The iridium-catalyzed decarbonylation of aldehydes under mild conditions†

Tomohiro Iwai, Tetsuaki Fujihara and Yasushi Tsuji*

Received (in Cambridge, UK) 1st August 2008, Accepted 1st October 2008
First published as an Advance Article on the web 29th October 2008
DOI: 10.1039/b813171f

The catalytic decarbonylation of aldehydes has been developed using commercially available [IrCl(cod)]$_2$ and PPh$_3$ under mild conditions, and the method could be widely applicable to various substrates with different functionalities.

The removal of formyl functionalities, the decarbonylation of aldehydes, is one of the essential protocols of synthetic chemistry, including in the total syntheses of natural products.[1] The decarbonylation reaction of aldehydes was first discovered by Tsuji and Ohno using a stoichiometric amount of Wilkinson's complex, $RhCl(PPh_3)_3$.[2] As for catalytic reactions, Doughty and Pignolet found that rhodium complexes with *chelating diphosphines* were much more reactive as catalysts.[3] Since then, rhodium catalysts with chelating phosphines have been extensively studied in decarbonylation reactions of aldehydes.[4] Recently, Madsen and co-workers reported a mechanism for the rhodium-catalyzed decarbonylation of aldehydes by DFT calculations.[5a] They mentioned that the reaction involves a rapid oxidative addition into the C(O)–H bond, followed by a rate-limiting extrusion of CO. Some Pd[6] and Ru,[7] as well as Ir,[8] complexes were also reported as catalysts for decarbonylation and related reactions.

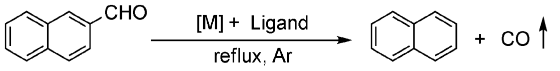
However, in order to realize the efficient catalytic (or even stoichiometric) decarbonylation of aldehydes, elevated reaction temperatures (typically >160 °C)[1a,b,g,3,4a,b,d,5a,6] or an associated chemical scavenger of the evolved CO (*i.e.*, by an accompanying carbonylation reaction[4c,8,9] or with added diphenylphosphoryl azide[10] to remove the evolved CO) are indispensable. Actually, more than a stoichiometric, not a catalytic, amount of $RhCl(PPh_3)_3$ is still being used to obtain efficient decarbonylations of aldehyde functionalities as an important step in various total syntheses.[1a–g] Hence, a much more active catalyst system to realize the reliable catalytic decarbonylation of aldehydes at lower temperatures, and without a chemical scavenger for CO, is highly desirable.

In the present study, we describe a highly active iridium catalyst system that realizes the efficient catalytic decarbonylation of aldehydes at lower temperatures (66 °C–101 °C) and without any chemical scavenger of CO (eqn (1)). A simple combination of commercially available [IrCl(cod)]$_2$ (cod = 1,5-cyclooctadiene) and an easily accessible phosphine, such as PPh$_3$ or P(n-Bu)$_3$, provides a highly active and practical catalyst system.

$$\mathrm{R{-}CHO} \xrightarrow[\text{at } 66\ ^\circ\mathrm{C}-101\ ^\circ\mathrm{C}]{\text{cat. }[\mathrm{IrCl(cod)_2}]\text{-}\mathrm{PR'_3}} \mathrm{R-H + CO}\uparrow \qquad (1)$$

Firstly, the decarbonylation of 2-naphthaldehyde was carried out to examine the effect of the catalyst system (Table 1). In the presence of a catalytic amount of [IrCl(cod)]$_2$ (5.0 mol% with respect to Ir) and PPh$_3$ (PPh$_3$: Ir = 1 : 1) in refluxing diglyme (bp 162 °C), the decarbonylation product, naphthalene, was obtained in 92% yield (Table 1, entry 1). The best decarbonylation catalyst reported so far, $RhCl_3{\cdot}3H_2O$ with dppp (1,3-bis(diphenylphosphino)propane),[4b] also afforded the product in a high yield in refluxing diglyme (Table 1, entry 2). However, the catalytic activity dropped drastically when the reaction was carried out in refluxing dioxane (bp 101 °C) (Table 1, entry 3). Thus, the elevated temperature is a requisite for rhodium catalysts. In contrast, the [IrCl(cod)]$_2$–PPh$_3$ catalyst system showed a high catalytic activity, even in refluxing dioxane, and gave the product in 79% yield in 24 h and in 95% yield in 48 h (Table 1, entries 4 and 5). As catalyst precursors, $IrCl_3{\cdot}3H_2O$, [Ir(cod)$_2$]BF$_4$ and [IrCl$_2$Cp*]$_2$ (Cp* = η^5-pentamethylcyclopentadienyl) gave the

