1

Dimerization of Alkynes and Alkenes

Homo- or cross-dimerization of alkynes and/or alkenes is a straightforward, atom economical method to approach the conjugated enynes, 1,3-dienes, or higher alkenes. Particularly, the homo- and cross-dimerization of terminal alkynes can afford conjugated enynes, which are the important moieties in organic materials [1], biologically important molecules [2], and the versatile synthetic intermediates [3]. The functional 1,3-dienes from the cross-dimerization of alkynes with alkenes via hydrovinylation are also important intermediates in organic syntheses [4].

The catalytic dimerization of terminal alkynes can yield theoretically four unsaturated products: 2,4-disubstituted enyne (via head to tail or Markovnikov), E- and Z-1,4-disubstituted enynes (via head to head or $anti$-Markovnikov), and butatriene (Scheme 1.1).
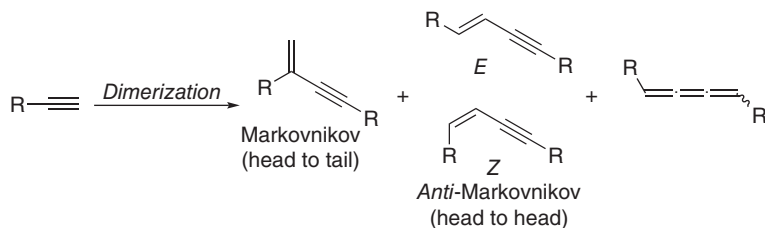
The transition metal-catalyzed formation of 2,4- and 1,4-disubstituted enynes via alkyne dimerization can be explained by a series of conventional reaction steps: oxidative addition of C≡H, insertion of C≡C of the second alkyne molecule, and then reductive elimination [5].

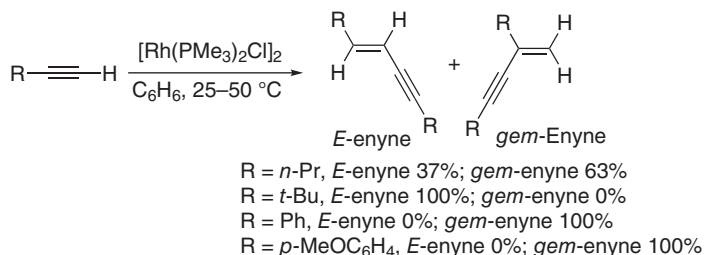## 1.1 Markovnikov Dimerization of Terminal Alkynes

The regioselective Markovnikov dimerization (head to tail) of terminal alkynes will afford gem-enynes (2,4-disubstituted enynes). [(Rh(PMe$_3$)$_2$Cl]$_2$ has been found to be the efficient catalyst to catalyze the insertion of terminal alkynes into benzene C—H bonds under irradiation, and it also shows catalytic activity for the dimerization of terminal alkynes with the gem-enynes as the major products in most cases (Scheme 1.2) [6].

[Rh(cod)Cl]$_2$/dppf can efficiently catalyze the dimerization of N-protected propargylamines to regioselectively give gem-enynes, which can subsequently undergo intramolecular hydroamination reaction to afford 2-(aminomethyl)pyrrole derivatives in the presence of AuCl$_3$ (Scheme 1.3) [7]. [Rh(cod)Cl]$_2$/PPh$_3$ was then applied in the cross-dimerization between aromatic alkynes and propargylic alcohols, ethers, or amides with high chemo- and regioselectivity [8].
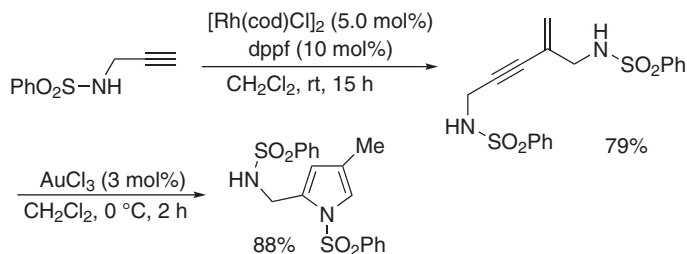
Nolan and coworker studied the catalytic activity of palladium/imidazolium system in the dimerization of aromatic and aliphatic terminal alkynes [9]. It was found

**Scheme 1.1** Dimerization products of terminal alkynes.

R = *n*-Pr, *E*-enyne 37%; *gem*-enyne 63%
R = *t*-Bu, *E*-enyne 100%; *gem*-enyne 0%
R = Ph, *E*-enyne 0%; *gem*-enyne 100%
R = *p*-MeOC$_6$H$_4$, *E*-enyne 0%; *gem*-enyne 100%

Scheme 1.2 [Rh(PMe$_3$)$_2$Cl]$_2$-catalyzed dimerization of terminal alkynes.


Scheme 1.3 Synthesis of trisubstituted pyrroles by cyclization of *N*-functionalized *gem*-enynes.

that Pd(OAc)$_2$/IMes·HCl is a highly efficient and regio- and stereoselective catalytic system depending on the use of the base and alkynes to control the product distribution. As shown in Scheme 1.4, in the case of K$_2$CO$_3$ used, the dimerization of 1-heptyne and phenyl acetylene affords *gem*-enyne and *E*-enyne, respectively, as the major products. However, in the former reaction, replacement of K$_2$CO$_3$ with Cs$_2$CO$_3$ results in a significant increase of *E*-enyne from the head-to-head dimerization as the predominant products.

   In the presence of PdCl$_2$(PPh$_3$)$_2$/CuI/PPh$_3$, the aromatic terminal alkynes undergo the trimerization to first afford (*Z*)-1,3-diaryl-2-arylethynyl-1,3-butadienes in moderate to excellent yields with high regioselectivity, and the structures and stereochemistry of dienyne were confirmed by X-ray crystal analyses [10]. As shown in Scheme 1.5, upon heating phenyl acetylene in dimethylfomamide (DMF) or acetonitrile with a mixture of PdCl$_2$(PPh$_3$)$_2$, PPh$_3$, NEt$_3$, and CuI, the angular dienyne could be obtained with high regioselectivity in 87 and 94% yield, respectively. This
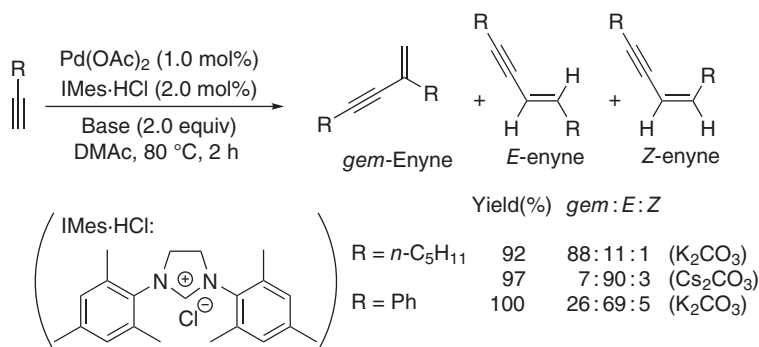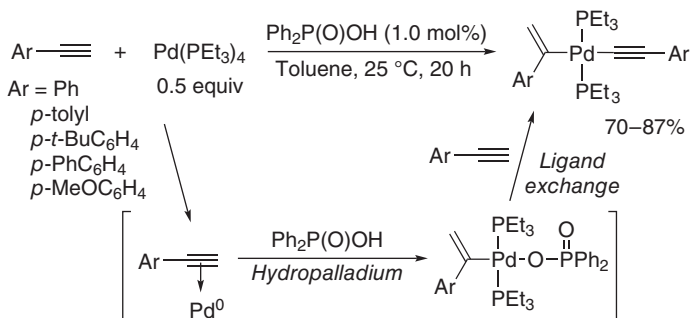
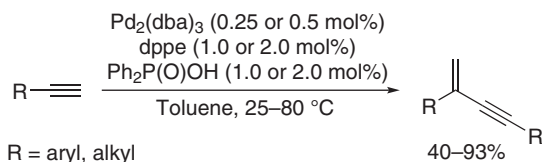**Scheme 1.4** Dimerization of terminal alkynes to enynes catalyzed by Pd(OAc)$_2$/IMes·HCl/base system.
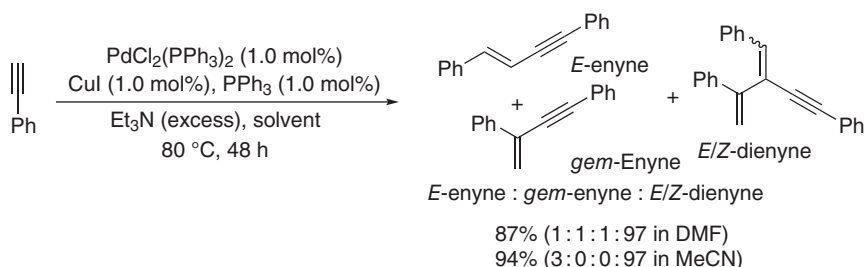
Scheme 1.5 Palladium-catalyzed synthesis of (*Z*)-dienynes via regioselective trimerization of alkynes.

protocol indicates that *gem*-enynes are much more reactive than aromatic terminal alkynes toward hydroalkynylation to yield dienynes.

Han and coworker reported a Brønsted acid Ph$_2$P(O)OH-promoted reaction of Pd(PEt$_3$)$_4$ with terminal alkynes to successfully isolate and characterize the complex of alkenyl(alkynyl)-palladiums from the oxidative addition of C—H bond of terminal alkyne to Pd(0) and subsequent ligand exchange reactions (Scheme 1.6). Then, a selective head-to-tail dimerization of terminal alkynes efficiently affording *gem*-enynes was developed by using Pd(0)/Brønsted acid (Scheme 1.7) [11].

**Scheme 1.6** Ph$_2$P(O)OH-catalyzed formation of alkenyl (alkynyl) palladium.

Scheme 1.7 Palladium(0)/Ph$_2$P(O)OH-catalyzed head-to-tail dimerization of terminal alkynes.

