J|A|C|S
ARTICLES
Published on Web 03/08/2006

Highly Stable Cp*−Ir(III) Complexes with *N*-Heterocyclic Carbene Ligands as C−H Activation Catalysts for the Deuteration of Organic Molecules

Rosa Corberán,[†] Mercedes Sanaú,[‡] and Eduardo Peris*,[†]

Contribution from the Departamento de Química Inorgánica y Orgánica, Universitat Jaume I, Avenida Vicente Sos Baynat s/n, Castellón, E-12071 Spain, and the Departamento de Química Inorgánica, Universitat de Valencia, C/Dr. Moliner s/n, Burjassot-Valencia, E-46100 Spain

Received December 15, 2005; E-mail: eperis@qio.uji.es

Abstract: The preparation of a series of complexes of the type $Cp^*IrX_2(NHC)$ provides effective catalysts for the H/D exchange of a wide range of organic molecules in methanol-d_4. The reaction proceeds with higher yields under milder reaction conditions than previous Cp*Ir systems reported thus far. For comparative purposes, we also studied the catalytic activity of $Cp^*IrCl_2(PMe_3)$ under the same reaction conditions. The molecular structures of two of the new Cp*Ir(NHC) complexes are described.

Introduction

Deuterium labeled compounds can be used in a wide range of applications such as the study of biologically active systems, solvents for NMR spectroscopy, and the study of reaction mechanisms.[1] Among the catalysts used for H/D exchange reported in the literature, those containing the "$Cp^*Ir^{III}(PMe_3)$" fragment described by Bergman and co-workers have shown excellent results in the sense that they can activate a wide range of organic molecules using a variety of deuterium sources (D_2, CD_3OD, $(CD_3)_2CO$, D_2O, and others).[2,3] The use of the basic phosphine in the catalyst seems to be essential in the activity of the compound, since this type of complex has shown activity toward H/D reactions (or other C−H activation processes) only when alkylphosphines such as PMe_3, $P(C_6H_{11})_3$, and $P(CH_2\text{-}t\text{-}Bu)_3$ are used.[4] A recent study by Herbert and co-workers showed that the basicity of the phosphines bound to iridium is an important factor influencing substrate selectivity and efficiency of deuteration.[5] *N*-Heterocyclic carbenes (NHCs) are known to be better σ-donor ligands than even basic alkylphosphines,[6,7] and some NHC complexes have shown improved activities toward C−H activation, but most of them refer to intramolecular processes,[8,9] intermolecular or catalytic examples being scarce.[10,11] Some organometallic species are known to be stabilized when NHC ligands are used,[12] and therefore the possibility to obtain stable catalysts for C−H activation can be envisaged.

With this in mind, we synthesized a series of $Cp^*IrCl_2(NHC)$ complexes with the aim of evaluating their capabilities in C−H activation, specifically in H/D exchange reactions of hydrocarbon molecules. Yamaguchi and co-workers recently described similar complexes that showed high catalytic activity toward the Oppenauer-type oxidation of alcohols.[13] Other related chelate biscarbene complexes of Cp^*Ir^{III} were reported by Heinekey and co-workers, who also obtained a cationic dihydrogen species of the type $[Cp^*Ir(H_2)(bis\text{-}NHC)]^+$.[14]

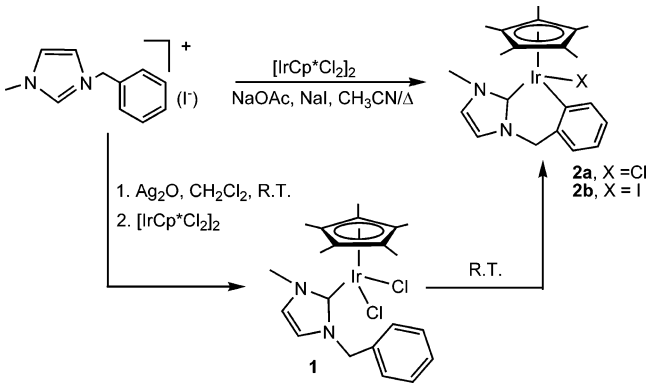
In this article, we describe the preparation of a series of $Cp^*IrCl_2(NHC)$ complexes that show a high efficiency in the deuteration of a wide range of organic molecules. The deuteration capabilities of these complexes are compared to that shown by $Cp^*IrCl_2(PMe_3)$. The molecular structures of two of these new complexes are also described.

[†] Universitat Jaume I.
[‡] Universitat de Valencia.

