Synthetic Studies on Fluorine-containing Novel Liquid-crystalline Materials

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Chapter I

General Introduction

I-1. Historical Background of Organofluorine Material Chemistry

Remarkable biological activities[1] and material characteristics[2] of partially fluorinated compounds[3-5] have attracted great attention in the fields of pharmaceuticals, agrochemicals, and material science. Recent theoretical and experimental studies have revealed that those characteristic features are attributed to the physicochemical properties such as the effect of fluorine isosteric to oxygen, block effect of metabolism,[6] hydrogen bonding ability,[7] large C–F bond energy, and large dipole moment of a C–F bond.[8]

In contrast to those features of partially fluorinated compounds, highly fluorinated compounds show different properties: biological inertness, weak intermolecular interaction, high stability against most of chemicals, immiscibility with both water and organic solvents, and partial solubility of gaseous solutes like molecular oxygen.[5,9] Advantages of these properties have been taken intensively for the development of novel functional materials. The clue is brought by the discoveries of dichlorodifluoromethane in 1928, a non-toxic and incombustible refrigerant called CFC-12,[10] and poly(tetrafluoroethylene) in 1938, a highly heat- and chemicals-resisting polymer called Teflon®.[11] Recently, novel heat- and weather-resisting materials, artificial blood,[12] and media for organic synthesis[13] have been introduced.

Such extended use of organofluorine compounds has required needs for novel fluorination methods. Accordingly, development of mild and efficient synthetic methods for both partially and highly fluorinated compounds is an urgent problem in synthetic organofluorine chemistry.[14]

Historically speaking, three fluorination methods are important: i) nucleophilic halogen substitution reaction of alkyl halides with antimony(III) fluoride (Swarts, 1892),[15] ii) aromatic substitution reaction of arenediazonium salts with anhydrous hydrogen fluoride (AHF) for the synthesis of arylfluorides (Balz-Schemann, 1927),[16] and iii) electrochemical fluorination of alkanes to give perfluoroalkanes in AHF (Simons, 1948).[17]

Remarkable progress in synthetic organofluorine chemistry was made in United States during the World War II, because uranium(VI) fluoride was utilized to collect and condense radioactive uranium for production of an atomic bomb. For this purpose, novel equipment, tools, and materials were invented that tolerate fluorine gas and AHF generated during the whole process.[18] The fluorine-technologies allowed use of fluorine gas and AHF as the most basic electrophilic and nucleophilic reagents for fluorination, respectively.

Use of these reagents was quite limited because of extremely high toxicity and

explosive reactivity that hampered the isolation of fluorine until 1886 (Moissan).[19]

Synthetic methods of organofluorine compounds are briefly classified into two depending on the timing of fluorine introduction. The one involves C–C bond formation using readily available partially fluorinated small molecules and is called a building block method. The other consists of C–F bond formation with an electrophilic or a nucleophilic reagent and is called electrophilic fluorination or nucleophilic fluorination, respectively. Synthesis of organofluorine compounds by way of the building block approach has been developed mostly by synthetic organic chemists,[20] because highly toxic and explosive fluorination reagents and special equipments are not required.

A goal in synthetic organofluorine chemistry is the development of mild, selective, low-cost, and effective fluorination methods that can be carried out without special care, techniques, and conditions. Although many fluorination reactions and reagents are available for non-functionalized molecules, fluorination reactions applicable to highly functionalized molecules have remained unexplored.

In the next section, the Author briefly reviews synthetic methods of organofluorine compounds, especially focusing on nucleophilic fluorination.

1-2. Syntheses of Organofluorine Compounds

1-2-1. Electrophilic Fluorination

The simplest reagent for electrophilic fluorination is fluorine gas.[21] However, its high reactivity and toxicity have hampered everyday-use in conventional laboratories for organic synthesis. To overcome the difficulties, electrophilic fluorinating agents are exploited that are endowed with mild reactivity.[14,22-26]

1-2-2. Nucleophilic Fluorination

Nucleophilic fluorination using a fluoride ion is the most familiar tool for the preparation of organofluorine compounds, because a variety of fluoride reagents is commercially available. A classical and inexpensive nucleophilic fluorinating agent are AHF.[14] However, its volatility (bp 19.5 °C) and toxicity make its handling very difficult and dangerous, especially for laboratory use. Furthermore, fluorination reaction with AHF is sometimes accompanied by undesired side reactions owing to high acidity and low nucleophilicity. To overcome these problems, various types of HF equivalents and fluoride reagents with high nucleophilicity as well as low basicity and volatility have been developed and utilized for the synthesis of organofluorine compounds.

In the following, the Author briefly summarizes properties of representative HF

equivalents for nucleophilic fluorination and their synthetic applications. Details of fluoride reagents such as metal fluorides,[27] sulfur tetrafluoride (SF_4),[28] di(alkylamino)-sulfur trifluoride (DAST),[29] and fluoroalkylamine reagents[30] were reviewed in literatures.

To reduce high acidity and volatility and low nucleophilicity of AHF, various types of HF/base complexes such as HF/THF,[32] HF/pyridine (HF/py),[33] HF/melamine (HF/mel),[34] HF/triethylamine (HF/Et_3N),[35] and HF/diisopropylamine (HF/iPr_2NH)[36] have been developed. By complexation, the drawback of AHF is much improved. In particular, 70% HF/py and its polymer supported version, poly(vinylpyridinium) poly(hydrogen fluoride) (PVPHF)[37] were studied by Olah *et al.*[33] and found many applications.

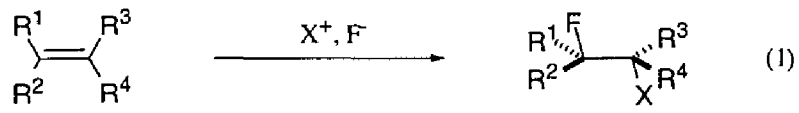
Further enhancement of nucleophilicity of AHF is realized by use of tetrabutylammonium fluoride (TBAF), tetrabutylammonium hydrogendifluoride ($TBAHF_2$), or tetrabutylammonium dihydrogentrifluoride ($TBAH_2F_3$). All of these are now commercially available. These salts are soluble in aprotic solvents and form a loose ion pair in which fluoride (F^-), hydrogendifluoride (HF_2^-), or dihydrogentrifluoride ($H_2F_3^-$) anion is considered to be naked and thus responsible for high reactivity. These anions display varying sensitivity to specific hydration, decreasing in the order: $F^- >> HF_2^- > H_2F_3^-$.[38]

$TBAH_2F_3$ is readily prepared from TBAF and 48% hydrofluoric acid (aq. HF).[39] This reagent allows hydrofluorination of olefins[40] and oxiran ring-opening reaction in a glass vessel without special care.

1-2-3. Combination of an Electrophile and a Fluoride Reagent: Oxidative Fluorination

Because a fluoride ion is a weak nucleophile, a substrate needs to be electrophilic enough or to be mildly oxidized to generate an electrophilic species. To this end, a combination of an oxidant and a fluoride ion reagent is effective. Depending on the substrate, both the oxidant and the fluoride ion reagent can be optimized for high yields of products.

Using a reagent system consisting of an electropositive heteroatom oxidant and a nucleophilic fluoride source (eq. 1), halo-,[42] thio-,[43] seleno-,[44] or nitro-fluorination[45] has been readily achieved under mild conditions with Markovnikov selectivity.



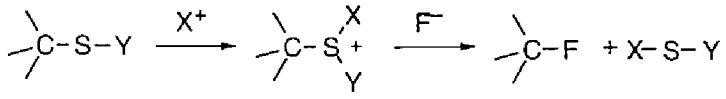
(1)

X = Br, I, S, Se, N

F^- = HF/amine complexes, $TBAF{\bullet}3H_2O$, $TBAH_2F_3$, SiF_4

Since organosulfur compounds are easily oxidized chemically or electrochemically[46] and afford electrophilic species, oxidative desulfurization-fluorination is achieved by a combined reagent system of an oxidant and a fluoride ion with high nucleophilicity (Scheme 1).

Scheme 1. Oxidative desulfurization-fluorination of organosulfur compounds



X^+: positive halogen oxidant

F^-: a fluoride reagent such as from $TBAH_2F_3$, $Et_3N/3HF$, 50-70% HF/py, or 80% HF/melamine

According to this method, fluorine substitution[47-50] and fluoro-Pummerer reaction[51] of phenyl sulfides are readily achieved. Similarly, oxidative desulfurization-fluorination of dithioacetals gives *gem*-difluoromethylenes.[52-57] In particular, a reagent system consisting of $TBAH_2F_3$ and an *N*-halo imide tolerates the substrates with an acid-labile functional group. This reaction, as applied to aromatic orthothioesters[58] and dithioesters,[59] affords trifluoromethyl-substituted aromatics. When the reaction is applied to orthothioestes of alkanoic acids[60] and dithioalkanoates,[61] 1,1-difluoro-1-(alkylthio)alkanes result as sole products. Furthermore, thione esters and thione carbonates are readily fluorinated to give α,α-difluoro ethers and difluoromethylenedioxy compounds.[62,63] Although this transformation can be performed with BrF_3, this reagent must be handled with great care.[63]

I-3. Syntheses of Trifluoromethylamines and Trifluoromethyl Ethers

At the outset of the present study, trifluoromethylamines were only accessible by the reaction using highly toxic and explosive reagents under special conditions,[64-72] and a limited number of compounds were available. Therefore, physicochemical properties of trifluoromethylamines remained unexplored.

Likewise, limited availability and expensiveness of trifluoromethyl ether building blocks were serious problems in view of development of advanced materials and pharmaceuticals. These disadvantages were attributed to the synthetic difficulties of these compounds.[73-78]

I-4. Brief History of LC Compounds

The first thermotropic LC compound was discovered in 1888 by the Austrian chemist and botanist F. Reinitzer.[79] In determining molecular formula of cholesterol, he found unusual melting property of cholesteryl benzoate on heating. He also observed unusual color behavior of the compound upon cooling: the phase is now known as chiral nematic (N*) or cholesteric (Ch) phase. The concept of LCs was first defined in 1889 by German crystallographer O. Lehmann as compounds having combined properties of fluidity of liquids and optical anisotropy of crystals. He initially called "Fließende Krystalle".[80]

Until the early 20th century, it became clear that mesogenic compounds consisted in common of rod-like (calamitic) and fairly rigid molecules. In 1922, LC phases of these compounds were classified by G. Friedel into nematic, smectic, and cholesteric phases depending on the structure of unidirectional order, layer, or helix, respectively. Nematic and smectic phases are coined according to optical textures corresponding to Greek *nematos* (thread-) and *smectos* (soap-), respectively. The cholesteric phase was named after the first materials exhibiting this phase.

Studies on chemistry and physics of LCs later diminished, because no practical applications were anticipated. Since the utility of these compounds in flat panel displays was suggested by G. H. Heilmeir in the late 60s,[81] LC research rapidly grew active acquiring interest in material science, synthetic organic chemistry, electrical engineering, and physics.

Today, super twisted nematic (STN)[82] and thin film transistor[83] (TFT, active matrix LC) mode displays are evolving rapidly and becoming the major technology for flat panel displays that make it possible to commercialize colored large size displays. At present, most of economical display modes are based on the principle of twisted nematic (TN) cell invented by M. Schadt in 1971.[84] For TN cell, various types of LCs with positive dielectric anisotropy are employed. The first and representative LCs are 4-cyano-4'-pentylbiphenyl and its analogs as introduced by G. W. Gray. The cyano-substituted LCs, however, cannot be used for TFT-mode displays because of low voltage holding ratio.

Among recent LC displays, those of STN-TFT-modes, in-plane switching (IPS) TFT-modes,[85] and vertical alignment (VA) TFT-modes[86] especially have created large demand for new LC materials that exhibit high voltage holding ratio as well as positive or negative dielectric anisotropy.[87]

Recently, ferroelectric and antiferroelectric LCs based on chiral smectic C and *anti*-smectic C phases, respectively, have been shown to respond much faster than nematic LCs. The properties of large dipole moment and low viscosity of fluorine-substituted LCs are

quite appropriate to the displays.

Accordingly, exploration of novel fluorine-containing LC materials is growing indispensable in the fields of material science and synthetic organofluorine chemistry.

I-5. Fluorine Containing LCs

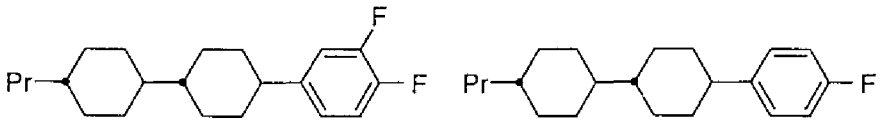
Recent remarkable progress of synthetic methods has enabled us to design and synthesize novel types of LC materials. However, syntheses of fluorine-containing LCs are strongly limited by the inaccessibility of fluorinated starting materials. Furthermore, abnormal reactivities of organofluorine compounds often prevent their use of conventional synthetic derivatization.[88] Fluorination methods are hardly employed because of explosiveness and/or toxicity of fluorination reagents.

In this section, the Author briefly summarizes the synthesis and properties of fluorine-containing nematic LCs that are classified into two depending on $\Delta\varepsilon$.

I-5-1. LCs with Positive Dielectric Anisotropy

Fluorine-substituted LCs with positive $\Delta\varepsilon$ have attracted great attention as the materials for TFT-mode LC displays. The most important material properties for the displays are high voltage holding ratio (specific resistance) and high photochemical and thermal stability. Voltage holding ratio of cyano-substituted materials for TN displays tends to decrease upon prolonged UV irradiation or to solvate ubiquitous ionic impurities.[89] Therefore, cyano-substituted compounds are not suitable for TFT displays. Fluorine-substituted LCs overcome such disadvantages due to high voltage holding ratio, low viscosity, appropriate $\Delta\varepsilon$, high chemical and thermal stability, and high nematic liquid-crystallinity. Thus, fluorine-substituted LCs are now commonly used as major components of materials for TFT-displays. Representative LCs are summarized below.

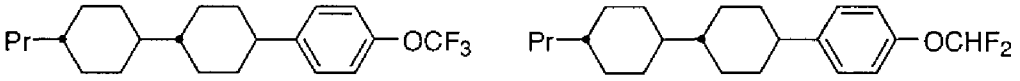
LCs with a 3,4-difluorophenyl subunit are the most widely used materials for TFT-displays (Figure 1).[87a] Effect of fluorine on a mesogen unit is recognized obviously by comparison with the corresponding 4-fluorobenzene and 3,4,5-trifluorobenzene derivatives.[90] For example, nematic to isotropic transition temperature (T_{NI}) is decreased by fluorine introduction with increase of $\Delta\varepsilon$. This type of compounds are prepared by a palladium catalyzed cross-coupling reaction of bromofluorobenzenes and bis[4-(*trans*-4-propylcyclohexyl)cyclohexyl]zinc.[91]



Cr 44 N 118 Iso, $\Delta\varepsilon = +5.3$ Cr 88 N 159 Iso, $\Delta\varepsilon = +4.8$

Figure 1. LCs containing fluorine-substitutents

Because CF_3O– (2.36 debye) and CHF_2O– (2.46 debye) groups are more polar than F– (1.47 debye), LCs with a CF_3O– or CHF_2O– group exhibit large positive $\Delta\varepsilon$ without decrease of liquid-crystallinity and thus are widely used for TFT displays. Representative examples are shown in Figure 2.[92] Although LCs with a CF_3– (2.56 debye) group have already been shown to exhibit large $\Delta\varepsilon$, inferior nematic liquid-crystallinity and high viscosity of these compounds are not suitable.[93]

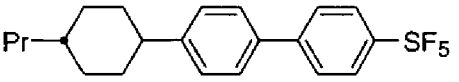


Cr 39 S_B 68 N 149 Iso
$\Delta\varepsilon = +5.2$, $\Delta n = 0.095$

Cr 51 S_X 69 N 172 Iso
$\Delta\varepsilon = +5.0$, $\Delta n = 0.095$

Figure 2. CF_3O- or CHF_2O-substituted LCs with positive dielectric anisotropy

Quite recently, LCs with a pentafluorosulfuranyl group (F_5S–, 3.44 debye) as a polar substituent were invented.[94] This functional group is more stable than a trifluoromethyl group against hydrolysis and heat (Figure 3). Upon comparison with representative LCs, pentafluorosulfuranyl-substituted LCs were revealed to exhibit the largest $\Delta\varepsilon$ among the materials for TFT displays.



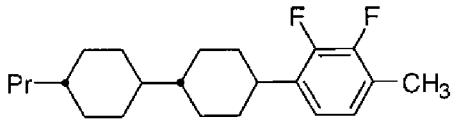
Cr 109 N (88) Iso, $\Delta\varepsilon = +14.3$

Figure 3. An LC with a pentafluorosulfuranyl group

I-5-2. LCs with Negative Dielectric Anisotropy[95]

Recently developed LC displays based on vertical alignment TFT (VA-TFT) mode offer precise picture quality with a wide view angle (160 °), high contrast, and video-compatible switching times (< 20 ms). The properties required for the display are high negative $\Delta\varepsilon$, low Δn (~ 0.08), and high voltage holding ratio. Materials containing no heteroatoms other than fluorine are found to display the best voltage holding ratio values. Nowadays, laterally difluorinated LCs are utilized as mixtures for VA-TFT mode displays because of the high negative $\Delta\varepsilon$ values.[96,97] A representative example is shown in Figure 4. Although LCs with a 2,3-difluorobenzene subunit show high nematic liquid-

crystallinity, slow switching resulted owing to relatively high rotational viscosity.



Cr 67 N 145 Iso, $\Delta\varepsilon = -2.7$

Figure 4. Laterally fluorinated-LC with negative dielectric anisotropy

Introduction of an aromatic mesogen induces the increase of Δn, a feature unsuitable for the VA-TFT mode. To overcome this problem, LCs with axially fluorinated cyclohexane units are designed and synthesized (Figure 5).[98] Such fluorine is introduced by hydrofluorination of olefins with 70% HF/py.[33] Although this type of LCs have high negative $\Delta\varepsilon$ and low Δn, low synthetic efficiency, less liquid-crystallinity, and low thermal stability are serious problems.

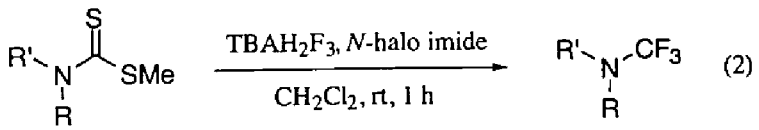
R = C_3H_7, Cr 78 S_B 104 Iso, $\Delta\varepsilon = -4.6$; R = C_5H_{11}, Cr 68 S_B 120 Iso, $\Delta\varepsilon = -4.2$

Figure 5. LCs with axially fluorinated cyclohexane units

I-6. Summary of This Thesis

In this Thesis, the Author describes details of synthetic studies on novel fluorine-containing liquid-crystalline materials.

In Chapter II, he discusses the synthesis of trifluoromethylamines through oxidative desulfurization-fluorination of dithiocarbamates using $TBAH_2F_3$ and an *N*-halo imide (eq. 2).



(2)

The procedure has following advantages:

i) Methyl dithiocarbamates, synthetic precursors of trifluoromethylamines, are readily prepared from the corresponding amines.

ii) Experimental operation is easily performed by using $TBAH_2F_3$ that allows the use of conventional glassware under mild conditions.

iii) Regioselective aromatic bromination accompanying the fluorination can be achieved in

excellent yields at higher reaction temperatures.

The Author has applied this procedure to the synthesis of novel LC materials having a trifluoromethylamino-substituent as a polar group (Figure 6). Details are summarized in Chapter III. He particularly focused on 4-bromo(trifluoromethylamino)heteroarenes that are readily prepared according to the procedure described in Chapter II. LCs with heterobiaryls or (4-cyclohexylcyclohexyl)arenes exhibit a smectic phase in a temperature range wider than the corresponding methylamines. Efficiency of the LCs as a dopant for ferroelectric LCs is also demonstrated.

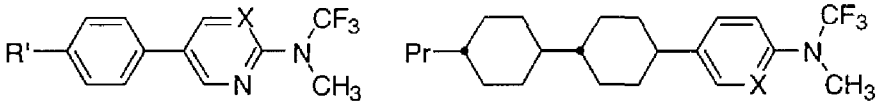
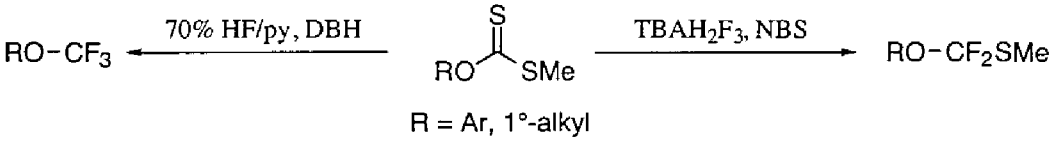


Figure 6. Trifluoromethylamino-substituted LCs

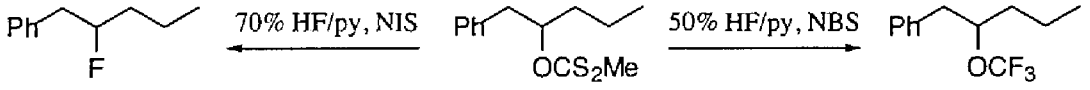
Chapter IV describes the oxidative desulfurization-fluorination reaction of dithiocarbonates derived from phenols and primary alcohols, which are ultimately transformed to trifluoromethyl or difluoro(methylthio)methyl ethers (Scheme 2).

Scheme 2. Synthesis of trifluoromethyl ethers or difluoro(methylthio)methyl ethers



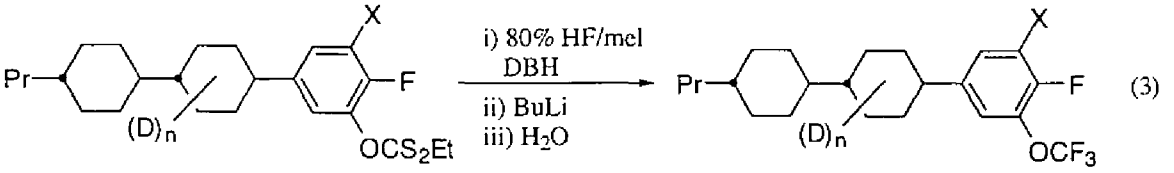
On the other hand, dithiocarbonates derived from secondary alcohols are converted into fluorination products or trifluoromethyl ethers, selectively depending on the reaction conditions (Scheme 3).[99] The results sharply contrast to the reaction using iodotoluene difluoride that solely affords fluorination products.[100]

Scheme 3. Fluorination of dithiocarbonates derived from secondary alcohols



The conditions for the preparation of trifluoromethyl ethers are applied to the synthesis of novel LC materials in Chapter V and VI.

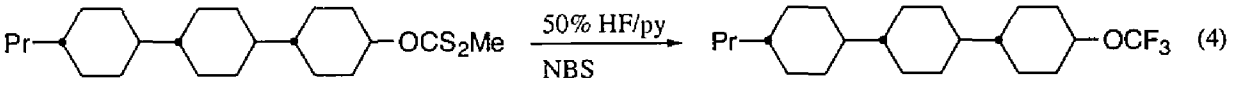
Initially, a trifluoromethoxy group introduced into a lateral position of mesogenic core of LCs was considered to lower $\Delta\varepsilon$ and viscosity. Therefore, 1-cyclohexyl-4-fluoro-3-trifluoromethoxybenzenes were designed and synthesized (eq. 3).



(3)

Although all of those compounds did not exhibit any mesophase, they were shown to lower threshold voltage, $\Delta\varepsilon$, and Δn as compared with the corresponding 4-trifluoromethoxyl-substituted LCs, features favorable to TFT-LCDs. The experimental details and electro-optical properties are summarized in Chapter V.

In Chapter VI, are discussed the synthesis and electro-optical properties of LCs with a trifluoromethoxycyclohexane mesogen that was expected to improve the physical and electro-optical properties of trifluoromethoxybenzene derivatives. Thus, the LCs with a cyclohexyl trifluoromethyl ether moiety as shown in eq. 4 were synthesized and shown to exhibit physical and electro-optical properties favorable to materials for not only TN-LCDs but TFT-LCDs.



(4)

The Author further synthesized LCs containing a trifluoromethoxy group connected to an alkyl tail. These LCs show characteristic properties independent of the mesogenic structure (Figure 7).

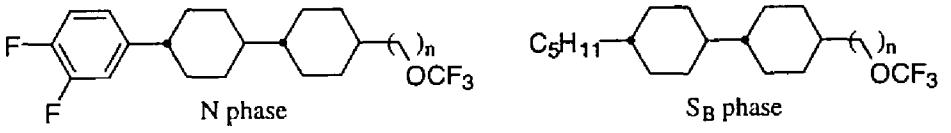
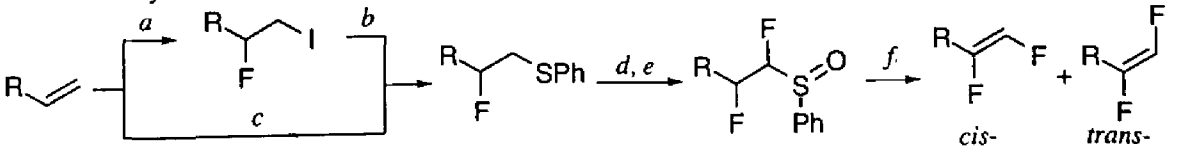


Figure 7. Structures of ω-trifluoromethoxyalkylcyclohexane-LCs

The final Chapter deals with a facile transformation of terminal olefins to *vic*-difluoro olefins and the synthesis of LCs with a *vic*-difluoro olefinic moiety. The synthetic route is shown in Scheme 4.

Scheme 4. Synthesis of *vic*-difluoro olefins from olefins



a: $TBAH_2F_3$, NIS. *b*: PhSH, NaH. *c*: 70% HF/py, *N*-PhS-phthalimide. *d*: $TBAH_2F_3$, DBH. *e*: *m*CPBA. *f*: Δ

According to this procedure, both *cis*- and *trans-vic*-difluoro olefinic LCs are readily prepared. The starting olefinic LCs are utilized as the materials for current LCDs. The Author disclosed that the properties changed extensively by a $(CH_2)_nCF=CHF$ group depending on the olefinic configuration and the value of n.

In conclusion, the Author succeeded in syntheses of trifluoromethylamines, trifluoromethyl ethers, and *vic*-difluoro olefins through oxidative fluorination as the key transformation. The synthetic efficiency has enabled him to develop fluorine-containing novel LCs especially of aliphatic trifluoromethyl ethers that are quite useful as materials for TFT-LCDs.

Thus, the Author has disclosed that the development of mild and effective transformations are closely linked to invention of novel class of LC materials.

1-7. References

1) a) R. Filler and Y. Kobayashi, "*Biomedical Aspects of Fluorine Chemistry*," Kodansha Ltd. and Elsevier Biochemical, Tokyo and Amsterdam (1982); b) Y. Kobayashi, I. Kumadaki, and T. Taguchi, "*Fusso Yakugaku,*" Hirokawa Shoten, Tokyo (1993).
2) a) R. E. Banks, Ed., "*Preparation, Properties, and Industrial Applications of Organofluorine Compounds,*" Ellis Horwood, Chichester, England (1982); b) N. Ishikawa, Ed., "*Fusso Kagobutu no Gosei to Kinou*," CMC, Tokyo (1993).
3) C. Heidelberger, N. K. Chaudhuri, P. Danneberg, D. Mooren, L. Griesbach, R. Duschinsky, R. J. Schnitzer, E. Pleven, and J. Schneiner, *Nature,* **179**, 663 (1957).
4) P. Goldman, *Science,* **164**, 1123 (1969).
5) T. Hiyama, "*Organofluorine Compounds, Chemistry and Applications*," Chapter 6, p 183, Springer, Berlin (2000).
6) a) J. T. Welch, *Tetrahedron*, **43**, 3123 (1987); b) T. Allmendinger, P. Furet, and E. Hungerbuhler, *Tetrahedron Lett.*, **31**, 7297 (1990); c) D. O'Hagan and H. S. Rzepa, *Chem. Commun.*, **1997**, 645.
7) a) H. Plenio, *Chem. Rev.*, **97**, 3363 (1997); b) J. A. K. Howard, V. J. Hoy, D. O'Hagan, and G. T. Smith, *Tetrahedron*, **52**, 12613 (1996); c) L. Shimoni, J. P. Glusker, and C. W. Bock, *J. Phys. Chem.*, **99**, 1194 (1995); d) V. R. Thalladi, H. C. Weiss, D. Bläser, R. Boese, A. Nangia, and G. R. Desiraju, *J. Am. Chem. Soc.*, **120**, 8702 (1998); e) T. A. Evans and K. R. Seddon, *Chem. Commun.*, **1997**, 2023; f) K. M. Guckian and E. T. Kool, *Angew. Chem. Int. Ed. Engl.*, **36**, 2825 (1997); g) D. Cantacuzene, K. L. Kirk, H. McCuiioh, and C. R. Creveling, *Science*, **204**, 1217 (1979).
8) B. E. Smatt, "*Chemistry of Organic Fluorine Compounds II, A Critical Review* " (M. Hudlick´y and A. E. Pavlath Eds.), ACS Monograph 187, p 979, American Chemical

Society, Washington, DC (1995).
9) a) Ref. 5 Chapter 1, p 1; b) G. L. Cantrell and R. Filler, *J. Fluorine Chem.*, **27**, 35 (1985).
10) T. Midgley and A. L. Henne, *Ind. Eng. Chem.*, **22**, 542 (1930).
11) R. J. Plunkett, *US Patent* 2,230,654 (1941) (*Chem. Abstr.*, **35**, 3365 (1941)).
12) a) L. C. Clark Jr. and F. Gollan, *Science*, **152**, 1755 (1966); b) J. G. Riess and M. L. Blanc, *Pure and Appl. Chem.*, **54**, 2383 (1982).
13) a) T. Hiyama, "*Organofluorine Compounds, Chemistry and Applications*," Chapter 7, p 235, Springer, Berlin (2000); b) B. Cornils, *Angew. Chem. Int. Ed. Engl.*, **36**, 2057 (1997); c) I. T. Horváth, *Acc. Chem. Res.*, **31**, 641 (1998).
14) a) T. Kitazume and T. Yamazaki, *Experimental Methods in Organic Fluorine Chemistry*, Kodansha-Gordon & Breach Science, Tokyo (1998); b) G. A. Olah, R. D. Chambers, and G. K. S. Prakash, Eds., "*Synthetic Fluorine Chemistry,*" John Wiley & Sons, New York (1992); c) J. T. Welch, Ed, "*Selective Fluorination in Organic and Bioorganic Chemistry,*" American Chemical Society, Washington, DC (1991).
15) F. Swarts, *Bull. Acad. Roy. Belg.*, **24**, 309 (1892).
16) G. Baltz and G. Schiemann, *Chem. Ber.*, **60**, 1186 (1927).
17) J. H. Simons, *J. Fluorine Chem.*, **32**, 7 (1986).
18) H. Goldwhite *J. Fluorine Chem.*, **33**, 109 (1986).
19) H. Moissan, *Compt. Rend.*, **102**, 1534 (1886).
20) a) Ref. 5, Chapter 3, p 77; b) T. Kitazume, T. Ishihara, T. Taguch, "*Fusso no Kagaku*," Kodansha, Tokyo (1993); c) T. Umemoto, *Chem. Rev.*, **96**, 1757 (1996).
21) S. T. Purrington, B. S. Kagen, and T. B. Patric, *Chem. Rev.*, **86**, 997 (1986).
22) M. A. Tius, *Tetrahedron*, **51**, 6605 (1995).
23) S. Rozen, *Chem. Rev.*, **96**, 1717 (1996).
24) T. Umemoto, S. Fukami, G. Tomizawa, K. Hasegawa, K. Kawada, and K. Tomita, *J. Am. Chem. Soc.*, **112**, 8563 (1990).
25) G. S. Lal, *J. Org. Chem.*, **58**, 2791 (1993).
26) S. Singh, D. D. DesMarteau, S. S. Zuberi, M. Witz, and H.-N. Huang, *J. Am. Chem. Soc.*, **109**, 7194 (1987).
27) J. A. Wilkinson, *Chem. Rev.*, **92**, 505 (1992); b) J. H. Clark, *Chem. Rev.*, **80**, 429 (1980).
28) G. A. Boswell, Jr., W. C. Ripka, R. M. Schibner, and C. W. Tullock, *Org. React.*, **21**, 1 (1974).
29) M. Hudlicky, *Org. React.*, **35**, 513 (1988).
30) a) N. N. Yarovenko and M. A. Raksha, *J. Gen. Chem. USSR*, **29**, 2125 (1959); b) A. Takaoka, H. Iwakiri, and N. Ishikawa, *Bull. Soc. Chem. Jpn.*, **52**, 3377 (1979).
31) N. Yoneda, *Tetrahedron*, **47**, 5329 (1991).
32) a) R. F. Hirscmann, R. Miller, J. Wood, and R. E. Jones, *J. Am. Chem. Soc.*, **78**, 4956 (1956); b) D. Taub, R. D. Hoffsommer, and W. L. Wendler, *J. Am. Chem. Soc.*, **79**,

452 (1957).
33) G. A. Olah, J. T. Welch, Y. D. Vanker, M. Nojima, I. Kerekes, and J. A. Olah, *J. Org. Chem.*, **44**, 3872 (1979).
34) T. Fukuhara, N. Yoneda, T. Abe, S. Nagata, and A. Suzuki, *Nippon Kagaku Kaishi*, **10**, 1951 (1985).
35) R. Franz, *J. Fluorine Chem.*, **15**, 423 (1980).
36) G. Aranda, J. Jullien, and J. A. Martin, *Bull. Soc. Chim. Fr.*, **1965**, 1890.
37) G. A. Olah, X.-Y. Li, Q. Wang, and G. K. S. Prakash, *Synthesis*, **1993**, 693.
38) a) G. A. Olah and X.-Y. Li, "*Synthetic Fluorine Chemistry,*" (G. A. Olah, R. D. Chambers, and G. K. S. Prakash, Eds.,) John Wiley & Sons, New York, pp 163 (1992); b) O. A. Mascaretti, *Aldrichimica Acta*, **26**, 47 (1993).
39) J. Cousseau and P. Albert, *Bull. Soc. Chim. Fr.*, **6**, 910 (1986).
40) P. Albert and J. Cousseau, *J. Chem. Soc. Chem. Commun.*, **1985**, 961.
41) D. Landili and M. Penso, *Tetrahedron Lett.*, **31**, 7209 (1990).
42) Ref. 5, Chapter 2, p 25.
43) C. Saluzzo, A.-M. L. Spina, D. Picq, G. Alvernhe, D. Anker, D. Wolf, and G. Haufe, *Bull. Soc. Chim. Fr.*, **131**, 831 (1994).
44) C. Saluzzo, G. Alvernhe, D. Anker, and G. Haufe, *Tetrahedron Lett.*, **31**, 663 (1990).
45) C. York, G. K. S. Prakash, and G. A. Olah, *J. Org. Chem.*, **59**, 6493 (1994).
46) a) T. Fuchigami, A. Konno, K. Nakagawa, and M. Shimojo, *J. Org. Chem.*, **59**, 5937 (1994); b) S. Higashiya, T. Sato, and T. Fuchigami, *J. Fluorine Chem.*, **87**, 203 (1998).
47) R. E. Dolle and K. C. Nicolaou, *J. Am. Chem. Soc.*, **107**, 1691 (1985).
48) S. Caddick, L. Gazzard, W. B. Motherwell, and J. A. Wilkinson, *Tetrahedron*, **52**, 149 (1996).
49) C. York, G. K. S. Prakash, and G. A. Olah, *Tetrahedron*, **52**, 9 (1996).
50) J. Ichikawa, K. Sugimoto, T. Sonoda, and H. Kobayashi, *Chem. Lett.*, **1987**, 1985.
51) S. Furuta, M. Kuroboshi, and T. Hiyama, *Tetrahedron Lett.*, **36**, 8243 (1995).
52) S. C. Sondej and I. A. Katzenellebogen, *J. Org. Chem.*, **51**, 3508 (1986).
53) G. K. S. Prakash, D. Hoole, V. P. Reddty, and G. A. Olah, *Synlett*, **1993**, 691.
54) M. Kuroboshi and T. Hiyama, *Synlett*, **1991**, 909.
55) W. B. Motherwell and J. A. Wilkinson, *Synlett*, **1991**, 191.
56) T. Fuchigami and T. Fujita, *J. Org. Chem.*, **59**, 7190 (1994).
57) M. Kuroboshi and T. Hiyama, *J. Fluorine Chem.*, **69**, 127 (1994).
58) D. P. Matthews, J. P. Whitten, and J. R. McCarthy, *Tetrahedron Lett.*, **27**, 4861 (1986).
59) a) M. Kuroboshi and T. Hiyama, *Chem. Lett.*, **1992**, 827; b) S. Furuta and T. Hiyama, *Synlett*, **1996** 1199.
60) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1939 (1998).
61) K. Kim and J. R. McCarthy, *Tetrahedron Lett.*, **37**, 3223 (1996).
62) M. Kuroboshi and T. Hiyama, *Synlett*, **1994**, 251.

63) S. Rozen and E. Mishani, *J. Chem. Soc. Chem. Commun.*, **1993**, 1761.
64) G. Klöter, W. Lutz, K. Seppelt, and W. Sundermeyer, *Angew. Chem. Int. Ed. Engl.*, **16**, 707 (1977).
65) R. A. DeMarco and J. M. Shreeve, *Chem. Commun.*, **1971**, 788.
66) W. Dmowski and M. Kaminski, *J. Fluorine Chem.*, **23**, 207 (1983).
67) R. J. Hardek and W. C. Smith, *J. Am. Chem. Soc.*, **83**, 3422 (1961).
68) L. N. Markovskij, V. E. Pashinnik, and A. V. Kirsanov, *Synthesis*, **1973**, 787.
69) L. M. Yagupol'skii, N. V. Kondratenko, G. N. Timofeeva, M. I. Dronkina, and Y. L. Yagupol'skii, *J. Jeneral Chem. USSR*, **16**, 2139 (1981).
70) E. Klauke, *Angew. Chem. Int. Ed. Engl.*, **5**, 848 (1966).
71) G. Pawelke, *J. Fluorine Chem.*, **52**, 229 (1991).
72) K. Adachi, S. Ishihara, and T. Umemoto, *the 21st Fluorine Conference of Japan*, P-44, 182 (1997).
73) L. M. Yagupolski, *Dokl. Akad. Nauk SSSR*, **105**, 100 (1955) (*Chem. Abstr.*, **50**, 11270 (1956)).
74) A. E. Feiring, *J. Org. Chem.*, **44**, 2907 (1979).
75) W. A. Sheppard, *J. Org. Chem.*, **29**, 1 (1964).
76) P. E. Aldrich and W. A. Sheppard, *J. Org. Chem.*, **29**, 11 (1964).
77) F. Mathey and J. Bensoam, *Tetrahedron Lett.*, **25**, 2253 (1973).
78) I. Ben-David, D. Rechavi, E. Mishani, and S. Rozen, *J. Fluorine Chem.*, **97**, 75 (1999).
79) F. Reinitzer, *Monatshefte Für Chemie*, **9**, 421 (1888), English translation, *Liq. Cryst.*, **5**, 7 (1989).
80) O. Lehmann, *Z. Physik. Chem.*, **4**, 462 (1889).
81) a) G. H. Heilmeier, L. A. Zanoni, and L. A. Barton, *Proc. IEEE.*, **56**, 1162 (1968); b) G. H. Heilmeier and L. A. Zanoni, *Appl. Phys. Lett.*, **13**, 91 (1968).
82) T. J. Scheffer and J. Nehring, *Appl. Phys. Lett.*, **45**, 1021 (1984).
83) A. Sasaki, T. Uchida, and S. Miyagami, *Japan Display '86*, **1986**, 62.
84) M. Schadt and W. Helfrich, *Appl. Phys. Lett.*, **18**, 127 (1971).
85) M. Oh-e, M. Ohta, S. Aratani, and K. Kondo, *Asia Display '95*, 577 (1995).
86) K. Ohmura, S. Kataoka, T. Sasaki, and Y. Koike, *SID 97 Digest*, 845 (1997).
87) a) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.*, **209**, 1 (1991); b) M. Schadt, R. Buchecker, and A. Villiger, *Liq. Cryst.*, 7, 519 (1990).
88) a) H. Matsutani, T. Kusumoto, and T. Hiyama, *Chem. Lett.*, **1999**, 529; b) T. Yamazaki, N. Shinohara, T. Kitazume, and S. Sato, *J. Org. Chem.*, **60**, 8140 (1995).
89) M. Bremer, S. Naemura, and K. Tarumi, *Jpn. J. Appl. Phys.*, **37**, L88 (1998).
90) a) A. Beyer, B. Schuler, and K. Tarumi, *22. Freiburger Arbeitstagung Flüssigkristalle*, p 13 (1993); b) D. Demus, Y. Goto, S. Sawada, E. Nakagawa, H. Saito, and R. Tarao, *Mol. Cryst. Liq. Cryst.*, **260**, 1 (1995).
91) E. Postsch, *Kontakte*, **2**, 15 (1988).
92) a) E. Bartmann, D. Dorsch, U. Finkenzeller, H. A. Kurmeier, and E. Poetsch, *19th*

Freiburger Arbeitstagung Flussigkristalle, p 8 (1990); b) A. I. Pavluchenko, N. I. Smirnova, and V. F. Petrov, *Mol. Cryst. Liq. Cryst.*, **209**, 225 (1991).
93) A. Griffin and N. W. Buckley, *Mol. Cryst. Liq. Cryst.*, **41**, 141 (1978).
94) P. Kirsch, M. Bremer, M. Heckmeier, and K. Tarumi, *Angew. Chem. Int. Ed.*, **38**, 1989 (1999).
95) P. Kirsch, V. Reiffenrath, and M. Bremer, *Synlett,* **1998**, 389.
96) V. Reiffenrath, J. Krause, H. J. Plach, and G. Weber, *Liq. Cryst.*, **5**, 159 (1989).
97) a) M. Hard, G. W. Gray, and K. J. Toyne, *Liq. Cryst.*, **11**, 531 (1992); b) S. J. Lock, J. W. Goodby, M. Hird, and K. J. Toyne, *Liq. Cryst.*, **21**, 279 (1996).
98) P. Kirsch and K. Tarumi, *Angew. Chem. Int. Ed.*, **37**, 484 (1998).
99) G. A. Boswell, Jr., W. C. Ripka, R. M. Scribner, and C. W. Tullock, *Org. React.*, **21**, 1 (1974).
100) M. J. Koen, F. L. Guyader, and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, **1995**, 1241.

Abbreviations

AHF	anhydrous hydrogen fluoride
Ar	aryl
Ac	acetyl
aq.	aqueous
Bn	benzyl
bp	boiling point
brs	broad singlet (in NMR)
BuLi	butyllithium
°C	degree Celsius
calcd	calculated
d	doublet (in NMR)
DBH	1,3-dibromo-5,5-dimethylhydantoin
DMAP	4-(*N,N*-dimethylamino)-pyridine
DMF	*N,N*-dimethylformamide
δ	scale (in NMR)
Δε	dielectric anisotropy
Δ*n*	birefringence
eq.	equation
Et_2O	diethyl ether
ε	dielectric constant
HF	hydrogen fluoride
HF/py	hydrogen fluoride-pyridine
Hz	hertz (s^{-1}, in NMR)
IR	infrared (spectrum)
J	coupling constant (in NMR)
LC	liquid crystal or liquid-crystalline
m	multiplet (in NMR)
M	molar concentration (1 M = 1 mol dm^{-3})
Me	methyl
mL	1 cm^3
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
NMR	nuclear magnetic resonance
mmol	millimol
mp	melting point
Ph	phenyl
Pr	propyl
q	quartet (in NMR)
R_f	relative mobility
rt	room temperature
s	singlet (in NMR)
t	triplet (in NMR)
τ	response time
$TBAH_2F_3$	tetrabutylammonium dihydrogentrifluoride
THF	tetrahydrofuran
TLC	thin layer chromatography
V_{th}	threshold voltage

Chapter II

A Facile Synthesis of Trifluoromethylamines by Oxidative Desulfurization–Fluorination of Dithiocarbamates

Abstract: Trifluoromethylamines are easily synthesized from dithiocarbamates by a reagent system consisting of $TBAH_2F_3$ and an *N*-halo imide under mild conditions. When this reaction was applied to dithiocarbamates ($ArN(R)CS_2Me$) at higher temperatures, the trifluoromethylation was accompanied by halogen substitution at a *p*-position of the Ar group. Synthesis of trifluoromethyl-substituted adenosine also is described.

II-1. Introduction

Because fluorine is the most electronegative element and the van der Waals radius is close to hydrogen, introduction of fluorine often improves the properties of the parent compounds and/or induces novel activities.[1] Recently, many new fluorinated materials, drugs, and agrochemicals have been designed[2] and synthesized[3] taking advantages of the properties as described in Chapter I.

In view of the strongly electron-withdrawing nature of a trifluoromethyl group, trifluoromethylamines are apparently much less basic and less nucleophilic than the corresponding methylamines,[4] and thus the physical, chemical, and/or biological properties of trifluoromethylamines should be remarkably modified as compared with those of the corresponding methylamines. For example, aryl(trifluoromethyl)amines resist oxidation compared with the corresponding methylamines and can be applied to liquid-crystalline materials.[5] Thanks to these properties, trifluoromethylamino-substituted agrochemicals[6] and artificial bloods[7] containing a trifluoromethylamines or perfluoroalkylamine moiety have been developed, and reagents substituted by a trifluoromethylamino group are utilized in organic synthesis as oxidants[8-10] or fluorination reagents.[11]

Preparative methods of trifluoromethylamines are classified into: i) fluorination of *N*-formylamines with SF_4 and KF,[12] ii) fluorine substitution of trichloromethylamines with SbF_3,[13] iii) fluorination of thiuram sulfides with SF_4[14] or R_2NSF_3,[15] iv) reaction of secondary amines with CBr_2F_2 and tetrakis(dimethylamino)ethylene,[16] v) fluorination of isocyanates with AHF,[17] vi) electrochemical fluorination of alkylamines,[18] and vii) electrophilic trifluoromethylation of amines by treatment with *O*-(trifluoromethyl)dibenzofuranium salts.[19] Most of these methods use such highly toxic and/or corrosive reagents as SF_4, SbF_3, F_2 and/or anhydrous hydrogen fluoride under harsh conditions, and the yield of the desired products are not always high enough. These technical problems have hampered the systematic study on trifluoromethylamines.

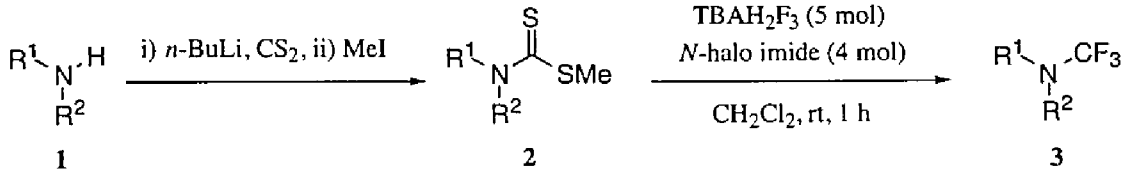
The oxidative desulfurization-fluorination reaction using an *N*-halo imide and a fluoride source has been recently demonstrated to be a convenient entry to the synthesis of organofluorine compounds.[20] This reaction allows to replace a C–S bond with a C–F bond under extremely mild conditions. The Author has applied this reaction to methyl dithiocarbamates $R^1R^2NC(S)SMe$ to find that trifluoromethylamines $R^1R^2NCF_3$ are readily prepared in good yields.[5a, 21]

II-2. Results and Discussion

II-2-1. Synthesis of Trifluoromethylamines by the Oxidative Desulfurization-Fluorination of Dithiocarbamates

Secondary amines **1** were treated successively with *n*-BuLi, CS_2 and then with MeI to give corresponding dithiocarbamates **2** in high yields.[22] Oxidative desulfurization-fluorination of dithiocarbamates **2** was carried out using $TBAH_2F_3$ as a fluorinating reagent and an *N*-halo imide (Scheme 1). As summarized in Table 1, trifluoromethylamines **3** were obtained in yields of synthetic meaning.

Scheme 1. Synthesis of trifluoromethylamines by oxidative desulfurization-fluorination

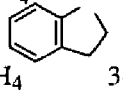


1 **2** **3**

Initially, the Author studied the optimization of the conditions using diphenyldithiocarbamate (**2a**) as a model substrate. For a halonium ion agent, he used NBS, DBH, *N*-chlorosuccinimide (NCS), NIS, or *N*-bromoacetamide (NBA). Compound **2a** was treated with $TBAH_2F_3$ (5 mol) and one of the *N*-halo imide (4 mol) in dichloromethane at room temperature for 1 h (Table 1, entries 1 to 5). All of these oxidants were found to promote the reaction to give diphenyl(trifluoromethyl)amine (**3a**). When DBH was used (entry 2), trifluoromethylation proceeded quantitatively, bromination of the phenyl ring being accompanied. Amoung the oxidants, NBS (entry 1) was concluded to be the most effective for the synthesis of **3a**.

He next examined the amount of $TBAH_2F_3$ (entries 6, 8 and 9) using **2b** for the substrate. When the amount of $TBAH_2F_3$ was reduced to 1.2 mol, **3b** was obtained in a 70% yield (entry 9). This means that all of the fluorine atoms of $TBAH_2F_3$ can be used for the fluorination. When the same reaction was carried out with $TBAF \cdot 3H_2O$ (5 mol) and NBS (4 mol), however, a complex mixture of products resulted. Accordingly, $H_2F_3^-$ ion is definitely superior to F^-. The trifluoromethylamine synthesis was applied to various kinds of cyclic and acyclic dithiocarbamates, and the corresponding trifluoromethylamines **3** could be readily isolated in good-to-excellent yields (entries 10 to 12, 16 and 18).

Table 1. Synthesis of trifluoromethylamines **3** or **4** from dithiocarbamates **2** according to Scheme 1.

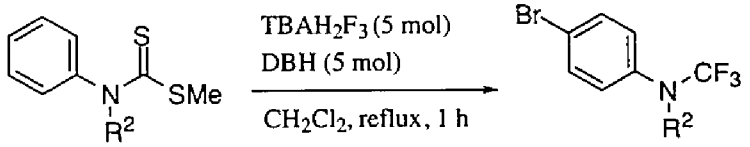
Entry	R^1	R^2	2	*N*-halo imide (mol)	Temp.	Yield of 3 or 4 (%)[a]	
1	Ph	Ph	**2a**	NBS (4)	rt	**3a**	78
2				DBH (4)			---[b]
3				NCS (4)			23
4				NIS (4)			60
5				NBA (4)			36
6	4-MeO-C_6H_4	$PhCH_2$	**2b**	NBS (4)		**3b**	99
7				NBS (1.5)			38[c]
8[d]				NBS (4)			84
9[e]							70
10	4-Cl-C_6H_4	$PhCH_2$	**2c**			**3c**	88
11	4-F-C_6H_4	$PhCH_2$	**2d**			**3d**	84
12	4-NC-C_6H_4	$PhCH_2$	**2e**			**3e**	78
13				DBH (4)			99
14[f]				NBS (4)			97
15[g]							99
16	4-MeO-C_6H_4	Me	**2f**			**3f**	90
17	4-O_2N-C_6H_4	Me	**2g**	DBH (4) (NBS)		**3g**	96 (68)
18			**2h**	NBS (4)		**3h**	76
19	3-Me-C_6H_4	3-Me-C_6H_4	**2i**	NIS (4) (NBS[b])		**3i**	74 (48)
20	4-Br-2-F-C_6H_3	Me	**2j**	DBH (5)		**3j**	87
21		Et	**2k**			**3k**	82
22		*n*-C_6H_{13}	**2l**			**3l**	87
23	Ph	Me	**2m**	NBS (4)		**3m**	66
24				DBH (5)	reflux	**4m**	96
25		Et	**2n**	NBS (4)	rt	**3n**	65
26				DBH (5)	reflux	**4n**	83
27		Pr	**2o**	NBS (4)	rt	**3o**	78
28				DBH (5)	reflux	**4o**	68
29		*n*-C_6H_{13}	**2p**	NBS (4)	rt	**3p**	68
30				DBH (5)	reflux (0 °C)	**4p**	71 (86)
31		*n*-C_8H_{17}	**2q**	NBS (4)	rt	**3q**	79
32				DBH (5)	0° C	**4q**	79
33[h]				NBS (5)			60
34[i]	$PhCH_2$	$PhCH_2$	**2r**	NBS (4)	rt	**3r**	86
35[i]		Pr	**2s**			**3s**	84

[a] Isolated yields. [b] Accompanied by aromatic bromination. [c] **2b** was recovered in 54% yield. [d] $TBAH_2F_3$ (2 mol) was used. [e] $TBAH_2F_3$ (1.2 mol) was used. [f] $(HF)_9$/py (1 mL/mmol, 80 mol of F^-) was used. [g] $(HF)_3/NEt_3$ (0.2 mL/mmol, 30 mol of F^-) was used. [h] $(HF)_9$/py (0.5 mL/mmol) was used. [i] $TBAH_2F_3$ (3 mol) was used.

When DBH or excess NBS was used as an oxidant, bromination of aromatic ring also took place (entries 2 and 19). For these substrates, NBS (4.0 mol) or NIS was proved to be a reagent of choice (compare entry 1 with 4; see also entry 19).

For the substrates bearing an electron-withdrawing group, a combination of $TBAH_2F_3$/DBH or an HF-amine complex/NBS was effective to afford the desired trifluoromethylamine quantitatively (entries 12 to 15). Upon use of an HF-amine complex, however, the reaction should be carried out in an effective hood to avoid the contact with hydrogen fluoride; also it is recommended to use a Teflon® bottle as a reaction vessel. Therefore, a combination of $TBAH_2F_3$/DBH is the best for the synthesis of **3** having an electron-withdrawing group (entries 17 and 20 to 22).

When alkyl(phenyl)dithiocarbamates **2** were treated with $TBAH_2F_3$ (5 mol) and NBS (4 mol) in dichloromethane at room temperature, trifluoromethylation only proceeded to afford compounds **3** in high yields. On the contrary, the reaction using $TBAH_2F_3$ (5 mol) and DBH (5 mol) in refluxing dichloromethane (eq. 1) gave alkyl(4-bromophenyl)(trifluoromethyl)amines **4** as sole products (entries 24, 26, 28 and 30). The formation of trifluorination-bromination products **4** was observed in some cases even at 0 °C (cf. entries 30 and 32).

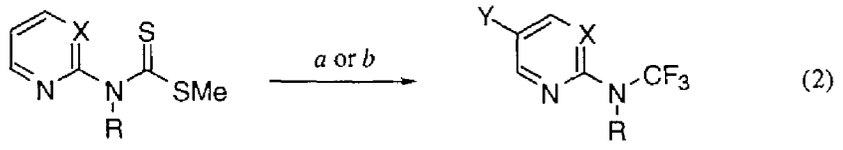


2 4 (1)

This fluorination reaction is also applicable to the synthesis of dialkyl(trifluoromethyl)amines (entries 34 and 35) that are readily hydrolyzed upon exposure to moisture. To isolate dialkyl(trifluoromethyl)amines **3r** and **3s**, filtration of insoluble materials generated during the reaction followed by concentration and distillation was suitable.

II-2-2. Synthesis of Trifluoromethylamino-substituted Pyridines and Pyrimidines

The fluorination reaction was applied to the synthesis of 2-(trifluoromethylamino)pyridines and -pyrimidines (eq. 2). The results, summarized in Table 2, clearly show that trifluoromethylation products **7** (and **11**) or trifluoromethylation-bromination products **8** (and **12**) were obtained in good-to-excellent yields from the corresponding dithiocarbamates **6** (and **10**) by use of $TBAH_2F_3$ (5 mol) and DBH (4-5 mol) in dichloromethane at 0 °C or at the refluxing temperature, respectively.



(2)

6 X = CH
10 X = N

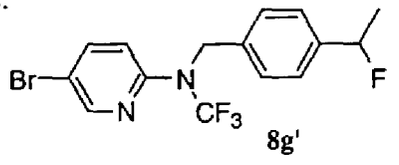
7 X = CH, Y = H **11** X = N, Y = H
8 X = CH, Y = Br **12** X = N, Y = Br

a: $TBAH_2F_3$ (5 mol), DBH (4 mol), CH_2Cl_2, 0 °C
b: $TBAH_2F_3$ (5 mol), DBH (5 mol), CH_2Cl_2, reflux

Table 2. Synthesis of trifluoromethylamino-substituted pyridines **7** (or **8**) and pyrimidines **11** (or **12**) according to equation 2.[a]

Entry	R	X	Carbamates	DBH (mol)	Temp.	Product(s) (% yield)[b]	
1	Me	CH	**6a**	4	0 °C	**7a** 72	
2				5	reflux	**8a** 78	
3	Et		**6b**	4	0 °C	**7b** 75	
4				5	reflux	**8b** 82	
5	*n*-C_6H_{13}		**6c**	4	0 °C	**7c** 67	
6				5	reflux	**8c** 89	
7	*n*-C_8H_{17}		**6d**	4	-20 °C	**7d** 76	
8				5	reflux	**8d** 89	
9	*n*-$C_{12}H_{25}$		**6e**	4	-20 °C	**7e** 86	
10				5	reflux	**8e** 90	
11	$PhCH_2$		**6f**	4	0 °C	**7f** 80	
12				5	reflux	**8f** 78	
13	4-Et-$C_6H_4CH_2$		**6g**	5	reflux	**8g** 41	**8g'** 38
14	Me	N	**10a**	4	0 °C	**11a** 38	
15				5	reflux	**12a** 84	
16	Pr		**10b**	4	0 °C	**11b** 50	
17				5	reflux	**12b** 81	
18	*n*-C_6H_{13}		**10c**	4	0 °C	**11c** 58	
19				5	reflux	**12c** 61	
20	*n*-C_8H_{17}		**10d**	4	0 °C	**11d** 80	**11d** 62
21				5	reflux	**12d** 24	
22	*n*-$C_{12}H_{25}$		**10e**	4	0 °C	**11e** 63	
23				5	reflux	**12e** 15	**11e** 65

[a] All the reactions were carried out with $TBAH_2F_3$ (5 mol), DBH (4-5 mol), in CH_2Cl_2 at 0 °C or at its refluxing temperature. [b] Isolated yields.

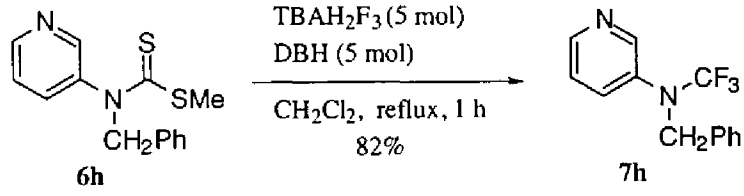


8g'

For the trifluorination of alkyl(2-pyridyl)dithiocarbamates **6**, the reaction conditions using $TBAH_2F_3$ (5 mol) and DBH (4 mol) at 0 °C in dichloromethane were effective, and trifluoromethylamines 7 were obtained in high yields. However, substrates **6d** and **6e** having a long alkyl chain were found to be sensitive to bromination even at 0 °C. Thus, carring out the reaction at –20 °C prevented the bromination (entries 7 and 9), and desired products **7d** and 7e could be isolated in high yields. When the reaction was performed in refluxing dichloromethane, 2-[alkyl(trifluoromethyl)amino]-5-bromopyridines **8a-8g** were obtained in high yields as sole products (entries 2, 4, 6, 8, 10, 12, and 13); none of the regio isomers or dibrominated compounds were produced. Under the similar conditions, alkyl(2-pyrimidinyl)dithiocarbamates **10** were also converted into 2-[alkyl(trifluoromethyl)amino]pyrimidines **11** or 2-[alkyl(trifluoromethyl)amino]-4-bromopyrimidines **12**, depending on the amount of DBH and the reaction temperature. However, the trifluorination-bromination of **10d** and **10e** having a long alkyl chain (entries 21 and 23) were sluggish: The aromatic bromination was not completed even at the reflux temperature of dichloromethane.

It is noteworthy that some of **6g** was converted into **8g'** under the forcing conditions (entry 13), probably *via* benzylic bromination and substitution by fluorine.

An isomer of **7f**, 3-[benzyl(trifluoromethyl)amino]pyridine (**7h**), was prepared in refluxing dichloromethane in a high yield from **6h** without bromination (eq. 3).



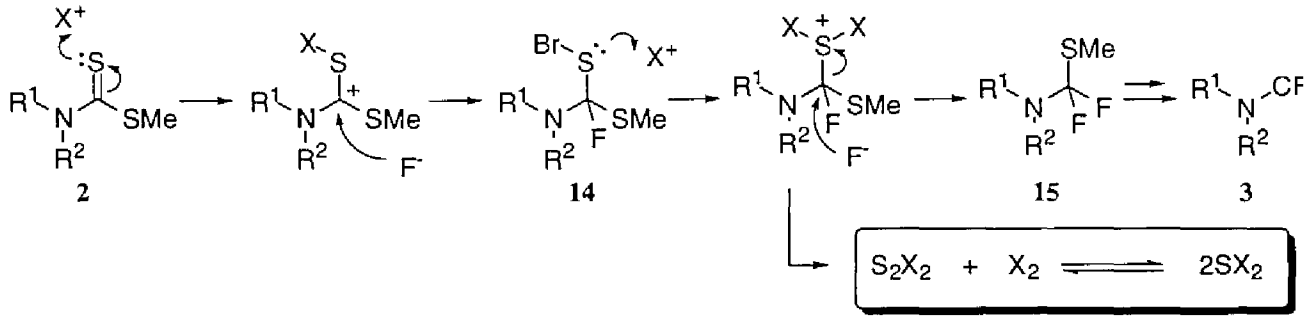
6h **7h** (3)

II-2-3. Reaction Mechanism

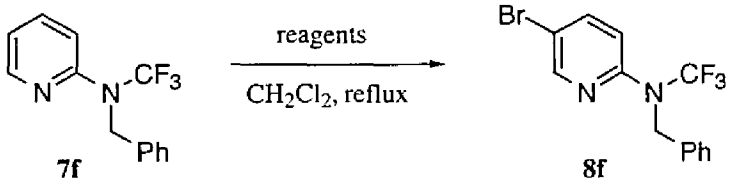
A plausible reaction mechanism of the oxidative desulfurization-fluorination of dithiocarbamates is shown in Scheme 2. The reaction is assumed to be initiated by an electrophilic attack of a halogen(I) cation towards the sulfur atom of a thiocarbonyl group, followed by a nucleophilic attack of a fluoride ion to the thiocarbonyl carbon to form a C–F bond. The thus formed **14** would undergo the similar electrophilic attack of X^+ at sulfur and substitution by a fluoride ion to give **15**. The difluorinated products of type **15** are isolable in the oxidative desulfurization-fluorination of dithiocarbonates.[23] Finally, the remaining MeS group could be substituted in a similar manner to give trifluoromethylated product **3**. The reaction of **2b** with less than 1.5 mol of NBS gave a

mixture of trifluoromethylamine **3b** and **2b** in 38 and 54% yields, respectively; none of mono-fluorinated product **14** or difluorinated product **15** could be detected (Table 1 entry 7). Based on this observation, the transformations of **2** to **14**, of **14** to **15**, and of **15** to **3** appear to be extremely fast in contrast to the trifluoromethyl ether synthesis.[23]

Scheme 2. A proposed reaction mechanism of trifluoromethylation.



When this reaction was performed at higher temperatures, the trifluorination was accompanied by regioselective ring bromination at the *p*-position (Table 1 entry 24 to 32 and Table 2). Since the regioselective bromination of the heteroaromatic ring, in particular, is noteworthy. Thus, the Author studied the bromination of **7f** in more detail (eq. 4).



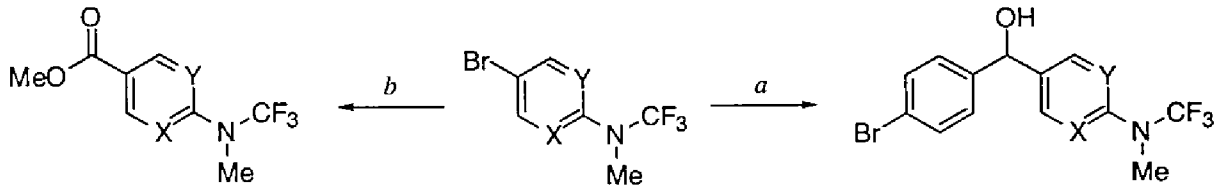
(4)

When the bromination of **7f** was performed using DBH (1.2 mol) in refluxing dichloromethane for 6 h, compound **8f** was obtained in only 49% yield. The reaction using Br_2 (1.1-2.2 mol) or a reagent system consisting of $TBAH_2F_3$ (2 mol) and DBH (1.2 mol) in refluxing dichloromethane were also ineffective, the bromination of **7f** was found to proceed slowly. However, a reaction using a combination of $TBAH_2F_3$ (2 mol) and Br_2 (2.2 mol) in refluxing dichloromethane for 1.5 h was quite effective to give **8f** in 84% yield. Therefore, the bromination under the oxidative desulfurization-fluorination conditions should be due to Br_2, probably *in situ* generated by heterolysis of SBr_2 (as shown in Scheme 2) and also to $TBAH_2F_3$ acting as a weak base.[24]

II-2-4. Derivatization of Bromoaryl(trifluoromethyl)amines

Lithium-bromine exchange of bromoaryl(trifluoromethyl)amines **4m**, **8a**, and **12a** was readily effected by means of *n*-BuLi at –78 °C, and the resulting aryllithiums were allowed to react with 4-bromobenzaldehyde to give the corresponding adducts **16**, **17**, and **18**, respectively, (Scheme 3, route *a*). Methyl esters **19**, **20**, and **21** also were obtained from the bromoaryl(trifluoromethyl)amines by treatment with *n*-BuLi at –78 °C, followed by carboxylation and esterification (Scheme 3, route *b*). During these transformations, both the trifluoromethylamino group and the aromatic ring remained intact. Thus, transformations of trifluoromethylamines are readily achieved by the use of an additonally introduced bromine functionality.[5]

Scheme 3. Reaction of bromoaryl(trifluoromethyl)amines.



19	X = Y = CH	98%	**4m** X = Y = CH	**16** X = Y = CH	69%
20	X = CH, Y = N	43%	**8a** X = CH, Y = N	**17** X = CH, Y = N	78%
21	X = Y = N	78%	**12a** X = Y = N	**18** X = Y = N	82%

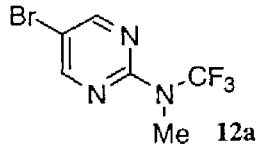
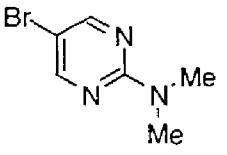
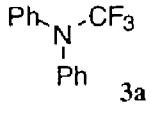
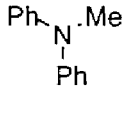
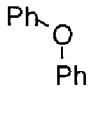
a: i) *n*-BuLi (1.1 mol), THF, –78 °C, 0.5 h; ii) *p*-Br-C_6H_4CHO (1.2 mol), –78 °C to rt, 12 h

b: i) *n*-BuLi (1.1 mol), THF, –78 °C, 0.5 h; ii) CO_2 (excess), –78 °C to rt; iii) $TMSCHN_2$ (2.0 mol), rt

II-2-5. Oxidation Potential of Trifluoromethylamines

The oxidation potential of trifluoromethylamines was measured by cyclic voltammetry. As shown in Table 3, diphenyl(trifluoromethyl)amine (**3a**) showed 1.90 V vs. SCE, 0.94 V higher than methyldiphenylamine (0.96 V), and comparable to diphenyl ether (1.87 V). Similarly, oxidation potential of 5-bromo-2-[methyl(trifluoromethyl)-amino]pyrimidine (**12a**) was 2.32 V vs SCE, 0.97 V higher than that of corresponding methylamine **25**. Therefore, trifluoromethylamines are highly tolerant of oxidation, as compared with ordinary methylamines, because of delocalization of the lone pair electrons on nitrogen by a strongly electron-withdrawing trifluoromethyl group.

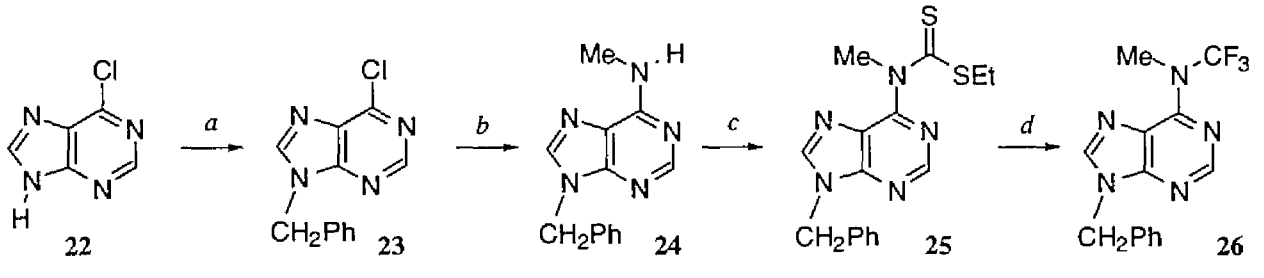
Table 3. Oxidation potential of trifluoromethylamines **3a** and **12a** (vs. SCE).

				
2.32 V	1.45 V	1.90 V	0.96 V	1.87 V

II-2-6. Synthesis of Trifluoromethylamino-substituted Adenosine

The present reaction was applied to the synthesis of trifluoromethylamino-substituted adenosine derivative **26**. Dithiocarbamate **25** was prepared as shown in Scheme 4, starting with 6-chloropurine (**22**), and was treated with $TBAH_2F_3$ (5 mol) and DBH (4 mol) in dichloromethane at 0 °C for 1 h to give desired trifluoromethylamine **26** in 25% yield.

Scheme 4. Synthesis of trifluoromethylamino-substituted adenosine **26**.



a: i) NaH (1.1 mol), DMF, 0 °C to rt, 30 min, ii) BnBr (2.0 mol), 0 °C to rt, 3 h, 69 %.
b: CH_3NH_2•HCl (5.0 mol), Et_3N (3.0 mol), CH_2Cl_2, rt, 12 d, 93%.
c: i) *n*-BuLi (1.1 mol), –78 to 0 °C, THF, 1 h, ii) $ClCS_2Et$ (2.0 mol), THF, rt, 2 h, 37%
d: $TBAH_2F_3$ (5.0 mol), DBH (4.0 mol), CH_2Cl_2, 0 °C, 1 h, 25%

II-3. Conclusion

The oxidative desulfurization-fluorination of readily accessible dithiocarbamates is shown to allow the synthesis of aryl-, heteroaryl-, and alkyl(trifluoromethyl)amines under extremely mild conditions. When the reaction is carried out at higher temperatures, bromination of the heteroaryl group at *p*-position sometimes takes place regioselectively.

It is also demonstrated that trifluoromethylamines resist oxidation, as compared with the corresponding methylamines. This novel synthetic reaction should find wide applications, particularly in the synthetic design of new drugs, agrochemicals, and opto-electrical materials.

II-4. Experimental

General.

Following general techniques apply to all of the experimental parts of this Thesis. All temperatures are uncorrected. Unless otherwise noted, reagents and solvents were purchased from Aldrich Chemical Co., Kanto Chemicals, Tokyo Kasei, or Wako Chemicals, Inc. and were used as received. All of the reactions were carried out under an argon atmosphere in a dry, freshly distilled solvent, unless otherwise noted. THF and Et_2O were distilled from sodium/benzophenone. DMF was distilled 2 times from calcium hydride under reduced pressure. CH_2Cl_2 was pre-dried with P_2O_5 and distilled from calcium hydride. Pyridine was distilled from KOH and kept over solid KOH at room temperature. NBS and NIS were purified by recrystallization from hot water and dioxane/CCl_4, respectively. $TBAH_2F_3$ was prepared according to the literature[25] procedure and dried *in vacuo* at room temperature overnight right before use. Unless otherwise stated, yields refer to materials purified by column chromatography or distillation under reduced pressure. The purchased reagents of the highest commercial quality and used without further purification unless otherwise noted. Reactions were monitored by thin-layer chromatography using 0.25 mm E. Merck silica-gel plates (Silica Gel F_{254}) with a visualizing device of UV light and/or by dipping the plates in an ethanolic phosphomolybdic acid or *p*-anisaldehyde solution by heating the plates. Silica gel from E. Merck (Kieselgel 60, 230-400 mesh) or Nacalai Tesque (silica gel 60, 150-325 mesh) were used for flash-column chromatography. Silica gel purchased from E. Merck (Kieselgel 60, 70-230 mesh) or Wako (Wakogel C-200) was used for column chromatography under an atmospheric or slightly positive pressure. Unless otherwise noted, NMR spectra were measured in a $CDCl_3$ solution. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a JEOL FX-100 spectrometer at 100 (^1H) and 94 (^{19}F) MHz, on a Bruker AC-200 spectrometer at 200 (^1H), 50.3 (^{13}C), and 188 (^{19}F) MHz, or on a Varian Mercury-300 spectrometer at 300 (^1H), 75.5 (^{13}C), and 282 (^{19}F) MHz, respectively. Chemical shifts of ^1H NMR, ^{13}C NMR, and ^{19}F NMR signals are quoted relative to internal standard Me_4Si (δ = 0.00), $CDCl_3$ (δ = 77.00), or $CFCl_3$ (δ = 0.00), respectively, and expressed by

chemical shift in ppm (δ), multiplicity, coupling constant (Hz), and relative intensity. IR spectra were recorded on a Shimadzu FTIR-8100A spectrometer in neat unless otherwise noted. Mass spectra were recorded on a Shimadzu GC/MS QP-5000 spectrometer or on a Hitachi H-80 double-focusing tandem gas chromatography mass spectrometer (70 eV). Measurement of melting points and phase transition temperatures and determination of liquid crystalline phases were carried out with an Olympus BH-2 optical polarizing microscope equipped with a Mettler FP-900 hot-stage. The thermal characterization was conducted with an SII DSC-200C (scanning rate 1 °C min^{-1}) differential scanning calorimeter (DSC) system. Recycling preparative HPLC was carried out using a Japan Analytical Industry LC-908 chromatograph.

Elemental analyses were carried out by Elemental Analysis Center, Tokyo Institute of Technology, using Yanako MT2 CHN Corder. High-resolution mass spectra were obtained on a JEOL Mstation spectrometer.

General Procedures for the Preparation of Secondary Amines: Method A.[26] Sodium borohydride (2.2 g, 59 mmol) was slowly added portionwise to a stirred suspension of a primary aromatic amine (10 mmol), an aldehyde (11 mmol), acetic acid (8.7 mL), anhydrous sodium acetate (2.7 g, 33 mmol), and sodium sulfate (1.56 g, 11 mmol) in ethanol (20 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred until all of the amine was consumed. Ethanol and acetic acid were then removed under reduced pressure. The residue was treated with aq. sodium hydroxide (1 M, 30 mL) and diethyl ether (100 mL). The organic phase was separated, and the aq. phase was extracted with diethyl ether three times. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography or bulb-to-bulb distillation to give the desired secondary amine.

Method B. A hexane solution of *n*-BuLi (11 mmol) was slowly added to a stirred solution of a primary aromatic amine (10 mmol) in THF (20 mL) at –78 °C. After the solution was allowed to warm to 0 °C over 1 h, an alkyl iodide (20 mmol) was added dropwise to the reaction mixture at 0 °C. The resulting mixture was stirred at room temperature until all of the substrate was consumed and was then treated with aq. $NaHCO_3$ solution. The organic phase was separated and the aq. phase was extracted with diethyl ether three times. Workup and purification described in Method A gave the desired secondary amine.

Method C.[27] A suspension of sodium methoxide (2.7 g, 50 mmol), paraformaldehyde (420 mg, 14 mmol) and a primary aromatic amine (10 mmol) in methanol (25 mL) was stirred for 15 h at 40 °C before sodium borohydride (0.38 g, 10

mmol) was added at room temperature. The resulting mixture was heated at 50 °C for 4 h, and the methanol was removed under reduced pressure. The crude white solid was dissolved in sat. $NaHCO_3$ aq. solution and diethyl ether, and the organic phase was separated. The aq. phase was extracted with diethyl ether three times. Workup and purification described as above gave the desired secondary amine.

Method D. To a stirred solution of a substituted 2-chloropyrimidine (4.0 g, 35 mmol) in THF (50 mL) was added a 40% solution of an alkylamine in methanol (175 mmol) at 0 °C. The reaction mixture was stirred at 50 °C until all of the substrate was then consumed and was poured into sat. $NaHCO_3$ aq. solution. Workup and purification by column chromatography gave the desired 2-(alkylamino)pyrimidine.

Method, isolated yield and spectroscopic properties of products are shown below.

Benzyl(4-methoxyphenyl)amine (1b). Method A, 85%. Colorless crystals, mp 40.5-41.5 °C; R_f= 0.44 (hexane : Et_2O = 2 : 1). IR (KBr) 3380, 2998, 2950, 2903, 2832, 1642, 1514, 1462, 1441, 1406, 1296, 1238, 1036, 828, 768, 704 cm^{-1}; ^1H NMR (100 MHz) δ = 3.77 (s, 3 H), 3.78 (br s, 1 H), 4.31 (s, 2 H), 6.63 (d, J = 9 Hz, 2 H), 6.81 (d, J = 9 Hz, 2 H), 7.4-7.3 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 49.2 (s), 55.8 (s), 114.1 (s), 114.8 (s), 127.1 (s), 127.5 (s), 128.5 (s), 139.6 (s), 142.4 (s), 152.1 (s); MS *m/z* (rel intensity) 214 (M^++1, 10), 213 (M^+, 59), 212 (11), 211 (25), 196 (28), 122 (88), 107 (6), 106 (7), 105 (7), 95 (14), 91 (100), 77 (13), 65 (27). Found: *m/z* 213.1166. Calcd for $C_{14}H_{15}NO$: M, 213.1154.

Benzyl(4-chlorophenyl)amine (1c). Method A, 86%. A pale yellow oil; R_f= 0.39 (hexane : EtOAc = 10 : 1). IR 3428, 3063, 2853, 1601, 1505, 1453, 1321, 1296, 1266, 1246, 1179, 1123, 1028, 816, 773, 698 cm^{-1}; ^1H NMR (100 MHz) δ = 4.07 (br s, 1 H), 4.31 (s, 2 H), 6.55 (d, J = 9 Hz, 2 H), 7.12 (d, J = 9 Hz, 2 H), 7.3-7.4 (m, 5 H); ^{13}C NMR (50.3 MHz) δ = 48.3 (s), 113.8 (s), 122.0 (s), 127.3 (s), 127.4 (s), 128.6 (s), 129.0 (s), 138.9 (s), 146.6 (s); MS *m/z* (rel intensity) 219 (M^++2, 10), 218 (M^++1, 6), 217 (M^+, 32), 216 (M^+-1, 6), 140 (5), 111 (6), 91 (100), 77 (7), 75 (6), 65 (20). Found: *m/z* 217.0662. Calcd for $C_{13}H_{12}{}^{35}ClN$: M, 217.0658.

Benzyl(4-fluorophenyl)amine (1d). Method A, 85%. A colorless oil, bp 185-190 °C/2 mmHg; R_f= 0.52 (hexane : EtOAc = 5 : 1). IR 3410, 3030, 1618, 1521, 1494, 1450, 1325, 1296, 1275, 1215, 1118, 1075, 1028, 812, 724, 690, 500 cm^{-1}; ^1H NMR (100 MHz) δ = 3.94 (br s, 1 H), 4.31 (s, 2 H), 6.58 (dd, J = 4, 9 Hz, 2 H), 6.91 (dd, J = 9, 9 Hz, 2 H), 7.3-7.4 (m, 5 H); ^{19}F NMR (94 MHz) δ = −128.4 (septet, J = 4 Hz); ^{13}C NMR (75.5 MHz) δ = 48.8 (s), 113.6 (d, J = 8 Hz), 115.6 (d, J = 22 Hz), 127.2 (s), 127.4 (s), 128.6 (s), 139.2 (s), 144.4 (d, J = 2 Hz), 155.8 (d, $^1J_{C\text{-}F}$ =235 Hz); MS *m/z* (rel intensity) 202 (M^++1, 5), 201 (M^+, 34), 200 (M^+-1, 64), 91 (100). Found: *m/z* 201.0955. Calcd for $C_{13}H_{12}FN$: M, 201.0954.

Benzyl(4-cyanophenyl)amine (1e). Method A, 72%. A pale orange powder, mp 64.4-64.8 °C; R_f = 0.66 (hexane : Et_2O = 1 : 1). IR 3372, 3349, 2215, 1609, 1576, 1534, 1455, 1343, 1296, 1273, 1134, 1028, 830, 814 cm^{-1}; ^1H NMR (200 MHz) δ = 4.37 (d , J = 6 Hz, 2H), 4.65 (m, 1 H), 6.59 (d, J = 9 Hz, 2 H), 7.3-7.4 (m, 5 H), 7.42 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 47.4 (s), 99.0 (s), 112.4 (s), 120.4 (s), 127.3 (s), 127.6 (s), 128.8 (s), 133.7 (s), 137.8 (s), 151.1 (s); MS *m/z* (rel intensity) 209 (M^++1, 4), 208 (M^+, 10), 207 (M^+-1, 2), 91 (100). Found: *m/z* 208.0991. Calcd for $C_{13}H_{12}N_2$: M, 208.1000.

(4-Bromo-2-fluorophenyl)methylamine (1j). Method C, 84%. Colorless needles, mp 41.7-42.3 °C; R_f = 0.65 (hexane : Et_2O = 5 : 1). IR (KBr) 3338, 3007, 2878, 2818, 1617, 1584, 1518, 1449, 1410, 1325, 1270, 1196, 1159, 1105, 1046, 873, 860, 803 cm^{-1}; ^1H NMR (100 MHz) δ = 2.86 (d, J = 5 Hz, 3 H), 3.93 (br, 1 H), 6.53 (dd, J = 9, 9 Hz, 1 H), 7.04-7.17 (m, 2 H); ^{19}F NMR (188 MHz) δ = –135.0 (dd, J = 7, 9 Hz); ^{13}C NMR (50.3 MHz) δ = 29.9 (s), 106.5 (d, J = 9 Hz), 112.2 (d, J = 4 Hz), 117.1 (d, J = 22 Hz), 127.3 (d, J = 4 Hz), 136.9 (d, J = 12 Hz), 151.1 (d, $^1J_{C\text{-}F}$ = 243 Hz); MS *m/z* (rel intensity) 206 (M^++3, 9), 205 (M^++2, 96), 204 (M^++1, 89), 203 (M^+, 100), 202 (96), 163 (13), 161 (13), 157 (14), 155 (15), 123 (17), 122 (11), 103 (20), 94 (18), 82 (10), 81 (14), 77 (14), 76 (14), 75 (19), 74 (12), 63 (13), 62 (13), 61 (16). Found: C, 41.38; H, 3.22; N, 6.85%. Calcd for C_7H_7BrFN: C, 41.21; H, 3.46; N, 6.89%.

(4-Bromo-2-fluorophenyl)ethylamine (1k). Method B, 84%. A colorless oil, bp 120 °C/0.55 mmHg; R_f = 0.46 (hexane : EtOAc = 10 : 1), 0.18 (hexane : CH_2Cl_2 = 4 : 1). IR 3428, 2973, 2874, 1617, 1514, 1483, 1337, 1266, 1194, 1156, 868, 797 cm^{-1}; ^1H NMR (200 MHz) δ = 1.27 (t, J = 7 Hz, 3 H), 3.15 (qm, J = 7 Hz, 2 H), 3.79 (br s, 1 H), 6.53 (dd, J = 9, 9 Hz, 1 H), 7.06-7.13 (m, 2 H); ^{19}F NMR (188 MHz) δ = –134.7 (t, J = 10 Hz); ^{13}C NMR (50.3 MHz) δ = 14.56 (s), 38.00 (s), 106.6 (d, J = 9 Hz), 112.7 (d, J = 4 Hz), 117.1 (d, J = 22 Hz), 127.4 (d, J = 4 Hz), 136.1 (d, J = 12 Hz), 151.0 (d, $^1J_{C\text{-}F}$ = 243 Hz); MS *m/z* (rel intensity) 220 (M^++3, 5), 219 (M^++2, 58), 218 (M^++1, 9), 217 (M^+, 59), 205 (14), 204 (96), 202 (100), 157 (20), 155 (18), 123 (32), 109 (16), 103 (18), 102 (15), 94 (27), 83 (16), 82 (16), 81 (17), 76 (21), 75 (23), 68 (15), 63 (21). Found: C, 44.31; H, 4.34; N, 6.45%. Calcd for C_8H_9BrFN: C, 44.06; H, 4.16; N, 6.42%.

(4-Bromo-2-fluorophenyl)hexylamine (1l). Method B, 100%; A colorless oil, bp 167 °C/0.5 mmHg; R_f = 0.56 (hexane : EtOAc = 10 : 1). IR 3434, 2930, 2859, 1617, 1514, 1412, 1337, 1267, 1194, 1156, 868, 797 cm^{-1}; ^1H NMR (200 MHz) δ = 0.97 (t, J = 8 Hz, 3 H), 1.14-1.49 (m, 6 H), 1.49-1.71 (m, 2 H), 3.06 (q, J = 6 Hz, 2 H), 3.82 (br s, 1 H), 6.53 (dd , J = 9, 9 Hz, 1 H), 7.06-7.12 (m, 2 H); ^{19}F NMR (188 MHz) δ = –134.8 (m); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.7 (s), 29.3 (s), 31.6 (s), 40.3 (s), 106.4 (d, J = 9 Hz), 112.7 (d, J = 4 Hz), 117.7 (d, J = 22 Hz), 127.4 (d, J = 4 Hz), 136.2 (d, J = 12 Hz),

151.1 (d, $^{1}J_{C\text{-}F}$ = 243 Hz); MS *m/z* (rel intensity) 276 (M^++3, 8), 275 (M^++2, 57), 274 (M^++1, 8), 273 (M^+, 61), 204 (99), 202 (100), 191 (23), 189 (25), 157 (30), 155 (32), 130 (35), 94 (39), 76 (50). Found: *m/z* 273.0527. Calcd for $C_{12}H_{17}{}^{79}BrFN$: M, 273.0529.

Benzyl(propyl)amine (1s). Method B (prepared from benzylamine), 50%; A colorless oil; R_f = 0.36 (hexane : EtOAc : Et_3N = 10 : 10 : 1). IR 3310, 2960, 2932, 2874, 2815, 1605, 1495, 1455, 1379, 1123, 1028, 733, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 0.92 (t, *J* = 8 Hz, 3 H), 1.38 (br s, 1 H), 1.53 (sextet, *J* = 8 Hz, 2 H), 2.60 (t, *J* = 8 Hz, 2 H), 3.79 (s, 2 H), 7.20-7.38 (m, 5 H); ^{13}C NMR (50.3 MHz) δ = 11.8 (s), 23.2 (s), 51.3 (s), 54.0 (s), 126.8 (s), 128.0 (s), 128.3 (s), 140.5 (s); MS *m/z* (rel intensity) 149 (M^+, 7), 120 (43), 92 (7), 91 (100), 65 (14). Found: *m/z* 149.1207. Calcd for $C_{10}H_{15}N$: M, 149.1204.

Ethyl(2-pyridyl)amine (5b). Method B, 55%; A colorless oil, bp 105 °C/7 mmHg; R_f = 0.67 (hexane : EtOAc = 1: 3). IR 3420, 3264, 2971, 2361, 1603, 1512, 1447, 1329, 1287, 1154, 1090, 984, 772, 735 cm^{-1}; ^1H NMR (200 MHz) δ = 1.25 (t, *J* = 7 Hz, 3 H), 3.29 (dq, *J* = 6, 7 Hz, 2 H), 4.50 (br s, 1 H), 6.36 (ddm, *J* = 1, 8 Hz, 1 H), 6.54 (ddd, *J* = 1, 5, 7 Hz, 1 H), 7.40 (ddm, *J* = 2, 7 Hz, 1 H), 8.07 (dm, *J* = 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 12.9 (s), 42.3 (s), 105.4 (s), 110.7 (s), 136.9 (s), 148.1 (s), 157.5 (s); MS *m/z* (rel intensity) 123 (M^++1, 9), 122 (M^+, 54), 121 (31), 107 (63), 94 (47), 80 (41), 79 (100), 67 (42), 66 (29); Found: C, 68.49; H, 8.13; N, 22.95%. Calcd for $C_7H_{10}N_2$: C, 68.82; H, 8.25; N, 22.93%. Found: *m/z* 122.0844. Calcd for $C_7H_{10}N_2$: M, 122.0844.

Hexyl(2-pyridyl)amine (5c). Method B, 63%; A pale red oil; R_f = 0.75 (Et_2O : EtOAc = 1: 1). IR 3292, 2957, 2929, 2859, 1703, 1682, 1611, 1518, 1445, 1366, 1282, 1155, 770, 734 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.30-1.65 (m, 8 H), 3.18 (t, *J* = 7 Hz, 2 H), 4.40 (br s, 1 H), 6.42-6.60 (m, 2 H), 7.51 (ddd, *J* = 2, 7, 9 Hz, 1 H), 7.88 (dm, *J* = 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.6 (s), 29.0 (s), 31.4 (s), 42.3 (s), 106.5 (s), 111.6 (s), 139.1 (s), 144.7 (s), 157.9 (s); MS *m/z* (rel intensity) 179 (M^++1, 7), 178 (M^+, 48), 163 (4), 141 (12), 135 (10), 121 (64), 107 (100), 94 (85), 78 (61). Found: *m/z* 178.1472. Calcd for $C_{11}H_{18}N_2$: M, 178.1470.

Octyl(2-pyridyl)amine (5d). Method B, 51%; Colorless needles, mp 40.8-41.1 °C; R_f = 0.30 (hexane: Et_2O = 1 : 1). IR (KBr) 3257, 2955, 2924, 2854, 1605, 1574, 1531, 1441, 1292, 1156, 768 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.27-1.64 (m, 12 H), 3.23 (td, *J* = 6, 7 Hz, 2 H), 4.44 (br, 1 H), 6.35 (d, *J* = 8 Hz, 1 H), 6.54 (ddd, *J* = 2, 5, 7 Hz, 1 H), 7.40 (ddd, *J* = 2, 7, 8 Hz, 1 H), 8.06 (dm, *J* = 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 27.1 (s), 29.2 (s), 29.3 (s), 29.5 (s), 31.8 (s), 42.3 (s), 106.2 (s), 112.5 (s), 137.3 (s), 148.2 (s), 159.0 (s); MS *m/z* (rel intensity) 207 (M^++1, 4), 206 (M^+, 26), 190 (7), 177 (6), 163 (8), 149 (10), 121 (44), 107 (100), 94 (74), 78 (40). Found: *m/z* 206.1768. Calcd for $C_{13}H_{22}N_2$: M, 206.1783.

