Studies on Nickel-catalyzed Hydroarylation and Hydrocarbamoylation of Alkynes

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Contents

Abbreviations

Ac	acetyl	HRMS	high-resolution mass spectra
aq.	aqueous	Hz	hertz
Ar	aryl	*i*	iso
atm	atmospheric pressure	IR	infrared spectroscopy
br	broad	*J*	coupling constant
Bu	butyl	L	ligand
cat.	catalyst	$LiAlH_4$	lithium aluminum hydride
cf.	confer	M (m)	metal
cod	1,5-cyclooctadiene	min	minute(s)
Cy	cyclohexyl	mL	milliliter
Cyp	cyclopentyl	μL	microliter
d	doublet	mp	melting point
δ	scale (NMR)	*n*	normal
DIBAL-H	diisobutylaluminium-hydride	NMR	nuclear magnetic resonance
		nOe	nuclear Overhauser effect
E	electrophile	pin	pinacolato
EI	electron ionization	q	quartet
eq.	equation	quant	quantitative
equiv	equivalent	quint	quintet
Et	ethyl	ref.	reference
FAB	fast atom bombardment	rt	room temperature
FID	flame ionization detector	s	singlet
GC	gas chromatography	sept	septet
GPC	gel permeation chromatography	sext	sextet
		t	triplet
h	hour(s)	*t, tert*	tertiary
HetAr	heteroaryl	Temp.	temperature
Hex	hexyl	TLC	thin layer chromatography
HMBC	hetero-nuclear multiple-bond connectivity	UV	ultraviolet
		vic	vicinal

Chapter 1

Introduction and General Summary

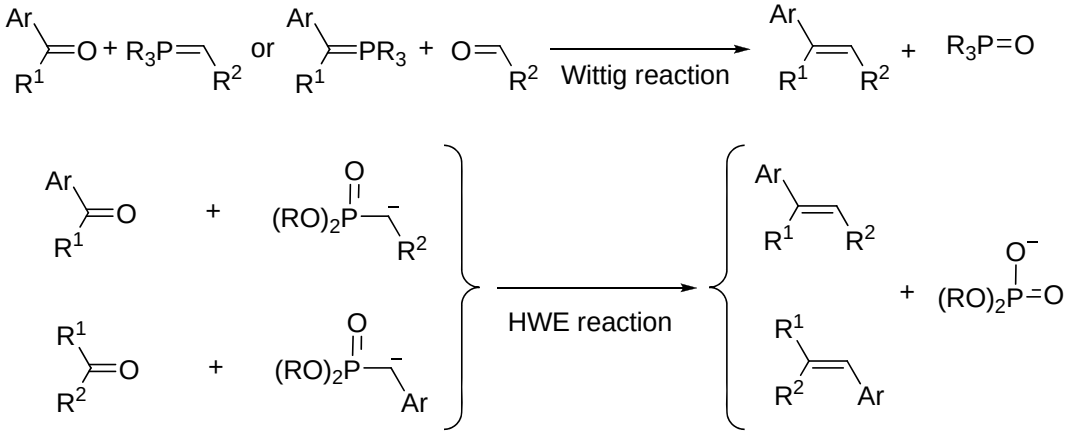
The advances in synthetic organic chemistry have provided numerous useful methods for construction of C–C frameworks,[1] which are ubiquitous in nature. Not only organic materials, pharmaceuticals, agrochemicals, and natural products, but all the living things are consisted of materials based on C–C bonds. On the other hand, most of conventional organic reactions, except for simple addition reactions, result in production of environmentally unfriendly byproducts or wastes alongside the desired compounds. Consequently, development of atom-efficient and environmentally benign methods for construction of target molecules is an important issue in modern organic synthesis.[2] An important consideration in making organic reactions more environmentally benign should be the design of processes that need not prefunctionalize substrates and involve simple addition of reacting materials, everything else needed being only catalytic. To this end, catalytic C–H bond functionalization[3] has emerged as an ultimate atom-economical approach for direct assembly of complex molecules from simple and readily available precursors.[4] Transition metal-catalyzed C–H bond activation and insertion of unsaturated bonds into the C–H bond provides a simple, economic, clean, and straightforward way to construct new C–C bonds. In particular, catalytic addition of aromatic compounds across internal alkynes through aryl–H bond activation is an ideal synthetic way to access disubstituted arylethenes, which have numerous applications as biologically active molecules[5] and versatile synthetic intermediates in organic synthesis.

Conventional synthetic methods for disubstituted arylethenes

a) Wittig olefination reaction and Horner-Wadsworth-Emmons reaction

The Wittig olefination and Horner-Wadsworth-Emmons (HWE) reactions are among the most well-established methodologies for preparation of functionalized disubstituted arylethenes containing an aryl or heteroaryl motif(s) (Scheme 1).[6] The Wittig reactions are commonly used to couple aldehydes and ketones with singly substituted phosphorous ylides. With unstable ylides, the transformation results in exclusive formation of *Z*-alkenes. In order to achieve *E*-alkenes, the Schlosser modification[7] of the Wittig reaction can be performed. The HWE reaction is also a modification of the Wittig reaction which employs carbanions stabilized by phosphonate to furnish *E*-alkenes preferentially upon reaction with aldehydes or ketones. Stereoselective preparation of *Z*-alkenes using the HWE reaction has also been developed.[8] Despite the extremely high

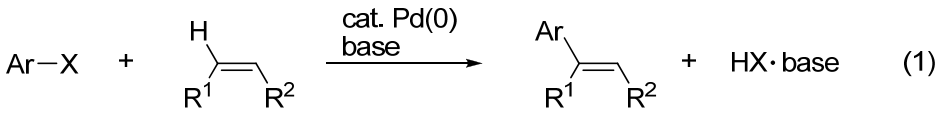
significance, these reactions give rise to stoichiometric amounts of phosphonium salts as wastes, and therefore development of alternative synthetic means has been desired.



Scheme 1. The Wittig olefination and HWE reactions.

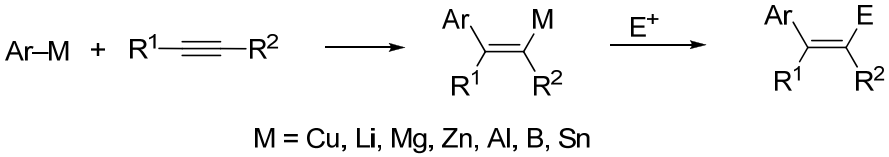
b) Mizoroki-Heck reaction

Palladium-catalyzed coupling reaction between haloarenes with alkenes, the Mizoroki-Heck reaction, is another significant means for preparation of disubstituted arylethenes (Eq. 1).[9] Usually, the reaction couples aryl, benzyl and vinyl halides and triflates with electron-deficient alkenes bearing at least one hydrogen, and requires a base to neutralize hydrogen halide coproduced.



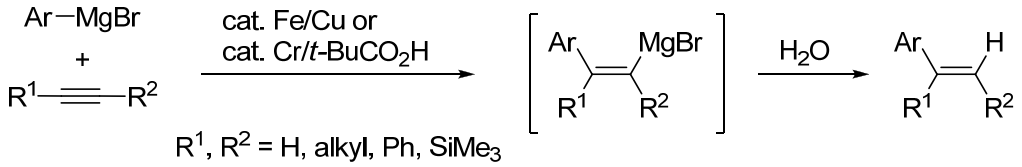
c) Hydroarylation of alkynes through arylmetalation

The addition of arylmetallic reagents to internal alkynes followed by hydrolysis of the resulting C–metal bonds is a versatile synthetic method for preparation of regio- and stereochemically defined disubstituted arylethenes.[10] Inter- and intramolecular arylmetalation of alkynes can be performed with a variety of organometallic reagents including Cu, Li, Mg, Zn, Al, B and Sn. In view of stereoselective synthesis of arylethenes, arylmetalation of alkynes is one of the most important and useful reactions, because the alkenylmetals thus obtained, upon reaction with electrophiles, provide variously substituted arylethenes (Scheme 2).



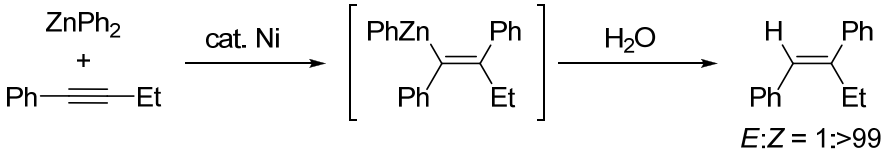
Scheme 2. Hydroarylation of alkynes through carbometalation followed by reactions with electrophiles.

Arylmagnesiation of various alkynes[11] has been reported recently to proceed by cooperative catalysts made of iron/copper[12] or chromium/pivalic acid[13] in highly efficient manners (Scheme 3). Hydrolysis of the resulting alkenylmagnesium bromides thus obtained gives a broad range of disubstituted arylethenes regio- and stereoselectively.



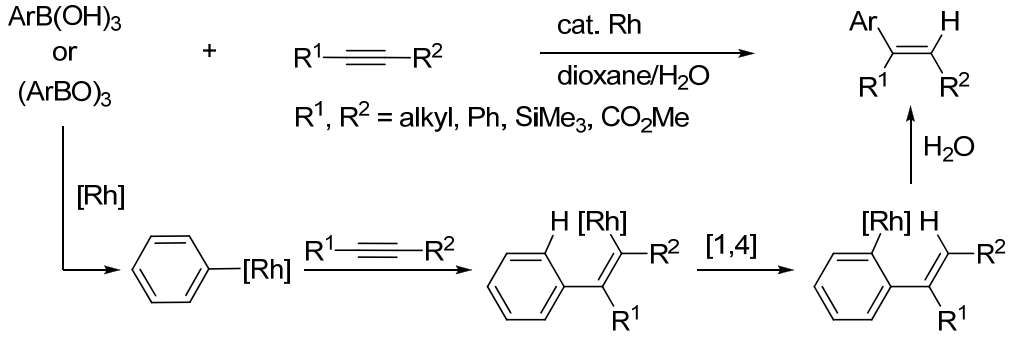
Scheme 3. Arylmagnesiation of alkynes catalyzed by iron/copper or chromium/pivalic acid.

Nickel catalyzes arylzincation of unactivated alkynes, to give, after hydrolysis, disubstituted arylethenes regio- and stereoselectively (Scheme 4).[14]



Scheme 4. Nickel-catalyzed arylzincation of alkynes.

Rhodium is unique to catalyze addition of arylboronic acids across alkynes. The reaction proceeds with high *syn*-selectivity through a catalytic cycle involving an interesting 1,4-shift of rhodium from an alkenyl carbon to an aryl carbon (Scheme 5).[15] From a synthetic point of view, this reaction is of great importance, because it can be carried out in an aqueous solvent, and tolerates various functional groups including ester motifs due totally to mild nucleophilicity of arylborane reagents.

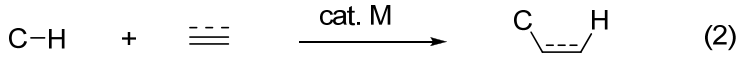


Scheme 5. Rhodium-catalyzed hydroarylation of alkynes.

These carbometalation reactions have nevertheless a serious drawback that they coproduce stoichiometric amounts of metal wastes, require preactivation of starting materials and suffer from poor functional group compatibility especially when highly nucleophilic organometallic reagents such as the Grignard reagents and organozincs are employed.

Carbon–hydrogen bond activation followed by insertion of unsaturated compounds

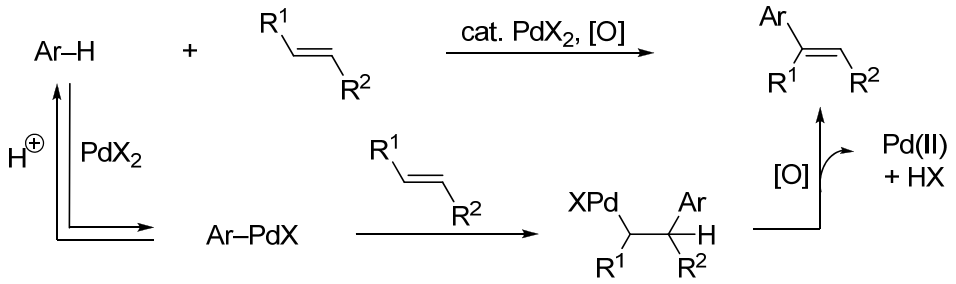
Ubiquitous in organic compounds are C–H bonds. Thus, direct functionalization of C–H bonds,[3] if available, should be one of the most powerful, valuable and straightforward tool for constructing carbon frameworks to prepare complex molecules. A potential catalyst for such transformations is expected to activate a relatively inert C–H bond selectively in the presence of other C–H bonds, and then allow efficient functionalization of the metalated carbon in order to provide the desired product. An additional challenge is the inherent bond stability of C–H bonds: the dissociation energy of C–H bonds is usually large, e.g. 105 kcal/mol for H–CH_3 and 110 kcal/mol for H–C_6H_5. Despite these demanding requirements, a number of reactions to activate and functionalize specific C–H bonds selectively by transition metal catalysis have been developed.[4] Among possible C–H bond functionalization reactions, insertion of unsaturated compounds into C–H bonds is considered to provide us with a highly atom- and step-efficient access to a variety of valuable synthetic intermediates and targets in a single operation (Eq. 2).



(2)

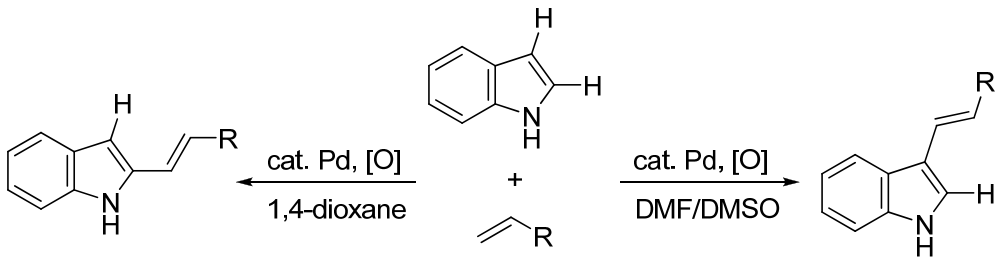
a) Electrophilic metalation of arene C–H bonds and its application to oxidative alkenylation reaction

Fujiwara, Moritani and coworkers disclosed in 1967 a coupling reaction of arenes with electron-deficient alkenes. The reaction was considered to proceed through a palladium-catalyzed oxidative process, which has found a widespread use in preparation of disubstituted arylethenes (Scheme 6).[16] The proposed reaction mechanism starts with electrophilic substitution of aromatic hydrogen by cationic $[PdX]^+$ species to form an aryl–Pd complex, followed by carbopalladation and β-hydride elimination to furnish *E*-alkenes stereoselectively.



Scheme 6. Fujiwara-Moritani oxidative alkenylation of arenes.

Although this reaction bypasses the need for prefunctionalization of the arene substrates and thus is much more straightforward than the conventional Mizoroki-Heck reaction, an oxidant in a stoichiometric amount is necessary in order to achieve the catalytic transformation, and a reaction site on arenes is hard to control except for electron-rich heterocycles such as indoles, which can be alkenylated regioselectively by tuning the solvent polarity (Scheme 7).[17]

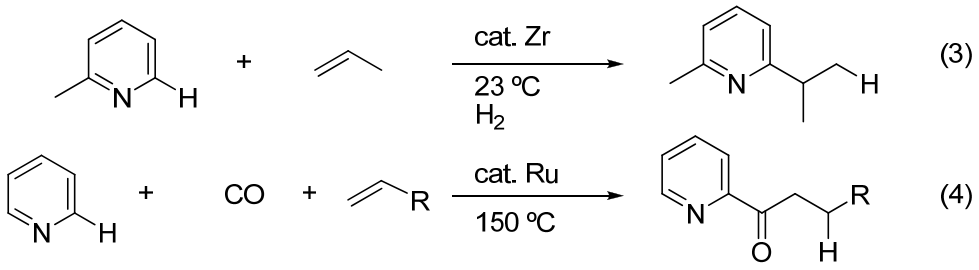


Scheme 7. Palladium-catalyzed regioselective oxidative C(2)- and C(3)-alkenylation of indoles.

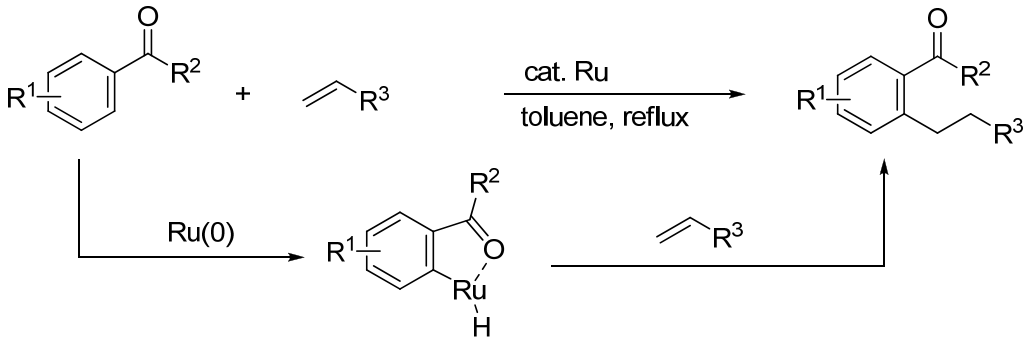
b) Heteroatom-directed activation of aromatic C–H bonds and alkenylation

As heteroatoms bear lone pair electrons, transition metals interact with heteroatoms

in substrates to facilitate regioselective C–H bond activation.[18] Particularly, activation of C–H bonds next to sp^2-nitrogen in a pyridine ring, followed by insertion of CO and olefins, readily takes place with the aid of a zirconium or ruthenium catalyst (Eqs. 3 and 4).[19] The reactions are initiated by coordination of the metal catalyst to nitrogen followed by oxidative addition of the C–H bonds.



Taking advantage of the directing effect of heteroatoms, direct alkylation of *ortho* C–H bonds of aryl ketones via insertion of olefins was developed in 1993 by Murai who used ruthenium catalyst (Scheme 8).[20] Recently, functional groups such as hydroxy, iminoacyl, carbamoyl, pyridyl and imidazolyl are found to induce a wide variety of C–H bond transformations.[18]

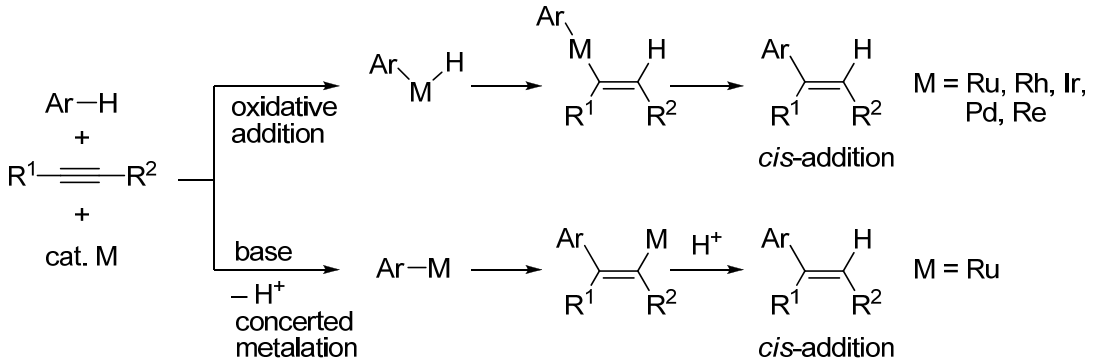


Scheme 8. Ruthenium-catalyzed C–H bond activation and insertion of olefins.

Hydroarylation of alkynes through C–H bond activation

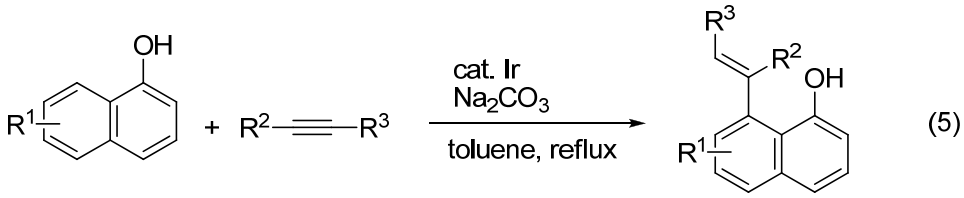
The strategy of aromatic C–H bond activation may be combined with insertion of alkynes to result in hydroarylation reactions of alkynes. This newly combined process allows synthesis of disubstituted arylethenes with ultimate atom efficiency.[21] Based on mechanistic types, transition metal-catalyzed hydroarylation of alkynes can be classified into two major groups as illustrated in Scheme 9 and Scheme 11, respectively. One of them is a direct cleavage of a C–H bond by a metal catalyst prior to reaction with

alkynes (Scheme 9). Hydroarylation reactions which proceed via oxidative addition[22] of C–H bonds or concerted metalation through base-assisted hydrogen abstraction[23] belong to this group. In the oxidative addition mechanism, reactions are initiated by insertion of a low-valent metal complex into a C–H bond. Most of the metal complexes applied are electron-rich late-transition metal complexes of ruthenium, rhodium, iridium, palladium, and rhenium. The insertion of alkynes takes place regioselectively in a *cis*-fashion.



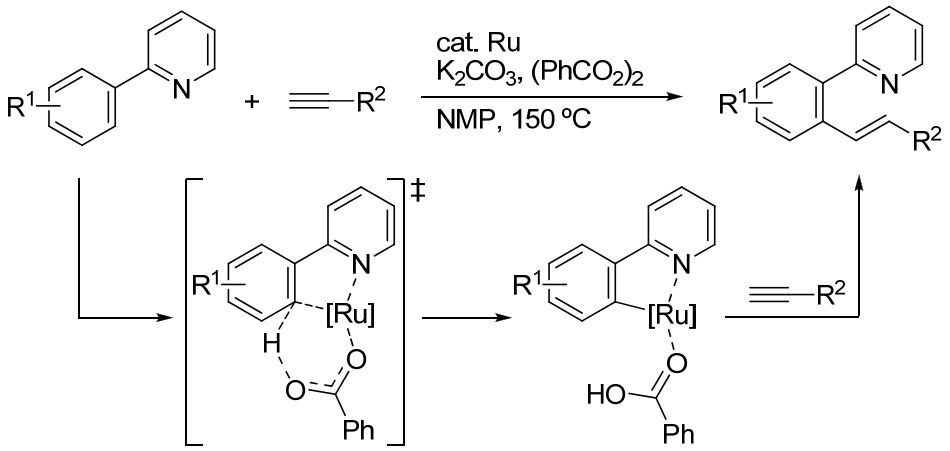
Scheme 9. Hydroarylation of alkynes initiated by Ar–H bond activation.

Through the oxidative addition mechanism, 1-naphthols couple with internal alkynes efficiently in the presence of an iridium catalyst to afford the corresponding 8-alkenyl-1-naphthols stereoselectively (Eq. 5).[22d]



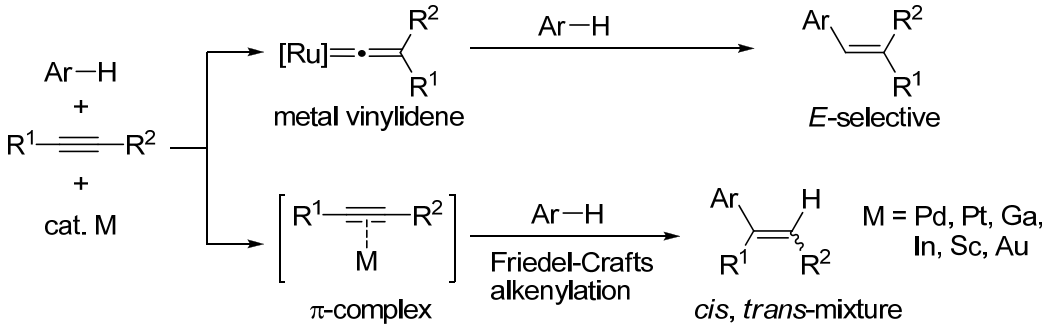
(5)

The concerted metalation mechanism shown in Scheme 9 suggests simultaneous C–H bond cleavage and C–metal bond formation.[24] An example is a direct *ortho*-alkenylation of 2-arylpyridines in the presence of a ruthenium catalyst (Scheme 10).[23] The reaction is initiated by coordination of the pyridyl nitrogen atom to ruthenium benzoate, then the benzoate ligand abstracts the hydrogen in the *ortho* position, allowing a simultaneous C–Ru bond formation to give an arylruthenium complex, which then adds across alkynes in a *cis*-fashion.

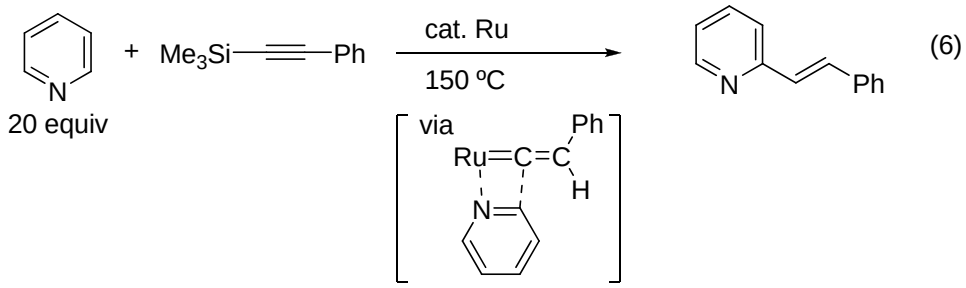


Scheme 10. Ruthenium-catalyzed direct alkenylation of 2-arylpyridines.

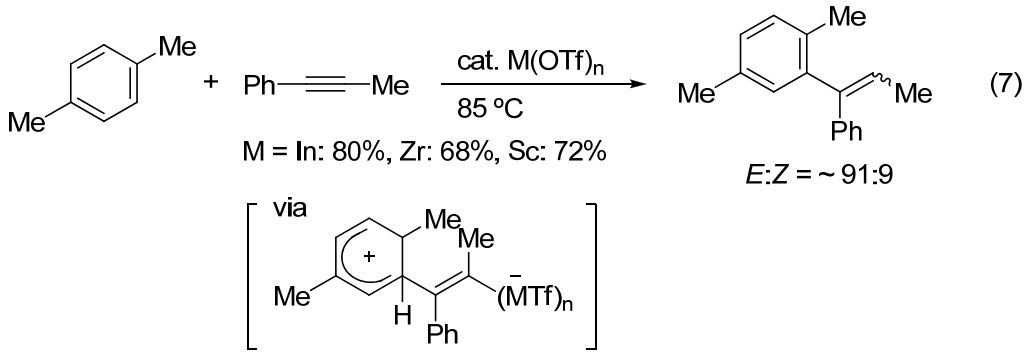
The other major group of hydroarylation involves activation of alkynes by metal catalysts prior to C–H bond cleavage (Scheme 11). A possible intermediate is a vinylidene or π-complex as shown in Scheme 11. A vinylidene is considered to be involved in alkenylation of pyridine derivatives at the C(2)-position under ruthenium catalysis to furnish (*E*)-2-phenylpyridine (Eq. 6).[25] The reaction is understood in terms of ruthenium vinylidene intermediates generated from silylacetylenes.[26] Although the target adducts are obtained in a highly stereoselective manner, a large excess amount of pyridine is used at high temperatures and desilylation is accompanied.



Scheme 11. Hydroarylation of alkynes initiated by activation of alkynes.

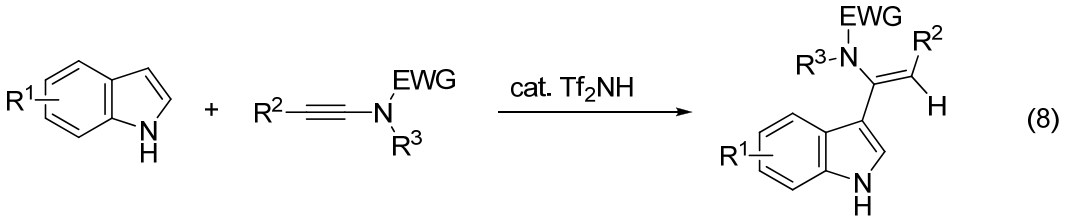


Alternative alkyne activation involves coordination of Lewis-acidic metal salt to an alkyne to form an activated π-complex (Scheme 11). Friedel-Crafts type electrophilic reaction of the π-complex with an arene gives an alkenyl metal intermediate, which after protonation gives the desired hydroarylation adduct as a stereoisomeric mixture.[27] For example, metal triflates [$M(OTf)_n$; M = In, Zr, Sc] catalyze the alkenylation of arenes with internal alkynes to give stereoisomeric mixtures of alkenylarenes (Eq. 7).[27c]



(7)

Proton also promotes[28] and catalyzes[29] hydroarylation of highly electron-rich alkynes, though examples are rare. An example is a highly regio- and stereoselective *cis*-hydroarylation of indoles with ynamides in the presence of a catalytic amount of Tf_2NH to give 3-alkenyl indoles (Eq. 8).[29b] The reaction also is understood in terms of the Friedel-Crafts type alkenylation mechanism.

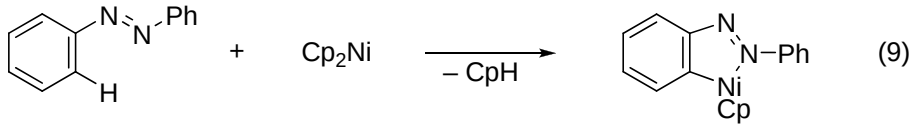


(8)

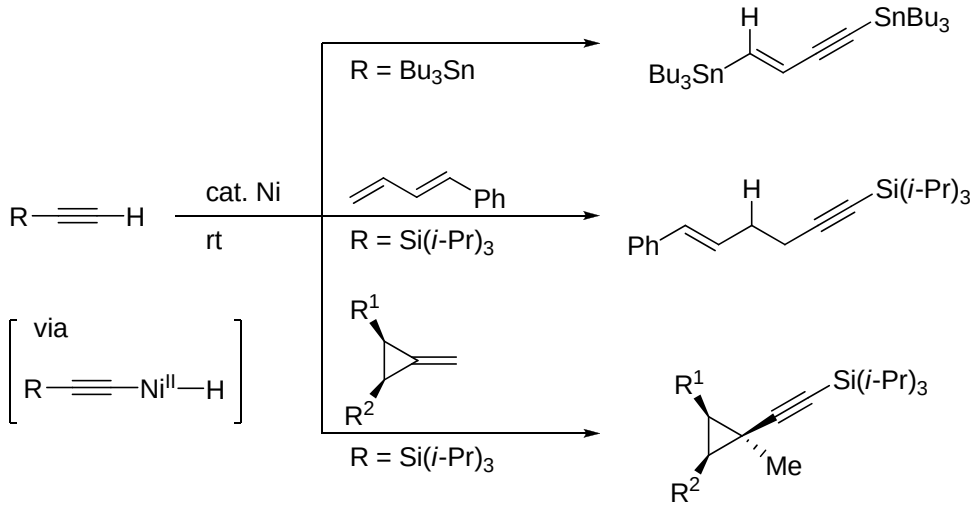
Scope of the hydroarylation reactions of alkynes reported so far is still limited; the reaction that proceeds through oxidative addition of C–H bonds requires the presence of a directing group and/or relatively harsh conditions in many cases, whereas the Lewis acid-catalyzed reaction proceeds only with electron-rich arenes and often suffers from poor functional group compatibility and stereoselectivity. Therefore, a catalyst system complementary to the known protocols for hydroarylation of alkynes, especially the one applicable to electron-deficient arenes, is yet to be developed.

Nickel-catalyzed C–H bond activation and insertion of unsaturated compounds

In contrast to the rich chemistry of such transition metal catalysts as palladium, ruthenium, rhodium, and iridium for catalytic C–H bond functionalization, nickel has been rarely explored for these transformations, in spite of an early report on the stoichiometric C–H bond activation of azobenzene by Cp_2Ni (Eq. 9).[30]

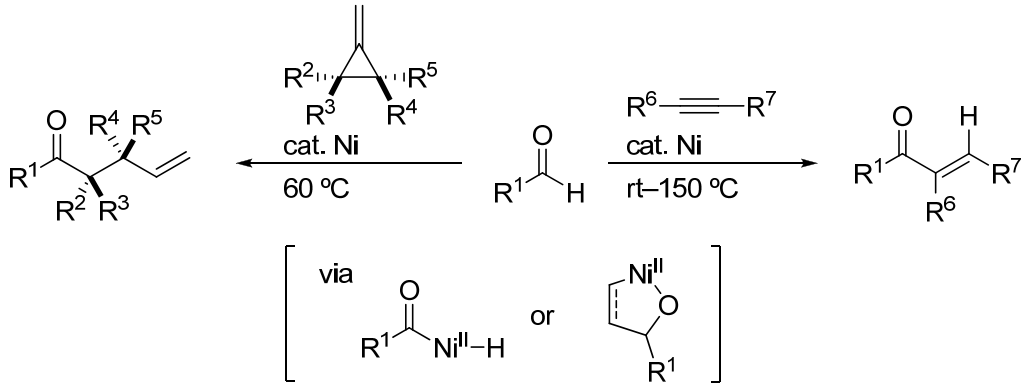


Only a limited number of examples for nickel-catalyzed C–H bond activation are available that include activation of C(sp)–H bonds of terminal alkynes followed by insertion of alkynes, 1,3-dienes, or methylenecyclopropanes (Scheme 12).[31] The reactions are suggested to be initiated by oxidative addition of the relatively acidic C(sp)–H bond to nickel(0).



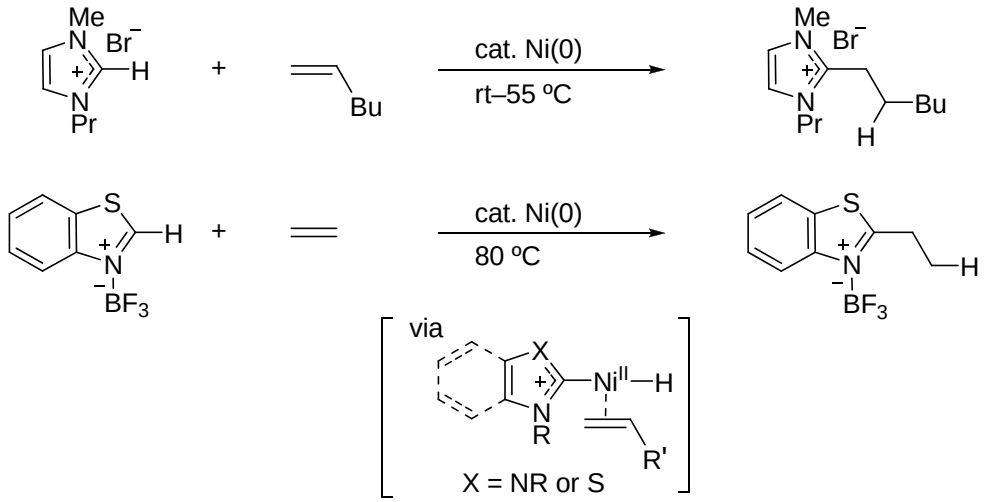
Scheme 12. Nickel-catalyzed hydroalkynylation of alkenes and alkynes.

Nickel also catalyzes hydroacylation of alkynes and methelenecyclopropanes (Scheme 13).[32] The reaction proceeds either through oxidative addition of the formyl C–H bond followed by insertion of the unsaturated compound or through a nickeladihydrofuran formed by oxidative cyclization of aldehyde and the unsaturated substrate.[32b]



Scheme 13. Nickel-catalyzed hydroacylation of alkynes and methylenecyclopropanes.

The C(2)–H bond in imidazolium salt or a benzothiazole–BF_3 complex can be activated by a nickel catalyst to undergo insertion of alkenes (Scheme 14).[33] Experimental and theoretical studies indicate that the reaction proceeds through oxidative addition of the C(2)–H bond to nickel(0) followed by migratory insertion of alkenes into the Ni–H bond and reductive elimination.[34]



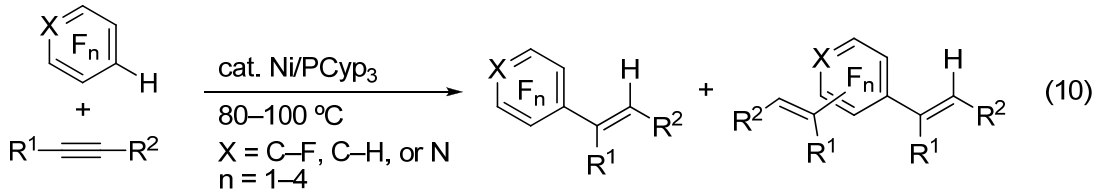
Scheme 14. Nickel-catalyzed olefin insertion into C(2)–H bonds in azolium salts.

Although these transformations demonstrate the potential of nickel as a catalyst for C–H bond activation and functionalization under relatively mild conditions, its application to other synthetically valuable transformations, especially hydroarylation of alkynes, have remained unexplored.

Summary of the present Thesis

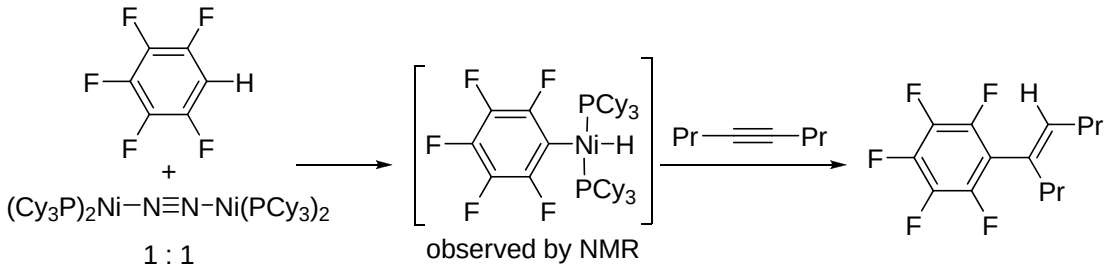
As mentioned above, only a few precedents have been reported for nickel-catalyzed insertion reactions of unsaturated compounds into C–H bonds.[35] The availability and relatively low cost of nickel complexes make them attractive catalysts for C–H bond functionalization reactions. From these view points, the author decided to start his study, aiming at establishing novel nickel-catalyzed C–H bond activation followed by insertion of alkynes to afford highly functionalized disubstituted arylethenes.

In view that a nickel catalyst appeared to activate relatively acidic C–H bonds, the author first envisaged that activation of C–H bonds of fluoroarenes followed by insertion of alkynes would provide an access to disubstituted fluoroarylethenes. A fluorine substituent bound to arenes is known to raise acidity of *ortho* hydrogens.[36] Infact, the author has found that hydroarylation reaction of alkynes using fluoroarenes proceeds in the presence of a nickel/$PCyp_3$ catalyst in a *cis*-fashion regio- and stereoselectively to furnish a wide variety of fluoroarylethenes in a single operation as described in Chapter 2 (Eq. 10).[37]



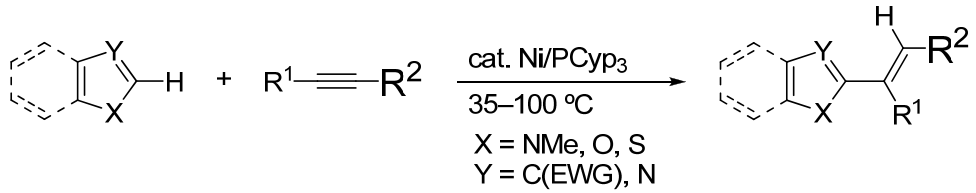
(10)

A catalytic cycle initiated by oxidative addition of Ar_F–H bonds to nickel(0) to form Ar_F–Ni^{II}–H species has been identified by NMR studies.[38] Stoichiometric reaction of the oxidative adduct with 4-octyne leads to the formation of the corresponding *cis*-hydrofluoroarylation product (Scheme 15).



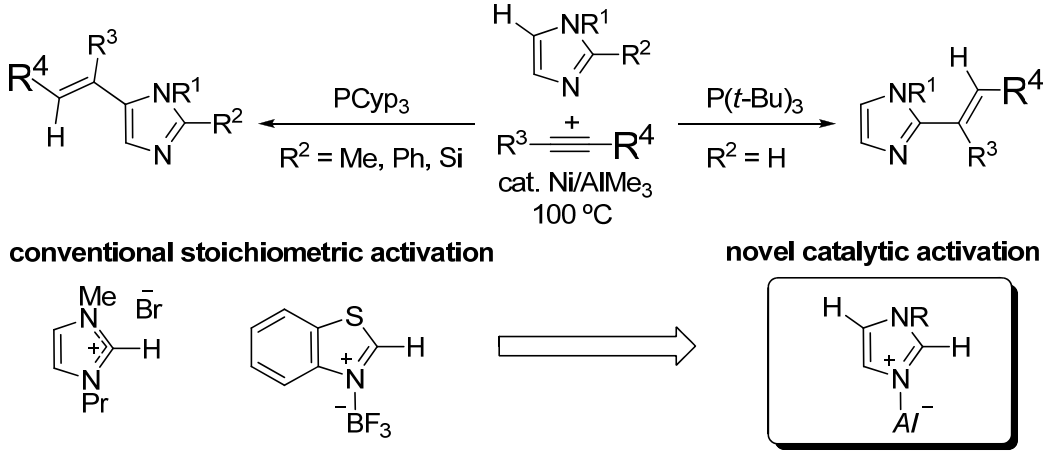
Scheme 15. Stoichiometric reaction of pentafluorobenzene, $Ni_2N_2(PCy_3)_4$ and 4-octyne.

The author next envisaged that the nickel catalyst might be effective for activation of relatively acidic C–H bonds in electron-deficient heteroarenes.[39] Described in Chapter 3 is nickel-catalyzed hydroheteroarylation of alkynes using five-membered heteroarenes (Eq. 11).[40] This addition reaction is applicable to a diverse range of heteroarenes such as indoles with a C-3 electron-withdrawing group, benzimidazole, benzofuran, benzothiophene, purine, and caffeine. A wide range of functional groups tolerate the reaction conditions. Excellent regioselectivity is observed with unsymmetrical alkynes to furnish the corresponding heteroarylethenes having a larger substituent *trans* to an heteroaryl group.



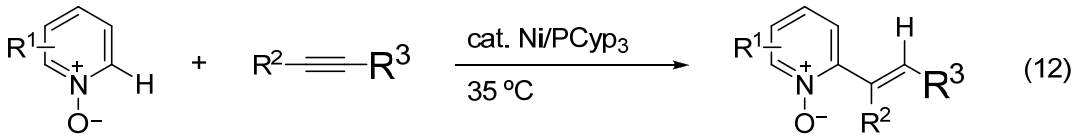
(11)

Although only low yields resulted with imidazoles as the substrates under these reaction conditions, the author has disclosed that use of a Lewis acid (LA) co-catalyst together with the nickel catalyst allows an easy access for regio- and stereochemically defined C(2)- and C(5)-alkenylated imidazoles (Scheme 16).[41] A LA catalyst likely binds to the sp^2-nitrogen in imidazoles to enhance the reactivity of C(2)–H or C(5)–H bonds and assist oxidative addition to nickel(0). Only a catalytic amount of LA is required in this transformation in sharp contrast to the conventional stoichiometric azole activation through imidazolium salts[33a] or BF_3–complexes (cf. Scheme 14).[33b]



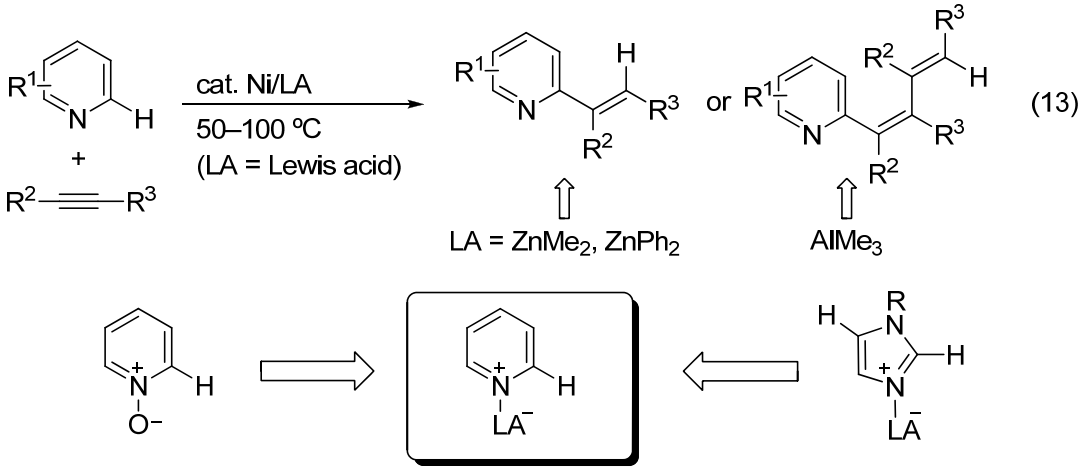
Scheme 16. Nickel/$AlMe_3$-catalyzed hydroheteroarylation of alkynes with imidazoles.

Described in Chapter 4 is the alkenylation of 6-membered heteroarenes by the nickel catalysis. First described is C(2)-alkenylation of pyridine-*N*-oxides through activation of their C(2)–H bond followed by regioselective insertion of alkynes in the presence of a nickel(0)/$PCyp_3$ catalyst (Eq. 12).[42] The addition reaction provides trisubstituted ethenes bearing a pyridine-*N*-oxide motif under mild conditions. However, under these conditions parent pyridines never participate in this transformation even at elevated temperatures.



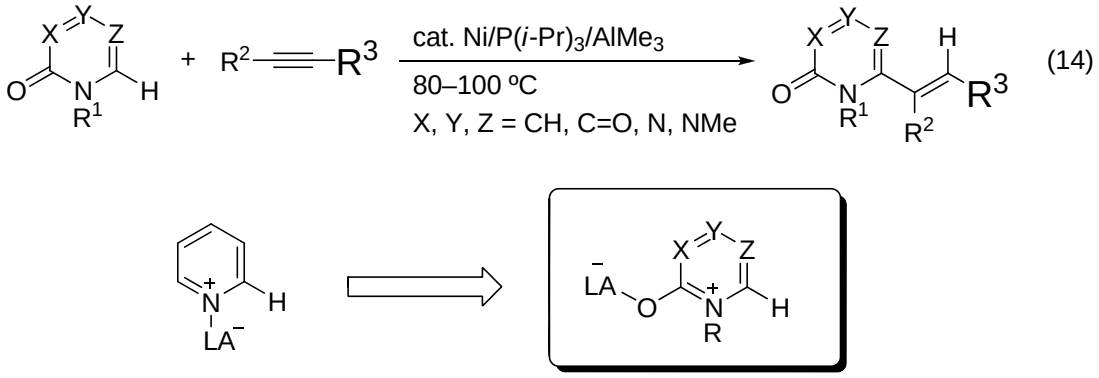
(12)

Since the enhanced reactivity of pyridine-*N*-oxides is apparently ascribed to an electron-deficient nitrogen that possibly increases the acidity of the C(2)–H bond, the author envisioned that a similarly activated pyridinium species could be generated *catalytically in situ* by coordination of the pyridine nitrogen to a LA catalyst in a manner similar to the imidazole activation (Eq. 13). This approach led to the discovery of direct selective C(2)-alkenylation of pyridine derivatives under nickel(0)/LA binary catalysis.[43] Whereas diorganozinc reagents as the LA catalyst give C(2)-monoalkenylation products, $AlMe_3$ changes the reaction course to afford C(2)-dienylated products via double insertion of alkynes into the C(2)–H bond. The reaction clearly demonstrates a broad scope both in pyridines and alkynes, and proceeds with high chemo-, regio-, and stereoselectivity.



(13)

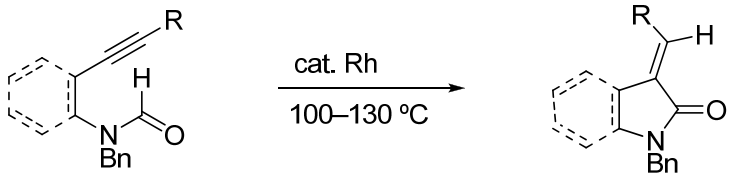
Similar nickel(0)/LA binary catalysis allows C(6)-alkenylation of 2-pyridone derivatives: possibly a reactive pyridinium species is generated *in situ* by coordination of their carbonyl group to the LA catalyst (Eq. 14).[44]



(14)

Hydrocarbamoylation of alkynes

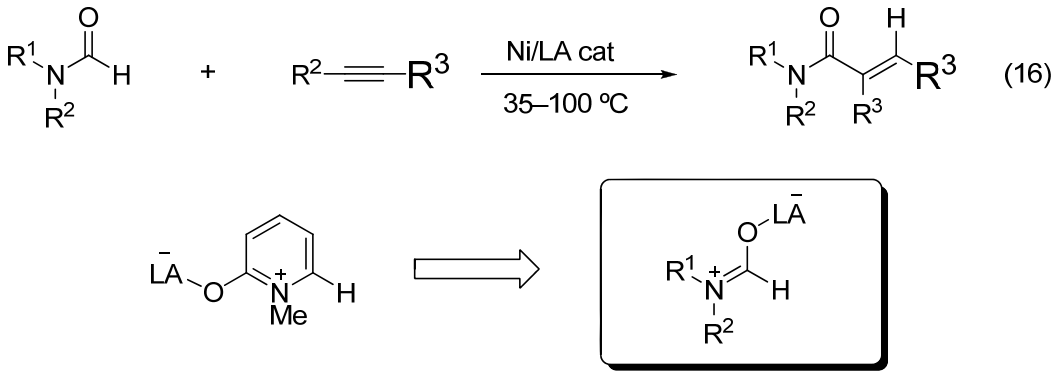
Manipulation of the formyl C–H bond in formamide to form C–C bonds has great synthetic potential for the straightforward synthesis of higher homologs of amides.[45] In particular, hydrocarbamoylation of unsaturated compounds provides a simple and atom-economical method to synthesize amides without forming a metal waste.[46] However, most of the reported reactions to achieve this transformation require harsh reaction conditions and/or the presence of a directing group to assist the oxidative addition of the C–H bond to metal complexes. Rhodium-catalyzed intramolecular hydrocarbamoylation of alkynes provides an efficient synthetic means for (*E*)-α-alkylidene-γ-lactams and (*E*)-3-alkylideneoxindoles, and represents the only example of alkyne-hydrocarbamoylation reaction (Eq. 15).[46f]



(15)

Upon coordination of formamides to LA, the formyl C–H bond located α to the positively charged nitrogen thus may become reactive toward the nickel catalyst as is the case with the C(6)–H activation of 2-pyridone derivatives discussed in Chapter 4. Chapter 5 thus describes realization of a nickel(0)/LA-catalyzed hydrocarbamoylation of alkynes (Eq. 16).[47] The reaction proceeds under mild conditions to give variously

substituted α,β-unsaturated amides from simple and readily available starting materials.



In summary, the present Thesis describes the invention of novel nickel-catalyzed hydroarylation and hydrocarbamoylation reactions across alkynes which provide a direct and atom efficient access to highly functionalized disubstituted arylethenes and α,β-unsaturated amides in chemo-, regio- and stereoselective manners. The nickel catalyst appears to activate relatively acidic C–H bonds of electron-poor heteroarenes: the requisite is pK_a estimated to fall in 24–30 in DMSO by theoretical calculations.[39c,48] The addition reactions described herein will find many synthetic applications complimentary to the known protocols by other transition metals. Also, a combination of low-valent transition metal/LA cooperative catalysts represents a new strategy to activate otherwise unreactive C–H bonds and will stimulate further development of novel synthetic reactions useful for organic synthesis.

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(48) For activation of C–H bond of heteroarenes or fluoroarenes whose pK_a values are estimated to be 30–40, either a LA catalyst or high temperature is necessary.

Chapter 2

Hydroarylation of Alkynes with Fluoroarenes

A combination of $Ni(cod)_2$ and $PCyp_3$ is found to be an effective catalyst for chemoselective activation of the C–H bond of fluoroarenes over C–F bonds followed by insertion of alkynes to allow direct alkenylation of the electron-deficient arenes. The characteristics of the reactions are as follows: a C–H bond *ortho* to a fluorine substituent is selectively activated; the reactivity of fluorobenzenes is roughly proportional to the number of fluorine atoms. The reaction conditions tolerate a broad range of fluoroarenes with both electron-withdrawing and -donating groups and alkynes to allow efficient synthesis of a variety of substituted ethenes containing a fluoroaryl motif in high regio- and stereoselective manners. Mechanistic studies including both labeling experiments and stoichiometric reactions reveal that oxidative addition of C–H bonds in fluoroarenes to nickel(0) is highly facile.

Introduction

The presence of fluorine atom(s) in an organic compound influences its physical, chemical and biological properties significantly.[1] In particular, organic molecules containing fluoroaryl motifs find increasing applications in pharmaceutical,[2] agrochemical[3] and material sciences.[4] Accordingly, invention of effective methods for rapid and concise preparation of fluoroaryl containing compounds, either by direct introduction of fluorine or by use of fluoroaryl-containing building blocks, is of great significance in both academia and industry. In most cases, traditional methods for introduction of a fluorine atom into an aromatic framework usually require special equipments to perform the experiments and/or harsh conditions that are incompatible with many functional groups.[5] Although fluoroarenes can be functionalized via deprotonation of their acidic hydrogens with a stoichiometric amount of organometallic bases followed by reactions with electrophiles,[6] this method results in organometallic wastes in stoichiometric amounts. Therefore, invention of strikingly efficient alternative synthetic means is desired.

Transition metal-catalyzed C–H bond transformation has emerged as a atom-efficient way for functionalization of organic molecules.[7] Nevertheless, direct functionalization of C–H bonds of fluoroarenes remain relatively unexplored compared to electron-rich arenes.[8] An intriguing problem to achieve a useful reaction for direct functionalization of C–H bonds of fluoroarenes is the challenge of activating C–H bonds over C–F bonds chemoselectively. Although several transition metals have been reported to activate C–H bonds over C–F bonds,[9] applications of these elemental reactions in catalytic functionalization of fluoroarenes are rare. Recently, Fagnou[10] and Daugulis[11] demonstrated pioneering works for direct coupling reactions at C–H bonds of fluoroarenes with aryl and alkenyl halides using Pd and Cu catalysts, respectively. On the other hand, a transition metal-catalyzed addition of fluoroarenes across alkynes should be an attractive method for preparation of multifunctionalized fluoroarylethenes, in terms of atom- and step economy.[12]

Nickel catalysts have been reported to be effective for activation of rather acidic C(sp)–H bonds of terminal alkynes[13] and activated azoles[14] to undergo insertion of unsaturated compounds into these C–H bonds. On the other hand, fluorine bound to arenes is known to raise acidity of *ortho* hydrogens.[15] Based on these facts, the author

envisaged that activation of C–H bonds of fluoroarenes by nickel(0) species followed by insertion of alkynes could be feasible. Described in Chapter 2 is a nickel-catalyzed activation of C–H bonds of fluoroarenes over C–F bonds followed by insertion of alkynes to furnish a variety of disubstituted fluoroarylethenes in regio- and stereoselective manners.[16] The addition reaction can also be carried out with a Ni(0)/$PCyp_3$ catalyst generated *in situ* by reduction and deprotonation of a bench-stable Ni(II) complex and a phosphonium salt, respectively.[17] The stoichiometric reaction of pentafluorobenzene and $Ni_2N_2(PCy_3)_4$[18] reveals that the reaction is initiated by oxidative addition of C–H bond to nickel(0) to form a *trans*-$(C_6F_5)(H)Ni(PCy_3)_2$ complex.[19] Whereas the oxidative addition step is highly facile and occur at room temperature, insertion of alkyne and reductive elimination are likely slow at temperatures below 50 ºC.

Results and discussion

Nickel-catalyzed hydroarylation of alkynes with fluoroarenes

The author first examined the reaction of pentafluorobenzene (**1a**, 0.50 mmol) with 4-octyne (**2a**, 0.75 mmol) in the presence of a catalytic amount of $Ni(cod)_2$ with various ligands (Table 1). Among the numerous ligands screened for the reaction, tri(*sec*-alkyl)phosphines gave the desired product (**3aa**) in excellent yields (entries 1–3). The *cis*-stereochemistry of the addition reaction was unambiguously confirmed by nOe experiments of **3aa**. Other trialkylphosphines gave no detectable amount of **3aa** (entries 4 and 5). Neither triaryl- nor diarylalkylphosphine ligand such as PPh_3 or $PCyPh_2$ were effective (entries 6 and 7). Increase in the amount of a ligand was deleterious to the reaction (entry 8), furnishing the required product in only 62% yield as estimated by GC. The reaction performed in such solvents as hexane, 1,4-dioxane and DMF also gave **3aa** albeit in moderate yields (entries 9–11).

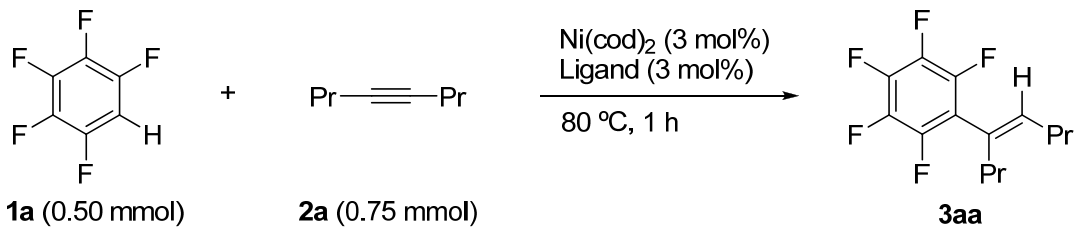


Table 1. Nickel-catalyzed addition of pentafluorobenzene (**1a**) across 4-octyne (**2a**).[a]

Entry	Ligand	Solvent	Yield (%)[b]
1	$PCyp_3$	toluene	>95 (99)[c]
2	PCy_3	toluene	94
3	$P(i\text{-}Pr)_3$	toluene	>95
4	$P(n\text{-}Bu)_3$	toluene	<1
5	$P(t\text{-}Bu)_3$	toluene	2
6	PPh_3	toluene	12
7	$PCyPh_2$	toluene	6
8[d]	$PCyp_3$	toluene	62
9	$PCyp_3$	hexane	70
10	$PCyp_3$	1,4-dioxane	53
11	$PCyp_3$	DMF	69

[a] All the reaction was carried out using **1a** (0.50 mmol), **2a** (0.75 mmol), $Ni(cod)_2$ (0.015 mmol), and a ligand (0.015 mmol) in toluene (0.5 mL) at 80 ºC for 1 h. [b] Estimated by GC using undecane as an internal standard. [c] Isolated yield obtained with a 1.00 mmol scale for 3 h. [d] $PCyp_3$ (6 mol%) was used.

With the optimized conditions in hand, the author next studied the scope of fluoroarenes with **2a** as an alkyne substrate (Table 2). The addition of 1,2,3,4-tetrafluorobenzene (**1b**) across **2a** proceeded smoothly to give the corresponding mono-adduct **3ba** in 71% yield (entry 1). A trace amount of dialkenylated adduct **4ba** was also detected. The reactions of 2 equivalents of tetrafluorobenzenes, **1c** and **1d,** with **2a** also gave the respective mono-adducts selectively in moderate yields (entries 2 and 4). On the other hand, when the amount of **2a** was increased to 4 equivalents compared to the fluoroarenes, dialkenylated products **4ca** and **4da** were obtained in high and excellent yields, respectively (entries 3 and 5). Similar results were obtained with **1e** as a fluoroarene substrate (entries 6 and 7). Trifluorobenzenes **1f**, **1g** and **1h** also added across **2a** smoothly, although a mixture of mono- and dialkenylation products resulted (entries 8–11). Noteworthy, among possible reaction sites, the C–H bond *ortho* to a fluorine substituent was primarily activated.[10,11] The higher reactivity is attributable to enhanced acidity of the C–H bonds,[15] or the more-stabilized Ni–fluoroaryl bond in the oxidative adducts by *ortho* fluorine atoms (*vide infra*).[20] Apparently, non-alkenylated fluoroarenes are more reactive than mono- and dialkenylated adducts, due possibly to steric hindrance induced by an alkenyl group, which may inhibit

η^2-coordination of the fluoroarenes prior to C–H bond activation. Whereas the reaction of **2a** with 1,2- and 1,4-difluorobenzene (**1j** and **1k**) gave the desired products in only low yields, 1,3-difluorobenzene (**1i**) reacted at the C-2 position exclusively to give the corresponding mono-adduct selectively in moderate yield (cf. entries 12–14). Relatively high reactivity of **1i** is attributed to the presence of two fluorine substituents *ortho* to the C–H bond to be activated, compared to **1j** and **1k**. This is consistent with the observations reported by Fagnou and Dauglus, whereby the most acidic C–H bonds flanked by two fluorine substituents are more prone to be activated. Noteworthy is that *mono*-fluorobenzene also participated in the addition reaction, albeit in a low yield (entry 15). Both electron-withdrawing and -donating groups tolerated the reaction conditions to give multifunctionalized fluoroarylethenes in moderate to high yields (entries 16–19). The chemoselective activation of the C–H bond in presence of an Ar–OMe bond in **1p** is in sharp contrast to the fact that Ni(0)/PCy_3 catalyst cleaves the Ar–OMe bond.[21] Interestingly, the hydrofluoroarylation reaction occurred at *ortho* position of the fluorine substituent regardless of the nature of other functional groups on the fluoroarene ring. These data suggest that the activation of C–H bonds *ortho* to fluorine is preferred kinetically and/or thymodynamically.[22] Fluoropyridines also participated in the addition reaction to afford the desired adducts in moderate to excellent yields (entries 20–23). These results represent another feature of the present system to be noted: a Ni(cod)$_2$/PEt_3 combination is reported to activate C–F bonds of polyfluoropyridines over C–H bonds.[23] All the reaction proceeded with exclusive *cis*-addition of the fluoroarenes as confirmed by nOe experiments of some selected adducts.

