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Note

A convenient synthesis of 2,3,4-tri-*O*-methyl-D-allopyranose

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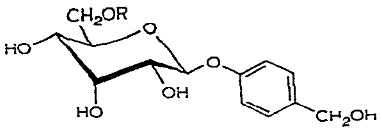
The leaves of *Protea rubropilosa* Beard contain[1] D-allopyranose linked glycosidically in the form of the 6-cinnamate **1** (R = COCH=CHPh, rubropilosin) and the 6-benzoate **1** (R = Bz, pilorubrosin). The position of the ester substituents in these naturally occurring glycosides was located by methylation, followed by de-esterification and hydrolysis with acid to give 2,3,4-tri-*O*-methyl-D-allopyranose[1]. Since no reference compound was available for identifying the methylated sugar, it was characterized by oxidation with periodate both before and after reduction with sodium borohydride. Direct comparison with an authentic sample of 2,3,4-tri-*O*-methyl-D-allopyranose would undoubtedly aid in future studies of naturally occurring D-allose derivatives related to rubropilosin and pilorubrosin.



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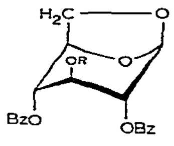
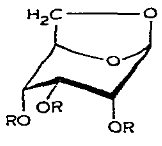
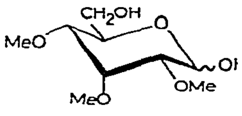


2 R = H
3 R = Ms



4 R = Bz
5 R = H
6 R = Ac
7 R = Me



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Although syntheses of 2,3,4-tri-*O*-methyl-D-allopyranose (**8**) can be devised from derivatives of D-allose obtained by recent oxidative procedures[2], we were attracted by the simplicity of an approach involving methylation of 1,6-anhydro-β-D-allopyranose (**5**). However, this approach rests on designing a convenient synthesis of 1,6-anhydro-β-D-allopyranose (**5**), which has been prepared hitherto by heating D-allose in dilute, acid solution; under these conditions, the anhydro sugar is present[3] to the extent of ~14%. The following procedure yields this anhydro sugar in five steps from the readily accessible 1,6-anhydro-β-D-glucopyranose[4].

Dimolar benzoylation of 1,6-anhydro-β-D-glucopyranose is known[5] to furnish the 2,4-diester **2**, presumably for steric reasons. Methanesulphonylation of the diester **2** gave the 3-sulphonate **3** having both benzoyloxy groups ideally situated for rearside attack on the methanesulphonyloxy group. Solvolysis of the methanesulphonate **3** was readily effected by heating in moist *N*,*N*-dimethylformamide to give, after benzoylation, 1,6-anhydro-2,3,4-tri-*O*-benzoyl-β-D-allopyranose (**4**). That inversion of configuration at C-3 had occurred, presumably with participation of one or other of the benzoyloxy groups, was established when debenzoylation of the tribenzoate **4** yielded 1,6-anhydro-β-D-allopyranose[3] (**5**), which was further characterized as the crystalline triacetate[3] **6**. The physical constants of both compounds **5** and **6** were in very good agreement with those previously recorded. Methylation of the anhydro sugar **5** afforded 1,6-anhydro-2,3,4-tri-*O*-methyl-β-D-allopyranose (**7**), which was hydrolysed with acid to give 2,3,4-tri-*O*-methyl-D-allopyranose (**8**). This material was indistinguishable (m.p., $[\alpha]_D$, and i.r. spectrum) from that[1] derived from natural sources.

EXPERIMENTAL

Kieselgel G (Merck) was used for t.l.c., and spots were detected with vanillin–sulphuric acid[6]. I.r. spectra were recorded for Nujol mulls, using a Perkin–Elmer Infracord spectrometer, and n.m.r. spectra were routinely measured for solutions in deuteriochloroform (1% tetramethylsilane as an internal standard) with a Perkin–Elmer R-10 spectrometer; the spectra were entirely compatible with the structures assigned. Optical rotations were measured at ambient temperature with a Perkin–Elmer 141 automatic polarimeter. Light petroleum refers to the fraction having b.p. 60–80°.

1,6-Anhydro-2,4-di-O-benzoyl-β-D-glucopyranose (**2**). — A solution of 1,6-anhydro-β-D-glucopyranose (10 g, m.p. 181–182°, prepared by pyrolysis of starch *in vacuo*[4]) in pyridine (50 ml) was treated with benzoyl chloride (17.5 g, ~2 mol.) at room temperature for 30 min, and water (200 ml) was then added. After decantation of most of the solvent, the syrupy residue was dispersed in methanol (100 ml), and the fine precipitate that formed was filtered off and recrystallized from dichloromethane–methanol to give 1,6-anhydro-2,3,4-tri-*O*-benzoyl-β-D-glucopyranose (7 g, 24%), m.p. 204–205°, $[\alpha]_D$ −36° (*c* 1, chloroform); lit.[5] m.p. 202–203°, $[\alpha]_D$ −36° (*c* 1.1, chloroform). The original mother liquors were treated with water until turbid and then stored at ~0° overnight. The material that precipitated was filtered off and dissolved in hot methanol, and any insoluble tribenzoate was filtered off. On cooling (0°), the filtrate deposited the dibenzoate **2** (6.7 g, 29%), m.p. 128–129°, $[\alpha]_D$ −34° (*c* 1, chloroform); lit.[5] m.p. 136–138°, $[\alpha]_D$ −34° (*c* 0.8, chloroform). After removal of the dibenzoate, the mother liquors were concentrated and combined with the crystalline tribenzoate, and the mixture was then heated under reflux with 0.1M sodium methoxide in methanol (100 ml) until debenzoylation was complete (~2 h). After deionization of the solution with Amberlite IR-120(H^+) resin (~25 ml) and concentration, the residue was recrystallized from ethanol to give the starting material (5.6 g); this could be recycled.

