Green Chemistry

Cite this: *Green Chem.*, 2012, **14**, 3410

www.rsc.org/greenchem

PAPER

Synthesis of substituted amines and isoindolinones: catalytic reductive amination using abundantly available $AlCl_3$/PMHS†‡

Vishal Kumar, Sushila Sharma, Upendra Sharma, Bikram Singh and Neeraj Kumar*

Received 17th August 2012, Accepted 9th October 2012
DOI: 10.1039/c2gc36305d

$AlCl_3$ has been employed for highly chemoselective reductive amination of carbonyl compounds in ethanol using polymethylhydrosiloxane as an inexpensive, stable and safe reducing agent without an inert atmosphere. A large range of functional groups such as nitro, carboxylic acid, acetyl, nitrile, halogen, methoxy, alkene and heterocycles were well tolerated. $AlCl_3$ also catalyzed tandem amination–amidation of 2-carboxybenzaldehyde with different amines to afford N-substituted isoindolinones. The catalyst can be recycled at least three times without any significant effect on activity and selectivity.

Introduction

Substituted amines are important building blocks for natural products, pharmaceuticals and agrochemicals (Fig. 1).[1] Owing to the immense importance of amines, their synthesis is an active field in medicinal chemistry and modern organic synthesis.[2] For the synthesis of substituted amines, methods involving imine reduction/direct reductive amination of carbonyl compounds remain the simplest approach.[2] Mainly, precious metal based catalysts such as Au, Pd, Pt, Rh, Ir, Ru, Re have been applied for this transformation.[2,3] Most of these precious metals are toxic and at a high risk of depletion, which is the continuous driving force for the development of abundantly available bio-relevant metal based catalysts. Although a few methods involving the use of abundant metal catalysts such as $Zn(ClO_4)_2{\cdot}6H_2O$,[4] $FeCl_3$,[5] $Zn(OTf)_2$,[6] and $Cu(OAc)_2$ [7] have been developed, the use of excess amounts of the catalyst, hydrogen sources and non-eco-friendly solvents limits the scope of these methods. Most of these methods are not efficient for reductive amination of acetophenone derivatives, generally considered challenging substrates for this reaction.[4,5]

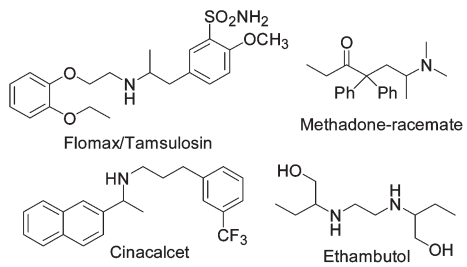


Fig. 1 Selected examples of therapeutically important substituted amines.

Aluminium is the most abundant metal in the earth's crust and has been explored as a catalyst for Lewis acid catalyzed organic transformations,[8] but has not been applied for reductive amination of carbonyl compounds. We have recently reported cobalt(II) phthalocyanine (CoPc) catalyzed reductive amination of carbonyl compounds using Ph_2SiH_2 as a silylating agent in ethanol.[9] Using an inexpensive metal with a green solvent was inspiring; the use of an abundantly available, inexpensive, stable and safe catalyst/reducing agent,[10] such as $AlCl_3$/polymethylhydrosiloxane (PMHS), could make the method highly attractive from a green catalysis point of view. Also, polysiliconates obtained as byproducts during hydrosilylation with PMHS are precursors of porous derivatives useful for absorbent properties.[11]

In continuation of our work on development of green reduction processes using abundantly available metal catalysts,[9,12] here we disclose $AlCl_3$ as a highly efficient catalyst for chemoselective reductive amination of carbonyl compounds and synthesis of N-substituted isoindolinones in ethanol using PMHS without applying an inert atmosphere.