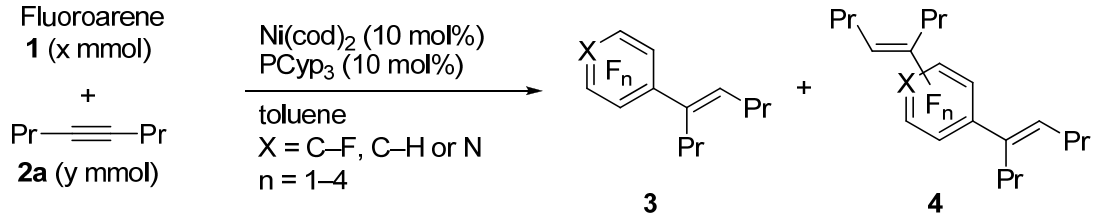
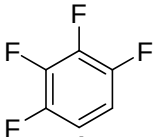
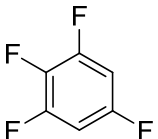
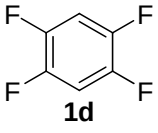
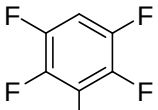
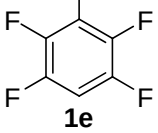
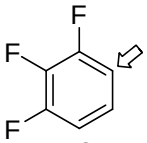
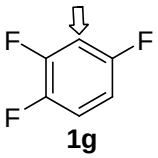
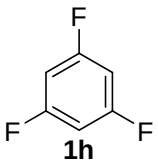
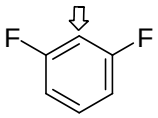
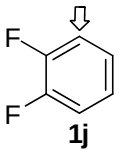
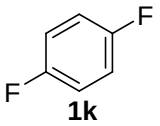
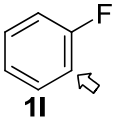
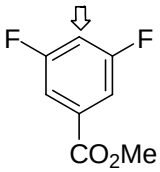
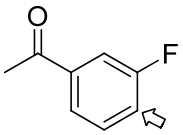
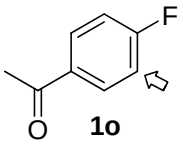
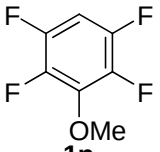
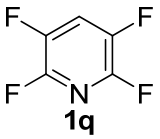
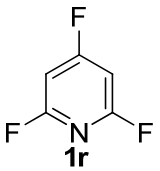
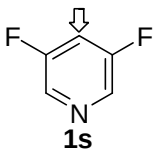


Table 2. Nickel/$PCyp_3$-catalyzed addition of fluoroarenes (**1**) across 4-octyne (**2a**).

Entry	Fluoroarene (**1**)	x	y	Temp (ºC)	Time (h)	Yield of **3** (%)[a]	Yield of **4** (%)[a]
1	 **1b**	1.0	1.5	80	12	71 (**3ba**)	<5 (**4ba**)
2[b]	 **1c**	2.0	1.0	80	5	48 (**3ca**)	7 (**4ca**)
3		1.0	4.0	80	14	<5 (**3ca**)	87 (**4ca**)
4[b]	 **1d**	2.0	1.0	80	1	53 (**3da**)	7 (**4da**)
5		1.0	4.0	80	10	<5 (**3da**)	99 (**4da**)
6[b]		1.0	3.0	80	10	<5 (**3ea**)	92 (**4ea**)
7[b]	 **1e**	2.0	1.0	80	1	61 (**3ea**)	9 (**4ea**)
8	 **1f**	2.0	1.0	100	3	35 (**3fa**)	2 (**4fa**)
9	 **1g**	1.0	1.5	80	2	75 (**3ga**)	16 (**4ga**)
10[c]	 **1h**	1.0	4.0	80	30	15 (**3ha**)	35 (**4ha**)
11		2.0	1.0	80	1	40 (**3ha**)	11 (**4ha**)
12	 **1i**	1.0	1.5	100	10	54 (**3ia**)	7 (**4ia**)
13	 **1j**	1.0	1.5	100	10	9 (**3ja**)	<5 (**4ja**)

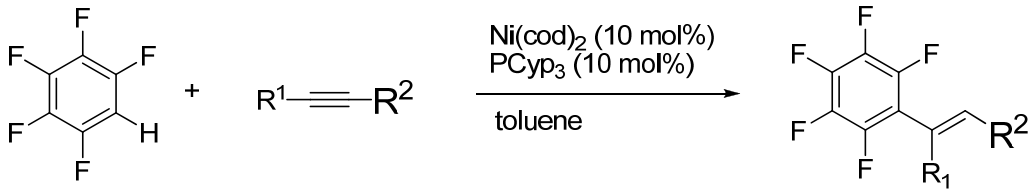
14	 **1k**	1.0	1.5	100	11	33 (**3ka**)	7 (**4ka**)
15	 **1l**	1.0	1.5	100	20	8 (**3la**)	<5 (**4la**)
16	 **1m**	1.0	1.5	80	2	71 (**3ma**)	<5 (**4ma**)
17	 **1n**	1.0	3.0	100	3	47 (**3na**)	5 (**4na**)
18	 **1o**	2.0	1.0	100	3	41 (**3oa**)	3 (**4oa**)
19	 **1p**	1.0	1.5	80	2	87 (**3pa**)	–
20[b]	 **1q**	1.0	1.0	80	18	85 (**3qa**)	–
21	 **1r**	1.0	3.0	80	9	<5 (**3ra**)	91 (**4ra**)
22		2.0	1.0	80	3	40 (**3ra**)	6 (**4ra**)
23[b]	 **1s**	2.0	1.0	80	2	99 (**3sa**)	<5 (**4sa**)

[a] Isolated yield obtained with a 1.00 mmol scale. [b] Run with 30 μmol of the catalyst. [c] 2,4,6-trialkenyltrifluorobenzene was also obtained in 21% yield.

The author next turned his attention to the scope of alkynes. The reaction of **1a** with 1,4-bis(trimethylsilyl)but-2-yne (**2b**) proceeded smoothly to give pentafluoroaryl-substituted allylsilane **3ab** (entry 1 in Table 2) in 75% yield. Addition

across 1,2-diphenylacetylene (**2c**) took place in good yield, although slow addition of the alkyne was essential to curb its competitive tri- and oligomerization (entry 2). The reactions with unsymmetrical internal alkynes, 4,4-dimethyl-2-pentyne (**2d**) and 1-trimethylsilylprop-1-yne (**2e**) proceeded with excellent regioselectivity to give the corresponding *cis*-adducts having a bulkier substituent *trans* to the pentafluorophenyl group exclusively (entries 3 and 4).[24] Other sterically biased unsymmetrical internal alkynes bearing phenyl and silyl groups also participate in this addition reaction to afford the respective adducts in good yields with defined regio- and stereoselectivity (entries 5 and 6). Terminal alkynes, however, failed to give the corresponding adducts due to rapid background tri- and oligomerization of alkynes.

Table 3. Nickel/$PCyp_3$-catalyzed hydroarylation of alkynes with **1a**.[a]



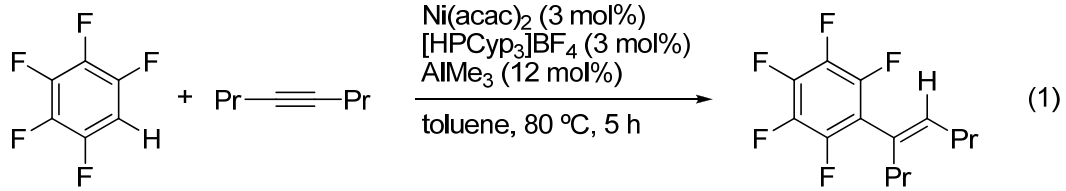
1a (1.0 mmol) **2** (1.5–3.0 mmol) **3**

Entry	R^1—≡—R^2	mmol	Temp (ºC)	Time (h)	Yield of **3** (%)[b]
1	Me_3Si—≡—$SiMe_3$ **2b**	3.0	80	6	75 (**3ab**)
2[b]	Ph—≡—Ph **2c**	3.0	80	3.5	68 (**3ac**)
3[c]	Me—≡—*t*-Bu **2d**	1.5	80	3	89 (**3ad**)
4	Me—≡—$SiMe_3$ **2e**	1.5	100	13	47 (**3ae**)
5	Ph—≡—$SiMe_3$ **2f**	1.5	100	15	63 (**3af**)
6[d]	Ph—≡—$SiMe_2Ar$ **2g**	1.0	100	24	63 (**3ag**)

[a] All the reaction was carried out using **1** (1.00 mmol), **2a** (1.50–3.00 mmol), $Ni(cod)_2$ (0.10 mmol), and $PCyp_3$ (0.10 mmol) in toluene (1.0 mL). [b] Slow addition of **2c** over 2.5 h. [c] Run with 0.030 mmol catalyst. [d] Ar = 2-$(CH_2OTHP)C_6H_4$, ratio of **1a**:**2g** = 2.0:1.0.

Since both $Ni(cod)_2$ and $PCyp_3$ are oxygen-sensitive, experimental practicality of the above method may be limited. To improve its convenience and applicability, the

author developed a method for generation of the active nickel(0)/$PCyp_3$ catalyst *in situ*, employing $AlMe_3$ to reduce and deprotonate air-stable and readily available nickel(II) complex and phosphonium salt.[17] Thus, the reaction of **1a** and **2a** using a catalyst generated *in situ* by reduction and deprotonation of bench-stable $Ni(acac)_2$ and $[HPCyp_3]BF_4$ with $AlMe_3$ following a standard Schlenk technique gave **3aa** in 87% isolated yield (Eq. 1).



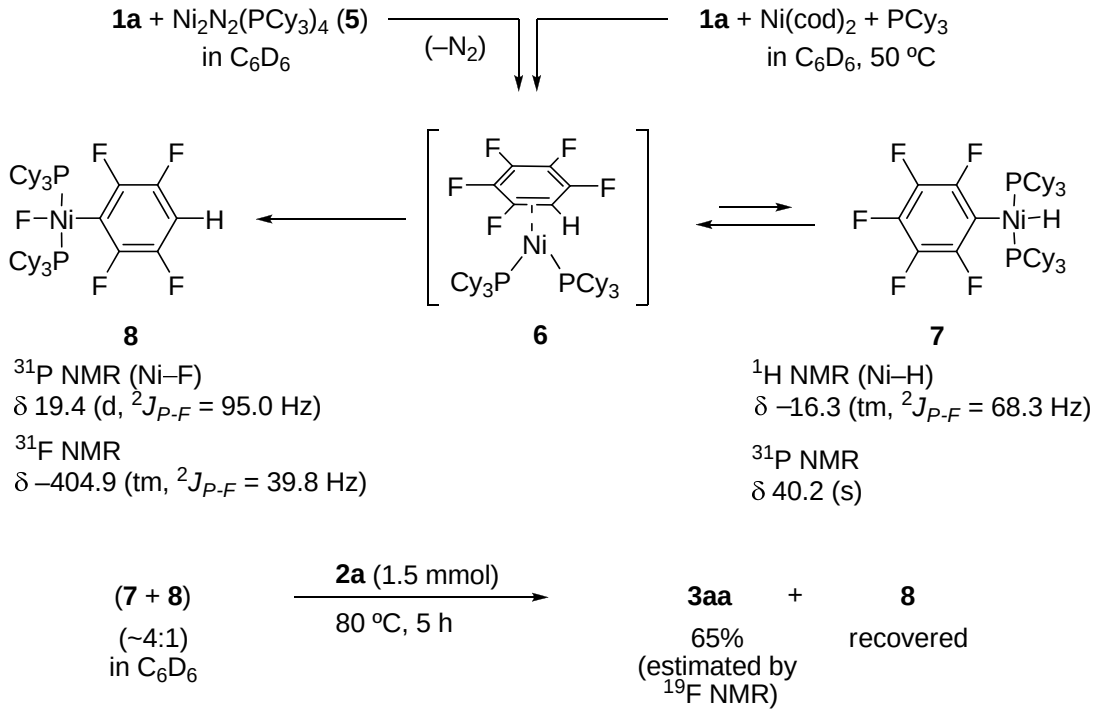
(1)

Mechanism of addition reaction of alkynes to fluoroarenes

To gain a mechanistic insight into the addition reaction, the author monitored a stoichiometric reaction using ^1H, ^{31}P and ^{19}F NMR spectroscopy. Upon mixing stoichiometric amounts of **1a** and $Ni_2N_2(PCy_3)_4$ (**5**) in C_6D_6, evolution of a gas (nitrogen), oxidative addition of the C–H and *para* C–F bonds in **1a** to nickel(0) took place to give a mixture of *trans*-$(C_6F_5)(H)Ni(PCy_3)_2$ (**7**) and *trans*-$(C_6F_4H)(F)Ni(PCy_3)_2$ (**8**) complexes (Scheme 1). The C–H and C–F bond activation possibly takes place via a η^2-complex (**6**), which would be formed by coordination of **1a** to Ni(0) complex.[25] The ratio of the two complexes after 1 h was estimated to be ~4:1 as determined by ^{31}P NMR. These observations are in agreement with those reported by Johnson and coworkers on the reaction of 1,2,4,5-tetrafluorobenzene with $(Et_3P)_2Ni(\eta^2\text{-}C_{10}H_{10})$.[25b] The ^1H NMR spectrum showed a multiplet of triplets at δ –16.3 with a $^2J_{P-H}$ value of 68.3 Hz, as anticipated for a nickel hydride complex.[25,26] The ^{31}P NMR spectrum featured a resonance for the hydride complex at δ 40.2 as a singlet, while the nickel fluoride complex was observed at δ 19.4 as a doublet with $^2J_{P-F}$ value of 95.0 Hz. The ^{19}F NMR of the nickel fluoride featured a triplet at δ –404.9 with $^2J_{P-F}$ value of 39.8 Hz. Although a similar stoichiometric reaction carried out using **1a**, $Ni(cod)_2$ and 1 or 2 equivalents of PCy_3 in C_6D_6 gave similar species by ^{31}P NMR, the reaction was sluggish possibly due to slow ligand exchange between cyclooctadiene (cod) and PCy_3. All attempts to isolate and crystallize the nickel hydride complex for X-ray analyses were

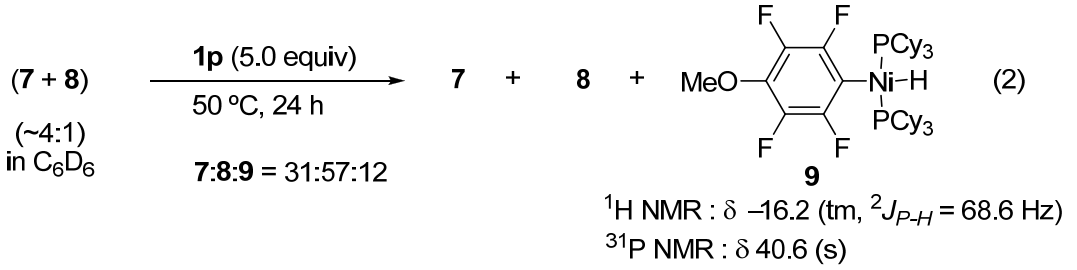
fruitless.

When **2a** (1.5 equiv) was added to a mixture of **7** and **8** (~4:1) in C_6D_6 and heated at 80 ºC, gradual conversion of the nickel hydride **7**, and simultaneous formation of **3aa** was observed. The reaction was complete in 5 h to give **3aa** in 65% yield as estimated by ^{19}F NMR. Upon the addition of **2a**, an unidentified species was also observed at δ 27.8 by ^{31}P NMR. The addition reaction was sluggish below 50 ºC; only slow formation of **3aa** was observed.

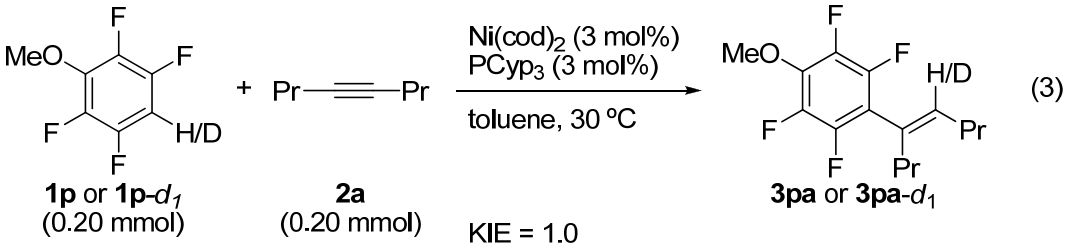


Scheme 1. Stoichiometric reactions of **1a**, $Ni_2N_2(PCy_3)_4$ (**5**), $Ni(cod)_2/PCy_3$ and **2a**.

Noteworthy, upon heating the crude mixture of **7** and **8** at 100 ºC, nickel fluoride **8** was observed as a major product (**7**:**8** = <5:95 after 2 h). Reversibility of the oxidative addition of C–H bond of **1a** to nickel(0) was further confirmed by the fact that addition of **1p** to the mixture of **7** and **8** (~4:1) in C_6D_6 followed by heating at 50 ºC for 24 h gave a mixture of nickel hydrides derived from **1a** and **1p** and an increased amount of **8** (Eq. 2). These observations clearly show that the oxidative addition of C–F bonds is irreversible and thermodynamically favored over that of C–H bonds, which is kinetically favored.[25b,c,27]



Similar phosphine species were observed in the catalytic reaction of **1a** with **2a** (1.5 equiv) in the presence of **5** (10 mol%) or $Ni(cod)_2$ (20 mol%) and PCy_3 (40 mol%) in C_6D_6 at 50 °C, although the reactions were sluggish. The same reaction but with 20 mol% of PCy_3 was faster to give **3aa** in 63% yield after 12 h as estimated by GC. These results indicate that the phosphine ligand in excess retards the reaction. To understand the mechanism further, the author measured initial rates of the reactions of **1p** or **1p**-d_1 with **2a** (Eq. 3). The estimated KIE value was 1.0 (Figure 1), indicating that neither C–H bond activation step nor hydronickelation are the rate-determining steps.



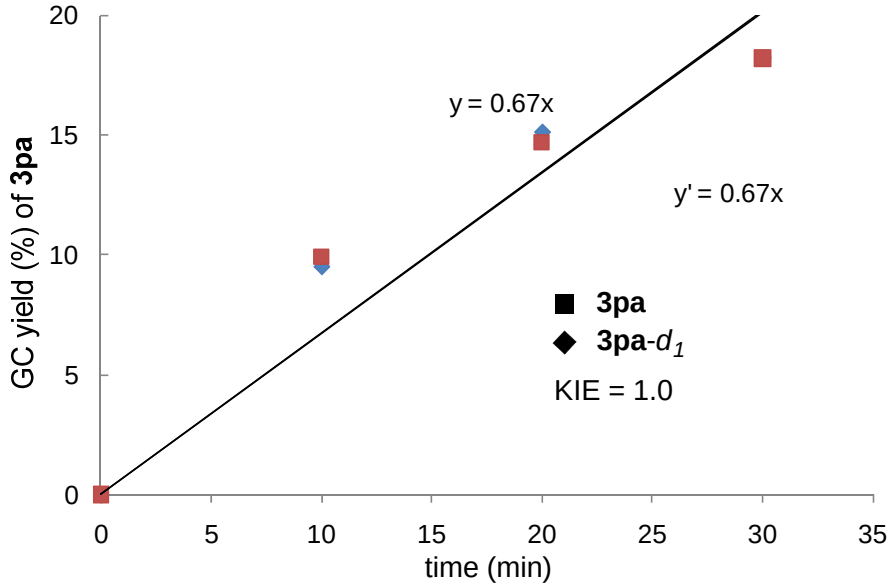
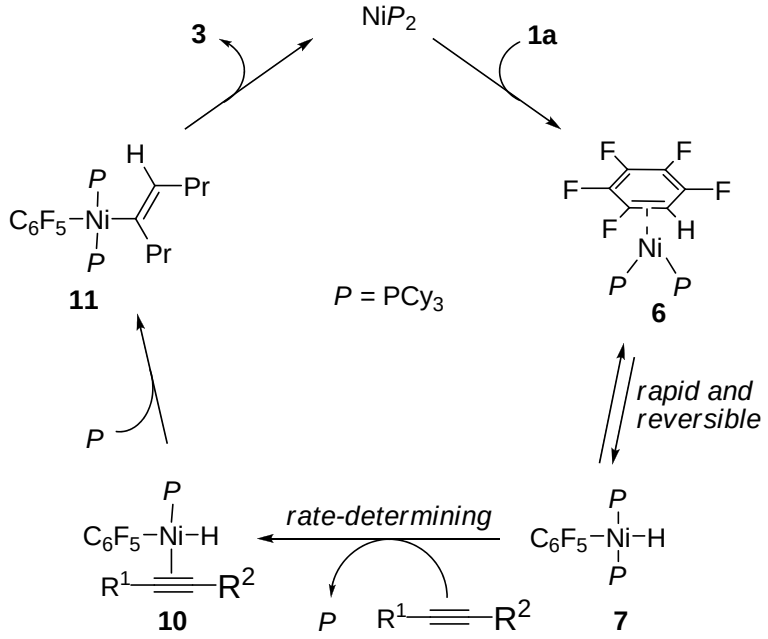


Figure 1. Estimation of KIE in hydrofluoroarylation of alkynes.

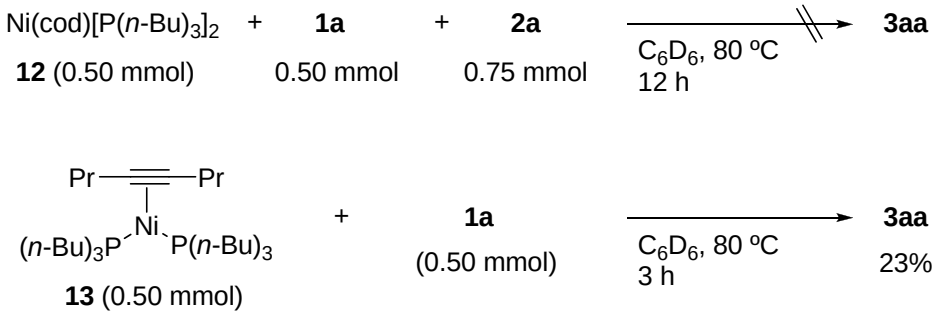
Based on these results, the catalytic cycle of the hydrofluoroarylation of alkynes should initiate through η^2-coordination of **1a** to nickel(0) complex to form η^2-arene complex **6** (Scheme 2). The intermediacy of the η^2-complex species is fully supported by literature precedents.[25,27] This is followed by a reversible oxidative addition of the C–H bond to nickel(0) to give *trans*-nickel hydride complex **7**. Ligand exchange between the coordinating phosphine ligand with an alkyne followed by migratory insertion of the coordinating alkyne into the Ni–H bond gives fluoroaryl–Ni(II)–alkenyl intermediate **11**. When unsymmetrical internal alkynes are used, the coordination and hydronickelation take place in the direction which avoids steric repulsion between bulkier R^2 and the fluoroaryl group in intermediate **10**. Subsequent reductive elimination of the C–C bond in **11** produces final product **3** and regenerates the Ni(0) species. Since the catalytic reaction is carried out using an equimolar amount of phosphine compared to nickel, the alkyne possibly acts as a ligand to stabilize some intermediates in the catalytic cycle. Excess phosphine ligand possibly retards the ligand exchange step, a plausible rate-determining step, thereby resulting in a lower rate and yield of the reaction (cf. entry 8 of Table 1).



Scheme 2. Plausible mechanism for hydrofluoroarylation across alkynes.

Comparison of PCy_3 and $P(n\text{-Bu})_3$ as ligand

As reported by Johnson and coworkers, activation of the C–H bond in fluoroarenes with a nickel(0)/tri(*n*-alkyl)phosphine complex, $(Et_3P)_2Ni(\eta^2\text{-}C_{10}H_{10})$, readily takes place.[25b] In contrast, Table 1 already shows that only tri(*sec*-alkyl)phosphine ligands are highly effective in the present addition reaction. To gain rationale for this observation, the author studied a stoichiometric reaction of **1a**, **2a** with $Ni(cod)[P(n\text{-Bu})_3]_2$ (**12**),[28] which was prepared *in situ* by reaction of $Ni(cod)_2$ with 2 equivalents of $P(n\text{-Bu})_3$, followed by removal of liberated cod *in vacuo*. Contrary to expectation, no hydroarylation reaction took place with the nickel complex, even at elevated reaction temperature of 80 ºC for 12 h (Scheme 3). In addition, monitoring the reaction by ^1H and ^{31}P NMR did not show formation of nickel hydride complex. On the other hand, a stoichiometric reaction of Ni(4-octyne)$[P(n\text{-Bu})_3]_2$ (**13**) with **1a** at 80 ºC proceeded to give **3aa** in a low yield, tri- and oligomerization of the alkyne being accompanied. These two experiments suggest that nickel complexes **12** and **13** having a phosphine with a small cone angle[29] are reluctant to undergo ligand exchange between the coordinating cyclooctadinene or **2a** with **1a** even at elevated temperatures. In contrast, such exchange reactions are feasible, when a ligand having a large cone angle is used, due presumably to steric hindrance. In addition, large cone angle may accelerate the reductive elimination step of the addition reaction.

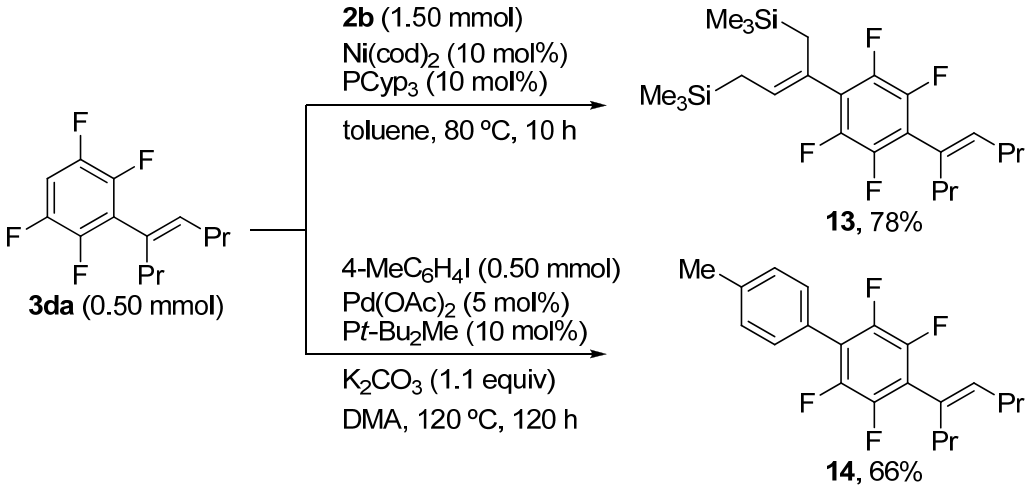


Scheme 3. Reactions of $Ni[P(n\text{-Bu})_3]_2$ complexes with **1a** and **2a**.

Transformations of 3da

Some synthetic transformations of the adducts thus obtained are demonstrated by sequential alkenylation of **3da** with **2b** under the nickel catalysis to afford dialkenylated tetrafluorobenzene **13** in 78% yield (Scheme 4). Also, direct C–H arylation of **3da** with

an equimolar amount of 4-iodotoluene using a palladium-catalyzed protocol reported by Fagnou and coworkers gave diarylethene **14** in 66% yield.[10a]



Scheme 4. Alkenylation and arylation reactions of **3da.**

In conclusion, the author has demonstrated addition reactions of fluoroarenes across alkynes under nickel catalysis. This hydrofluoroarylation reaction proceeds with high chemo-, regio-, and stereoselectivities to give rise to a wide variety of fluoroaryl ethenes in good to high yields. The reaction conditions tolerate a wide scope of fluoroarenes and alkynes. The versatility and applicability of the nickel catalysis may be drastically raised by the protocol that generates an active nickel(0) catalyst *in situ* from a bench-stable nickel(II) precursor, a phosphonium salt and $AlMe_3$. A catalytic cycle involving a nickel hydride intermediate derived from oxidative addition of the C–H bond in fluoroarenes and a rate-determining ligand exchange step has been elucidated by a series of mechanistic studies.

Experimental Section

General remarks compatible to all the experimental part in the present Thesis

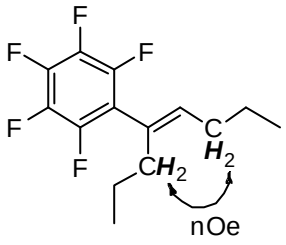
All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique or in a glove box under an argon or nitrogen atmosphere. Flash column chromatography was performed using Kanto Chemical silica gel (spherical, 40–50 μm). Analytical thin layer chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} (0.25 mm) plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating. Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Varian Mercury 400 (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm or C_6D_5H at 7.15 ppm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm or C_6D_6 at 128.62 ppm) as an external standard. Fluorine and phosphine nuclear magnetic resonance spectra (^{19}F NMR and ^{31}P NMR) were recorded on a Varian Gemini 300 (^{19}F NMR, 282 MHz; ^{31}P NMR, 121 MHz) spectrometer with $CFCl_3$ (0 ppm) as internal standard and phosphoric acid (0 ppm) as an external standard, respectively. Melting points (mp) were determined using a YANAKO MP-500D. Elemental analyses were performed by Elemental Analysis Center of Kyoto University. High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-700 (EI) or JEOL JMS-HX110A (FAB+) spectrometer. Preparative recycling gel permeation chromatography (GPC) and preparative recycling silica gel chromatography were performed with a JAI LC-908 chromatograph equipped with JAIGEL-1H and -2H (chloroform as an eluent) and JAIGEL-SIL or Nacalai tesque 5SL-II (hexane–ethyl acetate as an eluent). GC analyses were performed on a Shimadzu GC 2014 equipped with an ENV-1 column (Kanto Chemical, 30 m x 0.25 mm, pressure = 31.7 kPa, detector = FID, 290 °C) with a helium gas as a carrier. Unless otherwise noted, commercially available reagents were used without purification. Toluene was distilled from sodium/benzophenone ketyl or purchased from Kanto Chemical and degassed by purging vigorously with argon for 20 min and further purified by passing through activated alumina under positive argon pressure as described by Grubbs et al.[30]

Chemicals. 1,4-bis(trimethylsilyl)but-2-yne (**2b**)[31] and $Ni_2N_2(PCy_3)_4$[18] were prepared according to the respective literature procedure.

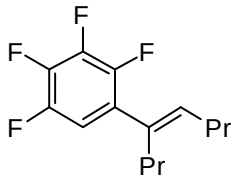
Nickel-catalyzed hydroarylation of alkynes with fluoroarenes. *General procedure.* In a glove box, a solution of $Ni(cod)_2$ (8.4 mg, 30 μmol) and $PCyp_3$ (7.2 mg, 30 μmol) in toluene (1.0 mL) was added to a solution of pentafluorobenzene (168 mg,

1.00 mmol) and 4-octyne (165 mg, 1.50 mmol) placed in a 3 mL-vial. Undecane (an internal standard, 78 mg, 0.5 mmol) was added. The vial was closed with a screw cap, taken out from the glove box, and heated at the temperature for the time specified in Tables 1, 2 and 3. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give the corresponding products in yields listed in Tables 1, 2 and 3. In some cases, a mixture of mono- and dialkenylated products and impurities (mainly tri- and oligomers of alkynes) were further separated by preparative recycling GPC or silica gel chromatography.

(*E*)-Pentafluoro(oct-4-en-4-yl)benzene (3aa). A colorless oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (t, *J* = 7.4 Hz, 1H), 2.35 (t, *J* = 7.6 Hz, 2H), 2.22 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.4 Hz, 2H), 1.29 (sext, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1 (dm, J_F = 244.9 Hz), 139.6 (dm, J_F = 252.6 Hz), 137.3 (dm, J_F = 252.6 Hz), 136.3, 126.3, 118.5–117.9 (m), 32.7, 30.3, 22.6, 21.5, 13.8 (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ –142.5 (dd, J_F = 24.8, 7.2 Hz, 2F), –158.1 (t, J_F = 20.5 Hz, 1F), –163.6 (td, J_F = 21.7, 8.1 Hz, 2F). IR (neat) 2963, 2928, 2874, 1518, 1493, 988. MS (EI, 70 eV) *m/z* (%) 278 (M^+, 24) 236 (16), 235 (100), 221 (16), 208 (73), 195 (11), 187 (30), 181 (79), 71 (15), 55 (15). Anal. Calcd for $C_{14}H_{15}F_5$: C, 60.43; H, 5.43. Found: C, 60.49; H, 5.67.

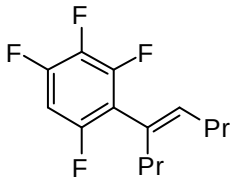


(*E*)-1,2,3,4-Tetrafluoro(oct-4-en-4-yl)benzene (3ba). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85–6.75 (m, 1H), 5.53 (t, *J* = 7.3 Hz, 1H), 2.40 (t, *J* = 7.7 Hz, 2H), 2.18 (q, *J* = 7.3 Hz, 2H), 1.47 (sext, *J* = 7.5 Hz, 2H), 1.30 (sext, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4 (dm, J_F = 246.4 Hz), 144.8 (dm, J_F = 242.4 Hz), 141.0 (dm, J_F = 252.6 Hz), 138.9 (dm, J_F = 251.8 Hz), 134.0, 133.5, 128.2–127.8 (m), 110.9 (dt, J_F = 19.2, 3.8 Hz), 32.3 (d, J_F = 2.3 Hz), 30.4, 22.8, 21.6, 13.94, 13.86; ^{19}F NMR (282 MHz, $CDCl_3$) δ –142.1 to –142.3 (m, 1F), –143.2 to –143.4 (m, 1F), –157.7 (t, J_F = 20.0 Hz, 1F), –160.1 to –160.4 (m, 1F). IR (neat) 2961, 2934, 2874, 1620, 1520, 1477, 1375, 1271, 1202, 1180, 1119, 1101, 1059, 1036, 1009, 966, 905, 862, 735, 712. MS (EI, 70 eV) *m/z* (%) 261 (M^++1, 38), 260 (M^+, 89), 231 (27), 218 (70), 217 (100), 215 (13), 204 (14), 203 (61), 201 (25), 200 (23), 197 (21), 195 (10), 191 (38), 190 (89), 189 (90), 188 (11), 187 (52), 183 (29),



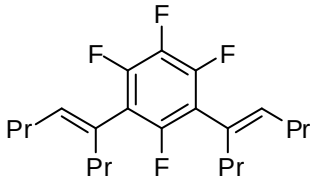
182 (36), 177 (57), 176 (29), 175 (42), 174 (27), 171 (11), 170 (17), 169 (73), 164 (32), 163 (83), 155 (17), 151 (33), 143 (12), 133 (15), 125 (14), 55 (58). Anal. Calcd for $C_{14}H_{16}F_4$: C, 64.61; H, 6.20. Found: C, 64.82; H, 6.40.

(*E*)-1,2,3,5-Tetrafluoro-4-(oct-4-en-4-yl)benzene (3ca). A yellow oil, R_f 0.50 (hexane).



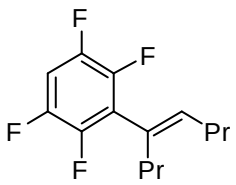
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77–6.67 (m, 1H), 5.48 (t, J = 7.3 Hz, 1H), 2.34 (t, J = 7.6 Hz, 2H), 2.20 (q, J = 7.3 Hz, 2H), 1.48 (sext, J = 7.5 Hz, 2H), 1.30 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4 (dm, J_F = 244.1 Hz), 148.9 (dm, J_F = 247.1 Hz), 137.0 (dm, J_F = 243.3 Hz), 135.3, 127.2, 118.6–118.0 (m), 100.2 (ddd, J_F = 29.7, 21.2, 3.8 Hz), 32.7, 30.2, 22.7, 21.5, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –117.4 (t, J_F = 8.9 Hz, 1F), –134.9 (d, J_F = 22.0 Hz, 1F), –136.0 to –136.1 (m, 1F), –166.1 to –166.4 (m, 1F). IR (neat) 2964, 2937, 2874, 1641, 1514, 1501, 1460, 1377, 1285, 1148, 1121, 1051, 968, 876, 833. MS (EI, 70 eV) *m/z* (%) 260 (M^+, 26), 218 (14), 217 (100), 203 (13), 190 (47), 189 (64), 177 (11), 175 (11), 169 (23), 163 (88), 55 (11). Anal. Calcd for $C_{14}H_{16}F_4$: C, 64.61; H, 6.20. Found: C, 64.64; H, 6.23.

(*E*,*E*)-1,2,3,5-Tetrafluoro-4,6-bis(oct-4-en-4-yl)benzene (4ca). A yellow oil, R_f 0.50 (hexane).



^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (t, J = 7.3 Hz, 2H), 2.34 (t, J = 7.6 Hz, 4H), 2.20 (q, J = 7.3 Hz, 4H), 1.48 (sext, J = 7.3 Hz, 4H), 1.30 (sext, J = 7.5 Hz, 4H), 0.97 (t, J = 7.3 Hz, 6H), 0.89 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0 (dm, J_F = 241.8 Hz), 146.9 (dm, J_F = 245.6 Hz), 136.8 (dm, J_F = 247.9 Hz), 135.0, 127.5, 117.4 (t, J_F = 23.1 Hz), 32.8, 30.3, 22.7, 21.6, 13.91, 13.88; ^{19}F NMR (282 MHz, $CDCl_3$) δ –120.6 (d, J_F = 8.2 Hz, 1F), –138.7 (d, J_F = 22.0 Hz, 2F), –166.6 (td, J_F = 22.3, 11.3 Hz, 1F). IR (neat) 2964, 2872, 1630, 1474, 1377, 1057, 976, 891. MS (EI, 70 eV) *m/z* (%) 370 (M^+, 23), 328 (24), 327 (100), 299 (12), 285 (22), 257 (10). Anal. Calcd for $C_{22}H_{30}F_4$: C, 71.32; H, 8.16. Found: C, 71.36; H, 8.08.

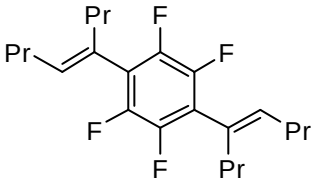
(*E*)-1,2,4,5-Tetrafluoro-3-(oct-4-en-4-yl)benzene (3da). A yellow oil, R_f 0.60 (hexane).



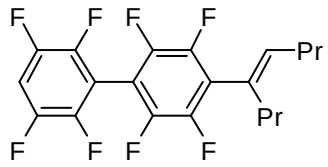
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99–6.86 (m, 1H), 5.52 (t, J = 7.3 Hz, 1H), 2.38 (t, J = 7.7 Hz, 2H), 2.23 (q, J = 7.3 Hz, 2H), 1.49 (sext, J = 7.3 Hz, 2H), 1.31 (sext, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7 (dm, J_F = 247.1 Hz), 143.8 (dm, J_F = 236.0 Hz), 135.6, 127.3, 124.1 (t, J_F = 18.9

Hz), 103.7 (t, J_F = 22.6 Hz), 32.6, 30.2, 22.7, 21.6, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –140.5 to –140.7 (m, 2F), –143.0 to –143.2 (m, 2F). IR (neat) 2924, 2855, 1643, 1607, 1493, 1285, 1171, 939, 899, 837, 714. MS (EI, 70 eV) *m/z* (%) 260 (M^+, 37), 218 (18), 217 (100), 203 (17), 197 (11), 190 (69), 189 (70), 187 (11), 183 (12), 182 (16), 177 (13), 176 (12), 169 (47), 163 (64), 55 (19). HRMS (EI) Calcd for $C_{14}H_{16}F_4$: M^+, 260.1188. Found: 260.1191.

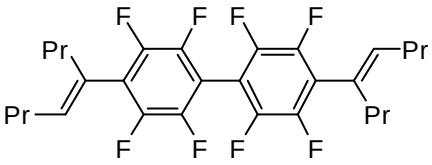
(*E*,*E*)-1,2,4,5-Tetrafluoro-3,6-bis(oct-4-en-4-yl)benzene (4da). A yellow oil, R_f 0.60 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (t, J = 7.3 Hz, 2H), 2.38 (t, J = 7.5 Hz, 4H), 2.23 (q, J = 7.3 Hz, 4H), 1.48 (sext, J = 7.3 Hz, 4H), 1.33 (sext, J = 7.4 Hz, 4H), 0.97 (t, J = 7.3 Hz, 6H), 0.91 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (d, J_F = 246.1 Hz), 135.4, 127.5, 121.0–119.6 (m), 32.7, 30.3, 22.7, 21.6, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –144.3 (s, 4F). IR (neat) 2976, 2880, 2835, 1470, 1454, 1377, 1308, 974, 897, 723. MS (EI, 70 eV) *m/z* (%) 370 (M^+, 32), 328 (25), 327 (100), 299 (12), 285 (22), 231 (15), 211 (12). Anal. Calcd for $C_{22}H_{30}F_4$: C, 71.32; H, 8.16. Found: C, 71.13; H, 8.13.



(*E*)-2,3,5,6,2',3',5',6'-Octafluoro-4-(oct-4-en-4-yl)biphenyl (3ea). A yellow oil, R_f 0.30 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.17 (m, 1H), 5.61 (t, J = 7.3 Hz, 1H), 2.42 (t, J = 7.7 Hz, 2H), 2.25 (q, J = 7.3 Hz, 2H), 1.50 (sext, J = 7.3 Hz, 2H), 1.36 (sext, J = 7.5 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1 (dm, J_F = 256.7 Hz), 145.8 (dm, J_F = 251.8 Hz), 144.1 (dm, J_F = 238.8 Hz), 143.8 (dm, J_F = 251.8 Hz), 136.4, 127.0, 125.4 (t, J_F = 18.5 Hz), 108.2 (t, J_F = 20.2 Hz), 107.5 (t, J_F = 22.3 Hz), 104.8 (t, J_F = 20.2 Hz), 32.6, 30.3, 22.6, 21.7, 13.89, 13.85; ^{19}F NMR (282 MHz, $CDCl_3$) δ –138.4 to –138.6 (m, 2F), –138.7 to –138.9 (m, 2F), –139.9 to –140.3 (m, 2F), –141.9 (dd, J = 22.9, 10.4 Hz, 2F). IR (neat) 2964, 2945, 2889, 2857, 2847, 1504, 1469, 1462, 1456, 1377, 1268, 1177, 988, 935, 849, 708. MS (EI, 70 eV) *m/z* (%) 409 (M^++1, 20), 408 (M^+, 76), 366 (64), 365 (100), 351 (39), 339 (35), 338 (95), 337 (85), 330 (20), 325 (29), 324 (36), 323 (16), 322 (24), 318 (16), 312 (29), 311 (89), 299 (12), 297 (11), 291 (20), 273 (22), 268 (13), 253 (14), 55 (20). Anal. Calcd for $C_{20}H_{16}F_8$: C, 58.83; H, 3.95. Found: C, 59.05; H, 4.10.

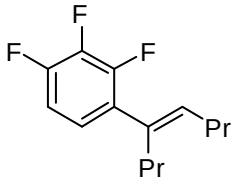


(*E*,*E*)-2,3,5,6,2',3',5',6'-Octafluoro-4,4'-bis(oct-4-en-4-yl)-biphenyl (4ea). A yellow solid, mp 56.5–57.4 ºC, R_f 0.30 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (t, J_F =



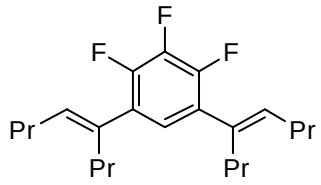
7.3 Hz, 2H), 2.43 (t, J = 7.6 Hz, 4H), 2.26 (q, J_F = 7.3 Hz, 4H), 1.51 (sext, J_F = 7.3 Hz, 4H), 1.38 (sext, J_F = 7.5 Hz, 4H), 0.99 (t, J_F = 7.4 Hz, 6H), 0.94 (t, J_F = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (dm, J_F = 246.4 Hz), 143.8 (dm, J_F = 251.9 Hz), 136.3, 127.1, 125.2 (t, J_F = 18.9 Hz), 105.2 (t, J_F = 16.2 Hz), 32.6, 30.3, 22.7, 21.7, 13.84, 13.79; ^{19}F NMR (282 MHz, $CDCl_3$) δ –139.9 to –140.3 (m, 4F), –142.0 to –142.4 (m, 4F). IR (KBr) 2961, 2932, 2872, 1651, 1479, 1462, 1401, 1379, 1367, 1339, 1287, 1261, 1165, 1094, 1071, 990, 968, 901, 818, 721, 656, 567. MS (EI, 70 eV) *m/z* (%) 519 (M^++1, 14), 518 (M^+, 37), 476 (36), 475 (100), 447 (18), 433 (18), 281 (13), 207 (20), 73 (11). Anal. Calcd for $C_{28}H_{30}F_8$: C, 64.86; H, 5.83. Found: C, 65.12; H, 6.01.

(*E*)-1,2,3-Trifluoro-4-(oct-4-en-4-yl)benzene (3fa). A yellow oil, R_f 0.60 (hexane). ^{1}H



NMR (400 MHz, $CDCl_3$) δ 6.92–6.83 (m, 2H), 5.50 (t, J = 7.3 Hz, 1H), 2.40 (t, J = 7.6 Hz, 2H), 2.18 (q, J = 7.3 Hz, 2H), 1.49 (sext, J = 7.4 Hz, 2H), 1.29 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4 (dm, J_F = 248.8 Hz), 148.0 (dm, J_F = 251.9 Hz), 139.7 (dt, J = 251.0, 15.4 Hz), 134.3, 133.1, 129.4 (dd, J = 11.5, 3.0 Hz), 123.6–123.2, 111.3 (dd, J = 16.9, 3.8 Hz), 32.4 (d, J = 2.3 Hz), 30.4, 22.9, 21.6, 14.0, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –137.5 (d, J_F = 25.4 Hz, 1F), –138.1 (d, J_F = 12.7 Hz, 1F), –161.7 (t, J_F = 19.1 Hz, 1F). IR (neat) 2924, 2855, 1607, 1508, 1464, 1310, 1273, 1231, 1182, 1038, 1016, 993, 808. MS (EI, 70 eV) *m/z* (%) 242 (M^+, 33), 200 (14), 199 (100), 185 (11), 172 (38), 171 (66), 151 (15), 145 (50). Anal. Calcd for $C_{14}H_{17}F_3$: C, 69.40; H, 7.07. Found: C, 69.68; H, 7.22.

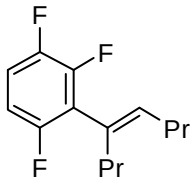
(*E*,*E*)-1,2,3-Trifluoro-4,6-bis(oct-4-en-4-yl)benzene (4fa). A yellow oil, R_f 0.60



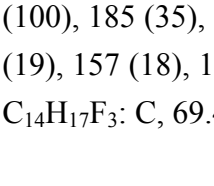
(hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (td, J = 7.8, 2.4 Hz, 1H), 5.51 (t, J = 7.3 Hz, 2H), 2.40 (t, J = 7.6 Hz, 4H), 2.17 (q, J = 7.3 Hz, 4H), 1.47 (sext, J = 7.3 Hz, 4H), 1.30 (sext, J = 7.4 Hz, 4H), 0.97 (t, J = 7.3 Hz, 6H), 0.87 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.0 (ddd, J_F = 248.4, 10.4, 3.0 Hz), 139.6 (dt, J_F = 249.5, 16.4 Hz), 134.4, 132.8, 128.1 (dd, J_F = 10.8, 5.4 Hz), 123.6 (dd, J_F = 3.9, 3.8 Hz), 32.5, 30.4, 22.9, 21.6, 14.0, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –140.3 (dd, J_F = 22.0, 8.2 Hz, 2F), –161.8 (t, J_F = 20.6 Hz). IR (neat) 2959, 2932, 2872, 1605, 1487, 1454, 1371, 1248, 1186, 1119, 1088, 1067, 1032, 974, 887, 739, 710. MS (EI, 70 eV) *m/z* (%) 353 (M^++1, 19), 352 (M^+, 75), 267 (17), 241 (19), 183 (14), 111

(17), 55 (30). HRMS (EI) Calcd for $C_{22}H_{31}F_3$: M^+, 352.2378. Found: 352.2366.

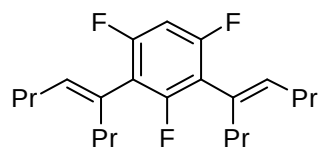
(*E*)-1,2,4-Trifluoro-3-(oct-4-en-4-yl)benzene (3ga). A yellow oil, R_f 0.40 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04–6.92 (m, 1H), 6.82–6.73 (m, 1H), 5.49 (t, J = 7.3 Hz, 1H), 2.38 (t, J = 7.7 Hz, 2H), 2.23 (q, J = 7.3 Hz, 2H), 1.49 (sext, J = 7.3 Hz, 2H), 1.31 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6 (dm, J_F = 245.4 Hz), 148.1 (dm, J_F = 262.5 Hz), 147.1 (dm, J_F = 245.8 Hz), 134.8, 128.0, 122.8 (dd, J_F = 22.9, 17.0 Hz), 114.4 (dd, J_F = 18.1, 9.5 Hz), 110.2 (ddd, J_F = 26.2, 6.9, 3.8 Hz), 32.7, 30.2, 22.8, 21.5, 13.92, 13.88; ^{19}F NMR (282 MHz, $CDCl_3$) δ –119.0 (s, 1F), –137.2 (dd, J_F = 22.6, 11.3 Hz, 1F), –143.3 to –143.6 (m, 1F). IR (neat) 2964, 2872, 1636, 1541, 1485, 1445, 1380, 1365, 1356, 1279, 1339, 1261, 1196, 1032, 972, 899, 860. MS (EI, 70 eV) *m/z* (%) 243 (M^++1, 10), 242 (M^+, 64), 200 (32), 199 (100), 185 (35), 183 (11), 173 (10), 172 (81), 171 (90), 169 (25), 164 (18), 159 (28), 158 (19), 157 (18), 156 (18), 151 (42), 146 (15), 145 (94), 137 (15), 55 (35). Anal. Calcd for $C_{14}H_{17}F_3$: C, 69.40; H, 7.07. Found: C, 69.69; H, 7.22.



(*E*)-1,3,5-Trifluoro-2-(oct-4-en-4-yl)benzene (3ha). A colorless oil, R_f 0.55 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67–6.57 (m, 2H), 5.44 (t, J = 7.3 Hz, 1H), 2.34 (t, J = 7.6 Hz, 2H), 2.20 (q, J = 7.3 Hz, 2H), 1.47 (sext, J = 7.3 Hz, 2H), 1.29 (sext, J = 7.5 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (dt, J_F = 241.1, 15.5 Hz), 160.3 (ddd, J_F = 241.1, 14.5, 10.8 Hz), 134.4, 127.7, 117.2 (t, J_F = 17.1 Hz), 99.8 (dd, J_F = 32.2, 25.1 Hz), 32.9, 30.2, 22.8, 21.5, 13.92, 13.87; ^{19}F NMR (282 MHz, $CDCl_3$) δ –110.7 (t, J_F = 6.1 Hz, 2F), –111.6 to –111.9 (m, 1F). IR (neat) 2922, 2853, 1595, 1462, 1452, 1420, 1377, 1144, 1036, 833. MS (EI, 70 eV) *m/z* (%) 243 (M^+, 20), 242 (M^+, 76), 213 (12), 200 (60), 199 (100), 197 (12), 186 (10), 185 (53), 183 (16), 182 (13), 173 (17), 172 (79), 171 (87), 169 (48), 165 (11), 164 (18), 159 (51), 158 (27), 157 (55), 156 (36), 151 (49), 146 (38), 145 (90), 137 (32), 125 (10), 67 (13), 55 (35). HRMS (EI) Calcd for $C_{14}H_{17}F_3$: M^+, 242.1282. Found: 242.1283.

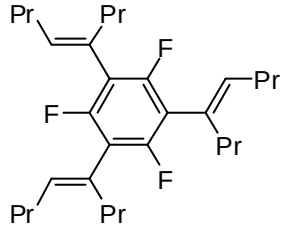


(*E*)-1,3,5-Trifluoro-2,4-bis(oct-4-en-4-yl)benzene (4ha). A colorless oil, R_f 0.55 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.59 (td, J = 9.3, 2.0 Hz, 1H), 5.44 (t, J = 7.3 Hz, 2H), 2.33 (t, J = 7.7 Hz, 4H), 2.20 (q, J = 7.3 Hz, 4H), 1.47 (sext, J = 7.3 Hz, 4H), 1.30 (sext, J = 7.4 Hz, 4H), 0.96 (t, J = 7.4 Hz, 6H), 0.89 (t, J =

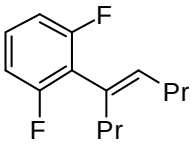


7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4 (ddd, J_F = 226.3, 15.3, 10.7 Hz), 157.7 (dt, J_F = 241.4, 10.1 Hz), 134.1, 128.2, 116.7 (dd, J_F = 25.5, 23.9 Hz), 99.3 (td, J_F = 27.8, 4.2 Hz), 33.0, 30.2, 22.8, 21.5, 14.0, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –113.5 (s, 1F), –114.6 (s, 2F). IR (neat) 2959, 2932, 2872, 1628, 1593, 1483, 1465, 1456, 1418, 1379, 1339, 1262, 1144, 1117, 1091, 1036, 974, 899, 833, 739, 577, 549. MS (EI, 70 eV) *m/z* (%) 353 (M^++1, 14), 352 (M^+, 57), 310 (48), 309 (100), 281 (29), 267 (24), 255 (36), 213 (10). Anal. Calcd for $C_{22}H_{31}F_3$: C, 74.97; H, 8.86. Found: C, 75.12; H, 9.01.

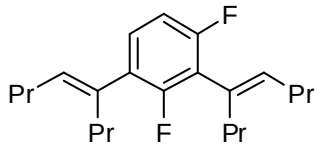
(*E*)-1,3,5-Trifluoro-2,4,6-tris(oct-4-en-4-yl)benzene (4'ha). A yellow oil, R_f 0.55 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, *J* = 7.3 Hz, 3H), 2.33 (t, *J* = 7.6 Hz, 6H), 2.19 (q, *J* = 7.3 Hz, 6H), 1.47 (sext, *J* = 7.3 Hz, 6H), 1.30 (sext, *J* = 7.5 Hz, 6H), 0.96 (t, *J* = 7.4 Hz, 9H), 0.89 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7 (dt, J_F = 242.6, 10.8 Hz), 133.7, 128.6, 116.1 (dd, J_F = 27.7, 23.2 Hz), 33.0, 30.3, 22.8, 21.6, 13.99, 13.95; ^{19}F NMR (282 MHz, $CDCl_3$) δ –117.2 (s, 3F). IR (neat) 2959, 2932, 2872, 1601, 1462, 1454, 1429, 1379, 1360, 1337, 1260, 1244, 1186, 1117, 1086, 1053, 1042, 1018, 993, 899, 859, 808, 739, 692, 598. MS (EI, 70 eV) *m/z* (%) 463 (M^+, 26), 462 (76), 433 (14), 421 (23), 420 (15), 419 (100), 405 (14), 392 (19), 391 (44), 379 (17), 377 (32), 366 (18), 365 (53), 349 (13), 335 (12), 69 (32), 55 (27). Anal. Calcd for $C_{30}H_{45}F_3$: C, 77.88; H, 9.80. Found: C, 78.03; H, 9.87.



(*E*)-1,3-Difluoro-2-(oct-4-en-4-yl)benzene (3ia). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (tt, *J* = 8.3, 6.4 Hz, 1H), 6.90–6.80 (m, 2H), 5.48 (t, *J* = 7.2 Hz, 1H), 2.39 (t, *J* = 7.5 Hz, 2H), 2.23 (q, *J* = 7.3 Hz, 2H), 1.49 (sext, *J* = 7.3 Hz, 2H), 1.32 (sext, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4 (dd, *J* = 245.4, 8.4 Hz), 133.9, 128.5, 127.5 (t, *J* = 10.0 Hz), 120.9 (t, *J* = 21.1 Hz), 111.0 (dd, *J* = 24.2, 7.6 Hz), 32.9, 30.2, 22.8, 21.6, 14.0, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ –113.9 (s, 2F). IR (neat) 2961, 2934, 2872, 1622, 1586, 1462, 1379, 1269, 1231, 995, 899, 785, 729. MS (EI, 70 eV) *m/z* (%) 225 (M^++1, 39), 224 (M^+, 88), 195 (19), 182 (73), 181 (100), 179 (16), 167 (70), 165 (31), 161 (10), 154 (83), 153 (89), 151 (62), 146 (26), 141 (67), 140 (40), 139 (54), 133 (60), 128 (45), 127 (89), 119 (42), 101 (18), 67 (16), 55 (46). HRMS (EI) Calcd for $C_{14}H_{19}F_2$: M^+, 224.1377. Found: 224.1374.

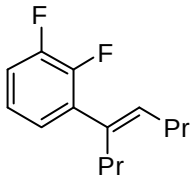


(*E*,*E*)-1,3-Difluoro-2,4-bis(oct-4-en-4-yl)benzene (4ia). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (td, *J* = 8.4, 6.4 Hz, 1H), 6.76 (td, *J* = 8.6, 1.5 Hz,



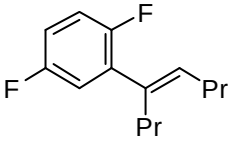
1H), 5.46 (br td, J = 7.3, 2.0 Hz, 2H), 2.40 (t, J = 7.4 Hz, 2H), 2.37 (t, J = 7.3 Hz, 2H), 2.21 (q, J = 7.3 Hz, 2H), 2.17 (q, J = 7.3 Hz, 2H), 1.53–1.41 (m, 4H), 1.37–1.23 (m, 4H), 0.972 (t, J = 7.3, Hz, 3H), 0.968 (t, J = 7.3, Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0 (dd, J_F = 244.8, 7.6 Hz), 157.0 (dd, J_F = 245.6, 7.9 Hz), 135.7, 133.6, 131.7, 128.9, 128.2 (dd, J_F = 9.3, 6.2 Hz), 127.6 (dd, J_F = 16.8, 3.8 Hz), 120.8 (dd, J_F = 22.3, 20.6 Hz), 110.2 (dd, J_F = 23.1, 3.8 Hz), 33.0, 32.6 (d, J_F = 3.1 Hz), 30.4, 30.2, 23.0, 22.8 x 2, 21.6, 14.03, 14.00, 13.9 x 2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –115.3 (t, J_F = 7.8 Hz, 1F), –116.6 (dd, J_F = 15.5, 6.8 Hz, 1F). IR (neat) 2961, 2934, 1614, 1584, 1479, 1456, 1418, 1379, 1339, 1260, 1229, 1182, 1022, 986, 879, 813. MS (EI, 70 eV) *m/z* (%) 335 (M^++1), 334 (M^+, 100), 305 (30), 292 (85), 291 (100), 264 (32), 263 (56), 249 (63), 237 (62), 223 (42), 221 (37), 207 (24), 195 (55), 193 (31), 181 (45), 179 (29), 177 (22), 173 (16), 167 (18), 165 (47), 159 (21), 153 (32), 151 (22), 146 (15), 127 (14), 111 (16), 69 (83), 55 (68), 53 (12). HRMS (EI) Calcd for $C_{22}H_{32}F_2$: 334.2472. Found: 334.2472.

(*E*)-1,2-Difluoro-3-(oct-4-en-4-yl)benzene (3ja). A yellow oil, R_f 0.50 (hexane). ^{1}H



NMR (400 MHz, $CDCl_3$) δ 7.06–6.88 (m, 3H), 5.54 (t, J = 7.3 Hz, 1H), 2.44 (t, J = 7.4 Hz, 2H), 2.19 (q, J = 7.3 Hz, 2H), 1.48 (sext, J = 7.4 Hz, 2H), 1.31 (sext, J = 7.4 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.6 (dd, J_F = 248.1, 13.9 Hz), 147.9 (dd, J_F = 247.2, 12.7 Hz), 134.8 (d, J_F = 2.2 Hz), 134.1 (d, J_F = 11.5 Hz), 132.7 (d, J_F = 1.5 Hz), 125.0 (t, J_F = 3.5 Hz), 123.3 (dd, J_F = 6.9, 4.8 Hz), 114.9 (d, J_F = 17.8 Hz), 32.5 (d, J_F = 2.3 Hz), 30.4, 22.9, 21.6, 13.99, 13.95; ^{19}F NMR (282 MHz, $CDCl_3$) δ –139.4 to –139.6 (m, 1F), –142.1 to –142.4 (m, 1F). IR (neat) 2959, 2932, 2872, 1377, 1265, 1213, 1061, 972, 885, 820, 785, 727. MS (EI, 70 eV) *m/z* (%) 224 (M^+, 36), 182 (15), 181 (100), 154 (32), 153 (55), 151 (10), 127 (35). HRMS (EI) Calcd for $C_{14}H_{18}F_2$: M^+, 224.1377. Found: 224.1378.

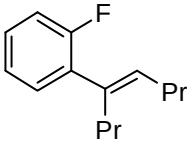
(*E*)-1,4-Difluoro-2-(oct-4-en-4-yl)benzene (3ka). A yellow oil, R_f 0.50 (hexane). ^{1}H



NMR (400 MHz, $CDCl_3$) δ 6.98–6.82 (m, 3H), 5.53 (t, J = 7.2 Hz, 1H), 2.42 (t, J = 7.6 Hz, 2H), 2.18 (q, J = 7.3 Hz, 2H), 1.47 (sext, J = 7.4 Hz, 2H), 1.31 (sext, J = 7.4 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (dd, J_F = 250.3, 2.9 Hz), 155.8 (dd, J_F = 250.3, 2.9 Hz), 135.2, 133.2 (dd, J_F = 17.5, 7.7 Hz), 132.7, 116.6 (dd, J_F = 23.8, 5.0 Hz), 116.2 (dd, J_F = 27.0, 8.5 Hz), 113.9 (dd, J_F = 23.9, 8.4 Hz), 32.3 (d, J_F =

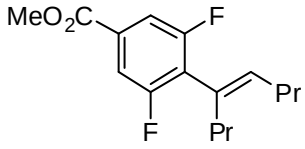
3.1 Hz), 30.4, 22.9, 21.6, 13.99, 13.96; ^{19}F NMR (282 MHz, $CDCl_3$) δ –120.5 to –120.9 (m, 1F), –122.3 to –122.6 (m, 1F). IR (neat) 2961, 2932, 2872, 1618, 1587, 1493, 1487, 1468, 1464, 1456, 1418, 1379, 1275, 1244, 1202, 1177, 1086, 874, 812, 756. MS (EI, 70 eV) *m/z* (%) 224 (M^+, 55), 182 (21), 181 (100), 167 (20), 165 (15), 164 (15), 154 (62), 153 (93), 151 (30), 141 (16), 133 (25), 127 (89), 119 (11), 55 (22). Anal. Calcd for $C_{14}H_{18}F_2$: C, 74.97; H, 8.09. Found: C, 75.03; H, 8.18.

