

Cleavage of Carbonyl Carbon and α -Carbon Bond of Acetophenones by Iridium(III) Porphyrin Complexes

Bao Zhu Li, Xu Song, Hong Sang Fung, and Kin Shing Chan*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, People's Republic of China

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Summary: Selective carbonyl carbon (C(=O)) and α -carbon (C(methyl)) bond activation of acetophenones was discovered by the high-valent, iridium(III) 5,10,15,20-tetrakis-4-tolylporphyrinato carbonyl chloride (Ir(tp)Cl(CO)), which also acted as a Lewis acid in catalyzing the aldol condensation of acetophenones together with release of the coproduct water. Preliminary mechanistic studies suggest that both aliphatic and aromatic carbon–hydrogen bond activation products are kinetic products, which can be converted by reaction with water to iridium porphyrin hydride (Ir(tp)H) via iridium porphyrin hydroxide (Ir(tp)OH). Both Ir(tp)OH and Ir(tp)H were the possible intermediates to cleave the C(=O)–C(methyl) bond of acetophenones and to generate iridium porphyrin acyl complexes as the thermodynamic products.

Activation of carbon–carbon bonds (CCA) adjacent to a carbonyl group by transition metal complexes has been widely investigated due to not only its mechanistic understandings but also its potential utility in organic synthesis.¹ Most examples of CCA reactions of carbonyl compounds involve strained systems.² Among these, cyclobutanones are the most widely used substrates, which have been proposed to undergo oxidative addition with low-valent transition metal complexes in the carbon–carbon bond activation.² Another approach for CCA reactions of carbonyl compounds is driven by chelation assistance of an adjacent coordinating atom.^{1,3}

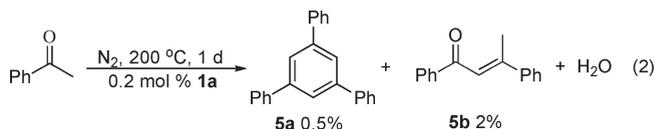
High-valent transition metal complexes are much less known to cleave carbon–carbon bonds since oxidative addition is uncommon with high-valent transition metal complexes.⁴ However, Cp*(PMe₃)Ir(CH₃)OTf has been shown recently to react with alkoxy- and siloxy-substituted cyclopropanes to undergo CCA reaction, and an Ir(V) alkyl intermediate was proposed.⁵

We have reported that high-valent metalloporphyrins of rhodium(III) and iridium(III) can activate aldehydic carbon–hydrogen bonds (CHA).⁶ These bond activations

are mechanistically intriguing due to the difficulty of forming high-valent transition metal(V) intermediates, which are particularly sterically demanding, with three substituents located in a *cis*-manner to the same face of a porphyrin plane. Herein, we report that iridium(III) 5,10,15,20-tetrakis-4-tolylporphyrinato carbonyl chloride (Ir(tp)Cl(CO)) **1a**⁷ cleaves the C(=O)–C(α) bonds of acetophenones to selectively give iridium porphyrin acyl complexes.^{6b}

Ir(tp)Cl(CO) **1a** was found to undergo successful selective CCA with a variety of *p*-substituted acetophenones in solvent-free conditions at the less sterically hindered C(=O)–C(methyl) bonds rather than the C(=O)–C(aryl) bonds to yield Ir(tp)COAr (Table 1, eq 1). For example, Ir(tp)Cl(CO) reacted with acetophenone at 200 °C in 20 days to give Ir(tp)COPh **3b** in 71% yield together with the aromatic CHA products Ir(tp)(*p*-COMe-Ph) **4b** in 4% yield and Ir(tp)(*m*-COMe-Ph) **4c** in 8% yield, respectively (Table 1, entry 2). Both electron-rich and electron-poor *p*-substituted acetophenones required shorter reaction times of 12 to 15 days to give **3a** and **3c,d** in similar product yields (Table 1, entries 1, 3, and 4), while these *p*-substituted acetophenones did not yield any aromatic CHA product.

