

## Preferential Bond Activation of $sp^3$ C–H over $sp^2$ C–H in $\alpha,\beta$ -Unsaturated Carboxylic Acids by Ruthenium Complex

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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 ruthenolactones  $Ru[OC(O)C(R)=CH-\kappa^2O,C](PMe_3)_4$  [ $R$  = Me (**2a**), Et (**2b**), Pr (**2c**),  $i$ Pr (**2d**)]. In contrast, reactions of *trans*-2-methyl-2-butenic acid and 2-methylcinnamic acid ( $R'CH=C(Me)COOH$ ) give  $Ru[OC(O)C(CH_2R')=CH-\kappa^2O,C](PMe_3)_4$  [ $R'$  = 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<sup>1–3</sup> 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.<sup>4</sup> This trend is accounted for both kinetic and thermodynamic reasons such as prior  $\pi$ -coordination of adjacent C=C bond to metal, and stability of the resulting M–C( $sp^2$ ) bond in the products.<sup>1b,3</sup> 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.<sup>5</sup> 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.<sup>5,6</sup> 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 ruthenolactones.<sup>7,8</sup> 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 ruthenolactones.

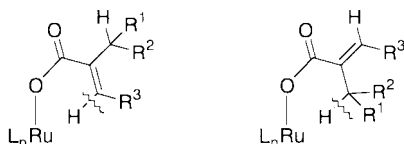
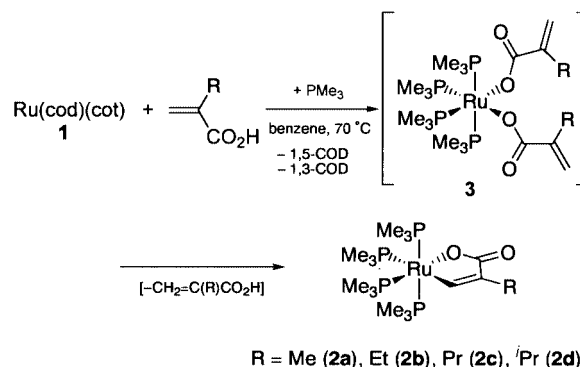


Chart 1

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 ruthenolactone  $cis-Ru[OC(O)C(Me)=CH-\kappa^2O,C](PMe_3)_4$  (**2a**) (31% NMR yield) accompanied by liberation of 1,5-COD and 1,3-COD (92% and 29% NMR yields)<sup>9</sup> (Scheme 1).



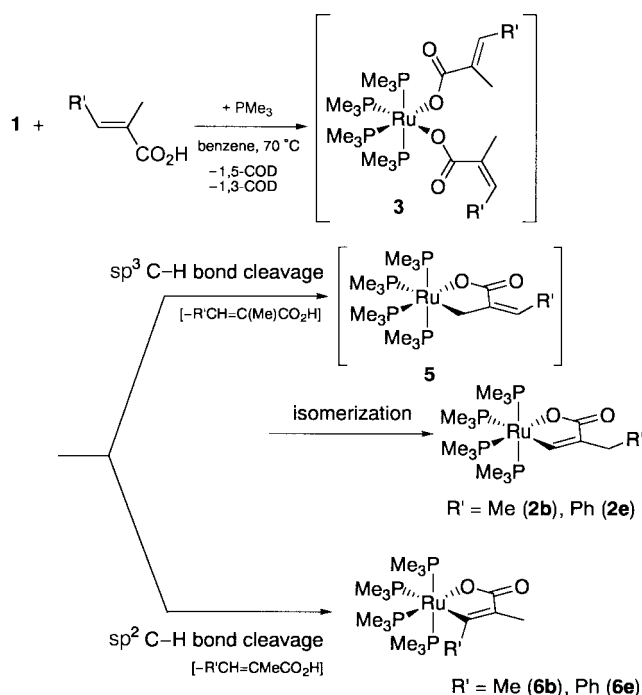
Scheme 1.

