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SYNTHESIS AND NUCLEOPHILIC SUBSTITUTION REACTIONS OF SOME IODO-DEOXY SUGARS

N. K. KOCHETKOV, A. I. USOV and K. S. ADAMYANTS

N. D. Zelinsky Institute of Organic Chemistry, Academy of Sciences, Moscow, USSR

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Abstract—$(PhO)_3P{\cdot}CH_3I$ reacts with methyl-2,3-O-isopropylidene-L-rhamnopyranoside (I) to give a mixture of methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-mannopyranoside (II), methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-β-D-allofuranoside (III), and methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-α-L-talofuranoside (IV) in the ratio of approx. 13:14:1. The course of substitution reactions at the iodine atoms in these compounds depends on nucleophilicity of the reagent used. Strong nucleophiles (e.g. PhCOSK) react with Walden inversion and without elimination. With the less nucleophilic NaN_3 the reaction proceeds also with inversion, but hydrogen iodide elimination and pyranose ring contraction (in II) also take place to some extent. In the action of PhCOONa the formation of unsaturated monosaccharides is the predominant process, while the substitution of the iodine atom by the benzoyloxy group proceeds to a small extent and gives rise to a mixture of epimeric benzoates.

INTRODUCTION

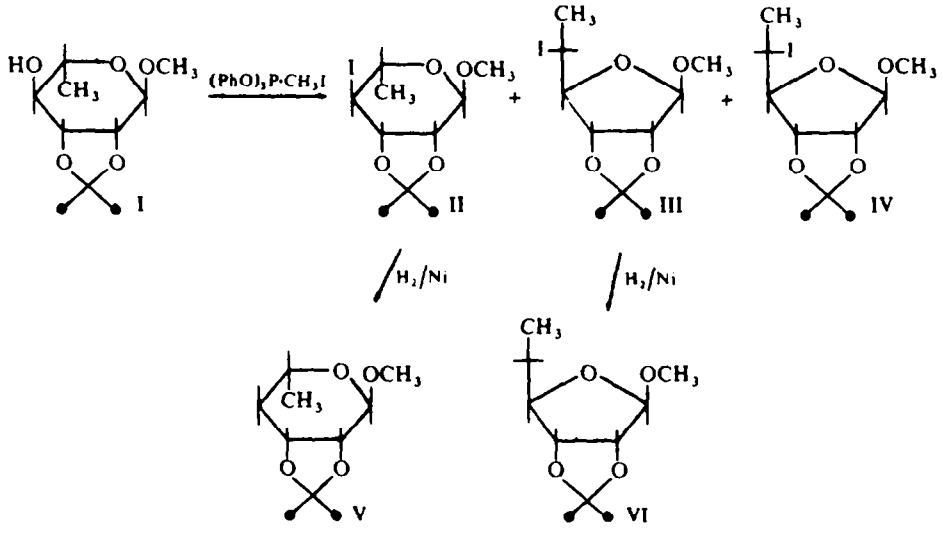
DURING our study of the synthesis and reactions of carbohydrate halogen derivatives[1] we have investigated the reaction of methyl-2,3-O-isopropylidene-α-L-rhamnopyranoside (I) with triphenyl phosphite methiodide. The displacement of the hydroxyl group by an iodine atom in this compound proved to be ambiguous giving two crystalline substances, methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-mannopyranoside (II)[2] and its isomer, which was erroneously assigned as methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-talopyranoside (VII).[2,3] Later this substance was shown to be methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-β-D-allofuranoside (III).[4,5] We have established that this crystalline substance may contain up to 10% of a third iodide, methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-α-L-talofuranoside (IV).[5] During the elucidation of the structures of iodides III and IV these compounds were synthesized independently.[5,6] We have investigated the applicability of the three isomeric iodides II, III, and IV to the introduction of various functional groups into a monosaccharide molecule. A study was made of the substitution of iodine atom by the azido group as a route to amino sugars,[3,6] by the thiolbenzoyl group to give thiosugars,[7] and by the benzoyl group to provide a possible method for establishing the structure of halogen derivatives.[8]

RESULTS AND DISCUSSION

Synthesis of iodo-deoxy sugars

Methyl-2,3-O-isopropylidene-α-L-rhamnopyranoside (I) was heated with triphenyl phosphite methiodide for 6–7 h at 70° in pure benzene to give a mixture of isomeric iodides, which was separated by chromatography on alumina with a 50% yield.[2]

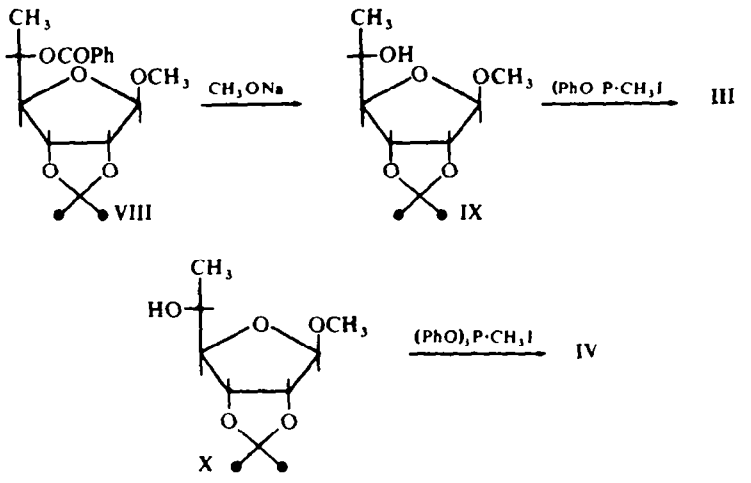
Two substances were separated from the mixture by crystallization. The first one



was identified from its NMR spectrum as methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-mannopyranoside (II). Its structure was confirmed by converting II into the dideoxy derivative V by hydrogenation over Raney nickel in the presence of KOH. After removal of the isopropylidene group from V followed by periodate oxidation[2] glyoxal and crotonaldehyde were isolated as their dinitrophenylhydrazones.

