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Cobalt- and Nickel-Catalyzed Regio- and Stereoselective Reductive Coupling of Alkynes, Allenes, and Alkenes with Alkenes

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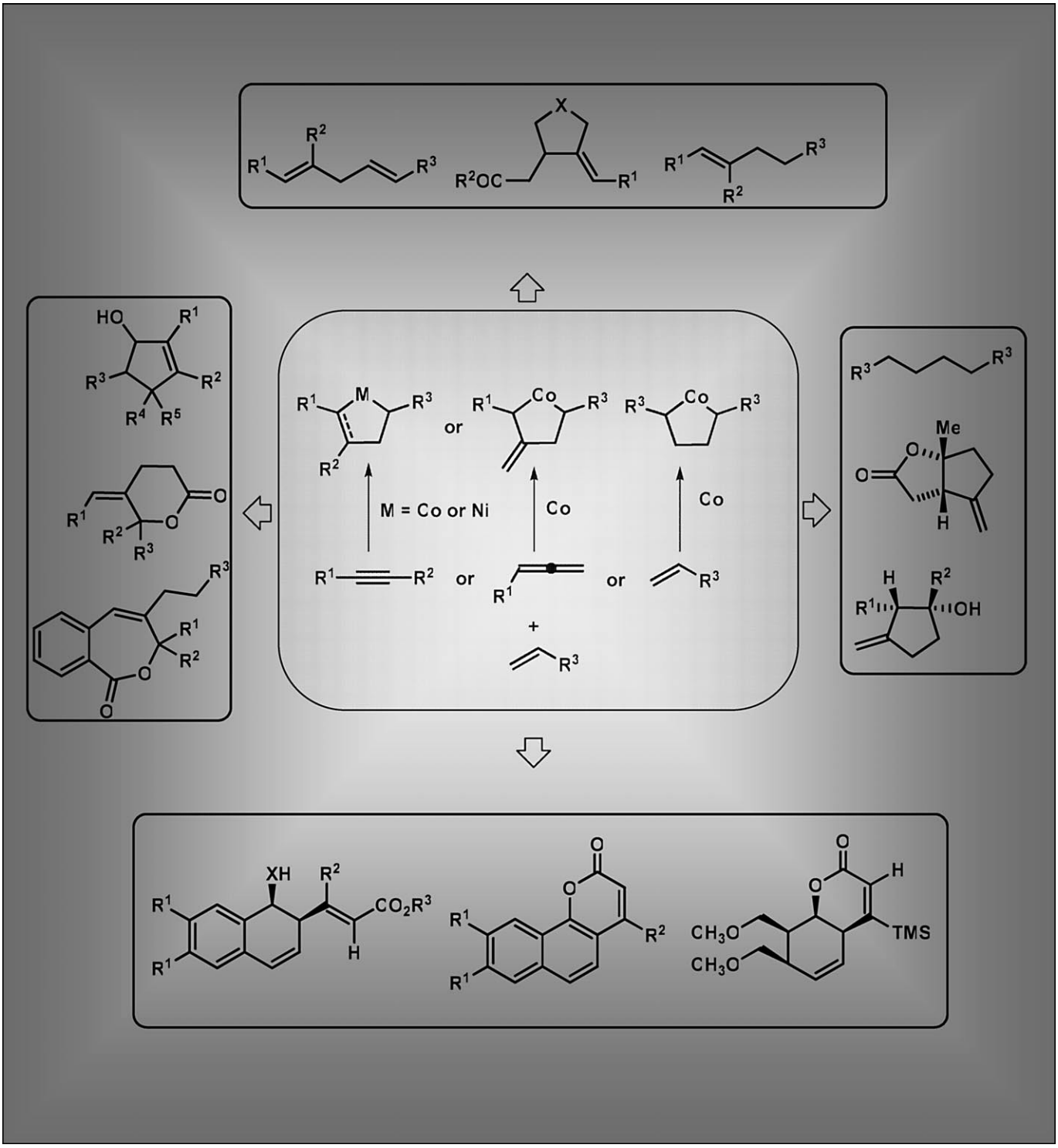

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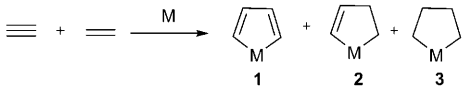
Abstract: Transition-metal-catalyzed coupling of two different C–C π components through a metallacycle intermediate is a highly atom economical method to construct C–C bonds in organic synthesis. The metal-catalyzed coupling of an alkene and alkyne generally gives an Alder-ene or reductive coupling product. In this article, we focus on the cobalt- and nickel-catalyzed reductive coupling of alkynes, allenes, and alkenes with alkenes. These reductive coupling reactions provide convenient methods for the synthesis of various alkenes, dienes, functionalized alkanes, lactones, lactams, and cyclic alcohols in a highly regio- and stereoselective manner. A chemselective formation of metallacyclopentene intermediate from the two different C–C π components and a low-valence metal species plays a key role for the high regio- and stereoselectivity of the catalytic reaction.

Keywords: cobalt · enyne coupling · homogeneous catalysis · nickel · reductive coupling

Introduction

The development of mild, chemo-, regio-, and stereoselective methods for the coupling of two different carbon–carbon π components catalyzed by metal complexes to construct carbon–carbon bonds has received considerable attention recently.[1–3] Examples of these coupling reactions include reductive coupling of alkyne/alkyne, alkyne/alkene, allene/alkene, and alkene/alkene.[1–3] Most of these coupling reactions are believed to proceed mechanistically via metallacycle intermediates. These coupling reactions provide convenient methods for the synthesis of various alkenes and functionalized alkanes in a highly regio- and stereoselective manner. It is known that ruthenium, rhodium, cobalt, nickel, and palladium complexes are efficient catalysts for these types of reactions.

The proposed mechanisms for the transition-metal-catalyzed coupling of an alkyne and alkene generally involves the coordination of these two substrates to a low-valence metal center followed by oxidative cyclometalation to give a metallacyclopentene intermediate as key steps. Theoretically, three types of metallacycles including metallacyclopentadiene **1**, metallacyclopentene **2**, and metallacyclopentane **3** can be formed in the reaction [see Eq. (1), the substituents on the alkyne and alkene are neglected for clarity]. In view of the fact that alkyne generally shows higher coordination ability and reactivity than alkene, we expect that the formation of **1** from an alkyne and alkene solution should be more favorable than **2** and **2** in turn is more favorable than **3**. To our surprise, in many of the coupling reactions of alkynes and alkenes, **2** appears to form more readily than the other two metallacycles.



