SYNTHESES WITH ANHYDRO SUGARS. XV.*

SYNTHESES OF 1,6-ANHYDRO-2,3,4-TRIDEOXY-β-D-*glycero*-HEXOPYRANOSE AND ITS UNSATURATED DERIVATIVES AS MODEL SUBSTANCES FOR STUDYING THE OPTICAL ROTATION OF SUGARS

J.PECKA and M.ČERNÝ

Department of Organic Chemistry,
Charles University, Prague 2

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In the present paper the authors describe the preparation of 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose (*III*) by three different processes: *a*) 1,6-Anhydro-2,4-dideoxy-β-D-*glycero*-hexopyranos-3-ulose (*I*) was converted by reaction with 1,2-ethanedithiol into the ethylenedithioacetal *II* which by desulphurization with Raney nickel afforded compound *III*. *b*) 1,6-Anhydro-4-O-benzyl-2-deoxy-3-O-*p*-toluenesulphonyl-β-D-*arabino*-hexopyranose (*V*) when treated with potassium tert-butoxide gave 1,6-anhydro-4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (*VI*) which on hydrogenation, debenzylation, and finally tosylation yielded 1,6-anhydro-2,3-dideoxy-4-O-*p*-toluenesulphonyl-β-D-*erythro*-hexopyranose (*IX*). From this compound was obtained the unsaturated derivative *X* which on hydrogenation gave compound *III*. *c*) Elimination of toluenesulphonic acid from 1,6-anhydro-3,4-dideoxy-2-O-*p*-toluenesulphonyl-β-D-*erythro*-hexopyranose (*XV*), prepared from the epoxy derivative *XIII*, afforded 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-2-enopyranose (*XVI*) which was then hydrogenated to give compound *III*. The significance of the compounds *III*, *X*, and *XVI* as models well suited for studying the optical rotation of hexopyranoses is shortly discussed.

The value for the optical rotation of the hitherto not described 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose (*III*) as the basic skeleton of the 1,6-anhydro-β-D-hexopyranoses has already been for some time a subject of discussions[1-3]. Also 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-2-enopyranose (*XVI*) and 1,6-anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-3-enopyranose (*X*) may serve as model substances for theoretical considerations about the optical rotation.** Therefore we decided to prepare these compounds within the framework of our study of the deoxysugars and to determine their properties. The trideoxyanhydride *III* was prepared by three different processes.

The starting compound in the first synthesis was the 2,4-dideoxy ketone[8] *I* which

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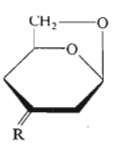
** Racemic mixtures of these compounds and also a number of related compounds have recently been prepared by Brown and coworkers by total synthesis[4-7] from acrolein.

by reaction with 1,2-enthanedithiol in dimethylsulphite under the catalysis of boron trifluoride etherate gave the ethylenedithioacetal *II* in 29% yield. The usual procedures for preparing the thioacetals without the presence of dimethylsulphite gave still lower yields. Desulphuration of the ethylenedithioacetal *II* with Raney nickel in ether afforded the trideoxy compound *III*. Its structure was confirmed by the IR, NMR and mass spectra which are in complete agreement with those of authentic 1,6-anhydro-2,3,4-trideoxy-β-DL-*glycero*-hexopyranose prepared from acrolein according to Brown and coworkers[4].

