Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters 49 (2008) 3264–3267

Tetrahedron Letters

Synthesis of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl with various anions for investigation of ionic liquids

Veronika Strehmel [a,*], Hans Rexhausen [a], Peter Strauch [b]

[a] University of Potsdam, Institute of Chemistry, Applied Polymer Chemistry, Karl-Liebknecht-Str. 24-25, D-14476 Potsdam-Golm, Germany
[b] University of Potsdam, Institute of Chemistry, Inorganic Chemistry, Karl-Liebknecht-Str. 24-25, D-14476 Potsdam-Golm, Germany

Received 16 February 2008; revised 11 March 2008; accepted 17 March 2008
Available online 20 March 2008

Abstract

A new synthetic way is described to prepare 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl bearing tetrafluoroborate, hexafluorophosphate or bis(trifluoromethylsulfonylimide) by an anion metathesis of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide using the corresponding silver salts. 4-Trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide is obtained by the methylation of 4-amino-2,2,6,6-tetramethylpiperidine-1-yloxyl with methyliodide. The new spin probe 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl bistrifluoromethylsulfonylimide and the spin probes containing tetrafluoroborate or hexafluorophosphate may be useful for an effective investigation of ionic liquids with similar anions.

Keywords: Spin probes; ESR spectroscopy; Nitroxides; Ionic liquids

Ionic liquids are new solvents distinguishing from traditional solvents by their higher viscosity and their tunability of solvent properties just by the variation of the cation or the anion structure resulting in the name 'designer solvents'. Furthermore, ionic liquids are interesting for various applications, such as in electrochemical devices, as solvents for extractions and for reactions in organic, inorganic, and polymer chemistry.[1–7] The specific structure of ionic liquids composed of cations and anions, and their interactions with solutes may cause advantages of ionic liquids compared to molecular solvents. However, the knowledge about the properties of ionic liquids on a molecular level and their interactions with solutes can be considered as rare. Spin probes are a versatile tool to explore molecular properties of these designer solvents in the molecular domain.[8–16] Positively or negatively charged spin probes are crucial for the investigation of ionic liquids because they directly interact with the individual ions of the ionic liquids. Recently, we described an improved synthesis for potassium 4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl and sodium 4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl.[16] These spin probes open the possibility to study especially interactions with the cation of the ionic liquid. This Letter describes the synthesis of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl salts bearing either bistrifluoromethylsulfonylimide, tetrafluoroborate or hexafluorophosphate as anions, which can also function as anions in ionic liquids. The selection of spin probes with similar counter ions as ionic liquids will improve the solubility of the spin probes in these ionic liquids and it will eliminate the counter ion exchange of charged spin probes dissolved in ionic liquids. Therefore, spin probes containing a similar counter ion as the investigated ionic liquid will increase the efficiency of the investigation of ionic liquids with spin probes.

4-Trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide can be obtained by the methylation of 4-dimethylamino-2,2,6,6-tetramethylpiperidine-1-yloxyl or 4-amino-2,2,6,6-tetramethylpiperidine-1-yloxyl with methyliodide.[17–19] The latter[19] cites a further reference, where

---

[*] Corresponding author. Tel.: +49 331 977 5224; fax: +49 331 977 5036.
E-mail address: vstrehme@uni-potsdam.de (V. Strehmel).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.03.073

the formation of another trimethylammonio substituted radical is described by the reaction of a primary amino substituted radical with methyliodide.[20] Nevertheless, the information about the experimental conditions to obtain 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide is rare in the literature.

