Nitrogen-containing Carbohydrate Derivatives. Part XXVII.† Synthesis and Reactions of 3-Cyano-3-deoxy-glycose Derivatives ‡

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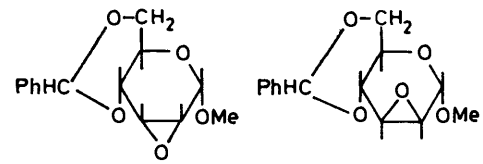
Treatment of sugar oxirans with hydrogen cyanide–triethylaluminium in ether has been shown to be a useful method for the synthesis of cyano-deoxy-glycoses. Reactions of such compounds have been studied, in particular epimerisation at the cyanide-bearing centre, and formation of cyano-olefin derivatives.

MANY naturally occurring monosaccharides are branched-chain sugars, in which the branch generally contains one but sometimes two or three carbon atoms. Such a branch is usually a simple alkyl group but may be a functional group such as formyl.[1] Branched-chain sugars may be further subdivided into those with R–C–OR′ at the branch point and those with R–C–H. Those of the former type are readily accessible from the appropriate carbonyl sugar by the action of alkyl-lithiums or Grignard reagents.[1] Little synthetic work has been reported on the second type of compound, and a general method for introduction of a carbon atom that would allow wide modifications in the branching group was therefore sought. The cyano-group was one with much potential and so methods of introducing it into sugar molecules were investigated. The most obvious precursors appeared to be oxirans.

The choice of a source of the cyano-group and a solvent for oxiran opening needed caution. Metal cyanides give rise to alkaline solutions whenever water is present and oxirans are opened by alkali; also any cyano-group introduced could well be hydrolysed in the alkaline solution. Non-aqueous systems are therefore preferable.

The first experiments were carried out on methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allo- and -manno-pyranosides (1) and (2), with sodium or potassium cyanide in *NN*-dimethylformamide (DMF). We were unable to characterise the products. During the course of these experiments, the opening of steroidal oxirans with hydrogen cyanide–triethylaluminium in tetrahydrofuran (THF) was reported.[2] In all cases cited, the only products were the cyano-alcohol expected to be formed by the Fürst–Plattner mode[3] of oxiran opening. The reaction of hydrogen cyanide-triethylaluminium with methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-manno-pyranoside (2) in THF was therefore studied. Chromatography of the product mixture gave two substances (A) and (B). Product (A), which gave mono-*O*-acetyl, -tosyl, and -brosyl derivatives, yielded correct analytical figures for a methyl 4,6-*O*-benzylidene-2(3)-cyano-2(3)-deoxy-α-D-glycopyranoside, which the Fürst–Plattner Rule[3,4] would predict to have the 3-cyano-3-deoxy-*altro*-structure (3). Hydrolytic removal of the benzylidene group gave a methyl cyano-deoxy-α-D-glycoside that consumed no periodate, confirming that the cyano-group was at C-3. Because no other compounds of this type were available, an *X*-ray structure determination of the brosyl derivative (5) was undertaken,[5]



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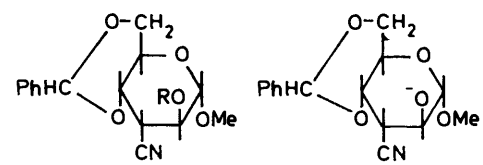


(3) R = H (3a)
(4) R = *p*-$MeC_6H_4SO_2$
(5) R = *p*-$BrC_6H_4SO_2$
(6) R = $[CH_2]_4 \cdot O \cdot [CH_2]_4 \cdot OH$

which confirmed that compound (A) was methyl 4,6-*O*-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside (3). N.m.r. data were in accord with this assignment.

Substance (B) contained OH, CN, and Ph groups, as shown by its i.r. spectrum. The molecular weight obtained by osmometry was 457 and that by mass spectrometry 434·905; product (B) mono-acetate gave a molecular ion at *m/e* 477·234. Thus (B) has the formula $C_{20}H_{33}NO_7$. The mass spectral fragmentation pattern and the i.r. spectrum both indicated that the benzylidene acetal and methoxy-groups had been retained. Thus any structural differences from the starting compound must be at C-2 and C-3. The n.m.r. spectrum of the acetate of (B) showed that a signal for *two* protons had shifted downfield with respect to the spectrum of (B), and so a $-CH_2 \cdot OH$ group must be present. Since a CN group is also present, a $C_7H_{14}O_2$-($CH_2 \cdot OH$) residue remains. THF is known to dimerise under the influence of alkylaluminiums, and indeed the reaction is known to be catalysed by epoxides such as

† Part XXVI, R. D. Guthrie and A. M. Prior, *Carbohydrate Res.*, 1971, **18**, 373.

