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Cobalt-Catalyzed Highly Regio- and Stereoselective Intermolecular Reductive Coupling of Alkynes with Conjugated Alkenes

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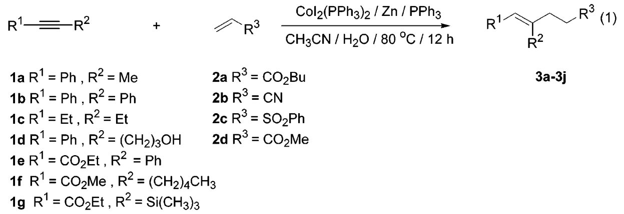
Intermolecular coupling of a carbon−carbon triple bond and double bond provides a convenient route for the carbon−carbon bond formation and for the assembling of two different stable organic molecules to form a new chain molecule. In view of the possibility that a vast number of stereo- and regioisomers can result from the coupling of an unsymmetrical alkyne and alkene, the control of regio- and stereochemistry of the reaction is crucial to make this type of coupling beneficial to organic synthesis. In this work, we wish to report an unusual cobalt-catalyzed intermolecular reductive coupling of a conjugated alkene and alkyne in a highly chemo-, regio-, and stereoselective fashion, providing an effective route for C−C formation under mild conditions. The result is significant in that cobalt-catalyzed C−C formation other than cyclotrimerization[1a,c] and carbonylation[1b,c] is underdeveloped. To the best of our knowledge, there is no catalytic intermolecular reductive ene−yne coupling reported, although several types of related reactions are known such as coupling of alkenes and alkynes to give dienes,[2a−d] three-component coupling of alkenes and alkynes with Cl^- to form vinyl chlorides,[2h−i] coupling of two alkenes to give new alkenes,[3] reductive coupling of a keto group with an unsaturated carbon−carbon bond,[2f,4] and intramolecular reductive coupling of electron-deficient alkenes with alkynes.[2f−g]

Treatment of methylphenylacetylene (**1a**) with *n*-butyl acrylate (**2a**) in the presence of $Co(PPh_3)_2I_2$ (5 mol %), PPh_3 (16 mol %), water, and zinc metal powder in acetonitrile at 80 °C led to reductive coupling of **1a** and **2a** to give product **3a** in 96% yield. The reaction is completely chemo-, regio-, and stereoselective. No regio- or stereoisomer other than **3a** was detected in the reaction mixture by ^{1}H NMR. In **3a**, the phenyl and methyl groups on the alkyne moiety are cis to each other, and the β-carbon of acrylate moiety is connected to the alkyne carbon where the methyl group is attached. The regio- and stereochemistry of this product was determined by NOE experiments.

Control experiments show that no reaction of **1a** and **2a** was observed in the absence of the cobalt complex, water, or zinc metal. The presence of a suitable amount of PPh_3 is important to ensure high yield of **3a**. The reaction without extra PPh_3 afforded only 74% yield of product **3a**; decomposition of the cobalt catalyst was observed as indicated by the decoloration of the catalytic solution. However, addition of more than 3 equiv of PPh_3 (0.32 mmol) appears to inhibit the catalytic reaction, giving **3a** in 76% yield. The presence of a stoichiometric amount of water is necessary as a proton source for the catalytic reaction, but a large excess of water deactivates the cobalt complex.

In addition to the $Co(PPh_3)_2I_2$/(3 PPh_3) system, CoI_2/(5 PPh_3) is also an effective catalyst system for the reductive coupling of **1a** and **2a**, providing **3a** in 79% yield. Other cobalt systems $Co(PPh_3)_2Cl_2$/(3 PPh_3), CoI_2(dppe), $CoCl_2$(dppe), and CoI_2(dppm) show lower catalytic activity for the same reaction, giving **3a** in 15, 40, 75, and 77% yields, respectively. The catalytic reaction also depends greatly on the solvent used. Of the solvents tested, acetonitrile is the best, affording **3a** in nearly quantitative yield. THF, DMF, and DMSO are much less effective, giving **3a** in 5, 19, and 15% yields, respectively. There is no desired product observed in toluene or dichloromethane.

Under similar reaction conditions, **1a** reacts smoothly with acrylonitrile **2b** and vinyl phenyl sulfone **2c** to give reductive coupling products **3b** and **3c** in 98 and 85% isolated yields, respectively (entries 2 and 3). For each of these coupling reactions only one isomer was observed, and the regio- and stereochemistry of these products is similar to that of product **3a**. It should be noted that alkenes with a conjugated electron-withdrawing group are required for the reduction coupling to proceed effectively.



This cobalt-catalyzed reductive coupling reaction is successfully extended to diphenylacetylene **1b** and diethylacetylene **1c**. Thus, the reaction of **1b** with **2a** and **2c** under similar reaction conditions affords **3d** and **3e** in 76 and 75% yield, respectively (entries 4 and 5). In each case, the two phenyl groups on the alkyne moiety are cis to each other, and an alkyne carbon is connected to the terminal vinyl carbon of **2a** or **2c**. Similarly, **1c** undergoes reductive coupling reaction with **2a** in completely regio- and stereoselective fashion to afford product **3f** in moderate yield (entry 6). The reaction of **1d** possessing a hydroxy group with acrylate **2a** also proceeds smoothly to give reductive coupling product **3g** albeit in lower yield (entry 7). The regiochemistry of **3g** is similar to that of product **3a** with the 3-hydroxypropyl group and the acrylate moiety being bonded to the same olefinic carbon of **3g**. Under the standard conditions, the reductive coupling of propiolates **1e**−**g** with acrylate and vinyl phenyl sulfone also proceeds readily to provide the corresponding reductive coupling products **3h**−**j** as shown in Table 1 (entries 8−10). In each of these reactions, a small amount of the cyclotrimerization product of propiolate was observed. The regio- and stereochemistry is intriguing as revealed by the formation of tail-to-tail reductive coupling products solely.

