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Direct reductive aminations with catalytic molybdenum dioxide dichloride and phenylsilane

Clive A. Smith [a,*], Laura E. Cross [b], Kimberley Hughes [c], Rebecca E. Davis [b], Duncan B. Judd [a], Andrew T. Merritt [a]

[a] Discovery Medicinal Chemistry, GlaxoSmithKline Pharmaceuticals, NFSP-North, Harlow, CM19 5AD, UK
[b] University of Bath, Claverton Down, Bath, BA2 7AY, UK
[c] University of Strathclyde, Glasgow, G1 1XL, Scotland, UK

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ABSTRACT

A powerful direct reductive amination (DRA) method is developed, using catalytic MoO_2Cl_2 and phenylsilane ($PhSiH_3$) as the reducing agent. The alkylation of a range of amines (pK_a 0–7.8) with both an electron-deficient and two electron-rich-aldehydes is achieved in good to excellent yields. The novel employment of this DRA in alcoholic solvents significantly improves the reaction scope and excellent functional group selectivity is exhibited.

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Direct reductive amination (DRA) is a powerful method for the reductive aminoalkylation of aldehydes and ketones with amines by either hydride-type reducing agents,[1] transfer hydrogenation,[2] hydrogenation[3] or by using a silane-containing reducing agent.[4] With the aim of improving the physico-chemical properties of a chemokine lead series, we wanted to carry out the DRA reaction on 4-formylphenylsulfonyl chloride (**1**) prior to any sulfonamide formation. Simple reaction of 4-formylphenylsulfonyl chloride with a variety of aryl amines **2** yields sulfonamides **3** as the major products.[5] In order to change the order of reactivity we envisioned converting **1** into its more stable synthetic equivalent, the pentafluorophenyl (PFP) sulfonate ester **4** (Scheme 1). The subsequent conversion of PFP-sulfonate esters, and more recently 2,4,6-trichlorophenyl (TCP) sulfonate esters,[6] into sulfonamides has been reported by Caddick et al.[7] The criteria for success were to find a reagent and suitable reaction conditions for the desired DRA, whilst minimizing possible sulfonamide formation or reduction of the aldehyde or the PFP-sulfonate ester group of **4**. Furthermore, if the product **5** was a 2° amine it has the possibility to react intermolecularly with a PFP-sulfonate ester group to form a sulfonamide dimer or higher oligomer. Thus, for these DRA reactions, only the 2° amines **6a–c** or the aryl amine **2a** were chosen for use with the PFP-sulfonate ester **4** to yield the higher order amine **5** (65–87%).

Conversion of 4-formylphenylsulfonyl chloride (**1**) into its PFP-sulfonate ester **4** was achieved in excellent yield at low temperature. The gold standard reagent and first choice for DRA reaction is sodium triacetoxyborohydride[1a,b] which was successfully employed for the reactions of this aldehyde **4** with the secondary amines **6a–c** to yield the tertiary benzylamines **5a–c** in good yields (Table 1). These reactions were carried out at room temperature in a chlorinated solvent mixture, under anhydrous conditions and with a slight excess of the 2° amine **6a–c** over the aldehyde **4**. An excess of acetic acid was also employed in order to both promote imine formation and to minimize sulfonamide formation. As the amines **6b** and **6c** were used as their hydrochloride salts, acetonitrile was added to improve their solubility. Carrying out the DRA reaction at room temperature ensured that the possible competing sulfonamide formation was relatively insignificant. With the aryl amine **2a**, the procedure gave only a moderate yield of the DRA product **5d** (Table 1).

Although the sodium triacetoxyborohydride method (Method A) showed reasonable selectivity with the 2° alkylamines, the reaction scope was relatively poor, especially for aromatic amines. As the nucleophilicity of the amine decreases, so does the rate of imine formation and hence the relative rate of aldehyde reduction increases. This suggested the need to find a reducing system, which favoured reduction of an imine over the aldehyde **4**. Recently,

* Corresponding author. Tel.: +44 01992 586639.
E-mail addresses: cliveadriansmith@googlemail.com (C.A. Smith), duncan.b.judd@gsk.com (D.B. Judd).

