

dithiocarbamates were more stable and were obtained in a pure condition.

Action of Thiobenzoic Acid.—Molar quantities of phenacyl thiocyanate and thiobenzoic acid were heated in benzene solution for four hours. The product isolated melted at 95° and corresponded to benzoyl-phenacyl-dithiocarbamate (VII), $C_6H_5CONHCSSCH_2COC_6H_5$, since on heating with dilute hydrochloric acid it gave benzoic acid and the thiazoline (VI), m. p. 168°.

As shown in the table, thiazolines were obtained from thiocyanates I–V, using thioacetic and thiobenzoic acids, but the intermediate dithiocarbamates were isolated only in some cases with thiobenzoic acid.

2-Thio-4,5-diphenylthiazoline (XVI).—Desyl thiocyanate and thioacetic acid gave in good yield this thiazoline (m. p. 214°).

Wheeler and Johnson³ on treating the desyl thiocyanate with thiobenzoic acid, had isolated an unidentified compound melting at 137°, which was doubtless the benzoyl addition product. Using the same reagents, evidence was obtained of an immediate product melting about 132–133° which went over readily into the diphenylthiazoline (m. p. 214°).

The enol nature of the thiazoline was shown by the

(3) Wheeler and Johnson, *Am. Chem. J.*, **26**, 202 (1901).

formation of a 2-benzyl ether (XVII) when the diphenylthiazoline was treated with benzyl chloride.

Rhodanine. 2-Thio-4-thiazolidone, XVIII.—Diethyl thiocyanomalonate was heated in benzene solution with thiobenzoic acid.⁴ On distilling off the benzene, an oil was left which failed to crystallize and had the odor of ethyl benzoate. When this oil was evaporated to dryness with dilute hydrochloric acid, rhodanine was obtained (m. p. 166°). Its identity was proved by analysis and comparison with a synthetic specimen.

Summary

This paper describes the syntheses of several substituted aryl thiocyanates and their behavior with thioacetic and thiobenzoic acids. The final products in all cases were 2-thio-4-arylthiazolines, but with thiobenzoic acid the more stable intermediates, benzoyl-phenacyl-dithiocarbamates, were isolated.

(4) Wheeler, *Am. Chem. J.*, **26**, 351 (1911), described the intermediate, the benzoyl-dithiourethan; but did not hydrolyze it. Rhodanine was also obtained by Miolati [*Ann.*, **262**, 62–85 (1891)] from chloroethyl acetate and ammonium dithiocarbamate.

LAWRENCE, KANSAS

RECEIVED MAY 15, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE, AND FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

2,4,6-Trimethyl- β -phenyl- and Benzyl-D-glucosides¹

BY NELSON K. RICHTMYER

In a previous study on the cleavage of glycosides by catalytic hydrogenation,² mention was made of a trimethyl- β -phenylglucoside and a trimethyl- β -benzylglucoside in which the methyl groups were located presumably in the 2,4,6-positions of the glucose chain. The appearance of four recent papers dealing with 2,4,6-trimethylglucose and its derivatives makes a description of the two named glucosides seem desirable at this time.

2,4,6-Trimethyl-D-glucose was obtained first by Haworth and Sedgwick³ through the hydrolysis of partially methylated glucose and sucrose. The allocation of methoxyl groups was confirmed later by Oldham⁴ through a synthesis, the details of which have just been published. Recently, Lake and Peat⁵ isolated 2,4,6-trimethylglucose by acid hydrolysis of the corresponding β -

methylglucoside which is one of the products resulting from the action of boiling sodium methylate on 4,6-dimethyl-2,3-anhydro- β -methyl-D-mannoside. Barker, Hirst and Jones⁶ have separated it from the products arising from incomplete methylation of α -methylglucoside with methyl iodide and thallous hydroxide. Freudenberg and Plankenhorn⁷ synthesized it by methylation of 3-benzylglucose, followed by reductive cleavage of the benzyl group and acid hydrolysis of the glycosidic methoxyl group. It is of interest to note also that, from the cell wall of yeast, Zechmeister and Tóth⁸ have isolated a glucose polysaccharide, which, after methylation and hydrolysis, furnished this same 2,4,6-trimethylglucose.

Tetraacetyl- β -phenylglucoside is readily accessible through the condensation of phenol with glucosyl pentaacetate, in the presence of *p*-toluenesulfonic acid as catalyst according to Helferich and Schmitz-Hillebrecht.⁹ The incomplete

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Richtmyer, *THIS JOURNAL*, **56**, 1637 (1934).

(3) Haworth and Sedgwick, *J. Chem. Soc.*, 2573 (1926).

(4) Oldham, *THIS JOURNAL*, **56**, 1360 (1934); Oldham and Oldham, *ibid.*, **61**, 1112 (1939).

(5) Lake and Peat, *J. Chem. Soc.*, 1417 (1938).

(6) Barker, Hirst and Jones, *ibid.*, 1695 (1938).

(7) Freudenberg and Plankenhorn, *Ann.*, **536**, 256 (1938).

(8) Zechmeister and Tóth, *Biochem. Z.*, **270**, 309 (1934).

(9) Helferich and Schmitz-Hillebrecht, *Ber.*, **66**, 380 (1933).

methylation of β -phenylglucoside or its tetraacetate with methyl sulfate and alkali, as described below, yields crystalline 2,4,6-trimethyl- β -phenyl-D-glucoside as the product most readily separated from the mixture¹⁰; this series of reactions, followed by acid hydrolysis of the glucoside, offers a suitable method for the preparation of crystalline 2,4,6-trimethyl-D-glucose.

