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Studies on Synthetic Reactions
of Ketene Dithioacetal Derivatives

Suguru Yoshida

2009
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Abbreviations

aq. aqueous
Ar aryl
Boc tert-butoxycarbonyl
br broad (spectral)
Bu butyl
°C degrees Celsius
cia. circa (about)
caled calculated
cat. catalytic
cm centimeter(s)
Co. corporation
cod 1,5-cyclooctadiene
conc. concentrated
Cp cyclopentadienyl
d doublet (spectral)
DMAP 4-(dimethylamino)pyridine
d.r. diastereomer ratio
ed(s.) editor(s)
equiv equivalent(s)
Et ethyl
et al. et alii (and others)
FAB fast atom bombardment
h hour(s)
Hex hexyl
HMPA hexamethylphosphoric triamide
HRMS high-resolution mass spectrum
Hz hertz (s\(^{-1}\))
i iso
IR infrared (spectral)
J coupling constant (spectral)
m multiplet (spectral)
M molar (1 M = 1 mol dm\(^{-3}\))
Me methyl
mg milligram(s)
MHz megahertz
min minute(s)

ml milliliter(s)
mm millimeter(s)
mmol millimole
Mp melting point

n normal

NMR nuclear magnetic resonance
p page(s)
Ph phenyl
ppm parts per million (spectral)
Pr propyl
q quartet (spectral)
ref reference

s (sec) secondary
s singlet (spectral)
t triplet (spectral)

\textit{t (tert)} tertiary

Tf trifluoromethanesulfonyl
THF tetrahydrofuran

TLC thin-layer chromatography
Ts \textit{p}-toluenesulfonyl
1. **Synthesis of Organosulfur Compounds Utilizing Stabilization Effect of Sulfur**

Organic molecules containing sulfur atoms are important compounds ranging from biological intriguing molecules to various organic materials. Moreover, organosulfur compounds are useful synthetic intermediates which are widely used for synthesis of complex compounds because various transformations of C–S bonds into C–H\textsuperscript{2}, C–C\textsuperscript{3}, C–O\textsuperscript{4}, C–N\textsuperscript{5}, C–F\textsuperscript{6}, \textit{etc} have been developed. Therefore, development of synthetic method that employs organosulfur compounds has attracted much attention.

Some characteristics of sulfur atom have been applied for synthesis of organosulfur compounds. A distinctive property of sulfur atom is stabilization of carbanion, carbocation, and carbon-centered radical next to sulfur atom.

1-1. **Reactions Utilizing Stabilization Effect of Sulfanyl Group**

Carbanion next to a sulfanyl group can be prepared from the corresponding sulfide, because the anion is stabilized due to the interaction between carbon-metal bond and the σ\textsuperscript{*} orbital of C–S bond.\textsuperscript{7} For example, phenylthiomethylolithium was readily generated by means of deprotonation of thioanisole with butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) and reacted with a variety of electrophiles such as benzophenone to provide the adducts in high yields (Scheme 1).\textsuperscript{8} Moreover, 1-lithio-1-sulfanylethene was prepared from sulfanylethene with \textit{sec}-butyllithium in the presence of hexamethylphosphoric triamide (HMPA) and also reacted with various electrophiles (Scheme 2).\textsuperscript{9} The products could be easily hydrolyzed into ketone in the presence of mercury chloride.
On the other hand, carbocation and carbon-centered radical next to a sulfanyl group are stabilized by conjugation of the lone pair of sulfur and have been utilized in various reactions, although the π conjugation of the 3p orbital of sulfur to the 2p orbital of carbon is weak. For example, a thionium intermediate, carbocation stabilized by sulfanyl groups, was also utilized in the cyclization of dithioacetal under typical acid catalysis to proceed in high yield (Scheme 3). As described above, intermediates stabilized by sulfanyl groups allow efficient construction of molecular skeleton.

### Scheme 3.

![Scheme 3 diagram](image)

**1-2. Reactions Utilizing Stabilization by Two Sulfanyl Groups**

Two sulfanyl groups strongly stabilize carbanion, carbocation, and carbon-centered radical. The intermediates have provided novel synthetic methods. In addition, gem-dithia compounds such as the dithioacetal can be transformed into carbonyl moiety effectively.

Carbanion stabilized by two adjacent sulfanyl groups can be also prepared by deprotonation.
For instance, treatment of 1,3-dithiane with butyllithium gave 2-lithio-1,3-dithiane which is used as an acyl anion equivalent for synthesis of a variety of carbonyl compounds (Scheme 4).\textsuperscript{11}

Carbocation next to two sulfanyl groups was also utilized to organic synthesis. In the presence of cerium ammonium nitrate as an oxidant, treatment of 2-tributylstannyl-1,3-dithiane with silyl enolate gave ketone in high yield (Scheme 5).\textsuperscript{12} In the reaction, oxidation of 2-stannyl-1,3-dithiane afforded a thionium intermediate followed by nucleophilic attack of silyl enolate to give the product 1.

1-3. Reactions Utilizing Stabilization by both One Sulfanyl and One Sulfinyl Groups

Because sulfoxide is a strong electron withdrawing group, carbanion and carbon-centered radical generated on the carbon sandwiched between sulfanyl and sulfinyl groups are well-stabilized.

Carbanion stabilized by sulfanyl and sulfinyl groups can be readily prepared and has been widely utilized as an acyl anion equivalent. For instance, deprotonation of methyl methylsulfinylmethyl sulfide (FAMSO) proceeded smoothly with sodium hydride and the resulting carbanion reacted with various electrophiles such as benzyl bromide to give the
corresponding product 2 (Scheme 6). The dithioacetal monoxide moiety was transformed into a carbonyl or acetal group under acidic conditions.

Scheme 6.

Carbon-centered radical bearing both sulfanyl and sulfinyl groups would be well-stabilized due to captodative effect. Addition of the radical to various olefins proceeded smoothly (Scheme 7).

Scheme 7.

\[ \text{DLP} = \text{dilauroyl peroxide} \]

1-4. Reactions of Ketene Dithioacetals and Ketene Dithioacetal Monoxides

Anionic, cationic and radical intermediates stabilized by two sulfur atoms have played key roles in organic synthesis. The author thus focused on ketene dithioacetals and ketene dithioacetal monoxides as useful precursors of the intermediates.

Ketene dithioacetals and ketene dithioacetal monoxides were synthesized easily. Typical examples are shown in Schemes 8 and 9. Ketene dithioacetals and ketene dithioacetal monoxides are regarded as ketene equivalents. Ketene dithioacetals are nucleophilic, and most
of ketene dithioacetals are sensitive to air, acid, and moisture which precludes silica gel column purification. On the other hand, ketene dithioacetal monoxides are electrophilic, and compatible with air, acid, moisture, and silica gel.

**Scheme 8.**

```
SR
1. n-BuLi
SR
2. Me₃SiCl
Me₃Si-SR
1. n-BuLi
2. R’CHO
```

**Scheme 9.**

```
ArCHO + SMe⁻ + SMe
Triton B
Ar
```

Anionic, cationic, and radical intermediates generated from ketene dithioacetals and ketene dithioacetal monoxides have been extensively utilized to organic synthesis. Some examples are shown below.

1-4-1. **Reactions via Anionic Intermediates**

Treatment of 2-methylene-1,3-dithiane (3) with alkyl lithium gave 2-alkyl-2-lithio-1,3-dithiane and the resulting anion reacted with alkyl halide to afford dialkyldithiane in high yield (Scheme 10). Ketene dithioacetal monoxides are good Michael acceptors to react with enolates, malonates, or enamines. As exemplified in Scheme 11, treatment of ketene dithioacetal monoxide 4 with lithium enolate gave the corresponding adduct and the resulting anion reacted further with electrophiles such as iodomethane.

**Scheme 10.**

```
n-BuLi + OLi
3
```

**Scheme 11.**

```
[O+SMe]
```

79%
1-4-2. Reactions via Cationic Intermediates

Ketene dithioacetals are nucleophilic, and many reactions with electrophiles in the presence of Lewis acids have been reported. For example, ketene dithioacetal 6 reacted with orthoester 5 in the presence of trityl chloride and tin(II) chloride followed by deprotonation to give ester 7 (Scheme 12).

Moreover, ketene dithioacetal 8 also reacted with acetal or aldehyde smoothly in the presence of trimethylsilyl triflate and the resulting cationic intermediate was trapped with nucleophiles (Scheme 13).

![Scheme 12](image)

![Scheme 13](image)

1-4-3. Reactions via Radical Intermediates

Ketene dithioacetals were rarely used as radical acceptors. For example, α-keto radical generated from β-keto carboxylic acid added to ketene dithioacetal followed by oxidation and deprotonation to afford ketone 9 (Scheme 14).
2. Overview of This Thesis

As described above, ketene dithioacetal derivatives have interesting reactivity. The author thus planned to develop some reactions by utilizing their characteristic reactivity and found several reactions of ketene dithioacetals and ketene dithioacetal monoxides via intermediates well-stabilized by the two sulfur atoms.

2-1. Radical Addition to Ketene Dithioacetal Derivatives (Chapters 1 and 2)

Although ketene dithioacetal derivatives would be good radical acceptors, few radical reactions with ketene dithioacetal derivatives have been reported. Addition of alkyl radical to a ketene dithioacatal derivative gives a radical intermediate which is well-stabilized by the two sulfur atoms. The author developed two radical reactions based on the addition of alkyl radical to 2-methylene-1,3-dithiane or 2-methylene-1,3-dithiane monoxide.

2-1-1. Zirconocene-Catalyzed Alkylative Dimerization of 2-Methylene-1,3-dithiane via a Single Electron Transfer Process to Provide Symmetrical vic-Bis(dithiane) (Chapter 1)

A mixture of tertiary alkyl halide and 2-methylene-1,3-dithiane was treated with butylmagnesium bromide in the presence of a catalytic amount of zirconocene dichloride. The reaction resulted in alkylative dimerization to yield the corresponding vic-bis(dithiane) (Scheme 15). The reaction would proceed as follows. A single electron transfer from low-valent zirconocene to alkyl halide would generate the corresponding alkyl radical. The radical adds to
2-methylene-1,3-dithiane to afford the corresponding radical stabilized by the two sulfur atoms. A couple of the stable radicals finally undergo dimerization.

2-1-2. Radical Addition of Alkyl Halides to 2-Methylene-1,3-dithiane Monoxide as a Ketene Equivalent (Chapter 2)

It is difficult to control the regioselectivity in the radical addition reactions to ketene. Thus, only few radical reactions using ketene have been reported. The author presumed that ketene dithioacetal monoxides should be good candidates for radical acceptors, because radical intermediates, generated by an addition of alkyl radical to ketene dithioacetal monoxides, would be well-stabilized by the sulfanyl and sulfinyl groups due to captodative effect (Scheme 16).

Radical addition reaction of alkyl halides with ketene dithioacetal monoxide in the presence of tributyltin hydride and a catalytic amount of 2,2’-azobis(isobutyronitrile) (AIBN) proceeded...
smoothly to give the corresponding adducts in moderate to high yields (Scheme 17). The products can be transformed into the corresponding aldehydes under acidic conditions.

**Scheme 17.**

\[
\begin{align*}
\text{RX} & \quad (3 \text{ equiv}) \\
+ \quad \text{Bu}_3\text{SnH} (2 \text{ equiv}) \quad \text{AIBN} (0.1 \text{ equiv}) \\
\text{benzene reflux, 2 h} \\
\rightarrow \quad \text{R} \quad \text{S} \quad \text{S} \quad \text{O} \quad \text{R} \\
58-91\% \\
\end{align*}
\]

\(\text{R} = \text{primary, secondary, tertiary alkyl}\)

2-2. **2-Alkylidene-1,3-dithiane Monoxides as Activated Alkenes in Rhodium-Catalyzed Addition Reaction of Arylboronic Acids (Chapter 3)**

Treatment of ketene dithioacetal derivatives with anionic species gives carbanions stabilized by the two sulfur atoms. However, the available nucleophiles had been strictly limited. The author thus focused on a transition-metal-catalyzed addition reaction of nucleophiles. Treatment of 2-alkylidene-1,3-dithiane 1-oxide with arylboronic acid under rhodium catalysis in aqueous dioxane at 25 °C provided the corresponding adduct, which is a useful 2-arylalkanal equivalent (Scheme 18).

**Scheme 18.**

\[
\begin{align*}
\text{ArB(OH)}_2 & \quad (1.2 \text{ equiv}) \\
+ \quad \text{[Rh(OH)(cod)]}_2 (5 \text{ mol%}) \\
\text{1,4-dioxane, H}_2\text{O} \\
25 ^\circ\text{C, 3 h} \\
\rightarrow \quad \text{Ar} \quad \text{S} \quad \text{O} \\
70-99\% \\
\end{align*}
\]

2-3. **Reactions of Ketene Dithioacetal Monoxides with Trifluoromethanesulfonic Anhydride (Chapters 4 and 5)**

Cationic intermediates stabilized by the two sulfur atoms are generated from ketene
dithioacetals and electrophiles. The author planned that reaction of ketene dithioacetal monoxides with trifluoromethanesulfonic anhydride would also give cationic intermediates stabilized by the two sulfur atoms. The reaction resulted in ring-closure or intermolecular Friedel-Crafts arylation, which depends on the substituent R\(^1\) (Scheme 19).

**Scheme 19.**

\[
\begin{align*}
R^2 \text{SR}^3 \text{O}^+ R^1 + \text{Tf}_2\text{O} \rightarrow & \quad \text{R}^2 \text{SR}^3 \text{O}^+ R^1 + 2\text{TfO}^- \\
& \rightarrow \text{R}^2 \text{SMe} \text{Ar} + \text{R}^2 \text{O} \text{ArH} \\
R^1 = \text{Ar, CF}_3 & \quad R^3 = \text{Me} \\
R^1 = \text{H} & \quad \text{ArH}
\end{align*}
\]

**2-3-1. Synthesis of Benzo[b]thiophenes by Cyclization of Arylketene Dithioacetal Monoxides under Pummerer-like Conditions (Chapter 4)**

When R\(^1\) is an aryl or trifluoromethyl group (Scheme 19), ring closure of the stabilized cationic intermediate, generated from arylketene dithioacetal monoxides by the action of trifluoromethanesulfonic anhydride, proceeded smoothly. Treatment of arylketene bis(methylthio)acetal monoxide with trifluoromethanesulfonic anhydride led to ring-closure to afford 2-methylthiobenzo[b]thiophene in high yield (Scheme 20). The reaction is useful for synthesizing multisubstituted benzo[b]thiophenes.

**Scheme 20.**

\[
\begin{align*}
\text{R}^2 \text{SR}^3 \text{O}^+ \text{Me} \text{Tf}_2\text{O} (1.3 \text{ equiv}) K_2\text{CO}_3 (5 \text{ equiv}) & \rightarrow \text{TfO}^- \\
& \rightarrow \text{R}^2 \text{SMe} \text{SMe} \\
& \rightarrow \text{HOCNH}_2 \text{25 °C, 3 h} & \rightarrow \text{86%}
\end{align*}
\]
2-3-2. Extended Pummerer Reaction of Arylketene Dithioacetal Monoxides with Aromatic Compounds by Means of Trifluoromethanesulfonic Anhydride (Chapter 5)

In the case of $R^1 = H$ (Scheme 19), extended Pummerer reaction of arylketene dithioacetal monoxides with aromatic compounds in the presence of trifluoromethanesulfonic anhydride proceeded smoothly (Scheme 21).

Scheme 21.

Additionally, in the case of intramolecular cyclization of (2-arylphenyl)ketene dithioacetal monoxides, phenanthrenes were obtained via ring-closure and skeletal rearrangement (Scheme 22).

Scheme 22.
2-4. **Trifluoromethylketene Dithioacetal Monoxide as a Trifluoromethylketene Equivalent (Chapter 6)**

The author attempted to utilize trifluoromethylketene dithioacetal monoxide as a trifluoromethylketene equivalent. Trifluoromethylketene dithioacetal monoxides 10 would react with nucleophile at C¹ under Pummerer reaction conditions to yield 11 which might be very attractive intermediate for further transformation (Scheme 23). Hydrolysis of ketene dithioacetal 11 could provide thiolester 12 which should react with nucleophile at C² to give α-trifluoromethyl ketone 13. Alternatively, reduction of 11 could afford dithiane 14, which should be converted into carbanion 15 by deprotonation of hydrogen adjacent to two sulfur atoms. Then, the carbanion could behave as an acyl anion equivalent. The addition of electrophile to the anion would provide another route to α-trifluoromethyl ketone 16.

![Scheme 23](image)

The author thus synthesized trifluoromethylketene dithioacetal monoxide. Malonate added to trifluoromethylketene dithioacetal monoxide in a Michael type fashion. The reaction is similar to the reactions of 2-methylene-1,3-dithioacetal monoxide (Scheme 24).

![Scheme 24](image)
The author found interesting reactivity of trifluoromethylketene dithioacetal monoxide in extended Pummerer reaction with allylsilane. Treatment of trifluoromethylketene dithioacetal monoxide with allylsilane in the presence of trifluoromethanesulfonic anhydride and 2,6-di-tert-butylpyridine afforded allylated ketene dithioacetal in good yield (Scheme 25). Interestingly, in the case of \( \gamma \)-substituted allylsilane, carbon-carbon bond formation took place at the \( \alpha \)-position of allylsilane.

Scheme 25.
References and Notes


Chapter 1

Zirconocene-Catalyzed Alkylative Dimerization of 2-Methylene-1,3-dithiane via a Single Electron Transfer Process to Provide Symmetrical vic-Bis(dithiane)

A mixture of tertiary alkyl halide and 2-methylene-1,3-dithiane is treated with butylmagnesium bromide in the presence of a catalytic amount of zirconocene dichloride. The reaction results in alkylative dimerization to yield the corresponding vic-bis(dithiane).
**Introduction**

Since the discovery of a convenient method for generating a low-valent zirconocene complex \( \text{Cp}_2\text{Zr}(1\text{-butene}) \), so-called the Negishi reagent, organic synthesis by using the zirconocene complex has been extensively developed.\(^1\) The reagent provides the corresponding zirconacycles upon treatment with unsaturated compounds such as alkene or alkyne. On the other hand, little attention has been paid to the reaction of \( \text{Cp}_2\text{Zr}(1\text{-butene}) \) with organic halides. Although the reactions with alkenyl or aryl halides result in the conventional oxidative addition reactions,\(^2\) the reactions are usually complicated when alkyl halides are subjected as substrates. From a mechanistic point of view, Schwartz investigated oxidation of \( \text{Cp}_2\text{ZrL}_2 \) (\( \text{L} = \text{PMePh}_2 \) or \( \text{PMe}_2\text{Ph} \)) with \( \text{RX} \) (\( \text{RX} = \text{alkyl halide} \)) and showed that the formal oxidative addition product \( \text{Cp}_2\text{ZrRX} \) was formed.\(^3\) It has been established that the oxidative addition involves the intermediacy of alkyl radicals generated by single electron transfer from zirconocene complexes to alkyl halides. However, the synthetic utility of the zirconocene-mediated single electron transfer remains largely unexplored.

Oshima et al. have been interested in single electron transfer from low-valent zirconocene complexes to organic halides and have applied the zirconocene-mediated electron transfer to intramolecular radical cyclization reactions.\(^4\) Here the author reports zirconocene-mediated intermolecular radical addition reactions of alkyl halides with 2-methylene-1,3-dithiane. The reaction proceeded smoothly to yield \( \text{vic-bis(dithiane)} \)s through dimerization of the sulfur-stabilized radicals generated by the addition of alkyl radicals to 2-methylene-1,3-dithiane.

**Results and Discussion**

Treatment of \( \text{tert-butyl bromide} \) (1a, 0.50 mmol) and 2-methylene-1,3-dithiane (2, 0.60 mmol) with butylmagnesium bromide (1.2 mmol) in the presence of a catalytic amount of zirconocene dichloride (0.10 mmol) in THF at 25 °C provided \( \text{vic-bis(dithiane)} \) 3a in 71% yield.
No products derived from the direct dimerization or disproportionation of the alkyl halide were observed, which underscores the excellent reactivity of 2 as a radical acceptor. Other tertiary alkyl bromides participated in the reaction (entries 2–4). Unfortunately, the reactions of secondary alkyl bromides such as 1e resulted in the formation of the corresponding 3 in much lower yields (entry 5), which was due to lower conversions as well as formations of rather complex mixtures. Use of secondary alkyl iodides led to full conversions, slightly improving the yields of 3 (entries 6 and 7). The reactions of activated tertiary alkyl bromides such as 2-bromo-N,N-diethyl-2-methylpropanamide afforded complex mixtures in which no desired products were observed.

