reactivities in reaction 3 are therefore not strongly affected by the cationic group Y or the value of a.

It should be stated explicitly that this mechanism for polysulfide oxidation predicts that the relative rates for reaction 8 will parallel those for this oxidation (Table V, column 5). The thiyl radical can be

$$RS\cdot + ArCH_3 \underset{9}{\overset{8}{\rightleftharpoons}} RSH + Ar\dot{C}H_2$$

generated at 25° by photochemical techniques, but as yet a study of reaction 8 has not been made.[37]

There are two oxidations of aralkyl compounds by metal ions that are relevant. The first is the rate of oxidation of aralkyl compounds by potassium permanganate in 54% acetic acid.[38] This reaction is believed to involve attack by a positively charged manganese species.[39,40] The relative rates (per methyl) for substituted toluenes are: H, 1.00; m-CH_3, 3.1; p-CH_3, 1.6; o-CO_2H, 0.89; m-CO_2H, 0.54; p-CO_2H, 0.48. Here the o-CO_2H, even as the neutral acid, has anomalous effect on an ionic reaction. However, this reaction does not show the usual effects of methyl substituents on an ionic reaction.

The second is oxidation of substituted diphenylmethanes by chromic acid in acetic acid. The effect on the rate of m-CH_3, p-CH_3 and p-Cl in that reaction is similar to the other reactions of type C given in Table V and the oxidation is concluded to involve free radical intermediates.[41]

Rate of Oxidation of Carbinol Relative to Methyl.—Another facet of the mechanism proposed involves the nature of steps subsequent to oxidation to the first stage. The very small steady state concentration of intermediates found[2] in the oxidation of m-toluic acid suggests that steps after removal of the first hydrogen are relatively fast and that a benzyl thiol or alcohol would be oxidized faster than is toluene.

The rate of oxidation of alcohols is less than or, at most, equal to the rate of oxidation of thiols.[42] It follows that if an alcohol is oxidized too rapidly to be an isolable intermediate, the same must be true of the related thiol.

Therefore, the rate of oxidation of $ArCH_2OH$ and $ArCH_3$ were compared, where Ar is m-$CH_3C_6H_4$–. The rate of oxidation of m-toluic acid is known[2] at 288° and 200° and Table III gives the rate of oxidation for m-xylene at 288°. Assuming the rate of oxidation of both compounds is affected similarly by temperature, the oxidation rate for m-xylene at 200° is 0.07×10^{-4} sec.$^{-1}$. This rate for m-tolylcarbinol is 4.1×10^{-4} sec.$^{-1}$. It appears, therefore, that the relative rates are: $ArCH_2SH \gtrsim ArCH_2OH$ ($\sim$60) > $ArCH_3$ ($\sim$1).

If reaction 3 were not reversible, the mechanism predicts[45] a maximum of 1.5% alcohol is reached in two minutes using these relative rates (ammonium polysulfide oxidant).[2] Experimental results indicate a maximum of 0.2% intermediates is found after 15 minutes.

Acknowledgment.—It is a pleasure to acknowledge encouraging and stimulating discussion with many of my associates and with Professor S. Winstein. Dr. L. L. Ferstandig read the manuscript. Messrs. N. D. McNair and A. J. Clecak gave valuable assistance with much of the experimental work.

(37) The detailed kinetics of the reaction between isobutyl thiyl radical and cumene have been reported, however; C. Walling and R. Rabinowitz, THIS JOURNAL, **81**, 1137 (1959).

(38) C. F. Cullis and J. W. Ladbury, *J. Chem. Soc.*, 1407, 2850, 4186 (1955).

(39) J. W. Ladbury and C. F. Cullis, *Chem. Revs.*, **58**, 403 (1958).

(40) L. S. Levitt, *J. Org. Chem.*, **20**, 1297 (1955); W. A. Waters, *Quart. Revs.*, **12**, 277 (1958).

(41) K. B. Wiberg, Abstracts of Papers, Organic Chemistry Symposium of the Amer. Chem. Soc., June 15, 1959, Seattle, Wash., p. 100.

(42) For example, 1-phenylethyl alcohol[43] and 1-phenylethyl thiol[58] are oxidized to 48 and 44% of phenylacetic acid, respectively, by aqueous ammonium polysulfide, in 4 hours at 210°. The 2-phenylethyl alcohol and thiol[44] are converted to 0 and 95% of phenylacetic acid, respectively, by aqueous ammonium polysulfide, in 4 hours at 205°.

(43) J. A. King and F. H. McMillan, THIS JOURNAL, **68**, 1369 (1946).

(44) J. A. King and F. H. McMillan, *ibid.*, **68**, 632 (1946).

(45) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 154.

RICHMOND, CALIF.

