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Note

Synthesis of L-arabinose 5-phosphate, 5-*O*-carbamoyl-D-arabinose and 6-*O*-carbamoyl-D-glucose*

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L-Arabinose 5-phosphate and 5-*O*-carbamoyl-D-arabinose were required as intermediates for the enzymic synthesis of labeled L-*gluco*-heptulose and the chemical synthesis of 2-amino-6-*O*-carbamoyl-2-deoxy-D-glucose, respectively. These latter compounds were needed for studies on the biosynthesis of the mitomycin antibiotics[1]. The synthesis of D-arabinose 5-phosphate has been reported[2–4], but the product of the earlier syntheses[2,3] has not been fully characterized. The synthesis reported by Stverteczky *et al.*[4] would not be convenient for the preparation of the L-enantiomer as L-glucose would be required as starting material.

Our synthesis of L-arabinose 5-phosphate started with L-arabinose and utilized 1,2,3-tri-*O*-acetyl-5-*O*-trityl-L-arabinofuranose (**1**) as an intermediate. The preparation of 5-*O*-carbamoyl-D-arabinose has not previously been reported and this compound was synthesized from D-arabinose by way of 1,2,3-tri-*O*-acetyl-5-*O*-trityl-D-arabinofuranose[5] (**2**). The route employed in these preparations appears to be a general one for certain terminally substituted aldoses. In order to explore this possibility, we have examined the synthesis of 6-*O*-carbamoyl-D-glucose from D-glucose by way of 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose[6] (**3**). Compounds **1**, **2**, and **3** were prepared from the corresponding acyclic dipropyl dithioacetals[7,8]. The terminal hydroxyl group was protected by tritylation and the thioacetal group was removed by using mercuric chloride in the presence of mercuric oxide[5]. The resulting terminally *O*-tritylated aldoses were then peracetylated with acetic anhydride in pyridine. The trityl groups of **1**, **2**, and **3** were conveniently removed by refluxing in 80% aqueous acetic acid[9], rather than by using other methods of detritylation[5,6], to afford the aldose acetates **4**, **5**, and **6**. Compound **4** was treated with diphenyl phosphochloridate[10] to give 1,2,3-tri-*O*-acetyl-5-*O*-(diphenylphosphono)-L-arabinofuranose (**7**), whereas **5** and **6** were treated with phenyl chloroformate[11] to give 1,2,3-tri-*O*-acetyl-5-*O*-phenoxycarbonyl-D-arabinofuranose (**8**) and 1,2,3,4-tetra-*O*-acetyl-6-*O*-phenoxycarbonyl-β-D-glucopyranose (**9**), respectively. Compound **7** was subjected to hydrogenolysis with palladium chloride in ethanol and, following cleavage of the acetate

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groups with sodium methoxide, L-arabinose 5-phosphate was obtained and characterized as the dilithium salt[4] **10**. Compounds **8** and **9** were treated with methanolic ammonia to yield 5-*O*-carbamoyl-D-arabinose (**11**) and 6-*O*-carbamoyl-D-glucose (**12**), respectively. The dilithium salt of L-arabinose 5-phosphate reduced 2.4 molar equivalents of periodate[12] whereas 5-*O*-carbamoyl-D-arabinose consumed 2.2 and 6-*O*-carbamoyl-D-glucose consumed 3.3 molar equivalents of the oxidant. The formation of formaldehyde[12] could not be detected in any one of these periodate oxidations.

The overall yield of L-arabinose 5-phosphate was 7%, based on L-arabinose, a yield presumably comparable to that obtained in the preparation of D-arabinose 5-phosphate[4] from D-glucose. The overall yield of 5-*O*-carbamoyl-D-arabinose based on D-arabinose was 20% and that for 6-*O*-carbamoyl-D-glucose was 37%.

EXPERIMENTAL

General methods. — Thin layer chromatography (t.l.c.) was used for monitoring reactions and for estimating the purity of products. Irrigants used were: A, 6:4:1 2-propanol–ethyl acetate–water and B, 4:1 benzene–methanol (v/v). Compounds were located by spraying the plates with 5% sulfuric acid in ethanol and then charring on a hot plate. Melting points were determined with a Thomas–Hoover apparatus and are not corrected. Optical rotations were determined with a Perkin–Elmer 141 recording polarimeter. Solutions were concentrated on a rotary evaporator at less than 40° under diminished pressure.

