*Carbohydrate Research*, 157 (1986) 65–81
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands



# TWO SYNTHESES OF 3-AMINO-3-DEOXY-α-D-ALTROPYRANOSYL 3-AMINO-3-DEOXY-α-D-ALTROPYRANOSIDE, A NEW ANALOG OF α,α-TREHALOSE, INVOLVING REDUCTION OF A DIAZIDE AND REDUCTIVE AMINATION OF A DIKETONE

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(Received February 7th, 1986; accepted for publication, April 7th, 1986)

ABSTRACT

A new diamino sugar, 3-amino-3-deoxy-α-D-altropyranosyl 3-amino-3-deoxy-α-D-altropyranoside (**5**) was synthesized by two routes starting from α,α-trehalose. The first route involved reduction and deprotection of a previously described, benzylidenated diazido analog. The second approach proceeded from the known 2,2′-di-*O*-benzyl-4,6;4′,6′-bis-*O*-benzylidene derivative of α-D-altropyranosyl α-D-altropyranoside, to the corresponding 3,3′-diketone, which was subjected to reductive amination with sodium cyanoborohydride and ammonium acetate. The major product, separated in 39% yield from by-products after *N*-acetylation, was deprotected to give **5**. Four by-products were isolated in low yields and determined to be monoaminated analogs which comprise two epimeric, 3′-hydroxy structures and two 3′-epimeric, 3′-cyano-3′-hydroxy structures in their non-aminated residues. A number of observations concerning the $^{13}C$- and $^{1}H$-n.m.r. spectra of the products are discussed, especially with regard to chemical-shift dependencies for certain ring and substituent protons, and attention is drawn to some inter-residue shielding phenomena.

## INTRODUCTION

The natural occurrence of several aminated disaccharides of the α,α-trehalose type as antibiotically active metabolites of fungi has prompted us to undertake the chemical synthesis of new analogs in this field, in the hope of generating compounds of biochemical or medicinal interest[1]. In continuation of these studies, the synthesis of the hitherto unknown 3-amino-3-deoxy-α-D-altropyranosyl 3-amino-3-deoxy-α-D-altropyranoside (**5**) is described, and physical and spectral data are recorded for some monoaminated analogs (**13–16**) that were obtained as minor products in the course of this work.

0008-6215/86/$ 03.50 

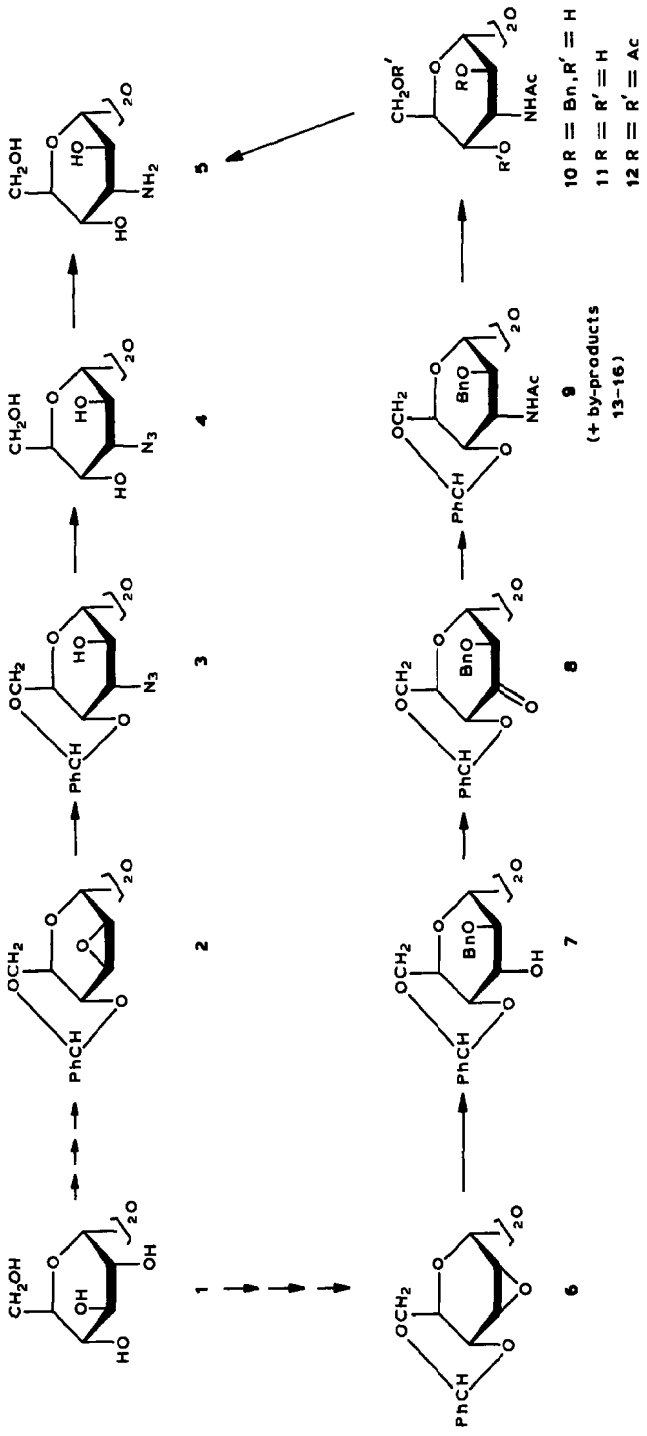
RESULTS AND DISCUSSION

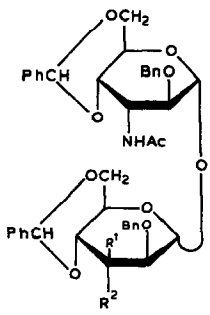
In 1973, Hough and his co-workers[2] studied the oxirane-ring opening, by azide ion, of various 2,3-anhydro derivatives obtainable from $\alpha,\alpha$-trehalose (**1**), and used this method for a synthesis of the 2,2′-diamino regioisomer of **5**. They also laid the groundwork for a convenient approach to **5** by preparing the D-*altro*, D-*altro* 3,3′-diazido-4,6;4′,6′-diacetal **3** in high yield (88%) from the D-*manno*,D-*manno* diepoxide **2**. Compound **3** has now been hydrolytically debenzylidenated to give **4** which, by transfer hydrogenation with palladium and cyclohexadiene, furnished the target disaccharide **5**. The overall yield was 21% from **2**, or 8% from **1**.

Simultaneously, an alternative synthesis of **5** was elaborated, also starting ultimately from **1**. It proceeds *via* the known[2] D-*allo*,D-*allo* diepoxide **6**, which is available somewhat more conveniently and in higher yield (67 *vs.* 37%)[3] than its stereoisomer **2**. Although this advantage is offset by the greater length of a synthetic sequence comprising six instead of only three steps from the respective epoxide to **5**, a study of the approach appeared worthwhile for reasons of general methodology. It was to be examined whether introduction of nitrogen by the procedure[4] of reductive amination of ketones using sodium cyanoborohydride can be profitable applied to amino disaccharide synthesis. The method has recently been used successfully[5] for the incorporation of diverse amine functions into oxycelluloses, but the aminations generally were incomplete and their stereochemistry was not investigated.