Results and discussion

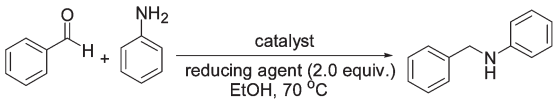
In our recent report on CoPc catalyzed reductive amination of carbonyl compounds, it was observed that the Lewis acidic character of CoPc played an important role in catalyzing the reaction.[9] In view of this point, it was further envisaged that stronger Lewis acidic Al based catalysts could catalyze this reaction more efficiently. For this, firstly the reductive amination of benzaldehyde with aniline was carried out in the presence of different hydrogen sources using various Al salts as the catalyst. Amongst the different catalysts, $AlCl_3$ (anhydrous) and $AlCl_3{\cdot}6H_2O$ were found to be most active at 70 °C with highest yield in the former

Natural Plant Products Division, CSIR-Institute of Himalayan Bioresource Technology, Palampur, H.P. 176001, India. E-mail: neerajnpp@rediffmail.com, neeraj@ihbt.res.in; Fax: (+)91-1894-230433; Tel: (+)91-1894-230426

† IHBT Communication No. 2401.

‡ Electronic supplementary information (ESI) available. See DOI: 10.1039/c2gc36305d

Table 1 Optimization of catalyst and reducing agent[a]



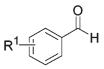
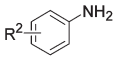
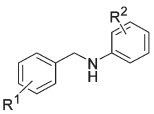
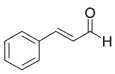
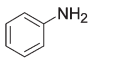
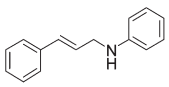
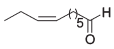
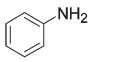
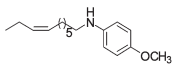
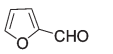
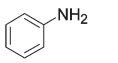
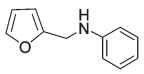
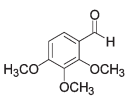
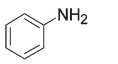
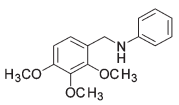
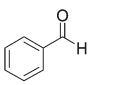
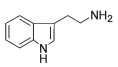
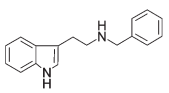
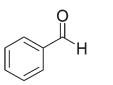
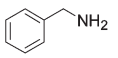
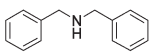
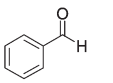
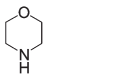
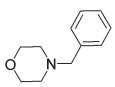
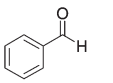
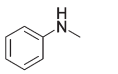
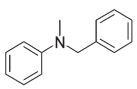
Entry	Catalyst	Quantity (mol%)	Reducing agent	Yield[b] (%)
1	$AlCl_3$	0.5	PMHS	57
2	$AlCl_3$	1.0	PMHS	71
3	$AlCl_3$	2.0	PMHS	>99
4	$AlCl_3$	3.0	PMHS	98
5	$AlCl_3$	5.0	PMHS	99
6[c]	$AlCl_3$	5.0	PMHS	NR
7	AlPc	5.0	PMHS	35
8	Al_2O_3 (acidic)	5.0	PMHS	8
9	Al_2O_3 (neutral)	5.0	PMHS	12
10	Al_2O_3 (basic)	5.0	PMHS	14
11	$Al_2(SO_4)_3$	5.0	PMHS	6
12	$AlCl_3{\cdot}6H_2O$	5.0	PMHS	82
13	$Al(NH_4)(SO_4)$	5.0	PMHS	16
14	—		PMHS	NR
15[d]	$AlCl_3$	2.0	$PhSiH_3$	97
16[d]	$AlCl_3$	2.0	Ph_2SiH_2	94
17[d]	$AlCl_3$	2.0	Ph_3SiH	96
18	$AlCl_3$	2.0	Et_3SiH	<5
19	$AlCl_3$	2.0	$(CH_3)_2CHOH$	10
20	$AlCl_3$	2.0	$HCOONH_4$	13
21	$AlCl_3$	2.0	—	NR

