*Carbohydrate Research*, 157 (1986) 242–250
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

## Note

# Formation of carbohydrate nitrocyclopropanes from nitroalditols*

BRUNO RADATUS, URSULA WILLIAMS, AND HANS H. BAER
*Ottawa-Carleton Institute for Research and Graduate Studies in Chemistry, Department of Chemistry, University of Ottawa, Ontario K1N 9B4 (Canada)*

(Received February 27th, 1986; accepted for publication, March 20th, 1986)

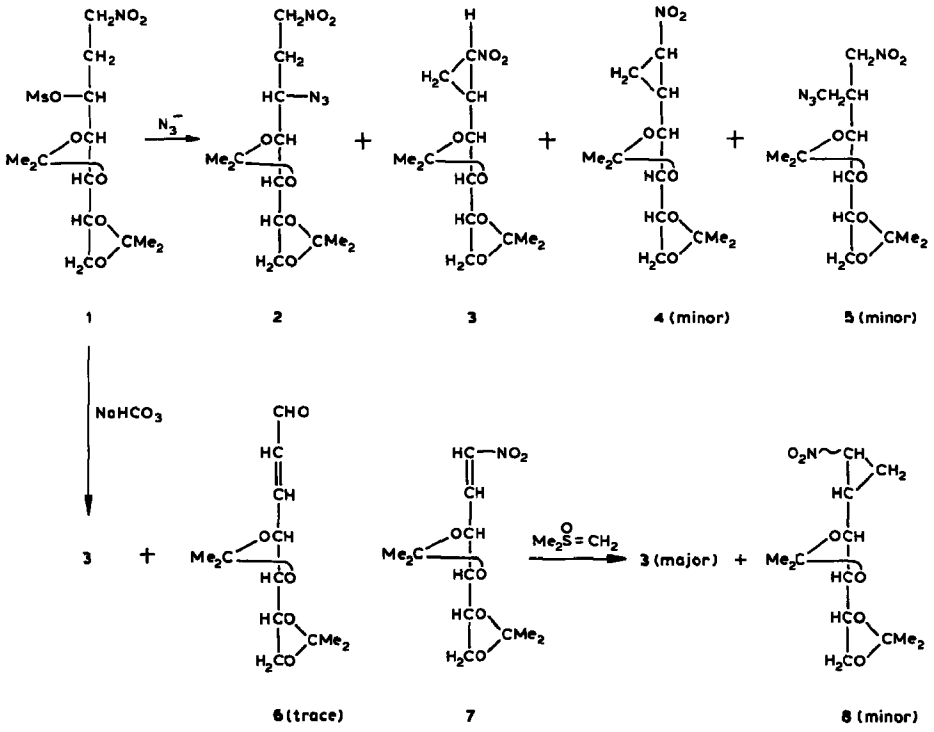
For a synthetic project currently underway in this laboratory, 3-azido-1,2,3-trideoxy-4,5;6,7-di-*O*-isopropylidene-1-nitro-D-*gluco*-heptitol (**2**) was required. As a potential precursor, the corresponding 1,2-dideoxy-3-*O*-mesyl derivative having the D-*manno* configuration (**1**) was prepared in several steps from D-mannose, and its reaction with azide ion was studied. Use of tetrabutylammonium azide in boiling toluene led within 1 h to a mixture of products from which the desired displacement-product **2** could in fact be isolated, but only in 46% yield; components having higher and lower chromatographic mobilities constituted about one-half of the mixture. Performance of the displacement reaction under phase-transfer conditions at 56°, using sodium azide in water–benzene and in the presence of tetrabutylammonium hydrogensulfate as the transfer catalyst, gave **2** in an improved yield (76%), with the previously observed by-produccts being diminished in proportion. However, the proportions of the latter rose again (up to 66%) when the same operation was performed at 80 and 100°. From the mixture produced in the aforementioned, homogeneous-phase reaction the by-products were isolated analytically pure by multiple chromatography. In addition to **2** (46%), three compounds were obtained, namely, the epimeric, *trans*- and *cis*-substituted nitrocyclopropanes **3** and **4** (yields, 25 and 4.5%, respectively), and the branched-chain azidonitro compound **5** (3%). Proof of structure was provided by elemental and spectroscopic analysis; see a subsequent section.

