# Synthesis of Methyl 3,6 Dideoxy-$\alpha$-D-*ribo*-hexopyranoside

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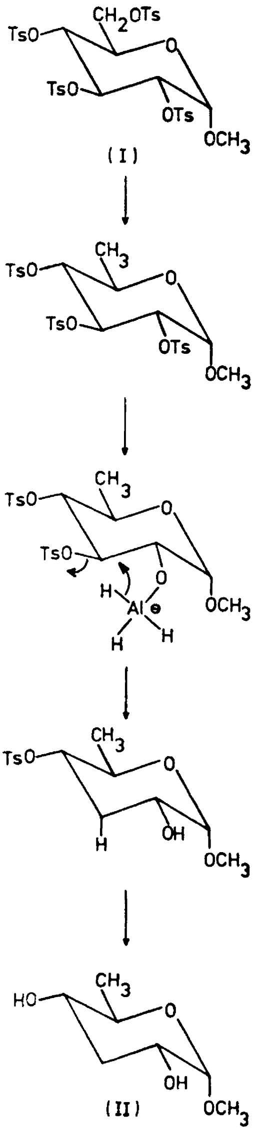
Paratose (3,6-dideoxy-D-*ribo*-hexose) is a constituent of the O-specific side chains of cell wall lipopolysaccharides from serogroup A *Salmonella* bacteria (*e.g. S. paratyphi* A).[1] The synthesis of methyl $\alpha,\beta$-paratopyranoside and paratose *via* 3-deoxy-D-glucose (3-deoxy-D-*ribo*-hexose) has been reported by Fouquey *et al.*[2] However, the preparation of 3-deoxy-D-glucose and its conversion into paratose is laborious and the overall yield is low.

The present communication reports a two step synthesis of methyl $\alpha$-paratopyranoside starting from methyl $\alpha$-D-glucopyranoside.

Methyl $\alpha$-D-glucopyranoside was converted into methyl 2,3,4,6-tetra-*O*-*p*-toluenesulphonyl-$\alpha$-D-glucoside (I) in nearly quantitative yield. This substance, on treatment with excess lithium aluminium hydride (LAH), yielded two components which were identified as methyl $\alpha$-paratopyranoside (II) and a methyl 4,6-dideoxyhexoside, respectively. If the reaction mixture was neutralized with aqueous phosphoric acid, the methyl 4,6-dideoxyhexopyranoside was destroyed, probably due to hydrolysis, and methyl $\alpha$-paratopyranoside could be isolated in a pure state by chromatography on silicic acid in a yield of 16 %. A possible mechanism for the transformation of (I) into (II) by reduction with LAH is depicted in Scheme 1.

The primary 6-*O*-tosyl group is first reduced to a deoxy function by LAH. The 2-*O*-tosyl group of this intermediate is then cleaved, and the LAH adduct formed can serve as a hydride donor for replacement of the 3-*O*-tosyl group.[3] Finally the 4-*O*-tosyl function is cleaved in the expected manner. When the reduction was performed with lithium aluminium deuteride (LAD), the resulting methyl $\alpha$-D-paratopyranoside contained one deuterium atom at C-6 and one axial deuterium atom at C-3 in agreement with the above mechanism.



*Scheme 1.*

The structures of the synthesized methyl $\alpha$-paratopyranoside and the deuterium labelled analogue were established by NMR and MS of the corresponding diacetates and were further corroborated by hydrolysis and identification of paratose and paratose labelled with deuterium atoms at C-3 and C-6, as their alditol acetates by GLC[4]–MS.[5] The NMR spectra of the diacetates of (I) and its deuterated analogue could be fully interpreted with the aid of spin decoupling and a shift reagent. The position of the deuterium atom at C-6 in the deuterated compound was established through the change of a three-proton doublet at $\tau$ 8.84 into a two-proton group of protons centered at $\tau$ 8.84. Further, the splitting pattern of H-5 was simplified. An axial deuterium atom at C-3 was adduced from the disappearance of H-3a at $\tau$ 8.10 and the changes in splitting patterns of H-3e, H-2, and H-4. The MS of the diacetates of I and its deuterated analogue (Fig. 1) exhibited, as expected, few degradation pathways.

