ORGANIC LETTERS

2001
Vol. 3, No. 12
1941−1944

A New Approach to 4-Alkylthio-1,3-dithiole-2-thione: An Unusual Reaction of a Zinc Complex of 1,3-Dithole-2-thione-4,5-dithiolate

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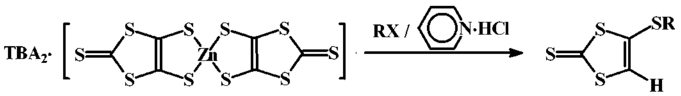
Received April 16, 2001

ABSTRACT



A new and facile approach to 4-alkylthio-1,3-dithiole-2-thione starting from easily accessible reactants was described. This approach was based on the unusual reaction of a zinc complex of 1,3-dithiole-2-thione-4,5-dithiolate with electrophilic reagents in the presence of 3-picolyl chloride hydrochloride/or 4-picolyl chloride hydrochloride/or pyridine hydrochloride.

Since the discovery of the first organic metal TTF·TCNQ (TTF, tetrathiafulvalene; TCNQ, 7,7,8,8-tetracyanoquinodimethane),[1] organic electron donors with a TTF backbone have been widely investigated in terms of synthetic and structural as well as physical aspects.[2] The most conventional route to these electron donors is based on the coupling of 1,3-thiole-2-thione (one) derivatives promoted by trialkyl phosphite.[3] Thus, the key precursors to these TTF-based electron donors are 1,3-thiole-2-thione (one) derivatives. Among them, 4,5-bisalkylthio-1,3-dithiole-2-thione **1** (Figure 1) can be routinely prepared by the reaction between a zinc complex of 1,3-dithiole-2-thione-4,5-dithiolate **2** (Figure 1) or the anion 1,3-dithiole-2-thione-4,5-dithiolate generated in situ and suitable electrophilic reagents.[4] The analogue of **1**, 4-alkylthio-1,3-dithiole-2-thione **3** (Figure 1), however, is not easily accessible. Only a few approaches to **3** were described, which include the electrochemical method[5] and that reported

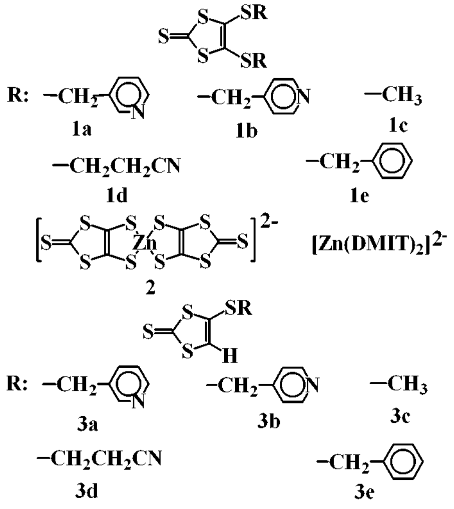


Figure 1.

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(1) Ferraris, J.; Cowan, D. O.; Walatka, V. J.; Perlstein, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 948.

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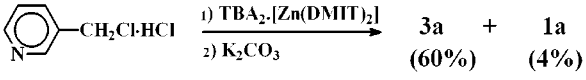
(3) (a) Bechgaard, K.; Cowan, D. O.; Bloch, A. N. *J. Org. Chem.* **1975**, *40*, 746. (b) Engler, E. M.; Scott, B. A.; Etemad, S.; Penney, T.; Patel, V. V. *J. Am. Chem. Soc.* **1977**, *99*, 5909. (c) Kini, A. M.; Parakka, J. P.; Geiser, U.; Wang, H.-H.; Rivas, F.; DiNino, E.; Thomas, S.; Dudek, J. D.; Williams, J. M. *J. Mater. Chem.* **1999**, *9*, 883. (d) Li, H.-X.; Zhang, D.-Q.; Zhang, B.; Yao, Y.-X.; Xu, W.; Zhu, D.-B.; Wang, Z.-M. *J. Mater. Chem.* **2000**, *10*, 2063.

