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Synthesis of a new ionic spin probe for investigation of polar and non-polar solvents

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ABSTRACT

A synthesis is described for the new ionic spin probe potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl. This new spin probe shows an improved solubility in both polar and non-polar solvents in comparison with the potassium-4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl. Furthermore, the solubility of potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl is also improved in ionic liquids relative to the potassium salt comprising no crown ether moiety. The spin probe potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl is highly suitable for investigation of both less polar and highly polar environments.

Spin probes have gained importance for investigation of biological systems, pharmaceutical products, synthetic polymers, ionic liquids, and for medical applications.[1–20] A sufficient solubility of the spin probes in distinct materials exhibiting either a polar or nonpolar environment is necessary to obtain reliable results in different applications. Main parameters obtained are the average rotational correlation time (τ) and the hyperfine coupling constant ($A_{iso}(N)$) of the spin probe dissolved in the matrix. These parameters give information about microviscosity and micropolarity of the surrounding matrix. Strong interactions between the ionic spin probes and ionic liquids make ionic spin probes interesting for investigation of ionic matrices. However, the solubility of ionic spin probes is very low in less polar materials. An insufficient solubility may lead to aggregation, and would result therefore in undesired phenomena during the measurement. This can be, for example, a spin exchange. Therefore, we developed a new spin probe with an ionic structure showing a significantly improved solubility in both highly polar and less polar solvents. The solubility of the new spin probe potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl is significantly improved compared to potassium-4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl. Our experiments indicate a significant reduce of aggregation by crown ether formation resulting in an increased solubility also in nonpolar solvents, that is, toluene.

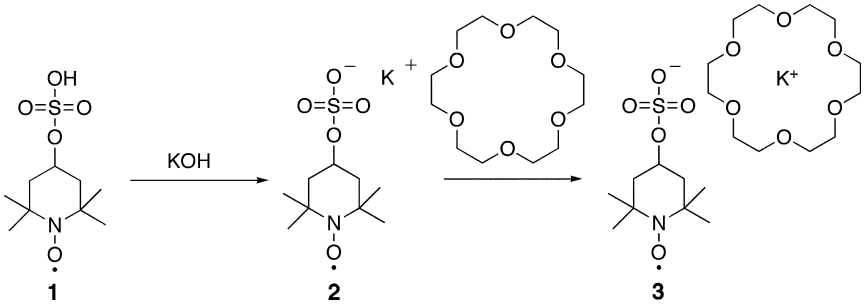

Figure 1. Formation of potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl by reaction of 4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl with potassium hydroxide[16] and complexation of the obtained potassium-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl with 18-crown-6.[21]

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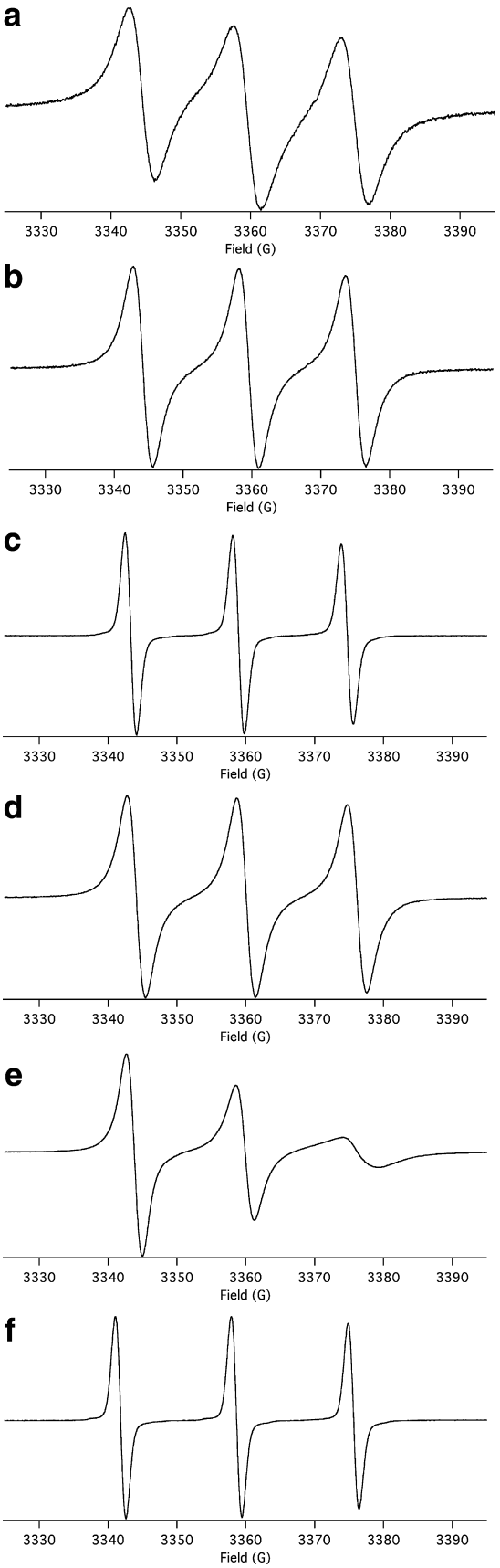

