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Cite this: *RSC Adv.*, 2015, 5, 2292

Received 18th November 2014  
Accepted 28th November 2014

DOI: 10.1039/c4ra14808h

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## Reductive amination using a combination of CaH<sub>2</sub> and noble metal†

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Amines were prepared by a reductive amination reaction in the presence of calcium hydride and Pt/C. The *in situ* formation of water seems to be the key to activate CaH<sub>2</sub> to reduce the intermediate imine.

Occurring in nature, amines are important building blocks in organic synthesis.<sup>1</sup> One way amongst others to prepare these compounds is the reductive amination reaction. This transformation, which supposes the reaction between a carbonyl and an amine then the reduction of the intermediate imine, is already well described.<sup>2</sup> Two main approaches are considered for the reductive amination: the first one supposes the formation of the imine before the addition of the reducing agent and in the second one all the reactants are present at the beginning of the reaction.<sup>3</sup> To perform this reaction several reducing agents have been employed: the most used are sodium borohydride derivatives<sup>4</sup> and hydrogen.<sup>5,6</sup> Unfortunately, it is well established now that even if boron and aluminium hydrides are efficient for the reduction of organic functions they should be substituted for security and environmental reasons. Hydrosilanes and hydrosiloxanes<sup>7</sup> or formates<sup>8</sup> have been associated with a metal complex or with an organocatalyst to realize reductive amination. Several reports are also dealing with Hantzsch esters.<sup>9</sup> Recently, amines were prepared *via* a hydrogen autotransfer in the presence of a metal catalyst.<sup>10</sup>

In the course to find alternative reducing agents to aluminium and boron hydrides, we have previously developed

several methods to reduce organic functions with 1,1,3,3-tetra-methylsiloxane (TMDS)<sup>11</sup> and hypophosphite derivatives.<sup>12</sup> After an analysis of the literature data, we were curious to notice that the calcium hydride was poorly explored for the reduction of organic functions. In fact, the calcium hydride alone is reported to reduce disulfide,<sup>13</sup> carbon monoxide<sup>14</sup> or tetrafluorosilane at temperatures up to 200 °C.<sup>15</sup> With a mechanical activation hexachlorobenzene could be dehalogenated and in the presence of a chelating agent silanes were prepared.<sup>16</sup> In an ionic liquid, AlCl<sub>3</sub>-Et<sub>3</sub>SBr, benzophenone was reduced.<sup>17</sup> The reduction of ketones and imines were performed with Lewis acids such as zinc halides with chlorosilane or Ti(Oi-Pr)<sub>4</sub>.<sup>18</sup> The authors generally mentioned the low reactivity of calcium hydride.<sup>19</sup> Probably for this reason, Harder reported the synthesis of an organic calcium hydride complex which is able to reduce several organic functions.<sup>20</sup>

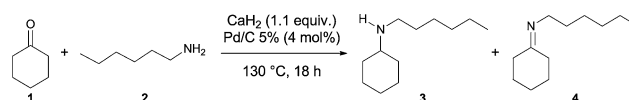
In our laboratory, we observed that the reaction of a 1 : 1 molar ratio of cyclohexanone **1** and hexylamine **2** in the presence of 4 mol% of Pd/C and 1.1 equivalent of CaH<sub>2</sub> at 130 °C in a sealed tube afforded the *N*-hexylcyclohexylamine **3** (Scheme 1). More precisely, analysis of the crude showed a complete conversion of the starting material toward the formation of several products (Fig. 1). The two major products were identified by GC-MS as *N*-hexylcyclohexylamine **3** and *N*-hexylcyclohexylimine **4**. The di- or tri-substituted amine **5**, **7** and **8** were formed from hexylamine by condensation reactions. The formation of bicyclic compounds **9** came from aldol reactions. The compounds **6** were identified as products from dehydrogenation reaction. This dehydrogenation reaction was already described in the presence of Pd/C including by our group.<sup>21</sup>

In order to increase the selectivity of the reaction, the different parameters were modified. A decrease of the

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c4ra14808h

‡ Carole Guyon held a doctoral fellowship from La Région Rhône-Alpes financed to the amount of 32 116 euros. The authors are grateful for the access to the MS analysis at the Centre Commun de Spectroscopie de Masse and NMR facilities at the Université Lyon 1.



Scheme 1 Reductive amination of cyclohexanone and hexylamine.

