ChemPubSoc Europe

DOI: 10.1002/chem.201501109

CHEMISTRY
A European Journal
Communication

Homogeneous Catalysis

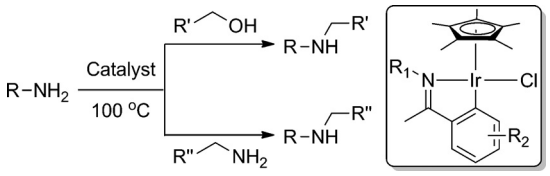
Alkylation of Amines with Alcohols and Amines by a Single Catalyst under Mild Conditions

Qingzhu Zou,[a] Chao Wang,*[a] Jen Smith,[b] Dong Xue,[a] and Jianliang Xiao*[a, b]

Abstract: An efficient catalytic system for the alkylation of amines with either alcohols or amines under mild conditions has been developed, using cyclometallated iridium complexes as catalysts. The method has broad substrate scope, allowing for the synthesis of a diverse range of secondary and tertiary amines with good to excellent yields. By controlling the ratio of substrates, both mono- and bis-alkylated amines can be obtained with high selectivity. In particular, methanol can be used as the alkylating reagent, affording *N*-methylated products selectively. A strong solvent effect is observed for the reaction.

The development of methods for the synthesis of amines is of great importance because of the widespread presence of amine moieties within natural products, pharmaceuticals and fine chemicals.[1] Classical methods for the preparation of amines include reduction of nitro,[2] nitrile or amide groups,[3] functionalisation of alkenes or alkynes,[1u,4] alkylation with alkyl halides[5] and reductive amination of carbonyl compounds.[1c,k,v,6] An alternative and greener method for the production of amines is the alkylation of amines with alcohols by the use of "borrowing hydrogen" or "hydrogen autotransfer" strategy.[7] The first examples of alkylation of amines with alcohols by homogeneous catalysis were reported independently by the groups of Grigg[8] and Watanabe.[9] Since then, great progress has been made in this area, allowing the reaction to be carried out under milder conditions,[7j,10] with broader substrate scope,[7h] or even in an enantioselective manner.[7m,11] Notable contributions have come from the groups of Beller,[3,7p,q,s,12] Williams,[7a,c,d,f,h,r,t–v,x,13] Fujita,[14] Kempe,[7z,10,15] Martín-Matute,[16] Crabtree,[17] Yus,[7b,18] Peris,[7g] Andersson,[7j] Milstein,[19] Zhao[7m,11b] and others.[20] The strategy could be further extended to the cross coupling of amines as reported by the groups of Beller,[7p,q] Peris[7g] and Williams.[7r] However, most of the catalysts reported only work for alkylation with alcohols or amines, but not with both. Shvo's catalyst,[7p] a [Cp*IrCl$_2$(NHC)] complex reported by Peris and co-workers,[7g] and a recent example from Li and co-workers[21] are the only catalysts that are able to catalyse both reactions under different reaction conditions or temperatures. Thus, a versatile catalyst capable of promoting alkylation both with alcohols and with amines is desirable. However, to perform amine alkylation with alcohols and amines using the same catalyst system under mild conditions is challenging, as the amine cross-coupling reaction normally requires high temperature ($>150\,^{\circ}C$). To our knowledge, a mild catalytic system for alkylation of amines with both alcohols and amines has not been reported to date.

We have developed efficient catalytic systems based on cyclometallated iridium complexes for the reductive amination of carbonyl compounds to afford amines.[6b,c,22] Apart from reduction reactions, these iridium complexes were found to be able to catalyse dehydrogenation reactions as well.[23] The dehydrogenation and reduction abilities of these iridium complexes render them possible catalysts for borrowing hydrogen reactions. This hypothesis has now been verified by the alkylation of amines with alcohols catalysed by a cyclometallated iridium complex. Compared with our previously reported reductive amination reactions, the alkylation with alcohols is greener, avoiding the use of extra reductant. Further studies have demonstrated that the catalyst is also viable for cross coupling of amines under relatively mild conditions, thus providing a versatile protocol for alkylation of amines with both alcohols and amines (Scheme 1). Herein, we report the details of our findings.



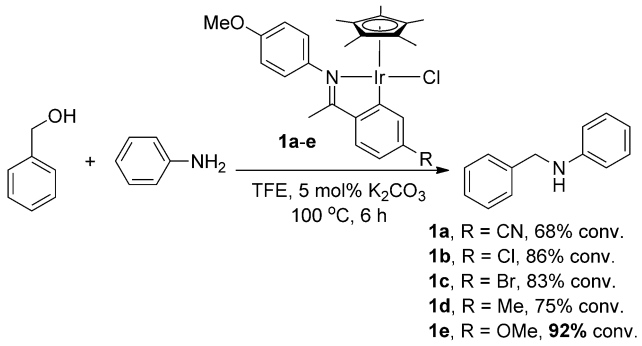
Scheme 1. Alkylation of amines with both alcohols and amines catalysed by a single cyclometallated iridium complex under the same mild conditions.

