

Facile Oxygen Atom Insertion into Unactivated C(sp³)–C(sp²) Single Bonds in Reactions of Ir(III) Complexes with O₂

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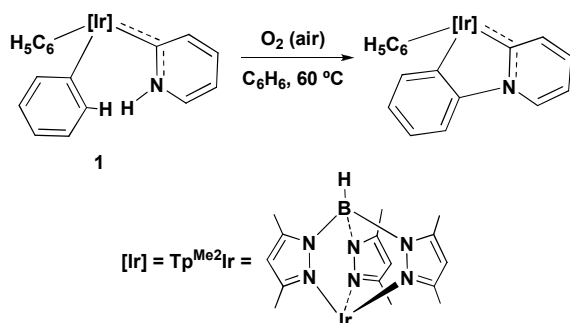
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ABSTRACT: The Ir(III) pyridylidene $\text{Tp}^{\text{Me}_2}\text{Ir}(\text{CH}_2\text{CH}_2\text{-}o\text{-C}_6\text{H}_4)(\text{CN}(\text{H})\text{CHCHCHCH})$ (**3**) (Tp^{Me_2} = hydrotris(3,5-dimethylpyrazolyl)borate) reacts with oxygen (air), under mild conditions, to afford a bicyclic ether-semiaminal species. The new structure derives formally from two oxidative events. One is dehydrogenative in nature (loss of 2 H) and the other consists in the insertion of an oxygen atom into a non-activated benzylic C—C bond. The reaction has been extended to a related iridacycle that contains a pyrazol co-ligand instead of the pyridylidene.

Nowadays, there is increasing interest in the use of O₂ as a terminal oxidant in many important organic reactions which usually need the aid of a transition metal catalyst.¹ Employing common Biochemistry terminology,^{1b} there are oxidase-like transformations that occur with dehydrogenation and no incorporation of oxygen into the end-products, whereas in other reactions of the oxygenase-type, the net

result is the incorporation of one or more oxygen atoms. One of the latter, particularly relevant to the present work, is the Baeyer–Villiger oxidation of ketones,² *i.e.* $\text{RC(O)R}' + [\text{O}] \rightarrow \text{RC(O)OR}'$, which can be performed with the aid of classical reagents (e.g. peracids) or with oxygen, under catalysis with specific enzymes^{2b} or by transition metal complexes.^{1,2c} We have recently reported³ on the reaction of the $\text{Tp}^{\text{Me}_2}\text{Ir(III)}$ bis(phenyl) pyridylidene⁴ complex **1** ($\text{Tp}^{\text{Me}_2} = \text{hydrotris(3,5-dimethylpyrazolyl)borate}$) with oxygen (Scheme 1). As can be observed, O_2 effects activation of the N—H bond of the carbenic unit along with that of an *ortho* C—H bond of one of the Ir— C_6H_5 groups, with concomitant formation of a C—N bond. KIE measurements are in accord with N—H bond activation being the rate determining step. In this note we wish to report that, in the course of the reaction of related pyridylidenes and pyrazol Ir(III) metallacycles with atmospheric oxygen under mild conditions, this process may be formally coupled to the unusual insertion of an oxygen atom into non-activated (*i.e.* non-acylic) $\text{C}(\text{sp}^3)\text{—C}(\text{sp}^2)$ benzylic single bonds. The resulting products are bicyclic structures possessing an ether-semiaminal functionality of the type $\text{RCH(OR')(NR''}_2)$. We are unaware of any literature precedent for this transformation.

Scheme 1. Reaction of Complex 1 with Oxygen

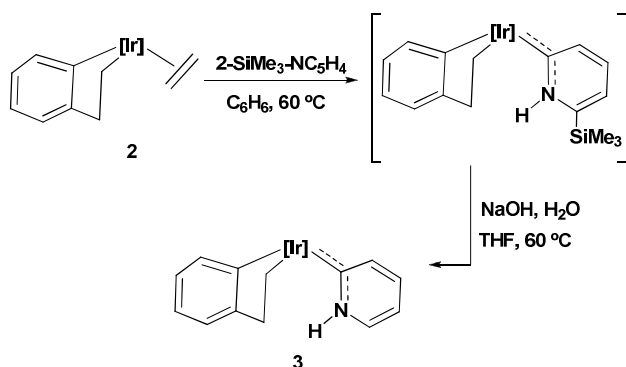


■ RESULTS AND DISCUSSION

Similarly to compound **1**,³ pyridylidene **3** was prepared in a one-pot, two-steps, procedure from the known⁵ metallacycle **2** and 2-trimethylsilylpyridine and found to exist in solution (CDCl_3) as a 4:1 mixture of rotamers, with the one depicted in Scheme 2, *i.e.* with the N—H bond pointing away the

