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# Selective Alkylation of Amines with Alcohols by Cp*–Iridium(III) Half-Sandwich Complexes

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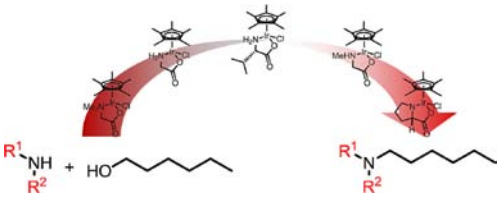
## ABSTRACT




**[Cp*Ir(Pro)Cl] (Pro = prolinato) was identified among a series of Cp*–iridium half-sandwich complexes as a highly reactive and selective catalyst for the alkylation of amines with alcohols. It is active under mild conditions in either toluene or water without the need for base or other additives, tolerates a wide range of alcohols and amines, and gives secondary amines in good to excellent isolated yields.**

Since Grigg et al.[1] reported $[RhH(PPh_3)_4]$ to be one of the first well-defined homogeneous catalysts for metal-catalyzed *N*-alkylations of amines with alcohols in 1981, this hydrogen-transfer process was established as a versatile, highly selective, and environmentally benign route to amines:[2] it starts from readily available reactants and gives water as a single side product.[3] Indeed, numerous catalysts based on iridium,[4] ruthenium,[5] and other transition metals[6] have been developed and already are applied industrially, e.g., in the kilogram-scale synthesis of a glycine transporter type 1 inhibitor.[7]

Soluble complexes based on iridium catalyze the formation of secondary or tertiary amines with high selectivity, e.g., Fujita's and Yamaguchi's $[Cp^*IrCl_2]_2$,[8] Crabtree's[9] and Peris'[10] Ir(III)–NHC complexes, or even $[Ir(COD)Cl]_2$

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(1) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. *J. Chem. Soc., Chem. Commun.* **1981**, 611–612.

(2) For a recent review, cf. (a) Hesp, K. D.; Stradiotto, M. *ChemCatChem* **2010**, *2*, 1192–1207. (b) Oro, L. A.; Claver, C. *Iridium Complexes in Organic Synthesis*: Wiley-VCH: Weinheim, 2009. Own contributions: (c) Cao, P.; Cabrera, J.; Padilla, R.; Serra, D.; Rominger, F.; Limbach, M. *Organometallics* **2012**, *31*, 921–929. (d) Lavy, S.; Miller, J. J.; Pažický, M.; Rodrigues, A.-S.; Rominger, F.; Jäkel, C.; Serra, D.; Vinokurov, N.; Limbach, M. *Adv. Synth. Catal.* **2010**, *352*, 2993–3000.

(3) Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681–703.

(4) (a) Andrushko, N.; Andrushko, V.; Roose, P.; Moonen, K.; Börner, A. *ChemCatChem* **2010**, *2*, 640–643. (b) Pontes da Costa, A.; Sanaú, M.; Peris, E.; Royo, B. *Dalton Trans.* **2009**, 6960–6966. (c) Pontes da Costa, A.; Viciano, M.; Sanaú, M.; Merino, S.; Tejeda, J.; Peris, E.; Royo, B. *Organometallics* **2008**, *27*, 1305–1309. (d) Cami-Kobeci, G.; Williams, J. M. J. *Chem. Commun.* **2004**, 1072–1073. (e) Tanaka, N.; Hatanaka, M.; Watanabe, Y. *Chem. Lett.* **1992**, *21*, 575–578. (f) Suzuki, T. *Chem. Rev.* **2011**, *111*, 1825–1845.

(5) (a) Hamid, M. H. S. A.; Allen, C. L.; Lamb, G. W.; Maxwell, A. C.; Maytum, H. C.; Watson, A. J. A.; Williams, J. M. J. *J. Am. Chem. Soc.* **2009**, *131*, 1766–1774. (b) Bähn, S.; Tillack, A.; Imm, S.; Mevius, K.; Michalik, D.; Hollmann, D.; Neubert, L.; Beller, M. *ChemSusChem* **2009**, *2*, 551–557.

