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Rhodium-Catalyzed Asymmetric Rearrangement of Alkynyl Alkenyl Carbinols: Synthetic Equivalent to Asymmetric Conjugate Alkynylation of Enones

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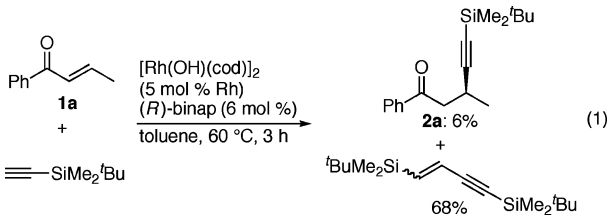
Rhodium-catalyzed asymmetric conjugate addition of organometallic reagents to electron-deficient alkenes has attracted increasing attention owing to its high catalytic activity and high enantioselectivity for a wide range of substrates.[1] One drawback of the rhodium-catalyzed asymmetric addition is that the organic groups successfully installed have been limited to aryl and alkenyl groups, and any alkynyl groups have not been applied to the rhodium-catalyzed asymmetric addition. There have been a few reports on the catalytic asymmetric alkynyl conjugate addition using a catalytic amount of chiral ligands for copper[2] and nickel[3] catalysts or alkynylboron reagents,[4] but the existing systems are still limited in terms of substrate's scope, thus a new method is certainly highly desirable. Although it has been reported that conjugate addition of terminal alkynes is catalyzed by rhodium complexes[5] as well as ruthenium[6] and palladium complexes,[7] high yielding addition has been reported only for β-unsubstituted enones such as methyl vinyl ketone. It follows that new methodology is required for the realization of rhodium-catalyzed asymmetric conjugate alkynylation because the use of β-substituted enones is essential for the creation of new stereogenic carbon centers at the β-position in the asymmetric conjugate addition.

Under one of the standard reaction conditions for the rhodium-catalyzed asymmetric addition,[8] the reaction of 1-phenyl-2-buten-1-one (**1a**) with (*tert*-butyldimethylsilyl)ethyne (1.0 equiv to **1a**) was examined (eq 1), which gave a very low yield of the conjugate alkynylation product **2a** as expected from the results reported so far.[5b] Thus, the reaction in the presence of a Rh/binap catalyst (5 mol % of Rh), generated from $[Rh(OH)(cod)]_2$ and (*R*)-binap, in toluene at 60 °C for 3 h gave 68% yield[9] of head-to-head dimers of the silylacetylene together with 6% yield of **2a**, indicating that the major problem is competing dimerization of the terminal alkyne. Assuming that the reaction proceeds by way of an alkynylrhodium species **A** which undergoes insertion of alkyne or enone, leading to an acetylene dimer or conjugate alkynylation product, respectively (Scheme 1), the wrong reaction pathway is caused by the presence of a terminal alkyne as a stoichiometric reagent,[10] which is more reactive than the β-substituted enone toward the insertion.

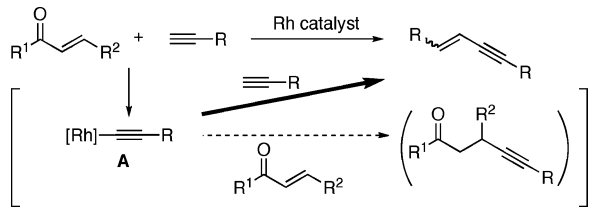
Our new approach is the asymmetric 1,3-rearrangement of an



