



Synthesis and Characterization of *bis*(Tetrahydrofurfuryl) Ether

John D. Stenger-Smith, Lawrence Baldwin, Andrew Chafin, and Paul A. Goodman*^[a]

Despite the availability of a large number of alkyl tetrahydrofurfuryl ethers that have a wide range of applications, pure *bis*(tetrahydrofurfuryl) ether (BTHFE) has not been previously synthesized. Here, we report the synthesis of BTHFE (consisting of the *RR*, *SS*, and *meso* stereoisomers) at greater than 99% purity from tetrahydrofurfuryl alcohol, using (tetrahydrofuran-2-yl)methyl methanesulfonate as an intermediate. Additionally, we demonstrate that BTHFE can be used as a non-volatile solvent in poly(3,4-propylenedioxythiophene)-based supercapacitors. Supercapacitor devices employing solutions of the ionic liquid 1-ethyl-3-methyl-imidizolium *bis*(trifluoromethylsulfonyl)imide in BTHFE display similar performances to those prepared by using the neat ionic liquid as an electrolyte, although solution-based devices exhibit a somewhat higher resistance.

A relatively large number of scientific publications and patents have analyzed, or proposed, the use of alkyl tetrahydrofurfuryl ethers for a diverse array of applications. In 1930, Kirner synthesized a small library of alkyl tetrahydrofurfuryl ethers, and analyzed their toxicity in mice and guinea pigs.^[1] His study demonstrated that this class of ethers exhibit significant anesthetic effects when administered intraperitoneally. Kirner also noted that, in larger doses, the compounds were toxic and, even at low doses, they appeared to initiate intestinal necrosis, which often proved fatal for the test animals. The synthetic methods employed by Kirner were very similar to those used by Wissell and Tollens when they first synthesized furfuryl ether derivatives in 1892.^[2] A significant body of published work shows the utility of these compounds as structural modifiers in rubbers. Modification of rubber with various alkyl tetrahydrofurfuryl ethers increases the static friction coefficient, and the rubber can be used in automobile tires.^[3] Additionally, these compounds have been proposed as components of heat pumps,^[4] paint strippers,^[5] and as fuel additives.^[6] There is clearly a potential market for these compounds, and there are

[a]	Dr. J. D. Stenger-Smith, Dr. L. Baldwin, A. Chafin, Dr. P. A. Goodman
	Chemistry Division, Code 4F0000D, Research Department
	Naval Air Warfare Center Weapons Division
	1 Administration Circle
	China Lake, CA 93555 (USA)
	E-mail: paul.goodman@navy.mil
	Supporting Information and the ORCID identification number(s) for the
D	author(s) of this article can be found under http://dx.doi.org/10.1002/
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© 2016 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited, and is not used for commercial purposes. several reports of methods for their synthesis.^[1,7] One tetrahydrofurfuryl ether derivative that has remained elusive is *bis*(tetrahydrofurfuryl) ether (BTHFE). We found one previous report of its synthesis, but this report lacked an in-depth characterization of the compound, which left some doubt as to the true identity of the reported product.^[8]

When Kirner attempted to make methyl tetrahydrofurfuryl ether using tetrahydrofurfuryl chloride and methanol as starting materials, he found that the chloride reacted very slowly, the reaction only occurred to a slight extent, and it had the added disadvantage of producing an unsaturated tetrahydrofuran derivative, 2-methylene tetrahydrofuran, as a byproduct.^[11] Previously, it has been reported that BTHFE had been produced by reacting tetrahydrofurfuryl bromide with sodium tetrahydrofurfurylate. In the previously published report of the synthesis, the chief spectroscopic evidence that the authors used to identify the compound was an IR spectrum.^[8] The IR spectrum for the BTHFE that we produced is shown in Figure 1. The peaks near 2800 cm⁻¹ (ca. 95% transmittance)



Figure 1. IR spectrum of BTHFE with the structure (ambiguous stereochemistry) inset.