In our previous work, the iridium complex **1a** demonstrated superior activity for the reduction of imines in 2,2,2-trifluoroethanol (TFE; Scheme 2).[6b] Thus, the reaction of benzyl alcohol with aniline was initially carried out with **1a** as precatalyst in TFE in the presence of 5 mol% of K_2CO_3 as base. Pleasingly, 68% conversion of benzyl alcohol to the alkylation product was observed in 6 h at 100 °C. The use of TFE as solvent is criti-

[a] Q. Zou, Prof. Dr. C. Wang, Prof. Dr. D. Xue, Prof. Dr. J. Xiao
Key Laboratory of Applied Surface and Colloid Chemistry
Ministry of Education, Department of Chemistry & Chemical Engineering
Shaanxi Normal University, Xi'an, 710062 (P. R. China)
E-mail: c.wang@snnu.edu.cn

[b] J. Smith, Prof. Dr. J. Xiao
Department of Chemistry, University of Liverpool
Liverpool, L69 7ZD (UK)
E-mail: j.xiao@liv.ac.uk

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201501109.



Scheme 2. The effect of different catalyst ligand substituents on the alkylation of aniline (0.6 mmol) with benzyl alcohol (0.5 mmol) in TFE (2.6 mL) at S/C = 100. Conversions were determined by ^{1}H NMR spectroscopy.

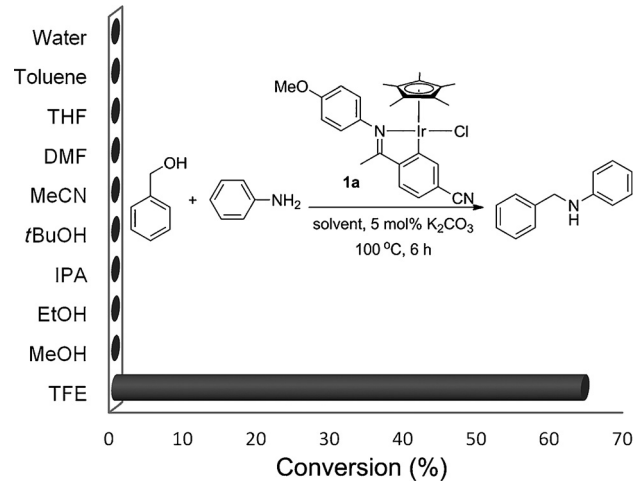
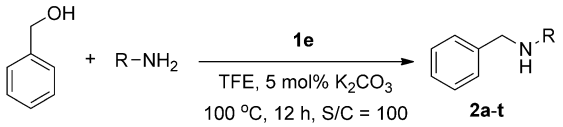


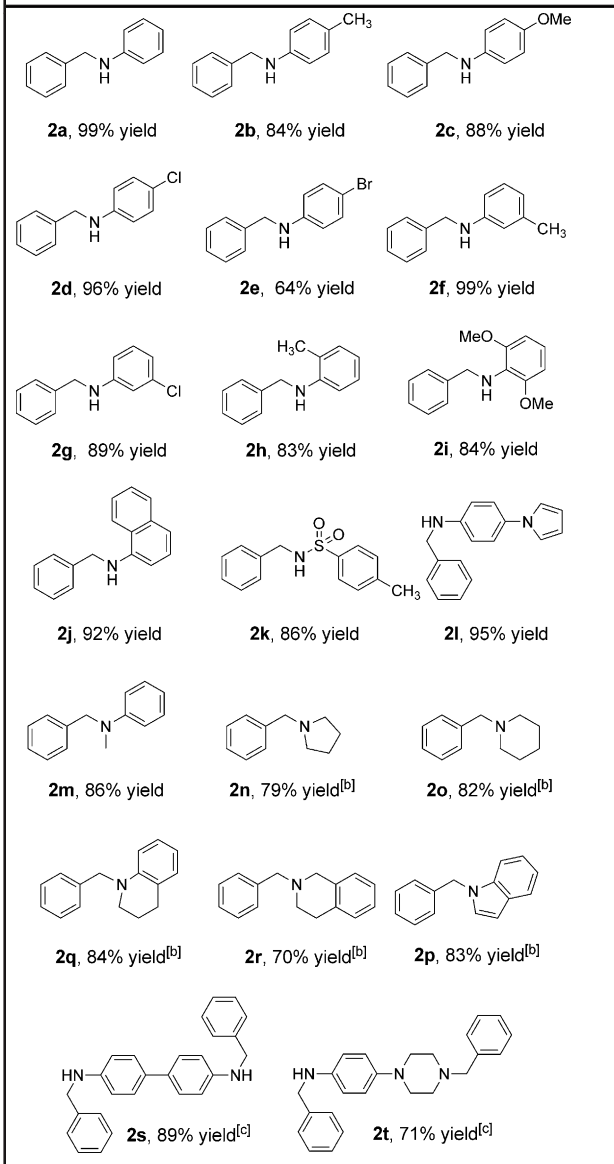
Figure 1. The effect of solvents on Ir catalysed alkylation of amine with benzyl alcohol. The substrate to catalyst ratio (S/C) was 100.

cal for the reaction to proceed, as no reaction was observed with all other solvents tested (Figure 1). Other cyclometallated iridium complexes with different substituents were subsequently evaluated in TFE (Scheme 2). Complex **1e** provided the highest conversion of 92% in 6 h. In contrast, only 22% conversion was obtained with [{Cp*IrCl$_2$}$_2$] under the same conditions and [{Cp*RhCl$_2$}$_2$] was totally inactive. By increasing the reaction time to 12 h and using a sealed reaction tube, a near-quantitative yield (99%) of product was isolated from the reaction with 1 mol% of **1e** as catalyst.

