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NOVEL FORMATION OF 1,2-DITHIOLANE-3-THIONE FROM β-DITHIOLACTONE

Toshiyuki Shigetomi,[†] Akiko Nojima,[†] Kosei Shioji,[†] Kentaro Okuma,[*†] and Yoshinobu Yokomori[‡]

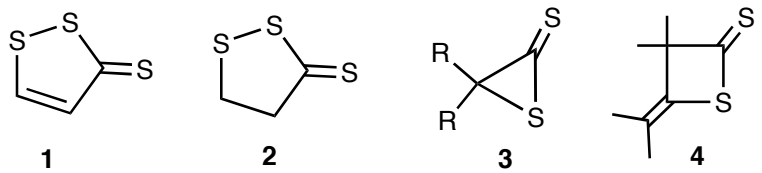
[†]Department of Chemistry, Faculty of Science, Fukuoka University, Jonan-ku, Fukuoka 814-0180, Japan

[‡]National Defense Academy, Hashirimizu, Yokosuka, 239-8686, Japan

e-mail kokuma@fukuoka-u.ac.jp

Abstract – The sulfurization of β-dithiolactone gave 1,2-dithiolane-3-thione via an ionic intermediate. The reaction of 1,2-dithiolane-3-thione with acetylenedicarboxylate esters gave the corresponding spirocyclic 1,3-dithioles in good yields, whereas the reaction of 5-methyl-1,2-dithiole-3-thione with DMAD afforded a 1:2 cycloadduct in 78% yield.

There is much interest in the synthesis of cyclic polysulfides such as lenthionin and 1,2-dithiole-3-thiones (**1**) because of their biological activity.[1] There are several reports on the reactions of 1,2-dithiole-3-thiones (**1**) because they possess biological and structural features of interest.[2] However, to our knowledge, there is no report on the reaction of 1,2-dithiolane-3-thiones (**2**). We recently reported the synthesis of α-dithiolactones (**3**), which reacted with benzyne to afford 1,3-benzodithioles in almost quantitative yields.[3] These results prompted us to investigate the synthesis of relatively unknown 1,2-dithiolane-3-thione (**2**) by sulfurization of β-dithiolactone (**4**), which was easily synthesized by reacting 2,2,4,4-tetramethyl-1,3-cyclobutanedione with P_4S_{10}.[4] In this communication, we report the synthesis of 5-isopropylidene-4,4-dimethyl-1,2-dithiolane-3-thione (**2a**) from β-dithiolactone (**4**) and its reactions.

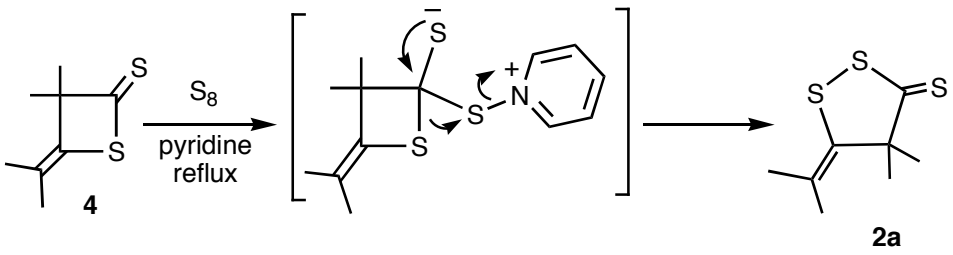


1 **2** **3** **4**

Scheme 1. Structures of **1**-**4**

When β-dithiolactone (**4**) was treated with elemental sulfur (2 equiv.) in refluxing pyridine and monitored by ^{1}H NMR, its amount was found to decrease rapidly. After 1 h, the reaction stopped and the

percentage conversion (50%) did not change anymore even after 5 h. After usual workup, 5-isopropylidene-4,4-dimethyl-1,2-dithiolane-3-thione (**2a**) was obtained in 80% yield. When 5 equiv. of elemental sulfur was used in this reaction, **2a** was obtained in low yield (28%) along with many side products. The structure of **2a** was confirmed by NMR and MS analyses. The ^{1}H NMR spectrum of **2a** showed methyl signals at 1.65 (6H), 1.95 (3H) and 1.99 (3H) ppm. The ^{13}C NMR spectrum showed signals at 248 ppm for thione and at 128 and 137 ppm for olefins. The MS spectrum showed M^{+} at 204.[5] How do we account for the formation of **2a**? The following observation that the thermolysis of **4** in refluxing toluene led to the recovery of **4** and the reaction of **4** with S_8 or P_4S_{10} in refluxing toluene gave only **2a** in 7% yield suggested that the concerted or radical process at this temperature was not operative. Thus, the following ionic mechanism might be plausible (Scheme 2).

