CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200801580

[$IrCl_2Cp^*$(NHC)] Complexes as Highly Versatile Efficient Catalysts for the Cross-Coupling of Alcohols and Amines

Amparo Prades, Rosa Corberán, Macarena Poyatos, and Eduardo Peris*[a]

Abstract: A comparative study on the catalytic activity of a series of [$IrCl_2Cp^*$(NHC)] complexes in several C–O and C–N coupling processes implying hydrogen-borrowing mechanisms has been performed. The compound [$IrCl_2Cp^*(I^{nBu})$] (Cp^* = pentamethyl cyclopentadiene; I^{nBu} = 1,3-di-*n*-butylimidazolylidene) showed to be highly effective in the cross-coupling reactions of amines and alcohols, providing high yields in the production of unsymmetrical ethers and N-alkylated amines. A remarkable feature is that the processes were carried out in the absence of base, phosphine, or any other external additive. A comparative study with other known catalysts, such as Shvo's catalyst, is also reported.

Keywords: alcohols · alkylation · amines · etherification · iridium · N-heterocyclic carbenes

Introduction

The search for efficient catalysts for "hydrogen-borrowing"[1] strategies is very challenging, since it can provide easy access to a wide variety of highly valuable organic molecules introducing environmental benefits. Although the principles governing hydrogen-transfer (or hydrogen-borrowing) processes are common to amines and alcohols, versatile catalysts capable of reacting with both types of substrates are not yet available, the only exception being Shvo's catalyst,[2–5] the exceptional features of which make it one of the most versatile catalysts described so far.

We recently described the base-free-catalyzed reduction of C=O and C=NR bonds with the complex [$IrCl_2Cp^*(I^{nBu})$] (**1**; Cp^* = pentamethyl cyclopentadiene; I^{nBu} = 1,3-di-*n*-butylimidazolylidene).[6] The same complex has been used for a wide range of C–H activation processes,[7,8] including the catalytic deuteration of organic molecules.[8] A related Ir complex with a Cp*–NHC functionalized ligand was also very active in the alkylation of amines with primary alcohols.[9] This latter compound was capable of dehydrogenating secondary alcohols to ketones in the presence of a base, although we did not quantify the process.[9] An example of a "ligand-promoted" dehydrogenation of alcohols using a $Ir^{III}Cp^*$ species was recently described by Fujita and Yamaguchi.[10] The dehydrogenation of alcohols is an interesting process, not only because it provides the more reactive carbonylated species, but because it also affords an easy way for the generation of hydrogen.[5,11]

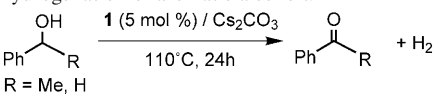
We now report a wide set of reactions that are effectively catalyzed by **1** and widens the scope of this versatile catalyst.

Results and Discussion

In the presence of a weak base, **1** is capable of dehydrogenating aromatic alcohols to the corresponding carbonylated species. The results for this reaction are shown in Table 1. Although the yields were moderate (the reactions were not optimized), this process establishes the basis for a full set of "hydrogen-borrowing" reactions.

Under base-free conditions, and with the addition of an excess of AgOTf, the same catalyst affords the etherification

Table 1. Dehydrogenation of aromatic alcohols.[a]



Entry	Alcohol	*t* [h]	Yield [%]
1	benzyl alcohol	24	50
2	1-phenylethanol	24	70

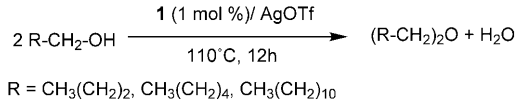
[a] Reaction conditions: alcohol (0.4 mmol), catalyst **1** (0.02 mmol; 5 mol%) and base (0.08 mmol; 20 mol%). Yields determined by ^1H NMR spectroscopy.

[a] A. Prades, Dr. R. Corberán, Dr. M. Poyatos, Prof. E. Peris
Departamento de Química Inorgánica y Orgánica
Universitat Jaume I, 12071-Castellón (Spain)
Fax: (+34) 964-728-214
E-mail: eperis@qio.uji.es

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200801580.

of aliphatic alcohols. The results for this reaction are shown in Table 2.

