

HETEROCYCLES, Vol. 68, No. 11, 2006, pp. 2243 - 2246. © The Japan Institute of Heterocyclic Chemistry
 Received, 31st July, 2006, Accepted, 7th September, 2006, Published online, 8th September, 2006. COM-06-10849

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

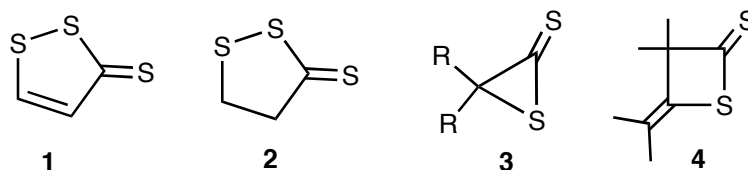
Toshiyuki Shigetomi,[†] Akiko Nojima,[†] Kosei Shioji,[†] Kentaro Okuma,^{*†} and
 Yoshinobu Yokomori[‡]

[†]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.

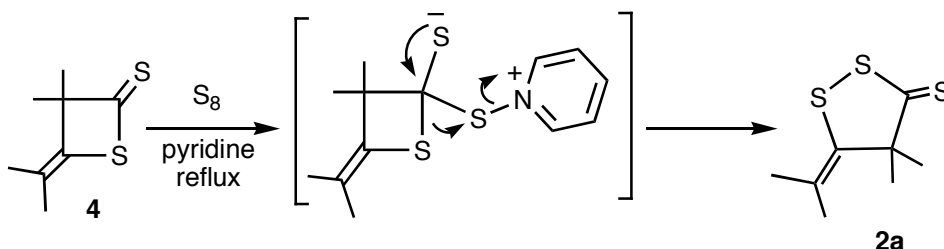
There is much interest in the synthesis of cyclic polysulfides such as lenthionin and 1,2-dithiole-3-thiones (**1**) because of their biological activity.¹ There are several reports on the reactions of 1,2-dithiole-3-thiones (**1**) because they possess biological and structural features of interest.² 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.



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

When β -dithiolactone (**4**) was treated with elemental sulfur (2 equiv.) in refluxing pyridine and monitored by ¹H 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 ^1H 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).

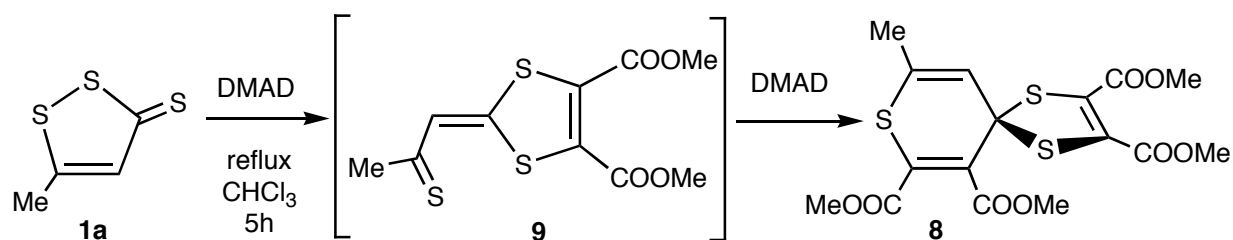
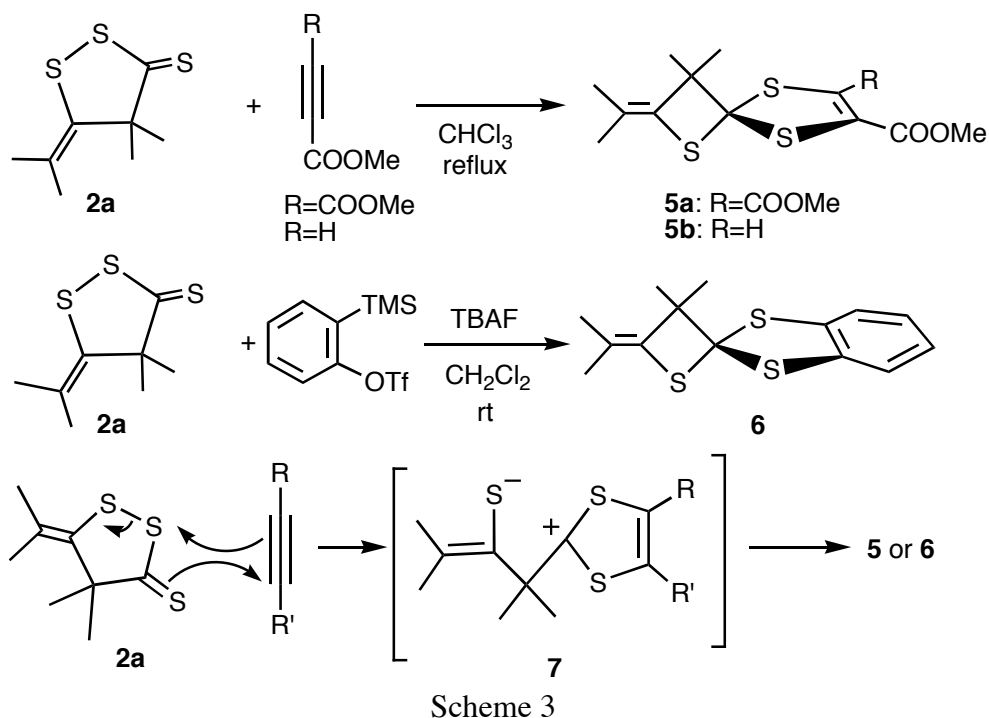


