Synthetic Nucleosides. LVI.[1,2] Facile Displacement Reactions in the D-Mannitol Series. III. Transformation of Tetrahydropyranyl Derivatives

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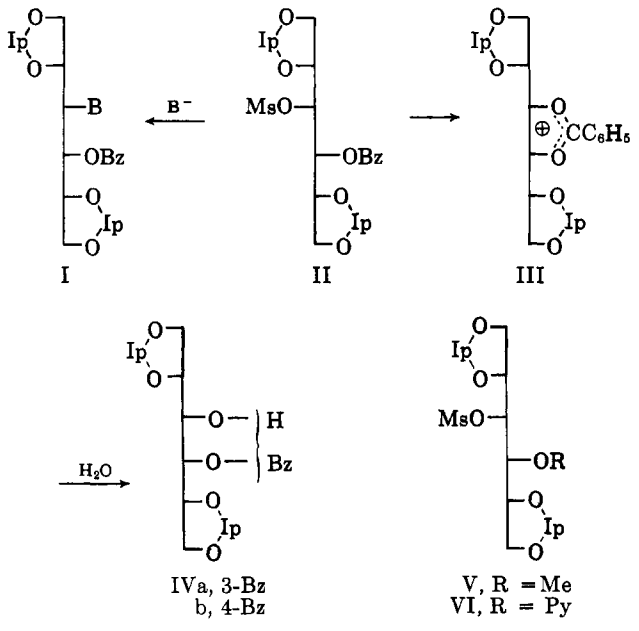
Acid-catalyzed reaction of 3-O-benzoyl-1,2:5,6-di-O-isopropylidene-D-mannitol (VII) with dihydropyran gave a 73% yield of the crystalline 4-O-(2-tetrahydropyranyl) derivative (VIII). Base-catalyzed methanolysis of VIII afforded a 73% yield of crystalline 1,2:5,6-di-O-isopropylidene-3-O-(2′-tetrahydropyranyl)-D-mannitol (XI). The latter could be oxidized with chromium trioxide–pyridine to the corresponding 3-*arabo*-hexulose (XI) in 40% yield or mesylated to the key intermediate, 1,2:5,6-di-O-isopropylidene-3-O-mesyl-4-O-(2-tetrahydropyranyl)-D-mannitol (VI), in 80% yield. The mesyloxy group of VI could be bimolecularly displaced with either acetate or azide ions which, by further transformations, gave 1,2:5,6-di-O-isopropylidene-D-talitol (XXII) and 3-benzamido-4-O-benzoyl-3-deoxy-1,2:5,6-di-O-isopropylidene-D-altritol (XVII), respectively. A key reaction to these transformations was the selective removal of the tetrahydropyranyl group by acid-catalyzed methanolysis with retention of the isopropylidene blocking groups.

Previous papers in this area[1,3] on displacement reactions of 3-O-benzoyl-1,2,5,6-di-O-isopropylidene-4-O-mesyl-D-mannitol have shown that the reaction can proceed *via* anchimeric formation of the ortho ester ion (III) or by direct SN2 reaction (II→I) depending upon the relative strengths of the attacking nucleophile (B^-) and the anchimeric group. With a strong nucleophile such as azide ion, the SN2 reaction was



favorably competitive with formation of I (B = N_3^-). However, with weaker nucleophiles the anchimeric reaction predominated with resultant formation of talitol derivatives (IV) sans introduction of the nucleophile. A neighboring methyl ether group of V is such a poor anchimeric group that only SN2 reaction took place with acetate ion.

The success with the ether group suggested that an ether group more easily removable than the methyl might make the mannitol displacement reactions more attractive as a source for synthesis of unusual carbohydrates. The acid-labile tetrahydropyranyl blocking group meets these requirements and its use in the mannitol series is the subject of this paper.

Reaction of 3-O-benzoyl-1,2:5,6-di-O-isopropylidene-D-mannitol (VII)[4] with dihydropyran in the presence of a trace of *p*-toluenesulfonic acid gave the tetrahydropyranyl ether (VIII). A short reaction time was essential; after fifteen minutes the product was crystallized in 73% by addition of petroleum ether, but with a longer reaction time the product could not be crystallized.

