Carbon−Carbon Bond Formation on a Bis(oxazolinyl)phenyl−Rhodium Complex in a Reduction and Oxidative Addition Sequence

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*Summary: The unique C−C bond formation reaction between diisopropylamine and CH_2Cl_2 proceeding on a bis(oxazolinyl)-phenyl rhodium complex (tBu-Phebox-dm)RhCl$_2$(H_2O) (**1**) was discovered. The intermediary chloromethyl complex, (tBu-Phebox-dm)Rh(CH_2Cl)Cl(NEt_3), which was obtained by reaction of **1** with CH_2Cl_2 in the presence of amine, underwent C−C bond formation with imine to give an azarhodacyclopentene complex, **2**.*

Reduction of transition metal complexes can readily be promoted by action of tertiary or secondary amines, involving activation of the α-hydrogen atom adjacent to the nitrogen atom.[1] Such an activation of an sp^3 C−H bond has also been recognized as a potential derivatization method of amino compounds accompanied with subsequent carbon-chain elongation.[2] Recently Murai et al. reported a catalytic C−C bond formation by efficient activation of a C−H bond of amines followed by reaction with alkenes.[3] We have so far studied bis(oxazolinyl)phenyl (Phebox) ligands, which can make a metal−carbon covalent bond and meridional stereochemistry, and their related rhodium complexes as catalysts for asymmetric reactions.[4] Recently, we have demonstrated a conjugate reduction of acrylates and sequential aldol reaction with Phebox-Rh^{III} catalysts and hydrosilanes, where it is essential that the initial trivalent rhodium atom is reduced to the monovalent species by the action of hydrosilanes. As alternative reducing agents, we have pursued other hydride species and alkylamines. In this communication, we will disclose a unique C−C bond formation reaction on the Phebox-Rh skeleton and the related reduction and oxidative addition sequences.

Treatment of (*t*Bu-Phebox-*dm*)RhCl$_2$(H_2O) (**1**) with diisopropylamine (10 equiv) in a dichloromethane solution at 50 °C for 12 h resulted in formation of an azarhodacyclopentene complex, **2**, accompanied with a small amount of the primary isopropylamine rhodium complex **3** in the ratio **2**:**3** = 96:4 based on ^{1}H NMR of the crude mixture (Scheme 1). Complex **2** was isolated in ca. 50% yield after crystallization.[5]

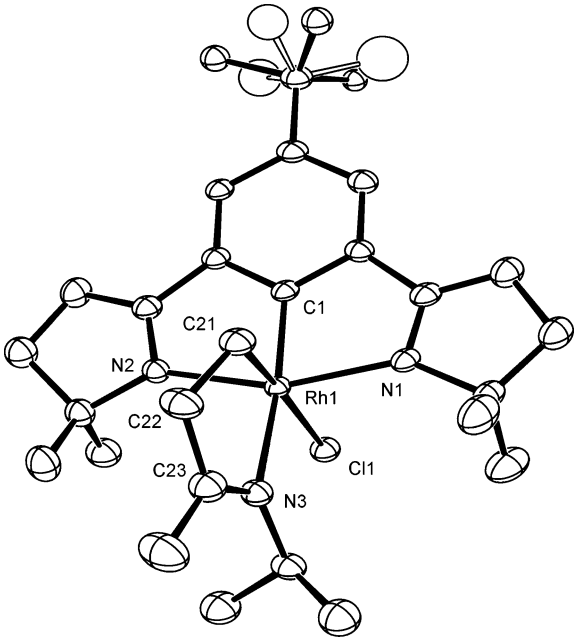

Figure 1. Molecular structure of **2**. Selected bond lengths (Å) and angles (deg): Rh1−C1 1.913(5), Rh1−C21 2.045(6), Rh1−N1 2.078(4), Rh1−N2 2.095(4), Rh1−N3 2.211(4), Rh1−Cl1 2.4977-(12), N3−C23 1.278(7), C21−C22 1.528(9), C22−C23 1.511(8), N1−Rh1−N2 156.72(16), C1−Rh1−N3 169.16(18), C21−Rh1−Cl1 173.28(18), C23−N3−Rh1 112.8(4), N3−C23−C22 117.3-(5), C23−C22−C21 114.0(5), C22−C21−Rh1 108.6(4).