Guo and coworker reported an interesting counterion-controlled reactivity shift between dimerization and hydration of aromatic terminal alkynes catalyzed by Pd(PPh$_3$)$_4$ (Scheme 1.8) [12]. It is proposed that the use of acetate as counterion favors the formation of an alkenyl alkynyl palladium intermediate, resulting in the formation of 1,3-diaryl-substituted conjugated enynes via reductive elimination, while chloride is used, which is a better leaving group, leading to anion exchange on the alkenyl palladium intermediate with hydroxide to afford hydration products via reductive elimination and tautomerization (Scheme 1.9).
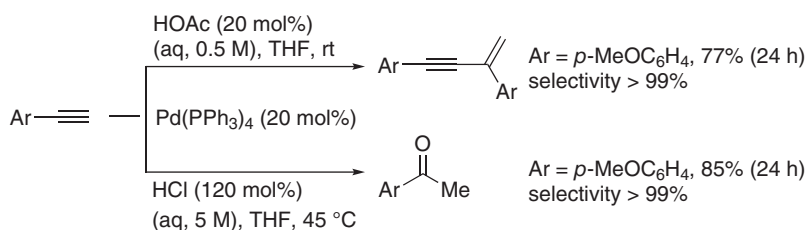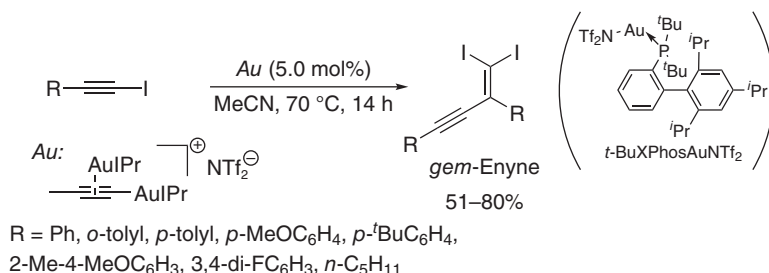

**Scheme 1.8** A counterion-controlled reactivity of terminal aromatic alkynes catalyzed by Pd(PPh$_3$)$_4$.
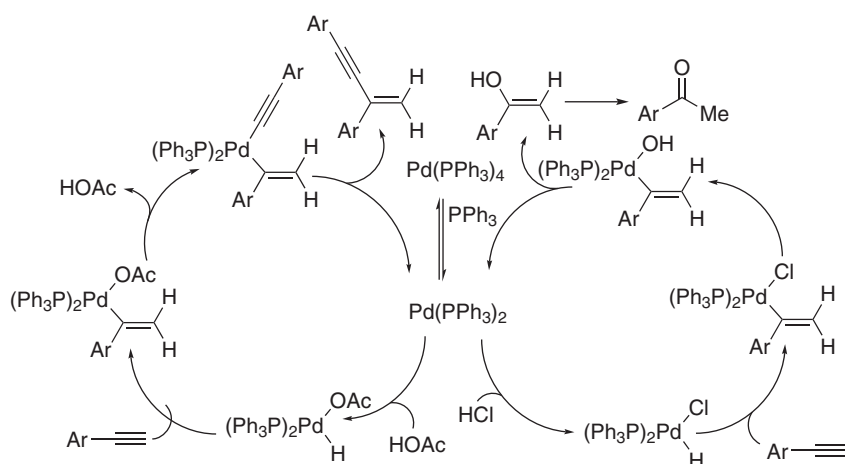
Scheme 1.9 A proposed mechanism for counterion-controlled reactivity shift of terminal aromatic alkynes.

In the presencea of *t*-BuXPhosAuNTf$_2$, the head-to-tail dimerization of aliphatic terminal alkynes occurs to give *gem*-enynes in good yields with excellent regioselectivity with the use of NaOAc as an additive [13]. Very interestingly, Hashmi and coworker have also developed a dual gold-catalyzed head-to-tail dimerization of haloalkynes (halo = Cl, Br, I) to afford *gem*-dihalogenated enynes, which are expected to be the valuable building blocks in organic synthesis. In the cases of iodoalkynes used, the dimerization occurs smoothly to give *gem*-deoxygenated enynes in good yields (Scheme 1.10) [14].

R = Ph, *o*-tolyl, *p*-tolyl, *p*-MeOC$_6$H$_4$, *p*-^{t}BuC$_6$H$_4$,
2-Me-4-MeOC$_6$H$_3$, 3,4-di-FC$_6$H$_3$, *n*-C$_5$H$_{11}$

Scheme 1.10 Gold-catalyzed Markovnikov dimerization of iodoalkynes.

Methylaluminoxane (MAO) has been found to be an active catalytic precursor in benzene for the chemo- and regioselective head-to-tail dimerization of aromatic and aliphatic terminal alkynes to produce the corresponding *gem*-enynes in the excellent yields without formation of any other dimers (Scheme 1.11) [15]. Interestingly, in the case of terminal alkynes bearing an alkenyl functional group used, the *gem*-enyne can undergo an intermolecular [4 + 2] cycloaddition reaction to give alkynyl-substituted cyclohexene. A plausible pathway for the MAO-catalyzed dimerization of terminal alkynes is shown in Scheme 1.12; it involves a sequence of Al-alkynyl complex formation, a regioselective 1,2-head-to-tail insertion of alkyne into the Al-carbon bond, and the protonolysis of alkenyl complex.

R = ^{i}Pr, ^{n}Bu, ^{t}Bu, Ph, Me, *p*-^{t}BuC$_6$H$_4$,
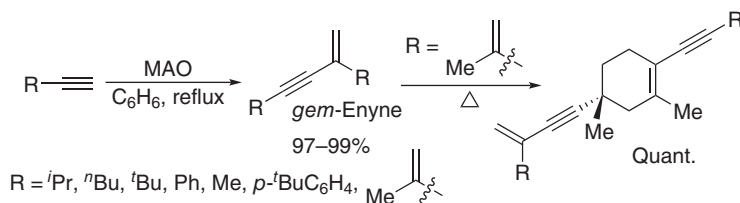
Scheme 1.11 MAO-promoted head-to-tail dimerization of terminal alkynes.

The intramolecular cyclic dimerization of α,ω-diynes is one of the atom economic synthetic ways for the construction of macrocyclic 1-en-3-ynes. Trost and coworker first reported the Pd(OAc)$_2$/tris(2,6-dimethoxyphenyl)phosphine (TDMPP)-catalyzed synthesis of the *exo*-macrocyclic 14-membered ring compound in 41% yield with high regioselectivity (Scheme 1.13) [16].
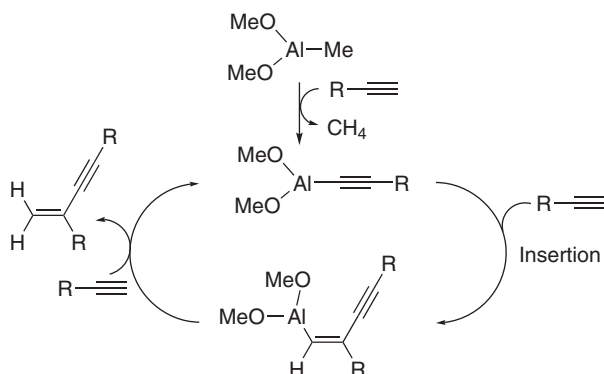
Scheme 1.12 Proposed mechanism for head-to-tail dimerization of terminal alkynes promoted by MAO.
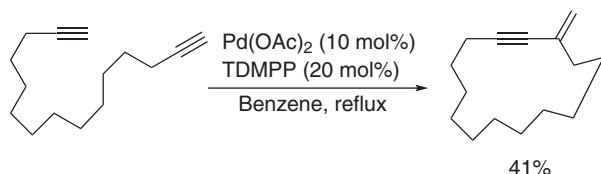
Scheme 1.13 Palladium-catalyzed synthesis of the *exo*-macrocycles.

In the presence of rare-earth silylamides, $Ln[N(SiMe_3)_2]_3$ (Ln = Y, La, Sm), the regio- and stereoselective dimerization of terminal alkynes occurs to give enynes in high yields with the use of amines as additives [17]. It has been found that the amine additives play a crucial role to depress the oligomerization and to control the regio- and stereochemistry of the dimerization. As shown in Scheme 1.14, when primary amine of aniline was used as the additive, the dimers of (*Z*)-head-to-head enynes from aromatic terminal alkynes could be obtained as the exclusive products. In contrast, when tertiary amine of $N(SiMe_2)_3$ was employed as the additive, nearly complete formation of head-to-tail dimers from aliphatic terminal alkynes was realized.
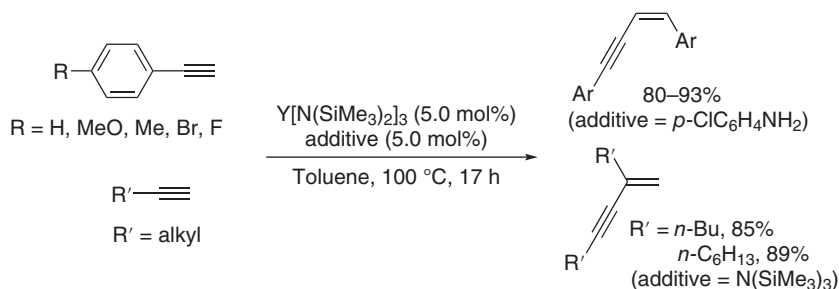
Scheme 1.14 Dimerization of terminal alkynes catalyzed by $Y[N(SiMe_3)_2]_3$/additive.

Interestingly, when α,ω-diynes were subjected to the dimerization conditions, a novel double dimerization takes place, leading to the formation of bisenynes (Scheme 1.15).
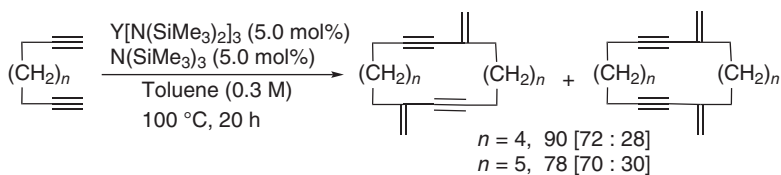
**Scheme 1.15** Bisenynes formation via double dimerization of diynes.