Crystalline 2,4,6-trimethyl- β -benzyl-D-glucoside has been obtained similarly from the incomplete methylation of β -benzylglucoside.

Experimental

2,4,6-Trimethyl- β -phenyl-D-glucoside.—To a solution of 100 g. of β -phenyl-D-glucoside dihydrate in 200 cc. of water (or an equivalent amount of tetraacetyl- β -phenyl-D-glucoside suspended in sufficient 50% aqueous sodium hydroxide to deacetylate it) was added 180 cc. of 50% aqueous sodium hydroxide and 100 cc. of methyl sulfate. The mixture was stirred mechanically, heated to 95° in a water-bath, cooled, and the process repeated until a total of 2160 cc. of alkali and 1200 cc. of methyl sulfate had been added. The methylated phenylglucoside, which crystallized in needles or small pellets when the reaction mixture was cooled, was extracted completely with ether, and the ethereal solution washed with water, dried with granular calcium chloride and concentrated. From the sirup, by fractional crystallization with ether and petroleum ether (b. p. 26–30°), was isolated 14.5 g. of 2,4,6-trimethyl- β -phenyl-D-glucoside in glistening, prismatic needles, melting at 108–109°, and with $[\alpha]_D -57.5^\circ$ in chloroform (*c*, 2).

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 60.37; H, 7.44; OCH_3 , 31.21. Found: C, 60.38; H, 7.58; OCH_3 , 30.95.

A second product having the composition also of a trimethyl- β -phenyl-D-glucoside was isolated in small amounts. It melted at 105–106°; a mixture with the 2,4,6-isomer melted at 80–95°.

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 60.37; H, 7.44; OCH_3 , 31.21. Found: C, 60.31; H, 7.33; OCH_3 , 31.21.

Hydrolysis to 2,4,6-Trimethyl-D-glucose.—A solution of 3 g. of the 108–109° trimethylphenylglucoside in 200 cc. of 5% aqueous hydrochloric acid was boiled four hours under a reflux condenser. The solution was neutralized with solid barium carbonate, concentrated *in vacuo* to a small volume, and extracted with ether in a Soxhlet apparatus arranged for the continuous extraction of liquids. The ethereal solution deposited prismatic needles of 2,4,6-trimethyl-D-glucose which was identified by direct com-

parison with a specimen supplied through the courtesy of Dr. J. W. H. Oldham.⁴ The two specimens, alone or mixed, melted at 122–123° when heated rapidly, and at 113–122° when heated slowly in soft glass melting point tubes. A mixture of the new 2,4,6-isomer with an authentic sample of 2,3,6-trimethylglucose melted at 87–105°. The rotation, $[\alpha]^{20}_D +111^\circ$ in methyl alcohol (*c*, 1), changed in six days at 20° to $[\alpha]^{20}_D +71^\circ$ (constant) upon the addition of a drop of concentrated hydrochloric acid; these values are in agreement with the earlier data, and distinguish clearly between the 2,4,6- and the 2,3,6-trimethylglucoses.⁷

Anal. Calcd. for $C_9H_{18}O_6$: C, 48.62; H, 8.17; OCH_3 , 41.90. Found: C, 48.58; H, 7.96; OCH_3 , 41.93.

2,4,6-Trimethyl- β -benzyl-D-glucoside.—To a solution of 32 g. of β -benzyl-D-glucoside in 100 cc. of water was added 44 cc. of methyl sulfate and 80 cc. of 50% aqueous sodium hydroxide; the mixture was stirred mechanically, heated to 70° with a water-bath, cooled, and the process repeated with nine more portions of methyl sulfate and alkali. After the final addition, the water was kept at 100° for one hour to decompose any excess methyl sulfate. The product was extracted with chloroform, concentrated, and methylated again with the same quantities of reagents. The methylated benzylglucoside was extracted with chloroform, and the chloroform solution washed with water, dried over calcium chloride, and concentrated *in vacuo*. With the aid of ether and petroleum ether (b. p. 26–30°) there was obtained 4.6 g. of 2,4,6-trimethyl- β -benzyl-D-glucoside; a thrice recrystallized sample melted at 94–95°, and showed $[\alpha]^{20}_D -49.1^\circ$ in chloroform (*c*, 2).

Anal. Calcd. for $C_{16}H_{24}O_6$: C, 61.50; H, 7.75; OCH_3 , 29.81. Found: C, 61.54; H, 8.15; OCH_3 , 29.50.

Hydrolysis to 2,4,6-Trimethyl-D-glucose.—A 1.5-g. sample of the trimethylbenzylglucoside was heated with 5% aqueous hydrochloric acid, and the product isolated and identified as described above.

This work has been aided by a grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences. The author desires to thank the Chemical Foundation of New York for a Research Associateship which he held while completing a portion of the research.

Summary

2,4,6-Trimethyl- β -phenyl-D-glucoside has been obtained through incomplete methylation of β -phenyl-D-glucoside. The method is recommended for the preparation of 2,4,6-trimethyl-D-glucose.

2,4,6-Trimethyl- β -benzyl-D-glucoside has been described.

WASHINGTON, D. C.

RECEIVED MAY 8, 1939

(10) Work on the separation of the other components has been discontinued; tetramethyl- β -phenyl-D-glucoside is described by Voss and Wachs, *Ann.*, **522**, 252 (1936).