Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 4429–4431

Tetrahedron Letters

New chiral imidazolium ionic liquids: 3D-network of hydrogen bonding

Jonathan J. Jodry and Koichi Mikami*

Department of Applied Chemistry, Tokyo Institute of Technology, Meguro-ku, Tokyo 152-8552, Japan

Received 5 March 2004; revised 10 April 2004; accepted 14 April 2004

Abstract—New hydrophobic chiral ionic liquids bearing an imidazolium core have been stereospecifically prepared from the chiral pool; their enantiomeric purity and 3D-network of hydrogen bonding were analysed by NMR and X-ray diffraction, respectively.

In the last years, intensive research has transformed ionic liquids from the curiosity they used to be to a new type of medium with interesting properties: they cannot evaporate nor inflame, can be used at a large range of temperature, easily recycled and reused, making them solvents of choice for *green chemistry*; Furthermore, they can enhance the rate and increase the selectivity of a number of valuable reactions.[1] The possibility to use chiral ionic liquids (CILs) as inducers for asymmetric reactions has recently prompted researchers to synthesise such chiral solvents, in particular. Seddon prepared the chiral lactate salt of 1-butyl-3-methylimidazolium (bmim) **1** (Fig. 1), and investigated asymmetric Diels–Alder reactions therein (however <5% ee were obtained).[2] Wasserscheid synthesised CIL **2** as chiral shift reagent in ^{19}F NMR, on kilogram scale from (*R*)-2-amino-butan-1-ol.[3] Imidazolium salts with planar chirality (**3**, resolved by NMR)[4] and chiral lateral chains (**4**),[5] as well as thiazolinium salt **5**,[6] were also prepared. Herein, we wish to report the straightforward synthesis of new chiral ionic liquids bearing an imidazolium core, an easy and efficient procedure to determine their enantiomeric purity and the 3D-network of hydrogen bonding obtained in the solid state.

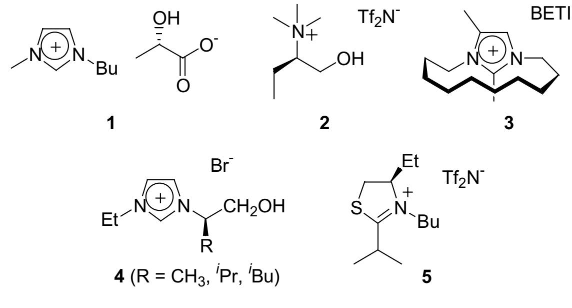


Figure 1. Examples of chiral ionic liquids.

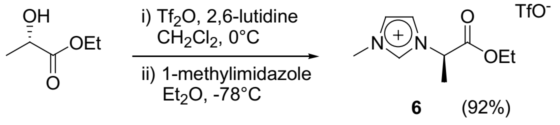
Imidazolium-based cations usually lead to ionic liquids with favourable properties, namely low melting point and viscosity, which explain that they represent the biggest class of ionic liquids. We therefore were interested in the introduction of chirality on such derivatives. The following properties were also targeted: (i) straightforward and easy preparation, applicable on larger scale; (ii) presence of functional groups that could lead to favourable interactions with substrates. Previously synthesised CILs have shown to form diastereomeric interactions with a chiral shift reagent in NMR; however, either the magnitude of the splitting of the signals is small, preventing a precise measurement of the enantiopurity,[4] or affording only a qualitative result.[3,7] Therefore, there is a need for a new procedure allowing the direct measurement of the enantiomeric purity by NMR.

Commercially available and inexpensive (*S*)-ethyl lactate was transformed onto its triflate derivative, which upon reaction with 1-methylimidazole afforded the triflate salt **6** as a solid (melting point 73 °C), in excellent yield (Scheme 1). The enantiomeric purity of this salt can easily be measured by using Lacour's TRISPHAT

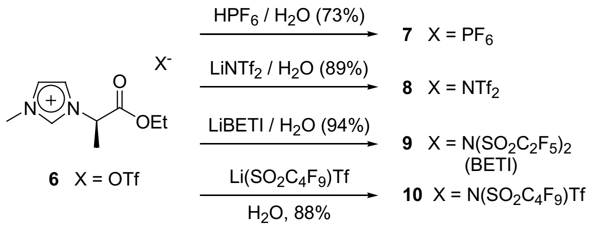
Keywords: Ionic liquids; Chirality; Green chemistry.

