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New chiral imidazolinic derivatives

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Abstract—Novel C-2 substituted 4,5-dihydroimidazoles and imidazoles bearing an N-linked stereogenic group were rapidly prepared from a chiral primary amine. Quaternization of these derivatives resulted in a range of scalemic room temperature ionic liquids. The ability of the imidazolium species to act as reaction medium and/or phase transfer catalyst was also assessed.

1. Introduction

Chiral non-racemic pyridinium salts bearing a stereogenic center connected to the nitrogen atom have already received much attention (Fig. 1).[1] They have proven to be highly valuable synthetic intermediates[2] and have lately given rise to a new family of chiral room temperature ionic liquids (RTILs).[3,4]

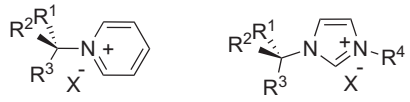


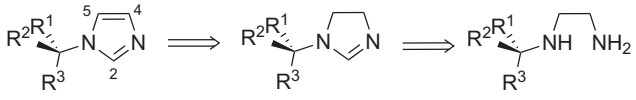
Figure 1.

The imidazolinic equivalents of these pyridinium salts have been far less exploited, only recently being described for the first time.[5] These imidazolium derivatives may, however, represent interesting candidates for RTIL and/or asymmetric phase transfer catalysis development. The use of a water/RTIL biphasic system has been applied to base-catalyzed alkylation of glycine esters[6] or Michael addition to enones.[7,8] Furthermore, it has been proposed that the RTIL plays a dual role of solvent and phase transfer catalyst over the course of biphasic hydrogen peroxide epoxidation of α,β-unsaturated compounds.[9] It might therefore be expected that some enantioselection arises from the association between the negatively charged nucleophilic reagent and a chiral imidazolium cation during such RTIL-mediated transformations. In addition, the electron-rich dihydroimidazole and imidazole precursors of these salts could also be of interest as chiral bases and/or nucleophiles.[10]

We thus report herein the preparation of new imidazolinic derivatives with an N-linked stereogenic appendage and, as a first illustration of their usefulness, their transformation into novel chiral RTILs.

2. Results and discussions

Our synthetic route was based on the preparation of the key imidazolinic moiety by oxidative dehydrogenation of the partially saturated heterocycle (Scheme 1). Synthesis of the 4,5-dihydroimidazole intermediate was in turn envisioned via condensation of a chiral 1,2-ethanediamine with a carboxylic acid equivalent.



Scheme 1.

Preparation of the required monosubstituted diamine precursor was thus studied (Scheme 2). Alkylation of a chiral primary amine with chloroethylamine appeared

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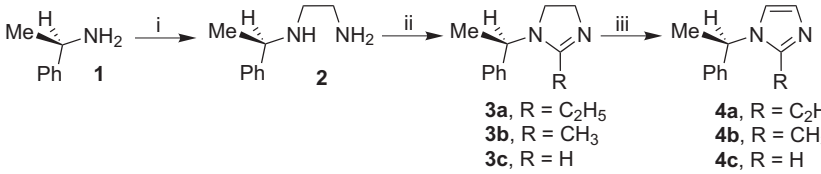


Scheme 2. Reagents and conditions: (i) $ClCH_2CH_2NH_2$ (0.5 equiv), 100 °C, 3 h of addition then 3 h additional, 45% based on the chloride; (ii) $RC(OEt)_3$ (1.06 equiv), AcOH (1.06 equiv), CH_3CN, reflux, 1 h, 93% (**3a** or *ent*-**3a**), 81% (*ent*-**3b**), 80% (*ent*-**3c**); (iii) $BaMnO_4$ (1000 wt%), 4 Å MS (100 wt%), CH_2Cl_2, reflux, 20 h, 58% (**4a** or *ent*-**4a**), 59% (*ent*-**4c**); or $KMnO_4$ (1.4 equiv), $BnEt_3NBr$ (0.05 equiv), benzene/water (1:2), rt, 1 h, 66% (**4a** or *ent*-**4a**), 61% (*ent*-**4b**).

to be the most direct option and the readily available α-methylbenzylamine was chosen as a suitable starting material. After careful optimization, it was established that slow addition of an aqueous solution of the electrophile to a 2-fold excess of neat primary amine **1** heated at 100 °C allowed the formation of the desired monoalkylation product **2** (or *ent*-**2** from *ent*-**1**) in 45% purified yield. The 1-fold excess of starting amine could be easily recovered during purification over Al_2O_3 and enantiomeric purity of the recovered material was checked by determination of its specific rotation. The only isolated side product was the dimeric triamine resulting from the alkylation of **2**.

