Cyclizations of Dialdehydes with Nitromethane. XV. Synthesis of Four Stereoisomeric Deoxynitroinositol Monomethyl Ethers[1]

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Received January 4, 1973

Methylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) followed by hydrolysis of the 5,6-ketal group and periodate oxidation gave 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose (**4**). Addition of nitromethane to **4** afforded a mixture of 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-nitro-α-D-glucofuranose (**5**) and -β-L-idofuranose (**6**). Removal of the 1,2-ketal group led to a mixture of 6-deoxy-3-*O*-methyl-6-nitro-D-glucose (**7**) and -L-idose (**8**) from which the crystalline β-anomer of **7** could be isolated. Cyclization of the nitro hexoses by internal Henry reaction furnished four stereoisomeric deoxynitroinositol monomethyl ethers which were obtained in crystalline condition, in part directly and in part via acetone and acetyl derivatives. The *scyllo* (**9**), DL-*myo*-1 (**10**), *muco*-3 (**14**), and *epi*-3 (**16**) configurations were assigned to the products by n.m.r. spectroscopy.

La méthylation du di-*O*-isopropylidène-1,2:5,6-α-D-glucofuranose (**1**) suivie de l'hydrolyse du groupe cétal-5,6 et de l'oxydation périodique, conduit à l'*O*-isopropylidène-1,2-*O*-méthyl-3-α-D-*xylo*-pentodialdofuranose-1,4 (**4**). L'addition de nitrométhane à **4** conduit à un mélange de déoxy-6-*O*-isopropylidène-1,2-*O*-méthyl-3 nitro-6-α-D-glucofuranose (**5**) et de -β-L-idofuranose (**6**). L'enlèvement du groupe cétal-1,2 conduit au mélange de déoxy-6-*O*-méthyl-3 nitro-6-D-glucose (**7**) et de -L-idose (**8**) à partir duquel l'anomère β cristallin de **7** a pu être isolé. La cyclisation des nitrohexoses par une réaction de Henry interne fournit quatre éthers déoxynitroinositolmonométhylés diastéréoisomères qui ont été obtenus cristallisés soit par voie directe, soit par les dérivés acétone et acétyle. Les configurations *scyllo* (**9**), DL-*myo*-1 (**10**), *muco*-3 (**14**), et *épi*-3 (**16**) ont été attribuées aux produits par spectroscopie r.m.n.

[Traduit par le journal]

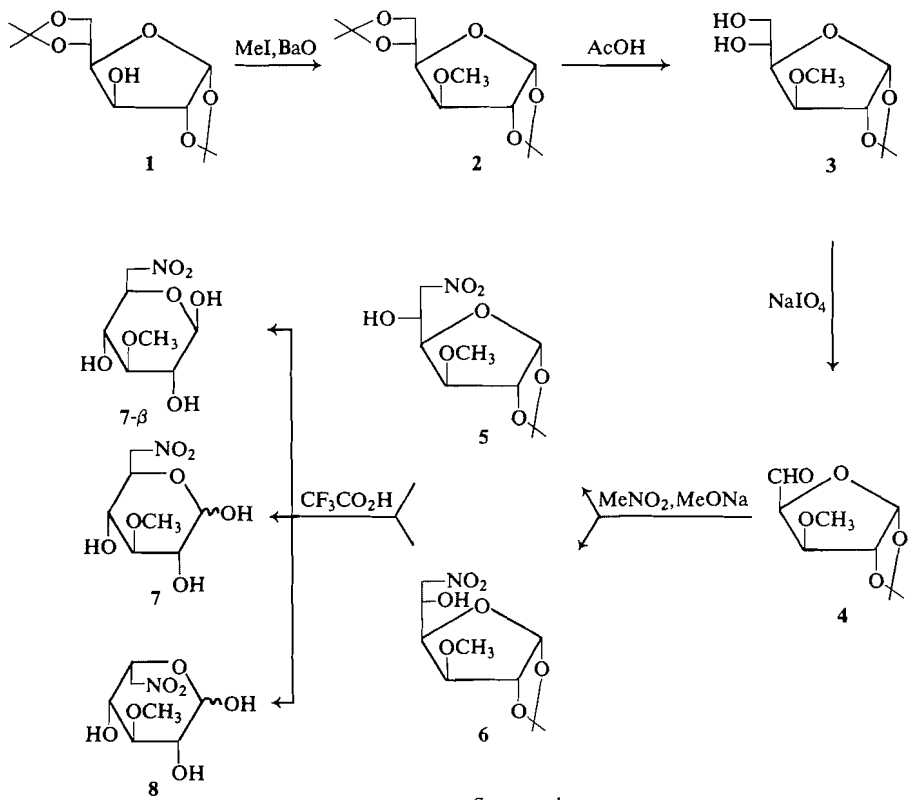
Can. J. Chem., 51, 1801 (1973)

Several recent articles from this laboratory dealt with non-bonded interactions between hydroxyl groups and nitro groups in vicinal position on pyranoside rings, with special reference to the formation and stability of glycoside nitronates. Conformational preferences and configurational equilibrations in such glycosides were correlated with such interactions, and the studies led to new insights into chemical reactivities and mechanisms in this field (2–5). It became desirable to seek, along similar lines, a better understanding of certain aspects of the formation and mutual interconversion of stereoisomeric deoxynitroinositols (6–10), and it now seemed profitable to apply the newly developed concepts and methods of study to this related group of compounds.

It was reasoned that the planned investigations might be facilitated if there were available a number of stereoisomeric deoxynitroinositols that carry an *O*-methyl group in opposition to the nitro function. The methyl group, it was hoped, should render the isomers more readily distinguishable by n.m.r. spectroscopy and thus aid in the analysis of product mixtures while at the same time this functionality would be distant from, and not interfere with, the nitrodiol moiety whose chemistry was to be examined. Consequently we synthesized such methyl ethers as will be reported here, and studied mechanistic aspects of their formation and epimerization as will be communicated elsewhere (11).

The synthesis was to be patterned after the Fischer–Grosheintz nitroinositol synthesis (6, 12) which involves a stepwise nitromethane cyclization of a partially blocked pentodialdose. It was therefore necessary, first, to synthesize 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-pentodialdo-1,4-furanose (**4**) and thence 6-deoxy-3-*O*-methyl-6-nitro-D-glucose (**7**) and (or) its L-*ido* isomer (**8**). The pathway that led to the crystalline β-anomer of **7**, and also to a mixture of **7** and **8** which could not be separated, is delineated in Scheme 1. 1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (**1**) was methylated by the Kuhn method (13), which proved simple and furnished the 3-*O*-methyl derivative **2** in 83% yield. Partial hydrolysis to give 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-glucofuranose (**3**) was readily achieved with 90% acetic acid. The product

[1]For part XIV in this series see ref. 1.