During the reaction, water-like droplets were observed to form and likely come from the Ir(tp)Cl(CO)-catalyzed aldol condensation of acetophenone. Indeed, we found that acetophenone did undergo an Ir(tp)Cl(CO)-catalyzed aldol condensation reaction to give **5a** and **5b** in a shorter reaction time of 1 day. Therefore, the coformation of water in reactions of **1a** and **2a–d** was confirmed (eq 2).^{8,9}



Upon more careful examination of the reaction mixture of acetophenone with **1a** at a lower temperature of 120 °C in 5 days, only the α -CHA product **4a** was isolated in 11% yield¹⁰

(7) Yeung, S. K.; Chan, K. S. *Organometallics* **2005**, *24*, 6426–6430.

(8) Lyle, R. E.; DeWitt, E. J.; Nichols, N. M.; Cleland, W. *J. Am. Chem. Soc.* **1953**, *75*, 5959–5961.

(9) For the Lewis acid-catalyzed aldol condensation of acetophenone via the Rh(oep)CH₂COR (oep = octaethylporphyrinato) intermediate from a more reactive Rh(oep)ClO₄: Aoyama, Y.; Tanaka, Y.; Yoshida, T.; Toi, H.; Ogoshi, H. *J. Organomet. Chem.* **1987**, *329*, 251–266.

(10) According to TLC analysis, most Ir(tp)Cl(CO) still remained, while it decomposed upon chromatography on alumina.

*Corresponding author. E-mail: ksc@cuhk.edu.hk.

(1) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222–234.

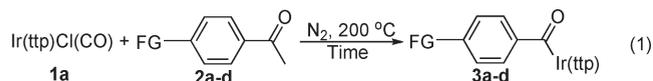
(2) (a) Murakami, M.; Ashida, S. *Chem. Commun.* **2006**, 4599–4601. (b) Matsuo, J.-i.; Sasaki, S.; Tanaka, H.; Ishibashi, H. *J. Am. Chem. Soc.* **2008**, *130*, 11600–11601.

(3) Ahn, J.-A.; Chang, D.-H.; Park, Y. J.; Yon, Y. R.; Loupy, A.; Jun, C.-H. *Adv. Synth. Catal.* **2006**, *348*, 55–58.

(4) For oxidative addition (OA) of the C–H bond, see: (a) Gómez, M.; Robinson, D. J.; Maitlis, P. M. *J. Chem. Soc., Chem. Commun.* **1983**, 825–826. For OA of the Si–H bond, see: (b) Klei, S. R.; Tilley, T. D.; Bergman, R. G. *J. Am. Chem. Soc.* **2000**, *122*, 1816–1817.

(5) Anstey, M. R.; Yung, C. M.; Du, J.; Bergman, R. G. *J. Am. Chem. Soc.* **2007**, *129*, 776–777.

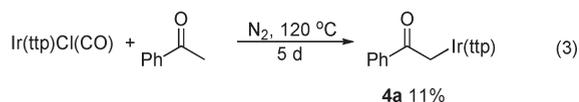
(6) (a) Chan, K. S.; Lau, C. M. *Organometallics* **2006**, *25*, 260–265. (b) Song, X.; Chan, K. S. *Organometallics* **2007**, *26*, 965–970.

Table 1. CCA of Acetophenones by Ir(tp)Cl(CO)

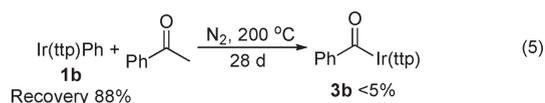
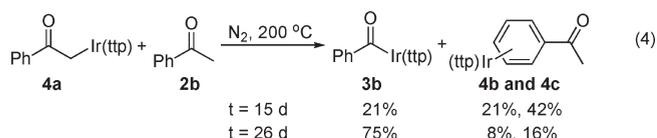
| entry | FG | time/d | product (yield/%) |
|-------|---------------|--------|--|
| 1 | F 2a | 13 | Ir(tp)CO(4-F-Ph) 3a (74) |
| 2 | H 2b | 20 | Ir(tp)COPh 3b (71) ^a |
| 3 | Me 2c | 12 | Ir(tp)CO(4-Me-Ph) 3c (78) |
| 4 | OMe 2d | 15 | Ir(tp)CO(4-OMe-Ph) 3d (79) |

^aAromatic CHA products of Ir(tp)(*p*-COMe-Ph) **4b** and Ir(tp)(*m*-COMe-Ph) **4c** were also isolated in 4% and 8% yield, respectively. For the typical experimental details see ref 20.