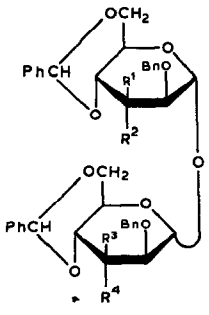
The 2,2′-di-*O*-benzyl-3,3′-diol **7**, recently obtained[3] from **6** in 79% yield, was converted into the diketone **8** by Pfitzner–Moffatt oxidation with dimethyl sulfoxide and acetic anhydride (yield, 82%). Treatment of **8** with ammonium acetate and sodium cyanoborohydride in methanolic solution at 25° led to a very complex mixture of products which, prior to partial, chromatographic resolution, was treated with acetic anhydride in methanol, in order to *N*-acetylate any amines present. The major product then isolated, in up to 39% yield, proved to be the desired D-*altro*,D-*altro* bisacetamido sugar **9**. Hydrolytic debenzylidenation afforded the crystalline derivative **10**, and subsequent, catalytic transfer hydrogenolysis using formic acid[6] removed the benzyl ether groups, to give the deprotected bisacetamido disaccharide **11**, characterized also as its per-*O*-acetyl derivative **12**. *N*-Deacetylation of **11** with aqueous barium hydroxide produced **5**, identical with the product obtained in the aforedescribed, stereospecific synthesis. Confirmation of structure is provided by the $^1$H-n.m.r. data for **9**–**12** (Table I). the overall yield for the six steps from **6** was 10.4%, corresponding to 7% from **1**. With most of the functional-group adjustments proceeding satisfactorily (66–92% yields), it was clearly the crucial amination which was the troublesome link in the chain of reactions. We were curious to uncover the nature of the side-reactions that interfered, especially since the diketone **8** was virtually completely consumed.

Thin-layer chromatography performed following *N*-acetylation of the reaction mixture obtained from **8** revealed a plethora of products ranging widely in

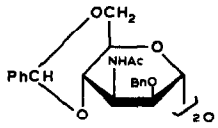

1
2
3
4
5
6
7
8
9
(+ by-products 13–16)
10 R = Bn, R′ = H
11 R = R′ = H
12 R = R′ = Ac



13 $R^1$ = H, $R^2$ = OH
14 $R^1$ = OH, $R^2$ = H
15 $R^1$ = CN, $R^2$ = OH
16 $R^1$ = OH, $R^2$ = CN



17 $R^1$ = $R^3$ = CN, $R^2$ = $R^4$ = OH
18 $R^1$ = $R^4$ = CN, $R^2$ = $R^3$ = OH
19 $R^1$ = $R^3$ = OH, $R^2$ = $R^4$ = CN



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mobility ($R_F$ 0.0–0.9). Column chromatography on silica gel resulted in incomplete recovery (~50%) of the material applied. Numerous homogeneous and inhomogeneous fractions were collected, and the former included four fractions that contained small proportions of components having $R_F$ 0.47, 0.40, 0.38, and 0.33, respectively, eluted prior to **9** ($R_F$ 0.10). These products, isolated in ~4, 2, 8, and 1.5% yield, were characterized by physical, spectral, and microanalytical data, and were determined to be monoaminated, hydroxyl-containing disaccharides. Each gave in the $\delta$ 2.0 region of its $^1$H-n.m.r. spectrum a 3-proton singlet for an acetamido group, and a second singlet appeared after *O*-acetylation. The H-3 signals for the acetamidated pyranosyl residues, occurring in the range of $\delta$ 4.6–4.9 as wide doublet ($J_{3,NH}$ 7–9 Hz) of narrow multiplets ($J_{2,3}$ and $J_{3,4}$ both small), indicated that H-3 was positioned equatorially; the appurtenant NH-3 signals were doublets at lower field in each case. The four by-products, therefore, possessed one 3-acetamidoaltroside unit in common with **9** (which showed the corresponding features). For corroboration, we also analyzed the D-*manno*,D-*manno* isomer* (**20**) of **9**, in which H-3 expectedly resonated as a multiplet with one small and two large couplings. Further spectral analysis revealed that the products having $R_F$ 0.38 and 0.33 had the D-*altro*,D-*altro* (**13**) and D-*altro*,D-*manno* (**14**) structures, respectively, determined from the splitting patterns given by H-3′ and H-4′ in the non-aminated moieties of the compounds and (or) their *O*-acetyl derivatives. It thus became clear that incomplete immonium salt formation[4] prior to reduction is one of the factors liable to curtail the preparative usefulness of the procedure. In fact, small amounts of diols produced by complete reduction of **9** were also detected (see Experimental).

The by-products having $R_F$ 0.47 and 0.40 were found, by elemental analysis, to contain a higher percentage of nitrogen than their less-mobile counterparts.

*Prepared from 3-azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-D-mannopyranosyl 3-azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-D-mannopyranoside[1d] by reduction with lithium aluminum hydride, followed by *N*-acetylation.

Upon brief treatment with alcoholic potassium hydroxide and ferrous sulfate they gave a positive Prussian Blue reaction that indicated the presence of cyanide. (The same test was negative for **13** and **14**.) Although CN stretching vibrations, expected near 2250 $cm^{-1}$ in the i.r. spectrum, were indistinctive (as is often the case for oxygen-containing cyano compounds), the $^{13}C$-n.m.r. spectra exhibited unmistakable signals for the cyano group ($\delta$ 117). Accordingly, the compounds were assigned the cyanohydrin structures **15** and **16**, which were supported by the presence, in their $^{1}H$-n.m.r. spectra and those of their acetates, of clear *doublets* for H-2′ ($J_{1,2}$ ~1 Hz) and H-4′ ($J_{4,5}$ 9–10 Hz).

To facilitate configurational assignment for the quaternary centers (C-3′) in **15** and **16**, the bis-cyanohydrins **17–19** were prepared for spectral comparison. Treatment of the diketone **8** with potassium cyanide in methanol at pH 8 (18 h) gave a mixture of isomers which by chromatography yielded **17** (38%), **18** (36%), and **19** (14%). The proportions of isolated products implied a ratio of 1.75:1 for epimer formation at C-3′, similar to the ratio (2:1) of **15** and **16** isolated. Winternitz and Lukacs[7,8] have found for related, 3-epimeric cyanohydrins (and other C-3 branched analogs) that the $^{13}C$ chemical shifts for C-5 are diagnostic of configuration: when, in a pair of epimers, the oxygen atom is oriented *syn*-axially to H-5, the C-5 resonance occurs at slightly higher field than in the opposite case. Although the differences were small, they appeared consistent and significant. Table II shows good correlations in this regard, justifying the indicated assignments. Thus, the C-5 chemical shift for the cyanohydrin residue in **15** (59.5 p.p.m.) corresponds closely with that for **17** (59.6 p.p.m.) and with one of the C-5 shifts (59.2 p.p.m.) for unsymmetrical **18**, whereas the other C-5 resonance in **18** coincides with that in **16** (62.8 p.p.m.), at lower field. A similar C-5′ chemical-shift difference (3.8 p.p.m.) manifested the C-3′ epimerism in the pair **13**/**14** whose configurations were independently revealed by proton spectra as mentioned before.