In order to carry out certain transformations to be discussed later, it was necessary to remove the tetrahydropyranyl group with minimal effect on the isopropylidene blocking groups. Since the tetrahydropyranyl group can be removed only under acid conditions, unless proper conditions could be found, the hexitol would lose more or less of its isopropylidene blocking groups. The usual conditions of aqueous mineral acid[5] or dilute acetic acid[6] also could be expected to cause partial or total loss of the isopropylidene groups. In contrast, it can be anticipated that acid-catalyzed interchange of the tetrahydropyranyl group with a monohydric alcohol should show great selectivity since the dioxalane ring formed from a glycol such as in VIII should not exchange readily with a monohydric alcohol.

Treatment of VIII with reagent methanol containing a catalytic amount of *p*-toluenesulfonic acid at room temperature did indeed remove the tetrahydropyranyl group with formation of VII in about 30% yield; investigation of the mother liquor showed that the material had still lost some isopropylidene blocking groups. In order to minimize the dioxalane exchange reaction, 2,2-dimethoxypropane and acetone were used in addition to methanol and an 82% yield of VII was obtained; the dimethoxypropane served either to keep the equilibrium of isopropylidene removal in favor of the dioxalane (VII) or acted as a scavenger for traces of water or both, whereas acetone could contribute to the former.

Debenzoylation of VIII with methanol containing a trace of sodium methoxide gave a mixture of IX and methyl benzoate. After removal of the methyl

(1) For the previous paper of this series (LV), see B. R. Baker and A. H. Haines, *J. Org. Chem.*, **28**, 442 (1963).

(2) This work was generously supported by grant no. CY-5845 from the National Cancer Institute, U. S. Public Health Service.

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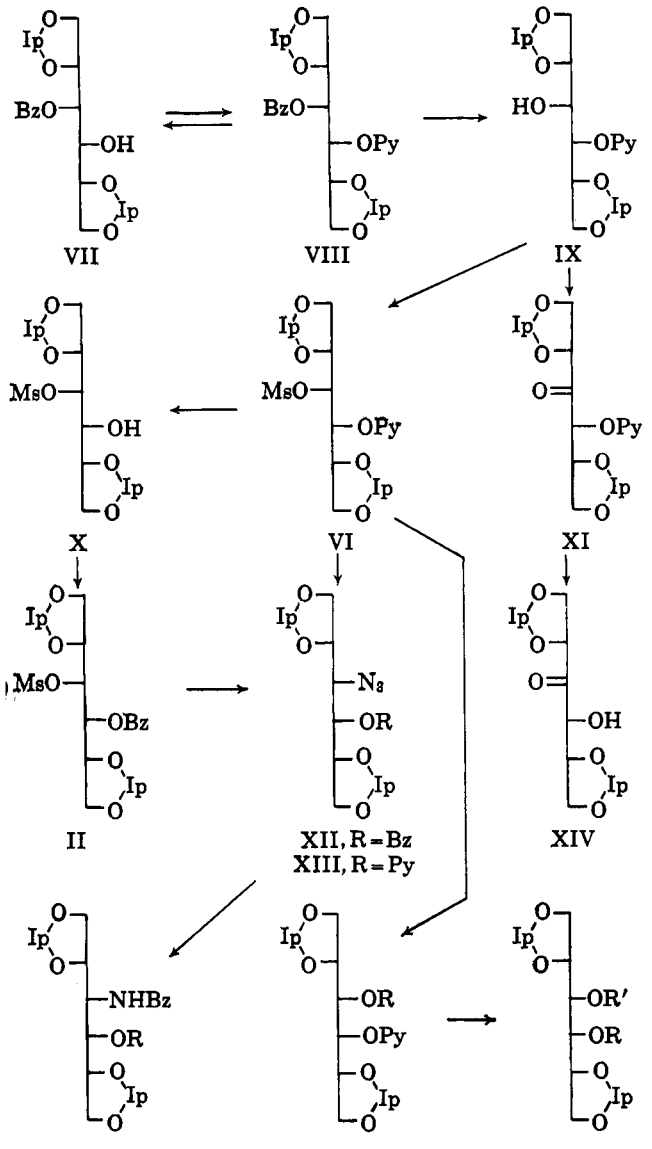

XV, R = Py
XVI, R = H
XVII, R = Bz

XVIII, R = Ac
XIX, R = H
XX, R = Bz

IVa, R = H, R′ = Bz
IVb, R = Bz, R′ = H
XXI, R = R′ = Bz
XXII, R = R′ = H

Bz = Benzoyl; Py = 2-tetrahydropyranyl; Ms = methanesulfonyl; Ac = acetate; Ip = isopropylidene

benzoate by steam distillation *in vacuo*, IX could be crystallized from petroleum ether as a low-melting solid in 73% yield.

