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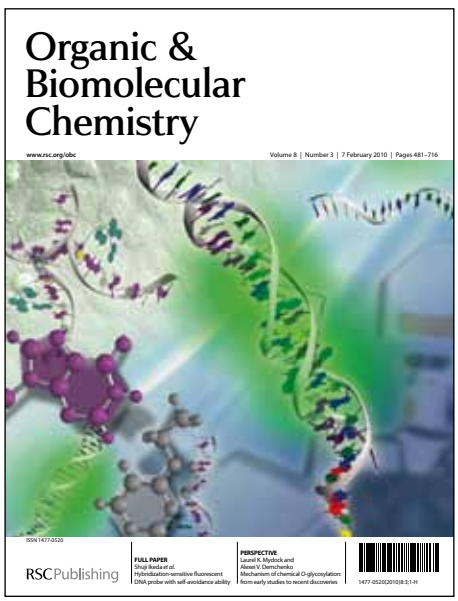

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DOI: 10.1039/C3OB41635F

Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Coordinating chiral ionic liquids

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A practical synthesis of novel coordinating chiral ionic liquids with amino alcohol structural motive was developed starting from commercially available amino alcohols. These basic chiral ionic liquids could be successfully applied as catalysts in the asymmetric alkylation of aldehydes and gave high enantioselectivities of up to 91% ee.

Introduction

During the last years, ionic liquids (ILs) have been established as alternatives to organic solvents and as new reaction media for chemical reactions and separation techniques.[1] The combination of a constantly growing number of possible cations and anions permits the creation of tailor-made ILs, including chiral species.[2] It was early recognized that the properties of chiral ionic liquids (CILs) might provide a new and attractive approach to asymmetric synthesis. However, despite the rapid growth of numbers of papers dealing with CILs successful applications remained hidden for some time, and many CILs failed to induce significant selectivity if used as sole source of chirality. Incidentally, it seems to be not sufficient to attach any chiral unit on an IL moiety to obtain high enantioselectivities, but necessary to carefully design CILs for a specific asymmetric reaction. This could be recently demonstrated for the application of CILs in organocatalytic aldol or Michael-type reactions[3], aza-Baylis-Hillman reaction[4], Diels-Alder reactions[5], Mukayama aldol reactions[5], hydrogenation[6], enantioselective sulfide oxidation[7] or Sharpless-type dihydroxylation.[8]

Chiral 1,2-amino alcohols with acyclic as well ascyclic core structure are successfully used as auxiliaries or ligands in asymmetric synthesis in an immense variety.[9] Therefore, we want to present the design and synthesis of CILs with a chiral amino alcohol unit to access highly coordinating CILs which could be used as ligands, catalysts and auxiliaries similar to chiral amino alcohols in a wide range of transformations.

Results and Discussion

In a general strategy, a nitrogen-containing IL precursor is grafted onto a chiral 1,2-amino alcohol L* to obtain tridentate ligands (Figure 1) which are then further functionalized to obtain a chiral ionic ligand.

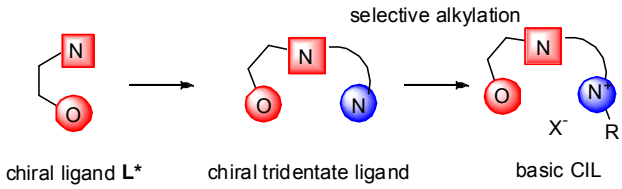

Figure 1. Design of basic chiral ionic liquids

Designing CILs with an amino alcohol sub-structure as shown in figure 1, there are two major synthetic tasks to accomplish: (*a*) a grafting strategy is necessary that allows selective linkage of the chiral amino alcohol L* nitrogen with the IL precursor without reaction of the alcohol; (*b*) selective alkylation of the external nitrogen unit has to be performed. While the first issue can be solved easily, the major problem in the design of basic CILs is the selective alkylation of the IL part in the presence of the amino alcohol functionality that has to be kept unsubstituted, preferably without the use of protecting groups.

Based on this synthetic strategy, we aimed for a small set of commercially available amino alcohols as precursors where some examples can be directly obtained from the chiral pool: Camphor derived amino isoborneol **1**, the natural amino alcohols ephedrine **6** and pseudoephedrine **10**, the amino acid derived amino alcohols valinol **19**, leucinol **23**, phenylalaninol **27**, and prolinol **31** as well as the diphenyl derivative **14** were used and gave access to a small library of chiral ionic liquids with chelate formation capability.

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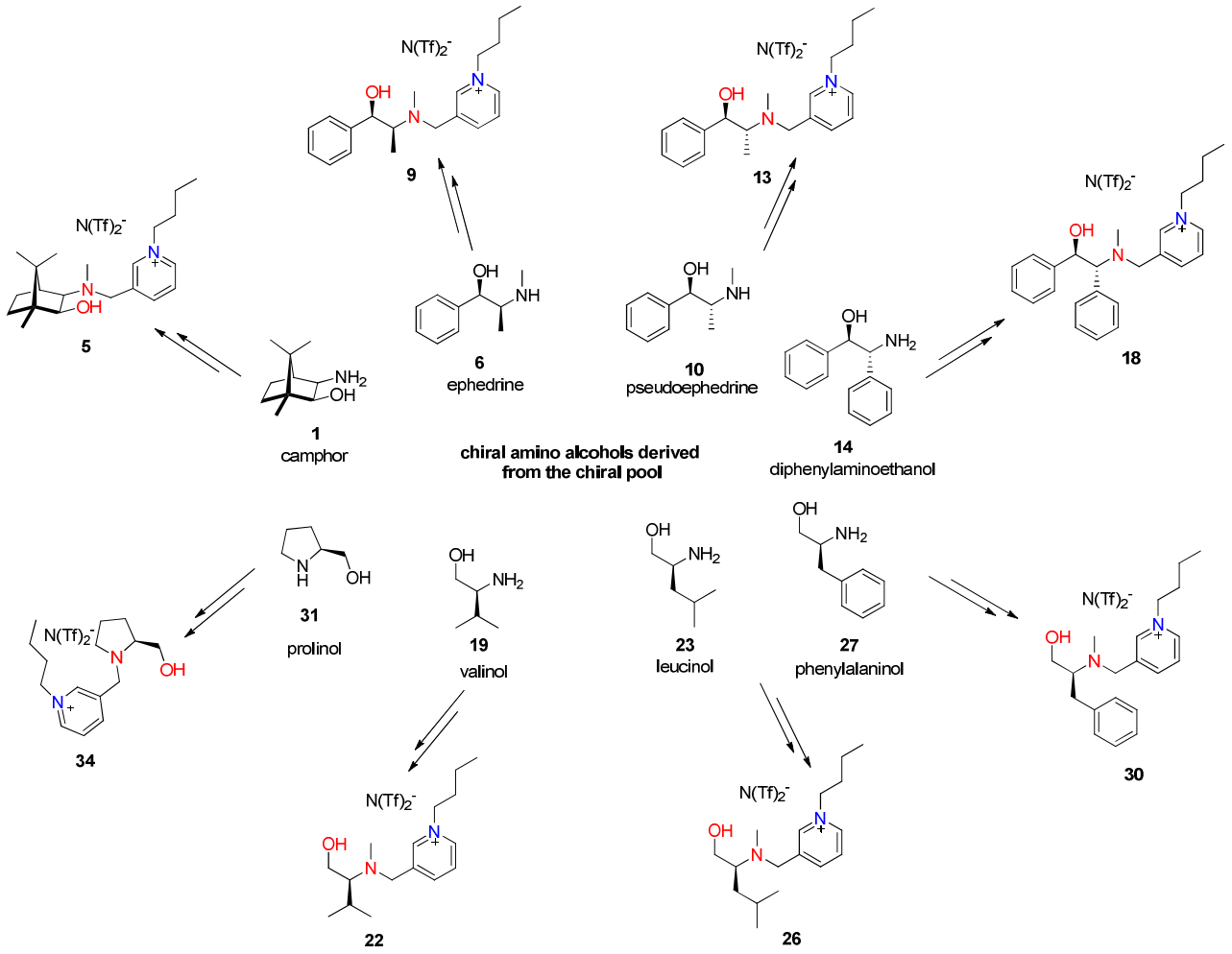

Figure 2: Coordinating chiral ionic liquids obtained from commercially available amino alcohols.

We decided to use a pyridinium ring system not only for the simple availability of the precursor pyridine-3-carbaldehyde, but – more important – for the absence of acidic protons present in the more common imidazolium ILs that restrict the use in basic conditions.[10] Selective alkylation of the pyridine unit should allow the formation of highly coordinating basic CILs that can be applied not only as chiral reaction media, but also show the possibility for direct interaction with substrates or metals. Reaction in the presence of freshly activated molecular sieve in anhydrous methanol and successive reduction gave intermediate tridentate ligands (Scheme 1). In case of primary amino alcohol precursors **1**, **14**, **19**, **23** and **27**, we included a successive *N*-methylation step according to the classical Leukart-Wallach protocol to obtain tertiary central amine functionalities, since our previous work in this area has shown that a central secondary amine could limit the application of these ligands.[11]

Selective alkylation of the terminal pyridine was best done with *n*-butyl bromide at 60 °C overnight under solvent-free conditions (Scheme 1). Despite the higher basicity of tertiary amines compared to pyridine, alkylation can be selectively performed on the pyridine moiety which might be explained by sterical reasons and an easier accessibility for alkylation. When the less reactive *n*-butyl chloride was used as alkylation reagent, no conversion could be obtained even under harsh conditions (neat, 80 °C, 7 days) or microwave-assisted chemistry. However, even with a 3-fold excess of alkyl bromide, a selective alkylation of the pyridine took place and no substitution of the amino group was observed. In fact, the forced double alkylation was observed when ephedrine-based tridentate ligand **7** was refluxed with an excess of the very reactive alkylation reagent methyl iodide. In this case, a quantitative formation of the di-cation **35** was observed. The diiodide salt could be crystallized from ethanol/H_2O to give large plate-like crystals with remarkable triangular structure which reflected the polar character of the solid state structure (see ESI for details).

