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PREPARATION, AND NUCLEOPHILIC ADDITION-REACTIONS, OF 1,5-ANHYDRO-4,6-*O*-BENZYLIDENE-2,3-DIDEOXY-2-NITRO-D-*erythro*-HEX-2-ENITOL*†

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ABSTRACT

Nucleophilic addition-reactions of the title compound, prepared from the corresponding 3-nitrohex-2-enitol, were investigated under kinetically controlled conditions; such sterically bulky nucleophiles as *tert*-butyl peroxide and 2,4-pentanedionate ions (except in 1,4-dioxane) were found to engage almost exclusively in equatorial attack, whereas, for hydroperoxide and deuteride ions, axial attack is favored. All the products thus obtained, other than the nitro epoxides, were subjected to an equilibration test. Factors potentially controlling the addition reactions under thermodynamically, as well as kinetically, controlled conditions are discussed, based on the results described herein.

INTRODUCTION

On the basis of our extensive studies on the stereochemistry of the Michael-type reactions of 3-nitro-2-enopyranosides[2,3], 2-nitro-2-enopyranosides[1,4,5], 2-cyano-2-enopyranosides[6], hex-2-enopyranosid-4-uloses[7], and others[8], we recently proposed[5] that the approaching direction of a nucleophile under kinetically controlled conditions is presumably governed by three factors, *viz.*, (*i*) the relative stability of an intermediate bearing a chair and a boat conformation derived by stereoelectronic control[9], (*ii*) the presence or absence of electrostatic and steric repulsion ($A^{1,3}$ strain)[10] in such an intermediate, and (*iii*) the electrostatic and steric repulsion between an approaching nucleophile and substituents around the reactive site.

In order to elucidate the relative importance of the factors involved in categories *i* and *iii*, we have prepared 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-D-*erythro*-hex-2-enitol (**2**), and have performed relevant reactions with some nucleophiles**.

*Stereochemistry of Nucleophilic Addition Reactions. Part XV. For Part XIV, see ref. 1.
†Dedicated to Professor Sumio Umezawa on the occasion of his 73rd birthday and the 25th anniversary of the Microbial Chemistry Research Foundation.
**Concerned with the thermodynamic stabilities of some products, and already reported in preliminary form[11].

TABLE I

CHEMICAL SHIFTS (δ) AT 100 MHz OF THE PRODUCTS IN CHLOROFORM-d[a]

Compound	*H-1*a	*H-1*e	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*a	*H-6*e	*H-8*[b]	*PhCH*	*COMe*
2	4.64	4.68	—	~7.40	~4.36	3.49	3.80	~4.39	—	5.61	—
3[c]	4.53	4.87	—	4.15	3.77	3.54	3.77	4.26	—	5.70	—
4[c]	4.32	5.16	—	←4.30–4.23→		~3.57	3.76	←4.30–4.23→	—	5.73	—
5	3.81	4.35	5.02	3.12	4.17	3.42	3.69	4.13	3.81	5.44	2.17, 2.20
6	3.90	4.57	5.05	3.21	4.29	3.46	3.72	4.26	~3.96	5.50	2.10, 2.25
9[d]	3.78	4.58	4.25				←4.23–3.55→			5.46	1.99, 2.19
11	3.84	4.72	4.62	[e]	3.93	3.36	3.69	4.24	—	5.58	—

[a]Me_4Si as the internal standard. [b]Methine proton of the substituent at C-3. [c]Recorded in acetone-d_6. [d]Recorded at 250 MHz. [e]H-3*a*, 2.00; H-3*e*, 2.97.

TABLE II

FIRST-ORDER COUPLING-CONSTANTS (Hz) AT 100 MHz FOR SOLUTIONS IN CHLOROFORM-*d*

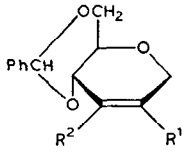
Compound	$J_{1a,1e}$	$J_{1a,2}$	$J_{1e,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6e}$	$J_{6a,6e}$	$J_{3,8}$
2[a]	~0	—	—	—	3.0	8.3	10	4.5	10	—
3[b]	12.8	—	—	—	~0	9.0	9.6	3.8	9.6	—
4[b]	13.1	—	—	—			10.2	4.5	10.2	—
5	10.5	10.5	4.9	10.5	10.5	9.0	9.8	4.5	9.8	4.1
6	13.1	2.6	1.5	4.5	10.5	8.3	9.8	4.5	9.8	11.2
9[c]	13.7	2.5	~0.7	~1.0						
11	13.9	2.7	1.5	[d]	[d]	10	10.2	4.5	10.2	—

[a] $J_{1a,3}$ 1.0 and $J_{1e,3}$ 2.3 Hz. [b] Recorded in acetone-d_6. [c] Recorded at 250 MHz. [d] $J_{2,3a}$ 4.5, $J_{2,3e}$ 2.3, $J_{3a,3e}$ 14.3, $J_{3a,4}$ 11.5, $J_{3e,4}$ 4.5, and $J_{1e,3e}$ 2.3 Hz.