Table 1 The iridium-catalyzed decarbonylation of 2-naphthaldehyde: effect of catalyst precursors, ligands and solvents[a]



Entry	[M]	Ligand	Solvent	Time/h	Yield (%)[b]
1	[IrCl(cod)]$_2$	PPh$_3$	Diglyme	6	92
2	$RhCl_3{\cdot}3H_2O$	dppp[c]	Diglyme	24	90
3	$RhCl_3{\cdot}3H_2O$	dppp[c]	Dioxane	24	1
4	[IrCl(cod)]$_2$	PPh$_3$	Dioxane	24	79
5	[IrCl(cod)]$_2$	PPh$_3$	Dioxane	48	95 (87[d])
6	$IrCl_3{\cdot}3H_2O$	PPh$_3$	Dioxane	24	2
7	[Ir(cod)$_2$]BF$_4$	PPh$_3$	Dioxane	24	14
8	[IrCl$_2$Cp*]$_2$	PPh$_3$	Dioxane	24	3
9	[IrCl(cod)]$_2$	P(n-Bu)$_3$	Dioxane	24	95 (81[d])
10	[IrCl(cod)]$_2$	PCy$_3$	Dioxane	24	89 (82[d])
11	[IrCl(cod)]$_2$	dppe	Dioxane	24	28
12	[IrCl(cod)]$_2$	dppp	Dioxane	24	7
13	[IrCl(cod)]$_2$	(±)-BINAP	Dioxane	24	49
14	[IrCl(cod)]$_2$	P(n-Bu)$_3$	DME	48	84
15	[IrCl(cod)]$_2$	PPh$_3$	DME	48	31
16	[IrCl(cod)]$_2$	PPh$_3$	Toluene	24	86

[a] Reaction conditions: 2-naphthaldehyde (0.50 mmol), [M] (0.025 mmol with respect to Ir or Rh), ligand (0.025 mmol), solvent (1.0 cm^3), reflux, Ar atmosphere. [b] GC yields. [c] dppp (0.050 mmol). [d] In air with unpuirifed dioxane.

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan.
E-mail: ytsuji@scl.kyoto-u.ac.jp

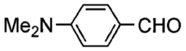
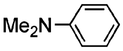
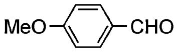
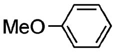
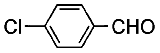
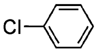
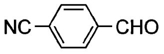
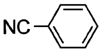
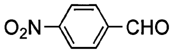
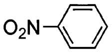
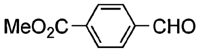
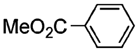
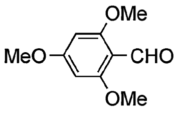
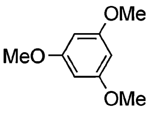
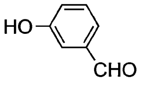
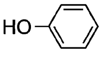
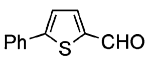
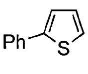
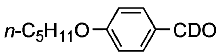
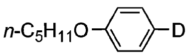
† Electronic supplementary information (ESI) available: Experimental procedures and measurement of the kinetic isotope effect. See DOI: 10.1039/b813171f

product in only low yields (Table 1, entries 6–8). The phosphines $P(n\text{-}Bu)_3$ and tricyclohexylphosphine (PCy_3), of higher basicity, were more efficient and afforded the product in 95 and 89% yields, respectively (Table 1, entries 9 and 10, *cf.* entry 4), in 24 h. Although bidentate phosphines such as dppe (1,2-bis(diphenylphosphino)ethane), dppp and (±)-BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) were found to be noticeably effective in the Rh catalyst system,[4b–d] they were not as efficient as PPh_3 with the iridium catalyst (Table 1, entries 11–13). These results suggest that the use of a monodentate phosphine is more favorable in iridium-catalyzed decarbonylation reactions. However, with excess PPh_3 (PPh_3 : Ir = 2 : 1), the yield decreased to 4% under otherwise identical conditions to those in Table 1, entry 4. Furthermore, the iridium catalyst system with $P(n\text{-}Bu)_3$ showed a good catalytic activity, even in refluxing 1,2-dimethoxyethane (DME, bp 85 °C) (Table 1, entry 14), although PPh_3 was not such an efficient ligand in DME (Table 1, entry 15). Hydrocarbon solvents, such as toluene, can also be employed in this reaction, as shown in Table 1, entry 16. It is noteworthy that this decarbonylation reaction can be carried out in unpurified (as received) dioxane and in air, albeit with slightly decreased yields (Table 1, entries 5, 9 and 10).

