Combinatorial synthesis of functionalized chiral and doubly chiral ionic liquids and their applications as asymmetric covalent/non-covalent bifunctional organocatalysts†

Long Zhang,[a] Sanzhong Luo,*[b] Xueling Mi,[b] Song Liu,[b] Yupu Qiao,[b] Hui Xu[b] and Jin-Pei Cheng*[a]

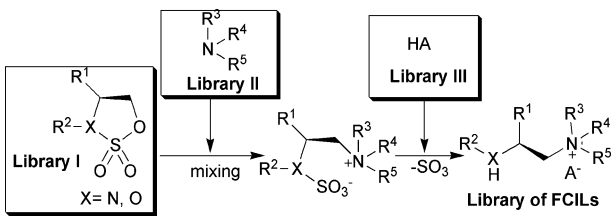
Received 10th September 2007, Accepted 4th December 2007
First published as an Advance Article on the web 20th December 2007
DOI: 10.1039/b713843a

A facile combinatorial strategy was developed for the construction of libraries of functionalized chiral ionic liquids (FCILs) including doubly chiral ionic liquids and bis-functional chiral ionic liquids. These FCIL libraries have the potential to be used as asymmetric catalysts or chiral ligands. As an example, novel asymmetric bifunctional catalysts were developed by simultaneously incorporating functional groups onto the cation and anion. The resultant bis-functionalized CILs showed significantly improved stereoselectivity over the mono-functionalized parent CILs.

Introductions

Functionalized ionic liquids (FILs, or task-specific ionic liquids, TSILs), are receiving growing attention due to their tunable features for various targeted chemical tasks[1] and their advantages as reusable homogeneous supports and dual solvent-catalysts with green credentials.[2] Recently, chiral ionic liquids (CILs) have emerged as an important kind of ionic liquid in the development of task-specific ionic liquids.[3] Following the initial works of Howarth[4a] and Seddon,[4b] a number of CILs have been synthesized and applied as chiral resolution reagents, chiral solvents or asymmetric catalysts.[3] For example, the use of CILs as reaction media has been shown to induce significant chiral induction in several reactions including the Baylis–Hillman reaction,[5] photoisomerization,[6] Michael addition[7] and hydrogenation.[8] Recently, we and other groups have reported that CILs with specific functional groups served as highly effective asymmetric organocatalysts for the direct aldol reaction and the Michael addition reaction.[9] Functionalized CILs have also been shown to be effective chiral ligands in asymmetric transition metal catalysis.[10] Overall, as the unique properties of ILs become well-established, more promising applications of CILs are ensured, and the bottleneck now is in the development and synthesis of new kinds of CILs.

In general, CILs have been generated by introducing chirality into the cation, anion or both *via* a "chiral pool" strategy[11] or asymmetric synthesis.[12] Of the two approaches, the former strategy has normally been employed to produce optically pure CILs. In the chiral pool synthesis, the judicious selection of chiral precursors and the corresponding IL-forming reaction are considered critical steps. Ideally, a successful synthesis would encompass a modular and combinatorial strategy, an easy, quick and clean reaction and readily available chiral precursors. Despite much success achieved in this area,[13] most of the syntheses have been applied to only a few selected substrates with limited structural diversity. A facile and combinatorial synthesis of CILs with a wide variety of structural patterns has not been reported until now.[14] Herein, we describe such a method for the synthesis of CILs by choosing chiral cyclic sulfates and cyclic sulfamidates as the key precursors (Scheme 1).[15] In this procedure, ring opening of cyclic sulfates or sulfamidates with tertiary amines serves as the key IL-forming reaction. This reaction, with characteristics resembling "click" reactions,[16] allows for facile and combinatorial construction of libraries of chiral ionic liquids with structural diversity. Besides being highly modular, this new protocol opens access to a wide variety of CILs with hydroxyl or amino chiral centers in a highly efficient and halide-free manner.



Scheme 1 Strategy for the click synthesis of FCILs.

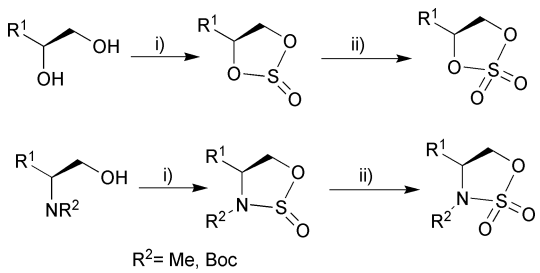
Results and discussion

Synthesis of cyclic sulfates and sulfamidates

The chiral cyclic sulfates and sulfamidates were synthesized from readily available chiral diols and chiral amino alcohols,[15] respectively. The chiral diols or chiral amino alcohols were treated with $SOCl_2$ and the cyclic sulfites or cyclic sulfimidates obtained were oxidized with $RuCl_3/NaIO_4$ to afford the final products (Scheme 2). Alternatively, the sulfamidates could also be accessed from chiral diols by use of the Burgess reagent[17] or direct asymmetric intramolecular amidation of simple alcohols by

[a]*Department of Chemistry and State-key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin, 300071, China*
[b]*Beijing National Laboratory for Molecular Sciences (BNLMS), Centre for Chemical Biology, Institute of Chemistry, Chinese Academy of Science, Beijing, 100080, China. E-mail: luosz@iccas.ac.cn; Fax: +86-10-62554449; Tel: +86-1062554446*

† Electronic supplementary information (ESI) available: Experimental details and characterization of all the new ionic liquids synthesized. See DOI: 10.1039/b713843a



Scheme 2 Synthesis of cyclic sulfate and sulfamidates. *Reagents and conditions*: i) $SOCl_2$, NEt_3, imidazole, CH_2Cl_2, rt, 12 h; ii) $RuCl_3$, $NaIO_4$, CH_3CN–H_2O, rt, 12 h, 56–86% yield.

C–H activation,[18] which would eventually make the process more atom-economic.

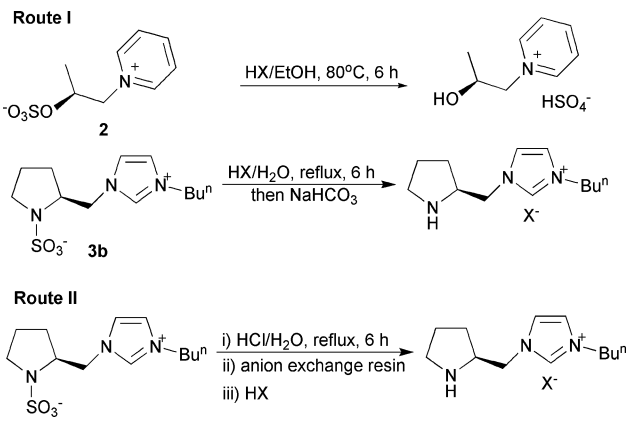
Ring-opening reactions of cyclic sulfates and sulfamidates

The ring-opening reactions were simply carried out by mixing the two reactants in a 1 : 1 molar ratio. In cases where liquid substrates were involved, no solvent is necessary to facilitate the reaction. Gratifyingly, the ring-opening reactions of both cyclic sulfates and cyclic sulfamidates proceeded smoothly, affording the desired zwitterionic products. These were insoluble in non-polar solvents and precipitated from reaction mixture, thus making the work-up very straightforward. In all the cases examined, simple washing with ether or ethyl acetate was sufficient to give the pure zwitterionic products in quantitative yields (Table 1). Several notable features of the alkylation reactions are evident: (1) the reactions are very clean and quick, thus accelerating the synthesis of CILs, (2) only stoichiometric alkylation reagents are employed. This stands in contrast to the commonly practised ionic liquid synthesis with alkyl halides, where excess reagents and extending heating are normally required to complete the reaction; and (3) the cyclic sulfate or sulfamidate moieties also serve as masked functional groups, thus diminishing protection–deprotection manipulations. For example, our present synthesis of chiral hydroxyl ionic liquid from the cyclic sulfate of (*R*)-propane-1,2-diol were conveniently conducted in one pot, and the reactions went to completion cleanly in minutes at room temperature, a significant improvement over the previous synthesis that required multiple protections and deprotections.[13m]

Some selected zwitterionic products are summarized in Table 1. As shown, the current method accommodates a variety of chiral cyclic sulfates and cyclic sulfamidates as well as a wide range of nucleophiles, including alkylated imidazoles and pyridines. With cyclic sulfates, the reactions took place exclusively on the less substituted side, leading to a single product in quantitative yields. Judged from the data in Table 1, combinatorial synthesis is clearly viable by combination of different cyclic sulfates/sulfamidates and nucleophiles (*e.g.* entries 9–14).

Synthesis of the final functionalized chiral ionic liquids

The zwitterions were next treated with strong acids to afford, as initially predicted, Brønsted acidic CILs. Unfortunately, this type of acidic CIL is unstable, and slow decomposition of the sulfuric/sulfamic acid groups was observed in most of the cases examined. However, this instability provides us with a chance to remove the sulfonyl groups to achieve functionalized CILs. The zwitterionic products, *e.g.* **2** and **3b**, were therefore heated in the presence of a strong acid to completely remove the sulfonyl groups. This step could be accelerated using microwave heating. After treatment, the sulfuric zwitterions were cleanly transferred to functionalized CILs with hydrogen sulfate anions. For sulfamic zwitterions, this step could introduce the anion of the final FCILs when excess strong acids such as HCl, CF_3SO_3H, $HClO_4$ or HBF_4 were used (Scheme 3, route I). Alternatively, the anions of FCILs could also be introduced following an anion exchange (OH^-) and neutralization procedure (Scheme 3, route II). It should be noted that the neutralization strategy allowed for the incorporation of all kinds of acids, either strong or weak, especially with chiral acids as the final anions. The diversity of our combinatorial synthesis is therefore significantly enhanced, and a facile combinatorial synthesis of doubly chiral ILs (with chirality on both cation and anion) and bis-functional CILs (with functional groups on both cation and anion) was achieved for the first time. Following routes I and II, an initial library of functionalized chiral ionic liquids were easily constructed (Fig. 1). In general, the final functionalized chiral ionic liquids were obtained in quantitative yields starting from the corresponding zwitterions. Fig.1 lists the selected examples of functionalized chiral ionic liquids, doubly chiral ILs and bifunctional CILs.



