One-pot multi-component synthesis of 1,4-dihydropyridine derivatives in biocompatible deep eutectic solvents

SUHAS PEDNEKAR, RAHUL BHALERAO and NITIN GHADGE*

Organic Chemistry Research Laboratory, Department of Chemistry, Ramnarain Ruia College,
Matunga, Mumbai 400 019, India
e-mail: nitin.ghadge3@gmail.com

MS received 24 May 2012; revised 29 September 2012; accepted 6 November 2012

Abstract. An efficient protocol for the synthesis of differently substituted 1, 4-dihydropyridines in deep eutectic solvents under solvent-free conditions is reported here. Excellent yields of the resultant products have been obtained. Recyclability studies have also been performed for deep eutectic solvents with very little loss in activity up to five recycles.

Keywords. Green chemistry; one-pot synthesis; 1,4-dihydropyridines; deep eutectic solvents; recyclability.

1. Introduction

1,4-Dihydropyridines (1,4-DHPs) are an important class of bioactive molecules, well-known for their role as calcium channel modulators and used extensively for the treatment of hypertension.^{1–3} The derivatives of 1,4-DHP have shown a variety of biological activities such as vasodilator, bronchodilator, antitumour, hepatoprotective and geroprotective activities.^{4,5} Commercial drugs such as Nifedipine which are a prototype of the 1,4-DHP structure have been used extensively in both antianginal and antihypertensive treatment.⁶

One-pot multi-component reactions are of increasing academic and ecological interest due to the possibility of achieving high synthetic efficiency and reaction design.⁷ The classical method for synthesis of 1,4-DHPs involves one-pot condensation of three or more components under relatively harsh conditions using ammonia as the nitrogen source.⁸ Drastic reduction in reaction time and improved reactivity of the synthetic procedures have been brought about by the application of microwaves.⁹ Although, impressive levels of activity could be achieved, large-scale synthesis is a problem. Similarly, Lewis acid catalysts such as Yb(OTf)₃ have been shown to catalyse the reactions at ambient temperature.¹⁰

Recently, Zhao-Qin Jiang *et al.* reported the synthesis of 1,4-DHP derivatives in ionic liquids.¹¹ Ionic liquids have attracted much attention during the last decade in the context of green chemistry due to their low vapour pressure, high thermal stability and their solvation properties which make them such unique solvents in synthesis.¹² However, serious limitations have emerged for the industrial scale application of ionic liquids such as high cost,¹³ environmental toxicity¹⁴ and demand for high purity which could otherwise lead to change in the physical properties of ionic liquids.^{15,16} The development of alternative solvents from components that are inexpensive, non-toxic towards the environment and are biodegradable is therefore highly desirable to overcome these drawbacks.

One such alternative approach could be the use of deep eutectic solvents (DES) which were first synthesized by Abbott *et al.*¹⁷ and since then found wide scope in an array of biological applications due to their biodegradable properties. Most common among them are biological transformations such as hydrolase-catalysed biotransformation¹⁸ and extraction of glycerol from biodiesel into a eutectic-based solvent.¹⁹ Although attractive, deep eutectic solvents have seldom been used for organic transformations.²⁰ We therefore thought it would be interesting to try the application of DES in one-pot synthesis of 1,4-DHPs and it worked very efficiently. A mixture of substituted aldehyde **2a–n**, dimedone **3**, ethyl acetoacetate **4** and ammonium acetate **5** in DES **1a** on heating resulted in the formation of 1,4-DHPs **6a–n**.

*For correspondence

2. Experimental

2.1 Materials

All common reagents and solvents were used as obtained from commercial supplies without further purification.

2.2 Apparatus

All melting points were determined in open capillaries using Gallen Kamp melting point apparatus and are uncorrected. All ^1H NMR (nuclear magnetic resonance) spectra were recorded in CDCl_3 (chemical shift in delta) using Bruker AV 200 spectrophotometer (300 MHz).

2.3 Representative procedure for the preparation of deep eutectic solvent **1a**

Choline chloride **A** (2.8 g, 20 mmol) and urea **B** (**a**) (2.4 g, 40 mmol) were placed in a round bottomed flask and heated to 60°C , until liquid began to form. After 10 min, a homogenous colourless liquid was formed which was used directly for the reactions.

