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Reversible 1,3-Dipolar Cycloaddition of Dimethyl 2-Thiono-1,3-dithiole-4,5-dicarboxylate with Dimethyl Acetylenedicarboxylate

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ABSTRACT: *It was shown that dimethyl 2-thiono-1,3-dithiole-4,5-dicarboxylate (***2***) and dimethyl acetylenedicarboxylate (DMAD) undergo a 1,3-dipolar cycloaddition to produce a short-lived ylide intermediate (***3***). The 1,3-dipolar cycloaddition took place even at room temperature, although sluggishly, but took place much more rapidly under application of a high pressure of 500 MPa. The 1,3-dipolar cycloaddition is reversible and the ylide* **3** *immediately splits into* **2** *and DMAD. When the reaction of* **2** *with DMAD was carried out at room temperature without solvent, a spiro-1,3-dithiole (***11***) was formed in 11% yield, whereas the reaction at 150°C provided a thiophene derivative (***13***) in 41% yield. It was found that* **11** *undergoes a thermal rearrangement to* **13**. *Results of attempted chemical trapping of the ylide* **3** *are also reported.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:434–440, 2000

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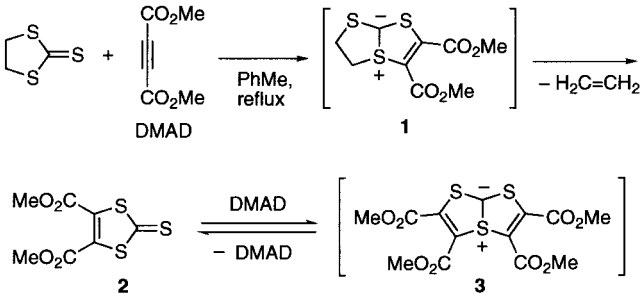
INTRODUCTION

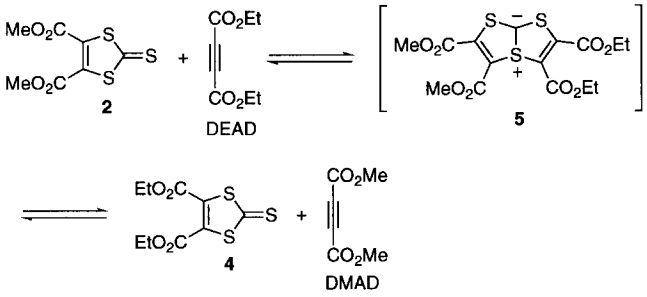
It is well documented that ethylene trithiocarbonate reacts with dimethyl acetylenedicarboxylate (DMAD) in refluxing toluene to furnish dimethyl 2-thiono-1,3-dithiole-4,5-dicarboxylate (**2**) in a satisfactory yield [1]. This synthetically useful reaction, a key step for the preparation of tetrathiafulvalene (TTF), has been believed to take place through a 1,3-dipolar cycloaddition that yields an ylide intermediate (**1**), which undergoes a retro-1,3-dipolar cycloaddition to produce **2** and ethylene. A question that emerges here is whether **2** is capable of further reaction with DMAD to give another ylide (**3**). However, even if such a cycloaddition had taken place, it would not be observable since the retro-1,3-dipolar cycloaddition of **3** to the starting materials occurs quickly (Scheme 1) [2]. The present study answers the question whether the above 1,3-dipolar cycloaddition actually takes place.

