

It seems that compounds such as phenyliodoarsine, triphenyldiarsyl, triphenylchlorodiarsyl and pentaphenyltriarsine are not produced by interaction of the above-mentioned arsines although the formation of these substances has been reported by other investigators.

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RESEARCHES ON NITROGENOUS GLYCOSIDES. I. THE UTILIZATION OF GLYCOSE ISOCYANATES FOR GLYCOSIDE SYNTHESSES

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So far as the writers are aware, only one sugar isocyanate derivative has been described in the chemical literature, namely, tetraacetyl-*d*-glycose-*l*-isocyanate, $C_{14}H_{19}O_9NCO$. This interesting compound was described by Emil Fischer in a paper entitled "Synthese neuer Glycoside," in 1914² but since this publication, apparently no attention has been paid to its chemistry. Fischer obtained this sugar derivative by the action of silver cyanate on tetraacetobromoglycose, but the chief product of this reaction was an amorphous substance having the same composition as the glycose isocyanate but whose constitution was not established by Fischer.³

We have now repeated Fischer's preliminary experiments in order to obtain his isocyanate derivative for new glycoside syntheses. We find that silver cyanate interacts with tetraacetylbromoglycose in xylene solution to give, besides resinous substances, three definite compounds which have been identified, namely, two modifications of the glycose isocyanate (A and B), melting at 120 and 92°, respectively, and the amorphous substance previously described by Fischer as a product of this reaction. We conclude that this amorphous material is without doubt impure *sym*-octaacetyl-*d*-diglycose urea, which is formed by the interaction of tetraacetylglycose isocyanate with water. It can be purified easily to give a beautiful crystalline substance melting at 160–161°. That this is octaacetyl-glycose urea is not only established by the results of our analyses, but also by its characteristic behavior toward aqueous ammonia. By treatment with this reagent it is transformed by hydrolysis smoothly into *sym*-*d*-diglycose urea. The

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² E. Fischer, *Ber.*, **47**, 1377 (1914).

³ Fischer also examined the behavior of silver isothiocyanate toward tetraacetylbromoglycose and observed the smooth formation of the corresponding glycose-isothiocyanate derivative, $C_{14}H_{19}O_9NCS$. Here also practically no attention has been paid to the chemistry of this mustard oil since Fischer's work in 1914. The results of a new research dealing with specific reactions of this interesting compound will be discussed in a future paper from this Laboratory by Miss Katherine Haring.

latter glycoside proved to be identical with the diglycose urea prepared recently by Helferich and Kosche⁴ by the action of aqueous ammonia on octabenzoyldiglycose urea.

Tetraacetyl-*d*-glycose-*l*-isocyanate is characterized by its behavior toward ammonia and alcohol. By the action of aqueous ammonia it is converted smoothly into the glycose urea previously described by Schoorl.⁵ The lower melting modification of the glycose isocyanate is unstable and rearranges on heating into Fischer's original glycose isocyanate, melting at 120°. The behavior toward alcohol is also characteristic of the isocyanate structure. We observed that *n*-amyl alcohol and ethylene chlorohydrin both interact smoothly at the boiling point of the respective alcohols, giving the corresponding urethans. A complete description of these various compounds and their preparation is given in the experimental part of this paper.

Tetraacetyl-*d*-glycose-*l*-isocyanate promises to be a fruitful starting point for the development of several new and important syntheses of biochemical interest. Our future program calls for coupling with various amino acids and peptide combinations leading to the formation of important glycosido-ureide constructions.⁶

Experimental Part

Tetraacetyl-*d*-glycose-*l*-isocyanate, C₁₄H₁₉O₉NCO (A).—To a solution of 33 g. of tetraacetobromoglycose in 120 cc. of xylene, dried over sodium, 12 g. of freshly prepared, dried and pulverized silver cyanate is added. The reaction flask is connected with a rubber stopper fitted with a calcium chloride tube and heated on the steam-bath with frequent shaking. The silver cyanate soon turns yellow due to the formation of silver bromide. After one-half and one hour, respectively, 6 g. of silver cyanate is added and the mixture is finally heated for one hour more. The liquid is then filtered by suction and the insoluble silver salts are once more extracted with 80 cc. of xylene. The united liquids are then poured into 200 cc. of petroleum ether (30–60°), whereby a slightly yellow resin is precipitated. The mother liquor is at once decanted from the resin, mixed with 100 cc. more petroleum ether and allowed to stand overnight. One thus obtains a crystalline product, which consists of two distinctly different forms of crystals, needles and blocks. The yield of crystalline material is about 16–17 g. The melting point fluctuates between 80 and 110°, according to the proportion of needles or blocks which is obtained. The crystalline material is filtered and washed with petroleum ether.