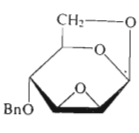
As the starting compound for the second synthesis of the trideoxyanhydride *III* and its 3,4-unsaturated derivative *X* was used 1,6:2,3-dianhydro-4-O-benzyl-β-D-mannopyranose[10] (*IV*). The reductive cleavage of the oxiran ring of this compound was performed with lithium aluminium hydride in tetrahydrofuran by a modification of the procedure of Seib[11] under formation of 1,6-anhydro-4-O-benzyl-2-deoxy-β-D-*arabino*-hexopyranose. The reaction of this compound with *p*-toluene sulphochloride in pyridine afforded the 3-O-tosyl derivative *V* which, treated with potassium tert-butoxide in tert-butyl alcohol, eliminated *p*-toluenesulphonic acid and furnished 1,6-anhydro-4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (*VI*). In hydrogenating the double bond of the benzyl derivative in acetic acid in the presence of palladium on charcoal debenzylation took place, and 1,6-anhydro-2,3-dideoxy-β-D-*erythro*-hexopyranose[9] (*VIII*) was produced. Notwithstanding that hydrogenation of the double bond proceeds more rapidly than the debenzylation, the preparative separation of these reactions is very difficult. However, when carrying out the reaction in ethanol in the presence of potassium hydroxide, the selectivity of the reaction of the double bond increases to such an extent that hydrogenolysis of the benzyl group does not occur, and 1,6-anhydro-4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hexopyranose (*VII*) is exclusively formed. Debenzylation of this compound in acetic acid in the presence of palladium on charcoal gave the dideoxy alcohol *VIII* which by tosylation in pyridine was converted to 1,6-anhydro-2,3-dideoxy-4-O-*p*-toluenesulphonyl-β-D-*erythro*-hexopyranose (*IX*). This substance, when treated with a solution of tert-butoxide in tert-butyl alcohol, eliminated *p*-toluenesulphonic acid under the formation of the 3-hexenopyranose *X* which contained as impurity a small amount of the 2-hexenopyranose *XVI* formed by a consecutive base-catalysed isomerisation of the initial substance. The structure of substance *X* was proved by its PMR spectrum (see Experimental part) which was essentially in accord with that of the DL-form of compound[5] *X*. The by-product *XVI* is unstable in chloroform of commercial quality, a property which was utilized for its elimination from the mixture. Compound *X* afforded on hydrogenation of its double bond in ether over platinum on charcoal the trideoxyanhydride *III*.

For the further preparation of compound *III* we used as the starting material 1,6-anhydro-4-deoxy-2-O-*p*-toluenesulphonyl-β-D-*xylo*-hexopyranose[12] (*XI*) which was converted by mesylation in pyridine into 1,6-anhydro-4-deoxy-3-O-methane-

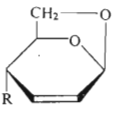
sulphonyl-2-O-*p*-toluenesulphonyl-β-D-*xylo*-hexopyranose (*XII*) and this then by treatment with sodium methoxide in methanol–tetrahydrofuran mixture into 1,6 : 2,3-dianhydro-4-deoxy-β-D-*ribo*-hexopyranose (*XIII*). This modification of the original procedure[12] suppressed the consecutive side reaction of opening the oxiran ring in the dianhydride *XIII* with sodium methoxide and increased the yield markedly. By reducing the dianhydride *XIII* over Raney nickel was prepared 1,6-anhydro-3,4-dideoxy-β-D-*erythro*-hexopyranose[9] (*XIV*), and this in turn was converted by tosylation in pyridine to the 2-O-tosyl derivative *XV*. The reaction of this compound with sodium ethoxide proceeded under elimination of the tosyl group and formation of compound *XVI*, but at the same time occurred also to a considerable extent fission



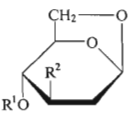
I; R = O=
II; R = —S(CH$_2$)$_2$S—
III; R = H$_2$



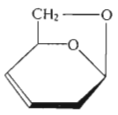
IV
Bn = C$_6$H$_5$CH$_2$
Ts = *p*-CH$_3$C$_6$H$_4$SO$_2$



VI; R = C$_6$H$_5$CH$_2$O
XVI; R = H



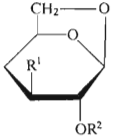
V; R^1 = C$_6$H$_5$CH$_2$, R^2 = OTs
VII; R^1 = C$_6$H$_5$CH$_2$, R^2 = H
VIII; R^1 = R^2 = H
IX; R^1 = Ts, R^2 = H

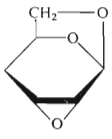


X

of the tosyl ester into the starting alcohol *XIV*. Structure *XVI* was confirmed by the PMR spectrum of this substance which was essentially in accord with that of the DL-form of compound[4,5] *XVI*. Substitution of sodium ethoxide for potassium tert-butoxide, an agent which would be unable to split the bond of the sulphoester, was in this case not possible, as the elimination proceeds much slower than with the tosyl ester *IX*, and the formed unsaturated compound has sufficient time to undergo isomerisation to the 3,4-unsaturated anhydride *X*. On hydrogenation the 2,3-unsaturated derivative *XVI* over platinum on charcoal we obtained the trideoxyanhydride *III*.