Table 1. Zirconocene-mediated alkylative dimerization of 2-methylene-1,3-dithiane (2)

<table>
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<th>Entry</th>
<th>R-X</th>
<th>1</th>
<th>3</th>
<th>Yield / %</th>
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<tr>
<td>1</td>
<td></td>
<td>1a</td>
<td>3a</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>1b</td>
<td>3b</td>
<td>69</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>1c</td>
<td>3c</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>1d</td>
<td>3d</td>
<td>52</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>1e</td>
<td>3e</td>
<td>21(^a)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>1f</td>
<td>3f</td>
<td>44(^b)</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>1g</td>
<td>3g</td>
<td>42(^b)</td>
</tr>
</tbody>
</table>

\(^a\)The reaction was performed for 4 h. \(^b\)1.5 eq of 2 was used.
The author is tempted to assume the reaction mechanism as follows (Scheme 1), based on the previous reports of Oshima.\textsuperscript{4b,4c} A low-valent zirconocene complex \( \text{Cp}_2\text{Zr}^{\text{II}} \) is initially formed. The zirconocene complex effected single electron transfer to an alkyl halide \( \text{1} \) to generate \( \text{Cp}_2\text{Zr}^{\text{III}} \) and the radical anion of \( \text{1} \). The radical anion immediately liberates a halide ion to yield an alkyl radical. The alkyl radical adds to \( \text{2} \) to generate the corresponding sulfur-stabilized radical. The radical is so stabilized and bulky that the radical is neither captured by \( \text{Cp}_2\text{Zr}^{\text{III}} \) nor abstracts hydrogen from a solvent molecule. Pair of the long-lived radicals finally dimerize to yield \( \text{3} \).\textsuperscript{7} \( \text{Cp}_2\text{Zr}^{\text{III}} \) would be reduced by the action of an excess of \( \text{BuMgBr} \) to form the initial low-valent \( \text{Cp}_2\text{Zr}^{\text{II}} \), although the exact mechanism of the reduction process is not clear.

**Scheme 1.**

![Scheme 1 diagram](image)

The following experiment justifies the intermediacy of alkyl radicals (Scheme 2). Treatment of \( \text{1h} \) under similar reaction conditions afforded \( \text{3h} \) having two cyclopentane rings in high yield. Single electron transfer to \( \text{1h} \) furnishes 6-methyl-5-heptenyl radical (4), which undergoes a well-known 5-exo-trig radical cyclization\textsuperscript{8} to yield radical 5. The following radical addition to \( \text{2} \) and dimerization provided \( \text{3h} \).

**Scheme 2.**

![Scheme 2 diagram](image)
Conclusion

The alkylative dimerization of 2-methylene-1,3-dithiane proceeds with the aid of the BuMgBr/cat.Cp$_2$ZrCl$_2$ combination. Tertiary alkyl bromides are the best alkyl sources. The transformation features single electron transfer from electron-rich zirconocene to alkyl halides. The products, \textit{vic}-bis(dithiane)s, had not been readily accessible. The present easy preparation has made bis(dithiane)s accessible and hence being potentially interesting intermediates.$^9$
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz) and $^{13}$C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl$_3$. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H and relative to CDCl$_3$ at 77.2 ppm for $^{13}$C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. X-ray crystal structure analysis was carried out with a Bruker SMART APEX CCD diffractometer with Mo-Kα radiation. The structure was solved by direct methods and refined by full-matrix least squares methods on F$^2$ with the SHELXL-97. Mass spectra (FAB unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Zirconocene dichloride was purchased from TCI. Butylmagnesium bromide was prepared from magnesium metal and 1-bromobutane in THF. THF was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. All reactions were carried out under argon atmosphere. Halide $^{1}$h was prepared according to the literature.$^{10}$ Dithiane 2 was prepared as described in the following section.

Preparation of 2-methylene-1,3-dithiane (2)

Butyllithium (1.60 M in hexane, 15.9 mL, 25.4 mmol) was added to a solution of 2-trimethylsilyl-1,3-dithiane (4.19 g, 22.1 mmol) in THF (20 mL) at −40 °C. After being stirred for 2 h at the same temperature, paraformaldehyde (0.90 g, 30 mmol) was added to the resulting solution. The reaction mixture was allowed to warm to room temperature gradually over 12 h. Water (20 mL) was added to the reaction mixture, and the mixture was extracted with ethyl
acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure. Distillation (51 °C/0.1 torr) in the presence of hydroquinone (a few milligram) gave 2-methylene-1,3-dithiane ($2$, 1.68 g, 12.7 mmol, 58%). The NMR spectrum of the product was identical with the date described in the literature.\textsuperscript{11}

**Typical procedure for zirconocene-catalyzed alkylative dimerization (Table 1, Entry 1)**

Zirconocene dichloride (29.0 mg, 0.10 mmol) was placed in a flask under an atmosphere of argon. A THF (1.0 mL) solution of 2-methylene-1,3-dithiane ($2$, 80.0 mg, 0.61 mmol) and tert-butyl bromide (67.6 mg, 0.49 mmol) was added. A THF solution of butyllmagnesium bromide (0.86 M, 1.40 mL, 1.2 mmol) was added, and the mixture was stirred at 25 °C for 1 h. The reaction mixture was poured into saturated aqueous NH\textsubscript{4}Cl and extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and concentrated in vacuo. Purification by chromatography on silica gel (hexane) provided 2,2'-bis(2,2-dimethylpropyl)-2,2'-bi-1,3-dithianyl ($3a$, 66.0 mg, 71%).

**Characterization data**

**2-bromo-4-(4-methoxyphenyl)-2-methylbutane (1d)**

IR (neat) 2931, 1613, 1514, 1456, 1248, 1038 cm\textsuperscript{–1}; $^1$H NMR (CDCl\textsubscript{3}) $\delta$ 1.83 (s, 6H), 2.05–2.08 (m, 2H), 2.79–2.82 (m, 2H), 3.81 (s, 3H), 6.85 (dd, $J = 6.5, 2.0$ Hz, 2H), 7.14 (dd, $J = 6.5, 2.0$ Hz, 2H); $^{13}$C NMR (CDCl\textsubscript{3}) $\delta$ 32.2, 34.6, 50.0, 55.6, 67.9, 114.2, 129.6, 133.9, 158.2. HRMS (FAB\textsuperscript{+}) (m/z) Observed: 256.0460 ($\Delta = –1.2$ ppm). Calcd for C\textsubscript{12}H\textsubscript{17}OBr: 256.0463.

**1-iodo-6-methyl-5-heptene (1h)**

IR (neat) 2929, 2855, 1436, 1377, 1224 cm\textsuperscript{–1}; $^1$H NMR (CDCl\textsubscript{3}) $\delta$ 1.44 (tt, $J = 7.5, 7.5$ Hz, 2H), 1.61 (s, 3H), 1.70 (d, $J = 1.0$ Hz, 3H), 1.83 (tt, $J = 7.5, 7.5$ Hz, 2H), 2.01 (dt, $J = 7.5, 7.5$ Hz, 2H),
3.20 (t, $J = 7.5$ Hz, 2H), 5.10 (dt, $J = 7.5, 1.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 7.4, 17.9, 26.0, 27.1, 30.9, 33.4, 124.1, 132.3. Found: C, 40.12; H, 6.30%. Calcd for C$_8$H$_{15}$I: C, 40.35; H, 6.35%.

2,2'-bis(2,2-dimethylpropyl)-2,2'-bi-1,3-dithianyl (3a)

Mp 119–120 °C; IR (nujol) 2925, 2855, 1464, 1456 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.21 (s, 18H), 1.80–2.30 (m, 8H), 2.73 (ddd, $J = 13.5, 4.5, 4.5$ Hz, 4H), 3.20–3.80 (br s, 4H); $^{13}$C NMR (CDCl$_3$) $\delta$ 23.1, 30.4, 31.9, 33.3, 52.3, 67.9. Found: C, 57.24; H, 9.11%. Calcd for C$_{18}$H$_{34}$S$_4$: C, 57.08; H, 9.05%. Crystal data. CCDC 627902, C$_{18}$H$_{34}$S$_4$, $M = 378.69$, orthorhombic, $a = 12.0851(13)$, $b = 11.1164(12)$, $c = 15.2028(17)$ Å, $V = 2042.4(4)$ Å$^3$, $T = 293(2)$ K, space group $Pbca$, $Z = 4$, $\mu$(Mo-$K\alpha$) = 0.461 mm$^{-1}$, 10778 reflections measured, 2214 unique ($R_{int} = 0.0273$) which were used in all calculations. The final $wR(F^2)$ was 1.136 (all data). The largest residual electron density hole was $-0.181$ eÅ$^{-3}$.

2,2'-bis(2,2-dimethyldecyl)-2,2'-bi-1,3-dithianyl (3b)

IR (neat) 2925, 2854, 1468, 1456 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t, $J = 7.0$ Hz, 6H), 1.18 (s, 12H), 1.19–1.33 (m, 24H), 1.43–1.48 (m, 4H), 1.70–2.50 (m, 8H), 2.62–2.78 (m, 4H), 3.00–3.90 (br s, 4H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.4, 23.0, 23.3, 24.5, 29.4, 29.7, 30.0, 30.7, 30.9, 32.2, 36.1, 45.2, 50.3, 68.3. Found: C, 66.57; H, 10.67%. Calcd for C$_{32}$H$_{62}$S$_4$: C, 66.83; H, 10.87%.

2,2'-di[(1-methylcyclohexyl)methyl]-2,2'-bi-1,3-dithianyl (3c)

Mp 107–108 °C; IR (nujol) 2925, 2855, 1464, 1456 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.34 (s, 6H), 1.38–1.68 (m, 20H), 1.80–2.50 (m, 8H), 2.73 (ddd, $J = 13.5, 4.5, 4.5$ Hz, 4H), 3.20–3.80 (br s, 4H); $^{13}$C NMR (CDCl$_3$) $\delta$ 22.4, 23.3, 24.8, 26.6, 30.8, 36.2, 40.5, 52.8, 68.5. HRMS (FAB$^+$) (m/z) Observed: 459.2242 ($\Delta = -1.3$ ppm). Calcd for C$_{24}$H$_{43}$S$_4$ [MH$^+$]: 459.2247.

2,2'-bis[4-(4-methoxyphenyl)-2,2-dimethylbutyl]-2,2'-bi-1,3-dithianyl (3d)

IR (neat) 2919, 2859, 1506, 1464, 1456, 1247, 1176, 1039 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.28 (s,
12H), 1.60–2.50 (m, 12H), 2.55–2.65 (m, 4H), 2.65–2.70 (m, 4H), 3.00–3.60 (m, 4H), 3.79 (s, 6H), 6.82 (dd, $J = 6.5$, 2.0 Hz, 4H), 7.14 (dd, $J = 6.5$, 2.0 Hz, 4H); $^{13}$C NMR (CDCl$_3$) δ 29.7, 30.3, 30.8, 31.8, 36.3, 47.1, 49.5, 55.5, 66.4, 113.9, 129.5, 136.1, 157.7. Found: C, 65.80; H, 8.04%. Calcd for C$_{34}$H$_{50}$O$_2$S$_4$: C, 65.97; H, 8.14%.

2,2'-di(cyclopentylmethyl)-2,2'-bi-1,3-dithianyl (3e)

Mp 118–119 °C; IR (nujol) 2924, 2854, 1456, 1416, 1377, 1284 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.18–1.25 (m, 4H), 1.47–1.64 (m, 8H), 1.90–1.97 (m, 2H), 1.98–2.05 (m, 6H), 2.24 (d, $J = 5.5$ Hz, 4H), 2.37–2.46 (m, 2H), 2.84 (ddd, $J = 14.0$, 7.5, 5.0 Hz, 4H), 3.12 (ddd, $J = 14.0$, 7.5, 5.0 Hz, 4H); $^{13}$C NMR (CDCl$_3$) δ 23.4, 25.0, 28.8, 35.3, 38.2, 45.3, 68.3. Found: C, 59.37; H, 8.25%. Calcd for C$_{20}$H$_{34}$S$_4$: C, 59.64; H, 8.51%.

2,2'-di(2-methylpropyl)-2,2'-bi-1,3-dithianyl (3f)

Mp 126–127 °C; IR (nujol) 2926, 2857, 1456 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.07 (d, $J = 8.0$ Hz, 12H), 1.92 (doublet of septet, $J = 8.0$, 4.5 Hz, 2H), 1.99 (d, $J = 4.5$ Hz, 4H), 2.03–2.10 (m, 2H), 2.29–2.36 (m, 2H), 2.81 (ddd, $J = 14.5$, 7.0, 5.0 Hz, 4H), 3.17 (ddd, $J = 14.5$, 9.0, 4.5 Hz, 4H); $^{13}$C NMR (CDCl$_3$) δ 23.7, 25.7, 26.5, 29.2, 47.8, 68.9. Found: C, 54.77; H, 8.70%. Calcd for C$_{18}$H$_{30}$S$_4$: C, 54.80; H, 8.62%.

2,2'-di(cyclohexylmethyl)-2,2'-bi-1,3-dithianyl (3g)

Mp 114–115 °C; IR (nujol) 2917, 2848, 1654, 1559, 1457 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.00–1.06 (m, 4H), 1.13–1.18 (m, 2H), 1.26–1.34 (m, 4H), 1.55–1.68 (m, 6H), 1.88–2.00 (m, 12H), 2.01–2.10 (m, 2H), 2.79 (ddd, $J = 14.0$, 6.5, 4.5 Hz, 4H), 3.17 (ddd, $J = 14.0$, 9.0, 5.0 Hz, 4H); $^{13}$C NMR (CDCl$_3$) δ 23.7, 26.6, 26.9, 29.3, 35.7, 36.1, 46.4, 69.0. Found: C, 61.30; H, 8.91%. Calcd for C$_{22}$H$_{36}$S$_4$: C, 61.34; H, 8.89%.

2,2'-di(2-cyclopentyl-2-methylpropyl)-2,2'-bi-1,3-dithianyl (3h)
Chapter 1

Mp 131–132 °C; IR (nujol) 2924, 2855, 1684, 1653, 1558 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.25–1.32 (m, 16H), 1.41–1.50 (m, 8H), 1.61–1.68 (m, 4H), 1.70–2.40 (m, 10H), 2.73 (ddd, \(J = 13.5, 4.5, 4.5\) Hz, 4H), 3.00–3.80 (br s, 4H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 23.3, 25.8, 26.2, 27.4, 30.8, 37.8, 50.0, 53.6, 68.4. Found: C, 63.96; H, 9.26%. Calcd for C\(_{26}\)H\(_{46}\)S\(_4\): C, 64.14; H, 9.52%.
References and Notes


5. In the absence of zirconocene dichloride and 2, no reaction took place between 1a and butylmagnesium bromide. The reaction of 1b with butylmagnesium bromide in the presence of zirconocene dichloride and in the absence of 2 afforded a mixture of 2-methyl-1-decene (24%), 2-methyl-2-decene (10%), 2-methyldecane (34%), and 9,9,10,10-tetramethyloctadecane (8%).

6. Use of 0.05 mmol of zirconocene dichloride resulted in a slightly lower yield (65%). Much lower catalyst loadings such as 0.025 mmol led to poor reproducibility.

7. The dimerization is practically irreversible.


Chapter 2

Radical Addition of Alkyl Halides to 2-Methylene-1,3-dithiane Monoxide as a Ketene Equivalent

Radical addition reaction of alkyl halides with ketene dithioacetal monoxide in the presence of tributyltin hydride and a catalytic amount of 2,2’-azobis(isobutyronitrile) (AIBN) proceeds smoothly to provide the corresponding adducts in moderate to high yields.
**Introduction**

Ketene is one of the most important building blocks for synthesis of carbonyl compounds, such as β-lactam and β-lactone.\(^1\) However, few radical reactions using ketene have been reported,\(^3\) because of the difficulty to control the regiochemistry in the addition of radicals to ketene\(^4\) (Scheme 1). Limited numbers of radical addition to ketene equivalents, instead of ketene itself, have also been reported,\(^5\) although the reaction provides us with an alternative route to various carbonyl compounds via radical pathways. Therefore, development of new method for the radical addition reaction to a novel ketene equivalent as radical acceptor would provide a powerful synthetic tool.

![Scheme 1.](image)

The author has been pursuing the synthetic utility of ketene dithioacetal monoxides as ketene equivalents.\(^6\) Ketene dithioacetal monoxides should be good candidates for a radical acceptor, because radical intermediate 2, generated by the addition of alkyl radical to ketene dithioacetal monoxide 1, would be well-stabilized by both sulfanyl and sulfinyl groups due to captodative effect\(^7\) (Scheme 2). The stability of intermediate 2 could prevent undesired side reactions such as polymerization. Here, the author reports radical addition of alkyl halides to ketene dithioacetal monoxide 1 as a ketene equivalent.

![Scheme 2.](image)
Results and Discussion

Tributyltin hydride (2.0 equiv) was added to a mixture of tert-butyl bromide (5a) (3.0 equiv) and ketene dithiocacetal derivative 1a, 1b, or 1c (1.0 equiv) over 1 h in the presence of 0.1 equiv of 2,2'-azobis(isobutyronitrile) (AIBN) as a radical initiator in boiling benzene (Scheme 3). Among three ketene dithiocacetal derivatives, 2-methylene-1,3-dithiane 1-oxide (1a) was found to be the best radical acceptor. The reaction of 5a with 1a afforded 3a in 84% yield. On the other hand, 2-methylene-1,3-dithiane (1c) provided the desired product in only 43% yield upon treatment with 5a. The corresponding adduct, sulfoxide 3a, could be separated by silica-gel column purification without contamination by tin residues due to the high polarity of sulfoxide 3a.

The use of triphenyltin hydride instead of tributyltin hydride could decrease an amount of halide. Thus, the reaction of tert-butyl bromide (5a) (1.0 equiv) with ketene dithiocacetal monoxide 1a (1.2 equiv) in the presence of triphenyltin hydride (2.0 equiv) and AIBN (0.2 equiv) gave the corresponding adduct 3a in 70% yield.

Scheme 3.

\[ \text{5a (3 equiv)} + \text{Bu}_3\text{SnH (2 equiv)}^a \text{AIBN (0.1 equiv)} \rightarrow \text{3a–c} \]

\[ \begin{align*}
1a & \quad 84\% (70\%)^b \\
1b & \quad 0\%
\end{align*} \]

\[ \begin{align*}
1c & \quad 43\%
\end{align*} \]

^aSlow addition over 1h.
^b5a (1.0 equiv), 1a (1.2 equiv), AIBN (0.2 equiv), Ph3SnH (2.0 equiv, slow addition over 1h), benzene, reflux, 2 h.
Then, the author examined the scope of alkyl halides (Table 1). In the case of tertiary alkyl bromides (entries 1–4), desired products were obtained in high yields. The phenylthio group was tolerated under the reaction conditions (entry 4). Secondary and primary alkyl halides also underwent the radical reaction smoothly with 1a. Secondary alkyl iodides 5e and 5f gave the corresponding adducts in good yields in the reaction with 1a, although the products were mixtures of two diastereomers. Primary alkyl iodide 5g reacted with 1a to provide 3g in moderate yield.

![Reaction of sulfoxide 1a with alkyl halide in the presence of tributyltin hydride and a catalytic amount of AIBN.](image)

**Table 1.** Reaction of sulfoxide 1a with alkyl halide in the presence of tributyltin hydride and a catalytic amount of AIBN.

<table>
<thead>
<tr>
<th>Entry</th>
<th>RX</th>
<th>5</th>
<th>3</th>
<th>Yield / %&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Br</td>
<td>5a</td>
<td>3a</td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td>n-C&lt;sub&gt;8&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;Br</td>
<td>5b</td>
<td>3b</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>Br</td>
<td>5c</td>
<td>3c</td>
<td>91 (d.r. = 17:1)</td>
</tr>
<tr>
<td>4</td>
<td>PhS&lt;sub&gt;5&lt;/sub&gt;Br</td>
<td>5d</td>
<td>3d</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>I</td>
<td>5e</td>
<td>3e</td>
<td>75&lt;sup&gt;b&lt;/sup&gt; (d.r. = 8:1)</td>
</tr>
<tr>
<td>6</td>
<td>I</td>
<td>5f</td>
<td>3f</td>
<td>80&lt;sup&gt;b&lt;/sup&gt; (d.r. = 6:1)</td>
</tr>
<tr>
<td>7</td>
<td>n-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;I</td>
<td>5g</td>
<td>3g</td>
<td>58&lt;sup&gt;b&lt;/sup&gt; (d.r. = 3:1)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yields. <sup>b</sup>AIBN (0.2 equiv).