The second crystalline substance, isolated from the mixture of iodides, produced three peaks on gas-liquid chromatography, one of which corresponded to the iodo-derivative II.[5] This compound was removed from the preparation by additional recrystallization. However, the resulting III contained up to 10% of isomeric IV. This product upon hydrogenation on freshly prepared Raney nickel in the presence of KOH gave methyl-5,6-dideoxy-2,3-O-isopropylidene-β-D-ribohexofuranoside (VI) in a 70% yield. Its structure was established by its NMR spectrum and by comparison with data in the literature.[9] Similar results have been reported elsewhere.[4]

The structures of III and IV were confirmed by independent synthesis of these two C_5-epimeric iodides: methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-β-D-allofuranoside (III)[5] and methyl-5,6-dideoxy-5-iodo-2,3-O-isopropylidene-α-L-talofuranoside (IV).[6] Methyl-6-deoxy-2,3-O-isopropylidene-α-L-talofuranoside (IX), obtained by saponification of benzoate VIII, served as a starting compound for the synthesis of III. The properties of VIII and IX were found to be in agreement with those reported for these compounds.[10] Their structures were supported by NMR spectra. IX readily reacts with $(PhO)_3P \cdot CH_3I$ to yield iodide III, obtained, after purification by chromatography, in crystalline form. The NMR spectrum of III agrees well with the suggested structure. The spin-spin coupling constant $J_{4,5}$ of ~ 11 Hz provides evidence for its D-allo-configuration (cf.[4]). The retention time on GLC and m.p., specific rotation, and IR spectrum of the synthetic sample are identical with those of III isolated from the above mixture of iodides.[5]

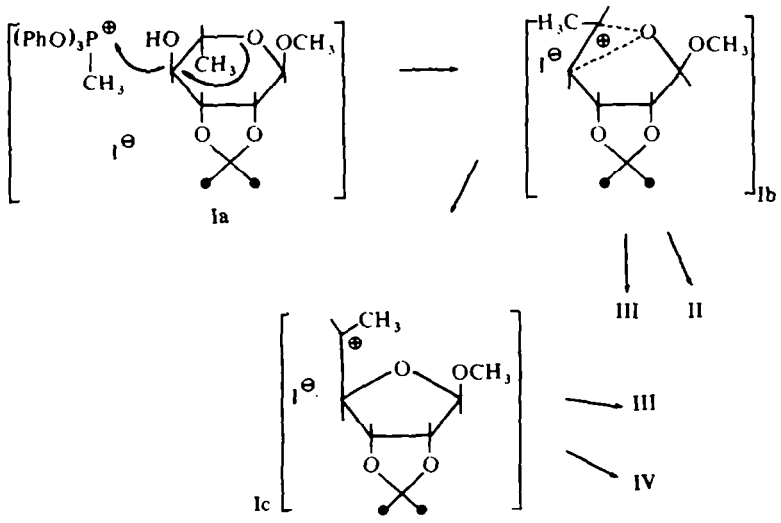


Iodide IV with the L-talo-configuration was synthesized by the action of $(PhO)_3P \cdot CH_3I$ on methyl-6-deoxy-2,3-O-isopropylidene-β-D-allofuranoside (X), obtained from L-rhamnose.[10] The structure of IV was confirmed by its NMR spectrum.[6]

