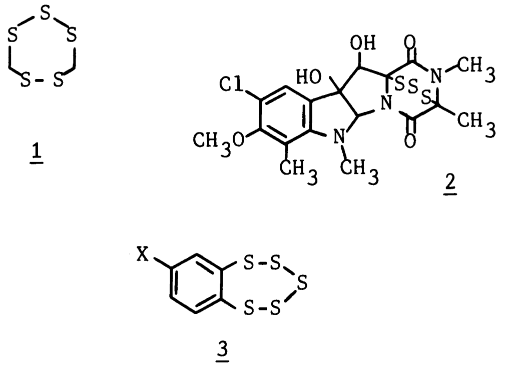
May, 1988] *Bull. Chem. Soc. Jpn., 61, 1647—1651 (1988)* 1647

Synthesis of Cyclic Polysulfides. Reactions of Dithiols and Related Compounds with Elemental Sulfur in Liquid Ammonia[1]

Ryu Sato,* Satoru Saito, Hiroshi Chiba, Takehiko Goto,
and Minoru Saito
Department of Resource Chemistry, Faculty of Engineering, Iwate University, Morioka 020
(Received August 31, 1987)

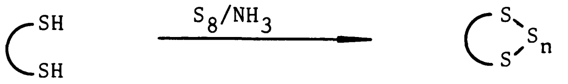
Many cyclic polysulfides, i.e., benzopentathiepins (**3a—d**), 6*H*-1,2,3,4,5-benzopentathiocin, 5*H*-1,2,3,4-benzotetrathiepin, 3*H*-1,2-benzodithiole, 1,5-dihydro-2,3,4-benzotrithiepin, 1,4-dihydro-2,3-benzodithiin, naphtho[1,8-*cd*]-1,2-dithiole, 1,2,3-trithiane, 1,2-dithiane, 2,3,4,5-tetrathiabicyclo[4.4.0]decane, and 2,3,4,5,6-pentathiabicyclo[5.4.0]undecane, were synthesized in high yields by new reactions of their corresponding dithiols and related compounds, 1,3-benzodithiole-2-thiones (**5**) and 1,3-dithiolane-2-thione, with elemental sulfur in liquid ammonia at ambient temperature. In the synthesis of **3a—d** from 1,2-benzenedithiol or **5**, considerable increase in the product yield was observed upon adding 1,3-dinitrobenzene to the solvent used in work-up.

Much interest of organic sulfur chemists has centered on cyclic polysulfides from the viewpoint of synthesis of natural products which show biological activity, such as lenthionine (**1**)[2] and sporidesmin (**2**)[3]. Various procedures for the synthesis of these compounds have been developed in the past few years.[4]



Scheme 1.

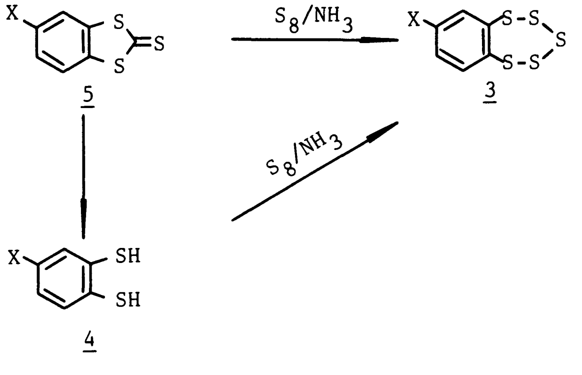
There have been published a few reports[5] on the synthesis of sulfur containing compounds such as benzopentathiepins (**3**). Very recently, Chenard et al.[5] reported the synthesis of **3** from benzothiadiazoles with elemental sulfur in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) at high temperatures such as 180 °C in moderate yields, and **3** were shown to have acaricidal and fungicidal effects.[6] In the course of our studies on the reactions of organic compounds with elemental sulfur in liquid ammonia,[7] we have reported on synthesis of polysulfides from corresponding thiols.[8] The above situation urged us to pursue a new synthesis of various cyclic polysulfides from corresponding dithiols and related compounds with elemental sulfur in liquid ammonia. Consequently, we could obtain many cyclic polysulfides **3, 7, 8, 9, 11, 12, 14, 17, 19, 21,** and **22** in moderate to excellent yields (Scheme 2). Moreover, in the case of synthesis of **3**, addition of 1,3-dinitrobenzene in the work-up procedure was found to increase the yield of **3**. This effect was explained in terms of the electron-transfer effect of thiolate species which accelerates the formation of sulfur–sulfur bond.



