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Note

Reduction of 2,3,5-tri-*O*-benzyl-α (and β)-D-ribofuranosylethyne*†

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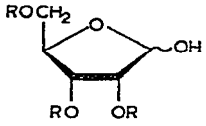
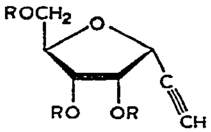
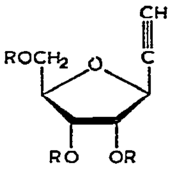
In a programme directed towards the synthesis of *C*-nucleoside antibiotics[2] and related compounds, we have used 2,3,5-tri-*O*-benzyl-D-ribofuranose[3] (**1**) as a starting material for the preparation of 2,3,5-tri-*O*-benzyl-α(and β)-D-ribofuranosylethyne[4] (**2** and **5**). The ether **1** was first prepared by Barker and Fletcher[3], for use in α-ribonucleoside synthesis[5], and as part of a more extensive study of syntheses from partially benzylated carbohydrates[6].



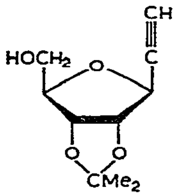
1 R = CH_2Ph



2 R = CH_2Ph
3 R = H
4 R = Ac



5 R = CH_2Ph
6 R = H



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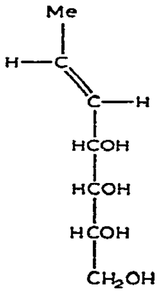

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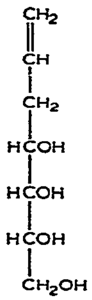

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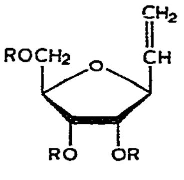

10 R = CH_2Ph

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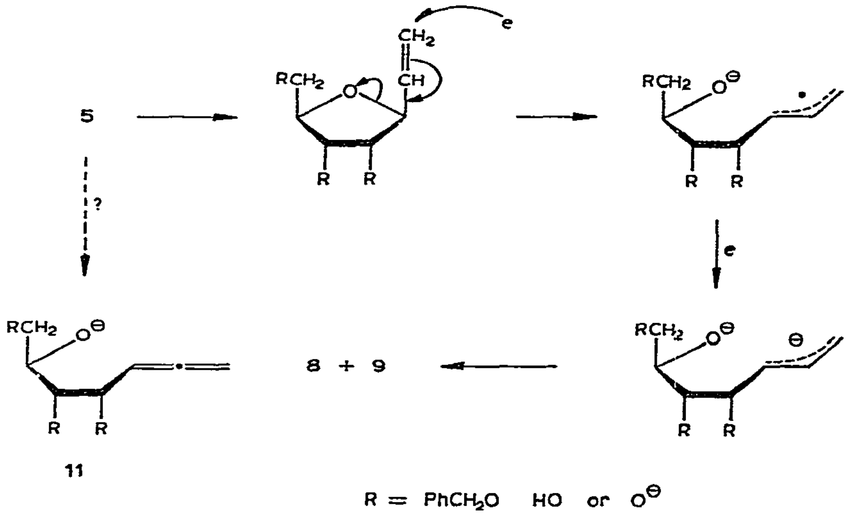
*Dedicated to the memory of Dr. Hewitt G. Fletcher, Jr.
†*C*-Nucleoside Studies: Part IV. For Part III, see Ref. 1.

We wished to have available derivatives of α(and β)-D-ribofuranosylethyne carrying a range of protecting groups and have therefore converted the ethers **2** and **5** into the parent triols **3** and **6**. A general method for the removal of benzyl ether protecting groups is the use of sodium in liquid ammonia[7]. This reagent reduces acetylenes to *trans*-olefins[8], but reduction of a terminal acetylene may be prevented by its conversion, in ammonia solution, into the anion by means of sodamide[9] prior to the reduction. Under these conditions, the ether **2** was converted into the triol **3**, which was isolated as the triacetate **4** (61%). Deacetylation of **4** gave the crystalline triol **3**[10] in 84% yield. Similarly, the ether **5** was converted into the crystalline triol **6**, isolated by chromatography, in 54% yield. The 2,3-*O*-isopropylidene derivative **7** of the β-ethyne **6** was prepared.