(*E*)-Fluoro-2-(oct-4-en-4-yl)benzene (3la). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR



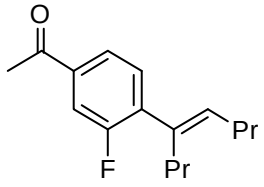
(400 MHz, $CDCl_3$) δ 7.22–7.15 (m, 2H), 7.08–6.96 (m, 2H), 5.51 (t, *J* = 7.3 Hz, 1H), 2.45 (t, *J* = 7.5 Hz, 2H), 2.19 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.3 Hz, 2H), 1.31 (sext, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8 (d, J_F = 246.3 Hz), 136.0, 131.814, 131.810 (d, J_F = 14.6 Hz), 130.5 (d, J_F = 4.5 Hz), 127.8 (d, J_F = 8.4 Hz), 123.6 (d, J_F = 3.8 Hz), 115.3 (d, J_F = 23.1 Hz), 32.6 (d, J_F = 2.3 Hz), 30.4, 23.3, 21.6, 14.0 x 2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –116.3 (s, 1F). IR (neat) 2959, 2931, 2872, 1613, 1576, 1487, 1451, 1379, 1258, 1221, 1206, 1091, 1034, 897, 824, 754. MS (EI, 70 eV) *m/z* (%) 206 (M^+, 44), 164 (18), 163 (100), 149 (14), 136 (31), 135 (67), 133 (16), 109 (47). HRMS (EI) Calcd for $C_{14}H_{19}F$: M^+, 206.1471. Found: 206.1477.

Methyl (*E*)-3,5-difluoro-4-(oct-4-en-4-yl)benzoate (3ma). A colorless oil, R_f 0.20



(hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.48 (m, 2H), 5.50 (t, *J* = 7.3 Hz, 1H), 3.92 (s, 3H), 2.39 (t, *J* = 7.5 Hz, 2H), 2.22 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.3 Hz, 2H), 1.29 (sext, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 160.0 (dd, J_F = 248.0, 7.7 Hz), 134.8, 129.9 (t, J_F = 9.6 Hz), 128.0, 125.7 (t, J_F = 21.2 Hz), 112.4 (dd, J_F = 20.0, 8.5 Hz), 52.5, 32.6, 30.2, 22.7, 21.6, 13.89, 13.87; ^{19}F NMR (282 MHz, $CDCl_3$) δ –112.1 (s, 2F). IR (neat) 2961, 2934, 2874, 1732, 1566, 1435, 1421, 1379, 1331, 1232, 1188, 1105, 1086, 1030, 1003, 887, 770, 746. MS (EI, 70 eV) *m/z* (%) 283 (M^++1, 47), 282 (M^+, 91), 253 (20), 251 (69), 240 (80), 239 (100), 225 (69), 213 (41), 212 (88), 211 (89), 199 (66), 198 (26), 197 (36), 186 (43), 185 (87), 181 (53), 179 (26), 167 (34), 166 (12), 165 (44), 164 (41), 157 (60), 152 (40), 151 (60), 138 (15), 133 (26), 127 (35), 126 (34), 59 (38), 55 (36). Anal. Calcd for $C_{16}H_{20}F_2O_2$: C, 68.07; H, 7.14. Found: C, 68.34; H, 7.17.

(*E*)-3-fluoro-4-(oct-4-en-4-yl)acetophenone (3na). A yellow oil, R_f 0.10 (hexane–ethyl acetate = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.58 (dd,



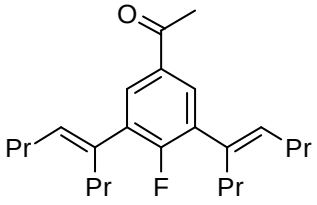
J = 11.1, 1.6 Hz, 1H), 7.28 (t, J = 7.7 Hz, 1H), 5.58 (t, J = 7.3 Hz, 1H), 2.58 (s, 3H), 2.46 (t, J = 7.6 Hz, 2H), 2.20 (q, J = 7.3 Hz, 2H), 1.48 (sext, J = 7.3 Hz, 2H), 1.29 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2 (d, J_F = 2.3 Hz), 159.6 (d, J_F = 248.7 Hz), 136.9 (d, J_F = 3.1 Hz), 136.8 (d, J_F = 11.5 Hz), 135.3 (d, J_F = 1.5 Hz), 133.3, 130.5 (d, J_F = 3.8 Hz), 123.7 (d, J_F = 3.1 Hz), 115.1 (d, J_F = 24.6 Hz), 32.1 (d, J = 3.1 Hz), 30.3, 26.6, 22.8, 21.6, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –114.8. IR (neat) 3364, 2961, 2934, 2856, 1694, 1682, 1614, 1562, 1495, 1465, 1454, 1416, 1360, 1279, 1242, 1188, 1123, 1099, 1076, 963, 891, 831, 646, 560. MS (EI, 70 eV) *m/z* (%) 249 (M^++1, 52), 248 (M^+, 100), 233 (25), 219 (34), 206 (42), 205 (92), 191 (49), 179 (14), 178 (79), 177 (37), 165 (21), 163 (80), 161 (22), 151 (46), 147 (47), 146 (57), 134 (17), 133 (70), 123 (37), 115 (18), 108 (16), 107 (11), 55 (15). HRMS (EI) Calcd for $C_{16}H_{21}FO$: M^+, 248.1576. Found: 248.1572.

(*E*,*E*)-3-fluoro-2,4-bis(oct-4-en-4-yl)acetophenone (4na). A yellow oil, R_f 0.10 (hexane–ethyl acetate = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.1 Hz, 1H), 7.09 (dd, J = 7.9, 7.0 Hz, 1H), 5.53 (t, J = 7.2 Hz, 1H), 5.35 (t, J = 7.3 Hz, 1H), 2.47 (s, 3H), 2.44 (t, J = 7.6 Hz, 2H), 2.36 (br, 2H), 2.18 (q x 2, J = 7.7 Hz, 4H), 1.53–1.22 (m, 8H), 0.97 (t, J = 7.3 Hz, 3H), 0.96 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.4 (d, J_F = 34.1 Hz), 157.0 (d, J_F = 245.6 Hz), 140.0 (d, J_F = 33.0 Hz), 135.9, 134.6 (d, J = 17.7 Hz), 133.6, 133.0, 132.6, 130.7 (d, J_F = 20.1 Hz), 128.5 (d, J_F = 5.5 Hz), 122.9 (d, J_F = 3.9 Hz), 34.6 (d, J_F = 1.5 Hz), 32.4 (d, J_F = 3.4 Hz), 30.6, 30.5, 30.4, 22.9, 22.6, 21.7, 21.6, 14.6, 14.1, 14.03, 14.00; ^{19}F NMR (282 MHz, $CDCl_3$) δ –116.2 (s, 1F). IR (neat) 2961, 2932, 2872, 1694, 1601, 1465, 1454, 1412, 1379, 1354, 1279, 1260, 1017, 891, 826, 743. MS (EI, 70 eV) *m/z* (%) 358 (M^+, 18), 340 (16), 330 (35), 329 (89), 317 (23), 315 (100), 311 (16), 273 (41), 257 (22), 215 (13), 69 (16). HRMS (EI) Calcd for $C_{24}H_{35}FO$: M^+, 358.2672. Found: 358.2670.

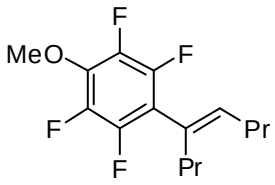
(*E*)-4-fluoro-3-(oct-4-en-4-yl)acetophenone (3oa). A yellow oil, R_f 0.10 (hexane–ethyl acetate = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.78 (m, 2H), 7.10–7.02 (m, 1H), 5.54 (t, J = 7.3 Hz, 1H), 2.60 (s, 3H), 2.45 (t, J = 7.6 Hz, 2H), 2.20 (q, J = 7.4 Hz, 2H), 1.48 (sext, J = 7.3 Hz, 2H), 1.29 (sext, J = 7.5 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H),

0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 162.8 (d, J_F = 254.9 Hz), 135.1, 133.1 (d, J_F = 3.1 Hz), 132.9, 132.2 (d, J_F = 16.2 Hz), 131.1 (d, J_F = 6.2 Hz), 128.6 (d, J_F = 9.3 Hz), 115.6 (d, J_F = 26.4 Hz), 32.4 (d, J_F = 2.3 Hz), 30.4, 26.6, 22.9, 21.6, 13.98, 13.94; ^{19}F NMR (282 MHz, $CDCl_3$) δ –108.3 (s, 1F). IR (neat) 2961, 2932, 2872, 1688, 1605, 1580, 1489, 1458, 1431, 1412, 1379, 1358, 1304, 1288, 1242, 1202, 1119, 1099, 957, 897, 829, 731, 652, 600, 567. MS (EI, 70 eV) *m/z* (%) 249 (M^++1, 100), 248 (M^+, 100), 233 (32), 219 (18), 206 (41), 205 (96), 191 (51), 179 (12), 178 (73), 177 (39), 175 (21), 165 (20), 164 (16), 163 (80), 161 (23), 159 (12), 151 (63), 149 (23), 147 (37), 146 (46), 136 (14), 135 (23), 134 (13), 133 (52), 127 (10), 115 (12), 109 (17), 108 (11), 55 (12). HRMS (EI) Calcd for $C_{16}H_{21}FO$: M^+, 248.1576. Found: 248.1581.

(*E*,*E*)-4-fluoro-3,5-di(oct-4-en-4-yl)acetophenone (4oa). A yellow oil, R_f 0.10 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 6.8 Hz, 2H), 5.52 (t, J = 7.2 Hz, 2H), 2.59 (s, 3H), 2.44 (t, J = 7.6 Hz, 4H), 2.19 (q, J = 7.3 Hz, 4H), 1.48 (sext, J = 7.3 Hz, 4H), 1.30 (sext, J = 7.5 Hz, 4H), 0.98 (t, J = 7.3 Hz, 6H), 0.87 (t, J = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.0, 160.0 (d, J_F = 254.9 Hz), 135.6, 132.5, 132.2 (d, J_F = 17.8 Hz), 129.3 (d, J_F = 6.2 Hz), 32.6 (d, J_F = 2.3 Hz), 30.4, 26.7, 22.9, 21.6, 14.1, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ –110.9 (t, J_F = 2.4 Hz, 1F). IR (neat) 2959, 2932, 2872, 1688, 1584, 1456, 1416, 1377, 1360, 1240, 1202, 1137, 1082, 889, 760, 741, 650, 577. MS (EI, 70 eV) *m/z* (%) 359 (M^++1, 64), 358 (M^+, 100), 343 (16), 329 (20), 316 (53), 315 (95), 288 (12), 287 (21), 285 (12), 273 (42), 271 (42), 259 (11), 245 (20), 243 (11), 231 (10), 229 (41), 217 (17), 216 (17), 215 (69), 203 (19), 201 (12), 189 (24), 187 (12), 175 (30), 173 (12), 147 (11), 69 (20), 55 (13). HRMS (EI) Calcd for $C_{24}H_{35}FO$: M^+, 358.2672. Found: 358.2656.

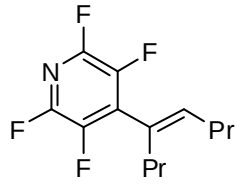


(*E*)-2,3,5,6-Tetrafluoro-4-(oct-4-en-4-yl)anisole (3pa). A colorless oil, R_f 0.20 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 (t, J = 7.3 Hz, 1H), 4.06 (s, 3H), 2.35 (t, J = 7.6 Hz, 2H), 2.21 (q, J = 7.3 Hz, 2H), 1.48 (sext, J = 7.3 Hz, 2H), 1.30 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (dm, J_F = 242.3 Hz), 140.7 (dm, J_F = 246.2 Hz), 136.6–136.2 (m), 135.6, 126.9, 116.8 (t, J_F = 19.7 Hz), 62.1, 32.8, 30.3, 22.7, 21.6, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –144.3 (dd, J_F = 21.8, 8.6 Hz, 2F), –159.4 (dd, J_F = 24.0, 10.4 Hz, 2F). IR (neat) 2961, 2934, 2874, 1647, 1504, 1481, 1470, 1439, 1420, 1381, 1200, 1126, 1107, 1063, 1018, 984, 945, 903, 864. MS (EI, 70 eV) *m/z* (%) 291 (M^++1, 40), 290 (M^+,

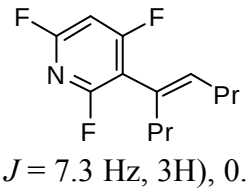


92), 261 (35), 248 (64), 247 (100), 233 (47), 221 (23), 220 (83), 219 (84), 217 (19), 207 (40), 205 (45), 204 (21), 200 (10), 199 (10), 194 (36), 193 (91), 189 (22), 188 (20), 187 (26), 176 (17), 169 (32), 162 (12), 161 (10), 157 (13), 151 (16), 81 (10), 67 (10), 55 (21). Anal. Calcd for $C_{15}H_{18}F_4O$: C, 62.06; H, 6.25. Found: C, 62.33; H, 6.53.

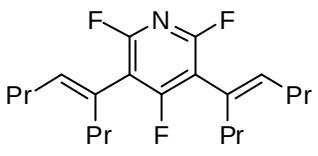
(*E*)-2,3,5,6-Tetrafluoro-4-(oct-4-en-4-yl)pyridine (3qa). A yellow oil, R_f 0.30 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (t, J = 7.3 Hz, 1H), 2.43 (t, J = 7.6 Hz, 2H), 2.26 (q, J = 7.3 Hz, 2H), 1.50 (sext, J = 7.5 Hz, 2H), 1.32 (sext, J = 7.5 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4 (dm, J_F = 245.3 Hz), 139.6 (dm, J_F = 256.0 Hz), 137.6, 136.8–136.3 (m), 126.7, 31.9, 30.3, 22.5, 21.6, 13.8, 13.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ –92.1 to –92.5 (m, 2F), –143.9 to –144.1 (m, 2F). IR (neat) 2965, 2936, 2876, 1640, 1454, 1410, 1368, 1286, 1171, 1069, 961, 903, 878. MS (EI, 70 eV) *m/z* (%) 261 (M^+, 47), 219 (37), 218 (32), 204 (18), 191 (100), 190 (35), 184 (12), 177 (18), 170 (35), 164 (16), 55 (12). HRMS (EI) Calcd for $C_{13}H_{15}F_4N$: M^+, 261.1141. Found: 261.1146.



(*E*)-2,4,6-Trifluoro-3-(oct-4-en-4-yl)pyridine (3ra). A yellow oil, R_f 0.20 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (ddd, J = 7.7, 1.2, 0.6 Hz, 1H), 5.51 (t, J = 7.4 Hz, 1H), 2.34 (t, J = 7.6 Hz, 2H), 2.20 (q, J = 7.5 Hz, 2H), 1.47 (sext, J = 7.4 Hz, 2H), 1.29 (sext, J = 7.4 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1 (ddd, J_F = 261.1, 12.3, 9.2 Hz), 159.8 (dt, J_F = 242.6, 17.8 Hz), 159.6 (ddd, J_F = 243.3, 17.7, 12.3 Hz), 135.9, 126.1 (d, J_F = 3.8 Hz), 112.8–112.1 (m), 94.9 (ddd, J_F = 39.3, 26.2, 6.2 Hz), 32.4, 30.2, 22.6, 21.5, 13.8 (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ –67.8 (dd, J_F = 21.4, 13.0 Hz, 1F), –68.5 (t, J_F = 17.1 Hz, 1F), –94.7 to –95.2 (m, 1F). IR (neat) 2964, 2941, 2874, 1593, 1462, 1406, 1377, 1144, 1049, 1013, 833. MS (EI, 70 eV) *m/z* (%) 243 (M^+, 20), 201 (13), 200 (80), 186 (17), 184 (15), 173 (51), 172 (63), 170 (17), 160 (12) 159 (12), 158 (12), 157 (16), 152 (18), 147 (11), 146 (100), 138 (21), 57 (27), 56 (16), 55 (14). Anal. Calcd for $C_{13}H_{16}F_3N$: C, 64.18; H, 6.63. Found: C, 64.35; H, 6.89.

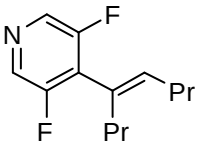


(*E*,*E*)-2,4,6-Trifluoro-3,5-di(oct-4-en-4-yl)pyridine (4ra). A yellow oil, R_f 0.20 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (t, J = 7.3 Hz, 2H), 2.34 (t, J = 7.6 Hz, 4H), 2.20 (q, J = 7.3 Hz, 4H), 1.48 (sext, J = 7.3 Hz, 4H), 1.30 (sext, J = 7.5 Hz, 4H), 0.96 (t, J = 7.4 Hz, 6H), 0.89 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz,

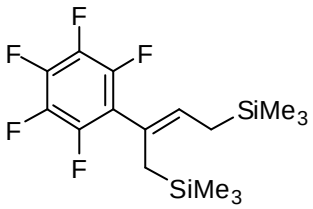


$CDCl_3$) δ 167.1 (d, J_F = 258.8 Hz), 157.0 (ddd, J_F = 242.2, 18.5, 12.3 Hz), 135.5, 126.6, 112.1 (dd, J_F = 22.3, 18.5 Hz), 32.5, 30.2, 22.6, 21.6, 13.9 (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ 71.5 (d, J_F = 17.2 Hz, 2F), –97.7 (t, J_F = 18.0 Hz, 1F). IR (neat) 2948, 2926, 2855, 1585, 1458, 1423, 1377, 1045. MS (EI, 70 eV) *m/z* (%) 353 (M^+, 21), 311 (22), 310 (100), 282 (17), 268 (18), 256 (14), 149 (13), 55 (10). Anal. Calcd for $C_{21}H_{30}F_3N$: C, 71.36; H, 8.55. Found: C, 71.62; H, 8.77.

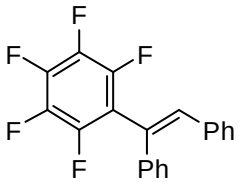
(*E*)-3,5-Difluoro-4-(oct-4-en-4-yl)pyridine (3sa). A yellow oil, R_f 0.20 (hexane–ethyl acetate = 19:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 2H), 5.57 (t, *J* = 7.3 Hz, 1H), 2.40 (t, *J* = 7.6 Hz, 2H), 2.22 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.5 Hz, 2H), 1.29 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7 (dd, J_F = 247.7, 3.4 Hz), 135.9, 133.9 (dd, J_F = 29.9, 6.1 Hz), 128.2 (t, J_F = 17.2 Hz), 126.6, 32.1, 30.2, 22.6, 21.5, 13.84, 13.79; ^{19}F NMR (282 MHz, $CDCl_3$) δ –129.1 (s, 2F). IR (neat) 2924, 2855, 1461, 1420, 1377, 1283, 1258, 1225, 1026, 874. MS (EI, 70 eV) *m/z* (%) 226 (M^++1, 12), 225 (M^+, 79), 196 (15), 184 (10), 183 (67), 182 (100), 168 (46), 167 (11), 166 (17), 155 (95), 154 (90), 153 (28), 142 (59), 141 (36), 134 (23), 128 (48), 127 (71), 120 (11), 55 (54). Anal. Calcd for $C_{13}H_{17}F_2N$: C, 69.31; H, 7.61. Found: C, 69.46; H, 7.58.



(*E*)-[1,4-Bis(trimethylsilyl)but-2-en-2-yl]pentafluorobenzene (3ab). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (t, *J* = 8.6 Hz, 1H), 1.84 (s, 2H), 1.61 (d, *J* = 8.6 Hz, 2H), 0.06 (s, 9H), –0.08 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (dm, J_F = 244.9 Hz), 139.3 (dm, J_F = 252.6 Hz), 137.3 (dm, J_F = 252.6 Hz), 129.9, 120.4, 120.3–118.7 (m), 21.8, 20.2, –1.2, –1.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ –142.6 (dd, J_F = 23.3, 6.2 Hz, 2F), –159.3 (t, J_F = 21.6 Hz, 1F), –164.3 (td, J_F = 22.5, 7.2 Hz, 2F). IR (neat) 2963, 2860, 1518, 1489, 1468, 1420, 1377, 1315, 1250, 1144, 1121, 1063, 988, 876, 858, 694. MS (EI, 70 eV) *m/z* (%) 366 (M^+, 100), 263 (16), 259 (11), 200 (16), 183 (30), 182 (81), 177 (18), 163 (32), 151 (11), 143 (12), 102 (12), 81 (13), 77 (79), 75 (56), 74 (82), 73 (98), 72 (23), 59 (16), 58 (12). HRMS (EI) Calcd for $C_{16}H_{23}F_5Si_2$: M^+, 366.1258. Found: 366.1240.

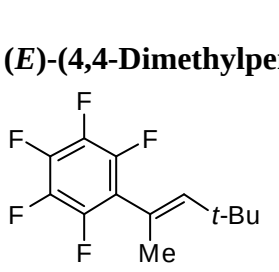


(*E*)-(1,2-Diphenylethenyl)pentafluorobenzene (3ac).[32] A yellow oil, R_f 0.60 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.15 (m, 8H), 7.14–7.08 (m, 2H), 6.76 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4 (dm, J_F = 247.2 Hz), 140.7 (dm, J_F = 254.1 Hz), 138.0, 137.4 (dm, J_F = 253.4 Hz), 135.4, 135.3, 129.4, 128.9, 128.6, 128.0, 128.88, 128.82,



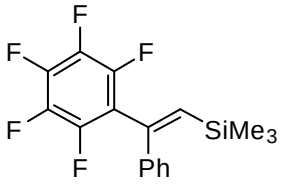
127.3, 127.4, 118.7–118.0 (m) (2C); ^{19}F NMR (282 MHz, $CDCl_3$) δ –141.5 (dd, J_F = 22.0, 8.2 Hz, 2F), –156.2 (t, J_F = 20.6 Hz, 1F), –162.7 (td, J = 22.0, 7.2 Hz, 2F). IR (neat) 3061, 3042, 3023, 1653, 1520, 1495, 1445, 1427, 1119, 1076, 1030, 983, 921, 880, 864, 795, 750, 735, 704, 561, 542. MS (EI, 70 eV) *m/z* (%) 347 (M^++1, 27), 346 (M^+, 100), 331 (26), 325 (17), 324 (13), 306 (10), 179 (16), 178 (12). HRMS (EI) Calcd for $C_{20}H_{11}F_5$: M^+, 346.0781. Found: 346.0781.

(*E*)-(4,4-Dimethylpent-2-en-2-yl)pentafluorobenzene (3ad). A yellow oil, R_f 0.60 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52–5.49 (m, 1H), 2.05–2.02 (m, 3H), 1.22 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.1, 143.8 (dm, J_F = 247.7 Hz), 139.5 (dm, J_F = 252.6 Hz), 137.3 (dm, J_F = 250.3 Hz), 120.9–120.4 (m), 120.0, 33.5, 30.6, 18.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ –143.7 (dd, J_F = 22.7, 8.2 Hz, 2F), –158.7 (t, J_F = 20.6 Hz, 1F), –163.6 (td, J = 22.0, 7.5 Hz, 2F). IR (neat) 2963, 2872, 1651, 1520, 1487, 1385, 1366, 1314, 1163, 1076, 1038, 1017, 984, 943, 872, 845, 665. MS (EI, 70 eV) *m/z* (%) 264 (M^+, 67), 250 (21), 249 (100), 221 (13), 207 (28), 195 (69), 187 (12), 181 (44). HRMS (EI) Calcd for $C_{13}H_{13}F_5$: M^+, 264.0937. Found: 264.0928.

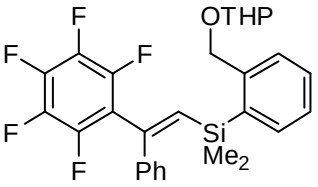


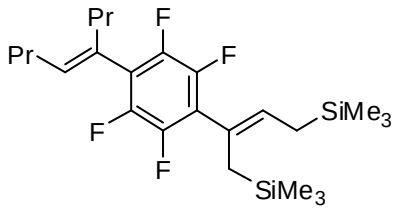
(*E*)-[1-(Trimethylsilyl)propen-2-yl]pentafluoro benzene (3ae). A green oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (s, 1H), 2.11 (s, 3H), 0.22 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2 (dm, J_F = 249.6 Hz), 139.6 (dm, J_F = 252.6 Hz), 137.8, 137.4, 137.3 (dm, J_F = 253.3 Hz), 121.8–121.1 (m), 22.4, –0.17; ^{19}F NMR (282 MHz, $CDCl_3$) δ –143.4 (dd, J_F = 24.3, 6.8 Hz, 2F), –158.1 (t, J_F = 20.6 Hz, 1F), –163.3 (td, J_F = 23.0, 6.9 Hz, 2F). IR (neat) 2959, 1651, 1607, 1591, 1520, 1495, 1443, 1250, 1119, 1072, 1036, 988, 885, 866, 839, 762, 700. MS (EI, 70 eV) *m/z* (%) 280 (M^+, 6), 267 (23), 266 (67), 265 (100), 225 (47), 187 (20), 183 (45), 182 (13), 181 (11), 170 (33), 169 (82), 165 (39), 164 (59), 163 (13), 159 (16), 151 (11), 149 (16), 145 (18), 143 (19), 133 (22), 125 (48), 119 (15), 99 (12), 81 (28), 78 (17), 77 (81), 75 (14), 73 (61), 59 (25). HRMS (EI) Calcd for $C_{12}H_{13}F_5Si$: M^+, 265.0472. Found: 265.0472 ($M^+ - CH_3$).

(*E*)-[2-Phenyl-1-(trimethylsilyl)ethen-2-yl]pentafluoro benzene (3af). A yellow oil, R_f 0.50 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.29 (m, 3H), 7.27–7.21 (m, 2H), 6.06 (s, 1H), 0.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 143.5 (dm, J_F = 246.4 Hz), 142.0, 140.8, 140.0 (dm, J_F = 258.8 Hz), 137.3 (dm, J_F = 250.9 Hz), 128.2, 127.99,



127.93, 119.9–119.5, –0.05; ^{19}F NMR (282 MHz, $CDCl_3$) δ –142.2 (dd, J_F = 22.7, 8.2 Hz, 2F), –157 (t, J_F = 20.6 Hz, 1F), –163.1 (td, J = 21.9, 8.2 Hz, 2F). IR (neat) 2959, 1593, 1520, 1495, 1250, 1175, 990, 945, 864, 843, 758, 700. MS (EI, 70 eV) *m/z* (%) 343 (M^++1, 21), 342 (M^+, 84), 328 (26), 327 (100), 309 (11), 250 (25), 231 (14), 230 (12), 225 (13), 135 (15), 77 (14), 73 (21). Anal. Calcd for $C_{17}H_{15}F_5Si$: C, 59.64; H, 4.42. Found: C, 59.49; H, 4.37.

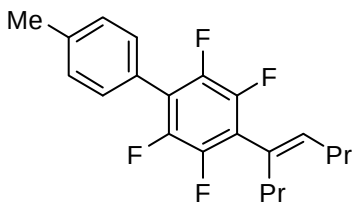
(*E*)-Dimethyl(2-(pentafluorophenyl)-2-phenylethenyl)[2-((tetrahydro-2*H*-pyran-2-yloxy)methyl)phenyl]silane (3ag).  A yellow oil, R_f 0.30 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.5 Hz, 1H), 7.42 (dd, J = 7.5, 1.0 Hz, 1H), 7.38 (td, J = 7.5, 1.3 Hz, 1H), 7.26–7.18 (m, 2H), 7.15 (t, J = 7.5 Hz, 2H), 7.08 (d, J = 7.1 Hz, 2H), 6.28 (s, 1H), 4.84 (d, J = 12.1 Hz, 1H), 4.69 (t, J = 3.5 Hz, 1H), 4.57 (d, J = 12.3 Hz, 1H), 3.90 (ddd, J = 11.3, 8.4, 2.9 Hz, 1H), 3.53 (ddd, J = 10.9, 4.7, 4.1 Hz, 1H), 1.91–1.46 (m, 6H), 0.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5 (dm, J_F = 248.0 Hz), 143.4, 142.9, 140.05, 139.99 (dm, J_F = 258.6 Hz), 139.4, 137.3 (dm, J_F = 253.4 Hz), 136.7, 134.4, 129.4, 128.1, 128.0, 127.8, 126.8, 119.5 (t, J_F = 17.2 Hz), 109.7, 97.9, 68.9, 62.1, 30.7, 25.6, 19.5, –0.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ –142.0 (d, J_F = 24.6 Hz, 2F), –156.7 (d, J_F = 24.6 Hz, 1F), –162.8 (t, J_F = 24.4 Hz, 2F). IR (neat) 3057, 2926, 2856, 1647, 1589, 1518, 1493, 1340, 1260, 1250, 1182, 1119, 1078, 1069, 1032, 907, 871, 851, 833, 816, 775, 749, 735, 700. MS (EI, 70 eV) *m/z* (%) 417 (M^+–OTHP, 11), 281 (10), 270 (11), 260 (11), 245 (16), 237 (14), 219 (11), 165 (18), 164 (19), 163 (29), 149 (44), 147 (11), 135 (10), 105 (17), 91 (24), 85 (100), 75 (10), 71 (11), 57 (43), 55 (14). Anal. Calcd for $C_{28}H_{27}F_5O_2Si$: C, 64.85; H, 5.25. Found: C, 64.95; H, 5.27.

(*E*)-6-(Oct-4-en-4-yl)-(*E*)-3-[1,4-bis(trimethylsilyl)but-2-en-2-yl]-1,2,4,5-tetrafluorobenzene (13).  A yellow oil, R_f 0.60 (hexane only). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (t, J = 7.5 Hz, 1H), 5.46 (t, J = 8.8 Hz, 1H), 2.38 (t, J = 7.5 Hz, 2H), 2.22 (q, J = 7.3 Hz, 2H), 1.87 (s, 2H), 1.61 (d, J = 8.6 Hz, 2H), 1.48 (sext, J = 7.3 Hz, 2H), 1.29 (sext, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H), 0.07 (s, 9H), –0.08 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (dm, J_F = 241.8 Hz, 2C), 135.4, 129.0, 127.4, 122.8 (t, J_F = 18.9 Hz), 121.7, 120.7 (t, J_F = 18.5 Hz), 32.6, 30.3, 22.7, 21.7, 21.5, 20.1, 13.9 x 2, –1.2, –1.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ –143.7 (dd, J_F = 26.6, 10.6 Hz, 2F),

–144.4 (dd, J_F = 24.0, 13.3 Hz, 2F). IR (neat) 2959, 2936, 2901, 2874, 1715, 1695, 1647, 1636, 1468, 1456, 1306, 1249, 1161, 1144, 1063, 974, 939, 895, 842, 758, 694. MS (EI, 70 eV) *m/z* (%) 459 (M^++1, 51), 458 (M^++1, 100), 328 (17), 327 (63), 299 (17), 274 (19), 273 (73), 245 (40), 231 (20), 217 (19), 203 (20), 183 (13), 178 (14), 177 (18), 77 (22), 75 (16), 74 (37), 73 (91). HRMS (EI) Calcd for $C_{24}H_{38}F_4Si_2$: M^+, 458.2448. Found: 458.2432.

KIE Experiment. In a glove box, a solution of $Ni(cod)_2$ (1.7 mg, 6.0 μmol) and $PCyp_3$ (1.4 mg, 6.0 μmol) in toluene (0.6 mL) were added to a solution of **1p** (36 mg, 0.20 mmol) placed in a 3 mL-vial. In another vial were placed the same catalyst and **1o**-d_1 in equimolar amount. To each vial were added 4-octyne (22.0 mg, 0.2 mmol) and dodecane (internal standard, 17.0 mg, 0.10 mmol). Each vial was closed with a screw cap, and heated at 30 °C. Aliquots of the reaction mixture were taken from each vial and analyzed by GC to monitor the reactions. The set of experiments was repeated twice and the average yields for the three sets were calculated and plotted in Figure 1.

Palladium-catalyzed arylation of 3da with 4-iodotoluene. $Pd(OAc)_2$ (6.0 mg, 25 μmol), K_2CO_3 (76 mg, 0.55 mmol) and 4-iodotoluene (109 mg, 0.5 mmol) were measured into a 3.0 mL-vial. The vial was purged three times with argon and put into a glove box. DMA (1.0 mL), P(*t*-Bu)$_2$Me (6.0 mg, 50 μmol), **3da** (130 mg, 0.5 mmol) and undecane (internal standard, 78 mg, 0.5 mmol) were added. The vial was closed with a screw cap, taken out from the glove box and heated at 120 ºC for 120 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give **4'-methyl-(*E*)-4-(oct-4-en-4-yl)-2,3,5,6-tetrafluorobiphenyl** (**14**, 120 mg, 0.33 mmol, 66%) as a colorless solid, mp 55.6–56.2 ºC, R_f 0.35 (ethyl acetate–hexane = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 5.58 (t, J = 7.3 Hz, 1H), 2.43 (s, 3H), 2.42 (t, J = 7.5 Hz, 2H), 2.25 (q, J = 7.3 Hz, 2H), 1.50 (sext, J = 7.4 Hz, 2H), 1.37 (sext, J = 7.5 Hz, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (dm, J_F = 241.8 Hz), 143.6 (dm, J_F = 248.0 Hz), 138.8, 135.7, 129.8, 129.1, 127.4, 124.6, 121.9 (t, J_F = 19.3 Hz), 118.4 (t, J_F = 16.5 Hz), 32.7, 30.3, 22.7, 21.6, 21.4, 13.9, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ –143.6 (dd, J_F = 49.9, 13.7 Hz, 2F), –145.8 (dd, J_F = 24.8, 13.8 Hz, 2F). IR (KBr) 3038, 3024, 2957, 2930, 2870, 2837, 1522, 1474, 1460, 1402, 1381, 1370, 1308, 1188, 1146, 1113, 1081, 1067, 1025, 970,



945, 905, 849, 818, 789, 766, 746, 712, 681, 583, 513. MS (EI, 70 eV) *m/z* (%) 351 (M^++1, 27), 350 (M^+, 85), 308 (48), 307 (100), 293 (16), 281 (11), 280 (56), 279 (48), 267 (12), 265 (14), 264 (16), 254 (17), 253 (76). Anal. Calcd for $C_{21}H_{22}F_4$: C, 71.98; H, 6.33. Found: C, 72.32; H, 6.52.

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Chapter 3

Hydroheteroarylation of Alkynes with Five-membered Heterocycles

Nitrogen-containing five-membered heterocycles are found to add across alkynes in the presence of a nickel/tri(*sec*-alkyl)phosphine catalyst. The addition reaction can also be achieved by a simple and convenient protocol using air-stable and commercially available $Ni(acac)_2$ and $[HPCyp_3]BF_4$ as catalyst precursors. Furthermore, nickel/Lewis acid binary catalysis is found effective to direct regioselective C(2)- and C(5)-alkenylation of imidazoles. The nickel catalysis is applicable to a diverse range of heterocycles to furnish a broad scope of disubstituted heteroarylethenes stereoselectively in modest to excellent yields. Excellent regioselectivity is observed with unsymmetrical alkynes to give the corresponding heteroaryl-substituted ethenes having a bulkier substituent *trans* to an heteroaryl group.

Introduction

Nitrogen-containing five-membered heterocycles such as indoles and imidazoles are recurring structural units in a vast number of natural products and biologically active compounds.[1] Accordingly, development of efficient methods for their rapid and concise synthesis and functionalization is of considerable importance in organic synthesis.[2] Transition metal-catalyzed C–H bond activation has emerged as a powerful and environmentally-friendly method for direct functionalization of heteroarenes, because it overcomes several limitations of classical and traditional cross-coupling reactions such as the need to prefunctionalize starting materials.[3] In contrast to much more developed direct C–H arylation reactions,[3] direct alkenylation of indoles[4] and imidazoles have received less attention. Only a few protocols which couple the heteroarenes with activated olefins through oxidative C–H alkenylation has been reported.[5]

A transition metal-catalyzed hydroheteroarylation of alkynes with five-membered heterocycles should be an attractive and atom-efficient method for preparation of variously substituted alkenylated heteroarenes.[6] As discussed in Chapter 2, a nickel catalyst is effective for activation of C–H bonds of fluoroarenes followed by direct insertion of alkynes to furnish disubstituted fluoroarylethenes in a single operation.[7] Since C–H bonds positioned *ortho* to heteroatoms in five-membered heteroaromatic compounds are known to be relatively acidic,[8] the author postulated that their activation followed by insertion of alkynes could be effected by a nickel catalyst.

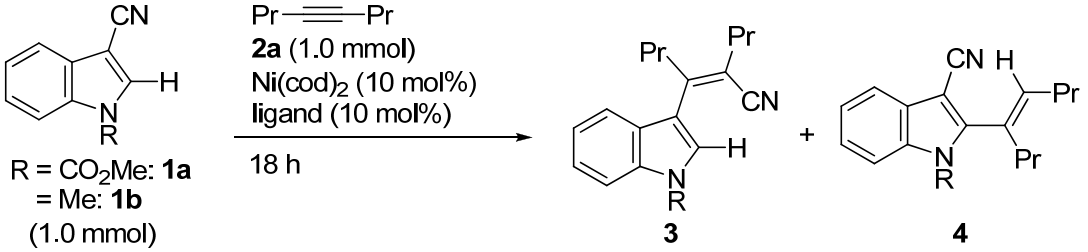
Described in this Chapter is nickel(0)/$PCyp_3$-catalyzed direct alkenylation of electron-deficient 5-membered heterocycles including such fused ones as indoles substituted with an electron-withdrawing group at the C-3 position, benzimidazole, benzofuran, benzothiophene, purine, and caffeine.[9] The addition reaction can also be achieved by a catalyst prepared from air-stable and commercially available $Ni(acac)_2$ and $[HPCyp_3]BF_4$ as catalyst precursors by reduction and deprotonation with $AlMe_3$.[10] Direct regioselective C(2)- and C(5)-alkenylation of imidazoles by nickel(0)/Lewis acid (LA) binary catalysis is also demonstrated.[11] The catalysis is applicable to a diverse range of heteroarenes (hetAr–H) to furnish a broad scope of disubstituted heteroarylethenes stereoselectively in modest to excellent yields. Excellent regioselectivity is observed with unsymmetrical alkynes to give the corresponding heteroaryl-substituted ethenes having a bulkier substituent *trans* to heteroaryl group.

Results and discussion

Nickel-catalyzed hydroheteroarylation of alkynes

At the onset, the author examined the reaction of methyl 3-cyano-1*H*-indole-1-carboxylate (**1a**, 1.0 mmol) with 4-octyne (**2a**, 1.0 mmol) in the presence of $Ni(cod)_2$ (10 mol%) and PMe_3 (10 mol%) in toluene at 100 ºC for 18 h to obtain methyl 3-(5-cyanooct-4-en-4-yl)-1*H*-indole-1-carboxylate (**3aa**) and methyl 3-cyano-2-(oct-4-en-4-yl)-1*H*-indole-1-carboxylate (**4aa**) in 68% and 6% yields, respectively, after purification by flash column chromatography on silica gel (entry 1 of Table 1). Heteroarylcyanation product **3aa** is clearly derived from insertion of **2a** into the hetAr–CN bond at the C-3 position of **1a**,[12] whereas the formation of hydroheteroarylation product **4aa** can be ascribed to insertion of **2a** into the hetAr–H bond at the C-2 position. The stereochemistry of **3aa** and **4aa** was unambiguously assigned by nOe experiments. Next, the author optimized reaction conditions to improve the yield and selectivity of **4aa**. An identical reaction run with $PCyp_3$ as a ligand instead of PMe_3 gave **4aa** in 16% yield together with 3% of **3aa**, the activation of the hetAr–CN bond being preceded by that of the hetAr–H bond (entry 2). With 1-methyl-1*H*-indole-3-carbonitrile (**1b**), the corresponding hydroheteroarylation product **4ba** became dominant even under the nickel(0)/PMe_3 catalysis (entry 3), and the catalysis was found effective even at 35 ºC using $PCyp_3$ as a ligand to afford **4ba** in 95% yield (entry 4). It is worth noting that the bond to be activated is controllable by choosing a ligand and/or an *N*-protecting group to induce a different catalysis of nickel.[13] Other bulky tri(*sec*-alkyl)phosphines such as PCy_3 and $P(i\text{-Pr})_3$ also gave comparable results (>90% yield estimated by GC, entries 5 and 6), whereas $P(t\text{-Bu})_3$ and PPh_3 were found completely ineffective for the hydroheteroarylation reaction (entries 7 and 8). Bulky electron-rich carbene ligands were also effective to give **4ba** in moderate to high yields (entries 9 and 10). Other solvents such as hexane, 1,4-dioxane, ethyl acetate and DMF were also effective to give **4ba** in moderate to high yields (entries 11–14). Use of 1 mol% of the catalyst still worked well to give **4ba** in 88% isolated yield, although the reaction took 96 h for completion (entry 15).

Table 1. Nickel-catalyzed hydroheteroarylation of 4-octyne (**2a**).[a]



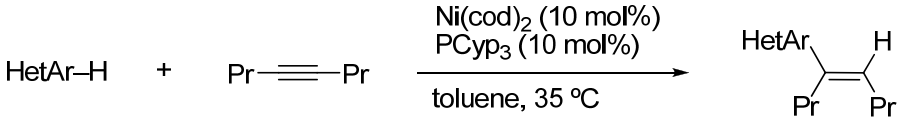
Entry	**1**	Ligand	Solvent	Temp. (ºC)	Yield of **3** (%)[b]	Yield of **4** (%)[b]
1	**1a**	PMe_3	toluene	100	68[c]	6[c]
2	**1a**	$PCyp_3$	toluene	100	3[c]	16[c]
3	**1b**	PMe_3	toluene	100	<3	35[c]
4	**1b**	$PCyp_3$	toluene	35	<3	95[c]
5	**1b**	PCy_3	toluene	35	<3	91
6	**1b**	P(*i*-Pr)$_3$	toluene	35	<3	>95
7	**1b**	P(*t*-Bu)$_3$	toluene	35	<3	<3
8	**1b**	PPh_3	toluene	35	<3	<3
9[d]	**1b**	IPr	toluene	35	<3	61
10[e]	**1b**	IMes	toluene	35	<3	88
11	**1b**	$PCyp_3$	hexane	35	<3	59
12	**1b**	$PCyp_3$	1,4-dioxane	35	<3	>95
13	**1b**	$PCyp_3$	AcOEt	35	<3	>95
14	**1b**	$PCyp_3$	DMF	35	<3	94
15[f]	**1b**	$PCyp_3$	toluene	35	<3	88[c]

[a] All the reaction was carried out using **1** (1.00 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.10 mmol), and ligand (0.10 mmol) in a solvent (2.5 mL) for 18 h. [b] Estimated by GC using undecane as an internal standard. [c] Isolated yield based on **1**. [d] IPr = 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene. [e] IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene. [f] Run with $Ni(cod)_2$ (1 mol%) and $PCyp_3$ (1 mol%) for 96 h.

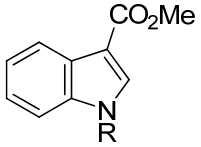
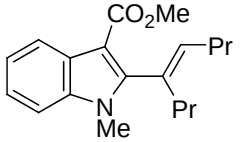
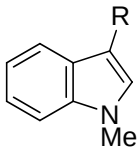
With the optimized conditions in hand, the author next examined scope of the reaction (Table 2). Methyl 1*H*-indole-3-carboxylates bearing methyl, benzyl and methoxymethyl groups (**1c**–**1e**) reacted with an equimolar amount of **2a** in modest to good yields, irrespective of the kind of *N*-substituents (entries 1–3). Indoles having an electron-withdrawing functional group at the C-3 position (**1f**–**1i**) all gave the corresponding *cis*-hydroheteroarylation products in modest to high yields at 35 ºC (entries 4–7), whereas elevation of temperature was required for

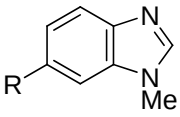
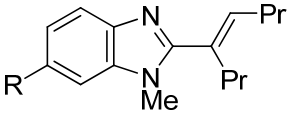
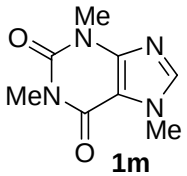
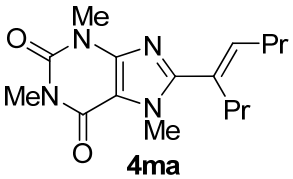
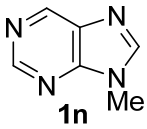
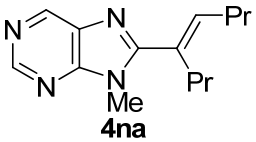
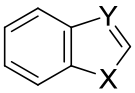
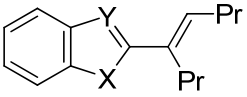
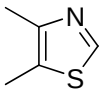
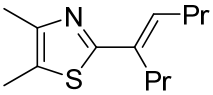
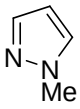
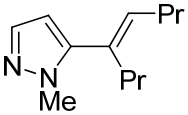
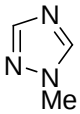
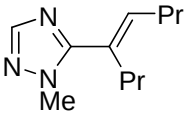
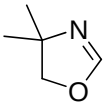
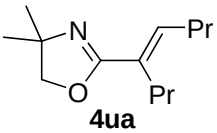
1-methyl-3-phenyl-1*H*-indole (**1j**) to achieve satisfactory yield (entry 8). The exclusive reaction of the hetAr–H bond over the formyl C–H bond of **1g** is remarkable, because the latter may also be activated to undergo addition across an alkyne under nickel(0)/P(*n*-Bu)$_3$ catalysis.[14] The reaction of **2a** with substituted benzimidazoles (**1k**–**1l**) occurred exclusively at the C-2 position even in the presence of a reactive hetAr–Cl bond (entries 9 and 10). Caffeine (**1m**) and 9-methyl-9*H*-purine (**1n**), which are prevalent in various bioactive compounds, also added across **2a** smoothly at their C-2 position over other acidic C–H bonds (entries 11 and 12). The reactions of **2a** with benzofuran (**1o**), benzothiophene (**1p**) and benzoxazole (**1q**) also proceeded smoothly (entries 13–15). Other heterocycles such as 4,5-dimethylthiazole (**1r**), 1-methyl-1*H*-pyrazole (**1s**), 1-methyl-1*H*-1,2,4-triazole (**1t**) and 4,4-dimethyl-4,5-dihydrooxazole (**1u**) participated in the reaction to give the corresponding products in good to high yields.

Table 2. Nickel-catalyzed hydroheteroarylation of 4-octyne (**2a**).[a]



1 (1.0 mmol) **2a** (1.0 mmol) **4**

Entry	HetAr–H (**1**)	Time (h)	Product	Yield (%)[b]
				
1	R = Me (**1c**)	15	R = Me (**4ca**)	85
2	CH_2Ph (**1d**)	15	CH_2Ph (**4da**)	57
3[c]	CH_2OMe (**1e**)	120	CH_2OMe (**4ea**)	84
				
4	R = C(O)Me (**1f**)	30	R = C(O)Me (**4fa**)	70
5	CHO (**1g**)	6	CHO (**4ga**)	91
6	(*E*)-CH=CHCO_2Me (**1h**)	10	(*E*)-CH=CHCO_2Me (**4ha**)	88
7	CH=NS(O)*t*-Bu (**1i**)[d]	10	CH=NS(O)*t*-Bu (**4ia**)	41

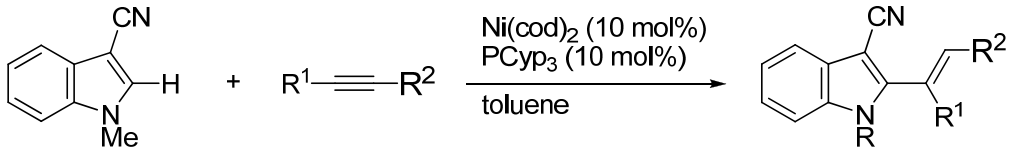
8	Ph (**1j**)	35	Ph (**4ja**)	67
				
9	R = H (**1k**)	12	R = H (**4ka**)	92
10	Cl (**1l**)	10	Cl (**4la**)	80
11	 **1m**	10	 **4ma**	94
12	 **1n**	6	 **4na**	94
				
13	X, Y = O, CH (**1o**)	6	X, Y = O, CH (**4oa**)	94
14	S, CH (**1p**)	24	S, CH (**4pa**)	47
15	O, N (**1q**)	8	O, N (**4qa**)	89
15	 **1r**	15	 **4ra**	89
16	 **1s**	17	 **4sa**	85
17	 **1t**	24	 **4ta**	93
18	 **1u**	15	 **4ua**	79

[a] All the reaction was carried out using **1** (1.00 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.10 mmol), and $PCyp_3$ (0.10 mmol) in toluene (2.5 mL) at 35 ºC. [b] Isolated yield based on **1**. [c] Run at 50 ºC using 4.0 mmol of **2a**. [d] (*R*)-enantiomer was used as starting material.

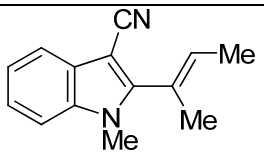
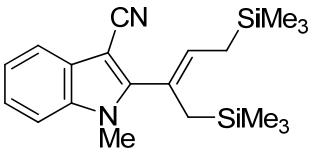
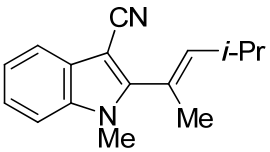
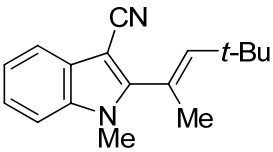
The author next turned his attention to examine the scope of alkynes using **1b** as a heteroarene substrate (Table 3). The addition reaction of **1b** across 2-butyne (**2b**) proceeded to give the corresponding product **4bb** in a low yield, due possibly to fast

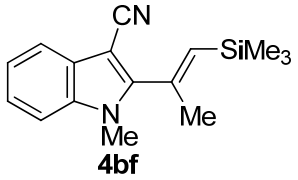
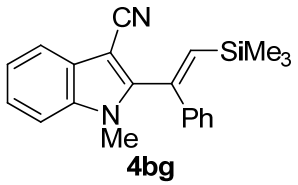
competitive tri- and oligomerization of the alkyne (entry 1). Bis(silylmethyl)-substituted acetylene **2c** participated in the reaction to give the corresponding *cis*-adduct **4bc,** which has allylsilane substructures in 62% yield. Unsymmetrical internal alkynes, 4-methyl-2-pentyne (**2d**) and 4,4-dimethyl-2-pentyne (**2e**), reacted with **1b** in excellent regioselectivity to give the corresponding adducts having a larger substituent *trans* to the indolyl group in high yields (entries 3 and 4). Sterically biased unsymmetrical silylacetylenes **2f** and **2g** participated in the reaction to afford the corresponding adducts regio- and stereoselectively in high yields, although elevated temperatures were required (entries 5 and 6).

Table 3. Nickel-catalyzed hydroheteroarylation of alkynes with **1b**.[a]



1b (1.0 mmol) **2** (1.0 mmol) **4**

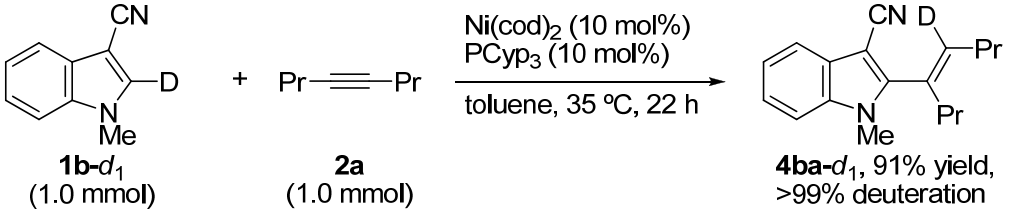
Entry	R^1, R^2 in **2**	Temp. (ºC)	Time (h)	Product	Yield (%)
1	Me, Me (**2b**)	35	15	 **4bb**	32
2	CH_2SiMe_3, CH_2SiMe_3 (**2c**)	80	15	 **4bc**	62
3	Me, *i*-Pr (**2d**)	35	6	 **4bd**	97
4	Me, *t*-Bu (**2e**)	35	10	 **4be**	81

5	Me, $SiMe_3$ (**2f**)	50	40	 **4bf**	74
6[c]	Ph, $SiMe_3$ (**2g**)	100	35	 **4bg**	67

[a] All the reaction was carried out using **1b** (1.00 mmol), **2** (1.00 mmol), $Ni(cod)_2$ (0.10 mmol), and $PCyp_3$ (0.10 mmol) in toluene (2.5 mL). [b] Isolated yield based on **1b**. [c] Run with 2.0 mmol of **2g**.

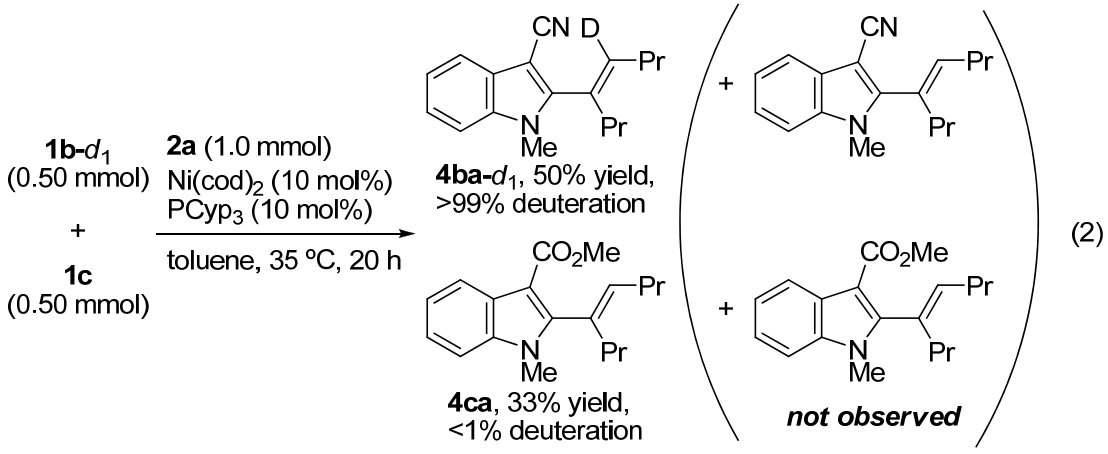
Insights into the reaction mechanism

In order to gain insights into the reaction mechanism, isotope-based experiments were carried out. First, the reaction of **1b**-d_1 with **2a** gave the corresponding deuterated adduct **4ba**-d_1 as a sole product in 91% yield with >99% deuteration (Eq. 1).



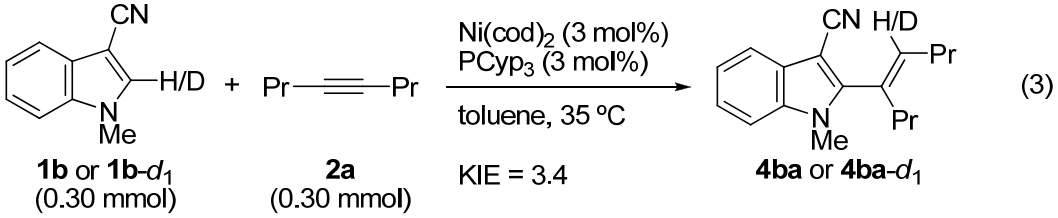
(1)

The reaction of an equimolar (0.50 mmol) mixture of **1b**-d_1 and **1c** with **2a** (1.0 mmol) under the identical reaction conditions did not cause any intermolecular hydrogen–deuterium crossover: only **4ba**-d_1 and **4ca** were obtained (Eq. 2). These observations support a mechanism in which the activated/cleaved hydride is attached to the nickel complex throughout the catalytic cycle.



(2)

Finally, a kinetic isotope effect (KIE) was determined by comparing the initial rate of the reaction of **1b** or **1b**-d_1 with **2a** (Eq. 3). The estimated average KIE value of three sets of experiments was 3.4, indicating that oxidative addition of the hetAr–H bond to nickel(0) or hydronickelation is likely to be the rate-determining step.



(3)

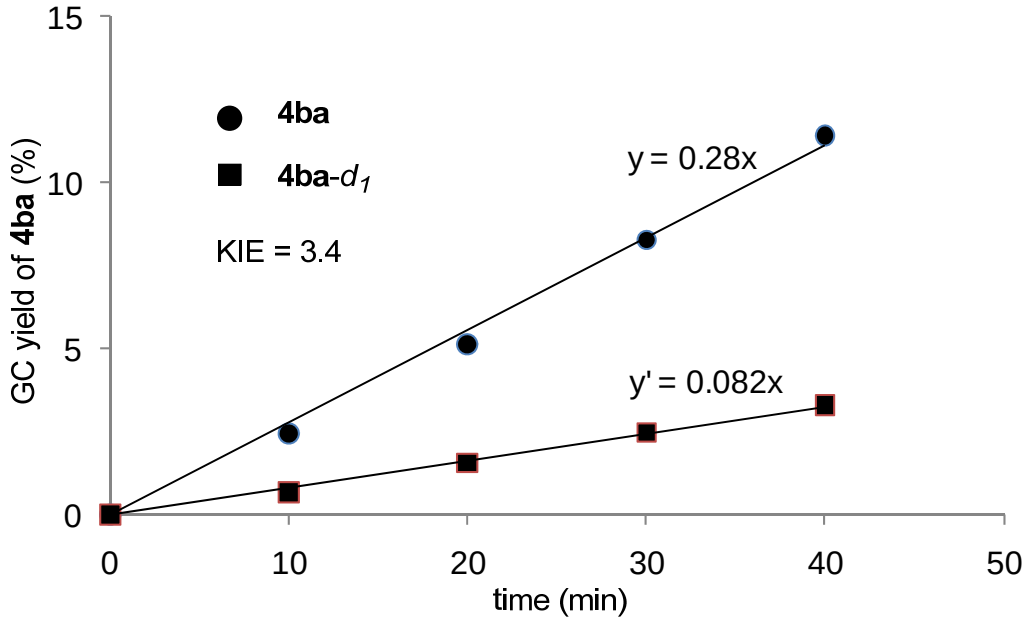
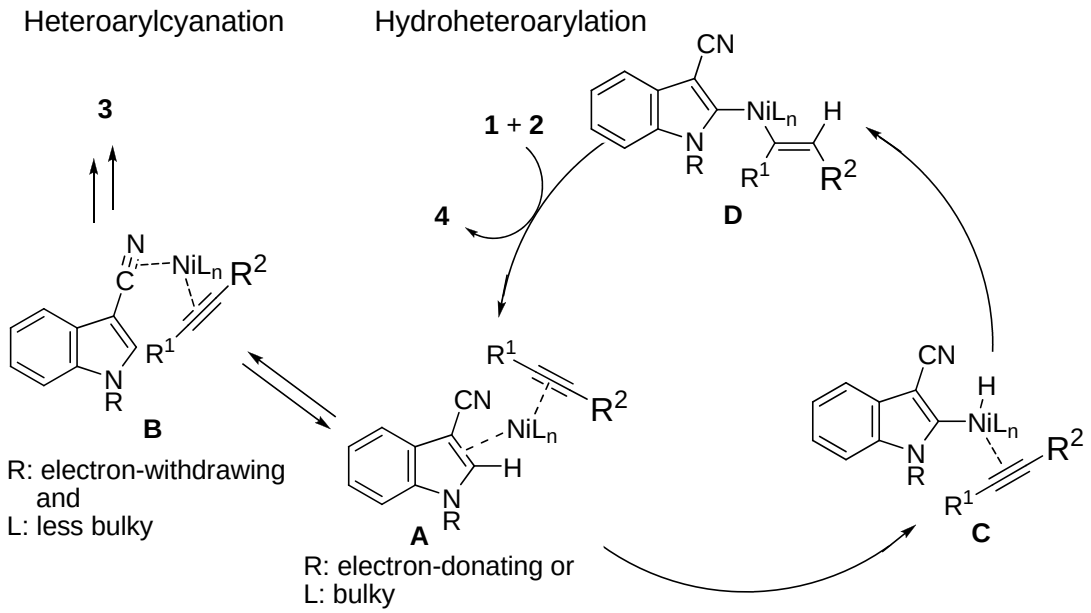


Figure 1. Estimation of KIE for hydroarylation of 5-membered heterocycles.

Based on these observations, a catalytic cycle may be initiated by η^2-coordination of heteroarene **1** and alkyne **2** to nickel(0) to form complex **A**,[15] which would be in equilibrium with cyano- and alkyne-coodinating nickel(0) species **B**. Subsequent oxidative addition of the hetAr–H bond at the C-2 position to nickel(0) gives hetAr–Ni(II)–H intermediate **C,**[16] wherein the alkyne coordinates to the nickel center in a direction that avoids steric repulsion between the nickel-center and R^2. Hydronickelation across **2** gives hetAr–Ni(II)–alkenyl intermediate **D**, which upon reductive elimination gives *cis*-hydroheteroarylation product **4** and regenerates the active nickel(0) species. On the other hand, oxidative addition of the hetAr–CN bond in

B followed by heteroarylnickelation across **2** and reductive elimination results in heteroarylcyanation product **3**.[12,17] A bulky tri(*sec*-alkyl)phosphine ligand would retard η^2-coordination of a cyano group in **1a** or **1b** and/or oxidative addition of the hetAr–CN bond because of steric hindrance. In addition, an electron-donating *N*-substituent would increase π-electron density on the heteroaromatic ring and thus prefer the η^2-coordination of **1** to nickel(0) species, whereas an electron-withdrawing group at C-3 position raises acidity of the C(2)–H bond to facilitate oxidative addition to nickel(0). A mechanism proposed for the Friedel-Crafts alkenylation[18] may not be operative since the reaction proceeds best with relatively electron-deficient heteroarenes and requires electron-rich nickel(0) species, which is likely effective for activation of a rather acidic C–H bond adjacent to a heteroatom. Furthermore, nickel(II) complexes, such as $Ni(acac)_2$ and $NiCl_2$, which might activate alkynes according to the Friedel-Crafts mechanism, failed to catalyze the reaction in the presence or absence of external bases, such as Et_3N and Cs_2CO_3.



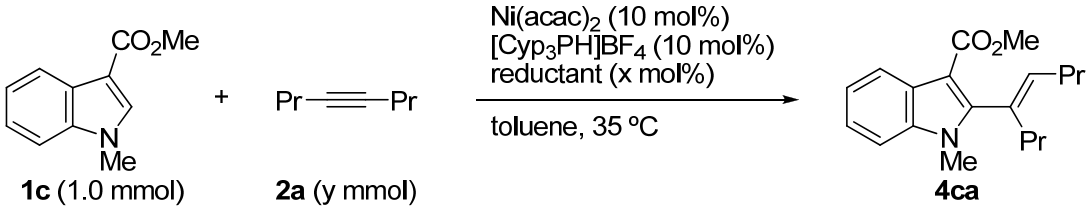
Scheme 1. Plausible reaction mechanism.