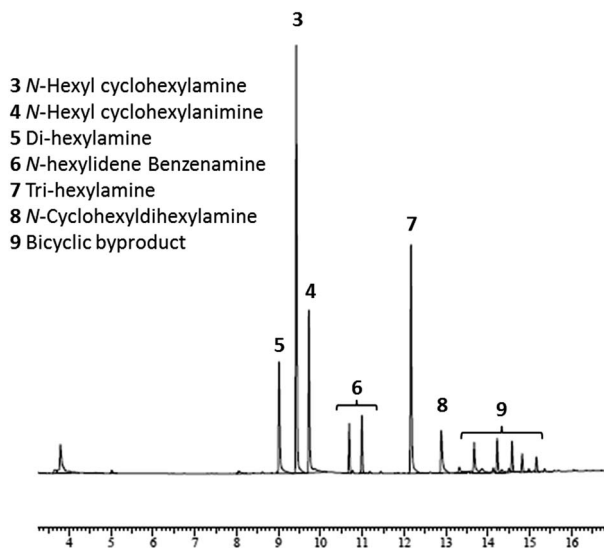
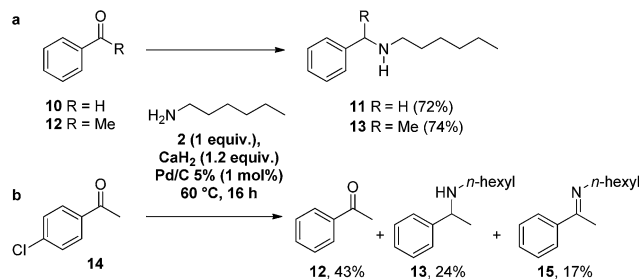


Fig. 1 Gas chromatogram of the crude.

temperature (60 °C) and the load of the catalyst (1 mol% of Pd/C) allowed the isolation of the compound 3 with 68% yield. These conditions were then applied to the formation of amines from benzaldehyde 10 or acetophenone 12 (Scheme 2a). The reaction of benzaldehyde 10 and hexylamine 2 gave the corresponding amine 11 with a 72% of isolated yield. Similar results were obtained with acetophenone 12 as compound 13 was isolated with 74% yield.

When chloride derivative 14 reacted with hexylamine the desired product was not formed. Only dehalogenated compounds 12, 13 and 15 were obtained as shown in Scheme 2b. As a consequence, the parameters of the reaction were investigated. The reductive amination of benzaldehyde 10 and hexylamine 2 in the presence of calcium hydride (1.2 equiv.), Pd/C (1 mol%), 60 °C, 16 h led to the incomplete reduction of the formed imine 16 (8% GC yield), the formation of the amine 11 (72% GC yield) and toluene 17 (9% GC yield). The reduction of CaH<sub>2</sub> equivalent from 1.5 to 0.6 did not affect the conversion into the amine 11 and reduced the formed quantity of imine (5% GC yield) and toluene (5% GC yield).

In order to reduce the amount of toluene 17, metal catalysts were screened with calcium hydride (60 mol%), metal (1 mol%) at 60 °C for 16 h (Table 1). With Ru/C the conversion of



Scheme 2 (a) Reductive amination of carbonyls; (b) limitation of the reductive amination reaction.

benzaldehyde 10 into imine 16 was complete however reduction of the *in situ* formed imine 16 yielded only 5% of amine 11 (Table 1, entry 1). The reductive amination in the presence of palladium or platinum catalysts led to the formation of the amine 11 with 71–79% GC yields (Table 1, entries 2–6). The platinum catalysts had the advantage to afford less toluene 17 than palladium catalysts respectively 2% against 5–10% GC yields. The conditions using Pt/SiO<sub>2</sub> as catalyst were applied to the reductive amination of acetophenone 12 and hexylamine 2. After 16 h, only 45% GC yield of the corresponding amine 13 was observed (Table 1, entry 9). Screening of the catalysts showed a strong effect of the support in this case. Palladium and platinum on carbon led to the complete conversion of acetophenone 12 and 76–77% GC yields into the amine 13 against 37–45% with palladium and platinum on silica (Table 1, entries 7–10). In addition, with palladium on silica incomplete conversion of acetophenone 12 was observed while with platinum on silica 20% GC yield of unreduced imine 15 was detected with 21% GC yield of 1-phenylethanol 20 (Table 1, entries 8 and 9).

The following conditions were retained for the study of the scope and limitations of the reaction: platinum on carbon (1 mol%), CaH<sub>2</sub> (60 mol%), 60 °C for 16 h (Table 2).

Reductive amination of benzaldehyde 10 with benzylamine 21 proceeded with an excellent isolated yield of 87% in dibenzylamine 22 (Table 2, entry 1). The reaction with secondary amines such as dibutylamine 23, morpholine 25 and piperidine 27 afforded the corresponding tertiary amines 24, 26 and 28 with moderate to good isolated yields of 40–82% (Table 2, entries 2–4). The formation of benzyl alcohol 18 (12–17% GC yields), as co-product, was observed when morpholine 25 and piperidine 27 were used (Table 2, entries 3 and 4). The reaction of benzaldehyde 10 with aniline 29, a less nucleophilic amine than aliphatic ones, allowed the formation of 30 with moderate 58% yield (Table 2, entry 5). The benzamide 31, poor nucleophile and poorly soluble, did not react. Benzaldehyde 10 was detected in 84% GC yield after reaction with the formation of 10% GC yield of benzyl alcohol 18 (Table 2, entry 6). The reaction with phenylalanine ester hydrochloride salt 33 led to the amine 34 with 71% isolated yield (Table 2, entry 7). The reaction with ammonium acetate led to the formation of dibenzylamine 22 with 67% isolated yield (Table 2, entry 8). The reactions starting from benzaldehyde 10 and acetophenone 12 as carbonyl compounds gave good isolated yields of respectively 88% and 80% into amine 11 and 13 (Table 2, entries 9 and 11).