Scheme 2.

Results and Discussion

1,2-Benzenedithiols **4a** and **4b** and other dithiols **6, 10, 13, 15, 16,** and **18** or their synthetic equivalents such as 1,3-dithiole-2-thiones **5a—d** and 1,3-dithiolane-2-thione **20** were chosen as substrate for the synthesis of cyclic polysulfides and allowed to react with elemental sulfur in liquid ammonia, affording desired cyclic polysulfides together with an unidentified polymer (Scheme 3). As a typical synthesis of cyclic polysulfides, an optimization of the synthesis of **3** was studied.



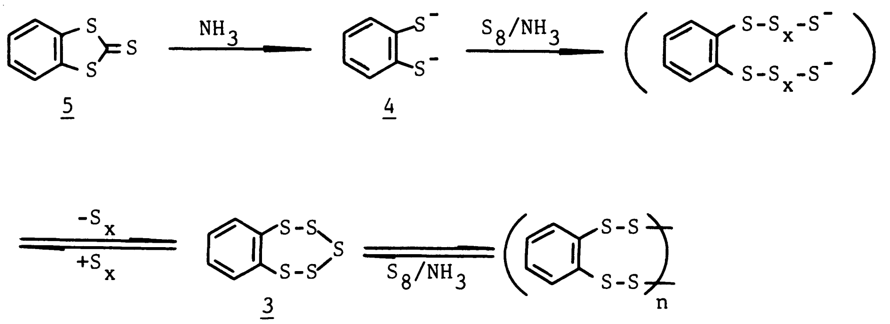
Scheme 3.

1,3-Benzodithiole-2-thione (**5a**) as a substrate gave better yields of **3** than **4** did (Runs 2, 4, 7, 12, and 13, Table 1). The quantity in equivalents of elemental sulfur used affected considerably the yields of **3**. For example, a use of 3 or 5 mg atom of elemental sulfur (6 or 10 milli equivalents, respectively) gave **3a** quantitatively (Runs 4 and 5), but in a reaction using 0.5 mg-atom of elemental sulfur the desired **3a** was

Table 1. Synthesis of Benzopentathiepins (**3**) with S_8/NH_3

Run	Substrate	S_8		Solvent	DNB		Yield of **3**	Mp θ_m/°C (lit)
		mg-atom	milli equiv		mmol	milli equiv	%	
1	**5a**	3.0	6.0	—	0	0	**3a** Trace	64 (60)[5]
2	**5a**	3.0	6.0	CH_2Cl_2	0.5	1	**3a** 82 (64)	
3	**5a**	3.0	6.0	CH_3CN	0.5	1	**3a** 75	
4	**5a**	3.0	6.0	Benzene	0.5	1	**3a** 97 (89)	
5	**5a**	5.0	10.0	Benzene	0.5	1	**3a** 97	
6	**5a**	0.5	1.0	Benzene	0.5	1	**3a** 2	
7	**5b**	3.0	6.0	CH_2Cl_2	1.5	3	**3b** 59 (30)	87 (89)[5]
8	**5b**	3.0	6.0	Benzene	1.5	3	**3b** 41 (30)	
9	**5c**	3.0	6.0	Benzene	0.5	1	**3c** 99 (90)	101 (98)[5]
10	**5d**	3.0	6.0	Benzene	1.5	3	**3d** 91 (20)	123
11	**5e**	3.0	6.0	Benzene	0.5	1	**3e** 0	
12	**4a**	3.0	6.0	Benzene	0.5	1	**3a** 78 (5)	
13	**4b**	3.0	6.0	CH_2Cl_2	1.5	3	**3b** 54 (19)	