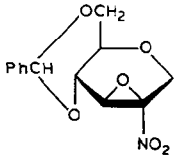
RESULTS AND DISCUSSION

Treatment of 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-D-*erythro*-hex-2-enitol (**1**) with sodium nitrite in benzene–water, in the presence of tributylhexadecylphosphonium bromide as a phase-transfer catalyst, provided **2** in 44% yield. The nitroalkenic structure of **2** was determined by elemental analysis, and i.r. [ν 1535 cm^{-1} (C=C-NO_2)], and ^{1}H-n.m.r. spectroscopy (alkenic-proton signal at δ ~7.40).

Epoxidation of **2** with 35% aqueous hydrogen peroxide in benzene–0.5M sodium hydroxide solution in the presence of the phase-transfer catalyst, or in 1,4-



1 R^1 = H, R^2 = NO_2
2 R^1 = NO_2, R^2 = H



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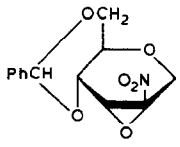

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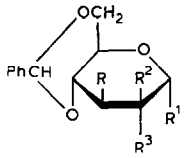
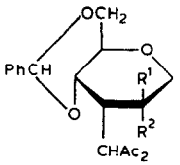
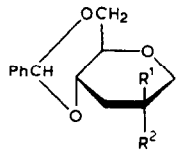


5 R^1 = R^2 = H, R^3 = NO_2
6 R^1 = R^3 = H, R^2 = NO_2
7 R^1 = OMe, R^2 = H, R^3 = NO_2
8 R^1 = OMe, R^2 = NO_2, R^3 = H
R = $CHAc_2$



9 R^1 = NO_2, R^2 = H
10 R^1 = H, R^2 = NO_2



11 R^1 = NO_2, R^2 = H
12 R^1 = H, R^2 = NO_2

dioxane–M sodium hydroxide solution, respectively afforded a 1:3.2 or a 1.1:1 mixture of the *manno* (**3**) and *allo* isomer (**4**). On the other hand, similar epoxidation with *tert*-butyl peroxide ion yielded **3**, together with a trace of **4**. The *manno* configuration was assigned to **3**, based on the coupling constant[8b,12], $J_{3,4}$ ~0 Hz (see Tables I and II), and, therefore, the alternative isomer **4** may be assumed to have the *allo* configuration, although the ^{1}H-n.m.r. evidence was insufficient to permit assignment of its stereochemistry.

Subsequently, the reaction of **2** with 2,4-pentanedionate ion in various solvents was investigated, and the results thus obtained are summarized in Table III. All of the reactions in solvents other than 1,4-dioxane afforded no *altro* isomer **9**; it was detectable neither by t.l.c. nor by ^{1}H-n.m.r. spectroscopy. The reactions in acetonitrile and in oxolane (tetrahydrofuran) afforded an ~1:1 mixture of the *gluco* (**5**) and *manno* isomer (**6**) (Entries 4 and 5), whereas those in dimethyl sulfoxide and in benzene–water afforded a mixture in which **6** preponderated over **5** (**5**:**6** = 1:3–8).

TABLE III

REACTIONS OF **2** WITH 2,4-PENTANEDIONE IN VARIOUS SOLVENTS[a]

Entry	*Solvent (mL)*	*Reaction time (min)*	*Yield (%)*	*Product ratios*[b]		
				gluco **5**	manno **6**	altro **9**
1	Me_2SO (1.5)	5	86	1	3.2	—
2	Me_2CO (2)	25	93	1	4.2	—
3	benzene (2)[c]	20	92	1	8.0	—
4	MeCN (2)	25	85	1	1	—
5	oxolane (2)	25	91	1.2	1	—
6	1,4-dioxane (1.5)	20	91	3.8	—	1
7	1,4-dioxane (12)	60	90	1	—	5.8

[a]A solution of **2** (20 mg, 75 μmol) in the solvent indicated was stirred at ~25° with 2,4-pentanedione (11.4 mg, 114 μmol) in the presence of 0.1M aqueous sodium hydroxide (0.2 mL). [b]Determined by ^{1}H-n.m.r. spectroscopy on the basis of area-ratios of the benzylidene methine-proton signals; the symbol — in each column indicates: no product formation. [c]Tributylhexadecylphosphonium bromide (2.5 mg) was added as the phase-transfer catalyst.

