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A New c*ine*-Substitution of Alkenyl Sulfones with Aryltitanium Reagents Catalyzed by Rhodium: Mechanistic Studies and Catalytic Asymmetric Synthesis of Allylarenes

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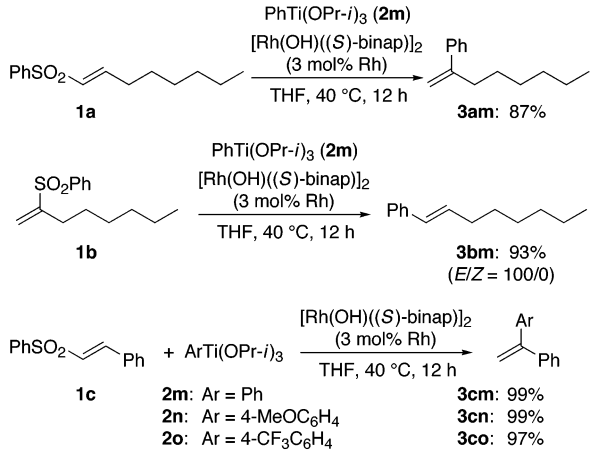
The *cine*-substitution reaction has attracted considerable attention as a result of its rather unusual substitution pattern and its synthetic utility.[1] It takes place mostly in aromatic systems, and only a few types have been reported on the *cine*-substitution in nonaromatic systems, the representatives being those observed as competing side reactions in palladium-catalyzed cross-couplings of alkenylstannanes and -silanes.[2] On the other hand, we have reported the rhodium-catalyzed asymmetric addition of organoboron[3,4] and -titanium[5] reagents to various types of electron-deficient olefins which proceeds through carbo-rhodation of the olefins as a key step, giving the corresponding 1,4-addition products with high enantioselectivity. On using alkenyl sulfones[6] as substrates for the rhodium-catalyzed addition of organometallic reagents, we found a new type of *cine*-substitution where the sulfonyl group is eliminated after the carbo-rhodation step.[7] Here we wish to report the catalytic *cine*-substitution reaction, its catalytic cycle established by deuterium-labeling studies and its application to catalytic asymmetric synthesis of allylarenes with over 99% enantioselectivity.

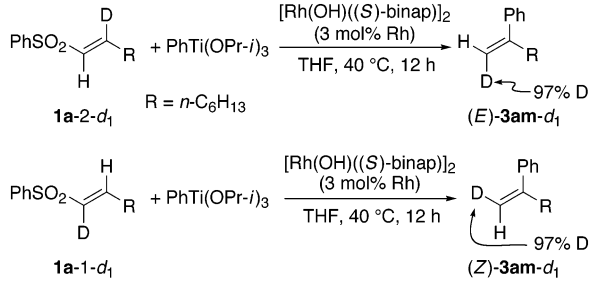
In the first set of experiments, a pair of regioisomeric alkenyl sulfones, (*E*)-1-phenylsulfonyl-1-octene (**1a**) and 2-phenylsulfonyl-1-octene (**1b**), were allowed to react with phenyltitanium triisopropoxide (PhTi(OPr-*i*)$_3$)[8] (**2m**) in the presence of 3 mol % of [Rh(OH)((*S*)-binap)]$_2$[3j] in THF at 40 °C for 12 h (Scheme 1). The reaction of **1a** gave 87% yield of 2-phenyl-1-octene (**3am**), and that of **1b** gave 93% yield of (*E*)-1-phenyl-1-octene (**3bm**) with perfect regioselectivity in both reactions. Thus, *cine*-substitution where the phenylsulfonyl group is substituted with the phenyl group on the next carbon took place in both regioisomeric alkenyl sulfones **1a** and **1b**. The *cine*-substitution was also observed in the reaction of (*E*)-1-phenylsulfonyl-2-phenylethene (**1c**) with PhTi(OPr-*i*)$_3$ (**2m**) and those containing an electron-donating or -withdrawing group on the phenyl **2n**,**o**, which gave the corresponding substitution products **3cm**, **3cn**, and **3co**, respectively, in a quantitative yield. With organoboron reagents such as phenyl-9BBN or triphenylcyclotriboroxane ((PhBO)$_3$) in place of the aryltitanium reagents, neither this type of *cine*-substitution nor the 1,4-addition took place.