SCHEME 1

could be purified with advantage by chromatography on silica gel instead of distillation as was practiced earlier (14). However, crude **3** was satisfactory for immediate use in the subsequent step. Its periodate oxidation smoothly afforded the partially blocked dialdose **4** as a chloroform-soluble syrup. Because of its apparent sensitivity, purification of **4** for elemental analysis was not pursued, but the n.m.r. spectrum proved its structure beyond doubt. The data (see Experimental) also gave an indication of the conformation of **4** and its precursors **2** and **3**. At 1000 Hz sweep width the signals of H-2 and -3 appeared as doublets due to coupling with H-1 and -4, respectively; the observed splittings were 2.5–4 Hz, and coupling between H-2 and -3 was too small to be observable. These features showed that the furanose ring in these compounds exhibits the same conformational preference as that in 1,2-*O*-isopropylidene-α-D-glucofuranose and related derivatives (15–17). Originally the $^3T_2$ twist conformation had been proposed (15) for this system, but more recent studies indicate (17) that it may better be described by the segment $^3T_4 \rightleftarrows E_4 \rightleftarrows {}^0T_4$ of the cycle of furanose conformers. Another noteworthy signal in the spectrum of **4** was a low-field doublet (δ 9.66, J = 1.5 Hz) whose intensity corresponded to 80% of one proton and tended to decrease when attempts were made to purify the product by repeated distribution between chloroform and water. The signal was assigned to the aldehydic H-5, and the implication is that the compound as prepared under our conditions exists largely as the free aldehyde depicted (**4**) but is prone to undergo hydration and perhaps dimerization. The 3-*O*-benzyl analog of **4** has been regarded as a free aldehyde, whereas the 3-hydroxy analog is known to form, reversibly, a dimeric product (18–20).

The aldehyde **4** was combined with nitromethane in the presence of sodium methoxide in the usual manner. After acidification, the addition product was purified chromatographically to give analytically pure nitro sugar as a syrup which, although exhibiting a single spot on t.l.c., was revealed by its n.m.r. spectrum to be a 2:1 mixture of two components (**5** and **6**). In the

expected resonance position of H-1 a slightly asymmetric, apparent triplet consisting of two partially overlapping doublets was found (δ 5.79 and 5.90; $J_{1,2}$ = 4–5 Hz). The outer lines had an intensity ratio 2:1, and the stronger signal could be attributed to 6-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-6-nitro-α-D-glucofuranose (**5**) when, at a later stage, pure **5** became available for comparison. The second component was judged to be the β-L-*ido* isomer (**6**). The configurational assignments were supported by circular dichroism data (see later).

The preponderance of the D-*gluco* epimer **5** in the expected formation of two epimers from **4** deserves comment since the 3-*O*-benzyl analog of **4** has been shown to react with Grignard reagents to give preponderantly L-*ido* derivatives, with the degree of stereoselectivity being influenced by the solvent (19, 20). It has been suggested that the transition state in those Grignard reactions may involve coordination between the magnesium and the carbonyl and ring oxygen atoms (21). It can be seen in a molecular model that such a cyclic complex requires the aldehyde group to be so oriented as to expose its *si* face to the less hindered, rear side of the molecule, and attack from that direction will generate the *S* configuration at C-5 and therefore produce L-*ido* derivatives. In our reaction, which is characterized by methanenitronate ion preferentially attacking the *re* face to produce the *R* configuration at C-5, the rotameric orientation of the aldehyde group is not constrained by complexing. A preferred arrangement of the carbonyl double bond antiperiplanar to the C_4—O bond, plausible on grounds of dipole considerations, would be able to account for the result.

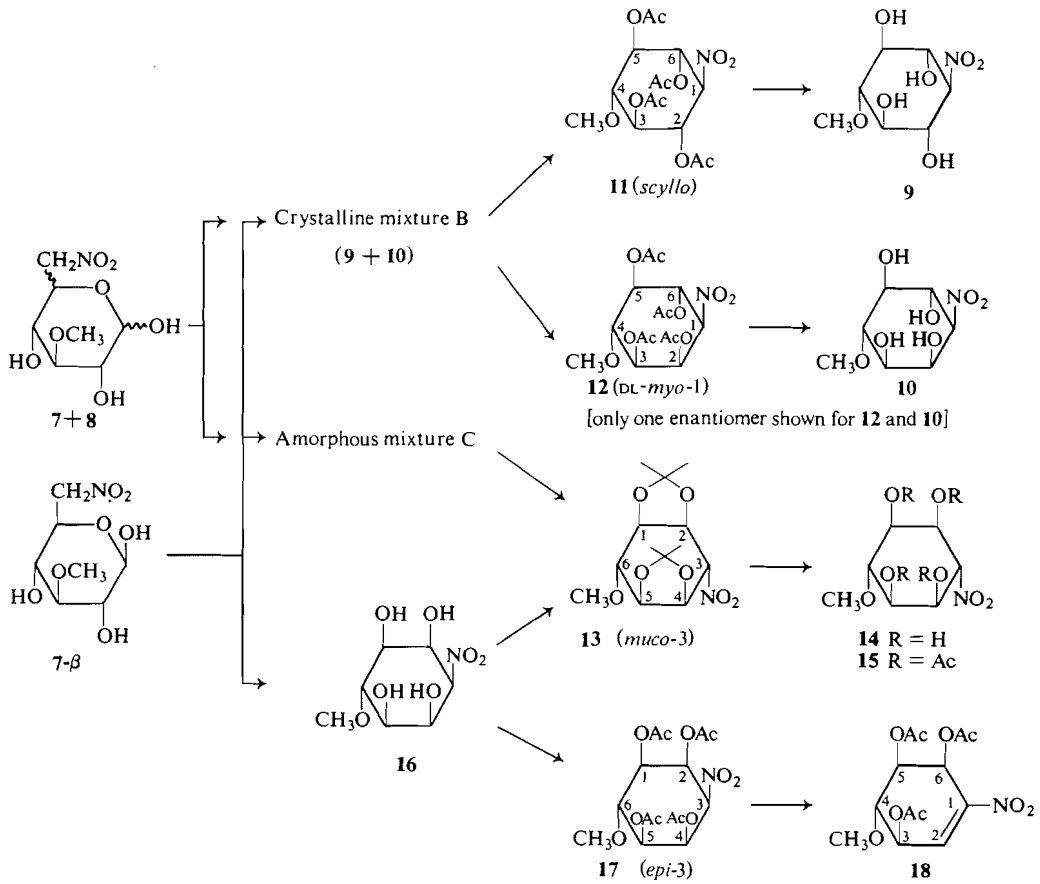
The mixture of **5** and **6** was hydrolyzed with 90% trifluoroacetic acid for removal of the isopropylidene group. One of the products was obtained in crystalline form in 49% yield. It exhibited a negative Cotton effect, indicative of the *R* configuration at C-5, the asymmetric carbon atom next to the nitromethyl group (22), and was thereby revealed to be the D-*gluco* derivative **7**. The crystalline substance (termed **7**-β) was assigned the β-anomeric configuration as it exhibited upward mutarotation. The mother liquor of the reaction yielded an additional 32% of product as a non-mutarotating syrup which showed a positive Cotton effect such as would accord with a mixture containing preponderantly the L-*ido* isomer **8** along with some **7**. The syrup could be used in the subsequent reactions so that the practical, over-all yield in nitro sugars based on **1** was about 45%.

