

centrated hydrochloric acid. Because of their amino substituent, these hydantoin possess solubility in acid as well as the usual solubility in alkali.

The hydantoin were recrystallized readily from dilute alcohol, and are soluble in the ordinary organic solvents, and are insoluble in water. The compounds are stable, white, crystalline solids which melt without decomposition to clear straw-colored liquids. Analytical data and cor-

rected melting points for the hydantoin are reported in Table I.

### Summary

1. Ten examples have been prepared of a new type of disubstituted aminohydantoin in which the two substituents are not alike.

AUSTIN, TEXAS

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[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

## The Preparation and Properties of 6-Halogenated Carvacrylamines from *p*-Cymene

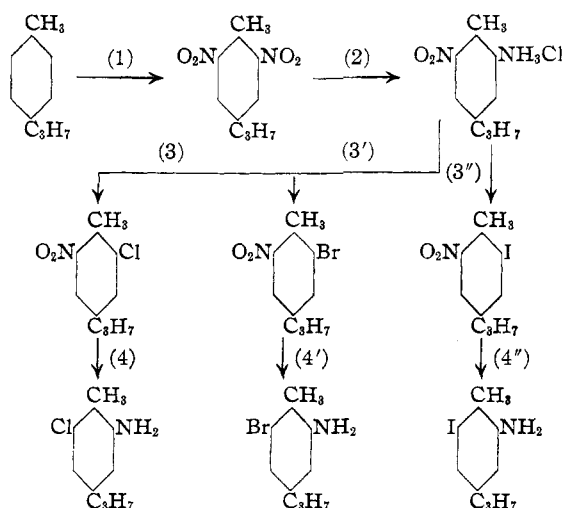
BY R. W. BOST AND GRANVIL C. KYKER<sup>1</sup>

The preparation of 6-halogenated carvacrylamines by a method which locates the position of the halogen has not been reported. Wheeler and Early<sup>2</sup> and Inoue and Horiguchi<sup>3</sup> independently obtained a product by the direct chlorination of 2-nitro-*p*-cymene from which a chloronitro-*p*-cymene was separated. In each case the substance was taken to be 2-chloro-6-nitro-*p*-cymene and the subsequent reduction product to be 6-chloro-carvacrylamine. The chlorination is accompanied by low yields and a mixture of difficultly separable products since positions 3, 5 and 6 are open to substitution and other chlorination products were recognized.<sup>2</sup> The method of these investigators<sup>2,3</sup> is not applicable to the preparation of analogous bromine and iodine compounds. A method for preparing 6-halogenated carvacrylamines from *p*-cymene which is equally applicable to chloro, bromo, and iodo-carvacrylamines has been investigated. The steps in the process are shown in the diagram.

Steps (1) and (2) have been reported in a previous paper.<sup>4</sup>

Since the position of the substituents in 2,6-dinitro-*p*-cymene and 6-nitrocarvacrylamine have been established<sup>5</sup> an orientation of the substituent groups in 6-halogenated carvacrylamines is obtained.

Diazotized 6-nitrocarvacrylamine gave 2-chloro-6-nitro-*p*-cymene when treated with cup-



rous chloride according to the procedure of Marvel and McElvain.<sup>6</sup> An azo dye, 2-nitro-5(?)-(6-nitrocarvacrylazo)-6-hydroxy-*p*-cymene was isolated from the reaction product; its occurrence is explained by the formation of 6-nitrocarvacrol, through a side reaction, which served as a coupler with the diazo compound. The reduction of 2-chloro-6-nitro-*p*-cymene with either tin or a mixture of tin and zinc in hydrochloric acid yielded 6-chlorocarvacrylamine.

