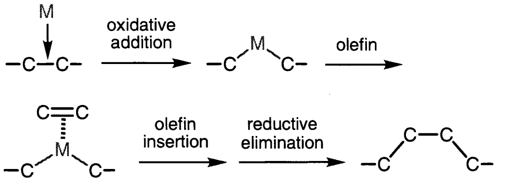
J|A|C|S
COMMUNICATIONS

Catalyzed Intramolecular Olefin Insertion into a Carbon−Carbon Single Bond

Masahiro Murakami,* Tamon Itahashi, and Yoshihiko Ito
Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Yoshida, Kyoto 606-8501, Japan

Received August 7, 2002

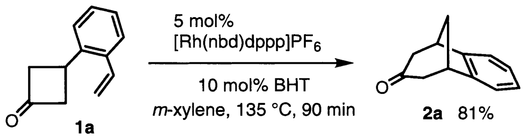
A wide variety of synthetic transformations are currently available for the functionalization of organic compounds. Nevertheless, the controlled insertion of an unsaturated organic functionality such as a carbon−carbon double bond into a carbon−carbon single bond would be a synthetic protocol of considerable novelty as well as utility. Such a transformation requires a particular method for the activation of carbon−carbon single bonds, for example, by way of oxidative addition to a transition metal (eq 1).[1]



(1)

However, carbon−carbon single bonds are arguably one of the least reactive functional groups especially with respect to transition metals. Hence, catalytic reactions in which oxidative addition of carbon−carbon single bonds is the elementary step are still difficult to achieve.[2] We recently found that the bond between the carbonyl carbon and the α-carbon of a cyclobutanone can be catalytically cleaved by a rhodium(I) complex.[3] Here we report the rhodium-catalyzed intramolecular insertion reaction of a carbon−carbon double bond into a carbon−carbon single bond which occurs as depicted in eq 1. In a single step, the insertion reaction creates a complex bicyclo[3.2.1]octane skeleton from cyclobutanone. In addition, novel regioselectivity was observed in the key process of carbon−carbon bond cleavage, presumably being brought about through the ligation of the metal by a pendant vinyl group.

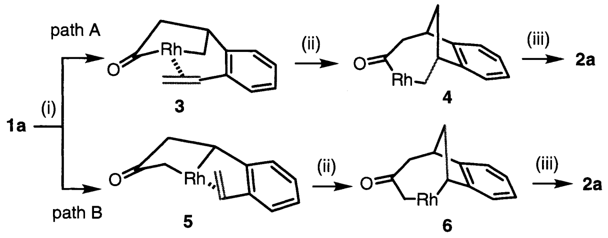
Our previous studies on the activation of carbon−carbon single bonds[3] led us initially to attempt intermolecular insertion reactions, all of which have so far proved unsuccessful. We then envisaged that the desired transformation can be accomplished by situating an unsaturated organic functionality at an appropriate position within the substrate. The key substrate, that is, cyclobutanone equipped with an *o*-substituted styryl group at the 3-position (**1a**), was prepared from 1,2-divinylbenzene by [2 + 2] cycloaddition with dichloroketene and the subsequent dechlorination with zinc. When heated at 135 °C in xylene in the presence of [Rh(nbd)(dppp)]PF_6 (5 mol %)[4] and 2,6-di(*tert*-butyl)-4-methylphenol (BHT, 10 mol %),[5] cyclobutanone **1a** was converted into benzobicyclo[3.2.1]octan-3-one (**2a**) which was isolated in 81% yield after heating for 90 min. Obviously, this complex skeleton resulted from intramolecular insertion of the vinyl group into a carbon−carbon single bond of the cyclobutanone, as discussed below. The present reaction proceeded much faster than the carbon−carbon bond cleaving reactions of cyclobutanones previously reported, which normally took more than one-half of a day.[3] It is likely that intramolecular coordination of the vinyl group to rhodium facilitates its insertion.



(2)

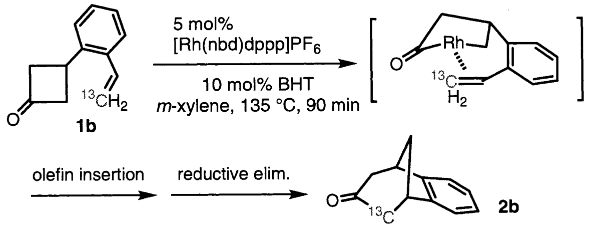
The production of **2a** can be explained by assuming the pathway pictured below (path A in eq 3). Initially, rhodium(I) is inserted between the carbonyl carbon and the α-carbon of **1a** to generate a five-membered cyclic acylrhodium intermediate (**3**) with the vinyl group coordinating to rhodium. Migratory insertion of the vinyl group into the rhodium−carbon bond affords the bicyclic acylrhodium intermediate (**4**).[6] Subsequent reductive elimination gives rise to **2a** and regenerates the rhodium(I) catalyst.