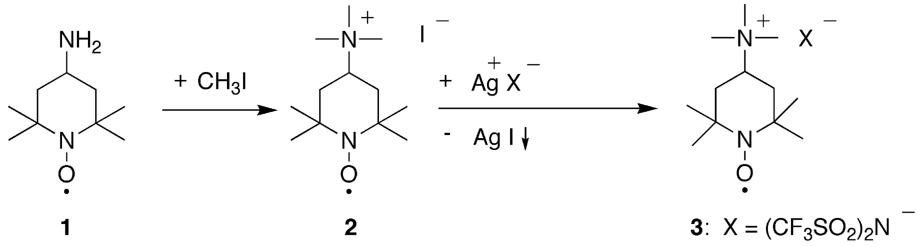
Furthermore, exchange of the iodide can be done by using KPF_6 to obtain 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl hexafluorophosphate.[21] However, no experimental details are given for this anion exchange in the literature. Anion exchange is important to tailor-made spin probes for the investigation of ionic liquids. Therefore, we developed an improved procedure for anion exchange of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide to obtain 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl derivatives bearing similar counter ions as ionic liquids, such as bistrifluoromethylsulfonylimide, tetrafluoroborate, and hexafluorophosphate.

In a first step the commercially available 4-amino-2,2,6,6-tetramethylpiperidine-1-yloxyl is converted into 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide by reaction with methyliodide (Fig. 1).[22] Then, anion metathesis of the iodide occurs when 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide is stirred with silver bistrifluoromethylsulfonylimide, silver tetrafluoroborate or silver hexafluorophosphate in acetone.[23] High yields on the new spin probe 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl bistrifluoromethylsulfonylimide (**3**, mp 229–248 °C dec), 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl tetrafluoroborate (**4**, mp 259–268 °C dec), and 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl hexafluorophosphate (**5**, mp 250–256 °C dec) are obtained because silver iodide precipitates, and it can be easily separated from the reaction mixture by the filtration resulting in the crystalline 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl salts after the evaporation of acetone in vacuo (Fig. 1).[23]

In principle, **3** can be obtained from **2** and lithium bistrifluoromethylsulfonylimide as well. However, purification is difficult in this case, and a paste-like product is obtained. The significant decrease in the melting point of **3** may be attributed to the presence of a small amount of the lithium salt. Therefore, anion metathesis using silver bistrifluoromethylsulfonylimide is preferred because the formed silver iodide precipitates, and it can be easily removed resulting in **3** with a higher purity.

The spin probes are well soluble in dimethylsulfoxide. The ESR spectrum of **3** dissolved in dimethylsulfoxide consists of the expected three lines (Fig. 2), which are characteristic for 2,2,6,6-tetramethylpiperidine-1-yloxyl derivatives. Examples for ESR spectra of **3**–**5** dissolved in 1-butyl-3-methylimidazolium salts containing similar anions as the spin probes are depicted in Figure 2 as well. The ESR spectra of the spin probes in the ionic liquids show line broadening and changes in the habitus in comparison with the ESR spectrum of **3** in dimethylsulfoxide due to the stronger interactions between the spin probes and the individual ions of the ionic liquids and the higher viscosity of the ionic liquids. Furthermore, the observed differences between the ESR spectra of the spin probes in the ionic liquids may be attributed to the viscosity of these ionic liquids that increase in the order 1-butyl-3-methylimidazolium bistrifluoromethylsulfonylimide < 1-butyl-3-methylimidazolium tetrafluoroborate < 1-butyl-3-methylimidazolium hexafluorophosphate.[24,25] This is also mirrored in the rotational correlation times (τ) of the spin probes (figure caption of Fig. 2) determined using the method of Budil et al.[26] The τ values increase in the same order as the solvent viscosity: dimethylsulfoxide < 1-butyl-3-methylimidazolium bistrifluoromethylsulfonylimide < 1-butyl-3-methylimidazolium tetrafluoroborate < 1-butyl-3-methylimidazolium hexafluorophosphate.[24,25,27] Moreover, slight distinct values are obtained for the isotropic hyperfine coupling constant ($A_{\text{iso}}(^{14}N)$) of the spin probes dissolved in dimethylsulfoxide and in ionic liquids.