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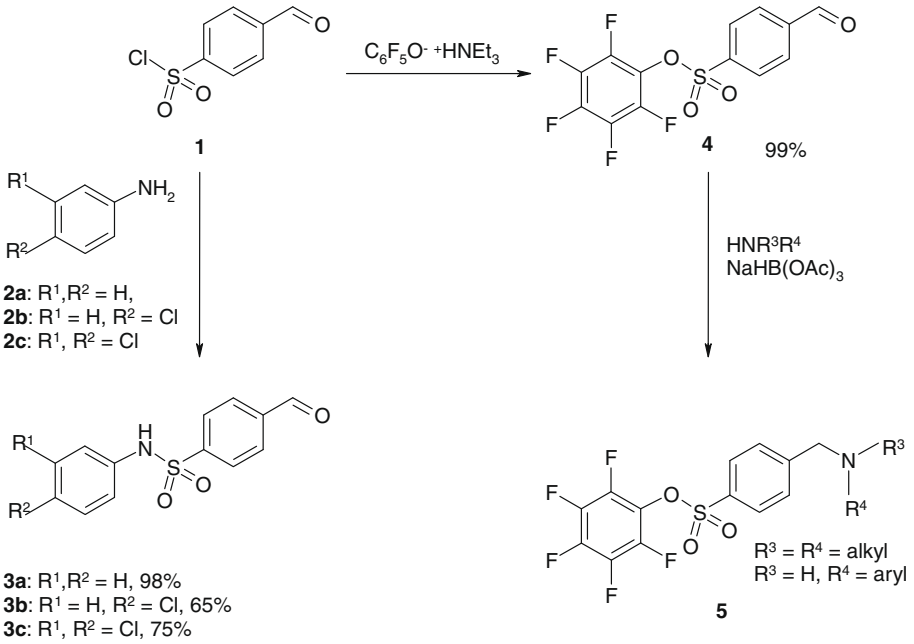
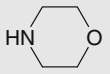
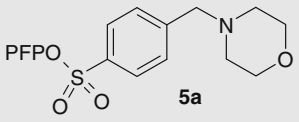
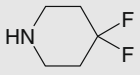
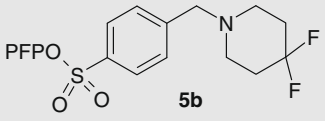
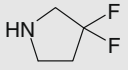
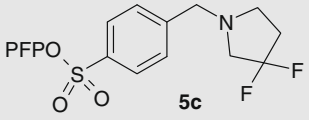
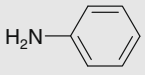
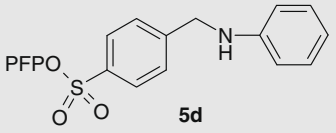


Scheme 1.

Table 1
Direct reductive amination of aldehyde **4** with the 2° amines **6a–c** and aryl amine **2a** using sodium triacetoxyborohydride

Amine	Structure	Product	Yield (%)
6a		 **5a**	69
6b		 **5b**	75[a]
6c		 **5c**	87[b]
2a		 **5d**	65