2.4 Representative procedure for the synthesis of 1,4-DHP derivatives **6a–n**

2a–n (1.0 mmol), **3** (0.140 g, 1.0 mmol), **4** (0.130 g, 1.0 mmol), **5** (0.115 g, 1.5 mmol) and DES **1a** (2.0 mL) were successively charged into a Schlenk tube equipped with a magnetic stirrer. Then the reaction was stirred at 60°C for 20 min and a solid product gradually formed. After the completion of reaction as indicated by thin-layer chromatography (TLC), water was added, the reaction mass was stirred and the mixture was filtered. The crude product obtained was purified by recrystallization using absolute alcohol. Further, water was removed under vacuum at 80°C leaving behind DES

which was used up to 5 recycles. A detailed account of the recycle studies is mentioned in results and discussion.

2.5 Spectroscopic data of selected compounds

2.5a Ethyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxo-4-phenylquinoline-3-carboxylate (6a): M.p: $203\text{--}204^\circ\text{C}$. IR (KBr in cm^{-1}) 3233, 3210, 3080, 1696, 1602, 1059, 692, ^1H NMR (CDCl_3 , 300 MHz): δ 0.94 (s, 3H), 1.07 (s, 3H), 1.21 (t, $J = 7.1$ Hz, 3H), 2.13–2.29 (m, 4H), 2.35 (s, 3H), 4.06 (q, $J = 7.1$ Hz, 2H), 5.07 (s, 1H), 6.25 (s, 1H), 7.08–7.13 (m, 1H), 7.18–7.23 (m, 2H), 7.28–7.33 (m, 2H). ESI-MS (m/z) 340 ($\text{M} + \text{H}^+$). Analysis calculated for $\text{C}_{21}\text{H}_{25}\text{NO}_3$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.27; H, 7.39; N, 4.08.

2.5b Ethyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxo-4-p-tolylquinoline-3-carboxylate (6b): M.p: $260\text{--}262^\circ\text{C}$. IR (KBr in cm^{-1}) 3287, 3031, 2958, 1644, 1596, 1480, 1334, 1213, 757, ^1H NMR (CDCl_3 , 300 MHz): δ 0.94 (s, 3H), 1.08 (s, 3H), 1.21 (t, $J = 7.1$ Hz, 3H), 2.10–2.24 (m, 4H), 2.26 (s, 3H), 2.37 (s, 3H), 4.06 (q, $J = 7.1$ Hz, 2H), 5.03 (s, 1H), 5.96 (s, 1H), 7.02 (d, $J = 8.0$ Hz, 2H), 7.19 (d, $J = 8.0$ Hz, 2H). ESI-MS (m/z) 354 ($\text{M} + \text{H}^+$). Analysis calculated for $\text{C}_{22}\text{H}_{27}\text{NO}_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.74; H, 7.65; N, 3.91.

2.5c Ethyl-1,4,5,6,7,8-hexahydro-4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (6c): M.p: $256\text{--}257^\circ\text{C}$. IR (KBr in cm^{-1}) 3281, 3199, 3080, 1708, 1607, 1224, 837, ^1H NMR (CDCl_3 , 300 MHz): δ 0.94 (s, 3H), 1.07 (s, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 2.09–2.20 (m, 4H), 2.36 (s, 3H), 3.73 (s, 3H), 4.04 (q, $J = 7.2$ Hz, 2H), 4.99 (s, 1H), 6.06 (s, 1H), 6.65 (d, $J = 7.3$ Hz, 2H), 7.24 (d, $J = 7.3$ Hz, 2H). ESI-MS (m/z) 370 ($\text{M} + \text{H}^+$). Analysis calculated

Scheme 1. Optimization studies.

Table 1. Preparation of deep eutectic solvents **1a–f**.

Compound A	Compound B (a–f)	Ratio A:B (1a–f)
Choline chloride	Urea (a)	1:2 (1a)
Choline chloride	1-Methyl urea (b)	1:2 (1b)
Choline chloride	Thiourea(c)	1:2 (1c)
Choline chloride	Malonic acid (d)	1:1 (1d)
Choline chloride	Phenyl acetic acid (e)	1:1 (1e)
Choline chloride	Glycerin (f)	1:1 (1f)

Table 2. Optimization studies.