The author next examined the utility of the products (Scheme 4). The dithioacetal monoxide moiety could be removed smoothly without using toxic mercury reagents. Treatment of
sulfoxide 3b with a catalytic amount of sulfuric acid in hot toluene afforded aldehyde 6 in almost quantitative yield. In addition, sulfoxide 3b could be reduced easily into 1,3-dithiane. Treatment of sulfoxide 3b with trifluoroacetic anhydride and sodium iodide gave 1,3-dithiane 7 in high yield.

Scheme 4.

In order to develop the further utility of the radical addition products of ketene dithioacetal monoxide, tertiary alkyl bromide 8 bearing an amide moiety was subjected to the reaction with 1a. The reaction proceeded efficiently to give desired adduct 9 in high yield. Then, the product 9 was treated with hydrochloric acid followed by an addition of benzoyl chloride to provide dihydropyrrole 10 bearing a quaternary carbon atom in good yield. This result shows that the radical addition reaction would be useful for the synthesis of heterocycles bearing such a quaternary carbon moiety.

Scheme 5.
Chapter 2

Conclusion

The author has developed radical addition reaction of alkyl halides to 2-methylene-1,3-dithiane 1-oxide as a ketene equivalent in the presence of tributyltin hydride and a catalytic amount of AIBN. The reaction afforded alkanal equivalents protected as dithioacetal monoxide, which can be removed easily with sulfuric acid. The products would be subjected to a variety of organic transformations.
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz) and $^{13}$C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl$_3$. Chemical shifts ($\delta$) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H and relative to CDCl$_3$ at 77.23 ppm for $^{13}$C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (FAB unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Benzene was purchased from Wako Pure Chemical and dried over slices of sodium. Substrates 1a and 1b were prepared according to the literature.$^{10,11}$ Dithiane 1c was prepared as described in Chapter 1. Most of alkyl halides 5 and AIBN were purchased from Wako Pure Chemical. Alkyl halides 5b$^{12}$ and 5d$^{13}$ were prepared by bromination of the corresponding alcohol with hydrobromic acid. Tributyltin hydride and triphenyltin hydride were purchased from Aldrich. Alkyl halides 8 was prepared according to the literature.$^9$ All reactions were carried out under argon atmosphere.

Typical procedure for radical addition to 1a (Table 1, Entry 1)

A benzene (1.0 mL) solution of 2-methylene-1,3-dithiane 1-oxide (1a, 49.4 mg, 0.33 mmol), 2-bromo-2-methylpropane (0.10 mL, 0.89 mmol), and 2,2'-azobis(isobutyronitrile) (5.0 mg, 0.030 mmol) was placed in a flask under an atmosphere of argon. Then, a benzene (1.0 mL) solution of tributyltin hydride (0.18 mL, 0.66 mmol) was added over 1 h with a syringe pump at reflux. After the addition was completed, the mixture was stirred for additional 1 h at the same
temperature. The reaction mixture was poured into sat. aq NaHCO$_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 1/2) provided 2-(2,2-dimethylpropyl)-1,3-dithiane 1-oxide (3a, 58.0 mg, 84%).

Characterization data

**2-(2,2-dimethylpropyl)-1,3-dithiane 1-oxide (3a)**

IR (neat) 2955, 2907, 2868, 2844, 1474, 1425, 1367, 1241 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.05 (s, 9H), 1.41 (dd, $J = 14.5$, 4.5 Hz, 1H), 2.25–2.34 (m, 1H), 2.37 (d, $J = 14.5$ Hz, 1H), 2.45–2.50 (m, 1H), 2.53–2.58 (m, 1H), 2.67 (ddd, $J = 10.0$, 10.0, 2.0 Hz, 1H), 2.75 (dd, $J = 12.0$, 12.0 Hz, 1H), 3.40–3.45 (m, 1H), 3.56 (d, $J = 9.5$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 29.4, 30.2, 30.6, 31.4, 42.1, 53.9, 63.0. Found: C, 52.55; H, 8.75%. Calcd for C$_9$H$_{18}$OS$_2$: C, 52.38; H, 8.79%.

**2-(2,2-dimethyldecyl)-1,3-dithiane 1-oxide (3b)**

IR (neat) 2925, 2853, 1468, 1425, 1389, 1367, 1171, 1038, 870, 830, 404 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.87 (t, $J = 7.0$ Hz, 3H), 0.97 (s, 3H), 0.98 (s, 3H), 1.21–1.36 (br, 14 H), 1.41 (dd, $J = 15.0$, 5.0 Hz, 1H), 2.20–2.34 (m, 2H), 2.40–2.58 (m, 2H), 2.64 (ddd, $J = 13.0$, 13.0, 3.0 Hz, 1H), 2.72 (dd, $J = 12.0$, 12.0 Hz, 1H), 3.39 (br d, $J = 12.0$ Hz, 1H), 3.53 (d, $J = 9.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.2, 22.8, 24.1, 27.6, 27.9, 29.2, 29.5, 29.8, 30.4, 30.6, 32.0, 33.7, 40.2, 42.8, 53.9, 62.9. HRMS (FAB$^+$) (m/z) Observed: 305.1979 ($\Delta = +1.9$ ppm). Calcd for C$_{16}$H$_{33}$OS$_2$ [MH$^+$]: 305.1973.

**2-(1-adamantylmethyl)-1,3-dithiane 1-oxide (3c, the major diastereomer)**

Mp 130–131 °C; IR (nujol) 2922, 2853, 1685, 1654, 1559, 1507, 1378, 1279, 1024 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.27 (dd, $J = 15.0$, 4.5 Hz, 1H), 1.58–1.75 (m, 12 H), 1.99 (br s, 3H), 2.20 (d, $J = 15.0$ Hz, 1H), 2.23–2.33 (m, 1H), 2.42–2.56 (m, 2H), 2.65 (ddd, $J = 13.0$, 13.0, 2.0 Hz, 1H), 3.40–3.45 (m, 1H), 3.56 (d, $J = 9.5$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 29.4, 30.2, 30.6, 31.4, 42.1, 53.9, 63.0. Found: C, 52.55; H, 8.75%. Calcd for C$_9$H$_{18}$OS$_2$: C, 52.38; H, 8.79%.
2.75 (dd, $J = 13.0$, 13.0 Hz, 1H), 3.38–3.44 (m, 1H), 3.59 (d, $J = 10.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 28.7, 29.3, 30.5, 33.1, 37.0, 42.8, 42.9, 53.8, 61.2. HRMS (FAB$^+$) (m/z) Observed: 284.1268 ($\Delta = -0.2$ ppm). Calcd for C$_{15}$H$_{24}$O$_2$: 284.1269.

2-(7-phenylthio-2,2-dimethylheptyl)-1,3-dithiane 1-oxide (3d)

IR (neat) 2921, 2853, 1584, 1480, 1471, 1438, 1425, 1367, 1092, 1038, 740, 691 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.99 (s, 6H), 1.26–1.36 (m, 4H), 1.37–1.44 (m, 3H), 1.62–1.70 (m, 2H), 2.22–2.36 (m, 2H), 2.42–2.48 (m, 1H), 2.50–2.55 (m, 1H), 2.65 (ddd, $J = 10.0$, 10.0, 2.0 Hz, 1H), 2.73 (dd, $J = 12.0$, 12.0 Hz, 1H), 2.93 (t, $J = 7.0$ Hz, 2H), 3.38–3.43 (m, 1H), 3.53 (d, $J = 8.0$ Hz, 1H), 7.15–7.19 (m, 1H), 7.26–7.30 (m, 2H), 7.31–7.35 (m, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 23.6, 27.7, 27.8, 29.3, 29.7, 30.5, 33.7, 33.8, 40.1, 42.5, 53.9, 62.7, 125.9, 129.1, 129.2, 137.3. HRMS (FAB$^+$) (m/z) Observed: 370.1462 ($\Delta = +0.9$ ppm). Calcd for C$_{19}$H$_{30}$O$_3$: 370.1459.

2-(cyclohexylmethyl)-1,3-dithiane 1-oxide (3e, the major diastereomer)

Mp 93–94 °C; IR (nujol) 2920, 2853, 1685, 1559, 1507, 1447, 1375, 1023 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.85–1.45 (m, 6H), 1.46–1.76 (m, 5H), 1.80–1.86 (m, 1H), 2.20–2.32 (m, 2H), 2.42–2.48 (m, 1H), 2.52–2.70 (m, 3H), 3.38–3.44 (m, 1H), 3.65 (ddd, $J = 11.0$, 3.5 Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 26.1, 26.3, 26.5, 29.5, 30.1, 32.1, 34.1, 34.2, 36.3, 54.0, 64.1. Found: C, 56.62; H, 8.39%. Calcd for C$_{11}$H$_{20}$O$_2$: C, 56.85; H, 8.67%.

2-(2-methylpropyl)-1,3-dithiane 1-oxide (3f, the major diastereomer)

IR (neat) 2957, 2911, 2869, 2826, 1469, 1426, 1368, 1034, 682, 657 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.97 (d, $J = 6.5$ Hz, 3H), 1.01 (d, $J = 7.0$ Hz, 3H), 1.91–1.96 (m, 1H), 2.16–2.34 (m, 2H), 2.43–2.49 (m, 1H), 2.54–2.72 (m, 3H), 3.38–3.46 (m, 1H), 3.63 (ddd, $J = 11.0$, 3.5 Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 21.4, 23.6, 25.0, 29.5, 30.1, 37.8, 54.0, 64.6. Found: C, 50.06; H, 8.35%. Calcd for C$_8$H$_{16}$O$_2$: C, 49.96; H, 8.38%.
2-heptyl-1,3-dithiane 1-oxide (3g, the major diastereomer)
IR (neat) 2955, 2926, 2855, 1466, 1426, 1036, 754, 698, 663 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.88 (t, $J = 7.0$ Hz, 3H), 1.25–1.50 (m, 9H), 1.62–1.77 (m, 2H), 2.22–2.35 (m, 2H), 2.42–2.49 (m, 1H), 2.57–2.73 (m, 3H), 3.40 (m, 1H), 3.60 (dd, $J = 9.5$, 3.5 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 22.8, 26.0, 28.9, 29.2, 29.5, 29.7, 30.2, 31.9, 54.1, 66.5. HRMS (FAB$^+$) (m/z) Observed: 234.1112 ($\Delta = 0.0$ ppm). Calcd for C$_{11}$H$_{22}$OS$_2$: 234.1112.

3,3-dimethylundecanal (6)
IR (neat) 2958, 2928, 2854, 2729, 1723, 1468, 1368, 1267 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.89 (t, $J = 7.0$ Hz, 3H), 1.04 (s, 6H), 1.23–1.36 (br, 14H), 2.25 (d, $J = 3.0$ Hz, 2H), 9.84 (t, $J = 3.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 22.9, 24.2, 27.8, 29.5, 29.8, 30.5, 32.1, 33.7, 43.0, 55.0, 204.0. HRMS (m/z) Observed: 197.1909 ($\Delta = +1.8$ ppm). Calcd for C$_{13}$H$_{25}$O [M–H]: 197.1905.

2-(2,2-dimethyldecyl)-1,3-dithiane (7)
IR (neat) 2927, 2900, 2853, 1559, 1507, 1458, 1275 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.89 (t, $J = 7.0$ Hz, 3H), 0.95 (s, 6H), 1.23–1.32 (m, 14H), 1.58 (d, $J = 5.5$ Hz, 2H), 1.76–1.86 (m, 1H), 2.05–2.12 (m, 1H), 2.77–2.82 (m, 2H), 2.92–2.99 (m, 2H), 4.04 (t, $J = 5.5$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.4, 22.9, 24.3, 25.6, 27.6, 29.6, 29.9, 30.7, 31.6, 32.1, 34.0, 42.6, 43.5, 48.3. HRMS (m/z) Observed: 288.1941 ($\Delta = –1.5$ ppm). Calcd for C$_{16}$H$_{32}$S$_2$: 288.1945.

2-[2-(tert-butoxycarbonylaminomethyl)-2-ethylbutyl]-1,3-dithiane 1-oxide (9)
IR (neat) 3307, 2880, 1683, 1505, 1366, 1250, 1161, 1022 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.84 (t, $J = 7.5$ Hz, 6H), 1.15–1.40 (m, 5H), 1.41 (s, 9H), 2.18–2.31 (m, 2H), 2.42–2.56 (m, 2H), 2.59–2.66 (m, 1H), 2.72–2.84 (m, 2H), 3.35 (dd, $J = 14.5$, 9.0 Hz, 1H), 3.41–3.50 (m, 2H), 3.80 (br s, 1H); $^{13}$C NMR (CDCl$_3$) δ 7.4, 7.6, 25.5, 26.5, 28.6, 29.6, 31.1, 34.5, 40.5, 44.2, 54.3, 60.4, 78.8, 156.7. HRMS (m/z) Observed: 349.1742 ($\Delta = –1.1$ ppm). Calcd for C$_{16}$H$_{31}$O$_3$NS$_2$: 349.1746.
**N-benzoyl-3,3-diethyl-2,3-dihydropyrrole (10)**

IR (neat) 2963, 2922, 1610, 1578, 1448, 1406, 1374, 831, 716, 700 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 0.90 (t, \(J = 7.5\) Hz, 6H), 1.48–1.56 (m, 4H), 3.74 (s, 2H), 4.99 (d, \(J = 4.0\) Hz, 1H), 6.43 (d, \(J = 4.0\) Hz, 1H), 7.40–7.46 (m, 3H), 7.48–7.52 (m, 2H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 8.8, 31.4, 49.8, 55.0, 119.2, 128.0, 128.6, 129.6, 130.5, 135.8, 167.1. HRMS (m/z) Observed: 229.1466 (\(\Delta = -0.2\) ppm). Calcd for C\(_{15}\)H\(_{19}\)ON: 229.1466.
References and Notes


Chapter 3

2-Alkylidene-1,3-dithiane Monoxides as Activated Alkenes in Rhodium-Catalyzed Addition Reaction of Arylboronic Acids

2-Methylene-1,3-dithiane 1-oxide reacts with arylboronic acids in the presence of a rhodium catalyst in aqueous dioxane to afford 2-arylmethyl-1,3-dithiane 1-oxides in good yields.
Introduction

Ketene dithioacetal and its derivatives are useful two-carbon building blocks as ketene equivalents in organic synthesis.\(^1\) In the course of the author’s studies on the use of ketene dithioacetal as substrates for metal-catalyzed organic reactions,\(^2\) he now reports that 2-alkylidene-1,3-dithiane 1-oxide undergoes rhodium-catalyzed addition of arylboronic acids.\(^3\) Rhodium-catalyzed 1,4-additions of arylboronic acids to α,β-unsaturated carbonyl compounds are extensively studied.\(^4\) On the other hand, the reactions of heteroatom-substituted electron-deficient alkenes are still unexplored.\(^5\)

Results and Discussion

Treatment of 2-methylene-1,3-dithiane 1-oxide (1a) with phenylboronic acid (2a, 1.2 equiv) in the presence of [Rh(OH)(cod)]\(_2\) (5 mol\%, COD = 1,5-cyclooctadiene) in aqueous dioxane at 25 °C for 3 h provided the corresponding adduct 3a in 97% yield (Table 1, entry 1). The reaction afforded the cis isomer, which is a known compound,\(^7\) exclusively, and the trans isomer of 3a was not detected. A variety of arylboronic acids participated in the reaction. The electronic nature of the substituents of arylboronic acids proved to have little influence on the efficiency of the reactions (entries 2–5). Sterically demanding ortho-substituted arylboronic acids 2f and 2g added to 1a under the rhodium catalysis to yield the corresponding adducts in excellent yields (entries 6 and 7). Although alkenylboronic acid 2h was less reactive, use of an excess of 1,5-cyclooctadiene and a larger amount of the rhodium complex led to a satisfactory yield (Scheme 1).
Table 1. Rhodium-Catalyzed Arylation of 1a with Various Arylboronic Acids

<table>
<thead>
<tr>
<th>Entry</th>
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<th>3</th>
<th>Yield / %</th>
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<td>H</td>
<td>2a</td>
<td>3a</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
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</tr>
<tr>
<td>3</td>
<td>4-Me</td>
<td>2c</td>
<td>3c</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>4-CF₃</td>
<td>2d</td>
<td>3d</td>
<td>&gt;99</td>
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<tr>
<td>5</td>
<td>4-MeOOC</td>
<td>2e</td>
<td>3e</td>
<td>90</td>
</tr>
<tr>
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<td>2-BocNH</td>
<td>2g</td>
<td>3g</td>
<td>96</td>
</tr>
</tbody>
</table>

aTwo equivalents of 2g were used.

Scheme 1.

It is worth noting that acyclic ketene dithioacetal monoxide 4 was the less reactive Michael acceptor than cyclic 1a (Scheme 2). Addition of 2a to 4 furnished 5 in only 41% yield, and 40% of 4 was recovered even at an elevated temperature and with an excess of 2a. The reaction of 4 provided a 6:4 (determined by $^1$H NMR) separable mixture of stereoisomers, which is different from the reaction of 1a.
Phenyl-substituted 1b was less reactive because of the steric hindrance of the phenyl group. Although the phenylation reaction of 1b required a longer reaction time and two equivalents of phenylboronic acid, the reaction afforded the corresponding product 6a in high yield with exclusive stereoselectivity (Scheme 3).

The reaction of 1b with arylboronic acid 2d yielded 6b with high diastereoselectivity (Scheme 4). The relative stereochemistry of 6b was unambiguously determined by X-ray crystallographic analysis. Based on the configuration of 6b, the author is tempted to assume the reaction mechanism as follows. Arylrhodium, generated by transmetalation between 2d and the rhodium catalyst, would be coordinated by the oxygen of 1b to form 7. The aryl group on the rhodium would attack to the activated double bond in a diastereoface-selective fashion to yield 8. Protonation of 8 would take place from the same side where the aryl group would have attacked, affording 6b selectively.
The reaction of \(1c\) required a large excess of phenylboronic acid, a larger amount of \([\text{Rh(OH)}(\text{cod})]_2\), and a prolonged reaction time to proceed to completion (Scheme 5). Product \(6c\) was contaminated with a small amount of a stereoisomer, the relative configuration of which the author was unable to assign. Unfortunately, \(\text{gem}\)-diphenyl-substituted 2-alkylidene-1,3-dithiane 1-oxide \(1d\) resisted the reaction (Scheme 6).
The products 3 and 6 are useful building blocks as 2-arylalkanal equivalents. However, a number of attempts to convert 3a to phenylacetaldehyde resulted in either formation of a complex mixture or no conversion. The failure would be due to the instability of phenylacetaldehyde under strongly acidic or basic conditions. Instead, treatment of 3a with ethylene glycol in the presence of sulfuric acid in toluene at 100 °C provided 2-benzyl-1,3-dioxolane (9) in 84% yield (Scheme 7). Deprotonation of 3a with lithium diisopropylamide followed by addition of iodomethane afforded a methylated product 10 in good yield. Intriguingly, attempted acetalization of 10 with ethylene glycol unexpectedly furnished benzyl methyl ketone (11) in high yield.

### Scheme 7.

![Scheme 7](image)

Treatment of 3g with trifluoroacetic anhydride in nitromethane provided N-Boc-protected indole 12 in excellent yield (Scheme 8). The trifluoroacetylation of the sulfoxide followed by the cleavage of the carbon-sulfur bond would afford a cationic intermediate 14. Intramolecular nucleophilic attack of the Boc-protected amino group led to ring closure to yield dihydroindole 15 with concomitant liberation of trifluoroacetate. Elimination of dithiaecyclopentane yielded 12. The series of the transformations from 1a is a new method for constructing indole skeletons.
Conclusion

The author has found rhodium-catalyzed addition of arylboronic acids to ketene equivalents 1. The products are 2-arylalkanal equivalents, which can be subjected to a variety of organic transformation.
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz) and $^{13}$C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl$_3$. Chemical shifts ($\delta$) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H and relative to CDCl$_3$ at 77.2 ppm for $^{13}$C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. X-ray crystal structure analysis was carried out with a Bruker SMART APEX CCD diffractometer with Mo-K$_\alpha$ radiation. The structure was solved by direct methods and refined by full-matrix least squares methods on F$^2$ with the SHELXL-97. Mass spectra (EI unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F$^{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. The rhodium catalyst was prepared according to the literature.$^{12}$ Dioxane was purchased from Wako Pure Chemical and dried over slices of sodium. Distilled water was used for the addition reaction. Substrate 1 was prepared according to the literature.$^{13}$ Most of arylboronic acids 2 were purchased from Wako Pure Chemical. Arylboronic acid 2g was prepared according to the literature.$^{14}$ All reactions were carried out under argon atmosphere.