It was apparent that azide ion, besides effecting SN2 displacement at C-3 in **1**, acted for part of the substrate as a base to generate the nitronate anion, which then produced **3** and **4** by internal displacement. This mechanistic view received

*Part XLIV of a series "Reactions of Nitro Sugars". For Part XLIII, see ref. 1. Financial support of this work by the United States Public Health Service through grant GM 35244 to H. H. B. is gratefully acknowledged. Dr. D. R. Bundle, National Research Council of Canada, Ottawa, is thanked for measuring some spectra.

†Compound **1** was obtained by acetonation, followed by mesylation, of 1,2-dideoxy-1-nitro-D-*manno*-heptitol which, in turn, had been prepared from D-mannose by chain elongation employing conventional nitromethane methodology[2].

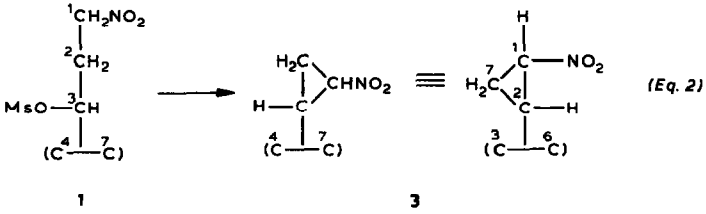
0008-6215/86/$ 03.50 



support when **1** was converted with high yield (85%) into **3** by treatment with solid sodium hydrogencarbonate in refluxing toluene, although only a trace of epimer **4** was detected in this case. The reaction conditions were those commonly used for dehydroacyloxylation of β-nitro esters (the Schmidt–Rutz reaction[3]) to give nitroalkenes; as far as we are aware, the present example is the first where a γ-nitro ester was analogously transformed into a nitrocyclopropane. However, a closely related precedent[4] is the potassium acetate-induced dehydrobromination of [α-alkyl (or aryl) -β-nitroethyl]bromomalonates (Eq. *1*).

The mechanism of formation of **3** (and **4**) implies actual inversion of configuration at C-3. However, as a consequence of renumbering of the chain in accord with carbohydrate nomenclature, the *manno* designation is retained. Thus, **3** is (1*R*)-1,2-dideoxy-3,4;5,6-di-*O*-isopropylidene-1,2-*C*-methylene-1-nitro-D-mannitol, and **4** is its 1*S* diastereomer. (See Eq. *2*)

In the reaction of **1** with hydrogencarbonate to give **3**, a minute proportion of

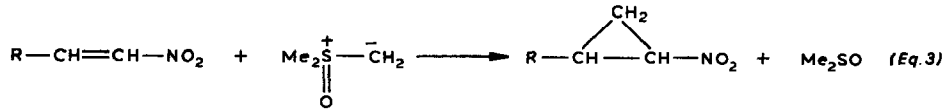


(Eq. 2)

1 3

another by-product arose which, after isolation, was spectroscopically identified as the unsaturated aldehyde **6**. Its mode of formation evidently involved β-elimination of methanesulfonic acid, and extrusion of the elements of nitroxyl (HNO)*.

It was decided, next, to investigate an alternative approach to **3**. Asunskis and Shechter[8] had reported the synthesis of several, simple nitrocyclopropane derivatives by methylene addition to nitroalkenes with dimethylsulfoxonium methylide (Eq. *3*), and this procedure had been applied to two 2,3-dideoxy-3-nitro-hex-2-enopyranoside anomers by Sudoh and his co-workers[9,10], who obtained 2,3-*C*-methylene derivatives in yields of 16.5 and 72%.

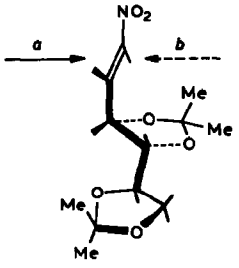


(Eq. 3)

Reaction of the ylide with the known[11], nitroalkenic alditol **7** gave **3** as a distillable syrup, in disappointing yield (28% after distillation). Although the i.r. and 300-MHz $^1$H-n.m.r. spectra of the distilled product (homogeneous in t.l.c.) were superposable on those of the previously obtained **3**, the optical rotation deviated slightly, and 500-MHz, $^1$H-n.m.r. as well as 125-MHz, $^{13}$C-n.m.r. spectra revealed ~6% of an isomer to be present. The small extra signals in the carbon spectrum were all close satellites to the signals for **3**, but did *not* coincide with those for **4**. For instance, the nitromethine carbon resonated at 57.5, versus 56.8 and 58.5 p.p.m. for **3** and **4**, respectively. It can be concluded that the accompanying isomer was the D-glucitol derivative **8**, resulting from attack on the *si,si* face of the nitroalkene. The high, diastereofacial selectivity of this addition is remarkable. However, a strong preference for *re,re* face addition is plausible if one assumes for the nitroalkene a favored conformation as depicted in formula **7a**, with O-3 eclipsing the ethylenic double bond. (For justification of this assumption, see a discussion in ref. 12.)