correspond to C–H stretching. The peaks at 1460 and 1360 cm⁻¹ (ca. 97% transmittance) correspond to C–H bending, and the large peak near 1070 cm⁻¹ (ca. 75% transmittance) corresponds to ether C–O stretching. This spectrum is largely in agreement with the one presented by Prutkov et al., except for the area around 1700 cm⁻¹. In the spectrum presented by Prutkov et al., there is a medium intensity peak at approximately 1700 cm⁻¹ that is absent in our spectrum.^[8] Alkene stretching occurs at this frequency, and we suspect, based on the evidence presented by Kirner related to the diffi-

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culty of producing alkyl tetrahydrofurfuryl ethers using tetrahydrofurfuryl halides as reagents, that the previously reported synthesis of BTHFE actually produced a mixture of the ether and 2-methylene tetrahydrofuran.

Additionally, Prutkov et al. determined that the molecular weight of their product was 172.5 g mol⁻¹, as determined by freezing-point depression in benzene. The true molecular weight of BTHFE is 186 g mol^{-1} . It is possible that the 172.5 g mol⁻¹ that they observed is within the expected error of the freezing-point depression measurement; however, given the peak at 1700 cm⁻¹ in the IR spectrum that they presented, it seems equally, if not more, likely that their freezing-point depression analysis solutions contained a mixture of BTHFE and 2-methylene tetrahydrofuran, which has a molar mass of only 84 g mol⁻¹. A mixture that contained approximately 87% BTHFE with 13% 2-methylene tetrahydrofuran would result in an observed molar mass of 172.5 g mol⁻¹ in a freezing-point depression experiment. Based on these observations, we believe that, although Prutkov et al. did synthesize BTHFE, we have successfully improved upon their synthesis by using (tetrahydrofuran-2-yl)methyl methanesulfonateas a starting material. We were able to limit the side reaction that produces 2methylene tetrahydrofuran, because the methanesulfonate ion is a better leaving group for an SN₂ reaction than bromide, which resulted in substitution, rather than elimination, being the strongly preferred reaction pathway.

The total ion chromatogram obtained through GC-MS analysis showed product purity of >99%. The molecular ion was not observed, because electron ionization resulted in significant fragmentation in the GC-MS measurements. We performed chemical ionization (CI) mass spectrometry with methane to identify the molecular ion and help verify the identity of the product. The most abundant ion observed in these measurements was m/z = 187, which corresponds to the M+H ion. The spectrum contained a peak with approximately 10% abundance, relative to the M+H ion, at m/z = 188, which corresponds to the expected ¹²C/¹³C isotopic effect for a molecule with 10 carbon atoms, such as the molecular ion. The second most abundant peak in the CI mass spectrum was m/z=85, which is consistent with fragmentation at the central oxygen atom that results in an ion with the molecular formula $C_5H_9O^+$. An additional peak at m/z = 86 proved to have 5% abundance relative to the peak at m/z=85, which is consistent with the ¹²C/¹³C isotopic effect expected for this fragmentation.

Interestingly, the BTHFE produced for this work can be thought of as pure, based on the IR and GC–MS analysis, but, because it contains two stereocenters, it can also be considered a mixture of three distinct compounds (*RR*, *SS*, and *meso*), as evidenced by the ¹H, ¹³C, and ¹H–¹³C heteronuclear multiquantum correlation (HMQC) NMR spectra (Figure 2). The ¹H spectral assignments are shown in Figure 2, and they were deduced based on a paper by Plavec et al., wherein the chemical shifts and three-bond proton–proton coupling constants for (*S*)-tetrahydrofurfuryl alcohol were reported.^[9] As the sample contains a combination of stereoisomers that have overlapping resonances, we observe broad multiplets in the ¹H spectrum. The ¹³C NMR assignments of the BTHFE ether mixture were de-



Figure 2. The ¹H (top axis), ¹³C (left axis), and HMQC (in plane) NMR spectra for BTHFE with peak assignments noted in plane. The structure of the molecule is in the inset with the hydrogens labeled.

termined by using HMQC experiments. In the ¹³C NMR spectrum, two resonances are observable for each carbon, except for C1. Each individual shift of the carbon resonance pairs represents the *RR/SS* isomers, which have identical chemical shifts, and the *meso* isomer, which has a slightly different resonance. The singlet assigned as C1 is likely a result of overlap, as this carbon is isolated from the stereocenter enough to dampen its effect on the chemical shift. Temperature-dependent peak shifts were observed in the ¹H spectra that were not observed by Plavec et al., and the shifts were particularly large for the H₅ and H_{5'} resonances. The cause of these apparently unique shifts is beyond the scope of this paper, but further analysis is underway.