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

Thiazolothiazoles. I. The Reaction of Aromatic Aldehydes with Dithioöxamide[1]

BY JOHN R. JOHNSON AND ROGER KETCHAM[2]

RECEIVED NOVEMBER 7, 1959

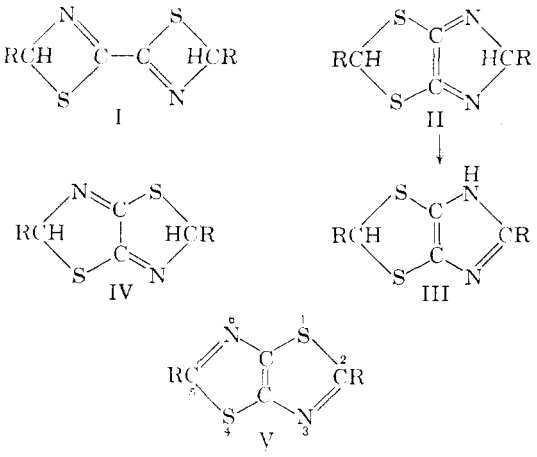
It has been shown that the reaction of dithioöxamide (rubeanic acid) with aromatic aldehydes is a condensation process involving concurrent loss of two hydrogen atoms. In one instance it was possible to isolate a labile intermediate condensation product that had not undergone dehydrogenation. The two aryl groups in the typical reaction products were shown to be structurally equivalent and the heterocyclic system to be remarkably stable thermally and chemically. A structure having two four-membered heterocycles (VI) has been rejected and the compounds are formulated as aryl derivatives of a new fused heterocyclic system of aromatic character, thiazolo[5,4-d]thiazole (V). The reaction appears to be general for aldehydes of aromatic type, including furfural and cinnamaldehyde. Aliphatic aldehydes and aryl methyl ketones did not furnish condensation products with dithioöxamide.

Ephraim[3] effected the condensation of benzaldehyde with dithioöxamide (rubeanic acid) and obtained in good yield a crystalline product, which was assigned the molecular formula $C_{16}H_{12}N_2S_2$ and represented as 2,2′-diphenyl-4,4′-bithiazetine (I, R = C_6H_5–). The lack of any structural evidence to support this formulation led us to consider two different structures, each containing two fused five-

(1) This paper is based upon the doctoral thesis of Roger Ketcham, Cornell University, September, 1956.

(2) National Science Foundation Pre-doctoral Fellow, 1953–1954; General Electric Co. Fellow, 1955–1956.

(3) J. Ephraim, *Ber.*, **24**, 1027 (1891).



membered rings, that should be formed more readily than the four-membered rings proposed by Ephraim. One of these was a fused imidazo-1,3-dithiolane system (II or III), in which the positions of attachment of the two aryl substituents are structurally dissimilar. The second and preferred formulation was the centro-symmetrical 2,5-dihydrothiazolothiazole system (IV), in which the substituents occupy equivalent positions. The latter seemed of particular interest since it should be capable of undergoing dehydrogenation to afford the aromatized thiazolo[5,4-d]thiazole system (V) a new analog of naphthalene.[4]

Ephraim[3] described also a similar condensation product from salicylaldehyde and dithioöxamide, which is subject to the same structural considerations (R = *o*-HOC_6H_4–). The presence in this compound of two phenolic functions capable of stepwise alkylation enabled us to obtain evidence bearing on the structural equivalence of the two aryl groups in the condensation products. Methylation of the salicylaldehyde derivative under mild conditions furnished in good yield a *single* monomethyl ether, m.p. 217–218° (soluble in Claisen alkali), and a small amount of a dimethyl ether, m.p. 253–254°, identical with the condensation product from *o*-methoxybenzaldehyde and dithiooxamide. Similarly, ethylation gave in high yield a *single* monoethyl ether, m.p. 236–237°, and a small quantity of a diethyl ether.

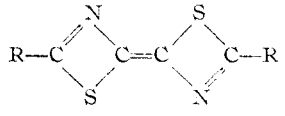
Isolation of a single monoalkylation product implies either that the two hydroxyaryl groups are equivalent *or*, if they are not equivalent, that one of them is alkylated selectively. Unambiguous demonstration of the equivalence of the hydroxyaryl groups was effected through conversion of the monomethyl and the monoethyl ether by subsequent ethylation and methylation, respectively, into the same monomethyl monoethyl ether, m.p. 214–217°. Identity of the specimens resulting from the inverse sequences of alkylation was established by means of their infrared spectra and melting point comparisons. Since all of the condensation products are similar to the salicylaldehyde compound, as indicated by their ultraviolet absorption spectra, formulas II and III were excluded from further consideration.

(4) The systematic name of this heterocycle is derived by analogy to soxazolo[5,4-d]isoxazole; "The Ring Index," No. 591.

Attempts to effect dehydrogenation of the benzaldehyde and salicylaldehyde condensation products with a variety of reagents under favorable conditions generally led to recovery of a large fraction of unchanged starting material. Likewise, addition of a hydrogen acceptor such as nitrobenzene to the reaction mixture did not change the nature or affect materially the yields of the normal condensation products. Such observations suggested that the postulated dihydro compounds (IV) are merely transient intermediates that undergo dehydrogenation spontaneously to the thiazolothiazoles (V) under the vigorous conditions of reaction (temperatures of 160–200° in presence of a large excess of the aldehyde).

