chloroform – hexane gave 1.60 g of II, m.p. 147 °C (decomp.), $[\alpha]_D$ −183° (*c* 0.5, in chloroform). (Found: C 42.8; H 4.94; N 4.88; O 34.4; Cl 12.9. $C_{10}H_{14}NO_6Cl$ requires C 42.9; H 5.05; N 5.01; O 34.3; Cl 12.7.)

*Methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-*L*-galacto-hexoside (IV).* The above nitrosyl chloride adduct II (1.40 g) was refluxed with methanol (0.32 g) and pyridine (0.79 g) in dry tetrahydrofuran (40 ml) for 1 h and concentrated. The residue was taken up in chloroform and the chloroform solution shaken with water, dried over magnesium sulfate, filtered and concentrated to yield III as a colourless syrup (1.38 g) which was used directly in the next step. The oxime III (1.38 g) in tetrahydrofuran (35 ml) was refluxed under nitrogen with lithium aluminium hydride (0.66 g) for 3 h. Excess hydride was decomposed by adding, in turn, ethyl acetate and 50 % aqueous methanol (135 ml). The mixture was filtered, the filtrate was neutralized (HCl) to pH 4.5, low-boiling solvents were removed by evaporation and the residual water solution was freeze-dried. The product was acetylated overnight at room temperature with acetic anhydride (8 ml) and pyridine (20 ml). The solution was poured into ice-water and the mixture extracted with chloroform. The combined chloroform phases were washed with ice-cold 1 M sulfuric acid, saturated aqueous sodium hydrogen carbonate and finally water, dried over magnesium sulfate, filtered and concentrated to yield 1.44 g of crude product. GLC at 200 °C showed the presence of two components in an approximate ratio of 7:3. The major component crystallized from diethyl ether – hexane to yield 0.31 g of IV, m.p. 150 °C, $[\alpha]_D$ −144° (*c* 0.25, chloroform). (Found: C 51.7; H 6.91; N 4.82. $C_{13}H_{21}NO_7$ requires C 51.5; H 6.98; N 4.62.)

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1. Jeanloz, R. W. *The Amino Sugars IA*, Academic, New York and London 1969.
2. Perry, M. B. and Daoust, V. *Can. J. Chem. 51* (1973) 974.
3. Liav, A., Hildesheim, J., Zehavi, U. and Sharon, N. *Carbohyd. Res. 33* (1974) 217.
4. Serfontein, W. J., Jordaan, J. H. and White, J. *Tetrahedron Lett.* (1964) 1069.
5. Lemieux, R. U., Nagabhushan, T. L. and O'Neill, I. K. *Tetrahedron Lett.* (1964) 1909.
6. Lemieux, R. U., Nagabhushan, T. L. and O'Neill, I. K. *Can. J. Chem. 46* (1968) 413.
7. Lemieux, R. U., James, K., Nagabhushan, T. L. and Ito, Y. *Can. J. Chem. 51* (1973) 33.
8. Iselin, B. and Reichstein, T. *Helv. Chim. Acta 27* (1944) 1200.

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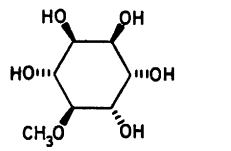
Synthesis of 3-Deuterio-2,3-diphospho-D-glyceric Acid

BERTIL ERBING, PER J. GAREGG and BENGT LINDBERG

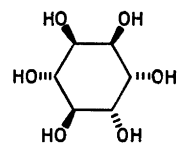
Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-104 05 Stockholm, Sweden

2,3-Diphospho-D-glyceric acid, labelled with deuterium at C-3, was required for NMR studies of its association with hemoglobin [1] and the present paper describes the synthesis of this substance. The key intermediate, 2,3:4,5-di-*O*-cyclohexylidene-D-*manno*-hexodialdose (III) was obtained in a manner similar to that described by Angyal and Hoskinson for the synthesis of 2,3:4,5-di-*O*-isopropylidene-L-*manno*-hexodialdose, an intermediate in the synthesis of L-mannitol from quebrachitol.[2]

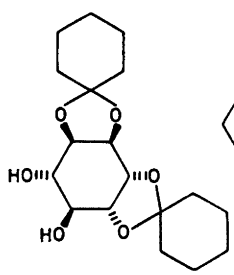
D-*chiro*-Inositol (I), obtained by demethylation of pinitol, was converted into the 1,2:5,6-dicyclohexylidene derivative (II) as described by Angyal and co-workers for the enantiomer.[3]



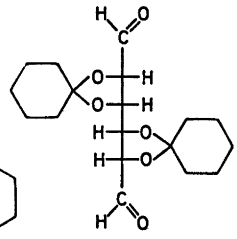
Pinitol



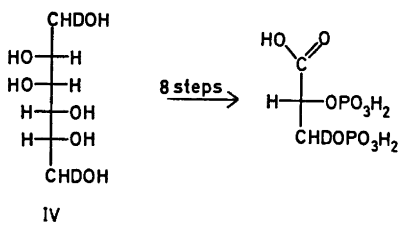
I



II



III



IV

Periodate oxidation afforded the hexodialdo derivative III which, without purification, was converted into 1,6-dideuterio-D-mannitol (IV). The deuterium labelling was confirmed by NMR and by GLC-MS of its hexaacetate. 1,6-Dideuterio-D-mannitol was converted into the title compound by established procedures previously described for unlabelled 2,3-diphospho-D-glyceric acid.[4-6] The various intermediates were characterized by NMR and, when appropriate, by GLC-MS.

