Preferential Bond Activation of sp^3 C–H over sp^2 C–H in α,β-Unsaturated Carboxylic Acids by Ruthenium Complex

Susumu Kanaya, Nobuyuki Komine, Masafumi Hirano, and Sanshiro Komiya*
Department of Applied Chemistry, Faculty of Technology, Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588

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Reactions of Ru(1,5-cod)(1,3,5-cot) (**1**)/PMe_3 [cod = cyclooctadiene, cot = cyclooctatriene] with propenoic acids (CH_2=CH(R)COOH) give unsaturated ruthenalactones Ru[OC(O)C(R)=CH-κ^2*O,C*](PMe_3)$_4$ [R = Me (**2a**), Et (**2b**), Pr (**2c**), ^{i}Pr (**2d**)]. In contrast, reactions of *trans*-2-methyl-2-butenoic acid and 2-methylcinnamic acid (R'CH=C(Me)COOH) give Ru[OC(O)C(CH_2R')=CH-κ^2*O,C*](PMe_3)$_4$ [R' = Me (**2b**), Ph (**2e**)] as major products, suggesting the preferential activation of the sp^3 C–H over sp^2 C–H bond on ruthenium(II) center.

Much attention has been currently paid for C–H bond activation by transition-metal complexes[1–3] because of its potential applications in environmentally benign organic synthesis. It is generally accepted that transition metal complexes favor to cleave sp^2 C–H bond than sp^3 C–H bond, though the former bond dissociation energy is slightly larger (8–14 kJ/mol) than the latter.[4] This trend is accounted for both kinetic and thermodynamic reasons such as prior π-coordination of adjacent C=C bond to metal, and stability of the resulting M–C(sp^2) bond in the products.[1b,3] However, the selectivity control in transition metal mediated C–H activation is still limited and is rather unsettled.

We previously reported successive O–H and sp^3 C–H bond activation of ortho substituents of phenols by Ru(cod)(cot) (**1**) in the presence of tertiary phosphines to give novel 5-membered oxaruthenacycle complexes.[5] In these reactions, protonation of **1** by phenols is a crucial step to provide an anchoring phenoxo ligand, which would force the *ortho*-methyl C–H bond close to the metal center.[5,6] In a similar vein, unsaturated carboxylic acids are subjected to the reaction with **1**/PMe_3 to cleave C–H bonds in these acids giving ruthenalactones.[7,8] In the reactions of 2-alkyl-2-alkenoic acids, both sp^2 and sp^3 C–H bonds are susceptible to be cleaved as shown in the following Chart. We now found preferential sp^3 C–H bond activation over sp^2 bond in 2-alkyl-2-alkenoic acids by **1**/PMe_3 giving unsaturated ruthenalactones.

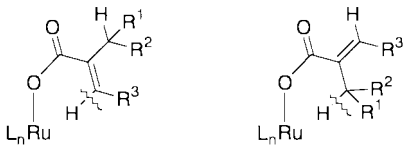
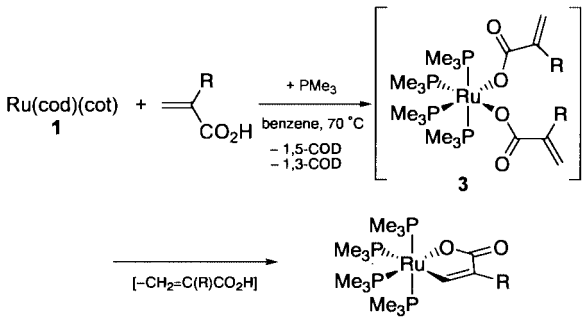


Chart 1

Reaction of **1** with methacrylic acid at 70 °C in the presence of PMe_3 resulted in the successive activation of O–H and C–H bonds to give an unsaturated ruthenalactone *cis*-Ru[OC(O)C(Me)=CH-κ^2*O,C*](PMe_3)$_4$ (**2a**) (31% NMR yield) accompanied by liberation of 1,5-COD and 1,3-COD (92% and 29% NMR yields)[9] (Scheme 1).



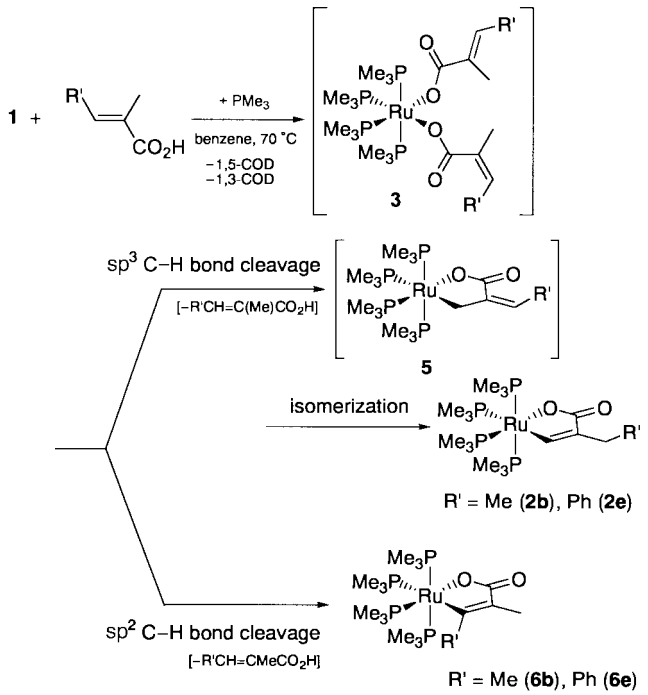
Scheme 1.

