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Selective Generation, Isolation, and Purification of Tetrathiafulvalenetetrathiolate: A Versatile Building Block for New Materials

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Tetrathiafulvalene (TTF) and its derivatives are fully π conjugated organic molecules[1] which, upon one-electron oxidation, form very stable, aromatic radical cations. Crystals of these radical cation salts have the unique ability to form organic metals and, in some cases, superconductors.[2] Over the past few years, significant progress has been made toward understanding the chemistry and physics of these interesting advanced materials.[3] Recent research has led to the discovery of the κ-phase structure in TTF-based conductors.[3a] This structural arrangement containing either bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF or ET)[3a] or some unsymmetrical tetrathiafulvalene derivatives[4] can lead to some of the highest T_c organic superconductors.[3a,5] The κ-phase salts form a unique two-dimensional array of conducting networks which accounts for the stability of the metallic state.[2,3b] Such discoveries continue to be the motivation behind the design and synthesis of new conducting materials which display unique electronic properties because of their three-dimensional stuctures.

We are interested in developing the synthesis and exploring the properties of coordination complexes of tetrathiafulvalenetetrathiolate ($\mathrm{TTFS_4}^{4-}$) (**2**) as potential building blocks for new two-dimensional electrical conductors and metal–TTF hybrid magnetic materials.[6] Compounds of this type have recently been targeted as potential new materials[7,8] for molecular electronics, molecular optical switches, and other telecommunication devices. The lack of development of these metal–TTF hybrid materials has been severly hampered by the inability to synthesize well-defined materials. Although a number of polymeric coordination complexes[9] of TTF have been reported, only one non-polymeric complex has been prepared. Although none of these compounds have been well characterized, their electrical and optical properties are extremely interesting.[9,10] One problem with the preparation of these inorganic compounds could be that the Schumaker and Engler preparation of **2**[11] produces ketones or carbonates and/or anionic species (which are derived from the reaction of dithiapendione and sodium methoxide or methyl lithium), which can compete for metal coordination sites with ligand **2**. This must lead to a mixture of products and subsequently cause difficulties in purification.

Theoretically, compound **2** can also be synthesized by the treatment of TTF with 4 equiv of LDA,[12,13] followed by 4 equiv of sulfur. However, recent work by Zambounis and Mayer[14] and Chiang[15,16] demonstrates that this route is generally ineffective in the synthesis of $\mathrm{TTFS_4}^{4-}$. Consequently, this procedure has not been used to make inorganic coordination complexes. We believed that it was important to develop a method to synthesize *only* $\mathrm{TTFS_4}^{4-}$ (**2**). Herein is described the first method for the exclusive generation, isolation, and purification of the highly air- and water-sensitive $\mathrm{TTFS_4}^{4-}$ (**2**).

The synthesis of **2**, from TTF and LDA, involves an equilibration between TTF/LDA and lithiated TTF/diisopropylamine (DIA).[12] A recent report claims that the equilibrium reaction does not provide "$\mathrm{TTFLi_4}$" exclusively with 4 equiv of LDA and that increasing the amount of base does not improve the yield of "$\mathrm{TTFLi_4}$".[14] This analysis was determined by trapping **2**, derived from "$\mathrm{TTFLi_4}$", with SEMCl. We have determined that an excess of base *can* shift the equilibrium and increase the amount of "$\mathrm{TTFLi_4}$". The treatment of TTF with 10 equiv of LDA, followed by 4.1 equiv of S (Scheme I, pathway A), provides a greatly improved yield of **2**,as determined from quenching studies. We purified the intermediate **2** by the following method. The reaction mixture was filtered in a dry box in order to remove excess sulfur and any other solid impurities. Compound **2** was then precipitated by the addition of excess dry hexane to the filtrate. Subsequent filtration and washing of **2** with hexane removed DIA and other hexane-soluble impurities. Solid $\mathrm{TTFS_4}^{4-}$ (**2**) was redissolved in dry THF and was then considered to be pure and ready for further reactions.

