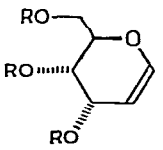
Carbohydrate Research, 72 (1979) 285–288

Note

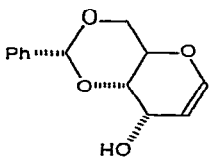
A facile synthesis of D-allal and its derivatives

R. D. GUTHRIE AND ROBERT W. IRVINE
School of Science, Griffith University, Nathan, Queensland 4111 (Australia)
(Received June 22nd, 1978; accepted for publication, July 17th, 1978)

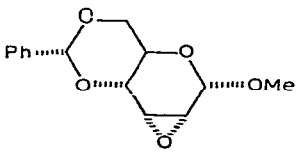
As part of a study of the chemistry of glycals (1,5-anhydro-2-deoxy-hex-1-enitols), we required reasonable quantities of D-allal (**1**) and its tri-*O*-substituted derivatives. Considerable research has been done on D-glucal, the C-3 epimer of **1**, but little on **1**.



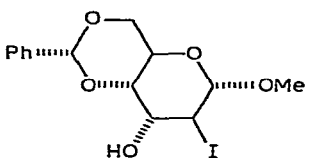
1 R = H
2 R = Ac
3 R = Bz
4 R = Bzl



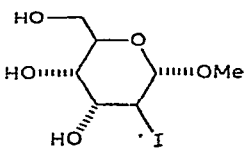
5



6



7



8

The first D-allal derivative (**5**) was prepared[1] from the reaction of the epoxide **6** with methyl-lithium (see also Refs. 2 and 3). The yield of the allal **5** was increased[3] to 85% by treating the iodo-altroside **7** with butyl- or methyl-lithium. Compound **5** is of little use as a precursor for D-allal, because of the lability of the double bond under the acidic conditions necessary to remove the acetal group[4].

3,4,6-Tri-*O*-acetyl-D-allal (**2**) was isolated[5] as a syrup (12%) from penta-*O*-acetyl-β-D-altropyranose by a modification of the Fischer glycal synthesis[6]. Compound

2 was isolated[9] crystalline (76%) by using the corresponding allopyranose derivative, but when we repeated this synthesis, we obtained the lower yield reported by Mallams and co-workers[8].

We now describe an easy, high-yielding synthesis of D-allal and its derivatives. Because, as noted above, the benzylidene group cannot efficiently be removed from **5**, we investigated the possibility of removing the acetal function from **7**, *prior* to the introduction of the double bond.

Compound **7**, prepared essentially quantitatively from the readily available[3] epoxide **6**, afforded an excellent yield of methyl 2-deoxy-2-iodo-α-D-altropyranoside (**8**), which, like **7**, was unstable to heat and light. Treatment of **8** with butyl-lithium in tetrahydrofuran gave good yields of syrupy D-allal, best isolated by conversion into the crystalline triacetate **2** and subsequent deacetylation. The overall yield of D-allal from **6** was 60%. Conventional methods were used to convert D-allal into the hitherto unknown tribenzoate **3** and tri-*O*-benzyl derivative **4**.

EXPERIMENTAL

General. — Melting points are uncorrected. I.r. spectra were recorded with a Perkin–Elmer 377 spectrophotometer, and optical rotations were measured on a Perkin–Elmer 241 polarimeter. P.m.r. spectra (60 MHz, internal Me_4Si) were recorded with a Varian EM-360 spectrometer. ^{13}C-N.m.r. spectra (22.628 MHz) were recorded with a Bruker HX-90 spectrometer and assigned by analogy with those of known compounds[9]. P.l.c. was performed on Kieselgel GF 254 (Merck), and detection was effected by iodine vapour or u.v. light (254 nm).

Methyl 2-deoxy-2-iodo-α-D-altropyranoside (**8**). — A solution of methyl 4,6-*O*-benzylidene-2-deoxy-2-iodo-α-D-altropyranoside (**7**, 2 g) in methanol (50 ml) was stirred with Amberlite IR-120(H^+) resin (2 ml) for 16 h at room temperature, filtered through Celite, and concentrated below 40°. Ether (50 ml) was added to the syrupy residue to give a crystalline product, which was collected and washed with cold ether to give **8** (1.36 g). Concentration and cooling of the mother liquors afforded a second crop (0.17 g; total yield, 99%) sufficiently pure for the next step.

Recrystallisation from acetone gave colourless needles, m.p. 134° (dec.), $[\alpha]_D^{22}$ +44° (*c* 1, water). P.m.r. data (Me_2SO-d_6): δ 5.08 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.87 (d, 1 H, OH; $^3J_{OH,H}$ 4.5 Hz disappeared upon addition of D_2O), 4.34 (d, 1 H, OH; $^3J_{OH,H}$ 5.5 Hz disappeared upon addition of D_2O), 4.28 (d, 1 H, OH; $^3J_{OH,H}$ 5.5 Hz disappeared upon addition of D_2O), 3.40–4.24 (m, 6 H, H-2,3,4,5,6,6′), and 3.28 (3 H, OMe).

Anal. Calc. for $C_7H_{13}IO_5$: $M^{+\cdot}$ 303.9809. Found: $M^{+\cdot}$ 303.9806.

