Carbohydrate Research, 74 (1979) 309–318

CHAIN ELONGATION BY A SEEMINGLY STEREOSPECIFIC CYANOHYDRIN SYNTHESIS: THE PREPARATION AND CONFIGURATIONAL ASSIGNMENT OF 3,7-ANHYDRO-D-*threo*-L-*talo*- AND -L-*galacto*-OCTOSE

HANS FRITZ, JOCHEN LEHMANN, AND PETER SCHLESSELMANN

Chemisches Laboratorium der Universität Freiburg i.Br., Albertstrasse 21, D-7800 Freiburg im Breisgau (West Germany)

(Received January 10th, 1979; accepted for publication, March 7th, 1979)

ABSTRACT

2,6-Anhydro-D-*glycero*-L-*manno*-heptose (**1**) is converted by the cyanohydrin reaction into crystalline D-*threo*-L-*talo*-octononitrile (**3**), which shows mutarotation in water. The equilibrium mixture, as measured by ^{13}C-n.m.r. spectroscopy, contains about equal amounts of **3** and its epimer, D-*threo*-L-*galacto*-octononitrile. On evaporation of the aqueous mixture, pure, crystalline **3** is again obtained. Labelling experiments in ^3H_2O proved that epimerization proceeds through reversible deprotonation. Stabilization of **3** in the solid state is explained by intramolecular hydrogen-bonding. In pyridine, rapid isomerization of **3** occurs. When acetylation of **3** is conducted in this solvent, the yield of 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*talo*-octononitrile (**4**) depends strongly on the conditions of acetylation. Acetylation after equilibration produces an equimolar mixture of **4** and its isomer 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octononitrile. Structural assignment for both was achieved by 360-MHz, ^{1}H- and ^{13}C-n.m.r. spectroscopy. Reduction of **4** in pyridine–acetic acid–water in the presence of *N,N*-diphenylethylenediamine yields a 1:2.36 mixture of 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*talo*-octose *N,N*-diphenylimidazolidine (**6**) and 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octose *N,N*-diphenylimidazolidine (**8**). Compounds **6** and **8** could be separated and obtained as crystalline solids, and their structure proved by ^{1}H- and ^{13}C-n.m.r. spectroscopy. Hydrolysis of **6** and **8** gave 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octose and -D-*threo*-L-*talo*-octose.

INTRODUCTION

Although it is one of the oldest methods for carbon-bond formation, the cyanohydrin or Kiliani synthesis[1] is still widely applied in carbohydrate chemistry. Its usefulness for linear carbon-chain elongation[2], for introduction of carbon branches[3], and, especially, for ^{14}C-labelling of sugars[4] is demonstrated in numerous, recent publications. The elegant conversion of a cyano group into an aldehyde group performed by Moffatt *et al.*[5] significantly increased the value of the cyanohydrin synthesis.

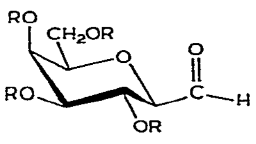
However, one of its disadvantages is the poor stereoselectivity during the conversion of aldehyde groups into cyanohydrins having a newly formed, asymmetric carbon atom[2,6]. It is, therefore, surprising that 2,6-anhydro-D-*glycero*-L-*manno*-heptose[8] (**1**) yields only one crystalline cyanohydrin on evaporation of the reaction mixture; this reaction was carried out in order to obtain *C*-galactosyl derivatives having extended carbon-chains. Such compounds might be converted into substrates[7], and competitive[8], as well as irreversible[9], inhibitors of β-D-galactosidase.

RESULTS AND DISCUSSION

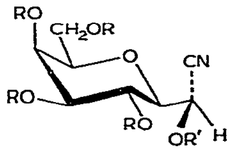
2,6-Anhydro-D-*glycero*-L-*manno*-heptose[8] (**1**) reacts with sodium cyanide in aqueous solution to give, after removal of sodium ions, and evaporation, the crystalline cyanohydrin 3,7-anhydro-D-*threo*-L-*talo*-octononitrile (**3**). From **3**, the pure, crystalline peracetate **4** can be obtained in up to 70% yield.

