Ruthenium-Catalyzed Coupling of Aromatic Carbon-Hydrogen Bonds in Aromatic Imidates with Olefins

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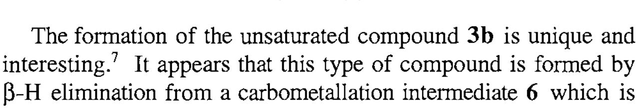
(Received September 28, 1998; CL-980749)

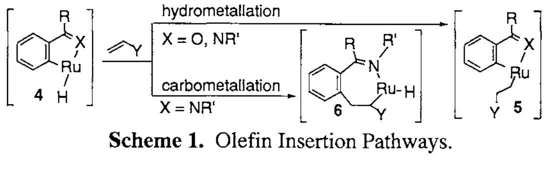
Catalytic C-H/olefin coupling can be directed by *N,O*-heterocyclic substituents. The $Ru_3(CO)_{12}$-catalyzed reaction of 4,4-dimethyl-2-(2-methylphenyl)-5,6-dihydro-4*H*-1,3-oxazine (**1**) with triethoxyvinylsilane gave a mixture of the corresponding 1:1 addition product (**3a**) and its olefinic analogue (**3b**) in good yields in ca. a 1:1 ratio. In the case of the reaction of 4,4-dimethyl-2-(2-methylphenyl)-4,5-dihydro-1,3-oxazole (**7**), the olefinic analogue (**8b**) of the coupling product (**8a**) was obtained as the major product. The existence of a new reaction pathway is discussed.

The synthetic potential of dihydrooxazole and dihydrooxazine functional groups, which are referred to as imidates, has continued to provide efficient and convenient routes for the synthesis of a variety of organic molecules, since these functions can be easily converted to carboxyl, amino, and formyl groups.[1] It is noteworthy that these imidate functions can be used as the directing group in lithiation chemistry using organolithium reagents.[2] During our ongoing efforts with respect to a catalytic use of otherwise unreactive C-H bonds in organic synthesis,[3] we became interested in the possibility that the imidate function might be useful as a directing group for ruthenium-based catalysts, since the coupling products would be expected to be very useful. In this communication, we report that the addition of C-H bonds in aromatic imidates to olefins can be catalyzed by $Ru_3(CO)_{12}$ and that an olefinic analogue of the coupling product was also formed and, in some cases, was isolated as the major product. These novel findings open a new opportunity in the rapidly expanding area of catalytic C-H/olefin coupling.

The reaction of 4,4-dimethyl-2-(methylphenyl)-5,6-dihydro-4*H*-1,3-oxazine (**1**) with triethoxyvinylsilane (**2**) proceeded with the aid of $Ru_3(CO)_{12}$[4] to afford the corresponding 1:1 addition product **3a** and a dehydrogenative coupling product **3b** in 35% and 30% yields, respectively (Eq. 1). The two methyl groups are necessary in order for this reaction to proceed. A similar compound without the methyl group, i.e., 2-(methylphenyl)-5,6-dihydro-4*H*-1,3-oxazine, gave no coupling product at all. This result indicates that the hydrogen α to the nitrogen atom strongly suppresses the desired catalytic C-H/olefin coupling reaction. This deactivation of the catalyst might be the result of the cleavage of the C-H bond α to the nitrogen atom by the ruthenium complex.[5,6]

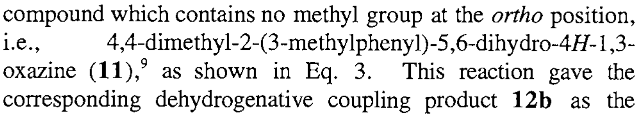


The formation of the unsaturated compound **3b** is unique and interesting.[7] It appears that this type of compound is formed by β-H elimination from a carbometallation intermediate **6** which is formed only when the directing center is a nitrogen atom (**4**, X = NR') but not an oxygen atom[8] (**4**, X = O) (Scheme 1). The ease of carbometallation (**4** → **6**) can be attributed to the stabilization of the seven-membered ruthenacycle by the strong coordination of nitrogen (**4**, X = NR'), whereas coordination by a carbonyl oxygen (**4**, X = O) is not sufficiently strong to stabilize the similar seven-membered ruthenacycle.



Scheme 1. Olefin Insertion Pathways.

