174–179°. It was purified by crystallization from absolute ethanol by addition of ether. The m.p. was 175–179°, and the compound showed $[\alpha]_D$ +51.0° (*c* 2, water).

Anal. Calcd. for $C_{17}H_{27}O_4N$ (309): C, 66.1; H, 8.8; N, 4.5. Found: C, 66.3; H, 9.1; N, 4.9.

Methyl 2-*O*-Benzyl-D-*erythro*-2,3-dihydroxybutyrate.—Two grams of the cyclohexylammonium salt above was dissolved in 10 ml. of 1 *N* hydrochloric acid and 10 ml. of water. The solution was extracted three times with 50-ml. portions of ether, the combined ether extract was dried over anhydrous sodium sulfate, and then filtered. An ether solution containing 0.4 g. of diazomethane was added to the dry ether solution of the carboxylic acid. Esterification took place instantaneously. When a slight excess of diazomethane remained, the solution was concentrated to a sirup *in vacuo*, then freed of traces of solvent in a high vacuum. The product weighed 1.4 g. (97%), and showed $[\alpha]^{25}_D$ +76° (*c* 1.5, ethanol).

Anal. Calcd. for $C_{12}H_{16}O_4$ (224): C, 64.4; H, 7.15; OCH_3, 13.8. Found: C, 64.5; H, 7.26; OCH_3, 13.5.

D-*erythro*-2,3-Dihydroxybutyric Acid 3-Phosphate.—A solution of 1.4 g. of the methyl ester above in 10 ml. of dry pyridine was cooled to 5° in ice-water, 1.7 g. of diphenylphosphorochloridate was added dropwise, and the mixture was left at 5° overnight. A few drops of water were added to destroy the excess phosphorylating reagent, and most of the pyridine was distilled off *in vacuo*. The residue was taken up in chloroform, the solution washed with water, ice-cold 1 *N* hydrochloric acid, ice-cold 1 *M* potassium bicarbonate and finally with water. The chloroform layer was dried over sodium sulfate and concentrated to a sirup of crude methyl 2-*O*-benzyl 3-diphenylphosphonyl D-*erythro*-2,3-dihydroxybutyrate that weighed 2.4 g. (86%).

This intermediate was unblocked by reductive cleavage with hydrogen and palladium in absolute ethanol (hydrogen uptake 150 ml. in 2 hr.), followed by hydrogen and platinum (hydrogen uptake 1450 ml. in 1 hr.).[1] The catalyst was removed and 20 ml. of 1 *N* sodium hydroxide was added to the ethanol solution. The mixture was concentrated *in vacuo* to remove the alcohol, 25 ml. of water was added and the solution was left overnight to complete saponification of the methyl ester.

The alkaline solution was treated with Dowex-50 in the hydrogen form to remove all cations, and after removal of the resin, was brought to *p*H 8–9 with cyclohexylamine. Concentration of the solution to dryness left a crystalline residue that was recrystallized from absolute ethanol. The pure tricyclohexylammonium D-*erythro*-2,3-dihydroxybutyrate 3-phosphate showed $[\alpha]_D$ −14.5° (*c* 1, free acid in 1 *N* hydrochloric acid), and $[\alpha]_D$ −737° (*c* 0.2, free acid in neutral molybdate).

Anal. Calcd. for $C_{22}H_{48}O_7N_3P$ (497): N, 8.47; P, 6.24. Found: N, 8.54; P, 6.13.

D-*erythro*-2,3-Dihydroxybutyric Acid 2-Phosphate.—Two grams of methyl 2-*O*-benzyl-D-*erythro*-2,3-dihydroxybutyrate was benzoylated in 10 ml. of dry pyridine with 2.0 g. of benzoyl chloride. The reaction was left overnight at room temperature, and was then worked up in the manner of the phosphorylation described above, to give 2.9 g. (99%) of methyl 2-*O*-benzyl-3-*O*-benzoyl-D-*erythro*-2,3-dihydroxybutyrate.

The benzyl group was removed from this compound, without further purification, by reductive cleavage in absolute ethanol with hydrogen and palladium.[1] The hydrogen uptake was 200 ml. in 2 hr. The catalyst was removed, and the alcohol solution was concentrated to a dry sirup. The yield of crude methyl 3-*O*-benzoyl-D-*erythro*-2,3-dihydroxybutyrate was 2.0 g. (95%).