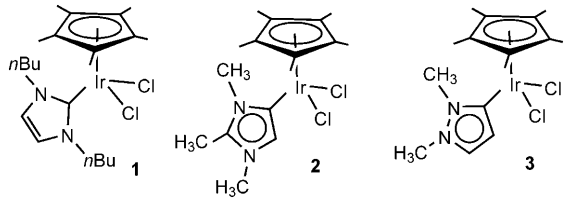
Table 2. Homo-coupling of alcohols.[a]



Entry	Alcohol	*t* [h]	Yield [%]
1	*n*-butanol	12	95
2	*n*-hexanol	12	71
3	*n*-dodecanol	12	87

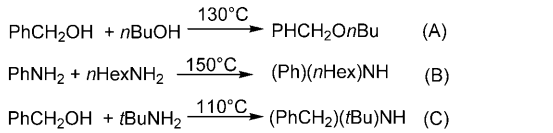
[a] Reaction conditions: alcohol (0.4 mmol), catalyst **1** (0.004 mmol; 1 mol %) and AgOTf (0.012 mmol). Yields determined by ^{1}H NMR spectroscopy.

Based on these two preliminary results and on our previous research on hydrogen-transfer processes, we thought that {IrCp*(NHC)} complexes may be good candidates for reactions implying the cross-coupling of alcohols and amines, in all three possible combinations. For the studies reported herein we used the [$IrCl_2$Cp*(NHC)] catalysts **1**–**3**.



Complexes **1**[8] and **2**[12] have been previously reported, and the preparation of compound **3** is described in the Experimental Section. For comparison, we also tested the catalytic activity of [{$IrCl_2$Cp*}$_2$]. For a rapid screening of the catalytic activities of these four compounds we performed a set of three experiments implying the cross-coupling of: 1) benzyl alcohol with *n*-butanol, 2) aniline with *n*-hexylamine, and 3) benzyl alcohol with *tert*-butylamine (Table 3). Addition of AgOTf was needed in order to activate the catalysts. However, the isolation of the triflate compounds, [IrCp*(NHC)$(OTf)_2$], and their use under the same catalytic conditions did not show any differences in the activities obtained. All four catalysts showed good activities in the three model reactions, although catalyst **1** achieved the best catalytic performances (Table 3, entries 1, 5, and 9). The fact that **1** behaves as a very active catalyst in such a wide set of catalytic reactions is

Table 3. Comparison of the different catalysts towards cross-coupling of alcohols and amines.[a]



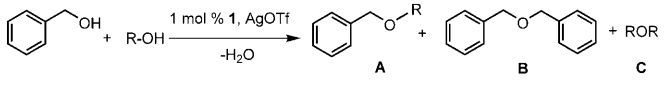
Entry	Reaction	Catalyst	*t* [h]	Yield [%]
1	A	**1**	2	>95
2	A	**2**	3	91
3	A	**3**	2	>95
4	A	[{$IrCl_2$Cp*}$_2$]	3	90
5	B	**1**	24	>95
6	B	**2**	24	75
7	B	**3**	24	70
8	B	[{$IrCl_2$Cp*}$_2$]	24	70
9	C	**1**	7	>95
10	C	**2**	7	75
11	C	**3**	7	83
12	C	[{$IrCl_2$Cp*}$_2$]	7	80

[a] Reaction conditions: entries 1–4: benzyl alcohol (0.4 mmol), *n*-butanol (2 mmol), catalyst (0.004 mmol; 1 mol %) and AgOTf (0.012 mmol); entries 5–8: aniline (0.2 mmol), *n*-hexylamine (0.4 mmol), catalyst (0.01 mmol; 5 mol %) and AgOTf (0.03 mmol) in [D_8]toluene; entries 9–12: amine (0.2 mmol), alcohol (0.24 mmol), catalyst (0.01 mmol; 5 mol %) and AgOTf (0.03 mmol). Yields determined by ^{1}H NMR spectroscopy.

of great interest, specially if we take into account all the synthetic applications that can be obtained by combination of these three model reactions. It should be mentioned that the catalytic activity displayed by [{$IrCl_2$Cp*}$_2$] in the presence of AgOTf in these reactions, although not as good as that shown by **1**, is remarkable, and encourages the use of this simple combination of reagents in other catalytic reactions for which [{$IrCl_2$Cp*}$_2$] has proved to be active.

To study the scope of catalyst **1**, we decided to perform a series of reactions using a wider set of substrates for each individual cross-coupling reaction. Table 4 shows the catalytic results for the cross-coupling of benzyl alcohol with primary and secondary alcohols to provide unsymmetrical ethers. As can be seen from the results shown, the reaction is quantita-

Table 4. Etherification of benzyl alcohol with primary and secondary alcohols with catalyst **1**.[a]