When crystalline **7**-β was reacetonated, syrupy but analytically pure **5** was obtained. It showed the n.m.r. doublet for H-1 at δ 5.90 and exhibited a negative Cotton effect. Similar reacetonation of the mother liquor mixture **8** + **7** gave a mixture of **5** and **6** similar to that described above, except that the intensity ratio of the H-1 doublets was reversed, indicating a 2:1 preponderance of **6**. This mixture showed a positive Cotton effect.

Cyclization of the nitro hexoses **7** and **8** to furnish inositol derivatives was performed in a manner similar to the cyclization of the non-methylated analogs (6). Two procedures were used, namely, reaction in aqueous barium hydroxide solution, and reaction in a mixture of methanol and nitromethane in the presence of sodium methoxide. The first-mentioned procedure gave better yields and was more convenient in work-up; the results shown in Scheme 2 and to be discussed in detail first refer to it. The results of the second procedure, to be mentioned briefly afterwards, were qualitatively similar although there were some minor differences.

When amorphous mixtures of **7** and **8**[2] were employed for cyclization, a partly crystalline mixture of isomeric inositols arose. The smaller, crystalline part (21–30%) of the product melted above 200°, was sparingly soluble in ethanol, and was shown by chromatography to consist of of two compounds (**9** and **10**). They could not be separated directly but gave separable tetraacetates (**11** and **12**) whose acid-catalyzed methanolysis then furnished pure **9** and **10**. The tetraacetates arose in yields of, for instance, 58 (**11**) and 32% (**12**), and presumably **9** and **10** had constituted the crystalline part of that particular cyclization mixture in a similar ratio. The *scyllo* and *myo*-1 configurations were assigned to these isomers on evidence to be given below. The larger, non-crystalline part (36–56%) of the cyclization mixture contained, besides colored impurities, very little of **9** or **10** but consisted chiefly of at least one other isomer.

[2]This refers to both the mother liquor material (richer in **8**) remaining after isolation of crystalline **7**-β, and to the total mixture (richer in **7**) as obtained prior to such isolation.



SCHEME 2

Acetonation of this part led to a di-*O*-isopropylidene derivative (**13**) whose deacetonation afforded the crystalline *muco*-3 isomer **14**. For further characterization, **14** was acetylated to its tetraacetate **15**. From the isolated amount of diacetone derivative **13**, one might have concluded that the mixture subjected to acetonation had contained at least 31% of **14**. This was not the case, however. Compound **14** can be distinguished readily by n.m.r. spectroscopy (see later), and it was found that only small proportions of **14** (never more than 10%) were present in the mixture prior to acetonation. The bulk of **13** must therefore have originated from a secondary reaction, the nature of which will be disclosed later on.

Use of crystalline **7**-β in the barium hydroxide-induced cyclization again furnished a partly crystalline product. However, fractional recrystallization of the crystalline portion not only yielded mixtures of **9** and **10** as before, though in somewhat smaller amounts (18–19%), but gave in addition a fourth isomer (m.p. 165–167°) as the chief component (27–45%). The amorphous portion of the reaction product (29–41%) had similar characteristics as in the previous experiment; although it contained little, if any, of the *muco*-3 isomer **14**, it was acetonated to produce the diacetone derivative **13**. The crystalline, fourth nitroinositol isomer just mentioned was allocated the *epi*-3 configuration (**16**). Acetylation gave a crystalline tetraacetate (**17**) that was characterized by n.m.r. spectroscopy but proved too unstable for purification for elemental analysis. In attempted recrystallization from ethanol a sample deteriorated due to dehydroacetylation. This became evident by the appearance of a low-field n.m.r. signal (δ 7.25) attributable to an olefinic proton, and eventually a small amount of the nitroolefin [3,5,6/4]-3,5,6-

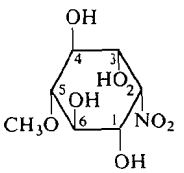
triacetoxy-4-methoxy-1-nitrocyclohexene (**18**) was isolated.[3]

An unexpected observation was made when the *epi*-3 isomer **16** was acetonated. A di-*O*-isopropylidene derivative was formed, but the isolated product (yield, 36%) evidently had undergone epimerization during work-up or chromatography on silica gel and proved identical with **13**. This was verified by acid-catalyzed methanolysis which did not regenerate **16** but gave **14** instead. The epimerization is reminiscent of the facile conversion of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-nitro-α-D-glucofuranose into its D-*allo* isomer (16).

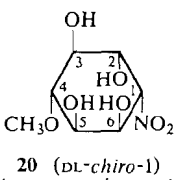
Cyclization of crystalline **7**-β in a methanol–nitromethane solvent containing sodium methoxide furnished a crystalline mixture of **9** and **10** (16%), crystalline **14** (8%), and an amorphous material (61%) that appeared similar in composition to that obtained in the barium hydroxide-promoted reactions.

Configurational Assignments

In the cyclization of the 6-deoxy-6-nitrohexoses considered here, two centers of prochirality (C-1 and -6) are directly involved in producing two new chiral centers in the products. A third chiral center affecting the number of possible epimers stems from chiral C-5 in the hexoses. Due to possibilities of over-all symmetry, however, only six stereoisomeric deoxynitroinositols can thus arise, namely, four meso forms (with the *scyllo*, *myo*-2, *muco*-3, and *epi*-3 configurations) and two racemic forms (with the *myo*-1 and *chiro*-1 configurations). Of these, the *myo*-2 (**19**) and *chiro*-1 (**20**) isomers seemed unlikely to arise under the present conditions because of conformational energy considerations, and the remaining four have all been encountered in this work.



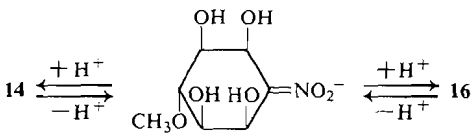
19 (*myo*-2)



20 (DL-*chiro*-1)
[only one enantiomer shown]

[3]It is interesting to note in this connection that the stereoisomeric tetraacetates **11** and **15** were completely stable, whereas **12** was somewhat prone to decomposition if much less so than **17**.

The two isomers that gave a diisopropylidene derivative (in a non-forcing procedure of acetonation) must each possess two *cis*-glycol groupings, a condition met only by **14** and **16**. The fact that the diisopropylidene derivative of one isomer was converted during work-up into that of the other isomer, shows that they were epimeric at the carbon bearing the nitro group where epimerization through the common nitronate ion can occur. Confirming this, the n.m.r. spectra given by **14** and **16** in the presence of excess sodium deuteroxide in D_2O were identical, in accord with the existence of one common nitronate (**21**).