1,2-Diamines are known to undergo facile ring closure to form 4,5-dihydroimidazoles when treated with an appropriate electrophile, such as an orthoester.[11] Indeed, diamine **2** (or *ent*-**2**) was condensed cleanly with triethylorthopropionate in the presence of an equimolar amount of acetic acid to give the expected five-membered ring heterocycle **3a** (or *ent*-**3a**) in 93% yield (Scheme 2). Running the cyclization with triethylorthoacetate readily gave the corresponding 2-methyl-4,5-dihydroimidazole *ent*-**3b** in 81% yield from *ent*-**2**. Similarly, the C-2 unsubstituted derivative *ent*-**3c** was also obtained in 80% yield from *ent*-**2** and triethylorthoformate. Introduction of a substituent at the sensitive C-2 position of the imidazolinic moiety was important to ensure stability of the corresponding imidazolium cation toward basic medium. Moreover, such C-2 substituted chiral imidazole derivatives have never been described.[12] We therefore focused the rest of our study on this series.

We were then in a position to consider the key oxidative aromatization of the heterocyclic core (Scheme 2). An extensive study, conducted with the 2-ethyl derivate **3a**, revealed that this transformation suffered from the sensitivity of the benzylic portion of the molecule toward either reductive or oxidative conditions. The use of palladium as a hydrogen acceptor[13] appeared attractive for its simplicity. However, prolonged reflux in toluene, xylene, or acetic acid (in the presence of 100 wt% of 10% Pd/C) did not yield any appreciable transformation, whereas carrying out the reaction at a higher temperature was hampered by the sensitivity of the benzylic chiral appendage to hydrogenolysis. Clean formation of 2-ethylimidazole in ca. 60% yield was indeed observed in refluxing *p*-cymene.

Manganese-based oxidants have been employed to produce various heterocycles such as oxazole[14] imidazole,[15] and triazole.[16] The mild γ-MnO_2 (500 wt% γ-MnO_2, 100 wt% 4 Å MS, benzene, reflux, 4 h, 30% yield)[14] required forcing conditions and gave a rather complicated transformation. On the other hand, the moderate reactivity of $BaMnO_4$ allowed a clean reaction,[15] delivering the essentially pure imidazole **4a** in 58% yield. Moreover, it was found that the powerful $KMnO_4$ could give rise to even better results if used under phase transfer catalysis conditions[16] rather than in homogeneous conditions (2 equiv, acetone, 0 °C to rt, 7 h, 43% yield). The 2-methyl analogue *ent*-**4b** was prepared in similar yield by this method. The sensitivity of the phenylethyl radical to benzylic oxidation likely constituted a limit to the efficiency of this transformation, as suggested by the traces of benzophenone present in the crude reaction mixture. The C-2 unsubstituted substrate *ent*-**3c** behaved in a comparable fashion, the corresponding imidazole *ent*-**4c**, for example, being prepared in 59% yield with $BaMnO_4$.

X-ray diffraction analysis of a single crystal of imidazole *ent*-**4b** chlorhydrate unambiguously confirmed the proposed chemical structure[17–19] and (*S*)-configuration[20] (Fig. 2). Interestingly, this solid-state conformation corresponds to a minimized A[1,3] strain with a quasi-synperiplanar arrangement between the chiral carbon hydrogen and the C-2 (dihedral angle 30.2°), as a consequence of the methyl radical in this position. It is worth noting that, to the best of our knowledge, no existing method allows access to such C-2 substituted chiral imidazoles.

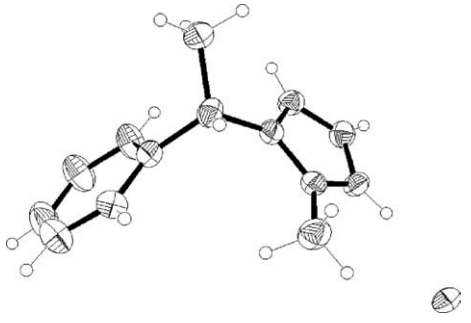
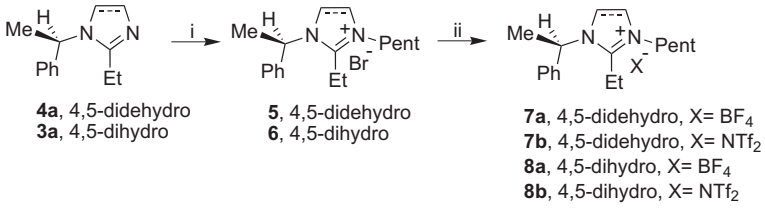


Figure 2. Crystal structure for chiral imidazole *ent*-**4b** chlorhydrate.[17–20]

With these new imidazoles in hands, we next looked at their quaternization with the prospect of preparing novel chiral RTILs for possible use under aqueous biphasic conditions. It was reasoned that a C_5 alkyl chain could provide enough lipophilicity, while maintaining suitably



Scheme 3. Reagents and conditions: (i) *n*-PentBr (5 equiv), 1,1,1-trichloroethane, reflux, 5 days, 91% (**5** or *ent*-**5**), 83% (**6**); (ii) $NaBF_4$ (1 equiv), acetone, rt, 4 days, 93% (*ent*-**7a**), 91% (**8a**); or $LiNTf_2$ (1 equiv), water, 70 °C, 30 min, 76% (**7b**), 81% (**8b**).

low viscosity and liquid–solid transition temperature.[21] The 2-ethyl derivative **4a** (or *ent*-**4a**) was thus reacted smoothly with *n*-pentyl bromide to form the expected imidazolium bromide salt **5** (or *ent*-**5**) isolated as a foam (Scheme 3).