Complex **2** was fully characterized on the basis of NMR and X-ray study. The characteristic signal appearing at δ_H 0.79 ppm with the Rh−H coupling (J_{RhH} = 2.1 Hz) was assigned to the methylene protons bound to the Rh atom. The doublet signal assigned to the α-carbon atom bound to the Rh atom was observed at δ_C 11.2 ppm with the Rh−C coupling (J_{RhC} = 23.5 Hz), and the other doublet signal assigned to the imine carbon atom was observed at δ_C182.3 ppm with the Rh−C coupling (J_{RhC} = 1.7 Hz). As shown in Figure 1, complex **2** consists of the azarhodacycle structure with Rh, N, and three C atoms.[6] Furthermore, the Rh−C(21) bond length of 2.045(6) Å indicates that the bond Rh−C is a single bond, and the N(3)−C(23) bond length of 1.278(7) Å is consistent with the N=C double bond.

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(1) (a) Trzeciak, A. M.; Ciunik, Z.; Ziokowski, J. J. *Organometallics* **2002**, *21*, 132−137. (b) Hidai, M.; Kokura, M.; Uchida, Y. *J. Organomet. Chem.* **1973**, *52*, 431−435. (c) Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890−1901.

(2) (a) Murahashi, S.-I. *Angew. Chem.* **1995**, *107*, 2670−2693. (b) Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312−15313. (c) Li, Z.; Li. C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 11810−11811. (d) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 6968−6969.

(3) (a) Chatani, N.; Asaumi, T.; Ikeda, T.; Yorimitsu, S.; Ishii, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **2000**, *122*, 12882−12883. (b) Chatani, N.; Asaumi, T.; Yorimitsu, S.; Ikeda, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **2001**, *123*, 10935−10941.

(4) (a) Kanazawa, Y.; Tsuchiya, Y.; Kobayashi, K.; Shiomi, T.; Itoh, J.; Kikuchi, M.; Yamamoto, Y.; Nishiyama, H. *Chem. Eur. J.* **2006**, *12*, 63−71. (b) Tsuchiya, Y.; Kanazawa, Y.; Shiomi, T.; Kobayashi, K.; Nishiyama, H. *Synlett* **2004**, 2493−2496. (c) Nishiyama, H.; Shiomi, T.; Tsuchiya, Y.; Matsuda, I. *J. Am. Chem. Soc.* **2005**, *127*, 6972−6973. (d) Motoyama, Y.; Okano, M.; Narusawa, H.; Makihara, N.; Aoki, K.; Nishiyama, H. *Organometallics* **2001**, *20*, 1580−1591.

(5) Complex **3** was characterized by comparison with an authentic sample prepared by the reaction of **1** with N^iPrH_2.

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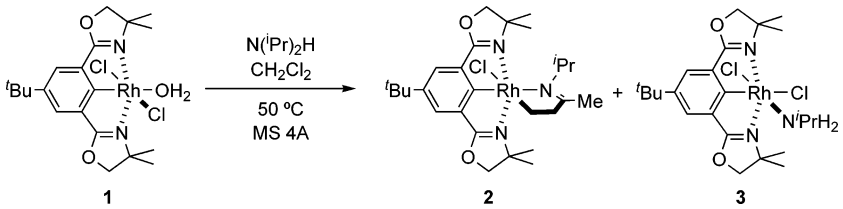
Scheme 1



1 2 3

By monitoring the reaction of **1** with diisopropylamine in CD_2Cl_2 by ^1H NMR spectroscopy at room temperature, the formation of free *N*-isopropylpropylideneamine (**4**) was observed. When the reaction was carried out in the presence of water (ca. 30 equiv), the ratio of **2**:**3** decreased to 23:76. As the formation of acetone molecules was detected in the reaction medium by NMR study, isopropylamine of complex **3** should be derived by hydrolysis of **4**, which was formed by oxidative hydride elimination of starting diisopropylamine.