1 **2** **3** (1)

A possible explanation for the high chemoselectivity of metallacyclopentene **2** relative to **1** is based on the bond-angle strain of the metallacycle rings. Lower bond-angle strain is expected for **2** than for **1** and **3**, due to the difference of normal bond angle of sp^3 and sp^2 carbon atoms in the metallacycle ring. It is known that for a planar five-membered ring, the total of the five angles of the ring is 540°, which is the largest value for a five-membered ring. The value becomes smaller, if the five-membered ring becomes nonplanar. By assuming that the normal bond angle for a carbon–metal–carbon in a five-membered metallacycle is ≈80° (based on the results of X-ray structural determination of five-membered metallacycles)[4–6] and the bond angles for sp^2 and sp^3 carbons are 120 and 109.5°, the ideal total value of the five angles in the ring for **1**, **2**, and **3** should be 560, 539, and 518°, respectively. Comparing with the value of 540° for a planar five-membered ring, the bond angle strain of metallacyclopentene **2** is expected to be smallest, because the ideal total angle of 539° is very close to the value of 540°. However, for the formation of metallacycle **1**, substantial contraction of the bond angle from 560 to 540° is necessary and thus, its bond-angle strain is expected to be larger than that of **2**. It is worth noting that a nonplanar structure (<540°) of **1** further increases the angle strain, but should reduce the repulsion between the substituents on the ring. For metallacycle **3**, some angle strain is expected, if the metallacycle is close to planar. However, the angle strain can be reduced, if the metallacycle becomes nonplanar. As a result, we expect that **3** should also have a small bond-angle strain, but is likely to be bigger than **2**. In the literature, the structures of many five-membered metallacycles have been reported.[4–6] In agreement with the above analysis, structure **1** is generally planar, **3** is nonplanar, and **2** generally showed slight distortion to the planar structure. Thus, the bond-angle strain analysis appears to favor the formation of **2** relative to **1** and **3**. In addition, for disubstituted alkynes, the formation of metallacyclopentadiene **1** is further inhibited by the steric repulsion raised by the substituents on the planar ring. Based on our experience and the results of literature reports, a suitable pairing of

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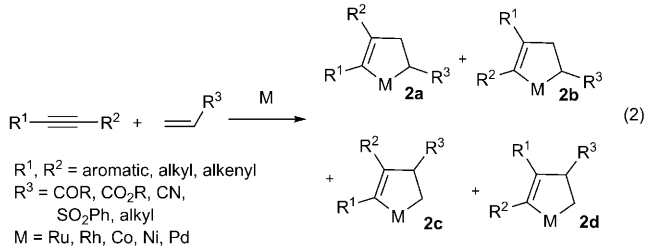
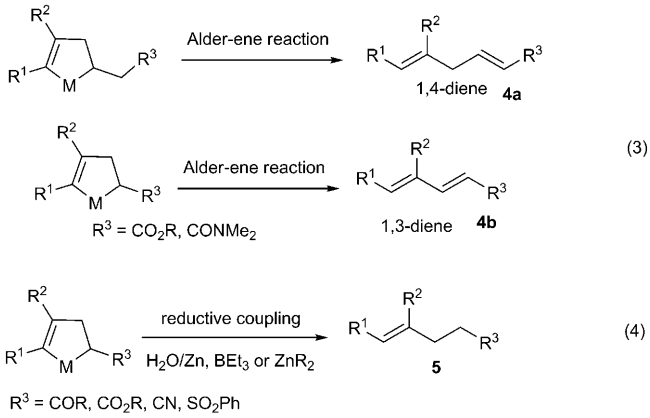
alkyne and alkene for an enyne coupling reaction would be a disubstituted alkyne and an activated alkene.

For the enyne coupling to be beneficial to organic synthesis, the control of regiochemistry of metallacyclopentene intermediate is crucial. In principle, four different regioisomers of metallacyclopentenes **2a–d** can be formed from the intermolecular coupling of an unsymmetrical alkyne and alkene [Eq. (2)]. Such control can be achieved by tuning both electronic and steric effects of the alkyne and alkene substrates and the choice of the catalyst. In general, a large or electron-withdrawing group prefers to stay at the *ortho* position near to the metal of the metallacyclopentene. As a result, **2a** or **2b** is more favorable than the other two regioisomers. Moreover, if R^1 is more electron-withdrawing or larger in size than R^2, **2a** should be most favorable.



(2)

There are two familiar types of products, Alder-ene and reductive coupling products, from transition-metal-catalyzed intermolecular coupling reaction of alkynes and alkenes. Metallacyclopentene is a common intermediate in both reactions. If β-hydride elimination of the metallacyclopentene intermediate is faster than protonation, the Alder-ene type product **4a** or **4b** is obtained [Eq. (3)]. On the other hand, if protonation is faster than β-hydride elimination, the reductive coupling product **5** is produced [Eq. (4)]. The reaction type is mainly determined by the nature of metal complex, reaction conditions, and alkenes used.[1–3]



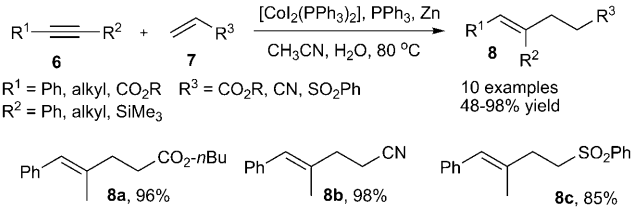
(3)

(4)

Previously, the Alder-ene type enyne coupling reaction was reviewed by Trost's group[1a–c] and the reductive-type three-component coupling reactions and the coupling of carbon–carbon π components with carbonyl compounds or imines were reviewed by Montgomery,[2b–c] Ikeda,[2d–e] and Jamison.[2f–g] Up to now, there is no review available in the literature mainly for the reductive coupling of two different carbon–carbon π components. In this article, we will highlight cobalt- or nickel-catalyzed reductive coupling reactions of alkynes, alkenes, and allenes with alkenes and the related reactions.

Cobalt-Catalyzed Intermolecular Reductive Enyne Coupling

In 2001, we observed a cobalt-catalyzed intermolecular reductive coupling of alkynes and activated alkenes using water as a proton source and zinc as a reducing agent.[7a] Thus, the reaction of 1-phenyl-1-propyne (**6a**) with *n*-butyl acrylate (**7a**) in the presence of $[Co(PPh_3)_2I_2]$ (5 mol%), PPh_3, water, and zinc metal in CH_3CN at 80 °C gave reductive coupling product **8a** in excellent yield (Scheme 1). The



Scheme 1. Cobalt-catalyzed intermolecular reductive coupling of alkynes and activated alkenes.

catalytic reaction is highly regio- and stereoselective with the β-carbon of acrylate group attached to the methyl-substituted alkyne carbon and the phenyl and methyl groups from the alkyne moiety *cis* to each other. The presence of suitable amount of PPh_3 and water are crucial for the success of catalytic reaction.

Under similar reaction conditions, 1-phenyl-1-propyne (**6a**) also undergoes reductive coupling with acrylonitrile and vinyl phenyl sulfone to provide products **8b** and **8c** in 98 and 85% yields, respectively. Similarly, various symmetrical and unsymmetrical alkynes react with activated alkenes to give the corresponding reductive coupling products **8** in 48–81% yields in a highly regio- and stereoselective manner. The structures and yields of products **8a–c** are shown in Scheme 1.

