Iridium-Catalyzed Selective C-C Bond Cleavage of Nitriles and Ketones

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Abstract: Selective and catalytic C-C bond cleavage of pentanedinitriles and 5-oxohexanenitriles can be performed in the presence of iridium hydride complex $IrH_5(Pi-Pr_3)_2$ (1). The key steps of this reaction are α -C-H activation of the cyano or carbonyl group and subsequent β -carbon elimination.

Key words: iridium hydride complex, C-H activation, β -carbon elimination, nitrile, ketone

The selective catalytic cleavage of C-C single bond by transition metals under homogeneous conditions has received much interest in recent years, because this type of reaction enables us to perform a novel one-step transformation of molecular skeleton^{1,2} which cannot be achieved by conventional organic synthesis. Furthermore, this type of C-C bond cleavage could form a key part of environmentally friendly processes for recycling polymer to the corresponding monomer.^{3,4}

Recent studies on transition-metal-catalyzed C-C single bond cleavage⁵ are roughly classified into two categories: i) oxidative addition, and ii) β -carbon elimination. Direct oxidative addition of transition metals into the C-C bonds is generally driven by release of ring strain⁶ or by chelation assistance.⁷ Transition metal-mediated β -carbon elimination, well recognized as an important mechanism for chain scission of polymer,⁸ has a potent ability to cleave unstrained inactive C-C single bonds. However, except for a few examples,⁹ strain release strategy has been widely used for most β -carbon eliminations.^{10,11}

Currently, we are investigating catalytic C-C single bond cleavage of non-strained compounds via β -carbon elimination. In this report, we describe iridium-catalyzed C-C single bond cleavage of nitriles and ketones via β -carbon elimination. Our investigation was based on the following concept (Scheme 1).

Both nitriles (X = -CN) and ketones (X = -COR) readily react with metals to give nitrile- or ketone-coordinated complex **2**. Iridium hydride complexes have proven to be effective catalysts for C-H bond activation of nitriles.¹² The activation of C-H bond adjacent to X would give an alkyliridium intermediate **3**.^{13,14} The C-C bond β - to X could be cleaved by β -carbon elimination to yield an ole-

SYNLETT 2004, No. 12, pp 2185–2187 Advanced online publication: 01.09.2004 DOI: 10.1055/s-2004-831333; Art ID: U15804ST © Georg Thieme Verlag Stuttgart · New York



Scheme 1

fin-coordinated iridium intermediate **4**. Reductive elimination of iridium from **4** would produce R-H and olefin with regeneration of the iridium catalyst.

In order to assess the catalytic activity of various iridium complexes, a series of C-C bond cleavage reactions was carried out by adding iridium catalysts to a solution of 2-methyl-2-phenyl-pentanedinitrile (**5**) in toluene at 150 °C (Scheme 2).¹⁵

Scheme 2 Catalytic activities of various iridium complexes for the C-C bond cleavage of 1,3-dicyano-3-phenylbutane (5)

Heating the solution for five hours in the presence of 10 mol% of iridium complex catalysts gave the corresponding 2-phenylpropionitrile (6). In this trial, the reaction time was shortened in order to estimate the initial reaction rate. The iridium-pentahydride complex, $IrH_5(Pi-Pr_3)_2$ (1) has proven to be the best catalyst. The hydride ligands easily leave as molecular hydrogen from pentahydride iridium complexes to form coordinatively unsaturated active species.¹⁶ The strong electron donating triisopropyl phosphine ligand would also facilitate C-H activation. Complexes such as IrH(CO)(PPh₃)₂, IrCl(CO)(PPh₃)₂, $Ir(CO)_2(acac),$ $IrHCl_2(PCy_3)_2$, $Ir(acac)_3$, IrCl₂, [IrCl₂Cp*]₂, [IrCl(coe)₂]₂, Na₃IrCl₆ were not effective as catalysts. Phosphine ligands such as Pi-Pr3, PCy3, and PPh₃ also showed no catalytic activity.

 Table 1
 C-C Bond Cleavage Reactions Catalyzed by IrH₅(Pi-Pr₃)₂

 (1)
 (1)



Representative results of this reaction are shown in Table 1.

In the presence of catalytic amounts of IrH₅(Pi-Pr₃)₂ (0.10 mmol) (1), the β -selective C-C bond cleavage of nitriles or ketones (1.0 mmol) proceeds to give the corresponding product in good yields.¹⁷ The reaction of nitriles having two phenyl groups at 2-position proceeds more effectively than that of the nitrile with one phenyl group. For example, 2,2-diphenyl-pentanedinitrile could react to produce diphenylacetonitrile almost quantitatively (entry 2). Phenyl group at 2-position is essential for this reaction. It is noteworthy that the iridium-catalyzed C-H activation tolerates bulky substituents at α -position of the nitriles. Typically, the reaction of 2,4-dimethyl-2- phenypentanedinitrile gave better yield than the reaction of 5 (entry 3). Generally, ketones are less reactive than nitriles toward α -C-H activation because of their poor coordination ability to metals. However, in the presence of catalyst 1, the C-C bond cleavage of ketones can be performed as shown in entries 4-6. A similar rate enhancement due to two phenyl groups was also observed in the reaction of ketone (entry 5).

