Heterocyclic Amino Sugar Derivatives. II. Preparation of D-Glucopyranosido[2,3:4′,5′]-2′-oxazolidinones[1]

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Received September 12, 1968

trans-Fused oxazolidinone derivatives of glucosamine (benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranoside-2,3-carbamates) could be obtained in three ways. A synthesis utilizing *N,N′*-carbonyldiimidazole gave the best results. The compounds prepared demonstrate the usefulness of *trans*-fused 2,3-carbamates as a novel protective group for amino sugars.

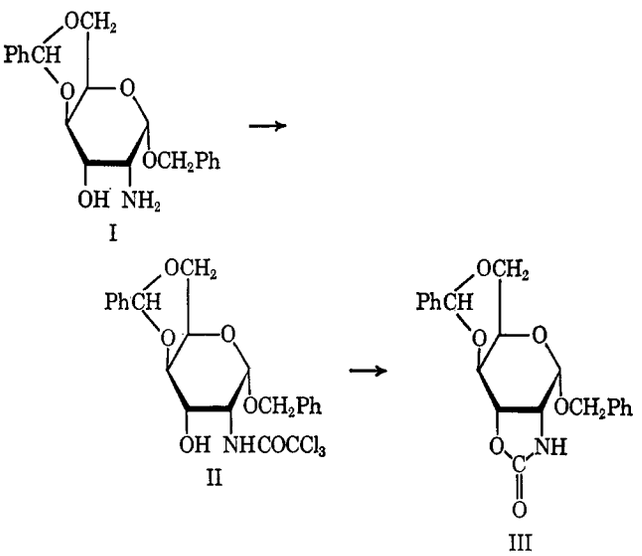
Many natural products contain amino sugars in biologically important 1,4-linked oligosaccharides. Synthesis of model substances having this type of linkage requires protection groups at C-2 and C-3 of 2-amino-2-deoxy-D-hexopyranoses that do not participate in and/or sterically hinder reactions at C-1 and C-4.

Heterocyclic derivatives, bridging C-2 and C-3 of 2-amino-2-deoxy-D-hexopyranoses, would be useful as blocking groups in the preparation of such oligosaccharides. Specifically, 2-oxazolidinone compounds of D-gulosamine and D-glucosamine were of interest. In the preceding paper,[2] new methods for the preparation of a cyclic carbamate (oxazolidinone) of D-allosamine were investigated. One method utilized hexachloroacetone for the generation of this protective group.

We demonstrated the general usefulness of this reaction for the synthesis of *cis*-fused cyclic carbamates when benzyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-α-D-gulopyranoside (II) and subsequently benzyl 4,6-*O*-benzylidene-α-D-gulopyranosido-[2,3:4′,5′]-2′-oxazolidinone (III) were prepared with hexachloroacetone from benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-gulopyranoside (I) (Scheme I). However, the two most frequently occuring amino sugars, 2-amino-2-deoxy-D-glucose and 2-amino-2-deoxy-D-galactose, have the amino group and the hydroxyl group of C-3 in a *trans* configuration. In these amino sugars, the *C1* conformation of the pyranose ring has a 2,3-*trans*-diequatorial arrangement and, if a five-membered ring should be fused to positions C-2 and C-3 of the pyranose ring, is a steric requirement. The 2,3-*trans*-diequatorial arrangement in D-glucosamine can be maintained by forming the 4,6-*O*-benzylidene derivative.

Stable heterocyclic rings fused *trans*-diequatorial to C-2 and C-3 of the 2-amino sugars have been unknown until 1963 when Carroll[3] obtained muramolactams in attempts to acetylate muramic acid. In these lactams the six-membered heterocyclic derivative, morpholinone, is fused *trans* diequatorial to C-2 and C-3 of the 2-amino-2-deoxy-D-glucopyranose ring. Gross and Jeanloz[4] synthesized stereospecifically such morpholinones from the anomeric benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranosides. There is no example in which a five-membered ring is fused *trans* diequatorial

SCHEME I



to an amino sugar. However, considering work on nitrogen-free sugars, such compounds should be possible.

In 1961 and 1962, Angyal and coworkers[5,6] have reported the preparation of *trans*-ketal derivatives of cyclitols. These preparations have demonstrated that five-membered rings can be fused to *trans*-diequatorial positions of carbohydrates. Similar work was reported by Bissett and coworkers[7] in 1967. Later, Evans, Parrish, and Long[8] have reported successful preparation of *trans*-ketal compounds of methyl D-glucopyranoside and methyl D-galactopyranoside. Very recently, cyclic thiocarbonate and carbonate fused *trans* diequatorially to C-2 and C-3 of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside were reported by Stout, Doane, Shasha, Russell, and Rist.[9,10] Their synthetic method was improved by application of the method of Bokadia, *et al.*,[11] who had prepared carbonates of a flavan *trans*-3,4-diol The similar compound with galactose configuration was reported by Sibral and Schmid.[12] Brimacombe and coworkers[13] in 1967 and Marvel and

(1) A preliminary communication was presented at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., March 1968, by K. Miyai and P. H. Gross, Abstracts C-017. Taken from the doctoral thesis of K. Miyai, University of the Pacific, 1968. This work was partially supported by Grant No. GP-4587 of the U. S. National Science Foundation.