The air-sensitive nature of $Ni(cod)_2$ and tri(*sec*-alkyl)phosphine ligands makes the practical utility of this hydroheteroarylation reaction limited, because a glove box technique is required to set up the reaction. To raise the convenience and applicability of the present transformation, the author explored a protocol using an air-stable and readily

available nickel(II) complex to generate the active Nickel(0)/$PCyp_3$ catalyst *in situ*.[19]

Using methyl 1-methyl-1*H*-indole-3-carboxylate (**1c**) and 4-octyne (**2a**) as standard substrates, the author first screened a suitable organometallic reagent which acts as a reductant and a base at the same time to convert air-stable $Ni(acac)_2$ and $[HPCyp_3]BF_4$ to Nickel(0) and $PCyp_3$, respectively (Table 4).[10] Whereas the Louie's protocol,[20] namely a combination of $Ni(acac)_2$, $[HPCyp_3]BF_4$ and *n*-BuLi resulted in poor conversion of **1c** and poor yield of **4ca** (entry 1), use of $AlMe_3$ instead of *n*-BuLi led to considerably fair conversion of **1c**, and **4ca** was produced in 55% yield as estimated by GC (entry 2). Further optimization revealed that at least 1.5 equivalents of **2a** was necessary to achieve high conversion of **1c** (entry 3). Although the need of excess alkynes is not fully rationalized, it could stabilize a nickel(0) species produced *in situ*. Whereas a small excess of $AlMe_3$ was required to achieve sufficient conversion of **1c** (entry 4), the amount of DIBAL–H could be reduced to 30 mol% (entry 8). Importantly, this protocol works well with a standard Schlenck technique.

Table 4. Optimization of reductants for nickel-catalyzed hydroheteroarylation of **2a** with **1c**.

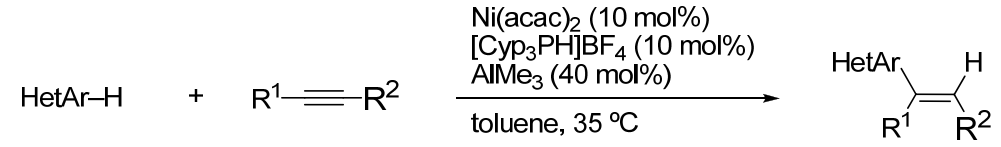


Entry	Reductant (x)	y	Time (h)	Conv. of **1c** (%)[a]	Yield of **4ca** (%)[a]
1	BuLi (40)	1.0	30	20	14
2	$AlMe_3$ (30)	1.0	30	70	55
3	$AlMe_3$ (30)	1.5	30	81	75
4	$AlMe_3$ (40)	1.5	12	91	92 (89)[b]
5	DIBAL–H (40)	1.0	30	60	64
6	DIBAL–H (40)	1.5	18	89	82
7	DIBAL–H (40)	2.0	18	94	89
8	DIBAL–H (30)	2.0	18	88	92 (91)[b]

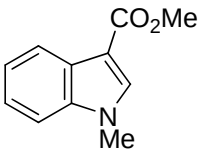
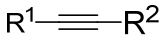
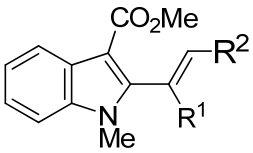
[a] Estimated by GC using $C_{12}H_{26}$ as an internal standard. [b] Isolated yields based on **1c**.

The nickel(0)/$PCyp_3$ catalyst prepared *in situ* was found equally effective for hydroheteroarylation of alkynes using a variety of heteroarenes (Table 5), compared with the results obtained with the $Ni(cod)_2$/$PCyp_3$ system (Table 2). Thus, heterocycles **1b**, **1f**, **1k**, **1o**, **1p**, **1s**, and **1u** all added across **2a** smoothly to give their respective adducts in excellent chemo- and stereoselectivities (entries 1–7). Scope of alkynes was briefly examined with **1c** as a heteroarene substrate. Unsymmetrical internal alkynes (**2d**, **2e** and **2g**) all reacted to give *cis*-adducts having a larger substituent *trans* to the heteroaryl group (entries 8–10) (*vide supra*).

Table 5. Hydroheteoarylation of alkynes with a nickel/$PCyp_3$ catalyst generated *in situ*.[a]



1 (1.0 mmol) **2** (1.5 mmol) **4**

Entry	HetAr–H	Alkyne	Time (h)	Product	Yield (%)[b]
1	**1b**	**2a**	12	**4ba**	84
2	**1f**	**2a**	12	**4fa**	84 (89)[c]
3	**1k**	**2a**	12	**4ka**	87
4	**1o**	**2a**	8	**4oa**	92
5	**1p**	**2a**	12	**4pa**	86
6	**1s**	**2a**	12	**4sa**	96
7	**1u**	**2a**	12	**4ua**	75
					
		R^1, R^2 =		R^1,R^2 =	
8	**1c**	Me, *i*-Pr: **2d**	14	Me, *i*-Pr: **4cd**	93
9	**1c**	Me, *t*-Bu: **2e**	18	Me, *t*-Bu: **4ce**	82
10[d]	**1c**	Ph, $SiMe_3$: **2g**	36	Ph, $SiMe_3$: **4cg**	85

[a] All the reaction was carried out using **1** (1.00 mmol), **2** (1.50 mmol), $Ni(acac)_2$ (10 mmol), and $[HPCy_3]BF_4$ (10 mmol), $AlMe_3$ (1.03 M solution in hexane, 0.40 mmol) in toluene (2.5 mL) at 35 ºC. [b] Isolated yield based on **1**. [c] DIBAL–H (30 mmol) and **2a** (2.0 mmol) were used. [d] Run with 3.0 mmol of **2g** at 100 ºC.

Nickel/Lewis acid-catalyzed hydroheteroarylation of alkynes with imidazoles

Encouraged by these results, the author envisaged the hydroheteroarylation reaction of alkynes might be applicable to imidazoles. Thus, 1-methyl-1*H*-imidazole (**5a**, 3.0 mmol) was reacted with **2a** (1.0 mmol) in the presence of $Ni(cod)_2$ (10 mol%) and $PCyp_3$ (10 mol%) at 100 ºC in toluene for 4 h, and (*E*)-1-methyl-2-oct-4-en-4-yl-1*H*-imidazole (**6aa**) and 2,5-dienylated imidazole (**6'aa**) were produced in 5% and 20% ^{1}H NMR yields, respectively (Table 6, entry 1). The stereochemistry of the products was unambiguously determined based on nOe experiments. The poor yields of the hydroheteroarylation adducts is attributable to competitive tri- and oligomerization of **2a** under the reaction conditions.

Since BF_3•OEt_2 has been reported to enhance the reactivity of C(2)–H bonds of azoles to undergo oxidative addition to nickel(0) in a stoichiometric manner through coordination of their sp^2-nitrogen to the LA,[21] the author considered that use of LA might generate such active imidazolium species *catalytically in situ* to allow the direct functionalization of the C(2)–H or C(5)–H bonds efficiently in a regioselective manner. Thus, when a similar reaction was performed in the presence of $Ni(cod)_2$ (3 mol%), $PCyp_3$ (12 mol%), and $AlMe_3$ (6 mol%) as a LA cocatalyst, **6aa** and **6'aa** were obtained in increased yields: 15% and 24% ^{1}H NMR yields, respectively (entry 2). Whereas P(*i*-Pr)$_3$ as a ligand resulted in almost the same combined yields but with poorer regioselectivity (entry 3), P(*t*-Bu)$_3$ dramatically improved the regioselectivity to afford C(2)-alkenylated adduct **6aa** exclusively in 70% yield after isolation by flash column chromatography on silica gel (entry 4). P(*n*-Bu)$_3$ and PPh_3 ligands were not effective (entries 5 and 6). $ZnMe_2$ was also found effective for the C(2)-alkenylation to a less extent compared to $AlMe_3$ (entry 7).

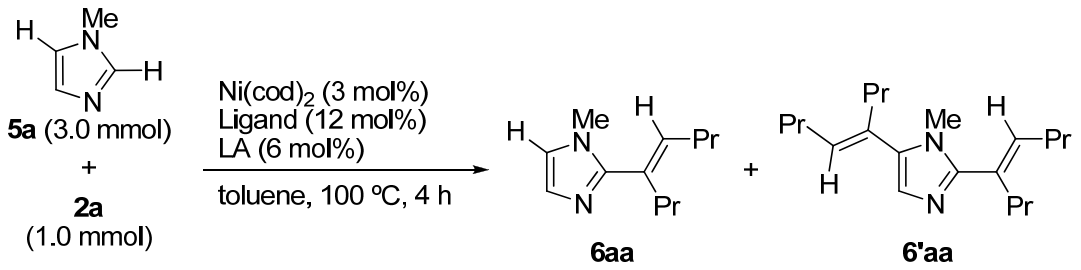


Table 6. Optimization of reaction conditions for C(2)-alkenylation of imidazoles.[a]

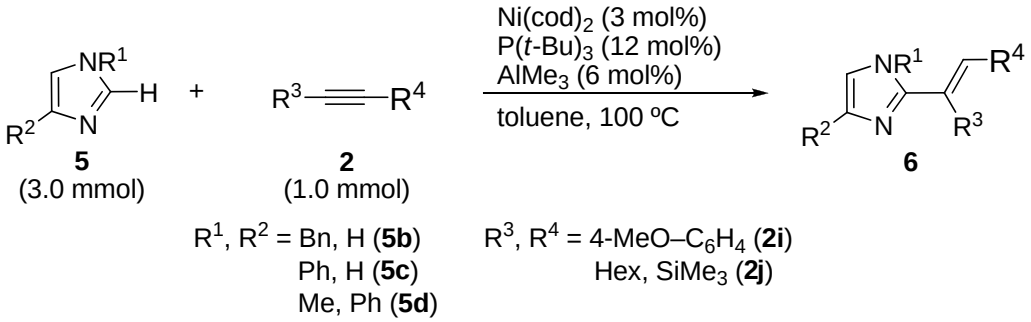
Entry	Ligand	LA	Yield of **6aa** (%)[b]	Yield of **6'aa** (%)[b]
1[c]	$PCyp_3$	none	5	20
2	$PCyp_3$	$AlMe_3$	15	24
3	P(*i*-Pr)$_3$	$AlMe_3$	16	16
4	P(*t*-Bu)$_3$	$AlMe_3$	76 (70)[d]	<1
5	P(*n*-Bu)$_3$	$AlMe_3$	6	2
6	PPh_3	$AlMe_3$	7	1
7	P(*t*-Bu)$_3$	$ZnMe_2$	40	<1

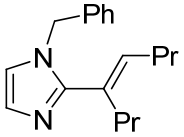
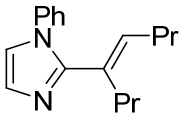
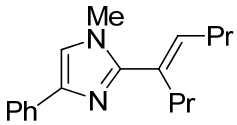
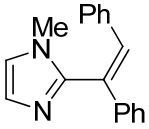
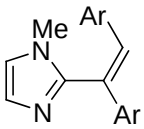
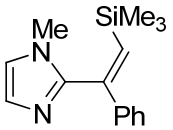
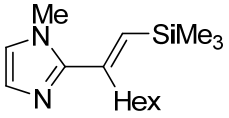
[a] All the reaction was carried out using **5a** (3.00 mmol), **2a** (1.00 mmol), Ni(cod)$_2$ (30 μmol), a ligand (0.12 mmol) and a LA (60 μmol) in toluene (0.68 mL) at 100 ºC for 4 h. [b] Estimated by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Run with Ni(cod)$_2$ (10 mol%) and $PCyp_3$ (10 mol%). [d] Isolated yield based on **2a**.

With the optimized set of a ligand and LA for the regioselective C(2)-alkenylation of imidazoles in hand, several imidazole derivatives were tested for the reaction with **2a**. Imidazoles with an *N*-benzyl or *N*-phenyl substituent **5b** and **5c** participated in the reaction to give **6ba** and **6ca** highly regio- and stereoselectively in 63% and 42% yields, respectively (entries 1 and 2 of Table 7). A phenyl substituent at the C-4 position in **5d** did not affect the reaction to give **6da** in 63% yield (entry 3). C(2)-Alkenylation of **5a** with other alkynes was examined next. Aryl-substituted alkynes **2g, 2h** and **2i** underwent the reaction to give the respective triarylethenes and diarylethene in good yields but with reversed stereoselectivity (entries 4–6). In both cases, initially formed *cis*-adducts apparently isomerized to *trans*-adducts under the reaction conditions. Thus, the *E*/*Z* ratios of **6ag** and **6ai** at 1 h were 88:12 and 31:69, respectively. The isomerization was proved further by the fact that treatment of isolated pure *E*-isomer of **6ag** with Ni(cod)$_2$ (3 mol%), P(*t*-Bu)$_3$ (12 mol%), and $AlMe_3$ (6 mol%) in toluene at 100 ºC for 6 h induced quantitative isomerization to the *Z*-isomer. Nevertheless, partial formation of the *trans*-adducts kinetically via isomerization of alkenylnickel intermediates cannot be ruled out.[22] The aryl substituent may electronically stabilize intermediates of such isomerization and facilitate it. Unsymmetrical alkyne **2j** underwent the hydroheteroarylation reaction with perfect stereo- and regioselectivity to give the corresponding adduct **6aj**, in which the silyl substituent is located *trans* to the imidazolyl ring (entry 7), whereas terminal alkynes did not give any trace amount of

adducts due to rapid tri- and/or oligomerization of the alkynes under these conditions.

Table 7. Nickel/LA-catalyzed C-2 alkenylation of imidazoles with alkynes.[a]

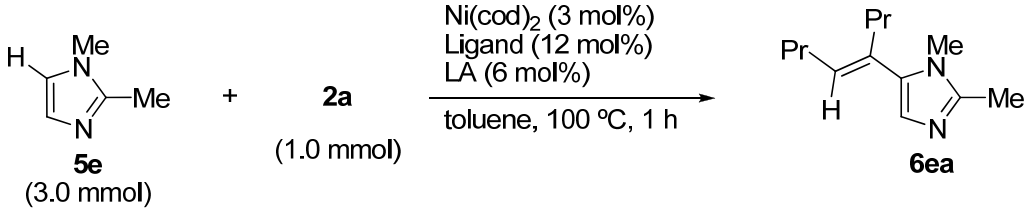


Entry	**5**	**2**	Time (h)	Major product	Yield (%)[b]	*E*/*Z*[c]
1	**5b**	**2a**	3		63 (**6ba**)	93:7
2	**5c**	**2a**	10		42 (**6ca**)	92:8
3	**5d**	**2a**	2		63 (**6da**)	>99:1
4	**5a**	**2h**	10		75 (**6ah**)	<1:99
5[d]	**5a**	**2i**	18		53 (**6ai**)	<1:99
6	**5a**	**2g**	20		69 (**6ag**)	20:80
7[e]	**5a**	**2j**	26		60 (**6aj**)	>99:1

[a] All the reaction was carried out using **5** (3.00 mmol), **2** (1.00 mmol), $Ni(cod)_2$ (30 μmol), $P(t\text{-}Bu)_3$ (12 mmol), and $AlMe_3$ (60 μmol) in toluene (0.68 mL). [b] Isolated yield based on **2**. [c] Estimated by ^1H NMR analysis of a crude product. [d] Ar = 4-MeO-C_6H_4. [e] Run with $Ni(cod)_2$ (10 mol%), $P(t\text{-}Bu)_3$ (40 mol%), and $AlMe_3$ (20 mol%).

The author next optimized reaction conditions for C(5)-selective alkenylation of C(2)-substituted imidazoles. P(*t*-Bu)$_3$ was ineffective to give expected adduct **6ea** in poor yield (Table 8, entry 3), whereas PCyp$_3$ and P(*i*-Pr)$_3$ gave moderate yields of **6ea** (entries 1 and 2). Use of ZnMe$_2$, a milder LA catalyst, also provided the hydroheteroarylation adduct in a comparable yield (entry 4). In any case, the alkenylation took place exclusively at the C-5 position, and no trace amount of C(4)-alkenylated imidazole was observed.

Table 8. Optimization of reaction conditions for C(5)-alkenylation of imidazoles.[a]

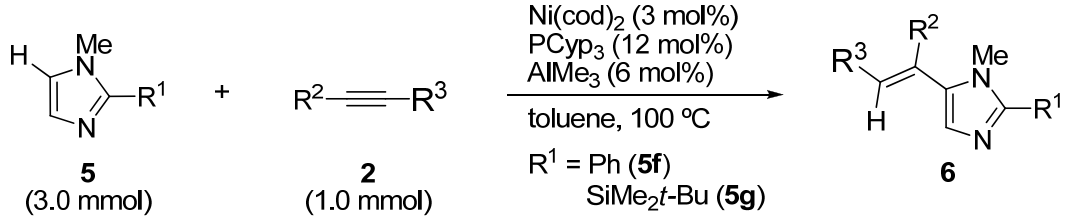


Entry	Ligand	LA	Yield of **6ea** (%)[b]
1	PCyp$_3$	AlMe$_3$	59 (55)[c]
2	P(*i*-Pr)$_3$	AlMe$_3$	59
3	P(*t*-Bu)$_3$	AlMe$_3$	12
4	PCyp$_3$	ZnMe$_2$	51

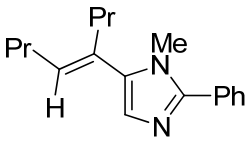
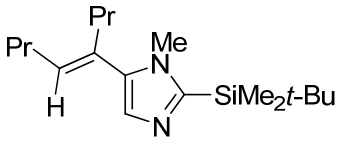
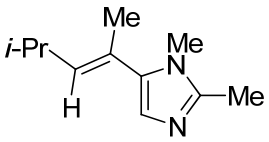
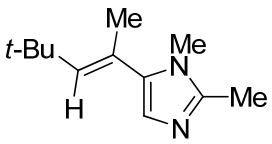
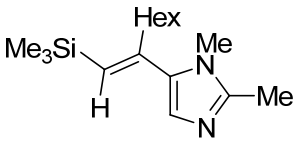
[a] All the reaction was carried out using **5e** (3.00 mmol), **2a** (1.00 mmol), Ni(cod)$_2$ (30 μmol), a ligand (12 mmol), and a Lewis acid (60 μmol) in toluene (0.68 mL) at 100 °C for 1 h. [b] Estimated by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Isolated yield after 1.5 h, *E*:*Z* = >99:1.

The author further examined the scope of 2-substituted imidazoles and alkynes using the optimum conditions thus established (Table 9). The reaction of 1-methyl-2-phenyl-1*H*-imidazole (**5f**) with **2a** proceeded smoothly to give the corresponding C(5)-alkenylated product **6fa** in 81% yield (entry 1), whereas *tert*-butyldimethylsilyl-substituted one **5g** reacted sluggishly to give **6ga** in 42% yield (entry 2). The hydroheteroarylation of 4-methyl-2-pentyne (**2d**), 4,4-dimethyl-2-pentyne (**2e**) and 1-trimethyl-silyl-1-octyne (**2i**) with **5e** also proceeded smoothly in excellent regio- and stereoselectivities to give the corresponding adducts all with a bulkier substituent located *trans* to the imidazolyl ring (entries 3–5).

Table 9. Nickel/LA-catalyzed C-5 alkenylation of 2-substituted imidazoles with alkynes.[a]



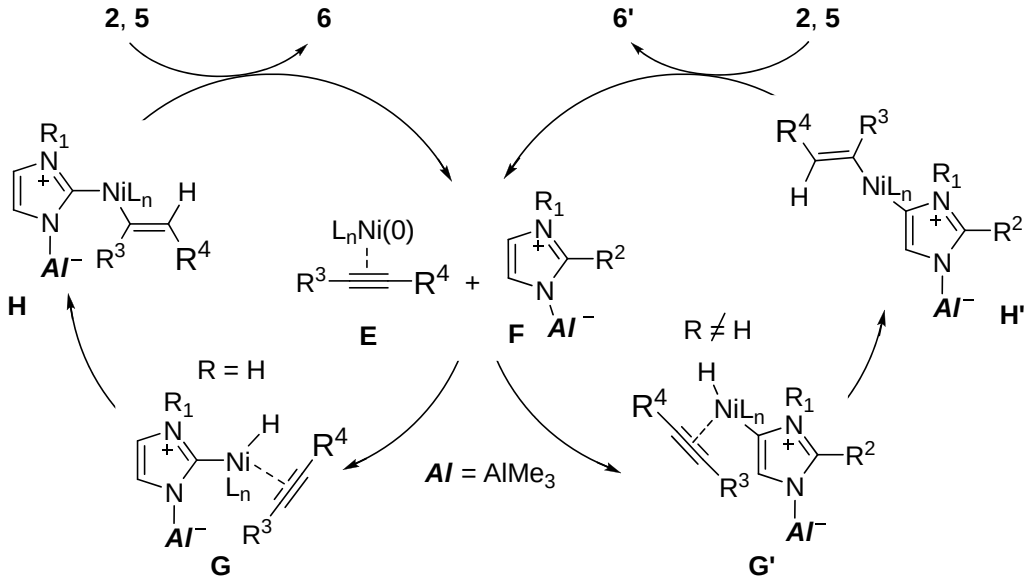
5 (3.0 mmol) + **2** (1.0 mmol) → **6**

Entry	**5**	**2**	Time (h)	Major product	Yield (%)[b]	*E*:*Z*[c]
1	**5f**	**2a**	2		81 (**6fa**)	>95:5
2	**5g**	**2a**	1		42 (**6ga**)	96:4
3	**5e**	**2d**	4		75 (**6ed**)	>95:5
4	**5e**	**2e**	4		71 (**6ee**)	>95:5
5[d]	**5e**	**2i**	31		63 (**6ei**)	>95:5

[a] All the reaction was carried out using **5** (3.00 mmol), **2** (1.00 mmol), $Ni(cod)_2$ (30 μmol), $PCyp_3$ (12 mmol) and $AlMe_3$ (60 μmol) in toluene (0.68 mL). [b] Isolated yield based on **2**. [c] Estimated by ^1H NMR analysis of a crude product. [d] Run with $Ni(cod)_2$ (10 mol%), P(*t*-Bu)$_3$ (40 mol%), and $AlMe_3$ (20 mol%).

Following is a plausible reaction mechanism (Scheme 2). First, nickel(0) species **E**[15] and imidazolium species **F**[21] are formed *in situ* by coordination of an alkyne to nickel(0) and nitrogen in imidazole nucleus to $AlMe_3$, respectively. Oxidative addition of the imidazolium C–H bond to the nickel species gives alkyne-coordinating hetAr–Ni(II)–H intermediates **G** or **G'**.[16] Hydronickelation across the coordinating alkyne takes place to give imidazolyl–Ni(II)–alkenyl intermediates **H** or **H'**, respectively. Subsequent

reductive elimination gives *cis*-hydroheteroarylation products **6** or **6'**, and regenerates nickel(0) species **E**. Exclusive C(5)–H bond activation with 2-substituted imidazoles may be ascribed to resonance structure **F**, wherein the C(5)–H bond locates α to the formally positively charged nitrogen. The observed preferences for ligands depending on the site of alkenylation is not clarified yet.



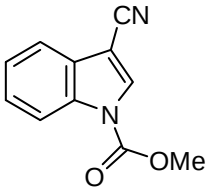
Scheme 2. Plausible mechanism for C(2)- and C(5)-alkenylation of imidazoles.

In summary, the author has demonstrated that a nickel catalyst is effective for the activation of relatively acidic C–H bonds of 5-membered heterocycles and insertion of alkynes into the C–H bonds. Use of LA co-catalysts was found to significantly improve regioselective C(2)- and C(5)-alkenylation of imidazoles. The catalysis is applicable to a diverse range of 5-membered heterocycles to provide a broad range of disubstituted heteroarylethenes with defined stereochemistry in modest to excellent yields. Excellent regioselectivity is observed with unsymmetrical alkynes to give the corresponding heteroaryl-substituted ethenes having a bulkier substituent *trans* to the heteroaryl group.

Experimental section

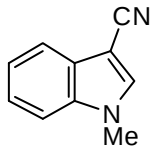
Chemicals. 9-Methyl-9*H*-purine (**1n**),[23] 1-benzyl-1*H*-imidazole (**5b**),[24] 1-phenyl-1*H*-imidazole (**5c**),[25] 1-methyl-4-phenyl-1*H*-imidazole (**5f**),[26] 1-methyl-2-phenyl-1*H*-imidazole (**5f**),[26] and 2-(*tert*-butyldimethylsilyl)-1-methyl-1*H*-imidazole (**5g**)[27] were prepared according to the respective literature procedure.

Methyl 3-cyano-1*H*-indole-1-carboxylate (1a). Following the reported procedure,[28]



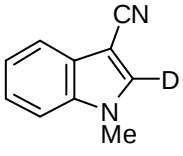
1*H*-indole-3-carbonitrile (1.00 g, 7.0 mmol) was treated with NaH (0.26 g, 10.9 mmol) in DMF (15 mL) at 0 ºC for 10 min, and then methyl chloroformate (1.35 g, 14.2 mmol) was added to the resulting mixture at rt, which was stirred for 1 h, then quenched with H_2O and extracted with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give **1a** (1.12 g, 80%) as a colorless solid, mp 89.2–90.2 ºC, R_f 0.75 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 1H), 8.13 (s, 1H), 7.73 (dq, J = 7.9, 0.7 Hz, 1H), 7.51–7.37 (m, 2H), 4.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 134.2, 132.8, 127.9, 126.6, 124.7, 119.9, 115.6, 113.9, 93.3, 54.8. Anal. Calcd for $C_{11}H_8N_2O_2$; C, 66.00; H, 4.03. Found: C, 66.18; H, 4.20.

1-Methyl-1*H*-indole-3-carbonitrile (1b).[29] 1*H*-Indole-3-carbonitrile (2.0 g, 14.1 mmol)



was treated with NaH (0.40 g, 16.8 mmol) in DMF (30 mL) at 0 ºC for 10 min, and then iodomethane (2.4 g, 16.8 mmol) was added to the resulting mixture at rt. The reaction mixture was stirred for 1 h, treated with H_2O and extracted with ethyl acetate. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give **1b** (1.38 g, 84%) as a colorless solid, mp 60.5–61.5 ºC, R_f 0.50 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.9 Hz, 1H), 7.55 (s, 1H), 7.42–7.27 (m, 3H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 135.5, 127.8, 123.8, 122.1, 119.8, 115.9, 110.3, 85.4, 33.6.

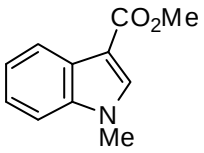
2-Deuterio-1-methyl-1*H*-indole-3-carbonitrile (1b-*d*$_1$). A 1.6 M solution of BuLi in



hexane (3.5 mL, 5.6 mmol) was added to **1b** (0.50 g, 3.2 mmol) dissolved in THF (10 mL) at –78 ºC. The resulting mixture was stirred at –78 ºC for 30 min, then quenched with D_2O (0.55 g, 27 mmol). The

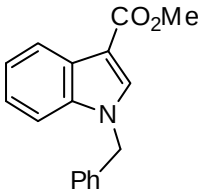
mixture was warmed gradually to rt, and extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give **1b**-d_1 (0.36 g, 71%) as a colorless solid, mp 58.0–59.0 ºC, R_f 0.50 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dt, J = 7.9, 1.0 Hz, 1H), 7.42–7.27 (m, 3H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 135.2 (t, J = 28.8 Hz), 127.4, 123.5, 121.8, 119.3, 115.8, 110.2, 84.7, 33.3. HRMS (EI) Calcd for $C_{10}H_7N_2D$: M^+, 157.0750. Found: m/z 157.0748.

Methyl 1-methyl-1*H*-indole-3-carboxylate (1c).[29] Following the procedure for **1b**, the



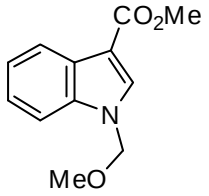
reaction using methyl 1*H*-indole-3-carboxylate (3.0 g, 17.1 mmol) gave **1c** (2.8 g, 87%) as a colorless solid, mp 87.6–88.7 ºC, R_f 0.60 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.14 (m, 1H), 7.78 (s, 1H), 7.39–7.25 (m, 3H), 3.91 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 137.1, 135.1, 126.6, 122.7, 121.8, 121.6, 109.7, 106.9, 50.9, 33.4.

Methyl 1-benzyl-1*H*-indole-3-carboxylate (1d).[30] Methyl 1*H*-indole-3-carboxylate



(1.00 g, 5.7 mmol) was treated with NaH (0.164 g, 6.8 mmol) in THF (30 mL) at 0 ºC for 10 min at rt, and then benzyl bromide (0.98 g, 5.7 mmol) was added to the resulting mixture. After stirring for 1 h, the reaction was quenched with H_2O and extracted with CH_2Cl_2. Combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give **1d** (1.41 g, 93%) as a brownish solid, mp 70.2–71.2 ºC, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, J = 7.9, 0.7 Hz, 1H), 7.85 (s, 1H), 7.36–7.22 (m, 6H), 7.18–7.13 (m, 2H), 5.34 (s, 2H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 136.7, 135.9, 134.5, 129.0, 128.1, 127.1, 126.8, 122.9, 122.0, 121.8, 110.3, 107.5, 51.0, 50.7.

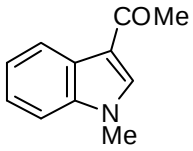
Methyl 1-methoxymethyl-1*H*-indole-3-carboxylate (1e). Methyl



1*H*-indole-3-carboxylate (1.00 g, 5.7 mmol) was treated with NaH (0.164 g, 6.8 mmol) in DMF (30 mL) at 0 ºC for 15 min, and then chloromethyl methyl ether (0.92 g, 11.4 mmol) was added to the resulting mixture at rt. After stirring for 1 h, the reaction was quenched with H_2O and extracted with ethyl acetate. Combined

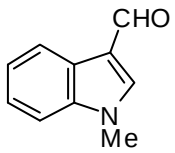
organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give **1e** (1.25 g, 100%) as a colorless solid, mp 64.9–65.7 ºC, R_f 0.80 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.16 (m, 1H), 7.89 (s, 1H), 7.55–7.49 (m, 1H), 7.35–7.28 (m, 2H), 5.48 (s, 2H), 3.93 (s, 3H), 3.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 136.5, 134.3, 126.9, 123.4, 122.5, 121.8, 110.5, 108.4, 78.1, 56.2, 51.1. Anal. Calcd for $C_{12}H_{13}NO_3$; C, 65.74; H, 5.98. Found: C, 65.78; H, 5.88.

1-(1-Methyl-1*H*-indol-3-yl)ethanone (1f).[31] Following the procedure for **1b**, the



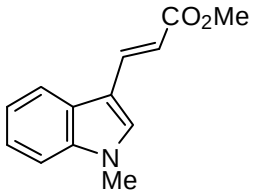
reaction using 1-(1*H*-indol-3-yl)ethanone (2.0 g, 12.6 mmol) gave **1f** (1.70 g, 80%) as a colorless solid, mp 106.0–107.0 ºC, R_f 0.40 (hexane–ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40–8.34 (m, 1H), 7.69 (s, 1H), 7.35–7.28 (m, 3H), 3.84 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 137.4, 135.7, 126.2, 123.3, 122.5, 116.9, 109.7, 109.5, 33.4, 27.6.

1-Methyl-1*H*-indole-3-carbaldehyde (1g).[29] Following the procedure for **1b**, the



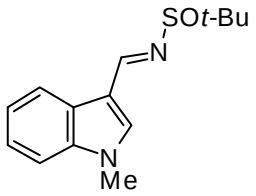
reaction using 1*H*-indole-3-carboxaldehyde (2.0 g, 13.8 mmol) gave **1g** (1.67 g, 83%) as a colorless solid, mp 69.9–70.8 ºC, R_f 0.60 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.31 (d, J = 6.4 Hz, 1H), 7.67 (s, 1H), 7.38–7.30 (m, 3H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.6, 139.4, 138.1, 125.5, 124.3, 123.2, 122.3, 118.3, 110.1, 33.9.

Methyl (*E*)-3-(1-methyl-1*H*-indol-3-yl)acrylate (1h).[29] Following the procedure for **1b**,



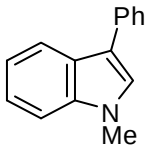
(*E*)-methyl 3-(1*H*-indol-3-yl)acrylate (0.25 g, 1.23 mmol)[32] was transformed to **1h** (0.26 g, 100%) as a reddish solid, mp 97.9–98.8 ºC, R_f 0.45 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.87 (m, 2H), 7.37–7.24 (m, 4H), 6.42 (d, J = 15.9 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 138.2, 138.0, 133.1, 126.0, 122.9, 121.3, 120.5, 112.1, 112.0, 109.9, 51.3, 33.1.

(*E*)-2-methyl-*N*-[(1-methyl-1*H*-indol-3-yl)methylene]propane-2-sulfinamide (1i).[33] (*R*)-(+)-2-methyl-2-propanesulfinamide (0.80 g, 6.6 mmol) was placed in a 80 mL Schlenk flask equipped with a magnetic stirring bar, and dissolved into ethanol (20 mL).

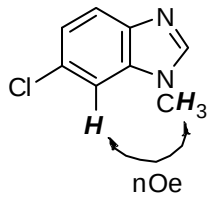


$FeCl_3$ (42 mg, 0.3 mmol) and 1-methyl-1*H*-indole-3-carboxaldehyde (**1g**, 1.31 g, 8.25 mmol) were added sequentially, then the resulting solution was stirred at rt for 12 h. The reaction mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give **1i** (0.86 g, 50%) as a pale colorless solid, mp 149.5–150.3 ºC, R_f 0.25 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.31 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.41–7.28 (m, 3H), 3.88 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 137.9, 136.1, 125.4, 123.6, 122.2, 122.1, 113.6, 109.7, 57.0, 33.6, 22.6.

1-Methyl-3-phenyl-1*H*-indole (1j). Following the procedure for **1b**, 3-phenyl-1*H*-indole (0.68 g, 3.5 mmol)[34] gave **1j** (0.71 g, 97%) as a colorless solid, mp 48.5–49.0 ºC, R_f 0.65 (hexane–ethyl acetate = 3:1). ^{1}H and ^{13}C spectra of the obtained compound were identical with those reported for the title compound.[35]



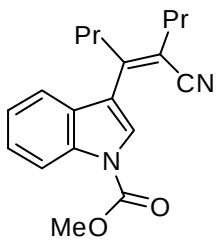
6-Chloro-1-methyl-1*H*-benzimidazole (1l). 5-Chloro-1*H*-benzimidazole (1.07 g, 7.0 mmol) was treated with NaH (0.26 g, 10.8 mmol) in THF (30 mL) at 0 ºC for 15 min. Iodomethane (2.7 g, 19.2 mmol) was added slowly to the resulting mixture. The whole mixture was warmed to rt, stirred for 30 min, and quenched with H_2O. The organic layer was separated by extraction with CH_2Cl_2. The combined organic layers were washed with H_2O and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give a mixture of 5- and 6-chloro-1-methyl-1*H*-benzimidazole (0.73 g, 62%), which after recrystallization from hexane–Et_2O (9:1) for three times gave **1l** as colorless crystals, mp 119.0–120.0 ºC, R_f 0.60 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.36 (d, *J* = 1.6 Hz, 1H), 7.23 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 142.4, 128.7, 123.3, 122.7, 122.1, 109.5, 31.1. Anal. Calcd for $C_8H_7ClN_2$; C, 57.67; H, 4.23. Found: C, 57.41; H, 4.19.



Nickel-catalyzed hydroheteroarylation of alkynes. *General procedure.* In a glove box, $Ni(cod)_2$ (28 mg, 0.10 mmol) and $PCyp_3$ (24 mg, 0.10 mmol) were placed in a 3 mL-vial and dissolved in toluene (2.5 mL). An heteroarene (1.0 mmol) and an alkyne (1.0 mmol) were added to the solution. The vial was closed with a screw cap,

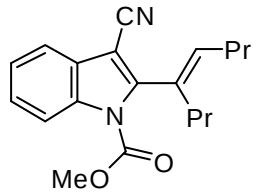
taken out from the glove box and heated at the temperature for the time specified in Tables 1, 2 and 3. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding hydroheteroarylation products in yields listed in Tables 1, 2 and 3.

(*Z*)-3-*(*1-Methoxycarbonyl-3-indol-yl)-2-propyl-2-hexenenitrile (3aa). A colorless oil,



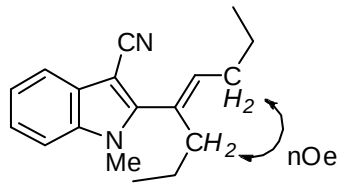
R_f 0.65 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (br d, *J* = 8.1 Hz, 1H), 7.70 (s, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.38 (td, *J* = 7.8, 1.1 Hz, 1H), 7.30 (td, *J* = 7.6, 1.1 Hz, 1H), 4.04 (s, 3H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.43 (t, *J* = 7.6 Hz, 2H), 1.73 (sext, *J* = 7.5 Hz, 2H), 1.37 (sext, *J* = 7.5 Hz, 2H), 1.06 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 150.4, 135.3, 128.5, 125.0, 124.2, 123.1, 120.8, 119.8, 119.2, 115.3, 113.5, 53.8, 35.0, 32.1, 21.7, 21.3, 13.7, 13.4. IR (neat) 2959, 2932, 2874, 2211, 1804, 1751, 1744, 1699, 1628, 1605, 1584, 1560, 1454, 1439, 1379, 1341, 1285, 1273, 1252, 1231, 1207, 1169, 1138, 1109, 1084, 1057, 1017, 943, 810, 762, 694, 611, 567, 498, 451, 424 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 311 (M^++1, 21), 310 (M^+, 100), 282 (15), 281 (75), 267 (14), 251 (12), 249 (18), 239 (13), 221 (14), 207 (14), 193 (18), 192 (14), 180 (11), 167 (12). Anal. Calcd for $C_{19}H_{22}N_2O_2$; C, 73.52; H, 7.14. Found: C, 73.42; H, 7.19.

Methyl (*E*)-3-cyano-2-(oct-4-en-4-yl)-1*H*-indole-1-carboxylate (4aa, containing 9% of *Z*-isomer). A colorless oil, R_f 0.60 (hexane–ethyl acetate = 1:1).

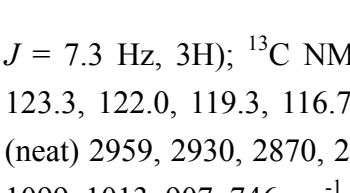


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.40–7.22 (m, 3H), 5.79 (t, *J* = 7.4 Hz, 1H), 3.69 (s, 3H), 2.48 (t, *J* = 7.8 Hz, 2H), 2.30 (q, *J* = 7.4 Hz, 2H), 1.54 (sext, *J* = 7.3 Hz, 2H), 1.37 (sext, *J* = 7.6 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2, 138.5, 136.2, 129.4, 127.3, 123.3, 123.2, 122.0, 119.3, 116.7, 110.2, 110.1, 32.9, 31.1, 30.3, 22.5, 21.7, 13.92, 13.87. IR (neat) 2959, 2932, 2872, 2359, 2341, 2214, 1742, 1526, 1468, 1437, 1398, 1379, 1360, 1329, 1248, 1130, 1099, 1013, 907, 746 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 311 (M^++1, 22), 310 (M^+, 100), 282 (15), 281 (74), 267 (15), 251 (13), 249 (18), 239 (13), 221 (15), 207 (15), 195 (10), 194 (11), 194 (11), 193 (21), 192 (16), 180 (12), 179 (12), 168 (11), 167 (13), 59 (11). HRMS (EI) Calcd for $C_{17}H_{19}N_2$: $[M–CO_2Me]^+$, 251.1548. Found: *m/z* 251.1545.

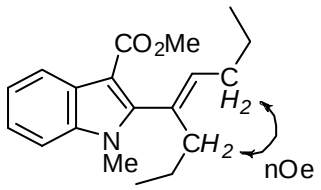
(*E*)-1-Methyl-2-(oct-4-en-4-yl)-1*H*-indole-3-carbonitrile (4ba). A colorless oil, R_f 0.65 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dt, *J* = 7.3, 1.0 Hz, 1H), 7.38–7.24 (m, 3H), 5.78 (t, *J* = 7.4 Hz, 1H), 3.69 (s, 3H), 2.49 (t, *J* = 7.7 Hz, 2H), 2.30 (q, *J* = 7.4 Hz, 2H), 1.54 (sext, *J* = 7.4 Hz, 2H), 1.37 (sext, *J* = 7.6 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2, 138.5, 136.2, 129.4, 127.3, 123.3, 122.0, 119.3, 116.7, 110.1, 84.9, 32.9, 31.1, 30.3, 22.5, 21.7, 13.90, 13.85. IR (neat) 2959, 2930, 2870, 2214, 1526, 1468, 1435, 1398, 1379, 1360, 1329, 1248, 1130, 1099, 1013, 907, 746 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 267 (M^++1, 25), 266 (M^+, 100), 251 (14), 238 (21), 237 (90), 224 (24), 223 (72), 212 (11), 210 (21), 209 (52), 208 (11), 207 (16), 196 (33), 195 (32), 194 (11), 193 (24), 192 (24), 183 (13), 182 (14), 181 (23), 180 (18), 179 (22), 169 (36), 168 (11), 167 (11), 157 (23). Anal. Calcd for $C_{18}H_{22}N_2$; C, 81.16; H, 8.32. Found: C, 81.37; H, 8.47.



(*E*)-1-Methyl-2-(5-deuteriooct-4-en-4-yl)-1*H*-indole-3-carbonitrile (4ba-*d*$_1$). A colorless oil, R_f 0.65 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dt, *J* = 7.3, 1.0 Hz, 1H), 7.36–7.23 (m, 3H), 3.68 (s, 3H), 2.48 (t, *J* = 7.7 Hz, 2H), 2.29 (t, *J* = 7.3 Hz, 2H), 1.54 (sext, *J* = 7.4 Hz, 2H), 1.37 (sext, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2, 138.1 (t, *J* = 23.4 Hz), 136.2, 129.2, 127.3, 123.2, 121.9, 119.2, 116.7, 110.1, 84.8, 32.8, 31.1, 30.2, 22.4, 21.7, 13.9, 13.8. IR (neat) 3059, 2959, 2932, 2870, 2214, 1526, 1468, 1435, 1396, 1379, 1360, 1329, 1254, 1165, 1130, 1099, 1013, 808, 746 cm^{-1}. MS (FAB+) *m/z* (%) 269 (M^++2, 22), 268 (M^++1, 100), 267 (M^+, 91), 154 (23), 137 (13), 136 (19). HRMS (FAB+) Calcd for $C_{18}H_{21}DN_2$; M^+, 267.1846. Found: *m*/*z* 267.1848.

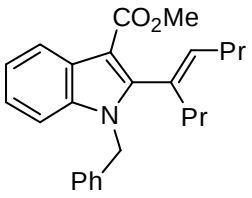


Methyl (*E*)-1-methyl-2-(oct-4-en-4-yl)-1*H*-indole-3-carboxylate (4ca). A colorless oil, R_f 0.65 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20–8.14 (m, 1H), 7.35–7.23 (m, 3H), 5.51 (t, *J* = 7.3 Hz, 1H), 3.87 (s, 3H), 3.68 (s, 3H), 2.50 (t, *J* = 8.1 Hz, 2H), 2.30 (q, *J* = 7.3 Hz, 2H), 1.53 (sext, *J* = 7.4 Hz, 2H), 1.29 (sext, *J* = 7.9 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 150.0, 134.7, 131.9, 126.6, 122.3, 121.8, 121.7, 109.6, 108.17, 108.15, 50.6, 34.1, 30.4, 30.2, 22.7, 21.8, 14.4, 13.9. IR (neat) 2957, 2932, 2870, 1701, 1518, 1466, 1437, 1394, 1373, 1331, 1273, 1217, 1190,



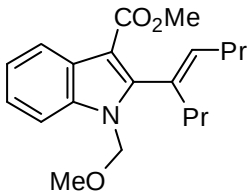
1155, 1132, 1101, 1029, 1016, 791, 752, 741 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 329 (17), 293 (12), 286 (14), 281 (22), 269 (12), 243 (16), 236 (23), 231 (26), 224 (10), 219 (22), 194 (12), 193 (12), 181 (48), 169 (41), 131 (54), 119 (46), 100 (11), 69 (100), 57 (13), 55 (10). Anal. Calcd for $C_{19}H_{25}NO_2$; C, 76.22; H, 8.42. Found: C, 76.25; H, 8.41.

Methyl (*E*)-1-benzyl-2-(oct-4-en-4-yl)-1*H*-indole-3-carboxylate (4da). A colorless oil,



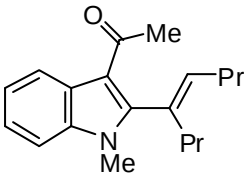
R_f 0.55 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.30–7.07 (m, 6H), 6.96 (d, *J* = 7.9 Hz, 2H), 5.48 (t, *J* = 7.3 Hz, 1H), 5.35 (s, 2H), 3.89 (s, 3H), 2.44 (br, 2H), 2.19 (br q, *J* = 7.3 Hz, 2H), 1.40–1.19 (m, 4H), 0.93–0.78 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 150.0, 137.2, 136.0, 135.0, 131.4, 128.6, 127.3, 126.8, 125.8, 122.5, 122.0, 121.7, 110.8, 104.3, 50.7, 47.5, 34.1, 30.1, 22.4, 21.7, 14.4, 13.7. IR (neat) 3032, 2957, 2930, 2870, 1701, 1638, 1605, 1522, 1497, 1481, 1460, 1437, 1400, 1369, 1348, 1281, 1231, 1186, 1159, 1132, 1115, 1078, 1030, 908, 790, 752, 931, 696 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 376 (M^++1, 15), 375 (M^+, 52), 360 (22), 346 (19), 33 (13), 332 (40), 318 (11), 316 (18), 224 (12), 91 (M–$PhCH_2$, 100). Anal. Calcd for $C_{25}H_{29}NO_2$; C, 79.96; H, 7.78. Found: C, 80.20; H, 7.79.

Methyl (*E*)-1-methoxymethyl-2-(oct-4-en-4-yl)-1*H*-indole-3-carboxylate (4ea). A



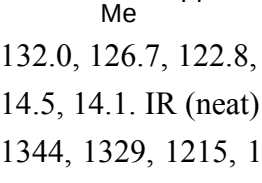
colorless oil, R_f 0.60 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.23–8.13 (m, 1H), 7.56–7.44 (m, 1H), 7.34–7.21 (m, 2H), 5.64 (t, *J* = 7.4 Hz, 1H), 5.40 (br, 2H), 3.88 (s, 3H), 3.31 (s, 3H), 2.47 (br t, *J* = 8.1 Hz, 2H), 2.30 (q, *J* = 7.4 Hz, 2H), 1.53 (sext, *J* = 7.3 Hz, 2H), 1.30 (sext, *J* = 7.9 Hz, 2H), 1.02 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 149.6, 136.0, 135.7, 130.9, 126.7, 122.8, 122.3, 121.7, 110.5, 105.2, 74.8, 55.9, 50.7, 34.2, 30.3, 22.6, 21.5, 14.4, 13.9. IR (neat) 2957, 2932, 2872, 1701, 1526, 1481, 1460, 1437, 1394, 1331, 1259, 1244, 1219, 1149, 1155, 1123, 1101, 1035, 1018, 964, 916, 793, 754, 742, 713 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 329 (17), 293 (12), 286 (14), 281 (22), 269 (12), 243 (16), 236 (23), 231 (26), 224 (10), 219 (22), 194 (12), 193 (12), 181 (48), 169 (41), 131 (54), 119 (46), 100 (11), 69 (100), 57 (13). Anal. Calcd for $C_{20}H_{27}NO_3$; C, 72.92; H, 8.26. Found: C, 72.84; H, 8.08.

1-[1-Methyl-2-(oct-4-en-4-yl)-1*H*-indol-3-yl]ethanone (4fa). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.42–8.35 (m, 1H),

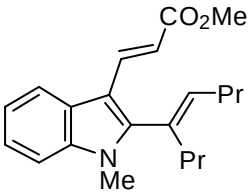


7.35–7.25 (m, 3H), 5.66 (t, J = 7.3 Hz, 1H), 3.66 (s, 3H), 2.52 (s, 3H), 2.48 (br, 2H), 2.32 (q, J = 7.4 Hz, 2H), 1.54 (sext, J = 7.3 Hz, 2H), 1.34 (sext, J = 8.0 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 149.4, 136.4, 132.0, 126.7, 122.8, 122.5, 122.4, 114.6, 109.5, 108.2, 35.1, 30.6, 30.4, 30.0, 22.4, 21.7, 14.5, 14.1. IR (neat) 3051, 2957, 2932, 2870, 1639, 1611, 1578, 1502, 1464, 1433, 1393, 1344, 1329, 1215, 1178, 1153, 1130, 1099, 1016, 930, 908, 750, 725 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 283 (M^+, 26), 254 (35), 241 (85), 240 (100), 212 (19), 211 (18), 210 (14), 198 (17), 197 (12), 196 (21), 183 (11), 182 (30), 181 (13), 180 (11), 168 (19), 167 (24). Anal. Calcd for $C_{19}H_{25}NO$; C, 80.52; H, 8.89. Found: C, 80.37; H, 8.83.

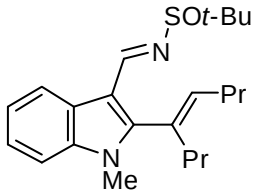
(*E*)-1-Methyl-2-(oct-4-en-4-yl)-1*H*-indole-3-carboxaldehyde (4ga). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.39–8.34 (m, 1H), 7.35–7.28 (m, 3H), 5.75 (t, J = 7.4 Hz, 1H), 3.67 (s, 3H), 2.43 (br, 2H), 2.31 (q, J = 7.4 Hz, 2H), 1.53 (sext, J = 7.3 Hz, 2H), 1.35 (sext, J = 7.6 Hz, 2H), 1.01 (t, J = 7.3 Hz, 3H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.4, 154.9, 139.3, 137.0, 128.8, 125.1, 123.6, 122.9, 122.0, 115.5, 109.4, 33.7, 30.7, 30.4, 22.6, 21.5, 14.1, 13.9. IR (neat) 2957, 2932, 2870, 1690, 1651, 1612, 1580, 1516, 1466, 1439, 1408, 1381, 1325, 1256, 1126, 1099, 1049, 750 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 269 (M^+, 18), 240 (42), 227 (33), 226 (100), 198 (14), 184 (12), 182 (15), 168 (15), 167 (13). HRMS (EI) Calcd for $C_{18}H_{23}NO$: M^+, 269.1780. Found: *m/z* 269.1790.



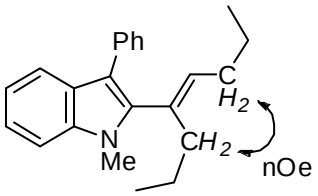
Methyl (*E*)-3-[(*E*)-1-methyl-2-(oct-4-en-4-yl)-1*H*-indol-3-yl]acrylate (4ha). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 6.9, 1.3 Hz, 1H), 7.88 (dd, J = 15.9, 1.1 Hz, 1H), 7.34–7.20 (m, 3H), 6.44 (d, J = 15.9 Hz, 1H), 5.60 (t, J = 7.3 Hz, 1H), 3.78 (s, 3H), 3.62 (s, 3H), 2.37 (br, 2H), 2.31 (q, J = 7.3 Hz, 2H), 1.55 (sext, J = 7.3 Hz, 2H), 1.30 (sext, J = 7.7 Hz, 2H), 1.03 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 148.6, 139.4, 138.2, 137.4, 129.8, 125.5, 122.5, 121.3, 120.4, 111.0, 109.7, 109.6, 51.1, 33.8, 30.6, 30.3, 22.6, 21.4, 14.1, 13.8. IR (neat) 3051, 3018, 2957, 2932, 2870, 1713, 1651, 1620, 1574, 1506, 1468, 1433, 1406, 1369, 1339, 1285, 1242, 1196, 1170, 1132, 1097, 1051, 1016, 984, 908, 847, 835, 808, 745, 731 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 325 (26), 293 (12), 282 (22), 281 (23), 250 (11), 243 (15), 231 (28), 219 (20), 193 (12), 181 (44), 169 (38), 131 (51), 119 (48), 69 (100). Anal. Calcd for $C_{21}H_{27}NO_2$; C,



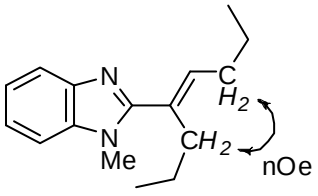
77.50; H, 8.36. Found: C, 77.23; H, 8.33.

(1,*E*)-2-Methyl-*N*-[(1-methyl-2-(oct-4-en-4-yl)-1*H*-indol-3-yl)methylene]propane-2-sulfinamide (4ia). 

A colorless oil, R_f 0.55 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.92 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.37–7.26 (m, 3H), 5.69 (t, *J* = 7.3 Hz, 1H), 3.67 (s, 3H), 2.56–2.20 (br, 2H), 2.31 (q, *J* = 7.4 Hz, 2H), 1.55 (sext, *J* = 7.4 Hz, 2H), 1.32 (sext, *J* = 7.7 Hz, 2H), 1.27 (s, 9H), 1.02 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 151.2 138.8, 137.2, 130.0, 125.3, 123.1, 122.0, 122.0, 111.4, 109.4, 56.7, 34.0, 30.8, 30.5, 22.8, 22.5, 21.6, 14.3, 14.1. IR (neat) 3053, 2957, 2930, 2870, 1586, 1568, 1468, 1439, 1410, 1319, 1254, 1182, 1128, 1076, 1053, 1015, 907, 833, 764, 748, 732, 723, 691, 590, 579, 548, 517 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 317 (10), 316 (40), 315 (M^+–*t*-Bu, 82), 274 (18), 273 (M^+–99, 100,), 267 (42), 266 (20), 253 (12), 252 (26), 237 (19), 225 (42), 224 (36), 223 (20), 209 (20), 196 (20), 195 (38), 182 (10), 181 (12), 169 (10), 57 (12).

(*E*)-1-Methyl-2-(oct-4-en-4-yl)-3-phenyl-1*H*-indole (4ja). 

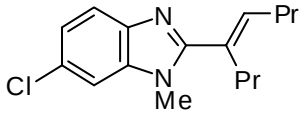
A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.1 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 2H), 7.36 (q, *J* = 7.6 Hz, 3H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 5.68 (t, *J* = 7.3 Hz, 1H), 3.70 (s, 3H), 2.25 (q, *J* = 7.3 Hz, 2H), 2.12 (t, *J* = 7.8 Hz, 2H), 1.51 (sext, *J* = 7.3 Hz, 2H), 1.15 (sext, *J* = 7.6 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.70 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 136.7, 136.6, 135.9, 131.8, 129.4, 128.1, 127.0, 125.5, 121.4, 119.8, 119.2, 113.4, 109.4, 33.6, 30.4, 30.3, 22.8, 21.5, 14.1, 14.0. IR (neat) 3051, 2981, 2930, 2866, 1599, 1529, 1489, 1466, 1429, 1398, 1367, 1329, 1256, 1090, 772, 750, 737, 704 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 317 (M^+, 100), 288 (23), 275 (12), 274 (54), 244 (18), 232 (36), 231 (39), 230 (17), 218 (11), 217 (18), 207 (14). Anal. Calcd for $C_{23}H_{27}N$; C, 87.02; H, 8.57. Found: C, 87.25; H, 8.66.

(*E*)-1-Methyl-2-(oct-4-en-4-yl)-1*H*-benzimidazole (4ka). 

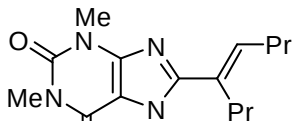
A colorless oil, R_f 0.55 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.73 (m, 1H), 7.33–7.21 (m, 3H), 5.77 (t, *J* = 7.3 Hz, 1H), 3.74 (s, 3H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.30 (q, *J* = 7.4 Hz, 2H), 1.52 (sext, *J* = 7.4 Hz, 2H), 1.39 (sext, *J* = 7.5 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR

(101 MHz, $CDCl_3$) δ 155.9, 142.5, 136.6, 135.9, 130.9, 122.2, 121.9, 119.4, 109.3, 32.3, 31.2, 30.4, 22.6, 21.7, 13.9, 13.8. IR (neat) 3051, 2959, 2930, 2870, 1612, 1486, 1460, 1435, 1387, 1360, 1323, 1283, 1254, 1151, 1123, 1109, 1096, 1007, 906, 824, 766, 746 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 242 (M^+, 47), 227 (37), 214 (24), 213 (100), 199 (23), 197 (17), 185 (24), 184 (12), 183 (26), 172 (19), 171 (12), 169 (12), 157 (16). Anal. Calcd for $C_{16}H_{22}N_2$; C, 79.29; H, 9.15. Found: C, 78.99; H, 9.06.

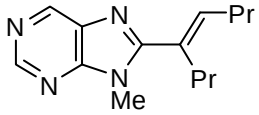
(*E*)-6-Chloro-1-methyl-2-(oct-4-en-4-yl)-1*H*-benzimidazole (4la). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 2.0 Hz, 1H), 7.21 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.78 (t, *J* = 7.4 Hz, 1H), 3.73 (s, 3H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.30 (q, *J* = 7.3 Hz, 2H), 1.53 (sext, *J* = 7.4 Hz, 2H), 1.38 (sext, *J* = 7.5 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 141.2, 137.0, 136.6, 130.6, 127.9, 122.6, 120.2, 109.5, 32.3, 31.3, 30.4, 22.6, 21.8, 13.9, 13.8. IR (neat) 2959, 2930, 2870, 1609, 1458, 1425, 1377, 1329, 1273, 1055, 918, 837, 810 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 276 (M^+, 12), 269 (11), 247 (20), 245 (10), 243 (17), 231 (27), 219 (19), 207 (17), 205 (11), 193 (12), 181 (42), 169 (34), 131 (52), 119 (41), 69 (100), 57 (14), 55 (10). HRMS (EI) Calcd for $C_{16}H_{21}ClN_2$: M^+, 276.1393. Found: *m*/*z* 276.1393.



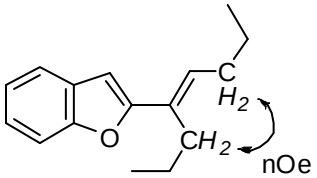
(*E*)-1,3,7-Trimethyl-8-(oct-4-en-4-yl)-3,7-dihydro-1*H*-purine-2,6-dione (4ma). A colorless solid, mp 92.7–93.6 ºC, R_f 0.60 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (t, *J* = 7.4 Hz, 1H), 3.89 (s, 3H), 3.53 (s, 3H), 3.36 (s, 3H), 2.48 (t, *J* = 7.6 Hz, 2H), 2.23 (q, *J* = 7.4 Hz, 2H), 1.47 (sext, *J* = 7.3 Hz, 2H), 1.32 (sext, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 154.4, 151.7, 147.8, 137.6, 129.4, 107.5, 33.4, 32.0, 30.3, 29.6, 27.8, 22.4, 21.7, 13.9, 13.8. IR (KBr) 2957, 2932, 2870, 1705, 1659, 1603, 1541, 1489, 1429, 1373, 1339, 1286, 1221, 1042, 978, 918, 758, 745 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 304 (M^+, 38), 289 (17), 276 (19), 275 (100), 67 (14). Anal. Calcd for $C_{16}H_{24}N_4O_2$; C, 63.13; H, 7.95. Found: C, 62.91; H, 8.04.



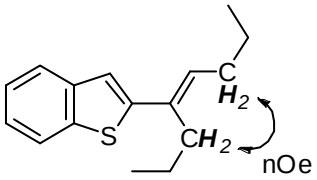
(*E*)-9-Methyl-8-(oct-4-en-4-yl)-9*H*-purine (4na). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 9:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.87 (s, 1H), 5.91 (t, *J* = 7.4 Hz, 1H), 3.80 (s, 3H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.28 (q, *J* = 7.4 Hz, 2H), 1.49 (sext, *J* = 7.4 Hz,



2H), 1.36 (sext, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 153.1, 152.0, 147.0, 138.8, 133.6, 130.4, 31.8, 30.5, 30.3, 22.5, 21.8, 13.9, 13.8. IR (neat) 2957, 2932, 2872, 1697, 1651, 1589, 1491, 1464, 1404, 1375, 1354, 1340, 1298, 1236, 1101, 908, 795, 740, 727, 619 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 245 (M^++1, 19), 244 (M^+, 96), 230 (11), 229 (73), 216 (45), 215 (100), 201 (52), 200 (13), 199 (36), 187 (54), 186 (29), 185 (54), 174 (54), 173 (27), 172 (20), 171 (18), 161 (22), 159 (34), 148 (20), 134 (12). HRMS (EI) Calcd for $C_{14}H_{20}N_4$: M^+, 244.1688. Found: *m*/*z* 244.1688.

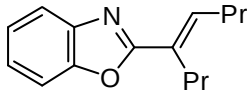
(*E*)-2-(Oct-4-en-4-yl)benzofuran (4oa). A colorless oil, R_f 0.50 (hexane–ethyl acetate = 1:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.41 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.21 (td, *J* = 7.7, 1.2 Hz, 1H), 7.16 (td, *J* = 7.4, 1.4 Hz, 1H), 6.54 (s, 1H), 6.38 (t, *J* = 7.5 Hz, 1H), 2.43 (t, *J* = 7.8 Hz, 2H), 2.23 (q, *J* = 7.4 Hz, 2H), 1.62–1.47 (m, 4H), 1.03–0.95 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 154.5, 129.8, 129.5, 129.3, 123.7, 122.5, 120.4, 110.7, 100.8, 30.2, 30.0, 22.8, 22.7, 14.2, 14.0. IR (neat) 3479, 2961, 2934, 2872, 1728, 1682, 1614, 1556, 1454, 1377, 1308, 1286, 1256, 1161, 1142, 1101, 1009, 974, 881, 810, 750 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 228 (M^+, 42), 214 (21), 201 (17), 200 (100), 186 (15), 170 (12), 159 (11). HRMS (EI) Calcd for $C_{16}H_{20}O$: M^+, 228.1514. Found: *m*/*z* 228.1513.

