Studies on Addition to 1-Aryl-1-alkynes and *N*-Alkynyl Amides

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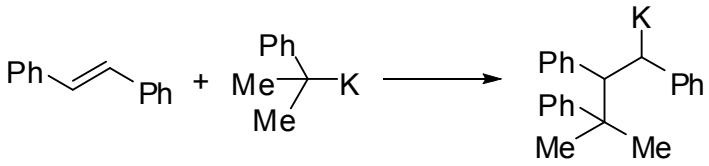
Contents

General Introduction

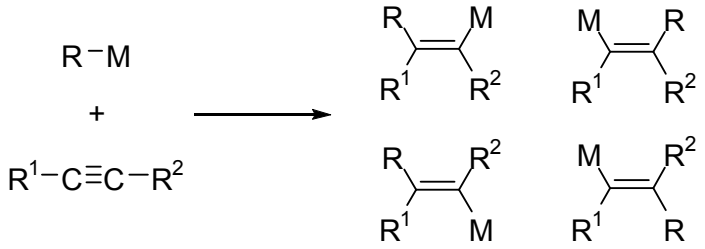
1. Carbometalation of Alkynes

Addition of organometallic reagents to carbon–carbon multiple bonds leading to new organometallic compounds are called carbometalation reactions. The resultant organometallic compounds can be used for further synthetic transformation, and then carbometalation reactions are among the most powerful synthetic methods.[1] Since the report by Ziegler and Bähr in 1928 (Scheme 1),[2] carbometalation reactions have been investigated very actively. It is known that various organometallic reagents such as organolithium, organomagnesium, organozinc, organoboron, organoaluminium, organocopper, organotin, organosilane, and organomercury add to a carbon–carbon multiple bonds in the presence or absence of a catalyst.



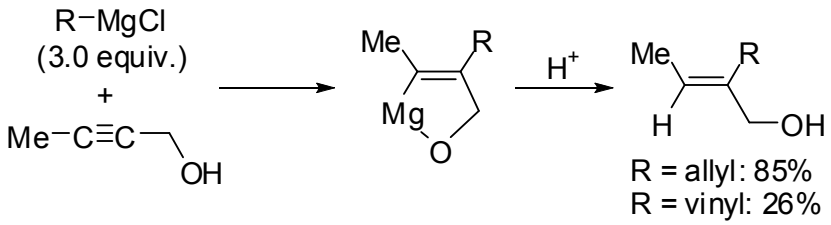
Scheme 1.

In this section, carbometalation of a carbon–carbon triple bond is focused. The vinylmetals generated by carbometalation of alkynes reacted with various electrophiles to afford multi-substituted alkenes. Carbometalation of alkynes can lead to regio- and stereoisomers (Scheme 2). In order that the carbometalation is synthetically useful, high regio- and stereoselectivity is required.



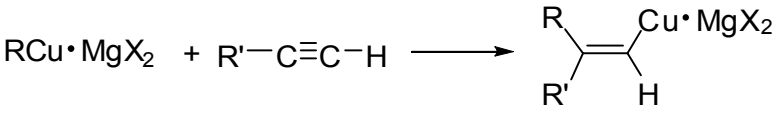
Scheme 2.

Regio- and stereoselective carbometalation of alkynes containing an adjacent heteroatom have been well studied.[1c] For example, reactions of propargyl alcohol derivatives with Grignard reagents resulted in *anti* additions to afford the corresponding adducts with exclusive regio- and stereoselectivity (Scheme 3).[3]



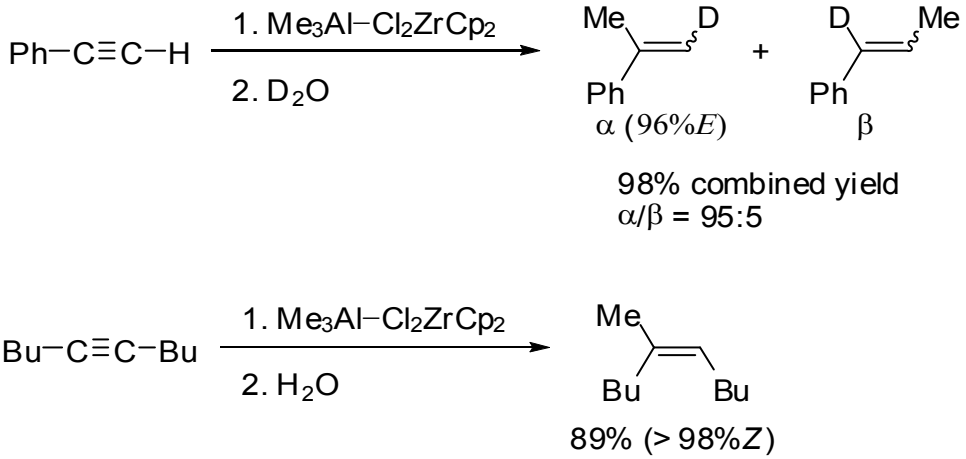
Scheme 3.

In 1971, Normant *et al.* reported that organocopper reagents add to terminal alkynes in a syn fashion with high regio- and stereoselectivity (Scheme 4).[4]



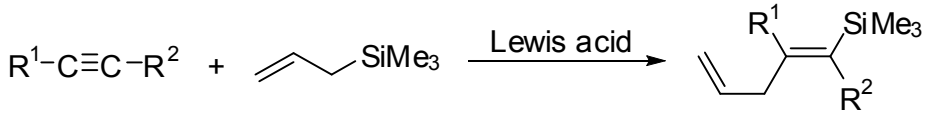
Scheme 4.

The uncatalyzed carboalumination of alkynes occurs generally under severe conditions. The reaction is of limited synthetic interest due to the low chemo-, regio- and stereoselectivity. In 1978, Negishi *et al.* reported that reactions of terminal and internal alkynes with organometallic reagents obtained by mixing organoalanes with zirconocene dichloride (Cp_2ZrCl_2) resulted in regio- and stereoselective carbometalation to produce the corresponding alkenes (Scheme 5).[5]



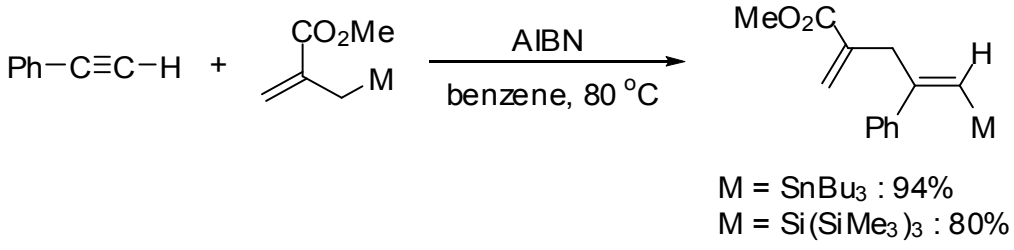
Scheme 5.

Lewis-acid catalyzed allylsilylation of alkynes that proceeds in an *anti* fashion was reported by Jung *et al.* and Y. Yamamoto *et al* (Scheme 6).[6]



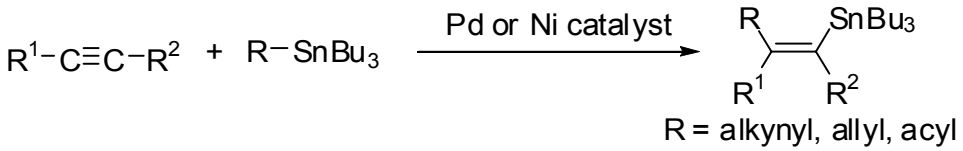
Scheme 6.

Allylstannylation and allylsilylation of alkynes via a radical process in an *anti* fashion was found by Hosomi (Scheme 7).[7] Allylstannanes and allylsilanes having an electron-withdrawing group at the β position participated in the reaction smoothly.



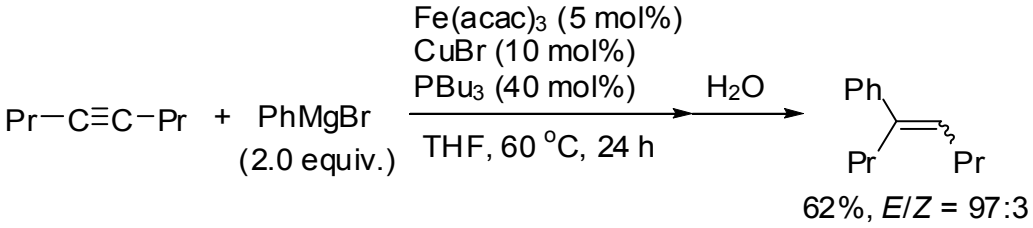
Scheme 7.

Transition-metal-catalyzed *syn*-carbostannylation such as alkynylstannylation, allylstannylation and acylstannylation of alkynes was found by Hiyama's group (Scheme 8).[8]



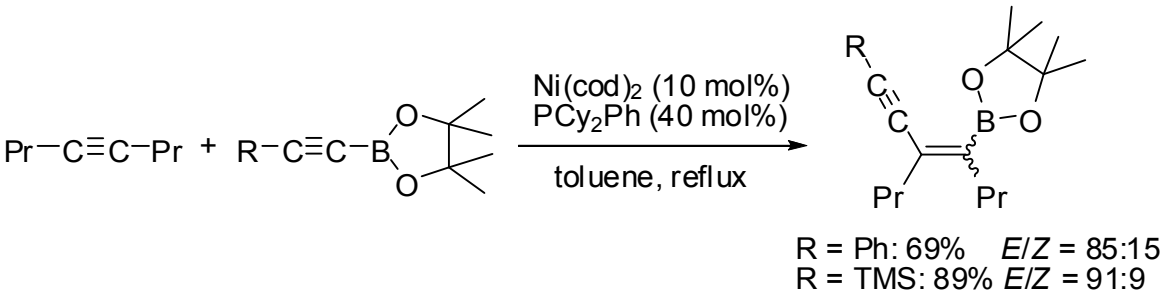
Scheme 8.

Hayashi's group reported arylmagnesiation of unfunctionalized alkynes catalyzed cooperatively by iron and copper complex (Scheme 9).[9] Oshima's group also reported chromium-catalyzed arylmagnesiation of unfunctionalized alkynes.[10]



Scheme 9.

Nickel-catalyzed alkynylboration of alkynes to provide vinylboranes was reported by Suginome (Scheme 10).[11] Suzuki-Miyaura cross-coupling of the vinylborane proceeded smoothly to afford a tetra-substituted alkene in a high yield.

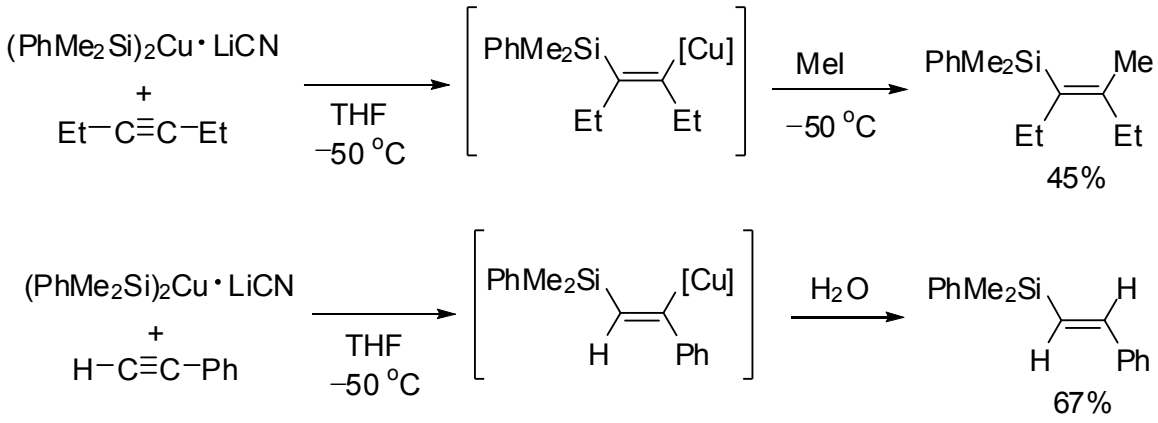


Scheme 10.

2. Silylmetalation of Alkynes

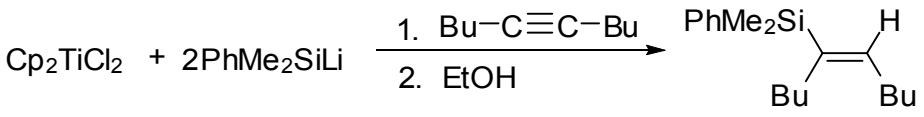
Vinylsilanes play an important role as synthetic building blocks because they react with various electrophiles in the presence or absence of Lewis acid and they are widely used for palladium-catalyzed cross-coupling reactions.[12] Silylmetalation of alkynes is one of the most general methods for synthesis of multi-substituted vinylsilanes.

Fleming *et al.* reported silylcupration of alkynes in 1981.[13] Bis(dimethylphenylsilyl)copper•lithium cyanide added to terminal and internal alkynes in a *syn* fashion (Scheme 11). The resultant vinylcopper reacted with various electrophiles smoothly. When terminal alkynes were used, the silyl group attached to the terminal carbon atom with high regioselectivity.



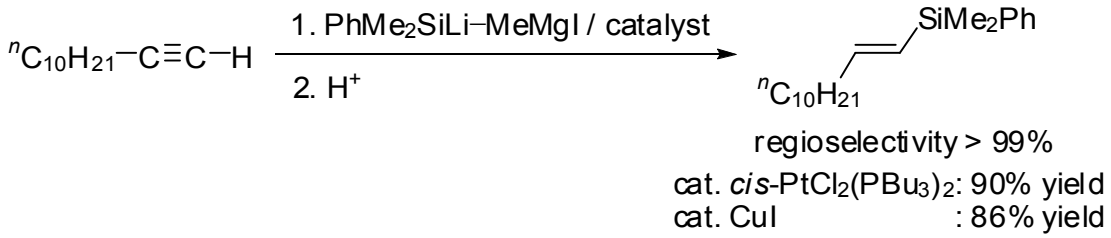
Scheme 11.

Silyltitanation of alkynes was reported by Tamao and Kumada *et al.*[14] A Ti^{III}–Si active species, $Cp_2TiSiMe_2Ph$, added to alkynes to provide vinylsilanes after protonolysis (Scheme 12).



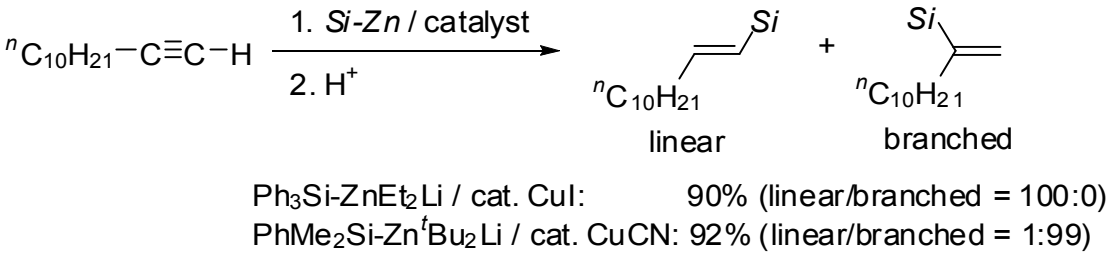
Scheme 12.

Transition-metal-catalyzed silylmetalation of alkynes was found by Oshima's group.[15] Silylmagnesium reagents prepared from silyllithium and methylmagnesium iodide added to 1-dodecyne under copper or platinum catalysis with high regioselectivity (Scheme 13).



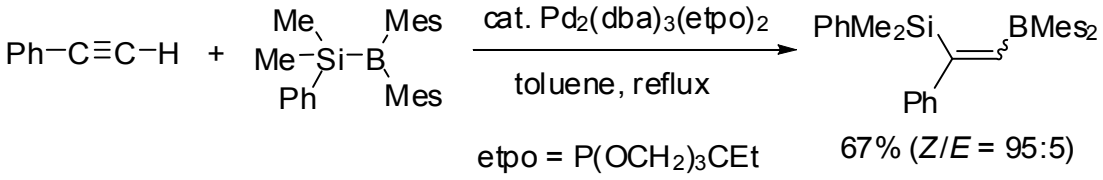
Scheme 13.

Oshima *et al.* also reported transition-metal-catalyzed silylzincation and silylalumination of alkynes.[16] Interestingly, both linear- and branched vinysilanes were synthesized from terminal alkynes selectively (Scheme 14).



Scheme 14.

Palladium-catalyzed silylboration of alkynes with stable silylboranes possessing mesityl (Mes = 2,4,6-trimethylphenyl) groups was reported by Birot and Pillot *et al* (Scheme 15).[17]

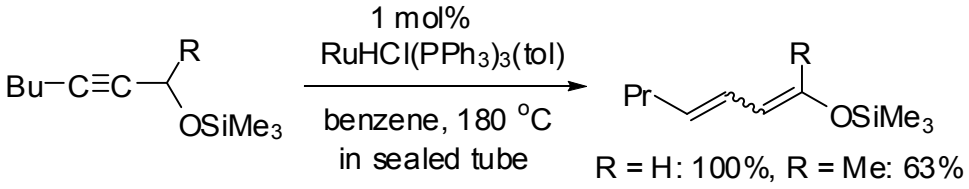


Scheme 15.

3. Isomerization of Alkynes under Transition-Metal-Catalysis

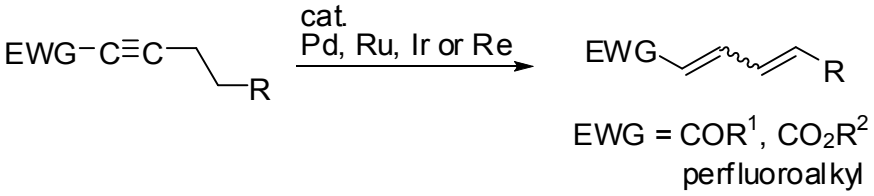
Transition-metal-catalyzed isomerization of alkenes to other alkenes is a well-known process. However, efficient isomerization of alkynes to 1,3-dienes is rare under transition metal catalysis unless particular alkynes described as follows.

Hydridoruthenium-catalyzed isomerization of propargyl ethers to the corresponding 1,3-dienyl ethers was reported (Scheme 16).[18] This isomerization is well explained by the mechanism involving addition and elimination of hydridoruthenium via allene intermediates.



Scheme 16.

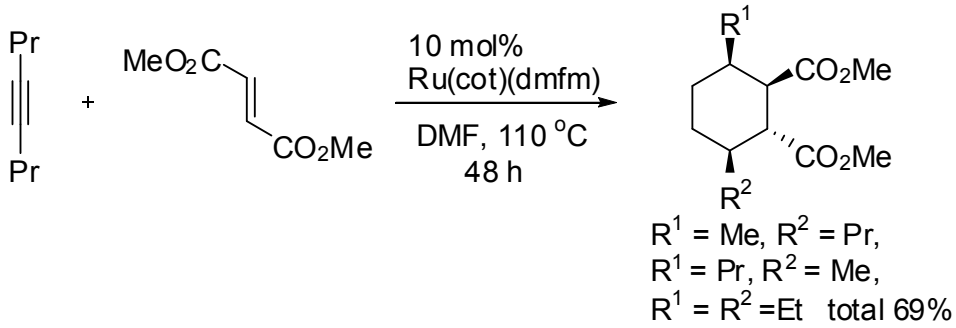
Isomerization of electron-deficient alkynes to the corresponding conjugated dienes was reported (Scheme 17). Palladium-catalyzed isomerization of 2-alkyn-1-one to 2,4-alkadien-1-one was reported by Trost *et al*.[19] Lu's group reported isomerization of 2-alkyn-1-one under ruthenium, rhenium or iridium catalysis.[20] Additionally, Lu *et al.* reported isomerization of 2-alkynoate esters[21] and perfluoroalkylated alkynes[22] to the corresponding conjugated dienes. In most cases, (*E*,*E*)-dienes were obtained stereoselectively.



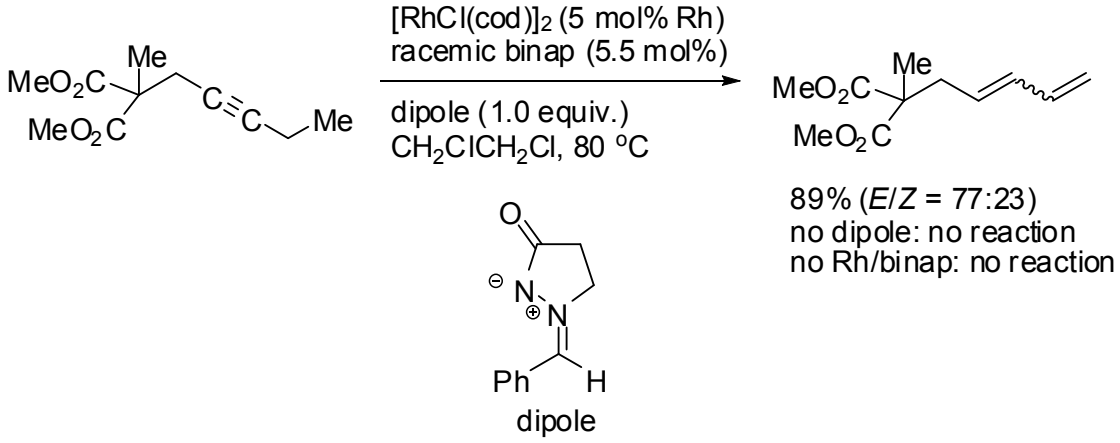
Scheme 17.

There are few reports on isomerization of simple alkynes under transition metal catalysis. Unexpectedly, Yamamoto *et al*. found palladium-catalyzed isomerization of a 1-phenyl-1-alkyne derivative to the corresponding diene during studies on hydroamination reactions.[23]

Isomerization of simple alkynes to the corresponding dienes in the presence of catalytic amount of Ru(cot)(dmfm) (cot = 1,3,5-cyclooctatriene, dmfm = dimethyl fumarate) was found by Mitsudo.[24] This isomerization was performed in the presence of an electron-deficient alkene such as dimethyl fumarate to afford Diels-Alder adducts (Scheme 18). Very recently, Hayashi *et al*. found that simple alkynes were isomerized to the corresponding 1,3-dienes in the presence of a rhodium catalyst and a dipole as the promoter (Scheme 19).[25]



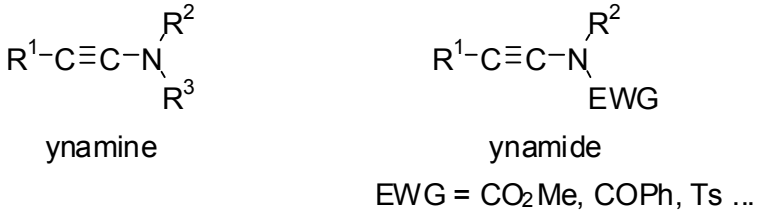
Scheme 18.



Scheme 19.

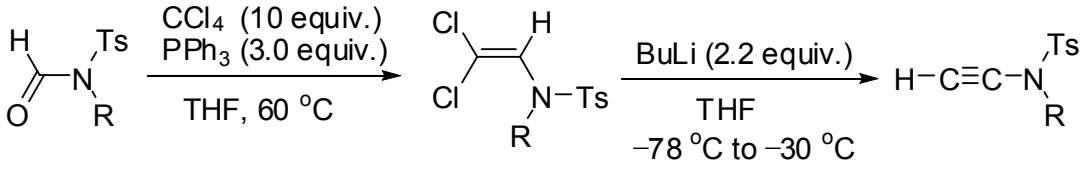
4. Synthesis and Reactions of Ynamides

Ynamines have proved to be useful building blocks in organic synthesis for a long time.[26] However, the widespread synthetic use of ynamines has remained limited because of the difficulty in preparation and handling of them. Recently, ynamides have attracted considerable attention as ynamines having both good reactivity and sufficient stability due to an electron-withdrawing group (EWG) on the nitrogen. The organic synthesis using ynamides have been studied actively.[27] In this section, the chemistry of ynamides is described.



a) Synthesis of Ynamides

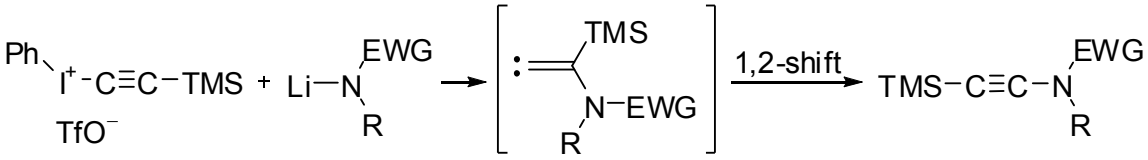
A elimination protocol that starts from *gem*-dichloroenamides to afford terminal ynamides was reported by Brückner (Scheme 20).[28] Internal ynamides can be synthesized by additional transformations such as Sonogashira reaction. However, multisteps are needed to obtain internal ynamides.



Scheme 20.

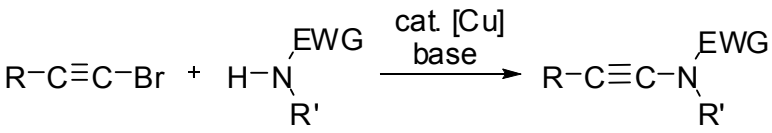
Direct alkynylation of amides using 1-alkynyliodonium salts was developed by Feldman and Witulski.[29] Treatment of pheny(trimethylsilylethynyl)iodonium trifluoromethanesulfonates with lithium amides afforded the corresponding ynamides via 1,2-shift of alkylidenecarbene intermediates (Scheme 21). This protocol is important because terminal ynamides can be

provided easily by protodesilylation of trimethylsilylethynylamides obtained.



Scheme 21.

Alkynylation of amides using 1-bromo-1-alkyne under copper catalysis was developed by Hsung and Danheiser (Scheme 22).[30] This protocol has great generality and direct synthesis of internal ynamides involving 1-alkynylamides and phenylethynylamides was accomplished.

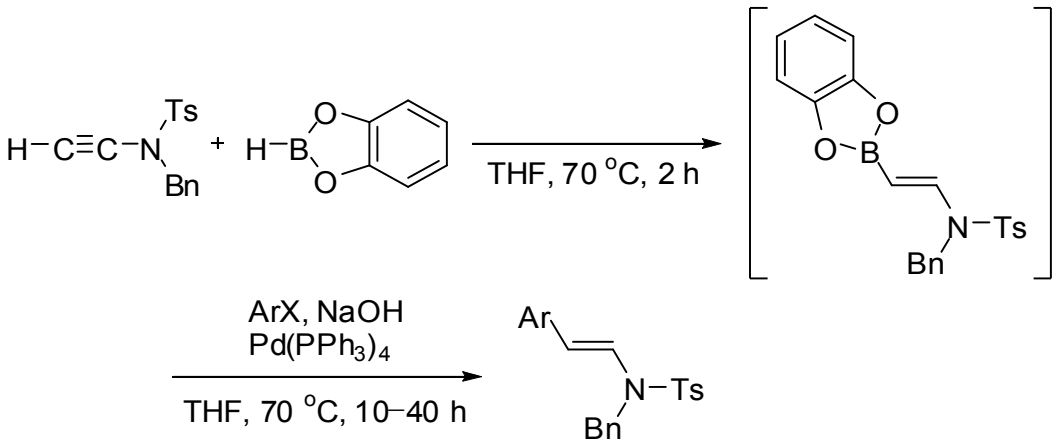


Scheme 22.

b) Reactions of Ynamides

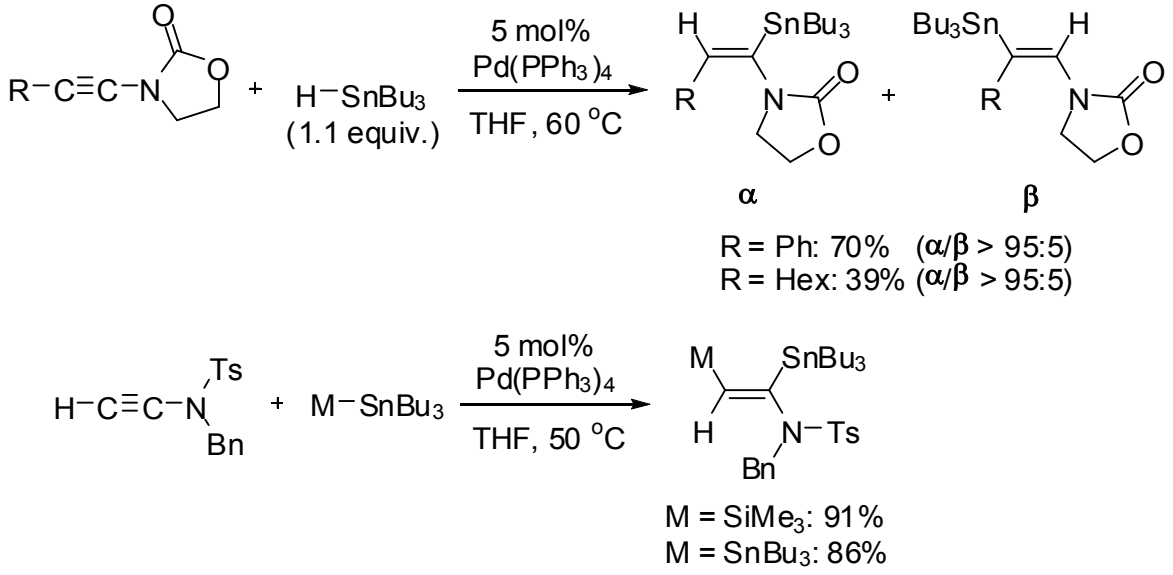
Since convenient and straightforward synthesis of ynamides was developed, organic synthesis using ynamides has been studied actively.

Addition of organometallic reagents to ynamides have been extensively explored. Hydroboration of terminal ynamides was reported by Witulski *et al*. (Scheme 23).[31] Suzuki-Miyaura coupling reactions of the obtained vinylboronate with aryl halides were performed to afford (*E*)-β-arylenamides.



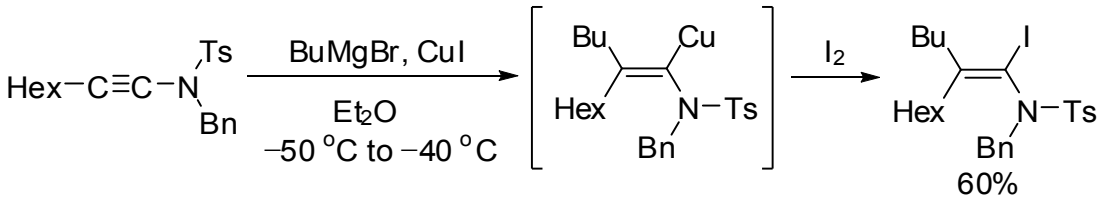
Scheme 23.