* Corresponding author. Tel.: +81-3-5734-2142; fax: +81-3-5734-2776; e-mail: kmikami@o.cc.titech.ac.jp

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2004.04.063



Scheme 1. Preparation of ester-imidazolium salt.



Scheme 2. Anion metathesis.

Table 1. Melting points and glass transition temperatures of CIL **6**–**10** (°C, DSC)

CIL	Anion	Melting point	Glass transition[a]
6	OTf	73	−50
7[b]	PF_6	—	−58
8	NTf_2	45[c]	−57
9	$N(SO_2C_2F_5)_2$	—	−56
10	$N(SO_2C_4F_9)Tf$	—	−54

[a] Measured by heating samples cooled at −120 °C.

[b] Viscous oil.

[c] From solid obtained by slow recrystallisation; once melted, this CIL only displayed a glass transition at −57 °C during repetitive cooling/warming cycles.

anion[7] as NMR chiral shift reagent.[8] Addition of this salt to a $CDCl_3$ solution of the racemic triflate salt **6** (obtained from (*rac*)-ethyl lactate) showed a baseline separation between the signals of the two enantiomers (Fig. 2, spectrum b, $\Delta\delta_{max} = 0.12$ ppm), while only one set of signals was observed with **6** obtained from (*S*)-ethyl lactate (spectrum c, >97% ee). Control of the reaction temperature is crucial: when the triflate derivative reacted with 1-methylimidazole at 0 °C, salt **6** was obtained as a racemic mixture. No enantiospecificity was obtained starting from halide, mesylate or tosylate derivatives.

Anion metathesis was performed to get salts **7**–**10** (Scheme 2). This synthetic pathway has a double advantage: salt **6** is obtained as a white solid, allowing to get rid of the colouration, which can appear during the quaternisation of the 1-methylimidazole; and no trace of halide—incompatible with several asymmetric processes and difficult to remove completely—is present in the products. All CILs **7**–**10** are hydrophobic, and therefore can be washed with water to ensure that no triflate anion remains. They are obtained as colourless liquids at room temperature. While **7** has an oily consistency, salts **8**–**10** are free-flowing, low-viscous liquids. CIL **8**, whose preparation can be easily scaled-up (50 g, overall yield 82%), does not solidify upon cooling but rather becomes very viscous at around −20 °C. DSC measurements (Table 1) showed that this liquid phase undergoes a glass transition (−57 °C). All other CILs (**7**, **9**, **10**) exhibit a similar phase transition. Despite multiple attempts, none of those CILs could be crystallised. However, when a flask containing neat salt **8** was left open on the bench for two months, small crystals melting at 45 °C appeared.

The structure of **8** was resolved by low temperature X-ray diffraction analysis (Fig. 3).[9] To our surprise, a complete racemisation of the salt was observed. All cations are surrounded closely by three NTf_2 anions. C–H···O and C–H···N hydrogen bonds are observed between hydrogens of the cations and the oxygen or nitrogen of the anions (Table 2).[10] Due to the negative charge of the anion, very short distances are observed. Typically, interactions between protons C(1′) and C(2)—the most acidic of the cation—with, respectively, the nitrogen and the two oxygens of anions can be considered as relatively strong, in regards of their lengths (2.36–2.44 Å) and angles (140°–160°).[10a,11]