Terminally O-tritylated aldose acetates (**1**, **2**, *and* **3**). — Compounds **1** and **2** were prepared from L- and D-arabinose, respectively, in 32.4% overall yield; **1** had $[\alpha]_D^{20}$ −29° (*c* 1.0, chloroform), and **2** had $[\alpha]_D^{20}$ +30° (*c* 1.0, chloroform) [lit.[5] $[\alpha]_D^{16}$ +28.5° (*c* 2.0, chloroform)]. Compound **3** was prepared from D-glucose in 66% overall yield; m.p. 162°, $[\alpha]_D^{20}$ +49° (*c* 3.0, pyridine) [lit.[6] m.p. 166°, $[\alpha]_D^{18}$ +45° (*c* 9.0, pyridine)].

Aldose acetates (**4**, **5**, *and* **6**). — A mixture of **1**, **2**, or **3** (10 g) and 100 ml of 80% aqueous acetic acid was heated, with stirring for 30 min on a steam bath, although solution was complete within 5 min. Water (100 ml) was added to the cooled solution and triphenylmethanol was removed by filtration. The filtrate was saturated with sodium chloride and extracted with chloroform (4 × 40 ml), washed with aqueous sodium hydrogen carbonate and water, and dried (sodium sulfate). Concentration of the filtrate gave **4**, **5**, and **6**; the first two compounds were obtained in 63% yield as gums[5], whereas **6** was obtained as crystals in 72% yield; m.p. 124–127°, $[\alpha]_D^{20}$ +13° (*c* 3.0, chloroform), [lit.[6] m.p. 128–129°, $[\alpha]_D^{25}$ +12° (*c* 6.0, chloroform)].

L-*Arabinose 5-(dilithium phosphate)* (**10**). — To a cooled solution of **4** (10 g) in pyridine (20 ml) was added diphenyl phosphochloridate (7 ml). The reaction mixture was stirred overnight at room temperature. Water was added to decompose the excess of phosphorylating reagent and the solution was extracted with chloroform (4 × 50 ml). The extract was then washed with water, ice-cold 5% aqueous acetic acid, aqueous sodium hydrogen carbonate and water, and dried (sodium sulfate) to give, on concentration, 13.8 g (75%) of **7**. One gram of **7** was dissolved in ethanol (50 ml) and

reduced by hydrogen at room temperature and atmospheric pressure with palladium chloride (0.2 g). When the reduction was complete (3–4 h), the mixture was filtered. The filtrate was rendered akaline by addition of 0.1M sodium methoxide, and then kept for 4 h at room temperature. The solvent was removed and the syrup obtained was dissolved in water (10 ml) and extracted with ether (3 × 10 ml). The aqueous phase was then passed through a column (1.8 × 20 cm) of Amberlite IR-120 (H^+). The resulting solution was neutralized (pH 7.1) with M lithium hydroxide and concentrated to low volume (5 ml). The lithium salt was precipitated by ethanol; yield 0.2 g (42.6%), $[\alpha]_D^{20}$ −12.8° (*c* 2.3, 0.1M hydrochloric acid), [lit.[4] for the D-enantiomer $[\alpha]_D^{22}$ +10°, +13° (*c* 2.0, 0.1M hydrochloric acid]. The product was homogeneous on t.l.c. (R_F 0.12, $R_{D\text{-arabinose}}$ 0.50, irrigant A, run twice).

Anal. Calc. for $C_5H_9Li_2O_8P \cdot H_2O$: C, 23.08; H, 4.23; P, 11.92. Found: C, 23.24; H, 4.45; P, 11.50.

*1,2,3-Tri-*O*-acetyl-5-*O*-phenoxycarbonyl-*D*-arabinofuranose* (**8**). — To a stirred solution of **5** (0.3 g) in pyridine (3 ml) was added phenyl chloroformate (0.3 ml) and the solution was kept overnight at room temperature. The reaction mixture showed one spot on t.l.c. with irrigant B. Water was added and the solution was extracted with chloroform (4 × 20 ml). The extract was washed with ice-cold, dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and dried (sodium sulfate). Concentration of the filtrate gave the title compound (**8**) as a pale-yellow, viscous syrup (yield 0.4 g (95.2%), ν_{max}^{neat} 1740 (–O(C=O)–] and 1780 cm^{-1} (–O(C=O)O–].