On performing the reaction in 1,4-dioxane, on the other hand, **9** was formed besides **5** (**5**:**9** = 3.8:1) (Entry 6), and **9** became the major product when the proportion of the solvent was increased (**5**:**9** = 1:5.8) (Entry 7). Incidentally, similar solvent-effects have also been observed in the Michael reaction of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-α-D-*erythro*-hex-2-enopyranoside[4]. The configurations of these products were deduced from the coupling constants, *i.e.*, $J_{1a,2}$ 10.5, $J_{1e,2}$ 4.9, $J_{2,3}$ 10.5, and $J_{3,4}$ 10.5 Hz for **5**; $J_{1a,2}$ 2.6, $J_{1e,2}$ 1.5, $J_{2,3}$ 4.5, and $J_{3,4}$ 10.5 Hz for **6**; $J_{1a,2}$ 2.5, $J_{1e,2}$ ~0.7, and $J_{2,3}$ ~1.0 Hz for **9**.

In order to elucidate if the reaction was kinetically controlled, epimerization of the products isolated (**5**, **6**, and **9**) was examined. As may be seen from Table IV,

TABLE IV

EPIMERIZATION[a] OF THE ADDUCTS **5**, **6**, AND **9**

Entry	*Starting material*	*Solvent (mL)*	*Reaction time (min)*	*Yield (%)*	*Product ratios*[b]		
					gluco **5**	manno **6**	altro **9**
8	**9**	Me_2SO (0.5)	5	98	—	—	1
9	**9**	benzene (0.7)[c]	20	98	—	—	1
10	**5**	1,4-dioxane (4.3)	60	97	1	—	—
11	**5**	Me_2CO (0.72)	25	100	1	3.2	—
12	**6**	Me_2CO (0.72)	25	100	t	1	—
13	**5**	benzene (0.72)[c]	20	95	1	5.5	—
14	**6**	benzene (0.72)[c]	20	97	1	6.5	—
15	**5**	1,4-dioxane (0.54)	20	99	1	t	—
16	**6**	1,4-dioxane (0.54)	20	98	—	1	—

[a]A solution of the starting material (10 mg, 0.03 mmol) in the solvent indicated was stirred at ~23° with 2,4-pentanedione (4.1 mg, 41 μmol) in the presence of 0.1M aqueous solution of sodium hydroxide (0.07 mL). [b]The product ratios were calculated on the basis of area-ratios of the benzylidene methine-proton signals in the ^{1}H-n.m.r. spectra; the symbol t indicates that a weak spot was detectable in t.l.c., but not by ^{1}H-n.m.r. spectroscopy, and —, that the compound was detectable neither by t.l.c. nor by ^{1}H-n.m.r. spectroscopy. [c]Tributylhexadecylphosphonium bromide (0.9 mg) was added as the phase-transfer catalyst.

(*i*) treatment of **9** under the conditions employed for obtaining a mixture of **5** and **6** resulted in almost quantitative recovery of **9** (Entries 8 and 9), (*ii*) epimerization of **5** or **6** into **9** was not observed, even in 1,4-dioxane, wherein **9** was produced from **2** (Entries 10–16).

These results show that, on addition of nucleophile, the reaction proceeds under kinetic control, and that the approaching direction of the nucleophile is strongly affected by the solvents employed. Furthermore, in 1,4-dioxane, wherein a mixture of **5** and **9** (3.8 : 1) was produced, epimerization of **5** into **6** was negligible (Entry 15), and *vice versa* from **6** (Entry 16). It is apparent from these results that, under such conditions, not only addition of a nucleophile, but also protonation were kinetically controlled. Alternatively, formation of the *gluco* isomer **5** is kinetically more favorable than that of the *manno* isomer **6**, at least in 1,4-dioxane.

However, studies on nucleophilic addition to 3-nitro-2-enopyranosides[2,3] on protonation (as well as halogenation) of sugar 3-nitronates[13], and on conformational analysis of nitrocyclohexane derivatives[14], revealed the strong tendency of their nitro group to assume the equatorial orientation. If the same tendency holds for 2-nitro sugar derivatives, preponderant formation of the *manno* isomer **6** over the *gluco* isomer **5** is unreasonable, as the former is an unfavorable product from the standpoint of both thermodynamic and kinetic grounds. Therefore, we compared the mutual, thermodynamic stability of **5** and **6** as follows. Epimerization of **5** and of **6** (10 mg of each, separately) was induced in acetone-d_6 (0.3 mL) in the presence of 0.1M sodium hydroxide (33 mg), and was monitored by ^{1}H-n.m.r. spectroscopy.

