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Full Paper

Ionic Thiourea Organocatalysis of the Morita–Baylis–Hillman Reaction

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An ionic thiourea based organocatalyst has been shown to promote a 1,4-diazabicyclo[2.2.2]octane, (DABCO) catalysed Morita-Baylis-Hillman reaction between benzaldehyde and cyclohex-2-en-1-one. The ionic thiourea catalyst was easily prepared from a pyrrolidinium salt containing an arylamine moiety and 3,5-di(trifluoromethyl)phenylisothiocyanate. X-ray crystallographic analysis of the ionic thiourea catalyst shows an acetone molecule doubly hydrogen bonded to the Lewis acidic thiourea N-H protons. Entrainment of the ionic thiourea co-catalyst in the ionic liquid *N*-butyl-*N*-methylpyrrolidinium bistriflimide, [BMPyr][$N(Tf)_2$], facilitates catalyst recycling and affords very good yields with reaction times reduced through use of microwave heating.

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Introduction

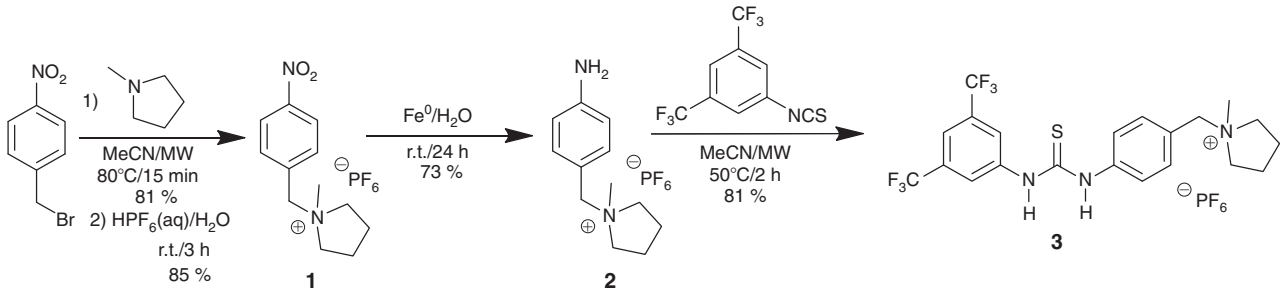
The Morita–Baylis–Hillman (MBH) reaction is a valuable carbon–carbon bond-forming reaction, affording allylic alcohol products with high functional group density and is typically catalyzed by a tertiary amine or tertiary phosphine.[1] The salient drawback of the MBH reaction is the slow rate of reaction, resulting in long reaction times. Several methods are known to accelerate the MBH reaction such as the use of protic additives,[2] Lewis acids,[3] and ionic liquid solvents.[4] Schreiner and coworkers have shown that electron-deficient thiourea derivatives can behave as Lewis acids and accelerate Diels–Alder reactions.[5] As Lewis acids can also promote the MBH reaction, electron-deficient thiourea derivatives are therefore expected to also accelerate the MBH reaction. This was demonstrated by Nagasawa and coworkers – the authors showed that the MBH reaction could be accelerated using a thiourea organocatalyst.[6]

Organocatalysis, which refers to the use of a sub-stoichiometric quantity of an organic molecule to accelerate a chemical reaction, is an area that has experienced rapid growth since the turn of the twenty-first century.[7] Despite the emergence of organocatalysis over the past number of years, organocatalysis using ionic liquid systems remains relatively unexplored, namely with respect to thiourea-based organocatalysts. Several examples of ionic liquid-functionalized proline derivatives have been reported for use as organocatalysts.[8] To our knowledge, there are no reports on the use of ionic liquid-based thiourea deriviatives as organocatalysts.