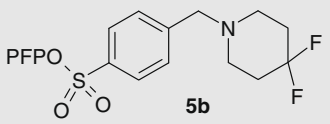
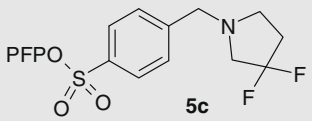
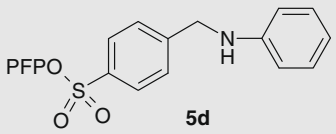
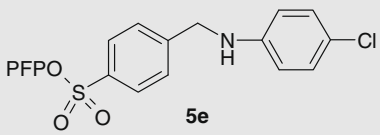
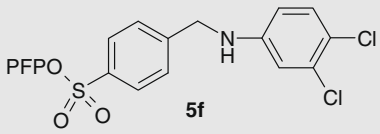
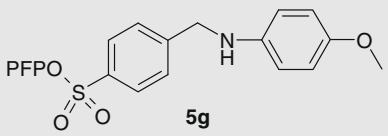
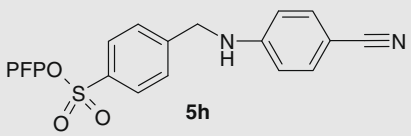
Method A: $NaHB(OAc)_3$ (1.0 mol equiv), CH_2Cl_2–THF (1:1), AcOH (1.1 mol equiv), amine (1.1 mol equiv), 4 Å molecular sieves, room temperature, 16–20 h.
[a] Reaction solvent: CH_2Cl_2–THF–MeCN (1:1:1), $NaHB(OAc)_3$ (1.5 mol equiv).
[b] Reaction solvent: DCE–THF–MeCN (60:8:4), $NaHB(OAc)_3$ (1.5 mol equiv).

the use of catalytic MoO_2Cl_2 and phenylsilane ($PhSiH_3$), in THF at reflux, has been reported for reduction of imines derived from a variety of benzaldehydes with either aniline or 2-chloroaniline.[8] The reported yields are generally excellent for the more electron-deficient benzaldehydes (4-NO_2, 4-F, 4-CF_3, 4-CO_2Me), but only moderate with more electron-rich benzaldehydes (4-H, 4-OMe). It was encouraging to observe that the DRA was possible using a catalytic $MoO_2Cl_2/PhSiH_3$ system, in CH_2Cl_2–THF–MeCN (1:1:1) at 50 °C, in the presence of a slight excess of acetic acid, although the yield of **5b** was only moderate (41%). Changing the reaction solvent to 1,4-dioxane (Method B, Table 2) and carrying out the reaction at reflux improved both the isolated yield and the reaction scope of the benzylamine product **5**. Methanol has been reported to be superior to both THF and 1,2-dichloroethane (DCE) in increasing both the rate and extent of imine formation in solution as judged by ^1H NMR and GC.[1b] As the $MoO_2Cl_2/PhSiH_3$ reduction system behaved well in the presence of acetic acid, it was reasoned that it should also tolerate an alcoholic reaction solvent. We found this was the case and using $MoO_2Cl_2/PhSiH_3$ in refluxing ethanol (Method C, Table 2) not only gave improved yields, but also further increased the reaction scope. Finally, two examples using methanol as the reaction solvent (Method D, Table 2) have been included for comparison.

The use of catalytic MoO_2Cl_2 and $PhSiH_3$ in refluxing 1,4-dioxane (Method B, Table 2) gave essentially identical results to those obtained when using sodium triacetoxyborohydride (Method A, Table 1) at room temperature with aldehyde **4**. Changing the reaction solvent to refluxing ethanol (Method C, Table 2) showed an improvement in yield and also increased the scope of the reaction, allowing the use of the less nucleophilic amines **2b** (pK_a 4.0) and **2c** (pK_a 2.9). In the reaction of aniline **2a** with aldehyde **4,** replacement of acetic acid with hydrogen chloride showed essentially no difference. However, omission of the acetic acid from this reaction appeared to show a slight improvement in yield. The two examples using methanol as the reaction solvent at room temperature (Method D, Table 2) suggest that this is an even more selective DRA procedure. The first example shows an improvement in yield of product **5e** (84%) and the reaction scope is further improved with amine **2e** (pK_a 1.7) giving **5h** (81%) in good yield. Probably even more notable is that no anhydrous precautions were taken with Method D and that HPLC grade methanol was used as the reaction solvent, again with the relatively electron-deficient aldehyde **4**.