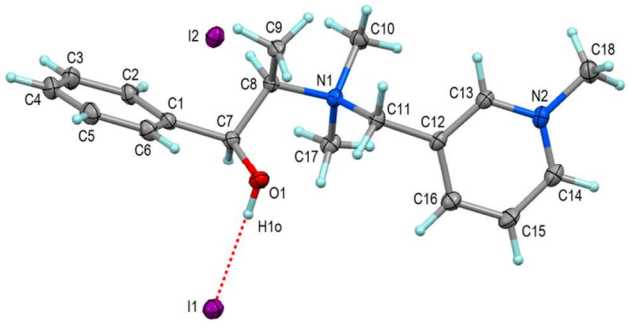

Figure 3: Crystal structure of diiodide salt of ephedrine-based ligand **35**. †

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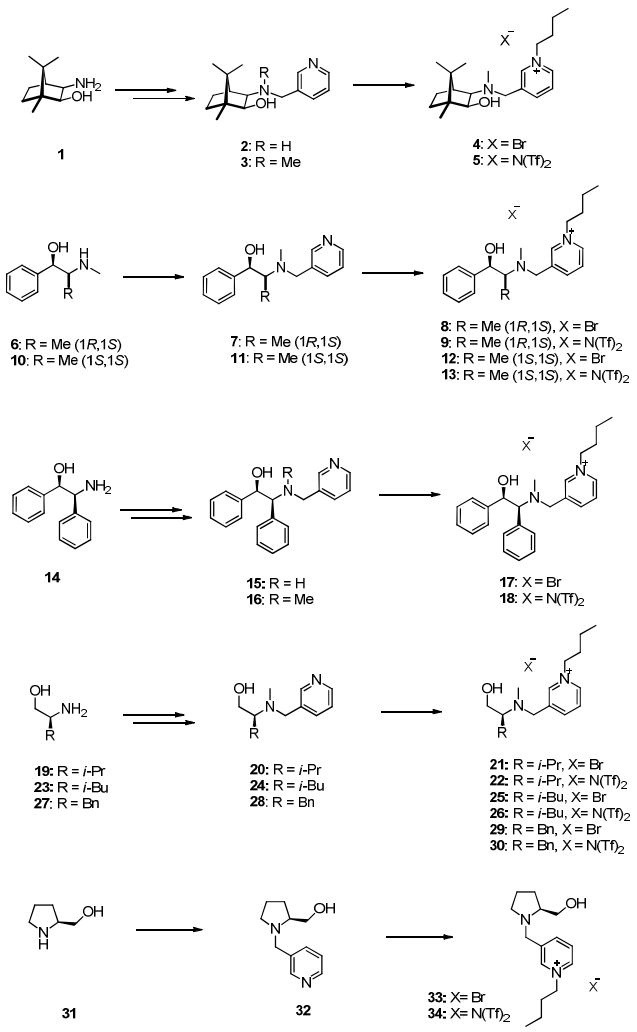

Scheme 1: Coordinating chiral ionic liquids obtained from commercially available amino alcohols.

The obtained chiral ionic liquids provide the possibility for multiple interactions with racemic substrates. In order to evaluate the chiral recognition properties we investigated the diasteromeric interactions with Mosher's acid potassium salt as racemic probe via ^{19}F NMR spectroscopy. This technique has been previously introduced by Wasserscheid et al.[12] in a pioneering paper on chiral-pool derived ionic liquids, and has soon become a popular tool for quantifying of diastereomeric interactions with chiral ionic liquids. To evaluate the chiral recognition ability of these new functionalized CILs potassium salt of racemic Mosher's acid was mixed with 5 equivalents of the enantiopure coordinating ionic liquid and dissolved in CD_2Cl_2. One equivalent of the crown ether 18C6 was added to trap the potassium cation, and the resulting clear solution was examined by ^{19}F NMR spectroscopy. In case of diastereomeric interactions, a splitting of the CF_3 signal at -70.15 Hz was observed.

Table 1: Evaluation of chiral recognition properties via ^{19}F-NMR

Entry	CIL	Δppm[a]
1	ephedrine-derived **9**	17.5
2	diphenylaminoethanol-derived **18**	12.6
3	leucin-derived **26**	8.3
4	valine-derived **22**	6.3
5	pseudoephedrine-derived **13**	3.6
6	phenylalanin-derived **30**	-[b]
7	aminoisoborneol-derived **5**	-[b]
8	prolinol-derived **34**	-[b]

[a] Chemical shift difference of the CF_3 signal (^{19}F NMR, 376.5 MHz) of racemic Mosher's acid carboxylate (potassium salt) in the presence of 5 eq. chiral ionic liquid. [b] Broadening but no measurable splitting of the CF_3 signal.

A significant splitting of the CF_3 signal was observed for the CILs **9**, **18** whereas lower Δppm values were obtained for CILs **26**, **22**, **13**. Surprisingly, no splitting of the signal was observed for aminoisoborneol- and prolinol-derived CILs **5** and **34** in ^{19}F NMR under these conditions, and it seems that an aromatic system and the possibility for π-π interactions is advantageous for chiral recognition of racemic Mosher's acid.

The results from chiral recognition in ^{19}F NMR can to some extent be connected to their performance in the asymmetric alkylation of benzaldehyde **36** (Figure 4): To investigate the chiral induction properties of the synthesized CILs, we selected as test reaction the asymmetric alkylation of carbonyls using organozinc reagents. For this reaction, the presence of a coordinating ligand – typically a chiral amino alcohol – is crucial to obtain satisfying conversion and enantioselectivities. The catalytic enantioselective addition of organometallic reagents to carbonyl groups is one of the most useful methods for the preparation of chiral secondary alcohols and therefore has been studied extensively.[13] Of all organometallic reagents, dialkylzinc organyls are most frequently used, since it is a ligand accelerated reaction in which chemoselective alkylation of functionalized carbonyls is possible and high enantioselectivities can be achieved.[14]

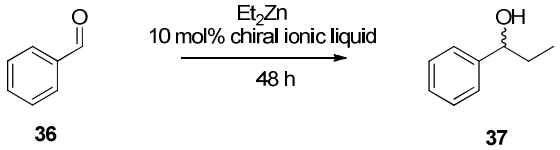

Figure 4: Asymmetric addition of diethylzinc to benzaldehyde **36** catalyzed by basic chiral ionic liquids

The asymmetric alkylation of benzaldehyde **36** has been previously performed using CILs as inducer for chirality and selectivities of up to 82% ee could be obtained with a BINOL-derived CIL.[15] However, in all cases chiral imidazolium salts were applied where the involvement of N-heterocyclic carbene (NHC) ligands formed from the CILs might play an additional role.[16] To evaluate optimal reaction conditions, different solvents were chosen and homogeneous and heterogeneous systems examined. A sub-stochiometric amount of amino alcohol CIL (10 mol%) was reacted with a 1 M solution of diethylzinc in *n*-hexane and benzaldehyde **36** at 0 °C. The reaction was performed under homogenous conditions using the conventional solvent CH_2Cl_2 as well as under biphasic conditions in the system 1-butyl-2,3-dimethylimidazolium bistriflimide

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($[C_4m_2im]N(Tf)_2$)/hexane. This immobilization of ionic liquid-tagged chiral ligands, e.g. a bisoxazoline derivative in hydrophobic ionic liquids has already been reported by Doherty et al., and the biphasic methodology proved to be extremely suitable for catalyst recycling.[5] When using dichloromethane as a solvent we could obtain excellent yield and selectivity with camphor-derived CIL **5** (entry 1). The addition of the Lewis acid $Ti(OiPr)_4$ in dichloromethane resulted in a decrease of yield to 74% and in a complete loss of selectivity (entry 2), thus highlighting the importance of the amino alcohol structural motive in the chiral ionic liquid for coordination to the metal organyl.

Table 2: Asymmetric addition of diethylzinc to benzaldehyde catalyzed by coordinating chiral ionic liquids

Entry[a]	CIL	Conditions	Yield [%][c]	ee [%][d,e]
1	camphor-derived **5**	CH_2Cl_2	79	91(*R*)
2[b]		CH_2Cl_2	74	2 (*R*)
3		$[C_4m_2im]NTf_2$	85	50 (*R*)
4	ephedrine-derived **9**	CH_2Cl_2	81	74 (*R*)
5		$[C_4m_2im]NTf_2$	79	70 (*R*)
6	pseudoephedrine-derived **13**	CH_2Cl_2	67	55 (*R*)
7		$[C_4m_2im]NTf_2$	74	56 (*R*)
8	diphenylaminoethanol-derived **18**	CH_2Cl_2	92	66 (*R*)
9		$[C_4m_2im]NTf_2$	90	59 (*R*)
10	valinol-derived **22**	CH_2Cl_2	78	32 (*S*)
11		$[C_4m_2im]NTf_2$	59	54 (*S*)
12	leucinol-derived **26**	CH_2Cl_2	72	20 (*S*)
13		$[C_4m_2im]NTf_2$	83	21 (*S*)
14	phenylalaninol-derived **30**	CH_2Cl_2	26	23 (*S*)
15		$[C_4m_2im]NTf_2$	98	18 (*S*)
16	prolinol-derived **34**	CH_2Cl_2	<1	n.d.
17		$[C_4m_2im]NTf_2$	86	15 (*S*)

[a] Performed with 2 mmol benzaldehyde, 4.4 mmol of a 1 M solution of Et_2Zn in *n*-hexane and 0.2 mmol CIL at 0 °C for 24-48 hrs. [b] Addition of 2.4 mmol $Ti(OiPr)_4$. [c] Isolated yield. [d] Determined by HPLC using a DAICEL Chiralcel IB column. [e] Absolute configuration determined via optical rotation and comparison with literature values.

When comparing the chiral ionic liquids derived from the diastereomers ephedrine **6** and pseudoephedrine **10** we found that ephedrine is better suited: Good yields and selectivities of 79% and 70%ee could be obtained with the ephedrine derivative, whereas both yield and selectivity decrease in case of the diastereomer. Chiral ionic liquids obtained from the diphenylaminoalcohol **14** or valinol **19** also performed very well, whereas leucinol **23-** or prolinol **31**-derived CILs gave lower selectivities. Surprisingly, the prolinol-derived CIL completely failed as catalyst in the asymmetric alkylation of benzaldehyde **36**: Although excellent yield could be observed under heterogenic conditions, the enantioselectivity remained low, and no conversion at all was observed under homogenous conditions.