a) Reaction conditions: reaction temp, 20 °C; reaction time, 0.5 h; liquid ammonia, 30 ml; substrate, 0.5 mmol; solvent, 80 ml. b) These solvents were used in work up. c) 1,3-Dinitrobenzene. d) Isolated yield based on the substrate. Yields in the absence of 1.3-dinitrobenzene are shown in parentheses.



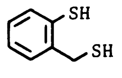
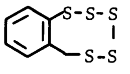
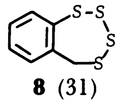
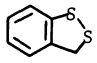
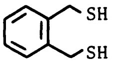
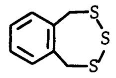
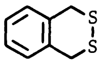
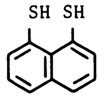
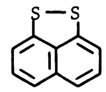
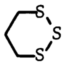
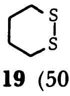
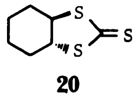
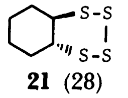
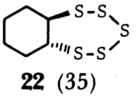
Scheme 4.

obtained only in 2% yield (Run 6). Only a trace of **3a** was obtained when no solvent was used in the work up of reaction and a use of an organic solvent such as dichloromethane or benzene significantly improved the yield of **3a** as shown in Table 1 (Runs 1—4; see Experimental). Moreover the kind of the solvent used in the work up also influenced the yield of benzopentathiepin **3**. Thus, the best yield was achieved when benzene was employed (Runs 2—4). These solvent effects may be accounted for in terms of the dilution effect of solvent which inhibits the collision of reactive species such as thiolate. A generality of the synthesis of **3** is indicated by Runs 7—11. We could not, however, obtain 5-nitro-1,2,3,4,5-benzopentathiepin (**3e**) by the present method. It should be noted that **3a** is obtained in a better yield (Run 4) from **5** than from **4** (Run 12), which is generally obtained by solvolysis of **5** (Scheme 3). In these reactions seven-membered benzopentathiepin **3a** was the sole isolated and stable product. Our further important finding is that a considerable increase in the yield of **3** was observed by addition of 1,3-dinitrobenzene to the solvent used in the work up (Runs 2, 7—10, and 12; see Experimental). In the absence of 1,3-dinitrobenzene, the amount of unidentified polymer increased. Interestingly, **3a** was also obtained by treating the polymer with elemental sulfur in liquid ammonia under similar conditions. Based on the above results, it seems that there are certain equilibriums between **3** and the polymer in both the reaction mixture and the work-up solution, and that 1,3-dinitrobenzene serves as a trapper of electron from thiolate intermediates to accelerate the formation of sulfur-linked product **3**, since it is well-known that 1,3-dinitrobenzene can trap one electron in electron-transfer systems. Plausible pathways of this reaction are depicted in Scheme 4.

To extend this method to other compounds, some dithiols, e.g., 1,2-bis(mercaptomethyl)benzene (**10**) and 1,3-propanedithiol (**16**), were treated with elemental sulfur in liquid ammonia similarly to **3**. Ten desired cyclic polysulfides **7, 8, 9, 11, 12, 14, 17, 19, 21,** and **22** were consequently obtained in moderate yields as shown in Table 2. It is noteworthy that the first two cyclic polysulfides having one benzylic methylene group were obtained by the reaction of 2-(mercaptomethyl)benzenethiol (**6**). Thus, an eight-membered ring product, 6*H*-1,2,3,4,5-benzopentathiocin (**7**), and a seven-membered ring compound, 5*H*-1,2,3,4-benzotetrathiepin (**8**), were obtained together with a five-membered ring product, 3*H*-benzo[*d*]-1,2-dithiole (**9**).

