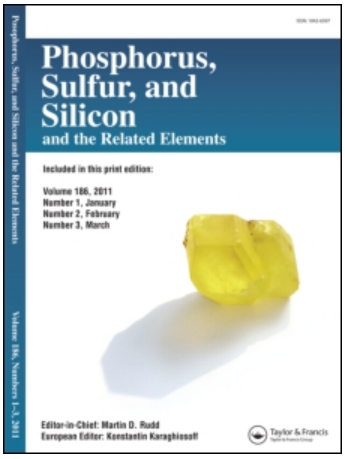

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THE CHEMISTRY OF α, ω-MERCAPTOALCOHOLS IN THE PRESENCE OF DIETHOXYTRIPHENYLPHOSPHORANE. TEMPERATURE DEPENDENCE OF CYCLODEHYDRATIONS AND S-ETHYLATIONS

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THE CHEMISTRY OF α,ω-MERCAPTOALCOHOLS IN THE PRESENCE OF DIETHOXYTRIPHENYLPHOSPHORANE. TEMPERATURE DEPENDENCE OF CYCLODEHYDRATIONS AND S-ETHYLATIONS

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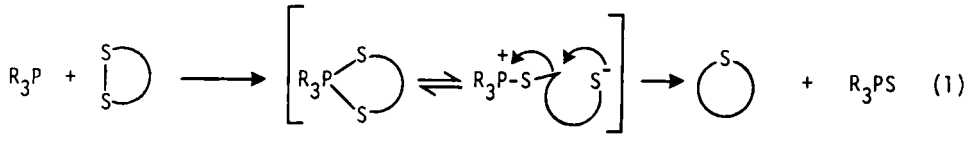
Diethoxytriphenylphosphorane (DTPP) is easily prepared by oxidative addition of triphenylphosphine with diethyl peroxide. DTPP converts a variety of mercaptoalcohols to cyclic sulfides as well as hydroxythioethers. The temperature dependence (+25 → −25°C) of the product distribution has synthetic potential.

INTRODUCTION

The importance of cyclic thioethers in natural products chemistry[1] and the need for regio- and enantiomeric synthesis of organic molecules containing the —S— functional group[2] have put heavy demands on existing synthetic methodology[3] and a more concentrated focus on more efficient reagents[4] and milder reaction conditions.[5] Existing strategies take advantage of the availability of simple precursors capable of functionalization by latent divalent sulfur nucleophiles, followed by demasking and intramolecular displacement of a suitable leaving group.[6]

A number of cyclic organosulfur compounds have been prepared using various organophosphorus reagents. In most cases, these reactions involve oxidative addition of the labile disulfide bond (—S—S—) to trivalent phosphorus atoms of phosphines[7] and phosphites,[8] followed by intramolecular displacement of phosphine sulfide or thiophosphate[9] (Equation 1).

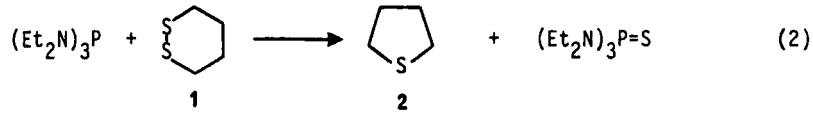


(1)

R=Alkyl, Aryl, Alkoxy, Aryloxy

Tris(diethylamino)phosphine (TDAP) also desulfurizes a number of cyclic disulfides including 1,2-dithiane (**1**) to afford tetrahydrothiophene (**2**) in essentially quantitative yield.[10] (Equation 2). Desulfurization of substituted 1,2-

diothiolanes using TDAP provides a valuable synthetic approach to substituted thietanes.[11]

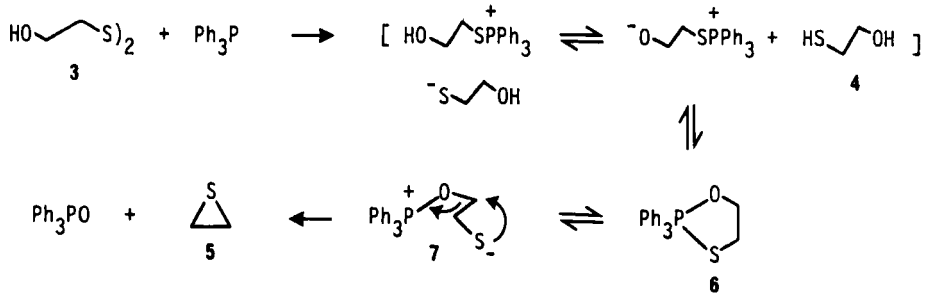


(2)