Coupling products **8a** and **8b** were obtained in 10% and 87% yields, respectively from the five-membered ring analogue, 4,4-dimethyl-2-(2-methylphenyl)-4,5-dihydro-1,3-oxazole (**7**) (Eq. 2). Interestingly, in this case the dehydrogenative coupling product **8b** was formed as the major product. We presume that this different selectivity to **3b** and **8b** is caused by steric repulsion between the methyl group on the aromatic ring and the oxygen atom in the dihydrooxazine ring, which results in the suppression of the formation of a seven-membered ruthenacycle such as **9** (a precursor to **3b**) (Chart 1).



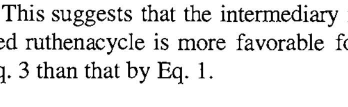
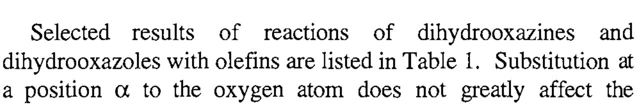


Chart 1.

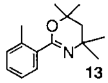
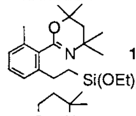
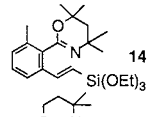
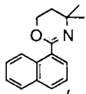
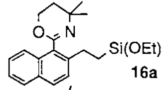
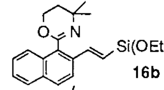
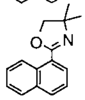
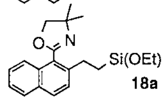
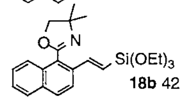
To verify this hypothesis, we investigated the reaction of a compound which contains no methyl group at the *ortho* position, i.e., 4,4-dimethyl-2-(3-methylphenyl)-5,6-dihydro-4*H*-1,3-oxazine (**11**),[9] as shown in Eq. 3. This reaction gave the corresponding dehydrogenative coupling product **12b** as the major isomer. This suggests that the intermediary formation of a seven-membered ruthenacycle is more favorable for the reaction described in Eq. 3 than that by Eq. 1.



Selected results of reactions of dihydrooxazines and dihydrooxazoles with olefins are listed in Table 1. Substitution at a position α to the oxygen atom does not greatly affect the product distribution (Run 1 and Eq. 1). Interestingly, the reaction of naphthyldihydrooxazine **15** with **2** gave the 1:1 addition product **16a** as a major product in 84% yield (Run 2). However, the dehydrogenative coupling product **18b** was formed as the product distribution again appears to stem from the steric congestion around the peri hydrogen atom (at the C8 position).

Therefore, the formation of a seven-membered ruthenacycle (from **15**; similar to **9**) seems to be thwarted by steric repulsion between the peri hydrogen and the ring oxygen.

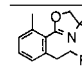
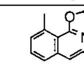
Table 1. Reactions of Several Aromatic Imidates with **2**[a]

Run	Aromatics	Products and Yields[b]	
1	 **13**	 **14a** 30%	 **14b** 35%
2[c]	 **15**	 **16a** 84%	 **16b** 5%
3[d]	 **17**	 **18a** 15%	 **18b** 42%

[a]Reaction conditions: imidates (2 mmol), **2** (10 mmol), $Ru_3(CO)_{12}$ (0.12 mmol), toluene (3 cm^3), 135 °C (bath temp.), 24 h. [b]GC yield. [c]10 h. [d]4 h.

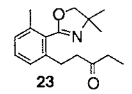
Several olefins are also applicable to the present C-H/olefin coupling reaction (Table 2). The reaction of **7** with ethoxy(dimethyl)vinylsilane afforded the simple 1:1 addition product **19a** and dehydrogenative coupling product **19b** in 6% and 52% yield, respectively (Run 1 in Table 2). This represents an interesting new route for vinylsilanes which are well known as versatile synthetic intermediates.[10] Styrene can be also used in place of the vinylsilanes as the olefin (Run 3 in Table 2). This coupling reaction proceeded to give the corresponding dehydrogenative coupling product **21b** in 45% yield. In this case, ethylbenzene was also formed in nearly equimolecular amounts (1 mmol) to **21b**. This result suggests that the hydrogen atoms generated in the olefin forming step were transferred to another molecule of the starting olefin. In contrast to this result, in the cases of reactions with vinylsilanes, even though dehydrogenative coupling products were obtained in high yields, the hydrogenation products of the vinylsilanes were not detected by GC. It has previously been shown that two molecules of a vinylsilane catalytically give bis(silyl)ethylene and ethylene.[11] Therefore, in the present reaction using vinylsilanes, the ethylene, produced *in situ*, must have functioned as the hydrogen scavenger in the catalytic cycle.[12,13]

Table 2. Reactions of **7** with Olefins[a]

		Products and Yields[b]			
Run	R				
1	$SiMe_2(OEt)$	**19a**	6%	**19b**	52%
2	$SiMe_2Ph$	**20a**	8%	**20b**	84%
3	Ph	**21a**	4%	**21b**	45%
4[c,d]	H	**22a**	53%	**22b**	trace

[a]Reaction conditions: **7** (2 mmol), olefin (10 mmol), $Ru_3(CO)_{12}$ (0.12 mmol), toluene (3 cm^3), 24 h. [b]GC yield. [c]Ethylene (7 atm, 14 mmol). [d]A CO incorporated product **23** was also formed in 20% yield.