We have synthesized tetrakis(methylthio)tetrathiafulvalene (**3**)[17] in 50% yield after trapping **2** with excess

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(1) For reviews on the synthesis of TTF derivatives, see: (a) Krief, A. *Tetrahedron* **1986**, *42*, 1209. (b) Narita, M.; Pittman, C. *Synthesis* **1976**, 489. (c) Schukat, G.; Richter, A.; Fanghänel, E. *Sulfur Rep.* **1987**, *7*, 155.

(2) For an excellent introduction to the field, see: Cowan, D. O.; Wiygul, F. M. *Chem. Eng. News* **1986**, *64*, 28.

(3) For some recent reviews, see: (a) Williams, J. M.; Schultz, A. J.; Geiser, U.; Carlson, K. D.; Kini, A. M.; Wang, H. H.; Kwok, W.-K.; Whangbo, M.-H.; Schirber, J. E. *Science* **1991**, *252*, 1501. (b) Jerome, D. *Science* **1991**, *252*, 1509. (c) Bryce, M. R. *Chem. Soc. Rev.* **1991**, *20*, 355.

(4) For representative examples, see: (a) Kikuchi, K.; Kikuchi, M.; Namiki, T.; Saito, K.; Ikemoto, I.; Murata, K.; Ishiguro, T.; Kobayashi, K. *Chem. Lett.* **1987**, *931*. (b) Papavasssiliou, G. C.; Mousdis, G. A.; Zambounis, J. S.; Terzis, A.; Hountas, A.; Hilti, B.; Mayer, C. W.; Pfeiffer, J. *Synth. Met.* **1988**, *27*, B379. (c) Kikuchi, K.; Honda, Y.; Ishikawa, Y.; Saito, K.; Ikemoto, I. *Solid State Commun.* **1988**, *66*, 405. (d) Kini, A. M.; Beno, M. A.; Son, D.; Wang, H. H.; Carlson, K. D.; Porter, L. C.; Welp, U.; Vogt, B. A.; Williams, J. M.; Jung, D.; Evain, M.; Whangbo, M.-H.; Overmeyer, D. L.; Schirber, J. E. *Solid State Commun.* **1989**, *69*, 503.

(5) Very recently, fullerene-based superconductors have been found to possess superconductivity at temperatures higher than the ET-based superconductors, presumbly due to fullerene's three-dimensional band structure. The added dimensionality is thought to suppress structural phase transitions that are detrimental to the conducting state.

(6) (a) McCullough, R. D.; Seth, J.; Belot, J. A. *Synth. Met.* **1993**, *56*, 1989. (b) McCullough, R. D.; Belot, J. A.; Seth, J.; Proulx, G.; Talham, D. R. Unpublished results.

(7) Alverez, A.; Vicente, R.; Hoffman, R. *J. Am. Chem. Soc.* **1985**, *107*, 6253.

(8) (a) Oliver, S.; Winter, C. *Adv. Mater.* **1992**, *4*, 119. (b) Winter, C. S.; Hill, C. A. S.; Underhill, A. *Appl. Phys. Lett.* **1991**, *58*, 107.

(9) (a) In fact, only one molecular coordination complex of TTF has been reported, see: Rivera, N. M.; Engler, E. M.; Schumaker, R. R. *J. Chem. Soc., Chem. Commun.* **1979**, 184. (b) Poleschner, H.; John, W.; Hoppe, F.; Fanghänel, E. *J. Prakt. Chem.* **1983**, *325*, 957.

(10) Fanghänel, E.; Bierwisch, J.; Richter, A. M.; Beye, N. *Synth. Met.* **1992**, *47*, 87.

(11) Schumaker, R. R.; Engler, E. M. *J. Am. Chem. Soc.* **1977**, *99*, 5521. While the Schumaker and Engler preparation of **2** is useful for the synthesis of tetrathioalkyl derivatives of TTF, it is generally not useful for the preparation of well-characterized inorganic compounds.

(12) Aharom-Shalom, E.; Becker, J. Y.; Bernsteir, J.; Bittner, S.; Shark, S. *Tetrahedron Lett.* **1985**, *26*, 273.