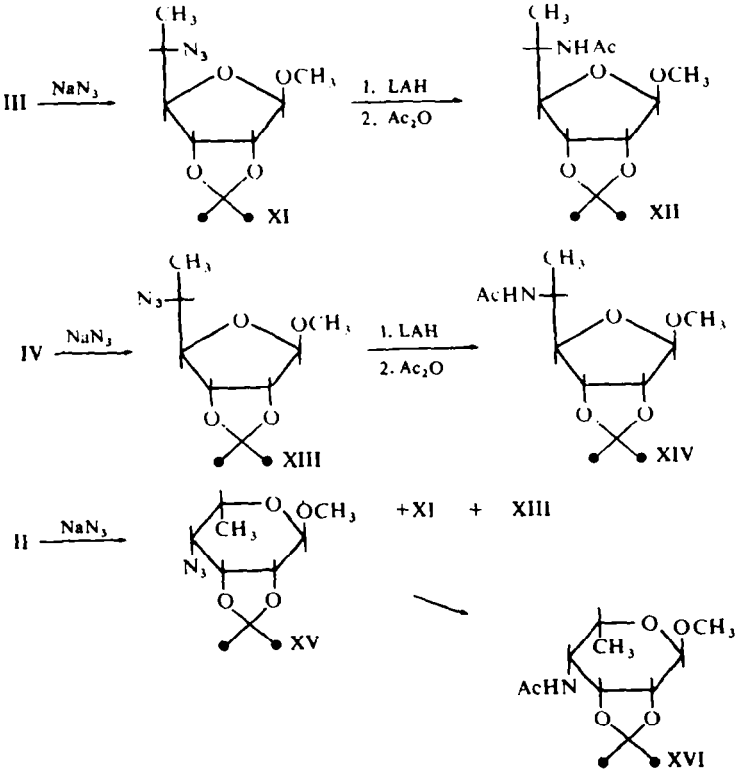
Using individual samples of II, III, and IV as reference compounds it was possible to show by GLC, that the mixture, resulting from the reaction of $(PhO)_3P \cdot CH_3I$ with I, consists of these iodides in the approximate ratio of 13:14:1, slightly varying with the reaction conditions.[5] Thus, instead of the expected displacement of hydroxyl group accompanied by Walden inversion, the interaction between $(PhO)_3P \cdot CH_3I$ and I involves, on the one hand, rearrangement with ring contraction and formation of furanose derivatives with an iodine atom at C_5, and, on the other hand, the substitution of the hydroxyl at C_4 by an iodine atom without inversion. It may be suggested that the reaction proceeds *via* an intermediate complex of the type of Ia, which converts into Ib as a result of a transformation involving inversion at C_4. Next, cation Ib is attacked by iodide anion either at C_4 or at C_5 producing II and III, respectively. In this case the original inversion at the asymmetric centres is reversed. Simultaneously a part of Ib undergoes rearrangement to produce Ic. The latter reacts with iodide anion to give IV and, evidently, some III. However, it is not unlikely that the less favoured methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-talopyranoside (product of "normal" hydroxyl group displacement) may be formed first. It could then undergo rearrangement to produce II, III, and IV *via* the same intermediate cations Ib and Ic.

Reaction with sodium azide

On heating in dimethylformamide with an excess of NaN_3 for 10 hours at 120° iodide III reacts completely to form the azido-deoxy sugar XI. Unsaturated monosaccharides are also formed as by-products, the yield being less than 10%. They have not been studied in this case. XI was isolated by chromatography on alumina in a 50% yield. Its retention time upon GLC, IR spectrum, and specific rotation correspond to those of an authentic sample of methyl-5-azido-5,6-dideoxy-2,3-O-isopropylidene-α-L-talofuranoside.[11] The NMR spectrum of XI is similar to that of iodide IV with



L-talo-configuration, for example, protons H_2 and H_3 are equivalent and produce an A_2-system in the spectra of IV and XI. Azide XI was converted into acetamido-deoxy sugar XII in 90% yield by reducing with LAH in ether followed by acetylation. The specific rotation, IR, NMR, and mass spectra of XII are in agreement with the



data reported for methyl-5-acetamido-5,6-dideoxy-2,3-O-isopropylidene-α-L-talofuranoside.[11] Thus, the displacement of the iodine atom in III by azido group proceeds with Walden inversion at C_5.*

Iodide IV reacts readily with sodium azide as well,[6] the unsaturated sugars being formed as by-products. Under optimal conditions (boiling in DMF for two hours) the content of azido-deoxy sugar XIII is twice as high as that of the unsaturated monosaccharides. XIII was isolated by chromatography on neutral alumina in 46% yield. Its IR spectrum shows a band at 2100 cm^{-1} and, in fact, does not differ from that of XI, but the specific rotations and NMR spectra are different. Iodide IV (as well as its epimer III) appears to substitute azido group for iodine atom with Walden inversion, giving methyl-5-azido-5,6-dideoxy-2,3-O-isopylidene-β-D-allofuranoside. The NMR spectrum of XIII, similar to that of iodide III with D-allo-configuration, is in a full agreement with the structure suggested for XIII. XIII was converted into its acetamido derivative XIV by reducing with LAH followed by acetylation. The stability to hydrolysis of the glycosidic linkage, and the mass spectra of XIV are practically the same as those of the epimeric XII. The structure of methyl-5-acetamido-5,6-dideoxy-2,3-O-isopropylidene-β-D-allofuranoside is confirmed by its NMR spectrum.[6]

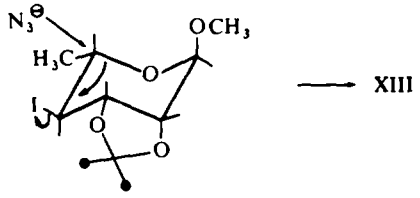
The synthesis of the two epimeric acetylaminosugars XII and XIV outlined above suggests that aminosugars might be obtained via carbohydrate iodo-derivatives. This is true, in particular, for the unknown 5-acetylaminoalloside XIV, as its preparation by other routes would present considerable difficulties.