Various derivatives of 6-chlorocarvacrylamine were studied. The amine produced crystalline salts with hydrochloric, hydrobromic, nitric, sulfuric, phenylsulfonic, *p*-tolylsulfonic, dichloroacetic, trichloroacetic, oxalic, 3,5-dinitrobenzoic, 2,4,6-trinitrobenzoic and picric acids. These salts are soluble in alcohol, insoluble in water, easily hydrolyzed, and stable in the dry state. The amine has been characterized by its acetyl, benzoyl, 3,5-dinitrobenzoyl, benzenesulfonyl, *p*-tolyl-

(1) This paper is an abstract of part of the dissertation submitted by Granvil C. Kyker to the Graduate Faculty of the University of North Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy, in June, 1938.

(2) Wheeler and Early, unpublished thesis by Early, "The Chlorination of 2-Nitro-*p*-cymene," Department of Chemistry, University of North Carolina, 1933.

(3) Inoue and Horiguchi, *J. Soc. Chem. Ind., Japan*, **36**, Suppl. binding 189-190 (1933).

(4) Kyker and Bost, *THIS JOURNAL*, **61**, 2469 (1939).

(5) Wheeler and Harris, *ibid.*, **49**, 494 (1927).

(6) Marvel and McElvain, "Org. Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1932, Coll. Vol. I, p. 163.

TABLE I

	Wheeler and Early <sup>7</sup>	Inoue and Horiguchi <sup>8</sup>	This study
2-Chloro-6-nitro- <i>p</i> -cymene			
B. p., °C.	123–125 at 6–7 mm.	146–148 at 15 mm.	132–133 at 2 mm.
Density	1.1965 <sup>20</sup>	1.1592 <sup>20</sup>	1.1834 <sup>25</sup>
Refractive index	1.4934 <sup>26</sup>	1.53917 <sup>20</sup>	1.5397 <sup>25</sup>
6-Chlorocarvacrylamine			
B. p., °C.	130–132 at 7–8 mm.	156–157 at 15 mm.	134–136 at 1 mm.
Density	1.0968 <sup>20</sup>	1.0866 <sup>20</sup>	1.0977 <sup>20</sup>
Refractive index	1.5583	1.50930	1.5604 <sup>20</sup>
M. p., °C. HCl	200–205		225–226
<i>n</i> -Benzoyl-		134	139
Azo-2-naphthol-		162	202

sulfonyl, *p*-bromosulfonyl, *m*-nitrobenzenesulfonyl and picryl derivatives all of which are easily prepared and purified and possess very sharp melting points. The picryl derivative has a melting point almost identical to that of the picrate but the two are easily distinguished by crystal form, solubility, color, stability to water, and mixed melting point. A substituted urea was made by condensing the amine hydrochloride with potassium cyanate. 2,2'-Diazoamino-6,6'-dichloro-*p*-cymene resulted from coupling the amine with itself in half-saturated sodium acetate.

The diazotized 6-chlorocarvacrylamine gave an azo dye with 2-naphthol and disazo dyes with phenol, resorcinol, phloroglucinol, and 1,8-dihydroxy-3,6-naphthalene disulfonic acid. *m*-Phenylenediamine, 1-naphthylamine, 2-naphthylamine, naphthionic acid and 1-amino-8-hydroxy-4-naphthalenesulfonic acid coupled easily to give dyes but these dyes resisted every attempt toward purification and no analyses were obtained on these dyes. Each of the dyestuffs was applied to wool, silk, cotton, and rayon giving varying shades of red, yellow, and brown to the fibers. The vegetable fibers were previously mordanted with tannic acid. The colors are very brilliant on animal fibers and are fast to light, washing, alkali, and perspiration.

The data of previous studies<sup>2,3</sup> are compared to those of this investigation in Table I.

6-Bromocarvacrylamine hydrochloride and 6-iodocarvacrylamine hydrochloride were prepared in two steps from 6-nitrocarvacrylamine, the former by a process similar to that used for the chloro analog and the latter by the method of Griess.<sup>7</sup> The intermediate compounds, 2-bromo-6-nitro-*p*-cymene and 2-iodo-6-nitro-*p*-cymene and the free bases of these amines have not been isolated and characterized.

(7) Griess, *Ann.*, **137**, 76 (1866).