Alternatively, that reaction was performed using 1 g of the IL $[C_4m_2im]N(Tf)_2$ as co-solvent. All chiral amino alcohol-derived ILs were readily soluble in this IL and a biphasic system was obtained when a solution of diethylzinc in *n*-hexane was added. After complete reaction and hydrolysis with diluted hydrochloric acid, a three-phase system was obtained and 1-phenyl-1-propanol **37** was isolated from the upper organic layer. Again, we observed excellent yields and good selectivities for camphor-, ephedrine- and diphenylaminoethanol-derived CILs **5**, **9**, and **18**. When compared to conventional solvents the use of the IL as co-solvent lead to better yields and comparable enantioselectivities. Additionally, the isolation of the product was facilitated, as the product could be simply decanted in the *n*-hexane layer in very pure form, whereas a chromatographic purification was required when CH_2Cl_2 was used.

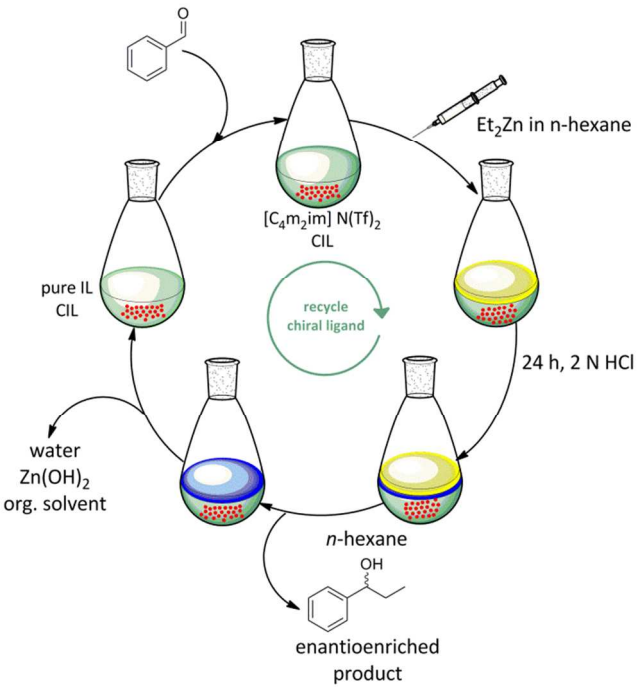

Fig. 5: Recycling strategy for the re-use of coordinating CILs

The ease of work-up and IL recovery in case of biphasic systems motivated us to investigate recycling of the chiral ionic liquid immobilized in $[C_4m_2im]N(Tf)_2$. This could be easily achieved *via* phase separation in the 3-layer system that is obtained after hydrolysis with 2 N HCl once the reaction was complete. However, despite our efforts we could not maintain the excellent selectivity observed with the ephedrine-derived coordinating chiral ionic liquid **9**: Although excellent conversion and yield was observed for five consecutive runs, the enantioselectivity dropped in the third run and only 20 %ee could be obtained after the 5th recycling step (Table 3).

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Table 3: Yields and enantioselectivities during recycling of the coordinating chiral ionic liquid **9** for five runs.

Entry[a]	Run	Yield [%][b]	ee [%][c]
1	1st	79	70
2	2nd	93	60
3	3rd	97	16
4	4th	94	18
5	5th	98	20

[a] Performed with 2 mmol benzaldehyde, 4.4 mmol of a 1 M solution of Et_2Zn in *n*-hexane and 0.2 mmol CIL at 0 °C for 24-48 hrs. [b] Isolated yield. [c] Determined by HPLC using a DAICEL Chiralcel IB column. [d] Absolute configuration determined via optical rotation and comparison with literature values.

Conclusion

In summary, we could develop a simple and efficient synthesis for novel coordinating CILs with an amino alcohol sub-unit. Additionally to the ionic liquid pyridinium moiety two non-functionalized coordination sites are free and therefore best conditions for high selectivity should be present. When tested as chiral ligands in the enantioselective alkylation of benzaldehyde with diethylzinc, excellent yields and high enantioselectivities of up to 91% ee were observed. These results are among the best selectivities ever obtained with CILs in asymmetric synthesis and by far the most convincing one in asymmetric alkylation. However, the recycling of coordinating chiral ionic liquids did not proceed to our satisfaction, and better recycling strategies including the development of silica-supported chiral ionic liquids will have to be developed.

We expect that this novel type of coordinating chiral ionic liquids offers a broad range of applications covering not only asymmetric synthesis but also separation sciences, and more investigations are currently ongoing in our lab.

Experimental

Commercially available reagents and solvents were used as received from the supplier unless otherwise specified. Amino alcohols valinol, leucinol, prolinol and phenylalaninol were prepared via reduction of the respective amino acids with $LiAlH_4$ in THF according to standard procedures.[17] Tridentate ligands **3**, **7**, **20**, **24**, **28**, **32** have been previously reported in literature and detailed experimental and analytical data are published elsewhere.[11] A racemic sample of 1-phenylethanol for comparison was prepared by addition of EtMgBr to benzaldehyde followed by standard extractive work-up.

^1H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker AC 200 at 200 and 50 MHz or on a Bruker AC 400 at 400, 100 and 376.5 MHz, resp., using the solvent peak or TMS as reference.Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin.= quintet, sext.=sextet, m = multiplet, brs = broad. Infrared spectra were recorded on a Perkin-Elmer Spectrum 65 FT IR spectrometer equipped with a specac MK II Golden Gate Single Reflection ATR unit.

TLC-analysis was done with precoated aluminium-backed plates (Silica gel 60 F_{254}, Merck). Compounds were visualised by spraying with 5% phosphomolybdic acid hydrate in ethanol and heating. Vacuum flash chromatography (VFC) was carried out with silica gel Merck 60. Elemental analysis was carried out at Vienna University, Laboratory for Microanalysis Services, Währinger Str. 42, A-1090 Vienna.

HPLC analysis was performed on Daionex UPLC chromatograph with a PDA plus detector (190-360 nm). A DAICEL IB column (250 × 4.60 mm) was used as stationary phase with n-hexane/i-propanol as solvent and a flow of 0.7 ml/min; detection was done at 254 and 219 nm. Specific rotations were measured on an Anton Paar MCP 500 polarimeter. $[\alpha]_D$ values are given in deg cm^2 g^{-1}. Thermal stabilities were determined on a Netzsch TGA in a range of 25 to 500 °C with a heating rate of 10 °C/min. Decomposition temperatures ($T_{5\%onset}$) were reported from onset to 5 wt% mass loss. Melting points above room temperature were measured on a Kofler hot-stage microscope or on an automated melting point system OPTI MELT of Stanford ResearchSystems and are uncorrected.

1-Butyl-3-[[[(1*S*,2-exo,3-exo)-3-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]methyl]amino]methyl]-pyridinium bromide 4

Cmp. **3** (2.91 g, 10.6 mmol) and freshly distilled *n*-butyl bromide (1.59 g, 11.66 mmol) were mixed in a round-bottom flask, sealed, and stirred at 60 °C for 24 h. Excess *n*-butyl bromide was evaporated and the brown oil was washed twice with anhydrous ethyl acetate. Remaining volatile materials were removed under reduced pressure at 60 °C to yield pyridinium bromide **4** as light brown solid in 99% yield. Crystallization from acetonitrile/ethyl acetate gave colourless crystals.

^1H-NMR (200 MHz, $CDCl_3$): δ_H = 9.38 (s, 1H, H-arom.), 9.29 (d, J = 6.1 Hz, 1H, H-arom.), 8.30 (d, J = 7.8 Hz, 1H, H-arom.), 7.96 (dd, J_1 = 7.8 Hz, J_2 = 6.3 Hz, 1H, H-arom.), 4.78 (t, J = 7.3 Hz, 2H, N-CH_2-CH_2), 3.97 (d, J = 14.5 Hz, 1H, CH_2-NMe), 3.49 (m, 3H, CH_2-NMe, C*H*-OH and O*H*), 2.51 (d, 1H, J = 6.3 Hz, C*H*-NMe), 2.07 (s, 3H, CH_3-N), 1.88 (m, 3H, CH_2-CH_2-CH_2, C*H*-C-CH_3), 1.59-1.28 (m, 4H, H-6_{exo}, H-5_{exo}, CH_2-CH_2-CH_3), 1.03 (s, 3H, CH_3-C), 0.94-0.75 (m, 5H, H-6_{endo}, H-5_{endo}, CH_2-CH_2-CH_3), 0.81/0.61 (2s, 6H, 2 CH_3);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.8/144.6 (2d, C-arom.), 143.5 (d, C-arom.), 141.4 (s, C-arom.), 127.9 (d, C-arom.), 79.7 (d, C-OH), 73.6 (s, C-NMe), 61.4 (t, *C*H_2-CH_2-CH_2), 58.0 (t, *C*H_2-NMe), 49.4 (d, *C*-CH_3), 46.8 (s, *C*-2CH_3), 46.5 (d, *C*H-C-2CH_3), 40.9 (q, N-*C*H_3), 33.6 (t, *C*H_2-CH_2-CH_3), 32.4 (t, *C*H_2-CH_2-CH), 27.5 (t, CH_2-*C*H_2-CH), 21.7/20.8 (2q, 2 CH_3), 19.2 (t, CH_2-*C*H_2-CH_3), 13.5 (q, CH_2-CH_2-*C*H_3), 11.6 (q, C-*C*H_3);

Anal. Calcd. for $C_{21}H_{35}BrN_2O$: C, 61.31; H, 8.57; Found: C, 61.09; H, 8.81; ν_{max}/cm^{-1}: 3272 (OH), 2958 (NH), 1638 (C-N), 1370 (C-CH_3), 1282 (C-H); $[\alpha]_D^{20}$: -1.8 (c 1.03 in EtOH,); mp 146-149 °C (from acetonitrile/ethyl acetate); $T_{5\%onset}$: 187 °C.