RESULTS AND DISCUSSION

When equimolar amounts of **2** and diethyl acetylenedicarboxylate (DEAD) in $CDCl_3$ were allowed to react at room temperature for 16 days, diethyl 2-



SCHEME 1



SCHEME 2 The equilibrium is attained when either **2** and DEAD or **4** and DMAD are allowed to react for three weeks at room temperature, for 70 hours under 500 MPa at room temperature, or for 3 hours in refluxing toluene (see Figure 2).

thiono-1,3-dithiole-4,5-dicarboxylate (**4**) and DMAD were formed in equal amounts, even though **2** and DEAD were still the major components (Scheme 2 and Figure 1). A mixture containing the same compounds was also obtained by starting from **4** and DMAD (Figure 1). The reactions are sluggish at room temperature, however, and more than three weeks were required to attain the equilibrium. It is known that 1,3-dipolar cycloadditions are accelerated under high pressure [3]. Therefore, if these exchange reactions take place through the common ylide intermediate (**5**), which is formed by 1,3-dipolar cycloaddition in a concerted manner, application of high pressure should accelerate the reactions. Thus, equimolar amounts of **2** and DEAD were allowed to react under 500 MPa in $CDCl_3$ at room temperature for 20 hours. The reaction gave a mixture of **2, 4,** DEAD, and DMAD in the ratio 1.2:1.0:1.2:1.0, and after 70 hours, a 1:1:1:1 equilibrium mixture was obtained (Figure 2). The reaction of **4** with DMAD for 70 hours under the same conditions also provided a mixture of these compounds in the ratio ca. 1:1:1:1 (Figure 2).

The same equilibrium mixture was also obtained by heating **2** and DEAD in refluxing toluene for 3 hours. These findings, though indirect, prove that the 1,3-dipolar cycloadditions of **2** with DMAD to produce the ylide **3** actually take place probably in a concerted manner. In addition, the occurrence of the reaction, even at room temperature without application of high pressure, is rather surprising, when we recall that (1) the reaction of ethylene trithiocarboxylate with DMAD was carried out in refluxing toluene [1] and (2) the reaction of 2-seleno-1,3-dithiole (**6**) with DMAD, which furnished 2-thiono-1,3-thiaselenole (**8**) probably through the intermediary formation of the ylide (7), was also carried out in refluxing toluene (Scheme 3) [4].

When a solution of **2** in DMAD was allowed to stand at room temperature for 10 days, a spiro-compound (**11**) was formed in 11% yield with recovery of **2** in 33% yield. In accordance with the assigned structure, the ^1H NMR spectrum of **11** showed three methyl signals at δ 3.78, 3.86, and 3.93, and the ^{13}C NMR spectrum exhibited three ester carbonyl carbon peaks at δ 159.9, 161.0, and 164.6, three sp^2 carbon peaks at δ 127.1, 128.0, and 133.5, three methyl carbon peaks at δ 53.1, 53.2, and 53.8, and one quaternary carbon peak at δ 66.2. The most plausible mechanism, which explains the formation of **11**, is shown in Scheme 4. Competing with the 1,3-dipolar cycloaddition would be a [2 + 2] cycloaddition. Thus, **3** reacts with DMAD to give a thiete (**9**) probably via a zwitterion. The ring-opening of **9,** followed by a [4 + 2] cycloaddition of the resulting (**10**) with DMAD, would produce the spiro-compound **11** [5].

On the other hand, heating **2** with excess DMAD without solvent at 150°C for 4 hours furnished a thiophene derivative (**13**) in 41% yield with recovery of **2** in 27% yield; the dimerization product (**16**) and the tetramerization product (**17**) of DMAD were also isolated in small amounts [6]. The reaction in refluxing toluene for 5 hours also provided **13** in 35% yield. The structure of **13,** which could not be elucidated unambiguously by spectroscopic methods, was determined by X-ray crystallographic analysis. Figure 3 shows an ORTEP structure of **13.** Any particular deviation of bond angles and bond lengths was not found in the molecular structure of **13.** A separate experiment proved that **13** is formed by thermal rearrangement of **11**; heating **11** in refluxing toluene for 3 hours resulted in the quantitative formation of **13.** The formation of heteroaromatic 1,3-dithiolylium ion (**12**) [7,8] and thiophene **13** would serve as a driving force of this novel rearrangement (Scheme 5). An alternative mechanism, involving a heterolytic cleavage of the carbon-sulfur bond that produces (**14**) and then (**15**), may also explains the formation of **13** (Scheme 5) [9].

