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Cyclometallation and Hydrogen/Deuterium Exchange Reactions of an Arylphosphine Ligand upon Coordination to {Ir(η^5-C_5Me_5)}

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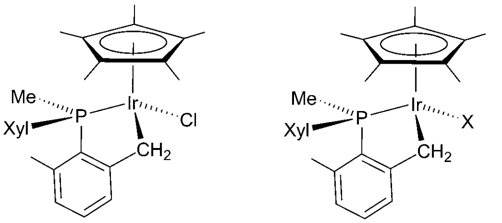
Dedicated to Professor Jennifer Green on the occasion of her retirement

The cyclopentadienyl ligand has played a pivotal role in organometallic chemistry ever since the synthesis and structural characterization of ferrocene was achieved in the early 1950s.[1] Half-sandwich metallocenes of rhodium and especially iridium, particularly those that contain the C_5Me_5 ligand, have provided truly remarkable advances in the field of C–H bond activation. An early important milestone was the observation in 1982 by the groups of Bergman and Graham of the intermolecular addition of alkane C–H bonds to electron-rich [(η^5-C_5Me_5)Ir(L)] centers.[2] A subsequent, also impressive, breakthrough in this field was the discovery by Bergman and co-workers that the electron-deficient cationic Ir^{III} species [(η^5-C_5Me_5)Ir(Me)(PMe_3)($ClCH_2Cl$)]$^+$, isolated as the [BAr_4^F]$^-$ salt ([BAr_4^F]$^-$ = [B-(3,5-$C_6H_3(CF_3)_2)_4$]$^-$), effects the selective cleavage of the C–H bonds of alkanes and arenes under unusually mild conditions (for example, C_6H_6 at −30 °C and CH_4 at 10 °C).[3]

Numerous studies of inter- and intramolecular C–H bond activation reactions employing neutral or cationic complexes of the (η^5-C_5Me_5)M (M = Rh, Ir) fragments have been reported to date,[4–8] including a number of catalytic transformations. Considering the high activity and selectivity of the [(η^5-C_5Me_5)Ir(Me)(PMe_3)($ClCH_2Cl$)]$^+$ ion in C–H activation,[3] it is surprising that information on related complexes with different cyclopentadienyl or P-donor ligands is scarce. The analogous rhodium complex [(η^5-C_5Me_5)Rh(Me)(PMe_3)($ClCH_2Cl$)]$^+$ has also been isolated as its [BAr_4^F]$^-$ salt.[7c] Since an important strategy that is frequently employed in organometallic chemistry to fine-tuning metal reactivity and improve metal performance in terms of efficiency and selectivity is the search for different ligand environments, we have recently programmed a study of rhodium and iridium compounds based on [(η^5-Cp′)M(PR_3)] units with differently substituted cyclopentadienyl ligands, Cp′, and bulky tertiary phosphines. Here we present preliminary results based on the parent {(η^5-C_5Me_5)Ir} metal fragment, but bound to the bis(aryl) phosphine PMe(Xyl)$_2$ (Xyl = 2,6-$Me_2C_6H_3$) that is clearly prone to cyclometallation.[9] The cyclometallated chloro precursor **1**, as well as the corresponding methyl and hydride derivatives, **2** and **4**, respectively (Scheme 1), are herein described, along with carbon–hydrogen/carbon–deuterium exchange reactions of some of these complexes. A compound related to **2**, in which the Ir–Me unit has been formally replaced by an Ir–CH_2–P bond, as a consequence of metallation of the P–Me group (compound **3**) is also reported.



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X = Me, **2**; H, **4**

Scheme 1. Schematic structural representations of the major diastereoisomers of compounds **1**, **2** and **4**.

Reaction of the Ir^{III} dimer [{(η^5-C_5Me_5)$IrCl_2$}$_2$] with one equivalent of PMe(Xyl)$_2$ does not permit isolation of the expected phosphine adduct. Instead, this purported intermediate undergoes fast cyclometallation with concomitant elimination of HCl, which is trapped as the corresponding phosphine hydrochloride [HPMe(Xyl)$_2$]Cl. Consequently, only half of the starting iridium dimer converts into the desired

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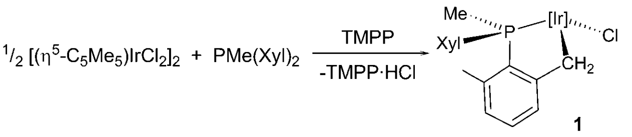
product. To circumvent this problem the reaction was performed in the presence of the weakly coordinating base 2,2,6,6-tetramethylpiperidine (TTMP in Scheme 2), giving the desired complex **1** in the form of two diastereomers (ca. 7:3 ratio). Mild heating (CH_2Cl_2/MeOH, 40 °C) of this mixture causes conversion into its major component as the exclusive product, isolated in 90 % yield. This is assumed to be the sterically more favorable stereomer with a *syn* orientation of chloride and methyl phosphine groups (Scheme 2), as confirmed by NOE experiments for the related methyl complex **2** obtained from it (see the Supporting Information).