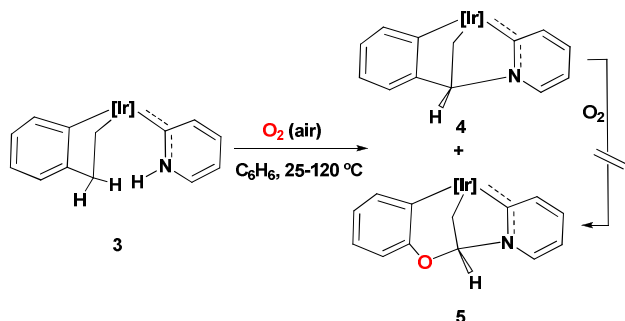
Tp^{Me2} ligand, predominating (NOESY evidence). Interestingly, the thermodynamic preference for one of the rotamers is an unexpected result as it contrasts with the reported behavior of complex **1**, where the corresponding rotamers are, as reasonably expected, isoenergetic.

Scheme 2. Synthesis of the Pyridylidene Complex **3**



When a benzene solution of **3** was stirred in a glass ampoule in contact with air (25 °C, 24 h) a mixture of two new complexes, **4** and **5** (Scheme 3) was cleanly generated in a *ca.* 1:5 relative ratio, normal laboratory light having no influence in the course of the reaction. The two compounds were separated by column chromatography on silica gel and fully characterized by spectroscopy. The benzylic CH unit of **4** gives rise to a doublet ($^3J_{\text{HH}} = 2.5$ Hz) at 5.63 ppm in the ¹H NMR spectrum (CDCl₃), and to a ¹³C resonance at 90.2 ppm which features a one-bond C—H coupling constant of 142 Hz. In contrast, the corresponding ¹³C signal of **5** shifts to 102.0 ppm and it is characterized by a ¹J_{CH} value of 160 Hz. Additionally, the Ir—C_{Ph} resonance of **4** at 150.9 ppm, finds its counterpart in **5** significantly shielded to 114.9 ppm. Comparative mass spectrometry measurements demonstrate the presence in **5** of an extra oxygen atom. Furthermore, when the reaction of Scheme 3 was carried out under ¹⁸O₂, compound **5** resulted labelled, thus demonstrating that the oxygen atom incorporated into **5** comes from dioxygen.

Scheme 3. Reaction of Complex 3 with O₂ in C₆H₆ Solution



These data along with those resulting from a single crystal X-ray study performed with **5** (Figure 1) demonstrate the structures shown for these complexes in Scheme 3.

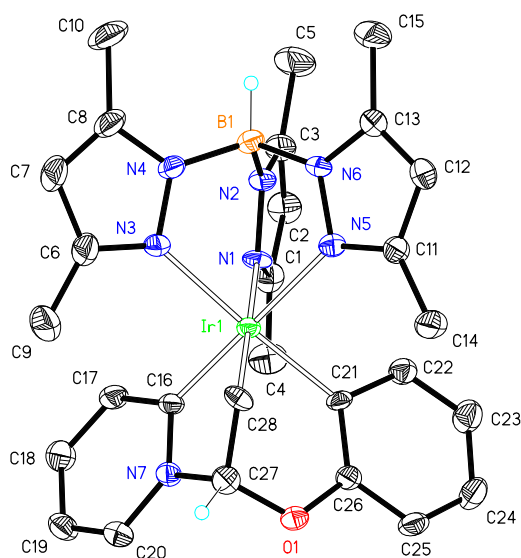


Figure 1. X-ray structure of complex **5** (50% displacement ellipsoids, H atoms except the H atoms on C(27) and B(1) omitted for clarity). Selected bond distances (Å) and angles (deg): Ir(1)—C(16) 1.952(5), Ir(1)—C(21) 2.044(5), Ir(1)—C(28) 2.076(6), Ir(1)—N(1) 2.158(4), Ir(1)—N(5) 2.159(5), Ir(1)—N(3) 2.166(5), N(7)—C(20) 1.360(7), N(7)—C(16) 1.376(7), N(7)—C(27) 1.486(7), O(1)—

C(26) 1.400(7), O(1)—C(27) 1.409(8), C(27)—C(28) 1.503(8), C(16)—Ir(1)—C(21) 91.2(2), C(16)—Ir(1)—C(28) 80.2(2), C(21)—Ir(1)—C(28) 85.4(2), C(26)—O(1)—C(27) 119.9(4).