The reported use of catalytic MoO_2Cl_2 and $PhSiH_3$, in anhydrous THF, for the indirect reductive amination (IRA) of the imines formed between aniline **2a** and a series of aryl aldehydes showed

Table 2
Comparison of the direct reductive amination of aldehyde **4** with MoO_2Cl_2/$PhSiH_3$, in either 1,4-dioxane (Method B), ethanol (Method C) or methanol (Method D), with 2° amines **6b**, **c** and the aryl amines **2a**–**e**

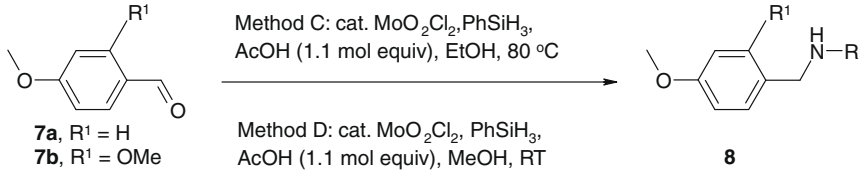
Amine	pK_a	Product structure	Method B yield (%)	Method C yield (%)	Method D yield (%)
6b	7.8	 **5b**	77	78	–
6c	6.6	 **5c**	81	81	–
2a	4.6	 **5d**	61	93 98[a] 91[b]	–
2b	4.0	 **5e**	36	51	84
2c	2.9	 **5f**	–	60 51[c]	–
2d	5.2	 **5g**	–	82	–
2e	1.7	 **5h**	–	–	81

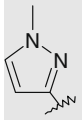
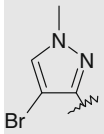
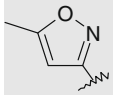
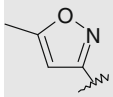
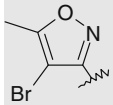
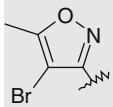
Method B: MoO_2Cl_2 (10 mol %), $PhSiH_3$ (3.0 mol equiv), AcOH (1.1 mol equiv), amine (1.1 mol equiv), 4 Å molecular sieves, 1,4-dioxane, reflux, 16–20 h.
Method C: MoO_2Cl_2 (10 mol %), $PhSiH_3$ (3.0 mol equiv), AcOH (1.1 mol equiv), amine (1.1 mol equiv), 4 Å molecular sieves, ethanol, reflux, 16–20 h.
Method D: MoO_2Cl_2 (5 mol %), $PhSiH_3$ (1.5 mol equiv), AcOH (1.1 mol equiv), amine (1.1 mol equiv), methanol, rt, 3–4 h.
[a] No AcOH added.
[b] HCl (4.0 M in 1,4-dioxane, 1.1 mol equiv) used in place of AcOH.
[c] Reaction in a microwave reactor for 2 h at 80 °C.

that the most electron-rich example, 4-methoxybenzaldehyde **7a,** gave the lowest reported yield of 2° benzylamine **8a** (50%)[8] (Table 3). In order to compare this IRA reaction with the DRA reaction methods C (ethanol) and D (methanol) four reactions were carried out between aniline **2a** and the aldehydes 4-methoxybenzaldehyde **7a** and 2,4-dimethoxybenzaldehyde **7b** to give the 2° benzylamines **8a** and **8b**, respectively (Table 3). Both DRA methods C and D gave excellent results for the preparation of **8a**, but only method D gave a good yield of **8b** (77%). Therefore, we sought to optimize the DRA methods C and D with the more problematical and electron-rich aldehyde, 2,4-dimethoxybenzaldehyde **7b**, and in the process of doing so, further improve the reaction scope. During optimization, we investigated the effects of the stoichiometry of the catalyst and $PhSiH_3$, the reaction temperature, the nature of the alcoholic solvent and the presence of additives, especially water (Table 3).