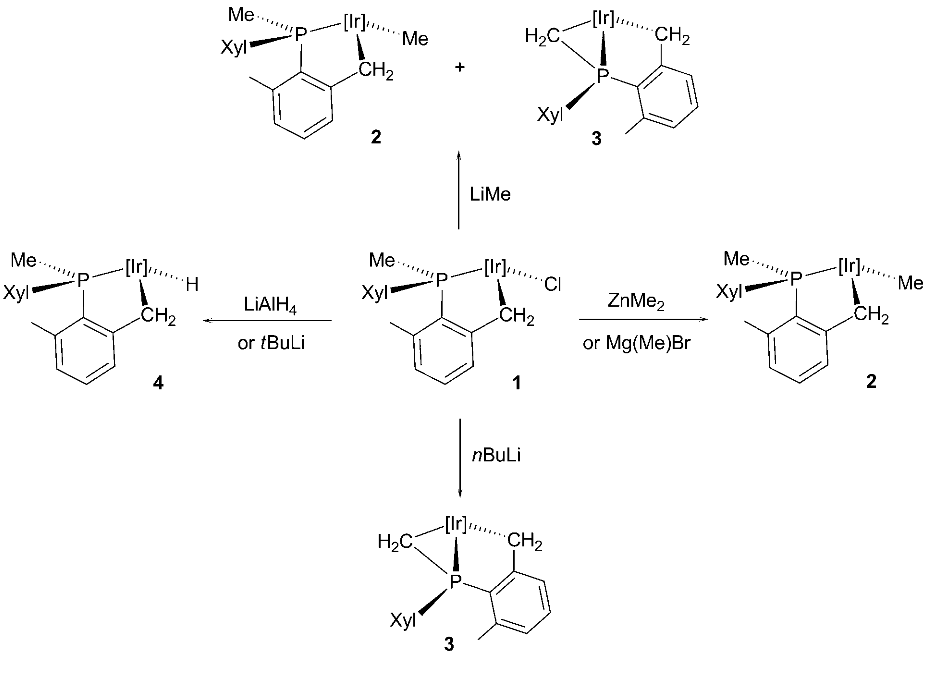


Scheme 2. Synthesis of cyclometallated compound **1**. In this and other schemes, [Ir] represents {(η^5-C_5Me_5)Ir}.

Complex **1** is a yellow crystalline solid, soluble in common organic solvents. It displays moderate stability toward oxygen and moisture, particularly in the solid state. NMR data (see the Supporting Information) permit unambiguous characterization of the ligand framework. In the ^{1}H NMR spectrum there is a prominent doublet at δ = 1.32 ppm ($^4J_{HP}$ = 1.9 Hz, 15 H) due to the C_5Me_5 group, as well as three singlets with chemical shifts δ = 1.47, 1.78, and 2.35 ppm (3 H each), which correspond to the inequivalent methyl aryl protons. The phosphorus-bound methyl group appears as a doublet (δ = 2.28 pm, 10.4 Hz), whereas the diastereotopic protons of the methylene group bonded to the iridium center provide a characteristic pattern of lines. This may be identified as the AB part of an ABX spin system, in which only one of the protons features observable coupling to ^{31}P (δ_A = 4.15, δ_B = 3.87 ppm; $^2J_{AB}$ = 14.5, $^3J_{AX}$ = 3.8 Hz). Corresponding signals are found in the ^{13}C{^{1}H} NMR spectrum. Interestingly, the Ir−CH_2 resonance appears at δ = 20.3 ppm and exhibits negligible coupling to phosphorus, whereas the two methyl groups of the nonmetallated xylyl (δ = 22.7 and 25.0 ppm) show three-bond couplings with the ^{31}P nucleus of 4 and 8 Hz, respectively. The ^{31}P{^{1}H} NMR spectrum consists of a singlet at δ = 11.3 ppm, that is significantly shifted to higher frequency in comparison with the free ligand (δ = −33.1 ppm).