The decarbonylation of aromatic aldehydes was carried out in refluxing unpurifed dioxane under air (Table 2).‡ Both electron-rich (Table 2, entries 1 and 2) and electron-poor (Table 2, entries 3–6) aldehydes provided the corresponding products in good-to-high yields. In the $RhCl_3{\cdot}3H_2O$–dppp-catalyzed decarbonylation reaction in refluxing diglyme, *para*-nitrobenzaldehyde was reported to be partially decomposed and afforded the decarbonylation product in only 12% yield.[4b] However, with the iridium catalyst, the decarbonylation could be carried out smoothly in refluxing dioxane, and the product was isolated in 87% yield (Table 2, entry 5). Sterically hindered 2,4,6-trimethoxybenzaldehyde was smoothly decarbonylated (Table 2, entry 7). While, the decarbonylation of salicylaldehyde did not proceed, possibly due to intramolecular coordination of the OH functionality, *meta*-hydroxybenzaldehyde provided the decarbonylation product in an excellent yield (Table 2, entry 8). 5-Phenylthiophene-2-carboxyaldehyde gave 2-phenylthiophene in 94% yield (Table 2, entry 9), and the decarbonylation of *para*-amyloxybenzaldehyde-d_1 afforded the product bearing the deuterium at the *para*-position in 81% yield (Table 2, entry 10).

Table 2 The iridium-catalyzed decarbonylation of aromatic aldehydes[a]

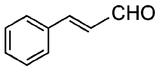
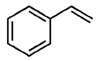
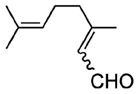
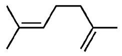
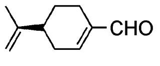
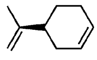
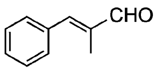
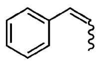
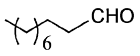
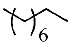
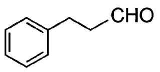
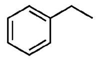
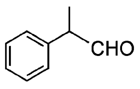
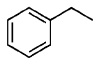
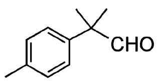
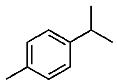
$$\mathrm{Ar{-}CHO} \xrightarrow[\text{dioxane, reflux, air, 48 h}]{[\mathrm{IrCl(cod)_2}]\text{-}\mathrm{PPh_3}} \mathrm{Ar{-}H + CO}\uparrow$$

Entry	Aldehyde	Product	Yield (%)[b]
1			91
2			76
3			79
4			84
5			87
6			91
7			78
8			95[c]
9			94
10			81[d]

[a] Reaction conditions: aldehyde (1.0 mmol), $[IrCl(cod)]_2$ (0.025 mmol), PPh_3 (0.050 mmol), refluxing dioxane (unpurified, 1.0 cm^3) for 48 h in air. [b] Isolated yields. [c] GC yield. [d] For 72 h.

Table 3 The iridium-catalyzed decarbonylation of various aldehydes[a]

$$\mathrm{R{-}CHO} \xrightarrow[\text{solvent, reflux, air}]{[\mathrm{IrCl(cod)_2}]\text{-phosphine}} \mathrm{R{-}H + CO}\uparrow$$

Entry	Aldehyde	Solvent	Time/h	Product	Yield (%)[b]
1		Dioxane	9		84 (99)
2		Dioxane	32		(94)[cd]
3		DME	24		(79)[c]
4		DME	24		(91)[ce]
5		THF	96		(82)[ce]
6		Dioxane	24		92
7		Dioxane	24		82
8		Dioxane	24		63[f]
9		Dioxane	24		91[g]
10		Dioxane	24		72[h]
11		Dioxane	24		81[i]
12		Dioxane	24		3[j]

[a] Reaction conditions: aldehyde (1.0 mmol), $[IrCl(cod)]_2$ (0.025 mmol), PPh_3 (0.050 mmol), refluxing dioxane (unpurified, 1.0 cm^3) for 24 h in air. [b] Isolated yields. [c] Under argon. [d] $[IrCl(cod)]_2$ (0.0025 mmol), PPh_3 (0.0050 mmol). [e] With PCy_3 in place of PPh_3. [f] $E : Z = 16 : 84$. [g] In addition, nonenes were obtained in 5% yield. [h] In addition, styrene was obtained in 6% yield. [i] In addition, styrene was obtained in 10% yield. [j] In addition, 1-isopropenyl-4-methylbenzene was obtained in 6% yield.