Entry	Alcohol	*T* [°C]	*t* [h]	Conv. [%]	**A** [%][b]	**B** [%][b]	**C** [%][c]
1	methanol	110	12	94	88	6	0
2	ethanol	110	12	>95	>95	0	6
3	*n*-butanol	130	2	>95	>95(90)[d]	0	8
4	*n*-hexanol	130	6	>95	94	5	10
5	*n*-dodecanol	130	3	>95	95(93)[d]	2	14
6	benzyl alcohol	130	12	>95[e]	10	–	–
7	allyl alcohol	110	12	93	85	8	15
8	isopropyl alcohol	110	12	>95	80	16	10
9	cyclohexanol	110	10	81	70	11	–

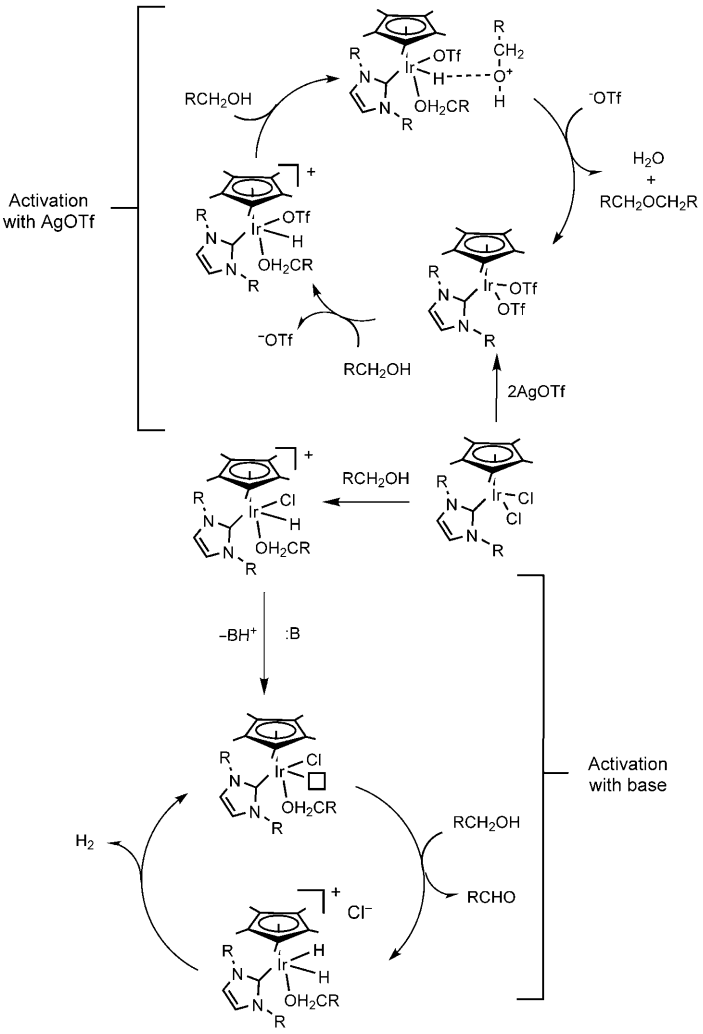
[a] Reaction conditions: benzyl alcohol (0.4 mmol), primary or secondary alcohol (2 mmol), catalyst (0.004 mmol; 1 mol %) and AgOTf (0.012 mmol). Conversion and yields determined by ^{1}H NMR spectroscopy. [b] Yield based on the amount of benzyl alcohol. [c] Yield based on the amount of primary or secondary alcohol. [d] Isolated yields [e] Benzaldehyde was formed in 80 % yield.

tive or almost quantitative for all the experiments performed, showing a high selectivity to the unsymmetrical ethers. Only for the homocoupling of benzyl alcohol did we obtain a very low yield in the formation of benzyl ether (entry 6), but this is because the dehydrogenation to form benzaldehyde is a highly favorable process for this alcohol. The results compare well and in some cases are even an improvement in comparison with recently reported results in which the same or similar substrates were used.[13–15] In particular, we observed that **1** provided higher yields in the formation of the unsymmetrical ethers than the highly active catalyst $[ReBr(CO)_5]$,[15] a result that is even more interesting if we consider that **1** needed lower temperatures and shorter reaction times. It is also important to point out the high performances obtained when allyl alcohol is used (85% yield, entry 7). Allyl ethers are important starting materials for a wide variety of organic reactions, and our result is clearly improving recent reports for the same process.[14]