A possible reaction mechanism for the reductive enyne coupling is shown in Scheme 2. Reduction of Co^{II} to Co^{I} by zinc powder initiates the catalytic reaction. Highly chemoselective coordination of an alkyne and alkene to the Co^{I} center followed by regioselective oxidative cyclometalation yields cobaltacyclopentene intermediate **9**. Protonation of **9** by water affords reductive coupling product **8** in a highly regio- and stereoselective manner and a Co^{III} species. The latter is then reduced by Zn to regenerate the active Co^{I} species. An isotope-labeling experiment with D_2O as the proton source for the reductive coupling of **6a** and vinyl sulfone **7c** supports the proposed protonation step (Scheme 2).

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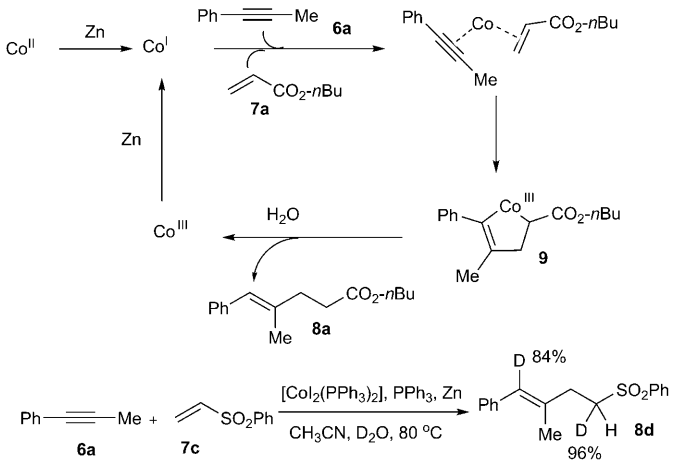
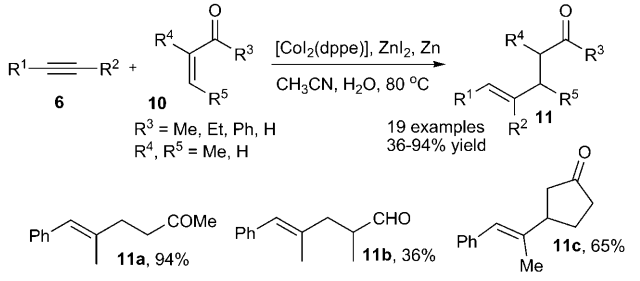


Scheme 2. A proposed mechanism for the reductive coupling of alkyne and acrylate.

In product **8d**, the olefinic proton and one of the protons attached to the α-carbon of SO_2Ph in **8d** were deuterated in 84 and 96%, respectively.

Although the present cobalt-catalyzed reductive enyne coupling reaction worked well with acrylates, acrylonitrile, and vinyl sulfone, the reductive coupling does not proceed with enones and enals. Fortunately, we observed that use of the Lewis acid ZnI_2 successfully led to the reductive coupling of enone and enal with alkyne in the presence of a bidentate cobalt complex, Zn, and water.[7b] Other Lewis acids such as $ZnCl_2$, CuI, and CuCl were also active. Thus, treatment of **6a** with methyl vinyl ketone (**10a**) in the presence of $[CoI_2(dppe)]$ (5 mol%; dppe = 1,2-bis(diphenylphosphino)ethane), ZnI_2 (10 mol%), water, and zinc metal powder in CH_3CN at 80°C gave reductive coupling product **11a** in excellent yield (Scheme 3). A similar regio- and stereoselectivity as that shown in Scheme 1 was also found for the present reaction. Examples of the structures of products **11** and yields are shown in Scheme 3. ZnI_2 probably plays two roles in the reaction. First, it likely acts as a mild Lewis acid to remove a halide from the Co^I center and to assist the coordination of the alkynes and alkenes to the Co^I center. Second, it activates the vinyl ketone through coordination to the keto oxygen.

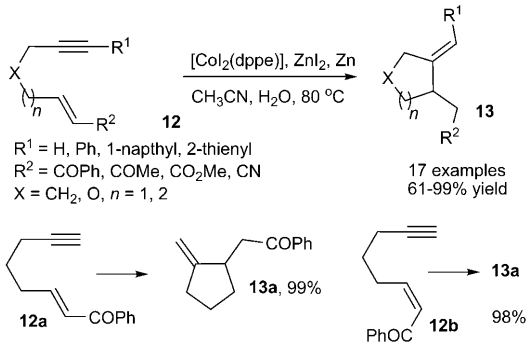


Scheme 3. Cobalt-catalyzed intermolecular reductive coupling of alkynes and enones or enals.

The catalytic reaction is compatible with various internal alkynes and substituted enones and enals. Interestingly, even cyclic enones efficiently participate in the reductive coupling with alkynes.

Cobalt-Catalyzed Intramolecular Reductive Coupling of Alkynes with Activated Alkenes

An intramolecular version of reductive enyne coupling was also examined under the cobalt-catalyzed reaction conditions shown in Scheme 4.[7b] Enyne **12a** with an electron-deficient *trans*-alkene tethered to a terminal alkyne moiety was converted to cyclic product **13a** in 99% yield in the presence of $[CoI_2(dppe)]$, ZnI_2, water, and zinc metal powder in CH_3CN. Under similar reaction conditions, *cis*-enyne **12b** also worked equally well to give the same product **13a** in 98% yield. It is interesting to note that in the intermolecular enyne reductive coupling, terminal alkynes generally do not react with activated alkenes, but undergo self cyclotrimerization to give the corresponding aromatics.[8] Internal alkynes with an aryl or alkyl substituent are compatible for the intramolecular reductive coupling. Similarly, acrylonitrile- and acrylate-tethered alkynes also worked very well.



Scheme 4. Cobalt-catalyzed intramolecular reductive enyne coupling.

Cobalt-Catalyzed Intermolecular Reductive Coupling of Propargyl Alcohols with Activated Alkenes

The cobalt-catalyzed reductive enyne coupling methodology was successfully applied to the synthesis of various six-membered lactones and lactams (Scheme 5).[7b] The reductive coupling of 3-phenylpropargyl alcohol (**14a**) with methyl acrylate (**7b**) in the presence of $[CoI_2(dppe)]$ (5 mol%), PPh_3, water, and zinc metal powder in an 1:3 ratio of CH_3CN and 1,4-dioxane at 80°C provided six-membered lactone **15a** in 80% yield with an excellent *Z* stereoselectivity of the *exo* carbon–carbon double bond (Scheme 5). The use of the mixed CH_3CN/1,4-dioxane solvent is crucial to get **15a** in