Anal. Calc. for $C_{18}H_{20}O_{10}$: C, 54.54; H, 5.05. Found: C, 54.62; H, 4.92.

*5-*O*-Carbamoyl-*D*-arabinose* (**11**). — To a solution of **8** (0.4 g) in methanol (5 ml) was added 50% methanolic ammonia (10 ml) and the solution was kept at room temperature. After 10 h, the solution was evaporated, the residue was dissolved in water (10 ml) and the solution was extracted with ether (4 × 10 ml). The aqueous layer was then concentrated and the last traces of water were removed by azeotropic distillation with abs. ethanol, to give **11** as a chromatographically homogeneous (R_F 0.47, $R_{D\text{-arabinose}}$ 0.25, irrigant A) pale-yellow, viscous syrup; yield 0.18 g (92.6%), $[\alpha]_D^{20}$ 0° (*c* 4.2, ethanol).

Anal. Calc. for $C_6H_{11}NO_6$: C, 37.35; H, 5.70; N, 7.25. Found: C, 37.52; H, 5.51; N, 7.42.

*1,2,3,4-Tetra-*O*-acetyl-6-*O*-phenoxycarbonyl-*D*-glucopyranose* (**9**). — To a solution of **6** (1 g) in dry pyridine (10 ml) was added phenyl chloroformate (0.8 ml) and the reaction mixture was stirred overnight at room temperature. T.l.c. analysis (irrigant B) showed one spot. Water was added and the reaction mixture was processed as described for the preparation of **8**. On concentration, the residue was crystallized from ethanol; yield 1.2 g (91.6%), m.p. 137–138°, $[\alpha]_D^{20}$ 0° (*c* 4.0, chloroform); ν_{max}^{KBr} 1740 (–O(C=O)–] and 1780 cm^{-1} (–O(C=O)O–].

Anal. Calc. for $C_{21}H_{24}O_{12}$: C, 53.84; H, 5.13. Found: C, 53.64; H, 5.28.

*6-*O*-Carbamoyl-*D*-glucose* (**12**). — A solution of **9** (0.94 g) in methanol (10 ml) was treated with 50% methanolic ammonia (40 ml) for 15 h at room temperature. The solvent was then evaporated off and the residue was processed as described for

11. The residue was recrystallized from ethanol to afford **12** as a chromatographically homogeneous material (R_F 0.38, $R_{D\text{-glucose}}$ 0.23, irrigant A); yield 0.36 g (85.7%), m.p. 165–167° (dec.), $[\alpha]_D^{20}$ −49.6° (*c* 1.3, water).

Anal. Calc. for $C_7H_{13}NO_7$: C, 37.67; H, 5.83; N, 6.28. Found: C, 37.86; H, 5.99; N, 6.56.

REFERENCES

1 U. Hornemann, J. P. Kehrer, C. S. Nunez, and R. L. Ranieri, *Develop. Ind. Microbiol.*, 15 (1974) 82.
2 P. A. Levene and C. C. Christman, *J. Biol. Chem.*, 123 (1938) 607.
3 W. A. Volk, *Biochim. Biophys. Acta*, 37 (1960) 365.
4 J. Stverteczky, P. Szabó, and L. Szabó, *J. Chem. Soc., Perkin Trans.*, 1 (1973) 872.
5 N. W. Bristow and B. Lythgoe, *J. Chem. Soc.*, (1949) 2306.
6 B. Helferich and W. Klein, *Ann.*, 450 (1926) 219; A. E. Talley, *Methods Carbohyd. Chem.*, 2 (1963) 337.
7 H. Zinner, H. Brander, and G. Rembarz, *Chem. Ber.*, 89 (1956) 800.
8 W. Schneider, J. Sepp, and O. Stiehler, *Ber.*, 51 (1918) 220.
9 R. E. Schaub and M. J. Weiss, *J. Amer. Chem. Soc.*, 80 (1958) 4683.
10 C. E. Ballou and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 77 (1955) 3329.
11 H. Kuzuhara and S. Emoto, *Tetrahedron Lett.*, (1973) 5051.
12 G. Dryhurst, *Periodate Oxidation of Diol and Other Functional Groups*, Pergamon Press, 1970, pp. 121, 140.