*p*-Chlorobenzaldehyde 36 led efficiently to the corresponding product of reductive amination 37 in 67% isolated yield without formation of dehalogenated products. The GC analysis of the crude showed a proportion between amine and imine of 78/22 explaining the moderate yield. The reaction of *p*-nitrobenzaldehyde with hexylamine led to complete conversion of the starting materials and a mixture of imines: imine from *p*-nitrobenzaldehyde with hexylamine and imine from *p*-formylaniline. No product of reductive amination has been observed. After column chromatography, 58% of the *p*-nitrobenzaldehyde was recovered. *p*-Formylbenzaldehyde and *p*-nitrosobenzaldehyde were isolated respectively with 8% and

Table 1 Screening of catalyst

Entry	Metal	Conversion of benzaldehyde <b>10</b>	GC yields <sup>a</sup>			
			Amine <b>11</b>	Imine <b>16</b>	Toluene <b>17</b>	Benzylalcohol <b>18</b>
1	Ru/C	100	5	80	0	2
2	Pd/Al <sub>2</sub> O <sub>3</sub>	100	76	6	5	0
3	Pd/C	100	71	5	5	0
4	Pd/SiO <sub>2</sub>	100	71	5	10	0
5	Pt/SiO <sub>2</sub>	100	79	3	2	1
6	Pt/C	100	73	4	2	0
		Conversion of acetophenone <b>12</b>	GC yields <sup>a</sup>			
			Amine <b>13</b>	Imine <b>15</b>	Ethylbenzene <b>19</b>	1-Phenylethanol <b>20</b>
7	Pd/C	100	76	0.5	N.D.	0
8	Pd/SiO <sub>2</sub>	66	37	4	N.D.	12
9	Pt/SiO <sub>2</sub>	96	45	20	N.D.	21
10	Pt/C	100	77	4	N.D.	7

<sup>a</sup> GC yields were determined by GC using dodecane as internal standard; N.D. = not determined.

18% yield. Electro donating group on acetophenone such as *para* methoxy did not impair the reactivity with 81% isolated yield of **39** compared with acetophenone where **13** was obtained with 80% yield (Table 2, entries 11 and 12). The reaction in the presence of  $\alpha$ -tetralone **40** led to the amine **41** with an average yield of 62% (Table 2, entry 13). The crude of the reaction contained an important quantity of unreduced imine (GC proportion: amine/imine = 81/19). However, no other side-product was observed. The reductive amination of hexylamine **2** with aliphatic carbonyl compounds such as cyclohexanone **1** and 3-phenylpropionaldehyde **42** proceeded well leading to the corresponding amines **3** and **43** in moderate yields of 62 and 58% (Table 2, entries 14 and 15).

The reductive amination of *p*-cyanobenzaldehyde **44** with hexylamine **2** in toluene under the optimized conditions did not lead to the expected product of reductive amination but led to the diamine **45** resulting from the pinacol reaction of the intermediate imine (Scheme 3). The diamine **45** was isolated with 73% yield as a mixture of *rac/meso* mixture in a 50/50 ratio. This family of diamines have already been observed in the radical reduction of imines of *p*-cyanobenzaldehyde **44** by NaTeH<sup>22</sup> or by sodium metal.<sup>23</sup> More generally, the pinacol reaction of imine can take place in the presence of Zn/TMSCl.<sup>24</sup> This method has been applied to the synthesis of ligand (*R,R*)- and (*S,S*)-*N,N'*-dimethyl-1,2-diphenylethylene-1,2-diamine on 10 g scale.<sup>25</sup> Recently, this method has been selected for the synthesis on 100 g.<sup>26</sup>

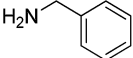
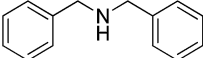

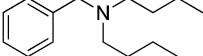
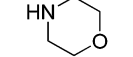
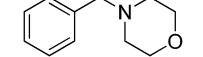
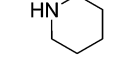
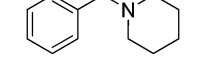
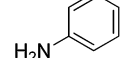
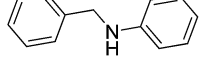
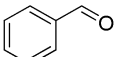
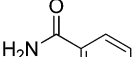
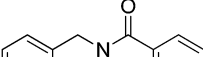
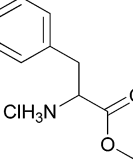
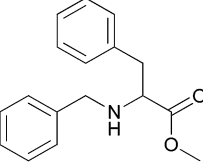
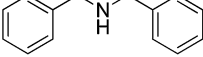
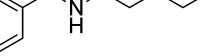
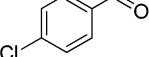
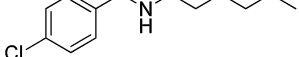
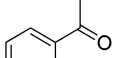
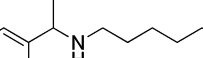
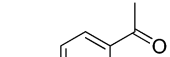

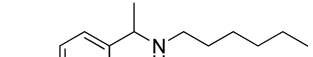
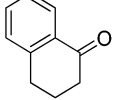
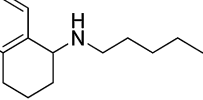