‡ Preliminary reports, *Chem. Comm.*, 1968, 1273: *Carbohydrate Res.*, 1969, **9**, 254.

[1] For recent examples see ' Carbohydrate Chemistry,' (Chem. Soc. Specialist Periodical Reports), Vols. 1—4, 1967—1970.

[2] W. Nagata, M. Yoshioka, and T. Okumura, *Tetrahedron Letters*, 1966, 847; full details in W. Nagata, M. Yoshioka, and T. Okumura, *J. Chem. Soc.* (*C*), 1970, 2365.

[3] A. Fürst and P. A. Plattner, Abstracts of 12th Internat. Congress Pure Appl. Chem., New York, 1951, p. 409.

[4] N. R. Williams, *Adv. Carbohydrate Chem.*, 1970, **25**, 109.

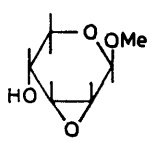
[5] B. E. Davison and A. T. McPhail, *J. Chem. Soc.* (*B*), 1970, 660.

epichlorhydrin.[6] The foregoing residue is therefore presumed to be the system O·[CH_2]$_4$·O·[CH_2]$_4$·OH. The anomeric proton signal occurred as a singlet in the n.m.r. spectrum and so the group at C-2 is in an axial position. Further experiments showed that (A) and (B) were formed independently from the epoxide and also that (A) was unchanged when exposed to the reaction conditions for several days. It is concluded therefore that both (A) and (B) arise from the intermediate anion (3a), which either picks up a proton or attacks THF, so that (B) has the *altro*-configuration (6). No product of this type was reported [2] in any of the steroid ring-opening reactions.

The reaction was considerably improved by replacing the THF by diethyl ether. Triethylaluminium was more reactive in ether than in THF, as shown by the vigorous reaction on addition of hydrogen cyanide. The reaction with compound (2) yielded only the required cyanohydrin (3) as shown by t.l.c. This was obtained in 65% yielded by crystallisation; no by-products were observed.

Attempts were then made to extend the reaction to methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (1), using ether as solvent. Five products were formed, all showing OH and CN bands in their i.r. spectra and one a carbonyl band; we were unable to prepare crystalline derivatives of any of the compounds. The reactions of this epoxide with triethylaluminium in hydrogen cyanide were not therefore studied further. The more complicated nature of the reaction with the anhydro-alloside (1) may be due to further reaction of the expected 2-cyano-2-deoxy-*altro*-product. In this the carbon–oxygen bonds in the ring and the methoxy-group are β to the cyano-group and therefore labile to base. In this connection it is interesting that the benzylidene group was removed from compound (3) on treatment with alkali. Similar situations have been observed with the analogous nitro-sugars.[7]

During the work with the hydrogen cyanide–triethylaluminium reagent, Williams [8] published details of the ring-opening of methyl 2,3-anhydro-β-D-ribopyranoside (7) with cyanide ion in an aqueous buffered system (pH 8·5). The product was a mixture of methyl 3-cyano-3-deoxy-β-D-xylo- and -ribopyranosides [(8) and (9), respectively]. The latter was shown to arise



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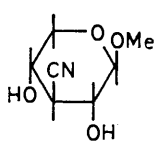

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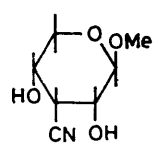


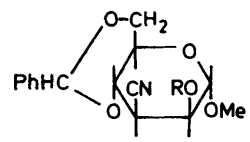
(9)

from the former by epimerisation at C-3 during the reaction. Use of the triethylaluminium–hydrogen cyanide reagent on the L-isomer of (7) gave the expected L-isomer of (8) (60%); as predicted no epimerisation occurred by this method.