Concerning cyanohydrin epimerism, glycos-3-uloses have been known to give kinetic or thermodynamic products depending on reaction conditions[7–12]. The conditions used for the reaction of **8** with cyanide would seem likely to favor thermodynamic control, and the inference may be drawn that the configuration generated preponderantly (D-*altro*) is the more-stable one. However, this remains to be verified by experimentation, in light of previous work. Thus, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose, a monosaccharidic analog of **8** lacking the axial C-2 substituent, gave the D-*ribo* epimer (equatorial CN) under kinetic, and the D-*arabino* epimer (axial CN) under thermodynamic control[7,9,10], and the same was true for 4-*O*-methyl[11] and 4-*O*-methoxymethyl[10] derivatives of 2,6-dideoxy-*erythro*-hexopyranosid-3-uloses. In these cases, the observed stabilities qualitatively conformed with expectations based on conformational free energy, which is[13] lower for CN than for OH. On the other hand, the situation was surprisingly found to be the opposite for cyanohydrins formed from corresponding 4,6-*O*-benzylidene[8] and 4-*O*-methyl[12] derivatives having the D-*threo* configuration. The latter compounds, bearing, like **8**, an axial oxygen atom vicinal to the carbonyl

TABLE I

$^1$H-N.M.R. DATA AT 300 MHz FOR COMPOUNDS **8–20** IN CHLOROFORM-*d* SOLUTION

| *Compound*[a] | *Chemical shifts*[b] *(δ)* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *H-1* | *H-2* | *H-3* | *H-4* | *H-5* | *H-6a* | *H-6e* | *Ph–CH*[c] | *PH–CH$_2$*[d] | *N–H* | *O–H* | *CO–Me*[c] |
| **8** | 5.24d | 3.78d | | 4.83d | ⊢—3.82–3.94m—⊣ | | 4.23q[e] | 5.56 | 4.64,4.46 | | | |
| **9** | 4.84s | 3.89d | 4.52nm | 4.11dd | 3.44dt | 3.75t | 4.16dd | 5.58 | 4.80,4.59 | 5.75d | 1.94 | |
| **10**[f] | 5.23bs | 3.89dd | 4.44t[g] | 3.97dd[g] | ⊢——3.75–3.63 (2 m, 3 H)——⊣ | | | | 4.71s | 6.92d | 1.91 | |
| **11**[h] | 4.91d | ~3.73[i] | 4.08t | 3.86dd | ~3.73[i] ⊢—3.59dd, 3.67dd——⊣ | | | | | | | 1.87 |
| **12** | 5.08d | 4.87dd | 4.70nm | 5.07dd | 3.98m ⊢— 4.21m (2 H)——⊣ | | | | | 6.02d | | 2.01, 2.05, 2.07, 2.13 |
| **13** | 5.01d | 3.56dd | 4.93nm | ~4.11[j] | 3.87dt | 3.78,3.75 | ~4.11[j] | 5.62,5.59 | 4.78, 4.56 | 6.91d | | 1.95 |
| | 5.05bs | 3.69dd | 4.26t | 3.99dd | ~4.09[j] | | ~4.14[j] | | 4.66, 4.59 | | 2.28d | |
| **13ac** | 4.83bs | 3.64dd | 4.67nm | 4.06[k] | 3.39dt | 3.70t | ~4.10[k] | 3.58, 3.56 | 4.78, 4.58 | 5.81 | | 1.99, 1.90 |
| | 4.88bs | 3.71[l] | 5.20t | 4.19dd | 3.87dt | 3.75t | ~4.10[k] | | 4.80, 4.61 | | | |
| **14** | 4.92bs | 3.76dd | 4.66nm | 4.14dd | 3.67dt | 3.78t | 4.14dd | 5.61, 5.52 | 4.80, 4.59 | 5.88d | | 1.96 |
| | 5.03d | 3.71nm[m] | ⊢— 3.90m ——⊣ | | 3.44dt | 3.71t | 4.04dd | | 4.76, 4.68 | | 2.10d | |
| **14ac** | 4.94s | 3.71[n] | 4.77nm | ~4.14dd[o] | 3.71dt | 3.79, 3.78 | 4.14, 4.09 | 5.60, 5.54 | 4.81, 4.58 | 6.08d | | 2.06, 2.03 |
| | 5.02d | 3.96dd | 5.03dd | 4.20dd | 3.56dt | | | | 4.64, 4.56 | | | |
| **15** | 4.90~s | 3.52dd | 4.85nm | 4.06dd | 3.71m | 3.74m | 4.09, 4.07 | 5.67, 5.58 | 4.76, 4.52 | 6.49d | | 1.93 |
| | 4.96d | 3.78d | | 4.14d | 3.92dt | 3.74m | | | 4.88, 4.68 | | 3.64s | |
| **15ac** | 4.67bs | 3.50dd | 4.54m | 4.01[o] | 2.92dt | 3.67t | 4.02dd | 5.62, 5.56 | 4.78, 4.54 | 5.39d | | 2.03, 1.94 |
| | ⊢ 4.53nm (2 H) | | | 4.25d | 3.63dt | 3.75t | 4.19dd | | 4.99, 4.76 | | | |
| **16** | 4.90bs | 3.66dd | 4.86nm | 4.08[o] | 3.77,~3.75 | 3.73t | ~4.07 | 5.59, 5.54 | 4.88, 4.70 | 6.27d | | 2.03 |
| | 5.03d | 3.86d | | 4.03d | | 3.73t | ~4.07 | | 4.81, 4.57 | | 3.50bs | |
| **16ac** | 4.89s | 3.71nm | 4.88nm | ~4.12[o] | ~3.75[p] | ~3.75[p] | ~4.12 | 5.61, 5.57 | 4.81, 4.56 | 6.34d | | 2.10, 2.08 |
| | 4.99d | 4.63d | | 4.19d | 3.93dt | ~3.75[p] | ~4.12 | | 4.58, 4.51 | | | |
| **17** | 4.76d | 3.74d | | 4.11d | 3.77dt | 3.71t | 4.04q[e] | 5.64 | 4.89, 4.69 | | 3.70s | |
| **17ac** | 4.42s | 4.25s | | 4.13d | 3.17dt | 3.62t | 4.03dd | 5.59 | 4.97, 4.68 | | | 2.07 |
| **18** | 4.81d | 3.86d | | 4.10d | 3.83dt | 3.70t | 4.06dd | 5.63, 5.53 | 4.87, 4.62 | | 3.50s | |
| | 4.67bs | 3.83bs | | 3.99d | 3.49dt | 3.67t | 3.98dd | | 4.93, 4.60 | | 3.36s | |
| **18ac** | 4.46bs | 4.61bs | | 4.21d | 3.24dt | 3.62t | 4.05dd | 5.63, 5.51 | 4.99, 4.73 | | | 2.30, 2.09 |
| | 4.61s | 4.37s | | 4.06d | 3.56dt | 3.67t | 3.89dd | | 4.61, 4.36 | | | |
| **19** | 4.57d | 4.05d | | 3.96d | 3.38dt | 3.67t | 4.00dd | 5.54 | 4.92, 4.57 | | 3.37s | |
| **19ac** | 4.84d | 4.49d | | 4.11d | 3.54dt | 3.67t | 3.96dd | 5.55 | 4.68, 4.38 | | | 2.11 |
| **20** | 4.99d | 3.89dd | 4.48dt | ⊢——~3.75m (3 H)——⊣ | | | 4.10q[e] | 5.46 | 4.63, 4.51 | 5.56d | | 1.85 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **8** | 1.4 | | | | 9.3 | | | | |
| **9** | <1 | 3.1 | 6.2 | 4.5 | 9.9 | 10.0 | | 5.0 | 10.3 |
| **10** | 1.3 | 4.0 | 7.3 | 4.0 | 10.0 | | | | |
| **11** | 2.9 | 5.1 | | 4.6 | 8.1 | | 6.4, 2.7 | | 12.2 |
| **12** | 2.7 | 6.1 | 9.5 | 3.2 | 8.1 | | 5.6, 2.9 | | |
| **13** | 1.5 | 2.7 | 9.3 | 4.5 | 9.0 | 9.8 | | 4.4 | 9.0 |
| | 0.5 | 2.7 | | 2.7 | 9.0 | | | | |
| **13ac** | 1 | 2.5 | 8.0 | | | 10.5 | | 4.5 | 10.5 |
| | <1 | | | 2.9 | | 10.5 | | 4.5 | 10.5 |
| **14** | 1 | 2.5 | 7.5 | 4.0 | 10.0 | 10.0 | | 4.5 | 10.5 |
| | 1.4 | | | | | 10.0 | | 5.0 | 10.5 |
| **14ac** | <0.5 | | 8.0 | | | 10.0 | | | 10.3 |
| | 1.7 | 3.3 | | 10.5 | 9.6 | 10.0 | | 4.6 | 10.1 |
| **15** | 1 | 2.2 | 9.0 | 4 | 10 | | | | |
| | 1.0 | | | | 9.5 | 10.0 | | 4.5 | 10.0 |
| **15ac** | 0.8 | 2.5 | 7.0 | 4.1 | 9.6 | 10.0 | | 4.5 | 9.8 |
| | 1.0 | | | | 9.0 | 10.0 | | 4.2 | 9.5 |
| **16** | ~1.3 | ~2 | 8.0 | | | | | | |
| | 0.9 | | | | 9.3 | 10.0 | | 4.5 | 10.0 |
| **16ac** | | ~2 | 9.0 | ~4 | | | | | |
| | 1.2 | | | | 9.7 | 10.0 | | 4.5 | 10.0 |
| **17** | 2.6 | | | | 9.4 | 10.0 | | 3.8 | 10.4 |
| **17ac** | 0.6 | | | | 9.5 | 10.3 | | 5.1 | 10.6 |
| **18** | 1.8 | | | | 9.2 | 10.2 | | 5.1 | 9.6 |
| | <1 | | | | 9.9 | 10.0 | | 5.0 | 10.1 |
| **18ac** | | | | | 9.2 | 10.1 | | 5.0 | 10.1 |
| | | | | | 9.8 | 10.3 | | 5.0 | 10.5 |
| **19** | 1.7 | | | | 9.9 | 10.2 | | 5.6 | 11.0 |
| **19ac** | 1.2 | | | | 9.7 | 10.1 | | 5.0 | 10.1 |
| **20** | 1.7 | 3.5 | 8.0 | ~9 | | | | | |