The hydroxyl group of IX smoothly reacted with mesyl chloride in pyridine at 0° to give the crystalline mesylate (VI) in 80% yield, showing the stability of the tetrahydropyranyl group to cold pyridine–pyridine hydrochloride. That the tetrahydropyranyl group also was stable to pyridine–chromium trioxide was shown by oxidation of IX to the crystalline pyranyl ketone (XI)[7] in 43% yield under conditions previously used for oxidation of VII to the corresponding ketone,[4] where a similar yield was obtained.

Depyranylation of the mesyl derivative (VI) by the methanolysis procedure gave an 88% yield of the hydroxy mesylate (X) which could not be crystallized, but which was converted to the known crystalline benzoyl derivative (II)[3] in 61% yield. The hydroxy mesylate (X) should serve as a useful intermediate for introducing neighboring groups that could be used for anchimeric introduction of functions into the hexitol chain.

The displacement reactions of the pyranyl mesylate (VI) were studied with both acetate and azide ions; although the mesylate group of VI was somewhat less active than the mesylate of II, the pyranyl group was, fortunately, sufficiently stable to the displacement conditions that the reactions proceeded smoothly.

Treatment of VI with sodium acetate in boiling dimethylformamide for twenty-four hours caused complete displacement of the mesyloxy group; the product was an oil, primarily the talitol acetate (XVIII) contaminated slightly with the alcohol (XIX) formed by partial hydrolytic loss of the acetyl group. The mixture of XVIII and XIX was deacetylated with methanolic sodium methoxide giving XIX as an oil in 67% yield.

Depyranylation of crude XIX by acid-catalyzed methanolysis to give 1,2:5,6-di-O-isopropylidene-D-talitol (XXII) afforded an oil with an infrared spectrum almost identical to authentic XXII; purification at this stage by crystallization appeared unpromising, due in part to the relatively low melting point of XXII.[3,4] Hence the sequence XIX → XX → IVa → XXII was used in a search for an easily isolable crystalline derivative; unfortunately, none of the intermediates could be crystallized. However, benzoylation of XIX and purification on an alumina column gave a 55% yield of analytically pure pyranyl benzoate (XX) as an oil.[8]

Depyranylation of XX gave a sirupy benzoate from which the previously described[3] 1,2:5,6-di-O-isopropylidene-D-talitol (XXII) monobenzoate crystallized slowly in 12% yield. Since this monobenzoate is an easily crystallizable substance and since the oily benzoate in the mother liquor from this crystalline benzoate could be debenzoylated to crystalline XXII in 45% yield, or benzoylated to XXI, probable structural assignments for the crystalline and noncrystalline benzoates can be made.

The product from depyranylation of XX should be the talitol 4-benzoate (IVa); since a mixture of the two isomeric benzoates are obtained, any structural assignment can only be tentative. It previously has been shown that the oily benzoate could slowly rearrange to the crystalline benzoate.[3] Therefore, the predominant isomer obtained in the depyranylation should be the talitol 4-benzoate (IVa), which slowly rearranges to the crystalline talitol 3-benzoate (IVb). The current experiments give further credence to the suggestion[3] that the ortho ester ion (III) reacts with water to give a

(7) Attempts to depyranylate XI to XIV with methanol–acetone–dimethoxypropane containing a trace of *p*-toluenesulfonic acid gave an oil which on benzoylation afforded a small yield of O-benzoyl derivative, m.p. 122°, that was isomeric to the O-benzoyl derivative of XIV[4]; the oily residue from the mother liquor contained what appeared to be a mixture of isomeric ketone benzoates. Either the depyranylation conditions, the benzoylation conditions, or both cause an equilibration of isomers at the 3- and 4-positions probably through an enediol[4]; it also is possible that the supposed intermediate, XIV, is actually an enediol, since it shows no ketone absorption, but does show strong hydroxyl absorption. The n.m.r. spectrum of XIV showed no O–CH_3 hydrogens which could have arisen by formation of a stable hemiketal between XIV and methanol, or formation of a dimethyl ketal.

(8) *A posteriori*, it would be simpler to prepare the pyranyl benzoate (XX) by reaction of the pyranyl mesylate (VI) with sodium benzoate, rather than sodium acetate and subsequent transformation; *cf.* E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **24**, 1689 (1959), and references therein.

mixture of both isomeric benzoates (IV), thus showing no unusual selectivity during ring opening.