(1) (a) Thomas, A. F. *Deuterium Labeling in Organic Chemistry*; Appleton-Century-Crofts: New York, 1971. (b) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper & Row: New York, 1987. (c) Pleiss, U.; Voges, R. *Synthesis and Applications of Isotopically Labeled Compounds*; Wiley: New York, 2001. (d) Junk, T.; Catallo, W. J. *Chem. Soc. Rev.* **1997**, *26*, 401.
(2) (a) Skaddan, M. B.; Yung, C. M.; Bergman, R. G. *Org. Lett.* **2004**, *6*, 11. (b) Klei, S. R.; Golden, J. T.; Burger, P.; Bergman, R. G. *J. Mol. Catal. A: Chem.* **2002**, *189*, 79. (c) Klei, S. R.; Tilley, T. D.; Bergman, R. G. *Organometallics* **2002**, *21*, 4905. (d) Golden, J. T.; Andersen, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **2001**, *123*, 5837.
(3) Yung, C. M.; Skaddan, M. B.; Bergman, R. G. *J. Am. Chem. Soc.* **2004**, *126*, 13033.
(4) (a) Arndtsen, B. A.; Bergman, R. G. *Science* **1995**, *270*, 1970. (b) Bergman, R. G. *Science* **1984**, *223*, 902.
(5) Ellames, G. J.; Gibson, J. S.; Herbert, J. M.; Kerr, W. J.; McNeill, A. H. *J. Labelled Compd. Radiopharm.* **2004**, *47*, 1.
(6) (a) Hillier, A. C.; Sommer, W. J.; Yong, B. S.; Petersen, J. L.; Cavallo, L.; Nolan, S. P. *Organometallics* **2003**, *22*, 4322. (b) Dorta, R.; Stevens, E. D.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2003**, *125*, 10490. (c) Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 2485.
(7) Chianese, A. R.; Li, X. W.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2003**, *22*, 1663.
(8) (a) Scott, N. M.; Pons, V.; Stevens, E. D.; Heinekey, D. M.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2005**, *44*, 2512. (b) Dorta, R.; Stevens, E. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5054. (c) Huang, J. K.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2000**, *19*, 1194. (d) Danopoulos, A. A.; Winston, S.; Hursthouse, M. B. *J. Chem. Soc., Dalton Trans.* **2002**, 3090. (e) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T. L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546.
(9) Prinz, M.; Grosche, M.; Herdtweck, E.; Herrmann, W. A. *Organometallics* **2000**, *19*, 1692.
(10) Fructos, M. R.; Belderrain, T. R.; de Fremont, P.; Scott, N. M.; Nolan, S. P.; Diaz-Requejo, M. M.; Perez, P. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 5284.
(11) Clement, N. D.; Cavell, K. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3845.
(12) Scott, N. M.; Nolan, S. P. *Eur. J. Inorg. Chem.* **2005**, 1815.
(13) Hanasaka, F.; Fujita, K.; Yamaguchi, R. *Organometallics* **2005**, *24*, 3422.
(14) Vogt, M.; Pons, V.; Heinekey, D. M. *Organometallics* **2005**, *24*, 1832.

10.1021/ja058253l CCC: $33.50

Scheme 1



Results and Discussion

(a) Preparation and Characterization of the Compounds. Scheme 1 depicts the preparation of complexes **1**, **2a**, and **2b**. Compound **1** can be obtained by transmetalation of 1-methyl-3-benzylimidazolylidene from the corresponding silver carbene derivative to $[Cp^*IrCl_2]_2$ in CH_2Cl_2. However, this compound is unstable and at room temperature undergoes orthometalation to give compound **2a** (X = Cl) in 5 h. The reaction of $[Cp^*IrCl_2]_2$ and 1-benzyl-3-methylimidazolium iodide in the presence of NaOAc and NaI affords the preparation of compound **2b** (X = I). The addition of NaI to the reaction mixture favors the formation of the iodine complex and minimizes the presence of mixtures of **2b** with **2a**.

The $^{13}C\{^1H\}$ NMR spectra of compounds **2a** and **2b** reveal that both coordination of the NHC and orthometalation have occurred, as shown by the two C−Ir signals (δ = 157.4 $C_{carbene}$, δ = 144.4, C_{Ph} in **2a**; δ = 154.7 $C_{carbene}$, δ = 141.2, C_{Ph} in **2b**). The signal of the carbene−carbon in **1** appears at 156.5 ppm, as in previously reported Cp*−Ir−(NHC) complexes.[9,13,14]

Crystals of compounds **1** and **2b** suitable for X-ray diffraction were obtained from concentrated CH_2Cl_2/hexane solutions and allowed confirmation of both structures. Figure 1 shows the molecular diagram of **1** and the most representative distances and angles. The structure of **1** can be regarded as a three-legged piano stool. The Ir−$C_{carbene}$ distance is 2.06 Å, similar to that found by Yamaguchi and co-workers in a related Cp*Ir(NHC) complex[13] and other Ir^{III}−NHC species.[7,15,16] The Ir−Cl (2.415 and 2.425 Å) and Ir−Cp*(centroid) (1.803 Å) distances lie in the expected range for other known Cp*Ir(NHC) complexes.[13,14]

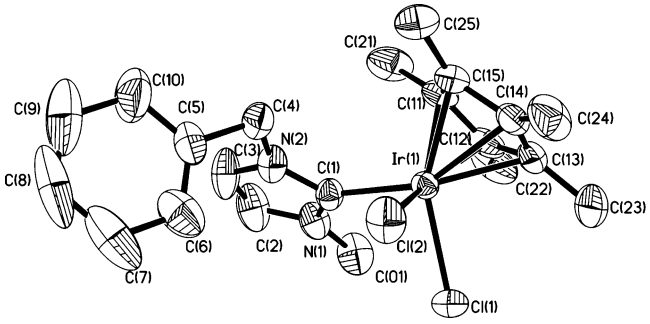


Figure 1. Molecular diagram of compound **1**. Selected bond distances (Å) and angles (deg): Ir(1)−C(1) 2.061(5), Ir(1)−Cl(1) 2.415(11), Ir(1)−Cl(2) 2.425(11), Ir(1)−$Cp_{centroid}$* 1.803(15), C(1)−Ir(1)−Cl(1) 93.36(13), C(1)−Ir(1)−Cl(2) 91.53(13), Cl(1)−Ir(1)−Cl(2) 86.32(4), $Cp_{centroid}$*−Ir(1)−C(1) 127.9(5), $Cp_{centroid}$*−Ir(1)−Cl(1) 120.4(5), $Cp_{centroid}$*−Ir(1)−Cl(2) 126.0(5).

