liberated phenylhydrazine was removed from the precipitated benzimidazole by washing the filtered product with alcohol and ether.

Barium D-Gala-L-*gluco*-heptonate.—Pure D-gala-L-*gluco*-heptonic phenylhydrazide remaining from an earlier research in this Laboratory[11] was decomposed by heating with aqueous copper sulfate and the liberated heptonic acid converted to its barium salt in the usual manner. Kiliani[12] mentioned that this salt is very beautifully crystalline but gave no further details. We found that it crystallizes readily from water in clusters of elongated prisms that are anhydrous when dried in the air at room temperature. Its rotation is negative, $[\alpha]^{20}D$ −4.1° in water (*c* 2), in accord with Levene's rule of rotation for the salts of aldonic acids.[13] For its additional characterization we have measured the mutarotation it undergoes when dissolved in an excess of *N* hydrochloric acid (Table I).

Anal. Calcd. for $C_{14}H_{26}BaO_{16}$: C, 28.61; H, 4.46; Ba, 23.37. Found: C, 28.56; H, 4.48; Ba, 23.18.

TABLE I

ROTATION OF BARIUM D-GALA-L-*gluco*-HEPTONATE IN *N* HCl (*c* 5)

Time, min.	$[\alpha]^{20}D$
3	− 5.0°
10	− 6.4
30	− 7.9
60	− 9.1
120	−10.0
180	−10.7
240	−11.0
300	−11.1
480	−11.2
1440 (constant)	−11.6

Final rotation, calculated as lactone, −16.3°

2-(D-*gala*-L-*gluco*-*hepto*-1,2,3,4,5,6-Hexahydroxyhexyl)-benzimidazole.—A solution of 5.9 g. (0.010 mole) of the barium salt just described, 2.4 g. (0.022 mole) of *o*-phenylenediamine, 8.8 ml. (0.044 mole) of 5 *N* hydrochloric acid and 10 ml. of water in a test-tube was heated at 135 ± 5° for 2.5 hours. The thick residue was dissolved in hot water, decolorized with activated carbon, and the filtered solution made alkaline with aqueous ammonia. No crystallization occurred, so the solution was concentrated to a powder and the excess *o*-phenylenediamine removed by several extractions with ether. The residue was redissolved in hot water and concentrated in a current of air, the product then separating as small, granular crystals which were filtered, washed with water, and dried at 70° to yield 3.5 g. with m.p. 185–189°. The substance was recrystallized first from water by the addition of ethanol to form long needles, and then from water alone as clusters of small, radiating needles. This benzimidazole is unusual, first, because it is hydrated and secondly, because the analyses of the samples dried to constant weight at 20° *in vacuo* indicate the presence of only three-quarters of a mole of water. It was because of the latter circumstance that we prepared the benzimidazole not only from the phenylhydrazide directly but also from the barium salt derived from a sample of carefully purified phenylhydrazide in order to minimize the possibility that we might have either a mixture or a double compound containing 75% of a monohydrated benzimidazole of D-gala-L-*gluco*-heptonic acid and 25% of the known, anhydrous benzimidazole of D-gala-L-*manno*-heptonic acid. The melting point of the hydrated benzimidazole varied with the rate of heating, a value of 198° being observed when the compound was heated slowly from room temperature. Its rotation $[\alpha]^{20}D$ −13.8° in *N* hydrochloric acid (*c* 2) is equivalent to −14.4° for the anhydrous compound.

Anal. Calcd. for $C_{13}H_{18}N_2O_6 \cdot 0.75H_2O$: C, 50.07; H, 6.31; N, 8.99; H_2O, 4.34. Found: C, 50.25, 50.36; H, 6.18, 6.32; N, 8.78, 9.11, 9.12; H_2O (100° *in vacuo*), 4.11, 4.28, 4.38.

(11) R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 548 (1937).

(12) H. Kiliani, *Ber.*, **55**, 96 (1922).