Palladium-catalyzed hydrostannylation of internal ynamides was developed by Cintrat (Scheme 24).[32] α-Stannylenamides were obtained as the major products. Cintrat also reported that palladium-catalyzed silylstannylation and bisstannylation of terminal ynamides furnished the corresponding adducts as single isomers.[33]



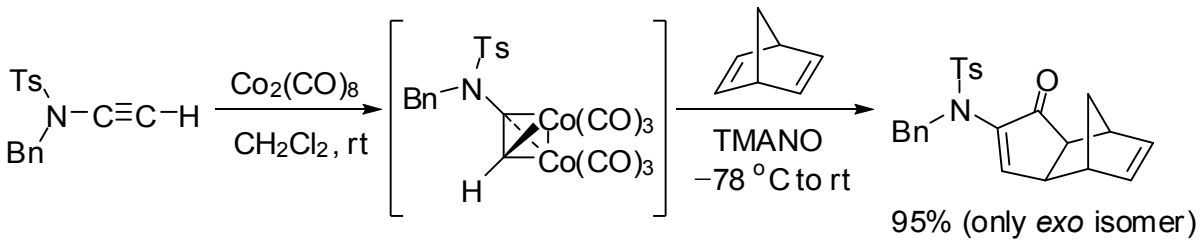
Scheme 24.

In addition, regio- and stereoselective carbocupration of internal ynamides was performed by Marek's group.[34] The resultant vinylcopper compounds reacted with electophiles such as allyl bromide and iodine (Scheme 25). The directing effect of the sulfonyl group of the ynamide would play a major role in determining the regiochemistry in the carbocupration. Copper-catalyzed carbomagnesiation was also reported.



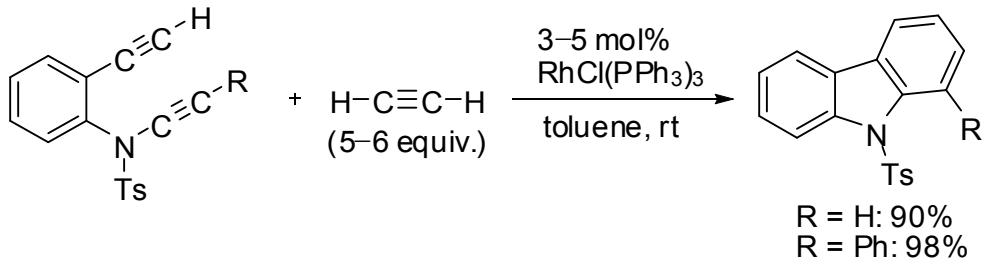
Scheme 25.

Cycloaddition reactions of ynamides have been well studied. In particular, there are many reports about cycloaddition reactions using a transition metal complex. The formal [2+2+1] cycloaddition reactions (Pauson-Khand reactions) of ynamides mediated with $Co_2(CO)_8$ were reported by Witulski (Scheme 26).[29b] Trimethylamine *N*-oxide (TMANO) was added as a promoter.



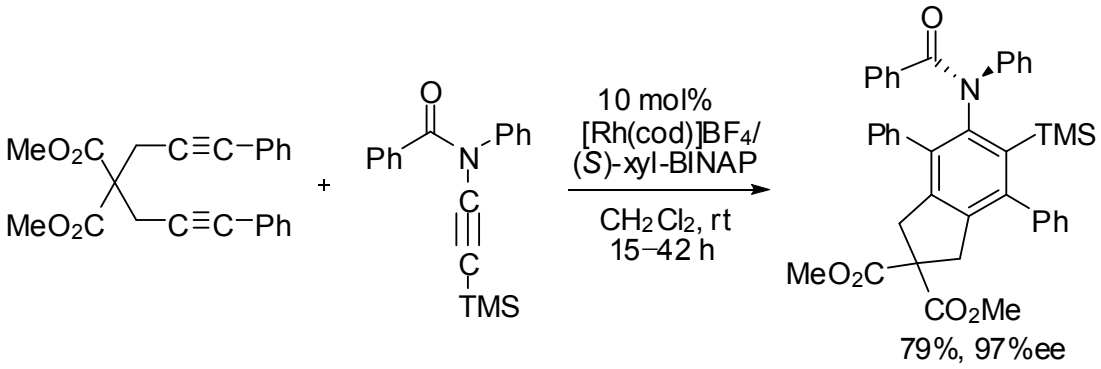
Scheme 26.

The formal [2+2+2] cycloaddition reactions utilizing ynamides were reported by Witulski.[35] Treatment of *N*-alkynyl-*N*-[*o*-(1-alkynyl)phenyl]-*p*-toluenesulfonamides with alkynes in the presence of Wilkinson catalyst afforded carbazoles (Scheme 27).



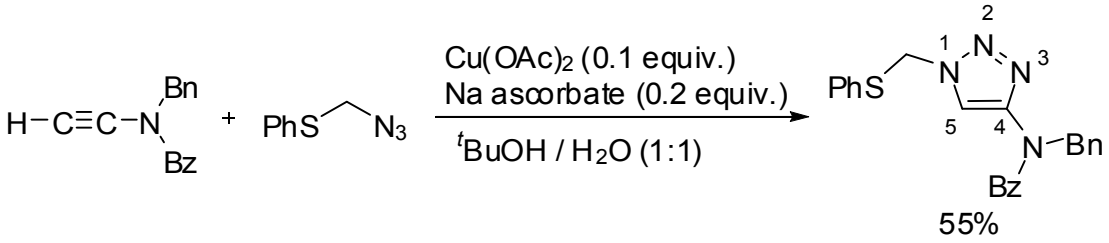
Scheme 27.

Enantioselective formal [2+2+2] cycloaddition reaction of ynamides and 1,6-diynes in the presence of catalytic amounts of $[Rh(cod)]BF_4$ and (*S*)-xyl-BINAP was reported by Tanaka (Scheme 28).[36] Enantioselective synthesis of axially chiral anilides was accomplished.



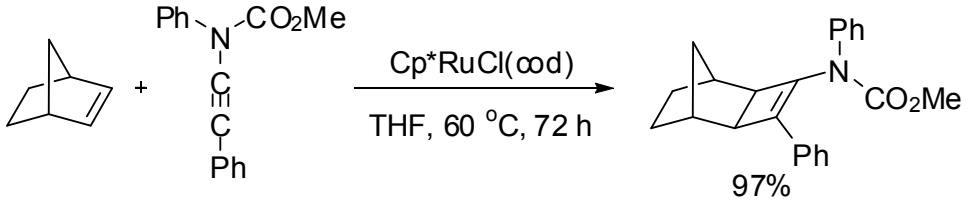
Scheme 28.

Cintrat found that ynamides can be good partners for formal [3+2] cycloaddition reactions with azides. Treatment of terminal ynamides with organic azides in the presence of catalytic amounts of copper acetate and sodium ascorbate afforded 1-substituted 4-amino-1,2,3-triazole regioselectively (Scheme 29).[37] He also reported synthesis of 1-substituted 5-amino-1,2,3-triazole from ynamides and azides under ruthenium catalysis.[38]



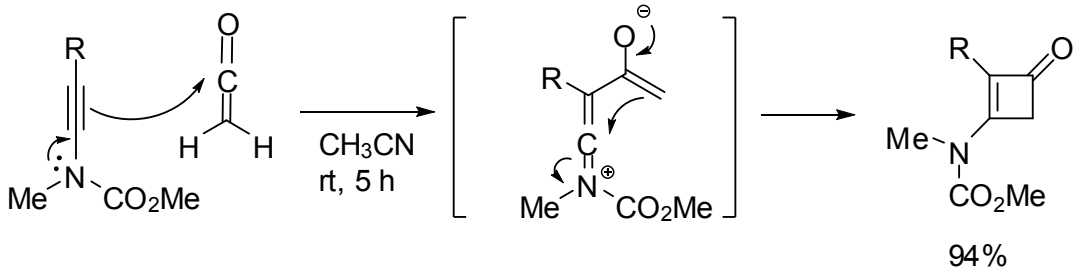
Scheme 29.

Ruthenium-catalyzed formal [2+2] cycloaddition of ynamides with norbornene was explored by Tam *et al* (Scheme 30).[39] The *exo* cycloadducts were formed as single stereoisomers.



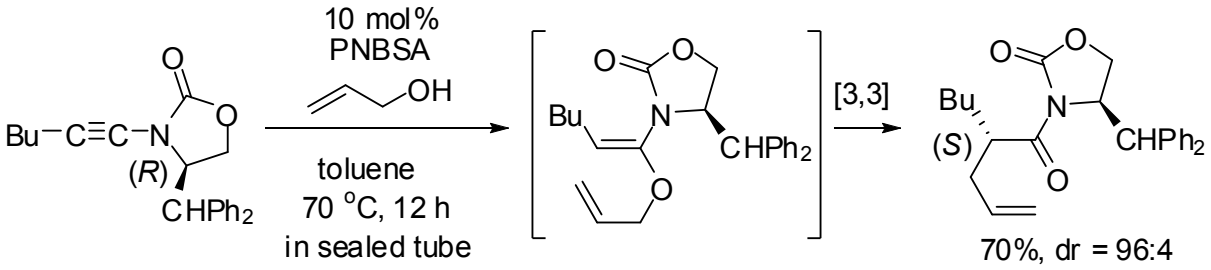
Scheme 30.

Reactions of ynamides have been developed on the basis of the reactivity of the electron-rich carbon–carbon triple bonds. The formal [2+2] cycloaddition of ynamides with ketenes was reported by Danheiser (Scheme 31).[40] This reaction suggests that ynamides have the reactivity similar to ynamine.



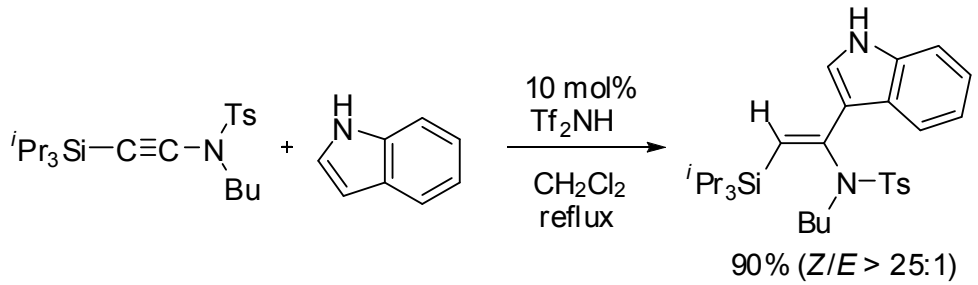
Scheme 31.

Reactions of ynamides catalyzed by Brϕnsted- and Lewis acid via active ketene iminium intermediates have been well studied. In the presence of a catalytic amount of *p*-nitrobenezenesulfonic acid (PNBSA), treatment of ynamides with allyl alcohols generated ketene aminal intermediates. The [3,3] sigmatropic rearrangement (Ficini–Claisen rearrangement) of the intermediates proceeded diastereoselectively (Scheme 32).[41] Propargyl alcohols can be utilized in similar reactions.[42]



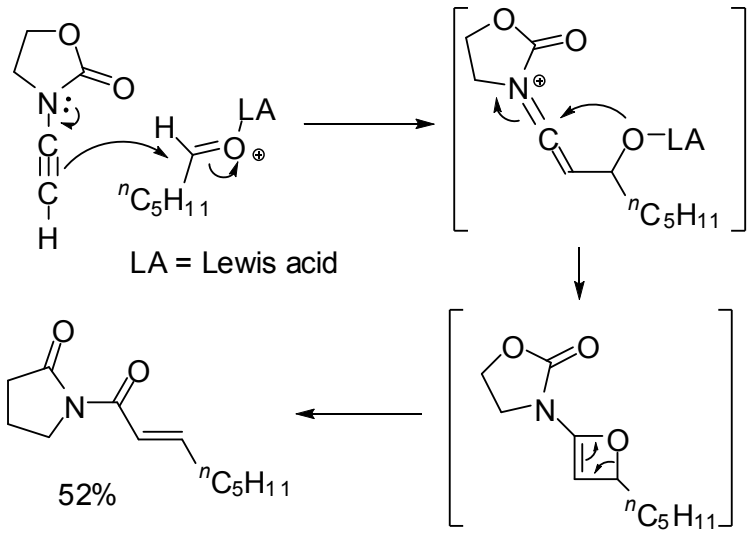
Scheme 32.

Brϕnsted acid-catalyzed regio- and stereoselective *cis*-hydroarylation of ynamides was reported. Reactions of ynamides with indoles in the presence of 10 mol% of bis(trifluoromethylsulfonyl)amine (Tf_2NH) afforded the corresponding vinylindoles (Scheme 33).[43] Intramolecular hydroarylation was also developed.[44]



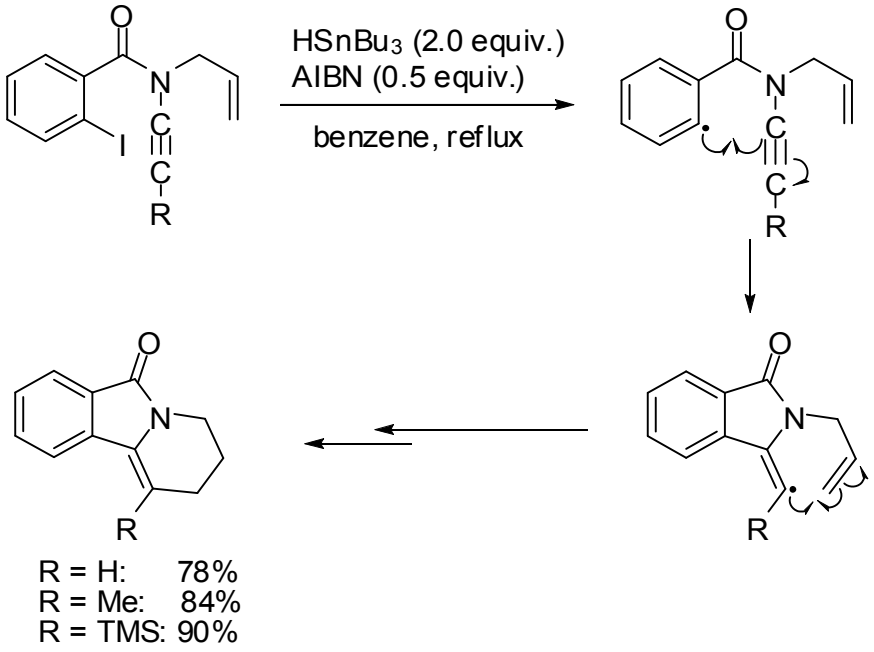
Scheme 33.

Reaction of ynamides with aldehydes or ketones under Lewis acid catalysis provided acrylic amides (Scheme 34).[45] The reaction would proceed as follows. First, ynamides reacted with aldehydes or ketones activated by Lewis acid to afford the oxetenes. Next, ring-opening of the oxetenes furnished acrylic amides. The intramolecular version was also reported.[46]



Scheme 34.

Malacria *et al.* used ynamides in radical cyclizations leading to polycyclic nitrogen heterocycles (Scheme 35).[47] It was shown that ynamides could be used as radical acceptors.



Scheme 35.

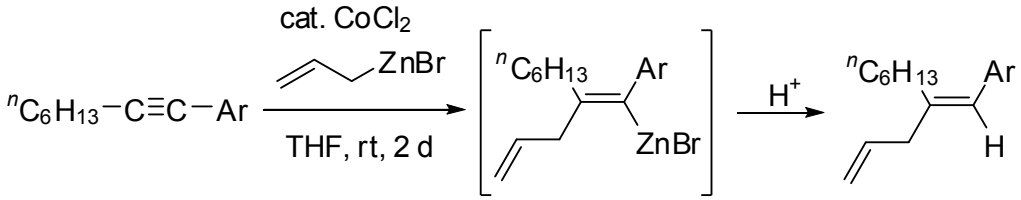
5. Summary of Thesis

The author studied carbometalation of unfunctionalized internal alkynes under transition metal catalysis. In chapter 1, the author describes cobalt-catalyzed *syn*-allylzincation of internal alkynes. During the study on transition-metal-catalyzed carbometalation of alkynes, the author found isomerization of alkynes to the corresponding conjugated dienes unexpectedly. In chapter 2, isomerization of simple internal alkynes under palladium or rhodium catalysis is thus described.

In addition, the author developed organic reactions using ynamides. In chapter 3, silylcupration of ynamides is discussed. Application of copper-catalyzed carbometalation to ynamides to aza-Claisen rearrangement is also described. In chapter 4, regio- and stereoselective hydrothiolation of ynamides with diphenyldithiophosphinic acid is described.

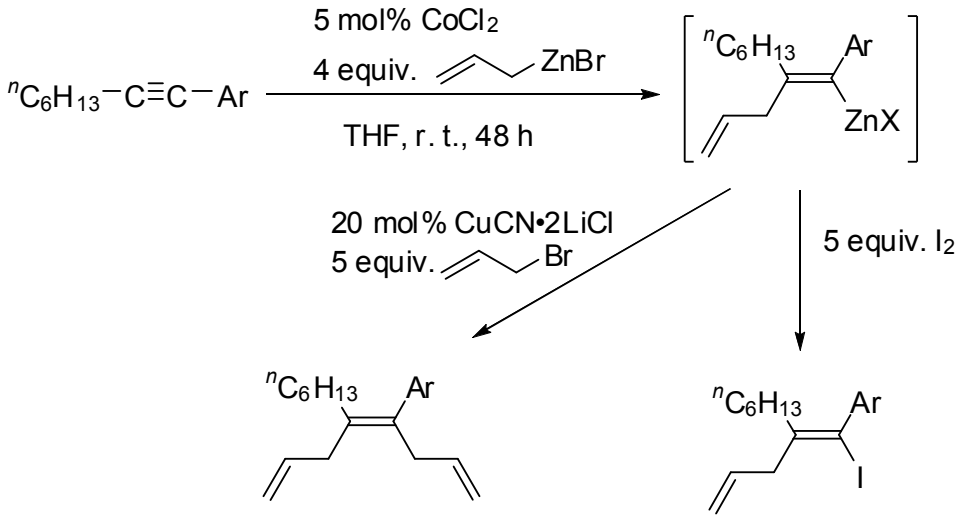
5.1) Cobalt-Catalyzed *Syn*-Allylzincation of Internal Alkynes

Reaction of 1-aryl-1-octyne with allylzinc bromide in the presence of a catalytic amount of cobalt(II) chloride in THF at ambient temperature resulted in allylzincation to afford the corresponding allylated product after hydrolysis (Scheme 36). The reaction proceeded regio- and stereoselectively.



Scheme 36.

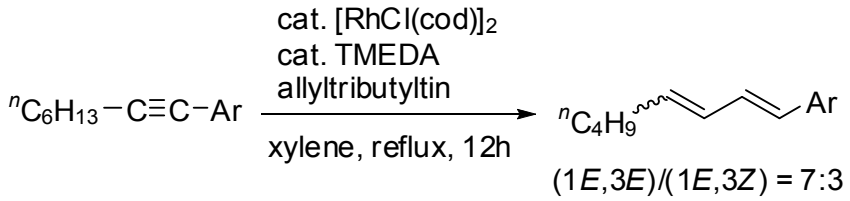
In addition, the resultant alkenylzinc compounds reacted with electrophiles such as allyl bromide and iodine to provide the corresponding tetra-substituted alkenes (Scheme 37).



Scheme 37.

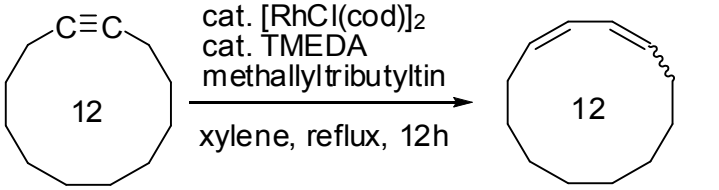
5.2) Isomerization of Simple Internal Alkynes under Palladium or Rhodium Catalysis

Reaction of 1-aryl-1-octynes in the presence of allyltributyltin and catalytic amounts of [RhCl(cod)]$_2$ and *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA) in refluxing xylene afforded a mixture of (1*E*,3*E*)- and (1*E*,3*Z*)-1-aryl-1,3-octadienes in a good combined yield (Scheme 38).



Scheme 38.

Interestingly, rhodium-catalyzed isomerization of alkynes to the conjugated dienes did not occur without allyltributyltin, although the role of allyltributyltin is not clear. An aromatic ring was not needed on the acetylenic carbon in the isomerization. Isomerization of cyclododecyne provided to the corresponding cyclododecadiene under similar conditions smoothly (Scheme 39). A cyclic allene was also isomerized to a cycloalkadiene under similar conditions. In addition, the isomerization of alkynes under palladium catalysis is also disclosed.

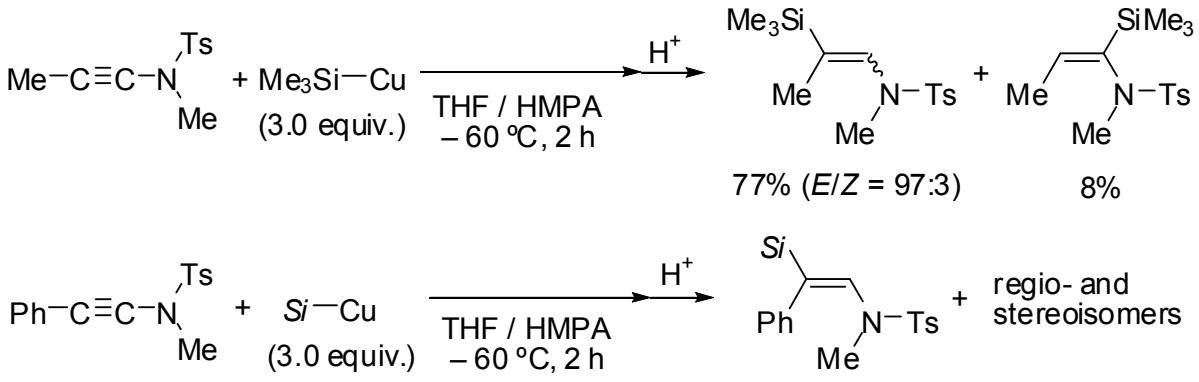


(*E*,*E*)/(*E*,*Z*) = 94:6

Scheme 39.

5.3) Silylcupration and Copper-Catalyzed Carbomagnesiation of Ynamides: Application to Aza-Claisen Rearrangement

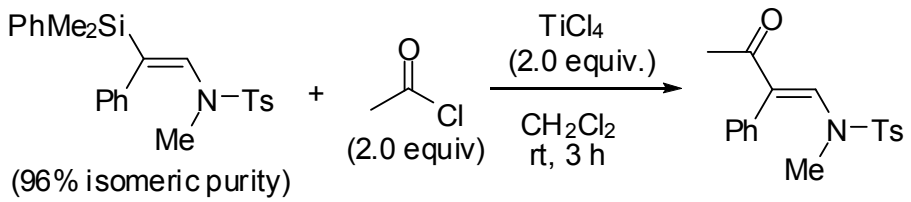
Treatment of ynamides with silylcopper reagents resulted in silylcupration to afford (*E*)-β-silylenamides, after protonolysis, in good yields with high regio- and stereoselectivity (Scheme 40).



Si = $SiMe_3$, 89% (92% isomeric purity)
Si = $SiPhMe_2$, 81% (93% isomeric purity)

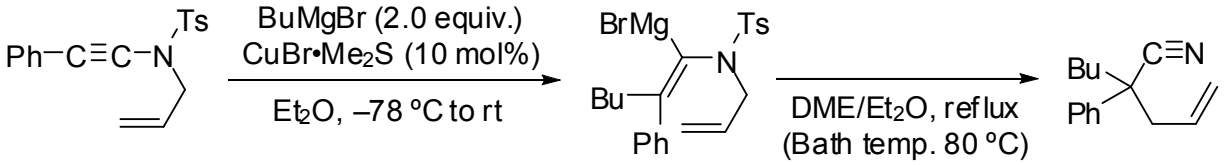
Scheme 40.

Reaction of (*E*)-β-silylenamides with acetyl chloride in the presence of titanium tetrachloride provided the corresponding acetylated product (Scheme 41).



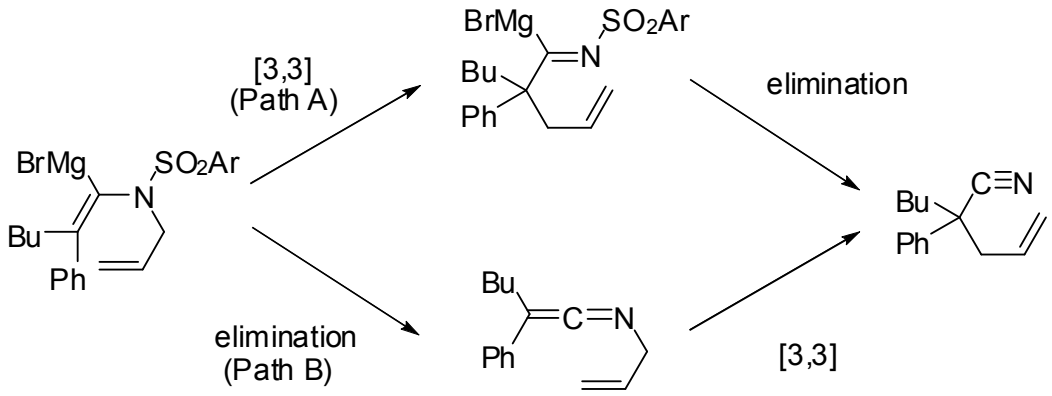
Scheme 41.

Reaction of ynamides having an allyl group on the nitrogen with Grignard reagents in the presence of a copper catalyst resulted in carbomagnesiation across the alkynyl parts and the subsequent heating provided 4-pentenenitriles via aza-Claisen rearrangement (Scheme 42).



Scheme 42.

There are two possible mechanisms for the formation of 4-pentenenitrile (Scheme 43). The [3,3] sigmatropic rearrangement of the vinylmagnesium compound and the subsequent elimination of magnesium sulfinate would afford the nitrile (Path A). The other mechanism (Path B) is as follow. First, the elimination of magnesium sulfinate would take place to give ketene imine intermediate. Then, [3,3] sigmatropic rearrangement of the ketene would proceed to furnish the product.

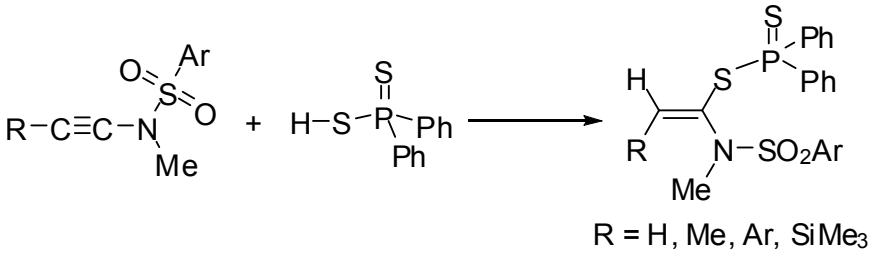


Scheme 43.

.

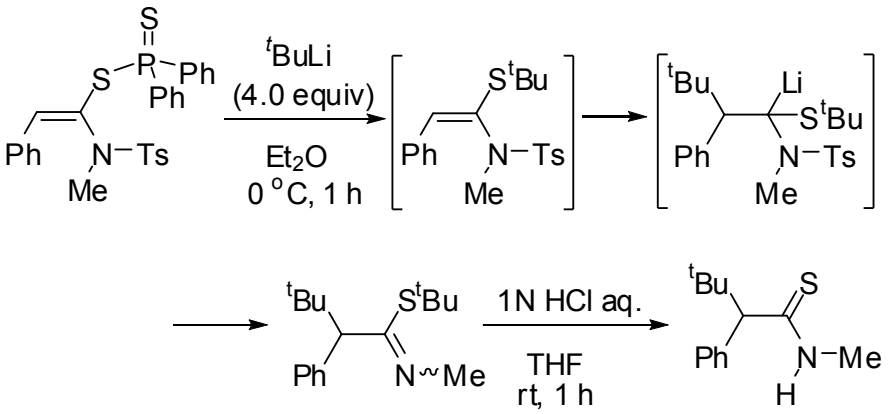
5.4) Regio- and Stereoselective Hydrothiolation of Ynamides with Diphenyldithiophosphinic Acid: Straightforward Synthesis of Ketene *N*,*S*-Acetal Derivatives

Treatment of *N*-1-alkynyl-*N*-methylarenesulfonamides with diphenyldithiophosphinic acid (Ph_2PS_2H) resulted in hydrothiolation reactions to provide ketene *N*,*S*-acetal derivatives with regio- and stereoselectivity (Scheme 44). The reaction would proceed via ketene iminium intermediates.



Scheme 44.

In addition, the reactivity of the ketene *N*,*S*-acetal obtained was examined (Scheme 45). Treatment of ketene *N*,*S*-acetal with 4.0 equimolar amounts of *tert*-butyllithium in diethyl ether at 0 ˚C provided thioimidate. Hydrolysis of the thioimidate led to *tert*-butyl-substituted thioamide.



Scheme 45.

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Abbreviations

Ac	acetyl
aq.	aqueous
Ar	aryl
Bn	benzyl
brs	broad singlet (spectral)
Bu	butyl
Bz	benzoyl
˚C	degrees Celsius
ca	*circa* (about)
calcd	calculated
cat.	catalytic
cm	centimeter(s)
Co.	company
cod	1,5-cyclooctadiene
conc.	concentrated
Cp	cyclopentadienyl
d	doublet (spectral)
DME	1,2-dimethoxyethane
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
de	diastereomeric excess
Ed(s).	editor(s)
ee	enantiomeric excess
eq	equation
equiv.	equivalent(s)
Et	ethyl
et al.	*et alii* (and others)
FAB	fast atom bombardment
h	hour(s)
Hex	hexyl
HMPA	hexamethylphosphoric triamide
HRMS	high-resolution mass spectrum
Hz	hertz (s^{-1})
i	iso
IR	infrared (spectrum)
J	coupling constant (spectrum)
m	multiplet (spectral)
M	molar (1 M = 1 mol dm^{-3})
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mm	millimeter(s)
mmol	millimole
m.p.	melting point
n	normal
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
p.	page(s)
Ph	phenyl
ppm	parts per million (spectrum)
Pr	propyl
q	quartet (spectral)
quant.	quantitative
ref	reference
r. t.	room temperature (25 ± 3 ˚C)
s (*sec*)	secondary
s	singlet (spectral)
sept	septet (spectral)
t	triplet (spectral)
t (*tert*)	tertiary
TBDMS	*tert*-butyldimethylsilyl
temp.	temperature
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	trimethylsilyl
Ts	*p*-tolylsulfonyl

Instrumental and Materials

^{1}H NMR (500 MHz), ^{13}C NMR (125.7 MHz) and ^{31}P NMR (121.5 MHz) spectra were taken on Varian UNITY INOVA 500 and Mercury 300 spectrometers. ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ with tetramethylsilane as an internal standard. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^{1}H and relative to $CDCl_3$ at 77.2 ppm for ^{13}C unless otherwise noted. ^{31}P NMR was obtained in $CDCl_3$ with 85% phosphoric acid solution as an external standard. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra were determined on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. The analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. THF and ether were purchased from Kanto Chemical Co., stored under nitrogen, and used as they are.