The epimers **3** and **4** were interconvertible by catalysis with sodium hydroxide

*The Nef reaction, which produces carbonyl compounds from nitronates with release of HNO (that emerges as $N_2O$), generally requires a strongly acidic medium and is therefore unlikely to account for the formation of **6**. Rather, one of two related, carbonyl-forming processes may have been responsible: nitronate autoxidation in basic[5], or oxido-reduction in weakly acidic[6] medium[7].




7a

*a,Re,Re* face attack
*b,Si,Si* face attack

in methanol at room temperature, either compound giving an equilibrium mixture in which the *E* isomer **3** strongly preponderated. Although equilibration occurred within 3 min when 1.2M sodium hydroxide was used, it required 1–1.5 h with 0.12M base. Evidently, more-strongly basic conditions were needed than for nitromethine epimerizations observed in other ring systems*. This was not surprising as nitrocyclopropanes are known to be deprotonated with difficulty. Thus, nitrocyclopropane itself and alkyl derivatives thereof are insoluble in aqueous sodium hydroxide at room temperature[8,14], and the pK value for nitrocyclopropane in dimethyl sulfoxide solution is ~27, as compared to 16.9 for 2-nitropropane[15]. The phenomenon is attributed to sharply increased ring strain in the anion due to bond rehybridization[15,16]. By contrast, variations in pK of up to 3 units observable in different nitrohexopyranoside derivatives are associated with $A^{(1,3)}$ strain developing in the nitronate ion[17].

The structures of the new compounds were derived from spectroscopic data. Thus, **3** and **4** showed i.r. bands at 1545 ($NO_2$) and 3105 $cm^{-1}$ (cyclopropane C–H). The $^{13}C$-n.m.r. spectra exhibited methine carbon resonances near $\delta$ 57–58 for C-1 and near $\delta$ 27 for C-2, and methylene carbon signals for C-7 (in the cyclopropane ring) near 15 p.p.m. By contrast, the branched-chain molecule **5** displayed methylene carbon signals at 68.0 ($CH_2NO_2$) and 40.1 p.p.m. ($CH_2N_3$), with a methine signal at 26.9 p.p.m. for C-2. The products **3** and **4** gave perfectly resolved, first-order, high-field $^1H$-n.m.r. spectra, showing multiplets at lowest field for H-1 coupled to multiplets for H-2, H-7a, and H-7b at high field. Coupling constants present in **3** were $J_{1,7a} = J_{1,2} = 3.4$ and $J_{1,b} = 6.8$ Hz, indicating for the nitromethine proton H-1 two *trans* and one *cis* vicinal protons, and consequently the *E* geometry. Conversely, the corresponding signals in **4** contained two large (8.7 and 6.7 Hz) and one small (4.2 Hz) couplings, indicating for H-1 one *trans* and two *cis* relationships and hence the *Z* geometry. (It is to be noted that the nitro substituent markedly decreases the couplings of H-1; normally in cyclopropanes, *trans* coupl-

*For example, 3-deoxy-1,2;5,6-di-*O*-isopropylidene-3-nitro-α-D-allofuranose and -glucofuranose were equilibrated in acetone solution in the presence of solid sodium hydrogencarbonate[13a], and nitroinositols were found to epimerize in aqueous sodium hydrogencarbonate solution[13b].

ings are 7–8, and *cis* couplings, 10–12 Hz.) Compound **5** showed at lowest field two separate doublets of doublets for the nitromethyl (magnetically nonequivalent) and similarly, two doublets of doublets at intermediate field for the azidomethyl protons, with a complex, one-proton multiplet for H-2 at the branch point occurring at high field. It was not possible to deduce the C-2 configuration from the spectrum or prove it otherwise, and the assumed *manno* configuration of the product is based solely on the mechanistic consideration that it was formed from **3** (or **4**) by nucleophilic opening of the nitrocyclopropane ring. Finally, the determinant parameters for the enal **6** (which lacked $NO_2$ bands in the infrared) were an aldehydic, one-proton doublet ($J_{1,2}$ 7.9 Hz) at $\delta$ 9.57 and two vinylic proton signals at $\delta$ 6.86 (H-3) and 6.41 (H-2), mutually coupled ($J_{2,3}$ 15.8 Hz, $J_{2,4}$ −1.6 Hz).