[a] Reaction conditions: all reactions were carried out with benzaldehyde (1 mmol) and aniline (1 mmol) in EtOH (5 mL) at 70 °C for 12 h. [b] Yield based on GC-MS analysis of the reaction mixture. [c] The reaction was carried out at room temperature. NR = no reaction. [d] The reaction was carried out for 1 h.

case (Table 1, entries 3 and 12). No reaction was observed at room temperature (Table 1, entry 6). Aluminium phthalocyanine (AlPc) and other aluminium salts under the same reaction conditions were not able to provide comparable yields of the desired product (Table 1, entries 7–11 and 13). Comparable yields were recorded with PMHS, $PhSiH_3$, Ph_2SiH_2 and Ph_3SiH in the presence of $AlCl_3$ (Table 1, entries 4 and 15–17). Although the reaction with phenylsilanes was very fast as compared to PMHS, PMHS was selected for further studies, considering the cost and safety factors. Et_3SiH, isopropanol and ammonium formate gave the desired product in very low yields (Table 1, entries 18–20). As expected, no reaction was observed in the absence of a catalyst or a reducing agent showing the necessity of both (Table 1, entries 14 and 21).

With optimized reaction conditions, the scope of the method was explored by carrying out the reductive amination of different aldehydes with various amines (Table 2). The $-NO_2$ group is highly susceptible to reduction,[3i,13] however, in the present case the reductive amination of 2-nitro and 4-nitrobenzaldehyde with aniline afforded the desired products in good to high yields leaving the aromatic nitro group unaltered (Table 2, entries 2 and 3). One of the major problems associated with reductive amination is intolerance of C=C bonds,[14] however, in the present case >99% chemoselectivity was observed with conjugated as well as isolated C=C bonds containing aldehydes (Table 2, entries 13 and 14). Functional groups such as chloro, bromo and cyano present on the aldehyde remained unaffected and the

Table 2 Reductive amination of different aldehydes with amines[a]

Entry	Aldehyde	Amine	Product	Yield[b] (%)
				
1	R^1 = H	R^2 = H		95[c]
2	R^1 = 2-NO_2	R^2 = H		80[c]
3	R^1 = 4-NO_2	R^2 = H		95
4	R^1 = 4-Cl	R^2 = H		91
5	R^1 = 4-Br	R^2 = H		93
6	R^1 = 3-CN	R^2 = H		80
7	R^1 = H	R^2 = 2-I		77
8	R^1 = H	R^2 = 4-F		91
9	R^1 = H	R^2 = 4-NO_2		48
10	R^1 = H	R^2 = 4-CO_2H		64[c]
11	R^1 = H	R^2 = 4-$COCH_3$		94[c]
12	R^1 = H	R^2 = 4-OCH_3		92
13				89[c]
14				97
15				92[c]
16				95[c]
17				96
18				80
19				51(91)[d]
20				26(81)[d]

[a] Reaction conditions: aldehyde (1 mmol), amine (1 mmol), $AlCl_3$ (2 mol%), PMHS (2 mmol), EtOH (5 mL) at 70 °C for 12 h. [b] Yield based on GC-MS analysis of the reaction mixture. [c] The reaction was carried out with 1 g of aldehyde and isolated yield is reported. [d] Yield given in parentheses corresponds to the reaction carried out using $PhSiH_3$ (1.5 equiv.) as the reducing agent.

desired products were obtained in high yields (Table 2, entries 4–6). The method was also successful in reductive amination of a heteroaromatic aldehyde, 2-furaldehyde (Table 2, entry 15). Excellent yield and chemoselectivity (>99%) was observed in the case of a polysubstituted aldehyde, 2,3,4-trimethoxybenzaldehyde, with aniline (Table 2, entry 16).

