Improved Synthesis of the π-Electron Donor Bis(ethylenethio)tetrathiafulvalene (BET-TTF)

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Received 7 August 1998; revised 18 November 1998

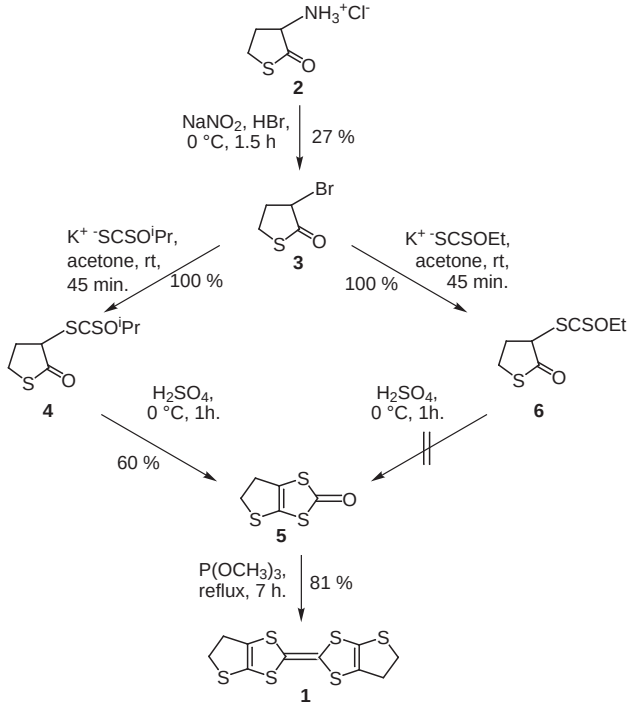
Abstract: Following a three step route, 5,6-dihydrothieno[2,3-*d*]-1,3-dithiol-2-one **(5)** was synthesized in gram quantities starting from commercially available reagents. Coupling of **5** with trimethyl phosphite gave the π-donor bis(ethylenethio)tetrathiafulvalene **1** in 80% yield.

Key words: tetrathiafulvalene analog, 1,3-dithiol-2-one, trimethyl phosphite, coupling reactions

Since the discovery of the metallic charge transfer complex TTF-TCNQ,[1,2] a large number of TTF analogs have been designed as electron-donating components to produce metallic or even superconducting cation radical salts.[3,4] The physical properties of these salts strongly depend on the electronic and structural features of the TTF derivative used, i.e. on its substituent pattern; those with sulfur atoms in cyclic substituents being the π-donors which gave rise to a larger number of superconductors.[3,4] We have been involved in the synthesis of new π-donors of the TTF family having a five-membered ring containing a sulfur atom as substituent of the TTF core.[5] One of them, BET-TTF (**1),** is an excellent donor which forms highly conducting cation radical salts with both diamagnetic[6–9] and paramagnetic counterions.[10] However, the previously reported syntheses of the BET-TTF donor[5, 11] produce only small amounts (~130 milligrams) of pure donor in each synthesis due to the poor yields of the steps involved and to the difficult purification of the intermediate compounds. Moreover, it takes more than one month to perform the complete synthesis. These facts have prompted us to improve the synthesis of the BET-TTF donor by changing the synthetic pathway towards one which gives the desired donor in gram quantities, thus allowing the preparation of different charge-transfer salts.

Since it is well known that to obtain TTF derivatives having sulfur atoms directly attached to the TTF core, the coupling of ketones gives better results than the coupling of thiones,[12–15] we have now developed a synthesis based on the coupling of the 1,3-dithiol-2-one **5**. The previous thiadiazole route[5] gave the thione precursors in very poor yields and the coupling of the thione gave the donor in only 23% yield.