We consider **3** to be potentially useful for a variety of synthetic pursuits. Its chief significance is seen in the presence of a stereospecifically established point of chain branching vicinal to a nitrogen function, and studies to elaborate the molecule with the intent of taking advantage of that feature are in progress. Only a few carbohydrate nitrocyclopropanes have been described previously, including the 2,3-*C*-methylene-3-nitrohexopyranosides referred to[9,10] and two isomers obtained[18] by thermal degradation of nitropyrazolino sugars, and no experiences regarding the chemical reactivity of such molecules have been gathered.

## EXPERIMENTAL

*General methods.* — For general, preparative, and instrumental techniques, see ref. 1. Solvents used for t.l.c. and column chromatography on silica gel were: *A*, 1:4 (v/v) ethyl acetate–hexane; *B*, 1:19 (v/v) ethyl acetate–hexane; and *C*, dichloromethane. The $^1$H- and $^{13}$C-n.m.r. data refer to spectra measured at 300 and 75.43 MHz, respectively, except for **3** which was measured at 500 and 125.76 MHz. The solvent was chloroform-*d* for all determinations. Signal assignments were made or confirmed with the aid of the HOMCOR and ADEPT methods.

*Preparation of 3-azido-1,2,3-trideoxy-4,5;6,7-di-*O*-isopropylidene-1-nitro-*D*-gluco-heptitol* (**2**), *and isolation of by-products* **3**–**5**. — A solution of tetrabutylammonium bromide (10 g) and sodium azide (15 g) in water (30 mL) was extracted twice with chloroform, and the extract evaporated. The resulting residue and fresh $NaN_3$ (15 g) were dissolved in water (30 mL), and the solution was extracted twice with chloroform. Drying ($MgSO_4$) and evaporation of the extract gave a residue of tetrabutylammonium azide, from which added toluene was evaporated before further use. Methanesulfonate[19] **1** (3.9 g) and toluene (30 mL) were then added. No reaction was evident at room temperature after 30 min (t.l.c. with solvent *A*), but boiling of the mixture under reflux generated rapidly new products as revealed by 3 spots, A ($R_F$ 0.59), B ($R_F$ 0.42), and C ($R_F$ 0.29). All of **1** ($R_F$ 0.12) was consumed after 1 h. The mixture was diluted with some benzene, washed with water (4×), dried ($Na_2SO_4$), and evaporated, to give a brown syrup (2.9 g) which was chromatographed on a column of silica gel (60 × 2 cm). Elution with solvent

*B* gave fractions of A (772 mg), A + B (240 mg), and B (1.394 g), isolated as syrups. Subsequent elution with solvent *A* produced syrupy C (131 mg). Rechromatography of A + B on a smaller column separated the mixture into A (58 mg) and B (150 mg).

The fractions B (total, 1.544 g) proved to be compound **2** (yield, 46%), $[\alpha]_D$ +16° (*c* 0.7, chloroform), $\nu_{max}$ 2105 ($N_3$) and 1550 $cm^{-1}$ ($NO_2$); $^1$H-n.m.r.: $\delta$ 4.55 (dd, 2 H, $J_{1,2}$ 6.4, $J_{1,2'}$ 8.1 Hz, H-1,1'), 4.13 (m, H-6), 4.02–3.85 (m, 4 H, H-4,5,7,7'), 3.46 (dt, $J_{2,3} = J_{2',3} = 3.8$, $J_{3,4} = 8.8$ Hz, H-3), 2.40 (m, 2 H, H-2,2'), and 1.42, 1.36, 1.35, 1.30 (s, 4 × 3 H, 4 Me); $^{13}$C-n.m.r.: $\delta$ 110.0 and 110.4 (–O–C–O–), 82.8, 78.1, and 77.1 (C-4,5,6), 72.1 (C-1), 68.0 (C-7), 58.6 (C-3), 29.1 (C-2), and 27.1, 26.7, 26.5, 25.1 (4 × Me).

*Anal.* Calc. for $C_{13}H_{22}N_4O_6$ (330.3): C, 47.26; H, 6.71; N, 16.96. Found: C, 47.49; H, 6.65; N, 16.88.