Typical Procedure for Rhodium-Catalyzed Addition Reaction (Table 1, Entry 1)

$[\text{Rh(OH)(cod)}]_2$ (7.3 mg, 0.016 mmol) was placed in a 20-mL reaction flask under argon. Water (0.30 mL) and a solution of 2-methylene-1,3-dithiane 1-oxide (1a, 44.1 mg, 0.30 mmol) in dioxane (3.0 mL) were added. Phenylboronic acid (2a, 43.8 mg, 0.36 mmol) was added, and the resulting mixture was stirred at 25 °C for 3 h. The mixture was poured into saturated aqueous NaHCO$_3$ (5 mL) and extracted with EtOAc (10 mL × 3). The combined organic layer was dried
over anhydrous sodium sulfate and concentrated in vacuo. Chromatographic purification on silica gel (hexane/AcOEt = 1/2) yielded 2-benzyl-1,3-dithiane 1-oxide (3a, 65.6 mg, 0.29 mmol, 97%).

Transformation of 3a to 9

A toluene (3.0 mL) solution of 1,2-cis-2-benzyl-1,3-dithiane 1-oxide (3a, 69.3 mg, 0.30 mmol) was placed in a flask under an atmosphere of argon. Then, ethylene glycol (0.10 mL, 1.8 mmol) and sulfuric acid (0.050 mL, 0.94 mmol) were added and the mixture was stirred at 100 °C for 2 h. The reaction mixture was poured into saturated aqueous NaHCO$_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 5/1) provided 2-benzyl-1,3-dioxolane (9, 42.0 mg, 84%).

Transformation of 3a to 11

A THF (2.0 mL) solution of diisopropylamine (0.052 mL, 0.37 mmol) was placed in a flask under an atmosphere of argon. Then, butyllithium in hexane (1.6 M, 0.22 mL, 0.36 mmol) was added at 0 °C, and the resulting mixture was stirred for 10 min at the same temperature. The mixture was added to a THF (3.0 mL) solution of 1,2-cis-2-benzyl-1,3-dithiane 1-oxide (3a, 61.3 mg, 0.27 mmol) at –78 °C, and the resulting mixture was stirred for 1 h at the same temperature. Iodomethane (0.037 mL, 0.59 mmol) was then added, and the reaction was allowed to warm to rt gradually over 2 h. The reaction mixture was poured into saturated aqueous NH$_4$Cl (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatographic purification on silica gel (hexane/AcOEt = 1/2) afforded 2-benzyl-2-methyl-1,3-dithiane 1-oxide (10, 52.1 mg, 0.22 mmol, 80%).

A toluene (3.0 mL) solution of 2-benzyl-2-methyl-1,3-dithiane 1-oxide (10, 58.7 mg, 0.26 mmol) was placed in a flask under an atmosphere of argon. Ethylene glycol (0.10 mL, 1.8
mmol) and sulfuric acid (0.050 mL, 0.94 mmol) were added and the mixture was stirred at 100 °C for 1 h. The reaction mixture was poured into saturated aqueous NaHCO$_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Silica gel column purification (hexane/AcOEt = 10/1) provided 1-phenyl-2-propanone (11, 28.4 mg, 0.21 mmol, 87%).

Synthesis of Boc-Protected Indole 12

A nitromethane (4.0 mL) solution of 1,2-cis-2-[2-(tert-butoxycarbonylamino)phenylmethyl]-1,3-dithiane 1-oxide (3g, 70.3 mg, 0.21 mmol) was placed in a flask under an atmosphere of argon. Then, trifluoroacetic anhydride (0.057 mL, 0.41 mmol) was added at 0 °C, and the resulting mixture was stirred for 30 min at the same temperature. The reaction mixture was poured into saturated aqueous NaHCO$_3$ (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 10/1) provided N-tert-butoxycarbonylindole (12, 41.2 mg, 0.19 mmol, 92%).

Characterization Data

Compounds 1a, 4, 3a, 7, 3h, 15 and 4 16 showed the identical spectra reported in the literature. The $^1$H NMR spectra of 9 and 12 are identical to the corresponding commercially available compounds.

(E)-2-(benzylidene)-1,3-dithiane 1-oxide (1b)

Mp 67–68 °C; IR (nujol) 2923, 2854, 1559, 1457, 1057, 752 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.50–2.67 (m, 3H), 2.84–2.92 (m, 2H), 3.42–3.46 (m, 1H), 7.35–7.38 (m, 1H), 7.39–7.44 (m, 2H), 7.53 (s, 1H), 7.77–7.79 (m, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 27.3, 32.0, 55.2, 128.6, 129.4, 130.3, 133.9, 134.7, 137.0. Found: C, 58.84; H, 5.35%. Calcd for C$_{11}$H$_{12}$O$_2$: C, 58.89; H, 5.39%.
(E)-2-ethylidene-1,3-dithiane 1-oxide (1c)
Mp 41–42 °C; IR (nujol) 2923, 2854, 1609, 1457, 1429, 1373, 1040 cm⁻¹; ¹H NMR (CDCl₃) δ 2.03 (d, J = 7.0 Hz, 3H), 2.35–2.45 (m, 1H), 2.52–2.62 (m, 2H), 2.66–2.77 (m, 2H), 3.25–3.32 (m, 1H), 6.74 (q, J = 7.0 Hz, 1H); ¹³C NMR (CDCl₃) δ 14.8, 26.8, 31.4, 54.7, 134.4, 137.2.
Found: C, 44.16; H, 6.20%. Calcd for C₆H₁₀O₂S₂: C, 44.41; H, 6.21%.

2-(diphenylmethylene)-1,3-dithiane 1-oxide (1d)
Mp 203–204 °C; IR (nujol) 2924, 2854, 1559, 1457, 1052, 1043 cm⁻¹; ¹H NMR (CDCl₃) δ 1.94–1.98 (m, 1H), 2.75–2.79 (m, 1H), 2.84–2.90 (m, 1H), 2.94–3.05 (m, 2H), 3.16–3.20 (m, 1H), 7.14–7.16 (m, 2H), 7.20–7.22 (m, 2H), 7.34–7.39 (m, 6H); ¹³C NMR (CDCl₃) δ 15.4, 30.8, 48.1, 128.3, 128.4, 129.0, 129.0, 130.0, 130.3, 136.5, 139.1, 139.7, 153.5. Found: C, 67.94; H, 5.46%. Calcd for C₁₇H₁₆O₂S₂: C, 67.96; H, 5.37%.

1,2-cis-2-(4-methoxyphenylmethyl)-1,3-dithiane 1-oxide (3b)
Mp 112–113 °C; IR (nujol) 2923, 2854, 1610, 1513, 1456, 1247, 1057 cm⁻¹; ¹H NMR (CDCl₃) δ 1.99–2.06 (m, 1H), 2.48–2.55 (m, 1H), 2.60–2.72 (m, 3H), 2.92 (dd, J = 14.5, 5.5 Hz, 1H), 3.00–3.08 (m, 1H), 3.34 (dd, J = 14.5, 9.0 Hz, 1H), 3.80 (s, 3H), 3.84 (dd, J = 9.0, 3.0 Hz, 1H), 6.86–6.89 (m, 2H), 7.20–7.23 (m, 2H); ¹³C NMR (CDCl₃) δ 20.8, 26.1, 31.6, 46.2, 55.5, 61.1, 114.3, 128.7, 130.7, 159.0. Found: C, 56.22; H, 6.29%. Calcd for C₁₂H₁₆O₂S₂: C, 55.93; H, 6.00%.

1,2-cis-2-(4-tolylmethyl)-1,3-dithiane 1-oxide (3c)
Mp 113–114 °C; IR (nujol) 2923, 2854, 1460, 1051, 994, 811 cm⁻¹; ¹H NMR (CDCl₃) δ 1.96–2.08 (m, 1H), 2.34 (s, 3H), 2.48–2.55 (m, 1H), 2.59–2.64 (m, 1H), 2.68–2.72 (m, 2H), 2.93 (dd, J = 14.0, 5.0 Hz, 1H), 3.00–3.05 (m, 1H), 3.37 (dd, J = 13.5, 9.0 Hz, 1H), 3.86 (dd, J = 9.0, 3.0 Hz, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 21.1, 21.3, 26.0, 32.0, 46.2, 60.9, 129.6, 129.6, 133.8, 137.0. Found: C, 59.86; H, 6.62%. Calcd for
Chapter 3

C$_{12}$H$_{16}$OS$_2$: C, 59.96; H, 6.71%.

1,2-cis-2-(4-trifluoromethylphenylmethyl)-1,3-dithiane 1-oxide (3d)
Mp 130–131 °C; IR (nujol) 2923, 2854, 1327, 1158, 1106, 1044 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.04–2.11 (m, 1H), 2.49–2.55 (m, 1H), 2.59–2.63 (m, 1H), 2.70–2.80 (m, 2H), 2.96–3.04 (m, 2H), 3.50 (dd, $J = 9.0$, 14.0 Hz, 1H), 3.87 (dd, $J = 9.0$, 4.5 Hz, 1H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.60 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 21.8, 25.6, 31.7, 46.3, 60.0, 124.3 (q, $J_{C-F} = 270$ Hz), 125.8 (q, $J_{C-F} = 3.4$ Hz), 129.8 (q, $J_{C-F} = 32$ Hz), 130.1, 141.2. Found: C, 48.81; H, 4.41%. Calcd for C$_{12}$H$_{15}$F$_3$OS$_2$: C, 48.96; H, 4.45%.

1,2-cis-2-(4-methoxycarbonylphenylmethyl)-1,3-dithiane 1-oxide (3e)
Mp 108–109 °C; IR (nujol) 2922, 2854, 1718, 1437, 1285, 1044, 753 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.05–2.10 (m, 1H), 2.49–2.56 (m, 1H), 2.59–2.64 (m, 1H), 2.70–2.80 (m, 2H), 3.00–3.05 (m, 2H), 3.50 (dd, $J = 14.0$, 9.0 Hz, 1H), 3.90 (dd, $J = 9.0$, 4.0 Hz, 1H), 3.92 (s, 3H), 7.37–7.39 (m, 2H), 8.01–8.03 (m, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 21.8, 25.7, 31.9, 46.3, 52.3, 60.1, 129.4, 129.8, 130.2, 142.4, 167.0. Found: C, 54.78; H, 5.64%. Calcd for C$_{13}$H$_{16}$O$_3$S$_2$: C, 54.90; H, 5.67%.

1,2-cis-2-(2-methoxyphenylmethyl)-1,3-dithiane 1-oxide (3f)
Mp 81–82 °C; IR (nujol) 2923, 2854, 1586, 1496, 1244, 1020, 755 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.95–2.00 (m, 1H), 2.48–2.55 (m, 1H), 2.59–2.72 (m, 3H), 3.01–3.08 (m, 2H), 3.37 (dd, $J = 14.0$, 8.5 Hz, 1H), 3.85 (s, 3H), 4.07 (dd, $J = 8.5$, 3.0 Hz, 1H), 6.88–6.94 (m, 2H), 7.22 (dd, $J = 8.0$, 6.0 Hz, 1H), 7.27 (ddd, $J = 8.0$, 8.0, 2.0 Hz, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 20.3, 26.4, 28.3, 46.2, 55.6, 58.9, 110.7, 120.7, 124.8, 128.8, 131.8, 157.9. Found: C, 55.95; H, 6.38%. Calcd for C$_{12}$H$_{16}$O$_2$S$_2$: C, 56.22; H, 6.29%.

1,2-cis-2-[2-(tert-butoxycarbonylamino)phenylmethyl]-1,3-dithiane 1-oxide (3g)
Mp 57–58 °C; IR (nujol) 2923, 2854, 1717, 1452, 1158, 1024 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.53
(s, 9H), 2.04–2.15 (m, 1H), 2.45–2.54 (m, 1H), 2.61–2.69 (m, 1H), 2.71–2.84 (m, 2H), 2.94–3.03 (m, 2H), 3.44 (dd, $J = 14.5, 6.0$ Hz, 1H), 3.85 (dd, $J = 6.0, 6.0$ Hz, 1H), 7.08 (ddd, $J = 7.0, 7.0, 3.5$ Hz, 1H), 7.25–7.31 (m, 2H), 7.49 (brs, 1H), 7.79 (d, $J = 7.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 22.4, 25.5, 28.2, 28.6, 45.7, 58.9, 80.5, 123.9, 124.5, 128.1, 128.4, 130.8, 136.9, 154.1. HRMS (m/z) Observed: 341.1120 (Δ = +0.1 ppm). Calcd for C$_{16}$H$_{23}$O$_3$NS$_2$: 341.1119.

1-methylsulfinyl-1-methylthio-2-phenylethane (5)
The major isomer: $^1$H NMR (CDCl$_3$) δ 2.17 (s, 3H), 2.64–2.69 (m, 4H), 3.65–3.70 (m, 2H), 7.27–7.37 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 16.2, 31.3, 32.3, 67.4, 127.2, 128.9, 129.6, 137.5.
The minor isomer: $^1$H NMR (CDCl$_3$) δ 2.15 (s, 3H), 2.78 (s, 3H), 2.85 (dd, $J = 14.0, 11.0$ Hz, 1H), 3.54 (dd, $J = 14.0, 3.5$ Hz, 1H), 3.69 (dd, $J = 11.0, 3.5$ Hz, 1H), 7.27–7.38 (m, 5H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 33.7, 36.9, 69.7, 127.3, 128.9, 129.5, 137.0. Found: C, 56.28; H, 6.48%. Calcd for C$_{10}$H$_{14}$OS$_2$: C, 56.03; H, 6.58%.

(1$^R$,2$^S$*)-2-(diphenylmethyl)-1,3-dithiane 1-oxide (6a)
Mp 188–189 °C; IR (nujol) 2923, 2854, 1457, 1044, 710 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.74–1.80 (m, 1H), 2.41–2.60 (m, 3H), 2.84–2.90 (m, 1H), 3.10–3.14 (m, 1H), 4.23 (d, $J = 12.5$ Hz, 1H), 4.46 (d, $J = 12.0$ Hz, 1H), 7.22–7.42 (m, 10H); $^{13}$C NMR (CDCl$_3$) δ 14.1, 29.3, 46.5, 52.6, 65.4, 127.4, 127.6, 128.5, 128.6, 128.7, 129.1, 139.7, 139.9. Found: C, 67.23; H, 6.00%. Calcd for C$_{17}$H$_{18}$OS$_2$: C, 67.51; H, 6.00%.

(1$^R$,2$^S$*)-2-[($^S$*)-phenyl(4-trifluoromethylphenyl)methyl]-1,3-dithiane 1-oxide (6b)
Mp 173–174 °C; IR (nujol) 2923, 2854, 1417, 1326, 1161, 1128, 1070, 1051, 735, 697 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.78–1.84 (m, 1H), 2.45–2.64 (m, 3H), 2.86–2.91 (m, 1H), 3.15–3.19 (m, 1H), 4.31 (d, $J = 12.0$ Hz, 1H), 4.46 (d, $J = 12.0$ Hz, 1H), 7.25–7.29 (m, 1H), 7.32–7.37 (m, 4H), 7.53 (d, $J = 8.0$ Hz, 2H), 7.60 (d, $J = 8.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$) δ 14.2, 29.4, 46.7, 52.5, 65.0, 124.1 (q, $J_{C-F} = 271$ Hz), 126.2 (q, $J_{C-F} = 3.8$ Hz), 127.9, 128.6, 129.1 (Two signals...
merge.), 130.0 (q, $J_{C-F} = 32.0$ Hz), 138.9, 144.0. Found: C, 58.15; H, 4.58%. Calcd for $C_{18}H_{17}OF_{3}S_{2}$: C, 58.36; H, 4.63%. X-ray quality crystals were grown from acetonitrile/hexane. CCDC No.: 681750. Copies of the X-ray crystallographic data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: 44-1223-3360033 or E-mail: deposit@ccdc.cam.ac.uk.

(1$R^{*},2S^{*}$)-2-[(S*)-1-phenylethyl]-1,3-dithiane 1-oxide (6c, the major isomer)
Mp 126–128 °C; IR (nujol) 2924, 2854, 1454, 1375, 1038 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.45 (d, $J = 7.0$ Hz, 3H), 1.72–1.78 (m, 1H), 2.33 (ddd, $J = 13.5$, 13.5, 3.0 Hz, 1H), 2.50–2.61 (m, 1H), 2.66–2.70 (m, 1H), 2.83–2.90 (m, 1H), 3.01–3.06 (m, 1H), 3.13–3.19 (m, 1H), 3.80 (d, $J = 5.5$ Hz, 1H), 7.27–7.33 (m, 3H), 7.34–7.38 (m, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.4, 19.3, 29.2, 41.5, 46.8, 68.5, 127.6, 128.1, 129.0, 142.5. Found: C, 59.70; H, 6.62%. Calcd for $C_{12}H_{16}OS_{2}$: C, 59.96; H, 6.71%.

2-benzyl-2-methyl-1,3-dithiane 1-oxide (10)
Mp 126–128 °C; IR (nujol) 2923, 2853, 1456, 1374, 1071, 1006, 748, 699 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.62 (s, 3H), 2.13–2.22 (m, 1H), 2.32–2.39 (m, 2H), 2.62–2.68 (m, 1H), 2.76 (ddd, $J = 13.5$, 13.5, 3.0 Hz, 1H), 3.07 (ddd, $J = 13.5$, 4.0, 4.0 Hz, 1H), 3.21 (s, 2H), 7.27–7.35 (m, 5H); $^{13}$C NMR (CDCl$_3$) $\delta$ 13.9, 25.0, 28.8, 43.4, 46.4, 62.4, 127.6, 128.2, 131.3, 133.8. Found: C, 59.79; H, 6.42%. Calcd for $C_{12}H_{16}OS_{2}$: C, 59.96; H, 6.71%.
References and Notes


3. Ketene dithioacetal monoxides are known to serve as Michael acceptors. 


5. Addition to alkenylphosphonates:  

6. Addition to nitroalkenes:  


8. Intermediate 8 can be in equilibrium with 8’ and 8’’.

![Equilibrium Diagram]


10. The relative stereochemistry of 10 has not been determined.

Chapter 3

1995, 73.


Synthesis of Benzo[b]thiophenes by Cyclization of Arylketene Dithioacetal Monoxides under Pummerer-like Conditions

Treatment of arylketene bis(methylthio)acetal monoxide with trifluoromethanesulfonic anhydride leads to ring-closure to afford 2-methylthiobenzo[b]thiophene in high yield. The reaction is useful for synthesizing multisubstituted benzo[b]thiophenes.
Introduction

The benzo[b]thiophene skeleton is a ubiquitous structure found in various compounds ranging from biologically intriguing molecules\(^1\) to advanced organic materials.\(^2\) Construction of the benzo[b]thiophene skeleton is hence important. There are several representative methods for the construction, most of which employ benzenethiol derivatives as the starting materials.\(^3,4\) However, methods for synthesis of multisubstituted benzo[b]thiophenes are still limited, and hence have to be explored.

The author has been interested in ketene dithioacetal monoxides as interesting synthetic intermediates.\(^5\) Here the author reports a new approach to benzo[b]thiophenes starting from ketene dithioacetal monoxides. His idea is outlined in Scheme 1. Treatment of aryl-substituted ketene dithioacetal monoxide 1 with an oxophilic electrophile would result in cleavage of the oxygen-sulfur bond with concomitant Friedel-Crafts-type electrophilic aromatic substitution to yield 4. Removal of the methyl group on the cationic sulfur would afford 3-substituted 2-(methylthio)benzo[b]thiophene 5. The synthesis of the starting material 1 was facile and scalable, starting from aryl ketone and formaldehyde dimethyl dithioacetal S-oxide (FAMSO) in 3 steps.\(^6\) Thus, his approach to 5 will be useful for the synthesis of multisubstituted benzo[b]thiophenes.
Results and Discussion

The synthesis of the starting material 1 is summarized in Figure 1. Although all steps were unoptimized, the overall transformations were facile to give 1a–g in satisfactory yields. The products except for 1a were obtained as 1:1 stereoisomeric mixtures. The stereoisomers of 1b were separable from each other on silica gel.