One intriguing property of BTHFE is its relatively high boiling point (62°C at 0.3 mmHg). One of the drawbacks to typical electrochemical capacitors is that they contain relatively lowboiling, flammable solvents (e.g. acetonitrile), which limit their useful temperature range and present a safety hazard. The use of ionic liquids (ILs) as electrolytes can eliminate the temperature and safety concerns, but they often come with their own limitations, like cost and the fact that they generally have a lower conductivity than traditional electrolyte solutions.^[10] Previously, this laboratory has performed extensive analysis of conducting polymer supercapacitors that employed neat EMIBTI as an electrolyte.^[11] We chose to do a preliminary analysis of BTHFE as a solvent for EMIBTI in poly(3-4, propylenedioxythiophene) capacitor devices, with the hope that solvation of the IL would increase the conductivity of the electrolyte by breaking up ion-pairing interactions, and, because BTHFE has a high boiling point, it does not introduce the same temperature limitations as other solvents. For this preliminary analysis, we compared devices that used neat EMIBTI as an electrolyte against devices containing 1 M EMIBTI in BTHFE as an electrolyte. Voltammetrically, the devices prepared by using either electrolyte system showed a typical box-like response (Figures S1a and S1b in the Supporting Information). In fact, aside

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from a slight difference in capacitance, which is evident from the difference in the magnitude of the plateau current in the voltammograms (Figure S1c) and is attributed to slightly different amounts of polymer being present on the electrodes in each device, the devices appear to perform identically. Based solely on the cyclic voltammetry, one might incorrectly conclude that the addition of the solvent made no difference to device performance.

We performed electrochemical impedance spectroscopy (EIS) measurements on the devices to shed light on any subtle differences in capacitive performance, as well as to gain insight into the resistance of the electrolyte that contributed to the systems. The high-frequency plateau in the Bode magnitude plot, which can be used to determine the solution resistance of the device, shows that the 1 M EMIBTI solution has a resistance that is approximately 20 Ω higher than that of neat EMIBTI (see Figure S1d). This result was consistent for each device analyzed. To verify that this resistance was caused by the electrolyte solution, and not caused by the conducting polymer that was on the electrodes, we performed EIS measurements on devices that contained only the separator paper soaked in electrolyte and electrodes that did not have any polymer on them. These measurements yielded device resistances of 18 $\pm\,6$ and 45 $\pm\,$ 10 Ω at the 90 % confidence level for the neat EMIBTI and 1 M EMIBTI solutions, respectively. The difference between the resistances measured for devices that contained polymer and those that did not contain polymer is not statistically significant, but the difference between neat EMIBTI and the 1 M EMIBTI solution is statistically significant. These results are counter to our hypothesis that the addition of solvent would lower the resistance by breaking up the ionpairing interactions that are present in neat EMIBTI. Further exploration showed that the conductivities of EMIBTI/BTHFE solutions are directly proportional to the concentration of EMBTI, up to approximately 90% EMIBTI, where it plateaus, at about 9 mS cm^{-1} (see Figure S2 in the Supporting Information).

The Bode phase-angle plot (see Figure S1e) shows that, at frequencies below approximately 1 Hz, the phase angle for both neat EMIBTI and the BTHFE solution approaches -90%, and is indicative of nearly ideal capacitive behavior. These results suggest that BTHFE solutions warrant further analysis in electrochemical capacitors, because it appears that the solvent is relatively stable electrochemically.