The ^1H NMR spectra of **8** showed a peak at δ=4.77 (AB pattern, $\Delta\delta$=0.96, J=16 Hz, 2H) characteristic of the two protons of the methylene group, whereas the methylene group in **7** appeared in a singlet peak at δ=4.41. Measurements of the molecular weights of the new compounds **7** and **8** by the Rast method gave the values of 283 and 235 respectively,[9] suggesting that the products **7** and **8** were not dimerized compounds. Similarly, a six-membered cyclic disulfide, 1,4-dihydro-2,3-benzodithiin (**12**), and 1,5-dihydro-2,3,4-benzotrithiepin (**11**) were obtained as expected when **10** was treated with elemental sulfur in liquid ammonia under similar conditions, as shown in Table 2. These results suggest that one, two, or three sulfur atoms in the molecule were incorporated from elemental sulfur to form the stable seven- or eight-membered ring compounds **7, 8, 9, 11,** and **12**. 1,8-Naphthalenedithiol (**13**) did not incorporate any sulfur atoms at all upon being treated with elemental sulfur, but naphtho[1,8-*cd*]-1,2-dithiole (**14**) was formed quantitatively. The formation of **14** may be explained on the basis of facile sulfur–sulfur bond formation to give the stable product **14**, since the two sulfur atoms in **13** lie close to each other at the peri position of the naphthalene ring. Subsequently, cyclizations of α,ω-alkanedithiols, 1,2-ethanedithiol (**15**), **16** and 1,4-butanedithiol (**18**), with elemental sulfur in liquid ammonia were carried out in a similar manner. Except the reaction of **15**, two expected six-membered cyclic polysulfides, 1,2,3-trithiane (**17**) and 1,2-dithiane (**19**), were obtained from the corresponding dithiols **16** and **18**, respectively. An unidentified polymer was mainly formed in the reaction of **15**. The results of the reactions of **16** or **18** suggest that these six-membered products are very stable in this system, in contrast to the results of the reactions of **6** or **10**.

Table 2. Synthesis of Cyclic Polysulfides **7, 8, 9, 11, 12, 14, 17, 19, 21,** and **22** with Elemental Sulfur in Liquid Ammonia

Run	Substrate	Condition	Solvent	Product (Yield/%) and Mp θ_m/°C (lit)		
1	 **6**	A	CH_2Cl_2	 **7** (18) 61	 **8** (31) 49	 **9** (36) oil[15]
2	 **10**	A	CH_3CN	 **11** (57) 101 (101)[16]	 **12** (26) 78 (78)[17]	
3	 **13**	B	Benzene	 **14** (98) 122 (123)[13]		
4	HS-CH_2CH_2-SH **15**	B	Benzene	Polymer		
5	HS-$(CH_2)_3$-SH **16**	B	CH_3CN	 **17** (38) 46 (46)[18]		
6	HS-$(CH_2)_4$-SH **18**	C	DMF	 **19** (50) 34 (31)[19]		
7	 **20**	D	CH_3CN	 **21** (28) 88 (89)[20]	 **22** (35) 68 (67)[20]	

a) Substrate, 0.5 mmol; liquid ammonia, 30 ml; solvent, 80 ml. b) Reaction conditions, A: r.t., 0.5 h, and 6 equiv of S_8. B: r.t., 2 h, and 6 equiv of S_8. C: r.t., 2 h, and 3 equiv of S_8. D: 40 °C, 3 h, and 6 equiv of S_8.

The 1,3-dithiolane-2-thione containing a cyclohexane ring, **20**, also reacted with elemental sulfur in liquid ammonia at 40 °C to give two correspoding cyclic polysulfides **21** and **22** in moderate yields (Run 7, Table 2).