1-Butyl-3-[[[(1*S*,2-*exo*,3-*exo*)-3-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]methyl]amino]methyl]-pyridinium bis(trifluoromethanesulfonyl)imide 5

Cmp. **4** (0.99 g, 2.98 mmol) was dissolved in 3 ml of distilled water and a solution of $Li[N(CF_3SO_2)_2]$ (0.86 g, 3.00 mmol) in 2

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ml H_2O_{dest} was added drop wise under stirring. A second phase separated immediately. After 15 minutes, the biphasic system was extracted with CH_2Cl_2. The combined organic layers were washed with small portions of water until no more halide-ions could be detected in the washings (checked by addition of an aqueous acidic solution of $AgNO_3$), dried with Na_2SO_4 and concentrated under reduced pressure. Remaining volatile materials were removed under high-vacuum to yield **5** as light yellow viscous liquid in 93% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.72 (s, 1H, H-arom.), 8.68 (d, J = 6.1 Hz, 1H, H-arom.), 8.40 (d, J = 7.8 Hz, 1H, H-arom.), 7.95 (dd, J_1 = 7.8 Hz, J_2 = 6.3 Hz, 1H, H-arom.), 4.55 (t, J = 7.3 Hz, 3H, C*H*$_3$), 3.95 (d, J = 14.5 Hz, 1H, C*H*$_2$-NMe), 3.56 (m, 2H, C*H*-OH, C*H*$_2$-NMe), 3.21 (brs, OH), 2.62 (d, 1H, J = 6.3 Hz, C*H*-NMe), 2.16 (s, 3H, C*H*$_3$-N), 2.14-1.15 (m, 7H, C*H*-C-2CH$_3$, H-6$_{exo}$, H-5$_{exo}$, C*H*$_2$-CH$_2$-CH$_3$, CH$_2$-C*H*$_2$-CH$_3$), 1.16 (s, 3H, CH$_3$-C), 1.02-0.85 (m, 5H, H-6$_{endo}$, H-5$_{endo}$, CH$_2$-CH$_2$-C*H*$_3$), 0.96/0.78 (2s, 6H, 2 CH$_3$);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 145.1/144.0 (2d, C-arom.), 142.9 (d, C-arom.), 142.1(s, C-arom.), 129.3 (d, C-arom.), 119.5 (q, J = 321.4 Hz, CF3), 80.0 (d, C-OH), 73.7 (s, 1C, C-NMe), 62.2 (t, CH$_2$-CH$_2$-*C*H$_2$), 58.0 (t, *C*H$_2$-NMe), 49.5 (d, *C*-CH$_3$), 46.9 (s, *C*-2CH$_3$), 46.6 (d, *C*H-C-2CH$_3$), 40.7 (q, N-*C*H$_3$), 33.3 (t, *C*H$_2$-CH$_2$-CH$_3$), 32.4 (t, *C*H$_2$-CH2), 27.5 (t, CH$_2$-*C*H2), 21.7/20.7 (2q, 2 CH$_3$), 19.1 (t, CH$_2$-*C*H$_2$-CH$_3$), 13.1 (q, CH$_2$-CH$_2$-*C*H$_3$), 11.3 (q, CH$_3$); Anal. Calcd. for $C_{23}H_{35}F_6N_3O_5S_2$: C, 45.16; H, 5.77; Found: C, 45.13; H, 5.54; ν_{max}/cm^{-1}: 2879 (NH), 1636 (C-N), 1348 (C-CH$_3$), 1179 (C-F$_3$), 1133 (S=O), 1052 (NH-CH$_3$); $[\alpha]_D^{20}$: +2.1 (c 0.97 in EtOH); $T_{5\%onset}$: 191 °C.

1-Butyl-3-[[[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenyl-ethyl]methylamino]methyl]pyridinium bromide 8

Preparation from **7** (0.77 g, 3.00 mmol) similar to the procedure described for compound **4** gave **8** as viscous brown oil in 89% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 9.20 (d, J = 5.9 Hz, 1H, H-arom.), 8.90 (d, J = 2.0 Hz, 1H, H-arom.), 7.90 (d, J = 7.8 Hz, 1H, H-arom.), 7.81 (dd, J_1 = 7.5 Hz, J_2 = 6.4 Hz, 1H, H-arom.), 7.24 (m, 5H, H-arom.), 4.88 (d, 1H, J = 5.3 Hz, C*H*-OH), 4.67 (t, J = 7.6 Hz, 2H, CH-N arom.), 4.12 (brs, 1H, OH), 4.13/3.67 (2d, J = 15.5 Hz/J = 15.3 Hz, 2H, CH$_2$-N), 2.90 (m, 1H, H-NMe), 2.18 (s, 3H, CH$_3$-N), 1.84 (q, J = 7.7 Hz, 1H, C*H*$_2$-CH$_2$-CH$_2$), 1.31 (sext, J = 7.3 Hz, 2H, CH$_2$-C*H*$_2$-CH$_2$), 1.07 (d, 3H, J = 6.9 Hz, C*H*$_3$-CH$_2$-CH$_2$), 0.90 (t, J = 7.2 Hz, 3H, C*H*$_3$-CH);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.4/144.2 (2d, C-arom.), 144.1 (s, C-arom.), 143.1 (d, C-arom.), 142.5 (s, C-arom.), 128.0 (d, C-arom.), 127.7 (d, C-arom.), 126.9 (d, C-arom.), 126.6 (d, C-arom.), 75.3 (d, *C*-OH), 64.6 (d, *C*-N-CH$_3$), 61.4 (t, *C*H$_2$-CH$_2$-CH$_2$), 54.4 (t, *C*H$_2$), 39.0 (q, NH-*C*H$_3$), 33.7 (t, CH$_2$-*C*H$_2$-CH$_2$), 19.3 (t, CH$_2$-CH$_2$-*C*H$_2$), 13.5 (q, *C*H$_3$-CH$_2$-CH$_2$), 8.9 (q, *C*H$_3$);

Anal. Calcd. for $C_{20}H_{29}BrN_2O \cdot 0.1\ H_2O$: C, 59.43; H, 7.53; Found: C, 59.45; H, 7.24; ν_{max}/cm^{-1}: 3374 (OH), 2873 (NH), 1638 (C-N), 1371 (C=C), 1201(C-H), 703 (C-H arom);

$[\alpha]_D^{20}$: -2.2 (c 1.00 in EtOH,); $T_{5\%onset}$: 213 °C.

1-Butyl-3-[[[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenyl-ethyl]methylamino]methyl]pyridinium bis(trifluoromethane-sulfonyl)imide 9

Preparation from **8** (0.78 g, 2.00 mmol) according to procedure for compound **5** gave **9** as brown viscous liquid in 86% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.48 (d, J = 5.9 Hz, 1H, H-arom.), 7.91 (m, 2H, H-arom.), 7.71 (dd, J_1 = 7.5 Hz, J_2 = 6.4 Hz, 1H, H-arom.), 7.30 (m, 5H, H-arom.), 4.62 (d, 1H, J = 7.4 Hz, H-OH), 4.28 (t, J = 7.6 Hz, 2H, CH-N arom), 3.79/3.77 (2d, J = 15.9 Hz, 2H, CH$_2$-N), 2.89 (m, 1H, H-NMe), 2.67 (br s, 1H, OH), 2.14 (s, 3H, C*H*$_2$-CH$_2$-CH$_2$), 1.77 (q, J = 7.8 Hz, 1H, CH$_2$-C*H*$_2$-CH$_2$), 1.29 (sext, J = 7.8 Hz, 2H, CH$_2$-CH$_2$-C*H*$_2$), 1.17 (d, 3H, J = 6.7, C*H*$_3$-CH$_2$-CH$_2$), 0.93 (t, J = 7.3 Hz, 3H, C*H*$_3$-CH);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.7/143.9 (2d, C-arom.), 143.1/142.9 (2s, C-arom.), 142.4 (d, C-arom.), 128.3 (d, C-arom.), 127.7/127.4 (2d, C-arom.), 126.7 (d, C-arom.), 119.5 (q, J = 321.31 Hz, CF$_3$), 76.0 (d, *C*-OH), 64.4 (d, 1C, *C*-NH), 62.0 (t, *C*H$_2$-CH$_2$-CH$_2$), 54.7 (t, *C*H$_2$), 37.7 (q, NH-*C*H$_3$), 33.3 (t, CH$_2$-*C*H$_2$-CH$_2$), 19.2, (t, CH$_2$-CH$_2$-*C*H$_2$), 13.2 (q, 1C, *C*H$_3$-CH$_2$-CH$_2$), 9.5 (t, *C*H$_3$);

Anal. Calcd. for $C_{22}H_{29}F_6N_3O_5S_2$: C, 44.51; H, 4.92; Found: C, 44.28; H, 4.75; ν_{max}/cm^{-1} = 3534 (OH), 2960 (NH), 1350 (C=C), 1330 (C-H), 690 (C-H arom); $[\alpha]_D^{20}$ = -14.5 (c 1.03 in EtOH); $T_{5\%onset}$: 251 °C.

(1*S*,2*S*)-2-[Methyl(pyridin-3-ylmethyl)amino]-1-phenyl-propan-1-ol 11

To a suspension of commercial available (1*S*,2*S*)-pseudoephedrine **10** (4.90 g, 30 mmol) and molecular sieve 4 Å (10 g) in 100 mL anhydrous MeOH, freshly distilled pyridine-2-carboxaldehyde (3.21 g, 30 mmol) was added dropwise. The reaction mixture was refluxed for 15 h until TLC showed complete conversion. The mixture was filtrated over celite to remove the molecular sieve and acetic acid (9.00 g, 150 mmol) and $NaCNBH_3$ (5.65 g, 90 mmol) were added to the solution. The mixture was stirred 2 h at room temperature until TLC showed full conversion of the intermediate. Solid $NaHCO_3$ (15 g) was added and the mixture was allowed to rest for 2 hours. Methanol was removed under reduced pressure and ethyl acetate was added to the residue. The organic layer was extracted three times with small amounts of water, dried over Na_2SO_4, filtrated and the remaining solvent was removed. The obtained raw material was purified via MPLC (CH_2Cl_2:MeOH 10:1) and gave **11** in 68% yield as colourless liquid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.48 (m, 1H, H-arom.), 7.65 (td, J_1 = 1.8 Hz, J_2 = 7.6 Hz, 1H, H-arom.), 7.23 (m, 6H, H-arom.), 4.87 (brs, 1H, OH), 4.26 (d, J = 9.8 Hz, 1H, C*H*-OH), 3.69 (d, J = 13.1 Hz, 1H, C*H*$_2$-NMe), 3.44 (d, J = 13.3 Hz, 1H, C*H*$_2$-NMe), 2.68 (m, 1H, C*H*-N), 2.16 (s, 3H, N-CH$_3$), 0.74 (d, J= 6.7 Hz, 3H, C*H*$_3$-CH);

^{13}C-NMR (100 MHz, $CDCl_3$): δ_C = 150.3 (d, C-arom.), 149.0 (d, C-arom.), 141.6 (s, C-arom.), 136.5 (d, C-arom.), 134.0 (s, C-arom.), 128.3 (d, C-arom.), 127.8 (d, C-arom.), 127.3 (d, C-arom.), 123.6 (d, C-arom.), 74.8 (d, *C*-OH), 65.1 (d, N-*C*H), 55.5 (q, N-*C*H$_3$), 35.7 (t, *C*H$_2$), 7.4 (q, *C*H$_3$);

Anal. Calcd. For $C_{16}H_{20}N_2O \cdot 0.01\ H_2O$: C, 74.44; H, 7.89; Found: C, 74.58; H, 7.38; ν_{max}/cm^{-1}: 3370 (O-H), 1576 (C-C), 1451 (C=C), 1480 (C-H), 1025.38 (NH-CH$_3$), 756 (C-H arom.); $[\alpha]_D^{20}$: +108.2 (c 0.91 in CH_2Cl_2); $T_{5\%onset}$: 215 °C.