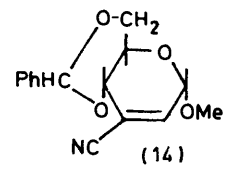
[6] Belg. Pat. 630,098 (Japanese Chemical Fibres Research Institute).

A A

In view of Williams' work [8] and of the known lability of the proton in an H–C–CN system, it was expected that the 3-cyano-3-altroside (3) could be epimerised with alkali to the *manno*-isomer (10). Treatment with cold



(10) R = H
(11) R = Me
(12) R = Et
(13) R = *p*-$BrC_6H_4SO_2$



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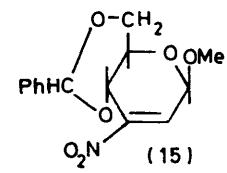

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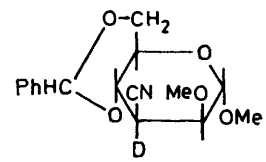

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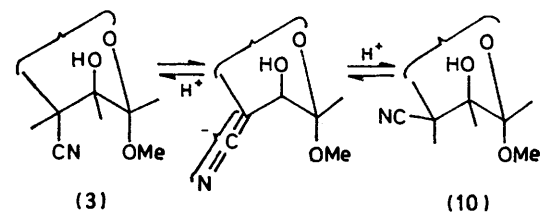


(3) (10)

SCHEME 1

dilute methanolic sodium methoxide for 5 days effected the epimerisation in 80% yield. The equilibrium would be expected to lie on the side of (10) rather than (3), because of the 1,3-interaction between the 1-OMe and 3-CN groups in the latter (Scheme 1). [This interaction in (3) is seen clearly in the *X*-ray structural study.[5]]

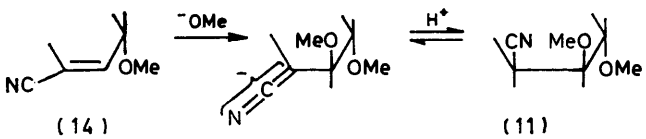
It was thought of interest to make an *X*-ray structural study of a derivative of (10) for comparison with that of (3) and so attempts were made to prepare the 2-*O*-brosyl derivative (13). Treatment of compound (10) with brosyl chloride in cold pyridine, however, did not give the required ester, but the cyano-olefin (14), formed presumably by elimination in the required compound, in which the C-3 proton and the *O*-brosyl leaving group are *trans*-diaxial. The structure of compound (14) followed from its n.m.r. spectrum (see Experimental section) and elemental analysis. Analogous nitro-olefins, such as (15), have been successfully used [7] as intermediates in a wide range of amino-sugar syntheses, and it was possible therefore that (14) could fulfill a similar role in branched-chain sugar chemistry. Other methods (see Experimental section) were therefore sought for its preparation, the most convenient of

[7] H. H. Baer, *Adv. Carbohydrate Chem.*, 1969, **24**. 67.
[8] N. R. Williams, *Chem. Comm.*, 1967, 1012.

which was treatment of (4) with diethylamine (90% yield). The reaction with diethylamine is interesting in that this reagent adds to nitro-olefins;[7] this difference reflects the greater activation of the double bond by a nitro-group than by a cyano-group.

As expected, the cyano-olefin added methanol or ethanol in the presence of a trace of sodium to give the appropriate 2-alkoxy-3-cyano-3-deoxy-product; these compounds were shown to have the *manno*-configuration [(11) or (12)] by n.m.r. spectroscopy ($J_{1.2}$ *ca.* 1; $J_{2.3}$ 3; $J_{3.4}$ 11 Hz), and in the case of the methoxy-derivative by synthesis[9] by standard procedures from (10). Compounds (11) and (12) were presumably formed as shown in Scheme 2, in which the incoming alkoxy-group approached from the opposite side of the molecule from the anomeric methoxy-group. Treatment of compound (4) with methanol containing a little sodium also gave (11) in high yield. Addition of methan[^{2}H]ol to compound (14) gave the [3-^{2}H]-analogue (16) of (10). Compound (14) would probably undergo a wide variety of other additions.