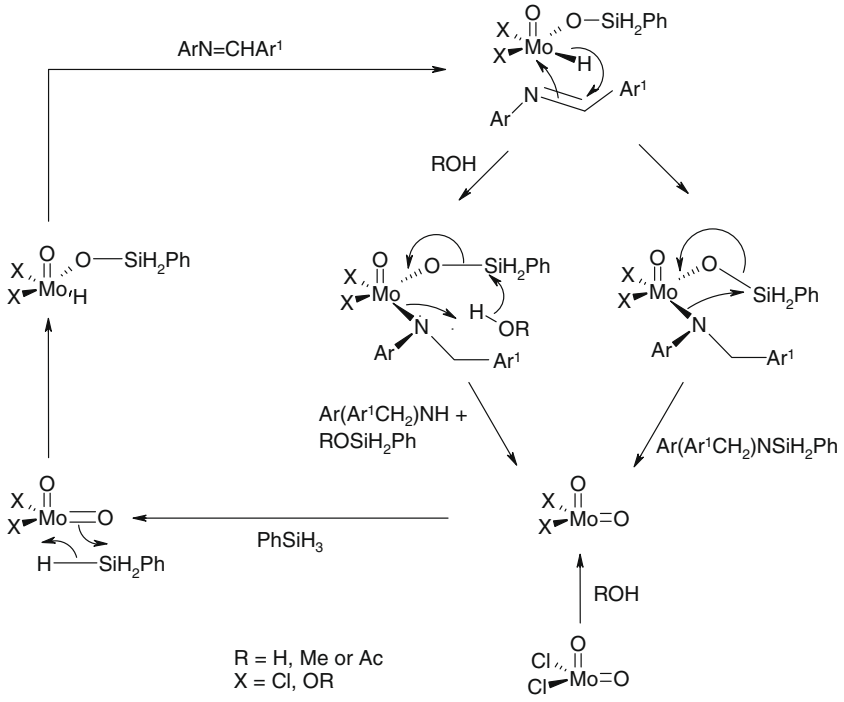
Whilst processing the MoO_2Cl_2 for these reactions, it was noted that the catalyst was slightly hygroscopic. As such, we could not be sure how much water we were adding to our reactions. In order to minimize any unintentional addition of water for methods A and B, the addition of both molecular sieves and anhydrous solvents was used. However, to be more confident of the possible effects of the presence of water in our reactions we decided to use it as an additive during imine formation (5–30 min) and preceding the addition

Table 3
Comparison of the direct reductive amination using $MoO_2Cl_2/PhSiH_3$, with Method C (ethanol) or Method D (methanol), with aldehydes **7a**, **b** and aryl amines **2a**, **e-n**



Aryl amine (R)	pK_a	Aldehyde	MoO_2Cl_2 (mol %)	$PhSiH_3$ (mol equiv)	Method	H_2O (mol equiv)	Product yield
C_6H_5 **2a**	4.6	**7a**	10	3.0	C	1.0	**8a**,[11] 96%
C_6H_5 **2a**	4.6	**7a**	5	1.5	D	0	**8a**,[11] 89%
C_6H_5 **2a**	4.6	**7b**	10	3.0	C	1.0	**8b**, 38%
C_6H_5 **2a**	4.6	**7b**	5	1.5	D	0	**8b**, 77%
 **2f**	4.0	**7b**	5	1.5	D	1.0	**8f**, 71%
 **2g**	3.6	**7b**	5	1.5	D	1.0	**8g**, 68%
4-$MeO_2CC_6H_4$ **2h**	2.5	**7b**	10	1.5	C[a]	1.0	**8h**, 51%
4-$MeO_2CC_6H_4$ **2h**	2.5	**7b**	10	1.2	D[a]	1.0	**8h**, 69%
4-$MeO_2CC_6H_4$ **2h**	2.5	**7b**	10	2.0	D[a]	1.0	**8h**, 78%
 **2i**	2.4	**7b**	10	3.0	C	1.0	**8i**, 9%
 **2i**	2.4	**7b**	10	1.5	D	1.0	**8i**, 82%
2-Cl-4-IC_6H_3 **2j**	1.9	**7b**	5	1.5	D	1.0	**8j**, 83%
4-NCC_6H_4 **2e**	1.7	**7b**	10	1.5	D	1.0	**8e**, 49%
4-NCC_6H_4 **2e**	1.7	**7b**	10	1.5	D	10.5	**8e**, 63%
4-NCC_6H_4 **2e**	1.7	**7b**	5	1.5	D	1.0	**8e**, 82%
4-$O_2NC_6H_4$ **2k**	1.0	**7b**	10	2.0	C	1.0	**8k**, 31%
4-$O_2NC_6H_4$ **2k**	1.0	**7b**	10	1.2	D[a]	1.0	**8k**, 70%
4-$O_2NC_6H_4$ **2k**	1.0	**7b**	5	1.5	D	1.0	**8k**, 90%
4-$O_2NC_6H_4$ **2k**	1.0	**7b**	5	1.5	D	10.5	**8k**, 93%
 **2l**	0.3	**7b**	5	1.5	D	1.0	**8l**, 68%
 **2l**	0.3	**7b**	5	1.5	D	10.5	**8l**, 52%
2-F-5-$O_2NC_6H_3$ **2m**	0.0	**7b**	5	1.5	D	10.5	**8m**, 88%
3-F-2-$O_2NC_6H_3$ **2n**	0.0	**7b**	5	1.5	D	10.5	**8n**, 74%