The unsaturated anhydro derivatives *X* and *XVI* establish in strong alkaline medium an equilibrium which was in the DL-series utilized for preparative purposes[6]. We studied the course of this reaction $X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} XVI$ quantitatively by measuring the constants of the pseudofirst order, k_1 and k_2, at 50°C in 1M-solution of potassium tert-butoxide in tert-butyl alcohol. The measurements were performed by starting the reaction either from the pure compound *X* or *XVI*, and the reaction was allowed to proceed with compound *X* only to a conversion of 2% and with compound *XVI* to a conversion of 6%, in order thus to prevent the occurrence of side reactions by prolonged treatment with the base (after some longer time, the reaction mixture becomes yellow).





XI; $R^1 = OH$, $R^2 = Ts$
XII; $R^1 = OMs$, $R^2 = Ts$
XIV; $R^1 = R^2 = H$
XV; $R^1 = H$, $R^2 = Ts$

XIII
$Ts = p\text{-}CH_3C_6H_4SO_2$
$Ms = CH_3SO_2$

The graphical representation of the dependence of the concentration ratios $[XVI]/[X]$ and $[X]/[XVI]$ gave straight lines whose slopes equal the rate constant $k_1 = 3{\cdot}67 \,.\, 10^{-3}\ h^{-1}$ and $k_2 = 19{\cdot}9 \,.\, 10^{-3}\ h^{-1}$, from which follows the equilibrium constant $K = k_1/k_2 = 0{\cdot}18$. This result is consistent with the composition of the mixture of *X* and *XVI* in the DL-series (ref.[6] gives $K = 0{\cdot}25$ and $0{\cdot}175$, respectively). It seems therefore that side reactions do not appreciably affect the composition of the equilibrium mixture (these reactions proceed slower than the establishment of the equilibrium). On the assumption that the entropies of the compounds *X* and *XVI* do not differ, it follows from the equilibrium constant that the energy content of substance *XVI* is 1·1 kcal/mol higher than that of substance *X*. By measuring the ratio of the hydrogenation rates of the compounds *XVI* and *X* under the catalysis of platinum on charcoal we found the ratio of the rate constants $k_{XVI}/k_X = 1{\cdot}47$.

Of interest is the question of the optical rotations of the compounds *III*, *X* and *XVI*. For compound *III* which is the basic skeleton of the 1,6-anhydro-β-D-hexopyranoses has by the method of optical "superposition"[1] been calculated the value $[\alpha]_D -112°$ (by relating the hypothetical value $[\alpha]_D -79°$ for the molecular weight of 162 to the molecular weight of 114 for substance *III*), and in the present work has been measured the value $[\alpha]_D -105°$ (water). Horton and Wander[2] calculated the optical rotations of the 1,6-anhydro-β-D-hexopyranoses by summation the rotatory contributions of the conformational elements and obtained for substance *III* the value $[\alpha]_D -75°$ (covering also the conformational contribution of the equatorial hydroxyl group in position 4) which they later[3] modified to $-127°$ on the basis of the $[\alpha]_D$ values for the 1,6-anhydro-4-deoxy-β-D-hexopyranoses. Though formally the method of "superposition"[1] and