In addition, the actinide amides $U[N(SiMe_3)_2]_3$ also show good catalytic activity for conversion of terminal alkynes into dimers, trimers, and trisubstituted benzenes; the outcome of products greatly depends on the nature of terminal alkynes and the catalyst loading [18].

In addition, other rhodium complexes [19], hafnium carboranyl complex [20], have been also confirmed to be the efficient catalysts for the dimerization of terminal alkynes to selectively give *gem*-enynes, and a series of pincer complexes of Rh(I) has been found to be the efficient catalysts for the dimerization of terminal alkynes to afford a regioisomer mixture of *E*- and *gem*-enynes [21].

Moreover, very recently, *gem*-cross-dimerization of aryl alkynes and aliphatic alkynes or gas acetylene under mild reaction conditions has been developed in the presence of $Co(OAc)_2 \cdot 4H_2O$ and phosphine ligand [22].

1.2 *Anti*-Markovnikov (Head-to-Head) Dimerization of Terminal Alkynes

Gevorgyan and coworker studied the dimerization of aromatic terminal alkynes in the presence of $[(\pi\text{-allyl})PdCl]_2$/TDMPP to give the head-to-head *E*-dimers in fair to high yields with excellent regio- and stereoselectivity, although aliphatic terminal alkynes could not produce the corresponding head-to-head dimer at all (Scheme 1.16) [23]. Further studies have revealed that both good yields and high selectivity are observed only for the dimerization of aromatic terminal
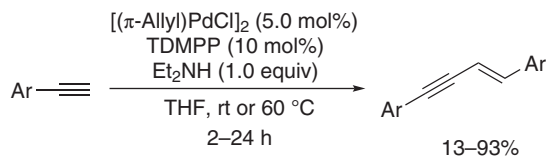

Ar = Ph, *p*-MeC$_6$H$_4$, *p*-MeOC$_6$H$_4$, *p*-NCC$_6$H$_4$, *p*-F$_3$CC$_6$H$_4$, 1-naphthyl, 2-naphthyl, 9-anthryl

Scheme 1.16 Palladium-catalyzed head-to-head dimerization of terminal aromatic alkynes.

alkynes possessing *ortho*-hydrogen atoms. Therefore, it has been found that the introduction of one group at *ortho*-position substantially diminishes the efficiency of the head-to-head dimerization, and substitution of both *ortho*-hydrogen atoms completely inhibits the process.

However, the combination of bis-*N*-heterocyclic carbene (NHC) palladium complex (IPr—Pd—IPr) and TDMPP has been found to show highly regio- and stereoselective head-to-head dimerization not only for aliphatic terminal alkynes but also for aromatic terminal alkynes even without *ortho*-hydrogen atoms. The reaction is general for a variety of terminal alkynes possessing various functional groups such as aryl, heteroaryl, alkyl, hydroxyl, propargyl ether, and amino groups [24]. In addition, the density functional theory (DFT) calculations have revealed that the reaction proceeds via a hydropalladation pathway (Scheme 1.17). Interestingly, further studies in the same group have found that combination of several NHC-based palladium precursors with phosphine additives selectively promotes head-to-head dimerization of terminal alkynes, but the addition of carboxylate anion to the catalytic system dramatically affects the selectivity favoring the head-to-tail dimerization reaction [25]. On the basis of computational studies, it has been disclosed that the formation of anionic palladium complexes or ion pairs in the presence of carboxylate anion deactivates the hydropalladation pathway, and the head-to-tail dimerization via the carbopalladation pathway is found to be preferential for the carboxylate-assisted reaction.
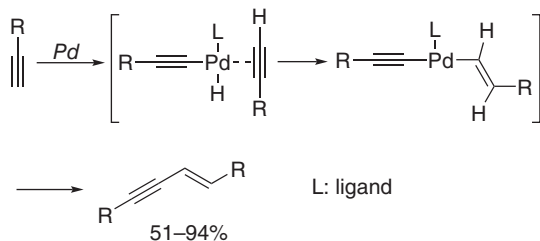
Scheme 1.17 Head-to-head dimerization of terminal acetylenes via a hydropalladation pathway.

In addition, in the presence of a catalytic amount of diethylphosphite, $Ni(cod)_2/t\text{-}Bu_3P$ [26], an iridium(III) hydride complex $IrHCl(TIMP_3)$ (Scheme 1.18) [27], copper(I) or copper(II) salts and oxides [28], and $[ReBr(CO)_3(thf)]_2/TBAF$
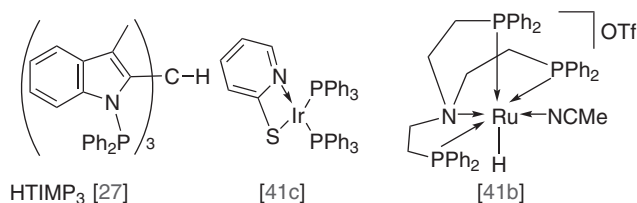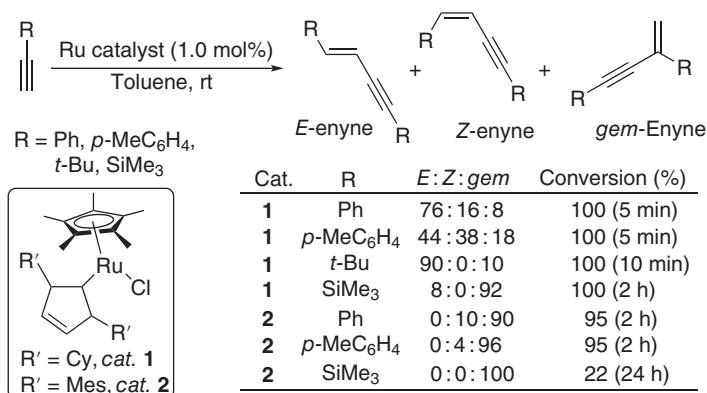

Scheme 1.18 Ligands and catalysts for dimerization of terminal alkynes.

[29] can also promote regioselective head-to-head dimerization of terminal alkynes with the *E*-enynes as major product.
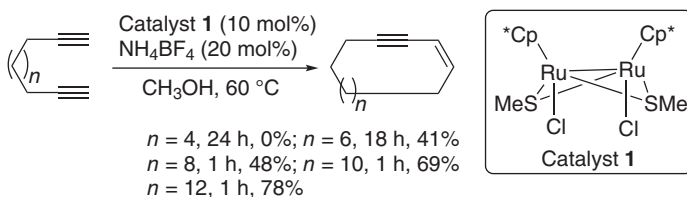
A series of ruthenium complexes have been used as the efficient catalysts in the *anti*-Markovnikov dimerization of terminal alkynes. As shown in Scheme 1.19, the NHC-coordinating unsaturated 16-electron half-sandwich ruthenium complexes can be easily prepared by the reaction of $[Cp*Ru(OMe)]_2$ with 1,3-diorganylimidazolium chloride in THF and show high catalytic activity in the dimerization of terminal alkynes without α-CH_2 moiety [30]. The regioselectivity of dimerization and the catalytic activity of catalysts greatly depend on the substituent's property of terminal alkynes. In addition, it is surprising that in the case of primary alkynes such as $PhCH_2{\equiv}CH$ used, no catalytic reaction occurs at all.

Cat.	R	E : Z : gem	Conversion (%)
1	Ph	76 : 16 : 8	100 (5 min)
1	p-MeC_6H_4	44 : 38 : 18	100 (5 min)
1	t-Bu	90 : 0 : 10	100 (10 min)
1	$SiMe_3$	8 : 0 : 92	100 (2 h)
2	Ph	0 : 10 : 90	95 (2 h)
2	p-MeC_6H_4	0 : 4 : 96	95 (2 h)
2	$SiMe_3$	0 : 0 : 100	22 (24 h)

Scheme 1.19 Ruthenium/*N*-heterocyclic carbene-catalyzed dimerization of terminal alkynes.

The thiolate-bridged diruthenium complexes $[Cp*RuCl(\mu_2\text{-}SR)_2RuCp*Cl]$ (R = Me, Et, *n*-Pr) have been found not only to be the effective catalysts for the head-to-head *Z*-dimerization of terminal alkynes [31] but also to show the good catalytic activity for the intramolecular cyclic dimerization of α,ω-diynes to produce the *endo*-cyclic (*Z*)-1-en-3-ynes in moderate to high yields with complete stereoselectivities (Scheme 1.20) [32].

Kirss and coworker found that ruthenium η^5-pentadienyl complex $(\eta^5\text{-}C_5H_7)$$(PPh_3)_2RuCl$ shows catalytic activity in the dimerization of phenyl acetylene in benzene at 20 °C for 24 hours with nearly quantitative conversion to afford a

n = 4, 24 h, 0%; n = 6, 18 h, 41%
n = 8, 1 h, 48%; n = 10, 1 h, 69%
n = 12, 1 h, 78%

Scheme 1.20 Ruthenium-catalyzed synthesis of the *endo*-macrocycle.

mixture of enynes with an 8 : 1 : 1 ratio of *Z*/*E*/*gem*-enyne (Scheme 1.21) [33]. It was also observed that the reaction so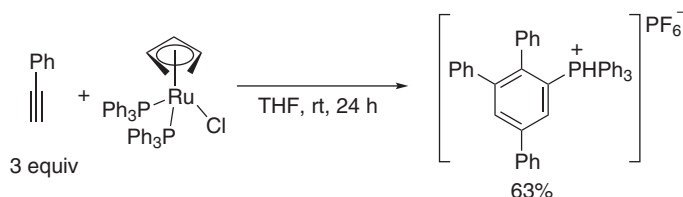lution slowly darkened to a brown color over 30 minutes, which was assumed to be the formation of polyphenyl phosphonium salts generated in situ by cyclotrimerization of phenyl acetylene with a stoichiometric amount of $(\eta^5\text{-}C_5H_7)(PPh_3)_2RuCl$ in the presence of KPF_6 in THF by Lin's group work (Scheme 1.22) [34].