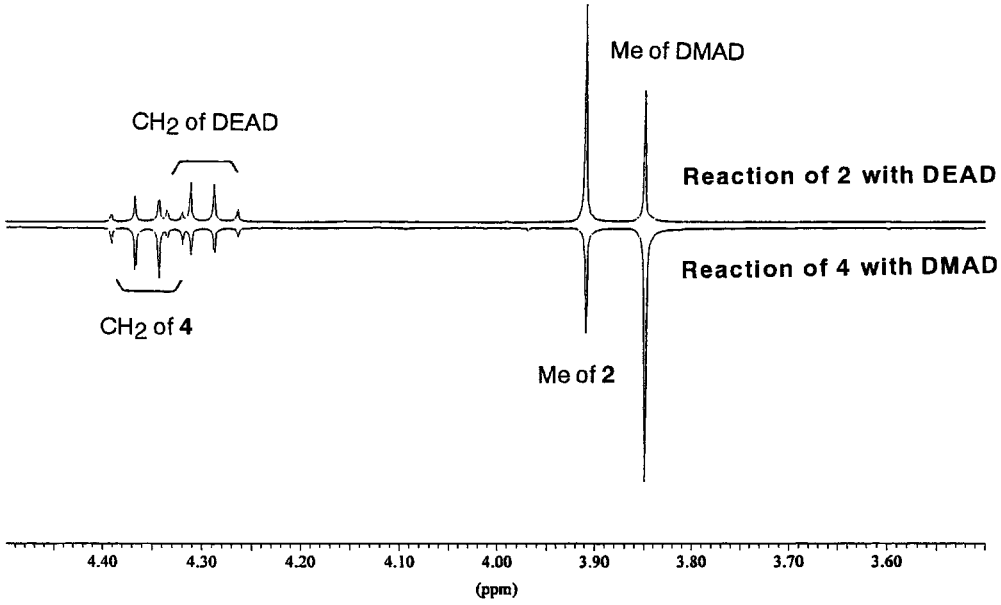


FIGURE 1 ^{1}H NMR spectra of the reaction mixture of **2** with DEAD (top) and the reaction mixture of **4** with DMAD (bottom) at room temperature for 16 days (methyl signals of **4** and DEAD are out of these spectra).

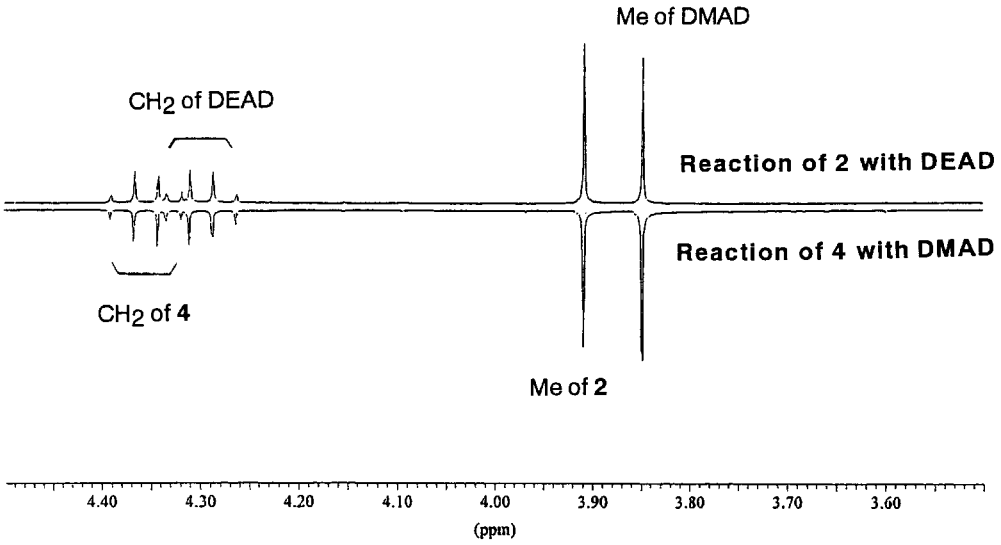
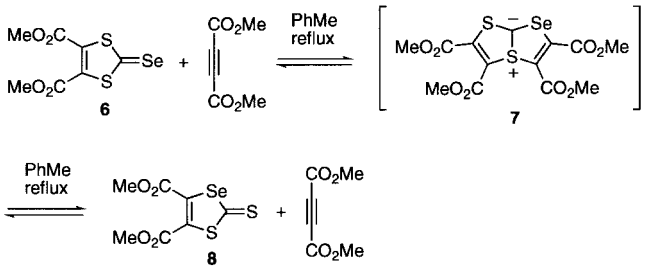