Pyranoside II reacts with sodium azide under more vigorous conditions (boiling DMF for 20 hours) and gives a mixture of azides XI, XIII, and XV in a ratio of 1:6·5:6·5 (GLC).[3] We have not succeeded in separating the mixture of XI and XIII, but azide XV, which has a different chromatographic mobility, was obtained by chromatography on alumina in 25% yield. The retention times on GLC of azides XI and XIII proved to be the same as those of authentic samples of methyl-5-azido-5,6-dideoxy-2,3-O-isopropylidene-α-L-talofuranoside and 5-azido-5,6-dideoxy-2,3-O-isopropylidene-β-D-allofuranoside respectively. This provides evidence in favour of the suggested structures for XI and XIII. Azide XV was converted into the acetylamino sugar XVI. The structures of XV and XVI were established by their IR, NMR, and mass spectra as well as by the coincidence of the m.p. and specific rotation of XVI with the data reported for methyl-4-acetamido-4,6-dideoxy-2,3-O-isopropylidene-α-L-talopyranoside.[12]

Thus, the reaction of II with NaN_3 proceeds by two routes: rearrangement together with the ring contraction (azides XI and XIII), and substitution with Walden inversion at C_4 (azide XV). It is worth mentioning that the 4-sulphonates of α-L- and β-D-rhamnopyranosides are known[11, 13] to react with NaN_3 only with ring contraction. However, when reproducing the reaction of methyl-2,3-O-isopropylidene-4-O-p-toluenesulphonyl-α-L-rhamnopyranoside with NaN_3, we detected a small amount of azide XV, resulting from the direct displacement of the p-toluenesulphonyloxy group with Walden inversion at C_4.

* Since III was originally assigned the structure of methyl-4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-talopyranoside, the previous interpretation[3] of the conversion of III into azide XI is not valid.

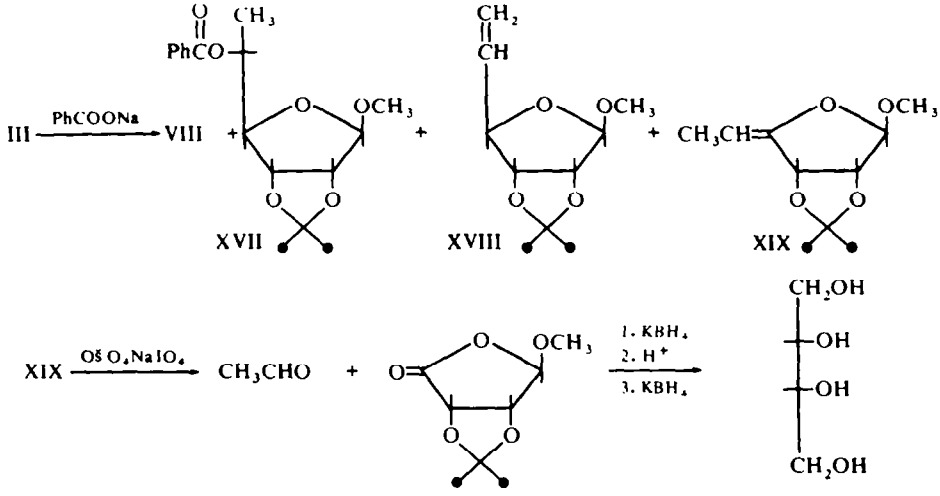
Rearrangement with ring contraction gives rise mainly to XIII having the D-allo-configuration. The formation of XIII is likely to be due to the attack of azide anion at C_5, which would proceed simultaneously with the substitution at C_4 by the oxygen atom of the pyranose ring.



Reaction with PhCOONa

Sodium benzoate has a lower nucleophilicity and higher basicity than sodium azide. Therefore one may expect the substitution of iodine atom by benzoyloxy group to be more hindered, with a greater proportion of elimination. This proved to be the case. Iodide II reacts very little with sodium benzoate even under vigorous conditions (boiling in DMF for 20 hours).[8] As indicated by GLC, 85% of II survived, the remaining 15% having similar retention times to the unsaturated monosaccharides XVIII and XIX.

The more reactive iodide III is converted in boiling DMF for 6–7 hours into a complex mixture of unsaturated derivatives and benzoates XVII and VIII.[8]



The unsaturated monosaccharide XVIII (yield 4%), the mixture of benzoates VIII and XVII (the ratio 4:1 determined by GLC, overall yield 9%), and the mixture of unsaturated monosaccharides containing XIX (overall yield 33%) were isolated by chromatography on neutral alumina. The mixture of VIII and XVII was separated by thin-layer chromatography on silica gel. VIII and XVII were identified by their IR and mass spectra and from the results of mild hydrolysis as isomeric furanosides. The properties of benzoate VIII are in agreement with those reported for methyl-5-O-benzoyl-6-deoxy-2,3-O-isopropylidene-α-L-talofuranoside,[10] and XVII proved to be identical with an authentic sample of methyl-5-O-benzoyl-6-deoxy-2,3-O-isopropylidene-β-D-allofuranoside.[10]

The specific rotation and NMR spectrum of unsaturated monosaccharide XVIII are in agreement with those reported for 5,6-dideoxy-2,3-O-isopropylidene-β-D-ribohex-5-enofuranoside.[9]