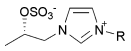
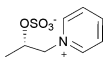
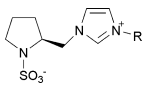
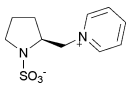
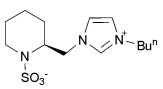
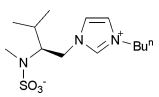
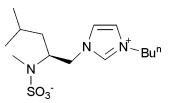
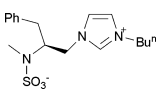
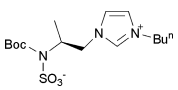
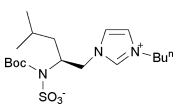
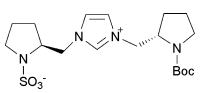
Scheme 3 Synthesis of final FCILs.

Table 2 summarizes the thermal properties of the selected final FCILs **20** and **21**. These functionalized CILs demonstrated good thermal stability (>163 °C) as determined by TGA. Given the multi-functionalized structural features, FCILs **20** and **21** are still viscous liquids with glass transition temperaturesranging from −37 °C to −67 °C. These properties suffice for potential applications of the FCILs.[11]

Catalytic applications of functionalized chiral ionic liquids

To illustrate the potential of current combinatorial synthesis, the obtained functionalized chiral ionic liquids, in particular the doubly chiral ionic liquids and the bis-functionalized chiral ionic liquids, were next applied as catalysts in asymmetric direct aldol reactions. Previously, we have shown that functionalized chiral ionic liquids such as **20** can serve as highly efficient and reusable organocatalysts for Michael addition reactions[9a,b,d] and direct aldol reactions.[9c] Though excellent stereoselectivities were achieved in Michael reactions with the catalysis of **20**, FCILs such

Table 1 Synthesis of zwitterions

Entry	Product		Conditions[a]	Time	Yield (%)[b]
1		R = Me (**1a**)	A	15 min	>99
2		R = *n*-C_4H_9 (**1b**)	A	15 min	>99
3		R = *n*-C_8H_{17} (**1c**)	B	1 min	>99
4		R = *n*-$C_{12}H_{25}$ (**1d**)	B	1 min	97
5[c]		**2**	B	10 h	>99
6		R= Me (**3a**)	B	30 min	>99
7		R = *n*-C_4H_9 (**3b**)	B	1.5 h	>99
8		R = *n*-C_8H_{17} (**3c**)	C	5 h	>99
9		**4**	C	10 h	72
10		**5**	B	3 h	99
11		**6**	B	3 h	71
12		**7**	B	3 h	>99
13		**8**	C	5 h	>99
14		**9**	C	7 h	98
15		**10**	C	3 h	75
16		**11**	C	5 h	96

[a] *Reagents and conditions*: A: 1.0 equiv. Nu, CH_2Cl_2, 0 °C; B: 1.0 equiv. Nu, neat, rt; C: 1.0 eq. Nu, toluene, 80 °C. [b] Isolated yield. [c] Excess pyridine was used.

as **20a** demonstrated poor stereoselectivities in aldol reactions.[9c] Further evolution of the catalysts is therefore necessary. In this regard, the current combinatorial synthesis might provide promising solutions. A initial library of doubly chiral ionic liquids and bis-functionalized CILs were briefly examined in the model reaction of cyclohexanone and *p*-nitrobenzaldehyde (Table 3).

A variety of doubly chiral ionic liquids such as **21** were first tested and showed reasonably high catalytic activities in the model reactions but with marginal effect on the stereoselectivity (Table 3, entries 2–4 *vs.* entry 1), suggesting the second chirality on anions is insignificant in influencing stereocontrol. We next examined possible bifunctional catalysis by introducing an additional functional group (namely, a hydrogen-bonding group), onto FCIL anions. As is known, bifunctional catalysis is a well-explored motif in asymmetric organocatalysis.[19] A prominent example is L-proline, for which both the pyrrolidine and carboxylic groups have been shown to be essential for asymmetric catalysis in many transformations.[20] Previously, we have shown that acidic additives have a dramatic impact on the catalytic performance of FCILs.[9a,c] Bearing these observations in mind, we prepared a series of

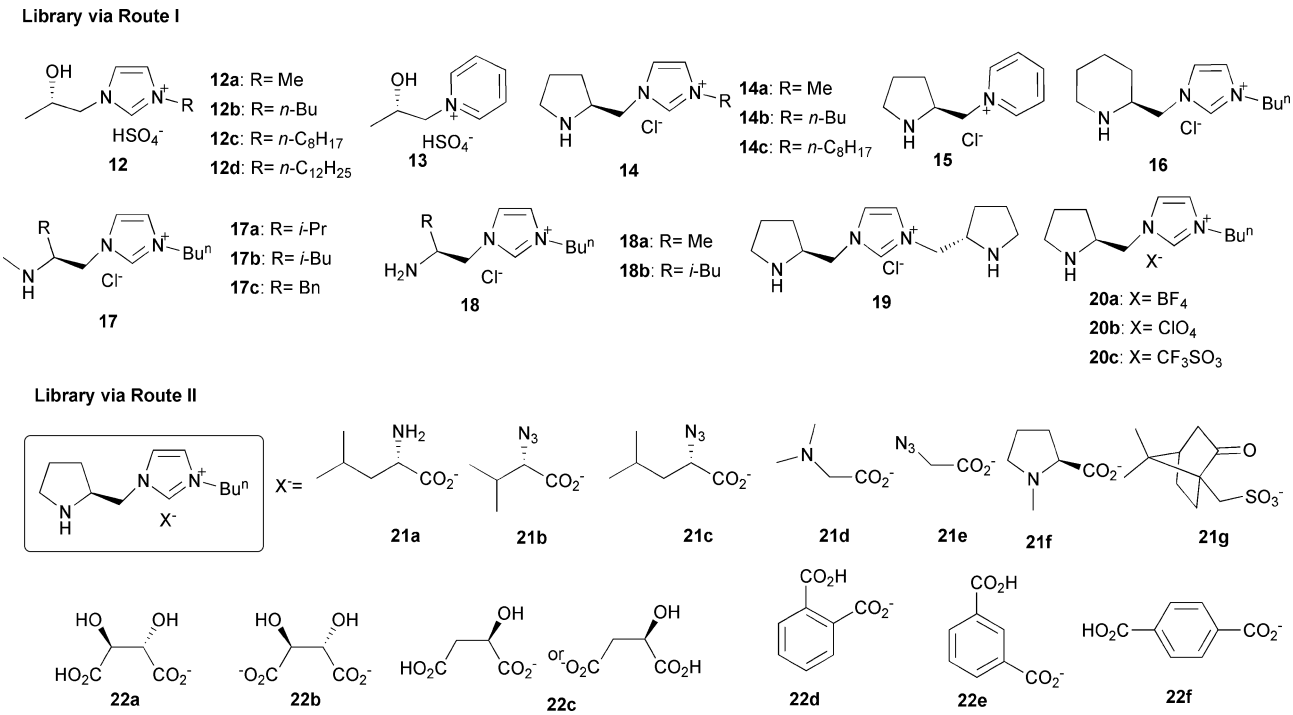


Fig. 1 Library of final FCILs.

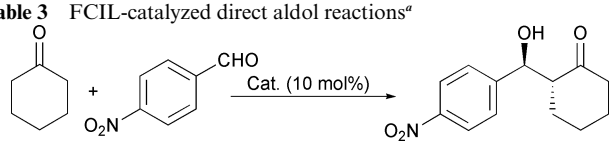
Table 2 Thermal properties of the FCILs

Entry	FCIL	T_g/°C[a]	T_{decomp}/°C[b]	$[\alpha]_D^{20}$
1	**20a**	−52	232	+25.5 (c = 1.0, $CHCl_3$)
2	**20b**	−67	263	+24.6 (c = 1.0, EtOH)
3	**20c**	−63	228	+17.6 (c = 1.0, EtOH)
5	**21a**	−54	197	+6.1 (c = 1.0, CH_3OH)
6	**21b**	−52	163	+2.9 (c = 1.0, $CHCl_3$)
7	**21c**	−41	179	+9.8 (c = 1.0, $CHCl_3$)
8	**21d**	−38	235	+11.6 (c = 1.0, $CHCl_3$)
9	**21e**	−64	167	+20.2 (c = 1.0, CH_3OH)
10	**21f**	−37	226	−31.2 (c = 1.0, CH_3OH)
11	**21g**	−44	229	+46.4 (c = 1.0, $CHCl_3$)

[a] Determined by DSC. [b] Determined by TGA.

bis-functionalized FCILs **22**, *i.e.* hydroxy- or carboxy-functionalized ILs, by incorporating acidic groups onto anions following the neutralization strategy (Fig. 1, route II). FCILs **22** were generated *in situ* and used directly in the model reaction (Table 3). To our delight, improvement on stereoselectivity was indeed observed (Table 3, entries 5–10) and the best results were achieved with FCIL **22d** bearing a phthalic mono-anion. In the presence of **22d** (10 mol%), the reaction gave 94% yield, 70 : 30 *anti*/*syn* and 55% ee (*anti*) in 23 h, showing a significant improvement over the parent FCIL **20a** (Table 3, entry 8 *vs.* entry 1). Interestingly, FCILs **22e** and **22f** (prepared from the phthalic acid isomers isophthalic acid and terephthalic acid, respectively), showed much lower stereoselectivity than that of FCIL **22d**, though they maintained similar activities (Table 3, entries 9 and 10 *vs.* entry 8). These results strongly suggest that the carboxylic acid group is involved in the catalytic cycle, wherein its orientation in the chiral ion pair is vital for stereocontrol. FCIL **22d** may therefore represent a rare example of non-covalent bifunctional organocatalysts with its two acting functional groups residing