Chapter 1

Cobalt-Catalyzed Allylzincation of Internal Alkynes

Cobalt salts such as cobalt(II) chloride catalyze allylzincation reactions of 1-aryl-1-alkynes. The allylzincations proceed in a *syn* fashion to form 2-allyl-1-aryl-1-alkenylzinc species. Other internal alkynes such as 6-dodecyne or 2-nonyn-1-ol are much less reactive than 1-aryl-1-alkynes.

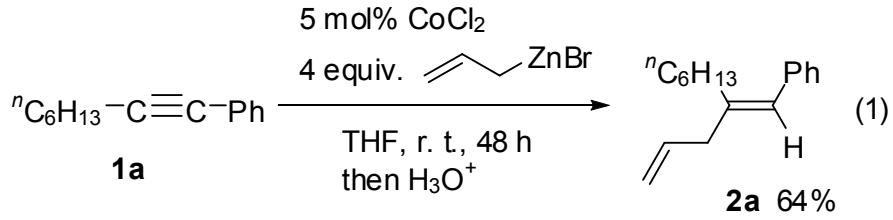
Introduction

Due to the importance of allylic groups, allylmetalation reactions of alkynes and alkenes represent powerful methods for the construction of complex organic molecules.[1] Among them, allylzincation reactions of internal alkynes are rather difficult processes.[1f,2] Oshima *et al.* have been interested in allylation reactions under cobalt catalysis.[3] Here the author reports cobalt-catalyzed allylzincation reactions of internal alkynes.[4]

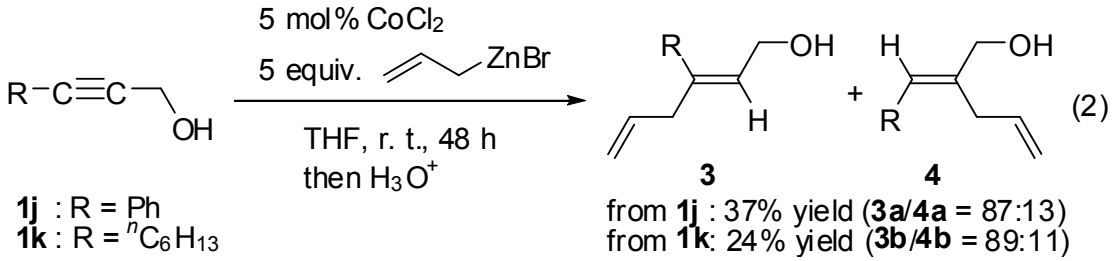
Results and Discussion

As a model substrate, 1-phenyl-1-octyne (**1a**) was subjected to various conditions for cobalt-catalyzed allylzincation reaction (eq 1). Treatment of **1a** with 4 equiv of allylzinc bromide in the presence of 5 mol% of cobalt(II) chloride in THF at room temperature for 48 h provided the corresponding allylated product **2a** in 64% yield. No traces of regio- or stereoisomers were obtained. The formation of 2-allyl-1-aryl-1-alkenylzinc species was confirmed by quantitative deuterium incorporation upon quenching with deuterated hydrochloric acid. THF was chosen as the solvent. The use of other solvents such as toluene, hexane, and Et_2O resulted in a slight decrease of the yield of **2a**. Cobalt(II) bromide, (8-quinolinolato)cobalt(II), and acetylacetonatocobalt(III) also catalyzed the reaction to provide **2a** in 64%, 59%, and 53% yields, respectively. Cobalt(II) fluoride did not promote the allylzincation reaction. In the presence of a phosphine ligand, the yield of **2a** was significantly decreased (13% with 5 mol% of PPh_3). The reaction did not go to completion when the reaction was carried out for 24 h (53% yield). A smaller amount, 3.0 equiv for instance, of allylzinc bromide also furnished a 56% yield of **2a**. The use of 10 equiv of allylzinc bromide slightly increased the yield of **2a** to 73%. Reaction at 40 ˚C gave rise to a lower conversion of **1a** (43% recovery) and 30% of **2a** was obtained, probably because the cobalt catalyst lost its activity upon heating. In the absence of a cobalt(II) catalyst, the reaction did not occur and the starting

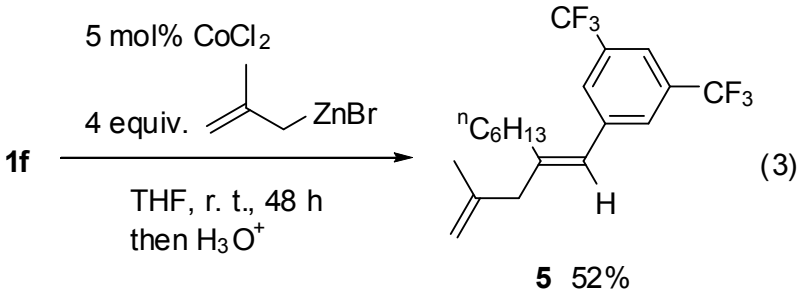
material remained untouched. It is noteworthy that the use of allylmagnesium bromide instead of allylzinc bromide resulted in no conversion of **1a**.



A variety of internal alkynes were subjected to the cobalt-catalyzed allylzincation reaction (Table 1). An electron-donating substituent on the aromatic ring rendered the reaction less efficient (entry 1). On the other hand, 1-aryl-1-alkynes having electron-withdrawing groups underwent the allylzincation to yield the corresponding products in high yields (entries 2–5). Unfortunately, an attempted allylzincation reaction of 1,2-diphenylacetylene (**1g**) provided the desired product **2g** in only 41% yield (entry 6). The reaction of 6-dodecyne (**1h**) and the homopropargyl methyl ether **1i** afforded the corresponding products in only 18% and 34% yields, respectively (entries 7 and 8). The allylzincation reaction of 3-phenyl-2-propyn-1-ol (**1j)** gave a mixture of the allylzincation products **3a** and **4a**, albeit the yield was low (eq 2). The formation of **4a** was often observed in the previous allylmetalation reactions.[1a,5] Similarly, a mixture of **3b** and **4b** was formed in the reaction of 2-nonyn-1-ol (**1k**).

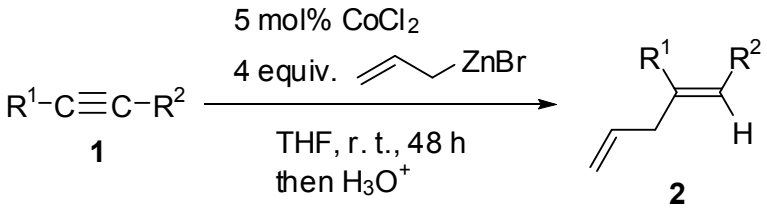


The reaction of **1f** with substituted allylic zinc reagents was studied. 2-Methyl-2-propenylzinc bromide reacted with **1f** under catalysis of $CoCl_2$ to afford **5** in 52% yield (eq 3). An attempt to use a 2-butenylzinc reagent resulted in the formation of a complex mixture.



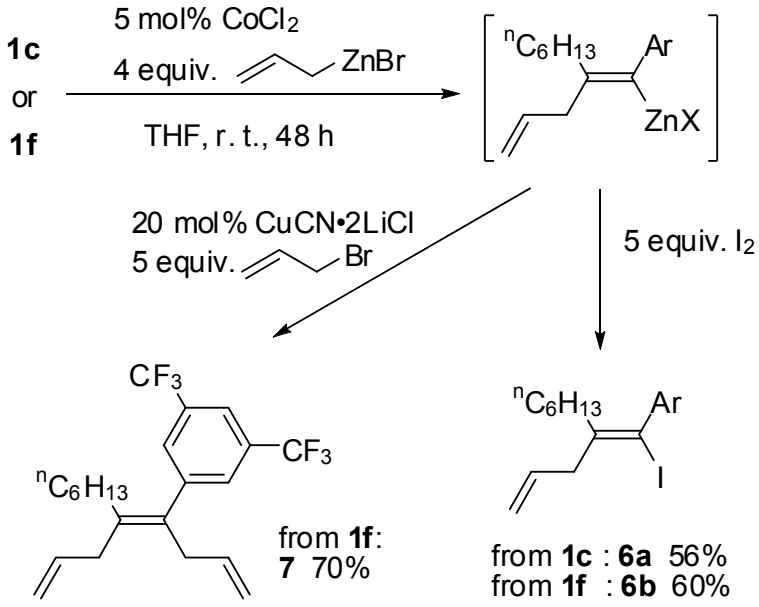
(3)

Table 1. Cobalt-catalyzed allylzincation reactions of internal alkynes



Entry	**1**	R^1	R^2	**2**	Yield / %
1	**1b**	$^nC_6H_{13}$	4-$MeOC_6H_4$	**2b**	51
2	**1c**	$^nC_6H_{13}$	4-ClC_6H_4	**2c**	67
3	**1d**	$^nC_6H_{13}$	4-FC_6H_4	**2d**	70
4	**1e**	$^nC_6H_{13}$	4-$CF_3C_6H_4$	**2e**	73
5	**1f**	$^nC_6H_{13}$	3,5-$(CF_3)_2C_6H_3$	**2f**	73
6	**1g**	Ph	Ph	**2g**	41
7	**1h**	$^nC_5H_{11}$	$^nC_5H_{11}$	**2h**	18
8	**1i**	$^nC_6H_{13}$	CH_2CH_2OMe	**2i**	34

The intermediary alkenylzinc compounds obtained by the allylzincation reaction reacted with electrophiles (Scheme 1). The cobalt-catalyzed allylzincations of **1c** and **1f** followed by the addition of iodine provided the corresponding tetrasubstituted alkenes **6** in moderate yields. Copper(I) cyanide mediated a carbon-carbon bond formation reaction with allyl bromide.



Scheme 1. Reactions of alkenylzinc intermediates.

Conclusion

Cobalt salts such as cobalt(II) chloride proved to catalyze the allylzincation reaction of 1-aryl-1-alkynes efficiently. The cobalt catalysis did not efficiently promote the allylzincation reactions of other internal alkynes such as 6-dodecyne and propargylic alcohols.

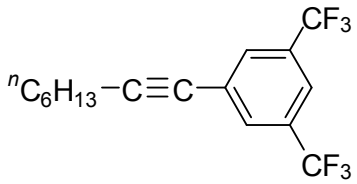
Experimental Section

Materials. The starting materials **1** were prepared by the conventional Sonogashira coupling reaction or were commercially available. Allylic zinc reagents were prepared and titrated according to the literature.[3a]

Typical Procedure for the Cobalt-Catalyzed Allylzincation of Internal Alkynes. The synthesis of **7** is representative. Cobalt(II) chloride (3.2 mg, 0.025 mmol) was placed in a 20 mL reaction flask under argon. A solution of **1f** (161 mg, 0.50 mmol in 1 mL of THF) was added to the reaction flask. A solution of allylzinc bromide (1.50 mL, 1.34 M THF solution, 2.0 mmol) was added at room temperature. The mixture was stirred for 48 h at room temperature. Allyl bromide (0.22 mL, 2.5 mmol) and CuCN•2LiCl (0.1 mL, 1.0 M THF solution, 0.1 mmol) were then added. The resulting mixture was stirred for an additional 3 h. The mixture was poured into 1 M hydrochloric acid. The organic compounds were extracted with ether three times. The combined organic part was dried and concentrated in vacuo. Chromatographic purification on silica gel afforded **7** (142 mg, 0.35 mmol) in 70% yield.

Characterization Data. The spectral data of the products **2g**,[6] **2i**,[7] **3a**,[8] **3b**,[7] and **4a**[9] can be found in the literature. The stereochemistry of **2a**[6,9,10] and **2h**[11] was determined by comparison with their closely related analogues. The stereochemistry of **2b**–**2f** was tentatively assigned compared to that of **2a**.

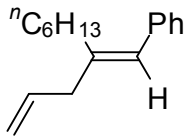
1-[3,5-Bis(trifluoromethyl)phenyl]-1-octyne (1f)



IR (neat) 2936, 2862, 2232, 1464, 1385, 1279, 1234, 1180, 1138, 1106, 896, 848, 701, 684 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.91 (t, *J* = 7.5 Hz, 3H), 1.31–1.35 (m, 4H), 1.42–1.48 (m, 2H), 1.62 (tt, *J* = 7.5, 7.5 Hz, 2H), 2.43 (t, *J* = 7.5 Hz, 2H), 7.74 (s, 1H), 7.81 (s, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.04, 19.34, 22.53, 28.34, 28.62, 31.31, 78.05, 94.65, 120.83 (m), 123.02 (q, *J* = 271.5 Hz),

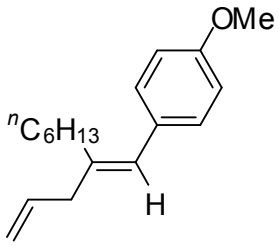
126.39, 131.47 (m), 131.66 (q, J = 33.4 Hz); Found: C, 59.63; H, 5.02%. Calcd for $C_{16}H_{16}F_6$: C, 59.63; H, 5.00%.

(*E*)-2-Hexyl-1-phenyl-1,4-pentadiene (2a)



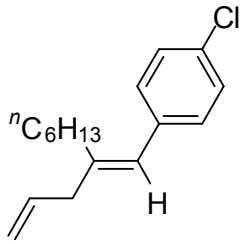
IR (neat) 2956, 2927, 2857, 1466, 995, 913, 748, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, J = 7.0 Hz, 3H), 1.22–1.31 (m, 6H), 1.44–1.50 (m, 2H), 2.22 (t, J = 6.0 Hz, 2H), 2.91 (d, J = 7.0 Hz, 2H), 5.07–5.14 (m, 2H), 5.88 (ddt, J = 17.0, 10.0, 7.0 Hz, 1H), 6.28 (s, 1H), 7.17–7.21 (m, 3H), 7.29–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.07, 22.60, 28.10, 29.38, 30.83, 31.62, 41.73, 116.25, 125.82, 125.94, 128.03, 128.56, 136.70, 138.41, 141.95; Found: C, 89.54; H, 10.67%. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59%.

(*E*)-2-Hexyl-1-(4-methoxyphenyl)-1,4-pentadiene (2b)



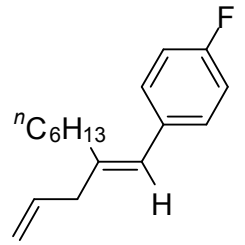
IR (neat) 2955, 2929, 1609, 1511, 1464, 1249, 1176, 1039, 911 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.89 (t, J = 7.5 Hz, 3H), 1.21–1.34 (m, 6H), 1.44–1.51 (m, 2H), 2.22 (t, J = 8.0 Hz, 2H), 2.90 (d, J = 6.5 Hz, 2H), 3.82 (s, 3H), 5.08–5.15 (m, 2H), 5.89 (ddt, J = 17.5, 10.0, 6.5 Hz, 1H), 6.23 (s, 1H), 6.87 (d, J = 8.5 Hz, 2H), 7.16 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.09, 22.62, 28.10, 29.43, 30.81, 31.65, 41.83, 55.20, 113.44, 116.10, 125.22, 129.65, 130.97, 136.88, 140.59, 157.75; Found: C, 83.45; H, 9.98%. Calcd for $C_{18}H_{26}O$: C, 83.67; H, 10.14%.

(*E*)-1-(4-Chlorophenyl)-2-hexyl-1,4-pentadiene (2c)



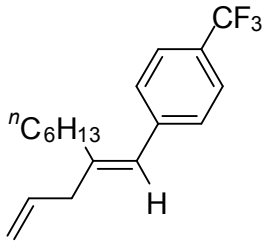
IR (neat) 2958, 2927, 2857, 1490, 1093, 1015, 914 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, *J* = 7.5 Hz, 3H), 1.21–1.31 (m, 6H), 1.42–1.48 (m, 2H), 2.18 (t, *J* = 8.0 Hz, 2H), 2.90 (dd, *J* = 7.0, 1.5 Hz, 2H), 5.08–5.14 (m, 2H), 5.86 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 6.21 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.07, 22.59, 28.01, 29.34, 30.82, 31.59, 41.67, 116.48, 124.63, 128.17, 129.86, 131.60, 136.40, 136.84, 142.81; Found: C, 77.96; H, 8.81%. Calcd for $C_{17}H_{23}Cl$: C, 77.69; H, 8.82%.

(*E*)-1-(4-Fluorophenyl)-2-hexyl-1,4-pentadiene (2d)



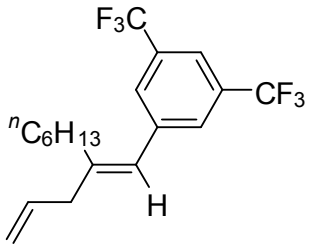
IR (neat) 2928, 2858, 1603, 1505, 1229, 1156, 913, 837, 823 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, *J* = 7.0 Hz, 3H), 1.20–1.32 (m, 6H), 1.42–1.48 (m, 2H), 2.18 (t, *J* = 8.5 Hz, 2H), 2.89 (dd, *J* = 7.0, 1.5 Hz, 2H), 5.07–5.14 (m, 2H), 5.87 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 6.22 (s, 1H), 6.97–7.02 (m, 2H), 7.13–7.16 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.27, 22.80, 28.23, 29.55, 30.92, 31.80, 41.81, 115.05 (d, *J* = 21.0 Hz), 116.56, 124.92, 130.24 (d, *J* = 7.6 Hz), 134.58 (d, *J* = 3.4 Hz), 136.76, 142.19, 161.37 (d, *J* = 243.4 Hz); Found: C, 82.76; H, 9.42%. Calcd for $C_{17}H_{23}F$: C, 82.88; H, 9.41%.

(*E*)-2-Hexyl-1-[4-(trifluoromethyl)phenyl]-1,4-pentadiene (2e)



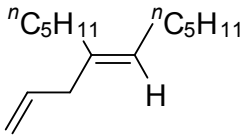
IR (neat) 2930, 1615, 1326, 1165, 1127, 1069, 1017 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.87 (t, *J* = 7.0 Hz, 3H), 1.20–1.33 (m, 6H), 1.44–1.50 (m, 2H), 2.20 (t, *J* = 8.0 Hz, 2H), 2.93 (dt, *J* = 6.0, 1.0 Hz, 2H), 5.10–5.16 (m, 2H), 5.88 (ddt, *J* = 17.0, 10.5, 6.0 Hz, 1H), 6.28 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.22, 22.81, 28.26, 29.54, 31.13, 31.81, 41.90, 116.89, 124.58 (q, *J* = 270.0 Hz), 124.89, 125.14–125.23 (m), 128.20 (q, *J* = 32.0 Hz), 128.99, 136.37, 142.32, 144.51; Found: C, 72.81; H, 7.68%. Calcd for $C_{18}H_{23}F_3$: C, 72.95; H, 7.82%.

(*E*)-1-[3,5-Bis(trifluoromethyl)phenyl]-2-hexyl-1,4-pentadiene (2f)



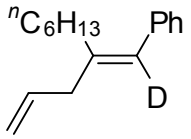
IR (neat) 2932, 2861, 1387, 1368, 1279, 1177, 1138, 918, 897, 708, 683 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.88 (t, *J* = 7.0 Hz, 3H), 1.23–1.33 (m, 6H), 1.48–1.54 (m, 2H), 2.19 (t, *J* = 8.0 Hz, 2H), 2.96 (dd, *J* = 7.5, 1.5 Hz, 2H), 5.14–5.18 (m, 2H), 5.84–5.92 (m, 1H), 6.31 (s, 1H), 7.64 (s, 2H), 7.71 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 13.96, 22.53, 28.06, 29.20, 31.02, 31.49, 41.59, 117.19, 119.65 (m), 123.14, 123.42 (q, *J* = 271.6 Hz), 128.54 (m), 131.29 (q, *J* = 33.0 Hz), 135.62, 140.30, 146.17; Found: C, 62.90; H, 6.11%. Calcd for $C_{19}H_{22}F_6$: C, 62.63; H, 6.09%.

(*E*)-4-Pentyl-1,4-decadiene (2h)



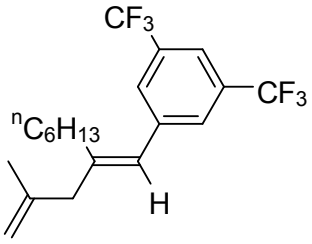
IR (neat) 2958, 2927, 2858, 1467, 994, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.82 (t, *J* = 7.5 Hz, 6H), 1.16–1.31 (m, 12H), 1.49–1.94 (m, 4H), 2.65 (d, *J* = 7.0 Hz, 2H), 4.91–4.97 (m, 2H), 5.07 (t, *J* = 7.0 Hz, 1H), 5.72 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 14.07, 14.09, 22.59, 22.60, 27.77, 27.95, 29.74, 30.00, 31.62, 31.90, 41.52, 115.34, 126.14, 137.57, 137.70; HRMS(EI) Found: 208.2194. Calcd for $C_{15}H_{28}$: 208.2192 [M^+].

(*E*)-1-Deuterio-2-hexyl-1-phenyl-1,4-pentadiene (2a-*d*)



IR (neat) 2956, 2926, 2857, 1494, 1467, 1443, 995, 913, 754, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, *J* = 7.0 Hz, 3H), 1.22–1.32 (m, 6H), 1.46–1.50 (m, 2H), 2.22 (t, *J* = 9.0 Hz, 2H), 2.91 (d, *J* = 7.0 Hz, 2H), 5.08–5.14 (m, 2H), 5.89 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 7.17–7.22 (m, 3H), 7.29–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.07, 22.60, 28.09, 29.38, 30.82, 31.63, 41.71, 116.24, 125.48 (t, *J* = 22.9 Hz), 125.94, 128.03, 128.56, 136.70, 138.33, 141.85; ^{2}H NMR ($CHCl_3$) δ 6.32 (br). Found: C, 89.21; H and D, 10.73%. Calcd for $C_{17}H_{23}D$: C, 89.02; H and D, 10.99%.

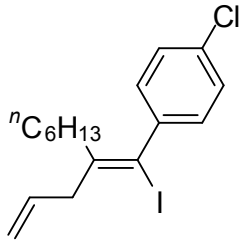
(*E*)-1-[3,5-Bis(trifluoromethyl)phenyl]-2-hexyl-4-methyl-1,4-pentadiene (5)



IR (neat) 2960, 2932, 1387, 1365, 1279, 1174, 1138, 896, 705, 683 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, *J* = 7.5 Hz, 3H), 1.22–1.32 (m, 6H), 1.46–1.55 (m, 2H), 1.74 (s, 3H), 2.15 (t, *J* = 8.0 Hz, 2H), 2.91 (s, 2H), 4.82 (s, 1H), 4.90 (s, 1H), 6.33 (s, 1H), 7.64 (s, 2H), 7.70 (s, 1H); ^{13}C NMR

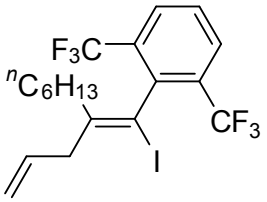
($CDCl_3$) δ = 14.15, 22.18, 22.73, 28.31, 29.45, 30.66, 31.68, 46.47, 113.49, 119.83–119.89 (m), 123.64 (q, *J* = 271.5 Hz), 124.14, 128.70, 131.53 (q, *J* = 33.0 Hz), 140.47, 143.17, 145.76; Found: C, 63.74; H, 6.47%. Calcd for $C_{20}H_{24}F_6$: C, 63.48; H, 6.39%.

(*Z*)-1-(4-Chlorophenyl)-2-hexyl-1-iodo-1,4-pentadiene (6a)



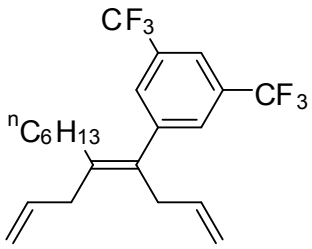
IR (neat) 2955, 2926, 2857, 1486, 1091, 1016, 914, 815 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.83 (t, *J* = 7.5 Hz, 3H), 1.09–1.13 (m, 4H), 1.18–1.23 (m, 2H), 1.29–1.34 (m, 2H), 2.02 (t, *J* = 8.0 Hz, 2H), 3.18 (dt, *J* = 6.5, 1.5 Hz, 2H), 5.13–5.16 (m, 1H), 5.18–5.22 (m, 1H), 5.84 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.01, 22.45, 28.26, 28.88, 31.36, 32.28, 45.38, 95.28, 116.65, 128.38, 129.90, 133.17, 134.09, 143.20, 146.29; HRMS (FAB) Found: 388.0459. Calcd for $C_{17}H_{22}{}^{35}ClI$: 388.0455 [M^+].

(*Z*)-1-[3,5-Bis(trifluoromethyl)phenyl]-2-hexyl-1-iodo-1,4-pentadiene (6b)



IR (neat) 2930, 1376, 1278, 1178, 1140, 917, 684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.81 (t, *J* = 7.5 Hz, 3H), 1.09 (m, 4H), 1.18–1.21 (m, 2H), 1.34–1.37 (m, 2H), 1.99 (t, *J* = 7.0 Hz, 2H), 3.22 (d, *J* = 9.5 Hz, 2H), 5.18–5.26 (m, 2H), 5.85 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 7.65 (s, 2H), 7.75 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 14.08, 22.53, 28.45, 29.00, 31.47, 32.74, 45.53, 91.97, 117.47, 121.44, 123.26 (q, *J* = 271.1 Hz), 129.07, 131.80 (q, *J* = 33.4 Hz), 133.69, 146.62, 148.90; HRMS (FAB) Found: 490.0593. Calcd for $C_{19}H_{21}F_6I$: 490.0592 [M^+].

(*E*)-4-[3,5-Bis(trifluoromethyl)phenyl]-5-hexyl-1,4,7-octatriene (7)



IR (neat) 2960, 2930, 2860, 1383, 1278, 1177, 1138, 992, 916, 897, 847, 711, 683, 684 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.82 (t, *J* = 7.0 Hz, 3H), 1.09–1.14 (m, 4H), 1.18–1.22 (m, 2H), 1.30–1.36 (m, 2H), 1.82 (t, *J* = 8.0 Hz, 2H), 2.99 (dt, *J* = 6.0, 1.5 Hz, 2H), 3.11 (d, *J* = 6.0 Hz, 2 H), 4.93–5.01 (m, 2H), 5.09–5.16 (m, 2H), 5.69 (ddt, *J* = 17.0, 10.0, 6.0 Hz, 1H), 5.85 (ddt, *J* = 17.5, 10.0, 6.0 Hz, 1H), 7.55 (s, 2 H), 7.75 (s, 1H); ^{13}C NMR ($CDCl_3$) δ = 14.08, 22.63, 28.74, 29.36, 31.66, 33.30, 35.78, 38.79, 116.04, 116.44, 120.25–120.43 (m), 123.68 (q, *J* = 271.1 Hz), 126.94, 129.35–129.37 (m), 131.44 (q, *J* = 32.9 Hz), 135.00, 135.92, 138.33, 145.70; Found: C, 65.10; H, 6.52%. Calcd for $C_{22}H_{26}F_6$: C, 65.34; H, 6.48%.

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10. J. G. Duboudin, B. Jousseaume, A. Bonakdar, *J. Organomet. Chem*. **1979**, *168*, 227.
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Chapter 2

Isomerization of Alkynes to 1,3-Dienes under Rhodium or Palladium Catalysis

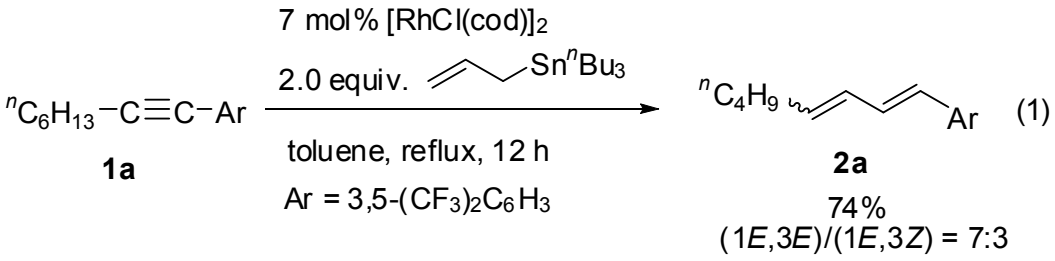
Treatment of 1-aryl-1-octynes with allyltributylstannane under rhodium catalysis provided 1-aryl-1,3-octadienes in good yields. A combination of allyl acetate and a palladium catalyst also effected the isomerization of alkynes to 1,3-dienes.

Introduction

Transition metal-catalyzed isomerization of alkenes to other alkenes is a well-known process. In contrast, efficient isomerization of alkynes to 1,3-dienes is rare under transition metal catalysis. Although the isomerization of 2-alkyn-1-one and 2-alkynoate to 1,3-alkadien-1-one and 1,3-alkadienoate proceeds smoothly,[1] there are a limited number of reports on the isomerization of simple alkynes.[2] Here the author reports a couple of new catalytic systems that realize the isomerization of simple alkynes to 1,3-dienes.

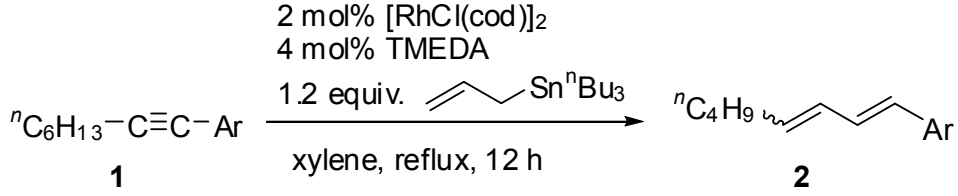
Results and Discussion

Treatment of 1-[3,5-bis(trifluoromethyl)phenyl]-1-octyne (**1a**) with allyltributylstannane (2.0 equiv.) in the presence of 7 mol% of $[RhCl(cod)]_2$ in refluxing toluene for 12 h provided 1-[3,5-bis(trifluoromethyl)phenyl]-1,3-octadiene (**2a**) in 74% yield (eq 1). The diene **2a** consisted of stereoisomers, (1*E*,3*E*)-**2a** and (1*E*,3*Z*)-**2a** in a ratio of 7:3. Interestingly, the addition of allyltributylstannane is essential for the rhodium-catalyzed isomerization. Without the allylstannane, no reaction took place. Instead of allyltributylstannane, tributylmethallylstannane similarly promoted the reaction to yield **2a** in 58% yield. The use of other allylmetal reagents such as allylmagnesium chloride, allylzinc bromide, and allyltrimethylsilane resulted in the recovery of **1a**. Organostannanes including tributylhydrostannane, tributylvinylstannane, 3-butenyltributylstannane failed to promote the isomerization.[3]



After further optimization of reaction conditions, the author could reduce the amounts of the rhodium catalyst and allyltributylstannane by using *N,N,N',N'*-tetramethylethylenediamine (TMEDA) as an additive (Table 1). Treatment of **1a** with 1.2 equiv. of allyltributylstannane, 2 mol% of $[RhCl(cod)]_2$, and 4 mol% of TMEDA in refluxing xylene for 12 h furnished **2a** in 66% yield (entry 1). Other 1-aryl-1-octynes were converted to the corresponding 1-aryl-1,3-octadienes in reasonable yields. It is worth noting that the keto groups in **1e** and **1f** survived under the reaction conditions (entries 5 and 6). The ratios of (1*E*,3*E*)-**2** and (1*E*,3*Z*)-**2** were always 8:2 to 7:3.