The ionic liquid *N*-butyl-*N*-methylpyrrolidinium bistriflimide, [BMPyr][$N(Tf)_2$], is an excellent solvent for a variety of organic, organometallic, and inorganic compounds; however, it is immiscible in selected organic solvents. Hence, the incorporation of an ionic liquid moiety based on the pyrrolidinium cation into a thiourea organocatalyst allows dissolution of the ionic organocatalyst in the ionic liquid solvent, thereby facilitating homogenous reaction conditions in the ionic liquid phase. Furthermore, a pyrrolidinium cationic tag would avoid any potential side reactions that have been shown to occur when other ions, such as the imidazolium cation, are present in MBH reaction mixtures.[4] Separation of the ionic catalyst and ionic liquid phase from the reactants and products using an organic solvent such as diethyl ether, Et_2O, is then possible. This strategy provides a very simple method to recycle the catalyst for use in subsequent reactions and mimics the advantages of both homogeneous and heterogeneous catalytic systems.

Microwave heating using ionic liquids as a reaction medium has been shown to be very efficient due to the microwave-absorbing properties of ionic liquids.[9] Microwave irradiation has also been shown to accelerate the Morita–Baylis–Hillman reaction.[10] Inspired by previous studies using ionic liquid-tagged molecules for catalytic applications,[11] an ionic liquid-tagged thiourea was designed for use as an organocatalyst. Herein, we report the synthesis and application of an ionic thiourea organocatalyst, wherein the ionic nature of the thiourea catalyst renders the catalyst ionophilic and thus very suitable for use and recycling in an ionic liquid. This system is hence well suited to the use of microwave heating due to the ionic nature of the organocatalyst and the use of an ionic liquid reaction medium.

We report herein the use of an ionic thiourea oragnocatalyst for the MBH reaction using an ionic liquid reaction medium with microwave irradiation. The ionic thiourea derivative **3** reported herein is a salt and solid at room temperature and hence is not an 'ionic liquid'. Rather, as a salt, it is 'ionophilic' and readily dissolves in an ionic liquid reaction medium. Hence,



Scheme 1. Synthesis of ionic thiourea catalyst **3**. MW = microwave heating; r.t. = room temperature.

this reaction system and protocol offers the advantages of (1) catalytic recyclability, (2) solvent recyclability, and (3) reduced reaction times while permitting comparable yields of products relative to those obtained from more conventional systems reported to date.

Results and Discussion

The criteria necessary for organocatalytic activity in thiourea derivatives include the presence of sufficiently electron-deficient secondary amine protons, thereby enabling them to act as effective Lewis acids.[12] Thus, the aryl substituents on the thiourea moiety need to bear electron-withdrawing groups. Substitution of the aryl groups at the *ortho* position has been shown to be unfavourable and ought to be avoided. Rigidifying interactions between the *ortho* protons of the aryl rings and the sulfur lone pair electrons are also required. A previously prepared ionic thiourea derivative, specifically and intentionally designed for metal extractions, lacked these structural and electronic features and hence would be unlikely to be organocatalytic.[13] To incorporate these required features in our ionic thiourea derivative, *p*-nitrobenzylbromide was alkylated using *N*-methylpyrrolidine to afford a pyrrolidinium bromide salt that was then metathesized to the hexafluorophosphate salt **1**, thus enabling facile purification (Scheme 1). The nitro group was then easily reduced using Fe^0 in water to afford the amine **2**, which then underwent reaction with 3,5-di(trifluoromethyl) phenyl isothiocyanate under microwave irradiation to give the ionic thiourea derivative **3**.

The product was recrystallized from acetone, and the structure was determined unequivocally as an acetone solvate of **3** using single-crystal X-ray diffraction (Fig. 1).

The X-ray structure displays an acetone molecule doubly hydrogen-bonded to the Lewis acidic thiourea N–H protons of **3**. Such an interaction has been proposed as a key interaction for the acceleration of the MBH reaction by thiourea organocatalysts.[12] Additionally, the rigidifying interactions determined to be necessary for catalytic activity by Schreiner and coworkers between the *ortho* protons of the phenyl rings and the sulfur atom of the thiourea backbone are also observed.[12]

Using Schreiner's thiourea, *N*,*N*′-bis[3,5-bis(trifluoromethyl) phenyl]thiourea (**4**), as a benchmark, the ionic thiourea derivative **3** was tested for catalytic activity using neat conditions in an ionic liquid and in an ionic liquid under microwave irradiation (Table 1).

