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Water-soluble iridium N-heterocyclic carbene complexes for alkylation of amines with alcohols

Ana Fernandes,^[a] and Beatriz Royo*^[a]

Abstract: A new series of water-soluble Cp*Ir(NHC)Cl₂ complexes with N-heterocyclic carbene (NHC) ligands bearing ester- and amide-groups have been obtained and fully characterised. The new complexes are highly reactive and selective catalysts for the alkylation of amines with alcohols, using 1:1 ratio of reactants, in water and in the absence of base or other additives. The catalytic system has broad substrate scope, allowing the synthesis of a variety of primary and secondary amines in excellent yields. Tolerance to a large range of functional groups was obtained.

Introduction

The development of water soluble catalysts has gained increasing attention in the last years.^[1] The use of water as a solvent in synthetic organic chemistry plays a key role in green chemistry, since water is relatively inexpensive, non-toxic, and non-flammable. The most general approach for designing water soluble catalysts is the functionalization of ligands with organic groups capable to form H-bonds with water, commonly P- and N-based ligands.^[2,3] N-heterocyclic carbene (NHC) ligands offer attractive features for the development of water-soluble metal catalysts, because they can be easily functionalised, and confer great stability to their metal complexes.^[4] However, this area of research is still in its early stage, and few transition metals containing water soluble NHCs have been described in the literature.^[3,5] In particular, reports on aqueous catalysis with iridium N-heterocyclic carbenes are scarcely found in the literature, despite the prominent role of iridium NHCs in homogeneous catalysis.^[6] Catalytic applications using Ir-NHC complexes in water includes hydroamination,^[7] hydrogenation,^[8] C-H activation^[8a,9] and water oxidation reactions.^[10]

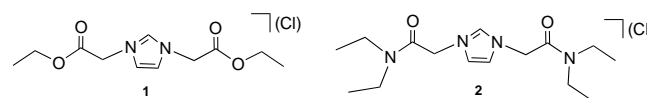
Recently, we became interested in developing water-soluble Ir-NHC complexes for their application in catalytic dehydrogenative processes. Direct N-alkylation of amines with alcohols provides a green and atom economy method for the synthesis of substituted amines, which are important building blocks in different industries, like the pharmaceutical industry.^[11] Since the

first reports, independently disclosed by Watanabe and Grigg,^[12a,12b] significant progress has been made in this field,^[11,12] and a variety of successful catalytic systems were developed using Ir(III)-NHC complexes.^[13] Interesting results were reported by Peris using IrCl₂Cp*(NHC) complexes, which displayed excellent catalytic performances in the cross-coupling reactions of amines with alcohols in the absence of base.^[13a] However, little work has been done towards the development of catalytic systems operating in water.^[14] To the best of our knowledge, this work represents the first examples of iridium NHC-based catalysts for alkylation of amines with alcohols operating in water. Herein, we report the preparation of iridium(III) complexes having ester-, and amide-functionalised NHC ligands and their catalytic activity in the alkylation of amines with alcohols in water.

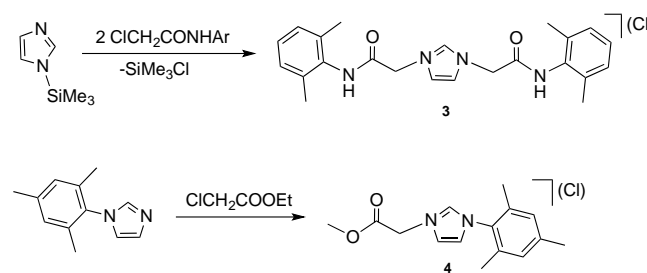
Results and Discussion

Synthesis and characterisation

The synthesis of the NHC ligand precursors **1** and **2** (Scheme 1) was performed as previously described in the literature.^[15] The novel NHC proligand **3** was prepared following similar approach by reacting N-(2,6-dimethylphenyl)chloroacetamide with 1-(trimethylsilyl)imidazole (Scheme 2). The new unsymmetrical NHC proligand **4** was synthesised by refluxing 1-(mesityl)imidazole with ethyl chloroacetate (Scheme 2). Compounds **3** and **4** were isolated as pale yellow solids in good yield (85 % and 80%, respectively). They were soluble in water, chlorinated solvents, methanol, acetonitrile, and dimethylsulfoxide, and insoluble in diethyl ether and hexane.