Spectroscopic examination of different fractions just designated as A, giving a single spot in t.l.c. with solvent *A* ($R_F$ 0.49), revealed that they were in fact inhomogeneous. In particular, i.r. spectra showed different relative intensities of peaks attributable to azide and cyclopropyl groups (2100 and 3100 $cm^{-1}$). T.l.c. with solvent *C* effected separation into two components, $A_1$ ($R_F$ 0.22) and $A_2$ ($R_F$ 0.30). The total amount of A (~830 mg), in which $A_1$ strongly preponderated, was subjected to multiple chromatography on silica gel columns with dichloromethane as the eluant (and partly with ethyl acetate–hexane mixtures), to procure the components $A_1$ and $A_2$ in pure or almost-pure form. The aforementioned product C, which showed trace impurities in t.l.c., was purified by another passage through silica gel by means of solvent *B*, and was so obtained as a colorless, homogeneous syrup (110 mg).

*(1R)-1,2-Dideoxy-3,4;5,6-di-*O*-isopropylidene-1,2-*C*-methylene-1-nitro-*D*-mannitol* (**3**). — The component $A_1$ (see the preceding section) proved to be **3**. From the amount of crude A originally isolated (830 mg) and the amount of $A_2$ (100 mg) removed therefrom chromatographically, its yield was estimated as ~25% Chromatographically purified **3** still contained traces of $A_2$, invisible in t.l.c. but detectable by i.r. (small $N_3$ peak). The contaminant was completely removed by distillation of a sample (179 mg) in an oil-pump vacuum, using a cold-finger apparatus (yield of pure distillate, 172 mg); $[\alpha]_D$ −55.1° (*c* 0.5, chloroform); $\nu_{max}$ 3105 (cyclopropyl) and 1545 $cm^{-1}$; $^1$H-n.m.r. (500 MHz): $\delta$ 4.32 (dt, $J_{1,2}$ 3, $J_{1,7}$ 3.5, $J_{1,7'}$ 7.5 Hz, H-1), 4.10 (dd, *J* 6 and 8.5 Hz, H-6'), 3.98 (ddd, *J* 4, 6, and 8.5 Hz, H-5), 3.94 (dd, *J* 4 and 8.5 Hz, H-6), 3.81 (dd, $J_{2,3}$ 4.5, $J_{3,4}$ 8 Hz, H-3), 3.64 (dd, $J_{3,4}$ 8, $J_{4,5}$ 8.5 Hz, H-4), 2.34 (12-line m, $J_{1,2}$ 3, $J_{2,3}$ 4.6, $J_{2,7}$ 7.7, $J_{2,7'}$ 11 Hz, H-2), 1.83 (ddd, $J_{1,7}$ 3.5, $J_{7,7'}$ 6, $J_{2,7'}$ 11 Hz, H-7'), 1.40 (dt, $J_{7,7'}$ 6, $J_{1,7'}$ 7.5, $J_{2,7}$ 7.7 Hz, H-7), 1.34 and 1.32 (s, 3 H each, 2 Me), and 1.30 (s, 6 H, 2 Me); $^{13}$C-n.m.r.: $\delta$ 109.8, 109.6 (2 O–C–O), 81.2, 77.7, 76.8 (C-3,4,5), 67.7 (C-6), 56.9 (C-1), 27.1 (C-2), 26.8, 26.75, 26.60, and 25.1 (4 Me), and 15.5 (C-7).

*Anal.* Calc. for $C_{13}H_{21}NO_6$ (287.3): C, 54.34; H, 7.37; N, 4.87. Found: C, 54.30; H, 7.36; N, 4.91.

*(1S)-1,2-Dideoxy-3,4;5,6-di-O-isopropylidene-1,2-C-methylene-1-nitro-D-mannitol* (**4**). — The aforementioned syrup C (crude yield, 4.5%; pure, 3.7%) proved to be **4**; $[\alpha]_D$ +25.8° (*c* 0.6, chloroform); $\nu_{max}$ 3105 (cyclopropyl) and 1545 $cm^{-1}$ ($NO_2$); $^1$H-n.m.r.: $\delta$ 4.42 (ddd, $J_{1,7'}$ 4.2, $J_{1,7}$ 6.7, $J_{1,2}$ 8.7 Hz, H-1), 4.13 (dd, *J* 5.6 and 7.6 Hz, H-6'), 4.06 (m, H-5), 4.02 (dd, *J* 7.3 and 9.3, H-3), 3.95 (dd, $J_{5,6}$ 4, $J_{6,6'}$ 7.7 Hz, H-6), 3.76 (~t, $J_{3,4} \approx J_{4,5} \approx$ 7.5 Hz, H-4), 1.96 (ddd, $J_{1,7'}$ 4.2, $J_{7,7'}$ 6.8, $J_{2,7'}$ 8.5 Hz, H-7'), 1.64 (sym. quintet with poorly resolved splitting of inner peaks, width 35.3 Hz, compatible with $J_{1,2} \approx J_{2,7} \approx J_{2,7'}$ = 8.5–8.8, $J_{2,3}$ 9.3 Hz, H-2), 1.38 (m, for H-7, obscured by Me signals), 1.39, 1.37, 1.33, and 1.23 (s, 3 H each, 4 Me); $^{13}$C-n.m.r.: $\delta$ 109.70, 109.65 (2 O–C–O), 81.4, 77.0, 76.3 (C-3,4,5), 67.6 (C-6), 58.5 (C-1), 27.1 (Me), 26.75 and 26.70 (C-2, Me), 25.1 (2 Me), and 14.35 (C-7).