Scheme 1.21 Ruthenium-catalyzed dimerization of phenylacetylene affording *Z*-enyne as a major product.
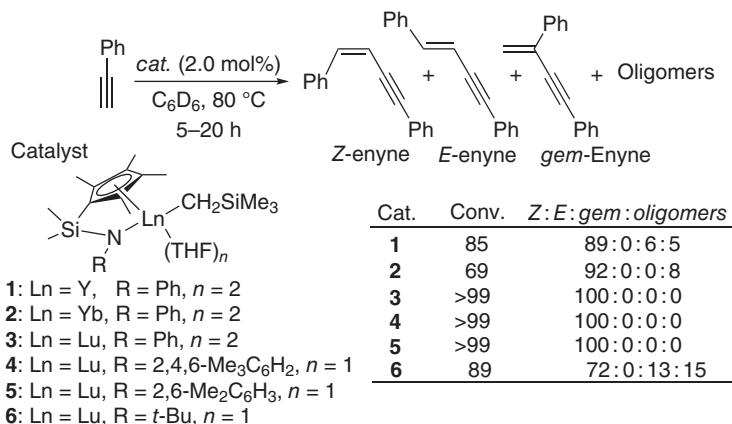

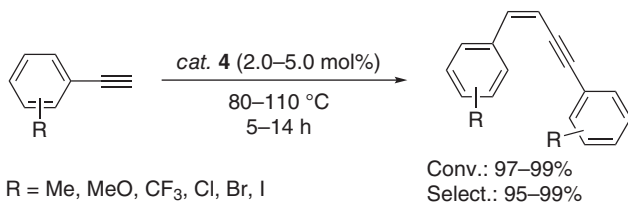**Scheme 1.22** The formation of aryl phosphonium salts.

It has been reported that in AcOH [35] or $AcOH/H_2O$ [36] mixture (1 : 1, v/v) at room temperature, $[RuCl(\mu\text{-}Cl)(\eta^6\text{-}p\text{-cymene})]_2$ could catalyze the dimerization of aromatic alkynes to give (*E*)-1,4-diaryl-1-buten-3-ynes with excellent regio- and stereoselectivity. In addition, $[RuCl(\mu\text{-}Cl)(\eta^6\text{-}p\text{-cymene})]_2/AcOH$ could promote the polyaddition of aromatic diynes affording conjugated homo- and copolymers featuring the repeat unit (—Ar—C≡C—CH=CH—) [37].

On the other hand, the (*Z*)-1,4-diphenyl-1-buten-3-yne could be obtained from the dimerization of phenyl acetylene, when a Ru(II) *cis*-dihydride $[(PP_3)RuH_2]$ was used as catalyst [38]. Other ruthenium complexes have been also used as the efficient catalysts in the head-to-head dimerization of aromatic terminal alkynes [39].

Hou and coworker have found that the lanthanide half-metallocene complexes show high catalytic activity in C_6D_6 to catalyze the dimerization of phenylacetylene to extremely afford head-to-head (*Z*)-dimer (Scheme 1.23) [40]. The representative results of the dimerization of various aromatic terminal alkynes with the use of complex **4** as a catalyst are summarized in Scheme 1.24. However, it should be noted that a novel solvent effect on the regioselectivity was also observed. For example, the dimerization of 4-methoxyphenyl acetylene in pure toluene gave a 67 : 33 mixture of the head-to-head and head-to-tail dimers, whereas that in the presence of a small amount of THF (c. 5 equiv per 4) yielded solely the head-to-head

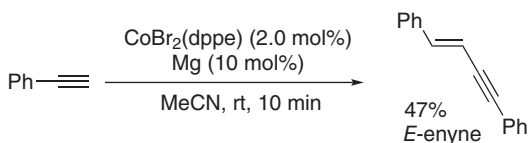**Scheme 1.23** Dimerization of phenylacetylene catalyzed by lanthanide half-metallocene complexes.

Cat.	Conv.	Z : E : gem : oligomers
1	85	89 : 0 : 6 : 5
2	69	92 : 0 : 0 : 8
3	>99	100 : 0 : 0 : 0
4	>99	100 : 0 : 0 : 0
5	>99	100 : 0 : 0 : 0
6	89	72 : 0 : 13 : 15

1: Ln = Y, R = Ph, *n* = 2
2: Ln = Yb, R = Ph, *n* = 2
3: Ln = Lu, R = Ph, *n* = 2
4: Ln = Lu, R = 2,4,6-Me₃C₆H₂, *n* = 1
5: Ln = Lu, R = 2,6-Me₂C₆H₃, *n* = 1
6: Ln = Lu, R = *t*-Bu, *n* = 1

Scheme 1.24 (*Z*)-dimerization of aromatic terminal alkynes.

R = Me, MeO, CF₃, Cl, Br, I

Conv.: 97–99%
Select.: 95–99%

(*Z*)-dimer. Similarly, the dimerization of 1-octyne, an aliphatic terminal alkyne in toluene-d_8, gave the head-to-tail dimer in 76% yield, while that in THF-d_8 afforded the head-to-head *Z*-dimer in 95% yield.

In addition, the excellent regio- and stereoselective dimerization of terminal alkynes to give (*Z*)-enynes can be also achieved by using other transition metal complexes (Scheme 1.18) [41].

It is very important and interesting to develop the cheap catalyst systems for dimerization of terminal alkynes to afford enynes.

With the use of magnesium as activator, CoBr₂(dppe) catalyzes the dimerization of phenyl acetylene in acetonitrile, leading to linear (*E*)-enyne in 47% yield as the best result in the absence of a Lewis acid, accompanied with the formation of cyclic trimers (Scheme 1.25) [42]. In the presence of a Lewis acid, the cyclotrimerization process is favored.

Scheme 1.25 Cobalt-catalyzed dimerization of phenylacetylene in the absence of Lewis acid.

Petit and coworker have also developed a HCo(PMe$_3$)$_4$-catalyzed highly regio- and stereoselective dimerization of various aromatic terminal alkynes at room temperature to afford corresponding (*E*)-1,4-enynes in good to high yields with excellent selectivity (Scheme 1.26) [43]. This method represent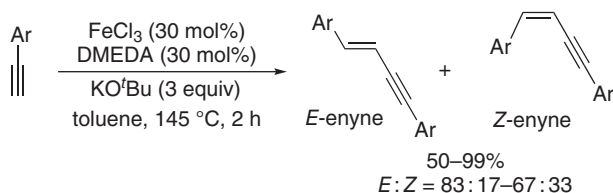s the first general (*E*)-selective dimerization of aromatic terminal alkynes under cobalt catalysis, and the mild catalytic conditions are tolerant of a large range of functionalized aromatic moieties. In addition, DFT calculations have revealed that the reaction proceeds via a C—H activation/hydrocobaltation pathway.

Scheme 1.26 Cobalt-catalyzed dimerization of aromatic terminal alkynes.

Iron salts are inexpensive and readily available. Dash and coworker reported the *E*-selective head-to-head dimerization of aromatic terminal alkynes catalyzed by FeCl$_3$/*N,N*-dimethylethylenediamine (DMEDA) in the presence of KO^{t}Bu (Scheme 1.27) [44]. Although the regioselectivity of dimerization is not ideal, this catalytic system represents an alternative to toxic and expensive transition metals for such kind of transformation.
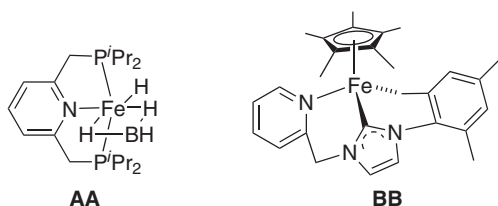

Ar = Ph, *p*-F/Br/CF$_3$/Me/MeOC$_6$H$_4$, *m*-F/Me/MeOC$_6$H$_4$,
3,5-di-F/di-MeC$_6$H$_3$, *o*-F/OMeC$_6$H$_4$

Scheme 1.27 FeCl$_3$-catalyzed dimerization of aromatic terminal alkynes.

On the other hand, Milstein and coworker have also developed an efficient [Fe(H)(BH$_4$)(^{i}Pr-PNP)]-catalyzed homodimerization of terminal alkynes and cross-dimerization of aromatic alkynes with trimethylsilylacetylene at room temperature, without the need for a base or other additives, to give *Z*-enynes in good to high yields, and the homodimerization of trimethylsilylacetylene afforded *gem*-enyne (Scheme 1.28, **AA**) [45]. As the complementary to *E*- and *Z*-selective iron catalyst, Song and coworker reported a *gem*-specific homo- and cross-dimerization of terminal alkynes catalyzed by a well-defined iron(II) complex containing Cp* and picolyl NHC ligands (Scheme 1.28, **BB**) [46].

Zhao and coworker also reported a catalytic system of CuSO$_4$·5H$_2$O (0.5 equiv)/diethyl phosphonate (1.1 equiv)/HNEt$_2$ (0.3 equiv) could promote the

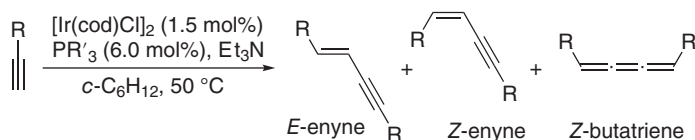**Scheme 1.28**   Iron catalysts for dimerization of terminal alkynes.

regioselective head-to-head dimerization of aromatic and aliphatic terminal alkynes to give the conjugated enynes in good to high yields with (*E*)-isomer as major product [47].

In addition, NHCs as the organocatalysts have been applied in the diverse organic transformation [48], and NHCs have also shown the catalytic activity in the head-to-head dimerization of styrenes [49] and dimerization of methacrylonitrile [50].