The generality of the **1e**-catalysed alkylation reaction was first tested in the reaction of benzyl alcohol with various amines (Table 1). Substituents at the *ortho*, *meta* and *para* positions of aromatic amines were all tolerated (**2a–i**). Good yield was obtained even for the very bulky 2,6-dimethoxyaniline (**2i**). The electronic properties of the substituents exerted strong influence on the reactivity of substrates. Thus, low yields (< 20%) were observed for the very electron-deficient amines, 4-nitroaniline and 4-(trifluoromethyl)aniline, indicating that the reaction of the amine with the intermediate aldehydes may be involved in or before the turnover limiting step. 1-naphthylamine, benzenesulfonamide and heterocycle-substituted aniline are all viable substrates, affording the desired products in good to excellent yields (**2j–l**). Secondary amines, including heterocyclic aliphatic secondary amines, all reacted well with benzyl alcohol to afford the alkylated products in good yields (**2m–r**). Interestingly, the dehydrogenated indole product (**2p**) was obtained when indoline was used as a substrate. When

Table 1. Alkylation of amines with benzyl alcohols.[a]





[a] Reaction conditions (unless otherwise stated): Benzyl alcohol (0.5 mmol), amine (0.6 mmol), **1e** (0.005 mmol), K_2CO_3 (0.025 mmol), TFE (2.6 mL), 100 °C, 12 h; yields refer to isolated products; [b] benzyl alcohol (1 mmol), amine (1.2 mmol), **1e** (0.01 mmol), K_2CO_3 (0.75 mmol), TFE (2 mL), 100 °C, 12 h; [c] benzyl alcohol (1.1 mmol), amine (0.5 mmol).

two amino groups were presented, both could be alkylated (**2s** and **2t**) to afford products hitherto thought difficult to prepare.[15e, 16b]

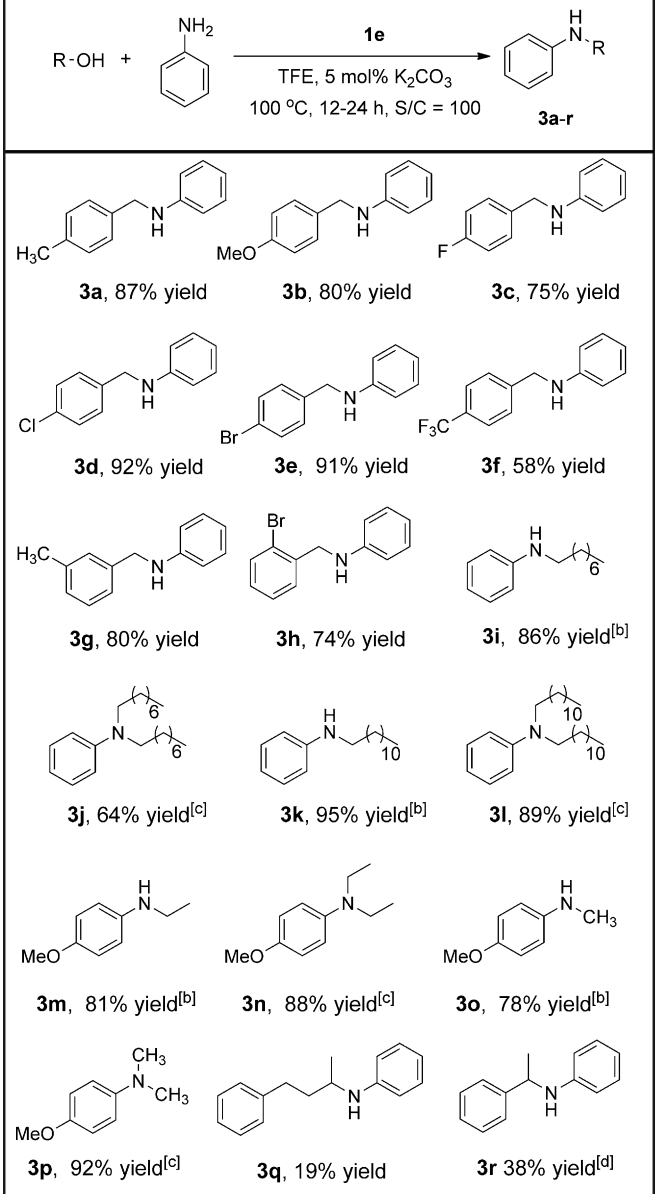
The substrate scope of the system was further examined by reaction of different alcohols with aniline (Table 2). Various benzylic alcohols and aliphatic alcohols could act as alkylating reagents, affording good yields in general. However, no correlation could be established between the electronic properties of substituents and yields (**3a**–**f**). This appears in line with the dehydrogenation step not being turnover limiting. Substituents at the *meta* and *ortho* positions of benzylic alcohols could be tolerated (**3g** and **3h**). Remarkably, by varying the ratio of substrates, both mono- and bis-alkylated amines could be obtained with good selectivity (**3i**–**p**). Only a few examples are known in which control of this selectivity has been demonstrated in borrowing hydrogen reactions.[9, 14e] Notably, methanol could be used as substrate, affording mono- and bis-alkylated amines with good yields (**3o** and **3p**) and thus providing a green and selective method for *N*-methylation of amines.[24] The use of methanol as an alkylating reagent is rare in the literature[7a,b] and the selective formation of mono-methylated amines is a still difficult issue in *N*-methylation reactions.[24a,c–e] Secondary alcohols displayed lower activities, however, even with a higher catalyst loading and longer reaction time (**3q** and **3r**).

