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Preliminary communication

Reactions of α-nitroepoxides*

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The α-nitrooxirane grouping has been described, as a novel functionality, only a few years ago and its chemical reactivity and potentialities for synthesis have received but limited study in general organic chemistry[1,2]. In the meantime, a number of carbohydrate α-nitroepoxides have been synthesized in our laboratory[3–5] and by Nakagawa and co-workers[6]. The latter investigators have also communicated[7] some chemical transformations performed with methyl 2,3-anhydro-4,6-*O*-benzylidene-3-nitro-β-D-allopyranoside[4–6] (**1**) and the analogous phenyl glycoside. We now report results of related studies on **1** and its stereoisomers[4,5] having the β-D-*talo* (**5**), α-D-*manno* (**7**), and β-D-*gulo* (**12**) configurations.

Reduction of **1** by sodium borohydride in ethanol (1 h at 25°) gave[3] methyl 4,6-*O*-benzylidene-2-deoxy-β-D-*arabino*-hexopyranoside (**2**), m.p. 155–156°, $[\alpha]_D$ −67° (in $CHCl_3$), which was identified by conversion into the known[8] aniline derivative of 2-deoxy-D-*arabino*-hexose†. Similarly, **5** furnished methyl 4,6-*O*-benzylidene-2-deoxy-β-D-*lyxo*-hexopyranoside (**6**), m.p. 202°, $[\alpha]_D$ −40.5° ($CHCl_3$), whereas the stereoisomeric epoxides **7** and **12** did not react with sodium borohydride under the conditions stated. The reductive denitrations of **1** and **5** no doubt occur by attack of hydride at C-2 from the rear of the oxirane ring followed by elimination of nitrite ion and reduction of an intermediary 2-deoxyglycosid-3-ulose. In **7** and **12**, such attack appears to be hindered by the (pseudoaxial) oxygen function at C-1 and C-4, respectively. In the reaction of **1**, a second product was isolated; it proved to be methyl 4,6-*O*-benzylidene-2-*O*-ethyl-β-D-mannopyranoside (**3**), m.p. 129°, $[\alpha]_D$ −126° (in EtOH), and evidently resulted from competitive attack of ethoxide ion. 3-Epimers of **2**, **3**, and **6**, which could conceivably arise in these borohydride reductions, have not as yet been detected among the products.

Catalytic hydrogenation of α-nitroepoxides with palladium on carbon in ethanol at 25° caused opening of the oxirane ring between its oxygen atom and C-3. Thus, **1** gave known[9] methyl 4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-glucopyranoside (**4**) as the main