## Experimental Part

**2-Chloro-6-nitro-*p*-cymene.**—Precipitated cuprous chloride, prepared from 312 g. (1.25 moles) of hydrated copper sulfate, 87.5 g. (1.5 moles) of sodium chloride, 66.6 g. (0.64 mole) of sodium bisulfite, and 44 g. (1.1 moles) of sodium hydroxide, was washed several times by decantation and dissolved in 400 cc. of concd. hydrochloric acid in a stoppered flask. At 0°, 230.5 g. (1 mole) of 6-nitrocarvacrylamine hydrochloride was stirred for thirty minutes with 1200 cc. of water, 575 g. (6 moles) of concd. hydrochloric acid, and 74.5 g. (1.08 moles) of sodium nitrite. The excess nitrous acid was destroyed with urea. With vigorous stirring the cold diazo solution was added rapidly to the cuprous chloride solution which had been cooled previously to 0°. Stirring was continued for two hours at room temperature and for thirty minutes at 60°.

The oily layer was separated and distilled with superheated steam at 155–160°. About 10 liters of distillate was collected. The yellowish-red oil in the distillate was separated, stirred with an equal volume of concd. sulfuric acid at 0° for an hour, diluted and stirred with 1 kg. of cracked ice, separated, washed successively with water, dilute sodium hydroxide and water, taken up with ether and dried over anhydrous calcium chloride. After removal of the drier and ether the oil was distilled at reduced pressure. The fraction boiling at 132–133° at 2 mm. was collected. The distillate was a highly refractive, light yellow oil,  $n_D^{25}$  1.5397,  $d_4^{25}$  1.1834, soluble in ethanol, methanol, ether, acetone, carbon tetrachloride, benzene, petroleum ether and other organic solvents; yield 165.7 g.; 77.5%.

A more rapid isolation of the product was obtained by ether extraction in place of superheated steam distillation, followed by the same treatment as above but purification was easier when the steam distillation was used.

*Anal.* Calcd. for  $C_{10}H_{12}O_2NCl$ : Cl, 16.60. Found: Cl, 16.60, 16.49.

**2-Nitro-5(?)-(6-nitrocarvacrylazo)-6-hydroxy-*p*-cymene.**—A solid, insoluble in water and ether, was found in the isolation of 2-chloro-6-nitro-*p*-cymene as a residue in the steam distillation and as a flocculent precipitate at the interface in the ether extraction. It was purified by crystallization from acetone. The brilliant red, irregular platelets melted at 186–187°.

*Anal.* Calcd. for  $C_{20}H_{24}O_6N_4$ : N, 13.99. Found: 13.82, 13.84.

TABLE II

Procedure	Salt	Color	Crystal form	M. p., °C.	Analysis for acid, %	
					Calcd.	Found
A	Hydrobromide	White	Needles	231-232	30.60	30.61
A	Nitrate	White	Needles	153	25.56	25.49
A	Oxalate	White	Plates	155	19.69	19.75
A	Trichloroacetate	White	Blades	157	47.09	47.01
A	2,4,6-Trinitrobenzoate	Light yellow	Needles	161	58.33	58.54
B	3,5-Dinitrobenzoate	White	Needles	133-134	53.60	53.55
B	Picrate	Deep yellow	Needles	151	55.53	55.76
C	Acid sulfate	White	Needles	166	34.82	34.72
C	Phenylsulfonate	White	Needles	184	46.27	46.69
C	<i>p</i> -Tolylsulfonate	White	Needles	193-194	48.39	48.60
D	Dichloroacetate	White	Irreg. plates	92-93	41.24	41.25

**6-Chlorocarvacrylamine. (A) Hydrochloride.**—To a 3-liter flask, under reflux condenser and heated on a steam-bath containing 107 g. (0.5 mole) of 2-chloro-6-nitro-*p*-cymene, 50 cc. of ethanol and 178 g. of mossy tin, was added with frequent shaking 280 cc. of concd. hydrochloric acid during a period of two hours. Refluxing and shaking was continued for two hours after the addition of the acid. The cooled reaction product was treated with an excess of sodium hydroxide, a cold saturated solution containing about 450 g. The oil was extracted with five 300-cc. portions of ether. A troublesome emulsion accompanied the extraction. The combined extracts were dried over solid sodium hydroxide, decanted from the drier, and saturated with dry hydrogen chloride. The precipitated salt weighed 100 g., was decomposed by water, stable and only slightly soluble in hydrochloric acid, and gave glistening white needles when crystallized from alcohol and hydrochloric acid; yield 91%; softens at 210-220°; m. p. 225-226° with decomposition.