At this stage of our study, the stereospecificity of our approach was checked running ^{1}H NMR analysis of imidazolium bromides *rac*-**5**, **5**, and *ent*-**5** in the presence of tris[3-(trifluoromethylhydroxymethylene)-D-camphorato]europium(III). No sign of epimerization was noted.

The potential of imidazolium **5** as a phase transfer catalyst was briefly explored. It was shown to catalyze the condensation of dimethyl malonate and chalcone under solid–liquid biphasic conditions (1 equiv chalcone, 1.5 equiv dimethyl malonate, 6 equiv K_2CO_3, 0.1 equiv salt **5**, toluene/CH_2Cl_2, 9:1; rt, 10 h) affording the expected Michael adduct, although as a racemic mixture, in a satisfactory 75% yield.[22] The catalyst proved to be stable under these conditions, as judged by ^{1}H NMR analysis and optical rotation measurement.

Counter anion metathesis was finally required to reach the targeted RTILs. In order to ensure once again a compromise between viscosity, solidification temperature, and water immiscibility, the highly fluorinated tetrafluoroborate and bis(trifluoromethanesulfonyl)amide anion were selected. Imidazolium *ent*-**7a** and **7b** could be readily prepared from bromide salt *ent*-**5** and **5**, respectively. Gratifyingly, they were both found to be water immiscible liquids at room temperature. Differential scanning calorimetry (DSC) analysis was conducted in order to gain more information about their thermal behavior. Salts *ent*-**7a** and **7b** were shown to be liquid down to −39 and −48 °C, respectively, temperatures at which they exhibited a glass transition. These solidification points (T_g) are appreciably low considering the presence of a C-2 alkyl substituent and phenyl ring, expected to favor ion–ion pairing through aromatic and H-bonding interactions. Preliminary experiments were conducted with derivative **7b** in order to assess the ability of these molten salts to act as reaction medium. Ionic liquid mediated Michael addition of dimethyl malonate to chalcone in the presence of solid K_2CO_3 was shown to proceed smoothly (1 equiv chalcone at 0.3 M in **7b**, 1.5 equiv dimethyl malonate, 6 equiv K_2CO_3, rt, 10 h) affording 74% yield of the desired condensation product, yet as an unexpected epimeric mixture.

We were also able to prepare chiral RTILs of a novel type from 2-ethyl dihydroimidazole **3a**. Following the pathway described above, counter anion metathesis was applied to the quaternized dihydroimidazolium bromide **6** prepared in 83% yield. Tetrafluoroborate **8a** and bis(trifluoromethanesulfonyl)imide **8b** were obtained (91% and 81% yields, respectively) as water immiscible liquids. A glass transition was observed in DSC at even lower temperatures (T_g = −50 and −55 °C, respectively) than for the related imidazolium species. Salts **8a** and **8b** were also found to be notably less viscous than their imidazolium congeners, although this empirical observation has not yet been quantified. This behavior may be attributed to the disruption of the aromatic imidazolium nucleus detrimental to H-bonding and π–π stacking-based ion–ion interactions.

3. Conclusion

We have accessed scalemic C-2 substituted dihydroimidazole and imidazole derivatives, available in two or three steps, respectively, from a chiral primary amine. These derivatives, otherwise potentially interesting as chiral nucleophilic bases, proved useful for the preparation of a range of novel chiral non-racemic RTILs. The capacity of the imidazolium species to act as reaction medium and/or phase transfer catalyst was also assessed. More extensive analysis of physicochemical properties as well as further development of these molten salts in asymmetric synthesis will be reported in due course.

4. Experimental

The following solvents were dried prior to use: acetonitrile (from calcium hydride, stored over 3 Å MS), and dichloromethane (freshly distilled from calcium hydride). $BaMnO_4$ was prepared according to the described procedure.[23] Thin layer chromatography reaction monitoring was carried out with Macherey–Nagel ALUGRAM® SIL G/UV_{254} (0.2 mm) plates visualized with a Dragendorff reagent as dipping solution. Neutral grade I Macherey–Nagel alumina was used, from which grade III was prepared by addition of 6% v/v of water. Bulb to bulb distillations were realized with a Büchi GKR-51 apparatus. NMR spectroscopic data were obtained with Bruker AC250 instrument operating ^{1}H spectra at 250 MHz and ^{13}C spectra at 63 MHz. Chemical shifts are quoted in parts per million (ppm) downfield from tetramethylsilane and coupling constants given in hertz. Mass spectrometry (MS) data were obtained on a NERMAG R10-10 (DCI) or a Perkin–Elmer SCIEX API365

spectrometer (ES). High resolution mass spectra (HRMS) were performed on a ThermoFinnigan MAT 95 XL spectrometer. Optical rotations were measured on a Perkin–Elmer model 141 polarimeter. Differential scanning calorimetry (DSC) analysis were conducted on a Perkin–Elmer DSC 7 apparatus.