Table 3 FCIL-catalyzed direct aldol reactions[a]



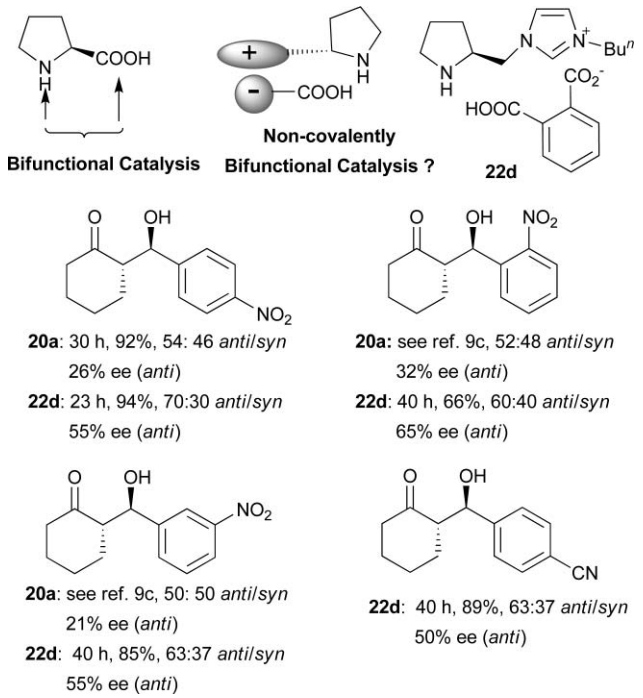
Entry	Catalyst	Time/h	Yield (%)	*Anti*/*syn*[b]	ee (%)[c] *Anti*	ee (%)[c] *Syn*
1	**20a**	30	92	46 : 55	26	71
2	**21b**	36	90	64 : 36	7	4
3	**21c**	60	94	60 : 40	15	46
4	**21e**	36	97	60 : 40	21	6
5	**22a**	36	94	50 : 50	23	58
6	**22b**	50	90	57 : 43	35	34
7	**22c**	96	66	70 : 30	47	24
8	**22d**	**23**	**94**	**70 : 30**	**55**	**73**
9	**22e**	30	90	54 : 46	23	<5
10	**22f**	30	80	50 : 50	16	7

[a] *Conditions*: 0.25 mmol of substrate in the presence of 10 equiv. of cyclohexanone, neat. [b] Determined by ^1H NMR. [c] Determined by chiral HPLC.

separately on cation and anion. To further prove the bifunctional catalysis of FCIL **22d**, several other substrates were examined (Scheme 4) and consistent results were obtained, all showing significantly improved stereoselectivity over the parent FCIL **20a**. Importantly, the ionic liquid type catalyst **22d** maintains good biphasic properties, and can be easily recycled and reused as previously demonstrated.[9]

Conclusions

In conclusion, we have presented herein a facile and combinatorial synthesis of functionalized chiral ionic liquids by utilizing



Scheme 4 Non-covalent bifunctional catalysis of the asymmetric direct aldol reaction.

ring-opening reactions of chiral cyclic sulfates/sulfamidates. As a result, parallel synthesis of library of FCILs is not only accelerated but allows for a much richer family of functionalized structures. This versatility was demonstrated in the parallel synthesis of doubly chiral ionic liquids and bis-functional CILs. These series of ionic liquids, endowed with multiple functional groups, still maintain good ionic liquid properties. The potential of these FCILs was further demonstrated in asymmetric direct aldol reactions. Novel non-covalent bifunctional organocatalysts have been evolved by screening a series of doubly chiral and bis-functionalized ionic liquids. FCIL **22d**, endowed with a carboxylic acid group on the anion, showed significantly improved stereoselectivity over its parent FCILs. This bifunctional strategy can be applied to many other bifunctional organocatalytic transformations. Furthermore, the chiral imidazolium zwitterions would also serve as good nitrogen heterocyclic carbene (NHC) ligands and catalysts,[21] and these features are also currently being investigated by our groups.

Experimental

General

Commercial reagents were used as received, unless otherwise stated. ^{1}H and ^{13}C NMR were recorded on a Bruker-DPX 300 spectrometer, and chemical shifts are reported in ppm relative to tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations are used to designate chemical shift mutiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Mass spectra were obtained using a fast-atom bombardment (FAB) spectrometer, electron impact ionization (EI) mass spectrometer or electrospray ionization (ESI) mass spectrometer. Glass transition temperatures (T_g) were determined by scanning differential chromatography on a DSC 822e instrument with a heating rate of 10 °C min^{-1} after initially cooling to −80 to −100 °C. Decomposition temperatures (T_{dec}) were determined with a STA 409 PC instrument with a heating rate of 10 °C min^{-1}. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Perkin-Elmer 341 digital polarimeter and are reported as $[a]_D^{20}$ values (c in g per 100 mL of solvent). The cyclic sulfates and cyclic sulfamidates were synthesized following previous procedures with minor modifications.

Synthesis of FCILs 12 and 13

FCIL 12a (Condition A). The chiral cyclic sulfate of (*S*)-propane-1,2-diol (69 mg, 0.5 mmol) was dissolved in *ca.* 3 mL CH_2Cl_2, followed by the dropwise addition of *N*-methylimidazole (41 mg, 0.5 mmol, dissolved in *ca.* 3 mL CH_2Cl_2). The mixture was stirred for another 15 min, concentrated in *vacuo*, the residue washed with Et_2O (5 mL × 6), and dried in *vacuo* to afford **1a** as white solid in quantitative yield. ^{1}H NMR (300 MHz, D_2O): δ 1.41 (3H, d, J = 5.46 Hz), 3.94 (3H, s), 4.25–4.33 (1H, m), 4.50–4.55 (1H, m), 4.70–4.84 (1H, m), 7.48 (1H, s), 7.54 (1H, s), 8.79 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 17.25, 35.86, 53.37, 74.59, 123.24, 123.47, 136.86; MS (ESI) for $C_7H_{13}N_2O_4S^+$ (M^+ + 1): calcd. 221.06, found 221.18.

The zwitterion **1a** obtained above was dissolved in 5 mL 4 N HCl in EtOH solution and refluxed for 6 h. The the reaction mixture was then evaporated and dried in *vacuo* to afford the FCIL **12a** as a colorless viscous liquid in quantitative yield. $[a]_D^{20}$ = +1.8 (c = 1.0, CH_3CH_2OH); ^{1}H NMR (300 MHz, D_2O): δ 1.06–1.09 (3H, m), 3.76–3.77 (3H, m), 3.90–4.03 (2H, m), 4.14–4.19 (1H, m), 7.31 (1H, s), 7.35 (1H, s), 8.58 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 18.92, 25.73, 55.59, 65.79, 122.92, 123.38, 136.40; IR (film): ν 3348.8, 3150.2, 3099.1, 2973.7, 1571.7, 1457.9, 1427.1, 1379.8, 1168.7, 1114.7 cm^{-1}; HRMS (FAB) for $C_7H_{13}N_2O^+$ (M^+): calcd. 141.1022, found 141.1015.

FCIL 12b. The corresponding zwitterion **1b** was obtained following Condition A in quantitative yield in 15 min, **1b**: ^{1}H NMR (300 MHz, D_2O): δ 0.87 (3H, t, J = 7.41 Hz), 1.23–1.34 (5H, m), 1.76–1.85 (2H, m), 4.15–4.25 (3H, m), 4.43–4.49 (1H, m), 7.47 (2H, s), 8.77 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.70, 17.24, 18.76, 31.29, 49.50, 53.40, 74.52, 122.29, 123.28, 136.13; MS (ESI) for $C_{10}H_{19}N_2O_4S^+$ (M^+ + 1): calcd. 263.11, found 263.27. The desired FCIL **12b** was obtained as a colorless viscous liquid in quantitative yield after desulfonation with HCl/EtOH. $[a]_D^{20}$ = +2.8 (c = 1.0, CH_3CH_2OH); ^{1}H NMR (300 MHz, D_2O): δ 0.80–0.85 (3H, m), 1.13–1.16 (2H, m), 1.19–1.30 (3H, m), 1.75–1.80 (2H, m), 3.98–4.26 (5H, m), 7.44 (2H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.67, 18.75, 18.99, 31.19, 49.34, 55.61, 65.77, 122.18, 123.04. IR (film): ν 3348.8, 3144.0, 3087.0, 2967.9, 2933.2, 2875.3, 1540.9, 1457.9, 1410.7, 1376.9, 1188.9, 1115.6 cm^{-1}; HRMS (FAB) for $C_{10}H_{19}N_2O^+$ (M^+): calcd. 183.1492, found 183.1486.

FCIL 12c (Condition B). The chiral cyclic sulfate of (*S*)-propane-1,2-diol (69 mg, 0.5 mmol) was mixed with 1-octylimidazole (90 mg, 0.5 mmol). The mixture was stirred for 1 min, then washed with ether six times, and dried *in vacuo*

to afford **1c** as a colorless solid in quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (3H, t, $J = 7.16$ Hz), 1.14–1.24 (13H, m), 1.74–1.78 (2H, m), 4.05–4.20 (3H, m), 4.53–4.57 (1H, m), 4.69–4.73 (1H, m), 7.30 (1H, m), 7.61 (1H, s), 9.10 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.98, 18.08, 22.48, 26.16, 28.86, 28.94, 30.08, 31.59, 49.90, 53.62, 71.76, 121.40, 124.18, 136.84; MS (ESI) for $C_{14}H_{27}N_2O_4S^+$ ($M^+ + 1$): calcd. 319.17, found 319.26.