*Anal.* Calc. for $C_{13}H_{21}NO_6$ (287.3): C, 54.34; H, 7.37; N, 4.87. found: C, 54.87; H, 7.45; N, 4.68.

*2-C-(Azidomethyl)-1,2-dideoxy-3,4;5,6-di-O-isopropylidene-1-nitro-D-mannitol* (**5**). — All fractions of component $A_2$ ($R_F$ 0.30 with solvent *C*; see a preceding section) were combined, and trace impurities were removed by another passage through silica gel (16 × 1.8 cm) with solvent *B*. A colorless syrup (99 mg, 2.9%) of **5** was obtained, $[\alpha]_D$ +16.5° (*c* 0.7, chloroform); $\nu_{max}$ 2109 ($N_3$) and 1560 $cm^{-1}$ ($NO_2$); $^1$H-n.m.r.: $\delta$ 4.60 (dd, $J_{1,2}$ 4.3, $J_{1,1'}$ 13.7 Hz, H-1), 4.45 (dd, $J_{1',2}$ 7.8, $J_{1,1'}$ 13.7 Hz, H-1'), 4.15 (dd, $J_{5,6}$ 4.9, $J_{6,6'}$ 8.3 Hz, H-6), 4.06 (dd, $J_{2,3}$ 5.2, $J_{3,4}$ 6.7 Hz, H-3), 4.00 (dt, H-5), 3.92 (dd, $J_{5,6'}$ 5.5, $J_{6,6'}$ 8.3 Hz, H-6'), 3.68 (dd, $J_{3,4}$ 6.7, $J_{4,5}$ 9.0 Hz, H-4), 3.63 (dd, $J_{2,7}$ 4.7, $J_{7,7'}$ 11.5 Hz, H-7), 3.57 (dd, $J_{2,7'}$ 5.5, $J_{7,7'}$ 11.5 Hz, H-7'), 2.77 (m, H-2), 1.40, 1.34, 1.32 and 1.31 (s, 3 H each, 4 Me); $^{13}$C-n.m.r.: $\delta$ 110.1, 109.9 (2 O–C–O), 80.1, 78.9, 77.0 (C-3,4,5), 73.6 (C-1), 68.0 (C-6), 50.3 (C-7), 40.1 (C-2), 26.85 (2 Me), 26.6 (Me) and 25.1 (Me).

*Anal.* Calc. for $C_{13}H_{22}N_4O_6$ (330.3): C, 47.26; H, 6.71; N, 16.96. Found: C, 47.56; H, 7.00; N, 16.76.

*Preparation of* **3**. A. *From* **1** *with sodium hydrogencarbonate.* A solution of methanesulfonate[19] **1** (0.96 g) in toluene (25 mL) was stirred with dry $NaHCO_3$ (5 g) and boiled under reflux for 24 h. A major product ($R_F$ 0.5) and two trace spots ($R_F$ 0.4 and 0.3) were indicated by t.l.c. (solvent *A*). The cooled mixture was diluted with benzene and shaken with water. The separated phases were extracted with water and benzene, respectively, and combined with the corresponding extracts. The organic phase was dried ($Na_2SO_4$), and evaporated, to yield a faintly yellowish syrup (695 mg). The material was chromatographed on a column of silica gel (24 × 1.8 cm) with solvent *B* as the eluant, which effected clean separation to give **3**, $R_F$ 0.5 (615 mg, 85.5%); **4**, $R_F$ 0.3 (7 mg, ~1%); and **6**, $R_F$ 0.4 (4.2 mg, 0.6%). Compounds **3** and **4** were identical with the previously described products according to their 300-MHz, $^1$H-N.m.r. and i.r. spectra; for **3**, $[\alpha]_D$ −55.2° (*c* 0.5, chloroform).