Method C: MoO_2Cl_2 (10 mol %), $PhSiH_3$ (1.2–3.0 mol equiv), AcOH (1.1 mol equiv), amine (1.1 mol equiv), ethanol, reflux, 16–20 h.
Method D: MoO_2Cl_2 (5–10 mol %), $PhSiH_3$ (1.2–2.0 mol equiv), AcOH (1.1 mol equiv), amine (1.1 mol equiv), methanol, rt, 3–4 h.
HPLC grade solvents were used in all experiments.
Adamantis Pro (GSK's proprietary physico-chemical and ADMET comparison software) was used to calculate the pK_a of the amines, with values between 0 and 14.
[a] Reaction carried out at 50 °C.



Scheme 2. Proposed reaction mechanism for the direct reductive amination of an imine with MoO_2Cl_2/$PhSiH_3$ in methanol with acetic acid and water additives.

of the MoO_2Cl_2 catalyst and $PhSiH_3$ in ethanol (Method C) and methanol (Method D). The interpretation of the results shown in Table 3 is that addition of at least one equivalent of water gave good yields, and generally the addition of 10.5 equiv of water was, in most cases, beneficial. The reactions performed in methanol at room temperature were better in all cases than those carried out in ethanol at reflux, except for one example when water was not added. All the reactions carried out in methanol were more efficient at room temperature than when carried out at 50 °C and also when less catalyst (5 mol %) was employed. The reactions carried out in methanol gave the desired reductive amination product more quickly at ambient temperature than those performed in ethanol at reflux. The reaction conditions do not appear to be sensitive to oxygen as none of the reaction solvents were degassed, but all the reactions were carried out under an inert gas atmosphere in order to control the amount of water available to the reaction system. As the preferred DRA protocol uses a number of potential oxygen nucleophiles (ROH, where R = Ac, Me or H) we cannot be sure whether the active catalyst is MoO_2Cl_2, $MoO_2Cl(OR)$, $MoO_2(OR)_2$ or even some other Mo(VI) species. The mechanism of the imine reduction is possibly similar to that proposed for the hydrosilation of aldehydes and ketones with MoO_2Cl_2/$PhSiH_3$,[9a,b] with an initial [2+2]-addition of the Si–H bond to the metal oxide (Mo=O), resulting in the formation of the active reducing agent, Si–O–Mo–H being most likely.[9b] Following hydride transfer to the iminium carbon, either the iminium nitrogen could pick up the silane or the catalyst could be regenerated by direct attack of an oxygen nucleophile (ROH, where R = Ac, Me or H) on the silane itself. Although we cannot rule out the possibility of a radical mechanism, the rate enhancement observed on moving to more polar solvents suggests the presence of polar or charged transition state complexes. For simplicity, the proposed mechanism in Scheme 2 depicts a fully concerted process taking place; however, a stepwise process could be equally likely. The replacement of MoO_2Cl_2 with MoO_3 failed to reproduce the DRA reaction to any appreciable level. Interestingly, the reactions were chemoselective; notably we failed to observe any appreciable nitro or ester reduction, as has been reported with MoO_2Cl_2/$PhSiH_3$ in refluxing toluene.[10]