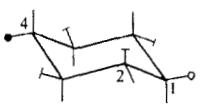
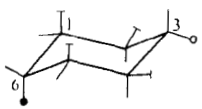
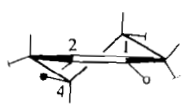


21

Finally, unambiguous allocation of formulas **14** and **16**, and of **9** and **10** to the other two isomers, was possible by analysis of n.m.r. spectra of their tetraacetates in chloroform-*d* (Table 1).[4] The *muco*-3 and *epi*-3 tetraacetates (**15** and **17**) each exhibited in order of decreasing field a one-proton signal for H-6, a one-proton signal for H-3, and two two-proton signals for the enantiotopic pairs H-1, H-5 and H-2, H-4. Two pairs of enantiotopic acetyl groups gave two 6-proton singlets in each compound, and the methoxy group gave a three-proton singlet. Compound **17** showed large coupling in the triplet for H-6 ($J_{1,6} = J_{5,6} = 10$ Hz), indicating a 1,6,5-triaxial proton arrangement and therefore equatorial substituents in these positions. The coupling $J_{1,2}$ ($= J_{4,5}$) was small, requiring the substituents at C-2 and -4 to be axial and hence *cis* to those at C-1 and -5, in accord with the chemical evidence of facile acetonation. The triplet for H-3 showed small coupling (3 Hz), but this feature, even though it was consistent with an equatorial nitro group flanked by two axial acetoxyls as depicted in Table 1, did not disprove an axial nitro group. The *epi*-3 configuration could nevertheless be allocated to **17** with certainty since inversion at C-3 would result in the *muco*-3 configuration which, it was found, must be reserved for compound **15** for the

[4]The spectra of the free nitroinositols in aqueous trifluoroacetic acid were in complete agreement; see Experimental.

TABLE 1. Nuclear magnetic resonance data of acetates in $CDCl_3$

Compound*	Chemical shifts (δ, from TMS)								Couplings (Hz)					
	H-1	H-2	H-3	H-4	H-5	H-6	CH_3O	CH_3CO_2	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,1}$
 **11**	4.80	5.58	5.14	3.55	5.14	5.58	3.45	2.06, 2.00	10.5	10	9.5	9.5	10	10.5
 **12**	4.76	5.96	4.95	3.70	5.07	5.90	3.45	2.10, 2.07, 2.03, 1.97	3	2	10	10	10	11
 **15**	5.52	5.65	5.16	5.65	5.52	3.68	3.54	2.09, 1.97	3	11	11	3	3	3
 **17**	5.02	6.30	4.82	6.30	5.02	3.85	3.48	2.13, 2.09	3	3	3	3	10	10
 **18**		7.25	5.59	3.82	5.13	6.40	3.51	2.17, 2.11, 2.06		3	8	11	4	

*Symbols: ⚲ OMe, ⊤ OAc, ⚲ NO_2, | H.

following reason. Compound **15** exhibited large splitting in its triplet of H-3 ($J_{2,3} = J_{3,4} = 11$ Hz), clearly requiring a 2,3,4-triequatorial substituent arrangement. This condition is realized only in one conformer, namely that of the *muco*-3 epimer shown in Table 1. The remaining coupling constants, all small, were in harmony with substituent orientations as depicted. It is noteworthy that the non-acetylated *muco*-3 isomer **14** in aqueous solution also adopts the same conformation, with an equatorial nitro group and an axial methoxyl group, as was revealed by analogous n.m.r. data (see Experimental). Evidently when **21**, the nitronate common to **14** and **16**, is protonated, the rule of equatorial nitro group preference (2) is obeyed for both products. In **14**, the methoxyl proton signal is found markedly upfield (by 0.15–0.2 p.p.m.) from the corresponding signals of its three isomers, rendering **14** easily recognizable.

Assignment of the *scyllo* and *myo*-1 configurations to the tetraacetates **11** and **12**, respectively, was straightforward. Thus **11** (and also its parent compound **9**) revealed molecular symmetry by the presence of two pairs of enantiotopic hydrogen atoms (H-2, H-6 and H-3, H-5) which each gave rise to a two-proton signal. All the coupling constants were large (9.5–10.5 Hz), indicating the all-*trans* substituent orientation. By contrast compound **12** and its parent **10**, which lack molecular symmetry, exhibited six individual one-proton signals for their ring hydrogen atoms. The observed multiplicities and splittings demanded the formula depicted. The data of Table 1 also rule out the *myo*-2 (**19**) and *chiro*-1 (**20**) configurations for any of the products obtained.

Experimental

Melting points were determined in capillaries in an electrically heated aluminum block. The n.m.r. data (100 MHz) were obtained on a Varian HA-100 instrument. Optical rotations were measured at room temperature in a Perkin–Elmer automatic polarimeter, Model 141. Circular dichroism was determined with a Jasco ORD/UV-5 instrument. I.r. spectra of new nitro compounds were compatible with the assigned structures.

1,2:5,6-Di-O-isopropylidene-3-O-methyl-α-D-glucofuranose (2)

A mixture of diacetone glucose **1** (8.0 g), methyl iodide (11.4 g), barium oxide (10.0 g) and *N,N*-dimethylformamide (80 ml) in a stoppered flask was vigorously shaken for 67 h at ambient temperature (29°). The mixture was filtered with suction through a layer of Celite and the residue washed successively with ether (100 ml) and water (125 ml). The phases of the filtrate were separated and the water layer was extracted twice with ether which was combined with the organic phase. The latter was washed twice with water, dried ($MgSO_4$), and evaporated to furnish a pale yellow oil (8.2 g; $[\alpha]_D$ −32° in ethanol). The oil was distilled *in vacuo*; following a forerun (0.4 g) the main fraction was collected at 85° (bath temperature) and 0.1 Torr. Compound **2** was thus obtained as a colorless oil (7.0 g, 83%); $[\alpha]_D$ −33° (*c*, 0.4 in ethanol); lit. (23), b.p. (0.3 Torr) 105°, $[\alpha]_D$ −34° in ethanol.

The n.m.r. data (in $CDCl_3$; TMS): δ 5.88 (1H d, H-1, $J_{1,2} = 4$ Hz), 4.57 (1H d, H-2, $J_{1,2} = 4$ Hz), 3.9–4.3 (4H m, H-4, -5, -6, -6′), 3.78 (1H d, H-3, $J_{3,4} = 2.5$ Hz), 3.47 (3H s, OCH_3), 1.50, 1.43, 1.37, 1.33 (four 3H s, isopropylidene methyl groups). The undistilled crude product gave virtually the same spectrum, with additional weak signals due to DMF (δ 2.80, 2.72).

1,2-O-Isopropylidene-3-O-methyl-α-D-glucofuranose (3)

A solution of **2** (7.0 g) in acetic acid (70 ml) and water (7 ml) was kept at 40° for 1.5 h and then evaporated under reduced pressure. Added toluene and benzene were successively evaporated from the residue which was a colorless, viscous oil. The material contained some unreacted **2** (*ca.* 1.1 g) which was removed by two extractions with ether (25 and 10 ml) from an aqueous solution (25 ml) of the crude **3**. The aqueous solution then contained about 5.0 g of **3** and could be used directly for the preparation of **4**.