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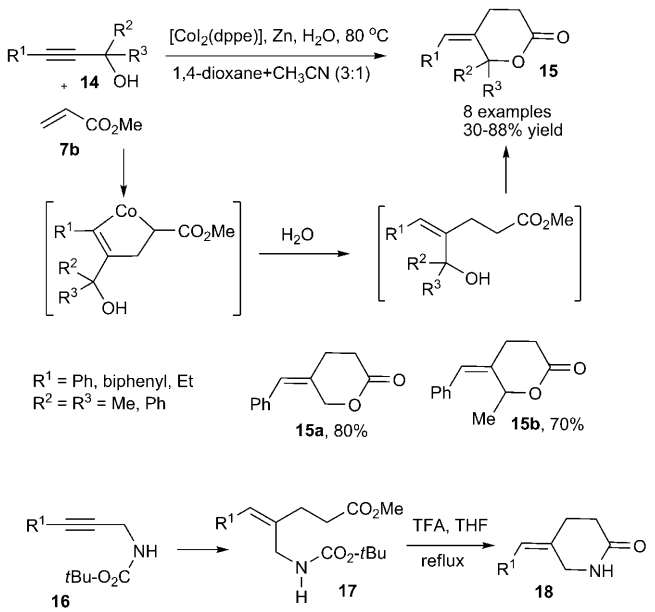
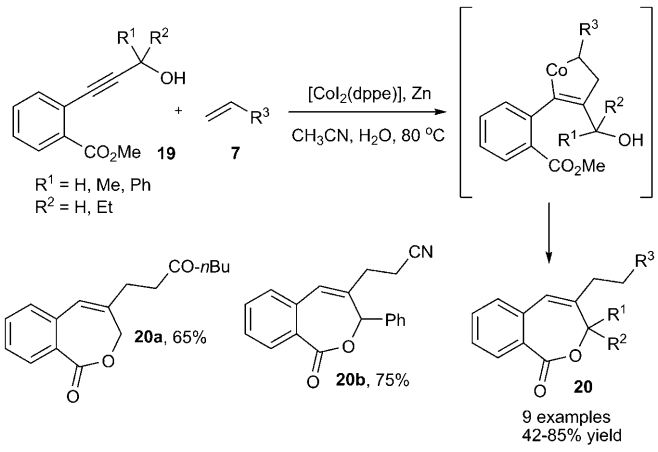


Scheme 5. Cobalt-catalyzed reductive coupling of propargyl alcohols and amines with methyl acrylate.

very high yield. Similarly, various propargyl alcohols gave six-membered ring lactones **15** in good yields. In addition, the synthesis of lactam **18** was achieved from propargylcarbamate **16** and methyl acrylate under similar cobalt-catalyzed reaction conditions, followed by treatment of product **17** with TFA in THF (Scheme 5).

This methodology was further applied to the synthesis of seven-membered lactones (Scheme 6).[7b] 2-(3-Hydroxyprop-1-ynyl)benzoate **19a** possessing an ester group at the *ortho* position of the phenyl ring reacted with *n*-butyl acrylate (**7a**) in the presence of $[CoI_2(dppe)]$ (5 mol%), water, and zinc metal powder in CH_3CN at 80°C to give seven-membered lactone **20a** in 65% yield. In the reaction two different types of lactonization products are possible. As in

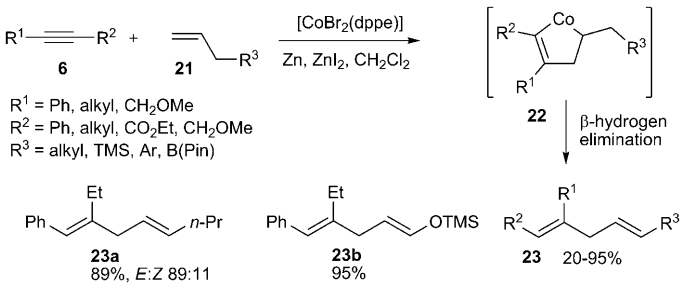


Scheme 6. Cobalt-catalyzed reductive coupling of substituted 3-arylpropargyl alcohols and activated alkenes.

Scheme 6, the hydroxyl group at the propargyl alcohol moiety might cyclize with the ester group on the acrylate moiety to afford a six-membered-ring product. Another possibility is an intramolecular cyclization of the hydroxyl group to the ester group on the phenyl ring to give a seven-membered lactone. In the reaction, the seven-membered cyclic lactone was only observed. These results are interesting in view of the fact that it is generally more favorable for the formation of a six-membered ring than of a seven-membered ring. This high selectivity might be explained based on the cobaltacycles formed in the reaction. The cobaltacyclopentene intermediate will place the hydroxyl group in proximity to the aromatic ester group, thereby facilitating the formation of seven-membered ring lactone even before the catalytic cycle is complete. Various activated alkenes **7** and alkynes **19** with different substituents at the propargylic position were successfully employed in the reaction. In all cases, seven-membered ring lactone **20** was observed exclusively in good to moderate yields.

Cobalt-Catalyzed Coupling of Alkynes and Unactivated Alkenes

Very recently, Hilt and Treutwein reported a cobalt-catalyzed intermolecular coupling (Alder-ene reaction) of unactivated alkenes with alkynes (Scheme 7).[9] In the reaction,



Scheme 7. Cobalt-catalyzed Alder-ene reaction of alkynes and unactivated alkenes.

alkynes **6** couple with alkenes **21** in the presence of $[CoBr_2(dppe)]$, Zn, and ZnI_2 in CH_2Cl_2 to give 1,4-diene products **23** in good to excellent yields with a high stereoselectivity. The structures of products **23a**,**b** and the corresponding yields are shown in Scheme 7.

It is surprising that in the cobalt-catalyzed reaction of alkynes with activated alkenes, the reductive coupling product **8** or **11** was observed, but in the present reaction the 1,4-diene coupling product was formed. Presumably, *exo* β-hydrogen elimination of the cobaltacyclopentene intermediate **22** from an alkyne and unactivated alkene is very efficient relative to other competing processes (Scheme 7).

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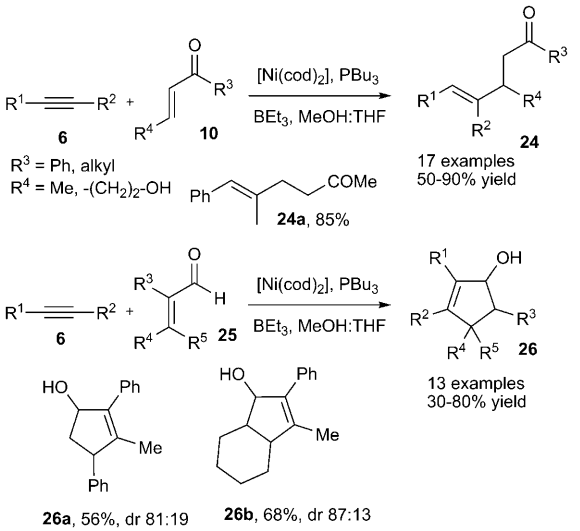
Nickel-Catalyzed Reductive Coupling of Alkynes and Activated Alkenes

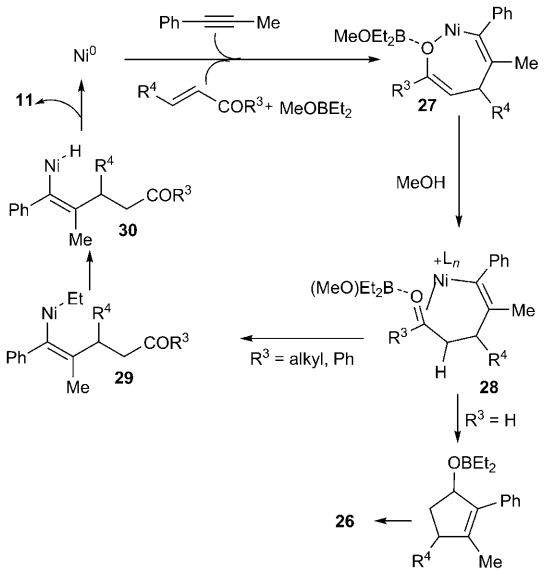
Recently, Montgomery's group reported a nickel-catalyzed intermolecular reductive coupling of alkynes and activated alkenes using BEt_3 as the hydride source (Scheme 8).[10] The