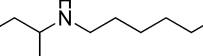
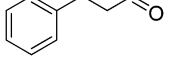
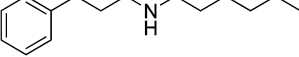
From 2,6-dimethylcyclohexanone **46** (83/17 *cis/trans* mixture) two diastereoisomers **47A** and **47C** were isolated respectively in 23% and 25% yield (Scheme 4). Three different products could have been obtained: two diastereoisomers (**47A** and **47B**) and one pair of enantiomers (**47C**). **47A** and **47C** had been assigned

thanks to carbon and NOESY RMN<sup>27</sup> and supported by the literature.<sup>28</sup>

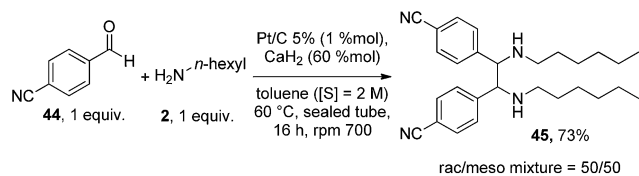
The monomethylation of amines is a challenge in spite of the number of pathways.<sup>29</sup> The alkylation reaction remains difficult as the monomethylated product is more reactive than the starting materials.<sup>30</sup> Reductive amination reactions issue from Eschweiler-Clarke reaction often affords a mixture of products.<sup>31</sup> In this case, under the optimized conditions in toluene (1 M) in the presence of Pt/C and CaH<sub>2</sub>, the reaction of para-formaldehyde **48** (1 equiv.) and hexylamine (1.06 equiv.) gave a mixture of hexylamine **2** (11%), *N*-methylhexylamine **49** (67%) and *N,N*-dimethylhexylamine **50** (22%) with a global yield of 95% (Scheme 5). The products have not been separated. The distillation is difficult due to close boiling points: hexylamine **2** (130 °C), *N*-methylhexylamine **49** (135 °C), *N,N*-dimethylhexylamine **50** (145 °C). Even if the major product is the monomethylated and this result is similar to the literature, the selectivity should be improved.

A mechanism is proposed to explain these results (Scheme 6). The amine reacts with the carbonyl group to form the corresponding imine after elimination of water. The water would then react with calcium hydride to release one molecule of hydrogen. The hydrogen could be adsorbed on the metal catalyst and hydrogenate the *in situ* formed imine into amine. A control experiment was carried out on the reductive amination of benzaldehyde and hexylamine **2** under the optimized conditions in the absence of Pt/C: CaH<sub>2</sub> (60 mol%), 60 °C. After 16 h, only the imine **16** was observed showing the importance of the catalyst. The reaction of CaH<sub>2</sub> (60 mol%) and Pt/C (1 mol%) on the dry imine **16** at 60 °C for 16 h led to the formation of 44% of the amine **11**. It has been attributed to the presence of water in the Pt/C.<sup>25</sup> It has been observed with different batch of Pt/C.

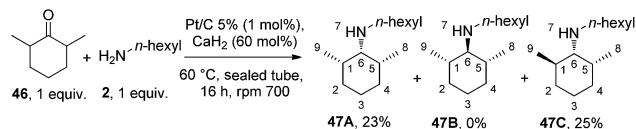
Table 2 Scope of the reductive amination catalyzed by Pt/C

Entry	Carbonyl derivative	Amine	Product	GC yield <sup>a</sup> (%) amine product	Isolated yield (%)
1				22 94	87
2 <sup>b</sup>				24 96	82
3 <sup>b</sup>				26 87	75
4 <sup>b</sup>				28 48	40
5 <sup>b</sup>				30 58	58
6 <sup>c</sup>		10 		32 0	0
7 <sup>b,d,e</sup>				34 N.D. <sup>f</sup>	71
8 <sup>b,d,e</sup>		NH <sub>4</sub> OAc		22 N.D. <sup>f</sup>	67
9				11 89	88
10 <sup>b</sup>		36		37 N.D. <sup>f</sup>	67
11		12		13 77	80
12		38 	2 	39 94	81
13		40		41 N.D. <sup>f</sup>	62
14		1		3 63	62
15		42		43 62	58

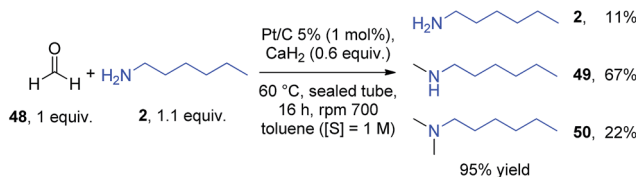
<sup>a</sup> GC yields were determined by GC using dodecane as internal standard. <sup>b</sup> Toluene ([S] = 2 M). <sup>c</sup> Ethyl acetate ([S] = 0.5 M). <sup>d</sup> CaH<sub>2</sub> (1.2 equiv.). <sup>e</sup> 2.2 equiv. of CaH<sub>2</sub>. <sup>f</sup> N.D. = not determined; general conditions: 1 equiv. of carbonyl, 1 equiv. of amine, Pt/C (1 mol%), CaH<sub>2</sub> (60 mol%), 60 °C, sealed tube, 16 h, stirring 700 rpm.