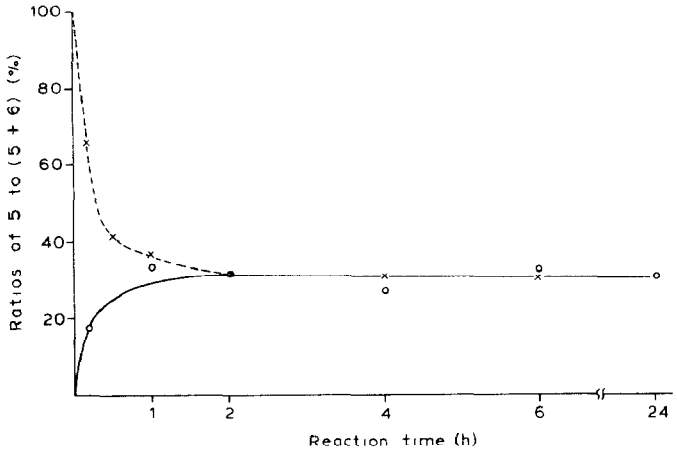


Fig. 1. Epimerization of the adducts (**5** and **6**); the reactions of **5** or **6** (10 mg) in acetone-d_6 (0.3 mL) in the presence of 0.1M sodium hydroxide (33 mg) were performed in an n.m.r. sample-tube at ~23°, and monitored by ^{1}H-n.m.r. spectroscopy (---x---, from **5**, and —○—, from **6**).

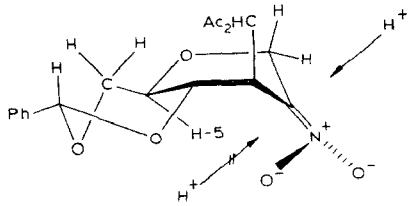


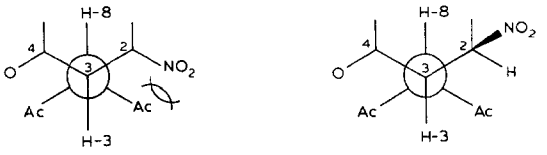
Fig. 2.

The results thus obtained are outlined in Fig. 1. It was thus proved that the same equilibrium mixture, composed of **5** and **6** (1 :2.2) was obtained from both **5** and **6**, and **6** was concluded to be thermodynamically more stable than **5** by ~2.1 kJ/mol (~0.5 kcal/mol)*.

Exclusive formation of the *gluco* isomer **5**, instead of the *manno* isomer **6** (Entries 6 and 7), may be explained as follows. An intermediary nitronate should have the $B_{2,5}$ conformation in order to maintain a maximum overlap of molecular orbitals between the nitro alkene species and the 2,4-pentanedionate ion (stereo-electronic control[9]). In this conformation, protonation from the down side would experience steric hindrance due to H-5, but that from the up side would not experience so serious a steric hindrance, giving the isomer **5** (see Fig. 2).

Similar treatment of the *altro* isomer **9** in acetone-d_6 in the presence of sodium deuteroxide gave **9** quantitatively (95% recovery yield) after 24 h; deuteration at C-2

*Similar treatment of **5** in the presence of sodium deuteroxide (instead of sodium hydroxide) gave a simple decrement curve up to 24 h, whereas that of **6** under the same conditions gave a maximum value after ~1.5 h, and then a simple decrement curve, as had been found in that of **5** on plotting the percentage of **5** in the mixture against the reaction time. The reason why such different phenomena were observed among these reactions is at present ambiguous, although it might arise from the so-called "isotope effect".



I (10) II (9)

Fig. 3. "Newman" projection of the most stable conformation, showing C-3 to C-8.

was found to be almost complete after 2.75 h, and to be complete after 24 h. The use of sodium hydroxide instead of sodium deuteroxide for this treatment resulted in almost quantitative recovery of **9**. The results* indicated that **9** was much more stable than the *allo* isomer **10**, and this was supported by the conformational analysis. The α-proton of the 2,4-pentanedionate moieties (H-8) in the *altro* and *allo* isomers would orient towards the sterically crowded ring, and the acetyl groups point away from the ring, in the sterically favored rotamers. In this conformation, the *allo* isomer I, having a considerable 1,3-diaxial repulsion between the nitro and acetyl group, must be less stable than the *altro* isomer II, having no such repulsion (see Fig. 3).