I.r. Spectra of Cyano-deoxy-sugars.—Bellamy[10] has noted that the intensity of the C≡N absorption is very variable and in general is diminished by neighbouring oxygen functions. The point was made that absence of a band cannot be taken as absence of the group. The i.r. spectra of esters of (3) provided an example of this phenomenon, the intensity of $\nu_{C\equiv N}$ varying with the group on C-2 in the order OH > OAc > OTs > OBs, which is the order of the electron-withdrawing capacity of the groups. In all cases the absorption occurred at 2250—2265 cm^{-1}.



SCHEME 2

N.m.r. Spectra.—The spectra of the compounds discussed showed the expected features. Detailed analysis is reserved for a later paper. The only new feature concerns the proton on the CN-bearing carbon atom, which gave a signal in the region τ 6·65—6·80, so that in several cases the signal was partly obscured by the methoxy-signal. The assignment was verified by preparation of compound (16), in the spectrum of which such a signal was absent.

EXPERIMENTAL

T.l.c., p.l.c., and column chromatography were all performed on silica gel (Merck GF_{254}). All solvent extracts were washed and dried ($MgSO_4$) before evaporation and solvents were then removed at <50° in *vacuo*. The chromatography solvent was ether–benzene (1 : 1) unless otherwise stated. Compounds were identified by comparison of i.r. and n.m.r. spectra, and by t.l.c. Optical rotations quoted are for chloroform solutions.

Reaction of Potassium Cyanide with Methyl 2,3-Anhydro-4,6-O-benzylidene-α-D-allo- and -manno-pyranosides in DMF.—Potassium cyanide (0·08 g), methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside (1) (0·2 g), and ammonium chloride (0·2 g) were dissolved in DMF (35 ml) and water (1·5 ml). The solution was heated under reflux for 4 h, cooled, poured into water (180 ml), and extracted with chloroform. Evaporation of the extracts gave a syrup, which crystallised from ethanol to give the anhydro-alloside (1) (0·05 g), m.p. 202—204°. The aqueous liquors were evaporated to give a red oil, the i.r. spectrum of which indicated the presence of carbonyl and hydroxy-groups. Chromatography failed to separate the mixture. Use of sodium cyanide in DMF gave a similar red oil from which again no characterised products were isolated.

Similar reactions with the anhydro-mannoside (2) gave uncharacterised coloured oils.

Reactions of Triethylaluminium–Hydrogen Cyanide with Methyl 2,3-Anhydro-4,6-O-benzylidene-α-D-mannopyranoside (2) in THF.—Triethylaluminium (55 ml) was transferred under nitrogen to a 1 l flask. Anhydrous THF (440 ml) (prepared by distillation from lithium aluminium hydride and stored over sodium) was cautiously added under nitrogen. A solution of hydrogen cyanide (5·2 ml) in anhydrous THF (50 ml) was added dropwise with stirring; evolution of ethane occurred. The anhydro-mannoside (2) (14 g) in anhydrous THF (200 ml) was added under nitrogen and the solution was set aside for 16 h. The pale yellow product mixture was poured cautiously into 2N-sodium hydroxide solution (140 ml) and ice (140 ml) cooled in ice–water; the temperature was kept below 3°. After evolution of gas had ceased, the suspension was extracted with chloroform and the combined extracts were evaporated to give a syrup (21·3 g). Two products were detected by t.l.c. The syrup was chromatographed on silica (1 kg).

Crystallisation from benzene–light petroleum of the first component (A) gave *methyl 4,6-O-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (3) (5·2 g, 31%), m.p. 150—150·5°, $[\alpha]_D^{25}$ +159° (*c* 1·0) (Found: C, 61·8; H, 5·8; N, 4·7. $C_{15}H_{17}NO_5$ requires C, 61·85; H, 5·9; N, 4·8%).

Continued elution gave a clear syrup (B) which we could not crystallise, *methyl 4,6-O-benzylidene-3-cyano-3-deoxy-2-O-[4-(4-hydroxybutoxy)butyl]-α-D-altropyranoside* (6) [M^+, 434·905. $C_{23}H_{33}NO_7$ requires *M*, 434·905. *M* (osmometry), 457].