First we made an adaptation of the thiolactone route developed by Larsen and Lenoir for the synthesis of bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF).[13] This synthesis consists of four steps (see Scheme 1) involving commercially available starting materials and the BET-TTF donor is obtained in good yields and gram quantities. The first step was the diazotization-bromination of DL-homocysteine thiolactone hydrochloride (**2)** to produce the α-bromo-γ-thiobutyrolactone (**3**), as reported by Miller and Heindel.[16] The nucleophilic displacement of the bromine atom in **3** by the *O*-isopropylxanthic group was achieved in 45 minutes and gave the crude product **4** pure enough to be used in further reactions.[17]



Scheme 1

The cyclization of the isopropylxanthic derivative **4** proceeds via its dehydration to give the corresponding 1,3-dithiol-2-one **5**. In contrast, the ethylxanthic derivative **6** (Scheme 1) does not give the ketone **5** but a dark red oil composed by a complex mixture of compounds that was not characterized.

Finally, the coupling of the ketone **5** to give **1** was accomplished in 7 hours by refluxing it with $P(OMe)_3$ in 81% yield. This yield is, as expected, much higher than that obtained by coupling of the corresponding thione (23%).[5] By recrystallization from chlorobenzene, high quality single crystals of the donor **1** were obtained and by X-ray dif-

fraction it was concluded that **1** exists in the crystals principally as the *E*-isomer as was also observed when the donor was obtained by coupling of the thione.[5]

Attempts to prepare the oxygen-containing analogue of **1** (bisethyleneoxo-tetrathiafulvalene) following the same procedure used in the synthesis of **1** failed because the precursor ketone **10** is not obtained, but instead, the disulfide **9** is formed (Scheme 2). Even though the acid-catalyzed ring closure of **8** was attempted by changing sulfuric acid for $HClO_4$[18] or CF_3CO_2H/AcOH/*p*-toluenesulfonic acid mixture,[19] the ketone **10** was never detected. The ring closure of **8** was also attempted with P_2O_5 in refluxing decalin but surprisingly the former oxygen atom of the lactone was replaced by sulfur giving **5** instead of the analogue **10**. A similar exchange was described by Engler et al. for the cyclization of the ethyl analogue of **8** with P_4S_{10}.[11] This procedure for the synthesis of **5** directly from **8** is very interesting since it starts from a commercial product, α-bromo-γ-butyrolactone (**7**), and avoids the tedious synthesis of the α-bromo-γ-thiobutyrolactone **(3)**. Moreover, the total yield for the synthesis of the ketone **5** following the route **2** → **3** → **4** → **5** (Method A, 15%) is similar to the yield obtained following the route **7** → **8** → **5** (Method B, 10%).

In conclusion, we have presented an improved synthesis of the π-electron donor bis(ethylenethio)tetrathiafulvalene (BET-TTF) (**1**) based on the coupling of the 1,3-dithiol-2-one **5**. With the current methodology it is possible to produce gram amounts of the donor in 2–3 days (Method A) starting from commercially available products, since not only the overall yield has been improved but also the intermediate compounds are readily purified; one of them, compound **5**, should be valuable in the synthesis of new disymmetric TTF derivatives.

DL-Homocysteine thiolactone hydrochloride **(2)**, α-bromo-γ-butyrolactone **(7)**, potassium *O*-ethyldithiocarbonate and potassium *O*-(isopropyl)dithiocarbonate were purchased from Aldrich and used as received. α-Bromo-γ-thiobutyrolactone **(3)** was obtained following the procedure reported by Miller and Heindel.[16]

FT-IR spectra were recorded on a Nicolet 710 spectrometer, ^{1}H NMR and ^{13}C NMR on a Bruker ARX 300, and the mass spectra on a Hewlett-Packard 5989X. Elemental analyses were performed using the Elemental Analyser EA 1108 (Carlo Erba Instruments). Melting points were measured in an electrothermal apparatus and were uncorrected.