Reduction of **2** with sodium borohydride in methanol for 30 min at room temperature yielded a mixture of the *arabino* (**11**) and *ribo* isomer (**12**) in the ratio of ~3.7:1, as determined by ^{1}H-n.m.r. spectroscopy. Isomer **11** was readily isolated by fractional recrystallization, whereas only a small amount of **12** was obtained by column chromatography**. Therefore, an attempt was made to ascertain conditions proper for the formation of **12** as the major product; however, all attempts with respect to reaction temperature, time, proportions of reagents, and solvents were unsuccessful. The *arabino* configuration and the $^4C_1$ conformation were assigned on the basis of the coupling constants ($J_{1a,2}$ 2.7, $J_{1e,2}$ 1.5, $J_{2,3a}$ 4.5, $J_{2,3e}$ 2.3, $J_{3a,4}$ 11.5, and $J_{3e,4}$ 4.5 Hz). Although the stereochemistry of **12** could not be deduced by ^{1}H-n.m.r. spectroscopy, the assignment of the *ribo* structure to **12** seems to be valid from the theoretical viewpoint, and was supported by the successful epimerization of **11** into **12**.

Similar reduction of **2** with sodium borodeuteride gave a mixture of deuterio derivatives of **11** and **12** in the ratio of 4.8:1, as estimated by ^{1}H-n.m.r. spectroscopy. The isolated *arabino* isomer (deuterio-**11**) had the axial and equatorial deuterio substituents in the ratio of 2.8:1, as estimated by ^{1}H-n.m.r. spectroscopy, suggesting that a deuteride ion attacked predominantly from the axial side of **2**. Treatment of the *arabino* isomer (deuterio-**11**) in acetone-d_6 in the presence of 0.1M sodium deuteroxide for 24 h at room temperature gave a 7:1 mixture of the *arabino* and *ribo* isomers; deuteration at C-2 was complete during this reaction time. Similar treatment of the *arabino* isomer in the presence of sodium hydroxide, instead of sodium deuteroxide, also afforded a 7:1 mixture of **11** and **12**; the ratio did not change, even after

*A similar result had also been obtained in the case of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-(diacetylmethyl)-2-nitro-α-D-altropyranoside[4].

Compound **12 was mostly decomposed during column chromatography.

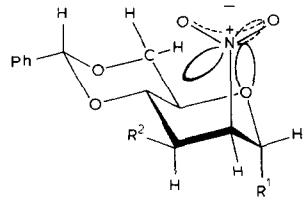
48 h. The proportions should be those of a mixture in equilibrium, so indicating that **11** is thermodynamically more stable than **12** by 4.6 kJ/mol (1.1 kcal/mol). In 1,4-dioxane, equilibrium was attained within 48 h, to yield a 3.9 : 1 mixture of **11** and **12**; **11** is thus thermodynamically more stable than **12** by 3.3 kJ/mol (0.8 kcal/mol).

The results showed that peroxide (in the heterogeneous system) and deuteride ions attacked from the axial and equatorial sides of **2** in the ratio of $\sim 3:1$, suggesting that the factors in categories *i* and *iii* were competitive in these reactions; *tert*-butyl peroxide and 2,4-pentanedionate ions approached exclusively from the equatorial side of **2**, except for the latter in 1,4-dioxane; *i.e.*, the factor in category *iii* was indicated to be crucial in the reactions with these bulky nucleophiles. A $B_{2,5}$ conformation in a transition state derived by equatorial attack on **2** should be relatively stable, due to the lack of bowsprit–flagpole interaction[15], because carbon atom 2 is sp^2-hybridized. Therefore, the factor in category *i* should be underestimated in the present investigation (in comparison with the case involving such an interaction).