**Figure 1.** Synthesis of ketene dithioacetal monoxides, precursors of benzo[b]thiophenes.

```latex
\begin{align*}
\text{O}^{-} & \text{S'}\text{Me} & \text{SMe} & \text{O}^{-} & \text{S'}\text{Me} & \text{SMe} & \text{O}^{-} & \text{S'}\text{Me} & \text{SMe} \\
\text{R}^{1} & \text{R}^{2} & \text{O} & \text{R}^{1} & \text{R}^{2} & \text{O} & \text{R}^{1} & \text{R}^{2} & \text{O} \\
& 1) n-\text{BuLi (1.0 equiv)} & \text{THF, } -20^\circ\text{C, 30 min} & 2) R^{1} & (1.2 equiv) & R^{2} & -20^\circ\text{C, 6 h} & 3) \text{Ac}_{2}\text{O, (1.1 equiv)} & -20^\circ\text{C, 12 h} & \text{t-BuOK} & \text{t-BuOH / benzene} & 25^\circ\text{C, 1 h} \\
\text{Ph} & 1a & 66\% & \text{CF}_{3} & 1b & 53\% & \text{MeO} & 1c & 56\% \\
\text{MeO} & 1d & 46\% & \text{MeO} & 1e & 79\% & \text{Ph} & 1f & 65\% & \text{CF}_{3} & 1g & 57\% \\
\end{align*}
```
Treatment of 1a with trifluoromethanesulfonic anhydride (Tf₂O) in the presence of potassium carbonate in toluene at 25 °C followed by addition of ethanolamine to the reaction mixture provided benzo[b]thiophene 5a in 86% yield (Table 1, entry 1). It is worth noting that no addition of a nucleophile at the diphenyl-substituted olefinic carbon was observed under the Pummerer-like conditions. None of 5a was obtained when trifluoroacetic anhydride, p-toluenesulfonyl chloride, or trifluoromethanesulfonic acid was used instead of Tf₂O.
Table 1. Synthesis of Benzo[b]thiophenes from 1

<table>
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<th>Entry</th>
<th>1\textsuperscript{a}</th>
<th>5</th>
<th>Yield /%</th>
</tr>
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<tbody>
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<td>1</td>
<td>( \text{Ph} )</td>
<td>( \text{Ph} ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{Ph} ) SMe SMe SMe</td>
</tr>
<tr>
<td>2</td>
<td>( \text{CF}_3 )</td>
<td>( \text{CF}_3 ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{CF}_3 ) SMe SMe SMe</td>
</tr>
<tr>
<td>3</td>
<td>( \text{Ph} )</td>
<td>( \text{Ph} ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{Ph} ) SMe SMe SMe</td>
</tr>
<tr>
<td>4</td>
<td>( \text{MeO} )</td>
<td>( \text{MeO} ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{MeO} ) SMe SMe SMe</td>
</tr>
<tr>
<td>5</td>
<td>( \text{MeO} ) ( \text{Ph} )</td>
<td>( \text{MeO} ) ( \text{Ph} ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{MeO} ) ( \text{Ph} ) SMe SMe SMe</td>
</tr>
<tr>
<td>6</td>
<td>( \text{MeO} ) ( \text{Ph} )</td>
<td>( \text{MeO} ) ( \text{Ph} ) SMe SMe ( \text{O}^- ) SMe</td>
<td>( \text{MeO} ) ( \text{Ph} ) SMe SMe SMe</td>
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</table>
Table 1. (Continued)

<table>
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<th>Entry</th>
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<th>5</th>
<th>Yield /%</th>
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<tr>
<td>8</td>
<td><img src="image3.png" alt="Image" /></td>
<td>1g</td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
</tbody>
</table>

In the reactions of 1c–f, ca. 1:1 mixtures of stereoisomers were used. In the reaction of 1g, a 7:1 mixture of the stereoisomers was used, although the stereochemistry of each isomer could not be assigned.

Trifluoromethyl-substituted (E)-1b was subjected to the cyclization reaction to yield benzo[b]thiophene 5b\(^9,10\) having a trifluoromethyl group at the 3 position in high yield (entry 2). Interestingly, its stereoisomer (Z)-1b also underwent the cyclization to afford 5b in good yield (entry 3). The participation of (Z)-1b in the cyclization suggests a detailed reaction mechanism (Scheme 2). The sulfur-oxygen bond cleavage by Tf₂O would produce a highly stabilized dication 7. The C\(^a\)–C\(^b\) single bond of 7 would rotate to form 8. The dication 8 has a suitable conformation for the cyclization to yield 3b.

Scheme 2

![Image](image5.png)
When a 1:1 stereoisomeric mixture of 1c was treated under the cyclization conditions, the cyclization onto the more electron-rich methoxyphenyl group took place exclusively (entry 4). The reaction of m-methoxyphenyl-substituted 1d led to the C–S bond formation at the para position to the methoxy group selectively (entry 5). Neither C–S bond formations at the ortho position to the methoxy group nor on the other phenyl group was observed. The cyclization reaction of a stereoisomeric mixture of 1e also took place absolutely onto the methoxyphenyl group (entry 6). In the reaction of 1f, the cyclization onto the naphthalene is highly preferable to that onto the phenyl ring (entry 7). The reaction of 1g bearing a trifluoromethylphenyl group and a phenyl group yielded 5g selectively (entry 8). In cases where R² are alkyl groups such as methyl and ethyl, the reactions afforded complex mixtures.

The methylthio group of 1 plays an important role for the synthesis (Scheme 3). Treatment of 9 bearing no methylthio group under the same conditions afforded a complex mixture. On the other hand, methyl 1,2,2-triphenylethenyl sulfoxide (10) reacted to provide 2,3-diphenylbenzo[b]thiophene (12) in good yield. These results suggest that sufficient stability of the dicationic intermediate 13/14 would be quite important for the success of the ring-closure.

Scheme 3

1) Tf₂O (1.3 equiv)
   K₂CO₃ (3 equiv)
   toluene, 25 °C, 1 h
2) ethanolamine (5.0 equiv)
   25 °C, 3 h
Chapter 4

The synthesis of 18, a highly substituted benzo[b]thiophene, underscores the utility of the present method (Scheme 4). Bromination of o-chlorophenol\(^{11}\) followed by methylation yielded 15. Trifluoroacetylation of magnesiated 15 yielded trifluoromethyl ketone 16 on a large scale. Nucleophilic addition of lithiated FAMSO to 16 followed by elongating conjugation\(^6\) yielded 17. The ring-closure of 17 by Tf\(_2\)O afforded 18.

**Conclusion**

Treatment of arylketene bis(methylthio)acetal monoxide with trifluoromethanesulfonic anhydride leads to ring-closure to afford 2-methylthiobenzo[b]thiophene in high yield. The reaction is useful for synthesizing multisubstituted benzo[b]thiophenes. Multisubstituted benzo[b]thiophenes can find many applications in various fields of chemistry. The present protocol provides a conceptually new and useful approach to the benzo[b]thiophene skeleton.
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz) and $^{13}$C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl$_3$. Chemical shifts ($\delta$) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H and relative to CDCl$_3$ at 77.2 ppm for $^{13}$C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (EI unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Trifluoromethanesulfonic anhydride and ethanolamine were purchased from TCI. Toluene and potassium carbonate were purchased from Wako Pure Chemical and toluene was dried over slices of sodium. All reactions were carried out under argon atmosphere.

Typical Procedure for Synthesis of Ketene Dithioacetal Monoxides

Formaldehyde dimethyl dithioacetal S-oxide (1.0 mL, 10 mmol) and THF (10 mL) were placed in a flask under an atmosphere of argon. Butyllithium in hexane (1.62 M, 6.0 mL, 10 mmol) was added to the solution at –20 °C, and the mixture was stirred at the same temperature for 30 min. Benzophenone (2.2 g, 12 mmol) was added to the reaction mixture, and the mixture was stirred at –20 °C for 6 h. Acetic anhydride (1.0 mL, 11 mmol) was added to the reaction mixture, and the mixture was stirred at –20 °C for 12 h. Saturated aqueous NH$_4$Cl was poured into the mixture, and the product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. The crude mixture, benzene (10 mL), and tert-butyl alcohol (10 mL) were placed in a flask under an atmosphere of argon. Potassium tert-butoxide was added to the solution at 25 °C, and the mixture was stirred
for 1 h. Saturated aqueous NH₄Cl was poured into the mixture and the product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 1/2) provided methyl 1-methylsulfinyl-2,2-diphenylethenyl sulfide (1a, 1.84g, 66%).

Typical Procedure for Synthesis of Benzo[b]thiophenes (Table 1, entry 1)

Methyl 1-methylsulfinyl-2,2-diphenylethenyl sulfide (1a, 54.9 mg, 0.19 mmol), K₂CO₃ (90.4 mg, 0.66 mmol), and toluene (4.0 mL) were placed in a flask under an atmosphere of argon. Trifluoromethanesulfonic anhydride (0.045 mL, 0.27 mmol) was added, and the mixture was stirred at 25 °C for 1 h. Ethanolamine (0.060 mL, 1.0 mmol) was added to the reaction mixture, and the mixture was stirred at 25 °C for 3 h. Saturated aqueous NaHCO₃ was poured into the mixture and the product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 50/1) provided 2-methylthio-3-phenylbenzo[b]thiophene (5a, 42.2 mg, 0.16 mmol, 86%).

Characterization Data

methyl 1-methylsulfinyl-2,2-diphenylethenyl sulfide (1a)
Mp 106–107 °C; IR (nujol) 2855, 1442, 1318, 1029, 765, 696 cm⁻¹; ¹H NMR (CDCl₃) δ 2.24 (s, 3H), 2.74 (s, 3H), 7.14–7.16 (m, 2H), 7.35–7.38 (m, 8H); ¹³C NMR (CDCl₃) δ 20.3, 38.6, 128.5, 128.6, 129.0, 129.2, 129.6, 129.7, 139.9, 140.4, 143.5, 156.6. Found: C, 66.76; H, 5.62%. Calcd for C₁₆H₁₆OS₂: C, 66.63; H, 5.59%.

methyl (E)-3,3,3-trifluoro-1-methylsulfinyl-2-phenyl-1-propenyl sulfide (1b)
(E)-isomer: Mp 104–105 °C; IR (nujol) 2854, 1447, 1378, 1296, 1114, 1046, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 2.56 (s, 3H), 2.69 (s, 3H), 7.10–7.25 (br, 2H), 7.45–7.48 (m, 3H); ¹³C NMR
(CDCl$_3$) $\delta$ 21.9, 38.8, 121.6 (q, $J_{C-F} = 276$ Hz), 129.0, 129.1, 130.1, 131.7, 143.7 (q, $J_{C-F} = 31.0$ Hz), 155.7.  **(Z)-isomer:** IR (neat) 2928, 1564, 1489, 1444, 1293, 1124, 1074, 847, 704, 676 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.08 (s, 3H), 2.80 (s, 3H), 7.30–7.32 (m, 2H), 7.43–7.46 (m, 3H); $^{13}$C NMR (CDCl$_3$) $\delta$ 19.1, 40.2, 122.0 (q, $J_{C-F} = 276$ Hz), 128.9, 129.2, 129.6, 133.1, 138.1 (q, $J_{C-F} = 31.0$ Hz), 157.8.  Found: C, 47.02; H, 3.96%.  Calcd for C$_{11}$H$_{11}$F$_3$OS$_2$: C, 47.13; H, 3.96%.

**methyl 2-(2-methoxyphenyl)-1-methylsulfinyl-2-phenylethenyl sulfide (1c, 1:1 mixture of stereoisomers)**

Mp 118–119 °C; IR (nujol) 2923, 1488, 1248, 1035, 1020, 758, 700 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.20–2.40 (br, 3H), 2.50–2.74 (br, 3H), 3.65–3.90 (br, 3H), 6.80–7.22 (br, 3H), 7.28–7.36 (m, 4H), 7.40 (dd, $J = 1.5$, 8.0 Hz, 2H); $^{13}$C NMR (CDCl$_3$) $\delta$ 20.3 (Two signals merge.), 55.4, 55.8, 111.0, 111.5, 120.4, 121.0, 128.1 (Three signals merge.), 128.4 (Four signals merge.), 128.7 (br, Two signals merge.), 129.9 (br), 130.3 (Two signals merge.), 140.0 (Two signals merge.), 143.4 (br), 144.6 (br), 151.6 (br), 152.6 (br), 155.5 (br), 156.1 (br).  Found: C, 64.19; H, 5.71%.  Calcd for C$_{17}$H$_{18}$O$_2$S$_2$: C, 64.12; H, 5.70%.

**methyl 2-(3-methoxyphenyl)-1-methylsulfinyl-2-phenylethenyl sulfide (1d, 3:2 mixture of stereoisomers)**

Mp 105–106 °C; IR (nujol) 2854, 1576, 1486, 1226, 1034, 941, 779 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.24 (s, 0.4 $\times$ 3H), 2.27 (s, 0.6 $\times$ 3H), 2.74 (s, 0.4 $\times$ 3H), 2.75 (s, 0.6 $\times$ 3H), 3.79 (s, 0.4 $\times$ 3H), 3.80 (s, 0.6 $\times$ 3H), 6.64–6.65 (m, 0.4 $\times$ 1H), 6.74–6.76(m, 0.4 $\times$ 1H), 6.89–6.92 (m, 0.6 $\times$ 2H, 0.4 $\times$ 1H), 6.95–6.96 (m, 0.6 $\times$ 1H), 7.14–7.16 (m, 0.4 $\times$ 3H), 7.29 (dd, $J = 7.5$, 7.5 Hz, 0.6 $\times$ 2H), 7.35–7.40 (m, 0.6 $\times$ 4H, 0.4 $\times$ 3H); $^{13}$C NMR (CDCl$_3$) $\delta$ 20.2, 20.3, 38.6 (Two signals merge.), 55.5 (Two signals merge.), 114.3, 114.5, 115.2 (Two signals merge.), 122.0 (Two signals merge.), 128.5, 128.6, 129.0, 129.2, 129.4, 129.5, 129.6 (Two signals merge.), 139.8, 140.1, 141.2, 141.6, 143.6 (Two signals merge.), 156.0, 156.2, 159.5, 159.7.  Found: C, 63.85; H, 5.66%.  Calcd for
methyl 2-(4-methoxyphenyl)-1-methylsulfinyl-2-phenylethenyl sulfide (1e, 3:2 mixture of stereoisomers)

Mp 111–112 °C; IR (nujol) 2854, 1604, 1507, 1253, 775, 691 cm⁻¹; ¹H NMR (CDCl₃) δ 2.22 (s, 0.4 × 3H), 2.26 (s, 0.6 × 3H), 2.73 (s, 0.6 × 3H), 2.76 (s, 0.4 × 3H), 3.83 (s, 3H), 6.86–6.89 (m, 2H), 7.06–7.07 (m, 0.4 × 2H), 7.13–7.15 (m, 0.6 × 2H), 7.33–7.39 (m, 5H); ¹³C NMR (CDCl₃) δ 20.2, 20.4, 38.5, 38.6, 55.5 (Two signals merge.), 113.7, 113.9, 128.4, 128.5, 128.9, 129.1, 129.7, 129.8, 131.4, 131.5, 132.2, 132.5, 140.3, 140.8, 142.0, 142.2, 156.0, 156.8, 160.2, 160.5. Found: C, 63.94; H, 5.86%. Calcd for C₁₇H₁₈O₂S₂: C, 64.12; H, 5.70%.

methyl 1-methylsulfinyl-2-(2-naphthyl)-2-phenylethenyl sulfide (1f, 4:3 mixture of stereoisomers)

Mp 116–117 °C; IR (nujol) 2922, 1442, 1377, 1028, 693 cm⁻¹; ¹H NMR (CDCl₃) δ 2.22 (s, 0.45 × 3H), 2.29 (s, 0.55 × 3H), 2.78 (s, 0.55 × 3H), 2.80 (s, 0.45 × 3H), 7.19–7.22 (m, 0.45 × 2H, 0.55 × 1H), 7.37–7.43 (m, 4H), 7.48–7.57 (m, 0.45 × 3H, 0.55 × 2H), 7.67 (d, J = 1.5 Hz, 0.55 × 1H), 7.78–7.86 (m, 0.45 × 3H, 0.55 × 4H); ¹³C NMR (CDCl₃) δ 20.3 (Two signals merge.), 38.5, 38.6, 126.7, 126.9 (Two signals merge.), 127.0, 127.2, 127.3, 127.9, 128.0 (Two signals merge.), 128.1, 128.5 (Three signals merge.), 128.6, 129.1, 129.3 (Two signals merge.), 129.6, 129.7, 129.9, 132.8, 133.0, 133.4, 133.4, 137.2, 137.8, 139.9, 140.2, 143.5, 143.6, 156.7 (Two signals merge.). Found: C, 70.89; H, 5.36%. Calcd for C₂₀H₁₈OS₂: C, 70.97; H, 5.36%.

methyl 2-(4-trifluoromethylphenyl)-1-methylsulfinyl-2-phenylethenyl sulfide (1g, the major isomer)

Mp 119–121 °C; IR (nujol) 2920, 1329, 1126, 1034, 706 cm⁻¹; ¹H NMR (CDCl₃) δ 2.27 (s, 3H), 2.76 (s, 3H), 7.13 (dd, J = 2.0, 7.5 Hz, 2H), 7.34–7.41 (m, 3H), 7.49 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 20.4, 38.6, 124.0 (q, J_C–F = 263 Hz), 125.5 (q,
$J_{C-F} = 3.9 \text{ Hz}$), 128.8, 129.5, 129.6, 129.9, 130.8 ($q$, $J_{C-F} = 32.5 \text{ Hz}$), 139.0, 143.9, 145.2, 155.1.

Found: C, 57.31; H, 4.33%. Calcd for $C_{17}H_{12}F_{3}OS_{2}$: C, 57.29; H, 4.24%.

2-methylthio-3-phenylbenzo[b]thiophene (5a)
IR (neat) 2918, 1423, 1314, 1071, 965, 767, 732, 699 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.50 (s, 3H), 7.31–7.36 (m, 2H), 7.44–7.58 (m, 6H), 7.79–7.83 (m, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 20.2, 122.0, 122.9, 124.5, 124.8, 128.0, 128.7, 130.2, 134.8, 135.5, 137.6, 139.9, 140.1. Found: C, 70.41; H, 4.98%. Calcd for $C_{15}H_{12}OS_{2}$: C, 70.27; H, 4.98%.

3-trifluoromethyl-2-methylthiobenzo[b]thiophene (5b)
IR (neat) 1507, 1463, 1367, 1219, 1156, 1111, 757, 730 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.68 (s, 3H), 7.33 (ddd, $J = 1.0, 7.5, 7.5 \text{ Hz}$, 1H), 7.42 (ddd, $J = 1.0, 7.5, 7.5 \text{ Hz}$, 1H), 7.74 (d, $J = 7.5 \text{ Hz}$, 1H), 7.84 (d, $J = 7.5 \text{ Hz}$, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 18.7 (q, $J_{C-F} = 1.5 \text{ Hz}$), 120.0 (q, $J_{C-F} = 34 \text{ Hz}$), 121.6, 122.0 (q, $J_{C-F} = 2.9 \text{ Hz}$), 123.5 (q, $J_{C-F} = 271 \text{ Hz}$), 124.4, 125.7, 137.2 (q, $J_{C-F} = 1.5 \text{ Hz}$), 138.1, 145.8 (q, $J_{C-F} = 2.9 \text{ Hz}$). Found: C, 48.63; H, 2.94%. Calcd for $C_{10}H_{7}F_{3}S_{2}$: C, 48.37; H, 2.84%.

4-methoxy-2-methylthio-3-phenylbenzo[b]thiophene (5c)
IR (neat) 2919, 1600, 1423, 1245, 1114, 1027, 755, 731 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.49 (s, 3H), 3.78 (s, 3H), 7.07–7.12 (m, 2H), 7.28–7.36 (m, 4H), 7.45 (ddd, $J = 2.0, 7.5, 7.5 \text{ Hz}$, 1H), 7.79 (dd, $J = 1.0, 7.5 \text{ Hz}$, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$ 20.0, 55.5, 111.3, 120.5, 121.7, 123.0, 123.4, 124.1, 124.2, 129.6, 131.9, 134.6, 136.0, 139.7, 140.0, 157.5. Found: C, 66.86; H, 4.91%. Calcd for $C_{16}H_{14}OS_{2}$: C, 67.10; H, 4.93%.

5-methoxy-2-methylthio-3-phenylbenzo[b]thiophene (5d)
IR (neat) 1596, 1421, 1264, 1229, 1140, 1036, 700 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 2.49 (s, 3H), 3.79 (s, 3H), 6.98–7.01 (m, 2H), 7.44–7.56 (m, 5H), 7.67 (d, $J = 8.5 \text{ Hz}$, 1H); $^{13}$C NMR (CDCl$_3$) $\delta$
20.1, 55.7, 105.3, 114.3, 122.7, 128.0, 128.8, 130.1, 132.2, 134.9, 136.8, 137.2, 141.1, 158.0.

Found: C, 66.81; H, 5.00%. Calcd for C\textsubscript{16}H\textsubscript{14}OS\textsubscript{2}: C, 67.10; H, 4.93%.