Using the ionic thiourea organocatalyst **3** afforded a slightly lower conversion to the allylic alcohol product under neat reaction conditions at 25°C under conventional heating using a hotplate (Table 1, Entries 1 and 2); no conversion to product was observed in the absence of **3** (Table 1, Entry 3). The use of our ionic thiourea co-catalyst **3** gave comparable yields to those

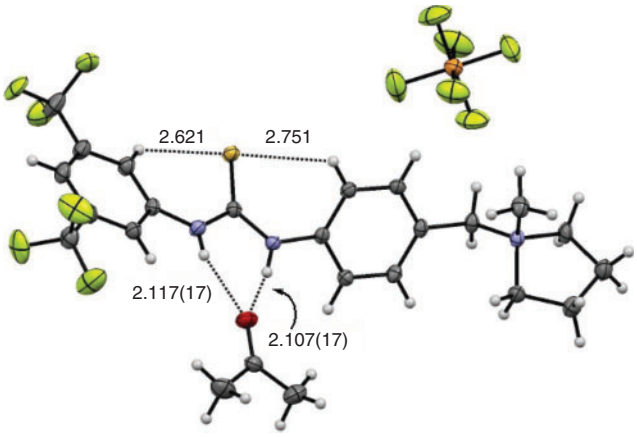


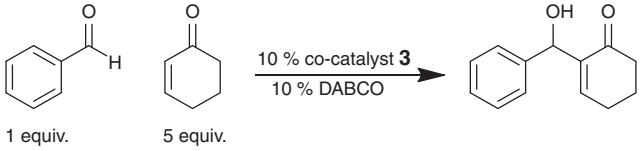
Fig. 1. X-ray crystal structure of ionic thiourea co-catalyst **3**. Ellipsoids drawn at 50% probability level. (Disorder of the cation and anion, and a complete disordered acetone solvent molecule have been omitted for clarity).

obtained using Schreiner's neutral thiourea derivative **4** when the reaction was performed over 2 days in ionic liquid [BMPyr][$N(Tf)_2$] while using conventional heating (Table 1, Entries 4 and 5a).

An advantage of our ionic thiourea co-catalyst **3** employing the ionic liquid [BMPyr][$N(Tf)_2$] as a reaction medium was revealed in a series of recycling experiments (Table 1, Entries 5a–5c); no apparent loss of catalytic activity was observed over three cycles using the ionic thiourea catalyst/ionic liquid system. Furthermore, we conducted leaching experiments that revealed that no ionic thiourea co-catalyst **3** was leached out of the ionic liquid phase/reaction medium, as observed by ^{1}H NMR analysis, during Et_2O extractions of reaction products. Hence, the ionic thiourea co-catalyst **3** was successfully entrained in the ionic liquid phase. Conversely, neutral thiourea catalyst **4** readily leached into Et_2O from the ionic liquid phase during extraction of products, thereby making the recycling of the neutral catalyst **4** problematic. Unsurprisingly, no allylic alcohol product was observed after 2 days of conventional heating at 25°C in the ionic liquid-mediated reaction in the absence of catalyst **3** (Table 1, Entry 6).