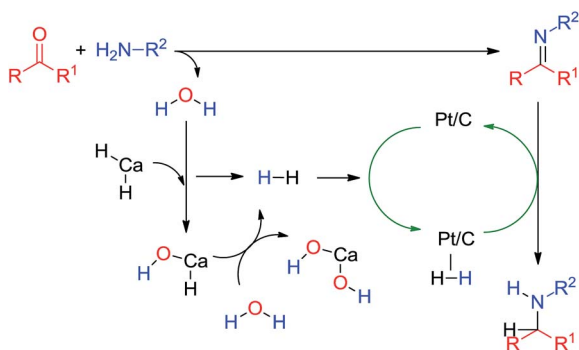
Scheme 3 Reductive amination of *p*-cyanobenzaldehyde with hexylamine.



Scheme 4 Reductive amination of the 2,6-dimethylcyclohexanone with hexylamine.



Scheme 5 Methylation of hexylamine.



Scheme 6 Proposed mechanism.

## Conclusion

We have showed that calcium hydride can be used directly in the reductive amination of carbonyl compounds. The calcium hydride seems to react with the formed water and then liberate hydrogen.  $\text{CaH}_2$  could be considered as a hydrogen reservoir. This hydrogen adsorbed on the metal catalyst could reduce the formed imine. The reaction leads to good yield in amines, however, it is sensitive to the nucleophilicity of the amine and the steric hindrance of the substrates.

This method allows an easy to handle reductive amination without the need of dedicated equipment and selectivity issue due to excess of hydrogen.

## Notes and references

- 1 S. Gomez, J. A. Peters and T. Maschmeyer, *Adv. Synth. Catal.*, 2002, **344**, 1037.
- 2 (a) A. Tarasevich and N. G. Kozlov, *Russ. Chem. Rev.*, 1999, **68**, 55; (b) A. F. Abdel-Magid and S. J. Mehrman, *Org. Process Res. Dev.*, 2006, **10**, 971; (c) R. O. Hutchins, Reduction of  $\text{C}=\text{N}$  to  $\text{CHNH}$  by Metal Hydrides, in *Comprehensive Organic Synthesis*, ed. B. N. Trost and I. Fleming, Pergamon Press, New York, 1991, vol. 8, p. 47; (d) K. S. Hayes, *Appl. Catal.*, A, 2001, **221**, 187; (e) S. G. Ouellet, A. M. Walji and D. W. C. Macmillan, *Acc. Chem. Res.*, 2007, **40**, 1327; (f) V. I. Tararov and A. Börner, *Synlett*, 2005, 203; (g) T. C. Nugent and M. El-Shazly, *Adv. Synth. Catal.*, 2010, **352**, 753; (h) M. Klusmann, *Angew. Chem., Int. Ed.*, 2009, **48**, 7124.
- 3 R. P. Tripathi, S. S. Verma, J. Pandey and V. K. Tiwari, *Curr. Org. Chem.*, 2008, **12**, 1093.
- 4 (a) G. W. Gribble, P. D. Lord, J. Skotnicki, S. E. Dietz, J. T. Eaton and J. L. Johnson, *J. Am. Chem. Soc.*, 1974, **96**, 7812; (b) A. F. Abdel-Magid, C. A. Mayanoff and K. G. Carson, *Tetrahedron Lett.*, 1990, **31**, 5595; (c) A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff and R. D. Shah, *J. Org. Chem.*, 1996, **61**, 3849; (d) E. R. Burkhardt and K. Matos, *Chem. Rev.*, 2006, **106**, 2617; (e) M. D. Bomann, I. C. Guch and M. DiMare, *J. Org. Chem.*, 1996, **60**, 5995; (f) S. Sato, T. Sakamoto, E. Miyazawa and Y. Kikugawa, *Tetrahedron*, 2004, **60**, 7899; (g) S. Yoshida, J. Hayashida, Y. Morinaga, S. Mizobata, A. Okada, K. Kawai, S. Tanoue, T. Nakata, M. Kitayama, A. Ohigashi, M. Matsuura, T. Takahashi, S. Ieda and M. Okada, *Org. Process Res. Dev.*, 2014, **18**, 725; (h) R. F. Borch, M. D. Bernstein and H. D. Durst, *J. Am. Chem. Soc.*, 1971, **93**, 2897.
- 5 (a) M. O. Frederick, S. A. Frank, J. T. Vicenzi, M. E. LeTourneau, K. Derek Berglund, A. W. Edward and C. A. Alt, *Org. Process Res. Dev.*, 2014, **18**, 546; (b) F. Fache, L. Jacquot and M. Lemaire, *Tetrahedron Lett.*, 1994, **35**, 3313; (c) T. Mohy El Dine, S. Chapron, M.-C. Duclos, N. Duguet, F. Popowycz and M. Lemaire, *Eur. J. Org. Chem.*, 2013, 5445; (d) G. S. Vanier, *Synlett*, 2007, 131; (e) N. Levi and R. Neumann, *ACS Catal.*, 2013, **3**, 1915; (f) H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner and M. Studer, *Adv. Synth. Catal.*, 2003, **345**, 103; (g) T. Ikenaga, K. Matsushita, J. Shinozawa, S. Yada and Y. Takagi, *Tetrahedron*, 2005, **61**, 2105; (h) M. Freifelder, *J. Org. Chem.*, 1966, **31**, 3875; (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; (j) T. Ikawa, Y. Fujita, T. Mizusaki, S. Betsuin, H. Takamatsu, T. Maegawa, Y. Monguchi and H. Sajiki, *Org. Biomol. Chem.*, 2012, **10**, 293; (k) S. K. Sharma, J. Lynch, A. M. Sobolewska, P. Plucinski, R. J. Watson and J. M. J. Williams, *Catal. Sci. Technol.*, 2013, **3**, 85.
- 6 (a) W. S. Emerson and H. W. Mohrman, *J. Am. Chem. Soc.*, 1940, **62**, 69; (b) W. S. Emerson and C. A. Ura-neck, *J. Am.*