On the other hand, the cumulated butatrienes (C=C=C=C) with two sp^2 and two sp carbon atoms are highly reactive, which are interesting structures, and their derivatives are the versatile synthons in organic transformations; thus the synthetic methodology and applications of 1,2,3-butatrienes are one of the important topics in organic chemistry [51]. The transition metal-catalyzed dimerization of terminal alkynes has been developed as one of the efficient synthetic methods for the synthesis of 1,2,3-butatrienes.

As an earlier work, Wakatsuki and coworker reported on a catalytic version of the dimerization reaction using ruthenium complexes and phosphine ligands to give 1,2,3-butatrienes [52].

In the case of [Ir(cod)Cl]$_2$/PR$'_3$ used as catalyst system, the outcome of dimerization of terminal alkynes greatly depends on the nature of substituent of alkynes and the use of ligands to give (*E*)-enynes, (*Z*)-enynes, or 1,2,3-butatrienes [53]. As shown in Scheme 1.29, the use of PPh$_3$ resulted in the selective formation of (*E*)-enynes for dimethylphenyl alkyne, while the PPr$_3$ complex provided linear (*Z*)-enynes for the same alkyne or 1,2,3-butatrienes for 3,3-dimethyl-1-butyne.

PR$'_3$ = PPh$_3$, R = SiMe$_2$Ph: 93% (4 h); *E*-enyne : *Z*-enyne = 96 : 4
PR$'_3$ = PPr$_3$, R = SiMe$_2$Ph: 75% (26 h); *E*-enyne : *Z*-enyne : *Z*-butatriene = 2 : 96 : 2
PR$'_3$ = PPr$_3$, R = *t*-Bu: 74% (18 h); *E*-enyne : *Z*-enyne : *Z*-butatriene = 0 : 7 : 93

Scheme 1.29   Iridium-catalyzed dimerization of terminal alkynes.

Esteruelas and coworker have reported that in the presence of Et$_2$NH, OsHCl(CO)(P^{i}Pr$_3$)$_2$ catalyzes the dimerization of terminal alkynes (R = *t*-Bu, Cy,

Scheme 1.30 Osmium-catalyzed synthesis of butatrienes from dimerization of terminal alkynes.

Ph, and Me$_3$Si) to initially give *Z*- or *E*-1,4-disubstituted butatrienes (Scheme 1.30) [54]. It has been found that when R is *t*-Bu or Cy, the corresponding butatrienes are stable under the reaction conditions, and when R is phenyl group, the butatriene undergoes polymerization. In addition, in the case of trimethylsilyl acetylene used, the butatriene isomerizes into the *Z*-enyne.

1.3 Dimerization and Cross-dimerization of Terminal Alkenes

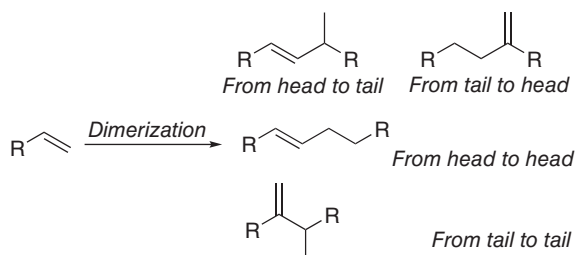The homo- and cross-dimerization of alkenes are important reactions for synthesis of higher alkenes, which are fundamental unsaturated hydrocarbons in the organic synthesis. The homodimerization of alkenes can afford theoretically four homodimers (Scheme 1.31).

Scheme 1.31 Dimers from dimerization of terminal alkenes.

The study on the homo- and cross-dimerization of alkenes catalyzed by the transition metal complexes has been a long history, and the catalyst systems generally gave (*E*)-1,3-disubstituted-1-butenes via a head-to-tail dimerization [55].

The catalytic dimerization of vinylarenes has been well studied, and the reactions can produce three dimer's isomers depending on the reaction conditions and catalysts (Scheme 1.31) [56].

Shirakawa and coworker have reported a Pd(OAc)$_2$/PPh$_3$/In(OTf)$_3$-catalyzed head-to-tail dimerization of vinylarenes to give (*E*)-1,3-diaryl-1-butenes

(Scheme 1.32) [57]. Since lack of $In(OTf)_3$ resulted in no reaction, thus the proposed mechanism involves the activation of vinylarenes by $In(OTf)_3$ to accept nucleophilic attack of palladium(0) complexes, giving oxidative adduct equivalents, which accept insertion of another vinylarene as shown in Scheme 1.33.

Ar = Ph, 2-naphtyl, *p*-$CF_3C_6H_4$, *p*-$HOCOC_6H_4$,
p-ClC_6H_4, *p*-BrC_6H_4, *p*-$ClCH_2C_6H_4$, *p*-MeC_6H_4

Scheme 1.32 Dimerization of vinylarenes catalyzed by $Pd(OAc)_2/In(OTf)_3$.

Scheme 1.33 Proposed mechanism of dimerization of vinylarenes catalyzed by $Pd(OAc)_2/In(OTf)_3$.
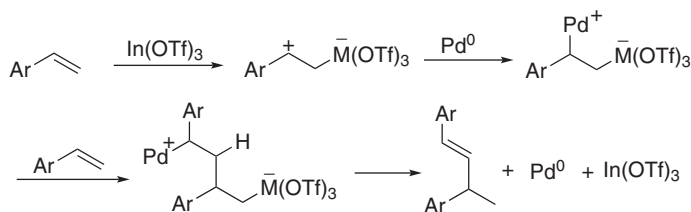
$NiCl_2(dppp)$ also shows high catalytic activity for the head-to-tail dimerization of vinylarenes having electron-donating and electron-withdrawing groups to give (*E*)-1,3-diaryl-1-butenes in high yields [58].

The examples of tail-to-head dimerization of terminal alkenes are very few. Jun and coworker have reported the dimerization of vinylsilanes promoted by a catalyst system of $[(COE)_2IrCl]_2$ and HCl to afford exclusive tail-to-head dimers at room temperature (Scheme 1.34) [59].

The simple $RuCl_3 \cdot nH_2O$ has been found to be the efficient catalyst in the dimerization of alkenes to afford either Markovnikov adducts or *anti*-Markovnikov adducts in a high stereospecific manner depending on the substituents of alkenes [60]. For example, the dimerization of α-methylstyrene in THF under N_2 for 24 hours produced Markovnikov dimer in 78%, and the dimerization of *N*,*N*-dimethylacrylamide with the relatively low reactivity gave *anti*-Markovnikov

R, R′, R″ = alkyl, Ph, $OSiPh_3$

Scheme 1.34 Iridium-catalyzed dimerization of vinylsilanes.

(head-to-head) dimer in 17% yield (Scheme 1.35). However, Kondo and coworker have found that in the presence of primary alcohols, the zero-valent ruthenium complex [Ru(η⁶-cot)(η²-dmfm)$_2$] can efficiently catalyze the head-to-head dimerization of styrenes to give (*E*)-1,4-diaryl-1-butenes (Scheme 1.36) [61]. In addition, this catalyst system is also effective for the selective linear cross-dimerization of styrenes with ethylene to give (*E*)-1-aryl-1-butenes in good yields and high selectivity.

Scheme 1.35 RuCl$_3$·nH$_2$O-catalyzed dimerization of terminal alkenes.

R = H, Me, OMe, F

Scheme 1.36 Ruthenium-catalyzed head-to-head dimerization of styrenes.

In addition, in a primary or secondary alcoholic solvents, RuCl$_3$(tpy)/Zn or [RuCl$_2$(C$_6$H$_6$)]$_2$/Zn can catalyze a linear codimerization of 2-no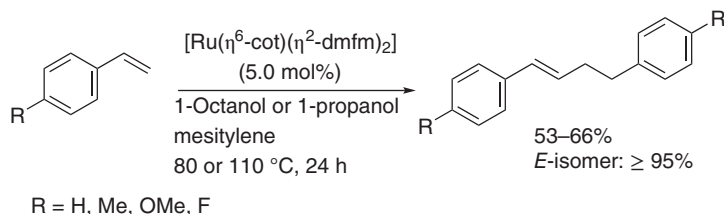rbornenes with acrylic compounds to afford the *exo-trans*-2-norbornylacrylates as major products with regio- and stereoselectivity [62].

The cross-dimerization of terminal alkenes via the addition of C—H bond to the other alkenes is one of the efficient synthetic methods to prepare higher alkenes.

Rhodium chloride has been found to be the efficient catalyst to catalyze the addition of ethylene or propylene to dienes, such as butadiene, isoprene, and 1,3-pentadiene, to afford 1,4-dienes, and rhodium and ruthenium chlorides also catalyze the dimerization of ethylene to butenes, butadiene to 2,4,6-octatriene, and methyl acrylate to dimethyl 2-hexenedioate [63].

Yi and coworker have reported an efficient catalytic system of RuCl(PCy$_3$)$_2$(CO)H/ HBF$_4$·OEt$_2$ for the hydrovinylation of alkenes [64]. For example, the reaction of styrene with excess amount of ethylene at room temperature produced the hydrovinylation product in 93% isolated yield (Scheme 1.37). Both terminal alkenes and dienes were found to give the hydrovinylation products in good to high yields.

Ph
+
RuCl(PCy$_3$)$_2$(CO)H (0.5 mol%)
HBF$_4$·OEt$_2$ (2.0 equiv)
Benzene, rt, 6 h

6.4 equiv

Ph
93%
+
Ph
Trace

Scheme 1.37 Ruthenium-catalyzed hydrovinylation of alkenes.

The transition metal-catalyzed asymmetric hydrovinylation [65] of alkenes (cross-dimerization of alkene with ethylene) has become one of the efficient methods for synthesis of chiral alkenes.