Less troublesome emulsions were encountered in the ether extraction when the reduction was obtained by using a mixture of tin (10%) and zinc (90%). After completion of the reduction, the hot solution was decanted from any undissolved material and cooled. The crystals which formed were filtered and the filtrate was concentrated and cooled as long as it yielded more crystals. The above procedure of making alkaline and isolating the amine was repeated.

*Anal.* Calcd. for  $C_{10}H_{13}NCl_2$ : HCl, 16.57. Found: HCl, 16.66, 16.68.

**(B) Free Base.**—The hydrochloride suspended in 500 cc. of water was made alkaline with dilute sodium hydroxide. The oil was extracted with ether (five 100-cc. portions), dried over solid sodium hydroxide, decanted, ether removed and distilled at 1 mm.; b. p. 134-136°. The colorless amine became red when exposed to light and air, was soluble in common organic solvents,  $n_D^{20}$  1.5604, and  $d_4^{20}$  1.0977.

*Anal.* Calcd. for  $C_{10}H_{14}NCl$ : Cl, 19.32. Found: Cl, 19.38, 19.48.

**Salts of 6-Chlorocarvacrylamine.**—The following procedures gave good yields of pure salts: (A) To a dry ether solution containing the required amount of acid was added 0.005 mole of the amine in ether solution. The precipitated salt was filtered and washed with ether. (B) The amine and acid, 0.005 mole of each, were dissolved in a small amount of alcohol and heated on a steam-

bath. Water was added until a slight turbidity was produced and the salt separated on cooling; it was recrystallized from alcohol and water. (C) The amine, 0.005 mole, was boiled with sufficient quantity of 5% solution of the acid to dissolve it. The hot charcoaled, filtered solution gave the salt in crystalline form when cooled. (D) The amine and acid, 0.005 mole of each, were dissolved in 10 cc. of benzene and heated to boiling on a steam-bath. The hot solution was diluted with 20 cc. of hot heptane and cooled in ice. The salt was washed in cold benzene and heptane mixture.

The data on the salts are found in Table II.

**N-Acyl Derivatives of 6-Chlorocarvacrylamine.**—To the amine, 0.005 mole, dissolved in pyridine, 0.006 mole, was added the acyl chloride, 0.006 mole. The mixture was stirred and placed on a steam-bath for ten to fifteen minutes. The reaction product was worked with cracked ice until it solidified. The solid was washed successively with water, dilute alkali, water, dilute acid and water and recrystallized from a suitable solvent. In each case a needle crystal resulted, white in color except in the presence of nitro groups where a straw color was observed. The data on the acyl derivatives are found in Table III.

TABLE III

Acyl derivative	Solvent	M. p., °C.	Cl Analyses, %	
			Calcd.	Found
N-Acetyl	Heptane-pet. ether	117-118	15.72	15.68
N-Benzoyl	Alc.-water (3:1)	139	12.33	12.40
N-3,5-Dinitrobenzoyl	Alc.-water (4:1)	197-198	9.39	9.40

**Sulfonyl Derivatives of 6-Chlorocarvacrylamine.**—The amine, 0.005 mole, dissolved in pyridine, 0.006 mole, was treated with the sulfonyl chloride, 0.006 mole, stirred and warmed on a steam-bath for ten to fifteen minutes. The solid was stirred with water and ice until it solidified, then filtered, washed, dissolved in 2% sodium hydroxide, stirred with charcoal, filtered, and acidified with hydrochloric acid. The filtered and washed precipitate was recrystallized in each case from alcohol and water mixture (2:1). The crystals were white in each case except in the presence of a nitro group where a yellow color was noted. The data on the sulfonyl derivatives are given in Table IV.