(6) (a) Zhao, Y.; Foo, S. W.; Saito, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 3006–3009. (b) He, L.; Lou, X.-B.; Ni, J.; Liu, Y.-M.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Chem.—Eur. J.* **2010**, *16*, 13965–13969. (c) Bähn, S.; Imm, S.; Neubert, L.; Zhang, M.; Neumann, H.; Beller, M. *ChemCatChem* **2011**, *3*, 1853–1864.

(7) (a) Berliner, M. A.; Dubant, S. P. A.; Makowski, T.; Ng, K.; Sitter, B.; Wager, C.; Zhang, Y. *Org. Process Res. Dev.* **2011**, *15*, 1052–1062. (b) Watson, A. J. A.; Maxwell, A. C.; Williams, J. M. J. *J. Org. Chem.* **2011**, *76*, 2328–2331.

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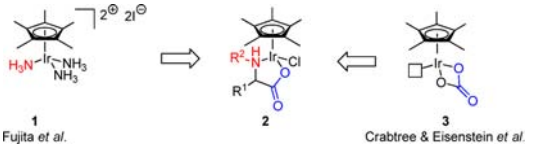
in combination with a phosphine ligand.[11] However, although single base-free systems are known,[12,13] harsh reaction conditions (temperature > 100 °C) and activation by inorganic bases is crucial for high catalytic activity.

Fujita's dicationic complex $[Cp^*Ir(NH_3)_3][I]_2$ (**1**) (Scheme 1) is highly active in the alkylation of aqueous $NH_3$ and amines in water.[12c] On the other hand, DFT calculations of Eisenstein and Crabtree suggest that **3** forms from $[Cp^*IrCl_2]_2$ and $K_2CO_3$.

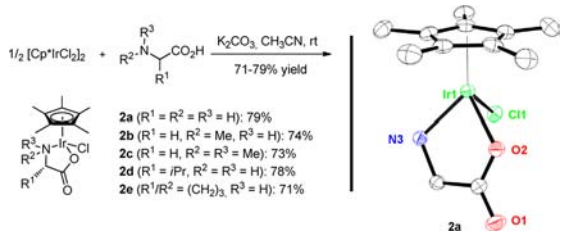
**Scheme 1.** Aminoacidato Ligands in the Cp*−Iridium-Catalyzed Alkylation of Amines with Alcohols




The $\kappa^2$-carbonato ligand is supposed to stabilize the newly generated 16-electron iridium−alkoxy intermediate as an electron donor.[14] Thus, we envisaged a compromise of both approaches, i.e., aminoacidates, to be suitable ligands leading to high catalytic activity paired with high selectivity. Cp*Ir(III) half-sandwich complexes of type **2** bearing either α-,[15,16] β-aminoacidato,[17] or even peptide-derived ligands[18] have been known for decades, but they have only scarcely been used in catalysis.[19] Their application for catalytic *N*-alkylation of amines with alcohols has no precedent.

Cp*−iridium complexes **2a**−**e** (Cp* = $\eta^5$-$C_5Me_5$, cf. Scheme 2) were synthesized in $CH_3CN$ from $[Cp^*IrCl_2]_2$, the corresponding amino acid, and $K_2CO_3$ in good yields (70−80%).[16] Remarkably, they are stable under air at ambient temperature for months. While those complexes with achiral $\kappa^2$-*N*,*O*-glycinato ligands (**2a**[16b] and **2c**) form enantiomers, the metal as well as the *N*-atom of the sarcosinato ligand in [Cp*Ir(Sar)Cl] (**2b**)[15c] are chiral.