The use of ruthenium complex with chiral (*S*,*S*)-2-methylbicyclo[3.3.1]nona-2,6-diene ligand results in the asymmetric linear cross-dimerization between methyl methacrylate and 2,5 dihydrofuran to give the cross-dimer in 74% yield in 80% ee (Scheme 1.38) [66].
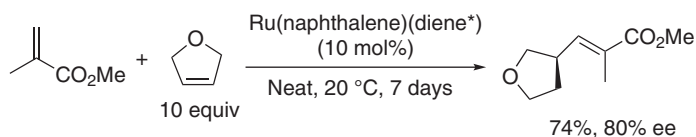
CO$_2$Me
+
O
Ru(naphthalene)(diene*)
(10 mol%)
Neat, 20 °C, 7 days

10 equiv

O
CO$_2$Me

74%, 80% ee

Scheme 1.38 Ruthenium-catalyzed asymmetric cross-dimerization.

The dinuclear rhodium complexes, [(Cp*Rh)$_2$(μ-CH$_2$)$_2$(MeCN)$_2$](BF$_4$)$_2$, [(Cp*Rh)$_2$(μ-CH$_2$)$_2$(CO)$_2$](BF$_4$)$_2$ [67], and Ru(η^6-naphthalene)(η^4-1,5-cod), show the catalytic activity for head-to-head dimerization of methyl methacrylate (MMA) in MeCN [68].

Ura and coworker have recently found that when RuCl$_3$·nH$_2$O/Zn—Cu/EtOH is used as a catalytic system, *N*-methyl-*N*-vinylacetamide and ethyl acrylate in dimethylamine (DMA) undergo a linear cross-dimerization to give two head-to-head cross-dimers (Scheme 1.39) [69]. The ratio of two cross-dimers greatly depends on the reaction temperature; at 100 °C, the cross-dimerization affords *N*-vinyl product selectively, and at 130 °C, *N*-alkyl product is also formed. In addition, the effect of solvents is considerable to affect the outcome of two products.

O
N
Me
1.1 equiv
+
CO$_2$Et
RuCl$_3$·nH$_2$O (5.0 mol%)
Zn-Cu (50 mol%)
EtOH (30 mol%)
DMA, temp.

O
N
Me
CO$_2$Et
N-vinyl product
+
O
N
Me
CO$_2$Et
N-alkyl product

100 °C, 5 h: 51% (100 : 0)
130 °C, 3 h: 72% (74 : 26)

Scheme 1.39 Ruthenium-catalyzed cross-dimerization of terminal alkenes.

The results of stoichiometric and catalytic reactions have revealed that the present cross-dimerization proceeds via ruthenacyclopentane intermediates.

The first highly selective intermolecular tail-to-tail homodimerization of styrenes and cross-dimerization of styrenes with unactivated alkenes to produce branched 1,1-disubstituted alkenes were reported by Ho's group [70]. As shown in Scheme 1.40, in the presence of a catalytic amount of in situ generated [(IPr)NiH]OTf, at room temperature styrene and 1-octene (3 equiv) undergo the tail-to-tail cross-dimerization to give 2-(1-phenylethyl)-1-octene, accompanied with the formation of 2,3-diphenyl-1-butene from the tail-to-tail homodimerization of styrene in a total yield of 95%. The ratio of cross-dimer: homodimer is 90 : 10.

R = Ar
R′ = Ar, alkyl

1,1-Disubstituted alkenes

R = Ph, R′ = *n*-hexyl, total yield: 95%; ratio: 90 : 10

Scheme 1.40 Nickel/NHC-catalyzed intermolecular tail-to-tail hydroalkenylation of styrenes with alkenes.

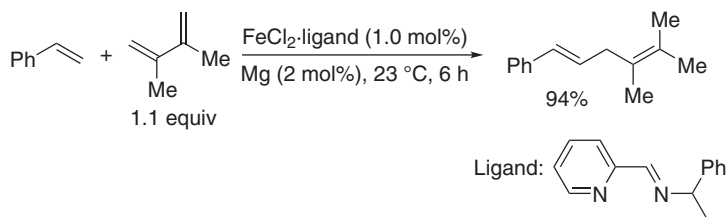Interestingly, Ritter and coworker reported an FeCl$_2$/iminopyridine-catalyzed 1,4-addition of α-alkenes to 1,3-dienes with high stereo- and regioselectivity to give linear 1,4-diene adducts [71]. For example, the addition of styrene to 2,3-dimethylbutadiene affords 1,4-diene in 94% yield, providing an efficient method for access to 1,4-dienes from 1,3-dienes (Scheme 1.41).

Scheme 1.41 Iron-catalyzed 1,4-addition of α-alkenes to 1,3-dienes.

Very recently, the iridium-catalyzed asymmetric hydroalkenylation of norbornenes with terminal alkenes has been reported [72].

1.4 Cross-dimerization of Different Alkynes or Alkynes with Alkenes

Development of the cross-dimerization of terminal alkynes or alkynes with alkenes is one of the challenging research topics due to the competitive homodimerization or di- and trimerization of the terminal alkynes and terminal alkenes (Scheme 1.42).

Scheme 1.42 Cross-dimerization of different alkynes or alkynes with alkenes.

In order to realize the chemoselective cross-dimerization, the catalyst systems should be able to selectively catalyze the reaction.

Trost and coworker reported the first Pd(OAc)$_2$/TDMPP-catalyzed cross-dimerization of a variety of terminal alkynes, RC≡CH (donor alkyne, R = alkyl, aryl, silyl) with electron-deficient internal alkynes and R′C≡C—EWG (acceptor alkyne or activated alkyne, R′ = alkyl, silyl; EWG = CO$_2$Me, COMe, SO$_2$Ph) affording *E*-regioisomer as single geometric isomer arising from head-to-tail cross-coupling reaction (Scheme 1.43) [73].

Scheme 1.43 Cross-dimerization of terminal alkynes with electron-deficient internal alkynes.

Their further studies disclosed that under the similar reaction conditions, the "unactivated" internal alkynes such as 2-butyn-l,4-diol and its diacetate derivative, 1-trimethylsilylpropargyl alcohol, could also undergo the cross-dimerization with terminal alkynes with good chemo-, regio-, and stereoselectivities [74]. Scheme 1.44 shows the cross-dimerization of trimethylsilylacetylene (5.0 equiv) to the propargyl alcohol at room temperature for 48 hours to afford the correspondin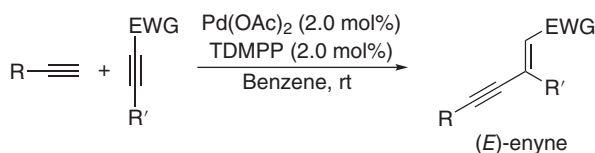g cross-dimer in 58% yield. The highly selective cross-dimerization of terminal alkynes with propargyl alcohol was applied in the synthesis of caulerpenyne analog.

Scheme 1.44 Palladium-catalyzed cross-dimerization of terminal alkynes with unactivated internal alkynes.

The combination of CuBr (5.0 mol%) and PdCl$_2$(PPh$_3$)$_2$ (2.5 mol%) in water has been also found to be the efficient catalyst system to catalyze only the addition of terminal alkynes to electron-deficient alkynes selectively, but not the homodimerization of the terminal alkynes (Scheme 1.45) [75].

$$R \!-\!\!\equiv\!\!- \quad + \quad R' \!-\!\!\equiv\!\!-EWG \xrightarrow[\text{H}_2\text{O, 60 °C or rt}]{\substack{\text{CuBr (5.0 mol\%)} \\ \text{PdCl}_2(\text{PPh}_3)_2 \text{ (2.5 mol\%)}}}$$

R = Ph, 1-cyclohexenyl, alkyl, Me$_3$Si
R′ = Ph, Me
EWG = COMe, CO$_2$Me

48–86%

Scheme 1.45 Copper-/palladium-catalyzed cross-dimerization of terminal alkynes with activated alkynes in water.

[IrCl(cod)]$_2$/phosphines also show the catalytic activation to catalyze the cross-dimerization of electron-rich terminal alkyne with an equivalent of electron-deficient internal alkyne such as alkynyl esters and alkynyl aldehydes [76]. The regioselectivity of *cis*-adduct via the addition of C—H bond to internal alkynes markedly depends on the ligands used, and when (*rac*)-bis(diphenylphosphino)-1,1′-binaphthalene (BINAP) was employed as a ligand, the cross-dimerization occurred with excellent regioselectivity. In addition, when dppe was used as a ligand, the substituted benzene derivatives from 1:2 cross-cyclotrimerizati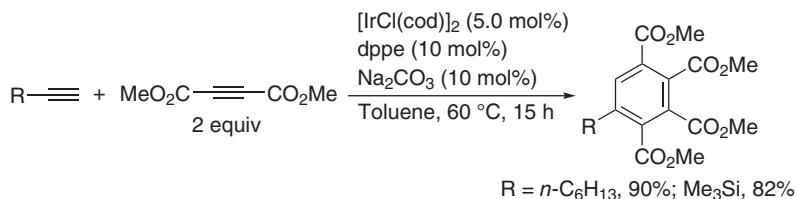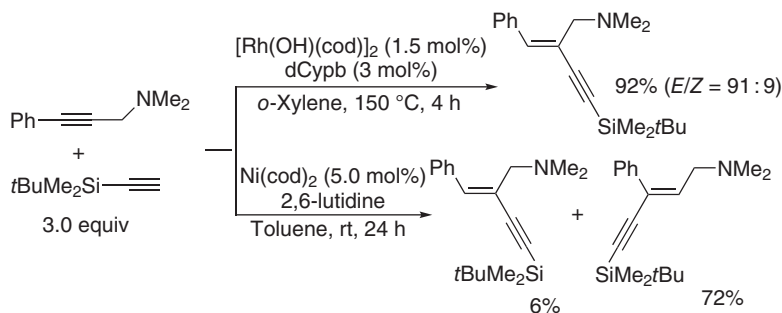on of terminal alkynes with dimethyl acetylenedicarboxylate (two equivalents) could be obtained in fair yield, and the yield can be improved in the presence of a small amount of Na$_2$CO$_3$ under mild conditions (Scheme 1.46).

$$R \!-\!\!\equiv\!\!- \quad + \quad \text{MeO}_2\text{C} \!-\!\!\equiv\!\!- \text{CO}_2\text{Me} \xrightarrow[\text{Toluene, 60 °C, 15 h}]{\substack{\text{[IrCl(cod)]}_2 \text{ (5.0 mol\%)} \\ \text{dppe (10 mol\%)} \\ \text{Na}_2\text{CO}_3 \text{ (10 mol\%)}}}$$

2 equiv

CO$_2$Me, CO$_2$Me, CO$_2$Me, CO$_2$Me

R = *n*-C$_6$H$_{13}$, 90%; Me$_3$Si, 82%

Scheme 1.46 Synthesis of substituted benzenes via 1:2 cross-cyclotrimerization.