1,6-Anhydro-2,4-di-O-benzoyl-3-O-methanesulphonyl-β-D-glucopyranose (**3**). — A solution of the dibenzoate **2** (14.3 g) in pyridine (40 ml) was treated with methanesulphonyl chloride (6 g), and the mixture was set aside for 2.5 h at room temperature. Work-up in the usual manner furnished the methanesulphonate **3** (15.8 g, 92%), m.p. 167–168° (from dichloromethane–light petroleum), $[\alpha]_D$ −24° (*c* 1, chloroform) (Found: C, 56.3; H, 4.5; S, 7.2. $C_{21}H_{20}O_9S$ calc.: C, 56.2; H, 4.4; S, 7.1%).

1,6-Anhydro-2,3,4-tri-O-benzoyl-β-D-allopyranose (**4**). — A solution of the methanesulphonate **3** (15.6 g) in *N,N*-dimethylformamide (350 ml) and water (70 ml) containing a suspension of calcium carbonate (7 g) was heated for 3 days at 150°, whereafter the solvents were removed with repeated additions of toluene. The residue was extracted with acetone, and the extract was filtered and concentrated; t.l.c. (dichloromethane) revealed the presence of at least three components. The mixture of products was taken up in pyridine (30 ml) and treated with benzoyl chloride (7.5 g). After 2 h at room temperature, methanol (50 ml) was added, followed by water to incipient turbidity. The material that deposited was filtered off and recrystallized from ether–light petroleum to give the tribenzoate **4** (11.5 g, 70%), m.p. 140–141°, $[\alpha]_D$ −37.5° (*c* 1, chloroform) (Found: C, 68.3; H, 4.6. $C_{27}H_{22}O_8$ calc.: C, 68.3; H, 4.6%).

1,6-Anhydro-β-D-allopyranose (**5**). — A solution of the tribenzoate **4** (5 g) in 0.1M sodium methoxide in methanol (100 ml) was heated under reflux for 2 h to effect complete debenzoylation. The resulting solution was deionized [Amberlite IR-120(H^+) resin] and concentrated to afford **5** (1.2 g, 72%), m.p. 182–183° (from ethanol), $[\alpha]_D$ −76° (*c* 1, water); lit.[3] m.p. 178.5–180°, $[\alpha]_D$ −76° (*c* 0.6, water). A mixture of **5** and 1,6-anhydro-β-D-glucopyranose had m.p. 82–85°.

Acetylation of **5** in the usual way afforded 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-allopyranose (**6**), m.p. 86–87° (from ether–light petroleum), $[\alpha]_D$ −73° (*c* 1, chloroform); lit.[3] m.p. 88–89°, $[\alpha]_D$ −71° (*c* 1, chloroform).

1,6-Anhydro-2,3,4-tri-O-methyl-β-D-allopyranose (**7**). — A stirred solution of the anhydro sugar **5** (0.81 g) in *N,N*-dimethylformamide (10 ml) containing methyl iodide (3.1 ml, ~10 mol.) and sodium hydride (1.15 g) was stirred for 5 h at room temperature, whereafter sufficient water was carefully added to decompose the excess of reagent. The solvents were removed, the residue was dissolved in water (100 ml), and the aqueous solution was extracted with dichloromethane (5 × 50 ml). The combined and dried ($MgSO_4$) extracts were concentrated and the residue was taken up in ether. The filtered and decolourized (charcoal) solution was concentrated, with repeated additions of toluene, to give the methylated derivative **7** (0.76 g, 75%), m.p. 81–82° (from ether–light petroleum), $[\alpha]_D$ −82.5° (*c* 1, chloroform) (Found: C, 52.9; H, 7.6. $C_9H_{16}O_5$ calc.: C, 52.9; H, 7.8%).

2,3,4-Tri-O-methyl-D-allopyranose (**8**). — The methylated derivative **7** (0.41 g) was heated with M sulphuric acid (10 ml) on a boiling water-bath for 6 h, and the cooled solution was then neutralized with conc. ammonia (2 ml). The solvent was removed and toluene was distilled from the residue several times before it was extracted with dichloromethane. The dried ($MgSO_4$) and filtered extract was concentrated to yield a syrup that crystallized on standing. Recrystallization from benzene gave the free sugar **8** (0.27 g, 60%), m.p. 109–110°, $[\alpha]_D$ +5.5 (initial)→ +21.5° (24 h, final; *c* 1, water), $[\alpha]_D$ +26.5° (final; *c* 0.5, methanol) (Found: C, 48.5; H, 8.2. $C_9H_{18}O_6$ calc.: C, 48.6; H, 8.2%); lit.[1] m.p. 106.5–108°, $[\alpha]_D$ +25° (*c* 0.4, methanol). The i.r. spectrum (KBr disc) of the synthetic material was indistinguishable from that of 2,3,4-tri-*O*-methyl-D-allopyranose obtained[1] from natural sources, and no depression of m.p. was observed when the two materials were mixed.

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