(2) K. Miyai, H. K. Zimmerman, and P. H. Gross, *J. Org. Chem.*, **34**, 1635 (1969).

(3) P. M. Carroll, *Nature*, **197**, 694 (1963).

(4) P. H. Gross and R. W. Jeanloz, Abstracts of Papers, Winter Meeting of the American Chemical Society, 1966, C-033.

(5) S. J. Angyal, M. E. Tate, and S. D. Gero, *J. Chem. Soc.*, 4116 (1961).

(6) S. J. Angyal and R. M. Hoskinson, *ibid.*, 2985 (1962).

(7) F. H. Bissett, M. E. Evans, and F. W. Parrish, *Carbohyd. Res.*, **5**, 184 (1967).

(8) M. E. Evans, F. W. Parrish, and L. Long, *ibid.*, **3**, 453 (1967).

(9) E. I. Stout, W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *ibid.*, **3**, 354 (1967).

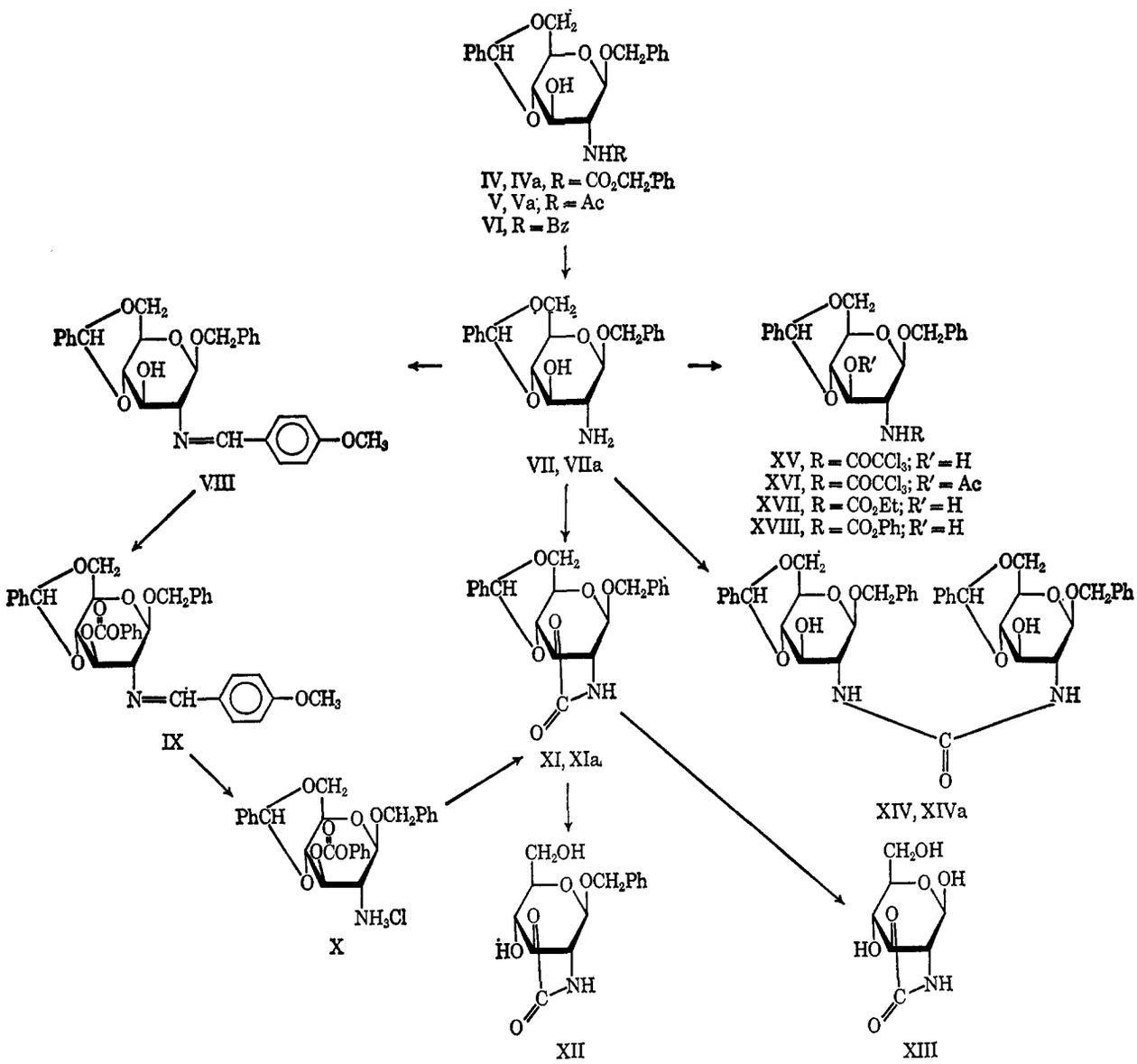
(10) W. M. Doane, B. S. Shasha, E. I. Stout, C. R. Russell, and C. E. Rist, *ibid.*, **4**, 445 (1967).