In conclusion, **3** and analogous cyclic polysulfides **7**, **8**, **9**, **11**, **12**, **14**, **17**, **19**, **21**, and **22** were synthesized by this new method, which has a great advantage over precedent methods in that high yields may be obtained under mild conditions. Since these cyclic polysulfides are well known to exhibit remarkable properties and especially **3** are soluble in usual organic solvents, the use of **3** as sulfurization reagents is extensively applicable. These studies are now under progress in our laboratory.[10]

Experimental

All melting points were measured by the capillary method and uncorrected. IR spectra were obtained on a Hitachi 295 spectrophotometer, and ^{1}H NMR spectra were obtained on a Hitachi R-22 spectrometer by using tetramethylsilane as an internal standard. All reactions were monitered by TLC (Merck Kieselgel 60-GF). The silica gel used for column chromatography was Wako gel C-200. Mass spectra were taken with a Hitachi RMU-6M mass spectrometer. Elemental analyses were carried out with a Yanagimoto MT-3.

Materials. All reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Kasei Co., Ltd., or Aldrich Chemical Co. The reagents were further purified by general methods. 1,3-Benzodithiole-2-thiones (**5**) were synthesized from 2-aminobenzenethiol by the literature method.[11] 1,2-Benzenedithiols (**4**) were obtained by hydrolysis of **5**.[11] **6** was synthesized from bis(2-carboxyphenyl) disulfide by thiation with phosphorus pentasulfide followed by reduction with lithium aluminium hydride.[12] **10** was obtained from 1,2-bis(bromomethyl)benzene by the literature method.[4] **13** was given by two-step synthesis from 1,8-dichloronaphthalene.[13] **15**, **16**, and **18** were commecially available. Hexahydro-1,3-benzodithiole-2-thione (**20**) was prepared from cyclohexene oxide with potassium hydroxide and carbon disulfide by the literature method.[14]

Reactions of Dithiols 4a-b, 6, 10, 13, 15, 16, and 18, 1,3-Benzodithiole-2-thiones 5a—e or 1,3-Dithiolane-2-thione 20 with Elemental Sulfur in Liquid Ammonia. A typical procedure is as follows: **5a** (0.5 mmol) and elemental sulfur (3.0 mg atom) were taken into a titanium autoclave (volume 50 ml) and the autoclave was evacuated. Liquid ammonia (30 ml) was charged and then the mixture was stirred at 20 °C for 0.5 h. After completion of the reaction, the reaction mixture in liquid ammonia was added dropwise to benzene (80 ml) containing 1,3-dinitrobenzene (0.5 mmol) through a needle bulb and the solution was stirred at room temperature until liquid ammonia was evaporated completely (for about 2 h). An evaporation of benzene under vacuum and a subsequent column chromatography on silica gel (Wako gel C-200) using CCl_4/hexane as an eluent gave the desired benzopentathiepin **3a** (114 mg) as yellow crystals. The products were identified with ^{1}H NMR, IR, mass spectra, and elemental analyses. In the reaction of **6** with elemental sulfur in liquid ammonia, the yields of the products, **7** and **8**, were determined by the proton ratio for methylene groups in ^{1}H NMR spectra after separation of reaction mixture by column chromatography.

7-Amino-1,2,3,4,5-benzopentathiepin (3d): Yellow crystals (ether); mp 123 °C; IR (KBr) 1020, 1235, 1570, and 1620 cm^{-1}; ^{1}H NMR (CDCl) δ=4.01 (2H, br, $-NH_2$), 6.49 (1H, dd, J=9.0 and 3.0 Hz, arom), 7.02 (1H, d, J=3.0 Hz, arom) and 7.53 (1H, d, J=9.0 Hz, arom); MS m/z 251 (M$^+$). Found: C, 28.42; H, 1.92%. Calcd for $C_6H_5NS_5$: C, 28.66; H, 2.00%.