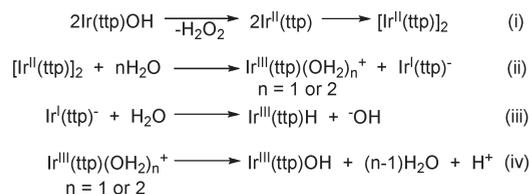
without any **3b** formed (eq 3). The α -CHA reaction is a facile, kinetic process.



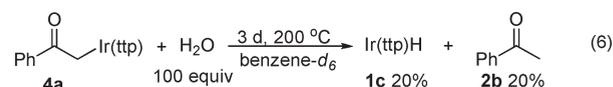
The possible intermediacy of **4a** for CCA was further examined by independent reactions between **4a** and **2b** at 200 °C. After 15 days, **4b** and **4c** were produced in 21% and 42% yield, respectively, together with **3b** in 21% yield (eq 4). After 26 days, **3b** was formed in 75% yield, while **4b,c** still remained in 8% and 16% yield, respectively (eq 4). Furthermore, when the more accessible Ir(tp)Ph¹¹ **1b** was used as an analogue of Ir(tp)(*p*- and *m*-COMe-Ph) (**4b** and **4c**) to react with acetophenone, the CCA product **3b** was isolated in trace amount (<5%) only with the recovery of **1b** in 88% yield after heating for 28 days at 200 °C (eq 5). These results suggest that **4b,c** are less likely the direct intermediates for CCA, as they reacted very slowly. Furthermore, a direct σ -bond metathesis of metal-C and C-C bonds is sterically difficult and unprecedented.¹² We therefore considered other more plausible mechanistic fates for **4a-c**.



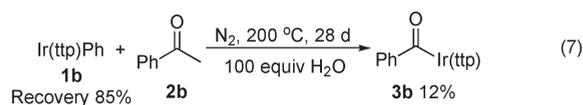
Indeed, Ir(tp)H⁷ **1c** was observed in 20% yield together with acetophenone **2b** in 20% yield when Ir(tp)CH₂COPh

Scheme 1. Transformation from Ir(tp)OH to Ir(tp)H

4a was hydrolyzed by water (100 equiv) in benzene-*d*₆ at 200 °C for 3 days (eq 6).¹³ Likely, water attacks at the iridium center to give Ir(tp)OH¹⁴ and acetophenone. Ir(tp)OH can undergo reduction at high temperature to yield Ir^{II}(tp);¹⁵ Ir^{II}(tp) further rapidly disproportionates into Ir^{III}(tp)(OH₂)_{*n*}⁺ (*n* = 1 or 2) and Ir^I(tp)⁻,¹⁶ which upon protonation with H₂O gives Ir(tp)H (Scheme 1). We propose that Ir(tp)CH₂COPh **4a**, as the kinetic product, likely converts to Ir(tp)OH and Ir(tp)H in the presence of water, or Ir(tp)Cl in the presence of HCl at high temperature. As Ir(tp)H did not react with benzene to give the aromatic CHA product of Ir(tp)Ph, more likely Ir(tp)OH cleaves the aromatic C-H bond to form **4b-c**.^{14d,17}



Similar to **4a**, **4b,c** can be hydrolyzed to convert to Ir(tp)OH and Ir(tp)H or Ir(tp)Cl in the presence of water or HCl. Indeed, with the addition of 100 equiv of water in the reaction of Ir(tp)Ph and acetophenone, a higher yield of Ir(tp)COPh **3b** was obtained in 12% yield (eq 7 vs eq 5). The slower rate of hydrolysis of **1b** compared with **4a** is likely due to the stronger and more hindered metal aryl bond than the metal alkyl bond.¹⁸



As both Ir(tp)OH and Ir(tp)H are proposed intermediates for CCA, the more accessible and observed Ir(tp)H was reacted with acetophenone independently.