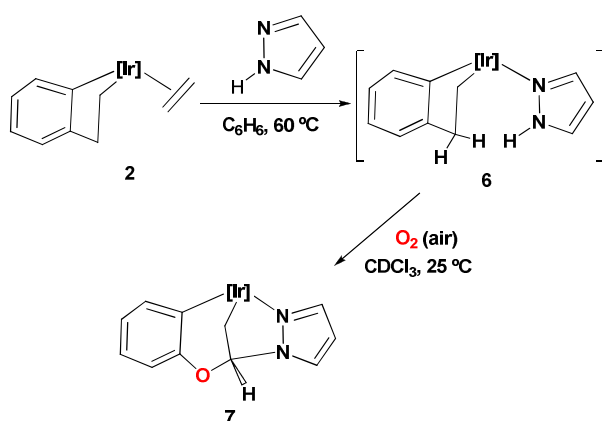
While it is clear that compound **4** results from a dehydrogenation process closely related to that shown in Scheme 1, formation of **5** constitutes a much more interesting reaction outcome. Indeed, complex **5** may be viewed as a bimetalacycle that contains an ether-semiaminal functionality of type RCH(OR')(NR''₂), formally related to **4** by insertion of an oxygen atom into its benzylic C_{Ar}—CH bond. Hence, in its formation oxygen is performing a dual role, with both enzymatic oxidase- and oxygenase-type reactivity. Interestingly, the copper-containing enzyme PPO (polyphenol oxygenase) catalyzes monophenols oxidation to *o*-quinones in a two step process, the first of the oxygenase kind and the second of oxidase nature.⁶

Complex **5** was not formed from **4** and O₂ under the reaction conditions, but we have found that the formation of the former was disfavored as the reaction temperature increased, the **4:5** ratio being *ca.* 0.6:1 and *ca.* 1:1 at 90 and 120 °C, respectively; increase of temperature caused as well the formation of other unidentified byproducts, which amounted at most to *ca.* 20% of the crude mixture. These ratios were independent of the oxygen concentration in the C₆H₆ solvent, *i.e.* the same values were obtained when the reactions were carried out under 2 atm of pure O₂. Interestingly, and in a very clean reaction, only complex **5** was observed when CDCl₃ was used as the solvent (both at 25 or at 90 °C). In addition, and as expected from our previous work,³ the oxidation events of Scheme 3 are suppressed when the reaction was carried out in the presence of *o*-hydroquinone, this indicating the participation of radicals in the processes.

Finally, we have demonstrated that the unusual oxidation under consideration is not restricted to pyridilydene derivatives. Thus, the metallacyclic complex **6**, prepared *in situ* from complex **2** and pyrazol, was also found to react, although at a slower rate, with oxygen (air) at 25 °C with formation of complex **7** (Scheme 4). However, in this case the reaction was much more complex, with the formation of several unidentified byproducts, but with no compound analogous to **4** being generated, as is deduced

by the absence of any resonance in the ^{13}C NMR spectra in the fingerprint ranges expected for this hypothetical product (see above). Compound **7** is unambiguously characterized by ^{13}C NMR spectroscopy where the O—CH functionality resonates at 89.9 ppm with a $^1J_{\text{CH}}$ coupling constant of 160 Hz, which compares well with the corresponding values found for **5** (102.0 ppm and 160 Hz, respectively).

Scheme 4. Reaction of the Pyrazol Derivative **6** with Oxygen

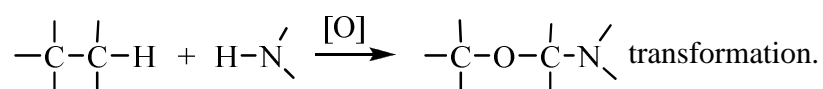


In closing, it has to be noted that, as in the case of many O_2 -mediated reactions with organic or organometallic substrates, it is not possible to advance mechanistic proposals for the oxidations described herein. The complexity of these type of reactions is highlighted by the fact that when the reaction of Scheme 3 is carried out with crude **3**, *i.e.* without being purified by column chromatography, only complex **4** is obtained under normal reaction conditions.