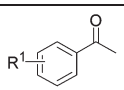
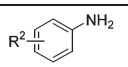
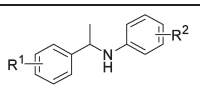
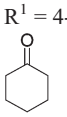
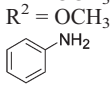
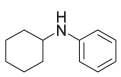
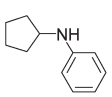
Other amines were also tested for reductive amination under the present reaction conditions. Halogen-substituted amines such as 2-iodo- and 4-fluoroaniline were efficiently utilized for the reductive amination of benzaldehyde (Table 2, entries 7 and 8)

without the formation of any byproduct. The reaction of benzaldehyde with 4-nitroaniline afforded relatively low yield (48%) with high chemoselectivity (Table 2, entry 9). Good to high yields were obtained in the case of functional groups such as carboxylic acid and acetyl on amines, which are generally not considered in reductive amination due to their low reactivity and incompatibility with reducing agents (Table 2, entries 10 and 11).[3a–d] The reaction of benzaldehyde with 4-methoxyaniline gave an excellent yield of the product (Table 2, entry 12). Aliphatic primary amines were also tested and the desired products were obtained in very good yields (Table 2, entries 17 and 18). Secondary amines (aliphatic as well as aromatic) were found to be incompatible with the $AlCl_3$/PMHS system giving a low yield of the product, whereas the $AlCl_3$/$PhSiH_3$ system showed efficient conversion to the desired products (Table 2, entries 19 and 20).

One of the major advantages of the present method is the reductive amination of acetophenones, which are otherwise considered difficult substrates for this reaction resulting in low yields of the products[15] or require higher quantities of the catalyst.[16] Under the present reaction conditions, the reductive amination of different acetophenones with amines afforded the desired products in good to excellent yields (Table 3, entries 1–5). Also, very good yields of products were obtained in the reaction of aliphatic ketones and aniline (Table 3, entries 6 and 7). When the method was applied on larger scales (up to gram scale), with some important substrates containing functional groups such as nitro, carboxylic acid, ketone, alkene, heterocycle, 2,3,4-trimethoxy and bromo (Table 2, entries 2, 10, 11, 13, 15 and 16, Table 3, entries 3 and 4), good isolated yields were obtained in all the cases.

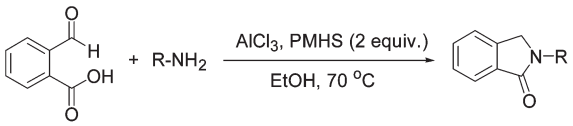
Furthermore, the scope of the method was extended for the synthesis of biologically important[17] N-substituted isoindolinones by tandem amination–amidation of 2-carboxybenzaldehyde.[18] Under the present reaction conditions, a wide range of amines was investigated for tandem amination–amidation of 2-carboxybenzaldehyde to synthesize the corresponding N-substituted isoindolinones (Table 4). Interestingly, both aromatic and aliphatic amines produced the corresponding isoindolinones in good to excellent yields. The reaction with aniline afforded the desired isoindolinone in excellent yield (Table 4, entry 1). Aromatic amines having electron-donating substituents such as 4-OCH_3, 4-CH_3 and 4-I gave good yields of the desired products (Table 4, entries 2–4). In the reaction of 4-nitroaniline high chemoselectivity was observed and the desired product was obtained in good yield (Table 4, entry 5). Amines with strongly electron-withdrawing substituents like 4-$COCH_3$ generally give low yields of the product,[13] but, in the present case, the reaction of 4-acetylaniline proceeded smoothly to give high yields of the product (Table 2, entry 6). The effect of steric hindrance was seen in the reaction of *o*-substituted anilines giving the desired product in comparatively lower yields (Table 4, entries 7 and 8).