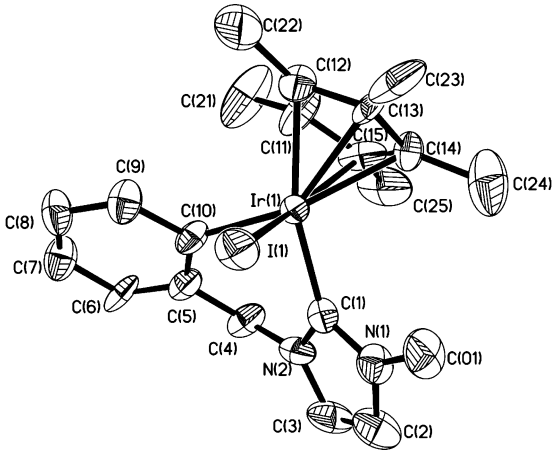
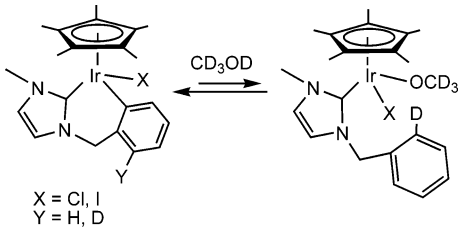


Figure 2. Molecular diagram of compound **2b**. Selected bond distances (Å) and angles (deg): Ir(1)−C(1) 2.014(7), Ir(1)−I(1) 2.7079(6), Ir(1)−C(10) 2.068(8), Ir(1)−$Cp_{centroid}$* 1.85(3), C(1)−Ir(1)−C(10) 85.7-(3), C(1)−Ir(1)−I(1) 90.4(2), C(10)−Ir(1)−I(1) 88.4(2), $Cp_{centroid}$*−Ir(1)−C(1) 128.9(11), $Cp_{centroid}$*−Ir(1)−C(10) 127.9(10), $Cp_{centroid}$*−Ir(1)−I(1) 123.4(11).

Scheme 2



The molecular diagram of compound **2b** is depicted in Figure 2. The structure of **2b** confirms that the orthometalation of the phenyl ring of the imidazolylidene ligand has occurred, thus leading to a chelate coordination of the ligand with a bite angle of 85.7°. The Ir−$C_{carbene}$ and Ir−C_{phenyl} distances are 2.01 and 2.06 Å, respectively. The Ir−I (2.708 Å) and Ir−Cp*(centroid) (1.85 Å) distances lie in the expected range.[13,14]

The fact that **1** orthometalates at room temperature to yield **2a** gives us an idea of the potentialities of Cp^*IrCl_2(NHC) complexes in C−H activation reactions. Furthermore, the reaction of **2a** and **2b** in refluxing CD_3OD affords quantitative deuteration of the ortho-position of the metalated phenyl group in 24 h, thus suggesting that a dynamic metalation/demetalation equilibrium (Scheme 2) process is occurring.

With these results in mind, we decided to test complex **2** (**2a** or **2b**) and other related complexes in the deuteration of several organic compounds. In this sense, the new complexes Cp^*IrCl_2-(I^{nBu}), **3**, and Cp^*IrCl_2($^{Cl}I^{nBu}$), **4** (I^{nBu} = 1,3-di-*n*-butylimidazolylidene; $^{Cl}I^{nBu}$ = 1,3-di-*n*-butyl-4,5-dichloroimidazolylidene), were obtained by transmetallating the carbene from a silver−NHC complex in a way similar to that used for compound **1** shown in Scheme 1. The idea was to study both the differences in the activity between the bidentate complex **2** and monodentate complexes **3** and **4** and the effect of the introduction of the chloro substituents in the 4,5-positions of the azole ring, hence

(15) (a) Viciano, M.; Mas-Marza, E.; Poyatos, M.; Sanau, M.; Crabtree, R. H.; Peris, E. *Angew. Chem., Int. Ed.* **2005**, *44*, 444. (b) Miecznikowski, J. R.; Crabtree, R. H. *Organometallics* **2004**, *23*, 629. (c) Albrecht, M.; Miecznikowski, J. R.; Samuel, A.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2002**, *21*, 3596.

(16) Chianese, A. R.; Kovacevic, A.; Zeglis, B. M.; Faller, J. W.; Crabtree, R. H. *Organometallics* **2004**, *23*, 2461.

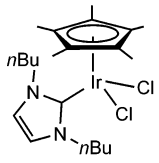
Table 1. H/D Exchange Reactions Using $Cp^*IrCl_2(PMe_3)$, **2**, and **3**[a]