(*E*)-2-(Oct-4-en-4-yl)benzothiophene (4pa). A colorless oil, R_f 0.60 (hexane–ethyl acetate = 1:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.66 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.31–7.22 (m, 2H), 7.13 (s, 1H), 6.01 (t, *J* = 7.3 Hz, 1H), 2.51 (t, *J* = 7.8 Hz, 2H), 2.21 (q, *J* = 7.4 Hz, 2H), 1.62–1.45 (m, 4H), 1.02–0.94 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 140.6, 138.4, 134.0, 130.9, 124.1, 123.9, 123.0, 121.9, 118.6, 31.7, 30.6, 22.8, 22.4, 14.1, 14.0. IR (neat) 3445, 3057, 2959, 2930, 2870, 1713, 1666, 1516, 1456, 1435, 1377, 1302, 1248, 1155, 1069, 1016, 856, 824, 745, 725 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 243 (M^+–1, 17), 231 (29), 219 (20), 193 (11), 191 (41), 169 (39), 162 (10), 161 (13), 147 (19), 131 (54), 119 (47). Anal. Calcd for $C_{16}H_{20}S$; C, 78.63; H, 8.25. Found: C, 78.83; H, 8.35.

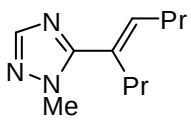
(*E*)-2-(Oct-4-en-4-yl)benzoxazole (4qa). A colorless oil, R_f 0.50 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.68 (m, 1H), 7.49–7.45 (m, 1H), 7.31–7.25 (m, 2H), 6.88 (t, *J* = 7.6 Hz, 1H), 2.63 (t, *J* = 7.8 Hz, 2H), 2.31 (q, *J* = 7.4 Hz, 2H),



1.68–1.50 (m, 4H), 1.04–0.96 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 150.4, 142.1, 138.8, 128.5, 124.6, 124.0, 119.7, 110.1, 30.6, 29.4, 22.43, 22.39, 14.0, 13.8. IR (neat) 3053, 2961, 2932, 2872, 1711, 1643, 1537, 1454, 1377, 1344, 1286, 1244, 1196, 1134, 1103, 1003, 974, 920, 906, 893, 813, 762, 745 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 229 (M^+, 38), 216 (10), 214 (25), 201 (16), 200 (92), 186 (20), 184 (12), 172 (14), 170 (18), 159 (14), 158 (11), 146 (17), 133 (10), 120 (15). Anal. Calcd for $C_{15}H_{19}NO$; C, 78.56; H, 8.35. Found: C, 78.55; H, 8.24.

(*E*)-4,5-Dimethyl-2-(oct-4-en-4-yl)thiazole (4ra). A purple oil, R_f 0.60 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (t, *J* = 7.5 Hz, 1H), 2.51 (t, *J* = 7.7 Hz, 2H), 2.31 (s, 3H), 2.30 (s, 3H), 2.18 (q, *J* = 7.4 Hz, 2H), 1.58–1.43 (m, 4H), 0.98–0.89 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 148.1, 134.5, 131.9, 124.5, 31.3, 30.5, 22.6, 22.3, 14.8, 14.01, 13.97, 11.3. IR (neat) 3434, 3366, 2961, 2930, 2872, 1708, 1680, 1551, 1528, 1461, 1431, 1377, 1308, 1034, 1115, 1034, 945, 885, 754 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 224 (M^++1, 11), 223 (M^+, 78), 218 (23), 195 (25), 194 (100), 180 (14), 178 (10), 166 (13), 165 (14), 164 (16), 153 (10). HRMS (EI) Calcd for $C_{13}H_{21}NS$: M^+, 223.1395. Found: *m/z* 223.1394.

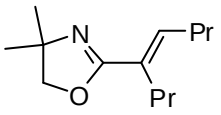
(E)-1-Methyl-5-(oct-4-en-4-yl)-1*H*-pyrazole (4sa). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 1.6 Hz, 1H), 6.05 (d, *J* = 1.6 Hz, 1H), 5.51 (t, *J* = 7.2 Hz, 1H), 3.81 (s, 3H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.48 (sext, *J* = 7.2 Hz, 2H), 1.39–1.27 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 137.8, 133.5, 130.2, 104.5, 37.1, 33.2, 30.2, 22.8, 21.6, 13.92, 13.88. IR (neat) 3216, 3192, 3115, 2961, 2932, 2871, 1655, 1614, 1466, 1418, 1377, 1279, 1173, 1134, 1011, 905, 878, 741, 716, 615 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 193 (M^++1, 24), 181 (29), 180 (11), 178 (27), 169 (28), 165 (16), 164 (100), 150 (15), 136 (14), 131 (37), 123 (10), 119 (34), 69 (76). Anal. Calcd for $C_{12}H_{20}N_2$; C, 74.95; H, 10.48. Found: C, 74.76; H, 10.43.



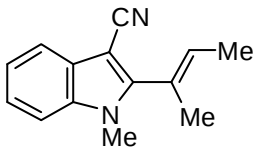
(*E*)-1-Methyl-5-(oct-4-en-4-yl)-1*H*-1,2,4-triazole (4ta). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 5.72 (t, *J* = 7.3 Hz, 1H), 3.87 (s, 3H), 2.51 (t, *J* = 7.7 Hz, 2H), 2.26 (q, *J* = 7.2 Hz, 2H), 1.52 (sext, *J* = 7.4 Hz, 2H), 1.36 (sext, *J* = 7.4 Hz, 2H),,

0.99 (t, J = 7.4 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 149.8, 136.3, 128.9, 36.5, 32.0, 30.3, 22.5, 21.7, 13.94, 13.85. IR (neat) 3458, 2959, 2932, 2872, 1651, 1503, 1418, 1377, 1279, 1173, 1134, 1109, 978, 905, 878, 741, 714, 665 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 193 (M^+, 21), 178 (24), 165 (14), 164 (100), 150 (13), 136 (13). Anal. Calcd for $C_{11}H_{19}N_3$; C, 68.35; H, 9.91. Found: C, 68.16; H, 9.98.

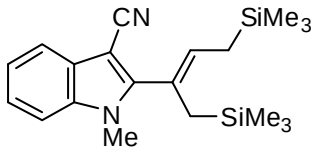
(*E*)-4,4-dimethyl-2-(oct-4-en-4-yl)-4,5-dihydrooxazole (4ua). A colorless oil, R_f 0.75 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (t, J = 7.6 Hz, 1H), 3.91 (s, 2H), 2.35 (t, J = 7.4 Hz, 2H), 2.15 (q, J = 7.6 Hz, 2H), 1.52–1.39 (m, 4H), 1.29 (s, 6H), 0.88–0.98 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 137.7, 129.1, 78.3, 67.2, 30.5, 29.6, 28.4, 22.6, 22.5, 14.1, 14.0. IR (neat) 3344, 3217, 2961, 2932, 2872, 1655, 1616, 1464, 1377, 1362, 1350, 1436, 1132, 1011, 908, 719 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 209 (M^+, 37), 194 (64), 181 (18), 180 (100), 166 (28), 152 (15), 139 (12), 81 (13), 55 (10). Anal. Calcd for $C_{13}H_{23}NO$; C, 74.59; H, 11.07. Found: C, 10.82; H, 74.59.



(*E*)-2-(But-2-en-2-yl)-1-methyl-1*H*-indole-3-carbonitrile (4bb). A colorless oil, R_f 0.75 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (ddd, J = 7.5, 1.5, 0.8 Hz, 1H), 7.36–7.24 (m, 3H), 5.95 (dt, J = 6.8, 1.5 Hz, 1H), 3.70 (s, 3H), 2.08 (q, J = 1.2 Hz, 3H), 1.91 (dq, J = 6.8, 1.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 136.1, 132.7, 127.1, 124.7, 123.2, 121.8, 119.1, 116.6, 110.0, 85.8, 31.4, 16.7, 14.4. IR (neat) 3050, 2922, 2853, 2112, 1724, 1524, 1468, 1439, 1400, 1381, 1358, 1329, 1250, 1161, 1130, 1069, 1013, 858, 823, 746 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 210 (M^+, 43), 209 (15), 195 (30), 193 (16), 183 (14), 181 (51), 169 (47), 168 (11), 155 (11), 131 (60), 119 (52), 100 (50), 69 (100), 57 (16). Anal. Calcd for $C_{14}H_{14}N_2$; C, 79.97; H, 6.71. Found: C, 79.86; H, 6.82.



(*Z*)-2-[1,4-Bis(trimethylsilyl)but-2-en-2-yl]-1-methyl-1*H*-indole-3-carbonitrile (4bc). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (ddd, J = 7.9, 1.5, 0.9 Hz, 1H), 7.26–7.13 (m, 3H), 5.67 (t, J = 8.7 Hz, 1H), 3.62 (s, 3H), 1.89 (s, 2H), 1.63 (d, J = 8.8 Hz, 2H), 0.00 (s, 9H), –0.16 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 136.2, 132.4, 127.3, 123.5, 123.1, 121.9, 119.2, 116.9, 110.0, 84.2, 31.7, 22.0, 20.8, –1.0, –1.3. IR (neat) 2953, 2895, 2212, 1738, 1715, 1626, 1522, 1508, 1468, 1435, 1495, 1358, 1329, 1250, 1165, 1142, 1109, 1061,



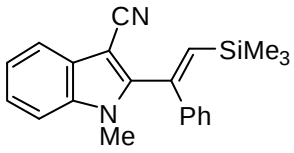
1015, 988, 841, 746, 694, 660, 502 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 355 (M^++1, 15), 354 (46), 339 (29), 283 (11), 282 (46), 281 (100), 73 (48). Anal. Calcd for $C_{20}H_{30}N_2Si_2$; C, 67.74; H, 8.53. Found: C, 67.49; H, 8.56.

(*E*)-1-Methyl-2-(4-methylpent-2-en-2-yl)-1*H*-indole-3-carbonitrile (4bd). A pale yellow solid, mp 98.5–99.0 ºC, R_f 0.50 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (ddd, *J* = 7.9, 1.4, 0.6 Hz, 1H), 7.36–7.24 (m, 3H), 5.68 (dq, *J* = 9.5, 1.5 Hz, 1H), 3.70 (s, 3H), 2.84–2.74 (m, 1H), 2.09 (d, *J* = 1.5 Hz, 3H), 1.12 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 145.7, 136.2, 127.3, 123.3, 122.0, 121.6, 119.2, 116.6, 110.1, 83.9, 31.2, 27.9, 22.3, 16.6. IR (KBr) 3042, 2958, 2863, 2206, 2158, 1950, 1911, 1790, 1693, 1651, 1607, 1576, 1522, 1452, 1404, 1399, 1327, 1246, 1231, 1161, 1130, 1121, 1099, 1067, 1001, 961, 935, 908, 854, 758, 708, 692, 664 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 238 (M^+, 40), 231 (27), 224 (11), 223 (57), 219 (22), 196 (11), 193 (13), 181 (46), 169 (45), 164 (18), 131 (52), 119 (48), 69 (100). Anal. Calcd for $C_{16}H_{18}N_2$; C, 80.63; H, 7.61. Found: C, 80.44; H, 7.64.

(E)-2-(4,4-Dimethylpent-2-en-2-yl)-1-methyl-1*H*-indole-3-carbonitrile (4be). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (ddd, *J* = 7.5, 1.3, 0.8 Hz, 1H), 7.35–7.23 (m, 3H), 5.81 (q, *J* = 1.4 Hz, 1H), 3.70 (s, 3H), 2.17 (d, *J* = 1.4 Hz, 3H), 1.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 148.2, 135.8, 127.0, 123.1, 122.4, 121.8, 119.0, 116.5, 110.0, 83.6, 33.7, 31.1, 30.4, 17.9. IR (neat) 2959, 2905, 2868, 2214, 1524, 1468, 1437, 1398, 1360, 1329, 1250, 1192, 1130, 1082, 1011, 926, 880, 745, 704, 664, 473 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 253 (M^++1, 13), 252 (68), 238 (18), 237 (100), 210 (11), 196 (21), 195 (13), 183 (12). Anal. Calcd for $C_{17}H_{20}N_2$; C, 80.91; H, 7.99. Found: C, 80.81; H, 7.99.

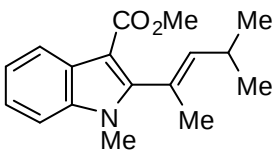
(*E*)-1-Methyl-2-[1-(trimethylsilyl)prop-1-en-2-yl]-1*H*-indole-3-carbonitrile (4bf). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.5 Hz, 1H), 7.37–7.24 (m, 3H), 5.91 (q, *J* = 1.0 Hz, 1H), 3.72 (s, 3H), 2.27 (d, *J* = 1.1 Hz, 3H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 140.6, 139.2, 136.3, 127.3, 123.6, 122.2, 119.5, 116.5, 110.3, 83.3, 31.4, 22.0, –0.3. IR (neat) 2949, 2303, 2210, 1597, 1493, 1468, 1394, 1373, 1358, 1246, 1207, 1130, 1078, 976, 880, 839, 750, 710, 687 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 269 (M^+, 16), 268 (66), 267

(43), 254 (22), 253 (100), 238 (29), 223 (29), 213 (43), 73 (19). Anal. Calcd for $C_{16}H_{20}N_2Si$; C, 71.59; H, 7.51. Found: C, 71.59; H, 7.55.

(*E*)-1-Methyl-2-(1-phenyl-2-(trimethylsilyl)ethen-2-yl)-1*H*-indole-3-carbonitrile (4bg). 

A colorless solid, mp 79.6–80.6 ºC, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.39–7.22 (m, 8H), 6.49 (s, 1H), 3.36 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.8, 144.9, 142.4, 139.9, 136.5, 128.9, 128.6, 128.4, 127.3, 123.8, 122.1, 119.6, 116.5, 110.1, 86.5, 31.6, –0.1. IR (KBr) 3059, 2955, 2895, 2205, 1560, 1470, 1387, 1358, 1323, 1248, 966, 864, 841, 770, 746, 704 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 331 (M^++1, 20), 330 (M^+, 64), 329 (35), 316 (28), 315 (100), 285 (13), 213 (32). Anal. Calcd for $C_{21}H_{22}N_2Si$; C, 76.32; H, 6.71. Found: C, 76.16; H, 6.73.

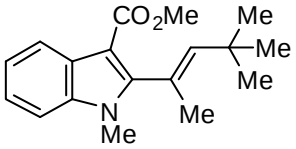
Nickel-Lewis acid catalyzed hydroheteroarylation of alkynes using a bench-stable Nickel catalyst. *General procedure.* $Ni(acac)_2$ (26 mg, 0.10 mmol), $[HPCyp_3]BF_4$ (33 mg, 0.10 mmol) and toluene (2.5 mL) were placed in a 20 mL Schlenk tube. To the suspension was added a 1.03 M solution of $AlMe_3$ in hexane (0.39 mL, 0.40 mmol) dropwise, and then the resulting black suspension was stirred for additional 5 min. Heteroarene (1.0 mmol) and alkyne (1.5 mmol) were added sequentially, and the mixture was stirred at 35 ºC for the time listed in Tables 4 and 5. The mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified on flash column chromatography on silica gel to give the corresponding hydroheteroarylation products in yields listed in Tables 4 and 5.

Methyl (*E*)-1-methyl-2-(4-methylpent-2-en-2-yl)-1*H*-indole-3-carboxylate (4cd). 

A colorless solid, mp 96.5–97.5 ºC, R_f 0.35 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.13 (m, 1H), 7.33–7.20 (m, 3H), 5.32 (dq, *J* = 9.4, 1.6 Hz, 1H), 3.86 (s, 3H), 3.65 (s, 3H), 2.87–2.74 (m, 1H), 2.00 (d, *J* = 1.6 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 150.1, 141.5, 136.1, 126.4, 124.1, 122.1, 121.7, 121.5, 109.5, 103.3, 50.6, 30.1, 27.7, 22.5, 17.2. IR (KBr) 3057, 5957, 2926, 2866, 1888, 1767, 1690, 1576, 1514, 1464, 1441, 1391, 1363, 1331, 1271, 1229, 1198, 1157, 1136, 1103, 1017, 999, 961, 928, 885, 858, 816, 789, 750, 729, 698, 685, 652, 586, 554, 503, 473, 434 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 271 (M^+, 46), 229 (16),

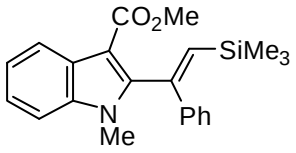
228 (100), 213 (12) 212 (38), 197 (14), 196 (21), 182 (15), 181 (11). Anal. Calcd for $C_{17}H_{21}NO_2$; C, 75.25; H, 7.80. Found: C, 75.26; H, 7.81.

Methyl (*E*)-1-methyl-2-(4,4-dimethylpent-2-en-2-yl)-1*H*-indole-3-carboxylate (4ce).



A colorless solid, mp 99.5–100.0 ºC, R_f 0.33 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.20 (m, 1H), 7.32–7.21 (m, 3H), 5.48 (q, *J* = 1.6 Hz, 1H), 3.86 (s, 3H), 3.65 (s, 3H), 2.09 (d, *J* = 1.6 Hz, 3H), 1.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 151.3, 143.8, 135.9, 126.4, 125.7, 122.1, 121.6, 121.4, 109.4, 102.7, 50.5, 33.1, 30.5, 29.9, 18.4. IR (KBr) 3055, 2982, 2961, 2930, 2903, 2866, 1923, 1886, 1850, 1802, 1690, 1653, 1611, 1580, 1514, 1464, 1437, 1391, 1364, 1331, 1273, 1254, 1234, 1200, 1184, 1163, 1157, 1134, 1103, 1024, 1009, 963, 926, 880, 843, 812, 791, 770, 752, 737, 698, 691, 652, 596, 556, 505, 475, 449, 413 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 285 (M^+, 12), 229 (25), 228 (100), 196 (11). Anal. Calcd for $C_{18}H_{23}NO_2$; C, 75.76; H, 8.12. Found: C, 75.77; H, 8.03.

Methyl (*E*)-1-methyl-2-(1-trimethylsilyl-2-phenylethen-2-yl)-1*H*-indole-3-carboxylate (4cg).



A colorless solid, mp 126.5–127.5 ºC, R_f 0.30 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.17 (m, 1H), 7.32–7.23 (m, 8H), 6.05 (s, 1H), 3.78 (s, 3H), 3.57 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 149.1, 147.6, 140.5, 139.0, 136.2, 128.6, 127.9, 127.7, 126.6, 122.5, 121.8, 121.7, 109.5, 104.1, 50.6, 30.7, 0.32. IR (KBr) 3055, 3023, 2922, 2870, 1946, 1879, 1807, 1757, 1699, 1599, 1493, 1456, 1441, 1408, 1379, 1372, 1155, 1072, 1030, 1003, 991, 966, 910, 849, 785, 758, 746, 700, 658, 583, 523 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 331 (23), 330 (68), 329 (35), 316 (28), 315 (100), 285 (13), 213 (31), 69 (14). Anal. Calcd for $C_{22}H_{25}NO_2Si$; C, 72.69; H, 6.93. Found: C, 72.57; H, 6.75.

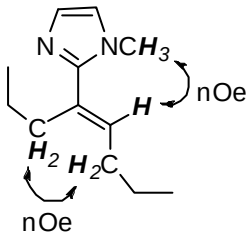
KIE Experiment. In a glove box, a solution of $Ni(cod)_2$ (2.5 mg, 9.0 μmol) and $PCyp_3$ (2.1 mg, 9 μmol) in toluene (1.5 mL) were added to a solution of **1b** (47 mg, 0.30 mmol) placed in a 3 mL-vial. In another vial were placed the same catalyst and **1b**-d_1 in equimolar amounts. To each vial were added 4-octyne (33.0 mg, 0.3 mmol) and dodecane (internal standard, 26 mg, 0.15 mmol). The two vials were closed with screw caps, taken out from the glove box and heated at 35 ºC. Aliquots of the reaction mixtures were taken from each vial and analyzed by GC to monitor the reaction in each

vial. The set of experiments was repeated additionally twice and the average yields for three sets were calculated and plotted in Figure 1.

Deuterium crossover experiment. In a glove box, a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and $PCyp_3$ (24 mg, 0.10 mmol) in toluene (2.5 mL) was placed in a 3 mL-vial. Then, **1b**-d_1 (134 mg, 0.50 mmol), **1c** (150 mg, 0.50 mmol), and 4-octyne (110 mg, 1.00 mmol) were added. The vial was closed with a screw cap, taken out of the glove box and heated at 35 ºC for 20 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give a mixture of **4ba**-d_1 and **4ca** (220 mg, 50% of **4ba**-d_1 and 33% of **4ca** based on **2a** as estimated by ^{1}H NMR analysis).

Nickel-Lewis acid catalyzed hydroheteroarylation of alkynes with imidazoles. *General procedure.* In a glove box, a solution of $Ni(cod)_2$ (8.2 mg, 30 μmol) and P(*t*-Bu)$_3$ (24 mg, 0.12 mmol) in toluene (0.38 mL) was put into a 3 mL-vial. A solution of imidazole (3.0 mmol), a Lewis acid [60 μmol, $AlMe_3$: 58 μL (a 1.03 M solution in hexane); $ZnMe_2$: 60 μL (a 1.00 M solution in hexane)], and an alkyne (1.0 mmol) in toluene (0.3 mL) was added. After addition of undecane (internal standard, 78 mg, 0.5 mmol), the vial was closed with a screw cap, taken out from the glove box and heated at 100 ^{o}C for the time specified in Tables 6–9. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding products in yields listed in Tables 6–9. In some cases, *E*- and *Z*-isomers of the products were separated by preparative recycling GPC or silica gel chromatography.

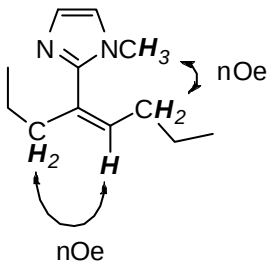
(*E*)-1-Methyl-2-(oct-4-en-4-yl)-1*H*-imidazole [(*E*)-6aa, *E*/*Z* = 95:5]. A colorless oil,



R_f 0.20 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 1.1 Hz, 0.05H), 7.00 (d, *J* = 1.1 Hz, 0.95H), 6.86 (d, *J* = 1.1 Hz, 0.05H), 6.81 (d, *J* = 1.1 Hz, 0.95H), 5.74 (t, *J* = 7.3 Hz, 0.05 Hz), 5.57 (t, *J* = 7.3 Hz, 0.95 Hz), 3.63 (s, 2.85 H), 3.52 (s, 0.15H), 2.52 (t, *J* = 7.7 Hz, 1.90H), 2.32 (t, *J* = 7.7 Hz, 0.10H), 2.21 (q, *J* = 8.1 Hz, 1.90H), 1.80 (q, *J* = 8.1 Hz, 0.10H), 1.49 (sext, *J* = 7.3 Hz, 2H), 1.35 (sext, *J* = 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR [for (*E*)-**3aa**, 101 MHz, $CDCl_3$] δ 149.5, 133.7, 130.7, 127.2, 120.7, 34.1, 32.4, 30.3, 22.8, 21.9, 14.01, 13.98. IR (neat) 2959, 2932, 2870, 1421, 1406, 1377, 1281, 1134, 984, 914, 901, 822, 721, 664 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 192 (M^+, 35), 177

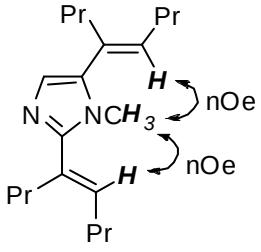
(25), 164 (15), 163 (100), 149 (15), 147 (19), 135 (14), 134 (11), 133 (16), 121 (11), 96 (13), 85 (10), 83 (12), 71 (12), 69 (10), 57 (17), 55 (12). Anal. Calcd for $C_{12}H_{20}N_2$: C, 74.95; H, 10.48. Found: C, 74.83; H, 10.23.

(*Z*)-1-Methyl-2-(oct-4-en-4-yl)-1*H*-imidazole [(*Z*)-6aa, *E*/*Z* = 1: >99] A colorless oil,



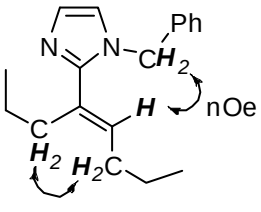
R_f 0.20 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 1.1 Hz, 1H), 6.85 (d, *J* = 1.1 Hz, 1H), 5.73 (tt, *J* = 7.3, 1.2 Hz, 1H), 3.51 (s, 3H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.78 (q, *J* = 7.4 Hz, 2H), 1.362 (sext, *J* = 7.4 Hz, 2H), 1.358 (sext, *J* = 7.4 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H). HRMS (EI) Calcd for $C_{12}H_{20}N_2$: M^+ 192.1626. Found: *m*/*z* 192.1617.

2,5-Bis(oct-4-en-4-yl)-1-methyl-1*H*-imidazole (6'aa, *EE*/*others* = 96:4) A colorless



oil, R_f 0.50 (hexane–ethyl acetate = 1:1). ^{1}H NMR [for (*EE*)-**3'aa**, 400 MHz, $CDCl_3$] δ 6.83 (s, 1H), 5.61 (t, *J* = 7.3 Hz, 1H), 5.51 (t, *J* = 7.3 Hz, 1H), 3.48 (s, 3H), 2.51 (t, *J* = 7.7 Hz, 2H), 2.36–2.14 (m, 6H), 1.48 (sext, *J* = 7.4 Hz, 4H), 1.37 (sext, *J* = 7.4 Hz, 4H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR [for (*EE*)-**3'aa**, 101 MHz, $CDCl_3$)] δ 150.3, 135.8, 133.8, 132.4, 131.3, 129.7, 125.2, 33.4, 33.1, 32.5, 30.5, 30.4, 23.0, 22.9, 22.1, 21.9, 14.2 (2C), 14.12, 14.06. IR (neat) 2959, 2930, 2870, 1456, 1389, 1377, 1103, 899, 818, 731 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 303 (M^++1, 19), 302 (M^+, 59), 289 (29), 288 (11), 287 (47), 274 (49), 273 (100), 271 (16), 261 (18), 259 (24), 247 (29), 245 (12), 217 (12), 215 (17). HRMS (EI) Calcd for $C_{20}H_{34}N_2$: M^+ 302.2722. Found: *m*/*z* 302.2737.

1-Benzyl-2-(oct-4-en-4-yl)-1*H*-imidazole (6ba, *E*/*Z* = 97:3) A colorless oil, R_f 0.30



(hexane–ethyl acetate = 1:1). ^{1}H NMR [for (*E*)-**3ba**, (400 MHz, $CDCl_3$] δ 7.36–7.26 (m, 3H), 7.12–7.00 (m, 3H), 6.82 (d, *J* = 1.2 Hz, 1H), 5.74 (t, *J* = 7.2 Hz, 0.03H), 5.51 (t, *J* = 7.2 Hz, 0.97H), 5.15 (s, 2H), 2.49 (t, *J* = 7.6 Hz, 2H), 2.16 (q, *J* = 7.4 Hz, 2H), 1.48–1.26 (m, 4H), 0.92–0.84 (m, 6H); ^{13}C NMR [for (*E*)-**3ba**, 101 MHz, $CDCl_3$] δ 149.9, 137.1, 133.9, 130.6, 128.6, 127.7, 127.5, 126.4, 120.0, 50.1, 32.7, 30.3, 22.7, 21.9, 14.1, 13.9. IR (neat) 2959, 2930, 1497, 1456, 1420, 1375, 1362, 1279, 1117, 909, 729, 649 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 269 (M^++1, 11), 268 (M^+, 50),

253 (23), 240 (27), 239 (100), 226 (15), 225 (59), 177 (37), 133 (12), 119 (10), 91 (53). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01. Found: C, 80.30; H, 8.80.

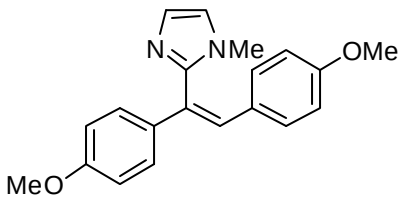
(*E*)-2-(Oct-4-en-4-yl)-1-phenyl-1*H*-imidazole (6ca) A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.33 (m, 3H), 7.29–7.23 (m, 2H), 7.11 (d, *J* = 1.3 Hz, 1H), 6.99 (d, *J* = 1.3 Hz, 1H), 5.38 (t, *J* = 7.4 Hz, 1H), 2.33 (t, *J* = 7.7 Hz, 2H), 2.00 (q, *J* = 7.3 Hz, 2H), 1.40 (sext, *J* = 7.5 Hz, 2H), 1.19 (sext, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.3 Hz, 3H), 0.75 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR 101 MHz, $CDCl_3$) δ 148.8, 138.9, 135.3, 129.8, 129.1, 127.7, 127.6, 125.6, 121.6, 31.7, 30.3, 22.5, 22.2, 14.2, 13.9. IR (neat) 2959, 2930, 2870, 1684, 1599, 1499, 1456, 1418, 1377, 1300, 1120, 1126, 1099, 1072, 899, 845, 766, 743, 719, 694 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 254 (M^+, 26), 239 (27), 226 (19), 225 (100), 211 (19), 209 (14), 197 (12), 195 (18), 182 (10), 169 (15), 85 (10), 77 (14), 71 (13), 69 (10), 57 (18), 55 (10). Anal. Calcd for $C_{17}H_{22}N_2$: C, 80.27; H, 8.72. Found: C, 80.12; H, 8.75.

(*E*)-2-(Oct-4-en-4-yl)-1-methyl-4-phenyl-1*H*-imidazole (**6da**). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.34 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.20 (tt, *J* = 7.0, 1.4 Hz, 1H), 7.11 (s, 1H), 5.62 (t, *J* = 7.3 Hz, 1H), 3.65 (s, 3H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.25 (q, *J* = 7.4 Hz, 2H), 1.50 (sext, *J* = 7.5 Hz, 2H), 1.40 (sext, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 139.9, 134.30, 134.26, 130.8, 128.3, 126.2, 124.7, 116.5, 34.1, 32.8, 30.4, 22.8, 22.0, 14.1 (2C). IR (neat) 2959, 2930, 2870, 1719, 1686, 1609, 1497, 1456, 1437, 1397, 1377, 1339, 1194, 945, 909, 748, 731, 694 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 269 (M^++1, 14), 268 (M^+, 62), 239 (32), 212 (20), 211 (56), 210 (11), 209 (30), 200 (34), 199 (20), 198 (40), 197 (31), 196 (13), 195 (12), 186 (14), 185 (100), 184 (21), 183 (19), 136 (17). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01. Found: C, 80.62; H, 9.06.

(*Z*)-2-(1,2-Diphenylethenyl)-1-methyl-1*H*-imidazole (6ah). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 6H), 7.23–7.14 (m, 4H), 6.90 (d, *J* = 1.3 Hz, 1H), 6.88–6.83 (m, 2H), 3.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6, 140.0, 136.1, 132.8 (2C), 130.6, 128.8, 128.4, 128.3, 127.8, 127.6, 126.4, 120.5, 32.8. IR (neat) 3059, 3021, 2947, 2205, 1493, 1454, 1443, 1404, 1281, 1134, 1078, 1032, 910, 766, 731, 710, 694, 640,

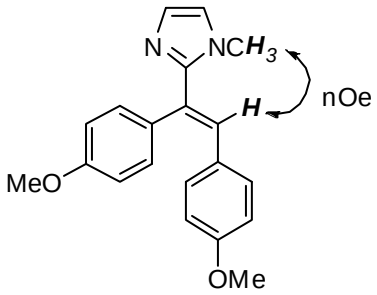
602, 557, 513 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 261 (M^++1, 11), 260 (M^+, 88), 259 (100), 243 (29), 189 (13), 183 (25). HRMS (EI) Calcd for $C_{18}H_{16}N_2$: M^+ 260.1313. Found: *m*/*z* 260.1319.

(*Z*)-2-[1,2-bis(4-methoxyphenyl)ethenyl]-1-methyl-1*H*-imidazole [(Z)-6ai]. A



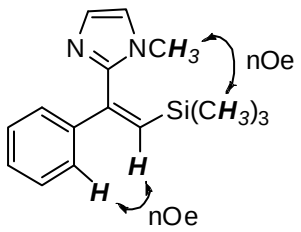
colorless oil, R_f 0.60 (CH_2Cl_2–acetone = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 1.1 Hz, 1H), 7.15 (s, 1H), 6.91 (d, *J* = 1.1 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 2H), 6.78–6.71 (m, 4H), 3.81 (s, 3H), 3.77 (s, 3H), 3.19 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 158.7, 146.1, 132.9, 130.6, 129.6, 129.2, 128.8, 127.9, 127.4, 120.3, 113.81, 113.79, 55.4, 55.2, 32.8. IR (neat) 3001, 2953, 2936, 2835, 1711, 1607, 1572, 1514, 1454, 1416, 1404, 1300, 1281, 1250, 1179, 1132, 1115, 1032, 912, 833, 731, 536 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 321 (M^+, 28), 320 (M^+, 100), 305 (15), 304 (19), 276 (13), 275 (12), 261 (11), 213 (29). HRMS (EI) Calcd for $C_{20}H_{20}N_2O_2$: M^+ 320.1525. Found: *m*/*z* 320.1521.

(*E*)-2-[1,2-Bis(4-methoxyphenyl)ethenyl]-1-methyl-1*H*-imidazole [(*E*)-6ai]. A



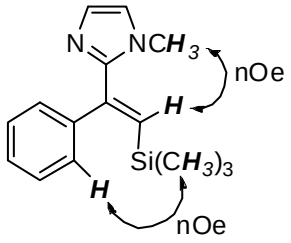
colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.07 (s, 1H), 7.06 (s, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.83 (s, 1H), 6.70 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H), 3.77 (s, 3H), 3.21 (s, 3H). HRMS (EI) Calcd for $C_{20}H_{20}N_2O_2$: M^+ 320.1525. Found: *m*/*z* 320.1514.

(*Z*)-2-[1-Phenyl-2-(trimethylsilyl)ethenyl]-1-methyl-1*H*-imidazole [(Z)-6ag)]. A



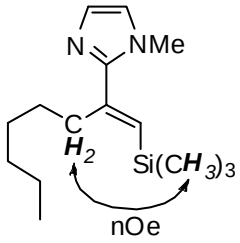
colorless oil, R_f 0.50 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 7.09 (d, *J* = 1.3 Hz, 1H), 6.88 (d, *J* = 1.3 Hz, 1H), 6.66 (s, 1H), 3.26 (s, 3H), –0.06 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 145.4, 140.3, 137.1, 128.3, 128.0, 127.9, 126.0, 120.4, 32.1, –0.8. IR (neat) 3057, 2951, 2895, 1591, 1572, 1495, 1481, 1445, 1404, 1281, 1246, 1130, 932, 903, 862, 837, 764, 739, 702 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 242 (22), 241 (M^+–Me, 100), 73 (10). Anal. Calcd for $C_{15}H_{20}N_2Si$: C, 70.26; H, 7.86. Found: C, 70.36; H, 7.66.

(*E*)-2-[1-Phenyl-2-(trimethylsilyl)ethenyl]-1-methyl-1*H*-imidazole [(*E*)-6ag)]. A

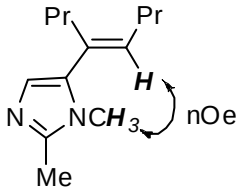


colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.37–7.21 (m, 5H), 7.01 (d, *J* = 1.1 Hz, 1H), 6.77 (d, *J* = 1.1 Hz, 1H), 6.48 (s, 1H), 3.20 (s, 3H), –0.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 146.3, 140.6, 136.5, 128.8, 128.0, 127.9, 127.7, 122.3, 34.6, 0.2. IR (neat) 2953, 2895, 1586, 1570, 1493, 1462, 1443, 1402, 1281, 1248, 1207, 1140, 1074, 937, 899, 860, 835, 785, 752, 704, 667 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 242 (23), 241 (M^+–Me, 100), 73 (14). Anal. Calcd for $C_{15}H_{20}N_2Si$: C, 70.26; H, 7.86. Found: C, 69.97; H, 7.88.

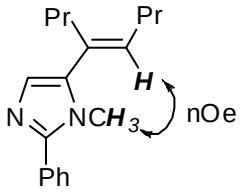
(*E*)-1-methyl-2-[1-(trimethylsilyl)octen-2-yl]-1*H*-imidazole (6aj). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.78 (s, 1H), 5.54 (s, 1H), 3.60 (s, 3H), 2.60 (t, *J* = 7.7 Hz, 2H), 1.35–1.13 (m, 8H), 0.82 (t, *J* = 6.8 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.7, 147.7, 123.0, 127.1, 121.3, 36.1, 34.2, 31.7, 29.45, 29.38, 22.6, 14.1, 0.2. IR (neat) 2955, 2928, 2857, 1607, 1508, 1458, 1404, 1339, 1279, 1248, 1142, 914, 860, 839, 777, 750, 729, 619 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 250 (21), 249 (M^+–Me, 100), 193 (11), 191 (16), 179 (28), 149 (19). Anal. Calcd for $C_{15}H_{28}N_2Si$: C, 68.12; H, 10.67. Found: C, 68.26; H, 10.39.



(*E*)-1,2-Dimethyl-5-(oct-4-en-4-yl)-1*H*-imidazole (**6ea**). A colorless oil, R_f 0.10 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (s, 1H), 5.43 (t, *J* = 7.3 Hz, 1H), 3.41 (s, 3H), 2.36 (s, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.15 (q, *J* = 7.3 Hz, 2H), 1.44 (sext, *J* = 7.3 Hz, 2H), 1.33 (sext, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 134.9, 132.4, 129.6, 124.6, 33.3, 31.2, 30.3, 23.0, 21.8, 14.00, 13.99, 13.8. IR (neat) 3198, 2959, 2932, 2872, 1740, 1506, 1458, 1437, 1400, 1375, 1242, 1047, 812 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 207 (M^++1, 11), 206 (M^+, 67), 205 (14), 197 (10), 178 (17), 177 (100), 149 (11), 147 (11), 136 (48), 121 (11), 95 (11), 56 (11). HRMS (EI) Calcd for $C_{13}H_{22}N_2$: M^+ 206.1783. Found: *m/z* 206.1775.

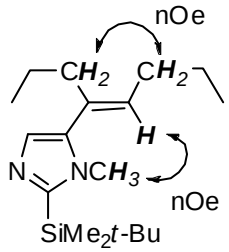


(*E*)-1-Methyl-5-(oct-4-en-4-yl)-2-phenyl-1*H*-imidazole (**6fa**). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.61 (m, 2H), 7.49–7.35 (m, 3H), 6.96 (s, 1H), 5.58 (t, *J* = 7.3 Hz, 1H), 3.60 (s, 3H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.21 (q, *J* = 7.3 Hz, 2H), 1.56–1.36 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J*

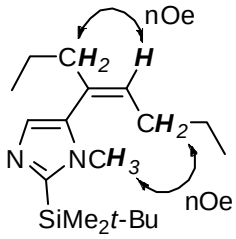


= 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 137.0, 133.0, 131.0, 129.5, 128.5, 128.3, 128.2, 126.4, 33.7, 33.2, 30.4, 23.0, 21.9, 14.1 (2C). IR (neat) 2957, 2930, 2870, 1605, 1508, 1464, 1433, 1387, 1074, 1024, 936, 899, 820, 771, 698 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 268 (M^+, 42), 253 (24), 240 (22), 239 (100), 209 (14). HRMS (EI) Calcd for $C_{18}H_{24}N_2$: M^+ 268.1939. Found: *m/z* 268.1937.

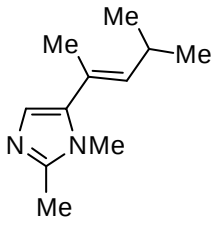
2-(*Tert*-butyldimethylsilyl)-1-methyl-5-(oct-4-en-4-yl)-1*H*-imidazole [(*E*)-6ga, *E*/Z = 96:4]. A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR [for (*E*)-**6ga**, 400 MHz, $CDCl_3$] δ 6.98 (s, 1H), 5.45 (t, *J* = 7.3 Hz, 1H), 3.60 (s, 3H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.17 (q, *J* = 7.5 Hz, 2H), 1.46 (sext, *J* = 7.4 Hz, 2H), 1.32 (sext, *J* = 7.5 Hz, 2H), 0.963 (t, *J* = 7.5 Hz, 3H), 0.957 (s, 9H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.40 (s, 6H); ^{13}C NMR [for (*E*)-**3ga**, 101 MHz, $CDCl_3$] δ 149.8, 137.5, 133.2, 129.5, 128.3, 33.6, 33.3, 30.4, 26.8, 23.0, 21.8, 18.1, 14.1, 14.0, -4.5. IR (neat) 3113, 2957, 2930, 2857, 1497, 1464, 1377, 1360, 1252, 1111, 1007, 1063, 1007, 897, 833, 772, 664, 650 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 306 (M^+, 83), 251 (21), 250 (69), 249 (M^+-*t*-Bu, 100), 221 (24), 207 (13), 192 (13), 191 (12), 163 (20), 113 (15), 85 (14), 83 (13), 75 (21), 71 (18), 69 (16), 57 (28), 56 (13), 55 (19). HRMS (EI) Calcd for $C_{18}H_{34}N_2Si$: M^+ 306.2491. Found: *m/z* 306.2484.



(*Z*)-2-(*Tert*-butyldimethylsilyl)-1-methyl-5-(oct-4-en-4-yl)-1*H*-imidazole [(*Z*)-6ga, *E*/*Z* = 5:95]. A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR [for (*Z*)-**3ga**, 400 MHz, $CDCl_3$] δ 6.92 (s, 1H), 5.68 (t, *J* = 7.4 Hz, 1H), 3.51 (s, 3H), 2.17 (t, *J* = 7.6 Hz, 2H), 1.77 (q, *J* = 7.4 Hz, 2H), 1.42–1.24 (m, 4H), 0.94 (s, 9H), 0.88 (t, *J* = 7.3 Hz, 3H), 0.83 (t, *J* = 7.3 Hz, 3H), 0.41 (s, 6H). HRMS (EI) Calcd for $C_{18}H_{34}N_2Si$: M^+ 306.2491. Found: *m/z* 306.2488.

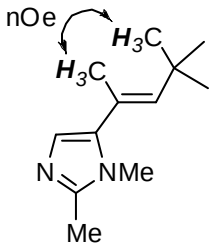


(*E*)-1,2-Dimethyl-5-(4-methylpent-2-en-2-yl)-1*H*-imidazole (6ed). A colorless oil, R_f 0.30 (CH_2Cl_2–methanol = 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 5.29 (dq, *J* = 9.2, 1.3 Hz, 1H), 3.44 (s, 3H), 2.72–2.56 (m, 1H), 2.36 (s, 3H), 1.91 (d, *J* = 1.4 Hz, 3H), 1.02 (d, *J* = 8.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 138.9, 136.0, 123.9, 122.1, 31.5, 27.7, 22.9, 17.2, 13.7. IR (neat) 3381, 2957, 2928, 2868, 1645, 1541, 1501, 1464, 1433, 1402, 1383, 1180, 1153, 988, 872, 810, 673, 550 cm^{-1}. MS (EI,



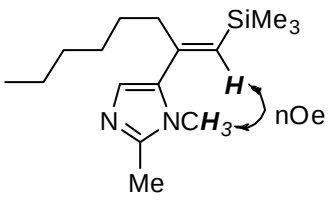
70 eV) *m/z* (%) 179 (M^++1, 11), 178 (M^+, 87), 177 (28), 164 (13), 163 (100), 149 (10) 123 (12), 122 (52), 121 (10), 108 (10), 107 (13), 93 (13), 81 (18), 56 (22), 55 (10). HRMS (EI) Calcd for $C_{11}H_{18}N_2$: M^+ 178.1470. Found: *m/z* 178.1463.

(*E*)-1,2-Dimethyl-5-(4,4-dimethylpent-2-en-2-yl)-1*H*-imidazole (6ee). A colorless oil,



R_f 0.30 (CH_2Cl_2–methanol = 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (s, 1H), 5.48 (q, *J* = 1.5 Hz, 1H), 3.43 (s, 3H), 3.36 (s, 3H), 2.01 (d, *J* = 1.5 Hz, 3H), 1.20 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ144.4, 142.2, 137.6, 123.7, 123.5, 32.9, 31.1, 30.8, 18.5, 13.7. IR (neat) 3381, 2955, 2866, 1636, 1541, 1497, 1464, 1433, 1402, 1362, 1233, 1146, 988, 812, 673, 550 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 192 (M^+, 63), 178 (13), 177 (100), 136 (26), 122 (10), 121 (16), 95 (16), 56 (16). HRMS (EI) Calcd for $C_{12}H_{20}N_2$: M^+ 192.1626. Found: *m/z* 192.1618.

(*E*)-1,2-Dimethyl-4-[1-(trimethylsilyl)octen-2-yl]-1*H*-imidazole (6ei). A colorless oil,



R_f 0.35 (CH_2Cl_2–methanol = 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81(s, 1H), 5.41 (s, 1H), 3.48 (s, 3H), 2.44–2.36 (m, 5H), 1.40–1.18 (m, 8H), 0.87 (t, *J* = 7.1 Hz, 3H), 0.19 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 145.7, 135.5, 128.9, 124.9, 37.0, 31.7, 29.7, 29.4, 22.6, 14.1, 13.9, 0.4. IR (neat) 2953, 2928, 2857, 1597, 1533, 1466, 1400, 1248, 860, 837, 775, 750, 691, 671 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 278 (M^+, 12), 263 (20), 221 (18), 209 (10), 208 (44), 207 (53), 205 (19), 194 (18), 193 (100), 192 (15), 191 (46), 153 (16), 73 (21). Anal. Calcd for $C_{16}H_{30}N_2Si$: C, 69.00; H, 10.86. Found: C, 68.76; H, 10.77.

References and notes:

(1) (a) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*, Wiley-VCH, Weinheim, 1996, Chapters 2, 4, 8 and 33. (b) Nicolaou, K. C.; Snyder, S. A. *Classics in Total Synthesis II*, Wiley-VCH, Weinheim, 2003, Chapters 8, 12, 18, 19, 20 and 33.

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Chapter 4

Hydroheteroarylation of Alkynes with Pyridine-*N*-oxides, Pyridines, and Pyridones

Pyridine-*N*-oxides are found to add across alkynes by nickel(0) catalysis to give C(2)-alkenylated pyridine-*N*-oxide derivatives regioselectively in modest to high yields. Couse of a Lewis acid (LA) catalyst allows direct activation of C(2)–H bonds of parent pyridine nucleus and insertion of alkynes to afford C(2)-alkenylated pyridines under mild conditions. The reaction possibly proceeds through a pyridinium species generated *catalytically in situ* by coordination of pyridine nitrogen to a LA catalyst. Regioselective C(6)-alkenylation of 2-pyridone derivatives is also achieved by the nickel(0)/LA binary catalysis possibly through a similar reactive pyridinium species generated by coordination of their carbonyl group to a LA catalyst. The catalysis is applicable to a diverse range of pyridine-*N*-oxides, pyridines and 2-pyridones to afford *cis*-hydroheteroarylation products in chemo-, stereo-, and regioselective manners to give heteroaryl-substituted ethenes having a larger substituent *trans* to the heteroaryl group.

Introduction

In view of the prevalence of an azine nucleus in pharmaceuticals, functional materials and natural products, development of a new and efficient methodology to derivatize the azine nucleus is becoming an important issue in organic synthesis.[1] However, due to the electron-deficiency of azines towards aromatic electrophilic substitution reactions such as the Friedel-Crafts reaction, most of the synthetic methods to functionalize azines require preactivation, for example, halogenation or metalation, before subsequent transformations to introduce substituents. In addition, azines bearing a metal adjacent to nitrogen pose problems in cross-coupling reactions due to their instability and difficulty in synthesis.[2] Alternatively, transition metal-catalyzed C–H bond activation[3] and direct installation of carbonaceous groups has emerged as a new protocol for functionalization of azine derivatives. Although direct catalytic alkylation,[4] acylation,[5] and arylation[6] of azines have been achieved, direct alkenylation[7] by reacting azines with unactivated alkynes has remained elusive.[8] Accordingly, development of new reactions which allow for C–H bond activation and direct alkenylation of the azine nucleus is highly desired.

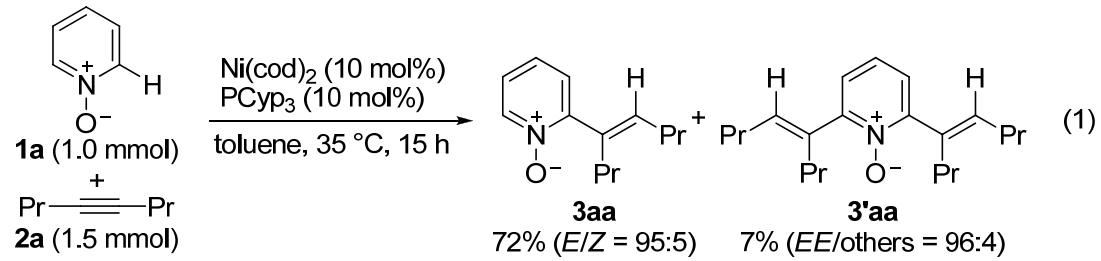
Described in this Chapter is the alkenylation of azines by nickel catalysis. First described is C(2)-alkenylation of activated pyridines,[9] namely, pyridine-*N*-oxides through activation of the C(2)–H bond followed by regioselective insertion of alkynes in the presence of a nickel(0)/$PCyp_3$ catalyst.[10] Deoxygenative functionalization of the adducts is demonstrated by allylation[11] and transfer of the oxygen moiety.[12] The author further describes direct addition of pyridines across alkynes through a similarly active pyridinium species generated catalytically *in situ* by coordination of pyridine nitrogen to a Lewis acid (LA) catalyst.[13] Whereas use of diorganozinc compounds as the LA catalyst gives C(2)-monoalkenylation products, $AlMe_3$ changes the reaction course to afford C(2)-dienylated products via double insertion of alkynes into the C(2)–H bond. Lastly, the author describes C(6)-alkenylation of 2-pyridone derivatives[14] by similar nickel(0)/LA binary catalysis possibly through a reactive pyridinium species generated *in situ* by coordination of their carbonyl group to the LA catalyst.[15] The reactions demonstrate a broad scope of pyridine-*N*-oxides, pyridines, 2-pyridones and alkynes, and proceed with high chemo-, regio- and stereoselectivity to give the corresponding heteroaryl-substituted ethenes having a larger substituent *trans* the heteroaryl group

under mild conditions compared to previously reported examples of direct C–H functionalization of respective azines.[4–8]

Results and discussion

Hydroheteroarylation of alkynes with pyridine-*N*-oxides

The reaction of pyridine-*N*-oxide (**1a**, 1.0 mmol) with 4-octyne (**2a**, 1.5 mmol) in the presence of a nickel catalyst prepared from $Ni(cod)_2$ (10 mol%) and $PCyp_3$ (10 mol%) in toluene at 35 ºC for 15 h proceeded to give (*E*)-2-(oct-4-en-4-yl)pyridine-*N*-oxide [(*E*)-**3aa**] in 72% isolated yield (Eq. 1). When the catalyst amount was decreased to 1–5 mol%, yield of **3aa** was much lower (37%–55% by ^{1}H NMR) even after 24 h. Adduct (*E*)-**3aa** was contaminated by a small amount of a *Z*-isomer produced most probably by isomerization of the initial *cis*-adduct. Indeed, ^{1}H NMR analysis of the reaction mixture showed gradual formation of (*Z*)-**3aa** during the reaction course. Thus, the *E*/*Z* ratio of **3aa** at 2 h was 98:2. A mixture of stereoisomers of 2,6-dialkenylated product **3'aa** was also obtained in 7% yield. On the other hand, parent pyridines never participate in this transformation under these conditions even at elevated temperatures.

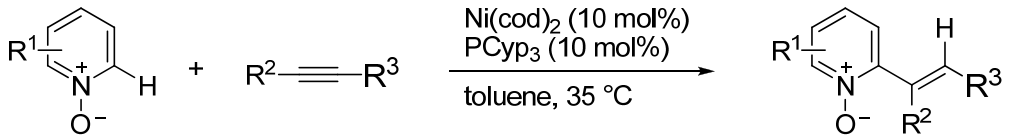


(1)

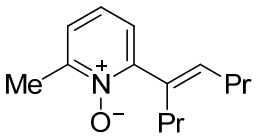
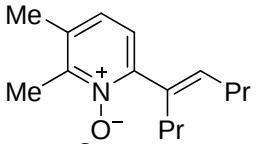
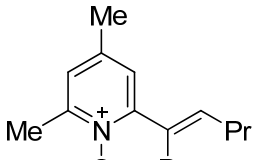
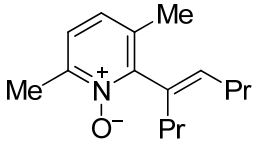
The present conditions were applicable to a diverse range of pyridine-*N*-oxides (Table 1). The addition of 2-picoline-*N*-oxide (**1b**) across **2a** gave a 93:7 (*E*/*Z*) mixture of 2-alkenylated product **3ba** in 67% yield (entry 1). Analogous results were obtained with 3- and 4-methylpicoline-*N*-oxides (**1c** and **1d**) (entries 2 and 3). However, no trace amount of a stereoisomer was observed from 5-methylpicoline-*N*-oxide (**1e**), probably owing to a steric hindrance caused by the 5-methyl group to exhibit the isomerization (entry 4). Whereas the ester functionality of 5-methoxycarbonyl-2-picoline-*N*-oxide (**1f**) tolerated the present reaction conditions to give the corresponding adduct **3fa** in high yield (entry 5), Cl, Br, and NO_2 groups did not. Isoquinoline-*N*-oxide (**1g**) also reacted

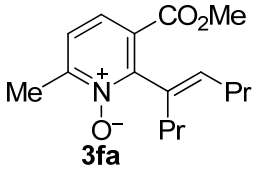
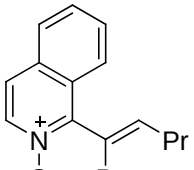
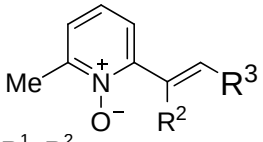
with **2a** selectively at the C-1 position (entry 6). The regioselectivity observed in this case implies that the reactivity may be controlled by acidity of C–H rather than steric reasons, since the benzylic C(1)–H bond next to the nitrogen atom is more acidic than C(3)–H bond. Hydroheteroarylation of 4-methyl-2-pentyne (**2b**) and 4,4-dimethyl-2-pentyne (**2c**) with **1b** also proceeded smoothly to give the respective adducts with excellent regio- and stereoselectivities, that a bulkier substituent is located *trans* to the pyridyl ring (entries 7 and 8). Terminal alkynes such as 1-octyne and phenylacetylene failed to participate in the reaction due to their rapid oligomerization under the reaction conditions.

Table 1. Nickel-catalyzed hydroheteroarylation of alkynes with pyridine-*N*-oxides.



1 (1.0 mmol) **2** (1.5 mmol) **3**

Entry	**1**	**2**	Time (h)	Major product (**3**)	Yield,[a] *E*/*Z*[b]
1	**1b**	**2a**	15	 **3ba**	67%, 93:7
2	**1c**	**2a**	22	 **3ca**	59%, 97:3
3	**1d**	**2a**	22	 **3da**	54%, 94:6
4	**1e**	**2a**	40	 **3ea**	66%, >99:1

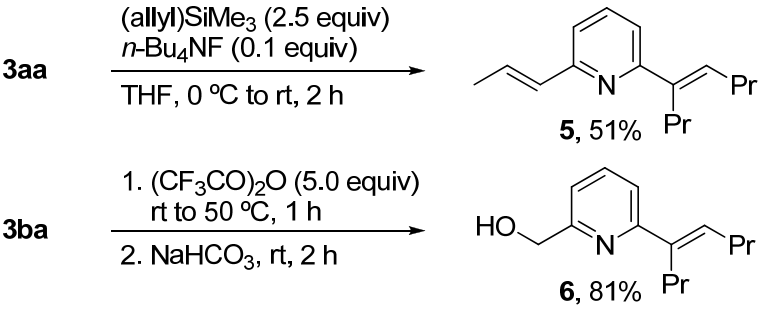
5	**1f**	**2a**	24	 **3fa**	81%, >99:1
6[c]	**1g**	**2a**	24	 **3ga**	60%, >99:1
				 R^1, R^2 =	
7	**1b**	**2b**	15	Me, *i*-Pr (**3bb**)	56%, >99:1
8	**1b**	**2c**	15	Me, *t*-Bu (**3bc**)	63%, >99:1

[a] Yield of isolated product based on **1**. [b] Estimated by ^{1}H NMR spectroscopy. [c] (*E*,*E*)-1,3-Di(oct-4-en-4-yl)isoquinoline-*N*-oxide (**3'ga**) was also isolated in 5% yield.

Alkenylated pyridine-*N*-oxides thus obtained were readily deoxygenated by treatment with PCl_3, and 2-alkenylpyridines were isolated in excellent yields (Eq. 2).

(2)

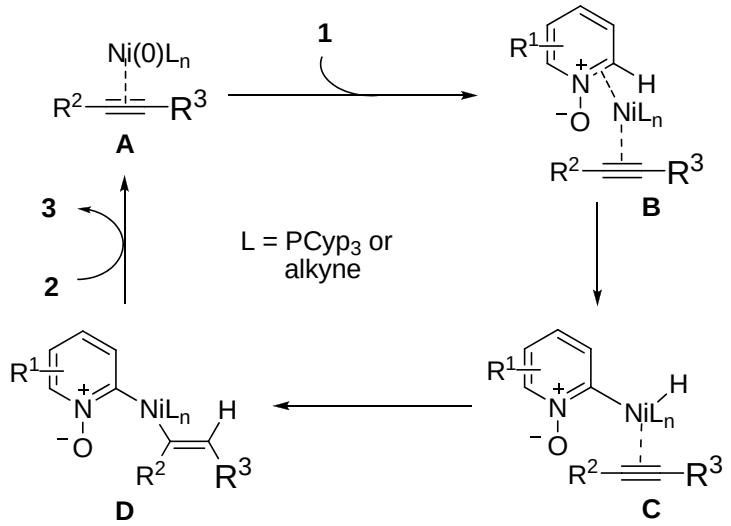
Furthermore, deoxygenative functionalization of the adducts was successfully demonstrated by the reaction of **3aa** with allyl(trimethyl)silane in the presence of a catalytic amount of *n*-Bu_4NF to afford **5** in 51% yield (Eq. 3).[11] Another transformation is an oxygen migration in **3ba** to the benzylic position to give **6** in 81% yield (Eq. 4).[12]



(3)

(4)

A plausible mechanism for the hydroheteroarylation reaction is suggested in Scheme 1. Oxidative addition of alkyne-coordinated nickel(0) species **A**[16] to the C(2)–H bond[17] via η^2 complex **B** gives pyridyl(hydride)nickel species **C**. Hydronickelation in a *cis* fashion then provides the alkenyl(pyridyl)nickel intermediate **D**. Reductive elimination followed by coordination of an alkyne affords 2-alkenylpyridine-*N*-oxide **3** and regenerates active nickel(0) species **A**. Similar regioselectivity has been observed in hydronickelation of unsymmetrical alkynes.[18] The presence of the *N*-oxide functionality could prevent nonproductive binding of the nickel catalyst to the nitrogen lone pair electrons and favor η^2-coordination of the pyridine ring to the nickel center. Furthermore, the *N*-oxide moiety enhances the acidity of the adjacent pyridyl C(2)–H bond to possibly facilitate the oxidative addition.[19]



Scheme 1. Plausible mechanism for hydroheteroarylation of alkynes with pyridine-*N*-oxides.

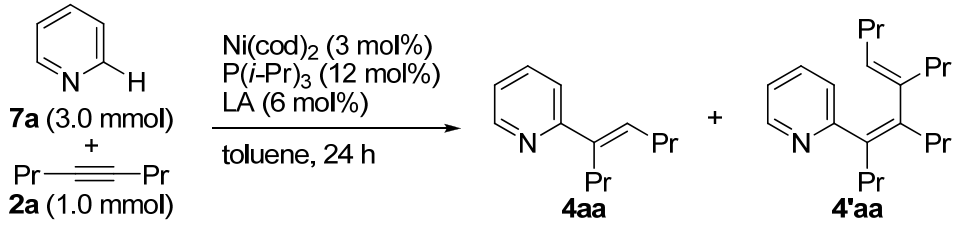
Nickel/Lewis acid-catalyzed hydroheteroarylation of alkynes with pyridines

Since the enhanced reactivity of pyridine-*N*-oxides is apparently ascribed to the electron-deficient nitrogen, possibly increasing the acidity of the C(2)–H bond to allow oxidative addition to nickel(0), the author envisioned that a similarly activated pyridinium species could be generated *in situ* by coordination of the pyridine nitrogen to a LA catalyst in a manner similar to the imidazole activation discussed in Chapter 3.[20] Thus, the author examined the reaction of pyridine (**7a**, 3.0 mmol) with **2a** (1.0 mmol) in the presence of a catalytic amount of $Ni(cod)_2$ with various ligands and LA catalysts

(Table 2). Whereas reactions performed in the absence of either a LA catalyst, $Ni(cod)_2$ or P(*i*-Pr)$_3$ did not give any detectable amount of hydroheteroarylation product **4aa** (entries 1–3, 9 and 10), the reaction using $Ni(cod)_2$ (3 mol%), P(*i*-Pr)$_3$ (12 mol%), and $ZnMe_2$ (6 mol%) as a LA catalyst furnished C(2)-alkenylated product **4aa** highly stereoselectively in 95% yield as estimated by GC (entry 4). C(2)-Dienylated product **4'aa** was also observed in a small amount. Formation of **4'aa** was suppressed by running the reaction at 80 ºC (entry 5). $ZnPh_2$ was equally effective to give **4aa** in 88% yield after isolation by flash column chromatography on silica gel (entry 6). On the other hand, a stronger zinc LA catalyst, $ZnCl_2$, was completely ineffective (entry 7). Reducing the amount of **7a** to an equimolar amount of **2a** resulted in a low yield (55% by GC), due possibly to competitive oligomerization of **2a** (entry 8). Nevertheless, no trace amount of a C(2), C(6)-dialkenylated product was observed in this nickel/ZnR_2-catalyzed system.

In contrast, use of $AlMe_3$ as a LA catalyst dramatically changed the reaction course producing **4'aa** as a major adduct in 80% isolated yield together with a small amount of **4aa** (entry 11). The reaction run at 80 ºC, however, gave a mixture of **4aa** and **4'aa** (entry 12), suggesting that a higher reaction temperature preferred formation of **4aa** over **4'aa** irrespective of the kind of LA catalysts used (entry 4 vs entry 5 and entry 11 vs entry 12). Again, aluminum-based LA catalysts with stronger Lewis acidity were inferior (entries 13–15). In either system, the direct C–H bond functionalization of pyridines by nickel/LA dual catalysis under relatively mild conditions at 50–80 ºC is worth noting, compared with the reported ruthenium and rhodium catalysis.[4b,5,6a,7]

Table 2. Direct C(2)-alkenylation of **7a** with **2a** by nickel/LA catalysis.