**Scheme 2.** Preparation and Structure of **2a**−**e**[a]




[a] Solid-state (X-ray) molecular structure of **2a**; ellipsoids drawn at the 50% probability level. Two independent molecules are present in the unit cell. Hydrogen atoms omitted for clarity.[20]

Thus, **2b** forms diastereomers (ratio 4:1),[15a] such as [Cp*Ir(Val)Cl] (**2d**)[16b] and [Cp*Ir(Pro)Cl] (**2e**),[15i] which bear stereogenic centers at the metal and in the backbone of the chiral amino acids (*S*)-valine and (*S*)-proline (1:1 and 6:1, respectively). Crystals of **2a** suitable for X-ray analysis were grown from $CH_2Cl_2$ layered with *n*-pentane (Scheme 2). The geometry at the metal is that of a three-legged piano stool. The two angles Cl−Ir−O and Cl−Ir−N are slightly smaller than the ideal value of 90°, and the N−Ir−O angle is even below that (ca. 78°), similar to the analogous complex of valine.[16a]

In toluene at 140 °C the reaction of 1-octylamine and 1-hexanol catalyzed by [Cp*Ir(Gly)Cl] (**2a**) (2 mol %) gave besides the desired hexyloctylamine (**4**) an almost equivalent amount of dioctylamine (**5**) resulting from amine homocoupling (Table 1, a),[21] accompanied by small amounts of the tertiary amines **6** and **7** (ratio 45:44:4:7). At 95 °C the selectivity for the desired amine **4** increased to >90%, and only minor amounts of byproducts **5**−**7** formed (Table 1, b−d).[22]

At 75 °C, conversion dropped significantly (Table 1, e), and not even an excess of 1-hexanol prevented the formation of small amounts of byproducts at 95 °C (Table 1, f). Remarkably, **2a** is quite soluble in water, and here its

(8) (a) Fujita, K.-i.; Enoki, Y.; Yamaguchi, R. *Tetrahedron* **2008**, *64*, 1943–1954. (b) Fujita, K.-i.; Yamaguchi, R. *Synlett* **2005**, *2005*, 560–571. (c) Fujita, K.-i.; Fujii, T.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 3525–3528. (d) Fujita, K.-i.; Li, Z.; Ozeki, N.; Yamaguchi, R. *Tetrahedron Lett.* **2003**, *44*, 2687–2690. (e) Fujita, K.-i.; Yamamoto, K.; Yamaguchi, R. *Org. Lett.* **2002**, *4*, 2691–2694.

(9) Gnanamgari, D.; Sauer, E. L. O.; Schley, N. D.; Butler, C.; Incarvito, C. D.; Crabtree, R. H. *Organometallics* **2008**, *28*, 321–325.

(10) Prades, A.; Corberán, R.; Poyatos, M.; Peris, E. *Chem.—Eur. J.* **2008**, *14*, 11474–11479.

(11) (a) Blank, B.; Michlik, S.; Kempe, R. *Chem.—Eur. J.* **2009**, *15*, 3790–3799. (b) Sakaguchi, S.; Yamaga, T.; Ishii, Y. *J. Org. Chem.* **2001**, *66*, 4710–4712.

(12) (a) Saidi, O.; Blacker, A. J.; Lamb, G. W.; Marsden, S. P.; Taylor, J. E.; Williams, J. M. J. *Org. Process Res. Dev.* **2010**, *14*, 1046–1049. (b) Kawahara, R.; Fujita, K.-i.; Yamaguchi, R. *Adv. Synth. Catal.* **2011**, *353*, 1161–1168. (c) Kawahara, R.; Fujita, K.-i.; Yamaguchi, R. *J. Am. Chem. Soc.* **2010**, *132*, 15108–15111.

(13) Zhang, W.; Dong, X.; Zhao, W. *Org. Lett.* **2011**, *13*, 5386–5389.

(14) Balcells, D.; Nova, A.; Clot, E.; Gnanamgari, D.; Crabtree, R. H.; Eisenstein, O. *Organometallics* **2008**, *27*, 2529–2535.