R-H $\xrightarrow[CD_3OD,\ 100°C]{2\ mol\%\ catalyst,\ AgOTf}$ R-D

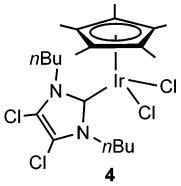
entry	substrate	catalyst	% D_{inc}	time (h)
1	diethyl ether	**2**	CH_3: 45; CH_2: 65	12
2		**3**	CH_3, CH_2 > 99	12
3		**Cp*Ir Cl_2 (PMe_3)**	CH_3: 61; CH_2: 56	12
4	THF	**2**	α-CH_2: 4, β-CH_2: 4	6
5		**3**	α-CH_2: 25, β-CH_2: 20	12
6		**Cp*Ir Cl_2 (PMe_3)**	α-CH_2, β-CH_2: 0	12
7	ethylmethyl ketone	**2**	α-CH_3 > 99; α-CH_2 > 99; β-CH_3: 8	6
8		**3**	α-CH_3 > 99; α-CH_2 > 99; β-CH_3: 71	3
9		**Cp*Ir Cl_2 (PMe_3)**	α-CH_3 > 99; α-CH_2 > 99; β-CH_3: 30	3
10	acetophenone	**2**	*o*: 30; *m*: 13; *p*: 28; CH_3 > 99	3
11		**3**	*o*: 40; *m*: 49; *p*: 40; CH_3 > 99	3
12			*o*: 51; *m*: 85; *p*: 58; CH_3 > 99	12
13		**Cp*Ir Cl_2 (PMe_3)**	*o*, *m*, *p*: 0; CH_3: 82	3
14			*o*, *m*, *p*: 0; CH_3: 87	12
15	1,3,5-trimethoxybenzene	**2**	Ar > 99; CH_3: 0	13
16		**3**	Ar > 99; CH_3: 0	3
17		**Cp*Ir Cl_2 (PMe_3)**	Ar > 99; CH_3: 0	3
18	2-propanol	**2**	CH: 91; CH_3: 82	6
19		**3**	CH_3: 92; CH: 80	3
20		**Cp*Ir Cl_2 (PMe_3)**	CH_3, CH: 0	3
21	styrene	**2**	vinyl > 99; Ph: 0	12
22		**3**	vinyl > 99; *o*: 58; *m*,*p*: 51	3
23			vinyl > 99; *o* > 99; *m*,*p*: 65	12
24		**Cp*Ir Cl_2 (PMe_3)**	vinyl: 28; *o*: 8; *m*,*p*: 0	3
25			vinyl > 99; *o*: 51; *m*,*p*: 0	12
26	*tert*-butylethene (tbe)	**3**	vinyl: 90; *t*-Bu: 59	12
27		**Cp*Ir Cl_2 (PMe_3)**	vinyl: 85; *t*-Bu: 50	12

[a] All reactions carried out using J. Young-style NMR tubes loaded with 0.5 mL of CD_3OD, 0.0095 mmol of catalyst, and 0.475 mmol of substrate. Reaction progress measured by ^1H NMR spectroscopy.

reducing the basicity of the NHC ligand. We also tested the activity of the complex $Cp^*IrCl_2(PMe_3)$ to check whether the introduction of the NHC ligand is in fact implying any enhancement in both the catalytic activity and the stability of the catalyst.



3



4

The experimental details of the preparation and characterization of complexes **3** and **4** are described in the Experimental Section. The most significant features in the ^{13}C NMR spectrum of **3** and **4** are the signals of the carbene carbons at 150.6 and 152.1 ppm (**3** and **4**, respectively), as for other reported Cp*−Ir−(NHC) complexes.[9,13,14]

(b) Catalytic Experiments. Deuteration of several organic substrates was carried out at 100 °C with catalyst loadings of 2% mol, using methanol-d_4 and acetone-d_6 as the deuterium sources. Both sources were effective, but we observed that methanol-d_4 afforded better conversions at lower reaction times (data shown in Table 1). For the activation of the catalysts, addition of AgOTf was necessary to remove the halide ligands and form the corresponding triflate species, which we did not isolate. Table 1 lists all the substrates and their corresponding extents of deuterium incorporation. Compounds **2** and **3** showed high levels of deuteration in a wide range of molecules, including ethers, ketones, alcohols, and terminal olefins (Table 1). In general, **2** and **3** showed a much higher activity than $Cp^*IrCl_2(PMe_3)$ in the activation of aliphatic C−H bonds, although the latter one also showed high activity in the deuteration of terminal olefins. For all the experiments studied, the monodentate complex **3** showed higher activity than the orthometalated species **2**. Probably the chelate coordination of the ligand is reducing the catalytic activity of **2** due to the blocking of one of the active coordination sites. Although we have shown that under the reaction conditions the dynamic metalation/demetalation of the phenyl ring is occurring (Scheme 2), we believe that this process is competing with the intermolecular catalytic process, hence reducing the efficiency of the latter one.

For the ether compounds, we observed that diethyl ether was more easily deuterated than THF, with complete deuterium incorporation in both the methyl and methylene positions after

12 h of reaction when **3** was used (entry 2). For the same substrate, **2** yielded a more rapid deuteration in the internal methylene position, as expected for the weaker secondary C−H bonds compared to the primary C−H bonds in the methyl group (entry 1). This result contrasts with the previously reported results by Bergman and co-workers when using the catalyst $Cp^*IrCl_2(PMe_3)$ with the same substrate,[17] as we have also observed (entry 3). When using **3**, THF shows faster deuteration at the α-position, although with very low level of D-incorporation after 12 h of reaction (entry 5). If the reaction is carried out at 135 °C, the conversion rose to 69% (α-) and 65% (*β*-position). Both **2** and $Cp^*IrCl_2(PMe_3)$ are ineffective toward the deuteration of this substrate.