Dodecyl(2-pyridyl)amine (5e). Method B, 45%; Colorless needles, mp 58.9-59.7 °C; R_f = 0.40 (hexane : Et_2O = 1 : 1). IR (KBr) 3257, 2955, 2919, 2877, 1606, 1574, 1531, 1470, 1454, 1441, 1332, 1293, 1156, 1136, 1079, 984, 767, 735, 720 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.26-1.65 (m, 20 H), 3.23 (td, J = 6, 7 Hz, 2 H), 4.42 (br s, 1 H), 6.35 (ddd, J = 1, 2, 9 Hz, 1 H), 6.53 (ddd, J = 1, 5, 7 Hz, 1 H), 7.39 (ddd, J = 2, 7, 9 Hz, 1 H), 8.44 (ddd, J = 1, 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.6 (s), 27.1 (s), 29.4 (s), 31.9 (s), 42.3 (s), 106.2 (s), 112.5 (s), 137.3 (s), 148.2 (s), 159.0 (s); MS *m/z* (rel intensity) 262 (M^+, 11), 246 (5), 177 (4), 163 (4), 146 (7), 135 (4), 122 (4), 121 (27), 108 (34), 107 (100), 94 (56), 78 (18). Found: *m/z* 262.2408. Calcd for $C_{17}H_{30}N_2$: M, 262.2409.

Ethylbenzyl(2-pyridyl)amine (5g). Method B, 23%. Colorless needles, mp 80.8-81.2 °C; R_f = 0.56 (hexane : Et_2O = 1 : 3). IR (KBr) 3241, 3094, 2965, 2928, 2870, 1929, 1601, 1574, 1532, 1455, 1442, 1422, 1335, 1293, 1156, 1125, 1080, 982, 818, 768 cm^{-1}; ^1H NMR (200 MHz) δ = 1.23 (t, J = 8 Hz, 3 H), 2.64 (t, J = 8 Hz, 2 H), 4.46 (d, J = 6 Hz, 2 H), 4.80 (br s, 1 H), 6.37 (ddd, J = 1, 1, 8 Hz, 1 H), 6.58 (ddd, J = 1, 5, 7 Hz, 1 H), 7.17 (d, J = 9 Hz, 2 H), 7.28 (d, J = 9 Hz, 1 H), 7.40 (ddd, J = 2, 7, 8 Hz, 1 H), 8.11 (ddd, J = 1, 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 15.6 (s), 28.5 (s), 46.1 (s), 106.7 (s), 120.0 (s), 127.4 (s), 128.1 (s), 136.3 (s), 137.3 (s), 143.2 (s), 148.2 (s), 158.7 (s); MS *m/z* (rel intensity) 213 (M^++1, 8), 212 (M^+, 49), 211 (23), 183 (23), 134 (100), 119 (45), 117 (14), 105 (15), 104 (13), 91 (52), 79 (61), 78 (65), 77 (25), 62 (11). Found: *m/z* 212.1320. Calcd for $C_{14}H_{16}N_2$: M, 212.1313.

Benzyl(3-pyridyl)amine (5h). Method A, 78%. Colorless needles, mp 88.3-89.4 °C; R_f = 0.59 (Et_2O : methanol = 10 : 1). IR (KBr) 3263, 3098, 3029, 1591, 1578, 1528, 1485, 1450, 1327, 1317, 1303, 1244, 1120, 1069, 1029, 1008, 903, 798, 713, 702 cm^{-1}; ^1H NMR (200 MHz) δ = 4.05-4.32 (br s, 1 H), 4.33 (d, J = 5 Hz, 2 H), 6.85 (ddd, J = 1, 3, 8 Hz, 1 H), 7.05 (ddd, J = 1, 5, 8 Hz, 1 H), 7.27-7.36 (m, 5 H), 7.95 (dd, J = 1, 5 Hz, 1 H), 8.06 (dd, J = 1, 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 47.7 (s), 118.5 (s), 123.8 (s), 127.4 (s), 127.4 (s), 128.8 (s), 136.2 (s), 138.6 (s), 138.8 (s), 144.3 (s); MS *m/z* (rel intensity) 185 (M^++1, 4), 184 (M^+, 33), 107 (5), 91 (100), 78 (18). Found: *m/z* 184.1002. Calcd for $C_{12}H_{12}N_2$: M, 184.1000.

2-(Methylamino)pyrimidine (9a). Method D, 91%. Colorless needles, mp 63.1-63.9 °C; R_f = 0.16 (hexane : Et_2O = 5 : 1). IR (KBr) 2964, 2934, 2876, 1606, 1534, 1510, 1409, 1328, 1284, 1253, 1242, 1178, 1069, 971, 838, 827 cm^{-1}; ^1H NMR (200 MHz) δ = 3.00 (d, J = 5 Hz, 3 H), 4.65-5.30 (br, 1 H), 6.52 (t, J = 5 Hz, 1 H), 8.29 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 28.0 (s), 109.7 (s), 157.7 (s), 162.9 (s); MS *m/z* (rel intensity) 110 (M^++1, 13), 109 (M^+, 100), 108 (66), 81 (73), 80 (76). Found: *m/z* 109.0641. Calcd for $C_5H_7N_3$: M, 109.0640.

2-(Propylamino)pyrimidine (9b). Method D, 82%. A colorless oil; R_f = 0.64 (Et_2O). IR 3278, 3110, 2963, 2934, 2874, 1593, 1566, 1538, 1456, 1418, 1367, 1294, 1242, 1150, 1075, 803, 779 cm^{-1}; ^1H NMR (300 MHz) δ = 0.98 (t, J = 7 Hz, 3 H), 1.64 (sextet, J = 7 Hz, 2 H), 3.37 (q, J = 7 Hz, 2 H), 5.98 (br s, 1 H), 6.48 (t, J = 5 Hz, 1 H), 8.26 (d, J = 5 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 11.3 (s), 22.6 (s), 43.1 (s), 109.9 (s), 157.8 (s), 162.4 (s); MS *m/z* (rel intensity) 138 (M^++1, 4), 137 (M^+, 29), 136 (M^+-1, 3), 122 (9), 109 (13), 107 (100), 95 (26), 81 (23), 80 (7), 79 (20), 71 (14), 70 (12), 69 (18), 67 (11). Found: *m/z* 137.0954. Calcd for $C_7H_{11}N_3$: M, 137.0953.

2-(Hexylamino)pyrimidine (9c). Method D, 95%. A pale yellow oil; R_f = 0.45 (Et_2O : CH_2Cl_2 = 1 : 5). IR 3275, 2956, 2930, 2869, 2858, 1590, 1538, 1456, 1416, 1369, 1261, 802, 779, 732, 641 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 6 Hz, 3 H), 1.13-1.78 (m, 8 H), 3.29-3.51 (m, 2 H), 5.17-5.23 (br, 1 H), 6.50 (t, J = 5 Hz, 1 H), 8.26 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.5 (s), 26.6 (s), 29.5 (s), 31.5 (s), 41.5 (s), 110.1 (s), 157.9 (s), 162.4 (s); MS *m/z* (rel intensity) 179 (M^+, 20), 136 (4), 122 (12), 109 (22), 108 (100), 96 (4), 95 (18), 79 (20). Found: *m/z* 179.1417. Calcd for $C_{10}H_{17}N_3$: M, 179.1422.

2-(Octylamino)pyrimidine (9d). Method D, 88%. A pale yellow oil; R_f = 0.56 (Et_2O : CH_2Cl_2 = 1 : 2). IR 3283, 2956, 2856, 2827, 1596, 1538, 1457, 1416, 1370, 802 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.05 (m, 3 H), 1.20-1.72 (m, 12 H), 3.29-3.48 (m, 2 H), 4.95-5.25 (br, 1 H), 6.54 (t, J = 5 Hz, 1 H), 8.26 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 22.5 (s), 26.9 (s), 29.2 (s), 29.3 (s), 29.5 (s), 31.7 (s), 41.4 (s), 110.0 (s), 157.8 (s), 162.5 (s); MS *m/z* (rel intensity) 208 (M^++1, 4), 207 (M^+, 29), 122 (20), 109 (39), 108 (100), 96 (9), 95 (27), 79 (12). Found: *m/z* 207.1745. Calcd for $C_{12}H_{21}N_3$: M, 207.1735.

2-(Dodecylamino)pyrimidine (9e). Method D, 84%; Colorless needles, mp 51.3-51.9 °C; R_f = 0.34 (hexane : EtOAc = 3 : 1). IR (KBr) 3258, 3022, 2966, 2915, 2851, 1599, 1580, 1538, 1533, 1471, 1459, 1419, 1370, 800, 780, 716, 643 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 5 Hz, 3 H), 1.02-1.78 (m, 20 H), 3,38 (q, J = 6 Hz, 2 H), 5.05-5.14 (br, 1 H), 6.48 (t, J = 5 Hz, 1 H), 8.25 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.9 (s), 29.3 (s), 29.6 (s), 31.8 (s), 41.4 (s), 110.0 (s), 157.9 (s), 162.5 (s); MS *m/z* (rel intensity) 263 (M^+, 13), 150 (6), 136 (5), 122 (12), 108 (100), 96 (9), 95 (17). Found: *m/z* 263.2362. Calcd for $C_{16}H_{29}N_3$: M, 263.2361.

A General Procedure for the Preparation of Dithiocarbamates: Butyllithium (1.6 M in hexane, 0.75 mL, 12 mmol) was slowly added dropwise to a stirred solution of secondary amine **1**, **5**, **9**, or **13** (10 mmol) in THF (20 mL) at –10 °C. After the solution was allowed to warm to 0 °C over 1 h, CS_2 (1.2 mL, 20 mmol) was added dropwise to this mixture at 0 °C. The mixture was stirred for 12 h at room temperature, and MeI (1.3 mL,

20 mmol) was added dropwise to the reaction mixture at 0 °C. The mixture was stirred at room temperature for 3-5 h and was then treated with sat. aq. $NaHCO_3$. The organic phase was separated, and the aq. phase was extracted with diethyl ether for three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography or recrystallization to give the desired dithiocarbamates. Yields and spectra of products are as follows.

Methyl *N,N*-Diphenyldithiocarbamate (2a). Yield: 83%. A pale yellow powder, mp 128.3-128.7 °C; R_f = 0.40 (hexane : EtOAc = 10 : 1). IR (KBr) 3080, 3050, 3028, 3000, 2908, 1582, 1484, 1448, 1418, 1354, 1312, 1264, 1161, 1148, 1070, 1048, 1020, 1000, 956, 910, 889, 759, 743, 700, 690 cm^{-1}; ^1H NMR (90 MHz) δ = 2.56 (s, 3 H), 7.39 (m, 10 H). ^{13}C NMR (75.5 MHz) δ = 20.9 (s), 127.9 (s), 128.3 (s), 129.6 (s), 145.2 (m), 202.0 (s); MS *m/z* (rel intensity) 260 (M^++1, 2), 259 (M^+, 10), 212 (19), 167 (13), 151 (11), 150 (100), 135 (8), 109 (30), 91 (45), 77 (45), 65 (9). Found: *m/z* 259.0492. Calcd for $C_{14}H_{13}NS_2$: M, 259.0489.

Methyl *N*-Benzyl-*N*-(4-methoxyphenyl)dithiocarbamate (2b). Yield: 97%. A brown oil; R_f = 0.46 (hexane : Et_2O = 2 : 1). IR 3052, 3028, 3000, 2951, 2910, 2832, 1720, 1602, 1580, 1503, 1429, 1391, 1350, 1296, 1248, 1205, 1180, 1168, 1100, 1078, 1028, 980, 958, 908, 832, 758, 724, 699, 648, 621 cm^{-1}; ^1H NMR (90 MHz) δ = 2.57 (s, 3 H), 3.80 (s, 3 H), 5.58 (s, 2 H), 6.84 (d, *J* = 9 Hz, 2 H), 6.93 (d, *J* = 9 Hz, 2 H), 7.2-7.3 (m, 5 H); MS *m/z* (rel intensity) 303 (M^+, 4), 165 (4), 164 (7), 92 (11), 91 (100), 65 (12). Found: *m/z* 303.0754. Calcd for $C_{16}H_{17}ONS_2$: M, 303.0752.

Methyl *N*-Benzyl-*N*-(4-chlorophenyl)dithiocarbamate (2c). Yield: 86%. A pale brown oil; R_f = 0.54 (hexane : Et_2O = 3 : 1). IR 2917, 1603, 1487, 1455, 1387, 1350, 1242, 1206, 1102, 1088, 1015, 957, 833, 700 cm^{-1}; ^1H NMR (300 MHz) δ = 2.56 (s, 3 H), 5.56 (s, 2 H), 6.95 (d, *J* = 9 Hz, 2 H), 7.27 (s, 5 H), 7.32 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 20.9 (s), 60.4 (s), 127.8 (s), 128.4 (s), 128.7 (s), 129.5 (s), 129.6 (s), 135.0 (s), 135.5 (s), 141.1(m), 201.9 (s); MS *m/z* (rel intensity) 310 (M^++3, 0.4), 309 (M^++2, 2), 308 (M^++1, 1), 307 (M^+, 6), 164 (12), 91 (100). Found: *m/z* 307.0265. Calcd for $C_{15}H_{14}ClNS_2$: M, 307.0256.

Methyl *N*-Benzyl-*N*-(4-fluorophenyl)dithiocarbamate (2d). Yield: 90%. A brown oil; R_f = 0.33 (hexane : EtOAc = 10 : 1). IR 3054, 3024, 2910, 1600, 1500, 1432, 1388, 1348, 1238, 1203, 1152, 1100, 1078, 953, 838, 764, 720, 699 cm^{-1}; ^1H NMR (90 MHz) δ = 2.58 (s, 3 H), 5.58 (s, 2 H), 7.0-7.1 (m, 4 H), 7.28 (s, 5 H); ^{19}F NMR (188 MHz) δ = −111.62 (m); ^{13}C NMR (75.5 MHz) δ = 21.0 (s), 60.6 (s), 116.4 (d, *J* = 23 Hz), 127.9 (s), 128.5 (s), 128.8 (s), 130.1 (d, *J* = 9 Hz), 135.6 (s), 138.6 (m), 162.4 (d, $^1J_{C\text{-}F}$ = 245 Hz), 202.2 (s); MS *m/z* (rel intensity) 293 (M^++2, 1), 292 (M^++1, 1), 291 (M^+, 6), 91

(100). Found: *m/z* 291.0571. Calcd for $C_{15}H_{14}FNS_2$: M, 291.0552.

Methyl *N*-Benzyl-*N*-(4-cyanophenyl)dithiocarbamate (2e). Yield: 88%. Brown needles, mp 65.7-67.2 °C; R_f = 0.24 (hexane : EtOAc = 10 : 1). IR (KBr) 3080, 3052, 3025, 2950, 2352, 2225, 1596, 1496, 1452, 1380, 1346, 1222, 1204, 1092, 964, 952, 852, 838, 758, 737, 700 cm^{-1}; ^1H NMR (90 MHz) δ = 2.58 (s, 3 H), 5.58 (s, 2 H), 7.0-7.1 (m, 4 H), 7.28 (s, 5 H); ^{13}C NMR (75.5 MHz) δ = 20.9 (s), 60.1 (s), 112.8 (s), 117.7 (s), 128.0 (s), 128.5 (s), 129.3 (s), 133.3 (s), 135.0(s), 146.6 (s), 201.4 (s); MS *m/z* (rel intensity) 300 (M^++2, 1), 299 (M^++1, 2), 298 (M^+, 9), 91 (100). Found: *m/z* 298.0603. Calcd for $C_{16}H_{14}N_2S_2$: M, 298.0598.

Methyl *N*-(4-Methoxyphenyl)-*N*-methyldithiocarbamate (2f). Yield: 68%. Colorless needls, mp 93.7-94.6 °C; R_f = 0.42 (hexane : benzene = 1 : 1). IR (KBr) 3050, 3000, 2950, 2920, 2832, 1600, 1504, 1479, 1440, 1420, 1362, 1298, 1243, 1186, 1169, 1096, 1030, 948, 840, 752, 720 cm^{-1}; ^1H NMR (90 MHz) δ = 2.53 (s, 3 H), 3.76 (s, 3 H), 3.85 (s, 3 H), 7.00 (d, *J* = 8 Hz, 2 H), 7.18 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 20.8 (s), 46.2 (s), 55.4 (s), 114.7 (s), 127.9 (s), 137.4 (m), 159.6 (s), 200.8 (s); MS *m/z* (rel intensity) 228 (M^++1, 3), 227 (M^+, 12), 186 (9), 180 (10), 165 (28), 139 (9), 136 (10), 122 (7), 91 (17), 88 (100), 77 (9), 64 (12). Found: *m/z* 227.0459. Calcd for $C_{10}H_{13}NOS_2$: M, 227.0439.

Methyl *N*-Methyl-*N*-(4-nitrophenyl)dithiocarbamate (2g). Yield: 79%. A brown powder, mp 128.5-129.4 °C; R_f = 0.40 (hexane : EtOAc = 5 : 1). IR (KBr) 3098, 3062, 2910, 1606, 1590, 1523, 1486, 1462, 1430, 1340, 1308, 1290, 1260, 1094, 1010, 957, 860, 800, 694 cm^{-1}; ^1H NMR (90 MHz) δ = 2.57 (s, 3 H), 3.77 (s, 3 H), 7.47 (d, *J* = 9 Hz, 2 H), 8.32 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 20.1 (s), 45.2 (s), 125.1 (s), 128.3 (s), 147.3 (s), 150.3 (s), 200.5 (s); MS *m/z* (rel intensity) 243 (M^++1, 7), 242 (M^+, 58), 196 (16), 195 (100), 150 (15), 149 (40), 134 (18), 93 (12), 92 (5), 91 (92), 88 (69), 77 (21), 75 (16), 74 (19), 64 (14), 63 (24). Found: *m/z* 242.0171. Calcd for $C_9H_{10}N_2O_2S_2$: M, 242.0184.

Methyl 2,3-Dihydro-1-indolyldithiocarbamate (2h). Yield: 92%. A white powder, mp 86.8-87.4 °C; R_f = 0.45 (hexane : EtOAc = 10 : 1). IR (KBr) 3108, 3043, 2940, 2928, 2910, 1477, 1458, 1396, 1350, 1318, 1296, 1252, 1218, 1165, 1100, 1060, 1021, 970, 948, 783, 760, 702 cm^{-1}; ^1H NMR (90 MHz) δ = 2.71 (s, 3 H), 3.20 (t, *J* = 8 Hz, 2 H), 4.51 (t, *J* = 8 Hz, 2 H), 7.1-7.3 (m, 3 H), 9.0-9.2 (br s, 1 H); ^{13}C NMR (75.5 MHz) δ = 19.5 (s), 27.3 (s), 54.5 (m), 118.4 (s), 125.1 (s), 125.2 (s), 126.7 (s), 134.4 (s), 144.0 (m), 193.4 (s); MS *m/z* (rel intensity) 211 (M^++2, 6), 210 (M^++1, 7), 209 (M^+, 66), 163 (10), 162 (88), 129 (13), 128 (100), 118 (29), 91 (70), 89 (15), 77 (37), 74 (32), 69 (13), 65 (15), 63 (13). Found: *m/z* 209.0347. Calcd for $C_{10}H_{11}NS_2$: M, 209.0333.

Methyl *N*,*N*-Di(*m*-tolyl)dithiocarbamate (2i). Yield: 82%. Orange crystals, mp

103.1-104.2 °C; R_f = 0.44 (hexane : EtOAc = 10 : 1). IR (KBr) 2919, 1603, 1584, 1356, 1287, 1184, 1055, 1003, 949, 772, 745 cm^{-1}; ^1H NMR (90 MHz) δ = 2.30 (s, 6 H), 2.53 (s, 3 H), 7.0-7.3 (m, 8 H); ^{13}C NMR (75.5 MHz) δ = 20.8 (s), 21.3 (s), 124.8 (s), 128.3 (s), 129.0 (s), 129.2 (s), 140.0 (s), 145.1 (m), 202.7 (s); MS *m/z* (rel intensity) 289 (M^++2, 3), 288 (M^++1, 18), 287 (M^+, 12), 286 (M^+-1, 19), 240 (16), 222 (23), 207 (33), 180 (13), 179 (14), 178 (23), 164 (100), 149 (26), 145 (19), 143 (47), 123 (17), 109 (19), 108 (31), 97 (32), 91 (46), 83 (36), 71 (33), 69 (36), 65 (35). Found: *m/z* 287.0804. Calcd for $C_{16}H_{17}NS_2$: M, 287.0802.

Methyl *N*-(4-Bromo-2-fluorophenyl)-*N*-methyldithiocarbamate (2j). Yield: 90%. A colorless solid, mp 74.5-74.7 °C (EtOH); R_f = 0.65 (hexane : Et_2O = 10 : 1). IR (KBr) 3031, 2924, 1595, 1576, 1489, 1404, 1364, 1312, 1211, 1098, 1063, 954, 874, 822, 779, 727 cm^{-1}; ^1H NMR (200 MHz) δ = 2.57 (s, 3 H), 3.70 (s, 3 H), 7.14-7.26 (m, 1 H), 7.35-7.43 (m, 2 H); ^{19}F NMR (188 MHz) δ = –117.47 (m); ^{13}C NMR (50.3 MHz) δ = 20.6 (s), 44.7 (s), 120.8 (d, J = 23 Hz), 123.4 (m), 130.4 (br), 130.8 (m), 157.0 (d, $^1J_{C-F}$ = 257 Hz), 201.5 (s); MS *m/z* (rel intensity) 297 (M^++2, 28), 295 (M^+, 25), 248 (40), 246 (41), 233 (39), 231 (38), 214 (17), 167 (19), 152 (14), 108 (22), 94 (26), 91 (56), 88 (100), 74 (12). Found: C, 36.94; H, 3.00; N, 4.82%. Calcd for $C_9H_9BrFNS_2$: C, 36.74; H, 3.08; N, 4.76%.

Methyl *N*-(4-Bromo-2-fluorophenyl)-*N*-ethyldithiocarbamate (2k). Yield: 87%. A pale brown oil, bp 210 °C/0.8 mmHg; R_f = 0.50 (hexane : Et_2O = 10 : 1). IR 2977, 1891, 1528, 1491, 1271, 1136, 912, 866, 808 cm^{-1}; ^1H NMR (200 MHz) δ = 1.24 (t, J = 7 Hz, 3 H), 2.55 (s, 3 H), 3.95-4.27 (m, 1 H), 4.27-4.60 (m, 1 H), 7.08-7.16 (m, 1 H), 7.36-7.44 (m, 2 H); ^{19}F NMR (188 MHz) δ = –116.41 (m); ^{13}C NMR (50.3 MHz) δ = 11.6 (s), 20.2 (s), 51.4 (s), 120.6 (d, J = 23 Hz), 123.4 (m), 129.0 (m), 131.2 (br s), 157.2 (d, $^1J_{C-F}$ = 257 Hz), 200.7 (s); MS *m/z* (rel intensity) 310 (M^++3, 4), 309 (M^++2, 37), 308 (M^++1, 3), 307 (M^+, 33), 290 (6), 288 (6), 262 (20), 260 (20), 234 (71), 233 (23), 232 (70), 231 (17), 216 (26), 153 (60), 152 (21), 137 (22), 133 (21), 108 (40), 102 (100), 94 (54), 91 (71). Found: C, 38.82; H, 3.60; N, 4.49%. Calcd for $C_{10}H_{11}BrFNS_2$: C, 38.97; H, 3.60; N, 4.54%.

Methyl *N*-(4-Bromo-2-fluorophenyl)-*N*-hexyldithiocarbamate (2l). Yield: 74%. A dark brown oil, bp 245 °C/0.45 mmHg; R_f = 0.24 (hexane). IR 2955, 2929, 1597, 1574, 1491, 1391, 1263, 1123, 1100, 1065, 878, 858, 818, 729, 610 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.16-1.42 (m, 6 H), 1.48-1.81 (m, 2 H), 2.55 (s, 3 H), 4.05 (m, 1 H), 4.35 (br s, 1 H), 7.07-7.16 (m, 1 H), 7.35-7.43 (m, 2 H); ^{19}F NMR (188 MHz) δ = –116.42 (dm, J = 5 Hz); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 20.3 (s), 22.4 (s), 26.1 (s), 26.4 (br), 31.3 (s), 56.6 (s), 120.7 (d, J = 23 Hz), 123.4 (m), 128.2 (d, J = 4 Hz), 129.5 (m), 157.3 (d, $^1J_{C-F}$ = 257 Hz), 201.1 (s); MS *m/z* (rel intensity) 366 (M^++2, 12),

364 (M^+, 10), 248 (16), 246 (15), 233 (25), 231 (24), 202 (13), 200 (11), 158 (39), 91 (63), 74 (32), 43 (100). Found: C, 45.82; H, 5.12; N, 3.73%. Calcd for $C_{14}H_{19}BrFNS_2$: C, 46.15; H, 5.26; N, 3.84%. Found: *m/z* 363.0130. Calcd for $C_{14}H_{19}{}^{79}BrFNS_2$: M, 363.0126.

Methyl *N*-Methyl-*N*-phenyldithiocarbamate (2m). Yield: 96%. Pale yellow crystals, mp 82.8-83.4 °C (EtOH); R_f = 0.54 (hexane : EtOAc = 10 : 1). IR (KBr) 2920, 1968, 1892, 1761, 1591, 1491, 1428, 1360, 1254, 1100, 955, 772, 696, 631 cm^{-1}; ^1H NMR (90 MHz) δ = 2.51 (s, 3 H), 3.78 (s, 3 H), 7.26 (m, 3 H), 7.42 (m, 2 H); ^{13}C NMR (50.3 MHz) δ = 20.7 (s), 45.9 (s), 126.8 (s), 128.8 (s), 129.6 (s), 144.8 (s), 200.3 (s); MS *m/z* (rel intensity) 197 (M^+, 62), 151 (15), 150 (100), 135 (58), 109 (54), 91 (39), 88 (41). Found: C, 54.59; H, 5.44; N, 7.01%. Calcd for $C_9H_{11}NS_2$: C, 54.79; H, 5.62; N, 7.10%.

Methyl *N*-Ethyl-*N*-phenyldithiocarbamate (2n). Yield: 86%. Pale yellow crystals, mp 47.1-47.9 °C (EtOH); R_f = 0.44 (hexane : Et_2O = 10 : 1). IR (KBr) 2980, 2910, 1595, 1489, 1454, 1397, 1345, 1279, 1238, 1103, 1076, 987, 901, 762, 696, 629 cm^{-1}; ^1H NMR (200 MHz) δ = 1.26 (t, *J* = 7 Hz, 3 H), 2.52 (s, 3 H), 4.25 (q, *J* = 7 Hz, 2 H), 7.19-7.23 (m, 2 H), 7.42-7.50 (m, 3 H); ^{13}C NMR (50.3 MHz) δ = 11.9 (s), 20.5 (s), 52.4 (s), 128.0 (s), 129.0 (s), 129.6 (s), 143.1 (s), 199.9 (s); MS *m/z* (rel intensity) 213 (M^++2, 3), 212 (M^++1, 4), 211 (M^+, 34), 164 (21), 136 (95), 120 (42), 109 (19), 104 (17), 102 (43), 91 (35), 78 (19), 77 (100), 74 (10), 64 (10). Found: C, 56.83; H, 6.24; N, 6.68%. Calcd for $C_{10}H_{13}NS_2$; C, 56.56; H, 6.20; N, 6.63%.

Methyl *N*-Phenyl-*N*-propyldithiocarbamate (2o). Yield: 96%. Pale yellow crystals, mp 60.7-61.5 °C (EtOH); R_f = 0.25 (hexane : CH_2Cl_2 = 3 : 1). IR (KBr) 2963, 2934, 2874, 1593, 1495, 1487, 1402, 1366, 1229, 1100, 953, 772, 700, 631 cm^{-1}; ^1H NMR (90 MHz) δ = 0.92 (t, *J* = 7 Hz, 3 H), 1.74 (m, 2 H), 2.52 (s, 3 H), 4.24 (t, *J* = 8 Hz, 2 H), 7.10-7.23 (m, 2 H), 7.42-7.67 (m, 3 H); ^{13}C NMR (50.3 MHz) δ = 11.0 (s), 20.0 (s), 20.6 (s), 59.1 (s), 127.9 (s), 128.9 (s), 129.6 (s), 143.4 (s), 200.4 (s); MS *m/z* (rel intensity) 226 (M^++1, 5), 225 (M^+, 33), 178 (15), 150 (23), 136 (100), 116 (24), 91 (33), 77 (72), 51 (32), 43 (42). Found: C, 59.05; H, 6.81; N, 6.32%. Calcd for $C_{11}H_{15}NS_2$: C, 58.65; H, 6.71; N, 6.22%. Found: *m/z* 225.0646. Calcd for $C_{11}H_{15}NS_2$: M, 225.0646.

Methyl *N*-Hexyl-*N*-phenyldithiocarbamate (2p). Yield: 100%. A dark brown oil, bp 220 °C/0.5 mmHg; R_f = 0.38 (hexane : EtOAc = 10 : 1). IR 2955, 2928, 2857, 1593, 1491, 1441, 1395, 1368, 1251, 1103, 957, 696 cm^{-1}; ^1H NMR (200 MHz) δ = 0.86 (t, *J* = 7 Hz, 3 H), 1.11-1.42 (m, 6 H), 1.49-1.95 (m, 2 H), 2.52 (s, 3 H), 4.27 (t, *J* = 8 Hz, 2 H), 7.15-7.26 (m, 2 H), 7.41-7.50 (m, 3 H); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 20.3 (s), 22.7 (s), 26.0 (s), 26.4 (s), 31.2 (s), 57.4 (s), 127.7 (s), 128.7 (s), 129.4 (s), 143.2 (s), 199.8 (s); MS *m/z* (rel intensity) 269 (M^++2, 3), 267 (M^+, 23), 158 (21), 150 (29), 136 (99), 135 (51), 106 (48), 104 (23), 91 (94), 85 (38), 77 (100). Found: C, 62.78; H, 7.90; N,

5.19%. Calcd for $C_{14}H_{21}NS_2$: C, 62.90; H, 7.92; N, 5.24%.

Methyl *N*-Octyl-*N*-phenyldithiocarbamate (2q). Yield: 92%. A dark brown oil, bp 235 °C/0.6 mmHg; R_f= 0.29 (hexane : CH_2Cl_2 = 4 : 1). IR 2926, 2855, 1593, 1491, 1395, 1368, 1248, 1103, 1073, 951, 770, 696 cm^{-1}; ^1H NMR (200 MHz) δ = 0.86 (t, *J* = 6 Hz, 3 H), 1.08-1.43 (m, 10 H), 1.43-1.98 (m, 2 H), 2.52 (s, 3 H), 4.27 (t, *J* = 8 Hz, 2 H), 7.17-7.42 (m, 2 H), 7.42-7.82 (m, 3 H); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 20.32 (s), 20.33 (s), 26.36 (s), 26.39 (s), 28.9 (s), 29.0 (s), 31.5 (s), 57.4 (s), 127.8 (s), 128.7 (s), 129.3 (s), 143.2 (s), 199.8 (s); MS *m/z* (rel intensity) 296 (M^++1, 6), 295 (M^+, 28), 186 (17), 183 (21), 150 (50), 136 (100), 91 (55), 77 (60). Found: C, 64.96; H, 8.59; N, 4.63%. Calcd for $C_{16}H_{25}NS_2$: C, 65.03; H, 8.53; N, 4.74%.

Methyl *N*,*N*-Dibenzyldithiocarbamate (2r). Yield: 99%. A pale red oil; R_f = 0.40 (hexane : EtOAc = 10 : 1). IR 3060, 3015, 2910, 1605, 1493, 1465, 1450, 1408, 1355, 1215, 1152, 1078, 1025, 970, 730, 690 cm^{-1}; ^1H NMR (300 MHz) δ = 2.73 (s, 3 H), 4.93 (s, 2 H), 5.37 (s, 2 H), 7.18-7.38 (m, 10 H); ^{13}C NMR (75.5 MHz) δ = 20.8 (s), 53.9 (s), 56.3 (s), 127.1 (s), 127.8 (s), 128.8 (s), 134.7 (m), 135.6 (m), 200.8 (s); MS *m/z* (rel intensity) 288 (M^++1, 3), 287 (M^+, 16), 196 (22), 148 (11), 137 (34), 123 (18), 92 (11), 91 (100), 65 (30). Found: *m/z* 287.0806. Calcd for $C_{16}H_{17}NS_2$: M, 287.0802.

Methyl *N*-Benzyl-*N*-propyldithiocarbamate (2s). Yield: 96%. A pale red oil; R_f= 0.49 (hexane : EtOAc = 10 : 1). IR 2965, 2930, 2917, 2874, 1605, 1495, 1476, 1455, 1435, 1410, 1381, 1302, 1231, 1188, 1121, 1078, 1030, 1001, 958, 731, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 0.90 (t, *J* = 8 Hz, 3 H), 1.65-1.80 (m, 2 H), 2.60-2.75 (m, 3 H), 3.45-3.65 (m, 1 H), 3.85-4.00 (m, 1 H), 4.97 (br s, 1 H), 5.37 (br s, 1 H), 7.20-7.70 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 11.1 (s), 20.1 (s), 20.2 (s), 53.0 (s), 57.1 (s), 126.7 (s), 127.4 (s), 128.5 (s), 135.8 (m), 199.4 (s); MS *m/z* (rel intensity) 240 (M^++1, 1), 239 (M^+, 11), 149 (5), 148 (8), 91 (100), 74 (6), 65 (12). Found: *m/z* 239.0802. Calcd for $C_{12}H_{17}NS_2$: M, 239.0824.

Methyl *N*-Methyl-*N*-(2-pyridyl)dithiocarbamate (6a). Yield: 96%. Colorless crystals, mp 47.5-47.7 °C; R_f = 0.18 (hexane : Et_2O = 2 : 1). IR (KBr) 3052, 3003, 2916, 1586, 1570, 1463, 1425, 1352, 1315, 1295, 1274, 1137, 1102, 995, 961, 791, 745, 656, 637, 621 cm^{-1}; ^1H NMR (200 MHz) δ = 2.59 (s, 3 H), 3.79 (s, 3 H), 7.32 (ddd, *J* = 1, 5, 8 Hz, 1 H), 7.40 (ddd, *J* = 1, 1, 8 Hz, 1 H), 7.80 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.59 (ddd, *J* = 1, 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 20.5 (s), 43.5 (s), 122.4 (s), 123.6 (s), 138.4 (s), 149.7 (s), 156.6 (s), 200.4 (s); MS *m/z* (rel intensity) 199 (M^++1, 5), 198 (M^+, 46), 183 (30), 151 (40), 137 (5), 107 (19), 91 (15), 78 (100). Found: *m/z* 198.0274. Calcd for $C_8H_{10}N_2S_2$: M, 198.0285.

Methyl *N*-Ethyl-*N*-(2-pyridyl)dithiocarbamate (6b). Yield: 83%. A pale yellow oil; R_f= 0.53 (hexane : CH_2Cl_2 : EtOAc = 4 : 2 : 1). IR 3052, 2975, 1586, 1466,

1433, 1389, 1348, 1273, 1111, 1013, 961, 911, 785, 745, 652 cm^{-1}; ^1H NMR (200 MHz) δ = 1.29 (t, *J* = 7 Hz, 3 H), 2.50 (s, 3 H), 4.41 (q, *J* = 7 Hz, 2 H), 7.30-7.38 (m, 2 H), 7.82 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.62 (dd, *J* = 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 12.3 (s), 20.3 (s), 50.8 (s), 123.6 (s), 123.9 (s), 138.4 (s), 150.0 (s), 155.5 (s), 199.8 (s); MS *m/z* (rel intensity) 214 (M^++2, 6), 213 (M^++1, 8), 212 (M^+, 53), 197 (22), 165 (22), 137 (94), 121 (100), 91 (35), 79 (41), 78 (96). Found: C, 50.84; H, 5.48; N, 13.01%. Calcd for $C_9H_{12}N_2S_2$: C, 50.91; H, 5.70; N, 13.19%.

Methyl *N*-Hexyl-*N*-(2-pyridyl)dithiocarbamate (6c). Yield: 88%. A dark red oil; R_f = 0.69 (hexane : Et_2O = 4 : 1). IR 2956, 2928, 2857, 1587, 1465, 1432, 1391, 1366, 1264, 1111, 995, 745 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85 (t, *J* = 7 Hz, 3 H), 1.13-1.41 (m, 6 H), 1.60-1.81 (m, 2 H), 2.57 (s, 3 H), 4.25-4.40 (m, 2 H), 7.28-7.41 (m, 2 H), 7.80 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.60 (dd, *J* = 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 20.2 (s), 22.5 (s), 26.3 (s), 26.9 (s), 31.4 (s), 55.8 (s), 123.5 (s), 123.7 (s), 138.2 (s), 149.9 (s), 155.8 (s), 200.0 (s); MS *m/z* (rel intensity) 269 (M^++1, 6), 268 (M^+, 35), 253 (14), 183 (4), 177 (78), 137 (100), 107 (11), 91 (26), 78 (50). Found: *m/z* 268.1066. Calcd for $C_{13}H_{20}N_2S_2$: M, 268.1068.

Methyl *N*-Octyl-*N*-(2-pyridyl)dithiocarbamate (6d). Yield: 93%. A pale yellow oil; R_f = 0.27 (hexane : Et_2O = 5 : 1). IR 3055, 2954, 2917, 2868, 2847, 1583, 1465, 1453, 1432, 1397, 1368, 1300, 1273, 1263, 1226, 1146, 1110, 1093, 994, 747, 634 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85 (t, *J* = 7 Hz, 3 H), 1.16-1.25 (m, 10 H), 1.67-1.71 (m, 2 H), 2.57 (s, 3 H), 4.29-4.37 (m, 2 H), 7.28-7.45 (m, 2 H), 7.80 (ddd, *J* = 2, 2, 8 Hz, 1 H), 8.60 (dd, *J* = 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 20.2 (s), 22.6 (s), 26.7 (s), 26.9 (s), 29.1 (s), 29.2 (s), 31.7 (s), 55.8 (s), 123.5 (s), 123.7 (s), 138.2 (s), 149.9 (s), 155.9 (s), 200.0 (s); MS *m/z* (rel intensity) 297 (M^++1, 5), 296 (M^+, 30), 281 (16), 249 (10), 205 (84), 137 (100), 91 (25), 78 (45). Found: *m/z* 296.1376. Calcd for $C_{15}H_{24}N_2S_2$: M, 296.1381.

Methyl *N*-Dodecyl-*N*-(2-pyridyl)dithiocarbamate (6e). Yield: 93%. A yellow powder, mp 54.8-55.3 °C; R_f = 0.40 (hexane : Et_2O = 5 : 2). IR (KBr) 2955, 2919, 2848, 1583, 1467, 1452, 1432, 1396, 1368, 1304, 1292, 1146, 1110, 953, 745 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85 (t, *J* = 7 Hz, 3 H), 1.16-1.75 (m, 20 H), 2.57 (s, 3 H), 4.29-4.37 (m, 2 H), 7.29-7.35 (m, 2 H), 7.80 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.60 (dd, *J* = 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 20.3 (s), 22.6 (s), 26.7 (s), 27.0 (s), 29.5 (s), 31.9 (s), 55.8 (s), 123.5 (s), 123.6 (s), 138.2 (s), 149.9 (s), 155.9 (s), 200.1 (s); MS *m/z* (rel intensity) 353 (M^++1, 5), 352 (M^+, 23), 337 (16), 262 (16), 261 (84), 137 (100), 107 (10), 78 (35). Found: *m/z* 352.2003. Calcd for $C_{19}H_{32}N_2S_2$: M, 352.2007.

Methyl *N*-Benzyl-*N*-(2-pyridyl)dithiocarbamate (6f). Yield: 88%. Colorless crystals, mp 86.8-87.3 °C; R_f = 0.18 (hexane : Et_2O = 2 : 1). IR (KBr) 3059, 3030,

2917, 1584, 1570, 1495, 1465, 1455, 1432, 1384, 1349, 1263, 1211, 1200, 1115, 996, 958, 744, 699 cm^{-1}; ^1H NMR (200 MHz) δ = 2.61 (s, 3 H), 5.68 (s, 2 H), 7.09 (ddd, *J* = 1, 1, 8 Hz, 1 H), 7.20-7.30 (m, 6 H), 7.65 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.59 (ddd, *J* = 1, 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 20.7 (s), 58.8 (s), 123.8 (s), 124.2 (s), 127.6 (s), 128.4 (s), 128.5 (s), 135.9 (s), 138.0, (s) 149.9 (s), 155.3 (s), 201.4 (s); MS *m/z* (rel intensity) 274 (M^+, 18), 184 (13), 183 (100), 148 (4), 137 (14), 91 (82), 78 (33). Found: *m/z* 274.0588. Calcd for $C_{14}H_{14}N_2S_2$: M, 274.0598.

Methyl *N*-(4-Ethylbenzyl)-*N*-(2-pyridyl)dithiocarbamate (6g). Yield: 96%. A dark red oil; R_f = 0.74 (hexane : Et_2O = 3 : 1). IR 2963, 1584, 1464, 1387, 1202, 1113, 997, 969, 743 cm^{-1}; ^1H NMR (200 MHz) δ = 1.19 (t, *J* = 8 Hz, 3 H), 2.59 (q, *J* = 8 Hz, 2 H), 2.60 (s, 3 H), 5.64 (s, 2 H), 7.04-7.13 (m, 1 H), 7.06 (d, *J* = 8 Hz, 2 H), 7.19 (d, *J* = 8 Hz, 2 H), 7.22-7.31 (m, 1 H), 7.66 (ddd, *J* = 2, 8, 8 Hz, 1 H), 8.59 (ddd, *J* = 1, 1, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 15.3 (s), 20.4 (s), 28.4 (s), 58.4 (s), 123.5 (s), 124.0 (s), 127.7 (s), 128.2 (s), 132.9 (s), 137.8 (s), 143.4 (s), 149.7 (s), 155.2 (s), 201.0 (s); MS *m/z* (rel intensity) 302 (M^+, 6), 211 (71), 183 (8), 137 (24), 136 (21), 121 (73), 105 (39), 91 (72), 79 (22), 78 (100), 77 (31). Found: *m/z* 302.0905. Calcd for $C_{16}H_{18}N_2S_2$: M, 302.0911.

Methyl *N*-Benzyl-*N*-(3-pyridyl)dithiocarbamate (6h). Yield: 93%. Colorless crystals, mp 113.9-114.4 °C; R_f = 0.55 (hexane : Et_2O = 1 : 4). IR (KBr) 3062, 2911, 1494, 1475, 1430, 1419, 1388, 1351, 1266, 1220, 1191, 1112, 985, 963, 957, 734, 708, 699 cm^{-1}; ^1H NMR (200 MHz) δ = 2.58 (s, 3 H), 5.59 (s, 2 H), 7.25-7.32 (m, 7 H), 8.32 (dd, *J* = 1, 2 Hz, 1 H), 8.58 (dd, *J* = 2, 5 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 21.1 (s), 60.4 (s), 123.9 (s), 128.1 (s), 128.7 (s), 128.8 (s), 135.3 (s), 136.0 (s), 139.5, (s) 149.5 (s), 149.9 (s), 202.4 (s); MS *m/z* (rel intensity) 274 (M^+, 20), 227 (7), 183 (7), 151 (5), 137 (5), 136 (5), 109 (21), 108 (78), 91 (100), 78 (11). Found: *m/z* 274.0590. Calcd for $C_{14}H_{14}N_2S_2$: M, 274.0598.

Methyl *N*-Methyl-*N*-(2-pyrimidyl)dithiocarbamate (10a). Yield: 76%. An orange powder, mp 61.5-62.1 °C; R_f = 0.40 (hexane : Et_2O = 1 : 2). IR (KBr) 1567, 1445, 1425, 1397, 1341, 1315, 1252, 1155, 1108, 810 cm^{-1}; ^1H NMR (200 MHz) δ = 2.62 (s, 3 H), 3.97 (s, 3 H), 7.22 (t, *J* = 5 Hz, 1 H), 8.78 (d, *J* = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 21.4 (s), 42.9, (s) 118.6 (s), 158.2 (s), 161.4 (s), 202.4 (s); MS*m/z* (rel intensity) 201 (M^++2, 6), 200 (M^++1, 7), 199 (M^+, 69), 184 (16), 152 (100), 108 (22), 91 (19), 79 (81). Found: *m/z* 199.0232. Calcd for $C_7H_9N_3S_2$: M, 199.0238.

Methyl *N*-Propyl-*N*-(2-pyrimidyl)dithiocarbamate (10b). Yield: 82%. A pale red oil; R_f = 0.41 (hexane : Et_2O = 1 : 2). IR 2965, 2932, 2874, 1566, 1462, 1406, 1366, 1294, 1283, 1148, 1119, 1073, 959, 814 cm^{-1}; ^1H NMR (300 MHz) δ = 0.92 (t, *J* = 8 Hz, 3 H), 1.78 (sextet, *J* = 8 Hz, 2 H), 4.51 (tm, *J* = 8 Hz, 2 H), 7.27 (t, *J* = 5 Hz, 1 H), 8.80 (d,

J = 5 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 11.0 (s), 20.5 (s), 20.8 (s), 56.4 (s), 119.0 (s), 158.4 (s), 161.2 (s), 201.5 (s); MS *m/z* (rel intensity) 229 (M^++2, 3), 228 (M^++1, 3), 227 (M^+, 28), 212 (7), 180 (10), 138 (100), 136 (33), 91 (23), 79 (56). Found: *m/z* 227.0552. Calcd for $C_9H_{13}N_3S_2$: M, 227.0551.

Methyl *N*-Hexyl-*N*-(2-pyrimidyl)dithiocarbamate (10c). Yield: 77%. A pale yellow oil; R_f = 0.38 (hexane : EtOAc = 3 : 1). IR 2955, 2928, 2857, 1564, 1408, 1381, 1294, 1249, 1191, 1145, 1120, 1073, 994, 955, 808, 671 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85 (t, J = 7 Hz, 3 H), 1.20-1.38 (m, 6 H), 1.72-1.80 (m, 2 H), 2.61 (s, 3 H), 4.53 (t, J = 8 Hz, 2 H), 7.24 (t, J = 5 Hz, 1 H), 8.79 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 20.9 (s), 22.5 (s), 26.3 (s), 27.2 (s), 31.3 (s), 55.0 (s), 119.1 (s), 158.4 (s), 161.4 (s), 201.5 (s); MS *m/z* (rel intensity) 270 (M^++1, 5), 269 (M^+, 35), 254 (8), 222 (14), 178 (31), 138 (100), 108 (16), 79 (30). Found: *m/z* 269.1023. Calcd for $C_{12}H_{19}N_3S_2$: M, 269.1020.

Methyl *N*-Octyl-*N*-(2-pyrimidyl)dithiocarbamate (10d). Yield: 75%. A pale yellow oil; R_f = 0.26 (hexane : EtOAc = 3 : 1). IR 2955, 2925, 2855, 1564, 1407, 1381, 1367, 1295, 1272, 1230, 1176, 1143, 1120, 1090, 1072, 954, 808, 671, 640 cm^{-1}; ^1H NMR (200 MHz) δ = 0.86 (t, J = 6 Hz, 3 H), 1.17-1.26 (m, 10 H), 1.69-1.80 (m, 2 H), 2.61 (s, 3 H), 4.49-4.57 (m, 2 H), 7.23 (t, J = 5 Hz, 1 H), 8.79 (d, J = 5 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 20.9 (s), 22.5 (s), 26.6 (s), 27.2 (s), 29.1 (s), 29.1 (s), 31.7 (s), 55.0 (s), 119.1 (s), 158.4 (s), 161.4 (s), 201.4 (s); MS *m/z* (rel intensity) 298 (M^++1, 6), 297 (M^+, 31), 282 (11), 250 (17), 206 (33), 138 (100), 108 (17), 91 (26), 79 (27). Found: *m/z* 297.1343. Calcd for $C_{14}H_{23}N_3S_2$: M, 297.1333.

Methyl *N*-Dodecyl-*N*-(2-pyrimidyl)dithiocarbamate (10e). Yield: 57%. A pale yellow oil; R_f = 0.32 (hexane : Et_2O = 3 : 1). IR 2957, 2920, 2849, 1577, 1564, 1406, 1376, 1366, 1296, 1226, 1153, 1112, 953, 804 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 6 Hz, 3 H), 1.24-1.40 (m, 18 H), 1.65-1.88 (m, 2 H), 2.61 (s, 3 H), 4.49-4.57 (m, 2 H), 7.22 (t, J = 5 Hz, 1 H), 8.78 (d, J = 5 Hz, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.0 (s), 20.8 (s), 22.6 (s), 26.6 (s), 27.1 (s), 29.1 (s), 29.2 (s), 29.37 (s), 29.42 (s), 29.5 (s), 31.8 (s), 54.9 (s), 119.0 (s), 158.3 (s), 161.2 (s), 201.3 (s); MS*m/z* (rel intensity) 354 (M^++1, 5), 353 (M^+, 24), 338 (10), 306 (18), 262 (30), 138 (100), 108 (14), 91 (23), 79 (20). Found: *m/z* 353.1958. Calcd for $C_{18}H_{31}N_3S_2$: M, 353.1959.

A General Procedure for the Preparation of Trifluoromethylamines: To a stirred solution of $TBAH_2F_3$ (3.0 g, 10 mmol) and a dithiocarbamate (2.0 mmol) in CH_2Cl_2 (4.0 mL) was added an *N*-halo imide (see Table 1, 8.0 mmol) in one portion at room temperature. The resulting mixture was stirred for 1 h at room temperature, then poured into an aq. solution of $NaHCO_3$, NaOH, and $NaHSO_3$ and extracted with diethyl

ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered through a Celite/silica gel (Wako Gel C-100) pad, and concentrated. The residue was purified by column chromatography or bulb-to-bulb distillation to give the desired trifluoromethylamine. Yields (*N*-halo imide) and spectroscopic properties of products are shown below.

Diphenyl(trifluoromethyl)amine (3a). Yield: 78% (NBS). A colorless oil; R_f = 0.74 (hexane : benzene = 4 : 1). IR 3068, 3045, 2960, 2925, 1950, 1872, 1800, 1720, 1591, 1494, 1452, 1382, 1318, 1299, 1270, 1201, 1096, 1074, 1032, 1001, 950, 921, 904, 771, 754, 740, 696 cm^{-1}; ^1H NMR (200 MHz) δ = 7.2-7.3 (m, 6 H), 7.3-7.4 (m, 4 H); ^{19}F NMR (188 MHz) δ = –54.77 (s); ^{13}C NMR (75.5 MHz) δ = 121.8 (q, $^1J_{C-F}$ = 256 Hz), 126.0 (q, J = 2 Hz), 126.4 (s), 129.2 (s), 141.5 (s); MS *m/z* (rel intensity) 239 (M^++2, 1), 238 (M^++1, 14), 237 (M^+, 100), 236 (39), 235 (3), 218 (7), 216 (7), 169 (4), 168 (34), 167 (65), 166 (11). Found: *m/z* 237.0769. Calcd for $C_{13}H_{10}F_3N$: M, 237.0765.

Benzyl(4-methoxyphenyl)(trifluoromethyl)amine (3b). Yield: 99% (NBS). A pale yellow oil: R_f = 0.74 (hexane : Et_2O = 10 : 1). IR 3090, 3062, 3000, 2928, 1720, 1608, 1581, 1511, 1454, 1440, 1380, 1291, 1248, 1223, 1180, 1167, 1100, 1078, 1052, 1034, 990, 908, 836, 734, 698 cm^{-1}; ^1H NMR (200 MHz) δ = 3.77 (s, 3 H), 4.47 (s, 2 H), 6.79 (d, J = 9 Hz, 2 H), 7.13 (d, J = 9 Hz, 2 H), 7.2-7.3 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.74 (s); ^{13}C NMR (75.5 MHz) δ = 53.5 (q, J = 1 Hz), 55.2 (s), 114.1 (s), 123.7 (q, $^1J_{C-F}$ = 255 Hz), 127.4 (s), 128.3 (s), 128.8 (s), 129.2 (m), 133.5 (s), 136.9 (s), 158.4 (s); MS *m/z* (rel intensity) 282 (M^++1, 6), 281 (M^+, 34), 204 (3), 190 (8), 126 (2), 92 (8), 91 (100). Found: *m/z* 281.1024. Calcd for $C_{15}H_{14}F_3ON$: M, 281.1027.

Benzyl(4-chlorophenyl)(trifluoromethyl)amine (3c). Yield: 88% (NBS). A colorless oil; R_f = 0.74 (hexane : Et_2O = 10 : 1). IR 3092, 3071, 3038, 2927, 1977, 1952, 1897, 1721, 1652, 1600, 1496, 1454, 1374, 1310, 1258, 1229, 1189, 1098, 1054, 1017, 996, 908, 837, 724, 698 cm^{-1}; ^1H NMR (200 MHz) δ = 4.52 (s, 2 H), 7.09 (d, J = 9 Hz, 2 H), 7.23 (d, J = 9 Hz, 2 H), 7.3-7.4 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.20 (s); ^{13}C NMR (50.3 MHz) δ = 53.2 (q, J = 1 Hz), 123.2 (q, $^1J_{C-F}$ = 256 Hz), 127.3 (q, J = 2 Hz), 127.6 (s), 127.9 (s), 128.5 (s), 129.2 (s), 132.1 (s), 136.4 (s), 139.5 (s); MS *m/z* (rel intensity) 288 (M^++3, 0.3), 287 (M^++2, 3), 286 (M^++1, 1), 285 (M^+, 9), 92 (8), 91 (100). Found: *m/z* 285.0534. Calcd for $C_{14}H_{11}{}^{35}ClF_3N$: M, 285.0532.

Benzyl(4-fluorophenyl)(trifluoromethyl)amine (3d). Yield: 84% (NBS). A colorless oil; R_f = 0.70 (hexane : Et_2O = 10 : 1). IR 3090, 3070, 3035, 2925, 2878, 1900, 1892, 1769, 1721, 1608, 1510, 1452, 1378, 1310, 1260, 1220, 1182, 1157, 1100, 1078, 1054, 991, 840, 820, 758, 728, 699 cm^{-1}; ^1H NMR (200 MHz) δ = 4.50 (s, 2 H), 6.96 (dd, J = 9, 9 Hz, 2 H), 7.16 (dd, J = 5, 9 Hz, 2 H), 7.2-7.4 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.68 (s, 3 F), –115.26 (dd, J = 5, 9 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 53.5

(q, J = 1 Hz), 115.9 (q, J = 23 Hz), 123.4 (q, $^1J_{C\text{-}F}$ = 256 Hz), 127.6 (s), 128.2 (s), 128.4 (s), 128.9 (dd, J = 2, 9 Hz), 136.5 (s), 136.7 (d, J = 3 Hz), 161.3 (d, $^1J_{C\text{-}F}$ = 247 Hz); MS *m/z* (rel intensity) 270 (M^++1, 1), 269 (M^+, 7), 92 (8), 91 (100). Found: *m/z* 269.0831. Calcd for $C_{14}H_{11}F_4N$: M, 269.0828.

Benzyl(4-cyanophenyl)(trifluoromethyl)amine (3e). Yield: 78% (NBS), 99% (DBH). A pale yellow oil; R_f = 0.72 (hexane : Et_2O = 2 : 1). IR 3092, 3064, 3032, 2928, 2224, 1720, 1608, 1515, 1452, 1378, 1332, 1296, 1260, 1224, 1194, 1108, 1080, 1060, 1000, 834, 736, 697 cm^{-1}; ^1H NMR (200 MHz) δ = 4.71 (s, 2 H), 7.19 (d, J = 9 Hz, 2 H), 7.2-7.4 (m, 5 H), 7.55 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –56.90 (s); ^{13}C NMR (75.5 MHz) δ = 52.1 (s), 107.7 (s), 118.4 (s), 121.9 (s), 122.5 (q, $^1J_{C\text{-}F}$ = 258.1 Hz), 126.7 (s), 127.7 (s), 128.9 (s), 133.1 (s), 136.0 (s), 145.1 (s); MS *m/z* (rel intensity) 277 (M^++1, 1), 276 (M^+, 3), 92 (8), 91 (100). Found: *m/z* 276.0879. Calcd for $C_{15}H_{10}F_3N_2$: M, 276.0874.

This compound was prepared alternatively in 97% or 99% yield by treatment with 70% HF/py or $(HF)_3/Et_3N$ (2.0 mL) and NBS (1.42 g, 8.0 mmol) at 0 °C for 1 h, respectively.

4-Methoxyphenyl(methyl)(trifluoromethyl)amine (3f). Yield: 90% (NBS). A colorless oil; R_f = 0.64 (hexane : Et_2O = 10 : 1). IR 2960, 2940, 2910, 2842, 1516, 1474, 1437, 1339, 1271, 1250, 1196, 1146, 1055, 835 cm^{-1}; ^1H NMR (200 MHz) δ = 2.98 (q, J = 1 Hz, 3 H), 3.81 (s, 3 H), 6.88 (d, J = 9 Hz, 2 H), 7.23 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.98 (s); ^{13}C NMR (75.5 MHz) δ = 36.8 (q, J = 2 Hz), 55.4 (s), 114.3 (s), 123.7 (q, $^1J_{C\text{-}F}$ = 255 Hz), 127.4 (s), 135.6 (s), 158.2 (s); MS *m/z* (rel intensity) 206 (M^++1, 9), 205 (M^+, 80), 191 (9), 190 (100), 186 (8), 162 (33), 92 (10), 83 (16), 77 (13), 69 (18), 65 (34). Found: *m/z* 205.0716. Calcd for $C_9H_{10}F_3ON$: M, 205.0714.

Methyl(4-nitrophenyl)(trifluoromethyl)amine (3g). Yield: 68% (NBS), 96% (DBH). A pale yellow oil; R_f = 0.46 (hexane : Et_2O = 5 : 1). IR 3120, 3085, 2928, 2850, 1720, 1601, 1518, 1478, 1441, 1380, 1334, 1263, 1201, 1141, 1100, 1062, 901, 849, 751, 731, 692 cm^{-1}; ^1H NMR (200 MHz) δ = 3.19 (q, J = 1 Hz, 3 H), 7.26 (d, J = 9 Hz, 2 H), 8.21 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.88 (s); ^{13}C NMR (75.5 MHz) δ = 35.1 (q, J = 2 Hz), 120.8 (q, J = 2 Hz), 122.3 (q, $^1J_{C\text{-}F}$ = 258 Hz), 124.8 (s), 143.6 (s), 147.9 (s); MS *m/z* (rel intensity) 221 (M^++1, 10), 220 (M^+, 100), 201 (13), 190 (41), 162 (17), 159 (23). Found: *m/z* 220.0456. Calcd for $C_8H_7F_3O_2N_2$: M, 220.0460.

1-Trifluoromethyl-2,3-dihydroindole (3h). Yield: 76% (NBS). A colorless oil; R_f = 0.72 (hexane : Et_2O = 10 : 1). IR 3074, 3050, 3035, 2992, 2954, 2918, 2885, 2851, 1794, 1720, 1602, 1483, 1440, 1374, 1339, 1318, 1301, 1270, 1242, 1200, 1180, 1169, 1120, 1090, 1058, 951, 874, 809, 750, 720, 682 cm^{-1}; ^1H NMR (200 MHz) δ = 3.11 (t, J

= 8 Hz, 2 H), 3.73 (t, J = 8 Hz, 2 H), 6.9-7.2 (m, 2 H), 7.2-7.4 (m, 2 H); ^{19}F NMR (188 MHz) δ = –61.74 (s); ^{13}C NMR (75.5 MHz) δ = 28.5 (s), 47.9 (q, J = 2 Hz), 112.2 (q, J = 3 Hz), 122.4 (s), 122.9 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 125.0 (s), 127.6 (s), 130.4 (s), 143.2 (s); MS *m/z* (rel intensity) 187 (M^+, 23), 186 (M^+-1, 41), 185 (37), 117 (45), 155 (11), 97 (11), 95 (12), 92 (11), 90 (17), 89 (31), 81 (16), 71 (30), 69 (100), 63 (43). Found: *m/z* 187.0602. Calcd for $C_9H_8F_3N$: M, 187.0609.

Bis(3-methylphenyl)(trifluoromethyl)amine (3i). Yield: 48% (NBS), 74% (NIS). A colorless oil; R_f = 0.70 (hexane : Et_2O = 10 : 1). IR 3038, 2952, 2924, 2858, 1720, 1603, 1583, 1491, 1450, 1380, 1310, 1299, 1269, 1247, 1209, 1153, 1082, 961, 904, 853, 840, 787, 695 cm^{-1}; ^{1}H NMR (200 MHz) δ = 2.36 (s, 6 H), 7.0-7.1 (m, 6 H), 7.2-7.3 (m, 2 H); ^{19}F NMR (188 MHz) δ = –54.51 (s); ^{13}C NMR (75.5 MHz) δ = 21.4 (s), 121.9 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 123.1 (s), 126.7 (s), 126.9 (s), 128.9 (s), 139.2 (s), 141.5 (s); MS *m/z* (rel intensity) 266 (M^++1, 17), 265 (M^+, 100), 264 (M^+-1, 12), 251 (2), 250 (15), 133 (19), 132 (12). Found: *m/z* 265.1073. Calcd for $C_{15}H_{14}F_3N$: M, 265.1078.

***N*-Methyl-*N*-trifluoromethyl-4-bromo-2-fluoroaniline (3j).** Yield: 87% (DBH). A colorless oil, bp 118 °C/10 mmHg; R_f = 0.57 (hexane). IR 2960, 1578, 1499, 1347, 1296, 1225, 1150, 1090, 1076, 1057, 907, 858, 820 cm^{-1}; ^{1}H NMR (200 MHz) δ = 3.00 (q, J = 1 Hz, 3 H), 7.16-7.33 (m, 3 H); ^{19}F NMR (188 MHz) δ = –61.55 (s, 3 F), –117.62 (m, 1 F); ^{13}C NMR (50.3 MHz) δ = 35.9 (s), 119.6 (s), 120.5 (d, J = 24 Hz), 121.0 (d, J = 9 Hz), 122.9 (q, $^{1}J_{C\text{-}F}$ = 256 Hz), 127.8 (d, J = 1 Hz), 129.6 (m), 158.8 (dm, $^{1}J_{C\text{-}F}$ = 256 Hz); MS *m/z* (rel intensity) 274 (M^++3, 9), 273 (M^++2, 100), 271 (M^+, 94), 270 (48), 252 (11), 204 (17), 203 (17), 202 (29), 201 (19), 177 (42), 157 (15), 155 (13), 123 (24), 122 (17), 108 (19), 103 (15), 95 (15), 94 (33), 81 (16), 75 (21), 69 (39). Found: C, 37.82; H, 2.57; N, 5.22%. Calcd for $C_8H_7BrF_3N$: C, 37.82; H, 2.78; N, 5.51%.

***N*-Ethyl-*N*-trifluoromethyl-4-bromo-2-fluoroaniline (3k).** Yield: 82% (DBH). A colorless oil, bp 85 °C/10 mmHg; R_f = 0.56 (hexane). IR 2988, 1578, 1499, 1408, 1352, 1271, 1242, 1223, 1146, 1074, 920, 860, 820 cm^{-1}; ^{1}H NMR (200 MHz) δ = 1.07 (t, J = 7 Hz, 3 H), 3.38 (q, J = 7 Hz, 3 H), 7.15-7.34 (m, 3 H); ^{19}F NMR (188 MHz) δ = –58.60 (s, 3 F), –117.04 (m, 1 F); ^{13}C NMR (50.3 MHz) δ = 13.4 (s), 43.2 (q, J = 1 Hz), 120.4 (d, J = 24 Hz), 121.5 (d, J = 27 Hz), 123.0 (q, $^{1}J_{C\text{-}F}$ = 265 Hz), 126.9 (d, J = 12 Hz), 127.8 (d, J = 4 Hz), 131.5 (qm, J = 1 Hz), 159.7 (dd, J = 1 Hz, $^{1}J_{C\text{-}F}$ = 256 Hz); MS *m/z* (rel intensity) 288 (M^++3, 6), 287 (M^++2, 37), 286 (M^++1, 7), 285 (M^+, 42), 273 (11), 272 (89), 271 (13), 270 (100), 257 (9), 240 (9), 239 (20), 237 (20), 203 (18), 201 (19), 177 (15), 108 (10), 94 (15), 69 (19). Found: C, 37.48; H, 2.76; N, 4.91%. Calcd for $C_9H_8BrF_3N$: C, 37.79; H, 2.82; N, 4.90%.

***N*-Hexyl-*N*-trifluoromethyl-4-bromo-2-fluoroaniline (3l).** Yield: 87% (DBH). A colorless oil, bp 110 °C/0.7 mmHg; R_f = 0.77 (hexane). IR 2959, 2934, 1578, 1497,

1458, 1408, 1287, 1242, 1207, 1196, 1102, 1076, 926, 860, 820, 735 cm^{-1}; ^1H NMR (200 MHz) δ = 0.86 (t, J = 6 Hz, 3 H), 1.16-1.48 (m, 8 H), 3.29 (t, J = 7 Hz, 3 H), 7.19-7.34 (m, 3 H); ^{19}F NMR (188 MHz) δ = –58.90 (s, 3 F), –116.76 (dm, J = 12 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.1 (s), 28.0 (s), 31.4 (s), 48.5 (q, J = 1 Hz), 120.3 (d, J = 7 Hz), 121.6 (d, J = 9 Hz), 122.9 (q, $^1J_{C\text{-}F}$ = 255 Hz), 127.2 (d, J = 12 Hz), 127.9 (d, J = 4 Hz), 131.6 (dd, J = 1, 1 Hz), 159.8 (dm, $^1J_{C\text{-}F}$ = 256 Hz); MS *m/z* (rel intensity) 343 (M^++3, 12), 342 (M^++2, 100), 341 (M^++1, 12), 340 (M^+, 100), 259 (37), 257 (38), 203 (29), 201 (30), 191 (31), 177 (19), 94 (37), 69 (30). Found: C, 45.98; H, 4.72; N, 4.05%. Calcd for $C_{13}H_{16}BrF_3N$: C, 45.63; H, 4.71; N, 4.09%.

***N*-Methyl-*N*-trifluoromethylaniline (3m).** Yield: 66%. A colorless oil; R_f = 0.47 (hexane). IR 3067, 2984, 2923, 1601, 1497, 1476, 1437, 1333, 1269, 1196, 1148, 1090, 1059, 889, 770, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 3.17 (t, J = 1 Hz, 3 H), 7.33-7.52 (m, 5 H); ^{19}F NMR (282 MHz) δ = –60.96 (s); ^{13}C NMR (75.5 MHz) δ = 36.3 (s), 123.4 (q, $^1J_{C\text{-}F}$ = 256 Hz), 124.9 (s), 126.1 (s), 129.1 (s), 142.8 (s); MS *m/z* (rel intensity) 176 (M^++1, 9), 175 (M^+, 84), 174 (51), 156 (31), 106 (37), 105 (13), 104 (22), 79 (27), 78 (76), 77 (100), 74 (10), 69 (44). Found: *m/z* 175.0609. Calcd for $C_8H_8F_3N$: M, 175.0609.

***N*-Ethyl-*N*-trifluoromethylaniline (3n).** Yield: 65%. A colorless oil; R_f= 0.48 (hexane). IR 2984, 2942, 1599, 1497, 1381, 1350, 1269, 1190, 1144, 1100, 1055, 909, 772, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 1.08 (t, J = 7 Hz, 3 H), 3.42 (qq, J = 1, 7 Hz, 2 H), 7.23-7.39 (m, 5 H); ^{19}F NMR (282 MHz) δ = –58.12 (s); ^{13}C NMR (75.5 MHz) δ = 13.7 (s), 43.8 (s), 123.5 (q, $^1J_{C\text{-}F}$ = 256 Hz), 126.6 (s), 126.8 (q, J = 2 Hz), 129.1 (s), 140.7 (s); MS *m/z* (rel intensity) 189 (M^+, 46), 174 (100), 141 (35), 105 (24), 91 (23), 78 (38), 77 (93), 69 (39), 66 (7), 65 (27). Found: *m/z* 189.0766. Calcd for $C_9H_{10}F_3N$: M, 189.0765.

***N*-Propyl-*N*-trifluoromethylaniline (3o).** Yield: 78%. A colorless oil; R_f = 0.52 (hexane). IR 2973, 2938, 2880, 1601, 1497, 1378, 1341, 1291, 1262, 1240, 1190, 1146, 1066, 932, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 1.02 (t, J = 8 Hz, 3 H), 1.60 (sextet, J = 8 Hz, 2 H), 3.41 (t, J = 8 Hz, 2 H), 7.36-7.52 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.29 (s); ^{13}C NMR (75.5 MHz) δ = 11.1 (s), 21.4 (s), 50.8 (s), 123.5 (q, $^1J_{C\text{-}F}$ = 255 Hz), 126.7 (s), 127.0 (q, J = 2 Hz), 129.1 (s), 141.0 (s); MS *m/z* (rel intensity) 204 (M^++1, 3), 203 (M^+, 25), 175 (9), 174 (100), 161 (3), 105 (12), 78 (24), 77 (59), 69 (10). Found: *m/z* 203.0922. Calcd for $C_{10}H_{12}F_3N$: M, 203.0922.

***N*-Hexyl-*N*-trifluoromethylaniline (3p).** Yield: 68%. A colorless oil; R_f = 0.67 (hexane). IR 2959, 2934, 2361, 1599, 1497, 1377, 1343, 1262, 1190, 1144, 1103, 1061, 924, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 0.86 (t, J = 7 Hz, 3 H), 1.15-1.50 (m, 8 H), 3.32 (qt, J = 1, 7 Hz, 2 H), 7.20-7.42 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.31 (s);

^{13}C NMR (75.5 MHz) δ = 14.0 (s), 22.5 (s), 26.2 (s), 28.1 (s), 31.3 (s), 49.0 (s), 123.5 (q, $^{1}J_{C-F}$ = 255 Hz), 126.7 (s), 127.0 (q, J = 1.2 Hz), 129.1 (s), 141.0 (s); MS *m/z* (rel intensity) 246 (M^++1, 2), 245 (M^+, 11), 175 (11), 174 (100), 161 (12), 83 (11), 78 (11), 77 (26), 71 (17), 69 (18). Found: *m/z* 245.1388. Calcd for $C_{13}H_{18}F_3N$: M, 245.1391.

***N*-Octyl-*N*-trifluoromethylaniline (3q).** Yield: 79%. A colorless oil; R_f= 0.53 (hexane). IR 2980, 2957, 2859, 1601, 1495, 1468, 1377, 1347, 1266, 1190, 1138, 1105, 1059, 907, 768, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.15-1.35 (m, 10 H), 1.36-1.50 (m, 2 H), 3.32 (t, J = 7 Hz, 2 H), 7.22-7.38 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.29 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.6 (s), 26.6 (s), 28.2 (s), 29.1 (s), 29.2 (s), 31.8 (s), 49.0 (s), 123.5 (q, $^{1}J_{C-F}$ = 255 Hz), 126.7 (s), 127.0 (s), 129.1 (s), 141.0 (s); MS *m/z* (rel intensity) 274 (M^++1, 8), 273 (M^+, 15), 175 (13), 174 (100), 161 (20), 78 (10), 77 (17). Found: *m/z* 273.1699. Calcd for $C_{15}H_{22}F_3N$: M, 273.1704.

Dibenzyl(trifluoromethyl)amine (3r). To a stirred solution of $TBAH_2F_3$ (0.95 g, 3.2 mmol) and **2r** (0.31 g, 1.1 mmol) in dichloromethane (1.0 mL) was added NBS (0.77 g, 4.3 mmol) in one portion at room temperature. The resulting mixture was stirred for 30 min at room temperature, and diluted with a mixture of pentane and diethyl ether (5 : 1). The resulting insoluble material was filtered through a short silica gel (Wako gel C-100) column. The filtrate was concentrated under reduced pressure. The residue was purified by bulb-to-bulb distillation to give **3r** in 86% yield as colorless oil, bp 195-205 °C/0.8 mmHg. The compound was kept in a hood since it easily liberated hydrogen fluoride upon exposure to moisture. IR 3067, 3034, 2926, 2876, 1497, 1456, 1399, 1266, 1225, 1096, 1075, 1022, 750, 698 cm^{-1}; ^1H NMR (100 MHz) δ = 4.04 (s, 4 H), 7.2-7.4 (m, 10 H); ^{19}F NMR (94 MHz) δ = –59.71 (s); ^{13}C NMR (75.5 MHz) δ = 49.5 (q, J = 2 Hz), 125.1 (d, $^{1}J_{C-F}$ = 256 Hz), 127.5 (s), 128.4 (s), 128.6 (s), 136.5 (s); MS *m/z* (rel intensity) 265 (M^+, 2), 174 (18), 152 (6), 149 (6), 93 (7), 92 (59), 91 (100), 77 (11), 69 (13), 65 (22). Found: *m/z* 265.1066; Calcd for $C_{15}H_{14}F_3N$: M, 265.1078.

Benzyl(propyl)(trifluoromethyl)amine (3s). This compound was similarly prepared in 84% yield as a colorless oil, bp 95-100 °C/0.8 mmHg. IR 3034, 2973, 2938, 2880, 1497, 1456, 1401, 1231, 1156, 1071, 1007, 735, 698 cm^{-1}; ^1H NMR (100 MHz) δ = 0.79 (t, J = 6 Hz, 3 H), 1.46 (sextet, J = 6 Hz, 2 H), 2.80 (qt, J = 1, 6 Hz, 2 H), 4.05 (s, 2 H), 7.3-7.4 (m, 5 H); ^{19}F NMR (94 MHz) δ = –60.90 (s); ^{13}C NMR (75.5 MHz) δ = 11.2 (s), 20.8 (s), 48.6 (s), 50.5 (q, J = 2 Hz), 125.3 (q, $^{1}J_{C-F}$ = 254 Hz), 127.4 (s), 128.0 (s), 128.4 (s), 137.5 (s); MS *m/z* (rel intensity) 217 (M^+, 2), 188 (5), 155 (2), 126 (8), 96 (4), 92 (10), 91 (100), 69 (17), 65 (29). Found: *m/z* 217.1080. Calcd for $C_{11}H_{14}F_3N$: M, 217.1078.

A General Procedure for the Preparation of Bromoaryl(trifluoromethyl)amines:

To a stirred suspension of $TBAH_2F_3$ (3.0 g, 10 mmol) and DBH (2.8 g, 10 mmol) in dichloromethane (4.0 mL) was added dropwise a solution of a dithiocarbamate (2.0 mmol) in dichloromethane (1.0 mL) at room temperature, and the reaction mixture was heated to reflux until all the substrate was consumed. The resulting mixture was treated with aq. $NaHSO_3/NaHCO_3/NaOH$ (pH 10) solution at 0 °C. The pH value of the mixture was adjusted at 10 with NaOH, and the organic phase was separated. The aq. phase was extracted with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered through a pad of Celite/silica gel (Wako Gel C-100), and concentrated. The residue was purified by column chromatography or bulb-to-bulb distillation to give the desired trifluoromethylamines. Yields and spectra of products are as follows.

***N*-Methyl-*N*-trifluoromethyl-4-bromoaniline (4m).** Yield: 96%. A colorless oil, bp 120 °C/10 mmHg; R_f = 0.70 (hexane : Et_2O = 10 : 1). IR 2984, 2920, 1495, 1437, 1281, 1262, 1198, 1148, 1090, 1059, 1013, 831 cm^{-1}; ^1H NMR (200 MHz) δ = 3.01 (q, J = 1 Hz, 3 H), 7.10-7.25 (m, 2 H), 7.43-7.49 (m, 2 H); ^{19}F NMR (188 MHz) δ = –61.12 (s); ^{13}C NMR (50.3 MHz) δ = 36.1 (q, J = 2 Hz), 119.6 (s), 123.2 (q, $^1J_{C-F}$ = 256 Hz), 126.4 (q, J = 2 Hz), 132.2 (s), 141.8 (s); MS *m/z* (rel intensity) 256 (M^++3; 6), 255 (M^++2, 63), 254 (M^++1, 23), 253 (M^+, 65), 236 (8), 234 (8), 186 (10), 185 (10), 184 (17), 183 (8), 182 (6), 174 (9), 173 (15), 159 (37), 157 (17), 155 (19), 105 (48), 104 (30), 90 (28), 77 (67), 78 (33), 76 (44), 69 (100), 63 (50). Found: C, 37.82; H, 2.57; N, 5.22%. Calcd for $C_8H_7BrF_3N$: C, 37.82; H, 2.78; N, 5.51%.

***N*-Ethyl-*N*-trifluoromethyl-4-bromoaniline (4n).** Yield: 83%. A colorless oil, bp 116 °C/0.6 mmHg; R_f = 0.65 (hexane). IR 2984, 2941, 1493, 1472, 1337, 1269, 1194, 1144, 1100, 1012, 908, 831 cm^{-1}; ^1H NMR (200 MHz) δ = 1.08 (dt, J = 1, 7 Hz, 3 H), 3.40 (dq, J = 1, 7 Hz, 3 H), 7.12 (d, J = 9 Hz, 2 H), 7.48 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.39 (s); ^{13}C NMR (50.3 MHz) δ = 13.6 (s), 43.8 (q, J = 2 Hz), 120.2 (s), 123.2 (q, $^1J_{C-F}$ = 256 Hz), 128.2 (q, J = 2 Hz), 132.3 (s), 139.8 (s); MS *m/z* (rel intensity) 288 (M^++3, 9), 287 (M^++2, 71), 286 (M^++1, 12), 285 (M^+, 68), 273 (18), 272 (58), 271 (21), 270 (100), 259 (15), 257 (17), 240 (14), 239 (38), 238 (16), 237 (35), 203 (42), 202 (23), 201 (44), 200 (20), 192 (28), 177 (24), 158 (17), 113 (23), 108 (26), 94 (44), 81 (18), 75 (17), 69 (47). Found: C, 40.42; H, 3.32; N, 5.19%. Calcd for $C_9H_9BrF_3N$: C, 40.32; H, 3.38; N, 5.22%.

***N*-Propyl-*N*-trifluoromethyl-4-bromoaniline (4o).** Yield: 68%. A colorless oil, bp 110 °C/1.5 mmHg; R_f = 0.62 (hexane). IR 2973, 2938, 2880, 1493, 1458, 1339, 1240, 1194, 1146, 1063, 1013, 930, 833, 795, 723 cm^{-1}; ^1H NMR (90 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.13-1.91 (m, 2 H), 3.27 (t, J = 7 Hz, 2 H), 7.12 (d, J = 9 Hz, 2 H), 7.47 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.57 (s); ^{13}C NMR (50.3 MHz) δ = 10.9

(s), 21.3 (s), 50.7 (q, J = 1 Hz), 120.3 (s), 123.2 (q, $^1J_{C\text{-}F}$ = 255Hz), 128.5 (q, J = 2 Hz). 132.3 (s), 140.1 (s); MS *m/z* (rel intensity) 284 (M^++3, 8), 283 (M^++2, 63), 282 (M^++1, 9), 281 (M^+, 64), 255 (21), 254 (97), 253 (24), 252 (100), 239 (11), 221 (15), 220 (15), 219 (13), 185 (34), 184 (19), 183 (31), 182 (17), 173 (74), 159 (19), 157 (39), 155 (36), 95 (19), 90 (14), 78 (48), 76 (58), 75 (54), 69 (40). Found: C, 42.49; H, 3.83; N, 4.89%. Calcd for $C_{10}H_{11}BrF_3N$: C, 42.58; H, 3.93; N, 4.97%.

***N*-Hexyl-*N*-trifluoromethyl-4-bromoaniline (4p).** Yield: 71% (in boiling CH_2Cl_2), 86% (0 °C). A colorless oil, bp 132 °C/0.68 mmHg; R_f = 0.73 (hexane). IR 2959, 2932, 2861, 1493, 1375, 1258, 1194, 1100, 1071, 1061, 1013, 920, 831 cm^{-1}; ^1H NMR (200 MHz) δ = 0.86 (t, J = 7 Hz, 3 H), 1.02-1.57 (m, 8 H), 3.27 (t, J = 7 Hz, 3 H), 7.11 (d, J = 9 Hz, 2 H), 7.52 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.57 (s); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.2 (s), 28.0 (s), 31.3 (s), 49.0 (q, J = 1 Hz), 120.3 (s), 123.2 (q, $^1J_{C\text{-}F}$ = 255 Hz), 128.5 (q, J = 2 Hz), 132.3 (s), 140.1 (s); MS *m/z* (rel intensity) 326 (M^++3, 8), 325 (M^++2, 47), 324 (M^++1, 8), 323 (M^+, 50), 301 (13), 255 (26), 254 (100), 252 (97), 241 (48), 240 (49), 232 (18), 230 (20), 219 (19), 217 (13), 186 (15), 185 (27), 184 (24), 183 (27), 182 (14), 174 (13), 173 (54), 159 (24), 157 (26), 155 (29), 95 (11), 90 (11), 78 (25), 77 (17), 76 (39), 75 (29), 69 (23). Found; C, 48.44; H, 5.15; N, 4.46%. Calcd for $C_{13}H_{17}BrF_3N$: C, 48.16; H, 5.29; N, 4.32%.

***N*-Octyl-*N*-trifluoromethyl-4-bromoaniline (4q).** Yield: 79% (0 °C). An alternative procedure follows. A polypropylene round-bottom tube was charged with NBS (0.45 g, 2.5 mmol), 70 wt% HF/py (0.26 mL), and CH_2Cl_2 (1.0 mL). To this suspension was added a solution of **2s** (0.16 g, 0.50 mmol) in dichloromethane (1.0 mL) at 0 °C, and the whole mixture was stirred for 30 min at 0 °C before quenching with an aq. $NaHSO_3$/$NaHCO_3$/NaOH (pH 10) solution at 0 °C. The organic phase was separated; the aq. phase was extracted with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtrated (Wako Gel C-100), and concentrated. The residue was purified by column chromatography (pentane) to give **4q** (0.10 g, 0.30 mmol) in 60% yield along with starting material **2q** (0.05 g, 0.16 mmol, 33%).

4q: A colorless oil, bp 183 °C/0.58 mmHg; R_f = 0.71 (hexane). IR 2957, 2930, 2860, 1493, 1375, 1273, 1260, 1192, 1073, 1051, 1013, 908, 831 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 6 Hz, 3 H), 0.91-1.37 (m, 12 H), 3.29 (t, J = 6 Hz, 2 H), 7.12 (d, J = 9Hz, 2 H), 7.48 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.59 (s); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.6 (s), 28.1 (s), 29.1 (s), 29.2 (s), 31.8 (s), 49.0 (q, J = 1 Hz), 120.3 (s), 123.3 (q, $^1J_{C\text{-}F}$ = 255 Hz), 128.5 (q, J = 2 Hz), 132.3 (s), 140.1 (s); MS *m/z* (rel intensity) 354 (M^++3, 11), 353 (M^++2, 55), 352 (M^++1, 11), 351 (M^+, 56), 255 (27), 254 (100), 253 (31), 252 (99), 241 (55), 239 (60), 186 (11), 185 (22), 184 (11), 183

(19), 174 (16), 173 (55), 159 (14), 157 (22), 155 (20), 78 (19), 77 (12), 76 (22), 75 (18), 71 (33), 69 (31). Found: *m/z* 351.0803. Calcd for $C_{15}H_{21}{}^{79}BrF_3N$: M, 351.0809.

A General Procedure for the Preparation of (Trifluoromethylamino)pyridines (7) and -pyrimidines (11). To a stirred suspension of $TBAH_2F_3$ (7.5 g, 25 mmol) and DBH (5.7 g, 20 mmol) in dichloromethane (10 mL) was added dropwise a solution of a dithiocarbamate (5.0 mmol) in dichloromethane (5.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C until all the substrate was consumed and was poured into an aq. buffer solution of $NaHCO_3$/NaOH/$NaHSO_3$ (pH = 10). The resultant was extracted with diethyl ether three times. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography or bulb-to-bulb distillation to give the corresponding trifluoromethylamines. The yields and spectroscopic properties of the products are given below.

Methyl(2-pyridyl)(trifluoromethyl)amine (7a). Yield: 72%. A colorless oil; R_f = 0.68 (hexane : Et_2O = 10 : 1). IR 3018, 2958, 2928, 1595, 1577, 1482, 1426, 1351, 1339, 1276, 1200, 1141, 1100, 1074, 778, 741, 663 cm^{-1}; ^1H NMR (200 MHz) δ = 3.26 (q, *J* = 2 Hz, 3 H), 6.97 (ddd, *J* = 1, 4, 6 Hz, 1 H), 7.06-7.13 (dm, *J* = 8 Hz, 1 H), 7.61 (ddd, *J* = 2, 7, 9 Hz, 1 H), 8.35 (ddd, *J* = 1, 2, 5 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (dq, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 32.1 (s), 113.6 (s), 118.3 (s), 122.9 (q, $^1J_{C\text{-}F}$ = 256 Hz), 137.5 (s), 147.9 (s), 153.8 (s); MS *m/z* (rel intensity) 176 (M^+, 28), 157 (7), 107 (56), 84 (100), 80 (15), 79 (69), 78 (55). Found: *m/z* 176.0587. Calcd for $C_7H_7F_3N_2$: M, 176.0561.

Ethyl(2-pyridyl)(trifluoromethyl)amine (7b). Yield: 75%. A colorless oil; R_f = 0.50 (hexane : Et_2O = 10 : 1). IR 2980, 2940, 1595, 1482, 1437, 1331, 1260, 1196, 1140, 1102, 941, 776 cm^{-1}; ^1H NMR (300 MHz) δ = 1.34 (t, *J* = 7 Hz, 3 H), 4.00 (qq, *J* = 2, 7 Hz, 2 H), 7.07 (ddd, *J* = 1, 5, 7 Hz, 1 H), 7.17 (ddd, *J* = 1, 1, 10 Hz, 1 H), 7.72 (ddd, *J* = 2, 7, 10 Hz, 1 H), 8.50 (ddd, *J* = 1, 2, 5 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.9 (s); ^{13}C NMR (75.5 MHz) δ = 14.2 (s), 40.4 (s), 113.5 (q, *J* = 4 Hz), 118.0 (s), 123.0 (q, $^1J_{C\text{-}F}$ = 258 Hz), 137.6 (s), 148.0 (s), 152.9 (s); MS *m/z* (rel intensity) 191 (M^++1, 2), 190 (M^+, 13), 176 (3), 175 (36), 155 (11), 142 (24), 121 (34), 80 (8), 79 (85), 78 (100), 69 (21). Found: *m/z* 190.0716. Calcd for $C_8H_9F_3N_2$: M, 190.0718.

Hexyl(2-pyridyl)(trifluoromethyl)amine (7c). Yield: 67%. A colorless oil; R_f = 0.68 (hexane : Et_2O = 5 : 1). IR 2959, 2933, 2861, 1593, 1481, 1437, 1388, 1334, 1257, 1194, 1145, 1099, 776 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 6 Hz, 3 H), 1.26-1.43 (m, 6 H), 1.53-1.63 (m, 2 H), 3.72-3.83 (m, 2 H), 6.94 (ddd, *J* = 1, 5, 7 Hz, 1 H), 7.05 (dm, *J* = 9 Hz, 1 H), 7.59 (ddd, *J* = 2, 7, 9 Hz, 1 H), 8.34 (ddd, *J* = 1, 2, 5 Hz, 1 H); ^{19}F NMR

(188 MHz) δ = –55.9 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 22.5 (s), 26.3 (s), 28.7 (s), 31.4 (s), 45.3 (s), 113.6 (s), 118.0 (s), 123.0 (q, $^{1}J_{C\text{-}F}$ = 256 Hz), 137.4 (s), 147.9 (s), 153.1 (s); MS *m/z* (rel intensity) 246 (M^+, 12), 206 (6), 189 (17), 177 (24), 175 (72), 169 (31), 162 (74), 156 (5), 142 (100), 107 (24), 78 (97). Found: *m/z* 246.1354. Calcd for $C_{12}H_{17}F_3N_2$: M, 246.1344.

Octyl(2-pyridyl)(trifluoromethyl)amine (7d). Yield: 76% as performed at –20 °C. A colorless oil; R_f = 0.77 (hexane : Et_2O = 5 : 1). IR 2958, 2932, 1730, 1607, 1573, 1497, 1436, 1393, 1357, 1330, 1297, 1276, 1199, 1126, 1072, 1020, 782, 617 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.87 (t, J = 6 Hz, 3 H), 1.17-1.43 (m, 10 H), 1.53-1.66 (m, 2 H), 3.72-3.83 (m, 2 H), 6.94 (ddd, J = 1, 5, 7 Hz, 1 H), 7.05 (dm, J = 9 Hz, 1 H), 7.59 (ddd, J = 2, 7, 9 Hz, 1 H), 8.34 (ddd, J = 1, 2, 5 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.8 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.7 (s), 28.8 (s), 29.2 (s), 31.8 (s), 45.3 (s), 113.7 (s), 118.0 (s), 123.0 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 137.5 (s), 148.0 (s), 153.1 (s); MS *m/z* (rel intensity) 274 (M^+, 10), 205 (12), 189 (13), 175 (53), 162 (93), 143 (22), 142 (80), 107 (18), 106 (16), 79 (41), 78 (100). Found: *m/z* 274.1663. Calcd for $C_{14}H_{21}F_3N_2$: M, 274.1657.

Dodecyl(2-pyridyl)(trifluoromethyl)amine (7e). Yield: 86% (prepared at –20 °C). A colorless oil; R_f = 0.66 (hexane : Et_2O = 10 : 1). IR 2927, 2856, 1594, 1575, 1481, 1468, 1437, 1387, 1334, 1264, 1194, 1163, 1138, 1100, 1078, 755, 738 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.87 (t, J = 6 Hz, 3 H), 1.15-1.37 (m, 18 H), 1.53-1.67 (m, 2 H), 3.72-3.82 (m, 2 H), 6.94 (ddd, J = 1, 5, 7 Hz, 1 H), 7.05 (dm, J = 9 Hz, 1 H), 7.59 (ddd, J = 2, 7, 9 Hz, 1 H), 8.34 (ddd, J = 1, 2, 5 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.8 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.7 (s), 26.7 (s), 28.8 (s), 29.3 (s), 29.5 (s), 29.6 (s), 31.9 (s), 45.3 (s), 113.7 (s), 118.0 (s), 122.9 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 137.4 (s), 148.0 (s) 153.1 (s); MS *m/z* (rel intensity) 330 (M^+, 5), 261 (8), 232 (11), 204 (7), 189 (16), 176 (12), 175 (52), 169 (22), 163 (10), 162 (100), 142 (76), 106 (21), 78 (83). Found: *m/z* 330.2285. Calcd for $C_{18}H_{29}F_3N_2$: M, 330.2283.