■ SUMMARY

O_2 -mediated N—H oxidation of pyridylidene or pyrrol ligands in $\text{Tp}^{\text{Me}_2}\text{Ir(III)}$ metallacycle derivatives, triggers a C—N bond forming event with the β -carbon (CH_2) of the metallacycle organic chain, accompanied by an oxygen atom insertion into an unactivated C—C bond, to form bicyclic structures

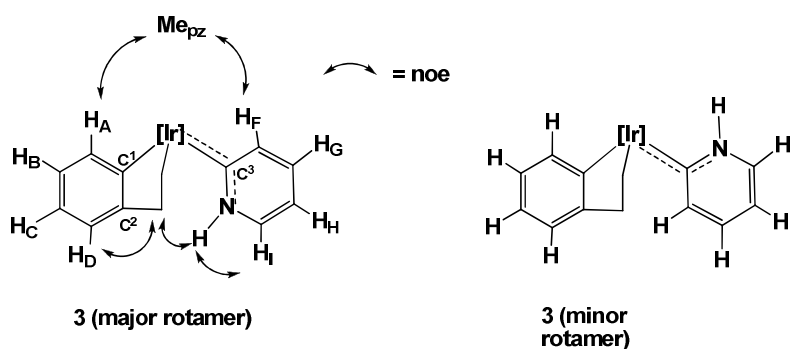
containing an ether-semiaminal functionality, *i.e.* effecting a



■ EXPERIMENTAL SECTION

General considerations. Microanalyses were by the Microanalytical Service of the Instituto de Investigaciones Químicas (Sevilla, Spain). The NMR Instruments were Bruker DRX-500, DRX-400, and DPX-300 spectrometers. Spectra were referenced to external SiMe₄ (δ 0 ppm) using the residual protio solvent peaks as internal standards (¹H NMR experiments) or the characteristic resonances of the solvent nuclei (¹³C NMR experiments). Spectral assignments were made by means of routine one- and two-dimensional NMR experiments where appropriate. All manipulations were performed under dry, oxygen-free dinitrogen, unless stated, following conventional Schlenk techniques. Compound **2**⁵ was obtained by using the published procedure. ¹⁸Oxygen was purchased from EURISO-TOP and charged through an appropriate valve into the reaction flask containing a degassed solution of compound **3**.

Synthesis and characterization of compound 3. Compound **2** (0.20 g, 0.32 mmol) was stirred overnight with 2-trimethylsilylpyridine (159 μ L, 0.96 mmol) in cyclohexane (10 mL) at 60 °C. The volatiles were removed under reduced pressure, the resulting residue dissolved in THF (10 mL) and a solution of NaOH (0.8 mL, 1.8 M) added. The mixture was heated at 60 °C overnight and the resulting solution was taken to dryness and methylene chloride (20 mL) added. The solution was washed with water (3 x 20 mL) and the organic fraction dried over MgSO₄. An analytically pure, bright yellow, sample of **3** was obtained by column chromatography on silica gel using a mixture of Et₂O:pentane (1:100) as eluent. Yield: 50%. **R_f** = 0.72 [silica gel, 6:1 pentane:diethylether]. In CDCl₃, at 0 °C, this complex exists as a 4:1 mixture of the rotamers depicted below and the spectroscopic data that follow correspond to the major one.



$^1\text{H NMR}$ (500 MHz, CDCl_3 , 0 °C) δ : 11.12 (br s, 1 H, NH), 7.56 (t, 1 H, $^3J_{\text{HH}} = 6.0$ Hz, H_I), 7.25 (d 1 H, H_D), 7.17 (d, 1 H, H_F), 6.94 (d, 1 H, H_A), 6.90 (m, 2 H, H_C and H_G), 6.63 (m, 2 H, H_H and H_B), 5.76, 5.74, 5.55 (s, 1 H each, CH_{pz}), 3.53, 3.13 (m, dd, 1 H each, $^2J_{\text{HH}} = 17.7$, $^3J_{\text{HH}} = 8.7$ Hz, IrCH_2CH_2), 2.79, 2.28 (q, t, 1 H each, $^2J_{\text{HH}} = 10.0$, $^3J_{\text{HH}} = 10.0$ Hz, IrCH_2CH_2), 2.41, 2.35, 1.84, 1.36, 1.31 (s, 2:1:1:1:1 ratio, 18 H, Me_{pz}). With the exception of the reported $^3J_{\text{IH}}$, all aromatic $^3J_{\text{HH}}$ are *ca.* 7.5 Hz.