The system could also be applied to the synthesis of heterocycles by reaction of amines with diols (Table 3). The formation of heterocycles requires two consecutive "borrowing hydrogen" reactions; thus a higher catalyst loading and a longer reaction time were necessary to obtain acceptable yields. Piperidines and pyrrolidines could be obtained with good to excellent yields with pentane-1,5-diol and butane-1,4-diol, respectively. 4-Phenylmorpholine was prepared with moderate yield by employing 2,2′-oxydiethanol as substrate (**4f**).

The synthesis of Piribedil, which is a piperazine dopamine agonist for the treatment of Parkinson's disease,[25] was successfully achieved employing our methodology. The method avoids the use of often toxic alkyl halides or hazardous reducing reagents[25b] (Scheme 3).

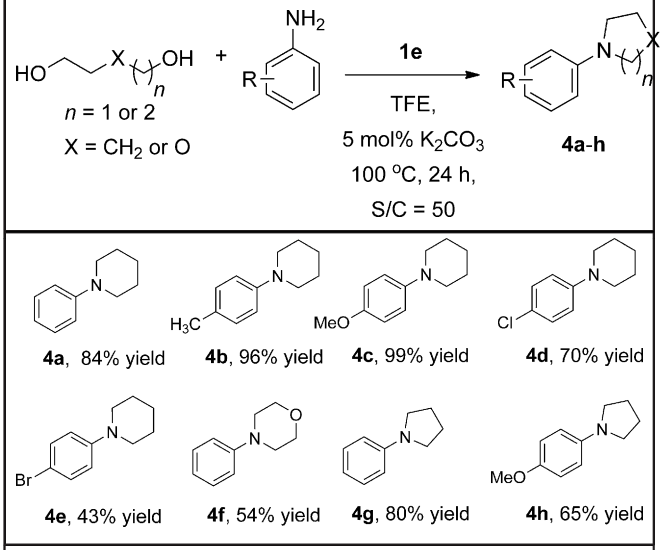
The versatility of the system was further examined for the cross-coupling of amines (Table 4), which is normally carried out at temperatures higher than 150 °C.[7g,p–r, 21] Delightfully, the reaction of aniline with diisopropylamine proceeded smoothly

Table 2. Alkylation of aniline with different alcohols.[a]

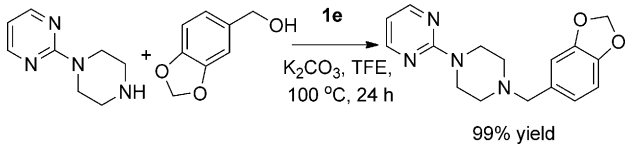


[a] Reaction conditions (unless otherwise stated): Alcohol (0.5 mmol), aniline (0.6 mmol), **1e** (0.005 mmol), K_2CO_3 (0.025 mmol), TFE (2.6 mL), 100 °C, 12 h; yields refer to isolated products; [b] alcohol (0.5 mmol), aniline (1.1 mmol); [c] alcohol (1.1 mmol), aniline (0.5 mmol); [d] **1e** (0.01 mmol), 24 h.

Table 3. Synthesis of heterocycles.[a]

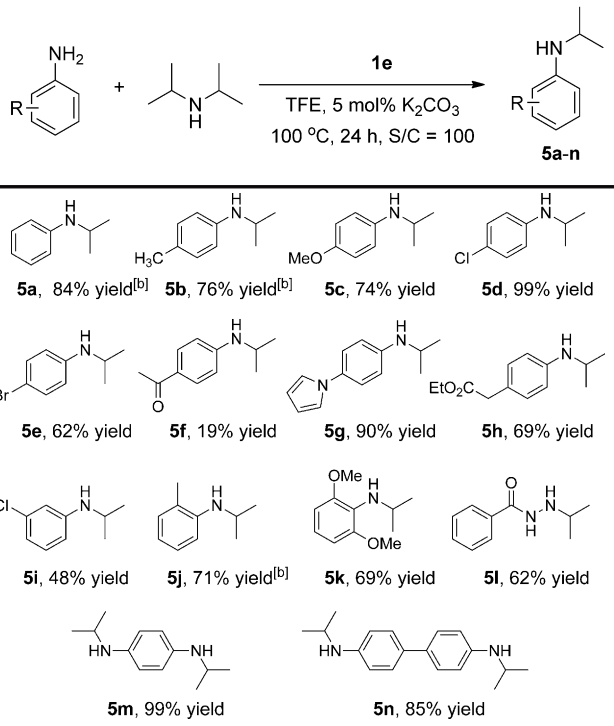


[a] Reaction conditions: Alcohol (0.5 mmol), aniline (0.5 mmol), **1e** (0.01 mmol), K_2CO_3 (0.025 mmol), TFE (2.6 mL), 100 °C, 24 h; yields refer to isolated products.



Scheme 3. Synthesis of Piribedil. Reactions conditions: Alcohol (0.5 mmol), amine (0.6 mmol), **1e** (0.005 mmol), K_2CO_3 (0.025 mmol), TFE (2.6 mL), 100 °C, 24 h. Yield refers to isolated product.