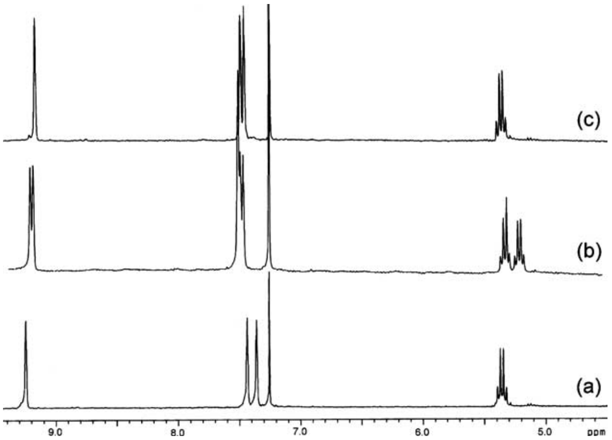


Figure 2. ^1H NMR chiral shift experiments. ^1H NMR (300 MHz, $CDCl_3$) of (a) (*rac*)-**6**; (b) (*rac*)-**6** + [*n*-Bu_4N][Δ-TRISPHAT] (1.6 equiv); (c) (*R*)-**6** + [*n*-Bu_4N][Δ-TRISPHAT] (3.0 equiv).

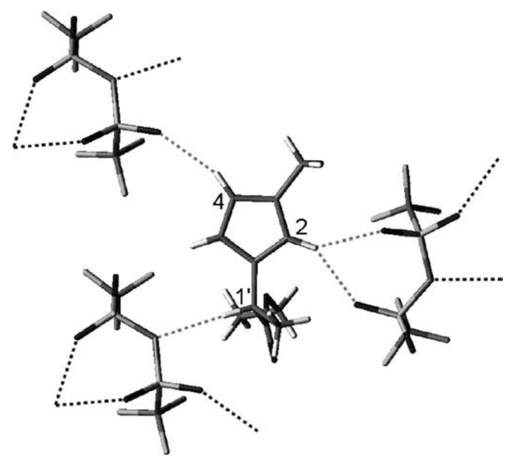


Figure 3. 3D-network of (*rac*)-**8** obtained by X-ray diffraction analysis.

Table 2. Distances [Å] and angles of C–H···(O/N) hydrogen bonds

	C···X	Angle C–H···X	Angle C–H···X
C(1′)–H···N	2.445	3.395	160.62
C(4)–H···O	2.444	3.329	156.85
C(2)–H···O	2.361	3.185	146.13
C(2)–H···O	2.509	3.287	140.18

Presence of this network of hydrogen bonding is in sharp contrast with the previously reported structure of a NTf_2 ionic liquid, in which substitution of the C(2) proton by a methyl group and absence of polar functional group prevented formation of strong hydrogen bonds.[12] In the meanwhile, the mother liquor from which the crystals *rac*-**8** were obtained was still enantiomerically pure. Separate experiments showed that in the presence of a base, racemisation occurs readily due to the acidity of the proton C(1′). However, the imidazolium-ester cation is configurationally stable in neutral or acidic conditions, even upon heating.

Experimental data

[1-(1-(*R*)-Ethoxycarbonyl-ethyl)-3-methyl-imidazolium]-[trifluoromethanesulfonate] **6**: To a solution of (*S*)-2-trifluoromethanesulfonyloxy-propionic acid ethyl ester (30.14 g) in dry Et_2O was added dropwise at −78 °C a cooled solution of 1-methyl-imidazole (9.910 g) in Et_2O. After 30 min, the mixture was warmed at rt, the white solid was filtered and washed with Et_2O to give 39.28 g of **6** (98%). NMR chiral shift experiments: To 5–10 mg of **6** in $CDCl_3$ (500 μL), were added 1–3 equiv of [*n*-Bu_4N][Δ-TRISPHAT] salt (prepared following Ref. 7). Ee was measured by direct integration. Similar procedure was successfully used for CILs **7** and **8**. CIL **7–10** were prepared by classical procedures from acid (HPF_6) or lithium salts ($LiNTf_2$, LiBETI, $LiN(SO_2C_4F_9)Tf$), washed with H_2O and dried.