(14) For Rh(oep)OH, see: (a) Del Rossi, K. J.; Wayland, B. B. *J. Am. Chem. Soc.* **1985**, *107*, 7941–7944. For Rh(tspp)OH (tspp = tetra-sulfonatophenylporphyrinato), see: (b) Fu, X.; Wayland, B. B. *J. Am. Chem. Soc.* **2004**, *126*, 2623–2631. (c) Fu, X.; Li, S.; Wayland, B. B. *J. Am. Chem. Soc.* **2006**, *128*, 8947–8954. For hydrolysis of Rh-(tspp)CH₂COR with water to form Rh(tspp)OH, see: (d) Zhang, J.; Li, S.; Fu, X.; Wayland, B. B. *Dalton Trans.* **2009**, 3661–3663. (e) Zhang, J.; Wayland, B. B.; Yun, L.; Li, S.; Fu, X. *Dalton Trans.* **2010**, *39*, 477–483. For Ir(acac)₂OH, see: (f) Tenn, W. J., III; Young, K. J. H.; Oxgaard, J.; Nielsen, R. J.; Goddard, W. A., III; Periana, R. A. *Organometallics* **2006**, *25*, 5173–5175. (g) Attempted synthesis of Ir(tp)OH from the reaction of Ir(tp)Cl(CO) with KOH remains unsuccessful.

(15) Hydroxide ion is an effective one-electron reducing agent; see: Sawyer, D. T.; Roberts, J. L., Jr. *Acc. Chem. Res.* **1988**, *21*, 469–476.

(16) Analogous disproportionation reactions of Rh(por)^{II}, see: (a) In excess MeOH: Li, S.; Cui, W.; Wayland, B. B. *Chem. Commun.* **2007**, 4024–4025. (b) By strong ligand: Wayland, B. B.; Balkus, K. J., Jr.; Farnos, M. D. *Organometallics* **1989**, *8*, 950–955. (c) Wayland, B. B.; Sherry, A. E.; Bunn, A. G. *J. Am. Chem. Soc.* **1993**, *115*, 7675–7684.

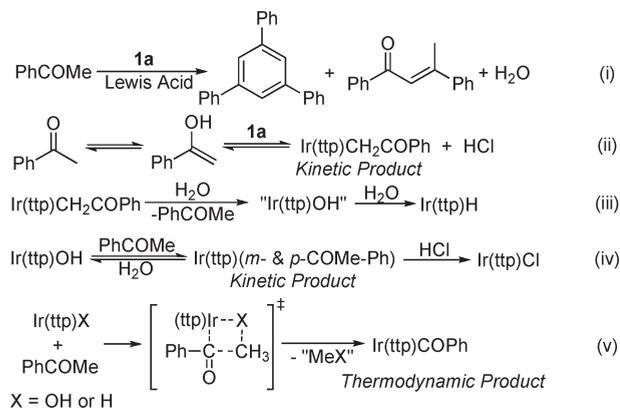
(17) For reported examples of the aromatic C-H bond cleavages by M^{III}OH, see: (a) Kloek, S. M.; Heinekey, D. M.; Goldberg, K. I. *Angew. Chem., Int. Ed.* **2007**, *46*, 4736–4738. (b) Hanson, S. K.; Heinekey, D. M.; Goldberg, K. I. *Organometallics* **2008**, *27*, 1454–1463. (c) Bercaw, J. E.; Hazari, N.; Labinger, J. A. *Organometallics* **2009**, *28*, 5489–5492.

(18) Clot, E.; Mègret, C.; Eisenstein, O.; Perutz, R. N. *J. Am. Chem. Soc.* **2006**, *128*, 8350–8357.

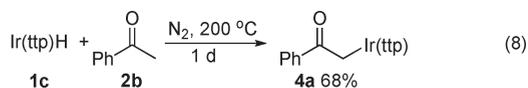
(11) Ogoshi, H.; Setsune, J.-i.; Omura, T.; Yoshida, Z.-i. *J. Am. Chem. Soc.* **1975**, *97*, 6461–6466.

(12) Direct σ -bond metathesis of the C-C bond is unprecedented, and it was proposed but later amended. See: Soulivong, D.; Copéret, C.; Thivolle-Cazat, J.; Basset, J.-M.; Maunders, B. M.; Pardy, R. B. A.; Sunley, G. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5366–5369.

(13) (a) The lower yield obtained is likely due to the competitive decomposition of Ir(tp)H. (b) **4a** was consumed completely, and no Ir(tp)COPh and Ir(tp)(*p*- and *m*-COMe-Ph) were observed. (c) The alternate nucleophilic attack on the α -carbon of **4a** would have produced PhCOCH₂OH, which was not detected. This mode of reaction has been reported in strongly alkaline media for analogous rhodium porphyrin complexes in intramolecular cases. See: Sanford, M. S.; Groves, J. T. *Angew. Chem., Int. Ed.* **2004**, *43*, 588–590.