Entry No.	Solvent	Time (min)	Temp (°C)	Yield (%) ^{a,b}
1	1a	20	60	95.0
2	1b	20	60	90.8
3	1c	20	60	89.7
4	1d	20	60	93.3
5	1e	20	60	90.0
6	1f	20	60	80.0
7	1a	60	60	95.0
8	1a	20	80	95.0
9	H ₂ O	20	60	73.4
10	–	360	60	65.7 ^c
11	DMF	20	60	52.3 ^c
12	CH ₃ CN	20	60	38.2 ^c
13	PhMe	20	60	55.3 ^c

^a**2a** (1.0 mmol), **3** (1.0 mmol), **4** (1.0 mmol), **5** (1.5 mmol), DES (2.0 mL) at 60°C for given time.

^bIsolated yields following purification by recrystallization.

^cLower selectivity obtained due to by-product formation

for C₂₂H₂₇NO₄: C, 71.54; H, 7.31; N, 3.79; Found: C, 71.59; H, 7.35; N, 3.84.

2.5d Ethyl-1,4,5,6,7,8-hexahydro-4-(4-hydroxyphenyl)-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6d**): M.p: 232–234°C. IR (KBr in cm^{−1}) 3285, 1690, 1617, 1229, ¹H NMR (CDCl₃, 300 MHz): δ 0.94 (s, 3H), 1.08 (s, 3H), 1.19 (t, *J* = 7.2 Hz, 3H), 2.09–2.19 (m, 4H), 2.34 (s, 3H), 4.06 (q, *J* = 7.6 Hz, 2H), 4.72 (s, 1H),

4.98 (s, 1H), 5.61 (s, 1H), 6.65 (d, *J* = 8.9 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H). ESI-MS (*m/z*) 356 (M + H)⁺. Analysis calculated for C₂₁H₂₅NO₄: C, 70.98; H, 7.04; N, 3.94; Found: C, 70.96; H, 7.02; N, 3.93.

2.5e Ethyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-4-(4-nitrophenyl)-5-oxoquinoline-3-carboxylate (**6e**): M.p: 241–243°C. IR (KBr in cm^{−1}) 3290, 3150, 1711, 1657, ¹H-NMR (CDCl₃ 300 MHz): δ 0.9 (s, 3H), 1.08 (s, 3H), 1.82 (t, *J* = 7.1 Hz, 3H), 2.16–2.36 (m, 4H), 2.40 (s, 3H), 4.01 (q, *J* = 7.1 Hz, 2H), 5.15 (s, 1H), 6.31 (s, 1H), 7.51 (d, *J* = 8.2 Hz, 2H), 8.09 (d, *J* = 8.3 Hz, 2H). ESI-MS (*m/z*) 385 (M + H)⁺. Analysis calculated for C₂₁H₂₅ N₂O₅ C, 65.45; H, 6.49; N, 7.27. Found: C, 65.43; H, 6.49; N, 7.28.

2.5f Ethyl-4-(2-chlorophenyl)-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6f**): M.p: 208–210°C. IR (KBr in cm^{−1}) 3062, 2955, 1720, 1640, 1610, 1468, 1385, 1228, 1020, 745, ¹H NMR (CDCl₃, 300 MHz): δ 0.95 (s, 3H), 1.07 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 2.15–2.23 (m, 4H), 2.30 (s, 3H), 4.04 (q, *J* = 7.1 Hz, 2H), 5.38 (s, 1H), 6.11 (s, 1H), 6.98 (m, 1H), 7.15–7.19 (m, 1H), 7.24–7.26 (m, 1H), 7.41–7.44 (m, 1H). ESI-MS (*m/z*) 374 (M + H)⁺. Analysis calculated for C₂₁H₂₄ClNO₃: C, 67.43; H, 6.47; N, 3.75. Found: C, 67.44; H, 6.48; N, 3.72.

2.5g Ethyl-4-(4-(dimethylamino)phenyl)-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6i**): M.p: 229–231°C. IR (KBr in cm^{−1}) 3287, 3018, 2964, 1602, 1510, 1377, 1207, 751, ¹H NMR (CDCl₃, 300 MHz): δ 0.96 (s, 3H), 1.07 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 2.18–2.27 (m, 4H), 2.35 (s, 3H), 2.86 (s, 6H), 4.05 (q, *J* = 7.1 Hz, 2H), 4.95 (s, 1H), 5.88 (s, 1H), 6.60 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H). ESI-MS (*m/z*) 383 (M + H)⁺. Analysis calculated for C₂₃H₃₀N₂O₃: C, 72.22; H, 7.91; N, 7.32. Found: C, 72.18; H, 7.85; N, 7.25.

Scheme 2. Synthesis of 1,4-DHP's **6a–n** using DES **1a** as the solvent.

