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Reaction of Thiochamphor with Disulfur Dichloride: Novel Formation of α-Disulfine

Kentaro Okuma,*[1] Toshiaki Tsubota,[1] Miki Tabuchi,[1] Masayuki Kanto,[1] Noriyoshi Nagahora,[1] Kosei Shioji,[1] and Yoshinobu Yokomori[2]
[1]*Department of Chemistry, Fukuoka University, Jonan-ku, Fukuoka 814-0180*
[2]*Department of Applied Chemistry, National Defense Academy, Hashirimizu, Yokosuka 239-8686*

(Received March 9, 2010; CL-100224; E-mail: kokuma@fukuoka-u.ac.jp)

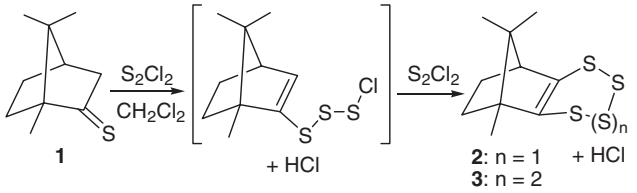
Reaction of thiocamphor with disulfur dichloride afforded six- and seven-membered tricyclic polysulfanes, which were oxidized by *m*-CPBA to afford bicyclic (*E*,*E*)-α-disulfine stereoselectively. Reaction of α-disulfine with the Lawesson reagent afforded tetrasulfane in 70% yield.

Synthesis of sulfur-containing heterocycles has been extensively studied because of many naturally occurring biologically active compounds, such as penicillin, lenthionine, and varacin.[1] Generally, cyclic polysulfanes are synthesized by the reaction of alkenes with elemental sulfur, reaction of dithiols with dihalosulfanes, and reaction of Bunte salts with sodium sulfide.[2] We have synthesized sulfur-containing heterocycles such as benzothietes,[3] 1,2,5-trithiolanes,[4] α-dithiolactones,[5] 1,2-dithietan-3-ones,[6] and 1,3-benzothiols.[7] In particular, dithietes are novel 4-membered cyclic disulfides, which are synthesized by the reaction of sterically hindered alkynes with elemental sulfur,[8] alkenes with S_2Cl_2,[9] or titanocene dithiolene complexes with SO_2Cl_2.[10] Stable aromatic α-dithione, 4,4′-bis(*p*-dimethylamino)dithiobenzil, which is an isomer of dithiete, was initially synthesized by Küsters and de Mayo.[11] Nakayama et al. have reported the synthesis of stable aliphatic dithiones from thiirene 1-oxide.[12] Sterically hindered dithietes were oxidized by *m*-CPBA to afford α-disulfines,[13] which were lately synthesized by oxidation of α-dithiones.[12] One synthetic approach to α-disulfines is the oxidation of cyclic polysulfanes. However, relatively little attention has been paid to the synthesis of sulfur-containing heterocycles by the reaction of bicyclic thiones such as thiocamphor (**1**). The only reported examples are the synthesis of norbornanethiazolines and 6*H*-[1,3]oxathiin-6-ones from thiofenchone.[14,15] This prompted us to investigate the reactivity of thiocamphor **1** in the hope of synthesizing tricyclic polysulfanes or tricyclic dithiete, which would be a good source of α-disulfine. Herein, we report the reaction of **1** with S_2Cl_2, which led to tricyclic polysulfanes and bicyclic α-disulfine by further oxidation.