To understand the role of water and to help elucidate the mechanism of the present catalytic reaction, an isotope-labeling experiment using D_2O (99.9%) to replace normal water for the reductive coupling of vinyl phenyl sulfone **2c** with alkyne **1a** was

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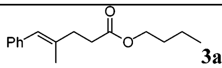
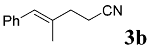
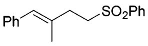
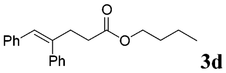
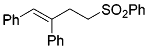
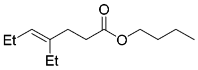
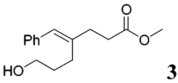
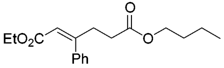
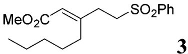
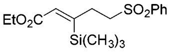
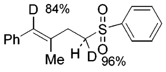
Table 1. Results of Co-Catalyzed Reductive Coupling of Alkenes and Alkynes[a]

Entry	Alkyne	Alkene	Product	Yield[b] (%)
1	**1a**	**2a**	 **3a**	96
2	**1a**	**2b**	 **3b**	98
3	**1a**	**2c**	 **3c**	85
4	**1b**	**2a**	 **3d**	76
5	**1b**	**2c**	 **3e**	75
6	**1c**	**2a**	 **3f**	76
7	**1d**	**2d**	 **3g**	48
8	**1e**	**2a**	 **3h**	61
9	**1f**	**2c**	 **3i**	82
10	**1g**	**2c**	 **3j**	81

[a] Reaction conditions: alkyne (1.00 mmol), alkene (1.20 mmol), $CoI_2(PPh_3)_2$ (0.050 mmol; 5.0 mol %), Zn (3.0 mmol), H_2O (0.60−1.0 mmol), PPh_3 (0.16 mmol), CH_3CN (2.0 mL) at 80 °C for 12 h. [b] Isolated yields.

carried out. The results show that the olefinic proton and one of the protons of the α-methylene group of product **3c′** were deuterated in 84 and 96%, respectively. No deuterium-labeling for other protons in this product was observed. The isotope abundance was determined by ^1H NMR integration method. In agreement with the results of ^1H NMR analysis, the ^{13}C NMR spectrum of **3c′** isolated from the above labeling study reveals two characteristic deuterium-coupled triplets at 54.54 and 127.11 ppm for the olefin and methylene carbons, respectively.

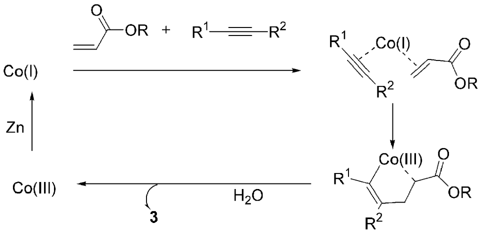


3c'

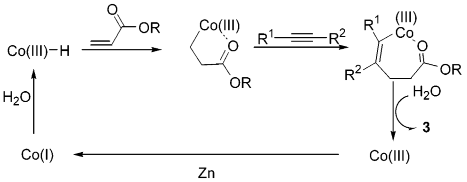
The mechanism of the present reductive coupling is interesting in view of the ability of the catalyst to assemble an alkyne and an alkene molecule for coupling and hydrogenation in one pot in a high regio- and stereoselective fashion. While the details of the catalytic steps is not clear, possible pathways may be proposed based on the known organometallic chemistry that relates to acrylates and alkynes. A straightforward route that can explain well the observed regio- and stereochemistry is the formation of a cobaltacyclopentene intermediate from cyclometalation of an alkyne and alkene to the cobalt(I) center followed by protonation of the intermediate by water (Scheme 1). Such a metallocyclopentene species has been proposed as a key intermediate[1b] in the ene−yne coupling catalyzed by ruthenium[2a,e,h] and nickel complexes.[6,2f−g] The results of the above deuterium isotope-labeling experiment strongly supports this pathway.

An alternative mechanism involving a cobalt(III) hydride generated from protonation of cobalt(I) by water cannot be ruled out. Insertion of an acrylate molecule into the metal-hydride bond gives a five-membered ring species. Further insertion of an alkyne molecule and protonation provides the expected reductive coupling product (Scheme 2). This pathway also explains excellently the results of the isotope-labeling experiment and account satisfactorily the observed regioselectivity of alkynes. A similar pathway has been used to explain the tail-to-tail coupling of acrylate catalyzed by rhodium [7] and cobalt complexes.[8]

Scheme 1



Scheme 2



In conclusion, we have developed a novel simple method for the assembling of an alkene and an alkyne via a cobalt-catalyzed reductive-coupling mode. This reaction is highly chemo-, regio-, and stereoselective. The mechanism of this interesting reaction is not yet clear. Further investigation on the mechanism, the scope, and the application of this reaction is underway.

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Supporting Information Available: Preparation details, characterization data, NOE experimental data of **3a−j** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org

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