The origin of the carbon atom α to the Rh atom of **2** was confirmed by the reaction of **1** with diisopropylamine in CD_2Cl_2 at 50 °C for 8 h. The obtained complex was determined to be complex **2-*d*$_2$**, in which the methylene protons bound to the Rh atom were exclusively replaced by deuterium, as evidenced by the disappearance of the signal for two protons at the C^1 carbon atom and the singlet signal for two protons at the C^2 carbon atom at δ 2.57 ppm (Figure 2). This fact unambiguously indicates that dichloromethane is the source for the C^1 carbon atom on the azarhodacyclopentene.

Oxidative addition of dichloromethane to Rh^I complexes is a common and basic reaction step.[7] We previously found oxidative addition of alkyl chlorides to a related Pybox-Rh^I complex (Pybox = bis(oxazolinyl)pyridine).[7a] First, we studied the process of oxidative addition of dichloromethane to the in-situ-generated Rh^I species by an action of amines. Only by use of NEt_3 could we isolate the chloromethyl-Rh^{III} complex **5** in 61% yield (Scheme 2). However, there was no reaction in the absence of NEt_3. The ^1H and ^{13}C NMR spectra showed the signals for the CH_2Cl group at δ_H 3.41 ppm (d, J_{RhH} = 3.3 Hz) and δ_C 48.79 ppm (d, J_{RhC} = 34.7 Hz), respectively. In place of dichloromethane, methyl chloroacetate was used to form the similar alkyl complex **6** in 95% yield. X-ray analysis of **6** reveals that the alkyl group is coordinated to the apical position (Figure 3).[6]

Second, we examined whether the free *N*-isopropylpropylideneamine **4** could be involved in the reaction. When the reaction of the chloromethyl complex **5** with 5 equiv of the imine **4** was carried out at 60 °C in THF for 20 h, complex **2** was formed in 28% yield accompanied with **1** (34%) and **3** (17%) (Scheme 3). The complexes **1** and **3** could be formed by hydrolysis of the starting compounds **4** and **5**, since treatment of **5** with H_2O in THF resulted in the clean formation of **1**.[7c] On the other hand, formation of **2** was not observed in the reaction of **1** with **4** in CH_2Cl_2 at 50 °C for 24 h. These results provide strong evidence that the chloromethyl group and the

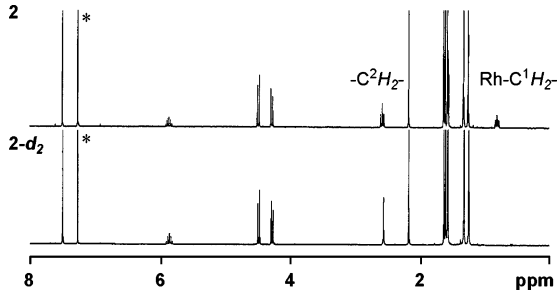


Figure 2. ^1H NMR spectra of **2** and **2-*d*$_2$** obtained by the reaction of **1** with $N(^iPr)_2H$ in CH_2Cl_2 and CD_2Cl_2 (*: $CHCl_3$).

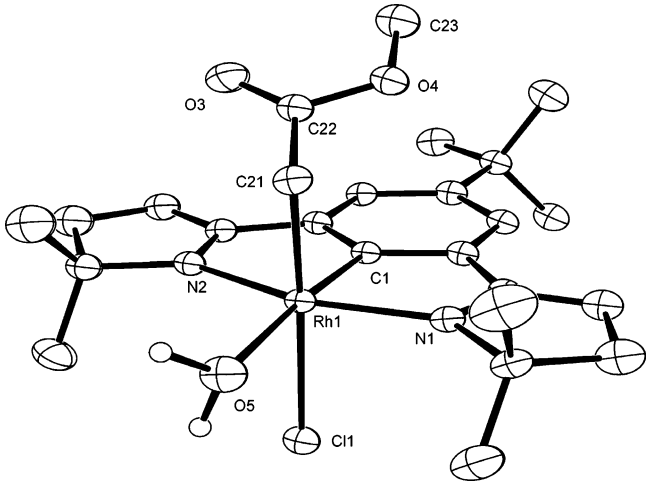
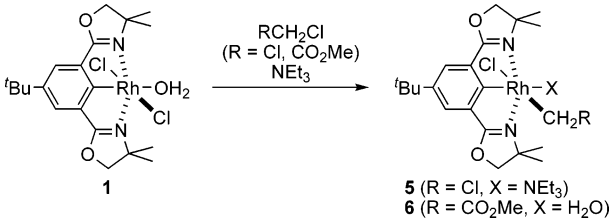


