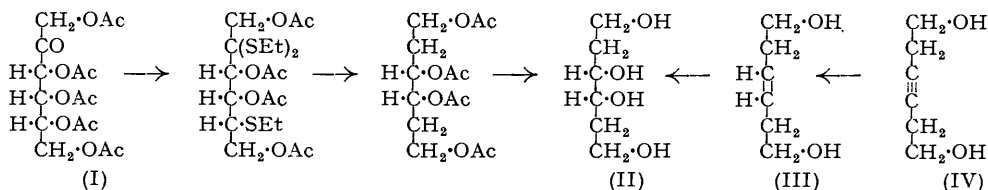


743. *Synthesis of Carbohydrates by Use of Acetylenic Precursors.*  
 Part III.\* *erythro-Hexane-1 : 3 : 4 : 6-tetrol.*

By R. A. RAPHAEL and C. M. ROXBURGH.

*erythro*-Hexane-1 : 3 : 4 : 6-tetrol has been prepared by the *cis*-hydroxylation of *cis*-hex-3-ene-1 : 6-diol which was obtained by partial catalytic hydrogenation of the corresponding acetylenic compound. It was not identical with the substance to which this constitution has hitherto been ascribed.

In an attempt to prepare 2-deoxy-D-allitol Wolfrom, Lew, and Goepf (*J. Amer. Chem. Soc.*, 1946, **68**, 1446) treated keto-D-psicose penta-acetate (I) with ethanethiol and zinc chloride and subjected the resulting crude thioketal to Raney nickel hydrogenolysis. Very surprisingly the product, after deacetylation, proved to be a hexanetetrol and, since the compound proved to be devoid of optical activity throughout the visible spectrum, the American workers assigned to it the plausible *meso*-configuration *erythro*-hexane-1 : 3 : 4 : 6-tetrol (II). The mechanism proposed to account for the formation of (II) involved the replacement of the 5-acetoxy-group as follows :



In view of the unusual nature of this postulated reaction it was deemed desirable to devise an unequivocal synthesis of (II) for purposes of comparison.

The required starting material was the hitherto unknown hex-3-yne-1 : 6-diol (IV). Preparation from ethylene oxide and acetylenedimagnesium bromide was unsuccessful, the sole product being ethylene bromohydrin; this type of reaction between ethylene oxide and Grignard reagents has been noted before (see Gaylord and Becker, *Chem. Reviews*, 1951, **49**, 414). In the successful preparation the lithium compound of 4-(tetrahydro-2-pyranyloxy)but-1-yne was treated in liquid ammonia solution with ethylene oxide; acid hydrolysis of the resulting 6-(tetrahydro-2-pyranyloxy)hex-3-yn-1-ol produced the needed hex-3-yne-1 : 6-diol. Partial hydrogenation of this compound with palladised charcoal as catalyst yielded *cis*-hex-3-ene-1 : 6-diol (III); the corresponding *trans*-diol was obtained when sodium in liquid ammonia was used as the reducing agent. Treatment of the *cis*-diol with a *tert*.-butyl alcoholic solution of hydrogen peroxide containing osmium tetroxide resulted in *cis*-hydroxylation to furnish the required *erythro*-hexane-1 : 3 : 4 : 6-tetrol (II) as a crystalline solid (cf. Part I, *J.*, 1949, S45). The melting point of this tetrol (113—114°) and that of its dimethylene derivative (146—147°) showed it to differ from the compound obtained by the American workers (m. p. 121—122°; dimethylene derivative, m. p. 97—98°). The nature of the latter product is obscure.

#### EXPERIMENTAL

6-(*Tetrahydro-2-pyranyloxy*)hex-3-yn-1-ol.—To a stirred solution of lithamide (from lithium, 2.3 g., in the presence of ferric nitrate catalyst) in liquid ammonia (400 c.c.) was added dropwise (15 minutes) a solution of 4-(tetrahydro-2-pyranyloxy)but-1-yne (45.4 g.; Jones, Shen, and Whiting, *J.*, 1950, 235) in dry ether (25 c.c.), and stirring was continued for 40 minutes. Ethylene oxide (40 c.c.) was then added all at once and the reaction mixture stirred for 9 hours after which it was decomposed by addition of ammonia solution (*d* 0.88; 5 c.c.) and set aside overnight for the ammonia to evaporate. Ether and water were added, the aqueous layer was extracted with ether, and the ethereal solution was washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and

\* Part II, *J.*, 1952, 401.

evaporated. Distillation gave 6-(tetrahydro-2-pyranyloxy)hex-3-yn-1-ol (45 g., 77%) as a liquid, b. p. 116°/0.4 mm.,  $n_D^{25}$  1.4828, after a small fore-run (5.5 g.) of starting material (Found: C, 66.3; H, 9.3.  $C_{11}H_{18}O_3$  requires C, 66.6; H, 9.15%). Catalytic hydrogenation of the compound in ethyl acetate in presence of platinum oxide resulted in the uptake of 2 mols. of hydrogen, to form 6-(tetrahydro-2-pyranyloxy)hexan-1-ol, b. p. 97°/0.5 mm.,  $n_D^{25}$  1.4570, the *bisphenylurethane* of which crystallised in plates, m. p. 73—74°, from light petroleum (b. p. 40—66°) (Found: N, 4.6.  $C_{18}H_{27}O_4N$  requires N, 4.4%).