We can conclude from the synthetic work that anion metathesis of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide using silver bistrifluoromethylsulfonylimide, silver tetrafluoroborate and silver hexafluorophosphate is an efficient way to obtain the corresponding 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl salts in a high yield. This new method opens the possibility to make further ammonio substituted spin probes with anions, which can be also found as the



3: $X = (CF_3SO_2)_2N^-$

4: $X = BF_4^-$

5: $X = PF_6^-$

Fig. 1. Formation of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide (**2**) by the methylation of 4-amino-2,2,6,6-tetramethylpiperidine-1-yloxyl (**1**) with methyl iodide[22] and anion metathesis using silver salts resulting in the cationic spin probes **3**–**5**.[23]

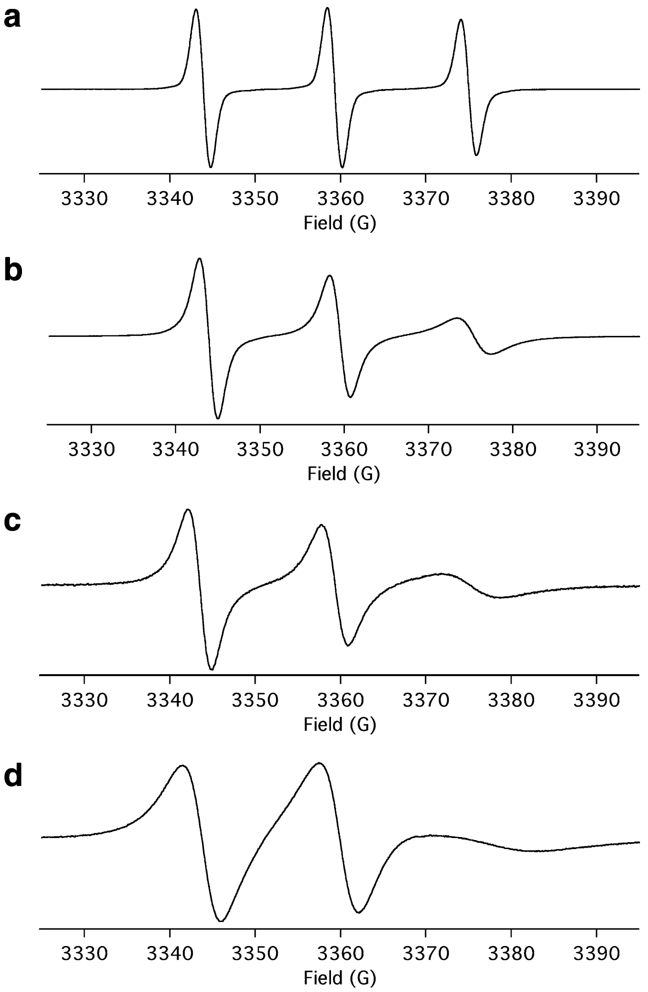


Fig. 2. ESR spectra of **3** dissolved in (a) dimethylsulfoxide ($A_{\mathrm{iso}}(^{14}\mathrm{N}) = 15.5$ G; $\tau = 0.7$ ns),[26,28] and of **3**–**5** dissolved in ionic liquids containing similar anions as the spin probes: (b) **3** in 1-butyl-3-methylimidazolium bistrifluoromethylsulfonylimide ($A_{\mathrm{iso}}(^{14}\mathrm{N}) = 15.7$ G; $\tau = 5.7$ ns), (c) **4** in 1-butyl-3-methylimidazolium tetrafluoroborate ($A_{\mathrm{iso}}(^{14}\mathrm{N}) = 15.8$ G; $\tau = 9.9$ ns), and (d) **5** in 1-butyl-3-methylimidazolium hexafluorophosphate ($A_{\mathrm{iso}}(^{14}\mathrm{N}) = 15.4$ G; $\tau = 17.2$ ns) at room temperature.

structural elements of ionic liquids. Such spin probes may be of great interest for the study of ionic liquids. These spin probes can be tailor made for ionic liquids, and possible counter ion exchange with the ionic liquid anion can be avoided. This should simplify the interpretation of results obtained by the investigation of ionic liquids with spin probes bearing cationic substituents.

Acknowledgments

The authors gratefully acknowledge A. Laschewsky for the use of laboratory equipment, the group of E. Kleinpeter, especially I. Starke and S. Fürstenberg from the University of Potsdam for mass spectrometric investigation, H. Wetzel from the Fraunhofer Institute for Applied Polymer Research Potsdam-Golm for elementary analysis, and the DFG for financial support within the priority programme SPP 1191.