(13) The reagent *n*-BuLi cannot be used for the metalation of TSF, because of ring-opening reactions, see: Rajeswari, S.; Jackson, Y. A.; Cava, M. P. *J. Chem. Soc., Chem. Commun.* 1988, 1089.

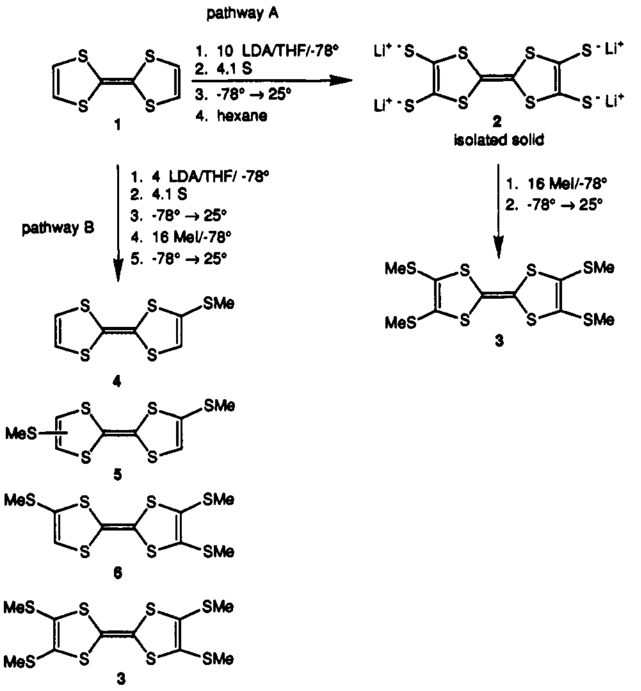
(14) Zambounis, J. S.; Mayer, C. W. *Tetrahedron Lett.* **1991**, *32*, 2741.

(15) Hsu, S.-Y.; Chiang, L.-Y. *J. Org. Chem.* **1987**, *52*, 3444.

(16) Although, the LDA route does not generally lead to $\mathrm{TTFS_4}^{4-}$ derivatives, the tetralithiated TTF can be effectively quenched with Se or Te metal. This method is generally used to synthesize $\mathrm{TTFSe_4}^{4-}$ and $\mathrm{TTFTe_4}^{4-}$ derivatives, see: (a) ref 15, (b) ref 12, (c) Okada, N.; Yamochi, H.; Shinozaki, F.; Ohima, K.; Saito, G. *Chem. Lett.* **1986**, 1861.

0022-3263/93/1958-6480\$04.00/0

Scheme I



MeI. Purification of **2** was surprisingly effective, as is seen by the ^{1}H NMR spectrum of the *isolated, crude product* (Figure 1, C). The NMR spectrum shows no visible TTF vinyl protons, even upon expanding the spectrum vertically 60×. In addition, the crude products derived from pathway A were examined by HPLC; this showed the presence of ≈85–95% of the desired product **3**. The HPLC was found to be slightly less accurate for the determination of absolute yield ratios since compound **3** is highly oxygen-sensitive and rapidly decomposes on the HPLC column.[18]

In contrast, the preparation of **2** via the literature method (Scheme I, pathway B),[12] followed by quenching the intermediate with MeI, produced a reaction mixture which contained at least 50–60% of mono-, di-, and trithiolated TTF derviatives (Scheme I, pathway B, **4**, **5**, and **6**) based on ^{1}H NMR of the quenched products. The results were variable from run to run, forming different product ratios of mono-, di-, and trithiolated TTFs (note Figure 1, A and B). This is apparently due to the highly sensitive nature of the numerous equilibrium reactions taking place. HPLC examination of the crude mixture, from one of these reactions, shows at least 10 products including five major products corresponding to **3**, **4**, two isomers of **5**, and **6**. In addition it was found that precipitation of the mixture of thiolate salts generated in the usual synthesis[12] of **2** using hexane followed by the quenching this mixture with MeI also gave approximately 50–60% yields of **4**–**6**. Zambounis and Mayer[14] have also found that the quenching of **2** gives a variety of products.

