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PREPARATION OF 2-AMINO-1,6-ANHYDRO-2,3-DIDEOXY-β-D-*arabino*-HEXOPYRANOSE. ^{1}H- AND ^{13}C-N.M.R. SPECTRA OF DEOXY DERIVATIVES OF 2-AMINO-1,6-ANHYDRO-2-DEOXY-D-GLUCOSE AND 2-AMINO-1,6-ANHYDRO-2-DEOXY-D-MANNOSE*

IVAN ČERNÝ, MILOŠ BUDĚŠÍNSKÝ,
Institute of Organic Chemistry and Biochemistry Czechoslovak Academy of Sciences, 166 10 Prague (Czechoslovakia)

TOMÁŠ TRNKA, AND MILOSLAV ČERNÝ
Department of Organic Chemistry, Charles University, 128 40 Prague (Czechoslovakia)

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ABSTRACT

Partial benzyloxycarbonylation of 1,6-anhydro-D-mannosamine, subsequent mesylation, and treatment with sodium methoxide gave 1,6:3,4-dianhydro-2-benzyloxycarbonylamino-2-deoxy-β-D-altropyranose (**9**). Oxirane-ring cleavage in **9** with potassium iodide, acetylation, and dehalogenation with tributylstannane, gave 4-*O*-acetyl-1,6-anhydro-2-benzyloxycarbonylamino-2,3-dideoxy-β-D-*arabino*-hexopyranose (**13**). Removal of protective groups in **13** by deacetylation and hydrogenolysis gave the hydrochloride of the title compound (**15**). 2-Amino-1,6-anhydro-2,3-dideoxy-β-D-*ribo*- (**18**) and -2,4-dideoxy-β-D-*xylo*-hexopyranose hydrochlorides (**21**) were prepared from the corresponding azido derivatives. ^{1}H- and ^{13}C-n.m.r. spectra of **15, 18, 21,** and of 2-amino-1,6-anhydro-2,4-dideoxy-β-D-*lyxo*-hexopyranose hydrochloride in D_2O were compared with those of the corresponding deoxy derivatives and other related compounds. Isomerization of 2-amino-1,6:3,4-dianhydro-2-deoxy-β-D-altropyranose into the 2,3-epimine was also studied.

INTRODUCTION

Recently, as a part of our program of synthesis of deoxy derivatives of 2-amino-2-deoxy-D-glucose and -D-mannose for biological studies, several aminodideoxy derivatives of 1,6-anhydro-β-D-hexopyranose were prepared[1,2]. As these compounds are convenient starting materials for further syntheses, and for ^{1}H- or ^{13}C-n.m.r. spectroscopic study, an additional compound of the series, 2-amino-1,6-anhydro-2,3-dideoxy-β-D-*arabino*-hexopyranose (**15**), was synthesized. Some intermediates of the synthesis are of interest for an understanding of the iso-

*Dedicated to Professor Raymond U. Lemieux.

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merization of *trans*-aminoepoxides into *trans*-hydroxyepimines described earlier[3,4].

RESULTS AND DISCUSSION

2-Amino-1,6-anhydro-2-deoxy-β-D-mannopyranose (**6**) was prepared according to a recently published[5] procedure *via* compounds **1, 2, 5,** and **6**. The key step of this sequence, the cyclization of urethane **1** into the oxazolidin-2-one **2** was modified, dimethylsulfoxide being used instead of 2-methyl-2-propanol as a solvent to improve the yield from 58 to 78%.

Treatment of **6** with benzyl chloroformate in pyridine gave the partially protected dibenzyloxycarbonyl derivative **7** in high yield which, on mesylation in pyridine, afforded **8**. In the next step, the 3,4-oxirane ring was formed by treatment of **8** with sodium methoxide in chloroform to give **9**; the ^{1}H-n.m.r. spectrum of **9** confirmed the D-*altro*-configuration and $^1H_\sigma$(D) conformation ($J_{1,2}$ 3, $J_{1,3}$ 2, $J_{2,3}$ 0, $J_{3,4}$ 4, $J_{4,5}$ 1.5, $J_{5,6endo}$ 1, $J_{5,6exo}$ 4, and $J_{6,6}$ 7.5 Hz being in agreement with the ^{1}H-n.m.r. parameters[6] for **10**).

Oxirane-ring cleavage in **9** with potassium iodide in acetic acid gave the iodo derivative **11** in a relatively low yield and a by-product **3** resulting from participa-