References and notes

1. Wasserscheid, P.; Keim, W. *Angew. Chem.* **2000**, *112*, 3926.
2. Rogers, R. D.; Seddon, K. R. *Ionic Liquids Industrial Applications to Green Chemistry.* ACS Symp. Ser. 818; American Chemical Society: Washington, DC, 2002.
3. Wasserscheid, P.; Welton, T. Ionic Liquids in Synthesis; Wiley-VCH: Weinheim, 2003.
4. Rogers, R. D.; Seddon, K. R.; Kubisa, P. Ionic Liquids as Green Solvents. ACS Symp. Ser. 856; American Chemical Society: Washington, DC, 2003.
5. Rogers, R. D.; Brazel, C. S. *Ionic Liquids in Polymer Systems.* ACS Symp. Ser. 913; American Chemical Society: Washington, DC, 2005.
6. Ohno, H. *Electrochemical Aspects of Ionic Liquids*; John Wiley & Sons: Hoboken, New Jersey, 2005.
7. Wang, J.; Tian, Y.; Zhao, Y.; Zhuo, K. *Green Chem.* **2003**, *5*, 618.
8. Noel, M. A. M.; Allendoerfer, R. D.; Osteryoung, R. A. *J. Phys. Chem.* **1992**, *96*, 2391.
9. Kawai, A.; Hidemori, T.; Shibuya, K. *Chem. Lett.* **2004**, *11*, 1464.
10. Kawai, A.; Hidemori, T.; Shibuya, K. *Chem. Phys. Lett.* **2005**, *414*, 378.
11. Evans, R. G.; Wain, A. J.; Hardacre, C.; Compton, R. G. *ChemPhysChem* **2005**, *6*, 1035.
12. Stoesser, R.; Herrmann, W.; Zehl, A.; Strehmel, V.; Laschewsky, A. *ChemPhysChem* **2006**, *7*, 1106.
13. Strehmel, V.; Laschewsky, A.; Stoesser, R.; Zehl, A.; Herrmann, W. *J. Phys. Org. Chem.* **2006**, *19*, 318.
14. Grampp, G.; Kattnig, D.; Mladenova, B. *Spectrochim. Acta A* **2006**, *63*, 821.
15. Stoesser, R.; Herrmann, W.; Zehl, A.; Laschewsky, A.; Strehmel, V. *Z. Phys. Chem.* **2006**, *220*, 1309.
16. Strehmel, V.; Rexhausen, H.; Strauch, P. *Tetrahedron Lett.* **2008**, *49*, 586.
17. Keith, A. D.; Snipes, W.; Mehlhorn, R.; Gunter, T. *Biophys. J.* **1977**, *19*, 205.
18. Hamada, K.; Iijima, T.; Mc Gregor, R. *J. Polym. Sci. Phys. Ed.* **1988**, *26*, 421.
19. Huang, W.; Charleux, B.; Chiarelli, R.; Marx, L.; Rassat, A.; Vairon, J.-P. *Macromol. Chem. Phys.* **2002**, *203*, 1715.
20. Reid, D. A.; Bottle, S. E.; Micallef, A. S. *Chem. Commun.* **1998**, 1907.
21. Aonuma, S.; Casellas, H.; Faulmann, C.; de Bonneval, B. G.; Malfant, I.; Lacroix, P. G.; Cassoux, P.; Hosokoshi, Y.; Inoue, K. *Synth. Met.* **2001**, *120*, 993.
22. For the synthesis of 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide (**2**), methyliodide from Aldrich (7 ml) is added to 4-amino-2,2,6,6-tetramethylpiperidine-1-yloxyl (**1**) from Acros (200 mg) dissolved in a *tert*-butylmethylether methanol mixture (10 ml: 10 ml) and stirred under nitrogen overnight. The 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide precipitates as red precipitate, which is filtered, washed with 10 ml *tert*-butylmethylether, and dried in vacuo (<40 °C, 1 mbar). The 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide is obtained with 28–39% yield (mass spectrometry: 214.2059 Da in the TOF MS ES$^+$ mode (calcd for $C_{12}H_{26}N_2O$: 214.2045 Da) and 126.9453 Da in the TOF MS ES$^-$ mode (calcd for I^-: 126.9050 Da), mp 244–246 °C dec determined by the microscopic observation of **2** during heating and thermogravimetric analysis).
23. 4-Trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide (100 mg) is stirred in 5 ml acetone under nitrogen at room temperature. Then, a silver salt (113.8 mg silver bistrifluoromethylsulfonylimide (Aldrich), 57 mg silver tetrafluoroborate (Aldrich) or 74.1 mg silver hexafluorophosphate (Aldrich)) dissolved in 10 ml acetone is dropped to the 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl iodide acetone solution within 15 min. The reaction mixture is