Figure 3. Molecular structure of **6**. Selected bond lengths (Å) and angles (deg): Rh1−C1 1.910(2), Rh1−C21 2.101(3), Rh1−N1 2.067(2), Rh1−N2 2.079(2), Rh1−Cl 2.4667(9), Rh1−O5 2.240(2), N1−Rh1−N2 158.30(9), C21−Rh1−Cl 172.10(8), C1−Rh1−O5 175.11(9), C22−C21−Rh1 115.53(18).

Scheme 2



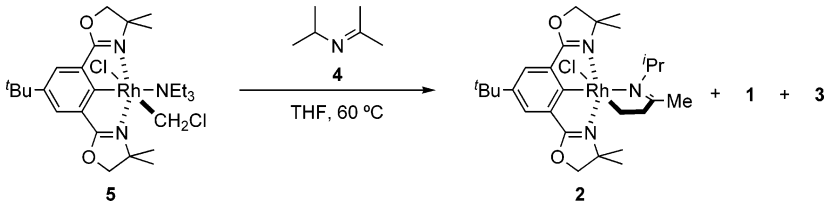
1

5 (R = Cl, X = NEt_3)
6 (R = CO_2Me, X = H_2O)

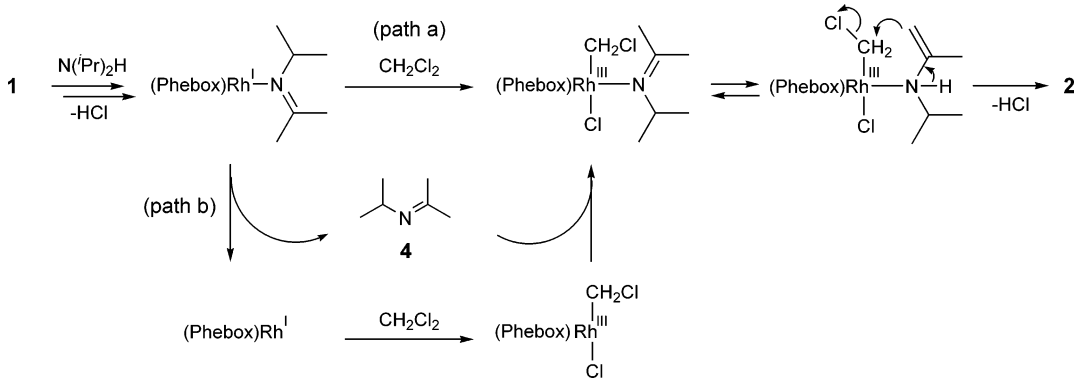
(6) Refinement details for **2**: empirical formula $C_{27}H_{41}ClN_3O_2Rh$; M_r = 577.99; crystal system orthorhombic; space group $P2_12_12_1$; a = 11.0643(10) Å, b = 11.9701(11) Å, c = 21.7303(19) Å, V = 2878.0(4) Å^3, Z = 4, d_{calcd} = 1.334 mg m^{-3}, μ = 0.713 mm^{-1}, $2\theta_{max}$ = 55°; reflections collected 19 889, independent reflections 6615 [R(int) = 0.0807]; max./min. transition 1.000000/0.670842; data/restrains/parameters 6615/16/320; goodness-of-fit on F^2 1.029; final R indices [$I > 2\sigma(I)$]: R1 = 0.0545, wR2 = 0.1034; R indices (all data): R1 = 0.0692, wR2 = 0.1080; absolute structure parameter 0.09(4); largest diff peak and hole 1.291 and −0.659 e Å^{-3}. Refinement details for **6**: empirical formula $C_{23}H_{34}ClN_2O_5Rh$; M_r = 556.88; crystal system monoclinic; space group $P2_1/c$; a = 10.064(4) Å, b = 11.050(4) Å, c = 23.182(9) Å, β = 100.009(9)°, V = 2538.8(17) Å^3, Z = 4, d_{calcd} = 1.457 mg m^{-3}, μ = 0.812 mm^{-1}, $2\theta_{max}$ = 55°; reflections collected 17 497, independent reflections 5811 [R(int) = 0.0450]; max./min. transition 1.000000/0.674537; data/restrains/parameters 5811/0/313; goodness-of-fit on F^2 1.081; final R indices [$I > 2\sigma(I)$]: R1 = 0.0386, wR2 = 0.0895; R indices (all data): R1 = 0.0475, wR2 = 0.0935; largest diff peak and hole 1.049 and −0.775 e Å^{-3}.