Scheme 8. Nickel-catalyzed intermolecular reductive coupling of alkynes and activated alkenes.

reaction of 1-phenyl-1-propyne (**6a**) with methyl vinyl ketone (**10a**) in the presence of [Ni(cod)$_2$] (cod = cyclooctadiene), PBu_3, and BEt_3 in 8:1 mixture of MeOH/THF at 50 °C provided reductive coupling product **24a** in 85 % yield with a 95:5 *E*/*Z* ratio.[10a] The catalytic reaction is highly regioselective with the β-carbon of methyl vinyl ketone group attached to the methyl-substituted carbon of alkyne. Various alkynes and acyclic and cyclic enones are compatible with the catalytic reaction.

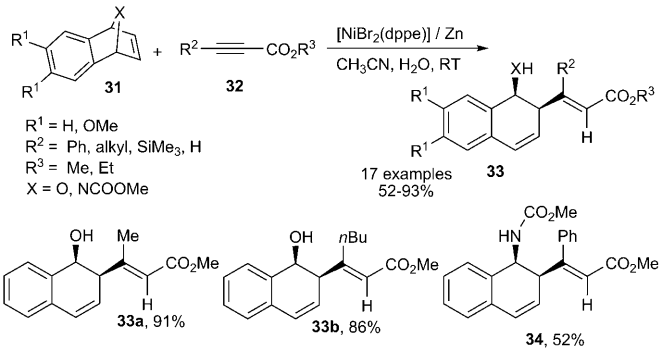
Under similar reaction conditions, enals **25** reacted with alkynes **6** to give [3+2] cycloaddition products, cyclopentanol derivatives, **26** in good to excellent yields with high diastereoselectivity (Scheme 8).[10b] The catalytic reaction proceeds through chemoselective coordination of an alkyne and alkene to the Ni^0 center followed by regioselective oxidative cyclometalation with the assistance of $MeOBEt_2$ yielding nickelacycle intermediate **27** (Scheme 9). Protonation of intermediate **27** by MeOH affords an alkenyl–nickel intermediate **28**. If the R^3 group is H, the alkenyl group of intermediate **28** adds intramolecularly to the tethered aldehyde, further hydrolysis affords [3+2] reductive cycloaddition product **26**. Alternatively, if the R^3 group is an aryl or alkyl, an ethyl group is transferred from boron to nickel in intermediate **28** to produce **29**. β-Hydride elimination followed by reductive elimination gives reductive coupling product **11** and regenerates the active Ni^0 catalyst.



Scheme 9. Proposed mechanism for nickel-catalyzed intermolecular reductive coupling of alkynes and activated alkenes.

Nickel-Catalyzed Reductive Ring-Opening Coupling of Bicyclic Alkenes and Propiolates

7-Oxa- and azabicyclic alkenes are a class of activated alkenes that show substantial coordinating ability to transition-metal centers due to the large bond-angle strain of the alkene group.[11] We had observed that they were efficient ene substrates for the reductive coupling reaction with various propiolates (Scheme 10).[12] Thus, the reaction of 7-oxabenzonorbornadiene (**31a**) and methyl but-2-ynoate (**32a**) in acetonitrile at room temperature in the presence of [Ni(dppe)Br$_2$] (5 mol %) and zinc powder gave a reductive ring-opening coupling product **33a** in 60 % yield (Scheme 10).[12a] Addition of water (1.5 mmol) in the reaction mixture greatly increased the yield of **33a** to 91 % yield. This catalytic reaction is highly regio- and stereoselective, that is, the propiolate moiety is added to bicyclic alkene **31a** at the exo face (*cis* to the oxygen atom) exclu-



Scheme 10. Nickel-catalyzed reductive ring-opening coupling of oxa- and azabenzonorbornadienes and propiolates.

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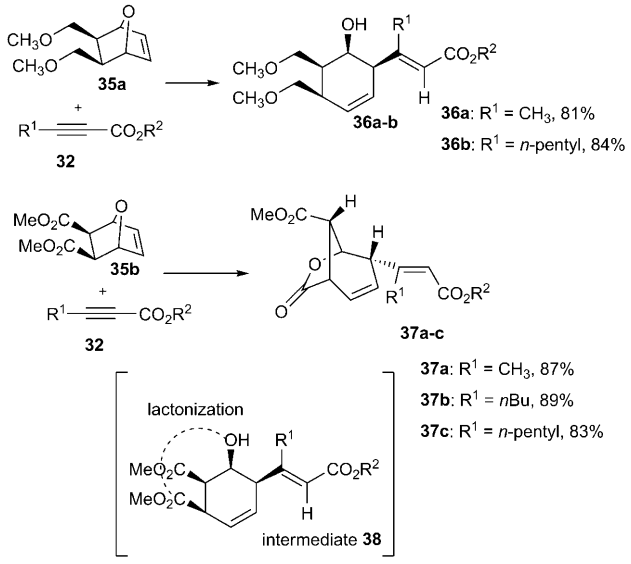
sively and the C–C bond formation occurs specifically at the triple-bonded carbon distal to the ester group of propiolate moiety. The present catalytic reaction is similar to an enyne reductive coupling except that the coupling is accompanied by a C–O bond cleavage leading to ring-opening of the bicyclic moiety. Likewise, various 7-oxabenzonorbornadienes and 7-azabenzonorbornadiene **31** also underwent reductive ring-opening coupling with alkyl propiolates **32** giving the corresponding *cis*-1,2- dihydronaphthalene derivatives **33** or **34** in good to excellent yields.

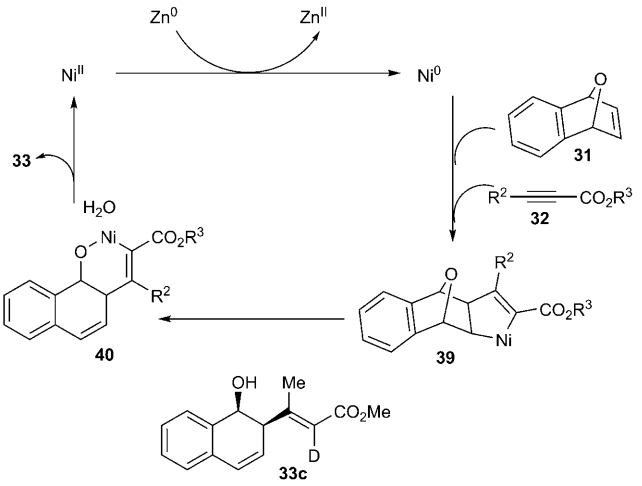
The scope of the reductive ring-opening coupling reaction was successfully extended to 7-oxanorbornenes (Scheme 11). The reaction of oxabicyclic alkene **35a** bearing two



Scheme 11. Reductive ring-opening coupling of oxanorbornenes and propiolates.