A sample of crude **3** (553 mg, from a similar experiment) was purified by column chromatography on silica gel (E. Merck AG., 15 g, with 10% of water added). Elution with benzene (180 ml) and benzene containing 2% of ethanol (150 ml) gave a material (45 mg) that was discarded, and further elution with benzene containing 5% of ethanol (120 ml) then gave pure **3** (466 mg, 84%), $[\alpha]_D$ −52.4° (*c*, 0.4 in chloroform); lit. (24) $[\alpha]_D$ −54° (*c*, 3.1 in chloroform). The n.m.r. data (in $CDCl_3$; TMS): δ 5.93 (1H d, H-1, $J_{1,2} = 4$ Hz), 4.62 (1H d, H-2, $J_{1,2} = 4$ Hz), 3.7–4.1 (5H m), 3.49 (3H s, OCH_3), 1.50, 1.33 (two 3H s, isopropylidene methyl groups). The hydroxyl protons were removed by deuterium exchange.

1,2-O-Isopropylidene-3-O-methyl-α-D-xylo-pentodialdo-1,4-furanose (4)

To a cooled (0°) solution of **3** (463 mg) in water (2.7 ml) was added sodium metaperiodate (463 mg) in two portions with a 20-min interval. After 2 h, a few drops of ethylene glycol were added and the reaction mixture was filtered. The filter residue was washed with chloroform and the aqueous filtrate was extracted with the same solvent. The combined chloroform solution was dried ($MgSO_4$) and evaporated to furnish a pale yellow oil which was dried *in vacuo*. The yield was 333 mg (83%); $[\alpha]_D$ −139° (*c*, 0.3 in $CHCl_3$). The n.m.r. data (in $CDCl_3$; TMS): δ 9.66 (1H d, $J_{4,5} = 1.5$ Hz, H-5); 6.10 (1H d, $J_{1,2} = 3.8$ Hz, H-1); 4.67 (1H d, $J_{1,2} = 3.8$ Hz, H-2); 4.57 (1H q, $J_{3,4} = 4$ and $J_{4,5} = 1.5$ Hz, H-4); 4.17 (1H d, $J_{3,4} = 4$ Hz, H-3); 3.37 (3H s, OCH_3); 1.47, 1.33 (two 3H s, $C(CH_3)_2$).

For use in subsequent experiments it was practical to prepare compound **4** as an alcoholic solution on a larger scale. Thus, a solution of **3** (5.62 g, 24 mmol) in water (35 ml) was stirred with ice cooling, and sodium metaperiodate (6.0 g, 28 mmol) was added in portions during

½ h, the temperature of the reaction mixture being maintained at 8–11°. Stirring was continued without cooling for another 90 min whereby the temperature gradually rose to 25°. The mixture was then cooled again and 0.2 ml of ethylene glycol followed by 25 ml of ethanol were added. The inorganic precipitate was filtered off and washed thoroughly with ethanol. The filtrate was evaporated to dryness and the residue was taken up in ethanol (10 ml). The solution was filtered from undissolved material which was washed with ethanol (5 ml). The filtrate so obtained (15 ml) was used directly for reaction with nitromethane.

6-Deoxy-1,2-O-isopropylidene-3-O-methyl-6-nitro-α-D-glucofuranose (5) and -β-L-idofuranose (6)

(a) Mixture of 5 and 6 from 4

A solution of oily aldehyde **4** (2.94 g) in nitromethane (4 ml) and methanol (8 ml) was rendered alkaline by the addition of 2.7 *N* sodium methoxide in methanol (6 ml) and stored for 18 h at room temperature, in a pure nitrogen atmosphere. The mixture was then cooled with Dry Ice, glacial acetic acid (1 ml) was added with stirring, and after removal from the cold bath it was shaken briefly with added chloroform (10 ml) and water (10 ml). Upon phase separation the aqueous layer was extracted twice with chloroform, which was combined with the organic layer. The latter was washed five times with 5 ml of water, dried over anhydrous $MgSO_4$, and evaporated to give a brown oil (3.70 g). The oil was chromatographed on silica gel (E. Merck AG; with 10% of water added). The column was eluted first with benzene (500 ml) and then with benzene containing 2% ethanol (900 ml). The last third of the second eluant produced a colorless syrup (3.27 g) of **5** and **6** in a yield of 85%. The t.l.c. with ethyl acetate – chloroform (1:1) showed a single spot, R_f 0.67. Optical rotations: $[\alpha]_{578}$ −48.8, $[\alpha]_{536}$ −56.2, $[\alpha]_{436}$ −102, $[\alpha]_{365}$ −213° (*c*, 0.6, methanol). The n.m.r. spectrum ($CDCl_3$) showed two overlapping H-1 doublets (an apparent triplet), δ 5.98 and 5.90 (J = 4–5 Hz), with an intensity ratio 1:2, indicating that **5** preponderated. The remaining part of the spectrum was identical with that of pure **5** (see below).

Alternatively, an ethanolic solution of **4** (obtained without isolation from 24 mmol of **3**, see earlier) was mixed under nitrogen with nitromethane (7.5 ml) and 3.25 *N* sodium methoxide in methanol (8.25 ml). After 18 h the mixture was cooled, neutralized with glacial acetic acid (1.65 ml, to p*H* 6), and worked-up by dilution with chloroform (25 ml) and addition of water (75 ml). The water layer was extracted four times with chloroform and the combined chloroform extracts were washed four times with 10 ml of water, each water portion being extracted again with chloroform. Drying of the combined chloroform solution ($MgSO_4$) and evaporation furnished a reddish-brown oil (6.62 g) which, according to t.l.c. and n.m.r. analysis, appeared to consist largely of **5** and **6**. Part of the oil (5.1 g) was chromatographed on silica gel as described and gave 4.1 g (84% based on **3**) of a colorless, n.m.r. spectroscopically pure mixture of **5** and **6**.

(b) Pure 5 from 7-β

Crystalline nitro sugar **7-β** (84 mg) was dissolved with Dry-Ice cooling in acetone (4 ml) containing concentrated sulfuric acid (0.08 ml) and then stirred with anhydrous cupric sulfate (0.2 g) for 2 h without further cooling. The mixture was thereafter cooled again, neutralized by addition of concentrated aqueous ammonia (0.33 ml), and filtered through a layer of Dowex 1 × 2 (acetate form; prewashed with acetone) and through a layer of Celite. The filtrate was evaporated to a residue which was taken up in chloroform. The filtered, dried ($MgSO_4$), and evaporated chloroform solution furnished **5** in quantitative yield (100 mg) as a colorless syrup (uniform on t.l.c., R_F 0.67 as in *a* above); $[\alpha]_D$ −34.0, $[\alpha]_{578}$ −35.9, $[\alpha]_{546}$ −41.5, $[\alpha]_{436}$ −88.5, $[\alpha]_{365}$ −256° (in methanol, *c*, 0.7). Circular dichroism (*c*, 0.5 in methanol): $[\theta]_{281}$ −1885. The n.m.r. data (in $CDCl_3$): δ 5.90 (1H d, H-1, $J_{1,2}$ = 4 Hz), 4.4–4.8 (4H m, H-2, -6, -6′, -4 or -5), 4.0–4.2 (1H m, H-4 or -5), 3.88 (d, H-3, J = 3.5 Hz), δ 3.49 (3H s, OCH_3), 1.48 and 1.33 (two 3H s, $C(CH_3)_2$).