**6-Chlorocarvacrylpicrylamine.**—Picryl chloride, 0.75 g. (0.003 mole), and 1.10 g. (0.006 mole) of 6-chlorocarvacrylamine were mixed in a test-tube, heated at 100° for an hour and then for an hour at 145°. During the latter

TABLE IV

Sulfonyl derivative	Crystal form	M. p., °C.	Halogen analyses, % Calcd.	Found
N-Benzenesulfonyl	Platelets	117.5	10.96	11.07
N- <i>p</i> -Tolylsulfonyl	Needles	115.5	10.50	10.75
N- <i>p</i> -Bromobenzenesulfonyl	Needles	131.5	28.66 <sup>a</sup>	28.86 <sup>a</sup>
N- <i>m</i> -Nitrobenzenesulfonyl	Needles	129.5	9.62	9.63

<sup>a</sup> Chlorine and bromine.

period the reaction mixture solidified. The solid recrystallized from alcohol as reddish-orange spear-shaped crystals which melted at 150.5–151.5°.

*Anal.* Calcd. for  $C_{10}H_{10}O_6N_2Cl$ : Cl, 8.99. Found: Cl, 8.84.

**2-Ureido-6-chloro-*p*-cymene.**—In 5 cc. of water, 0.74 g. (0.004 mole) of 6-chlorocarvacrylamine was suspended and treated with 2.5 g. of potassium cyanate and 1.25 cc. of concd. hydrochloric acid. A pink flocculent precipitate soon appeared. The solution was left on a steam-bath for three hours after evaporation to dryness. The solid was washed several times with water. The product recrystallized from alcohol and water (3:2) and melted at 180–182° with decomposition; at 185–187° with decomposition if placed in a bath at 160° and heated.

*Anal.* Calcd. for  $C_{11}H_{13}ON_2Cl$ : Cl, 15.59. Found: Cl, 15.44.

**2,2'-Diazamino-6,6'-dichloro-*p*-cymene.**—Two grams of 6-chlorocarvacrylamine hydrochloride (0.009 mole) in 20 cc. of water at 0° was treated with 0.318 g. (0.0046 mole) of sodium nitrite. After twenty minutes of stirring, an equal volume of cold saturated solution of sodium acetate was added. The reaction product stood for an hour at 0°, then was filtered, dried, and recrystallized from petroleum ether; m. p. 110°.

*Anal.* Calcd. for  $C_{20}H_{22}N_4Cl_2$ : Cl, 18.75; N, 11.11. Found: Cl, 18.47; N, 11.16.

**Azo Dyes from 6-Chlorocarvacrylamine.**—Diazotization of 1.1 g. (0.005 mole) 6-chlorocarvacrylamine hydrochloride was carried out in the usual manner and the excess nitrous acid was destroyed with urea. The diazo solution was added to the solution of the coupler dissolved in a slight excess of sodium hydroxide and stirred for ten to fifteen minutes. The dye was precipitated by making acid and was recrystallized from a suitable solvent. An azo dye was obtained with 2-naphthol whereas the other couplers gave diazo dyes. Data on the dyes are given in Table V.

**6-Bromocarvacrylamine Hydrochloride.**—Cuprous bromide was prepared by dissolving 62.4 g. (0.25 mole) copper sulfate and 35.6 g. (0.30 mole) potassium bromide in 300 cc. of boiling water. To this solution was added slowly

with stirring 150 cc. of alkaline sodium sulfite prepared from 13.3 g. (0.128 mole) of sodium bisulfite and 8.8 g. (0.22 mole) of sodium hydroxide. The precipitated cuprous bromide was washed several times by decantation, dissolved in 100 cc. of 48% hydrobromic acid and 50 cc. of water, stoppered, and cooled to 0°.