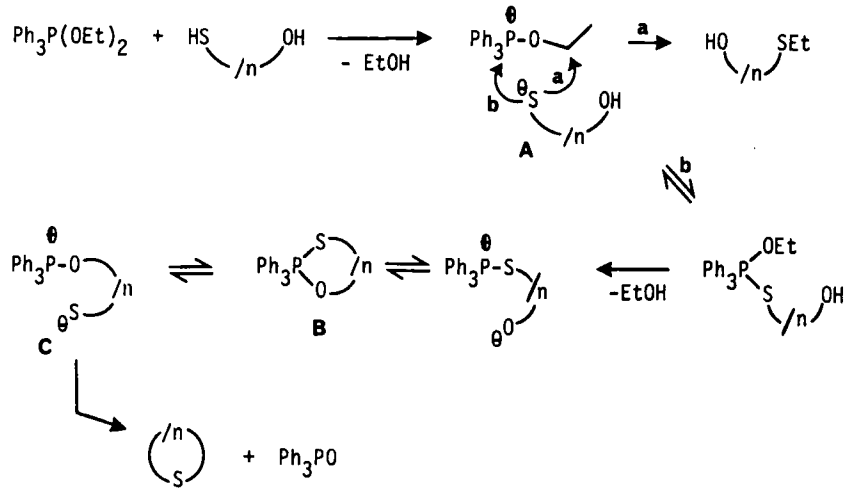
Although α,ω-mercaptoalcohols are easily prepared by a variety of simple synthetic procedures,[12] useful methodology for their direct conversion to cyclic thioethers is scarce.[13] In view of our previous success in establishing the scope and synthetic utility of diethoxytriphenylphosphorane (DTPP) as a useful reagent for effecting the cyclodehydration of diols to cyclic ethers,[14] it was desirable to ascertain the potential of DTPP for converting α,ω-mercaptoalcohols to cyclic sulfides in a single operation. Herein, we report the results of our investigation on this subject.

RESULTS AND DISCUSSION

Quite pertinent to the work reported here is the finding that bis(2-hydroxyethyl)-disulfide (**3**) reacts with triphenylphosphine (TPP) to afford 2-mercaptoethanol (**4**) and thiirane (**5**). Presumably, sulfide **5** arises from intramolecular mercaptide displacement of triphenylphosphine oxide (TPPO) from oxyphosphonium betaine **7**.[15] Based on these[15a] and other findings,[15b] we spectulated that bisphosphoranyl-ation of an α,ω-mercaptoalcohol with a suitably activated phosphorane reagent



[i.e., $Ph_3P(OEt)_2$] should afford betaine C via 1,3,2-oxathiophospholane B both of which are analogous to **7** and **6**, respectively, and thus provide a pathway for direct access to a range of cyclic sulfides. A sulfide synthesis by this process requires a *m*-exo-tet cyclization[16] involving mercaptide displacement of a phosphoryl moiety. The reaction sequences described in Scheme 1 summarize our expectations. Here, initial phosphoranylation of the thiol group by DTPP and subsequent loss of an equivalent of ethanol followed by the requisite heteroatom transposition via oxathiaphospholane B would give the desired cyclic sulfide through decomposition of oxyphosphonium betaine C (path b). Alternatively, ion pair A could simply decompose by thiolate displacement of TPPO (path a). Obviously, the success of this cyclodehydration scheme, particularly using DTPP, will depend heavily on the suppression of the S-ethylation side reaction (path a).



SCHEME 1 Cyclodehydration and S-Ethylation of Mercaptoalcohols with Diethoxytriphenylphosphorane.

We have examined the reactions of DTPP with several α,ω-mercaptoalcohols as a function of temperature in order to develop a comprehensive picture of the synthetic utility and scope of these transformations.

Ambient Temperature Reactions. 2-Mercaptoethanol (**4**) reacts with an equivalent of DTPP in toluene solvent to afford *ca.* 1:3 ratio of thiirane (**5**; 28%) and 2-ethylthioethanol (**8**; 72%) while 3-mercapto-1-propanol (**9**) reacts with DTPP to give 1:1 mixture of thietane (**10**) and 3-ethylthio-1-propanol (**11**). The fact that more thietane is formed than thiirane under similar reaction conditions is somewhat surprising considering the established facility with which the 3-exo-tet cyclization occurs (i.e., **4** → **5**) compared to the 4-exo-tet reaction (i.e., **9** → **10**). 2,2-Dimethylthietane (**13**) is obtained (56%) from reaction of 4-mercapto-4-methylbutanol (**12**) with DTPP. The other component of the reaction is 4-ethylthio-4-methylbutanol (**14**; 44%). Here, the gem-dialkyl effect[18] must be, in part, responsible for the slight increase in yield of thietane **13** over that for parent sulfide **10**. By contrast, 4-mercapto-4-methyl-2-pentanol (**15**) gave 4-ethylthio-4-methyl-2-pentanol (**17**) in quantitative yield in the presence of DTPP. Here, it seems clear that while the gem-dialkyl effect may increase the propensity for cyclodehydration, this effect is countered by the apparent inability of the sterically-congested, secondary carbinol to undergo effective phosphoranylation and subsequent conversion to the oxyphosphonium leaving group.