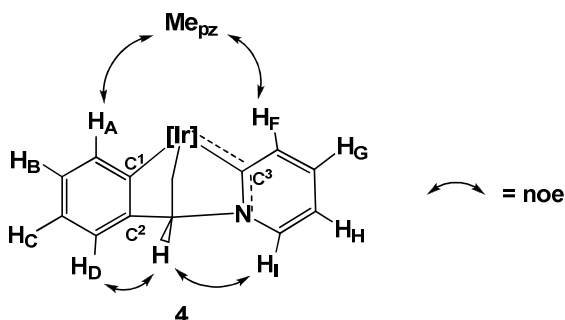
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3 , 0 °C) δ : 181.9 (C^3), 158.9 (C^2), 151.2, 149.9, 148.5, 143.1, 143.0, 142.6 (C_{qpz}), 150.1 (C^1), 143.8 (CH_F), 138.2 (CH_A), 136.8 (CH_I), 132.0 (CH_C), 123.2 (CH_D), 123.0 (CH_B), 121.3 (CH_G), 114.0 (CH_H), 108.2, 107.0, 106.4 (CH_{pz}), 40.0 (IrCH_2CH_2 , $^1J_{\text{CH}} = 122$ Hz), 15.2, 14.3, 13.2, 13.1, 13.1, 12.5 (Me_{pz}), -6.8 (IrCH_2 , $^1J_{\text{CH}} = 126$ Hz).

Anal. Calc. for $\text{C}_{28}\text{H}_{35}\text{BIrN}_7$: C, 50.0; H 5.2; N, 14.5. **Exp.:** C, 50.3; H 5.2; N, 14.4.

ESI-MS: m/z 694.3 [$\text{M}+\text{Na}$] $^+$.

Synthesis of compounds 4 and 5. Compound **3** dissolved in C_6H_6 (2 mL for 20 mg) was stirred overnight, at 25 °C, in a closed glass ampoule under an air atmosphere. NMR investigation of the crude mixture revealed the clean formation of compounds **4** and **5**, in a relative ratio 1:5 (**4**:**5**). Separation of both complexes was performed using a mixture obtained from a reaction carried out at 120 °C, where they formed in a 1:1 ratio. Complexes **4** and **5** were isolated, as bright yellow and yellow solids respectively, by column chromatography on silica gel using mixtures of Et_2O :pentane as eluent: (1:50)

→ (2:50) for **4** (30% yield), and (5:50) → (6:50) for **5** (35% yield). **RF (4)** = 0.8 (silica gel, pentane:diethyl ether 7:1); **RF (5)** = 0.34 (silica gel, pentane:diethyl ether 7:1).