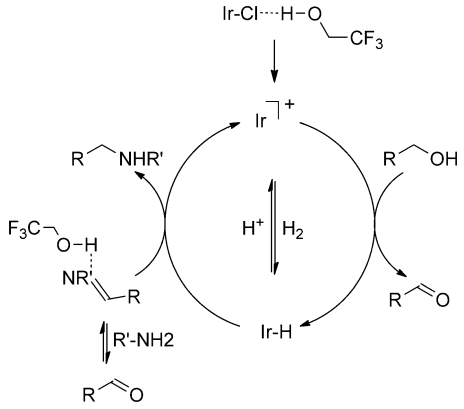
Table 4. Cross-coupling of amines.[a]



[a] Reaction conditions (unless otherwise stated): Amine (0.5 mmol), diisopropylamine (1.5 mmol), **1e** (0.005 mmol), K_2CO_3 (0.025 mmol), TFE (2.6 mL), 100 °C, 24 h; yields refer to isolated products; [b] yields were determined by ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as internal standard.

under the same mild reaction conditions as those for the alkylation with alcohols. Various *para*-substituted anilines reacted (**5a**–**h**), with all except *para*-acetyl aniline (**5f**) affording high yields, with heterocycle or ester groups tolerated (**5g** and **5h**). Anilines substituted at the *meta* or *ortho* positions are also viable substrates, as shown by the formation of **5i**–**k**. The alkylation of benzohydrazide proceeded in moderate yield (**5l**). When two amino groups are present, both amine groups were alkylated with excellent yields (**5m** and **5n**).

The mechanism of the reaction is believed to follow the conventional "borrowing hydrogen" pathway, which proceeds via a sequence of alcohol dehydrogenation, imine formation and imine reduction (Scheme 4).[7a–e] Indeed, when benzyl alcohol was subjected to the reaction conditions outlined in Table 1 but in the absence of aniline, benzyaldehyde was formed, indicating that dehydrogenation of alcohols by **1e** is involved in the alkylation of amines with alcohols. The fact that an improved yield was obtained in a sealed reaction vessel suggests that hydrogen gas might be released and reused. This is further supported by the observation that a lower conversion of benzyl alcohol was obtained when argon was continuously bubbled through the reaction mixture (15% vs 36% under standard conditions, 1 h reaction time). We have previously shown that cyclometallated iridium complexes catalyse the hydrogenation of imino bonds and isolated their hydride complexes.[26] The ability of such complexes to effect dehydrogenation of amines was also demonstrated,[23b] providing evidence that the cross-coupling of amines may proceed via a similar pathway. The beneficial effect of TFE as solvent might stem from its strong hydrogen-bond-donating ability, which could promote the dissociation of the chloride anion from **1e** to form the active catalyst and/or activate the imine toward hydride transfer (Scheme 4).



Scheme 4. Proposed mechanism for the alkylation of amines with alcohols.

In conclusion, we have developed a versatile catalytic system for alkylation of amines with either alcohols or amines under the same mild conditions. The system shows broad substrate scope for various alcohols and amines, allowing for the synthesis of a diverse range of secondary or tertiary amines, and excellent selectivity, which could be controlled by simple variation of substrate ratios. Of particular note is that methanol could be used as alkylating reagent, providing a green and selective *N*-methylation method. The cross-coupling of amines was achieved under the mildest conditions reported to date.

Experimental Section

Typical procedure for the reaction of alcohols and amines: Benzyl alcohol (0.5 mmol), aniline (0.6 mmol), **1e** (0.005 mmol), K_2CO_3 (0.025 mmol), and a magnetic stir bar were placed in a pressure tube. Into the mixture was injected TFE (2.6 mL). The mixture was bubbled with argon for 15 min, and then stirred at 100 °C for 12 h. After cooling to room temperature, the reaction solution was adjusted with hydrochloric acid (3 M) to pH 2 and stirred for 10 min. The solution was then adjusted to pH 10 with saturated NaOH solution, and extracted with DCM (3×10 mL). The organic layers were washed with brine (20 mL) and dried over Na_2SO_4. The organic solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica using petroleum ether/ethyl acetate (200:1) as eluent.

Acknowledgements

We are grateful for the financial support of the National Natural Science Foundation of China (21473109, 21103102), the Program for Changjiang Scholars and Innovative Research Team in University (IRT 14R33), the 111 project (B14041), Shaanxi Provincial Natural Science Foundation (2014JQ2048), the Fundamental Research Funds for the Central Universities (GK261001316, GK261001329, GK261001095), the Program for Key Science and Technology Innovative Team of Shaanxi Province (2012KCT-21 and 2013KCT-17), and the Scientific Research Foundation for the Returned Overseas Chinese Scholars, State Education Ministry.