Table 3. Synthesis of 1,4-DHPs **6a–n** using DES **1a** as the solvent.

Entry No.	R	Product	Yield (%) ^{a, b}
1	C ₆ H ₅	2a	6a 95
2	4-Me(C ₆ H ₄)	2b	6b 93
3	4-MeO(C ₆ H ₄)	2c	6c 94
4	4-OH(C ₆ H ₄)	2d	6d 94
5	4-O ₂ N(C ₆ H ₄)	2e	6e 95
6	2-Cl(C ₆ H ₄)	2f	6f 94
7		2g	6g 74

Table 3. (continued).

Entry No.	R	Product	Yield (%) ^{a,b}
8			73
9	4-(Me) ₂ N(C ₆ H ₄)		92
10	4-Cl(C ₆ H ₄)		94
11	3-O ₂ N(C ₆ H ₄)		93
12	CH ₃		83
13	C ₂ H ₅		81
14	n-C ₄ H ₉		79

^a**2a–n** (1.0 mmol), **3** (1.0 mmol), **4** (1.0 mmol), **5** (1.5 mmol), DES **1a** (2.0 mL) at 60°C for 20 min.^bIsolated yields following purification by recrystallization

2.5h Ethyl-4-(4-chlorophenyl)-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6j**): M.p: 245–246°C. IR (KBr in cm^{-1}) 3275, 3200, 3075, 2965, 1705, 1650, 1605, ^1H NMR (CDCl_3 , 300 MHz): δ 0.93 (s, 3H), 1.08 (s, 3H), 1.19 (t, $J = 7.1$ Hz, 3H), 2.15–2.23 (m, 4H), 2.38 (s, 3H), 4.04 (q, $J = 7.1$ Hz, 2H), 5.02 (s, 1H), 5.90 (s, 1H), 7.15–7.19 (m, 2H), 7.24–7.26 (m, 2H). ESI-MS (m/z) 374 ($\text{M} + \text{H}$)⁺. Analysis calculated for $\text{C}_{21}\text{H}_{24}\text{ClNO}_3$: C, 67.46; H, 6.47; N, 3.75. Found: C, 67.43; H, 6.49; N, 3.73.

2.5i Ethyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-4-(3-nitrophenyl)-5-oxoquinoline-3-carboxylate (**6k**): M.p: 177–178°C. IR (KBr in cm^{-1}) 3303, 2954, 1683, 1610, 1167, 759, ^1H NMR (CDCl_3 , 300 MHz): δ 0.89 (s, 3H), 1.05 (s, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 2.12–2.23 (m, 4H), 2.38 (s, 3H), 4.03 (q, $J = 7.1$ Hz, 2H), 5.16 (s, 1H), 6.85 (s, 1H), 7.36 (t, $J = 7.9$ Hz, 1H), 7.71 (d, $J = 7.9$ Hz, 1H), 7.97 (m, 1H), 7.99 (m, 1H). ESI-MS (m/z) 385 ($\text{M} + \text{H}$)⁺. Analysis calculated for $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_5$: C, 65.45; H, 6.49; N, 7.27. Found: C, 65.44; H, 6.48; N, 7.26.

2.5j Ethyl-1,4,5,6,7,8-hexahydro-2,4,7,7-tetramethyl-5-oxoquinoline-3-carboxylate (**6l**): M.p: 201–203°C. IR (KBr in cm^{-1}) 3287, 2947, 1685, 1147, 751, ^1H NMR (CDCl_3 , 300 MHz): δ 0.98 (d, 3H), 1.09 (s, 6H), 1.26–1.31 (t, 3H), 2.11–2.32 (m, 7H), 3.91–3.93 (q, 1H), 4.17–4.18 (m, 2H), 5.6 (s, 1H). ESI-MS (m/z) 278 ($\text{M} + \text{H}$)⁺. Analysis calculated for $\text{C}_{16}\text{H}_{23}\text{NO}_3$: C, 69.31; H, 8.30; N, 5.05. Found: C, 69.29; H, 8.29; N, 5.06.