Analyses do not afford a reliable criterion for distinguishing between structures IV and V, but it is significant that the observed hydrogen content of more than fifteen compounds examined, with the single exception of the bis-4-nitrophenyl derivative,[5] showed better agreement with values calculated for the dehydrogenated structures. Taken as a whole the analytical data give a consistent picture and support the contention that the condensation reaction is accompanied by dehydrogenation. Conclusive evidence for this view was obtained from nuclear magnetic resonance studies of the benzaldehyde condensation product in chloroform, which showed that the compound contains *only* benzenoid H–C bonds.[6]

The bithiazetine structure (I) proposed by Ephraim[3] is formally capable of giving rise to dehydro compounds (VI) that are isomeric with the thiazolothiazoles V, but that type of structure is not consistent with the thermal and chemical



VI

stability of the condensation products nor with our interpretation of the infrared and ultraviolet absorption spectra. For example, the heterocyclic system does not possess a strong, conjugated chromophore and does not exhibit absorption in the C=N region in the infrared; it has the character of a stabilized aromatic system and exerts an *ortho/para* directive effect in the attached aryl groups. Such evidence has led us to reject structure VI in favor of the thiazolothiazole system.

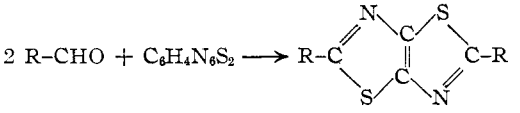
Efforts to prepare from dithioöxamide and benzaldehyde a product corresponding to the intermediate dihydro compound IV were unsuccessful. But from salicylaldehyde and dithioöxamide, after a very short reaction time, there resulted a new orange-yellow compound, m.p. 249–250° dec., that has a higher hydrogen content (3.6% *vs.* 3.2%; calcd. for a dihydro compound, 3.7% *vs.* 3.1%) than the normal yellow condensation product, m.p. 300–301° The new compound is decomposed

(5) The original analytical data of Ephraim[3] for the benzaldehyde condensation product also constitute an exception. His hydrogen values agreed better with the dihydro formula ($C_{16}H_{12}N_2S_2$) but the carbon values were closer to the dehydrogenated system ($C_{16}H_{10}N_2S_2$).

(6) For this observation we are indebted to Dr. W. D. Phillips, Central Research Department, E. I. du Pont de Nemours and Co.

TABLE I

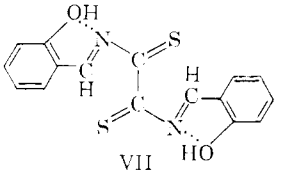
DISUBSTITUTED THIAZOLO[5,4-d]THIAZOLES FROM ALDEHYDES AND DITHIOÖXAMIDE



R–	R–CHO ratio[a]	Time,[b] min.	Yield, %	M.p., °C.	Solvent[c]	Subl.[d] temp., °C.	Analyses, % Calcd.[e] C	H	N	Found C	H	N
C_6H_5	10	40	78	209–210	C_6H_6	..	65.30	3.40	9.52	65.27	4.01	9.19[f]
								(4.05)[e]		65.67	3.81	9.55
o-HOC_6H_4	10	90	37	300–301.5	$C_6H_{10}O$	240	58.90	3.10	8.59	59.27	3.14	9.04
								(3.68)		59.18	3.23	8.84
m-HOC_6H_4	5	15	29, 38[g]	328–332	$C_6H_{10}O$	310	58.90	3.10	8.59	59.09	3.18	7.95
								(3.68)		59.14	3.00	7.76
p-HOC_6H_4	9	10	19, 29[g]	369–373	$C_6H_{10}O$	350	58.90	3.10	8.59	59.36	2.98	
								(3.68)				
o-$CH_3OC_6H_4$	8	5–30	47	253–254	$CHCl_3$	..						
p-$CH_3OC_6H_4$	8	40	64	360–362[h]	$C_6H_{10}O$	..	61.00	3.98	7.91	61.16	4.03	8.35
								(4.53)		61.44	4.25	8.15
p-BrC_6H_4	4	3	42	330–333	$C_6H_{10}O$	295	42.51	1.77	6.20	42.69	1.61	6.10
								(2.20)				
o-ClC_6H_4	11	30	17	218–219	$CHCl_3$–C_6H_{14}	210	52.90	2.22	7.71	53.13	2.26	7.48
								(2.74)				
p-ClC_6H_4	5	10	50	311–312[i]	$C_6H_{10}O$	285	52.90	2.22	7.71	53.13	2.12	7.96
								(2.74)				
m-$NO_2C_6H_4$	8	10	54	317–321	$C_6H_5NO_2$	..						
p-$NO_2C_6H_4$	8	5	59	400–405	$C_6H_5NO_2$	340	50.00	2.10	14.58	50.40	2.79	14.22
								(2.61)		50.15	2.55	14.28
$C_6H_5CH{=}CH$	9	15	7, 14[g]	242–243	C_6H_6	220	69.34	4.07	8.09	69.68	4.20	7.95
								(4.62)		69.92	4.01	7.85
2-Furyl	13	35	40	238–240	C_6H_6–C_6H_{14}	210	52.54	2.21	10.22	52.35	2.19	10.46
								(2.92)		52.63	2.09	10.35
p-$(CH_3)_2NC_6H_4$	8	10	18	365–372	C_6H_5OH–C_8H_{10}[j]	260	63.13	5.30	14.73	63.20	5.50	14.67
								(5.80)				
p-$CH_3C_6H_4$	5	90	70	292–293[k]	$C_6H_{10}O$	235	67.04	4.38	19.89	66.93	4.53	8.55
								(4.97)		66.82	4.44	8.74