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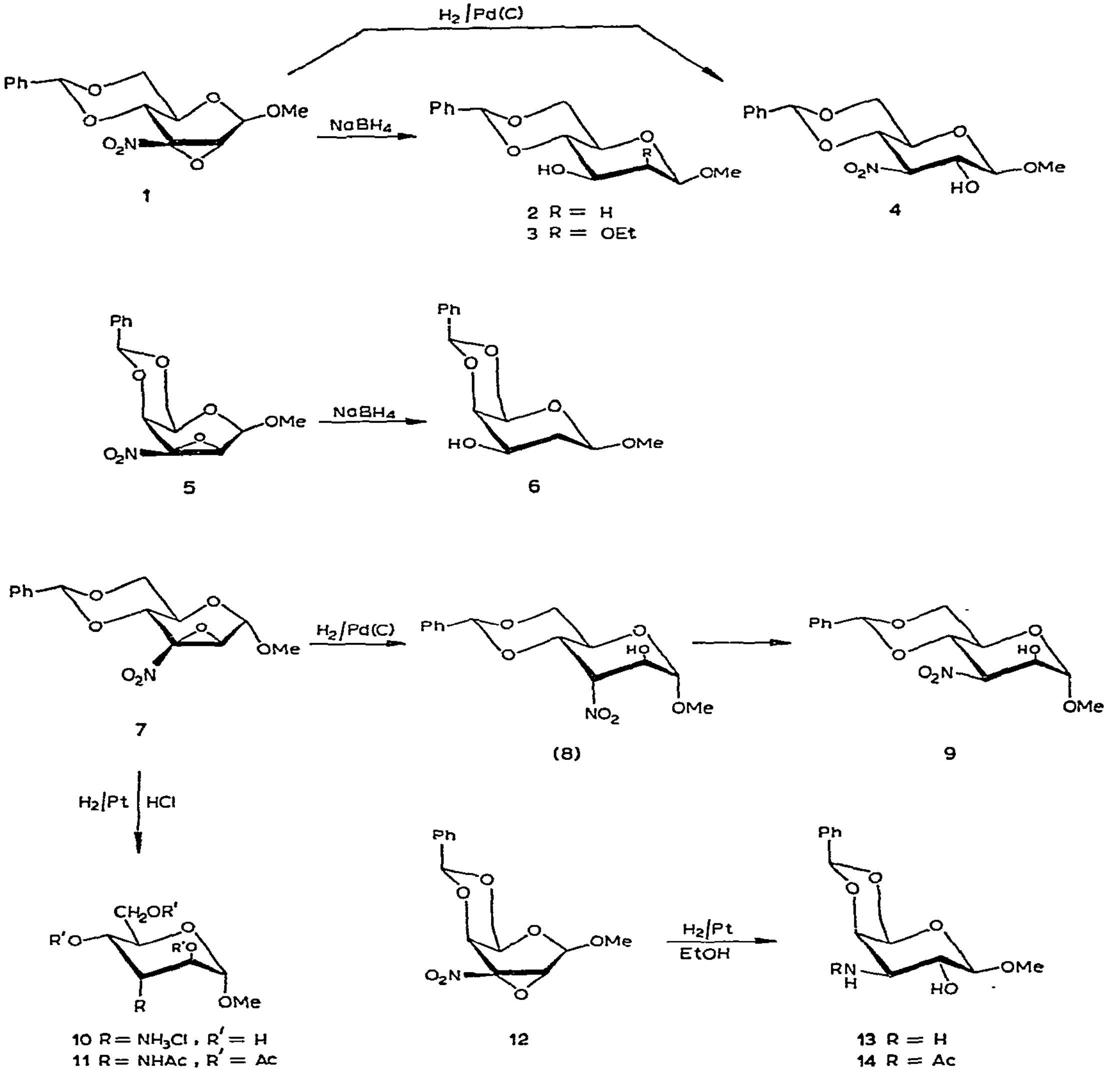
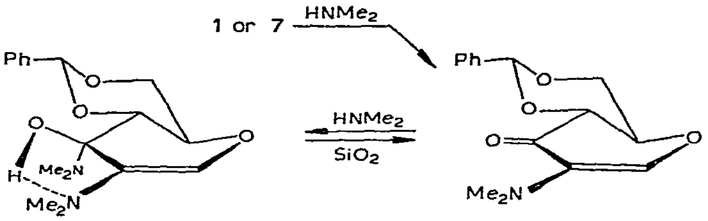
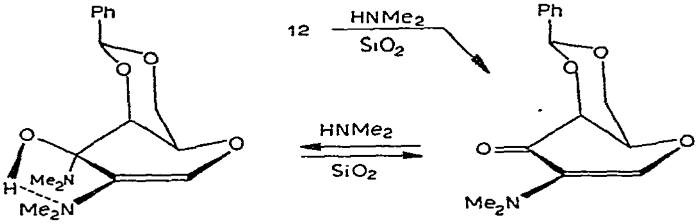
†All new compounds, characterized in this report by melting point and optical rotation, gave elemental analyses and spectral data consistent with the assigned structures. Physical constants of known compounds encountered in the course of this work were in satisfactory agreement with data in the literature cited.



product. Among minor by-products was a crystalline compound $C_{14}H_{17}NO_6$, m.p. 169° dec., $[\alpha]_D$ −55.7° (in $CHCl_3$), which presumably was the 3-oximino derivative that may arise by partial reduction of 4. The epoxide 7, in contrast to its behavior towards borohydride, was hydrogenated in the presence of palladium as, apparently, this hydrogenation takes place on the unhindered side of the molecule. The primary product, doubtless, was the (unknown) α-D-*altro* isomer (8) of 4, but the product isolated was the known[10] α-D-*manno* isomer (9). This was not unexpected as an axial C-3 nitro group is extremely prone to epimerization if traces of base are not excluded[11]. Epimerization was in fact forestalled when 7 was hydrogenated (20 h at 25°) with platinum in ethanol containing 1 equiv. of hydrochloric acid; under these conditions, full reduction of the nitro group and *O*-debenzylidenation took place to give methyl 3-amino-3-deoxy-α-D-altropyranoside



15 16



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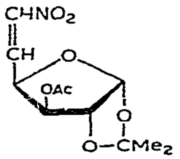