[a]For the unsymmetrical disaccharides **13–16** (and their acetates, which are designated by the suffix ac), the upper line refers to the 3-acetamido residue, and the lower line to the non-aminated residue, and for **18** (and its diacetate), to the D-*altro* and D-*manno* residues, respectively. Values that could not be specifically attributed to either moiety are centered between the two lines. [b]With reference to the $CHCl_3$ lock signal at 7.23 unless otherwise indicated. Signal assignments were aided by the homonuclear shift-correlation method. [c]Singlets. [d]Centers of doublets ($J_{gem}$ 11.5–12.0 Hz) constituting an AB quartet. [e]Distorted. [f]In acetone-$d_6$ with reference to acetone lock signal at 2.04. [g]After $D_2O$ exchange. [h]In $D_2O$, with acetone lock signal. [i]Part of coinciding multiplets for H-2 and -5. [j]Part of ill-resolved multiplets for H-4,6e,5′,6′e. [k]Part of 3 overlapping doublets of doublets for H-4,6e,6′e. [l]Superposed on center of H-6a triplet. [m]Superposed on center of H-6′a triplet and part of H-5 signal. [n]Narrow signal superposed on center of H-5 signal. [o]Superposed on dd for H-6e. [p]Part of ill-resolved multiplets.

TABLE II

$^{13}$C-N.M.R. SPECTRAL DATA AT 75.43 MHz

| *Compound*[a] | *Residue* | *Chemical shifts (p.p.m.)*[b,c] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | *CO* | *CN* | Ph*CH* | Ph$CH_2$ | *C-1* | *C-3* | *C-5* | *C-6* | $CH_3$ |
| **9** | *altro* | 170.9 | | 101.7 | 72.7 | 92.6 | 47.5 | 59.4 | 68.8 | 23.5 |
| **13** | *altro*[d] | | | 101.3 | 72.2 | 95.3 | 45.9 | 59.2 | 68.9 | 23.4 |
| | *altro*[e] | | | 102.1 | 72.9 | 95.9 | 67.1 | 60.5 | 68.9 | |
| **14** | *altro*[d] | ~170 | | 101.7 | 72.5 | 94.6 | 46.9 | 59.9 | 69.0 | 23.6 |
| | *manno*[e] | | | 102.2 | 74.0 | 93.9 | 68.7 | 64.3 | 68.3 | |
| **15** | *altro*[d] | 170.6 | | 101.5 | 72.2 | 95.6 | 45.8 | 60.4 | 68.8 | 23.4 |
| | *altro*[f] | | 117.8 | 102.1 | 74.9 | 93.9 | 70.5 | 59.5 | 68.2 | |
| **16** | *altro*[d] | 171.3 | | 101.5 | 72.5 | 95.6 | 46.0 | 59.9 | 68.8 | 23.5 |
| | *manno*[f] | | 117.5 | 102.6 | 75.4 | 96.2 | 69.9 | 62.8 | 68.0 | |
| **17** | *altro* | | 117.6 | 102.3 | 74.8 | 93.9 | 70.3 | 59.6 | 68.1 | |
| **18** | *altro* | | 117.5 } [g] | 102.2 | 75.1 | 93.4 | 70.2 | 59.2 | 68.0 } [g] | |
| | *manno* | | 118.0 } | 102.6 | 75.5 | 92.9 | 69.8 | 62.8 | 68.1 } | |

[a]In chloroform-*d*. [b]With reference to the tetramethylsilane signal. [c]The signals for C-2 and C-4 occurred at 74.0 and 74.2 (or reverse) p.p.m. in **9**, and at 76.3 and 76.4 (or reverse) p.p.m. in **17**. For the unsymmetrical compounds they occurred in the same region, and downfield to 78.7 p.p.m.; accurate determination was difficult because of overlap with chloroform signals. [d]3-Acetamido unit. [e]3-Hydroxy unit. [f]3-Cyano-3-hydroxy unit. [g]Or reverse assignment.

group (but at C-4), gave as thermodynamic products those containing an equatorial cyano group.

Inspection of Tables I and II reveals for some of the new compounds certain spectral features that merit additional comment. Thus, some remarkable *inter-residue* influences of structure on chemical shifts are evident in both $^{13}C$- and $^{1}H$-n.m.r. spectra. For example, the four identical 3-acetamido D-*altro* moieties of the unsymmetrical disaccharides **13**–**16**, although showing good general agreement in most of their corresponding $^{13}C$ shift values, do exhibit some minor variations that seem to exceed the expected precision of measurement, and especially noteworthy is the fact that the symmetrical analog **9** gives its C-1 signal 2.7 p.p.m. upfield, and its C-3 signal 1.4 p.p.m. downfield, from the average values for the corresponding signals in **13**–**16** (Table II). In the $^{1}H$ spectra (Table I), dramatic effects of structural change in one residue upon chemical shifts present in the other, structurally unaltered residue are observed. Thus, the NH signal for the 3-acetamido part incurs a great upfield shift upon *O*-acetylation of the second residue when the hydroxyl group in the latter is *axial* (**13**→**13**ac* and **15**→**15**ac, with $\Delta_\delta$ = 1.1 p.p.m. for each), whereas the signal is shifted slightly downfield ($-\Delta_\delta$ = 0.07–0.2 p.p.m.) when the hydroxyl group is equatorial (**14**→**14**ac and **16**→**16**ac). Such *O*-acetylation also affects the position of H-5′ (in the moiety that becomes acetylated), in the sense of moderate upfield shifts (0.2–0.3 p.p.m.) for **13** and **15** (axial O-3), and of small downfield shifts (−~0.1 p.p.m.) for **14** and **16** (equatorial O-3). Most interesting to note, however, is the strong effect on the resonance position of H-5 in the chemically *unaltered* residues of **13** and **15**, which are shifted upfield by 0.48 and 0.95 p.p.m., respectively, compared with the absence of such an effect in **14** and **16**. Similar correlations of chemical shifts for H-5 with configuration at C-3 are seen in the bis-cyanohydrins **17**–**19** and their acetates.

