Carbohydrate Research, 69 (1979) 308–310

Note

Selective tritylation: a general, one-step, method for synthesis of 5-*O*-trityl-D-pentofuranoses

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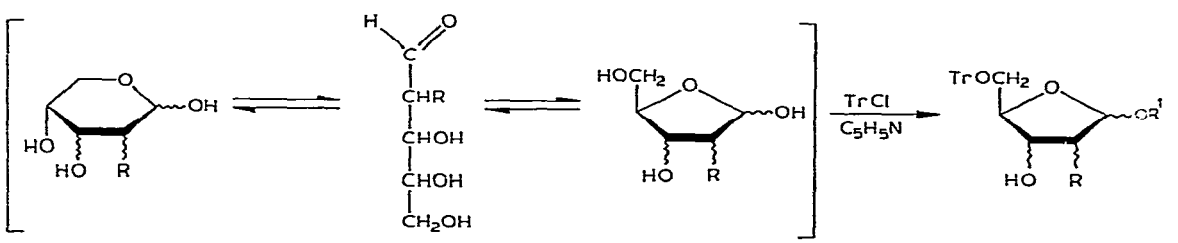
(Received January 26th, 1978; accepted for publication in revised form, March 27th, 1978)

In order to obtain large quantities of pentofuranoses having both an acid-labile blocking-group at O-5 and a free hydroxyl group at C-1, we have investigated the general synthesis of 5-*O*-tritylaldopentofuranoses. Two methods have been reported for their synthesis. The method of Bredereck *et al.*[1] involves treatment of D-ribose with chlorotriphenylmethane in pyridine (scheme 1a). The reported yields, however, are only ~30%, and subsequent work by Zeile *et al.*[2] has indicated that the method is not generally applicable to other pentoses, because of the formation of 1,5-di-*O*-trityl derivatives (scheme 1b). The second, and more-general method, is *via* 5-*O*-tritylation of aldopentose dithioacetals[3,4], and subsequent cyclization to the 5-*O*-tritylpentofuranose by treatment with mercuric oxide and mercuric chloride[5–8]. This multistep procedure is tedious and low-yielding, and the product is contaminated by mercuric ions[9,10], a factor significant in nucleoside synthesis, as Šorm *et al.*[10,11] have shown that concentrations of mercuric ions as low as 10^{-8}M in nucleoside samples may modify the results of biological tests.

To circumvent these problems, we have reexamined the direct tritylation of pentoses in pyridine. As an excess of chlorotriphenylmethane leads to ditrityl derivatives[2], we investigated the temperature-dependence of the reaction of equimolar



Tr = Trityl

a, R^1 = H R = H, OH
b, R^1 = Tr R = OH

Scheme 1

concentrations of chlorotriphenylmethane and D-arabinose in pyridine. At 20–23°, the yield of 5-*O*-trityl-D-arabinofuranose (**2**) is 60%; the yield of **2** at 37° is only 25%, and at 55° it is <10%. The observed temperature-dependence of monotritylation may therefore explain the previous report[2] that arabinose and xylose yield mainly the ditrityl derivatives, as both elevated temperature and an excess of chlorotriphenylmethane were used.

These results show that 5-*O*-tritylpentofuranoses can be synthesized directly by using stoichiometric amounts of pentose and chlorotriphenylmethane at a temperature <25°. The resulting 5-*O*-tritylated pentoses may be readily purified from the crude mixture, either by crystallization or by dry-column chromatography. These conditions afforded reasonable yields of 5-*O*-trityl-D-ribofuranose (**1**, 62%), 5-*O*-trityl-D-arabinofuranose (**2**, 60%), 5-*O*-trityl-D-xylofuranose (**3**, 57%), and 5-*O*-trityl-D-lyxofuranose (**4**, 32%; for lyxose, there is considerable formation of the ditrityl ether, even at room temperature). In addition, we have isolated, and describe for the first time, 2-deoxy-5-*O*-trityl-D-*erythro*-pentofuranose (**5**, 60%). The physical properties of the first four products are in agreement with literature values[1,6–8], and tritylation at O-5 is confirmed by ^{1}H-n.m.r. spectroscopy. The ready availability of these derivatives should extend their usefulness in carbohydrate and nucleoside chemistry.

EXPERIMENTAL

General methods. — Melting points were determined on a Thomas–Hoover apparatus and are uncorrected. Specific rotations were determined with a Perkin–Elmer 141 polarimeter. The n.m.r. spectra were recorded at 100 MHz on a Varian XL-100 n.m.r. spectrometer equipped with a Nicolet Technologies Fourier-transform system. Chemical shifts are reported in p.p.m. from internal tetramethylsilane, with Me_2SO-d_6 as a solvent. Except for the hydroxyl protons, the chemical shifts and coupling constants were obtained after the addition of 20 μL of D_2O.

Fluorescent silica-gel, plastic plates (Baker) developed with 1:4 methanol–chloroform were used for t.l.c., and spots were detected with a u.v. lamp or with iodine. Merck Silica gel 60 (230–440 mesh) was used for dry-column chromatography.