Another advantage of our ionic thiourea co-catalyst **3** used in an ionic liquid reaction medium becomes evident when the reaction is heated using microwave irradiation (Table 1, Entry 7). Owing to the enhanced microwave-absorbing properties of the ionic liquid used, [BMPyr][$N(Tf)_2$], reaction times were significantly decreased to 6 h (versus 48 h) when microwave heating at 50°C was employed affording useful percentage conversion to allylic alcohol product. It is possible that the ionic nature of **3** also was a factor on the microwave-irradiated

Table 1. Morita–Baylis–Hillman reaction using ionic thiourea co-catalyst 3



Entry	Co-Catalyst	Time [h]	Temperature [°C]	Solvent	Conversion [%][A]
1	3	24	25	Neat	80
2	4	24	25	Neat	96
3	None	24	25	Neat	0
4	4	48	25	[BMPyr][NTf_2]	98
5a	3	48	25	[BMPyr][NTf_2]	92
5b	3				90
5c	3				91
6	None	48	25	[BMPyr][NTf_2]	0
7	3	6	50[B]	[BMPyr][NTf_2]	78
8	4	6	50[B]	[BMPyr][NTf_2]	89
9	None	6	50[B]	[BMPyr][NTf_2]	5

[A]Percentage conversions determined by ^{1}H NMR.
[B]Dielectric heating using microwave irradiation.

reaction and hence provided a synergistic effect. However, this is yet to be confirmed in future experiments using a broader array of substrates. Although the neutral thiourea derivative **4** also gave comparable useful conversion to the allylic alcohol product under similar conditions (Table 1, Entry 8), it is not recyclable due to the leaching problems described earlier. Heating the ionic liquid-mediated reaction under microwave irradiation in the absence of ionic thiourea co-catalyst **3** afforded only a very small conversion to allylic alcohol product (Table 1, Entry 9), thus demonstrating the generally slow nature of the MBH reaction in the absence of a thiourea catalyst even at higher temperatures in an ionic liquid reaction medium.

Conclusion

Herein, we demonstrate that ionic thiourea co-catalyst **3** can be easily synthesized and successfully catalyzes the MBH reaction in a recyclable fashion and in shortened reaction times under microwave irradiation in an ionic liquid reaction medium. X-ray crystallographic analysis confirms the ionic nature of our catalyst (**3**). Very good percentage conversion to allylic alcohol product comparable with that obtained using a neutral thiourea catalyst **4**) can be obtained. The ionophillic nature of co-catalyst **3** facilitates preferential partitioning/entrainment into the ionic liquid [BMPyr][$N(Tf)_2$], consequently enabling recycling of the catalyst and solvent system under efficient microwave heating, leading to reduced reaction times. The MBH reaction involves charged intermediates making ionic solvents ideal reaction media. Our catalytic system presents the possibility for the scale-up of the MBH reaction to produce large quantities of allylic alcohol products with a high functional group density using a continuous flow approach. The scope and limitations of this catalytic strategy using a wider variety of aldehydes and enones are currently under investigation. The effect of varying the ionic liquid medium as well as the ionic thiourea derivative through simple alterations via our modular synthetic approach is also being further investigated.

Experimental

General Procedure

Ionic thiourea catalyst **3** (0.304 g, 10 mol-%) was placed in a 50-mL round-bottom flask and dissolved in the appropriate solvent (see Table 1) with stirring at room temperature. Cyclohex-2-en-1-one (0.49 mL, 5.00 mmol) and benzaldehyde (0.10 mL, 1.00 mmol) were then added sequentially to the reaction mixture. 1,4-diazabicyclo[2.2.2]octane (DABCO; 0.056 g, 10 mol-%) was then added to the reaction mixture. The reaction was stirred at room temperature (25°C) for a specified reaction time. Alternatively, reactions were heated using a CEM Discover microwave reactor operating at 20 W. Upon completion of the reaction, the organic materials were extracted using diethyl ether (5 × 10 mL). An aliquot of the ether extract was dissolved in $CDCl_3$, and the sample was analyzed via ^{1}H NMR spectroscopy to determine the percentage conversion to the allylic alcohol product, 2-(hydroxyphenylmethyl)cyclohex-2-en-1-one. To recycle the ionic liquid phase containing catalyst **3**, the ionic liquid phase was placed under vacuum to remove any residual ether. Benzaldehyde, cyclohex-2-en-1-one, and DABCO were added in the same quantities as those used in the first run. The mixture was stirred for 48 h and extracted using the same procedure with diethyl ether (5 × 10 mL). The third consecutive reaction in [BMPyr][$N(Tf)_2$] was performed using the same procedure as that used for the second reaction, and the results are summarized in Table 1 (Entries 5a–5c).