Further regularities are observed in the AB quartets given by the diastereotopic, benzylic protons. The quartet for the benzyl groups in **9** is essentially unchanged for the benzyl groups belonging to the acetamido residues in **13**–**16** and their acetates, but the quartets from the other residues of **13**–**16** as well as those from **17**–**19** are variable and, moreover, subject to characteristic changes with acetylation (Fig. 1). Thus, the signals generally are displaced slightly downfield for the acetate when OH-3 is axial (in **13**, **15**, **17**, and one set of **18**), but upfield when OH-3 is equatorial (in **14**, **16**, **19**, and the second set of **18**). It is seen, furthermore, that a vicinal *O*-acetyl group has almost the same effect on the signal pattern as a vicinal *N*-acetyl group; compare **13**ac with **9**, and **14**ac with **20**. However, acetylation of a given alcoholic residue does not necessarily result in an equal shifting of the A and B protons of the neighboring benzyloxy group; that is to say, the shift difference $\Delta_{A,B}$, which in some instances changes little if at all ($\Delta\Delta_{A,B}$ +0.03 p.p.m. for **15**→**15**ac, zero for **14**→**14**ac), is in other cases significantly increased or decreased, most notably for **13**→**13**ac ($\Delta\Delta_{A,B}$ +0.12 p.p.m.) and **16**→**16**ac ($\Delta\Delta_{A,B}$

*The suffix ac denotes the acetylated derivative.

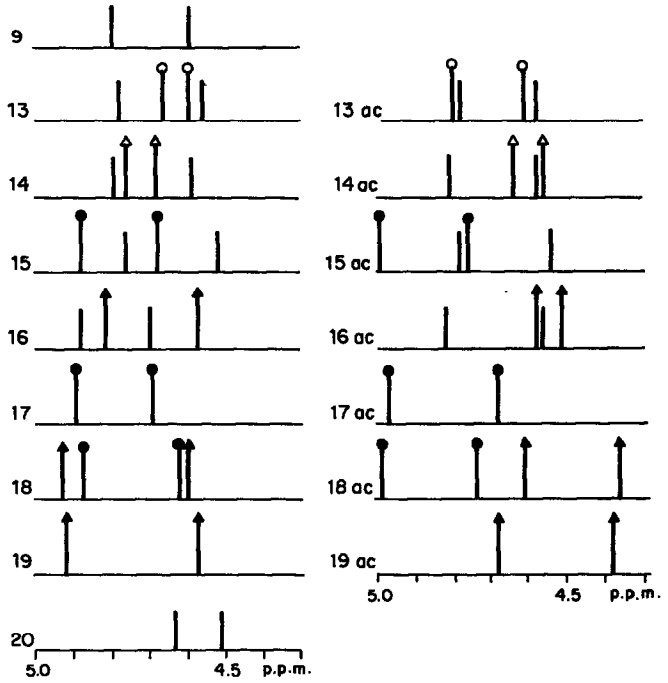


Fig. 1. Schematic representation of $^1$H-n.m.r. signals for the diastereotopic protons of the 2-*O*-benzyl group. The bars represent center lines of 1-proton doublets ($J$ 11.5–12.0 Hz) that form an AB quartet belonging to *a*, a 3-acetamido residue (short, uncapped bars); *b*, a 3-OH or 3-OAc residue, *altro* configuration (♀); *c*, the same, but *manno* configuration (↑); *d*, a 3-cyano-3-hydroxy (or OAc) residue, *altro* configuration (↑); and *e*, the same, but *manno* configuration (↑). For numerical data, see Table I.

−0.17 p.p.m.). Evidently, introduction of a geminal cyano group superposes an effect on that of the oxygen atom present. Equatorial CN deshields both benzylic protons (but unequally so, increasing $\Delta_{A,B}$; see **13**→**17**), whereas axial CN appears to exert deshielding on one and shielding on the other proton, thus likewise increasing $\Delta_{A,B}$ (see **14**→**19**). There are also some noticeable interresidue effects, for the signal pattern of unsymmetrical **18** is not an exact superposition of those of its symmetrical counterparts, and it is noted in particular that $\Delta_{A,B}$ values vary substantially for the constitutionally identical moieties in **19**ac, **18**ac, and **16**ac, which must be due to such long-range interaction.

Rao and Perlin[14] have recently recorded variable shifts for benzylic protons in 2- and 3-*O*-benzyl-α- and β-D-glucopyranosides, and suggested an explanation in terms of certain favored, conformational orientations of equatorial benzyloxy substituents that would expose the A and B protons to differential shielding influences of nearby oxygen atoms. Such considerations can probably be extended to compounds of the type discussed in this study, but at the present time we refrain from drawing more detailed conclusions about the rotameric behavior of axial benzyloxy groups, preferring to await the gathering of further supportive data. We believe,

however, that the spectral consistencies observable among analogous compounds in this investigation convincingly reinforce the structural assignments made.

## EXPERIMENTAL

*General methods.* — For general, preparative, and instrumental techniques see preceding papers[1b,c]. Unless otherwise stated, the following solvent combinations (v/v) were used for t.l.c. and in column chromatography on silica gel: *A*, 1:19 ethanol–ethyl acetate; *B*, the same solvents, but 1:4; *C*, the same, but 1:1; *D*, 1:1 ether–hexane; *E*, 1:3 ethyl acetate–hexane; *F*, the same solvents, but 2:3; *G*, the same, but 1:1; *H*, 5:4:1 methanol–chloroform–ammonia (conc., aqueous). The $^1$H-n.m.r. data refer to 300-MHz spectra.

*3-Azido-3-deoxy-α-D-altropyranosyl 3-azido-3-deoxy-α-D-altropyranoside* (**4**). — 2,3-Anhydro-4,6-*O*-benzylidene-α-D-mannopyranosyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (**2**) was prepared in three steps from α,α-trehalose by improved variants[3] of literature procedures[15]. For conversion into the known[2] bisacetal (**3**) of **4**, a mixture of **2** (0.65 g), sodium azide (1.0 g), water (1.5 mL), and 2-methoxyethanol (10 mL) was stirred for 12 h at the reflux temperature. Processing by partial evaporation of solvent, distribution of the material between water and dichloromethane, evaporation of the washed and dried ($N_2SO_4$) organic phase, and crystallization of the residue from chloroform afforded **3** (673 mg, 88%), m.p. 107–109°, $[\alpha]_D$ +38.3° (*c* 0.7, methanol); [lit.[2] m.p. 108–110° and $[\alpha]_D$ +336° (typographical error?) for **3** obtained in similar yield, but after a reaction performed in hexamethylphosphoric triamide–water medium for 48 h at 80°]; $\nu_{max}^{Nujol}$ 3420 (OH) and 2105 cm$^{-1}$ ($N_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.48 and 7.35 (m, Ph), 5.59 (s, *Ph*CH), 5.00 (s, H-1), 4.31–4.11 (m, unresolved, H-2, 3,4,5,6e), 3.77 (t, $J_{5,6a} = J_{6a,6e} = 10$ Hz, H-6a), and 2.08 (d, exchangeable with $D_2O$, OH).