Brønsted acids are known to catalyze the formation of ethers through the protonation of the hydroxy group that is converted into a better leaving group. For example, many studies in the homogeneous phases have been carried out with sulfuric acid,[16] although this procedure is known to give low yields when secondary and tertiary alcohols are used. In this case, the leaving groups are ROH_2^+ or $ROSO_2H^+$.[17] To rule out catalysis simply by AgOTf or even HOTf, we carried out the reaction of benzyl alcohol and *n*-butanol in the presence of each of these reactants without adding compound **1**. These experiments showed that addition of AgOTf did not provide any conversion to the desired ether, while addition of HOTf provided negligible conversions (22% after 4 h) to the desired unsymmetrical ether. This result confirms that the cross-coupling of alcohols to provide the unsymmetrical ethers (data in Table 4) is an Ir^{III}-catalyzed process. Also, the activation of **1** with $AgPF_6$ (instead of AgOTf) afforded much lower activities, probably because the generation of a dicationic species provides a compound with lower electron density than the neutral bistriflate adduct generated by addition of AgOTf, as we previously discussed in a recent paper.[6]

Although we do not have a clear explanation for the different behavior of **1** in the presence of alcohols depending on the addition of AgOTf or a base, we believe that Scheme 1 shows the two plausible mechanisms that may justify this difference.

Both processes rely on the oxidative addition of the alcohol (RCH_2OH) to one {IrCp*(NHC)} metal fragment, as we have previously proposed to justify our findings on the base-free reduction of ketones with *i*PrOH.[6] The key step of both processes is the formation of the corresponding $H-Ir^V$ species. In the presence of the base, this hydride is expected to be "deprotonated" to generate a neutral complex with a vacant coordination site, that is, the first active species in the oxidation of alcohols to ketones. On the other hand, for the AgOTf activation process, the cationic $H-Ir^V$ species acts as a Brønsted acid, and activates a second molecule of alcohol by electrophilic attack to the oxygen atom, with the



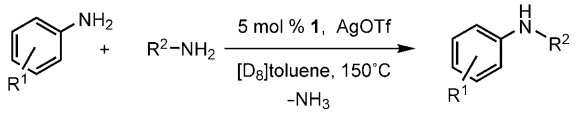
Scheme 1. Proposed mechanism for the activation of **1** with base and AgOTf.

subsequent coupling of the alkyl group to the coordinated alkoxide fragment and loss of H_2O. This latter mechanism is very interesting, since it combines a typical organometallic catalytic cycle, with an acid-catalyzed process in which the cationic $H-Ir^V$ intermediate acts as the protic acid. We are aware that this mechanism is merely speculative and needs a detailed study for its complete elucidation. Mechanistic studies based on DFT analysis of the process are currently underway.

The arylation of aliphatic amines with anilines has recently been described as a convenient method for the preparation of N-alkylated anilines.[2,3] For this process, Beller and co-workers elegantly showed that, from a series of Ru-based catalysts, Shvo's catalyst proved to be the most active.[2,3] We have recently observed that compound **1** resembles Shvo's catalyst in terms of reactivity and catalytic activity. For example, like Shvo's catalyst, **1** is able to catalyze the hydrogen-transfer reactions from alcohols to ketones at room temperature in the absence of an external base.[6] These similarities made us think that **1** would probably be

active in some other processes for which Shvo's catalyst has shown good catalytic performances. After proving that **1** is a good catalyst for the alkylation of aniline with *n*-hexylamine (Table 3, entry 5) we decided to study the generality of this reaction by using a wider set of substituted anilines and different alkyl amines. This process is known to proceed through a hydrogen-borrowing mechanism in which the alkyl amine is the hydrogen-transfer agent, although this strategy has only been proved once in the recent and pioneering work by Beller and co-workers.[3] The results that we obtained are summarized in Table 5. The catalytic activity of **1** was very high in the N-alkylation of a wide set of substituted anilines with several alkyl amines. For comparative reasons, we also performed a series of experiments using Shvo's catalyst under our reaction conditions (Table 1 in the Supporting Information). Both **1** and Shvo's catalyst showed similar catalytic performances, which in turn validates that the arylation of aliphatic amines with anilines under hydrogen-transfer conditions may be considered as a general and valuable method for the preparation of the corresponding aryl amines.

Table 5. N-alkylation of anilines with aliphatic amines with catalyst **1**.[a]

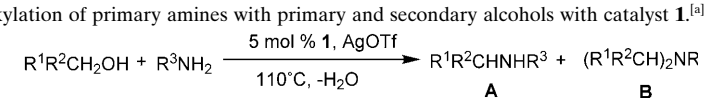


Entry	Aryl amine	Alkyl amine	Conv. [%]	Yield [%]
1	aniline	*n*-hexylamine	>95	>95 (85)[b]
2	aniline	benzylamine	>95	94
3	aniline	cyclohexylamine	>95	>95
4	aniline	*n*-dodecylamine	>95	>95
5	*o*-toluidine	*n*-hexylamine	>95	80
6	*o*-toluidine	benzylamine	90	80
7	*o*-toluidine	cyclohexylamine	>95	>95
8	*o*-toluidine	*n*-dodecylamine	>95	70
9	*p*-toluidine	*n*-hexylamine	90	70
10	*p*-fluoroaniline	*n*-hexylamine	>95	>95
11	*p*-chloroaniline	*n*-hexylamine	>95	>95 (80)[b]
12	*p*-methoxyaniline	*n*-hexylamine	50	50
13	2,4,6-methylaniline	*n*-hexylamine	90	90