Reaction of 4-mercapto-1-butanol (**18**) with DTPP gives 65% tetrahydrothiophene (**2**) and 35% 4-ethylthiobutanol (**19**). This finding is in contrast to an earlier report by Denney *et al.*[19] where only sulfide **19** was observed. Although Denney *et al.* did not report the experimental conditions for their reaction,[19] we suspect that the absence of sulfide **2** from their reaction is attributable to the relatively high temperatures (*ca.* 40–60°C) required for the *in situ* generation of

DTPP.[19] Apparently, at these temperatures the competitive potential of the S-ethylation reaction is also substantial (path a) such that formation of the requisite oxathiaphospholane B is suppressed and cyclodehydration cannot proceed. The results of the low-temperature (−25°C) cyclodehydration of **18** with DTPP supports this hypothesis (*Vide infra*).

5-Mercaptopentanol (**21**) and 6-mercaptohexanol (**24**) react with DTPP affording tetrahydrothiopyran (**22**) and thiepane (**25**) in 63 and 18%, respectively. the remaining materials are the respective S-ethylated alcohols, **23** and **26**. The low yield associated with conversion of hydroxythiol **24** to sulfide **25** is not totally unexpected considering the anticipated severe energetic constraints attending cyclization of betaine C (n = 6).[20]

The results of an examination of a series of regioisomeric 1,2-mercaptoalcohols were expected to shed valuable light on steric and possible electronic factors controlling regioselective cyclodehydration. Perhaps surprisingly, neither 1-mercapto-1-propanol (**27**) nor 2-mercapto-1-propanol (**30**) gave propylene sulfide (**28**) on treatment with DTPP; instead, both **27** and **30** afforded the respective S-ethylated alcohols in high yields: 1-ethylthio-2-propanol (**29**; 99%) and 2-ethylthio-1-propanol (**31**; 62%). Similarly, 2-mercapto-1-phenylethanol (**32**) also gave quantitative yield of 2-ethylthio-1-phenylethanol (**34**) on treatment with DTPP; however, the diastereoisomer, 2-mercapto-2-phenylethanol (**35**) afforded 63% styrene sulfide (**33**). If one compares the results of the chemistry between **32** and isomeric **35** with DTPP, it seems evident that both steric and electronic effects of the phenyl group attached to the secondary thiol tend to enhance the efficiency toward formation of oxathiophosphonium betaine C required for cyclodehydration. It is, however, surprising that a similar trend in reactivity is not manifested between the regioisomers **27** and **30** with DTPP.

Low Temperature (−25°C) Reactions. Of the reaction parameters most likely to alter the product distribution, we speculated that a lower reaction temperature might suppress the S-ethylation substantially and consequently increase chemoselectivity favoring the cyclic sulfide. To test this hypothesis, the reaction of mercaptoalcohol **18** with DTPP was examined by adding **18** in anhydrous toluene solvent dropwise to a toluene solution of DTPP at −25°C (ethylene glycol-dry ice) and allowing the resulting mixture to stir at −25°C for 6 h. ^{13}C NMR analysis of the reaction mixture revealed quantitative (>99%) conversion of **18** to **2**. This result was encouraging and suggested that formation of the intermediate seven-membered oxathiaphosphorane B (n = 4) occurs at −25°C with irreversible loss of ethanol faster than the hydroxymercaptide ion can displace TPPO from eoxytriphenylphosphonium cation A (path a).

We examined the reactions of other mercaptoalcohols with DTPP at −25°C (6 h). Each mercaptoalcohol that formed a cyclic sulfide at ambient temperature also formed the cyclic sulfide at −25°C with an enhancement in yield at the expense of the S-ethylation product. For example, the yield of thiirane arising from cyclodehydration of **4** with DTPP increased from 28 to 63%. The reaction of **9** with DTPP at −25°C gave essentially thietane (40%); however, the reaction rate is diminished significantly such that 60% mercaptoalcohol **9** remains after 6 h. Styrene sulfide (**33**) is formed in 83% compared to 63% at ambient

temperature and 2,2-dimethylthietane (**13**) is formed in >90% with only traces of ethylthioalcohol **14** at −25°C.

A summary of the results from the reactions of various mecaptoalcohols with DTPP at ambient temperature and −25°C is presented in Table I. One might reasonably conclude that the synthetic utility of DTPP-promoted cyclodehydrations of mercaptoalcohols is limited to formation of 3-, 4-, 5-membered ring sulfides. Future research in this area requires development of phosphoranes capable of effecting the cyclodehydration but devoid of possible S-alkylation chemistry. We are actively exploring various aspects of this research.

EXPERIMENTAL SECTION

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance spectra were recorded on the Varin Model XL-100-15 and the Bruker Model WM-250 NMR spectrometers and the chemical shift parameters are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si).