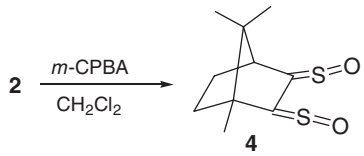
We first investigated the reaction of **1** with S_2Cl_2 under several conditions to determine whether the corresponding dithiete would occur. The results are shown in Table 1. When a solution of **1** and triethylamine (1 equiv) in dichloromethane was added to a solution of S_2Cl_2 (1 equiv) in dichloromethane at 0 °C, 1,11,11-trimethyl-3,4,5,6-tetrathiatricyclo[6.2.1.$0^{2,7}$]undeca-2(7)-ene (**2**) and 1,12,12-trimethyl-3,4,5,6,7-pentathiatricyclo[7.2.1.$0^{2,8}$]-dodeca-2(8)-ene (**3**) were obtained in 15% and 12% yields, respectively (Entry 1). In the absence of triethylamine, yields of **2** and **3** were improved (Entry 2). The best yields of **2** (69%) and **3** (12%) were obtained by using 1.5 equiv of S_2Cl_2 at 0 °C (Entry 3).[16] In contrast to Mlostoń's results,[17] no Wagner–Meerwein rearranged product was obtained, suggesting that α-proton abstraction is much faster than the rearrangement (Scheme 1). While reaction conditions (temperature, amount of S_2Cl_2, and time) were varied, no dithiete was formed. The reactions of norbornene with active sulfur to afford cyclic polysulfanes are well known.[18] However, there have been no reports of the synthesis of tricyclic polysulfanes from thiocamphor **1**. The present results provide the first synthetic method for cyclic polysulfanes with norbornene skeleton.

Table 1. Reaction of **1** with S_2Cl_2

Entry	S_2Cl_2 /equiv	Et_3N /equiv	Temp /°C	Products, yield/%	
				2	**3**
1	1.0	1.0	0	15	12
2	1.0	0	0	36	15
3	1.5	0	0	69	12
4	1.5	0	reflux	35	11
5	2.0	0	0	32	16



Scheme 1.



Scheme 2.

Since tricyclic polysulfanes **2** and **3** were in hand, we then tried the oxidation of tetrasulfane **2** to investigate whether α-disulfine would be formed. Treatment of **2** with *m*-CPBA (2 equiv) at rt resulted in the formation of 1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dithione *S*,*S*′-dioxide (**4**) (α-disulfine) as only one isomer in 95% yield (Scheme 2), suggesting that the reaction proceeded stereoselectively. Structure of dioxide **4** was confirmed by ^{1}H and ^{13}C NMR, mass spectrum, and elemental analysis (Scheme 2).[19] The IR spectrum of **4** shows peaks at 1044 (st), 1058, 1108, and 1124 cm^{-1} for C=S=O stretching.

To investigate the stereochemistry, we compared the ^{13}C NMR data of **4** with those of reported aliphatic α-disulfines, bis(*t*-butyl)sulfine (**5**). Nakayama et al. reported the synthesis of

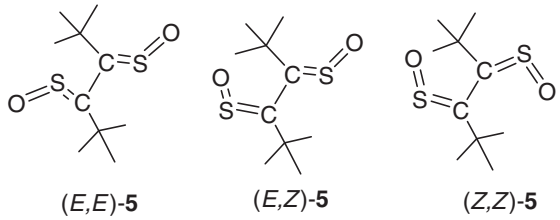
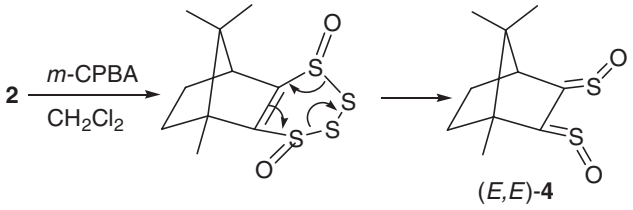
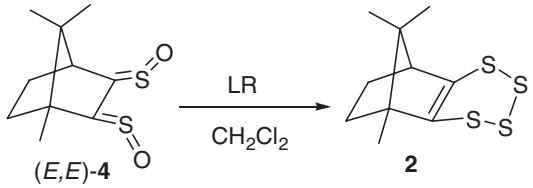


Figure 1.



Scheme 3.