The necessity for converting the ethyne into its anion in a separate step was shown when direct reduction of a solution of the ethyne **5** in tetrahydrofuran, with sodium in liquid ammonia, yielded the two alkenes **8** (44%) and **9** (22%). The crystalline products were separated from each other by chromatography on a strongly basic ion-exchange resin[11]. Their olefinic structures were shown clearly by p.m.r. spectroscopy, the D-*ribo* configuration being assumed in each case. In particular, the *trans*-geometry in **8** was shown by the high value (15.5 Hz) for the coupling of the vinylic protons. A possible reaction sequence is shown in Scheme 1, but a sequence involving the allenic intermediate **11** cannot be ruled out[12].



Scheme 1

We have previously studied the catalytic hydrogenation of the ethynes **2** and **5**, to give the corresponding ribofuranosylethanes[4], using palladium–charcoal as catalyst. The synthesis of the ethene **10**, which is a potential source of 2,5-anhydro-3,4,6-tri-*O*-benzyl-D-allose[13,14], has now been achieved by partial hydrogenation of the triple bond in **5**. When the ethyne **5** was hydrogenated using Lindlar catalyst[15] and in the presence of a small amount of quinoline[16], the ethene **10** could be isolated in 90% yield. No cleavage of the benzyl ether protecting groups was observed.

EXPERIMENTAL

Melting points are uncorrected. I.r. spectra were measured for potassium bromide discs or for films, using a Perkin–Elmer 257 or 157G spectrophotometer. Mass spectra were recorded with an A.E.I. MS 902 or MS 30 spectrometer. N.m.r. spectra were measured on a Perkin–Elmer R12B spectrometer at 60 Mz, a Varian HA-100D or JEOL MH 100 spectrometer at 100 MHz, and a Varian HR220 spectrometer at 220 MHz, with tetramethylsilane or sodium 3-trimethylsilylpropane-1-sulphonate as internal standard. Specific rotations were measured using a Bendix-NPL 143D automatic polarimeter (path length, 1 cm). Adsorption chromatography was carried out using silica gel (Merck; 70–230 mesh ASTM). For t.l.c., Kieselgel G (Merck) was used as adsorbent; carbohydrates were detected with anisaldehyde–sulphuric acid[17]. Evaporations were performed under reduced pressure below 40° on a rotary evaporator.

2,3,5-Tri-O-acetyl-α-D-ribofuranosylethyne (**4**). — The benzyl ether **2** (0.691 g) in dry ether (7 ml) was added to a suspension of sodamide (1.78 g, 28.3 equiv.) in liquid ammonia (180 ml) at $-40°$, and the resulting mixture stirred for 1 h. Sodium (0.83 g, 22.4 equiv.) was then added during 10 min, and stirring was continued for a further 30 min. Aqueous 10% ammonium chloride (100 ml) was added, and solvents were evaporated *in vacuo*, water being removed by azeotropic distillation with ethanol and benzene. Extraction of the residue with ethanol (2 × 100 ml) yielded a syrup, which was treated with acetic anhydride (7.33 g) in pyridine (10 ml) at $-35°$ and overnight at room temperature. The product was isolated using chloroform to yield a brown syrup which was chromatographed on silica gel (8 g). Benzene–ether (14:1) eluted the triacetate **4** as a pure syrup (0.281 g, 61%), $[\alpha]_D^{24}$ $+109.4°$ (*c* 1.06, chloroform); ν_{max}^{film} 3280 (HC≡), 2122 (C≡C), 1750 (C=O), and 1230 cm^{-1} (C–O); n.m.r. data (60 MHz, chloroform-*d*): δ 1.97–2.26 (2 s, 9 H, COMe), 2.58 (d, 1 H, ≡CH), and 4.1–5.6 (m, 6 H); *m/e* 285 (s) (M+1), 284 (w) (M), 242 (s) ($M-CH_2$=C=O), 225 (s) (M−OAc), 211 (s) ($M-CH_2OAc$), and 43 (s) (CH_3CO).