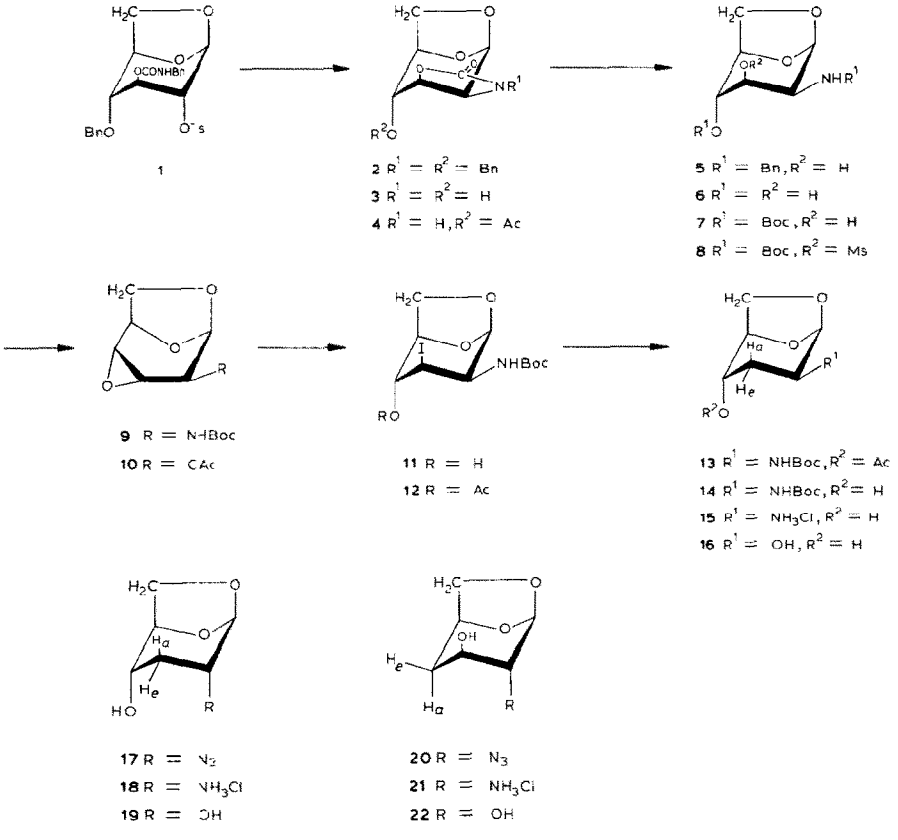


TABLE I

^{1}H-N.M.R DATA FOR 1,6-ANHYDRO-β-D-HEXOPYRANOSE DERIVATIVES[a]

Comp.	*Chemical shifts*[b]										*Vicinal and geminal coupling constants*[b,c]								
	H-1	*H-2*a	*H-2*e	*H-3*a	*H-3*e	*H-4*a	*H-4*e	*H-5*	*H-6en*	*H-6ex*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6en}$	$J_{5,6ex}$	$J_{6en,6ex}$	$J_{3,3'}$	$J_{4,4'}$
15	5.60	3.50		1.93	2.10		3.99	4.65	4.01	3.87	1.5(*e,e*)	11.2(*a,a*) 6.3(*a,e*)	4.3(*a,e*) 1.9(*e,e*)	2.4(*e,e*)	1.3	5.4	8.3	14.5	
16	5.36	3.88		1.71	1.99		3.92	4.53	3.87	3.79	1.8(*e,a*)	10.7(*a,a*) 6.2(*a,e*)	4.5(*a,e*) 2.0(*e,e*)	2.4(*e,e*)	1.3	5.3	8.1	14.5	
18	5.64		3.41	2.31	1.84		3.93	4.71	4.04	3.88	2.4(*e,e*)	5.2(*e,a*) 1.5(*e,e*)	4.0(*a,e*) 1.9(*e,e*)	2.4(*e,e*)	1.2	5.4	8.2	16.3	
19	5.40		3.64	2.12	1.72		3.79	4.59	3.91	3.80	2.3(*e,e*)	4.9(*e,a*) 1.5(*e,e*)	4.7(*a,e*) 2.3(*e,e*)	2.2(*e,e*)	1.3	5.5	8.2	16.3	
21	5.64		3.32		4.06	2.39	1.87	4.75	4.26	3.79	2.3(*e,e*)	1.3(*e,e*)	5.4(*e,a,*) 1.5(*e,e*)	4.5(*a,e,*) 1.6(*e,e*)	0.8	5.2	7.3		15.8
22	5.42		3.56		3.85	2.32	1.72	4.63	4.16	3.70	2.2(*e,e*)	1.7(*e,e*)	5.5(*e,a*) 1.6(*e,e*)	4.2(*a,e,*) 1.9(*e,e*)	1.0	5.3	7.2		15.6
23	5.59	3.49			4.26	2.29	2.03	4.72	4.34	3.79	1.8(*e,a*)	5.4(*a,e*)	4.5(*e,a*) 1.7(*e,e*)	4.1(*a,e*) 1.8(*e,e*)	0.9	5.4	7.2		15.6
24	5.36	3.67			4.13	2.19	1.97	4.62	4.23	3.72	1.9(*e,a*)	5.2(*a,e*)	4.5(*e,a*) 1.7(*e,e*)	4.1(*a,e*) 1.9(*e,e*)	0.9	5.4	7.1		15.6
25	5.68		3.33		3.88		3.83	4.74	4.26	3.83	1.8(*e,e*)	1.9(*e,e*)	2.2(*e,e*)	2.2(*e,e*)	1.1	5.7	7.9		
26	5.44		3.51		3.66		3.66	4.62	4.08	3.74	1.5(*e,e*)	2.1(*e,e*)	[d]	1.8(*e,e*)	1.2	5.8	7.8		
27	5.61	3.56			4.05		3.94	4.68	4.32	3.81	1.9(*e,a*)	5.7(*a,e*)	1.8(*e,e*)	2.1(*e,e*)	1.2	5.9	7.8		
28	5.39	3.77			3.94		3.92	4.58	4.20	3.76	1.5(*e,a*)	4.7(*a,e*)	1.8(*e,e*)	1.8(*e,e*)	1.1	5.9	7.8		
29[e]	5.60	2.11	1.75		3.84		3.73	4.58	4.25	3.73	2.0(*e,a*) 1.9(*e,e*)	5.7(*a,e*) 1.5(*e,e*)	4.0(*a,e*)	2.3(*e,e*)	1.2	5.9	7.8		

[a]For a solution in ^2H_2O. [b]Symbols *a* and *e* indicate axial and equatorial position of corresponding hydrogen atoms and they are used for specification of parameters in needed cases. [c]The following typical values of long-range couplings were observed for compounds **15, 16, 21–29** (absolute values of *J* are given only): $J_{1,3e}$ 1.5, $J_{2e,4e}$ 1.0, $J_{3e,5}$ 1.5, and $J_{4a\ 6ex}$ 1.5 Hz. [d]Value could not be determined owing to chemical-shift equivalence of corresponding hydrogen atoms. [e]$J_{2,2'}$ 15.6 Hz.