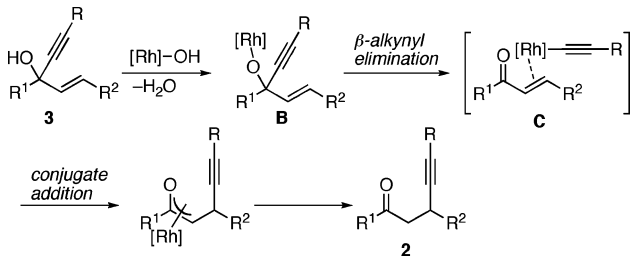
(1)

alkynyl group from alkynyl alkenyl carbinols **3** (Scheme 2), which involves the β-alkynyl elimination[11] as a key step. Thus, an alkoxyrhodium species **B** generated from the alkynyl alkenyl carbinol **3** undergoes β-alkynyl elimination to give alkynylrhodium complex **C**, which is coordinated with an enone released by the elimination. Conjugate addition of the alkynylrhodium to the enone

Scheme 1

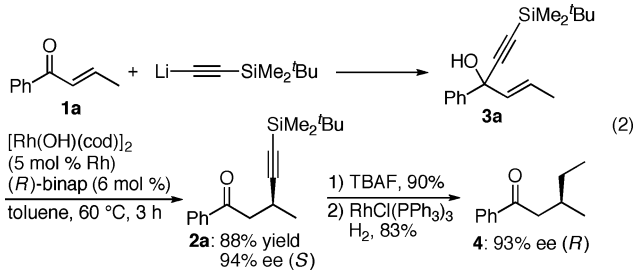


Scheme 2



will produce the β-alkynylketone **2** by way of an oxa-π-allylrhodium intermediate.[8] This rearrangement should proceed much more efficiently than the intermolecular alkynylation because the free terminal alkynes, which are responsible for the low yield of the conjugate addition, do not exist in the reaction media. In addition, the enone generated by the β-elimination is located close to rhodium, being ready to react with the alkynylrhodium species.

The asymmetric rearrangement took place very successfully.



(2)

Treatment of racemic (*E*)-1-(*tert*-butyldimethylsilyl)-3-phenyl-4-hexen-1-yn-3-ol (**3a**), which is readily accessible by 1,2-addition of (*tert*-butyldimethylsilyl)ethynyllithium to enone **1a**, with the Rh/(*R*)-binap catalyst in toluene at 60 °C for 3 h gave 88% yield of β-alkynylketone **2a** in 94% ee (eq 2).[12] The absolute configuration of **2a** was determined to be *S*-(−) by correlation with (*R*)-3-methyl-1-phenyl-1-pentanone (**4**),[13] which was obtained by deprotection of the silyl group followed by hydrogenation of the triple bond.

The absolute configuration of the product (*S*)-**2a** is in good agreement with the stereochemical pathway proposed for the asymmetric conjugate addition reactions catalyzed by Rh/binap,[14] the enone intermediate being attacked by the alkynylrhodium on its α-*re* face in the present reaction (Scheme 3).

The results obtained for the rhodium-catalyzed 1,3-alkynyl rearrangement of several types of alkynyl alkenyl carbinols are

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Scheme 3

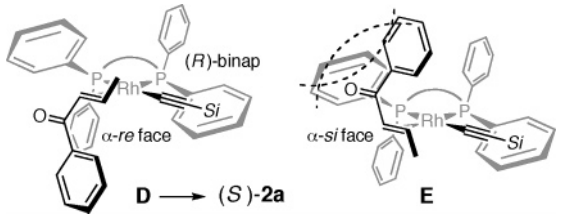
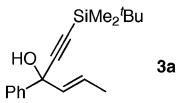
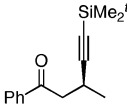
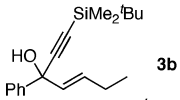
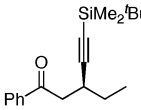
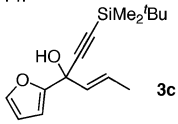
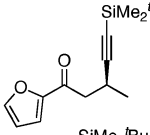
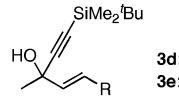
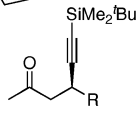
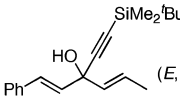
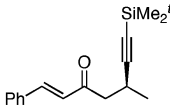
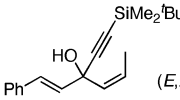
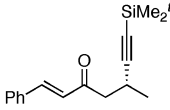
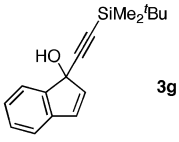
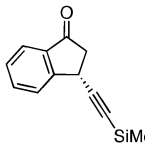
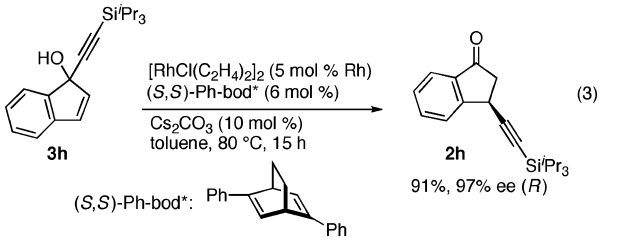