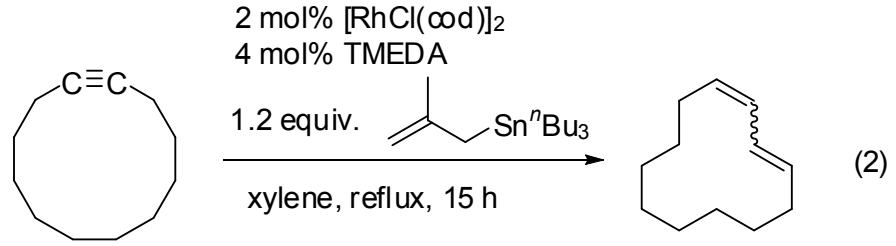
Table 1. Rhodium-catalyzed Isomerization of Alkynes to 1,3-Dienes



Entry	Ar	**1**	**2**	Yield/%[a]
1	3,5-$(CF_3)_2C_6H_3$	**1a**	**2a**	66 (79:21)
2	Ph	**1b**	**2b**	84 (69:31)
3	4-$MeOC_6H_4$	**1c**	**2c**	72 (76:24)
4	2-MeC_6H_4	**1d**	**2d**	48 (71:29)
5	3-AcC_6H_4	**1e**	**2e**	68 (73:27)
6	4-AcC_6H_4	**1f**	**2f**	49 (77:23)

[a] 1*E*,3*E*/1*E*,3*Z* ratios in parentheses

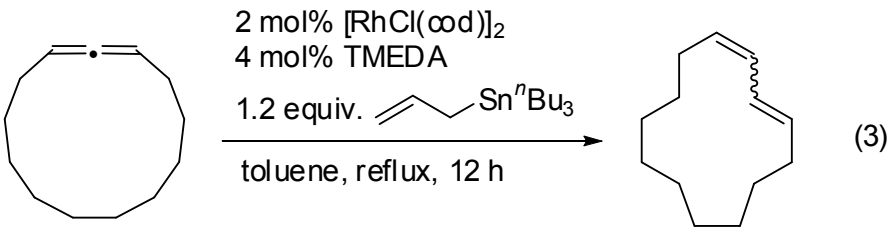
Cyclododecyne (**1g**) underwent the rhodium-catalyzed isomerization to yield 1,3-dodecadiene (**2g**) with the aid of tributylmethallylstannane (eq 2). Similar treatment of cyclic allene **1h** provided 1,3-tridecadiene (**2h**) (eq 3). Both of the products mainly comprised of the (*E*,*Z*) isomers, and no (*E*,*E*) isomers were detected. Unfortunately, the isomerization of an internal linear alkyne, 6-dodecyne, led to the formation of a mixture of conjugated dodecadienes. The reaction of 1-dodecyne provided a complex mixture containing no vinylic ^{1}H NMR signals.



1g

2g 63%
(*E*,*Z*)/(*Z*,*Z*) = 94:6

(2)



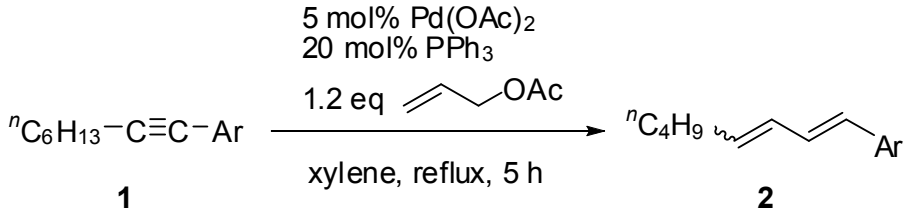
1h

2h 57%
(*E*,*Z*)/(*Z*,*Z*) = 88:12

(3)

An alternative system for the isomerization utilizes a combination of a palladium catalyst and allyl acetate. Heating a mixture of **1b**, 1.2 equiv. of allyl acetate, 5 mol% of $Pd(OAc)_2$, and 20 mol% of PPh_3 in xylene for 5 h afforded **2b** in 87% yield (Table 2, entry 1). Allyl acetate proved to enhance the efficiency of the reaction (entry 2). The exact role of allyl acetate is not clear at this stage. The author is tempted to assume that an allylpalladium complex can be the actual catalyst. The palladium-catalyzed conditions usually provided the better yields of **2** than the rhodium-catalyzed reactions.

Table 2. Palladium-catalyzed Isomerization of Alkynes to 1,3-Dienes



1 **2**

Entry	Ar	**1**	**2**	Yield/%[a]
1	Ph	**1b**	**2b**	87 (83:17)
2[b]	Ph	**1b**	**2b**	60 (83:17)
3	3,5-$(CF_3)_2C_6H_3$	**1a**	**2a**	97 (85:15)
4	4-$MeOC_6H_4$	**1c**	**2c**	53 (80:20)
5	2-MeC_6H_4	**1d**	**2d**	68 (84:16)
6	4-AcC_6H_4	**1f**	**2f**	90 (83:17)

[a] 1*E*,3*E*/1*E*,3*Z* ratios in parentheses. [b] Performed in the absence of allyl acetate.

Conclusion

The author has devised rhodium- and palladium-catalyzed isomerization reactions of alkynes to 1,3-dienes. The rhodium and palladium catalysts require allyltributylstannane and allyl acetate, respectively, to attain satisfactory results.

Experimental Section

Materials. The starting materials **1a**, **1b**, **1c**, **1d**, **1e**, and **1f** were prepared by the conventional Sonogashira coupling reaction. Cyclododecyne (**1g**) was prepared by bromination of commercially available cyclododecene and the following dehydrohalogenation. 1,2-Cyclotridecadiene (**1h**) was prepared according to the literature.[4]

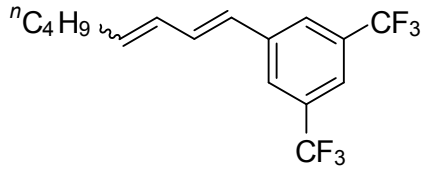
General Procedure for Rhodium-Catalyzed Isomerization of Alkynes. $[RhCl(cod)]_2$ (4.9 mg, 0.01 mmol) was placed in a 20-mL reaction flask under argon. TMEDA (2.3 mg, 0.02 mmol, dissolved in 2 mL of xylene), alkyne **1b** (93 mg, 0.50 mmol, dissolved in 2 mL of xylene), and allyltributylstannane (199 mg, 0.6 mmol, dissolved in 2 mL of xylene) were sequentially added at ambient temperature. After being stirred for 12 h at 140 ˚C, the reaction mixture was cooled to ambient temperature, and hydrochloric acid (6 M, 5 mL) was added. After being stirred for additional 1 h, the mixture was extracted with hexane (2 × 10 mL). The combined organic phase was dried over sodium sulfate. Evaporation followed by silica gel column purification afforded 1,3-diene **2b** (78.2 mg, 0.42 mmol, 84%).

General Procedure for Palladium-Catalyzed Isomerization of Alkynes. $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and PPh_3 (26 mg, 0.10 mmol) were placed in a 20-mL reaction flask under argon. Allyl acetate (60 mg, 0.60 mmol, dissolved in 2 mL of xylene) and alkyne **1a** (161 mg, 0.50 mmol) were sequentially added at ambient temperature. After being stirred for 5 h at 140 ˚C, the reaction mixture was filtrated. Evaporation followed by silica gel column purification afforded 1,3-diene **2a** (156 mg, 0.49 mmol, 97%).

Characterization Data. The spectral data of compound **1g**,[5] **1h**,[6] **2b**,[7] and **2g**[8] can be found in the literature.

(1*E*,3*E*)- and (1*E*,3*Z*)-1-[3,5-Bis(trifluoromethyl)phenyl]-1,3-octadiene

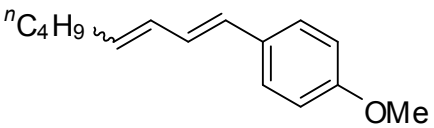
(2a, (1*E*,3*E*)/(1*E*,3*Z*) = 85:15)



IR (neat) 2962, 2932, 1645, 1468, 1381, 1279, 1134, 986, 939, 893, 846, 684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, *J* = 7.5 Hz, 3 × 0.85H), 0.96 (t, *J* = 7.5 Hz, 3 × 0.15H), 1.33–1.49 (m, 4H), 2.20 (dt, *J* = 7.5, 6.5 Hz, 2 × 0.85H), 2.35 (dt, *J* = 7.5, 6.0 Hz, 2 × 0.15 Hz), 5.70 (dt, *J* = 10.5, 7.5 Hz, 1 × 0.15H), 5.99 (dt, *J* = 15.0, 7.5 Hz, 1 × 0.85H), 6.16–6.26 (m, 1H), 6.47 (d, *J* = 16.0 Hz, 1 × 0.85H), 6.56 (d, *J* = 16.0 Hz, 1 × 0.15H), 6.89 (dd, *J* = 16.0, 10.5 Hz, 1 × 0.85H), 7.19 (ddd, *J* = 16.0, 11.0, 1.0 Hz, 1 × 0.15H), 7.68 (s, 1 × 0.85H), 7.70 (s, 1 × 0.15H), 7.77 (s, 2 × 0.85H), 7.80 (s, 2 × 0.15H); ^{13}C NMR ($CDCl_3$) (1*E*,3*E*)-isomer: δ 14.11, 22.45, 31.41, 32.81, 120.34–120.37 (m), 123.56 (q, *J* = 273 Hz), 125.86 (m), 126.76, 129.80, 132.06 (q, *J* = 33.2 Hz), 132.45, 139.65, 140.02; (1*E*,3*Z*)-isomer: δ 14.17, 22.53, 28.11, 31.91, 120.58–120.64 (m), 126.08 (m), 127.97, 128.12, 128.91, 132.12 (q, *J* = 32.7 Hz), 136.76, 139.97 (The signals for the carbons of CF_3 were not observed.); Found: C, 59.70; H, 4.94%. Calcd for $C_{16}H_{16}F_6$: C, 59.63; H, 5.00%.

Methyl *p*-[(1*E*,3*E*)-1,3-Octadienyl]phenyl Ether and

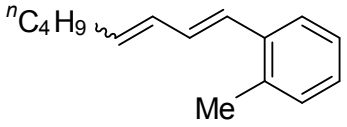
Methyl *p*-[(1*E*,3*Z*)-1,3-Octadienyl]phenyl Ether (2c, (1*E*,3*E*)/(1*E*,3*Z*) = 87:13)



IR (neat) 2926, 2360, 1604, 1511, 1253, 1178, 1031, 985 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84–0.96 (m, 3H), 1.29–1.46 (m, 4H), 2.13 (q, *J* = 7.0 Hz, 2 × 0.87H), 2.27 (q, *J* = 7.0 Hz, 2× 0.13H), 3.78 (s, 3 × 0.87H), 3.79 (s, 3 × 0.13H), 5.43–5.51 (m, 1 × 0.13H), 5.76 (pent, *J* = 7.0 Hz, 1 × 0.87H), 6.09–6.23 (m, 1H), 6.38 (d, *J* = 15.5 Hz, 1 × 0.87H), 6.46 (d, *J* = 15.5 Hz, 1 × 0.13H), 6.62 (dd, *J* = 15.5, 10.5 Hz, 1 × 0.87H), 6.78–6.88 (m, 2H), 6.93 (dd, *J* = 15.5, 11.0 Hz, 1 × 0.13H), 7.30 (d, *J* = 8.5 Hz, 2 × 0.87H), 7.34 (d, *J* = 8.5 Hz, 2 × 0.13H); ^{13}C NMR ($CDCl_3$) (1*E*,3*E*)-isomer:

δ 14.13, 22.44, 31.73, 32.71, 55.41, 114.18, 127.43, 127.68, 129.62, 130.70, 130.80, 134.93, 159.04; (1*E*,3*Z*)-isomer: δ 14.16, 22.53, 27.85, 32.10, 114.21, 122.76, 127.66, 129.01, 131.64, 132.35, 159.24 (The signals for the carbon of MeO and one of sp^2 carbons were not observed.); HRMS (EI) Found: 159.0809. Calcd for $C_{11}H_{11}O$: 159.0810 [M^+]; m.p. 29–34 ˚C.

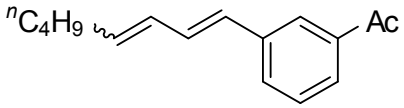
(1*E*,3*E*)- and (1*E*,3*Z*)-1-(2-methylphenyl)-1,3-octadiene (2d, (1*E*,3*E*)/(1*E*,3*Z*) = 82:18)



IR (neat) 2957, 2927, 2360, 1460, 987, 746 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.917 (t, *J* = 7.0 Hz, 3 × 0.82H), 0.924 (t, *J* = 7.0 Hz, 3 × 0.18H), 1.31–1.46 (m, 4H), 2.15 (q, *J* = 7.0 Hz, 2 × 0.82H), 2.25–2.32 (m, 2 × 0.18H), 2.34 (s, 3 × 0.82H), 2.35 (s, 3 × 0.18H), 5.50–5.57 (m, 1 × 0.18H), 5.83 (pent, *J* = 7.0 Hz, 1 × 0.82H), 6.16–6.30 (m, 1H), 6.61–6.77 (m, 1 + 1 × 0.82H), 6.97 (dd, *J* = 15.5, 11.0, 1 × 0.18H), 7.07–7.21 (m, 3H), 7.47 (d, *J* = 7.5 Hz, 1 × 0.82H), 7.51 (d, *J* = 7.5 Hz, 1 × 0.18H); ^{13}C NMR ($CDCl_3$) (1*E*,3*E*)-isomer: δ 14.15, 20.03, 22.48, 31.66, 32.73, 125.09, 126.22, 127.17, 127.72, 130.50, 130.78, 131.01, 135.49, 136.03, 136.71; (1*E*,3*Z*)-isomer: δ 22.54, 27.90, 32.07, 125.35, 125.86, 126.25, 127.42, 129.18, 129.75, 130.55, 133.41, 135.67, 136.77 (The signals for two of sp^3 carbons were not observed.); Found: C, 89.88; H, 10.08%. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06%.

1-{*m*-[(1*E*,3*E*)-1,3-Octadienyl]phenyl}ethanone and

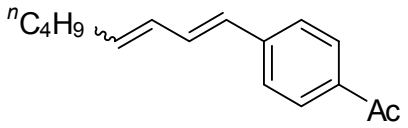
1-{*m*-[(1*E*,3*Z*)-1,3-Octadienyl]phenyl}ethanone (2e, (1*E*,3*E*)/(1*E*,3*Z*) = 89:11)



IR (neat) 2958, 2928, 1688, 1358, 1268, 988, 688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89–0.98 (m, 3H), 1.30–1.48 (m, 4H), 2.16 (q, *J* = 7.0 Hz, 2 × 0.89H), 2.31 (q, *J* = 7.0 Hz, 2 × 0.11 Hz), 2.61 (s, 3 × 0.89 H), 2.62 (s, 3 × 0.11H), 5.55–5.62 (m, 1 × 0.11 H), 5.89 (pent, *J* = 7.0 Hz, 1 × 0.89 H), 6.13–6.26 (m, 1H), 6.47 (d, *J* = 15.5 Hz, 1 × 0.89 H), 6.55 (d, *J* = 15.5 Hz, 1 × 0.11H), 6.83 (dd, *J* = 15.5, 10.5 Hz, 1 × 0.89 H), 7.09–7.17 (m, 1 × 0.11H), 7.34–7.44 (m, 1H), 7.56 (d, *J* = 7.5 Hz, 1 × 0.89 H), 7.60 (d, *J* = 8.0 Hz, 1 × 0.11H), 7.74–7.81 (m, 1H), 7.95 (s, 1 × 0.89 H), 7.98 (s, 1 × 0.11H); ^{13}C NMR ($CDCl_3$) (1*E*,3*E*)-isomer: δ 14.11, 22.44, 26.88, 31.56, 32.74, 125.95, 127.04, 128.88, 128.95, 130.32, 130.65, 131.00, 137.38, 137.61, 138.42, 198.36; Found: C, 84.35; H, 8.91%. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83%.

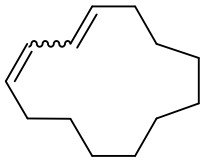
1-{*p*-[(1*E*,3*E*)-1,3-Octadienyl]phenyl}ethanone and

1-{*p*-[(1*E*,3*Z*)-1,3-Octadienyl]phenyl}ethanone (2f, (1*E*,3*E*)/(1*E*,3*Z*) = 83:17)



IR (neat) 2958, 2928, 1683, 1599, 1358, 1268, 1180, 989, 592 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90–0.96 (m, 3H), 1.31–1.47 (m, 4H), 2.17 (q, *J* = 7.5 Hz, 2 × 0.83H), 2.31 (dq, *J* = 8.0, 1.5 Hz, 2 × 0.17H), 2.575 (s, 3 × 0.83H), 2.583 (s, 3 × 0.17H), 5.60–5.67 (m, 1 × 0.17 H), 5.92 (pent, *J* = 7.5 Hz, 1 × 0.83 H), 6.14–6.27 (m, 1H), 6.45 (d, *J* = 15.5 Hz, 1 × 0.83H), 6.54 (d, *J* = 15.5 Hz, 1 × 0.17H), 6.86 (dd, *J* = 15.5, 10.5 Hz, 1 × 0.83H), 7.18 (ddd, *J* = 15.5, 11.0, 1.0 Hz, 1 × 0.17H), 7.43 (d, *J* = 8.0 Hz, 2 × 0.83H), 7.47 (d, *J* = 8.0 Hz, 2 × 0.17 H), 7.86–7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) (1*E*,3*E*)-isomer: δ 14.09, 22.42, 26.69, 31.48, 32.78, 126.20, 128.84, 128.94, 130.38, 132.46, 135.62, 138.41, 142.64, 197.60; Found: C, 83.97; H, 8.92%. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83%.

(*E*,*Z*)- and (*Z*,*Z*)-1,3-Cyclotridecadiene (2h, (*E*,*Z*)/(*Z*,*Z*)=88:12)



IR (neat) 2926, 2855, 1458, 1444, 982, 950, 728 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11–1.48 (m, 14H), 2.12–2.22 (m, 4H), 5.28 (dt, *J* = 8.5, 11.0 Hz, 1 × 0.88H), 5.31–5.36 (m, 2 × 0.12H), 5.57 (dt, *J* = 8.0, 15.5 Hz, 1 × 0.88H), 6.11 (m, 1 × 0.88H), 6.22 (d, *J* = 9.5 Hz, 2 × 0.12H), 6.34–6.40 (m, 1 × 0.88H); ^{13}C NMR ($CDCl_3$) (*E*,*Z*)-isomer: δ 25.24, 25.50, 26.23, 26.28, 27.22, 27.63, 27.71, 28.17, 33.09, 128.09, 129.84, 130.37, 132.88; (*Z*,*Z*)-isomer: 24.53, 25.55, 26.11, 26.55, 28.28, 125.65, 132.94; Found: C, 87.35; H, 12.19%. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44%.

References and Notes

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Chapter 3

Silylcupration and Copper-Catalyzed Carbomagnesiation of Ynamides: Application to Aza-Claisen Rearrangement

Treatment of ynamides with silylcopper reagents resulted in silylcupration to afford (*E*)-β-silylenamides, after protonolysis, in good yields with high regio- and stereoselectivity. Reaction of ynamides having an allyl group on the nitrogen with Grignard reagents in the presence of a copper catalyst resulted in carbomagnesiation across the alkynyl parts and the subsequent heating provided 4-pentenenitriles via aza-Claisen rearrangement.

Introduction

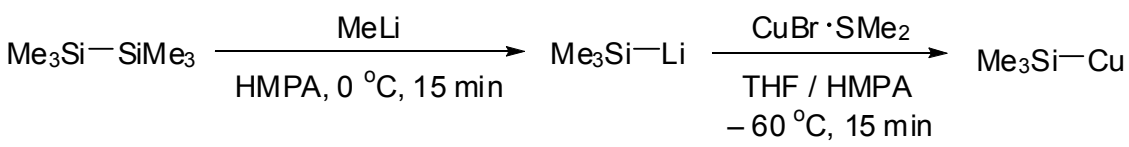
Ynamides are ynamines having sufficient stability to prepare and handle, due to the electron-withdrawing group on the nitrogen. Since direct and convenient synthesis of ynamides was accomplished, organic reactions of ynamides have been studied actively.[1] Among them, addition reactions of organometallic reagents to ynamides have been well investigated.[2] The author reports here highly regio- and stereoselective silylcupration of ynamides. He also describe copper-catalyzed carbomagnesiation reactions of ynamides having an allyl group followed by aza-Claisen rearrangement.[3]

Results and Discussion

(1) Silylcupration of Ynamides

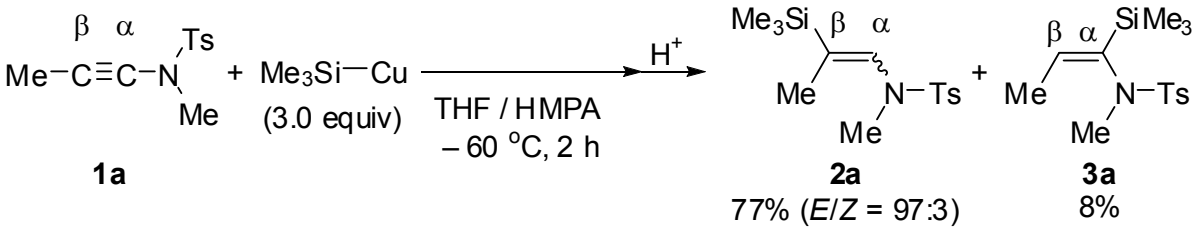
Vinylsilanes play an important role as synthetic building blocks because they react with various electrophiles in the presence or absence of Lewis-acid and they are used widely for palladium-catalyzed cross-coupling reactions.[4] Silylmetalation of alkynes is one of the most general methods for synthesis of multi-substituted vinylsilanes.[5] The author reports herein silylcupration of ynamides with high regio- and stereoselectivity.[6]

Treatment of hexamethyldisilane with methyllithium in hexamethylphosphoric triamide (HMPA) at 0 ˚C for 15 min generated trimethylsilyllithium (Me_3SiLi). Reaction of Me_3SiLi with $CuBr{\bullet}SMe_2$ in a mixed solvent of THF and HMPA at –60 ˚C for 15 min afforded trimethylsilylcopper (Me_3SiCu) (Scheme 1).



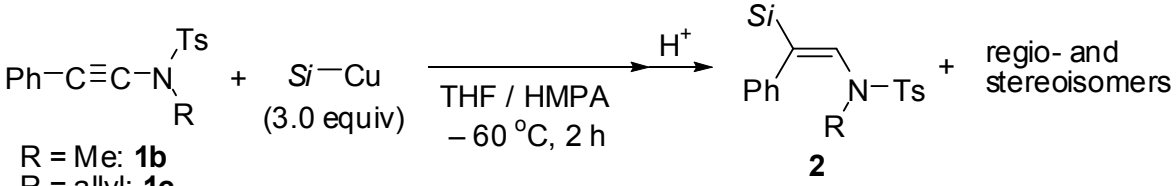
Scheme 1.

Reaction of *N*-1-propynylamide **1a** with Me_3SiCu furnished the corresponding products **2a** and **3a** in 77% and 8% yields, respectively (Scheme 2). It was revealed that the silyl group was mainly attached to the β carbon of the ynamide. The directing effect of the sulfonyl group of ynamides would play an important role in determining the regiochemistry of the silylcupration.[7]



Scheme 2.

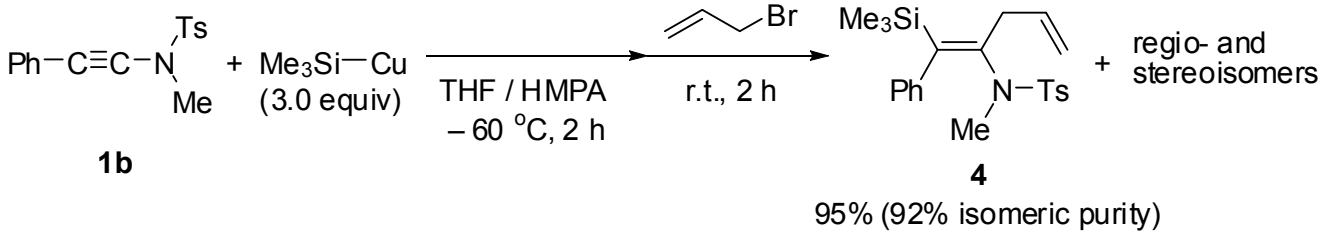
Reaction of *N*-phenylethynylamides **1b** with Me_3SiCu provided the desired product **2b** with high regio- and stereoselectivity (Scheme 3). Ynamide **1c** having an allyl group underwent to furnish the silylated product **2c** without difficulty. Silylcupration of **1b** with dimethylphenylsilylcopper ($PhMe_2SiCu$) also proceeded smoothly to afford **2d**.



Si = $SiMe_3$, R = Me: **2b** 89% (92% isomeric purity)
Si = $SiMe_3$, R = allyl: **2c** 75% (96% isomeric purity)
Si = $SiPhMe_2$, R = Me: **2d** 81% (93% isomeric purity)

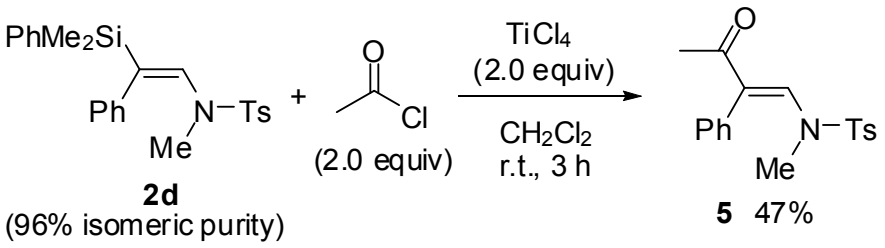
Scheme 3.

The vinylcopper generated by the silylcupration reacted with allyl bromide to provide the corresponding product **4** in a high yield (Scheme 4).



Scheme 4.

Then, Lewis-acid-catalyzed reaction of (*E*)-β-silylenamide with an electrophile was examined. Treatment of (*E*)-β-silylenamide **2d** with acetyl chloride in the presence of titanium tetrachloride ($TiCl_4$) in CH_2Cl_2 at room temperature afforded the corresponding product **5** in 47% NMR yield with regio- and stereoselectivity (Scheme 5).

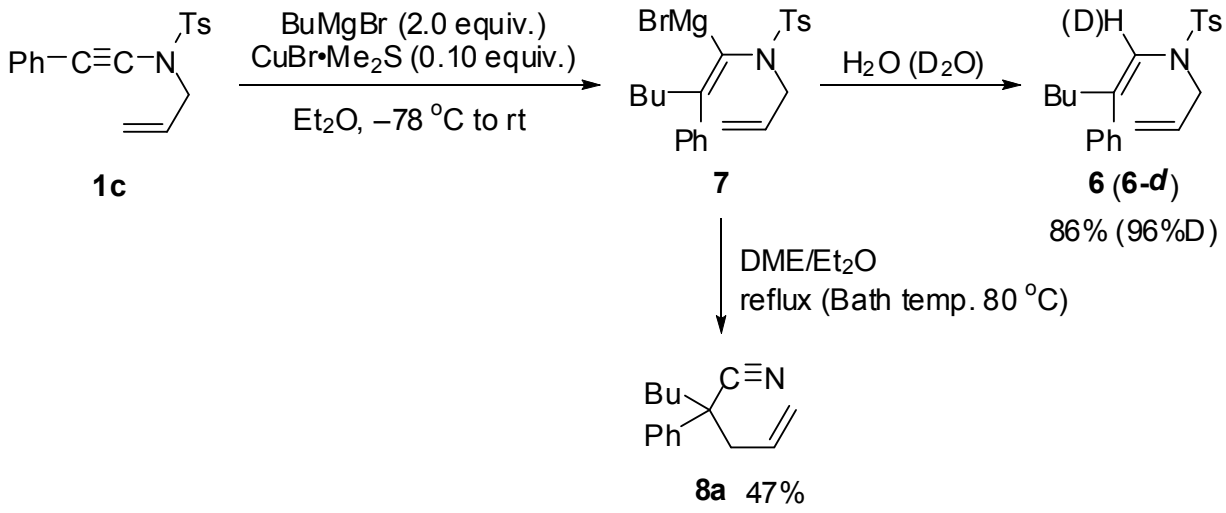


Scheme 5.

(2) Carbomagnesiation Reactions of Ynamides Followed by Aza-Claisen Rearrangement

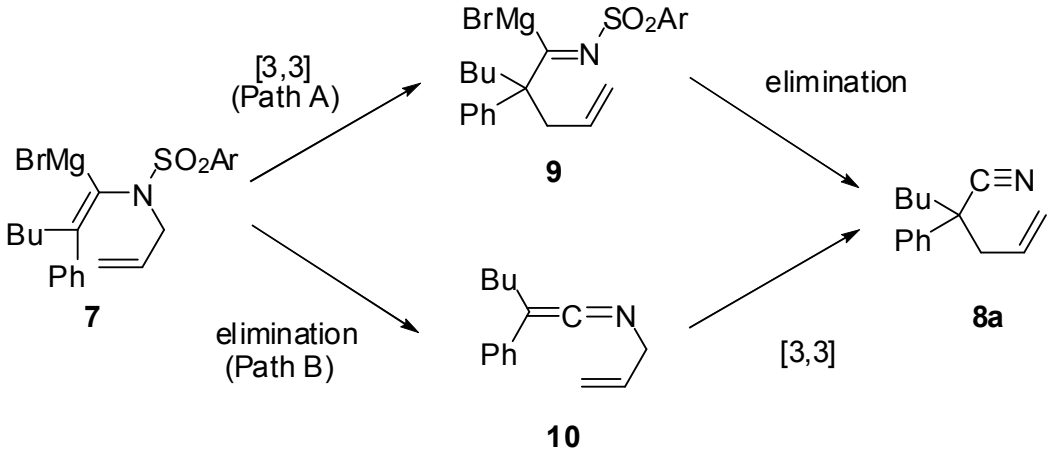
The [3,3] sigmatropic rearrangement of 3-aza-1,5-hexadienes is called aza-Claisen rearrangement and play an important role in organic synthesis.[8] The author describes herein carbomagnesiation reactions of *N*-allyl-*N*-(phenylethynyl)arenesulfonamides and the subsequent aza-Claisen rearrangement. The transformation offers a new repertoire to the synthesis of 4-pentenenitriles.