Scheme 2. Proposed Mechanism for CCA of Acetophenone by Ir(tp)Cl(CO)


However, Ir(tp)H **1c** reacted with acetophenone to give the α -CHA product Ir(tp)CH₂COPh **4a** in 68% yield in just 1 day at 200 °C (eq 8). The direct cleavage of the C–C bond by Ir(tp)H most likely is inhibited by the competitive α -CHA. The hydrolysis pathway must be responsible for the reconversion of **4a** back to Ir(tp)OH and Ir(tp)H.



On the basis of the above findings, we propose a mechanism for the C(=O)–C(α) bond activation of acetophenones by Ir(tp)Cl(CO) (Scheme 2). First, **1a** can react as a Lewis acid to catalyze the aldol condensation of acetophenone to give **5a,b** and water.⁹ On the other hand, **1a** can also react with acetophenone **2b** to give the α -CHA product **4a** as a result of the nucleophilic attack of the enol form of **2b**.⁹ **4a** undergoes interconversion with Ir(tp)Cl **1a'** and Ir(tp)H **1c** via Ir(tp)OH in acetophenone in the presence of HCl (coproduct of α -CHA) or H₂O (coproduct from the aldol condensation). Ir(tp)OH then reacts with **2b** to give the ArCHA products **4b,c**, which are more kinetically and thermodynamically stable than **4a**. However, in the presence of HCl, **4b,c** can convert back to Ir(tp)Cl or Ir(tp)OH and Ir(tp)H in the presence of H₂O. Besides the α -CHA^{14d,e} and aromatic CHA, Ir(tp)OH or Ir(tp)H, once formed again, cleaves the C(=O)–C(α) bond directly, most likely

undergoing σ -bond metathesis to give CCA product **3b** as the thermodynamic product, since oxidative addition of the C(=O)–C(α) bond to high-valent Ir(III) porphyrin complexes to form Ir(V) is sterically demanding.¹⁹ The cleavage of the carbonyl carbon and α -carbon bond is not more kinetically favorable than the carbon(α)–hydrogen bonds due to the steric hindrance. This proposed mechanism can also explain the faster reaction rates and higher yields for *p*-substituted acetophenones, as the *p*-substituents prevent the formation of nonproductive aromatic CHA intermediates and products.

In summary, we have discovered the selective carbonyl carbon and α -carbon bond activation of acetophenones by high-valent iridium porphyrin carbonyl chloride. The iridium porphyrin carbonyl chloride functions as a Lewis acid to catalyze the aldol condensation of acetophenones with water formed. Both aliphatic and aromatic carbon–hydrogen bond activation products are kinetic products, which can convert to intermediates Ir(tp)OH and/or Ir(tp)H in the presence of acid or water. Both Ir(tp)OH and Ir(tp)H are the possible intermediates to cleave the C(=O)–C(methyl) bond and give Ir(tp)COAr as the thermodynamic products. Further works to synthesize Ir(tp)OH and its chemistry are ongoing.

Acknowledgment. We are grateful for the Research Grants Council of Hong Kong of the SAR of China for financial support (No. 400308).

Supporting Information Available: Experimental details and characterizations of compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(19) We were not able to detect the coproduct of MeOH or MeH by GC-MS analysis; therefore, the possible intermediacy of Ir(tp)OH and Ir(tp)H can not be distinguished.

(20) Details for a typical experiment of the C(=O)–C(α) bond activation of acetophenone with Ir(tp)Cl(CO): Acetophenone (0.8 mL, 500 equiv) was added to Ir(tp)Cl(CO) (12.4 mg, 0.013 mmol) in a Teflon screw-head stoppered tube, and the mixture was degassed by the freeze–pump–thaw method (3 cycles). Then the mixture was heated at 200 °C for 20 days under N₂. The solvent was then removed under vacuum, and the crude product was purified by column chromatography on alumina. The purple solid of Ir(tp)COPh^{6b} **3b** (8.9 mg, 0.0092 mmol, 71%) and Ir(tp)(*p*-COMe-Ph) **4b** (0.5 mg, 0.0005 mmol, 4%) together with Ir(tp)(*m*-COMe-Ph) **4c** (1.0 mg, 0.0010 mmol, 8%) were isolated as the second fraction.