The configurational assignment of **4** and the other compounds described herein was achieved by combined use of ^{1}H- and ^{13}C-n.m.r.-spectroscopic results. The details of the assignment procedures are later given together for all compounds discussed. Parallel experiments with ^{14}C-labelled cyanide yielded a ^{14}C-labelled, acetylated cyanohydrin which could be incorporated (85%) into pure, crystalline **4**. The yield of **4** from **3** varied from 40 to 70%, depending on whether the substrate was dissolved in pyridine before adding acetic anhydride, or was dissolved in pyridine–acetic anhydride. Fast acetylation favored high yields. ^{13}C-N.m.r. data for the cyanohydrin **3** in pyridine-d_5 revealed the presence of an equal amount of its isomer **3a**. This confirmed the rapid epimerization of **3** when dissolved in pyridine.

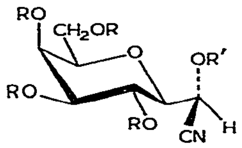
In water, the epimerization can be measured by observing the mutarotation. ^{13}C-N.m.r. investigation of the equilibrium mixture in water also showed an almost equal distribution of **3** and **3a**. Thus, **3** is not formed in a stereospecific, cyanohydrin synthesis, but as the result of crystallization of the mixture as one epimer (**3**) on evaporation of the aqueous solution. Strangely, the procedure of epimerization of **3** by dissolution and re-formation by evaporation, comparable to the anomerization and re-formation of a crystalline, free sugar when dissolved in water and crystallized from water, can be repeated without decomposition of the cyanohydrin **3** into its components. Thus, the epimerization can hardly proceed *via* retro-cyanohydrin reaction. When the cyanohydrin **3** is kept in $^{3}H_2O$ until mutarotation has ceased (2 days), the product (after acetylation) is labelled, showing that epimerization takes



1 R = H
2 R = Ac



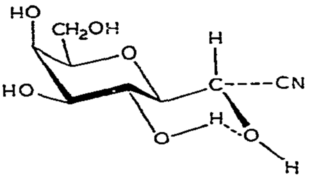
3 R = R' = H
4 R = R' = Ac
5 R = Ac, R' = H



3a R = R' = H
4a R = R' = Ac
5a R = Ac, R' = H

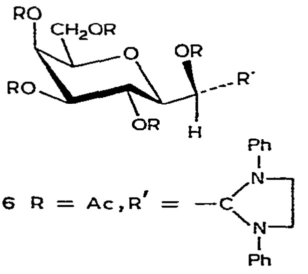
place through reversible deprotonation. Also, in the acetate **4**, the proton attached to C-2 exchanges with the medium (H_2O–pyridine), although, in this case, no epimerization can be observed by measuring the optical rotation.

A single, crystalline epimer could not be obtained when the cyanohydrin of 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose (**2**) was formed with hydrogen cyanide in pyridine. The product was an almost 1:1 mixture of 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-D-*threo*-L-*talo*-octononitrile (**5**) and 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octononitrile (**5a**). Acetylation of the mixture gave an equimolar mixture of **4** and **4a**, indicating a certain influence of the free hydroxyl groups upon the selective stabilization of epimer **3** as a crystalline compound. The stabilization may be due to intramolecular hydrogen-bonding between the hydroxyl groups attached to C-2 and C-4, and optimal orientation of the cyanide group in such a *quasi-trans*-decalin ring-system (**3b**).



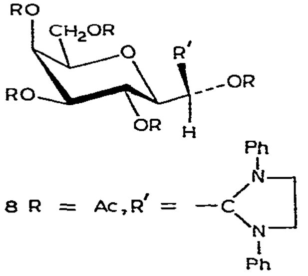
3 b

Reduction of pure **4** by the method of Moffatt *et al.*[5] in pyridine and aqueous acetic acid in the presence of *N*,*N*-diphenylethylenediamine again caused epimerization at C-2. The resulting imidazolidine derivatives 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octose *N*,*N*-diphenylimidazolidine (**8**) and 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*talo*-octose *N*,*N*-diphenylimidazolidine (**6**), formed in the ratio of 2.36:1, could be separated by fractional recrystallization, as well as by chromatography on a column of silica gel. Interestingly, the major product **8** has a configuration at C-2 the opposite of that of the starting material (**4**). By deprotecting the carbonyl group in both **6** and **8**, the aldehydes 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octose (**7**) and 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*talo*-octose (**9**) could be obtained in excellent yield.