Table 1. Asymmetric Rearrangement of Alkynyl Alkenyl Carbinols[a]

entry	alcohol	product
1	 **3a**	 **2a**: 88%, 94% ee (*S*)
2	 **3b**	 **2b**: 91%, 98% ee (*S*)
3	 **3c**	 **2c**: 89%, 91% ee (*S*)
4[b]	 **3d**: R = CH_3	 **2d**: 78%, 98% ee (*S*)
5	**3e**: R = C_5H_{11}	**2e**: 78%, 81% ee (*S*)
6[c]	 (*E*,*E*)-**3f**	 **2f**: 78%, 96% ee (*S*)
7[c]	 (*E*,*Z*)-**3f**	 **2f**: 88%, 81% ee (*R*)
8[d]	 **3g**	 **2g**: 86%, 71% ee (*S*)

[a] Reaction conditions: alcohol **3** (0.20 mmol), $[Rh(OH)(cod)]_2$ (5 mol % of Rh), (*R*)-binap (6 mol %), toluene (1.0 mL) at 60 °C for 3 h. Enantiomeric excess values were determined by HPLC analysis. The absolute configuration of **2b**−**g** were assigned by consideration of the stereochemical pathway. [b] At 50 °C for 12 h. [c] For 6 h. [d] For 24 h.

summarized in Table 1. The reaction of alcohol **3b** having a 1-butenyl group produced the corresponding β-ethynylketone **2b** in high yield (91%) and high enantioselectivity (98% ee) (entry 2). The 1,3-rearrangement was also observed on the carbinol **3c**, which is substituted with a 2-furyl group (entry 3). The carbinols **3d** and **3e**, which have a methyl substituent on the alcohol carbon, are another type of good substrates for the rearrangement (entries 4 and 5). It should be noted that the alkynyl migration took place exclusively to the 1-propenyl group in the reaction of **3f** where the enone intermediate is 2-phenylethenyl 1-propenylketone (entries 6 and 7). The absolute configuration of the alkynylation product **2f** was opposite in the reaction of (*E*)- and (*Z*)-propenyl isomers **3f**, which is as expected from the results observed for the asymmetric conjugate addition of phenylboronic acid.[15] In the reaction of cyclic allylic alcohol **3g** derived from indenone, the enantioselectivity was moderate under the standard conditions (71% ee, entry 8), but the use of chiral diene ligand, (*S*,*S*)-Ph-bod*,[16] for triisopropylsilylethynyl analogue **3h** resulted in a great increase of enantioselectivity (97% ee) (eq 3).



(3)

In summary, we found a new method of introducing alkynyl groups to the β-position of α,β-unsaturated ketones with high enantioselectivity, which was realized by rhodium-catalyzed asymmetric 1,3-migration of alkynyl groups from 1 position to 3 in alkynyl alkenyl carbinols. The catalytic cycle presumably involves the β-alkynyl elimination from an alkoxyrhodium intermediate as a key step.

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Supporting Information Available: Experimental procedures and spectroscopic and analytical data for the substrates and products (pdf). This material is available free of charge via the Internet at http://pubs.acs.org.

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