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Iridium solutes effect C–H bond activation and C–C bond forming reactions of C_6H_6–$MeOCH_2CH_2OMe$ solvent mixtures†

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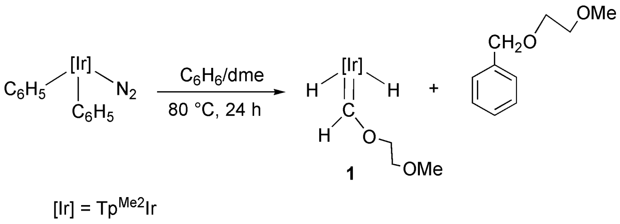
The *in situ* generated [$Tp^{Me2}Ir(C_6H_5)_2$] fragment induces both aromatic and aliphatic C–H bond activation reactions, along with C–C bond formation, when heated with benzene and 1,2-dimethoxyethane.

Soluble transition metal compounds that induce C–H bond activation and subsequent C–C bond formation have potential applications in the synthesis of complex molecules from simple, commonly available starting materials.[1] In recent years, transition metal complexes of different ligand environments have provided numerous examples of C–H[2] and other C–X bond activation reactions (X = F, O, N, *etc.*).[3] Here we report that the iridium compound[4a] $Tp^{Me2}Ir(C_2H_4)_2$ (Tp^{Me2} = hydrotris(3,5-dimethylpyrazolyl)borate) reacts with C_6H_6-plus-dme solvent mixtures (dme = 1,2-dimethoxyethane) with multiple C–H bond activation and C–C coupling between one molecule of either solvent. We also discuss preliminary mechanistic studies of this unusual transformation.

Heating a solution of $Tp^{Me2}Ir(C_2H_4)_2$ in C_6H_6, under argon, generates the unstable intermediate [$Tp^{Me2}Ir(C_6H_5)_2$], that can also be accessed from the N_2 complex $Tp^{Me2}Ir(C_6H_5)_2(N_2)$.[4b] Although experimentally the former procedure is more convenient than the latter, for the sake of simplicity the $Tp^{Me2}Ir(C_6H_5)_2(N_2)$ complex appears as precursor of the above unsaturated species in all reaction schemes throughout this paper. When either of these precursors is heated in C_6H_6, under argon, in the presence of dme, at 80 °C, (2-methoxy-ethoxymethyl)-benzene,[5] $C_6H_5CH_2OCH_2CH_2OCH_3$ is produced.‡ The transformation is complex and requires the participation of different organometallic intermediates (*vide infra*). Although minor amounts of different Ir-containing complexes are formed, the major end product (Scheme 1) is the bis(hydride) carbene **1** (50% spectroscopic yield, 30% isolated yield, following chromatography). Thus, two molecules of dme participate in this transformation. One undergoes double C–H bond activation to give a heteroatom-stabilized carbene ligand, whereas the other becomes involved in a C–C bond forming reaction with one molecule of benzene (following prior C–H activation) to afford the diether $C_6H_5CH_2OCH_2CH_2OCH_3$ (60% isolated yield).

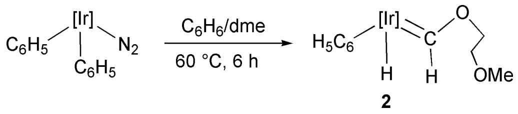
To gain mechanistic insight, the above reaction has been investigated under milder experimental conditions. Thus, after 6 h at 60 °C, NMR monitoring reveals quantitative formation of a hydride phenyl compound **2** (Scheme 2)§ that, like **1**, contains a heteroatom substituted carbene ligand. From the nature of this unit, it is evident that, similarly to previously reported systems,[6a] the reactive [$Tp^{Me2}Ir(C_6H_5)_2$] fragment has effected the regioselective cleavage of the two C–H bonds[6b] of one of the Me termini of the diether.¶ Moreover, only one of the CH_3 groups becomes activated, attempts to produce a dimetal dicarbene complex by the reaction of **2** with $Tp^{Me2}Ir(C_6H_5)_2(N_2)$ have proved fruitless. The Ir–H functionality of **2** is responsible for an IR absorption at 2140 cm^{-1} and a high-field ^1H NMR resonance at δ −16.46 ppm, while the metal-bound carbene carbon resonates at δ 262.9 in the $^{13}C\{^1H\}$ NMR spectrum. In the ^1H NMR, both the carbene and the hydride resonances are broad, due to the existence of two carbene rotamers.