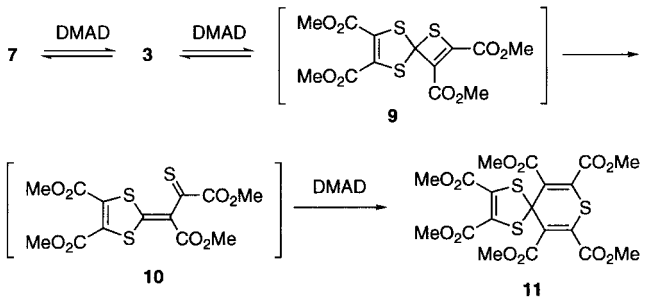
FIGURE 2 ^{1}H NMR spectra of the reaction mixture of 2 with DEAD (top) and the reaction mixture of 4 with DMAD (bottom) under 500 MPa at room temperature for 70 hours (methyl signals of **4** and DEAD are out of these spectra); formation of equilibrium mixtures.

Next, we tried chemical trapping of the ylide **3**. However, successful results were not necessarily obtained despite many efforts. The only successful trapping of this type of ylide was previously observed with the ylide (**18**), which was produced by reaction of 2-thiono-1,3-benzodithiole with benzyne and trapped by hydrogen chloride to furnish the sulfonium chloride (**19**) in good yield [2]. However, attempted trapping of **3** by acids, such as HBF_4 and TsOH, was unsuccessful. Some sulfonium ylides are known to react with elemental sulfur to afford thiocarbonyl compounds [10]. However, the reaction of **2** with DMAD in the presence of elemental sulfur did not result in the desired reaction under a variety of conditions.

Only trapping by benzaldehyde provided some meaningful results. Thus, the reaction of **2** with an equimolar amount of DMAD in benzaldehyde under