[a] Molar ratio of aldehyde to dithioöxamide. [b] Reaction time at reflux temperature. [c] Recrystallization solvent ($C_6H_{10}O$ = cyclohexanone; C_8H_{10} = xylene). [d] Sublimations at 1–2 mm. [e] Values for thiazolothiazole structures (V); H-values for the dihydro structures are shown in parentheses on the second line. [f] Analyses published by Ephraim (ref. 3). [g] Reaction mixture contained 2–3 g. of phenol per g. of dithioöxamide. [h] Solid–liquid crystal transition at 274–280°. [i] Solid–liquid crystal transition at 293–295°. [j] Following two crystallizations as the hydrochloride, from 20% hydrochloric acid; this salt undergoes hydrolysis if washed with water. [k] Solid–liquid crystal transition at 256–258°.

rapidly by hot aqueous alkali (slowly at 20°), whereas the normal product can be recovered unchanged after contact for several days with hot alkali. It can be converted to the normal product in low yields (20–30%) by refluxing with benzaldehyde, salicylaldehyde or nitrobenzene and 40% yields by heating at 250–270°, with or without addition of sulfur. The new substance has stronger general absorption than the normal product in the 230–300 mμ region of the ultraviolet, with a slight rise at 280 mμ (log ε 3.94), instead of two distinct maxima at 270 mμ (log ε 3.76) and 280 mμ (log ε 3.78). In the infrared spectrum there is a definite



VII

peak in the 5.9 μ region that is entirely lacking in the spectrum of the normal product. We conclude that the new substance is not the expected cyclic dihydro compound IV but is an uncyclized isomer, bis-salicylidenedithioöxamide (VII). The latter has a more extended conjugated chromophore and may be stabilized by proton bonding.

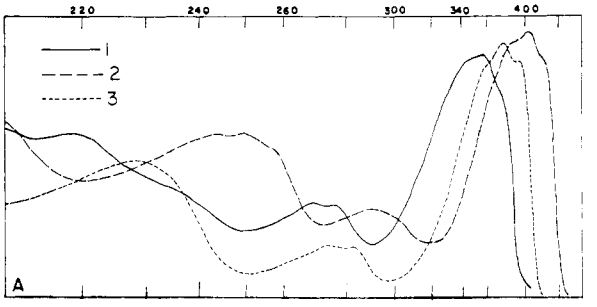


Fig. 1.—Ultraviolet absorption of thiazolo[5,4-d]thiazoles (V): 1, 2,5-diphenyl; 2, 2,5-bis-(2-furyl); 3, 2,5-bis-(β-styryl); solutions 2 × 10^{-5} molar in ethanol (for others, see Table II).

The formation of thiazolothiazoles from dithiooxamide and aromatic aldehydes appears to be a general reaction comparable in scope and limita-

tions to condensations like the Perkin reaction; *m*- and *p*-substituted benzaldehydes having a variety of substituents, including –OH, $-N(CH_3)_2$, $-CH_3$, –Cl, –Br and $-NO_2$, furnished the corresponding thiazolothiazoles in 20–60% yields (Table I). *o*-Substituents such as –OH and $-OCH_3$ are not unfavorable but *o*-chlorobenzaldehyde gives a lower yield and *o*-nitrobenzaldehyde did not react normally with dithioöxamide under the usual conditions. Furfural and cinnamaldehyde furnished typical condensation products in moderate yields. The addition of a solvent medium generally had little or no favorable effect, with the exception of phenol, which enhanced the yields in several instances but not in all.

Condensation products were not obtained from aliphatic aldehydes (formaldehyde, chloral, heptaldehyde, *n*-butyl glyoxylate).[7] Aryl methyl ketones (acetophenone, *o*-hydroxyacetophenone) also failed to give condensation products with dithioöxamide. An effort to synthesize thiazolothiazole derivatives by a different route, from thiobenzamide and glyoxal or glyoxime, was unsuccessful.

Reactions of the aryl substituents in the 2,5-diarylthiazolothiazoles are not affected appreciably by the heterocyclic system but the low solubility of these substances usually necessitated long reaction times or special techniques. Nitration of diphenylthiazolothiazole with concentrated nitric and sulfuric acids gave the bis-(4-nitrophenyl) derivative, m.p. 400°dec., identical with the condensation product from 4-nitrobenzaldehyde and dithioöxamide. Reduction of the dinitro compound with tin and hydrochloric acid in 1-butanol was extremely slow but furnished bis-(4-aminophenyl)-thiazolothiazole in almost quantitative yields.[8] Diazotization of the diamine and coupling with sodium 2-naphthol-3,6-disulfonate gave a sparingly soluble purple bis-azo dye.

Hydrolysis of bis-(4-methoxyphenyl)-thiazolothiazole was slow and difficult to bring to completion. The resulting bis-(4-hydroxyphenyl) compound was identical with the product from 4-hydroxybenzaldehyde and dithioöxamide. The hydroxyphenyl compounds were coupled with diazotized sulfanilic acid to give maroon and red bis-azo dyes.