General procedure for the synthesis of 5-O-trityl-D-pentoses. — To the D-pentose dissolved in pyridine (20 mL per mmol) was added an equimolar amount of chlorotriphenylmethane. The mixture was stirred for 18–20 h at room temperature. The resulting solution was evaporated to dryness and the pyridine removed from the residue by coevaporation with 1:4 (v/v) ethanol–toluene. The residue was then dissolved in chloroform and extracted with water. The chloroform phase was dried (sodium sulfate) and the solvent removed to give a mixture of the crude 5-*O*-trityl-D-pentofuranose and triphenylmethanol. The tritylated sugar was isolated by crystallization or by dry-column chromatography. The column was first eluted with chloroform to remove triphenylmethanol and then with 1:4 (v/v) methanol–chloroform to recover the 5-*O*-trityl-D-pentofuranose.

5-O-Trityl-D-ribofuranose (**1**). — This compound was isolated in 62% yield by successive recrystallization of the foregoing crude mixture with ethanol[1]; m.p. 125–126° (lit.[1] 125°), $[\alpha]_D^{24}$ −3.9° (20 h; *c* 2.5, pyridine) [lit.[1] +12.1 (4 min)→ −9.9° (12 days at 3°)]; R_F = 0.60; ^{1}H-n.m.r.: δ 5.20 (d, *J* 3.9 Hz, H-1α), 5.83 (d, *J* 7.7 Hz, HO-1α), 5.00 (d, *J* 1.5 Hz, H-1β), 6.26 (d, *J* 5.0 Hz, HO-1β), and 7.60–7.10 (m, 15H, Ph_3C).

5-O-Trityl-D-arabinofuranose (**2**). — Dry-column chromatography gave **2** as a foam in 60% yield; $[\alpha]_D^{24}$ +16.3° (*c* 0.85, ethanol, 20 h) (lit.[7] +16.5° after 25 h), R_F 0.55; ^{1}H-n.m.r. δ 5.01 (d, *J* 2.75 Hz, H-1α), 6.22 (d, *J* 5.27 Hz, HO-1α), 5.07 (d, *J* 3.60 Hz, H-1β), 6.10 (d, *J* 6.29 Hz, HO-1β), and 7.60–7.10 (m, 15H, Ph_3C).

5-O-Trityl-D-xylofuranose (**3**). — Dry-column chromatography gave **3** in 57% yield, and it was recrystallized from ethyl acetate–petroleum ether[8]; m.p. 124–126° (lit.[8] 124–126°), $[\alpha]_D^{24}$ −14.6° (*c* 1.85, pyridine, 3 h); (lit.[8] −14, 7 min, −19.5°, 90 min). R_F = 0.50; ^{1}H-n.m.r.: δ 5.18 (d, *J* 3.80 Hz, H-1α), 5.82 (d, *J* 6.5 Hz, HO-1α), 4.94 (d, *J* 1.75 Hz, H-1β), 5.92 (d, *J* 8.0 Hz, HO-1β), and 7.60–7.10 (m, 15H, Ph_3C).

5-O-Trityl-D-lyxofuranose (**4**). — Dry-column chromatography gave **4** in 32% yield. Attempts at crystallization from acetone–light petroleum ether gave an amorphous powder that had $[\alpha]_D^{24}$ +6.7° (*c* 0.65, chloroform; 20 h); (lit.[6] +10.1, 5 min, +7.9°, 2 h); R_F 0.55; ^{1}H-n.m.r. δ 4.81 (d, *J* 2.7 Hz, H-1α), 6.24 (d, *J* 5.9 Hz, HO-1α), 5.02 (d, *J* 3.5 Hz, H-1β), 6.22 (d, *J* 5.5 Hz, HO-1β), and 7.60–7.00 (m, 15H, Ph_3C).

5-O-Trityl-2-deoxy-D-erythro-pentofuranose (**5**). — Dry-column chromatography afforded **5** in 60% yield and it was recrystallized from ethyl ether–petroleum ether; m.p. 108–109°, $[\alpha]_D^{24}$ +16.7° (*c* 1.0, pyridine, 20 h); R_F = 0.63; ^{1}H-n.m.r.: δ 5.37 (q, $J_{1,2'}$ 5.6, $J_{1,2''}$ 2.1 Hz, H-1α), 6.08 (d, *J* 5.0 Hz, HO-1α), 4.88 (d, *J* 5.0 Hz, HO-3α), 5.43 (q, $J_{1,2'}$ 3.7, $J_{1,2''}$ = 1.7 Hz, H-1β), 6.14 (d, *J* 4.8 Hz, HO-1β), 4.94 (d, *J* 4.8 Hz, HO-3β), 2.40–2.10 (m, 1H, H-2′), 1.46–1.88 (m, 1H, H-2″), 4.11–3.71 (m, 2H, H-3,4), 3.17–2.85 (m, 2H, H-5,5′), and 7.50–7.20 (m, 15H, Ph_3C).

Anal. Calc. for $C_{24}H_{24}O_4$: C, 76.60, H, 6.38. Found: C, 76.54, H, 6.50.

ACKNOWLEDGMENTS

This research was supported, in part, by National Institutes of Health Grant GM-22982, and by University of California, San Francisco NMR Research Resource Center Grant NIH-RR-00892.

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