According to the general method of diazotization, 38.8 g. (0.2 mole) of 6-nitrocarvacrylamine suspended in 600 cc. of water was treated with 68 cc. of 48% hydrobromic acid and 14.9 g. (0.216 mole) of sodium nitrite dissolved in 200 cc. of water. The diazo solution was rapidly poured into the cold cuprous bromide solution. A purplish-brown addition product separated. The mixture was stirred for two hours at room temperature and for thirty minutes at 50 to 60°.

The oil which separated was stirred with an equal volume of concd. sulfuric acid at 0° for an hour, diluted with an equal volume of cracked ice, separated, washed with water, dilute sodium hydroxide, and water, and dried over calcium chloride; 39 g. oil.

A portion of the crude 2-bromo-6-nitro-*p*-cymene, 12.8 g., was reduced with 18.4 g. of tin and 28 cc. of concd. hydrochloric acid. The reduction product was rendered strongly alkaline with sodium hydroxide and extracted with ether. The dried ether solution was saturated with dry hydrogen chloride. The precipitated salt gave 10 g. of white needles when recrystallized from alcohol and hydrochloric acid; m. p. 213–214° with decomposition; yield 57.5%.

*Anal.* Calcd. for  $C_{10}H_{10}NClBr$ : HCl, 13.79. Found: HCl, 13.77.

**6-Iodocarvacrylamine Hydrochloride.**—6-Nitrocarvacrylamine, 48.5 g. (0.25 mole) in 500 cc. of water at 0° was treated with 57 g. of concd. sulfuric acid and 18.6 g. (0.27 mole) of sodium nitrite in 100 cc. of water. The excess nitrous acid was destroyed with urea. To the diazo solution was added gradually with stirring 72.6 g. (0.44 mole) of potassium iodide in 150 cc. of solution at 0°. The mixture was stirred for an hour after reaching room temperature and then for an hour on a steam-bath. The oily layer was separated, stirred for an hour at 0° with an equal volume of cracked ice, washed with water, dilute alkali, and water, and dried over calcium chloride; 46.5 g. of oil.

Part of the crude 2-iodo-6-nitro-*p*-cymene, 14.8 g., was reduced with 18.4 g. of tin and 28 cc. of hydrochloric acid. The reaction product was made strongly alkaline with sodium hydroxide and extracted with ether. The dried ether solution was saturated with dry hydrogen chloride. The hydrochloride gave 11.5 g. of white needles when crystallized from alcohol and hydrochloric acid; m. p. 244–245° with decomposition; yield 46.5%.

TABLE V

Coupler	Solvent	Color	Crystal form	M. p., °C.	Cl Analyses, %	
					Calcd.	Found
2-Naphthol	Gl. AcOH	Red	Needles	202	10.47	10.37
Phenol	Gl. AcOH	Brown	Needles	192–193	14.68	14.54
Resorcinol	Dil. AcOH-acetone	Dark red	Powder	233	14.21	14.10
Phloroglucinol	Benzene	Red	Plates	278	13.77	13.89
$C_{10}H_7-1,8-(OH)_2-3,6-(SO_3H)_2$	Gl. AcOH-ether	Purplish-black	Powder	Above 300	N, 7.90	7.83

*Anal.* Calcd. for  $C_{10}H_{15}NClH$ : HCl, 11.71. Found: HCl, 11.59, 11.49.

### Summary

1. A direct method for the synthesis of 6-halogenated carvacrylamines from *p*-cymene in good yields has been accomplished.

2. 6-Chlorocarvacrylamine as previously described has been shown to be impure.

3. The position of substituents in 2-chloro-6-nitro-*p*-cymene, 6-chloro, 6-bromo, and 6-iodo-carvacrylamines has been located by synthesis.

4. 6-Chlorocarvacrylamine has been characterized by twelve salts, three acyl and four sulfonyl derivatives, a secondary picrylamine, a substituted urea, 2,2'-diazoamino-6,6'-dichloro-*p*-cymene, one azo and four diazo dyes.

5. The dyes gave varying shades of yellow, red and brown when applied to wool, silk, cotton, and rayon; they were fast to washing, light, alkali, and perspiration.