[a] Reaction conditions: alkyl amine (0.2 mmol), aryl amine (0.4 mmol), catalyst (0.01 mmol; 5 mol%) and AgOTf (0.03 mmol) in [D_8]toluene, 24 h, 150°C. Conversions and yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene (0.02 mmol) as internal standard. [b] Isolated yields.

Finally, we studied the N-alkylation of primary amines with primary and secondary alcohols. This reaction is known to be catalyzed by Ir[18,19] and Ru[4,20] compounds. A recent computational study on the reaction mechanism for this process has been reported, showing that a three-step mechanism operates, implying: 1) metal-catalyzed oxidation of the alcohol, 2) nucleophilic addition of the amine to the aldehyde, and 3) metal-catalyzed reduction of the imine to the final secondary amine.[21] As observed from the data that we obtained (Table 6), all combinations of amines and alcohols provided high conversions to the corresponding N-alkylated amines. The selectivity of the process highly depended on the combination of amine and alcohol used. Full conversions to the corresponding secondary amines were observed for the reactions of aniline and benzyl alcohol (entry 1, Table 6) and benzylamine and 1-phenylethanol (entry 7, Table 6). Interestingly, the reaction afforded a high selectivity toward the tertiary amine in the reaction of benzylamine and benzyl alcohol (entry 2, Table 6), a result that clearly contrasts with the results previously described by Fujita and co-workers, who obtained full conversion to the secondary amine for the same process.[19] For comparative purposes we also tested Shvo's catalyst under our reaction conditions and observed that it provided lower catalytic activities (Table 2 in the Supporting Information). For example, the reaction of 1-phenylethanol with *n*-hexylamine yielded 30% of the secondary amine using Shvo's catalyst (39% yield using previously described conditions[4]), while we obtained 70% of the secondary amine (entry 6, Table 6) and 30% of the tertiary amine.

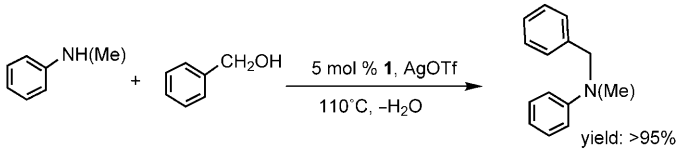
Table 6. N-alkylation of primary amines with primary and secondary alcohols with catalyst **1**.[a]



Entry	Alcohol	Amine	*t* [h]	Conv. [%]	**A** [%]	**B** [%]
1	benzyl alcohol	aniline	7	>95	>95	0
2		benzylamine	7	>95	0	>95(81)[b]
3	*n*-butanol	benzylamine	7	>95	50	50
4	*n*-butanol	benzylamine	24[c]	>95	35	65
5	1-phenylethanol	*n*-hexylamine	24	>95	51	19
6		*n*-hexylamine	24[c]	>95	70	30
7	1-phenylethanol	benzylamine	24	>95	>95	0
8		benzylamine	24[c]	>95	>95	0
9	1-phenylethanol	cyclohexylamine	24	>95	52	13
10		cyclohexylamine	24[c]	>95	45	10

[a] Reaction conditions: amine (0.2 mmol), alcohol (1.0 mmol), catalyst (0.01 mmol; 5 mol%) and AgOTf (0.03 mmol), 110°C. Conversions and yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene (0.02 mmol) as internal standard. [b] Isolated yield. [c] Amine/alcohol = 1:10.

Interestingly, **1** was also very active in the alkylation of the secondary amine N-methylaniline with benzyl alcohol affording full conversion to the corresponding tertiary amine (benzylmethylaniline), as shown in Scheme 2. We also tried the alkylation of other secondary amines (namely, dibutyl-



Scheme 2.

amine, diethylamine and diallylamine), but unfortunately the reactions gave mixtures that we were unable to identify.