This reaction product is extracted several times with anhydrous ether, when the needle form dissolves. The fraction insoluble in ether is dissolved in anhydrous chloroform, and ether then finally added until a separation of crystals begins. Under these conditions the beautiful crystalline glycose isocyanate "A" is obtained which melts sharply at 120°.

Anal. Calcd. for C₁₃H₁₉O₁₀N: C, 48.24; H, 5.13; N, 3.75. Found: C, 48.37;

⁴ Helferich and Kosche, *Ber.*, **59**, 69 (1926).

⁵ Schoorl, *Rec. trav. chim.*, **22**, 63 (1903).

⁶ We have observed also that silver cyanide and tetraacetylbromoglycose interact to give a beautiful crystalline isonitrile. The study of this substance will receive our attention later.

H, 5.19; N, 3.72. *Optical Rotation.* 0.8345 g. subs. in 25 cc. of CHCl_3 ; $l = 2$ dm.; $\alpha = -0.55^\circ$; $[\alpha]_D^{18} = -8.3^\circ$.

These analytical results, and the fact that the product is readily dissolved in concentrated ammonia giving *d*-glycose-urea, are conclusive evidence that the compound is the tetraacetyl-*d*-glycose-*l*-isocyanate previously described by E. Fischer.²

Tetraacetyl-*d*-glycose-*l*-isocyanate, $\text{C}_{14}\text{H}_{19}\text{O}_9\text{NCO}$ (B).—The ether solution of the above-mentioned needles is diluted with petroleum ether until cloudy. After some time, needles separate which are filtered off, dissolved in anhydrous ether and reprecipitated with petroleum ether. After repeating this precipitation again, well-developed needle-like crystals were obtained melting at 92° .

Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{O}_{10}\text{N}$: C, 48.24; H, 5.13; N, 3.75. Found: C, 48.26; H, 5.24; N, 3.84.

In all its reactions this glycose isocyanate modification "B" behaves like Fischer's compound "A." It rearranges into Fischer's isocyanate "A" if it is heated at its melting point. After cooling the fused mass and then reheating in a capillary tube, it melted at 115 – 120° . If a solution of the glycose isocyanate "B" in ether is mixed with petroleum ether, at first needles of this isocyanate will separate, but these slowly undergo a transformation, on standing, into the characteristic blocks of the isocyanate "A." During each recrystallization of the isocyanate "B" some of the isomeric modification "A" is always formed, which leads the authors to the conclusion that the modification "B" has not yet been obtained entirely pure and free from Fischer's glycose isocyanate.

Experience has shown that the highest yield of the isomer "B" is obtained if one filters the original xylene solution from the silver salts directly into a large excess of petroleum ether. At first a colorless amorphous mass separates, which soon takes on a crystalline form. This usually melts between 80 – 90° and probably consists of about 80% of the lower melting isomer.

Sym.-Octaacetyl-*d*-diglycose Urea, $(\text{C}_{14}\text{H}_{19}\text{O}_9)\text{NHCONH}(\text{C}_{14}\text{H}_{19}\text{O}_9)$.—The amorphous precipitate first obtained during the preparation of the tetraacetylglycose isocyanate is dissolved in xylene and carefully reprecipitated with petroleum ether, when it deposits again in the amorphous form. This product is then dissolved in ethyl acetate and reprecipitated several times by addition of ether and finally recrystallized from hot alcohol. On cooling this alcohol solution, needles were finally obtained which melted at 164° . This octaacetyl-diglycose urea is easily soluble in ethyl acetate, benzene, warm alcohol, acetone, difficultly soluble in hot water and insoluble in ether and petroleum ether. Large quantities of this urea may also be obtained easily by digesting the crude tetraacetyl-*d*-glycose-*l*-isocyanate in aqueous acetone and then precipitating the urea with water.

Anal. Calcd. for $\text{C}_{28}\text{H}_{40}\text{O}_{18}\text{N}_2$: C, 48.04; H, 5.56. Found: C, 48.04; H, 5.72. *Optical Rotation.* 0.0615 g. subs. in 3.2 cc. of CHCl_3 ; $l = 1$ dm.; $\alpha = -0.07^\circ$; $[\alpha]_D^{26} = -3.7^\circ$.