6-methoxy-2-methylthio-3-phenylbenzo[b]thiophene (5e)

IR (neat) 2919, 1600, 1468, 1233, 1084, 701, 645 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 2.43 (s, 3H), 3.89 (s, 3H), 6.94 (dd, \(J = 2.0, 8.5\ Hz\), 1H), 7.28 (d, \(J = 2.0\ Hz\), 1H), 7.42–7.54 (m, 6H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 20.9, 55.9, 104.7, 114.6, 123.9, 128.0, 128.6, 130.2, 131.7, 134.1, 135.0, 138.7, 141.6, 157.8. Found: C, 67.33; H, 4.91%. Calcd for C\textsubscript{16}H\textsubscript{14}OS\textsubscript{2}: C, 67.10; H, 4.93%.

2-methylthio-3-phenylnaphtho[1,2-b]thiophene (5f)

Mp 87–88 °C; IR (nujol) 2924, 1507, 1458, 1378, 809, 745, 690 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 2.52 (s, 3H), 7.46–7.49 (m, 1H), 7.51–7.61 (m, 7H), 7.70 (d, \(J = 9.0\ Hz\), 1H), 7.92 (d, \(J = 8.0\ Hz\), 1H), 8.10 (d, \(J = 8.0\ Hz\), 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 20.9, 121.5, 123.7, 125.8, 126.0, 126.9, 128.0, 128.6, 128.7, 129.1, 130.4, 131.1, 134.2, 134.9, 137.5, 137.7, 139.8. Found: C, 74.22; H, 4.80%. Calcd for C\textsubscript{19}H\textsubscript{14}S\textsubscript{2}: C, 74.47; H, 4.60%.

3-(4-trifluoromethylphenyl)-2-methylthiobenzo[b]thiophene (5g)

IR (neat) 2922, 1617, 1425, 1324, 1166, 1107, 1066, 852, 732 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 2.52 (s, 3H), 7.32–7.38 (m, 2H), 7.50–7.53 (m, 1H), 7.63 (d, \(J = 8.0\ Hz\), 2H), 7.79 (d, \(J = 8.0\ Hz\), 2H), 7.80–7.83 (m, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 20.1, 122.1, 122.5, 124.4 (q, \(J_{C-F} = 271\ Hz\)), 124.7, 125.1, 125.7 (q, \(J_{C-F} = 3.8\ Hz\)), 130.0 (q, \(J_{C-F} = 65\ Hz\)), 130.7, 135.8, 136.8, 138.6, 139.6, 139.9. Found: C, 59.04; H, 3.50%. Calcd for C\textsubscript{16}H\textsubscript{11}F\textsubscript{3}S\textsubscript{2}: C, 59.24; H, 3.42%.

methyl 2,2-diphenylethenyl sulfoxide (9)

Mp 88–89 °C; IR (nujol) 2925, 1448, 1020, 974, 763, 693 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \(\delta\) 2.74 (s, 3H), 6.83 (s, 1H), 7.22–7.24 (m, 2H), 7.32–7.45 (m, 8H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 41.0, 128.5 (Two signals merge.), 128.8, 129.4, 129.9, 130.0, 133.8, 137.3, 139.2, 152.6. Found: C, 74.29;
H, 5.96%. Calcd for $C_{15}H_{14}OS$: C, 74.34; H, 5.82%.

**methyl 1,2,2-triphenylethenyl sulfoxide (10)**

Mp 178–180 °C; IR (nujol) 2925, 1445, 1377, 1023, 740, 696 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.37 (s, 3H), 6.97–7.00 (m, 2H), 7.06–7.12 (m, 3H), 7.17–7.20 (m, 2H), 7.30–7.32 (m, 3H), 7.35–7.38 (m, 2H), 7.39–7.42 (m, 3H); $^{13}$C NMR (CDCl$_3$) δ 37.4, 128.0, 128.2, 128.3 (Two signals merge.), 128.4, 128.9, 130.4, 130.5, 131.6, 132.3, 139.2, 140.0, 142.4, 150.3. Found: C, 79.20; H, 5.74%. Calcd for $C_{21}H_{18}OS$: C, 79.21; H, 5.70%.

**methyl 2-(3-chloro-4-methoxyphenyl)-3,3,3-trifluoro-1-methylsulfinyl-1-propenyl sulfide (17, the major isomer)**

Mp 67–69 °C; IR (nujol) 2923, 1600, 1459, 1377, 1293, 1259, 1112, 815, 727, 665 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.39 (s, 3H), 2.68 (s, 3H), 3.96 (s, 3H), 6.97–7.01 (m, 1H), 7.01–7.15 (br, 1H), 7.15–7.26 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 21.2, 38.9, 56.5, 112.2, 121.5 (q, $J_{C-F} = 276$ Hz), 123.4, 124.4, 129.0, 130.9, 142.0 (q, $J_{C-F} = 31.5$ Hz), 156.4, 156.6. Found: C, 41.62; H, 3.41%. Calcd for $C_{12}H_{12}ClF_{3}O_{2}S_{2}$: C, 41.80; H, 3.51%.

**5-chloro-3-trifluoromethyl-6-methoxy-2-methylthiobenz[b] thiophene (18)**

Mp 135–136 °C; IR (nujol) 2923, 1460, 1266, 1141, 1098, 1048, 866, 824, 704 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.65 (s, 3H), 3.96 (s, 3H), 7.23 (s, 1H), 7.83 (q, $J_{H-F} = 1.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 19.0 (q, $J_{C-F} = 1.5$ Hz), 56.4, 103.8, 119.9 (q, $J_{C-F} = 33.4$ Hz), 122.5, 122.8 (q, $J_{C-F} = 271$ Hz), 123.0 (q, $J_{C-F} = 2.9$ Hz), 130.8 (q, $J_{C-F} = 2.0$ Hz), 137.7, 143.4 (q, $J_{C-F} = 2.8$ Hz), 152.6. Found: C, 42.16; H, 2.63%. Calcd for $C_{11}H_{8}ClF_{3}OS_{2}$: C, 42.24; H, 2.58%.
References and Notes

1. Selected examples:  

2. Selected examples:  


4. Selected recent examples:  


9. The biological activity of 3-trifluoromethylbenzo[b]thiophene has been attracting attention.

10. Synthesis of 3-trifluoromethylbenzo[b]thiophenes is not easy.  


Chapter 5

Extended Pummerer Reaction of Arylketene Dithioacetal Monoxides with Aromatic Compounds by Means of Trifluoromethanesulfonic Anhydride

Extended Pummerer reaction of arylketene dithioacetal monoxides and aromatic compounds with trifluoromethanesulfonic anhydride proceeds effectively to give diarylketene dithioacetals in moderate to good yields. In the case of intramolecular cyclization of (2-arylphenyl)ketene dithioacetal monoxides, phenanthrenes are obtained via ring-closure and skeletal rearrangement.
**Introduction**

The Pummerer reaction is regarded as an important synthetic method for preparation of α-substituted sulfides. Particularly, the Pummerer rearrangement has been utilized widely as a transformation from alkyl sulfoxides to aldehydes or ketones for synthesis of many natural products. However, extended Pummerer reactions using alkenyl or aryl sulfoxides are still limited. Especially, there are few reports on nucleophilic attack to cationic species generated from alkenyl sulfoxides via cleavage of the S–O bond.

The author has developed new method for the synthesis of benzo[b]thiophenes 4 by cyclization of arylketene dithioacetal monoxides 1 under Pummerer-like conditions (Scheme 1). The reaction should involve stabilized cationic intermediate 2 generated from arylketene dithioacetal monoxides with trifluoromethanesulfonic anhydride. Here, the author reports intermolecular nucleophilic attack to a similar cationic intermediate by aromatic compounds.

![Scheme 1](image)

**Results and Discussion**

First, 2-phenylmethylene-1,3-dithiane 1-oxide (5a) was treated with trifluoromethanesulfonic anhydride in toluene, as a nucleophile as well as solvent, at −78 °C (Scheme 2). The mixture
was warmed to 25 °C, and stirred for 12 h. Extractive work up followed by silica-gel column purification afforded 2-[phenyl(4-tolyl)methylene]-1,3-dithiane (6a) in 80% yield. A plausible reaction mechanism is as follows. At first, sulfoxide 5a gave intermediate 7a upon treatment with trifluoromethanesulfonic anhydride. Then, dicaticionic intermediate 8a could be generated after cleavage of the S–O bond. Friedel–Crafts-type nucleophilic attack to dicaticionic intermediate 8a followed by deprotonation would afford desired product 6a.

**Scheme 2.**

Then, the author has examined reactions of sulfoxide 5a with toluene (1.5 equiv) in the presence of trifluoromethanesulfonic anhydride (1.5 equiv) in several solvents. Although reactions in CH₂Cl₂, CH₃CN, THF, or diethyl ether gave complex mixtures, the use of CH₃NO₂ provided a good result due to the high polarity of the solvent (Scheme 3). Stabilization of caticionic intermediates by CH₃NO₂ could allow toluene to attack intermediate 8a intermolecularly. When acetic anhydride, trifluoroacetic anhydride, or trifluoromethanesulfonic acid was used instead of trifluoromethanesulfonic anhydride, no desired product was obtained.

**Scheme 3.**
The author examined the scope of the extended Pummerer reaction (Table 1). Nucleophilic attack of benzene or chlorobenzene to sulfoxide 5a with the aid of trifluoromethanesulfonic anhydride proceeded to give the expected products in moderate yields, although the nucleophiles were used as solvent (entries 2 and 3). In the case of anisole or naphthalene, the reaction proceeded effectively and the products were obtained as mixtures of regioisomers in high yields (entries 4 and 5). Treatment of mesitylene or \( p \)-chloroanisole gave desired multisubstituted benzene derivatives in good yields (entries 6 and 7).
Table 1. Reaction of sulfoxide 5 with aromatic compounds by means of Tf$_2$O

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nucleophile</th>
<th>Product</th>
<th>Yield/%$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeCl</td>
<td><img src="6a" alt="Image" /></td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td><img src="6b" alt="Image" /></td>
<td>50$^b$</td>
</tr>
<tr>
<td>3</td>
<td>ClMe</td>
<td><img src="6c" alt="Image" /></td>
<td>55$^b$</td>
</tr>
<tr>
<td>4</td>
<td>MeOCl</td>
<td><img src="6d" alt="Image" /></td>
<td>92 (o/p = 1/2)$^c$</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td><img src="6e" alt="Image" /></td>
<td>76 (1/2 = 4/1)</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td><img src="6f" alt="Image" /></td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>OMeCl</td>
<td><img src="6g" alt="Image" /></td>
<td>61</td>
</tr>
</tbody>
</table>

$^a$Isolated yields. 
$^b$Nucleophile was used as solvent instead of CH$_3$NO$_2$.
$^c$Tf$_2$O (2.5 equiv), K$_2$CO$_3$ (5.0 equiv), CH$_3$NO$_2$, 25 °C, 1 h.
Substituents on olefins affected the reaction significantly. Treatment of a mixture of 2-methylene- or 2-propylidene-1,3-dithiane 1-oxide and toluene with trifluoromethanesulfonic anhydride in CH$_3$NO$_2$ gave a complex mixture. In the case of 2-arylmethylene-1,3-dithiane 1-oxide, yields of 6 also heavily depended on substituents on the aromatic rings (Scheme 4). Although the reaction of 2-(4-chlorophenyl)methylene-1,3-dithiane 1-oxide (5b) afforded desired product 6h in good yield, 2-(4-trifluoromethylphenyl)methylene-1,3-dithiane 1-oxide (5c), a more electron-deficient substrate, afforded a complex mixture which did not contain 6i. 2-(4-Methoxyphenyl)methylene-1,3-dithiane 1-oxide (5d) gave desired product 6j in low yield due to some unidentified side reactions.

Scheme 4.

![Scheme 4 diagram]

Then, the author tried intramolecular extended Pummerer reactions. Trifluoromethanesulfonic anhydride was added to biphenylketene dithioacetal monoxide 10a in the presence of 2,6-di-tert-butylpyridine in toluene at $-20 \, ^\circ\text{C}$. The reaction did not give fluorene 12a, but afforded phenanthrene 11a in good yield (Scheme 5). Phenanthrene 11a should be formed via intramolecular extended Pummerer reaction and Wagner–Meerwein-type skeletal rearrangement of cationic intermediate 13a before deprotonation. Methyl-substituted biphenylketene dithioacetal monoxides 10b and 10c also gave the corresponding phenanthrenes 11b and 11c in good yields (Schemes 6 and 7).
Scheme 5.

\[
\begin{align*}
10a & \xrightarrow{\text{MeS}^+ \cdot \text{SMe}_2} 13a & \xrightarrow{T_2O (1.5 \text{ equiv})} 14a & \xrightarrow{\text{toluene} - 20^\circ C, 3 \text{ h}} 15a \\
10b & \xrightarrow{T_2O (1.5 \text{ equiv})} 11b & \xrightarrow{2,6-\text{di-t-butylpyridine (1.5 equiv)}} 11b \text{ (62\%)} \\
10c & \xrightarrow{T_2O (1.5 \text{ equiv})} 11c & \xrightarrow{2,6-\text{di-t-butylpyridine (1.5 equiv)}} 11c \text{ (81\%)}
\end{align*}
\]

Scheme 6.

```
10a 13a 14a 15a
```

Scheme 7.

```
10c 11c 11c'
```

(11c/11c' = 4/1)
Chapter 5

Conclusion

The author has developed an extended Pummerer reaction of arylketene dithioacetal monoxides and aromatic compounds. Nitromethane is the choice of solvent and allows for intermolecular Friedel–Crafts-type nucleophilic attack to cationic intermediates. In the intramolecular extended Pummerer reaction of arylphenylketene dithioacetal monoxides, phenanthrenes were obtained via cyclization and skeletal rearrangement.
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz) and $^{13}$C NMR (126 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl$_3$. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H and relative to CDCl$_3$ at 77.2 ppm for $^{13}$C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (EI unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Trifluoromethanesulfonic anhydride was purchased from TCI. Toluene and nitromethane were purchased from Wako Pure Chemical and toluene was dried over slices of sodium. 2,6-Di-tert-butylpyridine was purchased from Aldrich. All reactions were carried out under argon atmosphere.

Typical Procedure for Reaction of Arylketene Dithioacetal Monoxides with Aromatic Compounds by Means of Trifluoromethanesulfonic Anhydride (Table 1, Entry 1)

Toluene (0.080 mL, 0.75 mmol), trifluoromethanesulfonic anhydride (0.13 mL, 0.77 mmol), and nitromethane (3.0 mL) were placed in a flask under an atmosphere of argon. A solution of 2-(phenylmethylene)-1,3-dithiane 1-oxide (1a, 115.0 mg, 0.51 mmol) in nitromethane (2.0 mL) was added dropwise, and the mixture was stirred at 25 °C for 1 h. Saturated aqueous NaHCO$_3$ was poured into the mixture and the product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 40/1) provided 2-[phenyl(4-tolyl)methylene]-1,3-dithiane (6a, 134.2 mg, 0.45 mmol, 88%).
Characterization Data

(E)-2-[(4-chlorophenyl)methylene]-1,3-dithiane 1-oxide (5b, the major isomer)
Mp 92–93 °C; IR (nujol) 2924, 2853, 1460, 1377, 1265, 1169, 1059, 1043, 902, 823 cm⁻¹;¹H NMR (CDCl₃) δ 2.48–2.59 (m, 2H), 2.64 (ddd, J = 13.0, 4.0, 4.0 Hz, 1H), 2.82–2.90 (m, 2H), 3.40–3.46 (m, 1H), 7.35–7.38 (m, 2H), 7.45 (s, 1H), 7.69–7.72 (m, 2H);¹³C NMR (CDCl₃) δ 27.5, 32.0, 55.2, 128.8, 131.5, 132.3, 133.3, 135.1, 137.7. Found: C, 50.86; H, 4.24%. Calcd for C₁₁H₁₁ClOS₂: C, 51.05; H, 4.28%.

(E)-2-[(4-trifluoromethylphenyl)methylene]-1,3-dithiane 1-oxide (5c, the major isomer)
Mp 91–92 °C; IR (nujol) 2953, 1456, 1410, 1327, 1161, 1116, 1058, 1041, 843 cm⁻¹;¹H NMR (CDCl₃) δ 2.54–2.60 (m, 2H), 2.67 (ddd, J = 13.5, 3.5, 3.5 Hz, 1H), 2.85–2.94 (m, 2H), 3.45–3.51 (m, 1H), 7.56 (s, 1H), 7.66 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H);¹³C NMR (CDCl₃) δ 27.6, 32.1, 55.3, 124.1 (q, J_C–F = 271 Hz), 125.6 (q, J_C–F = 3.8 Hz), 130.4, 130.9 (q, J_C–F = 33 Hz), 133.1, 137.2, 140.3. Found: C, 49.43; H, 3.64%. Calcd for C₁₂H₁₁F₃OS₂: C, 49.30; H, 3.79%.

(E)-2-[(4-methoxyphenyl)methylene]-1,3-dithiane 1-oxide (5d, the major isomer)
Mp 74–75 °C; IR (nujol) 2920, 2853, 2398, 1609, 1507, 1457, 1260, 1226, 1171, 1114, 1054, 876 cm⁻¹;¹H NMR (CDCl₃) δ 2.45–2.60 (m, 3H), 2.80–2.87 (m, 2H), 3.36–3.42 (m, 1H), 3.84 (s, 3H), 6.91–6.94 (m, 2H), 7.43 (s, 1H), 7.76–7.80 (m, 2H);¹³C NMR (CDCl₃) δ 27.2, 31.9, 55.2, 55.5, 114.0, 126.7, 132.1, 133.6, 134.3, 160.5. Found: C, 56.67; H, 5.45%. Calcd for C₁₂H₁₄O₂S₂: C, 56.66; H, 5.55%.

2-[phenyl(4-tolyl)methylene]-1,3-dithiane (6a)
Mp 123–124 °C; IR (nujol) 2923, 2854, 1458, 1439, 1377, 1294, 1111, 1027, 918, 775, 750, 696 cm⁻¹;¹H NMR (CDCl₃) δ 2.12–2.17 (m, 2H), 2.37 (s, 3H), 2.96–2.99 (m, 4H), 7.11–7.17
m, 4H), 7.22–7.25 (m, 2H), 7.26–7.29 (m, 1H), 7.32–7.36 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 21.4, 24.2 (Two signals merge.). 29.7, 127.3, 128.0, 128.4, 129.8, 129.9, 137.1, 138.5, 139.6, 141.5. HRMS (m/z) Observed: 298.0850 ($\Delta = +0.0$ ppm). Calcd for C$_{18}$H$_{18}$S$_2$: 298.0850.

2-(diphenylmethylene)-1,3-dithiane (6b)
Mp 126–127 °C; IR (nujol) 2921, 2853, 1441, 1031, 970, 913, 846, 766, 736, 699 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.11 (quintet, $J = 6.5$ Hz, 2H), 2.96–2.98 (t, $J = 6.5$ Hz, 4H), 7.22–7.24 (m, 4H), 7.26–7.29 (m, 2H), 7.32–7.36 (m, 4H); $^{13}$C NMR (CDCl$_3$) δ 24.2, 29.7, 127.4, 128.1, 130.0, 130.3, 139.5, 141.4. Found: C, 71.58; H, 5.68%. Calcd for C$_{17}$H$_{16}$S$_2$: C, 71.78; H, 4.74%.

2-[(4-chlorophenyl)phenylmethylene]-1,3-dithiane (6c)
Mp 135–136 °C; IR (nujol) 2922, 2853, 1457, 1378, 1087, 1017, 840, 750 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.12–2.18 (m, 2H), 2.95–3.00 (m, 4H), 7.17 (d, $J = 8.5$ Hz, 2H), 7.20 (d, $J = 8.5$ Hz, 2H), 7.27–7.31 (m, 3H), 7.33–7.36 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 24.1, 29.6 (Two signals merge.). 127.6, 128.3, 130.0, 131.3, 131.4, 133.2, 138.0, 139.7, 141.0. Found: C, 64.28; H, 4.83%. Calcd for C$_{17}$H$_{16}$ClS$_2$: C, 64.03; H, 4.74%.

2-[(4-methoxyphenyl)phenylmethylene]-1,3-dithiane (6d, the major isomer)
Mp 112–113 °C; IR (nujol) 2923, 2853, 1683, 1653, 1594, 1559, 1506, 1490, 1457, 1437, 1236, 1029, 751, 700 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.11–2.17 (m, 2H), 2.95–2.99 (m, 4H), 3.82 (s, 3H), 6.85–6.88 (m, 2H), 7.14–7.17 (m, 2H), 7.20–7.23 (m, 2H), 7.25–7.29 (m, 1H), 7.31–7.36 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 24.3, 29.8 (Two signals merge.), 55.4, 113.5, 127.4, 128.1, 129.1, 130.1, 131.3, 133.9, 139.4, 141.7, 158.9. Found: C, 68.60; H, 5.78%. Calcd for C$_{18}$H$_{18}$OS$_2$: C, 68.75; H, 5.77%.