(11) M. M. Bokadia, B. R. Brown, P. L. Kokker, C. W. Love, J. Newbould, G. A. Somerfield, and P. M. Wood, *J. Chem. Soc.*, 4663 (1961).

(12) W. Sibral and L. Schmid, *Tetrahedron Lett.*, No. 43, 4239 (1967).

(13) J. S. Brimacombe, A. B. Foster, B. D. Jones, and J. J. Willard, *J. Chem. Soc.*, 2404 (1967).

SCHEME II[a]



[a] All reactions were carried out with β-glycosides. Where noted (*e.g.*, IVa) the corresponding α anomers were also prepared.

coworkers[14] in 1968 reported different cyclic acetals of methyl 4,6-*O*-benzylidene-D-glucopyranoside and the corresponding D-galactopyranoside. The ease of the ring-opening reaction of the *trans*-carbonate was utilized by Doane, Shasha, Stout, Russell, and Rist[15,16] to incorporate glucose units into starch with a carbonate linkage. This last work cited is the only one that reports in detail the chemical properties of these *trans*-fused bicyclic carbohydrate derivatives. It seems, however, that none of them possesses value as a protection group since they are sensitive to the conditions needed to give the compounds that are unprotected at C-1, C-4, and C-6.

In order to synthesize cyclic carbamates (oxazolidindones) fused *trans* diequatorial to glucosamine, benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranosides, VIIa and VII, seemed to be a suitable starting material (Scheme II). Both anomers were first prepared by Gross and Jeanloz.[17] We reinvestigated the synthesis of these compounds by alkaline hydrolysis of *N*-benzoyl, *N*-acetyl, and *N*-benzyloxycarbonyl compounds. Hydrolysis was fastest with *N*-benzyloxycarbonyl compounds IVa and IV and slowest with the *N*-benzoyl compound VI. Orientation of the aglycon seems to play no role in the hydrolysis of *N*-acyl compounds. It was found, however, that *N*-acyl-D-glucosamine derivatives hydrolyze faster than their corresponding D-allosamine derivatives.[2] Stability of the benzyl glycosides under severe alkaline conditions of hydrolysis seems to be a general feature.

Starting from an amino alcohol, it has been shown that phosgene, diphenylcarbonate, hexachloroacetone, and *N*,*N*′-carbonyldiimidazole are suitable reagents to prepare 2,3-*cis*-oxazolidinones.[2] The methods suitable for the preparation of model 2,3-*cis*-oxazolidinones were applied in the preparation of *trans*-oxazolidinones. The

(14) J. T. Marvel, S. K. Sen, F. T. Uenaka, J. W. Berry, and J. Deutschman, *Carbohyd. Res.*, **6**, 18 (1968).

(15) W. M. Doane, E. I. Stout, B. S. Shasha, C. R. Russell, and C. E. Rist, *ibid.*, **5**, 366 (1967).

(16) W. M. Doane, B. S. Shasha, E. I. Stout, C. R. Russell, and C. E. Rist, Abstracts of Papers, 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968, C-064.

(17) P. H. Gross and R. W. Jeanloz, *J. Org. Chem.*, **32**, 2759 (1967).

use of hexachloroacetone which was so successful in the preparation of *cis*-oxazolidinone gave benzyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (XV) as anticipated. This compound, however, failed to cyclize to give a *trans*-fused bicyclic compound. Reactions of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII) with diethyl carbonate or diphenyl carbonate gave the *N*-carbethoxy compound, XVII, and the *N*-carbophenoxy compound, XVIII, respectively. XVII and XVIII also failed to cyclize to give the *trans*-oxazolidinone compound.