The preparation of compound **2** presented here has also been used in the synthesis of new $\mathrm{TTFS_4}^{4-}$–CdSe quantum dots[6a] and the first preparation of a well-characterized, bimetallic TTF coordination complex.[6b] The properties of these novel materials are currently being investigated.

Experimental Section

All reactions were performed under prepurified nitrogen or argon, using dry glassware. Glassware was either dried in an oven overnight or flame dried and then cooled under a stream of argon or nitrogen. Tetrahydrofuran was dried over Na benzophenone ketyl radical and freshly distilled prior to use. Diisopropylamine and hexane were dried and distilled from CaH_2 and stored in the glovebox. Sulfur (99.999%) was purchased from the Aldrich Chemical Co., dried under vacuum, and stored in a drybox. Tetrathiafulvalene (TTF) and iodomethane were purchased from Aldrich and used as received.

^{1}H NMR spectra were recorded at 300 MHz. Elemental analysis was performed by Midwest Microlab, Indianapolis, IN.

Preparation of Tetrathiofulvalenetetrathiolate (2). The reagent *n*-BuLi (6.2 mL of a 1.6 M solution in hexane, 9.92 mmol) was added to a solution of diisopropylamine (1.4 mL, 1.01g, 10 mmol) in dry THF (20 mL) at −78 °C under argon. After the solution was stirred for 0.75 h, tetrathiafulvalene (TTF) (0.20 g, 0.98 mmol) in dry THF (12 mL) was slowly added over 15 min to the LDA and the solution was stirred at −78 °C for 2.5 h. During the formation of the tetralithiated TTF, the solution became bright yellow and some solid particles appeared. Elemental sulfur (0.14 g, 4.1 equiv) was suspended in 5 mL of THF and added to the reaction flask. The solution was stirred at −78 °C for 1 h and then the cold bath was removed and the solution was stirred for an additional 4 h.[19] The brown solution was warmed to 25 °C during this period. The reaction vessel was transferred into a dry box. The solution was filtered to remove any solids (including residual sulfur). Compound **2** was then precipitated by the addition of dry hexane (250 mL) to the filtrate. The complete precipitation of **2** was facilitated by cooling the solution to −20 °C for a total of 0.5 h. The solution was filtered through a fritted glass funnel (medium porosity), and the solid was washed with 50 mL of hexane to remove diisopropylamine and other soluble impurities. The solid remaining on the filter was quantitatively transferred to a clean round-bottomed flask, and dry THF (≈90 mL) was added. The flask was sealed and removed from the dry box and then cooled to −78 °C and stirred under argon for 0.5–1 h, in order to redissolve **2**.[20] Compound **2** could now be quenched with a wide variety of electrophiles and metal salts.

Reaction of Precipitated and Purified 2 with Methyl Iodide. The Synthesis of Tetrakis(methylthio)tetrathiafulvalene (3). Methyl iodide (2.28 g, 1.0 mL, 16 mmol) was added to a dark brown solution of compound **2** (0.98 mmol assumed) and dry THF (90 mL) at −78 °C under argon. Within 10 min the reaction mixture became orange-brown and was allowed to stir at −78 °C for 1 h. The mixture was warmed to 25 °C over 1 h and then quenched with H_2O. The product was extracted with Et_2O (3 × 25 mL). The Et_2O layer was washed with H_2O until the washings were neutral to pH paper. The organic layer was dried over Na_2SO_4 and the solvent was removed on rotary evaporator to yield the solid product. The ^{1}H NMR ($CDCl_3$) of this crude, reddish solid showed no vinyl protons, a methyl singlet at 2.43 ppm, and two small additional singlets at 2.46 and 2.41 ppm, due to decomposition products. Filtration of this solid (dissolved in 2:1 Et_2O:pentane) through silica followed by solvent removal provided pure **3**. Recrystallization (CH_3CN) gave yellow platelets of **3** (190 mg, 50%), mp 95–96 °C (lit.[17] mp 94.5–96.0 °C). ^{1}H NMR ($CDCl_3$): δ 2.43 (s) ppm. Anal. Calcd for $C_{10}H_{12}S_8$: C, 30.93; H, 3.09. Found: C, 30.79; H, 3.07.