Entry	Lewis Acid (LA)	Temp (ºC)	Yield of **4aa** (%)[a]	Yield of **4'aa** (%)[a]
1	none	50	<1	<1
2[b]	$ZnMe_2$	50	<1	<1

3[b,c]	$ZnMe_2$	50	<1	<1
4	$ZnMe_2$	50	95	3
5	***$ZnMe_2$***	***80***	***95[d]***	***<1***
6	***$ZnPh_2$***	***50***	***96 (88)[e]***	***3***
7	$ZnCl_2$	50	<1	<1
8[f]	$ZnMe_2$	50	55	<1
9[b]	$AlMe_3$	50	<1	<1
10[b,c]	$AlMe_3$	50	<1	<1
11	***$AlMe_3$***	***50***	***5***	***82 (80)[e]***
12	$AlMe_3$	80	17	56[f]
13	$AlMe_2Cl$	50	2	34
14	$AlMeCl_2$	50	<1	13
15	$AlCl_3$	50	<1	6

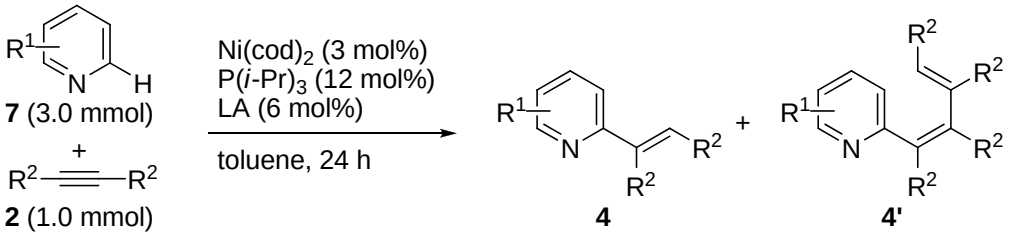
[a] Determined by GC based on **2a**. [b] Run in the absence of $Ni(cod)_2$. [c] Run in the absence of $P(i\text{-}Pr)_3$. [d] *E*/*Z* = 93:7. [e] Isolated yield based on **2a**. [f] Run with **7a** (1.00 mmol) and **2a** (1.00 mmol). [g] *ZE*/*EE*/*others* = 52:43:5.

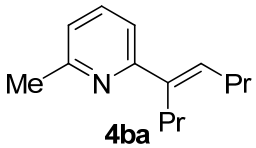
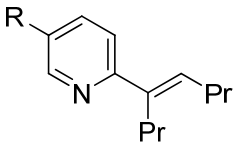
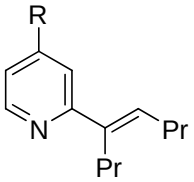
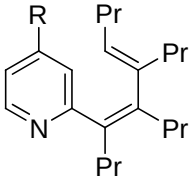
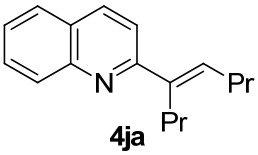
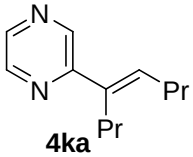
With the binary catalyst systems effective for the C(2)-selective alkenylation of pyridines, the author next tested the scope of this transformation (Table 3). The reaction of 2-picoline (**7b**) at 100 ºC gave adduct **4ba** in a modest yield (entry 1). This result suggests the sensitivity of the reaction toward a steric hindrance of substrates, and thus explains the suppression of dienylated products in the reaction of **7a**. Excellent regioselectivities were observed with 3-substituted pyridines **7c** and **7d**, which were alkenylated at their C-6 position exclusively (entries 2 and 3). A range of electron-withdrawing and -donating substituents at the 4-position of pyridine tolerated the reaction conditions to give adducts **7ea**–**7ia** in moderate to high yields (entries 4–8). Some of 4-substituted pyridines also participated in the dienylation reaction under nickel/$AlMe_3$ catalysis (entries 9 and 10). Quinoline (**7j**) and pyrazine (**7k**) also underwent the C-2 alkenylation (entry 11 and 12).

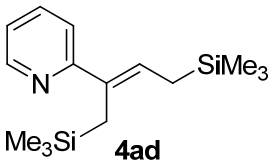
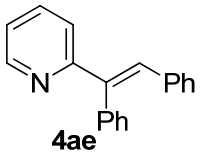
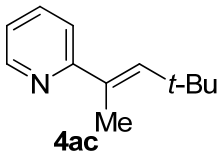
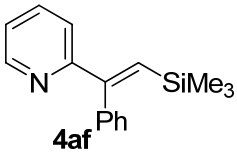
Scope of alkynes was also examined in this reaction. Bis(silylmethyl)acetylene **2d** underwent the reaction with **7a** to give pyridyl-substituted allylsilane **4ad** (entry 13), whereas the addition across diphenylacetylene (**2e**) was sluggish (entry 14). The reactions across unsymmetrical internal alkynes, 4,4-dimethyl-2-pentyne (**2c**) and trimethyl(phenylethynyl)silane (**2f**), were highly regioselective to give the corresponding adducts having a smaller substituent on the same side as the pyridyl

group (entries 15 and 16), although silyl-substituted adduct **4af** isomerized (*E*/*Z* = 80:20 at 0.7 h) under the reaction conditions to give a stereoisomeric mixture.

Table 3. Nickel/LA-catalyzed hydroheteroarylation of alkynes with pyridines.



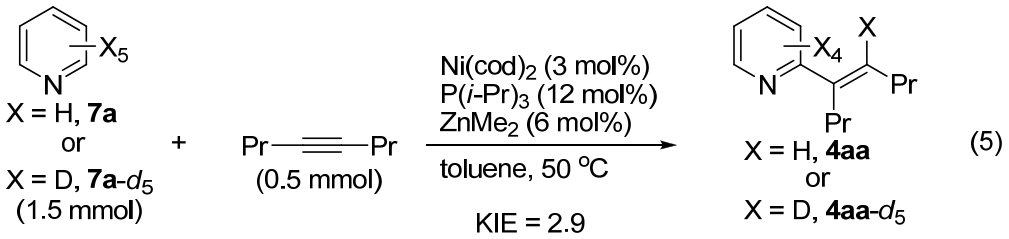
Entry	**7**	**2**	LA	Temp (ºC)	Time (h)	Major product (**4**)	Yield[a]	*E*/*Z*[b]
1	**7b**	**2a**	$ZnPh_2$	100	12	 **4ba**	42%	96:4
2	**7c**	**2a**	$ZnMe_2$	80	10	 R = MeO_2C (**4ca**)	69%	93:7
3	**7d**	**2a**	$ZnMe_2$	50	15	(pin)B (**4da**)	82%[c,d]	99:1
4	**7e**	**2a**	$ZnPh_2$	50	8	 R = Ph (**4ea**)	91%	98:2
5[e]	**7f**	**2a**	$ZnPh_2$	50	8	CF_3 (**4fa**)	69%[c]	96:4
6	**7g**	**2a**	$ZnMe_2$	80	12	*Si* (**4ga**)[f]	77%	95:5
7	**7h**	**2a**	$ZnMe_2$	50	8	MeO (**4ha**)	84%	>99:1
8	**7i**	**2a**	$ZnPh_2$	80	3	Me_2N (**4ia**)	81%[d]	97:3
9[g]	**7e**	**2a**	$AlMe_3$	50	30	 R = Ph (**4'ea**)	64%	>99:1
10	**7h**	**2a**	$AlMe_3$	50	40	MeO (**4'ha**)	46%[h]	>99:1
11	**7j**	**2a**	$ZnMe_2$	80	10	 **4ja**	65%	>99:1
12	**7k**	**2a**	$ZnMe_2$	100	5	 **4ka**	65[c,d]	97:3

13[g]	**7a**	**2d**	$ZnMe_2$	50	24	 **4ad**	61%	>99:1
14	**7a**	**2e**	$ZnMe_2$	100	10	 **4ae**	30%	>99:1
15	**7a**	**2c**	$ZnPh_2$	50	12	 **4ac**	87%	>99:1
16[g]	**7a**	**2f**	$ZnMe_2$	100	24	 **4af**	56%[d]	63:37

[a] Isolated yields based on **2**. [b] Determined by ^{1}H NMR of a crude product. [c] About 10% of **4** was also observed. [d] Isolated as a mixture of stereoisomers. [e] P(*t*-Bu)$_2$Me was used as a ligand. [f] *Si* = OCH_2SiMe_2t-Bu. [g] $Ni(cod)_2$ (10 mol%), P(*i*-Pr)$_3$ (40 mol%) and a LA catalyst (20 mol%) was used. [h] About 5% of **4ha** was also observed.

KIE Experiment

To determine the rate-determining step of the nickel/LA-catalyzed hydroheteroarylation reaction, kinetic isotope effect (KIE) of the addition reaction was estimated by comparing the initial rate of the reactions of **7a** or **7a**-d_5 with **2a**, first in the presence of $ZnMe_2$ (Eq. 5). A KIE value of 2.9 was observed (Figure 1). This data suggest that either the C–H or Ni–H cleavage step, namely, oxidative addition or hydronickelation step is slow, and therefore possibly the rate-determining step of the addition reaction catalyzed by nickel/organozincs.



(5)

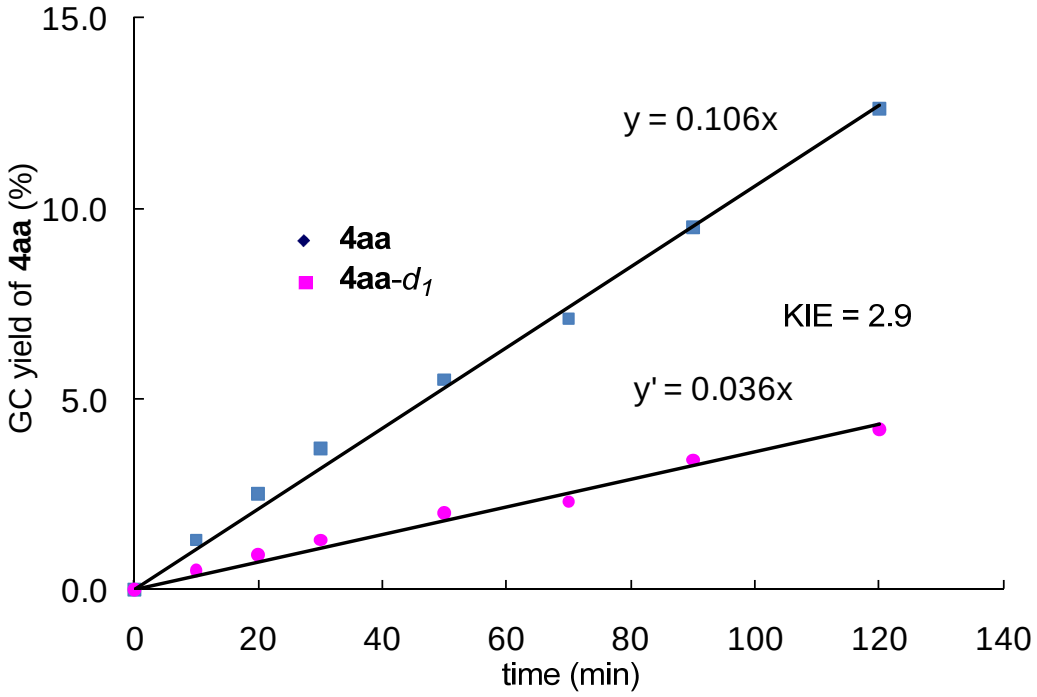
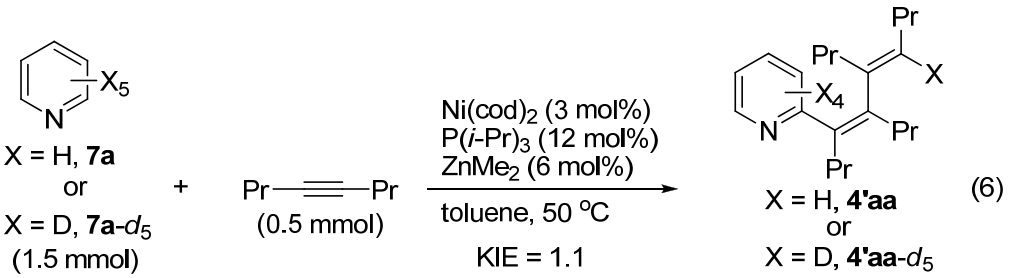


Figure 1. KIE study with $ZnMe_2$.

On the other hand, the KIE value of the reaction catalyzed by $AlMe_3$ as a LA catalyst was estimated to be 1.1 (Eq. 6 and Figure 2), indicating that both the oxidative addition and hydronickelation steps are facile, and insertion, reductive elimination or other elemental step is possibly the rate-determining step. This may be responsible for insertion of another alkyne molecule to give a dienylated product with $AlMe_3$ as a LA catalyst (*vide infra*).



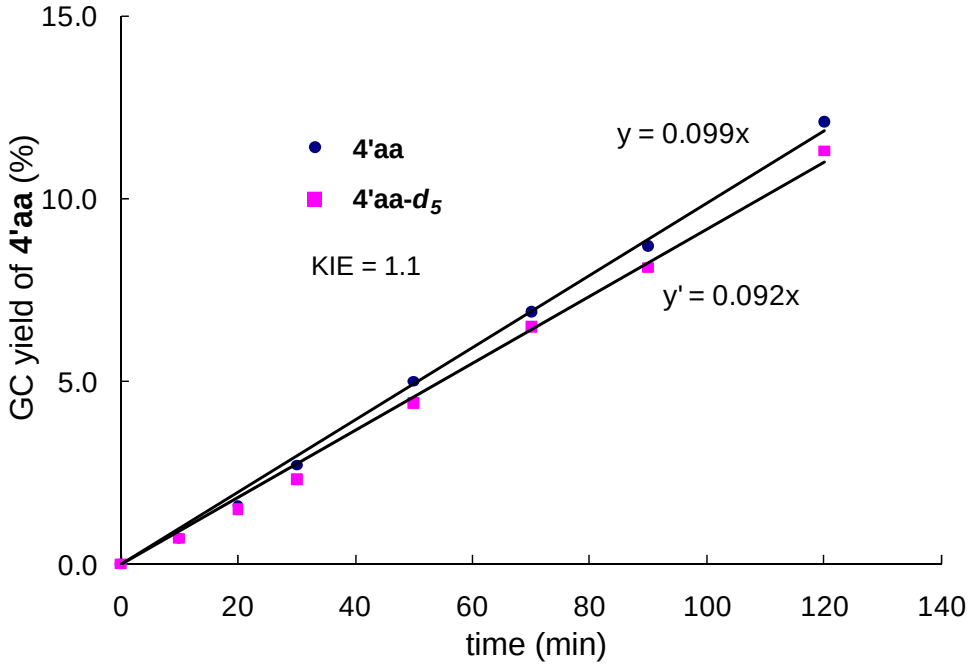
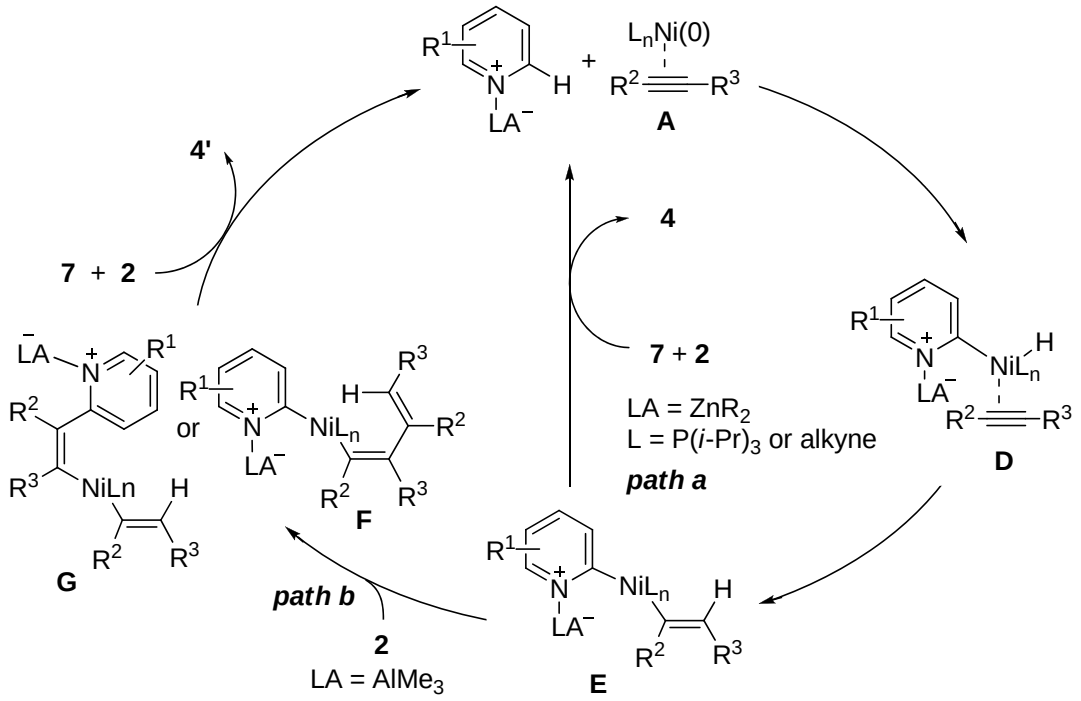


Figure 2. Estimation of KIE using $AlMe_3$.

Following is a plausible reaction mechanism. Pyridines activated by coordinating to a LA[21] catalyst would be responsible for oxidative addition of the C(2)–H bond to nickel(0) species **A**, a plausible initiation step of the present catalysis (Scheme 2). Hydronickelation across the alkyne coordinating to the nickel center in the direction that avoids steric repulsion between bulkier R^3 and the pyridyl group in **D** takes place to give **E**, which, in the presence of zinc LA catalysts, affords **4** upon reductive elimination (path a). Use of $AlMe_3$, a stronger LA than diorganozinc reagents,[21] or lower reaction temperature retards the reductive elimination and/or promotes the second insertion of another alkyne molecule into either of the C–Ni bonds in **E** to give **F** or **G**, resulting finally in the formation of dienylated product **4'** upon reductive elimination (path b). This observation contrasts the recent report that notes the C–N bond reductive elimination from pyridylpalladium amido complexes is accelerated by coordination of pyridyl nitrogen to LAs,[22] but in accord with the paper that records reductive elimination of C–C bonds is slow with an electron-withdrawing organic group.[23] Another reaction scenario involving a metallacycle formation[24] or carbene formation[25]

may be conceivable. Nevertheless, the mechanism described here is supported by KIE data (*vide supra*).



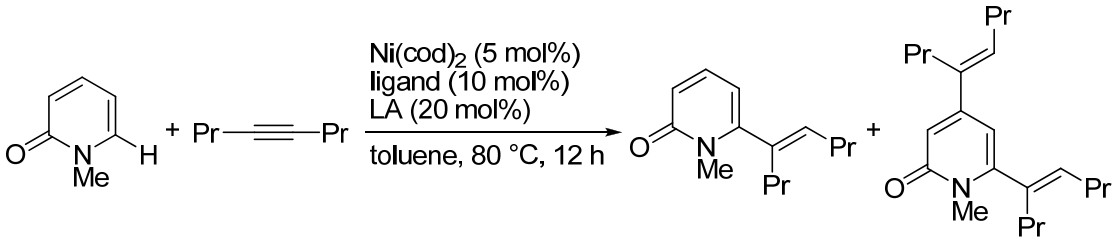
Scheme 2. Plausible mechanism for hydroheteroarylation of alkynes with pyridines.

Hydroheteroarylation of alkynes with 2-pyridones

The author next envisioned that 2-pyridone derivatives could also be similarly functionalized, because a similar reactive pyridinium species having the C(6)–H bond located α to a formally positively charged nitrogen is possibly generated *in situ* by coordination of their carbonyl group to the LA catalyst. To test this viability, he examined the reaction of *N*-methyl-2-pyridone (**8a**, 1.0 mmol) with **2a** (1.2 mmol) in the presence of $Ni(cod)_2$ (5 mol%), a ligand (10 mol%), and $AlMe_3$ (20 mol%) in toluene at 80 ºC for 12 h. While the reaction using P(*t*-Bu)$_3$ as a ligand gave low yield of (*E*)-1-methyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (**9aa**) (entry 1 of Table 4), tri(*sec*-alkyl)phosphine ligands gave good to excellent yields, P(*i*-Pr)$_3$ being the optimum to give **9aa** in 90% after isolation by flash column chromatography on silica gel (entries 2–4). The *cis* stereochemistry of the addition reaction was unambiguously identified by nOe experiments. Alkenylation at both the C(4) and C(6) positions also took place to a small extent (~5%). P(*n*-Bu)$_3$, PMe_3 and PPh_3 were ineffective to give

9aa in a trace or small amount (entries 5–7). The reactions performed in the absence of $Ni(cod)_2$, ligand or a LA catalyst were completely ineffective (entries 8–10). A brief screening of LA catalysts using P(*i*-Pr)$_3$ as a ligand revealed that $B(C_6F_5)_3$, $ZnMe_2$ and $ZnPh_2$ were completely ineffective in this hydroheteroarylation reaction, while $AlMe_2Cl$ and BPh_3 gave **9aa** in a moderate yield (entries 11–15).

Table 4. Optimization for nickel/LA-catalyzed C(6)-alkenylation of **8a** with **2a**.



8a (1.0 mmol) **2a** (1.2 mmol) **9aa** **9'aa**

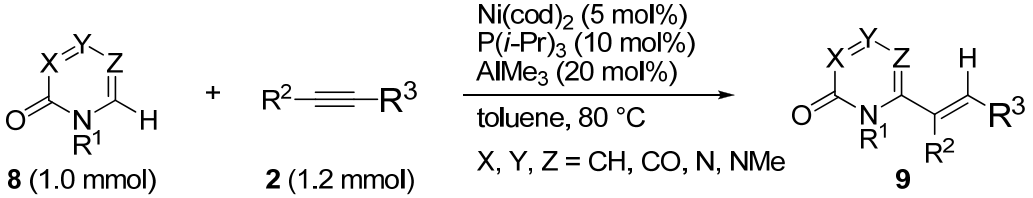
Entry	Ligand	LA	Yield of **9aa** (%)[a]	Yield of **9'aa** (%)[a]
1	P(*t*-Bu)$_3$	$AlMe_3$	12	<1
2	PCy_3	$AlMe_3$	83	2
3	$PCyp_3$	$AlMe_3$	70	2
4	***P(i-Pr)$_3$***	***$AlMe_3$***	***96 (90)***[b]	***3***
5	P(*n*-Bu)$_3$	$AlMe_3$	<1	<1
6	PMe_3	$AlMe_3$	12	<1
7	PPh_3	$AlMe_3$	<1	<1
8[c]	P(*i*-Pr)$_3$	$AlMe_3$	<1	<1
9	none	$AlMe_3$	<1	<1
10	P(*i*-Pr)$_3$	none	<1	<1
11	P(*i*-Pr)$_3$	$AlMe_2Cl$	60	<1
12	P(*i*-Pr)$_3$	BPh_3	44	<1
13	P(*i*-Pr)$_3$	$B(C_6F_5)_3$	<1	<1
14	P(*i*-Pr)$_3$	$ZnMe_2$	<1	<1
15	P(*i*-Pr)$_3$	$ZnPh_2$	<1	<1

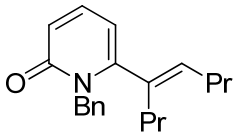
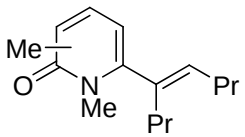
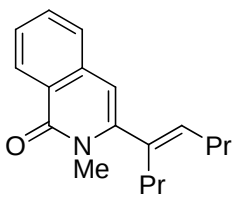
[a] Estimated by GC using dodecane as an internal standard. [c] Run in the absence of $Ni(cod)_2$.

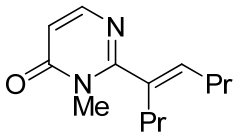
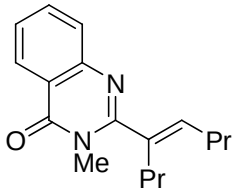
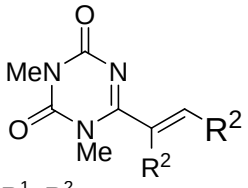
With the binary catalyst system effective for the C(6)-selective direct alkenylation of **8a** in hand, the author next tested the scope of substrates (Table 5). An *N*-benzyl

substituent (entry 1) and a methyl group at the C-3 or C-4 position did not affect the reaction (entries 2 and 3), whereas the C-5 methyl group of **8e** retarded the reaction, presumably because of steric repulsion (entry 4). *N*-Methylisoquinolin-1(2*H*)-one (**8f**), -pyrimidin-4(3*H*)-one (**8g**), and -quinazolin-4(3*H*)-one (**8h**) also participated in the alkenylation reaction, but in a modest yield or with low stereoselectivity (entries 5–7). Formal *trans*-adducts observed with **9ga** and **9ha** having an α,β-unsaturated imine substructure are likely derived from isomerization of the initial *cis*-adducts. In fact, an isolated sample of (*E*)-**9ha** readily isomerized to (*Z*)-**9ha** (*E*/*Z* = 57:43 at 1.5 h) under the reaction conditions in the presence of **8a** and **2a**. *N*-Methyl-4-pyridone did not give the alkenylated product under these reaction conditions. *N*,*N*-Dimethyluracil (**8i**) underwent the alkenylation reaction with **2a** and **2d** to give the corresponding adducts in excellent yields (entries 8–9). Perfect stereo- and regioselectivity was observed in the reaction of **8i** with unsymmetrical alkynes such as **2b, 2c**, **2g** and **2f** to give products with the heterocycle being introduced *trans* to a bulkier alkyl substituent (*vide supra*) (entries 10–13).

Table 5. Nickel/LA-catalyzed hydroheteroarylation of alkynes with 2-pyridones.

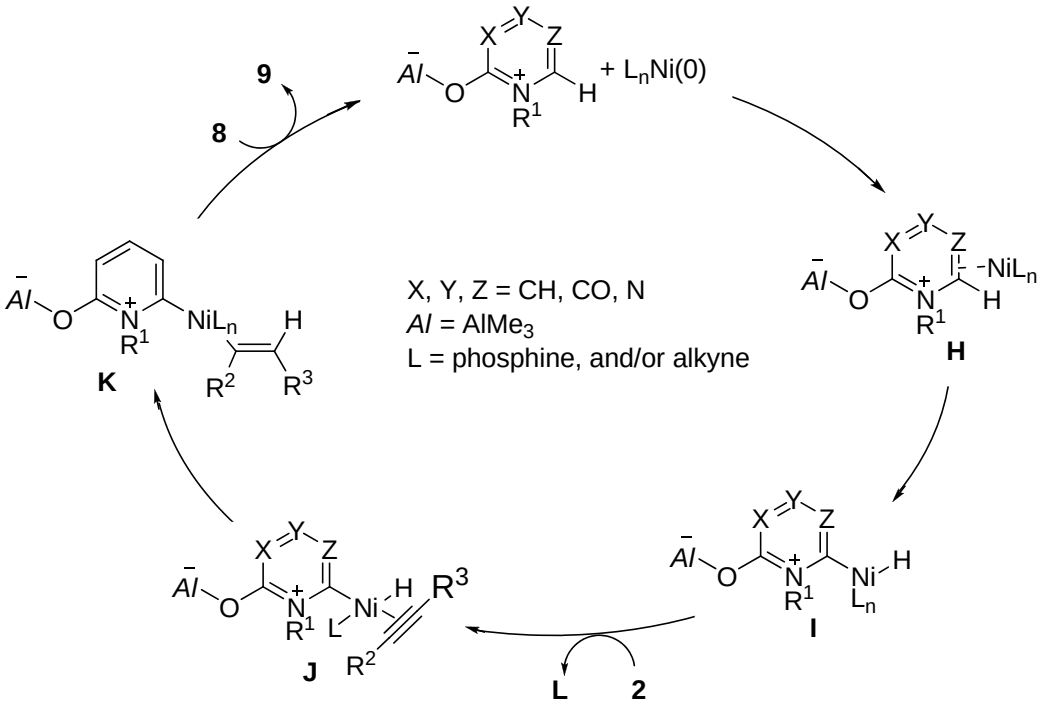


Entry	8	2	Time (h)	Major product		Yield (%)[a]
1	**8b**	**2a**	30			62 (**9ba**)[b]
2	**8c**	**2a**	16		3-Me	62 (**9ca**)
3	**8d**	**2a**	6		4-Me	88 (**9da**)
4	**8e**	**2a**	44		5-Me	29 (**9ea**)[b]
5	**8f**	**2a**	14			44 (**9fa**)

6	**8g**	**2a**	3		84 (**9ga**)[c]
7	**8h**	**2a**	3		99 (**9ha**)[d]
					
				R^1, R^2 =	
8	**8i**	**2a**	3	Pr, Pr	95 (**9ia**)
9	**8i**	**2d**	3	CH_2SiMe_3, CH_2SiMe_3	92 (**9id**)
10	**8i**	**2b**	4	Me, *i*-Pr	78 (**9ib**)
11	**8i**	**2c**	3	Me, *t*-Bu	97 (**9ic**)
12	**8i**	**2g**	6	Me, $SiMe_2$*t*-Bu	77 (**9ig**)
13	**8i**	**2f**	2	Ph, $SiMe_3$	77 (**9if**)[e]

[a] Isolated yield based on **8**. [b] 4,6-Dienylation product was also obtained (entry 1, 4%; entry 4, 1%). [c] *E*/*Z* = 50:50. [d] *E*/*Z* = 38:62. [e] *E*/*Z* = 97:3.

Hydroheteroarylation of alkynes with 2-pyridone derivatives is presumably initiated by η^2-coordination (**H** in Scheme 3) followed by oxidative addition of the activated 2-pyridones at the C-6 position to give nickel hydride intermediate **I**. Coordination of alkynes to the nickel center in the direction that minimizes steric repulsion between the bulkier R^3 group and the heterocycle (*vide supra*) forms intermediate **J**. Hydronickelation gives alkenylnickel intermediate **K**, which upon reductive elimination affords **9**.



Scheme 3. Plausible mechanism for hydroheteroarylation of alkynes with 2-pyridones.

Conclusion

In summary, the author has demonstrated that nickel catalysis is effective for hydroheteroarylation of alkynes with pyridine-*N*-oxides, pyridines and 2-pyridones. Use of Lewis acid cocatalysts allows to generate catalytic active species *in situ*, allowing activation of otherwise unreactive C–H bonds of pyridines and 2-pyridones and their direct functionalization. The catalysis is applicable to a diverse range of azines and alkynes to furnish a broad scope of disubstituted heteroarylethenes regio- and stereoselectively in modest to excellent yields.

Experimental section

Chemicals. 1-Benzyl-2-pyridone (**8b**)[26] and 1-(*tert*-butyldimethylsilyl)prop-1-yne (**2g**)[27] were prepared according to the respective literature procedures.

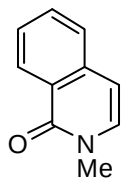
1,3-Dimethylpyridin-2(1*H*)-one (8c).[26] K_2CO_3 (2.2 g, 16.0 mmol) and MeI (0.75 mL, 12.0 mmol) were added to a solution of 3-methylpyridin-2(1*H*)-one (0.87 g, 8.0 mmol) in MeOH (10 mL). The mixture was heated to reflux for 22 h, filtered and concentrated *in vacuo*. The residue was diluted with water and extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$, filtered through a Celite pad and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give the title compound (0.77 g, 79%) as a colorless oil, R_f 0.30 (CH_2Cl_2–MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 6.8 Hz, 1H), 7.16 (d, *J* = 6.8 Hz, 1H), 6.07 (t, *J* = 6.8 Hz, 1H), 3.55 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 136.5, 135.4, 129.4, 105.3, 37.7, 17.2. IR (neat) 3509, 3077, 2943, 1657, 1651, 1593, 1562, 1443, 1406, 1379, 1319, 1227, 1103, 1047, 1009, 930, 866, 770, 756 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 123 (M^+, 95), 95 (22), 94 (100), 80 (11), 53 (13). HRMS (EI) Calcd for C_7H_9NO: M^+, 123.0684. Found: *m*/*z* 123.0690.

1,4-Dimethylpyridin-2(1*H*)-one (8d). Following the procedure for **8c**, 4-methylpyridin-2(1*H*)-one (0.55 g, 5.0 mmol) was methylated to give the title compound (0.49 g, 80%) as a colorless solid, mp 57.3–58.1 °C, R_f 0.30 (CH_2Cl_2–MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 6.8 Hz, 1H), 6.38 (s, 1H), 6.00 (d, *J* = 7.0 Hz, 1H), 3.51 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 150.5, 136.8, 117.9, 107.9, 36.6, 20.7. IR (KBr) 3429, 3059, 2970, 1665, 1591, 1545, 1435, 1418, 1381, 1342, 1329, 1254, 1182, 1128, 1057, 1030, 851, 773, 762, 748, 610, 519, 446, 428 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 123 (M^+, 100), 95 (19), 94 (89). HRMS (EI) Calcd for C_7H_9NO: M^+, 123.0684. Found: *m*/*z* 123.0679.

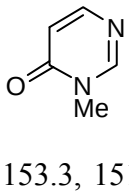
1,5-Dimethylpyridin-2(1*H*)-one (8e). Following the procedure for **8c**, 5-methylpyridin-2(1*H*)-one (0.87 g, 8.0 mmol) was methylated, and the title compound (0.74 g, 75%) was isolated as a colorless oil, R_f 0.35 (CH_2Cl_2–MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.05 (s, 1H), 6.52 (d, *J* = 9.3 Hz, 1H), 3.51 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 141.9, 135.6, 120.2, 114.8, 37.6, 17.1. IR (neat) 3447, 3048,

2947, 2868, 1667, 1597, 1541, 1433, 1418, 1368, 1323, 1271, 1211, 1150, 1051, 922, 829, 713, 532 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 123 (M^+, 100), 95 (21), 94 (82). HRMS (EI) Calcd for C_7H_9NO: M^+, 123.0684. Found: *m/z* 123.0683.

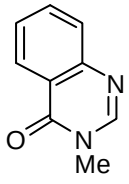
2-Methylisoquinolin-1(2*H*)-one (8f). Following the procedure for **8c**, isoquinolin-1(2*H*)-one (1.02 g, 7.0 mmol) was converted to the title compound (0.91 g, 81%) as a colorless solid, mp 68.3–68.9 °C, R_f 0.50 (ethyl acetate). ^1H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.1 Hz, 1H), 7.63 (td, *J* = 8.1, 1.3 Hz, 1H), 7.54–7.45 (m, 2H), 7.07 (d, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.3 Hz, 1H), 3.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 136.9, 132.2, 131.8, 127.4, 126.6, 125.9, 125.7, 105.8, 37.0. IR (KBr) 3065, 2943, 1651, 1620, 1601, 1555, 1491, 1454, 1433, 1404, 1348, 1317, 1298, 1258, 1194, 1153, 1099, 1059, 1024, 970, 947, 885, 791, 752, 692, 615, 577 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 160 (M^++1, 11), 159 (M^+, 100), 158 (12), 131 (15), 130 (26), 118 (15), 116 (32), 90 (11), 89 (21), 63 (10). Anal. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70. Found: C, 75.18; H, 5.45.



3-Methylpyrimidin-4(3*H*)-one (8g). The procedure for **8c** was applied to pyrimidin-4(3*H*)-one (1.02 g, 7.0 mmol), to give the title compound (0.67 g, 60%) as a colorless solid, mp 107.5–108.1 °C, R_f 0.45 (CH_2Cl_2–MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.89 (d, *J* = 6.6 Hz, 1H), 6.46 (d, *J* = 6.6 Hz, 1H), 3.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 153.3, 151.2, 115.4, 34.4. IR (KBr) 3044, 3001, 2888, 1663, 1595, 1537, 1495, 1451, 1424, 1348, 1236, 1211, 1167, 1150, 1074, 1030, 1005, 889, 856, 760, 731, 700, 621, 613, 552, 527, 471 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 110 (M^+, 100), 82 (12). HRMS (EI) Calcd for $C_5H_6N_2O$: M^+, 110.0480. Found: *m/z* 110.0484.

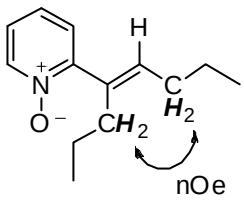


3-Methylquinazolin-4(3*H*)-one (8h). The procedure for **8c**, upon application to quinazolin-4(3*H*)-one (1.02 g, 7.0 mmol), gave **8h** (0.67 g, 60%) as a colorless solid, mp 117.4–118.2 °C, R_f 0.25 (CH_2Cl_2–MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.10 (s, 1H), 7.80–7.70 (m, 2H), 7.52 (ddd, *J* = 8.2, 6.9, 1.6 Hz, 1H), 3.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 147.7, 146.3, 133.6, 126.9, 126.7, 125.9, 121.4, 33.8. IR (KBr) 3017, 2988, 1670, 1613, 1560, 1470, 1397, 1341, 1321, 1294, 1265, 1186, 1152, 1107, 1067, 936, 874, 777, 694, 542 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 161 (M^++1, 10), 160 (M^+, 100), 159 (15), 132 (28), 131 (12), 119 (16). Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03. Found: C, 67.47; H, 5.10.

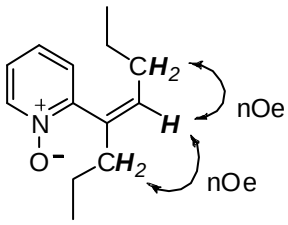


Hydroheteroarylation of alkynes with pyridine-*N*-oxides. G*eneral procedure.* In a glove box, a pyridine-*N*-oxide (1.0 mmol) and an alkyne (1.5 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and $PCyp_3$ (24 mg, 0.10 mmol) in toluene (2.5 mL) placed in a 3 mL-vial. The vial was closed with a screw cap, taken out of the glove box and heated at 35 ºC for the time specified in Eq. 1 and Table 1. The resulting mixture was filtered through a silica pad and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give the corresponding hydroheteroarylation product(s) in yields listed in Table 1.

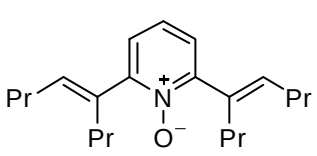
2-(Oct-4-en-4-yl)pyridine-*N*-oxide [(*E*)-3aa]. A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dt, *J* = 6.2, 1.0 Hz, 1H), 7.24–7.06 (m, 3H), 5.62 (t, *J* = 7.2 Hz, 1H), 2.65 (t, *J* = 7.3 Hz, 2H), 2.20 (q, *J* = 7.4 Hz, 2H), 1.49 (sext, *J* = 7.4 Hz, 2H), 1.26 (sext, *J* = 7.5 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 139.7, 136.3, 135.0, 127.2, 125.4, 123.9, 30.1, 29.5, 22.7, 22.0, 14.12, 14.07. IR (neat) 2959, 2932, 2870, 1483, 1458, 1422, 1377, 1248, 1211, 1144, 1113, 1092, 922, 907, 847, 766, 731, 642, 543 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 207 (M^++2, 18), 206 (M^++1, 100), 206 (M^+, 20). Anal. Calcd for $C_{13}H_{19}NO$; C, 76.06; H, 9.33. Found: C, 75.82; H, 9.49.



2-(Oct-4-en-4-yl)pyridine-*N*-oxide [(*Z*)-3aa]. A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 5.9 Hz, 1H), 7.25–7.08 (m, 3H), 5.73 (t, *J* = 7.5 Hz, 1H), 2.70–2.30 (br, 2H), 1.87 (q, *J* = 7.3 Hz, 2H), 1.43–1.20 (m, 4H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.1, 134.1, 132.5, 127.6, 124.9, 124.1, 36.5, 31.4, 22.8, 21.6, 14.0, 13.8.

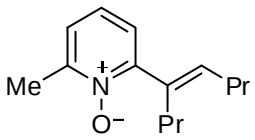


2,6-Bis(oct-4-en-4-yl)pyridine-*N*-oxide (3'aa, (*EE*/others = 94:6). A colorless oil, R_f 0.70 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.07 (m, 3H), 5.70–5.64 (m, 0.08H), 5.61 (t, *J* = 7.2 Hz, 1.92H), 2.65 (t, *J* = 7.8 Hz, 4H), 2.21 (q, *J* = 7.4 Hz, 4H), 1.48 (sext, *J* = 7.2 Hz, 4H), 1.25 (sext, *J* = 7.5 Hz, 4H), 0.97 (m, 6H), 0.85 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 136.8, 134.1, 125.2, 124.4, 30.1, 29.5, 22.6, 21.8, 14.1, 14.0. IR (neat) 2959, 2932, 1717, 1701, 1553, 1479, 1458, 1383, 1354, 1248, 1219, 1103, 1088, 1074, 899, 845, 793, 758 cm^{-1}. MS (EI, 70 eV)

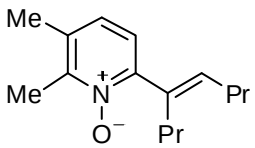


m/z (%) 317 (M^++2, 18), 316 (M^++1, 100), 315 (M^+, 27), 314 (M^+–1, 18). HRMS (FAB+) Calcd for $C_{21}H_{33}NO$: M^+, 315.2562. Found: *m/z* 315.2569.

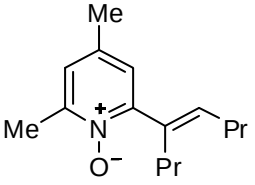
6-Methyl-2-(oct-4-en-4-yl)pyridine-*N*-oxide (3ba, *E*/*Z* = 93:7). A colorless oil, R_f 0.45 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–6.93 (m, 3H), 5.65 (t, *J* = 7.5, 0.07H), 5.57 (t, *J* = 7.2 Hz, 0.93H), 2.61 (t, *J* = 7.8 Hz, 2H), 2.51 (s, 0.21H), 2.49 (s, 2.79H), 2.19 (q, *J* = 7.4 Hz, 2H), 1.45 (sext, *J* = 7.4 Hz, 2H), 1.24 (sext, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.5 Hz, 3H), 0.84 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 148.8, 136.7, 133.9, 124.6, 124.5, 124.3, 29.9, 29.6, 22.5, 21.8, 18.1, 14.0, 13.9. IR (neat) 3393, 2959, 2932, 2870, 1717, 1705, 1559, 1489, 1456, 1389, 1375, 1263, 1246, 1096, 903, 841, 773, 731 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 220 (M^++1, 48), 219 (M^+, 11), 155 (19), 154 (54), 138 (19), 137 (38), 136 (43), 107 (11). HRMS (FAB+) Calcd for $C_{14}H_{21}NO$: M^+, 219.1623. Found: *m/z* 219.1613.



5,6-Dimethyl-2-(4-octen-4-yl)pyridine-*N*-oxide (3ca, *E*/*Z* = 97:3). A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.65 (t, *J* = 7.3 Hz, 0.03H), 5.54 (t, *J* = 7.3 Hz, 0.97H), 2.63 (t, *J* = 7.8 Hz, 2H), 2.52 (s, 0.09H), 2.50 (s, 2.91H), 2.34 (s, 0.09H), 2.32 (s, 2.91H), 2.20 (q, *J* = 7.3 Hz, 2H), 1.47 (sext, *J* = 7.4 Hz, 2H), 1.25 (sext, *J* = 7.5 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 147.8, 136.9, 133.4, 132.3, 126.2, 123.0, 29.9, 29.7, 22.6, 21.8, 19.5, 14.0, 13.9. IR (neat) 3420, 2957, 2930, 2870, 1497, 1456, 1377, 1348, 1271, 1244, 1173, 1094, 897, 870, 810, 716, 592, 507 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 93), 233 (M^+, 22), 154 (23), 137 (12), 136 (15). Anal. Calcd for $C_{15}H_{23}NO$; C, 77.21; H, 9.93. Found: C, 76.96; H, 10.20 .



4,6-Dimethyl-2-(oct-4-en-4-yl)pyridine-*N*-oxide (3da, *E*/*Z* = 94:6). A colorless oil, R_f 0.30 (CH_2Cl_2–acetone = 3:2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, *J* = 2.2 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 5.65 (t, *J* = 7.3, 0.06H), 5.57 (t, *J* = 7.2 Hz, 0.94H), 2.64(t, *J* = 7.8 Hz, 2H), 2.51 (s, 0.18H), 2.49(s, 2.82H), 2.31 8(s, 0.18), 2.29 (s, 2.82H), 2.20 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.4 Hz, 2H), 1.27 (sext, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.1, 148.1, 137.0, 135.6, 133.9, 125.4, 125.2, 30.1, 29.8, 22.8, 22.0, 20.3, 18.2, 14.20, 14.16. IR (neat)



3443, 2959, 2930, 2870, 1624, 1559, 1458, 1420, 1375, 1250, 1229, 1038, 860, 799, 627 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 100), 233 (M^+, 20), 190 (11), 154 (33), 137 (16), 136 (20). HRMS (FAB+) Calcd for $C_{15}H_{23}NO$: M^+, 233.1780. Found: *m/z* 233.1776.

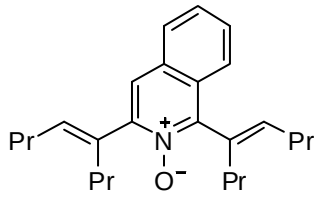
***(E)*-3,6-Dimethyl-2-(oct-4-en-4-yl)pyridine-*N*-oxide (3ea).** A colorless oil, R_f 0.50 (CH_2Cl_2–acetone = 3:2), ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.1 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 5.38 (t, *J* = 7.3 Hz, 1H), 2.54–2.41 (m, 2H), 2.45 (s, 3H), 2.24 (s, 3H), 2.32–2.22 (m, 2H), 1.56–1.36 (m, 2H), 1.34–1.18 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.9, 146.0, 133.8, 133.0, 132.3, 126.6, 123.2, 31.1, 30.0, 22.7, 22.1, 19.9, 18.0, 14.6, 14.2. IR (neat) 3447, 2959, 2932, 2872, 1736, 1559, 1489, 1458, 1449, 1435, 1354, 1304, 1261, 1207, 1140, 1071, 1038, 999, 916, 802, 773, 731, 642 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 74), 233 (M^+, 16), 155 (16), 154 (61), 138 (17), 137 (31), 136 (36). HRMS (FAB+) Calcd for $C_{15}H_{23}NO$: M^+, 233.1780. Found: *m/z* 233.1786.

***(E)*-3-(Methoxycarbonyl)-6-methyl-2-(oct-4-en-4-yl)pyridine-*N*-oxide (3fa).** A colorless oil, R_f 0.60 (CH_2Cl_2–acetone = 3:2), ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 5.40 (t, *J* = 7.2 Hz, 1H), 3.80 (s, 3H), 2.52 (s, 3H), 2.74–2.30 (m, 2H), 2.24–2.08 (m, 2H), 1.48–1.30 (m, 4H), 0.94 (t, *J* = 6.6 Hz, 3H), 0.91(t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 152.3, 151.2, 134.4, 134.0, 129.6, 124.3, 123.7, 52.5, 31.2, 30.3, 22.5, 21.7, 18.6, 14.7, 14.1. IR (neat) 3447, 2959, 2930, 2870, 1740, 1734, 1717, 1491, 1451, 1382, 1354, 1267, 1252, 1072, 1040, 922, 802, 731, 642 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 278 (M^++1, 10), 235 (26), 234 (100), 233 (33), 190 (15), 154 (37), 137 (18), 136 (21). Anal. Calcd for $C_{16}H_{23}NO_3$; C, 68.99; H, 8.29. Found: C, 69.29; H, 8.36.

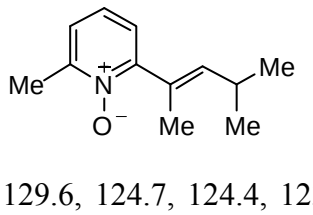
***(E)*-1-(Oct-4-en-4-yl)-isoquinoline-*N*-oxide (3ga).** A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 1:1), ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.1, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.59–7.48 (m, 3H), 5.58 (t, *J* = 7.2 Hz, 1H), 2.80–2.57 (m, 2H), 2.48–2.28 (m, 2H), 1.64–1.48 (m, 2H), 1.38–1.16 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 136.9, 135.9, 132.1, 129.5, 129.0, 128.5, 127.8, 126.6, 125.8, 122.3, 30.6, 30.3, 22.8, 21.9, 14.6, 14.2.

IR (neat) 2957, 2930, 2870, 1553, 1491, 1458, 1377, 1340, 1329, 1294, 1219, 1140, 1117, 961, 889, 752, 729, 660, 642 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 257 (M^++1, 12), 255 (M^+, 66), 155 (14), 154 (55), 138 (15), 137 (29), 136 (32). HRMS (FAB+) Calcd for $C_{17}H_{21}NO$: M^+, 255.1623. Found: *m/z* 255.1618.

***(E)*-1,3-Di(oct-4-en-4-yl)isoquinoline-*N*-oxide (3'ga).** A colorless oil, R_f 0.75 (CH_2Cl_2–acetone = 1:1), ^1H NMR (400 MHz, $CDCl_3$) δ 7.93–7.87 (m, 1H), 7.74–7.67 (m, 1H), 7.53–7.44 (m, 3H), 5.69 (t, *J* = 7.2 Hz, 1H), 5.57 (t, *J* = 7.2 Hz, 1H), 2.84–2.54 (m, 4H), 2.50–2.16 (m, 4H), 1.68–1.42 (m, 4H), 1.38–1.16 (m, 4H), 0.10–0.94 (m, 6H), 0.92–0.80 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 148.9, 136.9, 135.4, 134.2, 132.6, 129.2, 128.7, 127.5, 127.4, 126.3, 125.6, 122.3, 30.6, 30.4, 30.3, 22.84, 22.76, 21.83, 21.81, 14.6, 14.3, 14.2. IR (neat) 2959, 2930, 2870, 1697, 1618, 1578, 1559, 1491, 1456, 1377, 1335, 1146, 1071, 907, 883, 754, 735, 687 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 367 (M^++2, 31), 366 (M^++1, 100), 365 (M^+, 40), 364 (M^+, 28), 350 (14), 322 (18), 154 (16), 137 (11), 136 (15). HRMS (FAB+) Calcd for $C_{25}H_{35}NO$: M^+, 365.2719. Found: *m/z* 365.2709.



***(E)*-6-Methyl-2-(4-methylpent-2-en-2-yl)pyridine-*N*-oxide (3bb).** A colorless oil, R_f 0.60 (CH_2Cl_2–acetone = 3:2), ^1H NMR (400 MHz, $CDCl_3$) δ 7.17–7.04 (m, 3H), 5.50 (dq, *J* = 9.2, 1.3 Hz, 1H), 2.80–2.64 (m, 1H), 2.51 (s, 3H), 2.07 (d, *J* = 1.5 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7, 149.0, 141.5, 129.6, 124.7, 124.4, 123.8, 27.4, 22.6, 18.2, 14.4. IR (neat) 3447, 2959, 2926, 2870, 1559, 1489, 1447, 1389, 1373, 1263, 1246, 1179, 1096, 1007, 997, 847, 826, 779, 748, 611, 575, 527 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 192 (M^++1, 100), 191 (M^+, 15), 155 (24), 154 (88), 148 (18), 138 (25), 137 (47), 136 (54), 107 (13). HRMS (FAB+) Calcd for $C_{12}H_{17}NO$: M^+, 191.1310. Found: *m/z* 191.1303.

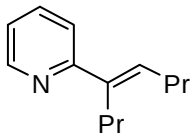


(*E*)-2-6-methyl(4,4-Dimethylpent-2-en-2-yl)-pyridine-*N*-oxide (3bc). A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 3:2), ^1H NMR (400 MHz, $CDCl_3$) δ 7.15–7.00 (m, 3H), 5.57 (q, *J* = 1.4 Hz, 1H), 2.49 (s, 3H), 2.12 (d, *J* = 1.5 Hz, 3H), 1.20 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 148.9, 143.7, 130.8, 124.7, 124.2, 123.7, 33.2, 30.5, 18.2, 15.7. IR (neat) 3420, 2959, 2905, 2871, 1560, 1489, 1458, 1447, 1387, 1364, 1263, 1244, 1207, 1163, 1092, 1011, 924, 858, 837, 781, 764, 731, 642, 619, 581, 527 cm^{-1}.

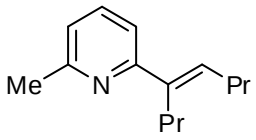
Anal. Calcd for $C_{13}H_{19}NO$. C, 76.05; H, 9.21. Found: C, 76.06; H, 9.33.

Deoxygenation of 3aa and 3ba. *General procedure*. PCl_3 (0.11 g, 1.30 mmol) was added dropwise to a solution of **3** (1.10 mmol) in toluene (5.0 mL). The resulting mixture was stirred at rt for 15 min, before careful addition of saturated $NaHCO_3$. The whole mixture was stirred for further 5 min. After extraction with with CH_2Cl_2/H_2O, the combined organic layers were washed with brine and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford the corresponding deoxygenated 2-alkenylpyridines **4aa** and **4ba**.

(*E*)-2-(Oct-4-en-4-yl)pyridine (4aa). A colorless oil, R_f 0.60 (hexane–ethyl acetate = 9/1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.58 (ddd, *J* = 8.0, 6.8, 1.9 Hz, 1H), 7.35 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.08 (ddd, *J* = 7.4, 4.9, 1.1 Hz, 1H), 6.21 (t, *J* = 7.4 Hz, 1H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.24 (q, *J* = 7.4 Hz, 2H), 1.58–1.36 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 148.6, 139.5, 136.0, 132.1, 121.0, 120.2, 30.9, 30.2, 22.9, 22.2, 14.22, 14.18. IR (neat) 2959, 2930, 2870, 1586, 1562, 1464, 1429, 1377, 1281, 1153, 1140, 1051, 991, 897, 772, 743, 702, 617 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 189 (M^+, 25), 174 (13), 161 (13), 160 (100), 146 (12), 144 (15), 132 (14), 131 (31), 130 (31), 118 (11), 117 (21). HRMS (FAB+) Calcd for $C_{13}H_{19}N$: M^+, 189.1517. Found: *m/z* 189.1525.

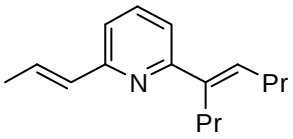


(*E*)-2-(Oct-4-en-4-yl)-6-methylpyridine (4ba). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 9:1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.22 (t, *J* = 7.3 Hz, 1H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.54 (s, 3H), 2.23 (q, *J* = 7.4 Hz, 2H), 1.50 (sext, *J* = 7.4 Hz, 2H), 1.41 (sext, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 157.1, 139.7, 136.1, 131.6, 120.5, 117.2, 30.8, 30.5, 24.9, 23.0, 22.2, 14.3, 14.2. IR (neat) 3057, 2959, 2930, 2870, 1699, 1584, 1574, 1456, 1375, 1217, 1159, 1094, 991, 899, 787, 743 cm^{-1}. HRMS (FAB+) Calcd for $C_{14}H_{21}N$: M^+, 203.1674. Found: *m/z* 203.1676.

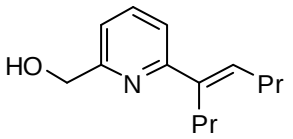


Synthesis of (*E*)-2(oct-4-en-4-yl)-6(propen-1-yl)pyridine (5).[11] Allyl(trimethyl)silane (0.40 g, 2.5 mmol) and a 1.0 M solution of Bu_4NF in THF (0.1 mL, 0.1 mmol) were added to a solution of **3aa** (1.0 mmol) in THF (5 mL) at 0 °C. The

mixture was stirred at 0–5 °C for 2 h, diluted with CH_2Cl_2 and then partitioned between water. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel using hexane–ethyl acetate as eluent to give the title compound (0.12 g, 51%) as a colorless oil. R_f 0.65 (hexane–ethyl aetate = 9/1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.7 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 6.79 (dq, *J* = 15.4, 6.8 Hz, 1H), 6.50 (dq, *J* = 14.1, 1.6 Hz, 1H), 6.27 (t, *J* = 7.4 Hz, 1H), 2.63 (t, *J* = 7.7 Hz, 2H), 2.25 (q, *J* = 7.5 Hz, 2H), 1.94 (dd, *J* = 6.7, 1.8 Hz, 3H), 1.58–1.38 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 154.6, 139.7, 136.3, 131.6, 131.5, 129.9, 118.2, 118.0, 30.9, 30.3, 23.0, 22.3, 18.4, 14.4, 14.2. IR (neat) 3026, 2959, 2932, 2870, 1778, 1717, 1701, 1659, 1578, 1566, 1452, 1377, 1161, 1088, 990, 966, 899, 833, 779, 739, 633 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 230 (M^++1, 100), 229 (M^+, 25), 228 (18), 200 (12), 148 (12), 154 (47), 138 (12), 137 (22), 136 (28). HRMS (FAB+) Calcd for $C_{16}H_{23}N$: M^+, 229.1830. Found: *m/z* 229.1836.



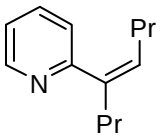
Synthesis of (*E*)-2-hydroxymethyl-6-(oct-4-en-4-yl)pyridine (6).[12] Trifluoroacetic anhydride (0.24 mL, 1.63 mmol) was added dropwise to **3ba** (70 mg, 0.33 mmol). The resulting orange mixture was stirred at rt for 30 min, then refluxed for further 30 min. After cooling the mixture to rt, a saturated aqueous $NaHCO_3$ solution was added slowly until the mixture indicated pH 8. Then the whole was stirred for 5 min and extracted with CH_2Cl_2. Combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude was purified by flash silica gel chromatography to afford **6** (58 mg, 81%) as a colorless oil. R_f 0.35 (hexane–ethyl acetate = 1:1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (t, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.9, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 6.29 (t, *J* = 7.4 Hz, 1H), 4.73 (s, 2H), 3.60–4.40 (br, 1H), 2.62 (t, *J* = 7.2 Hz, 2H), 2.25 (q, *J* = 7.0 Hz, 2H), 1.58–1.38 (m, 4H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.94(t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 156.8, 138.9, 136.8, 132.5, 118.5, 117.6, 63.5, 30.9, 30.2, 23.0, 22.3, 14.3, 14.2. IR (neat) 3403, 3368, 2959, 2932, 2870, 1638, 1586, 1572, 1458, 1377, 1339, 1296, 1219, 1159, 1090, 1069, 993, 897, 793, 746, 614 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 220 (M^++1, 100), 219 (M^+, 12), 155 (25), 154 (94), 139 (10), 138 (25), 137 (48), 136 (52), 107 (12). HRMS (FAB+) Calcd for $C_{14}H_{21}NO$: M^+, 219.1623. Found: *m/z* 219.1615.



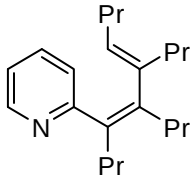
Hydroheteroarylation of alkynes with pyridines. *General procedure*. In a glove

box, a solution of pyridine (3.0 mmol) and a Lewis acid [60 μmol, $ZnMe_2$: 60 μL (a 1.00 M solution in hexane); $ZnPh_2$ (92% purity from Aldrich): 14.3 mg; $ZnPh_2$ (100% purity from Strem): 13.2 mg; $AlMe_3$: 53 μL (a 1.03 M solution in hexane)] in toluene (1.25 mL) was placed into a 3 mL-vial. A solution of $Ni(cod)_2$ (8.2 mg, 30 μmol) and P(*i*-Pr)$_3$ (19.2 mg, 0.12 mmol) in toluene (1.25 mL) was added. After an alkyne (1.0 mmol) and undecane (internal standard, 78 mg, 0.50 mmol) were added, the vial was closed with a screw cap, taken out of the glove box, and heated at the temperature for the time both specified in Table 3. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The crude was purified by flash column chromatography on silica gel to give the corresponding products in yields listed in Table 3. In some cases, **4** and **4'** were separated by preparative recycling GPC or silica gel chromatography.

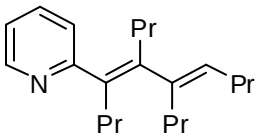
(*Z*)-2-(Oct-4-en-4-yl)pyridine [(*Z*)-4aa]. A colorless oil, R_f 0.50 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.6, 0.7 Hz), 7.53 (td, *J* = 7.6, 0.9 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 7.03 (ddd, *J* = 7.3, 4.9, 1.1 Hz, 1H), 5.51 (t, *J* = 7.3 Hz, 1H), 2.39 (t, *J* = 7.5 Hz, 2H), 1.93 (q, *J* = 7.3 Hz, 2H), 1.38–1.20 (m, 4H), 0.81 (t, *J* = 7.3 Hz, 3H), 0.78 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 148.9, 140.1, 135.2, 129.0, 123.6, 120.9, 39.6, 30.8, 23.1, 21.3, 13.7, 13.6. IR (neat) 3055, 2953, 2895, 1584, 1560, 1491, 1466, 1427, 1339, 1248, 1152, 1072, 1049, 991, 934, 907, 862, 835, 781, 739, 704, 608 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 189 (M^+, 25), 174 (13), 161 (13), 160 (100), 146 (12), 144 (15), 132 (14), 131 (31), 130 (31), 118 (11), 117 (21). Anal. Calcd for $C_{13}H_{19}N$; C, 82.48; H, 10.12. Found: C, 82.23; H, 10.11.



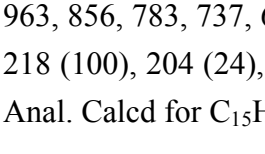
(4*Z*,6*E*)-5,6-Dipropyl-4-(2-pyridyl)deca-4,6-diene (4'aa). A colorless oil, R_f 0.75 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (dq, *J* = 4.8, 1.0 Hz, 1H), 7.44 (td, *J* = 7.6, 1.9 Hz, 1H), 7.03–6.96 (m, 2H), 4.91 (t, *J* = 7.3 Hz, 1H), 2.53 (t, *J* = 7.8 Hz, 2H), 2.23 (t, *J* = 7.8 Hz, 2H), 1.91 (t, *J* = 8.2 Hz, 2H), 1.73 (q, *J* = 7.3 Hz, 2H), 1.47–1.20 (m, 6H), 1.04–0.78 (m, 11H), 0.65 (*J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 148.2, 142.7, 138.9, 136.4, 134.7, 132.0, 125.1, 120.1, 34.7, 33.0, 32.6, 30.9, 22.6, 22.3, 21.7, 21.6, 14.9, 14.3, 14.1, 13.9. IR (neat) 2959, 2930, 2870, 1587, 1562, 1464, 1427, 1377, 1254, 1146, 1117, 1089, 1047, 893, 833, 797, 772, 746 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 299 (M^+, 5), 270 (15), 257 (27), 256 (100). HRMS (EI) Calcd for $C_{21}H_{33}N$: 299.2613. Found: *m*/*z* 299.2602.