The zwitterion **1c** obtained above was dissolved in 5 mL 4 N HCl in EtOH solution and refluxed for 6 h. The reaction mixture was then evaporated and dried in *vacuo* to afford the FCIL **12c** as a colorless viscous liquid in quantitative yield. $[\alpha]_D^{20} = +1.0$ ($c = 1.0$, CH_3CH_2OH); ^{1}H NMR (300 MHz, D_2O): δ 0.76–0.80 (3H, m), 1.17–1.30 (13H, m), 1.75–1.90 (2H, m), 4.06–4.32 (5H, m), 7.49 (1H, s) 7.54 (1H, s), 8.81 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 13.65, 19.02, 22.26, 25.67, 28.48, 28.64, 29.47, 31.37, 49.61, 55.72, 65.70, 122.10, 123.38, 135.88; IR (film): ν 3349.8, 3144.3, 3090.4, 2961.2, 2927.4, 2857.0, 1562.1, 1458.9, 1377.9, 1187.0, 1121.4 cm^{-1}; HRMS (FAB) for $C_{14}H_{27}N_2O^+$ (M^+): calcd. 239.2118, found 239.2120. HSO_4^- (X^-): calcd. 96.96, found 96.95.

FCIL 12d. The corresponding zwitterion **1d** was obtained following Condition B in 97% yield after 1 min, **1d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (3H, t, $J = 6.40$ Hz), 1.24–1.33 (21H, m), 1.75–1.96 (2H, br), 4.14–4.30 (3H, m), 4.61–4.66 (1H, m), 4.74–4.87 (1H, br), 7.38 (1H, m), 7.71 (H, s), 9.20 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.02, 18.11, 22.57, 26.21, 28.95, 29.23, 29.34, 29.46, 29.52, 30.11, 31.80, 49.89, 53.66, 71.77, 121.34, 124.17, 136.88; MS (ESI) for $C_{18}H_{35}N_2O_4S^+$ ($M^+ + 1$): calcd. 375.23, found 375.40. The desired FCIL **12d** was obtained as a pale yellow viscous solid in quantitative yield after desulfonation with HCl/EtOH. $[\alpha]_D^{20} = +3.6$ ($c = 1.0$, CH_3CH_2OH); ^{1}H NMR (300 MHz, D_2O): δ 0.82–0.86 (3H, m), 1.15–1.26 (21H, m), 1.75–1.90 (2H, m), 4.03–4.35 (5H, m), 7.34 (1H, s) 7.56 (1H, s), 8.99 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 14.06, 19.70, 22.64, 26.33, 29.13, 29.34, 29.51, 29.64, 29.67, 30.07, 31.89, 49.96, 55.97, 66.01, 121.69, 123.81, 136.32; IR (film): ν 3347.8, 3144.4, 3083.6, 2969.8, 2923.6, 2853.2, 1562.1, 1457.9, 1377.9, 1167.7, 1122.4 cm^{-1}; HRMS (FAB) for $C_{18}H_{35}N_2O^+$ (M^+): calcd. 295.2744, found 295.2742. HSO_4^- (X^-): calcd. 96.96, found 96.96.

FCIL 13. The corresponding zwitterion **2** was obtained follownig Condition B, except that 10 equiv. of pyridine was used and the reaction was carried out for 10 h at 0 °C, with quantitative yield. **2**: ^{1}H NMR (300 MHz, D_2O): δ 1.43 (3H, d, $J = 6.31$ Hz), 4.52–4.60 (1H, m), 4.78–4.90 (2H, m), 8.04 (2H, t, $J = 6.86$ Hz), 8.54 (1H, t, $J = 7.68$ Hz), 8.81 (1H, d, $J = 6.04$ Hz); ^{13}C NMR (D_2O, 75 MHz): δ 17.50, 64.81, 75.00, 128.10, 145.19, 146.36. MS (ESI) for $C_8H_{12}NO_4S^-$ ($M^+ + 1$): calcd. 218.05, found 218.13. The desired FCIL **13** was obtained as a colorless liquid in quantitative yield after desulfonation with HCl/EtOH. $[\alpha]_D^{20} = +5.9$ ($c = 1.0$, CH_3CH_2OH); ^{1}H NMR (300 MHz, D_2O): δ 1.18 (3H, d, $J = 6.31$ Hz), 4.13–4.18 (1H, m), 4.27–4.34 (1H, m), 4.62–4.66 (1H, m), 7.97 (2H, t, $J = 6.86$ Hz), 8.46 (1H, t, $J = 7.68$ Hz), 8.69 (1H, d, $J = 6.04$ Hz); ^{13}C NMR (D_2O, 75 MHz): δ 19.12, 66.56, 67.32, 128.01, 144.82, 146.00; IR (film): ν 3364.2, 3089.4, 3060.5, 2974.7, 2934.2, 1634.4, 1488.8, 1461.8, 1409.7, 1378.8, 1185.0 cm^{-1};MS (ESI) for $C_8H_{12}NO^+$ (M^+): calcd. 138.09, found 138.16, HSO_4^- (X^-): calcd. 96.96, found 96.93.

Synthesis of FCILs 14–19

FCIL 14a. The corresponding zwitterion **3a** was obtained using Condition B in quantitative yield after 30 min. **3a**: ^{1}H NMR (300 MHz, D_2O): δ 1.50–1.66 (1H, m), 1.67–1.81 (1H, m), 1.83–1.99 (1H, m), 2.05–2.22 (1H, m), 3.19–3.34 (2H, m), 3.94 (4H, s), 4.15–4.22 (1H, m), 4.36–4.42 (1H, m), 7.44 (1H, s), 7.54 (1H, s), 8.76 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 24.01, 28.66, 35.66, 49.83, 53.00, 59.08, 123.01, 123.35, 136.72. MS (ESI) for $C_9H_{16}N_3O_3S$ ($M^+ + 1$): calcd. 246.09, found 246.10. The zwitterion **3a** obtained above was dissolved in 5 mL aqueous 4 N HCl, refluxed for 6 h, and then the solution was cooled to rt and neutralized by solid $NaHCO_3$ until no further gas was evolved. The mixture was stirred for 1 h and concentrated to dryness *in vacuo*, extracted with $CHCl_3$ (10 mL × 4), and the combined organic layer concentrated in *vacuo* to afford FCIL **14a** (known compound)[9] as a pale yellow oil in quantitative yield. $[\alpha]_D^{20} = +3.3$ ($c = 1.0$, CH_3CH_2OH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.10–1.22 (1H, m), 1.41–1.51 (2H, m), 1.66–1.78 (1H, m), 2.57–2.71 (1H, m), 2.85–3.03 (1H, m), 3.14–3.40 (1H, m), 3.81–3.93 (4H, m), 4.09–4.16 (1H, m), 7.41 (1, s), 7.48 (1H, s), 10.07 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.69, 29.02, 36.22, 46.32, 53.97, 57.46, 122.80, 122.98, 137.90; IR (film): ν 3434.6, 3145.3, 3082.7, 2958.3, 2871.5, 1562.1, 1454.1, 1404.9, 1169.6 cm^{-1}.

FCIL 14b. The corresponding zwitterion **3b** was obtained using Condition B in quantitative yield after 1.5 h. **3b**: $[\alpha]_D^{20} = -39.5$ ($c = 1.0$, H_2O); ^{1}H NMR (300 MHz, D_2O): δ 0.94 (3H, t, $J = 7.34$ Hz), 1.24–1.40 (2H, m), 1.43–1.54 (1H, m), 1.67–1.76 (1H, m), 1.83–1.93 (3H, m), 2.06–2.18 (1H, m), 3.15–3.31 (2H, m), 3.91–3.99 (1H, m), 4.15–4.26 (3H, m), 4.40 (1H, apparent dd, $J =$ 4.14 Hz, 4.33 Hz, 13.94 Hz), 7.49 (1H, s), 7.54 (1H, s), 8.81 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.61, 18.73, 23.95, 28.60, 31.31, 49.31, 49.76, 53.00, 58.87, 121.82, 123.44, 135.97; MS (ESI) for $C_{12}H_{22}N_3O_3S$ ($M^+ + 1$): calcd. 288.14, found 288.15. The desired FCIL **14b** was obtained as a yellow viscous oil in 94% yield after desulfonation. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.69 (3H, t, $J =$ 7.16 Hz), 0.99–1.22 (3H, m), 1.41–1.48 (2H, m), 1.60–1.78 (3H, m), 2.58–2.85 (2H, m), 3.13–3.43 (2H, m), 3.90–3.98 (1H, m), 4.08 (2H, t, $J = 7.16$ Hz), 4.17 (1H, dd, $J = 3.58$ Hz, 13.56 Hz), 7.29–7.34 (1H, m), 7.54 (1H, s), 10.27 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.26, 19.24, 25.70, 29.01, 31.94, 46.40, 49.38, 53.93, 57.40, 121.22, 123.15, 137.55. IR (film): ν 3429.8, 3130.9, 3069.2, 2959.2, 2934.2, 2872.5, 1562.1, 1455.0, 1405.9, 1363.4, 1164.8 cm^{-1}; HRMS (FAB) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.1808, found 208.1805.