Methyl 2-O-Acetyl-4,6-O-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside.—The 3-cyano-altroside (3) (0·5 g) was acetylated with pyridine–acetic anhydride for 16 h and the product was worked up in the usual way. Crystallisation from aqueous methanol gave white needles of *methyl 2-O-acetyl-4,6-O-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (0·3 g, 52%), m.p. 129·5—130°, $[\alpha]_D^{26}$ +93·8° (*c* 0·98) (Found: C, 61·5; H, 5·9; N, 4·2. $C_{17}H_{19}NO_6$ requires C, 61·25; H, 5·75; N, 4·2%).

Acetylation of the Cyano-(hydroxybutoxy)butyl Ether (6).—The cyano-ether (6) (1 g) was acetylated with pyridine–acetic anhydride for 16 h. Work-up gave a syrup, which was purified by p.l.c. to give *methyl 2-O-[4-(4-acetoxybutoxy)-butyl]-4,6-O-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* as a clear syrup $[\alpha]_D^{22}$ +56·5° (*c* 0·84 in $CHCl_3$) (M^+, 477·234. $C_{25}H_{35}NO_8$ requires *M*, 477·236).

Reaction of Triethylaluminium–Hydrogen Cyanide in Diethyl Ether with Methyl 2,3-Anhydro-4,6-O-benzylidene-

[9] S. E. Creasey, D.Phil. Thesis, University of Sussex, 1971.
[10] L. J. Bellamy, 'The Infra-red Spectra of Complex Molecules,' Methuen, London, 1954.

α-D-*mannopyranoside* (2).—Triethylaluminium (4 ml) in anhydrous diethyl ether (35 ml) was treated under nitrogen with hydrogen cyanide (0·4 ml) in anhydrous diethyl ether (4 ml). The anhydro-mannoside (2) (1 g) was added as a suspension in anhydrous diethyl ether (50 ml); dissolution in the reaction medium was immediate. After 16 h the mixture was worked up as for the reaction in tetrahydrofuran to yield a glass. Crystallisation from benzene–light petroleum gave methyl 4,6-*O*-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside (3) (0·7 g, 65%), m.p. 148—149°, $[\alpha]_D^{25}$ +159°, characterised as the 2-acetate, m.p. 129—130°, $[\alpha]_D^{25}$ +94°.

Methyl 4,6-O-*Benzylidene-3-cyano-3-deoxy-2-O-p-tolylsulphonyl-α-D-altropyranoside* (4).—The cyano-altroside (3) (0·2 g.) in pyridine (10 ml) was treated at 0° with tosyl chloride (0·2 g). The solution was allowed to reach room temperature and left for 72 h. Pouring into water gave a white precipitate, which was collected and crystallised from methanol to give white needles of the *product* (0·2 g, 68%), m.p. 138—139·5°, $[\alpha]_D^{25}$ +59° (*c* 0·795) (Found: C, 59·35; H, 5·2; N, 3·0; S, 7·15. $C_{22}H_{33}NO_7S$ requires C, 59·35; H, 5·2; N, 3·2; S, 7·2%).

Methyl 4,6-O-*Benzylidene-2-O-p-bromophenylsulphonyl-3-cyano-3-deoxy-α-D-altropyranoside* (5).—The cyano-altroside (3) (0·5 g) in pyridine (25 ml) was treated with brosyl chloride (0·5 g) and left for 16 h. Pouring on to ice (100 ml) gave a white solid, which crystallised from methanol to give white needles of the *product* (0·24 g, 20%), m.p. 144—145° $[\alpha]_D^{26}$ +84° (*c* 0·855) (Found: C, 49·3; H, 3·9; Br, 15·9; N, 2·8; S, 6·2. $C_{21}H_{20}BrNO_7S$ requires C, 49·4; H, 3·95; Br, 15·7; N, 2·75; S, 6·3%).

Reaction of Methyl 4,6-O-*Benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (3) *with Triethylaluminium–Hydrogen Cyanide in THF*.—Triethylaluminium (2 ml) in anhydrous THF (20 ml) was treated under nitrogen with hydrogen cyanide (0·2 ml) in THF (2 ml). The 3-cyano-altroside (3) (0·5 g) was added and the solution was set aside for 14 days. Work-up as already described gave a solution in chloroform which contained one component. Evaporation gave a clear syrup which crystallised from benzene–light petroleum to yield starting material (0·5 g), m.p. 149—150°.