Tetrahydro-3-(*i*-propoxythiocarbonylthio)-2-oxothiophene (4)

α-Bromo-γ-thiobutyrolactone (**3**; 7.17 g, 0.04 mol) was added with stirring to a suspension of potassium *O*-(*i*-propyl)dithiocarbonate (7.28 g, 0.04 mol) in anhyd acetone (250 mL) at r.t. in the dark. After stirring for 45 min, the precipitate (KBr) formed was filtered off and the solvent was removed under reduced pressure to give a green oil.[20] The oil was washed with H_2O and extracted with Et_2O. The organic phase was dried ($MgSO_4$) and the solvent was evaporated to yield 9.3 g (~100%) of **4** as a stable orange oil. In order to obtain an analytically pure sample, the oil was purified by flash chromatography on silica gel, eluting with EtOAc/hexanes (1:3) to give **4** in an almost quantitative yield.

IR (film): ν = 1706 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.40 [dd, 6 H, *J* = 6.3 Hz, $CH(CH_3)_2$], 2.45 (m, 1 H, $SCHCH_2$), 2.85 (m, 1 H, $SCHCH_2$), 3.51 (m, 2 H, SCH_2), 4.55 (m, 1 H, SCH), 5.74 [sept, 1 H, *J* = 6.3 Hz, $CH(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 21.1, 30.0, 31.9, 57.6, 79.2, 202.4, 210.3

Anal. calcd for $C_8H_{12}O_2S_3$ (236.4): C, 40.65; H, 5.12; S, 40.69. Found C, 40.56; H, 5.11; S, 40.60.

5,6-Dihydrothieno[2, 3-d]-1, 3-dithiol-2-one (5)

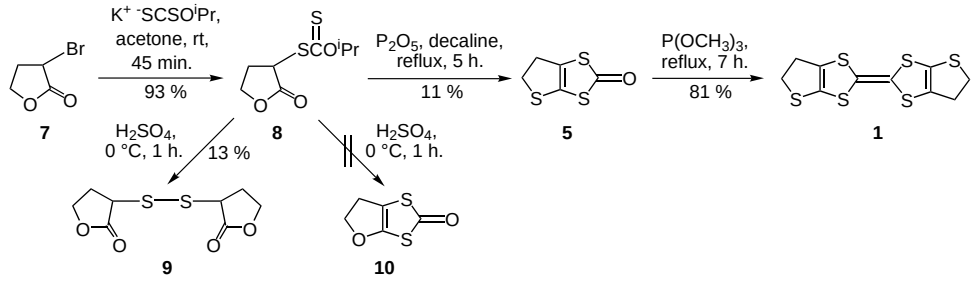
Method A: Compound **4** (9.3 g, 0.039 mol) was added dropwise to a stirred ice-cooled solution of concd H_2SO_4 (300 mL). After the addition was complete, the stirring was maintained for 1 h at r.t. and then the mixture was poured slowly onto ice (1 L) and extracted with toluene (4 × 300 mL). The combined organic layers were washed with H_2O (3 × 100 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with a mixture of CH_2Cl_2/hexanes (1:10). The ketone **5** was eluted pure in the second fraction or with the little less polar impurity which could be eliminated easily by recrystallization from hexanes to yield 4.15 g (60%) of **5** as white needles; mp 85–86 °C (Lit.[11] mp 84–85 °C).

^{1}H NMR ($CDCl_3$): δ = 3.10 (t, 2 H, *J* = 8.1 Hz, SCH_2CH_2), 3.55 (t, 2 H, *J* = 8.1 Hz, SCH_2).

^{13}C NMR ($CDCl_3$): δ = 33.0, 34.6, 118.0, 122.9, 195.1

Anal. calcd for $C_5H_4S_3O$ (176.3): C, 34.09; H, 2.27; S, 54.54. Found C, 34.32; H, 2.20; S, 54.35.

Method B: A solution of the compound **8** (6.85 g, 0.031 mol) in decalin (70 mL) was refluxed with P_2O_5 (4.37 g, 0.031 mol) for 4 h. The mixture was then stirred for 2 d at r.t. and purified by flash chromatography on silica gel eluting with a mixture of CH_2Cl_2/hexanes (1:10). Recrystallization from hexanes gave 0.6 g of white needles (11%) of **5**; mp 85–86 °C.