Table 3 shows the results of the decarbonylation of various aldehydes. The decarbonylation of α,β-unsaturated aldehydes proceeded somewhat more rapidly. *trans*-Cinnamaldehyde provided styrene in 99% yield in 9 h (Table 3, entry 1). The product was obtained in high yield, even if the catalyst loading was reduced to one tenth of the standard amount (Table 3, entry 2). In DME under reflux, styrene was obtained in 79% yield (Table 3, entry 3). When PCy_3 was used in place of PPh_3 in DME, the yield increased to 91% yield (Table 3, entry 4). Surprisingly, with the $[IrCl(cod)]_2$–PCy_3 catalyst system, the decarbonylation of *trans*-cinnamaldehyde proceeded in high yield, even in refluxing THF (bp 66 °C) (Table 3, entry 5). The corresponding decarbonylation products were isolated in high yields from citral (Table 3, entry 6) and (*S*)-perillaldehyde (Table 3, entry 7). (*E*)-2-Methyl-3-phenyl-2-propenal afforded the decarbonylation product in 63% yield in 24 h with *E*/*Z* isomerization to $E : Z = 16 : 84$ (Table 3, entry 8). In this case, by prolonging the reaction time to 48 h, the yield of β-methylstyrenes increased to 90%, but the isomerization proceeded further to $E : Z = 93 : 7$. In the case of aldehydes having β-hydrogens on an sp^3 carbon, the decarbonylation reaction proceeded smoothly, but alkenes formed simultaneously in 5–10% yields due to β-hydrogen elimination (Table 3, entries 9–11). As for limitations, the conversion of an α,α-dialkylated aldehyde was very low in the present catalyst system (Table 3, entry 12), as seen in previous rhodium catalyzed reactions.[4b]

To examine the reaction mechanism of the iridium-catalyzed decarbonylation of aldehydes, we measured the kinetic isotope effect. The rate of the iridium-catalyzed decarbonylation reaction has a first-order dependence on aldehyde concentration. Kinetic measurements with *para*-amyloxybenzaldehyde-d_1 (Table 2, entry 10) *vs.* *para*-methoxybenzaldehyde and a comparison of the k_D value with the k_H value for *para*-amyloxybenzaldehyde-d_0 afforded a deuterium isotope effect $k_H/k_D = 1.70$. This value is comparable to $k_H/k_D = 1.77$[5a] and 1.8[5b] reported previously for rhodium-catalyzed decarbonylations.

In conclusion, the iridium-catalyzed decarbonylation of aldehydes using a catalytic amount of commercially available $[IrCl(cod)]_2$ and an easily accessible monodentate phosphine such as PPh_3 or $P(n\text{-}Bu)_3$ was developed. The reaction proceeded smoothly under mild reaction conditions. This highly practical and reliable method should be widely applicable to various substrates containing different functionalities.

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Culture, Sports, Science and Technology, Japan. T. I. is grateful for a Research Fellowship from the Japan Society for the Promotion of Science (JSPS) for Young Scientists. We thank Professor Jun Terao at Kyoto University for helpful discussions.

Notes and references

‡ General procedure for the decarbonylation of aldehydes (Table 2, entry 1): A solution of $[IrCl(cod)]_2$ (16.8 mg, 0.025 mmol) and PPh_3 (13.1 mg, 0.050 mmol) in dioxane (unpurified, 1.0 cm^3) was stirred at room temperature for 10 min in air. *para*-Dimethylaminobenzaldehyde (149 mg, 1.0 mmol) was added to the flask and the reaction carried out under reflux for 48 h. After cooling to room temperature, the mixture was diluted with pentane, and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated carefully. The crude product was purified by silica gel column chromatography using pentane–CH_2Cl_2 (5 : 1) as an eluent to give *N*,*N*-dimethylaniline (110 mg, 91%) as a colorless oil.