Benzyl(2-pyridyl)(trifluoromethyl)amine (7f). Yield: 80%. A colorless oil; R_f = 0.42 (hexane : Et_2O = 10 : 1). IR 3067, 3034, 1591, 1479, 1436, 1382, 1332, 1270, 1232, 1105, 775, 698 cm^{-1}; ^{1}H NMR (200 MHz) δ = 5.05 (q, J = 2 Hz, 2 H), 6.95 (ddd, J = 1, 5, 7 Hz, 1 H), 7.07 (dm, J = 8 Hz, 1 H), 7.21-7.33 (m, 5 H), 7.59 (ddd, J = 2, 7, 9 Hz, 1 H), 8.33 (ddd, J = 1, 2, 5 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.6 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 48.5 (s), 113.35 (s), 113.43 (s), 118.4 (s), 123.0 (q, $^{1}J_{C\text{-}F}$ = 258 Hz), 127.2 (s), 128.5 (s), 137.8 (s), 138.2 (s), 148.1 (s), 153.0 (s); MS *m/z* (rel intensity) 253 (M^++1, 10), 252 (M^+, 71), 184 (11), 174 (9), 91 (100), 79 (52), 78 (35). Found: *m/z* 252.0867. Calcd for $C_{13}H_{11}F_3N_2$: M, 252.0874.

Methyl(2-pyrimidinyl)(trifluoromethyl)amine (11a). Yield: 38%. A colorless

oil; R_f = 0.57 (hexane : Et_2O = 1 : 1). IR 2970, 2950, 1588, 1568, 1470, 1409, 1372, 1326, 1266, 1210, 1135, 1071, 989, 926, 806, 679, 618 cm^{-1}; ^1H NMR (200 MHz) δ = 3.36 (q, J = 2 Hz, 3 H), 6.89 (t, J = 5 Hz, 1 H), 8.52 (d, J = 5 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –57.1 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 31.5 (s), 114.6 (s), 122.0 (q, $^1J_{C-F}$ = 258 Hz), 157.6 (s), 159.3 (s); MS *m/z* (rel intensity) 177 (M^+, 45), 158 (11), 108 (54), 84 (75), 80 (100), 79 (34), 78 (6). Found: *m/z* 177.0509. Calcd for $C_6H_6F_3N_3$: M, 177.0514.

Propyl(2-pyrimidinyl)(trifluoromethyl)amine (11b). Yield: 50%. A colorless oil; R_f = 0.22 (hexane : Et_2O = 10 : 1). IR 2971, 2882, 1588, 1564, 1470, 1429, 1389, 1331, 1304, 1267, 1235, 1140, 1107, 1073, 955, 806 cm^{-1}; ^1H NMR (300 MHz) δ = 1.05 (t, J = 8 Hz, 3 H), 1.81 (sextet, J = 8 Hz, 2 H), 3.95 (qt, J = 2, 8 Hz, 2 H), 6.99 (t, J = 5 Hz, 1 H), 8.63 (d, J = 5 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –57.9 (t, J = 2 Hz); ^{13}C NMR (75.5 MHz) δ = 11.0 (s), 22.0 (s), 46.6 (s), 114.4 (s), 122.1 (q, $^1J_{C-F}$ = 259 Hz), 157.6 (s), 158.9 (s); MS *m/z* (rel intensity) 206 (M^++1, 4), 205 (M^+, 32), 176 (44), 163 (16), 144 (15), 143 (33), 80 (45), 79 (100), 78 (44), 69 (14). Found: *m/z* 205.0823. Calcd for $C_8H_{10}F_3N_3$: M, 205.0827.

Hexyl(2-pyrimidinyl)(trifluoromethyl)amine (11c). Yield: 58%. A colorless oil; R_f = 0.51 (hexane : Et_2O = 5 : 1). IR 2960, 2933, 2861, 1588, 1565, 1470, 1429, 1391, 1333, 1250, 1194, 1143, 1104, 1072, 805, 637 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.30-1.36 (m, 6 H), 1.58-1.69 (m, 2 H), 3.80-3.91 (m, 2 H), 6.87 (t, J = 5 Hz, 1 H), 8.51 (d, J = 5 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –55.8 (t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.2 (s), 28.7 (s), 31.4, (s) 45.1 (s), 114.4 (s), 122.1 (q, $^1J_{C-F}$ = 259 Hz), 157.6 (s), 159.0 (s); MS *m/z* (rel intensity) 248 (M^++1, 7), 247 (M^+, 55), 205 (17), 190 (11), 177 (16), 176 (100), 163 (28), 144 (57), 143 (45), 80 (39), 79 (77). Found: *m/z* 247.1284. Calcd for $C_{11}H_{16}F_3N_3$: M, 247.1296.

Octyl(2-pyrimidinyl)(trifluoromethyl)amine (11d). Yield: 80%. A colorless oil; R_f = 0.44 (hexane : Et_2O = 5 : 1). IR 2958, 2929, 2858, 1588, 1564, 1470, 1429, 1391, 1383, 1333, 1255, 1235, 1206, 1177, 1141, 1104, 1072, 805, 637 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.26-1.30 (m, 10 H), 1.57-1.66 (m, 2 H), 3.80-3.91 (m, 2 H), 6.87 (t, J = 5 Hz, 1 H), 8.51 (d, J = 5 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –55.8 (t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.6 (s), 28.7 (s), 29.2 (s), 31.7 (s), 45.0 (s), 114.4 (s), 122.1 (q, $^1J_{C-F}$ = 259 Hz), 157.6 (s), 159.0 (s); MS *m/z* (rel intensity) 276 (M^++1, 10), 275 (M^+,62), 205 (22), 191 (14), 190 (12), 177 (20), 176 (100), 163 (31), 144 (73), 143 (50), 108 (13), 80 (44), 79 (86). Found: *m/z* 275.1615. Calcd for $C_{13}H_{20}F_3N_3$: M, 275.1609.

Dodecyl(2-pyrimidinyl)(trifluoromethyl)amine (11e). Yield: 63%. A colorless oil; R_f = 0.38 (hexane : Et_2O = 5 : 1). IR 2930, 2917, 2850, 1586, 1571, 1470, 1430,

1392, 1382, 1340, 1253, 1151, 1130, 1102, 854, 638 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 6 Hz, 3 H), 1.26-1.31 (m, 18 H), 1.57-1.69 (m, 2 H), 3.80-3.91 (m, 2 H), 6.86 (t, J = 5 Hz, 1 H), 8.50 (d, J = 5 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –55.8 (t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.6 (s), 28.7 (s), 29.2 (s), 29.3 (s), 29.6 (s), 31.9 (s), 45.0 (s), 114.4 (s), 122.2 (q, $^1J_{C-F}$ = 259 Hz), 157.6 (s), 159.0 (s); MS *m/z* (rel intensity) 332 (M^++1, 20), 331 (M^+, 100), 205 (18), 191 (11), 190 (10), 176 (79), 164 (20), 144 (63), 143 (30), 78 (49). Found: *m/z* 331.2248. Calcd for $C_{17}H_{28}F_3N_3$: M, 331.2235.

Preparation of 5-bromo-2-(trifluoromethylamino)pyridines **8** and -pyrimidines **12** was carried out in a procedure similar to that for **4**. Yields and spectroscopic properties are as follows.

5-Bromo-2-[methyl(trifluoromethyl)amino]pyridine (8a). Yield: 78%. A colorless oil; R_f = 0.56 (hexane : Et_2O = 5 : 1). IR 2992, 2956, 2935, 2899, 1583, 1563, 1526, 1478, 1434, 1384, 1355, 1324, 1273, 1244, 1199, 1121, 1108, 1071, 1002, 916, 821, 616 cm^{-1}; ^1H NMR (200 MHz) δ = 3.24 (q, J = 2 Hz, 3 H), 7.00 (dd, J = 2, 8 Hz, 1 H), 7.70 (dd, J = 2, 8 Hz, 1 H), 8.38 (d, J = 2 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 32.0 (s), 113.7 (s), 114.7 (s), 122.6 (q, $^1J_{C-F}$ = 257 Hz), 139.9 (s), 148.6 (s), 152.3 (s); MS *m/z* (rel intensity) 257 (M^++3, 5), 256 (M^++2, 28), 255 (M^++1, 9), 254 (M^+, 35), 187 (68), 185 (70), 160 (52), 159 (51), 158 (100), 157 (63), 156 (40), 106 (12), 78 (92). Found: *m/z* 253.9678. Calcd for $C_7H_6{}^{79}BrF_3N_2$: M, 253.9667.

5-Bromo-2-[ethyl(trifluoromethyl)amino]pyridine (8b). Yield: 82%. A colorless oil, bp 80 °C/2 mmHg; R_f = 0.48 (hexane : Et_2O = 20 : 1). IR 2986, 2940, 2860, 1584, 1559, 1480, 1381, 1320, 1260, 1244, 1194, 1132, 1105, 1067, 943, 819 cm^{-1}; ^1H NMR (200 MHz) δ = 1.21 (dt, J = 0.4, 7 Hz, 3 H), 3.86 (qq, J = 2, 7 Hz, 2 H), 6.96 (dqd, J = 1, 2, 9 Hz, 1 H), 7.68 (dd, J = 3, 9 Hz, 1 H), 8.38 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –56.10 (dm, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 40.4 (s), 113.3 (s), 114.4 (m), 122.7 (q, J = 258 Hz), 140.0 (s), 148.8 (s), 151.5 (s); MS *m/z* (rel intensity) 271 (M^++3, 4), 270 (M^++2, 38), 269 (M^++1, 6), 268 (M^+, 40), 256 (11), 255 (97), 254 (12), 253 (100), 235 (42), 233 (42), 223 (15), 222 (60), 220 (67), 201 (77), 199 (76), 159 (94), 158 (92), 157 (98), 156 (98), 119 (39), 92 (28), 78 (86), 77(63), 76 (84), 69 (90). Found: C, 35.89; H, 3.09; N, 10.52%. Calcd for $C_8H_8BrF_3N_2$: C, 35.71; H, 3.00; N, 10.41%.

5-Bromo-2-[hexyl(trifluoromethyl)amino]pyridine (8c). Yield: 89%. A colorless oil; R_f = 0.75 (hexane : Et_2O = 20 : 1). IR 2959, 2933, 2860, 1583, 1560, 1477, 1381, 1300, 1255, 1192, 1142, 1105, 1070, 1001, 819 cm^{-1}; ^1H NMR (200 MHz)

δ = 0.87 (t, J = 7 Hz, 3 H), 1.22-1.34 (m, 6 H), 1.43-1.62 (m, 2 H), 3.70-3.80 (m, 2 H), 6.94 (dm, J = 9 Hz, 1 H), 7.67 (dd, J = 3, 9 Hz, 1 H), 8.36 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –56.0 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.3 (s), 28.6 (s), 31.4 (s), 45.4 (s), 113.3 (s), 114.5 (s), 122.7 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 139.9 (s), 148.7 (s), 151.7 (s); MS *m/z* (rel intensity) 326 (M^++2, 15), 324 (M^+, 15), 255 (87), 253 (75), 242 (56), 240 (59), 222 (100), 220 (92), 187 (10), 186 (14), 185 (15), 184 (12), 158 (47), 156 (42), 77 (7). Found: *m/z* 324.0451. Calcd for $C_{12}H_{16}{}^{79}BrF_3N_2$: M, 324.0449.

5-Bromo-2-[octyl(trifluoromethyl)amino]pyridine (8d). Yield: 89%. A colorless oil; R_f = 0.68 (hexane : Et_2O = 20 : 1). IR 2958, 2929, 2857, 1583, 1560, 1477, 1379, 1320, 1302, 1266, 1244, 1192, 1141, 1106, 819 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.18-1.26 (m, 10 H), 1.53-1.62 (m, 2 H), 3.73-3.80 (m, 2 H), 6.95 (dm, J = 9 Hz, 1 H), 7.67 (dd, J = 3, 9 Hz, 1 H), 8.36 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –56.1 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.6 (s), 28.6 (s), 29.1 (s), 31.8 (s), 45.3 (s), 113.3 (s), 114.6 (s), 122.7 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 140.0 (s), 148.7 (s), 151.7 (s); MS *m/z* (rel intensity) 354 (M^++2, 5), 352 (M^+, 5), 291 (7), 289 (6), 255 (60), 253 (57), 242 (63), 240 (62), 222 (96), 220 (100), 158 (81), 156 (68), 77 (23). Found: *m/z* 352.0754. Calcd for $C_{14}H_{20}{}^{79}BrF_3N_2$: M, 352.0762.

5-Bromo-2-[dodecyl(trifluoromethyl)amino]pyridine (8e). Yield: 90%. A colorless oil; R_f = 0.81 (hexane : Et_2O = 20 : 1). IR 2956, 2926, 2855, 1583, 1477, 1380, 1320, 1305, 1264, 1244, 1193, 1157, 1138, 1107, 1071, 1000, 819 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.17-1.34 (m, 18 H), 1.53-1.62 (m, 2 H), 3.70-3.80 (m, 2 H), 6.95 (dm, J = 9 Hz, 1 H), 7.67 (dd, J = 3, 9 Hz, 1 H), 8.36 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –56.1 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.7 (s), 26.6 (s), 28.6 (s), 29.2 (s), 29.3 (s), 29.5 (s), 29.6 (s), 31.9 (s), 45.4 (s), 113.3 (s), 114.5 (s), 122.7 (q, $^{1}J_{C\text{-}F}$ = 257 Hz), 139.9 (s), 148.7 (s), 151.7 (s); MS *m/z* (rel intensity) 410 (M^++2, 5), 408 (M^+, 5), 341 (4), 339 (4), 312 (12), 310 (13), 298 (6), 296 (7), 284 (7), 282 (7), 242 (90), 240 (95), 222 (100), 220 (93), 200 (7), 198 (9), 186 (29), 184 (30), 158 (75), 156 (61), 77 (23). Found: *m/z* 408.1386. Calcd for $C_{18}H_{28}{}^{79}BrF_3N_2$: M, 408.1388.

5-Bromo-2-[benzyl(trifluoromethyl)amino]pyridine (8f). Yield: 78%. A colorless oil; R_f = 0.78 (hexane : Et_2O = 10 : 1). IR 3067, 3034, 2961, 1582, 1563, 1512, 1496, 1476, 1455, 1437, 1379, 1320, 1270, 1244, 1232, 1192, 1110, 1065, 1010, 1002, 820, 699 cm^{-1}; ^{1}H NMR (200 MHz) δ = 5.01 (q, J = 2 Hz, 2 H), 6.97 (dm, J = 8 Hz, 1 H), 7.25-7.31 (m, 5 H), 7.68 (dd, J = 3, 9 Hz, 1 H), 8.35 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.8 (dt, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 48.4 (s), 113.8 (s), 114.4 (s), 122.7 (q, $^{1}J_{C\text{-}F}$ = 258 Hz), 127.1 (s), 127.3 (s), 128.5 (s), 137.5 (s), 140.2 (s),

148.8 (s), 151.5 (s); MS *m/z* (rel intensity) 333 (M^++3, 6), 332 (M^++2, 42), 331 (M^++1, 12), 330 (M^+, 43), 263 (37), 261 (38), 174 (37), 158 (14), 156 (12), 91 (100), 78 (16). Found: *m/z* 329.9971. Calcd for $C_{13}H_{10}{}^{79}BrF_3N_2$: M, 329.9980.

5-Bromo-2-[4-ethylbenzyl(trifluoromethyl)amino]pyridine (8g). Yield: 41%. A colorless oil, bp 210 °C/0.7 mmHg; R_f = 0.76 (hexane : Et_2O = 10 : 1). IR 2967, 1584, 1559, 1479, 1377, 1319, 1269, 1190, 1109, 1101, 819 cm^{-1}; ^1H NMR (200 MHz) δ = 1.21 (t, *J* = 8 Hz, 3 H), 2.61 (q, *J* = 8 Hz, 2 H), 4.98 (q, *J* = 1 Hz, 2 H), 6.97 (dd, *J* = 1, 9 Hz, 1 H), 7.09-7.22 (m, 4 H), 7.68 (dd, *J* = 3, 9 Hz, 1 H), 8.36 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.77 (m); ^{13}C NMR (50.3 MHz) δ = 15.4 (s), 28.4 (s), 48.2 (q, *J* = 2 Hz), 112.7 (q, $^1J_{C-F}$ = 258 Hz), 113.7 (s), 114.6 (s), 127.1 (s), 127.9 (s), 134.7 (br), 140.1 (s), 143.3 (s), 148.7 (s), 151.5 (s); MS *m/z* (rel intensity) 359 (M^++1, 15), 358 (M^+, 88), 357 (M^+-1, 19), 356 (M^+-2, 89), 289 (42), 287 (43), 277 (5), 200 (73), 159 (28), 157 (27), 158 (39), 156 (37), 130 (15), 118 (79), 117 (100), 116 (42), 115 (99), 102 (21), 91 (98), 78 (50), 77 (35), 69 (54). Found: C, 50.11; H, 4.11; N, 7.83%. Calcd for $C_{15}H_{14}BrF_3N_2$: C, 50.16; H, 3.93; N, 7.80%.

5-Bromo-2-{[4-(1-fluoroethyl)benzyl](trifluoromethyl)amino}pyridine (8g'). Yield: 38%. A colorless oil, bp 220 °C/0.7 mmHg; R_f = 0.63 (hexane : Et_2O = 10 : 1). IR 2984, 2934, 2361, 1912, 1582, 1563, 1474, 1379, 1321, 1271, 1244, 1192, 1109, 1069, 1010, 1000, 820 cm^{-1}; ^1H NMR (200 MHz) δ = 1.61 (dd, *J* = 6, 24 Hz, 3 H), 5.01 (br, 2 H), 5.69 (dq, *J* = 6, 48 Hz, 1 H), 7.01 (dd, *J* = 1, 9 Hz, 1 H), 7.09-7.22 (m, 4 H), 7.69 (dd, *J* = 3, 9 Hz, 1 H), 8.36 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.83 (br, 3 F), –167.12 (dd, *J* = 24, 48 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 22.8 (d, *J* = 25 Hz), 48.5 (q, *J* = 2 Hz), 90.7 (d, $^1J_{C-F}$ = 168 Hz), 113.8 (s), 114.3 (q, *J* = 4.2 Hz), 122.6 (q, $^1J_{C-F}$ = 258 Hz), 125.4 (d, *J* = 8 Hz), 127.2 (s), 137.6 (m), 140.1 (s), 140.2 (s), 140.7 (s), 148.8 (s), 151.4 (s); MS *m/z* (rel intensity) 378 (M^++2, 9), 377 (M^++1, 2), 376 (M^+, 9), 375 (M^+-1, 1), 338 (3), 336 (3), 309 (13), 307 (10), 289 (5), 287 (5), 220 (18), 200 (11), 185 (6), 159 (10), 158 (20), 137 (86), 122 (24), 117 (100), 115 (62), 91 (40), 89 (12), 78 (36), 77 (18), 76 (26), 69 (28) ,65 (22), 64 (14). Found: C, 47.56; H, 3.45; N, 7.67%. Calcd for $C_{15}H_{13}BrF_4N_2$: C, 47.77; H, 3.47; N, 7.43%.

5-Bromo-2-[methyl(trifluoromethyl)amino]pyrimidine (12a). Yield: 84%. Colorless needles, mp 60.8-61.5 °C; R_f = 0.52 (hexane : EtOAc = 10 : 1). IR (KBr) 1579, 1544, 1486, 1467, 1414, 1373, 1319, 1253, 1177, 1138, 1118, 1089, 942, 922, 789, 779, 616 cm^{-1}; ^1H NMR (200 MHz) δ = 3.34 (q, *J* = 2 Hz, 3 H), 8.54 (s, 2 H); ^{19}F NMR (188 MHz) δ = –57.4 (s); ^{13}C NMR (50.3 MHz) δ = 31.8 (s), 111.9 (s), 121.7 (q, *J* = 259 Hz), 157.6 (s), 158.0 (s); MS *m/z* (rel intensity) 257 (M^++2, 69), 255 (M^+, 71), 188 (55), 186 (56), 160 (98), 158 (100), 133 (12), 131 (13), 106 (15), 104 (13), 79 (28). Found: *m/z* 254.9647. Calcd for $C_6H_5{}^{79}BrF_3N_3$: M, 254.9619 .

5-Bromo-2-[propyl(trifluoromethyl)amino]pyrimidine (12b). Yield: 81 %. A colorless oil; R_f = 0.70 (hexane : EtOAc = 10 : 1). IR (KBr) 3060, 2969, 1572, 1543, 1474, 1464, 1433, 1393, 1377, 1333, 1310, 1235, 1206, 1146, 1180, 1088, 959, 791 cm^{-1}; ^1H NMR (300 MHz) δ = 0.93 (t, J = 8 Hz, 3 H), 1.68 (sextet, J = 8 Hz, 2 H), 3.80 (qt, J = 2, 8 Hz, 2 H) 8.53 (s, 2 H); ^{19}F NMR (188 MHz) δ = –56.33 (s); ^{13}C NMR (75.5 MHz) δ = 10.9 (s), 21.8 (s), 46.9 (s), 111.6 (s), 121.8 (q, J = 260 Hz), 157.3 (s), 158.1 (s); MS *m/z* (rel intensity) 285 (M^++2, 62), 283 (M^+, 53), 256 (86), 254 (100), 243 (27), 241 (29), 224 (22), 223 (75), 222 (21), 221 (84), 216 (15), 214 (12), 205 (14), 204 (11), 186 (12), 174 (13), 172 (14), 160 (29), 159 (62), 158 (27), 157 (57), 120 (14), 119 (13), 106 (16), 105 (20), 91 (18), 83 (21), 78 (76), 69 (80). Found: *m/z* 282.9923. Calcd for $C_8H_9{}^{79}BrF_3N_3$: M, 282.9932.

5-Bromo-2-[hexyl(trifluoromethyl)amino]pyrimidine (12c). Yield: 61%. A colorless oil; R_f = 0.54 (hexane : Et_2O = 20 : 1). IR 2960, 2933, 2873, 2861, 1575, 1543, 1472, 1433, 1395, 1381, 1325, 1298, 1245, 1225, 1206, 1194, 1175, 1143, 1089, 792, 637 cm^{-1}; ^1H NMR (200 MHz) δ = 0.89 (t, J = 7 Hz, 3 H), 1.31-1.43 (m, 6 H), 1.61-1.67 (m, 2 H), 3.77-3.88 (m, 2 H), 8.53 (s, 2 H); ^{19}F NMR (188 MHz) δ = –56.2 (t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.9 (s), 22.5 (s), 26.2 (s), 28.5 (s), 31.4 (s), 45.4 (s), 111.6 (s), 121.8 (q, $^1J_{C\text{-}F}$ = 259 Hz), 157.2 (s), 158.1 (s); MS *m/z* (rel intensity) 327 (M^++2, 7), 326 (M^++1, 53), 325 (M^+, 8), 324 (M^+-1, 54), 285 (19), 283 (19), 270 (11), 268 (11), 255 (100), 253 (99), 243 (20), 241 (20), 223 (59), 221 (56), 187 (13), 185 (12), 159 (51), 157 (46), 78 (33). Found: *m/z* 325.0382. Calcd for $C_{11}H_{15}{}^{79}BrF_3N_3$: M, 325.0402.

5-Bromo-2-[octyl(trifluoromethyl)amino]pyrimidine (12d). Yield: 24% along with **11d** (62 % yield). A colorless oil; R_f = 0.91 (hexane : Et_2O = 10 : 1). IR 2929, 2858, 1575, 1543, 1472, 1432, 1395, 1380, 1325, 1300, 1250, 1233, 1208, 1183, 1144, 1089, 935, 806, 792, 637 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.27-1.43 (m, 10 H), 1.58-1.63 (m, 2 H), 3.76-3.87 (m, 2 H), 8.52 (s, 2 H); ^{19}F NMR (188 MHz) δ = –56.2 (t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.5 (s), 28.5 (s), 29.1 (s), 31.8 (s), 45.5 (s), 111.6 (s), 121.8 (q, $^1J_{C\text{-}F}$ = 260 Hz), 157.2 (s), 158.1 (s); MS *m/z* (rel intensity) 355 (M^++2, 10), 354 (M^++1, 64), 353 (M^+, 11), 352 (M^+-1, 66), 325 (5), 323 (5), 285 (23), 283 (23), 255 (100), 253 (99), 243 (21), 241 (20), 223 (59), 221 (57), 159 (51), 157 (45), 78 (32). Found: *m/z* 353.0716. Calcd for $C_{13}H_{19}{}^{79}BrF_3N_3$: M, 353.0715.

5-Bromo-2-[dodecyl(trifluoromethyl)amino]pyrimidine (12e). Yield: 15% along with **11e** (65 % yield). A colorless oil; R_f = 0.71 (hexane : Et_2O = 10 : 1). IR (KBr) 2981, 2956, 2916, 2874, 2849, 1575, 1547, 1467, 1427, 1381, 1331, 1245, 1227, 1141, 791, 639 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.17-1.30 (m, 18 H), 1.56-1.67 (m, 2 H), 3.76-3.87 (m, 2 H), 8.52 (s, 2 H); ^{19}F NMR (188 MHz) δ = –56.2

(t, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.7 (s), 26.5 (s), 28.5 (s), 29.2 (s), 29.3 (s), 29.6 (s), 31.9 (s), 45.5 (s), 111.6 (s), 121.8 (q, $^{1}J_{C\text{-}F}$ = 260 Hz), 157.3 (s), 158.1 (s); MS *m/z* (rel intensity) 412 (M^++3, 20), 411 (M^++2, 99), 410 (M^++1, 22), 409 (M^+, 100), 325 (5), 323 (5), 285 (22), 283 (23), 255 (89), 254 (88), 224 (46), 223 (52), 222 (48), 221 (48), 187 (9), 185 (8), 160 (16), 159 (42), 158 (17), 157 (35). Found: *m/z* 409.1335. Calcd for $C_{17}H_{27}{}^{79}BrF_3N_3$: M, 409.1341.

Synthesis of 3-[Benzyl(trifluoromethyl)amino]pyridine (7h). This compound was produced from **6h** in 82% yield as a colorless oil through a similar procedure for the preparation of **4**. R_f = 0.45 (hexane : Et_2O = 1 : 1). IR 3066, 3036, 2931, 1733, 1590, 1575, 1482, 1455, 1424, 1376, 1266, 1230, 1195, 1104, 1080, 1064, 1037, 994, 911, 813, 739, 713, 700, 650 cm^{-1}; ^{1}H NMR (200 MHz) δ = 4.57 (s, 2 H), 7.17-7.33 (m, 7 H), 7.47 (dm, J = 8 Hz, 1 H), 8.40-8.44 (m, 1 H); ^{19}F NMR (188 MHz) δ = –58.00 (s); ^{13}C NMR (50.3 MHz) δ = 53.0 (s), 123.0 (q, $^{1}J_{C\text{-}F}$ = 256 Hz), 123.6 (s), 127.8 (s), 128.0 (s), 128.6 (s), 133.0 (s), 135.9 (s), 137.4 (s), 147.5 (s), 147.6 (s); MS *m/z* (rel intensity) 252 (M^+, 19), 92 (14), 91 (100), 78 (4). Found: *m/z* 252.0857. Calcd for $C_{13}H_{11}F_3N_2$: M, 252.0874

Bromination of 2-[Benzyl(trifluoromethyl)amino]pyridine (7f). A solution of bromine (0.176 g, 1.1 mmol) in dichloromethane (1.2 mL) was added dropwised to a stirred solution of $TBAH_2F_3$ (0.30 g, 1.0 mmol) and **7f** (0.126 g, 0.50 mmol) in dichloromethane (1.0 mL) at room temperature. The reaction mixture was heated to reflux for 1.5 h, and the whole mixture was treated with aq. $NaHSO_3$/$NaHCO_3$/NaOH (pH 10) solution. The organic phase was separated, and the aq. phase was extracted with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtrated through a Celite/silica gel (Wako Gel C-100) pad, and concentrated under reduced pressure. The residue was purified by column chromatography to give **7f** (16 mg) and **8f** (0.139 g) in 14% and 84% yield, respectively.

Reaction of 4m, 8a, or 12a with *p*-Bromobenzaldehyde. A solution of *n*-BuLi in hexane (1.6 M, 0.38 mL, 0.60 mmol) was added dropwise to a stirred solution of bromoaryl(trifluoromethyl)amine **4m**, **8a**, or **12a** (0.50 mmol) in THF (2.0 mL) at –78 °C. The resulting mixture was stirred for 30 min at –78 °C before treatment with a solution of 4-bromobenzaldehyde (130 mg, 0.70 mmol) in THF (1.0 mL). The reaction mixture was warmed slowly up to room temperature, stirred for 12 h, poured into sat. $NaHCO_3$ aq. solution, and extracted with diethyl ether three times. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by column chromatography gave the desired adduct **21**, **22**, or **23**,

respectively. Yields and spectra of products are summarized below.

(4-Bromophenyl){4-[methyl(trifluoromethyl)amino]phenyl}methanol (16). Yield: 69%. A colorless oil; R_f = 0.23 (hexane : EtOAc = 5 : 1). IR 3280, 2977, 2872, 1790, 1700, 1651, 1514, 1374, 1276, 1113, 1071, 1011, 857, 731 cm^{-1}; ^1H NMR (300 MHz) δ = 2.74 (br s, 1 H), 3.14 (q, J = 1 Hz, 3 H), 5.87 (s, 1 H), 7.33 (d, J = 8 Hz, 2 H), 7.36 (d, J = 8 Hz, 2 H), 7.43 (d, J = 8 Hz, 2 H), 7.58 (d, J = 8 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –60.9 (s); ^{13}C NMR (75.5 MHz) δ = 36.1 (q, J = 2 Hz), 75.1 (s), 121.5 (s), 123.3 (q, $^1J_{C\text{-}F}$ = 256 Hz), 124.7 (q, J = 2 Hz), 127.2 (s), 128.1 (s), 131.6 (s), 141.0 (s), 142.2 (s), 142.4 (s); MS *m/z* (rel intensity) 361 (M^++2, 11), 359 (M^+, 8), 254 (10), 204 (22), 203 (18), 202 (76), 185 (50), 183 (37), 176 (62), 165 (43), 156 (65), 105 (30), 77 (100), 69 (40). Found: *m/z* 359.0133. Calcd for $C_{15}H_{13}{}^{79}BrF_3NO$: M, 359.0133.

(4-Bromophenyl){6-[methyl(trifluoromethyl)amino]-3-pyridyl}methanol (17). This compound was obtained in 78% as a colorless oil. R_f = 0.37 (hexane : Et_2O = 1 : 1). IR 3373, 2358, 2341, 1607, 1574, 1490, 1398, 1353, 1257, 1199, 1125, 1072, 1011, 824, 735 cm^{-1}; ^1H NMR (200 MHz) δ = 2.27 (d, J = 4 Hz, 1 H), 3.25 (q, J = 2 Hz, 3 H), 5.80 (d, J = 4 Hz, 1 H), 7.02-7.09 (m, 1 H), 7.21-7.28 (m, 2 H), 7.14-7.58 (m, 3 H), 8.32 (d, J = 2 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.8 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ 32.3 (s), 72.9 (s), 113.5 (s), 121.7 (s), 122.7 (q, $^1J_{C\text{-}F}$ = 257 Hz), 128.0 (s), 131.7 (s), 133.6 (s), 136.3 (s), 142.0 (s), 146.1 (s), 153.2 (s); MS *m/z* (rel intensity) 362 (M^++2, 38), 360 (M^+, 41), 345 (5), 343 (10), 293 (33), 291 (34), 266 (10), 265 (17), 264 (13), 263 (17), 205 (37), 203 (100), 185 (36), 183 (30), 157 (72), 106 (17), 92 (12), 77 (59). Found: *m/z* 360.0073. Calcd for $C_{14}H_{12}{}^{79}BrF_3N_2O$: M, 360.0086.

(4-Bromophenyl){2-[methyl(trifluoromethyl)amino]-5-pyrimidyl}methanol (18). Yield: 82%. A colorless powder, mp 67.8-69.4 °C; R_f = 0.41 (hexane : Et_2O = 1 : 2). IR (KBr) 3374, 2960, 2931, 2894, 2873, 1602, 1560, 1485, 1415, 1377, 1324, 1260, 1180, 1130, 1092, 1072, 1049, 1011, 805, 735, 618 cm^{-1}; ^1H NMR (200 MHz) δ = 2.38 (br s, 1 H), 3.35 (q, J = 2 Hz, 3 H), 5.79 (s, 1 H), 7.22-7.27 (m, 2 H), 7.49-7.53 (m, 2 H), 8.47 (d, J = 1 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –57.2 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 31.6 (s), 71.2 (s), 122.0 (s), 121.9 (q, J = 259 Hz), 128.0 (s), 129.7 (s), 131.9 (s), 141.4 (s), 156.3 (s), 158.4 (s); MS *m/z* (rel intensity) 363 (M^++2, 34), 361 (M^+, 41), 346 (9), 344 (10), 294 (17), 292 (16), 266 (19), 264 (21), 206 (39), 204 (100), 185 (21), 183 (16), 158 (48), 77 (46). Found: *m/z* 361.0042. Calcd for $C_{13}H_{11}{}^{79}BrF_3N_3O$: M, 361.0038.

Carboxylation of Bromoaryl(methyl)(trifluoromethyl)amines. A hexane solution of *n*-BuLi (1.6 M, 0.37 mL, 0.59 mmol) was slowly added to a stirred solution of **4m**, **8a**, or **12a** (0.47 mmol) in THF (1.0 mL) at –78 °C. The resulting mixture was stirred for 30 min at –78 °C, and carbon dioxide was bubbled into the mixture. The

reaction mixture was warmed to room temperature over 30 min during CO_2 bubbling, then treated with water (ca. 0.04 mL) and MeOH (0.4 mL), and again stirred for 10 min at room temperature before treatment with a 10 % hexane solution of trimethylsilyldiazomethane (0.94 mmol). The resulting mixture was stirred for 30 min at room temperature, poured into sat. aq. $NaHCO_3$, and extracted with diethyl ether three times. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash column chromatography gave **19**, **20**, or **21**. Yields and spectroscopic properties of products are shown below.

Methyl 4-[Methyl(trifluoromethyl)amino]benzoate (19). Yield: 98%. A colorless oil; R_f = 0.45 (hexane : Et_2O = 10 : 1). IR 2998, 2955, 2847, 1728, 1613, 1518, 1437, 1345, 1287, 1200, 1148, 1117, 1063, 1019, 774, 706 cm^{-1}; ^1H NMR (300 MHz) δ = 3.12 (q, J = 1 Hz, 3 H), 3.91 (s, 3 H), 7.23 (d, J = 9 Hz, 2 H), 8.01 (d, J = 9 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –59.44 (s); ^{13}C NMR (75.5 MHz) δ = 35.4 (q, J = 2 Hz), 52.1 (s), 121.8 (q, J = 2 Hz), 122.8 (q, J = 257 Hz), 126.3 (s), 130.6 (s), 1146.6 (s), 166.4 (s); MS *m/z* (rel intensity) 234 (M^++1, 5), 233 (M^+, 41), 214 (13), 203 (11), 202 (100), 154 (11), 132 (12), 105 (19), 104 (19), 90 (12), 77 (32), 69 (26), 63 (21). Found: *m/z* 233.0664. Calcd for $C_{10}H_{10}F_3NO_2$: M, 233.0664.

Methyl 2-[Methyl(trifluoromethyl)amino]pyridine-5-carboxylate (20). This ester was prepared in 45% yield from **8a** as a colorless oil by a procedure similar to that of **19** expect for treatment of solid CO_2 and an ethereal solution of diazomethane (excess). R_f = 0.44 (hexane : Et_2O = 5 : 1). IR 2958, 1730, 1607, 1573, 1497, 1436, 1393, 1357, 1330, 1297, 1276, 1199, 1126, 1072, 1020, 782 cm^{-1}; ^1H NMR (200 MHz) δ = 3.35 (q, J = 2 Hz, 3 H), 3.92 (s, 3 H), 7.09 (dm, J = 9 Hz, 1 H), 8.17 (dd, J = 9, 3 Hz, 1 H), 8.94 (dd, J = 3, 1 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.1 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 31.8 (s), 52.1 (s), 111.2 (s), 120.0 (s), 122.3 (q, J = 258 Hz), 138.6 (s), 150.0 (s), 156.2 (s), 165.6 (s); MS *m/z* (rel intensity) 235 (M^++1, 4), 234 (M^+, 41), 215 (10), 214 (18), 203 (33), 165 (100), 148 (27), 137 (82), 106 (27), 78 (25). Found: *m/z* 234.0661. Calcd for $C_9H_9F_3N_2O_2$: M, 234.0662.

Methyl 2-[Methyl(trifluoromethyl)amino]pyrimidine-5-carboxylate (21). Yield: 78%. A colorless solid, mp 110.5-111.8 °C; R_f = 0.32 (hexane : Et_2O = 5 : 1). IR 3056, 2965, 1719, 1607, 1553, 1497, 1418, 1399, 1320, 1254, 1196, 1136, 1092, 951, 808 cm^{-1}; ^1H NMR (300 MHz) δ = 3.44 (q, J = 2 Hz, 3 H), 3.95 (s, 3 H), 9.06 (s, 2 H); ^{19}F NMR (282 MHz) δ = –57.07 (q, J = 2 Hz); ^{13}C NMR (75.5 MHz) δ = 31.7 (q, J = 2 Hz), 52.2 (s), 117.4 (s), 121.4 (q, J = 261 Hz), 159.3 (s), 160.8 (s), 164.2 (s); MS *m/z* (rel intensity) 236 (M^++1, 6), 235 (M^+, 47), 216 (16), 204 (48), 166 (78), 149 (14), 139 (17), 138 (100), 107 (12), 80 (28), 79 (18), 69 (52). Found: *m/z* 235.0571. Calcd for $C_8H_8F_3N_3O_2$: M, 235.0569.

Synthesis of 6-Chloro-9-benzyl-9*H*-purine (23). A solution of 6-chloropurine (**22**, 0.31 g, 2.0 mmol) in DMF (2.0 mL) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil, 53 mg, 2.2 mmol) in DMF (1.0 mL) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then cooled to 0 °C. Benzyl bromide (0.48 mL, 4.0 mmol) was added dropwise at 0 °C, and the whole mixture was stirred at room temperature for 3 h before quenching with sat. aq. $NaHCO_3$ and extraction with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered through a Celite/silica gel (Wako Gel C-100) pad, and concentrated. The residue was purified by flash column chromatography (CH_2Cl_2 : MeOH = 25 : 1) to give **23** (0.34 g) and 6-chloro-7-benzylpurine (**23'**, 0.130 g) in 69% and 27% yield, respectively.

6-Chloro-9-benzyl-9*H*-purine (23). A white powder, mp 80.5-81.9 °C; R_f = 0.41 (CH_2Cl_2 : MeOH = 10 : 1). IR 3102, 3063, 3006, 1919, 1821, 1597, 1559, 1497, 1447, 1453, 1397, 1385, 1345, 1244, 1211, 1179, 1146, 1121, 953, 938, 858, 725 cm^{-1}; ^1H NMR (200 MHz) δ = 5.69 (s, 2 H), 7.15-7.22 (m, 2 H), 7.36-7.45 (m, 3 H), 8.22 (s, 1 H), 8.90 (s, 1 H); ^{13}C NMR (75.5 MHz) δ = 47.5 (s), 127 6 (s), 128.4 (s), 128.8 (s), 131.1 (s), 134.3 (s), 144.9 (s), 150.5 (s), 151.5 (s), 151.7 (s); MS *m/z* (rel intensity) 246 (M^++2, 11), 245 (M^++1, 20), 244 (M^+, 34), 243 (M^+-1, 48), 182 (9), 92 (9), 91 (100), 65 (36). Found: *m/z* 244.0517. Calcd for $C_{12}H_9{}^{35}ClN_4$: M, 244.0516.

6-Chloro-7-benzylpurine (23'). A white powder, mp 141.9-143.3 °C; R_f = 0.38 (CH_2Cl_2 : MeOH = 10 : 1). IR 3030, 1603, 1537, 1483, 1456, 1395, 1367, 1335, 1287, 1169, 1075, 968, 743 cm^{-1}; ^1H NMR (300 MHz) δ = 5.71 (s, 2 H), 7.15-7.23 (m, 2 H), 7.36-7.45 (m, 3 H), 8.26 (s, 1 H), 8.90 (s, 1 H); ^{13}C NMR (75.5 MHz) δ = 50.7 (s), 122.5 (s), 127.0 (s), 128.9 (s), 129.3 (s), 134.5 (s), 143.2 (s), 149.1 (s), 152.6 (s), 161.9 (s); MS *m/z* (rel intensity) 247 (M^++3, 1), 246 (M^++2, 8), 245 (M^++1, 6), 244 (M^+, 24), 243 (M^+-1, 9), 92 (8), 91 (100), 65 (22). Found: *m/z* 244.0515. Calcd for $C_{12}H_9{}^{35}ClN_4$: M, 244.0516.

Synthesis of 6-Methylamino-9-benzyl-9*H*-purine (24). Triethylamine (1.8 mL, 12.8 mmol) was added dropwise to a stirred solution of **23** (1.05 g 4.3 mmol) and methylamine hydrochloride (1.49 g, 22.0 mmol) in dichloromethane (5.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 d. Quenching with sat. $NaHCO_3$ aq. solution, extraction with diethyl ether three times, followed by purification by flash column chromatography (CH_2Cl_2 : MeOH = 20 : 1), gave **24** (0.95 g, 93% yield) as a colorless oil. R_f = 0.33 (CH_2Cl_2 : MeOH = 20 : 1). IR 3249, 3067, 1624, 1588, 1514, 1451, 1418, 1298, 1254, 1190, 729 cm^{-1}; ^1H NMR (300 MHz) δ = 3.20 (br s, 3 H), 5.37 (s, 2 H), 6.30 (br s, 1 H), 7.25-7.38 (m, 5 H), 7.72 (s, 1 H), 8.46 (s, 1

H); ^{13}C NMR (75.5 MHz) δ = 27.5 (m), 47.0 (s), 50.7 (s), 119.7 (s), 127.6 (s), 128.3 (s), 128.9 (s), 135.6 (s), 139.4 (s), 152.1 (s), 153.3 (s), 155.5 (s); MS *m/z* (rel intensity) 240 (M^++1, 11), 239 (M^+, 67), 238 (M^+-1, 66), 209 (10), 148 (59), 119 (11), 92 (11), 91 (100), 65 (40). Found: *m/z* 239.1162. Calcd for $C_{13}H_{13}N_5$: M, 239.1171.

Ethyl *N*-(9-Benzyl-9*H*-purine-6-yl)-*N*-methyldithiocarbamate (25). A hexane solution of *n*-BuLi (1.6 M, 0.20 mL, 0.33 mmol) was added dropwise to a solution of **24** (72 mg, 0.30 mmol) in THF (2.0 mL) at –78 °C. The reaction mixture was slowly warmed up to 0 °C over 1 h and then slowly treated with a solution of ethyl chlorodithioformate (81 mg, 0.60 mmol) in THF (1.5 mL) at 0 °C. The resulting mixture was stirred at room temperature for 2 h, poured into sat. aq. $NaHCO_3$. The aq. phase was extracted with diethyl ether three times; the combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography (hexane : Et_2O : EtOAc = 1 : 1 : 1) to give **25** (39 mg, 37% yield) as a brown oil. R_f = 0.43 (hexane : Et_2O : EtOAc = 1 : 1 : 1). IR 3067, 2969, 2929, 2870, 1595, 1499, 1456, 1406, 1244, 1154, 1096, 1038, 1003, 725, 698 cm^{-1}; ^1H NMR (300 MHz) δ = 1.30 (t, *J* = 8 Hz, 3 H), 3.27 (q, *J* = 8 Hz, 2 H), 3.95 (s, 3 H), 5.48 (s, 2 H), 7.28-7.40 (m, 5 H), 8.11 (s, 1 H), 8.94 (s, 1 H); ^{13}C NMR (75.5 MHz) δ = 13.0 (s), 32.0 (s), 43.0 (s), 47.7 (s), 127.0 (s), 127.2 (s), 128.0 (s), 128.8 (s), 129.2 (s), 134.6 (s), 144.7 (s), 152.3 (s), 153.9 (s), 200.9 (s); MS *m/z* (rel intensity) 345 (M^++2, 0.7), 344 (M^++1, 1), 343 (M^+, 7), 314 (16), 268 (6), 209 (7), 148 (5), 91 (100), 65 (18). Found: *m/z* 343.0926. Calcd for $C_{16}H_{17}N_5S_2$: M, 343.0925.

6-[Methyl(trifluoromethyl)amino]-9-benzyl-9*H*-purine (26). To a stirred solution of $TBAH_2F_3$ (0.24 g, 0.79 mmol) and dithiocarbamate **25** (54 mg, 0.157 mmol) in CH_2Cl_2 (0.5 mL) was added DBH (0.180 g, 0.63 mmol) in one portion at 0 °C. The resulting mixture was stirred for 1 h at 0 °C, then poured into aq. $NaHSO_3$/$NaHCO_3$/NaOH solution (pH 10), and extracted with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered through a Celite/silica gel (Wako Gel C-100) pad, and concentrated. The residue was purified by column chromatography (hexane : diethyl ether = 1 : 1) to give **26** (12 mg, 25% yield) as colorless needles; mp 89.6-90.9 °C; R_f = 0.67 (Et_2O). IR 2926, 2853, 1730, 1590, 1582, 1476, 1458, 1433, 1364, 1296, 1237, 1211, 1154, 1121, 1075, 731, 718 cm^{-1}; ^1H NMR (300 MHz) δ = 3.73 (q, *J* = 2 Hz, 3 H), 5.43 (s, 2 H), 7.23-7.40 (m, 5 H), 7.94 (s, 1 H), 8.68 (s, 1 H); ^{19}F NMR (188 MHz) δ = –57.7 (q, *J* = 2 Hz); ^{13}C NMR (75.5 MHz) δ = 33.6 (q, *J* = 2 Hz), 47.3 (s), 121.6 (q, *J* = 261 Hz), 125.1 (s), 127.8 (s), 128.1 (s), 128.6 (s), 129.1 (s), 135.1 (s), 141.5 (s), 151.6 (s), 152.4 (s); MS *m/z* (rel intensity) 308 (M^++1, 3), 307 (M^+, 19), 306 (M^+-1, 7), 210 (9), 119 (9), 92 (9), 91 (100), 69 (7), 65 (27). Found: *m/z* 307.1049. Calcd for $C_{14}H_{12}F_3N_5$: M, 307.1045.

II-5. References and Notes

1) a) J. T. Welch, *Tetrahedron*, **43**, 3123 (1987); b) R. Filler and Y. Kobayashi, Ed., "*Biomedical Aspects of Fluorine Chemistry*," Kodansha Ltd. and Elsevier Biochemical, Tokyo and Amsterdam (1982).
2) a) J. T. Welch and S. Eswarakrishnan, "*Fluorine in Bioorganic Chemistry*," John Wiley & Sons, New York (1991); b) P. Goldman, *Science*, **164**, 1123 (1969).
3) M. Hudlicky and A. E. Pavlath, "*Chemistry of Organic Fluorine Compounds II. A Critical Review*," ACS Monograph 187, Washington, DC (1995).
4) a) G. Klöter, W. Lutz, K. Seppelt, and W. Sundermeyer, *Angew. Chem. Int. Ed. Engl.*, **16**, 707 (1977); b) G. Klöter and K. Seppelt, *J. Am. Chem. Soc.*, **101**, 347 (1979).
5) a) M. Kuroboshi, K. Mizuno, K. Kanie, and T. Hiyama, *Tetrahedron Lett.*, **36**, 563 (1995); b) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683.
6) Y. Kobayashi, I. Kumadaki, and T. Taguchi, Ed., "*Fusso Yakugaku*," Hirokawa, Tokyo (1993).
7) R. P. Geyer, R. G. Monreo, and K. Taylor, *Fed. Proceedings*, **29**, 1699 (1970).
8) V. A. Petrov, V. Montanari, G. Resnati, and D. D. DesMarteau, *J. Fluorine Chem.*, **54**, 399 (1991).
9) D. D. DesMarteau, A. Donadelli, V. Montanari, V. A. Petrov, and G. Resnati, *J. Am. Chem. Soc.*, **115**, 4897 (1993).
10) A. Arnone, B. Novo, M. Pregnolato, G. Resnati, and M. Terreni, *J. Org. Chem.*, **62**, 6401 (1997).
11) W. Dmowski and M. Kaminski, *J. Fluorine Chem.*, **23**, 219 (1983).
12) W. Dmowski and M. Kaminski, *J. Fluorine Chem.*, **23**, 207 (1983).
13) L. M. Yagupol'skii, N. V. Kondratenko, G. N. Timofeeva, M. I. Dronkina, and Y. L. Yagupol'skii, *J. General Chem. USSR*, **16**, 2139 (1981).
14) R. J. Harder and W. C. Smith, *J. Am. Chem. Soc.*, **83**, 3422 (1961).
15) L. N. Markovskij, V. E. Pashinnik, and A. V. Kirsanov, *Synthesis*, **1973**, 787.
16) G. Pawelke, *J. Fluorine Chem.*, **52**, 229 (1991).
17) E. Klauke, *Angew. Chem., Int. Ed. Engl.*, **5**, 848 (1966).
18) T. Abe, E. Hayashi, H. Baba, and H. Fukaya, *J. Fluorine Chem.*, **48**, 257 (1990).
19) K. Adachi, S. Ishihara, and T. Umemoto, *Proceedings of the 15th International Symposium on Fluorine Chemistry, Vancouver*, Canada, Aug. 2-7, 1997.
20) a) M. Kuroboshi and T. Hiyama, *Yuki Gosei Kagaku Kyokai Shi*, **51**, 1124 (1993); b) K. Kanie, Y. Tanaka, M. Shimizu, M. Kuroboshi, and T. Hiyama, *Chem.*

Commun., **1997**, 309.

21) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.*, **33**, 4177 (1992); Perfluoroalkylamines are also prepared in a similar manner. See: b) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.*, **35**, 3983 (1994).
22) A. R. Katritzky, C. M. Marson, and H. Faid-Allah, *Heterocycles*, **26**, 1657, (1987).
23) M. Kuroboshi, K. Suzuki, and T. Hiyama, *Tetrahedron Lett.*, **33**, 4173 (1992).
24) J. H. Clark, *Chem. Rev.*, **80**, 429 (1980).
25) J. Cousseau and P. Albert, *Bull. Soc. Chim. Fr.*, **6**, 910 (1986).
26) K. A. Schellengerg, *J.Org. Chem.*, **28**, 3259 (1963).
27) J. Barluenga, A. M. Bayón, G. Asensio, *J. Chem. Soc., Chem. Commun.*, **1984**, 1334.

Chapter III

Syntheses and Properties of Novel Liquid Crystals Containing a Trifluoromethylamino Group

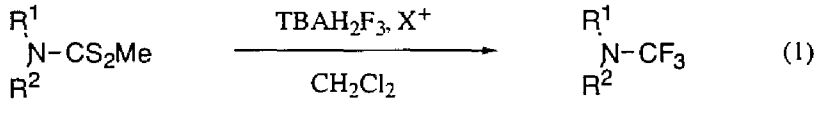
Abstract: LCs containing a trifluoromethylamino group are prepared by the cross-coupling reaction of *p*-bromo-substituted-(hetero)aryl(trifluoromethyl)amines that are derived from the corresponding dithiocarbamates through oxidative desulfurization-fluorination. The novel LCs are shown to exhibit mainly a smectic phase over a wide range of temperatures. Their electro-optical properties as a component of nematic LCs are compared with those of the corresponding methylamines.

III-1. Introduction

LCs having a fluorine-functional group show high polarity, high thermal and chemical stability, and low viscosity because of the most electronegative fluorine atom and the strong C–F bond.[1] Accordingly, various types of fluorinated LCs have been synthesized,[2] and their phase transition behaviors and electro-optical properties as an additive for LC materials have been shown to be superior to those of the corresponding cyano-substituted ones that are employed widely for twisted nematic displays at present.[3] Such fluorinated compounds are synthesized, in general, using highly toxic reagents such as hydrogen fluoride, metal fluorides, and/or elemental fluorine gas under harsh conditions.[4] Because of the operational difficulties in the syntheses, exploitation of novel fluorinated LCs has been hampered. To assist the development of LC materials, mild, efficient, and selective methods have been needed for the fluorination of organic substrates.

Recently, *the oxidative desulfurization-fluorination reaction* using an *N*-halo imide and a fluoride reagent is demonstrated to be a convenient fluorination method.[5] This reaction allows the replacement of C–S bonds with C–F bonds under extremely mild conditions. For example, when the reaction is applied to methyl dithiocarbamates $R^1R^2NC(S)SMe$, trifluoromethylamines $R^1R^2NCF_3$ are readily prepared in high yields.[6]

The Oxidative Desulfurization-Fluorination of Dithiocarbamates



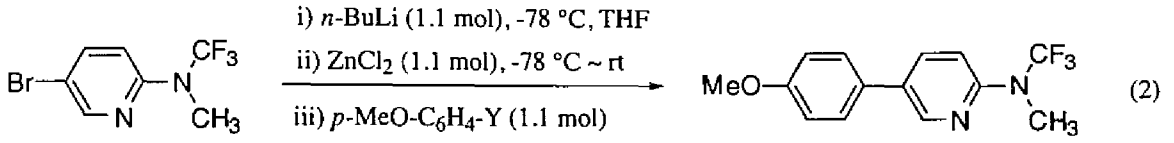
(1)

All of the preparative methods for trifluoromethylamines reported[7] so far involve the use of highly toxic and corrosive reagents under harsh conditions, and desired products are isolated usually in low yields. The inaccessibility has hampered the systematic studies on trifluoromethylamines, in spite of their unique properties such as resistance against oxidation,[6e] weak basicity and poor nucleophilicity[8] as compared with the corresponding methylamines. Thus, trifluoromethylamines are expected to show low viscosity and high thermal and chemical stabilities, properties essential for LC materials. Herein described are the syntheses, phase transition behaviors, and electro-optical properties of novel LCs containing a trifluoromethylamino group.[6d]

III-2. Results and Discussion

III-2-1. Synthesis of Trifluoromethylamino-substituted LCs with a Heterobiaryl Core

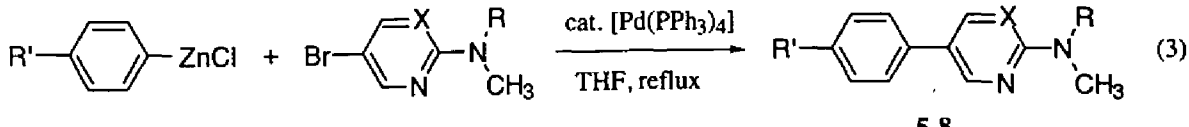
The oxidative desulfurization-fluorination of methyl *N*-methyl-*N*-2-pyridinyl-dithiocarbamate easily gives 5-bromo-2-[methyl(trifluoromethyl)amino]pyridine (**1**).[6c] The Author first treated **1** with *n*-BuLi and then with zinc chloride •tetramethylethylenediamine complex ($ZnCl_2$•TMEDA) to give a zinc reagent, which was reacted with 1-halo-4-methoxybenzene in the presence of a [$Pd(PPh_3)_4$] catalyst. Contrary to his expectation, the desired cross-coupled heterobiaryl **5** was not obtained in high yield, due probably to the instability of the zinc reagent (see Experimental).



1 → 5 (2)

Y = I, 20%; Br, 9%

The Author next examined the reaction of **1** with a 4-alkyl(oxy)-substituted arylzinc reagent prepared in the manner described above from 1-alkoxy-4-bromobenzene. Yields and phase transition temperatures of the resulting heterobiaryls are summarized in Table 1. As one readily sees, 5-(4-alkyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridines **5** and -pyrimidines **6** were obtained in moderate yields. In a similar way, corresponding 2-dimethylamino derivatives **7** and **8** were also prepared, but in lower yields (entries 5, 6, 12, and 13). When a Grignard reagent was used in lieu of the zinc reagent, only a trace amount of the desired heterobiaryl was obtained. Furthermore, a zinc reagent generated from $ZnCl_2$•TMEDA was more effective than that from $ZnCl_2$•Et_2O (compare entry 2 with 4). The coupling reaction was not applicable to the synthesis of 4-[alkyl(trifluoromethyl)amino]-4'-alkyloxybiphenyls, because these were easily hydrolyzed upon exposure to moisture.



(1.0 mol) **1-4** (1.2 mol) → **5-8** (3)

1, **5**; X = CH, R = CF_3 **3**, **7**; X = CH, R = CH_3

2, **6**; X = N, R = CF_3 **4**, **8**; X = N, R = CH_3

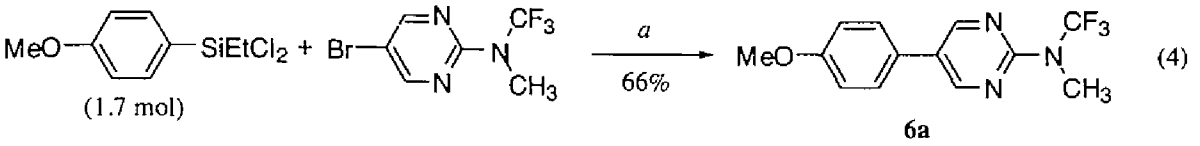
Table 1. Synthesis of trifluoromethylamino-substituted heterobiaryls accordinmg to equation 3.[a,b]

Entry	R'	X	R	Heterobiaryl	Yield/%[c]	Phase transition temperature/°C[d]
1	CH_3O	CH	CF_3	**5a**	20	Cr 69 Iso (Iso 53 Cr)
2	*n*-C_3H_7O	CH	CF_3	**5b**	58 (29)[e]	Cr 66 S_A 93 Iso (Iso 92 S_A 62 Cr)
3	*n*-$C_6H_{13}O$	CH	CF_3	**5c**	67	Cr 53 S_A 70 Iso (Iso 69 S_A 42 Cr)
4	*n*-$C_8H_{17}O$	CH	CF_3	**5d**	20[e]	Cr 51 S_A 62 Iso (Iso 60 S_A 36 Cr)
5	*n*-C_3H_7O	CH	CH_3	**7b**	39	Cr 128 Iso (Iso 116 Cr)
6	*n*-$C_6H_{13}O$	CH	CH_3	**7c**	35	Cr 104 Iso (Iso 96 Cr)
7	*n*-C_3H_7	CH	CF_3	**5e**	62	Cr 54 S_A 65 Iso[f]
8	CH_3O	N	CF_3	**6a**	71	Cr 101 Iso (Iso 52 Cr)
9	*n*-C_3H_7O	N	CF_3	**6b**	45	Cr 94 Iso (Iso 83 Cr)
10	*n*-$C_6H_{13}O$	N	CF_3	**6c**	38	Cr 84 Iso (Iso 60 Cr)
11	*n*-$C_8H_{17}O$	N	CF_3	**6d**	88	Cr 84 Iso (Iso 62 Cr)
12	*n*-C_3H_7O	N	CH_3	**8b**	48	Cr 106 Iso (Iso 95 Cr)
13	*n*-$C_6H_{13}O$	N	CH_3	**8c**	37	Cr 96 Iso (Iso 93 Cr)

[a]All the reaction performed with an organozinc reagent (1.0 mol) and an amine (1.2 mol) in the presence of $[Pd(PPh_3)_4]$ (1.8 mol%) in THF at a reflux temperature. [b]Respective organozinc reagent was prepared from1-alkyloxy-4-halobenzene by lithiation with *n*-BuLi and transmetallation with $ZnCl_2$•TMEDA. [c]Isolated yields are given. [d]Measured by a DSC on second heating. Values in parentheses were measured by DSC on first cooling. Cr: Crystal. Iso: Isotropic liquid. S_A: Smectic A phase. [e]$ZnCl_2$•Et_2O was used. [f]Determined by optical polarization microscopy.

Phase transition temperatures and textures of trifluoromethylamines **5** and **6** as well as the corresponding methylamines **7** and **8** are listed in Table 1. Methyl(trifluoromethyl)amino-substituted pyridines **5** exhibited smectic A (S_A) phase, whereas 2-(dimethylamino)pyridines **7** lost the LC phase. Thus, a trifluoromethylamino group appears to promote liquid crystallinity. This is the first example of LC compounds containing a trifluoromethylamino moiety.[6c,6d] The corresponding pyrimidines **6** and **8** showed melting points only. In addition, melting points of pyridines **5** and pyrimidines **6** turned out to be lower than those of **7** and **8**, respectively (compare entries 3 with 6; 10 with 13).

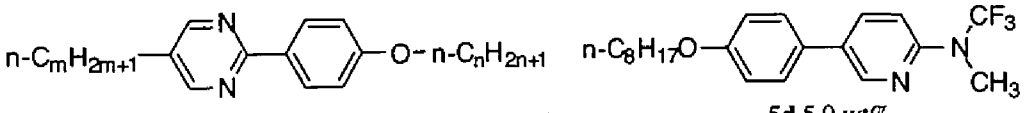
The cross-coupling reaction of dichloro(ethyl)(4-methoxyphenyl)silane[9] with **3** using a $Pd(OAc)_2$ catalyst, tri(*o*-tolyl)phosphine, and KF in excess gave rise to heterobiaryl **6a** in 66% yield (eq. 4). This procedure was also effective for the preparation of trifluoromethylamino-substituted LCs.



a: i) KF (9 mol), DMF, 60 °C, 3 h,
ii) $Pd(OAc)_2$ (8 mol%), P(*o*-Tol)$_3$ (8 mol%), DMF, 120 °C, 18 h

III-2-2. Trifluoromethylamino-substituted Heterobiaryls as a Dopant for Ferroelectric LCs

Ferroelectric LCs having an (*S*)-2-octylamino group show chiral smectic C (Sc*) phase in a range of temperatures wider than those with an (*S*)-2-octyloxy group.[10] Chiral *N*-alkyl-*N*-methylamino-substituted LCs are reported to possess relatively low viscosity values and an Sc* phase over a wide temperature range.[11] Although these properties are favorable as a switching element for surface stabilizing ferroelectric LC displays, the basicity and low oxidation potential of an amino group hampered their applications. In contrast, the low basicity and high oxidation potential of trifluoromethylamines apparently allow such applications. The Author thus prepared a host LC mixture containing trifluoromethylamine component **5d** (phase transition temperature of this mixture: see Figure 1) and then mixed in 2 wt% chiral dopant **9**.[12] The resulting mixture showed a phase transition of rt Sc* 48 S_A 67 N 69 Iso. Response time ($\tau_{0\text{-}90}$) of the mixture in a LC cell (2 μm thin) was 78 μs at 25 °C, whereas $\tau_{0\text{-}90}$ of a mixture lacking **5d** was 83 μs, indicating that **5d** improved both the range of the Sc* phase and the response speed.

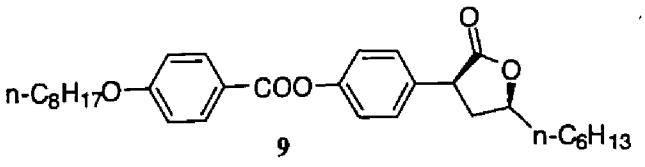


m = 7, n = 9: 28.5 wt%; m = 8, n = 10: 28.5 wt%
m = 8, n = 8: 19.0 wt%; m = 9, n = 9: 19.0 wt%

5d 5.0 wt%

host mixture: S_C 44 S_A 68.5 N 69.5 Iso

Figure 1. A host LC mixture containing **5d**.



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To estimate the thermal and chemical stability of trifluoromethylamino-substituted LC **5c**, the Author prepared an LC mixture consisting of **5c** (5 wt%) and 8 other LC compounds. The phase transition temperatures and color of the mixture did not change at all after heating at 100 °C for 50 h. Thus, the trifluoromethylamino-substituted LC compounds are demonstrated to be thermally stable. When the mixture shown in Figure 2 was kept at –20 °C for a week, no crystallization nor phase separation was detected. Thus, the miscibility of trifluoromethylamino-substituted LCs seems satisfactory.

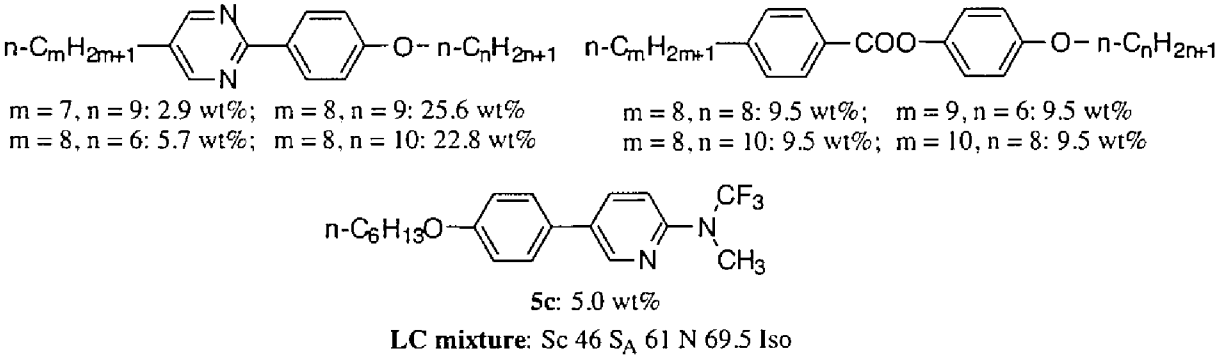
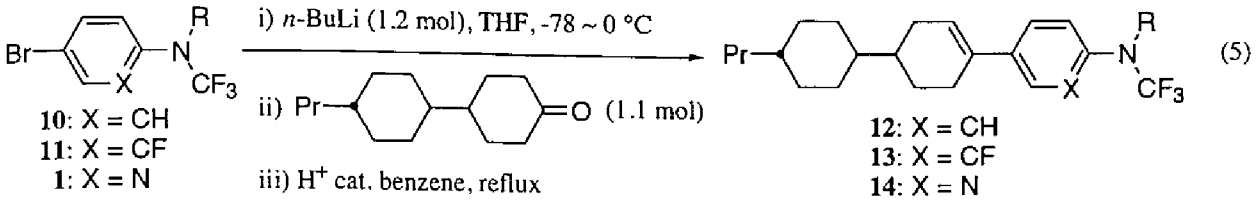


Figure 2. An LC mixture containing **5c** for stability test.

III-2-3. Trifluoromethylamino-substituted LCs with a 4-Cyclohexylcyclohexenylarene Core

The Author next planned the synthesis of 1-trifluoromethylamino-4-[4-(*trans*-4-substituted cyclohexyl)cyclohexen-1-yl]arenes, starting with 4-bromo-*N*-trifluoromethylaniline **10**, **11**, or **1**. Lithiation of **10**, **11**, or **1** with *n*-BuLi, followed by treatment with 4-(*trans*-4-propylcyclohexyl)cyclohexanone, gave a tertiary cyclohexanol, which was converted into cyclohexene derivative **12**, **13**, or **14** in hot benzene in the presence of an acid catalyst. Total yields and phase transition temperatures are summarized in Table 2. The yields turned out to be relatively low, probably because hydrolysis of a trifluoromethylamino group took place under the dehydration conditions. Indeed, a product tentatively assigned as fluoroformamide **15** was detected in the synthesis of **12a** (Table 2 entry 1, see Experimental). Compounds **12**, **13**, and **14** exhibited a smectic phase. In particular, cyclohexenylbenzene derivative **12** and its fluoro derivative **13** exhibited a smectic B (S_B), and cyclohexenylpyridine **14** showed an S_A phase over a wide range of temperatures. As readily seen in Table 2, either the fluorine atom on a phenyl ring or an ethyl group on nitrogen tends to make the temperature range of a smectic phase narrower and to lower the transition temperature from a smectic phase to an isotropic phase.

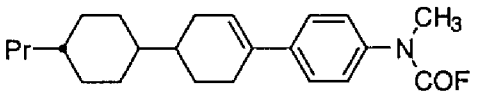


(5)

Table 2. The yields and phase transition temperatures of compounds **12**, **13**, or **14** according to equation 5.

Entry	X	R	H^+	Product	Yield/%	Phase transition temperature/°C	
						DSC (heating)	DSC (cooling)
1	CH	Me	PPTS	**12a**	10	Cr 24 S_B 158 Iso	Cr -23 S_B 155 Iso
2	CH	Et	MS 4A	**12b**	15	Cr 25 S_B 110 Iso	Cr -47 S_B 110 Iso
3	CF	Me	*p*-TsOH	**13a**	28	< 23 S_B 70 Iso[a]	
4	CF	Et	*p*-TsOH/MS 4A	**13b**	9	< 23 S_B 37 Iso[a]	
5	N	Me	*p*-TsOH	**14a**	49	Cr 82 S_A 139 Iso	Cr 64 S_A 138 Iso
6	N	Et	*p*-TsOH/MS 4A	**14b**	25	Cr 78 S_A 98 Iso	Cr 61 S_A 98 Iso

[a]Examined by optical polarization microscopy. S_B: Smectic B phase



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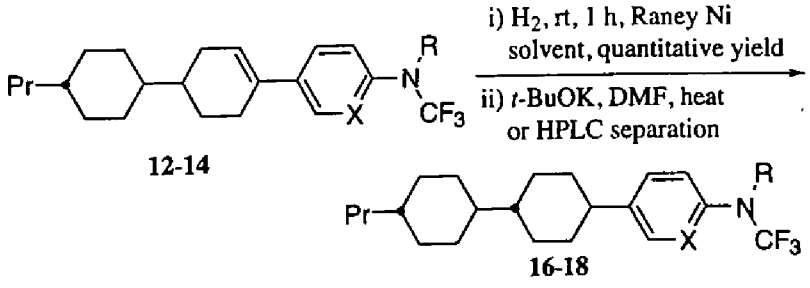
III-2-4. Trifluoromethylamino-substituted LCs with a 4-Cyclohexylcyclohexylarene Core

Hydrogenation of trifluoromethylamino-substituted cyclohexyl(cyclohexenyl)-benzenes **12**, **13**, or -pyridines **14** using a Raney Ni (W2) catalyst gave quantitatively 1 : 1 to 1 : 2 mixtures of *cis*- : *trans*-isomers of **16**, **17**, or **18**, respectively. The *trans*-isomers were separated by preparative HPLC. Alternatively, isomerization of the *cis*-isomers of **16**, **17**, or **18** to the *trans*-isomers was effected by treatment with excess *t*-BuOK in hot DMF.



12-14

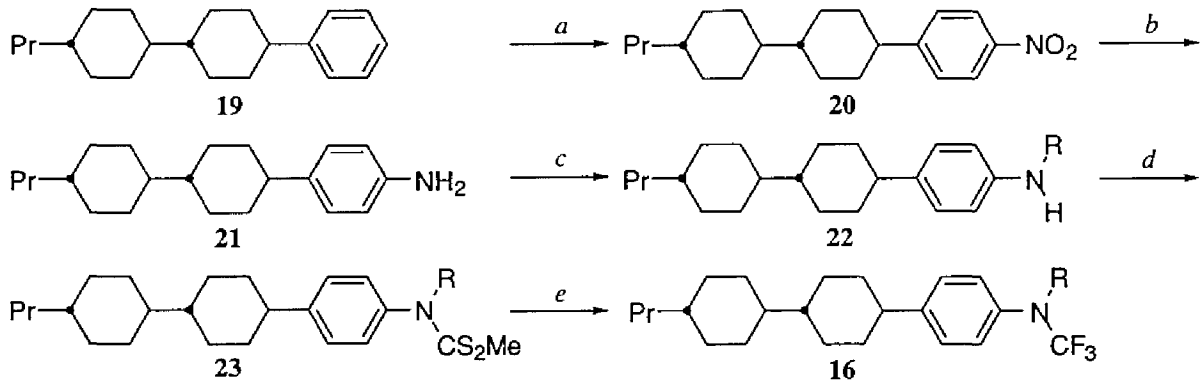
16-18

(6)

12, **16**; X = CH **13**, **17**; X = CF **14**, **18**; X = N

In order to facilitate the synthesis of **16** in large amounts, a sequence of reactions were carried out as shown in Scheme 1. Nitration of commercially available 1-phenyl-*trans*-4-(4-propyl)cyclohexylcyclohexane (**19**) and catalytic reduction of resulting nitrobenzene derivative **20** gave aniline derivative **21**. *N*-Alkylation of **21** by treatment with *n*-BuLi and an alkyl iodide gave **22**. To avoid dialkylation, **22a** was better prepared by the reaction of **21** with formaldehyde and $NaBH_4$ in the presence of sodium methoxide.[13] Treatment of **22** with *n*-BuLi, CS_2, and MeI gave dithiocarbamate **23** in high yields. Trifluoromethylation of **23** was quantitatively performed using $TBAH_2F_3$ and DBH.[6d]

Scheme 1. Synthesis of trifluoromethylamino-substituted LCs

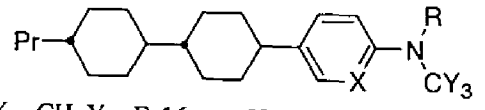


R = Me:	**22a**, 28%;	**23a**, 71%;	**16a**, quant.
R = Et:	**22b**, 79%;	**23b**, 94%;	**16b**, quant.
R = *n*-C_3H_7:	**22c**, 80%;	**23c**, 81%;	**16c**, 94%.

a: H_2SO_4/HNO_3, CH_2Cl_2, 0 °C to r.t., 2 h, 81% yield; *b*: Pd/C, H_2, EtOH, r.t., 3.5 h, 90% yield; *c*: i) *n*-BuLi (1.0 mol), -78 to 0 °C, ii) RI (1.0 mol); *d*: *n*-BuLi (1.0 mol), CS_2 (2.0 mol), MeI (2.0 mol); *e*: $TBAH_2F_3$ (5.0 mol), DBH (4.0 mol), CH_2Cl_2, 0 °C, 1 h.

Phase transition behaviors of **16-18** and **24** are summarized in Table 3. All of trifluoromethylamino-substituted compounds **16**, **17**, and **18** exhibited an S_B phase[14] over a wide range of temperatures. In addition, compound **18a** consisting of a (trifluoromethylamino)pyridine mesogen exhibited a nematic phase.

Worthy of note is that, with the carbon number of R increasing from 1 to 3 (or 2), the temperature ranges of LC phase of **16**, **17**, and **18** became narrower, and the phase transition took place at lower temperatures. Therefore, a long alkyl side-chain of R appears to destabilize the mesophase (see also Table 2). In contrast, the corresponding methylamine derivatives **24b** and **24c**[15] did not show any LC phase; these exhibited high melting points only. Therefore, the trifluoromethylamino substituent tends to induce liquid crystallinity.



X = CH, Y = F; **16** X = N, Y = F; **18**
X = CF, Y = F; **17** X = CH, Y = H; **24**

Table 3. Phase transition temperatures of compounds **16**, **17**, **18**, and the corresponding *N*-methyl coumterpart **24**.

Entry	X	Y	R	Compound	Phase transition temp./°C[a]
1	CH	F	Me	**16a**	< 20 S_B 173 Iso[b]
2	CH	F	Et	**16b**	Cr 35 S_B 141 Iso
					(Iso 141 S_B -50)
3	CH	F	Pr	**16c**	Cr 57 S_B 109 Iso
					(Iso 108 S_B -18 Cr)
4	CF	F	Me	**17a**	Cr 62 S_B 101 Iso[b]
5	CF	F	Et	**17b**	Cr 38 S_B 73 Iso[b]
6	N	F	Me	**18a**	Cr 62 S_X 73 S_B 120 N 121 Iso
					(Iso 121 N 119 S_B 70 S_X 37 Cr)
7	N	F	Et	**18b**	Cr 50 S_B 100 Iso
					(Iso 98 S_B 48 Cr)
8	CH	H	Me	**24a**	Cr 59 S_B 189 Iso[b]
9	CH	H	Et	**24b**	Cr 181 Iso[b]
10	CH	H	Pr	**24c**	Cr 168 Iso[b]

[a]Measured by DSC on 2nd heating. Values in parentheses were measured by DSC on 1st cooling. [b]Examined by a polarizing microscope. S_X: higher order smectic.

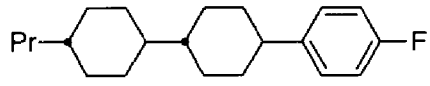
III-2-5. Electro-optical Properties of Trifluoromethylamino-substituted LCs with a 4-Cyclohexylcyclohexylarene Core

Trifluoromethylamine **16a**, **16b**, or **24b** was added (20 wt%) to the host nematic LC mixture[16] listed in Table 4. The physical and electro-optical properties of the resulting mixtures were measured and summarized in Table 4.

Table 4. Physical and electro-optical properties of mixtures[a] of nematic LC.

	T_{NI}/°C	V_{th}/V[b]	Δε	Δε'[c]	Δn[d]	$\eta_{20°C}$/cP[e]	$\eta_{0°C}$/cP[e]	τ/ms[b]	Applied Voltage/V
host	55	1.60	6.7	---	0.092	21.0	62.0	39.2	3.2
16a	59	1.62	5.92	2.8	0.091	---	---	46.4	3.6
16b	49	1.46	5.38	0.10	0.104	28.6	90.2	65.3	3.2
24b	68	1.84	6.59	6.1	0.100	---	---	53.9	4.0
26	73	1.91	6.31	4.75	0.096	---	---	---	---

[a]A mixture containing 80% of a host mixture[16] and 20% of **16a**, **16b**, **24b**, or **26**. [b]A 6 μm thick cell was used. [c]Extrapolated from Δε. [d]Anisotropy of refractive index. [e]Viscosity at 0°C and 20°C, respectively.



26

When one compares **16a** with **16b**, a substituent effect is obvious. For example, the nematic-isotropic phase transition temperature (T_{NI}) of a **16a**-host mixture was higher than that of the host, whereas T_{NI} of a **16b**-host mixture became lower. Thus, **16a** apparently stabilizes the nematic phase of the host.

The Δε value of the **16b**-host mixture was extrapolated to 100% purity to estimate Δε' of **16b** to be 0.10, much smaller than Δε' of **16a** or **24b**. When one compares Δε' of **16a** with that of **26**, it is obvious that a -N(CF_3)Me group induces Δε in a degree comparable with a fluoro-substituent.

Upon addition of **16a** to the host LC mixture, T_{NI} of the resulting mixture became slightly higher than that of the host without any change of threshold voltage (V_{th}) (compare **host** and **16a** in V_{th}). Since the phase transition temperatures remained unchanged after 50 h at 100 °C, trifluoromethylamines **16** can be used as a thermally stable nematic LC component. In particular, because the **16**-host mixture did not cause precipitation or phase separation when kept at –20 °C for 7 days, trifluoromethylamines **16a-16c** have excellent solubility in nematic LCs.

III-3. Conclusion

The Author has described the syntheses, phase transition behaviors, and electro-optical properties of CF_3N-substituted LCs. These compounds are easily accessible by

the reaction of *p*-bromo-substituted (hetero)aryl(trifluoromethyl)amines or by the oxidative desulfurization-fluorination of the dithiocarbamates with all the carbon frameworks fully set up. They show mostly a smectic phase over a wide range of temperatures. The liquid crystallinity and electro-optical properties of these compounds are better than those of the corresponding methylamines, and thus the CF_3N-substituted LCs should find wide applications as a stable component of a chiral smectic C or nematic LCs mixture.

III-4. Experimental

Measurements.

Following measurements of physical and electro-optical properties for LCs apply to all of the experimental parts of this Thesis. A sample for measurements of $\Delta\varepsilon$, Δn, V_{th}, and τ was prepared by mixing a compound with a standard LC material. The LC mixture was sealed in a polyimide rubbed cell of about 6 μm thickness. A rectangular electric field of 1 kHz was applied to the cell, and the intensity change of linearly polarized light transmitted through a pair of crossed polarizers was observed with a photodiode. Values of $\Delta\varepsilon$ were recorded on a YHP 4192A impedance analyzer by measuring electrical response. Values of Δn were obtained by an ATAGO 4T Abbe's refractometer. V_{th} was expressed as the voltage for 90% of maximum transmittance. Rising switching time (τ_r) and decay switching time (τ_d) were obtained respectively as electro-optical response from 100% to 10% and from 0% to 90%. Values τ were estimated when τ_r became equal to τ_d at a properly applied voltage.

General Procedure for the Preparation of Heterobiaryl-type LCs.

Method A: A hexane solution of *n*-BuLi (1.60 M, 0.69 mL, 1.1 mmol) was slowly added dropwise to a stirred solution of 5-bromo-2-[methyl(trifluoromethyl-amino)]pyridine[6e] (**1a**, 1.00 mmol) in THF (or DME) (2.0 mL) at −78 °C. The resulting mixture was stirred for 10 min at -78 °C before addition of $ZnCl_2$•TMEDA complex (1.10 mmol). The reaction mixture was warmed slowly up to room temperature and stirred for 1 h at room temperature before a solution of 1-alkyloxy-4-halobenzene (1.10 mmol) and [$Pd(PPh_3)_4$] (22 mg, 0.019 mmol, 1.9 mol%) in THF (or DME) (1.0 mL) was added. The resulting mixture was heated to reflux until all the substrate was consumed and then poured into sat. $NaHCO_3$ aq. solution. The organic layer was separated; the aq. layer was made alkaline (*p*H 10) with KOH and extracted three times with Et_2O. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated

in vacuo. The residue was purified by flash column chromatography followed by HPLC to give the desired heterobiaryl.

Method B: A 1.6 M solution of *n*-BuLi in hexane (0.75 mL, 1.2 mmol) was slowly added dropwise to a stirred solution of 1-alkyloxy-4-bromobenzene (1.00 mmol) in THF (2.0 mL) at –78 °C. The resulting mixture was stirred for 30 min at –78 °C before addition of a solution of $ZnCl_2$•TMEDA (1.00 M, 1.20 mL, 1.20 mmol). The reaction mixture was warmed slowly up to room temperature, stirred for 1 h at the same temperature, and then treated with a solution of **1a** (1.20 mmol) and [$Pd(PPh_3)_4$] (21 mg, 0.018 mmol, 1.8 mol%) in THF (4.0 mL). The resulting reaction mixture was heated to reflux, stirred until all the substrate was consumed, and poured into sat. $NaHCO_3$ aq. solution. Workup and purification by column chromatography followed by HPLC, gave the desired heterobiaryl.

5-(4-Methoxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridine (5a). Yield: 20% (Method A, from 1-iodo-4-methoxybenzene, in THF), 9% (Method A, from 1-bromo-4-methoxybenzene, in THF), 25% (Method A, from 4-methoxy-1-iodobenzene, in DME), 12% (Method A, from 1-bromo-4-methoxybenzene, in DME). Colorless needles, mp 69 °C (DSC on heating); R_f = 0.42 (CH_2Cl_2). IR (KBr) 2967, 2944, 2917, 2843, 1608, 1559, 1521, 1459, 1429, 1438, 1423, 1362, 1344, 1255, 1243, 1188, 1125, 1068, 1043, 1027, 916, 822, 702, 619 cm^{-1}; ^1H NMR (200 MHz) δ = 3.29 (q, J = 2 Hz, 3 H), 3.85 (s, 3 H), 6.95-7.03 (m, 3 H), 7.43-7.52 (m, 2 H), 7.78 (dd, J = 3, 9 Hz, 1 H), 8.55 (d, J = 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (s); ^{13}C NMR (50.3 MHz) δ = 32.3 (s), 55.3 (s), 113.6 (s), 114.5 (s), 122.9 (q, J = 256 Hz), 127.8 (s), 129.8 (s), 131.3 (s), 135.8 (s), 145.7 (s), 152.4 (s), 159.5 (s); MS *m/z* (rel intensity) 283 (M^++1, 16), 282 (M^+, 100), 213 (55), 198 (10), 186 (68), 185 (28), 170 (16), 143 (11), 142 (6), 141 (9), 140 (11). Found: *m/z* 282.0971. Calcd for $C_{14}H_{13}F_3N_2O$: M, 282.0980.

2-[Methyl(trifluoromethyl)amino]-5-(4-propoxyphenyl)pyridine (5b). Yield: 16% (Method A, from 1-iodo-4-propoxybenzene, in DME), 58% (Method B), 29% (Method B, $ZnCl_2$•Et_2O was used). Colorless needles, phase transition temp./°C: Cr 66 S_A 93 Iso (on heating), Iso 92 S_A 62 Cr (on cooling); R_f = 0.50 (CH_2Cl_2). IR (KBr) 2975, 2945, 1607, 1558, 1491, 1362, 1340, 1285, 1243, 1125, 1069, 976, 822 cm^{-1}; ^1H NMR (200 MHz) δ = 1.05 (t, J = 7 Hz, 3 H), 1.60-2.00 (m, 2 H), 3.29 (q, J = 2 Hz, 3 H), 3.96 (t, J = 6 Hz, 2 H), 6.94-7.19 (m, 3 H), 7.39-7.53 (m, 2 H), 7.78 (dd, J = 3, 9 Hz, 1 H), 8.54 (d, J = 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 10.5 (s), 22.6 (s), 32.3 (s), 69.8 (s), 113.7 (s), 115.1 (s), 122.9 (q, J = 257 Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.7 (s), 152.4 (s), 159.1 (s); MS *m/z* (rel intensity) 311 (M^++1, 14), 310 (M^+, 73), 268 (12), 267 (14), 248 (10), 199 (56), 172 (100),

170 (22), 143 (13), 141 (6). Found: *m/z* 310.1292. Calcd for $C_{16}H_{17}F_3N_2O$: M, 310.1293.

5-(4-Hexyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridine (5c). Yield: 11% (Method A, from 1-hexyloxy-4-iodobenzene, in DME), 67% (Method B). Colorless needles, phase transition temp./°C: Cr 53 S_A 70 Iso (on heating), Iso 69 S_A 42 Cr (on cooling); R_f = 0.65 (CH_2Cl_2). IR (KBr) 2965, 2941, 2868, 1605, 1492, 1438, 1421, 1359, 1286, 1252, 1246, 1189, 1096, 1076, 1026, 822 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 6 Hz, 3 H), 1.25-1.87 (m, 8 H), 3.29 (q, *J* = 2 Hz, 3 H), 4.00 (t, *J* = 6 Hz, 2 H), 6.93-7.17 (m, 3 H), 7.39-7.51 (m, 2 H), 7.78 (dd, *J* = 2, 9 Hz, 1 H), 8.54 (d, *J* = 2 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (s); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.6 (s), 32.3 (s), 68.1 (s), 113.6 (s), 115.1 (s), 122.9 (q, *J* = 256 Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.6 (s), 152.4 (s), 159.1 (s); MS *m/z* (rel intensity) 353 (M^++1, 14), 352 (M^+, 58), 268 (30), 248 (12), 199 (51), 172 (100), 171 (42), 170 (19), 115 (11). Found: *m/z* 352.1761. Calcd for $C_{19}H_{23}F_3N_2O$: M, 352.1762.

2-[Methyl(trifluoromethyl)amino]-5-(4-octyloxyphenyl)pyridine (5d). Yield: 15% (Method A, from 1-iodo-4-octyloxybenzene, in DME), 20% (Method B, $ZnCl_2$•Et_2O was used). Colorless needles, phase transition temp./°C: Cr 51 S_A 62 Iso (on heating), Iso 60 S_A 36 Cr (on cooling); R_f = 0.67 (CH_2Cl_2). IR (KBr) 2961, 2935, 2919, 2853, 1607, 1559, 1522, 1493, 1474, 1437, 1423, 1385, 1363, 1341, 1290, 1250, 1185, 1131, 1099, 1021, 918, 844, 825, 711 cm^{-1}; ^1H NMR (200 MHz) δ = 0.89 (t, *J* = 6 Hz, 3 H), 1.29-1.88 (m, 12 H), 3.29 (q, *J* = 2 Hz, 3 H), 3.99 (t, *J* = 6 Hz, 2 H), 6.93-7.19 (m, 3 H), 7.42-7.51 (m, 2 H), 7.77 (dd, *J* = 3, 9 Hz, 1 H), 8.54 (d, *J* = 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.6 (s), 26.1 (s), 29.3 (s), 29.4 (s), 31.8 (s), 32.3 (s), 68.1 (s), 113.6 (s), 115.1 (s), 122.9 (q, *J* = 256 Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.6 (s), 152.4 (s), 159.1 (s); MS *m/z* (rel intensity) 381 (M^++1, 24), 380 (M^+, 100), 268 (35), 248 (11), 199 (36), 172 (75), 171 (29), 170 (14), 143 (8). Found: *m/z* 380.2065. Calcd for $C_{21}H_{27}F_3N_2O$: M, 380.2075.

5-(4-Methoxyphenyl)-2-[methyl(trifluoromethyl)amino]pyrimidine (6a). Yield: 9% (Method A, from 1-iodo-4-methoxybenzene, in THF), 71% (Method B). Colorless needles, mp 101 °C (DSC on heating); R_f= 0.57 (CH_2Cl_2). IR (KBr) 2966, 2943, 2919, 2845, 1604, 1548, 1470, 1416, 1318, 1289, 1251, 1207, 1182, 1132, 1113, 1089, 1030, 926, 835, 823, 797, 713, 619 cm^{-1}; ^1H NMR (200 MHz) δ = 3.40 (q, *J* = 2 Hz, 3 H), 3.86 (s, 3 H), 6.97-7.05 (m, 2 H), 7.40-7.49 (m, 2 H), 8.70 (s, 2 H); ^{19}F NMR (188 MHz) δ = –57.0 (q, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 31.7 (s), 55.4 (s), 114.8 (s), 122.0 (q, *J* = 258 Hz), 126.8 (s), 127.6 (s), 155.3 (s), 158.0 (s), 159.9 (s); MS *m/z* (rel intensity) 284 (M^++1, 15), 283 (M^+, 100), 214 (54), 187 (69), 185 (23), 171 (24), 160 (23), 155 (15), 89 (42). Found: *m/z* 283.0941. Calcd for $C_{13}H_{12}F_3N_3O$: M, 283.0932.