Complex **1** is a suitable precursor for related complexes that contain Ir−C or Ir−H sigma bonds (Scheme 3). Treatment with LiMe yields the expected methyl derivative **2**, as the major reaction product. However, minor amounts (ca. 30 %) of the somewhat related complex **3**, additionally metallated in the phosphine methyl group, are also produced. Formation of the latter compound is avoided by the use of the milder dimethylzinc or methyl Grignard reagents, thus providing a straightforward, high-yield route to methyl complex **2**. Notably, *n*BuLi gives exclusively doubly metallated **3**, whereas *t*BuLi affords iridium hydride **4**. Complex **4** is best synthesized by reacting **1** with $LiAlH_4$ and results as an approximate 20:1 mixture of diastereomers.

Methyl complex **2** and the major diastereoisomer of hydride **4**, feature NMR signals for the C_5Me_5 and metallated phosphine ligands similar to those of chloride precursor **1**. For instance, both give ^{31}P{^{1}H} signals of nearly identical chemical shift values (δ = 8.4 ppm, **2**; δ = 8.3 ppm, **4** in C_6D_6), which are displaced by only about 3 ppm with respect to **1**. Characteristic NMR signals due to their Ir−CH_3 and Ir−H linkages are additionally observed. Thus, for **2** high-field ^{1}H and ^{13}C{^{1}H} doublets are recorded at δ = 0.35 ppm (5.2 Hz) and δ = −22.9 ppm (8 Hz), respectively. NOE studies for this predominant isomer reveal the *syn* distribution of Ir−Me and P−Me groups shown in Scheme 1. With respect to **4**, a strongly shielded resonance is recorded for the hydride ligand at δ = −17.24 ppm ($^2J_{HP}$ = 35.2 Hz). EXSY NMR studies performed at 0 °C give no evidence for exchange between the Ir−H and Ir−CH_2 sites. Furthermore, no H/D scrambling occurs at room temperature for solutions of either [D$_1$]-**4** (Ir−D) or [D$_{11}$]-**4** (Ir−H), although, the H/D

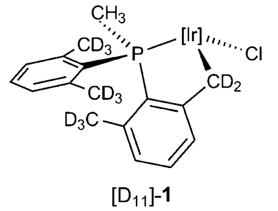


Scheme 3. Reactions of compound **1** to form iridium alkyl and hydride complexes **2**–**4**.

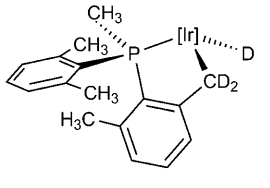
exchange becomes detectable at 90 °C ([D_1]-**4** is prepared from **1** and $LiAlD_4$ and [D_{11}]-**4** from [D_{11}]-**1** and $LiAlH_4$; see below and the Supporting Information). Since heating a solution of **4** in C_6D_6 at 200 °C (pressure vessel) for two days reveals no D incorporation into the metallated ligand, intramolecular C–H activation of the nonmetallated Ir^I intermediate [(η^5-C_5Me_5)Ir($PMeXyl_2$)] proceeds much faster than intermolecular benzene activation. This contrasts with results reported for somewhat related rhodium complexes.[9b,c,10]

At variance with the above, the metallation reaction of the P–Me unit[11] that gives rise to compound **3** causes a $^{31}P\{^1H\}$ shift of almost 50 ppm to higher field in comparison with **1**, **2**, and **4**. The corresponding signal is found at $\delta = -41.6$ ppm, that is about 8 ppm higher field than in the free ligand. In the ^1H NMR spectrum the doublet due to the P–Me group that appears in the vicinity of 2 ppm for compounds **1** and **2** is absent and is replaced by two multiplets at $\delta = 1.46$ and 0.17 ppm (see the Supporting Information) that correspond to the diastereotopic $IrCH_2P$ protons. The corresponding $^{13}C\{^1H\}$ resonance is found at $\delta = -18.4$ ppm and features negligible coupling to the ^{31}P nucleus.

The nature of compounds **1**–**4** support the notion of their utility as C–H bond-activation promoters. Current studies in our laboratory, to be reported in due course, confirm this assumption. H/D exchange reactions within the ligand backbone of chloride **1** and hydride **4** can, in the meantime, be discussed. Under similar conditions methyl derivative **2** does not undergo deuteration. The importance of deuterium labeling of organic molecules has sparked studies in this field by different research groups.[8c,g,12]