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DOI: 10.1039/C3OB41635F

1-Butyl-3-[[[(1*S*,2*S*)-1-hydroxy-1-phenylprop-2-yl]methylamino]methyl]pyridinium bromide 12

Preparation from **11** (1.13 g, 4.40 mmol) according to procedure for compound **4** gave **12** as yellow oil in 97% yield.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 9.68 (s, 1H, H-arom.), 9.22 (d, J = 6.0 Hz,1H, H-arom.), 8.34 (d, J = 7.9 Hz, 1H, H-arom.), 7.96 (t, J = 7.0 Hz, 1H, H-arom.), 7.20 (s, 5H, H-arom.), 4.80 (m, 3H, OH, CH_2-N arom.), 4.34 (d, J = 9.4 Hz, 1H, C*H*-OH), 3.97 (d, J = 14.9 Hz, 1H, CH_2-NMe), 3.76 (d, J = 14.8 Hz, 1H, CH_2-NMe), 2.78 (m, 1H, CH-OH), 2.22 (s, 3H, N-CH_3), 1.85 (m, 2H, CH_2-CH_2-CH_2), 1.26 (m, 2H, CH_2-CH_2-CH_2), 0.83 (t, J = 7.3 Hz, CH_3-CH_2-CH_2, 3H), 0.71 (d, J = 6.6 Hz, 3H, CH_3-C);

^{13}C-NMR (100 MHz, $CDCl_3$): δ_C = 145.1 (d, C-arom.), 144.7 (s, C-arom.), 143.5 (d, C-arom.), 141.8 (s, C-arom.), 140.8 (d, C-arom.), 128.2 (2d, C-arom.), 127.9 (d, C-arom.), 127.8 (d, C-arom.), 127.2 (d, C-arom.), 74.9 (d, *C*-OH), 65.3 (d, N-*C*H), 61.3 (t, *C*H_2-CH_2-CH_2), 54.5 (q, N-*C*H_3), 36.4 (t, *C*H_2), 33.7 (t, CH_2-*C*H_2-CH_2), 19.2 (t, CH_2-CH_2-*C*H_2), 13.5 (q, *C*H_3-CH_2-CH_2), 7.4 (q, *C*H_3);

Anal. Calcd. For $C_{20}H_{29}BrN_2O \cdot 0.5\ H_2O$: C, 59.57; H, 7.52; Found: C, 59.29; H, 7.15; ν_{max}/cm^{-1}: 3315 (O-H), 1632 (C-C), 1500 (C-C), 1453 (C=C), 1038 (NH-CH_3), 702 (C-H arom.); $[\alpha]_D^{20}$: +63.5 (c 1.22 in CH_2Cl_2); $T_{5\%onset}$: 221 °C.

1-Butyl-3-[[[(1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl]methyl-amino]methyl]pyridinium bis(trifluoromethanesulfonyl)imide 13

Preparation from **12** (1.00 g, 2.54 mmol) according to procedure for compound **5** gave **13** as yellow oil in 96% yield.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.72 (s, 1H, H-arom.), 8.58 (d, J = 6.0 Hz, 1H, H-arom.), 8.36 (d, J = 8.0 Hz, 1H, H-arom.), 7.89 (m, 1H, H-arom.), 7.25 (s, 5H, H-arom.), 4.50 (t, J = 7.6 Hz, OH, CH_2-N arom.), 4.33 (d, J = 9.6 Hz, 1H, C*H*-OH), 3.94 (d, J = 15.1 Hz, 1H, CH_2-NMe), 3.71 (d, J = 15.1 Hz, 1H, CH_2-NMe), 2.75 (m, 1H, CH-OH), 2.23 (s, 3H, N-CH_3), 1.88 (m, 2H, CH_2-CH_2-CH_2), 1.27 (m, 3H,), 0.89 (t, J = 7.3 Hz, 3H, CH_3-CH_2-CH_2), 0.77 (d, J = Hz 6.6, 3H, CH_3-C);

^{13}C-NMR (100 MHz, $CDCl_3$): δ_C = 145.3 (d, C-arom.), 143.8 (d, C-arom.), 142.9 (s, C-arom.), 141.6 (d, C-arom.), 141.3 (d, C-arom.), 128.4 (s, C-arom.), 128.2 (d, C-arom.), 128.1 (d, C-arom.), 127.3 (d, C-arom.), 119.6 (q, J = 324.6 Hz, CF_3), 75.0 (d, *C*-OH), 65.6 (d, N-*C*H), 62.2 (t, *C*H_2-CH_2-CH_2), 54.3 (q, N-*C*H_3), 36.1 (t, *C*H_2), 33.3 (t, CH_2-*C*H_2-CH_2), 19.2 (t, CH_2-CH_2-*C*H_2), 13.2 (q, *C*H_3-CH_2-CH_2), 8.0 (q, *C*H_3);

Anal. Calcd. For $C_{22}H_{29}F_6N_3O_5S_2 \cdot 0.9\ H_2O$: C, 43.33; H, 5.09; Found: C, 43.17; H, 4.71; ν_{max}/cm^{-1}: 2961 (O-H), 1504 (C-C), 1456 (C=C), 1348 (C-H), 1178 (C-F_3), 1132 (S=O), 1052 (NH-CH_3), 788 (C-H arom.); $[\alpha]_D^{20}$: +17.8 (c 0.88 in CH_2Cl_2); $T_{5\%onset}$: 250 °C.

(1*S*,2*R*)-1,2-Diphenyl-2-[(pyridin-3-ylmethyl)amino]ethanol 15

Freshly distilled pyridine-3-carboxaldehyde (1.00 g, 9.33 mmol) was added to a mixture of (1*S*,2*R*)-2-amino-1,2-diphenylethanol (2.00 g, 9.33 mmol) **14** and activated molecular sieve 3 Å (5.00 g) in 100 ml of anhydrous methanol and refluxed for 14 h. Sodium borohydride (0.35 g, 9.33 mmol) was added in small portions and the mixture was stirred at room temperature until TLC indicated complete conversion. The reaction mixture was filtered over silica and hydrolyzed with H_2O_{dest}. Methanol was removed under reduced pressure and the aqueous layer was extracted with dichloromethane to give crude product **15**, which was further purified via VFC (200 g silica, CH_2Cl_2:MeOH 40:1 + Et_3N) to yield **15** as white solid in 89% yield. Crystallization from toluene gave colourless crystals.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.38 (d, J = 4.8 Hz, 1H, H-arom.), 8.28 (s, 1H, H-arom.), 7.39 (m, 1H, H-arom.), 7.16 (m, 11H, H-arom.), 4.71 (d, J = 6.1 Hz, 1H, C*H*-OH), 3.81 (d, J = 6.1 Hz, 1H, C*H*-NH), 3.60 (d, J = 13.7 Hz, 1H, CH_2), 3.43 (d, J = 13.7 Hz, 1H, CH_2), 2.80 (brs, 1H, O*H*), 1.68 (brs, 2H, NH_2);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 149.6 (d, C-arom.), 148.4 (d, C-arom.), 140.6 (s, C-arom,), 138.9 (s, C-arom.), 135.7 (s, C-arom.), 135.2 (d, C-arom.), 128.4 (d, C-arom.), 128.1 (d, C-arom.), 127.9 (d, C-arom.), 127.8 (d, C-arom.), 127.2 (d, C-arom.), 126.9 (d, C-arom.), 123.3 (d, C-arom.), 76.4 (d, 1C, *C*-OH), 68.1 (d, *C*-NH), 48.4 (t, *C*H_2);

Anal. Calcd. for $C_{20}H_{20}N_2O \cdot 0.15\ H_2O$: C, 78.22; H, 6.66; Found: C, 78.12; H, 6.34; ν_{max}/cm^{-1}: 3175 (OH), 3028 (N-H), 1578 (C=C), 1450 (C-H), 752 (C-H arom.); $[\alpha]_D^{20}$: -17.8 (c 0.83 in CH_2Cl_2); mp: 144-146 °C (from toluene); $T_{5\%onset}$: 177 °C.