Some stereoselectivity during the reduction of the hexodialdo derivative III with sodium borodeuteride, due to asymmetric induction, is not excluded and has been observed in related reactions.[7,8]

Experimental. Concentrations were performed under reduced pressure. Precoated plates with Silica Gel F_{254} (Merck) were used for TLC and Silica Gel 60 (> 230 mesh, Merck) for column chromatography. Light petroleum refers to a fraction with b.p. 60 – 71 °C. NMR spectra were recorded with a Varian A 60-A instrument and were invariably in agreement with the postulated structures. Mass spectra were recorded with a Perkin-Elmer 270 instrument and optical rotations with a Perkin-Elmer 141 polarimeter. GLC was performed with a Perkin Elmer model 900 instrument using a column packed with ECNSS-M (3 %) on Gas-Chrom Q.

1,2:5,6-Di-O-cyclohexylidene-D-chiro-inositol (II). D-*chiro*-Inositol (11 g), cyclohexanone (275 ml), benzene (165 ml), and *p*-toluenesulfonic acid (0.55 g) were heated under reflux using a Dean and Stark separator. When, after 5 h, codistillation of water ceased, aqueous 10 % potassium carbonate (200 ml) was added and the excess reagent was removed by steam distillation. The crystals which formed on cooling the residue were filtered off. TLC (ethyl acetate – light petroleum 3:1) indicated the presence of both di- and tri-cyclohexylidene-D-*chiro*-inositol. The product was taken up in benzene – ethanol 10:1 (60 ml) and treated with acetic acid saturated with hydrogen bromide (0.6 ml) for 45 min at room temperature. The crystals which had separated were filtered off and washed with light petroleum. Recrystallization from ethanol afforded II (10 g) m.p. 208 – 209 °C $[\alpha]_{578}$ +18° (*c* 0.4, chloroform) in agreement with the values reported for its enantiomer. (Found: C 63.7; H 8.3. $C_{18}H_{28}O_6$ requires: C 63.5; H 8.3.)

1,6-Dideuterio-D-mannitol. The dicyclohexylidene-D-*chiro*-inositol (4.1 g), in methanol (800 ml) was treated with sodium metaperiodate (4.1 g) in water (80 ml) for 4 h with stirring at room temperature in the dark. Ethylene glycol (0.3 g) was added and the stirring continued for another 15 min. Precipitated sodium iodate was removed by filtration and the filtrate diluted with water (400 ml) and then extracted with chloroform. The combined chloroform extracts were washed with water, dried over sodium sulfate and concentrated to a syrup (crude III). This was dissolved in dioxane – methanol 3:1 (100 ml) and treated with sodium borodeuteride (0.4 g). The solution was kept at room temperature for 18 h. Excess deuteride was decomposed by adding acetic acid and the solution was concentrated. Boric acid was removed by repeated codistillations with methanol and the product purified by chromatography on a silica gel column using ethyl acetate and light petroleum (3:2) as eluent. The chromatographically pure product was hydrolyzed with aqueous acetic acid (60 %) at 100 °C for 5 h, cooled and concentrated. The resulting syrup was taken up in water (150 ml) and washed with chloroform. The water solution was concentrated to yield crystalline IV (2.0 g) m.p. 165 – 166 °C.

3-Deuterio-2,3-diphospho-D-glyceric acid was obtained from IV as described by Baer and Fischer[4-6] for unlabelled D-mannitol and purified as its barium salt. (Found: C 5.95; H 1.44 (recalculated for D_2H_{10}); Ba 54.5; P 9.59. $(C_3H_3DO_{10}P_2)_2Ba_5.3H_2O$ requires C 5.70; D + H 1.12; Ba 54.3; P 9.80.)

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1. Eaton, J. W., Brewer, G. J., Schultz, J. and Sing, C. In Brewer, G. J., Ed., *Red Cell Metabolism and Function*, Plenum, New York 1970, p. 21.
2. Angyal, S. J. and Hoskinson, R. M. *Methods Carbohyd. Chem. 2* (1963) 87, and the papers quoted therein.
3. Angyal, S. J., Irving, G. C., Rutherford, D. and Tate, M. E. *J. Chem. Soc.* (1965) 6662.
4. Baer, E. *J. Amer. Chem. Soc. 67* (1945) 338.
5. Baer, E. *J. Biol. Chem. 185* (1950) 763.
6. Baer, E. and Fischer, H. O. I. *J. Biol. Chem. 180* (1949) 145.
7. Lemieux, R. U. and Howard, J. *Can. J. Chem. 41* (1963) 308.
8. Gagnaire, D., Horton, D. and Taravel, F. *Carbohyd. Res. 27* (1973) 363.

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