Structural elucidation of the methyl 4,6-dideoxy-hexopyranoside and the mechanism of its formation are under investigation.

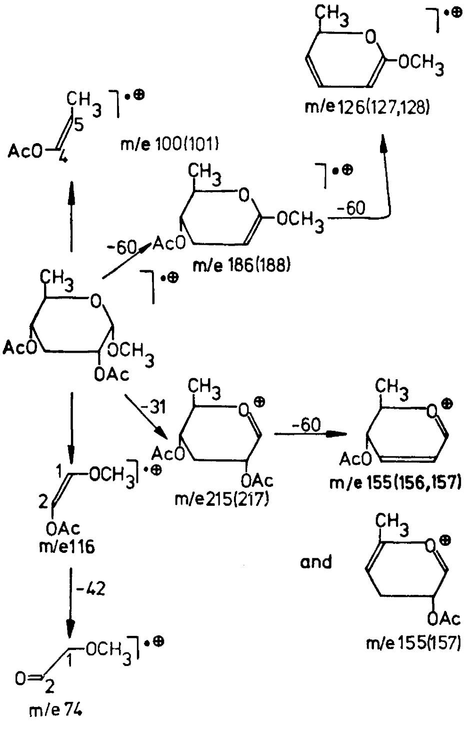


*Fig. 1.* Fragmentation routes for methyl 2,4-di-*O*-acetyl-α-paratoside. Values for the dideuterated analogue are given in brackets.

*Experimental.* Concentrations were performed at reduced pressure, at bath temperatures not exceeding 40°C. Melting points are corrected. Analytical TLC was performed on plates (20 × 20 cm) with a layer (0.25 mm) of Silica Gel $F_{254}$ (Merck). Ethyl acetate was used as solvent. Compounds were detected by spraying with 8 % aqueous sulphuric acid and subsequent heating at 140°C. Silica Gel 60 (<0.063 mm) was used for column chromatography. GLC was carried out on OV 225 SCOT- and OS 138 SCOT-columns (15 m × 0.5 mm) at 170 and 190°C, respectively. A Perkin-Elmer 900 Gas Chromatograph was used. For GLC-MS a Perkin-Elmer 270 instrument and the above columns were used. Mass spectra were recorded at a manifold temperature of 200°C, an ionization potential of 70 eV, ionization current of 80 μA and an ion source temperature of 80°C. Optical rotations were determined with a Perkin-Elmer 141 polarimeter and 1 dm microtubes. NMR spectra were recorded on a Varian XL100 (100 MHz) or a Varian A60A (60 MHz) instrument in chloroform-*d*, using TMS as internal standard.

*Methyl 2,3,4,6-tetra-*O*-*p*-toluenesulphonyl-α-*D*-glucoside (I).* This compound was prepared essentially as previously described[6] with the exceptions that the tosyl chloride was added at −10°C and that the reaction conditions were changed to 8 days at +4°C. These modifications minimized chlorine containing by-products.

*Methyl 3,6-dideoxy-α-*D*-*ribo*-hexopyranoside (II).* I (5.0 g) was mixed with Celite (10.0 g) and placed in the thimble of a Soxhlet apparatus. LAH (10.0 g) in dry ethyl ether (500 ml) was added to the reaction vessel and the mixture was refluxed for 15 h. The excess of LAH was destroyed by the addition of ethyl acetate at 0°C with vigorous stirring. The resulting slurry was neutralized with 1.0 M aqueous phosphoric acid, filtered and concentrated to a syrup. The crude product was fractionated on a silicic acid column (60 × 4 cm), using ethyl acetate as irrigant. The separation was monitored by polarimetry and TLC. The compound with *RF* 0.33 (ethyl acetate) was isolated as a syrup (0.16 g, 16 %), $[\alpha]_{578}^{23} + 170°$ (*c* 1.0, chloroform). NMR (60 MHz) showed, *inter alia:* $\tau$ 5.39, 1 proton, doublet, H-1, $J_{1,2}$ 3.5 Hz; $\tau$ 7.61–8.50, 2 protons, multiplet, H-3a and H-3e; $\tau$ 8.76, 3 protons, doublet, C–$CH_3$, $J_{5,6}$ 6.0 Hz. Part of the syrup (100 mg) was converted into the 2,4-di-*O*-3,5-dinitrobenzoyl derivative[7] which was recrystallized from ethanol (300 mg, 88 %). This compound melted at 147 – 148°C and on further heating new crystals were formed which melted at 184 – 186°C, $[\alpha]_{578}{}^{23} + 69°$ (*c* 1.7, chloroform). (Found: C 45.66; H 3.40; N 10.39. Calc. for $C_{21}H_{18}O_{14}N_4$: C 45.83; H 3.30; N 10.18.)