Keywords: alkylation · amines · cyclometallation · dehydrogenation · iridium

[1] a) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069; b) J. A. Ellman, T. D. Owens, T. P. Tang, *Acc. Chem. Res.* **2002**, *35*, 984; c) S. Gomez, J. A. Peters, T. Maschmeyer, *Adv. Synth. Catal.* **2002**, *344*, 1037; d) M. Besson, C. Pinel, *Top. Catal.* **2003**, *25*, 43; e) H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103; f) J. A. Ellman, *Pure Appl. Chem.* **2003**, *75*, 39; g) P. Kukula, R. Prins, *Top. Catal.* **2003**, *25*, 29; h) M. Breuer, K. Ditrich, T. Habicher, B. Hauer, M. Keßeler, R. Stürmer, T. Zelinski, *Angew. Chem. Int. Ed.* **2004**, *43*, 788; *Angew. Chem.* **2004**, *116*, 806; i) G. K. Friestad, *Eur. J. Org. Chem.* **2005**, *2005*, 3157; j) V. I. Tararov, A. Börner, *Synlett* **2005**, *2005*, 203; k) A. F. Abdel-Magid, S. J. Mehrman, *Org. Process Res. Dev.* **2006**, *10*, 971; l) D. Morton, R. A. Stockman, *Tetrahedron* **2006**, *62*, 8869; m) P. V. Ramachandran, T. E. Burghardt, *Pure Appl. Chem.* **2006**, *78*, 1397; n) G. K. Friestad, A. K. Mathies, *Tetrahedron* **2007**, *63*, 2541; o) J.-C. Kizirian, *Chem. Rev.* **2007**, *107*, 140; p) A. J. Minnaard, B. L. Feringa, L. Lefort, J. G. de Vries, *Acc. Chem. Res.* **2007**, *40*, 1267; q) M. Petrini, E. Torregiani, *Synthesis* **2007**, *2007*, 159; r) E. Skucas, M.-Y. Ngai, V. Komanduri, M. J. Krische, *Acc. Chem. Res.* **2007**, *40*, 1394; s) S.-L. You, *Chem. Asian J.* **2007**, *2*, 820; t) F. Spindler, H.-U. Blaser in *The Handbook of Homogeneous Hydrogenation* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim **2008**, Chapter 34; u) T. E. Müller, K. C. Hultzsch, M. Yus, F. Foubelo, M. Tada, *Chem. Rev.* **2008**, *108*, 3795; v) R. P. Tripathi, S. S. Verma, J. Pandey, V. K. Tiwari, *Curr Org Chem.* **2008**, *12*, 1093; w) T. C. Nugent, M. El-Shazly, *Adv. Synth. Catal.* **2010**, *352*, 753; x) C. Wang, B. Villa-Marcos, J. Xiao, *Chem. Commun.* **2011**, *47*, 9773.

[2] a) W. X. Dong, M. H. Liang, J. L. Zhang, W. Yuan, *Curr. Org. Chem.* **2007**, *11*, 299; b) H. U. Blaser, H. Steiner, M. Studer, *ChemCatChem* **2009**, *1*, 210; c) A. Corma, P. Serna, *Science* **2006**, *313*, 332; d) G. Wienhöfer, I. Sorribes, A. Boddien, F. Westerhaus, K. Junge, H. Junge, R. Llusar, M. Beller, *J. Am. Chem. Soc.* **2011**, *133*, 12875.

[3] S. Werkmeister, K. Junge, M. Beller, *Org. Process Res. Dev.* **2014**, *18*, 289.

[4] R. Severin, S. Doye, *Chem. Soc. Rev.* **2007**, *36*, 1407.

[5] R. N. Salvatore, C. H. Yoon, K. W. Jung, *Tetrahedron* **2001**, *57*, 7785.

[6] a) E. R. Burkhardt, K. Matos, *Chem. Rev.* **2006**, *106*, 2617; b) C. Wang, A. Pettman, J. Bacsa, J. Xiao, *Angew. Chem. Int. Ed.* **2010**, *49*, 7548; *Angew. Chem.* **2010**, *122*, 7710; c) Q. Lei, Y. Wei, D. Talwar, C. Wang, D. Xue, J. Xiao, *Chem. Eur. J.* **2013**, *19*, 4021.