Scheme 1. NHC proligands **1** and **2**.

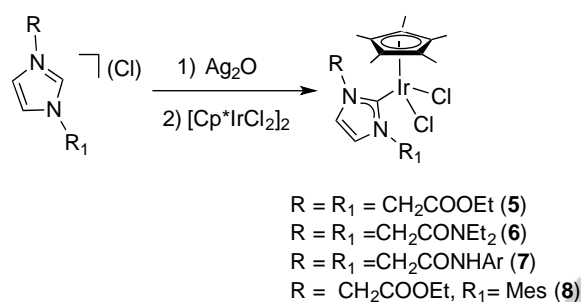


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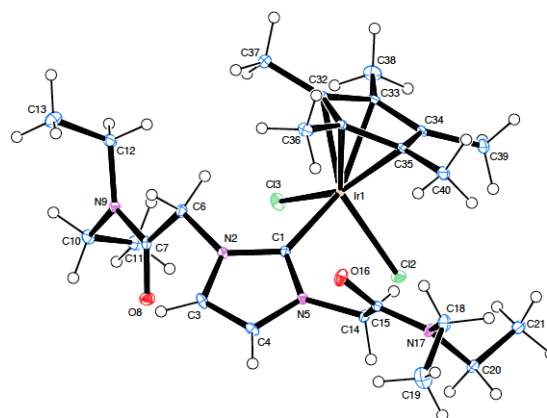
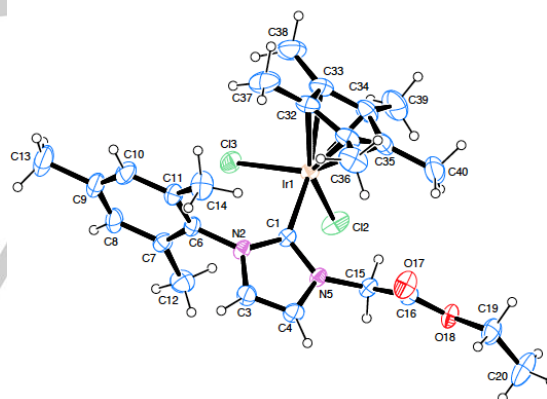
Supporting information for this article is given via a link at the end of the document.

Scheme 2. Synthesis of NHC proligands **3** and **4**.

Iridium-NHC complexes **5-8** were successfully synthesised via a transmetallation procedure, involving a stepwise reaction of the appropriate proligand **1-4** with Ag_2O followed by addition of $[\text{Cp}^*\text{IrCl}_2]_2$ ($\text{Cp}^* = \eta^5\text{-C}_5\text{Me}_5$) (Scheme 3). The identity of all complexes was established by spectroscopic methods, mass spectrometry (HRMS-ESI), and elemental analysis. The ^{13}C NMR spectra confirmed that coordination of the NHC have occurred, showing the characteristic signal of Ir-C_{NHC} at 166 ppm (for complexes **5-7**) and at 169 ppm (for complex **8**). All iridium NHC complexes were soluble in water (pH = 7) at 20 °C. Yellow solutions were obtained after stirring for 10 min, giving solubility values of 17, 56, 10 and 7 mg mL^{-1} for complexes **5**, **6**, **7**, and **8**, respectively. Complex **6**, bearing an acetamide group on the NHC wingtip, displayed the highest solubility in water. Remarkable, all complexes resulted to be stable in water for at least 24 h.