Debenzylidenation of Methyl 4,6-O-*Benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (3).—The cyano-altroside (0·5 g) was heated with 4% acetic acid (25 ml) for 30 min. The acetic acid and benzaldehyde were removed by co-distillation with water and the aqueous solution was evaporated to yield a water-white syrup (0·4 g).

T.l.c. [methanol–chloroform (7 : 25)] showed one main product and two minor ones. Separation was effected on a column using the same solvent system to give the main product, *methyl 3-cyano-3-deoxy-α-D-altropyranoside* as a clear syrup (0·35 g, 100%), $[\alpha]_D^{25}$ +93·5° (*c* 1·295 in H_2O) (Found: C, 45·2; H, 7·2; N, 6·7. $C_8H_{13}NO_5$ requires C, 47·3; H, 6·4; N, 6·9%); no M^+ in mass spectrum.

Attempts to form the triacetate, tritosylate, and tri-*p*-nitrobenzoate of methyl 3-cyano-3-deoxy-α-D-altroside by the usual methods gave rise to compounds with unsubstituted hydroxy-groups which were not further characterised.

Periodate Oxidation Studies on Methyl 3-Cyano-3-deoxy-α-D-altropyranoside.—Methyl 3-cyano-3-deoxy-α-D-altropyranoside was treated with excess of 0·02M-sodium periodate at pH 4·0. A similar solution of the methyl 4,6-*O*-benzylidene-3-cyano-3-deoxy-α-D-altropyranoside (3) and a blank were prepared. The periodate was estimated by titration (iodine liberation from potassium iodate and titration with N-sodium arsenite) and by optical density measurement at 223 nm. No periodate was taken up during 1 week by either cyano-sugar.

Action of Pyridine on Methyl 4,6-O-*Benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (3).—The cyano-altroside (3) was dissolved in pyridine at room temperature; t.l.c. showed that no change occurred during 20 h.

Reaction of Triethylaluminium–Hydrogen Cyanide in THF with Methyl 2,3-*Anhydro*-4,6-O-*benzylidene-α-D-allopyranoside* (1).—Triethylaluminium (13 ml) in anhydrous THF (110 ml) was treated under nitrogen with hydrogen cyanide (1 g) in anhydrous THF (10 ml). When the evolution of ethane had subsided, the anhydro-alloside (1) (3·5 g) in THF (50 ml) was added under nitrogen. The solution was set aside for 4 weeks and worked up as described previously; the temperature was not allowed to rise above 4° during the treatment with sodium hydroxide. A light yellow syrup (4·8 g) was obtained, the i.r. spectrum of which showed CN (2260), OH (3490), and phenyl (705 and 765 cm^{-1}) bands. T.l.c. [methanol–chloroform (1 : 40)] showed eight components. The syrup was introduced on to a silica gel (175 g) column and eluted with chloroform. Four fractions were collected, the main one (2·9 g) of which showed CN bands in the i.r. spectrum (2260), in addition to OH (3480) and phenyl (705 and 765 cm^{-1}). The first fraction (0·05 g, 1·4%) was shown to be starting material. Analysis showed fraction four to be a mixture of two compounds. Attempts to form derivatives for separation failed. Repetition of the foregoing reaction but for a 16 day period gave a mixture containing at least eight components (t.l.c.). Starting material (19%) was recovered.

Reaction of Triethylaluminium–Hydrogen Cyanide in Diethyl Ether with Methyl 2,3-*Anhydro*-β-L-*ribopyranoside*.—Triethylaluminium (8 ml) in diethyl ether (80 ml) was treated under nitrogen with hydrogen cyanide (0·8 ml) in diethyl ether (8 ml). The 2,3-anhydro-riboside (1 g) in diethyl ether (15 ml) was added under nitrogen and the resulting solution was set aside for 16 h. The mixture was poured on to ice (150 ml), with the temperature kept below 3°. Vigorous evolution of ethane ensued, concomitant with the formation of a gelatinous mass of hydrated alumina. The suspension was filtered and the alumina was washed with ethanol. The filtrate and washings were concentrated *in vacuo* to yield a semicrystalline mass (1·1 g; ν_{CN} 2265 cm^{-1}) which crystallised completely during 16 h. T.l.c. showed one component plus a trace of a second component. Crystallisation from ethyl acetate gave *methyl 3-cyano-3-deoxy-β-L-xylopyranoside* (0·7 g, 60%), m.p. 126·5—127·5°, $[\alpha]_D^{25}$ +49° (*c* 1·11 in H_2O) (in agreement with the data reported by Williams [8] for the D-compound: m.p. 127—128°, $[\alpha]_D$ −52°), which had i.r. and n.m.r. spectra identical with those of Williams' product.