CH_2OMe groups with methyl but-2-ynoate (**32a**) proceeded efficiently to give 3-cyclohexenol derivatives **36a** with all four substituents on the cyclohexene ring *cis* to each other in 81% yield. Very interestingly, the reaction of oxabicyclic alkene **35b**, bearing two ester groups, with methyl but-2-ynoate (**32a**) gave reductive cyclization product bicyclic γ-lactone **37a** in 87% yield, instead of the expected reductive coupling product **36**. The formation of product **37a** can be explained by the reductive ring-opening coupling of **35b** and **32a** leading to **38**, followed by chemoselective cyclization of the hydroxyl group with one of the ester groups on the cyclohexene ring. It is worth noting that the skeleton of these bicyclic γ-lactones are useful intermediates in the synthesis of natural products.[13]

A possible reaction mechanism is proposed for reductive ring-opening coupling of bicyclic alkenes and propiolates (Scheme 12). Reduction of Ni^{II} to Ni^0 by zinc powder initiates the catalysis reaction. Highly regioselective *exo* coordination of a bicyclic alkene **31** and propiolate **32** to the Ni^0 center followed by oxidative cyclometalation leads to a nickelacyclopentene intermediate **39**. Subsequent β-heteroatom elimination of intermediate **39** to give **40** followed by protonation affords reductive ring-opening coupling product **33** and Ni^{II} species. The latter is then reduced by Zn to regenerate the Ni^0 species. The proposed mechanism in Scheme 12 was strongly supported by the following isotope-labeling experiment. The reaction of **31a** with **32a** in the presence of D_2O (99.5%) instead of H_2O was carried out. The result showed that in product **33c**, the ester-substituted olefinic carbon is 75% deuterated.



Scheme 12. A proposed mechanism for nickel-catalyzed reductive ring-opening coupling of oxabicyclic alkenes with propiolates.

Nickel-Catalyzed Ring-opening Cyclization of Oxa Bicyclic Alkenes and Propiolates

In the absence of water, the reaction of 7-oxabenzonorbornadiene (**31a**) with methyl but-2-ynoate (**32a**) at 80°C in the presence of $[Ni(dppe)Br_2]$ (5 mol%) and zinc powder in CH_3CN provided benzocoumarin derivative **41a** in 87% yield (Scheme 13) instead of the reductive ring-opening coupling product **33**.[12b] Various 7-oxabenzonorbornadienes **31** were treated efficiently with propiolates **32** to give the corresponding benzocoumarin derivatives **41** in 62–89% yields. Similarly, treatment of 7-oxanorbornene **35a** with methyl 3-(trimethylsilyl)propiolate (**32c**) gave tetrahydrocoumarin **42** in a highly regio- and stereoselective manner. In the reaction all substituents in the ring are present in a *cis* fashion. It is important to say that benzocoumarins and tetrahydrocoumarins are key intermediates in various natural product synthesis.[14] In addition, benzocoumarins are also known as electron-transporting emitters.[15]

Similar to the reductive ring-opening coupling (Scheme 12), we believe that the present ring-opening cyclization also involves nickelacyclopentene **39** and the subsequent β-oxygen elimination product **40** as key intermediates (Scheme 14). In the absence of a proper proton source, β-hydride elimination of intermediate **40** dominates giving

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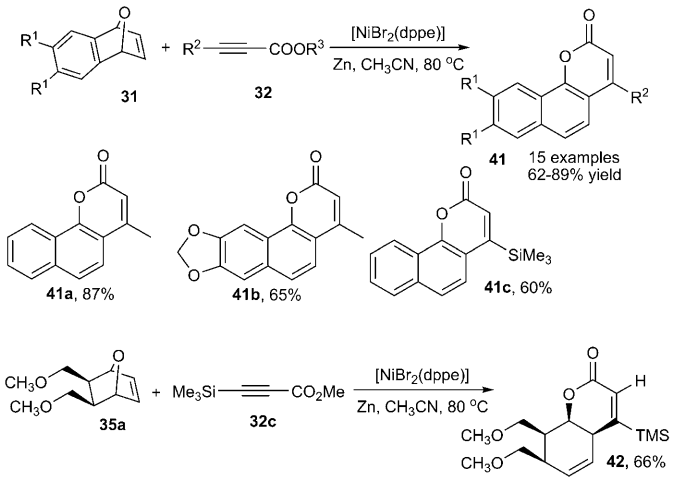
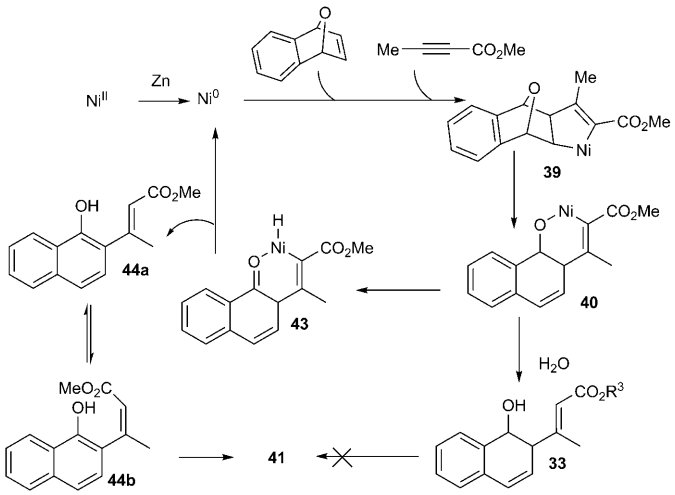


Scheme 13. Nickel-catalyzed ring-opening cyclization of oxabicyclic alkenes and propiolates.

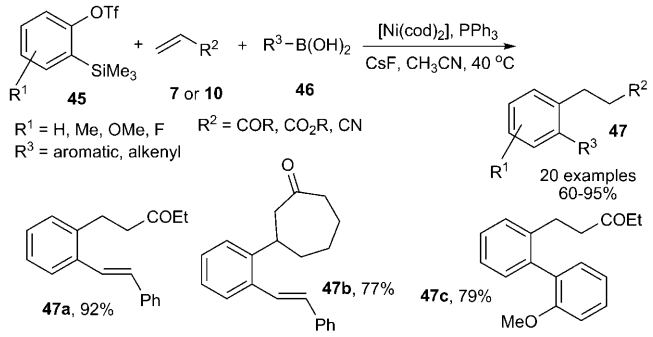


Scheme 14. A proposed mechanism for nickel-catalyzed ring-opening cyclization of oxabenzonorbornadienes with propiolates.

Ni–H intermediate **43**. Enolization and reductive elimination give product **44a** and Ni^0 species. *E*/*Z* isomerization of **44a** to **44b** followed by lactonization of **44b** provides the ring-opening cyclization product **41**. It should be noted that the reductive coupling product **33** failed to convert to benzocoumarin **41** under the catalytic conditions, although we cannot completely rule out **33** as an intermediate for the formation of **41**.