Another part of the syrup (4 mg) was hydrolysed with 0.25 M aqueous sulphuric acid (2 ml) at 100° for 1 h, neutralized and converted into the alditol acetate. This alditol acetate had the same retention time as an authentic sample of paratitol acetate on both the OV 225 and OS 138 columns. The MS was indistinguishable from that given by the authentic sample.

A sample of II (10 mg) was acetylated with acetic anhydride/pyridine. The diacetate was isolated in the usual manner as a chromatographically pure syrup. The MS of this compound had peaks, *inter alia*, at *m/e* (peak intensities relative to the base peak in brackets): 43(100), 44(4), 45(5), 71(12), 74(18), 83(8), 84(9), 100(25), 103(7), 113(5), 116(11), 143(1.5), 155(1.1), 186(1.1) and 215(3.3). The NMR spectrum (100 MHz) (first order analysis) gave the following results: τ 5.15, 1 proton, octet, H-2, $J_{1,2}$ 3.5 Hz, $J_{2,3e}$ 5 Hz, $J_{2,3a}$ 12 Hz; τ 5.25, 1 proton, doublet, H-1, $J_{1,2}$ 3.5 Hz; τ 5.43, 1 proton, octet, H-4, $J_{4,5}$ 10 Hz, $J_{4,3e}$ 5 Hz, $J_{4,3a}$ 11 Hz; τ 6.23, 1 proton, octet, H-5, $J_{4,5}$ 10 Hz, $J_{5,6}$ 6 Hz; τ 6.58, 3 protons, singlet, $OCH_3$; τ 7.78, 1 proton, sextet, H-3e, $J_{3e,3a}$ 11 Hz, $J_{3e,2}$ 5 Hz, $J_{3e,4}$ 5 Hz; τ 7.93, 3 protons, singlet, *O*-acetyl; τ 7.96, 3 protons, singlet, *O*-acetyl; τ 8.10, 1 proton, sextet, H-3a, $J_{3a,3e}$ 11 Hz, $J_{3a,2}$ 12 Hz, $J_{3a,4}$ 11 Hz; τ 8.84, 3 protons, doublet, $C-CH_3$, $J_{5,6}$ 6 Hz. The above analysis was made on the basis of decoupling experiments and by using $Eu(fod)_3$ as shift reagent to separate overlapping protons.

In another preparation of II the reduction was performed with LAD. The MS of the acetylated, deuterium labelled II had peaks at, *inter alia*, *m/e* (peak intensities relative to the base peaks in brackets): 43(100), 44(12), 45(8), 73(13), 75(22), 85(6), 86(5), 101(3), 102(24), 104(8), 117(11), 145(9), 157(0.9), 188(0.8), 217(2.3).

The NMR spectrum (100 MHz) was similar to that obtained for the non-deuterated diacetate with the following exceptions: The 1 proton sextet at τ 7.78 (H-3e) appeared as a triplet ($J_{3e,2}$ 5 Hz, $J_{3e,4}$ 5 Hz); the 1 proton sextet at τ 8.10 had disappeared; the 3 proton doublet at τ 8.84 was changed into a 2 proton doublet; further, the multiplets of H-2, H-4 and H-5 were altered.

When the reduction mixture was processed without neutralization, the combined yield of dideoxyglycosides was increased to 50 %. GLC – MS of the acetylated reaction product and of the derived alditol acetates established a ratio between II and a methyl 4,6-dideoxyhexoside of 3:2, reprectively.

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# Studies on Orchidaceae Alkaloids

## XXXVII.* Dendrowardine, a Quaternary Alkaloid from *Dendrobium wardianum* Wr.

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The occurrence in various *Dendrobium*, species of fourteen alkaloids of the

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* For number XXXVI of this series, see Ref. 1.