Horton's method do differ from each other, there does not exist between them any substantial difference. These methods can be transformed into each other,* but the quantities used in the calculation have a different significance, including the value for the basic skeleton. There differ also the premises on which the derivations are based. The superposition method[1] assumes different contributions from the hydroxyl groups at $C_{(2)}$ and $C_{(4)}$, but the same absolute value for the equatorial and axial orientation, and at the same time also a small, from zero different contribution from the hydroxyl group at $C_{(3)}$. Horton and Wander[2] consider besides the contributions of the mutual conformational[1,3] interactions** a contribution of $+10°$ for every axial hydroxyl group, on the basis of theory difficultly to be motivated. As the experimental determined value for the trideoxyanhydride *III* differs only little from the predicted value, we can suppose that both assumptions made in the superposition method[1] will not be far from reality. By using the parameters for the interactions according to Lemieux[14] or Brewster[16] we can estimate the high negative rotation of substance *III* to $[\alpha]_D \approx -100°$, whereby a decisive contribution makes the O/C_0 interaction of the axial oxygen atom in the 1,6-anhydro ring. But we cannot entirely exclude the concomitant deformation of the skeleton of *III*. However, from the PMR spectrum follows the approximately synclinal conformation of H_{2e}, H_1, and H_{2a}, and therefore does the deformation not markedly manifest itself at the bonds $C_{(1)}-C_{(2)}-C_{(3)}$. In this connection it is worth while to note the optical rotation of the unsaturated anhydro derivatives *X* ($[\alpha]_D -177°$) and *XVI* ($[\alpha]_D +137°$). By an imagined exchange of the oxygen atom for the methylene group in the 1,6-anhydro ring of these compounds (whereby from compound *XVI* with D-configuration is formed compound *X* with L-configuration), the value of the optical rotation undergoes a change of 40°. An analogous consideration for the trideoxyanhydride *III* leads, however, to a change of the optical rotation by 210°.

The experimental determined $[\alpha]_D$ value of the trideoxyanhydride *III* can be used together with the laws derived for the 1,6-anhydro-β-D-hexopyranoses also for the hexopyranoses if the changes of the interactions with variation of the conformation C_4^1 (in compound *III*) to C_1^4 (in most hexopyranoses) are respected and the conformations of the substituents at the anomeric oxygen atom and at $C_{(6)}$ also taken into account. Simple is the correlation of the $[M]_D$ values of the 1,6-anhydro-β-D-hexo-

* The calculation of the partial contributions from the hydroxyl groups in the 1,6-anhydro-β-D-hexopyranoses with the aid of the hypothetical deoxy derivatives implicitly covers[1] also the mutual O/O interactions. Therefore, in taking *e.g.* as contributions of the carbon atom $C_{(2)}$ the values $\mp(a - b/2 + f/2)$ and $\mp(a + b + f/2)$, as contributions at $C_{(4)}$ the values $\pm(c/2 - b/2 - f/2)$ and $\pm(c/2 + b - f/2)$, as contribution at $C_{(3)}$ the value $f/2$, and for the skeleton the value $d + 3/2f - c/2$, where the meaning for *a*, *b*, *c*, *d* and *f* is identical with the denotation of the interaction constants in the paper of Horton and Wander[2], we obtain for all eight 1,6-anhydro-β-D-hexopyranoses agreeing results. The value for the basic skeleton *III* differs of course.

** These authors, as well as Lemieux[14], neglect quite unfounded the mutual O/O 1,3-interaction for instance to be found in *trans*-1,3-cyclohexanediol: $[\alpha]_D \pm 16{,}2°$ (*c* 10; methanol)[15].

pyranoses with those of the corresponding methyl 6-deoxy-β-D-hexopyranosides[17,18]. With regard to this observation, it is to be expected that also the $[M]_D$ values of the basic skeleton *III* of the 1,6-anhydro-β-D-hexopyranoses and methyl 6-deoxy-β-D-hexopyranosides will not differ too much.

EXPERIMENTAL

Melting points were determined on a Boetius micro-melting point apparatus. Optical rotations were measured on an automatic polarimeter Bendix-Ericsson, type 143 A, at 23—25°C. The PMR spectra were taken in deuteriochloroform using a Varian HA-100 with tetrachloromethylsilane as internal standard. For measuring the IR spectra was used a prototype of the Research Institute for Instrumental Technique (Brno). The purity of the substances was checked by thin-layer chromatography and gas chromatography, respectively. Thin-layer chromatography was performed on silica gel in the solvent system benzene–acetone 10 : 1. The detection was effected by spraying with concentrated sulphuric acid and heating. Gas chromatography for analytical and kinetic measurements was carried out in a Chrom III apparatus. As stationary phase was used 15% Carbowax 20M on Chromosorb W. Column length 183 cm, internal diameter 6 mm. Overpressure at the entry into the column 0·53 atm, flow rate 30 ml N_2/min, temperature 132°C. The elution times of the compounds *III*, *X*, and *XVI* were 3·95 min, 5·12 min, and 7·56 min, respectively. The response on the flame-ionisation detector (area ratio of the peaks with the compounds in equal amounts) was in the ratio of 1 : 0·96 : 0·86. When analysing mixtures, the peak areas read off on a planimeter were converted into relative concentrations according to the response of the corresponding compounds.