6 R = Ac,R' =

7 R = Ac,R' = —CHO



8 R = Ac,R' =

9 R = Ac,R' = —CHO

TABLE I

^{1}H CHEMICAL-SHIFTS[a] AND H,H COUPLING-CONSTANTS[b] OF ATOMS H-1 TO H-8′ IN COMPOUNDS **4**, **4a**, AND **6**–**9**

Number of H atom	*Compound* **4**	**4a**[c]	**6**	**7**	**8**	**9**
1	—	—	5.95	9.52	5.89	9.49
2	5.50	5.58	5.03	5.11	5.25	5.27
3	3.84	3.82	3.59	4.11	3.76	4.01
4	5.40	5.30	5.24	5.39	5.60	5.51
5	5.09	5.08	4.92	5.07	4.92	5.04
6	5.44	5.46	5.43	5.45	5.34	5.43
7	3.98	4.02	3.90	3.90	3.91	3.95
8	4.16	4.23	4.49	4.08	4.30	4.12
8′	4.11	4.15	4.18	4.08	4.03	4.08
J(i,j)	**4**	**4a**[c]	**6**	**7**	**8**	**9**
1,2	—	—	9.0	0	8.0	0
2,3	2.5	3.0	1.5	2.3	2.1	2.2
3,4	10.0	10.0	10.0	10.0	10.0	10.0
4,5	10.0	10.0	10.1	10.0	10.0	10.0
5,6	3.5	3.5	3.5	3.5	3.3	3.3
6,7	1.0	1.0	1.0	1.0	1.0	1.0
7,8	6.8	7.0	7.5	6.5	6.0	7.0
7,8′	6.8	6.0	5.5	6.5	7.0	6.0
8,8′	11.5	11.5	11.5	—	11.0	11.5

[a] In p.p.m. (±0.01 p.p.m.) at 360 MHz; internal standard Me_4Si; solvent, $CDCl_3$; concentration, 10 mg/mL of solvent. [b] In Hz (±0.2 Hz), directly measured as line spacings in 360-MHz spectra. [c] Values are taken from the spectrum of a mixture of **4** and **4a**.

TABLE II

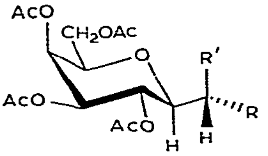
^{13}C-CHEMICAL SHIFTS[a] OF CARBON ATOMS 1 TO 8 IN COMPOUNDS **4**, **4a**, AND **6**–**9**

Number of C atom	*Compound* **4**	**4a**[b]	**6**	**7**	**8**	**9**
1	113.54	114.08	71.06	197.01	72.78	193.97
2	60.95	59.12	69.38	74.83	71.78	77.32
3	76.40	76.48	76.25	76.87	78.79	76.77
4	65.56	64.69	64.80	64.59	67.03	65.64
5	71.63	71.68	72.14	71.90	73.01	72.10
6	67.06	67.25	67.88	67.47	67.21	67.38
7	74.49	75.24	74.86	75.13	74.27	74.88
8	61.24	61.19	62.23	61.27	61.34	61.37

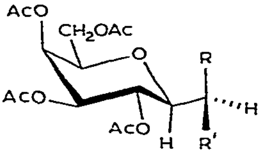
[a] In p.p.m. (±0.02 p.p.m.) at 90.53 MHz; internal standard Me_4Si; solvent $CDCl_3$; concentration, 100 mg/mL of solvent; for all compounds except **7** and **9**, which were measured at 25.16 MHz. [b] Values taken from the spectrum of a mixture of **4** and **4a**.

N.m.r.-spectral investigations. — ^{1}H-N.m.r.-spectral data for compounds **4**, **4a**, and **6–9** are given in Table I. At 360 MHz, the spectra are practically first-order, so assignment of the signals and evaluation of coupling constants was straightforward. ^{13}C-Chemical shifts for these compounds are given in Table II. Here, the assignments were unambiguously made by selective, proton-decoupling experiments.