(15) (a) Koch, D.; Sünkel, K.; Beck, W. *Z. Anorg. Allg. Chem.* **2003**, *629*, 1322–1328. (b) Carmona, D.; Lamata, M. P.; Viguri, F.; San José, E.; Mendoza, A.; Lahoz, F. J.; García-Orduña, P.; Atencio, R.; Oro, L. A. *J. Organomet. Chem.* **2012**, *717*, 152–163. (c) Jimineo, M. L.; Elguero *J. Magn. Reson.* **1996**, *34*, 42–46. (d) Poth, T.; Paulus, H.; Elias, H.; Dücker-Benfer, C.; van Eldik, R. *Eur. J. Inorg. Chem.* **2001**, 1361–1369. (e) Carmona, D.; Vega, C.; Lahoz, F. J.; Atencio, R.; Oro, L. A. *Organometallics* **2000**, *19*, 2273–2280. (f) Carmona, D.; Lahoz, F. J.; Atencio, R.; Oro, L. A.; Lamata, M. P.; San Josè, E. *Tetrahedron: Asymmetry* **1993**, *4*, 1425–1428. (g) Grotjahn, D. B.; Groy, T. L. *Organometallics* **1995**, *14*, 3669–3682. (h) Grotjahn, D. B.; Groy, T. L. *J. Am. Chem. Soc.* **1994**, *116*, 6969–6970. (i) Carmona, D.; Mendoza, A.; Lahoz, F. J.; Oro, L. A.; Lamata, M. P.; San Josè, E. *J. Organomet. Chem.* **1990**, *396*, C17–C21.

(16) (a) Grotjahn, D. B.; Joubran, C.; Hubbard, J. L. *Organometallics* **1996**, *15*, 1230–1235. (b) Krämer, R.; Polborn, K.; Wanjek, H.; Zahn, I.; Beck, W. *Chem. Ber.* **1990**, *123*, 767–778.

(17) Koch, D.; Hoffmüller, W.; Polborn, K.; Beck, W. *Z. Naturforsch.* **2001**, *56b*, 403–410.

(18) Hoffmüller, W.; Dialer, H.; Beck, W. *Z. Naturforsch.* **2005**, *60b*, 1278–1286.

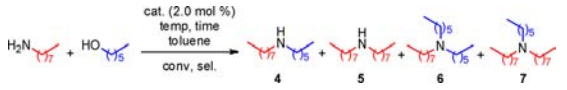
(19) Carmona, D.; Lahoz, F. J.; Atencio, R.; Oro, L. A.; Lamata, M. P.; Viguri, F.; San José, E.; Vega, C.; Reyes, J.; Joó, F.; Kathó, Á. *Chem.—Eur. J.* **1999**, *5*, 1544–1564.

(20) Selected bond lengths (Å) and angles (deg): Ir−Cl 2.4177(6)/2.4143(7), Ir−O 2.0992(18)/2.0998(18), Ir−N 2.120(2)/2.129(2), Cl−Ir−O 86.96(5)/85.25(6), Cl−Ir−N 83.95(6)/85.02(6), O−Ir−N 78.48(7)/78.39(8).

(21) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 7375–7378.

(22) The attempted alkylation of various $NH_3$ equivalents in neat benzyl alcohol (2 mol % **2a**, 140 °C, 24 h) yielded mostly tertiary amines ($NH_4BF_4$: 49% conv, 77% $Bn_3N$; $NH_4OAc$: 81% conv, 100% $Bn_3N$; urea: 69% conv, 26% $Bn_2NH$, 40% $Bn_3N$).

**Table 1.** Optimization of Reaction Conditions




| | | | | | selectivity[b] (%) | | | |
|---|---|---|---|---|---|---|---|---|
| entry | catalyst | temp (°C) | conv[a,b] (%) | time (h) | **4** | **5** | **6** | **7** |
| a | **2a** | 140 | 100 | 12 | 45 | 44 | 4 | 7 |
| b | **2a** | 120 | 100 | 17 | 83 | 12 | 3 | 2 |
| c | **2a** | 110 | 100 | 20 | 82 | 12 | 2 | 4 |
| d | **2a** | 95 | 100 | 24 | 94 | 3 | 1 | 2 |
| e | **2a** | 75 | 54 | 24 | 100 | 0 | 0 | 0 |
| f[c] | **2a** | 95 | 100 | 24 | 95 | 2 | 2 | 1 |
| g[d] | **2a** | 95 | 100 | 24 | 96 | 2 | 1 | 1 |
| h | $[Cp^*IrCl_2]_2$ | 95 | 29 | 24 | 100 | 0 | 0 | 0 |
| i | glycine | 95 | 0 | 24 | 0 | 0 | 0 | 0 |