2-[Methyl(trifluoromethyl)amino]-5-(4-propoxyphenyl)pyrimidine (6b). Yield: 24% (Method A, from 1-iodo-4-propoxybenzene, in THF), 45% (Method B). Colorless needles, mp 94 °C (DSC on heating); R_f = 0.65 (CH_2Cl_2). IR (KBr) 2968, 2945, 2914, 2884, 1602, 1544, 1489, 1472, 1420, 1386, 1335, 1289, 1252, 1209, 1181, 1133, 1120, 1092, 1021, 1011, 926, 839, 822, 799, 718, 629, 614 cm^{-1}; ^1H NMR (200 MHz) δ = 1.05 (t, *J* = 7 Hz, 3 H), 1.70-2.00 (m, 2 H), 3.40 (q, *J* = 2 Hz, 3 H), 3.96 (t, *J* = 7 Hz, 2 H), 6.95-7.07 (m, 2 H), 7.36-7.47 (m, 2 H), 8.70 (s, 2 H); ^{19}F NMR (188 MHz) δ = –57.0 (q, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 10.4 (s), 22.5 (s), 31.7 (s), 69.7 (s), 115.4 (s), 122.1 (q, *J* = 258 Hz), 126.5 (s), 127.6 (s), 155.2 (s), 158.0 (s), 159.5 (s); MS *m/z* (rel intensity) 312 (M^++1, 14), 311 (M^+, 81), 269 (29), 268 (12), 200 (57), 173 (100), 172 (33), 171 (3), 146 (18). Found: *m/z* 311.1238. Calcd for $C_{15}H_{16}F_3N_3O$: M, 311.1245.

5-(4-Hexyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyrimidine (6c). Yield: 9% (Method A, from 1-hexyloxy-4-iodobenzene, in THF), 38% (Method B). Colorless needles, mp 84 °C (DSC on heating); R_f = 0.74 (CH_2Cl_2). IR (KBr) 2963, 2937, 2920, 2877, 2856, 1602, 1545, 1485, 1469, 1419, 1382, 1333, 1285, 1208, 1183, 1126, 1086, 1028, 842, 822, 632, 614 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 6 Hz, 3 H), 1.10-2.00 (m, 8 H), 3.40 (q, *J* = 2 Hz, 3 H), 4.00 (t, *J* = 6 Hz, 2 H), 6.99 (d, *J* = 9 Hz, 2 H), 7.43 (d, *J* = 9 Hz, 2 H), 8.69 (s, 2 H); ^{19}F NMR (188 MHz) δ = –57.0 (q, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.5 (s), 31.8 (s), 68.2 (s), 115.4 (s), 122.1 (q, *J* = 258 Hz), 126.5 (s), 127.7 (s), 155.3 (s), 158.0 (s), 159.5 (s); MS *m/z* (rel intensity) 354 (M^++1, 13), 353 (M^+, 64), 269 (57), 200 (48), 173 (100), 146 (12). Found: *m/z* 353.1709. Calcd for $C_{18}H_{22}F_3N_3O$: M, 353.1715.

2-[Methyl(trifluoromethyl)amino]-5-(4-octyloxyphenyl)pyrimidine (6d). Yield: 10% (Method A, from 1-iodo-4-octyloxybenzene, in THF), 88% (Method B). Colorless needles, mp 84 °C (DSC on heating); R_f = 0.76 (CH_2Cl_2). IR (KBr) 2964, 2937, 2922, 2876, 2855, 1603, 1544, 1491, 1470, 1421, 1390, 1334, 1287, 1250, 1210, 1183, 1134, 1089, 1029, 993, 842, 829, 799, 721, 614 cm^{-1}; ^1H NMR (200 MHz) δ = 0.89 (t, *J* = 6 Hz, 3 H), 1.22-1.53 (m, 10 H), 1.73-1.87 (m, 2 H), 3.40 (q, *J* = 2 Hz, 3 H), 3.99 (t, *J* = 7 Hz, 2 H), 6.99 (d, *J* = 9 Hz, 2 H), 7.42 (d, *J* = 9 Hz, 2 H), 8.69 (s, 2 H); ^{19}F NMR (188 MHz) δ = –57.0 (q, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.0 (s), 29.2 (s), 29.3 (s), 31.8 (s), 68.2 (s), 115.4 (s), 122.1 (q, *J* = 258 Hz), 126.5 (s), 127.6 (s), 155.2 (s), 158.0 (s), 159.5 (s); MS *m/z* (rel intensity) 382 (M^++1, 14), 381 (M^+, 61), 269 (77), 268 (17), 249 (10), 200 (49), 173 (100), 172 (30), 171 (24). Found: *m/z* 381.2035. Calcd for $C_{20}H_{26}F_3N_3O$: M, 381.2028.

2-[Methyl(trifluoromethyl)amino]-5-(4-propylphenyl)pyridine (5e). Yield: 62% (Method B). Colorless needles, phase transition temp./°C: Cr 54 S_A 65 Iso; R_f = 0.78 (CH_2Cl_2). IR (KBr) 2965, 2935, 1606, 1558, 1490, 1362, 1342, 1280, 1245, 1127,

1071, 810, 677 cm^{-1}; ^1H NMR (200 MHz) δ = 0.97 (t, *J* = 7 Hz, 3 H), 1.68 (qt, *J* = 7, 7 Hz, 2 H), 2.63 (t, *J* = 7 Hz, 2 H), 3.29 (q, *J* = 2 Hz, 3 H), 7.15 (dm, *J* = 9 Hz, 1 H), 7.23-7.29 (m, 2 H), 7.46 (td, *J* = 2, 8 Hz, 2 H), 7.80 (dd, *J* = 3, 9 Hz, 1 H), 8.57 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –57.9 (q, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 24.5 (s), 32.3 (s), 37.7 (s), 113.6 (s), 122.9 (q, *J* = 257 Hz), 126.6 (s), 129.2 (s), 131.5 (s), 134.7 (s), 136.0 (s), 142.4 (s), 145.9 (s), 152.7 (s); MS *m/z* (rel intensity) 295 (M^++1, 18), 294 (M^+, 100), 265 (95), 225 (48), 198 (58), 197 (23), 169 (37), 168 (13). Found: *m/z* 294.1340. Calcd for $C_{16}H_{17}F_3N_2$: M, 294.1344.

Synthesis of Dimethylamino-substituted Heterobiaryls.

5-Bromo-2-(dimethylamino)pyridine (3). 2-Dimethylaminopyridine (0.25 mL, 2.0 mmol) was added dropwise to a stirred suspension of DBH (0.69 g, 2.4 mmol) in dichloromethane (4.0 mL) at –78 °C. The reaction mixture was stirred for 50 min at –78 °C and poured into sat. aq. $NaHCO_3$. Workup and silica-gel column chromatography (hexane : Et_2O = 5 : 1, R_f = 0.35) gave **3** (0.22 g, 54% yield) as colorless needles (mp 40.5-42.0 °C). IR (KBr) 2925, 2855, 1597, 1509, 1392, 1319, 1214, 1154, 983, 807, 764, 632 cm^{-1}; ^1H NMR (200 MHz) δ = 3.05 (s, 6 H), 6.38 (d, *J* = 9 Hz, 1 H), 7.47 (dd, *J* = 3, 9 Hz, 1 H), 8.15 (d, *J* = 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 38.1 (s), 105.9 (s), 107.2 (s), 139.3 (s), 148.3 (s), 157.8 (s); MS *m/z* (rel intensity) 203 (M^++3, 4), 202 (M^++2, 46), 201 (M^++1, 10), 200 (M^+, 48), 187 (54), 185 (56), 173 (71), 171 (71), 158 (34), 156 (26), 78 (50), 44 (100). Found: *m/z* 199.9957. Calcd for $C_7H_9{}^{79}BrN_2$: M, 199.9950.

5-Bromo-2-(dimethylamino)pyrimidine (4). Produced in 86% yield (1.74 g, 8.6 mmol) as colorless needles (mp 79.7-80.4 °C) from 2-dimethylaminopyrimidine (1.23 g, 10.0 mmol) by a procedure similar to that for the preparation of **3**. R_f = 0.58 (hexane : Et_2O = 1 : 1). IR (KBr) 3025, 3012, 2934, 2862, 2780, 1588, 1525, 1410, 1401, 1378, 1310, 1296, 1200, 1168, 1118, 1052, 968, 939, 785, 774, 643 cm^{-1}; ^1H NMR (200 MHz) δ = 3.15 (s, 6 H), 8.28 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 37.2 (s), 105.1 (s), 157.6 (s), 160.4 (s); MS *m/z* (rel intensity) 204 (M^++3, 7), 203 (M^++2, 99), 202 (M^++1, 30), 201 (M^+, 100), 188 (69), 186 (72), 174 (79), 172 (77), 160 (18), 158 (18). Found: *m/z* 200.9889. Calcd for $C_6H_8{}^{79}BrN_3$: M, 200.9902.

2-(Dimethylamino)-5-(4-propoxyphenyl)pyridine (7b). Yield: 39% (Method B). Colorless needles, mp 128 °C (DSC on heating); R_f = 0.24 (hexane : Et_2O = 3 : 1). IR (KBr) 2965, 2928, 1605, 1557, 1507, 1421, 1387, 1338, 1274, 1248, 1189, 1068, 988, 973, 960, 834, 822, 806, 668 cm^{-1}; ^1H NMR (200 MHz) δ = 1.04 (t, *J* = 6 Hz, 3 H), 1.72-1.92 (m, 2 H), 3.12 (s, 6 H), 3.94 (t, *J* = 6 Hz, 3 H), 6.57 (dd, *J* = 1, 9 Hz, 1 H), 6.94 (d, *J* = 9 Hz, 2 H), 7.42 (d, *J* = 9 Hz, 2 H), 7.64 (dd, *J* = 3, 9 Hz, 1 H), 8.38 (dd, *J* = 1, 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 10.5 (s), 22.6 (s), 38.2 (s), 69.6 (s), 105.7 (s), 115.7 (s), 124.4

(s), 127.1 (s), 131.1 (s), 135.5 (s), 145.7 (s), 158.2 (s), 158.3 (s); MS *m/z* (rel intensity) 257 (M^++1, 18), 256 (M^+, 100), 241 (21), 227 (48), 213 (44), 199 (15), 185 (31), 184 (14), 171 (18), 170 (17), 115 (12). Found: *m/z* 256.1579. Calcd for $C_{16}H_{20}N_2O$: M, 256.1576.

2-(Dimethylamino)-5-(4-hexyloxyphenyl)pyridine (7c). Yield: 35% (Method B). Colorless needles, mp 104 °C (DSC on heating); R_f = 0.24 (hexane : Et_2O = 3 : 1). IR (KBr) 2954, 2934, 2870, 2864, 1612, 1557, 1508, 1389, 1338, 1282, 1251, 1219, 1191, 1026, 961, 838, 806, 690, 669 cm^{-1}; ^1H NMR (200 MHz) δ = 0.90 (t, *J* = 6 Hz, 3 H), 1.25-1.83 (m, 8 H), 3.11 (s, 6 H), 3.98 (t, *J* = 6 Hz, 3 H), 6.56 (dd, *J* = 1, 9 Hz, 1 H), 6.94 (d, *J* = 9 Hz, 2 H), 7.42 (d, *J* = 9 Hz, 2 H), 7.64 (dd, *J* = 3, 9 Hz, 1 H), 8.38 (dd, *J* = 1, 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.3 (s), 31.6 (s), 38.2 (s), 68.1 (s), 105.7 (s), 115.0 (s), 124.4 (s), 127.1 (s), 131.1 (s), 135.5 (s), 145.6 (s), 158.2 (s), 158.3 (s); MS *m/z* (rel intensity) 300 (M^++2, 4), 299 (M^++1, 41), 298 (M^+, 100), 283 (17), 269 (48), 213 (59), 199 (34), 185 (78), 184 (17), 171 (27), 170 (21), 115 (12). Found: *m/z* 298.2044. Calcd for $C_{19}H_{26}N_2O$: M, 298.2045.

2-(Dimethylamino)-5-(4-propoxyphenyl)pyrimidine (8b). Yield: 48% (Method B). Colorless needles, mp 106 °C (DSC on heating); R_f = 0.38 (hexane : Et_2O = 1 : 1). IR (KBr) 2964, 2934, 2876, 2859, 1606, 1534, 1510, 1409, 1394, 1328, 1284, 1277, 1253, 1242, 1178, 1117, 1069, 993, 971, 838, 827, 795 cm^{-1}; ^1H NMR (200 MHz) δ = 1.04 (t, *J* = 6 Hz, 3 H), 1.60-2.00 (m, 2 H), 3.22 (s, 6 H), 3.95 (t, *J* = 6 Hz, 2 H), 6.96 (d, *J* = 9 Hz, 1 H), 7.38 (d, *J* = 9 Hz, 2 H), 8.51 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 10.5 (s), 22.6 (s), 37.2 (s), 69.6 (s), 115.2 (s), 121.9 (s), 126.9 (s), 128.2 (s), 155.4 (s), 158.6 (s), 161.3 (s); MS *m/z* (rel intensity) 258 (M^++1, 17), 257 (M^+, 100), 228 (16), 214 (6), 186 (60), 185 (7), 171 (16). Found: *m/z* 257.1525. Calcd for $C_{15}H_{19}N_3O$: M, 257.1528.

2-(Dimethylamino)-5-(4-hexyloxyphenyl)pyrimidine (8c). Yield: 37% (Method B). Colorless needles, mp 96 °C (DSC on heating); R_f = 0.22 (hexane : Et_2O = 3 : 1). IR (KBr) 2950, 2940, 2869, 2785, 1604, 1534, 1511, 1467, 1409, 1374, 1324, 1307, 1282, 1251, 1203, 1177, 1115, 1058, 1028, 972, 837, 822, 657 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 6 Hz, 3 H), 1.20-1.90 (m, 8 H), 3.23 (s, 6 H), 3.98 (t, *J* = 6 Hz, 2 H), 6.96 (d, *J* = 9 Hz, 2 H), 7.38 (d, *J* = 9 Hz, 2 H), 8.51 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.6 (s), 37.2 (s), 68.1 (s), 115.2 (s), 121.9 (s), 126.8 (s), 128.1 (s), 155.4 (s), 158.1 (s), 161.3 (s); MS *m/z* (rel intensity) 300 (M^++1, 20), 299 (M^+, 100), 215 (49), 214 (49), 200 (33), 186 (89), 171 (16). Found: *m/z* 299.2003. Calcd for $C_{18}H_{25}N_3O$: M, 299.1998.

Reaction of Dichloro(ethyl)-4-methoxyphenylsilane with 5-Bromo-2-[methyl(trifluoromethyl)amino)]pyrimidine (2a). To a suspension of potassium

fluoride (174 mg, 3.0 mmol) in DMF (1.0 mL) were added dichloro(ethyl)-4-methoxyphenylsilane (138 mg, 0.58 mmol) and **2a** (89 mg, 0.34 mmol); the resulting mixture was stirred for 3 h at 60 °C. The reaction mixture was allowed to cool to room temperature; a solution of palladium(II) acetate ($Pd(OAc)_2$, 6.0 mg, 0.026 mmol) and tri(*o*-tolyl)phosphine (8.0 mg, 0.026 mmol) in DMF (1.0 mL) was added dropwise to the mixture. The whole mixture was stirred at 120 °C for 18 h, then cooled to room temperature, poured into sat. aq. NaCl, and extracted three times with ethyl acetate. The combined organic extracts were then dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure afforded a crude material, which was purified by thin-layer silica-gel chromatography (CH_2Cl_2) to give **6a** (64 mg, 66%) as colorless needles.

1-{4-[Methyl(trifluoromethyl)amino]phenyl}-(*trans*-4-propylcyclohexyl)cyclohexene (12a). A hexane solution of *n*-BuLi (1.6 M, 1.35 mL, 2.2 mmol) was added dropwise to a stirred solution of 4-bromo-*N*-methyl-*N*-trifluoromethylaniline (**10a**, 0.50 g, 1.97 mmol) in THF (2.0 mL) at –78 °C under an argon atmosphere. The solution was allowed to warm to –30 °C over 1 h before a THF (2.0 mL) solution of 4-(*trans*-4-propylcyclohexyl)cyclohexanone (0.50 g, 2.2 mmol) was added dropwise at the same temperature. After being stirred for 3 h at room temperature, the resulting mixture was treated with aq. $NaHCO_3$ solution, the aq. phase was extracted three times with Et_2O. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated. A stirred solution of the residual oil in benzene (15 mL) and pyridinium *p*-toluenesulfonate (PPTS, 20 mg) was heated to reflux for 20 min. The reaction mixture was poured into a $NaHCO_3$ solution; the aq. phase was extracted with Et_2O three times. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (hexane) to give **12a** (73 mg, 10% yield) as colorless needles and carbamic acid fluoride derivative **15** (0.48 g, 68% yield).

Compound **12a** showed phase transition temperature/°C: Cr 24 S_B 158 Iso (on heating), Iso 155 S_B -23 Cr (on cooling) (recryst. from EtOH); R_f = 0.79 (hexane : Et_2O = 10 : 1). IR (KBr) 2915, 2849, 1613, 1518, 1445, 1345, 1283, 1260, 1208, 1148, 1094, 1061, 924, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 0.76-1.54 (m, 12 H), 1.64-2.05 (m, 6 H), 2.15-2.54 (m, 3 H), 3.02 (q, *J* = 1 Hz, 3 H), 6.06-6.16 (m, 1 H), 7.17 (d, *J* = 9 Hz, 2 H), 7.35 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.04 (s); MS *m/z* (rel intensity) 380 (M^{+}+1, 19), 379 (M^{+}, 75), 357 (21), 254 (25), 240 (36), 227 (100), 215 (65), 205 (22), 201 (47), 188 (50), 129 (68), 109 (26), 83 (42), 81 (34), 69 (97). Found: *m/z* 379.2485. Calcd for $C_{23}H_{32}F_3N$: M, 379.2487.

***N*-Methyl-*N*-[4-(*trans*-4-propylcyclohexyl)cyclohexen-1-ylphenyl]carbamic**

Fluoride (15) showed phase transition temperature/°C: Cr 85 S_X 107 Sc 117 N 137 Iso; R_f = 0.54 (hexane : Et_2O = 10 : 1). ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.84-1.45 (m, 12 H), 1.72-2.06 (m, 6 H), 2.19-2.50 (m, 3 H), 3.34 (s, 3 H), 6.02-6.13 (m, 1 H), 7.14 (d, J = 9 Hz, 2 H), 7.39 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –16.6 (s); MS *m/z* (rel intensity) 359 (M^++2, 4), 358 (M^++1, 24), 357 (M^+, 100), 233 (23), 232 (37), 218 (66), 205 (91), 193 (42), 180 (14), 179 (84), 166 (37), 164 (20), 157 (15), 129 (26), 123 (13), 115 (16), 109 (35), 83 (26), 81 (22), 69 (57).

1-{4-[Ethyl(trifluoromethyl)amino]phenyl}-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexene (12b). In a manner similar to the synthesis of **12a**, compound **12b** (48 mg, 15% yield) was prepared from **10b** (0.22 g, 0.81 mmol) as colorless needles using PPTS (3 mg) and MS 4A. Phase transition temperature/°C: Cr 25 S_B 110 Iso (on heating), Iso 110 S_B –47 Cr (on cooling) (recryst. from EtOH); R_f = 0.82 (hexane : EtOAc = 20 : 1). IR (KBr) 2915, 2849, 1800, 1518, 1449, 1379, 1269, 1191, 1146, 1098, 1057, 912, 804 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.07 (t, J = 7 Hz, 3 H), 0.78-1.43 (m, 11 H), 1.72-2.03 (m, 7 H), 2.20-2.51 (m, 3 H), 3.35-3.45 (m, 2 H), 6.08-6.14 (m, 1 H), 7.17 (d, J = 9 Hz, 2 H), 7.36 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.18 (s); MS *m/z* (rel intensity) 394 (M^++1, 18), 393 (M^+, 72), 371 (38), 268 (21), 254 (30), 241 (78), 232 (22), 229 (54), 215 (33), 202 (28), 193 (31), 129 (58), 128 (41), 109 (29), 83 (40), 69 (100). Found: *m/z* 393.2635. Calcd for $C_{24}H_{34}F_3N$: M, 393.2643.

1-{3-Fluoro-4-[methyl(trifluoromethyl)amino]phenyl}-4-(*trans*-4-propylcyclohexyl)cyclohexene (13a). Cyclohexene derivative **13a** (49 mg, 28% yield) was prepared from **11a** (117 mg, 0.43 mmol) using *p*-toluenesulfonic acid monohydrate (11 mg) as a catalyst. Colorless needles, phase transition temperature/°C: Cr 62 S_B 101 Iso (recryst. from EtOH); R_f = 0.46 (hexane). IR (KBr) 2921, 2851, 1570, 1516, 1437, 1345, 1296, 1210, 1152, 1084, 1067, 814, 741 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78-1.49 (m 12 H), 1.68-2.08 (m, 6 H), 2.18-2.43 (m, 3H), 3.00 (q, J = 1 Hz, 3 H), 6.11-6.14 (m, 1 H), 7.05-7.21 (m, 3 H); ^{19}F NMR (188 MHz) δ = –61.46 (d, J = 5 Hz, 3 F), –121.52 - –121.71 (m, 1 F); MS m/z (rel intensity) 398 (M^++1, 7), 397 (M^+, 28), 273 (8), 272 (12), 271 (8), 258 (23), 233 (21), 219 (30), 206 (29), 164 (17), 148 (17), 147 (100), 146 (18), 127 (17), 123 (19), 109 (19), 83 (32), 69 (88), 67 (41). Found: *m/z* 397.2391. Calcd for $C_{23}H_{32}F_3N$: M, 397.2392.

1-{4-[Ethyl(trifluoromethyl)amino]-3-fluorophenyl}-4-(*trans*-4-propylcyclohexyl)cyclohexene (13b). Similarly, this compound **13b** (73 mg, 9% yield) was prepared from **12b** (0.52 g, 2.0 mmol) as colorless needles. Phase transition temperature/°C: Cr 38 S_B 73 Iso (recryst. from EtOH); R_f = 0.55 (hexane). IR (KBr)

2957, 2917, 2849, 1619, 1570, 1516, 1387, 1356, 1275, 1244, 1202, 1146, 1100, 1065, 957, 916 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.06 (t, *J* = 7 Hz, 3 H), 0.78-1.46 (m, 12 H), 1.48-2.08 (m, 6 H), 2.15-2.52 (m, 3 H), 3.30-3.46 (m, 2 H), 6.12-6.22 (m, 1 H), 7.06-7.22 (m, 3 H); ^{19}F NMR (188 MHz) δ = –58.16 (d, *J* = 5 Hz, 3 F), –121.11 - –121.18 (m, 1 F); MS *m/z* (rel intensity) 412 (M^++1, 7), 411 (M^+, 23), 392 (6), 260 (12), 259 (11), 250 (11), 244 (13), 233 (30), 192 (18), 161 (14), 147 (44), 146 (14), 134 (14), 109 (14), 83 (29), 81(10), 79 (11), 77 (10), 69 (100), 67 (71). Found: *m/z* 411.2545. Calcd for $C_{24}H_{33}F_4N$: M, 411.2549.

1-{2-[Methyl(trifluoromethyl)amino]pyridin-5-yl})-4-(*trans*-4-propyl-cyclohexyl)cyclohexene (14a). Similarly, trifluoromethylamine **14a** (0.19 g, 49% yield) was obtained from **1a** (0.26 g, 1.00 mmol) as colorless needles. Phase transition temperature/°C: Cr 82 S_A 139 Iso (on heating), Iso 139 S_A 64 Cr (on cooling) (recryst. from EtOH); R_f = 0.64 (hexane : Et_2O = 3 : 1). IR (KBr) 2959, 2851, 1601, 1559, 1435, 1352, 1339, 1281, 1117, 1073, 1022, 916, 820, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 0.92-1.51 (m, 11 H), 1.62-2.10 (m, 7 H), 2.14-2.53 (m, 3 H), 3.24 (q, *J* = 2 Hz, 3 H), 6.07-6.10 (m, 1 H), 7.02 (ddd, *J* = 1, 2, 9 Hz, 1 H), 7.59 (dd, *J* = 3, 9 Hz, 1 H), 8.37 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –58.09 (m); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 26.4 (s), 27.8 (s), 29.8 (s), 30.0 (s), 30.2 (s), 32.3 (q, *J* = 2 Hz), 33.5 (s), 37.7 (s), 38.8 (s), 39.8 (s), 42.5 (s), 113.4 (q, *J* = 4 Hz), 123.0 (q, *J* = 257 Hz), 125.2 (s), 132.7 (s), 133.0 (s), 134.0 (s), 144.3 (s), 152.2 (s); MS *m/z* (rel intensity) 381 (M^++1, 23), 380 (M^+, 58), 255 (23), 241 (29), 228 (30), 227 (12), 207 (31), 197 (21), 189 (38), 159 (54), 154 (20), 132 (70), 131 (37), 130 (36), 117 (25), 116 (26), 83 (22), 79 (37), 77 (34), 69 (100), 67 (76), 65 (33). Found: *m/z* 380.2432. Calcd for $C_{22}H_{31}F_3N_2$: M, 380.2439.

1-{2-[Ethyl(trifluoromethyl)amino]pyridin-5-yl}-4-(*trans*-4-propyl-cyclohexyl)cyclohexene (14b). This compound (154 mg, 20% yield) was prepared from **1b** (0.54 g, 2.0 mmol) in a manner similar to the procedure for **11a**. Colorless needles, phase transition temperature/°C: Cr 78 S_A 98 Iso (on heating), Iso 98 S_A 61 Cr (on cooling) (recryst. from EtOH); R_f = 0.72 (hexane : Et_2O = 5 : 1). IR (KBr) 2924, 1800, 1603, 1559, 1499, 1389, 1260, 1220, 1022, 943, 811, 802 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.21 (t, *J* = 7 Hz, 3 H), 0.75-1.43 (m, 11 H), 1.62-2.10 (m, 7 H), 2.43-2.20 (m, 3 H), 3.78-3.96 (m, 2 H), 6.05-6.15 (m, 1 H), 6.97-7.02 (m, 1 H), 7.60 (dd, *J* = 3, 9 Hz, 1 H), 8.37 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –55.95 (m); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 14.4 (s), 20.0 (s), 26.4 (s), 27.7 (s), 29.8 (s), 30.0 (s), 30.2 (s), 33.5 (s), 37.6 (s), 38.8 (s), 39.8 (s), 40.5 (m), 42.5 (s), 113.3 (q, *J* = 4 Hz), 123.1 (q, *J* = 261 Hz), 125.2 (s), 132.4 (s), 133.1 (s), 134.0 (s), 144.5 (s), 151.3 (s); MS *m/z* (rel intensity) 394 (M^+, 10), 379 (16), 227 (19), 207 (29), 173 (8), 156 (10), 155 (22), 147 (14),

121 (14), 117 (15), 105 (27), 97 (14), 95 (17), 91 (21), 85 (26), 83 (31), 71 (30), 69 (100), 67 (39). Found: *m/z* 394.2602. Calcd for $C_{23}H_{33}F_3N_2$: M, 394.2596.

1-Nitro-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]benzene (20). To a stirred mixture of *trans*-4-(*trans*-4-propylcyclohexyl)cyclohexylbenzene (**19**, 22.8 g, 0.080 mol), conc. sulfuric acid (26 mL), and dichloromethane (15 mL) was added dropwise nitric acid (61 wt%, 28 mL) at 0 °C over 1 h. The resulting mixture was allowed to warm to room temperature in 1 h under vigorous stirring and then poured to ice. The resulting pale yellow precipitates were filtered by suction. The filtrate was neutralized with NaOH and extracted three times with Et_2O. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue and the precipitates were combined and purified by recrystallization from EtOH to give **20** (18.4 g, 81% yield) as a yellow powder. Phase transition temperature/°C: Cr 101 N 207 Iso (hexane-EtOH); R_f = 0.30 (hexane). IR (KBr) 2930, 2851, 1598, 1514, 1450, 1345, 1110, 980, 849, 860, 750 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78-1.55 (m 15 H), 1.63-2.00 (m, 8 H), 2.56 (tt, J = 3, 12 Hz, 1 H), 7.34 (d, J = 9 Hz, 2 H), 8.13 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.3 (s), 20.0 (s), 30.0 (s), 30.0 (s), 33.5 (s), 34.2 (s), 37.6 (s), 39.8 (s), 42.7 (s), 43.3 (s), 44.7 (s), 123.5 (s), 127.6 (s), 146.2 (s), 155.2 (s); MS *m/z* (rel intensity) 329 (M^+, 7), 312 (3), 299 (19), 133 (12), 132 (86), 126 (12), 119 (61), 109 (11), 107 (20), 106 (37), 95 (12), 93 (14), 83 (42), 81 (35), 69 (100), 67 (37), 65 (15). Found: C, 76.33; H, 9.62; N, 4.33%. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25%.

4-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]aniline (21). A mixture of **20** (17.6 g, 53 mmol) and palladium on activated carbon (10 wt%, 0.59 g) in EtOH (50 mL) was vigorously stirred for 3.5 h at room temperature under a hydrogen atmosphere with a slightly positive pressure. The mixture was filtered through a pad of Cellite, which was washed with Et_2O; the combined filtrates were concentrated under reduced pressure. The residue was purified by recrystallization from EtOH to give **21** (14.4 g, 90% yield) as a colorless powder (mp 174 °C). R_f = 0.12 (hexane : Et_2O = 5 : 1). IR (KBr) 3393, 3308, 3210, 2953, 2849, 1615, 1518, 1441, 1267, 1183, 826, 776, 708, 642 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.78-1.48 (m 15 H), 1.64-1.96 (m, 8 H), 2.33 (tt, J = 3, 12 Hz, 1 H), 3.51 (br, 2 H), 6.62 (d, J = 8 Hz, 2 H), 6.99 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.4 (s), 33.6 (s), 34.8 (s), 37.6 (s), 39.8 (s), 42.9 (s), 43.4 (s), 43.7 (s), 115.1 (s), 127.4 (s), 138.1 (s), 144.1 (s); MS *m/z* (rel intensity) 300 (M^++1, 5), 299 (M^+, 31), 212 (2), 191 (2), 158 (5), 135 (7), 133 (22), 132 (100), 121 (5), 120 (5), 119 (51), 106 (30), 81 (12), 65 (9). Found: *m/z* 299.2614. Calcd for $C_{21}H_{33}N$: M, 299.2613.

***N*-Methy-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (22a):**

Method A.[13] A suspension of sodium methoxide (1.54 g, 29 mmol), paraformaldehyde (0.26 g, 7.7 mmol) and **21** (1.53 g, 5.1 mmol) in methanol (80 mL) was stirred for 17 h at 40 °C before sodium borohydride (0.44 g, 12 mmol) was added at room temperature. The resulting mixture was heated at 50 °C for 9 h; the methanol was removed under reduced pressure. The solid residure was partitioned between aq. $NaHCO_3$ solution and diethyl ether; the organic phase was separated; the aq. phase was extracted three times with diethyl ether. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (CH_2Cl_2) to give **22a** (0.95 g, 59% yield) as a colorless powder.

Method B. A hexane solution of *n*-BuLi (1.6 M, 6.6 mL, 10.5 mmol) was slowly added to a stirred solution of **21** (3.0 g, 10.0 mmol) in THF (50 mL) at –78 °C. After the solution was allowed to warm to 0 °C over 1 h, methyl iodide (1.25 mL, 20 mmol) was added dropwise to the mixture at 0 °C. The resulting mixture was stirred at room temperature for 3 h and then treated with aq. $NaHCO_3$ solution. The organic phase was separated; the aq. phase was extracted with diethyl ether three times. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (hexane : Et_2O = 10 : 1) to give **22a** (0.88 g, 28% yield) and *N,N*-dimethyl derivative **24a** (0.23 g, 7% yield).

22a: A colorless powder, phase transition temperature/°C: Cr 62 S_B 132 Iso; R_f = 0.41 (hexane : Et_2O = 10 : 1). IR (KBr) 3297, 2955, 2936, 2849, 1615, 1520, 1443, 1265, 1186, 1148, 1057, 974, 816 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.80-1.52 (m, 15 H), 1.71-1.96 (m, 8 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 2.81 (s, 3 H), 3.57 (br, 1 H), 6.56 (d, *J* = 9 Hz, 2 H), 7.04 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.5 (s), 30.9 (s), 33.6 (s), 34.9 (s), 37.6 (s), 39.8 (s), 43.0 (s), 43.4 (s), 43.7 (s), 112.4 (s), 127.4 (s), 136.6 (s), 147.4 (s); MS *m/z* (rel intensity) 315 (M^++2, 1), 314 (M^++1, 10), 313 (M^+, 45), 147 (14), 146 (100), 133 (36), 132 (14), 120 (41), 107 (7), 106 (5), 81 (6), 69 (10). Found: *m/z* 313.2765. Calcd for $C_{22}H_{35}N$: M, 313.2769.

***N,N*-Dimethyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (24a).** A colorless powder, phase transition temperature/°C: Cr 59 S_B 189 Iso; R_f = 0.63 (hexane : Et_2O = 10 : 1). IR (KBr) 2951, 2849, 1617, 1524, 1447, 1350, 1229, 1165, 1063, 949, 808 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.76-1.51 (m, 16 H), 1.67-1.98 (m, 7 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 2.92 (s, 6 H), 6.66 (d, *J* = 9 Hz, 2 H), 7.06 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.1 (s), 30.1 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 43.6 (s), 112.9 (s), 127.3 (s), 136.3 (s), 149.0 (s); MS *m/z* (rel intensity) 329 (M^++2, 1), 328 (M^++1, 17), 327 (M^+, 65), 161 (15), 160 (100), 147 (33), 146 (22), 134 (55), 121 (7), 81 (8), 69 (8). Found: C, 83.95; H, 11.38; N, 4.26%. Calcd for $C_{23}H_{37}N$: C, 84.34; H, 11.39; N, 4.28%. Found: *m/z* 327.2930.

Calcd for $C_{23}H_{37}N$: M, 327.2926.

***N*-Ethyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (22b).** Aniline derivative **22b** (1.43 g, 79% yield) was obtained from **21** (1.65 g, 5.5 mmol) in a manner similar to the procedure of **22a** (Method B) except for the purification by recrystallization from EtOH-hexane and column chromatography (hexane : Et_2O = 5 : 1). A colorless powder, phase transition temperature/°C: Cr 94 N 225 Iso, R_f = 0.65 (hexane : Et_2O = 5 : 1). IR (KBr) 3450, 2920, 2840, 1869, 1616, 1522, 1446, 1350, 1229, 1165, 949, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 1.23 (t, *J* = 7 Hz, 3 H), 0.80-1.50 (m, 15 H), 1.71-1.96 (m, 8 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 3.13 (q, *J* = 7 Hz, 2 H), 3.40 (br, 1 H), 6.55 (d, *J* = 8 Hz, 2 H), 7.01 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 15.0 (s), 20.0 (s), 30.1 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.7 (s), 38.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 43.7 (s), 112.8 (s), 127.4 (s), 136.9 (s), 148.5 (s); MS *m/z* (rel intensity) 328 (M^++1, 8), 327 (M^+, 44), 312 (11), 254 (8), 207 (16), 161 (16), 160 (100), 148 (26), 134 (37), 132 (50), 128 (11), 121 (20), 118 (18), 117 (14), 115 (12), 91 (14), 83 (26), 81 (25), 71 (20), 69 (40). Found: C, 84.75; H, 11.70; N, 4.37%. Calcd for $C_{23}H_{37}N$: C, 84.34; H, 11.39; N, 4.28%. Found: *m/z* 327.2919. Calcd for $C_{23}H_{37}N$: M, 327.2926.

***N*-Propyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (22c).** In a manner similar to the procedure for **22a**, this compound (0.27 g, 0.80 mmol) was prepared from **21** (0.30 g, 80% yield) as a colorless powder. Phase transition temperature/°C: Cr 99 S_X 107 N 201 Iso; R_f = 0.52 (hexane : Et_2O = 5 : 1). IR (KBr) 3399, 2917, 2849, 1619, 1522, 1478, 1449, 1412, 1316, 1254, 1183, 978, 814 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.98 (t, *J* = 7 Hz, 3 H), 0.79-1.20 (m, 15 H), 1.47-1.95 (m, 10 H), 2.32 (tt, *J* = 3, 12 Hz, 1 H), 3.06 (t, *J* = 7 Hz, 2 H), 3.51 (br, 1 H), 6.54 (d, *J* = 9 Hz, 2 H), 7.01 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.7 (s), 14.5 (s), 20.1 (s), 22.9 (s), 30.2 (s), 30.6 (s), 33.7 (s), 35.0 (s), 37.8 (s), 38.9 (s), 43.1 (s), 43.6 (s), 43.8 (s), 46.2 (s), 112.8 (s), 127.5 (s), 136.8 (s), 146.7 (s); MS *m/z* (rel intensity) 342 (M^++1, 22), 341 (M^+, 85), 313 (18), 312 (100), 175 (15), 174 (99), 161 (25), 148 (24), 146 (13), 144 (12), 132 (50), 130 (10), 121 (10), 120 (12), 119 (12), 118 (11), 106 (17), 83 (14), 81 (19), 69 (35), 67 (22). Calcd for $C_{24}H_{39}N$: C, 84.39; H, 11.51; N, 4.10%. Found: C, 84.19; H, 11.31; N, 4.05%.

***N*-Ethyl-*N*-methyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}-amine (24b).** In a manner similar to the procedure for **22a**, compound **24b** was prepared from **22b** (90 mg, 0.27 mmol) in 91% yield as a colorless powder, mp 181 °C; R_f = 0.65 (hexane : Et_2O = 5 : 1). IR (KBr) 2930, 2850, 1867, 1614, 1530, 1466, 1370, 1269, 1211, 1157, 1082, 978, 812 cm^{-1}. ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 1.10 (t, *J* = 7 Hz, 3 H), 0.76-1.51 (m, 16 H), 1.67-1.98 (m, 7 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 2.87 (s, 3 H), 3.35 (q, *J* = 7 Hz, 2 H), 6.66 (d, *J* = 9 Hz, 2 H), 7.06 (d, *J* = 9 Hz, 2 H); ^{13}C NMR

(50.3 MHz) δ = 11.3 (s), 14.1 (s), 20.1 (s), 22.7 (s), 30.2 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.5 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 47.0 (s), 112.6 (s), 127.3 (s), 135.6 (s), 147.4 (s); MS *m/z* (rel intensity) 343 (M^++2, 4), 342 (M^++1, 25), 341 (M^+, 100), 327 (26), 326 (95), 175 (13), 174 (91), 161 (16), 160 (11), 148 (46), 146 (48), 131 (10), 120 (12), 81 (16), 69 (25), 67 (17). Found: *m/z* 341.3080. Calcd for $C_{24}H_{39}N$: M, 341.3082.

***N*-Methyl-*N*-propyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}-amine (24c).** This compound **24c** (0.33 g, 93% yield) was prepared from **22c** (0.34 g, 1.00 mmol) as a colorless powder, mp 168 °C. R_f = 0.50 (hexane : EtOAc = 10 : 1). IR (KBr) 2851, 1617, 1520, 1447, 1372, 1294, 1244, 1209, 1156, 1082, 968, 810 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 8 Hz, 3 H), 0.91 (t, *J* = 8 Hz, 3 H), 0.76-1.51 (m, 16 H), 1.58 (q, *J* = 8 Hz, 2 H), 1.63-1.98 (m, 7 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 2.88 (s, 3 H), 3.21 (t, *J* = 7 Hz, 2 H), 6.66 (d, *J* = 9 Hz, 2 H), 7.06 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.5 (s), 14.4 (s), 20.1 (s), 30.1 (s), 30.5 (s), 33.6 (s), 34.6 (s), 37.7 (s), 38.3 (s), 39.9 (s), 43.0 (s), 43.5 (s), 54.8 (s), 112.1 (s), 127.2 (s), 135.3 (s), 147.7 (s); MS *m/z* (rel intensity) 356 (M^++1, 7), 355 (M^+, 29), 327 (25), 326 (100), 200 (3), 188 (7), 146 (22), 131 (6), 120 (7), 93 (6), 81 (13), 69 (17). Found: *m/z* 355.3240. Calcd for $C_{25}H_{41}N$: M, 355.3239.

A General Procedure for the Preparation of Methyl Dithiocarbamates (23).

A hexane solution (1.6 M) of *n*-BuLi (7.5 mL, 12 mmol) was slowly added dropwise to a stirred solution of secondary amine **22** (10.0 mmol) in THF (20 mL) at –10 °C. The solution was allowed to warm to 0 °C over 1 h; CS_2 (1.2 mL, 20 mmol) was added dropwise to this mixture at 0 °C; the mixture was stirred for 12 h at room temperature; MeI (1.3 mL, 20 mmol) was added dropwise to the reaction mixture at 0 °C. The whole mixture was stirred at room temperature for 3-5 h and was poured to sat. aq. $NaHCO_3$. The organic phase was separated; the aq. phase was extracted three times with diethyl ether. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography or by recrystallization to give **23.** Yield and spectral properties of products were as follows.

Methyl *N*-Methyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}-dithiocarbamate (23a). Yield: 71%, pale yellow needles, mp 167.4-169.2 °C (EtOH). R_f = 0.57 (hexane : Et_2O = 10 : 1). IR (KBr) 2951, 2849, 1507, 1447, 1368, 1266, 1100, 1021, 955, 839 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 0.75-1.55 (m, 15 H), 1.64-2.01 (m, 8 H), 2.41-2.54 (m, 1 H), 2.53 (s, 3 H), 3.76 (s, 3 H), 7.14 (d, *J* = 8 Hz, 2 H), 7.28 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 20.8 (s), 30.1 (s), 30.2 (s), 33.6 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.8 (s), 43.4 (s), 44.3 (s), 46.8 (s), 126.5 (s), 128.0 (s), 142.5 (s), 148.9 (s), 200.5 (s); MS *m/z* (rel intensity) 404 (M^++1, 1), 403 (M^+,

4), 357 (2), 356 (6), 161 (2), 148 (2), 115 (1), 91 (5), 90 (5), 89 (5), 88 (100), 69 (5). Calcd for $C_{24}H_{37}NS_2$: C, 71.41; H, 9.24; N, 3.47%. Found: C, 71.29; H, 9.41; N, 3.39%.

Methyl *N*-Ethyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}-dithiocarbamate (23b). Yield: 95%, pale yellow needles, mp 152.1-153.0 °C (EtOH). R_f = 0.53 (hexane : Et_2O = 10 : 1). IR (KBr) 2924, 2851, 1503, 1456, 1450, 1406, 1273, 1235, 1103, 1073, 994, 961, 899, 812 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.26 (t, J = 7 Hz, 3 H), 0.79-1.57 (m, 15 H), 1.68-2.06 (m, 8 H), 2.42-2.55 (m, 1 H), 2.51 (s, 3 H), 4.33 (q, J = 7 Hz, 2 H), 7.10 (d, J = 9 Hz, 2 H), 7.28 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.9 (s), 14.4 (s), 20.0 (s), 20.5 (s), 30.1 (s), 30.2 (s), 33.5 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.8 (s), 43.3 (s), 44.3 (s), 52.5 (s), 127.5 (s), 127.9 (s), 140.7 (s), 148.9 (s), 199.9 (s); MS *m/z* (rel intensity) 417 (M^+, 5), 415 (2), 413 (1), 289 (1), 287 (1), 280 (1), 276 (2), 234 (2), 228 (1), 208 (2), 182 (2), 148 (4), 121 (6), 118 (7), 115 (3), 112 (5), 110 (4), 103 (11), 102 (100), 91 (7), 85 (8), 83 (10), 81 (10), 74 (12), 69 (20). Calcd for $C_{25}H_{39}NS_2$: C, 71.89; H, 9.41; N, 3.35%. Found: C, 71.51; H, 9.61; N, 3.16%. Found: *m/z* 417.2523. Calcd for $C_{25}H_{39}NS_2$: M, 417.2524.

Methyl *N*-Propyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}-dithiocarbamate (23c). Yield: 81%, pale yellow needles, mp 122.2-123.1 °C (EtOH-hexane). R_f = 0.66 (hexane : Et_2O = 10 : 1). IR (KBr) 2921, 2830, 1505, 1441, 1397, 1362, 1296, 1258, 1231, 1136, 1103, 955, 835, 828 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.91 (t, J = 7 Hz, 3 H), 0.72-1.58 (m, 15 H), 1.60-2.07 (m, 10 H), 2.41-2.62 (m, 1 H), 2.51 (s, 3 H), 4.18-4.25 (m, 2 H), 7.09 (d, J = 8 Hz, 2 H), 7.27 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.0 (s), 14.4 (s), 20.0 (s), 20.6 (s), 30.1 (s), 30.3 (s), 33.6 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.9 (s), 43.4 (s), 44.3 (s), 59.2 (s), 127.5 (s), 127.9 (s), 141.0 (s), 149.0 (s), 200.5 (s). Calcd for $C_{26}H_{41}NS_2$: C, 72.33; H, 9.57; N, 3.24%. Found: C, 72.18; H, 9.54, N, 3.07%.

A General Procedure for the Preparation of Trifluoromethylamino-substituted LCs with a Cyclohexylarene Core.

Method A: To a stirred suspension of $TBAH_2F_3$ (7.5 g, 25 mmol)[17] and DBH (5.7 g, 20 mmol) in dichloromethane (10 mL) was added dropwise a solution of dithiocarbamate **23** (5.0 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C until all the substrate was consumed and was then poured into an aq. buffer solution of $NaHCO_3$/NaOH/$NaHSO_3$ (pH = 10). The resultant was extracted three times with Et_2O. The combined organic layer was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give the corresponding trifluoromethylamines **16**.

Method B: A suspension of cyclohexene derivative **12**, **13**, or **14** (0.12 mmol) and

Raney Ni (W 2, 100 mg) in EtOAc (8 mL) was vigorously stirred for 1 h at room temperature under a hydrogen atmosphere with a slightly positive pressure. The mixture was filtered, and the filtrate was concentrated. The residue was purified by silica-gel column chromatography (hexane) to give **16**, **17**, or **18** and its *cis*-isomer. Separation of the stereoisomers was carried out with recycling preparative HPLC ($CHCl_3$ eluent).

1-{4-[Methyl(trifluoromethyl)amino]phenyl}-*trans*-4-(*trans*-4-propylcyclohexyl)-cyclohexane (16a). This compound was prepared by Method A in a quantitative yield as colorless needles. Recrystallization from EtOH gave an analytical sample, which showed phase transition temperature/°C: 20 S_B 173 Iso. R_f = 0.79 (hexane : Et_2O = 5 : 1). IR (KBr) 2957, 2919, 2849, 1617, 1518, 1447, 1345, 1267, 1204, 1150, 1092, 1059, 897, 833 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78-1.55 (m, 15 H), 1.68-2.00 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 3.00 (q, J = 1 Hz, 3 H), 7.17 (s, 4 H); ^{19}F NMR (188 MHz) δ = –61.23 (s); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.3 (s), 33.6 (s), 34.6 (s), 36.4 (q, J = 2 Hz), 37.7 (s), 39.8 (s), 42.9 (s), 43.4 (s), 44.1 (s), 123.6 (q, J = 257 Hz), 125.1 (s), 127.4 (s), 140.4 (s), 146.1 (s); MS *m/z* (rel intensity) 383 (M^++2, 1), 382 (M^++1, 17), 381 (M^+, 66), 359 (13), 215 (13), 214 (48), 202 (13), 201 (91), 188 (62), 179 (18), 166 (10), 144 (5), 132 (7), 115 (10), 111 (10), 109 (15), 97 (17), 95 (11), 91 (17), 83 (57), 81(19), 77 (12), 69 (100), 67 (40). Calcd for $C_{23}H_{34}F_3N$: C, 72.41; H, 8.98; N, 3.67%. Found: C, 72.42; H, 8.91; N, 3.74%.

1-[4-{Ethyl(trifluoromethyl)amino}phenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)-cyclohexane (16b). Method A, quantitative yield, colorless needles. Phase transition temperature/°C: Cr 35 S_B 141 Iso (EtOH); R_f = 0.79 (hexane : Et_2O = 10 : 1). IR (KBr) 2919, 2849, 1516, 1449, 1381, 1271, 1196, 1144, 1098, 1055, 912, 813 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.07 (t, J = 7 Hz, 3 H), 0.80-1.56 (m 15 H), 1.68-2.01 (m, 8 H), 2.44 (tt, J = 3, 11 Hz, 1 H), 3.37 (q, J = 7 Hz, 2 H), 7.16 (s, 4 H); ^{19}F NMR (188 MHz) δ = –58.22 (s); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 14.4 (s), 20.1 (s), 30.2 (s), 30.4 (s), 33.7 (s), 34.6 (s), 37.7 (s), 39.8 (s), 43.0 (s), 43.5 (s), 43.9 (q, J = 1.3 Hz), 44.2 (s), 123.7 (q, J = 255 Hz), 126.9 (q, J = 1 Hz), 127.4 (s), 138.3 (s), 146.1 (s); MS *m/z* (rel intensity) 396 (M^++1, 8), 395 (M^+, 33), 373 (21), 228 (23), 215 (33), 202 (20), 193 (25), 180 (15), 158 (7), 132 (8), 115 (9), 109 (12), 97 (12), 91 (8), 83 (38), 81 (33), 79 (14), 69 (100), 67 (33). Calcd for $C_{24}H_{36}F_3N$: C, 72.88; H, 9.17; N, 3.54%. Found: C, 73.11; H, 9.51; N, 3.46%. Found: *m/z* 395.2792. Calcd for $C_{24}H_{36}F_3N$: M, 395.2800.

1-(*trans*-4-Propylcyclohexyl)-*trans*-4-[4-{propyl(trifluoromethyl)amino}-phenyl]cyclohexane (16c). Method A, 94% yield. Colorless needles; phase transition temperature/°C: Cr 57 S_B 109 Iso (on heating), Iso 108 S_B –18 Cr (on cooling) (recryst. from EtOH); R_f = 0.62 (hexane). IR (KBr) 2923, 2851, 1514, 1451, 1381, 1358, 1293, 1258, 1240, 1190, 1148, 1057, 928, 837 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz,

6 H), 0.77-1.55 (m, 18 H), 1.64-2.00 (m, 7 H), 2.42 (tt, J = 3, 12 Hz, 1 H), 3.25 (dt, J = 1, 7 Hz, 2 H), 7.16 (s, 4 H); ^{19}F NMR (188 MHz) δ = –58.39 (s); ^{13}C NMR (50.3 MHz) δ = 11.0 (s), 13.8 (s), 20.1 (s), 21.5 (s), 30.2 (s), 30.4 (s), 33.7 (s), 34.6 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 44.2 (s), 50.9 (s), 123.7 (q, J = 254 Hz), 127.1 (q, J = 1 Hz), 127.4 (s), 138.6 (s), 146.6 (s); MS *m/z* (rel intensity) 410 (M^++1, 16), 409 (M^+, 58), 380 (13), 348 (8), 314 (7), 304 (9), 242 (29), 229 (23), 208 (15), 200 (29), 156 (12), 127 (13), 118 (16), 103 (18), 83 (23), 81 (36), 79 (20), 70 (28), 69 (100) 67 (58). Calcd for $C_{25}H_{38}F_3N$: C, 73.31; H, 9.35; N, 3.42%. Found: C, 72.77; H, 9.25; N, 3.33%. Found: m/z 409.2965. Calcd for $C_{25}H_{38}F_3N$: M, 409.2956.

1-[3-Fluoro-4-{methyl(trifluoromethyl)amino}phenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (17a). A 2 : 1 mixture of **17a** and *cis*-isomer (48 mg, quantitative) was obtained by Method B from **13a** (47 mg, 0.118 mmol). Separation of **17a** and its *cis*-isomer was carried out by recycling preparative HPLC ($CHCl_3$ eluent) to give **17a** as colorless needles, phase transition temperature/°C: Cr 62 S_B 101 Iso (EtOH). R_f = 0.89 (hexane : EtOAc = 10 : 1). IR (KBr) 2924, 2851, 1580, 1518, 1449, 1409, 1348, 1296, 1196, 1148, 1084, 1061, 956, 941, 889, 826 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.60-1.52 (m, 15 H), 1.60-1.98 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 2.99 (q, J = 1 Hz, 3 H), 6.98-7.02 (m, 2 H), 7.16-7.35 (m, 1 H); ^{19}F NMR (188 MHz) δ = –61.47 (dm, J = 5 Hz), –120.75—121.63 (m); MS *m/z* (rel intensity) 399 (M^+, 22), 377 (8), 232 (4), 220 (3), 219 (24), 206 (26), 197 (11), 136 (8), 83 (42), 81 (25), 69 (100), 66 (35). Calcd for $C_{23}H_{33}F_4N$: C, 69.15; H, 8.33; N, 3.51%. Found: C, 68.99; H, 8.38; N, 3.55%.

1-[4-{Ethyl(trifluoromethyl)amino}-3-fluorophenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (17b). A 2.7 : 1 mixture of compound **17b** and its *cis*-isomer was prepared (15 mg, 20% yield) from **13b** (73 mg, 0.177 mmol) by Method B. Purification of **17b** was carried out by recycling preparative HPLC ($CHCl_3$ eluent) as colorless needles, phase transition temperature/°C: Cr 38 S_B 73 Iso (EtOH). R_f = 0.55 (hexane). IR (KBr) 2924, 2851, 1578, 1541, 1449, 1387, 1271, 1284, 1196, 1146, 1096, 1061, 954, 826 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.06 (t, J = 7 Hz, 3 H), 0.80-1.58 (m, 15 H), 1.65-1.96 (m, 8 H), 2.44 (tt, J = 3, 12 Hz, 1 H), 3.37 (q, J = 7 Hz, 2 H), 6.92-6.98 (m, 2 H), 7.16-7.20 (m, 1 H); ^{19}F NMR (188 MHz) δ = –58.48 (dm, J = 5 Hz), –121.11—121.24 (m); MS *m/z* (rel intensity) 414 (M^+, 9), 413 (M^+, 51), 391 (19), 233 (20), 220 (18), 218 (14), 211 (10), 192 (12), 109 (8), 97 (8), 95 (11), 83 (44), 81 (25), 79 (15), 69 (100). Found: *m/z* 413.2697. Calcd for $C_{24}H_{35}F_4N$: M, 413.2705.

1-[2-{Methyl(trifluoromethyl)amino}pyridin-5-yl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (18a). A 1 : 1 mixture of **18a** and its *cis*-isomer (92 mg, quantitative) was obtained by Method B using EtOH as a hydrogenation solvent from **14a**

(92 mg, 0.24 mmol). *Trans*-isomer **18a** was separated by recycling preparative HPLC ($CHCl_3$ eluent) as colorless needles, phase transition temperature/°C: Cr 62 S_X 73 S_B 120 N 121 Iso (on heating), Iso 121 N 119 S_B 70 S_X 37 Cr (on coolong) (recryst. from EtOH). R_f = 0.67 (hexane : Et_2O = 5 : 1). IR (KBr) 2923, 2851, 1605, 1572, 1499, 1447, 1437, 1404, 1352, 1337, 1277, 1200, 1123, 1103, 1075, 1024, 830 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.75-1.53 (m, 15 H), 1.63-1.97 (m, 8 H), 2.43 (tt, *J* = 3, 12 Hz, 1 H), 3.22 (q, *J* = 2 Hz, 3 H), 7.03 (ddd, *J* = 1, 2, 9 Hz, 1 H), 7.45 (dd, *J* = 3, 9 Hz, 1 H), 8.20 (dd, *J* = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –58.36 (dq, *J* = 2, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.2 (s), 32.5 (s), 33.6 (s), 34.4 (s), 37.6 (s), 39.8 (s), 41.3 (s), 42.8 (s), 43.4 (s), 114.1 (q, *J* = 4 Hz), 123.1 (q, *J* = 256 Hz), 136.1 (s), 137.9 (s), 146.5 (s), 152.0 (s); MS *m/z* (rel intensity) 383 (M^++1, 10), 382 (M^+, 38), 381 (5), 362 (11), 313 (36), 286 (20), 215 (10), 189 (22), 183 (10), 157 (9), 133 (25), 120 (11), 116 (14), 106 (28), 105 (14), 104 (14), 93 (14), 83 (25), 81 (16), 79 (27), 78 (18), 77 (15), 69 (100), 67 (43). Calcd for $C_{22}H_{33}F_3N_2$: C, 69.08; H, 8.70; N, 7.32%. Found: C, 69.17; H, 9.24; N, 7.36%. Found: *m/z* 382.2590. Calcd for $C_{22}H_{33}F_3N_2$: M, 382.2596.

1-[2-{Ethyl(trifluoromethyl)amino}pyridin-5-yl}-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (18b). A 1 : 1 mixture of **18b** and its *cis*-isomer (122 mg, 79% yield) was obtained from **14b** (155 mg, 0.39 mmol) by Method B. Separation of **18b** was carried out by recycling preparative HPLC ($CHCl_3$ eluent). Colorless needles; phase transition temperature/°C: Cr 50 S_B 100 Iso (on heating), Iso 98 S_B 48 Cr (on cooling) (recryst. from EtOH); R_f = 0.68 (hexane : Et_2O = 5 : 1). IR (KBr) 2917, 2851, 2361, 1610, 1568, 1495, 1449, 1387, 1329, 1281, 1260, 1183, 1132, 1096, 1069, 1024, 945, 926, 822, 785, 758 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.20 (t, *J* = 7 Hz, 3 H), 0.76-1.55 (m, 15 H), 1.63-1.96 (m, 8 H), 2.43 (tt, *J* = 3., 12 Hz, 1 H), 3.75-3.89 (m, 2 H), 6.99 (dm, *J* = 9 Hz, 1 H), 7.44 (dd, *J* = 2, 9 Hz, 1 H), 8.20 (dm, *J* = 2 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –56.07 (dm, *J* = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.2 (s), 14.4 (s), 20.4 (s), 30.1 (s), 30.2 (s), 33.6 (s), 34.4 (s), 37.6 (s), 39.8 (s), 40.6 (br), 41.3 (s), 42.8 (s), 43.4 (s), 114.0 (q, *J* = 4 Hz), 123.1 (q, *J* = 256 Hz), 136.0 (s), 137.5 (s), 146.6 (s), 151.1 (s); MS *m/z* (rel intensity) 396 (M^+, 5), 382 (30), 381 (100), 361 (30), 327 (36), 203 (13), 181 (12), 160 (11), 155 (28), 147 (11), 131 (10), 120 (9), 116 (9), 105 (13), 83 (15), 81 (19), 79 (13), 70 (17), 69 (72), 67 (34). Calcd for $C_{23}H_{35}F_3N_2$: C, 69.67; H, 8.90; N, 7.06%. Found: C, 69.33; H, 8.98; N, 6.90%. Found: *m/z* 396.2745. Calcd for $C_{23}H_{35}F_3N_2$: M, 396.2752.

III-4. References and Notes

1) a) H. Nohira, *Nippon Kagaku Kaishi*, **1994**, 467; b) G. Weber, U. Finkenzeller, T. Geelhaar, H. J. Plach, B. Rieger, and L. Pohl, *Liquid Cryst.*, **5**, 1381 (1989); c) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.*, **209**, 1 (1991); d) G. W. Gray, M. Hird, and K. J. Toyne, *Mol. Cryst. Liq. Cryst.*, **204**, 91 (1991).

2) a) K. Kanie, Y. Tanaka, M. Shimizu, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1997**, 827; b) K. Kanie, Y. Tanaka, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1998**, 1169; c) K. Kanie, M. Kuroboshi, S. Takehara, and T. Hiyama, *J. Fluorine Chem.*, **97**, 201 (1999); d) P. Kirsch and K. Tarumi, *Angew. Chem., Int. Ed.*, **37**, 484 (1998); e) M. Hird, G. W. Gray, and K. J. Toyne, *Liq. Cryst.*, **11**, 531 (1992); f) M. Hird, K. J. Toyne, A. J. Slaney, J. W. Goodby, and G. W. Gray, *J. Chem. Soc., Perkin Trans. 2*, **1993**, 2337.

3) R. Eidenschink, *Mol. Cryst. Liq. Cryst.*, **94**, 119 (1983).

4) M. Hudlicky and A. E. Pavlath, "*Chemistry of Organic Fluorine Compounds II. A Critical Review*," ACS Monograph 187, Washington, DC (1995).

5) a) M. Kuroboshi and T. Hiyama, *Yuki Gosei Kagaku Kyokai Shi*, **51**, 1124 (1993); b) K. Kanie, Y. Tanaka, M. Shimizu, M. Kuroboshi, and T. Hiyama, *Chem. Commun.*, **1997**, 309; c) M. Kuroboshi, K. Suzuki, and T. Hiyama, *Tetrahedron Lett.*, **33**, 4173 (1992); d) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1939 (1998); e) M. Kuroboshi and T. Hiyama, *Synlett*, **1991**, 909.

6) a) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.*, **33**, 4177 (1992); perfluoroalkylamines are also prepared, see: b) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.*, **35**, 3983 (1994); c) M. Kuroboshi, K. Mizuno, K. Kanie, and T. Hiyama, *Tetrahedron Lett.*, **36**, 563 (1995); d) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683; e) K. Kanie, K. Mizuno, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1973 (1998).

7) a) W. Dmowski and M. Kaminski, *J. Fluorine Chem.*, **23**, 207 (1983); b) L. M. Yagupol'skii, N. V. Kondratenko, G. N. Timofeeva, M. I. Dronkina, and Yu. L. Yagupol'skii, *J. General Chem. USSR*, **16**, 2139 (1981); c) R. J. Harder and W. C. Smith, *J. Am. Chem. Soc.*, **83**, 3422 (1961); d) L. N. Markovskij, V. E. Pashinnik, and A. V. Kirsanov, *Synthesis*, **1973**, 787; e) G. Pawelke, *J. Fluorine Chem.*, **52**, 229 (1991); f) E. Klauke, *Angew. Chem., Int. Ed. Engl.*, **5**,

848 (1966); g) T. Abe, E. Hayashi, H. Baba, and H. Fukaya, *J. Fluorine Chem.*, **48**, 257 (1990); h) K. Adachi, S. Ishihara, and T. Umemoto, *Proceedings of the 15th International Symposium on Fluorine Chemistry, Vancouver*, Canada, Aug. 2-7, 1997.

8) a) G. Klöter, W. Lutz, K. Seppelt, and W. Sundermeyer, *Angew. Chem., Int. Ed. Engl.*, **16**, 707 (1977); b) G. Klöter and K. Seppelt, *J. Am. Chem. Soc.*, **101**, 347 (1979).

9) Y. Hatanaka, K. Goda, Y. Okahata, and T. Hiyama, *Tetrahedron*, **50**, 8301 (1994).

10) T. Ohinata, A. Sugiura, and T. Fujii, Japan Kokai Tokkyo Koho 63-2961 (1988); *Chem. Abstr.*, **109**, 83959n (1988)

11) A. Nishioka and C. Inoue, *Dyestuffs & Chemicals*, **38**, 2 (1993).

12) T. Kusumoto, A. Nakayama, K. Sato, K. Nishide, T. Hiyama, S. Takehara, T. Shoji, M. Osawa, T. Kuriyama, K. Nakamura, and T. Fujisawa, *J. Chem. Soc., Chem. Commun.*, **1991**, 311.

13) J. Barluenga, A. M. Bayón, and G. Asensio, *J. Chem. Soc., Chem. Commun.*, **1984**, 1334.

14) Miscibility test revealed that the texture was smectic B (hexatic) phase.

15) Compounds **23b** and **23c** were prepared by methylation of **21b** and **21c**, respectively; see experimental section.

16) The host nematic LCs mixture was composed of 3 compounds of a 4'-alkyl-4-cyanobiphenyl type and 6 compounds of a 4-alkyloxyphenyl *trans*-4-alkylcyclohexane-1-carboxylate type.

17) J. Cousseau and P. Albert, *Bull. Soc. Chim. Fr.*, **6**, 910 (1986).

Chapter IV

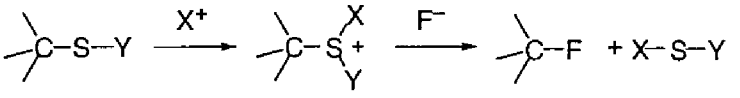
A Convenient Synthesis of Trifluoromethyl Ethers by Oxidative Desulfurization-Fluorination of Dithiocarbonates

Abstract: Trifluoromethyl ethers R–OCF_3 are easily synthesized from the corresponding dithiocarbonates R–OCS_2Me (R = aryl or primary alkyl) by a reagent system consisting of 70% HF/pyridine and an *N*-halo imide. When the reaction is applied to R–OCS_2Me wherein R = secondary alkyl, tertiary alkyl, or benzylic group, fluorination leading to the corresponding alkyl fluorides R–F is achieved, whereas a combination of 50% HF/pyridine and NBS affords the corresponding trifluoromethyl ethers R–OCF_3 (R = secondary alkyl).

IV-1. Introduction

Introduction of a fluorine functional group to pharmaceuticals or agrochemicals often brings enhancement of activity.[1,2] Accordingly, organofluorine compounds have attracted much attention in the pharmaceutical and material science fields. For the synthesis of fluorine-containing target molecules, introduction of fluorine atom(s) at the desired position of a molecule is preferably carried out at a late stage of synthesis.[3,4] Therefore, exploration of mild, efficient, and selective fluorination reactions with common reagents has been one of research topics in synthetic organofluorine chemistry.[3]

The oxidative desulfurization-fluorination reaction recently disclosed transforms organosulfur compounds to the corresponding organofluorine compounds through replacement of C–S bond(s) with C–F bond(s).[5] The reaction using an *N*-halo imide and a fluoride source provides with organofluorine compounds under extremely mild conditions with many functional groups being intact (Figure 1). According to the present method, trifluoromethyl-substituted aromatics[6] and trifluoromethylamines[7] are readily accessible. Due to high chemical stability, high lipophilicity, high oxygen solubility, and low toxicity, trifluoromethyl ethers[8] have found many applications in liquid-crystalline materials,[9] biologically active compounds,[1a-b] and artificial blood substitutes.[10]



X^+: halonium ion from an *N*-halo imide

F^-: from $TBAH_2F_3$, $Et_3N/3HF$, 50-70% HF/py, or 80% HF/melamine

Figure 1. Schematic illustration of *oxidative desulfurization-fluorination*

Aryl trifluoromethyl ethers have been prepared by i) fluorination of aryl trichloromethyl ethers with $SbF_3/SbCl_5$[11] or HF,[12] ii) trifluoromethylation of phenols with CCl_4/HF,[13] or iii) fluorination of aryl fluoroformate or -thioformate with SF_4[14] or MoF_6,[15] respectively. Alkyl trifluoromethyl ethers, though relatively ineffectively, have also been synthesized by i) the reaction of alkenes with CF_3OF,[16] ii) electrophilic trifluoromethylation of alcohols by treatment with *O*-(trifluoromethyl)dibenzofuranium salts,[17] or iii) fluorination of alkyl fluoroformates with SF_4.[18] All of these methods employ toxic and/or explosive reagents such as hydrogen fluoride, SF_4, and/or CF_3OF under specially cared conditions. The methods thus suffer from problems including difficult accessibility of starting materials and low chemoselectivity. These drawbacks

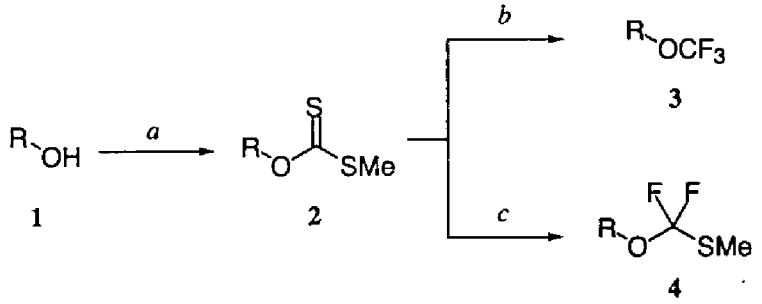
have hampered the flexibility in design of trifluoromethoxy-substituted agents and materials.

In contrast, the oxidative desulfurization-fluorination of dithiocarbonates using *N*-halo imides and 70% HF/pyridine (HF/py)[19] or 80% HF/melamine complexes[20] is a convenient entry to trifluoromethyl ethers. Transformation can be performed by a readily available reagent system consisting of HF/py and an *N*-halo imide. According to the method, primary- and secondary-aliphatic and aryl trifluoromethyl ethers can be readily prepared with many functional groups being intact.[8,9b] In this Chapter, the Author describes the trifluoromethyl ether synthesis.

IV-2. Results and Discussion

IV-2-1. Oxidative Desulfurization-Fluorination of Dithiocarbonates Derived from Aromatic and Primary Alkyl Alcohols: Synthesis of Trifluoromethyl Ethers and Difluoro(methylthio)methyl Ethers

Dithiocarbonates, the substrates of the oxidative desulfurization-fluorination, were easily obtained in high yields by treatment of the corresponding phenols or alcohols **1** with sodium hydride (NaH), CS_2, and then with MeI.[21] Oxidative desulfurization-fluorination of dithiocarbonates **2** was carried out using 70% HF/py[19] or $TBAH_2F_3$[22] with an *N*-halo imide as shown in Scheme 1. When the reaction was performed with 70% HF/py as a fluoride source, the fluorination proceeded effectively to give trifluoromethyl ethers **3**, whereas use of $TBAH_2F_3$ afforded difluoro(methylthio)methyl ethers **4** as a sole product. Fluorinated ethers **4** have no precedents. The results are summarized in Table 1.



1 2 3 4

a: i) NaH (1.2 mol), ii) CS_2 (5.0 mol), iii) MeI (2.0 mol)
b: 70% HF/py, *N*-halo imide, CH_2Cl_2, -78; 0 °C, 1 h
c: $TBAH_2F_3$, *N*-halo imide, CH_2Cl_2, rt, 1 h

Scheme 1. Synthesis of trifluoromethyl ethers **3** and difluoro(methylthio)methyl ethers **4**.

The Author first studied the optimization of the fluorination conditions using *S*-methyl *O*-4-propylphenyl dithiocarbonate (**2a**) as a substrate. For an *N*-halo imide, first tested were DBH and NBS that were already shown to be effective oxidants for the transformation.[7] Substrate **2a** was treated with NBS (3 mol) and 70% HF/py (80 mol) in dichloromethane to give **3a** in 16% yield (entry 1). Use of DBH improved the yield to 58%. The reaction with DBH (5 mol) achieved the trifluoromethylation, but was accompanied by mono- and dibromination of the phenyl ring in **3a**; these products could not be separated (entry 3). The reaction carried out with HF/py (40 mol) was not accompanied by bromination and gave **3a** in 81% yield as a sole product. Use of HF/py (20 mol) also promoted the reaction without ring bromination, though less efficiently.

The conditions in entry 2 for the trifluoromethyl ether synthesis were applied to various kinds of dithiocarbonates derived from phenols, and the corresponding aryl trifluoromethyl ethers **3** were readily obtained in moderate-to-high yields (entries 10, 14, 17, 19, 21, 24, and 25). For this transformation, exactly theoretical amounts of DBH (3 mol) should be used to avoid aromatic bromination by excess of the reagent particularly with a substrate lacking an electron-withdrawing group on an aromatic ring.[23] Indeed, this side reaction occurred readily with substrates containing an alkoxy group. For example, *O*-4-benzyloxyphenyl *S*-methyl dithiocarbonate (**2e**) was converted into 1-benzyloxy-2-bromo-4-trifluoromethoxybenzene (**3e'**) with 70% HF/py (80 mol) and DBH (4 mol) (entry 14), whereas a complex mixture resulted with DBH (3 mol). Compound **2d** having a methoxy group gave similar results (entry 12).

For the synthesis of alkyl trifluoromethyl ethers, the Author again optimized the conditions using *O*-2-(4-bromophenyl)ethyl *S*-methyl dithiocarbonate (**2l**) as the substrate. The reaction performed with 70% HF/py (60-80 mol) induced the trifluoromethylation effectively along with aromatic bromination (entries 27 and 28). When the reaction was performed with HF/py (40 mol), the trifluoromethylation proceeded with little ring bromination (< 2%) to give desired product **3l** in 81% yield (entry 29). Use of HF/py (20 mol) gave **3l** in only 20% yield (entry 30). The trifluoromethylation-bromination is applicable to **2m**, and 1-bromo-4-[3-(trifluoromethoxy)propyl]benzene (**3m'**) was obtained in 75% as a sole product (entry 32). Substrates without an aromatic ring effectively underwent the reaction with HF/py (80 mol) (entries 34 and 35). In summary, alkyl trifluoromethyl ethers of primary alcohols could be obtained in excellent yields by the oxidative desulfurization-fluorination procedure.[24]

Table 1. Synthesis of trifluoromethyl ethers **3** or difluoro(methylthio)methyl ethers **4** from **2**.

Entry	R	Yields of **2** (%)		Fluoride source (mol)[a]	*N*-Halo imide (mol)	Yields of **3** or **4** (%)[b]	
1	4-*n*-Pr-C_6H_4-	**2a**	80	70% HF/py (80)	NBS (3)	**3a**	16[c]
2				(80)	DBH (3)		58
3				(80)	(5)		--[d]
4				(40)	(3)		81[c]
5				(20)	(3)		60[c]
6				$TBAH_2F_3$ (5)	NBS (4)	**4a**	58
7				(4)	(3)		30
8				(6)	(5)		35
9	4-Me-C_6H_4-	**2b**	82	(5)	(4)	**4b**	64
10	4-*n*-Hex-C_6H_4-	**2c**	82	70% HF/py (80)	DBH (3)	**3c**	50
11				$TBAH_2F_3$ (5)	NBS (4)	**4c**	36
12	4-MeO-C_6H_4-	**2d**	56	70% HF/py (80)	DBH (3)	**3d**	--
13				$TBAH_2F_3$ (5)	NBS (4)	**4d**	33
14	4-$PhCH_2O$-C_6H_4-	**2e**	85	70% HF/py (80)	DBH (4)	**3e'**[e]	56
15					(3)		--
16				$TBAH_2F_3$ (5)	NBS (4)	**4e**	43
17	4-Br-C_6H_4-	**2f**	67	70% HF/py (80)	DBH (3)	**3f**	62
18				$TBAH_2F_3$ (5)	NBS (4)	**4f**	43
19	4-*n*-PrOC(O)-C_6H_4-	**2g**	33	70% HF/py (80)	DBH (3)	**3g**	30
20				$TBAH_2F_3$ (5)	NBS (4)	**4g**	42
21	3-MeOC(O)-C_6H_4-	**2h**	77	70% HF/py (80)	DBH (3)	**3h**	76
22				$TBAH_2F_3$ (5)	NBS (4)	**4h**	32
23	4-Ph-C_6H_4-	**2i**	84			**4i**	23
24	4-(4-AcO-C_6H_4)-C_6H_4-	**2j**	34[f]	70% HF/py (80)	DBH (3)	**3j**	80
25	4-(4-Br-C_6H_4)-C_6H_4-	**2k**	74			**3k**	52 (78)[g]
26				$TBAH_2F_3$ (5)	NBS (4)	**4k**	28
27	4-Br-C_6H_4-CH_2CH_2-	**2l**	99	70% HF/py (80)	DBH (3)	**3l**[d]	--
28				(60)			43 (47)[h]
29				(40)			81
30				(20)			20
31				$TBAH_2F_3$ (5)	NBS (4)	**4l**	19
32	Ph-$CH_2CH_2CH_2$-	**2m**	95	70% HF/py (80)	DBH (3)	**3m'**[i]	75
33				$TBAH_2F_3$ (5)	NBS (4)	**4m**	15
34	*n*-$C_{10}H_{21}$-	**2n**	66	70% HF/py (80)	DBH (3)	**3n**	80
35	*n*-$C_{16}H_{33}$-	**2o**	88			**3o**	95
36					$PhI(OCOCF_3)_2$ (3)		67
37				$TBAH_2F_3$ (5)	NBS (4)	**4o**	9

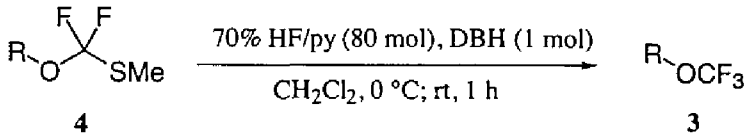
a) Mol amounts of F^- and $H_2F_3^-$ are indicated in parentheses for 70% HF/py and $TBAH_2F_3$, respectively. b) Isolated yields. c) Yields estimated by ^{19}F NMR using 1,3-$(CF_3)_2C_6H_4$ as internal standard. d) Accompanied by aromatic bromination. e) The product was 2-Br-4-CF_3O-C_6H_3-$OCH_2C_6H_5$ (**3e'**). f) Yields for 2 steps. See experimental. g) HF/py (40 mol) was used for the reaction. h) Brominated product 2,4-Br_2-C_6H_3-CH_2CH_2-OCF_3 (**3l'**) is produced. i) The product was 4-Br-C_6H_4-$CH_2CH_2CH_2$-OCF_3 (**3m'**).

In the meantime, Motherwell and his co-workers reported that the dithiocarbonates derived from primary and secondary alkanols were converted into the corresponding fluorides by means of 4-(difluoroiodo)toluene ($TolIF_2$).[25] For example, *O*-hexadecyl *S*-methyl dithiocarbonate (**2o**) was reportedly converted into the corresponding 1-fluorohexadecane in 48% yield by $TolIF_2$. In contrast, under the oxidative desulfurization reaction conditions, compound **2o** was converted into trifluoromethyl ether **3o** in 95% yield (entry 35) as a sole product, no trace of other products being detected. To compare the two reagents, the Author used [bis(trifluoroacetoxy)iodo]benzene (3 mol) in place of DBH and found that only trifluoromethyl ether **3o** was obtained again in 67% yield (entry 36). Thus, the reagent system consisting of 70% HF/py and an oxidant exhibited unique reactivity in sharp contrast to $TolIF_2$. The formation of different products may be attributed to different reaction pathways (*vide infra*).

The Author next studied the fluorination using $TBAH_2F_3$ as a fluorination reagent to find that novel products difluoro(methylthio)methyl ethers **4** were produced. In particular, the use of $TBAH_2F_3$ (5 mol) and NBS (4 mol) was the most effective for the difluorination (entry 6). Under these reaction conditions, no traces of trifluoromethyl ethers were produced. The difluorination reaction was applied to various kinds of dithiocarbonates, and a variety of aryl difluoro(methylthio)methyl ethers were obtained in fair yields from the corresponding *O*-aryl dithiocarbonates (entries 9, 11, 13, 16, 18, 20, 22, 23, and 26), whereas the alkyl difluoro(methylthio)methyl ethers were isolated in relatively low yields (entries 31, 33, and 37). In contrast to the trifluorination, aromatic rings having an alkoxy group remained intact under the difluorination conditions (entries 13 and 16).

IV-2-2. Conversion to Trifluoromethyl Ethers of Difluoro(methylthio)methyl Ethers

To examine the reactivity of difluoro(methylthio)methyl ethers **4**, these were treated with HF/py (80 mol) and DBH (1.0 mol) at 0 °C to room temperature (eq. 1). The results summarized in Table 2 clearly show that **4a**, **4h**, and **4m** smoothly gave trifluoromethyl ethers **3a**, **3h**, and **3m**, respectively, without ring bromination. However, substrate **4e** having a benzyloxyphenyl moiety was brominated to give **3e'**. Thus, DBH (2 mol) was necessary for the effective transformation. The results shown in Table 2 demonstrate that difluoro(methylthio)methyl ethers **4** are precursors of trifluoromethyl ethers **3**.



4 3 (1)

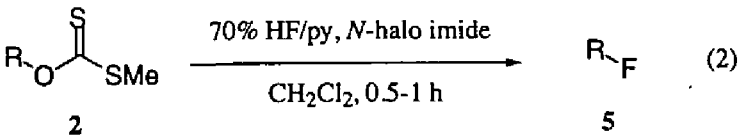
Table 2. Conversion of R-OCF_2SMe into R-OCF_3[a)]

Entry	R		DBH (mol)	Yields of 3 (%)[b)]	
1	4-*n*-Pr-C_6H_4-	**4a**	1	**3a**	42
2	4-$PhCH_2O$-C_6H_4-	**4e**	2	**3e'**[c)]	62
3	3-MeOC(O)-C_6H_4-	**4h**	1	**3h**	51
4	Ph-$CH_2CH_2CH_2$-	**4m**	1	**3m**	41

a) All the reaction were performed with 70% HF/py (80 mol of F^-) and DBH.
b) Isolated yields. c) The product was 2-Br-4-CF_3O-C_6H_3-$OCH_2C_6H_5$(**3e'**).

IV-2-3. Oxidative Desulfurization-Fluorination of Dithiocarbonates Derived from Secondary, Tertiary, or Benzylic Alcohols

To compare the reactivity of dithiocarbonates towards $TolIF_2$[25] with that towards 70% HF/py and an *N*-halo imide in more detail, the Author next examined the oxidative desulfurization-fluorination of dithiocarbonates derived from secondary, tertiary, or benzylic alcohols. In contrast to the dithiocarbonates of primary alcohols, these dithiocarbonates were converted into the corresponding fluorides **5** (eq. 2).



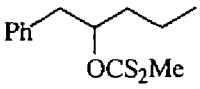
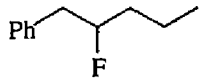
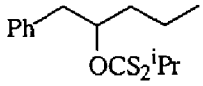
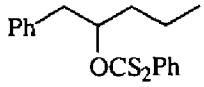
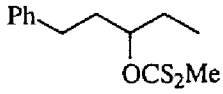
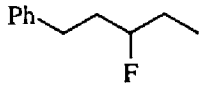
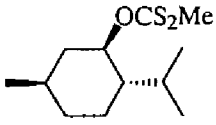
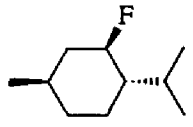
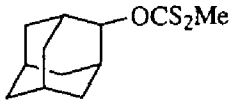
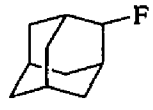
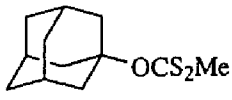
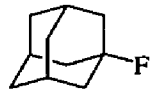
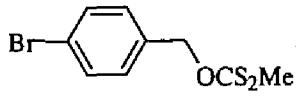
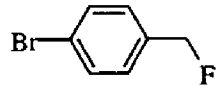
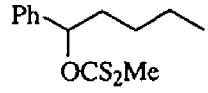
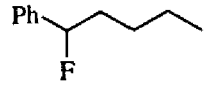
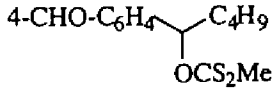
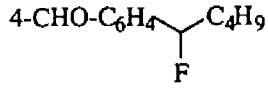
2 **5** (2)

(R = secondary alkyl)

The Author first optimized the reaction conditions using *O*-1-benzylbutyl *S*-methyl dithiocarbonate (**2p**) as a substrate. Initially, he applied the standard reaction conditions for primary dithiocarbonates using HF/py (80 mol) and DBH (3.0 mol). ^{19}F NMR and GC-MS of the crude inseparable mixture of products revealed the formation of **5p** in addition to its monobromo, dibromo, and tribromo derivatives. The results are summarized in entry 1 of Table 3. Use of NIS as an oxidant prevented the aromatic halogenation (entries 2-5). Upon use of HF/py (40 mol) and NIS (3 mol) (entry 2), the fluorination gave **5p** with a small amount of its iodination product. Use of HF/py (20 mol) was highly effective to produce **5p** in 70% yield without any ring halogenation (entry 3). Reduction of the amount of either HF/py (entry 4) or NIS (entry 5) decreased the yield of fluorination product **5p**. He next examined the influence of a substituent on sulfur using *S*-isopropyl or *S*-phenyl dithiocarbonates (**2q** or **2r**). Both of these were fluorinated to give **5p**; no trace of trifluoromethyl ether **3** was detected. The optimized fluorination conditions was applied to dithiocarbonates derived from various secondary, tertiary, and benzylic alcohols. The conditions and yields of products are summarized in Table 3.

As readily seen, both secondary (entries 8-10) and tertiary (entry 11) alkyl fluorides are readily available in high yields. Dithiocarbonate **2t** derived from menthol afforded **5t** as a single isolable product (entry 9). Although the reaction appears to have proceeded with retention of configuration, it is considered that **5t** was produced through a carbocationic intermediate. Similar stereochemical results are reported with other fluorination reagents.[25,26] Primary benzylic dithiocarbonate **2w** and secondary ones **2x** and **2y** gave the corresponding benzylic fluorides **5w**, **5x**, and **5y**, respectively. For **2w** and **2x**, DBH was the most effective oxidant (see, entry 13); bromination of aromatic ring was not observed. Substrate **2y** having a formyl functionality caused difluorination of the CHO group when DBH (3 mol) was used as an oxidant (entry 15). For this substrate, NIS was the best oxidant to produce fluorination product **5y** in 91% yield.

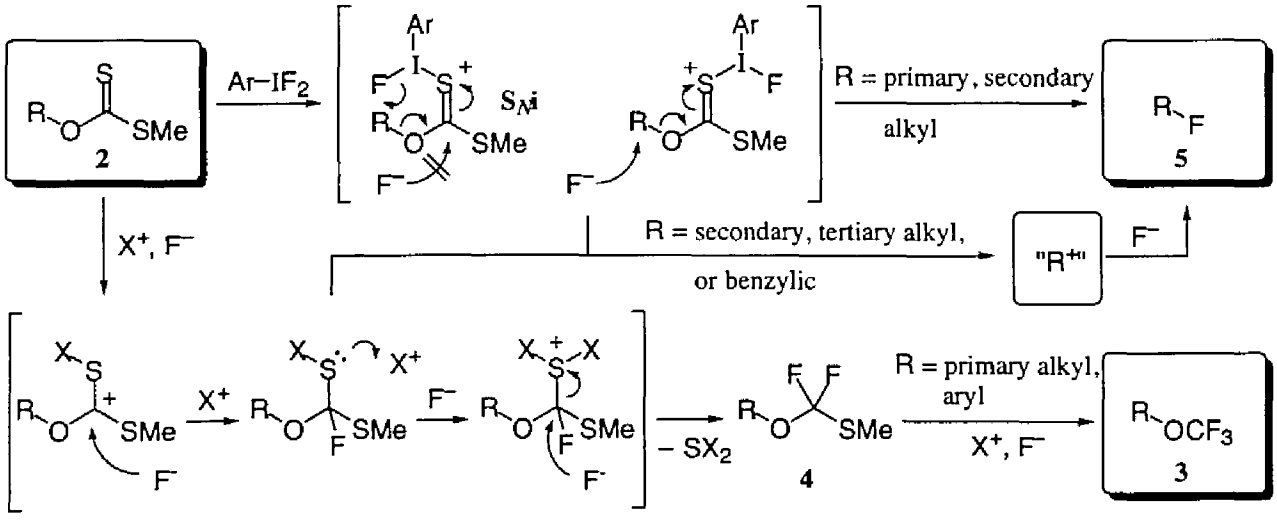
Table 3. Synthesis of alkyl fluorides **5** by oxidative desulfurization-fluorination[a)]

Entry	Dithiocarbonates **2**	70% HF/py (mol)	*N*-Halo imide (mol)	Products **5**	Yields of **5** (%)
1	 **2p**	80	DBH (3)	 **5p**	--[b, c)]
2	**2p**	40	NIS (3)	**5p**	48
3	**2p**	20	NIS (3)	**5p**	70
4	**2p**	5	NIS (3)	**5p**	no reaction
5	**2p**	40	NIS (1)	**5p**	45
6	 **2q**	40	NIS (3)	**5p**	78
7	 **2r**	40	NIS (3)	**5p**	42
8	 **2s**	40	NIS (3)	 **5s**	65
9	 **2t**	40	NIS (3)	 **5t**	48[d)]
10	 **2u**	40	NIS (3)	 **5u**	82[c)]
11	 **2v**	40	NIS (3)	 **5v**	78[c)]
12	 **2w**	40	DBH (3)	 **5w**	43[c)]
13	 **2x**	40	DBH (3)	 **5x**	94[c)] (76)[c, e)]
14	 **2y**	40	NIS (3)	 **5y**	91[c)]
15	**2y**	40	DBH (3)	**5y**	60 (23)[c, f)]

a) Unless otherwise noted, all the reaction was performed in CH_2Cl_2 at -42 °C for 1 h. b) Accompanied by aromatic bromination. c) The reaction was carried out at -78 °C then 0 °C for 1 h. d) The reaction was carried out at -78 °C then 0 °C for 0.5 h. e) NIS (3.0 mol) was used. f) Yield of 4-F_2CH-C_6H_4-CHF-C_4H_9 (**6**) is given in parentheses.

IV-2-4. Reaction Mechanism

A plausible reaction mechanism for the fluorination of dithiocarbonates is summarized in Scheme 2. As demonstrated above, the reagent system consisting of 70% HF/py and an *N*-halo imide converts R–OCS_2R' **2** into trifluoromethyl ethers R–OCF_3 **3** (R = primary and aryl) or alkyl fluorides R–F **5** (R = secondary, tertiary, and benzylic), depending on the cation stabilizing nature of R. In particular, the dithiocarbonates derived from primary alcohols gave trifluoromethyl ethers in striking contrast to the reaction with $TolIF_2$.[25] The reactivity difference may be attributed to an involvement of an S_Ni pathway with $TolIF_2$ as shown in Scheme 2. The oxidative desulfurization-fluorination appears to be initiated by an electrophilic reaction of a positive halogen (X^+) with a thiocarbonyl group of R–OC(S)SMe to generate a cationic species R–OC^+(SX)SMe; a subsequent nucleophilic attack by a fluoride ion at the electrophilic carbon forms a C–F bond. The resulting R–OCF(SX)SMe is again oxidized by X^+ and then fluorinated to yield difluorination product **4** as an isolable product. Further oxidation-fluorination affords trifluorination product R–OCF_3. The reagent combination clearly demonstrates that the fluorination proceeds via an intermolecular nucleophilic reaction three times to finally give trifluoromethyl ether **3**. Therefore, the fluorination of secondary, tertiary alkyl, and benzylic dithiocarbonates leading to fluoride **5** may be attributed to elimination of a –OCS_2Me, –OCF(SX)SMe, or –OCF_2SMe group to generate carbocationic species "R^+" under the weakly acidic conditions, followed by a fluoride attack.

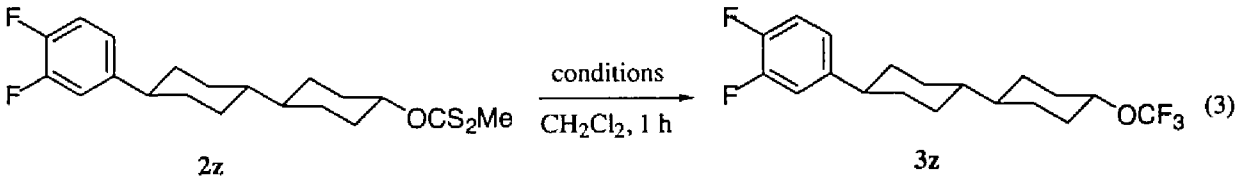


Scheme 2. A proposed mechanism for the fluorination of dithiocarbonates.