Ketones such as ethylmethyl ketone and acetophenone showed quantitative deuteration of the α-positions at reaction times of 3 (**3**) and 6 h (**2**), but this may also be due to an exchange via the enol, since we observed that the exchange process also occurs in the absence of catalyst (although at lower rates). The *β*-methyl group in ethylmethyl ketone was deuterated in moderate-high yield (71%) when **3** was used (entry 8). The deuteration of the aromatic ring in acetophenone showed a clear preference at the meta-position, with a maximum deuterium incorporation of 85% (entry 12). $Cp^*IrCl_2(PMe_3)$ only deuterated the *σ*-C−H bonds of ketones, not showing any activity toward the deuteration of the aromatic positions of acetophenone (entries 13 and 14), and only low activation of the *σ*-C−H bonds was achieved (entry 9), which in fact makes us believe that for this complex the H/D exchange may be mainly due to a keto−enolic equilibrium rather than to a Ir-mediated process.

Highly activated arenes as 1,3,5-trimethoxybenzene showed selective and quantitative deuteration at the aromatic positions, the methyl group being untouched (entries 15−17).

For the deuteration of 2-propanol (entries 18−20), both **2** and **3** showed a high activity, while $Cp^*IrCl_2(PMe_3)$ was completely inefficient.

For the terminal olefins, the three catalysts show a high activity in the deuteration of the vinylic positions of styrene (entries 21−25). Interestingly, **2** and $Cp^*IrCl_2(PMe_3)$ selectively deuterated the three olefinic positions, while **3** also deuterated in high yield the phenyl positions (entry 23; *o*: 99% and *m*,*p*: 65%). The deuteration of *tert*-butylethene (tbe) is produced in higher yields in the olefinic positions (90%) than in the methyl groups (59%), when **3** is used. Selective deuteration of the olefinic positions of styrene was previously reported by Milstein and co-workers using a Rh(III) catalyst, but a much lower efficiency was achieved for tbe.[18]

The introduction of chloro substituents in positions 4 and 5 of the azole ring in compound **4** strongly decreased the activity of the catalyst (for example, deuteration of the vinylic protons of styrene is only 5% after 12 h). As we expected, diminishing the electron richness of the metal center results in a poor cleavage of the C−H bonds of the substrate.

The progress of all the reactions described above can be easily followed by ^{1}H NMR spectroscopy. When monitoring the H/D exchange reactions in CD_3OD, we observed that the resonance for the $CH_3O\mathit{H}$ proton grew, rather than that corresponding to the $C\mathit{H}_3OH$ protons observed when the previously reported catalyst $[Cp^*Ir(H)_3(PMe_3)](OTf)$ was used.[3] For the reactions performed in acetone-d_6, the signals due to the protons of the methyl groups grew. A keto−enolic equilibrium may be justifying the behavior of acetone as deuterium source, thus implying O−D rather than C−D activation in the functioning of the D-source in the catalytic cycle.

Most of the H/D exchange catalysts reported to date are extremely air- and moisture-sensitive compounds that have to be prepared in situ and need to be handled under extreme inert atmosphere, although some examples can be found in the literature of air-stable H/D exchange catalysts that use D_2 or $^3H_2$ as deuterium/tritium source.[19] In our case, all manipulations were carried out in the presence of air. Also, we did not find any decomposition of **2** and **3** due to the disproportionation, as seen for complex $Cp^*IrCl_2(PMe_3)$ (generating $[Cp^*IrCl(PMe_3)_2]$-Cl and $[Cp^*IrCl_2]_2$),[17] probably due to the higher strength of the Ir−NHC compared to the Ir−PMe_3 bond. Furthermore, for our Ir−NHC catalysts **2** and **3**, we observed that increasing the temperature to 135 °C generally provided better catalytic results in terms of both conversions and rates, and no decomposition of the catalysts was observed according to the ^{1}HNMR spectra. In this sense, we also thought that the activation of the C(5)−H bond of the imidazolylidene ring may also occur, since this has been observed for other Ir−NHC complexes,[16,20] thus providing its deuteration or even any C−C bond coupling with the olefinic substrates, as has been previously reported,[11] but the ^{1}H NMR signals due to both C5−H and C4−H remained unperturbed all along the reaction experiments. This latter observation suggests that for the catalytic processes that we are describing, the NHC behaves as an spectator ligand.

In some of the experiments described above and summarized in Table 1, we tried to improve the catalytic performances of $Cp^*IrCl_2(PMe_3)$ by raising the temperature to 135 °C, but surprisingly this had the opposite effect. For example, under these new reaction conditions the deuteration of diethyl ether only reached 17 and 21% (related to the CH_2 and CH_3 groups, respectively) after 12 h, lower than the conversions achieved at 100 °C with the same catalyst (entry 3). Blank experiments carried out with $Cp^*IrCl_2(PMe_3)$ in CD_3OD at 135 °C in the absence of substrates showed that this complex completely decomposed after 12 h, providing the disproportionation products mentioned above.

Conclusions

We have obtained new $Cp^*IrCl_2(NHC)$ catalysts that have been tested in the deuteration of a wide range of organic molecules, using CD_3OD as deuterium source, providing high activities under relative mild conditions. Their catalytic activity has been compared to that shown by the phosphine analogue $Cp^*IrCl_2(PMe_3)$, showing that the Ir−NHC complexes displayed better results in terms of conversions, range of applicability, and catalyst stability. We believe that these results may provide