4.1. *N*-[(1*R*)-Phenylethyl]ethane-1,2-diamine, 2

Chlorethylamine hydrochloride (5.0 g, 43.1 mmol) was dissolved in water (8 mL) and the solution (pH 3–4) was alkalized (pH 8) by the addition of a few drops of a saturated aqueous K_2CO_3 solution. The resulting free amine solution was added dropwise over 3 h to neat (*R*)-α-methylbenzylamine (11.0 mL, 85.8 mmol, 2 equiv) heated at 100 °C with stirring. The heating with stirring was maintained for three additional hours after the end of addition. The reaction mixture was then allowed to cool to rt before being poured into a vigorously stirred mixture of 25% aqueous KOH (8 mL) and dichloromethane (50 mL). The aqueous layer (pH 8) was alkalized (pH 10) by the addition of KOH pellets, and the organic layer separated by decantation. The aqueous layer was further extracted with dichloromethane (3×100 mL) and the combined organic layers dried over anhydrous Na_2SO_4, filtered, and concentrated to dryness to give a residue that was chromatographed over neutral grade III Al_2O_3. Elution with CH_2Cl_2 allowed recovery of the unreacted starting chiral amine (5.0 g, 41.0 mmol) while the use of increasing amount of MeOH in CH_2Cl_2 (5%, 10%, 15%, and 20%) yielded the expected 1,2-ethanediamine **2** 3.2 g (19.5 mmol, 45% yield) as a colorless liquid. Compound **2** could also be purified by bulb to bulb distillation (heating at 80–90 °C under 0.05 mbar) for analysis. R_f 0.3 (EthOAc–MeOH, 95:5/NH_3 atmosphere). $[\alpha]_D^{20} = +51$ (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.36–7.28 (m, 4H, Ph), 7.28–7.19 (m, 1H, Ph), 3.76 (q, 1H, $J = 6.7$ Hz), 2.80–2.71 (m, 2H), 2.63–2.40 (m, 2H) 1.43 (br s, 3H), 1.36 (d, 3H, $J = 6.7$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 146.5 (Cquat., Ph), 128.9, 127.4, 127.1 (CH, Ph), 58.8 (CH), 51.0, 42.6 (CH_2), 25.1 (CH_3). MS (DCI/NH_3) *m*/*z* 165 ($M+H^+$). HRMS (CI) *m*/*z* calcd for $C_{10}H_{17}N_2$: 165.1392, found: 165.1391.

4.2. *N*-[(1*S*)-Phenylethyl]ethane-1,2-diamine, *ent*-2

Prepared from (*S*)-α-methylbenzylamine in the same way as **2**. $[\alpha]_D^{20} = -51$ (*c* 1.3, $CHCl_3$). HRMS (CI) *m*/*z* calcd for $C_{10}H_{17}N_2$: 165.1392, found: 165.1396.

4.3. 2-Ethyl-1-[(1*R*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazole, 3a

A mixture of diamine **2** (2.0 g, 12.2 mmol), ethyl orthopropionate (2.6 mL, 12.9 mmol, 1.06 equiv) and acetic acid (0.74 mL, 12.9 mmol, 1.06 equiv) in CH_3CN (12 mL) was refluxed for 1 h under inert atmosphere. The resulting mixture was then allowed to cool to rt before being concentrated to dryness, taken up in 40% aqueous KOH (6 mL) and extracted with dichloromethane (3×40 mL). The combined organic layers were then dried with KOH pellets, filtrated, and concentrated to dryness. Bulb to bulb distillation of the residue (heating at 120–130 °C at 0.05 mbar) gave the expected dihydroimidazole **3a** (2.3 g, 11.4 mmol, 93% yield) as a colorless liquid. R_f 0.3 (EthOAc–MeOH, 95:5/NH_3 atmosphere). $[\alpha]_D^{20} = -56$ (*c* 1.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.38–7.21 (m, 5H, Ph), 4.81 (q, 1H, $J = 7.0$ Hz), 3.75–3.58 (m, 2H), 3.40–3.26 (m, 1H), 3.17–3.03 (m, 1H), 2.28 (q, 2H, $J = 7.3$ Hz), 1.53 (d, 3H, $J = 7.0$ Hz), 1.22 (t, 3H, $J = 7.3$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 168.0 (Cquat. Imid.) 142.3 (Cquat. Ph), 129.2, 127.7, 127.1 (CH, Ph), 53.3 (Ch_2Imid.), 52.7 (CH), 44.9 (CH_2Imid.), 21.9 (CH_2CH_3), 18.5 (CH_3), 11.49 (CH_2CH_3). MS (DCI/NH_3) *m*/*z* 203 ($M+H^+$). HRMS (EI) *m*/*z* calcd for $C_{13}H_{18}N_2$: 202.1470, found: 202.1473.