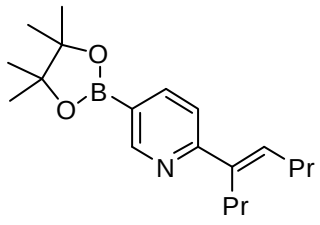
(4*E*,6*E*)-5,6-Dipropyl-4-(2-pyridyl)deca-4,6-diene (4"aa). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (ddd, *J* = 4.6, 1.8, 1.3 Hz, 1H), 7.60 (td, *J* = 6.6, 1.9 Hz, 1H), 7.13–7.07 (m, 2H), 5.24 (t, *J* = 7.3 Hz, 1H), 2.47 (t, *J* = 7.9 Hz, 2H), 2.16–2.07 (m, 4H), 1.84 (t, *J* = 7.8 Hz, 2H), 1.51–1.39 (m, 4H), 1.26 (sext, *J* = 7.5 Hz, 2H), 1.14 (sext, *J* = 7.6 Hz, 2H), 1.00–0.90 (m, 6H), 0.78 (t, *J* = 7.3 Hz, 3H), 0.71 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8, 149.1, 141.6, 138.5, 138.8, 135.3, 128.5, 124.2, 120.7, 36.5, 33.5, 31.8, 30.0, 23.3, 22.3, 21.8, 21.7, 14.8, 14.4, 14.10, 14.06. MS (EI, 70 eV) *m/z* (%) 299 (M^+, 3), 272 (20), 270 (23), 258 (12), 257 (23), 256 (100), 244 (17), 242 (10), 228 (10), 214 (11), 198 (12), 167 (11), 149 (20). HRMS (EI) Calcd for $C_{21}H_{33}N$: 299.2613. Found: *m/z* 299.2621.



Methyl-(*E*)-6-(oct-4-en-4-yl)nicotinate (4ca, *E*/*Z* = >99:1). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (q, *J* = 1.0 Hz, 1H), 8.17 (dt, *J* = 8.4, 1.1 Hz, 1H), 7.42 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.40 (t, *J* = 7.3 Hz, 1H), 3.93 (s, 3H), 2.62 (t, *J* = 7.7 Hz, 2H), 2.60 (q, *J* = 7.4 Hz, 2H), 1.59–1.21 (m, 4H), 1.04–0.81(m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 163.3, 150.0, 139.1, 137.1, 134.9, 123.1, 119.4, 52.2, 31.0, 30.0, 22.8, 22.2, 14.20, 14.17. IR (neat) 2959, 2932, 2872, 1728, 1593, 1557, 1458, 1435, 1387, 1379, 1292, 1271, 1194, 1119, 1022, 963, 856, 783, 737, 640 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 247 (M^+, 30), 232 (25), 219 (17), 218 (100), 204 (24), 202 (10), 190 (17), 189 (20), 188 (24), 177 (11), 137 (10), 58 (13). Anal. Calcd for $C_{15}H_{21}NO_2$; C, 72.84; H, 8.56. Found: C, 72.82; H, 8.47.



(*E*)-2-(4-Octen-4-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (4da, *E*/*Z* = 98:2). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (q, *J* = 0.9 Hz, 0.02H), 8.87 (q, *J* = 0.9 Hz, 0.98H), 8.00 (dd, *J* = 7.8, 1.9 Hz, 0.02H), 7.97 (dd, *J* = 7.8, 1.8 Hz, 0.98H), 7.34 (dd, *J* = 7.8, 0.9 Hz, 0.98H), 7.13 (dd, *J* = 7.8, 1.0 Hz, 0.02H), 6.27 (t, *J* = 7.4 Hz, 0.98H), 5.58 (t, *J* =7.4 Hz, 0.02H), 2.62 (t, *J* = 7.6 Hz, 1.96H), 2.44 (t, *J* = 7.5 Hz, 0.04H), 2.24 (q, *J* = 7.4 Hz, 1.96H), 1.98 (q, *J* = 7.5 Hz, 0.04H), 1.56–1.17 (m, 16H), 1.02–0.80 (m, 6H); ^{13}C NMR [for (*E*)-**4da**, 101 MHz, $CDCl_3$] δ 161.7, 154.3, 142.6, 139.4, 133.5, 119.6, 84.0, 31.0, 30.2, 24.9, 22.9, 22.1, 14.21, 14.19. IR (neat) 2959, 2932, 2872, 1595, 1543, 1458, 1400, 1371, 1358, 1312, 1215, 1146, 1134, 1109, 1098, 1020, 963, 858, 829, 770, 689, 669 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 315 (M^+, 42),



314 (M^+–1, 19), 300 (27), 287 (24), 286 (100), 285 (27), 272 (17), 186 (13), 181 (16), 169 (16), 131 (21), 119 (18), 69 (39). Anal. Calcd for $C_{19}H_{30}BNO_2$; C, 72.39; H, 9.59. Found: C, 72.35; H, 9.66.

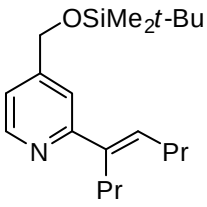
(*E*)-2-(Oct-4-en-4-yl)-4-phenylpyridine (4ea). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 5.1, 0.7 Hz, 1H), 7.69–7.61 (m, 2H), 7.58 (d, *J* = 1.9 Hz, 1H), 7.52–7.40 (m, 3H), 7.32 (dd, *J* = 5.1, 1.8 Hz, 1H), 6.30 (t, *J* = 7.4 Hz, 1H), 2.70 (t, *J* = 7.7 Hz, 2H), 2.29 (q, *J* = 7.4 Hz, 2H), 1.56 (sext, *J* = 7.4 Hz, 2H), 1.49 (sext, *J* = 7.5 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 149.0, 148.4, 139.7, 138.6, 132.2, 128.8, 128.6, 126.8, 119.2, 118.3, 30.9, 30.3, 22.9, 22.2, 14.22, 14.17. IR (neat) 2957, 2930, 2871, 1591, 1541, 1497, 1464, 1404, 1387, 1377, 1288, 1076, 887, 839, 760, 696, 613 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 237 (M^++1, 20), 236 (M^+, 100), 222 (18), 220 (14), 208 (16), 207 (22), 206 (33), 195 (11), 194 (12), 193 (21). Anal. Calcd for $C_{19}H_{23}N$; C, 85.99; H, 8.74. Found: C, 85.90; H = 8.80.

(4*E*,6*E*)-5,6-Dipropyl-4-(4-phenylpyridin-2-yl)deca-4,6-diene (4'ea). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.58–7.52 (m, 2H), 7.48–7.37 (m, 3H), 7.24 (s, 1H), 7.22 (dd, *J* = 5.1, 1.8 Hz, 1H), 4.99 (t, *J* = 7.3 Hz, 1H), 2.57 (t, *J* = 7.7 Hz, 2H), 2.26 (t, *J* = 7.8 Hz, 2H), 1.94 (t, *J* = 8.2 Hz, 2H), 1.75 (q, *J* = 7.3 Hz, 2H), 1.48–1.24 (m, 6H), 1.01–0.83 (m, 11H), 0.59 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 148.8, 147.1, 142.9, 139.1, 138.7, 136.6, 132.1, 128.8, 128.5, 126.8, 123.2, 118.3, 34.7, 33.2, 32.8, 30.1, 22.7, 22.5, 21.8, 21.7, 14.9, 14.3, 14.2, 13.8. IR (neat) 3055, 2953, 2918, 1584, 1560, 1491, 1466, 1441, 1427, 1339, 1248, 1207, 1152, 1094, 1072, 1049, 991, 934, 907, 862, 835, 781, 739, 704, 607, 556 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 376 (M^+, 20), 348 (13), 346 (16), 336 (13), 334 (23), 333 (29), 332 (M^+–Pr, 100), 318 (13), 304 (12), 292 (19), 290 (17), 288 (11), 274 (14), 246 (12), 58 (21). HRMS (EI) Calcd for $C_{27}H_{37}N$: 375.2926. Found: *m*/*z* 375.2922.

(*E*)-2-(Oct-4-en-4-yl)-4-(trifluoromethyl)pyridine (4fa). A colorless oil, R_f 0.60 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.9 Hz, 1H), 7.56 (t, *J* = 0.8 Hz, 1H), 7.30 (dd, *J* = 5.0, 1.0 Hz, 1H), 6.30 (t, *J* = 7.5 Hz, 1H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.27 (q, *J* = 7.4 Hz, 2H), 1.53 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.5 Hz, 2H), 0.99 (t, *J*

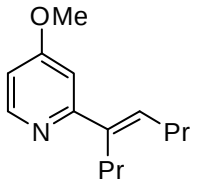
= 7.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 149.5, 139.0, 138.2 (q, *J* = 33.2 Hz), 134.1, 123.0 (q, *J* = 272.4 Hz), 116.4 (q, *J* = 3.3 Hz), 115.6 (q, *J* = 3.6 Hz), 31.0, 30.1, 22.8, 22.1, 14.21, 14.18; ^{19}F NMR (282 MHz, $CDCl_3$) δ -65.3. IR (neat) 3019, 2961, 2934, 2874, 1638, 1605, 1568, 1466, 1458, 1416, 1400, 1335, 1269, 1173, 1140, 1088, 893, 839, 737, 683, 667 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 257 (M^+, 56), 242 (32), 238 (11), 229 (28), 228 (100), 214 (41), 213 (13), 212 (25), 200 (35), 199 (44), 198 (60), 187 (19), 186 (26), 185 (31), 172 (10), 117 (13). Anal. Calcd for $C_{14}H_{18}F_3N$; C, 82.48; H, 10.12. Found: C, 82.20; H, 10.04.

(*E*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-2-(oct-4-en-4-yl)pyridine (4ga). A



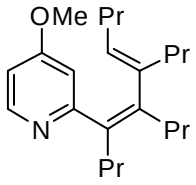
colorless oil, R_f 0.50 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 5.1 Hz, 1H), 7.34 (s, 1H), 7.04 (dd, *J* = 5.0, 0.6 Hz, 1H), 6.24 (t, *J* = 7.3 Hz, 1H), 4.73 (s, 2H), 2.60 (t, *J* = 7.7 Hz, 2H), 2.24 (q, *J* = 7.4 Hz, 2H), 1.51 (sext, *J* = 7.4 Hz, 2H), 1.42 (sext, *J* = 7.3 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.97 (s, 9H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.12 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 150.4, 148.5, 139.5, 132.0, 118.2, 117.0, 63.7, 30.9, 30.3, 26.0, 23.0, 22.2, 18.5, 14.25, 14.18, –5.2. IR (neat) 3030, 2955, 2930, 2886, 2874, 1603, 1562, 1472, 1462, 1414, 1379, 1362, 1319, 1254, 1219, 1202, 1113, 1080, 1065, 1007, 993, 939, 839, 797, 777, 669 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 222 (32), 167 (15), 166 (100), 147 (34), 136 (12), 73 (25). Anal. Calcd for $C_{20}H_{35}NOSi$; C, 72.01; H, 10.58. Found: C, 72.26; H, 10.44.

(*E*)-4-Methoxy-2-(oct-4-en-4-yl)pyridine (4ha). A colorless oil, R_f 0.60 (hexane–ethyl



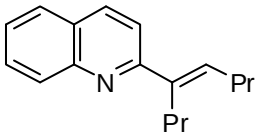
acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 5.6 Hz, 1H), 6.86 (d, *J* = 2.6 Hz, 1H), 6.64 (dd, *J* = 5.7, 2.4 Hz, 1H), 6.19 (t, *J* = 7.4 Hz, 1H), 3.89 (s, 3H), 2.57 (t, *J* = 7.7 Hz, 2H), 2.22 (q, *J* = 7.4 Hz, 2H), 1.49 (sext, *J* = 7.4 Hz, 2H), 1.40 (sext, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 161.6, 149.8, 139.5, 132.0, 107.0, 106.6, 55.0, 30.8, 30.4, 22.9, 22.1, 14.21, 14.17. IR (neat) 2959, 2932, 2870, 1591, 1564, 1470, 1422, 1414, 1377, 1308, 1260, 1236, 1204, 1177, 1130, 1113, 1044, 839, 812, 779, 731, 669 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 219 (M^+, 33), 204 (26), 191 (15), 190 (100), 176 (18), 174 (13), 167 (21), 166 (56), 162 (17), 161 (21), 160 (20), 149 (49), 147 (11). HRMS (EI) Calcd for $C_{14}H_{21}NO$: 219.1623. Found: *m/z* 219.1614.

(4*E*,6*E*)-5,6-Dipropyl-4-(4-methoxypyridin-2-yl)deca-4,6-diene (4'ha). A colorless



oil, R_f 0.75 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 5.5, 0.7 Hz, 1H), 6.58–6.53 (m, 2H), 4.95 (t, *J* = 7.4 Hz, 1H), 3.77 (s, 3H), 2.50 (t, *J* = 7.8 Hz, 2H), 2.22 (t, *J* = 7.8 Hz, 2H), 1.92 (t, *J* = 8.3 Hz, 2H), 1.76 (q, *J* = 7.3 Hz, 2H), 1.46–1.20 (m, 6H), 1.08–0.75 (m, 11H), 0.66 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 164.3, 149.4, 142.4, 139.0, 136.5, 131.5, 110.8, 106.8, 54.9, 34.6, 33.1, 32.6, 30.1, 22.7, 22.4, 21.71, 21.65, 14.9, 14.3, 14.1, 13.9. IR (neat) 2959, 2932, 2870, 1636, 1589, 1562, 1466, 1416, 1377, 1316, 1298, 1265, 1256, 1213, 1115, 1092, 1042, 853, 839, 777 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 329 (M^+, 5), 300 (36), 287 (95), 286 (100), 256 (12), 245 (15), 243 (30), 228 (35), 214 (14), 212 (12), 219 (11), 207 (10). HRMS (EI) Calcd for $C_{22}H_{35}NO$: 329.2719. Found: *m*/*z* 329.2716.

4-Dimethylamino-2-(oct-4-en-4-yl)pyridine (4ia, *E*/*Z* = 97:3). A colorless oil, R_f 0.70 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 5.8, 0.7 Hz, 0.03H), 8.18 (d, *J* = 6.0 Hz, 0.97H), 6.54 (d, *J* = 2.6 Hz, 1H), 6.35 (dd, *J* = 6.1, 2.6 Hz, 1H), 6.08 (t, *J* = 7.4 Hz, 0.97H), 5.48 (t, *J* = 7.5 Hz, 0.03H), 2.99 (s, 5.82 H), 2.98 (s, 0.18 H), 2.57 (t, *J* = 7.6 Hz, 1.94H), 2.40 (t, *J* = 7.3 Hz, 0.06H), 2.19 (q, *J* = 7.3 Hz, 1.94H), 2.01 (q, *J* = 7.4 Hz, 0.06H), 1.55–1.31 (m, 4H), 1.01–0.84 (m, 6H); ^{13}C NMR [for (*E*)-**4ia**, 101 MHz, $CDCl_3$] δ 160.4, 154.6, 148.6, 140.6, 130.8, 104.6, 103.3, 39.2, 30.8, 30.6, 23.0, 22.1, 14.23, 14.17. IR (neat) 3059, 2953, 2895, 2212, 1738, 1715, 1626, 1522, 1468, 1435, 1395, 1358, 1329, 1250, 1165, 1142, 1109, 1061, 1015, 988, 874, 841, 746, 694, 502 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 232 (M^+, 39), 217 (29), 204 (17), 203 (100), 189 (18), 187 (17), 175 (19), 174 (20), 173 (22), 166 (12), 162 (13), 160 (12). HRMS (EI) Calcd for $C_{15}H_{24}N_2$: 232.1939. Found: *m*/*z* 232.1945.



(*E*)-2-(Oct-4-en-4-yl)quinoline (4ja). A colorless oil, R_f 0.50 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.7 Hz, 2H), 7.75 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.66 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.46 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.32 (t, *J* = 7.4 Hz, 1H), 2.79 (t, *J* = 7.7, 2H), 2.32 (t, *J* = 7.4 Hz, 2H), 1.62–1.40 (m, 4H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 147.5, 140.6, 135.7, 133.7, 129.3, 129.0, 127.1, 126.7, 125.5, 119.1, 31.1, 30.4, 22.9, 22.4, 14.3, 14.2. IR (neat) 3059, 2959, 2930, 2870, 1634, 1616, 1597, 1555, 1503, 1456, 1425, 1377, 1337, 1304, 1217, 1138, 1107, 1017, 899, 820, 754, 704, 621 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 239 (M^+, 47), 238 (M^+–1, 12), 224 (23), 211 (18), 210 (100), 196 (22),

194 (18), 182 (20), 181 (25), 180 (36), 169 (15), 168 (19), 167 (30), 128 (10). HRMS (EI) Calcd for $C_{17}H_{21}N$: 239.1674. Found: *m*/*z* 239.1679.

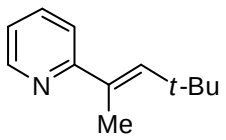
(*E*)-2-(Oct-4-en-4-yl)pyrazine (4ka). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (d, *J* = 1.5 Hz, 0.01H), 8.66 (d, *J* = 1.5 Hz, 0.99H), 8.56 (dd, *J* = 1.3 Hz, 0.01H), 8.46 (dd, *J* = 2.5, 1.6 Hz, 0.99H), 8.39 (d, *J* = 2.4 Hz, 0.01H), 8.34 (d, *J* = 2.5 Hz, 0.99H), 6.28 (t, *J* = 7.3 Hz, 0.99H), 5.71 (t, *J* = 7.4 Hz, 0.01H), 2.61 (t, *J* = 7.7 Hz, 1.98H), 2.46 (t, *J* = 7.0 Hz, 0.02H), 2.26 (q, *J* = 7.4 Hz, 1.98H), 2.03 (q, *J* = 7.4 Hz, 0.02H), 1.58–1.31 (m, 4H), 1.03–0.80 (m, 6H); ^{13}C NMR [for (*E*)-**4ka**, 101 MHz, $CDCl_3$] δ 155.2, 143.1, 142.0, 141.7, 137.1, 137.1, 134.3, 30.9, 29.8, 22.8, 22.1, 14.2, 14.1. IR (neat) 3368, 2957, 2930, 2870, 1690, 1630, 1595, 1541, 1501, 1458, 1429, 1375, 1292, 1225, 1065, 986, 841, 804, 752, 663 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 190 (M^+, 36), 189 (M^+–1, 10), 175 (24), 162 (14), 161 (100), 147 (24), 145 (10), 133 (24), 132 (19), 131 (19), 119 (20). Anal. Calcd for $C_{12}H_{18}N$; C, 75.74; H, 9.53. Found: C, 76.04; H, 9.76.

(*Z*)-2-[1,4-Bis(trimethylsilyl)but-2-en-2-yl]pyridine (4ad). A colorless oil, R_f 0.45 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (dt, *J* = 4.9, 0.9 Hz, 1H), 7.56 (td, *J* = 7.8, 1.8 Hz, 1H), 7.35 (dd, *J* = 8.0, 0.9, 1H), 7.05 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.09 (t, *J* = 8.7 Hz, 1H), 2.14 (s, 2H), 1.63 (d, *J* = 8.6 Hz, 2H), 0.06 (d, *J* = 0.6, 9H), –0.12 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 148.2, 135.7, 124.9, 120.5, 120.0, 20.8, 18.5, –0.7, –1.3. IR (neat) 2955, 2928, 1732, 1624, 1586, 1562, 1464, 1431, 1385, 1287, 1248, 1140, 1072, 968, 839, 787, 754, 692 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 277 (M^+, 10), 263 (26), 262 (96), 205 (11), 204 (51), 190 (51), 189 (10), 188 (24), 167 (22), 149 (61), 73 (60), 59 (12), 58 (100), 57 (15). HRMS (EI) Calcd for $C_{15}H_{27}NSi_2$: 277.1682. Found: *m*/*z* 277.1684.

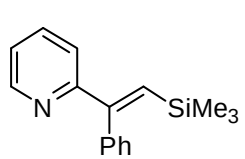
(*E*)-2-(1,2-diphenylvinyl)pyridine [(*E*)-4ae]. A colorless oil, R_f 0.50 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.1 Hz, 1H), 7.89 (s, 1H), 7.57 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.46–7.35 (m, 3H), 7.27–7.21 (m, 2H), 7.18 (dd, *J* = 6.7, 5.1 Hz, 1H), 7.16–7.01 (m, 5H), 6.98 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 149.0, 140.3, 139.0, 136.6, 136.2, 130.7, 130.1, 129.9, 128.9, 127.8, 127.5, 127.1, 122.3, 121.8. MS (EI, 70 eV) *m/z* (%) 258 (M^++1, 17), 257 (M^+, 100), 256 (M^+–1, 100), 180 (45), 178

(12), 153 (12), 128 (14), 127 (16). HRMS (FAB+) Calcd for $C_{19}H_{15}N$: 257.1204. Found: *m*/*z* 257.1201.

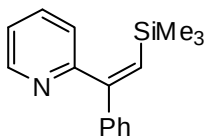
(*E*)-2-(4,4-Dimethylpent-2-en-2-yl)pyridine (4ac). A colorless oil, R_f 0.65 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (ddd, *J* = 4.8, 1.9, 0.8 Hz, 1H), 7.58 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.07 (ddd, *J* = 7.5, 4.8, 1.0 Hz, 1H), 6.31 (q, *J* = 1.3 Hz, 1H), 2.22 (d, *J* = 1.3 Hz, 3H), 1.25 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 148.3, 141.8, 136.0, 133.8, 121.0, 119.7, 32.8, 30.8, 15.6. IR (neat) 2957, 2905, 2866, 1638, 1584, 1564, 1464, 1431, 1383, 1362, 1271, 1252, 1198, 1152, 1099, 1047, 1003, 990, 862, 777, 760, 743, 619 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 174 (M^+–1, 13), 161 (13), 160 (M^+–Me, 100), 146 (10), 145 (11), 144 (13), 132 (12), 131 (28), 130 (25), 117 (16), 98 (20), 81 (35). Anal. Calcd for $C_{12}H_{17}N$; C, 82.23; H, 9.78. Found: C, 82.46; H, 9.99.



(*E*)-2-(1-Phenyl-2-(trimethylsilyl)ethenyl)pyridine [(*E*)-4af]. A colorless oil, R_f 0.30 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.52 (td, *J* = 7.6, 1.8, 1H), 7.42–7.31 (m, 3H), 7.30–7.20 (m, 2H), 7.17 (s, 1H), 7.13 (ddd, *J* = 7.5, 4.7, 1.1 Hz, 1H), 6.93 (dt, *J* = 8.1, 1.1 Hz, 1H), –0.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 155.0, 149.0, 141.2, 136.2, 133.1, 129.6, 127.9, 127.3, 122.1, 122.0, –0.04. IR (neat) 2959, 2932, 2872, 1690, 1632, 1595, 1551, 1466, 1456, 1377, 1179, 1088, 1001, 891, 843, 760, 696, 664, 615 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 253 (M^+, 16), 252 (42), 240 (45), 239 (85), 238 (M^+, –Me, 100), 236 (14), 209 (11), 208 (55), 194 (11), 181 (11), 180 (63), 176 (13), 135 (15), 106 (15), 106 (29), 105 (10), 73 (14). Anal. Calcd for $C_{16}H_{19}NSi$; C, 75.83; H, 7.56. Found: C, 75.59; H, 7.57.



(*Z*)-2-(1-Phenyl-2-(trimethylsilyl)ethenyl)pyridine [(*Z*)-4af]. A colorless oil, R_f 0.40 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.65 (td, *J* = 10.9, 1.9 Hz, 1H), 7.33–7.18 (m, 7H), 7.34 (s, 1H), –0.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 155.5, 148.8, 142.3, 135.7, 135.7, 133.5, 128.0, 127.5, 127.4, 124.2, 122.2, 0.3. IR (neat) 2961, 2932, 2872, 1701, 1638, 1570, 1518, 1466, 1404, 1377, 1290, 1163, 1136, 1059, 1013, 899, 851, 743 cm^{-1}. HRMS (EI) Calcd for $C_{16}H_{19}NSi$: 253.1287. Found: *m*/*z* 253.1277.



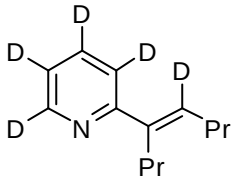
Protodesilylation of (*E*)-4af. 1.0 M solution of TBAF in THF (0.24 mmol, 0.24 mL) was added to **(*E*)-4af** (0.12 mmol, 31 mg) dissolved into THF (2.5 ml). The solution was heated at 60 ºC for 8 h. The organic phase was extracted with ethyl acetate, washed with brine, dried over $NaSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give 2-(1-phenylethenyl)pyridine in 81% yield as a colorless oil. The ^{1}H NMR and ^{13}C NMR spectra of the obtained product was in accordance with the previously reported one.[28]

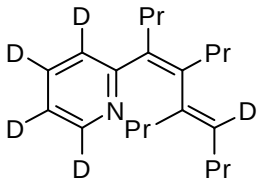
Protodesilylation of (*Z*)-4af. The reaction was done following the procedure above. 2-(1-phenylvinyl)pyridine was obtained quantitatively.

KIE experiment using $ZnMe_2$. In a glove box, $Ni(cod)_2$ (15 μmol, 4.1 mg), P*i*-Pr_3 (60 μmol, 9.6 mg), 1.0 M solution of $ZnMe_2$ in hexane (30 μmol, 30 μL) and toluene (1.25 mL) were placed in a 3 mL-vial before pyridine (**7a**, 1.50 mmol, 119 mg) was added. In another vial were placed the same catalyst and **7a**-d_5 in the same amount. To each vial were added 4-octyne (0.50 mmol, 55.0 mg) and undecane (internal standard, 78 mg, 0.50 mmol). Each vial was closed with a screw cap and heated at 50 ºC. Aliquots of each reaction mixture were taken and analyzed by GC to monitor each reaction. The set of experiments was repeated twice and the average yields for the three sets were calculated and plotted in Figure 1.

KIE experiment using $AlMe_3$. The reaction was carried out according to the procedure above but with 1.0 M solution of $AlMe_3$ in hexane (0.03 mmol, 30 μL) in lieu of $ZnMe_2$. Average yields for the three sets of experiments are plotted in Figure 2.

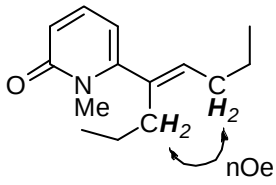
(*E*)-3,4,5,6-Tetradeuterio-2-(5-deuteriooct-4-en-4-yl)pyridine (4aa-d_5). A colorless oil, R_f 0.55 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (t, *J* = 7.7 Hz, 2H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.51 (sext, *J* = 7.4 Hz, 2H), 1.41 (sext, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 148.2 (t, *J* = 26.8 Hz), 139.4, 138.4 (t, *J* = 24.9 Hz), 131.7 (t, *J* = 23.0), 120.4 (t, *J* = 24.5 Hz), 119.8 (t, *J* = 24.2 Hz), 30.8, 30.2, 22.9, 22.1, 14.21, 14.17. IR (neat) 2959, 2930, 2870, 1626, 1553, 1530, 1462, 1456, 1377, 1316, 1250, 1098, 970, 897, 829, 723, 664, 590 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 194 (M^+, 35), 179 (23), 166 (14), 165 (100), 151 (18), 149 (15), 137 (14), 136 (20), 135 (33), 134 (10), 124 (11), 122 (17), 121 (11). Anal. Calcd for $C_{13}H_{14}D_5N$; C, 80.35; H, 7.26; D, 5.01. Found: C, 80.18; H, 7.22; D, 5.02.



(4*Z*,6*E*)-7-Deuterio-5,6-dipropyl-4-(3,4,5,6-tetradeuterio-2-pyridyl)deca-4,6-diene (4'aa-*d*$_5$). 

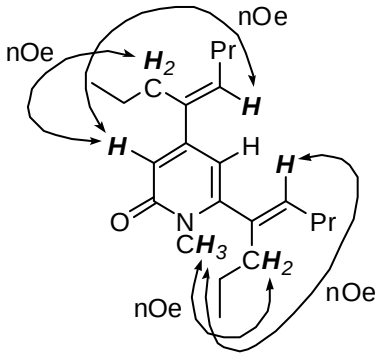
A colorless oil, R_f 0.55 (hexane–ethyl acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (t, *J* = 7.7 Hz, 2H), 2.23 (t, *J* = 7.9 Hz, 2H), 1.91 (t, *J* = 8.2 Hz, 2H), 1.73 (t, *J* = 7.3 Hz, 2H), 1.48–1.08 (m, 6H), 1.04–0.82 (m, 11H), 0.65 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 147.8 (t, *J* = 26.5 Hz), 142.6, 138.7, 136.4, 134.1 (t, *J* = 23.8 Hz), 131.6 (t, 23.0 Hz), 124.7 (t, *J* = 24.6 Hz), 119.5 (t, *J* = 25.3 Hz), 34.6, 33.0, 32.5, 29.9, 22.5, 22.2, 22.1, 21.6, 14.8, 14.7, 14.1, 13.8. IR (neat) 2957, 2930, 2870, 1591, 1553, 1530, 1464, 1456, 1377, 1316, 1109, 1092, 968, 883, 827, 746, 584 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 262 (M^+–Pr, 31), 261 (100), 203 (10). HRMS (EI) Calcd for $C_{21}H_{28}D_5N$: 304.2927. Found: *m/z* 304.2913.

Hydroheteroarylation of 4-octyne with 2-pyridones. *General procedure*. In a glove box, a pyridone (**8**, 1.00 mmol) and a 1.08 M solution of $AlMe_3$ in hexane (185 μL, 0.20 mmol) was placed in a 3 mL-vial. A solution of $Ni(cod)_2$ (13.8 mg, 50 μmol) and P(*i*-Pr)$_3$ (16.0 mg, 0.100 mmol) in toluene (1.0 mL) was added. After addition of 4-octyne (**2a**, 132 mg, 1.2 mmol) and dodecane (an internal standard, 85 mg, 0.50 mmol), the vial was closed with a screw cap, taken outside the dry box and heated with stirring at the temperature for the time specified in Table 5. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The crude was purified by flash chromatography on silica gel to give the corresponding products in yields listed in Table 5. Stereoisomers were further separated by preparative recycling GPC or silica gel chromatography.

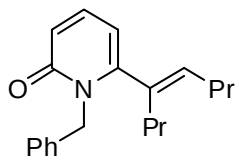
(*E*)-1-Methyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (9aa). 

A colorless oil, R_f 0.25 (hexane–ethyl acetate = 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 9.1, 6.8 Hz, 1H), 6.48 (dd, *J* = 9.1, 1.4 Hz, 1H), 5.94 (dd, *J* = 6.8, 1.5 Hz, 1H), 5.57 (t, *J* = 7.3 Hz, 1H), 3.44 (s, 3H), 2.25 (br t, *J* = 7.8 Hz, 2H), 2.16 (q, *J* = 7.3 Hz, 2H), 1.48 (sext, *J* = 7.4 Hz, 2H), 1.33 (sext, *J* = 7.5 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 152.2, 138.6, 135.7, 134.0, 117.9, 106.7, 33.5, 32.4, 30.0, 22.6, 21.5, 14.1, 14.0. IR (neat) 3487, 2959, 2932, 2872, 1667, 1651, 1582, 1549, 1464, 1427, 1377, 1283, 1157, 1117, 1090, 1057, 924, 907, 799, 731, 644 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 220 (M^++1, 17), 219 (M^+, 100), 204 (12), 191 (11), 190 (75), 177 (13), 176 (82), 162 (29), 149 (14), 148 (28), 134 (24). HRMS (EI) Calcd for $C_{14}H_{21}NO$: M^+, 219.1623. Found: *m/z* 219.1624.

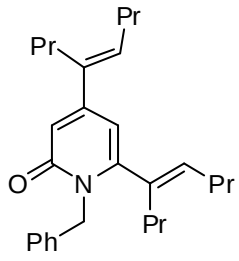
(*E*,*E*)-1-Methyl-4,6-di(oct-4-en-4-yl)pyridin-2(1*H*)-one (9'aa). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (d, *J* = 1.8 Hz, 1H), 5.98 (d, *J* = 1.8 Hz, 1H), 5.85 (t, *J* = 7.2 Hz, 1H), 5.58 (t, *J* = 7.3 Hz, 1H), 3.40 (s, 3H), 2.35 (t, *J* = 7.7 Hz, 2H), 2.24 (br t, *J* = 7.7 Hz, 2H), 2.16 (q, *J* = 7.4 Hz, 4H), 1.54–1.28 (m, 8H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 152.4, 150.7, 137.4, 136.0, 133.8, 132.0, 113.4, 105.6, 33.1, 32.5, 30.7, 30.6, 30.0, 22.8, 22.6, 21.9, 21.6, 14.14, 14.08, 14.0 (2C). IR (neat) 2959, 2932, 2870, 1659, 1651, 1584, 1530, 1456, 1436, 1377, 1348, 1094, 899, 862, cm^{-1}. MS (EI, 70 eV) *m/z* (%) 330 (M^++1, 24), 329 (M^+, 100), 301 (18), 300 (75), 287 (19), 286 (67), 246 (11), 244 (11), 218 (28), 207 (13), 152 (12), 57 (10), 55 (13). HRMS (EI) Calcd for $C_{22}H_{35}NO$: M^+, 329.2719. Found: *m*/*z* 329.2724.



(*E*)-1-Benzyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (9ba). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.15 (m, 4H), 7.07 (d, *J* = 7.5 Hz, 2H), 6.54 (d, *J* = 9.1 Hz, 1H), 5.94 (d, *J* = 6.8 Hz, 1H), 5.39 (t, *J* = 7.2 Hz, 1H), 5.19 (br, 2H), 2.13 (br, 2H), 2.03 (q, *J* = 7.1 Hz, 2H), 1.30 (br sext, *J* = 7.6 Hz, 4H), 0.84 (br t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 152.1, 138.8, 137.2, 134.8, 134.7, 128.1, 126.7, 126.2, 118.7, 107.0, 48.7, 32.8, 29.9, 22.3, 21.5, 14.0, 13.9. IR (neat) 2959, 2932, 2870, 1736, 1667, 1651, 1582, 1547, 1497, 1454, 1425, 1397, 1379, 1356, 1140, 1078, 1074, 1030, 905, 806, 797, 733, 696 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 295 (M^+, 18), 267 (10), 266 (49), 253 (19), 252 (100), 91 (36). Anal. Calcd for $C_{20}H_{25}NO$: C, 81.31; H, 8.53. Found: C, 81.42; H, 8.75.



(*E*,*E*)-1-Benzyl-4,6-di(oct-4-en-4-yl)pyridin-2(1*H*)-one (9'ba). A colorless oil, R_f 0.55 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.15 (m, 3H), 7.08 (d, *J* = 7.5 Hz, 2H), 6.51 (d, *J* = 1.8 Hz, 1H), 6.00 (d, *J* = 1.8 Hz, 1H), 5.92 (t, *J* = 7.3 Hz, 1H), 5.39 (t, *J* = 7.2 Hz, 1H), 5.17 (br, 2H), 2.38 (t, *J* = 7.8 Hz, 2H), 2.19 (q, *J* = 7.4 Hz, 2H), 2.12 (br, 2H), 2.03 (q, *J* = 7.3 Hz, 2H), 1.56–1.39 (m, 4H), 1.37–1.22 (m, 4H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9, 152.4, 150.6, 137.4, 137.3, 135.2, 134.5, 132.4, 128.2, 126.7, 126.3, 114.1, 106.0, 48.4,



32.9, 30.8, 30.6, 29.9, 22.9, 22.4, 22.1, 21.6, 14.2, 14.1, 14.0 (2C). IR (neat) 2959, 2932, 2872, 1661, 1651, 1582, 1530, 1497, 1454, 1431, 1379, 1350, 1148, 901, 862, 829, 725, 694 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 405 (M^+, 27), 377 (17), 376 (53), 363 (29), 362 (100), 207 (11), 91 (22). HRMS (EI) Calcd for $C_{28}H_{39}NO$: M^+, 405.3032. Found: *m/z* 405.3035.

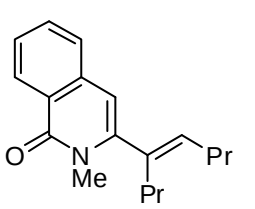
(*E*)-1,3-Dimethyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (9ca). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 6.9, 1.0 Hz, 1H), 5.87 (d, *J* = 6.8 Hz, 1H), 5.54 (t, *J* = 7.3 Hz, 1H), 3.44 (s, 3H), 2.23 (br t, *J* = 7.8 Hz, 2H), 2.15 (q, *J* = 7.3 Hz, 2H), 2.14 (s, 3H), 1.47 (sext, *J* = 7.3 Hz, 2H), 1.31 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 149.5, 135.94, 135.86, 133.8, 126.5, 106.2, 33.6, 32.5, 30.0, 22.6, 21.5, 17.4, 14.1, 14.0. IR (neat) 2959, 2932, 2872, 1651, 1645, 1599, 1566, 1462, 1456, 1427, 1373, 1211, 1115, 1092, 808, 770 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 17), 233 (M^+, 100), 218 (10), 204 (56), 190 (53), 176 (18), 162 (19), 148 (16), 124 (12). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93. Found: C, 77.18; H, 10.18.

(*E*)-1,4-Dimethyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (9da). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:2). ^1H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 1H), 5.79 (s, 1H), 5.54 (t, *J* = 7.3 Hz, 1H), 3.39 (s, 3H), 2.23 (br t, *J* = 7.6 Hz, 2H), 2.15 (q, *J* = 7.3 Hz, 2H), 2.14 (s, 3H), 1.47 (sext, *J* = 7.3 Hz, 2H), 1.32 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 151.0, 149.9, 135.7, 133.8, 116.4, 109.2, 33.0, 32.3, 29.9, 22.6, 21.5, 21.2, 14.1, 14.0. IR (neat) 2959, 2932, 2870, 1667, 1651, 1591, 1547, 1456, 1433, 1377, 1360, 1271, 1196, 1128, 1096, 905, 854, 818, 731, 646 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 16), 233 (M^+, 100), 218 (17), 205 (15), 204 (86), 191 (14), 190 (85), 176 (21), 174 (11), 163 (13), 162 (26), 161 (10), 160 (10), 148 (21), 147 (10), 146 (11), 53 (12). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93. Found: C, 76.92; H, 9.98.

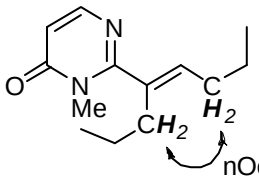
(*E*)-1,5-Dimethyl-6-(oct-4-en-4-yl)pyridin-2(1*H*)-one (9ea). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 9.1 Hz, 1H), 6.46 (d, *J* = 9.1 Hz, 1H), 5.45 (t, *J* = 7.4 Hz, 1H), 3.44 (s, 3H), 2.45 (dt, *J* = 14.2, 8.6 Hz, 1H), 2.22 (q, *J* = 7.3 Hz, 2H), 2.09–1.98 (m, 1H), 2.01 (s, 3H), 1.49 (sext, *J* = 7.3 Hz, 2H), 1.33 (sext, *J* = 7.7 Hz,

2H), 0.99 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 148.4, 142.1, 134.6, 133.7, 117.6, 112.6, 33.6, 33.4, 29.9, 22.5, 21.5, 18.3, 14.6, 14.1. IR (neat) 2959, 2932, 2872, 1667, 1661, 1651, 1587, 1537, 1456, 1414, 1379, 1352, 1260, 1234, 1161, 1088, 972, 926, 910, 826, 733, 644 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 234 (M^++1, 18), 233 (M^+, 100), 218 (13), 205 (10), 204 (67), 191 (13), 190 (82), 176 (16), 162 (21), 160 (11), 148 (21), 147 (13). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93. Found: C, 77.32; H, 10.11.

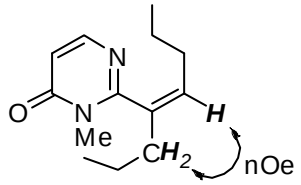
(*E*)-2-Methyl-3-(oct-4-en-4-yl)isoquinolin-1(2*H*)-one (9fa). A colorless oil, R_f 0.55 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.1 Hz, 1H), 7.60 (ddd, J = 8.2, 7.0, 1.4 Hz, 1H), 7.47–7.40 (m, 2H), 6.30 (s, 1H), 5.67 (t, J = 7.4 Hz, 1H), 3.51 (s, 3H), 2.29 (br t, J = 7.4 Hz, 2H), 2.19 (q, J = 7.3 Hz, 2H), 1.51 (sext, J = 7.3 Hz, 2H), 1.38 (sext, J = 7.5 Hz, 2H), 1.00 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 145.9, 136.5, 136.2, 133.8, 131.8, 127.5, 125.9, 125.4, 124.4, 106.0, 33.2, 32.6, 30.0, 22.7, 21.6, 14.2, 14.1. IR (neat) 2959, 2930, 2870, 1645, 1620, 1597, 1560, 1483, 1454, 1422, 1375, 1339, 1316, 1288, 1179, 1152, 1020, 905, 826, 756, 694 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 270 (M^++1, 21), 269 (M^+, 100), 240 (57), 227 (17), 212 (28), 210 (23), 199 (24), 197 (19), 196 (28), 184 (42), 182 (31), 168 (10), 167 (15), 160 (29), 154 (10), 141 (12), 128 (17), 127 (10), 115 (22). Anal. Calcd for $C_{18}H_{23}NO$: C, 80.26; H, 8.61. Found: C, 80.00; H, 8.52.



(*E*)-3-Methyl-2-(oct-4-en-4-yl)pyrimidin-4(3*H*)-one [(*E*)-9ga]. A colorless oil, R_f 0.25 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 6.6 Hz, 1H), 6.35 (d, J = 6.4 Hz, 1H), 5.70 (t, J = 7.3 Hz, 1H), 3.49 (s, 3H), 2.39 (t, J = 7.9 Hz, 2H), 2.21 (q, J = 7.3 Hz, 2H), 1.49 (sext, J = 7.3 Hz, 2H), 1.40 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.6, 152.1, 135.2, 134.9, 112.8, 33.4, 32.0, 30.0, 22.4, 21.7, 14.2, 14.1. IR (neat) 2959, 2932, 2872, 1688, 1682, 1578, 1518, 1464, 1424, 1406, 1358, 1277, 1175, 1155, 1121, 1107, 899, 829, 804 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 220 (M^+, 46), 205 (31), 192 (17), 191 (100), 177 (32), 163 (18), 150 (22), 149 (12), 135 (13), 122 (24). Anal. Calcd for $C_{13}H_{20}N_2O$: C, 70.87; H, 9.15. Found: C, 71.15; H, 9.36.

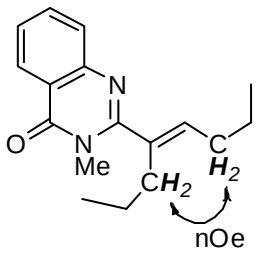


(*Z*)-3-Methyl-2-(oct-4-en-4-yl)pyrimidin-4(3*H*)-one [(*Z*)-9ga]. A colorless oil, R_f 0.20 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 6.6 Hz, 1H),



6.33 (d, *J* = 6.6 Hz, 1H), 5.63 (tt, *J* = 7.3, 1.3 Hz, 1H), 3.44 (s, 3H), 2.24 (br t, *J* = 8.1 Hz, 2H), 1.81 (q, *J* = 7.5 Hz, 2H), 1.55–1.31 (m, 4H), 0.92 (t, *J* = 7.23 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 161.4, 152.3, 134.4, 131.7, 112.8, 37.7, 32.2, 31.4, 22.2, 20.9, 13.9, 13.8. IR (neat) 2959, 2932, 2872, 1688, 1682, 1578, 1520, 1464, 1456, 1427, 1406, 1377, 1333, 1217, 1173, 1155, 1121, 1096, 1049, 906, 831, 804 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 220 (M^+, 41), 205 (22), 192 (15), 191 (100), 177 (12), 122 (13). Anal. Calcd for $C_{13}H_{20}N_2O$: C, 70.87; H, 9.15. Found: C, 71.16; H, 9.39.

(*E*)-3-Methyl-2-(oct-4-en-4-yl)quinazolin-4(3*H*)-one [(*E*)-9ha]. A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.7 Hz, 1H), 7.77–7.67 (m, 2H), 7.45 (ddd, *J* = 7.9, 6.0, 2.2 Hz, 1H), 5.77 (t, *J* = 7.3 Hz, 1H), 3.57 (s, 3H), 2.46 (t, *J* = 8.1 Hz, 2H), 2.26 (q, *J* = 7.5 Hz, 2H), 1.56–1.42 (m, 4H), 1.00 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 157.7, 147.2, 135.7 (2C), 134.3, 133.9, 127.1, 126.3, 120.2, 33.2, 32.3, 30.3, 22.4, 21.6, 14.3, 14.1. IR (neat) 2959, 2932, 2872, 1680, 1674, 1611, 1586, 1566, 1470, 1418, 1337, 1298, 1263, 1180, 1146, 1126, 1109, 1096, 1013, 907, 889, 773, 698, 654 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 270 (M^+, 32), 255 (26), 242 (19), 241 (100), 227 (30), 213 (23), 212 (11), 211 (19), 200 (20), 199 (22), 198 (11), 197 (10), 185 (28). Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20. Found: C, 75.22; H, 8.36.

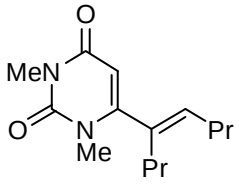


(*Z*)-3-Methyl-2-(oct-4-en-4-yl)quinazolin-4(3*H*)-one [(*Z*)-9ha]. A colorless solid, mp 62.0–62.8 °C, R_f 0.35 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.1 Hz, 1H), 7.77–7.68 (m, 2H), 7.47 (ddd, *J* = 8.1, 6.4, 1.7 Hz, 1H), 5.72 (t, *J* = 7.3 Hz, 1H), 3.56 (s, 3H), 2.34 (t, *J* = 8.0 Hz, 2H), 2.00 (dq, *J* = 14.5, 7.2 Hz, 1H), 1.87 (dq, *J* = 14.4, 7.1 Hz, 1H), 1.65–1.35 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 156.1, 147.4, 135.1, 133.9, 131.4, 127.2, 126.5, 126.4, 120.3, 38.0, 32.1, 31.6, 22.3, 20.9, 14.04, 14.00. IR (KBr) 2955, 2870, 1678, 1609, 1586, 1566, 1476, 1439, 1418, 1377, 1354, 1317, 1294, 1261, 1177, 1152, 1125, 1101, 1074, 1028, 1017, 905, 889, 876, 810, 799, 772, 741, 696, 654, 596, 552, 527, 496, 438 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 270 (M^+, 36), 255 (24), 242 (19), 241 (100), 227 (15), 213 (12), 211 (13), 199 (10), 185 (12).

Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.52; H, 8.20. Found: C, 75.75; H, 8.16.

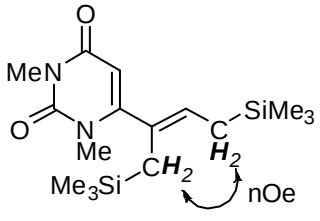
Hydroheteroarylation at C-6 in 1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (1i) with alkynes. *General procedure*. In a glove box, 1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**1i**, 140 mg, 1.00 mmol) and a 1.08 M solution of $AlMe_3$ in hexane (185 μL, 0.20 mmol) were placed in a 3 mL-vial. A solution of $Ni(cod)_2$ (13.8 mg, 50 μmol) and P(*i*-Pr)$_3$ (16.0 mg, 0.100 mmol) in toluene (1.0 mL) was added. After further addition of an alkyne (1.20 mmol) and dodecane (an internal standard, 85 mg, 0.50 mmol), the vial was closed with a screw cap, taken out from the glove box and heated at the temperature for the time specified in Table 5. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give the corresponding products in yields listed in Table 5.

(*E*)-1,3-Dimethyl-6-(oct-4-en-4-yl)pyrimidine-2,4(1*H*,3*H*)-dione [(*E*)-9ia]. A



colorless oil, R_f 0.25 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63 (t, *J* = 7.4 Hz, 1H), 5.54 (s, 1H), 3.35 (s, 3H), 3.29 (s, 3H), 2.22 (t, *J* = 7.8 Hz, 2H), 2.15 (q, *J* = 7.4 Hz, 2H), 1.47 (sext, *J* = 6.8 Hz, 2H), 1.39 (sext, *J* = 7.0 Hz, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 156.6, 152.5, 135.0, 134.0, 101.3, 33.6, 31.8, 29.9, 28.0, 22.5, 21.5, 14.04, 13.96. IR (neat) 2961, 2934, 2872, 1705, 1667, 1651, 1609, 1435, 1395, 1370, 1213, 1159, 1090, 955, 920, 909, 824, 764, 733 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 251 (M^++1, 16), 250 (M^+,100), 235 (45), 222 (12), 221 (77), 208 (11), 207 (52), 193 (23), 180 (57), 179 (17), 165 (38), 164 (19), 154 (13), 150 (19), 136 (33), 134 (10), 123 (12), 122 (34), 108 (16), 94 (15), 82 (15), 79 (11), 55 (11). Anal. Calcd for $C_{14}H_{22}N_2O_2$: C, 67.17; H, 8.86. Found: C, 67.15; H, 8.81.

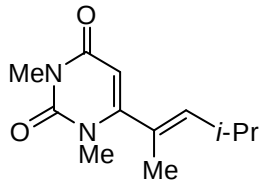
(*E*)-1,3-Dimethyl-6-[1,4-bis(trimethylsilyl)but-2-en-2-yl]pyrimidine-2,4(1*H*,3*H*)-dio



ne (9id). A colorless oil, R_f 0.65 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (t, *J* = 8.6 Hz, 1H), 5.57 (s, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 1.67 (br s, 2H), 1.54 (d, *J* = 8.6 Hz, 2H), 0.07 (s, 9H), 0.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ162.7, 158.6, 152.6 (2C), 129.0, 100.8, 33.9, 27.9, 20.9, 20.2, –0.5, –1.3. IR (neat) 2953, 2895, 1705, 1661, 1609, 1481, 1435, 1393, 1368, 1248, 1209, 1165, 1146, 1049, 999, 939, 874, 853, 841, 766, 694, 448, 434, 428 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 338 (M^+, 14), 323 (17), 266 (26), 265 (100), 251 (28), 73

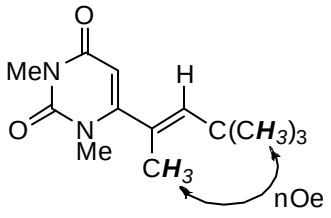
(13). HRMS (EI) Calcd for $C_{16}H_{30}N_2O_2Si_2$: M^+, 338.1846. Found: *m*/*z* 338.1840.

(*E*)-1,3-Dimethyl-6-(4-methylpent-2-en-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (9ib). A



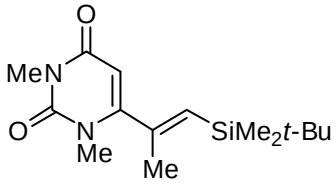
colorless oil, R_f 0.45 (hexane–ethyl acetate = 7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (s, 1H), 5.48 (dq, *J* = 9.5, 1.4 Hz, 1H), 3.35 (s, 3H), 3.29 (s, 3H), 2.62 (dsept, *J* = 9.5, 6.6 Hz, 1H), 1.87 (d, *J* = 1.5 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 157.6, 152.4, 141.9, 126.6, 100.1, 33.3, 27.9, 27.5, 22.2, 16.0. IR (neat) 2959, 2870, 1709, 1659, 1651, 1611, 1436, 1395, 1368, 1300, 1252, 1209, 1163, 1036, 1001, 980, 920, 883, 820, 764, 710, 689, 662, 542 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 223 (M^++1, 14), 222 (M^+, 100), 207 (33), 179 (30), 165 (13), 150 (26), 123 (13), 122 (52), 108 (12), 94 (10), 93 (11), 82 (23). Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16. Found: C, 64.60; H, 8.42.

(*E*)-1,3-Dimethyl-6-(4,4-dimethylpent-2-en-2-yl)pyrimidine-2,4(1*H*,3*H*)-dione (9ic).

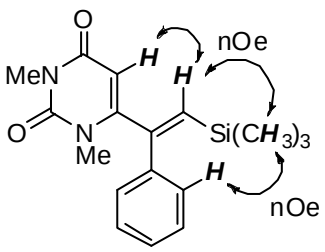


A yellow solid, mp 64.0–64.6 °C, R_f 0.30 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63 (q, *J* = 1.4 Hz, 1H), 5.54 (s, 1H), 3.35 (s, 3H), 3.30 (s, 3H), 1.97 (d, *J* = 1.3 Hz, 1H), 1.20 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 158.8, 144.4 (2C), 127.6, 99.9, 33.4, 33.2, 30.3, 27.9, 17.1. IR (KBr) 2957, 2905, 2868, 1705, 1692, 1659, 1609, 1530, 1439, 1395, 1362, 1252, 1233, 1209, 1059, 1044, 1026, 1009, 982, 895, 851, 822, 758, 718, 681, 669, 556, 492, 469, 417 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 237 (M^++1, 14), 236 (M^+, 93), 222 (15), 221 (100), 193 (11), 179 (41), 164 (40), 151 (10), 137 (10), 136 (79), 122 (34), 121 (14), 108 (16), 107 (13), 91 (11), 82 (20), 67 (10). Anal. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53. Found: C, 65.88; H, 8.60.

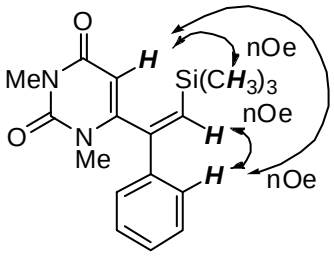
(*E*)-6-[1-(*tert*-Butyldimethylsilyl)prop-1-en-2-yl]-1,3-dimethylpyrimidine-2,4(1*H*, 3*H*)-dione (9ig). A colorless oil, R_f 0.40 (CH_2Cl_2–acetone = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (q, *J* = 1.1 Hz, 1H), 5.55 (s, 1H), 3.35 (s, 3H), 3.32 (s, 3H), 2.03 (d, *J* = 1.1 Hz, 3H), 0.93 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 159.0, 152.3, 145.9, 133.0, 99.0, 33.4, 28.0, 26.4, 21.4, 17.4, –4.5. IR (neat) 2953, 2930, 2884, 1709, 1667, 1651, 1605, 1528, 1470, 1462, 1435, 1393, 1368, 1308, 1250, 1211, 1186, 1148, 1057, 1036, 1007, 993, 955, 874, 860, 824, 783, 764, 683, 638, 521, 482 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 294 (M^+, 36), 239 (11), 238 (43), 237



(100), 223 (23), 182 (10), 181 (22), 180 (86). HRMS (FAB+) Calcd for $C_{15}H_{26}N_2O_2Si$: M^+, 294.1764. Found: *m*/*z* 294.1760.

(*E*)-1,3-Dimethyl-6-[2-phenyl-1-(trimethylsilyl)eth-1-en-2-yl]pyrimidine-2,4(1*H*, 3*H*)-dione [(*E*)-9if]. 

A colorless oil, R_f 0.15 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.34 (m, 3H), 7.30–7.16 (m, 2H), 6.15 (s, 1H), 5.82 (s, 1H), 3.36 (s, 3H), 3.08 (s, 3H), 0.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 157.1, 152.3, 149.9, 138.4, 137.6, 129.0, 128.5, 128.4, 102.0, 33.8, 28.1, 0.1. IR (neat) 2955, 1709, 1661, 1616, 1570, 1493, 1435, 1397, 1370, 1248, 1213, 1163, 991, 914, 864, 849, 764, 733, 709, 694, 444 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 314 (M^+, 31), 300 (12), 299 (50), 243 (21), 242 (100). HRMS (EI) Calcd for $C_{17}H_{22}N_2O_2Si$: M^+, 314.1451. Found: *m*/*z* 314.1455.

(*Z*)-1,3-Dimethyl-6-[2-phenyl-1-(trimethylsilyl)eth-1-en-2-yl]pyrimidine-2,4(1*H*, 3*H*)-dione [(*Z*)-9if]. 

A colorless oil, R_f 0.20 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.32 (m, 5H), 6.53 (s, 1H), 5.80 (s, 1H), 3.42 (s, 3H), 3.08 (s, 3H), 0.13 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 153.6, 152.2, 147.6, 137.4, 134.7, 129.1, 128.9, 125.6, 103.2, 33.0, 28.2, –0.3. IR (neat) 2955, 1703, 1667, 1645, 1611, 1589, 1572, 1526, 1476, 1435, 1393, 1370, 1250, 1211, 1190, 1161, 1105, 993, 916, 868, 839, 785, 762, 733, 706, 665, 652, 540 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 314 (M^+, 14), 299 (23), 243 (25), 242 (100), 184 (15), 159 (12), 128 (11), 115 (11), 99 (10), 82 (29), 73 (14), 58 (12). HRMS (EI) Calcd for $C_{17}H_{22}N_2O_2Si$: M^+, 314.1451. Found: *m*/*z* 314.1461.

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Chapter 5

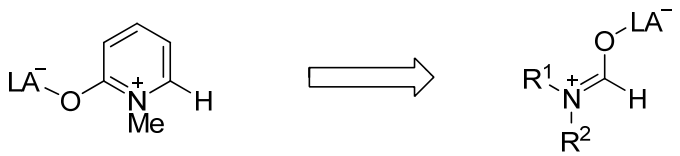
Hydrocarbamoylation of Alkynes

Formamides are found to undergo addition reactions across alkynes through activation of formyl C–H bonds under the nickel/Lewis acid catalysis to give a variety of α,β-unsaturated amides with stereo- and regioselectivity. The presence of Lewis acid cocatalysts is crucial, and formamide coordination to the Lewis acid is considered to be responsible for the C–H activation possibly through oxidative addition to nickel(0).

Introduction

The amide functionality is found in a large number of organic compounds, ranging from proteins to biological and insecticidal active compounds and materials.[1] Amides are also versatile and crucial intermediates in a wide range of organic synthesis. Accordingly, development of new and efficient ways for preparation of amides is of considerable importance in organic chemistry.[2] Manipulation of the formyl C(sp^2)–H bonds in formamides has great synthetic potential for the synthesis of amides with high atom efficiency.[3] Transition metal–catalyzed insertion of unsaturated bonds into the C(sp^2)–H bonds in formamides, namely hydrocarbamoylation reactions,[4] is one such transformation, and is a convenient alternative to aminocarbonylation reactions,[5] which require the use of toxic carbon monoxide. Most of the reported reactions to achieve this transformation require, however, harsh reaction conditions and/or the presence of directing groups to assist oxidative addition of the formyl C(sp^2)–H bond to transition metal complexes.

Activation of C(sp^2)–H bonds in formamides followed by insertion of alkynes is an ideal method for preparation of α,β-unsaturated amides. Nevertheless, only one example to achieve such a transformation has been reported, which utilizes a rhodium catalyst under harsh reaction conditions.[4f] Since the hydroheteroarylation reaction of alkynes with 2-pyridone derivatives reported in Chapter 4 is initiated by catalytic formation of an active pyridinium species *in situ* through coordination of their aminocarbonyl groups to a LA catalyst,[6] the author envisaged that similar activated formamides could be generated catalytically upon their coordination to LA, allowing oxidative addition of the formyl C(sp^2)–H bond located next to positively charged nitrogen (Scheme 1). Reported herein is realization of a nickel/LA-catalyzed hydrocarbamoylation of alkynes possibly via oxidative addition of the formyl C(sp^2)–H bond of formamides to nickel(0), followed by insertion of alkynes and reductive elimination.[7] The reaction proceeds under mild conditions to give variously substituted α,β-unsaturated amides from simple and readily available starting materials in moderate to high yields.



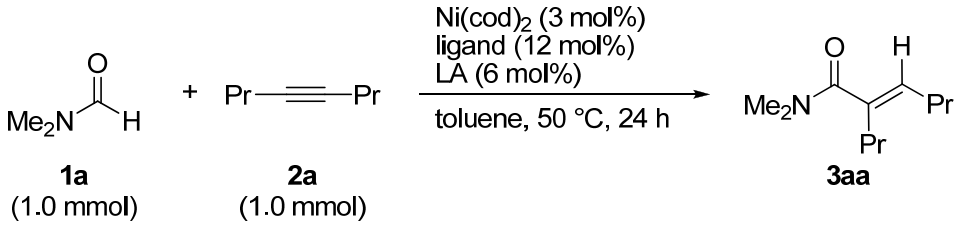
Scheme 1. Plausible C–H bond activation of formamides by nickel(0)/LA.

Results and Discussion

Nickel-catalyzed hydrocarbamoylation of alkynes

The author first examined the reaction of DMF (**1a**, 1.0 mmol) with 4-octyne (**2a**, 1.0 mmol) in toluene at 50 ºC for 24 h in the presence of a catalyst prepared *in situ* from $Ni(cod)_2$ (30 μmol), and various ligands and Lewis acids (Table 1). Reactions run in the absence of LA or a ligand gave no detectable amount of desired product **3aa** (entries 1, 2, 3 and 10). P(*n*-Bu)$_3$ as the ligand was ineffective, and only oligomerization of **2a** was observed (entry 4). Whereas combinations of either P(*i*-Pr)$_3$ or PCy_3 as the ligand with a BPh_3 LA catalyst gave **3aa** in low yields, $PCyp_3/BPh_3$ combination dramatically improved the yield to 65% (entries 5–7). The stereochemistry of **3aa** was unambiguously assigned by nOe experiments: irradiation of the allylic methylenes in ^1H NMR analyses resulted in enhancement of the intensity of other allylic methylenes by 3%. Further screening of ligands using $AlMe_3$ as the LA cocatalyst revealed that a combination of P(*t*-Bu)$_3$ and $AlMe_3$ gave 84% isolated yield of **3aa** after flash column chromatography on silica gel (entries 9, 11–15). No formation of **3aa** was observed for reactions carried out in the absence of $Ni(cod)_2$ (entries 8 and 16).