The pyranyl mesylate (VI) reacted with sodium azide in boiling dimethylformamide to give the azide (XIII). This oily azide (XIII), which showed a typical azido band at 2125 cm.$^{-1}$, was reduced with lithium aluminum hydride as described for XII[1]; the resultant amine was not obtained crystalline, but readily gave a crystalline N-benzoyl derivative (XV) in 40% over-all yield for the three steps from VI. Since the average yield per step was 74%, this was somewhat higher than an average yield of 72% for the three steps for the conversion of II → XII → XVII. Acid-catalyzed depyranylation of XV to XVI with methanol–acetone–dimethoxypropane, followed by benzoylation afforded the previously known[1] and easily crystallizable dibenzoylaminoaltritol (XVII) in 62% yield.

The synthesis of the aminoaltritol (XVII) and the talitol (XXI) from the pyranyl mesylate (VI) shows the utility of the tetrahydropyranyl blocking group for conversion of 1,2:5,6-di-O-isopropylidene-D-mannitol to other hexitol derivatives; further work on displacement reactions of VI with other nucleophiles, therefore, is warranted. In addition, the pyranyl ketone (XI) and the monomesyl pyranyl mannitol (X) may prove useful for introduction of groups into the hexitol chain.

Experimental[9]

3-O-Benzoyl-1,2:5,6-di-O-isopropylidene-4-O-(2-tetrahydropyranyl)-D-mannitol (VIII).—To a stirred suspension of 10 g. (0.033 mole) of VII[4] in 20 ml. of dihydropyran was added 50 mg. of *p*-toluenesulfonic acid over a period of 5 min., during which time a clear solution formed. After being stirred another 10 min., the solution was diluted with 100 ml. of petroleum ether, then kept overnight at −6°. The product was collected on a filter and washed with petroleum ether; yield, 6.7 g., m.p. 118–119°. The combined mother liquor and washings deposited an additional 2.3 g. (total 73%) of product after 3 more days at −6°. A similar preparation was recrystallized from petroleum ether giving white crystals, m.p. 119–120°; $[\alpha]^{25}D$ +22.4 ± 0.7° (0.7%); ν_{max}^{Nujol} 1710 (C=O); 1260, 1200, 1070 (C—O—C); 715 cm.$^{-1}$ (benzoate CH).

Anal. Calcd. for $C_{24}H_{34}O_8$: C, 64.0; H, 7.55. Found: C, 63.9; H, 7.44.

Selective Removal of the Tetrahydropyranyl Group from 3-O-Benzoyl-1,2:5,6-di-O-isopropylidene-4-O-(2-tetrahydropyranyl)-D-mannitol (VIII).—To a solution of 450 mg. (1 mmole) of VIII in 2 ml. of reagent methanol, 10 ml. of reagent acetone and 2 ml. of 2,2-dimethoxypropane was added 3 mg. of *p*-toluenesulfonic acid. After standing about 18 hr. at room temperature protected from moisture, the mixture was treated with 0.2 ml. of 5% aqueous sodium bicarbonate, then spin evaporated to dryness *in vacuo*. The residue was partitioned between 5 ml. of water and 20 ml. of chloroform, then the aqueous phase was extracted again with 20 ml. of chloroform. Washed with water, the combined organic extracts were evaporated to dryness *in vacuo*. Crystallization from ethyl acetate–petroleum ether gave 300 mg. (82%) of VII, m.p. 103–104°; a mixture with authentic VII gave no depression in melting point and the infrared spectra of the two samples were identical.

If the acetone and 2,2-dimethoxypropane were not present, the product suffered some deacetonation, and only about 30% of pure VII could be isolated.

1,2:5,6-Di-O-isopropylidene-3-O-(2-tetrahydropyranyl)-D-mannitol (IX).—A suspension of 5.3 g. (11.8 mmoles) of VIII in 90 ml. of reagent methanol containing 50 mg. of sodium methoxide was stirred for 48 hr. protected from moisture; solution occurred in about 24 hr. The solution was spin evaporated to dryness *in vacuo;* methyl benzoate was removed by spin evaporation with water *in vacuo*. Crystallization of the residue from petroleum ether at −6° gave 2.95 g. (73%) of product, m.p. 68°. Recrystallization from the same solvent gave the analytical sample, m.p. 69°[10]; $[\alpha]^{25}D$ −14.2 ± 0.6° (1.1%); ν_{max}^{Nujol} 3450 (OH); 1205, 1240, 1070 (C—O—C), and no benzoate absorption at 1710 and 715 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{30}O_7$: C, 59.0; H, 8.67. Found: C, 59.0; H, 8.47.