Conclusion

In summary, after performing a comparative study in which the catalytic activities of a series of $[IrCl_2Cp^*(NHC)]$ complexes and $[\{IrCl_2Cp^*\}_2]$ were evaluated, we observed that $[IrCl_2Cp^*(I^nBu)]$ (**1**) provided the best catalytic performances. A more detailed study showed that **1** provided excellent results in all three possible cross-coupling combinations between amines and alcohols. All the reactions constitute valuable processes for the preparation of biologically active species and industrial chemicals. The catalyst proved to be highly active in all the reactions tested, in most cases improving the catalytic performances of the most active catalysts recently described for the same processes. This feature confirms the extraordinary versatility and potential synthetic applications of this unique compound. Only Shvo's catalyst shows a similar activity for the case of the N-alkylation of anilines with aliphatic amines. The catalytic reactions that we studied were carried out in the absence of base, phosphine, or any other additive (for the use of the triflate adducts there is no need to add any extra amount of AgOTf), which in fact is not only simplifies the reaction workup processes (the products are more easily separated from the reaction mixtures), but also provides a more environmentally benign processes.

Experimental Section

Synthesis and characterization of the compounds

General procedures: $[\{IrCl_2Cp^*\}_2]$[22] and compounds **1**[8] and **2**[12] were prepared according to literature procedures. All other reagents were used as received from commercial suppliers and used without further purification. NMR spectra were recorded on a Varian Innova 300 MHz and 500 MHz, using $CDCl_3$ as solvent. Electrospray mass spectra (ESI-MS) were recorded on a Micromass Quatro LC instrument; nitrogen was employed as drying and nebulizing gas. Elemental analyses were carried out on a EuroEA3000 Eurovector Analyser.

Synthesis of ***3***: A suspension of 1,2-dimethylpyrazolium iodide (74 mg, 0.33 mmol) and silver oxide (176 mg, 0.50 mmol) in acetonitrile (20 mL) was stirred at room temperature for 2 h. The mixture was filtered through Celite and $[\{IrCl_2Cp^*\}_2]$ (120 mg, 0.15 mmol) was added. The mixture was refluxed for 3 h, the suspension was filtered through Celite and the solvent was evaporated under reduce pressure. The crude solid was purified by column chromatography. Elution with a mixture of CH_2Cl_2/acetone (1:1) afforded a yellow band that contained compound **3**. The pure compound was precipitated from a mixture of CH_2Cl_2/Et_2O as a yellow solid. Yield: 60 mg (40%). ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.36$ (d, $^3J_{H\text{-}H} = 2.70$ Hz, 1H; $CH_{pyrazole}$), 6.49 (d, $^3J_{H\text{-}H} = 2.70$ Hz, 1H; $CH_{pyrazole}$), 4.11 (s, 3H; NCH_3), 3.92 (s, 3H; NCH_3), 1.60 ppm (s, 15H; CH_{3Cp^*}); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): $\delta = 133.7$, 117.4 ($CH_{pyrazole}$), 87.9 ($C_5(CH_3)_5$), 37.1, 36.9 (NCH_3), 8.9 ppm ($C_5(CH_3)_5$); electrospray MS (30 V): m/z: 459.2 $[M-Cl]^+$; elemental analysis calcd (%) for $C_{15}N_2IrCl_2H_{23}$ (494.48): C 36.43, H 4.69, N 5.67; found: C 36.43, H 4.89, N 5.66.

Catalytic experiments

Dehydrogenation of aromatic alcohols: A mixture of benzyl alcohol or 1-phenylethanol (0.4 mmol), catalyst (5 mol%) and Cs_2CO_3 (20 mol%) was refluxed in toluene (1 mL) for 24 h. The reaction mixture was analyzed by ^1H NMR spectroscopy and the products were identified by comparison with the commercially available products benzaldehyde and acetophenone.

Homo-coupling of alcohols: A mixture of alcohol (0.4 mmol), catalyst (1 mol%), silver triflate (3 mol%) and $[D_8]$toluene (200 μL) was heated at 110°C in a thick-walled glass tube fitted with a Teflon cap. The reaction mixture was analyzed by ^1H NMR spectroscopy. Products were identified according to commercially available samples: dihexyl ether, dibutyl ether, and dodecyl ether.

Etherification of benzyl alcohol with primary and secondary alcohols: A mixture of benzyl alcohol (0.4 mmol), alkylating alcohol (2.0 mmol), catalyst (1 mol%), and silver triflate (3 mol%) was heated at 110°C or 130°C in a thick-walled glass tube fitted with a Teflon cap. The reaction mixture was analyzed by ^1H NMR spectroscopy. Products were identified according to commercially available samples (benzyl methyl ether, benzyl ethyl ether, benzyl butyl ether, benzyl hexyl ether, benzyl dodecyl ether, dibenzyl ether, allyl benzyl ether, and benzyl isopropyl ether) or previously reported spectroscopic data (benzyl cyclohexyl ether).[23] For the isolation of the products, the crude was extracted with dichloromethane and filtrated through a pad of Celite. The solvent was removed under vacuum, and the crude oil purified by column chromatography on silica gel using hexanes as eluent.

