FORMATION OF CYCLIC OLIGOSULFIDES BY REACTION OF HYDRAZONES WITH DISULFUR DICHLORIDE

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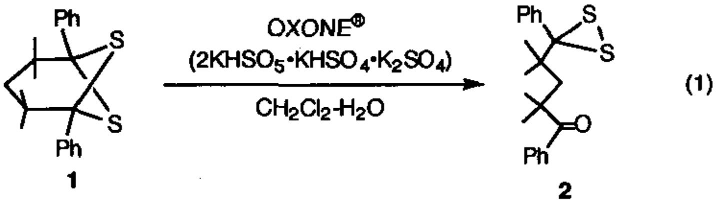
Abstract - Reactions of some hydrazones with disulfur dichloride were reinvestigated in the absence of a base with expectation of obtaining dithiirane or thiosulfine derivatives. However, treatment of hydrazones derived from 1-adamantyl phenyl ketone, pivalophenone, and benzophenone with disulfur dichloride gave pentathianes and hexathiepanes along with other products, while di-*t*-butyl ketone hydrazone gave a novel heterocyclic compound, 1,1-di-*t*-butyltetrathiolane, though in a low yield.

We have recently succeeded in the synthesis of the first isolable dithiirane derivative (**2**) by oxidative hydrolysis of bicyclic 1,3-dithietane (**1**) with $2KHSO_5{\bullet}KHSO_4{\bullet}K_2SO_4$ (OXONE®) (eq.1).[1]



Detailed study on the preparation of dithiiranes by the above procedure has reached a conclusion that the method is only applicable to bicyclic 1,3-dithietanes where a carbonyl group inevitably remains in the resulting dithiirane molecules.[2] Therefore, in order to expand the chemistry of dithiiranes, it is necessary

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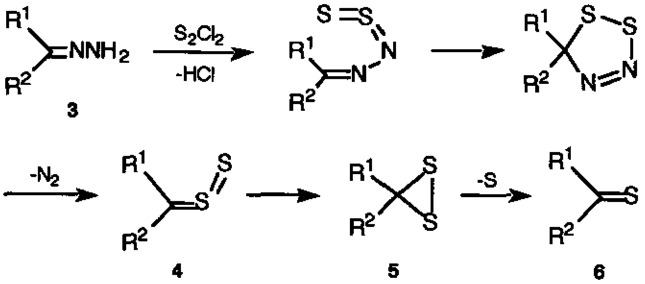
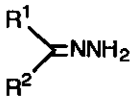
Dedicated to Professor Shigeru Oae on the occasion of his 77th birthday.

to devise a more general synthetic method for dithiiranes which uses simpler starting materials and gives no carbonyl-containing dithiiranes. We then focused our attention on the reaction of hydrazones (**3**) with disulfur dichloride (S_2Cl_2) that yields thioketones (Okazaki reaction).[3] It has been proposed that this reaction involves the intermediary formation of thiosulfines (**4**) and dithiiranes (**5**) which give thioketones (**6**) with loss of sulfur (Scheme 1). In this reaction, an amine is added to remove the hydrogen chloride formed. The dithiirane (**2**) is very sensitive to basic materials and thus, in the presence of basic materials, it decomposes to give the corresponding thione with loss of sulfur. We therefore reinvestigated the reaction of hydrazones with S_2Cl_2 in the absence of an amine with expectation of isolating proposed dithiirane intermediates.



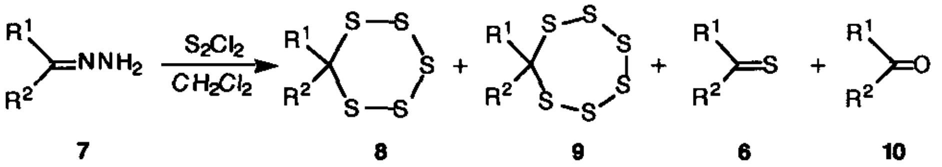
Scheme 1

The following four hydrazones (**7a-d**) were examined as the starting material.