TABLE II

^{13}C CHEMICAL SHIFTS OF 1,6-ANHYDRO-β-D-HEXOPYRANOSE DERIVATIVES[a]

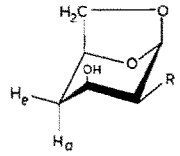
Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
15	101.33	50.47	30.43	68.11	79.38	69.33
16	104.60	69.66	33.99	68.25	79.06	68.76
18	101.15	50.53	28.56	67.48	79.99	68.79
19	104.03	68.37	31.95	68.14	79.52	67.82
21	100.65	55.13	66.37	34.39	74.88	70.60
22	103.47	72.35	69.91	34.44	74.46	69.80
23	100.52	53.68	64.38	37.70	74.64	70.63
24	103.92	71.08	68.35	37.20	74.82	70.46
25	100.68	54.33	71.45	72.13	78.96	68.07
26	104.14	72.91	75.22	73.53	78.97	67.89
27	100.61	51.49	69.40	73.68	78.43	67.68
28	103.84	68.57	72.82	74.17	78.41	67.31
29	102.65	36.64	69.67	73.43	78.21	67.03

[a]For a solution in ^2H_2O.

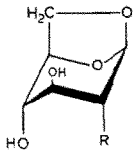
tion of the neighboring benzyloxycarbonylamino group adjacent to the oxirane ring. (An analogous reaction was found[7] to proceed with benzyl 3,4-anhydro-2-benzyloxycarbonylamino-2-deoxy-α-D-galactopyranoside at elevated temperatures). For identification purposes, **3** was acetylated to give **4**, identical with an authentic sample prepared independently.

Acetylation of crude **11** with acetic anhydride in pyridine provided **12** which, on reduction with tributylstannane in boiling benzene and subsequent deacetylation with sodium methoxide, afforded **13** and **14**, respectively. Catalytic hydrogenolysis of **14** in the presence of palladium-on-carbon and hydrochloric acid gave the desired compound **15**. For ^1H-n.m.r. studies, two additional aminodeoxy derivatives (**18** and **21**) were prepared from the corresponding azido derivatives[2] **17** and **20**.

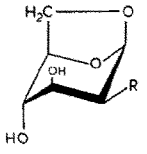
For a detailed evaluation of the influence of the C-2–NH_3^+ group on the conformation and thus n.m.r. parameters, the ^1H- and ^{13}C-n.m.r. spectra of NH_3^+-2 derivatives[8] **15, 18, 21, 23, 25, 27,** the corresponding OH-2 derivatives[8] **16, 19, 22, 24, 26,** and **28,** and the 2-deoxy derivative[8] **29** in ^2H_2O were determined. ^1H- and ^{13}C-N.m.r. data of all compounds **15, 16, 18, 19, 21–29** are reported in Tables I and II. Characteristic signals in the n.m.r. spectra of deoxy derivatives **15, 16, 18–24,** and **29** are those of the deoxy group in the upfield region of the spectra (^1H, δ 1.70–2.40; ^{13}C, δ 28–38). The orientation of neighboring substituents influences the chemical shifts of deoxy hydrogen atoms more profoundly than whether the hydrogen atom is axially or equatorially disposed. The signals for the deoxy group in the n.m.r. spectra are followed by those for the CH–N group (^1H, δ 3.30–3.60; ^{13}C, δ 50–55) which are easily assigned, especially those of ^{13}C-n.m.r. spectroscopy. Low-field regions of spectra contain the signals of C-5–H (^1H, δ 4.50–4.75; ^{13}C, δ 74–78) and anomeric C-1–H (^1H, δ 5.40–5.70; ^{13}C, δ 100–105). The relative chemical shifts



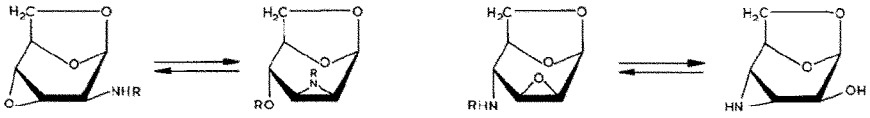
23 R = NH_3Cl
24 R = OH



25 R = NH_3Cl
26 R = OH



27 R = NH_3Cl
28 R = OH
29 R = H



30 R = H · HCl
31 R = H

32 R = H
33 R = Bz

34 R = H · HCl
35 R = H

36

of the remaining CH–O signals depend on the particular structure, and their assignment on the basis of chemical-shift values is ambiguous. The presence of a deoxy group is usually accompanied by upfield shifts of 3 to 5 p.p.m. of neighboring carbon atoms in comparison with the corresponding hydroxy derivatives. Similar effects were not observed in ^{1}H-n.m.r. spectra.