SCHEME 3



SCHEME 4

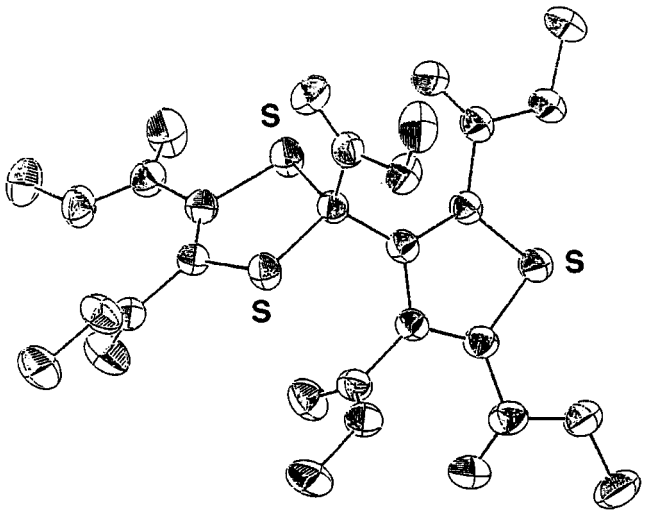


FIGURE 3 ORTEP drawing of the thiophene **13.**

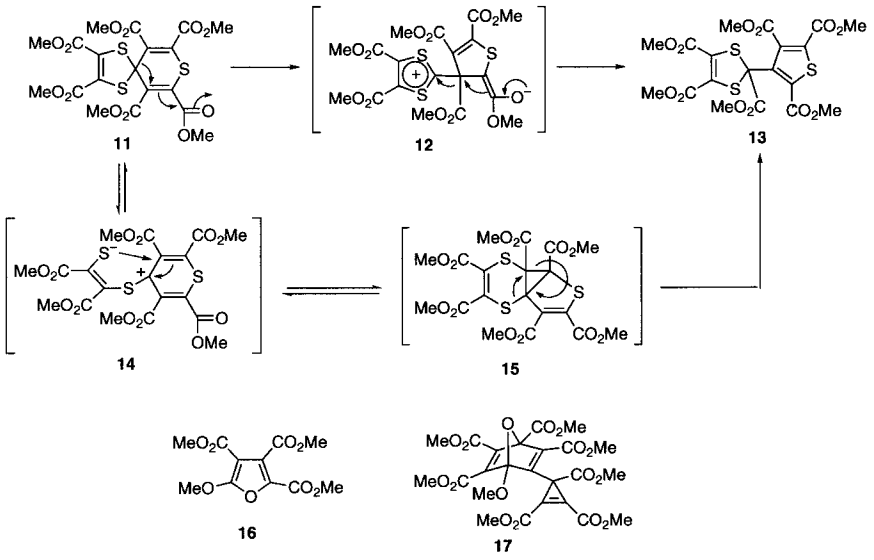
500 MPa for 70 hours provided the thiadiene **10** and the spiro- 1,3-dithiole **11** in 16% and 9% yields, respectively, with recovery of **2** in 42% yield. In addition, a crystalline compound (**20**), which gave satisfactory elemental analysis as $C_{20}H_{18}O_8S_3$, and the corresponding molecular ion peak in the MS spectrum, was obtained in 8% yield. The structure, given in the Scheme 7, was tentatively assigned to this compound; despite many attempts, **20** did not give single crystals suitable for X-ray crystallographic analysis. The reaction for 20 hours under the same conditions gave the same products in decreased yields. The structure of **20** corresponds to the deoxygenation product of the expected epoxide (**21**), the product of the reaction of the ylide **3** with benzaldehyde. The thiadiene **10** is the assumed intermediate for the formation of **11** (see Scheme 4). The following may explain why **10** was satisfactorily isolated only in this case. In the presence of a large excess of DMAD, the *s-cis* conformer that was formed by ring-opening of **9** and has a correct geometry for [4 + 2] cycloaddition, may react with DMAD immediately to give **11,** whereas, in the absence of a large excess of DMAD, the *s-cis* conformer might undergo a rapid conformational change to the thermodynamically more stable *s-trans* isomer which has an incorrect geometry for the [4 + 2] cycloaddition. The *s-trans* conformer, once formed, would not revert to the *s-cis* conformer without application of heat because of the contribution of the canonical structure (**10′**) which increases the energy barriers of the rotation about the C_1–C_2 bond.