Compound **3** (4.00 g) in 80% acetic acid (20 mL) was heated on a steam bath for 45 min, after which the acid was evaporated with sequential additions of water and ethanol. The syrupy residue, showing in t.l.c. (solvent *A*) a major spot for **4** ($R_F$ 0.3) and two minor spots due to contaminants ($R_F$ 0.6 and 0.55), was treated on a steam bath for 30 min with 12:5:3 methanol–water–triethylamine (20 mL), which effected removal of the faster-moving, and partial removal of the slower-moving contaminant. Upon recovery by evaporation of its solution, the material was purified further by passage through a column of silica gel (30 × 2.5 cm) with ethyl acetate followed by solvent *A* as eluants. Chromatographically homogeneous **4** was obtained as a solid foam (1.43 g, 52%), $[\alpha]_D$ +167° (*c* 0.7, methanol); $^1$H-n.m.r. (acetone-$d_6$): exchangeable signals for OH at δ 3.41 (t, *J* 4.9 Hz), 4.33 (d, *J* 6.1 Hz), and 4.79 (d, *J* 5.4 Hz); data recorded after $D_2O$ exchange: δ 5.00 (d, $J_{1,2}$ 2.2 Hz, H-1), 4.05 (dd, $J_{3,4}$ 3.9, $J_{4,5}$ 8.7 Hz, H-4), 3.95 (dd, $J_{1,2}$ 2.2, $J_{2,3}$ 4.6 Hz, H-2), 3.87 (2 H, ~t for H-3 superposed on m for H-5), 3.77 (dd, $J_{5,6}$ 3.4, $J_{6,6'}$ 11.5 Hz, H-6), and 3.66 (dd, $J_{5,6'}$ 5.6 Hz, H-6').

*Anal.* Calc. for $C_{12}H_{20}N_6O_9$ (392.3): C, 36.73; H, 5.14; N, 21.42. Found: C, 36.62; H, 5.46; N, 20.91.

*3-Amino-3-deoxy-α-*D*-altropyranosyl 3-amino-3-deoxy-α-*D*-altropyranoside* (**5**) *from* **4**. — To a suspension of Pd–C (10%, 1 g) in water (2 mL) and methanol (8 mL) was added a solution of **4** (981 mg) in methanol (10 mL), followed by 1,4-cyclohexadiene. The mixture was agitated at room temperature in a sonic bath under an $N_2$-atmosphere, and progress of the reaction was monitored by t.l.c. (solvent *H*). Compound **4** ($R_F$ 0.5) disappeared rapidly, an intermediate ($R_F$ 0.35) was seen temporarily, and the formation of **5** ($R_F$ 0.15) together with an almost immobile by-product was complete after 30 min. The catalyst was filtered off and washed with methanol (5 × 25 mL), and the filtrate was concentrated, decolorized with activated charcoal, and evaporated to give a colorless, solid foam (880 mg). The product was crystallized from methanol and ethanol, but the contaminant ($R_F$ 0.05) was troublesome to remove by multiple recrystallizations, and only a small part (66 mg) of **5** could thus be obtained as white, chromatographically homogeneous crystals, $R_F$ 0.14, $[\alpha]_D$ +150° (*c* 0.2, methanol). All of the impure fractions were combined, and acetylated by treatment overnight with acetic anhydride (4 mL) and pyridine (20 mL). After conventional processing of the mixture by evaporation of added portions of toluene the crude, syrupy acetate (1.005 g) gave in t.l.c. (solvent *A*) a major spot for **12** ($R_F$ 0.34) and a minor spot for an impurity ($R_F$ 0.52). Chromatography on a column of silica gel (20 × 2.8 cm) with ethyl acetate as the eluant yielded pure **12** (0.737 g) as a solid foam. This was saponified with $Ba(OH)_2 \cdot 8\ H_2O$ (1.5 g) in boiling water (20 mL) during 2.5 h. The cooled hydrolyzate was saturated with $CO_2$ and filtered, the filter residue was washed with water (3 × 20 mL), and the filtrate adjusted to pH 4 with M sulfuric acid. Following the removal of precipitated $BaSO_4$, the solution was treated with a strong-base anion exchange resin ($OH^-$ form) until it reached pH 8.5. Filtration and exhaustive washing of the resin with water (5 × 20 mL), concentration of the filtrate to a small volume and clarification with charcoal, and further evaporation with added ethanol gave chromatographically pure **5** ($R_F$ 0.14, 378 mg) as a white powder, $[\alpha]_D$ +148° (*c* 0.4, methanol), for a total yield of 444 mg (46.5%). The $^1$H-n.m.r. data ($D_2O$, acetone standard) were identical with those for **5** prepared from **11** (see a subsequent section): $\delta$ 4.90 (d, $J_{1,2}$ 2.2 Hz, H-1), 3.78 (dd, $J_{3,4}$ 4.2, $J_{4,5}$ 8.8 Hz, H-4), ~3.72 (m, 3 H, H-2,5,6), 3.60 (dd, *J* 6.5 and 12.6 Hz, H-6′), 2.95 (t, $J_{2,3} = J_{3,4}$ = 4.2 Hz, H-3), and 3.47q, 1.00t (2.5 H, ethanol of solvation).

In a separate experiment, the entire crude product obtained from 180 mg of **4** was purified *via* the peracetyl derivative as described, but without prior, partial crystallization of **5**. The yield of pure **5** then was 106 mg (60%).

*2-O-Benzyl-4,6-O-benzylidene-α-*D*-*arabino*-hexopyranosyl-3-ulose 2-O-benzyl-4,6-O-benzylidene-α-*D*-*arabino*-hexopyranosid-3-ulose* (**8**). — A solution of diol[3] **7** (7.0 g) in dimethyl sulfoxide (140 mL) and acetic anhydride (70 mL) was stored at room temperature for 24 h, and then introduced dropwise, with stirring, into ice–water (2.5 L). The precipitate was collected, washed with water, and dissolved in acetone without prior drying. The solution was concentrated (to remove most of the acetone), and the material was then distributed between

dichloromethane and water. The organic phase was washed twice with water, dried ($Na_2SO_4$), and evaporated to a syrup that crystallized, in part, from a small amount of warm ether, giving 4.845 g (69.7%) of **8**, m.p. 149–153°. The ethereal mother liquor was processed by evaporation, followed by precipitation of the residue, from acetone solution, with a large amount of water, extraction of the precipitate into dichloromethane, and crystallization of additional **8** (0.535 g, 7.7%) from ether as just described. A third crop (0.328 g), increasing the total yield to 5.708 g (82%), was obtained from the mother liquor by chromatography on a small column of silica gel (6 × 2.5 cm) with 1:4 ethyl acetate–hexane.

Chromatographically pure **8** ($R_F$ 0.25, solvent *D*) crystallized as stout prisms, m.p. 152–153°, $[\alpha]_D$ +74.8° (*c* 2.2, chloroform), $\nu_{max}^{Nujol}$ 1745 $cm^{-1}$.