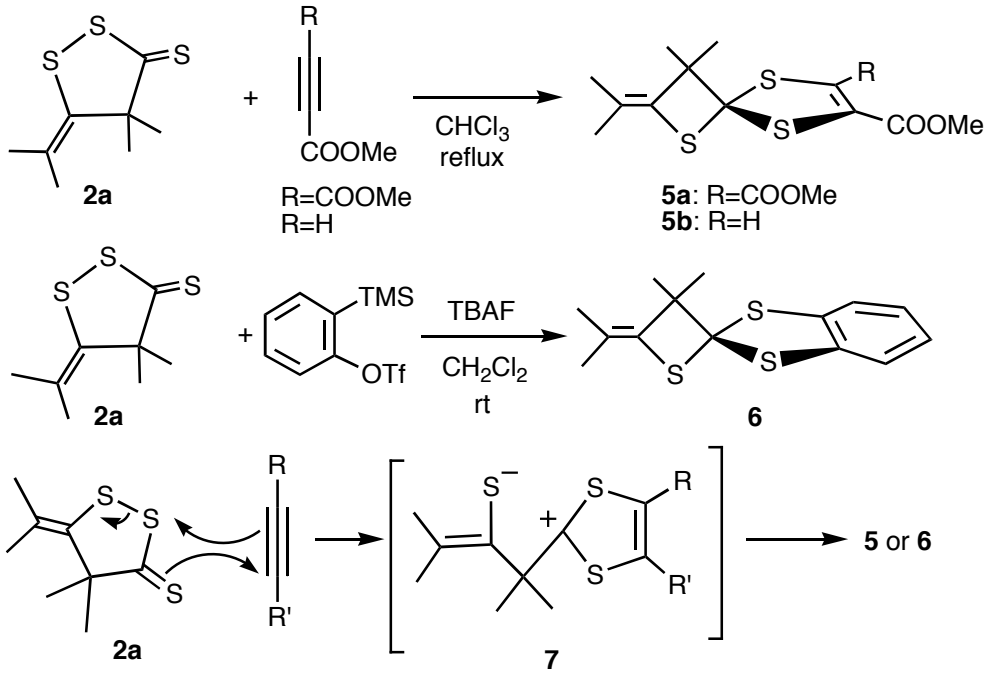


Scheme 2

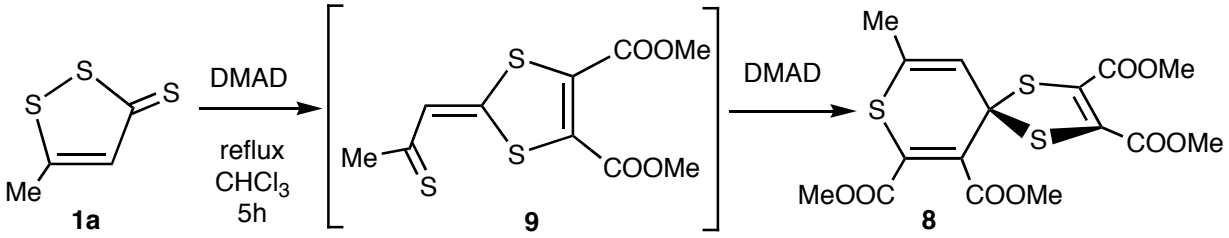
Since there is no report on the reaction of 1,2-dithiolane-3-thiones, we examined the reactivity of **2a** Treatment of **2a** with dimethyl acetylenedicarboxylate (DMAD) in refluxing chloroform gave the corresponding 1,3-dithiole (**5a**) in 87% yield. The structure of **5a** was confirmed by NMR analysis.[5] Similarly, the reaction with benzyne produced from *o*-trimethylsilylphenyl triflate[6] gave benzo-1,3-dithiole (**6**) in 85% yield. The reaction was surmised to proceed through a betaine intermediate; electron-deficient DMAD was initially attacked by **2a** to give betaine (**7**), which underwent intramolecular combination to give the product (Scheme 3). This result is quite different from that of 1,2-dithiole-3-thiones (**1**) that usually react with DMAD to afford the corresponding 2-(2-thioxoalkylidene)-1,3-dithioles.[2]

To check the possibility of obtaining spirocyclic 1,3-dithioles, we applied this method to the reaction of 1,2-dithiole-3-thione (**1**). Treatment of 5-methyl-1,2-dithiole-3-thione (**1a**) with excess DMAD resulted in the formation of spiro[2,3-bis(methoxycarbonyl)-4*H*-thiopyran-4,2'-4',5'-bis(methoxycarbonyl)-[1,3]dithiole] (**8**) in 78% yield. It is possible that initially formed 2-(2-thioxopropylidene)-1,3-dithiole (**9**) was further attacked by DMAD to afford **8** (Scheme 4). Thus, we have succeeded in the synthesis of two types of spirocyclic 1,3-dithioles.