1,6-Anhydro-2,4-dideoxy-β-D-*glycero*-hexopyranos-3-ulose Ethylenedithioacetal (*II*)

To 1,2-ethanedithiol (1·5 g) were added 2,4-dideoxy ketone[8] (600 mg), dimethyl sulphite (1 g), and boron trifluoride etherate (30 mg). After standing for 10 h at room temperature and adding further ethanedithiol (1 g), the mixture was set aside for an additional 15 h. Then was the reaction mixture diluted with benzene and extracted with 5% NaOH. The deposited solid was filtered off, and the organic layer was separated, extracted with water, and dried over anhydrous magnesium sulphate. Removal of the solvent under reduced pressure gave a residue (360 mg) which was chromatographed in benzene solution on silica gel. The fraction containing the main product was freed from benzene by evaporation, and the residue crystallised from cyclohexane. Yield, 280 mg (29%), m.p. 69—70°C, $[\alpha]_D$ −102° (*c* 0,47; chloroform). For $C_8H_{12}O_2S_2$ (204·3) calculated: 47·03% C, 5·92% H, 31·39% S; found: 47·05% C, 5·87% H, 31·47% S.

1,6-Anhydro-2,3,4-trideoxy-β-D-*glycero*-hexopyranose (*III*)

A) Raney nickel[19] T-1 (4 ml) was five times decanted with 15 ml of ether, then added dithioacetal *II* (280 mg) in ether (5 ml), and the mixture shaken for 1 h. Then was added more Raney nickel (2 ml) in ether (3 ml) and the mixture shaken another hour, whereupon the Raney nickel was filtered off under nitrogen and washed three times with 2 ml of ether. The ethereal solution was concentrated on a short column (c. 3 TP) and the residue distilled at 100 Torr at a bath temperature of 110—120°C. Yield, 65 mg (43%), m.p. 44—48°C, $[\alpha]_D$ −105° (*c* 0·47; water), −115° (*c* 0·41; hexane). For $C_6H_{10}O_2$ (114·1) calculated: 63·13% C, 8·83% H; found: 63·30% C, 8·79% H. PMR spectrum (p.p.m., δ scale, $J_{H,H}$ in Hz): 5·49 (H_1, singlet, w/2 3·5 Hz), 4·48 (H_5, symmetrical multiplet with 9 bands, w/2 10 Hz), 3·95 (H_{6endo}, doublet of doublets, $J_{6en,6ex}$ =

= 6·7; further splittings 1 Hz), 3·76 (H_{6exo}, quartet, $J_{6exo,6en} = 6·5$; $J_{6en5} \approx 5$; further splittings 1 Hz), 1·7 (H_2, H_3, H_4, centre of a complex multiplet). Mass spectrum (measured on a mass spectrometer MCH 1303; reported are peaks with a relative intensity above 15%): *m/e* 114 (32%), 86 (28%), 68 (39%), 67 (19%), 58 (37%), 57 (100%), 55 (19%), 41 (26%), 39 (18%), 29 (27%), 28 (28%), 27 (17%). *B*) Compound *X* (230 mg) in ether (5 ml) was hydrogenated in the presence of 5% platinum on charcoal (70 mg) at room temperature and atmospheric pressure for 1 h. Then was the catalyst filtered off and washed with ether. The ether was removed through a short column (c. 3TP) and the residue distilled at 100 Torr and the bath temperature of 110°C. Yield of compound *III*, 130 mg (56%), $[\alpha]_D$ −105° (*c* 0·90; water). *C*) Hydrogenation of compound *XVI* (10 mg) in ether (0·5 ml) over 5% platinum on charcoal (5 mg) yielded a substance identical by gas chromatography with the trideoxyanhydride *III*. *D*) The dianhydro derivative *XIII* (5 g) in ethanol (50 ml) was hydrogenated in the presence of Raney nickel[19] T-1 (10 ml) at room temperature and normal pressure for 4 h. The solvent was subsequently removed through a short column (c. 3TP) and the residue treated with light petroleum (which was distilled in a column and boiled between 30 and 40°C) to give crystals of 1,6-anhydro-3,4-dideoxy-β-*erythro*-hexopyranose[9] (*XIV*); after recrystallisation from ether–hexane mixture, yield 4·4 g (87%). The mother liquor was concentrated to small bulk on a short column and dissolved in light petroleum. This solution was extracted with water and the aqueous extract several times with carbon disulphide. The carbon disulphide extracts were combined with the light petroleum solution, dried over anhydrous magnesium sulphate, and the solvents removed by distillation through a short column giving a residue which was distilled at 100 Torr at a bath temperature of 110°C. Yield, 70 mg (1·6%) of compound *III*.

