Rhodium-catalyzed Selective Cross-coupling of Internal Alkynes with a Terminal Silylacetylene

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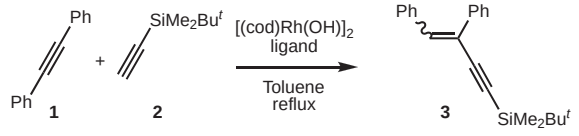
The cross-coupling of a number of internal arylalkynes with a representative terminal alkyne, *tert*-butyldimethylsilylacetylene, proceeds regio- and stereoselectively in the presence of a rhodium catalyst to produce the corresponding enyne compounds with good yield.

Alkyne coupling reactions by transition-metal catalysis are of genuine synthetic utility in preparing π-conjugated four carbon compounds such as enynes.[1–3,4a] Thus, the dimerization of terminal alkynes as a straightforward and practical method leading to enynes has been extensively studied to selectively synthesize one of the three possible head-to-tail and E and Z tail-to-tail products. However, the selective cross-coupling of two different alkynes is, in general, still difficult due to the fact that the formation of cross- and homo-coupled regio- and stereoisomers is possible, and thus, of a major challenge.[2,3] Among the rare, leading examples is the palladium-catalyzed reaction of internal alkynes having an electron-withdrawing group with terminal alkynes.[2] Such reactions have also been achieved by using ruthenium-[3b] and iridium-catalysts.[3f] During the course of our study of rhodium-catalyzed carbon–carbon bond-formation reactions,[4] we have found that a number of internal arylalkynes effectively and selectively couple with a representative terminal silylacetylene such as *tert*-butyldimethylsilylacetylene. The new findings are reported herein.[5]

In an initial attempt, the reaction of diphenylacetylene (**1**) (0.5 mmol) with *tert*-butyldimethylsilylacetylene (**2**) (0.6 mmol) was examined in the presence of $[(cod)Rh(OH)]_2$ (0.0075 mmol, 3 mol % Rh) with the addition of various phosphine ligands (P/Rh = 2) in refluxing toluene under nitrogen (Table 1).[6] The cross-coupled product **3** was obtained with moderate to excellent yields by using triarylphopsphines (Entries 1–3). Among them, the relatively more electron-donating ligand, $P(4\text{-}MeOC_6H_4)_3$, was most effective to afford **3** in 92% yield with an E/Z ratio of 83:17. The use of PCy_3 (Cy = cyclohexyl) having an electron-rich as well as bulky character[7a] resulted in selective formation of the E isomer (E/Z = 97:3), while the yield was decreased to 31% (Entry 4). The catalytic efficiency and stereoselectivity were also highly dependent on the identity of bidentate phosphines (Entries 5–9).[7b] The reaction was unexpectedly and remarkably accelerated by dCype $[Cy_2P(CH_2)_2PCy_2]$ compared with dppe $[Ph_2P(CH_2)_2PPh_2]$ (Entry 6 vs 5). Thus, dCype allowed the selective formation of the E isomer (E/Z = 97:3) with an almost quantitative yield. It is noted that in each entry, only a small amount of dimers of **2** was formed (see Table S1 in Supporting Information),[16] in spite of the fact that the dimerization of **2** by the Wilkinson complex is known to take place even at room temperature.[8a] It should also be cited that the reaction of **1** with **2** in the presence of $Ni(PEt_3)_4$ was reported previously, in which a 1:2-coupling product was mainly formed along with a minor amount of **3**.[8b,8c]

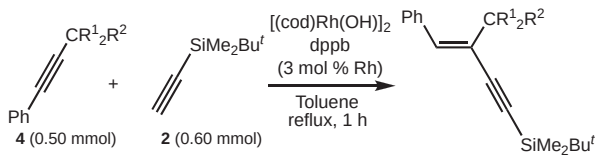
Table 1. Effect of phosphine ligands on rhodium-catalyzed cross-coupling of diphenylacetylene with *tert*-butyldimethylsilylacetylene[a]



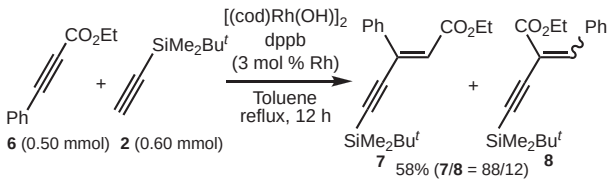
Entry	Ligand	Time/h	% Yield of **3**[b] (E/Z)[c]
1	$P(4\text{-}ClC_6H_4)_3$	6	58 (88/12)
2	PPh_3	3	64 (80/20)
3	$P(4\text{-}MeOC_6H_4)_3$	3	92 (83/17)
4	PCy_3	12	31 (97/3)
5	dppe	3	44 (98/2)
6	dCype	1	96 (96)[d] (97/3)
7	dppp	3	40 (94/4)
8	dppb	3	95 (88/12)
9	dCypb	1	95 (46/54)

[a]Reaction conditions: Diphenylacetylene (0.50 mmol), *tert*-butyldimethylsilylacetylene (0.60 mmol), $[(cod)Rh(OH)]_2$ (0.0075 mmol), ligand (0.03 mmol for monophosphine, 0.015 mmol for diphosphine) in refluxing toluene (5 mL) under N_2. [b]GC yield based on the amount of **1** used. [c]E/Z ratio. [d]Isolated yield.