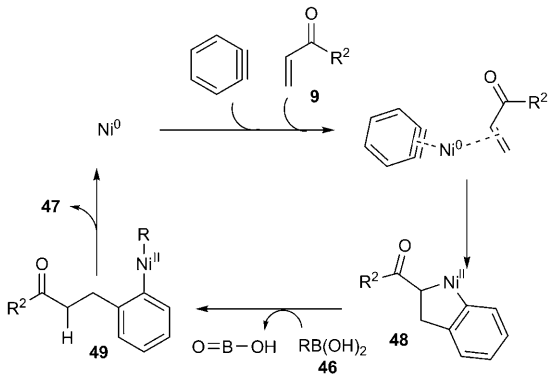
Nickel-Catalyzed Coupling of Benzynes, Activated Alkenes, and Organoboronic acids

In the reductive coupling of carbon–carbon π components, the most commonly employed π systems are alkynes, alkenes, dienes, allylic halides, and allenes. Very recently we demonstrated arynes also work as an efficient π component in the reductive coupling reaction.[16] Treatment of benzyne precursor **45** (2-(trimethylsilyl)phenyl triflate), ethyl vinyl ketone (**10b**) with (*E*)-2-phenylvinyl boronic acid (**46a**) in the presence of $[Ni(cod)_2]$ (10 mol%), PPh_3, and CsF in CH_3CN at 40 °C gave coupling product **47a** in 92% yield (Scheme 15). In the reaction, organoboronic acid likely



Scheme 15. Nickel-catalyzed coupling of benzynes, activated alkenes, and organoboronic acid.

plays dual roles acting as a proton source and as a carbon nucleophile. Under similar reaction conditions, a variety of aryne precursors **45**, organoboronic acids **46**, acyclic and cyclic enones, acrylates, and acrylonitrile also worked well for this coupling reaction. A possible catalytic reaction mechanism of coupling of benzynes, activated alkenes and organoboronic acids is proposed in Scheme 16. Coordinative



Scheme 16. A proposed mechanism for nickel-catalyzed coupling of benzynes, activated alkenes, and organoboronic acids.

cyclometalation of enone and aryne (generated from precursor **45** and CsF) with Ni^0 forms a nickelacycle **48**. Protonation of the α-carbon of ketone moiety in intermediate **48** by the boronic acid and transmetalation of the organic group onto the nickel center leads to intermediate **49**. Subsequent reductive elimination gives coupling product **47** and regenerates the Ni^0 catalyst.

Similar types of nickel-catalyzed three-component reductive couplings of π components, such as alkynes/alkenes, alkynes/allylic halides, and alkynes/imines or aldehydes with

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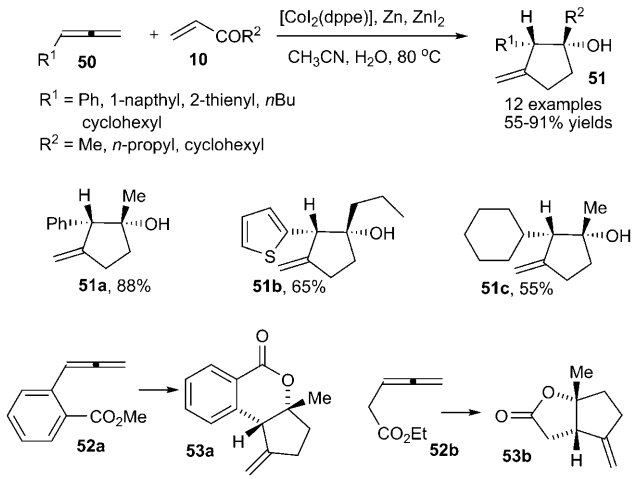
organometallic reagents or metal hydrides are known in the literature.[17–19] Ikeda's group studied intermolecular three-component reductive coupling of alkynes and activated alkenes with alkynyl stannanes[17] and Montgomery's group explored intramolecular three-component reductive coupling of enynes with organometallic reagents.[18] Recently, several other research groups also have paid considerable attention in this area.[19]

Cobalt-Catalyzed Reductive [3+2] Cycloaddition of Allenes and Enones

The observed reductive coupling of alkynes and alkenes prompted us to examine the feasibility of reductive coupling of allenes and alkenes (Scheme 17).[20] The reaction of

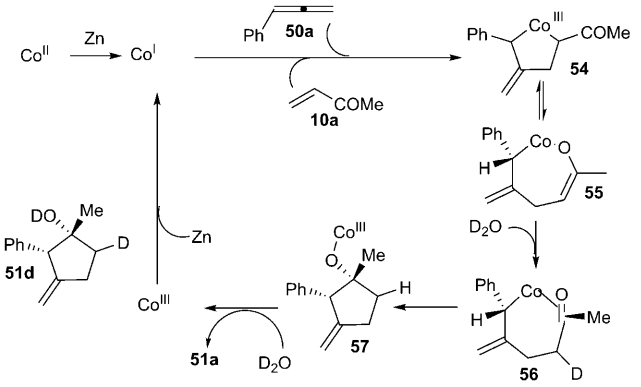


Scheme 17. Cobalt-catalyzed intermolecular reductive [3+2] cycloaddition of allenes and enones.

phenyl allene (**50a**) with methyl vinyl ketone (**10a**) in the presence of $[CoI_2(dppe)]$ (5 mol%), Zn, ZnI_2 (10 mol%), and water in CH_3CN gave cyclopentanol derivative **51a** in 88% yield (Scheme 17). The catalytic reaction is highly regio- and chemoselective, in that the internal double bond of allene is involved in the [3+2] cycloaddition and the phenyl and the methyl substituents in **51a** were *trans* to each other. The use of ZnI_2 and water were crucial for the success of the reaction. No [3+2] cycloaddition occurred without ZnI_2 and water. Various enones **10** and allenes **50** undergo reductive cyclization to give the corresponding cyclopentanols **51** in good yields with excellent diastereomeric selectivity. Very interestingly, a similar reaction using allenyl esters **52a**,**b** as the allene substrate gave tri- and bicyclic lactones **53a** and **53b** as a single diastereomer in 51 and 73% yields, respectively (Scheme 17).

A similar type of [3+2] cycloaddition of allenes and enones catalyzed by phosphine is known in the literature.[21] In the reaction, allene act as a three-carbon group adding to enone yielding cyclopentenes, whereas in our cobalt-catalyzed reaction, enone act as a three-carbon group adding to the internal double bond of allene leading to cyclopentanols. Meanwhile, a ruthenium-catalyzed intermolecular coupling of allenes and alkenes is also known in the literature. In this reaction, the Alder-ene type product (a 1,3-diene) was observed.[21]

A plausible mechanistic rationale of the reductive [3+2] cycloaddition is proposed in Scheme 18. Reduction of Co^{II} to Co^{I} by zinc powder initiates the catalytic reaction. Che-



Scheme 18. A proposed mechanism for the cobalt-catalyzed intermolecular [3+2] cycloaddition of allenes and enones.

moselective coordination of an internal double bond of phenyl allene and methyl vinyl ketone to the Co^{I} center followed by oxidative cyclometalation gives cobaltacyclopentene intermediate **54**. This intermediate **54** is in equilibrium with the *O*-enolate **55**. Selective protonation of the Co–O bond of intermediate **55** by water followed by carbonyl insertion into the Co–C bond in **56** affords cobaltalkoxide intermediate **57**. Protonation of **57** leads to **51a** and Co^{III} species. The latter is then reduced by Zn to regenerate the Co^{I} species. At the moment, the observed excellent diastereoselectivity of **51a** is unclear.