Reaction of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII) with phosgene gave a *trans*-fused bicyclic compound. The product obtained was difficult to purify but it confirmed that 2-oxazolidinones of anomeric benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranosides could be prepared. The reaction conditions were improved by the use of triethylamine with the result of better yields, but the difficulties in purification persisted. At present, the only way to work-up these products is the application of preparative thin layer chromatography or column chromatography. This purification problem was overcome when *N,N'*-carbonyldiimidazole was used as a reagent to prepare 2,3-*trans*-oxazolidinones. Formation of a urea, XIV, bridging two glucosamine units was observed as a side reaction. The urea, because of its low solubility, is separated easily from the desired product. Both the α and β anomer of benzyl 4,6-*O*-benzylidene-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XI) were obtained in good yield.

The structure of the 2,3-*trans*-oxazolidone is supported by the infrared spectrum, by elemental analysis, and by the easy alkaline hydrolytic regeneration of the starting material, VIIa and VII.

As an alternative synthetic approach, the preparation of the same 2,3-*trans*-oxazolidinone (XI) by cyclization from a C-3 substituent to a free amine group at C-2 has been carried out. Although benzyl 4,6-*O*-benzylidene-2-deoxy-2-(phenyloxycarbonyl)amino-β-D-glucopyranoside (XVIII) failed to cyclize to yield a *trans*-fused bicyclic compound, we have anticipated that benzyl 2-amino-4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-β-D-glucopyranoside (free base of X) would. Therefore, benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII) was treated with anisaldehyde to give the *N*-(*p*-methoxybenzylidene) compound VIII.[17] The *O* carbophenoxylation of VIII in absolute pyridine gave a 93% yield of benzyl 4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-2-[(*p*-methoxybenzyliden)imino]-β-D-glucopyranoside (IX). When IX was treated with hydrochloric acid (0.25 *N*) in acetone, benzyl 2-amino-4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-β-D-glucopyranoside hydrochloride (X) was obtained quantitatively in very pure form. Cyclization of X yielded benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XI) which was identical with the sample prepared from benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII) with phosgene or *N,N'*-carbonyldiimidazole.

It has been shown that the 2,3-*cis*-oxazolidinone derived from D-gulosamine is very stable toward acid.[18] Rhoads and Gross[19] have shown that the 2,3-*cis*-oxazolidinone derived from D-allosamine is stable under the conditions needed to remove a benzylidene group. However, this could not be said *a priori* for the oxazolidone with the D-*gluco* configuration. It was found, fortunately, that it is at least stable enough to withstand the conditions needed to remove the benzylidene group. Treatment of benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XI) with aqueous acetic acid at 70° for 70 min removed the benzylidene group but did not affect the oxazolidinone group. Thus, benzyl β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XII) was obtained in fair yield.

Hydrogenation of benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido[2,3:4′5′]-2′-oxazolidinone (XI) gave a compound which showed a characteristic carbonyl absorption band at 1750 cm^{-1} and a positive Benedict test. This compound is believed to be β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XIII) but needs to be characterized further. The test, however, showed that hydrogenation did not affect the oxazolidone blocking group.

Experimental Section

Melting points were taken in a Thomas–Hoover melting point apparatus, Model No. 6404H. All the melting points reported herein are uncorrected. Optical rotations were measured at the sodium D line with a O. C. Rudolph and Sons, Inc., Model No. 956 polarimeter. Infrared spectra were recorded with Perkin-Elmer spectrophotographs (Models 137 and 337) using the KBr pellet technique. The homogeneity of the compounds synthesized was determined by thin layer chromatography using silica gel G (Merck) and silica gel GF (Merck). The plates were developed with chloroform containing a sufficient portion of ethanol or *n*-hexane to produce R_f values between 0.2 and 0.7. The compounds were detected with ultraviolet light and also by subsequent spraying with 10–15% sulfuric acid–methanol and heating about 15 min at 120°. All the compounds reported herein are chromatographically homogeneous. The microanalyses were performed by Alfred Bernhardt of Mikroanalytisches Laboratorium im Max-Planck-Institut für Kohlenforschung, Mülheim (Ruhr), West Germany.

Benzyl 4,6-*O*-Benzylidene-2-deoxy-2-trichloroacetamido-α-D-gulopyranoside (II).—Benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-gulopyranoside (I, 2 g, 0.0056 mol)[20] was refluxed with hexachloroacetone (10.3 g) and dimethylmesidine (3 ml) in absolute chloroform (200 ml) for 6 hr. Additional hexachloroacetone (3 ml) was added and refluxing was continued for 1 more hr. The solvent was evaporated *in vacuo* to a syrup, which was dissolved in hot ethanol. The product was precipitated by addition of petroleum ether (bp 30–60°). The mixture was kept at 0° to complete precipitation and the precipitate collected by filtration. Recrystallization from absolute ethanol gave 2.5 g (0.0049 mol, 99.3% yield) of II melting at 199–201°, $[\alpha]^{27}D$ +111.4° (*c* 1.15, pyridine).