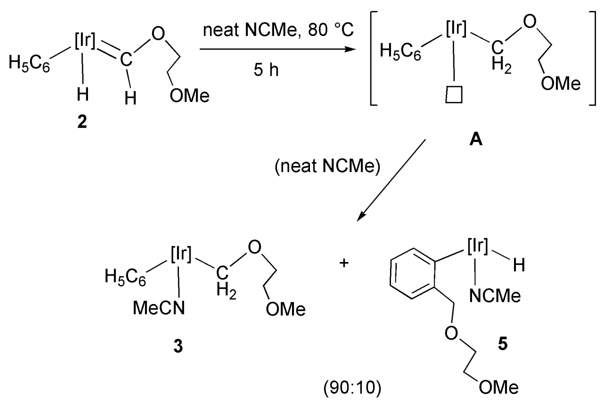
Scheme 1

Compound **2** undergoes a reversible 1,2-H shift[8] from iridium to the carbene carbon, as evinced by the formation of adduct **3** in its reaction with neat NCMe at 80 °C (Scheme 3). This demonstrates that the 16-electron, α-functionalized, alkyl intermediate [$Tp^{Me2}Ir(C_6H_5)(CH_2OCH_2CH_2OMe)$] **A** is accessible under the reaction conditions. Although **3** is the main compound formed in this reaction (*ca.* 90%), trapping of the above mentioned intermediate **A** by NCMe is not completely effective, since the isomeric adduct **5** is also formed as a minor product of the reaction. This observation suggests that **A** can alternatively generate a new hydride intermediate, and in accord with this assumption prolonged heating of **2** in C_6H_{12} (7 h), at the same temperature, gives the hydride complex **4** (Scheme 4)‖, that under the same reaction conditions converts cleanly and quantitatively into **5** when treated with NCMe.

Complex **4** contains an elaborated aryl ligand, $-C_6H_4$-*o*-$CH_2OCH_2CH_2OMe$, derived from a carbon–carbon bond forming reaction that involves the C_6H_5- and $-CH_2OCH_2CH_2OCH_3$ hydrocarbyl units of **A**. Evidently, prior aromatic C–H activation is needed, a plausible intermediate being the benzyne species **B** of Scheme 4.



Scheme 2



Scheme 3

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† Dedicated to Professor Malcolm L. H. Green on the occasion of his retirement.

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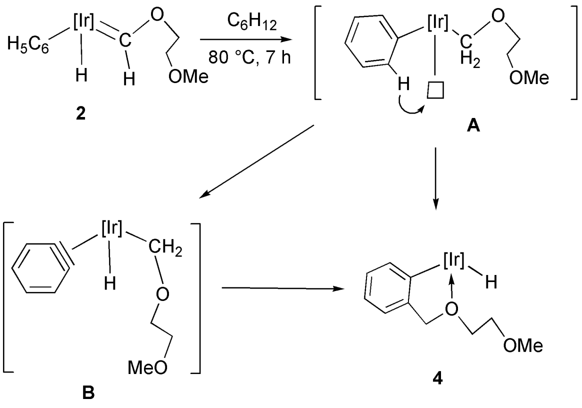
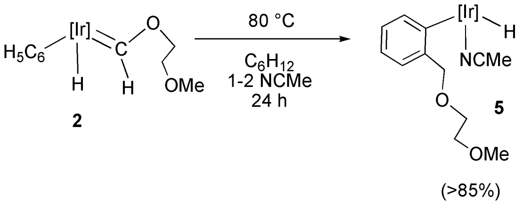


Scheme 4



Scheme 5

It is worth noting that coordination of NCMe in complex **3** is reversible, which implies that **A** can be generated from this acetonitrile adduct. This permits us to demonstrate that **5** is the thermodynamic product of the reaction of **2** with NCMe. Accordingly, prolonged heating of **2** or **3** in the presence of 1–2 equiv. of NCMe affords **5** in high yields (Scheme 5).

Both compounds **2** and **3** are active intermediates *en route* to **1** and $C_6H_5CH_2OCH_2CH_2OCH_3$, in the reaction of $[\mathrm{Tp^{Me2}Ir}(C_6H_5)_2]$ and dme, according to Scheme 1. Thus, when either of these species is heated in C_6H_6–dme mixtures, the bis(hydride) compound **1** plus the coupling organic product $C_6H_5CH_2OCH_2CH_2OCH_3$ are formed. In this process, the aryl ligand of **4** is likely extruded as the corresponding hydrocarbon, ArH, upon reaction of **4** with C_6H_6. An unsaturated $[\mathrm{Tp^{Me2}Ir}(C_6H_5)(H)]$ species would concomitantly be generated, which in the presence of dme gives rise to the bis(hydride) carbene complex **1**.