This substance (2.0 g.) was phosphorylated, without further purification, in 10 ml. of dry pyridine at 5° with 2.75 g. of diphenylphosphorochloridate added dropwise. The reaction mixture was left overnight at 5°, and was then worked up as described for the phosphorylation of the 3-isomer. The yield of methyl 2-*O*-diphenylphosphonyl 3-*O*-benzoyl-D-*erythro*-2,3-dihydroxybutyrate was 3.9 g. (99%).

This intermediate was unblocked by reductive cleavage with platinum oxide (1.0 g.) and hydrogen at atmospheric pressure in absolute ethanol.[1] The hydrogen uptake was 2450 ml. in one hr. The catalyst was removed, and 40 ml. of 1 *N* sodium hydroxide was added to the alcoholic solution. The mixture was concentrated *in vacuo* to remove the alcohol, and water was added to a volume of 25 ml. After 24 hr. at room temperature to complete saponification, the solution was freed of cations by treatment with Dowex-50 in the hydrogen form. The resin was removed, and the aqueous layer was extracted with ether to remove the benzoic acid. The aqueous layer was then brought to *p*H 8–9 with cyclohexylamine, and the solution was concentrated to dryness *in vacuo*. The solid residue was stirred up with ethyl acetate and filtered. It was reprecipitated from solution in absolute ethanol by addition of ethyl acetate. The tricyclohexylammonium D-*erythro*-2,3-dihydroxybutyrate 2-phosphate (2.5 g.) was dried in a vacuum desiccator at room temperature. It showed $[\alpha]_D$ +15° (*c* 1 free acid, 1 *N* hydrochloric acid), and had a very slight positive rotation in the presence of molybdate.

Anal. Calcd. for $C_{22}H_{48}O_7N_3P$ (497): N, 8.47; P, 6.24. Found: N, 8.50; P, 6.22.

Acid-catalyzed Isomerization of the Phosphates of 2,3-Dihydroxybutyric Acid.—Approximately 1% solutions of the compounds in 1 *N* hydrochloric acid were heated at 100° for two hr. After neutralization and addition of ammonium molybdate to a final concentration of 15%, the specific rotations were determined. The 2-isomer gave $[\alpha]_D$ −560° while the 3-isomer gave $[\alpha]_D$ −630°.

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BERKELEY 4, CALIFORNIA

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Cyclic Dimercaptals and Dimercaptols from Alkylene Dithiols[1]

BY C. S. MARVEL AND RALPH C. FARRAR, JR.

RECEIVED SEPTEMBER 10, 1956

The reaction of decamethylene dithiol with several aldehydes and one ketone has given further examples of 26-membered ring compounds containing 4 atoms of sulfur and 22 atoms of carbon. These cyclic dimercaptals and dimercaptols have been oxidized to tetrasulfones. Nonamethylene dithiol has also given a cyclic dimercaptal which is a 24-membered ring compound. Heptamethylene dithiol and vanillin did not give a crystalline cyclic material, but the 20-membered ring compound is formed with acetone. The cyclic dimercaptal from decamethylene dithiol and vanillin is converted to a polymer of about 13,000 mol. wt. on heating.

It has been found that a higher alkylene dithiol may react with an aldehyde or ketone to produce a cyclic dimercaptal or dimercaptol I or a linear polymer II.[2–5] The present study was under-

(1) The work discussed herein was performed as a part of the synthetic rubber research project sponsored by the National Science Foundation.

(2) W. Autenrieth and A. Geyer, *Ber.*, **41**, 4249 (1908).

(3) W. Autenrieth and F. Beuttel, *ibid.*, **42**, 4346, 4357 (1909).

(4) C. S. Marvel, E. H. H. Shen and R. R. Chambers, THIS JOURNAL, **72**, 2106 (1950).

(5) C. S. Marvel, E. A. Sienicki, M. Passer and C. N. Robinson, *ibid.*, **76**, 933 (1954).