Anal. Calcd for $C_{22}H_{22}NO_6Cl_3$ (502.8): C, 52.55; H, 4.41; N, 2.78; O, 19.10; Cl, 21.16. Found: C, 52.43; H, 4.84; N, 2.83; O, 19.13; Cl, 20.98.

Benzyl 4,6-*O*-Benzylidene-α-D-gulopyranosido[2,3:4′,5′]-2′-oxazolidinone (III). A.—Benzyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-α-D-gulopyranoside (II, 0.5 g, 0.001 mol) was heated in *N,N*-dimethylformamide (10 ml) with 1,5-diazabicyclo-[4.3.0]-5-nonene (0.25 g) for 15 hr at 110–115°. The product was precipitated by addition of excess ice–water. After several hours at 0° the precipitate was collected by filtration and recrystallized with decolorization by charcoal from absolute ethanol. This gave 0.36 g (0.00095 mol, 95% yield) of III melting at 216.5–217°, $[\alpha]^{25}D$ −9.2° (*c* 1.0, pyridine). Noorzad and Gross[20] reported melting point 210–211°, $[\alpha]^{30}D$ −9° (*c* 1, pyridine).

B.—Sodium phenoxide or sodium methoxide can also be used

(18) P. H. Gross, K. Brendel, and H. K. Zimmerman, *Ann.*, **680**, 159 (1964).

(19) W. D. Rhoads and P. H. Gross, Abstracts of Papers, 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968, C-019.

as the base catalyst in the cyclization reaction of benzyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-α-D-gulopyranoside.

Benzyl 2-Amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII).—Benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII) was prepared from benzyl 4,6-*O*-benzylidene-2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (IV), benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (V), and benzyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VI) in the manner described previously by Gross and Jeanloz.[17] The results were the following: reaction conditions—15 g of KOH (86.7% assay) and 0.01 mol of amino sugar in 50 ml of 95% ethanol; reaction temperature inside vessel—83–87°; reaction time required in hours (yield after recrystallization from methanol)—N-Cbz compound IV, 4.5–5.5 (80–85%), N-Ac compound V, 6–7 (80–85%), N-Bz compound VI, 19–31 (65–75%); mp 145–146°; $[\alpha]^{25}D$ −131° (*c* 1, pyridine).

Benzyl 2-Amino-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (VIIa).—Benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (VIIa)[17] was prepared by a procedure identical with that used for the preparation of the β anomer. Alkaline hydrolysis of benzyl 4,6-*O*-benzylidene-2-deoxy-2-benzyloxycarbonylamido-α-D-glucopyranoside (IVa) of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (Va) yielded VIIa: mp 173–174°; $[\alpha]^{25}D$ +90° (*c* 1.0, pyridine).

Benzyl 4,6-*O*-benzylidene-2-deoxy-2-[(*p*-methoxybenzylidene)imino]-β-D-glucopyranoside (VIII) was prepared in the manner described by Gross and Jeanloz:[17] mp 178–179°; $[\alpha]^{25}D$ −119° (*c* 1, pyridine).

Benzyl 4,6-*O*-Benzylidene-3-*O*-carbophenoxy-2-deoxy-2-[(*p*-methoxybenzyliden)imino]-β-D-glucopyranoside (IX).—Benzyl 4,6-*O*-benzylidene-2-deoxy-2-[(*p*-methoxybenzyliden)imino]-β-D-glucopyranoside (VIII, 2.375 g, 0.005 mol) in absolute pyridine (10 ml) was treated with phenyl chloroformate (1.2 g) at −5° for 24 hr. The mixture was then poured into ice–water and kept at 0° to complete precipitation. The product was collected by filtration, dried, and recrystallized from dichloromethane–diethyl ether–*n*-hexane to give 2.73 g (0.00465 mol, 93% yield) of IX melting at 153.5–154°, $[\alpha]^{25}D$ −119.2° (*c* 1.2, pyridine).

Anal. Calcd for $C_{35}H_{35}NO_8$ (595.6): C, 70.58; H, 5.58; N, 2.35; O, 21.50. Found: C, 69.80; H, 5.85; N, 2.73; O, 21.79.

Benzyl 2-Amino-4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-β-D-glucopyranoside Hydrochloride (X).—A solution of benzyl 4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-2-[(*p*-methoxybenzyliden)imino]-β-D-glucopyranoside (IX, 1.7 g, 0.003 mol) in acetone (60 ml) was cooled to 0° and 0.25 *N* hydrochloric acid (24 ml) was slowly added at 0°. After being kept with stirring for 3 hr at 0°, the product was collected by filtration, washed several times with acetone, and dried to give 1.435 g (0.0028 mol, 93% yield) of X melting at 250–250.5°. No suitable solvent was found for a measurement of optical rotation.