*1-Nitrobenzyl-1-methylpyrrolidinium Hexafluorophosphate (**1**)*

p-Nitrobenzyl bromide (1.00 g, 4.63 mmol) was dissolved in acetonitrile (MeCN; 10 mL), and *N*-methylpyrrolidine (0.48 mL, 4.63 mmol) was added dropwise at ambient temperature. The reaction vessel was heated using microwave irradiation to 80°C and held for 15 min. The product was precipitated from MeCN using an equal volume of ethyl acetate, filtered, and dried under vacuum to afford the intermediate product (1.13 g, 81 %), mp 168–169°C. ν_{max} (KBr)/cm^{-1} 2963, 1605, 1528, 1424, 1346. δ_H ([D6]DMSO, 300 MHz) 8.35 (2H, d, *J* 8.7), 7.94 (2H, d, *J* 8.7), 4.85 (2H, s), 3.65–3.69 (2H, m), 3.46–4.51 (2H, m), 2.97 (3H, s), 2.14–2.16 (2H, m). δ_C ([D6]DMSO, 75 MHz) 149.0, 136.9, 134.6, 124.3, 64.1, 63.5 47.7, 21.2. *m*/*z* (electrospray ionization; ESI^+) 221.9 (100 %, $[C_{12}H_{17}N_2O_2]^+$); calcd 221.1.

N-Methyl-*N*-(*p*-nitrobenzyl)pyrrolidinium bromide (1.23 g, 4.08 mmol) was dissolved in a minimum amount of water, and

an aqueous solution of HPF_6 (1.25 equiv., 0.43 mL) was added dropwise. The product which precipitated was then filtered off after 3 h, and dried under vacuum. The product obtained was a white solid (1.27 g, 85 %), mp 155–156°C. ν_{max} (KBr)/cm^{-1} 3081, 1610, 1530, 1431, 1359, 834, 557. δ_H ([D6]DMSO, 300 MHz) 8.34 (2H, d, *J* 8.8), 7.86 (2H, d, *J* 8.8), 4.72 (2H, s), 3.58–3.62 (2H, m), 3.41–3.47 (2H, m), 2.93 (3H, s), 2.14–2.16 (2H, m). δ_C ([D6]DMSO, 75 MHz) 149.0, 136.4, 134.5, 124.3, 64.5, 63.6, 47.8, 21.2. δ_P ([D6]DMSO, 121 MHz) −144.2 (septet, *J* 711.4). *m*/*z* (ESI$^+$) 221.1 (100 %, $[C_{12}H_{17}N_2O_2]^+$); calcd 221.1. *m*/*z* (ESI$^-$) 144.6 (100 %, $[PF_6]^-$); calcd 144.9.