4.4. 2-Ethyl-1-[(1*S*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazole, *ent*-3a

Prepared from diamine *ent*-**2** in the same way as **3a**. $[\alpha]_D^{20} = +55$ (*c* 1.3, $CHCl_3$). HRMS (EI) *m*/*z* calcd for $C_{13}H_{18}N_2$: 202.1470, found: 202.1471.

4.5. 2-Methyl-1-[(1*S*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazole, *ent*-3b

Diamine *ent*-**2** (1.0 g, 6.10 mmol) was reacted with ethyl orthoacetate according to the procedure described for the preparation of **3a** to give dihydroimidazole *ent*-**3b** (0.93 g, 4.95 mmol, 81% yield) as a colorless liquid. $[\alpha]_D^{20} = +67$ (*c* 1.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.40–7.20 (m, 5H, Ph), 4.78 (q, 1H, $J = 7.0$ Hz), 3.71–3.58 (m, 2H), 3.39–3.26 (m, 1H), 3.15–3.02 (m, 1H), 2.00 (s, 3H), 1.53 (d, 3H, $J = 7.0$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 163.7 (Cquat. Imid.), 142.1 (Cquat. Ph), 129.0, 127.6, 126.9 (CH Ph), 53.3 (CH), 52.2, 44.7 (CH_2 Imid.), 18.5, 15.2 (CH_3). MS (DCI/NH_3) *m*/*z* 189 ($M+H^+$). HRMS (EI) *m*/*z* calcd for $C_{12}H_{16}N_2$: 188.1313, found: 188.1318.

4.6. 1-[(1*S*)-1-Phenylethyl]-4,5-dihydro-1*H*-imidazole, *ent*-3c

Diamine *ent*-**2** (1.0 g, 6.10 mmol) was reacted with triethyl orthoformate according to the procedure described for the preparation of **3a** to give dihydroimidazole *ent*-**3c** (0.85 g, 4.90 mmol, 80% yield) as a colorless liquid. $[\alpha]_D^{20} = -27$ (*c* 1.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.40–7.22 (m, 5H, Ph), 7.00 (s, 1H), 4.33 (q, 1H, $J = 7.0$ Hz), 3.77 (dt, 2H, $J = 9.8$ Hz and 1.5 Hz), 3.10 (t, 2H, $J = 9.8$ Hz), 1.57 (d, 3H, $J = 7.00$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 155.9 (CH Imid.), 142.6 (Cquat. Ph), 129.2, 128.0, 127.1 (CH, Ph), 57.00 (CH), 55.0, 47.1 (CH_2 Imid.), 21.4 (CH_3). MS (DCI/NH_3) *m*/*z* 175 ($M+H^+$). HRMS (EI) *m*/*z* calcd for $C_{11}H_{14}N_2$: 174.1157, found: 174.1157.

4.7. 2-Ethyl-1-[(1*R*)-1-phenylethyl]-1*H*-imidazole, 4a

A mixture of dihydroimidazole **3a** (200 mg, 0.99 mmol), 4 Å molecular sieves (200 mg) and $BaMnO_4$ (2.0 g, 7.80 mmol, 1000 wt%) was refluxed for 20 h under an inert atmosphere. The reaction mixture was then filtered over Celite and the cake rinsed with dichloromethane.

The filtrate was concentrated to dryness to give imidazole **4a** (115 mg, 0.58 mmol, 58% yield) as a colorless liquid that solidified upon standing. Compound **4a** could also be purified by chromatography over neutral grade III Al_2O_3 eluted with dichloromethane for analysis. R_f 0.4 (CH_2Cl_2–EthOAc, 80:20/NH_3 atmosphere). $[\alpha]_D^{20} = +18$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.35–7.20 (m, 3H, Ph), 7.08–6.95 (4H, Ph and Imid.), 5.31 (q, 1H, $J = 7.0$ Hz), 2.70–2.41 (m, 2H), 1.78 (d, 3H, $J = 7.0$ Hz), 1.23 (t, 3H, $J = 7.5$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 149.9 (Cquat. Imid.), 142.6 (Cquat. Ph), 129.4, 128.2 (CH, Ph), 127.8 (CH Imid.), 126.2 (CH, Ph), 116.9 (CH, Imid.), 55.0 (CH), 23.1 (CH_3), 21.0 (CH_2CH_3), 12.5 (CH_2CH_3). MS (DCI/NH_3) *m/z* 201 ($M+H^+$). HRMS (EI) *m/z* calcd for $C_{13}H_{16}N_2$: 200.1313, found: 200.1314.