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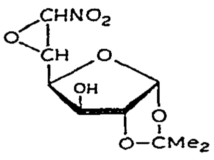

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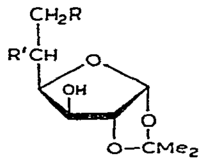
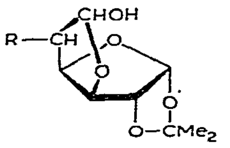


21 $R = OH, R' = H$
22 $R = NH_2, R' = OH$



23 $R = NMe_2$
24 $R = CH_2NO_2$

hydrochloride (**10**) as a hygroscopic solid characterized as its known[12], crystalline tetra-acetyl derivative **11**. Catalytic hydrogenation of **12** with platinum in ethanol (but without added HCl) furnished methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-β-D-galactopyranoside (**13**), m.p. 217–218°, $[\alpha]_D$ –40° (in EtOH), further characterized as *N*-acetyl derivative (**14**), m.p. 293–295°, $[\alpha]_D$ +23° (in $CHCl_3$) and structurally identified by conversion into the known[13] methyl 3-acetamido-3-deoxy-β-D-galactopyranoside.

Reaction of **1** with 25% aqueous dimethylamine for 75 min at 25° led to a 3-dimethylamino adduct (**15**; m.p. 131–133°, $[\alpha]_D$ –155.5° in $CHCl_3$ and –147.3° in EtOH) of 1,5-anhydro-4,6-*O*-benzylidene-2- deoxy-2-dimethylamino-D-*erythro*-hex-1-en-3-ulose (**16**). The α-D-*manno* epoxide **7** also gave **15**, although a reaction time of 48 h was required. The β-D-*gulo* isomer **12**, on brief heating with aqueous dimethylamine, gave a similar adduct (**17**; m.p. 136–137°, $[\alpha]_D$ +28.3° in $CHCl_3$) of the corresponding D-*threo*-glycos-3-ulose **18**. The configuration of C-3 in the vicinal amino alcohols **15** and **17** has not been established; however, indications are that strong chelation exists between the 3-OH and 2-NMe_2 groups, and molecular models suggest a pseudoequatorial 3-OH group to be in a more favorable position for such bonding than a pseudoaxial one. Passage of **15** through a silica gel column by means of 2:3 ethyl acetate–petroleum ether caused elimination of dimethylamine and produced the crystalline glyculose **16**, m.p. 132–133° (mixed m.p. with **15** strongly depressed), $[\alpha]_D$ +200° (in $CHCl_3$). Preliminary experiments showed that **17** undergoes an analogous conversion, although the expected product (**18**) has not yet been definitively characterized. The mechanism of formation of these products is assumed to involve nucleophilic attack by dimethylamine at C-2 of the nitroepoxide, which results in elimination of nitrite ion to give a 2-substituted, glycosid-3-ulose (see also the foregoing reactions with sodium borohydride, and[7] with lithium aluminum hydride and some other nucleophilic reagents). The base present in excess then produces the α,β-unsaturated ketone by β-elimination of methanol and finally adds itself reversibly to the keto group, giving the vicinal amino alcohol.

Epoxidation[4] of 3-*O*-acetyl-5,6-dideoxy -1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose[14] (**19**) yielded 5,6-anhydro-1,2-*O*-isopropylidene-6-nitro-α-D-glucofuranose (**20**; configuration at C-6 not determined), m.p. 134–135°, $[\alpha]_D$ –5° (in $CHCl_3$). Borohydride reduction of **20** in ethanol (15 min at 25°) gave known[15] 5-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexose (**21**), and platinum-catalyzed hydrogenation in ethanol (26 h) afforded 6-amino-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**22**), m.p. 123–125°, $[\alpha]_D$ –11.3° (in H_2O), which was identified by way of its known[16] *N*-acetyl derivative. Action of dimethylamine upon **20** (1 h at 25°) introduced a dimethylamino group at C-5 and caused denitration at C-6, where an aldehyde function was generated. However, the latter underwent intramolecular hemiacetalation, the product being a 5-deoxy-5-dimethylamino-1,2-*O*-isopropylidenehexodialdo-1,4;6,3-difuranose (**23**), m.p. 142–144°. An analogous product, the 5-deoxy-5-*C*-nitromethyl derivative **24**, m.p. 117–118°, $[\alpha]_D$ +63° (in $CHCl_3$), was formed on treatment of **20** with nitromethane in aqueous, saturated barium hydroxide solution for 16 h at 25°.

ACKNOWLEDGMENT

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