[7] a) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555; b) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* **2009**, *109*, 1611; c) T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Dalton Trans.* **2009**, 753; d) A. J. A. Watson, J. M. J. Williams, *Science* **2010**, *329*, 635; e) S. Pan, T. Shibata, *ACS Catal.* **2013**, *3*, 704; f) G. Cami-Kobeci, P. A. Slatford, M. K. Whittlesey, J. M. J. Williams, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 535; g) A. Prades, R. Corberán, M. Poyatos, E. Peris, *Chem. Eur. J.* **2008**, *14*, 11474; h) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc.* **2009**, *131*, 1766; i) W. Baumann, A. Spannenberg, J. Pfeffer, T. Haas, A. Köckritz, A. Martin, J. Deutsch, *Chem. Eur. J.* **2013**, *19*, 17702; j) J.-Q. Li, P. G. Andersson, *Chem. Commun.* **2013**, *49*, 6131; k) D. Weickmann, W. Frey, B. Plietker, *Chem. Eur. J.* **2013**, *19*, 2741; l) Q. Xu, Q. Li, X. Zhu, J. Chen, *Adv. Synth. Catal.* **2013**, *355*, 73; m) Y. Zhang, C.-S. Lim, D. S. B. Sim, H.-J. Pan, Y. Zhao, *Angew. Chem. Int. Ed.* **2014**, *53*, 1399; *Angew. Chem.* **2014**, *126*, 1423; n) C.-C. Lee, S.-T. Liu, *Chem. Commun.* **2011**, *47*, 6981; o) X. Cui, Y. Deng, F. Shi, *ACS Catal.* **2013**, *3*, 808; p) D. Hollmann, S. Bähn, A. Tillack, M. Beller, *Angew. Chem. Int. Ed.* **2007**, *46*, 8291; *Angew. Chem.* **2007**, *119*, 8440; q) D. Hollmann, S. Bähn, A. Tillack, R. Parton, R. Altink, M. Beller, *Tetrahedron Lett.* **2008**, *49*, 5742; r) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Angew. Chem. Int. Ed.* **2009**, *48*, 7375; *Angew. Chem.* **2009**, *121*, 7511; s) F. Shi, M. K. Tse, S. Zhou, M.-M. Pohl, J. Radnik, S. Hübner, K. Jähnisch, A. Brückner, M. Beller, *J. Am. Chem. Soc.* **2009**, *131*, 1775; t) M. G. Edwards, R. F. R. Jazzar, B. M. Paine, D. J. Shermer, M. K. Whittlesey, J. M. J. Williams, D. D. Edney, *Chem. Commun.* **2004**, 90; u) 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; v) D. J. Shermer, P. A. Slatford, D. D. Edney, J. M. J. Williams, *Tetrahedron: Asymmetry* **2007**, *18*, 2845; w) S. Whitney, R. Grigg, A. Derrick, A. Keep, *Org. Lett.* **2007**, *9*, 3299; x) S. J. Pridmore, J. M. J. Williams, *Tetrahedron Lett.* **2008**, *49*, 7413; y) T. Jensen, R. Madsen, *J. Org. Chem.* **2009**, *74*, 3990; z) B. Blank, R. Kempe, *J. Am. Chem. Soc.* **2010**, *132*, 924; aa) C. M. Wong, K. Q. Vuong, M. R. D. Gatus, C. Hua, M. Bhadbhade, B. A. Messerle, *Organometallics* **2012**, *31*, 7500; ab) B. Anxionnat, D. Gomez Pardo, G. Ricci, K. Rossen, J. Cossy, *Org. Lett.* **2013**, *15*, 3876; ac) I. S. Kim, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 6340; ad) J. R. Zbieg, J. Moran, M. J. Krische, *J. Am. Chem. Soc.* **2011**, *133*, 10582; ae) J. R. Zbieg, E. Yamaguchi, E. L. McInturff, M. J. Krische, *Science* **2012**, *336*, 324; af) E. Yamaguchi, J. Mowat, T. Luong, M. J. Krische, *Angew. Chem. Int. Ed.* **2013**, *52*, 8428; *Angew. Chem.* **2013**, *125*, 8586.

[8] R. Grigg, T. R. B. Mitchell, S. Sutthivaiyakit, N. Tongpenyai, *J. Chem. Soc. Chem. Commun.* **1981**, 611.

[9] Y. Watanabe, Y. Tsuji, H. Ige, Y. Ohsugi, T. Ohta, *J. Org. Chem.* **1984**, *49*, 3359.

[10] a) S. Ruch, T. Irrgang, R. Kempe, *Chem. Eur. J.* **2014**, *20*, 13279; b) V. R. Jumde, L. Gonsalvi, A. Guerriero, M. Peruzzini, M. Taddei, *Eur. J. Org. Chem.* **2015**, *2015*, 1829.

[11] a) N. J. Oldenhuis, V. M. Dong, Z. Guan, *J. Am. Chem. Soc.* **2014**, *136*, 12548; b) Z. Q. Rong, Y. Zhang, R. H. B. Chua, H. J. Pan, Y. Zhao, *J. Am. Chem. Soc.* **2015**, *137*, 4944.

[12] a) D. Hollmann, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J.* **2007**, *2*, 403; b) A. Tillack, D. Hollmann, K. Mevius, D. Michalik, S. Bähn, M. Beller, *Eur. J. Org. Chem.* **2008**, *28*, 4745; c) F. Shi, M. K. Tse, X. Cui, D. Gördes, D. Michalik, K. Thurow, Y. Deng, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 5912; *Angew. Chem.* **2009**, *121*, 6026; d) M. Zhang, S. Imm, S. Bähn, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2011**, *50*, 11197; *Angew. Chem.* **2011**, *123*, 11393.

[13] a) M. H. S. A. Hamid, J. M. J. Williams, *Chem. Commun.* **2007**, 725; b) M. H. S. A. Hamid, J. M. J. Williams, *Tetrahedron Lett.* **2007**, *48*, 8263; c) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden, J. M. J. Williams, *Chem. Commun.* **2010**, *46*, 1541.

[14] a) K.-i. Fujita, K. Yamamoto, R. Yamaguchi, *Org. Lett.* **2002**, *4*, 2691; b) K.-i. Fujita, Z. Li, N. Ozeki, R. Yamaguchi, *Tetrahedron Lett.* **2003**, *44*, 2687; c) K.-i. Fujita, T. Fujii, R. Yamaguchi, *Org. Lett.* **2004**, *6*, 3525; d) K.-i. Fujita, Y. Enoki, R. Yamaguchi, *Tetrahedron* **2008**, *64*, 1943; e) R. Kawahara, K.-i. Fujita, R. Yamaguchi, *J. Am. Chem. Soc.* **2010**, *132*, 15108; f) R. Kawahara, K.-i. Fujita, R. Yamaguchi, *Adv. Synth. Catal.* **2011**, *353*, 1161.