N-alkylation of aromatic amines with aliphatic amines: A mixture of aromatic amine (0.4 mmol), the corresponding aliphatic amine (0.2 mmol), catalyst (5 or 2 mol%), silver triflate (15 or 6 mol%), and $[D_8]$toluene (200 μL) was heated at 150°C in a thick-walled glass tube fitted with a Teflon cap. The reaction mixture was analyzed by ^1H NMR spectroscopy. 1,3,5-trimethoxybenzene (10 mol%) was used in all cases as an internal standard in order to determine conversions and yields. Products were identified according to previously reported spectroscopic data: *N*-hexylaniline,[24] *N*-hexyl-4-methylaniline,[3] *N*-hexyl-2-methylaniline,[3] *N*-hexyl-2,4,6-trimethylaniline,[3] 4-fluoro-*N*-hexylaniline,[3] 4-chloro-*N*-hexylaniline,[3] *N*-hexyl-4-methoxyaniline,[3] *N*-benzylaniline,[19] *N*-cyclohexylaniline,[19] *N*-dodecylaniline,[25] *N*-cyclohexyl-2-methylaniline,[25] *N*-dodecyl-2-methylaniline,[25] and *N*-benzyl-2-methylaniline.[26] For the isolation of the products, the crude was filtered through a pad of Celite and the solvent removed under vacuum. The crude alkyl aryl amine product was purified by column chromatography on silica gel using hexanes as eluent.

N-alkylation of primary amines with alcohols: A mixture of alcohol (0.24, 1.00 or 2.00 mmol), primary amine (0.20 mmol), catalyst (5 mol%), and silver triflate (15 mol%) was heated at 110°C in a thick-walled glass tube fitted with a Teflon cap. The reaction mixture was analyzed by ^1H NMR spectroscopy. 1,3,5-trimethoxybenzene (10 mol%) was used in all cases as an internal standard in order to determine conversions and yields. Products were identified according to commercially available samples (*N*-benzyl-*tert*-butylamine and dibenzylamine) or previously reported spectroscopic data (*N*-benzylidenebenzylamine,[27] *N*-benzyl-*n*-butylamine,[28] *N*,*N*′-di-*n*-butylbenzylamine,[28] *N*-hexyl-1-phenethylamine,[29] *N*-benzyl-1-phenethylamine,[27] and *N*-cyclohexyl-1-phenetylamine).[30] For the isolation of the products, the crude was extracted with dichloromethane and filtrated through a pad of Celite. The solvent was removed under vacuum, and the crude solid purified by flash chromatography on silica gel using hexanes as eluent.

Acknowledgements

We gratefully acknowledge financial support from the MEC of Spain (CTQ2007-31175) and Bancaixa (P1.1B2007-04). We would also like to thank the Spanish MEC for a fellowship (R.C.), and to the Juan de la Cierva program (M.P.).

[1] J. F. Bower, E. Skucas, R. L. Patman, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 15134–15135; S. Burling, B. M. Paine, D. Nama, V. S. Brown, M. F. Mahon, T. J. Prior, P. S. Pregosin, M. K. Whittlesey,

J. M. J. Williams, *J. Am. Chem. Soc.* **2007**, *129*, 1987–1995; P. J. Black, M. G. Edwards, J. M. J. Williams, *Eur. J. Org. Chem.* **2006**, 4367–4378; P. J. Black, G. Cami-Kobeci, M. G. Edwards, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Org. Biomol. Chem.* **2006**, *4*, 116–125; M. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555–1575; K. Fujita, R. Yamaguchi, *Synlett* **2005**, 560–571.

[2] D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Chem. Commun.* **2008**, 3199–3201.

[3] D. Hollmann, S. Bahn, A. Tillack, M. Beller, *Angew. Chem.* **2007**, *119*, 8440–8444; *Angew. Chem. Int. Ed.* **2007**, *46*, 8291–8294.

[4] D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J.* **2007**, *2*, 403–410.

[5] Y. Blum, D. Czarkie, Y. Rahamim, Y. Shvo, *Organometallics* **1985**, *4*, 1459–1461; Y. Shvo, D. Czarkie, *J. Organomet. Chem.* **1986**, *315*, C25-C28; Y. Shvo, D. Czarkie, Y. Rahamim, D. F. Chodosh, *J. Am. Chem. Soc.* **1986**, *108*, 7400–7402.

[6] R. Corberan, E. Peris, *Organometallics* **2008**, *27*, 1954–1958.