[a] 1-Octylamine, 1-hexanol (each 1.0 mmol), **2a** (2 mol %), toluene (0.3 mL). [b] Determined by GC. Conversion of 1-octylamine. [c] 1-Hexanol (2.0 mmol). [d] Solvent water (0.1 mL).

activity and selectivity were as high as in an organic solvent (Table 1, g). Thus, to the best of our knowledge, **2a** is the first Cp*−Ir(III) complex that catalyzes this reaction with high activity in organic as well as aqueous media without additives and at temperatures below 100 °C. In comparison, Fujita's and Yamaguchi's state-of-the-art catalyst $[Cp^*IrCl_2]_2$ was much less active under these conditions and glycine itself did not give any conversion (Table 1, h, i).

Under optimized conditions, **2b**−**e** were highly selective (>90%) toward the secondary amine (Figure 1) and within this group of catalysts [Cp*Ir(Pro)Cl] (**2e**) showed especially high activity. α-Substituents at the aminoacidato ligand diminished the catalyst's reactivity, cf. [Cp*Ir(Val)Cl] (**2d**) vs **2a**. On the other hand, *N*-alkylation activated the complex to a certain degree, and so **2b** is more active than **2a**.

The substrate scope of [Cp*Ir(Pro)Cl] (**2e**) is quite broad: *N*-alkylanilines **8a**−**f** formed in excellent isolated yields (83−99%, cf. Table 2) as did the secondary benzylamines **8g** and **8h** and the aliphatic amines **8i**,**j**. Bulky amines turned out to be more challenging (R = cyclohexyl, *t*-Bu), and even at 150 °C and prolonged reaction time in toluene (72 h) the secondary amines **8k** and **8l** did only form in poor yield (23 and <10%).

Compound **2e** was generally applicable and gave the secondary amines **8m**−**q** in high isolated yields (72−94%). Similarly, a wide variety of electron-rich ($R^1$ = 4-OMe/$MeC_6H_4$−) as well as electron-poor anilines ($R^1$ = 4-F/Cl/$CO_2MeC_6H_4$−) with benzyl alcohols led to secondary benzylamines **8r**−**z** in high to excellent isolated yields (79−100%), both in toluene and water (Table 2). Notably, *N*-benzyl-4-fluoroaniline (**8v**), a motif found in many biologically active compounds, formed in almost quantitative yield from benzyl alcohol and 4-fluoroaniline.[7] Substituents in the 4-position of the benzyl alcohols were of minor influence (isolated yields **8x**−**z** >90%). The yields obtained in water were again comparable or even slightly better than those in toluene.

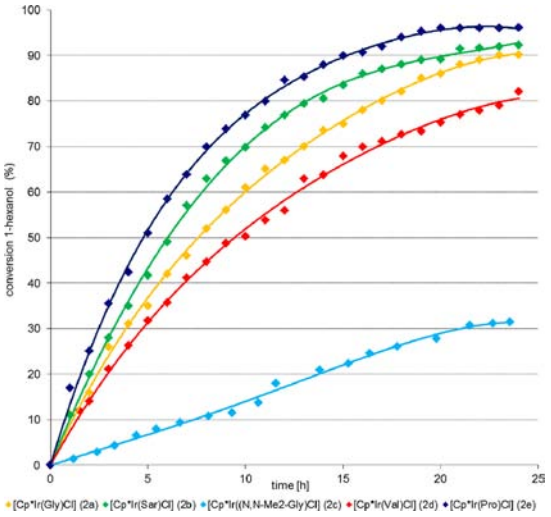



**Figure 1.** Ligand influence on catalyst activity of **2a**−**e**. Conditions: 1-octylamine, 1-hexanol (each 1.0 mmol), **2a**−**e** (2.0 mol %), toluene (0.3 mL), 95 °C. Conversion of alcohol monitored by NMR (internal standard biphenyl).