**Figure 1.** Synthesis of iridium(III) NHC complexes **5-8**.

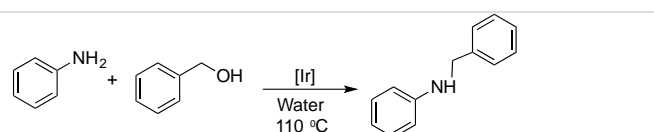
X-ray diffraction analyses of single crystals of **6** and **8** confirmed the expected three-legged piano-stool geometry of the complexes. Figures 1 and 2 show the ORTEP diagrams of **6** and **8**, respectively, and the more relevant bond lengths and angles. The molecular structure of complex **6** (Figure 1) has a symmetrically substituted NHC ligand coordinated to iridium, and two chlorides and a Cp^* ligand completes the coordination sphere of the metal. The Ir-C_{NHC} distance of 2.04 Å, lies in the expected range.^[16] The Ir-Cl (2.41 Å and 2.42 Å) and Ir-Cp^* (centroid) (2.18 Å) distances are within the found ranges for other known $\text{Cp}^*\text{Ir}(\text{NHC})$ complexes.^[16] The molecular structure of **8** (Figure 2) showed the unsymmetrically substituted NHC ligand coordinated to iridium (Ir-C_{NHC} distance of 2.06 Å), and two chlorides (Ir-Cl , 2.41 Å and 2.38 Å) and a Cp^* (2.16 Å) completing the coordination sphere about the metal. All distances and angles lie on the expected range, and compare well with other half-sandwich iridium(III) complexes reported in the literature.^[16]

**Figure 1.** ORTEP-3 diagram of **6**, using 30% probability level ellipsoids. Selected distances (Å): $\text{Ir}(1)\text{-C}(1)$ 2.0440(2), $\text{Ir}(1)\text{-Cl}(2)$ 2.4121(4), $\text{Ir}(1)\text{-Cl}(3)$ 2.4223(4), $\text{Ir}(1)\text{-Cpcentroid}^*$ 2.1831(6). Selected angles (°): $\text{C}(1)\text{-Ir}(1)\text{-Cl}(2)$ 90.11(5), $\text{C}(1)\text{-Ir}(1)\text{-Cl}(3)$ 91.16(5), $\text{Cl}(1)\text{-Ir}(1)\text{-Cl}(2)$ 86.010(2), $\text{Cpcentroid}^*\text{-Ir}(1)\text{-C}(1)$ 115.66(8), $\text{Cpcentroid}^*\text{-Ir}(1)\text{-Cl}(2)$ 141.37(5), $\text{Cpcentroid}^*\text{-Ir}(1)\text{-Cl}(3)$ 132.07.**Figure 2.** ORTEP-3 diagram of **8**, using 30% probability level ellipsoids. Selected distances (Å): $\text{Ir}(1)\text{-C}(1)$ 2.062(3), $\text{Ir}(1)\text{-Cl}(2)$ 2.4140(1), $\text{Ir}(1)\text{-Cl}(3)$ 2.3868(4), $\text{Ir}(1)\text{-Cpcentroid}^*$ 2.161(4). Selected angles (°): $\text{C}(1)\text{-Ir}(1)\text{-Cl}(2)$ 94.35(9), $\text{C}(1)\text{-Ir}(1)\text{-Cl}(3)$ 89.56(9), $\text{Cl}(1)\text{-Ir}(1)\text{-Cl}(2)$ 84.86(4), $\text{Cpcentroid}^*\text{-Ir}(1)\text{-C}(1)$ 113.47(1).**Catalytic studies**

The catalytic activity of the iridium(III) NHC complexes **5-8** in N-alkylation of amines with alcohols was studied using aniline and benzyl alcohol as a model reaction. The reaction was performed in water, in a closed vessel, using 2 mol % of catalyst in a 1:1 ratio of aniline:benzyl alcohol. Results are summarised in Table 1. Complexes **6** and **7** resulted to be the most active catalysts, affording quantitative yield of N-benzyl aniline in 16 h at 110 °C (Table 1, entries 2 and 3). Under similar conditions, complexes **5**

and **8** achieved lower yields of N-benzyl aniline (51 % and 38%, respectively, Table 2, entries 1 and 4). The presence of the amide group on the wingtip of the NHC seems to have a beneficial effect in the catalytic performance of the catalyst. When the catalyst loading was lowered to 1 and 0.5 mol %, a decrease of the catalytic activity was observed (Table 1, entry 6). An attempt to reduce the temperature to 70 °C resulted in a decrease of the activity (42 % yield, Table 1, entry 7). Notable, complexes **6** and **7** displayed good activity in the absence of base or other additives, using stoichiometric amount of alcohol. No reaction occurred in the absence of catalyst (Table 1, entry 8), and low yield was obtained using $[\text{Cp}^*\text{IrCl}_2]_2$ as catalyst (Table 1, entry 9).