The  $^{31}P\{^1H\}$  NMR spectrum of **2a** shows an  $AM_2X$  pattern and the  $^1H$  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  $^1H$  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  $1577\text{ cm}^{-1}$ .<sup>8</sup> 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  $\beta$ -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**)<sup>10</sup> 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).<sup>11</sup>

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 methacrylate ligands in **3a** acted as a hydrogen acceptor (Scheme 1).

Of particular interest is the reaction of **1** with (*E*)-2-methyl-2-butenic 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- $\kappa^2$ O,C](PMe<sub>3</sub>)<sub>4</sub> (**2b**) was obtained as a major product in 80% yield with concomitant formation of Ru[OC(O)C(Me)=C(Me)- $\kappa^2$ O,C](PMe<sub>3</sub>)<sub>4</sub> (**6b**) in 10% yield (Scheme 2).<sup>12</sup> Similar treatment with (*E*)-2-methylcinnamic acid also gave analogous products **2e** and **6e** in 70% and 30% NMR yields, respectively.<sup>13</sup> <sup>31</sup>P{<sup>1</sup>H} NMR of **2b** and **2e** showed a similar AM<sub>2</sub>X pattern to **2a** and <sup>1</sup>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-butenic acid in 60% and 12% yield, respectively. It should be noted that isomerization of these substrates was not catalyzed by **1**/PMe<sub>3</sub> at 70 °C. Thus, formation of **2b** and **2e** was consistently interpreted by the preferential sp<sup>3</sup> C-H bond cleavage of the 2-methyl group over sp<sup>2</sup> C-H on Ru(II) as follows. First of all, these acids react with **1**/PMe<sub>3</sub> to give *cis*-bis(carboxylato)ruthenium(II) complex **3**. The sp<sup>3</sup> C-H bond of the 2-methyl-2-alkenoato ligand is initially cleaved to give *cis*-Ru[OC(O)C(=CHR')CH<sub>2</sub>- $\kappa^2$ O,C](PMe<sub>3</sub>)<sub>4</sub> [R' = Me (**5b**), Ph (**5e**)], which spontaneously isomerizes to thermodynamically stable unsaturated ruthenolactone **2b** or **2e** by 1,3-shift of the hydrogen atom.

Although **2a** is considered to be apparently formed via cleavage of only sp<sup>2</sup> C-H bond of the methacrylate ligand, initial sp<sup>3</sup> 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 ruthenolactones **2b** (23%), **2c** (23%) and **2d** (47%)<sup>14</sup> were obtained, in which only sp<sup>2</sup> C-H bonds were cleaved. Therefore, steric factor at the  $\alpha$ - and  $\beta$ -carbon atoms seems to be important to control the selectivity between sp<sup>2</sup> and sp<sup>3</sup> C-H bond activation at Ru(II).

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- 2a**: Anal. Calcd for C<sub>16</sub>H<sub>40</sub>O<sub>2</sub>P<sub>4</sub>Ru: C, 39.26; H, 8.24%. Found: C, 39.00; H, 8.03%.
- 3a**: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  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). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -2.6 (t, *J* = 32 Hz, 2P), 14.5 (t, *J* = 32 Hz, 2P).
- 4a**: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  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). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  25.9 (br d, *J* = 38 Hz, 2P), 28.0 (br t, *J* = 38 Hz, 1P).
- Recrystallization of these products from THF/hexane gave a mixture of **2b** and **6b** in 7:3 molar ratio. **2b**: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  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). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -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**: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  2.24-2.27 (m, 6H) signals due to PMe<sub>3</sub> ligands are overlapped with those of **2b**. <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -14.6 (td, *J* = 24, 15 Hz, 1P), -0.2 (dd, *J* = 34, 24 Hz, 2P), 6.0 (td, *J* = 34, 15 Hz, 1P).
- Recrystallization of these products from THF/hexane exclusively gave **2e**. **2e**: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  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). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -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**: <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -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.
- 2c** as representative data: <sup>1</sup>H NMR (300 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  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). <sup>31</sup>P{<sup>1</sup>H} NMR (122 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  -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<sup>-1</sup>): 1580 (vs,  $\nu$ C=O), 945 (vs,  $\nu$ C-O).