Methyl 4,6-O-*Benzylidene-3-cyano-3-deoxy-α-D-mannopyranoside* (10) *from Methyl* 4,6-O-*Benzylidene-3-cyano-3-deoxy-α-D-altropyranoside* (3).—(*a*) The cyano-altroside (3) (1 g) in methanol (40 ml) was treated with sodium (0·05 g) and the solution was set aside for 5 days. T.l.c. showed a gradual change into a new product. Estimations based on charring of t.l.c. spots with 50% sulphuric acid gave the ratio of the new product to the cyano-altroside as at least 5 : 1.

The new product was separated by p.l.c. [light petroleum–ether (2 : 5); six passes]. The main band was removed and extracted with chloroform. Evaporation gave white

crystals of *methyl* 4,6-O-*benzylidene*-3-*cyano*-3-*deoxy*-α-D-*mannopyranoside* (10) (0·8 g, 80%), m.p. 164—165° raised by one crystallisation from benzene to 166—167°; $[\alpha]_D^{25}$ −11·3° (*c* 1·19) (Found: C, 61·9; H, 5·8; N, 5·0. $C_{15}H_{17}NO_5$ requires C, 61·85; H, 5·9; N, 4·8%).

The product was characterised [9] as its 2-O-*acetyl derivative*, m.p. 143—145°, $[\alpha]_D^{25}$ −48·8° (*c* 5·1) (Found: C, 60·7; H, 5·8; N, 4·25. $C_{17}H_{19}NO_6$ requires C, 61·3; H, 5·7; N, 4·2%).

(*b*) The cyano-altroside (3) (0·1 g) in methanol (4 ml) containing sodium (5 mg) was heated at reflux. T.l.c. as in (*a*) showed that after 10 min about 60% of the cyano-mannoside had been formed, and after 20 min about 75% (with three other components); after 45 min one slower moving spot was increasing in intensity. The mixture was treated with concentrated hydrochloric acid (0·05 ml) followed by water (20 ml). The white precipitate was collected and crystallised from benzene–light petroleum to yield the mannopyranoside (10) (0·05 g, 50%), m.p. 164—165°.

Attempted Formation of the p-*Bromophenylsulphonyl Derivative* (13) *of Methyl* 4,6-O-*Benzylidene*-3-*cyano*-3-*deoxy*-α-D-*mannopyranoside* (10); *Formation of Methyl* 4,6-O-*Benzylidene*-3-*cyano*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranoside* (14).—The methyl cyano-mannoside (10) (1·0 g) in pyridine (20 ml) was treated with brosyl chloride (1·0 g). The mixture was set aside for 10 days, then poured into ice–water (200 ml), and the white solid which separated was collected and crystallised from benzene–light petroleum. P.l.c. gave needles of *methyl* 4,6-O-*benzylidene*-3-*cyano*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranoside* (14) (0·44 g, 45%), m.p. 214·5—215·5°, $[\alpha]_D^{26}$ +58·3° (*c* 0·94) $\lambda_{max.}$ 211 nm, M^+ 273·099 ($C_{15}H_{15}NO_4$ requires *M*, 273·100), τ (100 MHz; $CDCl_3$) 2·4—2·9 (5H, m, Ph), 3·58 (1H, t, $J_{1.2} = J_{2.4} = 2·5$ Hz, H-2), 4·44 (1H, s, methine), 5·05 (1H, q, $J_{1.4}$ 1·0 Hz, H-1), 5·6—6·4 (4H, m, H-4, -5, -6, -6′), and 6·57 (3H, s, OMe).

Methyl 4,6-O-*Benzylidene*-3-*cyano*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranoside* (16).—(a) *From methyl* 4,6-O-*benzylidene*-3-*cyano*-3-*deoxy*-α-D-*altropyranoside* (3). (i) The 3-cyano-altroside (3) (0·2 g) in toluene (20 ml) was treated with methanol (1 ml) and dry alumina [Spence type H (0·5 g)] and the suspension was heated under reflux for 24 h. Cooling gave methyl 4,6-*O*-benzylidene-3-cyano-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (0·05 g, 26%), m.p. 212—214°.