In summary we have developed a novel and powerful method of carrying out DRA on both electron-deficient aldehyde **4** and the electron-rich aldehyde **7b** with amines possessing a wide pK_a range. The protocol is tolerant of a number of reducible functional groups (F, Cl, I, OMe, NO_2, CO_2Me, SO_3PFP and CN) and heterocyclic ring systems **2f, g, i, l**. The reactions are environmentally friendly, in that methanol is used in place of the standard chlorinated solvents (CH_2Cl_2 and DCE), and are carried out at ambient temperature. Method D requires only the use of commercial HPLC grade methanol and the addition of water (1.0 mol equiv) is recommended, as is a slight excess of acetic acid (1.1 mol equiv) to increase the rate of imine formation. The MoO_2Cl_2 catalyst (5 mol %), $PhSiH_3$ (1.5 mol equiv), with respect to the aldehyde, water, acetic acid and amine stoichiometry have not been optimized by a design of experiments procedure, as all reaction parameters are best examined for a particular reaction of interest. The addition of a large excess of water (10.5 mol equiv) is not only tolerated, but generally has a small positive effect on the yield. The tolerance of this protocol to relatively high water concentrations may be beneficial both to dissolve more polar or charged substrates, or with substrates with variable water content. Finally, the reactions are not sensitive to oxygen and are highly amenable to scale-up.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.071.

References and notes

1. (a) Abdel-Magid, A. H.; Maryanoff, C. A. *Synlett* **1990**, 537; (b) Abdel-Magid, A. H.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849; (c) Zhang, J.; Blazecka, P. G.; Davidson, J. G. *Org. Lett.* **2003**, *5*, 553; (d) Gutierrez, C. D.; Bavetsias, V.; McDonald, E. *Tetrahedron Lett.* **2005**, *46*, 3595; (e) Gribble, G. W. *Org. Process Res. Dev.* **2006**, *10*, 1062; (f) Bailey, H. V.; Heaton, W.;