(1*S*,2*R*)-2-[Methyl(pyridin-3-ylmethyl)amino]-1,2-diphenylethanol 16

Cmp. **15** (1.34 g, 4.40 mmol) was dissolved in 9 ml of concentrated formic acid and stirred for 30 minutes. Formaldehyde (7.5 ml, 37% solution in H_2O) was added and the mixture was refluxed overnight. Remaining formaldehyde was removed under reduced pressure, a 4 M NaOH solution in H_2O was added until pH>7 and the reaction mixture was extracted with CH_2Cl_2. The organic layers were washed with brine, dried with Na_2SO_4 and concentrated under reduced pressure to yield crude **16**. Crystallization from toluene gave **16** as colourless crystals in 65% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.36 (dd, J_1 = 1.6 Hz, J_2 = 4.8 Hz, 1H, H-arom.), 8.22 (d, J = 1.7 Hz, 1H, H-arom.), 7.18 (m, 12H, H-arom.), 5.26 (d, J = 6.7 Hz, 1H, C*H*-OH), 3.53 (m, 2H C*H*-NH, N-CH_2), 3.37 (d, J = 13.9 Hz, 2H, N-CH_2), 2.63 (brs, 1H, O*H*), 2.18 (s, 3H, NH-CH_3);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 149.9 (d, C-arom.), 148.4 (s, C-arom.), 142.0 (d, C-arom.), 136.3 (s, C-arom.), 135.6 (s, 1C, C-arom.), 134.5 (d, C-arom.), 129.5 (d, C-arom.), 128.0 (d, C-arom.), 127.9 (d, C-arom.), 127.7 (d, C-arom.), 127.4 (d, C-arom.), 126.7 (d, C-arom.), 123.3 (d, C-arom.), 74.5 (d, *C*-OH), 72.8 (d, *C*-NH), 56.8 (d, *C*H_2), 38.6 (q, NH-*C*H_3);

Anal. Calcd. For $C_{21}H_{22}N_2O \cdot 0.05\ H_2O$: C, 78.99; H, 6.98; Found: C, 79.08; H, 6.52; ν_{max}/cm^{-1}: 3269 (OH), 1574 (C=C), 1480 (C-H), 1027 (NH-CH_3), 756 (C-H arom.); $[\alpha]_D^{20}$: +61.1 (c 1.17 in CH_2Cl_2); mp: 103-106 °C (from toluene); $T_{5\%onset}$: 215 °C.

1-Butyl-3-[[[(1*R*,2*S*)-2-hydroxy-1,2-diphenylethyl]methyl-amino]methyl]pyridinium bromide 17

Preparation from **16** (0.50 g, 1.56 mmol) according to procedure for compound **4** gave **17** as light yellow viscous liquid in 99% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 9.23 (d, J = 5.4 Hz, 1H, H-arom.), 8.67 (s, 1H, H-arom.), 7.68 (m, 2H, H-arom.), 7.20 (m,

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DOI: 10.1039/C3OB41635F

10H, H-arom.), 5.31 (d, J = 7.0 Hz, 1H, CH_2-OH), 4.72 (t, J=7.5 Hz, 2H, CH-NH), 3.59 (m, 3H, CH_2-N, OH), 2.16 (s, 3H, NH-CH_3), 1.74 (m, 2H, CH_2-CH_2-CH_2), 11.27 (m, 2H, CH_2-CH_2-CH_2), 0.88 (t, J = 7.2 Hz, 3H, CH_3-CH_2-CH_2);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.1 (d, C-arom.), 143.4 (d, C-arom.), 142.7 (s, C-arom.), 135.2 (d, C-arom.), 129.6 (s, C-arom.) 128.1 (s, C-arom.), 128.0 (d, C-arom.), 127.8 (d, C-arom.), 127.3 (d, C-arom), 126.9 (d, C-arom), 74.9 (d, *C*-OH), 72.7 (d, *C*-NH), 61.5 (t, *C*H_2-CH_2-CH_2), 55.7 (t, *C*H_2), 39.34 (q, NH-*C*H_3), 33.7 (t, CH_2-*C*H_2-CH_2), 19.2 (t, CH_2-CH_2-*C*H_2), 13.5 (q, *C*H_3-CH_2-CH_2);

Anal. Calcd. For $C_{25}H_{31}BrN_2O \cdot 0.55\ H_2O$: C, 64.53; H, 6.95; Found: C, 64.54; H, 6.64; ν_{max}/cm^{-1}: 3284 (OH), 1631 (C-C), 1495 (C=C), 1480 (C-H), 1025 (NH-CH_3), 753 (C-H arom.);

$[\alpha]_D^{20}$: +52.0 (c 0.77 in CH_2Cl_2); $T_{5\%onset}$: 220 °C.

1-Butyl-3-[[[(1*R*,2S)-2-hydroxy-1,2-diphenylethyl]-methylamino]methyl]pyridinium bis(trifluoromethane-sulfonyl)imide 18

Preparation from **17** (0.60 g, 1.3 mmol) according to procedure for compound **5** gave **18** as yellow oil in 99% yield.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.47 (d, J = 6.0 Hz, 1H, H-arom.), 7.81 (s, 2H, H-arom.), 7.70 (s, 1H, H-arom.), 7.32 (m, 10H, H-arom.), 5.28 (d, J = 8.7 Hz, 1H, C*H*-OH), 4.29 (m, 2H, CH_2-N arom.), 3.82 (d, J = 7.9 Hz, 1H, C*H*-NH), 3.72/3.58 (2d, J = 15.0 Hz, 2H, N-CH_2), 2.13 (s, 3H, NH-CH_3), 1.77 (m, 2H, CH_2-CH_2-CH_3), 1.31 (m, 2H, CH_2-CH_2-CH_3), 0.97 (t, J = 7.2 Hz, 3H, CH_3-CH_2-CH_2);

^{13}C-NMR (100 MHz, $CDCl_3$): δ_C = 144.6 (d, C-arom.), 143.0 (d, C-arom.), 142.8 (d, C-arom.), 142.5 (s, C-arom.), 142.4 (d, C-arom.), 134.7 (s, C-arom.), 129.3 (d, 2 C-arom.), 128.6 (d, 2 C-arom.), 128.4 (d, 2 C-arom.), 128.2 (s, C-arom.), 127.9 (d, 2 C-arom.), 127.3 (d, 2 C-arom.), 119.7 (q, J = 321.5 Hz, CF_3), 74.4 (d, *C*-OH), 73.1 (d, *C*-NCH_3), 62.0 (t, *C*H_2-CH_2-CH_2), 55.4 (t, *C*H_2-NCH_3), 38.3 (q, NH-*C*H_3), 33.2 (t, CH_2-*C*H_2-CH_3), 19.3 (t, CH_2-*C*H_2-CH_3), 13.4 (q, *C*H_3-CH_2-CH_2);

Anal. Calcd. For $C_{27}H_{31}F_6N_3O_5S_2 \cdot 0.05\ H_2O$: C, 49.39; H, 4.77; Found: C, 49.41; H, 4.66; ν_{max}/cm^{-1}: 3529 (O-H), 1633 (C-C), 1498 (C=C), 1453 (C-H), 1178 (C-F_3), 1133 (S=O), 1035 (NH-CH_3), 703 (C-H arom.); $[\alpha]_D^{20}$: +43.7 (c 1.01 in CH_2Cl_2); $T_{5\%onset}$: 258 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-2-methylpropyl]methylamino]methyl]pyridinium bromide 21

Preparation from **20** (0.81 g, 2.36 mmol) according to procedure for compound **4** gave **21** as orange oil in 99% yield.[18]

^{1}H-NMR (200 MHz, MeOD): δ_H = 8.98 (s, 1H, H-arom), 8.90 (d, J = 5.9 Hz, 1H, H-arom), 8.57 (d, J = 8.0 Hz, 1H, H-arom), 8.06 (t, J = 7.3 Hz, 1H, H-arom), 4.66 (t, J = 7.5 Hz, 2H, CH_2-N-arom.), 4.13 (s, 2H, CH_2-N), 3.80 (m, 2H, CH_2-OH), 2.37 (m, 4H CH_2-CH_2, CH_2-CH_2-CH_2), 2.11-1.75 (m, 3H CH_3-CH_2-CH_2), 1.42 (sext., J = 7.4 Hz, 2H, CH_3-CH_2-CH_3), 1.03 (m, 9H, 2 CH_3, CH_3-CH_2-CH_2);

^{13}C-NMR (50 MHz, MeOD): δ_C = 146.5 (d, C-arom.), 145.4 (d, C-arom.), 144.2 (s, C-arom.), 128.9 (d, C-arom.), 72.4 (d, *C*-OH), 62.8 (t, N-*C*H_2), 60.9 (t, *C*H_2-CH_2-CH_2), 57.6 (t, CH_2-*C*H_2-CH_2), 37.3 (q, N-*C*H_3), 34.4 (d, *C*H-N-CH_3), 29.2 (d, CH_3-*C*H-CH_3), 21.9 (q, *C*H_3), 20.8 (q, *C*H_3), 20.4 (t, CH_2-CH_2-*C*H_2), 13.8 (q, *C*H_3-CH_2-CH_2);

ν_{max}/cm^{-1}: 3338 (OH), 2933 (N-C), 1633 (C-C), 1465 (C-H), 1049 (NH-CH_3); $[\alpha]_D^{20}$: -1.4 (c 0.61 in CH_2Cl_2); $T_{5\%onset}$: 223 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-2-methyl-propyl]methyl-amino]methyl]pyridinium bis (trifluoromethanesulfonyl)-imide 22

Preparation from **21** (0.28 g, 1.39 mmol) according to procedure for compound **5** gave **22** as viscous brown oil in 95% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.76 (s, 1H, H-arom), 8.63 (d, J = 5.9 Hz, 1H, H-arom.), 8.40 (d, J = 7.8 Hz, 1H, H-arom.), 7.94 (m, 1H, H-arom.), 4.56 (t, J = 7.5 Hz, 2H, CH_2-N-arom.), 4.11 (s, 2H, CH_2-N), 3.71 (m, 2H, CH_2-OH), 2.41 (m, 1H, C*H*-NMe), 2.35 (s, 3H, N-CH_3), 1.99-1.69 (m, 1H, CH_2-CH_2-CH_2), 1.68-1.03 (m, 3H, CH_2-CH_2, CH_2-CH_2-CH_2), 1.37 (sext, 2H, CH_3-CH_2-CH_3), 1.19- 0.71 (m, 9H, 2 CH_3, CH_3-CH_2-CH_2);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 145.1 (d, C-arom.), 143.8 (d, C-arom.), 142.8 (s, C-arom.), 142.6 (d, C-arom.), 128.1 (d, C-arom.), 122.9 (q, J = 321.3 Hz, CF_3), 71.1 (d, *C*H-NCH_3), 62.3 (t, *C*H_2-OH), 60.2 (t, CH_2-N-arom.), 56.2 (t, NMe-*C*H_2), 36.5 (q, N-*C*H_3), 33.3 (t, *C*H_2-CH_2-CH_2), 27.7 (d, CH_2-*C*H_2-CH_2), 21.6 (q, CH_3-*C*H-CH_3), 20.1 (q, 2 *C*H_3), 19.2 (t, CH_2-CH_2-*C*H_2), 13.2 (q, *C*H_3-CH_2-CH_2);