Anal. Calcd. for $C_{10}H_{17}NO_7$ (mol. wt. 263.2): C, 45.62; H, 6.51; N, 5.32. Found: C, 45.44; H, 6.38; N, 5.24.

(c) Mixture of 5 and 6 from 7 and 8

An amorphous mixture of **7** and **8** (from which crystalline **7-β** had been collected, see later) was acetonated as described under section *b*. The syrupy product (yield, 87%) gave an n.m.r. spectrum identical with that of the product described under section *a* except that the intensity ratio of the H-1 doublets at δ 5.98 and 5.90 was 3:2, indicating that **6** preponderated. Circular dichroism (*c*, 0.5 in methanol): $[\theta]_{310}$ +260. Assuming a 3:2 ratio for **6** and **5**, and using the [θ] value for pure **5**, the value for **6** may be extrapolated to +1700.

6-Deoxy-3-O-methyl-6-nitrohexoses 7 and 8

(a) Crystalline β-D-gluco Isomer (7-β)

A chromatographically purified mixture of isopropylidene derivatives **5** and **6** (1.56 g, ratio approximately 2:1) was dissolved in trifluoroacetic acid (5.5 ml), water (0.5 ml) was slowly added, and the reaction mixture was stirred for 45 min at room temperature and then evaporated *in vacuo*. From the syrupy residue a few milliliters of added water and subsequently some ethyl acetate were evaporated. The dried syrup (1.7 g) was then triturated with fresh ethyl acetate whereby it partially crystallized on scratching. The crystals (607 mg, 46%) were collected and washed with chloroform; m.p. 149–152°. An analytical sample was recrystallized from ethyl acetate – chloroform; m.p. 152–154°; homogeneous on t.l.c. in ethyl acetate (R_F 0.4) or 2:1 acetone–chloroform (R_F 0.65). The product exhibited upward mutarotation: $[\alpha]_D$ −4 (2 min) → +46° (24 h, final), $[\alpha]_{578}$ −4.3 → +47°, $[\alpha]_{546}$ −5.3 → +51°, $[\alpha]_{436}$ −31 → +61°, $[\alpha]_{365}$ −190 → −48°, in methanol; $[\alpha]_D$ and $[\alpha]_{578}$ +7 (2 min) → +40° (4 h, final), $[\alpha]_{546}$ +6 → +41°, $[\alpha]_{436}$ −10 → +49°, $[\alpha]_{365}$ −141 → −40°, in water.

Circular dichroism (*c*, 0.25 in 2.5 × 10^{-3} *N* acetic acid at anomeric equilibrium): $[\theta]_{319}$ −830, $[\theta]_{275}$ −2050.

The n.m.r. data (in 2 *N* CF_3CO_2D–D_2O with acetone reference): δ 3.0–1.8 (4H m), 1.43 (3H s, OCH_3), 1.4–1.1 (3H m).

Anal. Calcd. for $C_7H_{13}NO_7$ (mol. wt. 223.2): C, 37.66; H, 5.87; N, 6.28. Found: C, 37.90; H, 5.91; N, 6.23.

(b) Mixture of the D-gluco (7) and L-ido (8) Isomers

The ethyl acetate mother liquor obtained upon collection of crude **7-β** was concentrated and deposited an additional 53 mg of less pure **7-β**, which was removed.

Further evaporation gave a syrup (634 mg) which was partitioned between chloroform and water. The chloroform phase yielded a small amount of what appeared on t.l.c. to be impure starting material; it was discarded. The aqueous phase was decolorized by treatment with 0.5 ml of Dowex 1 × 2 (acetate) and evaporated. The remaining colorless syrup (420 mg, dried *in vacuo*) was a mixture of **7** and **8** (yield, 32%), R_F 0.4, 0.6 and 0.65, 0.8 (t.l.c. as described under section *a*). The material showed no mutarotation; $[\alpha]_{578}$ +9.7, $[\alpha]_{546}$ +11.3, $[\alpha]_{436}$ +23.3, $[\alpha]_{365}$ +68 (*c*, 0.52 in methanol); $[\alpha]_{578}$ +0.6, $[\alpha]_{546}$ +3.0, $[\alpha]_{436}$ +12, $[\alpha]_{365}$ +75° (*c*, 0.2 in water).

Circular dichroism (as for pure **7**): $[\theta]_{319}$ +170, $[\theta]_{272}$ −400. Assuming 40% **7** in the mixture, the ellipticities of **8** may be extrapolated to $[\theta]_{319}$ +840, $[\theta]_{272}$ +700.

The complex n.m.r. spectrum of the mixture showed prominent OCH_3 signals at δ 1.43 and 1.32.

Cyclization of Nitro Hexoses with Aqueous Barium Hydroxide

A suspension of crystalline 7-β (1.76 g, 7.88 mmol) in 0.0025 *N* acetic acid (8 ml) was stirred in an ice water bath in a nitrogen atmosphere, and a saturated solution of barium hydroxide (16 ml, approximately 0.5 *N*) was added in rapid flow. The mixture was stirred at 0° for 2.5 h and then kept at ambient temperature for 18 h. The dark solution was cooled again and acidified to p*H* 4–5 by dropwise introduction into ice cold, *N* acetic acid (20 ml). It was then passed sequentially through columns containing 5 ml of Dowex 1 × 2 (acetate) and 20 ml of Rexyn 101 (H^+), respectively, each column being washed with water (18 ml). Evaporation of the colorless effluent and drying of the residue *in vacuo* gave the nitroinositol mixture as a white semicrystalline mass (1.78 g).

Reactions using noncrystalline mixtures[3] of **7** and **8** were performed in the same fashion.

The reaction product (1.78 g, from 7-β) was triturated with absolute ethanol (5 ml). Upon storing overnight at 0°, a crop of crystals (1.30 g, m.p. 156–158°) was isolated. This material was not homogeneous but furnished, upon recrystallizations (once from methanol and three times from 95% ethanol), a pure product designated A (95 mg, m.p. 165–167°). Systematic fractional crystallization of the mother liquor materials gave another 145 mg of pure A and 234 mg of less pure A (m.p. 160–167°), the total yield being 27%. In addition, the procedure yielded 333 mg (19%) of a high-melting material designated B, (m.p. 185–205°, dec.), 97 mg (6%) of a mixture which melted in between (at 173–175°) and was dealt with no further, and finally there remained 731 mg (41%) of an amorphous foam designated C. It will be noted that a total of 904 mg of crystals was eventually isolated and the amount of noncrystallizable material remaining after the various recrystallizations was larger than the amount that did not crystallize in the first place. The relative amounts of products depended upon the number of recrystallizations performed, with amorphous C increasing with that number. Thus, an identical cyclization experiment furnished 45% of A (m.p. 165–166°), 18% of B (m.p. 209–215°), and 29% of C.