Anal. Calc. for $C_{13}H_{16}O_7$: C, 54.93; H, 5.63. Found: C, 54.70; H, 5.79.

α-D-Ribofuranosylethyne (**3**). — The triacetate **4** (135 mg) was treated with methanol (4 ml) containing a catalytic quantity of sodium methoxide at room temperature for 1.5 h. Passage through a short column of Amberlite IR-120 (H^+) resin, and subsequent evaporation yielded a syrup, which crystallised from ethyl acetate, yielding the triol **3** (63 mg, 84%), m.p. 99–100°, $[\alpha]_D^{24}$ $+6.3°$ (*c* 0.64, methanol); lit.[10] m.p. 102–102.5° (corr.), $[\alpha]_D$ $+4.0°$ (ethanol). Identity was confirmed by mixture m.p. and by comparison of i.r. spectra.

β-D-Ribofuranosylethyne (**6**). — Sodium (1.21 g, 15 equiv.) was added with stirring to liquid ammonia (250 ml), at $-40°$, containing hydrated ferric nitrate

(30 mg), and stirring was then continued for 45 min. The benzyl ether **5** (1.48 g) in dry ether (15 ml) was then added and the mixture stirred for 1 h. Sodium (1.20 g, 15 equiv.) was added and the reaction mixture stirred for 1.5 h. The ammonia was then evaporated at room temperature, and aqueous 10% ammonium chloride (25 ml) was added. After concentration of the solution *in vacuo*, and azeotropic removal of water with ethanol and benzene, the residue was extracted with hot ethyl acetate. Filtration and evaporation yielded a syrup which was chromatographed on silica gel (30 g). Elution with ether–ethyl acetate (1:1) yielded crystalline β-D-ribofuranosylethyne (**6**; 0.295 g, 54%). Recrystallised from ethyl acetate–light petroleum, the triol **6** had m.p. 63–64°, $[\alpha]_D^{23}$ −18.2° (*c* 0.71, methanol); ν_{max}^{KBr} 3720–3020 br (OH) and 2110 cm^{-1} (C≡C); n.m.r. (100 MHz, acetone-d_6) data: δ 2.98 (d, 1 H, ≡CH) and 3.40–4.60 (m, 9 H); *m/e* 127 ($M - CH_2OH$).

Anal. Calc. for $C_7H_{10}O_4$: C, 53.16; H, 6.33. Found: C, 53.32; H, 6.01.

2,3-O-Isopropylidene-β-D-ribofuranosylethyne (**7**). — A mixture of the ethyne **6** (50 mg), dry acetone (5 ml), and *p*-toluenesulphonic acid (15 mg) was stirred at room temperature for 6 h, neutralised (solid Na_2CO_3), filtered, and evaporated to a syrup. Chromatography on silica gel (1:1 light petroleum–ether) gave pure **7** as a syrup (59 mg, 94%), $[\alpha]_D^{22}$ −21.15° (*c* 0.94, chloroform); ν_{max}^{film} 3425 (OH), 3268 (≡C–H), 2114 (C≡C), 1374 and 1382 cm^{-1} (both CMe_2); n.m.r. (60 MHz, chloroform-*d*) data: δ 1.37, 1.55 (2 s, 6 H, CMe_2), 2.07–2.57 (broad s, 1 H, OH), 2.66 (d, 1 H, ≡CH), and 3.6–5.0 (m, 6 H); *m/e* 199 (m) (M+1), 198 (w) (M), and 183 (s) ($M - CH_3$).

Anal. Calc. for $C_{10}H_{14}O_4$: C, 60.61; H, 7.07. Found: C, 60.40; H, 7.26.