Interproton coupling-constants are extensively used in the conformational analysis of saccharides[9,10]. The bicyclic system of 1,6-anhydro-β-D-hexopyranoses restricts the conformational mobility so that the pyranose ring can assume only two basic types of conformation, the chair $^1C_4$(D) and boat $B_{\sigma,3}$(D). A detailed analysis of $^3J_{H,H}$ values in the series of 1,6-anhydro-β-D-hexopyranoses indicated[11,12] the preference of the $^1C_4$(D) form, more or less flattened, depending on the configurations of substituents at positions 2, 3, and 4. The flattened chair form $^1C_4$(D) has been found also in the crystalline state of *gluco* derivative **26** by X-ray diffraction analysis[13]. The only known case of the preference of the boat form $B_{\sigma,3}$(D) was 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose and its hydrochloride[14]. From this point of view, it was interesting to study the conformational behavior of 2-amino-1,6-anhydrohexopyranoses. As shown in Table I, the coupling constants of **15, 18, 21, 23, 25,** and **27** have values very similar to or identical with those of the corresponding 2-hydroxy analogs **16, 19, 22, 24, 26,** and **28**. Thus, it is possible to conclude unambiguously that all 2-amino derivatives studied prefer the $^1C_4$(D) conformation for solutions in water. This conformational homogeneity over this entire

TABLE III

CHEMICAL-SHIFT DIFFERENCES AT PAIRS OF C-2 EPIMERS OF 1,6-ANHYDRO-β-D-HEXOPYRANOSE DERIVATIVES

C-2 Substituent	*Compounds* (R_{ax}–R_{eq})	*H-1*	*H-2*	*H-3*a	*H-3*e	*H-4*a	*H-4*e	*H-5*	*H-6en*	*H-6ex*
NH_3Cl	**(18 – 15)**	0.04	−0.17	0.38	−0.26		−0.06	0.06	0.03	0.01
	(21 – 23)	0.05	−0.17		−0.20	0.10	−0.16	0.03	−0.08	0.00
	(25 – 27)	0.07	−0.24		−0.17		−0.11	0.06	−0.06	0.02
OH	**(19 – 16)**	0.04	−0.24	0.41	−0.27		−0.13	0.06	0.04	0.01
	(22 – 24)	0.06	−0.11		−0.28	0.13	−0.25	0.01	−0.07	−0.02
	(26 – 28)	0.05	−0.25		−0.27		−0.26	0.04	−0.14	0.00

		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
NH_3Cl	**(18 – 15)**	−0.18	0.06	−1.87	−0.63	0.61	−0.54
	(21 – 23)	0.13	1.45	1.99	−3.31	0.24	−0.03
	(25 – 27)	0.07	2.84	2.05	−1.55	0.53	0.39
OH	**(19 – 16)**	−0.57	−1.29	−2.04	0.11	0.46	−0.94
	(22 – 24)	−0.45	1.27	1.56	−2.76	−0.36	−0.66
	(26 – 28)	0.30	4.34	2.40	−0.64	0.56	0.58

TABLE IV

SUBSTITUENT EFFECTS IN N.M.R. SPECTRA UPON REPLACEMENT OF OH BY NH_3^+ GROUP AT C-2 OF 1,6-ANHYDRO-β-D-HEXOPYRANOSE DERIVATIVES

Substituent position	*Compounds*	*H-1*	*H-2*	*H-3*a	*H-3*e	*H-4*a	*H-4*e	*H-5*	*H-6en*	*H-6ex*
2-Axial	**(18 – 19)**	0.24	−0.23	0.19	0.12		0.14	0.12	0.13	0.08
	(21 – 22)	0.22	−0.24		0.21	0.07	0.15	0.12	0.14	0.09
	(25 – 26)	0.24	−0.22		0.22		0.17	0.12	0.18	0.09
2-Equat.	**(15 – 16)**	0.24	−0.30	0.22	0.11		0.07	0.12	0.14	0.08
	(23 – 24)	0.23	−0.18		0.13	0.10	0.06	0.10	0.11	0.07
	(27 – 28)	0.22	−0.21		0.11		0.02	0.10	0.12	0.05

		C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
2-Axial	**(18 – 19)**	−2.88	−17.84	−3.39	−0.66	0.47	0.97
	(21 – 22)	−2.82	−17.22	−3.54	−0.05	0.42	0.80
	(25 – 26)	−3.46	−18.58	−3.77	−1.40	−0.01	0.18
2-Equat.	**(15 – 16)**	−3.27	−19.19	−3.56	−0.14	0.32	0.57
	(23 – 24)	−3.40	−17.40	−3.97	0.50	−0.18	0.17
	(27 – 28)	−3.23	−17.08	−3.42	−0.49	0.02	0.37

series of compounds allowed us to derive an empirical correlation of substituent effects on chemical shifts. Table III gives the comparison of pairs of C-2 epimers and shows the chemical shift differences of hydrogen and carbon atoms in compounds having an axial and equatorial NH_3^+ or OH group at C-2. The values for individual protons on the pyranose ring are either positive or negative, and they are approxi-