1,2:5,6-Di-O-isopropylidene-3-O-mesyl-4-O-(2-tetrahydropyranyl)-D-mannitol (VI).—To a stirred solution of 2.8 mmoles) of IX in 8 ml. of reagent pyridine cooled in an ice bath and protected from moisture was added 1.1 g. (9.5 mmoles) of methanesulfonyl chloride over a period of 20 min. After being stirred for an additional 3 hr. at 0°, then allowed to stand overnight at room temperature, the mixture was poured into 25 ml. of ice–water and extracted with chloroform (three 20-ml. portions). Combined extracts were washed with 10 ml. of 5% aqueous sodium bicarbonate, then water. Dried with magnesium sulfate, the organic solution was spin evaporated to dryness *in vacuo* at room temperature. Traces of pyridine were removed by addition and spin evaporation of toluene. Crystallization from petroleum ether afforded 2.8 g. (80%) of product, m.p. 59–61°, that was suitable for further transformations. Recrystallization from ethyl acetate–petroleum ether gave white crystals, m.p. 63°; $[\alpha]^{25}D$ +4.8 ± 0.5° (1%); ν_{max}^{Nujol} 1340, 1165 (—SO_3—); 1265, 1200, 1080, 1060 cm.$^{-1}$ (C—O—C).

Anal. Calcd. for $C_{18}H_{32}O_9S$: C, 50.9; H, 7.55; S, 7.55. Found: C, 51.0; H, 7.62; S, 7.76.

1,2:5,6-Di-O-isopropylidene-4-O-(2-tetrahydropyranyl)-D-*arabo*-3-hexulose (XI).—To the chromium trioxide–pyridine complex from 4 g. of chromium trioxide and 50 ml. of reagent pyridine, prepared according to Sugihara and Yuen[4] with observation of their precautions to avoid detonation, was added a solution of 3.0 g. (8.7 mmoles) of IX in 10 ml. of reagent pyridine. After being heated with stirring at 60° for 8 hr., the mixture was cooled, poured into 100 ml. of ice–water, then extracted with ether (four 40-ml. portions). Combined extracts were washed with water, dried with magnesium sulfate, then evaporated *in vacuo*. Traces of pyridine were removed by addition and spin evaporation of toluene *in vacuo*. Crystallization from petroleum ether gave 1.2 g. (40%) of white crystals, m.p. 83°; $[\alpha]^{25}D$ −16.1 ± 0.6° (0.6%); ν_{max}^{Nujol} 1720 (C=O); 1255, 1200, 1120, 1120, 1065 cm.$^{-1}$ (C—O—C).

Anal. Calcd. for $C_{17}H_{28}O_7$: C, 59.3; H, 8.14. Found: C, 59.2; H, 8.23.

1,2:5,6-Di-O-isopropylidene-3-O-mesyl-D-mannitol (X).—Depyranylation of 424 mg. (1 mmole) of VI as described for the depyranylation of VIII gave 300 mg. (88%) of X as an oil which could not be crystallized; ν_{max}^{film} 3500 (OH); 1360, 1170 (—SO_3—); 1260, 1210, 1070 cm.$^{-1}$ (C—O—C).

For characterization, 300 mg. of X was benzoylated with 154 mg. of benzoyl chloride in 5 ml. of reagent pyridine for 2 hr. at 0° and 24 hr. at room temperature, then worked up as usual.[1,3] Crystallization from ethyl acetate–petroleum ether gave 250 mg. (61%) of II, m.p. 73–74°, that was identical with an authentic sample of II as shown by mixture melting point and comparative infrared spectra.