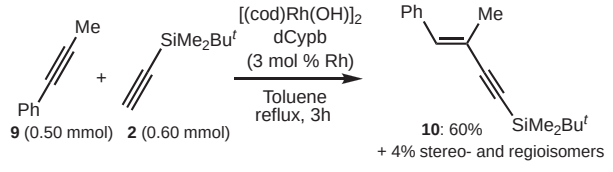
We recently reported that in the presence of $[(cod)Rh(OH)]_2$ and dppb, 1,1,3-triphenyl-2-propyn-1-ol (**4a**) and 1,1-dimethyl-3-phenyl-2-propyn-1-ol (**4b**) undergo a unique homo-coupling with liberation of one benzophenone and acetone molecule, respectively, to produce the corresponding 2-hydroxymethyl-(*E*)-enynes.[4a] The reaction proceeds through C–C bond cleavage by β-carbon elimination in an initially formed alkoxyrhodium to afford an alkynylrhodium as a key intermediate. It was of quite interest that treatment of **4a** in the presence of **2** using the same catalyst system and conditions led to the selective formation of cross-coupled (*Z*)-enyne **5a** in 92% yield after isolation (Scheme 1). Thus, the dppb ligand was enough effective to control the regio- and stereoselectivity and only a minor amount of each of the homo-coupling products (less than 5%) was produced. Note that the configuration of **5a** is reverse to the



Scheme 1.



Scheme 2.



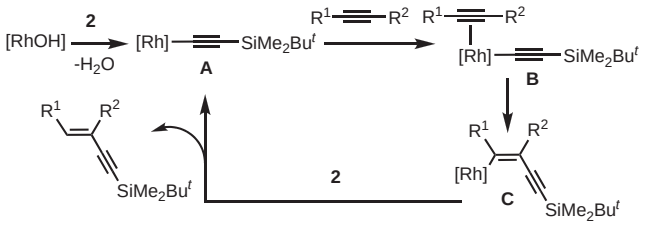
Scheme 3.

homo-coupling product of **4a**.[4a] The reaction of **4b** with **2** proceeded similarly.[9,10]

The reactions of 3-phenyl-2-propyn-1-ol (**4c**) and 4-phenyl-3-butyn-1-ol (**4d**), which possess α-methylene hydrogens, with **2** also gave enynes **5c** and **5d** selectively, while no byproduct fromed via β-H elimination of the corresponding alkoxyrhodium species was observed.[11] These results indicate that the C–H cleavage of **2** is relatively faster than the formation of the alkoxyrhodium species.

We also undertook the reactions of representative electronically activated and unactivated arylalkynes, ethyl 3-phenyl-2-propynoate (**6**) and 3-phenyl-2-propyne (**9**) (Schemes 2 and 3). The reaction of **6** gave the regioisomeric enynes **7** and **8** in a ratio of 88:12 with 58% combined yield.[12] From the reaction of **9** using dCypb as a ligand, enyne **10** was obtained in 60% yield and 94% selectivity along with small amounts of its stereo- and regioisomers (in the case using dppb, the yield and selectivity were 34 and 66%, respectively).[12,13] The use of dCype in the reactions of **6** and **9** was less effective. The reactions of aliphatic internal alkynes were sluggish; as an example, in the reaction of 8-hexadecyne with **2** using dppb as a ligand for 3 h, a mixture of stereoisomeric enynes (ca. 20%) was detected by GC-MS.

A plausible mechanism for the enyne formation is illustrated in Scheme 4, in which neutral ligands are omitted. The first step involves the reaction of hydroxyrhodium(I) species with **2** to form alkynylrhodium **A**.[4a,5a,14] The successive insertion of an internal alkyne via π-complex **B** gives vinylrhodium **C**. Then, the reaction with another molecule of **2** affords an enyne product with regeneration of **A**. The regioselectivity determined in the transformation of **B** to **C** may be mainly due to steric reasons, while in the case of **6**, the electronic bias in the substrate is the key.[2] The E/Z-isomerization probably takes place in the vinylrhodium intermediate via carbene-like zwitterionic species.[15]



Scheme 4.

The observed high syn selectivity in the present couplings may imply that the reaction of **C** with **2** is relatively fast. To establish this, however, further investigation is required.

In summary, we have demonstrated that the regio- and stereoselective cross-coupling of internal arylalkynes with a terminal silylacetylene is accomplished by using the catalyst system consisting of $[(cod)Rh(OH)]_2$ and bidentate phosphines. This appears to provide a new, effective method for constructing π-conjugated systems, as the silyl function may be subjected to further structural transformations. Work is underway toward a better understanding of the catalysis.

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