Remarkably, **2e** also catalyzes the 2-fold amination of diols and with benzylamine in very good yields (89−94%) in a one-pot reaction to form the heterocycles *N*-benzylpyrrolidine (**9a**), *N*-benzylpiperidine (**9b**), and *N*-benzylazepane (**9c**), even in water (Table 3).

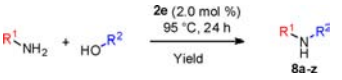
For all those substrates, overalkylation to the tertiary amines turned out to be favored at elevated temperature and prolonged reaction time (cf. Table 1): within 36 h at 130 °C, the tertiary amines **10a**−**e** formed cleanly from a series of secondary amines and 1-hexanol (yields 84−90%, cf. Table 4).

We finally were able to realize the one-pot synthesis of an unsymmetrical tertiary amine by subsequent alkylation of a primary amine by two different alcohols (Scheme 3). Thus, benzylamine was first alkylated with 1-butanol at 100 °C for 24 h in the presence of **2e**. Subsequently, 1-hexanol was added and the temperature was increased to 130 °C for further 24 h to finally isolate **11** in 77% yield over two steps.

The course of the reactions on a molecular level might follow the generally accepted hydrogen-borrowing mechanism.[7a,8a,12c,14] The formation of *N*-benzylaniline in 81% yield within 24 h from aniline, benzaldehyde, the hydrogen donor *i*PrOH and **2e** is in accord with this pathway (Scheme 4a), as was the futile alkylation of aniline with *t*BuOH that bears no *β*-H.

Surprisingly, the reduction of *N*-benzylideneaniline with *i*-PrOH and **2e** gave *N*-benzylaniline in virtually quantitative yield (Scheme 4b), although we would have expected considerable product inhibition as reported for other Cp*Ir complexes.[7a,8a,12c,14] The ease of this transformation (4 h, 85 °C) suggests this is not necessarily the rate-determining step in the catalytic cycle and does not occur in the coordination sphere of iridium. Alternatively, the simultaneous proton transfer from the aminoacidato ligand and a hydrido-iridium complex to the imine through

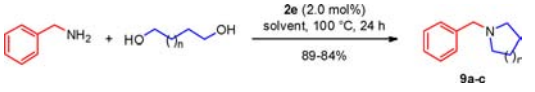
**Table 2.** *N*-Alkylation of Various Amines with Alcohols by [Cp*Ir(Pro)Cl] (**2e**) in Toluene or Water[a]




| entry | $R^1$ | $R^2$ | yield of **8a**–**z**[b] (%) | |
|---|---|---|---|---|
| a | Ph | *n*-hexyl | 98[c] | 97[d] |
| b | 4-OMeC$_6$H$_4$– | *n*-hexyl | 99[c] | [d] |
| c | 4-ClC$_6$H$_4$– | *n*-hexyl | 85[c] | [d] |
| d | 4-CO$_2$MeC$_6$H$_4$– | *n*-hexyl | 86[c] | 88[d] |
| e | 4-FC$_6$H$_4$– | *n*-hexyl | 98[c] | [d] |
| f | 2,4-Me$_2$C$_6$H$_4$– | *n*-hexyl | 83[c] | [d] |
| g | Bn | *n*-hexyl | 93[c] | 92[d] |
| h | 4-OMeBn | *n*-hexyl | 96[c] | [d] |
| i | *n*-octyl | *n*-hexyl | 93[c] | 96[d] |
| j | *n*-pentyl | *n*-hexyl | 92[c] | [d] |
| k[e] | cyclohexyl | *n*-hexyl | 23[c] | 27[d] |
| l[e] | *t*Bu | *n*-hexyl | <10[c,f] | <10[d,f] |
| m | *n*-octyl | *n*-pentyl | 90[c] | [d] |
| n | *n*-octyl | Bn | 94[c] | [d] |
| o | *n*-octyl | phenethyl | 89[c] | [d] |
| p | *n*-octyl | cyclohexyl | 89[c] | 84[d] |
| q | *n*-octyl | (CH$_2$)$_2$OMe | 72[c] | 79[d] |
| r | Ph | Bn | 96[c] | 95[d] |
| s | 4-OMeC$_6$H$_4$– | Bn | 100[c] | [d] |
| t | 4-ClC$_6$H$_4$– | Bn | 95[c] | [d] |
| u | 4-CO$_2$MeC$_6$H$_4$– | Bn | 81[c] | 86[d] |
| v | 4-FC$_6$H$_4$– | Bn | 99[c] | [d] |
| w | 2,4-Me$_2$C$_6$H$_4$– | Bn | 82[c] | 79[d] |
| x | Ph | 4-OMeBn | 93[c] | [d] |
| y | Ph | 4-ClBn | 90[c] | [d] |
| z | Ph | 4-CO$_2$MeBn | 96[c] | 94[d] |