*Anal.* Calc. for $C_{40}H_{38}O_{11}$ (694.7): C, 69.15; H, 5.51. Found: C, 69.07; H, 5.62.

Crude crystal fractions normally were contaminated by a trace of a by-product having $R_F$ 0.45, which was removable by chromatography, or by recrystallization from ether with addition of a small proportion of hexane. A sample of the contaminant, isolated chromatographically (solvent *D*) gave microanalytical values (C, 66.94, and H, 6.05%) fitting the composition $C_{42}H_{44}O_{11}S$ for a product bearing a (methylthio)methyl ether group in one, and a keto group in the other, sugar ring. (Methylthio)methoxy compounds are common by-products in the Pfitzner–Moffatt oxidation of alcohols[16].

*Reductive amination of* **8**. — A. *Formation and isolation of products*. A mixture of diketone **8** (3.474 g, 5 mmol), ammonium acetate (8.0 g), 3-Å molecular sieve (8 g) and dry methanol (100 mL) was stirred at room temperature for 5 min, with exclusion of atmospheric moisture; sodium cyanoborohydride (0.65 g, reagent grade, 95%; 10 mmol) was then added, and stirring was continued for 18 h. Virtually complete consumption of **8** ($R_F$ 0.95) and formation of a large number of products varying widely in polarity ($R_F$ 0.0–0.9) was indicated by t.l.c. (ethyl acetate). The mixture was filtered through Celite, which was washed with methanol, and the filtrate concentrated to a thin, cloudy syrup that was partitioned between water and dichloromethane. The aqueous phase was extracted with fresh dichloromethane, and the combined organic phase was washed once with water, dried ($Na_2SO_4$), and evaporated to give a dry foam. For *N*-acetylation, the material was treated overnight at 25° with acetic anhydride (10 mL) in methanol (50 mL). The solvent was evaporated with several portions of added toluene, and the vacuum-dried, syrupy residue (2.95 g) was placed on a silica gel column with the aid of a little benzene. Elution with solvent *E* followed by solvent *G* effected partial separation of the products. Fractions containing two or more components were appropriately pooled for repeated chromatography. Eventually, 9 fractions showing either one or two spots in t.l.c. (solvent *F*) were obtained: A, 65 mg ($R_F$ 0.71 and 0.69); B, 112 mg ($R_F$ 0.62 and 0.58); C, 49 mg ($R_F$ 0.56); C, 24 mg ($R_F$ 0.53); E, 137 mg ($R_F$ 0.47); F, 67 mg ($R_F$ 0.40); G, 299 mg ($R_F$ 0.38); H, 56 mg ($R_F$ 0.33); and I, 629 mg ($R_F$ 0.10), for a total of 1.438 g of products (49% recovery in the chromatographic procedures).

In a modified procedure, the filtered solution from the reductive amination was introduced dropwise into 4 volumes of vigorously stirred ice–water. The fine, almost white precipitate was collected, washed with water, and dried in the air. The dry powder (3.29 g) was dissolved in methanol (45 mL), and acetic anhydride (2.2 mL) and triethylamine (3 mL) were added. After 4 h the solution was concentrated to ~15 mL and stirred into ice–water (100 mL). A few drops of brine were added to the resulting, white emulsion which rapidly coagulated, and the solid precipitate was isolated, washed with water, and dried (3.40 g). Its complex t.l.c. pattern was similar to that observed in the previous procedure. Column chromatography on silica gel (70 g) was performed with the aim only of isolating the slow-moving, major component that corresponded to the aforementioned fraction I ($R_F$ 0.10), since this had proved to be the desired compound **9**. Elution of the column was commenced with ether, which produced the components having high and medium mobility and, in late fractions, small proportions of **9**. The bulk of the latter was then eluted with ethyl acetate, and mixed fractions containing appreciably amounts of **9** were rechromatographed in the same way. The chromatographically homogeneous **9** thus isolated (dry weight, 1.52 g, 39%) was dissolved in a small quantity of methanol and, by precipitation with 2–3 volumes of water at 4°, and careful trituration, obtained as a semicrystalline, faintly yellowish powder whose $^1$H-n.m.r. and i.r. spectra were identical with those of fraction I from the preceding experiment; it weighed 1.38 g (35.4%).

B. *3-Acetamido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-altropyranosyl 3-acetamido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-altropyranoside* (**9**). Isolated as just described, **9** melted in the range of 93–115° and showed $[\alpha]_D$ +65.8° (*c* 0.6, chloroform); $\nu_{max}^{Nujol}$ 3425 (NH) and 1665 cm$^{-1}$ (amide CO).

*Anal.* Calc. for $C_{44}H_{48}N_2O_{11}$ (780.8): C, 67.68; H, 6.12; N, 3.59. Found: C, 67.82; H, 6.28; N, 3.58.

*3-Acetamido-2-*O*-benzyl-3-deoxy-α-*D*-altropyranosyl 3-acetamido-2-*O*-benzyl-3-deoxy-α-*D*-altropyranoside* (**10**). — A suspension of **9** (600 mg) in 80% acetic acid (10 mL) was heated on a steam bath for 30 min, whereby **9** gradually dissolved. The solution was evaporated with several portions of water and ethanol, added sequentially. The resulting syrup was taken up in hot ethanol (6 mL), some water (10–15 drops) was added, the solution was filtered through Celite, concentrated slightly on the steam bath, and set aside for crystallization of **10**. The crystals (306 mg, 66%) had m.p. 265–267° (dec.), raised to 266.5–267.5° (dec.) by recrystallization from hot ethanol; $[\alpha]_D$ +94.8° (*c* 0.1, methanol); $\nu_{max}^{Nujol}$ 3300 (NH) with shoulder at 3380 (OH), and 1643 cm$^{-1}$ (amide CO).

*Anal.* Calc. for $C_{30}H_{40}N_2O_{11}$ (604.5): C, 59.59; H, 6.67; N, 4.63. Found: C, 59.63; H, 6.83; N, 4.63.

*3-Acetamido-3-deoxy-α-*D*-altropyranosyl 3-acetamido-3-deoxy-α-*D*-altropyranoside* (**11**) *and its 2,4,6,2',4',6'-hexaacetate* (**12**). — Compound **10** (227 mg) and Pd–C (10%, 440 mg, moistened with methanol) were suspended in hot methanol (10 mL), formic acid (2 mL) was added, an $N_2$-atmosphere provided, and the vessel

placed in a sonic bath, the temperature of which rose from 20 to 47° in the course of 2 h. All of the (fast-moving) **10** was consumed within 1 h (t.l.c., solvent *B*). After 2 h, the catalyst was filtered off and washed exhaustively with methanol. The filtrate and washings were evaporated to a syrup which, after treatment with activated charcoal (in a small volume of methanol), recovery by evaporation, and drying *in vacuo*, weighed 170 mg. Crystallization from hot 2-propanol gave **11** (149 mg, 84%), $R_F$ 0.40, containing a trace of an impurity, $R_F$ 0.55 (t.l.c., solvent *C*). Recrystallization from 2-propanol gave chromatographically pure **11** (67 mg, 38%) as a solvate, m.p. 92–98°, $[\alpha]_D$ +105.5° (*c* 0.5, methanol).

*Anal.* Calc. for $C_{16}H_{28}N_2O_{11} \cdot H_2O \cdot 0.5\ C_3H_6O$ (472.5): C, 44.48; H, 7.25; N, 5.93. Found: C, 44.51; H, 7.24; N, 5.80.