Table 1. N-Alkylation of aniline with benzyl alcohol catalysed by Ir-NHC complexes **5-8**.^[a]



Entry ^[a]	Catalyst	Loading (%)	T (h)	Yield (%) ^[b]
1	5	2	16	51
2	6	2	16	99
3	7	2	16	99
4	8	2	16	38
5	6	1	24	57
6	6	0.5	24	38
7	6	2	24	42 ^[c]
8	None	-----	24	0
9	$[\text{Cp}^*\text{IrCl}_2]_2$	2	16	20

[a] Reaction conditions: benzyl alcohol (1 mmol), aniline (1 mmol), catalyst, water (0.25 mL), 110 °C. [b] Yield determined by ¹H NMR using 1,4-di-tert-butylbenzene as an internal standard. [c] Reaction carried out at 70 °C.

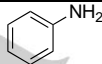
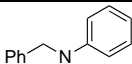
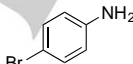
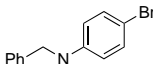
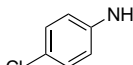
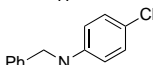
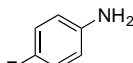
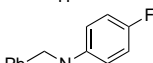
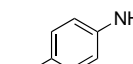
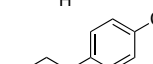
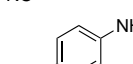
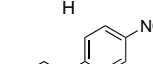
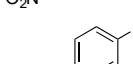
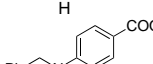
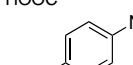
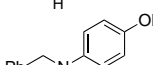
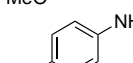
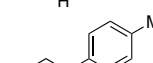
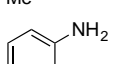
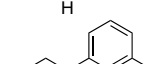
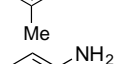
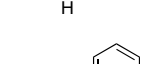
Catalyst **6** was recycled and reused for three catalytic cycles without losing its activity. Recovery of the catalyst was achieved by a simple phase separation (water/ CH_2Cl_2). ¹H and ¹³C NMR spectra of the recovered catalyst confirmed the identity of the iridium species **6**.

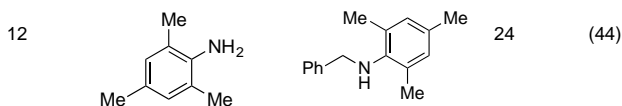
Then, we decided to explore the scope of the reaction, and we choose complex **6** for this study due to its high reactivity, better accessibility and lower cost. The scope of the reaction was explored using 2 mol % of catalyst **6** at 110 °C in water. Results are summarised in Table 2. A variety of substituted anilines were selectively alkylated with benzyl alcohol (in a ratio 1:1) to yield the corresponding N-benzyl anilines in good yields (>88 %).

Electron-donating and electron-withdrawing groups were well tolerated; high yields of N-benzyl anilines were obtained in all cases (Table 2, entries 1-10). Anilines containing *ortho* and *meta* substituents were also quantitatively alkylated with benzyl alcohol (Table 2, entries 9 and 10). An exception was the bulky 2,4,6-trimethylaniline, which was alkylated in a lesser extent, giving a 44% yield of the corresponding N-benzyl aniline after 24 hours of reaction (Table 2, entry 12).