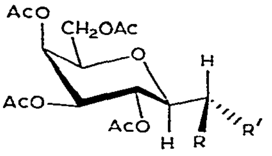
The H,H coupling-constants of H-3 to H-7 of the ring verified the expected chair conformation of the sugar, with all substituents equatorially attached, except the acetoxyl group at C-6. In all compounds examined, a small coupling constant ^3J (H-2,3) was observed, indicating that H-2 and H-3 are *gauche*-oriented. Of the two possible *gauche* forms, g_1 and g_2, only in g_1 are unfavorable, steric interactions between the equatorial acetoxyl substituent on C-4 and one of the substituents on C-2 avoided. (Such interactions would also occur in the *anti* form *a*; this form is, therefore, also less favored.) Similar, favored forms have been observed for related compounds (*e.g.*, methoxymenthane *versus* neomethoxymenthane[11]). All of the configurational assignments rest on the very plausible assumption that, in all compounds, the g_1 disposition is highly favored.



g_1



g_2



a

On the basis of this conformational assignment, configurations can be assigned for **4** and **4a** from the coupling constants observed between C-1 and H-3. There is experimental and theoretical evidence that vicinal, C,H couplings have a dependence on dihedral angles similar to that of the corresponding H,H couplings[12]. The signals for the cyano carbon atom (C-1) in **4** and **4a** appear as doublets of doublets in the proton-undecoupled, ^{13}C-n.m.r. spectra, because of coupling to H-2 and H-3. By

TABLE III

C,H COUPLING-CONSTANTS TO CARBON ATOM 1 IN COMPOUNDS **4**, **4a**, **7**, AND **9**[a]

Compound	*Coupling constant*		
	^3J(C-1,H-3)	^2J(C-1,H-2)	^1J(C-1,H-1)
4	4.6	7.8	—
4a	1.6	7.7	—
7	—	4.6	185.0
9	2.9	4.4	184.4

[a] In Hz (±0.2 Hz), measured as line spacings in 25.16- (**4**, **7**, and **9**) and 90.53- (**4** and **4a**) MHz, ^{13}C-n.m.r. spectra for CDCl$_3$ solutions. Values for **4a** are taken from measurements made for a mixture of **4** and **4a**.

selectively decoupling from H-2, the two coupling-constants can unambiguously be differentiated; the resulting assignments are given in Table III. The vicinal, C,H coupling-constants are quite different for **4** and **4a**, as expected for either the antiperiplanar or the gauche arrangement of the two coupling atoms (H-3 and C-1). Configuration **4** is, therefore assigned to the compound having the larger ^3J (C-1, H-3) value. In the same way, configurational assignments may be made for the two aldehydes **7** and **9**, the relevant coupling-constants for which are also given in Table III. The smaller values observed for the aldehydes are a consequence of the well-known dependence of two- and three-bond, C,H coupling-constants on the hybridization of the coupling carbon atom[12].

An independent determination of the configuration is possible for the two diphenylimidazolidine derivatives **6** and **8**. These compounds also have the favored, g_1 orientation with respect to the C-2,C-3 bond. From the large coupling-constant ^3J (H-2,H-1), the favored, antiperiplanar arrangement can be deduced for these two hydrogen atoms. As may be seen from Tables I and II, the chemical shifts for some of the hydrogen and carbon atoms are quite different for the two diastereomers. Even larger differences are, however, found for the diastereotopic groups of the diphenylimidazolidine rings, whose chemical-shift values are given in Table IV. From selective, decoupling experiments, it was shown that the chemical-shift differences between the protons of one CH$_2$ group are small compared to the differences between the two diastereotopic groups. Also, by decoupling experiments, the *ortho*- and *para*-protons can be connected, showing that the set of signals at higher field belongs to protons on the same ring. The ^{13}C signals can also be assigned by selective decoupling, again showing that the set of ortho and para signals at high field belong to carbon

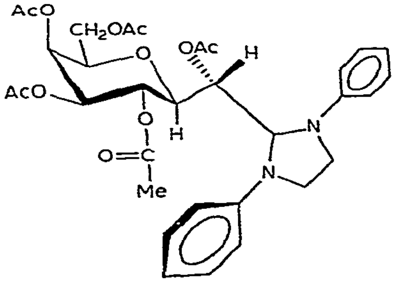
TABLE IV

^{1}H AND ^{13}C CHEMICAL-SHIFTS[a] OF THE DIASTEREOTOPIC GROUPS IN THE DIPHENYLIMIDAZOLIDINE RINGS IN COMPOUNDS **6** AND **8**