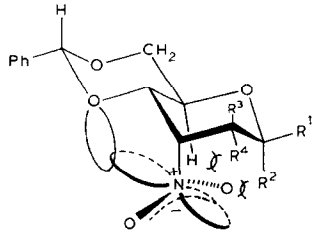
Concerned with the difference in the thermodynamic stability between an axial and an equatorial nitro group on a pyranose ring, examples in the present study, as well as in the literature, furnish such categories as the following (*1*) the nitro group in 3-nitro sugar derivatives always assumes the equatorial disposition[13], (*2*) the *manno* isomers of 3-*C*-(diacetylmethyl) derivatives **6** and **8** are more stable than the corresponding 2-epimers **5** and **7** by 2.1 and 0.84 kJ/mol (0.5 and 0.2 kcal/mol), respectively, (*3*) the 2,3-dideoxy-2-nitro-arabinitol **11** is more stable than its 2-epimer by 4.6 (1.1) (in acetone) and 3.3 kJ/mol (0.8 kcal/mol) (in 1,4-dioxane), (*4*) three isomers, except the *manno*, could be detected in the reaction of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-D-*erythro*-hex-2-enopyranoside with methanol[1], and (*5*) the compound having the axial nitro group could not be detected in methyl 2-nitro-β-D-hexopyranoside derivatives[5]. The fact in category *5* could be explained in terms of the Δ^2 effect[16]. The facts in categories *2* and *3* obviously conflict with the previous interpretation[13] for the equatorial preference of the nitro group on the basis of steric repulsion as well as dipole–dipole interaction. Incidentally, Eliel and his co-workers[17] found that the 5-axial isomer of 2-isopropyl-5-nitro-1,3-dioxane was preponderant over the corresponding 5-equatorial isomer by 3.4 kJ/mol (0.81 kcal/mol) in dichloromethane. They explained the fact in terms of (*a*) attractive electrostatic interaction between the positively polarized nitrogen atom of the nitro group and the negatively polarized ring-oxygen atom, and (*b*) p-π^* overlap of the ring-oxygen unshared electron pairs with the π^* orbitals of the nitro group*. Inspection of Stuart models revealed that 4,6-*O*-benzylidene-2-nitro sugars in categories *2* and *3* are likely to assume conformation III, due to stabilization by the aforementioned factors in contrast with the situation for 4,6-*O*-benzylidene-3-nitro sugars. If the latter assume the conformation having an axial nitro group, the nitro group should bring about 1,3-diaxial interaction with the substituents at both C-1 and C-5,

*A "p-π^*" overlap should be appropriate for stabilization[18], although they explained it by "p-π" overlap.

as may be seen from IV, which may exceed the same type of stabilization as already described, to force the conformation to change into V. However, conformation V is also destabilized by steric[13] and electrostatic repulsion between O-4 and one of the oxygen atoms of the nitro group. A similar argument should be applicable to the fact in category *4*, *i.e.*, the conformer stabilized by the factors already cited should be destabilized by steric and electrostatic repulsion between the methoxyl group on C-3 and one of the oxygen atoms of the nitro group. Steric hindrance between the 2,4-pentanedione moiety and the nitro group in **6** and **8** seems to be more serious than that between the methoxyl group on C-3 and the nitro group of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-nitro-α-D-mannopyranoside. However, **6** and **8** are more stable than the corresponding 2-epimers, different from the 3-*O*-methyl derivatives, suggesting that electrostatic repulsion present in the latter is important.



III



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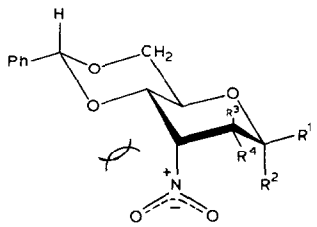

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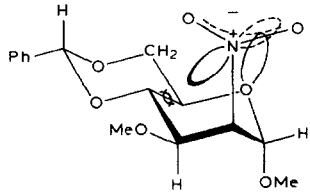

VI

EXPERIMENTAL

General methods. — All melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 polarimeter. Solutions were dried with anhydrous sodium sulfate, and were evaporated under diminished pressure. Column chromatography was conducted on silica gel (Wakogel C-300). T.l.c. was performed with silica gel GF 254 (Merck, Darmstadt). The catalyst used refers to tributylhexadecylphosphonium bromide. I.r. spectra were recorded for potassium bromide pellets, and ^{1}H-n.m.r. spectra were recorded with a JNM PS-100 (JEOL) spectrometer.

*1,5-Anhydro-4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-*D*-erythro-hex-2-enitol* (**2**). — A mixture of compound[3b] **1** (59 mg, 0.22 mmol), sodium nitrite (71.9 mg, 1 mmol), the catalyst (4.7 mg), benzene (4.72 mL), and water (0.47 mL) was stirred for 4.5 h at room temperature. Benzene (10 mL) was then added to the mixture, and the organic layer was separated, washed with water, dried (anhydrous magnesium sulfate), and evaporated. The residue (58.7 mg) was chromatographed, with benzene as the eluant, to give **2** (25.9 mg, 44% yield), which was pure enough for elemental analysis; m.p. 155–155.5°, $[\alpha]_D^{22}$ +25.3° (*c* 1, acetone); ν_{max} 1535 cm^{-1} (alkenic nitro group).