Deuterium-labeling experiments shown in Scheme 2 gave us an insight into the mechanism of the present *cine*-substitution. The rhodium-catalyzed reaction of (*E*)-2-deuterio-1-phenylsulfonyl-1-octene (**1a**-2-d_1) (99% D) with PhTi(OPr-*i*)$_3$ (**2m**) gave (*E*)-1-deuterio-2-phenyl-1-octene ((*E*)-**3am**-d_1) where the deuterium content at the *E* position is 97%. Consistent with this deuterium shift, the reaction of (*E*)-1-deuterio-1-phenylsulfonyl-1-octene (**1a**-1-d_1) (99% D) gave (*Z*)-1-deuterio-2-phenyl-1-octene ((*Z*)-**3am**-d_1) with the deuterium content of 97% at the *Z* position. Scheme 3 illustrates the formation of the *cine*-substitution product using for an example the reaction starting from **1a**-2-d_1. Addition of a phenylrhodium species[5] to the alkenyl sulfone in a *syn* fashion generating alkyl-rhodium intermediate **A** followed by β-deuterium elimination with *syn* stereochemistry and readdition of the deuterium−rhodium to the double bond with *syn* stereochemistry and with opposite regiochemistry forms new alkyl-rhodium intermediate **B**. The last step, elimination of the sulfonyl group and the rhodium from **B**, should proceed in an *anti* fashion to give the *cine*-substitution product (*E*)-**3am**-d_1 where the deuterium is at *E* position to the phenyl.[9] It is likely that the last step consists of nucleophilic attack of the phenyltitanium on the rhodium and E_2 elimination of the phenylsulfonyl as a leaving group.

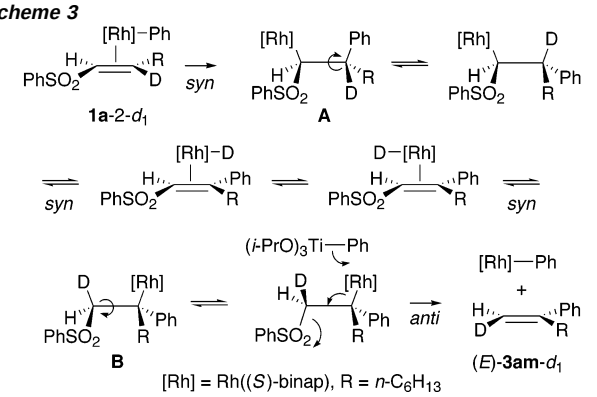
Scheme 1



Scheme 2

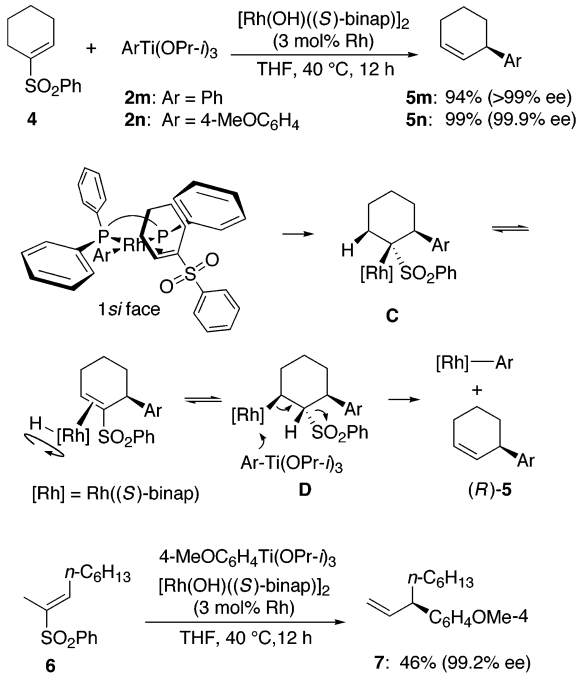


Scheme 3



10.1021/ja0295568 CCC: $25.00

Scheme 4



In the reaction of cyclic alkenyl sulfone, the asymmetric carbon center created at the carbo-rhodation step is retained in the substitution product (Scheme 4). Thus, the reaction of 1-phenylsulfonylcyclohexene (**4**) with PhTi(OPr-*i*)$_3$ (**2m**) in the presence of [Rh(OH)((*S*)-binap)]$_2$ gave 94% yield of (*R*)-3-phenylcyclohexene (**5m**) whose enantiomeric excess turned out to be over 99% ee by GC analysis with a chiral stationary phase column.[10] The very high enantioselectivity (99.9% ee) was also observed in the reaction with 4-MeOC$_6$H$_4$Ti(OPr-*i*)$_3$ (**2n**) giving the corresponding 3-arylcyclohexene (**5n**).[11,12] The coordination of **4** to the (*S*)-binap/Rh with its 1*si* face at the insertion into the aryl-rhodium intermediate[3a,c,e] leads to the *R* configuration of the substitution products **5**. Because the alkyl-rhodium intermediate **C** formed by the insertion does not have the *syn* β-hydrogen on the aryl-substituted carbon, the β-hydrogen elimination takes place for the *syn* β-hydrogen on the other neighboring carbon. Subsequent *syn* hydro-rhodation and the *anti* elimination from **D** produces the allylic arenes **5**.

The selective formation of allylic arene was also observed in the reaction of (*E*)-2-phenylsulfonyl-2-nonene (**6**) which is a sulfone of internal alkene. Although the yield was not high enough, the enantioselectivity forming allylarene **7** in the reaction with **2n** was surprisingly high (99.2% ee).[13] For this alkenyl sulfone **6**, the hydrogen on the methyl carbon is abstracted at the β-hydrogen elimination on the alkyl-rhodium intermediate much more readily than that on the sterically congested carbon substituted with phenyl and hexyl groups, resulting in the selective formation of **7**.