2-[(1-naphthyl)phenylmethylene]-1,3-dithiane (6e, the major isomer)
Mp 151–152 °C; IR (nujol) 2853, 1440, 1416, 1378, 1301, 799, 794, 779, 767, 735, 698 cm$^{-1}$;
\(^{1}\)H NMR (CDCl\(_3\)) δ 2.09–2.14 (m, 2H), 2.82–2.87 (m, 1H), 2.92–3.01 (m, 2H), 3.03–3.08 (m, 1H), 7.19–7.24 (m, 1H), 7.28–7.36 (m, 2H), 7.35–7.38 (m, 2H), 7.40 (d, J = 7.0 Hz, 1H), 7.46–7.53 (m, 3H), 7.84 (d, J = 8.0 Hz, 1H), 7.86–7.89 (m, 1H), 7.96–8.00 (m, 1H); \(^{13}\)C NMR (CDCl\(_3\)) δ 24.0, 29.6, 29.7, 125.7, 125.8, 126.0, 126.5, 127.3, 127.9, 128.0, 128.1, 128.6, 129.2, 131.7, 132.1, 134.1, 137.2, 139.5, 140.5. Found: C, 75.60; H, 5.47%. Calcd for C\(_{21}\)H\(_{18}\)S\(_2\): C, 75.40; H, 5.42%.

2-(mesitylphenylmethylene)-1,3-dithiane (6f)

Mp 97–99 °C; IR (nujol) 2853, 1685, 1654, 1559, 1507, 1490, 758.0 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\)) δ 2.17–2.22 (m, 2H), 2.26 (s, 6H), 2.38 (s, 3H), 2.99–3.04 (m, 4H), 6.99 (s, 2H), 7.25–7.29 (m, 1H), 7.32–7.37 (m, 4H); \(^{13}\)C NMR (CDCl\(_3\)) δ 20.0, 21.4, 24.2, 29.4, 29.9, 127.0, 127.8, 128.7, 129.3, 129.8, 136.5, 137.3, 137.5, 138.0, 138.8. Found: C, 73.79; H, 6.84%. Calcd for C\(_{20}\)H\(_{22}\)S\(_2\): C, 73.57; H, 6.79%.

2-[(5-chloro-2-methoxyphenyl)phenylmethylene]-1,3-dithiane (6g)

Mp 129–130 °C; IR (nujol) 2323, 1734, 1700, 1684, 1653, 1558, 751 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\)) δ 2.11–2.16 (m, 2H), 2.93–2.96 (m, 4H), 3.74 (s, 3H), 6.84 (d, J = 9.0 Hz, 1H), 7.15 (d, J = 2.5 Hz, 1H), 7.22–7.28 (m, 4H), 7.30–7.33 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) δ 24.1, 29.6 (Two signals merge.), 56.2, 112.8, 125.4, 127.3, 128.0, 128.7, 129.4, 131.0, 131.7, 132.4, 134.7, 140.3, 155.7. Found: C, 61.91; H, 4.79%. Calcd for C\(_{18}\)H\(_{17}\)ClO\(_{2}\)S\(_2\): C, 61.96; H, 4.91%.

2-[(4-chlorophenyl)(4-tolyl)methylene]-1,3-dithiane (6h)

Mp 143–144 °C; IR (nujol) 2922, 2853, 1685, 1559, 1457, 1437, 1302, 1089, 826 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\)) δ 2.12–2.17 (m, 2H), 2.36 (s, 3H), 2.94–3.00 (m, 4H), 7.06–7.10 (m, 2H), 7.14–7.18 (m, 4H), 7.28–7.31 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) δ 21.5, 24.1 (Two signals merge.), 29.7, 128.3, 129.0, 129.9, 130.6, 131.4, 133.1, 137.5, 138.1, 138.2, 139.9. Found: C, 64.79; H, 5.09%. Calcd for C\(_{18}\)H\(_{17}\)ClO\(_{2}\): C, 64.94; H, 5.15%.
2-[(4-methoxyphenyl)(4-tolyl)methylene]-1,3-dithiane (6j)
Mp 111–112 °C; IR (nujol) 2923, 2853, 1507, 1490, 1457, 1245, 1176, 1111, 1037, 840, 761 cm⁻¹; ¹H NMR (CDCl₃) δ 2.11–2.19 (m, 2H), 2.35 (s, 3H), 2.94–2.98 (m, 4H), 3.81 (s, 3H), 6.84–6.87 (m, 2H), 7.08–7.16 (m, 6H); ¹³C NMR (CDCl₃) δ 21.5, 24.4 (Two signals merge.), 29.9, 55.4, 113.4, 128.3, 128.8, 129.9, 131.3, 134.0, 137.2, 138.8, 139.5, 158.8. Found: C, 69.18; H, 6.00%. Calcd for C₁₉H₂₀OS₂: C, 69.47; H, 6.14%.

(E)-2-(2-biphenyl)-1-(methylsulfinyl)ethenyl methyl sulfide (10a, the major isomer)
IR (nujol) 3059, 2995, 2923, 1472, 1450, 1435, 1417, 1286, 1067, 1009, 954, 934, 906, 778, 758, 742, 724, 702 cm⁻¹; ¹H NMR (CDCl₃) δ 2.25 (s, 3H), 2.66 (s, 3H), 7.28–7.30 (m, 2H), 7.32–7.46 (m, 6H), 7.60 (s, 1H), 7.88–7.92 (m, 1H); ¹³C NMR (CDCl₃) δ 18.0, 40.2, 127.3, 127.8, 128.4, 129.3 (Two signals merge.), 129.7, 130.3, 132.2, 136.5, 140.3, 142.1, 142.5. Found: C, 66.36; H, 5.70%. Calcd for C₁₆H₁₆OS₂: C, 66.63; H, 5.59%.

(E)-2-[2-(4-tolyl)phenyl]-1-(methylsulfinyl)ethenyl methyl sulfide (10b, the major isomer)
Mp 74–75 °C; IR (nujol) 2923, 2853, 1467, 1445, 1377, 1068, 1007, 976, 825, 759, 750 cm⁻¹; ¹H NMR (CDCl₃) δ 2.27 (s, 3H), 2.38 (s, 3H), 2.68 (s, 3H), 7.17–7.22 (m, 4H), 7.38–7.44 (m, 3H), 7.60 (s, 1H), 7.91–7.93 (m, 1H); ¹³C NMR (CDCl₃) δ 18.1, 21.5, 40.3, 127.1, 129.2, 129.4 (Two signals merge.), 129.7, 130.4, 132.2, 136.9, 137.4, 137.7, 141.8, 142.7. Found: C, 67.55; H, 6.10%. Calcd for C₁₇H₁₈OS₂: C, 67.51; H, 6.00%.

(E)-2-[2-(3-tolyl)phenyl]-1-(methylsulfinyl)ethenyl methyl sulfide (10c, the major isomer)
Mp 80–81 °C; IR (nujol) 2924, 2853, 1456, 1377, 1053, 956, 926, 907, 877, 791, 774, 762, 750, 701 cm⁻¹; ¹H NMR (CDCl₃) δ 2.28 (s, 3H), 2.39 (s, 3H), 2.67 (s, 3H), 7.07–7.12 (m, 2H), 7.15–7.18 (m, 1H), 7.29 (dd, J = 8.0, 8.0 Hz, 1H), 7.38–7.46 (m, 3H), 7.60 (s, 1H), 7.90–7.94 (m, 1H); ¹³C NMR (CDCl₃) δ 18.0, 21.6, 40.2, 126.9, 127.2, 128.3, 128.5, 129.2 (Two signals merge.), 130.2, 130.4, 132.2, 136.7, 137.9, 140.2, 141.8, 142.7. HRMS (m/z) Observed:
302.0796 (Δ = –1.0 ppm). Calcd for C₁₇H₁₈OS₂: 302.0799.

9,10-di(methylsulfanyl)phenanthrene (11a)
Mp 78–80 °C; IR (nujol) 2923, 2853, 1685, 1654, 1558, 1507, 1457, 967, 752, 723 cm⁻¹; ¹H NMR (CDCl₃) δ 2.52 (s, 6H), 7.69–7.73 (m, 4H), 8.70–8.74 (m, 2H), 8.89–8.94 (m, 2H); ¹³C NMR (CDCl₃) δ 21.1, 123.1, 127.6, 127.7, 128.8, 131.3, 132.7, 140.8. Found: C, 71.09; H, 5.14%. Calcd for C₁₆H₁₄S₂: C, 71.07; H, 5.22%.

2-methyl-9,10-di(methylsulfanyl)phenanthrene (11b)
Mp 89–90 °C; IR (nujol) 2923, 2853, 1559, 1507, 1457, 1156, 964, 758 cm⁻¹; ¹H NMR (CDCl₃) δ 2.51 (s, 3H), 2.52 (s, 3H), 2.64 (s, 3H), 7.54 (dd, J = 8.5, 1.0 Hz, 1H), 7.64–7.70 (m, 2H), 8.60 (d, J = 8.5 Hz, 1H), 8.66–8.68 (m, 1H), 8.70 (s, 1H), 8.86–8.90 (m, 1H); ¹³C NMR (CDCl₃) δ 21.1, 21.2, 22.1, 122.9, 123.1, 127.2, 127.6, 128.3, 128.7, 129.1, 129.4, 131.3, 132.3, 132.8, 137.5, 140.5, 140.8. Found: C, 71.63; H, 5.88%. Calcd for C₁₇H₁₆S₂: C, 71.78; H, 5.67%.

3-methyl-9,10-di(methylsulfanyl)phenanthrene (11c, the major isomer)
Mp 79–80 °C; IR (nujol) 2854, 1559, 1490, 968, 818, 761, 727 cm⁻¹; ¹H NMR (CDCl₃) δ 2.50 (s, 3H), 2.51 (s, 3H), 2.65 (s, 3H), 7.53 (dd, J = 8.0, 1.0 Hz, 1H), 7.67–7.71 (m, 2H), 8.50 (s, 1H), 8.69–8.72 (m, 1H), 8.78 (d, J = 8.0 Hz, 1H), 8.88–8.91 (m, 1H); ¹³C NMR (CDCl₃) δ 21.1 (Two signals merge.), 22.1, 122.9, 123.1, 127.4, 127.5, 128.7 (Two signals merge.), 129.3, 130.7, 131.0, 131.3, 132.8, 137.6, 139.5, 140.8. Found: C, 71.75; H, 5.73%. Calcd for C₁₇H₁₆S₂: C, 71.78; H, 5.67%.
References and Notes


6. According to chapter 4, the generation of dicationic intermediate 8a is possible. However, the possibility of attack of toluene to intermediate 7a in an SN2’ mode cannot be excluded.

7. Treatment of 10a with trifluoromethanesulfonic anhydride in CH$_3$NO$_2$ gave a complex mixture. After extensive screening of the reaction conditions for the cyclization, the author has found the best conditions.


Chapter 6

Trifluoromethylketene Dithioacetal Monoxide
as a Trifluoromethylketene Equivalent

Preparative method of trifluoromethylketene dithioacetal monoxide and its interesting reactivity under Pummerer-like conditions are developed. Treatment of a mixture of trifluoromethylketene dithioacetal monoxide and allylsilanes with trifluoromethanesulfonic anhydride in nitromethane in the presence of 2,6-di-tert-butylpyridine afforded the corresponding allylated ketene dithioacetals in good yields. The products should be converted into various trifluoromethylated compounds which have interesting properties.
Introduction

Trifluoromethylated compounds have attracted much attention because of their important applications as biologically active agents and advanced organic materials, which exhibit specific biological and physical properties.¹ The methods for introducing a trifluoromethyl group into an organic compound have thus been investigated extensively.² However, α-trifluoromethylation of carbonyl compounds has remained difficult.³ Therefore, a novel trifluoromethylketene equivalent should be a useful building block for synthesis of α-trifluoromethyl carbonyl compounds.⁴

Recently, the author has been developing the synthetic utility of ketene dithioacetal monoxides as ketene equivalents.⁵ Thus, the author has been interested in the chemical behavior of trifluoromethylketene dithioacetal monoxide ¹a. He anticipated that trifluoromethylketene dithioacetal monoxide ¹a would react with nucleophile at C¹ under extended Pummerer reaction conditions to yield ² which might be very attractive intermediate for further transformation (Scheme 1). Hydrolysis of ketene dithioacetal ² could provide thiolester ³ which should react with nucleophile at C² to give α-trifluoromethyl ketone ⁴. Alternatively, reduction of ² could afford dithiane ⁵, which should be converted into carbanion by deprotonation of hydrogen adjacent to two sulfur atoms. Then, the carbanion could behave as an acyl anion equivalent. The addition of electrophile to the anion would provide another route to α-trifluoromethyl ketone ⁶. Here, the author reports the synthetic method for trifluoromethylketene dithioacetal monoxide ¹a and its interesting reactivity in extended Pummerer reaction.
Results and Discussion

Trifluoromethylketene dithioacetal monoxide 1a was prepared starting from 1,3-dithiane and ethyl trifluoroacetate as stereoisomeric mixtures (E/Z = 4/1) (Scheme 2). The method is facile and scalable. Trifluoroacetylation of 1,3-dithiane followed by reduction and tosylation afforded dithiane 7. Oxidation of 7 to monosulfoxide and subsequent treatment with potassium tert-butoxide yielded trifluoromethylketene dithioacetal monoxide 1a. The stereoisomers of 1a were separated from each other by column chromatography on silica gel.
The author then examined the reactivity of trifluoromethylketene dithioacetal monoxide \((E)-1a\) as a Michael acceptor.\(^6\) Treatment of \((E)-1a\) with di-\(\text{tert}\)-butyl malonate in the presence of potassium \(\text{tert}\)-butoxide gave the corresponding adduct \(8\) in high yield (Scheme 3).

\[\text{Scheme 3.} \]

\[
\begin{align*}
\text{CF}_3\text{S}^\text{O} & \quad \text{t-BuOK (1.0 equiv)} \quad \text{THF} \quad 25^\circ\text{C}, 6\text{ h} \\
\text{(E)-1a} & \quad t-\text{BuO}_2\text{C} \quad t-\text{BuO}_2\text{C} \\
& \quad 83\% \\
& \quad (\text{single isomer})
\end{align*}
\]

An interesting reactivity of trifluoromethylketene dithioacetal monoxide \(1a\) was observed in extended Pummerer reaction\(^5c,7\) using allylsilanes. Treatment of \((E)-1a\) with allyltrimethylsilane \((9a)\) in the presence of trifluoromethanesulfonic anhydride and 2,6-di-\(\text{tert}\)-butylpyridine provided the corresponding allylated ketene dithioacetal \(10a\) in high yield (Table 1, entry 1). A mixture of \(E\) and \(Z\) isomers of \(1a\) \((E/Z = 2/3)\) reacted equally as \((E)-1a\) to afford \(10a\). Perfluoroalkylketene dithioacetal monoxide \((E)-1b\) also reacted with allylsilane \(9a\) under the same reaction conditions (entry 2). On the other hand, the reactions of phenyl- and methyl-substituted ketene dithioacetal monoxides \((E)-1c\) and \((E)-1d\) gave complex mixtures (entries 3 and 4). Thus, the trifluoromethyl or perfluoroalkyl group played an important role for the successful reaction.

\[\text{Table 1. Reaction of 1 with allylsilane in the presence of Tf}_2\text{O.} \]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>1</th>
<th>10</th>
<th>Yield /%(^a)</th>
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<tbody>
<tr>
<td>1</td>
<td>CF(_3)</td>
<td>1a</td>
<td>10a</td>
<td>86 (85)(^b)</td>
</tr>
<tr>
<td>2</td>
<td>C(_2)F(_7)</td>
<td>1b</td>
<td>10b</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>CH(_3)</td>
<td>1c</td>
<td>10c</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>1d</td>
<td>10d</td>
<td>7</td>
</tr>
</tbody>
</table>

\(^a\)Isolated yields.
\(^b\)An \(E/Z\) mixture was used instead of pure \(E\) isomer.
Then, the author examined the scope and limitation using various allylsilanes and allylstannane (Table 2). The reaction with allyl-tert-butyl dimethylsilane (9b) also proceeded effectively to give allylated ketene dithioacetal 10a in good yield (entry 2). On the other hand, allyltributylstannane (9c) failed to cause efficient allylation and afforded 10a in only 29% yield (entry 3). The reactions with β-methyl- and β-phenyl-substituted allylsilanes 9d and 9e afforded the corresponding products 10e and 10f, respectively, in high yields (entries 4 and 5). In the reactions with γ-substituted allylsilanes (entries 6–9), unusual regioselectivity was found. γ-(2-Phenylethyl)-substituted allylsilane 9f reacted with 1a to yield ketene dithioacetal 10g stereo- and regioselectively (entry 6), which was produced via carbon-carbon bond formation at the α-position of 9f. γ-Heptyl-substituted allylsilane 9g also reacted at the α position exclusively (entry 7). However, the reaction with cinnamylsilane 9h gave a complex mixture with no trace amount of the expected product 10i (entry 8). γ,γ-Disubstituted allylsilane 9i was not a good allylating agent (entry 9).
Table 2. Reaction of 1a with allylsilane 9 in the presence of Tf$_2$O.

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Entry</th>
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<th>10</th>
<th>Yield /%$^a$</th>
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</thead>
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<td>1</td>
<td>$\text{SiMe}_3$</td>
<td>$\text{Me}$</td>
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</tr>
<tr>
<td>2</td>
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<td>$\text{Ph}$</td>
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<tr>
<td>3</td>
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<td>$\text{Me}$</td>
<td>29</td>
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<tr>
<td>4</td>
<td>$\text{SiMe}_3$</td>
<td>$\text{Ph}$</td>
<td>86</td>
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<tr>
<td>5</td>
<td>$\text{SiMe}_3$</td>
<td>$\text{Ph}$</td>
<td>87$^b$</td>
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<td>$\text{Ph}$</td>
<td>$\text{SiMe}_3$</td>
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<tr>
<td>7</td>
<td>$\text{C}<em>7\text{H}</em>{15}$</td>
<td>$\text{SiMe}_3$</td>
<td>75$^c$</td>
</tr>
<tr>
<td>8</td>
<td>$\text{Ph}$</td>
<td>$\text{SiMe}_3$</td>
<td>0$^b$</td>
</tr>
<tr>
<td>9</td>
<td>$\text{C}<em>7\text{H}</em>{15}$</td>
<td>$\text{SiMe}_3$</td>
<td>19$^d$</td>
</tr>
</tbody>
</table>

$^a$Isolated yields. $^b$2.0 equiv of 9 was used and the reaction was performed at 0 °C for 1 h. $^c$CH$_2$Cl$_2$ was used as solvent instead of CH$_3$NO$_2$. $^d$CH$_2$Cl$_2$/CH$_3$NO$_2$ (1/1) was used as solvent.
A plausible reaction mechanism was shown in Scheme 4. Treatment of 1a with trifluoromethanesulfonic anhydride gives sulfonium salt A.\textsuperscript{5b,5c} Allylsilane 9 then attacks to sulfur along with liberation of trimethylsilyl triflate to afford sulfonium salt B. Sulfonium salt B then undergoes [3, 3]-sigmatropic rearrangement, followed by deprotonation, to afford 10 with high stereo- and regioselectivity.\textsuperscript{10} Although the role of the trifluoromethyl group is still unclear, the trifluoromethyl group might prevent generation of dicationic species via cleavage of the S–O bond.\textsuperscript{5b,5c}

The product 10 should be a useful synthetic intermediate. Treatment of ketene dithioacetal 10a with aqueous hydrochloric acid in acetonitrile yielded thiolester 11, which is a good electrophile in the reactions with various nucleophiles.\textsuperscript{11} Reduction of ketene dithioacetal 10a proceeded smoothly in the presence of NaBH\textsubscript{4} and hydrochloric acid to afford trifluoromethylated dithiane 12, which could be used further as an acyl anion equivalent.\textsuperscript{12}
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Conclusion

The author has synthesized trifluoromethylketene dithioacetal monoxide and disclosed its interesting reactivity under Pummerer-like conditions. The trifluoromethyl group plays an important role for the extended Pummerer reaction. The product should provide a new entry to various trifluoromethylated compounds.
Experimental Section

Instrumentation and Chemicals

$^1$H NMR (500 MHz), $^{13}$C NMR (126 MHz), and $^{19}$F NMR (282 MHz) spectra were taken on Varian UNITY INOVA 500 and Mercury 300 spectrometers and were recorded in CDCl$_3$. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for $^1$H, relative to CDCl$_3$ at 77.2 ppm for $^{13}$C, and relative to C$_6$F$_6$ at 0.00 ppm unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra (EI unless otherwise noted) were determined on a JEOL MStation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F$_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Trifluoromethanesulfonic anhydride was purchased from TCI. Nitromethane was purchased from Wako Pure Chemical. Allylsilane $^{5e}$, $^{13}$ $^{5f}$, $^{14}$ $^{5g}$, $^{14}$ $^{5h}$, $^{13}$ and $^{5i}$ $^{14}$ were prepared according to the literature. All reactions were carried out under argon atmosphere.