10.1021/ol015990n CCC: $20.00

by Otsubo et al. starting from trimethylsilylacetylene.[6] In this Letter, we wish to report a new approach to 4-alkylthio-1,3-dithiole-2-thione **3**.

With the initial goal of synthesizing 4,5-bis(3-picolylthio)-1,3-dithiole-2-thione **1a** (Figure 1), 3-picolyl chloride hydrochloride was reacted with the tetra(*n*-butyl)ammonium salt of **2**, TBA_2•[Zn(DMIT)$_2$], at 50−60 °C (method A).[7] After neutralization with K_2CO_3 and purification, in contrast to our expectation, a new compound in addition to **1a**[8] (isolated in 4% yield) was obtained in 60% yield (Scheme 1). In its FAB-MS spectrum, a molecular ion peak at *m*/*z* 258 was detected. Signals at 4.13 (s), 6.97 (s), and 7.64−8.78 (m) ppm in a 2:1:4 ratio were found in its ^{1}H NMR spectrum, and nine signals at 210.0, 128.8, 130.9, 136.7, 144.7, 149.9, 150.3, 123.7, and 39.7 ppm in its ^{13}C NMR spectrum. On the basis of these spectroscopic data, we proposed the chemical structure of this new compound as 4-(3-picolylthio)-1,3-dithiole-2-thione (**3a**).

Scheme 1



To establish the structure of this unexpected compound completely, single crystals of good quality were grown from dichloromethane, and the X-ray diffraction analysis results[9] confirmed that this compound was **3a**. Figure 2 shows the molecular structure of **3a**.

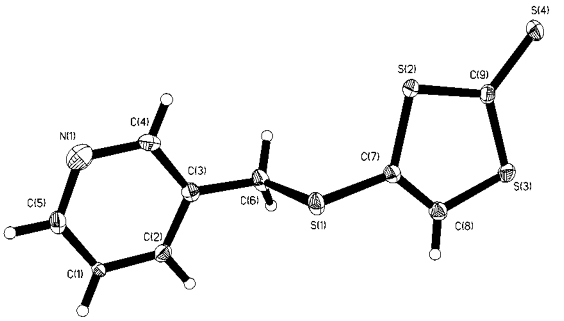
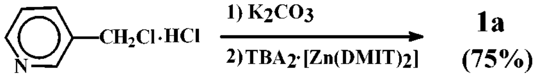


Figure 2. Molecular structure of compound **3a**.

By varying the reaction sequences, i.e., 3-picolyl chloride hydrochloride was first neutralized by K_2CO_3 and reacted further with TBA_2•[Zn(DMIT)$_2$] (method B)[10] at 50−60 °C, only compound **1a** was detected, as expected (Scheme 2).

Scheme 2



Efforts were also made to prepare single crystals of **1a**, and its crystal structure was also determined.[11] Figure 3 displays the chemical structure of **1a**.

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(5) (a) Falsig, M.; Lund, H. *Acta Chem. Scand. B* **1980**, *34*, 591. (b) Wawzonek, S.; Heilmann, S. M. *J. Org. Chem.* **1974**, *39*(4), 511.

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(7) **The reaction was performed as follows:** The mixture of TBA_2•[Zn(DMIT)$_2$] (2.15 g, 2.28 mmol) and 3-picolyl chloride hydrochloride (1.5 g, 9.15 mmol) dissolved in 50 mL of acetonitrile was stirred at 50−60 °C for 2 h. After that, solvents were removed under reduced pressure. The resulting solid was treated with 40 mL of a saturated solution of K_2CO_3. The above suspension was extracted with CH_2Cl_2 (3 × 50 mL), and the organic phase was combined, washed with water (3 × 20 mL), and dried with anhydrous $MgSO_4$. This dichloromethane solution was decolorized by heating with activated charcoal. Column chromatography of the crude product after removing the solvents on silica gel with ethyl acetate afforded compound **3a** as a yellow solid (0.70 g, 60%) and **1a** as a yellow solid (6.7 mg, 4%).