1,5-Anhydro-2-deoxy-D-ribo-*hex-1-enitol* (D-*allal*) (**1**). — A solution of butyl-lithium in hexane (12 mmol) was added dropwise to a stirred solution of **8** (608 mg, 2 mmol) in tetrahydrofuran (50 ml) at 0° under dry nitrogen. After 5 min, the excess of butyl-lithium was decomposed with ice and the solvent was evaporated. The thoroughly dried residue was conventionally acetylated with pyridine (10 ml) and

acetic anhydride (2 ml), to give 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*ribo*-hex-1-enitol (**5**), m.p. and mixture m.p. 81–83°, $[\alpha]_D^{20}$ +314° (*c* 1); lit.[7] m.p. 81–83°, $[\alpha]_D^{24}$ +310.3° (chloroform). P.l.c. of the mother liquors (acetone–hexane, 1:5; 3 developments) afforded a second crop of pure material (total yield, 380 mg, 70%).

A solution of **2** (380 mg) in methanol (20 ml) was treated with sodium (2 mg) for 16 h at 20°. After neutralisation with solid carbon dioxide, the methanol was evaporated and the residue was extracted with boiling ethyl acetate (3 × 50 ml). The extract was boiled with activated charcoal for 5 min, dried ($MgSO_4$), filtered, and concentrated to yield **1** as a colourless syrup (182 mg, 90%), $[\alpha]_D^{22}$ +309° (*c* 1.69, water); ν_{max} 1645 (-C=C-O-), 1248 (-C-O-C=), and 1077 cm^{-1} (-C-O-C-). P.m.r. data (acetone-d_6): δ 6.43 (d, 1 H, $J_{1,2}$ 6.0 Hz H-1), 4.27 (s, 3 H, OH; disappeared upon addition of D_2O), 4.09 (dd, 1 H, $J_{3,4}$ 2.5 Hz, H-3), and 3.70–4.00 (m, 5 H, H-2,4,5,6,6').

Anal. Calc. for $C_6H_{10}O_4$: $M^{+\cdot}$ 146.0579. Found: $M^{+\cdot}$ 146.0582.

Conventional treatment of **1** with pyridine (10 ml) and benzoyl chloride (2.5 ml) gave the 3,4,6-tribenzoate as a pale-yellow syrup (665 mg, 72.6%), $[\alpha]_D^{22.5}$ +383° (*c* 0.95, chloroform). P.m.r. data ($CDCl_3$): δ 7.80–8.30 (m, 6 H, aromatic), 7.09–7.72 (m, 9 H, aromatic), 6.63 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 5.90 (dd, 1 H, $J_{2,3}$ 6.0, $J_{3,4}$ 4.2 Hz, H-3), 5.67 (dd, 1 H, $J_{4,5}$ 10 Hz, H-4), 5.14 (dd, 1 H, H-2), and 4.48–4.95 (m, 3 H, H-5,6,6'). ^{13}C-N.m.r. data ($CDCl_3$): C-1, 148.3; C-2, 97.7; C-3, 63.9; C-4, 67.5; C-5, 71.2; and C-6, 63.0 p.p.m.

Anal. Calc. for $C_{27}H_{22}O_7$: C, 70.7; H, 4.8. Found: C, 70.8; H, 5.0.

*1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-*D-ribo-*hex-1-enitol* (**4**). — A solution of **1** (190 mg) in dry methyl sulphoxide (10 ml) was added dropwise to a stirred suspension of oil-free sodium hydride (200 mg) in methyl sulphoxide (10 ml) under dry nitrogen. After stirring for 2 h at 20°, benzyl chloride (440 µl) was added dropwise, and the mixture was stirred for a further 16 h, poured into water (100 ml), and extracted with ether (3 × 50 ml). The combined extracts were washed with water (2 × 50 ml) and dried ($MgSO_4$), and the solvent was evaporated. P.l.c. (acetone–hexane, 1:5; 2 developments) gave **4** as a colourless syrup (145 mg, 27%), $[\alpha]_D^{21}$ +230° (*c* 1.1 chloroform). P.m.r. data ($CDCl_3$): δ 7.17–7.52 (15 H, aromatic), 6.45 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.92 (t, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.27–4.72 (m, 7 H, H-3 and 3 benzyl CH_2), and 3.70–4.11 (m, 4 H, H-4,5,6,6'). ^{13}C-N.m.r. data ($CDCl_3$): C-1, 146.6; C-2, 98.2; C-3, 73.1; C-4, 73.1; C-5, 74.0; and C-6, 68.9 p.p.m.

Anal. Calc. for $C_{27}H_{28}O_4$: C, 77.9; H, 6.8. Found: C, 77.5; H, 6.5.

REFERENCES

1 A. A. J. Feast, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, (1965) 7378–7388.
2 M. Sharma and R. K. Brown, *Can. J. Chem.*, 44 (1966) 2825–2835.
3 R. U. Lemieux, E. Frage, and K. A. Watanabe, *Can. J. Chem.*, 46 (1968) 61–69.
4 I. D. Blackburne, P. M. Fredericks, and R. D. Guthrie, *Aust. J. Chem.*, 29 (1976) 381–391.
5 H. Paulsen and J. Thiem, *Chem. Ber.*, 106 (1973) 3850–3876.
6 E. Fischer and K. Zach, *Sitzungsber K. Preuss. Akad. Wiss.*, 16 (1913) 113.

7 M. HAGA AND S. TEJIMA, *Carbohydr. Res.*, 34 (1974) 214–218.
8 M. K. GELMANN, A. K. MALLAMS, AND H. F. VERNAY, *J. Chem. Soc., Perkin Trans. 1*, (1976) 1113–1126.
9 A. I. R. BURFITT, R. D. GUTHRIE, AND R. W. IRVINE, *Aust. J. Chem.*, 30 (1977) 1037–1043.