TABLE I

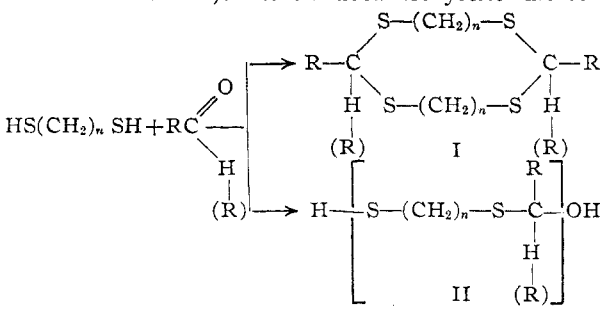
REACTIONS OF DECAMETHYLENE DITHIOL AT 30°

Dithiol, g.	19.28	12.9	19.3	19.3
Carbonyl compd.	Benzaldehyde diethyl acetal	Vanillin	Acetone	*p*-Chlorobenzaldehyde diethyl acetal
Amt., g.	16.83	9.52	5.425	20.052
Dioxane, ml.	80	80	70	80
Catalyst, ml. dioxane satd. with dry HCl	9	20	15	9
Reacn. time, days	12	5	5	44
Isolation method	A	B	B	A
Polymer, g.	19.1(69.5%)	0	0	20.1(60.0%)
Inherent visc.	0.21	...	...	0.18
Cyclic prod., g.	8.23(29.9%)	21[a](98.9%)	19.3(83.9%)	12.08(39.4%)
M.p., °C.	133–134	163–164	120–121	144–145
Analyses, % Calcd. C		63.48	63.35	62.06
Obsd. C		63.51	63.29	62.28
Calcd. H		8.29	10.63	7.66
Obsd. H		8.45	10.42	7.35
Calcd. S		18.83	26.02	19.50
Obsd. S		18.93	26.61	19.39[b]
Calcd. mol. wt.		681	493	658
Obsd. mol. wt.[c]		659	463	623

[a] At the end of five days stirring this product precipitated suddenly from the solution. [b] *Anal.* Calcd.: Cl, 10.78 Found: Cl, 10.50. [c] Average of 5 by boiling point elevation method of Menzies and Wright.[7]

taken to extend our knowledge of these reactions.

In this reaction, acetals of aromatic aldehydes can be used as well as the aldehydes. The character of the product seems to depend on the value of n (that is, the number of methylene groups between the sulfur atoms). With decamethylene dithiol



which was used in most of the current experiments, the major product is usually the large ring dimercaptal, and there is a minor yield of polymeric material. Autenrieth and Geyer[2] showed that when n is 5, acetone reacted to give the cyclic dimercaptal. Earlier work in this Laboratory[4] demonstrated that hexamethylene dithiol produces linear polymercaptals. Heptamethylene dithiol gave a low molecular weight linear product with vanillin. Both heptamethylene dithiol and nonamethylene dithiol gave good yields of the cyclic dimercaptols with acetone.

It has been found that the cyclic dimercaptal prepared from decamethylene dithiol and vanillin can be converted to a polymer of a molecular weight of about 13,000 when it is heated above its melting point. The cyclic product from acetone and decamethylene dithiol could not be changed to a polymer even though it was heated with acidic catalysts.

Most of the cyclic products have been characterized by analyses, molecular weight determinations, oxidation to sulfones and by their ultraviolet absorption spectra. The ultraviolet spectra of these cyclic products showed peaks which have been established as characteristic for mercaptals and mercaptols by Fehnel and Carmack.[6]

The experimental work was terminated earlier than had been intended because of a most severe skin rash caused by the alkylene dimercaptans. Other workers in this Laboratory have found that these compounds cause severe rashes.

Experimental

Reactions of Decamethylene Dithiol.—The general procedure followed was to dissolve the dithiol in purified dioxane in a glass stoppered erlenmeyer flask and then add the carbonyl compound (or acetal), stir for a minute or two with a magnetic stirrer and finally introduce the catalyst. A nitrogen atmosphere was introduced; then stirring was continued as long as the reaction was allowed to proceed at 30°. The solid product was isolated either by direct filtration (procedure B) or by neutralization with solid sodium bicarbonate, then filtration and separation of the organic material from the salt by dissolving in benzene and recrystallizing (procedure A). In either case the residual dioxane solution from the first filtration was concentrated by evaporation and then poured into methanol to precipitate polymeric products. The results of some typical experiments are collected in Table I.