Methyl Iodide Quenching of 2 As Prepared Using 4 equiv of LDA and 4 equiv of S[12] without Precipitation. Tetrathiafulvalene (0.15 g, 0.74 mmol) in dry THF (12 mL) was slowly added over 15 min to a solution of LDA (3 mmol) in THF (6 mL) and the solution was stirred at −78 °C for 2.5 h. Subsequently, 4.1 equiv of sulfur (0.097 g) suspended in 3 mL of THF was added, and the solution was then stirred at −78 °C for 1 h. The cold bath was removed and the solution was stirred for an additional 3.5 h. The brown solution warmed to 25 °C during this period. The solution was cooled to −78 °C, and 16 equiv of MeI was added. The reaction mixture was allowed to stir at −78 °C for 1 h. The reaction was warmed to 25 °C over 1 h and quenched with H_2O, and the product was extracted with Et_2O (3 × 25 mL). The Et_2O layer was washed with H_2O until neutral

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(17) Moses, P. R.; Chambers, J. Q. *J. Am. Chem. Soc.* **1974**, *96*, 945.

(18) HPLC conditions were as follows: C-18 column, CH_3CN eluent.

(19) This time can range from 3 to 5 h.

(20) We have found that it is not necessary to completely redissolve 2 before allowing it to react with electrophiles or metal salts.