Anal. Calcd. for $C_{16}H_{29}F_6N_3O_5S_2$: C, 39.63; H, 5.36; Found: C, 39.43; H, 5.03; ν_{max}/cm^{-1}: 3310 (O-H), 1627 (C-C), 1469 (C=C), 1466 (C-H), 1230 (C-F_3), 1134 (S=O), 1045 (NH-CH_3); $[\alpha]_D^{20}$: -3.9 (c 1.00 in EtOH); $T_{5\%onset}$: 226 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-3-methyl-butyl]methylamino]methyl]pyridinium bromide 25

Preparation from **24** (0.67 g, 3 mmol) according to procedure for compound **4** gave **25** as yellow oil in 99% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 9.40 (d, J = 5.9 Hz, 1H, H-arom.), 9.19 (d, J = 5.9 Hz, 1H, H-arom.), 8.28 (d, J = 8.0 Hz, 1H, H-arom.), 7.94 (dd, J_1 = 7.6 Hz, J_2 = 6.1 Hz, 1H, H-arom.), 4.76 (t, J = 7.3 Hz, 2H, CH_2-N arom.), 3.96/3.71 (2d, J = 15.3 Hz, 2H, CH_2-N), 3.37 (m, 2H, CH_2-OH), 2.63 (m, 1H, C*H*-NMe), 2.11 (s, 3H, N-CH_3), 1.85 (q, J = 7.5 Hz, 2H, CH_2-CH_2-CH_2), 1.58-1.05 (m, 4H, CH_2-CH_2-CH_3, CH_2-CH_2-CH_3), 0.91 (m, 1H, CH_3-C*H*-CH_3), 0.75 (t, J = 7.5 Hz, 3H, CH_3-CH_2-CH_2), 0.68/0.64 (2d, 6H, J = 6.5 Hz, 2 CH_3);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.5 (2d, C-arom.), 143.1 (d, C-arom.), 142.2 (s, C-arom.), 128.0 (d, C-arom.), 62.3 (d, NMe-*C*H), 62.0/61.4 (2t, *C*-N arom., *C*-OH), 54.8 (t, *C*H_2-NMe), 36.3 (q, N-*C*H_3), 35.5 (t, CH-*C*H_2-CH_2), 33.7 (t, CH_2-*C*H_2-CH_2), 25.3 (t, CH_3-*C*H_2-CH_3), 23.0/22.5 (2q, 2 *C*H_3), 19.2 (t, CH_2-CH_2-*C*H_2), 13.4 (q, *C*H_3-CH_2-CH_2);

Anal. Calcd. for $C_{17}H_{31}BrN_2O \cdot 0.3\ H_2O$: C, 55.98; H, 8.73; Found: C, 55.90; H, 8.47; ν_{max}/cm^{-1}: 3330 (OH), 2957 (NH), 1643 (C-N), 1367 (C-CH_3), 1055 (C-H); $[\alpha]_D^{20}$ = +12.8 (c 0.94 in EtOH); $T_{5\%onset}$: 188 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-3-methylbutyl]methylamino]methyl]pyridinium bis(trifluoromethanesulfonyl)imide 26

Preparation from **25** (0.85 g, 2.36 mmol) according to procedure for compound **5** gave **26** as light yellow oil in 92% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.74 (s, 1H, H-arom), 8.60 (d,

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DOI: 10.1039/C3OB41635F

J = 6.6 Hz, 1H, H-arom.), 8.37 (d, J = 8.0 Hz, 1H, H-arom.), 7.90 (dd, J_1 = 7.8 Hz, J_2 = 6.3 Hz, 1H, H-arom.), 4.51 (t, J = 7.6 Hz, 2H, CH_2-N-arom.), 3.96/3.81 (2d, J = 15.3 Hz, 2H, CH_2-N), 3.49 (m, 2H, CH_2-OH), 2.76 (m, 2H, C*H*-NMe and OH), 2.21 (s, 3H, N-CH_3), 1.90 (q, J = 7.5 Hz, 2H, CH_2-CH_2-CH_2), 1.68-0.99 (m, 5 H, CH_2-CH_2, CH_2-CH_2-CH_2, CH_3-C*H*-CH_3), 0.89 (t, J = 7.14 Hz, 3H, CH_3-CH_2-CH_2), 0.90 (m, 2H, CH_3-CH_2-CH_3), 0.91/0.83 (2d, 6H, J = 6.45 Hz, 2 CH_3);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 145.1 (d, C-arom.), 143.9 (d, C-arom.), 142.8 (d, C-arom.), 142.5 (s, C-arom.), 128.1 (d, C-arom.), 119.7 (q, J = 321.3 Hz, CF_3), 62.7 (d, *C*H-NMe,), 62.3 (t, C, *C*-OH), 61.9 (t, CH_2-N-arom.), 54.5 (t, NMe-*C*H_2), 36.1 (q, N-*C*H_3), 34.8 (t, CH-*C*H_2-CH), 33.3 (t, CH_2-*C*H_2-CH_2), 25.3 (d, 1C. CH_3-*C*H-CH_3), 23.1/22.2 (2q, 2 CH*3*), 19.2 (t, CH_2-CH_2-*C*H_2), 13.1 (t, *C*H_3-CH_2-CH_2);

Anal. Calcd. for $C_{19}H_{31}F_6N_3O_5S_2$: C, 40.78; H, 5.58; Found: C, 40.59; H, 5.29; ν_{max}/cm^{-1}: 3562 (OH), 2969 (NH), 1635 (C-N), 1348 (C-CH_3), 1179 (C-F_3), 1132 (S=O), 1052 (NH-CH_3); $[\alpha]_{365}^{20}$: +7.2 (c 0.97 in EtOH); $T_{5\%onset}$: 244 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-2-phenylethyl]methylamino]methyl]pyridinium bromide 29

Preparation from **28** (0.37 g, 2.67 mmol) according to procedure for compound **4** gave **29** as brown oil in 99% yield.

^{1}H-NMR (200 MHz, MeOD): δ_H = 8.82 (d, J = 8.8 Hz, 1H, H-arom.), 8.60 (s, 1H, H-arom.), 8.26 (d, J = 8.0 Hz, 1H, H-arom.), 7.92 (t, 1H, H-arom.), 7.26 (m, 5H, H-arom.), 4.50 (t, J = 7.5 Hz, 2H, CH-N arom.), 4.03 (s, 2H,CH_2-OH), 3.86-3.50 (m, 2H, CH_2-NMe), 3.05 (m, 1H, CH_2-CH_2-OH), 2.92-2.64 (m, 2H, CH_2-Ph), 2.41 (m, 3H, CH_3-N), 1.93 (quin., J = 3.6, 2H, CH_2-CH_2-CH_2), 1.40 (sext. J = 4.9, 2H, CH_2-CH_2-CH_2), 1.02 (t, 3H, J = 3.9, CH_2-CH_2-CH_3);

^{13}C-NMR (50 MHz, MeOD): δ_C = 146.3 (d, C-arom.), 145.2 (d, C-arom.), 144.0 (d, C-arom.), 141.6 (s, C-arom.), 141.2 (s, C-arom.), 130.4 (d, C-arom.), 129.5 (d, 2C, C-arom.), 128.7 (d, C-arom.), 127.2 (d, C-arom.), 67.9 (d, *C*H-NH), 62.8 (t, *C*H_2-CH_2-CH_2), 62.2 (t, CH_2-*C*H_2-CH_2), 36.6 (q, N-*C*H_3), 34.7 (t, *C*H_2-OH), 34.4 (t, *C*H_2-NH), 20.4 (t, *C*H_2- C arom.), 13.8 (q, CH_2-CH_2-*C*H_3); Anal. Calcd. for $C_{12}H_2ON_2O$ · 2.3 H_2O: C, 55.25; H, 7.79; Found: C, 55.30; H, 8.16; ν_{max}/cm^{-1}: 3309 (O-H), 2872 (N-C), 1632 (C-C), 1495 (C=C), 1453 (C-H), 1031 (NH-CH_3); $[\alpha]_D^{20}$: -2.3 (c 0.27 in CH_2Cl_2); $T_{5\%onset}$: 225 °C.

1-Butyl-3-[[[(1*S*)-1-(hydroxymethyl)-2-phenylethyl]methylamino]methyl]pyridinium bis (trifluoromethane sulfonyl)imide 30

Preparation from **29** (1.28 g, 5 mmol) according to procedure for compound **5** gave **30** as dark brown oil in 99% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 8.48 (d, J = 6.1 Hz, 1H, H-arom.), 8.26 (s, 1H, H-arom.), 8.03 (d, J= 8.0 Hz, 1H), 7.73 (m, 1H, H-arom.), 7.31-7.05 (m, 5H, H-arom.), 4.34 (t, J = 7.6 Hz, 2H, C*H*-N arom), 3.92 (dd, J_1 = 15.6 Hz, J_2 = 14.5 Hz, 2H, CH_2-N), 3.60 (m, 2H, CH_2-OH), 2.99 (m, 1H, C*H*-CH_2-OH), 2.61 (m, 2H, CH_2-Ph), 2.32 (s, 3H, N-CH_3), 1.80 (q, J = 7.6 Hz, 2H, CH_2-CH_2-CH_3), 1.25 (sext, J = 7.5 Hz, 2H, CH_3-CH_2-CH_2), 0.89 (t, J = 7.3 Hz, 3H, CH_3-CH);

^{13}C-NMR (50 MHz, $CDCl_3$): δ_C = 144.9/143.6 (2d, C-arom.), 142.6/142.4 (2s, C-arom.), 139.5 (d, C-arom.), 129.2 (d, C-arom.), 128.5 (2d, C-arom.), 127.8 (d, C-arom.), 119.5 (q, J = 321.3 Hz, CF_3), 66.3 (d, *C*-OH), 62.1 (t, *C*-NH), 61.6 (t, *C*H_2-CH_2-CH_2), 55.3 (t, *C*H_2), 35.9 (q, NH-*C*H_3), 33.4 (t, CH_2-*C*H_2-CH_2), 33.3 (t, NH-*C*H_3), 19.2 (t, CH_2-CH_2-*C*H_2), 13.2 (q, *C*H_3-CH_2-CH_2);

Anal. Calcd. for $C_{22}H_{29}F_6N_3O_5S$: C, 44.51; H, 4.92; Found: C, 44.85; H, 4.96; ν_{max}/cm^{-1}: 2855 (O-H), 1577 (C-C), 1453 (C=C), 1328 (C-H), 1284 (C-F_3), 1027 (NH-CH_3); $[\alpha]_D^{20}$: -14.3 (c 0.96 in EtOH); $T_{5\%onset}$: 265 °C.