mately constant not only for different pairs having the same substituent (not influenced by the presence or the position, or both, of the deoxy group) but even for both NH_3^+ and OH substituents. The following approximate values may be considered as typical for C-2 epimers: 0.05 (H-1), −0.20 (H-2), 0.40 (H-3a), −0.25 (H-3e), −0.10 (H-4a), −0.15 (H-4e), and 0.05 p.p.m. (H-5). On the other hand, analogous shift differences for carbon atoms are much more dependent on the adjacent substituents and cannot be used for characterization. Replacement of an OH-2 by an NH_3^+ group (Table IV) resulted, for individual hydrogen atoms, in rather constant chemical-shift differences, practically independent of the configuration at C-2. These differences are positive for all protons except H-2. Carbon-substituent effects have significant (1 p.p.m.) and characteristic negative values for C-1, -2, and -3 in α- and β-position, respectively, independent of the configuration at C-2. Typical observed values (−17.5 for C-2 and −3.5 p.p.m. for C-1 and -3) were in good agreement with literature data[15,16] for substituted alkanes.

Isomerization of *trans*-aminoepoxides into *trans*-hydroxyepimines has been described several times for 1,6-anhydrohexopyranoses[3,4,17]. Thus, it was suggested[3] that conversion of epimine **32** into **6** in alkaline solution proceeds through the intermediary epoxide **31** which, however, was not found in the reaction mixture. In this work, the latter compound was prepared from **9** by hydrogenolysis in the presence of palladium-on-carbon and its isomerization studied. After heating of either **31** or **32** in water for 8 h at 100°, practically no hydrolysis was observed and both equilibrium mixtures were identical (t.l.c.). Equlibration of **31** on a larger scale and separation of the products gave epimine **32**, which was identified as its benzoate **33**, and the starting compound **31**, identified as **30**. For determining the composition of the equilibrium mixture, a sample of **32** was heated in ^2H_2O; the components **31** and **32** were present in the ratio 13:7 as determined from integration of the ^{1}H-n.m.r. signals of H-1 for both compounds.

In comparison to these results, the equilibrium of an analogous pair, **35** and **36**, strongly favors **36** (99%). It may be concluded that, generally, the preponderant compounds in the equilibrium mixtures possess an *exo*-oriented, three-membered ring with respect to the 6,8-dioxabicyclo[3.2.1.] octane skeleton[3,17–19]. However, in addition to steric effects, the greater stability of the aziridine ring, as compared to the oxirane ring, also controls the proportion of compounds in the equilibrium mixtures.

EXPERIMENTAL

General. — Melting points were determined on a Boëtius micro melting-point apparatus and optical rotations with a Bendix–Ericsson ETL 143A or Perkin–Elmer M-141 polarimeter at 23–25°. I.r. spectra were recorded with a Zeiss Jena UR-20 spectrophotometer. ^{1}H- and ^{13}C-n.m.r. spectra were measured on Varian XL-200 spectrometer at 200 MHz, resp. 50.31 MHz frequency, for solutions of ~10 mg of substance in ^2H_2O (0.4 mL) and sodium 4,4-dimethyl-4-silapentane-1-

sulfonate (DSS) as the internal reference at 30°. For the assignment of protons in ^{1}H-n.m.r. spectra, a series of homonuclear decoupling experiments was done. Exponential multiplication and Gaussian apodization were used for resolution enhancement. The chemical shifts and coupling constants were determined by first-order analysis from the expanded spectral plots (2 Hz/cm). ^{13}C-Chemical shifts were determined from proton-broadband decoupled spectra. The assignment of signals was based on the attached-proton test measurement (distinguishing of CH_2 and CH carbon atoms by positive or negative amplitudes), general chemical-shift arguments, and comparison with literature data[16,20,21]. T.l.c. was performed on Silica gel G (according to Stahl, Woelm). Detection was effected with ninhydrin (for amines) or by charring with sulfuric acid. Solutions were evaporated at ~40° (bath temperature) and 2 kPa after being dried with Na_2SO_4 or $MgSO_4$.

*3-Benzyl-(1,6-anhydro-4-O-benzyl-2,3-dideoxy-β-*D*-mannopyrano)-[2,3-*d*]-2-oxazolidinone* (**2**). — Potassium (4.9 g, 125 mmol) was gradually dissolved in 2-methyl-2-propanol (200 mL) boiling under reflux and argon. The solution was concentrated to 100 mL, diluted with dimethyl sulfoxide (50 mL), and added dropwise to a stirred solution of **1** (22 g, 41 mmol) in dimethyl sulfoxide (100 mL) cooled with ice. After additional stirring for 30 min at room temperature (t.l.c. in 4:1 ether–cyclohexane), the solution was made neutral with 10% sulfuric acid under cooling, and the mixture diluted with water (500 mL). After extraction with chloroform (3 × 200 mL), the organic layers were combined and evaporated. The residual solvent was twice coevaporated with toluene, and the residue dried at 25 Pa and 50–60°. Crystallization from acetone–ether gave **2** (11.5 g, 78%), m.p. 84–85° in agreement with lit.[5].