Acknowledgements

We thank Prof. M. Wakihara and Dr. H. Ikuta (Tokyo Institute of Technology) for DSC measurements, Dr. M. Hatano (from our group) for X-ray measurement, Central Glass Co, Ltd for the generous gift of triflic anhydride and lithium salts, and the Japan Society for the Promotion of Science for funding.

References and notes

1. For books, see: (a) *Ionic Liquids in Synthesis*; Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Weinheim, 2002; (b) *Green Industrial Applications of Ionic Liquids*; Rogers, R. D., Seddon, K. R., Volkov, S., Eds.; Kluwer Academic: Dordrecht, 2002; For reviews, see: (c) Welton, T. *Chem. Rev.* **1999**, *99*, 2071; (d) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772; (e) Sheldon, R. *Chem. Commun.* **2001**, 2399; (f) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157; (g) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667; (h) Mikami, K. Ed. *New Environmentally Benign Reaction Media*; Scheffield Academic Press, in press.
2. Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, *1*, 23.
3. Wasserscheid, P.; Boesmann, A.; Bolm, C. *Chem. Commun.* **2002**, 200.
4. Ishida, Y.; Miyauchi, H.; Saigo, K. *Chem. Commun.* **2002**, 2240.
5. Bao, W.; Wang, Z.; Li, Y. *J. Org. Chem.* **2003**, *68*, 591.
6. Levillain, J.; Dubant, G.; Abrunhosa, I.; Gulea, M.; Gaumont, A.-C. *Chem. Commun.* **2003**, 2914.
7. (a) Lacour, J.; Ginglinger, C.; Grivet, C.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 608; (b) Lacour, J.; Ginglinger, C.; Favarger, F. *Tetrahedron Lett.* **1998**, *39*, 4825; (c) Jodry, J. J.; Lacour, J. *Chem. Eur. J.* **2000**, *6*, 4297.
8. (a) Lacour, J.; Goujon-Ginglinger, C.; Troche-Haldimann, S.; Jodry, J. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3695; (b) Lacour, J.; Jodry, J. J.; Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 2379.
9. Crystal data of *rac*-**8**: $C_{11}H_{15}F_6N_3O_6S_2$, $M = 463.38$, monoclinic, $a = 13.1697(3)$, $b = 8.5394(3)$, $c = 17.4529(4)$ Å, $U = 1871.91(9)$ Å^3, $T = 223$ K, space group $P2_1/c$ (#14), $Z = 4$, $\mu(\mathrm{MoK}_\alpha) = 0.377\ \mathrm{mm}^{-1}$, 3940 reflections measured, 3651 unique ($R_{\mathrm{int}} = 0.0594$), which were used in all calculations. The final $wR(F^2)$ was 0.1587 (all data). CCDC 200303 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
10. (a) Desiraju, G. R. *Acc. Chem. Res.* **1996**, *29*, 441; (b) Steiner, T.; Desiraju, G. R. *Chem. Commun.* **1998**, 891; (c) Thaimattam, R.; Reddy, D. S.; Xue, F.; Mak, T. C. W.; Nangia, A.; Desiraju, G. R. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1783; (d) Calhorda, M. J. *Chem. Commun.* **2000**, 801.
11. Similar C–H···O hydrogen bonds have already been observed in ionic liquids: (a) Wilkes, J. S.; Zaworotko, M. J. *J. Chem. Soc., Chem. Commun.* **1992**, 965; (b) Holbrey, J. D.; Reichert, W. M.; Swatloski, R. P.; Broker, G. A.; Pitner, W. R.; Seddon, K. R.; Rogers, R. D. *Green Chem.* **2002**, *4*, 407; (c) Holbrey, J. D.; Visser, A. E.; Reichert, W. M.; Swatloski, R. P.; Broker, G. A.; Rogers, R. D. *Green Chem.* **2003**, *5*, 129.
12. Golding, J. J.; MacFarlane, D. R.; Spiccia, L.; Forsyth, M.; Skelton, B. W.; White, A. H. *Chem. Commun.* **1998**, 1593.