The trace product **6** was identified as (2,3*E*)-2,3-dideoxy-4,5;6,7-di-*O*-isopropylidene-*aldehydo*-D-*arabino*-hept-2-enose by its $^1$H-n.m.r. data: $\delta$ 9.57 (d, $J_{1,2}$ 7.9 Hz, H-1), 6.86 (dd, $J_{2,3}$ 15.8, $J_{3,4}$ 4.2 Hz, H-3), 6.41 (ddd, *J* 7.9 and 15.8 Hz, $J_{2,4}$

−1.6 Hz, H-2), 4.61 (ddd, $J_{2,4}$ −1.6, $J_{3,4}$ 4.2, $J_{4,5}$ 7.8 Hz, H-4), 4.12 (m, 2 H, H-7,7'), 3.93 (td, H-6), 3.65 (t, $J_{4,5} = J_{5,6}$ = 7.8 Hz, H-5), 1.41, 1.38, 1.37, and 1.32 (s, 3 H each, 4 Me).

B. *From* **7** *with dimethylsulfoxonium methylide.* Sodium hydride (0.16 g of a 61% oil dispersion; 4 mmol) was rinsed three times with hexane and dried by evacuation of the reaction-vessel, which was then flushed with $N_2$ gas, and trimethylsulfoxonium iodide[20] (0.87 g, 4 mmol) was added. Dry dimethyl sulfoxide (5 mL) was added dropwise with stirring, to give under $H_2$ evolution a milky-white suspension of dimethylsulfoxonium methylide[21]. The mixture was cooled (+10°), and 1,2-dideoxy-3,4;5,6-di-*O*-isopropylidene-1-nitro-D-*arabino*-hex-1-enitol[11] (**7**; 1.0 g, 3.7 mmol) in dry dimethyl sulfoxide (5 mL) was added dropwise. After 10 min, t.l.c. (solvent *A*) suggested that the reaction was essentially complete, with **7** ($R_F$ 0.55, visible under u.v. light) having been replaced by **3** ($R_F$ 0.50, not visible under u.v.) as a major product, accompanied by several more-slowly moving, minor products. The mixture was kept at ambient temperature for 10 min and then processed by addition of ice–water and extraction with ether. The extract was washed 3 times with water, dried ($Na_2SO_4$), and evaporated, to give a yellow oil (671 mg). Column chromatography on silica gel (30 g) with solvent *B* furnished syrupy **3** (310 mg, 29.5%), chromatographically homogeneous and indistinguishable from pure **3** obtained previously, by comparison of i.r. and 300-MHz $^1$H-n.m.r. spectra. However, the optical rotation was $[\alpha]_D$ −47.8°. Distillation in an oil-pump vacuum at 65° gave **3** (295 mg, 28%) showing $[\alpha]_D$ −49.2° and an unchanged 300-MHz spectrum. At 500 MHz, a trace impurity became discernible in the spectrum, and this was particularly noticeable in a 125.75-MHz, $^{13}$C-n.m.r. spectrum. There were small satellite peaks (5–6% estimated intensity) close to the main peaks that exactly coincided with those found for pure **3**. Extra peaks not obscured by main peaks were at δ 109.86, 109.65, 81.28, 78.18, 67.86, 57.46, 26.55, 26.47, and 14.38, and although some of these were quite close to resonances found in the epimer **4**, others clearly differed (notably the C-1 peak at δ 57.46). It was concluded that this preparation of **3** contained a small proportion of the D-*gluco* isomer **8**.

In an experiment performed in the same way but on a 5-fold scale (20 mmol), the yield of **3** after chromatography was only 23.5%. Further processing of the aqueous solution that had remained after ether extraction, by continued extractions with chloroform followed by ethyl acetate, gave substantial amounts of material composed largely of slow-moving, unidentified products. Only an insignificant quantity of additional **3** could be isolated (~1%) by chromatography. After vacuum distillation, the total yield was 21%; $[\alpha]_D$ −46.1° (*c* 1, chloroform).