The semicrystalline reaction product (3.21 g) obtained from a mixture (3.89 g) of **7** and **8** was triturated with cold ethanol (7 ml) to give inhomogeneous crystals (1.77 g, m.p. 199–205° dec.) and an amorphous material (1.32 g). After fractional crystallizations using methanol and ethanol there was obtained 1.18 g (30%) of B (m.p. 205–222°), a total of 0.43 g (11%) of unresolved mixtures melting anywhere between 100 and 175°, and 1.40 g (36%) of amorphous C. No pure A could be isolated. A similar experiment yielded 21% of B and 56% of C.

*3-Deoxy-6-O-methyl-3-nitro-epi-inositol (**16**)*

The crystalline product A, m.p. 165–167° (see above) represented compound **16**. The n.m.r. data (in 2.1 *N* CF_3CO_2D–D_2O with acetone standard): δ 2.62–2.57 (2H m, H-2, -4), 2.47 (1H t, J = 3 Hz, H-3), 1.47–1.44 (3H m, H-1, -5, -6), 1.42 (3H s, OCH_3).

Anal. Calcd. for $C_7H_{13}NO_7$ (mol. wt. 223.2): C, 37.66; H, 5.87; N, 6.28. Found: C, 37.55; H, 5.71; N, 6.40.

*1,2,4,5-Tetra-O-acetyl-3-deoxy-6-O-methyl-3-nitro-epi-inositol (**17**) and (3,5,6/4)-3,5,6-Triacetoxy-4-methoxy-1-nitrocyclohexene (**18**)*

An ice-cooled suspension of **16** (126 mg) in acetic anhydride (1.3 ml) was stirred for 6 h after addition of 2 drops of boron trifluoride etherate. The inositol dissolved when the catalyst was added, and crystalline **17** began to precipitate soon afterwards. It was collected and washed with ethanol (3 × 0.2 ml); yield, 104 mg; m.p. 172–182°. For the n.m.r. data see Table 1.

The product decomposed on attempted recrystallization from ethanol, becoming extremely soluble in the solvent and developing a low-field, olefinic proton signal which was not present in its original n.m.r. spectrum. A small amount of the nitroalkene **18**, m.p. 120–122°, was eventually isolated by crystallization from ether and ether–ligroin. For the n.m.r. data see Table 1.

Anal. Calcd. for $C_{13}H_{17}NO_9$ (mol. wt. 331.3): C, 47.13; H, 5.17; N, 4.23. Found: C, 47.31; H, 5.32; N, 4.18.

*2,3,5,6-Tetra-O-acetyl-1-deoxy-4-O-methyl-1-nitro-scyllo-inositol (**11**)*

The high-melting crystalline cyclization products previously designated B represented mixtures of the *scyllo* and *myo*-1 isomers **9** and **10**. Such a mixture (0.85 g) was acetylated with acetic anhydride (8.5 ml) in the presence of BF_3 etherate (12 drops) by stirring for 10 h at 0° and another 10 h at room temperature. The reaction mixture was then cooled again (0°) and filtered through sintered glass. The crystals (**11**) were washed with 5 ml of cold ethanol in three portions and dried *in vacuo*, and the combined filtrates containing isomeric acetate **12** were set aside. The crystals (0.87 g, 58.5%) were pure according to their n.m.r. spectrum (Table 1). The m.p. of 257–258° observed at this stage did not appear to be reproducible, as higher (270–272°) or lower (230–232°) values were found on occasion in similar preparations which exhibited, nevertheless, exactly the same well-defined n.m.r. spectrum. Recrystallization of a sample (0.47 g) from glacial acetic acid (3 ml) containing acetic anhydride (0.15 ml) gave translucent prisms (0.43 g) of m.p. 220–222°, whereas recrystallization from methanol (44 mg in 4 ml) gave long needles (35 mg) of m.p. 214–216°. The recrystallized samples gave n.m.r. spectra superimposable on those of the original product, and both gave correct microanalyses.

Anal. Calcd. for $C_{15}H_{21}NO_{11}$ (mol. wt. 391.3): C, 46.03; H, 5.41; N, 3.58. Found: C, 45.90; H, 5.46; N, 3.59. C, 45.92; H, 5.47; N, 3.73.

*2,3,5,6-Tetra-O-acetyl-1-deoxy-4-O-methyl-1-nitro-*D,L*-myo-inositol (**12**)*

To the filtrate of the acetylation mixture, from which crystalline **11** had been collected (see preceding section), was added excess ethanol; after decomposition of the remaining acetic anhydride the solution was evaporated, and two portions of added ethanol were evaporated from the residue which after drying weighed 0.64 g and consisted of at least 80% of **12** (n.m.r.). After two crystallizations from small volumes of hot ethanol (performed rapidly without prolonged heating, lest losses due to formation of low-melting, unsaturated products occurred), 475 mg (32%) of the tetraacetate **12** was obtained, m.p. 139–140°. Further recrystallization did not change the n.m.r. spectrum (Table 1) although variations in m.p. from 135–136° to 140–142° were observed.

Anal. Calcd. for $C_{15}H_{21}NO_{11}$ (mol. wt. 391.3): C, 46.03; H, 5.41; N, 3.58. Found: C, 45.95; H, 5.44; N, 3.67.

*1-Deoxy-4-O-methyl-1-nitro-scyllo-inositol (**9**)*

A suspension of tetraacetate **11** (430 mg) in anhydrous methanol (25 ml) containing methyl *p*-toluenesulfonate (0.5 ml) was boiled in a flask fitted with a Vigreux column. Distillation was maintained at a slow rate so that 15 ml of distillate was collected in 5 h. Fresh methanol was introduced during the operation so as to approximately maintain the original volume. The solid gradually dissolved, and the resulting solution was subsequently refluxed for another 20 h and then evaporated. Trituration of the residue with ethanol produced a white powder (277 mg) which was recrystallized from 90% ethanol (7 ml) to give **9** (202 mg, 83%) as needles, m.p. 258–260° (dec.). Recrystallization of a sample from water gave large grains that melted with decomposition at 248–249° (with apparent change in crystal structure from 220°). The n.m.r. data (in 2.1 *N* CF_3CO_2D–D_2O, with acetone as reference): δ 2.39 (1H t, H-1, J = 10.5 Hz), 1.81 (2H t, H-2 and -6, J = 10.5 Hz), 1.41 (3H s, OCH_3), 1.35 (2H t, H-3 and -5, J = 9.5 Hz), 1.02 (1H t, H-4, J = 9.5 Hz).

Anal. Calcd. for $C_7H_{13}NO_7$ (mol. wt. 223.2): C, 37.66; H, 5.87; N, 6.28. Found: C, 37.58; H, 5.82; N, 6.44.

*1-Deoxy-4-O-methyl-1-nitro-*D,L*-myo-inositol (**10**)*

The tetraacetate **12** (315 mg) was methanolyzed as described for **11**. The residue obtained upon evaporation of the reaction solution was dissolved in 1–2 ml of ethanol, and addition of benzene caused crystallization of **10** (178 mg, 99%) which was collected and washed with benzene; m.p. 198–203°. Recrystallization from ethanol–benzene gave very fine needles (150 mg, 83%), m.p. 203–205°. The n.m.r. data (in 2.1 *N* CF_3CO_2D–D_2O, with acetone reference): δ 2.49 (1H q, H-1, $J_{1,2}$ = 2.5, $J_{1,6}$ = 10 Hz), 2.30 (1H t, H-2, J = 2.5 Hz), 2.13 (1H, quartet of narrow doublets, H-6, $J_{1,6}$ = 10, $J_{5,6}$ = 9 Hz, and a 1.5 Hz splitting, presumably due to long-range coupling), 1.6–1.2 (3H m, H-3, -4, -5), 1.39 (3H s, OCH_3).