We then attempted the photoreaction of **2a**. UV irradiation (354 nm) of **2a** in a Pyrex photoreactor produced 3,3,5,5-tetramethyl-4-thioxothiolane-2-thione (**10**)[7] in 84% yield.

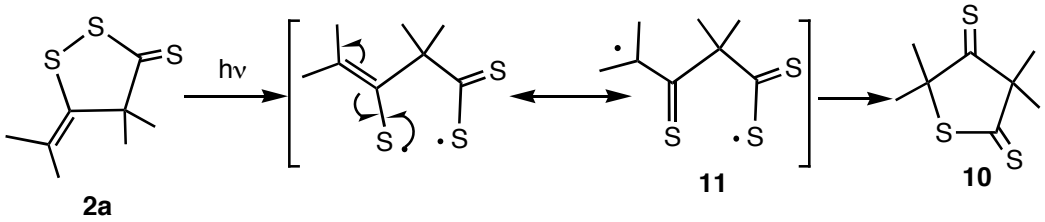


Scheme 3



Scheme 4

Sulfur-sulfur bond cleavage of **2a** gave a corresponding biradical that rearranged to form carbon radical (**11**). The recombination of biradical (**11**) finally produced **10** (Scheme 5).



Scheme 5

In summary, we have synthesized 1,2-dithiolane-3-thione (**2a**) by reacting dithiolactone (**4**) with elemental sulfur. The reaction of **2a** with acetylenic acids gave spirocyclic 1,3-dithioles in good yields. The photoreaction of **2a** afforded isomer (**10**).

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5, Compound (**2a**): yellow oil. ^{1}H NMR ($CDCl_3$) δ=1.65 (s, 6H, Me), 1.95 (s, 3H, Me), 1.99 (s, 3H, Me). ^{13}C NMR ($CDCl_3$) δ= 21.63 (Me), 26.60 (Me), 29.13 (2Me), 64.43 (q-C), 128.43 (=C), 137.37 (=C), 248.05 (C=S). Anal. Calcd for $C_8H_{12}S_3$: C, 47.01; H, 5.92. Found C, 46.66; H, 5.81; MS: m/z 204 (M^+). Compound (**5a**): yellow crystals. mp 75-76 °C. ^{1}H NMR ($CDCl_3$) δ=1.36 (s, 3H, Me), 1.59 (s, 6H, Me), 1.69 (s, 3H, Me), 3.77 (s, 6H, Me). ^{13}C NMR ($CDCl_3$) δ= 19.89 (Me), 21.51 (Me), 26.62 (2 x Me), 53.63 (2 x OMe), 62.24 (q-C), 84.50 (S-C-S), 120.31 (=C), 127.81 (=C), 129.65 (=C), 161.10 (C=O). Compound (**5b**): 84% yield: yellow oil. ^{1}H NMR ($CDCl_3$) δ=1.34 (s, 3H, Me), 1.56 (s, 3H, Me), 1.59 (s, 3H, Me), 1.67 (s, 3H, Me), 3.73 (s, 3H, OMe), 7.04 (=CH). ^{13}C NMR ($CDCl_3$) δ= 19.91 (Me), 21.54 (Me), 26.75 ((Me), 26.95 (Me), 52.58 (OMe), 62.02 (q-C), 87.57 (S-C-S), 119.06 (=C), 122.65 (=C), 128.42 (=CH), 129.22 (=C), 161.19 (C=O). Anal. Calcd for $C_{12}H_{16}O_2S_3$: C, 48.53; H, 5.24. Found C, 48.67; H, 5.12. Compound (**8**): yellow needles. mp 114-115 °C. ^{1}H NMR ($CDCl_3$) δ=2.05 (s, 3H, Me), 3.78 (s, 6H, OMe), 3.83 (s, 3H, OMe), 3.90 (s, 3H, OMe), 6.36 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$) δ= 21.88 (Me), 53.31 (3 x OMe), 53.83 (OMe), 68.66 (S-C-S), 117.76 (2 x =C), 127.71 (=C), 128.89 (=C), 129.39 (=C), 129.49 (=C), 161.04 (2 x C=O), 162.35 (C=O), 169.54 (C=O). Anal. Calcd for $C_{16}H_{16}O_2S_3$: C, 44.43; H, 3.73. Found C, 44.14; H, 3.69.

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