*Epimerization of* **3** *and* **4**. — Samples (1 mg) of **4** were dissolved at 25° in (*a*) 10 drops of 1.2M NaOH in methanol, and (*b*), 10 drops of 0.12M NaOH in methanol. T.l.c. with solvent *A* showed for (*a*) that equilibration was virtually complete within 3 min, with formation of **3** ($R_F$ 0.5) as the strongly preponderant product, and retention of a small proportion of **4** ($R_F$ 0.3) that remained unchanged thereafter. For (*b*), the same pattern was reached after 1.5 h. Samples (1 mg) of **3**

were treated in the same ways, and for (*a*) the same equilibrium pattern was seen after 3 min, with the proportion of **4** appearing to remain constant; for (*b*), **4** was barely detectable after 12 min but approached the previously observed equilibrium proportion after ~1 h.

## REFERENCES


1 H. H. BAER AND Z. H. HANNA, *Carbohydr. Res.*, 85 (1980) 136–142.
2 J. C. SOWDEN, *Adv. Carbohydr. Chem.*, 6 (1951) 291–318; H. H. BAER, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 67–138; M. B. PERRY AND D. T. WILLIAMS, *Methods Carbohydr. Chem.*, 7 (1976) 44–48.
3 H. H. BAER AND L. URBAS, in H. FEUER (Ed.), *The Chemistry of the Nitro and Nitroso Groups*, Interscience Publ., Part 2 (1970), 75–200, especially pp. 168–171.
4 E. P. KOHLER AND S. F. DARLING, *J. Am. Chem. Soc.*, 52 (1930) 1174–1181; A. S. SOPOVA, O. I. YURCHENKO, AND V. V. PEREKALIN, *J. Org. Chem. USSR*, 1 (1965) 1732–1733.
5 G. A. RUSSELL, *J. Am. Chem. Soc.*, 76 (1954) 1595–1600.
6 J. ARMAND, P. SOUCHAY, AND S. DESWARTE, *Tetrahedron*, 20, Suppl. 1 (1964) 249–255; J. ARMAND, *Bull. Soc. Chim. Fr.*, (1965) 3246–3255.
7 A. T. NIELSEN, in H. FEUER (Ed.), *loc. cit.* ref. 3, part 1 (1969) 349–486, especially pp. 384–389, 400–403.
8 J. ASUNSKIS AND H. SHECHTER, *J. Org. Chem.*, 33 (1968) 1164–1168.
9 T. SAKAKIBARA AND R. SUDOH, *J. Chem. Soc., Chem. Commun.*, (1977) 7–8; *Bull. Chem. Soc. Jpn.*, 51 (1978) 1193–1196.
10 T. SAKAKIBARA, T. TAKAMOTO, R. SUDOH, AND T. NAKAGAWA, *Chem. Lett.*, (1972) 1219–1222; T. SAKAKIBARA, R. SUDOH, AND T. NAKAGAWA, *Bull. Chem. Soc. Jpn.*, 51 (1978) 1189–1192.
11 H. PAULSEN AND M. BUDZIS, *Chem. Ber.*, 107 (1974) 1998–2008.
12 E. L. ELIEL, N. L. ALLINGER, S. J. ANGYAL, AND G. A. MORRISON, *Conformational Analysis*, Interscience Publ., (1965) pp. 19–21.
13 (a) J. KOVÁŘ AND H. H. BAER, *Can. J. Chem.*, 49 (1971) 3203–3209; (b) H. H. BAER AND J. KOVÁŘ, *Carbohydr. Res.*, 45 (1975) 161–180.
14 H. B. HASS AND H. SHECHTER, *J. Am. Chem. Soc.*, 75 (1953) 1382–1384.
15 F. G. BORDWELL, N. R. VANIER, W. S. MATTHEWS, J. B. HENDRICKSON, AND P. L. SKIPPER, *J. Am. Chem. Soc.*, 97 (1975) 7160–7162.
16 H. E. ZIMMERMAN AND B. S. THYAGARAJAN, *J. Am. Chem. Soc.*, 82 (1960) 2505–2511.
17 H. H. BAER AND W. RANK, *Can. J. Chem.*, 49 (1971) 3197–3202.
18 H. H. BAER, F. LINHART, AND H. R. HANNA, *Can. J. Chem.*, 56 (1978) 3087–3095.
19 H. H. BAER, I. ARAI, B. RADATUS, J. RODWELL, AND C. NGUYEN, *Can. J. Chem.*, in press.
20 R. KUHN AND H. TRISCHMANN, *Justus Liebigs Ann. Chem.*, 611 (1958) 117–121.
21 E. J. COREY AND M. CHAYKOVSKY, *J. Am. Chem. Soc.*, 84 (1962) 867–868.