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An Improved Route to 3,4-Thiophenedithiolate

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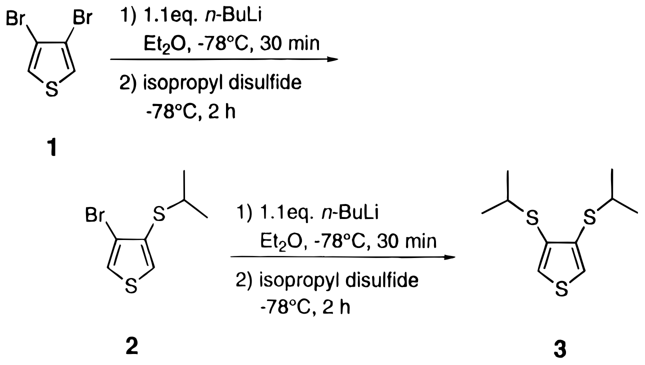
Molecules bearing thiol groups have become increasingly important as entries into self-assembled materials[1] and unique coordination compounds for electronic, magnetic, and optical materials.[2] In particular, thiol-containing compounds in which the nucleus is a heterocyclic ring allows for the facile coupling of open sites through chemical or electrochemical means. Thiophene is an extremely attractive choice as its chemistry has been well explored and offers a myriad of synthetic options.

To date, there has been no convenient source of 3,4-thiophenedithiolate. The most common synthesis[3] is a one-pot reaction involving monolithiation of 3,4-dibromothiophene, treatment with elemental sulfur, and repetition of the cycle once again. However, for ease of purification, the dithiolate is treated with CS_2, allowing cyclization to the thione derivative. (Upon recrystallization, the thione can be treated with alkali metal to regenerate the dithiolate.) While the original paper reports a yield of 33% for the thione, based on 3,4-dibromothiophene, other work has found yields to be less than 25%.[4] Preliminary experiments in our laboratories confirm these lower yields, and we have found this reaction to be temperamental. A second method utilizes the formation of 3,4-dilithiothiophene and subsequent trapping with sulfur flowers.[5] We found this route to be unacceptable due to the large amount of butylthiophenes formed in the reaction. With the wealth of applications existing for the use of the dithiolate, such as various poly(alkylthio)thiophenes[6] and electropolymerizable coordination compounds, an alternative synthesis was sought.

There are many examples in the literature that involve the conversion of (isopropylthio)benzenes to their corresponding benzenethiolates by treatment with alkali metals in solvents such as NH_3, HMPA, and pyridine.[7] We chose to pursue this alternative pathway to determine its applicability to heterocycles, namely thiophene. To arrive at the target molecule 3,4-thiophenedithiolate **4** in this manner, the precursor 3,4-bis(isopropylthio)thiophene (BITT) (**3**) was required. Initial attempts using 3,4-dibromothiophene and cuprous mercaptide resulted almost exclusively in monosubstitution, even after variation of solvent and reaction time. Yabukov *et al.*[8] had prepared a number of dimercaptothiophenes, and a variation of their method was employed.

Scheme 1



The synthesis of **3** was accomplished in two steps, starting from 3,4-dibromothiophene (**1**), in 60−70% yield based on **1** (Scheme 1).

In a typical procedure, **1** was treated with 1.1 equiv of *n*-butyllithium at low temperatures to promote lithium−halogen exchange. The lithiothiophene species was then treated with isopropyl disulfide to yield compound **2**, which was isolated by simple extraction and removal of solvent. It is imperative that the thienyllithium derivatives not be allowed to warm above −30 °C, as rearrangements take place. The products of these rearrangements have not been identified, but they likely involve lithium exchange from the β-carbon to the α-carbon. Crude **2**[9] was then subjected to the same treatment as with **1**, and similar workup gave the target molecule **3**, which was purified by vacuum distillation. We have attempted to condense this procedure by generating the dilithio species; however, the result is usually a mixture of isomeric products, which are inseparable by standard distillation.

Treatment of **3** with sodium in pyridine at 105 °C was found to generate 3,4-thiophenedithiolate with exceptional ease as illustrated by Scheme 2. Trapping experiments with methyl iodide indicate that cleavage of the aliphatic carbon−sulfur bond appears to be near quantitative, as the ^{1}H NMR of the product (crude **5**) shows no signals due to isopropyl groups within the sensitivity of the instrument.

We have also begun preliminary derivitization of **4** to demonstrate the utility of this synthon. Alkylation, arylation, esterification, and transition metal complexation will yield a number of unique molecular building blocks for electronic materials and polymers.