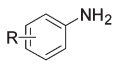
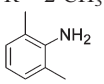
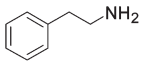
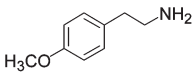
Table 3 Reductive amination of ketones[a]

Entry	Ketone	Amine	Product	Yield[b] (%)
				
1	R^1 = H	R^2 = H		73
2	R^1 = H	R^2 = OCH_3		98
3	R^1 = 4-NO_2	R^2 = OCH_3		83[c]
4	R^1 = 4-Br	R^2 = OCH_3		74[c]
5	R^1 = 4-OCH_3	R^2 = OCH_3		70
6				96
7				89

[a] Reaction conditions: ketone (1 mmol), amine (1 mmol), $AlCl_3$ (2 mol%), PMHS (2 mmol), EtOH (5 mL) at 70 °C for 12 h. [b] Yield based on GC-MS analysis of the reaction mixture. [c] The reaction was carried out with 1 g of ketone and isolated yield is reported.

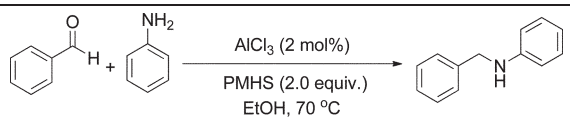
Table 4 $AlCl_3$ catalyzed synthesis of N-substituted isoindolinones[a]



Entry	Amine	Yield[b] (%)
		
1	R = H	96
2	R = 4-OCH_3	96
3	R = 4-CH_3	91
4	R = 4-I	72
5	R = 4-NO_2	78[c]
6	R = 4-$COCH_3$	92[c]
7	R = 2-CH_3	74[c]
8		62
9		95
10		98

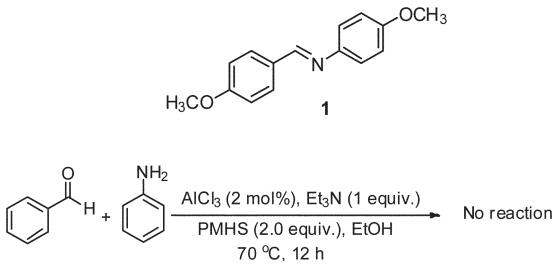
[a] Reaction conditions: ketone (1 mmol), amine (1 mmol), $AlCl_3$ (2 mol%), PMHS (2 mmol), EtOH (5 mL) at 70 °C for 12 h. [b] Isolated yield. [c] Yield based on GC-MS analysis of the reaction mixture.

Table 5 Recyclability of the catalyst



Cycle	1st	2nd	3rd	4th
Yield[a] (%)	>99	92	94	65

[a] Yield based on GC-MS analysis of the reaction mixture.



Scheme 1 Preferential interaction of Al(III) with Et_3N leading to no reaction.

Excellent yields were obtained with aliphatic amines (Table 4, entries 9 and 10).

The reusability study of the catalyst on the model reaction showed that it can be reused up to three cycles without any loss in catalytic activity (Table 5).

As far as the mechanism of the reaction is concerned, it was proposed in our recent report that Lewis acid–base interaction between CoPc and an imine helps in the activation of the imine towards reduction.[9] Expecting a similar mechanism in the present case, the model reaction was carried out in the presence of triethylamine and no reaction was observed (Scheme 1), which may be due to preferential interaction of Et_3N with Al(III). To further confirm the interaction between $AlCl_3$ and an imine (4-(methoxybenzylidene)-4-methoxyaniline, **1**), a UV-Vis study was carried out. Addition of $AlCl_3$ to an ethanolic solution of **1** resulted in a bathochromic shift in λ_{max} of **1** from 335 nm to 375 nm and the color of the solution changed from colorless to dark yellow confirming the coordination of **1** with $AlCl_3$, which was consistent with the previous reports (for spectra see ESI‡).[19,20] When Et_3N was added to the mixture of the imine (**1**) and $AlCl_3$, the yellow color of the solution as well as the band at λ_{max} 375 nm in the UV-Vis spectrum disappeared and a new band at 342 nm for free imine was observed due to preferential coordination of Et_3N with Al(III). The observation of low yield in the case of amines with strong electron-withdrawing groups such as $–NO_2$, $–CO_2H$ *etc.* may be due to lesser Lewis basic character of the corresponding imines, which further supports the crucial role of Lewis acid–base interaction in catalyzing the reaction (Table 2, entries 9 and 10). Also, Lewis acids are known to activate hydrosilanes for hydride transfer. To confirm this, the reaction of PMHS with $AlCl_3$ in ethanol was carried out for 12 h and analyzed by ^1H NMR. The appearance of new peaks at δ 3.8 (2H) and 1.2 (3H) corresponding to Si–OEt and the decrease in intensity of the peak at δ 4.7 for Si–H confirmed the activation of PMHS by $AlCl_3$. This observation provides evidence for the consumption of PMHS under the action of $AlCl_3$. On the basis of the above observations, it can be proposed that $AlCl_3$ activates imine through Lewis acid–base interaction and also helps in the hydride transfer to imine.