FCIL 14c (Condition C). The cyclic sulfamidate of L-prolinol (0.326 g, 2 mmol) was dissolved in 20 mL toluene, and 1-octylimidazole (0.361 g, 2 mmol) was added with stirring. The mixture was stirred at 80 °C until TLC showed complete conversion to a product that did not migrate on TLC (*ca.* 5 h, ethyl acetate–petrol ether = 1 : 4). The solvent was removed in *vacuo*. The residue was washed with ether, and dried *in vacuo* to afford **3c** as a colorless gluey liquid in quantitative yield. $[\alpha]_D^{20} = -39.7$ ($c = 1.0$, H_2O); ^{1}H NMR (300 MHz, D_2O): δ 0.83 (3H, d, $J = 3.01$ Hz), 1.27 (11H, d, $J = 19.59$ Hz), 1.64–1.78 (1H, br), 1.79–2.00 (3H, br), 2.08–2.20 (1H, m), 3.16–3.28 (2H, m), 3.95–4.00 (1H, m), 4.24–4.34 (3H, m), 4.48–4.53 (1H, m), 7.56 (1H, s), 7.64 (1H, s), 8.93 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 13.67, 22.33, 24.07, 25.71, 28.62, 28.66, 28.78, 29.62, 31.44, 49.59, 49.85,

53.05, 58.60, 121.75, 123.89, 136.36. MS (ESI) for $C_{16}H_{30}N_3O_3S$ ($M^+ + 1$): calcd. 344.20, found 344.13. The zwitterion **3c** was desulfonated following the same procedure as for **3a** to afford FCIL **14c** as a pale yellow viscous oil in 68% yield. $[a]_D^{20} = +2.4$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.67 (3H, t, $J = 6.97$ Hz), 1.05–1.29 (11H, m), 1.44–1.55 (2H, m), 1.69–1.85 (3H, m), 2.64–2.78 (2H, m), 3.23–3.49 (1H, m), 3.97–4.05 (1H, m), 4.13 (2H, t, $J = 7.54$ Hz), 4.22–4.28 (1H, m), 7.29 (1H, s), 7.59 (1H, s), 10.42 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.87, 22.38, 25.77, 26.09, 28.78, 28.85, 29.08, 30.13, 31.48, 46.48, 49.74, 54.02, 57.48, 121.03, 123.23, 137.91. IR (film): ν 3434.6, 3130.9, 3064.3, 2956.3, 2926.5, 2856.1, 1563.1, 1451.2, 1409.7, 1359.6, 1162.9 cm^{-1}; HRMS (FAB) for $C_{16}H_{30}N_3^+$ (M^+): calcd. 264.2434, found 264.2435.

FCIL 15. The corresponding zwitterion **4** was obtained following Condition C in 72% yield after 10 h. **4**: $[a]_D^{20} = +9.7$ ($c = 1.0$, H_2O); ^1H NMR (300 MHz, D_2O): δ 1.70–1.90 (2H, m), 1.95–2.07 (1H, m), 2.13–2.27 (1H, m), 3.26–3.39 (2H, m), 4.08–4.16 (1H, m), 4.43 (1H, dd, $J = 8.67$ Hz, 13.19 Hz), 4.80–4.84 (1H, m), 8.08 (2H, t, $J = 6.97$ Hz), 8.58 (1H, t, $J = 7.72$ Hz), 8.85 (2H, d, $J = 6.03$ Hz); ^{13}C NMR (D_2O, 75 MHz): δ 24.17, 28.84, 49.70, 59.93, 64.57, 127.60, 145.17, 145.69. MS (ESI) for $C_{10}H_{15}N_2O_3S$ ($M^+ + 1$): calcd. 243.08, found 243.06. The desired FCIL **15** was obtained as red viscous oil in 88% yield after desulfonation. $[a]_D^{20} = +64$ ($c = 0.5$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.34–1.46 (1H, m), 1.58 (2H, h, $J = 6.78$ Hz), 1.90–2.02 (1H, m), 2.78 (2H, t, $J = 6.78$ Hz), 3.00–3.28 (2H, br m), 3.58–3.67 (1H, m), 4.60 (1H, dd, $J = 8.48$ Hz, 12.62 Hz), 5.05 (1H, dd, $J = 3.77$ Hz, 12.43 Hz), 7.98 (2H, t, $J = 7.35$ Hz), 8.42 (1H, t, $J = 7.72$ Hz), 9.49 (2H, d, $J = 5.65$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.76, 29.10, 46.27, 58.67, 64.63, 127.44, 144.87, 145.84. IR (film): ν 3416.3, 3043.1, 2961.2, 2925.5, 2871.5, 2376.8, 2348.9, 1727.9, 1633.4, 1488.8, 1122.4 cm^{-1}; HRMS (FAB) for $C_{10}H_{15}N_2^+$ (M^+): calcd. 163.1230, found 163.1229.

FCIL 16. The corresponding zwitterion **5** was obtained following Condition B in 99% yield after 3 h. **5**: $[a]_D^{20} = +0.6$ ($c = 1.0$, H_2O); ^1H NMR (300 MHz, D_2O): δ 0.94 (3H, t, $J = 7.34$ Hz), 1.28–1.40 (2H, m), 1.57–1.72 (5H, m), 1.87 (3H, h, $J = 7.54$ Hz), 3.07–3.16 (1H, m), 3.60 (1H, d, $J = 13.38$ Hz), 4.10–4.17 (1H, br), 4.22 (2H, t, $J = 6.79$ Hz), 4.32 (1H, dd, $J = 5.09$ Hz, 14.32 Hz), 4.63 (1H, dd, $J = 9.61$ Hz, 14.13 Hz), 7.50 (1H, s), 7.53 (1H, s), 8.79 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.75, 18.65, 18.80, 23.29, 24.99, 31.32, 41.42, 48.52, 49.39, 53.53, 122.08, 122.93, 135.71; MS (ESI) for $C_{13}H_{24}N_3O_3S$ ($M^+ + 1$): calcd. 302.15, found 302.13. The desired FCIL **16** was obtained as a brown viscous oil in quantitative yield after desulfonation. $[a]_D^{20} = +2.0$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.62 (3H, t, $J = 7.35$ Hz), 0.70–0.79 (1H, m), 0.92–1.10 (3H, m), 1.20 (1H, d, $J = 11.30$ Hz), 1.36–1.48 (1H, m), 1.58 (2H, h, $J = 7.54$ Hz), 2.18–2.26 (1H, m), 2.62–2.72 (3H, m), 3.98 (3H, t, $J = 7.35$ Hz), 4.02–4.22 (2H, m), 7.28 (1H, s), 7.47 (1H, s), 9.94 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.18, 19.16, 23.82, 25.63, 29.31, 31.75, 46.06, 49.36, 54.08, 55.69, 121.21, 123.48, 137.27. IR (film): ν 3433.6, 3134.7, 3067.2, 2931.3, 2858.0, 1639.2, 1562.1, 1444.4, 1334.5, 1166.7, 1114.6 cm^{-1}; HRMS (FAB) for $C_{13}H_{24}N_3^+$ (M^+): calcd. 222.1965, found 222.1963.

FCIL 17a. The corresponding zwitterion **6** was obtained following Condition B in 71% yield after 3 h. **6**: ^1H NMR (300 MHz, D_2O): δ 0.98 (3H, t, $J = 7.35$ Hz), 1.08 (6H, apparent dd, $J = 6.59$ Hz, 6.78 Hz, 14.51 Hz), 1.32–1.44 (2H, m), 1.82–2.04 (3H, m), 2.74 (3H, s), 3.73–3.81 (1H, m), 4.31–4.30 (3H, m), 4.46 (1H, apparent dd, $J = 3.58$ Hz, 3.77 Hz, 14.51 Hz), 7.49–7.52 (2H, m), 8.74 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.63, 18.76, 19.30, 20.20, 28.17, 28.43, 31.25, 48.70, 49.32, 65.07, 121.93, 122.90, 135.85; MS (ESI) for $C_{13}H_{26}N_3O_3S$ ($M^+ + 1$): calcd. 304.17, found 304.14. The desired FCIL **17a** was obtained as a yellow oil in quantitative yield after desulfonation. $[a]_D^{20} = +0.9$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.89–0.99 (9H, m), 1.27–1.39 (2H, m), 1.80–1.87 (3H, m), 2.27 (3H, s), 2.49–2.54 (2H, m), 4.15–4.31 (3H, m), 4.54 (1H, s), 7.34 (1H, s), 7.51 (1H, s), 10.19–10.24 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.39, 17.97, 18.92, 19.39, 28.64, 32.09, 34.29, 49.69, 50.73, 64.92, 121.12, 122.79, 138.14. IR (film): ν 3418.2, 3134.7, 3063.3, 2960.2, 2932.3, 2873.4, 1636.3, 1562.1, 1463.7, 1373.0, 1165.8, 1097.3 cm^{-1}; HRMS (FAB) for $C_{13}H_{26}N_3^+$ (M^+): calcd. 224.2121, found 224.2119.

FCIL 17b. The corresponding zwitterion **7** was obtained following Condition B in quantitative yield in 3 h. **7**: $[a]_D^{20} = +5.2$ ($c = 0.25$, H_2O); ^1H NMR (300 MHz, D_2O): δ 0.93–1.00 (9H, m), 1.39–1.49 (3H, m), 1.61–1.75 (2H, m), 1.89 (2H, h, $J = 7.35$ Hz), 2.70 (3H, s), 4.05–4.15 (1H, m), 4.20–4.26 (4H, m), 7.49–7.51 (2H, m), 8.76 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.64, 18.75, 21.67, 21.87, 24.31, 28.09, 31.26, 37.46, 49.36, 50.24, 56.46, 122.03, 122.85, 135.73; MS (ESI) for $C_{14}H_{28}N_3O_3S$ ($M^+ + 1$): calcd. 318.18, found 318.13. The desired FCIL **17b** was obtained as a yellow viscous oil in 63% yield after desulfonation. $[a]_D^{20} = +8.0$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.85–0.93 (9H, m), 1.09–1.23 (2H, m), 1.25–1.36 (2H, m), 1.57–1.68 (1H, m), 1.84 (2H, h, $J = 7.72$ Hz), 2.33 (3H, s), 2.43–2.61 (1H, br), 2.75–2.84 (1H, m), 4.20–4.33 (4H, m), 7.37 (1H, d, $J = 1.32$ Hz), 7.47 (1H, d, $J = 1.32$ Hz), 10.07 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.37, 19.37, 22.53, 22.86, 24.77, 32.04, 34.46, 40.63, 49.69, 52.32, 59.94, 121.14, 123.04, 137.98; IR (film): ν 3434.6, 3285.1, 3131.8, 2957.3, 2933.2, 2869.6, 2797.2, 1621.8, 1562.1, 1464.7, 1367.3, 1165.8, 1114.7 cm^{-1}; HRMS (FAB) for $C_{14}H_{28}N_3^+$ (M^+): calcd. 238.2278, found 238.2275.