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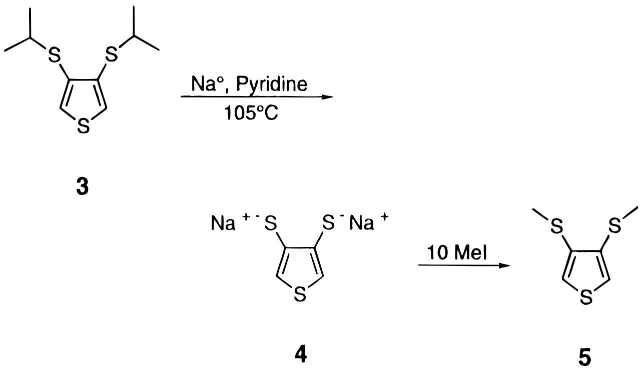
(9) Compound **2** can be purified by vacuum fractional distillation if desired (123 °C, 5 Torr): ^{1}H NMR δ 1.26 (d, 6H), 3.31 (m, 1H), 7.21 (br, 2H).

S0022-3263(96)00336-2 CCC: $12.00

Scheme 2



Experimental Section

All reactions were performed under prepurified nitrogen or argon, using Schlenk-type techniques. Glassware was dried in an oven overnight or flame dried and then cooled under a stream of inert gas. All melting points are uncorrected. NMR spectra were obtained on a 300 MHz spectrometer with Me_4Si as internal standard and $CDCl_3$ as solvent. Mass spectral anaylses were performed by the University of Florida Mass Spectral Services, Gainesville, FL. Elemental Analyses were performed by Robertson Microlabs, Madison, NJ.

Tetrabromothiophene[10] and 3,4-dibromothiophene[11] were prepared by previously reported procedures. Tetrahydrofuran and diethyl ether were dried over Na/K benzophenone ketyl radical, methanol over magnesium metal, and pentane over CaH_2, and all were distilled prior to use. Thiophene, isopropyl disulfide, *n*-butyllithium (2.5 M in hexanes), and methyl iodide were purchased from Aldrich Chemical Co. and used as received.

Note: All reactions using the disulfide are accompanied by a stench, which is caused by the thiolate byproduct! All manipulations should be carried out in an efficient fume hood with KOH traps placed between the product and any aspirators.

3-Bromo-4-(isopropylthio)thiophene (2). A solution of 3,4-dibromothiophene (15 g, 0.062 mol) in anhydrous diethyl ether (125 mL) was stirred and cooled to −78 °C under argon while *n*-butyllithium (27.3 mL, 0.0682 mol) was slowly added *via* syringe. After the mixture was stirred for 0.5 h, isopropyl disulfide (10.23 g, 0.0682 mol) was added. The entire mixture was stirred at −78 °C for 2 h and the dry ice−acetone bath removed. The reaction was allowed to warm naturally, and when the temperature reached −35 °C 20 mL of water was added. The contents of the flask were poured into 300 mL of water and the phases separated, and the aqueous phase was extracted several times with ether (3 × 25 mL). The combined organic phases were washed twice with a 2 M KOH solution and then once with water. Upon drying with $MgSO_4$, the solvent was removed under reduced pressure, yielding **2** as a viscous oil (crude yield: 11.77 g, 80%).

Bis(isopropylthio)thiophene (BITT) (3). **2** (11.77 g, 0.05 mol) was treated using a procedure that was identical for its preparation. Identical workup yielded a colored viscous oil, which upon distillation at reduced pressure (150 °C, 5 Torr) gave **3** as a colorless oil (7.80 g, 76.7%). ^1H NMR: δ 1.27 (d, 12 H), 3.38 (m, 2 H), 7.19 (s, 2H). ^{13}C NMR: 23.0, 38.1, 125.4, 133.9. Anal. Calcd: C, 51.68; H, 6.94. Found: C, 51.44; H, 6.72. FAB-HRMS: calcd for $C_{10}H_{16}S_3$ 233.049 (M + 1), found 233.049.

Methyl Iodide Trapping of 4. Pyridine (30 mL) and **3** (0.580 g, 0.005 mol) were stirred and heated to 105 °C, whereupon sodium metal (0.75 g atom) was added. The resulting blue/purple solution was stirred at this temperature for 1.5 h and allowed to cool to rt, and methanol (5 mL) was *CAUTIOUSLY* added *via* syringe. Methyl iodide (1.42 g, 0.1 mol) was then added, and the reaction mixture was stirred for 0.5 h. The contents of the flask were poured into water (300 mL) and the product extracted with ether. The ether layer was washed with water until neutral and dried over $MgSO_4$ and the solvent removed. The resulting dark oil was then placed on a vacuum line (10^{-2} Torr) to further remove any residual volatiles, leaving behind **5**. This crude material was analyzed by ^1H and ^{13}C NMR and showed no detectable amount of $-CH(CH_3)_2$ residue relative to product integration.

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