*1-Aminobenzyl-1-methylpyrrolidinium Hexafluorophosphate (**2**)*

$FeSO_4{\cdot}7H_2O$ (5.75 g, 20.69 mmol) and sodium citrate (0.44 g, 1.72 mmol) were added to water (100 mL). $NaBH_4$ (1.30 g, 34.49 mmol) was added slowly, and the iron was reduced to black Fe^0. The water was decanted, and the nanoparticles were washed and decanted twice more with water (50 mL). *N*-Methyl-*N*-(*p*-nitrobenzyl)pyrrolidinium hexafluorophosphate (1.26 g, 3.45 mmol) was added, and the reaction was stirred at ambient temperature for 24 h. The reaction mixture was passed through a vacuum frit to remove water and other aqueous impurities. The residue in the frit was washed with MeCN (3 × 20 mL). MeCN from the washings was removed under vacuum, and the product was dried under vacuum. The product was obtained as a yellow solid (0.85 g, 73 %), mp 143–144°C. ν_{max} (KBr)/cm^{-1} 3489, 3401, 2981, 1632, 1426, 835, 558. δ_H ([D6]DMSO, 300 MHz) 7.16 (2H, d, *J* 8.4), 6.60 (2H, d, *J* 8.4), 5.53 (s, 2NH), 4.30 (2H, s), 3.44–3.48 (2H, m), 3.26–3.30 (2H, m), 2.83 (3H, s), 2.09 (2H, s). δ_C ([D6]DMSO, 75 MHz) 150.8, 133.8, 115.4, 114.0, 66.1, 62.3, 47.5, 21.3. δ_P ([D6]DMSO, 121 MHz) −144.2 (septet, *J* 711.3). *m*/*z* (ESI$^+$) 191.2 (99.5 %, $[C_{12}H_{19}N_2]^+$); calcd 191.1. *m*/*z* (ESI$^-$) 144.6 (100 %, $[PF_6]^-$); calcd 144.9. ESI HRMS (positive mode) *m*/*z* 191.1535 (99.5 %, $[C_{12}H_{19}N_2]^+$); calcd for $[C_{12}H_{19}N_2]^+$ 191.1548.

*1-{4-[((3,5-Di(trifluoromethyl)anilino)carbothioyl)amino] benzyl}-1-methylpyrrolidinium Hexafluorophosphate (**3**)*

N-Methyl-*N*-(*p*-aminobenzyl)pyrrolidinium hexafluorophosphate (**2**) (0.334 g, 0.99 mmol) was dissolved in MeCN (5 mL), and 3,5-bis(trifluoromethyl)phenyl isothiocyanate was added (0.18 mL, 0.99 mmol) and was heated to 50°C under microwave irradiation for 2 h. Solvent was removed under vacuum followed by column chromatography using acetone as the eluting solvent. The acetone was removed under vacuum affording a pale yellow solid (0.49 g, 81 %). ν_{max} (KBr)/cm^{-1} 3378, 1614, 1537, 1473, 1384, 1280, 1178, 1133, 841, 558. δ_H ([D6]DMSO, 300 MHz) 10.46 (s, 1NH), 10.36 (s,1NH), 8.25 (2H, s), 7.82 (1H, s), 7.66 (2H, d, *J* 8.6), 7.56 (2H, d, *J* 8.6), 4.53 (2H, s), 3.54–3.58 (2H, m), 3.36–3.41 (2H, m), 2.91 (3H, s), 2.14–2.15 (4H, m). δ_C ([D6]DMSO, 75 MHz) 180.3, 142.1, 141.0, 133.4, 130.8, 130.4, 125.6, 123.9, 121.9, 65.2, 63.1, 47.7, 21.3. δ_P ([D6]DMSO, 121 MHz) −144.2 (septet, *J* 711.4). *m*/*z* (ESI$^+$) 462.3 (100 %, $[C_{21}H_{22}N_3F_6S]^+$]; calcd 462.1. *m*/*z* (ESI$^-$) 144.6 (100 %, $[PF_6]^-$); calcd 144.9. ESI HRMS (positive mode) *m*/*z* 462.1424 (100 %, $[C_{21}H_{22}N_3F_6S]^+$); calcd for $[C_{21}H_{22}N_3F_6S]^+$ 462.1439.

Supplementary Material

Spectroscopic data, including ^{1}H and ^{13}C NMR spectra, of all intermediate products, ionic thiourea derivative **3**, and reaction products are available on the Journal's website. The crystallographic data for **3** have been deposited (CCDC 1010910). The data can be obtained from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax +44 1223 336033; Email: deposit @ccdc.cam.ac.uk or from www.ccdc.cam.ac.uk.