FCIL 17c. The corresponding zwitterion **8** was obtained following Condition C in quantitative yield in 3 h. **8**: $[a]_D^{20} = -46.4$ ($c = 0.25$, H_2O); ^1H NMR (300 MHz, D_2O): δ 0.97 (3H, t, $J = 7.16$ H z), 1.30–1.38 (2H, m), 1.85 (2H, h, $J = 7.35$ Hz), 2.84 (3H, s), 2.89–2.93 (1H, m), 3.23–3.29 (1H, m), 4.15–4.20 (3H, m), 4.23–4.31 (1H, br), 4.32–4.40 (1H, m), 7.34–7.50 (7H, m), 8.63 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.63, 18.73, 29.14, 31.18, 34.95, 49.01, 49.33, 60.25, 121.99, 122.62, 126.98, 128.98, 129.28, 135.66, 137.97; MS (ESI) for $C_{17}H_{26}N_3O_3S$ ($M^+ + 1$): calcd. 352.17, found 352.05. The desired FCIL was obtained as a yellow viscous oil in 91% yield after desulfonation. $[a]_D^{20} = +2.2$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.83–0.95 (3H, m), 1.23–1.39 (2H, m), 1.78–1.89 (2H, m), 2.27–2.33 (3H, m), 2.70–2.76 (2H, m), 3.02–3.10 (4H, m), 4.21–4.35 (4H, m), 7.14–7.22 (5H, m), 7.33 (1H, s), 7.38 (1H, s), 9.77–10.07 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.37, 19.34, 31.95, 33.60, 37.55, 49.64, 52.04, 60.38, 121.32, 123.03, 126.70, 128.76, 129.14, 137.47. IR (film): ν 3419.2, 3137.6, 3061.4, 2960.2, 2931.3, 2872.5, 1636.3, 1561.1,

1494.6, 1455.0, 1164.8 cm^{-1}; HRMS (FAB) for $C_{17}H_{26}N_3^+$ (M^+): calcd. 272.2121, found 272.2116.

FCIL 18a. The corresponding zwitterion **9** was obtained following Condition C in 98% yield after 7 h. **9**: ^1H NMR (300 MHz, D_2O): δ 0.91–0.96 (3H, m), 1.23–1.35 (5H, m), 1.46–1.51 (9H, m), 1.81–1.90 (2H, m), 4.19–4.25 (2H, m), 4.29–4.37 (1H, m), 4.65–4.73 (1H, m), 4.80–4.88 (1H, m), 7.51–7.52 (2H, m), 8.71 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 12.65, 15.96, 18.77, 27.39, 31.34, 49.45, 51.94, 54.74, 84.35, 122.26, 123.09, 135.68, 183.11. MS (ESI) for $C_{15}H_{28}N_3O_2$ ($M^+ - SO_3^- + 1$): calcd. 282.22, found 282.15. The desired FCIL **18a** was obtained as a pale yellow viscous oil in 82% yield after desulfonation. $[\alpha]_D^{20} = +12.6$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.74 (3H, t, J = 7.54 Hz), 0.94 (3H, d, $J = 6.40$ Hz), 1.11–1.23 (2H, m), 1.39–1.56 (2H, br), 1.65–1.75 (2H, m), 3.13–3.22 (1H, m), 4.05–4.14 (3H, m), 4.20–4.26 (1H, m), 7.37 (1, s), 7.64 (1H, s), 10.23 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.27, 19.28, 21.26, 31.93, 46.93, 49.51, 56.30, 121.25, 123.51, 137.50. IR (film): ν 3426.9, 3134.7, 3071.1, 2961.2, 2934.2, 2873.4, 1562.1, 1459.9, 1375.0, 1164.8, 1113.7 cm^{-1}; HRMS (FAB) for $C_{10}H_{20}N_3^+$ (M^+): calcd. 182.1652, found 182.1653.

FCIL 18b. The corresponding zwitterion **10** was obtained following Condition C in 75% yield after 3 h. **10**: ^1H NMR (300 MHz, D_2O): δ 0.89–0.95 (9H, m), 1.25–1.67 (13H, m), 1.83 (2H, h, $J = 7.72$ Hz), 1.91–2.19 (1H, br), 4.20 (2H, t, $J = 6.78$ Hz), 4.30–4.35 (1H, m), 4.52–4.75 (2H, br), 7.38–7.51 (2H, m), 8.61–8.80 (1H, br); ^{13}C NMR (D_2O, 75 MHz): δ 12.76, 18.81, 21.07, 22.77, 24.61, 27.48, 31.40, 49.45, 51.71, 57.79, 83.97, 122.20, 123.25, 135.84; MS (ESI) for $C_{13}H_{24}N_3O_3S^+$ ($M^+ + 1$): calcd. 302.15, found 302.20. The desired FCIL **18b** was obtained as a yellow-brown viscous oil in quantitative yield after desulfonation. $[\alpha]_D^{20} = -2.0$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.59–0.69 (9H, m), 0.94–0.99 (2H, m), 1.03–1.13 (2H, m), 1.43–1.53 (1H, m), 1.63 (2H, h, $J = 7.35$ Hz), 2.85–2.94 (1H, m), 3.95–4.19 (4H, m), 7.36 (1H, s), 7.46 (1H, s), 10.16 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.23, 19.21, 21.49, 23.24, 24.26, 31.87, 44.08, 49.17, 49.39, 55.56, 121.39, 123.14, 137.73. IR (film): ν 3418.2, 3137.6, 3066.3, 2957.3, 2934.2, 2870.5, 1747.2, 1562.1, 1465.6, 1368.3, 1165.8, 1048.1 cm^{-1}; HRMS (FAB) for $C_{13}H_{26}N_3^+$ (M^+): calcd. 224.2121, found 224.2119.

FCIL 19. The corresponding zwitterion **11** was obtained following Condition C in 96% yield after 5 h. **11**: ^1H NMR (300 MHz, D_2O): δ 1.41 (9H, s), 1.56–1.65 (1H, m), 1.68–1.77 (1H, m), 1.81–1.88 (2H, m), 1.90–1.99 (2H, m), 2.08–2.21 (2H, m), 3.18–3.48 (4H, m), 3.93–4.00 (1H, m), 4.20–4.29 (2H, m), 4.39–4.49 (3H, m), 7.51–7.66 (2H, m), 8.86 (1H, s); ^{13}C NMR (D_2O, 75 MHz): δ 22.22, 23.99, 27.68, 28.20, 28.70, 46.21, 49.83, 51.77, 53.07, 58.96, 82.06, 122.95, 123.68, 136.52. MS (ESI) for $C_{18}H_{31}N_4O_5S^+$ ($M^+ + 1$): calcd. 415.20, found 415.16. The desired FCIL was obtained as a pale yellow viscous oil in 80% yield after desulfonation. $[\alpha]_D^{20} = +27.9$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.17–1.45 (2H, br), 1.45–1.74 (4H, m), 1.74–1.98 (2H, br), 2.70–3.10 (3H, m), 3.15–3.33 (1H, br), 3.46–3.63 (1H, br m), 3.84–4.00 (1H, br), 4.11–4.52 (4H, m), 5.54–6.52 (1H, br), 7.39 (1H, s), 7.60 (1H, m), 9.65–10.13 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.94, 24.20, 24.64, 28.18, 28.67, 44.81, 45.32, 46.24, 51.74, 52.29, 52.70, 53.31, 55.86, 56.78, 57.58, 121.97, 137.07, 161.01. IR (film): ν 3418.2, 3141.5, 3080.7, 2963.1, 2873.4, 1637.3, 1561.1, 1449.2, 1396.2, 1358.6, 1163.8, 1118.5 cm^{-1}; HRMS (FAB) for $C_{13}H_{23}N_4^+$ (M^+): calcd. 235.1917, found 235.1917.

Synthesis of FCILs 20a–c

FCIL 20a. Zwitterion **3b** (86 mg) was dissolved in 3 mL H_2O, and 415 μL HBF_4 (40% in water, *ca.* 8 equiv. of acid) was added. The mixture was refluxed for 6 h, cooled to rt, and solid $NaHCO_3$ was added portionwise until pH = 10. The solvent was removed *in vacuo*, the residue was dried and extracted with chloroform (10 mL × 4), and the organic layers were combined and concentrated to afford **20a** in 94% yield as a pale yellow oil (known compound).[9]

FCIL 20b. Following the above procedure, but using $HClO_4$. $[\alpha]_D^{20} = +24.6$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.90 (3H, t, $J = 7.14$ Hz), 1.25–1.41 (3H, m), 1.58–1.73 (2H, m), 1.78–1.88 (2H, m), 1.89–2.00 (1H, m), 2.50 (1H, s), 2.77–2.93 (2H, m), 3.48–3.57 (1H, m), 3.93–4.00 (1H, m), 4.14–4.24 (3H, m), 7.33 (1H, s), 7.49 (1H, s), 8.83 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.35, 19.37, 25.82, 29.02, 31.85, 46.49, 49.80, 54.33, 57.47, 121.75, 123.29, 135.83; IR (film): ν 3432.7, 3137.6, 3075.9, 2958.3, 2932.2, 2872.5, 2461.7, 1564.0, 1453.1, 1410.7, 1383.7, 1101.2 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 228.34; ClO_4^- (X^-): calcd. 98.95, found 98.93.