Miura and coworker have described a remarkable ligand effect on the Ni(cod)$_2$-catalyzed cross-dimerization of aromatic alkynes with terminal silylacetylenes [77], and then they have also developed an interesting transition metal catalyst-controlled

Ph $\!-\!\!\equiv\!\!-$ NMe$_2$

+

*t*BuMe$_2$Si $\!-\!\!\equiv\!\!-$

3.0 equiv

$$\xrightarrow[\text{o-Xylene, 150 °C, 4 h}]{\substack{\text{[Rh(OH)(cod)]}_2 \text{ (1.5 mol\%)} \\ \text{dCypb (3 mol\%)}}}$$

Ph, NMe$_2$
92% (*E/Z* = 91:9)
SiMe$_2$*t*Bu

$$\xrightarrow[\text{Toluene, rt, 24 h}]{\substack{\text{Ni(cod)}_2 \text{ (5.0 mol\%)} \\ \text{2,6-lutidine}}}$$

Ph, NMe$_2$ + Ph, NMe$_2$
*t*BuMe$_2$Si, SiMe$_2$*t*Bu
6%, 72%

**Scheme 1.47** Catalyst-dependent regioselective cross-dimerization of terminal silylacetylene to propargyl amine.

switching of regioselective cross-dimerization terminal silylacetylenes to γ-arylated propargyl amines [78]. As shown in Scheme 1.47, in the presence of [Rh(OH)(cod)]$_2$/dCypb, the reaction of *t*-butyldimethylsilyl-acetylene with dimethyl(3-phenyl-2-propynyl)amine in *o*-xylene at 150 °C (bath temperature) produced 2-alkynylallylamine as the sole regioisomer in excellent yield with good stereoselectivity. On the other hand, if the same reaction was carried out using Ni(cod)$_2$/2,6-lutidine as catalyst system in toluene at room temperature, 3-alkynylallylamine was obtained as the major adduct in good yield.

Other rhodium complexes [79] and CoCl$_2$·6H$_2$O/dipime/Zn [80] have been also used in the cross-dimerization of terminal alkynes or internal alkynes with terminal alkynes.

Yi and coworker have reported a ruthenium acetylide complex Cp*(PPh$_3$) RuC≡CPh, generated in situ from the reaction of Cp*(PPh$_3$)(Cl)Ru=C=CHPh with a base to be the efficient catalyst for the cross-dimerization of terminal alkynes with activated and unactivated internal alkynes to yield enynes with high regio- and stereoselectivities, when R groups of terminal alkynes are *t*-Bu, *s*-Bu, and Me$_3$Si (Scheme 1.48) [81]. In addition, an intermediate of β-agostic species could be isolated from the reaction of Cp*(PPh$_3$)(Cl)Ru=C=CH^{t}Bu with 2-butyne in the presence of NaOMe, which showed an equally effective catalyst for the cross-dimerization (Scheme 1.49).
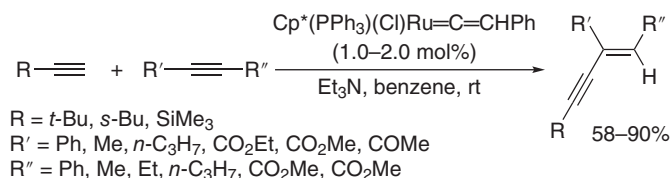
Scheme 1.48 Ruthenium-catalyzed cross-dimerization of terminal alkynes with internal alkynes.
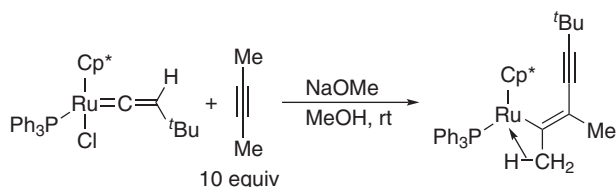
Scheme 1.49 Preparation of ruthenium β-agostic intermediate.

In addition, the use of Pd(OAc)$_2$ with some P,N-ligands shows effective activity for the homodimerization of terminal alkynes and cross-dimerization of terminal alkynes with internal alkynes with excellent yields even under solvent-free conditions. More importantly, in case of racemic propargylic alcohols employed as one of the reactants, the use of enantiomerically pure ligands resulted in the kinetic resolution of racemic propargylic alcohols [82]. For example, in the presence of

PHOX-ligand, the solvent-free reaction of 2.2 equiv of racemate 1-nonyn-3-ol with 1.0 equiv of ethyl 2-butyrate produced the cross-dimer in 43% yield with 53% ee (Scheme 1.50).
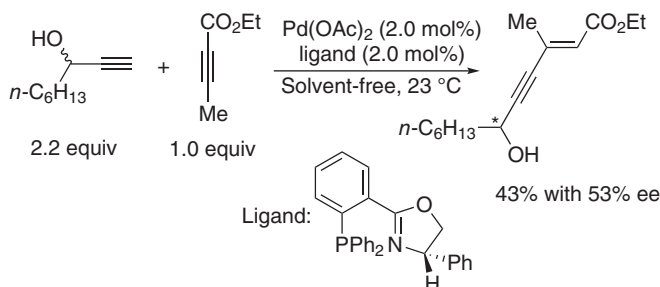
Scheme 1.50 Palladium-catalyzed cross-dimerization with kinetic resolution.

In addition, in the presence of palladium, the *E*-enynes formed in situ have been found to undergo a subsequent [4 + 2] benzannulation with 1,3-diynes to give pentasubstituted benzenes in moderate to good yields. Therefore, Yamamoto and coworker have developed a highly chemo- and regioselective formation of the benzene ring by a formal [2 + 2 + 2] sequential intermolecular trimerization of alkynes from three different acetylenic units (Scheme 1.51) [83].
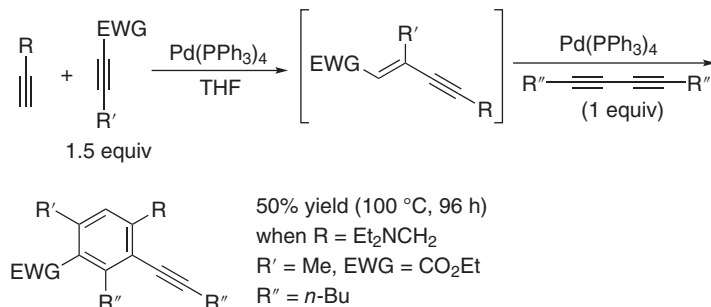
Scheme 1.51 Synthesis of pentasubstituted benzenes via formal [2 + 2 + 2] sequential cycloaddition of alkynes.

Other palladium complexes have been also found to be the efficient catalysts in the cross-dimerization of intermolecular terminal alkynes with internal alkynes [84].

It is much more interesting and challenging to develop the efficient catalyst system for the cross-dimerization between two kinds of terminal alkynes.

It has been found that the reaction of $(\eta^5\text{-}C_5Me_5)_2TiCl_2$ with two equivalents of ^iPrMgBr generated in situ will be the species of $(\eta^5\text{-}C_5Me_5)_2TiH$, which behaves as an efficient catalyst not only for the regioselective dimerization of terminal alkynes to 2,4-disubstituted 1-buten-3-ynes (head to tail, selectivity > 99%) in excellent yields but also for the chemoselective cross-dimerization of ethynyl-1-cyclohexene or phenylacetylene with less acidic terminal alkynes ($R'C\equiv CH$) (Scheme 1.52) [85].
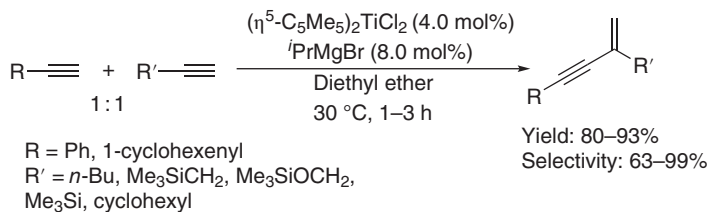
Scheme 1.52 Chemoselective head-to-tail cross-dimerization of two terminal alkynes.

However, note that when the cross-dimerization was carried out using a 1 : 1 mixture of two different normal alkyl-substituted alkynes, for example, 1-butyne and 1-hexyne, the four isomers were obtained with low chemoselectivity. The chemoselectivity can be improved by using one of the alkyne bearing secondary or tertiary alkyl substituents or Me_3Si group.

At room temperature, although $RuCl_2(=C=CHPh)(P^iPr_3)_2$/*N*-methylpyrrolidine shows high catalytic activity for the selective dimerization of electron-rich arylacetylenes to yield (*Z*)-ArCH=CH—C≡CAr in 90–97% selectivities, and the dimerization of (trimethylsilyl)acetylene affords a 15 : 85 mixture of (*E*)- and *gem*-dimerization products, but as shown in Scheme 1.53, the same catalyst system serves as good catalyst precursor for (*Z*)-selective cross-dimerization between two kinds of terminal alkynes: arylacetylenes and silylacetylenes [86]. The role of *N*-methylpyrrolidine is to abstract HCl, when a proposed catalytically active intermediate of alkynylruthenium species $[RuCl(C≡CPh)(P^iPr_3)_2]$ is formed.
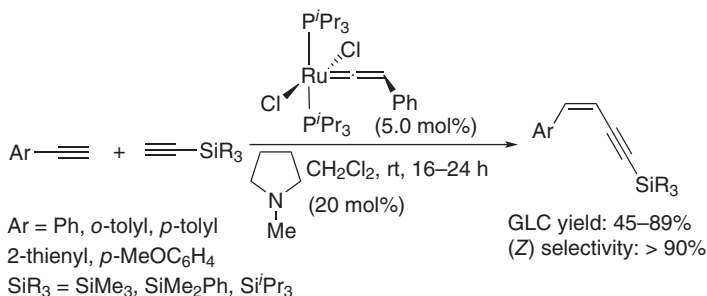
Scheme 1.53 Cross-dimerization of arylacetylenes with silylacetylenes catalyzed by vinylideneruthenium complexes.