Complex **6** displayed comparable catalytic activity to the iridium(III) complex $[\text{Cp}^*\text{Ir}(\text{Pro})\text{Cl}]$ (Pro = prolinato), recently described by Limbach and co-workers^[14d] as the first iridium complex catalysing this reaction without additives at 95 °C in water. Both **6** and $[\text{Cp}^*\text{Ir}(\text{Pro})\text{Cl}]$ complexes, are identified among $\text{Cp}^*\text{Ir}(\text{III})$ state-of-the-art catalysts, as highly reactive catalysts for the alkylation of amines with alcohols in water under base-free conditions. Other base-free catalytic systems are known, but in all cases temperature higher than 100 °C and activation by inorganic salts is needed.^[14b, 4c, 17]

Table 2. Alkylation of anilines with benzyl alcohol using **6**.^[a]


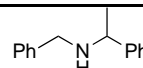

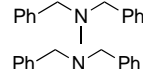

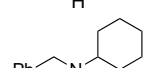

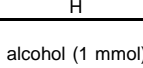
Entry	Amine	Product	Time (h)	Yield (%) ^[b]
1			16	95 (99)
2			24	93 (98)
3			16	86 (93)
4			16	83 (92)
5			24	92 (99)
6			16	87 (92)
7			24	84 (90)
8			24	84 (88)
9			24	90 (94)
10			24	93 (99)
11			16	91 (96)



[a] Reaction conditions: benzyl alcohol (1 mmol), amine (1 mmol), catalyst **6** (2 mol%), water (0.25 mL), 110 °C. [b] Isolated yields. In parenthesis, yield determined by ¹H NMR using 1,4-di-tert-butylbenzene as an internal standard.

The catalytic system has also been tested with aliphatic amines such as α-methylbenzylamine, N-benzylmethylamine, benzyl amine, and cyclohexylamine (Table 3). Good to moderate yields of the corresponding secondary and tertiary amines were obtained, except in the alkylation of cyclohexylamine with benzyl alcohol that afforded 35% yield of N-benzylcyclohexylamine.

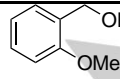
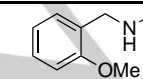
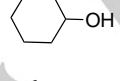
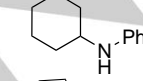
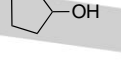
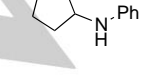
Table 3. Alkylation of primary and secondary aliphatic amines with benzyl alcohol using **6**.^[a]

Entry	Amine	Product	Time (h)	Yield (%) ^[b]
1			16	60 (64)
2			16	87 (93)
3			24	69 (77)
4			24	(35)

[a] Reaction conditions: benzyl alcohol (1 mmol), primary or secondary amine (1 mmol), 2 mol % catalyst **6**, water (0.25 mL). [b] Isolated yields. In parenthesis, yield determined by ¹H NMR using 1,4-di-tert-butylbenzene as an internal standard.

In addition, secondary amines were obtained in high yields by alkylation of aniline with 2-methoxybenzyl alcohol, cyclohexanol, and cyclopentanol (Table 4, entries 1-3).

Table 4. Alkylation of aniline with primary and secondary alcohols using **6**.^[a]

Entry	Alcohol	Product	T (h) ^[1]	Yield (%) ^[b]
1			16	75 (80)
2			24	90 (99)
3			16	88 (95)

[a] Reaction conditions: alcohol (1 mmol), aniline (1 mmol), catalyst **6** (2 mol%), water (0.25 mL), 110 °C. [b] Isolated yields. In parenthesis, yield determined by ¹H NMR using 1,4-di-tert-butylbenzene as an internal standard.

Conclusions

We have developed a versatile catalytic system for alkylation of amines with alcohols in water using a new series of water-soluble Cp*Ir(NHC)Cl₂ complexes bearing ester- and amide-functionalised NHCs. For the first time, iridium NHC complexes have been applied as catalyst for alkylation of amines with alcohols in water. All the iridium complexes resulted to be stable in water solutions for at least 24 h. The best catalyst displayed a broad substrate scope for various alcohols and amines, allowing for the synthesis of a diverse range of secondary aromatic and aliphatic amines, in excellent yields and selectivity. Notable, the catalytic system is operating under base-free conditions and without adding any additive.