[15] a) B. Blank, M. Madalska, R. Kempe, *Adv. Synth. Catal.* **2008**, *350*, 749; b) B. Blank, S. Michlik, R. Kempe, *Adv. Synth. Catal.* **2009**, *351*, 2903; c) B. Blank, S. Michlik, R. Kempe, *Chem. Eur. J.* **2009**, *15*, 3790; d) S. Michlik, R. Kempe, *Chem. Eur. J.* **2010**, *16*, 13193; e) S. Michlik, T. Hille, R. Kempe, *Adv. Synth. Catal.* **2012**, *354*, 847.

[16] a) I. Cumpstey, S. Agrawal, K. E. Borbas, B. Martin-Matute, *Chem. Commun.* **2011**, *47*, 7827; b) S. Agrawal, M. Lenormand, B. Martín-Matute, *Org. Lett.* **2012**, *14*, 1456; c) A. Bartoszewicz, R. Marcos, S. Sahoo, A. K. Inge, X. Zou, B. Martín-Matute, *Chem. Eur. J.* **2012**, *18*, 14510.

[17] a) D. Balcells, A. Nova, E. Clot, D. Gnanamgari, R. H. Crabtree, O. Eisenstein, *Organometallics* **2008**, *27*, 2529; b) D. Gnanamgari, E. L. O. Sauer, N. D. Schley, C. Butler, C. D. Incarvito, R. H. Crabtree, *Organometallics* **2008**, *27*, 321.

[18] A. Martínez-Asencio, D. J. Ramón, M. Yus, *Tetrahedron Lett.* **2010**, *51*, 325.

[19] C. Gunanathan, D. Milstein, *Angew. Chem. Int. Ed.* **2008**, *47*, 8661; *Angew. Chem.* **2008**, *120*, 8789.
[20] a) K. Yamaguchi, J. He, T. Oishi, N. Mizuno, *Chem. Eur. J.* **2010**, *16*, 7199; b) M. Bertoli, A. Choualeb, A. J. Lough, B. Moore, D. Spasyuk, D. G. Gusev, *Organometallics* **2011**, *30*, 3479; c) R. N. Monrad, R. Madsen, *Org. Biomol. Chem.* **2011**, *9*, 610; d) A. B. Enyong, B. Moasser, *J. Org. Chem.* **2014**, *79*, 7553; e) T. Yan, B. L. Feringa, K. Barta, *Nat. Commun.* **2014**, *5*, 5602; f) S. Bartolucci, M. Mari, A. Bedini, G. Piersanti, G. Spadoni, *J. Org. Chem.* **2015**, *80*, 3217; g) A. J. Rawlings, L. J. Diorazio, M. Wills, *Org. Lett.* **2015**, *17*, 1086.
[21] D. Wang, K. Zhao, C. Xu, H. Miao, Y. Ding, *ACS Catal.* **2014**, *4*, 3910.
[22] a) D. Talwar, N. P. Salguero, C. M. Robertson, J. Xiao, *Chem. Eur. J.* **2014**, *20*, 245; b) Y. Wei, C. Wang, X. Jiang, D. Xue, J. Li, J. Xiao, *Chem. Commun.* **2013**, *49*, 5408.
[23] a) J. H. Barnard, C. Wang, N. G. Berry, J. Xiao, *Chem. Sci.* **2013**, *4*, 1234; b) J. Wu, D. Talwar, S. Johnston, M. Yan, J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6983; *Angew. Chem.* **2013**, *125*, 7121.
[24] a) M. Selva, P. Tundo, A. Perosa, *J. Org. Chem.* **2002**, *67*, 9238; b) T. Oku, Y. Arita, H. Tsuneki, T. Ikariya, *J. Am. Chem. Soc.* **2004**, *126*, 7368; c) M. Selva, P. Tundo, T. Foccardi, *J. Org. Chem.* **2005**, *70*, 2476; d) A. B. Shivarkar, S. P. Gupte, R. V. Chaudhari, *J. Mol. Catal. A* **2005**, *226*, 49; e) M. Selva, A. Perosa, P. Tundo, D. Brunelli, *J. Org. Chem.* **2006**, *71*, 5770; f) M. Selva, A. Perosa, *Green Chem.* **2008**, *10*, 457; g) K. Beydoun, T. vom Stein, J. Klankermayer, W. Leitner, *Angew. Chem. Int. Ed.* **2013**, *52*, 9554; *Angew. Chem.* **2013**, *125*, 9733; h) O. Jacquet, X. Frogneux, C. Das Neves Gomes, T. Cantat, *Chem. Sci.* **2013**, *4*, 2127.
[25] a) M. Jaber, S. W. Robinson, C. Missale, M. G. Caron, *Neuropharmacology* **1996**, *35*, 1503; b) M. A. J. Duncton, J. R. A. Roffey, R. J. Hamlyn, D. R. Adams, *Tetrahedron Lett.* **2006**, *47*, 2549.
[26] a) B. Villa-Marcos, W. Tang, X. Wu, J. Xiao, *Org. Biomol. Chem.* **2013**, *11*, 6934; b) W. Tang, C. Lau, X. Wu, J. Xiao, *Synlett* **2014**, *25*, 81; c) C. Wang, H. Y. T. Chen, J. Bacsa, C. R. A. Catlow, J. L. Xiao, *Dalton Trans.* **2013**, *42*, 935.

Received: March 21, 2015
Published online on June 3, 2015