2.5k Ethyl-4-ethyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6m**): M.p: 143–145°C. IR (KBr in cm^{-1}) 3288, 2954, 1686, 1167, 759, ^1H NMR (CDCl_3 , 300 MHz): δ 0.74 (t, $J = 7.2$ Hz, 3H), 1.10 (s, 6H), 1.26–1.30 (m, 5H), 2.12–2.34 (m, 7H), 4.02 (t, $J = 6.2$ Hz, 1H), 4.16 (m, 2H), 5.58 (s, 1H). ESI-MS (m/z) 292 ($\text{M} + \text{H}$)⁺. Analysis calculated for $\text{C}_{17}\text{H}_{25}\text{NO}_3$: C, 70.10; H, 8.59; N, 4.89. Found: C, 70.12; H, 8.57; N, 4.87.

2.5l Ethyl-4-butyl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylate (**6n**): M.p: 165–167°C. IR (KBr in cm^{-1}) 3290, 3090, 1690, 1197, 751, ^1H NMR (CDCl_3 , 300 MHz): δ 0.82 (t, $J = 7.1$ Hz, 3H), 1.09 (s, 6H), 1.15–1.41 (m, 9H), 2.19–2.30 (m, 7H), 4.01 (t, $J = 6.1$ Hz, 1H), 4.17 (m, 2H), 5.77 (s, 1H). ESI-MS (m/z) 320 ($\text{M} + \text{H}$)⁺. Analysis calculated for $\text{C}_{19}\text{H}_{29}\text{NO}_3$: C, 71.47; H, 9.09; N, 4.38. Found: C, 71.45; H, 9.07; N, 4.40.

3. Results and discussion

We first set out to prepare a series of DESs as mixtures of **A** with amides **Ba–c** (ratio 1:2) and **A** with carboxylic acids **Bd–f** (ratio 1:1) (scheme 1, table 1).¹⁷

We first tested DES **1a–f** as solvents for the synthesis of 1,4-DHPs in a one-pot multi-component reaction between **2a–n**, **3**, **4** and **5**. A direct comparison of DES as solvent, with water and under solventless conditions was also carried out. Initial experiments suggested that the reactions initiated in DES **1a–f** gave better yields of the desired products at an optimum temperature of 60°C as compared to water as solvent and under solventless conditions. Interestingly, **1a** proved superior to others, enabling the synthesis of the 1,4-DHPs in excellent yield (95.0%, entry 1, table 2). Polar and non-polar organic solvents (entry 11–13, table 2) when employed as solvents under similar reaction conditions showed poor conversion to the 1,4-DHPs. These results highlight the potential of DESs **1a–f** for promoting synthetically important transformations in comparison to the conventional solvent systems. Easy work-up procedures could be employed to obtain the product for DESs as they could be easily washed away with water suggesting their biocompatible nature.

Encouraged by the above results, we probed the applicability of DES **1a** as optimum solvent for synthesis of 1,4-DHPs in scheme 2. A variety of substituted aldehydes underwent smooth conversion to the desired products. The presence of electron-withdrawing or electron-donating substituents had no influence on the outcome of the reaction with both giving excellent yields. Unsubstituted benzaldehyde (entry 1, table 3) gave the best results followed by electron-withdrawing $-\text{NO}_2$ (entry 5, table 3) and $-\text{Cl}$ (entry 6, table 3) groups. The electron-donating $-\text{OMe}$ (entry 3, table 3) or $-\text{Me}$ (entry 2, table 3) were not far behind. Highly substituted aldehydes such as vanillin (entry 7, table 3)

Table 4. Recycling of deep eutectic solvent in synthesis of 1,4-DHPs.

Recycle of DES	Yield (%) ^{a,b}
Fresh (non-recycled)	95.0
First	92.9
Second	91.7
Third	90.3
Fourth	89.8
Fifth	87.0

^a**2a** (1.0 mmol), **3** (1.0 mmol), **4** (1.0 mmol), **5** (1.5 mmol), DES **1a** (2.0 mL) at 60°C for 20 min.

^bIsolated yields following purification by recrystallization

and 5-bromo vanillin (entry 8, table 3) also gave good to excellent yields of the 1,4-DHP products. It was further observed that even aliphatic aldehydes gave products in good yields (entry 12–13, table 3). The generality of the protocol is thus exhibited allowing efficient synthesis of differently substituted 1,4-DHPs.

3.1 Recycle study of DESs

The ability to recover and recycle the solvent used in the reaction is an important aspect of green chemistry. Therefore in the present study, we also evaluated the recyclability and reusability of this DES (table 4).

4. Conclusion

In summary, a very simple approach towards one-pot multi-component synthesis of 1,4-dihydropyridine derivatives was developed using biocompatible DESs. The DES gave excellent recyclability without loss of activity up to 5 cycles, hence providing a greener alternative. A milder and highly efficient protocol was developed which can easily replace existing methods.