The initial carbomagnesiation proceeded smoothly by using Grignard reagents and a copper catalyst.[9] Treatment of *N*-allyl-*N*-phenylethynyl-*p*-toluenesulfonamide (**1c**) with 2.0 equimolar amounts of butylmagnesium bromide in the presence of CuBr•Me_2S (10 mol%) in diethyl ether at ambient temperature afforded **6** in 86% yield after hydrolysis.[10] Quenching the reaction with deuterium oxide provided the corresponding deuterium-labeled product **6-*d*** (96%D). Hence, it is suggested that the intermediate **7** was formed in the reaction flask. When organomagnesium **7** was heated in a mixed solvent of 1,2-dimethoxyethane (DME) and diethyl ether, pentenenitrile **8a** was obtained in 47% yield, along with 34% of **6** (Scheme 6).

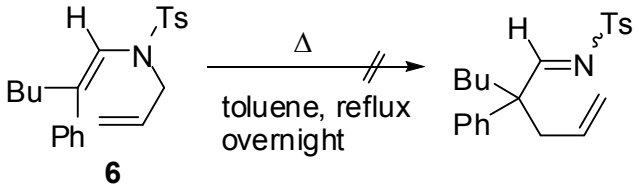


Scheme 6.

There are two possible mechanisms of the formation of nitrile **8a** (Scheme 7). The [3,3] sigmatropic rearrangement of the organomagnesium **7** and the subsequent elimination of magnesium sulfinate from **9** would afford **8a** (Path A). The other mechanism (Path B) is as follows. First, the elimination of magnesium sulfinate from organomagnesium **7** would take place to give ketene imine intermediate **10**. Then, [3,3] sigmatropic rearrangement of **10** would proceed to furnish nitrile **8a**. The [3,3] sigmatropic rearrangement of 3-aza-1,2,5-hexatrienes has been known to proceed smoothly.[11] It is worth noting that heating **6** in boiling toluene resulted in complete recovery of **6** (Scheme 8).



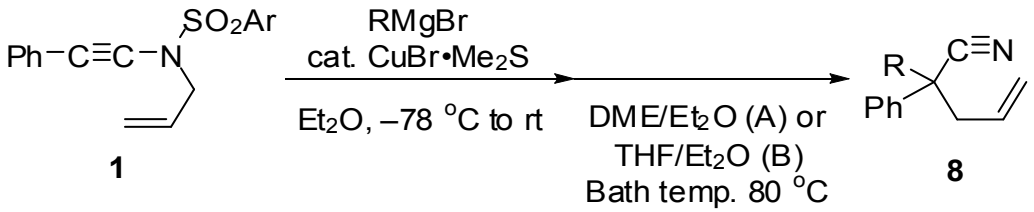
Scheme 7.



Scheme 8.

Table 1 summarizes the synthesis of 4-pentenenitriles starting from Grignard reagents and ynamides having an allyl group on the nitrogen. Primary alkyl Grignard reagents including a bulky neopentylmagnesium reagent participated in the reaction. When aryl and secondary alkyl Grignard reagents were used, the yields of desired products were much lower (Entries 4 and 7). Ynamides **1d**, having a *p*-fluorophenylsulfonyl group on the nitrogen, provided the corresponding pentenenitriles in better yields (Entries 5 and 6).

Table 1. Carbomagnesiation of ynamides followed by aza-Claisen rearrangement



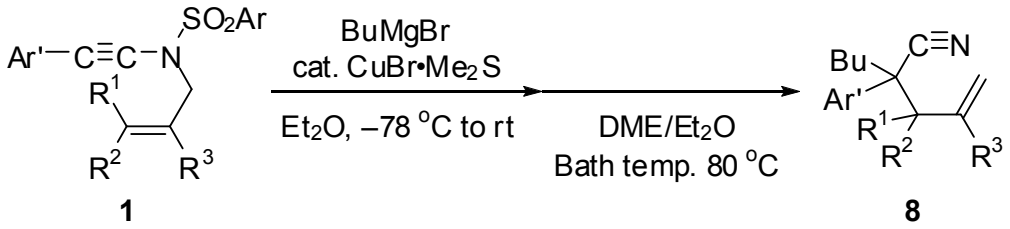
1 **8**

Entry	**1**	Ar	RMgBr	Solvent	Time[a]/h	**8**	Yield[b]/%
1	**1c**	*p*-tolyl	BuMgBr	A	5	**8a**	47
2	**1c**	*p*-tolyl	EtMgBr	B	4	**8b**	47
3	**1c**	*p*-tolyl	^{t}BuCH$_2$MgBr	B	18	**8c**	46
4	**1c**	*p*-tolyl	PhMgBr	B	4	**8d**	27
5	**1d**	*p*-FC$_6$H$_4$	BuMgBr	A	4	**8a**	61
6	**1d**	*p*-FC$_6$H$_4$	EtMgBr	B	4	**8b**	50
7	**1d**	*p*-FC$_6$H$_4$	^{i}PrMgBr	B	19	**8e**	23

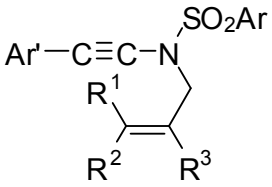
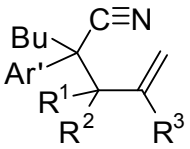
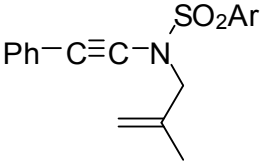
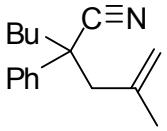
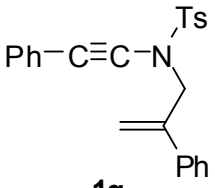
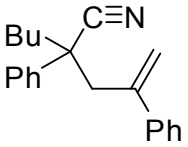
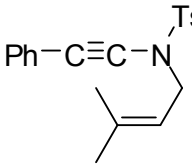
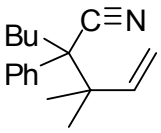
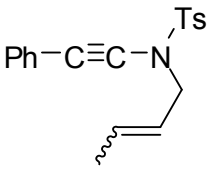
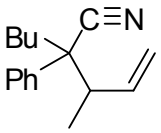
[a]Time for the rearrangement. [b]Isolated yield.

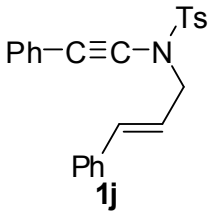
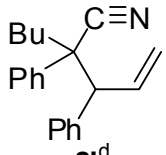
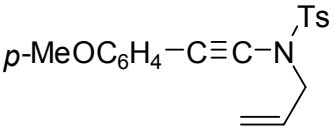
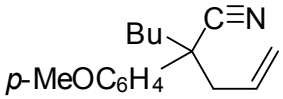
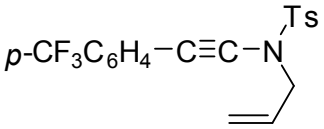
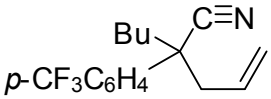
Scope of substrates was investigated (Table 2). *N*-Methallylamides (**1e** and **1f**) and *N*-(2-phenyl-2-propenyl)amide **1g** participated in the reaction (Entries 1−3). Due to the inherent regiospecificity of the aza-Claisen rearrangement, 2,2,3,3-tetrasubstituted 4-pentenenitrile **8h** was obtained in the reaction of *N*-prenylamide **1h** (Entry 4). It is difficult to synthesize such a sterically congested nitrile by the conventional methods. The reactions of *N*-crotyl- and *N*-cinnamylamides (**1i** and **1j**) afforded mixtures of diastereomers (Entries 5 and 6). The reactions of **1k** and **1l** with butylmagnesium bromide gave the corresponding nitriles **8k** and **8l** in lower yields of 33% and 34% yields, respectively (Entries 7 and 8). The phenyl group at the acetylenic terminus proved to be indispensable for the success of the reaction. A similar reaction of *N*-allyl-*N*-1-octynyl-*p*-toluenesulfonamide resulted in formation of a complex mixture containing 6% of the anticipated nitrile and 31% of *N*-allyl-*p*-toluenesulfonamide. Unfortunately, silylcupration of ynamide **1c** followed by heating gave no desired aza-Claisen rearrangement product.

Table 2. Scope and limitation of carbomagnesiation followed by aza-Claisen rearrangement.



1 **8**

Entry	 **1**	 **8**	Yield[a]/%
1	 **1e** (Ar = *p*-tolyl) **1f** (Ar = *p*-FC_6H_4)	 **8f**	48 (from **1e**) 58 (from **1f**)
2			
3	 **1g**	 **8g**	37
4	 **1h**	 **8h**	61
5	 **1i**[b]	 **8i**[c]	57

6	 **1j**	 **8j**[d]	49
7	 **1k**	 **8k**	33
8	 **1l**	 **8l**	34

[a]Isolated yield. [b]E/Z = 4:1. [c]Diastereomer ratio = 1.4:1. [d]Diastereomer ratio = 1.6:1

Experimental Section

Material. Ynamides **1** were prepared by copper-catalyzed alkynylation of amides.[12] Trimethylsilyllithium and dimethylphenylsilyllithium were prepared by the conventional methods.[13]

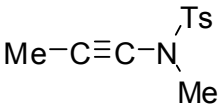
Typical Procedure for Silylcupration of Ynamides. A solution of methyllithium (1.1 mL, 1.1 mol/L diethyl ether solution, 1.2 mmol) was added to hexamethyldisilane (0.37 mL, 1.8 mmol) in freshly distilled hexamethylphosphoric triamide (1.2 mL) at 0 ˚C under argon. The mixture was stirred at 0 ˚C for 15 min. After THF (3 mL) was added, the reaction mixture was cooled to –60 ˚C. CuBr•SMe_2 (247 mg, 1.8 mmol) was added and the resulting mixture was stirred at –60 ˚C for 15 min. A solution of ynamide **1b** (114 mg, 0.4 mmol) in THF (3 mL) was added. After stirring at –60 ˚C for 2 h, allyl bromide (0.17 mL, 2.0 mmol) was added and the reaction mixture was warmed to room temperature. A saturated aqueous solution of ammonium chloride (2 mL) was added. The organic compounds were extracted with a mixture of ethyl acetate and hexane twice. The combined organic part was dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatographic purification on silica gel afforded **2b** (151 mg, 0.38 mmol, 92% isomeric purity) in 95% yield.

Typical Procedure for Carbomagnesiation Reaction of Ynamides Followed by Aza-Claisen Rearrangement. CuBr•SMe_2 (6 mg, 0.03 mmol) and *N*-allyl-*N*-phenylethynyl-*p*-fluorobenzenesulfonamide (**1d**, 95 mg, 0.30 mmol) were placed in a 20-mL reaction flask under argon. Diethyl ether (3 mL) was added. A solution of butylmagnesium bromide (0.53 mL, 1.13 mol/L diethyl ether solution, 0.60 mmol) was added at –78 ˚C. The mixture was stirred at room temperature for 1 h. DME (5 mL) was added, and the reaction mixture was refluxed for 4 h (bath temp, 80 ˚C). A saturated aqueous solution of ammonium chloride (2 mL) was added. The organic compounds were extracted with a mixture of ethyl acetate and hexane twice. The combined organic part was dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatographic purification on silica gel afforded **8a** (39 mg,

0.18 mmol) in 61% yield.

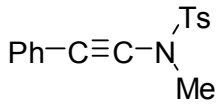
Characterization Data. The ^{1}H and ^{13}C NMR spectral data of compounds **1c**[12] and **8d**[14] can be found in the literature.

***N*-Methyl-*N*-1-propynyl-*p*-toluenesulfonamide (1a)**



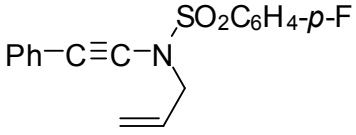
IR (nujol) 2924, 2855, 2265, 1456, 1355, 1168, 1158, 1042, 816, 677, 566, 545 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.88 (s, 3H), 2.46 (s, 3H), 3.01 (s, 3H), 7.34–7.39 (m, 2H), 7.76–7.81 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 3.39, 21.83, 39.43, 64.26, 73.90, 127.97, 129.87, 133.49, 144.64; Found: C, 59.16; H, 5.82%. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87%; m.p. 99–100 ˚C.

***N*-Methyl-*N*-phenylethynyl-*p*-toluenesulfonamide (1b)**



IR (nujol) 2924, 2233, 1595, 1365, 1164, 764, 676, 546 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 3H), 3.15 (s, 3H), 7.27–7.31 (m, 3H), 7.34–7.38 (m, 4H), 7.83–7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.85, 39.49, 69.19, 84.11, 122.87, 128.02, 128.04, 128.44, 129.98, 131.57, 133.40, 144.97; Found: C, 67.07; H, 5.25%. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30%; m.p. 85–86 ˚C.

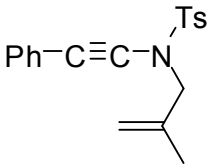
***N*-Phenylethynyl-*N*-2-propenyl-*p*-fluorobenzenesulfonamide (1d)**



IR (nujol) 2925, 2855, 2235, 1492, 1367, 1181, 545 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.08 (dt, J = 6.5, 1.0 Hz, 2H), 5.24–5.33 (m, 2H), 5.79 (ddt, J = 16.5, 10.0, 6.5 Hz, 1H), 7.23–7.30 (m, 5H), 7.34–7.36 (m, 2H), 7.97–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 54.67, 71.30, 81.99, 116.66 (d, J = 22.4 Hz), 120.51, 122.68, 128.19, 128.48, 130.74, 130.82, 131.61, 133.85, 165.93 (d, J = 254.8 Hz). Found: C, 64.97; H, 4.70%. Calcd for $C_{17}H_{14}NO_2FS$: C, 64.75; H, 4.47%; m.p.

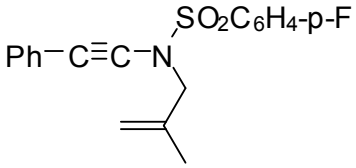
77.7–79.6 ˚C.

***N*-(2-Methyl-2-propenyl)-*N*-phenylethynyl-*p*-toluenesulfonamide (1e)**



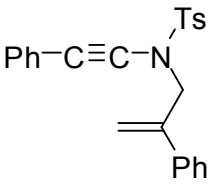
IR (neat) 2976, 2920, 2235, 1597, 1366, 1169, 756, 691, 589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (s, 3H), 2.43 (s, 3H), 3.94 (s, 2H), 4.97 (s, 2H), 7.25–7.27 (m, 3H), 7.32–7.35 (m, 4H), 7.84 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 19.82, 21.74, 58.05, 70.85, 82.43, 115.98, 122.95, 127.79, 127.81, 128.32, 129.86, 131.32 134.60, 138.80, 144.81. Found: C, 69.96; H, 6.07%. Calcd for $C_{19}H_{19}NO_2S$: C, 70.13; H, 5.88%.

***N*-(2-Methyl-2-propenyl)-*N*-phenylethynyl-*p*-fluorobenzenesulfonamide (1f)**



IR (neat) 3081, 2237, 1592, 1495, 1368, 1175, 1156, 837, 756, 589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.76 (s, 3H), 3.98 (s, 2H), 4.98 (s, 1H), 4.99 (s, 1H), 7.23–7.34 (m, 7H), 7.97–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 19.91, 58.26, 71.13, 82.05, 116.28, 116.63 (d, *J* = 22.5 Hz), 122.76, 128.10, 128.46, 128.60, 130.71 (d, *J* = 9.6 Hz), 131.53, 138.68, 165.89 (d, *J* = 255.3 Hz); HRMS (FAB) Found: 330.0958. Calcd for $C_{18}H_{17}NO_2FS$: 330.0964 [MH^+].

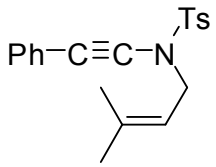
***N*-Phenylethynyl-*N*-(2-phenyl-2-propenyl)-*p*-toluenesulfonamide (1g)**



IR (nujol) 2924, 2854, 2248, 1362, 1174, 915, 758, 608, 550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 4.43 (s, 2H), 5.33 (s, 1H), 5.53 (s, 1H), 7.24–7.33 (m, 10H), 7.40–7.41 (m, 2H), 7.78 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.81, 55.50, 71.43, 82,29, 117.94, 122.95, 126.52, 127.84,

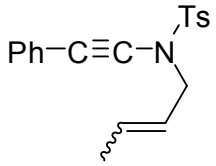
127.93, 128.23, 128.33, 128.56, 129.87, 131.40, 134.40, 138.16, 141.44, 144.83. Found: C, 74.33; H, 5.43%. Calcd for $C_{24}H_{21}NO_2S$: C, 74.39%; H, 5.46%. m.p. 100.7–101.0 ˚C

***N*-(3-Methyl-2-butenyl)-*N*-phenylethynyl-*p*-toluenesulfonamide (1h)**



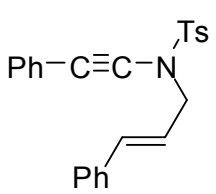
IR (neat) 2360, 2235, 1363, 1169, 1091, 754, 691, 584 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (d, J = 1.0 Hz, 3H), 1.70 (d, J = 1.0 Hz, 3H), 2.44 (s, 3H), 4.05 (d, J = 8.0 Hz, 2H), 5.20 (tsept, J = 8.0, 1.0 Hz, 1H), 7.24–7.35 (m, 7H), 7.81–7.84 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.20, 21.81, 25.91, 49.80, 70.68, 83.05, 117.21, 123.26, 127.72, 127.92, 128.39, 129.80, 131.28, 135.07, 139.45, 144.65; HRMS (EI) Found: 339.1293. Calcd for $C_{20}H_{21}NO_2S$: 339.1293 [M^+].

***N*-2-Butenyl-*N*-phenylethynyl-*p*-toluenesulfonamide (1i, a 8:2 mixture of stereoisomers)**



IR (neat) 2919, 2234, 1366, 1171, 1091, 937, 756, 582, 546 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65–1.68 (m, 3H), 2.43 (s, 3H), 3.96–3.98 (m, 2 × 0.8H), 4.11 (d, J = 6.5 Hz, 2 × 0.2H), 5.40–5.46 (m, 1H), 5.68–5.75 (m, 1H), 7.23–7.35 (m, 7H), 7.81–7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) (*E*-isomer) δ 17.80, 21.71, 54.10, 71.04, 82.73, 123.10, 123.74, 127.78, 127.89, 128.34, 129.79, 131.31, 132.28, 134.96, 144.70; HRMS (FAB) Found: 325.1138. Calcd for $C_{19}H_{19}NO_2S$: 325.1136 [M^+].

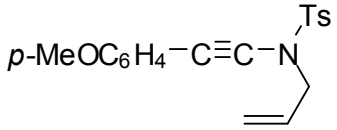
***N*-Phenylethynyl-*N*-[(*E*)-3-phenyl-2-propenyl]-*p*-toluenesulfonamide (1j)**



IR (neat) 3029, 2235, 1597, 1495, 1363, 1169, 1090, 753, 692, 586 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.38 (s, 3H), 4.21 (dd, J = 7.0, 1.5 Hz, 2H), 6.07 (dt, J = 16.0, 7.0 Hz, 1H), 6.55 (d, J = 16.0 Hz,

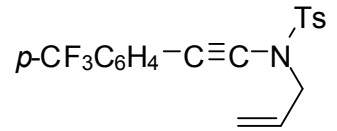
1H), 7.20–7.33 (m, 12H), 7.84–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.68, 54.34, 71.16, 82.66, 121.84, 122.86, 126.69, 127.84, 127.92, 128.20, 128.33, 128.65, 129.86, 131.37, 134.83, 135.34, 136.09, 144.85; HRMS (EI) Found: 387.1291. Calcd for $C_{24}H_{21}NO_2S$: 387.1293 [M^+].

***N*-*p*-Methoxyphenylethynyl-*N*-2-propenyl-*p*-toluenesulfonamide (1k)**



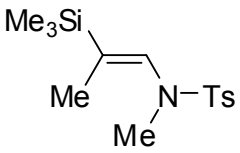
IR (neat) 2935, 2839, 2237, 1606, 1512, 1363, 1250, 1171, 664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 3H), 3.81 (s, 3H), 4.04 (dt, *J* = 6.5, 1.5 Hz, 2H), 5.20–5.24 (m, 1H), 5.24–5.32 (m, 1H), 5.79 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 6.80–6.85 (m, 2H), 7.28–7.34 (m, 2H), 7.34–7.39 (m, 2H), 7.82–7.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.76, 54.56, 55.40, 70.61, 80.94, 114.00, 114.80, 120.05, 127.90, 129.84, 131.11, 133.47, 134.80, 144.85, 159.61; HRMS (FAB) Found: 341.1082. Calcd for $C_{19}H_{19}NO_3S$: 341.1086 [M^+].

***N*-2-Propenyl-*N*-[*p*-(trifluoromethyl)phenylethynyl]-*p*-toluenesulfonamide (1l)**



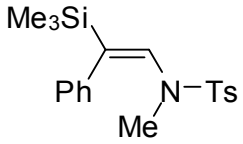
IR (neat) 2929, 2235, 1615, 1370, 1323, 1171, 1126, 1105, 1066, 842, 664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 3H), 4.08 (dt, *J* = 6.5, 1.5 Hz, 2H), 5.26–5.34 (m, 2H), 5.80 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.84–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.89, 54.53, 70.61, 85.19, 120.55, 124.21 (q, *J* = 270.7 Hz), 125.41 (q, *J* = 3.9 Hz), 127.13, 128.01, 129.47 (q, *J* = 32.5 Hz), 130.11, 130.97, 131.21, 134.91, 145.22; HRMS (FAB) Found: 380.0936. Calcd for $C_{19}H_{17}NO_2F_3S$: 380.0932 [MH^+].

***N*-Methyl-*N*-[(*E*)-2-(trimethylsilyl)-1-propenyl]-*p*-toluenesulfonamide (2a)**



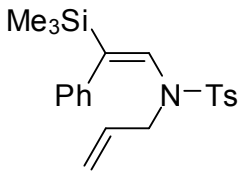
IR (neat) 2955, 1614, 1349, 1250, 1166, 839, 713 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 9H), 1.77 (s, 3H), 2.43 (s, 3H), 2.80 (s, 3H), 5.88 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ –2.04, 14.86, 21.69, 37.57, 127.31, 127.77, 129.56, 129.66, 132.41, 143.64; Found: C, 56.69, 7.80%. Calcd for $C_{14}H_{23}NO_2SiS$: C, 56.52; H, 7.79%.

_N_-Methyl-_N_-[(_E_)-2-phenyl-2-(trimethylsilyl)ethenyl]-_p_-toluenesulfonamide (2b)



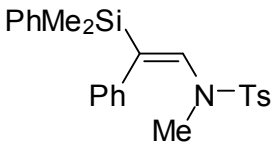
IR (neat) 2955, 1607, 1353, 1248, 1169, 838, 758, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (s, 9H), 2.42 (s, 3H), 2.47 (s, 3H), 6.69–6.71 (m, 2H), 6.73 (s, 1H), 7.09–7.16 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ –1.20, 21.77, 35.76, 125.96, 126.67, 127.23, 127.97, 128.52, 129.90, 131.48, 135.24, 140.00, 143.87; Found: C, 63.37; H, 6.93%. Calcd for $C_{19}H_{25}NO_2SiS$: C, 63.47; H, 7.01%.

_N_-[(_E_)-2-Phenyl-2-(trimethylsilyl)ethenyl]-_N_-2-propenyl-_p_-toluenesulfonamide (2c)



IR (neat) 2956, 1605, 1353, 1249, 1167, 1092, 837, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06 (s, 9H), 2.46 (s, 3H), 3.53–3.55 (m, 2H), 4.77–4.81 (m, 1H), 4.91–4.93 (m, 1H), 5.29 (ddt, *J* = 17.0, 10.5, 6.0 Hz, 1H), 6.54 (s, 1H), 6.71–6.73 (m, 2H), 7.12–7.18 (m, 3H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ –1.20, 21.73, 49.58, 117.29, 126.21, 127.32, 127.93, 128.23, 129.54, 129.80, 131.30, 132.80, 136.71, 139.73, 143.76; Found: C, 65.50; H, 7.00%. Calcd for $C_{21}H_{27}NO_2SiS$: C, 65.41; H, 7.06%.

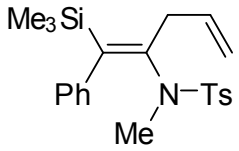
_N_-[(_E_)-2-Dimethylphenylsilyl-2-phenylethenyl]-_N_-methyl-_p_-toluenesulfonamide (2d)



IR (neat) 2957, 1594, 1354, 1248, 1168, 936, 810, 754, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.32 (s,

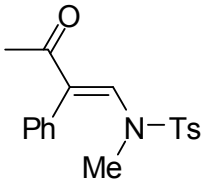
6H), 2.43 (s, 3H), 2.47 (s, 3H), 6.67–6.69 (m, 2H), 6.75 (s, 1H), 7.10–7.12 (m, 3H), 7.34 (d, J = 8.0 Hz, 2H), 7.38–7.44 (m, 3H), 7.51–7.52 (m, 2H), 7.59 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ –2.82, 21.69, 35.67, 124.36, 126.01, 127.14, 127.86, 127.89, 128.65, 129.32, 129.83, 133.34, 134.22, 134.99, 137.59, 139.49, 143.84; Found: C, 67.97; H, 6.49%. Calcd for $C_{24}H_{27}NO_2SiS$: C, 68.37; H, 6.45%.

***N*-Methyl-*N*-[(*E*)-1-phenyl(trimethylsilyl)methylene-3-butenyl]-*p*-toluenesulfonamide (4)**



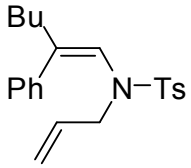
IR (neat) 2954, 1600, 1344, 1251, 1151, 840, 718, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 9H), 2.39 (s, 3H), 2.57 (s, 3H), 3.38 (d, J = 6.5 Hz, 2H), 4.93–4.96 (m, 1H), 4.99–5.02 (m, 1H), 5.76 (ddt, J = 17.0, 10.5, 6.5 Hz, 1H), 7.01 (br, 2H), 7.18–7.19 (m, 3H), 7.24–7.28 (m, 2H), 7.47 (d, J =8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.43, 21.51, 38.77, 40.35, 117.60, 125.68, 127.51, 127.90 (br, 2C), 129.36, 135.09, 137.45, 141.90, 142.92, 143.98, 146.09; Found: C, 65.85; H, 7.37%. Calcd for $C_{22}H_{29}NO_2SiS$: C, 66.12; H, 7.31%.

***N*-Methyl-*N*-[(*E*)-3-oxo-2-phenyl-1-butenyl]-*p*-toluenesulfonamide (5)**



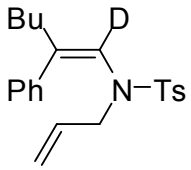
IR (nujol) 2924, 2854, 1657, 1613, 1357, 1347, 1292, 1169, 1155, 971, 754, 724, 702, 664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 3H), 2.46 (s, 6H), 7.00–7.02 (m, 2H), 7.27–7.29 (m, 3H), 7.37 (d, J = 8.0 Hz, 2H), 7.71—7.73 (m, 2H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.83, 28.00, 35.14, 123.49, 127.43, 128.12, 128.34, 130.34, 131.01, 134.55, 135.29, 138.07, 144.99, 197.89; HRMS (EI) Found: 329.1085. Calcd for $C_{18}H_{19}NO_3S$: 329.1086 [M^+].

***N*-[(*Z*)-2-Phenyl-1-hexenyl]-*N*-2-propenyl-*p*-toluenesulfonamide (6)**



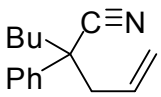
IR (nujol) 2924, 2855, 1347, 1159, 934, 770, 664 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (t, *J* = 7.5 Hz, 3H), 1.21–1.30 (m, 4H), 2.33 (m, 2H), 2.45 (s, 3H), 3.51 (dt, *J* = 6.5, 1.5 Hz, 2H), 4.84–4.88 (m, 1H), 4.95–4.98 (m, 1H), 5.41 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.88 (s, 1H), 6.97–6.98 (m, 2H), 7.21–7.24 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.93, 21.72, 22.09, 30.18, 36.25, 52.08, 118.22, 121.06, 127.46, 127.64, 128.13, 128.22, 129.72, 133.13, 136.09, 138.45, 140.79, 143.58. Found: C, 71.57; H, 7.36%. Calcd for $C_{22}H_{27}NO_2S$: C, 71.51; H, 7.36%. m.p. 81.2–81.7 ˚C

***N*-[(*Z*)-1-Deuterio-2-phenyl-1-hexenyl]-*N*-2-propenyl-*p*-toluenesulfonamide (6-*d*)**



IR (nujol) 2925, 2855, 1340, 1158, 935, 822, 771, 703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (t, *J* = 7.5 Hz, 3H), 1.21–1.30 (m, 4H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.45 (s, 3H), 3.51 (dt, *J* = 6.5, 1.0 Hz, 2H), 4.84–4.88 (m, 1H), 4.95–4.98 (m, 1H), 5.41 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 6.95–6.97 (m, 2H), 7.21–7.23 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.94, 21.73, 22.09, 30.19, 36.22, 52.01, 118.20, 120.75 (t, *J* = 26.3 Hz), 127.46, 127.63, 128.13, 128.23, 129.73, 133.16, 136.16, 138.46, 140.46, 143.58. Found: C, 71.58; H + D, 7.58%. Calcd for $C_{22}H_{26}DNO_2S$: C, 71.31; H + D, 7.61%. m.p. 81.1–82.3 ˚C.

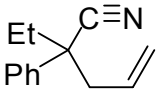
2-Butyl-2-phenyl-4-pentenenitrile (8a)



IR (neat) 2933, 2863, 2236, 1495, 1449, 924, 699, 519 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.5 Hz, 3H), 1.09–1.45 (m, 4H), 1.89 (dt, *J* = 13.5, 4.5 Hz, 1H), 2.00 (dt, *J* = 13.5, 4.5 Hz, 1H),

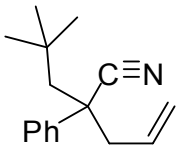
2.67 (d, J = 7.0 Hz, 2H), 5.11–5.15 (m, 2H), 5.64 (ddt, J = 17.0, 10.0, 7.0 Hz, 1H), 7.30–7.33 (m, 1H), 7.37–7.41 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 13.96, 22.72, 27.43, 39.87, 45.55, 48.20, 120.05, 122.35, 126.23, 127.85, 128.98, 132.06, 138.34. Found: C, 83.84; H, 9.25%. Calcd for $C_{15}H_{19}N$: C, 83.92; H, 9.55; N, 6.52%.