(13) P. A. Levene, *J. Biol. Chem.*, **23**, 145 (1915); P. A. Levene and G. M. Meyer, *ibid.*, **26**, 355 (1917).

2,2'-(L-*threo*-1,2-Dihydroxyethylene)-dibenzimidazole.—A mixture of 15 g. (0.10 mole) of L-threaric acid (the common, dextrorotatory tartaric acid), 21.6 g. (0.20 mole) of *o*-phenylenediamine and 44 ml. (0.22 mole) of 5 *N* hydrochloric acid was heated in an oil-bath at 135 ± 5° for 2.5 hours. The resulting dark blue, nearly solid mass was dissolved in 100 ml. of water and the solution made alkaline with aqueous ammonia. The original gummy precipitate became granular overnight and was then filtered and washed thoroughly with water. The air-dried, lilac-colored powder weighed 15.8 g. Two extractions with boiling ether removed only a very small amount of soluble material. Boiling methanol was then used to dissolve a large part of the remaining solid and the dark red solution was decolorized with activated carbon. Concentration of the methanol solution to 200 ml. *in vacuo* and the addition of an equal volume of water, followed by refrigeration overnight, yielded a flask full of long needles, with small clusters of compact crystals on top. When the solution was allowed to warm to room temperature the long needles dissolved and appeared to be replaced by clusters of tiny needles. After several days the product was filtered and dried; it weighed 4.0 g., and an additional smaller amount was obtained from the mother liquor. The dibenzimidazole thus prepared was recrystallized four times from methanol. The small, colorless needles began to discolor when heated to about 260°, and showed a definite melting and flowing to a red mass at about 275°; the residue solidified, and a small amount of distilled oil was observed to crystallize in the melting point tube just above the metal block used in heating the sample. The $[\alpha]^{20}D$ value was +212° in *N* hydrochloric acid (*c* 0.8).

Anal. Calcd. for $C_{16}H_{14}N_4O_2$: C, 65.29; H, 4.79; N, 19.04. Found: C, 65.48; H, 4.91; N, 19.16.

2,2'-(L-*threo*-1,2-Dihydroxyethylene)-dibenzimidazole Dihydrochloride Dihydrate.—When a solution of the dibenzimidazole in *N* hydrochloric acid was allowed to evaporate in a current of air the dihydrochloride crystallized readily as plate-like prisms; it was recrystallized from 95% ethanol by the addition of pentane. On heating, the dihydrochloride began to turn yellowish at about 200°, then gradually darkened until it melted at 270° to a red liquid with the evolution of gas.

Anal. Calcd. for $C_{16}H_{14}N_4O_2 \cdot 2HCl \cdot 2H_2O$: C, 47.65; H, 5.00; Cl, 17.58; N, 13.89; H_2O, 8.93. Found: C, 47.94; H, 5.17; Cl, 17.48; N, 14.12; H_2O (100° *in vacuo*), 9.38.

Acknowledgment.—The authors wish to thank Mr. Edward W. Tracy for preparing the 5-methyl-2-D-gluco-benzimidazole, and Dr. William C. Alford, Miss Paula M. Parisius and Mrs. Evelyn G. Peake for carrying out the microchemical analyses.

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE
FEDERAL SECURITY AGENCY, BETHESDA, MARYLAND

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The Reaction of 2-Aminobenzenethiol with Aldoses and with Hydroxymethylfurfural

BY LOUIS SATTLER,[1a] F. W. ZERBAN,[1b] G. L. CLARK[1c] AND CHIA-CHEN CHU[1d]

Benzothiazolines are readily formed when 2-aminobenzenethiol reacts with aldehydes[2] and it was therefore considered that a corresponding reaction with aldoses might also take place. We find that the reaction goes quantitatively with D-mannose, D-glucose, D-arabinose and with hydroxymethylfurfural. The formation of thiazolidine derivatives of aldoses has been reported by Schu-

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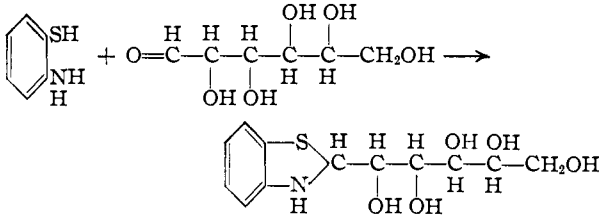
(2) H. P. Laukelma and P. X. Sharnoff, THIS JOURNAL, **53**, 2654 (1931); M. T. Bogert and B. Naiman, *ibid.*, **57**, 1529 (1935).