Scheme 2

5,5', 6,6'-Tetrahydro-$\Delta^{2,2'}$-bithieno[2,3-*d*]-1,3-dithiol (1)
Ketone **5** (2.05 g, 0.0116 mol) was dissolved in freshly distilled trimethyl phosphite (26 mL) and refluxed for 7 h under an argon atmosphere, during which time red crystals of **1** precipitated. After cooling to r.t., the product was filtered off, washed with Et_2O and dried; yield: 1.5 g (81%). Recrystallization from chlorobenzene afforded 1.40 g (75 %) of **1** as scarlet crystals. All spectroscopic data were in accordance with those previously reported;[5,11] mp 194–197 °C (dec) (Lit.[11] mp 195–196°C).

2-Oxo-3-(*i*-propoxythiocarbonylthio)tetrahydrofuran (8)
α-Bromo-γ-butyrolactone (**7**; 15.84 g, 0.096 mol) was added with stirring to a suspension of potassium *O*-(*i*-propyl)dithiocarbonate (16.74 g, 0.096 mol) in anhyd acetone (170 mL) at r.t.in the dark. After stirring for 45 min, the precipitate (KBr) formed was filtered off and the solvent was eliminated under reduced pressure to give a pink oil.[20] The crude product was washed with H_2O and extracted with Et_2O. The organic phase was dried ($MgSO_4$) and the solvent was evaporated to yield 19.7 g (93%) of **8** as a stable yellow oil.

IR (film): ν = 1776 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21 [dd, 6 H, *J* = 6.2 Hz, $CH(CH_3)_2$], 2.28 (m, 1 H, $SCHCH_2$), 2.70 (m, 1 H, $SCHCH_2$), 4.21 (m, 3 H, SCH, OCH_2), 5.55 [sept, 1 H, *J* = 6.2 Hz, $CH(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 21.1, 29.7, 45.6, 66.6, 79.4, 173.4, 209.5

Anal. calcd for $C_8H_{12}O_3S_2$. (220.3): C, 43.63; H, 5.50; S, 29.06. Found C, 43.21; H, 5.44; S, 28.82.

3, 3'-Dithiobisdihydro-2-furanone (9)
Compound **8** (8 g, 0.0363 mol) was added dropwise to a magnetically stirred ice-cooled solution of concd H_2SO_4 (300 mL). After the addition was complete, the stirring was maintained for 1 h at r.t. and then the solution was poured onto ice (1 L) and extracted with toluene (4 × 300 mL). The solvent was removed at reduced pressure to give a yellow oil. Et_2O and acetone were added to the oil until a homogeneous solution was formed. The solution was chilled at 5 °C for 2 d to give a white solid that was purified by flash chromatography on silica gel eluting with CH_2Cl_2/acetone (1:1). White needles of **9** were obtained (560 mg, 13%); mp 115–116 °C (Lit.[21] mp 111–113 °C).

IR (KBr) ν = 1747, 1774, 3472, 3520 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.53 (m, 1 H, SCH_2CH_2), 2.79 (m, 1 H, SCH_2CH_2), 3.92 (m, 1 H, SCH_2), 4.35 (m, 1 H, SCH_2), 4.50 (m, 1 H, SCH).

^{13}C NMR ($CDCl_3$): δ = 29.3, 46.2, 66.7, 174.6.

Anal. calcd for $C_8H_{10}O_4S_2$ (170.3): C, 41.01; H, 4.30; S, 27.37. Found C, 40.96; H, 4.23; S, 27.39.

MS: *m*/*z* (%) = 86 (26), 118 (100), 149 (4), 234 (M^+, 9).

Acknowledgement

This work was supported by the Ministerio de Educación y Cultura (DGCYT), Grant PB 96-0872-C02-01) and the Generalitat de Catalunya (CIRIT) SGR 96-00106. A. P-B. thanks the CONACyT for a predoctoral fellowship and the Universidad Autónoma de Puebla for on live permission.

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