IV-2-5. Synthesis of Secondary Alkyl Trifluoromethyl Ethers through the Oxidative Desulfurization-Fluorination

To the best of knowledge, no synthetic method has been available for the synthesis of trifluoromethyl ethers from secondary aliphatic alcohols.[27] An already reported alternative approach involves addition of CF_3OF to alkenes to give *vic*-fluoro(trifluoromethoxy)alkanes.[16] As CF_3OF is highly explosive and toxic, special equipments and techniques should be employed with great care. Furthermore, the reaction is often accompanied by the formation of regio-isomers and formal F_2 adducts, and thus the desired trifluoromethyl ethers are produced generally in low yields.

Based on the mechanism suggested in Scheme 2, it is essential to prevent the elimination of a $-OCS_2Me$, $-OCF(SX)SMe$, or $-OCF_2SMe$ group for the synthesis of trifluoromethyl ethers derived from secondary alcohols. The Author thus envisaged that, if the acidity of the reaction conditions might be controlled by a proper choice of the reagent system, it would be possible to switch the reaction pathway to the trifluoromethyl ether formation. To this end, he initially used HF/py complex with HF content lower than the Olah reagent. The results using **2z** as a model substrate are summarized in Table 4.



2z **3z** (3)

Table 4. Synthesis of substituted cyclohexyl trifluoromethyl ether **3z**

Entry	Conditions (mol)	Temp (°C)	Isolated yield of **3z** (%)
1	55% HF/py (40), NBS (5)	0	37
2	50% HF/py (40), NBS (5)	0	42
3	50% HF/py (80), NBS (5)	0	38
4	50% HF/py (40), NBS (5)	–42	29
5	45% HF/py (40), NBS (5)	0	trace
6	70% HF/py (40), NBS (5), KHF_2 (40)	–42	trace
7	70% HF/py (40), NBS (5), KHF_2 (20)	–42	30
8	70% HF/py (40), DBH (5), KHF_2 (15)	–42	31
9	70% HF/py (40), DBH (5), KHF_2 (10)	–78	27

Dilution of 70% HF/py with appropriate amounts of dry pyridine gave reagents 45-55% HF/py (40-80 mol of F^-). When a reaction was performed using 50% HF/py (40 mol) and NBS (5 mol) in dichloromethane at 0 °C, compound **2z** was converted into the corresponding cyclohexyl trifluoromethyl ether derivative **3z** in 42% yield without any fluorination product being detected (entry 2). DBH (5 mol) was not effective for this transformation. Use of 55% HF/py (40 mol) (run 1) or 50% HF/py (80 mol) (run 3) at –42 °C also gave **3z** but in lower yields. When 45% HF/py (40 mol) was employed for the reaction, the fluorination did not complete, and the formation of a difluoro(methylthio)methyl ether (R–OCF_2SMe) was detected by ^{19}F NMR (entry 5). A combined use of 70% HF/py and KHF_2 was also effective for this transformation; when the reaction was performed with 70% HF/py and KHF_2 (20, 15, or 10 mol), **3z** was obtained in 30, 31, or 27% yield, respectively. Potassium hydrogendifluoride is known to enhance the fluoride nucleophilicity and reduce the acidity of 70% HF/py.[28]

The trifluoromethyl ether synthesis was applied to the dithiocarbonates derived from several secondary aliphatic alcohols. The products and isolated yields are shown in Figure 2. As one can readily see, the corresponding secondary aliphatic trifluoromethyl ethers were prepared under the oxidative desulfurization-fluorination conditions, though the yields are not striking. It is worthy to emphasize that either alkyl fluorides **5p** and **5s** or trifluoromethyl ethers **3p** and **3s** are available from dithiocarbonates **2p** and **2s**, respectively, only by tuning the HF content of the Olah reagent.

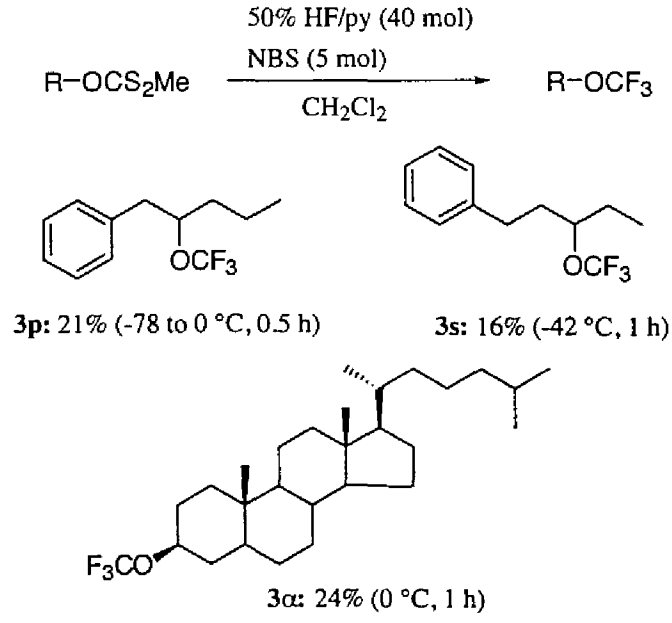


Figure 2. Synthesis of secondary aliphatic trifluoromethyl ethers.

IV-3. Conclusion

It is demonstrated that synthesis of trifluoromethyl ethers is conveniently achieved by the oxidative desulfurization-fluorination of dithiocarbonates that are readily accessible from the corresponding alcohols or phenols. When the reaction is carried out using a reagent system consisting of 70% HF/py and an *N*-halo imide, R–OCS_2Me (R = aryl or primary alkyl) is transformed selectively to trifluoromethyl ethers R–OCF_3. When the similar conditions are applied to R–OCS_2Me (R = secondary and tertiary alkyl or benzylic), fluorination leading to alkyl fluorides R–F proceeds without any formation of R–OCF_3. Furthermore, a combination of 50% HF/py and NBS converts R–OCS_2Me (R = secondary alkyl) to afford trifluoromethyl ethers R–OCF_3. Thus, the reaction pathway towards secondary alkyl fluorides or trifluoromethyl ethers can be controlled simply by an appropriate choice of the fluorination reagent starting with the same substrate.

The convenient transformations disclosed herein should find further applications particularly in LC materials, pharmaceuticals, and agrochemicals. Applications to LCs will be discussed in the following Chapters.

IV-4. Experimental

General Procedure for the Preparation of Dithiocarbonates 2.

To a stirred solution of alcohol **1** (80 mmol) in THF (or DMF) (160 mL), sodium hydride (NaH, 60% in oil, 3.8 g, 96 mmol) was slowly added portionwise at 0 °C. After the resulting mixture was stirred for 1 h at room temperature, carbon disulfide (9.6 mL, 0.16 mol) was added dropwise at 0 °C. The resulting mixture was stirred for 10 h at room temperature before MeI (6.0 mL, 96 mmol) was added dropwise to the reaction mixture at 0 °C. The resulting mixture was stirred for 1 h at room temperature, treated with aqueous NH_4Cl solution, and extracted with Et_2O. The organic phase was separated; the aqueous phase was extracted with Et_2O three times. The combined organic phase was washed with sat. NaCl solution containing small portions of sodium hydrogensulfite, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography or recrystallization from EtOH to give dithiocarbonates **2**. Yields and spectral properties of **2** are as follows.

***S*-Methyl *O*-4-Propylphenyl Dithiocarbonate (2a).** Prepared in 80% yield upon use of DMF in lieu of THF. A pale yellow oil; R_f = 0.83 (hexane : Et_2O = 2 : 1). IR 2960, 2930, 2870, 1500, 1175, 1040, 965, 819 cm^{-1}; ^1H NMR (300 MHz) δ = 0.94 (t, *J* = 8 Hz, 3 H), 1.05-1.64 (m, 2 H), 2.59 (t, *J* = 8 Hz, 2 H), 2.65 (s), 6.99 (d, *J* = 9 Hz, 2 H), 7.20 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 13.8 (s), 19.9 (s), 24.4 (s), 37.4 (s), 121.5 (s), 129.3 (s), 141.0 (s), 152.6 (s), 215.9 (s); MS *m/z* (rel intensity) 226 (M^+, 6), 200 (2), 198 (20), 121 (5), 93 (9), 91 (100), 65 (5). Found: *m/z* 226.0485. Calcd for $C_{11}H_{14}OS_2$: M, 226.0486.

***S*-Methyl *O*-4-Methylphenyl Dithiocarbonate (2b).** Yield, 82% with DMF as a reaction solvent. A pale yellow oil; R_f = 0.57 (hexane : EtOAc = 10 : 1). IR 3042, 2924, 1884, 1720, 1597, 1503, 1420, 1413, 1382, 1213, 1192, 1180, 1103, 1041, 1020, 962, 821 cm^{-1}; ^1H NMR (200 MHz) δ = 2.36 (s, 3 H), 2.70 (s, 3 H), 7.02 (d, *J* = 9 Hz, 2 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 19.9 (s), 20.9 (s), 121.6 (s), 130.0 (s), 136.2 (s), 152.4 (s), 216.0 (s); MS *m/z* (rel intensity) 199 (M^++1, 0.5), 198 (M^+, 3), 170 (28), 138 (2), 107 (5), 91 (100), 77 (13), 65 (10). Found: *m/z* 198.0177. Calcd for $C_9H_{10}OS_2$: M, 198.0173.

***O*-4-Hexylphenyl *S*-Methyl Dithiocarbonate (2c).** Yield, 82% with DMF as a reaction solvent. A pale yellow oil; R_f = 0.50 (hexane). IR 2926, 2857, 1505, 1460, 1415, 1383, 1179, 1042, 965, 831 cm^{-1}; ^1H NMR (100 MHz) δ = 0.89 (t, *J* = 6 Hz, 3 H), 1.15-1.80 (m, 8 H), 2.65 (t, *J* = 7 Hz, 2 H), 2.67 (s, 3 H), 7.03 (d, *J* = 6 Hz, 2 H), 7.25 (d, *J* = 6 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 19.9 (s), 22.6 (s), 29.0 (s), 31.3 (s), 31.7 (s), 35.4 (s), 121.6 (s), 129.3 (s), 141.3 (s), 152.6 (s), 216.0 (s); MS *m/z* (rel intensity) 270 (M^++2, 1), 269 (M^++1, 2), 268 (M^+, 13), 240 (47), 169 (18), 121 (14), 107 (11), 93 (26), 91 (100), 75 (14), 65 (10). Found: *m/z* 268.0961. Calcd for $C_{14}H_{20}OS_2$: M, 268.0956.

***O*-4-Methoxyphenyl *S*-Methyl Dithiocarbonate (2d).** Yield, 56% with DMF as a reaction solvent. A pale yellow oil; R_f = 0.44 (hexane : EtOAc = 10 : 1). IR 3000, 2875, 2820, 1500, 1250, 1185, 1170, 1040, 830 cm^{-1}; ^1H NMR (100 MHz) δ = 2.64 (s, 3 H), 3.80 (s, 3 H), 6.87 (d, *J* = 7 Hz, 2 H), 7.05 (d, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 19.9 (s), 55.5 (s), 114.4 (s), 122.7 (s), 148.2 (s), 157.7 (s), 216.4 (s); MS *m/z* (rel intensity) 214 (M^+, 7), 186 (23), 149 (20), 123 (22), 111 (12), 109 (11), 105 (18), 97 (26), 95 (34), 91 (100), 83 (38), 71 (52). Found: *m/z* 214.0119. Calcd for $C_9H_{10}O_2S_2$: M, 214.0122.

***O*-4-Benzyloxyphenyl *S*-Methyl Dithiocarbonate (2e).** Yield, 85% with DMF as a reaction medium. A pale yellow oil; R_f = 0.66 (hexane : Et_2O = 2 : 1). IR 3010, 2860, 1500, 1383, 1242, 1185, 1150, 1055, 1019, 838, 742, 695 cm^{-1}; ^1H NMR (100 MHz) δ = 2.67 (s, 3 H), 5.08 (s, 2 H), 7.03 (s, 4 H), 7.30-7.60 (m, 5 H); ^{13}C NMR (75.5

MHz) δ = 19.9 (s), 70.4 (s), 115.4 (s), 122.8 (s), 127.5 (s), 128.1 (s), 128.6 (s), 136.7 (s), 148.4 (s), 157.0 (s), 216.3 (s); MS *m/z* (rel intensity) 292 (M^++2, 1), 291 (M^++1, 2), 290 (M^+, 9), 262 (11), 151 (2), 93 (10), 92 (198), 91 (100), 65 (35). Found: *m/z* 290.0435. Calcd for $C_{15}H_{14}O_2S_2$: M, 290.0435.

***O*-4-Bromophenyl *S*-Methyl Dithiocarbonate (2f).** Yield, 67% with DMF as a reaction medium. A pale yellow oil; R_f = 0.43 (hexane). IR 3120, 2950, 1883, 1724, 1582, 1482, 1420, 1400, 1190, 1172, 1100, 1037, 1015, 965, 832, 806, 715 cm^{-1}; ^1H NMR (200 MHz) δ = 2.66 (s, 3 H), 7.01 (d, *J* = 9 Hz, 2 H), 7.55 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 20.1 (s), 119.8 (s), 123.9 (s), 132.6 (s), 153.5 (s), 215.5 (s); MS *m/z* (rel intensity) 264 (M^++2, 2), 262 (M^+, 1), 236 (10), 234 (8), 145 (4), 143 (3), 119 (4), 93 (10), 91 (100), 75 (16), 64 (9). Found: *m/z* 261.9115. Calcd for $C_8H_7{}^{79}BrOS_2$: M, 261.9122.

***S*-Methyl *O*-4-(Propoxycarbonyl)phenyl Dithiocarbonate (2g).** Obtained in 33% yield by the reaction in DMF. A pale yellow oil; R_f = 0.53 (hexane : Et_2O = 5 : 1). IR 2969, 2922, 1721, 1601, 1501, 1412, 1275, 1194, 1159, 1113, 1040, 1015, 776, 702 cm^{-1}; ^1H NMR (100 MHz) δ = 1.05 (t, *J* = 6 Hz, 3 H), 1.79 (tq, *J* = 6, 6 Hz, 2 H), 2.66 (s, 3 H), 4.30 (t, *J* = 6 Hz, 2 H), 7.18 (d, *J* = 9 Hz, 2 H), 8.12 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 10.5 (s), 20.0 (s), 22.1 (s), 66.7 (s), 122.2 (s), 128.7 (s), 131.1 (s), 157.8 (s), 165.6 (s), 215.0 (s); MS *m/z* (rel intensity) 271 (M^++1, 1), 270 (M^+, 1), 242 (12), 194 (9), 152 (52), 135 (88), 107 (10), 93 (10), 82 (19), 91 (100), 77 (21), 75 (25), 64 (14). Found: *m/z* 270.0380. Calcd for $C_{12}H_{14}O_3S_2$: M, 270.0384.

***O*-3-(Methoxycarbonyl)phenyl *S*-Methyl Dithiocarbonate (2h).** Isolated in 77% yield by the reaction carried out in DMF. A pale yellow oil; R_f = 0.46 (hexane : Et_2O = 5 : 1). IR 2950, 1725, 1580, 1440, 1295, 1265, 1175, 1100, 1040, 1000, 760, 695 cm^{-1}; ^1H NMR (100 MHz) δ = 2.69 (s, 3 H), 3.93 (s, 3 H), 7.22-7.64 (m, 2 H), 7.72-8.04 (m, 2 H); ^{13}C NMR (75.5 MHz) δ = 20.0 (s), 52.4 (s), 123.4 (s), 126.8 (s), 127.7 (s), 129.5 (s), 131.8 (s), 154.4 (s), 165.9 (s), 215.5 (s); MS *m/z* (rel intensity) 242 (M^+, 1), 214 (26), 135 (4), 121 (2), 119 (3), 105 (4), 97 (3), 93 (10), 91 (100), 75 (9). Found: *m/z* 242.0071. Calcd for $C_{10}H_{10}O_3S_2$: M, 242.0071.

***O*-4-Biphenyl *S*-Methyl Dithiocarbonate (2i).** Yield, 84% (DMF as a reaction solvent). Pale yellow crystals, mp 80.2-80.9 °C; R_f = 0.23 (hexane). IR (KBr) 3057, 2924, 1888, 1510, 1481, 1184, 1036, 1005, 839, 766, 725 cm^{-1}; ^1H NMR (100 MHz) δ = 2.70 (s, 3 H), 7.21 (d, *J* = 6 Hz, 2 H), 7.35-7.81 (m, 7 H); ^{13}C NMR (75.5 MHz) δ = 20.0 (s), 122.3 (s), 127.1 (s), 127.4 (s), 128.2 (s), 128.7 (s), 139.6 (s) 140.0 (s), 154.0 (s), 215.7 (s); MS *m/z* (rel intensity) 262 (M^++2, 1), 261 (M^++1, 2), 260 (M^+, 12), 232 (36), 185 (9), 152 (13), 141 (11), 115 (23), 93 (16), 91 (100), 76 (15), 75 (16). Found: *m/z* 260.0331. Calcd for $C_{14}H_{12}OS_2$: M, 260.0330.

***O*-4'-Bromo-4-biphenyl *S*-Methyl Dithiocarbonate (2k).** Yield, 74% (in DMF). Pale yellow crystals, mp 109.8-110.6 °C; R_f = 0.26 (hexane). IR (KBr) 3040, 2925, 1584, 1478, 1387, 1182, 1051, 1001, 961, 822 cm^{-1}; ^1H NMR (200 MHz) δ = 2.71 (s, 3 H), 7.19 (d, *J* = 9 Hz, 2 H), 7.46 (d, *J* = 9 Hz, 2 H), 7.42-7.67 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 20.0 (s), 121.8 (s), 122.5 (s), 128.0 (s), 128.7 (s), 131.9 (s), 138.3 (s), 139.0 (s), 154.2 (s), 215.7 (s); MS *m/z* (rel intensity) 340 (M^++2, 5), 338 (M^+, 4), 312 (11), 310 (10), 152 (7), 139 (10), 91 (100), 75 (8). Found: *m/z* 337.9435. Calcd for $C_{14}H_{11}{}^{79}BrOS_2$: M, 337.9435.

***O*-2-(4-Bromophenyl)ethyl *S*-Methyl Dithiocarbonate (2l).** Obtained in 99% yield, a pale yellow oil; R_f = 0.26 (hexane). IR 2941, 2921, 1489, 1406, 1219, 1175, 1071, 1049, 1013, 812 cm^{-1}; ^1H NMR (300 MHz) δ = 2.52 (s, 3 H), 3.05 (t, *J* = 7 Hz, 2 H), 4.76 (t, *J* = 7 Hz, 2 H), 7.11 (d, *J* = 9 Hz, 2 H), 7.58 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 34.0 (s), 73.4 (s), 120.6 (s), 130.6 (s), 131.6 (s), 136.2 (s), 215.6 (s); MS *m/z* (rel intensity) 292 (M^++2, 0.01), 290 (M^+, 0.01), 185 (20), 184 (96), 183 (21), 182 (100), 104 (98), 103 (41), 102 (11), 91 (18), 89 (12), 78 (26), 77 (41), 76 (14), 75 (14), 63 (13). Found: *m/z* 289.9434. Calcd for $C_{10}H_{11}{}^{79}BrOS_2$: M, 289.9435.

***S*-Methyl *O*-3-Phenylpropyl Dithiocarbonate (2m).** Yield, 95%. A pale yellow oil; R_f = 0.19 (hexane). IR 3025, 2950, 2920, 1718, 1495, 1455, 1380, 1220, 1175, 1060, 740, 700 cm^{-1}; ^1H NMR (200 MHz) δ = 1.90-2.38 (m, 2 H), 2.55 (s, 3 H), 2.76 (t, *J* = 7 Hz, 2 H), 4.61 (t, *J* = 7 Hz, 2 H), 7.10-7.48 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 29.8 (s), 32.0 (s), 73.1 (s), 126.0 (s), 128.3 (s), 128.4 (s), 140.8 (s), 215.7 (s); MS *m/z* (rel intensity) 226 (M^+, 11), 205 (21), 153 (12), 123 (12), 119 (25), 118 (86), 92 (13), 91 (100), 71 (24). Found: *m/z* 226.0487. Calcd for $C_{11}H_{14}OS_2$: M, 226.0486.

***O*-Decyl *S*-Methyl Dithiocarbonate (2n).** Yield, 66%. A pale yellow oil; R_f = 0.50 (hexane). IR 2924, 2855, 1725, 1464, 1383, 1223, 1063, 966, 725 cm^{-1}; ^1H NMR (100 MHz) δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.04-1.62 (m, 14 H), 1.68-2.05 (m, 2 H), 2.56 (s, 3 H), 4.62 (t, *J* = 6 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.7 (s), 25.9 (s), 28.2 (s), 29.2 (s), 29.3 (s), 29.46 (s), 29.48 (s), 31.9 (s), 74.3 (s), 215.9 (s); MS *m/z* (rel intensity) 248 (M^+, 3), 215 (11), 141 (11), 140 (75), 109 (27), 91 (23), 75 (61), 71 (100), 69 (92). Found: *m/z* 248.1235. Calcd for $C_{12}H_{24}OS_2$: M, 248.1269.

***O*-Hexadecyl *S*-Methyl Dithiocarbonate (2o).** Yield, 88%. A pale yellow oil; R_f = 0.79 (hexane : EtOAc = 10 : 1). IR 2924, 2853, 1466, 1223, 1063, 967 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.20-1.50 (m, 26 H), 1.72-1.87 (m, 2 H), 2.56 (s, 3 H), 4.59 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.7 (s), 25.9 (s), 28.2 (s), 29.2 (s), 29.4 (s), 29.47 (s), 29.54 (s), 29.62 (s), 29.65 (s), 29.68 (br), 31.9 (s), 74.2 (s), 215.9 (s); MS *m/z* (rel intensity) 333 (M^++1, 0.2), 332 (M^+, 0.4), 299 (7), 285 (5), 224 (24), 125 (11), 111 (35), 109 (77), 108 (13), 98 (12), 97 (53), 91 (29), 85

(39), 83 (57), 71 (100), 69 (89). Found: *m/z* 332.2209. Calcd for $C_{18}H_{36}OS_2$: M, 332.2208.

***O*-1-Benzylbutyl *S*-Methyl Dithiocarbonate (2p).** Yield, 90%. A pale yellow oil; R_f = 0.63 (hexane : EtOAc = 10 : 1). IR 3029, 2959, 2872, 1456, 1219, 1129, 1051, 964, 741, 700 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.24-1.84 (m, 4 H), 2.52 (s, 3 H), 2.91 (dd, *J* = 7, 14 Hz, 1 H), 3.12 (dd, *J* = 6, 14 Hz, 1 H), 5.82-5.96 (m, 1 H), 7.20-7.30 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 13.8 (s), 18.5 (s), 18.7 (s), 34.8 (s), 39.6 (s), 84.4 (s), 126.5 (s), 128.3 (s), 129.4 (s), 136.8 (s), 215.4 (s); MS *m/z* (rel intensity) 254 (M^+, 0.13), 147 (12), 146 (84), 117 (47), 115 (11), 105 (13), 104 (24), 92 (17), 91 (100), 77 (8), 69 (4), 65 (21). Found: *m/z* 254.0797. Calcd for $C_{13}H_{18}OS_2$: M, 254.0799.

***O*-1-Benzylbutyl *S*-1-Methylethyl Dithiocarbonate (2q).** Prepared by treatment with 2-iodopropane in lieu of MeI and isolated in 84% yield as a pale yellow oil; R_f = 0.61 (hexane : EtOAc = 10 : 1). IR 2961, 2930, 2872, 1497, 1455, 1246, 1217, 1069, 1038, 787, 700 cm^{-1}; ^1H NMR (300 MHz) δ = 0.84 (t, *J* = 6 Hz, 3 H), 1.25-1.80 (m, 10 H), 2.90 (dd, *J* = 7, 14 Hz, 1 H), 3.12 (dd, *J* = 6, 14 Hz, 1 H), 3.78 (heptet, *J* = 7 Hz, 1 H), 5.86-5.95 (m, 1 H), 7.19-7.32 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 18.6 (s), 22.2 (s), 22.4 (s), 34.8 (s), 39.7 (s), 40.5 (s), 83.9 (s), 126.5 (s), 128.4 (s), 129.5 (s), 136.9 (s), 214.1 (s); MS *m/z* (rel intensity) 282 (M^+, 0.2), 147 (6), 146 (33), 117 (16), 105 (8), 104 (8), 92 (9), 91 (100), 65 (7). Found: *m/z* 282.1111. Calcd for $C_{15}H_{22}OS_2$: M, 282.1112.

***O*-(1-Ethyl-2-phenylethyl) *S*-Methyl Dithiocarbonate (2s).** Isolated in 80% yield as a pale yellow oil, R_f = 0.69 (hexane : EtOAc = 10 : 1). IR 3027, 2969, 1456, 1223, 1132, 1048, 965, 747, 698 cm^{-1}; ^1H NMR (200 MHz) δ = 0.94 (t, *J* = 7 Hz, 3 H), 1.78 (dq, *J* = 7, 7 Hz, 2 H), 1.90-2.20 (m, 2 H), 2.54 (s, 3 H), 2.58-2.76 (m, 2 H), 5.64-5.76 (m, 1 H), 7.13-7.35 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 9.2 (s), 18.7 (s), 26.4 (s), 31.4 (s), 34.8 (s), 84.9 (s), 125.8 (s), 128.1 (s), 128.2 (s), 141.2 (s), 215.6 (s); MS *m/z* (rel intensity) 254 (M^+, 0.2), 221 (0.6), 146 (27), 131 (5), 116 (15), 104 (10), 92 (10), 91 (100), 65 (5). Found: *m/z* 254.0790. Calcd for $C_{13}H_{18}OS_2$: M, 254.0799.

***O*-(–)-Menthyl *S*-Methyl Dithiocarbonate (2t).** Yield, 97%. A pale yellow oil; R_f = 0.72 (hexane : Et_2O = 10 : 1). IR 2957, 2924, 2870, 1456, 1370, 1246, 1219, 1148, 1051, 943, 901 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80 (d, *J* = 7 Hz, 3 H), 0.88-1.19 (m, 9 H), 1.42-1.78 (m, 4 H), 1.84-1.94 (m, 1 H), 2.18-2.26 (m, 1 H), 2.55 (s, 3 H), 5.52 (ddd, *J* = 5, 11, 11 Hz, 1 H); ^{13}C NMR (75.5 MHz) δ = 17.0 (s), 18.8 (s), 20.6 (s), 22.0 (s), 23.8 (s), 26.6 (s), 31.3 (s), 34.1 (s), 39.6 (s), 47.2 (s), 84.4 (s), 215.4 (s); MS *m/z* (rel intensity) 246 (M^+, 0.6), 171 (2), 140 (3), 139 (9), 138 (42), 97 (17), 95 (29), 91 (21), 83 (100), 81 (32), 71 (19), 69 (52), 67 (30). Found: *m/z* 246.1105. Calcd for $C_{12}H_{22}OS_2$: M, 246.1112.

***O*-2-Adamantyl *S*-Methyl Dithiocarbonate (2u).** Yield, 91%. Pale yellow needles, mp 106.4-107.6 °C; R_f = 0.70 (hexane : EtOAc = 10 : 1). IR (KBr) 2905, 2855, 1703, 1451, 1426, 1406, 1356, 1340, 1225, 1211, 1177, 1049, 963, 914 cm^{-1}; ^1H NMR (200 MHz) δ = 1.60-1.68 (m, 2 H), 1.72-1.96 (m, 8 H), 1.98-2.08 (m, 2 H), 2.20-2.28 (m, 2 H), 2.56 (s, 3 H), 5.62-5.78 (m, 2 H); MS *m/z* (rel intensity) 244 (M^++2, 2), 243 (M^++1, 3), 242 (M^+, 17), 182 (34), 136 (37), 135 (100), 107 (34), 93 (62), 91 (54), 81 (42), 79 (59), 77 (38), 67 (34). Found: *m/z* 242.0804. Calcd for $C_{12}H_{18}OS_2$: M, 242.0799.

***O*-1-Adamantyl *S*-Methyl Dithiocarbonate (2v).** Yield, 78%. Pale yellow needles, mp 110.6-111.2 °C; R_f = 0.76 (hexane : EtOAc = 10 : 1). IR (KBr) 2912, 2849, 1456, 1354, 1186, 1105, 1048, 1024, 954, 860, 714 cm^{-1}; ^1H NMR (200 MHz) δ = 1.69 (s, 6 H), 2.24 (brs, 3 H), 2.43 (s, 3 H), 2.45 (s, 6 H); ^{13}C NMR (75.5 MHz) δ = 19.1 (s), 31.4 (s), 36.0 (s), 41.1 (s), 91.2 (s), 212.5 (s); MS *m/z* (rel intensity) 242 (M^+, 0.8), 167 (1), 149 (2), 107 (9), 93 (19), 91 (13), 79 (25), 67 (8). Found: *m/z* 242.0793. Calcd for $C_{12}H_{18}OS_2$: M, 242.0799.

***O*-4-Bromophenylmethyl *S*-Methyl Dithiocarbonate (2w).** Obtained in 99% yield as a pale yellow oil; R_f = 0.62 (hexane : EtOAc = 10 : 1). IR 2921, 1900, 1595, 1489, 1406, 1368, 1223, 1197, 1177, 1071, 1013, 967, 851, 803, 731 cm^{-1}; ^1H NMR (200 MHz) δ = 2.56 (s, 3 H), 5.57 (s, 2 H), 7.26 (d, *J* = 8 Hz, 2 H), 7.50 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 19.1 (s), 73.8 (s), 122.5 (s), 129.9 (s), 131.5 (s), 133.5 (s), 215.2 (s); MS *m/z* (rel intensity) 278 (M^++2, 3), 276 (M^+, 2), 218 (3), 216 (3), 171 (81), 169 (100), 90 (33), 89 (28), 63 (20). Found: *m/z* 275.9280. Calcd for $C_9H_9{}^{79}BrOS_2$: M, 275.9279.

***S*-Methyl *O*-1-Phenyl-1-pentyl Dithiocarbonate (2x).** Yield, 95%. A pale yellow oil; R_f = 0.61 (hexane : EtOAc = 10 : 1). IR 3033, 2957, 2930, 1456, 1244, 1211, 1055, 964, 758, 698 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.23-1.45 (m, 4 H), 1.80-2.01 (m, 1 H), 2.04-2.34 (m, 1 H), 2.53 (s, 3 H), 6.51 (dd, *J* = 6, 8 Hz, 1 H) 7.23-7.36 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 18.9 (s), 22.5 (s), 27.5 (s), 35.9 (s), 85.3 (s), 125.8 (s), 126.8 (s), 128.0 (s), 128.4 (s), 215.0 (s); MS *m/z* (rel intensity) 254 (M^+, 3), 147 (71), 146 (15), 137 (8), 117 (44), 115 (23), 105 (32), 104 (27), 92 (26), 91 (100), 78 (11), 77 (18), 75 (11), 65 (16). Found: *m/z* 254.0792. Calcd for $C_{13}H_{18}OS_2$: M, 254.0799.

***O*-1-(4-Formylphenyl)pentyl *S*-Methyl Dithiocarbonate (2y).** Yield, 25%. A pale yellow oil; R_f = 0.48 (hexane : EtOAc = 10 : 1). IR 2957, 2924, 2870, 1713, 1456, 1370, 1246, 1219, 1159, 1051, 1005, 943, 901 cm^{-1}; ^1H NMR (200 MHz) δ = 0.89 (t, *J* = 7 Hz, 3 H), 1.22-1.50 (m, 4 H), 1.85-2.25 (m, 2 H), 2.56 (s, 3 H), 6.52 (dd, *J* = 6, 8 Hz, 1 H), 7.49 (d, *J* = 8 Hz, 2 H), 7.87 (d, *J* = 8 Hz, 2 H), 10.00 (s, 1 H); ^{13}C NMR (75.5 MHz)

δ = 13.9 (s), 19.1 (s), 22.4 (s), 27.4 (s), 36.0 (s), 84.3 (s), 127.2 (s), 129.9 (s), 135.9 (s), 146.5 (s), 191.7 (s), 215.1 (s); MS *m/z* (rel intensity) 283 (M^++1, 1), 282 (M^+, 13), 207 (12), 197 (17), 178 (22), 149 (24), 147 (40), 135 (40), 121 (21), 117 (24), 111 (29), 105 (35), 97 (100), 83 (61). Found: *m/z* 282.0740. Calcd for $C_{14}H_{18}O_2S_2$: M, 282.0748.

***O*-{*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexyl} *S*-Methyl Dithiocarbonate (2z).** Yield, 86%. Pale yellow needles, phase transition temperature/°C: Cr 95 N 148 Iso; R_f = 0.71 (hexane : EtOAc = 10 : 1) IR (KBr) 2961, 2921, 2857, 1605, 1516, 1497, 1449, 1429, 1356, 1285, 1271, 1190, 1161, 1051, 1021, 968, 870, 824, 777, 749 cm^{-1}; ^1H NMR (200 MHz) δ = 1.00-1.30 (m, 6 H), 1.31-1.61 (m, 4 H), 1.76-1.98 (m, 6 H), 2.14-2.30 (m, 2 H), 2.41 (tt, *J* = 3, 12 Hz, 1 H), 2.55 (s, 3 H), 5.45 (tt, *J* = 4, 11 Hz, 1 H), 6.84-7.07 (m, 3 H); ^{19}F NMR (188 MHz) δ = −139.1 (ddd, *J* = 8, 12, 21 Hz, 1 F), −143.0 (dddd, *J* = 5, 8, 10, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.6 (s), 27.7 (s), 30.1 (s), 31.0 (s), 34.3 (s), 41.82 (s), 41.84 (s), 43.5 (d, *J* = 1 Hz), 115.2 (d, *J* = 17 Hz), 116.6 (d, *J* = 16 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.5 (dd, *J* = 4, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.0 (dd, *J* = 13, 247 Hz), 215.0 (s); MS *m/z* (rel intensity) 384 (M^+, 0.17), 277 (15), 276 (47), 195 (17), 179 (19), 153 (22), 140 (37), 127 (100), 109 (18), 95 (20), 83 (50), 81 (58), 79 (31), 67 (51). Found: C, 62.27; H, 6.92%. Calcd for $C_{20}H_{26}F_2OS_2$: C, 62.47; H, 6.82%.

***O*-3β-Cholestanyl *S*-Methyl Dithiocarbonate (2α).** Yield, 93%. A colorless powder, mp 98.8-100.0 °C; R_f = 0.66 (hexane). IR (KBr) 2868, 2851, 1468, 1447, 1383, 1367, 1331, 1258, 1246, 1221, 1194, 1154, 1129, 1059, 1030, 995, 963, 922 cm^{-1}; ^1H NMR (200 MHz) δ = 0.60-2.15 (m, 47 H), 2.53 (s, 3 H), 5.38-5.60 (m, 1 H); ^{13}C NMR (50.3 MHz) δ = 12.1 (s), 12.2 (s), 18.7 (s), 18.8 (s), 21.2 (s), 22.5 (s), 22.8 (s), 23.8 (s), 24.2 (s), 26.8 (s), 28.0 (s), 28.2 (s), 28.6 (s), 32.0 (s), 33.3 (s), 35.5 (s), 35.8 (s), 36.2 (s), 36.7 (s), 39.5 (s), 40.0 (s), 42.6 (s), 44.6 (s), 54.2 (s), 56.3 (s), 56.4 (s), 83.6 (s), 215.2 (s); MS *m/z* (rel intensity) 478 (M^+, 0.2), 371 (29), 370 (40), 355 (13), 316 (13), 215 (34), 163 (16), 161 (21), 111 (20), 109 (43), 107 (43), 95 (79), 91 (53), 83 (44), 81 (100), 67 (73). Found: *m/z* 478.3264 (M^+). Calcd for $C_{29}H_{50}OS_2$: M, 478.3303 Found: C, 72.28; H, 10.46%. Calcd for $C_{29}H_{50}OS_2$: C, 72.74; H, 10.53%.

Synthesis of *O*-4-(4'-Acetoxy)biphenyl *S*-Methyl Dithiocarbonate (2j)

According to the general procedure for the preparation of dithiocarbonates described above, *O*-4'-hydroxy-4-biphenyl *S*-methyl dithiocarbonate was prepared in 42% yield with DMF as the reaction medium. A mixture of the dithiocarbonate (1.5 mmol), pyridine (2.5 mL), and DMAP (10 mg) was treated with Ac_2O (1.8 mL, 0.17 mmol) overnight. Workup and purification gave **2j** in 82% as a pale yellow powder, mp 112.8-113.4 °C; R_f = 0.23 (hexane : EtOAc = 10 : 1). IR (KBr) 3059, 2924, 1905, 1751, 1599, 1491, 1431,

1367, 1317, 1213, 1062, 1003, 914, 839, 800, 721 cm^{-1}; ^1H NMR (200 MHz) δ = 2.32 (s, 3 H), 2.70 (s, 3 H), 7.06-7.20 (m 4 H), 7.52-7.71 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 20.0 (s), 21.1 (s), 115.7 (s), 121.9 (s), 122.4 (s), 128.2 (s), 137.9 (s), 138.8 (s), 150.3 (s), 154.1 (s), 169.4 (s), 215.7 (s); MS *m/z* (rel intensity) 319 (M^++1, 1), 318 (M^+, 4), 312 (11), 310 (10), 152 (7), 139 (10), 91 (100), 75 (8). Found: *m/z* 318.0377. Calcd for $C_{16}H_{14}O_3S_2$: M, 318.0384.

***O*-1-Benzylbutyl *S*-Phenyl Dithiocarbonate (2r).** This substrate was prepared from 1-phenyl-2-pentanol (0.53 g, 3.2 mmol) by treatment with phenyl chlorodithioformate (0.55 mL, 3.9 mmol), pyridine (0.5 mL, 9.4 mmol), and DMAP (61 mg, 0.50 mmol) in dichloromethane (2.0 mL) at room temperature for 1 h. Workup and purification afforded **2r** (0.31 g, 30% yield) as a pale yellow oil; R_f = 0.50 (hexane : EtOAc = 10 : 1). IR 3061, 3028, 2959, 2872, 1497, 1473, 1456, 1233, 1129, 1078, 1040, 1021, 999, 746, 700 cm^{-1}; ^1H NMR (300 MHz) δ = 0.83 (t, *J* = 7 Hz, 3 H), 1.14-1.39 (m, 2 H), 1.43-1.60 (m, 2 H), 2.83 (dd, *J* = 7, 14 Hz, 1 H), 2.99 (dd, *J* = 6, 14 Hz, 1 H), 5.75-5.84 (m, 1 H), 7.02-7.10 (m, 2 H), 7.16-7.28 (m, 3 H), 7.38-7.49 (m, 5 H); ^{13}C NMR (75.5 MHz) δ = 13.8 (s), 18.3 (s), 34.6 (s), 39.4 (s), 84.9 (s), 126.5 (s), 128.3 (s), 129.1 (s), 129.4 (s), 129.8 (s), 129.9 (s), 135.1 (s), 136.7 (s), 212.3 (s); MS *m/z* (rel intensity) 316 (M^+, 1), 268 (2), 240 (8), 167 (4), 146 (8), 91 (100), 77 (10). Found: *m/z* 316.0956. Calcd for $C_{18}H_{20}OS_2$: M, 316.0956.

A General Procedure for the Preparation of Trifluoromethyl Ethers of Primary Alcohols and Phenols.

An oven-dried polypropylene round bottom tube equipped with a rubber septum, a Teflon®-coated magnetic stirring bar, and an argon inlet, was flushed with argon and charged with DBH (0.86 g, 3.0 mmol) and dry CH_2Cl_2 (3.0 mL). The suspension was cooled to –78 °C using an external acetone-dry ice bath and stirred at –78 °C for 10 min. To the mixture was slowly added 70% HF/py (2.0 mL, 40 mmol of HF/mL) over 5 min using a polypropylene/polyethylene syringe under an argon atmosphere. The resulting suspension was stirred vigorously. To this mixture was added dropwise a solution of **2** (1.0 mmol) in CH_2Cl_2 (3.0 mL) at –78 °C via a cannula by positive argon pressure. After the addition was completed, the acetone-dry ice bath was replaced by an ice-cold NaCl solution bath. The resulting red-brown reaction mixture was stirred at the same temperature for 30 min, diluted with diethyl ether at 0 °C, carefully (*caution!! during this operation, vigorous evaporation of hydrogen fluoride often occurs*), and quenched by careful addition of an ice-cold aqueous $NaHSO_3$/$NaHCO_3$/NaOH (pH 10) solution until a red-brownish color of the mixture disappeared at 0 °C. The pH value was readjusted to 10 at 0 °C by slow addition of ice-cooled 30% NaOH aq. solution and diluted with diethyl

ether. The contents were transferred to a separatory funnel; the organic phase was separated. The aqueous phase was extracted four times with portions of diethyl ether; the combined organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The pyridine in the residue was removed by double toluene azeotrope under reduced pressure. The residue was purified by flash column chromatography or bulb-to-bulb distillation to give trifluoromethyl ethers **3**. Yields and spectral properties of products are as follows.

4-Propyl-1-trifluoromethoxybenzene (3a). Isolated in 58% yield as a colorless oil; R_f = 0.68 (hexane). IR 2962, 2934, 2874, 1728, 1599, 1508, 1487, 1464, 1387, 1262, 1221, 1169, 1073, 846, 743 cm^{-1}; ^1H NMR (200 MHz) δ = 0.95 (t, J = 7 Hz, 3 H), 1.64 (tq J = 7, 7 Hz, 2 H), 2.59 (t, J = 7 Hz, 2 H), 7.12 (d, J = 9 Hz, 2 H), 7.19 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.46 (s); MS *m/z* (rel intensity) 205 (M^++1, 4), 204 (M^+, 6), 189 (11), 187 (13), 175 (38), 117 (12), 115 (18), 107 (16), 105 (15), 91 (15), 89 (19), 88 (14), 84 (100), 77 (44), 74 (20), 69 (85). Found: *m/z* 204.0755. Calcd for $C_{10}H_{11}F_3O$: M, 204.0762.

4-Hexyl-1-trifluoromethoxybenzene (3c). Yield, 50%. A colorless oil; R_f = 0.70 (hexane). IR 2932, 2861, 1510, 1262, 1223, 1165, 1020, 842, 808 cm^{-1}; ^1H NMR (100 MHz) δ = 0.90 (t, J = 6 Hz, 3 H), 1.10-1.87 (m, 8 H), 2.63 (t, J = 7 Hz, 2 H), 7.03 (d, J = 6 Hz, 2 H), 7.22 (d, J = 6 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.50 (s); MS *m/z* (rel intensity) 247 (M^++1, 3), 246 (M^+, 22), 176 (22), 175 (100), 109 (5), 78 (3). Found: C, 63.72; H, 6.97%. Calcd for $C_{13}H_{17}F_3O$: C, 63.40; H, 6.96%.

2-Benzyloxy-1-bromo-3-trifluoromethoxybenzene (3e'). Yield, 56%. A colorless oil; R_f = 0.41 (hexane). IR 2928, 1595, 1582, 1491, 1252, 1219, 1169, 1073, 1049, 1011, 808, 719 cm^{-1}; ^1H NMR (200 MHz) δ = 5.15 (s, 2 H), 6.91 (d, J = 9 Hz, 2 H), 7.14 (dd, J = 3, 9 Hz, 1 H), 7.4-7.6 (m, 6 H); ^{19}F NMR (188 MHz) δ = –58.94 (s); MS *m/z* (rel intensity) 348 (M^++2, 1), 346 (M^+, 1), 257 (2), 171 (58), 170 (9), 169 (100), 149 (6), 90 (18), 89 (12), 79 (3), 69 (11), 63 (9), 58 (8). Found: *m/z* 345.9810. Calcd for $C_{14}H_{10}{}^{79}BrF_3O_2$: M, 345.9816.

4-Bromo-1-trifluoromethoxybenzene (3f).[29] Obtained in 62% yield. ^1H NMR (200 MHz) δ = 7.06 (d, J = 8 Hz, 2 H), 7.51 (d, J = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.63 (s).

Propyl 4-Trifluoromethoxybenzoate (3g). Yield, 30%. A colorless oil; R_f = 0.46 (hexane : Et_2O = 10 : 1). IR 2973, 2884, 1725, 1609, 1507, 1416, 1307, 1260, 1221, 1169, 1103, 1019, 770, 710 cm^{-1}; ^1H NMR (300 MHz) δ = 1.03 (t, J = 7 Hz, 3 H), 1.80 (tq, J = 7, 7 Hz, 2 H), 4.29 (t, J = 7 Hz, 2 H), 7.27 (d, J = 7 Hz, 2 H), 8.10 (t, J = 7 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.14 (s); ^{13}C NMR (75.5 MHz) δ = 10.5 (s), 22.1 (s), 66.8 (s), 120.2 (s), 120.3 (q, J = 259 Hz), 128.9 (s), 131.5 (s), 152.5 (s), 165.4 (s); MS

m/z (rel intensity) 249 (M^++1, 0.1), 248 (M^+, 0.7), 207 (20), 206 (58), 190 (10), 189 (100), 161 (12), 95 (37), 75 (8), 69 (8), 64 (13). Found: *m/z* 248.0663. Calcd for $C_{11}H_{11}F_3O_3$: M, 248.0660._

Methyl 3-Trifluoromethoxybenzoate (3h). Yield, 76%. A colorless oil; R_f = 0.24 (hexane) IR 2959, 1732, 1592, 1449, 1302, 1256, 1171, 1102, 1078, 997, 760, 708 cm^{-1}; ^1H NMR (200 MHz) δ = 3.94 (s, 3 H), 7.42 (d, *J* = 8 Hz, 1 H), 7.48 (dd, *J* = 8, 8 Hz, 1 H), 7.90 (s, 1 H), 7.98 (d, *J* = 8 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –58.45 (s); ^{13}C NMR (75.5 MHz) δ = 52.4 (s), 120.4 (q, *J* = 258 Hz), 122.0 (s), 125.3 (s), 127.9 (s), 129.9 (s), 132.2 (s), 149.2 (q, *J* = 2 Hz), 165.7 (s); MS *m/z* (rel intensity) 222 (M^++2, 1), 221 (M^++1, 4), 220 (M^+, 33), 190 (10), 189 (100) 161 (31), 135 (9), 111 (3), 95 (43), 92 (11), 75 (12), 69 (19), 63 (21). Found: *m/z* 220.0348. Calcd for $C_9H_7F_3O_3$: M, 220.0347.

4-Acetoxy-4'-trifluoromethoxybiphenyl (3j). Isolated in 80% yield as colorless crystals, mp 126 °C; R_f = 0.68 (hexane : CH_2Cl_2 = 1 : 1). IR (KBr) 3072, 2930, 1911, 1761, 1604, 1496, 1373, 1292, 1215, 1167, 1006, 914, 842, 798 cm^{-1}; ^1H NMR (200 MHz) δ = 2.33 (s, 3 H), 7.21 (d, *J* = 9 Hz, 2 H), 7.34 (d, *J* = 9 Hz, 2 H), 7.55 (d, *J* = 9 Hz, 2 H), 7.57 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.34 (s); ^{13}C NMR (75.5 MHz) δ = 21.1 (s), 120.5 (q, *J* = 258 Hz), 121.2 (s), 122.0 (s), 128.1 (s), 128.4 (s), 137.5 (s), 139.1 (s), 148.7 (s), 150.4 (s), 169.4 (s); MS *m/z* (rel intensity) 297 (M^++1, 2), 296 (M^+, 10), 255 (14), 254 (100), 185 (13), 157 (7), 128 (6), 69 (3). Found: C, 60.69; H, 3.86%. Calcd for $C_{15}H_{11}F_3O_3$: C, 60.82; H, 3.74%.

4-Bromo-4'-trifluoromethoxybiphenyl (3k). Obtained in 52% yield with HF/py (80 molar amounts) or in 78% yield with HF/py (40 molar amounts) as colorless needles, mp 59.9-61.2 °C; R_f = 0.70 (hexane). IR (KBr) 3060, 3030, 1906, 1589, 1514, 1481, 1389, 1260 1163, 1003, 834, 808 cm^{-1}; ^1H NMR (200 MHz) δ = 7.29 (d, *J* = 9 Hz, 2 H), 7.42 (d, *J* = 9 Hz, 2 H), 7.54 (t, *J* = 8 Hz, 2 H), 7.58 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –58.33 (s); MS *m/z* (rel intensity) 320 (M^++4, 1), 319 (M^++3, 13), 318 (M^++2, 96), 317 (M^++1, 14), 316 (M^+, 100), 249 (27), 247 (27), 221 (25), 219 (26), 152 (18), 140 (26), 139 (49), 69 (25). Found: C, 48.96; H, 2.47%. Calcd for $C_{13}H_8BrF_3O$: C, 49.24; H, 2.54%.

1-Bromo-4-(2-trifluoromethoxyethyl)benzene (3l). Yield, 81%. A colorless oil, bp 120 °C/6 mmHg; R_f = 0.47 (hexane). IR 2975, 2915, 1595, 1491, 1404, 1267, 1144, 1075, 1013, 826, 804 cm^{-1}; ^1H NMR (300 MHz) δ = 2.95 (t, *J* = 7 Hz, 2 H), 4.13 (t, *J* = 7 Hz, 2 H), 7.10 (d, *J* = 8 Hz, 2 H), 7.44 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.23 (s); ^{13}C NMR (75.5 MHz) δ = 34.6 (s), 67.3 (q, *J* = 4 Hz), 120.8 (s), 121.5 (q, *J* = 255 Hz), 130.6 (s), 131.7 (s), 135.6 (s); MS *m/z* (rel intensity) 271 (M^++3, 3), 270 (M^++2, 24), 269 (M^++1, 3), 268 (M^+, 24), 251 (10), 249 (22), 247 (11), 171 (80), 170 (12), 169

(100), 90 (36), 89 (36), 86 (37), 84 (61), 77 (23), 75 (15), 74 (24), 69 (54), 63 (54). Found: *m/z* 267.9714. Calcd for $C_9H_8{}^{79}BrF_3O$: M, 267.9711.

1-Bromo-4-[3-(trifluoromethoxy)propyl]benzene (3m'). Yield, 75%. A colorless oil, R_f = 0.33 (hexane). IR 2973, 1489, 1408, 1271, 1140, 1073, 1013, 855, 835, 797 cm^{-1}; ^1H NMR (300 MHz) δ = 1.97 (tt, *J* = 6, 8 Hz, 2 H), 2.68 (t, *J* = 8 Hz, 2 H), 3.94 (t, *J* = 6 Hz, 2 H), 7.05 (d, *J* = 8 Hz, 2 H), 7.41 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.17 (s); ^{13}C NMR (75.5 MHz) δ = 30.1 (s), 31.0 (s), 66.2 (q, *J* = 3 Hz), 120.0 (s), 121.7 (q, *J* = 254 Hz), 130.2 (s), 131.6 (s), 139.5 (s); MS *m/z* (rel intensity) 285 (M^++3, 2), 284 (M^++2, 23), 283 (M^++1, 2), 282 (M^+, 19), 172 (15), 171 (55), 169 (100), 117 (14), 115 (13), 104 (11), 91 (41), 90 (33), 89 (29), 77 (25), 69 (47), 65 (13). Found: *m/z* 281.9866. Calcd for $C_{10}H_{10}{}^{79}BrF_3O$: M, 281.9868.

1-Trifluoromethoxydecane (3n). Yield, 80%. A colorless oil; R_f = 0.75 (hexane). IR 2928, 2857, 1728, 1466, 1408, 1383, 1273, 1142, 1044, 725 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.15-1.48 (m, 14 H), 1.60-1.79 (m, 2 H), 3.94 (*J* = 6 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.14 (s); MS *m/z* (rel intensity) 227 (M^++1, 0.7), 226 (M^+, 57), 141 (1), 112 (5), 97 (13), 83 (14), 69 (26), 57 (57), 43 (100). Found: *m/z* 226.1540. Calcd for $C_{11}H_{21}F_3O$: M, 226.1544.

1-Trifluoromethoxyhexadecane (3o). Isolated in 95% yield with DBH or in 67% yield using [bis(trifluoroacetoxy)iodo]benzene as an oxidant, respectively. A colorless oil; R_f = 0.78 (hexane). IR 2926, 2855, 1468, 1408, 1273, 1223, 1142, 860, 722 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 6 Hz, 3 H), 1.18-1.48 (m, 26 H), 1.60-1.79 (m, 2 H), 3.94 (*J* = 7 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.18 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 25.4 (s), 28.7 (s), 29.1 (s), 29.37 (s), 29.45 (s), 29.54 (s), 29.63 (s), 29.67 (s), 29.69 (s), 29.71 (s), 31.9 (s), 67.5 (q, *J* = 3 Hz), 121.7 (q, *J* = 254 Hz); MS *m/z* (rel intensity) 312 (M^++2, 0.2), 311 (M^++1, 0.9), 310 (M^+, 5), 224 (3), 211 (4), 169 (7), 155 (8), 141 (5), 140 (4), 126 (13), 111 (33), 99 (36), 98 (68), 97 (68), 96 (12), 85 (94), 84 (39), 83 (72), 75 (15), 71 (100), 70 (74), 69 (93). Found: *m/z* 310.2484. Calcd for $C_{17}H_{33}F_3O$: M, 310.2483.

Oxidative Desulfurization-Fluorination of Difluoro(methylthio)methyl Methyl Ethers.

Difluoro(methylthio)methyl methyl ethers **4** were fluorinated under the conditions for the fluorination of dithiocarbonates **2**. Yields (amounts and reagent) and spectral properties of products are as follows:

Compound **3a**: 42% yield, (70%, HF/py 80 mol; DBH, 1 mol).

Compound **3e'**: 62% yield, (70%, HF/py 80 mol; DBH, 2 mol).

Compound **3h**: 51% yield, (70%, HF/py 80 mol; DBH, 1 mol).

3-(Trifluoromethoxy)propylbenzene (3m): Obtained in 41% yield as a colorless oil using 70% HF/py (80 mol) and DBH (1 mol); R_f = 0.32 (hexane). IR 2928, 2862, 1456, 1408, 1270, 1141, 1033, 852 cm^{-1}; ^1H NMR (200 MHz) δ = 2.00 (tq, J = 7, 7 Hz, 2 H), 2.71 (t, J = 7 Hz, 2 H), 3.96 (t, J = 7 Hz, 2 H), 7.0-7.4 (m, 5 H); ^{19}F NMR (188 MHz) δ = –61.09 (s); MS *m/z* (rel intensity) 205 (M^++1, 3), 204 (M^+, 6), 167 (2), 150 (8), 149 (100), 1117 (3), 107 (6), 92 (10), 91 (33), 85 (12), 83 (10), 71 (26), 69 (27). Found: *m/z* 204. 758. Calcd for $C_{10}H_{11}F_3O$: M, 204.0762.

A General Procedure for the Difluorination of Dithiocarbonate.

Method A. To a stirred solution of $TBAH_2F_3$ (1.51 g, 5.0 mmol) and dithiocarbonate **2** (1.0 mmol) in CH_2Cl_2 (2.0 mL) was added NBS (0.71 g, 4.0 mmol) in one portion at room temperature. The resulting mixture was stirred for 1 h at room temperature, then poured into an aq. solution of $NaHCO_3$, NaOH, and $NaHSO_3$, and extracted three times with dichloromethane. The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered through a pad of Celite/silica gel (Wako Gel C-100), and concentrated. The residue was purified by flash column or preparative thin layer chromatography to give difluoro(methylthio)methyl ether **4**.

Method B. The reaction was carried out by a procedure similar to that described in Method A. Work-up was effected as follows. The reaction mixture was diluted with a mixture of pentane and diethyl ether (5 : 1). The resulting insoluble material was filtered through a short silica gel (Wako gel C-100) column. The filtrate was concentrated under reduced pressure. The residue was purified by flash column or preparative thin layer chromatography to give **4**.

Method, yield, and spectroscopic properties of products follow:

1-Difluoro(methylthio)methoxy-4-propylbenzene (4a). Method A, 58% yield. A colorless oil; R_f = 0.35 (hexane : CH_2Cl_2 = 40 : 1). IR 2955, 2930, 1720, 1502, 1205, 1198, 1138, 1108, 1050, 1028, 963, 838, 796 cm^{-1}; ^1H NMR (200 MHz) δ = 0.93 (t, J = 7 Hz, 3 H), 1.60 (qt, J = 7, 8 Hz, 2 H), 2.36 (s, 3 H), 2.60 (t, J = 8 Hz, 2 H), 7.10 (d, J = 7 Hz, 2 H), 7.16 (d, J = 7 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.55 (s); MS *m/z* (rel intensity) 276 (M^++2, 1), 275 (M^++1, 4), 274 (M^+, 22), 203 (9), 161 (9), 97 (100), 91 (11). Found: C, 56.79; H, 6.05%. Calcd for $C_{11}H_{14}F_2OS$: C, 56.88; H, 6.08%.

4-[Difluoro(methylthio)methoxy]toluene (4b). Method A, 64% yield. A colorless oil; R_f = 0.69 (hexane : Et_2O = 5 : 1). IR 3048, 2942, 1724, 1508, 1440, 1382, 1218, 1200, 1171, 1142, 1113, 1053, 1034, 973, 872, 721 cm^{-1}; ^1H NMR (200 MHz) δ = 2.35 (s, 3 H), 2.37 (s, 3 H), 7.10 (d, J = 9 Hz, 2 H), 7.16 (d, J = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.49 (s); ^{13}C NMR (75.5 MHz) δ = 12.4 (t, J = 3 Hz), 20.8 (s), 121.3 (s), 129.8 (t, J = 292 Hz), 129.9 (s), 135.8 (s), 148.4 (s); MS *m/z* (rel intensity) 205

(M^++1, 6), 204 (M^+, 33), 154 (13), 107 (8), 97 (100), 95 (11), 91 (32), 71 (18). Found: *m/z* 204.0425. Calcd for $C_9H_{10}F_2OS_2$: M, 204.0420.

1-Difluoro(methylthio)methoxy-4-hexylbenzene (4c). Method A, 36% yield. A colorless oil; R_f = 0.33 (hexane : CH_2Cl_2 = 40 : 1). IR 2930, 2859, 1726, 1507, 1466, 1383, 1200, 1144, 1055, 972 cm^{-1}; ^1H NMR (200 MHz) δ = 0.89 (t, *J* = 7 Hz, 3 H), 1.05-1.85 (m, 8 H), 2.36 (s, 3 H), 2.61 (t, *J* = 7 Hz, 2 H), 6.81-7.49 (m, 4 H); ^{19}F NMR (188 MHz) δ = –46.40 (s); MS *m/z* (rel intensity) 276 (M^++2, 1), 275 (M^++1, 4), 274 (M^+, 22), 203 (9), 161 (9), 97 (100), 91 (11). Found: C, 61.26; H, 7.17%. Calcd for $C_{14}H_{20}F_2OS$: C, 61.29; H, 7.35%.

1-Difluoro(methylthio)methoxy-4-methoxybenzene (4d). Method A, 33% yield. R_f = 0.56 (hexane : Et_2O = 5 : 1). IR 2946, 2840, 1720, 1600, 1500, 1250, 1190, 1140, 1110, 1030, 830 cm^{-1}; ^1H NMR (200 MHz) δ = 2.36 (s, 3 H), 3.80 (s, 3 H), 6.83 (d, *J* = 8 Hz, 2 H), 7.21 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.84 (s); MS *m/z* (rel intensity) 222 (M^++2, 2), 221 (M^++1, 3), 220 (M^+, 31), 123 (26), 107 (13), 97 (100), 92 (10), 77 (13). Found: C, 49.25; H, 4.63%. Calcd for $C_9H_{10}F_2O_2S$: C, 49.08; H, 4.58%.

1-Benzyloxy-4-difluoro(methylthio)methoxybenzene (4e). Method A, 43% yield. A colorless oil; R_f = 0.64 (hexane : Et_2O = 5 : 1). IR 3030, 2940, 1500, 1455, 1245, 1196, 1140, 1110, 1025, 830, 740, 690 cm^{-1}; ^1H NMR (200 MHz) δ = 2.39 (s, 3 H), 5.06 (s, 2 H), 6.94 (d, *J* = 8 Hz, 2 H), 7.16 (d, *J* = 8 Hz, 2 H), 7.28-60 (m, 5 H); ^{19}F NMR (188 MHz) δ = –46.82 (s); MS *m/z* (rel intensity) 298 (M^++2, 0.5), 297 (M^++1, 1), 296 (M^+, 8), 97 (13), 92 (10), 91 (100), 65 (11). Found: C, 60.78; H, 4.68%. Calcd for $C_{15}H_{14}F_2O_2S$: C, 60.80; H, 4.76%.

1-Bromo-4-[difluoro(methylthio)methoxy]benene (4f). Method A, 43% yield. A colorless oil; R_f = 0.68 (hexane : Et_2O = 5 : 1). IR 3125, 2950, 2880, 1890, 1730, 1584, 1489, 1440, 1383, 1201, 1168, 1140, 1100, 1068, 1011, 973, 863, 830, 780 cm^{-1}; ^1H NMR (200 MHz) δ = 2.38 (s, 3 H), 7.11 (d, *J* = 10 Hz, 2 H), 7.49 (d, *J* = 10 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.96 (s); ^{13}C NMR (75.5 MHz) δ = 12.3 (t, *J* = 3 Hz), 123.2 (s), 129.7 (t, *J* = 294 Hz), 132.5 (s), 132.6 (s), 149.6 (s); MS *m/z* (rel intensity) 271 (M^++3, 0.7), 270 (M^++2, 7), 269 (M^++1, 0.7), 268 (M^+, 7), 223 (0.6), 221 (0.6), 157 (6), 155 (6), 145 (2), 143 (2), 119 (1), 117 (1), 97 (100). Found: *m/z* 267.9371. Calcd for $C_8H_7{}^{79}BrF_2OS_2$: M, 267.9369.

Propyl 4-[Difluoro(methylthio)methoxy]benzoate (4g). Method A, 25% yield. A colorless oil; R_f = 0.46 (hexane : Et_2O = 5 : 1). IR 2961, 2930, 1728, 1601, 1466, 1273, 1123, 1073, 1042, 743 cm^{-1}; ^1H NMR (200 MHz) δ =1.03 (t, *J* = 6 Hz, 3 H), 1.80 (tq, *J* = 6, 6 Hz, 2 H), 2.44 (s, 3 H), 4.30 (t, *J* = 6 Hz, 2 H), 7.25 (d, *J* = 9 Hz, 2 H), 8.10 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.87 (s); ^{13}C NMR (75.5 MHz) δ = 10.5 (s), 12.4 (t, *J* = 3 Hz), 22.1 (s), 66.7 (s), 120.6 (s), 122.2 (s), 129.7 (t, *J* = 294 Hz), 131.2 (s),

154.0 (s), 165.7 (s); MS *m/z* (rel intensity) 276 (M^+, 9), 167 (36), 149 (100), 104 (6), 83 (8), 71 (29), 70 (25). Found: *m/z* 276.0630. Calcd for $C_{12}H_{14}F_2O_3S$: M, 276.0632.

Methyl 3-[Difluoro(methylthio)methoxy]benzoate (4h). Method A, 32% yield. A colorless oil; R_f = 0.38 (hexane : Et_2O = 5 : 1). IR 2950, 1727, 1585, 1442, 1382, 1296, 1285, 1272, 1203, 1130, 1103, 1058, 748 cm^{-1}; ^1H NMR (100 MHz) δ = 2.32 (s, 3 H), 3.86 (s, 3 H), 7.27-7.49 (m, 2 H), 7.72-7.95 (m, 2 H); ^{19}F NMR (188 MHz) δ = –46.98 (s); MS *m/z* (rel intensity) 249 (M^++1, 2), 248 (M^+, 13), 217 (6), 135 (12), 97 (100), 76 (6), 63 (5). Found: C, 48.56; H, 4.13%. Calcd for $C_{10}H_{10}F_2O_3S$: C, 48.38; H, 4.06%.

4-[Difluoro(methylthio)methoxy]biphenyl (4i). Method A, 23% yield. A colorless oil; R_f = 0.58 (hexane : EtOAc = 10 : 1). IR 3034, 2934, 1726, 1605, 1514, 1485, 1207, 1142, 1057, 1008, 972, 841, 760, 698 cm^{-1}; ^1H NMR (200 MHz) δ = 2.59 (s, 3 H), 7.29-7.61 (m, 9 H); ^{19}F NMR (188 MHz) δ = –47.91 (s); ^{13}C NMR (75.5 MHz) δ = 12.4 (s), 121.7 (s), 127.0 (s), 127.1 (s), 127.4 (s), 128.1 (s), 128.8 (s), 129.6 (t, J = 290 Hz), 139.1 (s), 140.1 (s); MS *m/z* (rel intensity) 268 (M^++2, 2), 267 (M^++1, 7), 266 (M^+, 41), 169 (6), 153 (17), 152 (15), 141 (8), 115 (11), 97 (100). Found: C, 62.99; H, 4.38%. Calcd for $C_{14}H_{12}F_2OS$: C, 63.14; H, 4.54%.

4-Bromo-4'-[difluoro(methylthio)methoxy]biphenyl (4k). Method A, 28% yield. Colorless crystals, mp 37.5-38.3 °C; R_f = 0.60 (hexane : EtOAc = 10 : 1). IR (KBr) 3042, 2942, 1902, 1586, 1512, 1480, 1387, 1213, 1090, 1028, 818, 785, 720 cm^{-1}; ^1H NMR (200 MHz) δ =2.40 (s, 3 H), 7.27 (d, J = 9 Hz, 2 H), 7.42 (d, J = 9 Hz, 2 H), 7.52 (d, J = 8 Hz, 2 H), 7.56 (d, J = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –46.64 (s); MS *m/z* (rel intensity) 347 (M^++3, 2), 346 (M^++2, 14), 345 (M^++1, 2), 344 (M^+, 14), 152 (15), 139 (8), 97 (100). Found: C, 48.57; H, 3.19%. Calcd for $C_{14}H_{11}BrF_2OS$: C, 48.71; H, 3.21%.

1-Bromo-4-{2-[difluoro(methylthio)methoxy]ethyl}benzene (4l). Method B, 19% yield. A colorless oil; R_f = 0.69 (hexane : Et_2O = 5 : 1). IR 2934, 1709, 1489, 1406, 1266, 1152, 1073, 1048, 1013, 972, 814, 723 cm^{-1}; ^1H NMR (300 MHz) δ = 2.21 (s, 3 H), 2.92 (t, J = 7 Hz, 2 H), 4.09 (t, J = 7 Hz, 2 H), 7.10 (d, J = 8 Hz, 2 H), 7.42 (d, J = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –50.70 (s); ^{13}C NMR (75.5 MHz) δ = 12.1 (t, J = 3 Hz), 34.9 (s), 66.3 (t, J = 4 Hz), 120.5 (s), 130.2 (t, J = 290 Hz), 130.6 (s), 131.6 (s), 136.3 (s); MS *m/z* (rel intensity) 298 (M^++2, 3), 296 (M^+, 3), 204 (2), 202 (2), 185 (39), 184 (100), 183 (42), 182 (99), 171 (16), 169 (15), 104 (77), 103 (26), 97 (18), 90 (13), 89 (13), 77 (30). Found: *m/z* 295.9717. Calcd for $C_{10}H_{11}{}^{79}BrF_2OS$: M, 232.0733.

{3-[Difluoro(methylthio)methoxy]propyl}benzene (4m). Method B, 15% yield. A colorless oil; R_f = 0.60 (hexane : Et_2O = 5 : 1). IR 3028, 2932, 2855, 1712, 1454, 1313, 1147, 1030, 746, 700 cm^{-1}; ^1H NMR (300 MHz) δ = 1.98 (tt, J = 7, 8 Hz, 2 H),

2.31 (s, 3 H), 2.72 (t, J = 8 Hz, 2 H), 3.93 (t, J = 7 Hz, 2 H), 7.17-7.32 (m, 5 H); ^{19}F NMR (188 MHz) δ = –50.51 (s); ^{13}C NMR (75.5 MHz) δ = 12.2 (t, J = 3 Hz), 30.6 (s), 31.8 (s), 65.4 (t, J = 5 Hz), 126.0 (s), 128.38 (s), 128.43 (s), 130.2 (t, J = 290 Hz), 141.0 (s); MS *m/z* (rel intensity) 232 (M^+, 0.4), 207 (2), 186 (2), 161 (40), 159 (100), 131 (12), 113 (14), 111 (41), 76 (10), 75 (55), 73 (12). Found: *m/z* 232.0734. Calcd for $C_{11}H_{14}F_2OS$: M, 232.0733.

1-[Difluoro(methylthio)methoxy]hexadecane (4o). Method B, 9% yield. A colorless oil; R_f = 0.78 (hexane : EtOAc = 10 : 1). IR 2924, 2855, 1715, 1468, 1352, 1150, 740 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.20-1.40 (m, 28 H), 1.62-1.71 (m, 2 H), 2.33 (s, 3 H), 4.21 (t, J = 7 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –50.96 (s); ^{13}C NMR (75.5 MHz) δ = 13.4 (s), 14.1 (s), 22.7 (s), 25.8 (s), 28.7 (s), 29.0 (s), 29.2 (s), 29.4 (s), 29.5 (s), 29.55 (s), 29.62 (s), 29.66 (s), 29.7 (s), 31.9 (s), 67.7 (s), 128.7 (t, J = 290 Hz); MS *m/z* (rel intensity) 338 (M^+, 3), 270 (6), 229 (4), 167 (10), 149 (6), 99 (14), 97 (16), 85 (45), 75 (16), 71 (100), 69 (32). Found: *m/z* 338.2452. Calcd for $C_{18}H_{36}F_2OS$: M, 338.2455.

A General Procedure for the Fluorination of Dithiocarbonates Derived from Secondary, Tertiary Aliphatic, and Benzylic Alcohols.

To a suspension of NIS (0.34 g, 1.5 mmol) in dichloromethane (2.0 mL) in an oven-dried polypropylene round-bottom tube was added dropwise 70% HF/py (0.5 mL, 20 mmol of HF) at –42 °C (CCl_4-dry ice bath) under stirring with a Teflon®-coated magnetic bar under an argon atmosphere. A dichloromethane solution (0.5 mL) of dithiocarbonate **2p** to **2y** (0.5 mmol) was added dropwise to the mixture at –42 °C via a cannula by an argon positive pressure. The resulting mixture was stirred at –42 °C for 1 h, poured into an ice-cold pH = 10 buffer solution ($NaHCO_3$, $NaHSO_3$, and NaOH) carefully, and extracted with diethyl ether three times. The combined ethereal layer was washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to give fluorinated products **5**. Yields and spectral properties of **5** follow.

(2-Fluoropentyl)benzene (5p). Isolated in 70% yield as a colorless oil; R_f = 0.79 (hexane : EtOAc = 10 : 1). IR 3065, 2961, 2936, 1605, 1417, 1466, 1381, 1192, 1129, 1082, 1009, 961, 829, 747, 739, 700 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.92 (t, J = 7 Hz, 3 H), 1.25-1.70 (m, 4 H), 2.70-3.05 (m, 2 H), 4.70 (dm, J = 51 Hz, 1 H), 7.15-7.40 (m, 5 H); ^{19}F NMR (188 MHz) δ = –179.32 (dm, J = 51 Hz); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 18.4 (d, J = 5 Hz), 36.8 (d, J = 21 Hz), 41.7 (d, J = 22 Hz), 94.3 (d, J = 171 Hz), 126.5 (s), 128.4 (s), 129.3 (s), 137.4 (s); MS *m/z* (rel intensity) 167 (M^++1, 2), 166 (M^+, 15), 151 (2), 117 (2), 109 (1), 105 (2), 104 (2), 103 (2), 92 (22), 91 (100), 65 (11).

Found: *m/z* 166.1165. Calcd for $C_{11}H_{15}F$: M, 166.1158.

(3-Fluoropentyl)benzene (5s). Yield, 65%. A colorless oil; R_f = 0.30 (hexane). IR 2969, 2941, 1605, 1497, 1455, 1385, 1362, 1115, 1059, 945, 745, 700 cm^{-1}; ^1H NMR (300 MHz) δ = 0.96 (t, *J* = 8 Hz, 3 H), 1.51-2.04 (m, 4 H), 2.62-2.86 (m, 2 H), 4.41 (dm, *J* = 49 Hz, 1 H), 7.16-7.31 (m, 5 H); ^{19}F NMR (282 MHz) δ = –183.21—183.72 (m); ^{13}C NMR (75.5 MHz) δ = 9.3 (d, *J* = 6 Hz), 28.1 (d, *J* = 21 Hz), 31.4 (d, *J* = 5 Hz), 36.5 (d, *J* = 21 Hz), 94.6 (d, *J* = 168 Hz), 125.9 (s), 128.40 (s), 128.43 (s), 141.6 (s); MS *m/z* (rel intensity) 167 (M^++1, 8), 166 (M^+, 45), 117 (27), 115 (17), 109 (14), 104 (13), 103 (13), 92 (100), 78 (22), 77 (25), 65 (37). Found: *m/z* 166.1156. Calcd for $C_{11}H_{15}F$: M, 166.1158.

(–)-Menthyl Fluoride (5t).[25] Yield, 48%; A colorless oil. IR 2957, 2930, 2872, 1458, 1385, 1371, 1183, 1013, 992, 976, 845 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80-0.98 (m, 9 H), 0.99-1.50 (m, 5 H), 1.54-1.74 (m, 2 H), 1.98-2.18 (m, 2 H), 4.31 (ddt, *J* = 5, 11, 50 Hz); ^{19}F NMR (188 MHz) δ = –175.40 (dm, *J* = 50 Hz); ^{13}C NMR (75.5 MHz) δ =17.0 (s), 20.4 (s), 22.0 (s), 23.6 (d, *J* = 9 Hz), 26.5 (d, *J* = 2 Hz), 31.2 (d, *J* = 11 Hz), 34.1 (d, *J* = 2 Hz), 41.5 (d, *J* = 17 Hz), 48.3 (d, *J* = 17 Hz), 93.2 (d, *J* = 173 Hz); MS *m/z* (rel intensity) 158 (M^+, 17), 138 (25), 123 (35), 99 (11), 97 (29), 96 (69), 95 (90), 81 (100), 73 (38), 72 (20), 67 (69), 59 (47), 55 (80), 53 (59), 41 (93). Found: *m/z* 158.1467. Calcd for $C_{10}H_{19}F$: M, 158.1471.

2-Fluoroadamantane (5u).[25] Yield, 82%. Colorless crystals, mp 84.2-84.7 °C. IR (KBr) 2909, 2857, 1453, 1383, 1363, 1102, 1048, 1007, 934, 816 cm^{-1}; ^1H NMR (300 MHz) δ = 1.50-1.95 (m, 10 H), 2.04-2.20 (m, 4 H), 4.68 (dm, *J* = 50 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –174.42 (dm, *J* = 50 Hz); ^{13}C NMR (75.5 MHz) δ = 14.9 (s), 26.8 (d, *J* = 2 Hz), 27.2 (s), 27.6 (d, *J* = 14 Hz), 31.4 (s), 31.9 (s), 32.5 (s), 32.6 (s), 32.9 (s), 35.6 (s), 35.7 (s), 37.2 (s), 37.8 (s), 38.7 (s), 94.6 (d, *J* = 178 Hz); MS *m/z* (rel intensity) 155 (M^++1, 5), 154 (M^+, 32), 111 (16), 109 (12), 99 (11), 98 (42), 97 (100), 93 (43), 71 (42), 69 (49), 67 (40). Found: *m/z* 154.1155. Calcd for $C_{10}H_{15}F$: M, 154.1158.

1-Fluoroadamantane (5v). Yield, 78%. Colorless crystals, mp 108 °C (sublimation). IR (KBr) 2915, 2853, 1456, 1352, 1318, 1300, 1111, 1103, 1088, 968, 918, 812 cm^{-1}; ^1H NMR (200 MHz) δ = 1.55-1.76 (m, 6 H), 1.80-1.90 (m, 6 H), 2.15-2.35 (m, 3 H); ^{19}F NMR (188 MHz) δ = –128.95—129.01 (m); ^{13}C NMR (75.5 MHz) δ = 31.5 (d, *J* = 10 Hz), 35.9 (d, *J* = 2 Hz), 42.7 (d, *J* = 17 Hz), 92.5 (d, *J* = 184 Hz); MS *m/z* (rel intensity) 155 (M^++1, 2), 154 (M^+, 17), 136 (13), 135 (100), 111 (6), 107 (8), 97 (4), 93 (25), 92 (12), 91 (20), 79 (64), 77 (26), 67 (69), 34 (64). Found: *m/z* 154.1160. Calcd for $C_{10}H_{15}F$: M, 154.1158.

4-Bromobenzyl Fluoride (5w). Yield, 43%. A colorless oil; R_f = 0.42 (hexane). IR 2961, 2897, 1902, 1595, 1489, 1468, 1408, 1373, 1213, 1071, 1013, 988,

837, 799 cm^{-1}; ^1H NMR (200 MHz) δ = 5.33 (d, *J* = 48 Hz, 2 H), 7.26 (d, *J* = 8 Hz, 2 H), 7.52 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –208.71 (t, *J* = 48 Hz); ^{13}C NMR (75.5 MHz) δ = 83.7 (d, *J* = 167 Hz), 122.7 (d, *J* = 4 Hz), 129.0 (d, *J* = 6 Hz), 131.7 (s), 135.1 (d, *J* = 17 Hz); MS *m/z* (rel intensity) 191 (M^++3, 3), 190 (M^++2, 3), 189 (M^++1, 10), 188 (M^+, 24), 187 (7), 110 (8), 109 (100), 108 (11), 107 (12), 83 (24), 63 (18). Found: *m/z* 187.9641. Calcd for C_7H_6BrF: M, 187.9637.

(1-Fluoropentyl)benzene (5x). Yield, 94% (DBH). A colorless oil; R_f = 0.48 (hexane). IR 2959, 2934, 1489, 1458, 1073, 1013, 822, 718 cm^{-1}; ^1H NMR (200 MHz) δ = 0.90 (t, *J* = 7 Hz, 3 H), 1.25-1.55 (m, 4 H), 1.60-2.10 (m, 2 H), 5.41 (ddd, *J* = 5, 8, 48 Hz, 1 H), 7.20-7.50 (m, 5 H); ^{19}F NMR (188 MHz) δ = –174.69 (ddd, *J* = 17, 27, 48 Hz); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 22.5 (s), 27.2 (d, *J* = 4 Hz), 36.9 (d, *J* = 24 Hz), 94.7 (d, *J* = 171 Hz), 125.5 (d, *J* = 7 Hz), 128.1 (d, *J* = 2 Hz), 128.3 (s), 140.6 (d, *J* = 20 Hz); MS *m/z* (rel intensity) 167 (M^++1, 2), 166 (M^+, 15), 146 (32), 118 (10), 117 (74), 115 (42), 110 (21), 109 (100), 104 (29), 91 (32), 77 (10), 65 (11). Found: *m/z* 166.1164. Calcd for $C_{11}H_{15}F$: M, 166.1158.

4-(1-Fluoropentyl)benzaldehyde (5y). Yield, 91% (NIS), 60% (DBH). A colorless oil; R_f = 0.50 (hexane : Et_2O = 5 : 1). IR 2959, 2934, 2735, 1705, 1611, 1306, 1210, 1169, 1048, 831 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 7 Hz, 3 H), 1.14-1.55 (m, 4 H), 1.63-2.05 (m, 2 H), 5.50 (ddd, *J* = 5, 8, 48 Hz, 1 H), 7.48 (d, *J* = 8 Hz, 2 H), 7.90 (d, *J* = 8 Hz, 2 H), 10.02 (s, 1 H); ^{19}F NMR (188 MHz) δ = –179.69 (ddd *J* = 20, 27, 48 Hz); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 22.4 (s), 28.5 (d, *J* = 4 Hz), 37.0 (d, *J* = 23 Hz), 93.8 (d, *J* = 173 Hz), 125.8 (d, *J* = 8 Hz), 129.9 (s), 136.0 (s), 147.4 (d, *J* = 20 Hz), 191.8 (s); MS *m/z* (rel intensity) 195 (M^++1, 7), 194 (M^+, 39), 193 (6), 165 (19), 151 (7), 147 (11), 138 (62), 137 (100), 133 (13), 132 (15), 131 (12), 110 (24), 109 (96), 108 (15), 107 (11), 105 (15), 91 (60), 77 (21). Found: *m/z* 194.1110. Calcd for $C_{12}H_{15}FO$: M, 194.1107.

1-Difluoromethyl-4-(1-fluoropentyl)benzene (6). Yield, 23% (DBH). A colorless oil; R_f = 0.38 (hexane). IR 2961, 1773, 1684, 1559, 1541, 1375, 1221,1075, 1032 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 7 Hz, 3 H), 1.20-1.45 (m, 4 H), 1.70-2.10 (m, 2 H), 5.46 (ddd, *J* = 5, 8, 48 Hz, 1 H), 6.65 (t, *J* = 56 Hz, 1 H), 7.40 (d, *J* = 8 Hz, 2 H), 7.52 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –111.19 (d, *J* = 56 Hz, 2 F), –177.50 (ddd *J* = 18, 28, 52 Hz, 1 F); MS *m/z* (rel intensity) 216 (M^+, 12), 198 (3), 197 (20), 160 (14), 159 (80), 155 (30), 154 (12), 141 (100), 140 (9), 109 (15), 63 (6). Found: *m/z* 216.1123. Calcd for $C_{12}H_{15}F_3$: M, 216.1126.

A General Procedure for the Preparation Trifluoromethyl Ethers of Secondary Alcohols.

To a suspension of NBS (0.89 g, 5.0 mmol) and dichloromethane (2.5 mL) placed in an oven-dried polypropylene round-bottom tube equipped with a rubber septum and Teflon®-coated magnetic stirring bar were added dropwise distilled pyridine (0.46 mL) and subsequently 70% HF/py (1.0 mL, 40 mmol of HF) at –42 °C (cooled by a CCl_4/dry ice bath) under an argon atmosphere. The resulting mixture was stirred at room temperature for 5 min and then cooled to 0 °C using an ice-water bath. A dichloromethane (1.5 mL) solution of dithiocarbonate **2p**, **2s**, **2α**, or **2z** (1.0 mmol) was added dropwise to the suspension at 0 °C. The dark-red reaction mixture was stirred at 0 °C for 1 h, diluted carefully with Et_2O (5 mL), and poured into an ice-cold buffer solution (pH = 10, $NaHCO_3$, $NaHSO_3$, and NaOH). The pH of the mixture was adjusted to 10 by careful addition of ice-cold 10% NaOH aqueous solution. The whole was diluted with Et_2O, and the organic phase was separated. The aqueous phase was extracted with diethyl ether three times. The combined organic phase was washed with sat aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash column chromatography (cyclohexane) afforded the corresponding trifluoromethyl ether.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-trifluoromethoxycyclohexane (3z).** Yield, 42%. A colorless powder, mp 43 °C; R_f = 0.41 (hexane). IR (KBr) 2928, 2861, 1607, 1520, 1455, 1270, 1208, 1129, 1032, 860, 773 cm^{-1}; ^1H NMR (200 MHz) δ = 0.96-1.26 (m, 6 H), 1.30-62 (m, 4 H), 2.06-2.20 (m, 2 H), 2.41 (tt, J = 3, 12 Hz, 1 H), 4.09 (tt, J = 5, 11 Hz, 1 H), 6.82-7.18 (m, 3 H); ^{19}F NMR (188 MHz) δ = –58.1 (s, 3 F), –139.1 (dddd, J = 1, 8, 12, 21 Hz, 1 F), –142.9 (dddd, J = 3, 7, 12, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 27.8 (s), 30.2 (s), 32.6 (s), 34.4 (s), 41.6 (s), 41.9 (s), 43.7 (s), 78.4 (q, J = 2 Hz), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 121.7 (q, J = 254 Hz), 122.5 (dd, J = 3, 6 Hz), 144.5 (dd, J = 4, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 363 (M^++1, 6), 362 (M^+, 30), 153 (23), 140 (93), 128 (10), 127 (100), 97 (21), 95 (20), 85 (18), 83 (27), 81 (87), 79 (27), 67 (47). Found: *m/z* 362.1668 (M^+). Calcd for $C_{19}H_{23}F_5O$: M, 362.1669.

1-Phenyl-2-trifluoromethoxypentane (3p). Yield, 21%. A colorless oil. R_f = 0.45 (hexane). IR 3032, 2963, 2876, 1456, 1284, 1217, 1136, 1009, 747, 700 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.25-1.66 (m, 4 H), 2.82-3.10 (m, 2 H), 4.30-4.50 (m, 1 H), 7.13-7.38 (m, 5 H); ^{19}F NMR (188 MHz) δ = –58.14 (s); MS *m/z* (rel intensity) 232 (M^+, 12), 123 (2), 117 (3), 115 (3), 104 (2), 103 (4), 92 (36), 91 (100), 89 (2), 77 (9), 75 (26), 69 (10), 65 (24). Found: *m/z* 232.1077. Calcd for $C_{12}H_{15}F_3O$: M, 232.1075.

(3-Trifluoromethoxypentyl)benzene (3s). Yield, 16%. A colorless oil. R_f =

0.48 (hexane). IR 2957, 2925, 2855, 1464, 1378, 1366, 1261, 1123, 771, 721 cm^{-1}; ^1H NMR (200 MHz) δ = 0.95 (t, *J* = 7 Hz, 3 H), 1.64-1.80 (m, 2 H), 1.82-1.98 (m, 2 H), 2.56-2.84 (m, 2 H), 4.12-4.25 (m, 1 H), 7.15-7.35 (m, 5 H); ^{19}F NMR (188 MHz) δ = –57.74 (s); MS *m/z* (rel intensity) 232 (M^+, 23), 146 (8), 118 (9), 117 (56), 115 (6), 105 (19), 104 (35), 92 (37), 91 (100), 78 (13), 77 (11), 69 (35), 65 (24), 61 (12). Found: *m/z* 232.1073. Calcd for $C_{12}H_{15}F_3O$: M, 232.1075.

3β-Trifluoromethoxycholestane (3α). Yield, 24%. Colorless needles, mp 92-94 °C (EtOH); R_f = 0.79 (hexane). IR (KBr) 2930, 2870, 1468, 1447, 1385, 1283, 1219, 1134, 1021, 853 cm^{-1}; ^1H NMR (200 MHz) δ = 0.60-2.15 (m, 46 H), 4.05-4.20 (m, 1 H); ^{19}F NMR (188 MHz) δ = –58.02 (s); ^{13}C NMR (50.3 MHz) δ = 12.1 (s), 12.2 (s), 18.7 (s), 21.2 (s), 22.6 (s), 22.8 (s), 23.8 (s), 24.2 (s), 28.0 (s), 28.2 (s), 28.4 (s), 28.5 (s), 31.9 (s), 34.8 (s), 35.2 (s), 35.4 (s), 35.8 (s), 36.2 (s), 36.6 (s), 39.5 (s), 39.9 (s), 42.6 (s), 44.6 (s), 54.2 (s), 56.2 (s), 56.4 (s), 78.6 (q, *J* = 2.2 Hz), 121.6 (q, *J* = 254.1 Hz); MS *m/z* (rel intensity) 457 (M^++1, 7), 456 (M^+, 23), 302 (54), 301 (100), 287 (28), 233 (23), 149 (11), 147 (11), 135 (13), 123 (27), 121 (25), 109 (33), 108 (37), 107 (47), 95 (60), 93 (45), 81 (67), 67 (78). Found: C, 73.59; H, 10.52%. Calcd for $C_{28}H_{47}F_3O$: C, 73.64; H, 10.37%.

IV-5. References and Notes

1) a) J. T. Welch and S. Eswarakrishnan, "*Fluorine in Bioorganic Chemistry*," John Wiley & Sons, New York (1991); b) "*Biomedical Aspects of Fluorine Chemistry*," ed by R. Filler and Y. Kobayashi, Kodansha Ltd. and Elsevier Biochemical, Tokyo and Amsterdam (1982); c) C. Hansch, A. Leo, and R. W. Tafts, *Chem. Rev.*, **91**, 165 (1991); d) C. Hansch and A. Leo, "*Substituent Constants for Correlation Analysis in Chemistry and Biology*," John Wiley & Sons, New York (1979).

2) a) H. Nohira, *Nippon Kagaku Kaishi*, **1994**, 467; b) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.*, **209**, 1 (1991).

3) a) "*Chemistry of Organic Fluorine Compounds II. A Critical Review*," ed by M. Hudlicky and A. E. Pavlath, ACS Monograph 187, Washington, DC (1995); b) "*Synthetic Fluorine Chemistry*," ed by G. A. Olah, R. D. Chambers, and G. K. S. Prakash, John Wiley & Sons, New York (1991); c) "*Preparation, Properties, and Industrial Applications of Organofluorine Compounds*," ed by R. E. Banks,

John Wiley & Sons, New York (1982); d) J. T. Welch, *Tetrahedron,* **43**, 3123 (1987).

4) a) H. Matsutani, T. Kusumoto, and T. Hiyama, *Chem. Lett.,* **1999**, 529; b) T. Yamazaki, N. Shinohara, T. Kitazume, and S. Sato, *J. Org. Chem.,* **60**, 8140 (1995); c) T. Yamazaki, H. Umetani, and T. Kitazume, *Tetrahedron Lett.*, **38**, 6705 (1997); d) "*Fusso Kagaku Nyumon*," ed by H. Kobayashi, Nikkan Kogyo Shinbun Sha, Tokyo (1997).

5) a) M. Kuroboshi and T. Hiyama, *Yuki Gosei Kagaku Kyokai Shi,* **51**, 1124 (1993); b) M. Kuroboshi and T. Hiyama, *Synlett,* **1991**, 909; c) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.,* **71**, 1939 (1998); d) M. Kuroboshi and T. Hiyama, *Synlett,* **1994**, 251; e) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.,* **35**, 3983 (1994); f) M. Kuroboshi and T. Hiyama, *J. Fluorine Chem.,* **69**, 127 (1994); g) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683; h) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **72**, 2523 (1999).

6) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **72**, 805 (1999).

7) K. Kanie, K. Mizuno, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1973 (1998).

8) a) M. Kuroboshi, K. Suzuki, and T. Hiyama, *Tetrahedron Lett.,* **33**, 4173 (1992); b) K. Kanie, Y. Tanaka, M. Shimizu, M. Kuroboshi, and T. Hiyama, *Chem. Commun.,* **1997**, 309.

9) a) K. Kanie, Y. Tanaka, S. Takehara, and T. Hiyama, *Chem. Lett.,* **1998**, 1169; b) K. Kanie, M. Kuroboshi, S. Takehara, and T. Hiyama, *J. Fluorine Chem.,* **97**, 201 (1999); c) G. W. Gray, M. Hird, and K. J. Tony, *Mol. Cryst. Liq. Cryst.,* **204**, 91 (1991).

10) L. C. Clark and F. Gollan, *Science,* **152**, 1755 (1966).