References

1. Bossert F, Meyer H and Wehinger E 1981 *Angew. Chem. Int. Ed. Engl.* **20** 762
2. Mannhold R, Jablonka B, Voigdt W, Schoenafinger K and Schrava K 1992 *Eur. J. Med. Chem.* **27** 229
3. Reid G L, Meredith P A and Pasanisi F 1985 *J. Cardio-vasc. Pharmacol.* **7** S18
4. Shan R, Velazquez C and Knaus E 2004 *J. Med. Chem.* **47** 254
5. Kawase M, Shah A, Gaveriya H, Motohashi N, Sakagami H, Varga A and Molnar J 2002 *Bioorg. Med. Chem.* **10** 1051
6. a) Janis R A and Triggler D J 1983 *J. Med. Chem.* **26** 775; b) Loev B, Goodman M M, Snader K M, Tedeschi R and Macko E 1974 *J. Med. Chem.* **17** 956
7. a) Tietze L F 1996 *Chem. Rev.* **96** 115; b) Tietze L F, Brasche G and Gericke K M 2006 *Domino reactions in organic synthesis*, Weinheim: Wiley-VCH
8. Love B and Sander K M 1965 *J. Org. Chem.* **30** 1914
9. Tu S-J, Yu C-X, Liu X-H, Yao C-S, Liu F and Gao Y 2002 *Chin. J. Struct. Chem.* **21** 99
10. Wang L-M, Sheng J, Zhang L, Han J-W, Fan Z-Y, Tian H and Qian C-T 2005 *Tetrahedron* **61** 1539
11. Ji S J, Jiang Z Q, Lu J and Loh T P 2004 *Synlett* 831
12. a) Welton T 1999 *Chem. Rev.* **99** 2071; b) Ranke J, Stolte S, Stormann R, Arning J and Jastorff B 2007 *Chem. Rev.* **107** 2183; c) Jastorff B, Stormann R, Ranke J, Molter K, Stock F, Oberheitmann B, Hoffmann W, Hoffmann J, Nuhter M, Ondruschka B and Filser J 2003 *Green Chem.* **5** 136; d) Stolte S, Arning J, Bottin-Weber U, Matzke M, Stock F, Thiele K, Uerdingen M, Welz-Biermann U, Jastorff B and Ranke J 2006 *Green Chem.* **8** 621; e) Anastas P T 2010 *Green solvents: ionic liquids*, P Wasserscheid and A Stark (eds) Weinheim: Wiley-VCH, vol. 6
13. Park S and Kazlauskas R J 2003 *Curr. Opin. Struct. Biol.* **14** 432
14. Gericke M, Fardim P and Heinze P 2012 *Molecules* **17** 7458
15. a) Aparicio S, Atilhan M and Karadas F 2010 *Ind. Eng. Chem. Res.* **49** 9580; b) Seddon K R, Stark A and Torres M J 2000 *Pure Appl. Chem.* **72** 2275; c) Ab Rani M A, Brant A, Crowhurst L, Dolan A, Lui M, Hassan N H, Hallett J P, Hunt P A, Niedermeyer H and Perez-Arlandis J M 2011 *Phys. Chem. Chem. Phys.* **13** 16831; d) Gallo V, Mastroilli P, Nobile C F, Romanazzi G and Suranna G P 2002 *J. Chem. Soc. Dalton* **23** 4339; e) Lee S, Ha S, Lee S and Koo Y M 2006 *Biotechnol. Lett.* **28** 1335
16. Shamsuri A A and Abdullah D K 2010 *MAKARA SAINS.* **14** 101
17. a) Abbot A, Capper G, Davies D, Munro H, Rasheed R and Tambyrajah V 2001 *Chem. Commun.* 2010; b) Abbott A, Capper G, Davies D, Rasheed R and Tambyrajah V 2003 *Chem. Commun.* 70; c) Abbott A, Capper G, Davies D and Rasheed R 2004 *J. Am. Chem. Soc.* **126** 9142
18. Gorke J, Srienc F and Kazlauskas R 2008 *Chem. Commun.* 1235
19. Abbott A, Cullis P, Gibson M, Harris R and Raven E 2007 *Green Chem.* **9** 868
20. Jain N, Kumar A and Chauhan S 2005 *Tetrahedron* **61** 1015