(17) Klei, S. R.; Golden, J. T.; Tilley, T. D.; Bergman, R. G. *J. Am. Chem. Soc.* **2002**, *124*, 2092.
(18) Rybtchinski, B.; Cohen, R.; Ben-David, Y.; Martin, J. M. L.; Milstein, D. *J. Am. Chem. Soc.* **2003**, *125*, 11041.
(19) (a) Johansen, S. K.; Sorensen, L.; Martiny, L. *J. Labelled Compd. Radiopharm.* **2005**, *48*, 569. (b) Shu, A. Y. L.; Heys, J. R. *Tetrahedron Lett.* **2000**, *41*, 9015.
(20) (a) Appelhans, L. N.; Zuccaccia, D.; Kovacevic, A.; Chianese, A. R.; Miecznikowski, J. R.; Macchioni, A.; Clot, E.; Eisenstein, O.; Crabtree, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 16299. (b) Grundemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *Chem. Commun.* **2001**, 2274. (c) Grundemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 10473. (d) Kovacevic, A.; Grundemann, S.; Miecznikowski, J. R.; Clot, E.; Eisenstein, O.; Crabtree, R. H. *Chem. Commun.* **2002**, 2580.

new perspectives in the design of a novel generation of NHC-based C−H activation catalysts.

Experimental Section

General Procedures. $[Cp^*IrCl_2]_2$,[21] $Cp^*IrCl_2(PMe_3)$,[22] 1-benzyl-3-methylimidazolium iodide,[23] and 1,3-di-*n*-butylimidazolium iodide[24] were prepared according to literature procedures. NMR spectra were recorded on a Varian Innova 300 and 500 MHz, using $CDCl_3$ and CD_3OD as solvents. Elemental analyses were carried out in an EA 1108 CHNS-O Carlo Erba analyzer. Electrospray mass spectra (ESI-MS) were recorded on a Micromass Quatro LC instrument, and nitrogen was employed as drying and nebulizing gas. All other reagents were used as received from commercial suppliers.

Synthesis of 1-*n*-Butyl-4,5-dichloroimidazole. To an RB flask was added 4,5-dichloroimidazole (2.74 g, 20 mmol), KOH (1.40 g, 25 mmol), TBABr (193 mg, 0.6 mmol), and droplets of H_2O. The mixture was stirred at room temperature for 1 h, and then *n*-BuI (5.52 g, 30 mmol) was added. After being stirred for 48 h at room temperature, the reaction mixture was extracted with CH_2Cl_2/H_2O and the organic extracts were collected and dried over Na_2SO_4. Evaporation of the solvent under vacuum gave an oil, which was the desired product. Yield: 3.5 g (70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (s, 1H, NC*H*N), 3.96 (t, 2H, N−C*H*$_2$ *n*-Bu), 1.67 (m, 2H, C*H*$_2$ *n*-Bu), 1.26 (m, 2H, C*H*$_2$ *n*-Bu), 0.88 (t, 3H, C*H*$_3$ *n*-Bu).

Synthesis of 1,3-di-*n*-butyl-4,5-dichloroimidazolium Iodide. *n*-BuI (4.3 g, 23.4 mmol) was added to 1-*n*-butyl-4,5-dichloroimidazole (3.5 g, 18 mmol), and the mixture was heated at 120 °C overnight. The resultant oil was extracted with CH_2Cl_2/H_2O to remove excess of *n*-BuI. Yield: 5.43 g (80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.65 (s, 1H, NC*H*N), 4.41 (t, 4H, N−C*H*$_2$ *n*-Bu), 1.98 (m, 4H, C*H*$_2$ *n*-Bu), 1.47 (m, 4H, C*H*$_2$ *n*-Bu), 1.01 (t, 6H, C*H*$_3$ *n*-Bu). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 136.19 (NCHN), 119.42 (*C*-Cl dichloroimidazole), 49.45 (N-*C*H$_2$ *n*-Bu), 31.21 (*C*H$_2$ *n*-Bu), 19.54 (*C*H$_2$ *n*-Bu), 13.46 (*C*H$_3$ *n*-Bu). Anal. Calcd for $C_{11}H_{19}N_2Cl_2I$: C, 35.04; H, 5.08; N, 7.43. Found: C, 35.15; H, 5.07; N, 7.45.

Synthesis of 1. Silver oxide (44 mg, 0.19 mmol) was added to a solution of 1-benzyl-3-methylimidazolium iodide (75 mg, 0.25 mmol) in 10 mL of dichloromethane. The mixture was stirred at room temperature for 1 h, and then $[Cp^*IrCl_2]_2$ (100 mg, 0.13 mmol) was added. The mixture was stirred at room temperature for another 4 h and filtered through Celite. The solvent was removed under vacuum, and the resultant product was immediately characterized. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34 (m, 5H, benzene), 6.93 (s, 1H, C*H*, imidazole), 6.66 (s, 1H, C*H*, imidazole), 6.02 (d, ^2J(H,H) = 14.5 Hz, 1H, −C*H*$_2$−Ph), 5.18 (d, ^2J(H,H) = 14.5 Hz, 1H, −C*H*$_2$−Ph), 3.99 (s, 3H, C*H*$_3$−imidazole), 1.62 (s, 15H, C*H*$_3$, Cp*). ^{13}C NMR ($CDCl_3$, 500 MHz): δ 156.52 ($C_{carbene}$−Ir), 136.75 (Ph), 128.74 (Ph), 128.63 (Ph), 128.36 (Ph), 128.27 (Ph), 128.04 (Ph), 123.47 (*C*H imidazole), 121.66 (*C*H imidazole), 88.72 ($C_5(CH_3)_5$), 54.23 (*C*H$_2$−Ph), 38.65 (N−*C*H$_3$), 9.20 ($C_5(CH_3)_5$).