2-Ethyl-2-phenyl-4-pentenenitrile (8b)



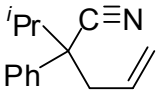
IR (neat) 2973, 2938, 2236, 1495, 1449, 925, 762, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 7.5 Hz, 3H), 1.94 (dq, J = 14.5, 7.5 Hz, 1H), 2.08 (dq, J = 14.5, 7.5 Hz, 1H), 2.67–2.69 (m, 2H), 5.10–5.15 (m, 2H), 5.65 (ddt, J = 17.5, 10.5, 7.0 Hz, 1H), 7.29–7.33 (m, 1H), 7.37–7.41 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 9.75, 33.26, 45.17, 48.97, 120.04, 122.15, 126.35, 127.90, 128.99, 132.08, 137.96. Found: C, 84.17; H, 8.37%. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16%.

2-Neopentyl-2-phenyl-4-pentenenitrile (8c)



IR (neat) 2956, 2909, 2236, 1642, 1601, 1449, 924, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (s, 9H), 1.98 (d, J = 14.5 Hz, 1H), 2.06 (d, J = 14.5 Hz, 1H), 2.67 (d, J = 7.0 Hz, 2H), 5.09–5.14 (m, 2H), 5.56–5.64 (m, 1H), 7.29–7.32 (m, 1H), 7.36–7.40 (m, 2H), 7.46–7.48 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 31.03, 32.18, 45.97, 48.95, 52.37, 120.25, 122.78, 126.61, 127.80, 128.82, 131.83, 138.58. Found: C, 84.24; H, 9.26%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31%.

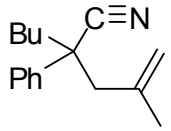
2-Isopropyl-2-phenyl-4-pentenenitrile (8e)



IR (neat) 2967, 2235, 1495, 1449, 923, 761, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.81 (d, J = 6.5 Hz, 3H), 1.21 (d, J = 6.5 Hz, 3H), 2.18 (sept, J = 6.5 Hz, 1H), 2.65 (ddt, J = 14.0, 7.0, 1.0 Hz, 1H), 2.86 (ddt, J = 14.0, 7.5, 1.0 Hz, 1H), 5.01–5.04 (m, 1H), 5.06–5.10 (m, 1H), 5.43–5.51 (m, 1H), 7.28–7.31 (m, 1H), 7.36–7.38 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 18.70, 18.95, 37.24, 42.26, 53.89,

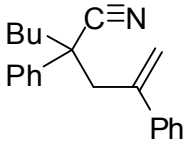
119.62, 121.07, 126.89, 127.78, 128.80, 132.39, 137.74. Found: C, 84.53; H, 8.67%. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60%.

2-Butyl-4-methyl-2-phenyl-4-pentenenitrile (8f)



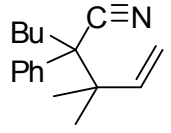
IR (neat) 3078, 2958, 2864, 2236, 1647, 1495, 1449, 900, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, J = 7.5 Hz, 3H), 1.05–1.12 (m, 1H), 1.24–1.34 (m, 2H), 1.41–1.49 (m, 1H), 1.53 (s, 3H), 1.92 (dt, J = 13.5, 4.5 Hz, 1H), 2.01 (dt, J = 12.5, 4.5 Hz, 1H), 2.60 (d, J = 14.0 Hz, 1H), 2.70 (d, J = 14.0 Hz, 1H), 4.71 (s, 1H), 4.83 (s, 1H), 7.26–7.31 (m, 1H), 7.36–7.42 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 13.98, 22.74, 23.83, 27.42, 41.06, 47.81, 49.17, 116.65, 122.75, 126.31, 127.79, 128.89, 138.51, 140.17. Found: C, 84.76; H, 9.46%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31%.

2-Butyl-2,4-diphenyl-4-pentenenitrile (8g)



IR (neat) 2958, 2933, 2236, 1686, 1627, 1600, 1495, 1448, 907, 778, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79 (t, J = 7.5 Hz, 3H), 1.01–1.42 (m, 4H), 1.87 (dt, J = 13.5, 4.5 Hz, 1H), 1.95 (dt, J = 12.0, 4.5 Hz, 1H), 3.07 (d, J = 13.5 Hz, 1H), 3.16 (d, J = 13.5 Hz, 1H), 5.09 (s, 1H), 5.28 (s, 1H), 7.15–7.33 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 13.88, 22.67, 27.42, 40.22, 46.50, 48.64, 118.84, 122.18, 126.38, 126.67, 127.53, 127.66, 128.26, 128.68, 138.12, 144.81, 143.72; HRMS (FAB) Found: 290.1901. Calcd for $C_{21}H_{24}N$: 290.1908 [MH^+].

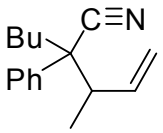
2-Butyl-3,3-dimethyl-2-phenyl-4-pentenenitrile (8h)



IR (neat) 2961, 2934, 2874, 2233, 1469, 1448, 922, 750, 703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (t, J = 7.5 Hz, 3H), 1.02 (s, 3H), 1.17 (s, 3H), 1.27–1.39 (m, 4H), 1.94–2.00 (m, 1H), 2.05–2.12 (m,

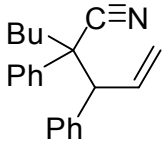
1H), 5.02 (d, J = 18.0 Hz, 1H), 5.15 (d, J = 10.5 Hz, 1H), 5.89 (dd, J = 18.0, 10.5 Hz, 1H), 7.29–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.03, 23.03, 23.14, 24.48, 28.03, 32.39, 43.23, 56.06, 115.13, 122.71, 127.81, 127.96, 128.77, 134.95, 142.87. Found: C, 84.49; H, 9.76%. Calcd for $C_{17}H_{23}N$: C, 84.59; H, 9.60%.

2-Butyl-3-methyl-2-phenyl-4-pentenenitrile (8i, a 59:41 mixture of diastereomers)



IR (neat) 2959, 2933, 2865, 2235, 1714, 1601, 1495, 1449, 923, 762, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 (t, J = 7.5 Hz, 3 × 0.59H), 0.84 (t, J = 7.5 Hz, 3 × 0.41H), 0.87 (d, J = 6.5 Hz, 3 × 0.59H), 1.21 (d, J = 7.0 Hz, 3 × 0.41H), 0.78–1.52 (m, 4H), 1.71–1.82 (m, 1 × 0.59H), 1.90–1.99 (m, 1 × 0.41H), 1.99–2.12 (m, 1H), 2.52–2.60 (m, 1 × 0.59H), 2.62–2.72 (m, 1 × 0.41H), 4.88–5.00 (m, 2 × 0.41H), 5.18–5.26 (m, 2 × 0.59H), 5.50 (ddd, J = 17.0, 10.0, 8.0 Hz, 1 × 0.41H), 5.88–5.98 (m, 1 × 0.59H), 7.20–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.93, 13.96, 16.37, 17.23, 22.70, 22.82, 27.59, 27.61, 37.14, 38.87, 47.10, 48.51, 52.51, 52.62, 117.12, 117.61, 121.26, 121.97, 126.52, 127.10, 127.71, 127.74, 128.60, 128.94, 137.03, 137.93, 138.09, 139.18. Found: C, 84.65; H, 9.55%. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31%.

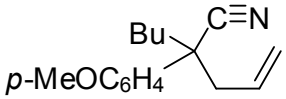
2-Butyl-2,3-diphenyl-4-pentenenitrile (8j, a 60:40 mixture of diastereomers)



IR ($CDCl_3$) 2958, 2932, 2865, 2234, 1602, 1494, 1449, 925, 724, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.75 (t, J = 3 × 0.60H), 0.84 (t, J = 7.0 Hz, 3 × 0.40H), 0.86–1.06 (m, 1H), 1.09–1.47 (m, 3H), 1.68 (ddd, J = 13.5, 12.0, 4.5 Hz, 1 × 0.60H), 1.89 (ddd, J = 14.0, 12.5, 4.5 Hz, 1 × 0.60H), 1.96 (ddd, J = 14.0, 12.5, 4.5 Hz, 1 × 0.40H), 2.24 (ddd, J = 12.5, 12.5, 4.5 Hz, 1 × 0.40H), 3.54 (d, J = 9.5 Hz, 1 × 0.40H), 3.64 (d, J = 8.5 Hz, 1 × 0.60H), 4.77–4.81 (m, 1 × 0.60H), 4.98–5.01 (m, 1 × 0.60H), 5.26–5.32 (m, 2 × 0.40H), 6.05 (ddd, J = 17.0, 10.5, 8.5 Hz, 1 × 0.60H), 6.41 (ddd, J = 16.5, 10.0, 9.5 Hz, 1 × 0.40H), 6.90–6.95 (m, 2 × 0.40H), 7.06–7.10 (m, 2 × 0.60H), 7.12–7.24

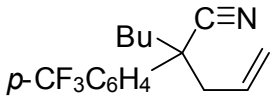
(m, 2H), 7.28–7.42 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 14.01, 14.08, 22.77, 22.88, 27.60, 27.68, 37.92, 38.53, 52.99, 53.13, 60.14, 60.84, 118.96, 119.26, 121.85, 121.88, 127.08, 127.21, 127.23, 127.71, 127.89, 127.99, 128.19, 128.59, 128.74, 128.79, 128.83, 129.45, 135.94, 136.71, 136.78, 137.46, 139.06, 139.23. Found: C, 86.95; H, 8.27%. Calcd for $C_{21}H_{23}N$: C, 87.15; H, 8.01%.

2-Butyl-2-*p*-methoxylphenyl-4-pentenenitrile (8k)



IR (neat) 2937, 2863, 2235, 1611, 1514, 1253, 1185, 1036, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.0 Hz, 3H), 1.07–1.16 (m, 1H), 1.21–1.46 (m, 3H), 1.84 (dt, *J* = 13.5, 4.5 Hz, 1H), 1.97 (dt, *J* = 12.5, 4.5 Hz, 1H), 2.59–2.68 (m, 2H), 3.82 (s, 3H), 5.099–5.104 (m, 1H), 5.12–5.14 (m, 1H), 5.60–5.69 (m, 1H), 6.89–6.92 (m, 2H), 7.28–7.32 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.97, 22.72, 27.44, 39.97, 45.63, 47.47, 55.45, 114.26, 119.91, 122.60, 127.37, 130.34, 132.22, 159.08. Found: C, 78.72; H, 8.59%. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70%.

2-Butyl-2-*p*-trifluoromethylphenyl-4-pentenenitrile (8l)



IR (neat) 2962, 2936, 2866, 2238, 1620, 1329, 1169, 1122, 1071, 1018, 927, 839 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.5 Hz, 3H), 1.03–1.12 (m, 1H), 1.22–1.38 (m, 2H), 1.41–1.49 (m, 1H), 1.90 (dt, *J* = 13.5, 4.5 Hz, 1H), 2.03 (dt, *J* = 12.0, 4.5 Hz, 1H), 2.63–2.74 (m, 2H), 5.10–5.14 (m, 2H), 5.58–5.66 (m, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.86, 22.64, 27.40, 39.79, 45.37, 48.30, 120.65, 121.64, 124.02 (q, *J* = 270.6 Hz), 126.03 (m), 126.81, 130.0 (q, *J* = 32.6 Hz), 131.36, 142.40. Found: C, 68.37; H, 6.45%. Calcd for $C_{16}H_{18}NF_3$: C, 68.31; H, 6.45%.

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7. A similar directing effect was reported in carbocupration reactions of ynamides. See ref 2c.
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9. Carbometalation of ynamides was reported. See ref 2c.
10. The *syn* mode in the addition was determined according to the literature. See ref 2c.

11. a) K. C. Brannock, R. D. Burpitt, *J. Org. Chem.* **1965**, *30*, 2564. b) M. A. Walters, *J. Org. Chem.* **1996**, *31*, 978.

12. Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151.

13. a) R. D. Singer, In *Science of Synthesis*, *Organometallics*, ed by I. Fleming, Thieme, **2002**, p. 237. For preparation of Me_3SiLi, see: b) W. C. Still, *J. Org. Chem.* **1976**, *41*, 3063. For preparation of $PhMe_2SiLi$, see: c) H. Gilman, G. D. Lichtenwalter, *J. Am. Chem. Soc.* **1958**, *80*, 607. d) I. Fleming, R. S. Roberts, S. C. Smith, *J. Chem. Soc., Perkin Trans. 1* **1998**, 1209.

14. C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2005**, *127*, 1070.

Chapter 4

Regio- and Stereoselective Hydrothiolation Reactions of Ynamides with Diphenyldithiophosphinic Acid: Straightforward Synthesis of Ketene *N*,*S*-Acetal Derivatives

Treatment of *N*-1-alkynyl-*N*-methylarenesulfonamides with diphenyldithiophosphinic acid resulted in hydrothiolation reactions to provide ketene *N*,*S*-acetal derivatives regio- and stereoselectively.

Introduction

Ynamides are ynamines having both good reactivity and sufficient stability to handle, thanks to the electron-withdrawing group on the nitrogen. In the past few years, the chemistry of ynamides has attracted considerable attention.[1] Reactions of ynamides have been developed on the basis of the reactivity of the electron-rich carbon–carbon triple bonds. Among them, Brϕnsted acid- or Lewis acid-promoted addition reactions to ynamides have been actively explored.[2] The author reports here hydrothiolation of ynamides with diphenyldithiophosphinic acid[3] leading to ketene *N*,*S*-acetal derivatives.

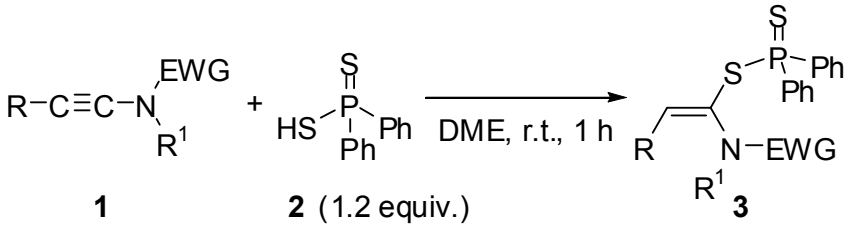
Results and Discussion

Treatment of *N*-ethynyl-*N*-methyl-*p*-toluenesulfonamide (**1a**) with diphenyldithiophosphinic acid (**2**) in 1,2-dimethoxyethane (DME) at room temperature for 1 h afforded 1-[methyl(*p*-tolylsufonyl)amino]ethenyl diphenyldithiophosphinate (**3a**) in 86% isolated yield regioselectively (Table 1, Entry 1).

A wide range of ynamides **1** were tested for the hydrothiolation reactions with **2**. Interestingly, internal ynamides also reacted with **2** smoothly. All the reactions proceeded in a syn fashion to furnish (*E*)-isomers as the sole isomers.[4] Both *N*-1-propynylamide **1b** and *N*-phenylethynylamide **1c** afforded the corresponding products in high yields (Entries 2 and 3). In addition, *N*-arylethynylamides having an electron-donating group or an electron-withdrawing group on the aromatic rings provided the corresponding hydrothiolation products without difficulty (Entries 4–7). It is worth noting that the keto group in **1g** survived under the reaction conditions (Entry 7). Ynamide **1h**, which has a silyl group on the terminus of the triple bond, also furnished the desired product **3h** (Entry 8). Even *N*-methyl-*N*-phenylethynyl-*p*-nitrobenzenesulfonamide (**1j**), the carbon–carbon triple bond of which would be more electron-deficient, reacted with **2** smoothly to afford the corresponding

product **3j** in 97% isolated yield (Entry 10).

Table 1. Hydrothiolation reactions of ynamides with diphenyldithiophosphinic acid



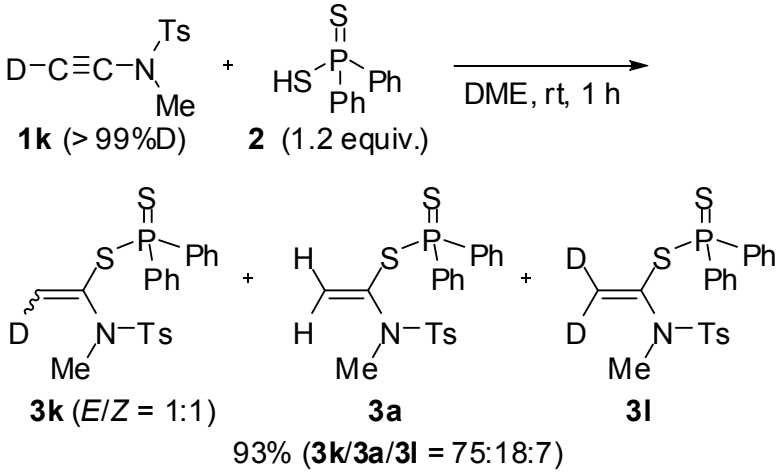
1 **2** (1.2 equiv.) **3**

Entry	**1**	R	R^1	EWG	**3**	Yield /%[a]
1	**1a**	H	Me	Ts	**3a**	86
2	**1b**	Me	Me	Ts	**3b**	76
3	**1c**	Ph	Me	Ts	**3c**	87
4	**1d**	*p*-tolyl	Me	Ts	**3d**	91
5	**1e**	*o*-tolyl	Me	Ts	**3e**	97
6	**1f**	*p*-ClC_6H_4	Me	Ts	**3f**	88
7	**1g**	*p*-AcC_6H_4	Me	Ts	**3g**	97
8	**1h**	TMS	Me	Ts	**3h**	63[b]
9	**1i**	Ph	allyl	Ts	**3i**	95
10	**1j**	Ph	Me	*p*-Ns[c]	**3j**	97

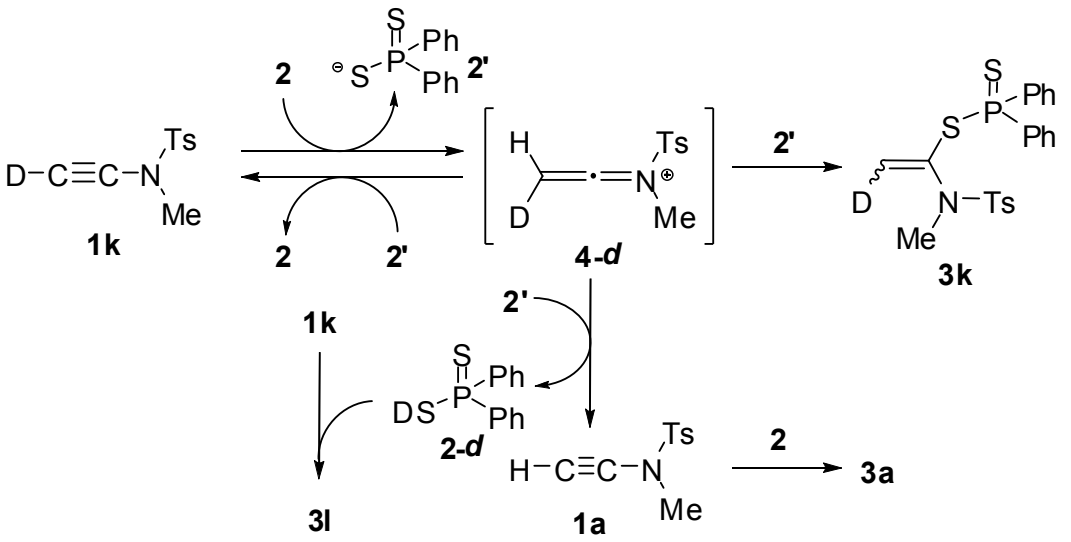
[a]Isolated yields by silica gel column chromatography unless otherwise noted. [b]Isolated yield obtained by recrystallization.

[c] *p*-nitrophenylsulfonyl.

In order to reveal the mechanism of the hydrothiolation, the reaction of deuterium-labeled ynamide **1k** was performed. As a result, a mixture of adducts **3k**, **3a**, and **3l** was obtained in 93% combined yield in a ratio of 75:18:7 (Scheme 1). It is worth noting that **3k** was obtained as a 1:1 mixture of the E and Z isomers. The formation of the stereoisomeric mixture of **3k** suggests the stepwise mechanism for the hydrothiolation as shown in Scheme 2. Namely, protonation of **1k** with **2** would generate ketene iminium intermediate **4-*d*** and diphenyldithiophosphinate anion **2'** as the first step.[5] Next, **2'** would add to the intermediate **4-*d*** to furnish **3k**. Instead of the addition of **2'** to **4-*d***, abstraction of the deuterium in **4-*d*** by **2'** would generate **1a** and **2-*d***. Then the reaction of **1a** with **2** would afford **3a**. In addition, the reaction of **1k** with **2-*d*** would provide **3l**.

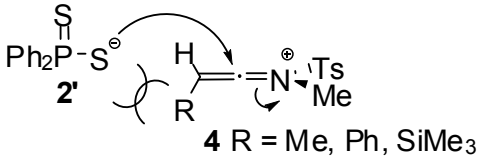


Scheme 1.



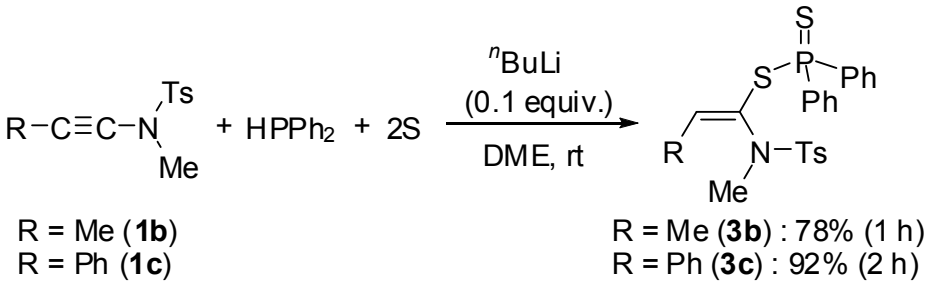
Scheme 2.

The selective formation of (*E*)-isomers from **1b**~**1j** is suggested as follows. Dithiophosphinate anion **2'** would attack ketene iminium intermediate **4** from the same side of hydrogen to avoid steric hindrance with a substituent R (Scheme 3).



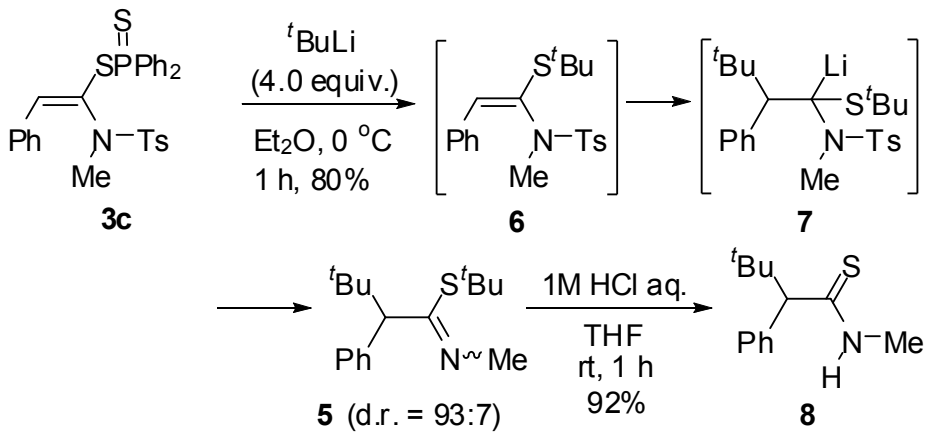
Scheme 3.

The author found that treatment of ynamides **1b** or **1c** with commercially available diphenylphosphine and sulfur in the presence of a catalytic amount of butyllithium in DME at room temperature afforded the same product **3b** or **3c** respectively in high yield (Scheme 4). It is reasonable that diphenyldithiophosphinic acid (**2**) would be generated in situ.[6] Indeed, treatment of diphenylphosphine with a catalytic amount of butyllithium in the presence of sulfur in DME at room temperature for 1 h afforded diphenyldithiophosphinic acid in 56% ^{31}P NMR yield (^{31}P NMR; δ 53.78 ppm in $CDCl_3$), after acid-base extraction.



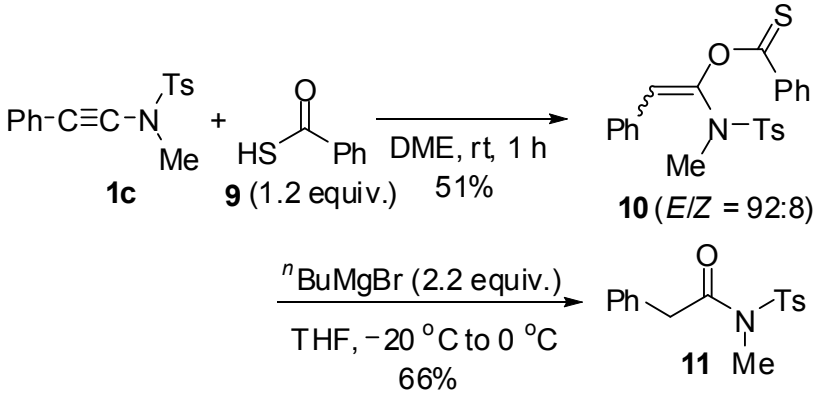
Scheme 4.

Finally, the author examined the reactivity of the ketene *N*,*S*-acetal **3**. Treatment of **3c** with 4.0 equimolar amounts of *tert*-butyllithium in diethyl ether at 0 ˚C provided thioimidate **5** in 80% yield (Scheme 5).[7] The formation of thioimidate **5** would proceed as follows. An attack of *tert*-butyl anion to the sulfur atom which attaches to olefinic carbon directly in **3c** gave **6**. Then another *tert*-butyllithium added to **6** to give **7,** and the subsequent elimination of lithium *p*-toluenesufinate furnished thioimidate **5**. Hydrolysis of thioimidate **5** led to *tert*-butyl-substituted thioamide **8** in 92% yield. Treatment of **3c** with 1.2 equimolar amounts of *tert*-butyllithium in THF at –40 ˚C for 90 min afforded the intermediate **6** in only 34% NMR yield. Unfortunately, the use of other organolithium compounds or organomagnesium compounds instead of *tert*-butyllithium provided complex mixtures.



Scheme 5.

When ynamide **1c** was treated with thiobenzoic acid (**9**) instead of **2** under otherwise the same conditions, ketene aminal **10** in 51% isolated yield (Scheme 6). Reaction of adduct **10** with butylmagnesium bromide in tetrahydrofuran (THF) afforded amide **11** in 66% yield. Therefore, the result suggested that the adduct **10** was not *S*-alkenyl thioester but *O*-alkenyl thioester. On the other hand, when ynamide **1c** was treated with thiols such as benzenethiol and 1-dodecanethiol under otherwise the same conditions, no hydrothiolation reactions took place.[8] The result suggests that the acidity of the reagents is important.[9]



Scheme 6.

Conclusion

The author has developed hydrothiolation reactions of ynamides with diphenyldithiophosphinic acid without any activation to afford ketene *N*,*S*-acetal derivatives. In addition, the reactivity of the ketene *N*,*S*-acetal obtained was examined.

Experimental Section

Material. Ynamide **1h** was prepared by the procedure described in the literature.[10] Ynamide **1a** and **1k** was prepared by treatment of **1h** with an excess amount of potassium carbonate in methanol or methanol-d_1. Preparation of other ynamides **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, **1i**, and **1j** were performed according to the literature.[11]

General Procedure for the Hydrothiolation Reactions of Ynamides with Diphenyldithiophosphinic Acid. Ynamide **1a** (105 mg, 0.50 mmol) was placed in a 30-mL reaction flask under argon. A solution of **2** (150 mg, 0.60 mmol in 5 mL of DME) was added to the reaction flask at room temperature. The mixture was stirred for 1 h at room temperature. The resulting mixture was concentrated in vacuo. A ^{31}P NMR analysis with trimethyl phosphate as an internal standard revealed formation of the corresponding product **3a** in 91% yield. Purification of the crude product by silica gel column chromatography provided **3a** (198 mg, 0.43 mmol) in 86% yield as white crystal.

Hydrothiolation of Ynamides with Diphenylphosphine and Sulfur in the Presence of a Catalytic Amount of Butyllithium. The reaction of ynamide **1b** is representative. DME (3 mL), butyllithium (1.6 mol/L, 31 μL, 0.050 mmol), and freshly distilled diphenylphosphine (0.13 mL, 0.75 mmol) were sequentially added to a 50-mL reaction flask under argon at room temperature. After the reaction mixture was stirred for 10 min at room temperature, S_8 (48 mg) and ynamides **1b** (112 mg, 0.5 mmol, dissolved in 3 mL of DME) were successively added. The resulting mixture was stirred at room temperature for 1 h, and saturated NH_4Cl aq. (2 mL) was

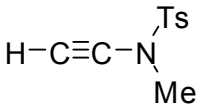
added. The organic compounds were extracted with ethyl acetate twice. The combined organic part was washed with brine and dried over anhydrous Na_2SO_4. After evaporation, the resulting residue was purified by silica gel column chromatography to afford **3b** (185 mg, 0.39 mmol) in 78% yield.

Reaction of Ketene *N*,*S*-Acetal 3c with *tert*-Butyllithium. Ketene *N*,*S*-acetal **3c** (161 mg, 0.30 mmol) was placed in a 30-mL reaction flask under argon. Diethyl ether (5 mL) and *tert*-butyllithium (1.58 mol/L, 0.76 mL, 1.2 mmol) were sequentially added at 0 ^oC. After being stirred for 1 h at 0 ^oC, water (5 mL) was added. The organic compounds were extracted with ethyl acetate twice. The combined organic part was washed with brine and dried over anhydrous Na_2SO_4. After evaporation, the resulting residue was purified by silica gel column chromatography to afford thioimidate **5** (67 mg, 0.24 mmol) in 80% yield.

Hydrolysis of Thioimidate. Thioimidate **5** (65 mg, 0.24 mmol) was placed in a 30-mL reaction flask under argon. THF (3 mL) and hydrochloric acid (1.0 mol/L, 3 mL) were sequentially added at ambient temperature. After the mixture was stirred for 1 h at ambient temperature, water (5 mL) was added. The organic compounds were extracted with ethyl acetate twice. The combined organic part was washed with brine and dried over anhydrous Na_2SO_4. After evaporation, the resulting residue was purified by silica gel column chromatography to afford thioamide **8** (48 mg, 0.22 mmol) in 92% yield.

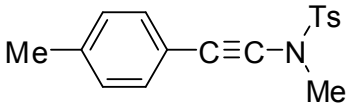
Characterization Data. The spectral data of **1h**[10] and **1i**[11] are found in the literature.