Oxidation of the bis-(2-furyl) and bis-(β-styryl) derivatives by permanganate in pyridine resulted in the formation of thiazolothiazole-2,5-dicarboxylic acid in 75–80% yields. Decarboxylation of this acid leads to thiazolothiazole-2-carboxylic acid and to the parent unsubstituted heterocycle, thiazolo-[5,4-d]thiazole. Studies of these compounds and their derivatives will be reported in a later paper.

(7) α-Hydroxymethylenecyclohexanone reacted with dithioöxamide to furnish 3–4% yields of a condensation product, m.p. 215–225°. This substance was difficult to purify and was not subjected to further study. Recently Dr. J. F. Oneto at the School of Pharmacy, University of California Medical Center, has obtained typical condensation products from dithioöxamide and 4-cyano-2,2-dimethylbutyraldehyde, and also pyridine aldehydes (private communication to R. K.).

(8) Ephraim[3] reported that nitration of the diphenyl compound with fuming nitric acid gave a dinitro derivative, m.p. 269°, but we have been unable to confirm this observation. He obtained 4-nitrobenzoic acid on chromic oxidation of his dinitro compound and stated that it was not reduced by tin and hydrochloric acid but gave 4-aminobenzylamine by reduction with hydrogen iodide.

Experimental

Condensation of Dithioöxamide with Aldehydes.—Dithioöxamide (rubeanic acid) prepared from cyanogen and hydrogen sulfide in ethanol[9] or obtained from commercial sources was recrystallized from ethanol. On heating gradually dithioöxamide begins to decompose rapidly at 190–200°; on a hot-block it melts instantaneously at 240° before decomposing. The aldehydes obtained from commercial sources were recrystallized or redistilled before use. The condensation reaction does not appear to be particularly sensitive to small amounts of impurity in either reactant.

The mixed reactants were placed in a tube (about 3 × 10 cm.) fitted with a ground glass joint bearing a trap to collect the small amount of water formed, and heated to reflux temperatures in an oil-bath. Results of the preparations are summarized in Table I (all melting points are corrected; analyses are by Geller Laboratories and the Schwarzkopf Microanalytical Laboratories). These examples illustrate the procedures used, with and without the addition of phenol.

The 2,5-diarylthiazolo[5,4-d]thiazoles examined have high melting points (about 200°) and several of them exhibit solid–liquid crystal transition at temperatures below the true melting points. For example, the *p*-tolyl compound undergoes transition at 256–258° but the melt does not become clear until raised to 292–293°; unless the sample tube is observed closely the transition may be mistaken for the melting point.

(a) **Diphenylthiazolo[5,4-d]thiazole.**—Four grams (33 millimoles) of dithioöxamide and 37 g. (350 millimoles) of benzaldehyde were heated to the reflux temperature. The dithioöxamide dissolved and soon thereafter sputtering occurred as water was formed in the reaction mixture. After heating the reaction mixture for 40 minutes it was cooled and diluted with ethanol. The crude product after washing with ether weighed 6.7 g. (78% yield), m.p. 208–210°. Recrystallization from benzene gave faintly yellow crystals, m.p. 209–210° (92% recovery). Ephraim[3] reported a 30% yield of recrystallized product, m.p. 209°, after a 90-minute reaction period.

(b) **Bis-(3-hydroxyphenyl)-thiazolothiazole.**—A mixture of 3 g. (25 millimoles) of dithioöxamide, 15 g. (123 millimoles) of 3-hydroxybenzaldehyde and 9 g. of phenol was refluxed for 10 minutes. The warm reaction mixture was diluted with 75 g. of ethanol and cooled. The product was washed with ethanol and ether; weight 3.1 g. (38%), m.p. 318–327°. Recrystallizations from cyclohexanone and sublimation (310° at 2 mm.) furnished yellow crystals, m.p. 328–332°. The yield fell to less than 30% when phenol was omitted from the reaction mixture.

Alkylation Products of Bis-(2-hydroxyphenyl)-thiazolothiazole. (a) **2-Hydroxy-2′-methoxydiphenylthiazolothiazole.**—A sample of 2.3 g. (7 millimoles) of the bis-(2-hydroxyphenyl) compound was dissolved in 12 ml. of 10% sodium hydroxide (28 millimoles) at room temperature and methyl sulfate was added dropwise, with shaking, until the solution became acidic. Another portion of alkali (10 ml.) was added and after shaking for 15 minutes the precipitate was collected. To the filtrate, methyl sulfate was added as before, until it became acidic, and a final portion of alkali (6 ml.) was introduced. The precipitate was collected and combined with that obtained previously. Acidification of the alkaline filtrate gave only a small amount of unchanged starting material (10–20 mg., m.p. 290–297°).

The precipitate of methylated products was dissolved in chloroform and treated with Norit. The filtrate, when concentrated to 30 ml. and diluted with 50 ml. of hexane, furnished 2.1 g. of crystals, m.p. 203–209° (cloudy to 230°). This material was treated with 20 ml. of Claisen alkali (35 g. of potassium hydroxide, 25 ml. of water and 125 ml. of methanol) and warmed to 50°. After collecting the alkali-insoluble fraction (see below), the alkaline filtrate upon acidification furnished the monomethyl ether. After recrystallization from chloroform–hexane the product weighed 1.8 g. (78% yield), m.p. 206–211°. Repeated crystallizations from benzene–hexane and sublimation (210° at 2 mm.) gave yellow crystals, m.p. 217–218°.