Scheme 4.

mixtures of (*E*,*E*)-, (*E*,*Z*)-, and (*Z*,*Z*)-bis(*t*-butyl)sulfines (**5**) by oxidation of 1,2-dithietes and 1,2-dithiones.[12,13] The ^{13}C NMR of compound **4** shows peaks at 193.20 and 195.00 ppm for the C=S=O carbon. The ^{13}C NMR of the C=S=O carbon of disulfines **5** appears at 192.56 ppm for *E*,*E*-configuration, 197.80 and 198.52 ppm for *E*,*Z*-configuration, and 199.69 ppm for *Z*,*Z*-configuration (in $CDCl_3$) (Figure 1).

These data clearly show that sulfine **4** is in *E*,*E*-configuration. Thus, the present oxidation proceeded by the following pathway: oxidation of **2** initially formed the corresponding dioxide, which cycloreversed to give (*E*,*E*)-α-disulfine exclusively (Scheme 3). Thus, stereoselective synthesis of α-disulfine **4** from tetrasulfane **2** was achieved.

The obtained α-disulfine **4** was relatively unstable, and decomposed upon standing for 15 h at rt in chloroform to give a complex mixture. Interestingly, reaction of α-disulfine **4** with the Lawesson reagent (LR) in dichloromethane at rt afforded tetrasulfane **2** in 70% yield (Scheme 4).

In summary, we have successfully synthesized tricyclic polysulfanes by the reaction of thione **1** with S_2Cl_2. Stereoselective oxidation of tricyclic tetrasulfane **2** gave unusual bicyclic α-disulfine **4**. Further attempts to investigate the reaction of **2**, **3**, and **4** are underway in our laboratory.

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16 Typical reaction: To a solution of S_2Cl_2 (1.5 mmol) in CH_2Cl_2 was added a solution of **1** (1.0 mmol) in CH_2Cl_2 at rt. After stirring for 1.5 h, the reaction mixture was evaporated to give pale yellow oil, which was chromatographed over silica gel and then subjected to Gel HPLC to give **2** and **3**. Compound **2**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.28–1.36 (m, 2H, CH_2), 1.64–1.70 (m, 1H, CH_2), 1.89–1.95 (m, 1H, CH_2), 2.56 (d, $J = 3.0$ Hz, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.53, 18.71, 18.93, 26.30, 33.24, 53.04, 59.71, 60.02, 129.98, 131.62. Anal. Calcd for $C_{10}H_{14}S_4$: C, 45.76; H, 5.38%. Found: C, 45.36; H, 5.22%. Compound **3**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.49–1.57 (m, 2H, CH_2), 1.76–1.82 (m, 1H, CH_2), 2.06–2.12 (m, 1H, CH_2), 2.64 (d, $J = 3.9$ Hz, 1H, CH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 11.95, 18.63, 18.78, 24.99, 31.82, 56.53, 61.54, 61.63, 152.08, 155.86. Anal. Calcd for $C_{10}H_{14}S_5$: C, 40.78; H, 4.79%. Found: C, 40.70; H, 4.94%.

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19 Synthesis of **4**: To a solution of **2** (0.5 mmol) in CH_2Cl_2 was added a solution of *m*-CPBA (1.2 mmol) in CH_2Cl_2 at rt. After stirring for 1.5 h, the reaction mixture was filtered and evaporated to give yellow solid, which was chromatographed over silica gel by elution with hexane–dichloromethane (2:1) to give yellow leaflets of α-disulfine **4** (0.47 mmol). Mp 72 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.45 (m, 1H, C*H*H), 1.53 (m, 1H, C*H*H), 1.95 (m, 1H, C*H*H), 2.07 (m, 1H, C*H*H), 3.89 (d, 1H, $J = 4.0$ Hz, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.50 (Me), 18.18 (Me), 20.12 (Me), 25.89 (CH_2), 34.82 (CH_2), 51.99 (CH), 53.65 (q-C), 57.44 (q-C), 193.20 (C=S=O), 195.30 (C=S=O). Anal. Calcd for $C_{10}H_{14}O_2S_2$: C, 52.14; H, 6.13%. Found: C, 52.01; H, 6.12%.