A plausible mechanism of this reaction is shown in Scheme 3. The catalytically active species seems to be unsaturated iridium complexes IrL_n (L = P*i*-Pr₃ and H) which would be formed by dissociation of molecular hydrogen from 1.¹⁶ Nitriles or ketones would coordinate to the iridium active catalyst IrL_n to give intermediate 7. The activation of C-H bond adjacent to X would provide inter-



Scheme 3

mediate $8^{.18}$ Subsequent β -carbon elimination from 8 would proceed to afford olefin-coordinated intermediate 9. Dissociation of the olefin (X = -CN; acrylonitrile, X = -COR; methylvinylketone) from 9 would lead to alkyliridium intermediate 10. Reductive elimination of iridium in 10 would yield product 11 with regeneration of the catalyst. During this catalytic cycle, thermodynamic stability of Ir-C bond²⁰ might contribute to generation of intermediates 8-10.

Acknowledgment

This work was supported by the Research for the Future Program from the Japan Society for the Promotion of Science, and a Grantin-Aid for Scientific Research, the Ministry of Education, Science, Sports, and Culture, Japan. This work was also supported by Sasagawa Scientific Research Grant from The Japan Science Society and Kansai Research Foundation for Technology Promotion (KRF). The authors express special thanks to the center of excellence (21COE) program 'Creation of Integrated EcoChemistry of Osaka University'. The authors thank Professor Takeshi Naota of Osaka University for his helpful discussion and generous support.

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- (15) General Procedure for the Iridium-Catalyzed C-C Bond Cleavage of 2-Methyl-2-phenyl-pentanedinitrile (5). In a 25 mL sealed tube, iridium catalysts (0.1 mmol), 5 (1 mmol), and toluene (0.5 mL) were placed and stirred for 12 h at 150 °C under argon atmosphere. The yield of 2-phenylpropionitrile 6 was determined by NMR using dibenzyl as an internal standard.
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- (17) General Procedure for the Iridium-Catalyzed C-C Bond Cleavage of Nitriles and Ketones. In a 25mL of sealed tube, IrH₅ (Pi-Pr₃)₂ (1, 0.2 mmol), nitriles or ketones (1 mmol), and toluene (0.5 mL) were placed and stirred for 12 h at 150 °C under argon atmosphere. The yields of products were determined by NMR using dibenzyl as an internal standard. All the products were confirmed by ¹H NMR, ¹³C NMR, and HRMS.
- (18) In the case of the reaction of 2-methyl-2- phenylhexanedinitrile (**12**), the formation of 2-amino-1-cyano-3-methyl-3-phenylcyclopentene (**13**) was observed.¹⁹ The cyclization would proceed via nucleophilic addition of alkyliridium intermediate to the CN triple bond of nitriles (Scheme 4). This cyclic product unequivocally supports the occurrence of α -C-H bond activation and the formation of intermediate **8** (Scheme 4).





- (19) In a 25mL of sealed tube, 2-methyl-2- phenylhexanedinitrile (12, 200 mg, 1.0 mmol), IrH₅(P*i*-Pr₃)₂ (1, 52 mg, 0.1 mmol), and toluene (0.5 mL) were placed and stirred for 24 h at 150 °C under argon atmosphere. After removal of the solvent, the mixture was purified by silica gel column chromatography and by Kugelrohr distillation to give 2amino-1-cyano-3-methyl-3-phenylcyclopentene (13, 1:0.8 diastereomer mixture) as a colorless oil (47 mg, 24%). ¹H NMR (270 MHz, CDCl₃): $\delta = 1.54$ (s, 3 H, -CH₃), 1.95–2.15 [m, 2 H, -CH₂-C(Me)(Ph)-], 2.48–2.53 [m, 2 H, -CH₂-C(CN)-], 4.25 (br, 2 H, -NH₂), 7.22–7.40 (m, 5 H, -C₆H₅). ¹³C NMR (68 MHz, CDCl₃): δ = 167.2 (*C*-NH₂), 144.1 (-C₆H₅), 128.4 (-C₆H₅), 126.7 (-C₆H₅), 126.2 (-C₆H₅), 118.8 (-CN), 74.2 (C-CN), 53.0 (C-CH₃), 41.5 [-CH₂-C(Me)(Ph)-], 28.1 [-CH₂-C(CN)-], 22.9 (-CH₃). MS (EI, 70 eV): m/z (%) = 198, 183, 168, 166, 140, 129, 115, 105, 91, 77.
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