The reaction of decamethylene dithiol and *m*-nitrobenzaldehyde was carried out in a slightly different manner. To the reaction mixture of 19.3 g. of decamethylene dithiol, 18.9 g. of *m*-nitrobenzaldehyde in 250 ml. of dioxane was added 25 ml. of dioxane saturated with hydrogen chloride. The solution was stirred for 5 days at 30° and filtered to give 0.34 g. of product. The filtrate was saturated with dry hydrogen chloride and allowed to stand one day and filtered again to yield 3.32 g. of product. After another day 5.1 g. of product was removed by filtration and after the ninth day 3.19 g. Then the filtrate was again saturated with dry hydrogen chloride and on the eleventh day 8.63 g. of product was removed by filtration. On the sixteenth day an additional 4.14 g. was collected. The total yield of crystalline product after 16 days was 24.42 g. (77%) of the cyclic dimercaptal, m.p. 142–143°. No polymeric material was isolated from the filtrate.

Anal. Calcd. for $C_{34}H_{50}N_2O_4S_4$: C, 60.14; H, 7.42; S, 18.89; N, 4.13. Found: C, 60.51; H, 7.35; S, 18.57; N, 4.34.

(6) E. A. Fehnel and M. Carmack, THIS JOURNAL, **71**, 84 (1949).

(7) A. W. C. Menzies and S. L. Wright, Jr., *ibid.*, **43**, 2315 (1921).

Oxidation of Dimercaptals to Tetrasulfones.—The cyclic dimercaptals and dimercaptol were oxidized to the corresponding tetrasulfones by the method of Drew.[8] The vanillin derivative could not be converted to the sulfone because of oxidative attack of the phenolic ring. The oxidation of the *p*-chlorobenzaldehyde derivative is typical.

A mixture of 4.068 g. of the cyclic dimercaptal from *p*-chlorobenzaldehyde and decamethylene dimercaptan in 200 ml. of chloroform was stirred with 272 ml. of a cold 0.417 *N* solution of monoperphthalic acid in ether. An additional 100 ml. of ether was added to increase the volume of solvent. After three days of stirring an additional 136 ml. of the monoperphthalic acid solution was added, and stirring was continued another three days. The reaction mixture was filtered and the precipitate washed repeatedly with 5% sodium bicarbonate solution and then water to remove phthalic acid. The white solid tetrasulfone after drying in a desiccator weighed 4.67 g. (96%). The sulfone was quite insoluble in common solvents. A sample was recrystallized repeatedly from a large volume of chloroform to give crystals, m.p. 166–170° dec.

Anal. Calcd. for $C_{34}H_{50}Cl_2O_8S_4$: C, 51.96; H, 6.41; S, 16.32. Found: C, 52.28; H, 6.53; S, 15.78.

The acetone cyclic dimercaptol gave a tetrasulfone, m.p. 213–218°. *Anal.* Calcd. for $C_{26}H_{52}S_4O_8$: C, 50.29; H, 8.44; S, 20.66. Found: C, 50.27; H, 8.75; S, 20.33.

The *m*-nitrobenzaldehyde cyclic dimercaptal gave a 93.3% yield of a tetrasulfone, m.p. 151–154° dec. *Anal.* Calcd. for $C_{34}H_{50}O_{12}N_2S_4$: C, 50.60; H, 6.24; S, 15.89; N, 3.47. Found: C, 50.70; H, 6.40; S, 15.48; N, 3.48.

Reaction of Heptamethylene Dithiol and Vanillin.—To a solution of 6.5 g. of heptamethylene dithiol and 6.02 g. of vanillin in 100 ml. of dioxane was added 20 ml. of dioxane saturated with dry hydrogen chloride. After 22 days no solid had crystallized. Evaporation of the solvent left a viscous liquid soluble in benzene but insoluble in methanol. This oil weighed 10.9 g. and had an inherent viscosity in benzene of only 0.03. It was not further investigated.

Reaction of Heptamethylene Dithiol and Acetone (By Eugene D. Vessel).—To a solution of 16.4 g. of heptamethylene dithiol and 5.8 g. of acetone in 80 ml. of dry dioxane was added 20 ml. of dioxane saturated with dry hydrogen chloride. The mixture was placed in a closed flask and stirred at room temperature for 8 days. Filtration gave 15.7 g. of crystals, m.p. 128–129°. From the mother liquors 3.5 g. of viscous material was obtained. On recrystallization from dioxane additional crystalline material (about 4–5 g.) was obtained until finally less than 0.5 g. of residual viscous polymeric material remained.