4.8. 2-Ethyl-1-[(1*S*)-1-phenylethyl]-1*H*-imidazole, *ent*-4a

Prepared from dihydroimidazole *ent*-**3a** in the same way as **4a**. $[\alpha]_D^{20} = -19$ (*c* 1.0, $CHCl_3$). HRMS (EI) *m/z* calcd for $C_{13}H_{16}N_2$: 200.1313, found: 200.1316.

4.9. 2-Methyl-1-[(1*S*)-1-phenylethyl]-1*H*-imidazole, *ent*-4b

A biphasic mixture of dihydroimidazole *ent*-**3b** (214 mg, 1.14 mmol) in benzene (6 mL) and $KMnO_4$ (270 mg, 1.71 mmol, 1.5 equiv) in water (12 mL) containing benzyltriethylammonium bromide (13 mg, 0.06 mmol, 0.05 equiv) was vigorously stirred at rt for 1 h. A saturated aqueous solution of $Na_2S_2O_3$ (3 mL) was then added and the reaction mixture diluted with dichloromethane before being filtered over Celite. The cake was rinsed with dichloromethane and water. The organic layer was separated, washed with water and brine, dried over Na_2SO_4, filtered, and concentrated to dryness to afford imidazole *ent*-**4b** (130 mg, 0.70 mmol, 61% yield) as a colorless liquid that solidified upon standing. Compound *ent*-**4b** could also be purified by chromatography over neutral grade III Al_2O_3 eluted with dichloromethane for analysis. R_f 0.6 (CH_2Cl_2–EthOAc, 80:20/NH_3 atmosphere). $[\alpha]_D^{20} = -14$ (*c* 1.4, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.40–7.22 (m, 3H, Ph), 7.11–6.95 (m, 4H, Ph and Imid.), 5.30 (q, 1H, $J = 7.0$ Hz), 2.27 (s, 3H), 1.80 (d, 3H, $J = 7.0$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 145.3 (Cquat. Imid.), 142.4 (Cquat. Ph), 129.5, 128.3 (CH Ph), 127.7 (CH Imid.), 126.3 (CH Ph), 117.1 (CH Imid.), 55.5 (CH), 22.9, 14.1 (CH_3). MS (DCI/NH_3) *m/z* 187 ($M+H^+$). HRMS (EI) *m/z* calcd for $C_{12}H_{14}N_2$: 186.1157, found: 186.1156. Anal. Calcd for $C_{12}H_{14}N_2 \cdot HCl + 1/4\ H_2O$: C, 63.43; H, 6.87; N, 12.33. Found: C, 63.51; H, 6.73; N, 12.55.

4.10. 1-[(1*S*)-1-Phenylethyl]-1*H*-imidazole, *ent*-4c

Dihydroimidazole *ent*-**3c** (213 mg, 1.24 mmol), was reacted with $BaMnO_4$ according to the procedure used for the preparation of **4a** to afford *ent*-**4c** (126 mg, 0.73 mmol, 59% yield) as a yellow liquid. R_f 0.6 (CH_2Cl_2–EthOAc, 80:20/NH_3 atmosphere). $[\alpha]_D^{20} = -5$ (*c* 1.9, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.60 (s, 1H, Imid.), 7.39–7.25 (m, 3H, Ph), 7.17–7.11 (m, 2H, Ph), 7.08 (s, 1H, Imid.), 6.93 (s, 1H, Imid.), 5.35 (q, 1H, $J = 7.0$ Hz), 1.86 (d, 3H, $J = 7.0$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 142.2 (Cquat. Ph), 136.7, 130.0 (CH, Imid.), 129.5, 128.7, 126.6 (CH, Ph), 118.6 (CH, Imid.), 57.2 (CH), 22.7 (CH_3). MS (DCI/NH_3) *m/z* 173 ($M+H^+$). HRLSIMS (FAB +) *m/z* calcd for $C_{11}H_{12}N_2$: 172.1000, found: 172.1003.

4.11. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-1*H*-imidazolium bromide, 5

A solution of imidazole **4a** (225 mg, 1.10 mmol) and bromopentane (0.90 mL, 7.30 mmol, 6.6 equiv) in 1,1,1-trichloroethane (3.5 mL) was refluxed for 3 days. The insoluble oily material was separated by decantation and washed several times with 1,1,1-trichloroethane to give **5** (360 mg, 1.00 mmol, 91% yield) as light brown foam. $[\alpha]_D^{20} = +17$ (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.8 (d, 1H, $J = 2.1$ Hz, Imid.), 7.56 (d, 1H, $J = 2.1$ Hz, Imid.), 7.41–7.22 (m, 5H, Ph), 6.00 (q, 1H, $J = 7.0$ Hz), 4.31–4.11 (m, 2H), 3.45–3.26 (m, 1H), 3.15–2.98 (m, 1H), 1.94 (d, 3H, $J = 7.0$ Hz), 1.91–1.79 (m, 2H), 1.42–1.28 (m, 4H), 0.97 (t, 3H, $J = 7.6$ Hz), 0.92–0.83 (m, 3H). ^{13}C NMR (CD_3OD) δ (ppm): 149.0 (Cquat. Imid.), 140.9 (Cquat. Ph), 130.4, 129.9, 127.3 (CH, Ph), 122.8, 120.4 (CH, Imid.), 59.0 (CH), 49.0, 30.8, 29.5, 23.2 (CH_2), 22.0 (CH_3), 17.9 (CH_2), 14.2, 11.8 (CH_3). MS (DCI/NH_3) *m/z* 271 (M^+). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{27}N_2$: 271.2174, found: 271.2172.