Gas–Liquid Chromatographic (GLC) analyses were obtained on the Hewlett–Packard Model 5754B research gas chromatograph using a stainless-steel column (0.125 in (i.d.) × 10 ft packed with 15% Carbowax DC-550 on Chromosorb W-HP-AW-DMCS, 80–100 mesh).

Thin-layer Chromatography (TLC) analyses were performed on plastic sheets coated with silica gel (Baker–Flex) and used for confirmation of sample homogeneity. Iodine vapor was used for visualization.

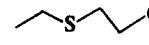
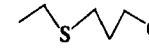
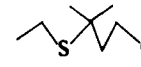
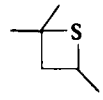
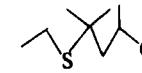
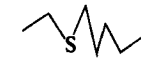
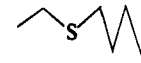
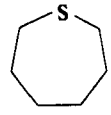
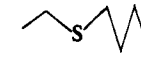
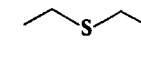
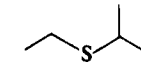
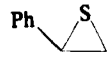
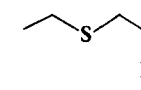
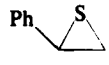
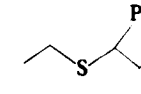
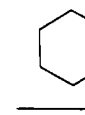
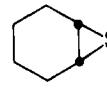
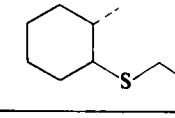
Toluene solvent was distilled from benzophenone ketyl, formed by addition of sodium to benzophenone in toluene solvent.[21]

General Procedure for the Reaction of DTPP with Mercaptoalcohols. The yields of the various product components of the cyclodehydration reactions were determined using ^{13}C NMR and GLC analyses. The identities of the product components were ascertained by coincidence of their NMR spectra and GLC retention times with authentic samples when possible. All experiments were performed in essentially the same manner, first at ambient temperature and then at −25°C (ethylene glycol/dry ice or tetrachloromethane/dry ice). The detailed procedure described for the reaction of 2-mercapto-2-phenylethanol with DTPP is illustrative. All experimental results are summarized in Table I.

Styrene sulfide (**33**). *Ambient Temperature.* 2-Mercapto-2-phenylethanol (**35**; 462 mg, 3 mmol)[22] in C_6D_6 solvent (1 mL) was added to a toluene solution of DTPP (3.1 mL, 1M in toluene, 3.1 mmol) at ambient temperature. The reaction mixture warmed noticeably for approximately 5 min during the initial mixing and the reaction was complete after the mixture cooled to ambient temperature. ^{13}C NMR analysis of the mixture indicated the presence of styrene sulfide (**33**; 63%; ^{13}C NMR δ 35.9 and 27.0) and 2-ethylthiol-2-phenylethanol (**36**; 37%; ^{13}C NMR δ 66.2, 52.5, 25.0 and 14.7). The identity of the latter substance was assured by comparison of its ^{13}C NMR spectrum with material prepared by

TABLE I

Cyclodehydration and S-ethylation of α,ω-mercaptoalcohols with DTPP at ambient temperature and −25°C.[a]

Mercaptoalcohol		Cyclic Sulfide (%)		Amb Temp	−25°C	Ethylthioalcohol (%)		Amb Temp	−25°C
	**4**		**5**	28	63		**8**	72	37
	**9**		**10**	50	40		**11**	50	trace[b]
	**12**		**13**	56	>90		**14**	44	<1
	**15**		**16**	0	--		**17**	>99	--
	**18**		**2**	65	>99		**19**	35	<1
	**21**		**22**	63	35[b]		**23**	37	30[b]
	**24**		**25**	18	16[b]		**26**	82	63[b]
	**27**		**28**	0	0		**29**	>99	90
	**30**		**28**	0	0		**31**	62[b]	90
	**32**		**33**	0	0		**34**	>99	60[b]
	**35**		**33**	63	83		**36**	27	60[b]
	**38**		**39**	0	--		**40**	>99	17

[a] The yields were determined by GLC/^{13}C NMR analysis of the reaction mixtures.
[b] The remaining material in the reaction mixture was starting mercaptoalcohol.

ethylation of 2-mercapto-2-phenylethanol with ethyl iodide in the presence of sodium hydride.

Low Temperature (*−25°C*). 2-Mercapto-2-phenylethanol (**35**; 462 mg, 3 mmol) in toluene solvent (2 mL) was added to DTPP (3.1 mL, 3 mmol, 1M in toluene) at −25°C. The mixture was maintained at −25°C for 6 h, then allowed to warm to ambient temperature. ^{13}C NMR analysis of the reaction mixture (1 mL C_6D_6 solvent added to maintain the deuterium NMR lock signal) revealed the presence of sulfide **33** (83%) and 2-ethylthio-2-phenylethanol (17%).

The requisite mercaptoalcohols are obtainable by two synthetic routes: (i) reaction of thiourea with a halohydrin to form the thiouronium halide salt, followed by basic hydrolysis to afford urea and the mercaptoalcohol after subsequent acidic neutralization.[23] This method was used to prepare 4-mercapto-1-butanol (**18**; 43%)[23] from 4-bromo-1-butanol, 5-mercapto-1-pentanol (**21**; 60%)[23] from 5-chloro-1-pentanol, and 6-mercapto-1-hexanol (**24**; 42%)[23] from 6-chloro-1-hexanol (See Experimental text). Acid-catalyzed (H_2SO_4) ring opening of cyclohexene oxide with thiourea followed by basic hydrolysis of the thiouronium salt gave *trans*-2-mercapto-cyclohexanol (**37**; 19%).[24] (ii) displacement of halide ion from a halohydrin or halocarbonyl substrate by an alkali metal methylxanthate[22] followed by simultaneous reduction ($LiAlH_4$) of the xanthate ester and carbonyl functions (when present) to the mercaptoalcohols.[22] Mercaptoalcohols prepared by this procedure include (a) 3-mercapto-1-propanol (**9**; 35%)[25] from 3-chloro-1-propanol, (b) 2-mercapto-2-phenyl-1-ethanol (**35**; 35%)[22] from α-bromo-α-phenylacetic acid, and 2-mercapto-1-phenyl-1-ethanol (**32**; 37%)[22] from α-bromoacetophenone.

Lithium aluminum hydride reduction of thiolactic acid give 2-mercapto-1-propanol (**30**; 39%).[26]

The hydroxythioethers were obtained by (i) reaction of sodium ethyl mercaptide (from ethanethiol and sodium hydroxide) with the appropriate halohydrin and include 3-ethylthio-1-propanol (**11**; 70%)[25], 4-ethylthio-1-butanol (**20**; 90%)[25], 5-ethylthio-1-pentanol (**23**; 50%),[25]and 6-ethylthio-1-hexanol (**26**; 25%) and (ii) formation of the appropriate sodium mercaptide (from the mercaptoalcohol and sodium hydride in toluene solvent) followed by ethylation with ethyl iodide gave 2-ethylthio-1-ethanol (**9**; 99%),[27] 2-ethylthio-1-propanol [**31**; 90%; ^{13}C NMR ($CDCl_3$) δ 60.6 ($\underline{C}H_2OH$), 34.9 ($\underline{C}H_2SCH_2CH_3$), 25.6 ($CH_3\underline{C}H_2S$), and 14.9 ($\underline{C}H_3$)], 2-ethylthio-1-phenyl-1-ethanol (**34**; 90%), and 2-ethylthio-2-phenyl-1-ethanol (**36**; 60%).

trans-2-Ethylthiocyclohexanol (**40**) was prepared from reaction of ethanethiol in potassium hydroxide/ethanol with cyclohexene oxide.[28] ^{13}C NMR ($CDCl_3$) δ 72.3 (C-1), 53.3 (C-2), 33.1 (C-3), 24.1 (C-4), 24.5 (C-5), 34.0 (C-6), 26.4 ($\underline{C}H_2S$), and 15.5 ($\underline{C}H_3$). Calcd for $C_8H_{16}OS$: C, 60.00; H, 9.99. Found: C, 59.65; H, 9.81.

It was also convenient to prepare some of the thioethyl derivatives by reacting the appropriate mercaptoalcohol with DTPP. In a typical procedure, 6-hydroxyhexanethiol (402 mg, 3.0 mmol) was combined with 3.0 mL of 1.0 M DTPP in toluene solvent under a nitrogen or argon atmosphere and allowed to stir overnight at ambient temperature. The S-ethylated derivative was chromat-

ographed using 10–30% ethyl acetate and 90–70% hexanes. The fractions containing the appropriate material were concentrated under reduced pressure and any additional solvent was removed under high vacuum. Samples requiring elemental analysis were sealed in vials under an argon atmosphere.

5-Ethylthiopentanol (**23**): ^{13}C NMR ($CDCl_3$) δ 14.9 ($\underline{C}H_3$), 24.8,* 25.3* ($SCH_2\underline{C}H_2\underline{C}H_2$), 29.7 ($\underline{C}H_2\underline{C}H_2OH$), 31.6,* 32.7* ($\underline{C}H_2S\underline{C}H_2$), and 62.2 ($\underline{C}H_2OH$). *Anal.* Calcd for $C_7H_{16}OS$: C, 56.70; H, 10.80. Found: C, 56.84; H, 10.92. (The asterisk denotes that assignments may be interchangeable.)

6-Ethylthiohexanol (**26**): ^{13}C NMR ($CDCl_3$) δ 14.6 ($\underline{C}H_2CH_2OH$), 25.6 ($SCH_2\underline{C}H_2$), 28.3*, 28.7* ($\underline{C}H_2\underline{C}H_2CH_2CH_2OH$), 31.5* ($\underline{C}H_2CH_2OH$), 31.9*, 32.9* ($\underline{C}H_2S\underline{C}H_2$), and 61.8 ($\underline{C}H_2OH$). *Anal.* Calcd for $C_8H_{18}OS$: C, 59.26; H, 11.10. Found: C, 59.40; H, 10.94. (The asterisk denotes that assignments may be interchangeable).

3-Ethylthiopropane-2-ol (**29**): ^{13}C NMR ($CDCl_3$) δ 14.9 ($\underline{C}H_3CH_2$), 22.0 ($\underline{C}H_3CH$), 26.2 ($CH_3\underline{C}H_2S$), 41.2 ($\underline{C}H_2S$), and 65.6 ($\underline{C}HOH$). *Anal.* Calcd for $C_5H_{12}OS$: C, 50.00; H, 9.99. Found: C, 50.21; H, 9.99.

2-Ethylthio-1-phenylethanol (**34**): ^{13}C NMR ($CDCl_3$) δ 15.0 ($\underline{C}H_3$), 26.6 ($CH_3\underline{C}H_2S$), 41.7 ($\underline{C}H_2S$), and 73.7 ($\underline{C}HOH$). *Anal.* Calcd for $C_9H_{14}OS$: C, 65.93; H, 7.68. Found: C, 66.20; H, 7.49.

2-Ethylthio-2-phenylethanol (**36**): ^{13}C NMR ($CDCl_3$) δ 65.5 ($\underline{C}H_2OH$), 52.6 ($\underline{C}HS$), 25.1 ($CH_3\underline{C}H_2S$) and 14.7 ($\underline{C}H_3$). *Anal.* Calcd for $C_9H_{14}OS$: C, 65.93; H, 7.68. Found: C, 65.50; H, 7.80.

A number of the cyclic sulfides are commerically available or their preparation have been reported elsewhere.[5,6a,30] The ^{13}C NMR shifts of a number of cyclic sulfides are also presented below.

Thiirane (**5**): ^{13}C NMR ($CDCl_3$) δ 17.5 ($\underline{C}H_2$); ^{31}Thietane (**10**): ^{13}C NMR ($CDCl_3$) δ 25.7 ($\underline{C}H_2S\underline{C}H_2$) and 27.8 ($CH_2\underline{C}H_2CH_2$);[31] 2,2-Dimethylthietane (**13**): ^{13}C NMR ($CDCl_3$) δ 17.6 ($\underline{C}H_2S$), 32.9 ($\underline{C}H_3$), 41.3 (C-3) and 47.2 (C-2; Thiolane (**2**): ^{13}C NMR ($CDCl_3$) δ 26.5 ($\underline{C}H_2CH_2CH_2S$), 27.8 ($\underline{C}H_2CH_2S$), and 29.0 ($\underline{C}H_2S$);[31] Thiane (**22**): ^{13}C NMR ($CDCl_3$) δ 26.5 ($\underline{C}H_2CH_2CH_2S$), 27.8 ($\underline{C}H_2CH_2S$), and 29.0 ($\underline{C}H_2S$);[31] Hexamethylene sulfide (**25**): ^{13}C NMR ($CDCl_3$) δ 29.5 ($\underline{C}H_2CH_2CH_2S$), 29.7 ($\underline{C}H_2CH_2S$) and 32.0 ($\underline{C}H_2S$);[31] Styrene sulfide (**33**): ^{13}C NMR ($CDCl_3$) δ 27.0 ($CH\underline{C}H_2$) and 35.9 ($\underline{C}HCH_2$).

1-Phenyl-1-mertcaptoetanol (**32**). (i) α-Bromoacetophenone (8.0 g, 0.04 mol) in 15 mL of acetone was added dropwise (10°C, 0.5 h) to an acetone solution (40 mL) of sodium benzylxanthate (20 mL, 0.04 mol). After stirring for 1 h at ambient temperature, the mixture was filtered and the filtrate was concentrated to an oil under reduced pressure (0.5 torr, 70°C). The oily residue was dissolved in dry ether (15 mL), then added dropwise to a suspension of lithium aluminum hydride (5.0 g, 0.13 mol) in anhydrous ether (50 mL). After refluxing overnight, the suspension was treated with acetone (100 mL) followed by 6N H_2SO_4 (100 mL). The ethereal layer was separated and washed with 10% aqueous sodium hydroxide (5 × 100 mL). The combined basic extracts were acidified (conc. HCl) and the resulting suspension was extracted with ether (5 × 100 mL). The ethereal portions were dried (Na_2SO_4), then concentrated (rotary evaporator) to afford 3.4 g of crude mercaptoalcohol 32.

(ii) α-Bromoacetophenone (11.2 g, 0.056 mol) in 60 mL acetone was added

dropwise (1 h, 10°C) to a solution of sodium ethylxanthate (30 mL, 0.056 mol) in acetone (60 mL). After stirring for 1 h at ambient temperature, the mixture was filtered and the resulting solution was concentrated under reduced pressure (60°C, 1 torr) to an oil. The resulting oily residue was dissolved in dry ether (50 mL) and added dropwise to a suspension of lithium aluminum hydride (5.0 g, 0.13 mod) in dry ether (75 mL). After refluxing overnight, the suspension was treated with acetone (100 mL) followed by 6N H_2SO_4 (100 mL). The ether layer was separated and washed with 10% aqueous sodium hydroxide (5 × 100 mL). The combined basic extracts were acidified (conc. HCl) and extracted with ether (5 × 100 mL). The combined ether portions were dried (Na_2SO_4) then concentrated (rotary evaporator) to afford 4.2 g of crude **32**.

The two crude samples of **32** were combined and distilled under reduced pressure to afford homogeneous 1-phenyl-2-mercaptoethanol (5.4 g, 37%): bp 84–7° (1.5–1.0 torr) (lit.,[20] bp 93–95° (3 torr)); ^{1}NMR ($CDCl_3$) δ 1.40 (*t*, J = 9 Hz, 1H, SH), 2.66–2.86 (*m*, 2H CH_2), 3.02 (*bs*, 1H, OH), 4.66 (*dd*, J_1 = 3 Hz, J_2 = 4 Hz, 1H, CH), and 7.32 (*s*, 5H, aromatic CH); ^{13}C NMR ($CDCl_3$) δ 142.1, 128.5, 128.0, 124.9 (aromatic CH), 74.7 (CHOH), and 33.7 (CH_2SH).

5-Mercapto-1-pentanol (**21**). Thiourea (10.2 g, 0.135 mol) in water (15 mL) was added to 5-chloro-1-pentanol (12.2 g, 0.10 mol) and the resulting mixture was kept at reflux for 4 h then at ambient temperature for 16 h. Ten-percent sodium hydroxide (4.39 g in 45 mL H_2O) was added and the mixture was refluxed an additional 3 h. Aqueous sulfuric acid (10% w/w, *ca.* 4 mL) was added to lower the pH to approximately 4 (pH paper indicator) and the mercaptoalcohol was extracted into ether (5 × 100 mL). The ethereal extracts were dried (Na_2SO_4) and the solvent removed (reduced pressure). Distillation of the resulting oil afforded 5-mercapto-1-pentanol (7.2 g, 60% yield): bp 103–105°C (12–15 torr) [lit.,[23] bp 100–105°C (15 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.35 (*t*, J = 8 Hz, 1H, SH), 1.30–1.88 (*m*, 6H, C_2, C_3, C_4-CH_2), 2.26 (*s*, 1H, OH), 2.54 (*q*, J = 8 Hz, 2H, CH_2SH), and 3.62 (*t*, J = 7 Hz, 2H, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 78.3 (CH_2OH), 62.5 (CH_2SH), 33.6 (C_3-CH_2), 32.1 (C_2-CH_2), and 24.5 (C_4-CH_2).

6-Mercapto-1-hexanol (**24**) was prepared (42% yield) by the reaction of thiourea (5.1 g, 0.069 mol) with 6-chloro-1-hexanol (7.0 g, 0.051 mol) followed by sodium hydroxide hydrolysis (2.24 g in 23 mL H_2O) of the thiouronium salt: bp 104–105°C (8 torr) [lit.,[23] bp 121–122°C (15 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.40 (*t*, J = 8 Hz, 1H, SH), 1.20–1.80 (*m*, 8H, C_2, C_3, C_4, C_5-CH_2), 1.80 (*s*, 1H, OH), 2.54 (*g*, J = 8 Hz, 2H, CH_2SH, and 3.62 (*t*, J = 6 Hz, 2H, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 62.7 (CH_2OH), 33.9, 32.6, 28.1, 25.2, and 24.5 (C_2-C_6).

4-Mercapto-1-butanol (**18**) was prepared (43% yield) by the reaction of thiourea (10 g, 0.135 mol) with 4-bromo-1-butanol (15.3 g, 0.10 mol) followed by basic hydrolysis (4.4 g of NaOH in 45 mL H_2O) of the thiouronium salt: bp 59–60°C (1 torr) [lit.,[23] bp 69–71°C (5 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.38 (*t*, J = 8 Hz, 1H, SH), 1.56–1.84 (*m*, 4H, C_2, C_3-CH_2), 2.36 (*s*, 1H, OH), 2.42–2.74 (*m*, 2H, CH_2SH), and 3.66 (*t*, J = 6 Hz, 2H, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 62.2 (CH_2OH), 31.4 and 30.3 (CH_2SH and CH_2CH_2OH; may be interchangeable), and 24.5 (C_3-CH_2).

trans-2-Mercaptocyclohexanol (**37**) was prepared by reaction of cyclohexene oxide (49.0 g, 0.5 mol) with thiourea (40.0 g, 0.5 mol) and sulfuric acid (15 mL,