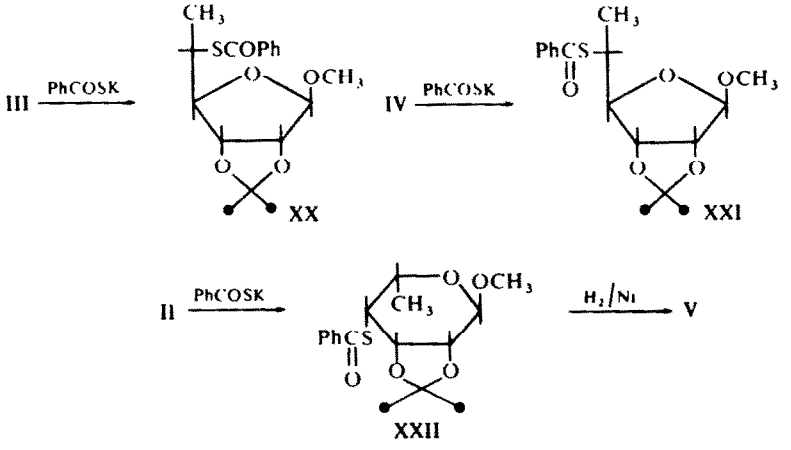
We failed to separate the mixture of XIX with other unsaturated derivatives. An attempt was undertaken to establish the structure of the unsaturated sugars, without their separation, by hydroxylation of the double bond and periodate oxidation of the resulting α-glycol grouping. The reaction mixture contained acetaldehyde, which was identified as its 2,4-dinitrophenylhydrazone. The other oxidation products were converted into polyols by two-stage reduction before and after acidic hydrolysis. The paper chromatography and GLC data showed erythritol and glycerol to be present, the former prevailing. Thus, the structure of methyl-5,6-dideoxy-2,3-O-isopropylidene-β-D-*erythro*-hex-4-enofuranoside assigned to XIX is supported by the formation of acetaldehyde and erythritol upon degradation. Unfortunately, the data available are insufficient to establish the structures of the other components of the mixture.

According to the thin-layer chromatography data, iodide IV is also converted largely into unsaturated monosaccharides by the action of sodium benzoate.

The results obtained provide evidence that sodium benzoate is but of little use in the substitution of iodine atom in iodo-deoxy sugars. Due to its low nucleophilicity the substitution proceeds only to a very insignificant extent and is accompanied with some epimerization. The main reaction process is the formation of unsaturated monosaccharides. If the elimination of HI is sterically hindered, as in the case of II, the reaction with sodium benzoate hardly takes place.

Reaction with PhCOSK

Iodide III is converted into thiolbenzoate XX by heating in dimethylformamide for 2 hours at 110° under nitrogen with a large excess of potassium thiolbenzoate.[7] No products of hydrogen iodide elimination from III have been found in the reaction mixture by thin-layer chromatography. The m.p., specific rotation, IR, NMR, and mass spectra of thiolbenzoate XX proved to be completely identical with those of methyl-5-S-benzoyl-6-deoxy-2,3-O-isopropylidene-5-thio-α-L-talofuranoside.[14] Thus, the substitution of iodine atom by thiolbenzoyl group in III proceeds with inversion at C_5.



Iodide IV reacts similarly with potassium thiolbenzoate.[7] The reaction product XXI was isolated by preparative thin-layer chromatography on alumina in a 39% yield. Its structure was determined from IR, NMR, and mass-spectra. It should be mentioned that no unsaturated monosaccharides have been found in this reaction, although the substitution of iodine atom by azido group in IV is accompanied by a considerable elimination of hydrogen iodide (see above).

Iodide II, less reactive than the isomeric III and IV, reacts with potassium thiolbenzoate completely only in 28 hours at 120°.[7] The main reaction product is the thiolbenzoate XXII (yield 35%). Its specific rotation, NMR and mass spectra are different from those of the isomeric furanosides XX and XXI. XXII is converted into 4,6-dideoxyhexopyranoside V on desulphurisation with Raney nickel in alcohol. This indicates its pyranoid structure with the thiolbenzoyl group at C_4. The NMR spectrum of XXII confirmed that it possesses the IC-conformation. Spin-decoupling data give the spin–spin coupling constant $J_{4,5}$ as ~ 4 Hz. Since the position of H_5 in the IC-conformation of XXII is axial, H_4 would be equatorial, and XXII would be 4-S-benzoyl-6-deoxy-2,3-O-isopropylidene-4-thio-α-L-talopyranoside. Hence, the substitution of iodine atom by thiolbenzoyl group in II proceeds with Walden inversion at C_4.

EXPERIMENTAL

NMR spectra were determined in CCl_4 with a Varian-DA-60-IL instrument. Chemical shifts are given in τ values with TMS as internal standard. The mass spectra were determined on a MX-1303 mass spectrometer. The IR spectra were obtained on a UR-10 spectrometer. The specific rotations were measured on a Hilger M412 polarimeter; m.ps. were determined by using a Kofler hot stage and are uncorrected. Thin-layer chromatography was performed on glass plates with a non-fixed layer of alumina or with a fixed layer of silica gel KCK; the solvents employed were: benzene(A), benzene-isooctane-MeOH 100:30:1 (B), benzene-acetone 50:1·3 (C). Column chromatographic separations were performed on III activity grade neutral alumina "for chromatography" or on silica gel KCK.

The reaction of methyl 2,3-O-*isopropylidene*-α-L-*rhamnopyranoside* (*I*) *with* $(PhO)_3P \cdot CH_3I$. A soln of I (2·1 g) in dry benzene (10 ml) was added to a suspension of $(PhO)_3P \cdot CH_3I$ (8·8 g) in dry benzene (20 ml). The mixture was heated at 70° for 7 h. Chromatography of the reaction mixture on an alumina column (elution with benzene) afforded a syrupy mixture of II, III and IV (1·55 g, 49%), R_f 0·6 (A), the ratio being approximately 13:14:1 (GLC on 300 × 0·3 cm column with 20% Apiezone M on Chromosorb WS, 210°) The syrup crystallized on storage and III mixed with IV (10%, GLC) was isolated by three crystallizations from light petroleum; m.p. 55° (Found (III): C, 36·56; H, 5·29; I, 39·48. (IV): C, 36·68; H, 5·19; I, 39·46. $C_{10}H_{17}IO_4$ requires: C, 36·61; H, 5·20; J. 38·69%).