1,6-Anhydro-4-O-benzyl-2-deoxy-3-O-*p*-toluenesulphonyl-β-D-*arabino*-hexopyranose (*V*)

To 1,6 : 2,3-dianhydro-4-O-benzyl-β-D-mannopyranose[10] (*IV*) (10 g) in tetrahydrofuran (50 ml) was added lithium aluminium hydride (1·5 g) in tetrahydrofuran (50 ml), and the reaction mixture was left standing for 24 h. Then were added ethyl acetate (10 ml) and, after the reaction was over, 4 ml of water. The precipitated hydroxides were filtered off with suction and washed with chloroform. The resulting solution was evaporated to give crude 1,6-anhydro-4-O-benzyl-2-deoxy-β-D-*arabino*-hexopyranose[11] (10·5 g) which was dissolved in a mixture of pyridine and acetone 1 : 1 (21 ml). To this solution was with stirring and cooling with water added *p*-toluene sulphochloride (11 g) over 10 min. After standing at room temperature for 70 h, the meantime solidified mixture was triturated with water. The deposited material was collected with suction, washed with water and, after drying, recrystallised from ethanol and afterwards from acetone–hexane mixture. Yield, 11·9 g (71%), m.p. 128—129°C (after melting it undergoes decomposition), $[\alpha]_D$ +26° (*c* 1·43; chloroform). Halbych[9] reports m.p. 125°C (decomposition after melting), $[\alpha]_D$ +23° (*c* 0·8; chloroform).

1,6-Anhydro-4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranose (*VI*)

The benzyltosyl derivative *V* (3·9 g) was dissolved in hot benzene (20 ml) and treated with 15 ml of 1M potassium tert-butoxide in tert-butyl alcohol, whereupon the reaction mixture was left overnight. Then it was decomposed with water, the benzene layer separated, and the aqueous layer extracted three times with chloroform. The extracts were combined with the benzene layer, dried over anhydrous magnesium sulphate, and the solvents removed under reduced pressure. The residue dissolved in ether–hexane was put in the refrigerator for crystallisation. Yield, 1·94 g (89%), m.p. 56—57°C, $[\alpha]_D$ +155° (*c* 0·50; chloroform). For $C_{13}H_{14}O_3$ (218·2) calculated: 71·54% C, 6·47% H; found: 71·92% C, 6·67% H.

1,6-Anhydro-4-O-benzyl-2,3-dideoxy-β-D-*erythro*-hexopyranose (*VII*)

To a solution of KOH (50 mg) and compound *VI* (2 g) in ethanol (45 ml) was added 10% palladium on charcoal (0·3 g), and then was the hydrogenation performed at room temperature and atmospheric pressure in the course of 5 h. The catalyst was then filtered off and washed with ethanol. After removing the ethanol under reduced pressure, the residue was dissolved in chloroform and the solution dried over anhydrous magnesium sulphate. The solvent was removed by distillation and the residue crystallised from hexane to give 1·4 g (69%) of *VII*; m.p. 47°C, $[\alpha]_D$ −66° (*c* 0·86; chloroform). For $C_{13}H_{16}O_3$ (220·2) calculated: 70·89% C, 7·32% H; found: 70·99%, 7·41% H.