Preparation of 2-(2,2,2-trifluoro-1-tosyloxyethyl)-1,3-dithiane (7)

Butyllithium (1.60 M in hexane, 13.0 mL, 20.8 mmol) was added to a solution of 1,3-dithiane (2.40 g, 20.0 mmol) in THF (20 mL) at –20 °C. After being stirred for 1 h at the same temperature, the reaction mixture was added dropwise to a THF (20 mL) solution of ethyl trifluoroacetate (6.0 mL, 50 mmol) at –78 °C. After the mixture was stirred for 1 h at the same temperature, the reaction mixture was allowed to warm to room temperature gradually over 12 h. Water (20 mL) was added to the reaction mixture, and the mixture was extracted with ethyl acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure.
A Et₂O (20 mL) solution of the crude product was placed in a flask under an atmosphere of argon, and LiAlH₄ (0.38 g, 10 mmol) was added to the solution at −78 °C. After the mixture was stirred for 1 h at the same temperature, ethyl acetate (5 mL) was added slowly. Then, aqueous hydrochloric acid (1 M, 20 mL) was added to the reaction mixture. The mixture was extracted with ethyl acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure.

A CH₂Cl₂ (30 mL) solution of the crude product, p-tolylsulfonyl chloride (4.40 g, 22.9 mmol), and triethylamine (3.0 mL, 22 mmol) was treated with 4-(dimethylamino)pyridine (5 mg, 0.04 mmol). After the mixture was stirred for 12 h at room temperature, water (20 mL) was added to the reaction mixture. The mixture was extracted with chloroform (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure. Purification by silica-gel column chromatography (hexane/AcOEt = 10/1) provided 2-(2,2,2-trifluoro-1-tosyloxyethyl)-1,3-dithiane (7, 5.26 g, 14.1 mmol, 71%).

**Preparation of 2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide (1a)**

Sodium periodate (1.4 g, 6.5 mmol) in water (15 mL) was added dropwise over 1 h to a methanol (50 mL) solution of 2-(2,2,2-trifluoro-1-tosyloxyethyl)-1,3-dithiane (7, 2.3 g, 6.2 mmol) at 0 °C. After being stirred for 1 h at the same temperature, the reaction mixture was stirred at room temperature for 12 h. After filtration, the filtrate was concentrated in vacuo, and extracted with ethyl acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure.

Potassium tert-butoxide (0.80 g, 7.1 mmol) was added to the crude product in tert-butyl alcohol (20 mL) at room temperature. After being stirred for 4 h, water (20 mL) was added to the reaction mixture. The mixture was extracted with ethyl acetate (10 mL) three times. The combined organic extract was washed with brine, dried over sodium sulfate, and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 1/1) provided 2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide (1a, E/Z = 4/1, 0.96 g, 4.4 mmol, 72%).
Typical Procedure for Reaction of Trifluoromethylketene Dithioacetal Monoxide with Allylsilane in the Presence of Trifluoromethanesulfonic Anhydride (Table 1, Entry 1)

A nitromethane solution of allyltrimethylsilane (5a, 0.048 mL, 0.30 mmol), (E)-2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide (1a, 43.7 mg, 0.20 mmol), and 2,6-di-tert-butylpyridine (0.053 mL, 0.30 mmol) was placed in a flask under an atmosphere of argon. Trifluoromethanesulfonic anhydride (0.040 mL, 0.24 mmol) was added, and the mixture was stirred at 25 °C for 30 min. Saturated aqueous NaHCO$_3$ was poured into the mixture and the product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. Purification by chromatography on silica gel (hexane/AcOEt = 10/1) provided 2-(1-trifluoromethyl-3-butenylidene)-1,3-dithiane (10a, 41.3 mg, 0.17 mmol, 86%).

Characterization Data

(E)-2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide (1a, the major isomer)
IR (neat) 2922, 1616, 1420, 1256, 1132, 1046, 901, 879, 655 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.52–2.63 (m, 2H), 2.72–2.78 (m, 1H), 2.91–2.98 (m, 2H), 3.52 (dddd, $J = 11.5, 4.0, 4.0, 1.5$ Hz, 1H), 6.80 (q, $J_{H-F} = 8.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 27.7, 31.9, 54.9, 122.2 (q, $J_{C-F} = 271$ Hz), 123.4 (q, $J_{C-F} = 36$ Hz), 153.1 (q, $J_{C-F} = 4.3$ Hz); $^{19}$F NMR (CDCl$_3$) δ 34.3–34.2 (m, 2F), 53.2–55.5 (m, 2F), 81.0 (t, $J_{F-H} = 8.0$ Hz, 3F). Found: C, 33.42; H, 3.38%. Calcd for C$_6$H$_7$F$_3$OS$_2$: C, 33.33; H, 3.26%.

(E)-2-(2,2,3,3,4,4,4-heptafluorobutylidene)-1,3-dithiane 1-oxide (1b, the major isomer)
IR (neat) 2922, 1616, 1420, 1256, 1132, 1046, 1008, 901, 879, 655 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 2.50–2.64 (m, 2H), 2.73–2.79 (m, 1H), 2.89–2.97 (m, 2H), 3.50–3.56 (m, 1H), 6.73 (t, $J_{H-F} = 14.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 27.8, 32.0, 55.1, 108.0–119.3 (m), 120.9 (t, $J_{C-F} = 25$ Hz), 155.5; $^{19}$F NMR (CDCl$_3$) δ 34.3–34.2 (m, 2F), 53.2–55.5 (m, 2F), 81.0 (t, $J = 8.9$ Hz, 3F). HRMS (FAB$^+$) (m/z) Observed: 316.9900 ($\Delta = –1.5$ ppm). Calcd for C$_8$H$_8$F$_7$OS$_2$ [MH$^+$]:
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316.9905.

2-(2,2,2-trifluoro-1-tosyloxyethyl)-1,3-dithiane (7)
Mp 81–82 °C; IR (nujol) 2924, 2853, 1365, 1282, 1173, 1143, 1073, 972, 819, 682 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.97–2.10 (m, 2H), 2.47 (s, 3H), 2.73–2.83 (m, 2H), 2.99–3.08 (m, 2H), 4.16 (d, \(J = 6.0\) Hz, 1H), 5.24 (dq, \(J = 6.0\) Hz, \(J_{H-F} = 6.0\) Hz, 1H), 7.34–7.38 (m, 2H), 7.84–7.87 (m, 2H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 22.0, 24.9, 28.2 (q, \(J_{C-F} = 12\) Hz), 42.4 (Two signals merge.), 78.1 (q, \(J_{C-F} = 32\) Hz), 122.3 (q, \(J_{C-F} = 282\) Hz), 128.4, 130.0, 133.3, 145.8; \(^19\)F NMR (CDCl\(_3\)) \(\delta\) 89.6 (d, \(J_{F-H} = 9.0\) Hz, 3F). HRMS (m/z) Observed: 372.0140 (\(\Delta = +1.3\) ppm). Calcd for C\(_{13}\)H\(_{15}\)F\(_3\)O\(_3\)S\(_3\): 372.0135.

di-tert-butyl 2-[2,2,2-trifluoro-1-(2-oxo-2,6-dithiacyclohexyl)ethyl]malonate (8)
Mp 100–101 °C; IR (nujol) 2924, 2853, 1744, 1728, 1369, 1339, 1121, 1036, 744 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.47 (s, 9H), 1.50 (s, 9H), 2.25–2.36 (m, 1H), 2.43–2.49 (m, 1H), 2.53–2.68 (m, 3H), 3.54–3.60 (m, 1H), 3.75 (d, \(J = 9.0\) Hz, 1H), 4.17 (ddq, \(J = 9.0, 3.0\) Hz, \(J_{H-F} = 9.0\) Hz, 1H), 4.28 (d, \(J = 3.0\) Hz, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 27.9, 28.0, 29.9, 31.8, 40.1 (q, \(J_{C-F} = 14\) Hz), 51.5, 56.5, 64.5, 83.4 (Two signals merge.), 124.8 (q, \(J_{C-F} = 282\) Hz), 165.3, 165.6; \(^19\)F NMR (CDCl\(_3\)) \(\delta\) 97.9 (d, \(J = 9.0\) Hz, 3F). HRMS (FAB\(^+\)) (m/z) Observed: 433.1329 (\(\Delta = –0.3\) ppm). Calcd for C\(_{17}\)H\(_{28}\)F\(_3\)O\(_5\)S\(_2\) [MH\(^+\)]: 433.1330.

2-(1-trifluoromethyl-3-butenylidene)-1,3-dithiane (10a)
IR (neat) 2930, 1639, 1564, 1421, 1299, 1216, 1108, 1074, 918 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.11 (tt, \(J = 7.0, 7.0\) Hz, 2H), 2.98 (t, \(J = 7.0\) Hz, 2H), 3.00 (t, \(J = 7.0\) Hz, 2H), 3.18 (d, \(J = 6.0\) Hz, 2H), 5.05–5.13 (m, 2H), 5.71–5.79 (m, 1H); \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 23.4, 28.5, 28.8, 34.5 (q, \(J_{C-F} = 2.4\) Hz), 116.4, 121.5 (q, \(J_{C-F} = 29\) Hz), 124.0 (q, \(J_{C-F} = 273\) Hz), 133.6, 145.0 (q, \(J_{C-F} = 2.9\) Hz); \(^19\)F NMR (CDCl\(_3\)) \(\delta\) 103.2 (s, 3F). HRMS (m/z) Observed: 240.0258 (\(\Delta = +1.4\) ppm). Calcd for C\(_9\)H\(_{11}\)F\(_3\)S\(_2\): 240.0255.
2-(1-heptafluoropropyl-3-butenylidene)-1,3-dithiane (10b)

IR (neat) 1685, 1546, 1507, 1420, 1340, 1219, 1178, 1107, 912 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.13 (tt, \(J = 7.0, 7.0\) Hz, 2H), 2.94 (t, \(J = 7.0\) Hz, 2H), 3.01 (t, \(J = 7.0\) Hz, 2H), 3.13–3.16 (m, 2H), 5.06–5.14 (m, 2H), 5.76 (ddt, \(J = 10.0, 7.0, 4.0\) Hz, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 23.3, 28.7, 28.9, 35.1, 106.0–121.7 (m), 133.8, 148.9; \(^{19}\)F NMR (CDCl\(_3\)) \(\delta\) 36.2–36.3 (m, 2F), 56.9–57.1 (m, 2F), 80.8 (t, \(J = 9.9\) Hz, 3F). HRMS (m/z) Observed: 341.0261 (\(\Delta = -2.3\) ppm). Calcd for C\(_{11}\)H\(_{12}\)F\(_7\)S\(_2\) [MH\(^+\)]: 341.0269.

2-(1-trifluoromethyl-3-methyl-3-butenylidene)-1,3-dithiane (10e)

IR (neat) 1560, 1420, 1301, 1159, 1089, 901 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.76 (s, 3H), 2.14 (tt, \(J = 7.0, 7.0\) Hz, 2H), 2.98–3.00 (m, 4H), 3.13 (s, 2H), 4.70 (s, 1H), 4.78–4.81 (m, 1H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 22.7, 23.4, 28.5, 28.8, 38.3 (q, \(J_{C-F} = 2.4\) Hz), 111.2, 122.0 (q, \(J_{C-F} = 30\) Hz), 124.0 (q, \(J_{C-F} = 273\) Hz), 141.6, 145.8 (q, \(J_{C-F} = 3.4\) Hz); \(^{19}\)F NMR (CDCl\(_3\)) \(\delta\) 103.0 (s, 3F). Found: C, 47.49; H, 5.07%. Calcd for C\(_{10}\)H\(_{13}\)F\(_3\)S\(_2\): C, 47.22; H, 5.15%.

2-(1-trifluoromethyl-3-phenyl-3-butenylidene)-1,3-dithiane (10f)

IR (neat) 2930, 1562, 1495, 1420, 1300, 1161, 1108, 910, 779, 706 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.12–2.18 (m, 2H), 2.97–3.03 (m, 4H), 3.60 (s, 2H), 5.03 (s, 1H), 5.35 (s, 1H), 7.29–7.38 (m, 3H), 7.44–7.47 (m, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 23.4, 28.5, 28.8, 38.3 (q, \(J_{C-F} = 2.4\) Hz), 111.2, 122.0 (q, \(J_{C-F} = 30\) Hz), 124.0 (q, \(J_{C-F} = 273\) Hz), 126.3, 127.8, 128.5, 141.4, 143.7, 146.8; \(^{19}\)F NMR (CDCl\(_3\)) \(\delta\) 103.0 (s, 3F). Found: C, 56.96; H, 4.83%. Calcd for C\(_{15}\)H\(_{15}\)F\(_3\)S\(_2\): C, 56.94; H, 4.78%.

\((E)\)-2-(1-trifluoromethyl-6-phenyl-3-hexenylidene)-1,3-dithiane (10g)

IR (neat) 2929, 2853, 1564, 1496, 1420, 1298, 1107, 967, 747, 699 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.14 (tt, \(J = 7.0, 7.0\) Hz, 2H), 2.33 (dt, \(J = 8.0, 8.0\) Hz, 2H), 2.68 (t, \(J = 8.0\) Hz, 2H), 2.97–3.01 (m, 4H), 3.12 (d, \(J = 6.0\) Hz, 2H), 5.37 (dt, \(J = 15.0, 6.0\) Hz, 1H), 5.53–5.59 (m, 1H), 7.16–7.21 (m,
3H), 7.27–7.30 (m, 2H); $^{13}$C NMR (CDCl$_3$) δ 23.4, 28.4, 28.7, 33.5 (q, $J_{C-F} = 2.8$ Hz), 34.6, 36.1, 122.4 (q, $J_{C-F} = 29$ Hz), 124.0 (q, $J_{C-F} = 274$ Hz), 125.6, 125.9, 128.4, 128.7, 131.8, 142.2, 144.1; $^{19}$F NMR (CDCl$_3$) δ 103.2 (s, 3F). Found: C, 59.16; H, 5.62%. Calcd for C$_{17}$H$_{19}$F$_3$S$_2$: C, 59.28; H, 5.52%.

(E)-2-(1-trifluoromethyl-3-undecenylidene)-1,3-dithiane (10h)
IR (neat) 2926, 2854, 1564, 1420, 1299, 1160, 1110, 967 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 0.89 (t, $J = 7.0$ Hz, 3H), 1.24–1.35 (m, 10H), 1.99 (dt, $J = 7.5$, 7.5 Hz, 2H), 2.14 (tt, $J = 7.0$, 7.0 Hz, 2H), 2.96–3.02 (m, 4H), 3.11 (d, $J = 6.0$ Hz, 2H), 5.34 (dt, $J = 15.0$, 6.0 Hz, 1H), 5.50 (dt, $J = 15.0$, 7.5 Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 14.3, 22.9, 23.5, 28.4, 28.8, 29.2, 29.4, 29.5, 32.1, 32.6, 33.6 (q, $J_{C-F} = 2.9$ Hz), 122.7 (q, $J_{C-F} = 29$ Hz), 124.1 (q, $J_{C-F} = 274$ Hz), 124.7, 133.0, 143.8 (q, $J_{C-F} = 3.4$ Hz); $^{19}$F NMR (CDCl$_3$) δ 103.2 (s, 3F). Found: C, 56.93; H, 7.28%. Calcd for C$_{16}$H$_{25}$F$_3$S$_2$: C, 56.77; H, 7.44%.

2-(3-cyclohexylidene-1-trifluoromethyl-3-butenylidene)-1,3-dithiane (10j)
IR (neat) 2929, 2854, 1564, 1300, 1158, 1107, 1080 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.45–1.60 (m, 6H), 2.05–2.10 (m, 2H), 2.13 (tt, $J = 7.0$, 7.0 Hz, 2H), 2.17–2.23 (m, 2H), 2.96–3.02 (m, 4H), 3.14 (d, $J = 7.0$ Hz, 2H), 4.95 (t, $J = 7.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$) δ 23.5, 27.1, 27.8, 28.5, 28.7 (Two signals merge.), 28.9 (q, $J_{C-F} = 2.4$ Hz), 29.0, 37.4, 116.3, 123.6 (q, $J_{C-F} = 28$ Hz), 124.2 (q, $J_{C-F} = 274$ Hz), 141.5, 142.9 (q, $J_{C-F} = 3.8$ Hz); $^{19}$F NMR (CDCl$_3$) δ 103.4 (s, 3F). HRMS (m/z) Observed: 308.0881 ($\Delta = +0.1$ ppm). Calcd for C$_{14}$H$_{19}$F$_3$S$_2$: 308.0881.

S-(3-mercaptopropyl) 2-trifluoromethyl-4-pentenethioate (11)
IR (neat) 2928, 2861, 1684, 1259, 1122, 1097, 938, 855, 704 cm$^{-1}$; $^1$H NMR (CDCl$_3$) δ 1.40 (t, $J = 7.5$ Hz, 1H), 1.91 (tt, $J = 7.0$, 7.0 Hz, 2H), 2.53–2.60 (m, 2H), 2.60–2.73 (m, 1H), 3.03–3.13 (m, 2H), 3.32–3.40 (m, 2H), 5.12–5.20 (m, 2H), 5.67–5.76 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 23.4, 28.0, 31.2 (q, $J_{C-F} = 2.4$ Hz), 33.3, 57.1 (q, $J_{C-F} = 26$ Hz), 119.2, 124.1 (q, $J_{C-F} = 280$ Hz), 132.2,
192.9. HRMS (m/z) Observed: 258.0363 (Δ = +1.4 ppm). Calcd for C\textsubscript{9}H\textsubscript{13}F\textsubscript{3}OS\textsubscript{2}: 258.0359.

2-(1-trifluoromethyl-3-butenyl)-1,3-dithiane (12)
IR (neat) 2903, 1643, 1424, 1372, 1278, 1224, 1165, 1097, 1070, 993, 923 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) δ 1.82–1.92 (m, 1H), 2.09–2.16 (m, 1H), 2.48–2.68 (m, 3H), 2.83–3.02 (m, 4H), 4.45 (d, J = 2.5 Hz, 1H), 5.11–5.24 (m, 2H), 5.81–5.89 (m, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 26.2, 30.3 (q, J\textsubscript{C–F} = 2.4 Hz), 31.4, 32.0, 47.4 (q, J\textsubscript{C–F} = 1.9 Hz), 49.0 (q, J\textsubscript{C–F} = 25 Hz), 118.3, 126.7 (q, J\textsubscript{C–F} = 281 Hz), 134.6; \textsuperscript{19}F NMR (CDCl\textsubscript{3}) δ 95.2 (d, J\textsubscript{F–H} = 7.9 Hz, 3F). HRMS (m/z) Observed: 242.0410 (Δ = –0.3 ppm). Calcd for C\textsubscript{9}H\textsubscript{13}F\textsubscript{3}S\textsubscript{2}: 242.0411.
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References and Notes


9.  Dichloromethane was used as solvent instead of nitromethane.  In the case of nitromethane, 6h was obtained in low yield probably due to the poor solubility of 5g.


Chapter 6


Publication List

1. Parts of the present thesis have been published in the following journals.

   Chapter 1  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima

   Chapter 2  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima
              Submitted.

   Chapter 3  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima
              *Synlett* 2007, 1622–1624.

   Chapter 4  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima

   Chapter 5  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima

   Chapter 6  Suguru Yoshida, Hideki Yorimitsu, and Koichiro Oshima
              Submitted.

2. Other Publications not included in this thesis.

   (1) 1,8-Bis(diphenylmethylium)naphthalenediyld Cation as an Organic Oxidant: Synthesis of
       Benzidines via Self-Coupling of *N,N*-Dialkylanilines
       T. Saitoh, S. Yoshida, and J. Ichikawa

   (2) Naphthalene-1,8-diylbis(diphenylmethylium) as an Organic Two-Electron Oxidant:
       Benzidine Synthesis via Oxidative Self-Coupling of *N,N*-Dialkylanilines
       T. Saitoh, S. Yoshida, and J. Ichikawa

   (3) Synthesis of Bulky Arylphosphanes by Rhodium-Catalyzed Formal [2+2+2] Cycloaddition
       Reaction and Their Use as Ligands
       T. Kobatake, A. Kondoh, S. Yoshida, H. Yorimitsu, and K. Oshima
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Suguru Yoshida