H(C)	*^1H*		*^{13}C*	
	6	**8**	**6**	**8**
N—CH$_2$	3.81–3.69	3.80–3.69	47.21	50.57
N—CH$_2$	3.54	3.38–3.27	45.17	45.58
s	—	—	146.30	146.76
o	6.72	6.73	113.02	112.79
m	7.22	7.20	129.01[b]	129.01[b]
p	6.72	6.72	117.41	117.25
s′	—	—	147.33	149.22
o′	6.86	6.93	113.40	117.42
m′	7.28	7.21	129.56[b]	129.21[b]
p′	6.82	6.86	118.82	120.71

[a] For the conditions of measurement, see footnotes to Tables I and II. [b] The assignments may be reversed.

atoms in the same ring. In **8**, one phenyl ring exhibits carbon signals (s,o,m,p) that are quite untypical for an *N*-substituted phenyl ring. The chemical shifts are more typical for a situation wherein the resonance interaction between the nitrogen substituent and the ring is (at least partially) inhibited. As may be found by inspection of models, only for **8** does such an inhibition of resonance-interaction occur for one of the phenyl rings because of steric interaction with the sugar ring (see also, **8a**). The configurational assignment following from this rather unusual phenomenon of steric inhibition of resonance (by a substituent that is far removed) through bonds is fully consistent with the assignment made from the coupling constants for aldehyde **9**.



8a

EXPERIMENTAL

General methods. — Optical rotations were measured with a Perkin–Elmer 141 polarimeter. T.l.c. was performed on silica gel F_{254} (Merck) using the following solvent-systems: *A*, 4:1 (v/v) ether–light petroleum (b.p. 60–70°) for fully acetylated compounds; *B*, 4:1 (v/v) benzene–methanol for partially acetylated compounds; and *C*, 25:14:7 (v/v/v) ethyl acetate–2-propanol–water for nonacetylated sugars. Detection was effected by charring with sulfuric acid. ^{1}H-N.m.r. spectra ($CDCl_3$, internal standard Me_4Si) were recorded with a Varian EM 390 (90 MHz) and a Bruker HX 360-MHz spectrometer, and ^{13}C-n.m.r. spectra at 25.2 MHz were recorded in the Fourier mode with a Varian spectrometer XL 100/15 and, at 90.53 MHz, with a Bruker HX 360 spectrometer. Radioactive samples were measured in a Berthold BF 815 liquid scintillation counter (LSC); "Cocktail": 5.0 g of PPO and 62.5 mg of POPOP in 1 L of toluene.

3,7-Anhydro-D-threo-L-talo-*octononitrile* (**3**). — A solution of 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose *N*,*N*-diphenylimidazolidine[8] (20 g) in dichloromethane (300 mL) was treated at 0° with a solution of *p*-toluenesulfonic acid monohydrate (20 g) in acetone (200 mL). After 1 h, the precipitate was filtered off with suction, and washed once with dichloromethane (200 mL). The combined filtrates were successively washed with 1% aqueous sodium hydrogencarbonate solution and water (twice), dried (magnesium sulfate), and evaporated *in vacuo*. The residue was deacetylated with 0.01M sodium methoxide (200 mL), and after 2 h at room temperature, the solution was evaporated to dryness under diminished pressure. The residue was dissolved in water (75 mL), sodium cyanide (3.61 g) was added, and the solution was kept for 24 h at 0°. By stirring the solution with Amberlite IR-120 (H^+) ion-exchange resin, sodium ions were removed, and the neutral filtrate was evaporated *in vacuo*, to yield crystalline **3** (6.72 g, 85%), m.p. 159°, $[\alpha]_{578}^{22}$ $-14.0 \rightarrow +30°$ (3.5 h; *c* 10.0, H_2O); t.l.c., R_F 0.45 (system *C*); ν_{max}^{KBr} 3300 cm^{-1} (OH).

Anal. Calc. for $C_8H_{13}NO_8$: C, 43.84; H, 5.98; N, 6.39. Found: C, 43.73; H, 6.09; N, 6.05.