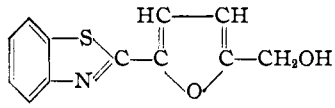
bert[3] and by Ågren[4] who prepared them by the action of cysteine on simple sugars.

Because the benzothiazolines give a negative test for the SH group with sodium nitroprusside, the reaction with D-mannose, for example, presumably goes as follows



In this reaction a new asymmetric center is produced on carbon 1 of the aldose, and consequently two isomeric compounds should be expected to be produced. However, at present there is no simple way to establish the identities of such substances, and X-ray powder diffraction analysis gives no assistance in elucidating the exact nature of the obtained products.

The aldose benzothiazolines are not only light sensitive, but they are unstable in water solution. An aqueous solution of the glucose derivative becomes turbid on standing exposed to the air. In a few days a yellow crystalline solid deposits which on recrystallization from methanol yields glistening, elongated hexagonal plates melting at 91.7–92.2°. Analysis shows it to be bis-(2-aminophenyl) disulfide. The water solution contains D-glucose which was isolated in the form of its phenylosazone. Schubert[3] correspondingly obtained cystine on mild oxidation of his compound. While it is known[2] that benzothiazolines are readily oxidized by air to yield benzothiazoles, only hydroxymethylfurfural gave a product which, based on quantitative analysis, appeared to be the benzothiazole derivative.



Experimental[5,6,7]

Synthesis of 2-(D-*manno*-Pentahydroxypentyl)-benzothiazoline.—To a solution of 1 ml. of commercial 2-amino benzenethiol in 8 ml. of glacial acetic acid was added one gram of D-mannose and the mixture was shaken from time to time at room temperature in a glass-stoppered erlenmeyer flask. The reaction was practically completed within a half-hour because the product gave only a faint color test with anthrone.[8] However, the reaction mixture was permitted to stand overnight when an additional 15 ml. of glacial acetic acid was added. The stiff, creamy paste was filtered on a buchner funnel, and the fine crystalline mass was washed with glacial acetic acid and then with cold isopropyl alcohol. The D-mannose derivative was recrystallized from dilute isopropyl alcohol, and on standing in the refrigerator overnight, extremely minute crystals deposited. They were filtered on a dense fritted glass funnel, and at a magnification of 960 × the crystals appeared rectangular, and were of the order of 0.5–3 microns in length; m.p. 192°. The compound is very sparingly soluble in cold water; soluble in hot. It is insoluble in 99% isopropyl alcohol, benzene, dioxane and tetrahydrofurfuryl alcohol, but it is soluble in pyridine at room temperature. After standing 3 hours, $[\alpha]^{20}D$ +39.6° (*c* 0.5204, pyridine).

Anal. Calcd. for $C_{12}H_{17}O_5NS$: C, 50.16; H, 5.97; N, 4.88. Found: C, 50.33; H, 6.13; N, 4.90.

Preparation of 2-(D-*gluco*-Pentahydroxypentyl)-benzothiazoline.—The reaction with anhydrous D-glucose was carried out as previously. After standing three days at room temperature, the reaction mixture was diluted with an equal volume of 99% isopropyl alcohol, and then put into the refrigerator. At the end of two days, the fluffy solid was removed on a buchner funnel, washed with cold 99% isopropyl alcohol, and recrystallized from that solvent (1 g. in 25 ml. of solvent) in which it is abundantly soluble at elevated temperatures. Beautiful long silky needles were obtained. This compound on analysis showed the presence of one mole of isopropyl alcohol of crystallization; $[\alpha]^{20}D$ −9.22° (*c* 1.3184, water).