In conclusion, we have demonstrated that common solvents like C_6H_6 and dme participate in C–H activation and C–C bond forming reactions in the presence of $\mathrm{Tp^{Me2}Ir}(C_2H_4)_2$. Extension of this chemistry to other aliphatic, mono- and diethers is currently underway.

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Notes and references

‡ *Synthesis*: **1**: Compound $[\mathrm{Tp^{Me2}Ir}(C_2H_4)_2]$ (0.40 g, 0.73 mmol) was dissolved in C_6H_6 (8 mL) and an excess of $CH_3OCH_2CH_2OCH_3$ was added (0.7 mL). The solution was stirred for 24 h at 80 °C and the solvent evaporated under vacuum. NMR monitoring of the crude product revealed the formation of compound **1** and the organic derivative $C_6H_5CH_2OCH_2$-CH_2OCH_3, along with other Ir-containing byproducts. Following column chromatography through silica gel (hexane–Et_2O, 10 : 1 → 3 : 1), the organic product (60%) and compound **1** (30% yield) were isolated. Compound **1** can be crystallized by cooling to −20 °C its solutions in a hexane–CH_2Cl_2 mixture (3 : 2). Analytical data for **1**: IR (nujol mull): ν(Ir–H) 2135 $\mathrm{cm^{-1}}$. ^{1}H NMR ($CDCl_3$, 25 °C): δ 15.39 (s, 1 H, Ir=CH), 5.81, 5.79 (s, 2 : 1, 3 CH_{pz}), 4.84 (br s, 2 H, $\mathrm{OC}H_2\mathrm{CH_2OCH_3}$), 3.94 (br s, 2 H, $\mathrm{OCH_2C}H_2\mathrm{OCH_3}$), 3.48 (br s, 3 H, OCH_3), 2.44, 2.39, 2.39, 1.95 (s, 2 : 1 : 1 : 2, 6 Me_{pz}), −17.80 (br s, 2 H, IrH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 25 °C): δ 262.3 (br s, Ir=CH, $^1J_{CH}$ = 150 Hz), 152.2, 149.6, 144.2, 143.6 (1 : 2 : 1 : 2, C_{qpz}), 105.5 (CH_{pz}), 80.3 (br s, $^1J_{CH}$ = 146 Hz, $\mathrm{O}C\mathrm{H_2CH_2OCH_3}$), 70.2 ($^1J_{CH}$ = 145 Hz, $\mathrm{OCH_2}C\mathrm{H_2OCH_3}$), 59.1 ($^1J_{CH}$ = 141 Hz, OCH_3), 17.2, 15.4, 12.7 (1 : 2 : 3, Me_{pz}). Calcd. for $C_{19}H_{32}BN_6O_2Ir$: C, 39.4; H, 5.6; N, 14.5; found: C, 39.5; H, 5.5; N, 14.2%.