Interestingly, the reaction of **7** with ethylene (Run 4 in Table 2) gave the corresponding 1:1 addition product **22a** in 53% yield. In addition to **22**, the carbon monoxide[14] incorporated product **23** was also obtained in 20% GC yield. It appears that product **23** is formed *via* a carbometallation pathway (Scheme 1; **6**, Y = H). Thus, the dehydrogenative coupling products such as **3b** or **8b** appear to be produced through the insertion of an olefin into the ruthenium-carbon bond followed by a β-hydride elimination sequence.



23

To enhance the utility of the present C-H/olefin coupling, the *in situ* hydrogenation of the product mixture to one component (i.e., saturated products) is successfully carried out. After the C-H/olefin coupling reaction was complete, the reaction mixture was directly exposed to hydrogen (1 atm). In the cases of the hydrogenation **8b** and **18b**, the reaction was carried out at 100 ℃ for 1h, resulting in complete conversions to **8a** and **18a**, respectively. No additional catalyst was necessary. In the case of the hydrogenation of a mixture of **3a** and **3b**, prolonged reaction period (24 h) was required to attain complete conversion to **3a**.

It has been found that dihydrooxazines and dihydrooxazoles on the aromatic ring are capable of effecting the C-H/olefin coupling. In addition to the simple coupling reaction pathway (i.e., addition), the existence of a new pathway, i.e., olefinic product formation, has been found. This will provide for new opportunities for the use of these catalytic systems in the future.

Supporting Information (7 pages) including typical experimental procedures and spectral data of new compounds are available on request to the author by telefax (+81-6-879-7396).

This work was supported, in part, by a Grant-in-Aid for Scientific Research on Priority Areas (No. 283, "Innovative Synthetic Reactions") from Monbusho, Japan.

References and Notes

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3 a) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, and N. Chatani, *Nature*, **366**, 529 (1993). b) F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, and S. Murai, *Bull. Chem. Soc. Jpn.*, **68**, 62 (1995). c) M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, and S. Murai, *Chem. Lett.*, **1996**, 109. d) F. Kakiuchi, M. Yamauchi, N. Chatani, and S. Murai *Chem. Lett.* **1996**, 111.

4 The $Ru_3(CO)_{12}$ complex is effective in the coupling reaction of aromatic imines with olefins. See, Ref. 3d.

5 For the examples of the cleavage of a C-H bond adjacent to a nitrogen atom, see: S.-I. Murahashi, T. Naota, and K. Yonemura, *J. Am. Chem. Soc.*, **110**, 8256 (1988).

6 Very recently, we reported on a new catalytic reaction involving the cleavage of a C-H bond adjacent to a nitrogen atom, see: Y. Ishii, N. Chatani, F. Kakiuchi, and S. Murai, *Organometallics*, **16**, 3615 (1997); Y. Ishii, N. Chatani, F. Kakiuchi, and S. Murai, *Tetrahedron Lett.*, **38**, 7565 (1997).

7 A similar olefinic product was observed in the catalytic reaction of aromatic imines but only in low yields (Ref. 3d)

8 The Ru-catalyzed coupling of aromatic ketones with olefins did not give rise to any unsaturated by-products. See, Refs. 3a-c.

9 The introduction of a methyl group on the aromatic ring is important in suppressing the formation of the 1:2 coupling product.

10 J. Y. Corey, "Advances in Silicon Chemistry," ed by G. L. Larson, JAI Press, Greenwich, Conneticut (1991), pp. 327-387.

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12 The corresponding bis(silyl)ethylenes have been detected in ca. 20-40% yields (2 mmol-4 mmol) based the vinylsilane charged.

13 Since the reactions of **7** with vinylsilanes were carried out in vigorously refluxing toluene, ethylene that should have been generated by the disproportionation of the vinylsilanes seemed to have gone away from the reaction mixture. So, the corresponding ethylation product could have not been detected by GC analysis.

14 Carbon monoxide is assumed to arise from the ruthenium carbonyl complex.