7a : R^1 = 1-Ad, R^2 = Ph
7b : R^1 = *t*-Bu, R^2 = Ph
7c : R^1 = R^2 = Ph
7d : R^1 = R^2 = *t*-Bu

In the case of **7a**, **7b**, and **7c**, S_2Cl_2 was added slowly to a dry ice-cooled (-78 °C) dichloromethane solution of a hydrazone and then the mixture was stirred for 20 min at this temperature. During the mixture being warmed to room temperature, gas evolution probably due to nitrogen was observed at about -20 °C. The reaction was quenched by addition of water. The crude mixture was purifed by chromatography on a column of silica gel to give pentathianes (**8**) and hexathiepanes (**9**). Other products such as thiones (**10**) and ketones (**11**) were also obtained (eq. 2, Table 1). The formation of a hexathiepane was reported by the reaction of bis(trifluoromethyl) ketone hydrazone with S_2Cl_2 in the presence of triethylamine.[3] Meanwhile, Fehér reported that the reaction of dithiols with S_3Cl_2 produces the corresponding pentathiane derivatives,[4] and Okazaki and coworkers recently reported that the reaction of a sterically hindered diazomethane with S_8 gives the corresponding pentathiane and hexathiepane derivatives.[5]



(2)

Table 1. Yields of Products of the Reaction of Hydrazones (**7a-c**) with S_2Cl_2.

Hydrazones	R^1	R^2	Products (%)			
			8	**9**	**6**	**10**
7a	1-Ad	Ph	11	6	50	15
7b	*t*-Bu	Ph	7	3	10	63
7c	Ph	Ph	4	7	17	47

Structures of pentathianes (**8**) *and hexathiepanes* (**9**) *were determined by spectroscopic data and elemental* analysis. In addition, the molecular structure of **9b** was definitively determined by X-ray structure analysis. In the ^{13}C nmr spectra, S-C-S carbons of pentathianes (**8a**), (**8b**), and (**8c**) resonated at δ 66.2, 65.3, and 58.1, respectively, and those of hexathiepanes (**9a**), (**9b**), and (**9c**) at δ 108.6, 107.4, and 99.9, respectively. *The difference of chemical shift values between the pentathianes and the corresponding hexathiepanes reaches as large as ca. 42 ppm.* This observation is of much interest but no clear-cut explanation is available currently. Mass spectra of **8** and **9** showed not only the molecular ion peak (M^+) but also fragment peaks due to M^+-nS. An ORTEP drawing structure and selected bond length and angle data of **9b** are shown in Fig.1 and Table 2, respectively.

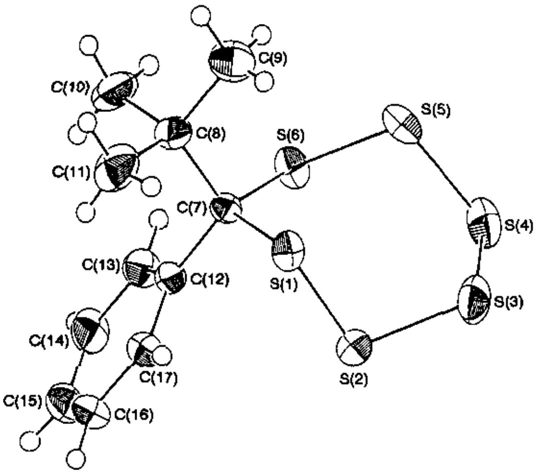
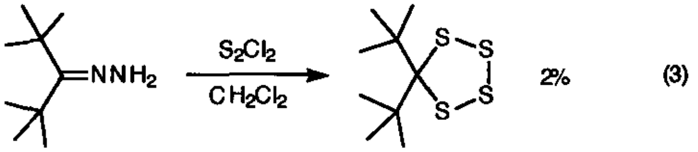


Figure 1. An ORTEP drawing of hexathiepane (**9 b**)

Table 2. Selected Bond Lengths (Å) and Bond Angles (deg) of **9b**.