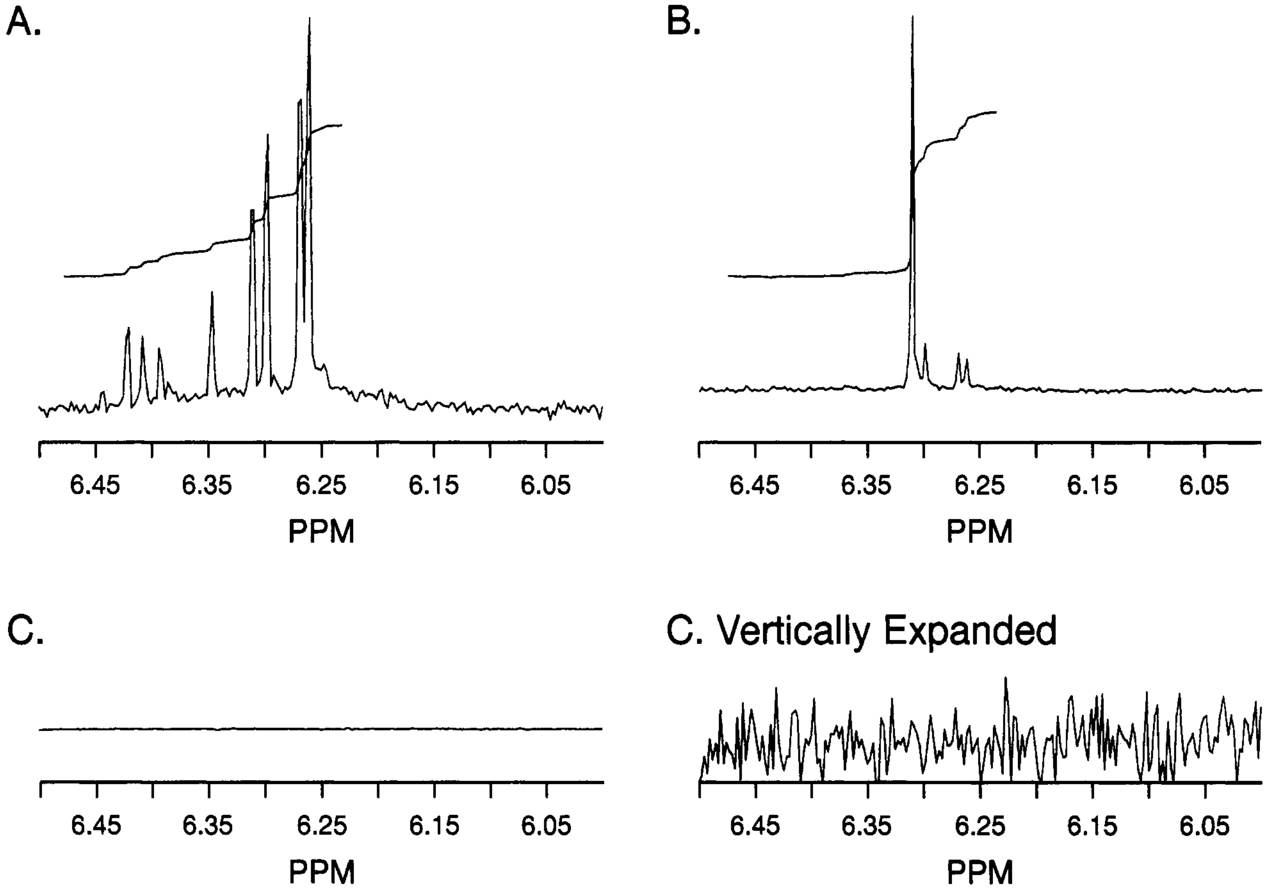

Figure 1. (A and B) Expanded ^1H NMR of vinyl region of the reaction of methyl iodide with the precipitated thiolate salts of **3**, **4**, **5**, and **6**, as prepared via literature method (see Experimental Section, reaction 3, runs 1 and 2, pathway B, with precipitation). Spectra A and B demonstrate the variability of the reaction. (C) Expanded ^1H NMR of vinyl region of a reaction of methyl iodide with **2** as prepared via new method. (C vertically expanded) Same vinyl region as (C), expanded vertically 60×.

and dried over Na_2SO_4, and the solvent was removed on a rotary evaporator to give an oil. The ^1H NMR ($CDCl_3$) of this crude mixture showed four major peaks at 6.32, 6.30, 6.27, and 6.26 ppm, which represent the vinyl protons on a tetrathiafulvalene skeleton. The spectrum showed five major methyl resonances, including singlets at 2.40, 2.39, 2.38, 2.37, and 2.27 ppm, which represent the five different TTF derviatives: monosubstituted, **4**, both *cis*-di- and *trans*-disubstituted, **5**, trisubstituted, **6**, and tetrasubstituted, **3**, TTFs). Chromatography of the crude product (silica, 3:1 pentane:CH_2Cl_2) did not lead to complete separation of the isomers. The weight and ^1H NMR spectrum of each isolated fraction indicates approximately 65% of **4**, **5**, and **6** and approximately 35% of **3**.

Methyl Iodide Quenching of Thiolate Salt Precursors of 3, 4, 5, and 6, with Precipitation. The general procedure for the preparation of **2** was identical to the above procedure.[12] After the sulfur was allowed to react completely, the reaction vessel was transferred into a dry box. The solution was filtered through a glass frit to remove any solids. The mixture of thiolate precursors of **3**, **4**, **5**, and **6** was precipitated by the addition of dry hexane (250 mL). This precipitation was facilitated by cooling the solution to −20 °C for 0.5 h. The solution was then filtered through a fritted glass funnel and the isolated solid was washed with hexane (50 mL). The solid on the filter was quantitatively transferred to a clean round-bottomed flask, and dry THF (≈90 mL) was added. The flask was removed from the dry box, cooled to −78 °C, and stirred under argon for 0.5–1 h in order to redissolve the mixture of thiolate precursors. Then MeI (2.28 g, 16 mmol) was added and the reaction mixture was allowed to stir at −78 °C for 1 h. The reaction was warmed to 25 °C over a 1-h period and then quenched with H_2O. The product was extracted with Et_2O (3 × 25 mL), the Et_2O layer was washed with H_2O until neutral and dried over Na_2SO_4, and the solvent was removed on a rotary evaporator to give an oil. Multiple runs of this reaction followed by the analysis of the products of the reaction mixture by ^1H NMR (Figure 1, A and B) and HPLC showed that 50–60% of **4**, **5**, and **6** and 40–50% of **3** were formed.

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