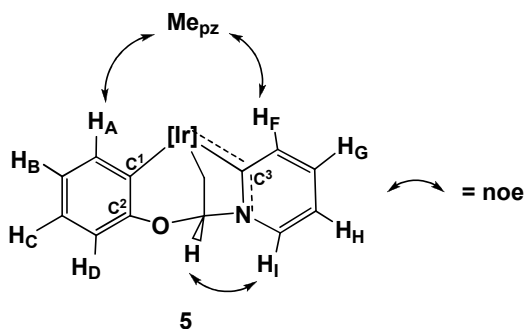


Data for 4: $^1\text{H NMR}$ (500 MHz, CDCl_3 , 25 °C) δ : 8.46 (d, 1 H, $^3J_{\text{HH}} = 6.0$ Hz, H_I), 7.50 (d, 1 H, H_F), 7.36 (d, 1 H, H_D), 7.16 (d, 1 H, H_A), 6.98 (t, 1 H, H_G), 6.85 (t, 1 H, H_C), 6.73 (t, 2 H, H_B and H_H), 5.78, 5.71, 5.68 (s, 1 H each, CH_{pz}), 5.63 (br d, 1 H, $^3J_{\text{HH}} = 2.5$ Hz, CHCH_2), 2.59, 2.42 (dd, d (from COSY), 1 H each, $^2J_{\text{HH}} = 9.4$, $^3J_{\text{HH}} = 2.5$ Hz, CHCH_2), 2.46, 2.43, 2.42, 1.59, 1.50, 1.44 (s, 3 H each, Me_{pz}). With the exception of the reported $^3J_{\text{HH}}$, all aromatic $^3J_{\text{HH}}$ are *ca.* 7.5 Hz.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3 , 25 °C) δ : 184.8 (C^3), 152.1, 150.4, 149.2, 143.2, 143.2, 142.5 (C_{pz}), 150.9 (C^1), 149.4 (C^2), 140.0 (CH_F), 138.2 (CH_A), 136.0 (CH_I), 130.5 (CH_G), 124.4 (CH_B), 120.5 (CH_C), 119.5 (CH_D), 115.7 (CH_H), 107.6, 107.2, 106.0 (CH_{pz}), 90.2 (CHCH_2 , $^1J_{\text{CH}} = 142$ Hz), 15.1, 14.2, 13.8, 13.1, 13.1, 13.0 (Me_{pz}), 12.7 (IrCH_2 , $^1J_{\text{CH}} = 129$ Hz).

Anal. Calc. for $\text{C}_{28}\text{H}_{33}\text{BIrN}_7$: C, 50.1; H 4.9; N, 14.6. **Exp.:** C, 50.2; H 5.3; N, 14.2.

ESI-MS: m/z 672.2 $[\text{M}+\text{H}]^+$.



Data for 5: ^1H NMR (500 MHz, CDCl_3 , 25 °C) δ : 8.39 (d, 1 H, $^3J_{\text{HH}} = 6.1$ Hz, H_I), 7.37 (d, 1 H, H_F), 7.03 (t, 1 H, H_G), 6.77 (t, 1 H, H_H), 6.68 (t, 1 H, H_C), 6.52 (d, 1 H, H_A), 6.42 (d, 1 H, H_D), 6.40 (t, 1 H, H_B), 6.07 (d, 1 H, $^3J_{\text{HH}} = 4.1$ Hz, CHCH_2), 5.81, 5.63, 5.61 (s, 1 H each, CH_{pz}), 2.92, 2.85 (d, dd, 1 H each, $^2J_{\text{HH}} = 12.2$ Hz, CHCH_2), 2.44, 2.38, 2.37, 1.61, 1.56, 1.38 (s, 3 H each, Me_{pz}). With the exception of the reported $^3J_{\text{HH}}$, all aromatic $^3J_{\text{HH}}$ are *ca.* 7.5 Hz.

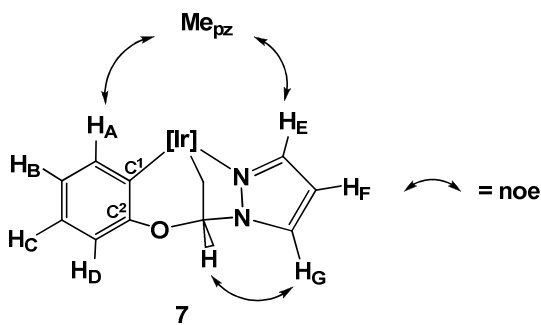
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3 , 25 °C) δ : 190.4 (C^3), 157.8 (C^2), 152.2, 149.5, 149.1, 143.3, 143.0, 142.8 (C_{qpz}), 142.7 (CH_A), 140.4 (CH_F), 136.1 (CH_I), 132.6 (CH_G), 122.1 (CH_C), 120.4 (CH_B), 115.9 (CH_H), 114.9 (C^1), 114.2 (CH_D), 107.8, 107.5, 106.5 (CH_{pz}), 102.0 (CHCH_2 , $^1J_{\text{CH}} = 160$ Hz), 15.5, 13.4, 13.1, 13.0, 12.7 (1:1:1:2:1 ratio, Me_{pz}), -4.4 (IrCH_2 , $^1J_{\text{CH}} = 129$ Hz).

Anal. Calc. for $\text{C}_{28}\text{H}_{33}\text{BIrN}_7\text{O}$: C, 48.9; H 4.8; N, 14.2. **Exp.:** C, 49.1; H 5.0; N, 14.0.

ESI-MS: m/z 710.3 [$\text{M}+\text{Na}$] $^+$; 687.4 [M] $^+$.

ESI-MS: m/z 689.4 [M] $^+$.