7: Yellow crystals (hexane/ether); mp 61 °C; IR (KBr) 450, 540, and 1400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.41(2H, s, $-CH_2-$) and 7.18—7.72(4H, m, arom); MS m/z 250 (M$^+$). Found: C, 33.77; H, 2.39%. Calcd for $C_7H_6S_5$: C, 33.57; H, 2.42%.

8: Yellow crystals (hexane/ether); mp 49 °C; IR (KBr) 445, 735, and 1390 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.28 (1H, d, J=15.0 Hz, $-CH_2-$), 5.26 (1H, d, J=15.0 Hz, $-CH_2-$) and 7.03—7.73 (4H, m, arom); MS m/z 218 (M$^+$). Found: C, 38.43; H, 2.74%. Calcd for $C_7H_6S_4$: C, 38.50; H, 2.77%.

Compounds 3a—c, 9, 11, 12, 14, 17, 19, 21, and 22: These were identified by comparing spectral and physical data with those of authentic samples. See Tables 1 and 2.

Reactions of Polymer obtained from 4 or 5 with Elemental Sulfur in Liquid Ammonia. The polymer (100 mg) obtained by reaction of **4a** or **5a** with elemental sulfur in liquid ammonia was taken into titanium autoclave (volume 50 ml) and then, after evacuation, liquid ammonia (30 ml) was charged into the autoclave. The mixture was allowed to react at 20 °C for 0.5 h. The reaction mixture obtained was treated in a similar manner as in the reaction of **5a** with elemental sulfur in liquid ammonia. **3a** of 53 mg was obtained.

References

1) A preliminary communication of a part of this work has already appeared: R. Sato, S. Saito, H. Chiba, T. Goto, and M. Saito, *Chem. Lett.*, **1986**, 349.

2) K. Morita and S. Kobayashi, *Chem. Pharm. Bull.*, **15**, 988 (1967); K. Morita and S. Kobayashi, *Tetrahedron Lett.*, **1966**, 573; I. W. J. Still and G. W. Kutney, *Tetrahedron Lett.*, **22**, 1939 (1981); S. J. Wratten and D. J. Faulkner, *J. Org. Chem.*, **41**, 2465 (1976).

3) For example: R. Rahman, S. Safe, and A. Taylor, *J. Chem. Soc. C*, **1969**, 1665; D. Brewer, R. Rahman, S. Safe, and A. Taylor, *J. Chem. Soc., Chem. Commun.*, **1968**, 1571.

4) For example: D. N. Harpp and R. A. Smith, *J. Am. Chem. Soc.*, **104**, 6045 (1982); R. Ballini, *Synthesis*, **1982**, 834; U. Anthoni, C. Christophersen, N. Jacobsen, and A. Svendsen, *Tetrahedron*, **38**, 2425 (1982); A. Kato, Y. Hashimoto, I. Otsuka, and K. Nakatsu, *Chem. Lett.*, **1978**, 1219; D. N. Harpp, R. A. Smith, and K. Steliu, *J. Org. Chem.*, **46**, 2072 (1981); D. N. Harpp and A. Granata, *J. Org. Chem.*, **44**, 4144 (1979); B. Milligan, B. Saville, and J. M. Swan, *J. Chem. Soc.*, **1965**, 2901; G. Goor and M. Antenius, *Synthesis*, **1975**, 329; S. Inoue, T. Tezuka, and S. Oae, *Phosphorus and Sulfur*, **4**, 219 (1978); J. Emsley and D. W. Gritfiths, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 228; G. Morel, E. Marchand, and A. Foucaud, *Synthesis*, **1980**, 918; N. Yamazaki, S. Nakahama, K. Yamaguchi, and T. Yamaguchi, *Chem. Lett.*, **1980**, 1355; E. A. Chernyshev, O. K. Kuzmin, A. V. Lebedev,

A. I. Gusev, N. I. Kirillova, N. S. Nametkin, V. D. Tyurin, and A. M. Krapivin, *J. Organomet. Chem.*, **252**, 133 (1983).