*1,6-Anhydro-4-O-benzyloxycarbonyl-2-benzyloxycarbonylamino-2-deoxy-β-*D*-mannopyranose* (**7**). — Benzyl chloroformate (14 mL, 0.1 mmol) was added within 1 h to a stirred solution of **6** (1.9 g, 11.8 mmol) in pyridine precooled to −15°. The temperature was kept below −10°. After additional stirring at room temperature for 1 h, (t.l.c. in 20:1 chloroform–methanol), the mixture was poured into ice–water (100 mL) and extracted with dichloromethane. The organic solution was washed with 5% sulfuric acid and water, and evaporated. The residue was purified by column chromatography on silica gel (100 g). Elution with 50:1 chloroform–methanol yielded **7** (4.5 g, 89%), m.p. 88–90°, $[\alpha]_D^{24}$ −72° (*c* 1.96, chloroform); $\nu_{max}^{CHCl_3}$ 3615 (OH), 3440 (NH), 1726, 1714, 1514, and 1506 (N-CO-OBn), 1750, 1738, 1268, and 1248 cm^{-1} (O-CO-OBn); ^{1}H-n.m.r. (60 MHz, $CDCl_3$): δ 5.14 (s, 2 H, CH_2O), 5.20 (s, 2 H, CH_2O), 5.46 (m, 1 H, H-1), 7.37 (m, 5 H, C_6H_5), and 7.41 (m, 5 H, C_6H_5).

Anal. Calc. for $C_{22}H_{23}NO_8$ (429.4): C, 61.53; H, 5.40; N, 3.26. Found: C, 61.72; H, 5.45; N, 3.13.

*1,6-Anhydro-4-O-benzyloxycarbonyl-2-benzyloxycarbonylamino-2-deoxy-3-O-methylsulfonyl-β-*D*-mannopyranose* (**8**). — To a stirred solution of **7** (4.5 g, 10.5 mmol) in pyridine (30 mL), cooled to 0°, was added dropwise methanesulfonyl chloride (4 mL, 52 mmol), and the mixture kept at room temperature overnight.

The mixture was poured into ice–water and, after 1 h, crystals were collected and washed with water. The crude product was dissolved in chloroform, filtered with charcoal, and crystallized from chloroform–methanol to give **8** (3.4 g, 64%), m.p. 155–156°, $[\alpha]_D^{24}$ −58° (*c* 0.18, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 1728, 1714, 1515, and 1505 (N-CO-OBn), 1748, 1268, 1247 (O-CO-OBn), 1333 and 1171 cm^{-1} ($O-SO_2-CH_3$).

Anal. Calc. for $C_{23}H_{25}NO_{10}S$ (507.5): C, 54.43; H, 4.96; N, 2.76; S, 6.32. Found: C, 54.58; H, 5.00; N, 2.69; S, 6.35.

*1,6:3,4-Dianhydro-2-benzyloxycarbonylamino-2-deoxy-β-*D*-altropyranose* (**9**). — To a stirred solution of **8** (3.2 g, 6.3 mmol) in chloroform (20 mL), cooled with an ice bath, was added dropwise a solution of sodium methoxide in methanol (1.4 g sodium in 20 mL). The mixture was stirred further for 1 h at room temperture, made neutral with acetic acid, diluted with chloroform, and washed with water. Drying and evaporation yielded an oil which, after column chromatography on silica gel (75 g) in 10:1 benzene–ether and on crystallization from ether, gave **9** (1.4 g, 80%), m.p. 82–83°, $[\alpha]_D^{24}$ −63° (*c* 0.18, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 1728, 1715, 1513, and 1506 cm^{-1} (N-CO-OBn); ^{1}H-n.m.r. (60 MHz, $CDCl_3$): δ 1.72 (m, 1 H, NH), 2.02 (dd, 1 H, $J_{1,3}$ 2, $J_{3,4}$ 4 Hz, H-3), 3.10 (bd, 1 H, $J_{3,4}$ 4 Hz, H-4), 3.81 (dd, 1 H, $J_{5,6exo}$ 4, $J_{6,6}$ 7.5 Hz, H-6exo), 4.03 (dd, 1 H, $J_{5,6endo}$ 1, $J_{6,6}$ 7.5 Hz, H-6endo), 4.74 (m, 2 H, H-2,5), 5.14 (s, 2 H, CH_2O), 5.29 (dd, 1 H, $J_{1,2}$ 3, $J_{1,3}$ 2 Hz, H-1), and 7.37 (s, 5 H, C_6H_5).

Anal. Calc. for $C_{14}H_{15}NO_5$ (277.3): C, 60.64; H, 5.45; N, 5.05. Found: C, 60.51; H, 5.40; N, 4.93.

*4-O-Acetyl-1,6-anhydro-2-benzyloxycarbonylamino-2,3-dideoxy-3-iodo-β-*D*-mannopyranose* (**12**) *and 4-O-acetyl-1,6-anhydro-2,3-dideoxy-β-*D*-mannopyrano-[2,3-d]-2-oxazolidinone* (**4**). — Compound **9** (1 g, 3.6 mmol) was dissolved in acetic acid (20 mL), sodium iodide (3.2 g, 21.3 mmol) was added, and the mixture was stirred and heated to 80°. After 5 min, the solution was chilled and poured into a stirred, saturated solution of $KHCO_3$ (200 mL). The mixture was extracted with dichloromethane, and the extract washed with 5% $Na_2S_2O_3$ (100 mL) and water. The organic solution was dried and evaporated. The residue (**11**, 1.1 g) was acetylated with acetic anhydride (3 mL) and pyridine (15 mL) at room temperature overnight. The mixture was then poured into ice–water and extracted with dichloromethane. The solution was dried and evaporated, and the residual solvent twice coevaporated with toluene. Column chromatography on silica gel (50 g) in 50:1 benzene–ether gave **12** as an oil (0.5 g, 31%), $[\alpha]_D^{24}$ −63° (*c* 0.54, chloroform); ^{1}H-n.m.r. (60 MHz, $CDCl_3$): δ 1.67 (bs, 1 H, NH), 2.13 (s, 3 H, CH_3), 3.4–4.7 (m, 6 H, H-2,3,4,5,6exo,6endo), 5.12 (s, 2 H, CH_2O), 5.34 (bs, 1 H, H-1), and 7.35 (s, 5 H, C_6H_5).