EXPERIMENTAL

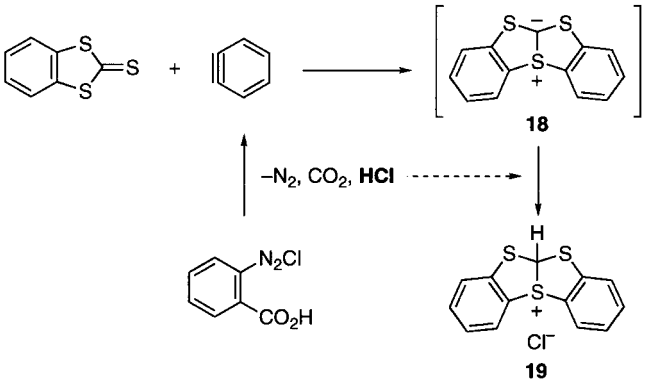
Solvents were purified and dried in the usual manner. All of the reactions, except the high-pressure reactions, were carried out under argon. Silica-gel column chromatography was performed on silica gel 7734 (Merck, 70-230 mesh). Melting points were determined on a Mel-Temp capillary tube apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX400, a Bruker AM400, a Bruker AM300, or a Bruker AM200 spectrometer using $CDCl_3$ as the solvent with TMS as the internal standard. Mass spectra were recorded on a JEOL JMS-DX303 spectrometer operating at 70 eV in the EI mode. Elemental analyses were performed by the Chemical Analysis Center of Saitama University. Diethyl 2-thiono-1,3-dithiole-4,5-dicarboxylate (**4**) was prepared by heating ethylene trithiocarbonate (1.4 g, 10 mmol) and diethyl acetylenedicarboxylate (3.4 g, 20 mmol) in refluxing toluene for 7 hours: b.p. 165°C/0.35 mmHg (bulb-to-bulb distillation), 2.5 g (89%), orange viscous oil. ^{1}H NMR (300 MHz) δ = 1.40 (t, 6H, J = 7.2 Hz), 4.36 (q, 4H, J = 7.2 Hz). ^{13}C NMR (100.6 MHz) δ = 13.9, 63.4, 138.3, 157.6, 207.5.

Reaction of **2** *with DEAD and Reaction of* **4** *with DMAD at Room Temperature*

A solution of 7.5 mg (0.03 mmol) of **2** and 5.1 mg (0.03 mmol) of DEAD in 0.4 mL of $CDCl_3$ was placed in an NMR tube. A solution of 8.5 mg (0.03 mmol) of **4** and 4.2 mg (0.03 mmol) of DMAD in 0.4 mL of $CDCl_3$ was also placed in an NMR tube. The pro-



SCHEME 5



SCHEME 6

gression of the reaction was monitored by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of the reaction mixture of **2** and DEAD and that of **4** and DMAD after 16 days are shown in Figure 1.

Reaction of **2** *with DEAD in Refluxing Toluene*

A mixture of 250 mg (1 mmol) of **2** and 173 mg (1 mmol) of DEAD in 5 mL of toluene was heated at reflux for 3 hours. The mixture was evaporated, and the analysis of the residue by ^{1}H NMR spectroscopy showed that an equilibrium mixture containing **2, 4,** DMAD, and DEAD in the ratio ca. 1:1:1:1 was formed.

Reaction of **2** *with DEAD and Reaction of* **4** *with DMAD at Room Temperature under 500 MPa*

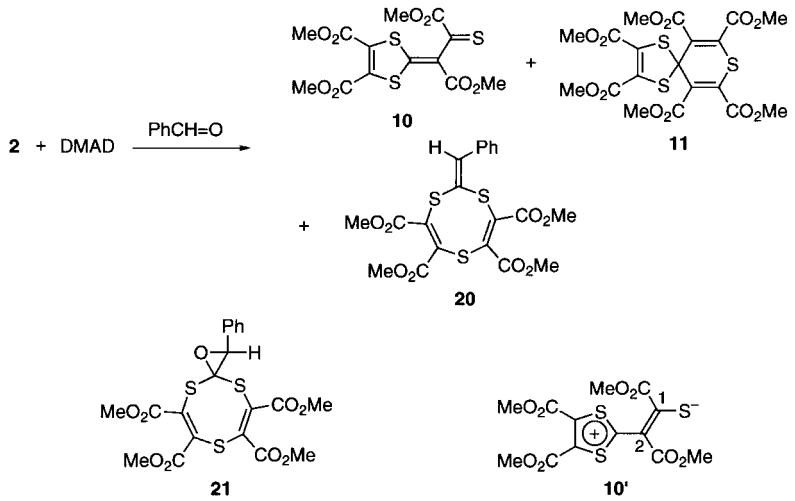
A solution of 75 mg (0.3 mmol) of **2** and 51 mg (0.3 mmol) of DEAD in 4 mL of $CDCl_3$ was placed in a sealed Teflon tube. A solution of 84 mg (0.3 mmol) of **4** and 43 mg (0.3 mmol) of DMAD in 4 mL of $CDCl_3$ was also placed in a sealed tube. These tubes were immersed in a high-pressure vessel and kept at 500 MPa for 20 hours or 70 hours. The ^{1}H NMR spectra of the reaction mixture of **2** and DEAD and that of **4** with DMAD after 70 hours are shown in Figure 1.