11) N. N. Iarovenko and A. S. Vasileva, *J. Gen. Chem. USSR,* **28**, 2539 (1958).

12) A. G. Fab. Hoechst, *Brevet Brit.* **1957**, 765527 (*Chem. Abstr.,* **51**, 14803f (1957)).

13) A. E. Feiring, *J. Org. Chem.,* **44**, 2907 (1979).

14) W. A. Sheppard, *J. Org. Chem.,* **29**, 1 (1964).

15) F. Mathey and J. Bensoam, *Tetrahedron Lett.,* **25**, 2253 (1973).

16) a) S. Rozen, *Chem. Rev.,* **96**, 1717 (1996); b) K. K. Johri and D. D. DesMarteau, *J. Org. Chem.,* **48**, 242 (1983); c) J. B. Levy and D. M. Sterling, *J. Org. Chem.,* **50**, 5615 (1985); d) T. B. Patrick, G. L. Cantrell, and S. M. Inga, *J. Org. Chem.,* **45**, 1409 (1980); e) D. H. R. Barton, L. J. Danks, A. K. Ganguly, R. H. Hesse, G. Tarzia, and M. M. Pechet, *Chem. Commun.*, **1969**, 227; f) J.

Adamson, A. B. Foster, L. D. Hall, and R. H. Hesse, *Chem. Commun.*, **1969**, 309; g) C. Corvaja, F. Cremonese, W. Navarrini, C. Tonelli, and V. Tortelli, *Tetrahedron Lett.*, **36**, 3543 (1995).

17) K. Adachi, S. Ishihara, and T. Umemoto, *Abstract of the 15th International Symposium on Fluorine Chemistry, Vancouver*, Canada, Aug. 2-7, 1997.

18) W. A. Sheppard, *J. Org. Chem.*, **29**, 11 (1964).

19) G. A. Olah, J. T. Welch, Y. D. Vankar, M. Nojima, I. Kerekes, and J. A. Olah, *J. Org. Chem.*, **44**, 3872 (1979).

20) T. Fukuhara, N. Yoneda, T. Abe, S. Nagata, and A. Suzuki, *Nippon Kagaku Kaishi*, **10**, 1951 (1985).

21) A. W. M. Lee, W. H. Chan, H. C. Wong, and M. S. Wong, *Synth. Commun.*, **19**, 547 (1989).

22) J. Cousseau and P. Albert, *Bull. Soc. Chim. Fr.*, **6**, 910 (1986).

23) Aromatic bromination under the similar conditions were reported: see, a) C. Chassaing, A. Haudrechy, and Y. Langlois, *Tetrahedron Lett.*, **38**, 4415 (1997); b) S. Rozen and O. Lerman, *J. Org. Chem.*, **58**, 239 (1993); c) S. Fujisaki, H. Eguchi, A. Omura, A. Okamoto, and A. Nishida, *Bull. Chem. Soc. Jpn.*, **66**, 1576 (1993).

24) I. Ben-David, D. Rechavi, E. Mishani, and S. Rozen, *J. Fluorine Chem.*, **97**, 75 (1999).

25) M. J. Koen, F. L. Guyader, and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, **1995**, 1241.

26) C. M. Sharts and W. A. Sheppard, *Org. React.*, **21**, 125 (1974).

27) G. A. Boswell, Jr., W. C. Ripka, R. M. Scribner, and C. W. Tullock, *Org. React.*, **21**, 1 (1974).

28) S. Kanemoto, M. Shimizu, and H. Yoshioka, *Bull. Chem. Soc. Jpn.*, **62**, 2024 (1989).

29) Compound **3f** was purchased from Tokyo Kasei Inc.

Chapter V

Synthesis and Electro-optical Properties of 3-Substituted Phenyl Trifluoromethyl Ethers

Abstract: A convenient synthetic method is described of 3-substituted aromatic trifluoromethyl ethers through an oxidative desulfurization-fluorination reaction. Upon addition to LC materials, these ethers lower Δn of the host liquid crystals.

V-1. Introduction

Fluorine-containing LCs are widely used as a switching element of LC displays (LCDs) as described in Chapter 1.[1-3] Recently, capabilities of such fluorine-containing LCs as 1-(4'-substituted cyclohexyl)-4-fluorobenzenes, trifluoromethoxy-benzenes, and *N*-alkyl-*N*-trifluoromethylanilines[4] as a component for LCs have attracted much attention because of low threshold voltage for low $\Delta\varepsilon$.

As discussed before, oxidative desulfurization-fluorination reaction[5,6] transforms the dithiocarbonates derived from phenols, primary alcohols,[7] and secondary alcohols[8] to the corresponding trifluoromethyl ethers under mild conditions. For this transformation, a readily available reagent system is extremely effective consisting of an *N*-halo imide such as DBH and a fluoride reagent such as 70% HF/py[9] or 80% hydrogen fluoride–20% melamine (80% HF/mel).[10]

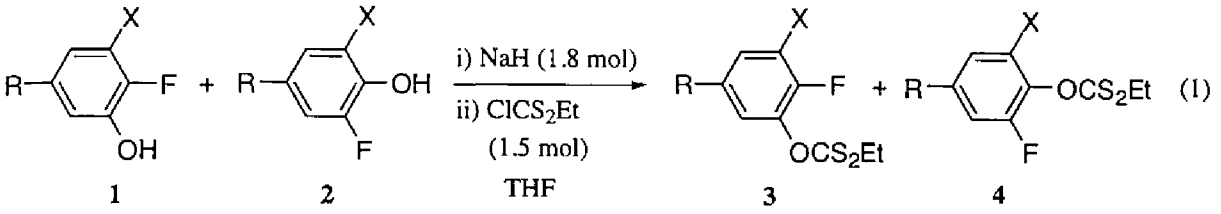
As introduction of a trifluoromethoxy group into C–3 of the LC molecules of type 1-cyclohexyl-4-fluorobenzene reduces the symmetry of molecule, the Author envisaged that such LC molecules would be an effective additive for lowering $\Delta\varepsilon$, viscosity, and Δn, as compared with the corresponding 4–CF_3O substituted LCs.

In this Chapter are discussed a convenient synthesis of LCs containing a 1-cyclohexyl-3-trifluoromethoxybenzenes unit through the oxidative desulfurization-fluorination reaction and the properties of the resulting trifluoromethyl ethers as a component of the LC compounds.

V-2. Results and Discussion

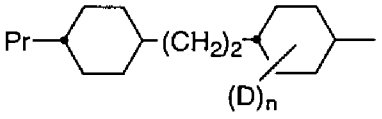
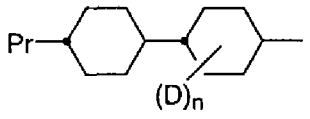
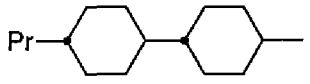
V-2-1. Synthesis

For the synthesis of 3-substituted phenyl trifluoromethyl ethers through the oxidative desulfurization-fluorination reaction, phenols **1**, obtained as a mixture with 4-isomers **2** expect for **1c** by the procedure described before,[11] were converted into *S*-ethyl dithiocarbonates **3** by the reaction with ethyl chlorodithioformate (eq. 1).



For this transformation, sodium hydride was a highly effective base to complete the reaction in a short period and gave **3** in high yields. The results are summarized in Table 1. The regioisomeric ratios in substrates and products were estimated by ^{19}F NMR. In entries 1 and 2, 4-substituted carbonates produced from the corresponding phenol were used also obtained as inseparatable minor products. Thus, the mixtures were used for the next fluorination reaction.

Table 1. Synthesis of *S*-ethyldithiocarbonates of **3** (and **4**)

R	substrates	X	yield of **3** (and **4**)/%	isomers ratio
	**1a** : **2a** = 12 : 1	F	96	**3a** : **4a** = 15 : 1
	**1b** : **2b** = 12 : 1	F	88	**3b** : **4b** = 14 : 1
	**1c** only	H	87	**3c** only

n = 1~3

The dithiocarbonates **3** (and **4**) were subjected to the oxidative desulfurization-fluorination reaction using 80% HF/mel (70 mol) and DBH (5.0 mol); bromotrifluoromethyl phenyl ethers **5** (and **6**) were isolated as shown in Scheme 1.

Scheme 1. Synthesis of 3-substituted phenyl trifluoromethyl ethers

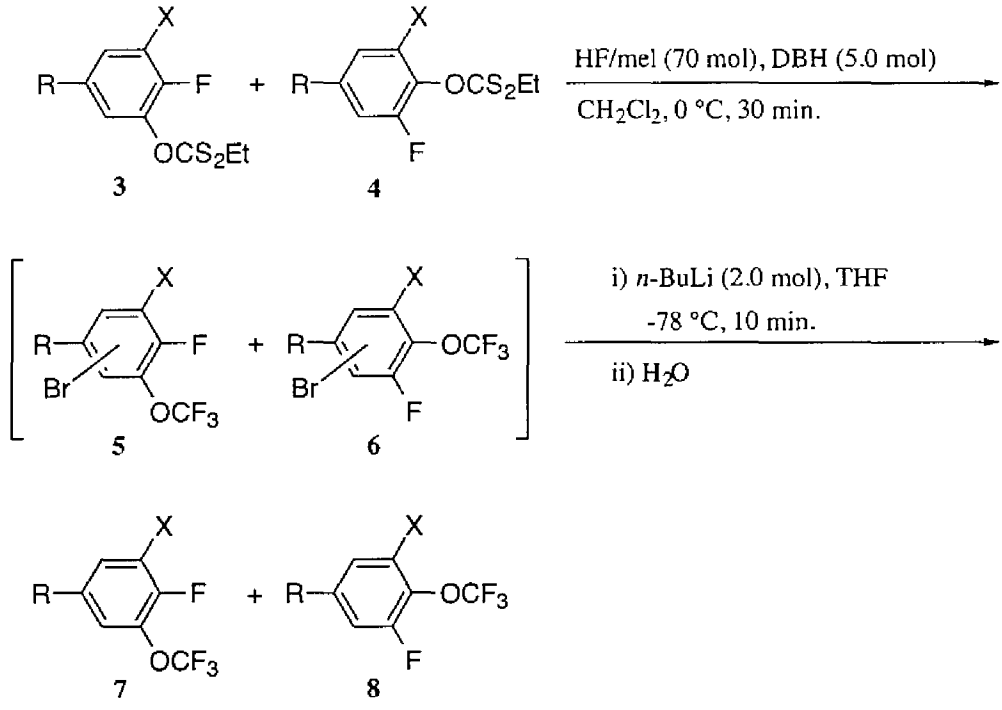
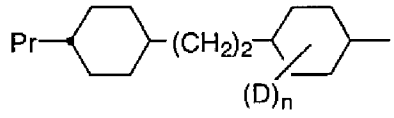
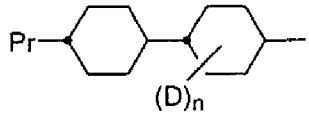
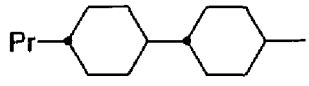


Table 2. Yields and isomers ratio of **7** (and **8**) prepared according to Scheme 1.

R	X	7 : 8	yield of **7** (and **8**)/%	products ratio
	F	15 : 1	60	**7a** : **8a** = 6 : 1
	F	14 : 1	62	**7b** : **8b** = 28 : 1
	H	1 : 0	35	**7c** : **8c** = 1 : 0

n = 1~3

Under the reaction conditions, trifluoromethylation as well as bromination of the phenyl ring took place. Debromination was performed by the treatment of **5** (and **6**) with *n*-BuLi (2.0 mol) at –78 °C for 10 min followed by quenching with H_2O at –78 °C to give **7** (and **8**) in moderate yields as a colorless oil. Results of the trifluorination are summarized in Table 2. Again, the separation of **8a** and **8b** from **7a** and **7b**, respectively, could not be performed by flash-silica gel column chromatography, preparative thin-layer chromatography, or HPLC (polystyrene-gel, $CHCl_3$ eluent). Use of 70% HF/py[7] was not effective for the fluorination reaction.

V-2-2. Electro-optical Properties of 3-Substituted Phenyl Trifluoromethyl Ethers

To examine the electro-optical properties of oily 3-substituted phenyl trifluoromethyl ethers **7a-c**, each was mixed in a **host** mixture (**7**/**host** = 15/85 w/w). The **host** mixture used was a 1 : 1 mixture of *trans*-1-(3,4-difluorophenyl)-4-[*trans*-4-(3-butenyl)-cyclohexyl]cyclohexane and *trans*-1-(3,4-difluorophenyl)-4-(*trans*-4-vinylcyclohexyl)-cyclohexane, typical materials for nematic LCDs. The following properties are summarized in Table 3: nematic-isotropic transition temperature (T_{NI}) on heating, $\Delta\varepsilon$, V_{th}, Δn, and τ with the applied voltages.

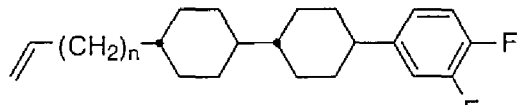
To estimate dielectric anisotropy ($\Delta\varepsilon'$) of a pure sample of **7**, $\Delta\varepsilon$ was extrapolated to 100%. The results also are listed in Table 3. The Author compared the properties of **7** with those of trifluoromethyl ethers **11**, currently employed LC materials for TFT displays. All the 3-substituted phenyl trifluoromethyl ethers exhibited $\Delta\varepsilon'$ lower than that of the 4-isomer **11**. In spite of the lower values of $\Delta\varepsilon'$, **7** showed V_{th} values similar to or lower than **11**. Furthermore, all 3-substituted trifluoromethyl ethers had especially low $\Delta n'$. Short response times (τ) of the **7**/**host** mixtures indicated that 3-trifluoromethoxy ether **7** switched faster than 4-isomer **11**. Thus, 3-trifluoromethoxy ether **7** should be a useful additive to lower $\Delta\varepsilon$, V_{th} , and Δn of LC materials and thus to achieve fast response.

Although it exhibited properties similar to methyl ether **10**, **7b** had a voltage holding ratio much higher than **10**. Therefore, the LCs of type 3-CF_3O substituted phenyl cyclohexanes synthesized here are suitable additives for TFT displays.

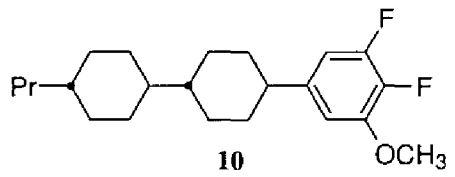
Table 3. Physical and electro-optical properties of **7**, **10**, and **11**[a)]

compound	T_{NI}/°C	$\Delta\varepsilon$	$\Delta\varepsilon'$[e)]	V_{th}/V[f)]	Δn	$\Delta n'$[g)]	τ/ms[f, h)]	applied voltage/V
host (9)	116.7	4.8	----	2.14	0.090	----	25.3	5.1
7a[b)]	97.0	5.2	7.7	1.76	0.082	0.037	43.0	4.1
7b[c)]	96.5	5.4	9.1	1.83	0.082	0.037	36.0	4.3
7c	98.5	4.9	5.6	1.94	0.083	0.043	33.0	4.4
10	102.4	5.7	11.1	1.85	0.084	0.050	42.0	4.4
11[d)]	110.5	5.9	11.9	1.90	0.087	0.070	73.5	4.0

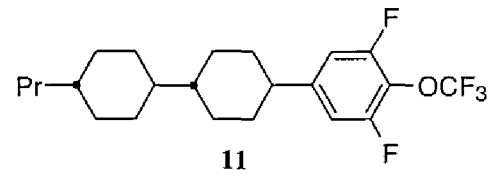
a) Measured in **host** (**9**) (15/85 w/w at 20 °C); b) A 6 : 1 mixture of **7a** and **8a**; c) A 28 : 1 mixture of **7b** and **8b**; d) Interpolated from 0 to 30 wt%; e) Extrapolated from $\Delta\varepsilon$; f) Corrected value for 6.0 μm cell; g) Extrapolated from Δn; h) Responce time ($\tau_r = \tau_d$).



host (9); (n = 0) : (n = 2) = 1 : 1 mixture



10



11

V-3. Conclusion

New LC compounds **7** were prepared through the oxidative desulfurization-fluorination reaction. Although **7** did not exhibit any mesophase, they were shown to induce lower threshold voltage, dielectric anisotropy, and birefringence than the 4-substituted isomers LC materials used now for TFT displays.

V-4. Experimental

The ratio of the regioisomers were estimated by the integration of ^{1}H NMR or ^{19}F NMR experiment.

A Typical Procedure for the Synthesis of *S*-Ethyl Dithiocarbonates.

***S*-Ethyl *O*-(2,3-Difluoro-5-{3,3,5,5-(D)$_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)-ethyl]cyclohexyl}phenyl) Dithiocarbonate (3a) and *S*-Ethyl *O*-(2,6-Difluoro-4-{3,3,5,5-(D)$_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)ethyl]cyclohexyl}phenyl) Dithiocarbonate (4a).** To a stirred suspension of sodium hydride (NaH, 60% in oil, 0.29 g, 7.2 mmol) in THF (2.0 mL) was slowly added dropwise a solution of a 12 : 1 mixture of 1,2-difluoro-3-hydroxy-5-{3,3,5,5-(D)$_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)ethyl]cyclohexyl}benzene (**1a**) and its regioisomer **2a** (1.46 g, 4.0 mmol) in THF (4.0 mL) at 0 °C under an argon atmosphere. The mixture was stirred for 30 min at 0 °C, chloro ethyldithioformate (0.86 g, 6.0 mmol) in THF (2.0 mL) solution was added dropwise. The resulting mixture was stirred for 1.5 h at 0 °C, treated with aq. $NaHCO_3$ and the aq. phase was extracted with Et_2O three times. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash-silica gel column chromatography (hexane : Et_2O = 30 : 1) to give a 15 : 1 mixture of **3a** and **4a** (1.79 g, 3.8 mmol) in a yield

of 96%.

These isomers could not be separated even by recycling preparative HPLC (polystyrene gel, $CHCl_3$ eluent) or recrystallization (from EtOH-hexane).

The mixture of **3a** and **4a** was pale yellow crystals, mp 56.7-58.4 °C; R_f = 0.57 (hexane). IR (KBr) 2921, 2849, 1520, 1454, 1439, 1331, 1167, 1065, 1055, 1040 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.78-0.95 (m, 4 H), 1.10-1.37 (m, 13 H), 1.43 (t, J = 8 Hz, 3 H), 1.65-1.78 (m, 3 H), 1.79-1.91 (m, 3 H), 2.42 (tt, J = 3, 12 Hz, 1 H), 3.24 (q, J = 8 Hz, 2H), 6.75 (ddd, J = 2, 2, 6 Hz, 1 H), 6.95 (ddd, J = 2, 7, 11 Hz, 1 H); MS *m/z*, as D_3 isomer (rel intensity) 472 (M^+, 0.8), 471 (1), 469 (1), 448 (1), 445 (5), 444 (11), 157 (9), 156 (11), 149 (19), 135 (16), 125 (15), 124 (6), 123 (15), 113 (9), 112 (7), 111 (20), 110 (13), 109 (16), 107 (13), 105 (100), 97 (38), 95 (26), 89 (38), 83 (50), 71 (52), 70 (22), 69 (59) Found: *m/z* 469.2390, Calcd for $C_{26}H_{37}DF_2OS_2$: M 469.2395. Found: *m/z* 470.2473, Calcd for $C_{26}H_{36}D_2F_2OS_2$: M 470.2458. Found: *m/z* 471.2513, Calcd for $C_{26}H_{35}D_3F_2OS_2$: M 471.2520.

3a: ^{19}F NMR (188 MHz) δ = −136.7 (ddd, J = 2, 11, 21 Hz), −154.1 (ddd, J = 6, 7, 21 Hz).

4a: ^{19}F NMR (188 MHz) δ = −126.4 (d, J = 9 Hz).

***S*-Ethyl *O*-(2,3-Difluoro-5-{[3,3,5,5-(D)$_n$-*trans*-4-(*trans*-4-propylcyclohexyl)]-cyclohexyl}phenyl) Dithiocarbonate (3b) and *S*-Ethyl *O*-(2,6-Difluoro-4-{[3,3,5,5-(D)$_n$-*trans*-4-(*trans*-4-propylcyclohexyl)]cyclohexyl}phenyl) Dithiocarbonate (4b).** A mixture of **3b** and **4b** was obtained in a similar manner in 88% yield (3.0 g, 9.0 mmol) as a 14 : 1 mixture from a 12 : 1 mixture of 2,3-difluoro-1-hydroxy-5-{[3,3,5,5-(D)$_n$-*trans*-4-(*trans*-4-propylcyclohexyl)]cyclohexyl}benzene (**1b**) and its regioisomer **2b** (3.5 g, 7.9 mmol).

A mixture of **3b** and **4b**: Pale yellow crystals, mp 59.8-62.2 °C (recryst. from EtOH-hexane); R_f = 0.57 (hexane). IR (KBr) 2940, 2845, 2190, 1609, 1520, 1431, 1333, 1275, 1236, 1171, 1060, 984, 860, 793, 700, 679 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.75-1.38 (m, 17 H), 1.43 (t, J = 7 Hz, 3 H), 1.60-1.95 (m, 6 H), 2.39 (m, 1 H), 3.24 (q, J = 7 Hz, 4 H), 6.75 (ddd, J = 1, 2, 6 Hz, 1 H), 6.94 (ddd, J = 2, 7, 12 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 13.0 (s), 14.4 (s), 20.0 (s), 29.9 (s), 30.1 (s), 31.7 (s), 33.6 (s), 34.1 (dm, J = 20 Hz), 37.6 (s), 39.8 (s), 42.7 (s), 43.3 (s), 113.4 (d, J = 17 Hz), 117.2 (d, J = 3 Hz), 140.9 (dd, J = 15, 250 Hz), 142.7 (dd, J = 3, 10 Hz), 144.0 (dd, J = 4, 6 Hz), 150.9 (dd, J = 11, 248 Hz), 213.0 (s); MS *m/z* as D_3 isomer (rel intensity) 444 (M^+, 1), 443 (1), 419 (1), 416 (2), 415 (5), 207 (5), 187 (2), 167 (3), 157 (6), 121 (6), 107 (13), 105 (100), 89 (40), 83 (15), 81 (16), 78 (15), 76 (62), 69 (45); Found: *m/z* 441.2050, Calcd for $C_{24}H_{33}DF_2OS_2$: M 441.2082. Found: *m/z* 442.2152, Calcd for $C_{24}H_{32}D_2F_2OS_2$: M 442.2145. Found: *m/z* 443.2208, Calcd for $C_{24}H_{31}D_3F_2OS_2$: M 443.2207.

3b: ^{19}F NMR (188 MHz) δ = –136.7 (ddd, *J* = 2, 12, 21 Hz), –154.1 (ddd, *J* = 6, 7, 21 Hz). **4b**: ^{19}F NMR (188 MHz) δ = –126.9 (ddd, *J* = 9 Hz).

***S*-Ethyl *O*-{2-Fluoro-5-[*trans*-4-(*trans*-4-propylcyclohexyl)]cyclohexyl}phenyl Dithiocarbonate (3c).** Compound **3c** was prepared similarly in 87% yield (0.62 g, 1.46 mmol) from 2-fluoro-1-hydroxy-5-{[*trans*-4-(*trans*-4-propylcyclohexyl)]cyclohexyl}-benzene (0.54 g, 1.68 mmol) as colorless needles, mp 65.0-66.4 °C (recryst. from EtOH-hexane), R_f = 0.28 (hexane). IR (KBr) 2923, 2849, 1601, 1510, 1447, 1418, 1408, 1374, 1266, 1254, 1175, 1113, 1046, 1038, 984, 970, 822, 679 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.87 (t, *J* = 7 Hz, 3 H), 0.70-1.45 (m, 16 H), 1.42 (t, *J* = 7 Hz, 3 H), 1.62-1.98 (m, 7 H), 2.44 (tt, *J* = 3, 12 Hz, 1 H), 3.23 (q, *J* = 7 Hz, 2 H), 6.96 (dm, *J* = 8 Hz, 1 H), 7.04-7.09 (m, 1 H); ^{19}F NMR (188 MHz) δ = –132.1 (dd, *J* = 7, 15 Hz); ^{13}C NMR (50.3 MHz) δ = 13.1 (s), 14.4 (s), 20.0 (s), 30.1 (s), 30.2 (s), 31.5 (s), 33.6 (s), 34.6 (s), 37.6 (s), 39.8 (s), 42.8 (s), 43.3 (s), 43.8 (s), 116.3 (d, *J* = 18 Hz), 122.2 (s), 125.8 (d, *J* = 7 Hz), 141.1 (d, *J* = 3 Hz), 144.6 (d, *J* = 4 Hz), 151.8 (d, *J* = 248 Hz), 213.5 (s); MS *m/z* (rel intensity) 422 (M^+, 1), 407 (1), 394 (2), 391 (2), 343 (3), 342 (14), 173 (29), 158 (18), 157 (100), 145 (28), 144 (48), 142 (21), 141 (10), 130 (16), 129 (37), 128 (29), 127 (11), 115 (24), 91 (25), 81 (17), 77 (25). Found: *m/z* 422.2097. Calcd for $C_{24}H_{35}OFS_2$: M, 422.2113.

Oxidative Desulfurization-Fluorination of 3a (and 4a).

A polypropylene round bottom tube was charged with DBH (0.71 g, 2.50 mmol), HF/mel (80 wt% of HF, 1.0 mL, 35 mmol) and CH_2Cl_2 (5.0 mL) under an argon atmosphere. To the suspension was added a solution of the 15 : 1 mixture of **3a** and **4a** (0.24 g, 0.52 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C; the mixture was stirred at 0 °C for 30 min and then poured into an aq. $NaHSO_3$/$NaHCO_3$/NaOH (pH 10) solution at 0 °C. The pH value of the whole mixture was adjusted to 10 with NaOH; precipitated white materials were filtered off; the aq. phase was extracted with Et_2O three times. The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash-silica gel column chromatography (hexane) to give a mixture of bromo-2,3-Difluoro-5-{3,3,5,5-(D)$_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)ethyl]-cyclohexyl}-1-trifluoromethoxybenzene (**5a**) and the regioisomer **6a** (0.19 g, 0.37 mmol). All of this was dissolved in THF (2.0 mL) and treated with *n*-BuLi (1.6 M in hexane, 0.50 mL, 0.81 mmol) at –78 °C for 10 min. Then the resulting mixture was treated with H_2O at –78 °C; and the aq. phase was extracted with Et_2O three times. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash silica gel column chromatography (hexane eluent) to give 2,3-difluoro-5-{3,3,5,5-(D)$_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)ethyl]-cyclohexyl}-1-trifluoromethoxybenzene

(**7a**) and 2,6-difluoro-5-{3,3,5,5-$(D)_n$-*trans*-4-[2-(*trans*-4-propylcyclohexyl)ethyl]-cyclohexyl}-1-trifluoromethoxybenzene (**8a**) as an inseparatable 6 : 1 mixture of the regioisomers (0.14 g, 0.31 mmol) in total 60% yield.

A mixture of **7a** and **8a**: Colorless oil, R_f = 0.78 (hexane). IR 2957, 2919, 2851, 1613, 1526, 1455, 1445, 1337, 1267, 1210, 1181, 1057, 864 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.70-0.94 (m, 4 H), 0.94-2.45 (m, 13 H), 1.60-1.79 (m, 4 H), 1.79-1.89 (m, 2 H), 2.43 (tt, J = 3, 12 Hz, 3 H), 6.85-7.20 (m, 2 H); MS *m/z* as D_3 isomer (rel intensity) 438 (M^++2, 10), 437 (M^++1, 25), 436 (M^+, 35), 435 (25), 434 (14), 239 (7), 238 (7), 225 (16), 224 (19), (100). Found: *m/z* 433.2533, Calcd for $C_{24}H_{32}DOF_5$: M, 433.2513. Found: *m/z* 434.2556, Calcd for $C_{24}H_{31}D_2OF_5$: M, 434.2575. Found *m/z* 435.2618, Calcd for $C_{24}H_{30}D_3OF_5$: M, 435.2637.

7a: ^{19}F NMR (188 MHz) δ –59.3 (s), –135.5 (ddd, J = 1, 11, 21 Hz), –156.3 (m).

8a: ^{19}F NMR (188 MHz) δ –59.3 (s), –135.7 (d, J = 20 Hz).

2,3-Difluoro-5-{3,3,5,5-$(D)_n$-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl}-1-trifluoromethoxybenzene (7b) and 2,6-Difluoro-4-{3,3,5,5-$(D)_n$-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl}-1-trifluoromethoxybenzene (8b). These were obtained in a way described above in 62% yield (0.45 g, 1.2 mmol) as a 28 : 1 mixture from a mixture of **3b** and **4b** (0.89 g, 2.0 mmol, 14 : 1 regioisomers mixture), a colorless oil, bp 190 °C/0.6 mmHg; R_f = 0.77 (hexane). IR 2960, 2920, 2850, 1612, 1525, 1438, 1338, 1275, 1210, 1185, 1060, 860 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.70-1.38 (m, 18 H), 1.60-1.95 (m, 6 H), 2.16-2.43 (m, 1 H), 6.83-7.05 (m, 2 H); MS *m/z* as D_3 isomer (rel intensity) 408 (M^+, 9), 407 (29), 406 (12), 226 (14), 225 (16), 213 (5), 212 (17), 69 (100); Found: *m/z* 404.2133, Calcd for $C_{22}H_{29}OF_5$: M, 404.2138. Found: *m/z* 405.2188, Calcd for $C_{22}H_{28}DOF_5$: M, 405.2200. Found: *m/z* 406.2255, Calcd for $C_{22}H_{27}D_2OF_5$: M, 406.2262. Found: *m/z* 407.2309, Calcd for $C_{22}H_{26}D_3OF_5$: M, 407.2324.

7b: ^{19}F NMR (188 MHz) δ = –59.3 (d, J = 7 Hz), –135.5 (ddd, J = 2, 10, 21 Hz), –156.4 (m).

8b: ^{19}F NMR (188 MHz) δ = –60.4 (d, J = 7 Hz), –135.8 (d, J = 20 Hz).

2-Fluoro-5-{*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl}-1-trifluoromethoxy-benzene (7c). Similarly, **7c** was obtained in 35% yield (0.17 g, 0.44 mmol) from **3c** (0.53 g, 1.3 mmol) as a colorless oil; R_f = 0.67 (hexane). IR 2920, 2860, 1518, 1445, 1278, 1265, 1228, 1205, 1178, 1120, 820; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.75-1.48 (m, 15 H), 1.58-1.95 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 7.06-7.14 (m, 3 H); ^{19}F NMR (188 MHz) δ = –59.2 (d J = 5 Hz), –134.03 (m); MS *m/z* (rel intensity)

388 (M^++2, 5), 387 (M^++1, 31), 386 (M^+, 82), 262 (21), 226 (14), 219 (31), 207 (35), 206 (100), 193 (93), 133 (40), 125 (62), 123 (43), 109 (53), 83 (83), 81 (72), 69 (87), 67 (91); Found: *m/z* 386.2250. Calcd for $C_{22}H_{30}OF_4$: M, 386.2233.

V-5. References and Notes

1) G. W. Gray, M. Hird, and K. J. Toyne, *Mol. Cryst. Liq. Cryst.*, **204**, 91 (1991).
2) R. Eidenschink, *Mol. Cryst. Liq. Cryst.*, **94**, 119 (1983).
3) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.*, **209**, 1 (1991).
4) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683.
5) M. Kuroboshi and T. Hiyama, *Yuki Gosei Kagaku Kyokai Shi*, **51**, 1124 (1993).
6) K. Kanie, K. Mizuno, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1973 (1998).
7) M. Kuroboshi, K. Suzuki, and T. Hiyama, *Tetrahedron Lett.*, **33**, 4173 (1992).
8) K. Kanie, Y. Tanaka, M. Shimizu, M. Kuroboshi, and T. Hiyama, *Chem. Commun.*, **1997**, 309.
9) G. A. Olah, J. D. Welch, Y. D. Vanker, M. Nojima, I, Kerekes, and J. A. Olah, *J. Org. Chem.*, **44**, 3832 (1979).
10) T. Fukuhara, N. Yoneda, T. Abe, S. Nagata, and A. Suzuki, *Nippon Kagaku Kaishi,* **10**, 1951 (1985).
11) S. Ogawa, S. Takehara, and H. Takatsu, Japan Patent, 08067647A (1996).
12) Deuterated cyclohexane derivatives were used for this reaction, but the influence of the deuterium to the electro-optical properties was small.

Chapter VI

A Facile Synthesis and Electro-optical Properties of Novel Liquid Crystalline Materials Having a Trifluoromethoxy Group

Abstract: Novel LCs containing a trifluoromethoxy group connected to a cyclohexane mesogen or to an alkyl tail were prepared through an oxidative desulfurization-fluorination reaction of the corresponding dithiocarbonates and compared with LCs containing a methoxy group with respect to phase transition behaviors and physical and electro-optical properties.

VI-1. Introduction

Remarkable properties of organofluorine compounds have attracted much attention in the development of new functional materials.[1] For example, LCs with a fluorinated aromatic mesogen are favorable to the materials for thin film transistor (TFT)-addressed twisted nematic (TN) LCDs.[2-4] In particular, LCs with a trifluoromethoxy-substituted aromatic mesogen show low viscosity and high voltage holding ratio.[5,6] However, trifluoromethoxy-benzene derivatives as the starting substrates are expensive and thus hardly available. Furthermore, introduction of a trifluoromethoxy moiety into an aromatic ring must be performed using highly toxic and/or explosive reagents under special conditions.[7-11]

According to the oxidative desulfurization-fluorination reaction,[12] both aromatic and aliphatic trifluoromethyl ethers (R–OCF_3) are readily prepared by the reaction of the corresponding dithiocarbonates (R–OCS_2R') as described in Chapter IV.[13] This reaction is an exclusive method[14] for the preparation of trifluoromethyl ethers from secondary aliphatic alcohols.[15] Accordingly, the reaction, leading to various types of trifluoromethyl ethers with many functional groups being intact, is a powerful tool for the synthesis of novel class of fluorinated functional materials.[6a,16]

Because LCs with a cyclohexane mesogen show lower viscosity and smaller Δn than those with a benzene mesogen,[17] the Author envisaged that LCs with a trifluoromethoxycyclohexane mesogen would exhibit physical and electro-optical properties better than LCs with a trifluoromethoxybenzene mesogen. In addition, because LCs containing an ω-methoxyalkyl moiety show high $\Delta\varepsilon$, broad nematic mesophase, and low viscosity as well as high voltage holding ratio favorable for TFT-addressed TN-LCDs,[18] he envisaged that the use of a trifluoromethoxy group in lieu of a methoxy group would increase chemical stability and voltage holding ratio and decrease the viscosity of parent LCs.[5,17b]

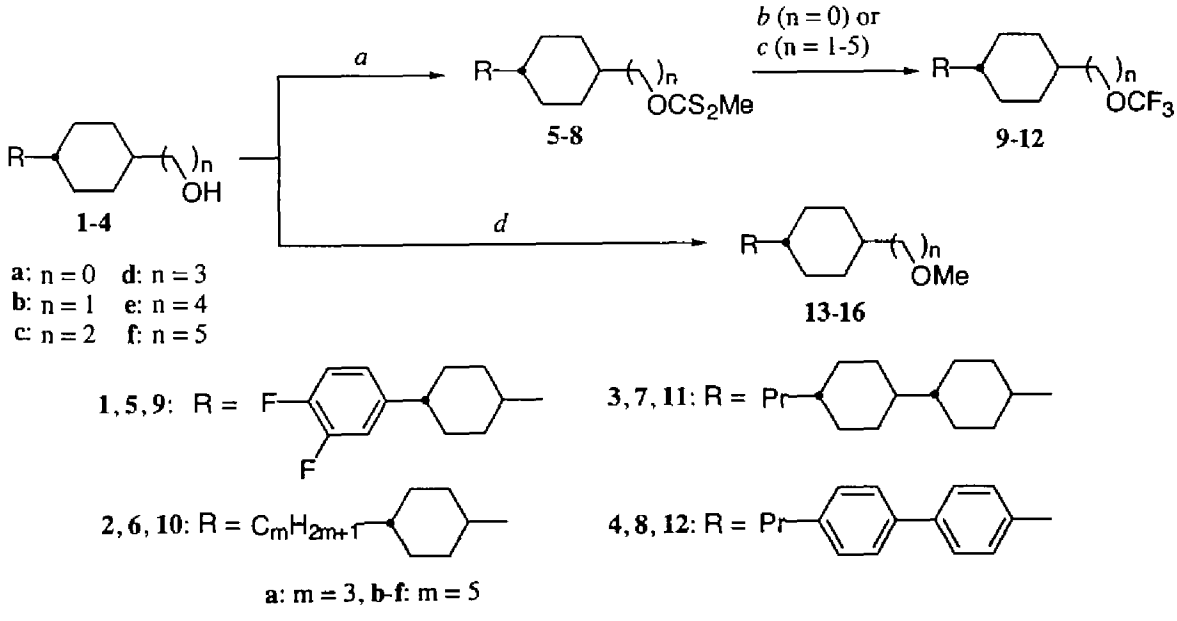
Herein described is the synthesis of novel LCs containing i) a trifluoromethoxycyclohexane mesogen or ii) an ω-trifluoromethoxyalkyl tail through the oxidative desulfurization-fluorination. Such LCs are compared in respect to phase transition behaviors and electro-optical properties with the corresponding LCs containing a trifluoromethoxybenzene mesogen or an ω-methoxyalkyl tail.

VI-2. Results and Discussion

VI-2-1. Synthesis of Trifluoromethoxycyclohexane-type LCs

Synthesis of LCs **9a**,[13a] **10a**, **11a**, and **12a**, all containing a trifluoromethoxycyclohexane mesogen, was carried out through the route shown in Scheme 1. Reduction of 4-substituted cyclohexanone with $LiAlH_4$ followed by separation by flash silica gel column chromatography and/or recrystallization gave *trans*-cyclohexanols **1a**, **2a**, **3a**, and **4a**, which were converted, respectively, into the corresponding dithiocarbonates **5a**,[13a] **6a**, **7a**, and **8a** in high yields by treatment successively with NaH, CS_2, and MeI. For the synthesis of **7a**, NaH was replaced by *n*-BuLi to solubilize the alkoxide generated from **3a**. Treatment of **5a**, **6a**, **7a**, and **8a** with 50% HF/py (40 mol, prepared by neutralization of 70% HF/py[19] with pyridine) and NBS (5.0 mol) in CH_2Cl_2 at 0 °C afforded cyclohexyl trifluoromethyl ethers **9a**, **10a**, **11a**, and **12a** in moderate yields.[13a]

Scheme 1. Synthesis of LCs **9-12** with a trifluoromethoxycyclohexane core.

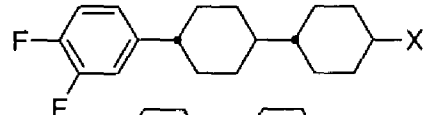
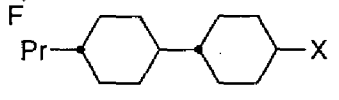
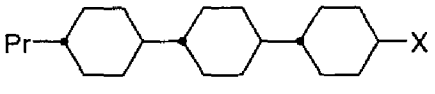
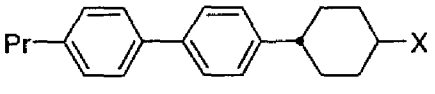
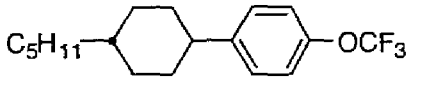
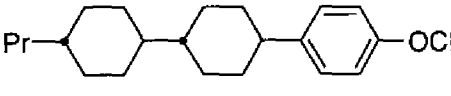
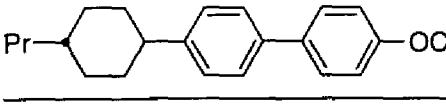


a: i) NaH [or *n*-BuLi] (1.2 mol), ii) CS_2 (5.0 mol), iii) MeI (2.0 mol), THF. *b*: 50% HF/py (40 mol), NBS (5.0 mol), CH_2Cl_2, 0 °C, 1 h. *c*: i) 70% HF/py (40 or 60 mol), DBH (3.0 mol), CH_2Cl_2, –78; 0 °C, 1 h, ii) [*n*-BuLi (1.2 mol), THF, –78 °C, 10 min, then H_2O.]. *d*: i) NaH [or *n*-BuLi] (1.2 mol), ii) MeI (2.0 mol), THF.

VI-2-2. Phase Transition Behavior of Trifluoromethoxycyclohexane-type LCs

Phase transition temperatures and LC phases of trifluoromethoxycyclohexanes **9a**, **10a**, **11a**, and **12a**, methoxycyclohexanes **13a**, **14a**, **15a**, and **16a**, and trifluoromethoxybenzenes **17**, **18**, and **19**[17] are summarized in Table 1. Although **9a** and **10a** showed only a melting point, trifluoromethyl ethers **11a** and **12a** exhibited nematic phase and smectic A phase, respectively, in a wide range of temperatures. DSC measurement of **11a** showed four endothermic peaks at 44, 112, 147, and 189 °C with enthalpy changes of 7.3, 2.7, 5.8, and 0.8 kJ/mol, respectively, on second heating. These peaks correspond to the phase transitions of Cr-to-S_X, S_X-to-S_B, S_B-to-N, and N-to-Iso, respectively.

Table 1. Phase transition temperatures of CF_3O-LCs and CH_3O-LCs

Compound		Phase transition temp./°C[a]
	**(9a)**	Cr 43 Iso[b]
	(13a)	Cr 68 Iso[b]
	**(10a)**	Cr 30 Iso
	(14a)	Cr 9 N 14 Iso
	**(11a)**	Cr 44 S_X 112 S_B 147 N 189 Iso
	(15a)	Cr 207 S_B 211 Iso
	**(12a)**	Cr 90 S_B 104 S_A 129 Iso
	(16a)	Cr 45 S_B 88 N 128 Iso
9a, 10a, 11a, 12a: X = OCF_3; **13a, 14a, 15a, 16a**: X = OCH_3		
	**(17)**	Cr 14 Iso
	**(18)**	Cr 38 S_B 69 N 153 Iso
	**(19)**	Cr 90 S_B 129 N 151 Iso

Cr: crystal, S_X: higher order smectic, S_B: smectic B, S_A: smectic A,
N: nematic, Iso: isotropic liquid.

[a]Measured by DSC on 2nd heating. [b]Observed with a polarizing microscope.

Trifluoromethyl ether **11a** exhibited nematic liquid crystallinity much higher than the corresponding methyl ether **15a**, but such a CF_3-- effect was not observed with **10a** and **12a**. Trifluoromethoxycyclohexane-type LCs **10a**, **11a**, and **12a** were compared in respect to phase transition behaviors with trifluoromethoxybenzene-type LCs **17**, **18**, and **19**, and the effect of a mesogenic core was studied. Clearing temperature of **10a** was found to be much higher than that of the counter part **17**. Trifluoromethoxycyclohexane-LC **11a** showed a higher nematic-to-isotropic transition temperature (T_{NI}) as compared with trifluoromethoxybenzene-LCs **18** and **19**. These results indicate that a cyclohexane mesogen more stabilizes nematic phase.

VI-2-3. Electro-optical Properties of Trifluoromethoxycyclohexane-type LCs

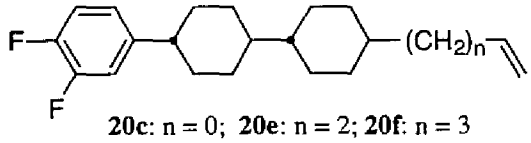
Physical and electro-optical properties of trifluoromethoxycyclohexane-type LCs **9a**, **10a**, **11a**, and **12a** were next studied as an additive for nematic LCs and compared with those of **13a**, **14a**, **15a**, and **16a**, respectively, all having a methoxycyclohexane mesogen, and with **18** containing a trifluoromethoxybenzene mesogen. Each of these was added by 20 wt% to **host** (a 1 : 1 mixture of **20c** and **20e**), and T_{NI}, $\Delta\varepsilon$, V_{th}, Δn, and τ of the resulting mixture were measured in a TN cell. The data are summarized in Table 2. The T_{NI} temperatures of the resulting LC mixtures reflected the clearing temperatures of the additive. For example, T_{NI} of the mixture of **11a** was much higher than that of **18**. Extrapolation of $\Delta\varepsilon$ to 100% allowed estimation of $\Delta\varepsilon'$. As $\Delta\varepsilon'$s of the mixtures containing trifluoromethoxycyclohexane-type LCs **10a**, **11a**, and **12** are positive, these LC mixtures are proved to be p-type, whereas methoxycyclohexanes **14a**, **15a**, and **16a** are n-type ($\Delta\varepsilon' < 0$). In contrast, the opposite was observed between **9a** and **13a** that have a 3,4-difluorobenzene mesogen. Negative $\Delta\varepsilon'$ of a **9a**/**host** mixture is apparently brought by compensation of dipole moment caused by F and CF_3O groups directing oppositely along the long axis of the molecule. In accord with the sign of $\Delta\varepsilon'$, trifluoromethoxycyclohexane-type LCs **10a**, **11a**, and **12a** reduced V_{th} of **host**, whereas **14a**, **15a**, and **16a** raised V_{th} of **host**. Thus, a trifluoromethoxy group connected to a cyclohexane mesogen contributes to the reduction of V_{th} of **host**. Each pair of **9a**/**13a**, **10a**/**14a**, **11a**/**15a**, and **12a**/**16a** showed similar and low Δn's, as estimated by extrapolation of Δn. Thus, Δn is governed by a mesogenic structure rather than a polar functional group. It is worth noting that **10a**, **11a**, and **12a** induced low Δn for relatively large $\Delta\varepsilon'$. Furthermore, V_{th} and Δn of **11a** were lower than those of **18** in spite of small $\Delta\varepsilon$ of **11a**. Thus, **11a** are better than **18** in reducing driving voltage and also in controlling cell

thickness[20] of TFT-addressed TN-LCDs. Trifluoromethoxycyclohexane-type LCs **9a**, **10a**, **11a**, and **12a** are apparently thermally stable, since T_{NI} of a mixture of **10a** and **host** did not change at all after heating at 80 °C for 10 h.

Table 2. Physical and electro-optical properties[a] of trifluoromethoxy-cyclohexanes **9a-12a** and the corresponding methyl ethers **13a-16a** as added by 20 wt% to **host**.

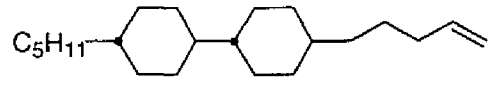
Compound	T_{NI}/°C	Δε	Δε'[b]	V_{th}/V[c]	Δn	Δn'[d]	τ/ms[c, e] (V)[f]
host	116.7	4.8	---	2.14	0.090	---	25.3 (5.1)
9a	90.9	3.2	-3.2	2.18	0.085	0.082	35.1 (5.0)
10a	90.1	5.2	6.7	1.86	0.078	0.030	34.3 (4.3)
11a	130.2	4.7	4.3	2.10	0.084	0.060	37.0 (4.6)
12a	106.2	5.9	10.3	2.11	0.109	0.185	37.6 (4.8)
13a	107.4	4.0	0.8	2.12	0.087	0.075	33.8 (4.8)
14a	93.5	3.6	-1.2	2.20	0.077	0.025	36.3 (4.9)
15a	137.3	3.4	-2.2	2.43	0.084	0.060	44.1 (5.1)
16a	112.7	3.4	-2.2	2.45	0.105	0.165	31.2 (5.4)
18	122.4	5.1	6.5	2.19	0.089	0.087	---

[a]Measured at 20 °C. [b]Extrapolated from Δε. [c]Corrected for 6.0 μm cell. [d]Extrapolated from Δn. [e]Responce time ($\tau_r = \tau_d$). [f]Applied voltage/V.



20c: n = 0; **20e**: n = 2; **20f**: n = 3

host (**20c** : **20e** = 1 : 1 mixture)

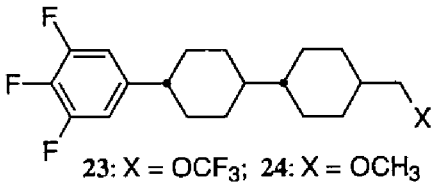


21f

VI-2-4. Synthesis of ω-Trifluoromethoxyalkyl-substituted LCs

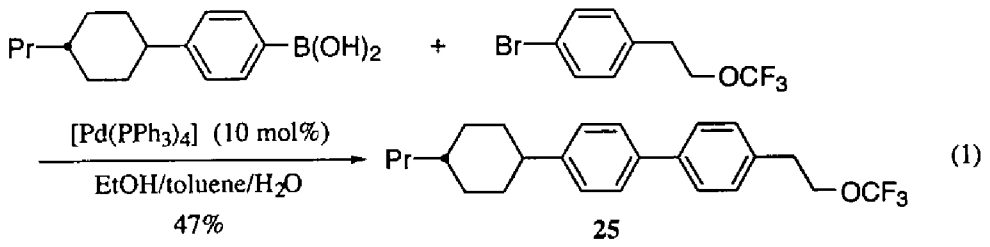
To examine the effect of tail length of LCs containing an ω-trifluoromethoxyalkyl group, the Author synthesized **9b-9f** and **10b-10f** having, respectively, *trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]cyclohexane and *trans*-4-(*trans*-4-pentylcyclohexyl)-cyclohexane mesogens. The corresponding methyl ethers **13b-13f** and **14b-14f** were also prepared to evaluate the fluorine substituent effect. The route is summarized in Scheme 1. Primary alcohols **1b-1f** and **2b-2f** were transformed to dithiocarbonates **5b-5f** and **6b-6f** in high yields by treatment with NaH (or *n*-BuLi), CS_2, and MeI. Trifluoromethoxylation of

the dithiocarbonates was performed with 70% HF/py and DBH. For the substrates **5b-5f**, having a difluorobenzene mesogen, trifluoromethoxylation leading to **9b-9f** was accompanied by bromination of the phenyl ring. The bromine functionality was removed by lithiation with *n*-BuLi followed by protonation with H_2O to give the desired trifluoromethyl ethers in high yields. Trifluoromethyl ethers **10b-10f** were obtained directly from **6b-6f**. Methyl ethers **13b-13f** and **14b-14f** were prepared respectively from **1b-1f** and **2b-2f** as usual. To examine the effect of fluorine attached to a benzene mesogen, trifluoromethyl ether **23** and methyl ether **24** were additionally prepared and compared.



23: X = OCF_3; **24**: X = OCH_3

Furthermore, in order to examine CF_3O and $CF_3OCH_2CH_2$ groups, **25** also was prepared and compared with **19** (eq. 1).



25 (1)

VI-2-5. Phase Transition Behaviors of ω-Trifluoromethoxyalkylcyclohexane-type LCs

Phase transition temperatures and LC phases of **9b-9f**, **10b-10f**, **13b-13f**, **14b-14f**, and **23-25** as well as trifluoromethoxycyclohexane-type LCs **9a**, **10a**, **13a**, and **14a** are listed in Table 3. LCs **9** and **13** with a *trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]-cyclohexane mesogen, **10** and **14** with a *trans*-4-(*trans*-4-pentylcyclohexyl)cyclohexane mesogen, and **25** with a *trans*-4-(*trans*-4-pentylcyclohexyl)biphenyl mesogen showed nematic, smectic B, and smectic A phases in a wide range of temperatures, respectively. Thus, the mesophase textures of trifluoromethoxy-substituted LCs are dependent mainly on the structure of a mesogen. The phase transition behaviors of LCs **9** and **13** are shown in Figure 1. Although LCs **9a** and **13a** with a *trans*-4-[*trans*-4-(3,4-difluoro-phenyl)cyclohexyl]cyclohexane mesogen exhibited only a melting point, LCs **9c-9f** and **13b-13f** having a methylene spacer between an ethereal oxygen and a mesogen exhibited nematic phase. A trifluoromethoxy group appears to lower clearing temperatures in comparison of **9** with **13**. With a longer alkyl chain (Figure 1), trifluoromethyl ethers **9** tend to have higher T_{NI} temperatures and more stabilize nematic phase. In contrast, methyl ethers **13** have variable T_{NI} depending on the odd-even number of methylene units, and **13b**, **13d**, and **13f** exhibit a nematic temperature range much wider than **13c** or **13e**. The odd-even effect in crystal-to-nematic (or smectic) transition temperatures (T_{CN} or (T_{CS})) was only observed with **9**. Figure 2 illustrates temperature behaviors of **10** and **14** having a *trans*-4-(*trans*-4-pentylcyclohexyl)cyclohexyl mesogen. These LCs mainly exhibited smectic B phase in a wide range of temperatures, and their smectic-to-isotropic transition temperatures (T_{SI}) and T_{CS} are influenced by the odd-even effect. A CF_3O group is shown to lower T_{SI} as compared with a CH_3O group.

Table 3. Phase transition temperatures of **9**, **10**, **13**, and **14**.

Compound	Phase transition temp./°C[a]	
	DSC (2nd heating)	DSC (1st cooling)
9a	Cr 43 Iso[b]	
9b	Cr 46 Iso[b]	
9c	Cr -7 S_B 8 N 17 Iso	Cr 7 N 16 Iso
9d	Cr 21 N 52 Iso	Cr -6 N 52 Iso
9e	Cr 14 S_B 17 N 55 Iso	G -1 N 54 Iso
9f	Cr 30 N 73 Iso	Cr 9 S_B 13 N 73 Iso
13a	Cr 68 Iso[b]	
13b	Cr 59 N 111 Iso	Cr 6 S_B 39 N 111 Iso
13c	Cr 48 N 80 Iso	Cr 2 N 79 Iso
13d	Cr 45 N 131 Iso	Cr 14 S_B 35 N 130 Iso
13e	Cr 57 N 102 Iso	Cr 56 N 101 Iso
13f	Cr 60 N 122 Iso	Cr 2 S_B 51 N 121 Iso
10a	Cr 30 Iso	Cr 13 Iso
10b	Cr 18 S_X 26 S_B 52 Iso	Cr -6 S_X 24 S_B 50 Iso
10c	Cr 4 S_B 53 Iso	Cr -10 S_X -9 S_B 52 Iso
10d	Cr 30 S_B 96 Iso	Cr 24 S_B 95 Iso
10e	Cr 4 S_B 90 Iso	Cr -12 S_B 90 Iso
10f	Cr 22 S_B 109 Iso	Cr 13 S_B 109 Iso
14a	Cr 9 N 14 Iso	Cr -2 S_B 3 N 14 Iso
14b	Cr -15 S_B 73 Iso	Cr -17 S_B 71 Iso
14c	Cr -12 S_B 72 Iso	Cr -19 S_B 71 Iso
14d	Cr 30 S_B 105 Iso	Cr 16 S_B 105 Iso
14e	Cr 9 S_B 97 Iso	Cr -1 S_B 96 Iso
14f	Cr 29 S_B 113 Iso	Cr 9 S_B 112 Iso
23	Cr 43 Iso[b]	
24	Cr 74 N 79 Iso	Cr 56 N 78 Iso
25	S_B 132 S_A 159 Iso	S_B 130 S_A 158 Iso

a) Iso: Isotropic liquid. N: Nematic phase. S_A: Smectic A phase. S_B: Smectic B phase. S_X: Higher order smectic phases. Cr: Crystal. G: Glass state.

b) Observed with an optical polarizing microscope on heating.

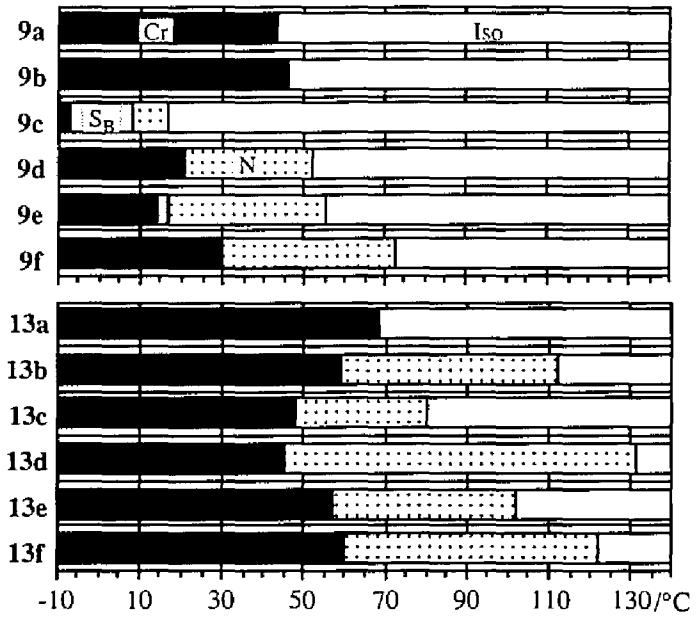


Figure 1. Phase transition behaviors of **9** and **13**.

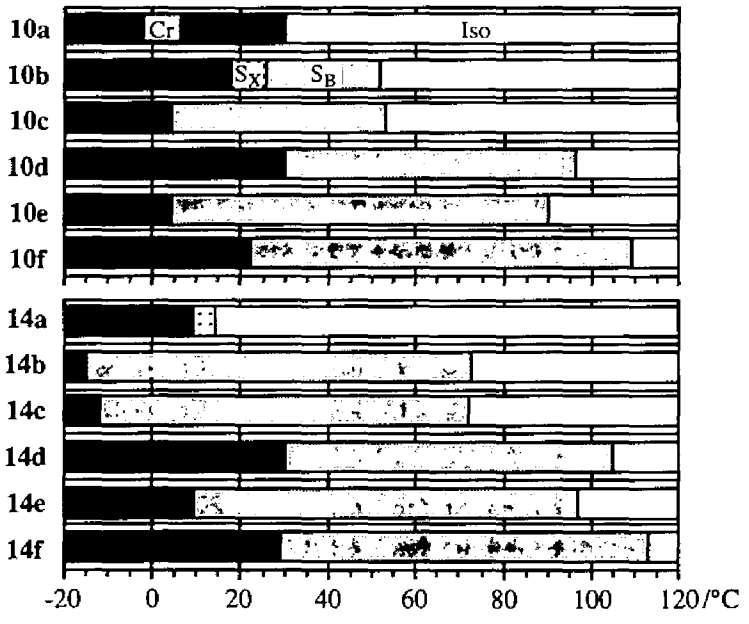


Figure 2. Phase transition behaviors of **10** and **14**.

VI-2-6. Physical and Electro-optical Properties of ω-Trifluoromethoxyalkylcyclohexane-type LCs: Tail Length Effect

The Author mixed by 20 wt% each of LCs **9b-9f**, **10b-10f**, **13b-13f**, **14b-14f**, **23**, and **25** with **host** (80 wt%) and measured the physical and electro-optical properties of the resulting mixtures. The data as well as those of **9a**, **10a**, **13a**, and **14a** are listed in Table 4. Among LCs with a *trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]cyclohexane mesogen, trifluoromethyl ethers **9b-9f** showed Δεs lower than the corresponding methyl ethers **13b-13f**, owing probably to the effect discussed for **9a** and **13a**. LCs with the same mesogen exhibited almost uniform values in Δε, V_{th}, Δ*n*, and τ, respectively, irrespective of the terminal structure of a tail. These values were found to be more dependent on the type of a mesogen. In general, V_{th} of an LC mixture increases when Δε of the LC mixture is reduced as was observed with **14**. In contrast, for small Δε, V_{th} of the mixture of **9** or **10** was not large. Therefore, the trifluoromethyl ethers are apparently suitable for the purpose of reducing driving voltage of LCDs. The fact that Δε of trifluoromethyl ether **10b**, **10c**, **10d**, **10e**, or **10f** with a *trans*-4-(*trans*-4-pentylcyclohexyl)cyclohexylalkyl mesogen was only slightly higher than that of the corresponding methyl ether **14c**, **14d**, **14e**, or **14f**, respectively, suggests that dipole moment induced by the trifluoromethoxy group in a tail of LCs is not striking. However, it is noteworthy that a trifluoromethoxy group connected directly to a cyclohexane mesogen raises Δε' as seen in **10a**, acting as a controlling polar functional group. Accordingly, introduction of a trifluoromethoxy group into a cyclohexane mesogen of LCs is highly effective for induction of Δε. In view that **13b** and **14b** having a methoxymethyl substituent did not form TN orientation in an LC cell, trifluoromethyl ethers **9b** and **10b** are favorable materials for TN-LCDs. Bulk viscosity (η_{20}) at 20 °C of **host** (η_{20} = 19.8) increased only slightly by a trifluoromethyl ether additive. For example, a mixture of **9b** and **host** (1 : 4 w/w) had η_{20} = 22.8; a mixture consisting of **23** and **host** (1 : 4 w/w), η_{20} = 23.2.

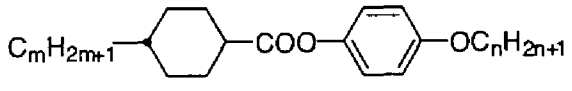
Table 4. Physical and electro-optical properties[a] of **9**, **10** and **13**, **14** as added by 20 wt% to **host**.

Compound	T_{NI}/°C	Δε	Δε'[b]	V_{th}/V[c]	Δ*n*	Δ*n*'[d]	τ/ms[c, e] (V)[f]
host	116.7	4.8	---	2.14	0.090	---	25.3 (5.1)
9a	90.9	3.2	-3.2	2.18	0.082	0.050	45.3 (4.8)
9b	103.4	3.2	-3.2	2.26	0.085	0.065	35.1 (5.0)
9c	101.0	3.2	-3.2	2.16	0.084	0.060	36.6 (4.9)
9d	107.5	3.2	-3.2	2.18	0.086	0.070	44.1 (4.7)
9e	105.5	3.3	-2.7	2.10	0.083	0.055	39.7 (4.9)
9f	109.0	3.2	-3.2	2.19	0.083	0.055	43.4 (4.8)
13a	107.4	4.0	0.8	2.12	0.087	0.075	33.8 (4.8)
13b	---	---	---	---	---	---	---
13c	110.9	4.3	2.3	2.03	0.086	0.070	33.8 (4.3)
13d	120.7	4.8	4.8	2.12	0.091	0.095	33.4 (4.9)
13e	114.6	4.3	2.2	1.98	0.087	0.075	41.1 (4.3)
13f	118.3	4.6	3.6	2.08	0.088	0.080	38.5 (4.6)
10a	90.1	5.2	6.7	1.86	0.078	0.030	34.3 (4.3)
10b	94.7	3.6	-1.2	2.16	0.079	0.035	31.8 (4.2)
10c	94.1	3.6	-1.2	1.97	0.078	0.030	34.8 (4.2)
10d	99.9	3.4	-2.0	2.18	0.079	0.035	36.8 (4.4)
10e	99.4	3.5	-1.8	2.02	0.079	0.035	39.4 (4.7)
10f	101.9	3.3	-2.7	2.10	0.078	0.030	37.9 (4.5)
14a	93.5	3.6	-1.2	2.20	0.077	0.025	36.3 (4.9)
14b	---	---	---	---	---	---	---
14c	100.2	3.1	-3.7	2.22	0.077	0.025	31.0 (4.5)
14d	110.1	3.2	-3.2	2.31	0.081	0.045	32.3 (4.9)
14e	105.2	3.1	-3.7	2.21	0.079	0.035	40.3 (4.6)
14f	109.4	3.2	-3.2	2.33	0.079	0.035	35.8 (5.0)
23	98.9	3.5	-1.8	2.10	0.084	0.060	36.4 (4.6)
25	117.1	4.0	0.8	2.15	0.101	0.145	36.5 (4.7)

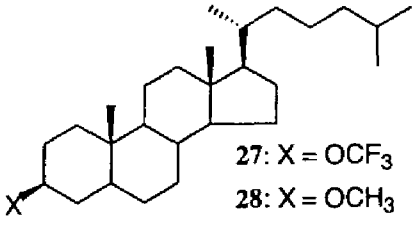
[a]Measured at 20 °C. [b]Extrapolated from Δε. [c]Corrected for 6.0 μm cell. [d]Extrapolated from Δ*n*. [e]Responce time ($\tau_r = \tau_d$). [f]Applied voltage/V.

VI-2-7. Trifluoromethoxy-substituted LCs as Chiral Dopants for TN- and TFT-addressed TN-LCDs

The Author next examined the possibility of LCs with a trifluoromethoxy group on a mesogen as a chiral dopant for TN-LCDs. As the chiral dopant for super-TN-LCDs, cholesteryl nonanoate (**26**) has been extensively utilized. He prepared 3β-trifluoromethoxycholestane (**27**)[13a] and 3β-methoxycholestane (**28**), mixed each by 1 wt% with **TN-host** consisting of 6-homologs (equal weight) of 4-alkoxyphenyl 4-alkylcyclohexane carboxylates, and measured helical pitch of each mixture at 25 °C. All of the mixtures exhibited chiral nematic phase below 72 °C with slight lowering of the clearing temperature of **TN-host**. Helical pitch of the mixture of **26**, **27**, or **28** was 15.9, 15.9, or 39.2 μm, respectively. The value for **27** was much smaller than that for **28**. Therefore, a trifluoromethoxy group in a chiral dopant is a polar functionality apparently better than a methoxy group. Furthermore, compound **27** induced helix of chiral nematic LCs to a degree comparable to **26** that is currently used for TN-LCDs. This means **27** may find applications as a chiral dopant for TFT-addressed TN-LC mixtures. Because LCs containing a cyano or alkoxycarbonyl group bring striking decrease in voltage holding ratio, compound **26** is not suitable for TFT-addressed TN-LCDs. Thus, he next examined voltage holding ratio of a mixture of **27** (2wt%) and **host** (98%) at 80 °C and was delighted to observe it was 97.4%; that of **host** was 97.5%. A mixture of **28** and **host** (2 : 98 w/w) showed 97.0% of voltage holding ratio at 80 °C. Helical pitch of the mixture of **27**/**host** or **26**/**host** was 8.0 μm at 25 °C. Therefore, compound **27** is concluded to be an excellent chiral dopant for not only TN-LCDs but also TFT-addressed TN-LCDs.



TN-host: a mixture of equal amounts of homologs
(m, n) = (3, 2), (3, 4), (3, 5), (4, 2), (5, 1), (5, 2)
T_{NI} = 73.8 °C



27: X = OCF_3
28: X = OCH_3

VI-2-8. Trifluoromethoxycyclohexane-type LCs as Materials for TFT-addressed TN-LCDs

The Author further investigated the possibility of **11** as an additive for TFT-addressed TN-LCDs and prepared an LC mixture containing **11** (20 wt%) in a TFT-host

mixture that exhibited T_{NI} = 82.5 °C, $\Delta\varepsilon$ = 3.6, V_{th} = 1.71 V, Δn = 0.072, τ = 48.6 ms. The resulting mixture showed T_{NI} = 102.5 °C, $\Delta\varepsilon$ = 4.15, V_{th} = 1.88 V, Δn = 0.074, and τ = 44.1 ms. Thus, use of **11** as an additive resulted in expansion of nematic phase range and improvement of response time of the TFT-host mixture without decrease of voltage holding ratio. Furthermore, T_{NI} of the **11**/TFT-host mixture did not lower at all upon heating at 80 °C for 10 h or under UV irradiation. Accordingly, LCs having a trifluoromethoxycyclohexane mesogen are very stable against heat and UV light.

VI-3. Conclusion

Novel LCs with a trifluoromethoxycyclohexane mesogen were prepared for the first time by the oxidative desulfurization-fluorination of dithiocarbonates derived from the corresponding cyclohexanols. LCs with an ω-trifluoromethoxyalkyl tail were also prepared in a similar way, starting with the corresponding primary alcohols. Most of the CF_3O-substituted LCs exhibited in a wide range of temperatures LC phases depending on the type of a mesogenic structure. LCs with a trifluoromethoxycyclohexane mesogen were shown to be thermally more stable than LCs with a trifluoromethoxybenzene mesogen. LCs having a trifluoromethoxyalkyl tail, e.g. **11**, show physical and electro-optical properties favorable to materials for not only TN-LCDs but TFT-addressed TN-LCDs. Furthermore, **27** was shown to be a potential chiral dopant for TFT-addressed TN-LCDs.

VI-4. Experimental

Materials. Followings were kindly donated by Dainippon Ink & Chemicals, Inc: 4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]cyclohexanone, 4-(*trans*-4-propylcyclohexyl)-cyclohexanone, 4-[*trans*-4-(*trans*-4-pentylcyclohexyl)cyclohexyl]cyclohexanone, 4-(4'-propylbiphenyl-4-yl)cyclohexanone, 4-[*trans*-4-(*trans*-4-pentylcyclohexyl)cyclohexyl]-phenol, {*trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]}cyclohexanecarbaldehyde, *trans*-4-[*trans*-4-(3,4,5-trifluorophenyl)cyclohexyl]cyclohexanemethanol, *trans*-1-pentyl-4-[*trans*-4-vinylcyclohexyl]-cyclohexane (**21c**), *trans*-1-[*trans*-4-(3,4-difluorophenyl)-cyclohexyl]-4-vinylcyclohexane (**20c**), and *trans*-1-[*trans*-4-(3-butenyl)cyclohexyl]-4-(3,4-difluorophenyl)cyclohexane (**20e**).

Measurements. A sample for the measurement of electro-optical properties was prepared by mixing a compound (20 wt%) with **host** (80%, Cr 11 N 117 Iso) consisting of equal amounts of **20c** and **20e**.

General Procedure for the Synthesis of Alcohols.

Method A: Reduction of Cyclohexanones. To a stirred suspension of lithium aluminum hydride (1.71 g, 45 mmol) in THF (60 mL) was added a solution of a 4-substituted cyclohexanone (30 mmol) in THF (40 mL) at 0 °C over a period of 5 min. The mixture was stirred at 0 °C for 10 min, quenched by slow addition of H_2O (1.7 mL) at 0 °C, and treated with 30% aq. NaOH. The resulting mixture was stirred at room temperature for 30 min before mixing with Celite, $MgSO_4$, and Et_2O (100 mL) under vigorous stirring at room temperature for 1 h. The insoluble material was filtered off through a Celite pad by suction funnel and washed with Et_2O (300 mL) and CH_2Cl_2 (50 mL). The filtrate was concentrated under reduced pressure, and the residue was recrystallized from hexane/EtOAc to give *trans*-4-substituted cyclohexanol. In some cases, the mother liquor was concentrated, and *cis*-4-substituted cyclohexanol was isolated by flash column chromatography.

Method B: Reduction of Phenols. A suspension of a 4-substituted phenol (14 mmol) and 10% Pd/C (1.9 g) in EtOAc (100 mL) was stirred vigorously under an H_2 atmosphere (20 atm) at 70 °C for 1 day. The insoluble material was filtered through a Celite pad by vacuum filtration and washed with a 100 mL portion of CH_2Cl_2 (totally 1 L). The filtrate was concentrated under reduced pressure; the residue was chromatographed to give *trans*- and *cis*-4-cyclohexanol.

Method C: Hydroboration-Oxidation of Terminal Olefins. In a two-necked flask were placed THF (200 mL) and a terminal olefin (91 mmol). To this solution was added dropwise a solution of borane in THF (BH_3, 1.0 M, 46 mL, 46 mmol) at 0 °C. The reaction mixture was stirred for 12 h at room temperature before slow addition of H_2O (1.0 mL), 3 M NaOH (22 mL) and then 30% aq. H_2O_2 (23 mL) at 0 °C. The resultant was stirred for 6 h at room temperature, and the excess peroxide was quenched with aq. $NaHSO_3$. The organic phase was separated; the aq. phase was extracted with Et_2O four times. The combined organic extracts were washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was recrystallized from hexane. The mother liquor was concentrated *in vacuo* and purified by flash column chromatography to give the desired alcohol.

Method D: Oxidative Cleavage of Terminal Olefins. To a mixture of formic acid (29 mL, 0.77 mol), 30% H_2O_2 (5.0 mL), and CH_2Cl_2 (2.0 mL), a terminal olefin (50

mmol) was added portionwise at 0 °C. The resulting mixture was stirred for 15 h at room temperature before quenching with 5% NaOH and aq. $Na_2S_2O_3$. The whole was diluted with CH_2Cl_2 (100 mL); the combined organic phase was separated; the aq. phase was extracted with CH_2Cl_2 eight times (totally 500 mL). The combined organic extracts were washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to give a 1,2-diol. To the diol dissolved in Et_2O (200 mL) was added an aq. solution of $NaIO_4$ (17.0 g) in H_2O (50 mL) at room temperature. The resulting mixture was stirred for 6 h; the organic phase was separated; the aq. phase was extracted with Et_2O four times (totally 500 mL). The organic extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a crude aldehyde, which was reduced to the corresponding alcohol by the procedure for the preparation of compound **1b** as described above.

Methods, yields, and spectral properties of alcohols are as follow.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanol (1a).** Method A, 86% yield. Colorless needles, mp 146.2-147.0 °C; R_f = 0.28 (hexane : EtOAc = 5 : 1). IR (KBr) 3438, 2980, 2851, 1605, 1520, 1454, 1282, 1212, 1116, 1060, 938, 822, 781, 627 cm^{-1}; ^1H NMR (200 MHz) δ = 0.98-1.49 (m, 11 H), 1.66-2.11 (m, 8 H), 2.41 (tt, *J* = 3, 12 Hz, 1 H), 3.54 (tt, *J* = 4, 10 Hz, 1 H), 6.82-7.11 (m, 3 H); ^{19}F NMR (188 MHz) δ = −139.2 (ddd, *J* = 8, 12, 21 Hz, 1 F), −143.0 (dddd, *J* = 5, 8, 10, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 28.1 (s), 30.2 (s), 34.4 (s), 35.8 (s), 43.7 (d, *J* = 1 Hz), 71.1 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 4, 6 Hz), 144.7 (dd, *J* = 4, 5 Hz), 148.5 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 294 (M^+, 7), 276 (23), 194 (11), 193 (23), 179 (35), 140 (57), 127 (84), 121 (24), 82 (15), 81 (100), 79 (31), 67 (38). Found: C, 73.14; H, 8.19%. Calcd for $C_{18}H_{24}F_2O$: C, 73.44; H, 8.22%.

***trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexanol (2a)** and ***cis*-4-(*trans*-4-Propylcyclohexyl)cyclohexanol (2a').** Alcohols **2a** and **2a'** were prepared in 63 and 16% yields, respectively, by Method A.

2a: Colorless needles, mp 125.3-126.7 °C; R_f = 0.24 (hexane : EtOAc = 5 : 1). IR (KBr) 3414, 3355, 2959, 2855, 1464, 1454, 1356, 1345, 1059, 943, 891 cm^{-1}; ^1H NMR (200 MHz) δ = 0.79-1.38 (m, 18 H), 1.61-1.84 (m, 7 H), 1.91-2.08 (m, 2 H), 3.51 (tt, *J* = 5, 10 Hz, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 28.1 (s), 30.2 (s), 33.5 (s), 35.9 (s), 37.5 (s), 39.8 (s), 42.3 (s), 42.8 (s), 71.2 (s); MS *m/z* (rel intensity) 224 (M^+, 0.2), 123 (0.4), 206 (83), 177 (12), 164 (13), 163 (46), 135 (11), 124 (36), 123 (56), 122 (36), 109 (53), 95 (53), 83 (89), 82 (91), 81 (100), 69 (87), 67 (87). Found: C, 80.09; H, 12.38%. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58%.

2a': Colorless needles, mp 100.2-101.0 °C; R_f = 0.39 (hexane : EtOAc = 5 : 1). IR

(KBr) 3347, 2935, 2848, 1444, 1264, 1150, 1040, 977, 957, 763 cm^{-1}; ^1H NMR (200 MHz) δ = 0.79-1.21 (m, 12 H), 1.24-1.58 (m, 9 H), 1.68-1.80 (m, 6 H), 3.95-4.01 (m, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 23.9 (s), 30.1 (s), 32.8 (s), 33.5 (s), 37.5 (s), 39.8 (s), 42.26 (s), 42.30 (s), 66.9 (s); MS *m/z* (rel intensity) 224 (M^+, 0.08), 206 (20), 163 (17), 123 (14), 109 (11), 96 (7), 95 (14), 83 (55), 82 (76), 81 (93), 79 (31), 69 (100), 67 (97). Found: *m/z* 224.2144. Calcd for $C_{15}H_{28}O$: M, 224.2140.

***trans*-4-[trans-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]cyclohexanol (3a)** and ***cis*-4-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]cyclohexanol (3a').** Alcohols **3a** and **3a'** were obtained in 36 and 11% yields, respectively, by Method A. According to Method B, **3a** and **3a'** were prepared in 32 and 56% yields, respectively.

3a: Colorless needles. Phase transition temperature/°C: Cr 152 S_B 225 Iso; R_f = 0.20 (hexane : EtOAc = 5 : 1). IR 3341, 2953, 2849, 1444, 1432, 1372, 1057, 1051, 967, 903 cm^{-1}; ^1H NMR (200 MHz) δ = 0.79-1.41 (m, 23 H), 0.86 (t, *J* = 7.1 Hz, 3 H), 1.57-1.85 (m, 9 H), 1.87-2.05 (m, 2 H), 3.46-3.54 (m, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 28.1 (s), 30.1 (s), 30.3 (s), 30.5 (s), 33.6 (s), 35.90 (s), 35.91 (s), 37.6 (s), 39.8 (s), 42.3 (s), 42.9 (s), 43.4 (s), 71.3 (s); MS *m/z* (rel intensity) 307 (M^++1, 0.2), 288 (30), 205 (10), 164 (13), 163 (16), 149 (11), 135 (8), 123 (15), 109 (20), 97 (10), 95 (30), 83 (41), 82 (39), 81 (100), 79 (27), 69 (71), 67 (72). Found: *m/z* 306.2920. Calcd for $C_{21}H_{38}O$: M, 306.2923

3a': A colorless powder. Phase transition temperature/°C: Cr 137 S_B 222 Iso; R_f = 0.30 (hexane : EtOAc = 5 : 1). IR (KBr) 3344, 2980, 2850, 1444, 1363, 1264, 1040, 980, 960, 898, 763 cm^{-1}; ^1H NMR (200 MHz) δ = 0.79-1.85 (m, 34 H), 0.87 (t, *J* = 7.2 Hz, 3 H), 3.98 (brs, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 23.9 (s), 30.1 (s), 30.3 (s), 30.4 (s), 32.8 (s), 33.6 (s), 37.6 (s), 39.8 (s), 42.3 (br s), 43.4 (s), 67.0 (s); MS *m/z* (rel intensity) 307 (M^++1, 1.5), 288 (29), 164 (11), 163 (18), 123 (13), 121 (14), 109 (18), 95 (27), 92 (15), 83 (48), 82 (37), 81 (100), 79 (38), 69 (67), 67 (85). Found: C, 82.06; H, 12.30%. Calcd for $C_{21}H_{38}O$: C, 82.29; H, 12.50%.

***trans*-4-(4'-Propylbiphenyl-4-yl)cyclohexanol (4a).** Method A, 65% yield. Colorless needles, mp 175.3-176.6 °C; R_f = 0.50 (CH_2Cl_2 : MeOH = 10 : 1). IR 3420, 2930, 2855, 1497, 1453, 1356, 1061, 1005, 804 cm^{-1}; ^1H NMR (200 MHz) δ = 0.97 (t, *J* = 7 Hz, 3 H), 1.33-1.78 (m, 7 H), 1.88-2.19 (m, 4 H), 2.42-2.70 (m, 3 H), 3.58-3.79 (m, 1 H), 7.20-7.27 (m, 4 H), 7.43-7.53 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 24.5 (s), 32.4 (s), 35.8 (s), 37.6 (s), 43.0 (s), 70.5 (s), 126.7 (s), 126.8 (s), 127.1 (s), 128.8 (s), 138.3 (s), 138.9 (s), 141.5 (s), 145.2 (s); MS *m/z* (rel intensity) 295 (M^++1, 15), 294 (M^+, 69), 276 (100), 261 (22), 147 (49), 222 (52), 205 (20), 193 (96), 178 (33), 165 (31), 91 (18). Found: C, 85.63; H, 9.21%. Calcd for $C_{21}H_{38}O$: C, 85.67; H, 8.90%.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanemethanol (1b).**

Sodium borohydride (0.98 g, 26 mmol) was added portionwise to a solution of *trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl] cyclohexanecarbaldehyde (7.3 g, 24 mmol) in methanol (20 mL) and THF (20 mL) at room temperature under stirring. The resulting mixture was stirred at room temperature for 4 h, and the methanol solvent was removed under reduced pressure. The white solid residue was partitioned in sat. aq. $NaHCO_3$ and Et_2O (200 mL), and the organic phase was separated. The aq. phase was extracted with Et_2O three times (totally 500 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by recrystallization to give **1b** (5.2 g) in 71% yield as colorless needles. Mp 97.7-99.1 °C; R_f = 0.15 (hexane : EtOAc = 5 : 1). IR (KBr) 3320, 2923, 2851, 1607, 1518, 1449, 1429, 1277, 1204, 1038, 812, 770 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80-1.58 (m, 11 H), 1.68-2.00 (m, 9 H), 2.28-2.68 (m, 1 H), 2.39 (tm, *J* = 12 Hz, 1 H), 3.42 (d, *J* = 6 Hz, 2 H), 6.86-7.04 (m, 3 H); ^{19}F NMR (282 MHz) δ = −139.09 (dd, *J* = 8, 12, 21 Hz, 1 F), −142.98 (dddd, *J* = 8, 11, 14, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.3 (s), 29.6 (s), 29.9 (s), 34.3 (s), 40.4 (s), 42.5 (s), 43.0 (s), 43.6 (s), 68.1 (s), 115.0 (d, *J* = 17 Hz), 116.5 (d, *J* = 17 Hz), 122.2 (dd, *J* = 3, 6 Hz), 144.6 (dd, *J* = 4, 4 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.0 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 309 (M^++1, 8), 308 (M^+, 100), 275 (9), 269 (4), 208 (19), 207 (13), 196 (14), 194 (40), 193 (49), 192 (28), 191 (19), 190 (15), 180 (18), 179 (93), 165 (23), 132 (4). Found: *m/z* 308.1949. Calcd for $C_{19}H_{26}F_2O$: M, 308.1952.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexaneethanol (1c).** Method C, 76% yield. A colorless powder. Phase transition temperature/°C: Cr 101 N 129 Iso; R_f = 0.29 (hexane : EtOAc = 5 : 1). IR (KBr) 3434, 2944, 2921, 2888, 2849, 1605, 1518, 1453, 1429, 1358, 1279, 1213, 1115, 1051, 1019, 862, 822, 781 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.40 (m, 8 H), 1.45-1.55 (m, 6 H), 1.70-1.95 (m, 8 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 3.69 (t, *J* = 7 Hz, 2 H), 6.84-7.09 (m, 3 H); ^{19}F NMR (282 MHz) δ = −139.0—139.2 (m, 1 F), −142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.9 (s), 30.1 (s), 33.5 (s), 34.4 (s), 34.5 (s), 40.3 (s), 42.7 (s), 43.1 (s), 43.8 (s), 60.9 (s), 115.3 (d, *J* = 17 Hz), 116.1 (d, *J* = 17 Hz), 122.4 (d, *J* = 3, 6 Hz), 144.8 (d, *J* = 5, 5 Hz), 148.4 (d, *J* = 13, 245 Hz), 150.1 (d, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 324 (M^++2, 1), 323 (M^++1, 9), 322 (M^+, 41), 275 (10), 194 (13), 193 (18), 179 (39), 166 (11), 153 (22), 140 (72), 127 (100), 109 (93), 95 (27), 81 (63), 67 (86). Found: *m/z* 322.2114. Calcd for $C_{20}H_{28}F_2O$: M, 322.2108.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanepropanol (1d).** Method D, 37% yield. Colorless needles. Phase transition temperature/°C: Cr 89 N 159 Iso; R_f = 0.19 (hexane : EtOAc = 5 : 1). IR (KBr) 3320, 2924, 2851, 1607, 1516, 1449, 1429, 1279, 1211, 1117, 1053, 1009, 943, 862, 818, 770 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.44 (m, 12 H), 1.46-1.68 (m, 3 H), 1.70-1.95 (m, 9 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H),

3.62 (t, J = 7 Hz, 2 H), 6.86-7.05 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.0—139.2 (m, 1 F), –142.8—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 30.0 (s), 30.1 (s), 30.2 (s), 33.3 (s), 33.5 (s), 34.5 (s), 37.7 (s), 42.7 (s), 43.2 (s), 43.8 (s), 63.4 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.8 (dd, J = 5, 5 Hz), 148.4 (dd, J = 13, 245 Hz), 150.1 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 338 (M^++2, 0.9), 337 (M^++1, 6), 336 (M^+, 27), 179 (24), 153 (15), 140 (49), 127 (71), 123 (26), 95 (33), 81 (100), 67 (87). Found: *m/z* 336.2263. Calcd for $C_{21}H_{30}F_2O$: M, 336.2265.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanebutanol (1e).** Method C, 88% yield. Colorless needles. Phase transition temperature/°C: Cr 97 N 152 Iso; R_f = 0.18 (hexane : EtOAc = 5 : 1). IR (KBr) 3434, 2919, 2849, 1609, 1518, 1495, 1451, 1435, 1289, 1211, 1115, 1045, 1021, 947, 817, 770 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.80-1.46 (m, 15 H), 1.48-1.62 (m, 2 H), 1.68-1.96 (m, 8 H), 2.06 (brs, 1 H), 2.40 (tt, J = 3, 12 Hz, 1 H), 3.65 (t, J = 7 Hz, 2 H), 6.86-7.06 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.1 (ddd, J = 8, 12, 21 Hz, 1 F), –143.0 (dddd, J = 8, 11, 14, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 23.1 (s), 30.0 (s), 30.1 (s), 33.0 (s), 33.5 (s), 34.5 (s), 37.2 (s), 37.8 (s), 42.7 (s), 43.2 (s), 43.8 (s), 63.1 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.6 (dd, J = 4, 4 Hz), 148.4 (dd, J = 13, 245 Hz), 150.2 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 351 (M^++1, 2), 350 (M^+, 6), 279 (12), 194 (12), 192 (14), 178 (14), 167 (31), 149 (100), 137 (50), 128 (11), 119 (13), 105 (18). Found: *m/z* 350.2421. Calcd for $C_{22}H_{32}F_2O$: M, 350.2421.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanepentanol (1f).** Method C, 86% yield. Colorless needles. Phase transition temperature/°C: Cr 93 N 158 Iso; R_f = 0.31 (hexane : EtOAc : CH_2Cl_2 = 4 : 1 : 1). IR (KBr) 3310, 2924, 2849, 1607, 1518, 1429, 1275, 1210, 1115, 1057, 951, 939, 862, 816, 772 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.80-1.64 (m, 19 H), 1.68-1.94 (m, 9 H), 2.40 (tt, J = 3, 12 Hz, 1 H), 3.64 (t, J = 7 Hz, 2 H), 6.87-7.06 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.1—139.2 (m, 1 F), –142.9--143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 26.1 (s), 26.8 (s), 30.0 (s), 30.2 (s), 32.8 (s), 33.6 (s), 34.6 (s), 37.4 (s), 37.8 (s), 42.8 (s), 43.3 (s), 43.8 (s), 63.1 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.6 (dd, J = 5, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 366 (M^++2, 0.4), 365 (M^++1, 4), 364 (M^+, 15), 193 (12), 179 (28), 153 (16), 151 (20), 140 (47), 127 (75), 109 (30), 95 (77), 81 (71), 67 (100). Found: *m/z* 364.2563. Calcd for $C_{23}H_{34}F_2O$: M, 364.2578.

***trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexanemethanol (2b).** Method D, 80% yield. A colorless solid, mp 129.3-131.0 °C. R_f = 0.20 (hexane : EtOAc = 10 : 1). IR (KBr) 3250, 2944, 2909, 1453, 1379, 1339, 1289, 1044, 895 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.75-1.48 (m, 21 H), 0.88 (t, J = 7 Hz, 3 H), 1.64-1.86 (m, 8 H), 3.40-3.44 (m, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.4 (s), 29.8

(s), 30.1 (s), 32.2 (s), 33.6 (s), 37.5 (s), 37.9 (s), 40.7 (s), 43.4 (s), 68.8 (s); MS *m/z* (rel intensity) 266 (M^+, 0.3), 248 (32), 219 (28), 177 (13), 151 (13), 137 (14), 123 (12), 113 (22), 109 (22), 97 (79), 95 (100), 83 (73), 81 (80), 79 (61), 69 (70), 67 (81). Found: *m/z* 266.2615. Calcd for $C_{18}H_{34}O$: M, 266.2610.

***trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexaneethanol (2c).**

Method C, 85% yield. Colorless needles. Mp 152.0-152.9 °C; R_f = 0.27 (hexane : EtOAc = 5 : 1). IR (KBr) 3428, 2953, 2919, 2851, 1468, 1453, 1360, 1051, 1022, 963, 893 cm^{-1}; ^1H NMR (200 MHz) δ = 0.82-1.34 (m, 24 H), 1.46 (dt, *J* = 7, 7 Hz, 2 H), 1.62-1.77 (m, 8 H), 3.68 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.9 (s), 30.1 (s), 32.2 (s), 33.60 (s), 33.64 (s), 34.5 (s), 37.5 (s), 37.9 (s), 40.4 (s), 43.3 (s), 43.4 (s), 60.9 (s); MS *m/z* (rel intensity) 280 (M^+, 0.7), 263 (7), 262 (32), 233 (12), 191 (13), 151 (14), 137 (11), 124 (6), 109 (100), 97 (66), 96 (46), 95 (45), 83 (67), 81 (76), 79 (52), 69 (57), 67 (81). Found: C, 81.19; H, 13.04%. Calcd for $C_{19}H_{36}O$: C, 81.36; H, 12.94%.

***trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexanepropanol (2d).**

Method C, 84% yield. A colorless solid. Mp 155.3-156.9 °C; R_f = 0.36 (hexane : EtOAc : CH_2Cl_2 = 5 : 1 : 1). IR (KBr) 3340, 2923, 2849, 1509, 1468, 1443, 1378, 1339, 1217, 1057, 959, 899, 723 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.45 (m, 23 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.48-2.00 (m, 10 H), 3.60 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 30.0 (s), 30.1 (s), 30.2 (s), 32.2 (s), 33.4 (s), 33.6 (s), 33.7 (s), 37.5 (s), 37.7 (s), 37.9 (s), 43.4 (s), 43.5 (s), 63.4 (s); MS *m/z* (rel intensity) 295 (M^++1, 3), 276 (21), 248 (17), 124 (16), 123 (41), 122 (19), 11 (15), 109 (13), 97 (61), 96 (48), 83 (54), 80 (100), 67 (63). Found: *m/z* 294.2928. Calcd for $C_{20}H_{38}O$: M, 294.2923.

***trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexanebutanol (2e).**

Method C, 67% yield. A colorless solid. Mp 160.4-161.2 °C; R_f = 0.24 (hexane : EtOAc = 5 : 1). IR (KBr) 3428, 3374, 2953, 2917, 2851, 1462, 1453, 1377, 1356, 1049, 1019, 992, 961, 893 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.42 (m, 24 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.53 (q, *J* = 7 Hz, 2 H), 1.62-1.82 (m, 9 H), 3.63 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 23.1 (s), 26.7 (s), 30.06 (s), 30.10 (s), 32.2 (s), 33.1 (s), 33.6 (s), 33.7 (s), 37.2 (s), 37.5 (s), 37.88 (s), 37.94 (s), 43.48 (s), 43.49 (s), 63.1 (s); MS *m/z* (rel intensity) 309 (M^++1, 8), 275 (18), 221 (12), 195 (15), 193 (29), 180 (17), 166 (45), 153 (26), 140 (56), 135 (36), 127 (100), 109 (45), 66 (32). Found: *m/z* 308.3070. Calcd for $C_{21}H_{40}O$: M, 308.3079.

***trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexanepentanol (2f).**

Method C, 55% yield. A colorless solid. Mp 158.9-160.4 °C; R_f = 0.17 (hexane : EtOAc = 5 : 1). IR (KBr) 3350, 2920, 2849, 1466, 1443, 1375, 1339, 1051, 988, 897, 725 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.45 (m, 28 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.50-

1.80 (m, 8 H), 3.05 (brs, 1 H), 3.65 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.0 (s), 26.7 (s), 26.8 (s), 30.06 (s), 30.09 (s), 32.3 (s), 32.6 (s), 33.6 (s), 33.7 (s), 37.4 (s), 37.5 (s), 37.85 (s), 37.93 (s), 43.5 (s), 63.1 (s); MS *m/z* (rel intensity) 322 (M^+, 3), 305 (18), 304 (78), 233 (24), 194 (16), 152 (49), 150 (43), 137 (40), 123 (30), 121 (34), 109 (100). Found: *m/z* 322.3237. Calcd for $C_{22}H_{42}O$: M, 322.3236.

***trans*-1-[*trans*-4-(4-Penten-1-yl)cyclohexyl]-4-pentylcyclohexane (21f).** A flask was charged with THF (150 mL), copper(I) iodide (4.8 g, 25 mmol), and 1-[*trans*-4-(2-iodoethyl)cyclohexyl]-*trans*-4-pentylcyclohexane[4e] (7.8 g, 20 mmol) and cooled at –78 °C. Allylmagnesium chloride (25 mL of 2.0 M THF solution, 50 mmol) was added dropwise to the mixture at –78 °C. After the addition was completed, the reaction mixture was allowed to warm to 0 °C over 4 h and stirred at room temperature for 2 h before quenching with aq. HCl (1.0 M). The organic phase was separated; the aq. phase was extracted with Et_2O three times (totally 300 mL). The combined organic extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **21f** (5.7 g) in 94% yield as a colorless mesomorphic oil. Phase transition temperature/°C: Cr –17 S_X 11 S_B 103 Iso (DSC 2nd heating); R_f = 0.88 (hexane). IR 2917, 2849, 1823, 1642, 1447, 1416, 1379, 1341, 1291, 1217, 989, 911, 895, 725 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.75-1.04 (m, 10 H), 0.88 (t, J = 7 Hz, 3 H), 1.06-1.42 (m, 14 H), 1.64-1.80 (m, 8 H), 2.01 (q, J = 7 Hz, 2 H), 4.90-5.02 (m, 2 H), 5.74-5.88 (m, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.4 (s), 26.7 (s), 30.10 (s), 30.13 (s), 32.3 (s), 33.65 (s), 33.70 (s), 34.2 (s), 37.0 (s), 37.5 (s), 37.9 (s), 38.0 (s), 43.50 (s), 43.53 (s), 114.1 (s), 139.3 (s); MS *m/z* (rel intensity) 304 (M^+, 12), 166 (9), 149 (17), 140 (22), 127 (27), 125 (11), 122 (16), 111 (19), 99 (12), 95 (59), 83 (49), 81 (87), 67 (100). Found: *m/z* 304.3142. Calcd for $C_{22}H_{40}$: M, 304.3130.

***trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexanebutanal.** Pyridinium chlorochromate (5.8 g, 27 mmol) was added in one portion to a solution of **1e** (6.3 g, 18 mmol) in CH_2Cl_2 (200 mL) at room temperature. The reaction mixture was stirred for 3 h at room temperature before addition of Celite. The insoluble material was filtered off; the filtrate was concentrated *in vacuo*; the residue was purified by flash column chromatography (hexane : EtOAc = 20 : 1) to give the title aldehyde (5.4 g) in 86% yield as a colorless solid. Phase transition temperature/°C: S_X 82 N 139 Iso; R_f = 0.57 (hexane : EtOAc = 5 : 1). IR (KBr) 2919, 2847, 1724, 1717, 1607, 1518, 1449, 1285, 1210, 1198, 1115, 945, 862, 816 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.80-1.46 (m, 13 H), 1.58-1.94 (m, 10 H), 2.34-2.48 (m, 3 H), 6.83-7.08 (m, 3 H), 9.74-9.77 (m, 1 H); ^{19}F NMR (282 MHz) δ = –139.0—139.2 (m, 1 F), –142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 19.5 (s), 29.9 (s), 30.1 (s), 33.3 (s), 34.5 (s), 36.8 (s), 37.6 (s), 42.7 (s), 43.2 (s),

43.8 (s), 44.2 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.8 (dd, J = 5, 5 Hz), 148.4 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 246 Hz), 203.0 (s); MS *m/z* (rel intensity) 349 (M^++1, 8), 348 (M^+, 17), 179 (26), 153 (26), 140 (50), 135 (75), 133 (17), 127 (100), 121 (18), 109 (25), 107 (21), 95 (34), 93 (37), 81 (59), 69 (32), 67 (98). Found: *m/z* 348.2251. Calcd for $C_{22}H_{30}F_2O$: M, 348.2265.

***trans*-1-(3,4-Difluorophenyl)-4-[*trans*-4-(4-penten-1-yl)cyclohexyl]cyclohexane (20f).** To triphenyl(methyl)phosphonium bromide (5.7 g, 16 mmol) suspended in Et_2O (100 mL) was added dropwise *n*-BuLi in hexane (1.6 M, 10 mL) at room temperature, and the mixture was stirred for 4 h at room temperature. To this ylide solution was added dropwise a solution of *trans*-4-[*trans*-4-(3,4-difluorophenyl)cyclohexyl]cyclohexane-butanal (14.1 g, 4.9 mmol) in Et_2O (100 mL) at room temperature; the resulting mixture was stirred for 10 h at room temperature before quenching with aq. NH_4Cl. The organic phase was separated; the aq. phase was extracted with Et_2O three times (300 mL). The combined organic extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **20f** (3.8 g) in 78% yield as a mesomorphic oil. Phase transition temperature/°C: Cr 17 N 88 Iso (DSC 2nd heating); R_f = 0.54 (hexane). IR 2923, 2851, 1607, 1518, 1449, 1431, 1279, 1211, 1117, 990, 911, 816 cm^{-1}; ^1H NMR (300 MHz) δ = 0.78-1.48 (m, 15 H), 1.70-1.94 (m, 8 H), 2.02 (q, J = 7 Hz, 2 H), 2.40 (tt, J = 3, 12 Hz, 1 H), 4.90-5.02 (m, 2 H), 5.74-5.88 (m, 1 H), 6.86-7.08 (m, 3 H); ^{19}F NMR (282 MHz) δ = −139.0—139.2 (m, 1 F), −142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 26.3 (s), 30.1 (s), 30.2 (s), 33.6 (s), 34.1 (s), 34.6 (s), 37.0 (s), 37.8 (s), 42.8 (s), 43.3 (s), 43.9 (s), 114.1 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 139.2 (s), 144.8 (dd, J = 5, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 348 (M^++2, 1), 347 (M^++1, 4), 346 (M^+, 21), 194 (11), 193 (17), 179 (37), 153 (15), 140 (37), 127 (69), 109 (27), 95 (49), 81 (67), 67 (100). Found: *m/z* 346.2472. Calcd for $C_{23}H_{32}F_2$: M, 346.2472.

Preparation of Dithiocarbonates: General Procedure.

Method A: An oven-dried, 1-L, three-necked, round-bottomed flask, equipped with an argon inlet and a Teflon®-coated magnetic stirring bar, and fitted with a rubber septum, was flushed with argon, charged with alcohol **1-4** (50 mmol) and THF (200 mL), and was cooled at 0 °C using an ice-water bath. To the solution was added portionwise NaH (2.4 g, 60 mmol, 60% dispersion in mineral oil) over 5 min at 0 °C under purging with argon via the inlet. The ice-water bath was removed, the resulting white suspension was allowed to warm to room temperature and stirred for 1 h. The mixture was recooled at 0 °C, and carbon disulfide (0.25 mol, 15 mL) was added dropwise to the mixture via a

syringe over 10 min. The resulting pale yellow suspension was allowed to warm to room temperature and stirred until all the substrate was consumed. The resulting yellow solution was recooled to 0 °C, and methyl iodide (6.2 mL, 0.10 mol) was added dropwise *via* a syringe over 10 min. The pale yellow creamy mixture was allowed to warm to room temperature, stirred for several hours, quenched by careful addition of 50% aq. NH_4Cl (100 mL) at 0 °C. The organic phase was separated; the aq. phase was extracted three times with portions of Et_2O (totally 500 mL). The combined organic phase was washed with sat. aq. NaCl (100 mL) containing 1 g of $NaHSO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. A yellow residue was flash column chromatographed or/and recrystallized to give dithiocarbonate **5-8**.

Method B: In the procedure for Method A, NaH (60 mmol) was replaced by BuLi (75 mmol).

***S*-Methyl *O*-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl] Dithiocarbonate (6a).** Method A, 79% yield. Pale yellow needles. Phase transition temperature/°C: Cr 61 N 75 Iso; R_f = 0.68 (hexane : EtOAc = 10 : 1). IR (KBr) 2950, 2907, 2856, 1702, 1464, 1442, 1237, 1215, 1050, 1018, 982, 918, 902, 733 cm^{-1}; ^1H NMR (200 MHz) δ = 0.73-1.55 (m, 16 H), 1.62-1.93 (m, 8 H), 2.20-2.35 (m, 2 H), 2.53 (s, 3 H), 5.43 (tt, *J* = 5, 11 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 18.7 (s), 20.0 (s), 27.8 (s), 30.1 (s), 31.2 (s), 33.4 (s), 37.5 (s), 39.7 (s), 42.1 (s), 42.6 (s), 83.5 (s), 215.1 (s); MS *m/z* (rel intensity) 314 (M^+, 0.4), 206 (37), 125 (12), 123 (16), 111 (22), 109 (29), 97 (126), 95 (29), 91 (17), 83 (63), 82 (25), 81 (62), 79 (24), 69 (100), 67 (68). Found: C, 64.65; H, 9.77%. Calcd for $C_{17}H_{30}OS_2$: C, 64.92; H, 9.61%.

***S*-Methyl *O*-{*trans*-4-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]cyclohexyl} Dithiocarbonate (7a).** Method B, 68% yield. Pale yellow needles. Phase transition temperature/°C: Cr 85 S_B 177 N 222 Iso; R_f = 0.29 (hexane). IR (KBr) 2951, 2934, 2888, 1464, 1443, 1234, 1208, 1092, 1049, 984 cm^{-1}; ^1H NMR (200 MHz) δ = 0.72-1.58 (m, 23 H), 0.86 (t, *J* = 7 Hz, 3 H), 1.60-1.88 (m, 8 H), 2.05-2.25 (m, 2 H), 2.53 (s, 3 H), 5.43 (tt, *J* = 5, 11 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 27.8 (s), 27.9 (s), 30.1 (s), 30.2 (s), 30.4 (s), 31.2 (s), 31.9 (s), 33.6 (s), 37.6 (s), 39.8 (s), 42.0 (s), 42.7 (s), 43.4 (s), 83.6 (s), 215.1 (s); MS *m/z* (rel intensity) 396 (M^+, 2), 287 (3), 286 (20), 203 (2), 202 (4), 160 (13), 146 (16), 135 (11), 121 (26), 108 (31), 94 (42), 83 (67), 81 (98), 69 (94), 67 (100). Found: *m/z* 396.2532. Calcd for $C_{23}H_{40}OS_2$: M, 396.2520.

***S*-Methyl *O*-[*trans*-4-(4'-Propylbiphenyl-4-yl)cyclohexyl] Dithiocarbonate (8a).** Method A, 95% yield. Colorless needles. Phase transition temperature/°C: Cr 115 N 153 Iso; R_f = 0.45 (hexane : EtOAc = 10 : 1). IR (KBr) 3024, 2947, 2931, 2866, 1898, 1495, 1495, 1448, 1220, 1210, 1050, 997, 957, 803, 778, 518 cm^{-1}; ^1H NMR (200 MHz) δ = 0.96 (t, *J* = 7 Hz, 3 H), 1.59-1.80 (m, 6 H), 1.86-2.12 (m, 2 H), 2.24-2.42 (m, 2

H), 2.53 (s, 3 H), 2.50-2.64 (m, 2 H), 5.52-5.67 (m, 1 H), 7.19-7.24 (m, 4 H), 7.45-7.51 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 13.8 (s), 18.8 (s), 24.4 (s), 31.3 (s), 32.0 (s), 37.6 (s), 42.8 (s), 82.6 (s), 126.7 (s), 126.9 (s), 127.0 (s), 128.8 (s), 138.2 (s), 139.1 (s), 141.5 (s), 144.6 (s), 215.2 (s); MS *m/z* (rel intensity) 385 (M^++1, 1), 384 (M^+, 5), 277 (22), 276 (76), 223 (18), 222 (58), 193 (100), 180 (16), 165 (19), 91 (11), 81 (27). Found: *m/z* 384.1577. Calcd for $C_{23}H_{28}OS_2$: M, 384.1582.

***O*-*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexylmethyl *S*-Methyl Dithiocarbonate (5b).** Method A, 92% yield. Pale yellow needles, mp 101.3-101.9 °C; R_f = 0.50 (hexane : EtOAc = 10 : 1). IR (KBr) 2920, 2892, 1605, 1516, 1449, 1426, 1291, 1227, 1216, 1073, 1059, 953, 938, 826, 774 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.95-1.25 (m, 8 H), 1.25-1.50 (m, 2 H), 1.70-1.95 (m, 9 H), 2.42 (tt, *J* = 3, 12 Hz, 1 H), 2.56 (s, 3 H), 4.41 (d, *J* = 6 Hz, 2 H), 6.85-7.08 (m, 3 H); ^{19}F NMR (282 MHz) δ = –138.9—139.1 (m, 1 F), –142.8—143.0 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.8 (s), 29.2 (s), 29.7 (s), 30.0 (s), 34.4 (s), 37.2 (s), 42.5 (s), 42.9 (s), 79.0 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.7 (dd, *J* = 5, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.0 (dd, *J* = 13, 247 Hz), 215.8 (s); MS *m/z* (rel intensity) 399 (M^++1, 0.3), 398 (M^+, 0.3), 291 (9), 290 (40), 193 (14), 179 (24), 153 (20), 140 (37), 136 (10), 127 (100), 109 (10), 107 (8). Found: *m/z* 398.1558. Calcd for $C_{21}H_{28}F_2OS_2$: M, 398.1550.

***O*-2-{*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexyl}ethyl *S*-Methyl Dithiocarbonate (5c).** Method A, 95% yield. A pale yellow powder, mp 73.4-74.6 °C; R_f = 0.75 (hexane : EtOAc = 10 : 1). IR (KBr) 2923, 2855, 1717, 1647, 1605, 1514, 1448, 1426, 1269, 1210, 1115, 1059, 968, 822, 777, 750 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.80-1.45 (m, 11 H), 1.65-1.90 (m, 10 H), 2.41 (tt, *J* = 3, 12 Hz, 1 H), 2.56 (s, 3 H), 4.64 (d, *J* = 6 Hz, 2 H), 6.85-7.07 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.0—139.2 (m, 1 F), –142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 29.8 (s), 30.1 (s), 33.3 (s), 34.5 (s), 34.8 (s), 35.5 (s), 42.6 (s), 43.0 (s), 43.8 (s), 72.6 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.7 (dd, *J* = 5, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 13, 247 Hz), 215.9 (s); MS *m/z* (rel intensity) 412 (M^+, 0.1), 379 (8), 305 (13), 304 (56), 193 (20), 179 (46), 166 (14), 153 (25), 141 (14), 140 (35), 127 (100), 111 (22), 109 (59), 97 (17), 95 (44), 81 (68), 69 (66), 67 (88). Found: *m/z* 412.1711. Calcd for $C_{22}H_{30}F_2OS_2$: M, 412.1706.

***O*-3-{*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexyl}propyl *S*-Methyl Dithiocarbonate (5d).** Method A, 83% yield. Pale yellow needles, mp 76.6-78.0 °C; R_f = 0.64 (hexane : EtOAc = 10 : 1). IR (KBr) 2946, 2915, 2845, 1869, 1610, 1518, 1489, 1447, 1289, 1273, 1219, 1207, 1065, 1052, 963, 939, 816, 772 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.82-1.45 (m, 13 H), 1.68-1.98 (m, 10 H), 2.41 (tt, *J* = 3, 12 Hz, 1 H), 2.56 (s, 3 H), 4.58 (t, *J* = 7 Hz, 2 H), 6.80-7.09 (m, 3 H); ^{19}F NMR (282 MHz) δ =

–139.0—139.2 (m, 1 F), –142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 25.7 (s), 29.9 (s), 30.1 (s), 33.4 (s), 33.4 (s), 34.5 (s), 37.5 (s), 42.7 (s), 43.2 (s), 43.8 (s), 74.6 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.8 (dd, *J* = 4, 4 Hz), 148.5 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 13, 247 Hz), 215.9 (s); MS *m/z* (rel intensity) 426 (M^+, 0.3), 393 (19), 319 (15), 318 (72), 276 (21), 195 (21), 193 (17), 179 (46), 140 (45), 127 (100), 123 (60), 109 (50), 95 (57), 81 (62), 69 (64), 67 (63). Found: *m/z* 426.1859. Calcd for $C_{23}H_{32}F_2OS_2$: M, 426.1863.

***O*-4-{*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexyl}butyl *S*-Methyl Dithiocarbonate (5e).** Method A, 92% yield. A pale yellow powder. Phase transition temperature/°C: Cr 55 S_B 63 N 88 Iso; R_f = 0.41 (hexane). IR (KBr) 2924, 2851, 1869, 1522, 1509, 1459, 1217, 1090, 1051, 939, 806, 770 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.80-1.48 (m, 15 H), 1.68-1.94 (m, 10 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 2.56 (s, 3 H), 4.59 (t, *J* = 7 Hz, 2 H), 6.80-7.09 (m, 3 H); ^{19}F NMR (188 MHz) δ = –139.0—139.2 (m, 1 F), –142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 23.3 (s), 28.5 (s), 30.0 (s), 30.1 (s), 33.4 (s), 34.5 (s), 36.9 (s), 37.7 (s), 42.7 (s), 43.2 (s), 43.8 (s), 74.3 (s), 115.4 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.8 (dd, *J* = 5, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 13, 247 Hz), 215.9 (s); MS *m/z* (rel intensity) 441 (M^++1, 0.3), 440 (M^+, 0.3), 407 (3), 333 (19), 332 (74), 193 (19), 179 (45), 153 (27), 139 (41), 127 (100), 109 (29), 95 (71), 81 (78), 69 (56). Found: *m/z* 440.2014. Calcd for $C_{24}H_{34}F_2OS_2$: M, 440.2019.

***O*-5-{*trans*-4-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]cyclohexyl}pentyl *S*-Methyl Dithiocarbonate (5f).** Method A, 86% yield. Pale yellow needles. Phase transition temperature/°C: Cr 71 S_B 77 N 81 Iso; R_f = 0.60 (hexane : EtOAc = 10 : 1). IR (KBr) 2944, 2917, 1869, 1522, 1221, 1208, 1069, 1053, 938, 868, 816, 772 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.79-1.45 (m, 17 H), 1.65-1.95 (m, 10 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 2.56 (s, 3 H), 4.59 (t, *J* = 7 Hz, 2 H), 6.80-7.09 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.1—139.2 (m, 1 F), –143.0—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 18.9 (s), 26.2 (s), 26.6 (s), 28.3 (s), 30.0 (s), 30.2 (s), 33.6 (s), 34.6 (s), 37.3 (s), 37.8 (s), 42.8 (s), 43.3 (s), 43.9 (s), 74.3 (s), 115.4 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.8 (dd, *J* = 5, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 13, 247 Hz), 216.0 (s); MS *m/z* (rel intensity) 455 (M^++1, 0.3), 454 (M^+, 0.6), 347 (14), 346 (52), 275 (8), 206 (4), 194 (8), 193 (17), 179 (8), 153 (23), 151 (23), 140 (30), 137 (13), 127 (100), 109 (39), 95 (57), 81 (71), 67 (80). Found: *m/z* 454.2173. Calcd for $C_{25}H_{36}F_2OS_2$: M, 454.2176.

***S*-Methyl *O*-[*trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexyl]methyl Dithiocarbonate (6b).** Method B, 96% yield. A pale yellow powder; mp 64.8-65.5 °C; R_f = 0.44 (hexane : EtOAc = 5 : 1). IR (KBr) 2919, 2851, 1456, 1238, 1165, 1061, 963, 895 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.75-1.35 (m, 18 H), 0.88 (t, *J* = 7 Hz, 3

H), 1.63-1.80 (m, 10 H), 2.55 (s, 3 H), 4.39 (d, J = 6 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.8 (s), 22.7 (s), 26.6 (s), 29.2 (s), 29.8 (s), 30.0 (s), 32.2 (s), 33.6 (s), 37.2 (s), 37.4 (s), 37.9 (s), 43.1 (s), 43.3 (s), 79.2 (s), 215.9 (s); MS *m/z* (rel intensity) 356 (M^+, 2), 249 (11), 248 (29), 152 (13), 151 (21), 149 (19), 137 (30), 111 (31), 109 (21), 95 (80), 83 (83), 79 (39), 71 (38), 69 (85), 67 (100). Found: *m/z* 356.2212. Calcd for $C_{20}H_{36}OS_2$: M, 356.2208.

***S*-Methyl *O*-2-[*trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexyl]ethyl Dithiocarbonate (6c).** Method B, 95% yield. A pale yellow powder; phase transition temperature/°C: Cr 30 N 41 Iso; R_f = 0.71 (hexane : EtOAc = 10 : 1). IR (KBr) 2920, 1559, 1509, 1466, 1443, 1375, 1225, 1086, 1055, 967, 897 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.75-1.40 (m, 20 H), 0.87 (t, J = 7 Hz, 3 H), 1.60-1.90 (m, 10 H), 2.53 (s, 3 H), 4.60 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.9 (s), 26.7 (s), 29.8 (s), 30.0 (s), 32.2 (s), 33.4 (s), 33.6 (s), 34.9 (s), 35.5 (s), 37.4 (s), 37.9 (s), 43.2 (s), 43.4 (s), 72 6 (s), 215.8 (s); MS *m/z* (rel intensity) 371 (M^+, 3), 308 (20), 307 (100), 193 (24), 189 (10), 179 (13), 178 (14), 167 (26), 149 (43), 139 (14), 133 (15), 127 (12), 123 (16), 113 (24), 105 (22). Found: *m/z* 370.2366. Calcd for $C_{21}H_{38}OS_2$: M, 370.2364.

***S*-Methyl *O*-3-[*trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexyl]propyl Dithiocarbonate (6d).** Method B, 96% yield. A pale yellow powder; mp 67.5-68.3 °C; R_f = 0.78 (hexane : EtOAc = 10 : 1). IR (KBr) 2951, 2923, 2849, 1717, 1445, 1420, 1217, 1061, 1052, 968, 899 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.75-1.05 (m, 10 H), 0.88 (t, J = 7 Hz, 3 H), 1.10-1.32 (m, 12 H), 1.65-1.85 (m, 10 H), 2.55 (s, 3 H), 4.57 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.7 (s), 25.7 (s), 26.7 (s), 29.9 (s), 30.1 (s), 32.2 (s), 33.4 (s), 33.5 (s), 33.7 (s), 37.48 (s), 37.52 (s), 37.9 (s), 43.39 (s), 43.43 (s), 74.6 (s), 215.9 (s); MS *m/z* (rel intensity) 385 (M^++1, 3), 384 (M^+, 3), 276 (13), 207 (15), 153 (20), 140 (23), 137 (21), 135 (18), 127 (36), 123 (29), 109 (51), 97 (59), 81 (56), 69 (63), 67 (100). Found: *m/z* 384.2526. Calcd for $C_{22}H_{40}OS_2$: M, 384.2521.

***S*-Methyl *O*-4-[*trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexyl]butyl Dithiocarbonate (6e).** Method B, 95% yield. A pale yellow powder; phase transition temperature/°C: Cr 59 N 65 Iso; R_f = 0.80 (hexane : EtOAc = 10 : 1). IR (KBr) 2847, 1709, 1655, 1446, 1450, 1220, 1152, 1086, 1055, 967, 899 cm^{-1}; ^{1}H NMR (300 MHz) δ = 0.75-1.04 (m, 10 H), 0.88 (t, J = 7 Hz, 3 H), 1.06-1.50 (m, 14 H), 1.64-1.82 (m, 10 H), 2.56 (s, 3 H), 4.58 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.7 (s), 23.3 (s), 26.7 (s), 28.5 (s), 30.0 (s), 30.1 (s), 32.2 (s), 33.5 (s), 33.7 (s), 37.5 (s), 37.7 (s), 37.9 (s), 43.4 (s), 43.5 (s), 74.3 (s), 215.9 (s); MS *m/z* (rel intensity) 400 (M^++2, 0.9), 399 (M^++1, 0.9), 398 (M^+, 2), 336 (16), 335 (85), 262 (15), 136 (22), 82 (100), 75 (26), 71 (25). Found: *m/z* 398.2666. Calcd for $C_{23}H_{42}OS_2$: M, 398.2677.

***S*-Methyl *O*-5-[*trans*-4-(*trans*-4-Pentylcyclohexyl)cyclohexyl]pentyl**

Dithiocarbonate (6f). Method B, 91% yield. A pale yellow powder; mp 76.9-78.3 °C; R_f = 0.38 (hexane : EtOAc = 10 : 1). IR (KBr) 2924, 2849, 1734, 1717, 1684, 1559, 1541, 1509, 1458, 1223, 1090, 1053 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.04 (m, 10 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.06-1.45 (m, 16 H), 1.64-1.84 (m, 10 H), 2.55 (s, 3 H), 4.58 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 18.9 (s), 22.7 (s), 26.2 (s), 26.6 (s), 26.7 (s), 28.2 (s), 30.0 (s), 30.1 (s), 32.2 (s), 33.59 (s), 33.63 (s), 37.3 (s), 37.5 (s), 37.8 (s), 37.9 (s), 43.4 (s), 74.2 (s), 215.8 (s); MS *m/z* (rel intensity) 413 (M^++1, 0.3), 412 (M^+, 0.1), 379 (12), 365 (6), 305 (20), 304 (83), 233 (26), 178 (12), 152 (27), 151 (59), 137 (17), 123 (20), 109 (100). Found: *m/z* 412.2829. Calcd for $C_{24}H_{44}OS_2$: M, 412.2834.

***S*-Methyl *O*-*trans*-4-[*trans*-4-(3,4,5-Trifluorophenyl)cyclohexyl]cyclohexylmethyl Dithiocarbonate (22).** This compound was prepared by Method A in 83% yield as a pale yellow powder from *trans*-4-[*trans*-4-(3,4,5-trifluorophenyl)cyclohexyl]-cyclohexanemethanol. Mp 96.8-98.2 °C; R_f = 0.43 (hexane : EtOAc = 10 : 1). IR (KBr) 2930, 2855, 1707, 1611, 1530, 1443, 1345, 1231, 1211, 1059, 1034, 959, 845, 777 cm^{-1}; ^1H NMR (200 MHz) δ = 0.95-1.53 (m, 10 H), 1.65-2.04 (m, 9 H), 2.39 (tm, *J* = 12 Hz, 1 H), 2.55 (s, 3 H), 4.41 (d, *J* = 6 Hz, 2 H), 6.79 (dd, *J* = 7, 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = −135.9 (dd, *J* = 9, 21 Hz, 2 F), −164.7 (tt, *J* = 7, 21 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 18.8 (s), 29.2 (s), 29.7 (s), 29.9 (s), 34.2 (s), 37.2 (s), 42.5 (s), 42.8 (s), 43.8 (s), 79.0 (s), 110.4 (dd, *J* = 7, 13 Hz), 137.7 (td, *J* = 16, 248 Hz), 143.9 (dt, *J* = 7, 7 Hz), 150.9 (ddd, *J* = 4, 10, 248 Hz), 215.8 (s); MS *m/z* (rel intensity) 416 (M^+, 0.1), 309 (21), 308 (94), 211 (22), 197 (54), 183 (10), 171 (22), 158 (38), 145 (100), 121 (17), 109 (29), 97 (73), 95 (99), 83 (68), 81 (88), 67 (88). Found: *m/z* 416.1458. Calcd for $C_{21}H_{27}F_3OS_2$: M, 416.1455.

Preparation of Trifluoromethoxycyclohexane-LC: General Procedure. To a suspension of NBS (0.89 g, 5.0 mmol) and CH_2Cl_2 (2.5 mL), placed in an oven-dried polypropylene round-bottom tube that was equipped with a rubber septum and a Teflon®-coated magnetic stirring bar, were added dropwise pyridine (0.46 mL) and subsequently 70% HF/py (1.0 mL, 40 mmol of HF) at −42 °C (cooled by a CCl_4/dry ice bath) under an argon atmosphere. The resulting mixture was stirred at room temperature for 5 min and then cooled at 0 °C. A solution of dithiocarbonate **5a**, **6a**, **7a**, or **8a** (1.0 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise to the suspension at 0 °C to give a dark-red mixture, which was stirred at 0 °C for 1 h, diluted carefully with Et_2O (5.0 mL), and quenched with an ice-cold buffer solution (pH = 10, $NaHCO_3$, $NaHSO_3$, and NaOH). The pH of the mixture was adjusted to 10 by careful addition of ice-cold 10% NaOH aq. solution. The whole was extracted with Et_2O; the aq. phase was extracted with Et_2O three times. The combined organic phase was washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and

concentrated under reduced pressure. Flash column chromatography (cyclohexane) afforded trifluoromethyl ether **9a**, **10a**, **11a**, or **12a**. Yields and spectral properties of products are as follows.

***trans*-1-(*trans*-4-Propylcyclohexyl)-4-trifluoromethoxycyclohexane (10a).** Obtained in 40% yield as colorless crystals, mp 30.8-31.1 °C; bp 160 °C/0.4 mmHg; R_f = 0.91 (hexane). IR 2980, 2850, 1452, 1442, 1366, 1305, 1130, 1024, 859, 673 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.92 (m, 19 H), 0.87 (t, J = 7 Hz, 3 H), 2.00-2.28 (m, 4 H), 4.07 (tt, J = 5, 11 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –58.0 (s, 3 F); MS *m/z* (rel intensity) 292 (M^+, 15), 263 (12), 220 (19), 194 (21), 182 (18), 164 (28), 149 (100), 135 (27), 121 (30), 104 (39). Found: *m/z* 292.2007. Calcd for $C_{16}H_{27}OF_3$: M, 292.2014.

***trans*-1-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]-4-trifluoromethoxy-cyclohexane (11a).** Prepared in 34% yield as a colorless powder; phase transition temperature/°C: Cr 44 S_X 112 S_B 147 N 189 Iso (DSC on 2nd heating); R_f = 0.77 (hexane). IR (KBr) 2952, 2908, 2854, 1445, 1366, 1265, 1253, 1156, 1023, 857 cm^{-1}; ^1H NMR (200 MHz) δ = 0.77-1.58 (m, 23 H), 0.87 (t, J = 7 Hz, 3 H), 1.65-1.90 (m, 8 H), 2.05-2.18 (m, 2 H), 4.07 (tt, J = 5, 11 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –58.0 (s, 3 F); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 28.0 (s), 30.1 (s), 30.2 (s), 30.4 (s), 32.7 (s), 33.6 (s), 37.6 (s), 39.8 (s), 41.8 (s), 42.6 (s), 43.38 (s), 43.40 (s), 78.6 (q, J = 2 Hz), 121.7 (q, J = 254 Hz); MS *m/z* (rel intensity) 374 (M^+, 10), 288 (26), 245 (20), 183 (7), 123 (18), 95 (36), 83 (53), 82 (66), 81 (88), 79 (29), 69 (100), 67 (58). Found: *m/z* 374.2795. Calcd for $C_{22}H_{37}OF_3$: M, 374.2796.

***trans*-1-(4'-Propylbiphenyl-4-yl)-4-trifluoromethoxycyclohexane (12a).** Isolated in 25% yield as a colorless powder; phase transition temperature/°C: Cr 90 S_X 104 S_A 129 Iso; R_f = 0.21 (hexane). IR (KBr) 2957, 1499, 1455, 1333, 1283, 1256, 1211, 1132, 1040, 982, 860, 806, 785 cm^{-1}; ^1H NMR (200 MHz) δ = 0.97 (t, J = 7 Hz, 3 H), 1.42-1.80 (m, 6 H), 1.94-2.12 (m, 2 H), 2.18-2.32 (m, 2 H), 2.43-2.68 (m, 3 H), 4.24 (tt, J = 5, 11 Hz, 1 H), 7.22-7.25 (m, 4 H), 7.46-7.53 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 13.9 (s), 24.6 (s), 32.0 (s), 32.8 (s), 37.7 (s), 42.4 (s), 77.7 (q, J = 2 Hz), 121.7 (q, J = 255 Hz), 126.8 (s), 127.00 (s), 127.02 (s), 128.8 (s), 138.2 (s), 139.2 (s), 141.7 (s), 144.4 (s); MS *m/z* (rel intensity) 363 (M^++1, 24), 362 (M^+, 100), 333 (78), 235 (13), 194 (13), 193 (76), 178 (23), 165 (19), 69 (10). Found: *m/z* 362.1857. Calcd for $C_{22}H_{25}OF_3$: M, 362.1857.

ω-Trifluoromethoxyalkyl-LCs 10b-10f. An oven-dried Teflon®-vessel equipped with a rubber septum, a Teflon®-coated magnetic stirring bar, and an argon inlet, was flushed

with argon and charged with DBH (5.2 g, 18.0 mmol) and CH_2Cl_2 (6.0 mL). The resulting suspension was stirred for 10 min at –78 °C. To the mixture was slowly added over 5 min under vigorous stirring 70% HF/py (40 mmol of HF/mL, 9.0 mL, 0.36 mol) using a polypropylene/polyethylene syringe under an argon atmosphere. To this mixture was added dropwise a solution of **6b-6f** (6.0 mmol) in CH_2Cl_2 (6.0 mL) at –78 °C *via* a cannula by applying positive argon pressure. The resulting red-brown mixture was stirred at 0 °C for 1 h, diluted with Et_2O (20 mL) carefully (*caution! during this operation, hydrogen fluoride is often freed vigorously*), and quenched by careful addition of an ice-cold aq. $NaHSO_3/NaHCO_3/NaOH$ (pH 10) solution at 0 °C until the red-brownish color of the mixture disappeared. The pH value was readjusted to 10 by slow addition of ice-cooled 30% NaOH aq. solution at 0 °C and diluted with Et_2O (200 mL). The organic phase was separated; the aq. phase was extracted four times with Et_2O; the combined organic phase was washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Pyridine of the residue was removed by double toluene azeotrope under reduced pressure. The residue was purified by flash column chromatography (hexane) to give trifluoromethyl ethers **10b-10f**.

ω-Trifluoromethoxyalkyl-LCs 9b-9f. Fluorination of dithiocarbonate **5b-5f** (5.0 mmol) using 70% HF/py (5.0 mL, 0.20 mol) and DBH (4.3 g, 15.0 mmol) was carried out according to the procedure for **10b-10f**. Purification of the resulting crude mixture afforded a mixture of **9b-9f** and a bromination product, *trans*-1-[*trans*-4-(bromo-3,4-difluorophenyl)cyclohexyl]-4-(trifluoromethoxy-alkyl)cyclohexane. The mixture dissolved in THF (10 mL) was treated with *n*-BuLi (1.6 M in hexane, 3.8 mL, 6.0 mmol) at –78 °C for 10 min before quenching with H_2O at –78 °C and extraction with Et_2O (three times, totally 200 mL). The combined organic extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated. Purification by flash column chromatography (hexane) gave **9b-9f**. Yields and spectral properties of products are as follows.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-(trifluoromethoxymethyl)-cyclohexane (9b).** Yield 82%. A colorless powder. Mp 45.5-46.4 °C; R_f = 0.40 (hexane). IR 2924, 2855, 1609, 1518, 1451, 1277, 1213, 1140, 1038, 951, 866, 818, 772 cm-1; ^{1}H NMR (200 MHz) δ = 0.82-1.50 (m, 10 H), 1.53-2.02 (m, 9 H), 2.41 (tm, J = 12 Hz, 1 H), 3.75 (d, J = 6 Hz, 2 H), 6.86-7.10 (m, 3 H); ^{19}F NMR (282 MHz) δ = –61.2 (s, 3 F), –139.2 (ddd, J = 8, 12, 21 Hz, 1 F), –143.0 (dddd, J = 4, 8, 11, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.1 (s), 29.4 (s), 30.1 (s), 34.5 (s), 37.3 (s), 42.6 (s), 43.0 (s), 43.81 (s), 43.83 (s), 72.4 (q, J = 3 Hz), 115.4 (d, J = 17 Hz), 116.8 (d, J = 17 Hz), 121.8 (q, J = 258 Hz), 122.5 (dd, J = 3, 6 Hz), 144.8 (dd, J = 4, 5 Hz), 148.7 (dd, J = 13, 245 Hz), 150.3 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 377 (M^++1, 13), 376 (M^+, 46), 207 (12), 205

(10), 195 (14), 153 (24), 149 (20), 140 (100), 127 (90), 121 (14), 109 (19), 95 (85), 91 (22), 83 (43), 81 (68), 71 (22), 69 (71). Found: *m/z* 376.1836. Calcd for $C_{20}H_{25}F_5O$: M, 376.1826.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-(2-trifluoromethoxyethyl)-cyclohexane (9c).** Yield 88%. A colorless oil. Phase transition temperature/°C: Cr –5 N 18 Iso (DSC on 2nd heating); R_f = 0.56 (hexane). IR 2923, 2853, 1609, 1518, 1449, 1431, 1410, 1297, 1138, 1028, 939, 866, 818, 772 cm^{-1}; ^1H NMR (300 MHz) δ = 0.88-1.20 (m, 8 H), 1.25-1.45 (m, 3 H), 1.50-1.63 (m, 2 H), 1.70-1.95 (m, 8 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 4.00 (t, *J* = 6 Hz, 2 H), 6.88-7.08 (m, 3 H); ^{19}F NMR (282 MHz) δ = –61.15 (s, 3 F), –139.1 (ddd, *J* = 8, 12, 21 Hz, 1 F), –143.0 (dddd, *J* = 4, 8, 11, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.8 (s), 30.1 (s), 33.2 (s), 34.2 (s), 34.5 (s), 36.0 (s), 42.7 (s), 43.0 (s), 43.8 (s), 65.6 (s), 115.4 (d, *J* = 16 Hz), 116.8 (d, *J* = 16 Hz), 121.7 (q, *J* = 254 Hz), 122.4 (dd, *J* = 3, 3 Hz), 144.8 (m), 148.5 (dd, *J* = 13, 245 Hz), 150.2 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 392 (M^++2, 2), 391 (M^++1, 11), 390 (M^+, 42), 195 (11), 140 (100), 128 (13), 127 (98), 109 (61), 95 (23), 91 (10), 83 (23), 81 (46), 79 (18), 67 (82). Found: *m/z* 390.1984. Calcd for $C_{21}H_{27}F_5O$: M, 390.1982.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-(3-trifluoromethoxypropyl)-cyclohexane (9d).** Yield 89%. A mesomorphic oil. Phase transition temperature/°C: Cr 21 N 52 Iso (DSC on 2nd heating); R_f = 0.42 (hexane). IR 2923, 2853, 1607, 1518, 1451, 1431, 1408, 1275, 1225, 1140, 1057, 939, 864, 818, 772 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.45 (m, 13 H), 1.52-1.95 (m, 10 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 3.92 (t, *J* = 6 Hz, 2 H), 6.86-7.05 (m, 3 H); ^{19}F NMR (282 MHz) δ = –61.1 (s, 3 F), –139.1 (ddd, *J* = 8, 12, 21 Hz, 1 F), –143.0 (dddd, *J* = 4, 8, 11, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 26.2 (s), 29.9 (s), 30.2 (s), 33.0 (s), 33.4 (s), 34.6 (s), 37.5 (s), 42.7 (s), 43.2 (s), 43.9 (s), 67.9 (s), 115.3 (d, *J* = 16 Hz), 116.7 (d, *J* = 16 Hz), 121.7 (q, *J* = 254 Hz), 122.4 (dd, *J* = 3, 3 Hz), 144.8 (m), 148.5 (dd, *J* = 13, 245 Hz), 150.2 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 405 (M^++1, 4), 404 (M^+, 16), 206 (10), 196 (13), 192 (15), 177 (10), 167 (24), 161 (10), 153 (14), 149 (100), 140 (39), 133 (14), 127 (48), 123 (35), 111 (29), 109 (31), 104 (12). Found: *m/z* 404.2139. Calcd for $C_{22}H_{29}F_5O$: M, 404.2139.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-(4-trifluoromethoxybutyl)-cyclohexane (9e).** Yield 88%. A mesomorphic oil. Phase transition temperature/°C: Cr 14 S_X 17 N 55 Iso (DSC on 2nd heating); R_f = 0.40 (hexane). IR 2923, 2853, 1609, 1518, 1449, 1410, 1275, 1215, 1140, 1038, 939, 864, 816, 772 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.49 (m, 15 H), 1.60-1.95 (m, 10 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 3.94 (t, *J* = 6 Hz, 2 H), 6.86-7.02 (m, 3 H); ^{19}F NMR (282 MHz) δ = –61.1 (s, 3 F), –139.1 (ddd, *J* = 8, 12, 21 Hz, 1 F), –143.0 (dddd, *J* = 4, 8, 11, 21 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 26.2 (s), 29.0 (s), 30.0 (s), 30.2 (s), 33.5 (s), 34.6 (s), 36.8 (s), 37.7 (s), 42.8 (s), 43.3 (s),

43.9 (s), 67.5 (q, J = 3 Hz), 115.3 (d, J = 16 Hz), 116.7 (d, J = 16 Hz), 121.7 (q, J = 254 Hz), 122.4 (dd, J = 3, 3 Hz), 144.9 (dd, J = 4, 4 Hz), 148.5 (dd, J = 13, 245 Hz), 149.3 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 420 (M^++2, 2), 419 (M^++1, 14), 418 (M^+, 51), 195 (10), 167 (12), 153 (24), 140 (96), 137 (17), 127 (100), 109 (12), 97 (12), 96 (13), 95 (37), 83 (26), 81 (54), 79 (18), 69 (90), 67 (62). Found: *m/z* 418.2300. Calcd for $C_{23}H_{31}F_5O$: M, 418.2295.

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-(5-trifluoromethoxypentyl)-cyclohexane (9f).** Yield 92%. A mesomorphic oil. Phase transition temperature/°C: Cr 32 N 74 Iso (DSC on 2nd heating); R_f = 0.58 (hexane). IR 2923, 2853, 1609, 1518, 1449, 1408, 1277, 1217, 1140, 939, 864, 817, 772 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80-1.45 (m, 17 H), 1.52-1.85 (m, 10 H), 2.39 (tt, J = 3, 12 Hz, 1 H), 3.93 (t, J = 7 Hz, 2 H), 6.80-7.15 (m, 3 H); ^{19}F NMR (282 MHz) δ = –61.1 (s, 3 F), –138.9—139.1 (m, 1 F), –142.8—143.0 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 25.8 (s), 26.5 (s), 28.8 (s), 30.0 (s), 30.2 (s), 33.6 (s), 34.6 (s), 37.3 (s), 37.8 (s), 42.8 (s), 43.3 (s), 43.9 (s), 67.5 (q, J = 3 Hz), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 121.7 (q, J = 253 Hz), 122.5 (dd, J = 3, 6 Hz), 144.9 (dd, J = 5, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.2 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 434 (M^++2, 2), 433 (M^++1, 18), 432 (M^+, 66), 196 (15), 195 (11), 181 (15), 153 (23), 149 (10), 141 (17), 140 (92), 127 (100), 109 (22). Found: *m/z* 432.2460. Calcd for $C_{24}H_{33}F_5O$: M, 432.2452.

***trans*-1-(*trans*-4-Pentylcyclohexyl)-4-trifluoromethoxymethylcyclohexane (10b).** Yield 89%. A mesomorphic oil. Phase transition temperature/°C: Cr 18 S_X 26 S_B 52 Iso (DSC on 2nd heating); R_f = 0.76 (hexane). IR 2917, 2851, 1470, 1447, 1410, 1379, 1260, 1140, 1078, 1038, 1022, 963, 895, 866, 725 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.36 (m, 18 H), 0.88 (t, J = 7 Hz, 3 H), 1.54-1.86 (m, 10 H), 3.73 (d, J = 6 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.2 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.1 (s), 29.4 (s), 30.1 (s), 32.3 (s), 33.6 (s), 37.3 (s), 37.5 (s), 37.9 (s), 43.1 (s), 43.3 (s), 72.5 (q, J = 3 Hz), 121.7 (q, J = 253 Hz); MS *m/z* (rel intensity) 335 (M^++1, 1), 334 (M^+, 11), 180 (22), 153 (15), 152 (17), 111 (19), 109 (12), 97 (100), 95 (50), 83 (89), 81 (56), 69 (72). Found: *m/z* 334.2491. Calcd for $C_{19}H_{33}F_3O$: M, 334.2483.

***trans*-1-(*trans*-4-Pentylcyclohexyl)-4-(2-trifluoromethoxyethyl)cyclohexane (10c).** Yield 100%. A mesomorphic oil. Phase transition temperature/°C: Cr 4 S_B 53 Iso (DSC on 2nd heating); R_f = 0.85 (hexane : EtOAc = 5 : 1). IR 2917, 2849, 1480, 1447, 1410, 1379, 1264, 1140, 1051, 1015, 895, 879, 855, 725 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.35 (m, 20 H), 0.87 (t, J = 7 Hz, 3 H), 1.50-1.57 (m, 2 H), 1.62-1.78 (m, 8 H), 3.96 (t, J = 7 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.2 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 26.7 (s), 29.8 (s), 30.1 (s), 32.3 (s), 33.3 (s), 33.7 (s), 34.2 (s), 36.0 (s), 37.5 (s), 38.0 (s), 43.3 (s), 43.4 (s), 65.5 (q, J = 3 Hz), 121.7 (q, J = 254 Hz); MS *m/z* (rel

intensity) 348 (M^+, 8), 221 (6), 194 (20), 181 (11), 167 (26), 163 (13), 152 (14), 150 (15), 149 (100), 139 (10), 129 (15), 127 (26), 121 (12), 119 (12), 113 (22), 109 (14). Found: *m/z* 348.2628. Calcd for $C_{20}H_{35}F_3O$: M, 348.2640.

***trans*-1-(*trans*-4-Pentylcyclohexyl)-4-(3-trifluoromethoxypropyl)cyclohexane (10d).** Yield 100%. A colorless oil. Phase transition temperature/°C: Cr 30 S_B 96 Iso (DSC on 2nd heating); R_f = 0.89 (hexane). IR (KBr) 2924, 2907, 2849, 1412, 1269, 1227, 1144, 1057, 862 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.38 (m, 22 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.62-1.80 (m, 10 H), 3.92 (t, *J* = 7 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.2 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 26.3 (s), 26.8 (s), 30.0 (s), 30.1 (s), 32.3 (s), 33.1 (s), 33.5 (s), 33.7 (s), 37.5 (s), 37.6 (s), 38.0 (s), 43.4 (s), 43.5 (s), 67.8 (q, *J* = 3 Hz), 121.7 (q, *J* = 254 Hz); MS *m/z* (rel intensity) 363 (M^++1, 11), 362 (M^+, 49), 235 (9), 209 (16), 208 (89), 153 (55), 152 (100), 137 (11), 125 (15), 124 (28), 123 (81), 111 (78), 109 (62). Found: *m/z* 362.2803. Calcd for $C_{21}H_{37}F_3O$: M, 362.2796.

***trans*-1-(*trans*-4-Pentylcyclohexyl)-4-(4-trifluoromethoxybutyl)cyclohexane (10e).** Yield 94%. A mesomorphic oil. Phase transition temperature/°C: Cr 4 S_B 90 Iso (DSC on 2nd heating); R_f = 0.84 (hexane). IR 2915, 2849, 1509, 1449, 1267, 1140, 895 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.04 (m, 10 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.06-1.43 (m, 14 H), 1.62-1.78 (m, 10 H), 3.93 (t, *J* = 7 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.2 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 22.9 (s), 26.8 (s), 29.1 (s), 30.1 (s), 30.2 (s), 32.3 (s), 33.6 (s), 33.8 (s), 36.9 (s), 37.6 (s), 37.8 (s), 38.0 (s), 43.50 (s), 43.53 (s), 67.5 (q, *J* = 3 Hz), 121.7 (q, *J* = 253 Hz); MS *m/z* (rel intensity) 377 (M^++1, 2), 376 (M^+, 7), 290 (5), 222 (16), 152 (24), 149 (16), 137 (24), 123 (12), 111 (18), 109 (18), 97 (90), 96 (80), 95 (57), 83 (99), 81 (95), 69 (100). Found: *m/z* 376.2959. Calcd for $C_{22}H_{39}F_3O$: M, 376.2953.

***trans*-1-(*trans*-4-Pentylcyclohexyl)-4-(5-trifluoromethoxypentyl)cyclohexane (10f).** Yield 81%. A mesomorphic oil. Phase transition temperature/°C: Cr 22 S_B 109 Iso (DSC on 2nd heating); R_f = 0.84 (hexane). IR 2917, 2849, 1445, 1266, 1140, 669 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.04 (m, 8 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.06-1.40 (m, 16 H), 1.62-1.78 (m, 12 H), 3.93 (t, *J* = 7 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.2 (s); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 25.9 (s), 26.5 (s), 26.8 (s), 28.6 (S), 28.8 (s), 30.1 (s), 30.2 (s), 32.4 (s), 33.69 (s), 33.75 (s), 37.4 (s), 37.6 (s), 37.9 (s), 38.1 (s), 43.6 (s), 67.5 (q, *J* = 3 Hz), 121.7 (q, *J* = 253 Hz); MS *m/z* (rel intensity) 391 (M^++1, 2), 390 (M^+, 9), 236 (22), 153 (9), 152 (26), 111 (15), 97 (80), 96 (100), 83 (71), 81 (57). Found: *m/z* 390.3110. Calcd for $C_{22}H_{39}F_3O$: M, 390.3109.

***trans*-1-Trifluoromethoxymethyl-4-[*trans*-4-(3,4,5-trifluorophenyl)cyclohexyl]-cyclohexane (23).** Synthesis of this compound was performed by a procedure similar to the one for **10** in 89% yield as a colorless powder. Mp 42.6-43.6 °C; R_f = 0.43 (hexane).

IR (KBr) 2923, 2855, 1717, 1684, 1617, 1534, 1509, 1264, 1237, 1215, 1154, 1036, 959, 847 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88-1.50 (m, 10 H), 1.53-2.08 (m, 9 H), 2.38 (tm, *J* = 12 Hz, 1 H), 3.75 (t, *J* = 7 Hz, 2 H), 6.78 (dd, *J* = 7, 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = –61.2 (s, 3 F), –135.9 (dd, *J* = 9, 21 Hz, 2 F), –165.4 (tt, *J* = 6, 21 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 29.1 (s), 29.4 (s), 30.0 (s), 34.3 (s), 37.3 (s), 42.6 (s), 42.9 (s), 72.4 (q, *J* = 3 Hz), 110.5 (dd, *J* = 7, 13 Hz), 121.8 (q, *J* = 253 Hz), 137.8 (td, *J* = 15, 248 Hz), 144.0 (dt, *J* = 7, 7 Hz), 150.1 (ddd, *J* = 4, 10, 248 Hz); MS *m/z* (rel intensity) 395 (M^++1, 13), 394 (M^+, 33), 259 (11), 213 (13), 171 (22), 158 (75), 151 (12), 145 (86), 99 (11), 95 (100), 81 (61), 69 (42), 67 (77). Found: *m/z* 394.1738. Calcd for $C_{20}H_{24}F_6O$: M, 394.1731.

4-(*trans*-4-Pentylcyclohexyl)-4'-(2-trifluoromethoxyethyl)biphenyl (25). A solution of 4-(*trans*-4-propylcyclohexyl)phenylboronic acid (2.2 g, 8.9 mmol) in EtOH (15 mL) was added to a stirred mixture of 1-bromo-4-(2-trifluoromethoxyethyl)benzene[13a] (1.61 g, 6.0 mmol), [$Pd(PPh_3)_4$] (70 mmol, 0.060 mmol) in toluene (30 mL) and aq. K_2CO_3 (2.3 M, 30 mL) at room temperature under an argon atmosphere. The resulting mixture was heated under reflux for 18 h before quenching by addition of H_2O (100 mL) and toluene (100 mL). The organic phase was separated; the aq. phase was extracted with toluene three times (300 mL). The combined organic extracts were washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane) and subsequent recrystallization from EtOH (four times) to give **25** in 47% yield as a colorless mesomorphic solid. Phase transition temperature/°C: S_B 132 S_A 159 Iso (DSC 2nd heating); R_f = 0.20 (hexane). IR (KBr) 2959, 2924, 2851, 1909, 1498, 1404, 1278, 1142, 1034, 811, 527 cm^{-1}; ^1H NMR (300 MHz) δ = 0.91 (t, *J* = 7 Hz, 3 H), 0.96-1.14 (m, 2 H), 1.16-1.56 (m, 5 H), 1.82-1.96 (m, 4 H), 2.50 (tt, *J* = 3, 12 Hz), 3.01 (t, *J* = 7 Hz, 2 H), 4.16 (t, *J* = 7 Hz, 2 H), 7.25 (d, *J* = 8 Hz, 2 H), 7.26 (d, *J* = 8 Hz, 2 H), 7.49 (d, *J* = 8 Hz, 2 H), 7.52 (d, *J* = 8 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –61.1 (s); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 35.6 (s), 34.3 (s), 34.9 (s), 37.0 (s), 39.7 (s), 44.3 (s), 67.7 (q, *J* = 3 Hz), 121.6 (q, *J* = 255 Hz), 126.9 (s), 127.2 (s), 129.2 (s), 135.1 (s), 138.2 (s), 138.7 (s), 139.9 (s), 147.0 (s); MS *m/z* (rel intensity) 392 (M^++2, 5), 391 (M^++1, 21), 390 (M^+, 67), 305 (23), 292 (33), 279 (22), 219 (37), 193 (56), 191 (27), 165 (20), 149 (100), 133 (15), 123 (14), 104 (14), 96 (20), 91 (24), 77 (28). Found: *m/z* 390.2168. Calcd for $C_{24}H_{29}F_3O$: M, 390.2170.

Preparation of Methyl Ethers: General Procedure.

Method A: To a stirred solution of an alcohol **1-4** (6.6 mmol) in THF (6.0 mL), sodium hydride (NaH, 60% in oil, 0.30 g, 7.4 mmol) was slowly added potionwise at 0 °C. After the mixture was stirred for 12 h at room temperature, MeI (0.60 mL, 9.6 mmol) was added

dropwise to the reaction mixture at room temperature. The resulting mixture was stirred for 10 h at room temperature before quenching with aq. NH_4Cl. The mixture was diluted with Et_2O (50 mL); the organic phase was separated; the aq. phase was extracted with Et_2O three times (200 mL). The combined organic phase was washed with sat. aq. NaCl, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography or recrystallization (EtOH) to give methyl ether **13-16**, **23**, or **24.**
Method B: Sodium hydride in Method A was replaced by *n*-BuLi (1.6 M, 9.3 mmol).

***trans*-1-[*trans*-4-(3,4-Difluorophenyl)cyclohexyl]-4-methoxycyclohexane (13a).** Method A, 100% yield. Colorless needles, mp 68.7-69.2 °C. R_f = 0.50 (hexane : EtOAc = 5 : 1). IR (KBr) 3042, 2941, 2928, 2861, 1604, 1516, 1442, 1096, 940, 926, 777, 753 cm^{-1}; ^1H NMR (200 MHz) δ = 0.98-1.49 (m, 10 H), 1.65-1.95 (m, 6 H), 2.00-2.18 (m, 2 H), 2.34 (tt, *J* = 3, 12 Hz, 1 H), 3.05 (tt, *J* = 4, 10 Hz, 1 H), 3.33 (s, 3 H), 6.82-7.13 (m, 3 H); ^{19}F NMR (188 MHz) δ = –138.8—139.2 (m, 1 F), –142.6—143.0 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 27.9 (s), 30.1 (s), 31.9 (s), 34.3 (s), 42.1 (s), 42.3 (s), 43.6 (d, *J* = 1 Hz), 79.6 (s), 115.2 (d, *J* = 17 Hz), 116.6 (d, *J* = 17 Hz), 122.3 (dd, *J* = 3, 6 Hz), 144.6 (dd, *J* = 4, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.0 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 308 (M^+, 10), 247 (17), 193 (31), 179 (36), 153 (32), 149 (24), 136 (19), 126 (27), 95 (21), 81 (72), 71 (100). Found: C, 74.03; H, 8.57%. Calcd for $C_{19}H_{26}F_2O$: C, 73.99; H, 8.50%.

***trans*-1-Methoxy-4-(*trans*-4-propylcyclohexyl)cyclohexane (14a).** Method B, 99% yield. Colorless oil, bp 145 °C/0.34 mmHg. R_f = 0.44 (hexane : EtOAc = 10 : 1). IR 2980, 2850, 2820, 1465, 1450, 1192, 1105, 929 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.35 (m, 13 H), 0.87 (t, *J* = 7 Hz, 3 H), 1.62-1.83 (m, 6 H), 2.00-2.13 (m, 4 H), 3.04 (tt, *J* = 4, 10 Hz, 1 H), 3.33 (s, 3 H); ^{13}C NMR (50.3 MHz) δ = 14.3 (s), 20.0 (s), 28.1 (s), 30.2 (s), 32.1 (s), 33.5 (s), 37.5 (s), 39.8 (s), 42.6 (s), 42.9 (s), 55.5 (s), 79.8 (s); MS *m/z* (rel intensity) 239 (M^++1, 0.2), 238 (M^+, 0.3), 206 (48), 176 (12), 163 (20), 124 (15), 123 (24), 109 (22), 93 (10), 83 (44), 82 (55), 81 (100), 79 (30), 71 (68), 67 (67). Found: C, 80.47; H, 12.75%. Calcd for $C_{16}H_{30}O$: C, 80.61; H, 12.68%.

***trans*-1-Methoxy-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]cyclohexane (15a).** Method B, 42% yield. A colorless powder. Phase transition temperature/°C: Cr 207 S_B 211 Iso (DSC on 2nd heating); R_f = 0.53 (hexane : EtOAc = 10 : 1); IR (KBr) 2930, 2855, 1495, 1451, 1372, 1098, 1005, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.40 (m, 21 H), 0.79 (t, *J* = 7 Hz, 3 H), 1.55-1.74 (m, 8 H), 1.94-2.14 (m, 4 H), 2.92-3.03 (m, 1 H), 3.27 (s, 3 H); ^{13}C NMR (75.5 MHz) δ = 14.4 (s), 20.0 (s), 28.1 (s), 30.1 (s), 30.3 (s), 30.5 (s), 32.1 (s), 33.60 (s), 33.65 (s), 37.6 (s), 39.8 (s), 42.6 (s), 43.0 (s), 43.5 (s), 55.5 (s), 79.9 (s); MS *m/z* (rel intensity) 322 (M^++2, 4), 321 (M^++1, 22), 374 (M^+,

25), 289 (14), 288 (32), 207 (21), 205 (13), 193 (9), 165 (11), 149 (35), 127 (7), 125 (25), 124 (20), 123 (22), 109 (39), 97 (38), 83 (91), 71 (78), 69 (100), 60 (41). Found: *m/z* 320.3083. Calcd for $C_{22}H_{40}O$: M, 320.3079.

***trans*-1-Methoxy-4-(4'-propylbiphenyl-4-yl)cyclohexane (16a).** Method A, 90% yield. A colorless powder. Phase transition temperature/°C: Cr 45 S_B 88 N 128 Iso (DSC on 2nd heating); R_f = 0.44 (hexane : EtOAc = 5 : 1). IR (KBr) 2930, 2855, 1495, 1451, 1372, 1098, 1005, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.95 (t, *J* = 7 Hz, 3 H), 1.22-1.61 (m, 4 H), 1.66 (sextet, *J* = 7 Hz, 2 H), 1.97 (dm, *J* = 12 Hz, 2 H), 2.19 (dm, *J* = 11 Hz, 2 H), 2.53 (tt, *J* = 3, 12 Hz, 1 H), 2.61 (t, *J* = 7 Hz, 2 H), 3.20 (tt, *J* = 4, 11 Hz, 1 H), 3.37 (s, 3 H), 7.19-7.25 (m, 4 H), 7.46-7.51 (m, 4 H); ^{13}C NMR (75.5 MHz) δ = 13.8 (s), 24.5 (s), 32.2 (s), 32.4 (s), 37.6 (s), 43.3 (s), 55.6 (s), 79.1 (s), 126.7 (s), 126.8 (s), 127.0 (s), 128.8 (s), 138.3 (s), 138.9 (s), 141.5 (s), 145.4 (s); MS *m/z* (rel intensity) 309 (M^++1, 10), 308 (M^+, 33), 277 (24), 276 (100), 261 (21), 247 (46), 233 (10), 219 (12), 205 (21), 193 (46), 191 (17), 178 (23), 165 (21), 91 (11), 73 (14), 71 (16). Found: *m/z* 308.2139. Calcd for $C_{22}H_{28}O$: M, 308.2140.

***trans*-1-[*trans*-(3,4-Difluorophenyl)cyclohexyl]-4-(methoxymethyl)cyclohexane (13b).** Yield 96% (Method A). A colorless powder. Phase transition temperature/°C: Cr 59 S_B 112 Iso (DSC on 2nd heating); R_f = 0.41 (hexane : EtOAc = 10 : 1). IR (KBr) 2920, 2851, 1869, 1605, 1516, 1458, 1298, 1211, 1107, 828 cm^{-1}; ^1H NMR (300 MHz) δ = 0.85-1.20 (m, 8 H), 1.24-1.44 (m, 2 H), 1.45-1.60 (m, 1 H), 1.72-1.96 (m, 8 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 3.18 (d, *J* = 6 Hz, 2 H), 3.32 (s, 3 H), 6.86-7.08 (m, 3 H); ^{19}F NMR (282 MHz) δ = −139.0—139.3 (m, 1 F), −142.9—143.2 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.5 (s), 30.1 (s), 30.2 (s), 34.5 (s), 38.2 (s), 42.7 (s), 43.2 (s), 43.8 (s), 58.8 (s), 78.8 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.8 (dd, *J* = 5, 5 Hz), 148.4 (dd, *J* = 13, 245 Hz), 150.1 (dd, *J* = 12, 247 Hz); MS *m/z* (rel intensity) 323 (M^++1, 1), 322 (M^+, 8), 290 (10), 261 (21), 179 (17), 153 (11), 140 (26), 127 (58), 121 (14), 95 (100), 81 (33), 67 (41). Found: *m/z* 322.2092. Calcd for $C_{20}H_{28}F_2O$: M, 322.2108.

***trans*-1-[*trans*-(3,4-Difluorophenyl)cyclohexyl]-4-(2-methoxyethyl)cyclohexane (13c).** Yield 98% (Method A). A colorless powder. Phase transition temperature/°C: Cr 48 N 80 Iso; R_f = 0.38 (hexane : EtOAc = 10 : 1). IR (KBr) 2920, 2845, 1717, 1684, 1609, 1522, 1429, 1389, 1289, 1271, 1208, 1125, 1105, 1162, 936, 868, 822, 772 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.20 (m, 8 H), 1.24-1.46 (m, 5 H), 1.64-1.94 (m, 8 H), 2.40 (tt, *J* = 3, 12 Hz, 1 H), 3.32 (s, 3 H), 3.40 (t, *J* = 7 Hz, 2 H), 6.86-7.07 (m, 3 H); ^{19}F NMR (282 MHz) δ = −139.0—139.3 (m, 1 F), −142.9—143.2 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.9 (s), 30.1 (s), 33.5 (s), 34.5 (s), 34.7 (s), 37.0 (s), 42.7 (s), 43.1 (s), 43.8 (s), 58.5 (s), 70.8 (s), 115.3 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 144.8

(dd, J = 5, 5 Hz), 148.4 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 336 (M^+, 9), 304 (14), 244 (11), 238 (18), 233 (20), 207 (18), 194 (23), 180 (20), 152 (22), 149 (100), 140 (29), 127 (32), 122 (20), 109 (38), 105 (38). Found: *m/z* 336.2273. Calcd for $C_{21}H_{30}F_2O$: M, 336.2265.

***trans*-1-[*trans*-(3,4-Difluorophenyl)cyclohexyl]-4-(3-methoxypropyl)cyclohexane (13d).** Yield 89% (Method A). A colorless oil. Phase transition temperature/°C: Cr 45 N 131 Iso; R_f = 0.43 (hexane : EtOAc = 10 : 1). IR (KBr) 2924, 2851, 1520, 1509, 1456, 1115, 939, 823 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80-1.22 (m, 11 H), 1.24-1.46 (m, 2 H), 1.52-1.64 (m, 2 H), 1.66-1.94 (m, 8 H), 2.40 (tt, J = 3, 12 Hz, 1 H), 3.33 (s, 3 H), 3.37 (t, J = 7 Hz, 2 H), 6.86-7.08 (m, 3 H); ^{19}F NMR (282 MHz) δ = –139.1—139.3 (m, 1 F), –142.9—143.1 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 27.1 (s), 30.0 (s), 30.2 (s), 33.5 (s), 33.7 (s), 34.6 (s), 37.8 (s), 42.8 (s), 43.2 (s), 43.8 (s), 58.5 (s), 73.3 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.8 (dd, J = 5, 5 Hz), 148.4 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 351 (M^++1, 3), 350 (M^+, 9), 318 (21), 193 (14), 179 (26), 140 (36), 127 (56), 123 (24), 121 (15), 95 (34), 81 (100), 79 (20), 67 (77). Found: *m/z* 350.2420. Calcd for $C_{22}H_{32}F_2O$: M, 350.2421.

***trans*-1-[*trans*-(3,4-Difluorophenyl)cyclohexyl]-4-(4-methoxybutyl)cyclohexane (13e).** Yield 97% (Method A). A colorless powder. Phase transition temperature/°C: Cr 57 N 102 Iso; R_f = 0.55 (hexane : EtOAc = 5 : 1). IR (KBr) 2930, 2847, 1607, 1522, 1509, 1458, 1289, 1210, 1192, 1117, 870, 820, 772 cm^{-1}; ^1H NMR (300 MHz) δ = 0.78-1.44 (m, 15 H), 1.48-1.60 (m, 2 H), 1.65-1.93 (m, 8 H), 2.39 (tt, J = 3, 12 Hz, 1 H), 3.32 (s, 3 H), 3.35 (t, J = 6 Hz, 2 H), 6.82-7.06 (m, 3 H); ^{19}F NMR (282 MHz) δ = –138.9--139.1 (m, 1 F), –142.8—143.0 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 23.5 (s), 30.0 (s), 30.1 (s), 33.5 (s), 34.5 (s), 37.3 (s), 37.8 (s), 42.7 (s), 43.2 (s), 43.8 (s), 58.4 (s), 72.9 (s), 115.2 (d, J = 17 Hz), 116.6 (d, J = 17 Hz), 122.3 (dd, J = 3, 6 Hz), 144.7 (dd, J = 4, 4 Hz), 148.4 (dd, J = 13, 245 Hz), 150.0 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 365 (M^++1, 2), 364 (M^+, 6), 332 (28), 194 (11), 193 (17), 179 (32), 153 (12), 140 (36), 137 (23), 135 (16), 127 (75), 123 (18), 121 (13), 109 (20), 97 (11), 95 (52), 93 (13), 81 (100), 67 (82). Found: *m/z* 364.2585. Calcd for $C_{23}H_{34}F_2O$: M, 364.2578.

***trans*-1-[*trans*-(3,4-Difluorophenyl)cyclohexyl]-4-(5-methoxypentyl)cyclohexane (13f).** Yield 93% (Method A). A colorless powder. Phase transition temperature/°C: Cr 60 N 122 Iso; R_f = 0.73 (hexane : EtOAc = 5 : 1). IR (KBr) 2919, 2851, 1522, 1509, 1489, 1289, 1213, 1117, 945, 837 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.45 (m, 17 H), 1.50-1.62 (m, 2 H), 1.65-1.93 (m, 8 H), 2.39 (tt, J = 3, 12 Hz, 1 H), 3.32 (s, 3 H), 3.36 (t, J = 7 Hz, 2 H), 6.85-7.07 (m, 3 H); ^{19}F NMR (282 MHz) δ = –138.9—139.1 (m, 1 F), –142.8—143.0 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 26.5 (s), 26.8 (s), 29.7 (s), 30.0 (s), 30.1 (s), 33.5 (s), 34.5 (s), 37.4 (s), 37.8 (s), 42.7 (s), 43.3 (s), 43.8 (s), 58.4 (s), 72.9 (s),

115.3 (d, J = 17 Hz), 116.6 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 144.8 (dd, J = 5, 5 Hz), 148.4 (dd, J = 13, 245 Hz), 150.1 (dd, J = 13, 247 Hz); MS *m/z* (rel intensity) 379 (M^++1, 3), 378 (M^+, 10), 346 (28), 194 (11), 193 (15), 179 (24), 153 (15), 140 (51), 127 (84), 121 (11), 109 (39), 95 (98), 81 (89), 67 (100). Found: *m/z* 378.2741. Calcd for $C_{24}H_{36}F_2O$: M, 378.2734.

***trans*-1-(Methoxymethyl)-4-(*trans*-4-pentylcyclohexyl)cyclohexane (14b).** Yield 100% (Method B). A mesomorphic oil. Phase transition temperature/°C: Cr 20 S_B 73 Iso (DSC on 2nd heating); R_f = 0.62 (hexane : EtOAc = 10 : 1). IR 2917, 2849, 2737, 2681, 1447, 1379, 1369, 1219, 1140,1103, 955, 895, 725 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.36 (m, 19 H), 0.88 (t, J = 7 Hz, 3 H), 1.42-1.58 (m, 1 H), 1.64-1.84 (m, 8 H), 3.16 (d, J = 6 Hz, 2 H), 3.31 (s, 3 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.5 (s), 30.1 (s), 30.3 (s), 32.2 (s), 33.6 (s), 37.5 (s), 37.9 (s), 38.3 (s), 43.4 (s), 43.5 (s), 58.8 (s), 78.9 (s); MS *m/z* (rel intensity) 280 (M^+, 0.5), 248 (28), 219 (18), 123 (10), 19 (11), 97 (30), 96 (27), 95 (100), 83 (34), 82 (17), 81 (49). Found: *m/z* 280.2776. Calcd for $C_{19}H_{36}O$: M, 280.2766.

***trans*-1-(2-Methoxyethyl)-4-(*trans*-4-pentylcyclohexyl)cyclohexane (14c).** Yield 95% (Method B). A mesomorphic oil; Phase transition temperature/°C: Cr –12 S_B 72 Iso (DSC on 2nd heating); R_f = 0.48 (hexane : EtOAc = 10 : 1). IR 2925, 2734, 2681, 1482, 1447, 1387, 1379, 1291, 1273, 1219, 1192, 1117, 992, 970, 895, 725 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.08 (m, 12 H), 1.10-1.38 (m, 10 H), 1.45 (q, J = 7 Hz, 2 H), 1.60-1.82 (m, 9 H), 3.32 (s, 3 H), 3.40 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.9 (s), 30.1 (s), 32.2 (s), 33.60 (s), 33.64 (s), 34.8 (s), 37.1 (s), 37.5 (s), 37.9 (s), 43.3 (s), 43.4 (s), 58.5 (s), 70.9 (s); MS *m/z* (rel intensity) 294 (M^+, 0.3), 262 (38), 233 (5), 151 (13), 111 (18), 110 (26), 109 (77), 108 (19), 97 (36), 83 (36), 81 (40), 69 (43), 67 (100). Found: *m/z* 294.2930. Calcd for $C_{20}H_{38}O$: M, 294.2923.

***trans*-1-(3-Methoxypropyl)-4-(*trans*-4-pentylcyclohexyl)cyclohexane (14d).** Yield 89% (Method B). A colorless oil. Phase transition temperature/°C: Cr 30 S_B 96 Iso (DSC on 2nd heating); R_f = 0.61 (hexane : EtOAc = 5 : 1). IR 2923, 2851, 1717, 1559, 1509, 1458, 1397, 1341, 1123 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.36 (m, 22 H), 0.87 (t, J = 7 Hz, 3 H), 1.52-1.62 (m, 2 H), 1.64-1.80 (m, 8 H), 3.33 (s, 3 H), 3.34 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 27.1 (s), 30.0 (s), 30.1 (s), 32.2 (s), 33.6 (s), 33.7 (s), 33.8 (s), 37.5 (s), 37.8 (s), 37.9 (s), 43.4 (s), 43.5 (s), 58.5 (s), 73.3 (s); MS *m/z* (rel intensity) 308 (M^+, 1), 277 (6), 276 (28), 248 (16), 152 (15), 149 (14), 137 (12), 123 (30), 122 (28), 110 (13), 109 (19), 97 (49), 95 (42), 83 (41), 82 (38), 81 (100), 71 (31), 67 (90). Found: *m/z* 308.3078. Calcd for $C_{21}H_{40}O$: M, 308.3079.

***trans*-1-(4-Methoxybutyl)-4-(*trans*-4-pentylcyclohexyl)cyclohexane (14e).** Yield 82% (Method B). A mesomorphic oil. Phase transition temperature/°C: Cr 7 S_X 9 S_B

97 Iso (DSC on 2nd heating); R_f = 0.61 (hexane : EtOAc = 5 : 1). IR 2925, 2734, 1732, 1480, 1447, 1387, 1379, 1219, 1119, 959, 895, 725 cm^{-1}; ^1H NMR (200 MHz) δ = 0.77-1.40 (m, 24 H), 0.89 (t, J = 7 Hz, 3 H), 1.48-1.59 (m, 2 H), 1.64-1.78 (m, 8 H), 3.33 (s, 3 H), 3.34 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 23.5 (s), 26.7 (s), 29.9 (s), 30.1 (s), 32.2 (s), 33.6 (s), 33.7 (s), 37.3 (s), 37.5 (s), 37.88 (s), 37.93 (s), 43.5 (s), 58.5 (s), 73.0 (s); MS *m/z* (rel intensity) 322 (M^+, 0.8), 290 (34), 178 (10), 137 (24), 136 (15), 123 (17), 121 (14), 111 (20), 109 (19), 97 (55), 96 (42), 95 (80), 83 (64), 81 (100), 69 (68). Found: *m/z* 322.3231. Calcd for $C_{22}H_{42}O$: M, 322.3236.

***trans*-1-(5-Methoxypentyl)-4-(*trans*-4-pentylcyclohexyl)cyclohexane (14f).** Yield 71% (Method B). A mesomorphic oil. Phase transition temperature/°C: Cr 60 S_B 114 Iso (DSC on 2nd heating); R_f = 0.56 (hexane : EtOAc = 10 : 1). IR (KBr) 2925, 2735, 1464, 1447, 1393, 1379, 1217, 1192, 1123, 961, 949, 895, 727 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.45 (m, 29 H), 1.55-1.80 (m, 10 H), 3.32 (s, 3 H), 3.35 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.5 (s), 26.7 (s), 26.9 (s), 29.7 (s), 30.07 (s), 30.09 (s), 32.3 (s), 33.6 (s), 33.7 (s), 37.4 (s), 37.5 (s), 37.8 (s), 37.9 (s), 43.5 (s), 58.5 (s), 72.9 (s); MS *m/z* (rel intensity) 337 (M^+, 0.2), 305 (22), 304 (97), 234 (22), 233 (22), 194 (19), 178 (11), 151 (78), 150 (68), 137 (39), 123 (27), 121 (26), 109 (100), 108 (26). Found: *m/z* 336.3398. Calcd for $C_{23}H_{44}O$: M, 336.3392.

***trans*-4-[*trans*-4-(3,4,5-trifluorophenyl)cyclohexyl]cyclohexanemethanol (24).** This compound was prepared by Method A from *trans*-4-[*trans*-4-(3,4,5-trifluorophenyl)cyclohexyl]cyclohexylmethanol in 93% yield as colorless needles. Phase transition temperature/°C: Cr 74 N 79 Iso (DSC on 2nd heating); R_f = 0.15 (hexane). IR (KBr) 2917, 2851, 1617, 1534, 1509, 1456, 1445, 1348, 1235, 1105, 1038, 850 cm^{-1}; ^1H NMR (300 MHz) δ = 0.86-1.68 (m, 11 H), 1.72-1.96 (m, 8 H), 2.38 (tt, J = 3, 12 Hz, 1 H), 3.18 (d, J = 6 Hz, 2 H), 3.30 (s, 3 H), 6.78 (dd, J = 7, 9 Hz, 2 H); ^{19}F NMR (282 MHz) δ = –136.0 (dd, J = 9, 20 Hz, 2 F), –165.4 (dd, J = 7, 20 Hz, 1 F); ^{13}C NMR (50.3 MHz) δ = 29.5 (s), 30.0 (s), 30.2 (s), 34.3 (s), 38.2 (s), 42.6 (s), 43.2 (s), 43.9 (s), 58.8 (s), 72.4 (q, J = 3 Hz), 110.5 (dd, J = 7, 13 Hz), 137.7 (td, J = 16, 248 Hz), 144.0 (dt, J = 7, 7 Hz), 150.9 (ddd, J = 4, 10, 248 Hz); MS *m/z* (rel intensity) 341 (M^++1, 1), 340 (M^+, 6), 308 (30), 280 (13), 279 (45), 151 (14), 149 (12), 145 (56), 137 (31), 135 (24), 125 (13), 123 (13), 197 (31), 158 (21), 121 (23), 109 (25), 83 (67), 81 (100), 67 (94). Found: *m/z* 340.2007. Calcd for $C_{20}H_{27}F_3O$: M, 340.2014.

3β-Methoxycholestane (28). Yield 75% (Method A). A colorless solid, mp 86.0-87.3 °C. R_f = 0.43 (hexane : EtOAc = 5 : 1). IR (KBr) 2930, 2850, 1472, 1374, 1173, 1106, 944, 929, 770 cm^{-1}; ^1H NMR (300 MHz) δ = 0.62-1.99 (m, 46 H), 3.07-3.17 (m, 1 H), 3.34 (s, 3 H); ^{13}C NMR (75.5 MHz) δ = 12.1 (s), 12.2 (s), 18.7 (s), 21.2 (s), 22.5 (s), 22.8 (s), 23.9 (s), 24.2 (s), 27.9 (s), 28.0 (s), 28.3 (s), 28.9 (s), 32.1 (s), 34.4 (s),

35.5 (s), 35.8 (s), 36.2 (s), 37.0 (s), 39.5 (s), 40.1 (s), 42.6 (s), 44.8 (s), 54.4 (s), 55.4 (s), 55.5 (s), 56.3 (s), 56.5 (s), 79.9 (s); MS *m/z* (rel intensity) 404 (M^++2, 2), 403 (M^++1, 10), 402 (M^+, 35), 387 (16), 355 (16), 262 (19), 248 (53), 216 (41), 215 (100), 201 (14), 179 (31), 161 (16), 149 (23), 147 (32), 138 (17), 135 (27), 121 (46), 107 (70). Found: C, 83.24; H, 12.58%. Calcd for $C_{28}H_{50}O$: C, 83.51; H, 12.51%.

VI-5. References and Notes

1) a) T. Hiyama, *"Organofluorine Compounds, Chemistry and Applications,"* Springer, Berlin (2000); b) H. Nohira, *Nippon Kagaku Kaishi*, **1994**, 467; c) M. Hudlicky and A. E. Pavlath, Eds., *"Chemistry of Organic Fluorine Compounds II. A Critical Review,"* ACS Monograph 187, Washington, DC (1995); d) R. E. Banks, Ed., *"Preparation, Properties, and Industrial Applications of Organofluorine Compounds,"* Ellis Horwood, New York (1982).

2) a) H. Takatsu, K. Takeuchi, and H. Sato, *Mol. Cryst. Liq. Cryst.*, **112**, 165 (1984); b) M. Hird, G. W. Gray, and K. J. Toyne, *Liq. Cryst.*, **11**, 531 (1992); c) G. W. Gray, M. Hird, and K. J. Toyne, *Mol. Cryst. Liq. Cryst.*, **204**, 43 (1991); d) P. Balkwill, D. Bishop, A. Pearson, and I. Sage, *Mol. Cryst. Liq. Cryst.*, **123**, 1 (1985).

3) a) T. Inukai, K. Miyazawa, *Ekisho,* **1**, 9 (1997); b) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.*, **209**, 1 (1991); c) M. Schadt, R. Buchecker, and A. Villiger, *Liq. Cryst.*, **7**, 519 (1990); d) F. Moia and M. Schadt, *Proceedings of the SID,* **32**, 361 (1991).

4) a) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **72**, 2523 (1999); b) M. Kuroboshi, K. Mizuno, K. Kanie, and T. Hiyama, *Tetrahedron Lett.*, **36**, 563 (1995); c) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683; d) K. Kanie, Y. Tanaka, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1998**, 1169; e) K. Kanie, Y. Tanaka, S. Takehara, and T. Hiyama, *Bull. Chem. Soc. Jpn., in press*; f) F. Guittard, E. Taffin de Givenchy, S. Geribaldi, and A. Cambon, *J. Fluorine Chem.*, **100**, 85 (1999); g) P. Kirsch and K. Tarumi, *Angew. Chem. Int. Ed.*, **37**, 484 (1998); h) P. Kirsch, M. Bremer, M. Heckmeier, and K. Tarumi, *Angew. Chem. Int. Ed.*, **38**, 1989 (1999); i) P. Kirsch, V. Reiffenrath, and M. Bremer, *Synlett,*

1999, 389; j) P. J. Collings and M. Hird, "*Introduction to Liquid Crystals, Chemistry and Physics*," Taylor & Francis, London (1997); k) K. Kitazima, O. Yokokohji, T. Tachibana, and S. Inoue, *The 23rd Symposium on Liquid Crystals*, 2PA12, Tokyo, 1997; l) F. Roussel, J.-P. Bayle, M. A. Khan, B. M. Fung, O. Yokokohji, T. Shimizu, H. Koh, and Kumai, *Liq. Cryst.*, **26**, 251 (1999).

5) a) G. W. Gray, M. Hird, and K. J. Toyne, *Mol. Cryst. Liq. Cryst.*, **204**, 91 (1991).

6) a) K. Kanie, M. Kuroboshi, S. Takehara, and T. Hiyama, *J. Fluorine Chem.*, **97**, 75 (1999); b) V. Reiffenrath, U. Finkenzeller, E. Poetsch, B. Rieger, and D. Coates, *Proc. of SPIE Conference*, **1990**, p. 84; c) A. Beyer, B. Schuler, and K. Tarumi, *Freiburger Arbeitstagung Flüssigkristalle*, **1993**, p. 13.

7) a) A. E. Feiring, *J. Org. Chem.*, **44**, 2907 (1979); b) A. G. Fab. Hoechst, *Brevet Brit.*, **1957**, 765527 (*Chem. Abstr.*, **51**, 14803f (1957)).

8) N. N. Iarovenko and A. S. Vasileva, *J. Gen. Chem. USSR*, **28**, 2539 (1958).

9) W. A. Sheppard, *J. Org. Chem.*, **29**, 1 (1964).

10) F. Mathey and J. Bensoam, *Tetrahedron Lett.*, **25**, 2253 (1973).

11) I. Ben-David, D. Rechavi, E. Mishani, and S. Rozen, *J. Fluorine Chem.*, **97**, 75 (1999).

12) a) M. Kuroboshi and T. Hiyama, *Yuki Gosei Kagaku Kyokai Shi*, **51**, 1124 (1993); b) M. Kuroboshi and T. Hiyama, *Synlett*, **1991**, 909; c) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1939 (1998); d) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 2687 (1998); e) M. Kuroboshi and T. Hiyama, *Synlett*, **1994**, 251; f) M. Kuroboshi and T. Hiyama, *Tetrahedron Lett.*, **35**, 3983 (1994); g) M. Kuroboshi and T. Hiyama, *J. Fluorine Chem.*, **69**, 127 (1994); h) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1995**, 683; i) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **72**, 805 (1999); j) K. Kanie, K. Mizuno, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1973 (1998).

13) a) Kanie, Y. Tanaka, K. Suzuki, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **73**, 471 (2000); b) M. Kuroboshi, K. Suzuki, and T. Hiyama, *Tetrahedron Lett.*, **33**, 4173 (1992); c) K. Kanie, Y. Tanaka, M. Shimizu, M. Kuroboshi, and T. Hiyama, *Chem. Commun.*, **1997**, 309.

14) a) S. Rozen, *Chem. Rev.*, **96**, 1717 (1996); b) K. K. Johri and D. D. DesMarteau, *J. Org. Chem.*, **48**, 242 (1983); c) J. B. Levy and D. M. Sterling, *J. Org. Chem.*, **50**, 5615 (1985); d) T. B. Patrick, G. L. Cantrell, and S. M. Inga, *J. Org. Chem.*, **45**, 1409 (1980); e) D. H. R. Barton, L. J. Danks, A. K. Ganguly, R. H. Hesse, G. Tarzia, and M. M. Pechet, *Chem. Commun.*, **1969**, 227; f) J. Adamson, A. B. Foster, L. D. Hall, and R. H. Hesse, *Chem. Commun.*, **1969**, 309; g) K. Adachi,

S. Ishihara, and T. Umemoto, *Abstract of the 15th International Symposium on Fluorine Chemistry, Vancouver*, Canada, Aug. 2-7, 1997; h) W. A. Sheppard, *J. Org. Chem.*, **29**, 11 (1964).

15) G. A. Boswell, Jr., W. C. Ripka, R. M. Scribner, and C. W. Tullock, *Org. React.*, **21**, 1 (1974).

16) K. Kanie, Y. Tanaka, M. Shimizu, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1997**, 827.

17) a) V. F. Petrov, S. I. Torgova, L. A. Karamysheva, and S. Takenaka, *Liq. Cryst.*, **26**, 1141 (1999); b) R. Eidenschink, *Mol. Crsst. Liq. Cryst.*, **94**, 119 (1983); c) R. Eidenschink, *Mol. Crsst. Liq. Cryst.*, **123**, 57 (1985).

18) H. Takatsu, K. Takeuchi, M. Saasaki, H. Ohnishi, and M. Schadt, *Mol. Cryst. Liq. Cryst.*, **206**, 159 (1991).

19) G. A. Olah, J. T. Welch, Y. D. Vankar, M. Nojima, I. Kerekes, and J. A. Olah, *J. Org. Chem.*, **44**, 3872 (1979).

20) C. H. Gooch and H. A. Tarry, *Appl. Phys.*, **8**, 1575 (1975).

Chapter VII

A Facile Transformation of Terminal Olefins to *vic*-Difluoro Olefins: Electro-optical Properties of Liquid Crystalline Materials Having a *vic*-Difluoro Olefinic Moiety

Abstract: A facile synthetic method of *vic*-difluoro olefins from the corresponding olefins is established and applied to the synthesis of LCs having a terminal *vic*-difluoro olefinic moiety. The physical and electro-optical properties of these LCs are compared with those of the corresponding parent olefinic LCs.

VII-1. Introduction

Because fluorine-containing LCs show properties[1,2] appropriate to the materials for the current LC display,[3] design and synthesis of novel LC materials having a fluorine substituent is an urgent synthetic problem in organofluorine chemistry and material science.[4] For the development of fluorinated functional materials, fluorine effect needs to be well understood in comparison with non-fluorinated materials. To evaluate the fluorine effect precisely, properties of fluorinated materials should be compared with those of parent non-fluorinated ones. Accordingly, a method for the introduction of fluorine(s) into non-fluorinated materials is highly desirable.

Because LCs containing an ω-alkenyl side chain induce lower viscosity and V_{th} and higher voltage holding ratio than those with an alkyl side chain, the olefinic LCs are being utilized for the materials for current LC displays.[5] On the other hand, LCs having a *vic*-difluoro olefinic functionality in a mesogenic core were demonstrated to exhibit low viscosity and high polarity.[6] With these precedents, the Author envisaged that LCs having an ω-*vic*-difluoroalkenyl group would exhibit favorable properties and thus studied novel strategies for the fluorination of terminal olefins.[7,8]

Synthetic methods of *vic*-difluoro olefins are briefly classified into two categories, depending on the timing of fluorine introduction. The one involves C-C bond formation, using readily available partially fluorinated small molecules called fluorinated building block approach; the other consists of C–F bond formation with an electrophilic or nucleophilic fluorination reagent. Construction of *vic*-difluoro olefinic functionality using a fluorinated building block has been attained by: i) alkylation or arylation of (trifluorovinyl)silanes,[9] ii) palladium catalyzed cross-coupling reaction of 1,2-difluoroalkenyl(or alkenyl)zinc reagent with alkenyl(or 1,2-difluoroalkenyl)iodide,[10] iii) reaction of 1,2-difluoroalkenyllithium with carbonyl compounds or epoxides,[11] or iv) reaction of enolates with 1,2-difluoroacetylene generated from 1,1,2-trifluoroethylene and *t*-BuLi.[12] To control the configuration of the *vic*-difluoro olefins, *cis*- and *trans*-1,2-difluoro olefinic precursors must be stereoselectively prepared.[13,14] Fluorination methods for *vic*-difluoro olefins[15] involve i) fluorination of β-keto esters with diethylaminosulfur trifluoride (DAST) to give 2,3-difluoro-2-alkenoate[16] or ii) dehydrofluorination of 1,2,2-trifluoroalkanes.[17] Furthermore, simultaneous use of the fluorinated building block method and the fluorination method leads to stereoselective preparation of *cis*- and *trans*-*vic*-difluoro olefins.[18] From the synthetic viewpoint of future functional materials, however, it is favorable to transform an olefinic moiety of prevailing materials to the corresponding *vic*-difluoro olefinic ones with other functional

groups being intact.