Scheme 2

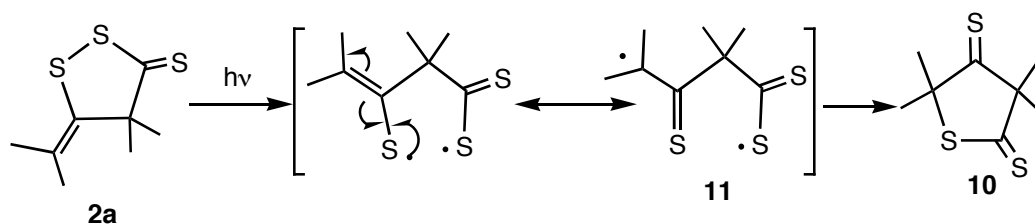
Since there is no report on the reaction of 1,2-dithiolane-3-thiones, we examined the reactivity of **2a**. Treatment of **2a** with dimethyl acetylenedicarboxylate (DMAD) in refluxing chloroform gave the corresponding 1,3-dithiole (**5a**) in 87% yield. The structure of **5a** was confirmed by NMR analysis.⁵ Similarly, the reaction with benzyne produced from *o*-trimethylsilylphenyl triflate⁶ 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.



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).



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-dithiols in good yields. The photoreaction of **2a** afforded isomer (**10**).

REFERENCES AND NOTES

- G. Mloston, A. Majchrzak, A. Senning, and I. Sotofte, *J. Org. Chem.*, 2002, **67**, 5690; R. Munday and C. M. Munday, *Carcinogenesis*, 2004, **25**, 1721; M. Navamal, C. McGrath, J. Stewart, P.

- Blans, F. Villamena, J. Tweier, and J. C. Fishbein, *J. Org. Chem.*, 2002, **67**, 9406; Y. Takikawa, T. Makabe, N. Hirose, T. Hiratsuka, R. Takoh, and K. Shimada, *Chem. Lett.*, **1988**, 1517; K. Yasumoto, K. Iwami, and H. Mitsuda, *Agr. Biol. Chem.*, 1971, **35**, 2070.
- H. Hehringer and R. Wiedenmann, *Tetrahedron Lett.*, **1965**, 3705; H. Davy and J. Vialle, *Bull. Soc. Chim. Fra.*, **1975**, 1435; P. Frerre, A. Belyasmine, A. Gorgues, G. Duguay, K. Boubekeur, and P. Batail, *Tetrahedron Lett.*, 1993, **34**, 4519; V. M. Timoshenko, J. -P. Bouillon, A. N. Chernega, Y. G. Shermolovich, and C. Portella, *Eur. J. Org. Chem.*, **2003**, 2471; S. Barriga, P. Fuertes, C. F. Marcos, and T. Torroba, *J. Org. Chem.*, 2004, **69**, 3672; A. M. Granados, J. Kreiker, R. H. de Rossi, P. Fuertes, and T. Torroba, *J. Org. Chem.*, 2006, **71**, 808.
 - K. Okuma, T. Shigetomi, K. Shioji, Y. Nibu, and Y. Yokomori, *J. Am. Chem. Soc.*, 2004, **126**, 9508; T. Shigetomi, H. Soejima, Y. Nibu, K. Shioji, K. Okuma, and Y. Yokomori, *Chem. Eur. J.*, in press.
 - E. U. Elam and H. E. Davis, *J. Org. Chem.*, 1967, **32**, 1562.
 - Compound (**2a**): yellow oil. ^1H 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 $\text{C}_8\text{H}_{12}\text{S}_3$: 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. ^1H 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. ^1H 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 $\text{C}_{12}\text{H}_{16}\text{O}_2\text{S}_3$: C, 48.53; H, 5.24. Found C, 48.67; H, 5.12. Compound (**8**): yellow needles. mp 114-115 °C. ^1H 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 $\text{C}_{16}\text{H}_{16}\text{O}_2\text{S}_3$: C, 44.43; H, 3.73. Found C, 44.14; H, 3.69.
 - Y. Himeshima, N. Sonoda, and H. Kobayashi, *Chem. Lett.*, **1983**, 1211.
 - K. Okuma, T. Tsubone, T. Shigetomi, K. Shioji, and Y. Yokomori, *Heterocycles*, 2005, **65**, 1553; R. Huisgen, J. Rapp, and H. Huber, *Liebigs Ann./Recueil*, **1997**, 1517; K. Muthuramu, B. Sundari, and V. Rammurthy, *J. Org. Chem.*, 1983, **48**, 4482.