§ **2**: Compound $\mathrm{Tp^{Me2}Ir}(C_2H_4)_2$ (0.50 g, 0.92 mmol) was dissolved in C_6H_6 (25 mL) and an excess of dme (1 mL) was added. The solution was stirred for 6 h at 60 °C. After this period of time, the solvent was removed under reduced pressure and the solid residue was chromatographed through silica gel (hexane : Et_2O, 7 : 1) to yield compound **2** in 84% isolated yield. Analytical data for **2**: IR (nujol mull): ν(Ir–H) 2140 $\mathrm{cm^{-1}}$. ^{1}H NMR ($CDCl_3$, 25 °C): δ 15.17 (br s, 1 H, Ir=CH), 8.01, 7.02, 6.81, 6.67, 6.34 (br s, br s, t, br s, br s, 1 H each, $^3J_{HH}$ ≈ 7 Hz, 5 CH_{ar}), 5.81, 5.76, 5.67 (s, 1 H each, 3 CH_{pz}), 4.46 (br m, 2 H, $\mathrm{OC}H_2\mathrm{CH_2OCH_3}$), 3.60 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{OCH_3}$), 3.29 (s, 3 H, OCH_3), 2.48, 2.39, 2.37, 1.63, 1.51 (s, 3 H each, 5 Me_{pz}), 2.05 (br s, Me_{pz}), −16.46 (br s, 1 H, IrH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 25 °C): δ 262.9 (br s, $^1J_{CH}$ = 169 Hz, Ir=CH), 152.3, 149.7, 143.4 (1 : 2 : 3, C_{qpz}), 141.5, 139.5, 126.0, 120.6 (br s, br s, s, s, 1 : 1 : 2 : 1, *o*, *m*, and *p* CH_{ar} resp.), 135.8 (br s, C_{qar}), 106.2, 106.1, 105.3 (CH_{pz}), 82.4 (br s, $^1J_{CH}$ = 144 Hz, $\mathrm{O}C\mathrm{H_2CH_2OCH_3}$), 70.3 ($^1J_{CH}$ = 141 Hz, $\mathrm{OCH_2}C\mathrm{H_2OCH_3}$), 58.8 ($^1J_{CH}$ = 139 Hz, OCH_3), 15.3, 14.7, 13.8, 12.7, 12.6 (1 : 1 : 1 : 2 : 1, Me_{pz}). Calcd. for $C_{25}H_{36}BN_6O_2Ir$: C, 45.8; H, 5.5; N, 12.8; found: C, 45.8; H, 5.5; N, 12.8%.

¶ Cleavage of the weaker C–H bonds of the $–OCH_2–$ unit does not occur, probably because the greater strength of the Ir–primary carbon bond makes activation of the stronger primary C–H thermodynamically more favourable than that of the secondary C–H bond.[7]

‖ **4**: Compound **2** (0.040 g, 0.061 mmol) was dissolved in C_6H_{12} (3 mL) and the solution was stirred for 7 h at 80 °C. The brown solution (> 70% spectroscopic yield of **4**) thus obtained was dried under reduced pressure, the residue dissolved in Et_2O (2 mL) and pentane (4 mL) was added, to precipitate compound **4** as a brown solid (0.012 g, 30% yield). A sample of analytical purity can be obtained by cooling to −20 °C a solution of **4** in a hexane–CH_2Cl_2 mixture (2 : 1). Analytical data for **4**: IR (nujol mull): ν(Ir–H) 2123 $\mathrm{cm^{-1}}$. ^{1}H NMR ($CDCl_3$, 25 °C): δ 7.00, 6.86, 6.80 (m, m, m, 1 : 1 : 2, 4 CH_{ar}), 5.85, 5.67, 5.63 (s, 1 H each, 3 CH_{pz}), 5.39, 5.15 (d, 1 H each, $^2J_{HH}$ = 10.2 Hz, $\mathrm{ArC}H_2\mathrm{O}$), 3.97, 3.80 (ddd, 1 H each, $^2J_{HH}$ = 12.4, $^3J_{HH}$ = 5.0, 3.1 and 6.7, 3.1 Hz, resp., $\mathrm{OC}H_2\mathrm{CH_2OCH_3}$), 3.18 (m, 2 H, $\mathrm{OCH_2C}H_2\mathrm{OCH_3}$), 3.11 (s, 3 H, OCH_3), 2.47, 2.41, 2.40, 2.33, 2.00, 1.30 (s, 3 H each, 6 Me_{pz}), −21.54 (s, 1 H, IrH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 25 °C): δ 151.7, 151.4, 150.1, 143.8, 143.1, 142.7 (C_{qpz}), 145.5, 143.9 (C_{qar}), 136.8, 124.7, 119.6, 118.4 (CH_{ar}), 106.8, 105.8, 105.5 (CH_{pz}), 90.0 ($^1J_{CH}$ = 146 Hz, $\mathrm{Ar}C\mathrm{H_2O}$), 78.0 ($^1J_{CH}$ = 145 Hz, $\mathrm{O}C\mathrm{H_2CH_2OCH_3}$), 71.6 ($^1J_{CH}$ = 142 Hz, $\mathrm{OCH_2}C\mathrm{H_2OCH_3}$), 58.7 ($^1J_{CH}$ = 141 Hz, OCH_3), 16.4, 15.8, 13.1, 12.6, 12.6, 11.8 (Me_{pz}). Calcd. for $C_{25}H_{36}BN_6O_2Ir$: C, 45.8; H, 5.5; N, 12.8; found: C, 45.5; H, 5.4; N, 12.3%.

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