4.12. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-1*H*-imidazolium bromide, *ent*-5

Prepared from imidazole, *ent*-**4a** in the same way as **5**. $[\alpha]_D^{20} = -17$ (*c* 1.1, $CHCl_3$).

4.13. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazolium bromide, 6

4,5-Dihydroimidazole **3a** (306 mg, 1.51 mmol) was reacted with bromopentane according to the procedure described for the preparation of **5** to give salt **6** (440 mg, 1.25 mmol, 83% yield) as a light brown foam. $[\alpha]_D^{20} = -16$ (*c* 1.4, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.37–7.19 (m, 5H, Ph), 5.15 (q, 1H, $J = 7.0$ Hz), 4.12–4.03 (m, 2H), 3.93–3.79 (m, 1H), 3.58–3.49 (m, 1H), 3.48–3.39 (m, 2H), 2.89–2.61 (m, 2H), 1.76 (d, 3H, $J = 7.0$ Hz), 1.63–1.49 (m, 2H), 1.30–1.18 (m, 4H), 1.16–1.10 (m, 3H), 0.79 (t, 3H, $J = 6.7$ Hz). ^{13}C NMR ($CDCl_3$) δ (ppm): 168.9 (Cquat. Imid.), 137.9 (Cquat. Ph), 129.5, 128.9, 127.1 (CH, Ph), 55.4 (CH), 47.9, 47.7 (CH_2, Imid.), 44.2, 28.9, 27.32, 22.5, 18.9 (CH_2), 18.8, 14.2, 11.2 (CH_3). MS (ES +) *m/z* 273 (M^+). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{29}N_2$: 273.2331, found: 273.2332.

4.14. 2-Ethyl-3-pentyl-1-[(1*S*)-1-phenylethyl]-1*H*-imidazolium tetrafluoroborate, *ent*-7a

A solution of imidazolium bromide *ent*-**5** (210 mg, 0.60 mmol) in acetone (0.5 mL) containing ammonium tetrafluoroborate (63 mg, 0.60 mmol, 1 equiv) was

allowed to stir at rt for 4 days. The reaction mixture was then filtered over Celite and concentrated to dryness. The residue was solubilized in dichloromethane and filtered again over Celite. The filtrate was concentrated to dryness to give *ent*-**7a** (200 mg, 0.56 mmol, 93% yield) as a reddish liquid. $[\alpha]_D^{20} = -25$ (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.45–7.33 (m, 5H, Ph), 7.22 (d, 1H, $J = 1.5$ Hz, Imid.), 7.20 (br s, 1H, Imid.), 5.68 (q, 1H, $J = 7.0$ Hz), 4.08 (t, 2H, $J = 7.6$ Hz), 3.19–2.89 (m, 2H), 1.92 (d, 3H, $J = 7.0$ Hz), 1.89–1.79 (m, 2H), 1.42–1.28 (m, 4H), 0.99 (t, 3H, $J = 7.6$ Hz), 0.94–0.86 (m, 3H). ^{13}C NMR ($CDCl_3$) δ (ppm): 148.0 (Cquat. Imid.), 139.6 (Cquat. Ph), 130.1, 129.5, 126.7 (CH, Ph), 122.3, 119.7 (CH, Imid.), 58.6 (CH), 48.9, 30.3, 28.9, 22.7 (CH_2), 22.4 (CH_3), 17.7 (CH_2), 14.4, 12.1 (CH_3). MS (ES +) *m/z* 271 (M^+). MS (ES −) *m/z* 87 (BF_4^-). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{27}N_2$: 271.2174, found: 271.2175.