Anal. Calc. for $C_{16}H_{18}INO_6$ (447.2): C, 42.97; H, 4.06; I, 28.37; N, 3.13. Found: C, 42.92; H, 4.11; I, 28.26; N, 3.17.

The aqueous solutions left after extraction of **11** were evaporated to dryness and the residue was extracted with ethanol. The extract was evaporated and the re-

sidue chromatographed on a column of silica gel (25 g) in 20:10:1 chloroform–methanol–25% aqueous ammonia. Crude **3** was acetylated with acetic anhydride (0.1 mL) and pyridine (2 mL) overnight. Processing as described for **12** and chromatography on silica gel (15 g) in 100:1 chloroform–methanol gave **4** (60 mg) after recrystallization from methanol, m.p. 210–215° (dec.), $[\alpha]_D^{24}$ −135° (*c* 0.37, methanol); ν_{max}^{KBr} 3448 (NH), 1768 (N-CO-O), 1732, and 1245 cm^{-1} (O-CO-CH_3); ^{1}H-n.m.r. [60 MHz, $CDCl_3$ + $(CD_3)_2SO$]: δ 2.18 (s, 3 H, $OCOCH_3$), and 5.43 (bd, 1 H, H-1). An authentic specimen prepared in the same manner from compound[5] **3** had m.p. 215–217° and other characteristics identical with those just described.

Anal. Calc. for $C_9H_{11}NO_6$ (229.20): C, 47.16; H, 4.84; N, 6.11. Found: C, 47.12; H, 5.03; N, 6.12.

*4-O-Acetyl-1,6-anhydro-2-benzyloxycarbonylamino-2,3-dideoxy-β-*D-arabino-*hexopyranose* (**13**). — Tributylstannane (2 mL, M solution in benzene) was added dropwise under argon atmosphere to a benzene solution (5 mL) of **12** (0.5 g, 1.12 mmol). 2,2′-Azobis(2-methylpropionitrile) (3 mg) was added, and the solution boiled under reflux for 10 min. After cooling, unreacted stannane was decomposed with tetrachloromethane (0.5 mL), the solution evaporated, and the product purified by column chromatography on silica gel (30 g) in 20:1 benzene–ether. Crystallization of the main fraction from ether gave **13** (270 mg, 75%), m.p. 151–152°, $[\alpha]_D^{24}$ −106° (*c* 1.73, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 1727, 1714, 1517, and 1506 (N-CO-OBn), 1739, 1247, and 1040 cm^{-1} (CH_3COO).

Anal. Calc. for $C_{16}H_{19}NO_6$ (321.3): C, 59.81; H, 5.96; N, 4.36. Found: C, 59.53; H, 5.91; N, 4.28.

*1,6-Anhydro-2-benzyloxycarbonylamino-2,3-dideoxy-β-*D-arabino-*hexopyranose* (**14**). — A solution of **13** (0.3 g, 0.93 mmol) in 1:1 benzene–methanol (10 mL) was kept for 24 h at room temperature with a sodium methoxide methanolic solution (0.1 mL, prepared from 0.1 g of sodium and 10 mL of methanol). Solid carbon dioxide was then added and the solvents were evaporated. After chromatography on silica gel (15 g) in 50:1 chloroform–methanol, the product crystallized from ether to give **14**, (220 mg, 85%), m.p. 94–95°, $[\alpha]_D^{24}$ −116° (*c* 1.8, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH). 1727, 1715, 1517, and 1505 cm^{-1} (N-CO-OBn).

Anal. Calc. for $C_{14}H_{17}NO_5$ (279.3): C, 60.20; H, 6.14; N, 5.02. Found: C, 60.20; H, 6.17; N, 4.91.

*2-Amino-1,6-anhydro-2,3-dideoxy-β-*D-ribo-*hexopyranose hydrochloride* (**18**). — A solution of **17** (ref. 2; 100 mg, 0.58 mmol) in a mixture of ethanol (8 mL), water (2 mL) and hydrochloric acid (azeotrop, 0.1 mL) was hydrogenated with 10% palladium-on-carbon (50 mg) under atmospheric pressure at room temperature for 2 h (t.l.c. in 10:1 chloroform–methanol). The catalyst was filtered off, the solution evaporated to dryness, and the residual solvent coevaporated with aqueous ethanol. The solution in aqueous ethanol was filtered with charcoal and evaporated. Crystallization from ethanol–water gave **18** (100 mg, 95%), dec. 190–210° $[\alpha]_D^{24}$ −54° (*c* 0.19, water); for ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II.

Anal. Calc. for $C_6H_{12}ClNO_3$ (181.6): C, 39.68; H, 6.66; Cl, 19.52; N, 7.71. Found: C, 39.42; H, 6.43; Cl, 19.61; N, 7.48.