FCIL 20c. Following the above procedure using CF_3SO_3H. $[\alpha]_D^{20} = +17.6$ ($c = 1.0$, CH_3CH_2OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.83 (3H, t, $J = 7.41$ Hz), 1.18–1.30 (2H, m), 1.35–1.47 (1H, m), 1.66–1.80 (4H, m), 1.94–2.06 (1H, m), 2.94 (2H, t, $J = 6.86$ Hz), 3.56–3.67 (1H, m), 4.04–4.12 (3H, m), 4.27–4.33 (1H, m), 4.81 (1H, s), 7.30 (1H, s), 7.49 (1H, s), 8.88 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.13, 19.21, 24.81, 28.41, 31.59, 46.32, 49.73, 52.48, 58.43, 113.98, 118.22, 122.04, 122.45, 123.13, 126.69, 135.94. IR (film): ν 3349.8, 3145.3, 3109.7, 2968.9, 2938.9, 2877.3, 1564.0, 1458.9, 1382.7, 1259.3, 1224.6, 1159.9, 1108.9, 1029.8 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.2, found 208.2; $CF_3SO_3^-$ (X^-): calcd. 149.0, found 148.9.

Synthesis of FCILs 21a–g

FCIL 21a. Zwitterion **3b** (0.330 g, 1.14 mmol) was dissolved in 10 mL of *ca.* 4 M HCl/EtOH, and the mixture was refluxed for 6 h. The solvent was then removed *in vacuo*. The residue was converted to a hydroxide-anion-type ionic liquid using anion exchange resin (IRA400). The compound obtained was dissolved in 40 mL water, and L-leucine (0.188 g, 1.1 equiv.) added. The reaction was stirred until pH = 7, and the solution concentrated to dryness *in vacuo*. The residue was dissolved in 50 mL solvent (acetonitrile–methanol = 9 : 1), stirred vigorously for 2 h, and then filtered to removed the excess amino acid. The filtrate was concentrated to afford **21a** in quantitative yield. $[\alpha]_D^{20} = +6.1$ ($c = 1.0$, CH_3OH); ^1H NMR (300 MHz, DMSO): δ 0.78–0.90 (9H, m), 1.03–1.13 (1H, m), 119–1.33 (3H, m), 1.36–1.46 (1H, m), 1.51–1.61 (2H, m), 1.70–1.81 (4H, m), 2.68–2.77 (2H, m), 2.79–2.86 (1H, m), 2.94–3.24 (3H, m), 3.35–3.43 (1H, m), 3.97–4.05 (1H, m), 4.15–4.24 (3H, m), 7.86 (2H, s), 9.89 (1H, s); ^{13}C NMR (DMSO, 75 MHz): δ 13.20, 18.73, 21.84, 23.62, 24.61, 25.36, 28.57, 31.43, 45.84, 48.32, 48.42, 53.25, 54.55, 57.11, 121.76, 122.93, 137.05, 178.07. IR (film): ν 3398.9, 3062.4, 2957.3, 2871.5,

1579.4, 1513.9, 1454.1, 1405.9, 1360.5, 1295.9, 1167.69 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.30; $C_6H_{12}NO_2^-$ (X^-): calcd. 130.09, found 130.15.

FCIL 21b. The title compound was prepared according to the general procedure. Yellow oil, quantitative yield. $[a]_D^{20} = +2.9$ ($c = 1.0$, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.69–0.78 (9H, m), 1.08–1.17 (2H, m), 1.24–1.32 (1H, m), 1.51–1.69 (4H, m), 1.75–1.83 (1H, m), 1.94–2.04 (1H, m), 2.75 (2H, t, $J = 6.59$ Hz), 3.29 (1H, d, $J = 5.76$ Hz), 3.44–3.54 (1H, m), 4.01–4.23 (4H, m), 4.46 (1H, br), 7.18 (1H, s), 7.50 (1H, s), 9.87 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.21, 17.99, 19.24, 20.16, 25.22, 28.81, 30.96, 31.82, 46.00, 49.42, 53.11, 57.70, 71.86, 121.26, 123.09, 137.67, 174.33. IR (film): ν 3409.5, 3139.5, 3083.6, 2963.1, 2873.4, 2102.0, 1606.4, 1564.0, 1462.7, 1384.6, 1268.0, 1166.7 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.29; $C_5H_8N_3O_2^-$ (X^-): calcd. 142.06, found 142.13.

FCIL 21c. The title compound was prepared according to the general procedure. Yellow oil, quantitative yield. $[a]_D^{20} = +9.8$ ($c = 1.0$, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.80–0.85 (9H, m), 1.20–1.38 (4H, m), 1.52–1.92 (9H, m), 2.80–2.84 (1H, m), 3.50–3.55 (1H, m), 4.13–4.30 (5H, m), 7.26 (1H, s), 7.54 (1H, s), 10.00 (1H, br); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.28, 19.30, 21.40, 23.19, 25.35, 25.42, 28.94, 31.92, 41.15, 46.20, 49.45, 53.53, 57.67, 63.87, 121.25, 123.07, 137.72, 175.52. IR (film): ν 3418.2, 3141.5, 3083.6, 2960.2, 2872.5, 2105.9, 1607.4, 1562.1, 1457.9, 1385.6, 1166.7 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.30; $C_6H_{10}N_3O_2^-$ (X^-): calcd. 156.08, found 156.15.

FCIL 21d. The title compound was prepared according to the general procedure. Yellow oil, 90% yield. $[a]_D^{20} = +11.6$ ($c = 1.0$, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.66 (3H, t, $J = 7.41$ Hz), 1.03–1.11 (2H, m), 1.16–1.25 (1H, m), 1.38–1.50 (1H, m), 1.53–1.63 (3H, m), 1.66–1.76 (1H, m), 2.09 (6H, s), 2.67 (1H, t, $J = 6.86$ Hz), 2.74 (2H, s), 3.40–3.47 (1H, m), 3.98–4.18 (4H, m), 5.06 (2H, br), 7.16 (1H, s), 7.48 (1H, s), 10.29 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.27, 19.33, 25.56, 29.04, 31.96, 45.35, 46.36, 49.38, 49.53, 53.79, 57.70, 64.18, 120.91, 122.85, 138.55, 175.62. IR (film): ν 3409.5, 3137.6, 3074.9, 2960.2, 2873.4, 1628.6, 1589.1, 1563.0, 1457.0, 1397.2, 1359.6, 1325.8, 1167.7 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.32; $C_4H_8NO_2^-$ (X^-): calcd. 102.60, found 102.00.

FCIL 21e. The title compound was prepared according to the general procedure. Pale yellow oil, 87% yield. $[a]_D^{20} = +20.2$ ($c = 1.0$, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.87 (3H, t, $J = 7.41$ Hz), 1.23–1.35 (2H, m), 1.38–1.48 (1H, m), 1.64–1.84 (3H, m), 1.90–2.00 (1H, m), 2.90 (2H, t, $J = 6.86$ Hz), 3.57 (2H, s), 3.61–3.69 (1H, m), 4.16–4.37 (6H, m), 7.21 (1H, s), 7.55 (1H, s), 10.2 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.34, 19.30, 25.40, 28.96, 31.94, 46.17, 49.62, 52.98, 53.32, 57.84, 121.03, 123.01, 138.29, 172.55; IR (film): ν 3408.6, 3137.6, 3074.9, 2962.1, 2935.1, 2874.4, 2100.1, 1598.7, 1565.9, 1457.9, 1376.9, 1282.4, 1260.3, 1164.8, 1106.0 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.31; $C_2H_2N_3O_2^-$ (X^-): calcd. 100.02, found 99.96.

FCIL 21f. The title compound was prepared according to the general procedure. Red viscous liquid, quantitative yield. $[a]_D^{20} = -31.2$ ($c = 1.0$, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.76 (3H, t, $J = 7.41$ Hz), 1.12–1.35 (3H, m), 1.48–1.60 (2H, m), 1.62–1.86 (5H, m), 1.91–2.09 (2H, m), 2.24 (3H, s), 2.57–2.66 (1H, m), 2.75 (1H, t, $J = 6.59$ Hz), 3.17–3.24 (1H, s), 3.44–3.53 (1H, m), 4.08–4.28 (4H, m), 4.52 (1H, br), 7.16–7.20 (1H, m), 7.50 (1H, s), 10.56 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.43, 19.44, 22.80, 25.86, 29.20, 30.37, 32.12, 41.17, 46.57, 49.38, 53.91, 56.42, 57.73, 71.96, 120.02, 122.50, 140.70, 179.35. IR (film): ν 3410.5, 3141.5, 3075.9, 2961.2, 2873.4, 1562.0, 1457.0, 1397.1, 1359.6, 1164.8, 1112.7 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.32; $C_6H_{10}NO_2^-$ (X^-): calcd. 128.07, found 128.12.

FCIL 21g. The title compound was prepared according to the general procedure. Pale yellow oil, quantitative yield. $[a]_D^{20} = +46.4$ ($c = 1.0$, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.65 (3H, s), 0.76 (3H, t, $J = 7.41$ Hz), 0.92 (3H, s), 1.11–1.32 (4H, m), 1.47–1.58 (3H, m), 1.65–1.88 (6H, m), 2.12 (1H, dt, $J = 18.11$ Hz, 3.29 Hz), 2.58 (1H, d, $J = 14.82$ Hz), 2.73 (2H, t, $J = 6.86$ Hz), 3.09 (1H, d, $J = 14.82$ Hz), 3.40–3.46 (4H, m), 4.00–4.13 (4H, m), 4.21 (1H, dd, $J = 13.72$ Hz, 4.67 Hz), 7.31 (1H, s), 7.55 (1H, s), 9.43 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.34, 19.30, 19.71, 19.87, 24.42, 25.38, 26.92, 28.93, 31.94, 42.47, 42.83, 46.30, 47.03, 47.72, 49.37, 53.55, 57.81, 58.42, 121.64, 123.25, 137.08, 216.98. IR (film): ν 3418.2, 3136.6, 3074.9, 2960.2, 2873.4, 1738.5, 1637.2, 1562.1, 1455.0, 1405.9, 1390.4, 1374.0, 1229.4, 1188.9, 1170.6 cm^{-1}; MS (ESI) for $C_{12}H_{22}N_3^+$ (M^+): calcd. 208.18, found 208.32; $C_{10}H_{15}O_4S^-$ (X^-): calcd. 231.07, found 231.23.