II was obtained from the mother liquor of the first crystallization upon seeding, m.p. 80° (from hexane), $[\alpha]_D 0°$ ($CHCl_3$) (Found: C, 36·46; 36·39; H, 5·15; 5·02; I, 39·11; 39·14. $C_{10}H_{17}IO_4$ requires: C, 36·61; H, 5·20; I, 38·69%). NMR data: s. 5·23 (H_1), q. 5·65 (H_3; $J_{2,3} \sim 5·2$ Hz, $J_{3,4} \sim 8·8$ Hz).

Methyl 4,6-*dideoxy*-2,3-O-*isopropylidene*-α-L-*lyxohexopyranoside* (V) *and methyl* 5,6-*dideoxy*-2,3-O-*isopropylidene*-β-D-*ribohexofuranoside*(VI). II (0·4 g) was hydrogenated in MeOH in the presence of Raney Ni: a soln of 0·07 g KOH in MeOH being added dropwise during the reaction. V (0·2 g, 80%) was obtained by chromatography on a silica gel column (elution with benzene), $[\alpha]_D$-40·4°($CHCl_3$). The substance was boiled in 10 ml of 2% MeOH/HCl for 6 h; the soln cooled, neutralized with $PbCO_3$, filtered and evaporated. Methyl 4,6-dideoxy-α-L-lyxohexopyranoside(XXIII) (0·14 g, 88%) was obtained by chromatography on a silica gel column, m.p. 102° (from ether), $[\alpha]_D$ − 63·5° ($CHCl_3$). (Found: C, 51·78; H, 8·72. $C_7H_{14}O_4$ requires: C, 51·84; H, 8·70%). XXIII (0·1 g) was oxidized with $NaIO_4$ in PO_4 buffer (pH 6·24). 1 mole of $NaIO_4$ per mole of XXIII was consumed in 24 h. Oxidized XXIII was treated with a soln of 2,4-dinitrophenylhydrazine in 2N HCl and crotonaldehyde 2,4-dinitrophenylhydrazone, m.p. 188° (from EtOH), λ_{max} 373 mμ ($CHCl_3$)] and glyoxal bis-2,4-dinitrophenylhydrazone [m.p. 320° (decomp, from nitrobenzene); λ_{max} ($CHCl_3$) 260, 395 mμ] were obtained by chromatography on a silica gel column (elution with $CHCl_3$) [lit for crotonaldehyde 2,4-dinitrophenylhydrazone: m.p. 190° (from benzene-

petroleum ether);[15] λ_{max} ($CHCl_3$) 373 mμ[16] and for glyoxal bis-2,4-dinitrophenylhydrazone: m.p. 319·5° (decomp, from nitrobenzene), λ_{max} ($CHCl_3$) 260, 395 mμ.[17]]

V (0·23 g, 70%) was obtained from III contaminated with 10% of IV (0·52 g) under similar conditions; $[\alpha]_D$-69° ($CHCl_3$) (lit[9] − 72·9°).

Methyl 5,6-dideoxy-5-iodo-2,3-O-isopropylidene-β-D-allofuranoside(III) *and methyl 5,6-dideoxy-5-iodo-2,3-O-isopropylidene-α-L-talofuranoside* (IV). IX was obtained as reported,[10] $[\alpha]_D$ − 51° (lit[10] $[\alpha]_D$ − 54°). 0·38 g IX was heated in dry benzene with $(PhO)_3P{\cdot}CH_3I$ (2 g) at 70° for 10 h. III (0·31 g, 54·5%) was obtained by chromatography on neutral alumina (elution with benzene); m.p. 57–58° (from light petroleum), $[\alpha]_D$ − 70·8° ($CHCl_3$) (Found: C, 36·65; 36·50; H, 5·20; 5·23; I, 38·58; 38·69; $C_{10}H_{17}IO_4$ requires: C, 36·61; H, 5·20; I, 38·69%]. NMR data: s. 5·08 (H_1); q. 5·20 (H_3 $J_{3,2}$ ~ 6 Hz; $J_{3,4}$ ~ 1 Hz); d. 5·56 (H_2, $J_{2,3}$ ~ 6 Hz); q. 5·90 (H_4, $J_{4,3}$ ~ 1 Hz; $J_{4,5}$ ~ 11·4 Hz).

X was also obtained,[10] $[\alpha]_D$ − 73·4° (lit[10] $[\alpha]_D$ − 73·8°). X (1·22 g) afforded IV (0·8 g, 44%); m.p. 35°. (Found: C, 36·67; 36·84; H, 5·41; 5·44; I, 38·46; 38·40. $C_{10}H_{17}IO_4$ requires: C, 36·61; H, 5·20; I, 38·69%). $[\alpha]_D$ + 17·5° ($CHCl_3$). NMR: s. 5·16 (H_1); s. 5·50 (H_2 and H_3).