1-Butyl-3-[[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]methyl]pyridinium bromide 33

Preparation from **32** (0.58 g, 3 mmol) according to procedure for compound **4** gave **33** as viscous brown oil in >99% yield.

^{1}H-NMR (200 MHz, $CDCl_3$): δ_H = 9.64 (s, 1H, H-arom.), 9.24 (d, J = 5.9 Hz, 1H, H-arom.), 8.41 (d, J = 7.8 Hz, 1H, H-arom.), 8.00 (dd, J_1 = 7.8 Hz, J_2 = 6.3 Hz, 1H, H-arom.), 4.85 (m, 2H, C*H*-N arom.), 4.42/3.72 (2d, J = 14.9 Hz, 2H, CH_2-N), 4.10 (brs, 1H, OH), 3.50 (m, 2H, CH_2-OH), 2.83 (m, 2H, CH_2-N pyr., CH-N pyr.), 2.29 (m, 1H, CH_2-N pyr.), 2.14-1.48 (m, 6H, CH_2-CH_2-CH_2, 2 CH_2-CH_2), 1.35 (sext, J = 7.75 Hz, 2H, CH_2-CH_2-CH_2), 0.91 (t, J = 7.2 Hz, 3H, CH_3-CH_2-CH_2);

^{13}C-NMR (50 MHz, d_6-DMSO): δ_C = 145.2 (d, C-arom.), 144.7 (d, C-arom.), 143.0 (d, C-arom.), 141.8 (s, C-arom.), 127.7 (d, C-arom.), 65.3 (d, *C*H-CH_2-OH), 63.8 (t, *C*H_2-OH), 63.8 (t, *C*H_2-N arom.), 55.6/54.8 (2t, *C*H_2- N- pyr., *C*H_2-N), 33.7 (t, CH_2-*C*H_2-CH_2), 27.2 (t, *C*H_2 pyr.), 23.3 (t, *C*H_2 pyr.), 19.3 (t, CH_2-CH_2-*C*H_2), 13.5 (q, *C*H_3-*C*H_2-CH_2);

Anal. Calcd. for $C_{15}H_{25}BrN_2O$ · 0.5 H_2O: C, 53.26; H, 7.75; Found: C, 53.34; H, 7.35; ν_{max}/cm^{-1}: 3535 (OH), 2879 (N-C), 1636(C-C), 1329 (C=C), 1052 (NH-CH_3); $[\alpha]_D^{20}$: +23.4 (c 0.76 in EtOH); $T_{5\%onset}$: 279 °C.

1-Butyl-3-[[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]methyl]-pyridinium bis(trifluoromethanesulfonyl)imide 34

Preparation from **33** (2.22 g, 6.76 mmol) according to procedure for compound **5** gave **34** as dark brown oil in 99% yield.

^{1}H-NMR (200 MHz, DMSO): δ_H = 9.04 (s, 1H, H-arom.), 8.97 (d, J = 5.9 Hz, 1H, H-arom.), 8.53 (d, J = 7.8 Hz, 1H, H-arom.), 8.08 (dd, J_1 = 7.8 Hz, J_2 = 6.3 Hz, 1H, H-arom.), 4.60 (m, 3H, C*H*-N arom., OH), 4.27/3.66 (2d, J = 14.5 Hz/ J = 14.7, 2H, CH_2-N), 3.42 (brs, 2H, CH_2-OH), 2.84/2.71 (m, 2H, CH_2-N pyr., CH-N pyr.), 2.27 (m, 1H, CH_2-N pyr.), 1.91 (m, 3H, CH_2-CH_2-CH_2, CH_2-CH_2), 1.75-1.42 (m, 3H, 2 CH_2-CH_2), 1.30 (sext, J = 7.8 Hz, 2H, CH_2-CH_2-CH_2), 0.92 (t, J = 7.3 Hz, 3H, CH_3-CH_2-CH_2); ^{13}C-NMR (50 MHz, d_6-DMSO): δ_C = 145.0 (d, C-arom.), 143.9 (d, C-arom.), 143.0 (s, C-arom.), 141.0 (d, C-arom.), 127.4 (d, 1C, C-arom.), 119.7 (q, J = 321.9 Hz, CF_3), 65.1 (d, CH-N pyr.), 63.7 (t, CH_2-OH), 60.5 (t, CH_2-N arom.), 54.7/54.0 (2t, CH_2- N pyr., CH_2-N), 32.6 (t, *C*H_2-CH_2-CH_2), 27.3 (t, *C*H_2 pyr.), 22.5 (t, CH_2-*C*H_2-CH_2), 18.7 (t, CH_2-CH_2-*C*H_2), 13.1 (q, *C*H_3-*C*H_2-CH_2);

Anal. Calcd. for $C_{17}H_{25}F_6N_3O_5S_2$ · 0.9 H_2O: C, 37.42; H, 4.95; Found: C, 37.32; H, 4.48; ν_{max}/cm^{-1}: 3551 (O-H), 2880 (N-C), 1636(C-C), 1346 (C=C), 1132 (S=O), 1178 (C-F_3), 1052 (NH-CH_3); $[\alpha]_D^{20}$: +16.9 (c 1.20 in EtOH); $T_{5\%onset}$: 280 °C.

1-Methyl-3-[[[dimethyl[(1*R*,2*S*)-2-hydroxy-1-methyl-2-phenyl]ethyl]ammonio]methyl]pyridinium diiodide 35

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DOI: 10.1039/C3OB41635F

Cmp. **7** (0.26 g, 1.00 mmol) and iodomethane (1.42 g, 10 mmol) were mixed in a round-bottom flask, sealed, and stirred at 60 °C for 24 h. Excess iodomethane was evaporated and remaining volatile materials were removed under reduced pressure to yield diiodo salt **35** as light yellow solid in quantitative yield. An analytical sample was crystallized from H_2O/EtOH.

^{1}H-NMR (200 MHz, d_6-DMSO): δ_H = 9.38 (s, 1H, H-arom.), 9.18 (d, J = 6.1 Hz, 1H, H-arom.), 8.89 (d, J = 8.0 Hz, 1H, H-arom.), 8.32 (t, J = 6.9 Hz, 1H, H-arom.), 7.40 (m, 5H, H-arom.), 6.1 (d, J = 3.7 Hz, 1H, C*H*-OH), 5.67 (br s, 1H, OH), 5.01/4.90 (2d, J = 13.1 Hz/J = 13.3 Hz, 2H, CH_2-N), 4.44 (s, 3H, CH_3-NPyr), 3.90 (m, 1H, C*H*-N), 3.36/3.25 (2s, 6H, N-2CH_3), 1.30 (d, 3H, J = 4.6 Hz, CH-C*H*$_3$);

^{13}C-NMR (50 MHz, d_6-DMSO): δ_C = 149.4/148.7 (2d, C-arom.), 146.5 (s, C-arom.), 141.5 (d, C-arom.), 128.5 (d, C-arom.), 128.2 (d, C-arom.), 127.9 (s, C-arom.), 127.6 (d, C-arom.), 125.9 (d, C-arom.), 75.7 (d, *C*H-CH_3), 67.3 (d, C-OH), 59.4 (t, *C*H_2-N), 48.4 (3q, N-CH_3), 7.2 (q, C-*C*H_3). Anal. Calcd. for $C_{18}H_{26}I_2N_2O$: C, 40.02; H, 4.85; N, 5.19. Found: C, 40.04; H, 4.81; N, 5.14.ν_{max}/cm^{-1}: 3304 (OH), 3019 (C-H), 1639 (C-C), 1449 (C=C), 992 (N-CH_3); $[\alpha]_D^{20}$ = -2.2 (H_2O, c = 1.00); mp: 206-209 °C (from H_2O/EtOH); $T_{5\%onset}$: 215 °C.

General procedure for the enantioselective alkylation of benzaldehyde

The chiral ionic liquid (0.1 mmol) was dissolved in 2 ml of anhydrous solvent under a dry argon atmosphere and cooled to 0 °C. A solution of diethylzinc (1.0 M in *n*-hexane, 2.2 mmol) was added slowly at 0 °C. After the reaction was stirred for 30 minutes, freshly distilled benzaldehyde **36** (0.1 g, 1 mmol) was added dropwise via microsyringe at 0 °C, the reaction was slowly warmed to room temperature and stirred for 48 hours at this temperature. The mixture was carefully hydrolysed with 1 M HCl and the aqueous phase was extracted with diethyl ether. The combined organic layers were washed with a small amount of brine, dried with anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (30 g silica, light petrol:diethyl ether 5:1) to yield 1-phenyl-1-propanol **37** as colourless liquid. Analytical data were comparable to those reported in literature.[11]

^{1}H-NMR: (200 MHz, $CDCl_3$): δ_H = 0.88 (t, J = 7.3 Hz, 3 H), 1.76 (m, 1H), 2.36 (br s, 1H, OH), 4.52 (t, J = 6.7 Hz, 1H), 7.30 (s, 5H).

For recycling experiments the raw reaction mixture was hydrolysed with 1 M HCl and washed carefully 3 times with *n*-hexane. The combined *n*-hexane layers were dried with anhydrous Na_2SO_4, filtered and concentrated to yield **36** as colourless liquid.

The aqueous layers were washed with CH_2Cl_2 and the combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated. The thus recycled chiral ionic liquid was dried under reduced pressure (0.01 mbar) and used for a consecutive runs.

Notes and references

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† Electronic Supplementary Information (ESI) available: Detailed crytallographic data of diiodo salt **35** as well as copies of ^{1}H and ^{13}C NMR spectra of all novel compounds. See DOI: 10.1039/b000000x/.

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18. Caused by the hygroscopy of pyridinium bromide **21** we were not able to obtain a matching elemental analysis. The compound was therefore directly used for anion exchange towards bistriflimide **22** that was completely characterized.