Experimental Section

General information

All experiments were carried out under nitrogen using standard Schlenk techniques and high vacuum, unless otherwise stated. Compounds [Cp*IrCl₂]₂,^[18] **1**,^[15] **2**,^[15] and 1-(mesityl)imidazole,^[19] were synthesised according to literature procedures. All other reagents were purchased from commercial suppliers and used without further purification. ¹H and ¹³C NMR spectra were recorded on a Bruker Avance III 400 MHz. Assignment of resonances was made from HMQC and HMBC experiments. CCDC-1531731 and CCDC-1531733 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of compound 3. A mixture of N-(2,6-Dimethylphenyl)chloroacetamide (1.5 g, 8.6 mmol) and 1-(trimethylsilyl)imidazole (0.5 g, 3.2 mmol) was heated to 60 °C and stirred for 24 h to obtain a yellow solid. The solid was cooled to room temperature, washed with diethyl ether (3 x 20 mL), filtered off, and dried under vacuo to yield **3** as a pale yellow solid in 70% yield. Data for **3**: ¹H NMR (298K, 400 MHz, DMSO-d₆): δ = 9.98 (s, 1H, NH), 9.28 (s, 1H, NCHN), 7.80 (s, 2H, NCHCHN), 7.08 (m, 6H, Ph), 5.37 (s, 4H, NCH₂CO), 2.17 (s, 12H, PhCH₃). ¹³C NMR (298K, 400 MHz, DMSO-d₆): δ 163.63 (CO), 138.72 (NCHN), 136.25 (Ph, C_{ipso}), 134.18 (Ph, CH), 127.92 (Ph, CH), 126.99 (Ph, C_{ipso}), 123.58 (NCHCHN), 50.78 (NCH₂CO), 18.25 (CH₃Ph). HRMS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₂₃H₂₇N₄O₂]⁺, 391.2134, found: 391.2133.

Synthesis of compound 4. A mixture of ethyl chloroacetate (0.66 g, 54 mmol) and 1-(mesityl)imidazole (1 g, 54 mmol) was heated to 60 °C and stirred for 24 h to afford a yellow solid. The solid was washed with diethyl ether (3 x 20 mL), filtered off, and dried under vacuo to yield **4** in 77% yield. Data for **4**: ¹H NMR (298K, 400 MHz, CDCl₃): δ = 10.31 (s, H,

NCHN), 7.94 (s, H, NCH), 7.14 (s, H, NCH), 6.99 (s, 2H, CHPh), 5.90 (s, 2H, NCH₂CO), 4.28-4.23 (m, 2H, CH₂CH₃), 2.33 (s, 3H, CH₃Ph), 2.08 (s, 6H, PhCH₃), 1.30 (t, 3H, ³J_{HH} = 7.1 Hz, CH₂CH₃). ¹³C NMR (298K, 400 MHz, CDCl₃): δ = 166.80 (CO), 141.47 (NCHN), 139.82 (Ph, C_{ipso}), 134.49 (Ph, C_{ipso}), 129.92 (Ph), 124.63 (NCHCHN), 122.46 (NCHCHN), 62.95 (CH₂CH₃), 50.76 (NCH₂CO), 21.21 (Ph, CH₃), 17.61 (Ph, CH₃), 14.14 (CH₂CH₃). HRMS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₁₆H₂₁N₂O₂]⁺, 273.1603, found: 273.1603.

General procedure for the synthesis of iridium complexes 5-8

Silver oxide was added to a solution of the appropriated proligand 1-4 in dichloromethane (10 mL). The suspension was stirred at room temperature for 1 h under the exclusion of light. Then, [Cp*IrCl₂]₂ was added, and the reaction mixture was stirred at room temperature for 4 h. The suspension was filtered through Celite, and the solvent was evaporated. The crude solid was purified by column chromatography on silica gel with a mixture dichloromethane/acetone (10/1).