Conclusions

An $AlCl_3$ catalyzed novel method has been reported for the synthesis of substituted amines and isoindolinones through reductive amination of carbonyl compounds with amines. Use of an eco-friendly hydrogen source and solvent with a low loading of recyclable abundant metal catalyst under ambient reaction conditions makes the present method superior to earlier reported methods in terms of environment safety and economy. In addition, there was no requirement of an inert atmosphere making the current method more economical and simple. Other remarkable advantages of this methodology include high isolated yields, clean reactions and easy work-up procedures.

Experimental section

General

$AlCl_3$ was purchased from Fisher Scientific India Pvt. Ltd (Acros Organics). Silica gel (60–120 mesh) used for column chromatography was purchased from Sisco Research Laboratories Pvt. Ltd India and all other chemicals were purchased from Spectrochem, India, Merck, Germany, and Sigma-Aldrich, USA and were used without further purification. NMR spectra were recorded on a Bruker Avance-300 spectrometer. Mass spectra were recorded on a QTOF-Micro of Waters Micromass and Maxis-Bruker. The GC-MS analysis was carried out on a Shimadzu (QP 2010) series Gas Chromatogram-Mass Spectrometer (Tokyo, Japan), an AOC-20i auto-sampler coupled, and a DB-5MS capillary column (30 m × 0.25 mm i.d., 0.25 μm). The initial temperature of the column was 70 °C held for 4 min and was programmed to 230 °C at 4 °C min^{-1}, then held for 15 min at 230 °C; the sample injection volume was 2 μl in GC grade dichloromethane. Helium was used as the carrier gas at a flow rate of 1.1 ml min^{-1} on split mode (1 : 50). UV-Vis spectra were recorded on a UV-Vis 2450 spectrophotometer from Shimadzu.

General experimental procedure for reductive amination of carbonyl compounds catalyzed by the $AlCl_3$/PMHS system

To a stirred suspension of $AlCl_3$ (0.02 mmol) in ethanol (4 mL) were added carbonyl compound (1.0 mmol), amine (1.0 mmol) and PMHS (2.0 H equiv.) at room temperature and then the temperature was raised to 70 °C. On completion of the reaction (as monitored by TLC), the reaction mixture was dried under vacuum and the crude product was analyzed directly by GC-MS. For the purification of the desired product column chromatography was carried out (*n*-hexane : ethyl acetate).

General experimental procedure for synthesis of N-substituted isoindolinones catalyzed by the $AlCl_3$/PMHS system

To a stirred suspension of $AlCl_3$ (0.02 mmol) in ethanol (4 mL) were added 2-carboxybenzaldehyde (1.0 mmol), amine (1.0 mmol) and PMHS (2.0 H equiv.) at room temperature and then the temperature was raised to 70 °C. On completion of the reaction (as monitored by TLC), the reaction mixture was dried under vacuum and the product was purified by crystallization with absolute ethanol.

Experimental procedure for recyclability of the catalyst

The recyclability of the catalyst was studied by carrying out the reductive amination of benzaldehyde with aniline as a test reaction. On completion of the reaction (as monitored by TLC), the reaction mixture was dried under vacuum and the crude product was extracted with ethyl acetate (2 × 5 mL). The residue left was dried under vacuum for 15 min. Successive reactions were carried out by sequential addition of fresh substrates, PMHS and ethanol to the crude remains after extracting the product.