(9) Trial experiments of the new synthesis devised by E. Urbschat [German Patent 868,908 (March 2, 1953)] also gave satisfactory results. This method involves the action of chlorine on aqueous ethanolic cyanide, and then reaction with ammonium sulfide.

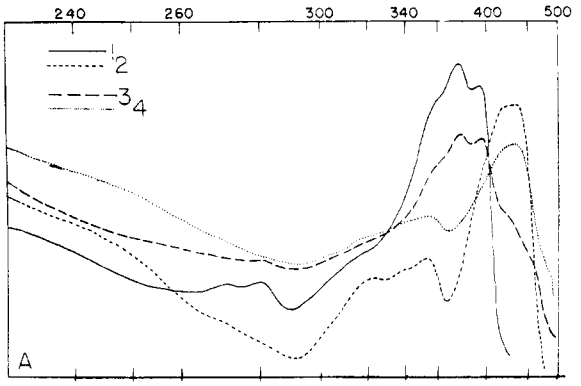


Fig. 2.—Ultraviolet absorption of salicylaldehyde derivatives: 1, 2,5-bis-(*o*-hydroxyphenyl)-thiazolo[5,4-d]thiazole (V); 2, sodium salt of (1); 3, bis-salicylidenedithioöxamide (VII); 4, sodium salt of (3), freshly prepared; solutions 2×10^{-5} molar, in ethanol + 10% chloroform.

Anal. Calcd. for $C_{17}H_{12}N_2O_2S_2$: C, 60.00; H, 3.56; N, 8.23. Found: C, 59.64, 59.67; H, 3.63, 3.57; N, 8.20, 8.13.

The alkali-insoluble fraction was washed with water, methanol and ether. This material (200 mg., m.p. 245–253°) proved to be the dimethyl ether (9% yield) and was identical with the condensation product from dithioöxamide and 2-methoxybenzaldehyde. Further methylation of the monomethyl ether in the presence of methanolic alkali furnished the dimethyl ether in high yields; yellow crystals, from chloroform, m.p. 253–254°.

(b) 2-Hydroxy-2'-ethoxydiphenylthiazolothiazole.—Ethylation of 600 mg. (1.83 millimoles) of the bis-(2-hydroxyphenyl) compound with 7 g. (56 millimoles) of ethyl sulfate, following the procedure used for methylation, furnished 500 mg. of the monoethyl ether (83% yield), m.p. 230–235°. Recrystallizations from benzene–hexane gave yellow needles, m.p. 236–237°.

Anal. Calcd. for $C_{18}H_{14}N_2O_2S_2$: C, 61.00; H, 3.98; N, 7.91. Found: C, 61.53, 61.23; H, 4.08, 4.15; N, 8.14, 7.96.

The fraction of ethylated material that was not soluble in Claisen alkali, after recrystallization from benzene–hexane, furnished pale yellow crystals of bis-(2-ethoxyphenyl)-thiazolothiazole, m.p. 235–237°. Although the monoethyl and diethyl ethers melt at essentially the same temperature, mixtures of the two show a marked depression (m.p. 206–220°).

(c) 2-Ethoxy-2'-methoxydiphenylthiazolothiazole.—Ethylation of 200 mg. (0.6 millimole) of the monomethyl ether with 3.5 g. of ethyl sulfate (2.3 millimoles), using four 2-ml. portions of 15% ethanolic potassium hydroxide, afforded 195 mg. (95% yield) of the monomethyl monoethyl ether. Recrystallizations from benzene–hexane, and then sublimation (215° at 2 mm.), gave yellow crystals, m.p. 217–218°.

Anal. Calcd. for $C_{19}H_{16}N_2O_2S_2$: C, 61.90; H, 4.38; N, 7.60. Found: C, 61.82; H, 3.85; N, 7.81.

Methylation of 30 mg. of the monoethyl ether with methyl sulfate and methanolic alkali afforded 25 mg. (82% yield) of the monomethyl monoethyl ether. After one crystallization from benzene–hexane this sample melted at 214–217° and its melting point was not depressed when mixed with the material prepared by ethylation of the monomethyl ether. The infrared spectra of the two samples were identical.

Bis-(salicylidene)-dithioöxamide (VII).—During the course of preparative experiments with salicylaldehyde and dithioöxamide it was observed that after heating for about 5 minutes at 220° (bath temperature) a precipitate formed, which dissolved slowly in the course of about 50 minutes. After a total heating time of about 90 minutes the reactants furnished 35–40% yields of the normal condensation product V, m.p. 290–300°. The initial labile substance was isolated by using a short reaction time.

Two grams of dithioöxamide (17 millimoles) was heated with 21 g. (170 millimoles) of salicylaldehyde to a bath temperature of 230° and heating was continued for 2–3 minutes after the evolution of water was first observed. The mixture was diluted with 50 ml. of 1:1 ether–ethanol and the precipitate collected. The yield was 3.9 g. (70%), m.p. 250–257°. Repeated recrystallizations from cyclohexanone gave orange-yellow crystals, m.p. 249–250° dec.