Synthesis of 2a. A quantity of 50 mg of **1** (0.08 mmol) was dissolved in CH_2Cl_2. The solution was stirred at room temperature for 5 h, and then the solvent was evaporated. The crude solid was purified by column chromatography. Yield: 21 mg (47%). ^{1}H NMR (CD_3OD, 500 MHz): δ 7.50 (d, ^3J(H,H) = 7.98 Hz, 1H, Ph), 7.23 (s, 1H, C*H*, imidazole), 7.18 (s, 1H, C*H*, imidazole), 6.99 (d, ^3J(H,H) = 7.50 Hz, 1H, Ph), 6.88 (t, 1H, Ph), 6.76 (t, 1H, Ph), 4.86 (d, ^2J(H,H) = 14.0 Hz, 1H, −C*H*$_2$−Ph), 4.79 (d, ^2J(H,H) = 14.0 Hz, 1H, −C*H*$_2$−Ph), 3.89 (s, 3H, C*H*$_3$−imidazole), 1.66 (s, 15H, C*H*$_3$, Cp*). ^{13}C NMR ($CDCl_3$, 500 MHz): δ 157.37 ($C_{carbene}$−Ir), 144.37 (C_{Ph}−Ir), 141.75 (Ph), 138.69 (Ph), 127.86 (Ph), 124.39 (Ph), 122.09 (Ph), 121.38 (*C*H imidazole), 120.58 (*C*H imidazole), 90.39 ($C_5(CH_3)_5$), 57.50 (*C*H$_2$−Ph), 37.10 (N−*C*H$_3$), 9.64 ($C_5(CH_3)_5$). Anal. Calcd for $C_{21}H_{26}ClIrN_2$: C, 47.22; H, 4.91; N, 5.24. Found: C, 47.48; H, 4.97; N, 5.57. Electrospray Ms. Cone 35 V. *m*/*z* (fragment): 499 $[Cp^*IrL]^+$.

Synthesis of 2b. A mixture of $[Cp^*IrCl_2]_2$ (300 mg, 0.37 mmol), 1-benzyl-3-methylimidazolium iodide (339 mg, 1.13 mmol), and NaOAc (139 mg, 1.70 mmol) in CH_3CN was refluxed overnight in the presence of an excess of NaI. The mixture was filtered through Celite, the solvent was evaporated, and the crude solid was purified by column chromatography. The pure compound **2b** was eluted with CH_2Cl_2/acetone (9:1) and precipitated in ether to give a yellow solid. Yield: 246 mg (53%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (d, ^3J(H,H) = 7.49 Hz, 1H, Ph), 6.94 (d, ^3J(H,H) = 7.99 Hz, 1H, Ph), 6.92 (s, 2H, C*H*, imidazole), 6.88 (t, 1H, Ph), 6.76 (t, 1H, Ph), 5.01 (d, ^2J(H,H) = 14.0 Hz, 1H, −C*H*$_2$−Ph), 4.67 (d, ^2J(H,H) = 14.0 Hz, 1H, −C*H*$_2$−Ph), 3.86 (s, 3H, C*H*$_3$−imidazole), 1.78 (s, 15H, C*H*$_3$, Cp*). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 154.72 ($C_{carbene}$−Ir), 147.43 (Ph), 141.19 (C_{Ph}−Ir), 138.19 (Ph), 127.49 (Ph), 124.13 (Ph), 121.96 (Ph), 121.18 (*C*H imidazole), 120.59 (*C*H imidazole), 90.94 ($C_5(CH_3)_5$), 57.19 (*C*H$_2$−Ph), 40.14 (N−*C*H$_3$), 10.21 ($C_5(CH_3)_5$). Anal. Calcd for $C_{21}H_{26}IIrN_2$: C, 40.32; H, 4.19; N, 4.48. Found: C, 40.56; H, 4.37; N, 4.59. Electrospray Ms. Cone 35 V. *m*/*z* (fragment): 499 $[Cp^*IrL]^+$.

Synthesis of 3. Silver oxide (58 mg, 0.25 mmol) was added to a solution of 1,3-di-*n*-butylimidazolium iodide (154 mg, 0.50 mmol) in CH_2Cl_2. The solution was stirred at room temperature for 1 h, and then $[Cp^*IrCl_2]_2$ (200 mg, 0.25 mmol) was added. The mixture was stirred at room temperature overnight and then filtered through Celite. The pure compound **3** was eluted with CH_2Cl_2/acetone (9:1) and precipitated in ether to give an orange solid. Yield: 160 mg (55%). ^{1}H NMR (500 MHz, CD_3OD): δ 7.31 (s, 2H, C*H*, imidazole), 4.59 (m, 2H, −C*H*$_2$ *n*-Bu), 3.83 (m, 2H, −C*H*$_2$ *n*-Bu), 1.92 (m, 2H, *n*-Bu), 1.81 (m, 2H, *n*-Bu), 1.57 (s, 15H, C*H*$_3$ Cp*), 1.22 (m, 4H, *n*-Bu) 0.99 (t, 6H, *n*-Bu). ^{13}C NMR (300 MHz, $CDCl_3$): δ 150.61 ($C_{carbene}$−Ir), 121.50 (*C*H imidazole), 89.90 ($C_5(CH_3)_5$), 53.78 (*n*-Bu), 33.59 (*n*-Bu), 20.01 (*n*-Bu), 14.09 (*n*-Bu), 10.54 ($C_5(CH_3)_5$). Anal. Calcd for $C_{21}H_{36}Cl_2IrN_2$: C, 45.29; H, 5.61; N, 5.03. Found: C, 45.20; H, 5.75; N, 4.86. Electrospray Ms. Cone 25V. *m*/*z* (fragment): 543 $[Cp^*IrLCl]^+$.