stirred for further 30 min in the case of the bistrifluoromethylsulfonylimide salt and for further 15 min in the case of the tetrafluoroborate and the hexafluorophosphate salts at room temperature and then cooled at 0 °C for 12 h. The precipitate is filtered off resulting in clear solutions. The acetone is evaporated from the clear solution (1 h at 10 mbar) and dried in vacuo (1 mbar) for 2 h resulting in 90% yield on the yellow to orange crystalline 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl bistrifluoromethylsulfonylimide **3** (mass spectrometry: 214.2034 Da in the TOF MS ES^+ mode (calcd for $C_{12}H_{26}N_2O$: 214.2045 Da) and 279.6999 Da in the TOF MS ES^- mode (calcd for $C_2F_6NO_4S_2^-$: 279.9178 Da); elementary analysis: 34.00% C, 5.30% H, 8.24% N, 13.20% S (calcd for $C_{14}H_{26}F_6N_3O_5S_2$: 34.00% C, 5.30% H, 8.50% N, 12.97% S); IR: characteristic vibrations for S–N–S (asymmetric vibration) at 1051 cm^{-1}, $-SO_2-$ (symmetric vibration) at 1137 cm^{-1}, CF_3 at 1188 cm^{-1}, $-SO_2-$ (asymmetric vibration) at 1330 cm^{-1} and 1345 cm^{-1}, mp 229–248 °C dec determined by the microscopic observation of **3** during heating and thermogravimetric analysis), 80% yield of yellow to orange crystalline 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl tetrafluoroborate **4** (mass spectrometry: 214.2039 Da in the TOF MS ES^+ mode (calcd for $C_{12}H_{26}N_2O$: 214.2045 Da), IR: characteristic vibration for BF_4^- at 1035 cm^{-1}, mp 259–268 °C dec determined by the microscopic observation of **4** during heating and thermogravimetric analysis), and 91% yield of yellow to orange crystalline 4-trimethylammonio-2,2,6,6-tetramethylpiperidine-1-yloxyl hexafluorophosphate **5** (mass spectrometry: 214.2040 Da in the TOF MS ES^+ mode (calcd for $C_{12}H_{26}N_2O$: 214.2045 Da) and 144.8458 Da in the TOF MS ES^- mode (calcd for PF_6^-: 144.9642 Da), IR: characteristic vibration for PF_6^- at 825 cm^{-1}, mp 250–256 °C dec determined by the microscopic observation of **5** during heating and thermogravimetric analysis).

24. Strehmel, V.; Laschewsky, A.; Wetzel, H.; Görnitz, E. *Macromolecules* **2006**, *39*, 923.
25. Jin, H.; O'Hare, B.; Dong, J.; Arzhantsev, S.; Baker, G. A.; Wishart, J. F.; Benesi, A. J.; Maroncelli, M. *J. Phys. Chem. B* **2008**, *112*, 81.
26. Budil, D. E.; Lee, S.; Saxena, S.; Freed, J. H. *J. Magnet. Res. A* **1996**, *120*, 155.
27. Ali, A.; Tewari, K.; Nain, A. K.; Chakravortty, V. *Phys. Chem. Liq.* **2000**, *38*, 459.
28. Methods: Mass spectra were taken in the ES^+ and the ES^- mode with an ESI Q-TOF instrument. ESR spectra of the spin probes were measured in X-band with a CW spectrometer E500 (Bruker). Thermogravimetric analysis was carried out using a Mettler-Toledo TGA/SDTA 851^e using a heating rate of 20 K/min.