General procedure for the direct aldol reactions

Procedure A. In a vial, FCIL (0.025 mmol) was mixed with cyclohexanone (0.3 mL) and the corresponding aldehyde (0.25 mmol) at rt. The solution was stirred until complete conversion of aldehyde, or the time indicated in Table 3 and Scheme 3. The reaction mixture was directly loaded onto a silica gel column and purified by FC to afford the desired aldol product. Alternatively, the reaction mixture was first treated with ether to precipitate the catalyst, and the organic layer separated and subjected to purification by FC after concentration.

Procedure B. The final FCIL catalyst **22** was prepared *in situ* by mixing pyrrolidinylimidazolium hydroxide (0.025 mmol) and the corresponding dicarboxylic acid (0.025 mmol) in CH_2Cl_2 (1.0 mL). The solution was stirred for 30 min at rt and the solvent was removed *in vacuo*. The residue was subjected to the model reaction following Procedure A. All the aldol products are known compounds.[9c]

Acknowledgements

This work was supported by the Natural Science Foundation of China (NSFC 20632060 and 20542007), the Ministry of Science and Technology (MoST) and the Chinese Academy of Sciences.

References

1 For reviews, see: (*a*) P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772–3789; (*b*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071–2083; (*c*) R. Sheldon, *Chem. Commun.*, 2001, 2399–2407; (*d*) C. E. Song, *Chem. Commun.*, 2004, 1033–1043; (*e*) Z. Fei, T. J. Geldbach, D. Zhao and P. J. Dyson, *Chem. Eur. J.*, 2006, **12**, 2123–2130.

2 For reviews, see: (*a*) J. Dupont, R. F. de Souza and P. A. Z. Suarez, *Chem. Rev.*, 2002, **102**, 3667–3692; (*b*) J. S. Wikes, *J. Mol. Catal.*

A: Chem., 2004, **214**, 11–17; (*c*) W. Miao and T. H. Chan, *Acc. Chem. Res.*, 2006, **39**, 897–908.
3 For reviews, see: (*a*) C. Baudequin, J. Baudoux, J. Levillain, D. Cahard, A.-C. Gaumont and J.-C. Plaquevent, *Tetrahedron: Asymmetry*, 2003, **14**, 3081–3093; (*b*) J. Ding and D. W. Armstrong, *Chirality*, 2005, **17**, 281–292; (*c*) C. Baudequin, D. Brégeon, J. Levillain, F. Guillen, J.-C. Plaquevent and A.-C. Gaumont, *Tetrahedron: Asymmetry*, 2005, **16**, 3921–3945; (*d*) S. T. Handy, *Chem. Eur. J.*, 2003, **9**, 2938.
4 (*a*) J. Howarth, K. Hanlon, D. Fayne and P. McCormac, *Tetrahedron Lett.*, 1997, **38**, 3097–3100; (*b*) M. J. Earle, P. B. McCormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23–25.
5 (*a*) B. Pégot, G. Vo-Thanh and A. Loupy, *Tetrahedron Lett.*, 2004, **45**, 6425–6428; (*b*) R. Gausepohl, P. Buskens, J. Kleinen, A. Bruckmann, J. Klankermayer and W. Leitner, *Angew. Chem., Int. Ed.*, 2006, **45**, 3689–3692.
6 J. Ding, V. Desikan, X. Han, T. L. Xiao, R. Ding, W. S. Jenks and D. W. Armstrong, *Org. Lett.*, 2005, **7**, 335–337.
7 (*a*) Z. Wang, Q. Wang, Y. Zhang and W. Bao, *Tetrahedron Lett.*, 2005, **46**, 4657–4660; (*b*) W. Ou and Z.-Z. Huang, *Green Chem.*, 2006, **8**, 731–734.
8 P. S. Schulz, N. Muller, A. Bosmann and P. Wasserscheid, *Angew. Chem., Int. Ed.*, 2007, **46**, 1293–1295.
9 (*a*) S. Luo, X. Mi, L. Zhang, S. Liu, H. Xu and J.-P. Cheng, *Angew. Chem., Int. Ed.*, 2006, **45**, 3093–3097; (*b*) S. Luo, X. Mi, S. Liu, H. Xu and J.-P. Cheng, *Chem. Commun.*, 2006, 3687–3689; (*c*) S. Luo, X. Mi, L. Zhang, S. Liu, H. Xu and J.-P. Cheng, *Tetrahedron*, 2007, **63**, 1923–1930; (*d*) S. Luo, L. Zhang, X. Mi, Y. Qiao and J.-P. Cheng, *J. Org. Chem.*, 2007, **72**, 9350–9352; (*e*) D. Xu, S. Luo, H. Yue, L. Wang, Y. Liu and Z. Xu, *Synlett*, 2006, 2569–2572; (*f*) W. Miao and T. H. Chan, *Adv. Synth. Catal.*, 2006, **348**, 1711–1718.
10 (*a*) L. C. Branco, P. M. P. Gois, N. M. T. Lourenco, V. B. Kurteva and C. A. M. Afonso, *Chem. Commun.*, 2006, 2371–2372; (*b*) S. V. Malhotra and Y. Wang, *Tetrahedron: Asymmetry*, 2006, **17**, 1032–1035.
11 P. Wasserscheid, A. Bösmann and C. Bolm, *Chem. Commun.*, 2002, 200–201.
12 For examples, see: (*a*) M. L. Patil, C. V. L. Rao, K. Yonezawa, S. Takizawa, K. Onitsuka and H. Sasai, *Org. Lett.*, 2006, **8**, 227–230; (*b*) Y. Ishida, H. Miyauchi and K. Saigo, *Chem. Commun.*, 2002, 2240–2241.
13 For recent examples of chiral pool synthesis, see: (*a*) H. Clavier, L. Boulanger, N. Audic, L. Toupet, M. Mauduit and J.-C. Guillemin, *Chem. Commun.*, 2004, 1224–1225; (*b*) W. Bao, Z. Wang and Y. Li, *J. Org. Chem.*, 2003, **68**, 591–593; (*c*) J. Levillain, G. Dubant, I. Abrunhosa, M. Gulea and A. C. Gaumont, *Chem. Commun.*, 2003, 2914–2915; (*d*) B. K. Ni, Q. Y. Zhang and A. D. Headley, *J. Org. Chem.*, 2006, **71**, 9857–9860; (*e*) B. Ni and A. D. Headley, *Tetrahedron Lett.*, 2006, **47**, 7331–7334; (*f*) J. Pernak and J. Feder-Kubis, *Tetrahedron: Asymmetry*, 2006, **17**, 1728–1737; (*g*) K. Fukumoto and H. Ohno, *Chem. Commun.*, 2006, 3081–3083; (*h*) V. Jurcik and R. Wilhelm, *Tetrahedron: Asymmetry*, 2006, **17**, 801–810; (*i*) F. Guillen, D. Bregeon and J. C. Plaquevent, *Tetrahedron Lett.*, 2006, **45**, 1245–1248; (*j*) B. K. Ni, A. D. Headley and G. G. Li, *J. Org. Chem.*, 2005, **70**, 10600–10602; (*k*) J. Pernak and J. Feder-Kubis, *Chem. Eur. J.*, 2005, **11**, 4441–4449; (*l*) G. Tao, L. He, N. Sun and Y. Kou, *Chem. Commun.*, 2005, 3562–3564; (*m*) Z. Wang, Q. Wang, Y. Zhang and W. Bao, *Tetrahedron Lett.*, 2005, **46**, 4657–4660; (*n*) E. J. Kim, S. Y. Ko and E. K. Dziadulewicz, *Tetrahedron Lett.*, 2005, **46**, 631–633; (*o*) K. Fukumoto, M. Yoshizawa and H. Ohno, *J. Am. Chem. Soc.*, 2005, **127**, 2398–2399.
14 For combinatorial synthesis of non-chiral ionic liquids, see: P. Wasserscheid, B. Drießen-Hölscher, R. van Hal, H. C. Steffens and J. Zimmermann, *Chem. Commun.*, 2003, 2038–2039.
15 For the applications of cyclic sulfamidates in organic synthesis, see: R. E. Meléndez and W. D. Lubell, *Tetrahedron*, 2003, **59**, 2581–2616.
16 For a review on click chemistry, see: H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004–2021.
17 K. C. Nicolaou, S. A. Snyder, D. A. Longbottom, A. Z. Nalbandian and X. Huang, *Chem. Eur. J.*, 2004, **10**, 5581–5606.
18 J.-L. Liang, S.-X. Yuan, J.-S. Huang, W.-Y. Yu and C.-M. Che, *Angew. Chem., Int. Ed.*, 2002, **41**, 3465.
19 (*a*) P. I. Dalko and L. Moisan, *Angew. Chem., Int. Ed.*, 2004, **43**, 5138; (*b*) A. Berkessel and H. Groger, *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, 2005.
20 (*a*) B. List, R. A. Lerner and C. F. Barbas, III, *J. Am. Chem. Soc.*, 2000, **122**, 2395–2396; (*b*) J. Seayad and B. List, *Org. Biomol. Chem.*, 2005, **3**, 719–724.
21 For reviews on these subjects, see: (*a*) O. Kühl, *Chem. Soc. Rev.*, 2007, **36**, 592–607; (*b*) D. Enders and T. Balensiefer, *Acc. Chem. Res.*, 2004, **37**, 534–541.