The $^{31}P\{^1H\}$ NMR spectrum of **2a** shows an AM_2X pattern and the ^{1}H NMR spectrum shows one virtual triplet and two doublets assignable to PMe_3 ligands trans to each other and two magnetically inequivalent PMe_3, respectively, indicating the cis configuration of **2a** in an octahedral geometry. The resonances at 7.86 (br) and 2.43 (s) ppm in the ^{1}H NMR are assigned to alkenyl and 2-methyl protons, respectively. In the IR spectrum of **2a**, a strong absorption band due to stretching vibration of the carbonyl group appears at 1577 cm^{-1}.[8] Acidolysis of **2a** by HCl gave methacrylic acid in 86% yield. Selective deuteration of alkenyl proton trans to the Me was observed on reaction of **2a** with DCl, suggesting that the β-carbon is directly bonded to ruthenium giving 5-membered ruthenacycle structure formed by the regioselective C–H bond cleavage.

In order to shed some light on the mechanism, the time-course of this reaction was monitored by NMR. At the initial stage of the reaction (12 h, at 50 °C), an A_2X_2 pattern assigned to *cis*-Ru[OC(O)C(Me)=CH_2]$_2$(PMe_3)$_4$ (**3a**)[10] was observed in NMR (25% NMR yield) together with free 1,5-COD and 1,3-COD (91% and 22% NMR yields, respectively). Then, signals due to **3a** gradually decreased, and instead an AM_2X pattern of **2a** increased with concomitant formation of two broad peaks due to (aqua)bis(carboxylato)ruthenium(II) complex Ru[OC(O)C(Me)=CH_2]$_2$(H_2O)(PMe_3)$_3$ (**4a**) in $^{31}P\{^1H\}$ NMR (24% NMR yield).[11]

Addition of PMe_3 (10 equiv) increased the yield of **2a** without retardation of reaction (69% NMR yield), while addition of water (ca. 1 equiv.) in this system enhanced the formation of **4a** (36% NMR yield). Thus, **2a** is considered to be obtained via an 18 e complex **3a** without liberation of PMe_3. The reaction proceeds via divalent species and one of the methacrylato ligands in **3a** acted as a hydrogen acceptor (Scheme 1).

Of particular interest is the reaction of **1** with (*E*)-2-methyl-2-butenoic acid in the presence of PMe_3. After 5 days at 70 °C



Scheme 2.

in benzene, an analogous but unexpected product *cis*-Ru[OC(O)C(Et)=CH-κ^2*O,C*](PMe$_3$)$_4$ (**2b**) was obtained as a major product in 80% yield with concomitant formation of Ru[OC(O)C(Me)=C(Me)-κ^2*O,C*](PMe$_3$)$_4$ (**6b**) in 10% yield (Scheme 2).[12] Similar treatment with (*E*)-2-methylcinnamic acid also gave analogous products **2e** and **6e** in 70% and 30% NMR yields, respectively.[13] ^{31}P{^{1}H} NMR of **2b** and **2e** showed a similar AM$_2$X pattern to **2a** and ^{1}H NMR indicated the existence of ethyl and benzyl moieties, respectively. Acidolyses of a mixture of **2b** and **6b** (7:3) with HCl give 2-ethylpropenoic acid and 2-methyl-2-butenoic acid in 60% and 12% yield, respectively. It should be noted that isomerization of these substrates was not catalyzed by **1**/PMe$_3$ at 70 °C. Thus, formation of **2b** and **2e** was consistently interpreted by the preferential sp^3 C–H bond cleavage of the 2-methyl group over sp^2 C–H on Ru(II) as follows. First of all, these acids react with **1**/PMe$_3$ to give *cis*-bis(carboxylato)ruthenim(II) complex **3**. The sp^3 C–H bond of the 2-methyl-2-alkenoato ligand is initially cleaved to give *cis*-Ru[OC(O)C(=CHR')CH$_2$-κ^2*O,C*](PMe$_3$)$_4$ [R' = Me (**5b**), Ph (**5e**)], which spontaneously isomerizes to thermodynamically stable unsaturated ruthenalactone **2b** or **2e** by 1,3-shift of the hydrogen atom.