We have synthesized *bis*(tetrahydrofurfuryl) ether (BTHFE) in a high purity by using (tetrahydrofuran-2-yl)methyl methanesulfonate as a starting material. The methanesulfonate ion is a more efficient leaving group for an SN₂ reaction than bromide, which had previously been employed to synthesize BTHFE, and its use prevented the previously observed side product, 2-methylene tetrahydrofuran, from forming. Generally, we have demonstrated that the use of (tetrahydrofuran-2-yl)methyl methanesulfonate, rather than tetrahydrofurfuryl halides, provides a versatile starting material that permits the synthesis of tetrahydrofurfuryl ethers with bulky substituents. The NMR analysis of BTHFE demonstrated that the product was a mixture of stereoisomers, as expected; although, we observed temperature-dependent peak shifts that have not previously been reported for molecules of this type. We also performed preliminary analysis of BTHFE as a solvent in electrochemical supercapacitors. In this capacity, the BTHFE proved to be electrochemically stable, even though 1 μ solutions of the IL 1-ethyl-3-methyl-imidizolium *bis*(trifluoromethylsulfonyl)imide had resistances that were approximately 20 Ω higher than the neat IL. Further analysis of both the NMR and electrochemical properties of BTHFE are ongoing.

Experimental Section

Tetrahydrofurfurylalcohol (THFA, Sigma Aldrich, ≥98%), tetrahydrofuran (THF, Sigma Aldrich, Reagent Grade, \geq 99%, BHT inhibited), sodium metal (Sigma Aldrich, Reagent Grade, dry stick), methanesulfonyl chloride (Sigma Aldrich, 99.7%), pyridine (Sigma Aldrich, Anhydrous, 99.8%), and propylene carbonate (Sigma Aldrich, Anhydrous, 99.7%) were purchased and used as received. 1-Ethyl-3methyl-imidizolium bis(trifluoromethylsulfonyl)imide (EMIBTI), for use in the electrochemical measurements, was synthesized as previously reported.^[11] Elemental analyses were performed independently by Atlantic Microlabs, Inc., Norcross, GA; Intertek Pharmaceutical Services, Whitehouse, NJ; and MHW Labs, Phoenix, AZ. The elemental analysis results reported with the synthetic procedures are averages of the results from all three laboratories. Electrochemical depositions and cyclic voltammetry were performed by using a Pine Instruments Model AFCBP1 potentiostat. EIS measurements were performed by using a Princeton Applied Research PARSTAT 2273 potentiostat. Conductivity measurements of EMIBTI/BTHFE solutions were performed by using a Jenway 4590 conductivity meter at 25 \pm 0.3 °C.

Synthesis of (Tetrahydrofuran-2-yl)methyl Methanesulfonate

A three-neck round-bottom flask was filled with 200 mL pyridine and 88 mL (91.8 g, 0.90 moles) THFA. The mixture was placed in an ice/water bath and purged with nitrogen for 1 h. Methanesulfonyl chloride (73 mL, 108.4 g, 0.94 moles) was added drop-wise to the continuously chilled mixture from an addition funnel over a period of 12 h. The mixture was then allowed to warm to room temperature over the next 48 h, at which time it was combined with 500 mL of 1.2 M HCl and extracted three times with 125 mL portions of dichloromethane. The organic phases were combined and then extracted once with 125 mL of 1.2 м HCl, followed by 125 mL of saturated NaCl. Finally, the dichloromethane solution was dried with MgSO₄, and the solvent was removed under reduced pressure. The crude product was a light yellow liquid, and the yield of crude material was 144 g (89%). Portions of the crude material were vacuum distilled at 0.34 mmHg to obtain pure product (125 g, 77% yield), which was a clear, colorless liquid. The headspace temperature during distillation of the pure material was 102 °C. This material was characterized by using ¹H and ¹³C NMR, 2-D NMR, GC-MS, FTIR, and elemental analysis. CAUTION: (Tetrahydrofuran-2-yl)methyl methanesulfonateis stable in air at room temperature, but will react violently if heated while exposed to air. ¹H NMR (CDCl₃ 500 MHz) $\delta = 1.60$ (m, 1 H), 1.8 (m, 2 H), 1.9 (m, 1 H), 3.03 (s, 3 H), 3.76 (m, 2 H), 4.0 (m, 2 H), ß4.14 ppm (m, 1 H). ¹³C NMR δ = 76.29, 71.65, 68.60, 37.55, 27.60, 25.75 ppm; elemental analysis: calcd: 39.93 % C, 6.71 % H, 17.79 % S; found: 40.1 % C, 6.7 % H, 18:01% S; GC-MS indicated 98.6% purity.