Anal. Calcd for $C_{27}H_{28}NO_7Cl$ (514): C, 63.09; H, 5.49; N, 2.73; O, 21.79; Cl, 6.90. Found: C, 63.33; H, 5.29; N, 2.55; O, 22.02; Cl, 6.91.

Benzyl 4,6-*O*-Benzylidene-β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XI). **A.**—A solution of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII, 3.57 g, 0.01 mol) in absolute tetrahydrofuran (150 ml) was added dropwise to a solution of *N,N′*-carbonyldiimidazole (3.24 g) in 150 ml of absolute tetrahydrofuran with stirring at room temperature (25–30°) for 24 hr. The mixture was filtered to remove the urea compound, XIV, which was insoluble in tetrahydrofuran. The filtrate was evaporated *in vacuo*. To the remaining residue, water was added and the mixture kept under refrigeration to complete precipitation. The product was collected by filtration, dried, and recrystallized from 2-propanol to give 3.33 g (0.0087 mol, 87% yield) of XI melting at 232–234°, $[\alpha]^{22}D$ −102.6° (*c* 1.67, pyridine).

Anal. Calcd for $C_{21}H_{21}NO_6$ (383.4): C, 65.78; H, 5.52; N, 3.66; O, 25.04. Found: C, 65.40; H, 5.74; N, 3.31; O, 25.44.

B.—To a solution of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII, 3.57 g, 0.01 mol), and triethylamine (1 g) in absolute pyridine (50 ml) was added dropwise a solution of phosgene (2.1 g) in dry toluene (20 ml) and the reaction mixture was stirred at room temperature for 12 hr. The mixture was then poured into ice–water–petroleum ether and kept under refrigeration to complete precipitation. The product was collected by filtration, washed with cold water, and dried to give 3.3 g (0.0087 mol, 87% yield) of crude product which was best purified by column chromatography on silica gel (Davison) with 2% ethanol in chloroform.

C.—Benzyl 2-amino-4,6-*O*-benzylidene-3-*O*-carbophenoxy-2-deoxy-β-D-glucopyranoside hydrochloride (X, 0.514 g, 0.001 mol) was heated in *N,N*-dimethylformamide (10 ml) with sodium phenoxide (0.30 g) for 10 hr at 95–100°. After neutralization with carbon dioxide, the product was precipitated by addition of excess ice–water. The mixture was kept at 0° for several hours to complete precipitation. The product was collected by filtration, dried, and recrystallized from tetrahydrofuran–petroleum ether and from 2-propanol to give 0.256 g (0.00067 mol, 67% yield) of XI.

Benzyl 4,6-*O*-benzylidene-α-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XIa) was prepared by procedure A identical with that used for the preparation of the β anomer XI: yield 67%; mp 214–215°; $[\alpha]^{22}D$ +59.3° (*c* 1.2, pyridine).

Anal. Calcd for $C_{21}H_{21}NO_6$ (383.4): C, 65.78; H, 5.52; N, 3.66; O, 25.04. Found: C, 65.44; H, 5.69; N, 2.97; O, 25.76.

Benzyl β-D-Glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XII).—Benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XI, 0.58 g, 0.0015 mol) was dissolved in glacial acetic acid (15 ml). The solution was heated to 70–71° and water (10 ml) was added dropwise over a period of 10 min. After the addition of water the reaction mixture was stirred for 60 min at 65–70°. The cooled solution was evaporated *in vacuo*, followed by repeated coevaporation with water and finally with toluene. Petroleum ether (bp 30–60°) was added to the remaining syrup and the mixture was kept at 0° to complete precipitation. The product was collected by filtration, dried, and recrystallized from diisopropyl ether–diethyl ether–petroleum ether–2-propanol to give 0.295 g (0.0010 mol, 68% yield) of XII melting at 159.5–160.5°, $[\alpha]^{29}D$ −38.8° (*c* 1.3, pyridine).

Anal. Calcd for $C_{14}H_{17}NO_6$ (295.3): C, 56.94; H, 5.80; N, 4.75; O, 32.51. Found: C, 57.32; H, 5.21; N, 4.29; O, 33.32.

Bis(benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosido)carbamide (XIV).—The precipitate (side-reaction product) of the preparation of benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidone (XI) with *N,N′*-carbonyldiimidazole was collected by filtration and dried. Recrystallization from dimethyl sulfoxide–tetrahydrofuran gave XIV melting at 291–293°, mol wt 740.8.

Bis(benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosido)carbamide (XIVa) was prepared by a procedure identical with that used for the preparation of the β anomer. Recrystallization from dimethyl sulfoxide–tetrahydrofuran–2-propanol gave XIVa melting at 304–305°, mol wt 740.8.

