Synthesis and Characterization of Chiral Imidazolium Salts

Mayra Y. Machado, Romano Dorta*
Departamento de Química, Universidad Simón Bolívar, Caracas, Venezuela
Fax +58(212)9063961; E-mail: rdorta@usb.ve
Received 27 January 2005; revised 12 March 2005

Abstract: Chiral imidazolium salts that can be classified as ionic liquids (ILs) were derived from the ‘chiral pool’ precursors camphor, β-pinene, and tartaric acid. ILs containing chiral imidazolium cations as well as chiral anions were synthesized. Furthermore, the anion of the IL 1-methyl-3-[(S)-2'-methylbutyl]imidazolium tosylate was substituted on an ion-exchange resin for the chiral (S)-camphorsulfonate anion thus forming the first well-characterized ‘doubly chiral’ IL.

Keywords: imidazolium salts, ionic liquids, chiral anions, chiral cations

Imidazolium salts have found major interest as a new class of solvents (ionic liquids, ILs) in synthesis and catalysis1 and as precursors of N-heterocyclic carbene (NHC) ligands.2 Chiral ILs (CILs)3 in general are still rare despite their potential as chiral solvents in synthesis, catalysis, and resolution, while chiral NHCs are a natural extension of this hugely successful class of ligands.4 Thus, the synthesis of chiral imidazolium salts is of twofold interest: On the one hand they form potentially useful chiral solvent systems5 and, on the other hand, they are the conjugate acids of chiral NHC ligands.

Three types of chiral salts may be conceived: (1) salts with chiral cations, (2) salts with chiral anions, and (3) salts with both, chiral anions and cations. Surprisingly, almost all reports on CILs are based on chiral cations, although the use of chiral anion based CILs6 in synthesis, catalysis, and resolution could be at least as promising. We report here the synthesis and characterization of examples of imidazolium salts of each of the three classes based on inexpensive ‘chiral pool’ derivatives (camphor, β-pinene, tartaric acid). Furthermore, we disclose the first example of a ‘doubly chiral’ IL, which contains both, a chiral cation and a chiral anion.

Since the imidazolium–myrtil motif was shown to be effective in chiral recognition experiments7 we believed that a corresponding IL would be a worthwhile synthetic target. Tosylate 1 [derived from commercially available (1S,2S,5S)-(−)-myrtanol, which in turn is accessed from readily available β-pinene] reacted in neat methylimidazole at 100 °C over 24 hours to form the imidazolium tosylate salt 2 (see Equation 1). In the 1H NMR spectrum a characteristic singlet of the proton between the two N atoms appeared at 9.81 ppm. The crude product mixture usually shows small amounts of methylimidazolium contamination,8 which was removed by washing and extracting the product in a CH3Cl–H2O mixture. Typical yields of purified product ranged from 60–80%.

The second example of a chiral imidazolium salt is based on the tartrate backbone. Commercially available tosyl tartrate 3 cleanly reacted with methylimidazol at 70 °C over 20 hours to afford the tartrate-based imidazolium tosylate 4 in acceptable yields (Equation 2). We note that 4 is one of the rare examples of a dicationic9 chiral imidazolium10 salt. A similar tartrate-based benzimidazolium derivative has recently been published and used as NHC ligand.10* However, no synthetic nor analytic details of the imidazolium synthesis were given.

SYNTHESIS 2005, No. 15, pp 2473–2475
Advanced online publication: 25.07.2005
DOI: 10.1055/s-2005-872102; Art ID: M00705SS
© Georg Thieme Verlag Stuttgart · New York
low-viscosity room temperature IL (RTIL) in good yields. The resulting salt was also readily exchanged for another chiral anion such as (S)-camphorsulfonate on a strong anion exchanger according to Equation 3. We found it beneficial to treat the resin (Dowex 1X2) in its Cl⁻ form first with an excess of NaOH (2 M) in order to remove the Cl⁻ ions completely followed, after washing, by an equimolar amount of (S)-camphorsulfonic acid (0.1 M). Generally, it seems that the use of ion-exchange resins for the synthesis of ILs has the advantage to reduce the problem of chloride or other unwanted anion contamination. The resulting salt 8 is a viscous pale yellow hygroscopic syrup at room temperature and to the best of our knowledge it represents the first example of a ‘doubly chiral’ RTIL.