Reaction of **2** *with DMAD without Solvent at Room Temperature*

A solution of 250 mg (1 mmol) of **2** in 2 mL of DMAD was allowed to stand at room temperature. The mixture turned orange after 10 days, and the DMAD was removed by bulb-to-bulb distillation below 30°C at 0.15 mmHg. The residue was purified by silica-gel column chromatography (elution with hexane/AcOEt, 1/1) and then by GPC (gel permeation chromatography) to give 83 mg (33%) of **2** and 60 mg (11%) of the spiro-compound **11**: yellow needles (from hexane/CH_2Cl_2); m.p. 139–143°C; **11** and the thiophene **13** showed the same melting point because of quantitative thermal rearrangement of **11** to **13**. ^{1}H NMR (300 MHz) δ = 3.78 (s, 6H), 3.86 (s, 6H), 3.93 (s, 6H). ^{13}C NMR (50 MHz) δ = 53.1, 53.2, 53.8, 66.2, 127.1, 128.0, 133.5, 159.9, 161.0, 164.6. Anal. Calcd for $C_{19}H_{18}O_{12}S_3$: C, 42.69; H, 3.39. Found: C, 42.88; H, 3.34. The reaction under 500 MPa at room temperature for 20 hours gave **11** in 2% yield with recovery of **2** in 82% yield.

Reaction of **2** *with DMAD without Solvent at 150°C*

A solution of 250 mg (1 mmol) of **2** in 2 mL of DMAD was heated at 150°C for 4 hours. The mixture was



SCHEME 7

evaporated under reduced pressure. The residue was chromatographed on a column of silica gel. Elution of the column with hexane/AcOEt (1:1) gave 68 mg (27%) of **2,** 23 mg of the DMAD tetramer **17**, and 322 mg of a mixture containing the thiophene **13.** The mixture was then purified by GPC to give 217 mg (41%) of **13** and 29 mg of the DMAD dimer **16**. **13**: yellow needles (from hexane/CH_2Cl_2); m.p. 139–143°C. ^{1}H NMR (300 MHz) δ = 3.79 (s, 6H), 3.85 (s, 3H), 3.87 (s, 3H), 3.89 (s, 3H), 3.92 (s, 3H). ^{13}C NMR (100.6 MHz) δ = 53.0, 53.06, 53.07, 53.2, 54.5, 67.0, 128.7, 131.5, 133.9, 140.6, 145,0, 159.9, 160.1, 161.8, 164.9, 167.6. Anal. Calcd for $C_{19}H_{18}O_{12}S_3$: C, 42.69; H, 3.39. Found: C, 42.86; H, 3.32.

Reaction of **2** *with DMAD in Refluxing Toluene*

A mixture of 250 mg (1 mmol) of **2** and 2 mL of DMAD in 10 mL of toluene was heated at reflux for 5 hours. The mixture was purified as previously described to give 186 mg (35%) of **13** together with 116 mg (46%) of recovered **2**.

Thermal Rearrangement of **11** *to* **13**

A solution of 10 mg of **11** in 3 mL of toluene was heated at reflux for 3 h. The mixture was evaporated. Analysis of the residue by ^{1}H NMR spectroscopy showed that the rearrangement of **11** to **13** took place quantitatively.