Preparation and characterisation of Cp*Ir(NHC)Cl₂, 5. Following the general procedure, proligand 1 (0.5 g, 1.8 mmol), Ag₂O (0.32 g, 1.37 mmol), and [Cp*IrCl₂]₂ (0.72 g, 0.9 mmol) afforded 5 as a yellow solid. Yield: 918 mg, 80%. Data for 5: ¹H NMR (298 K, 400MHz, CDCl₃): δ = 6.95 (s, 2H, NCHCHN), 5.96 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 18.49 Hz), 4.70 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 18.49 Hz), 4.23-4.15 (m, 4H, CH₂CH₃), 1.53 (s, 15H, CH₃Cp*), 1.26-1.22 (t, 6H, CH₂CH₃). ¹³C NMR (298 K, 400MHz, CDCl₃): δ 169.40 (CO), 159.80 (Clr), 123.50 (NCHCHN), 89.75 (C_{Cp*}), 61.87 (CH₂CH₃), 52.48 (NCH₂CO), 14.32 (CH₂CH₃), 8.88 (CH₃Cp*). Anal. Calcd. for C₂₁H₃₁N₂O₄Cl₂Ir (638.604): C, 39.50; H, 4.89; N, 4.39. Found: C, 39.27; H, 4.97; N, 4.26. HRMS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₂₁H₃₁N₂O₄IrCl]⁺, 603.1594, found: 603.1591.

Preparation and characterisation of Cp*Ir(NHC)Cl₂, 6. Following the general procedure, proligand 2 (0.5 g, 1.7 mmol), Ag₂O (0.30 g, 1.30 mmol), and [Cp*IrCl₂]₂ (0.72 g, 0.9 mmol) afforded 6 as a yellow solid. Yield: 962 mg, 82 %. Crystallisation from dichloromethane-pentane led to yellow crystals suitable for X-ray diffraction studies. Data for 6: ¹H NMR (298 K, 400MHz, CDCl₃): δ = 6.95 (s, 2H, NCHCHN), 6.23 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 17.50 Hz), 4.65 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 17.50 Hz), 3.60-3.57 (m, 2H, CH₂CH₃), 3.46-3.41 (m, 2H, CH₂CH₃), 3.32-3.19 (m, 4H, CH₂CH₃), 1.54 (s, 15H, CH₃Cp*), 1.24 (t, 6H, CH₂CH₃), 1.11 (t, 6H, CH₂CH₃). ¹³C NMR (298 K, 400MHz, CDCl₃): δ 166.75 (CO), 157.03 (NHClr), 123.58 (NCHCHN), 89.67 (C_{Cp*}), 52.39 (NCH₂CO), 41.29 (CH₂CH₃), 40.32 (CH₂CH₃), 14.15 (CH₂CH₃), 12.84 (CH₂CH₃), 8.62 (CH₃Cp*). Anal. Calcd. for C₂₅H₄₁N₄O₂Cl₂Ir (692.74): C, 43.34; H, 5.97; N, 8.09. Found: C, 43.45; H, 5.91; N, 7.81. HRMS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₂₅H₄₁N₄O₂Clr]⁺, 657.2540, found: 657.2540.

Preparation and characterisation of Cp*Ir(NHC)Cl₂, 7. Following the general procedure, proligand 3 (0.5 g, 1.2 mmol), Ag₂O (0.21 g, 0.9 mmol), and [Cp*IrCl₂]₂ (0.48 g, 0.6 mmol) afforded 7 as a yellow solid. Yield: 741 mg, 78%. Data for 7: ¹H NMR (298 K, 400MHz, CDCl₃): δ = 9.0 (s, 2H, NH), 7.46 (s, 2H, NCHCHN), 7.06-6.98 (m, 6H, CHPh), 6.09 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 12.96 Hz), 4.478 (dd, 2H, NCH₂CO, AB pattern, J_{HH} = 12.96 Hz), 2.13 (s, 12H, CH₃Ph), 1.66 (s, 15H, CH₃Cp*). ¹³C NMR (298 K, 400MHz, CDCl₃): δ 164.23 (CO), 157.81 (Clr), 133.95 (CPh), 132.316 (CPh), 127.10 (CHPh), 126.26 (CHPh), 121.97 (NCHCHN), 88.90 (Ar_{Cp*}), 53.68 (NCH₂CO), 28.67 (CPh), 17.57 (CH₃Ph), 8.10 (CH₃Cp*). Anal. Calcd. for C₃₃H₄₁N₄O₂Cl₂Ir (788.826): C, 50.25; H, 5.24; N, 7.01. Found: C, 49.87; H, 5.19; N, 6.92. MS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₃₃H₄₁N₄O₂Clr]⁺, 753.2541, found: 753.2549.