Synthesis of 4. Silver oxide (58 mg, 0.25 mmol) was added to a solution of 1,3-di-*n*-butyl-4,5-dichloroimidazolium iodide (154 mg, 0.50 mmol) in CH_2Cl_2. The solution was stirred at room temperature for 1 h, and then $[Cp^*IrCl_2]_2$ (200 mg, 0.25 mmol) was added. The mixture was stirred at room temperature overnight and then filtered though Celite. The solvent was evaporated, and the pure compound **4** was eluted with CH_2Cl_2/acetone (9:1) and precipitated in ether to give an orange

Table 2. Crystallographic Data

	1	**2b**
empirical formula	$C_{22}H_{29}Cl_4IrN_2$	$C_{21}H_{26}IIrN_2$
mol wt	655.47	625.54
radiation	Mo Kα (monochr); 0.71073 λ (Å)	
T (K)	273	273
cryst syst	monoclinic	orthorombic
space group	$P2_1/c$ (No. 14)	$P2_12_12_1$ (No. 19)
a (Å)	17.5521(9)	8.9105(5)
b (Å)	12.6090(6)	14.2032(7)
c (Å)	11.3366(5)	16.0373(8)
β (deg)	93.0040(10)	90.00
V (Å^3)	2505.5(2)	2029.64(18)
Z	4	4
D_{calcd} (g cm^{-3})	1.738	2.047
μ (Mo Kα) (cm^{-1})	5.767	8.105
total, unique no. of rflns	5718, 4486	6107, 4136
R_{int}	0.0394	0.0736
no. of params, restrictions	268, 0	232, 0
R, R_w	0.0447, 0.0836	0.0446, 0.0923
GOF	1.065	0.972
min, max resid dens (e Å^{-3})	−1.705, 1.003	−0.885, 1.265

(21) Ball, R. G.; Graham, W. A. G.; Heinekey, D. M.; Hoyano, J. K.; McMaster, A. D.; Mattson, B. M.; Michel, S. T. *Inorg. Chem.* **1990**, *29*, 2023.
(22) Isobe, K.; Bailey, P. M.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1981**, 2003.
(23) Day, G.; Glaser, R.; Shimomura, N.; Takamuku, A.; Ichikawa, K. *Chem.−Eur. J.* **2000**, *6*, 1078.
(24) Sala, A.; Ferrario, F.; Rizzi, E.; Catinella, S.; Traldi, P. *Rapid Commun. Mass Spectrom.* **1992**, *6*, 388.

solid. Yield: 163 mg (50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.84 (m, 2H, $-CH_2$, *n*-Bu), 3.61 (m, 2H, $-CH_2$, *n*-Bu), 2.12 (m, 2H, *n*-Bu), 1.76 (s, 15H, CH_3Cp*), 1.67 (m, 2H, *n*-Bu), 1.45 (m, 2H, *n*-Bu), 1.22 (m, 2H, *n*-Bu), 0.95 (t, 3H, *n*-Bu). ^{13}C NMR (300 MHz, $CDCl_3$): δ 152.08 ($C_{carbene}$−Ir), 117.89 (*C*−Cl imidazole), 91.02 ($C_5(CH_3)_5$), 53.88 (*n*-Bu), 33.39 (*n*-Bu), 19.96 (*n*-Bu), 14.23 (*n*-Bu), 10.90 ($C_5(CH_3)_5$). Anal. Calcd for $C_{21}H_{36}Cl_4IrN_2$: C, 38.77; H, 5.58; N, 4.31. Found: C, 38.43; H, 5.75; N, 4.09. Electrospray Ms. Cone 45 V. *m*/*z* (fragment): 611 $[Cp^*IrLCl]^+$.

X-ray Diffraction Studies. Single crystals of **1** and **2b** were mounted on a glass fiber in a random orientation. Data collection was performed at room temperature on a Siemens Smart CCD diffractometer using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) with a nominal crystal to detector distance of 4.0 cm. Space group assignment was based on systematic absences, E statistics, and successful refinement of the structures. The structure was solved by direct methods with the aid of successive difference Fourier maps and was refined using the SHELXTL 6.1 software package.[25] All non-hydrogens were refined anisotropically. Hydrogen atoms were assigned to ideal positions and refined using a riding model. Details of the data collection, cell dimensions, and structure refinement are given in Table 2. The diffraction frames were integrated using the SAINT package.[26]

Catalytic H/D Exchange. In a Young-style NMR tube, the catalyst (0.0095 mmol) was dissolved in 0.5 mL of CD_3OD. The organic substrate (0.475 mmol) and an excess of AgOTf were added to the solution. The resulting mixture was heated at 100 °C. Deuteration levels were monitored by ^{1}H NMR using an external standard capillary consisting of a solution of ferrocene in $CDCl_3$ (0.16 mg/μL).

Acknowledgment. We gratefully acknowledge financial support from the MEC of Spain (projects CTQ2005-05187) and Bancaixa (P1.1B2004-07). R.C. thanks the Spanish Ministerio de Educación y Ciencia for a fellowship.

Supporting Information Available: Crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA058253L

(25) Sheldrick, G. M. *SHELXTL*, version 6.1; Bruker AXS: Madison, WI, 2000.
(26) *SAINT*, version 5.0; Bruker AXS: Madison, WI, 1998.