Anal. Calcd. for $C_{12}H_{17}O_5NS \cdot C_3H_7OH$: C, 51.85; H, 7.25; N, 4.03. Found: C, 52.08; H, 7.30; N, 4.20.

After heating in an Abderhalden drier for four hours at the temperature of boiling carbon tetrachloride, and at 0.5 mm. pressure, the compound melted at 118–119.2°. After 20 minutes $[\alpha]^{20}D$ −15.6° (*c* 0.9214, water).

Anal. Calcd. for $C_{12}H_{17}O_5NS$: N, 4.88. Found: N, 4.92.

Preparation of 2-(D-*arabo*-Tetrahydroxybutyl)-benzothiazoline.—The reaction with D-arabinose was carried out exactly the same way as with D-mannose. The product was recrystallized from commercial anhydrous methanol; m.p. 173–174.2° with decomposition.

Anal. Calcd. for $C_{11}H_{15}O_4NS$: C, 51.34; H, 5.88; N, 5.45. Found: C, 51.65; H, 5.90; N, 5.31.

Preparation of 2-[5-(Hydroxymethyl)-2-furyl]-benzothiazole.—One gram of hydroxymethylfurfural was added to a slight excess of 2-aminobenzenethiol dissolved in glacial acetic acid. On standing two days at room temperature, the reaction was complete, and the yield quantitative. The solid was removed on a Hirsch funnel, dissolved in boiling dilute methanol, and decolorized with activated carbon. Long white needles were obtained melting at 171.5–172°.

Anal. Calcd. for $C_{12}H_9O_2NS$: C, 62.32; H, 3.92; N, 6.06. Found: C, 61.92; H, 4.11; N, 6.09.

Air Oxidation of the D-Glucose Derivative.—A solution of 2 g. of the compound in 100 ml. of water was placed in a beaker and stirred from time to time. In a few hours the solution became turbid and, after a few days, a yellow crystalline solid deposited. This was removed by filtration, and after air-drying, it was extracted with warm benzene. The benzene was removed by evaporation, and the crystalline residue was twice recrystallized from methanol. Shiny plates melting at 91.7–92.2° were obtained. The material had an odor associated with the disulfide obtained from 2-aminobenzenethiol, and it gave a negative test for the SH group. With a methanolic solution of silver nitrate, a reddish-brown precipitate formed. Its properties suggested that it is bis-(2-aminophenyl) disulfide.

Anal. Calcd. for $C_{12}H_{12}N_2S_2$: C, 58.03; H, 4.87; N, 11.28. Found: C, 58.02; H, 4.73; N, 10.94.

The X-ray diffraction data for this compound are: *d* (Å.) 11.30 (1), 6.67 (4), 6.16, 5.71 (5). 5.02 (2), 4.71, 4.35, 4.12, 3.85 (3), 3.67, 3.50, 3.20, 2.98, 2.79, 2.70, 2.57, 2.50, 2.39, 2.31, 2.24, 2.09, 1.91, 1.86, 1.72, 1.60, 1.53.

The aqueous solution from which the disulfide had been removed, was concentrated *in vacuo* to a small volume, and treated with a mixture of phenylhydrazine hydrochloride and sodium acetate. On heating in a water-bath, the characteristic phenylosazone of D-glucose was obtained. After recrystallization from ethanol, the osazone was mixed with an authentic sample of phenyl-D-glucosazone. There was no depression of the melting point.

The osazone was converted by the method of Hann and Hudson[9] into phenyl-D-glucosotriazole, m.p. 195°. A mixture made with it and authentic material gave no melting point depression.

The X-ray powder diffraction data are given in Table I.