CHAPEL HILL, NORTH CAROLINA

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF WISCONSIN]

## Synthesis of Glycol Glucosides<sup>1</sup>

BY SULO KARJALA AND KARL PAUL LINK

During the last ten years the production and extensive use of the glycol solvents has created a need for comprehensive toxicological studies on these compounds. This Laboratory recently undertook the preparation of large quantities of diethylene glycol  $\beta$ -*D*-monoglucoside for pharmacological investigations.<sup>2</sup> The synthesis of glucosides of other members of the glycol solvent series was studied during the course of this work.

Prior to the time that the work reported in this communication was started, ethylene glycol  $\beta$ -*D*-monoglucoside prepared by Fischer and Fischer<sup>3</sup> was the only substance of this class that had been obtained in the crystalline state. Subsequently Vintilescu, Ionescu and Kizyk<sup>4</sup> reported the enzymatic synthesis of this glucoside by emulsin. Bourquelot, Bridel and Aubry<sup>5</sup> had previously reported the biochemical synthesis of sirupy propylene glycol glucoside by the same enzyme.

A short time after our work was started, Helferich and Hiltmann<sup>6</sup> reported the preparation of the monoglucosides of ethylene glycol monomethyl ether, trimethylene glycol, tetramethylene glycol and the *cis* and *trans* forms of cyclopentanediol, as well as the diglucosides of ethylene, trimethylene, pentamethylene and hexa-

methylene glycols. Some of the work reported by them already had been completed in this Laboratory, and reference is made in the experimental part to agreement in data obtained.

### Experimental

**$\beta$ -*D*-Acetobromoglucose.**—The following procedure gave a stable product in yields above those reported previously.<sup>7,8</sup>

To 60 g. of acetic anhydride in a 500-cc. round-bottomed flask, fitted with a rubber stopper bearing an inlet tube reaching to the bottom of the flask and with a calcium chloride tube outlet, was added 60 g. of glucose pentaacetate. The suspension was cooled in ice and dry hydrogen bromide was introduced through the inlet tube. After all the glucose acetate had gone into solution, the passage of hydrogen bromide was interrupted, and an additional 60-g. portion of the acetate was added. Passage of the gas was resumed until the second portion of acetate had gone into solution and the mixture was saturated. With the use of a conventional naphthalene generator,<sup>9</sup> about 350 g. of bromine is required. The reaction takes about five hours. After the solution had stood overnight at room temperature, it was evaporated to a sirup under reduced pressure. Crystallization occurred during the concentration or upon the addition of a small amount of anhydrous ether. The crystalline product was dried and recrystallized from anhydrous ether. The mother liquors were concentrated and worked up in the same way. The yield is 109 g. (86%); m. p. 88–89°. The product could be kept indefinitely in a desiccator over phosphorus pentoxide.

**Ethylene Glycol  $\beta$ -*D*-Monoglucoside Tetraacetate.**—To 40 g. of ethylene glycol were added 12 g. of acetobromoglucose and 14.4 g. of dry silver carbonate. The mixture

(1) Published with the permission of the Director of the Wisconsin Agricultural Experiment Station.

(2) The pharmacological studies are being made by Dr. E. M. K. Geiling, Department of Pharmacology, University of Chicago.

(3) Fischer and Fischer, *Ber.*, **43**, 2529 (1910).

(4) Vintilescu, Ionescu and Kizyk, *Bull. soc. chim., Romania*, **16**, 151 (1934); *Chem. Abst.*, **29**, 4390 (1935).

(5) Bourquelot, Bridel and Aubry, *Compt. rend.*, **160**, 214 (1915).

(6) Helferich and Hiltmann, *Ann.*, **531**, 160 (1937).

(7) Freudenberg, Noë and Knopf, *Ber.*, **60**, 238 (1927).

(8) Levene and Raymond, *J. Biol. Chem.*, **90**, 247 (1931).

(9) Houben-Weyl, "Die Methoden der organischen Chemie," 3rd ed., Vol. III, Leipzig, 1930, p. 1156.