Equation 3

To summarize, chiral imidazolium salts of the three classes defined above were synthesized and characterized that may be classified as CILs. For the first time a ‘doubly chiral’ RTIL is disclosed. Since the CILs presented here are all readily accessible on gram scales their use as solvents is assured. Currently, these chiral imidazolium salts are all readily accessible on gram scales their use as solvents is assured.

Figure 1

Myrylotosylate 1 was synthesized according to a standard protocol. Reactions were carried out using standard Schlenk techniques unless otherwise stated. Elemental analyses were not performed under anhydrous conditions and values are corrected for water content. Optical rotations were measured on an Atago Polax-2L polarimeter. H and 13C NMR spectra were recorded on Bruker DPX300, Bruker DPX500 or Jeol Eclipse 400 (13C NMR spectra only) spectrometers.

[Myrtylimidazolium][Tosylate] (2)
Methylidazole (2.0 mL, 25 mmol) was added dropwise to 1 (1.00 g, 3.2 mmol) under a N2 atmosphere. The Schlenk tube was sealed and the reaction mixture was heated to 100 °C under stirring for 24 h affording a clear solution. Excess methylidazole was removed under vacuum followed by washing the mixture with Et2O (2 × 5 mL). High vacuum drying yielded a white solid, which was redissolved in CH2Cl2 (10 mL) and washed with H2O (2 × 10 mL). Evaporation of the volatiles afforded a white microcrystalline hygroscopic solid (780 mg, 63%); mp 102 °C.

1H NMR (300 MHz, CDCl3): δ = 0.87 (d, J = 9.9 Hz, 1 H), 0.74 (d, J = 1.6 Hz, 3 H), 1.15 (s, 3 H), 1.17 (s, 3 H), 1.35–1.55 (m, 1 H), 1.65–2.20 (m, 5 H), 2.25–2.40 (m, 1 H), 2.34 (s, 3 H), 2.40–2.55 (m, 1 H), 3.98 (s, 3 H), 4.00–4.25 (m, 2 H), 7.14 (d, J = 8 Hz, 2 H), 7.21 (s, 1 H), 7.45 (s, 1 H), 7.77 (d, J = 8 Hz, 2 H), 9.81 (s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 19.11, 21.28, 25.35, 25.55, 27.74, 32.79, 36.58, 38.59, 40.98, 41.47, 55.32, 76.80, 77.11, 77.43, 121.94, 123.40, 125.95, 126.69, 138.29, 139.34, 143.78.


[(4R,5S)-2,2-Dimethyl-1,3-dioxolane-4,5-bis(1′-methylene-3′-methyldimidazolium)][Tosylate]] (4)
(R/R)-2,2-Dimethyl-4,5-bis[(tosyl)methyl]-1,3-dioxolane (2.30 g, 4.90 mmol) was dissolved in 1-methyldimidazolium (1.64 mL, 20.6 mmol) and stirred at 70 °C for 20 h forming a slightly turbid brownish solution. Addition of anhyd Et2O (20 mL) caused the precipitation of an off-white solid. The mother liquors were decanted off and the solid was washed and slurried with two more Et2O portions. Drying in vacuo overnight yielded an off-white hygroscopic powder (1.9 g, 61%); mp 59–61 °C; [α]D +25 –21° (c = 2.07, CH3OH).