1,6-Anhydro-2,3-dideoxy-β-D-*erythro*-hexopyranose (*VIII*)

A) Compound *VI* (20 g) dissolved in acetic acid (250 ml) was hydrogenated in the presence of 5 g of 10% palladium on charcoal at room temperature and atmospheric pressure for 4·5 h. The catalyst was then filtered off and the acetic acid removed under reduced pressure over a short column (c. 3TP). The residue was treated with water (25 ml), alkalised, and 15 min refluxed with active charcoal. After filtering off the active charcoal was the solution extracted continuously for 5 h with chloroform. The chloroform extract was dried over anhydrous magnesium sulphate, freed from solvent, and the residue crystallised from ether–tetrachloromethane–hexane to yield 6·8 g (57%) of compound *VIII*; m.p. 65—70°C, $[\alpha]$ −119° (*c* 0·79; water). This substance is identical with an authentic specimen obtained[9] by a different route.

B) Compound *VII* (0·71 g) dissolved in acetic acid (7 ml) was hydrogenated in the presence of 200 mg of 10% palladium on charcoal at room temperature and atmospheric pressure for 4 hours. After filtering off the catalyst and removing the acetic acid under reduced pressure was the residue diluted with water, alkalised with sodium hydroxide, and extracted continuously with ether. The ethereal solution was dried over anhydrous magnesium sulphate and freed from the solvent. Crystallisation of the residue from ether–light petroleum mixture gave 0·27 g (67%) of compound *VIII*.

1,6-Anhydro-2,3-dideoxy-4-O-*p*-toluenesulphonyl-β-D-*erythro*-hexopyranose (*IX*)

To a solution of compound *VIII* (6·8 g) in pyridine (12 ml) was under cooling with water gradually added *p*-toluene sulphochloride (12 g). The reaction mixture was allowed to stand for 20 h, and was then diluted with water to give crystals which were collected with suction, washed with water, and recrystallised from aqueous ethanol. Yield, 13·1 g (88%), m.p. 93°C, $[\alpha]_D$ −72° (*c* 0·73; chloroform). For $C_{13}H_{16}O_5S$ (384·3) calculated: 54·91% C, 5·67% H, 11·28% S; found: 54·70% C, 5·68% H, 11·31% S.

1,6-Anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-3-enopyranose (*X*)

Compound *IX* (2·84 g) dissolved in hot tert-butyl alcohol (6 ml) was treated with 15 ml of 1M solution of potassium tert-butoxide in tert-butyl alcohol, and the mixture refluxed for 30 min. Then water (15 ml) was added and the reaction mixture fractionated on a c. 15 TP column. After the tert-butyl alcohol had passed over, the first 7 ml of the aqueous fraction containing the predominant part of the product were collected. This fraction was extracted three times with 5 ml of dichloromethane, the extract dried over anhydrous magnesium sulphate, and the solvent removed by distillation. The residue was distilled at 50 Torr to give substance *X* (0·72 g; 64%, which, according to gas chromatography, contained about 3% of compound *XVI* as admixture) Compound *X* can be freed from this admixture by standing in chloroform of usual commercial quality for 24 h, removal of the solvent and subsequent distillation of the residue: $[\alpha]_D$ −177°

(*c* 0·41; water); b.p. 75°C/50 Torr (b.p. of the racemate[6] 69—69·5°C/41 Torr). The PMR spectrum is consistent with that of the racemate[6]. For $C_6H_8O_2$ (112·1) calculated: 64·27% C, 7·19% H; found: 64·27% C, 7·38% H. IR spectrum: ν(C=C) 1 640 cm^{-1} (tetrachloromethane). PMR spectrum (deuteriochloroform, p.p.m., δ scale, $J_{H,H}$ in Hz): 6·03 (H_4, $J_{4,3} = 10·0$, $J_{4,5} = 4·5$, $J_{4,2ax} = 1·9$, $J_{4,2e} = 1·9$), ≈ 5·66 (H_1, $J_{1,2ax} = 2·5$, $J_{1,2e} = 0·8$, $J_{1,3} = 1·8$, $J_{1,6endo} \neq 0 < 0·5$, $J_{1,6exo} \neq 0 < 1$), 5·65 (H_3, $J_{3,4} = 10·0$, $J_{3,2ax} = 2·7$, $J_{3,2e} = 3·8$, $J_{3,1} = 1·8$), 4·59 (H_5, $J_{5,4} = 4·5$, $J_{5,6endo} = 0·6$, $J_{5,6exo} = 4·2$), 3·99 (H_{6endo}, $J_{6exo,6endo} = 6·3$, $J_{6endo,5} = 0·6$, $J_{6endo,1} \neq 0 < 0·5$), 3·74 (H_{6exo}, $J_{6exo,6endo} = 6·25$, $J_{6exo,5} = 4·15$, $J_{6exo,2ax} = 1·4$, $J_{6exo,2e} = 0·85$, $J_{6exo,1} \neq 0 < 1$), 2·53 (H_{2e}, $J_{2e,1} = 0·8$, $J_{2e,2ax} = 17·7$, $J_{2e,3} = 3·6$, $J_{2e,4} = 1·9$, $J_{2e,6exo} = 0·9$), 2·05 (H_{2ax}, $J_{2ax,1} = 2·5$, $J_{2ax,2e} = 17·7$, $J_{2ax,3} = 2·5$, $J_{2ax,4} = 1·9$, $J_{2ax,6exo} = 1·5$, $J_{2ax,5} = 0·5$).