Anal. Calc. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.27; H, 4.94; N, 5.29.

*1,5:2,3-Dianhydro-4,6-*O*-benzylidene-2-deoxy-2-nitro-*D*-mannitol* (**3**) *and* -*D*-*allitol* (**4**). — To a stirred solution of **2** (200 mg, 0.75 mmol) and 35% aqueous hydrogen peroxide (1.3 mL) in 1,4-dioxane (13 mL) was added M sodium hydroxide (1.3 mL) at room temperature. After stirring for 30 min, the base was neutralized with dilute hydrochloric acid, and dichloromethane was added. The organic layer was separated, successively washed with aqueous sodium hydrogencarbonate solution and water, dried, and evaporated, to afford a crystalline residue, the ^{1}H-n.m.r. spectrum of which showed the presence of the *manno* (**3**) and *allo* isomer (**4**) in the ratio of 1.1:1. The residue was chromatographed, with benzene as the eluant, to give **3** (95 mg, 45% yield) as the first fraction; m.p. 182–184°, $[\alpha]_D^{22}$ −3.6° (*c* 1, acetone); ν_{max} 1560 cm^{-1} (NO_2).

Anal. Calc. for $C_{13}H_{13}NO_6$: C, 55.91; H, 4.70; N, 5.02. Found: C, 55.80; H, 4.65; N, 4.93.

The slower-moving fraction (80 mg, 38% yield) was the *allo* isomer **4**; m.p. 201–202°, $[\alpha]_D^{22}$ +13° (*c* 1, acetone); ν_{max} 1564 cm^{-1} (NO_2).

Anal. Calc. for $C_{13}H_{13}NO_6$: C, 55.91; H, 4.70; N, 5.02. Found: C, 55.86; H, 4.59; N, 4.92.

A mixture of **2** (20 mg, 75 μmol), *tert*-butyl peroxide (1.39 mL), the catalyst (1.3 mg), benzene (1.36 mL), and 0.5M sodium hydroxide (0.13 mL) was stirred for 15 min at room temperature, and the base neutralized with dilute hydrochloric acid. The mixture was extracted with dichloromethane, and the extracts were combined, washed successively with aqueous sodium hydrogencarbonate solution and water, dried, and evaporated to a crystalline residue (20 mg), the ^{1}H-n.m.r. spectrum of which showed that **3** thus obtained was almost pure, but contained a trace of **4**.

Similar heterogeneous reaction of **2** (20 mg) with 35% aqueous hydrogen peroxide (1.3 mL) in benzene (1.36 mL)–0.5M sodium hydroxide (1.3 mL) in the presence of the catalyst (1.3 mg) for 15 min at room temperature afforded a mixture (20 mg) of **3** and **4** in the ratio of 1:3.2.

*1,5-Anhydro-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-(diacetylmethyl)-2-nitro-*D*-glucitol* (**5**). — To a solution of **2** (100 mg, 0.38 mmol) and 2,4-pentanedione (57 mg, 0.57 mmol) in 1,4-dioxane (7.5 mL) was added 0.1M sodium hydroxide (1 mL) at room temperature. The mixture was stirred for 20 min, made neutral with 0.1M aqueous hydrochloric acid, and extracted with dichloromethane. The extracts were

combined, washed with water, dried, and evaporated to a syrup (133 mg, 96% yield), the ^{1}H-n.m.r. spectrum of which revealed that it was a mixture of the *gluco* (**5**) and *altro* isomer (**9**) in the ratio of 3.8:1. Crystallization from ethanol gave **5** (22.2 mg, 16% yield); m.p. 127.5–129°, $[\alpha]_D^{22}$ −19.4° (*c* 1, acetone); ν_{max} 1726 (CO) and 1550 cm^{-1} (NO_2).

Anal. Calc. for $C_{18}H_{21}NO_7$: C, 59.49; H, 5.83; N, 3.86. Found: C, 59.63; H, 5.73; N, 3.89.

The mother liquor was evaporated, and the residue was chromatographed with 97:3 benzene–ethyl acetate as the eluant; the first fraction gave **5** (50 mg, 36% yield), and the second, **9** (20 mg, 14% yield).