Reaction of **2** *with DMAD in Benzaldehyde under 500 MPa*

A mixture of 250 mg (1 mmol) of **2,** 147 mg (1 mmol) of DMAD, and 2 mL of benzaldehyde was placed in a sealed Teflon tube. The tube was immersed in a pressure vessel and kept at 500 MPa for 20 hours at room temperature. The benzaldehyde was removed below 30°C under reduced pressure. The residue was chromatographed on a column of silica gel. Elution of the column with hexane/AcOEt (1:2) gave 185 mg (73%) of **2,** 25 mg (5%) of **11,** and 322 mg of a mixture containing **10** and **20.** The mixture fraction was further purified by GPC to give 35 mg (9%) of **10** and 10 mg (2%) of **20.** The reaction for 70 hours under the same conditions gave 107 mg (42%) of **2,** 48 mg (9%) of **11,** 61 mg (16%) of **10,** and 42 mg (8%) of **20**. **10**: red needles (from hexane/CH_2Cl_2); m.p. 116.0–117.5°C. ^{1}H NMR (400 MHz) δ = 3.90 (s, 3H), 3.94 (s, 3H), 3.98 (s, 3H), 3.99 (s, 3H). ^{13}C NMR (100.6 MHz) δ = 53.0, 53.2, 53.9, 54.0, 121.7, 131.7, 137.9, 159.4, 159.6, 164.5, 168.2, 174.1, 204.5. Anal. Calcd for $C_{13}H_{12}O_8S_3$: C, 39.79; H, 3.08. Found: C, 39.98; H, 3.00. **20:** yellow powder (from hexane/CH_2Cl_2), m.p. 97.5–99.0°C. ^{1}H NMR (400 MHz) δ = 3.79 (s, 6H), 3.87 (s, 3H), 3.88 (s, 3H), 3.91 (s, 3H), 6.60 (s, 1H), 7.45–7.49 (m, 2H), 7.58–7.62 (m, 1H), 8.10–8.12 (m, 2H). ^{13}C NMR (100.6 MHz) δ = 52.5, 53.0, 53.55, 53.57, 69.1, 106.5, 128.5, 129.0, 129.8, 130.1, 133.6, 136.6, 159.1, 159.9, 161.6, 165.2, 165.4, 167.4. MS *m/z* 482 (M^+), 451, 423, 361, 317, 221, 122, 105. Anal. Calcd for $C_{20}H_{18}O_8S_3$: C, 49.78; H, 3.76. Found: C, 49.66; H, 3.64.

X-Ray Crystallographic Analysis of the Thiophene **13**

The data were recorded on a Mac Science DIP3000 diffractometer equipped with a graphite monochrometer. Oscillation and nonscreen Weissenberg photographs were recorded on the imaging plates of

the diffractometer by using MoKα radiation (λ = 0.71073 Å), and the data reduction was made by the MAC DENZO program system. Cell parameters were determined and refined by using the MAC DENZO for all observed reflections. The structure was solved by direct methods using SIR in the CRYSTAN-GM program system. The atomic coordinates and anisotropic thermal parameters of the non-H atoms were refined by full-matrix least squares. Crystal data are as follows. Chemical formula, $C_{19}H_{18}O_{12}S_3$; formula weight, 534.50; crystal size, 0.26 × 0.15 × 0.10 mm; unit cell dimensions, a = 14.760(3), b = 18.162(4), c = 8.728(2) Å, β = 93.42(2)°, V = 2335.6(8) Å^3; crystal system, monoclinic; space group, $P2_1/n$; Z, 4; density, 1.520 Mg · m^{-3}; number of observed reflections, 3805; number of independent reflections, 4275; number of parameters varied, 379; R = 0.045; R_w = 0.066; GOF, 2.115.

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