The proposed mechanism is supported by the following isotope-labeling experiment (Scheme 18). The reaction of phenyl allene (**50a**) with methyl vinyl ketone (**10a**) was carried out in the presence of D_2O at 80°C to provide **51d**. The results showed that the 5-position in the cyclopentanol ring and the alcohol group of **51d** were deuterated.

Cobalt-Catalyzed Reductive Dimerization of Alkenes

The reductive coupling of alkynes and alkenes could be extended to alkenes alone (Scheme 19).[21] Thus, *n*-butyl acrylate (**7a**) undergoes reductive self-dimerization in the presence of $[CoI_2(PPh_3)_2]$ (5 mol%), PPh_3, zinc metal powder, and water in CH_3CN at 80°C to provide di(*n*-butyl) adipate (**58a**) in 90% yield. The catalytic reaction is completely regioselective and only the tail-to-tail product was observed. The addition of extra PPh_3 (16 mol%) was crucial to in-

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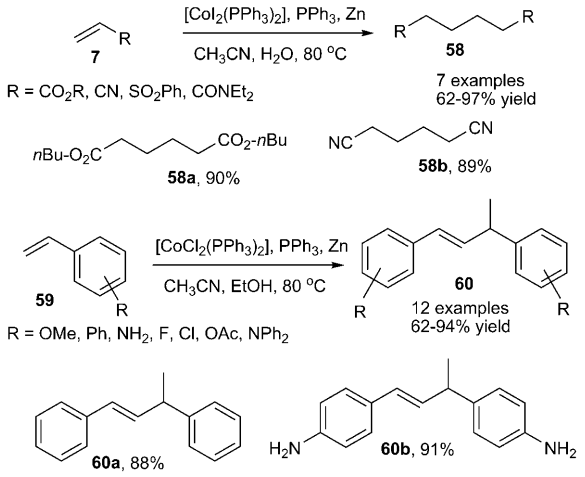
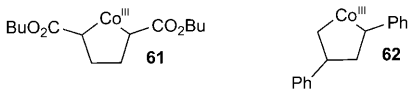


Scheme 19. Cobalt-catalyzed reductive dimerization of alkenes.

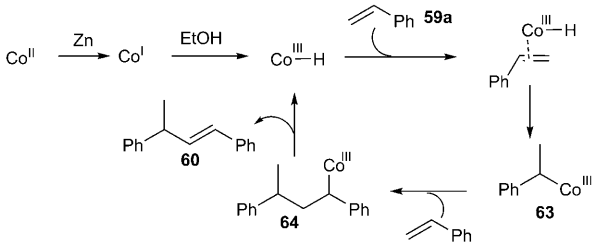
crease the yield of product **58a**, but if the amount of PPh_3 exceeds 16 mol%, the catalytic activity was inhibited. The catalytic reductive dimerization was successfully extended to other acrylates, acrylonitrile, phenyl vinyl sulfone, and *N*,*N*-disubstituted acrylamide **7**. A similar type of dimerization of alkenes were previously studied by various metal catalysts such as Rh, Ru, Pd, and Ni.[22–23]

The dimerization instead of reductive dimerization of vinylarenes occur using cobalt complexes as the catalyst (Scheme 19). Under slightly modified reaction conditions, $[CoCl_2(PPh_3)_2]$ (5 mol%), PPh_3, zinc metal, and EtOH, styrene **59** dimerizes to give alkene **60a** in 88% yield. The catalytic reaction is highly regioselective, only head-to-tail dimerization product was observed. It is worth noting that tail-to-tail reductive dimerization was observed for activated alkenes. Various substituted vinylarenes were successfully employed in the reaction.

The catalytic reaction mechanism of the reductive dimerization of activated alkenes is probably similar to that of enyne reductive coupling as shown in Scheme 2. Formation of regioselective cobaltacyclopentane intermediate **61** from two alkenes and Co^I and further protonation of **61** are probably the key steps for the tail-to-tail reductive dimerization.



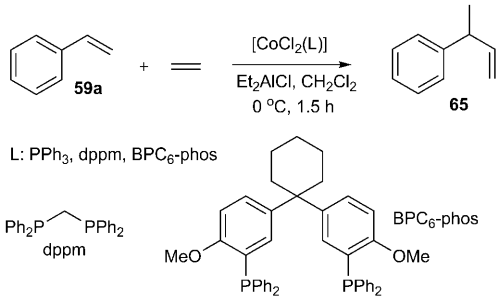
For the catalytic dimerization of styrenes, the key intermediate might also be a cobaltacyclopentane intermediate **62** with a different regiochemistry from **59** and Co^I. Further β-hydride elimination of **62** affords the coupling product **60**. Another possible mechanism involves a cobalt(III) hydride intermediate from the protonation of Co^I with EtOH. Coordinative insertion of vinylarene to the Co^{III}-H species gives intermediate **63** (Scheme 20). Further coordinative insertion of vinylarene to the Co^{III}–C species provides intermediate **64**. Subsequent β-hydrogen elimination of intermediate **64**



Scheme 20. A proposed mechanism for the dimerization of styrenes.

affords the dimerization product **60** and regenerates the Co^{III} hydride for further catalytic cycle.

Very recently, Vogt's group demonstrated a cobalt-catalyzed highly selective hydrovinylation of styrene (Scheme 21).[24] Treatment of styrene (**59a**) with ethylene



Scheme 21. Cobalt-catalyzed hydrovinylation of styrene with ethylene.

($p = 30$ bar) in the presence of $[CoCl_2(BPC_6\text{-phos})]$ (see ref. [24] for details of BPC_6-phos) and Et_2AlCl in CH_2Cl_2 at 0 °C for 1.5 h gave 3-phenyl-1-butene (**65**) in 95% yield. Under the catalytic reaction conditions, other phosphine ligands, such as PPh_3 and bis(diphenylphosphino)methane, were also active for the reaction. Hydrovinylation of styrenes catalyzed by other metals such as Ni, Pd, Ru, Rh, and Ir are also known in the literature.[24] In addition, 1,4-hydrovinylation of styrenes with 1,3-dienes was-studied by Hilt's group.[25]

Conclusion

In this concepts article, we have described various cobalt- and nickel-catalyzed reductive coupling of alkynes, allenes, and alkenes with alkenes. Mechanistically, we propose that the reactions proceed via metallacyclopentenes or metallacyclopentanes as key intermediates. In most of these reductive coupling reactions, zinc was used as the reducing agent and water as the proton source. These reactions are highly regio- and stereoselective providing an efficient route for the synthesis of various highly substituted alkenes, alkanes, cyclopentanols, and cyclic allylic alcohols and amines. The methodologies were also successfully applied to the synthesis six- and seven membered lactones, six-membered lactams, and benzocoumarin derivatives.

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