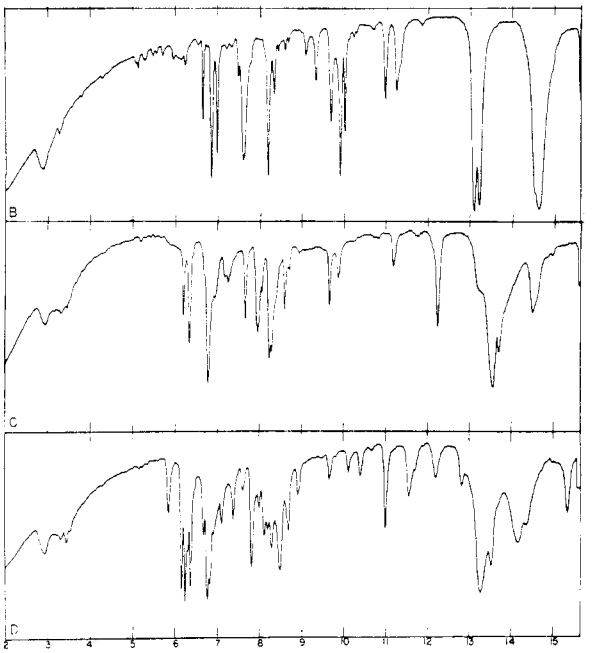


Fig. 3.—Infrared spectra: B, 2,5-diphenylthiazolo[5,4-d]-thiazole; C, 2,5-bis-(*o*-hydroxyphenyl)-thiazolo[5,4-d]thiazole (V); D, bis-salicylidenedithioöxamide.

Anal. Calcd for $C_{16}H_{12}N_2O_2S_2$: C, 58.55; H, 3.68; N, 8.54; S, 19.54. Found: C, 59.03, 59.18; H, 3.57, 3.57; N, 8.38, 8.42; S, 19.68, 19.41. (Calcd. for a dehydro compound, $C_{16}H_{10}N_2O_2S_2$: C, 58.90; H, 3.10; N, 8.59; S, 19.64.)

This substance dissolves in cold alkali and is reprecipitated unchanged if the solution is acidified within a few minutes. After standing at 20° for more than an hour in alkaline solution, or heating for 10–20 minutes, the substance cannot be recovered upon acidification. Heating at 270°, either alone or with 10% by weight of sulfur added, converts the substance to the normal condensation product (40% yields). Heating at reflux temperatures with benzaldehyde, salicylaldehyde or nitrobenzene effects the conversion in lower yields (20–30%).

Nitration of Diphenylthiazolothiazole: Bis-(4-nitrophenyl)-thiazolothiazole.—Three grams (10 millimoles) of diphenylthiazolothiazole was dissolved in 12 ml. of concentrated sulfuric acid and 12 ml. of concentrated nitric acid was added dropwise, with shaking and cooling. After standing for 5 minutes at 50°, the reaction mixture was poured onto 50 g. of ice and the yellow precipitate was collected and washed with water, ethanol and ether. The crude product was refluxed with 100 ml. of ethanol, collected, and washed with ether. Recrystallization from 150 ml. of nitrobenzene yielded 1.35 g. (34%) of the bis-(4-nitrophenyl) derivative, m.p. 395–402° dec. Three recrystallizations from nitrobenzene and sublimation (340° at 1–2 mm.) gave golden yellow crystals, m.p. 400–405° dec. Higher yields, up to 50%, were obtained when the reaction was run on a smaller scale. The infrared and ultraviolet spectra of this compound were identical with those of the authentic bis-(4-nitrophenyl) derivative, m.p. 394–400° dec., obtained from dithioöxamide and 4-nitrobenzaldehyde. The diacetate of 4-nitrobenzaldehyde did not react with dithiooxamide under the usual conditions (230°).

This compound is different from Ephraim's supposed bis-(4-nitrophenyl) derivative, m.p. 269°, which we have not succeeded in obtaining by his procedure.[8]

Bis-(4-aminophenyl)-thiazolothiazole.—To a suspension of 250 mg. (0.65 millimole) of the bis-(4-nitrophenyl) com-