In conclusion, we found a new type of *cine*-substitution reaction of alkenyl sulfones with aryltitanium reagents, which is catalyzed by a rhodium complex, and we established its catalytic cycle by deuterium-labeling studies. In some cases, the catalytic asymmetric carbon−carbon bond formation was realized with high enantioselectivity (>99% ee).

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

References

(1) For a review: Suwinski. J.; Swierczek K. *Tetrahedron* **2001**, *57*, 1639.
(2) (a) Kikukawa, K.; Umekawa, H.; Matsuda, T. *J. Organomet. Chem*. **1986**, *311*, C44. (b) Ennis, D. S.; Gilchrist, T. L. *Tetrahedron Lett.* **1989**, *30*, 3735. (c) Stork, G.; Isaacs, R. C. A. *J. Am. Chem. Soc*. **1990**, *112*, 7339. (d) Crisp, G. T.; Glink, P. T. *Tetrahedron* **1994**, *50*, 3213. (e) Busacca, C. A.; Swestock, J.; Johnson, R. E.; Bailey, T. R.; Musza, L.; Rodger, C. A. *J. Org. Chem*. **1994**, *59*, 7553. (f) Farina, V.; Hossain, M. A. *Tetrahedron Lett*. **1996**, *37*, 6997. (g) Chen, S.-H. *Tetrahedron Lett.* **1997**, *38*, 4741. (h) Quayle, P.; Wang, J.; Xu, J.; Urch, C. J. *Tetrahedron Lett.* **1998**, *39*, 489. (i) Flohr, A. *Tetrahedron Lett.* **1998**, *39*, 5177. (j) Anderson, J. C.; Anguille, S.; Bailey, R. *Chem. Commun*. **2002**, 2018.
(3) (a) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc*. **1998**, *120*, 5579. (b) Takaya, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron Lett.* **1998**, *39*, 8479. (c) Takaya, Y.; Senda, T.; Kurushima, H.; Ogasawara, M.; Hayashi, T. *Tetrahedron: Asymmetry* **1999**, *10*, 4047. (d) Takaya, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron Lett*. **1999**, *40*, 6957. (e) Hayashi, T.; Senda, T.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **1999**, *121*, 11591. (f) Takaya, Y.; Ogasawara, M.; Hayashi, T. *Chirality* **2000**, *12*, 469. (g) Hayashi, T.; Senda, T.; Ogasawara, M. *J. Am. Chem. Soc.* **2000**, *122*, 10716. (h) Hayashi, T. *Synlett* **2001**, 879. (i) Senda, T.; Ogasawara, M.; Hayashi, T. *J. Org. Chem*. **2001**, *66*, 6852. (j) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.
(4) (a) Sakuma, S.; Sakai, M.; Itooka, R.; Miyaura, N. *J. Org. Chem*. **2000**, *65*, 5951. (b) Kuriyama, M.; Tomioka, K. *Tetrahedron Lett.* **2001**, *42*, 921. (c) Sakuma, S.; Miyaura, N. *J. Org. Chem*. **2001**, *66*, 8944. (d) Reetz, M. T.; Moulin, D.; Gosberg, A. *Org. Lett*. **2001**, *3*, 4083. (e) Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett*. **2002**, *4*, 1311. (f) Kuriyama, M.; Nagai, K.; Yamada, K.; Miwa, Y.; Taga, T.; Tomioka, K. *J. Am. Chem. Soc*. **2002**, *124*, 8932.
(5) Hayashi, T.; Tokunaga, N.; Yoshida, K.; Han, J. W. *J. Am. Chem. Soc.* **2002**, *124*, 12102.
(6) For a review: Simpkins, N. S. *Tetrahedron* **1990**, *46*, 6951.
(7) Noncatalytic *cine*-substitution of alkenyl sulfones with potassium or lithium cyanides has been reported: (a) Taber, D. F.; Saleh S. A. *J. Org. Chem*. **1981**, *46*, 4817. (b) Bailey, P. L.; Jackson, R. F. W. *Tetrahedron Lett.* **1991**, *32*, 3119.
(8) For reviews on organotitanium reagents: (a) Duthaler, R. O.; Hafner, A. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 1, p 447. (b) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer: Verlag: 1986. (c) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835. (d) Ferreri, C.; Palumbo, G.; Caputo, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, p 139.
(9) A similar reaction mechanism has been reported in the palladium-catalyzed cross-coupling reaction (See ref 2a).
(10) GC analysis with chiral stationary phase column, CP-CHIRASIL-DEX-CB. For the asymmetric synthesis of **5** by nickel-catalyzed allylic alkylation: Chung, K.-G.; Miyake, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2725 and references therein.
(11) The enantiomeric purity was determined by HPLC analysis with chiral stationary phase column, Chiralcel OB-H (hexane).
(12) The reaction of 1-phenylsulfonylcyclpentene under the same conditions gave a lower yield (ca. 5%) of 3-phenylcyclopentene.
(13) The enantiomeric purity was determined by HPLC analysis with chiral stationary phase column, Chiralcel OJ (hexane).

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