Acknowledgements

The authors are grateful to Dr P. S. Ahuja, Director of the Institute, for encouragement and support. VK, SS and US also thank UGC and CSIR, New Delhi, India for granting research fellowships.

Notes and references

1 (*a*) A. W. Czarnik, *Acc. Chem. Res.*, 1996, **29**, 112–113; (*b*) J. P. Wolfe, S. Wagav, J. F. Marcoux and S. L. Buchwald, *Acc. Chem. Res.*, 1998, **31**, 805–818; (*c*) T. C. Nugent and M. El-Shazly, *Adv. Synth. Catal.*, 2010, **352**, 753–819.

2 For reviews see: (*a*) N. Fleury-Bregeot, V. De La Fuente, S. Castillon and C. Claver, *ChemCatChem*, 2010, **2**, 1346–1371; (*b*) J. H. Xie, S. F. Zhu and Q. L. Zhou, *Chem. Rev.*, 2011, **111**, 1713–1760; (*c*) R. P. Tripathi, S. S. Verma, J. Pandey and V. K. Tiwari, *Curr. Org. Chem.*, 2008, **12**, 1093–1115.

3 (*a*) Y. Yamane, X. Liu, A. Hamasaki, T. Ishida, M. Haruta, T. Yokoyama and M. Tokunaga, *Org. Lett.*, 2009, **11**, 5162–5165; (*b*) D. Gnanamgari, A. Moores, E. Rajaseelan and R. H. Crabtree, *Organometallics*, 2007, **26**, 1226–1230; (*c*) D. Imao, S. Fujihara, T. Yamamoto, T. Ohta and Y. Ito, *Tetrahedron*, 2005, **61**, 6988–6992; (*d*) V. I. Tararov, R. Kadyrov, T. H. Riermeierc and A. Borner, *Chem. Commun.*, 2000, 1867–1868; (*e*) E. Byun, B. Hong, K. A. De Castro, M. Lim and H. Rhee, *J. Org. Chem.*, 2007, **72**, 9815–9817; (*f*) B. Sreedhar, P. S. Reddy and D. K. Devi, *J. Org. Chem.*, 2009, **74**, 8806–8809; (*g*) A. Robichaud and A. N. Ajjau, *Tetrahedron Lett.*, 2006, **47**, 3633–3636; (*h*) B. Li, J. B. Sortais, C. Darcel and P. H. Dixneuf, *ChemSusChem*, 2012, **5**, 396–399; (*i*) L. Hu, X. Cao, D. Ge, H. Hong, Z. Guo, L. Chen, X. Sun, J. Tang, J. Zheng, J. Lu and H. Gu, *Chem.–Eur. J.*, 2011, **17**, 14283–14287.

4 (*a*) O. Y. Lee, K. L. Law, C. Y. Ho and D. Yang, *J. Org. Chem.*, 2008, **73**, 8829–8837; (*b*) O. Y. Lee, K. L. Law and D. Yang, *Org. Lett.*, 2009, **11**, 3302–3305.

5 S. Enthaler, *ChemCatChem*, 2010, **2**, 1411–1415.

6 S. Werkmeister, S. Fleischer, S. Zhou, K. Junge and M. Beller, *ChemSusChem*, 2012, **5**, 777–782.

7 S. Werkmeister, K. Junge and M. Beller, *Green Chem.*, 2012, **14**, 2371–2374.

8 (*a*) A. Kamal, M. N. A. Khan, K. S. Reddy, Y. V. V. Srikanth and T. Krishnaji, *Tetrahedron Lett.*, 2007, **48**, 3813–3818; (*b*) S. H. Cho, N. D. Walther, S. T. Nguyen and J. T. Hupp, *Chem. Commun.*, 2005, 5331–5333; (*c*) D. B. G. Williams, M. L. Shaw, M. J. Green and C. W. Holzapfel, *Angew. Chem.*, 2008, **120**, 570–573; (*d*) G. Rajagopal, S. S. Kim and S. C. George, *Appl. Organomet. Chem.*, 2007, **21**, 198–202; (*e*) D. B. G. Williams and M. Lawton, *Org. Biomol. Chem.*, 2005, **3**, 3269–3272; (*f*) D. B. G. Williams and M. C. Lawton, *Green Chem.*, 2008, **10**, 914–917.