Benzyl 4,6-*O*-Benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (XV). **A.**—Benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VIIb, 2 g, 0.0056 mol) was refluxed with hexachloroacetone (12 g) and dimethylmesidine (2 ml) in absolute chloroform (225 ml). Precipitation of the initial hexachloroacetone adduct occurred after 10–15 min refluxing. Refluxing was continued for 7 hr and after addition of hexachloroacetone (7 ml) for 8 more hr. The solvent was removed by evaporation *in vacuo*. The remaining syrup was dissolved in ethanol which was then evaporated. The product was precipitated by addition of *n*-heptane and collected by filtration after several hours at 0°. Recrystallization from absolute ethanol gave 2.1 g (0.0041 mol, 75% yield) of XV melting at 215–216°, $[\alpha]^{27}D$ −55.1° (*c* 1.3, pyridine).

Anal. Calcd for $C_{22}H_{22}NO_6Cl_3$ (502.8): C, 52.55; H, 4.41; N, 2.78; O, 19.10; Cl, 21.16. Found: C, 52.54; H, 4.81; N, 2.78; O, 18.94; Cl, 20.95.

B.—This compound was also prepared by treating benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VIIb) with trichloroacetyl chloride in pyridine at −5°, yield 47%.

Benzyl 3-*O*-Acetyl-4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (XVI).—Benzyl 4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (XV, 1.5 g, 0.0029 mol) in absolute pyridine (15 ml) was acetylated with acetic anhydride (2 ml) by stirring at room temperature for 36 hr. The mixture was then poured into ice–water and kept at 0° to complete precipitation. The product was collected by filtration and recrystallized from absolute ethanol to give 1.3 g (0.0023 mol, 82.8% yield) of XVI melting at 236–236.5°, $[\alpha]^{27}D$ −72.8° (*c* 1.42, pyridine).

Anal. Calcd for $C_{24}H_{24}NO_7Cl_3$ (544.8): C, 52.91; H, 4.44;

(20) H. M. Noorzad and P. H. Gross, Abstracts of Papers, 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968, C-018.

N, 2.57; O, 20.56; Cl, 19.53. Found: C, 52.88; H, 4.51; N, 2.66; O, 20.57; Cl, 19.32.

Benzyl 4,6-*O*-Benzylidene-2-deoxy-2-(ethoxycarbonyl)amino-β-D-glucopyranoside (XVII).—Ethyl chloroformate (0.33 g) was added dropwise with stirring to a solution of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII, 1 g, 0.0027 mol) in 20 ml of absolute pyridine. The resulting mixture was stirred for 1 hr, kept overnight at 0°, and poured into ice–water. After 3 hr at 0° the precipitate was collected by filtration, washed with cold water, and recrystallized from absolute methanol to give 1.02 g (0.0026 mol, 96.2% yield) of XVII melting at 233–233.5°, $[\alpha]^{23}D$ −87° (*c* 1.26, pyridine).

Anal. Calcd for $C_{23}H_{27}NO_7$ (429.4): C, 64.33; H, 6.34; N, 3.27; O, 26.08. Found: C, 64.25; H, 6.57; N, 3.37; O, 26.33.

Benzyl 4,6-*O*-Benzylidene-2-deoxy-2-phenoxycarbonylamino-β-D-glucopyranoside (XVIII).—Benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (VII, 1.07 g, 0.003 mol) in absolute pyridine (40 ml) was cooled to −5°, and phenyl chloroformate (0.52 g) was added dropwise with exclusion of moisture. The mixture was stirred 1 day at −5°. Pyridine was then removed by evaporation *in vacuo* until the volume was 15 ml and the mixture was poured into ice–water. The precipitate was collected by filtration, washed with cold water, and dried. Two recrystallizations from dioxane–hexane and absolute methanol gave 1.2 g (0.0025 mol, 87.5% yield) of XVIII melting at 247–247.5°, $[\alpha]^{27}D$ −84.5° (*c* 1.28, pyridine).

Anal. Calcd for $C_{27}H_{27}NO_7$ (477.5): C, 67.91; H, 5.70; N, 2.93; O, 23.46. Found: C, 67.46; H, 5.77; N, 3.28; O, 23.54.

Treatment of Benzyl 4,6-*O*-Benzylidene-D-glucopyranosido-[2,3:4′,5′]-2′-oxazolidinones (XIa and XI) with Alcoholic Potassium Hydroxide. Regeneration of Starting Compounds VIIa and VII.—A solution of benzyl 4,6-*O*-benzylidene-D-glucopyranosido[2,3:4′,5′]-2′-oxazolidinone (XIa or XI, 0.5 g, 0.00133 mol) in a hot mixture of potassium hydroxide (1 g) and 95% ethanol (60 ml) was refluxed for 5 hr at 85°. The mixture was then diluted with hot water (150 ml), allowed to cool, and kept at 0° to complete precipitation. The product was collected by filtration, washed with cold water, and dried. Recrystallization from absolute methanol gave 0.499 g (0.00126 mol, 95% yield) of benzyl 2-amino-4,6-*O*-benzylidene-2-deoxy-D-glucopyranoside (VIIa or VII).