TABLE II

ULTRAVIOLET ABSORPTION SPECTRA OF THIAZOLO[5,4-d]THIAZOLES

R–	$\lambda\lambda_{max}$ (log ϵ)[a]			R–	$\lambda\lambda_{max}$ (log ϵ)		
C_6H_5–	219 (4.3)	268 (3.95)	345 (4.61)	*m*-$NO_2C_6H_4$[b]	.....	276 (4.19)	350 (4.52)
		275 (3.95)	355 (4.65)				360 (4.55)
			370 (4.48)				375 (4.30)
o-HOC_6H_4	.....	270 (3.83)	360 (4.47)	*p*-$NO_2C_6H_4$[b]	247 (4.2)	288 (3.95)	396 (4.70)
		281 (3.83)	377 (4.62)				
			394 (4.53)	*o*-ClC_6H_4[c]	.....	279 (3.88)	345 (4.47)
							355 (4.44)
Sodium salt	235 (4.2)	323 (3.98)	445 (4.54)				
		352 (4.07)					
				p-ClC_6H_4[c]	.....	272 (3.87)[d]	355 (4.61)
m-HOC_6H_4	211 (4.5)	268 (3.88)	350 (4.55)[e]				364 (4.65)
		278 (3.83)[e]	362 (4.59)				381 (4.48)
			375 (4.47)[e]				
				p-$NH_2C_6H_4$	236 (4.2)	320 (3.11)	402 (4.70)
Sodium salt	214 (4.5)	250 (4.14)	357 (4.49)		250 (4.1)		
				Hydrochloride	218 (4.12)	270 (3.78)	365 (4.43)
p-HOC_6H_4	227 (4.3)	260 (3.93)	360 (4.63)[e]		235 (4.0)		377 (4.47)
		274 (3.90)[e]	375 (4.68)				395 (4.41)
Sodium salt	237 (4.3)	312 (3.82)	417 (4.74)				
				2-Furyl	228 (4.2)	273 (3.69)	360 (4.57)[e]
o-$CH_3OC_6H_4$	224 (4.2)	276 (3.75)	354 (4.56)			282 (3.69)	375 (4.72)
		286 (3.78)	370 (4.70)				392 (4.60)
			388 (4.56)				
p-$CH_3OC_6H_4$	237 (4.1)	268 (3.65)	360 (4.51)	β-Styryl	243 (4.3)	290 (3.93)	390 (4.72)[e]
		275 (3.66)	372 (4.55)		249 (4.3)		405 (4.81)
			388 (4.40)				420 (4.62)

[a] In 95% ethanol unless otherwise indicated. [b] In chloroform. [c] In 95% ethanol plus 10% chloroform. [d] The spectrum of the *p*-bromophenyl compound is almost identical with that of the *p*-chloro compound. [e] Shoulder or inflection.

pound in 3.8 ml. of 38% hydrochloric acid and 6 ml. of 1-butanol, 750 mg. (6.3 milliatoms) of mossy tin was added and the mixture refluxed for 2 hours. Two additional portions of 3.8 ml. of hydrochloric acid and 750 mg. of tin were added and the mixture refluxed for 4 and 8 hours, respectively, after these additions. The solid diamine hydrochloride was collected and washed with water, ethanol and ether; m.p. 315–340° dec. When prepared subsequently from the purified diamine, the hydrochloride melted at 338–348° dec.

The hydrochloride was heated on a steam-bath with 50 ml. of 3% sodium hydroxide; the resulting free base was collected and washed with water, ethanol and ether. The crude product (220 mg., m.p. 293–300°) after recrystallization from dioxane, with addition of Norite, gave 200 mg. (95% yield) of material melting at 298–300°. Recrystallizations from dioxane and sublimation (260° at 1 mm.) furnished yellow crystals of the pure diamine, m.p. 301–303°.

Anal. Calcd. for $C_{16}H_{12}N_4S_2$: C, 59.25; H, 3.73; N, 17.27. Found: C, 59.13, 59.29; H, 3.62, 3.89; N, 17.13, 17.13.

For diazotization, the diamine (100 mg.) was dissolved in 20 ml. of hot dioxane and the solution cooled to 20° and treated with 4 drops of concentrated hydrochloric acid in 10 ml. of water. The suspension of the hydrochloride was cooled to 0° and a solution of 50 mg. of sodium nitrite in 10 ml. of cold water was introduced. When the mixture was stirred at 0° for 15 minutes and poured into an alkaline solution of 2-naphthol-3,5-disulfonic acid, a maroon bis-azo dye was precipitated.

Bis-(4-hydroxyphenyl)-thiazolothiazole.—One gram (3 millimoles) of the bis-(4-methoxyphenyl) derivative, prepared from dithioöxamide and anisaldehyde, was refluxed for 9 hours with 30 ml. of 48% hydrobromic acid and 5 g. of phenol. The suspension was diluted with 30 ml. of water and the solid collected; this was partially purified by dissolving in 20 ml. of hot 5% sodium hydroxide, filtering, and reprecipitating with concentrated hydrochloric acid. Recrystallization from cyclohexanone gave 620 mg. (67% yield) of yellow crystals of the bis-(4-hydroxyphenyl) compound, m.p. 357–367° This substance can be obtained more satisfactorily and in purer condition by the direct condensation of dithioöxamide with 4-hydroxybenzaldehyde.

The bis-(hydroxyphenyl)-thiazolothiazoles were coupled with diazotized sulfanilic acid to obtain bis-azo dyes, as in the following example. A suspension of the diazonium salt prepared from 1.05 g. (5 millimoles) of sulfanilic acid was poured into an aqueous supension of the sodium salt of bis-(3-hydroxyphenyl)-thiazolothiazole (2.5 millimoles). The resulting bis-azo dye was deep tile-red in color.

Absorption Spectra.—The ultraviolet spectra were taken with a Beckman DK spectrophotometer, using a hydrogen lamp, with a scanning speed of three and a chart speed of two inches per minute. Compounds having maxima at wave lengths longer than 380 mμ were checked with a tungsten lamp. The data are collected in Table II. Three examples of typical compounds are shown in detail in Fig. 1.

The infrared spectra were taken in potassium bromide pellets with a Perkin-Elmer model 21 double beam spectrophotometer. Three significant curves are shown in Fig. 3.

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