*1,5-Anhydro-4,6-benzylidene-2,3-dideoxy-3-*C*-(diacetylmethyl)-2-nitro-*D*-mannitol* (**6**). — A mixture of **2** (100 mg, 0.38 mmol), 2,4-pentanedione (57 mg, 0.7 mmol), 0.1M sodium hydroxide (1 mL), the catalyst (12.5 mg), and benzene (10 mL) was stirred for 20 min at room temperature. The mixture was made neutral with 0.1M aqueous hydrochloric acid, and extracted with benzene. The extracts were combined, washed with water, dried, and evaporated to a syrup; ^{1}H-n.m.r. spectroscopy proved this to be a 1:8 mixture of the *gluco* (**5**) and the *manno* isomer (**6**). Crystallization from ethanol gave **6** (70 mg, 51% yield); m.p. 134–136°, $[\alpha]_D^{22}$ −20.8° (*c* 1, acetone); ν_{max} 1735, 1704 (CO), and 1543 cm^{-1} (NO_2).

Anal. Calc. for $C_{18}H_{21}NO_7$: C, 59.49; H, 5.83; N, 3.86. Found: C, 59.44; H, 5.82; N, 3.85.

The mother liquor was evaporated, and the residue was chromatographed with 97:3 (v/v) benzene–ethyl acetate as the eluant, to give **5** (21.3 mg, 15% yield) as the first fraction, and **6** (23.3 mg, 17% yield) as the second.

*1,5-Anhydro-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-(diacetylmethyl)-2-nitro-*D*-altritol* (**9**). — To a solution of **2** (100 mg, 0.38 mmol) and 2,4-pentanedione (57 mg, 0.57 mmol) in 1,4-dioxane (60 mL) was added 0.1M sodium hydroxide (1 mL), and the mixture was stirred for 1 h at room temperature, and made neutral with 0.1M aqueous hydrochloric acid; dichloromethane was added, and the organic layer was washed with water, dried, and evaporated to a syrup (130 mg, 94% yield), which was proved by ^{1}H-n.m.r. spectroscopy to be a 1:5.8 mixture. The syrup was chromatographed with 97:1 (v/v) benzene–ethyl acetate as the eluant; crystalline **5** (19.4 mg, 14% yield) was isolated as the first fraction (identical with an authentic specimen), and syrupy **9** (80.7 mg, 58% yield) as the second. Compound **9** had $[\alpha]_D^{22}$ −86.7° (*c* 1, acetone); ν_{max} 1730, 1695 (CO), and 1548 cm^{-1} (NO_2).

Anal. Calc. for $C_{18}H_{21}NO_7$: C, 59.49; H, 5.83; N, 3.86. Found: C, 59.44; H, 6.12; N, 3.78.

*1,5-Anhydro-4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-*D*-arabinitol* (**11**). — To a solution of **2** (100 mg, 0.38 mmol) in methanol (30 mL) was slowly added sodium borohydride (325 mg) at room temperature, and the mixture was stirred for 30 min at that temperature. After the addition of aqueous acetic acid, the mixture was extracted with dichloromethane, and the extracts were combined, washed successively with water, aqueous sodium hydrogencarbonate solution, and water, dried, and

evaporated, to give a crystalline residue which proved to be a 3.7:1 mixture of the *arabino* (**11**) and *ribo* isomer (**12**) (^{1}H-n.m.r. spectroscopy). Recrystallization from ethanol gave **11** (71 mg, 70% yield); m.p. 150–151°, $[\alpha]_D^{22}$ −65.5° (*c* 1, acetone): ν_{max} 1560 cm^{-1} (NO_2).

Anal. Calc. for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.61; H, 5.55; N, 5.22.

The mother liquor was evaporated to dryness, and the residue was chromatographed with benzene as the eluant. Although most of the product decomposed during column chromatography, a small amount (3 mg, 3% yield) of **12** was isolated; m.p. 160–162°, $[\alpha]_D^{22}$ +14.3° (*c* 0.3, acetone); ν_{max} 1550 cm^{-1} (NO_2).

Anal. Calc. for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 59.09; H, 5.71; N, 4.86.

Epimerization of **11**. — The reaction of **11** (10 mg, 38 μmol) in acetone-d_6 (0.3 mL) in the presence of 0.1M sodium deuteroxide (33 mg) or 0.1M sodium hydroxide (33 mg) was performed in an n.m.r. sample-tube at ~23°, and monitored by ^{1}H-n.m.r. spectroscopy. After 24 h, the ratio of **11** to **12** attained 7.1:1 and did not change, even after 48 h, judging from the area-ratio of their benzylidene methine-proton signals. The resulting mixture was de-ionized by treating with Amberlite IR-120 (H^+) cation-exchange resin, the resin was filtered off, and the filtrate was evaporated to dryness, to give a residue (9.7 mg).

Similar treatment of **11** (10 mg) in 1,4-dioxane (0.3 mL) afforded an equilibrium mixture (**11**:**12** = 3.9:1) after 48 h.

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