S(1)-S(2)	2.033	S(1)-S(7)	1.835
S(2)-S(3)	2.050	S(3)-S(4)	2.051
S(4)-S(5)	2.058	S(5)-S(6)	2.025
S(6)-S(7)	1.887		
S(2)-S(1)-C(7)	105.5	S(1)-S(2)-S(3)	102.7
S(2)-S(3)-S(4)	104.7	S(3)-S(4)-S(5)	103.6
S(4)-S(5)-S(6)	104.3	S(5)-S(6)-C(7)	109.4
S(1)-C(7)-S(6)	111.3	S(1)-C(7)-C(8)	105.3
S(1)-C(7)-C(12)	112.0	S(6)-C(7)-C(8)	111.6
S(6)-C(7)-C(12)	104.1		

We next examined the reaction of di-*t*-butyl ketone hydrazone (**7d**) with S_2Cl_2 in a similar manner. The reaction gave a complex mixture from which the corresponding pentathiane and hexathiepane were not isolated. However, interestingly enough, tetrathiolane (**11**) was isolated though in a low yield (2%) (eq. 3). To our knowledge, the tetrathiolane (**11**) is the first isolable example that has a ring system composed of one carbon atom and four sulfur atoms. The ^1H nmr spectrum of **11** showed a singlet due to two *t*-butyls at δ 1.38. On the other hand, in the ^{13}C nmr spectrum, the signal due to methyls was observed at δ 32.5 as a broad signal with a fine structure, while that due to the S-C-S carbon appeared at δ 113.9 as a sharp singlet. This implies that methyls of the *t*-butyl groups of **11** are not equivalent on a ^{13}C nmr time scale becasue of slow inversion of the tetrathiolane ring or of hindered rotation about the bonds between *t*-butyl groups and the five-membered ring carbon.



7d **11**

Next, mechanism for the formation of these cyclic oligosulfides was investigated. Thus, 1-adamantyl phenyl ketone hydrazone (**7a**) was allowed to react with S_2Cl_2 and then the solvent was removed under reduced pressure without aqueous workup. In the ^{13}C nmr spectrum of the residue, S-C-S carbon signals of the pentathiane (**8a**) and the hexathiepane (**9a**) were not found, while several signals were observed in the range of δ 101.6-102.6. On the other hand, when *t*-butyl phenyl thioketone (**6b**) was allowed to react with S_2Cl_2, the ^{13}C nmr spectrum of the crude mixture showed two characteristic peaks at δ 101.05 and 101.62. These peaks are not assignable to the pentathiane (**8b**) or the hexathiepane (**9b**), but their chemical shift values are very similar to those observed with the products of the reaction of **7a** with S_2Cl_2 (δ 101.6-102.6). In addition, the fact that tlc on silica gel shows the formation of **8b** and **9b** indicates that these compounds are produced during workup by decomposition of the primary products that give signals at δ 101.05 and 101.62. Still reported that the reaction of aromatic and aliphatic thiones with SCl_2 yields the corresponding chlorothiosulfenyl chlorides ($R_2C(Cl)SSCl$) whose chlorinated carbon signals appeared in the range of δ 75-106 in ^{13}C nmr spectra.[6] Therefore, it is probable that analogous compounds, chlorooligosulfanyl chlorides $RR'C(Cl)S_nCl$, are formed in the reactions of S_2Cl_2 with hydrazone (**7a**) and thione (**6b**) and are the precursor compounds of cyclic oligosulfides such as **8**, **9** and **12**.

In conclusion, the reaction of hydrazones (**7a-d**) with S_2Cl_2 in the absence of an amine gave cyclic oligosulfides and not dithiiranes. The tetrathiolane (**11**) is the first example of an isolable tetrathiolane derivative. In these reactions, the formation of chlorooligosulfanyl chlorides is suggested as the intermediates leading to the cyclic oligosulfides.

EXPERIMENTAL

Melting points were determined on a Mel-Temp capillary tube apparatus and are uncorrected. ^1H nmr spectra were determined at 400 MHz and ^{13}C nmr spectra at 100.6 MHz using $CDCl_3$ as the solvent on a Bruker AM-400 spectrometer. Mass spectra were obtained at 70 eV in the EI mode on a Shimadzu QP-1000 spectrometer and ir spectra on a Hitachi Model 270-50 spectrophotometer. Hplc was performed on an LC-908 (Japan Analytical Industry) using chloroform as the solvent. Elemental analyses were performed by Chemical Analysis Center of Saitama University.