Preparation of Sym.-*d*-diglycose Urea, $(\text{C}_8\text{H}_{11}\text{O}_5)\text{NHCONH}(\text{C}_8\text{H}_{11}\text{O}_5)$.—The octaacetyl-*d*-diglycose urea is suspended in ten times its weight of concentrated aqueous ammonia and the solution allowed to stand for three days. The urea finally dissolves completely. The solution is then concentrated in a vacuum, leaving behind an oily residue which easily dissolves in water. On adding alcohol to this aqueous solution the diglycose urea separates in a crystalline condition. It is purified by crystallization from dilute alcohol. When heated in a capillary tube this urea begins to turn brown at about 205° , and decomposes when heated above 230° .

Anal. Calcd. for $\text{C}_{16}\text{H}_{22}\text{O}_{10}\text{N}_2$: C, 40.61; H, 6.30. Found: C, 40.46; H, 6.16. *Optical Rotation.* 0.06633 g. subs. in 3.12 cc. of H_2O ; $l = 1$ dm.; $\alpha = 0.73^\circ$; $[\alpha]_D^{26} = -25.4^\circ$.

This urea agrees in all its properties with the *d*-diglycose urea already described by Helferich.⁴

Tetraacetyl-*d*-glycose-*n*-amyl Urethan, (C₄H₉O₉)NHCOOC₅H₁₁.—Tetraacetyl-*d*-glycose-*l*-isocyanate is dissolved in 20 cc. of *n*-amyl alcohol and the solution heated to boiling for thirty minutes. After concentration *in vacuo*, an oil is obtained which dissolves in ether completely with the exception of a small amount of octaacetyl-*d*-diglycose urea present as an impurity. Dilution of this ether solution with petroleum ether (30–60°) precipitates an oil which soon crystallizes when chilled to a low temperature. By repeated recrystallizations from a mixture of ether and petroleum ether or from dilute alcohol, the amyl urethan is obtained in the form of well-developed prismatic crystals melting at 88°. This urethan is easily soluble in ethyl acetate, alcohol, chloroform, and ether, and is insoluble in petroleum ether and water.

Anal. Calcd. for C₂₀H₃₁O₁₁N: C, 52.04; H, 6.77; N, 3.03. Found: C, 51.90; H, 6.70; N, 2.95. *Optical Rotation.* 0.0775 g. subs. in 3.2 cc. of ether; *l* = 1 dm.; $\alpha = -0.16$; $[\alpha]_D^{26} -6.61^\circ$.

Tetraacetyl-*d*-glycose-chlorethyl Urethan, (C₁₄H₁₉O₉)NHCOOCH₂CH₂Cl.—Tetraacetyl-diglycose-*l*-isocyanate and an excess of ethylene chlorohydrin are heated to boiling for ten minutes, and the solution concentrated *in vacuo*. An oil was obtained which dissolved immediately in cold ether. Dilution of this ether solution with petroleum ether led to the separation of needles which melted after repeated crystallizations at 110°. Recrystallization of this substance from dilute alcohol gave a product melting very sharply at 82–83° and containing liquid solvent of crystallization. After drying *in vacuo* at 80° the melting point was raised to 114°.

Anal. Calcd. for C₁₇H₂₄O₁₁NCl: C, 44.98; H, 5.33; Cl, 7.81. Found: C, 45.05; H, 5.36; Cl, 8.01. *Optical Rotation.* 0.0551 g. subs. in 3.2 cc. of ether; *l* = 1 dm.; $\alpha = -0.20^\circ$; $[\alpha]_D^{26} -11.6^\circ$.

Summary

1. Tetraacetyl bromoglycose interacts with silver cyanate in xylene solution to give three products, namely, two isomeric modifications of tetraacetyl-*d*-glycose-*l*-isocyanate melting at 92 and 120° and octaacetyl-*d*-diglycose urea.

2. The lower melting modification of the glycose isocyanate melting at 92° is rearranged by heating into the higher melting isomer (120°).

3. Tetraacetyl-*d*-glycose-*l*-isocyanate reacts with ammonia to form *d*-glycose urea and with *n*-amyl alcohol and ethylene chlorohydrin to form the corresponding urethans.

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