All mother liquors were combined and evaporated. The residue, which apparently contained incompletely debenzylated product, was subjected once more to hydrogenolysis as just described. The resulting syrup was acetylated (acetic anhydride and pyridine, 18 h, 25°), and the mixture conventionally processed by several evaporations of added toluene. Column chromatography on silica gel (6 × 2.8 cm), with ethyl acetate as the eluant, gave the hexaacetate **12** (76 mg, 30%), as a homogeneous, solid foam, $R_F$ 0.35 (solvent *A*), m.p. 94–104°, $[\alpha]_D$ +64° (*c* 0.7, chloroform).

*Anal.* Calc. for $C_{28}H_{40}N_2O_{17}$ (676.6): C, 49.70; H, 5.96; N, 4.14. Found: C, 49.88; H, 6.00; N, 4.02.

Zemplén *O*-deacetylation of **12** with 1% sodium methoxide in methanol (15 min at 25°), followed by deionization and evaporation of the solution, furnished pure **11** quantitatively. Its combined yield from **10** was, therefore, 68%.

*3-Amino-3-deoxy-α-*D*-altropyranosyl 3-amino-3-deoxy-α-*D*-altropyranoside* (**5**) *from* **11**. — A solution of **11** (118 mg) and $Ba(OH)_2 \cdot 8\ H_2O$ (0.5 g) in water (5 mL) was boiled under reflux for 1.5 h, after which the conversion of **11** ($R_F$ 0.4) into **5** ($R_F$ 0.15) was complete (t.l.c., solvent *H*). The cooled solution was saturated with $CO_2$, the precipitate washed well with water, and the filtrate carefully adjusted to pH 4 with M $H_2SO_4$ and, after removal of the precipitate, to pH 8.5 by means of a strongly basic, anion-exchange resin (J. T. Baker CGA-540, $OH^-$ form). The resin was removed and washed well with water (200 mL), and the filtrate concentrated to near-dryness. Evaporation of added ethanol from the residue gave **5** (88 mg, 92%) as a white, solid solvate. Recrystallized from 95% ethanol, the analytical sample had m.p. 60–65° (with subsequent swelling at 78–80°), $[\alpha]_D$ +155.5° (*c* 0.4, methanol). The $^1$H-n.m.r. spectrum was identical with that of **5** prepared from **4**.

*Anal.* Calc. for $C_{12}H_{24}N_2O_9 \cdot 0.5\ C_2H_6O$ (381.4): C, 40.94; H, 7.66; N, 7.34. Found: C, 40.76; H, 7.44; N, 7.14.

*Characterization of by-products* **13–16**. — The chromatographic fractions E, F, G, and H previously listed (see reductive amination of **8**, section *A*) were identified as compounds **15**, **16**, **13**, and **14**, respectively (yields, 3.6, 1.8, 8.1, and 1.5%). They were characterized as follows.

*3-Acetamido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-α-*D*-altropyranosyl 2-*O*-

*benzyl-4,6-O-benzylidene-α-D-altropyranoside* (**13**): m.p. 105–110°, $[\alpha]_D$ +68.6° (*c* 0.2, chloroform); $\nu_{max}^{Nujol}$ 3360 (sharp), 3180 (broad), and 1668 $cm^{-1}$.

*Anal.* Calc. for $C_{42}H_{45}NO_{11}$ (739.8): C, 68.18; H, 6.13; N, 1.89. Found: C, 68.18; H, 6.06; N, 2.08.

*3-Acetamido-2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-D-altropyranosyl 2-O-benzyl-4,6-O-benzylidene-α-D-mannopyranoside* (**14**): m.p. 94–104°, $[\alpha]_D$ +66.9° (*c* 0.5, chloroform); $\nu_{max}^{Nujol}$ 3430 (sharp), 3380 (broad), and 1665 $cm^{-1}$.

*Anal.* Calc. for $C_{42}H_{45}NO_{11}$ (739.8): C, 68.18; H, 6.13; N, 1.89. Found: C, 68.34; H, 6.14; N, 2.04.

*3-Acetamido-2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-D-altropyranosyl 2-O-benzyl-4,6-O-benzylidene-3-C-cyano-α-D-altropyranoside* (**15**): m.p. 105–115°, $[\alpha]_D$ +67.6° (*c* 0.5, chloroform); $\nu_{max}^{Nujol}$ 3382 (sharp), 3180 (broad), and 1670 $cm^{-1}$.

*Anal.* Calc. for $C_{43}H_{44}N_2O_{11}$ (764.8): C, 67.53; H, 5.80; N, 3.66. Found: C, 67.60; H, 5.91; N, 3.53.

*3-Acetamido-2-O-benzyl-4,6-O-benzylidene-3-deoxy-α-D-altropyranosyl 2-O-benzyl-4,6-O-benzylidene-3-C-cyano-α-D-mannopyranoside* (**16**): m.p. 112–118°, $[\alpha]_D$ +64.4° (*c* 0.3, chloroform); $\nu_{max}^{Nujol}$ 3410 (sharp), 3180 (broad), and 1660 $cm^{-1}$.

*Anal.* Calc. for $C_{43}H_{44}N_2O_{11}$ (764.8): C, 67.53; H, 5.80; N, 3.66. Found: C, 67.43; H, 5.92; N, 3.49.

The *3'-acetates* of **13–16** used for spectroscopy were prepared by treatment of 5-mg samples with acetic anhydride and pyridine (10 drops each), followed by evaporation of the reagents with added toluene. Whereas **14** and **16** were readily acetylated (3 h at 25°), **13** and **15** required more forceful conditions (4–5 h at 60°).

*Other by-products:* Fractions A–D displayed broad hydroxyl bands, but no bands attributable to keto or amide carbonyl groups (i.r.), and gave no *N*-acetyl signals ($^1$H-n.m.r.). The mixtures A and B were not examined further. Fraction C was identified as the diol **7** by its $^1$H-n.m.r. spectrum (superposable on that of authentic **7**). For fraction D, the spectrum indicated an analogous, but unsymmetrical structure, suggestive of the D-*altro*,D-*manno* isomer of **7**.

*2-O-Benzyl-4,6-O-benzylidene-3-C-cyano-α-D-hexopyranosyl 2-O-benzyl-4,6-benzylidene-3-C-cyano-α-D-hexopyranosides* **17–19**. — A solution of diketone **8** (250 mg) in methanol was stirred with a cation-exchange resin (carboxylic acid-type, $H^+$ form) at room temperature, and potassium cyanide (50 mg) in methanol was added portionwise, over the course of several h, so as to maintain the alkalinity of the solution below pH 8 (monitored potentiometrically). Stirring was then continued overnight, the filtered solution was evaporated, and the product mixture (286 mg), which showed 3 spots in t.l.c. ($R_F$ 0.6, 0.55, and 0.45; solvent *F*), was separated by column chromatography on silica gel with 1:9 ethyl acetate–hexane. There were eluted **17** (103 mg, 38%), **18** (98 mg, 36%), and **19** (37 mg, 14%) (order of decreasing mobility). Small samples were acetylated with acetic anhydride–pyridine at 25° (4 h for **18** and **19**, 60 h for **17**), to give the corresponding *diacetates* as syrups for n.m.r. spectroscopy ($R_F$ 0.5, 0.4, and 0.3; t.l.c. with 3:7 ethyl acetate–hexane).

ACKNOWLEDGMENTS

This work was supported by Grant GM 35244 from the United States Public Health Service. Mrs. Ho-chi Chin is thanked for skilful technical assistance.

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