9 V. Kumar, U. Sharma, P. K. Verma, N. Kumar and B. Singh, *Adv. Synth. Catal.*, 2012, **354**, 870–878.

10 M. Suguro, Y. Yamamura, T. Koike and A. Mori, *React. Funct. Polym.*, 2007, **67**, 1264–1276.

11 H. Mimoun and S. A. Firminich, *Pat.*, WO 00/37540 A1.

12 (*a*) U. Sharma, P. Kumar, N. Kumar, V. Kumar and B. Singh, *Adv. Synth. Catal.*, 2010, **352**, 1834–1840; (*b*) U. Sharma, P. K. Verma, N. Kumar, V. Kumar, M. Bala and B. Singh, *Chem.–Eur. J.*, 2011, **17**, 5903; (*c*) P. K. Verma, U. Sharma, N. Kumar, M. Bala, V. Kumar and B. Singh, *Catal. Lett.*, 2012, **142**, 907–913; (*d*) U. Sharma, N. Kumar, P. K. Verma, V. Kumar and B. Singh, *Green Chem.*, 2012, **14**, 2289–2293.

13 L. Shi, J. Wang, X. Cao and H. Gu, *Org. Lett.*, 2012, **14**, 1876–1879.

14 V. A. Tarasevich and N. G. Kozlov, *Russ. Chem. Rev.*, 1999, **68**, 55–72.

15 B. T. Cho and S. K. Kang, *Tetrahedron*, 2005, **61**, 5725–5734.

16 R. Apodaca and W. Xiao, *Org. Lett.*, 2001, **3**, 1745–1748.

17 (*a*) F. A. Luzzio, A. V. Mayorov, S. S. W. Ng, E. A. Kruger and W. D. Figg, *J. Med. Chem.*, 2003, **46**, 3793–3799; (*b*) W. T. Jiaang, Y. S. Chen, T. Hsu, T. H. Wu, C. H. Chien, C. N. Chang, S. P. Chang, S. J. Lee and X. Chen, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 687–691; (*c*) G. W. Muller, R. Chen, S. Y. Huang, L. G. Corral, L. M. Wong, R. T. Patterson, Y. Chen, G. Kaplan and D. I. Stirling, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1625–1630; (*d*) I. Takahashi, E. Hirano, T. Kawakami and H. Kitajima, *Heterocycles*, 1996, **43**, 2343–2346; (*e*) P. L. McCarthy, K. Owzar and C. C. Hofmeister, *N. Engl. J. Med.*, 2012, **366**, 1770–1781.

18 In our recent report on CoPc catalyzed highly chemoselective reductive amination of carbonyl compounds, we discovered a new route for the synthesis of N-substituted isoindolinone from 2-carboxybenzaldehyde.[8] The generality and extended scope of the CoPc catalyzed method for the synthesis of various isoindolinone derivatives has been submitted for publication elsewhere.

19 (*a*) X. Liu, W. Gao, Y. Mu, G. Li, L. Ye, H. Xia, Y. Ren and S. Feng, *Organometallics*, 2005, **24**, 1614–1629; (*b*) W. Yao, Y. Mu, A. Gao, W. Gao and L. Ye, *Dalton Trans.*, 2008, 3199–3206; (*c*) X. Liu, H. Xia, W. Gao, L. Ye, Y. Mu, Q. Su and Y. Ren, *Eur. J. Inorg. Chem.*, 2006, 1216–1222.

20 D. Malesev and V. Kuntic, *J. Serb. Chem. Soc.*, 2007, **72**, 921–939.