- Chem. Soc.*, 1941, **63**, 749; (c) Y. Yamane, X. Liu, A. Hamasaki, T. Ishida, M. Haruta, T. Yokoyama and M. Tokunaga, *Org. Lett.*, 2009, **11**, 5162; (d) V. I. Tararov, R. Kadyrov, T. H. Riermeier and A. Börner, *Chem. Commun.*, 2000, 1867; (e) T. Gross, A. M. Seayad, M. Ahmad and M. Beller, *Org. Lett.*, 2002, **4**, 2055; (f) C. Li, B. Villa-Marcos and J. Xiao, *J. Am. Chem. Soc.*, 2009, **131**, 6967; (g) P. Mattei, G. Moine, K. Püntener and R. Schmid, *Org. Process Res. Dev.*, 2011, **15**, 353; (h) S. Werkmeister, K. Junge and M. Beller, *Green Chem.*, 2012, **14**, 2371; (i) M. D. Bhor, M. J. Bhanushali, N. S. Nandurkar and B. M. Bhanage, *Tetrahedron Lett.*, 2008, **49**, 965; (j) S. Fleischer, S. Zhou, K. Junge and M. Beller, *Chem.-Asian J.*, 2011, **6**, 2240; (k) A. Pagnoux-Ozherelyeva, N. Pannetier, M. Diagne Mbaye, S. Gaillard and J.-L. Renaud, *Angew. Chem., Int. Ed.*, 2012, **51**, 4976; (l) S. Moulin, H. Dentel, A. Pagnoux-Ozherelyeva, S. Gaillard, A. Poater, L. Cavallo, J.-F. Lohier and J.-L. Renaud, *Chem.-Eur. J.*, 2013, **19**, 17881.
- 7 [Si] (a) O.-Y. Lee, K.-L. Law, C.-Y. Ho and D. Yang, *J. Org. Chem.*, 2008, **73**, 8829; (b) T. Mizuta, S. Sakaguchi and Y. Ishii, *J. Org. Chem.*, 2005, **70**, 2195; (c) F. Lehmann and M. Scobie, *Synthesis*, 2008, 1679; (d) D. Menche, F. Arikian, J. Li and S. Rudolph, *Org. Lett.*, 2007, **9**, 267; (e) R. Apodaca and W. Xiao, *Org. Lett.*, 2001, **3**, 1745; (f) J. R. Bernardo, S. C. A. Sousa, P. R. Florindo, M. Wolff, B. Machura and A. C. Fernandes, *Tetrahedron*, 2013, **69**, 9145; (g) T. Matsumura and M. Nakada, *Tetrahedron Lett.*, 2014, **55**, 1829; (h) T. Mizuta, S. Sakaguchi and Y. Ishii, *J. Org. Chem.*, 2005, **70**, 2195; (i) F.-M. Gautier, S. Jones, X. Li and S. J. Martin, *Org. Biomol. Chem.*, 2011, **9**, 7860; (j) J. P. Patel, A.-H. Li, H. Dong, V. L. Korlipara and M. J. Mulvihill, *Tetrahedron Lett.*, 2009, **50**, 5975; (k) S. Chandrasekhar, Ch. Raji Reddy and M. Ahmed, *Synlett*, 2000, 1655; (l) S. Enthaler, *Catal. Lett.*, 2011, **141**, 55; (m) H. Jaafar, H. Li, L. C. M. Castro, J. Zheng, T. Roisnel, V. Dorcet, J.-B. Sortais and C. Darcel, *Eur. J. Inorg. Chem.*, 2012, 3546; (n) R. Cano, M. Yus and D. J. Ramón, *Tetrahedron*, 2011, **67**, 8079; (o) V. Kumar, S. Sharma, U. Sharma, B. Singh and N. Kumar, *Green Chem.*, 2012, **14**, 3410; (p) J. Zheng, T. Roisnel, C. Darcel and J.-B. Sortais, *ChemCatChem*, 2013, **5**, 2861.
- 8 (a) R. Leuckart, *Ber. Dtsch. Chem. Ges.*, 1885, **18**, 2341; (b) J. Dalmolen, M. van der Sluis, J. W. Nieuwenhuijzen, A. Meetsma, B. de Lange, B. Kaptein, R. M. Kellogg and Q. B. Broxterman, *Eur. J. Org. Chem.*, 2004, 1544; (c) W. Eschweiler, *Ber. Dtsch. Chem. Ges.*, 1905, **38**, 880; (d) H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, *J. Am. Chem. Soc.*, 1933, **55**, 4571; (e) B. Basu, S. Jha, Md. M. H. Bhuiyan and P. Das, *Synlett*, 2003, 555; (f) E. E. Drinkel, R. R. Campedelli, A. M. Manfredi, H. D. Fiedler and F. Nome, *J. Org. Chem.*, 2014, **79**, 2574; (g) M. Allegretti, V. Berdini, M. Candida Cesta, R. Curti, L. Nicolini and A. Topai, *Tetrahedron Lett.*, 2001, **42**, 4257; (h) V. Berdini, M. C. Cesta, R. Curti, G. D'Anniballe, N. Di Bello, G. Nano, L. Nicolini, A. Topai and M. Allegretti, *Tetrahedron*, 2002, **58**, 5669; (i) E. Byun, B. Hong, K. A. De Castro, M. Lim and H. Rhee, *J. Org. Chem.*, 2007, **72**, 9815.