Synthesis and characterization of compound 7: A solution of complex **2** (0.20 g, 0.32 mmol) and pyrazol (0.036 g, 0.48 mmol) in C_6H_{12} (10 mL) was stirred, at 60 °C, overnight. The resulting solution was taken to dryness and methanol-free CHCl_3 (10 mL) added. Air was introduced into the glass ampoule and the solution stirred, at 25 °C, for 48 h. NMR investigation of the resulting solution revealed the formation of compound **7**, in *ca.* 30% spectroscopic yield, along with several unidentified products. Complex **7** has only been obtained with a (NMR) purity of *ca.* 80% even after many attempts of further purification by chromatography and/or crystallization. However, it was unambiguously characterized by NMR spectroscopy in such state.



^1H NMR (400 MHz, CDCl_3 , 25 °C) δ : 7.96 (d, 1 H, $^3J_{\text{HH}} = 2.6$ Hz, H_G), 7.23 (d, 1 H, $^3J_{\text{HH}} = 2.6$ Hz, H_E), 6.73 (t, 1 H, H_C), 6.52 (d, 1 H, H_A), 6.42 (m, 2 H, H_B and H_D), 6.19 (t, 1 H, H_F), 5.83, 5.66, 5.61 (s, 1 H each, CH_{pz}), 5.70 (d, 1 H, $^3J_{\text{HH}} = 4.6$ Hz, CHCH_2), 3.28, 2.92 (d, dd, 1 H each, $^2J_{\text{HH}} = 11.8$ Hz, CHCH_2), 2.44, 2.38, 1.67, 1.53, 1.23 (s, 1:2:1:1:1 ratio, 18 H, Me_{pz}). The non-reported aromatic $^3J_{\text{HH}}$ coupling constants are all *ca.* 7.5 Hz.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3 , 25 °C) δ : 158.1 (C^2), 152.6, 149.5, 149.2, 143.6, 143.4, 143.1 (C_{qpz}), 143.3 (CH_A), 140.7 (CH_E), 129.5 (CH_G), 122.9 (CH_C), 120.4 (CH_B), 114.3 (CH_D), 112.8 (C^1), 108.4, 107.4, 106.7 (CH_{pz}), 107.7 (CH_F), 89.9 (CHCH_2 , $^1J_{\text{CH}} = 160$ Hz), 15.1, 14.0, 13.6, 13.1, 13.0, 11.4 (Me_{pz}), -5.6 (IrCH_2 , $^1J_{\text{CH}} = 130$ Hz).

X-ray structure determination of compound 5. A single crystal of suitable size, coated with dry perfluoropolyether was mounted on a glass fiber and fixed in a cold nitrogen stream [$T = 173(2)$ K] to the goniometer head. Data collection was performed on Bruker-Nonius X8APEX-II CCD diffractometer, using monochromatic radiation $\lambda(\text{Mo K}\alpha_1) = 0.71073$ Å, by means of ω and ϕ scans. The data were reduced (SAINT)⁷ and corrected for Lorentz polarisation effects and absorption by multiscan method applied by SADABS.⁸ The structure was solved by direct methods (SIR-2002)⁹ and refined against all F^2 data by full-matrix least-squares techniques (SHELXTL).¹⁰ All the non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were included from calculated positions and refined riding on their respective carbon atoms with isotropic displacement parameters.

ASSOCIATED CONTENT

Supporting Information. Cif file for **5**. This material is available free of charge via the Internet at <http://pubs.acs.org>. CCDC 884959 also contains supplementary crystallographic data for complex **5**.

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FIGURE CAPTIONS

Figure 1. X-ray structure of complex **5** (50% displacement ellipsoids, H atoms except the H atoms on C(27) and B(1) omitted for clarity). Selected bond distances (Å) and angles (deg): Ir(1)—C(16) 1.952(5), Ir(1)—C(21) 2.044(5), Ir(1)—C(28) 2.076(6), Ir(1)—N(1) 2.158(4), Ir(1)—N(5) 2.159(5), Ir(1)—N(3) 2.166(5), N(7)—C(20) 1.360(7), N(7)—C(16) 1.376(7), N(7)—C(27) 1.486(7), O(1)—C(26) 1.400(7), O(1)—C(27) 1.409(8), C(27)—C(28) 1.503(8), C(16)—Ir(1)—C(21) 91.2(2), C(16)—Ir(1)—C(28) 80.2(2), C(21)—Ir(1)—C(28) 85.4(2), C(26)—O(1)—C(27) 119.9(4).

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Graphic for the TOC:

