475. *The Interaction of Aldehydes and Ketones with Monothioglycols.*

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The reaction of aldehydes and ketones with monothioglycols has been applied to the synthesis of several new 1 : 3-oxathiolans and 1 : 3-oxathians. A study of the reaction of benzil and benzoin with 2-hydroxyethanethiol has led to novel cyclic compounds containing oxygen and sulphur.

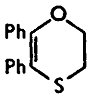
There are numerous references in the literature to the activity of phenoxathiin as an insecticide, anthelmintic, and bactericide. The present work arose as an attempt to find such activity in other ring systems containing oxygen and sulphur. The compounds described have been tested by routine screening but no useful activity has been found.

The reaction of aldehydes and ketones with 2-hydroxyethanethiol and 3-hydroxypropanethiol under acid dehydrating conditions generally gives 1 : 3-oxathiolans and 1 : 3-oxathians,[1,2] but Djerassi and Gorman [1] state that benzophenone does not react with hydroxyalkanethiols in boiling benzene in the presence of toluene-*p*-sulphonic acid. We have found, in four cases, that in boiling toluene reaction slowly gave moderate yields of oxathiolans and oxathians. The diphenyloxathiolans decompose slowly in refluxing toluene to the original benzophenone and an amorphous solid which is probably polyethylene sulphide.

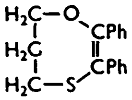
The water-separator method [1] has been applied to the preparation of 17 new oxathiolans and oxathians from various aldehydes and ketones. It failed with phenacyl chloride since the halogen atom is " positive " enough to oxidise the thiol, and hydrogen chloride was eliminated.

Chloral hydrate and 2-hydroxyethanethiol, in the absence of catalyst, yielded 2-trichloromethyl-1 : 3-oxathiolan as an unstable crystalline compound probably identical with that described by Bennett and Whincop [3] as a complex of chloral with 2-hydroxyethanethiol. Chloral mercaptals could not be obtained in aqueous suspension,[4] by the water-separator method, or by saturating an ethanolic solution of the components with hydrogen chloride.

Benzoin did not react with 2-hydroxyethanethiol in boiling benzene, but gave the expected oxathiolan in low yield in boiling toluene. A by-product, obtained in increasing yield with increased refluxing time, was undoubtedly 2 : 3-dihydro-5 : 6-diphenyl-1 : 4-oxathiin (I).



(I)



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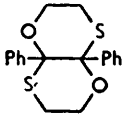

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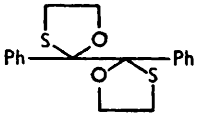

(IV)

This oxathiin can also be prepared easily by dehydration of α-(2-hydroxyethylthio)-deoxybenzoin (from desyl chloride and 2-hydroxyethanethiol). This route to these oxathiins is apparently general and 2 : 3-diphenylbenzoxathiin, 2 : 3-dihydro-6-phenyl-1 : 4-oxathiin, 6-*p*-bromophenyl-2 : 3-dihydro-1 : 4-oxathiin, and 2 : 3-dihydro-6-methyl-1 : 4-oxathiin have been similarly prepared. The corresponding 7-membered ring compound, 2 : 3-diphenyl-1-oxa-4-thia*cyclo*hept-2-ene (II), has been obtained by dehydration of α-(3-hydroxypropylthio)deoxybenzoin.

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[1] Djerassi and Gorman, *J. Amer. Chem. Soc.*, 1953, **75**, 3704.

[2] Jaeger and Smith, *Chem. and Ind.*, 1954, 1106; Djerassi and Grossman, *J. Amer. Chem. Soc.*, 1957, **79**, 2553; Kipnis and Ornfelt, *ibid.*, 1949, **71**, 3555.

[3] Bennett and Whincop, *J.*, 1921, 1860.

[4] Davey, *J. Inst. Petroleum*, 1947, **33**, 527.

2-Benzoyl-2-phenyl-1 : 3-oxathiolan could not be obtained from benzil and 2-hydroxyethanethiol, although Hurtley and Smiles [5] obtained the corresponding dithiolan from ethane-1 : 2-dithiol. The reaction in cold methanolic hydrogen chloride yielded two isomeric substances $C_{18}H_{18}O_2S_2$. Both isomers were degraded to benzoin with Raney nickel in acetone. Stereoisomeric forms of (III) and (IV) are possible structures for these compounds.

Oxathiolans and oxathians by the water-separator method.[1]

Substance	B. p./mm.	M. p.	n_D	Formula	Found (%) C	H	Required (% C	H)
1 : 3-*Oxathians*								
2-Methyl-2-phenyl-	106—108°/2·0	58—61°	1·5607/22°	$C_{11}H_{14}OS$	67·6	6·8	68·0	7·2
2-Ethoxycarbonylmethyl-2-methyl-	108°/1·2	—	1·4903/19°	$C_9H_{16}O_3S$	53·2	7·7	52·9	7·9
2-*p*-Chlorophenyl-	133°/1·2	48—50	—	$C_{10}H_{11}OClS$	55·7	5·0	55·9	5·1
1 : 3-Oxathian-2-*spiro*cyclohexane	86—87°/2	—	1·5212/24°	$C_9H_{16}OS$	62·5	9·0	62·8	9·3
1 : 3-*Oxathiolans*								
2-Ethyl-2-phenyl-	107°/2·4	—	1·5610/21°	$C_{11}H_{14}OS$	68·0	7·3	68·0	7·2
2-*p*-Chlorophenyl-2-methyl-	113°/1·5	—	1·5757/23°	$C_{10}H_{11}OClS$	56·3	5·1	55·9	5·1
2-(2 : 4-Dichlorophenyl)-2-methyl-	135°/1·5	—	1·5930/23°	$C_{10}H_{10}OCl_2S$	48·5	4·2	48·1	4·0
2-(2 : 5-Dichlorophenyl)-2-methyl-	136°/0·25	—	—	$C_{10}H_{10}OCl_2S$	48·4	4·0	48·1	4·0
2-Methyl-2-*p*-nitrophenyl- ...	—	50—52	—	$C_{10}H_{11}O_3NS$	53·1	4·9	53·3	4·9
2-*p*-Methoxyphenyl-2-methyl-	132°/1·1	—	1·5680/20°	$C_{11}H_{14}O_2S$	63·1	6·6	62·9	6·7
2-Benzyl-2-phenyl-	—	42—43·5	—	$C_{16}H_{16}OS$	75·0	6·0	75·0	6·3
2-*p*-Chlorophenyl-	124°/0·9	—	—	C_9H_9OClS	53·5	4·4	53·9	4·5
2-*o*-Chlorophenyl-	123°/1	—	—	C_9H_9OClS	53·7	4·4	53·9	4·5
2-*p*-Nitrophenyl-	—	73—77	—	$C_9H_9O_3NS$	51·4	4·4	51·2	4·3
2-*p*-Chlorobenzyl-2-phenyl-	—	60—63	—	$C_{16}H_{15}OClS$	66·5	5·2	66·1	5·2
2-*p*-Methylsulphonylphenyl-	—	102	—	$C_{10}H_{12}O_3S_2$	48·8	4·9	49·2	4·9
2-4′-Chlorobenzyl-2-*p*-chlorophenyl-	—	65—68	—	$C_{16}H_{14}OCl_2S$	59·0	4·2	59·1	4·3

EXPERIMENTAL

2-p-*Chlorophenyl-2-hydroxyethanethiol.*—2-Bromo-1-*p*-chlorophenylethanol (20 g.) was added to a saturated solution of hydrogen sulphide in ethanol (100 ml.) and sodium hydroxide (6·8 g.) at 60°. After 1 hr. at this temperature, the ethanol was evaporated and the residue treated with water. The solution was acidified with acetic acid, and the product separated with ether. Distillation gave 2-p-*chlorophenyl-2-hydroxyethanethiol* (5 g.), b. p. 132°/2 mm. (Found: C, 50·9; H, 4·7. C_8H_9OClS requires C, 50·9; H, 4·8%).

2 : 2-*Diphenyl-*1 : 3-*oxathiolan.*—2-Hydroxyethanethiol (30 g.), benzophenone (58 g.), and toluene-*p*-sulphonic acid (1 g.) were refluxed in toluene (250 ml.) for 3 hr. while water (7·2 ml.) was evolved. After cooling, an amorphous solid, probably polyethylene sulphide, was removed and washed with ether. The combined filtrates were washed with sodium hydrogen carbonate solution, dried, and evaporated. The residue was run in dry benzene through a column of active alumina (type 0) to remove remaining traces of the amorphous solid. The residue was obtained crystalline from methanol at 0° and recrystallised from propan-2-ol giving 2 : 2-*diphenyl-*1 : 3-*oxathiolan* (22 g.), m. p. 52° (Found: C, 74·2; H, 5·7. $C_{15}H_{14}OS$ requires C, 74·4; H, 5·8%).

The following were obtained similarly: the *compounds* in the Table were obtained as in ref. 1.

2 : 2-*Di-*(p-*chlorophenyl*)-1 : 3-*oxathiolan*, prisms (from propan-2-ol), m. p. 36° (Found: C, 58·0; H, 3·7. $C_{15}H_{12}OCl_2S$ requires C, 57·9; H, 3·9%). 2-p-*Chlorophenyl-2-phenyl-*1 : 3-*oxathiolan* (from methanol at −20°), m. p. 28° (Found: C, 65·1; H, 4·5. $C_{15}H_{13}OClS$ requires C, 65·1; H, 4·7%). 2 : 2-*Diphenyl-*1 : 3-*oxathian* (from methanol), m. p. 116—118° (Found: C, 74·9; H, 6·1. $C_{16}H_{16}OS$ requires C, 75·0; H, 6·3%).

2-*Trichloromethyl-*1 : 3-*oxathiolan.*—2-Hydroxyethanethiol (5 g.) and chloral hydrate

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[5] Hurtley and Smiles, *J.*, 1926, 2267.

(10·6 g.) were refluxed in benzene (70 ml.). After 1½ hr., when the evolution of water had ceased, the solution was concentrated at 170 mm. 2-*Trichloromethyl*-1 : 3-*oxathiolan* formed prisms, m. p. 70—85°, on cooling (Found: C, 23·3; H, 2·5. $C_4H_5OCl_3S$ requires C, 23·1; H, 2·4; Cl, 51·3. $C_4H_7O_2Cl_3S$ requires C, 21·3; H, 3·1; Cl, 47·2%). Bennett and Whincop[3] found Cl, 50·7, 51·2% for the condensation product of chloral and 2-hydroxyethanethiol. It is insoluble in cold water but dissolves rapidly with decomposition when heated; it also decomposes into volatile components on attempted distillation at 1 mm., and slowly deliquesces when exposed to the atmosphere.

2-*Methyl*-2-*phenyl*-1 : 3-*oxathiolan* 3 : 3-*Dioxide*.—2-Methyl-2-phenyl-1 : 3-oxathiolan (5 g.) in acetone (100 ml.) was stirred for 24 hr. with finely powdered potassium permanganate (6 g.). The mixture was filtered, and unchanged oxathiolan removed at 130°/2 mm. Strong cooling of the residue in methanol gave colourless prisms of the *dioxide* (*ca.* 2 g.), m. p. 56—57° (Found: C, 57·0; H, 5·6. $C_{10}H_{12}O_3S$ requires C, 56·6; H, 5·7%). The compound slowly decomposes at room temperature giving acetophenone. Attempts to carry out the oxidation with hydrogen peroxide in acetone or acetic acid led only to acetophenone.

α-(2-*Hydroxyethylthio*)*deoxybenzoin*.—Sodium hydroxide (2·8 g.) was added to an ethanolic solution of 2-hydroxyethanethiol (5 g.) and desyl chloride (14·8 g.). Reaction took place rapidly on warming. Water was added and the product separated with benzene. Light petroleum (b. p. 80—100°) (60 ml.) was added to a solution in benzene (40 ml.), and the precipitated oil obtained crystalline at 0°. Repetition of the process gave pure α-(2-*hydroxyethylthio*)*deoxybenzoin*, m. p. 51° (Found: C, 70·3; H, 5·9. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9%).

2 : 3-*Dihydro*-5 : 6-*diphenyl*-1 : 4-*oxathiin*.—α-(2-Hydroxyethylthio)deoxybenzoin (8·6 g.), when boiled for 1 hr., with separation of water, in toluene (100 ml.) containing toluene-*p*-sulphonic acid (0·5 g.), gave 2 : 3-*dihydro*-5 : 6-*diphenyl*-1 : 4-*oxathiin* (4 g.), m. p. 63—65°, very pale yellow prisms from methanol (charcoal) (Found: C, 75·7; H, 5·5. $C_{16}H_{14}OS$ requires C, 75·6; H, 5·5%).

2-(α-*Hydroxybenzyl*)-2-*phenyl*-1 : 3-*oxathiolan*.—2-Hydroxyethanethiol (30 g.), benzoin (82 g.), and toluene-*p*-sulphonic acid (2 g.) were refluxed in toluene (400 c.c.) for 1½ hr. while water (7·5 ml.) was evolved. On cooling, impure benzoin (40 g.) crystallised. After washing of the mixture with aqueous sodium hydrogen carbonate, the toluene was evaporated and the viscous yellow residue dissolved, as far as possible, in light petroleum (b. p. 80—100°) which was poured on a column (25 × 2·5 cm.) of alumina (type 0). The residue was repeatedly shaken with 100—200 ml. amounts of light petroleum, which were poured on the column, until an insoluble solid remained. The colourless first fractions of eluate contained 2 : 3-dihydro-5 : 6-diphenyl-1 : 4-oxathiin (8·6 g.). The next fractions of eluate were yellow and contained more oxathiin (9 g.), while still later fractions were less yellow and, on concentration, gave 2-(α-*hydroxybenzyl*)-2-*phenyl*-1 : 3-*oxathiolan* (5 g.), m. p. 95—96° (Found: C, 70·5; H, 5·8. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9%). In another experiment of 5½ hours' duration, the yield of oxathiin was 46% but no oxathiolan was isolated.

2 : 3-*Diphenylbenzoxathiin*.—2-Hydroxybenzenethiol (5 g.), benzoin (8·5 g.), and toluene-*p*-sulphonic acid (0·5 g.) in boiling toluene (100 ml.) yielded 2 : 3-*diphenylbenzoxathiin* (2·5 g.), m. p. 108—109°, nearly colourless prisms from methanol (Found: C, 79·8; H, 4·5. $C_{20}H_{14}OS$ requires C, 79·5; H, 4·6%).

α-(2-*Hydroxyphenylthio*)*deoxybenzoin*.—Sodium hydroxide (2 g.) in water was added to a solution of 2-hydroxybenzenethiol (5 g.) and desyl chloride (9·2 g.) in ethanol. After 20 min. at 100°, the mixture was poured into water and extracted with ether. The *deoxybenzoin* (6·2 g.), crystallised from methanol, had m. p. 102° (Found: C, 74·7; H, 4·9. $C_{20}H_{16}O_2S$ requires C, 75·0; H, 5·0%).

α-(3-*Hydroxypropylthio*)*deoxybenzoin*.—A similar preparation to the above gave the 3-*hydroxypropylthio-compound*, m. p. 46—48° [from light petroleum (b. p. 80—100°)–benzene at 0°] (Found: C, 71·3; H, 6·3. $C_{17}H_{18}O_2S$ requires C, 71·3; H, 6·3%).

This product (from 15 g. of desyl chloride) and toluene-*p*-sulphonic acid (0·25 g.), refluxed in benzene (150 ml.) for 3 hr., gave yellow needles of 2 : 3-*diphenyl*-1-*oxa*-4-*thia*cyclo*hept*-2-*ene* (3·4 g.), m. p. 119° (from ethanol) (Found: C, 76·1; H, 6·0. $C_{17}H_{16}OS$ requires C, 76·1; H, 6·0%).

6-*Aryl*-2 : 3-*dihydro*-1 : 4-*oxathiins*.—A methanolic solution of phenacyl chloride (21·8 g.), added to an aqueous-methanolic solution of 2-hydroxyethanethiol (10 g.) and sodium hydroxide

(5·2 g.) and heated for a short time, yielded 2 : 3-*dihydro*-6-*phenyl*-1 : 4-*oxathiin*, b. p. 126°/0·7 mm., n_D^{16} 1·6491 (Found: C, 67·7; H, 5·6. $C_{10}H_{10}OS$ requires C, 67·4; H, 5·6%). Similarly, *p*-bromophenacyl chloride gave 6-p-*bromophenyl*-2 : 3-*dihydro*-1 : 4-*oxathiin* (48%) as colourless crystals, m. p. 97° (from methanol) (Found: C, 46·7; H, 3·5. $C_{10}H_9OBrS$ requires C, 46·7; H, 3·5%); the crude product could not be obtained crystalline, but gave crystals only after ½ hour's heating at 150°.

2 : 3-*Dihydro*-6-*methyl*-1 : 4-*oxathiin*.—Chloroacetone (18 g.) was added to an aqueous-methanolic solution of 2-hydroxyethanethiol (15 g.) and sodium hydroxide (7·8 g.). An exothermic reaction took place. The mixture was evaporated at 100°/170 mm., and the residue taken up in ether. 2 : 3-*Dihydro*-6-*methyl*-1 : 4-*oxathiin* distilled at 56°/10 mm. and had n_D^{16} 1·5288 (Found: C, 51·8; H, 6·7. C_5H_8OS requires C, 51·7; H, 6·9%).

Condensation Products $C_{18}H_{18}O_2S_2$ *derived from Benzil and* 2-*Hydroxyethanethiol*.—A solution of benzil (26·25 g.) and 2-hydroxyethanethiol (19·5 g.) in methanol (100 ml.) was saturated with dry hydrogen chloride at 0—10°. After 1½ hr., water was added, and the product separated, washed, and dried. Recrystallisation from benzene gave colourless prisms. The crystals were solvated but readily effloresced to give an *isomer* (15 g.), m. p. 212° (Found: C, 65·3; H, 5·3. $C_{18}H_{18}O_2S_2$ requires C, 65·5; H, 5·5%). The viscous liquid obtained on evaporating the benzene mother-liquor to dryness gave thick needles of the second *isomer* (8·6 g.), m. p. 149° (from methanol) [Found: C, 65·5; H, 5·5%; *M* (Rast), 292. $C_{18}H_{18}O_2S_2$ requires C, 65·5; H, 5·5%; *M*, 330].

The isomer, m. p. 212° (1 g.), in acetone (50 ml.) was refluxed for 16 hr. with an aqueous suspension of Raney nickel (6 g.). The nickel was removed, and benzoin, m. p. 131°, was obtained from the solution by evaporation and recrystallisation from light petroleum (b. p. 60—80°)-benzene. Similarly the isomer, m. p. 149°, gave an impure specimen of benzoin which showed no m. p. depression when mixed with an authentic specimen but a large depression when mixed with hydrobenzoin.

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