(7) (a) Nishiyama, H.; Horihata, M.; Hirai, T.; Wakamatsu, S.; Itoh, K. *Organometallics* **1991**, *10*, 2706−2708. (b) de Pater, B, C.; Zijp, E. J.; Fruhauf, H.; Ernsting, J. M.; Elsevier, C. J.; Vrieze, K. *Organometallics* **2004**, *23*, 269−279. (c) Haarman, H. F.; Ernsting, J. M.; Kranenburg, M.; Kooijman, H.; Veldman, N.; Spek, A. L.; van Leeuwen, P. W. N. M.; Vrieze, K. *Organometallics* **1997**, *16*, 887−900. (d) Northcutt, T. O.; Lachicotte, R. J.; Jones, W. D. *Organometallics* **1998**, *17*, 5148−5152.

Scheme 3



Scheme 4



imine **4** are significant intermediates in the C−C bond formation described in Scheme 1.

On the basis of these observations, we propose the mechanism for the formation of the azarhodacyclopentene complex **2** as depicted in Scheme 4. First, the aqua ligand of **1** was replaced by diisopropylamine,[4d] and the Rh^{III} complex was then reduced to the Rh^{I} complex. Concurrently, the amine might be oxidized to isopropylidene derivative **4**.[8] Oxidative addition of dichloromethane to the Rh^{I} interemediate in the presence (path a) or absence (path b) of the imine ligand **4** on the metal center provides the chloromethyl intermediate. The coordinated imine **4** was converted to the corresponding enamine in tautomerization, probably on the metal center.[9] Finally, the enamine attacked the chloromethyl moiety to give the azarhodacyclopentene complex **2** via C−C bond formation.[10]

In summary, we have found a novel C−C bond formation in the transition metal complex between the enamine part and chloromethyl part producing the azarhodacyclopentene complex **2**, presumably via reduction, oxidative addition, and cyclization sequence. Further detailed experiments with a variety of substrates are proceeding including development of a new type of homogeneous catalytic reactions.

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Supporting Information Available: Experimental procedures and crystallographic information files (CIFs). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) An example of β-hydride elimination of amine ligands; Barrera, J.; Orth, S. D.; Harman, W. D. *J. Am. Chem. Soc.* **1992**, *114*, 7316−7318.

(9) Lu, C. C.; Peters, J. C. *J. Am. Chem. Soc.* **2004**, *126*, 15818−15832.

(10) (a) Ferguson, G.; Li, Y.; McAlees, A. J.; McCrindle, R.; Xiang, K. *Organometallics* **1999**, *18*, 2428−2439. (b) Grotjahn, D. B.; Gong, Y.; Zakharov, L.; Golen, J. A.; Rheingold, A. L. *J. Am. Chem. Soc.* **2006**, *128*, 438−453.