*Hex-3-yne-1 : 6-diol*.—6-(Tetrahydro-2-pyranyloxy)hex-3-yn-1-ol (5 g.) was added to a solution of concentrated sulphuric acid (4 c.c.) in methanol (90 c.c.) and set aside at room temperature for 48 hours. The mixture was then neutralised with methanolic sodium methoxide (phenolphthalein), the solution being kept cooled to room temperature. The methanol was then evaporated off under reduced pressure (an efficient splash-head was necessary) and the gelatinous solid residue extracted with hot ethyl acetate (3 × 50 c.c.). The filtered extract was taken to dryness and the residue dissolved in boiling benzene (50 c.c.). Filtration and cooling gave elongated plates (2 g., 70%) of *hex-3-yne-1 : 6-diol*, m. p. 77—79°; recrystallisation from benzene–light petroleum (b. p. 60—80°) gave the pure diol, m. p. 80—80.5° (Found: C, 63.25; H, 8.85.  $C_6H_{10}O_2$  requires C, 63.15; H, 8.85%). Setting aside a concentrated solution of the diol and phenyl isocyanate in dioxan at room temperature for several days gave the *bisphenylurethane* which crystallised from benzene, followed by ethanol, in plates, m. p. 173—174° (Found: C, 68.4; H, 5.6; N, 8.3.  $C_{20}H_{20}O_4N_2$  requires C, 68.2; H, 5.7; N, 7.95%). Complete hydrogenation with platinum oxide in ethyl acetate resulted in the uptake of 2 mols. of hydrogen to furnish hexane-1 : 6-diol, m. p. and mixed m. p. 39—41°.

*cis-Hex-3-ene-1 : 6-diol*.—A solution of hex-3-yne-1 : 6-diol (1.5 g.) in ethyl acetate (60 c.c.) was shaken under hydrogen with palladium–charcoal (10%; 150 mg.) until 1 mol. of hydrogen had been absorbed. Removal of catalyst and solvent followed by distillation gave *cis-hex-3-ene-1 : 6-diol* (1.1 g.) as a viscous hygroscopic liquid, b. p. 86—87°/0.3 mm.,  $n_D^{15}$  1.4750 (Found: C, 61.1; H, 10.8.  $C_6H_{12}O_2$  requires C, 62.0; H, 10.4%). The *bisphenylurethane* prepared at room temperature crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 107—108° (Found: C, 68.0; H, 6.2; N, 8.2.  $C_{20}H_{22}O_4N_2$  requires C, 67.8; H, 6.3; N, 7.9%).

*trans-Hex-3-ene-1 : 6-diol*.—Hex-3-yne-1 : 6-diol (1 g.) was transferred from a dropping funnel to a stirred solution of sodium (1 g.) in liquid ammonia (50 c.c.) by dripping liquid ammonia through it. The cooled (alcohol–carbon dioxide) reaction mixture was stirred for a further 2 hours and then decomposed by addition of ammonium chloride (4 g.). After evaporation any residual ammonia was removed by warming under reduced pressure and the residue extracted with boiling ethyl acetate. Filtration, evaporation, and distillation gave *trans-hex-3-ene-1 : 6-diol* (0.8 g.) as a viscous, hygroscopic liquid, b. p. 88—90°/0.3 mm.,  $n_D^{15}$  1.4747 (Found: C, 60.7; H, 10.7%). The *bisphenylurethane* crystallised from toluene in plates, m. p. 161—162° (Found: C, 68.0; H, 6.1; N, 7.9%).

*erythro-Hexane-1 : 3 : 4 : 6-tetrol*.—A cooled (0°) mixture of *cis-hex-3-ene-1 : 6-diol* (0.8 g.) and hydrogen peroxide–*tert.*-butanol (2.7M; 3 c.c.) was treated with a solution of osmium tetroxide in *tert.*-butyl alcohol (2%; 0.1 c.c.) and set aside at 0° for 24 hours. Removal of solvent under diminished pressure gave a viscous syrup which crystallised after several days at 0°. Crystallisation from ethanol gave *erythro-hexane-1 : 3 : 4 : 6-tetrol* (0.2 g.) as prisms, m. p. 113—114° (Found: C, 48.0; H, 9.2.  $C_6H_{14}O_4$  requires C, 48.0; H, 9.4%). Treatment of the tetrol with aqueous formaldehyde and hydrogen chloride by the method of Wolfrom, Lew, and Goepf (*loc. cit.*) gave a brown oil which was isolated by ether; evaporation gave an oil that rapidly solidified. Crystallisation from ethanol gave the *dimethylene* compound in plates, m. p. 146—147° (Found: C, 55.4; H, 7.8.  $C_8H_{14}O_4$  requires C, 55.2; H, 8.1%). This derivative was obtained both from the pure crystalline tetrol and from the syrupy residue derived from the mother-liquors.

We are indebted to the Chemical Society for a Research Grant. One of us (C. M. R.) thanks the Department of Scientific and Industrial Research for a Maintenance Award.