An alternative mechanism (path B) becomes conceivable when the new cleavage site (*β*-bond cleavage) discovered with the dppe ligand (vide infra) is taken into account. Rhodium(I) cleaves the bond between the α-carbon and the *β*-carbon of **1a** to generate a five-membered rhodacycle (**5**). Migratory insertion of the vinyl group into the rhodium−carbon bond and subsequent reductive elimination afford the same ketone **2a**.



(3)

To determine which path the reaction follows, ^{13}C-labeled substrate (**1b**) was synthesized in which a ^{13}C nuclide was installed at the terminal vinylic position. The reaction of **1b** furnished **2b** which contained a ^{13}C nuclide at the α-position of the carbonyl group. This experiment established that the initial insertion of rhodium occurred between the carbonyl carbon and the α-carbon of the cyclobutanone (path A), as with the previous cases.[3]



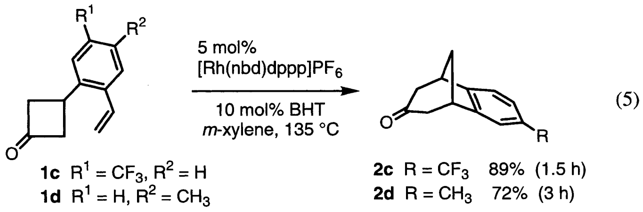
(4)

Other examples of the rhodium-catalyzed intramolecular insertion of a carbon−carbon double bond into a carbon−carbon single bond are shown in eq 5. The reaction of a cyclobutanone having an electron-withdrawing substituent (**1c**) proceeded slightly faster than that of **1d** possessing an electron-donating group.[7]

---

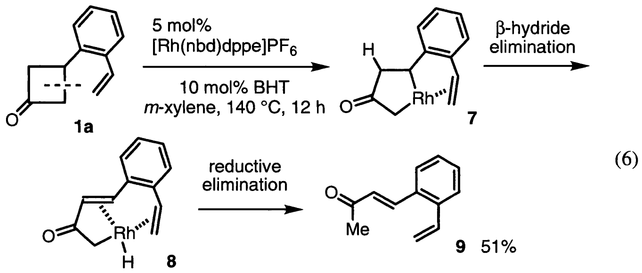
* To whom correspondence should be addressed. E-mail: murakami@sbchem.kyoto-u.ac.jp.

10.1021/ja021062n CCC: $22.00 © 2002 American Chemical Society



(5)

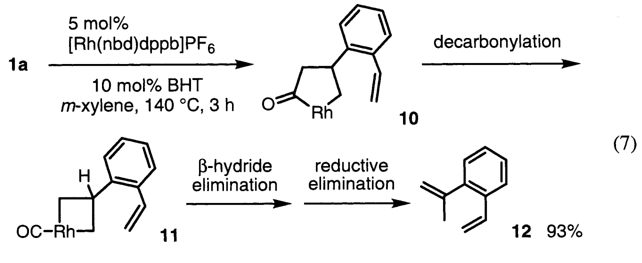
Surprisingly, decreasing the length of the tether between the two phosphorus atoms in the bidentate phosphine ligand dppp by only one carbon to dppe[4] gave a completely different result. While the dppp complex gave olefin insertion via α-bond cleavage, the [Rh(nbd)(dppe)]PF_6-catalyzed reaction of **1a** furnished the ring-opened α,β-unsaturated ketone (**9**) in 51% isolated yield. No formation of **2a** was observed in the NMR spectrum of the crude reaction mixture (the other starting material remained unreacted due to gradual deterioration of the catalyst). It is likely that rhodium(I) cleaves the β-bond, that is, the bond between the α sp^3 carbon and the β sp^3 carbon of **1a**, to generate the five-membered rhodacycle (**7**). Rhodacycle **7** then undergoes β-hydride elimination to give **8**. Finally, reductive elimination affords **9**.