[7] R. Corberan, M. Sanau, E. Peris, *Organometallics* **2006**, *25*, 4002–4008.

[8] R. Corberan, M. Sanau, E. Peris, *J. Am. Chem. Soc.* **2006**, *128*, 3974–3979.

[9] A. P. da Costa, M. Viciano, M. Sanau, S. Merino, J. Tejeda, E. Peris, B. Royo, *Organometallics* **2008**, *27*, 1305–1309.

[10] K. Fujita, N. Tanino, R. Yamaguchi, *Org. Lett.* **2007**, *9*, 109–111.

[11] H. Junge, B. Loges, M. Beller, *Chem. Commun.* **2007**, 522–524; J. H. Choi, N. Kim, Y. J. Shin, J. H. Park, J. Park, *Tetrahedron Lett.* **2004**, *45*, 4607–4610.

[12] M. Viciano, M. Feliz, R. Corberan, J. A. Mata, E. Clot, E. Peris, *Organometallics* **2007**, *26*, 5304–5314.

[13] A. Corma, M. Renz, *Angew. Chem.* **2007**, *119*, 302–304; *Angew. Chem. Int. Ed.* **2007**, *46*, 298–300; A. B. Cuenca, G. Mancha, G. Asensio, M. Medio-Simon, *Chem. Eur. J.* **2008**, *14*, 1518–1523.

[14] J. S. Yadav, D. C. Bhunia, K. V. Krishna, P. Srihari, *Tetrahedron Lett.* **2007**, *48*, 8306–8310; H. Saburi, S. Tanaka, M. Kitamura, *Angew. Chem.* **2005**, *117*, 1758–1760; *Angew. Chem. Int. Ed.* **2005**, *44*, 1730–1732.

[15] Y. Liu, R. M. Hua, H. B. Sun, X. Q. Qiu, *Organometallics* **2005**, *24*, 2819–2821.

[16] H. Feuer, J. Hooz, *The Chemistry of Ether Linkage*, Interscience, London, **1967**.

[17] J. March, *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, 4th ed., Wiley, New York, **1992**.

[18] K. Fujita, Z. Z. Li, N. Ozeki, R. Yamaguchi, *Tetrahedron Lett.* **2003**, *44*, 2687–2690; K. I. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett.* **2004**, *6*, 3525–3528; K. Fujita, K. Yamamoto, R. Yamaguchi, *Org. Lett.* **2002**, *4*, 2691–2694; B. Blank, M. Madalska, R. Kempe, *Adv. Synth. Catal.* **2008**, *350*, 749–758.

[19] K. I. Fujita, Y. Enoki, R. Yamaguchi, *Tetrahedron* **2008**, *64*, 1943–1954.

[20] A. Tillack, D. Hollmann, D. Michalik, M. Beller, *Tetrahedron Lett.* **2006**, *47*, 8881–8885; M. Hamid, J. M. J. Williams, *Chem. Commun.* **2007**, 725–727.

[21] D. Balcells, A. Nova, E. Clot, D. Gnanamgari, R. H. Crabtree, O. Eisenstein, *Organometallics* **2008**, *27*, 2529–2535.

[22] R. G. Ball, W. A. G. Graham, D. M. Heinekey, J. K. Hoyano, A. D. McMaster, B. M. Mattson, S. T. Michel, *Inorg. Chem.* **1990**, *29*, 2023–2025.

[23] M. B. Sassaman, K. D. Kotian, G. K. S. Prakash, G. A. Olah, *J. Org. Chem.* **1987**, *52*, 4314–4319.

[24] E. Byun, B. Hong, K. A. De Castro, M. Lim, H. Rhee, *J. Org. Chem.* **2007**, *72*, 9815–9817.

[25] J. Li, M. Cui, A. Yu, Y. Wu, *J. Organomet. Chem.* **2007**, *692*, 3732–3742.

[26] R. Y. Lai, C. I. Lee, S. T. Liu, *Tetrahedron* **2008**, *64*, 1213–1217.

[27] L. Blackburn, R. J. K. Taylor, *Org. Lett.* **2001**, *3*, 1637–1639.

[28] R. N. Salvatore, A. S. Nagle, K. W. Jung, *J. Org. Chem.* **2002**, *67*, 674–683.

[29] A. Johansson, P. Abrahamsson, O. Davidsson, *Tetrahedron: Asymmetry* **2003**, *14*, 1261–1266.

[30] B. C. Ranu, A. Majee, A. Sarkar, *J. Org. Chem.* **1998**, *63*, 370–373.

Received: August 1, 2008
Published online: November 19, 2008