4-O-Benzoyl-1,2:5,6-di-O-isopropylidene-3-O-(2-tetrahydropyranyl)-D-talitol (XX).—A mixture of 850 mg. (2 mmoles) of VI, 492 mg. (6 mmoles) of anhydrous sodium acetate, and 20 mg. of anhydrous dimethylformamide (Spectro Grade) was refluxed with stirring for 24 hr. Solvent was removed by spin evaporation *in vacuo* on a boiling water bath. The residue was suspended in 10 ml. of water and extracted with chloroform (three 30-ml. portions). Combined extracts were washed with water, dried with magnesium sulfate, and evaporated to dryness *in vacuo*. A solution of the residue in 20:1 petroleum ether–ethyl acetate was clarified with charcoal. Evaporation *in vacuo* gave 690 mg. of an oil that was predominately XVIII since it showed strong carbonyl absorption at 1740 cm.$^{-1}$ and weak hydroxyl absorption at 3500 cm.$^{-1}$ of some contaminating XIX; the product could not be crystallized.

The crude XVIII was deacetylated by solution in 50 ml. of reagent methanol containing 50 mg. of sodium methoxide. After

(9) Melting points were determined in capillary tubes with a Mel-Temp block and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 137B spectrophotometer. Optical rotations were measured in a 1-dm. microtube in chloroform solution. Petroleum ether refers to that fraction with b.p. 60–75°.

(10) Earlier preparations gave a low melting dimorph, m.p. 45°; only the high melting dimorph was encountered in later work.

about 18 hr. at room temperature protected from moisture, the solvent was removed *in vacuo*. The residue was suspended in 10 ml. of water and extracted with chloroform (two 30-ml. portions). Combined extracts were washed with water, dried with magnesium sulfate, and evaporated to dryness *in vacuo;* yield, 480 mg. (67% from VI) of oily XIX that could not be crystallized; ν_{max}^{film} 3550 (OH); 1255, 1210, 1065 (C—O—C) and no acetate C=O at 1740 cm.$^{-1}$.

To a stirred solution of 1.04 g. (3 mmoles) of a similar preparation of XIX in 6 ml. of reagent pyridine was added 490 mg. (3.5 mmoles) of benzoyl chloride with ice cooling. After 24 hr., the mixture was processed in the usual way[1,3] to give 0.95 g. of an oil showing benzoate C=O at 1710 cm.$^{-1}$. A solution of this crude XX in 20 ml. of benzene was poured onto a column of about 65 g. of neutral alumina (Brockmann activity III). Elution with 50 ml. of benzene, then 50 ml. of 1:1 chloroform–benzene gave 50 mg. of material with weak benzoyl absorption at 1710 cm.$^{-1}$ and was rejected. Further elution with 200 ml. of chloroform afforded 0.75 g. (56%) of pure XX as an oil that could not be crystallized; $[\alpha]^{25}D$ +18 ± 1° (0.2%); ν_{max}^{film} 1710 (ester C=O); 1260, 1200, 1070 (C—O—C); 715 cm.$^{-1}$ (benzoyl CH).

Anal. Calcd. for $C_{24}H_{34}O_8$: C, 64.0; H, 7.55. Found: C, 64.1; H, 7.73.

4-O-Benzoyl-1,2:5,6-di-O-isopropylidene-D-talitol (IVa).—Depyranylation of 200 mg. (0.44 mmole) of XX, as described for depyranylation of VIII, afforded 135 mg. (83%) of a syrup. Crystallization from ethyl acetate–petroleum ether slowly occurred over 2 days at −5° giving 20 mg. (12%) of the 3-benzoate (IVb), m.p. 123–124°, that was identical with the material previously prepared from II.[3] Spin evaporation of the mother liquor *in vacuo* gave the remainder of the product as the sirupy 4-benzoate (IVa) (115 mg., 71%) which had ν_{max}^{film} 3550 (OH); 1710, 710 (benzoate); 1260, 1080 cm.$^{-1}$ (C—O—C) and which was debenzoylated (description follows).

1,2:5,6-Di-O-isopropylidene-D-talitol (XXII).—The preceding sirupy 4-benzoate (IVa) was debenzoylated as described for the preparation of IX. Crystallization from petroleum ether gave 45 mg. (37% based on XX), m.p. 62–63°, that was identical with an authentic sample.