1H NMR (500 MHz, CDCl3): δ = 1.20 (s, 6 H), 2.25 (s, 6 H), 3.77 (s, 6 H), 4.09 (m, 2 H), 4.45 (m, 2 H), 4.80 (m, 2 H), 7.06 (d, J = 8 Hz, 4 H), 7.32 (m, 2 H), 7.51 (m, 2 H), 7.66 (d, J = 8 Hz, 4 H), 9.46 (s, 2 H).

13C NMR (100 MHz, CDCl3): δ = 21.30, 26.88, 36.37, 50.18, 76.82, 111.28, 123.32, 123.64, 125.82, 128.83, 138.08, 139.57, 143.66.


[1,3-Butylmethylimidazolium][(S)-Camphorsulfonate] (5)
Water (15 mL) was added to a mixture of 1,3-buty1methylimidazolium chloride (6.69 g, 33.3 mmol) and potassium (S)-camphorsulfonate (8.90 g, 33.3 mmol) affording a yellowish solution that was stirred for 3 h. Then the volatiles were removed in vacuo. The resulting white solid was treated with CH2Cl2 (25 mL) and the mixture was centrifuged for 1 h at 4000 rpm. The supernatant CH2Cl2 solution was decanted off, dried over activated MS 4 Å, pumped down and dried in vacuo overnight to afford a viscous yellowish oil (10.5 g, 85%); d = 1.15 g/cm³; [α]D20 20° (c = 1.634, CH3OH).

1H NMR (300 MHz, DMSO-d6): δ = 0.74 (s, 3 H), 0.90 (m, 3 H), 1.05 (s, 3 H), 1.20–1.35 (m, 4 H), 1.70–1.95 (m, 5 H), 2.15–2.30 (m, 1 H), 2.37 (d, J = 15 Hz, 1 H), 2.65–2.75 (m, 1 H), 2.86 (d, J = 15 Hz, 1 H), 3.85 (s, 3 H), 4.10–4.20 (m, 2 H), 7.71 (m, 1 H), 7.78 (m, 1 H), 9.16 (m, 1 H).
\[1\text{H NMR (300 MHz, CDCl}_3\text{)}: \delta = 0.70-0.75 (m, 3 H), 0.95-1.10 (m, 2 H), 1.35-1.50 (m, 2 H), 3.50 (s, 3 H), 3.60-3.70 (m, 2 H), 6.96 (s, 1 H), 6.87 (s, 1 H). \]
\[7.15-7.25 (m, 2 H), 7.30-7.40 (m, 4 H), 7.50-7.60 (m, 2 H), 7.75-7.90 (m, 4 H), 9.72 (s, 1 H). \]

13C NMR (100 MHz, CDCl3): \delta = 10.7, 15.9, 21.0, 26.0, 35.3, 36.0, 55.1, 122.5, 123.7, 125.6, 128.3, 130.1, 130.8, 132.3, 137.0, 149.7, 149.8.

\[1\text{3C NMR (100 MHz, CH}_2\text{Cl}_2-\text{CDCl}_3\text{): } \delta = 13.1, 19.1, 31.5, 35.8, 40.9, 121.1, 122.2, 123.0, 124.7, 126.0, 126.6, 128.3, 130.1, 130.8, 132.3, 137.0, 149.7, 149.8. \]

\[1\text{3P NMR (121.50 MHz, CDCl}_3\text{): } \delta = 7.71 (s). \]

Analysis: C, 64.36; H, 5.36; N, 5.98.


Acknowledgment

We thank Fonacit (Project S1-2001000851) for financial support and Ms Indira Vera (USB, BID-Fonacit project QF13) for NMR assistance.

References


(7) Probably, methylimidazolium formation is due to Hoffmann type elimination. NMR spectroscopy of crude reaction mixtures indicated concomitant alkene formation.


(12) The interchange of anions of similar size, such as OTf$, sulfonates, or BF4$ in the usual CH2Cl2–H2O system is not possible.

(13) We found that the classical ILs BMI-BF4$ or BMI-PIF4$ are obtained in a purer form by the ion-exchange method than by the standard CH2Cl2–H2O extraction method.