Preparation and characterisation of Cp*Ir(NHC)Cl₂, 8. Following the general procedure, proligand 4 (0.5 g, 1.6 mmol), Ag₂O (0.28 g, 1.2 mmol), and [Cp*IrCl₂]₂ (0.662 g, 0.83 mmol) afforded 8 as a yellow solid. Yield: 804 mg, 75%. Crystallisation from dichloromethane-pentane led to yellow crystals suitable for X-ray diffraction studies. Data for 8: ¹H NMR (298 K, 400MHz, CDCl₃): δ = 7.15 (s, 1H, NCHCHN), 6.84 (s, 2H, CHPh), 6.70 (s, 1H, NCHCHN), 4.27-4.22 (m, 2H, CH₂CH₃), 2.30 (s, 3H, CH₃Ph), 2.08 (s, 6H, CH₃Ph), 1.49 (s, 15H, CH₃Cp*), 1.30-1.27 (t, 3H, CH₂CH₃). ¹³C NMR (298 K, 400MHz, CDCl₃): δ = 168.71 (CO), 155.19 (NHClr), 137.56 (CPh), 132.16 (CPh), 127.10 (CHPh), 126.26 (NCHCHN), 121.90 (NCHCHN), 88.27 (Ar_{Cp*}), 60.79 (CH₂CH₃), 32.61 (NCH₂CO), 20.29 (CH₃Ph), 18.20 (CH₃Ph), 13.20 (CH₂CH₃), 7.98 (CH₃Cp*). Anal. Calcd. for C₂₆H₃₅N₂O₂Cl₂Ir (670.69): C, 46.56; H, 5.26; N, 4.18. Found: C, 46.26; H, 4.96; N, 3.87. MS (ESI-TOF) in acetonitrile: m/z [M]⁺ calcd for [C₂₆H₃₅N₂O₂Clr]⁺, 635.2009, found: 635.2020.

General procedure of N-alkylation of amines with alcohols

A mixture of amine (1 mmol), alcohol (1 mmol), and catalyst, was heated in water (0.25 mL) to 110 °C in a closed vessel for the time indicated in Tables 1-4. The organic products were extracted in dichloromethane. The solvent was evaporated to dryness and the corresponding amine was purified by column chromatography with silica gel (ethyl acetate/hexane). The yields were calculated based on isolated products. The identity of the products was established by comparison of their NMR spectral data with the reported data found in the literature.^[13d,14c,20] In addition, the yield was determined by ¹H NMR using 1,4-di-tert-butylbenzene as an internal standard.

Recycling of catalyst 6.

A mixture of amine (1 mmol), alcohol (1 mmol), catalyst 6 (2 mol%), and water (0.25 mL) was heated to 110 °C for 16 h. The mixture was allowed to cool down, and water (0.50 mL) and CH₂Cl₂ (0.20 mL) were added to the mixture. The organic phase was separated, and the water phase was concentrated to ca. 0.25 mL. New charges of aniline and benzyl alcohol were added to the water solution and the mixture was heated to 110 °C for further 16 h. Similar work up of the reaction was again applied to recover the catalyst for further catalytic cycles.

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Keywords: water-soluble • N-heterocyclic carbenes • iridium • alkylation of amines

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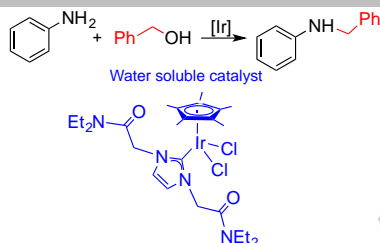
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Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

Water-soluble iridium NHC complexes containing ester- and amide-groups on the NHC wingtips, displayed excellent activity in the alkylation of amines with alcohols. Reactions are carried out in water under base-free conditions, and without the need of any additive.

*Ana Fernandes, Beatriz Royo****Page No. – Page No.****Water-soluble iridium N-heterocyclic carbene complexes for alkylation of amines with alcohols**