(8) All new compounds as well as **3c** and **3e** were characterized by spectroscopic methods and elemental analysis. **3a**: mp 90−91 °C; ^{1}H NMR ($CDCl_3$) δ 4.13 (s, 2H, -CH_2-), 6.97(s, 1H, olefinc), 7.64−8.78 (m, 4H, pyridine); ^{13}C NMR ($CDCl_3$) δ 210.0 (-C=S), 128.8, 130.9, 136.7, 144.7, 149.9, 150.3 (pyridine and olefinic), 123.7 (olefinic, CH) and 39.7 (-CH_2-); FAB-MS 258 (M + 1); IR ν (KBr) 1055 cm^{-1} (-C=S). Anal. Calcd for $C_9H_5NS_4$: C, 42.00; H, 2.74; N, 5.44. Found: C, 42.03; H, 2.55; N, 5.22. **3b**: mp 111−112 °C; ^{1}H NMR ($CDCl_3$) δ 3.94(s, 2H, -CH_2-), 6.897 (s, 1H, olefinic), 7.18−7.21 (“dd”, 2H), 8.59−8.62 (“dd”, 2H) (pyridine); ^{13}C NMR ($CDCl_3$) δ 40.1 (-CH_2-), 123.6 (CH, olefinic), 150.2, 145.1, 133.8, 133.5 (pyridine), 213.4 (-C=S); FAB-MS 258 (M + 1); IR ν (KBr) 1063 cm^{-1} (-C=S). Anal. Calcd for $C_9H_5NS_4$: C, 42.00; H, 2.74; N, 5.44. Found: C, 42.11; H, 2.57; N, 5.27. **3c**: mp 71−72 °C (lit.[6] mp 73.5−74.5 °C); ^{1}H NMR ($CDCl_3$) δ 2.51 (s, 3H, -CH_3), 6.90 (s, 1H, olefinic); EI-MS 180 (M$^+$, 100%); IR ν (KBr) 1061 cm^{-1} (−C=S). Anal. Calcd for $C_4H_4S_4$: C, 26.68; H, 2.24. Found: C, 26.45; H, 2.12. **3d**: mp 80−81 °C; ^{1}H NMR ($CDCl_3$) δ 2.76−2.82 (t, *J* = 6 Hz, -CH_2-), 3.12−3.19 (t, *J* = 6 Hz, -CH_2-), 7.18 (s, 1H, olefinic); ^{13}C NMR ($CDCl_3$) 18.6 (-CH_2-), 31.7 (-CH_2-), 117.0 (-CN), 132.6, 135.0 (olefinic), 213.7 (-C=S); EI-MS 219 (M$^+$, 100%); IR ν (KBr) 1062 cm^{-1} (-C=S). Anal. Calcd for $C_6H_5NS_4$: C, 32.85; H, 2.30; N, 6.39. Found: C, 32.76; H, 2.21; N, 6.36. **3e**: mp 44−45 °C (lit.[5a] mp 48 °C); ^{1}H NMR ($CDCl_3$) δ 3.99 (s, 2H, CH_2), 6.77 (s, 1H, olefinic), 7.21−7.40 (m, 5H, phenyl); EI-MS 256 (M$^+$, 22%). IR ν (KBr) 1062 cm^{-1} (-C=S). Anal. Calcd for $C_{10}H_8S_4$: C, 46.84; H, 3.14. Found: C, 46.42; H, 2.91. **1a**: mp 107−109 °C; ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 4H, -CH_2-), 7.15−7.31, 7.55−7.59, 8.49−8.58 (m, 8H, pyridine); ^{13}C NMR (CCl_4) δ 57.0 (-CH_2-), 123.8, 132.6, 136.6, 137.2, 148.9, 149.9 (pyridine, olefinic), 213.3 (-C=S); FAB-MS 381 (M + 1); IR ν (KBr) 1058 cm^{-1} (-C=S). Anal. Calcd for $C_{15}H_{12}N_2S_5$: C, 47.34; H, 3.18; N, 7.36. Found: C, 46.99; H, 3.14; N, 7.19. **1b**: mp 144−145 °C; ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 4H, -CH_2-), 7.16−7.19 (d, *J* = 6 Hz, 2H), 8.58−8.61 (d, *J* = 6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 38.6 (-CH_2-), 123.6, 133.8, 136.3, 149.3, 150.0 (pyridine, olefinic), 213.372 (C=S); FAB-MS 381 (M + 1); IR ν (KBr) 1063 cm^{-1} (−C=S). Anal. Calcd for $C_{15}H_{12}N_2S_5$: C, 47.34; H, 3.18; N, 7.36. Found: C, 46.95; H, 3.08; N, 7.12.