Figure 2. ESR spectra of **3** dissolved in (a) *tert*-butylmethylether ($A_{iso}(N) = 15.1$ G; $\tau = 3.2$ ns), (b) toluene ($A_{iso}(N) = 15.5$ G; $\tau = 1.3$ ns), (c) dimethylsulfoxide ($A_{iso}(N) = 15.7$ G; $\tau = 0.04$ ns), (d) ethanol ($A_{iso}(N) = 16.0$ G; $\tau = 1.1$ ns), (e) 1-butyl-3-methylimidazolium tetrafluoroborate ($A_{iso}(N) = 16.2$ G; $\tau = 7.3$ ns), (f) water ($A_{iso}(N) = 16.9$ G; $\tau = 0.2$ ns) at 293 K.

The new spin probe potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl (**3**) is synthesized from potassium-4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl (**2**), which is formed from 2,2,6,6-tetramethylpiperidine-1-yloxyl-sulfuric acid (**1**) (Fig. 1).[21] The synthesis of the latter is described in the literature.[16]

Examples for ESR spectra of **3** dissolved in selected solvents are given in Figure 2.

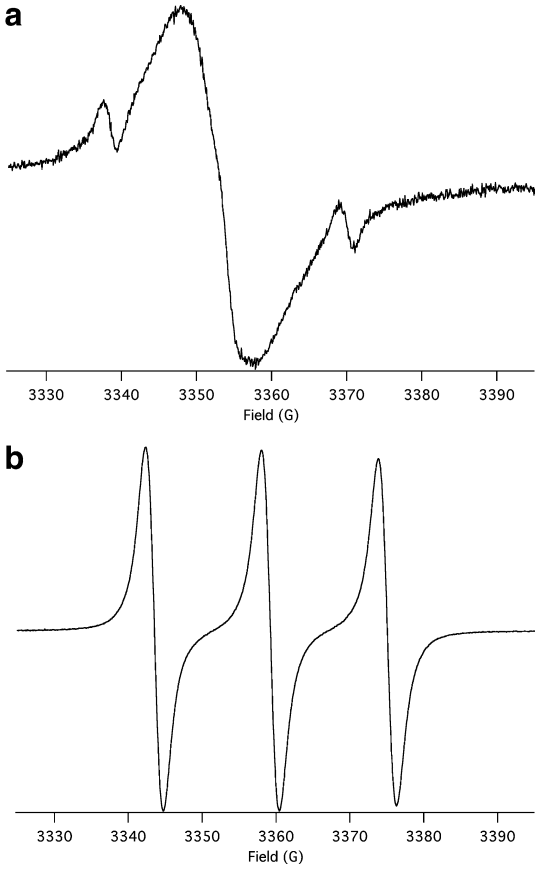

Figure 3. ESR spectra of **2** (a) and **3** ($A_{iso}(N) = 15.8$ G; $\tau = 0.1$ ns) (b) dissolved in methylenechloride at 293 K.

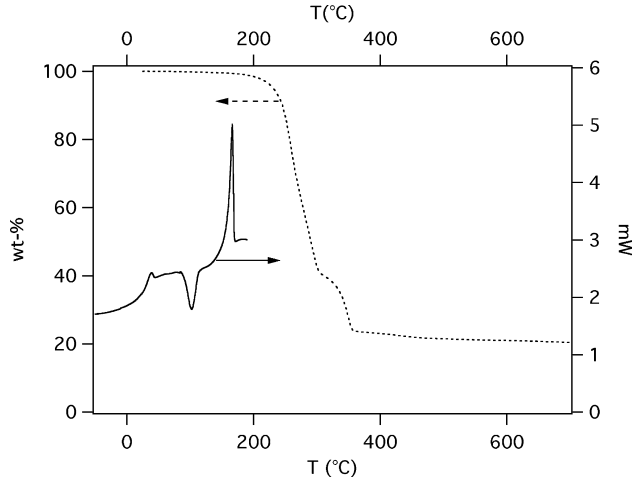

Figure 4. TGA and DSC analysis of **3** using a heating rate of 20 K/min for TGA and 10 K/min for DSC analysis.