*2,4,5,6,8-Penta-*O*-acetyl-3,7-anhydro-*D-threo-L-talo-*octononitrile* (**4**). — Acetylation of **3** (8.76 g) was conducted at 20° with 1 : 1 (v/v) pyridine–acetic anhydride (100 mL). Evaporation of the mixture under diminished pressure gave a syrup which, on addition of ether (50 mL), yielded **4** (11.85 g, 69%). If **3** was kept for 7 h in pyridine before acetic anhydride was added, the yield of **4** fell to 42%. Similarly, the yield of **4** decreased (to 49%) when the acetylation was performed for 30 min at 50°. Compound **4** had m.p. 142°, $[\alpha]_{578}^{22}$ +20.5° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1750 cm^{-1} (C=O).

Anal. Calc. for $C_{18}H_{23}NO_{11}$: C, 50.35; H, 5.40; N, 3.26. Found: C, 50.25; H, 5.45; N, 2.97.

*2,4,5,6,8-Penta-*O*-acetyl-3,7-anhydro-*D-threo-L-galacto-*octose* N,N-*diphenylimidazolidine* (**8**) *and 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-*D-threo-L-talo-*octose* N,N-*diphenylimidazolidine* (**6**). — Compound **4** (8.67 g) was added in one portion to a vigorously stirred mixture of Raney nickel (30 g), sodium hypophosphite monohydrate, and *N,N*-diphenylethylenediamine (17.88 g) in pyridine (150 mL) and 1 : 1 (v/v) acetic acid–water (150 mL). Stirring was continued for 20 h. The nickel was then filtered off, and rinsed with dichloromethane (3 × 200 mL), and the combined filtrates were washed with water (6 × 200 mL), dried ($MgSO_4$), and evaporated under diminished pressure, to yield a syrup which, on adding a small amount of methanol, crystallized partially. Recrystallization from methanol gave pure **8** (5.93 g, 46.8%), m.p. 242°, $[\alpha]_{578}^{22}$ −19.5° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1750 cm^{-1} (OAc).

Anal. Calc. for $C_{32}H_{38}N_2O_{11}$: C, 61.33; H, 6.13; N, 4.47. Found: C, 61.34; H, 6.36; N, 4.46.

The mother liquor, which contained mainly **6** and *N,N*-diphenylethylenediamine, was purified on a column (100 × 4 cm) of silica gel. Fractions containing **6** were combined and evaporated to dryness, yielding a syrup that could be crystallized, and recrystallized, from ether (2.5 g, 19.8%), m.p. 141°, $[\alpha]_{578}^{22}$ −40° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1750 cm^{-1} (OAc).

Anal. Calc. for $C_{32}H_{38}N_2O_{11}$: C, 61.33; H, 6.13; N, 4.47. Found: C, 61.25; H, 6.26; N, 4.41.

*2,4,5,6,8-Penta-*O*-acetyl-3,7-anhydro-*D-threo-L-galacto-*octose* (**7**) *and 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-*D-threo-L-talo-*octose* (**9**). — The free octoses **7** and **9** were generated from the corresponding imidazolidines **6** and **8** by treatment with *p*-toluene-sulfonic acid as described[8] for **2**. Compound **6** (2.0 g) gave colorless, foamy **7** (1.23 g, 89%), $[\alpha]_{578}^{22}$ +38.5° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1740 cm^{-1} (OAc).

Anal. Calc. for $C_{18}H_{24}O_{12}$: C, 50.00; H, 5.59. Found: C, 49.98; H, 5.80.

Compound **8** (2.0 g) gave **9**, a colorless foam (1.23 g, 89%), $[\alpha]_{578}^{22}$ −2.5° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1740 cm^{-1} (OAc).

Anal. Calc. for $C_{18}H_{24}O_{12}$: C, 50.00; H, 5.59. Found: C, 49.60; H, 5.59.

*Preparation of a mixture of 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-*D-threo-L-talo-*octononitrile* (**5**) *and 4,5,6,8-tetra-*O*-acetyl-3,7-anhydro-*D-threo-L-galacto-*octononitrile* (**5a**). — Compound **2**, prepared from the imidazolidine **1** (20 g) as described[8], was dissolved in pyridine (150 mL). Hydrogen cyanide, prepared from sodium cyanide (5.0 g) was condensed into the solution, and the mixture was kept for 24 h at 0°. After evaporation, the syrup remaining was shown by n.m.r. spectroscopy to be an ~1:1 mixture of **5** and **5a** (see Table I).