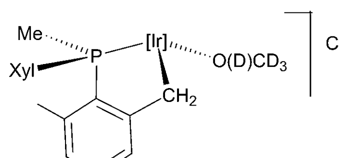


[D_{11}]-**1**



[D_3]-**4**

Deuterium incorporation into the methylene and methyl positions of the metallated ligand of **1** can be achieved by using CD_3OD as the deuterium source. Due to the poor solubility of **1** in this solvent, C_6H_6/CD_3OD or preferably CH_2Cl_2/CD_3OD solvent mixtures are employed in practice. Heating a solution of **1** in CH_2Cl_2/CD_3OD (1:1) at 45 °C results in the formation of [D_{11}]-**1**. Monitoring of the reaction by ^1H NMR spectroscopy provides evidence that incorporation of deuterium into the CH_2 and CH_3 sites of **1** occurs with the same rate and is characterized by a half-life, $t_{1/2} =$ 490 min (45 °C, 50 % CD_3OD). In parallel experiments, deuteration of **1** was effected with the same CD_2Cl_2/CD_3OD solvent mixture, in one case saturated with LiCl.[12b] A tenfold decrease in the rate of the H/D exchange was observed for the LiCl-containing solution, suggesting that chloride dissociation, and formation of a cationic species **A**, may be involved in the H/D exchange.



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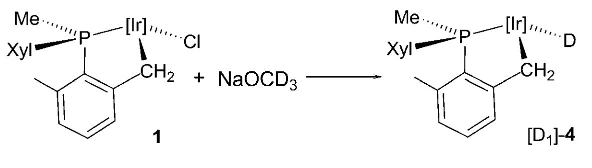
Hydride compound **4** undergoes deuteration too in the same CH_2Cl_2/CD_3OD solvent mixture, but important differences between the two systems are noticeable at first sight. Thus, only the hydride and methylene protons participate in the H/D exchange to yield [D_3]-**4**, both when the reaction is performed as for **1** (50 % CD_3OD, 45 °C), or with only 10 % CD_3OD at room temperature. Under the latter conditions $t_{1/2} = 130$ min. No difference in the rate of deuterium incorporation at these two chemically different sites of **4** becomes perceptible by ^1H NMR studies.

Before concluding, some comments on the mechanism of the H/D interchanges in **1** and **4** are appropriate. Clearly, different mechanistic pathways must be operative to explain the conspicuously dissimilar reaction outcomes, and this may be attributed, at least in part, to the good leaving-group characteristics of the chloride ligand of **1**, which facilitates formation of intermediate **A**. For this complex, acid addition causes only moderate acceleration of the H/D exchange since a 0.02 M solution of **1**, which is also 0.02 M in *p*-toluenesulfonic acid, experiences H/D interchange just three times faster than in the absence of the acid. However, remarkable acid catalysis has been uncovered for **4**, which in the presence of 5 % of the acid becomes immediately deuterated ($t_{1/2} \leq 3$ min) at the hydride and methylene sites. Furthermore, 20 % of the acid gives [D_{12}]-**4** additionally deuterated at the aryl methyl positions, almost instantly. In marked contrast with this observation, the addition of a base ($NaOCD_3$ or NaOH) inhibits completely H/D scrambling. The latter finding explains selective formation of [D_1]-**4** with $\geq$ 95 % deuterium content at the hydride position (no detectable mixing with the methylene protons) in the reaction of **1** with $LiAlD_4$, despite addition of H_2O to quench the excess of the deuteride reagent (see the Supporting Information). Besides, it has allowed the design of an alternative high-yield synthesis of [D_1]-**4** ($\geq$ 80 %) selectively labelled at the deuteride site (Scheme 4) in which $NaOCD_3$ acts as the source of deuterium.

The above results are consistent with the hypothesis that acid-catalyzed deuteration of **4** may also proceed through cationic species **A**, nevertheless generated catalytically by action of the acid (CD_3OD, *p*-$MeC_6H_4SO_3D$, or others like



Scheme 4. Synthesis of [D_1]-**4** employing $NaOCD_3$ as deuterium source.

CF_3CD_2OD). Intermediate **A** may find different paths to rearrange further along the H/D exchange scheme, including reversible α-H elimination within the Ir–CH_2 linkage. Additionally, C–H activation involving coordinated methanol might ensue according to well-known mechanistic routes.[13–15] However, the complexity of the system, in particular the different degree of deuterium incorporation in the reactions of **1** and **4** with CD_3OD, advises deferring a definitive mechanistic proposal until the results of ongoing experimental and theoretical studies become available.

In conclusion, cyclometallation of the bis(xylyl)phosphine $PMe(Xyl)_2$ by $[\{(\eta^5\text{-}C_5Me_5)IrCl_2\}_2]$, and subsequent functionalization of the resulting compound **1**, has provided a series of complexes that exhibit interesting H/D exchange reactions and have a high potential for C–H bond-activation chemistry. Work aimed at disclosing this reactivity, as well as the catalytic applications of these complexes in transfer hydrogenation and C–X coupling reactions, is presently going on in our laboratory.

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