*2-Amino-1,6-anhydro-2,3-dideoxy-β-*D-arabino-*hexopyranose hydrochloride* (**15**). — Compound **14** (190 mg, 0.68 mmol) was hydrogenated under the same conditions as described for **18** to yield **15** (75 mg, 60%), dec. 175–235°, $[\alpha]_D^{24}$ −117° (*c* 1.81, water); for ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II.

Anal. Calc. for $C_6H_{12}ClNO_3$ (181.6): C, 39.68; H, 6.66; Cl, 19.52; N, 7.71. Found: C, 39.93; H, 6.25; Cl, 19.69; N, 7.64.

*2-Amino-1,6-anhydro-2,4-dideoxy-β-*D-xylo-*hexopyranose hydrochloride* (**21**). — The hydrochloride **21** (97 mg, 92%) was prepared from **20** (ref. 2, 100 mg, 0.58 mmol) in the same manner as described for the preparation of **18**, dec. 190–210°, $[\alpha]_D^{24}$ −29° (*c* 0.23, water); for ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II.

Anal. Calc. for $C_6H_{12}ClNO_3$ (181.6): C, 39.68; H, 6.66; Cl, 19.52; N, 7.71. Found: C, 39.76; H, 6.68; Cl, 19.71; N, 7.55.

*2-Amino-1,6:3,4-dianhydro-2-deoxy-β-*D-*altropyranose hydrochloride* (**30**). — Compound **30** (100 mg, 78%) was prepared from **9** (200 mg, 0.72 mmol) as described for the preparation of **18**, m.p. 165–180° (dec.), $[\alpha]_D^{24}$ −85° (*c* 0.12, water).

Anal. Calc. for $C_6H_{10}ClNO_3$ (179.6): C, 40.13; H, 5.61; Cl, 19.74; N, 7.80. Found: C, 40.07; H, 5.66; Cl, 19.56; N, 7.54.

*Isomerization of 2-amino-1,6:3,4-dianhydro-2-deoxy-β-*D-*altropyranose* (**31**) *and 1,6-anhydro-2,3-dideoxy-2,3-epimino-β-*D-*mannopyranose* (**32**). — (*a*) *Preliminary experiments.* Compound **30** (10 mg) was dissolved in a glass-lined autoclave (volume of 3 mL) in water (1.5 mL) and an equivalent proportion of 0.1M potassium hydroxide (0.55 mL) was added. In a parallel experiment, **32** (10 mg) in water (2 mL) was placed in a similar vessel. Both vessels were heated to 100 ±2°, and the reaction course was monitored by t.l.c. in 20:20:2:2:1 chloroform–2-propanol–25% aqueous ammonia–water–ethanol. After 8 h the difference in composition of the mixtures was not distinguishable by means of t.l.c., and in both cases the aminoepoxide **31** prevailed. The product of hydrolysis, *i.e.* **6**, was not found.

(*b*) *Product identification.* Compound **30** (52 mg, 0.29 mmol) was treated as described under (*a*). After 8 h, the solvent was evaporated and the residual solvent twice coevaporated with ethanol. The solid residue was extracted with ethanol and chromatographed on a preparative silica gel t.l.c.-plate (20 × 20 cm) in 40:10:1 chloroform–2-propanol–25% aqueous ammonia. The fastest moving zone was eluted with aqueous ethanol and acidified with hydrochloric acid, the solvent was evaporated, and the residual hydrogen chloride removed by coevaporation with water. Crystallization of the residue from water–ethanol recovered **30** (27 mg, 52%), m.p. 170–180° (dec.), $[\alpha]_D^{24}$ −87° (*c* 0.1, water). A second zone gave, after elution with ethanol, **32** (12 mg, 30%) which did not crystallize. Benzoylation with benzoyl chloride (0.03 mL) and pyridine (0.5 mL) at room temperature overnight, processing by water–dichloromethane extraction, and crystallization from ethanol gave **33** (15 mg), m.p. 125–127°, $[\alpha]_D^{24}$ −67° (*c* 0.1, chloroform); {ref. 3, m.p. 126–127°, $[\alpha]_D^{24}$ −70° (*c* 0.91, chloroform)}; the i.r. spectrum was identical with that of an authentic sample.

(*c*) *Quantitative study.* A solution of **32** (3 mg) in ^2H_2O (0.5 mL) with a trace

of sodium 4,4-dimethyl-4-silapentan-1-sulfonate was heated to 100 ±2° in a sealed ^{1}H-n.m.r. measuring vessel. The ^{1}H-n.m.r. spectra were recorded at room temperature and the percentage composition was derived from integration of the signals of H-1 corresponding to **31** and **32**. The following data were obtained: after 8 h of heating, 53.5% of **31** and 46.5% of **32**; after 16 h, 62.6% of **31** and 37.4% of **32**; and after 24 h, 64.8% of **31** and 35.2% of **32** (final composition).

*Isomerization of 4-amino-1,6:2,3-dianhydro-4-deoxy-β-*D*-mannopyranose* (**35**). — Compound **35** (25 mg, 79%) was prepared from compound[4] **34** (40 mg, 0.22 mmol) by adding 0.1M potassium hydroxide (2.2 mL) evaporation to dryness, ethanol extraction, and chromatography on silica gel in 4:1 benzene–ethanol. Isomerization under the conditions described for **31** (*c*) gave the following data: after 0.25 h, 59% **35** and 41.0% **36**; after 0.5 h, 26.9% **35** and 73.1% **36**; after 1 h, 5.2% **35** and 94.8% **36**: and after 5 h 1% **35** and 99% **36**.

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