Exchange experiments with ^3H_2O. — Compound **3** (52 mg) was dissolved in ^3H_2O (0.5 mL; 26.123 Ci per mmol). After being kept for 48 h at room temperature, the ^3H_2O was removed by freeze-drying, and the residue (**3**) was submitted to acetylation as described for the preparation of **4**. After three recrystallizations from ether, the specific radioactivity (5.853 μCi/mmol) was constant. When [^{3}H]**4** (5.93 mg) was dissolved in 2:1:1 (v/v/v) pyridine–water–acetic acid (4 mL), and kept for 24 h at room temperature, 45.1% of the total ^{3}H-activity was volatile, and could be removed by freeze-drying; this indicated a significant ^{3}H-exchange also in the peracetylated cyanohydrin (**4**). Compound **4** could be recovered quantitatively.

*Determination of the stereochemical yield in the preparation of 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-*D-threo-L-talo-*octononitrile* (**4**). — Sodium cyanide (50 mg) was dissolved in water (1 mL), and a trace of $K^{14}CN$ (specific activity, 7.26 mCi/g) was added, to give a solution containing 625.64 μCi of ^{14}C-activity. Compound **1** (180 mg) was dissolved in this solution, and ^{14}C-labelled **4** was prepared as described for the unlabelled sample. Acetylation of **3**-^{14}C to give **4**-^{14}C was also performed as described before. The crude, ^{14}C-labelled sample (203 mg) was, after processing of the acetylation mixture, mixed with pure **4** (1.1 g), and recrystallized. After 6 recrystallizations, the specific radioactivity remained constant, indicating a yield of 85% of pure **4**. It may be assumed that the remaining 15% consisted of the epimeric 2,4,5,6,8-penta-*O*-acetyl-3,7-anhydro-D-*threo*-L-*galacto*-octononitrile (**4a**).

	Original mixture	*Recrystallization number*						
		1	*2*	*3*	*4*	*5*	*6*	*7*
μCi	312.82	184	232.5	244.7	256.6	265.8	271.2	272

ACKNOWLEDGMENTS

We thank the Deutsche Forschungsgemeinschaft for financial support, and Degussa for the donation of Raney nickel.

REFERENCES

1 H. KILIANI, *Ber.*, 18 (1885) 3066–3072; 19 (1886) 767–772, 1128–1130.

2 N. K. RICHTMYER, *Methods Carbohydr. Chem.*, 1 (1962) 160–167.

3 (a) J. M. BOURGEOIS, *Helv. Chim. Acta*, 58 (1975) 363–371; (b) K. SATO, J. YOSHIMURA, AND C. SHIN, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1191–1194.

4 (a) H. S. ISBELL, N. B. HOLT, AND H. L. FRUSH, *Methods Carbohydr. Chem.*, 1 (1962) 276–280; (b) R. SCHAFFER AND H. S. ISBELL, *ibid.*, 1 (1962) 281–285.

5 H. P. ALBRECHT, D. P. REPKE, AND J. G. MOFFATT, *J. Org. Chem.*, 38 (1973) 1836–1840.

6 G. TRUMMLITZ AND J. G. MOFFATT, *J. Org. Chem.*, 38 (1973) 1841–1845; N. P. DAMODARAN, G. H. JONES, AND J. G. MOFFATT, *J. Am. Chem. Soc.*, 93 (1971) 3812–3813; K. ICHIMURA, *Bull. Chem. Soc. Jpn.*, 43 (1970) 2501–2506; H. SAEKI, T. IWASHIGE, K. FURUYA, AND M. SHIRASAKA, *Ann. Sankyo Res. Lab.*, 19 (1967) 137–143; H. SAEKI AND E. OHKI, *Chem. Pharm. Bull.*, 18 (1970) 789–802.

7 M. BROCKHAUS AND J. LEHMANN, *Carbohydr. Res.*, 53 (1977) 21–31.

8 H.-M. DETTINGER, G. KURZ, AND J. LEHMANN, *Carbohydr. Res.*, 74 (1979) 301–307.

9 M. BROCKHAUS AND J. LEHMANN, *FEBS Lett.*, 62 2 (1976) 154–156.

10 D. DANNEELS AND M. ANTEUNIS, *Org. Magn. Reson.*, 8 (1976) 539–541.

11 F. W. WEHRLI AND T. WIRTHLIN, *Interpretation of Carbon-13 N.M.R. Spectra*, Heyden & Son, Ltd., London, New York, 1976, pp. 53–56.