- 9 (a) G. Li, Y. Liang and J. C. Antilla, *J. Am. Chem. Soc.*, 2007, **129**, 5830; (b) D. Menche and F. Arikian, *Synlett*, 2006, 841; (c) D. Menche, J. Hassfeld, J. Li, G. Menche, A. Ritter and S. Rudolph, *Org. Lett.*, 2006, **8**, 741; (d) Q. P. B. Nguyen and T. H. Kim, *Synthesis*, 2012, 1977.
- 10 Y. Zhang, C.-S. Lim, D. S. Boon Sim, H.-J. Pan and Y. Zhao, *Angew. Chem., Int. Ed.*, 2014, **53**, 1399.
- 11 [Cu], [Bi], [Al] (a) Y.-J. Zhang, W. Dayoub, G.-R. Chen and M. Lemaire, *Green Chem.*, 2011, **13**, 2737; (b) Y.-J. Zhang, W. Dayoub, G.-R. Chen and M. Lemaire, *Eur. J. Org. Chem.*, 2012, 1960; [Mo], [V]; (c) L. Pehlivan, E. Métay, S. Laval, W. Dayoub, D. Delbrayelle, G. Mignani and M. Lemaire, *Eur. J. Org. Chem.*, 2011, 7400; [Pd]; (d) Y. Shi, W. Dayoub, G.-R. Chen and M. Lemaire, *Tetrahedron Lett.*, 2011, **52**, 1281; (e) L. Pehlivan, E. Métay, O. Boyron, P. Demonchaux, G. Mignani and M. Lemaire, *Eur. J. Org. Chem.*, 2011, 4687; [Fe]; (f) L. Pehlivan, E. Métay, S. Laval, W. Dayoub, P. Demonchaux, G. Mignani and M. Lemaire, *Tetrahedron Lett.*, 2010, **51**, 1939; (g) L. Pehlivan, E. Métay, S. Laval, W. Dayoub, P. Demonchaux, G. Mignani and M. Lemaire, *Tetrahedron*, 2011, **67**, 1971; [In]; (h) L. Pehlivan, E. Métay, D. Delbrayelle, G. Mignani and M. Lemaire, *Eur. J. Org. Chem.*, 2012, 4689; (i) L. Pehlivan, E. Métay, D. Delbrayelle, G. Mignani and M. Lemaire, *Tetrahedron*, 2012, **68**, 3151; [Ti]; (j) S. Laval, W. Dayoub, L. Pehlivan, E. Métay, A. Favre-Réguillon, D. Delbrayelle, G. Mignani and M. Lemaire, *Tetrahedron Lett.*, 2011, **52**, 4072; (k) S. Laval, W. Dayoub, A. Favre Réguillon, P. Demonchaux, G. Mignani and M. Lemaire, *Tetrahedron Lett.*, 2010, **51**, 2092; (l) M. Berthod, A. Favre-Réguillon, J. Mohamad, G. Mignani, G. Docherty and M. Lemaire, *Synlett*, 2007, 1545; (m) C. Petit, A. Favre Réguillon, B. Albela, L. Bonneviot, G. Mignani and M. Lemaire, *Organometallics*, 2009, **28**, 6379; (n) C. Petit, E. Poli, A. Favre-Réguillon, L. Khrouz, S. Denis-Quanquin, L. Bonneviot, G. Mignani and M. Lemaire, *ACS Catal.*, 2013, **3**, 1431; (o) S. Laval, W. Dayoub, L. Pehlivan, E. Métay, A. Favre-Reguillon, D. Delbrayelle, G. Mignani and M. Lemaire, *Tetrahedron*, 2014, **70**, 975; (p) S. Laval, W. Dayoub, L. Pehlivan, E. Métay, D. Delbrayelle, G. Mignani and M. Lemaire, *Tetrahedron Lett.*, 2014, **55**, 23.
- 12 (a) C. Guyon, M. Baron, M. Lemaire, F. Popowycz and E. Métay, *Tetrahedron*, 2014, **70**, 2088; (b) M. Baron, E. Métay, M. Lemaire and F. Popowycz, *Green Chem.*, 2013, **15**, 1006; (c) C. Guyon, E. Métay, N. Duguet and M. Lemaire, *Eur. J. Org. Chem.*, 2013, 5439.
- 13 N. S. Gavande, S. Kundu, N. S. Badgular, G. Kaur and A. K. Chakraborti, *Tetrahedron*, 2006, **62**, 4201.
- 14 S. Reich and H. O. Serpek, *Helv. Chim. Acta*, 1920, **3**, 138.
- 15 (a) A. D. Bulanov, V. V. Balabanov, D. A. Pryakhin and O. Yu. Troshin, *Inorg. Mater.*, 2002, **38**, 283; *Neorg. Mater.*, 2002, **38**, 356; (b) G. G. Devyatikh, E. M. Dianov, A. D. Bulanov, O. Yu. Troshin, V. V. Balabanov and D. A. Pryakhin, *Dokl. Chem.*, 2003, **391**, 204; *Dokl. Akad. Nauk*, 2003, **391**, 638; (c) O. Yu. Troshin, A. D. Bulanov, V. S. Mikheev and A. Yu. Lashkov, *Russ. J. Appl. Chem.*, 2010, **83**, 984.