5) B. L. Chenard, U. S. Patent 84/00870 [*Chem. Abstr.*, **102**, 185115g (1985)]; B. L. Chenard and T. J. Miller, *J. Org. Chem.*, **49**, 1221 (1984); B. L. Chenard, R. L. Harlow, A. L. Johnson, and S. A. Vladuchick, *J. Am. Chem. Soc.*, **107**, 3871 (1985); J. Nakayama, M. Kashiwagi, R. Yomoda, and M. Hoshino, *Nippon Kagaku Kaishi*, **1987**, 1424.

6) F. Feher and M. Langer, *Tetrahedron Lett.*, **1971**, 2125; J. L. Moriss and C. W. Ress, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 211; J. Perregard, S. Sheibye, H. J. Meyer, I. Thomsen, and S. O. Lawesson, *Bull. Soc. Chim. Belg.*, **86**, 679 (1977).

7) For example: R. Sato, T. Goto, Y. Takikawa, and S. Takizawa, *Synthesis*, **1980**, 615; R. Sato, T. Etchu, Y. Takikawa, S. Takizawa, and M. Saito, *ibid.*, **1981**, 44; R. Sato, S. Chiba, Y. Takikawa, S. Takizawa, and M. Saito, *Chem. Lett.*, **1983**, 535; R. Sato, N. Saito, N. and M. Saito, *ibid.*, **1983**, 1603; R. Sato, N. Saito, Y. Takikawa, S. Takizawa, and M. Saito, *Synthesis*, **1983**, 1045; R. Sato, T. Senzaki, Y. Shikazaki, T. Goto, and M. Saito, *Chem. Lett.*, **1984**, 1423; R. Sato, K. Itoh, K. Ito, T. Goto, and M. Saito, *ibid.*, **1984**, 1913; R. Sato, M. Nakayama, Y. Yuzawa, T. Goto, and M. Saito, *Chem. Lett.*, **1985**, 1887.

8) R. Sato, T. Goto, Y. Takikawa, S. Takizawa, and S. Oae, *Phosphorus and Sulfur*, **7**, 289 (1979).

9) K. Hosaka, "Yuki-biryobunseki," Nankodo, Tokyo (1969), p. 633.

10) R. Sato, Y. Akutsu, T. Goto, and M. Saito, *Chem. Lett.*, **1987**, 2161.

11) S. Hunig and E. Fleckenstein, *Justus Liebigs Ann. Chem.*, **738**, 192 (1970).

12) A. Luttringhaus and K. Hagele, *Angew. Chem.*, **67**, 304 (1955); F. S. Fowkes and E. W. McCleland, *J. Chem. Soc.*, **1941**, 187.

13) K. Yui, Y. Aso, T. Otsubo, and F. Ogura, *Chem. Lett.*, **1986**, 551.

14) C. C. J. Culvenor, W. Davies, and K. H. Pausacker, *J. Chem. Soc.*, **1946**, 1051.

15) E. W. Mcleland, L. A. Warren, and J. H. Jackson, *J. Chem. Soc.*, **1929**, 1582; F. S. Fowes and E. W. Mcleland, *J. Chem. Soc.*, **1941**, 187.

16) S. Kabuss, A. Luttringhaus, H. Friebolin, and R. Mecke, *Z. Naturforsch., B: Anorg. Chem.*, **21**, 320 (1966).

17) P. K. Srivastava and L. Field, *J. Org. Chem.*, **37**, 4196 (1972).

18) G. Morel, E. Marchand, and A. Foucaud, *Synthesis*, **1980**, 918.

19) D. N. Harpp, S. J. Bodzay, and T. H. Chan, *Tetrahedron Lett.*, **27**, 441 (1986).

20) F. Feher and B. Degen, *Angew. Chem.*, **79**, 689 (1967).