0.5 mol in 175 mL water), followed by hydrolysis with sodium hydroxide (7.4 g in 135 mL H_2O). *trans*-2-Mercaptocyclohexanol (2.25 g, 19% yield): bp 84–86°C (7–5 torr) [lit.,[24] bp 97–99° (15 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.10–1.46 (*m*, 4H, ring CH's), 2.30–2.70 (*m*, 1H, CHSH), 2.85 (*bs*, 1H, OH), and 3.04–3.38 (*m*, 1H, CHOH); ^{13}C NMR ($CDCl_3$) δ 76.6 (COH), 47.6 (CHSH, 36.4 (C_2^*), 34.1 (C_5^*), 26.5 (C_3^*), 24.7 (C_4^*); the asterisk denotes tentative assignments. The major product was cyclohexene episulfide.

2-Mercapto-1-propanol (**30**) was prepared (39% yield) by reduction of thiolactic acid (21.2 g, 0.20 mol) with lithium aluminum hydride (8 g, 0.21 mol) followed with a workup analogous to that for the xanthate reductions (see compound 31): bp 47–50°C (5 torr) [lit.,[26] bp 56–60°C (15 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.34 (*d*, J = 7 Hz, 3H, CH_3), 1.62 (*d*, J = 7 Hz, 1H, SH), 3.04 (*s*, J = 7 Hz, 1H, CHSH), and 3.34–3.78 (*m*, 3H, CH_2OH); ^{13}C NMR ($CDCl_3$ δ 69.3 (CH_2OH), 37.9 (CHSH), and 20.9 (CH_3).

3-Mercapto-1-propanol (**9**) was prepared (35% yield), using the procedure previously described, from the reaction of 3-chloro-1-propanol with sodium ethylxanthate (54 mL, 0.1 mol) followed by reduction with lithium aluminum hydride (7.6 g, 0.2 mol): bp 50–53°C (2 torr) [lit.,[29] bp 75–80°C (7 torr)]; ^{1}H NMR ($CDCl_3$) δ 14.1 (*t*, J = 8 Hz, 1H, SH), 1.84 (*p*, J = 7 Hz, 2H, $HOCH_2CH_2$), 2.46 (*bs*, 1H, OH), 2.66 (*q*, J = 8 Hz, 2H, CH_2SH), and 3.75 (*t*, J = 7 Hz, 2H, CH_2OH); ^{13}C NMR ($CDCl_3$) δ 60.8 (CH_2OH), 36.2 (CH_2SH), and 21.2 ($HOCH_2CH_2$).

2-Phenyl-2-mercaptoethanol (**35**) was prepared (35% yield), using the procedure previously described, from the reaction of α-bromo-δ-phenylacetic acid (22.5 g, 0.100 mol) followed by reduction with lithium aluminum hydride (8.0 g, 0.21 mol) in THF solvent (100 mL): bp 99–105°C (0.07 torr) [lit.,[22,26] bp 90–103°C (1.6 torr)]; ^{1}H NMR ($CDCl_3$) δ 1.98 (*d*, J = 7 Hz, 1H, SH), 2.38 (*bt*, J = 7 Hz, 1H, OH), 3.60–4.20 (*m*, 3H, CH_2CH), and 7.34 (*s*, 5H, aromatic CH). ^{13}C NMR ($CDCl_3$) δ 140.6, 128.8, 127.8, 127.4 (aromatic CH), 68.3 (CH_2OH), and 46.3 (CHSH).

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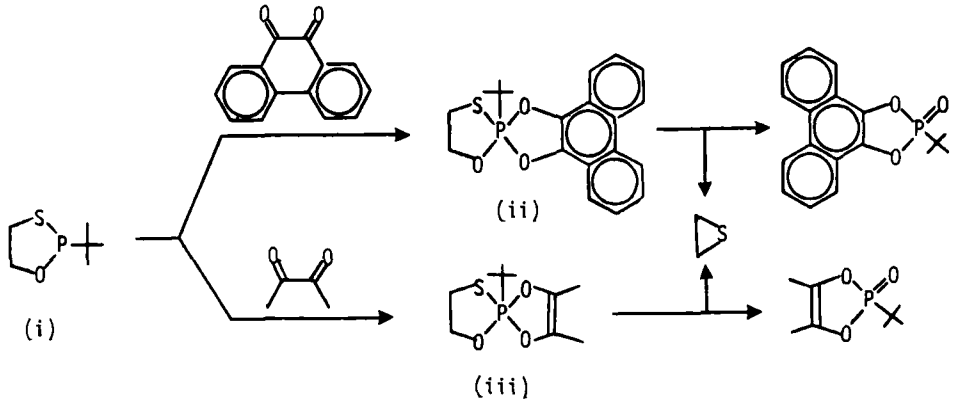

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