Disulfur dichloride was distilled over elemental sulfur and active carbon and stored in ampules in a refrigerator. Di-*t*-butyl ketone hydrazone (**7d**) was obtained by the reported method[7] and 1-adamantyl phenyl (**7a**) and *t*-butyl phenyl ketone hydrazones (**7b**) were prepared in a similar method. Benzophenone hydrazone (**7c**) was prepared from benzophenone and hydrazine hydrate.[8]

Reaction of 1-adamantyl phenyl ketone hydrazone (7a) with S_2Cl_2. A solution of S_2Cl_2 (282 mg, 2.1 mmol) in dichloromethane (5 ml) was added into a solution of **7a** (509 mg, 2.0 mmol) in dichloromethane (30 ml) at -78 °C. The reaction mixture was stirred for 20 min at -78 °C and the cooling bath was removed. During the mixture being warmed to room temperature, evolution of a gas probably due to nitrogen was observed at about -20 °C. The reaction was quenched by addition of water. The organic layer was washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gave a yellow residue, which was subjected to column chromatography (silica gel, hexane) to give 1-adamantyl phenyl pentathiane (**8a**) (81 mg, 11%), 1-adamantyl phenyl hexathiepane (**9a**) (47 mg, 6%), 1-adamantyl phenyl thioketone (**6a**) (253 mg, 49%) and 1-adamantyl phenyl ketone (**10a**) (72 mg, 15%).

8a: yellow needles, mp 183-184 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 1.51-1.64 (m, 6H), 1.80-1.81 (m, 6H), 1.98 (br s, 3H), 7.39-7.43 (m, 1H), 7.45- 7.53 (m, 2H), 7.61-7.63 (m, 2H); ^{13}C nmr (100 MHz, $CDCl_3$)δ 28.52, 36.49, 36.62, 43.33, 66.19 (S-*C*-S), 127.44, 127.59, 133.10, 134.33; ms *m/z* 384 (M^+), 320 (M^+-2S), 288 (M^+-3S), 256 (M^+-4S), 224 (M^+-5S). Anal. Calcd for $C_{17}H_{20}S_5$: C, 53.08; H, 5.24. Found: C, 53.08; H, 5.24.

9a: pale yellow crystals, mp 164-165 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 1.48-1.60 (m, 6H), 1.77-1.78 (m, 6H), 1.97 (br s, 3H), 7.26-7.31 (m, 1H), 7.33-7.37 (m, 2H), 7.58-6.61 (m, 2H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 28.76, 36.06, 39.61, 44.14, 108.64 (S-*C*-S), 127.62, 127.69, 130.51, 139.09; ms *m/z* 416 (M^+), 384 (M^+-S), 352 (M^+-2S), 320 (M^+-3S), 288 (M^+-4S), 256 (M^+-5S). Anal. Calcd for $C_{17}H_{20}S_6$: C, 49.00; H, 4.84. Found: C, 49.38; H, 4.91.

Reaction of *t*-butyl phenyl ketone hydrazone (7b) with S_2Cl_2. In a manner similar to that described above, the hydrazone (**7b**) (494 mg, 2.8 mmol) was allowed to react with S_2Cl_2 (370 mg, 2.7 mmol) to give *t*-butyl phenyl pentathiane (**8b**) (60 mg, 7%), *t*-butyl phenyl hexathiepane (**9b**) (30 mg, 3%), thiopivalophenone (**6b**) (51 mg, 10%), and pivalophenone (**10b**) (285 mg, 63%).

8b: white crystals, mp 135.0-135.5 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 1.09 (s, 9H), 7.38-7.41 (m, 1H), 7.48-7.51 (m, 2H), 7.63-7.68 (m, 2H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 25.58, 41.82, 65.30 (S-*C*-S), 127.56, 127.75, 133.83, 134.28; ms *m/z* 306 (M^+), 242 (M^+-2S), 178 (M^+-3S). Anal. Calcd for $C_{11}H_{14}S_5$: C, 43.10; H, 4.60. Found: C, 43.16; H, 4.58.

9b: pale yellow crystals, mp 144-145 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 1.39 (s, 9H), 7.27-7.31 (m, 1H), 7.33-7.38 (m, 2H), 7.65-7.67 (m, 2H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 28.79, 42.98, 107.35 (S-*C*-S), 127.75, 127.87, 130.11, 140.18; ms *m/z* 338 (M^+), 306 (M^+-S), 274 (M^+-2S), 242 (M^+-3S), 210 (M^+-4S), 178 (M^+-5S). Anal. Calcd for $C_{11}H_{14}S_6$: C, 39.02; H, 4.17. Found: C, 39.19; H, 4.16.