The crystals were recrystallized from benzene to give beautiful colorless plates, m.p. 129–129.5°.

Anal. Calcd. for $C_{20}H_{40}S_4$: C, 58.76; H, 9.86; S, 31.38; mol. wt., 408. Found: C, 58.73; H, 9.84; S, 31.47; mol. wt. Menzies–Wright b.p. elevation method[7] (av. of 3 runs), 415.5.

Reaction of Nonamethylene Dithiol and Acetone.—To a solution of 9.6191 g. of nonamethylene dithiol and 2.9039 g. of acetone in 40 ml. of dioxane was added 8 ml. of dioxane saturated with dry hydrogen chloride. The solution was stirred for 12 days at room temperature and then filtered to yield 5.57 g. (48%) of white crystals which proved to be the cyclic dimercaptol. After recrystallization from benzene the product melted at 128–129°.

Anal. Calcd. for $C_{24}H_{48}S_4$: C, 62.00; H, 10.41; S, 27.59; mol. wt., 464. Found: C, 62.00; H, 10.37; S, 27.20; Menzies–Wright b.p. elevation method[7] (av. of 3 runs), 437.

The infrared spectrum of this compound showed a C–SC band at 673 cm.$^{-1}$, $-(CH_2)_n-$ bands at 720 cm.$^{-1}$ and $(CH_3)_2$ bands at 1350, 1366 and 1379 cm.$^{-1}$ and aliphatic C–H at 2900 cm.$^{-1}$.

Ultraviolet Absorption Spectra of Cyclic Products.—The ultraviolet absorption of the cyclic dimercaptals and dimercaptols was taken in dioxane solution.

The results are listed in Table II.

TABLE II

Cyclic dimercaptal from	λ_{max}, mμ	log ε
Benzaldehyde and decamethylene dithiol	244[a]	3.50
m-Nitrobenzaldehyde and decamethylene dithiol	256	4.25
Vanillin and decamethylene dithiol	235	4.25
	285	4.01
p-Chlorobenzaldehyde and decamethylene dithiol	248[a]	3.72
Cyclic dimercaptol from		
Acetone and decamethylene dithiol	239	3.16
Acetone and nonamethylene dithiol	247	3.15

[a] Shoulders rather than peaks.

URBANA, ILL.

(8) H. F. Drew, Ph.D. Thesis, University of Minnesota, 1951, p. 52.

[CONTRIBUTION FROM THE MAYURBHANJA CHEMICAL LABORATORY, RAVENSHAW COLLEGE, UTKAL UNIVERSITY]

Synthesis of Isomeric Bromothiazolylamines and the Use of Their Mercurated Derivatives as Fungicides and Bactericides

BY G. N. MAHAPATRA

RECEIVED MAY 18, 1956

Fifteen isomeric bromothiazolylamines containing one, two or three bromine atoms have been synthesized. The relation between the position of bromine and biological activity has been studied. These bromothiazolylamines have been mercurated and the resulting compounds subjected to fungicidal and bactericidal assay with promising results.

In view of the antibacterial activity and other biological properties of 2-aminothiazoles and various N-substituted 2-amino thiazoles,[1-6] it was thought worthwhile to synthesize further N-substituted aminothiazoles. As the introduction of bromine into thiazolidone[7] and the thiazole[8] nucleus generally augments the antibacterial as well as antifungal activity, bromine has been introduced into these thiazole derivatives and the relation between the position of bromine in the molecules and their biological activity also has been studied.

Fifteen different phenyl-2-thiazolylamines having one, two or three bromine atoms at different positions of the molecule have been prepared.

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(3) D. Bovet, J. Bablet and J. Fournel, *Ann. Inst. Pasteur*, **72**, 105 (1946), *Semaine hopitaux Paris*, **37**, 8 (1945).

(4) C. W. Sondern and P. J. Breivogel, U. S. Patent 2,440,703, May 4 (1948); U. S. Patent 2,519,325, Aug. 15 ((1950).

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(8) G. N. Mahapatra, *Nature*, **177**, 938 (1956).