Table 1. Optimization of conditions for nickel/LA-catalyzed hydrocarbamoylation of **2a** with DMF (**1a**).[a]

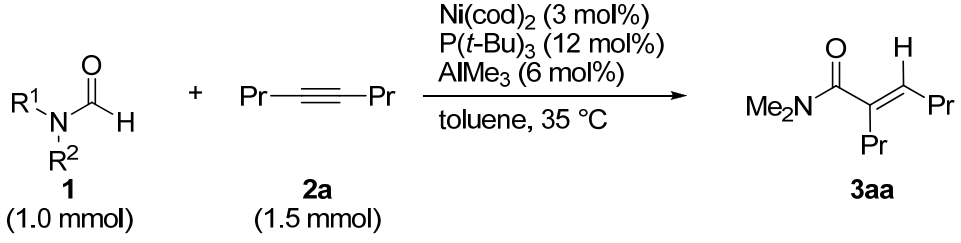


Entry	Ligand	Lewis acid	Yield of **3aa** (%)[b]
1	$PCyp_3$	none	<1
2	P(*t*-Bu)$_3$	none	<1
3	none	BPh_3	<1
4	P(*n*-Bu)$_3$	BPh_3	<1
5	P(*i*-Pr)$_3$	BPh_3	21
6	PCy_3	BPh_3	25
7	***$PCyp_3$***	***BPh_3***	***65***
8[c]	$PCyp_3$	BPh_3	<1

9	P(*t*-Bu)$_3$	BPh$_3$	<1
10	none	AlMe$_3$	<1
11	P(*n*-Bu)$_3$	AlMe$_3$	<1
12	P(*i*-Pr)$_3$	AlMe$_3$	6
13	PCy$_3$	AlMe$_3$	4
14	PCyp$_3$	AlMe$_3$	7
15	***P(t-Bu)$_3$***	***AlMe$_3$***	***96 (84)***[d]
16[c]	P(*t*-Bu)$_3$	AlMe$_3$	<1

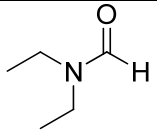
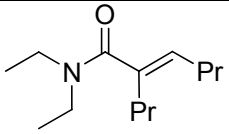
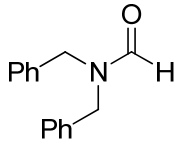
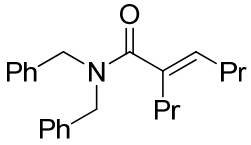
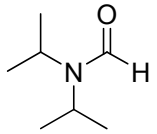
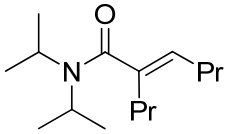
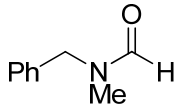
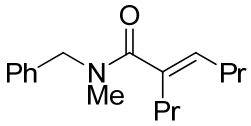
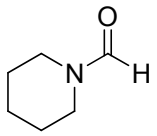
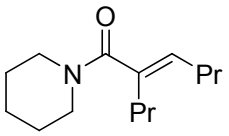
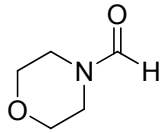
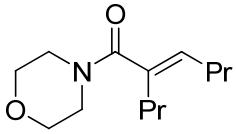
[a] All the reaction was carried out using **1a** (1.00 mmol), **2a** (1.00 mmol), Ni(cod)$_2$ (30 μmol), a ligand (0.12 mmol), and LA (60 μmol) in toluene (1.0 mL) at 50 °C for 24 h. [b] Estimated by GC using dodecane as an internal standard. [c] Run in the absence of Ni(cod)$_2$. [d] Isolated yield based on **1a**.

With the optimized conditions in hand, the author examined the scope of formamides using **2a** as a standard alkyne substrate (Table 2). *N*,*N*-Diethylformamide (**1b**) and *N*,*N*-dibenzylformamide (**1c**) participated in the reaction to give the corresponding α,β-unsaturated amides **3ba** and **3ca**, respectively, in excellent and high yield (entries 1 and 2). Long reaction time was necessary to achieve high yield with *N*,*N*-diisopropylformamide (**1d**), possibly due to steric hinderance of the bulky isopropyl groups, which may inhibit coordination of the formamide to LA and/or nickel center. High yield was also obtained in the reaction of *N*-benzyl-*N*-methylformamide (**1e**) with **2a** (entry 4). Piperidine-1-carbaldehyde (**1f**) and morpholine-4-carbaldehyde (**1g**) also participated in the reaction smoothly to give **3fa** and **3ga** stereoselectively in high yields. Attempted addition reactions of *N*-aryl-substituted and primary formamides shown below Table 1 were unsuccessful under the present reaction conditions.



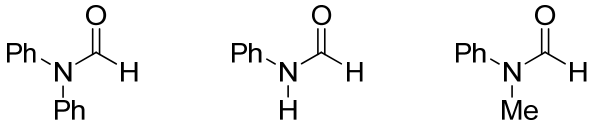
1 (1.0 mmol) **2a** (1.5 mmol) **3aa**

Table 2. Nickel/$AlMe_3$-catalyzed hydrocarbamoylation of **2a**: Scope of formamides.[a]

Entry	Formamide (**1**)		Time (h)	Product	Yield of **3** (%)[b]
1		**1b**	11		94 (**3ba**)
2		**1c**	46		83 (**3ca**)[c]
3		**1d**	120		77 (**3da**)[d]
4		**1e**	48		86 (**3ea**)
5		**1f**	9		84 (**3fa**)
6		**1g**	22		84 (**3ga**)

[a] All the reaction was carried out using **1** (1.00 mmol), **2a** (1.50 mmol), $Ni(cod)_2$ (30 μmol), $P(t\text{-}Bu)_3$ (0.12 mmol), $AlMe_3$ (60 μmol) in toluene (1.0 mL) at 35 °C. [b] Isolated yield based on **1a**. [c] 8% of **1c** was recovered. [d] Conversion of **1d** was estimated to be 85% by GC.

The substrates shown below were unreactive under the present reaction conditions.

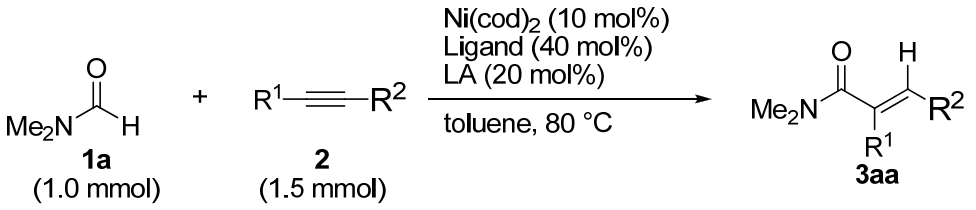


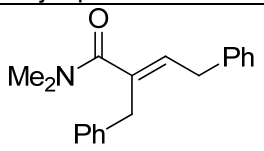
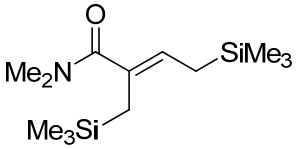
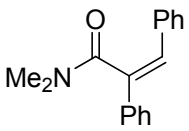
The author next turned his attention to the scope of alkynes with DMF (**1a**) as a standard formamide substrate. The reaction with 1,4-diphenylbut-2-yne (**2b**) was sluggish, and use of **1a** in large excess was necessary in order to obtain the corresponding product **3ab** in 38% yield (entry 1 of Table 3). Silylmethyl-substituted acetylene **2c** participated in the reaction to give the corresponding *cis*-adduct **3ac** albeit

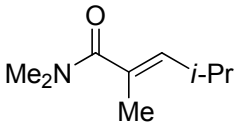
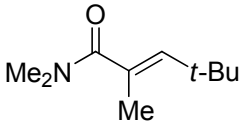
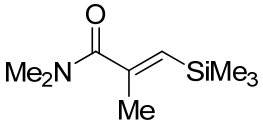
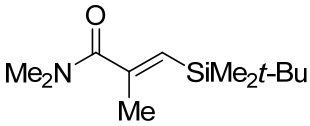
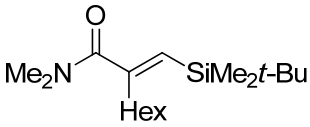
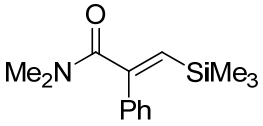
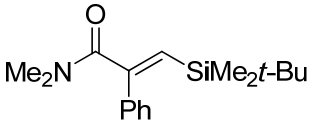
in a modest yield (entry 2), whereas the addition across diphenylacetylene (**2d**) gave *trans*-adduct (*Z*)-**3ad** as a major product (entry 3) likely via isomerization of initially formed *cis*-product (*E*)-**3ad** under the reaction conditions (*E*/*Z* = 30:70 at 0.5 h). Indeed, an isolated sample of (*E*)-**3ad** isomerized to (*Z*)-**3ad** under the reaction conditions in the presence of **1b** and **2a**. This experiment gave no detectable amount of crossover experiments (e.g. **3aa**), suggesting that the hydrocarbamoylation reaction is irreversible.

Alkynes with sterically biased substituents **2e**–**2k** reacted with excellent regioselectivities to give adducts having a larger substituent *trans* to the dimethylcarbamoyl group (entries 4–10). Use of bulky *tert*-butyldimethylsilylalkynes is important to obtain silyl-substituted *cis*-adducts selectively, because adducts derived from trimethylsilylalkynes isomerize relatively easily under the reaction conditions (cf. entry 7 *vs* entry 6). In some cases, the combination of $PCyp_3$ and BPh_3 (conditions B) or $P(t\text{-}Bu)_3$ and $ZnMe_2$ (conditions C) gave better yields. Terminal alkynes failed to give the corresponding adducts due to rapid background oligomerization of the alkynes.

Table 3. Nickel/Lewis acid-catalyzed hydrocarbamoylation of alkynes with DMF (**1a**).

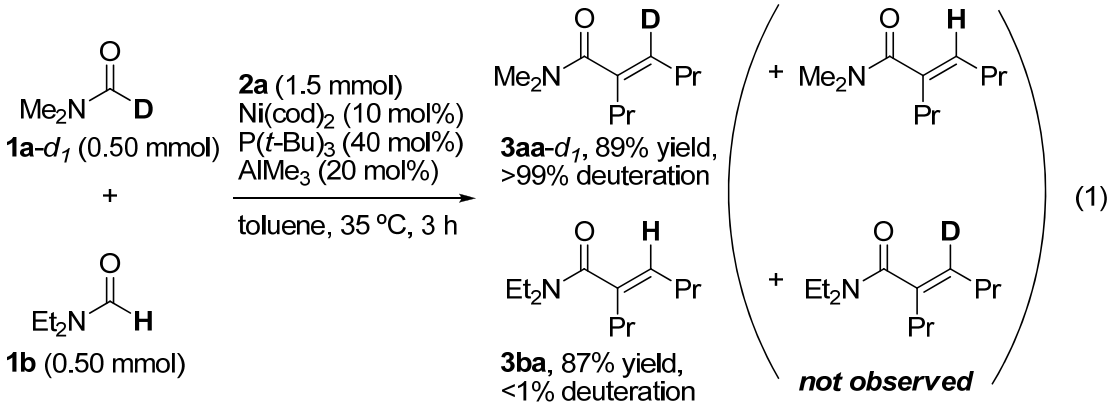


Entry	R^1, R^2 in **2**	Cond.[a]	Time (h)	Major product	Yield of **3** (%)[b]	*E*:*Z*
1[c]	CH_2Ph (**2b**)	A	1		38 (**3ab**)	>99:1
2[d]	CH_2SiMe_3 (**2c**)	B	3		55 (**3ac**)	>99:1
3[e]	Ph (**2d**)	A	3		83 (**3ad**)	7:93[f]

4	Me, *i*-Pr (**2e**)	B	1		84 (**3ae**)[g]	>99:1
5	Me, *t*-Bu (**2f**)	B	4		75 (**3af**)	>99:1
6[c]	Me, $SiMe_3$ (**2g**)	C	45		31 (3**ag**)	58:42[h]
7	Me, $SiMe_2t$-Bu (**2h**)	A	15		58 (**3ah**)	>99:1
8	Hex, $SiMe_2t$-Bu (**2i**)	A	72		47 (**3ai**)	>99:1
9	Ph, $SiMe_3$ (**2j**)	A	11		48 (**3aj**)[i]	96:4
10[d]	Ph, $SiMe_2t$-Bu (**2k**)	A	26		68 (**3ak**)	96:4

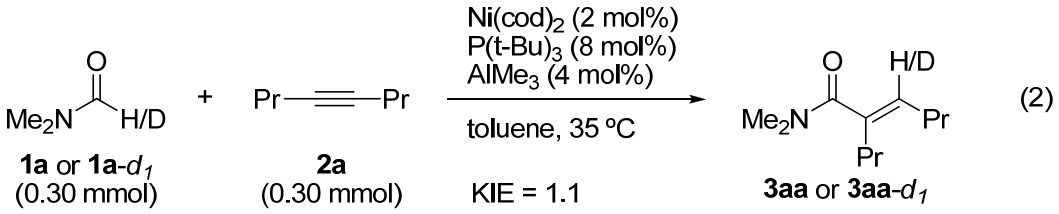
[a] Conditions A: P(*t*-Bu)$_3$ and $AlMe_3$. Conditions B: $PCyp_3$ and BPh_3. Conditions C: P(*t*-Bu)$_3$ and $ZnMe_2$. [b] Isolated yields based on **1a**. [c] Run with **1a** as a solvent, yields are based on the alkyne. [d] Run at 100 ºC. [e] Run with 1.00 mmol of the alkyne. [f] *E*:*Z* = 30:70 at 0.5 h. [g] Containing regioisomer **3'ae** (~3%). [h] *E*:*Z* = 77:23 at 7 h. [i] Containing regioisomer **3'aj** (~2%).

To gain an insight into the reaction mechanism, the author performed a deuterium crossover experiment using **1a**-d_1 (0.5 mmol) and **1b** (0.5 mmol) in the presence of $Ni(cod)_2$ (10 mol%), P(*t*-Bu)$_3$ (40 mol%) and $AlMe_3$ (20 mol%) in toluene at 35 ºC for 3 h (Eq. 1). The products obtained were **3aa**-d_1 and **3ba** only: no crossover products were observed. This observation reveal that the hydrocarbamoylation reaction proceeds via an oxidative addition mechanism, excluding the possibilities of radical and deprotonation mechanisms which can give crossover products.[4a,b,g]



KIE Experiment

To determine the rate determining step of the hydrocarbamoylation reaction, kinetic isotope effect (KIE) of the addition reaction was investigated by measuring initial rate for the reactions of **1a** or **1a**-d_1 with **2a** (Eq. 2).[8] A KIE value of 1.1 was observed. This data suggests that the cleavage of C–H or Ni–H bond, namely, oxidative addition or hydronickelation are fast enough, and therefore are unlikely to be the rate-determining steps of the reaction.



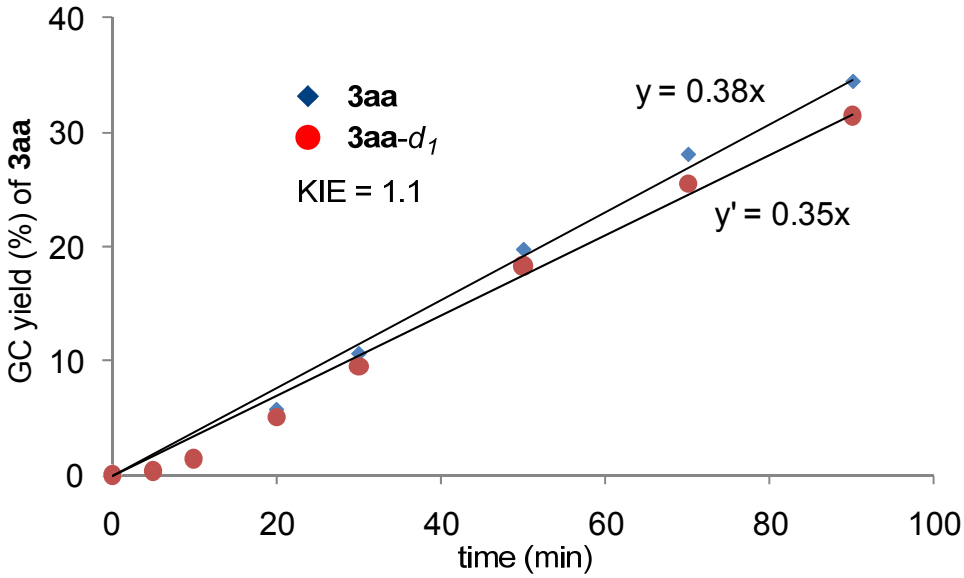
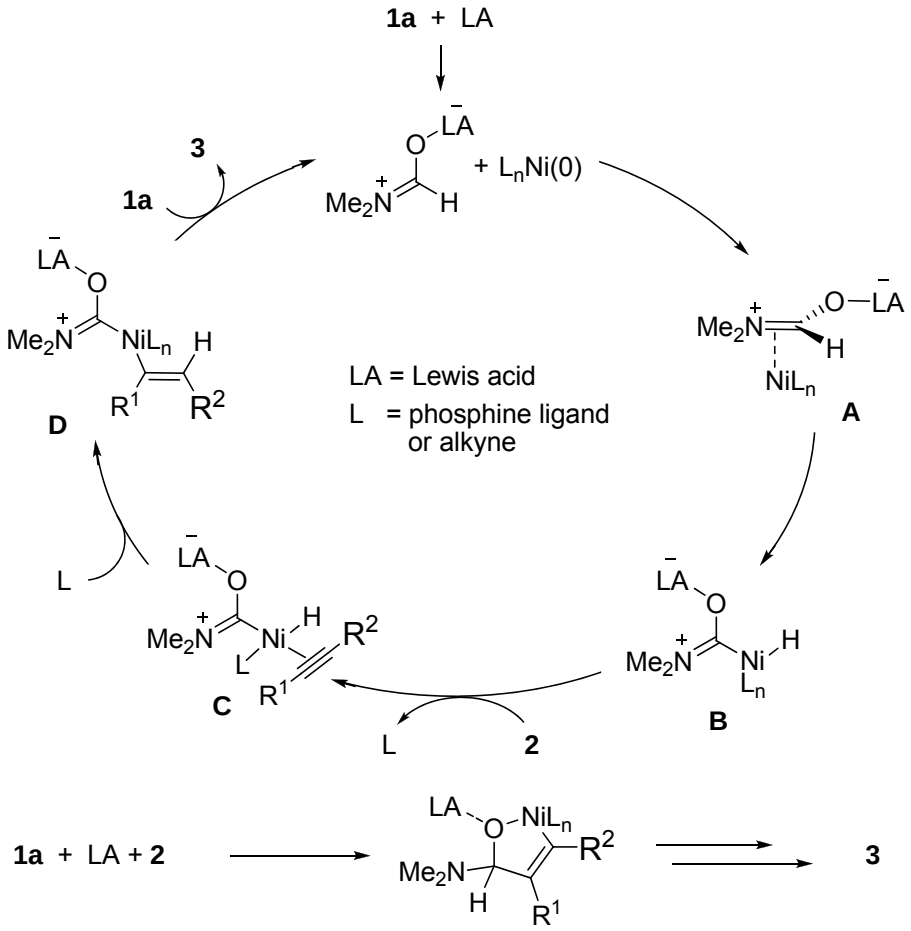


Figure 1. Estimation of KIE for hydrocarbamoylation of alkynes

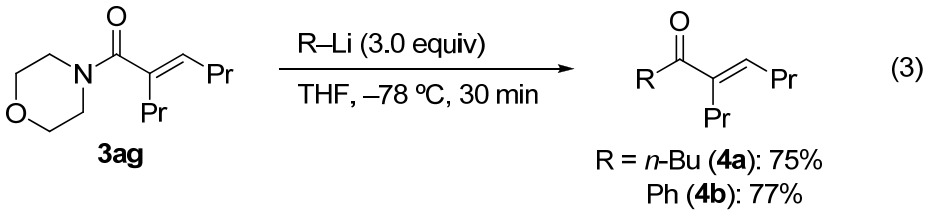
Based on these observations, the hydrocarbamoylation reaction is suggested to be initiated by activation of formamides through coordination to LA, making the formyl C(sp^2)–H bond reactive enough to undergo oxidative addition to the electron-rich nickel(0) complex via η^2-coordination of the activated formamides as shown in Scheme 2. Coordination of alkynes to the nickel center in the direction that avoids steric repulsion between the bulkier R^2 and the carbamoyl group followed by hydronickelation gives alkenylnickel intermediate **D**, which upon reductive elimination affords **3**. The fact that no crossover was observed in the reaction of **1a**-d_1 and **1b** with **2a** supports this mechanism which involves a nickel hydride intermediate **B,** rather than a carbamoylnickel intermediate with loss of a hydride ligand (*vide supra*). An alternative mechanism that proceeds through a nickeladihydrofuran intermediate (oxidative cyclization) cannot be ruled out.[9]



Scheme 2. Plausible reaction mechanism for the nickel/LA-catalyzed hydrocarbamoylation of akynes.

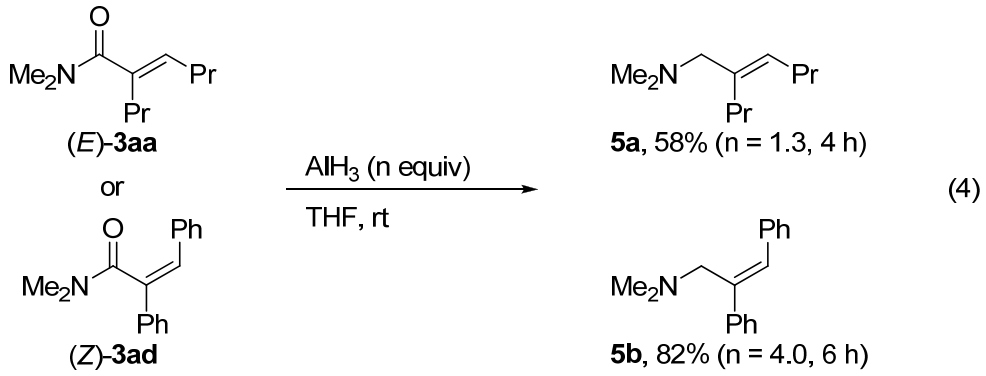
Manipulation of hydrocarbamoylation products

The hydrocarbamoylation products have a structure of α,β-disubstituted (*E*)-acrylamides and thus can be converted into α,β-unsaturated ketones. This fact is demonstrated by the smooth 1,2-addition of *n*-butyllithium and phenyllithium to **3ag** at –78 ºC in 30 min to give α,β-unsaturated ketones **4a** and **4b** in 75% and 77% yields, respectively (Eq. 3).[10]



(3)

Hydride reduction of (*E*)-**3aa** and (*Z*)-**3ad** with an alane prepared *in situ* from $LiAlH_4$ and H_2SO_4 gives allylamines **5a** and **5b** in 58% and 82% yields, respectively (Eq. 4).[11]



(4)

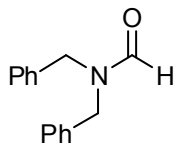
Conclusion

In conclusion, the author has demonstrated that formamides add across alkynes regio- and stereoselectively in the presence of a nickel/LA catalyst. The hydrocarbamoylation reaction allows for a straightforward and atom-efficient access to variously functionalized α,β-unsaturated amides from simple and commercially available formamides and alkynes in a single operation. The resulting hydrocarbamoylation products would serve as versatile precursors to synthetically important compounds such as α,β-unsaturated ketones and allylamines.

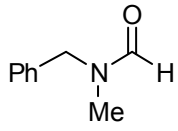
Experimental section

Chemicals. Apart from DMF, commercially available chemicals were distilled and degassed before use. Alkynes **2b**,[12] **2c**,[13] **2h**,[14] **2i**,[14] and **2k**,[14] were prepared according to the respective literature procedures.

Preparation of *N,N*-dibenzylformamide (1c). Following the reported procedure,[15] a solution of *N*-benzylformamide (1.35 g, 10 mmol) in DMF (5 mL) was added to a suspension of sodium hydride (0.26 g, 11 mmol) in DMF (20 mL). The mixture was stirred for 1.5 h at 60 °C before treatment with benzyl bromide (2.1 g, 12 mmol) at rt, stirred further for 22 h at rt, and then quenched with 30 mL of water. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 1:1) to give the title compound (**1c**, 1.79 g, 70%) as a colorless oil, R_f 0.45 (hexane–ethyl acetate = 1:1). ^{1}H and ^{13}C spectra for the title compound were identical with those reported in the literature.[16]

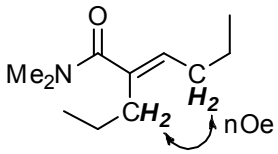


Preparation of *N*-benzyl-*N*-methylformamide (1e).[15] *N*-benzyl-*N*-methylamine (6.0 ml, 47 mmol) was dissolved in ethyl formate (75 mL) and heated under reflux for 12 h. The reaction mixture was concentrated *in vacuo*, and the residue purified by distillation under vacuum to give the title compound (**1e**, 6.0 g, 87%) as a colorless oil, bp 145–150 °C (0.4 mmHg). ^{1}H and ^{13}C spectra for the title compound were identical with those reported in the literature.[17]

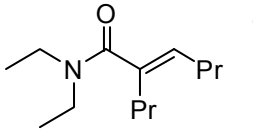


Nickel/Lewis acid-catalyzed hydrocarbamoylation of 4-octyne. *General procedure.* In a glove box, a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and P(*t*-Bu)$_3$ (81 mg, 0.40 mmol) in toluene (1.0 mL) was added to a solution of formamide (1.0 mmol) and a 1.08 M solution of $AlMe_3$ in hexane (185 μL, 0.20 mmol) placed in a 3 mL-vial. 4-Octyne (165 mg, 1.5 mmol) and dodecane (internal standard, 85 mg, 0.50 mmol) were added. The vial closed with a screw cap, taken out from the glove box and heated at the temperature for the time specified in Table 2. The resulting reaction mixture was filtered through a silica gel pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding products in yields listed in Table 2.

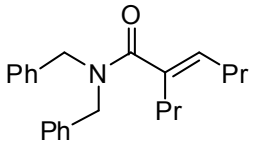
(*E*)-*N*,*N*-Dimethyl-2-propyl-2-hexenamide (3aa). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (t, *J* = 7.3 Hz, 1H), 3.01 (br, 6H), 2.28 (t, *J* = 7.8 Hz, 2H), 2.11 (q, *J* = 7.4 Hz, 2H), 1.49–1.36 (m, 4H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 136.0, 130.8, 39.0 (br), 34.8 (br), 30.9, 29.6, 22.5, 21.8, 14.3, 14.0. IR (neat) 2959, 2932, 2872, 1632, 1495, 1456, 1393, 1271, 1198, 1130, 1109, 1059, 908, 732, 627 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 183 (M^+, 58), 168 (14), 154 (44), 140 (27), 139 (65), 138 (12), 81 (14), 72 (46), 69 (100), 67 (18), 55 (42), 53 (19). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55. Found: C, 71.79; H, 11.48.



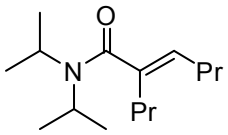
(*E*)-*N*,*N*-Diethyl-2-propyl-2-hexenamide (3ba). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, *J* = 7.2 Hz, 1H), 3.40 (q, *J* = 7.1 Hz, 2H), 2.27 (t, *J* = 7.9 Hz, 2H), 2.09 (q, *J* = 7.3 Hz, 2H), 1.49–1.37 (m, 4H), 1.15 (t, *J* = 7.0 Hz, 6H), 0.94 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 136.4, 129.0, 42.5 (br), 38.4 (br), 30.9, 29.4, 22.4, 21.5, 14.2, 13.8, 12.7 (br). IR (neat) 2961, 2934, 2872, 1620, 1462, 1425, 1379, 1364, 1317, 1287, 1238, 1221, 1132, 1101, 1080, 1069, 907, 791, 733 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 211 (M^+, 40), 196 (12), 183 (10), 182 (77), 169 (12), 168 (100), 140 (18), 139 (71), 138 (17), 126 (11), 81 (10), 72 (10), 69 (45), 55 (16). Anal. Calcd for $C_{13}H_{25}NO$: C, 73.88; H, 11.92. Found: C, 73.58; H, 11.80.



(*E*)-*N*,*N*-Dibenzyl-2-propyl-2-hexenamide (3ca). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 6H), 7.17 (brd, *J* = 7.1 Hz, 4H), 5.63 (t, *J* = 7.2 Hz, 1H), 4.54 (brs, 4H), 2.34 (t, *J* = 7.2 Hz, 2H), 2.07 (q, *J* = 7.3 Hz, 2H), 1.52 (sext, *J* = 7.5 Hz, 2H), 1.33 (sext, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.84 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 136.8 (br), 135.7, 130.7, 128.4 (br), 127.2 (br), 51.1 (br), 46.3 (br), 31.2, 29.6, 22.4, 21.9, 14.3, 13.9. IR (neat) 2959, 2930, 1632, 1495, 1454, 1416, 1364, 1312, 1271, 1219, 1165, 1080, 1030, 964, 902, 748, 698 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 335 (M^+, 22), 307 (10), 306 (43), 293 (23), 292 (100), 244 (23), 139 (26), 91 (44), 69 (19). HRMS (EI) Calcd for $C_{23}H_{29}NO$: M^+, 335.2249. Found: *m/z* $C_{23}H_{29}NO$: 335.2234.

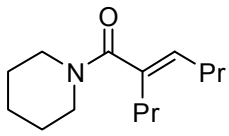


(*E*)-*N*,*N*-Diisopropyl-2-propyl-2-hexenamide (3da). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (t, *J* = 7.3 Hz, 1H),

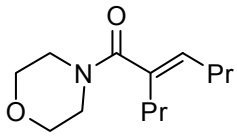


4.06 (br, 1H), 3.39 (br, 1H), 2.25 (t, J = 7.9 Hz, 2H), 2.07 (q, J = 7.3 Hz, 2H), 1.43 (sext, J = 7.4 Hz, 4H), 1.30 (br, 12H), 0.95 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 137.8, 127.4, 49.8 (br), 45.2 (br), 30.8, 29.2, 22.4, 21.4, 20.6, 14.1, 13.8. IR (neat) 2961, 2932, 2872, 1622, 1435, 1370, 1333, 1211, 1153, 1134, 1040, 922, 899, 733, 608 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 239 (M^+, 12), 210 (25), 197 (12), 196 (84), 168 (10), 140 (11), 139 (100), 69 (49), 55 (17). HRMS (EI) Calcd for $C_{15}H_{29}NO$: M^+, 239.2249. Found: *m/z* $C_{23}H_{29}NO$: 239.2254.

(*E*)-*N*-Benzyl-*N*-methyl-2-propyl-2-hexenamide (3ea). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 6:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.15 (m, 5H), 5.55 (br, 1H), 4.63 (s, 2H), 2.91 (s, 3H), 2.32 (brt, J = 7.6 Hz, 2H), 2.10 (br, 2H), 1.54–1.28 (m, 4H), 1.06–0.76 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2 (br), 136.9, 135.7, 130.7, 128.3, 127.7 (br), 127.0, 54.5 (br), 50.1 (br), 36.2 (br), 32.6 (br), 30.9, 29.5, 22.3, 21.7, 14.2, 13.8. IR (neat) 2959, 2930, 2872, 1626, 1493, 1454, 1396, 1360, 1273, 1223, 1171, 1103, 1078, 1028, 964, 907, 739, 698 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 259 (M^+, 5), 230 (38), 217 (16), 216 (100), 91 (43), 69 (28), 55 (14). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.44; H, 9.50.



***N*-(*E*)-(2-propyl-2-hexenoyl)piperidine (3fa).** A colorless oil, R_f 0.20 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, J = 7.2 Hz, 1H), 3.53 (br, 4H), 2.27 (t, J = 7.8 Hz, 2H), 2.09 (q, J = 7.3 Hz, 2H), 1.69–1.59 (m, 4H), 1.54 (br, 2H), 1.48–1.35 (m, 4H), 0.94 (t, J = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 136.0, 129.9, 48.1 (br), 42.5 (br), 31.0, 29.5, 26.5 (br), 26.0 (br), 24.8, 22.6, 21.7, 14.3, 14.0. IR (neat) 3231, 2934, 2859, 1626, 1429, 1377, 1283, 1258, 1223, 1134, 1026, 907, 853, 731 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 223 (M^+, 43), 208 (14), 195 (12), 194 (81), 181 (13), 180 (100), 139 (33), 138 (31), 123 (13), 84 (21), 82 (10), 81 (12), 69 (76), 67 (14), 56 (11), 55 (42), 53 (13). Anal. Calcd for $C_{14}H_{25}NO$: C, 75.28; H, 11.28. Found: C, 75.26; H, 11.47.



***N*-(*E*)-(2-propyl-2-hexenoyl)morpholine (3ga).** A colorless oil, R_f 0.40 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (t, J = 7.3 Hz, 1H), 3.64 (br, 4H), 3.62 (br, 4H), 2.28 (t, J = 7.9 Hz, 2H), 2.11 (q, J = 7.3 Hz, 2H), 1.49–1.36 (m, 4H), 0.941 (t, J = 7.3 Hz, 3H), 0.938 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 135.2, 131.3, 67.0, 47.6 (br),

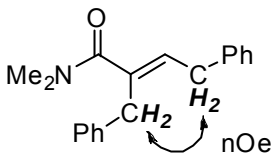
42.5 (br), 30.9, 29.6, 22.5, 21.8, 14.3, 14.1. IR (neat) 3472, 2959, 2930, 2870, 1631, 1454, 1427, 1300, 1281, 1227, 1169, 1117, 1069, 1038, 1020, 933, 910, 843, 739, 577 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 225 (M^+, 56), 196 (43), 182 (40), 140 (12), 139 (100), 138 (26), 123 (12), 81 (12), 70 (14), 69 (69), 67 (12), 55 (26). Anal. Calcd for $C_{13}H_{23}NO_2$: C, 69.29; H, 10.29. Found: C, 69.52; H, 10.56.

Nickel/Lewis acid-catalyzed hydrocarbamoylation of alkynes with DMF. *General procedure A.* In a glove box, a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and P(*t*-Bu)$_3$ (81 mg, 0.40 mmol) in toluene (1.0 mL) was added to a solution of DMF (**1a**, 73 mg, 1.0 mmol) and a 1.08 M solution of $AlMe_3$ in hexane (185 μL, 0.20 mmol) placed in a 3 mL-vial. An alkyne (1.5 mmol) and dodecane (internal standard, 85 mg, 0.50 mmol) were added. The vial was closed with a screw cap, taken out from the glove box and heated at the temperature for the time specified in Table 3. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding products in yields listed in Table 3. In some cases, isomers were separated by preparative recycling GPC or preparative recycling silica gel chromatography.

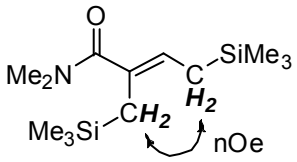
General procedure B. Following *general procedure A*, but with BPh_3 (48 mg, 0.20 mmol) and $PCyp_3$ (95 mg, 0.40 mmol) as LA and a ligand, respectively.

General procedure C. Following *general procedure A*, but with 1.08 M solution of $ZnMe_2$ in hexane (185 μL, 0.20 mmol) as LA.

(*E*)-*N*,*N*-Dimethyl-2-benzyl-4-phenyl-2-butenamide (3ab). A yellow oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.17 (m, 10H), 5.71 (tt, *J* = 7.3, 1.0 Hz, 1H), 3.80 (s, 2H), 3.63 (d, *J* = 7.3 Hz, 2H), 2.86 (br, 3H), 2.69 (br, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 139.3, 138.3, 135.4, 128.9, 128.53, 128.45, 128.3, 128.2, 126.2, 126.1, 38.7 (br), 34.9, 34.1. IR (neat) 3086, 3061, 3026, 2924, 2858, 1626, 1495, 1452, 1393, 1263, 1163, 1094, 1076, 1030, 926, 908, 749, 737, 731, 698, 619. MS (EI, 70 eV) *m/z* (%) 280 (M^++1, 22), 279 (M^+, 100), 235 (10), 234 (16), 206 (17), 188 (47), 156 (11), 129 (24), 115 (14), 91 (71), 72 (13). HRMS (EI) Calcd for $C_{19}H_{21}NO$: M^+, 279.1623. Found: *m*/*z* 279.1612.

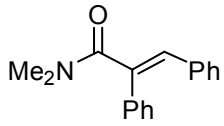


(*E*)-*N*,*N*-Dimethyl-4-trimethylsilyl-2-trimethylsilylmethyl-2-butenamide (3ac). A

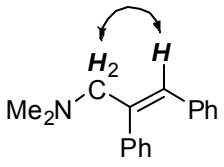


colorless oil, R_f 0.25 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (tt, J = 8.5, 1.1 Hz, 1H), 3.01 (brs, 6H), 1.75 (s, 2H), 1.50 (d, J = 8.6 Hz, 2H), 0.05 (s, 9H), 0.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 131.0, 125.7, 35.7 (br), 36.2 (br), 19.31, 19.25, –0.9, –1.3. IR (neat) 2953, 1641, 1622, 1495, 1443, 1385, 1248, 1140, 1061, 1009, 916, 841, 762, 694 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 271 (M^+, 6), 257 (11), 256 (44), 199 (16), 198 (95), 185 (16), 184 (100), 182 (11), 73 (68). HRMS (EI) Calcd for $C_{13}H_{29}NOSi_2$: M^+, 271.1788. Found: *m/z* 271.1781.

(*E*)-*N*,*N*-Dimethyl-2,3-diphenylpropenamide [(*E*)-3ad]. A colorless oil, R_f 0.10 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.09 (m, 10H), 6.71 (s, 1H), 3.03 (s, 3H), 3.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 137.6, 135.3, 135.2, 129.8, 129.2, 128.7, 128.5, 128.0, 127.8, 127.5, 38.7, 35.1. IR (neat) 3080, 3055, 3022, 2930, 3022, 2928, 1736, 1620, 1574, 1493, 1445, 1393, 1263, 1204, 1142, 1076, 1032, 1007, 928, 785, 733, 698, 671, 565, 517 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 252 (M^++1, 10), 251 (M^+, 52), 207 (15), 180 (15), 179 (100), 178 (59), 176 (10), 174 (10), 134 (20). HRMS (EI) Calcd for $C_{17}H_{17}NO$: M^+, 251.1310. Found: *m/z* 251.1301.



Reduction of (*E*)-3ad.[11] To a suspension of $LiAlH_4$ (15 mg, 0.40 mmol) in THF (4.0 mL) at 0 ºC, 98% H_2SO_4 (21 mg, 0.20 mmol) was added dropwise carefully. After stirring for 15 min, a solution of (*E*)-**3ad** (25 mg, 0.10 mmol) in THF (1.0 mL) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. After cooling to 0 ºC, the reaction was quenched by adding water/THF (1:1) dropwise, then the mixture was stirred further for 15 min. Diethyl ether (10 mL) and then a 2 M NaOH aqueous solution (2 mL) were added sequentially to form a thick precipitate of $Al(OH)_3$. The colorless precipitates were separated by suction filtration, then the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on aluminium oxide (hexane–ethyl acetate = 30:1) to give (*E*)-*N*,*N*-dimethyl-2,3-diphenylprop-2-en-1-ylamine (19.4 mg, 82%) as a colorless oil,



R_f 0.55 (aluminium oxide, hexane–ethyl acetate = 15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.19 (m, 5H), 7.14–7.04 (m, 3H), 6.98–6.93 (m, 2H) 6.60 (s, 1H) 3.27 (s, 2H) 2.29 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 139.7, 136.8, 129.1, 128.6, 128.44, 128.36, 127.7, 127.0, 126.4, 68.7, 45.6. IR (neat) 3078, 3055, 3023, 2972, 2942, 2853, 2812, 2770, 1946, 1881, 1804, 1688, 1599, 1574, 1493, 1464, 1447, 1354, 1263, 1175,

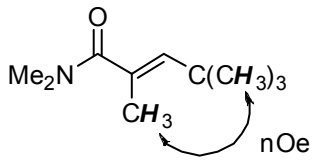
1148, 1084, 1065, 1044, 1030, 1018, 984, 918, 883, 847, 831, 777, 758, 737, 696, 563, 527 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 238, (M^++1, 12), 237 (M^+, 62), 222 (18), 191 (10), 178 (16), 160 (11), 115 (13), 91 (10), 58 (100). HRMS (EI) Calcd for $C_{17}H_{19}N$: M^+, 237.1517. Found: *m*/*z* 237.1518.

(*Z*)-*N*,*N*-Dimethyl-2,3-diphenylpropenamide [(*Z*)-3ad]. A colorless solid, mp 88.0–88.8 °C, R_f 0.25 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.50 (m, 2H), 7.41–7.23 (m, 8H), 6.98 (s, 1H), 3.08 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 136.5, 136.3, 135.5, 128.7, 128.5, 128.1, 127.93, 127.90, 127.1, 125.6, 37.5, 34.5. IR (KBr) 3057, 3024, 2928, 1634, 1495, 1445, 1398, 1261, 1140, 1078, 1057, 1032, 1001, 988, 924, 764, 731, 694, 575, 536, 517 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 252 (M^++1, 11), 251 (M^+, 56), 207 (17), 180 (16), 179 (100), 178 (57), 174 (10), 134 (20). HRMS (EI) Calcd for $C_{17}H_{17}NO$: M^+, 251.1310. Found: *m*/*z* 251.1301.

(*E*)-2,4,*N*,*N*-Tetramethyl-2-pentenamide (3ae). A colorless oil, R_f 0.25 (diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (dq, *J* = 9.3, 1.5 Hz, 1H), 2.99 (brs, 6H), 2.60 (d, sept, *J* = 9.3, 6.7 Hz, 1H), 1.84 (d, *J* = 1.5 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 138.0, 128.7, 38.9 (br), 34.8 (br), 27.0, 22.4, 14.2. IR (neat) 2959, 2928, 2870, 1632, 1497, 1456, 1393, 1265, 1140, 1080, 1005, 750, 733, 637 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 155 (M^+, 41), 112 (34), 111 (100), 110 (42), 83 (32), 72 (19), 55 (45). HRMS (EI) Calcd for $C_9H_{17}NO$: M^+, 155.1310. Found: *m*/*z* 155.1315.

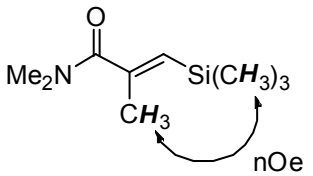
(*E*)-*N*,*N*-Dimethyl-2-isopropyl-2-butenamide (3'ae). A colorless oil, R_f 0.30 (diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (qd, *J* = 6.9, 0.7 Hz, 1H), 3.00 (brs, 3H), 2.97 (brs, 3H), 2.85 (sept, d, *J* = 7.0, 0.6 Hz, 1H), 1.72 (d, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 141.8, 122.9, 39.3, 34.3, 28.1, 21.3, 12.8. IR (neat) 2961, 2932, 1655, 1624, 1491, 1447, 1395, 1362, 1267, 1128, 1057, 997, 856, 837, 754, 610 cm^{-1}. MS (EI, 70 eV) *m*/*z* (%) 155 (M^+, 73), 140 (36), 126 (20), 112 (11), 111 (87), 110 (37), 98 (17), 84 (12), 83 (91), 82 (19), 72 (49), 67 (23), 55 (100). HRMS (EI) Calcd for $C_9H_{17}NO$: M^+, 155.1310. Found: *m*/*z* 155.1318.

(*E*)-2,4,4,*N*,*N*-Pentamethyl-2-pentenamide (3af). A colorless oil, R_f 0.25 (diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (q, *J* = 1.5 Hz, 1H), 2.98 (br, 6H), 1.94 (d, *J* = 1.5 Hz,

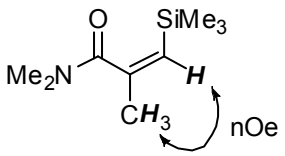


3H), 1.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.9, 129.7, 38.7 (br), 34.6 (br), 32.9, 30.3, 15.0. IR (neat) 2957, 2868, 1634, 1456, 1391, 1364, 1259, 1178, 1092, 1013, 729, 644 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 169 (M^+, 26), 155 (11), 154 (100), 126 (18), 125 (80), 112 (28), 109 (14), 97 (39), 96 (10), 81 (22), 72 (44), 69 (21), 67 (19), 57 (38), 56 (12), 55 (66), 53 (12). HRMS (EI) Calcd for $C_{10}H_{19}NO$: M^+, 169.1467. Found: *m*/*z* 169.1462.

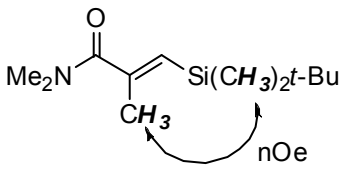
(*E*)-2,*N*,*N*-trimethyl-3-(trimethylsilyl)propenamide [(*E*)-3ag]. A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 (q, *J* = 1.1 Hz, 1H), 3.00 (br s, 3H), 2.97 (brs, 3H), 1.99 (d, *J* = 1.1 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 148.3, 129.1, 38.6, 34.6, 19.3, –0.2. IR (neat) 2953, 2907, 1643, 1614, 1497, 1445, 1394, 1306, 1257, 1248, 1159, 1082, 935, 864, 843, 783, 750, 735, 690, 617, 600, 513. MS (EI, 70 eV) *m/z* (%) 171 (33), 170 (M^+–Me, 100), 102 (28), 73 (36). Anal. Calcd for $C_9H_{19}NOSi$: C, 58.32; H, 10.33. Found: C, 58.49; H, 10.16.



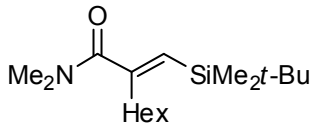
(*Z*)-2,*N*,*N*-trimethyl-3-(trimethylsilyl)propenamide [(*Z*)-3ag]. A colorless solid, mp 45.0–45.8 °C, R_f 0.35 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (q, *J* = 1.6 Hz, 1H), 2.99 (s, 3H), 2.95 (s, 3H), 2.02 (d, *J* = 1.6 Hz, 3H), 0.06 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 148.5, 129.1, 38.0, 34.1, 25.0, –1.0. IR (KBr) 2955, 2898, 1639, 1632, 1609, 1497, 1447, 1394, 1250, 1182, 1086, 1061, 993, 924, 860, 839, 760, 731, 692, 677, 623, 596. MS (EI, 70 eV) *m/z* (%) 171 (14), 170 (M^+–Me, 100), 112 (12), 102 (12), 73 (53). Anal. Calcd for $C_9H_{19}NOSi$: C, 58.32; H, 10.33. Found: C, 58.05; H, 10.48.



(*E*)-3-(*tert*-Butyldimethylsilyl)-2,*N*,*N*-trimethylpropenamide (3ah). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (q, *J* = 1.2 Hz, 1H), 3.01 (brs, 3H), 2.97 (brs, 3H), 2.00 (d, *J* = 1.3 Hz, 3H), 0.92 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 149.3, 126.6, 38.7, 34.6, 26.5, 19.5, 17.3, –4.4. IR (neat) 2953, 2928, 2857, 1643, 1634, 1607, 1497, 1464, 1447, 1393, 1254, 1182, 1086, 1007, 924, 826, 810, 766, 731 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 227 (M^+, 2), 171 (16), 170 (M^+–*t*-Bu, 100), 102 (11), 73 (10). Anal. Calcd for $C_{12}H_{25}NOSi$: C, 63.38; H, 11.08. Found: C, 63.24; H, 11.24.

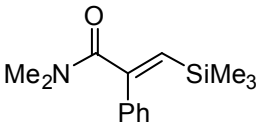


(*E*)-2-(*tert*-Butyldimethylsilylmethylidene)-*N*,*N*-dimethyloctanamide (3ai). A



colorless oil, R_f 0.45 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (s, 1H), 3.03 (brs, 3H), 3.00 (brs, 3H), 2.39 (t, *J* = 7.9Hz, 2H), 1.73–1.51 (m, 8H), 0.91 (s, 9H), 0.88 (t, *J* = 7.0Hz, 3H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 154.1, 125.9, 38.8, 34.6, 34.4, 31.7, 29.6, 28.7, 26.5, 22.6, 17.1, 14.1, –4.2. IR (neat) 2953, 2928, 2857, 1638, 1603, 1495, 1464, 1391, 1254, 1171, 1119, 1051, 1007, 839, 826, 810, 770, 731, 685, 613 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 241 (20), 240 (M^+–*t*-Bu, 100), 170 (10). Anal. Calcd for $C_{17}H_{35}NOSi$: C, 68.62; H, 11.86. Found: C, 68.91; H, 11.75.

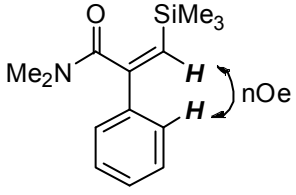
(*E*)-*N*,*N*-Dimethyl-2-phenyl-3-(trimethylsilyl)propenamide [(*E*)-3aj]. A colorless solid,



mp = 59.3–60.2 °C, R_f 0.20 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 5.89 (s, 1H), 2.980 (br s, 3H), 2.975 (br s, 3H), –0.02 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 152.9, 137.8 (2C), 131.7, 127.9, 127.8, 38.5, 34.6, 0.0 (The signals of the aryl group are overlapping.). IR (KBr) 3044, 2951, 2924, 2897, 1626, 1601, 1591, 1574, 1495, 1487, 1441, 1393, 1248, 1180, 1144, 1074, 991, 885, 864, 843, 769, 756, 708, 644. MS (EI, 70 eV) *m/z* (%) 247 (M^+, 1), 233 (22), 232 (M^+–Me, 100), 73 (30). HRMS (EI) Calcd for $C_{14}H_{21}NOSi$: M^+, 247.1392. Found: *m*/*z* 247.1388.

Protodesilylation of (*E*)-3aj. A 1.0 M solution of TBAF in THF (110 μL, 110 μmol) was added dropwise to a solution of (*E*)-**3aj** (25 mg, 0.10 mmol) in THF (0.20 mL) at 0 °C over 5 min. The resulting mixture was stirred for additional 5 min at 0 °C, then at rt for further 5 h before quenching with water. The mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and then concentrated *in vacuo*. The residue was purified by preparative TLC (hexane–ethyl acetate = 1:1) to give a colorless oil which exhibited ^{1}H NMR and ^{13}C NMR spectra identical with *N*,*N*-dimethyl-2-phenylpropenamide (14.4 mg, 82%) reported in a literature.[18]

(*Z*)-*N*,*N*-Dimethyl-2-phenyl-3-(trimethylsilyl)propenamide [(*Z*)-3aj]. A colorless oil,

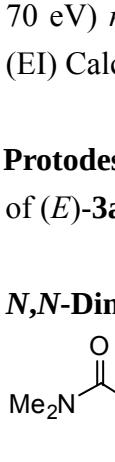


R_f 0.30 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 (m, 2H), 7.37–7.28 (m, 3H), 6.28 (s, 1H), 3.05 (s, 3H), 2.86 (s, 3H), 0.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 151.3, 137.2, 128.8, 128.6, 128.3, 125.3, 38.3, 34.4, –0.8. IR (neat) 2961, 2930, 2922, 1643, 1634, 1593, 1572,

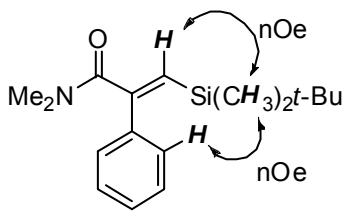
1495, 1445, 1397, 1263, 1246, 1138, 980, 891, 860, 839, 760, 696, 627, 581. MS (EI, 70 eV) *m/z* (%) 247 (M^+, 2), 233 (37), 232 (M^+–Me, 100), 102 (14), 73 (31). HRMS (EI) Calcd for $C_{14}H_{21}NOSi$: M^+, 247.1392. Found: *m*/*z* 247.1404.

Protodesilylation of (*E*)-3aj. Following the procedure described for protodesilylation of (*E*)-**3aj**, (*Z*)-**3aj** was protodesilylated to give the identical product in 60% yield.

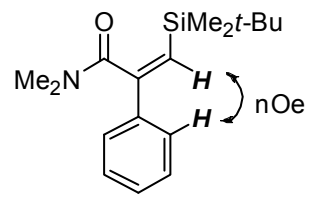
***N*,*N*-Dimethyl-3-phenyl-2-(trimethylsilyl)propenamide (3'aj).** A colorless solid, R_f 0.25 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 6.70 (s, 1H), 2.98 (s, 3H), 2.71 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 141.0, 137.7, 136.8, 128.4, 128.1, 127.8, 37.4, 34.3, –1.3. MS (EI, 70 eV) *m/z* (%) 247 (M^+, 18), 232 (17), 204 (20), 203 (97), 145 (10), 115 (10), 102 (37), 75 (21), 74 (17), 73 (100), 72 (28), 59 (22). HRMS (EI) Calcd for $C_{14}H_{21}NOSi$: M^+, 247.1392. Found: *m*/*z* 247.1387.



(*E*)-3-(*tert*-Butyldimethylsilyl)-*N*,*N*-dimethyl-2-phenylpropenamide [(*E*)-3ak]. A colorless solid, mp 60.4–60.8 °C, R_f 0.35 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 5.91 (s, 1H), 3.05 (s, 3H), 2.98 (s, 3H), 0.92 (s, 9H), –0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 153.7, 138.1, 129.0, 128.2, 127.9, 127.8, 38.8, 34.7, 26.7, 17.1, –4.6. IR (KBr) 2955, 2926, 2857, 1620, 1603, 1589, 1489, 1462, 1445, 1393, 1252, 1182, 1142, 1005, 988, 882, 853, 827, 764, 714 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 233 (20), 232 (M^+–*t*-Bu, 100). Anal. Calcd for $C_{17}H_{27}NOSi$: C, 70.53; H, 9.40. Found: C, 70.34; H, 9.63.

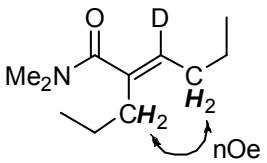


(*Z*)-3-(*tert*-Butyldimethylsilyl)-*N*,*N*-dimethyl-2-phenylpropenamide [(*Z*)-3ak. A colorless solid, mp 83.5–84.1 °C, R_f 0.50 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.39 (m, 2H), 7.37–7.26 (m, 3H), 6.32 (s, 1H), 3.03 (s, 3H), 2.85 (s, 3H), 0.97 (s, 9H), –0.10 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 152.4, 137.5, 128.6, 128.3, 126.0, 125.3, 38.3, 34.3, 26.7, 17.0, –5.8. IR (KBr) 2951, 2924, 2853, 1641, 1630, 1595, 1572, 1497, 1472, 1460, 1449, 1397, 1254, 1138, 982, 889, 858, 841, 828, 814, 789, 764, 702, 598, 500, 478 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 289 (31), 233 (19), 232 (M^+–*t*-Bu, 100), 207 (11). HRMS (EI) Calcd for $C_{17}H_{27}NOSi$: M^+, 289.1862. Found: *m*/*z* 289.1862.



Deuterium crossover experiment. In a glove box, a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and P(*t*-Bu)$_3$ (81 mg, 0.40 mmol) in toluene (1.0 mL) was added to a solution of **1a**-d_1 (37 mg, 0.50 mmol, 99% deuteration), **1b** (51 mg, 0.50 mmol) and a 1.08 M solution of $AlMe_3$ in hexane (185 μL, 0.20 mmol) placed in a 3 mL-vial. 4-Octyne (165 mg, 1.5 mmol) and dodecane (internal standard, 85 mg, 0.50 mmol) were added. The vial was closed with a screw cap, taken out from the glove box and heated at 80 °C for 3 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give **3aa**-d_1 (82 mg, 89%, 99% deuteration) and **3ba** (92 mg, 87%).

(*E*)-*N*,*N*-Dimethyl-3-deuterio-2-propyl-2-hexenamide (3aa-d_1). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 (br, 6H), 2.28 (t, *J* = 7.9 Hz, 2H), 2.10 (t, *J* = 7.3 Hz, 2H), 1.49–1.36 (m, 4H), 0.942 (t, *J* = 7.3 Hz, 3H), 0.935 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 135.8, 130.4 (t, *J* = 23.0 Hz), 38.9 (br), 34.7 (br), 30.8, 29.4, 22.4, 21.7, 14.2, 14.0. IR (neat) 2959, 2872, 1645, 1622, 1497, 1456, 1391, 1271, 1126 cm^{-1}. MS (EI, 70 eV) *m/z* (%) 185 (M^++1, 13), 184 (M^+, 100), 169 (20), 155 (66), 141 (38), 140 (98), 139 (21), 124 (14), 72 (45), 70 (70), 69 (41), 68 (14), 56 (24), 55 (25), 54 (12). Anal. Calcd for $C_{11}H_{20}DNO$: C, 71.69; H, 12.03. Found: C, 71.61; H, 11.75.

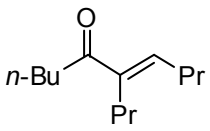


Determination of KIE. In a glove box, a solution of $Ni(cod)_2$ (1.7 mg, 6.0 μmol) and P(*t*-Bu)$_3$ (4.9 mg, 24 μmol) in toluene (0.6 mL) was added to a solution of [**1a** (22 mg, 0.30 mmol) and 1.08 M solution of a $AlMe_3$ in hexane (11.1 μL, 12 μmol)] and [**1a**-d_1 (22 mg, 0.30 mmol) and 1.08 M solution of a $AlMe_3$ in hexane (11.1 μL, 12 μmol)] placed in two separate 3 mL-vials. 4-Octyne (33.0 mg, 0.3 mmol) and dodecane (internal standard, 26 mg, 0.15 mmol) were added to each vial. The vials were closed with screw caps and heated at 35 °C. Aliquots of the reaction mixture were taken from the two vials and analyzed by GC to get initial yields of the two reactions. The set of experiments was repeated twice and the average yields for the three sets calculated and plotted in Figure 1.

Synthesis of 4a and 4b. *General procedure.*[10] A 1.6 M solution of *n*-butyllithium in hexane (0.94 mL, 1.5 mmol) [or 2.05 M solution of phenyllithium in dibutyl ether (0.73 mL, 1.5 mmol)] was added dropwise to a solution of **3ag** (113 mg, 0.50 mmol) in THF (2 mL) at –78 °C. The mixture was stirred for 30 min before quenching with saturated

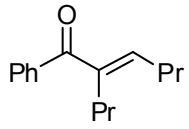
NH_4Cl aqueous solution. The resulting mixture was extracted with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding compounds in yields shown on Eq. 3.

(*E*)-6-Propyldec-6-en-5-one (4a). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 10:1).

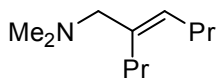


^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (t, *J* = 7.3 Hz, 1H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.30–2.20 (m, 4H), 1.63–1.54 (m, 2H), 1.51 (sext, *J* = 7.4 Hz, 2H), 1.34 (sext, *J* = 7.4 Hz, 2H), 1.33 (sext, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 142.1, 141.8, 37.2, 31.0, 27.8, 27.4, 22.6, 22.4 (2C), 14.3, 14.1 (2C). IR (neat) 2961, 2934, 2874, 1729, 1711, 1670, 1636, 1463, 1458, 1379, 1271, 1202, 1113, 1092, 955, 903, 803, 750. MS (EI, 70 eV) *m/z* (%) 196 (M^+, 7), 154 (14), 153 (36), 140 (10), 139 (M^+–Bu, 100), 85 (16), 71 (22), 69 (56), 57 (20), 55 (23). HRMS (EI) Calcd for $C_{13}H_{24}O$: M^+, 196.1827. Found: *m*/*z* 196.1828.

1-phenyl-2-propylhex-2-en-1-one (4b). A colorless oil, R_f 0.45 (hexane–ethyl acetate = 10:1). ^{1}H and ^{13}C spectra of the obtained compound were identical with those reported for the title compound.[19]



(*E*)-*N*,*N*-Dimethyl-2-propylhex-2-en-1-ylamine (5a).[11] Following the procedure for synthesis of **5b**, (*E*)-**3aa** (92 mg, 0.50 mmol) was reduced, and the product was purified by flash column chromatography on neutral aluminum oxide (hexane–ethyl acetate = 30:1) to give **5a** (49 mg, 0.29 mmol, 58%) as a colorless oil, R_f 0.35 (aluminum oxide, hexane–ethyl acetate = 15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (t, *J* = 7.2 Hz, 1H), 2.74 (d, *J* = 0.7 Hz, 2H), 2.16 (s, 6H), 2.05–1.98 (m, 4H), 1.47–1.32 (m, 4H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 128.4, 66.6, 45.5, 30.8, 29.8, 23.1, 21.6, 14.3, 14.0. Anal. Calcd for $C_{11}H_{23}N$: C, 78.03; H, 13.69. Found: C, 78.32; H, 13.61.



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List of Publications

I. Parts of the present Thesis have been or are to be published in the following journals.

Chapter 2

Nickel-Catalyzed Alkenylation and Alkylation of Fluoroarenes via Activation of C–H over C–F Bond

Nakao, Y.; Kashihara, N; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 16170–16171.

Nickel-Catalyzed Alkenylation of Fluoroarenes

Kanyiva, K. S.; Kashihara, N.; Nakao, Y.; Hiyama, T.; Ohashi, M.; Ogoshi, S. manuscript in preparation.

Chapter 3

Hydroheteroarylation of Alkynes under Mild Nickel Catalysis

Nakao, Y.; Kanyiva, K. S.; Oda, S.; Hiyama, T. *J. Am. Chem. Soc.* **2006**, *128*, 8146–8147.

Practical Approach for Hydroheteroarylation of Alkynes Using Bench-Stable Catalyst

Kanyiva, S. K.; Nakao, Y.; Hiyama, T. *Heterocycles* **2007**, *72*, 677–680.

Regioselective Alkenylation of Imidazoles by Nickel/Lewis Acid Catalysis

Kanyiva, K. S.; Löbermann, F.; Nakao, Y.; Hiyama, T. *Tetrahedron Lett.* **2009**, *50*, 3463–3466.

Chapter 4

Nickel-catalyzed Addition of Pyridine-*N*-oxides across Alkynes

Kanyiva, K. S.; Nakao, Y.; Hiyama, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 8872–8874.

A Strategy for C–H Activation of Pyridines: Direct C-2 Selective Alkenylation of Pyridines by Nickel/Lewis Acid Catalysis

Nakao, Y.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2008**, *130*, 2448–2449.

Direct Alkenylation and Alkylation of Pyridone Derivatives by Ni/$AlMe_3$ Catalysis

Nakao, Y.; Idei, H.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*,

15996–15997.

Chapter 5

Hydrocarbamoylation of Unsaturated Bonds by Nickel/Lewis Acid Catalysis

Nakao, Y.; Idei, H.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 5070–5071.

II. Following publication is not included in this Thesis.

Nickel-Catalyzed Hydroarylation of Vinyl Arenes

Nakao, Y.; Kashihara, N; Kanyiva, K. S.; Hiyama, T. manuscript in preparation.

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