In addition, other metal complexes have also been demonstrated to be the active precatalysts for the cross-dimerization of terminal alkynes: cationic actinide complex $[(Et_2N)_3U][BPh_4]$ with fair chemoselectivity [87], iridium(I) guanidinate complex phosphine [88], and dichlorocobalt(II) complex bearing a sterically demanding 2,9-bis(2,4,6-triisopropylphenyl)-1,10-phenanthroline [89].

On the other hand, 1,3-dienes are useful and versatile intermediates in organic synthesis via the transformation of carbon–carbon double bond and the activation of $C(sp^2)$—H bond. Therefore, it is one of the important and interesting research

topics to develop the efficient synthetic methods of 1,3-dienes. The transition metal-catalyzed intermolecular cross-dimerization of alkynes with alkenes via the activation of $C(sp^2)$—H bond has been well studied to be a straightforward and atom-efficient approach (Scheme 1.54).
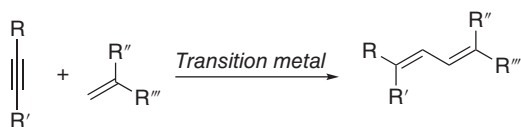
Scheme 1.54 Synthesis of 1,3-dienes via transition metal-catalyzed intermolecular enyne coupling reaction.

The first efficient catalytic linear cross-dimerization of alkynes with alkenes to give 1,3-dienes was reported in 1991 by Watanabe and coworker [90]. In the presence of Ru(cod)(cot), the intermolecular cross-dimerization of electron-rich alkynes, such as diphenylacetylene, 1-phenyl-1-propyne, 3-hexyne, and 3,3-dimethyl-1-butyne with electron-deficient α,β-unsaturated alkenes such as alkyl acrylates and *N*,*N*-dimethylacrylamide, occurs to give 1,3-dienes in fair to good yields with high regioselectivity. Scheme 1.55 shows the results from the reaction of diphenylacetylene with acrylates and acrylamide under different conditions.

R = OMe, 87%; R = OEt, 93%
in pyridine for 20 h
R = NMe$_2$, 81%, solvent-free, for 0.25 h
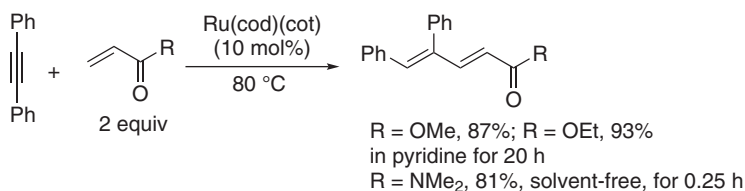
Scheme 1.55 Ruthenium-catalyzed synthesis of 1,3-dienes via cross-dimerization of alkynes with α,β-unsaturated alkenes.

With the use of bis(triphenylphosphine) iminium chloride ([PPN]Cl) or LiI as additives, Ru$_3$(CO)$_{12}$ catalyzes the reaction of terminal alkynes with alkyl acrylates in different chemoselective manner [91]. In the former case, γ,δ-alkynyl esters could

R = Ph, R′ = Me, 89%

R = Ph, R′ = Et, 64%
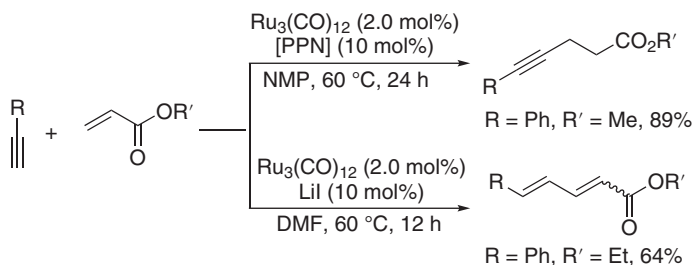
Scheme 1.56 Ru$_3$(CO)$_{12}$-catalyzed cross-dimerization of terminal alkynes with acrylates.

be obtained in good to high yields via a formal hydroalkynylation of alkyl acrylates; in the latter case, the linear cross-dimerization of terminal alkynes with alkyl acrylates via hydrovinylation of alkynes proceeds to give the corresponding conjugate dienes (Scheme 1.56). These two differently chemoselective carbon–carbon bond formation ways are controlled only by the nature of halide ions, either a chloride or an iodide with the use of additives.

In addition, the catalytic asymmetric hydroalkynylation of alkenes has been recently developed by Li's group [92].

$CpRu(PPh_3)_2Cl/NaPF_6$ shows the catalytic activity for the cross-dimerization of unactivated alkenes with unactivated alkynes in pyridine to provide an important method for the preparation of 1,3-dienes without electron-withdraw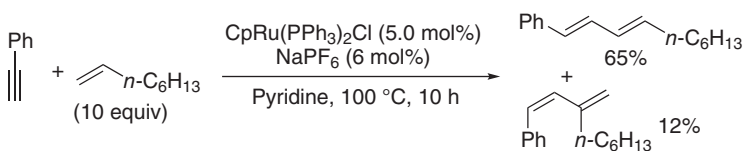ing group [93]. For example, the reaction of phenylacetylene with an excess amount of 1-octene yields linear and branched dienes in 65 and 12% yields, respectively (Scheme 1.57).

Ph
‖‖‖ + ⟍⟍ n-C$_6$H$_{13}$ →
(10 equiv)

$CpRu(PPh_3)_2Cl$ (5.0 mol%)
$NaPF_6$ (6 mol%)
Pyridine, 100 °C, 10 h

Ph ⟍⟍⟍ n-C$_6$H$_{13}$
65%
+
Ph n-C$_6$H$_{13}$ 12%

Scheme 1.57 Ruthenium-catalyzed cross-dimerization of unactivated alkene with unactivated alkyne.

Cheng and coworker have first developed a simple catalyst system for the reductive cross-dimerization of internal alkynes with electron-deficient conjugated alkenes in the presence of $CoI_2(PPh_3)_2/PPh_3/Zn$ with highly chemo-, regio-, and stereoselectivity (Scheme 1.58) [94].

R━━━R′ + ⟍⟍R″

$CoI_2(PPh_3)_2$ (5.0 mol%)
PPh_3 (16 mol%)
Zn (3.0 equiv)
$MeCN/H_2O$, 80 °C, 12 h

R ⟍⟍ R″
      |
      R′
48–98%

R = Ph, Et, CO_2Me, CO_2Et
R′ = alkyl, Ph, SiMe$_3$
R″ = CO_2Bu, CN, SO_2Ph, CO_2Me
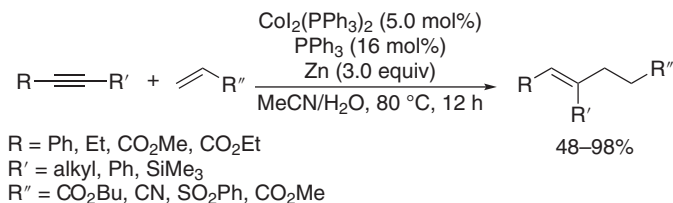
Scheme 1.58 Cobalt-catalyzed reductive cross-dimerization of internal alkynes with conjugated alkenes.

The cobalt-catalyzed Alder-ene reaction between internal alkynes and terminal alkenes to give 1,4-dienes was first reported by Hilt's group (Scheme 1.59) [95]. The reaction is proposed to involve the coordination of the two starting unsaturated compounds in the coordination sphere of the cobalt center to form a cobalt acycle intermediate and a subsequent β-hydride elimination and reductive elimination to yield 1,4-dienes.

Trost and coworker have reported a regioselective ruthenium complexes catalyzed by the cross-dimerization of silylalkynes with terminal alkenes with

R′, R″ = alkyl, aryl, COOEt
R‴ = alkyl, aryl, SiMe$_3$
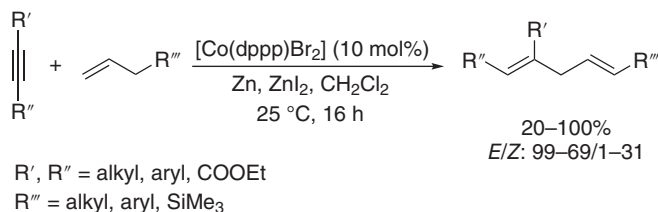
Scheme 1.59 1,4-Diene syntheses by a cobalt-catalyzed Alder-ene reaction.

complete control of regioselectivity by the silyl substituent to give geometrically defined vinylsilanes (Scheme 1.60) [96]. This protocol can be used as one of the key steps in the total synthesis of amphidinolide P [97].
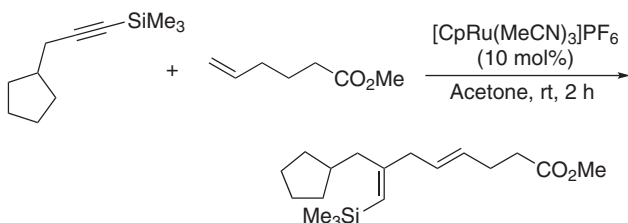
Scheme 1.60 Ruthenium-catalyzed regioselective cross-dimerization of silylalkyne with terminal alkene.

Also, [PdCl$_2$(cod)] or [Pd$_2$(dba)$_3$] [98], [Rh(cod)$_2$]BF$_4$ [99], CoI$_2$/Zn/ZnI$_2$ [100], and [(PPh$_3$)$_3$RuH(CO)Cl] [101] also have been reported in the applications of cross-dimerization of alkyne with alkenes to efficiently give 1,3-dienes.

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