Reaction of iodides II, III *and* IV *with* NaN_3. II (0·99 g) was boiled in DMF (20 ml) with NaN_3 (0·7 g) for 20 h. The mixture was poured into benzene, the benzene layer washed with water, dried over $MgSO_4$, filtered and evaporated. The mixture (0·47 g) of XI, XIII and XV in a ratio of 1 : 6·5 : 6·5 (GLC on 100 × 0·3 cm column with 5% polyethylene glycol 20000 on Celite, 140°) was obtained. Chromatography on an alumina column (gradient elution, 0 to 25% benzene in hexane) afforded a mixture of XI and XIII (0·22 g 30%), R_f 0·6 (silica gel, B), and XV (0·19 g, 26%), R_f 0·38 (silica gel, B), m.p. 76° (from MeOH), (Found: C, 49·95; 49·89; H, 7·07; 7·06; N, 17·22; 17·23. $C_{10}H_{17}N_3O_4$ requires: C, 49·39; H, 7·00; N, 17·28%); $[\alpha]_D$ 66° ($CHCl_3$). IR spectrum: 2100 cm^{-1}.

A soln of XV (0·2 g) in dry ether was added dropwise to a suspension of LAH (0·14 g) in dry ether and the mixture boiled for 6 h; the excess LAH was decomposed with dry EtOH; the mixture was filtered and evaporated. The residue was extracted with $CHCl_3$, the solution dried with $MgSO_4$, filtered and evaporated. The residue was acetylated with Ac_2O in dry pyridine to afford XVI, m.p. 151–152° (from benzene-hexane) (Found: N, 5·03; 5·13. $C_{12}H_{21}NO_5$ requires: N, 5·4%). $[\alpha]_D$ − 26° (MeOH); mass spectrum of XVI: m/e: 244 (M^+-15), 228 (M^+-OCH$_3$), 201 (M^+-CH_3CONH), 170 (M^+-OCH_3-CH_3COCH_3) (lit[12]: m.p. 152·5–153° (from acetone), $[\alpha]_D$ − 31°).

III (1·65 g) with NaN_3 (1·2 g) in DMF (30 ml) was heated at 120° for 10 h. The mixture was treated as described above and XI (0·62 g, 50%) was obtained by chromatography on an alumina column (gradient elution, 0 to 25% benzene in hexane); R_f 0·6 (silica gel, B) (Found: C, 49·40; 49·69; H, 7·04; 7·06; N, 16·87; 17·08. $C_{10}H_{17}N_3O_4$ requires: C, 49·39; H, 7·00; N, 17·28%). $[\alpha]_D$ − 23·4° (MeOH) (lit[11] $[\alpha]_D$ − 21°). IR spectrum: 2100 cm^{-1}. NMR data: s. 5·20 (H_1), s. 5·63 (H_2 and H_3). IR and NMR spectra of XI were identical with those of an authentic sample of XI.[11]

XII was obtained by reduction of XI with LAH followed by acetylation; $[\alpha]_D$ − 83° (MeOH) (lit[11] $[\alpha]_D$ − 84°). NMR data: s. 5·14 (H_1), two d. 5·40–5·75 (H_2 and H_3, $J_{2,3}$ ~ 6 Hz), mass spectrum of XII, m/e: 244 (M^+-15), 173 (M^+-$CH_3CHNHCOCH_3$), 86($CH_3CHNHCOCH_3$) (Found: C, 54·55; 54·52; H, 8·17; 8·19; N, 4·98; 5·12. $C_{12}H_{21}NO_5$ requires: C, 55·56; H, 8·16; N, 5·40%).

IV (0·9 g) with NaN_3 (0·3 g) was boiled in DMF (20 ml) for 2 h. The reaction mixture was treated as described above. XIII (0·3 g) was obtained by chromatography on an alumina column (gradient elution, 0 to 25% benzene in hexane); R_f 0·6 (silica gel, B). $[\alpha]_D$ − 31° (MeOH). IR spectrum: 2100 cm^{-1}. NMR data; s. 5·27 (H_1), q. 5·42 (H_3, $J_{3,2}$ 6 Hz, $J_{3,4}$ ~ 1Hz), d. 5·65 (H_2, $J_{2,3}$ ~ 6 Hz), q. 6·33 (H_4, $J_{4,3}$ ~ 1 Hz, $J_{4,5}$ ~ 10 Hz).

XIV was obtained by reduction of XIII with LAH and subsequent acetylation; $[\alpha]_D$ − 29° (MeOH). NMR spectrum: s. 5·27 (H_1), s. 5·55 (H_2 and H_3), mass spectrum of XIV, m/e: 244 (M^+-15), 173 (M^+-$CH_3CHNHCOCH_3$), 86 ($CH_3CHNHCOCH_3$) (Found: C, 55·61; 55·67; H, 8·18; 8·09; N, 5·35; 5·33. $C_{12}H_{21}NO_5$ requires: C, 55·56; H, 8·16; N, 5·40%).

Reaction of iodides II *and* III *with sodium benzoate*. II (0·15 g) was boiled in DMF (10 ml) with PhCOONa (0·3 g) for 20 h. The mixture was poured into benzene, the benzene layer washed with water, dried with $MgSO_4$, filtered and evaporated. The residue (0·07 g) contained II (85%) and unidentified substances (15%) (GLC on 200 × 0·3 cm column with polyethylene glycol 20000 on Celite, 150°).

III (0·44 g) was boiled in DMF (10 ml) with PhCOONa (0·6 g) for 6 h. The mixture was treated as described above. Chromatography of the resulting syrup (0·17 g) on an alumina column (gradient elution, 0 to 25% benzene in hexane) gave rise to a mixture of XIX with other unsaturated derivatives (0·09 g, 33%), R_f 0·65 (silica gel, C) and pure XVIII (0·01 g, 4%), R_f 0·53 (silica gel, C), $[\alpha]_D$ − 53° ($CHCl_3$) (lit[9] $[\alpha]_D$ − 57·9°).