4.15. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-1*H*-imidazolium bis(trifluoromethanesulfonyl)imide, 7b

A solution of dihydroimidazolium bromide **5** (240 mg, 0.68 mmol) in water (2 mL) containing lithium bis(trifluoromethanesulfonyl)imide (195 mg, 0.68 mmol, 1 equiv) was heated with stirring at 70 °C for 1 h and allowed to stand at rt overnight. The insoluble oily material was separated by decantation. It was then dissolved in dichloromethane, washed with water and brine, dried over Na_2SO_4, filtered, and concentrated to dryness. Salt **7b** (288 mg, 0.52 mmol, 76% yield) was obtained as a pale yellow liquid. $[\alpha]_D^{20} = +17$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.45–7.33 (m, 5H, Ph), 7.22 (d, 1H, $J = 2.1$ Hz, Imid.), 7.17 (br s, 1H, Imid.), 5.65 (q, 1H, $J = 7.0$ Hz), 4.12–4.02 (m, 2H), 3.15–2.87 (m, 2H), 1.93 (d, 3H, $J = 7.0$ Hz), 1.91–1.80 (m, 2H), 1.42–1.31 (m, 4H), 0.98 (t, 3H, $J = 7.6$ Hz), 0.94–0.89 (m, 3H). ^{13}C NMR ($CDCl_3$) δ (ppm): 147.9 (Cquat. Imid.), 139.4 (Cquat. Ph), 130.2, 129.7, 126.6 (CH, Ph), 122.1 (CH, Imid.), 120.5 (q, $J = 5.1$ Hz, $2 \times CF_3$), 119.7 (CH, Imid.), 58.8 (CH), 48.9, 30.2, 28.9, 22.6 (CH_2), 22.3 (CH_3), 17.8 (CH_2), 14.3, 11.9 (CH_3). MS (ES +) *m/z* 271 (M^+). MS (ES −) *m/z* 280 (Tf_2N^-). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{27}N_2$: 271.2174, found: 271.2179.

4.16. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazolium tetrafluoroborate, 8a

4,5-Dihydroimidazolium bromide **6** (154 mg, 0.44 mmol) was reacted with ammonium tetrafluoroborate according to the procedure described for the preparation of imidazolium tetrafluoroborate *ent*-**7a** to give salt **8a** (146 mg, 0.40 mmol, 91% yield) as a pale yellow liquid. $[\alpha]_D^{20} = -10$ (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.48–7.24 (m, 5H, Ph), 5.14 (q, 1H, $J = 7.0$ Hz), 4.11–3.93 (m, 2H), 3.92–3.73 (m, 1H), 3.62–3.50 (m, 1H), 3.45 (t, 2H, $J = 7.6$ Hz), 2.79–2.64 (m, 2H), 1.73 (d, 3H, $J = 7.0$ Hz), 1.71–1.56 (m, 2H), 1.42–1.26 (m, 4H), 1.24–1.17 (m, 3H), 0.93–0.88 (m, 3H). ^{13}C NMR ($CDCl_3$) δ (ppm): 169.1 (Cquat. Imid.), 138.4 (Cquat. Ph), 129.9, 129.2, 127.3 (CH, Ph), 55.6 (CH), 47.6 ($2 \times CH_2$, Imid.), 43.9, 29.2, 27.4, 22.8 (CH_2), 18.4 (CH_3), 18.3 (CH_2), 14.5, 10.9 (CH_3). MS (ES +) *m/z* 273 (M^+). MS (ES −) *m/z* 87 (BF_4^-). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{29}N_2$: 273.2331, found: 273.2331.

4.17. 2-Ethyl-3-pentyl-1-[(1*R*)-1-phenylethyl]-4,5-dihydro-1*H*-imidazolium bis(trifluoromethanesulfonyl)-imide, 8b

4,5-Dihydroimidazolium bromide **6** (149 mg, 0.42 mmol) was reacted with lithium bis(trifluoromethanesulfonyl)imide according to the procedure described for the preparation of imidazolium bis(trifluoromethanesulfonyl)imide **7b** to give **8b** (190 mg, 0.34 mmol, 81% yield) as a pale yellow liquid. $[\alpha]_D^{20} = -7$ (*c* 1.1, $CHCl_3$). ^1H NMR ($CDCl_3$) δ (ppm): 7.47–7.35 (m, 3H, Ph), 7.30–7.22 (m, 2H, Ph), 5.10 (q, 1H, $J = 7.0$ Hz), 4.06–3.87 (m, 2H), 3.85–3.73 (m, 1H), 3.62–3.51 (m, 1H), 3.42 (t, 2H, $J = 7.6$ Hz), 2.75–2.61 (m, 2H), 1.72 (d, 3H, $J = 7.0$ Hz), 1.69–1.59 (m, 2H), 1.42–1.26 (m, 4H), 1.23–1.17 (m, 3H), 0.94–0.88 (m, 3H). ^{13}C NMR ($CDCl_3$) δ (ppm): 169.0 (Cquat. Imid.), 138.0 (Cquat. Ph), 130.0, 129.4, 127.2 (CH, Ph), 120.5 (q, $J = 5.1$ Hz, $2 \times CF_3$), 55.9 (CH), 47.7, 47.6 (CH_2, Imid.), 43.9, 29.2, 27.5, 22.7, 18.5 (CH_2), 18.5, 14.4, 10.8 (CH_3). MS (ES +) *m/z* 273 (M^+). MS (ES −) *m/z* 280 (Tf_2N^-). HRLSIMS (FAB +) *m/z* calcd for $C_{18}H_{29}N_2$: 273.2331, found: 273.2334.

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