Figure 2 describes the use of the new spin probe **3** to explore polarity differences between polar solvents, such as dimethylsulfoxide, ethanol, 1-butyl-3-methylimidazolium tetrafluoroborate or water and less polar solvents, such as *tert*-butylmethylether or even toluene. Investigation of the latter becomes particularly possible by the increased solubility of **3** in these different solvents. Sharp line ESR spectra are obtained if dimethylsulfoxide or water is used as solvent for **3**. Line broadening is observed in the ESR spectra of **3** when this spin probe is dissolved in ethanol, *tert*-butylmethylether, or toluene. This may be caused by the lower polarity of these solvents in comparison with water or dimethylsulfoxide. The broadest lines are observed for **3** in 1-butyl-3-methylimidazolium tetrafluoroborate because of the significantly higher viscosity of the ionic liquid.

The $A_{iso}(N)$ values (Figs. 2 and 3) give an information about the polarity of the solvents detected by the spin probe ($A_{iso}(N)$: 15.1 G (*tert*-butylmethylether); 15.5 G (toluene); 15.7 G (dimethylsulfoxide); 16.0 G (ethanol); 16.2 G (1-butyl-3-methylimidazolium tetrafluoroborate); 16.9 G (water); 15.8 G (methylenechloride)). It shows the highest polarity for water and the lowest polarity for *tert*-butylmethylether. The polarity of the ionic liquid detected by **3** is rather similar to ethanol than to dimethylsulfoxide as detected by cationic spin probes.[17] The average rotational correlation times determined using the method of Budil et al. (Figs. 2 and 3) show significant differences (τ: 3.2 ns (*tert*-butylmethylether); 1.3 ns (toluene); 0.04 ns (dimethylsulfoxide); 1.1 ns (ethanol); 7.3 ns (1-butyl-3-methylimidazolium tetrafluoroborate); 0.2 ns (water); 0.1 ns (methylenechloride).[22] In general, the τ-values are lower if **3** is dissolved in the molecular solvents in comparison with the use of 1-butyl-3-methylimidazolium tetrafluoroborate as solvent for **3** caused by the significant higher viscosity of the ionic liquid.[18] The lowest τ-values are obtained in the case of using dimethylsulfoxide, methylenechloride, or water. Slightly higher τ-values are determined for the use of ethanol and toluene, although a significantly higher τ-value is found if **3** is dissolved in *tert*-butylmethylether.

The increased solubility of **3** in comparison with **2** can be also seen if these spin probes are dissolved in methylenechloride. Strong aggregation of the ionic species of **2** in methylenechloride results in the less-resolved ESR spectrum (Fig. 3a), although **3** gives a well-resolved three line spectrum in this solvent that is typical for 2,2,6,6-tetramethylpiperidine-1-yloxyl derivatives well dissolved in the matrix (Fig. 3b).

A further benefit of **3** in comparison with **2** is a reduced melting point without decomposition detected by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) investigation of **3**. DSC analysis shows a glass transition at 31 °C, a recrystallization with a minimum at 102 °C and a melting point at 168 °C (Fig. 4). Weight loss of **3** is observed above 200 °C (Fig. 4) indicating that nearly no thermal decomposition occurs below this temperature.

Acknowledgments

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21. For the synthesis of potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl (**3**), 200 mg of 2,2,6,6-tetramethylpiperidine-1-yloxyl-sulfuric acid (**1**) is dissolved in 8 ml of 0.1 N methanolic KOH at room temperature under nitrogen. The synthesis of **1** is described in Ref. 12 After stirring the reaction mixture for 20 min, 209 mg, 18-crown-6 dissolved in 5 ml methanol is added to the reaction mixture, which is further stirred for 1 h. The reaction mixture is kept at 0 °C for 48 h. Then, the reaction mixture is filtrated, and the resulting clear solution is evaporated at 20 °C and 10 mbar. The remaining red-like solid is dried in vacuo (1–3 mbar) at room temperature for 24 h. The potassium-(18-crown-6)-4-sulfonatooxy-2,2,6,6-tetramethyl-piperidine-1-yloxyl is obtained in 84% yield, melting point 168 °C determined by DSC. Elementary Anal.: C 45.40% measured (45.46% Calcd); H: 7.55% measured (7.40% Calcd); N: 2.5% measured (2.5% Calcd); S: 5.47% measured (5.77% Calcd). Mass spectrometric analysis gives 303.1186 Da in the positive mode (Calcd: 303.1210 Da) corresponding to $C_{12}H_{24}O_6K$, and 250.8938 Da in the negative mode corresponding to 4-sulfonatooxy-2,2,6,6-tetramethylpiperidine-1-yloxyl.
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