3,4-Di-O-benzoyl-1,2:5,6-di-*O*-isopropylidene-D-talitol (XXI).—Benzoylation of 115 mg. of syrupy benzoate (IVa) with 60 mg. of benzoyl chloride in 1.5 ml. of reagent pyridine, then work-up as usual,[1,3] gave 60 mg. of XXI, m.p. 144°, that was identical with an authentic sample.[3]

3-Benzamido-3-deoxy-1,2:5,6-di-O-isopropylidene-4-O-(2-tetrahydropyranyl)-D-altritol (XV).—A mixture of 0.85 g. (2 mmoles) of VI, 0.39 g. (6 mmoles) of sodium azide, and 10 ml. of dimethylformamide was refluxed for 6 hr. The solvent was removed by spin evaporation *in vacuo* on a boiling water bath. The residue was suspended in 20 ml. of ice–water and extracted with chloroform (three 20-ml. portions). Dried with magnesium sulfate, combined extracts were evaporated to residue *in vacuo;* yield, 0.66 g. (89%) of crude azide (XIII); ν_{max}^{film} 2125 (—N_3); 1255, 1210, 1065 cm.$^{-1}$ (C—O—C).

To a stirred suspension of 230 mg. (6 mmoles) of lithium aluminum hydride in 40 ml. of reagent ether was added a solution of 1.01 g. (2.73 mmoles) of crude azide (XIII) in 10 ml. of reagent ether at such a rate that gentle reflux was maintained. After being refluxed for 1 hr., the excess hydride was decomposed by the careful addition of 1 ml. of ethyl acetate followed by 0.35 ml. of water. The mixture was filtered and the salts washed with ether. The filtrate was decolorized with charcoal, then spin evaporated *in vacuo;* yield, 0.797 g. (90%) of 3-aminodeoxy-1,2:5,6-di-O-isopropylidene-4-O-(2′-tetrahydropyranyl)-D-altritol that could not be crystallized and had ν_{max}^{film} 3400 (NH); 1260, 1080 (C—O—C); and no azide absorption at 2125 cm.$^{-1}$.

To a stirred solution of 0.70 g. (2 mmoles) of the amine in 7 ml. of reagent pyridine cooled in an ice bath and protected from moisture was added 326 mg. (2.3 mmoles) of benzoyl chloride. After being stirred for 3 hr. in the ice bath and 18 hr. at room temperature, the mixture was processed in the usual manner.[1,3] Crystallization from ethyl acetate–petroleum ether gave 504 mg. (56%, or 40% from VI) of XV, m.p. 140°. Recrystallization from chloroform–petroleum ether afforded white needles, m.p. 141°; $[\alpha]^{25}D$ +8.2 ± 0.6° (0.8%); ν_{max}^{Nujol} 3325 (NH); 1640, 1525 (amide); 1250, 1210, 1065 (C—O—C); 705 cm.$^{-1}$ (benzoyl CH).

Anal. Calcd. for $C_{24}H_{35}NO_7$: C, 64.2; H, 7.78; N, 3.11. Found: C, 64.3; H, 7.99; N, 3.34.

3-Benzamido-4-O-benzoyl-3-deoxy-1,2:5,6-di-O-isopropylidene-D-altritol (XVIII).—Depyranylation of 150 mg. of XV as described for the depyranylation of VIII gave 110 mg. (90%) of crude XVI, which was benzoylated with 64 mg. of benzoyl chloride in 2 ml. of reagent pyridine in the usual manner.[3] Recrystallization of the product from ethyl acetate–methanol afforded 90 mg. (67%) of XVII, m.p. 202–203°, which was identical with an authentic sample prepared by a different route.[1]

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Synthetic Nucleosides. LVII.[1] Facile Displacement Reactions in the D-Mannitol Series. IV. Investigation of Thiourethane Derivatives[2]

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Reaction of the monosodium salt of 1,2:5,6-di-O-isopropylidene-D-mannitol (V) with phenyl isothiocyanate did not form the expected phenylthiourethane derivative (VI). Instead, a facile cyclization took place to give a cyclic carbonate (XIV), a thionocarbonate (IX), or a phenyliminocarbonate (X) derivative of V, depending upon the work-up conditions. Additional evidence to support a proposed mechanism for these reactions also is presented.

Possible routes to synthesis of sugars containing a *cis*-mercapto alcohol system (I) such as that in the 2-mercapto-2-deoxy-D-ribose or 3-mercapto-3-deoxy-D-ribose of Baker and co-workers[3–5] has been under investigation for several years; nucleosides containing such sugars might afford interesting biological properties.[3] Although thio sugars with a *trans* relationship of OH and SR groups (IV) are readily synthesized by ring opening of sugar epoxides (III) with mercaptides,[6] successful routes to *cis* compounds with a *cis* relation-

(1) For the previous paper in this series, see B. R. Baker and H. S. Sachdev, *J. Org. Chem.*, **28**, 2132 (1963).

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