Vicker, N.; Potter, B. V. L. *Synlett* **2006**, 2444; (g) Heydari, A.; Arefi, A.; Esfandyari, M. *J. Mol. Catal. A: Chem.* **2007**, *274*, 169; (h) Ignatovich, J.; Gusak, K.; Kovalyov, V.; Kozlov, N.; Koroleva, E. *Arkivoc* **2008**, *ix*, 42.
2. (a) Burling, S.; Whittlesey, M. K.; Williams, J. M. J. *Adv. Synth. Catal.* **2005**, *347*, 591; (b) Menche, D.; Arikan, F. *Synlett* **2006**, 841; (c) Menche, D.; Hassfeld, J.; Li, J.; Menche, G.; Ritter, A.; Rudolph, S. *Org. Lett.* **2006**, *8*, 741; (d) Liu, Z. G.; Li, N.; Yang, L.; Liu, Z. L.; Yu, W. *Chin. Chem. Lett.* **2007**, *18*, 458; (e) Gnanamgari, D.; Moores, A.; Rajaseelan, E.; Crabtree, R. H. *Organometallics* **2007**, *26*, 1226; (f) Li, D.; Zhang, Y.; Zhou, G.; Guo, W. *Synlett* **2008**, 225.
3. (a) Tararov, V. I.; Kadyrov, R.; Riermeier, T. H.; Fischer, C.; Börner, A. *Adv. Synth. Catal.* **2004**, *346*, 561; (b) Tararov, V. I.; Börner, A. *Synlett* **2005**, 203; (c) Storer, R. I.; Carrera, D. E.; Ni, Y.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 84; (d) Robichaud, A.; Ajjou, A. N. *Tetrahedron Lett.* **2006**, *47*, 3633; (e) Jaroskova, L.; Van der Veken, L.; de Belser, P.; Diels, G.; de Groot, A.; Linders, J. T. M. *Tetrahedron Lett.* **2006**, *47*, 8063; (f) Bhanushali, M. J.; Nandurkar, N. S.; Bhor, M. D.; Bhanage, B. M. *Tetrahedron Lett.* **2007**, *48*, 1273; (g) Nugent, T. C.; Ghosh, A. K. *Eur. J. Org. Chem.* **2007**, 3863; (h) Bhor, M. D.; Bhanushali, M. J.; Nandurkar, N. S.; Bhanage, B. M. *Tetrahedron Lett.* **2008**, *49*, 965; (i) Xing, L.; Cheng, C.; Zhu, R.; Zhang, B.; Wang, X.; Hu, Y. *Tetrahedron* **2008**, *64*, 11783.
4. (a) Kobayashi, S.; Yasuda, M.; Hachiya, I. *Chem. Lett.* **1996**, *25*, 407; (b) Lopez, R. M.; Fu, G. C. *Tetrahedron* **1997**, *53*, 16349; (c) Verdaguer, X.; Lange, U. E. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1998**, *37*, 1103; (d) Apodaca, R.; Xiao, W. *Org. Lett.* **2001**, *3*, 1745; (e) Miura, K.; Ootsuka, K.; Suda, S.; Nishikori, H.; Hosomi, A. *Synlett* **2001**, 1617; (f) Kangasmetsä, J. J.; Johnson, T. *Org. Lett.* **2005**, *7*, 5653; (g) Kato, H.; Shibata, I.; Yasaka, Y.; Tsunoi, S.; Yasuda, M.; Baba, A. *Chem. Commun.* **2006**, 4189; (h) Prakash, G. K. S.; Matthew, T.; Do, C.; Panja, C.; Olah, G. A., *Abstracts of Papers*, 233rd American Chemical Society National Meeting, Chicago, Il, March 25–29, 2007.
5. Arienti, K. L.; Brunmark, A.; Axe, F. U.; McClure, K.; Lee, A.; Blevitt, J.; Neff, D. K.; Huang, L.; Crawford, S.; Pandit, C. R.; Karlsson, L.; Breitenbucher, J. G. *J. Med. Chem.* **2005**, *48*, 1873.
6. Wilden, J. D.; Geldeard, L.; Lee, C. C.; Judd, D. B.; Caddick, S. *Chem. Commun.* **2007**, 1074.
7. (a) Caddick, S.; Wilden, J. D.; Judd, D. B. *J. Am. Chem. Soc.* **2004**, *126*, 1024; (b) Caddick, S.; Wilden, J. D.; Bush, H. D.; Judd, D. B. *QSAR Comb. Sci.* **2004**, *23*, 902; (c) Wilden, J. D.; Judd, D. B.; Caddick, S. *Tetrahedron Lett.* **2005**, *46*, 7637; (d) Caddick, S.; Wilden, J. D.; Judd, D. B. *Chem. Commun.* **2005**, 2727.
8. Fernandes, A. C.; Romão, C. C. *Tetrahedron Lett.* **2005**, *46*, 8881.
9. (a) Fernandes, A. C.; Fernandes, R.; Romão, C. C.; Royo, B. *Chem. Commun.* **2005**, 213; (b) Costa, P. J.; Romão, C. C.; Fernandes, A. C.; Royo, B.; Reis, P. M.; Calhorda, M. J. *Chem. Eur. J.* **2007**, *13*, 3934.
10. Fernandes, A. C.; Romão, C. C. *J. Mol. Catal. A: Chem.* **2006**, *253*, 96.
11. Analytical data confirms the structure, mp 63.8 °C, lit. mp 64.0 °C. Roe, A.; Montgomery, J. A. *J. Am. Chem. Soc.* **1953**, *75*, 910.