NMR data: s, 5·22(H_1), s. 5·56(H_2 and H_3), m. 4·55–5·15($2H_6$), m. 3·9–4·5(H^5), mass spectrum of XVIII, m/e: 200(M^+), 185($M^+ - 15$), 173(M^+-CH_2=CH—), 169(M^+-31). A mixture of VIII and XVII was also present (0·041 g, 9%). The ratio of VIII:XVII was 4:1 (GLC). This mixture was separated by preparative TLC on silica gel; crystalline VIII was obtained, m.p. 95° (from hexane), $[\alpha]_D$ − 36° (MeOH); mass spectrum of VIII, m/e: 307 (M^+-CH_3), 291 (M^+-OCH_3), 173 (M^+-$CH_3CHOCOPh$) 149 ($CH_3CHOCOPh$). Syrupy XVII has $[\alpha]_D$ − 75° ($CHCl_3$), NMR data: m. 4·90–5·15 (H_5), s. 5·15 (H_1), q. 5·35 (H_3, $J_{3,2} \sim 6$ Hz, $J_{3,4} \sim 1$ Hz), d. 5·50 (H_2, $J_{2,3} \sim 6$ Hz). Mass-spectra of VIII and XVII are identical (lit for VIII[10]: m.p. 93·5–95° (from MeOH), $[\alpha]_D$ − 38°). Authentic sample of XVII[10] had $[\alpha]_D$ − 78° ($CHCl_3$). Its IR and mass spectra were identical with those of XVII, obtained from III.

Destructive oxidation of a mixture of XIX *with other unsaturated monosaccharides.* A soln of a catalytic amount of OsO_4 in H_2O (2 ml) was stirred magnetically for 2 h at room temp. The mixture of XIX with other unsaturated monosaccharides (0·1 g, R_f 0·65 (C)) in dry ether was added and resulting emulsion stirred for 2 hr at room temp. $NaIO_4$ (0·1 g) was added stepwise. Acetaldehyde was removed from the resulting mixture by an N_2 stream and identified as its 2,4-dinitrophenylhydrazone: m.p. 163–164° (from EtOH) (lit[18] 167° (EtOH)); λ_{max} (hexane) 340 μ (lit[19] 340 μ (hexane)). Then the mixture was extracted with $CHCl_3$, washed with water, $Na_2S_2O_3$ soln, water again and then dried over $MgSO_4$, filtered and evaporated. The residue was treated with KBH_4 in MeOH at room temp, hydrolyzed with 2N H_2SO_4 at 100° for 2 h and reduced again with KBH_4 in MeOH at room temp. Erythritol and glycerol (in small amounts) were identified by paper chromatography (with three mobile phases: n-butanol: pyridin: H_2O; 6:4:3, methylethylketone: AcOH sat soln of H_3BO_3; 9:1:1 and n-butanol: EtOH: H_2O; 4:1:1) and by GLC (as acetates).

Reaction of iodides II, III *and* IV *with potassium thiolbenzoate.* III (0·8 g) and PhCOSK (2g) in DMF (20 ml) were heated at 110° for 2 h under N_2. The mixture was treated as described for the reaction of II with NaN_3 (see above). XX was obtained by chromatography on silica gel column (elution with benzene); m.p. 104° (from EtOH (lit[14] 104–105° (from EtOH)). (Found: S, 9·50; 9·37; $C_{17}H_{22}O_5S$ requires: S, 9·50%). $[\alpha]_D$ − 4·75° (CH_3OH). IR spectrum of XX: 1665 cm^{-1}, mass spectrum, m/e: 323 (M^+-15), 173 (M^+-$CH_3CHSCOPh$), 141 (M^+-$CH_3CHSCOPh$-CH_3OH), 115 (M^+-$CH_3CHSCOPh$-CH_3COCH_3). IR, NMR and mass spectra of XX[14] were identical with those of XX synthesized from III.

Similarly IV (0·1 g) reacted with PhCOSK (0·25 g); XXI (0·04 g, 39%) was obtained and purified by TLC on alumina. IR spectrum of XXI: 1660 cm^{-1}, $[\alpha]_D$ − 43° (CH_3OH). NMR spectrum: s. 5·3 (H_1), s. 5·54 (H_2 and H_3). Mass spectra of XXI and XX are practically identical.

II (0·41 g) and PhCOSK (0·8 g) in DMF (20 ml) were heated at 120° for 28 h under N_2. The reaction mixture was treated as described above. XXII (0·15 g, 35%) was obtained by column chromatography on silica gel; $[\alpha]_D$ − 58° (CH_3OH). IR spectrum of XXII: 1670 cm^{-1}. NMR data (in benzene): s. 5·14 (H_1), s. 7·05 (OCH_3 group), d. 8·75 ($3H_6$, $J_{5,6} \sim 6$ Hz), two s.: 8·49 and 8·88 (6H, isopropylidene group). The spin-spin coupling constant $J_{4,5}$ ($\sim$ 3·78 Hz) was found by spin decoupling exp. XXII (0·01 g) was boiled in EtOH in the presence of Raney Ni and the soln evaporated after filtration. The resulting syrup contained V without admixture of VI. The same result was obtained by treating the reaction mixture with Raney Ni before isolation of XXII by chromatography on silica gel.

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