Anal. Calcd. for $C_7H_{13}NO_7$ (mol. wt. 223.2): C, 37.66; H, 5.87; N, 6.28. Found: C, 37.56; H, 5.85; N, 6.34.

*3-Deoxy-1,2;4,5-di-O-isopropylidene-6-O-methyl-3-nitro-muco-inositol (**13**)*

(a) From Amorphous Cyclization Product C

A sample (372 mg) of the product C (see a previous section) was dissolved in acetone (10 ml) containing concentrated sulfuric acid (0.2 ml). (The reagent was freshly prepared under cooling with Dry Ice.) The mixture was stirred with anhydrous cupric sulfate (120 mg) for 2.5 h at room temperature, then cooled with Dry Ice and neutralized by adding concentrated aqueous ammonia (0.6 ml). The voluminous inorganic precipitate was filtered off and the solution passed through small columns of acetone – prewashed ion exchange resins (1 ml each) Dowex 1 × 2 (acetate) and Amberlite IR-120 (H^+). The columns were rinsed with acetone and methanol (10 ml each). Evaporation of the filtrate gave a syrup (387 mg) which upon extraction with chloroform (3.8 ml) left behind a dark mass (85 mg). The extract was chromatographed on Merck silica gel (10 g, with 1 ml of water added), whereby elution with chloroform furnished a crop (119 mg, 24%) of crystalline **13**, m.p. 160–162°, in the second 10 ml fraction. Further elution with chloroform (50 ml) followed by acetone (30 ml) produced syrups that were combined with the aforementioned insoluble material and acetonated again as described. In this way, a second crop of **13** (36 mg) was obtained (total yield, 31%). Recrystallization from ligroin raised the m.p. to 169–170°. The n.m.r. data (in $CDCl_3$, with TMS): δ 4.6–4.5 (3H m, H-2, -3, -4), 4.24 (2H q, H-1 and -5, $J_{1,6} = J_{5,6}$ = 8, $J_{1,2} = J_{4,5}$ = 5.5 Hz), 3.58 (3H s, OCH_3), 3.41 (1H t, H-6, $J_{5,6} = J_{1,6}$ = 8 Hz), 1.54 and 1.34 (two 6H s, for two isopropylidene groups).

Anal. Calcd. for $C_{13}H_{21}NO_7$ (mol. wt. 303.3): C, 51.48; H, 6.98; N, 4.62. Found: C, 51.34; H, 6.79; N, 4.74.

*(b) From the epi-3 Isomer **16***

A 268-mg sample of pure **16** (free from isomers according to n.m.r. spectrum) was acetonated by the method described in section *a*. By chromatography on silica gel 131 mg (36%) of pure **13**, m.p. 168.5–169.5°, was obtained. Its spectrum was superimposable on that of the previous product.

*3-Deoxy-6-O-methyl-3-nitro-muco-inositol (**14**)*

The compound **13** (93 mg) was deacetonated by treatment with trifluoroacetic acid (0.30 ml) containing water (1 drop) for 30 min at room temperature. Evaporation of the solution followed by crystallization of the residue from ethyl acetate gave **14** (66 mg, 96%) as large colorless prisms or flat rectangular plates, m.p. 161–163°. The n.m.r. data (in 2.1 *N* CF_3CO_2D–D_2O, with acetone as reference): δ 2.75 (1H t, H-3, $J_{2,3} = J_{3,4}$ = 10 Hz), 2.07 (2H q, H-2 and -4, $J_{2,3} = J_{3,4}$ = 10, $J_{1,2} = J_{4,5}$ = 3 Hz), 2.01 (2H t, H-1 and -5, $J_{1,2} = J_{1,6} = J_{4,5} = J_{5,6}$ = 3 Hz), 1.58 (1H t, H-6, $J_{1,6} = J_{5,6}$ = 3 Hz), 1.25 (3H s, OCH_3).

Anal. Calcd. for $C_7H_{13}NO_7$ (mol. wt. 223.2): C, 37.66; H, 5.87; N, 6.28. Found: C, 37.54; H, 6.00; N, 6.47.

*1,2,4,5-Tetra-O-acetyl-3-deoxy-6-O-methyl-3-nitro-muco-inositol (**15**)*

Compound **14** (66 mg) was treated with acetic anhydride (0.66 ml) and 1 drop of BF_3–etherate for 1 h at 0°. Ethanol (0.4 ml) was then added, and the tetraacetate **15** (101 mg, 88%) crystallized in part directly and in part upon evaporation of the solution. It was washed with a small amount of ethanol and melted at 187–188°. Recrystallization lowered the melting point: 170–172° (from ethanol), 175–176° (from ethyl acetate – ligroin). How-

ever, the n.m.r. spectra of the crude and recrystallized samples were indistinguishable (data see Table 1).

Anal. Calcd. for $C_{15}H_{21}NO_{11}$ (mol. wt. 391.3): C, 46.03; H, 5.41; N, 3.58. Found: C, 46.18; H, 5.54; N, 3.70.

Cyclization of Nitro Hexoses with Sodium Methoxide

To a suspension of crystalline 7-β (645 mg) in methanol (2 ml) and nitromethane (2.9 ml) was added 0.96 ml of a 3.25 *N* solution of sodium methoxide in methanol. The addition, which was performed at room temperature under nitrogen, caused 7-β to dissolve, and a new solid began to precipitate immediately afterwards. The reaction mixture was allowed to stand in a closed vessel for 4 days, then cooled with Dry Ice, and acidified with glacial acetic acid (0.3 ml). The solution was passed consecutively through short columns containing 5 ml of Dowex 1 × 2 (acetate) and 10 ml of Rexyn 101 (H^+), respectively. The columns were rinsed with methanol and then with water, the former eluant furnishing upon evaporation 418 mg of a brown syrup, and the latter, 246 mg of a yellow semicrystalline mass. Trituration of the products with ethanol and fractional crystallization gave 102 mg (16%) of a mixture of **9** and **10** (m.p. 190–210°), 52 mg (8%) of what according to an n.m.r. spectrum consisted mainly of **14** (although it melted over the range 102–145° and therefore was not pure), and 395 mg (61%) of an amorphous foam similar in composition to the amorphous material C encountered in the barium hydroxide-induced cyclizations.

A similar experiment starting with a noncrystalline mixture (670 mg) of **7** and **8** furnished, after a reaction time of 1 day, 173 mg (26%) of **9** + **10** (m.p. 200–220°) and 429 mg (64%) of amorphous material.

The amorphous products obtained from these cyclizations were acetonated and yielded pure **13** in yields of 30–35%.

Support of this work by the National Research Council of Canada is gratefully acknowledged.

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