(ii) The cyano-altroside (3) (0·1 g), tosyl chloride (0·065 g), and triethylamine (0·6 ml) in chloroform (6 ml) were stirred at room temperature for 7 days. Work-up by chloroform–water partition gave the cyano-ene (14), m.p. 209—210° (42%).

(b) *From methyl* 4,6-O-*benzylidene*-3-*cyano*-3-*deoxy*-2-O-*tosyl*-α-D-*altroside* (4). (i) Compound (4) (0·15 g) in THF hydrofuran (4·5 ml) containing diethylamine (was stirred for 2 h at room temperature; t.l.c. showed one product. Evaporation and crystallisation gave white needles of the cyano-olefin (14) (0·125 g, 89%), m.p. m.p. 213—214°.

(ii) [9] Use of triethylamine in place of diethylamine gave the cyano-ene (91%), m.p. 210—211°, but a reaction time of 96 h was needed. At reflux the reaction time was shortened to 4 h (yield 91%).

(iii) [9] The cyano-tosyl-altroside (4) was refluxed in pyridine for 4 h to give the cyano-ene (53%), m.p. 210—212°.

Methyl 4,6-O-*Benzylidene*-3-*cyano*-3-*deoxy*-2-O-*methyl*-α-D-*mannopyranoside* (11).—(*a*) The tosyl-altroside (4) (0·1 g) was suspended in methanol (7·5 ml), and sodium (9 mg) was added. The suspension was shaken for 16 h, after which time dissolution was complete. T.l.c. showed that all starting material had disappeared and that one new product had been formed. The solution was poured on ice–water (100 ml) and the white precipitate was collected. Crystallisation from aqueous methanol gave needles of *compound* (11) (90%), m.p. 141—141·5°, $[\alpha]_D^{26}$ −113·6° (*c* 0·85) (Found: C, 63·0; H, 6·6; N, 4·5. $C_{16}H_{19}NO_5$ requires C, 62·9; H, 6·3; N, 4·6%).

(*b*) The cyano-ene (14) (0·03 g) was treated with methanol (2 ml) containing sodium (10 mg). The solution was shaken for 20 h at room temperature and evaporated to dryness *in vacuo*, and the residue was crystallised from aqueous methanol to give methyl 4,6-*O*-benzylidene-3-cyano-3-deoxy-2-*O*-methyl-α-D-mannopyranoside (11) (0·023 g, 69%), m.p. 138—139°.

(*c*) [9] The cyano-mannoside (10) (97 mg) and methyl iodide (0·21 ml) were dissolved in the minimum amount of dry methanol at 0° and treated during 30 min with portions of freshly prepared dry silver oxide (total 387 mg). The mixture was stirred for 68 h. Work-up in the usual way gave a brown product which was subjected to p.l.c. to yield starting material (10) (40 mg) and the required product (11) [44 mg, 73% based on used (12)], m.p. 138·5—140°.

Addition of Methan[^{2}H]*ol to Methyl* 4,6-O-*Benzylidene*-3-*cyano*-2,3-*dideoxy*-α-D-erythro-*hex*-2-*enopyranoside* (14).—The reaction was performed as before using methan[^{2}H]ol and taking precautions to exclude all water. Evaporation gave *methyl* 4,6-O-*benzylidene*-3-*cyano*-3-*deoxy*-3-*deuterio*-2-O-*methyl*-α-D-*mannopyranoside*, m.p. 138—139°, n.m.r. spectrum identical with that of the non-deuteriated analogue except for the lack of the one-proton signal at τ 6·7.

Methyl 4,6-O-*Benzylidene*-3-*cyano*-3-*deoxy*-2-O-*ethyl*-α-D-*mannopyranoside* (12).[9]—Repeat of the foregoing methanol addition with ethanol gave the *product* (60%), m.p. 94—95·5° (Found: C, 63·7; H, 6·7; N, 4·5. $C_{17}H_{21}NO_5$ requires C, 63·95; H, 6·6; N, 4·4%).

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