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Synthesis of bis(Tetrahydrofurfuryl) Ether

A two-neck round-bottom flask was filled with 60 mL THF and 20.6 g (0.17 moles) of the sodium salt of THFA, which was prepared by adding sodium metal to excess THFA and collecting the resulting solid. The mixture was placed under a nitrogen flow, heated to approximately 70 °C by using an oil bath, and 29 g (0.16 moles) of distilled (tetrahydrofuran-2-yl)methyl methanesulfonatewas added drop-wise over several hours. Then, the temperature of the oil was increased to approximately 170 °C, and the THF was allowed to evaporate while the progress of the reaction was monitored by removing small aliguots from the mixture and recording the NMR spectrum. The mixture was allowed to cool to room temperature when the NMR spectrum indicated that the reaction was approximately 90% complete (after roughly 48 h). Diethyl ether (100 mL) was added to the room-temperature mixture, which was then filtered, and the ether was removed by rotary evaporation. The yield of crude material, which was a brown-colored liquid, was 19 g (63%). The crude material was purified by vacuum distillation and produced a clear, colorless liquid. The temperature of the distillate was 62 °C at 0.3 mmHg. The reaction yielded 14 g (47%) of product that was found to be approximately 99% pure by GC-MS. ¹H NMR (CDCl₃, 500 MHz) δ = 4.02–3.93 (broad m, 2H), 3.81–3.74 (m, 2H), 3.70-3.62 (m, 2H), 3.48-3.35 (m, 4H), 1.91-1.82 (broad m, 2H), 1.82-1.71 (broad m, 4H), 1.59-1.47 ppm (broad m); 13C NMR (CDCl₃, 500 MHz) δ = 77.95, 77.85, 74.18, 74.08, 68.25, 28.12, 28.10, 25.61, 25.58 ppm; elemental analysis: calcd: 64.5%C, 9.7% H, 25.8% O; found: 64.4%C, 9.7% H, 25.9% O.

Poly(3,4-propylenedioxythiophene) Electrochemical Supercapacitor Analysis

Poly(3,4-propylenedioxythiophene) (poly(ProDOT)) was potentiodynamically deposited onto 0.5 cm diameter gold disk electrodes from 30 mM solutions of 3,4-propylenedioxythiophene in propylene carbonate that contained 100 mM EMIBTI as a supporting electrolyte. The working electrode potential was swept between -1and +1.7 V versus Ag⁺/Ag six times at 100 mV s⁻¹ to produce the electroactive films. Two-electrode capacitor devices were constructed as previously reported.^[11] The charge capacity for each electrode was determined by integration of the voltammetric current corresponding to the neutralization of the polymer film on the electrode, and the difference in the capacity for electrodes that were used in a single device was limited to <10%. The devices were analyzed by using cyclic voltammetry and EIS.

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Keywords: electrochemistry · ion pairs · ionic liquids · supercapacitors · synthetic methods

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Finally! Many asymmetric alkyl tetrahydrofurfuryl ethers are available, and they have a wide range of potential applications. However, the preparation of the symmetric molecule, bis(tetrahydrofurfuryl) ether (BTHFE), has remained elusive, until now. High-purity BTHFE has been prepared and fully characterized for the first time. In addition, a preliminary investigation of BTHFE as a solvent in electrochemical supercapacitors is reported.



J. D. Stenger-Smith, L. Baldwin, A. Chafin, f P. A. Goodman*



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