***N*-Ethynyl-*N*-methyl-*p*-toluenesulfonamide (1a)**



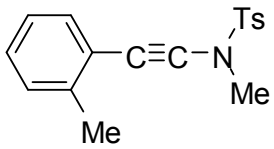
IR (Nujol) 2923, 2360, 2137, 1597, 1359, 1172, 960, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46 (s, 3H), 2.68 (s, 1H), 3.06 (s, 3H), 7.37 (d, J = 7.5 Hz, 2H), 7.80 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.84, 39.01, 57.63, 77.76, 128.00, 130.01, 133.41, 145.09; Found: C, 57.35; H, 5.47%. Calcd for $C_{10}H_{11}NO_2S$: C, 57.40; H, 5.30%; m.p. 75–76 ˚C.

***N*-Methyl-*N*-*p*-tolylethynyl-*p*-toluenesulfonamide (1d)**



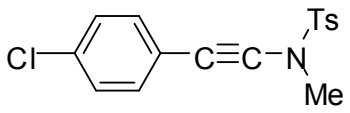
IR (Nujol) 2922, 2854, 2232, 1366, 1166, 728, 664, 567, 543 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H), 2.48 (s, 3H), 3.16 (s, 3H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.24–7.32 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.60, 21.83, 39.53, 69.15, 83.39, 119.69, 128.05, 129.20, 129.94, 131.66, 133.40, 138.21, 144.90; Found: C, 68.20; H, 5.60%. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72%; m.p. 73–74 ˚C.

***N*-Methyl-*N*-*o*-tolylethynyl-*p*-toluenesulfonamide (1e)**



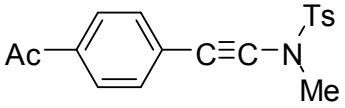
IR (neat) 2923, 2235, 1597, 1457, 1367, 1189, 1169, 962, 811, 758, 735, 676, 547 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.37 (s, 3H), 2.46 (s, 3H), 3.18 (s, 3H), 7.08–7.14 (m, 1H), 7.17 (dd, *J* = 5.0, 1.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.34–7.38 (m, 2H), 7.82–7.87 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.88, 21.93, 39.64, 68.21, 87.91, 122.70, 125.66, 127.92, 128.02, 129.56, 129.99, 131.55, 133.59, 139.91, 144.95; HRMS(EI) Found: 299.0986. Calcd for $C_{17}H_{17}NO_2S$: 299.0980 [M^+].

***N*-*p*-Chlorophenylethynyl-*N*-methyl-*p*-toluenesulfonamide (1f)**



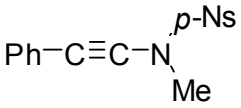
IR (Nujol) 2925, 2855, 2239, 1362, 1163, 1087, 960, 827, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46 (s, 3H), 3.15 (s, 3H), 7.24–7.30 (m, 4H), 7.36–7.40 (m, 2H), 7.80–7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.83, 39.38, 68.28, 85.00, 121.41, 127.99, 128.76, 130.02, 132.73, 133.41, 133.96, 145.10; Found: C, 59.81; H, 4.45%. Calcd for $C_{16}H_{14}NO_2SCl$: C, 60.09; H, 4.41%; m.p. 95–97 ˚C.

***N*-*p*-Acetylphenylethynyl-*N*-methyl-*p*-toluenesulfonamide (1g)**



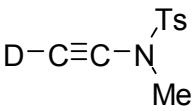
IR (Nujol) 2925, 2232, 1676, 1603, 1370, 1352, 1269, 1177, 1168, 714, 658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.47 (s, 3H), 2.59 (s, 3H), 3.18 (s, 3H), 7.36–7.44 (m, 4H), 7.82–7.86 (m, 2H), 7.86–7.91 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.87, 26.75, 39.38, 69.33, 87.70, 128.00, 128.13, 128.44, 130.11, 130.96, 133.44, 135.81, 145.25, 197.44; Found: C, 65.87; H, 5.39%. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23%; m.p. 131–133 ˚C.

***N*-Methyl-*N*-phenylethynyl-*p*-nitrobenzenesulfonamide (1j)**



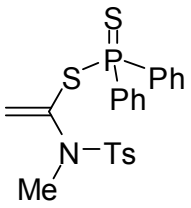
IR (Nujol) 2953, 2924, 2854, 2242, 1607, 1531, 1446, 1371, 1347, 1171, 769, 759, 598 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.23 (s, 3H), 7.28–7.40 (m, 5H), 8.15 (d, J = 8.5 Hz, 2H), 8.44 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 39.80, 69.99, 82.63, 122.04, 124.66, 128.62, 128.66, 129.22, 131.82, 141.82, 150.94; Found: C, 57.04; H, 3.88%. Calcd for $C_{15}H_{12}N_2O_4S$: C, 56.95; H, 3.82%; m.p. 150–153 ˚C.

***N*-Deuterioethynyl-*N*-methyl-*p*-toluenesulfonamide (1k)**



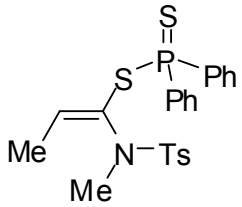
IR (Nujol) 2923, 2580, 2000, 1596, 1358, 1171, 955, 689, 544 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.45 (s, 3H), 3.05 (s, 3H), 7.34–7.49 (m, 2H), 7.78–7.82 (m, 2H); ^{13}C NMR (CD_2Cl_2) δ 21.94, 39.45, 57.48 (t, J = 40.1 Hz), 77.74 (t, J = 9.0 Hz), 128.30, 130.42, 133.65, 145.82; Found: C, 57.05; H+D, 5.61%. Calcd for $C_{10}H_{10}DNO_2S$: C, 57.12; H+D, 5.75%; m.p.74–76 ˚C.

1-[Methyl(*p*-tolylsulfonyl)amino]ethenyl Diphenyldithiophosphinate (3a)



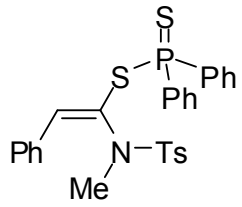
IR (Nujol) 2925, 2855, 2360, 1601, 1345, 1152, 930, 718, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H), 2.70 (s, 3H), 5.49 (dd, *J* = 3.5, 1.5 Hz, 1H), 5.55 (dd, *J* = 3.5, 1.5 Hz, 1H), 7.26–7.32 (m, 2H), 7.42–7.54 (m, 6H), 7.62–7.67 (m, 2H), 7.91–7.99 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.70, 37.08, 128.11, 128.36 (d, *J* = 6.6 Hz), 128.74 (d, *J* = 13.4 Hz), 129.70, 131.98 (d, *J* = 11.0 Hz), 132.28 (d, *J* = 2.9 Hz), 133.53 (d, *J* = 84.0 Hz), 134.10, 136.21 (d, *J* = 7.3 Hz), 144.11; ^{31}P NMR ($CDCl_3$) δ 63.97; Found: C, 57.24; H, 4.92%. Calcd for $C_{22}H_{22}NO_2PS_3$: C, 57.49; H, 4.82%; m.p. 99–100 ˚C.

(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-1-propenyl Diphenyldithiophosphinate (3b)



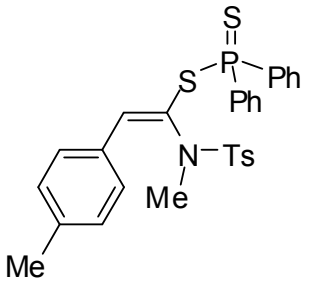
IR (neat) 3055, 2923, 1597, 1436, 1351, 1167, 1089, 957, 815, 720, 675, 654, 609 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.75 (dd, *J* = 7.0, 4.5 Hz, 3H), 2.45 (s, 3H), 2.54 (s, 3H), 6.13 (dq, *J* = 7.0, 3.5 Hz, 1H), 7.29–7.35 (m, 2H), 7.42 (br, 4H), 7.46–7.53 (m, 2H), 7.66–7.72 (m, 2H), 7.78–7.86 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 16.07 (d, *J* = 2.4 Hz), 21.79, 35.78, 126.47 (d, *J* = 7.6 Hz), 128.16, 128.69 (d, *J* = 13.4 Hz), 129.77, 131.87 (br), 132.11 (d, *J* = 3.4 Hz), 134.44 (d, *J* = 84.5 Hz), 135.58, 143.91, 147.52 (d, *J* = 7.1 Hz); ^{31}P NMR ($CDCl_3$) δ 64.47; Found: C, 58.39; H, 5.12%. Calcd for $C_{23}H_{24}NO_2PS_3$: C, 58.23; H, 5.27%; m.p. 83–84 ˚C.

(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-2-phenylethenyl Diphenyldithiophosphinate (3c)



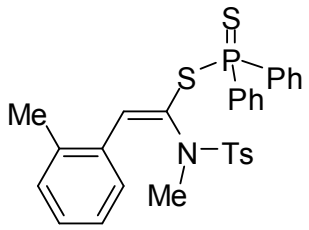
IR (Nujol) 2924, 2855, 1437, 1351, 1163, 693, 654 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 2.56 (s, 3H), 6.80 (d, *J* = 3.5 Hz, 1H), 7.22–7.54 (m, 13H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.73–7.89 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.77, 35.34, 125.73 (d, *J* = 8.1 Hz), 128.44, 128.51, 128.62 (d, *J* = 12.9 Hz), 129.31, 129.41 (d, *J* = 0.9 Hz), 129.54, 131.75 (d, *J* = 11.0 Hz), 132.11 (d, *J* = 2.9 Hz), 133.91 (d, *J* = 2.9 Hz), 134.19 (d, *J* = 83.1 Hz), 135.09, 143.98, 146.65 (d, *J* = 7.1 Hz); ^{31}P NMR ($CDCl_3$) δ 65.09; Found: C, 62.78; H, 4.93%. Calcd for $C_{28}H_{26}NO_2PS_3$: C, 62.78; H, 4.89%; m.p. 128–129 ˚C.

(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-2-*p*-tolylethenyl Diphenyldithiophosphinate (3d)



IR (Nujol) 2923, 2854, 1433, 1335, 1160, 1095, 975, 815, 686 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3H), 2.46 (s, 3H), 2.57 (s, 3H), 6.76 (d, *J* = 3.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.26–7.58 (m, 6H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.69–7.96 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 21.59, 21.79, 35.31, 124.52 (d, *J* = 8.1 Hz), 128.58, 128.69 (d, *J* = 13.4 Hz), 129.35, 129.57 (d, *J* = 1.4 Hz), 129.60, 131.27 (d, *J* = 2.9 Hz), 131.90 (d, *J* = 11.0 Hz), 132.13 (d, *J* = 3.4 Hz), 134.44 (d, *J* = 83.1 Hz), 135.35, 139.74, 143.96, 147.02 (d, *J* = 7.1 Hz); ^{31}P NMR ($CDCl_3$) δ 64.87; Found: C, 63.19; H, 5.01%. Calcd for $C_{29}H_{28}NO_2PS_3$: C, 63.36; H, 5.13%; m.p. 144–146 ˚C.

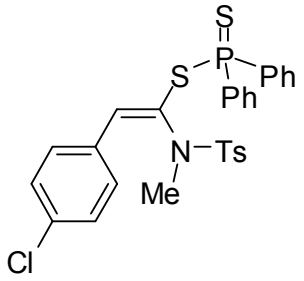
(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-2-*o*-tolylethenyl Diphenyldithiophosphinate (3e)



IR (Nujol) 2924, 2854, 1436, 1356, 1167, 1156, 1101, 723, 652 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3H), 2.39 (s, 3H), 2.57 (s, 3H), 6.90 (s, 1H), 7.02–7.26 (m, 5H), 7.30–7.66 (m, 9H), 7.78–8.02 (m,

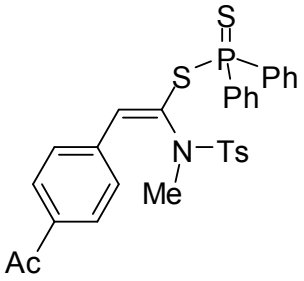
4H); ^{13}C NMR ($CDCl_3$) δ 20.21, 21.68, 35.83, 125.97, 127.15, 128.33, 128.46 (d, *J* = 1.4 Hz), 128.72 (d, *J* = 12.9 Hz), 128.87, 129.43, 130.02, 131.90 (d, *J* = 11.0 Hz), 132.16 (d, *J* = 2.9 Hz), 133.42, 134.21 (d, *J* = 83.5 Hz), 135.41, 137.09, 143.78, 143.84; ^{31}P NMR ($CDCl_3$) δ 64.35; Found: C, 63.54; H, 5.27%. Calcd for $C_{29}H_{28}NO_2PS_3$: C, 63.36; H, 5.13%; m.p. 165–167 ˚C.

(*E*)-2-*p*-Chlorophenyl-1-[methyl(*p*-tolylsulfonyl)aminoethenyl] Diphenyldithiophosphinate (3f)



IR (Nujol) 2924, 2855, 1437, 1351, 1162, 1090, 971, 815, 689 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.57 (s, 3H), 6.73 (d, *J* = 3.0 Hz, 1H), 7.22–7.58 (m, 12H) 7.67 (d, *J* = 8.5 Hz, 2H), 7.72–7.90 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 21.78, 35.33, 126.70 (d, *J* = 8.6 Hz), 128.51, 128.70, 128.81, 128.83, 129.70, 130.75, 131.88 (d, *J* = 10.9 Hz), 132.24 (d, *J* = 3.4 Hz), 132.55 (d, *J* = 2.9 Hz), 134.27 (d, *J* = 83.1 Hz), 135.12, 144.22, 145.21 (d, *J* = 7.1 Hz); ^{31}P NMR ($CDCl_3$) δ 65.48; Found: C, 59.11; H, 4.43%. Calcd for $C_{28}H_{25}NO_2PS_3$: C, 58.99; H, 4.42%; m.p. 109–111 ˚C.

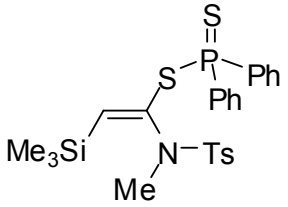
(*E*)-2-*p*-Acetylphenyl-1-[methyl(*p*-tolylsulfonyl)amino]ethenyl Diphenyldithiophosphinate (3g)



IR (Nujol) 2923, 2854, 1682, 1347, 1266, 1162, 973, 719, 682 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.58 (s, 3H), 2.60 (s, 3H), 6.80 (d, *J* = 3.0 Hz, 1H), 7.24–7.30 (m, 2H), 7.32–7.60 (m, 8H),

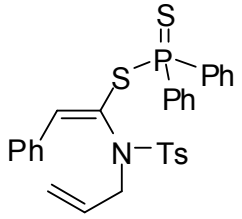
7.66–7.70 (m, 2H), 7.74–7.92 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 21.81, 26.82, 35.44, 128.53, 128.62, 128.68, 128.81 (d, J = 13.3 Hz), 129.56 (d, J = 1.4 Hz), 129.74, 131.92 (d, J = 11.0 Hz), 132.34 (d, J = 2.9 Hz), 134.14 (d, J = 83.5 Hz), 134.97, 137.10, 138.60 (d, J = 2.9 Hz), 144.30, 144.91 (d, J = 7.3 Hz), 197.60; ^{31}P NMR ($CDCl_3$) δ 65.70; Found: C, 62.25; H, 4.86%. Calcd for $C_{30}H_{28}NO_3PS_3$: C, 62.37; H, 4.89%; m.p. 132–134 ˚C.

(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-2-(trimethylsilyl)ethenyl Diphenyldithiophosphinate (3h)



Purification by recrystallization from a mixture of hexane and benzene was performed instead of silica gel column chromatography. IR (Nujol) 2924, 2854, 1439, 1348, 1245, 1166, 1157, 1103, 966, 864, 847, 721, 610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9H), 2.44 (s, 3H), 2.70 (s, 3H), 6.05 (d, J = 2.5 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.35–7.55 (m, 6H), 7.66–7.71 (m, 2H), 7.74–7.85 (m, 4H); ^{13}C NMR ($CDCl_3$) δ –0.61, 21.80, 36.06, 128.52, 128.69 (d, J = 13.3 Hz), 129.77, 132.01 (d, J = 10.5 Hz), 132.13 (d, J = 3.3 Hz), 134.15 (d, J = 83.9 Hz), 134.93, 136.27 (d, J = 6.4 Hz), 144.04, 151.42 (d, J = 5.1 Hz); ^{31}P NMR ($CDCl_3$) δ 64.19; Found: C, 56.20; H, 5.64%. Calcd for $C_{25}H_{30}NO_2SiPS_3$: C, 56.47; H, 5.69%; m.p. 160–162 ˚C.

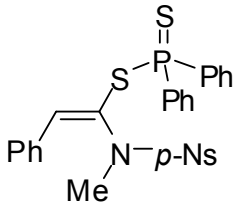
(*E*)-2-Phenyl-1-[(2-propenyl)(*p*-tolylsulfonyl)amino]ethenyl Diphenyldithiophosphinate (3i)



IR (Nujol) 2924, 2854, 1358, 1167, 1101, 723 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 3.72 (br, 2H), 4.85–4.92 (m, 1H), 4.94–5.02 (m, 1H), 5.64 (ddt, J = 17.0, 10.0, 7.0 Hz, 1H), 6.79 (d, J = 2.5 Hz, 1H), 7.17–7.27 (m, 5H), 7.30–7.54 (m, 8H), 7.70 (d, J = 8.0 Hz, 2H), 7.76–7.94 (m, 4H);

^{13}C NMR ($CDCl_3$) δ 21.73, 52.22, 118.83, 125.32 (d, J = 8.1 Hz), 128.30, 128.63, 128.75 (d, J = 13.3 Hz), 129.29, 129.57, 129.83 (d, J = 1.0 Hz), 131.95 (d, J = 11.0 Hz), 132.21 (d, J = 3.3 Hz), 132.98, 134.04, 134.30 (d, J = 83.5 Hz), 136.00, 144.09, 146.96 (d, J = 6.8 Hz); ^{31}P NMR ($CDCl_3$) δ 64.31; Found: C, 64.12; H, 5.09%. Calcd for $C_{30}H_{28}NO_2PS_3$: C, 64.15; H, 5.02%; m.p. 132–134 ˚C.

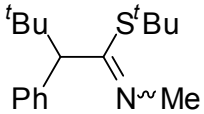
(*E*)-1-Methyl(*p*-nitrophenylsulfonyl)amino-2-phenylethenyl Diphenyldithiophosphinate (3j)



IR (Nujol) 2923, 2854, 1524, 1434, 1350, 1335, 1160, 718, 635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.76 (s, 3H), 6.75 (d, J = 3.0 Hz, 1H), 7.24–7.31 (m, 3H), 7.32–7.38 (m, 2H), 7.38–7.49 (m, 4H), 7.49–7.56 (m, 2H), 7.74–7.90 (m, 4H), 7.92–7.97 (m, 2H), 8.21–8.26 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 36.02, 124.11, 125.40 (d, J = 8.1 Hz), 128.78, 128.86 (d, J = 13.4 Hz), 129.31 (d, J = 1.4 Hz), 129.64, 129.72, 131.87 (d, J = 10.5 Hz), 132.44 (d, J = 3.3 Hz), 133.72 (d, J = 2.9 Hz), 134.03 (d, J = 83.0 Hz), 144.09, 147.10 (d, J = 7.1 Hz), 150.33; ^{31}P NMR ($CDCl_3$) δ 65.13; Found: C, 57.42; H, 4.23%. Calcd for $C_{27}H_{23}N_2O_4PS_3$: C, 57.23; H, 4.09%; m.p. 126–127 ˚C.

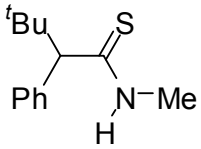
***tert*-Butyl *N*-Methyl-3,3-dimethyl-2-phenylbutanethioimidate**

(5, a 93:7 mixture of diastereomers)



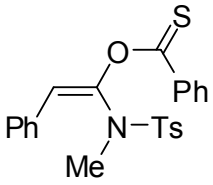
IR (neat) 2957, 2905, 1629, 1452, 1392, 1364, 1163, 976, 725, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.01 (s, 9 × 0.93H), 1.10 (s, 9 × 0.07H), 1.36 (s, 9 × 0.93H), 1.56 (s, 9 × 0.07H), 3.25 (s, 3 × 0.07H), 3.53 (s, 3 × 0.93H), 3.90 (s, 1 × 0.93H), 4.03 (s, 1 × 0.07H), 7.20–7.33 (m, 3H), 7.36–7.44 (m, 2H); ^{13}C NMR ($CDCl_3$) δ (major isomer) 28.66, 33.09, 36.60, 42.81, 49.02, 68.90, 126.53, 127.48, 131.32, 138.68, 162.42; Found: C, 73.47; H, 9.66%. Calcd for $C_{17}H_{27}NS$: C, 73.59; H, 9.81%.

***N*-Methyl-3,3-dimethyl-2-phenylbutanethioamide (8)**



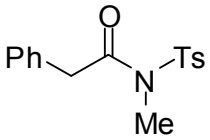
IR (Nujol) 3370, 2925, 2867, 1520, 1365, 1297, 1098, 1053, 740, 711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (s, 9H), 3.10 (s, 1.5H), 3.11 (s, 1.5H), 3.60 (s, 1H), 7.24–7.32 (m, 3H), 7.44 (br, 1H), 7.62–7.66 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 28.72, 32.99, 35.67, 72.63, 127.40, 127.98, 130.39, 138.26, 206.07; Found: C, 70.62; H, 8.51%. Calcd for $C_{13}H_{19}NS$: C, 70.54; H, 8.65%; m.p. 141–142 ˚C.

***O*-[(*E*)-1-Methyl(*p*-tolylsulfonyl)amino-2-phenylethenyl] Thiobenzoate ((*E*)-10)**



IR (Nujol) 2924, 2854, 1349, 1264, 1162, 1048, 1027, 990, 686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.28 (s, 3H), 3.10 (s, 3H), 6.26 (s, 1H), 7.02 (d, J = 8.0 Hz, 2H), 7.30–7.40 (m, 5H), 7.55–7.60 (m, 3H), 7.62–7.68 (m, 2H), 7.88–8.04 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.63, 37.51, 119.74, 127.77, 128.23, 128.60, 128.82, 128.85, 129.52, 129.61, 131.83, 133.58, 136.17, 137.30, 142.55, 143.99, 209.53; Found: C, 65.17; H, 5.15%. Calcd for $C_{23}H_{21}NO_3S_2$: C, 65.22; H, 5.00%; m.p. 138–140 ˚C.

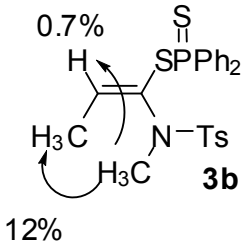
***N*-Methyl-*N*-phenylethanoyl-*p*-toluenesulfonamide (11)**



IR (neat) 3031, 1696, 1356, 1167, 1075, 673, 583 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.44 (s, 3H), 3.28 (s, 3H), 4.04 (s, 2H), 7.11–7.16 (m, 2H), 7.22–7.34 (m, 5H), 7.67–7.72 (m, 2H); ^{13}C NMR ($CDCl_3$) 21.78, 33.43, 43.23, 127.33, 127.69, 128.75, 129.54, 130.04, 133.62, 136.20, 145.12, 171.44; Found: C, 63.05; H, 5.66%. Calcd for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65%.

References and Notes

1. For reviews on the chemistry of ynamides, see: a) C. A. Zificsak, J. A. Mulder, R. P. Hsung, C. Rameshkumar, L.-L. Wei, *Tetrahedron* **2001**, *57*, 7575. b) J. A. Mulder, K. C. M. Kurtz, R. P. Hsung, *Synlett* **2003**, 1379.
2. For Brϕnsted acid-catalyzed addition reaction of allyl or propargyl alcohol followed by Claisen rearrangement, see: a) J. A. Mulder, R. P. Hsung, M. O. Frederick, M. R. Tracey, C. A. Zificsak, *Org. Lett.* **2002**, *4*, 1383. b) M. O. Frederick, R. P. Hsung, R. H. Lambeth, J. A. Mulder, M. P. Tracey, *Org. Lett.* **2003**, *5*, 2663. For hydrohalogenation, see: c) J. A. Mulder, K. C. M. Kurtz, R. P. Hsung, H. Coverdale, M. O. Frederick, L. Shen, C. A. Zificsak, *Org. Lett*. **2003**, *5*, 1547. For Brϕnsted acid-catalyzed hydroarylation, see: d) Y. Zhang, *Tetrahedron Lett.* **2005**, *46*, 6483. e) Y. Zhang, R. P. Hsung, X. Zhang, J. Huang, B. W. Slafer, A. Davis, *Org. Lett.* **2005**, *7*, 1047. For Lewis acid-catalyzed reaction with carbonyl compounds, see: f) K. C. M. Kurtz, R. P. Hsung, Y. Zhang, *Org. Lett.* **2006**, *8*, 231. g) L. You, Z. F. Al-Rashid, R. Figueroa, S. K. Ghosh, G. Li, T. Lu, R. P. Hsung, *Synlett* **2007**, 1656.
3. Diphenyldithiophosphinic acid was easily prepared from benzene and P_4S_{10} in the presence of $AlCl_3$. W. A. Higgins, P. W. Vogel, W. G. Craig, *J. Am. Chem. Soc.* **1955**, *77*, 1864.
4. Determined based on nuclear Overhauser effect. Syn addition reactions to ynamides under Brϕnsted acid catalysis was reported in Ref. 2d.



5. Ketene iminium intermediates were also proposed in Ref. 2a, 2d, 2e, 2f, and 2g.

6. It was reported that reaction of Ph_2PH and 2 equimolar amounts of sulfur in refluxing benzene afforded $Ph_2P(=S)SH$: G. Peters, *J. Org. Chem.* **1962**, *27*, 2198. Catalytic amounts of ^{n}BuLi would accelerate to form $Ph_2P(=S)SH$ due to generation of Ph_2PLi in situ.
7. Treatment of **3c** with 2.2 equimolar amounts of ^{t}BuLi under similar conditions provided **8** in 44% ^{1}H NMR yield along with the recovery of **3c** in 33% ^{31}P NMR yield. The reason, why 4.0 equimolar amounts of ^{t}BuLi were needed, was not clear.
8. Hydrothiolation with aromatic dithiocarbonic acid could not be performed due to difficulty in preparing and purifying dithiocarbonic acid.
9. pKa ($Ph_2P(=S)SH$, in 80% alcohol) = 2.6: a) M. I. Kabachnik, T. A. Mastrukova, A. E. Shipov, T. A. Melentyeva, *Tetrahedron* **1960**, *9*, 10. pKa (PhC(=O)SH, in DMSO) = 5.2, pKa (PhSH, in DMSO) = 9.8: b) J. Courtot-Coupez, M. Le Démézet, *Bull. Soc. Chim. Fr.* **1969**, 1033.
10. T. B. Clark, K. A. Woerpel, *Organometallics* **2005**, *24*, 6212.
11. Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett*. **2004**, *6*, 1151.

Appendix

Cobalt- and Rhodium-Catalyzed Cross-Coupling Reaction of Allylic Ethers and Halides with Organometallic Reagents

Reactions of 2-alkenyl methyl ether with phenyl, trimethylsilylmethyl, and allyl Grignard reagents in the presence of cobalt(II) complexes are discussed. The success of the reactions heavily depends on the combination of the substrate, ligand, and Grignard reagent. In the reaction of cinnamyl methyl ether, the formation of the linear coupling products predominates over that of the relevant branched products. In the cobalt-catalyzed allylation of allylic ethers, addition of a diphosphine ligand can change the regioselectivity, mainly providing the corresponding branched products. Rhodium complexes catalyze the reactions of allylic ethers and halides with allylmagnesium chloride and allylzinc bromide, respectively, in which the branched coupling product is the major product.

Appendix

Introduction

Palladium-, nickel-, and copper-catalyzed cross-coupling reactions of allylic substrates with organometallic reagents are recognized as one of the most useful reactions catalyzed by transition metals.[1] On the other hand, cobalt-catalyzed cross-coupling reactions of allylic substrates are quite rare.[2] Oshima have been interested in cobalt-catalyzed cross-coupling reactions.[3] Here the author reports the reactions of allylic ethers with phenyl, trimethylsilylmethyl, and allyl Grignard reagents in the presence of cobalt complexes.[4] Rhodium-catalyzed coupling reactions are also disclosed herein.[5]

Results and Discussion

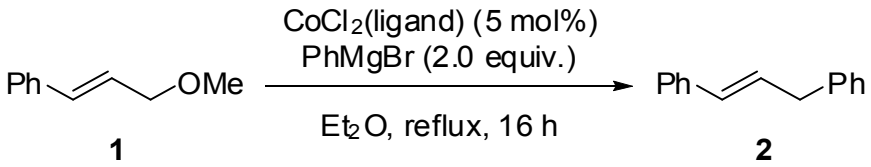
Cobalt-Catalyzed Phenylation Reaction of Allylic Ethers

The coupling reaction of cinnamyl methyl ether (**1**) with phenylmagnesium bromide was first performed (Table 1). A number of ligands were screened, and 1,5-bis(diphenylphosphino)pentane (DPPPEN) proved to be most effective for the phenylation reaction. 3,3-Diphenyl-1-propene was not detected at all. A small amount of β-methylstyrene was the only byproduct in each experiment, along with untouched **1**. The reaction of branched ether **3** with phenylmagnesium reagent under $CoCl_2$(dpppen) catalysis provided linear **2** selectively in good yield (eq. 1). The regioselectivity of the phenylations suggests that the reactions proceed via a π-allylcobalt intermediate. The phenylation reaction of **1** at 25 ˚C decreased the yield of **2**. The choice of the solvent was essential to obtain **2** in satisfactory yield. A similar reaction in THF resulted in very low conversion of **1**.

It is worth noting that treatment of cinnamyl bromide under similar conditions furnished a mixture of dimeric compounds such as 1,6-diphenyl-1,5-hexadiene and 3,4-diphenyl-1,5-hexadiene, in addition to a trace of **2**. The formation of the dimeric products implies that single electron transfer from a cobalt complex would yield cinnamyl radical that is

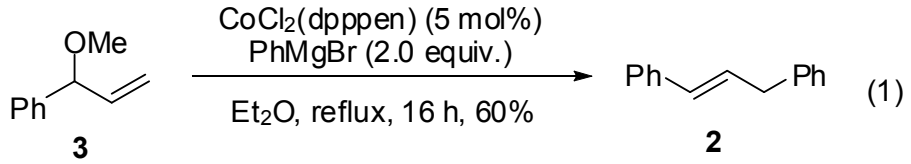
destined to dimerize.[2a,2c,2d]

Table 1. Cobalt-catalyzed reaction of cinnamyl methyl ether with phenylmagnesium bromide



Entry	Ligand	Yield/%
1	None	29
2	PPh_3 (10 mol%)	30
3	DPPM	24
4	DPPE	15
5	DPPP	27
6	DPPB	50
7	DPPPEN	72
8	DPPH	58

Ligands DPPM–DPPH represent $Ph_2P(CH_2)_nPPh_2$, n=1: DPPM; n=2: DPPE; n=3: DPPP; n=4: DPPB; n=5: DPPPEN; n=6: DPPH.