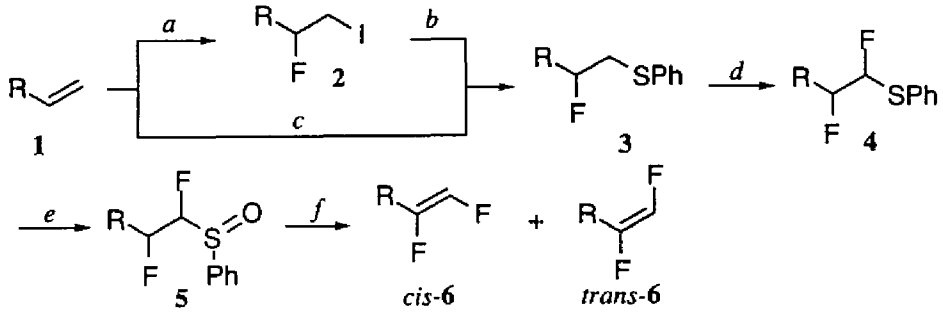
Herein described is a facile method for the synthesis of LC materials having a *vic*-difluoro terminal olefinic moiety from the corresponding parent olefins.[7] Also disclosed are the phase transition behaviors and electro-optical properties of the difluoro olefinic LCs.

VII-2. Results and Discussion

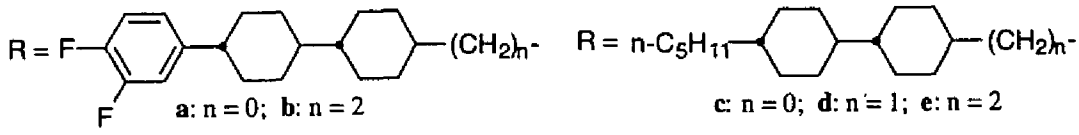
VII-2-1. Transformation of Terminal Olefins to *vic*-Difluoro Olefins

In order to achieve the transformation of terminal olefins **1** to the corresponding *vic*-difluoro olefins **6**, following sequence of reactions were performed: i) thio-fluorination of **1** to give β-fluoroalkyl phenyl sulfides **3**,[19] ii) fluoro-Pummerer rearrangement of **3** to give α,β-difluoroalkyl phenyl sulfides **4**,[20] iii) oxidation of **4** to sulfoxides **5**, and iv) thermolysis of **5**.[15,21,22] The route is shown in Scheme 1.

Scheme 1. Synthesis of *vic*-difluoro olefins **6**



a: $TBAH_2F_3$ (3 mol), NIS (1 mol), CH_2Cl_2, rt. *b:* PhSH (1.2 mol), NaH (1.1 mol), THF, 0 °C to rt. *c:* 70% HF/py (10 mol), *N*-PhS-phthalimide (1 mol), CH_2Cl_2, rt. *d:* $TBAH_2F_3$ (3 mol), DBH (1 mol), CH_2Cl_2, rt, 30 min. *e:* *m*CPBA (1.1 mol), CH_2Cl_2, -30 °C, 3 h. *f:* *o*-xylene, 170 °C



The Author chose LCs having an ω-alkenyl side chain for substrates that were used for current LC displays. Initially, parent olefins **1** were converted into **3** by thio-fluorination[19] or alternatively by iodo-fluorination using $TBAH_2F_3$ and NIS[23] followed by substitution of resulting iodo-fluorination products **2** with a phenythio nucleophile. Although the thio-fluorination reaction was straightforward, this was not applicable to vinylcyclohexanes **1a** and **1c**. Thus, an the alternative route was applied to these olefins. The fluoro-Pummerer rearrangement of **3** using $TBAH_2F_3$ and DBH[20a] gave **4** in high yields as 1 : 1 diastereomeric mixtures. The product ratios were assayed by ^{19}F NMR. As unstable in neat liquid, these **4** were immediately oxidized without isolation to give sulfoxides **5** by treatment with *m*CPBA. Finally, thermolysis of **5** at 170 °C in *o*-xylene (sealed tube) afforded a mixture of *cis*- and *trans*-difluoro olefins **6**. Each isomer was readily separated by flash column chromatography on silica gel. Isolation yields of intermediates **2**, **3**, **5**, and final products **6**, combined yields of **6**, and total yields of **6** from **1** are summarized in Table 1.

Table 1. Yields of **2**, **3**, **5**, and **6** in Scheme 1.

Compound	n	Isolated yield/%						
		2	**3**	**5**[a)]	*cis*-**6**	*trans*-**6**	*cis*-**6** + *trans*-**6**	total yields of **6**[b)]
1a	0	82 (**2a**)	91 (**3a**)	95 (**5a**)	46 (*cis*-**6a**)	16 (*trans*-**6a**)	62	44
1b	2		77 (**3b**)	94 (**5b**)	33 (*cis*-**6b**)	22 (*trans*-**6b**)	55	40
1c	0	68 (**2c**)	95 (**3c**)	88 (**5c**)	55 (*cis*-**6c**)	18 (*trans*-**6c**)	73	41
1d	1		81 (**3d**)	93 (**5d**)	45 (*cis*-**6d**)	29 (*trans*-**6d**)	74	56
1e	2		78 (**3e**)	87 (**5e**)	39 (*cis*-**6e**)	25 (*trans*-**6e**)	64	43

a) Yields for 2 steps from **3** are shown. b) Total yield from **1**.

II-2-2. Isomerization of *vic*-Difluoro Olefins

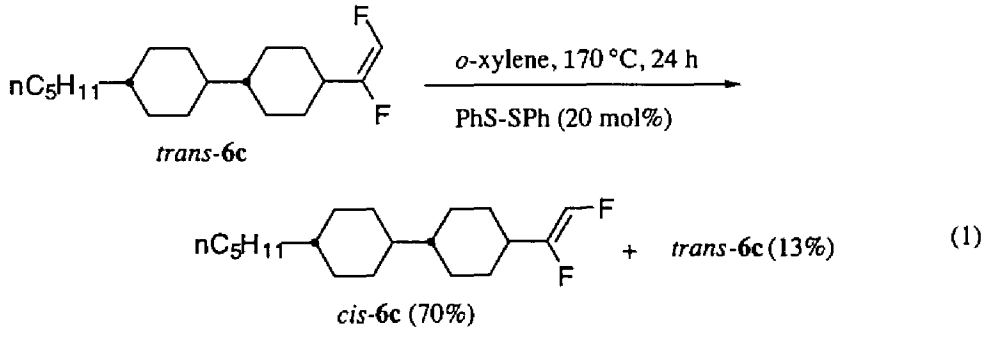
In general, thermal elimination of phenyl sulfoxides proceeds in a *syn*-stereochemical course. Therefore, the ratio of *cis*-**6** and *trans*-**6** should reflect the diastereomeric ratio of fluoro-Pummerer products **4**.[24] However, *cis*-**6** was favored over *trans*-**6** as compared with the diastereomeric ratios in **4**. Details are summarized in Table 2.

Table 2. Diastereoselectivity of fluoro-Pummerer reaction of **3**.

compound	diastereomeric ratio of **4**[a)]	*cis*-**6** : *trans*-**6**[b)]
4a	1.3 : 1	2.9 : 1
4b	1.4 : 1	1.5 : 1
4c	1.2 : 1	3.1 : 1
4d	1.0 : 1	1.6 : 1
4e	1.3 : 1	1.6 : 1

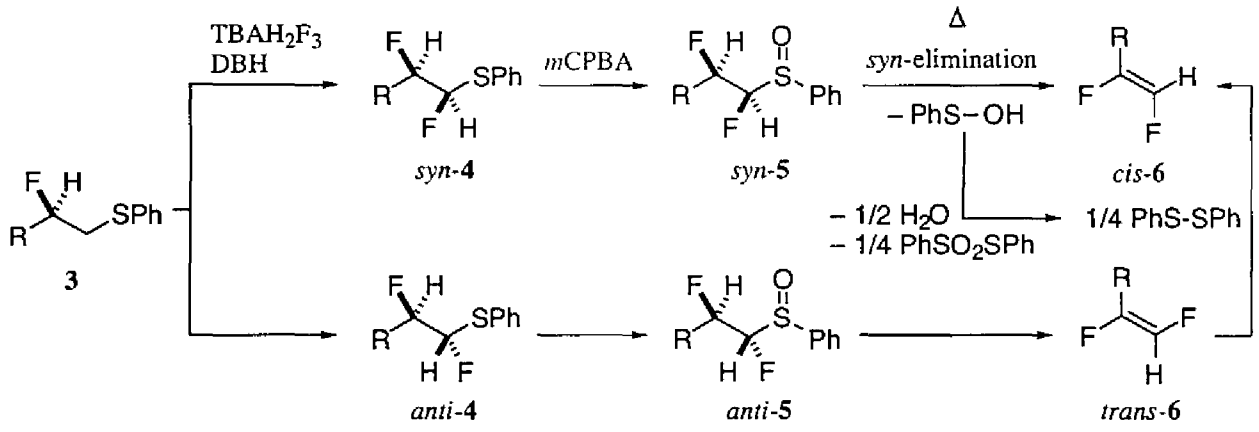
a) According to eq. 1. Determined by integration ratios of ^{19}F NMR.
b) Ratios of isolated yields of *cis*-**6** and *trans*-**6** according to Table 1.

Under the thermolytic conditions of **5** to give **6**, phenyl sulfenic acid is eliminated which is readily converted into diphenyl disulfide by dehydration and disproportionation.[25] Actually, the formation of diphenyl disulfide was detected by GC and TLC analyses. This suggests that the isomerization of the *trans*-1,2-difluoro olefins to the corresponding *cis*-isomers may be assisted by diphenyl disulfide, because *trans*-1,2-difluoro(triethyl)silylethane is known to isomerize to the corresponding *cis*-isomer in the presence of a catalytic amount of diphenyl disulfide under UV irradiation of 254 nm.[13] Indeed, pure *trans*-**6c** isomerized to a 70 : 13 mixture of *cis*-**6c** and *trans*-**6c** in the presence of 20 mol% of diphenyl disulfide as shown in eq. 1. In the absence of diphenyl disulfide, the isomerization did not occur at all, and *trans*-**6c** was recovered quantitatively. A plausible pathway is suggested in Scheme 2.



(1)

Scheme 2. Isomerization of *vic*-difluoro olefins



VII-2-3. Phase Transition Behavior of *vic*-Difluoro Olefinic LCs

Phase transition temperatures and enthalpies of *cis*-**6**, *trans*-**6**, and **1** as well as LC phases are summarized in Table 3. Although *trans*-**6a** and *trans*-**6b** showed a nematic phase in temperature ranges narrower than those of parent olefins **1a** and **1b**, *cis*-**6a** and *cis*-**6b** exhibited a nematic phase in similar ranges but at lower temperatures (Figure 1). The LCs having a *trans*-4-pentylcyclohexylcyclohexane mesogen are summarized in Figure 2. LC *cis*-**6c** exhibited a nematic temperature range much wider than **1c** or *trans*-**6c**, whereas those with a longer alkyl group diminished or lost the nematic phase. Among *trans*-difluoro olefins, *trans*-**6c** showed little liquid crystallinity; *trans*-**6d** and *trans*-**6e** exhibited an S_B phase in parallel with **1d** and **1e**. Thus, the fluorine effect was most striking in **6c**.

Table 3. Phase transition temperatures and enthalpies of compounds **1** and **6**.

Entry	Compound	Phase transition temperature/°C[a, b]	
		DSC (on 1st cooling)	DSC (on 2nd heating)
1	**1a**	Cr 24 (2.7) S_B 34 (9.4) N 107 (0.67) Iso	Cr 43 (13) N 109 (0.70) Iso
2	*cis*-**6a**	Cr -3 (13) N 92 (0.34) Iso	Cr 30 (12) S_B 38 (13) N 92 (0.51) Iso
3	*trans*-**6a**	Cr 52 (6.5) S_B 61 (13) N 83 (0.65) Iso	Cr 77 (29) N 83 (0.72) Iso
4	**1b**	Cr 35 (12) N 126 (1.1) Iso	Cr 42 (13) N 127 (0.99) Iso
5	*cis*-**6b**	Cr 0 (19) N 116 (0.49) Iso	Cr 35 (22) N 116 (0.48) Iso
6	*trans*-**6b**	Cr 12 (0.66) S_B 18 (11) N 92 (0.70) Iso	Cr 16 (5.8) S_X 25 (7.0) S_B 35 (14) N 92 (0.66) Iso
7	**1c**	Cr -4 (0.03) S_B 44 (2.9) N 53 (0.63) Iso	Cr -4 (0.08) S_B 49 (3.5) N 55 (1.0) Iso
8	*cis*-**6c**	Cr -14 (16) S_B 17 (3.1) N 70 (0.75) Iso	Cr 20 (3.0) S_B 22 (18) N 70 (0.75) Iso
9	*trans*-**6c**	Cr -4 (19) S_B 37 (3.3) N 41 (0.48) Iso	Cr 34 (21) S_B 38 (3.3) N 41 (0.42) Iso
10	**1d**	Cr -31 (9.4) S_B 77 (7.5) Iso	Cr -25 (7.5) S_{X1} -18 S_{X2} 14 (9.4) S_B 77 (7.6) Iso
11	*cis*-**6d**	Cr 36 (23) S_B 79 (11) Iso	Cr 57 (25) S_B 80 (11) Iso
12	*trans*-**6d**	Cr -12 (8.2) S_B 78 (8.0) Iso	Cr 2 (9.7) S_B 80 (8.2) Iso
13	**1e**	Cr -2 (18) S_B 89 (8.5) Iso	Cr 3 (23) S_B 90 (9.3) Iso
14	*cis*-**6e**	Cr -14 (24) S_B 84 (6.3) N 89 (1.0) Iso	Cr 20 (30) S_B 84 (6.4) N 89 (0.82) Iso
15	*trans*-**6e**	Cr -20 (23) S_B 81 (7.3) Iso	Cr 3 (27) S_B 83 (7.9) Iso

a) Cr: Crystal. N: Nematic phase. S_B: Smectic B phase. S_X: Higher order smectic phases.

b) Enthalpies of phase transitions in parentheses (KJ/mol).

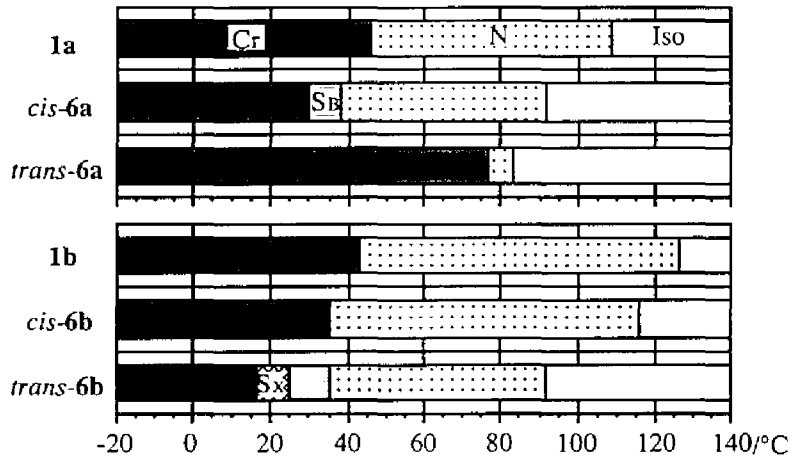


Figure 1. Phase transition behaviors of **6a** and **6b** on 2nd heating.

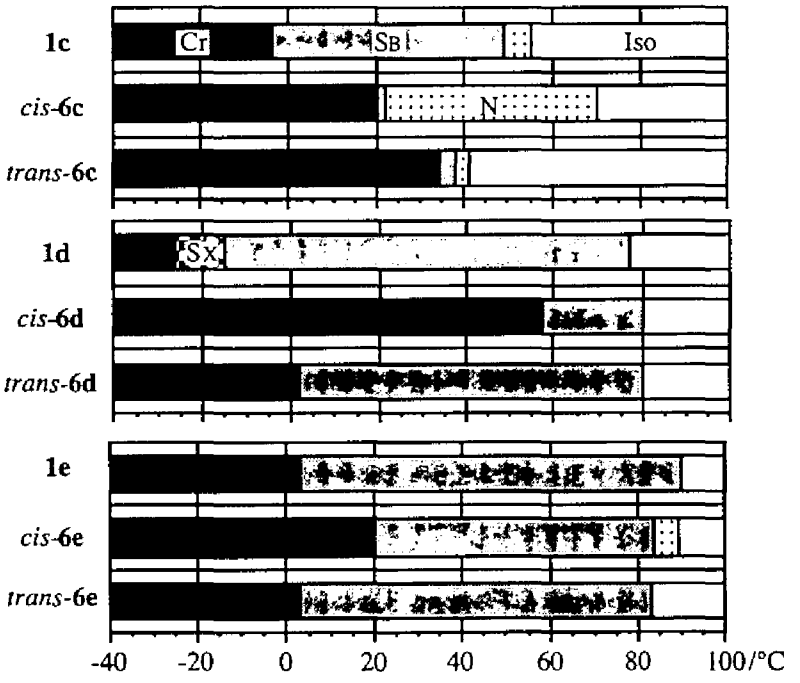


Figure 2. Phase transition behaviors of **6c**, **6d**, and **6e** on 2nd heating

VII-2-4. Electro-Optical Properties of *vic*-Difluoro Olefins

To examine the electro-optical properties of difluoro olefinic LCs, each of *cis*- and *trans*-isomers of **6a-6e** and parent olefinic LCs **1c-1e** were mixed by 20 wt% with **host**, a 1 : 1 mixture of **1a** and **1b**, and $\Delta\varepsilon$, V_{th}, Δn, and τ of the resulting mixtures were measured. The data are summarized in Table 4. The values of $\Delta\varepsilon$ and Δn were extrapolated to 100% to examine the dielectric anisotropy ($\Delta\varepsilon$') and birefringence (Δn') of pure samples of **6**. These values also are listed in Table 4.

Table 4. Physical and electro-optical properties[a] of **1c-1e** and *cis*- and *trans*-**6a-6e** as mixed by 20 wt% in **host**.

compound	T_{NI}/°C	$\Delta\varepsilon$	$\Delta\varepsilon$'[b]	V_{th}/V[c]	Δn	Δn'[d]	τ/ms[c,e] (V)[f]
host	116.7	4.8	—	2.14	0.090	—	25.3 (5.1)
cis-**6a**	116.0	3.2	-3.2	2.35	0.089	0.085	36.2 (5.5)
trans-**6a**	109.5	4.0	-0.8	2.01	0.090	0.090	33.2 (5.1)
cis-**6b**	117.4	3.6	-1.2	2.34	0.078	0.030	34.7 (5.2)
trans-**6b**	111.9	4.2	1.8	2.30	---	---	33.5 (5.0)
1c	102.8	3.6	-1.2	2.29	0.081	0.045	22.4 (5.3)
cis-**6c**	105.1	4.2	1.8	1.99	0.081	0.045	33.3 (4.3)
trans-**6c**	97.7	3.3	-2.7	2.16	0.081	0.045	31.2 (4.7)
1d	94.4	3.1	-3.7	2.08	0.077	0.025	32.6 (4.4)
cis-**6d**	87.4	3.0	-4.2	2.00	0.076	0.020	44.1 (4.2)
trans-**6d**	86.8	3.1	-3.7	2.04	0.075	0.025	43.1 (4.2)
1e	108.3	3.3	-2.7	2.29	0.082	0.050	26.9 (5.0)
cis-**6e**	108.6	4.0	0.8	2.15	0.083	0.055	29.4 (4.7)
trans-**6e**	101.6	3.2	-3.2	2.22	0.081	0.045	34.3 (4.7)

a) Measured at 20 °C. b) Extrapolated from $\Delta\varepsilon$. c) Corrected for 6.0 μm cell. d) Extrapolated from Δn. e) Responce time ($\tau_r = \tau_d$). f) Applied voltage/V.

In the case of **6a** and **6b** with a 3,4-difluorophenyl moiety in a mesogenic core, $\Delta\varepsilon$s of the resulting mixtures were lower as compared with **host**. The effect of *cis*-isomers was more striking than that of *trans*-ones owing probably to the cancelled dipole moment of C–F bonds in difluorophenyl and *cis*-difluoro olefinic moieties. Negative $\Delta\varepsilon$' of *cis*-**6a** also suggests the reduced dipole moment along the molecular long axis of **6a**. To examine the effect of the *vic*-difluoro olefinic moiety more precisely, properties of LCs **6c-e** were next measured. All *trans*-**6c-e** exhibited $\Delta\varepsilon$s to the extent similar to parent olefins **1c-e**, probably because the dipole moments of the two C–F bonds compensate each other, whereas *cis*-**6c-e** showed varying $\Delta\varepsilon$s depending on the kind of a side chain; *cis*-**6c** and *cis*-

6e were much larger in $\Delta\varepsilon$ than **1c** and **1e**, respectively; *cis*-**6d** had smaller $\Delta\varepsilon$ than **1d**. Since *cis*-**6d** has negative $\Delta\varepsilon'$, this is an n-type LC; both *cis*-**6c** and *cis*-**6e** shows positive $\Delta\varepsilon'$ and thus are p-type. All the *vic*-difluoro olefins lowered V_{th} of host LCs upon mixing by 20 wt% as compared with the parent olefins. In particular, the effect of *cis*-**6c-e** was remarkable in comparison with *trans*-**6c-e**. All the difluoro olefins had equally low Δn's as estimated by extrapolation, and thus mixing one of them in **host** results in lowering Δn of **host**. Accordingly, the difluoro olefins are a useful additive for reducing Δn of LC materials. Both *cis*- and *trans*-difluoro olefins are thermally stable, since no decomposition was observed by heating their xylene solutions at 170 °C for 24 h.

VII-3. Conclusion

The Author has demonstrated that LCs having a *vic*-difluoro olefinic moiety are readily prepared from the corresponding parent olefinic LCs. Studies on the phase transition behavior of the newly prepared LCs reveal that the fluorine introduction effect is most striking with **6c**. The electro-optical properties of the LCs having a $(CH_2)_nCF=CHF$ group change extensively depending on the configuration and the value of n. The difluoro olefinic LCs generally reduce V_{th} and Δn of host LCs upon mixing by 20 wt% more effectively than the corresponding parent olefins.

VII-4. Experimental

Measurements

A sample for the measurement of $\Delta\varepsilon$, Δn, V_{th}, and τ was prepared by mixing a compound (20 wt%) with **host** (80%, Cr 11 N 117 Iso) made of equal amounts of **1a** and **1b**.

LCs Having ω-Alkenyl Side Chain.

Compounds **1a-c** were commercially available from Dainippon Ink & Chemicals, Inc. Compounds **1d** and **1e** were prepared from **1c** as follows.

1-[*trans*-4-(2-Hydroxyethyl)cyclohexyl]-*trans*-4-pentylcyclohexane (7). In a

two-necked flask were placed THF (200 mL) and 1-[*trans*-4-(ethenyl)cyclohexyl]-*trans*-4-pentylcyclohexane **1c** (24 g, 91 mmol). The flask was immersed in an ice-water bath. A borane THF solution (1.00 M, 46 mL) was added dropwise to the solution. The reaction mixture was stirred for 12 h at room temperature before quenching with H_2O (1 mL) at 0 °C. The mixture was treated with 3 M NaOH (22 mL) and 30% H_2O_2 (23 mL), and the resulting suspension was stirred for 6 h at room temperature before quenching with aq. $NaHSO_3$. The organic phase was separated; the aqueous phase was extracted with Et_2O four times (400 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The product was recrystallized from hexane and purified by flash column chromatography (hexane : EtOAc = 5 : 1) to give **7** (22 g, 85% yield) as colorless needles, mp 152.0-152.9 °C, R_f = 0.27 (hexane : EtOAc = 5 : 1). IR (KBr) 3428, 2953, 2919, 2851, 1468, 1453, 1360, 1051, 1022, 963, 893 cm^{-1}; ^1H NMR (200 MHz) δ = 0.82-1.34 (m, 24 H), 1.46 (dt, *J* = 7, 7 Hz, 2 H), 1.62-1.77 (m, 8 H), 3.68 (t, *J* = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.9 (s), 30.1 (s), 32.2 (s), 33.60 (s), 33.64 (s), 34.5 (s), 37.5 (s), 37.9 (s), 40.4 (s), 43.3 (s), 43.4 (s), 60.9 (s); MS *m/z* (rel intensity) 280 (M^+, 0.7), 263 (7), 262 (32), 233 (12), 191 (13), 151 (14), 137 (11), 124 (6), 109 (100), 97 (66), 96 (46), 95 (45), 83 (67), 81 (76), 79 (52), 69 (57), 67 (81). Found: C, 81.19; H, 13.04%. Calcd for $C_{19}H_{36}O$: C, 81.36; H, 12.94%.

1-[*trans*-4-(Formylmethyl)cyclohexyl]-*trans*-4-pentylcyclohexane (8). To a solution of **7** (8.5 g, 30 mmol) in CH_2Cl_2 (200 mL) was added pyridinium chlorochromate (PCC, 9.7 g, 45 mmol) in one portion at room temperature. The reaction mixture was stirred for 3 h at the same temperature followed by the addition of Celite. The mixture was filtered through a Celite pad; the filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography (hexane : EtOAc = 5 : 1) to give **8** (7.2 g, 85% yield) as colorless solids. Phase transition temperature/°C: S_X 93 Iso; R_f = 0.61 (hexane : EtOAc = 5 : 1). IR 2915, 2849, 2716, 2361, 1723, 1468, 1447, 1408, 1379, 1352, 1291, 1217, 1024, 895 cm^{-1}; ^1H NMR (300 MHz) δ = 0.80-1.35 (m, 20 H), 0.88 (t, *J* = 7 Hz, 3 H), 1.64-1.84 (m, 8 H), 2.27 (dd, *J* = 2, 7 Hz, 2 H), 9.75 (t, *J* = 2 Hz, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.7 (s), 30.0 (s), 32.2 (s), 33.0 (s), 33.5 (s), 33.6 (s), 37.5 (s), 37.9 (s), 42.9 (s), 43.3 (s), 51.4 (s), 203.1 (s); MS *m/z* (rel intensity) 280 (M^++2, 5), 278 (M^+, 14), 234 (37), 149 (27), 137 (19), 135 (14), 125 (22), 115 (20), 108 (25), 97 (58), 95 (67), 81 (92), 69 (100). Found: *m/z* 278.2623. Calcd for $C_{19}H_{34}O$: M, 278.2610.

1-[*trans*-4-(2-Propenyl)cyclohexyl]-*trans*-4-pentylcyclohexane (1d). A solution of *n*-BuLi in hexane (1.60 M, 9.5 mL, 15.2 mmol) was added to methyltriphenylphosphonium bromide (5.7 g, 16 mmol) suspended in Et_2O (60 mL) at room temperature, and the resulting mixture was stirred for 4 h at room temperature.

Then an ethereal solution (18 mL) of **8** (4.1 g, 15 mmol) was added dropwise at room temperature. The resulting mixture was stirred for 4 h at the same temperature before quenching with aq. NH_4Cl. The organic phase was separated; the aq. phase was extracted with Et_2O three times (300 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **1d** (2.9 g, 72% yield). Phase transition temp./°C: Cr −25 S_{X1} −18 S_{X2} −14 S_B 77 Iso (DSC on 2nd heating); R_f = 0.89 (hexane). IR 3077, 2915, 2849, 1642, 1447, 1215, 994, 911, 895 cm^{-1}; ^1H NMR (200 MHz) δ = 0.77-1.34 (m, 23 H), 1.64-1.80 (m, 8 H), 1.93 (t, J = 7 Hz, 2 H), 3.68 (t, J = 7 Hz, 2 H), 4.90-4.93 (m, 1 H), 4.95-5.30 (m, 1 H), 5.65-5.90 (m, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 30.0 (s), 30.1 (s), 32.3 (s), 33.3 (s), 33.7 (s), 37.5 (s), 37.95 (s), 37.97 (s), 41.9 (s), 43.4 (s), 43.5 (s), 115.1 (s), 137.8 (s); MS *m/z* (rel intensity) 277 (M^++1, 1), 276 (M^+, 5), 234 (11), 219 (14), 206 (3), 192 (3), 179 (4), 165 (5), 151 (10), 137 (18), 123 (40), 109 (36), 97 (76), 95 (47), 83 (100), 81 (85), 69 (79), 67 (78). Found: *m/z* 276.2823. Calcd for $C_{20}H_{36}$: M, 276.2817.

1-[*trans*-4-(2-Iodoethyl)cyclohexyl]-*trans*-4-pentylcyclohexane (9). To a THF solution of borane (1.00 M, 80 mL) cooled at 0 °C was added dropwise 2-methyl-2-butene (12.8 mL, 120 mmol) over 10 min, and the resulting mixture was stirred for 3 h at 0 °C. To the reagent solution, a solution of **1c** (11.5 g, 44 mmol) in THF (20 mL) was added dropwise at 0 °C. The reaction mixture was warmed to room temperature and stirred for 11 h before quenching with methanol (1 mL) and iodine (34 g, 132 mmol). Then a methanol (40 mL) solution of sodium hydroxide (5.3 g) was added dropwise to the mixture. The whole mixture was stirred for 5 h at room temperature before treatment with aq. NaOH (3 M, 20 mL) and 30% H_2O_2 solution (10 mL). The resulting mixture was stirred for an additional period of 8 h at room temperature. The excess hydrogen peroxide was decomposed by careful portionwise addition of $NaHSO_3$, and the aqueous phase was extracted with Et_2O three times (500 mL). The combined organic extracts were washed by sat. aq. NaCl solution, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash column chromatography (hexane) afforded **9** (12.9 g, 75% yield) as a colorless powder, mp 132.3-134.4 °C, R_f = 0.81 (hexane). IR (KBr) 2923, 2851, 1468, 1441, 1289, 1219, 1184, 1159, 953, 897, 723 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.34 (m, 23 H), 1.67-1.78 (m, 10 H), 3.21 (t, J = 7 Hz, 2 H); ^{13}C NMR (75.5 MHz) δ = 5.2 (s), 14.1 (s), 22.7 (s), 26.7 (s), 29.7 (s), 30.1 (s), 32.2 (s), 32.7 (s), 33.6 (s), 37.5 (s), 37.9 (s), 38.8 (s), 41.2 (s), 43.3 (s), 43.4 (s); MS *m/z* (rel intensity) 391 (M^++1, 0.1), 390 (M^+, 0.5), 263 (19), 207 (3), 181 (9), 179 (8), 167 (13), 165 (12), 139 (19), 137 (19), 125 (26), 123 (24), 111 (64), 109 (53), 97 (100), 95 (48), 83 (94), 81 (73), 69 (85), 67 (86). Found: C, 58.50; H, 8.82%. Calcd for $C_{19}H_{35}I$: C, 58.46; H, 9.04%.

1-[*trans*-4-(3-Butenyl)cyclohexyl]-*trans*-4-pentylcyclohexane (1e). Vinylmagnesium bromide (1.0 M THF solution, 75 mL, 75 mmol) was added dropwise to a mixture of copper(I) iodide (7.1 g, 38 mmol) and **9** (12.1 g, 31 mmol) suspended in THF (150 mL) at –30 °C. The reaction mixture was then allowed to warm to 0 °C and stirred at 0 °C for 3 h before quenching with aq. 1.0 M HCl. The organic phase was separated; the aqueous phase was extracted with Et_2O three times (300 mL). The combined organic extracts were washed with sat. aq. NaCl solution, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **1e** (8.2 g, 90% yield) as a colorless mesomorphic oil. Phase transition temperature/°C: Cr 3 S_B 90 Iso (DSC on 2nd heating); R_f = 0.81 (hexane). IR 2927, 2849, 1642, 1468, 1447, 1379, 1219, 994, 909 cm^{-1}; ^1H NMR (300 MHz) δ = 0.75-1.36 (m, 22 H), 0.88 (t, J = 7 Hz, 3 H), 1.64-1.80 (m, 8 H), 2.00-2.10 (m, 2 H), 4.88-5.40 (m, 2 H), 5.74-5.88 (m, 1 H); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 30.0 (s), 30.1 (s), 31.3 (s), 32.3 (s), 33.5 (s), 33.7 (s), 36.7 (s), 37.4 (s), 37.5 (s), 37.9 (s), 43.46 (s), 43.49 (s), 113.9 (s), 139.5 (s); MS *m/z* (rel intensity) 291 (M^++1, 3), 290 (M^+, 12), 248 (3), 233 (4), 219 (7), 192 (3), 151 (11), 137 (33), 123 (14), 109 (17), 97 (54), 83 (61), 81 (100), 69 (59), 67 (83). Found: *m/z* 290.2967. Calcd for $C_{21}H_{38}$: M, 290.2974.

1-{*trans*-4-[3-Fluoro-4-(phenylthio)butyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)cyclohexane (3a). A 100 mL, dried, Teflon® bottle was charged with a solution of 1-[*trans*-4-(3-butenyl)cyclohexyl]-*trans*-4-(3,4-difluorophenyl)cyclohexane (**1a**) (3.3 g, 10.0 mmol), *N*-(phenylthio)phthalimide (2.7 g, 10.5 mmol) in CH_2Cl_2 (40 mL). To the reaction mixture stirred vigorously at room temperature, HF/py (70 wt% HF, 2.5 mL, 100 mmol) was added dropwise through a disposal polypropylene/polyethylene syringe. The mixture was stirred for 53 h at room temperature before quenching with aq. $NaHSO_3$/$NaHCO_3$/NaOH (*p*H 10). The organic phase was separated; the aqueous phase was extracted with Et_2O three times (150 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane : benzene = 6 : 1) to give **3a** (3.6 g, 77% yield) as a colorless powder, mp 69.3-69.8 °C, R_f = 0.41 (hexane : benzene = 5 : 1). IR (KBr) 2917, 2847, 1607, 1582, 1522, 1482, 1441, 1273, 1204, 1109, 1090, 945, 872, 820, 772, 741, 702, 691, 619, 581 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.45 (m, 13 H), 1.61-1.92 (m, 10 H), 2.40 (tm, J = 12 Hz, 1 H), 2.96-3.29 (m, 2 H), 4.58 (dm, J = 48 Hz, 1 H), 6.85-7.41 (m, 8 H); ^{19}F NMR (188 MHz) δ = –139.23 (ddd, J = 9, 12, 22 Hz, 1 F), –142.12 (dddd, J = 5, 8, 10, 22 Hz, 1 F), –176.73—177.43 (m, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.9 (d, J = 1 Hz), 30.1 (s), 31.7 (d, J = 21 Hz), 32.3 (d, J = 4 Hz), 33.3 (d, J =

13 Hz), 34.5 (s), 37.6 (s), 38.5 (d, J = 24 Hz), 42.7 (s), 43.2 (s), 43.8 (s), 92.3 (d, J = 173 Hz), 115.4 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.5 (dd, J = 4, 6 Hz), 126.5 (s), 129.0 (s), 129.8 (s), 135.7 (s), 144.8 (dd, J = 4, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 147 Hz); MS *m/z* (rel intensity) 461 (M^++1, 5), 440 (9), 330 (12), 179 (10), 153 (18), 135 (45), 127 (71), 123 (38), 110 (100), 95 (27), 81 (55), 67 (55). Found: C, 72.97; H, 7.80%. Calcd for $C_{28}H_{35}F_3S$: C, 73.01; H, 7.66%.

1-{*trans*-4-[2-Fluoro-3-(phenylthio)propyl]cyclohexyl}-*trans*-4-pentylcyclohexane (3d). In a similar manner as described for **3a**, **3d** (2.9 g, 81% yield) was prepared as a colorless powder from **1d** (2.4 g, 8.8 mmol). Mp 85.1-85.4 °C; R_f = 0.47 (hexane : benzene = 5 : 1). IR (KBr) 2953, 2923, 2907, 2890, 2847, 1586, 1482, 1439, 1094, 1069, 1051, 986, 961, 843, 820, 733, 702, 689 cm^{-1}; ^1H NMR (200 MHz) δ = 0.83-1.43 (m, 23 H), 1.59-1.83 (m, 10 H), 2.92-3.28 (m, 2 H), 4.70 (dm, J = 49 Hz, 1 H), 7.15-7.41 (m, 5 H); ^{19}F NMR (188 MHz) δ = –176.04—176.78 (m); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.8 (d, J = 12 Hz), 30.1 (s), 32.2 (s), 33.0 (s), 33.6 (s), 34.1 (s), 34.3 (d, J = 3 Hz), 37.5 (s), 37.9 (s), 39.1 (d, J = 24 Hz), 41.9 (d, J = 20 Hz), 43.3 (d, J = 13 Hz), 90.8 (d, J = 172 Hz), 126.5 (s), 129.0 (s), 129.9 (s), 135.8 (s); MS *m/z* (rel intensity) 406 (M^++2, 7), 405 (M^++1, 25), 404 (M^+, 88), 384 (12), 275 (9), 274 (34), 149 (14), 135 (17), 123 (81), 110 (90), 109 (56), 97 (43), 83 (57), 81 (86), 79 (59), 69 (65), 67 (100). Found: C, 77.01; H, 10.02%. Calcd for $C_{26}H_{41}FS$: C, 77.17; H, 10.21%.

1-{*trans*-4-[3-Fluoro-4-(phenylthio)butyl]cyclohexyl}-*trans*-4-pentylcyclohexane (3e). This compound (6.6 g, 78% yield) was prepared as a colorless powder from **1e** (5.8 g, 20 mmol). Phase transition temperature/°C: S_B 63 Iso; R_f = 0.38 (hexane : benzene = 5 : 1). IR (KBr) 3060, 2924, 2851, 2361, 1586, 1482, 1468, 1379, 1217, 1090, 1069, 1024, 895, 737, 691 cm^{-1}. ^1H NMR (200 MHz) δ = 0.79-1.43 (m, 25 H), 1.60-1.84 (m, 10 H), 2.93-3.27 (m, 2 H), 4.56 (ttd, J = 6, 6, 48 Hz, 1 H), 7.14-7.40 (m, 5 H); ^{19}F NMR (188 MHz) δ = –176.69—177.40 (m); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.9 (s), 30.1 (s), 31.7 (d, J = 21 Hz), 32.2 (s), 32.3 (d, J = 3 Hz), 33.4 (d, J = 13 Hz), 33.6 (s), 37.5 (s), 37.6 (s), 37.9 (s), 38.5 (d, J = 24 Hz), 43.3 (s), 43.4 (s), 92.8 (d, J = 173 Hz), 126.4 (s), 129.0 (s), 129.8 (s), 135.7 (s); MS *m/z* (rel intensity) 420 (M^++2, 5), 419 (M^++1, 18), 418 (M^+, 61), 288 (15), 183 (11), 136 (14), 135 (55), 123 (49), 111 (17), 110 (100), 109 (28), 97 (30), 95 (35), 83 (42), 81 (49), 79 (23), 69 (45), 67 (54) . Found: *m/z* 418.3076. Calcd for $C_{27}H_{43}FS$: M, 418.3070.

1-[*trans*-4-(1-Fluoro-2-iodoethyl)cyclohexyl]-*trans*-4-(3,4-difluorophenyl)-cyclohexane (2b). A solution of olefin **1b** (0.91 g, 3.0 mmol) in CH_2Cl_2 (4.0 mL) was added dropwise over 30 min to a mixture of $TBAH_2F_3$ (138 g, 4.6 mmol), NIS (3.4 g, 15 mmol), and CH_2Cl_2 (6.0 mL) placed in a 50 mL two-necked flask at 0 °C. The resulting

mixture was allowed to warm to room temperature and stirred for 23 h before quenching with aq. $NaHCO_3$ and solid $NaHSO_3$. The organic phase was separated; the aq. phase was extracted with hexane four times (200 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **2b** (1.10 g, 82% yield) as colorless needles. Phase transition temperature/°C: Cr 81 S_X 85 N 104 Iso; R_f = 0.25 (hexane). IR (KBr) 2923, 2853, 1605, 1516, 1451, 1269, 1211, 1186, 1117, 955, 939, 826, 772, 625, 581 cm^{-1}; ^1H NMR (200 MHz) δ = 1.00-1.46 (m, 10 H), 1.59-2.45 (m, 9 H), 2.41 (tt, *J* = 4,12 Hz, 1 H), 3.30 (ddd, *J* = 6, 11, 22 Hz, 1 H), 3.40 (ddd, *J* = 4, 11, 23 Hz, 1 H), 4.16 (dddd, *J* =4, 6, 6, 47 Hz, 1 H), 6.85-7.11 (m, 3 H); ^{19}F NMR (188 MHz) δ = –139.17 (ddd, *J* = 9, 12, 21 Hz, 1 F), –143.03 (dddd, *J* = 4, 8, 10, 21 Hz, 1 F), –178.10 (dddd, *J* = 15, 22, 23, 47 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 5.9 (d, *J* = 25 Hz), 27.3 (d, *J* = 5 Hz), 28.5 (d, *J* = 5 Hz), 29.1 (d, *J* = 18 Hz), 30.1 (s), 34.5 (s), 42.1 (d, *J* = 19 Hz), 42.6 (d, *J* = 15 Hz), 43.8 (s), 95.7 (d, *J* = 177 Hz), 115.4 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 2, 6 Hz), 144.7 (dd, *J* = 4, 4 Hz), 148.5 (dd, *J* = 13, 245 Hz), 150.9 (dd, *J* = 13, 247 Hz); MS *m/z* (rel intensity) 450 (M^+, 19), 323 (7), 320 (6), 303 (7), 302 (7), 241 (10), 215 (6), 195 (14), 165 (10), 153 (21), 140 (44), 127 (100), 95 (24), 91 (40), 67 (38). Found: C, 53.35; H, 6.04%. Calcd for $C_{20}H_{26}F_3I$: C, 53.34; H, 5.82%.

1-[*trans*-4-(1-Fluoro-2-iodoethyl)cyclohexyl]-*trans*-4-pentylcyclohexane (2c). In a similar manner, **2c** (0.55 g, 68% yield) was prepared as a colorless powder from **1c** (0.53 g, 2.0 mmol). Phase transition temperature/°C: Cr 67 N 71 Iso; R_f = 0.40 (hexane). IR (KBr) 2923, 2849, 1445, 1414, 1190, 965, 920, 899, 801, 590 cm^{-1}; ^1H NMR (300 MHz) δ = 0.77-1.35 (m, 22 H), 1.59-1.97 (m, 9 H), 3.29 (ddd, *J* = 7, 11, 22 Hz, 1 H), 3.39 (ddd, *J* = 4, 11, 23 Hz, 1 H), 4.13 (dddd, *J* = 4, 6, 7, 47 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –178.06 (dddd, *J* = 16, 22, 23, 47 Hz); ^{13}C NMR (75.5 MHz) δ = 6.0 (d, *J* = 25 Hz), 14.1 (s), 22.7 (s), 26.7 (s), 27.4 (d, *J* = 5 Hz), 28.5 (d, *J* = 5 Hz), 29.1 (d, *J* = 18 Hz), 30.0 (s), 32.2 (s), 33.6 (s), 37.4 (s), 37.9 (s), 42.1 (d, *J* = 19 Hz), 43.1 (d, *J* = 25 Hz), 95.8 (d, *J* = 177 Hz); MS *m/z* (rel intensity) 409 (M^++1, 0.96), 408 (M^+, 5), 317 (0.97), 281 (2), 261 (15), 235 (32), 221 (5), 205 (2), 179 (5), 165 (8), 153 (14), 139 (19), 123 (14), 109 (30), 97 (98), 83 (100), 67 (79). Found: *m/z* 408.1695. Calcd for $C_{19}H_{34}FI$: M, 408.1689.

1-{*trans*-4-[1-Fluoro-2-(phenylthio)ethyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)cyclohexane (3b) A flame dried, two-necked, 30 mL flask was charged with sodium hydride (132 mg, 5.5 mmol) and THF (5.0 mL). To the suspension cooled at 0 °C, thiophenol (0.62 mL, 6.0 mmol) was added dropwise. The mixture was stirred for 30 min at room temperature to generate sodium thiophenoxide, which was added *via*

cannula to a solution of **2b** (2.3 g, 5.0 mmol) in THF (5.0 mL) placed in a two-necked 50 mL flask and cooled at 0 °C. The thiophenoxide flask was washed with THF (10 mL). The THF also was added to the **2b** solution. The resulting mixture was allowed to warm to room temperature and stirred for 5 h before quenching with aq. NH_4Cl. The organic phase was separated; the aq. phase was extracted with Et_2O three times (50 mL). The combined organic phase was washed with sat. aq. NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane : benzene = 5 : 1) to give **3b** (1.98 g, 91% yield) as needles, mp 95.6-95.9 °C, R_f = 0.32 (hexane : benzene = 5 : 1). IR (KBr) 2923, 2853, 1607, 1582, 1516, 1480, 1273, 1211, 1117, 1090, 1053, 1024, 939, 741, 691 cm^{-1}; ^1H NMR (200 MHz) δ = 0.95-1.45 (m, 10 H), 1.65-1.98 (m, 9 H), 2.41 (tt, J = 3, 9 Hz, 1 H), 3.10-3.23 (m, 2 H), 4.39 (ddt, J = 6, 48, 6 Hz, 1 H), 6.84-7.41 (m, 8 H); ^{19}F NMR (188 MHz) δ = −139.19 (ddd, J = 8, 12, 21 Hz, 1 F), −143.06 (dddd, J = 5, 8, 10, 21 Hz, 1 F), −184.54 (ddt, J = 20, 48, 22 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 27.1 (d, J = 5 Hz), 28.8 (d, J = 5 Hz), 29.3 (d, J = 18 Hz), 30.1 (s), 34.5 (s), 36.4 (d, J = 24 Hz), 41.2 (d, J = 20 Hz), 42.6 (d, J = 20 Hz), 43.8 (s), 95.8 (d, J = 175 Hz), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 4, 6 Hz), 126.4 (s), 128.9 (s), 129.7 (s), 135.9 (s), 144.7 (dd, J = 4, 5 Hz), 148.5 (dd, J = 13, 246 Hz), 150.1 (dd, J = 12, 247 Hz); MS *m/z* (rel intensity) 433 (M^++1, 7), 432 (M^+, 25), 412 (18), 303 (13), 302 (33), 221 (5), 193 (10), 179 (16), 165 (8), 153 (24), 140 (18), 127 (94), 123 (94), 110 (100), 109 (61), 95 (38), 79 (62), 67 (68). Found: C, 72.13; H, 7.44%. Calcd for $C_{26}H_{31}F_3S$: C, 72.19; H, 7.22%.

1-{*trans*-4-[1-Fluoro-2-(phenylthio)ethyl]cyclohexyl}-*trans*-4-pentylcyclohexane (3c). In a similar way, **3c** (2.0 g, 95% yield) was obtained from **2c** (2.3 g, 5.5 mmol) as colorless needles, mp 59.8-60.7 °C, R_f = 0.50 (hexane : benzene = 5 : 1). IR (KBr) 3058, 2923, 2845, 1586, 1482, 1439, 1422, 1090, 1024, 968, 903, 830, 735, 702, 687 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.34 (m, 22 H), 1.66-1.92 (m, 9 H), 3.08-3.22 (m, 2 H), 4.37 (dtd, J = 6, 6, 48 Hz, 1 H), 7.15-7.40 (m, 5 H); ^{19}F NMR (188 MHz) δ = −184.47 (dtd, J = 19, 22, 48 Hz); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 27.2 (d, J = 5 Hz), 28.9 (d, J = 5 Hz), 29.3 (d, J = 18 Hz), 30.0 (s), 32.2 (s), 33.6 (s), 36.5 (d, J = 24 Hz), 37.4 (s), 37.9 (s), 41.3 (d, J = 19 Hz), 43.1 (d, J = 21 Hz), 95.9 (d, J = 175 Hz), 126.3 (s), 128.9 (s), 129.7 (s), 136.0 (s); MS *m/z* (rel intensity) 391 (M^++1, 6), 390 (M^+, 26), 370 (11), 261 (6), 260 (19), 189 (11), 165 (6), 163 (6), 135 (17), 123 (78), 110 (100), 109 (52), 95 (48), 81 (53), 79 (58), 69 (58), 67 (70). Calcd for $C_{25}H_{39}FS$: C, 76.87; H, 10.06%. Found: C, 76.88; H, 10.16%.

***trans*-1-(3,4-Difluorophenyl)-4-[*trans*-4-(3,4-difluoro-4-phenylsulfinylbutyl)-cyclohexyl]cyclohexane (5a).** A mixture of $TBAH_2F_3$ (2.7 g, 9.0 mmol), **3a** (1.38 g, 3.0

mmol), CH_2Cl_2 (10 mL), and DBH (0.87 g, 3.0 mmol) placed in a flame dried, two-necked, 30 mL flask was stirred for 30 min at room temperature before quenching with aq. $NaHCO_3$ and solid $NaHSO_3$ under vigorous agitation. The organic phase was separated; the aq. phase was extracted with Et_2O three times (200 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was transferred to a 100 mL round-bottomed flask dissolved in CH_2Cl_2 (10 mL) and cooled at –30 °C. To the mixture was added *m*CPBA (0.57 g, 3.3 mmol) in one portion; the whole was stirred for 3 h at –30 °C before quenching with solid $NaHSO_3$. The mixture was treated with water and then with 10% aq. NaOH. The organic phase was separated; the aq. phase was extracted with Et_2O three times (totally 200 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane : EtOAc = 5 : 1) to give **5a** (1.39 g, 94% yield) as colorless solids. Phase transition temperature/°C: S_X 45 S_B 93 Iso; R_f = 0.21, 0.35 (hexane : EtOAc = 5 : 1, diastereomeric mixtures). IR (KBr) 2920, 2848, 1605, 1518, 1446, 1428, 1272, 1214, 1118, 1091, 1048, 1023, 938, 817, 749, 686 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85-1.98 (m, 23 H), 2.40 (tm, *J* = 10 Hz, 1 H), 4.47-5.46 (m, 2 H), 6.85-7.10 (m, 3 H), 7.55-7.78 (m, 5 H); ^{19}F NMR (188 MHz) as diastereomeric mixtures; δ = –139.12—139.33 (m), –143.06—143.17 (m), –189.49—189.84 (m), –192.06—192.56 (m), –192.79—192.90 (m), –193.73—194.02 (m), –196.58—196.65 (m), –197.82—198.23 (m), –198.43—198.50 (m), –201.22—201.88 (m); MS *m/z* (rel intensity) 495 (M^++1, 0.7), 494 (M^+, 2), 479 (1), 478 (5), 477 (12), 459 (1), 458 (3), 195 (4), 179 (5), 167 (4), 153 (14), 140 (11), 127 (64), 126 (100), 125 (22), 109 (11), 95 (12), 81 (26), 79 (11), 78 (12), 77 (10), 69 (12), 67 (28). Found: *m/z* 494.2268. Calcd for $C_{28}H_{34}F_4OS$: M, 494.2266.

***trans*-1-(3,4-Difluorophenyl)-4-[*trans*-4-(1,2-Difluoro-2-phenylsulfinylethyl)-cyclohexyl]cyclohexane (5b).** This compound (1.31 g, 95% yield) was obtained from **3b** (1.30 g, 3.0 mmol) as a viscous oil by a procedure similar to the one for **5a**. R_f = 0.15 and 0.24 (hexane : EtOAc = 5 : 1, diastereomeric mixtures). IR (KBr) 2923, 2855, 1607, 1518, 1446, 1430, 1275, 1208, 1116, 1086, 1050, 999, 955, 863, 748, 689 cm^{-1}; ^1H NMR (200 MHz) δ = 0.98-1.45 (m, 11 H), 1.63-2.04 (m, 8 H), 2.32-2.46 (m, 1 H), 4.41-5.36 (m, 2 H), 6.85-7.11 (m, 3 H), 7.55-7.78 (m, 5 H); ^{19}F NMR (188 MHz) as diastereomeric mixtures; δ = –139.17—139.22 (m), –143.03—143.20 (m), –188.44--188.76 (m), –196.22—196.70 (m), –197.51—197.92 (m), –198.29—198.68 (m), –201.89--202.04 (m), –203.60—203.87 (m); MS *m/z* (rel intensity) 467 (M^++1, 2), 466 (M^+, 4), 452 (1), 450 (4), 449 (8), 431 (4), 430 (9), 321 (3), 195 (11), 181 (6), 179 (9), 167 (4), 153 (16), 141 (13), 140 (15), 128 (10), 127 (88), 126 (100), 125 (16), 110 (16), 109 (14), 97 (12), 95 (11), 83 (27), 81 (30), 79 (15), 77 (12), 67 (29). Found: *m/z* 466.1949. Calcd

for $C_{26}H_{30}F_4OS$: M, 466.1953.

1-[*trans*-4-(1,2-Difluoro-2-phenylsulfinylethyl)cyclohexyl]-*trans*-4-pentyl-cyclohexane (5c). Similarly, compound **5c** (1.13 g, 88% yield) was prepared from **3c** (1.18 g, 3.0 mmol) as a colorless powder. Phase transition temperature/°C: S_B 107 Iso; R_f = 0.27 and 0.39 (hexane : EtOAc = 5 : 1, diastereomeric mixtures). IR (KBr) 2922, 2850, 1445, 1378, 1341, 1084, 1044, 1000, 964, 748, 688 cm^{-1}; ^1H NMR (200 MHz) δ = 0.85-1.41 (m, 22 H), 1.59-1.99 (m, 9 H), 4.66-5.32 (m, 2 H), 7.56-7.76 (m, 5 H); ^{19}F NMR (188 MHz) δ = –185.23—185.79 (m), –188.46—188.87 (m), –196.31—196.72 (m), –197.57—198.02 (m), –198.32—198.67 (m), –201.34—202.14 (m), –203.36—203.78 (m); MS *m/z* (rel intensity) 425 (M^++1, 1), 424 (M^+, 3), 409 (2), 408 (7), 407 (10), 388 (7), 259 (4), 177 (2), 165 (4), 153 (6), 151 (7), 139 (8), 137 (11), 127 (12), 126 (100), 125 (21), 123 (17), 111 (19), 110 (26), 109 (29), 97 (66), 95 (28), 93 (14), 83 (83), 81 (46), 79 (22), 77 (17), 71 (15), 69 (55), 67 (46). Found: *m/z* 424.2566. Calcd for $C_{25}H_{38}F_2OS$: M, 424.2611.

1-[*trans*-4-(2,3-Difluoro-3-phenylsulfinylpropyl)cyclohexyl]-*trans*-4-pentyl-cyclohexane (5d). Compound **5d** (1.63 g) was isolated in 93% yield from **3d** (1.62 g, 4.0 mmol) as a colorless powder by a procedure similar to that for the preparation of **5a**. Phase transition temperature/°C: Cr 93 S_B 142 Iso; R_f = 0.22 and 0.28 (hexane : EtOAc = 5 : 1, diastereomeric mixtures). IR (KBr) 2918, 2849, 1445, 1377, 1305, 1084, 1044, 999, 968, 744, 689 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.53 (m, 23 H), 1.60-1.97 (m, 10 H), 4.43-5.47 (m, 2 H), 7.54-7.77 (m, 5 H); ^{19}F NMR (188 MHz) as diastereomeric mixtures; δ = –189.39—189.84 (m), –190.87—191.08 (m), –193.54—194.22 (m), –196.40--196.86 (m), –197.40—197.84 (m), –198.70—199.44 (m), –200.52—200.90 (m); MS *m/z* (rel intensity) 439 (M^++1, 2), 438 (M^+, 4), 422 (16), 421 (42), 141 (12), 127 (23), 126 (100), 125 (79), 111 (33), 110 (15), 109 (45), 97 (79), 83 (69), 81 (58), 69 (63), 67 (65); Found: *m/z* 438.2775. Calcd for $C_{26}H_{40}F_2OS$: M, 438.2768.

1-[*trans*-4-(3,4-Difluoro-4-phenylsulfinylbutyl)cyclohexyl]-*trans*-4-pentyl-cyclohexane (5e). In a similar manner as above, compound **5e** (1.20 g) was prepared in 87% yield from **3e** (1.25 g, 3.0 mmol) as a colorless powder. Phase transition temperature/°C: S_B 98 Iso; R_f = 0.24 and 0.36 (hexane : EtOAc = 5 : 1, diastereomeric mixtures). IR (KBr) 2920, 2850, 1445, 1378, 1320, 1090, 1050, 962, 897, 747, 688 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.50 (m, 25 H), 1.58-2.01 (m, 10 H), 4.47-5.39 (m, 2 H), 7.54-7.76 (m, 5 H); ^{19}F NMR (188 MHz) as diastereomeric mixtures; δ = –189.52--189.97 (m), –191.71—192.33 (m), –192.56—193.25 (m), –193.43—194.13 (m), –196.45--196.92 (m), –197.71—198.76 (m), –200.92—201.33 (m); MS *m/z* (rel intensity) 453 (M^++1, 0.5), 452 (M^+, 0.8), 435 (14), 127 (10), 126 (100), 125 (33), 111 (11), 109 (18), 97 (39), 95 (19), 83 (34), 81 (30), 77 (15), 69 (44), 67 (47); Found: *m/z* 452.2933. Calcd

for $C_{27}H_{42}F_2OS$: M, 452.2924.

1-{*trans*-4-[(*Z*)-3,4-Difluoro-3-butenyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)-cyclohexane (*cis*-6a) and **1-{*trans*-4-[(*E*)-3,4-Difluoro-3-butenyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)cyclohexane (*trans*-6a).** A solution of compound **5a** (1.39 g, 2.8 mmol) in *o*-xylene (15 mL) was placed in a thick-walled Pyrex pressure tube, and heated at 170 °C for 16 h under an argon atmosphere. The reaction mixture was cooled and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (10 mL) and treated with *m*CPBA (0.53 g, 3.1 mmol) in one portion at –30 °C. The whole was stirred for 6 h at –30 °C before quenching the excess peroxide with solid $NaHSO_3$ at –30 °C. The mixture was diluted with water and made alkaline with 10% aq. NaOH. The organic phase was separated; the aq. phase was extracted with Et_2O three times (200 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give *cis*-**6a** (0.34 g, 33% yield) and *trans*-**6a** (0.23 g, 22% yield) both as mesomorphic oils.

cis-**6a**: phase transition temperature/°C: Cr 35 N 116 Iso (DSC on 2nd heating); R_f = 0.38 (hexane). IR (KBr) 2928, 2855, 1727, 1607, 1516, 1453, 1271, 1202, 1140, 1088, 884, 866, 822, 779, 750, 631 cm^{-1}; ^1H NMR (200 MHz) δ = 0.81-1.44 (m, 13 H), 1.74-1.92 (m, 8 H), 2.00-2.20 (m, 2 H), 2.41 (tt, *J* = 3, 12 Hz, 1 H), 6.23 (tdd, *J* = 1, 18, 74 Hz, 1 H), 6.86-7.11 (m, 3 H); ^{19}F NMR (188 MHz) δ = –135.80 (ddt, *J* = 11, 18, 19 Hz, 1 F), –139.21 (ddd, *J* = 8, 12, 21 Hz, 1 F), –143.10 (dddd, *J* = 4, 8, 10, 21 Hz, 1 F), –167.70 (tdd, *J* = 5, 11, 74 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 24.8 (d, *J* = 22 Hz), 29.8 (s), 30.1 (s), 33.0 (d, *J* = 3 Hz), 33.2 (s), 34.5 (s), 37.0 (s), 42.7 (s), 43.1 (s), 43.8 (s), 115.4 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 132.4 (dd, *J* = 14, 250 Hz), 144.8 (dd, *J* = 4, 5 Hz), 148.5 (dd, *J* = 13, 245 Hz), 149.8 (dd, *J* = 6, 253 Hz), 150.1 (dd, *J* = 12, 247 Hz); MS *m/z* (rel intensity) 369 (M^++1, 5), 368 (M^+, 21), 290 (18), 193 (14), 179 (27), 166 (8), 153 (27), 141 (13), 140 (79), 127 (100), 111 (11), 95 (36), 81 (42), 79(24), 67 (54). Calcd for $C_{22}H_{28}F_4$: C, 71.72; H, 7.66%. Found: C, 71.63; H, 7.68%.

trans-**6a**: phase transition temperature/°C: Cr 16 S_X 25 S_B 35 N 92 Iso (DSC on 2nd heating); R_f = 0.56 (hexane). IR (KBr) 2923, 2853, 1609, 1518, 1497, 1451, 1433, 1285, 1208, 1138, 1119, 1094, 939, 870, 818, 770, 627 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88-1.51 (m, 13 H), 1.73-1.93 (m, 8 H), 2.28-2.49 (m, 3 H), 6.85-7.26 (m, 4 H); ^{19}F NMR (188 MHz) δ = –139.23 (ddd, *J* = 8, 12, 21 Hz, 1 F), –143.12 (dddd, *J* = 5, 8, 10, 21 Hz, 1 F), –160.63 (tdd, *J* = 3, 23, 127 Hz, 1 F), –184.20 (tdd, *J* = 5, 77, 127 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 23.6 (d, *J* = 24 Hz), 29.9 (s), 30.2 (s), 32.8 (d, *J* = 2 Hz), 33.2 (s), 34.6 (s), 37.2 (s), 42.8 (s), 43.2 (s), 43.9 (s), 115.4 (d, *J* = 17 Hz), 116.7 (d, *J* = 17 Hz), 122.4 (dd, *J* = 3, 6 Hz), 139.2 (dd, *J* = 68, 237 Hz), 144.8 (dd, *J* = 4, 5 Hz), 148.5 (dd, *J* =

13, 245 Hz), 150.2 (dd, J = 12, 247 Hz), 156.4 (dd, J = 40, 239 Hz); MS *m/z* (rel intensity) 369 (M^++1, 6), 368 (M^+, 26), 290 (7), 193 (11), 179 (24), 173 (8), 153 (35), 140 (82), 127 (100), 111 (14), 95 (37), 81 (42), 79 (28), 69 (22), 67 (62). Calcd for $C_{22}H_{28}F_4$: C, 71.72; H, 7.66%. Found: C, 71.61; H, 7.83%.

1-{*trans*-4-[(*Z*)-1,2-Difluoroethenyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)-cyclohexane (*cis*-6b) and **1-{*trans*-4-[(*E*)-1,2-Difluoroethenyl]cyclohexyl}-*trans*-4-(3,4-difluorophenyl)cyclohexane (*trans*-6b).** In a similar manner as for **6a**, *cis*-**6b** (0.44 g, 40% yield) and *trans*-**6b** (155 mg, 16% yield) were prepared both as mesomorphic oils from **5b** (1.31 g, 2.8 mmol).

cis-**6b**: phase transition temperature/°C: Cr 30 S_B 38 N 92 Iso (DSC on 2nd heating); R_f = 0.41 (hexane). IR (KBr) 2923, 1715, 1605, 1514, 1451, 1429, 1275, 1215, 1179, 1161, 1138, 1115, 997, 965, 864, 752, 722, 583 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88-1.53 (m, 10 H), 1.75-2.10 (m, 9 H), 2.41 (tt, J = 3,12 Hz, 1 H), 6.23 (dd, J = 18, 74 Hz, 1 H), 6.84-7.11 (m, 3 H); ^{19}F NMR (188 MHz) δ = –139.15 (ddd, J = 8, 12, 21 Hz, 1 F), –140.38 (ddd, J = 11, 17, 18 Hz, 1 F), –143.00 (dddd, J = 5, 8, 10, 21 Hz, 1 F), –171.32 (ddd, J = 4, 11, 74 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 29.2 (s), 29.7 (s), 30.0 (s), 34.4 (s), 37.1 (d, J = 21 Hz), 42.48 (s), 42.51 (s), 43.8 (s), 115.3 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 132.1 (dd, J = 14, 249 Hz), 144.7 (dd, J = 4, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 13, 247 Hz), 153.4 (dd, J = 6, 245 Hz); MS *m/z* (rel intensity) 341 (M^++1, 2), 340 (M^+, 11), 320 (8), 193 (18), 179 (34), 166 (18), 153 (25), 140 (66), 127 (100), 111 (8), 97 (11), 81 (25), 79 (23), 77 (16), 67 (30). Calcd for $C_{20}H_{24}F_4$: C, 70.57; H, 7.11%. Found: C, 70.55; H, 7.32%.

trans-**6b**: phase transition temperature/°C: Cr 77 N 83 Iso (DSC on 2nd heating); R_f = 0.59 (hexane). IR (KBr) 2917, 2857, 1607, 1516, 1491, 1451, 1433, 1345, 1283, 1215, 1111, 943, 864, 833, 816, 801, 779, 750, 631 cm^{-1}; ^1H NMR (200 MHz) δ = 1.05-1.66 (m, 10 H), 1.75-1.94 (m, 8 H), 2.34-2.69 (m, 2 H), 6.98 (dd, J = 4, 78 Hz, 1 H), 6.84-7.11 (m, 3 H); ^{19}F NMR (188 MHz) δ = –139.16 (ddd, J = 9, 12, 21 Hz, 1 F), –143.02 (dddd, J = 5, 8, 10, 21 Hz, 1 F), –169.43 (ddd, J = 4, 29, 127 Hz, 1 F), –184.97 (ddd, J = 5, 78, 127 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 28.7 (d, J = 3 Hz), 29.4 (s), 30.1 (s), 34.5 (s), 35.8 (dd, J = 2, 22 Hz), 42.3 (s), 42.7 (s), 43.8 (d, J = 1 Hz), 115.4 (d, J = 17 Hz), 116.7 (d, J = 17 Hz), 122.4 (dd, J = 3, 6 Hz), 138.3 (dd, J = 69, 237 Hz), 144.7 (dd, J = 4, 5 Hz), 148.5 (dd, J = 13, 245 Hz), 150.1 (dd, J = 12, 247 Hz), 159.2 (dd, J = 39, 241 Hz); MS *m/z* (rel intensity) 340 (M^+, 8), 320 (6), 193 (15), 179 (31), 166 (16), 153 (24), 140 (69), 127 (100), 111 (7), 97 (12), 81 (25), 80 (8), 79 (23), 77 (17), 67 (31). Found: *m/z* 340.1811. Calcd for $C_{20}H_{24}F_4$: M, 340.1814.

1-{*trans*-1-[(*Z*)-1,2-Difluoroethenyl)]cyclohexyl}-*trans*-4-pentylcyclohexane (*cis*-6c) and **1-{*trans*-1-[(*E*)-1,2-Difluoroethenyl)]cyclohexyl}-*trans*-4-pentylcyclohexane**

(*trans*-**6c**). A solution of compound **5c** (1.13 g, 2.7 mmol) in *o*-xylene (15 mL) was heated at 170 °C for 16 h. Concentration *in vacuo* followed by flash column chromatography (hexane) gave *cis*-**6c** (0.44 g, 55% yield) and *trans*-**6c** (143 mg, 18% yield).

cis-**6c**: phase transition temperature/°C: Cr 20 S_B 22 N 70 Iso (DSC on 2nd heating); R_f = 0.32 (hexane). IR 3131, 2924, 2853, 2361, 1719, 1451, 1377, 1329, 1310, 1242, 1190, 1138, 1123, 1103, 980, 772, 733 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.34 (m, 22 H), 1.66-2.04 (m, 9 H), 6.22 (ddd, *J* = 1, 17, 74 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –140.26 (ddd, *J* = 11, 17, 17 Hz, 1 F), –171.52 (ddd, *J* = 4, 11, 74 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.3 (s), 29.4 (s), 30.0 (s), 32.2 (s), 33.6 (s), 37.2 (d, *J* = 21 Hz), 37.4 (s), 37.9 (s), 42.7 (s), 43.3 (s), 132.2 (dd, *J* = 14, 249 Hz), 153.5 (dd, *J* = 6, 255 Hz); MS *m/z* (rel intensity) 299 (M^++1, 3), 298 (M^+, 13), 269 (2), 242 (2), 227 (11), 207 (3), 186 (8), 172 (8), 151 (18), 137 (14), 121 (7), 109 (21), 97 (79), 95 (46), 83 (91), 81 (87), 69 (81), 67 (100). Found: C, 76.18; H, 10.68%. Calcd for $C_{19}H_{32}F_2$: C, 76.46; H, 10.81%.

trans-**6c**: phase transition temperature/°C: Cr 34 S_B 38 N 41 Iso (DSC on 2nd heating); R_f = 0.60 (hexane). IR (KBr) 2924, 2851, 1447, 1379, 1339, 1258, 1210, 1123, 795, 600 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.50 (m, 22 H), 1.67-1.81 (m, 8 H), 2.38-2.67 (m, 1 H), 6.97 (dd, *J* = 4, 78 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –169.37 (ddd, *J* = 4, 29, 127 Hz, 1 F), –185.12 (ddd, *J* = 4, 78, 127 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 28.8 (d, *J* = 2 Hz), 29.5 (s), 30.0 (s), 32.3 (s), 33.6 (s), 35.8 (d, *J* = 22 Hz), 37.5 (s), 38.0 (s), 42.5 (s), 43.4 (s), 138.2 (dd, *J* = 69, 237 Hz), 159.3 (dd, *J* = 38, 241 Hz); MS *m/z* (rel intensity) 298 (M^+, 14), 242 (5), 207 (8), 191 (5), 173 (5), 151 (18), 149 (22), 137 (15), 121 (15), 109 (35), 97 (88), 95 (51), 83 (92), 81 (80), 71 (55), 69 (100), 67 (95). Found: *m/z* 298.2475. Calcd for $C_{19}H_{32}F_2$: M, 298.2472.

1-{*trans*-1-[(*Z*)-2,3-Difluoro-2-propenyl)]cyclohexyl}-*trans*-4-pentylcyclohexane (*cis*-6d) and **1-{*trans*-1-[(*E*)-2,3-Difluoro-2-propenyl)]cyclohexyl}-*trans*-4-pentylcyclohexane (*trans*-6d).** Compounds *cis*-**6d** (0.36 g, 45% yield) and *trans*-**6d** (0.23 g, 29% yield) were isolated from **5d** (1.14 g, 2.60 mmol) and showed following properties.

cis-**6d**: phase transition temperature/°C: Cr 57 S_B 80 Iso (DSC on 2nd heating); R_f = 0.71 (hexane). IR (KBr) 2951, 2907, 2847, 1727, 1441, 1325, 1223, 1200, 1148, 1113, 876, 797, 689, 586 cm^{-1}; ^1H NMR (200 MHz) δ = 0.80-1.52 (m, 23 H), 1.66-2.00 (m, 10 H), 6.18 (dd, *J* = 17, 74 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –134.80 (ddt, *J* = 10, 17, 23 Hz, 1 F), –166.17 (tdd, *J* = 4, 10, 74 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 26.7 (s), 29.7 (s), 30.1 (s), 32.3 (s), 33.0 (s), 33.6 (s), 34.6 (s), 34.9 (s), 37.5 (s), 37.9 (s), 43.1 (s), 43.3 (s), 132.9 (dd, *J* = 14, 251 Hz), 148.4 (dd, *J* = 6, 253 Hz); MS *m/z* (rel

intensity) 313 (M^++1, 0.2), 312 (M^+, 2), 241 (1), 160 (1), 153 (4), 151 (4), 139 (6), 123 (11), 111 (15), 109 (15), 97 (66), 95 (25), 83 (100), 81 (48), 79 (18), 71 (17), 69 (71), 67 (56). Found: *m/z* 312.2632. Calcd for $C_{20}H_{34}F_2$: M, 312.2629.

trans-**6d**: phase transition temperature/°C: Cr 2 S_B 80 Iso (DSC on 2nd heating); R_f = 0.83 (hexane). IR 2921, 2851, 1730, 1447, 1262, 1229, 1146, 1115, 895, 793 cm^{-1}; ^1H NMR (200 MHz) δ = 0.84-1.51 (m, 23 H), 1.66-1.81 (m, 8 H), 2.23 (ddd, *J* = 6, 6, 25 Hz, 2 H), 7.08 (dd, *J* = 4, 78 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –157.75 (dtd, *J* = 4, 25, 128 Hz, 1 F), –183.51 (tdd, *J* = 6, 78, 128 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 26.7 (s), 29.8 (s), 30.1 (s), 32.3 (s), 33.1 (s), 33.7 (s), 33.73 (dd, *J* = 2, 22 Hz), 34.9 (dd, *J* = 2, 2 Hz), 37.5 (s), 38.0 (s), 43.1 (s), 43.4 (s), 139.9 (dd, *J* = 67, 237 Hz), 155.2 (dd, *J* = 40, 240 Hz); MS *m/z* (rel intensity) 313 (M^++1, 3), 312 (M^+, 14), 235 (6), 179 (4), 165 (6), 151 (15), 139 (27), 123 (22), 109 (30), 97 (94), 95 (40), 83 (100), 81 (66), 69 (67), 67 (64). Found: *m/z* 312.2620. Calcd for $C_{20}H_{34}F_2$: M, 312.2629.

1-{*trans*-1-[(*Z*)-3,4-Difluoro-3-butenyl)]cyclohexyl}-*trans*-4-pentylcyclohexane (*cis*-6e) and **1-{*trans*-1-[(*E*)-3,4-Difluoro-3-butenyl)]cyclohexyl}-*trans*-4-pentyl-cyclohexane (*trans*-6e).** Compounds *cis*-**6e** (0.34 g, 39% yield) and *trans*-**6e** (0.22 g, 25% yield) were obtained from **5e** (1.2 g, 2.7 mmol) by a procedure similar to that for **6c**.

cis-**6e**: phase transition temperature/°C: Cr 20 S_B 84 N 89 Iso (DSC on 2nd heating); R_f = 0.69 (hexane). IR 2923, 2853, 1727, 1468, 1449, 1335, 1271, 1202, 1138, 1121, 885, 774 cm^{-1}; ^1H NMR (200 MHz) δ = 0.72-1.45 (m, 25 H), 1.57-1.85 (m, 8 H), 2.05-2.20 (m, 2 H), 6.20 (dd, *J* = 17, 74 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –135.71 (ddt, *J* = 11, 17, 19 Hz, 1 F), –167.74 (tdd, *J* = 5, 11, 74 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.7 (s), 24.8 (d, *J* = 22 Hz), 26.7 (s), 29.9 (s), 30.1 (s), 32.3 (s), 33.1 (d, *J* = 3 Hz), 33.2 (s), 33.6 (s), 37.1 (s), 37.5 (s), 37.9 (s), 43.3 (s), 43.4 (s), 132.3 (dd, *J* = 14, 250 Hz), 149.8 (dd, *J* = 6, 253 Hz); MS *m/z* (rel intensity) 327 (M^++1, 5), 326 (M^+, 11), 255 (7), 247 (16), 239 (13), 205 (11), 178 (15), 154 (21), 148 (13), 144 (17), 142 (13), 107 (39), 106 (35), 97 (100), 89 (19), 80 (22), 67 (50). Found: *m/z* 326.2783. Calcd for $C_{21}H_{36}F_2$: M, 326.2785.

trans-**6e**: phase transition temperature/°C: Cr 3 S_B 83 Iso (DSC on 2nd heating); R_f = 0.80 (hexane). IR 2925, 2851, 1719, 1672, 1655, 1468, 1449, 1379, 1339, 1298, 1215, 1208, 1137, 1122, 895, 791 cm^{-1}; ^1H NMR (200 MHz) δ = 0.75-1.47 (m, 25 H), 1.63-1.85 (m, 8 H), 2.26-2.48 (m, 2 H), 7.03 (dd, *J* = 4, 78 Hz, 1 H); ^{19}F NMR (188 MHz) δ = –160.58 (dtd, *J* = 4, 23, 128 Hz, 1 F), –184.22 (tdd, *J* = 6, 78, 128 Hz, 1 F); ^{13}C NMR (75.5 MHz) δ = 14.1 (s), 22.8 (s), 23.6 (d, *J* = 22 Hz), 26.7 (s), 29.9 (s), 30.1 (s), 32.3 (s), 32.8 (d, *J* = 1 Hz), 33.2 (s), 33.7 (s), 37.2 (s), 37.4 (s), 37.5 (s), 38.0 (s), 43.37 (s), 43.45 (s), 139.1 (dd, *J* = 68, 237 Hz), 156.4 (dd, *J* = 40, 239 Hz); MS *m/z* (rel intensity) 327 (M^++1, 2), 326 (M^+, 7), 306 (3), 248 (14), 233 (3), 192 (2), 172 (6), 152 (13), 137 (9), 123 (7), 111

(24), 97 (100), 83 (88), 81 (58), 69 (59), 67 (65). Found: *m/z* 326.2794. Calcd for $C_{21}H_{36}F_2$: M, 326.2785.

VII-5. References and Notes

1) a) T. Hiyama, *"Organofluorine Compounds, Chemistry and Applications,"* Springer, Berlin (2000); b) M. Hudlicky and A. E. Pavlath, Eds., *"Chemistry of Organic Fluorine Compounds II. A Critical Review,"* ACS Monograph 187, Washington, DC (1995); c) T. Kitazume, T. Ishikawa, and T. Taguchi, "Fusso no Kagaku," Kodansha, Tokyo (1993).

2) a) J. T. Welch, *Tetrahedron,* **43**, 3123 (1987); b) R. E. Banks, Ed., *"Preparation, Properties, and Industrial Applications of Organofluorine Compounds,"* Ellis Horwood, New York (1982); c) Y. Kobayashi, I. Kumadaki, and T. Taguchi, Eds., *"Fusso Yakugaku,"* Hirokawa Shoten, Tokyo (1992); d) J. T. Welch and S. Eswarakrishnan, *"Fluorine in Bioorganic Chemistry,"* John Wiley & Sons, New York (1991).

3) a) T. Inukai, K. Miyazawa, *Ekisho,* **1**, 9 (1997); b) G. W. Gray, M. Hird, and K. J. Toyne, *Mol. Cryst. Liq. Cryst.,* **204**, 91 (1991); c) R. Eidenschink, *Mol. Cryst. Liq. Cryst.,* **94**, 119 (1983); d) Y. Goto, T. Ogawa, S. Sawada, and S. Sugimori, *Mol. Cryst. Liq. Cryst.,* **209**, 1 (1991).

4) a) M. Kuroboshi, K. Mizuno, K. Kanie, and T. Hiyama, *Tetrahedron Lett.,* **36**, 563 (1995); b) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Chem. Lett.,* **1995**, 683; c) K. Kanie, K. Mizuno, M. Kuroboshi, S. Takehara, and T. Hiyama, *Bull. Chem. Soc. Jpn.,* **72**, 2523 (1999); d) K. Kanie, Y. Tanaka, M. Shimizu, S. Takehara, and T. Hiyama, *Chem. Lett.,* **1997**, 827; e) K. Kanie, M. Kuroboshi, S. Takehara, and T. Hiyama, *J. Fluorine Chem.,* **97**, 75 (1999); f) P. Kirsch, M. Bremer, M. Heckmeier, and K. Tarumi, *Angew. Chem. Int. Ed.,* **38**, 1989 (1999); g) P. Kirsch and K. Tarumi, *Angew. Chem. Int. Ed.,* **37**, 484 (1998); h) P. Kirsch, V. Reiffenrath, and M. Bremer, *Synlett,* **1999**, 389; i) P. J. Collings and M. Hird, *"Introduction to Liquid Crystals, Chemistry and Physics,"* Taylor & Francis, London (1997); j) M. Hird, G. W. Gray, and J. Toyne, *Liq. Cryst.,* **11**, 531 (1992); k) H. Takatsu, K. Takeuchi, M. Sasaki, H. Ohnishi, and M. Schadt, *Mol. Cryst. Liq. Cryst.,* **206**, 159 (1991); l) H. Liu and H. Nohira, *Liq. Cryst.,* **22**, 217 (1997); m) H. Nohira, *Nippon Kagaku Kaishi,* **1994**, 467.

5) M. Schadt, R. Buchecker, and A. Villiger, *Liq. Cryst.,* **7**, 519 (1990).

6) a) K. Kitazima, O. Yokokohji, T. Tachibana, and S. Inoue, The 23rd Symposium

on Liquid Crystals, 2PA12, Tokyo, 1997; b) F. Roussel, J.-P. Bayle, M. A. Khan, B. M. Fung, O. Yokokohji, T. Shimizu, H. Koh, and S. Kumai, *Liq. Cryst.*, **26**, 251 (1999).

7) K. Kanie, Y. Tanaka, S. Takehara, and T. Hiyama, *Chem. Lett.*, **1998**, 1169.

8) Phase transition behaviors of LCs having a difluoro olefinic functionality were reported, B. Ekkehard, Japan Kokai Tokkyo Koho 6-500343 (1994); B. Ekkehard, P. Herbert, E. Rudolf, R. Volker, P. Detlef, P. Eike, S. Sabine, M. Volker, J. Michael, and H. Reinhard, *Chem. Abstr.*, **120**, 285950r (1994).

9) a) S. Martin, R. Sauvetre, and J. F. Normant, *Tetrahedron Lett.*, **24**, 5615 (1983); b) S. Martin, R. Sauvetre, and J. F. Normant, *J. Organomet. Chem.*, **264**, 155 (1984).

10) F. Tellier, R. Sauvetre, and J. F. Normant, *J. Organomet. Chem.*, **292**, 19 (1985).

11) T. Dubuffet, R. Sauvetre, and J. F. Normant, *J. Organomet. Chem.*, **341**, 11 (1988).

12) A. S. Kende and P. Fludzinski, *J. Org. Chem.*, **48**, 1384 (1983).

13) S. A. Fontana, C. R. Davis, Y. B. He, and D. J. Burton, *Tetrahedron*, **52**, 37 (1996).

14) M. Fujita, M. Obayashi, and T. Hiyama, *Tetrahedron*, **44**, 4135 (1988).

15) Preparative methods of 1,1-difluoro olefins by way of oxidative fluorination of organosulfur compounds are reported in a) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 1939 (1998); b) K. Kim and J. R. McCarthy, *Tetrahedron Lett.*, **37**, 3223 (1996).

16) A. E. Asato and R. S. H. Liu, *Tetrahedron Lett.*, **27**, 3337 (1986).

17) J. Leroy, *J. Org. Chem.*, **46**, 206 (1981).

18) M. Shimizu, N. Yamada, Y. Takebe, T. Hata, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 2903 (1998).

19) C. Saluzzo, *Bull. Soc. Chim. Fr.*, **131**, 831 (1994).

20) a) S. Furuta, M. Kuroboshi, and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **71**, 2687 (1998); b) J. R. McCarthy, N. P. Peet, M. E. LeTourneau, and M. Inbasekaran, *J. Am. Chem. Soc.*, **107**, 735 (1985); c) M. J. Robins and S. F. Wnuk, *J. Org. Chem.*, **58**, 3800 (1993); d) S. F. Wnuk and M. J. Robins, *J. Org. Chem.*, 55, 4757 (1990); e) T. Umemoto and G. Tomizawa, *Bull. Chem. Soc. Jpn.*, **59**, 3625 (1986); f) G. S. Lal, *Synth. Commun.*, **25**, 725 (1995); g) T. Fuchigami, M. Shimojo, A. Konno, and K. Nakagawa, *J. Org. Chem.*, **55**, 6074 (1990); h) T. Brigaud and E. Laurent, *Tetrahedron Lett.*, **31**, 2287 (1990); i) S. Higashiya, T. Sato, and T. Fuchigami, *J. Fluorine Chem.*, **87**, 203 (1998); j) R. K. Marat and A. F. Janzen, *Can. J. Chem.*, **55**, 3031 (1977).

21) a) M. Fujita, M. Suzuki, K. Ogata, and K. Ogura, *Tetrahedron Lett.*, **32**, 1463 (1991).

22) a) V. Reutrakul and V. Rukachaisirikul, *Tetrahedron Lett.*, **24**, 725 (1983); b) S. T. Purrington and J. H. Pittman, *Tetrahedron Lett.*, **28**, 3901 (1987); c) M. L. Boys, E. W. Collington, H. Finch, S. Swanson, and J. F. Whitehead, *Tetrahedron Lett.*, **29**, 3365 (1988).

23) M. Kuroboshi and T. Hiyama, *Bull. Chem. Soc. Jpn.*, **68**, 1799 (1995).

24) Diastereoselectivity in the fluoro-Pummerer reaction is not high in general: a) S. Narizuka, H. Koshiyama, A. Konno, and T. Fuchigami, *J. Fluorine Chem.*, **73**, 121 (1995); b) M. J. Robins and S. F. Wnuk, *J. Org. Chem.*, **58**, 3800 (1993).

25) Disproportionation of sulfenic acid is discussed by R. Schubart, in "*Methoden der Organischen Chemie,*" **E11**, ed. by D. Klamann, Thieme, Stuttgart, New York, (1985), p. 63.

List of Publications

Chapter II

1. Synthesis of Trifluoromethylamino-substituted Pyridines and Pyrimidines by Oxidative Desulfurization-Fluorination
   Manabu Kuroboshi, Katsuya Mizuno, *Kiyoshi Kanie*, and Tamejiro Hiyama
   Tetrahedron Lett., **36**, 563-566 (1995).
2. A Facile Synthesis of Trifluoromethylamines by Oxidative Desulfurization-Fluorination of Dithiocarbamates
   Kiyoshi Kanie, Katsuya Mizumo, Manabu Kuroboshi, and Tamejiro Hiyama
   Bull. Chem. Soc. Jpn., **71**, 1973-1991 (1998).

Chapter III

3. Synthesis and Properties of New Liquid Crystals Containing a Trifluoromethylamino Group
   Kiyoshi Kanie, Katsuya Mizuno, Manabu Kuroboshi, Sadao Takehara, and Tamejiro Hiyama
   Chem. Lett., **1995**, 683-684.
4. Syntheses and Properties of Novel Liquid Crystals Containing a Trifluoromethylamino Group
   Kiyoshi Kanie, Katsuya Mizuno, Manabu Kuroboshi, Sadao Takehara, and Tamejiro Hiyama
   Bull. Chem. Soc. Jpn., **72**, 2523-2535 (1999).

Chapter IV

5. Oxidative Desulfurization-Fluorination of Alkanol Xanthates. Control of the Reaction Pathway to Fluorination or Trifluoromethoxylation
   Kiyoshi Kanie, Yoichiro Tanaka, Masaki Shimizu, Manabu Kuroboshi, and Tamejiro Hiyama
   Chem. Commun., **1997**, 309-310.
6. A Convenient Synthesis of Trifluoromethyl Ethers by Oxidative Desulfurization-Fluorination of Dithiocarbonates
   Kiyoshi Kanie, Yoichiro Tanaka, Kazundo Suzuki, Manabu Kuroboshi, and Tamejiro Hiyama
   Bull. Chem. Soc. Jpn., **73**, 471-484 (2000).

Chapter V

7. Synthesis and Electro-optical Properties of 3-Substituted Phenyl Trifluoromethyl Ethers
   Kiyoshi Kanie, Manabu Kuroboshi, Sadao Takehara, and Tamejiro Hiyama
   J. Fluorine Chem., **97**, 201-206 (1999).

Chapter VI

8. Synthesis and Electro-optical Properties of Novel Liquid Crystals Having a Cyclohexyl Trifluoromethyl Ether Moiety
   Kiyoshi Kanie, Yoichiro Tanaka, Masaki Shimizu, Sadao Takehara, and Tamejiro Hiyama
   Chem. Lett., **1997**, 827-828.
9. A Facile Synthesis and Electro-optical Properties of Novel Liquid Crystalline Materials Having a Trifluoromethoxy Group
   Kiyoshi Kanie, Sadao Takehara, and Tamejiro Hiyama
   Bull. Chem. Soc. Jpn., in press.

Chapter VII

10. A Facile Synthesis and Electro-optical Properties of New Liquid Crystals Having a *vic*-Difluoro Olefinic Moiety
    Kiyoshi Kanie, Yoidhiro Tanaka, Sadao Takehara, and Tamejiro Hiyama
    Chem. Lett., **1998**, 1169-1170.
11. A Facile Conversion of Olefins to *vic*-Difluoro Olefins: Electro-optical Properties of Liquid Crystalline Materials Having a *vic*-Difluoro Olefinic Moiety
    Kiyoshi Kanie, Yoichiro Tanaka, Sadao Takehara, and Tamejiro Hiyama
    Bull. Chem. Soc. Jpn., **73**, *in press.*

The Author also contributed to the following papers and books.

12. Reactions of *o*-Bromoacetylacylphenons with Several Primary Amines
    Seiko Nan'ya, Hirofumi Ishida, *Kiyoshi Kanie*, Noriyuki Ito, and Yasuo Butsugan
    J. Heterocyclic Chem., **32**, 1299-1302 (1995).

13. Synthesis and Photochemical Switching of the Antiferroelectric Liquid Crystals Containing a Diazenediyl Group
    Makoto Negishi, *Kiyoshi Kanie*, Tomiki Ikeda, and Tamejiro Hiyama

Chem. Lett., **1996**, 583-584.

14. Induction of Mesophases through the Complexation between Benzoic Acids with Lateral Groups and Polyamides Containing a 2,6-Diaminopyridine Moiety
Osamu Ihata, Hideyuki Yokota, *Kiyoshi Kanie*, Seiji Ujiie, and Takashi Kato
Liq. Cryst., **27**, 69-74 (2000).

15. Optical Switching and Alignment of Antiferroelectric Liquid Crystals Containing an Azo Group
Koichiro Shirota, Ichirou Yamaguchi, *Kiyoshi Kanie*, Tomiki Ikeda, Tamejiro Hiyama, Ichiro Kobayashi, and Yoshiichi Suzuki
Liq. Cryst., 27, 555-558 (2000).

16. Liquid-Crystalline Ion-Conductive Materials: Self-Organization Behavior and Ion-Transporting Properties of Mesogenic Dimers Containing Oxyethylene Moieties Complexed with Metal Salts
Toshihiro Ohtake, Yasuyuki Takamitsu, Kaori Ito-Akita, *Kiyoshi Kanie*, Masahiro Yoshizawa, Tomohiro Mukai, Hiroyuki Ohno, and Takashi Kato
Submitted.

17. Thermotropic Liquid-Crystalline Folic Acid Derivatives: Supramolecular Discotic and Smectic Aggregation
Kiyoshi Kanie, Takayasu Yasuda, Seiji Ujiie, and Takashi Kato
Submitted.

18. Oxidative Desulfurization-Fluorination: Facile Synthesis of Organofluorine Compounds and Development of Fluorine-Containing Novel Liquid-Crystalline Materials
Kiyoshi Kanie, Manabu Kuroboshi, and Tamejiro Hiyama
Nippon Kagaku Kai Shi, in press.

19. *Kiyoshi Kanie* and Takashi Kato, "*Ekisho Binran*", Chapter 4.1, Synthesis of Mesogens, Maruzen, Tokyo, *in press.*

20. Tamejiro Hiyama, "*Organofluorine Compounds: Chemistry and Applications*", Springer, Berlin (2000), (*Kiyoshi Kanie* contributed to Chapters 1, 2, and 7).

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