*1,2,3-Trideoxy-*trans-D-ribo*-hept-2-enitol* (**8**) *and 1,2,3-trideoxy-*D-ribo*-hept-1-enitol* (**9**). — The benzyl ether **5** (1.1 g) was suspended in liquid ammonia (50 ml), and dry tetrahydrofuran was added until the solution became homogeneous. Sodium (0.8 g, 13.5 equiv.) was then added in portions. After 15 min, solid ammonium chloride was added and the solution evaporated to dryness. The residue was extracted with ethanol, the extract was filtered and evaporated, and the residue, in water, was passed successively through columns of Dowex 50 (NH_4^+) (40 ml) and De-Acidite FF (HO^-) (40 ml) resins. Evaporation of the eluate yielded a syrup (0.38 g), a portion of which (0.20 g) was chromatographed on a column of De-Acidite FF (HO^-) resin (100 ml). Water eluted first the alkene **8**; recrystallisation from ethyl acetate gave material (95 mg, 44%) having m.p. 114–117°; n.m.r. (220 MHz, deuterium oxide) data: δ 1.74 (d, 3 H, Me), 3.5–3.9 (m, 4 H), 4.26 (dd, 1 H, H-4), 5.56 (dd, 1 H, $J_{2,3(trans)}$ 15.5 Hz, H-3), and 5.84 (dq, 1 H, H-2).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.84; H, 8.76. Found: C, 51.88; H, 8.80.

Further elution with water yielded **9**; recrystallisation from ethyl acetate gave material (48 mg, 22%) having m.p. 112–113°; n.m.r. (100 MHz, deuterium oxide) data: δ 2.38 (m, 2 H, H-3), 3.5–4.1 (m, 5 H), and 5.0–6.3 (m, 3 H, olefinic protons).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.84; H, 8.76. Found: C, 52.00; H, 8.49.

*3,6-Anhydro-4,5,7-tri-O-benzyl-1,2-dideoxy-*D-allo*-hept-1-enitol* (**10**). — The ethyne **5** (0.306 g) in benzene (7 ml) was shaken with Lindlar catalyst[15] (10.5 mg) and quinoline (0.03 ml) in a slightly positive pressure of hydrogen at room temperature.

After 50 min, hydrogen uptake virtually ceased, the catalyst was removed by filtration through Celite, and the filtrate was evaporated to a syrup which was dissolved in ether (25 ml). The ethereal solution was washed successively with aqueous 10% sulphuric acid, 10% aqueous potassium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated to yield a colourless syrup (0.3 g). Examination by t.l.c. (Kieselgel G, impregnated with silver nitrate, as adsorbent) indicated a new component together with unreacted ethyne **5**. The mixture was chromatographed on an intimate mixture of silica gel (10 g) and silver nitrate (1.5 g). Light petroleum–ether (4:1) eluted the ethene **10**, contaminated with a little silver nitrate which was removed by washing a chloroform solution of the ethene with water. Evaporation yielded a colourless syrup. The syrup was rechromatographed on silica gel (10 g). Light petroleum–ether (9:1) eluted the pure ethene **10** (0.276 g, 90%), $[\alpha]_D^{24}$ +0.01° (*c* 1.07, chloroform); n.m.r. (100 MHz, chloroform-*d*) data: δ 3.45 (d, 2 H, H-7,7′), 3.54 (dd, 1 H, $J_{3,4}$ 5.75 Hz, $J_{4,5}$ 4.5 Hz, H-4), 3.85 (t, 1 H, $J_{5,6}$ 4.5 Hz, H-5), 4.09 (m, 1 H, $J_{6,7'} = J_{6,7} = 8$ Hz, H-6), 4.34 (m, 1 H, $J_{2,3}$ 5.75 Hz, H-3), 4.45–4.60 (m, 6 H, Ph*CH*$_2$), 5.06 (ddd, 1 H, $J_{1,1'}$ 2.5 Hz, $J_{1,2(\mathrm{cis})}$ 10 Hz, $J_{1,3}$ 1 Hz, H-1), 5.29 (ddd, 1 H, $J_{1',2(\mathrm{trans})}$ 17 Hz, $J_{1',3}$ 1 Hz, H-1′), and 5.77 (ddd, 1 H, H-2).

Anal. Calc. for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02. Found: C, 78.08; H, 6.78.

ACKNOWLEDGMENT

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