Acknowledgments.—The writers take pleasure in thanking the American Cyanamid Company

(3) M. P. Schubert, *J. Biol. Chem.*, **130**, 601 (1939).
(4) G. Ågren, *Enzymologia*, **9**, 321 (1941).
(5) All melting points are uncorrected.
(6) Microanalyses by Clark Microchemical Laboratory.
(7) Optical rotations are of little significance due to changing values.
(8) L. Sattler and F. W. Zerban, THIS JOURNAL, **72**, 3814 (1950).
(9) R. M. Hann and C. S. Hudson, *ibid.*, **66**, 735 (1944).

TABLE I[10]

X-RAY DIFFRACTION DATA OF DERIVATIVES

D-Glucose, d (Å.)	D-Mannose, d (Å.)	D-Arabinose, d (Å.)	Hydroxymethyl furfuraldehyde, d (Å.)
(1) 15.55	(2) 13.55	10.80	(2) 9.08
(4) 9.60	6.65	8.56	(3) 8.36
7.28	5.11	5.37	7.66
6.17	(1) 4.84	4.92	7.06
5.54	4.52	4.35	(1) 5.83
5.28	4.18	4.00	5.43
4.95	3.92	3.62	5.00
(2) 4.45	(3) 3.31	3.39	4.51
(3) 4.16	3.13	3.20	4.22
3.86	2.86	3.03	3.97
3.64	2.74	2.62	3.69
3.19	2.41	2.23	3.49
2.81	2.33		3.33
2.70	2.21		3.21
2.40	2.12		2.82
	2.00		2.63
			2.51
			2.36
			2.09
			1.94
			1.82

for the 2-aminobenzenethiol, and Louis Lang of the National Sugar Refining Company for the hydroxymethylfurfural.

(10) Numbers in parenthesis indicate relative order of intensities.

NEW YORK SUGAR TRADE LABORATORY, INC.
NEW YORK, N. Y. RECEIVED JULY 9, 1951

Some Derivatives of 6,8-Dichloroquinoline[1]

BY CHARLES R. SAUNDERS, CLYDE E. SMITH, JR., AND JULIUS D. CAPPS

This investigation was conducted as part of a general study concerning the synthesis and establishment of molecular structures of various previously unreported derivatives of quinoline.

6,8-Dichloroquinoline (I), as prepared from either 2,4-dichloroaniline (II) or 2,4-dichloroacetanilide by a Skraup ring-closure, was nitrated to give the same compound obtained from ring-closure of 2,4-dichloro-5-nitroaniline[2] (III). III was produced by nitrating II with a solution of sodium nitrate in fuming sulfuric acid (20% oleum); its structure was verified by removing the amino grouping prior to reduction and subsequent bromination to yield 6-bromo-2,4-dichloroaniline, which was also obtained by brominating an authentic sample of II for comparison purposes.

An authentic sample of 2,6,8-trichloro-5-nitroquinoline (VII), synthesized from 6,8-dichloro-5-nitroquinoline *via* 6,8-dichloro-1-methyl-5-nitro-2-quinolone, was shown to be the same as the direct nitration-product of 2,6,8-trichloroquinoline (VI). Since the hydrolysis of VII gave the same compound as obtained by the nitration of 6,8-dichloro-2-hydroxyquinoline (IX), which resulted from the hydrolysis of VI, the chief nitration-product of IX was established as being 6,8-dichloro-2-hydroxy-5-nitroquinoline.

Hydrogen in presence of Raney nickel or metallic tin and hydrochloric acid under the usual conditions served for the reduction of the three nitroquinolines to the corresponding amines. Conditions previously reported for converting certain substituted aminoquinolines into arsonic acids, acetamido and benzamido derivatives[3] were employed successfully in preparing derivatives of these amines.

Experimental

6,8-Dichloroquinoline (I).—2,4-Dichloroacetanilide was subjected to a Skraup ring-closure under conditions similar to those reported by Richter and Smith[4] for synthesizing certain substituted quinolines; yield 35%; m.p. 103–104°.