Although **2a** is considered to be apparently formed via cleavage of only sp^2 C–H bond of the methacrylato ligand, initial sp^3 C–H activation of the Me group followed by isomerization can also explain the reaction pathway. However, when other 2-alkyl-2-alkenoic acids such as 2-ethylpropenoic acid, 2-propylpropenoic acid and 2-isopropylpropenoic acid were used as reactants, only ruthenalactones **2b** (23%), **2c** (23%) and **2d** (47%)[14] were obtained, in which only sp^2 C–H bonds were cleaved. Therefore, steric factor at the α- and β-carbon atoms seems to be important to control the selectivity between sp^2 and sp^3 C–H bond activation at Ru(II).

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7 Analogous reactions of **1**/PMe$_3$ and **1**/PPh$_3$ with 3-butenoic acid are reported to give Ru(η^5-C$_8$H$_{11}$)[OC(O)CH$_2$CH=CH$_2$-κ*O*, η^2-*C*^{3},*C*^{4}]-(PMe$_3$) [ref 6c] and Ru[OC(O)C$_3$H$_4$-κ*O*, η^3-*C*^{2},*C*^{2},*C*^{3}](PPh$_3$)$_2$ [ref 8], respectively.

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9 **2a**: Anal. Calcd for C$_{16}$H$_{40}$O$_2$P$_4$Ru: C, 39.26; H, 8.24%. Found: C, 39.00; H, 8.03%.

10 **3a**: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 1.08 (distorted vt, *J* = 4.5 Hz, 18H), 1.33 (vt, *J* = 1.5 Hz, 18H), 2.25 (s, 6H), 5.32 (s, 2H), 6.25 (d, *J* = 1.6 Hz, 2H). ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –2.6 (t, *J* = 32 Hz, 2P), 14.5 (t, *J* = 32 Hz, 2P).

11 **4a**: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 1.05 (br s, 27H), 2.09 (s, 6H), 5.25 (t, *J* = 1.8 Hz, 2H), 6.22 (d, *J* = 2.7 Hz, 2H), 10.3 (br s, 2H). ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ 25.9 (br d, *J* = 38 Hz, 2P), 28.0 (br t, *J* = 38 Hz, 1P).

12 Recrystallization of these products from THF/hexane gave a mixture of **2b** and **6b** in 7:3 molar ratio. **2b**: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 0.90 (d, *J* = 2.9 Hz, 9H), 0.97 (vt, *J* = 1.1 Hz, 18H), 1.08 (d, *J* = 2.7 Hz, 9H), 1.50 (t, *J* = 3.0 Hz, 3H), 2.83 (br q, *J* = 3.0 Hz, 2H), 7.89 (br, 1H). ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –11.7 (td, *J* = 26, 16 Hz, 1P), 0.16 (dd, *J* = 35, 26 Hz, 2P), 11.5 (td, *J* = 35, 16 Hz, 1P). **6b**: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 2.24–2.27 (m, 6H) signals due to PMe$_3$ ligands are overlapped with those of **2b**. ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –14.6 (td, *J* = 24, 15 Hz, 1P), –0.2 (dd, *J* = 34, 24 Hz, 2P), 6.0 (td, *J* = 34, 15 Hz, 1P).

13 Recrystallization of these products from THF/hexane exclusively gave **2e**. **2e**: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 0.87 (vt, *J* = 2.7 Hz, 18H), 0.90 (d, *J* = 7.2 Hz, 9H), 1.07 (d, *J* = 6.3 Hz, 9H), 3.99 (s, 2H), 7.02–7.68 (m, 5H), 7.89 (br, 1H). ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –11.6 (td, *J* = 26, 16 Hz, 1P), –0.1 (dd, *J* = 35, 26 Hz, 2P), 11.4 (td, *J* = 35, 16 Hz, 1P). **6e**: ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –15.6 (td, *J* = 24, 15 Hz, 1P), 6.3 (td, *J* = 30, 15 Hz, 1P), one of phosphorus signal is overlapped with the major signals.

14 **2c** as representative data: ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 0.88 (d, *J* = 7.5 Hz, 9H), 0.96 (vt, *J* = 2.7 Hz, 18H), 1.08 (d, *J* = 6.6 Hz, 9H), 1.22 (t, *J* = 7.5 Hz, 3H), 1.99 (qt, *J* = 7.5 Hz, 2H), 2.74 (br t, J = 7.2 Hz, 2H), 7.92 (br, 1H). ^{31}P{^{1}H} NMR (122 MHz, C$_6$D$_6$): δ –11.7 (br td, *J* = 25, 16 Hz, 1P), 0.3 (dd, *J* = 35, 25 Hz, 2P), 11.3 (td, *J* = 35, 16 Hz, 1P). IR (KBr, cm^{-1}): 1580 (vs, νC=O), 945 (vs, νC–O).