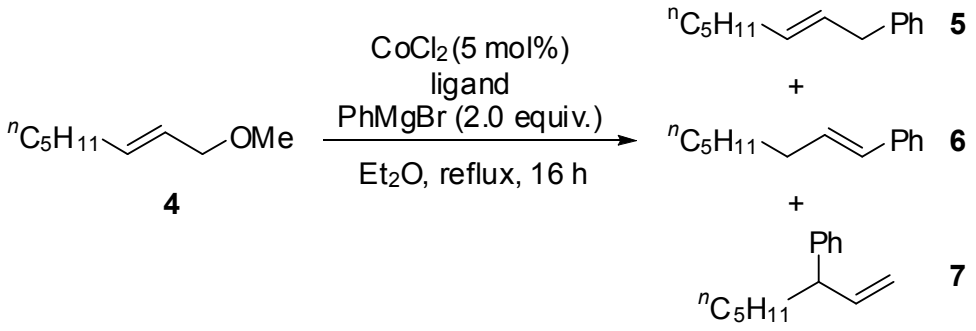


(1)

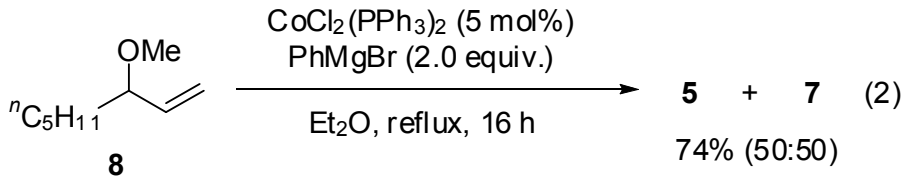
The cobalt-catalyzed phenylation reaction of *trans*-2-octenyl methyl ether (**4**) required triphenylphosphine as a ligand (Table 2, entry 4). A mixture of the corresponding coupling products **5**, **6**, and **7** was obtained. Under the reaction conditions, a part of **5** was transformed into **6**. In contrast to the reaction of **1**, the use of $CoCl_2$(dpppen) led to very poor conversion (entry 1). Without any phosphine ligand, coupling products were obtained in moderate

combined yield (entry 2). Other monodentate phosphine ligands were inferior to triphenylphosphine (entries 5–8). Under $CoCl_2(PPh_3)_2$ catalysis, branched ether **8** was also converted into **5** and **7** (eq. 2.), in which no isomerization from **5** to **6** was observed.

Table 2. Cobalt-catalyzed phenylation reaction of *trans*-2-octenyl methyl ether (**4**)

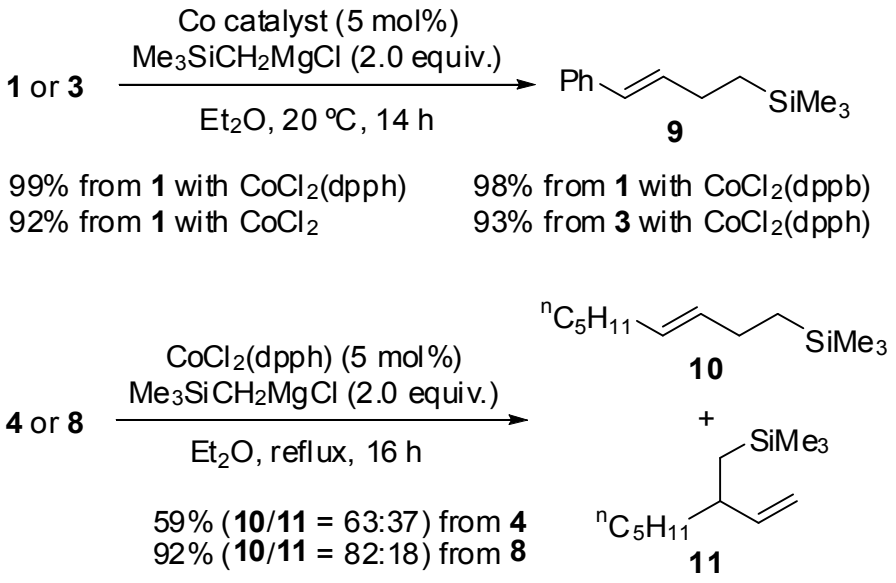


Entry	Ligand (amount)	Combined Yield/%	**5**/**6**/**7**
1	DPPPEN (5 mol%)	12	Not determined
2	None	47	58:10:32
3	DPPE (5 mol%)	32	10:53:37
4	PPh_3 (10 mol%)	78	36:7:57
5	$P(2\text{-}MeC_6H_4)_3$ (10 mol %)	39	66:<1:33
6	$P(4\text{-}MeC_6H_4)_3$ (10 mol %)	49	42:6:52
7	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$	Trace	Not determined
8	$P(4\text{-}MeOC_6H_4)_3$ (10 mol %)	41	31:16:53



Cobalt-Catalyzed Trimethylsilylmethylation Reaction of Allylic Ethers

Cross-coupling reaction with Me_3SiCH_2MgCl proceeded much more smoothly than that with PhMgBr (Scheme 1). Treatment of **1** with Me_3SiCH_2MgCl in the presence of $CoCl_2$(dpph) for 14 h at 20 ˚C afforded the corresponding linear product **9** in 99% yield. Whereas the choice of the ligand was crucial to establish the phenylation, ligandless $CoCl_2$ and $CoCl_2$(dppb) also effected the trimethylsilylmethylation to afford **9** in 92 and 98% yields, respectively. Reactions of branched **3** with Me_3SiCH_2MgCl afforded **9** in excellent yield. On the other hand, alkyl-substituted allylic ethers **4** and **8** were converted into mixtures of regioisomers **10** and **11**. The reaction required a higher temperature to complete the reaction within a satisfactory reaction time. Trimethylsilylmethylation of branched ether **8** afforded a higher yield of **10** and **11** than that of **4**.

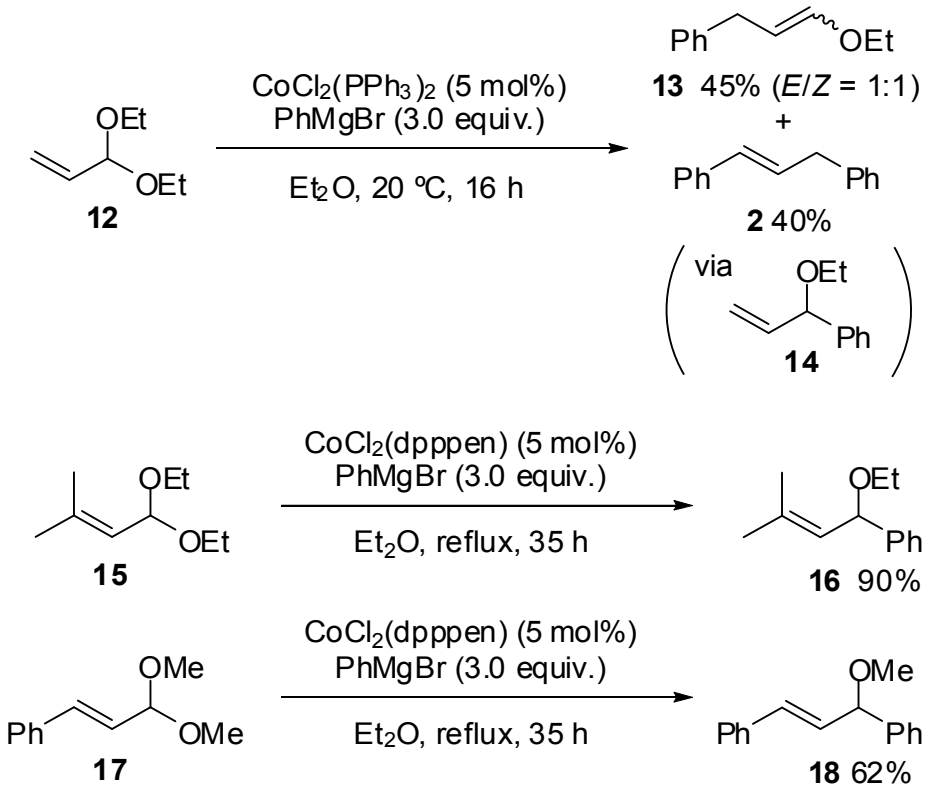


Scheme 1.

Cobalt-Catalyzed Reaction of α,β-Unsaturated Aldehyde Dialkyl Acetal

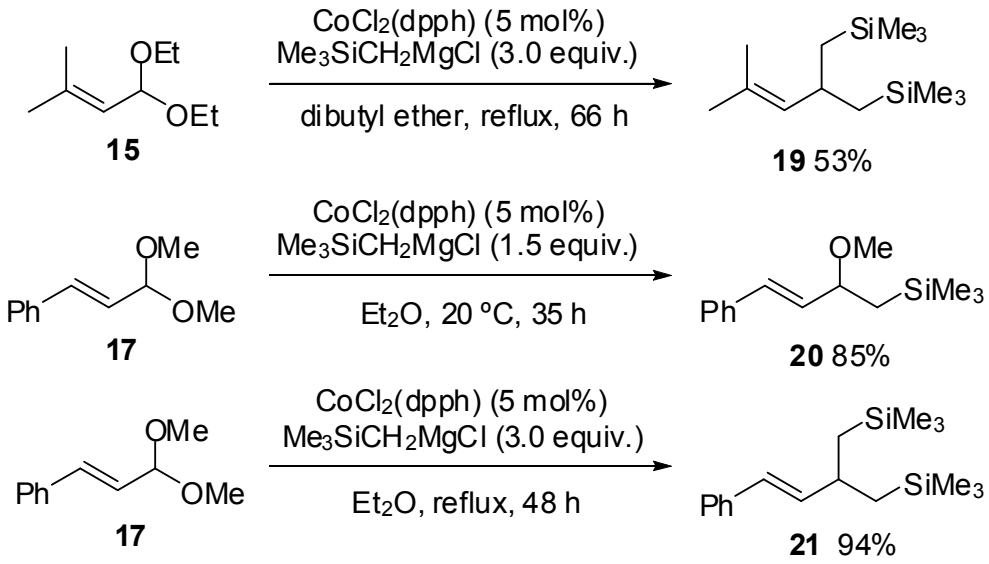
Treatment of acrolein diethyl acetal (**12**) with phenylmagnesium bromide in the presence of $CoCl_2(PPh_3)_2$ afforded a mixture of **2** and vinyl ether **13** (Scheme 2) Formation of doubly phenylated **2** would indicate a reaction path via the intermediate **14**. Monophenylation of

acetals **15** and **17** having substituents at the terminal olefinic positions was successful under $CoCl_2$(dpppen) catalysis. The dimethyl and phenyl groups of **16** and **18** would interfere with further phenylation.



Scheme 2.

In contrast to the reaction with phenylmagnesium bromide, bis(trimethylsilylmethylation) occurred in the reaction of **15** with three equimolar amounts of Me_3SiCH_2MgCl in refluxing dibutyl ether (Scheme 3). Intriguingly, in the reaction of **17**, we could completely control the distribution of the product by changing the amount of the Grignard reagent and reaction time. The reaction with 1.5 equimolar amounts of Me_3SiCH_2MgCl at ambient temperature for 35 h afforded monosubstituted product **20** exclusively in 85% yield. On the other hand, treatment of **17** with three equimolar amounts of the Grignard reagent in refluxing ether for 48 h furnished doubly substituted product **21** in 94% yield.



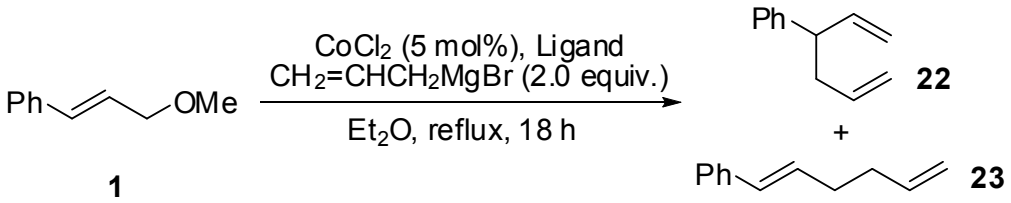
Scheme 3.

Cobalt-Catalyzed Cross-Coupling Reaction of Cinnamyl Methyl Ether with Allyl Grignard Reagent

To extend the scope of the cobalt-catalyzed cross-coupling reactions, the allylation reaction of cinnamyl methyl ether was examined. The regioselectivity of the title reaction heavily depended on the ligand used (Table 3). Cobalt(II) chloride by itself catalyzed the cross-coupling to yield linear **23** exclusively (entry 1). Addition of amines as a ligand did not influence the regioselectivity (entries 2, 3). Phosphine ligands allowed us to obtain significant amounts of branched **22**. Among them, DPPP exhibited the highest **22**/**23** selectivity, 70:30.

Judging from the results of Table 1, Scheme 1, and Table 3, trimethylsilylmethylmagnesium reagent proved to be the most reactive, and phenyl- and allylmagnesium reagents have similar reactivity. The low reactivity of allylmagnesium reagent may be due to the formation of π-allylcobalt that has less vacant coordination sites than phenyl- or trimethylsilylmethylcobalt has and that hence interacts weakly with the substrates at the initial oxidative addition stage.

Table 3. Cobalt-catalyzed coupling reaction of **1** with allylmagnesium bromide



Entry	Ligand	Yield/%	**22**/**23**
1	None	78	<1:99
2	NBu_3	79	<1:99
3	TMEDA	75	<1:99
4	DPPE	57	51:49
5	DPPP	70	70:30
6	DPPB	54	19:81
7	DPPF	32	54:46

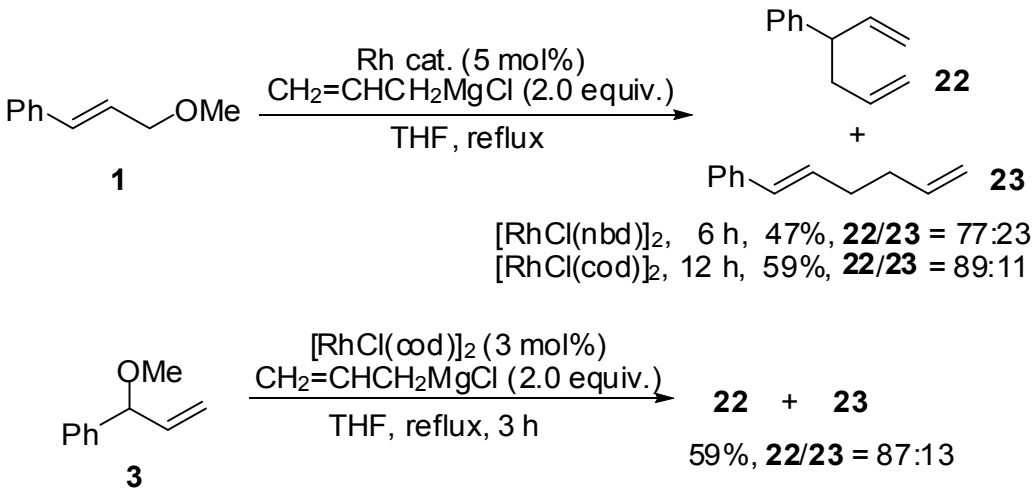
TMEDA and DPPF denote *N,N,N,'N'*-tetramethylethylenediamine and 1,1'-bis(diphenylphosphino)ferrocene, respectively.

The reactions of **1** and **3** with other Grignard reagents including vinylmagnesium bromide, methylmagnesium iodide, and alkynylmagnesium bromide failed to yield satisfactory amounts of the cross-coupling products.

Rhodium-Catalyzed Cross-Coupling Reaction of Allylic Ethers with Allylmagnesium Reagents

Although the catalytic activity of rhodium is lower than that of cobalt, rhodium complexes also catalyzed allylation of **1** (Scheme 4). Treatment of **1** with allylmagnesium chloride in the presence of $[RhCl(nbd)]_2$ (NBD = norbornadiene) in refluxing THF yielded the corresponding dienes in 47% combined yield. The branched form **22** was mainly obtained, and the selectivity is opposite to that of cobalt-catalyzed allylation. The use of $[RhCl(cod)]_2$ (COD = 1,5-cyclooctadiene) instead of $[RhCl(nbd)]_2$ slightly improved the efficiency and selectivity of

the reaction. Other rhodium complexes such as Wilkinson's catalyst and rhodium(III) acetylacetonate as well as an iridium complex $[IrCl(cod)]_2$ exhibited no catalytic activity. Branched ether **3** yielded **22** and **23** in good yield in a similar ratio under the $[RhCl(cod)]_2$ catalysis.

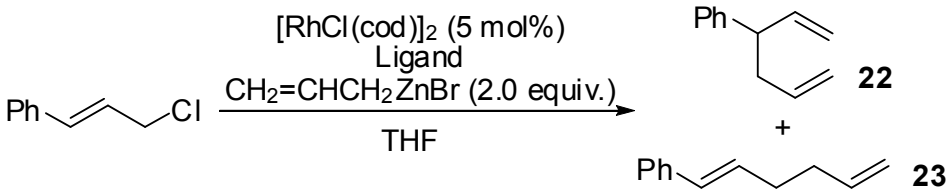


Scheme 4.

Rhodium-Catalyzed Cross-Coupling Reaction of Cinnamyl Chloride with Allylzinc Reagents

Rhodium complexes also mediated the reaction of cinnamyl chloride with allylzinc bromide (Table 4). The reaction at –40 ˚C in the presence of $[RhCl(cod)]_2$ for 30 min furnished **22** and **23** in 75% yield in a ratio of 77:23 (entry 2). The author screened many ligands to find that TMEDA is the best ligand with respect to the regioselectivity as well as the efficiency (entry 8). It is worth noting that a catalytic amount of diphosphine ligands such as DPPB (entry 3) and a stoichiometric amount of TMEDA (entry 9) completely inhibited the reaction. Interestingly, ligandless $CoCl_2$ effected the allylation to yield linear **23** exclusively (entry 13). An iridium complex $[IrCl(cod)]_2$ exhibited no catalytic activity.

Table 4. Rhodium-catalyzed coupling reaction of cinnamyl chloride with allylzinc bromide



Entry	Ligand (amount)	Temp./˚C	Time/h	Yield/%	**22**/**23**
1	None	–80	2	No Reaction	–
2	None	–40	0.5	75	77:23
3	DPPB (10 mol%)	–40	2	Trace	–
4	PBu_3 (20 mol%)	–40	3	57	86:14
5	NEt_3 (20 mol%)	–40	2	70	83:17
6	NBu_3 (20 mol%)	–40	3.5	54	81:19
7	TMEDA (10 mol%)	–40	6.5	53	85:15
8	TMEDA (10 mol%)	–20	1.5	87	83:17
9	TMEDA (2.0 eq of substrate)	–20	1.5	No Reaction	–
10	$Me_2NCH_2NMe_2$ (10 mol%)	–20	1.5	73	87:13
11	$Me_2N(CH_2)_3NMe_2$ (10 mol%)	–20	1	62	84:16
12	2,2’-Bipyridyl (10 mol%)	–20	1	68	84:16
13	None, $CoCl_2$	–20	3	66	<1:99

Conclusion

The cobalt-catalyzed cross-coupling reaction with phenyl Grignard reagent proved to be a function of a substrate as well as of solvent and ligand. To attain high yields in the phenylation reaction, intensive tunings of variants are needed. In contrast, introduction of trimethylsilylmethyl group was facile and clean under cobalt catalysis. The reactions of cinnamyl methyl ether with both phenyl and trimethylsilylmethyl Grignard reagents yielded the corresponding linear products, irrespective of reaction conditions. The cross-coupling reactions of allylic ethers with allyl Grignard reagent with the aid of ligandless cobalt(II) chloride afforded the corresponding linear dienes. Interestingly, addition of DPPP could reverse the regioselectivity, leading to predominant formation of the branched dienes. Rhodium salts catalyzed the reactions of allylic ethers and halides with allylmagnesium chloride and allylzinc bromide, respectively. Under rhodium catalysis, the branched coupling product was primarily formed. In both cobalt- and rhodium-catalyzed systems, π-allylmetal intermediates would be the key intermediates. The regioselectivity would depend on the ways how the carbon-carbon bonds are formed, i.e., via the outer-sphere mechanism or the inner-sphere mechanism. The exact mechanism is not clear at this stage.

Experimental Section

Material. The starting materials **1**, **3**, **4**, and **8** were prepared by the conventional Williamson ether synthesis.

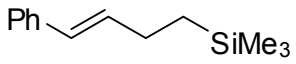
General Procedure for the Cross-Coupling Reactions with Grignard Reagents. The reaction of **1a** with trimethylsilylmethyl Grignard reagent is representative. Anhydrous $CoCl_2$ (7 mg, 0.05 mmol) was placed in a 50-mL two-necked flask and heated with a hair dryer in vacuo for 3 min. DPPH (27 mg, 0.06 mmol) and ether (1 mL) were sequentially added under argon. After the mixture was stirred for 30 min to obtain blue suspension, cinnamyl methyl ether (**1a**, 0.15 g, 1.0 mmol) and Me_3SiCH_2MgCl (1.0 M in ether, 2.0 mL, 2.0 mmol) were successively added to the reaction mixture at 0 ˚C. After being stirred for 14 h at 20 ˚C, the reaction mixture was poured into saturated NH_4Cl solution. The products were extracted with ethyl acetate (20 mL ×3) and the combined organic layer was dried over sodium sulfate and concentrated. Silica gel column purification of the crude product provided **9** (0.20 g, 0.99 mmol) in 99% yield as colorless oil.

Rhodium-Catalyzed Cross-Coupling Reactions of Cinnamyl Chloride with Allylzinc Bromide. Zinc powder (2.94g, 45 mmol) was placed in a 50-mL reaction flask under argon. THF (3.4 mL) was added. Chlorotrimethylsilane (0.1 mL, 0.8 mmol) and dibromoethane (0.1 mL, 2 mmol) were sequentially added at ambient temperature to activate zinc. After the mixture was stirred for 5 min, allyl bromide (2.6 mL, 30 mmol) in THF (24 mL) was added dropwise to the suspension with vigorous stirring over 15 min at 0 ˚C. The mixture was stirred for an additional 1 h at 25 ˚C. The gray supernatant liquid obtained was transferred to another flask filled with argon. The concentration of allylzinc bromide was determined by quantitative allylation reaction of an excess of benzaldehyde with allylzinc bromide prepared. The concentration was 0.87 M. $[RhCl(cod)]_2$ (25 mg, 0.05 mmol) was placed in another 50-mL two-necked flask under argon. THF (5 mL) and TMEDA (15 μL, 0.10 mmol) were successively added. The resulting solution was stirred for 5 min. Cinnamyl chloride (153 mg, 1.0 mmol,

dissolved in 5 ml of THF) was added. The solution was cooled at –20 ˚C, and allylzinc bromide (0.87 M in THF, 2.3 mL, 2.0 mmol) was added. After being stirred for 1.5 h at –20 ˚C, the reaction mixture was poured into 1 M hydrochloric acid. The product was extracted with ethyl acetate (2 × 20 mL). The combined organic phase was dried over sodium sulfate. Evaporation followed by silica gel column purification afforded a mixture of **22** and **23** (87% combined ^{1}H NMR yield) in a ratio of 83:17.

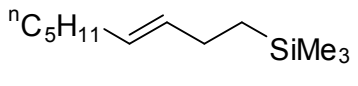
Characterization Data. The spectral data of the products **5**,[6] **6**,[6] **7**,[7] **13**,[8] **18**,[9] **22**,[10] and **23**[10] were found in the literature.

(*E*)-4-Trimethylsilyl-1-phenyl-1-butene (9)

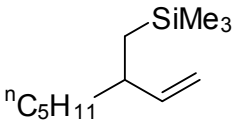


IR (neat) 3061, 2953, 2903, 1497, 1248, 962, 862, 837, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.27–7.35 (m, 4H), 7.17–7.20 (m, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.27 (dt, *J* = 16.0, 6.5 Hz, 1H), 2.23 (ddt, *J* = 10.0, 1.0, 6.5 Hz, 2H), 0.68–0.71 (m, 2H), –0.10–0.16 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 137.98, 133.83, 128.45, 128.26, 126.66, 125.87, 27.39, 16.27, –1.59. Found: C, 76.27; H, 9.73%. Calcd for $C_{13}H_{20}Si$: C, 76.40; H, 9.86%.

(*E*)-1-(Trimethylsilyl)-3-nonene/3-(trimethylsilylmethyl)-1-octene (10/11 = 82:18**)**



10

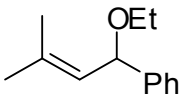


11

IR (neat) 2955, 2926, 1460, 1248, 968, 862, 835, 756, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.52–5.59 (m, 0.18 × 1H), 5.35–5.46 (m, 0.82 × 2H), 4.91 (ddd, *J* = 17.0, 2.0, 0.5 Hz, 0.18 × 1H), 4.87 (ddd, *J* = 10.0, 2.0, 0.5 Hz, 0.18 × 1H), 2.05–2.13 (m, 0.18 × 1H), 1.95–2.02 (m, 0.82 ×4H), 1.23–1.37 (m, 0.82 ×6H + 0.18 × 8H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.55–0.59 (m, 2H), –0.01 (s, 9H); ^{13}C NMR ($CDCl_3$) For major isomer, δ 113.03, 128.87, 32.48, 31.44, 29.35, 26.85, 22.57, 16.58, 14.08, –1.58. For minor isomer, δ 145.53, 112.56, 40.38, 38.55, 31.93, 23.26, 22.69, 14.12, –0.58. One of the sp^3-hybridized carbons of **11** could not been observed, probably due to overlapping.

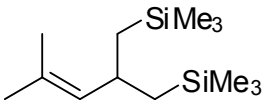
Found: C, 72.34; H, 12.94%. Calcd for $C_{12}H_{26}Si$: C, 72.69; H, 13.21%.

1-Ethoxy-3-methyl-1-phenyl-2-butene (16)



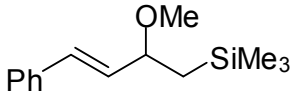
IR (neat) 2974, 2930, 1425, 1086, 756, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31–7.35 (m, 4H), 7.26–7.23 (m, 1H), 5.35 (d, *J* = 9.0 Hz, 1H), 5.01 (d, *J* = 9.0 Hz, 1H), 3.45–3.51 (m, 1H), 3.35–3.42 (m, 1H), 1.79 (s, 3H), 1.74 (s, 3H), 1.22 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.81, 134.99, 128.40, 127.19, 126.59, 126.43, 78.13, 63.39, 25.91, 18.40, 15.36. Found: C, 81.84; H, 9.54%. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54%.

2-Methyl-5-trimethylsilyl-4-(trimethylsilylmethyl)-2-pentene (19)



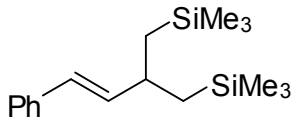
IR (neat) 2953, 2909, 1248, 837, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.86 (d, *J* = 10.0 Hz, 1H), 2.51–2.58 (m, 1H), 1.62 (s, 3H), 1.59 (s, 3H), 0.67 (dd, *J* = 14.7, 5.3 Hz, 2H), 0.57 (dd, *J* = 14.7, 8.5 Hz, 2H), –0.17–0.07 (m, 18H); ^{13}C NMR ($CDCl_3$) δ 134.73, 126.19, 30.41, 28.54, 25.63, 18.19, –0.72 . Found: C, 64.59; H, 12.24%. Calcd for $C_{13}H_{30}Si_2$: C, 64.38; H, 12.47%.

(*E*)-3-Methoxy-4-trimethylsilyl-1-phenyl-1-butene (20)



^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.41 (m, 4H), 7.22–7.25 (m, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.01 (dd, *J* = 15.9, 8.4 Hz, 1H), 3.81 (q, *J* = 7.8 Hz, 1H), 3.27 (s, 3H), 1.14 (dd, *J* = 14.3, 6.8 Hz, 1H), 0.94 (dd, *J* = 14.3, 7.7 Hz, 1H), 0.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.04, 131.15, 128.49, 127.51, 126.34, 106.68, 80.60, 55.72, 25.05, –0.62. Found: C, 71.79; H, 9.45%. Calcd for $C_{14}H_{22}OSi$: C, 71.73; H, 9.46%.

(*E*)-1-Phenyl-4-trimethylsilyl-3-(trimethylsilylmethyl)-1-butene (21)



^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.33 (m, 4H), 7.15–7.21 (m, 1H), 6.27 (d, *J* = 15.6 Hz, 1H), 5.98 (dd, *J* = 15.6, 9.0 Hz, 1H), 2.47–2.59 (m, 1H), 0.70–0.84 (m, 4H), –0.02 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.22, 128.37, 126.61, 126.54, 125.82, 106.68, 36.42, 28.13, –0.41. Found: C, 70.21; H, 10.28%. Calcd for $C_{17}H_{30}Si_2$: C, 70.26; H, 10.41%.

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Appendix

Publication List

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

Chapter 1 Hiroto Yasui, Toshihiro Nishikawa, Hideki Yorimitsu, and Koichiro Oshima
Bull. Chem. Soc. Jpn. **2006**, *79*, 1271–1274.

Chapter 2 Hiroto Yasui, Hideki Yorimitsu, and Koichiro Oshima
Synlett **2006**, 1783–1785.

Chapter 3 Hiroto Yasui, Hideki Yorimitsu, and Koichiro Oshima
Chem. Lett. **2007**, *36*, 32–33.
Bull. Chem. Soc. Jpn. in press..

Chapter 4 Hiroto Yasui, Hideki Yorimitsu, and Koichiro Oshima
Chem. Lett. in press.

Appendix Hiroto Yasui, Keiya Mizutani, Hideki Yorimitsu, and Koichiro Oshima
Tetrahedron **2006***, 62,* 1410–1415.

2. Other Publications not included in this thesis.

(1) Stereoselective Synthesis of Di- and Tri-substituted Aminoalkenes: Tandem Isomerization/Aza-Claisen Rearrangement/Hydride Reduction Sequence
Kiyoshi Honda, Hiroto Yasui, and Seiichi Inoue
Synlett **2003**, 2380–2382.

(2) Copper-Catalyzed Intermolecular Generation of Ammonium Ylides with Subsequent [2,3]Sigmatropic Rearrangement: Efficient Synthesis of Bifunctional Homoallylamines
Kiyoshi Honda, Hiromasa Shibuya, Hiroto Yasui, Yujiro Hoshino, and Seiichi Inoue
Bull. Chem. Soc. Jpn. in press.

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