6,8-Dichloro-5-nitroquinoline (IV) (A).—Nitration of 6,8-dichloroquinoline under conditions similar to those employed by de Arce, Greene and Capps[3] for the nitration of 8-bromo-6-methylquinoline gave IV in yields of 66–78%; m.p. 125.5–126.5°.

Anal. Calcd. for $C_9H_4Cl_2N_2O$: Cl, 29.18; N, 11.53. Found: Cl, 29.21; N, 11.65.

(B).—2,4-Dichloro-5-nitroaniline (5.0 g.), arsenic pentoxide (5.5 g.), acetic anhydride (3 ml.), anhydrous glycerol (6.9 g.) and sulfuric acid (3.4 ml.) were mixed well and heated together under a reflux condenser by means of an oil-bath maintained at 155–160° for five hours. The cooled mass was poured with stirring into cracked ice–water mixture and finally filtered. Extraction of the water-washed and dried residue with boiling benzene removed the 6,8-dichloro-5-nitroquinoline that was deposited upon evaporation of the benzene. The crude product was purified by a combination of decolorizing carbon treatments and crystallizations from 95% ethanol; yield 3 g.

2,4-Dichloro-5-nitroaniline (III).—2,4-Dichloroaniline (5 g.) dissolved in fuming sulfuric acid (20% oleum, 50 ml.) was added dropwise, with mechanical stirring, to a solution of sodium nitrate (2.6 g.) in fuming sulfuric acid (20% oleum, 25 ml.) maintained at 0°. When an additional 30 minutes had elapsed, the temperature of the system was slowly increased to 40° and maintained for 15 minutes. An orange-colored solid formed upon pouring the reaction mixture into cracked ice and water (800 ml.). The acid was neutralized with sodium hydroxide prior to filtering and washing the residue with water. A combination of dissolutions in 95% ethanol and decolorizing carbon treatments followed by addition of water (30% by volume) gave yellow needles; 2.7 g.; m.p. 107–108°.

The molecular structure of III as obtained by procedure listed above was verified by deamination according to conditions reported by Morton and McGookin,[5] for changing 4-amino-2,3-dinitrotoluene into 2,3-dinitrotoluene, followed by reduction of the resulting 2,4-dichloronitrobenzene with tin and hydrochloric acid to 2,4-dichloroaniline and bromination in hydrochloric acid solution (sp. gr. 1.19) to give 6-bromo-2,4-dichloroaniline.

6,8-Dichloro-1-methyl-2-quinolone (V).—6,8-Dichloroquinoline (40 g.) was converted into V (43 g., m.p. of crude, 80–86°) according to modifications of conditions employed by de Arce, Greene and Capps[3] for synthesis of 8-bromo-1,6-dimethyl-2-quinolone. Dimethyl sulfate (100 ml.) acted upon 6,8-dichloroquinoline at 140–150° (temperature of oil-bath) for three hours and oxidation with potassium ferricyanide was conducted at 60–65°.

Super-heated steam distillation of some of the crude quinolone gave a solid in distillate that was analyzed.

Anal. Calcd. for $C_{10}H_7Cl_2NO$: N, 6.14. Found: N, 6.33.

2,6,8-Trichloroquinoline (VI).—Crude 6,8-Dichloro-1-methyl-2-quinolone (21 g.) was converted into VI (12.7 g., m.p. 165–166°) by treatment with phosphorus pentachloride according to the procedure of Perkin and Robinson[6] for

(1) Condensed in part from a thesis presented by Clyde E. Smith, Jr., to the Graduate School of the Alabama Polytechnic Institute in partial fulfillment of the requirements for the degree of Master of Science.

(2) See *C. A.*, **5**, 1270 (1911).

(3) H. Diaz de Arce, J. L. Greene, Jr., and J. D. Capps, THIS JOURNAL, **72**, 2971 (1950).

(4) F. Richter and G. F. Smith, *ibid.*, **66**, 396 (1944).

(5) A. Morton and A. McGookin, *J. Chem. Soc.*, 910 (1934).

(6) W. H. Perkin and R. Robinson, *ibid.*, **103**, 1977 (1913).