Catalytic Hydrogenation of *trans*-Oxazolidinone XI.—Palladium black (1 g) was suspended in ethyl acetate (125 ml) in a hydrogenation flask. Benzyl 4,6-*O*-benzylidene-β-D-glucopyranosido-[2,3:4′5′]-2′-oxazolidinone (XI, 0.8138 g, 0.0021 mol) was then introduced, followed by hydrogen at atmospheric pressure. The hydrogen uptake started immediately and the hydrogenation was stopped after 30 min. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo*. The remaining syrup was taken up in dioxane–acetone–petroleum ether and the mixture was kept at 0° for 2 weeks. Compound XIII, giving a characteristic carbonyl absorption at 1750 cm^{-1} and a positive test with Benedict reagent, was obtained.

Registry No.—II, 19358-93-1; III, 19358-94-2; IX, 19358-95-3; X, 19358-96-4; XI, 19358-97-5; XIa, 19358-98-6; XII, 19358-99-7; XIV, 19359-00-3; XIVa, 19359-01-4; XV, 19359-02-5; XVI, 19359-03-6; XVII, 19359-04-7; XVII, 13347-81-4.

Reactions of Chlorine with Some Thiocarbonyl Sugar Derivatives[1a]

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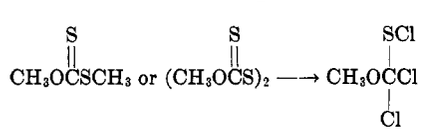
Received October 9, 1968

The reactions between chlorine and some thiocarbonyl sugar derivatives were investigated. In each reaction the major product(s) was (were) isolated and identified. Both bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (**1**) and bis[methyl 4,6-*O*-benzylidene-2- (and 3-) *O*-thiocarbonyl-α-D-glucopyranoside] disulfide (**3**) added four chlorine atoms (two chlorine atoms to each carbon–sulfur double bond) to yield corresponding chloromethylsulfenyl chloride derivatives **2** and **4**. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-(methylthio)thiocarbonyl-α-D-glucofuranose (**5**) reacted in a similar fashion to give **6**. On further reaction with chlorine, **6** lost the methylthio group and gave a dichloromethanesulfenyl chloride derivative (**7**). 1,2-*O*-Isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (**8**), methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-thionocarbonate (**10**), and 3-*O*-ethoxythiocarbonyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**12**) yielded the corresponding carbonates **9**, **11**, and **13**. Conversion of **8** → **9** in the presence of $H_2{}^{18}O$ established the origin of the carbonyl oxygen atom. A dithiocarbonate derivative (**17**) was obtained from 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose 5,6-trithiocarbonate (**16**). Two major reaction products from methyl 4,6-*O*-benzylidene-2- (and 3-) *O*-[(1-piperidyl)thiocarbonyl]-α-D-glucopyranoside (**14**) were identified as the corresponding carbonyl compound **15** and the cyclic carbonate **11**.

The formation of sulfenyl chlorides by reaction of chlorine with certain organic disulfides and dithio esters has been reported.[2] Douglas and Osborne[3] studied the action of anhydrous chlorine at low temperature on some simple thio esters. Such dithio esters as the methyl ester of methyl xanthate undergo chlorinolysis with removal of the methylthio group as methylsulfur trichloride and with formation of methoxydichloromethanesulfenyl chloride. This product is also formed during chlorinolysis of bis(methoxythiocarbonyl) disulfide. Although this reaction has been conducted with a number of organic sulfur derivatives,



no information is available on such a reaction with similar sulfur derivatives of carbohydrates. We have now extended our studies[4] on the preparation and reactions of thiocarbonyl derivatives of carbohydrates to the reaction of these derivatives with chlorine. We examined the behavior of carbohydrate bis(*O*-thiocarbonyl) disulfides, (alkylthio) dithiocarbonates, cyclic

(1) (a) Presented before the Division of Carbohydrate Chemistry, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968. (b) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

(2) I. B. Douglass in "Organic Sulfur Compounds," Vol. 1, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, pp 350–360.

(3) I. B. Douglass and C. E. Osborne, *J. Amer. Chem. Soc.*, **75**, 4582 (1953).

(4) W. M. Doane, B. S. Shasha, C. R. Russell, and C. E. Rist, *J. Org. Chem.*, **30**, 3071 (1965); **32**, 1080 (1967); references cited therein.