(9) Crystal data for **3a**: $C_9H_7NS_4$, $M = 257.40$, monoclinic, $C2/c$, $a = 12.996(3)$, $b = 7.934(2)$, and $c = 22.205(4)$ Å, $\beta = 109.62(3)°$, $V = 2156.6(8)$ Å^3, $Z = 8$, $D_c = 1.585$ g•cm^{-3}. A total of 2152 observed reflections [$I > 2\sigma(I)$] and 130 variable parameters converged to $R = 0.0357$ and wR = 0.1062.

(10) A total of 42.15 mg (0.3mmol) of K_2CO_3 was dissolved in less than 5 mL of water, and 100 mg (0.61 mmol) of 3-picolyl chloride hydrochloride was added at room temperature. After the gas evolution was stopped, a colorless dense liquid was present. Subsequently, 143.35 mg (0.15 mmol) of TBA_2•[Zn(DMIT)$_2$] dissolved in 15 mL of acetonitrile was mixed with this dense liquid, and the solution was stirred at 50−60 °C for 1.5−2 h. The reaction mixture was filtered, and the solid residue was washed twice with dichloromethane (20 mL). The combined filtrate and washings were decolorized by activated charcoal. After removing the solvent, column chromatography of the crude reaction mixture on silica gel with ethyl acetate/methanol (10:1) afforded compound **1a** as a yellow solid (85.5 mg, 75%).

(11) Crystal data for **1a**: $C_{30}H_{24}N_4S_{10}$, $M = 380.57$, monoclinic, $P2(1)/c$, $a = 19.646(4)$, $b = 5.849(1)$, and $c = 29.643(6)$ Å, $\beta = 101.67(3)°$, $V = 3335.8(11)$ Å^3, $Z = 4$, $D_c = 1.516$ g•cm^{-3}. A total of 5037 observed reflections [$I > 2\sigma(I)$] and 397 variable parameters converged to $R = 0.0384$ and wR = 0.1007.

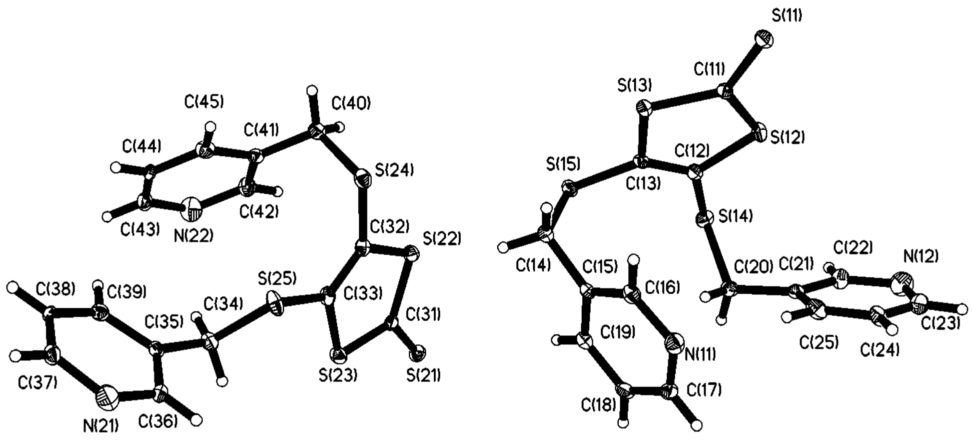

Figure 3. The asymmetric unit of crystal **1a**.