- 16 (a) S. Loisel, M. Branca, G. Mulas and G. Cocco, *Environ. Sci. Technol.*, 1997, **31**, 261; (b) G. Mulas, S. Loisel, L. Schiffrini and G. Cocco, *J. Solid State Chem.*, 1997, **129**, 263; (c) G. Cao, S. Doppiu, M. Monagheddu, R. Orrù, M. Sannia and G. Cocco, *Ind. Eng. Chem. Res.*, 1999, **38**, 3218; (d) G. Cao and R. Orrù, *Chem. Eng. J.*, 2002, **87**, 239; (e) I. Pri-Bar and B. R. James, *J. Mol. Catal. A: Chem.*, 2007, **264**, 135; (f) R. Calas and P. Bourgeois, *Bull. Soc. Chim. Fr.*, 1971, 3263; (g) G. Soula and J.-L. Lepage, FR Patent 2576902, 1985.
- 17 L. Xiao and K. E. Johnson, *Can. J. Chem.*, 2004, **82**, 491.
- 18 (a) T. Aida, N. Kuboki, K. Kato, W. Uchikawa, C. Matsuno and S. Okamoto, *Tetrahedron Lett.*, 2005, **46**, 1667; (b) A. Tshakho, J.-Q. He, M. Mihara, N. Saino and S. Okamoto, *Tetrahedron Lett.*, 2007, **48**, 9120.
- 19 (a) S. Harder, *Chem. Commun.*, 2012, **48**, 11165; (b) S. Harder, *Chem. Rev.*, 2010, **110**, 3852.
- 20 (a) S. Harder and J. Brettar, *Angew. Chem., Int. Ed.*, 2006, **45**, 3474; (b) J. Spielmann and S. Harder, *Chem.–Eur. J.*, 2007, **13**, 8928; (c) J. Spielmann and S. Harder, *Eur. J. Inorg. Chem.*, 2008, 1480.
- 21 M. Sutter, M.-C. Duclos, B. Guicheret, Y. Raoul, E. Métay and M. Lemaire, *ACS Sustainable Chem. Eng.*, 2013, **1**, 1463.
- 22 D. H. R. Barton, L. Bohé and X. Lusinchi, *Tetrahedron Lett.*, 1988, **29**, 2571.
- 23 J. G. Smith and I. Ho, *J. Org. Chem.*, 1973, **38**, 2776.
- 24 A. Alexakis, I. Aujard and P. Mangeney, *Synlett*, 1998, 873.
- 25 A. Alexakis, I. Aujard, T. Kanger and P. Mangeney, *Org. Synth.*, 1999, **76**, 23.
- 26 S. Karlsson, J. Lindberg and H. Sorensen, *Org. Process Res. Dev.*, 2013, **17**, 1552.
- 27 Further information can be found in the ESI.†
- 28 C. L. Barney, E. W. Huber and J. R. McCarthy, *Tetrahedron Lett.*, 1990, **31**, 5547.
- 29 (a) L. Aurelio, R. T. C. Brownlee and A. B. Hughes, *Chem. Rev.*, 2004, **104**, 5823; (b) C. Wu, R. Li, D. Dearborn and Y. Wang, *Int. J. Org. Chem.*, 2012, **2**, 202.
- 30 (a) M. Selva and P. Tundo, *Tetrahedron Lett.*, 2003, **44**, 8139; (b) A. Dhakshinamoorthy, M. Alvaro and H. Garcia, *Appl. Catal., A*, 2010, **378**, 19; (c) T. Lebleu, X. Ma, J. Maddaluno and J. Legros, *Chem. Commun.*, 2014, **50**, 1836.
- 31 R. A. da Silva, I. H. S. Estevamb and L. W. Bieber, *Tetrahedron Lett.*, 2007, **48**, 7680.