X-Ray structure analysis of **9b**. —*Crystal Data.* $C_{11}H_{14}S_6$, $M = 338.60$. Monoclinic, $a = 9.174(4)$, $b = 23.478(8)$, $c = 7.397(4)$ Å, $\beta = 111.66(4)$°, $V = 1481(1)$ Å^3 (by least-squares refinement on diffractometer angles for 22 automatically centered reflections, $\lambda = 1.54178$ Å), space group $P2_1/n$, $Z = 4$, $D_c = 1.52$ g cm^{-3}, $F(000) = 703$. Crystal dimensions: 0.46 × 0.40 × 0.38 mm, μ(Cu-Kα) = 82.384 cm^{-1}. *Data Collection and Processing.*—Mac Science MXC3K diffractometer, $\omega/2\theta$ mode with ω scan width = $2.33 + 0.20\tan\theta$, ω scan speed const. 8.0° min^{-1}, graphite-monochromated Cu-Kα radiation; 3212 reflections measured ($3.0 \leq 2\theta \leq 140$°), 3070 unique reflections. *Structure Analysis and refinement.*—The structure was solved by direct methods using SIR[9] 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[10] to minimize the functions $\Sigma(w|F_o|-|F_c|)^2$, where $w=\exp(5.00\sin^2\theta/\lambda^2)/[\sigma^2(F_o)+0.001|F_o|^2]$, for 2562 reflections with $I>3\sigma I$. The final R and R_W values are 0.037 and 0.044, respectively. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, vol. IV). All calculations were carried out on a SUN SPARC 10 workstation.

Reaction of benzophenone hydrazone (7c) with S_2Cl_2. In a method similar to that described above, the hydrazone (**7c**) (330 mg, 1.7 mmol) was allowed to react with S_2Cl_2 (270 mg, 2.0 mmol) to give diphenyl pentathiane (**8c**) (20 mg, 4%), diphenyl hexathiepane (**9c**) (40 mg, 7%), thiobenzophenone (**6c**) (58 mg, 17%), and benzophenone (**10c**) (140 mg, 47%).

8c: yellow crystals, mp 115-117 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 7.22-7.33 (m, 5H), 7.47-7.52 (m, 1H), 7.56-7.61 (m, 2H), 7.83-7.85 (m, 2H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 58.10 (S-*C*-S), 128.32, 128.83, 128.90, 129.96, 132.60, 136.05, 142.93; ms *m/z* 326 (M$^+$), 262 (M$^+$-2S), 230 (M$^+$-3S), 198 (M$^+$-4S). Anal. Calcd for $C_{13}H_{10}S_5$: C, 47.82; H, 3.09. Found: C, 47.56; H, 2.99.

9c: pale yellow crystals, mp 119-120 °C. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 7.33-7.40 (m, 10H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 99.93 (S-*C*-S), 128.40, 128.79, 128.97, 140.04; ms *m/z* 358 (M$^+$), 326 (M$^+$-S), 294 (M$^+$-2S), 262 (M$^+$-3S), 230 (M$^+$-4S), 198 (M$^+$-5S). Anal. Calcd for $C_{13}H_{10}S_6$: C, 43.54; H, 2.81. Found: C, 43.78; H, 2.73.

Reaction of di-*t*-butyl ketone hydrazone (7d) with S_2Cl_2. In a manner similar to that described above, the hydrazone (**7d**) (469 mg, 3 mmol) was allowed to react with S_2Cl_2 (641 mg, 4.8 mmol). The reaction mixture was subjected to column chromatography (silica gel, hexane) to give a mixture (146 mg) of elemental sulfur and the tetrathiolane (**11**). The mixture was further purified with hplc to give di-*t*-butyl tetrathiolane (**11**) (17.9 mg, 2%), di-*t*-butyl thioketone (59 mg, 12%), and an unidentified yellow oil (30 mg).

11: yellow oil. ^{1}H Nmr (400 MHz, $CDCl_3$) δ 1.38 (s, 18H); ^{13}C nmr (100 MHz, $CDCl_3$) δ 32.45 (br s), 45.08, 113.94 (S-*C*-S); ms *m/z* 254 (M^+), 190 (M^+-2S), 158 (M^+-3S). Anal. Calcd for $C_9H_{18}S_4$: C, 42.47; H, 7.13. Found: C, 42.73; H, 7.13.

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