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References

[1] (a) K. Morita, Z. Suzuki, H. Hirose, *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2732. doi:10.1246/BCSJ.42.2732
(b) A. B. Baylis, M. E. D. Hillman, *German Patent 2155113* **1972**; *Chem. Abstr*., **1972**, *77*, 34174q
(c) S. J. Connon, *Chem. – Eur. J.* **2006**, *12*, 5418. doi:10.1002/CHEM.200501076
(d) D. Basavaiah, G. Veeraraghavaiah, *Chem. Soc. Rev.* **2012**, *41*, 68. doi:10.1039/C1CS15174F
(e) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.* **2010**, *110*, 5447. doi:10.1021/CR900291G

[2] V. K. Aggarwal, D. K. Dean, A. Mereu, R. J. Williams, *J. Org. Chem.* **2002**, *67*, 510. doi:10.1021/JO016073Y

[3] V. K. Aggarwal, J. G. Tarver, R. McCague, *Chem. Commun.* **1996**, 2713. doi:10.1039/CC9960002713

[4] V. K. Aggarwal, I. Emme, A. Mereu, *Chem. Commun.* **2002**, 1612. doi:10.1039/B203079A

[5] P. R. Schreiner, A. Wittkopp, *Org. Lett.* **2002**, *4*, 217. doi:10.1021/OL017117S

[6] Y. Sohtome, A. Tanatani, Y. Hashimoto, K. Nagasawa, *Tetrahedron Lett.* **2004**, *45*, 5589. doi:10.1016/J.TETLET.2004.05.137

[7] D. W. C. MacMillan, *Nature* **2008**, *455*, 304. doi:10.1038/NATURE07367

[8] (a) N. A. Larionova, A. S. Kucherenko, D. E. Siyutkin, S. G. Zlotin, *Tetrahedron* **2011**, *67*, 1948. doi:10.1016/J.TET.2011.01.017
(b) G. Tang, X. Hu, H. J. Altenbach, *Tetrahedron Lett.* **2011**, *52*, 7034. doi:10.1016/J.TETLET.2011.10.009
(c) X. Ding, H. Liang, C. Zhu, Y. Cheng, *Tetrahedron Lett.* **2010**, *51*, 6105. doi:10.1016/J.TETLET.2010.09.036

[9] J. Hoffmann, M. Nuchter, B. Ondruschka, P. Wasserscheid, *Green Chem.* **2003**, *5*, 296. doi:10.1039/B212533A

[10] (a) M. K. Kundu, S. B. Mukherjee, N. Balu, R. Padmakumar, S. V. Bhat, *Synlett* **1994**, 444. doi:10.1055/S-1994-22883
(b) R. Octavio, M. A. de Souza, M. L. A. A. Vacsoncellos, *Synth. Commun.* **2003**, *33*, 1383. doi:10.1081/SCC-120018699

[11] (a) P. U. Naik, G. J. McManus, M. J. Zaworotko, R. D. Singer, *Dalton Trans.* **2008**, 4834. doi:10.1039/B811232K
(b) S. Sonar, K. Ambrose, A. D. Hendsbee, J. D. Masuda, R. D. Singer, *Can. J. Chem.* **2012**, *90*, 60. doi:10.1139/V11-106
(c) K. Ambrose, B. B. Hurisso, R. D. Singer, *Can. J. Chem.* **2013**, *91*, 1258. doi:10.1139/CJC-2013-0336

[12] (a) A. Wittkopp, P. Schreiner, *Chem. – Eur. J.* **2003**, *9*, 407. doi:10.1002/CHEM.200390042
(b) K. M. Lippert, K. Hof, D. Gerbig, D. Ley, H. Hausmann, S. Guenther, P. Schreiner, *Eur. J. Org. Chem.* **2012**, 5919. doi:10.1002/EJOC.201200739

[13] A. E. Visser, R. P. Swatloski, W. M. Reichert, R. Mayton, S. Sheff, A. Wierzbicki, J. H. Davis, R. D. Rogers, *Chem. Commun.* **2001**, 135. doi:10.1039/B008041L