(6)

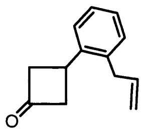
When 3-phenylcyclobutanone lacking a vinyl group was subjected to identical conditions, no reaction occurred, and 3-phenylcyclobutanone remained unreacted. Moreover, diphenylacetylene (1 equiv) or ethylene (7 atm) as a coordinating additive completely hampered the reaction of **1a**. These results demonstrate that cleavage at the β carbon−carbon bond of **1a** is guided by the vinyl substituent; it acts as a ligand bringing rhodium into the immediate vicinity of the β carbon−carbon bond and promotes cleavage of this otherwise unreactive bond.

The use of dppb[4] as a ligand for rhodium yielded a third distinct and exclusive reaction pathway for **1a**. As was often the case with dppb,[3b,d] **1a** underwent decarbonylation to furnish diolefin (**12**, 93% GC yield) when treated with [Rh(nbd)(dppb)]PF_6. Similarly to the case with dppp, rhodium initially inserted into the α C−C bond to form **10**. Expulsion of the carbonyl group was followed by β-hydride elimination and reductive elimination, leading to **12**. The preference the dppb ligand has for expulsion of the carbonyl group from **10** may be attributed to the wider P−Rh−P angle, which is expected to squeeze the ligated substrate to form a rhodacycle of a smaller ring size through decarbonylation.



(7)

For comparison, analogous reactions of cyclobutanone **13** having an allyl group instead of a vinyl group were studied. Only decarbonylation took place to form diolefin or a mixture of cyclopropane and diolefin with a catalysis of either dppe, dppp, or dppb complex. Appropriate location of a C−C double bond in a molecule or η^4-type coordination of a styryl unit is important for olefin insertion (with dppp) as well as for β bond cleavage (with dppe).



13

In summary, a new rhodium-catalyzed synthetic sequence was developed in which a carbon−carbon double bond was inserted into a carbon−carbon single bond. Construction of a complex bicyclic carbon framework from a simple cyclobutanone in a single step is noteworthy. While the full potential awaits exploration, this new insertion process may eventually lead to a general synthetic protocol. An additional highlight is that the reaction patterns of cyclobutanone **1a** change dramatically according to the chain length separating two phosphorus atoms of the employed ligand. In particular, the use of the dppe ligand found a new site selection in the carbon−carbon bond cleavage of cyclobutanone. A bond between two sp^3 carbon atoms is the most inert one because no π-orbital participation is available for incipient interaction with a metal orbital. The present example proved it promising that the aid of a coordinating directive group steers the position of activation even to such an inert bond.

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research on Priority Areas (A) “Exploitation of Multi-Element Cyclic Molecules” from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

Supporting Information Available: Preparation of **1**, spectroscopic data, and experimental procedure for **2**, **9**, and **12** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For reviews, see: (a) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (b) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed.* **1999**, *38*, 870. (c) Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S., Ed.; Springer: Berlin, 1999; p 97.

(2) (a) Kaneda, K.; Azuma, H.; Wayaku, M.; Teranishi, S. *Chem. Lett.* **1974**, 215. (b) Suggs, J. W.; Jun, C.-H. *J. Chem. Soc., Chem. Commun.* **1985**, 92. (c) Edelbach, E. L.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2843. (d) Liou, S.-Y.; van der Boom, M. E.; Milstein, D. *Chem. Commun.* **1998**, 687. (e) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880. (f) Jun, C.-H.; Lee, D.-Y.; Kim, Y.-H.; Lee, H. *Organometallics* **2001**, *20*, 2928. (g) Miller, J. A. *Tetrahedron Lett.* **2001**, *42*, 6991. (h) Müller, C.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **2002**, *21*, 1975.

(3) (a) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (b) Murakami, M.; Amii, H.; Shigeto, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8285. (c) Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307. (d) Murakami, M.; Itahashi, T.; Amii, H.; Takahashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9949. (e) Murakami, M.; Tsuruta, T.; Ito, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 2484.

(4) nbd = 2,5-norbornadiene, dppp = $Ph_2PCH_2CH_2CH_2PPh_2$, dppe = $Ph_2PCH_2CH_2PPh_2$, dppb = $Ph_2PCH_2CH_2CH_2CH_2PPh_2$.

(5) 2,6-Di(*tert*-butyl)-4-methylphenol (BHT) was used to prevent polymerization of the styryl group. When the reaction was carried out in the absence of BHT, the yield of **2a** decreased to 15%, while **1a** was consumed.

(6) Migratory insertion into the rhodium−(acyl carbon) linkage is also conceivable.

(7) For promotion by o-$CF_3C_6H_4CH{=}CH_2$, see: Giovannine, R.; Stüdemann, T.; Dussin, G.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2387.

JA021062N