1 (*a*) A. Padwa and H. Zhang, *J. Org. Chem.*, 2007, **72**, 2570–2582; (*b*) H. Zhang and A. Padwa, *Tetrahedron Lett.*, 2006, **47**, 3905–3908; (*c*) S. Ikeda, M. Shibuya and Y. Iwabuchi, *Chem. Commun.*, 2007, 504–506; (*d*) J. P. Malerich, T. J. Maimone, G. I. Elliott and D. Trauner, *J. Am. Chem. Soc.*, 2005, **127**, 6276–6283; (*e*) M. Harmata and S. Wacharasindhu, *Org. Lett.*, 2005, **7**, 2563–2565; (*f*) T. Kato, M. Hoshikawa, Y. Yaguchi, K. Izumi, Y. Uotsu and K. Sakai, *Tetrahedron*, 2002, **58**, 9213–9222; (*g*) C.-M. Zeng, M. Han and D. F. Covey, *J. Org. Chem.*, 2000, **65**, 2264–2266; (*h*) F. Sobrio, M. Amokhtari, F. Gourand, M. Dhilly, F. Dauphin and L. Barré, *Bioorg. Med. Chem.*, 2000, **8**, 2511–2518; (*i*) G. S. Weatherhead, G. A. Cortez, R. R. Schrock and A. H. Hoveyda, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 5805–5809; (*j*) R. K. Boeckman, Jr, J. Zhang and M. R. Reeder, *Org. Lett.*, 2002, **4**, 3891–3894.

2 (*a*) J. Tsuji and K. Ohno, *Tetrahedron Lett.*, 1965, **6**, 3969–3971; (*b*) K. Ohno and J. Tsuji, *J. Am. Chem. Soc.*, 1968, **90**, 99–107.

3 D. H. Doughty and L. H. Pignolet, *J. Am. Chem. Soc.*, 1978, **100**, 7083–7085.

4 (*a*) C. M. Beck, S. E. Rathmill, Y. J. Park, J. Chen, R. H. Crabtree, L. M. Liable-Sands and A. L. Rheingold, *Organometallics*, 1999, **18**, 5311–5317; (*b*) M. Kreis, A. Palmelund, L. Bunch and R. Madsen, *Adv. Synth. Catal.*, 2006, **348**, 2148–2154; (*c*) T. C. Fessard, S. P. Andrews, H. Motoyoshi and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2007, **46**, 9331–9334; (*d*) E. Taarning and R. Madsen, *Chem.–Eur. J.*, 2008, **14**, 5638–5644.

5 (*a*) P. Fristrup, M. Kreis, A. Palmelund, P. Norrby and R. Madsen, *J. Am. Chem. Soc.*, 2008, **130**, 5206–5215; (*b*) F. Abu-Hasanayn, M. E. Goldman and A. S. Goldman, *J. Am. Chem. Soc.*, 1992, **114**, 2520–2524.

6 J. Tsuji and K. Ohno, *J. Am. Chem. Soc.*, 1968, **90**, 94–98.

7 (*a*) G. Domazetis, B. Tarpey, D. Dolphin and B. R. James, *J. Chem. Soc., Chem. Commun.*, 1980, 939–940; (*b*) K. H. Park, S. U. Son and Y. K. Chung, *Chem. Commun.*, 2003, 1898–1899.

8 (*a*) T. Shibata, N. Toshida, M. Yamasaki, S. Maekawa and K. Takagi, *Tetrahedron*, 2005, **61**, 9974–9979; (*b*) F. Y. Kwong, H. W. Lee, W. H. Lam, L. Qiu and A. S. C. Chan, *Tetrahedron: Asymmetry*, 2006, **17**, 1238–1252.

9 For recent papers and references cited therein, see: (*a*) H. W. Lee, L. N. Lee, A. S. C. Chan and F. Y. Kwong, *Eur. J. Org. Chem.*, 2008, 3403–3406; (*b*) T. Morimoto, M. Fujioka, K. Fuji, K. Tsutsumi and K. Kakiuchi, *Pure Appl. Chem.*, 2008, **80**, 1079–1087.

10 J. M. O'Connor and J. Ma, *J. Org. Chem.*, 1992, **57**, 5075–5077.