Similar reactions were conducted with 4-picolyl chloride hydrochloride. Compounds **3b** and **1b** (Figure 1) were obtained after purification in yields of 60% and 9%, respectively, by method A. Only compound **1b** was produced (68%) with method B. Although method A and method B differ only in the reaction sequences, completely different reactions take place. Since both 3-picolyl chloride hydrochloride and 4-picolyl chloride hydrochloride are weakly acidic, it seems that acidic reaction medium is essential for the formation of **3a** and **3b**. Thus, we assume that compound **4** (Figure 4) is the key reaction intermediate for the above reactions with method A. The unusual chemical reactivity of **4** was once reported by Rauchfuss et al.[12] A detailed investigation of this reaction mechanism is in progress.

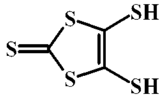

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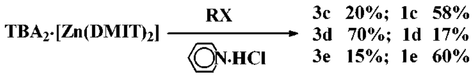
Figure 4.

Accordingly, both 3-picolyl chloride hydrochloride and 4-picolyl chloride hydrochloride may be considered to have two roles for the reactions in method A: weak acid and electrophile. Therefore, by replacing 3-picolyl chloride hydrochloride or 4-picolyl chloride hydrochloride with pyridine hydrochloride and an appropriate electrophilic reagent, it would be possible to prepare other analogues of **3a** and **3b** by an approach similar to method A. Preliminary experimental results were rather encouraging. Namely, pyridine hydrochloride and $TBA_2 \cdot [Zn(DMIT)_2]$ were reacted with an electrophilic reagent such as methyl iodide, 3-bromopropionitrile, or benzyl chloride at 50−60 °C for 1−2 h.[13] After separation and purification, the corresponding 4-alkylthio-1,3-dithole-2-thiones **3c**, **3d**, and **3e** (Figure 1) were obtained in addition to the 4,5-bisalkylthio-1,3-dithole-2-thiones **1c**, **1d**, and **1e** (Figure 1) as indicated in Scheme 3.

Scheme 3



The reaction yield for **3c** and **3e** was not high, probably due to the high reactivity of methyl iodide and benzyl chloride which will induce them to react with $TBA_2 \cdot [Zn(DMIT)_2]$ directly, forming **1c** and **1e**, respectively. Compound **3d**, on the contrary, was separated in fairly high yield. It should be mentioned that the reaction condition was not optimized for each case. Efforts are being made in this regard to improve the reaction yield for **3c**, **3d**, and **3e**. Among the compounds **3a−e**, **3d** is most interesting since 2-cyanoethyl is a good protecting group widely employed in the chemistry of 1,3-dithiole-2-thione-4,5-dithiolate,[4] and it can be used for the synthesis of other derivatives of 4-alkylthio-1,3-dithole-2-thione.

In summary, a new and facile approach to 4-alkylthio-1,3-dithole-2-thione starting from easily accessible chemicals was described. The reaction procedure including separation and purification is rather straightforward. We are currently

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(13) **Typical procedure is as follows:** To the solution of $TBA_2 \cdot [Zn(DMIT)_2]$ (568.3 mg, 0.6 mmol) in 15 mL of acetonitrile were added 0.2 mL (2.4 mmol) of 3-bromopropionitrile and 279.66 mg (2.4 mmol) of pyridine hydrochloride. The mixture was heated to 50−60 °C and stirred for 2 h at this temperature. The resulting mixture was filtered ho, and the remaining solid was further washed with dichloromethane (3 × 20 mL) for complete extraction of the product. The combined filtrate and washings were decolorized by use of activated charcoal. After removing the solvent, column chromatography of the crude reaction mixture on silica gel with dichloromethane afforded compound **3d** as a yellow solid (184 mg 70%) and **1d** (62 mg, 17%).

doing mechanism studies for this novel method, in particular, studying the effect of pyridine hydrochloride. We are also investigating the possibility of replacement of pyridine hydrochloride by other acids and whether only a catalytic amount of suitable acid is needed for the formation 4-alkylthio-1,3-dithole-2-thione. These results will be reported in due course.

Acknowledgment. The present research work was financially supported by the Chinese Academy of Sciences and the Major State Basic Research Development Program (G2000077500). The authors thank Prof. Xianglin Jin of Peking University for his kind help on crystal structural analysis.

Supporting Information Available: CIF files of compounds **1a** and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL015990N