[a] Amine, alcohol (each 1.0 mmol), **2e** (2.0 mol %). [b] Isolated yield. [c] In toluene (0.3 mL). [d] In water (0.1 mL). [e] 72 h, 150 °C. [f] GC yield. Bn: benzyl, Ph: phenyl.

**Table 3.** Preparation of *N*-Heterocycles **9a**–**c**[a]



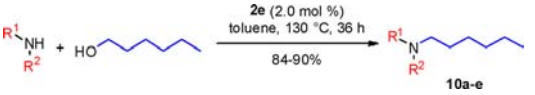

| entry | *n* | yield of **9a**–**c**[b] (%) | |
|---|---|---|---|
| a | 1 | 94[c] | [d] |
| b | 2 | 89[c] | [d] |
| c | 3 | 91[c] | 92[d] |

[a] Amine, diol (each 1.0 mmol), **2e** (2.0 mol %). [b] Isolated yield. [c] In toluene (0.3 mL). [d] In water (0.1 mL).

a six-membered cyclic intermediate is a viable pathway, as proposed by Carmona et al.[23]

(23) (a) Carmona, D.; Lamata, M. P.; Oro, L. A. *Eur. J. Inorg. Chem.* **2002**, 2239–2251. (b) Carmona, D.; Viguri, F.; Lamata, M. P.; Ferrer, J.; Bardaji, E.; Lahoz, F. J.; Garcia-Orduna, P.; Oro, L. A. *Dalton Trans.* **2012**, *41*, 10298–10308.

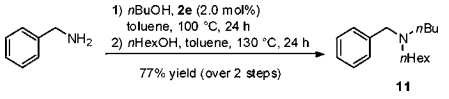
**Table 4.** Preparation of Tertiary Amines **10a**–**e**[a]



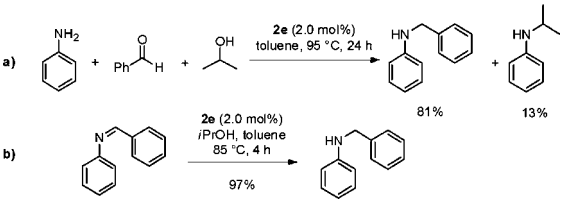

| entry | $R^1$ | $R^2$ | yield of **10a**–**e**[b] (%) |
|---|---|---|---|
| a | | piperidine | 84 |
| b | | morpholine | 87 |
| c | Bn | Bn | 85 |
| d | *n*-hexyl | *n*-hexyl | 90 |
| e | Me | Ph | 88 |

[a] Amine, alcohol (each 1.0 mmol), **2e** (2.0 mol %) in toluene (0.3 mL). [b] Isolated yield.

**Scheme 3.** Subsequent Alkylation of Primary Amine




**Scheme 4.** Preliminary Mechanistic Information




In summary, Cp*–iridium(III) half-sandwich complexes with aminoacidato ligands are highly active and selective catalysts for the alkylation of amines with alcohols. In contrast to state-of-the-art catalysts, they do not require basic additives or harsh reaction conditions for high activity. They work both in an organic solvent and in water. This opens the door for functionalization of both highly polar and unpolar substrates.

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**Supporting Information Available.** Experimental details and spectral characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.