1,6-Anhydro-4-deoxy-3-O-methanesulphonyl-2-O-*p*-toluenesulphonyl-β-D-*xylo*-hexopyranose (*XII*)

To a solution of 1,6-anhydro-4-deoxy-2-O-toluenesulphonyl-β-D-xylo-hexopyranose[12] (*XI*) (14 g) in pyridine (30 ml) was under cooling with water dropwise added methane sulphochloride (5·4 ml). The mixture was allowed to stand for 16 h and then stirred with water. The produced crystals were collected with suction, washed with water and recrystallised from ethanol. Yield, 16·6 g (94%), m.p. 140°C, $[\alpha]_D$ −33° (*c* 1·66; chloroform). For $C_{14}H_{18}O_8S_2$ (378·4) calculated: 44·43% C, 4·79% H, 16·95% S; found: 44·39% C, 4·88% H, 16·87% S.

1,6 : 2,3-Dianhydro-4-deoxy-β-D-*ribo*-hexopyranose (*XIII*)

To a solution of compound *XII* (20 g) in tetrahydrofuran (200 ml) was added a methanolic solution (100 ml) of sodium methoxide prepared from 5 g of natrium. The reaction mixture was kept for 2·5 h at 40°C, and after cooling were the sulphonates filtered off with suction. The filtrate was concentrated under reduced pressure to about 50 ml, treated with water (150 ml), neutralised with diluted sulphuric acid, and extracted with dichloromethane. The extract was dried over magnesium sulphate, and dichloromethane removed by distillation. The residue was crystallised from ether–light petroleum. Yield, 5·4 g (80%), m.p. 65—66°C, $[\alpha]_D$ +33° (*c* 1·2; water), in agreement with the literature[12].

1,6-Anhydro-2,3,4-trideoxy-β-D-*glycero*-hex-2-enopyranose (*XVI*)

To a solution of 0·4 g natrium in 10 ml of 96% ethanol was added compound *XV* (3·1 g; m.p. 87—88°C, $[\alpha]_D$ −42° (*c* 0·8; chloroform)) prepared by *p*-toluenesulphonation of *XIV* according to Halbych and Černý[9]. The mixture was heated under reflux for 2 h at a bath temperature of 100—110°C, then cooled, treated with water (20 ml) and distilled in a column of c. 15 TP. After ethanol had passed over, the aqueous fraction (about 10 ml) was collected and extracted four times with dichloromethane. The extract was dried over anhydrous magnesium sulphate, freed from solvent, and the residue distilled under reduced pressure. Yield, 170 mg (14%), b.p. 80—85°C/50 Torr, $[\alpha]_D$ +137° (*c* 0·67; water); on gas chromatography it shows one peak. IR spectrum: ν(C=C) 1 641 cm^{-1} (tetrachloromethane). The PMR spectrum was identical to that of the DL-form[4] (ref.[4–6] give b.p. 58°C/15 Torr; 83—84°C/51·5 Torr; 84°C/50 Torr; IR spectrum: ν(C=C) 1 638 cm^{-1}). PMR spectrum (deuteriochloroform, p.p.m., δ scale, $J_{H,H}$ in Hz): 5·91 (H_2, $J_{2,3} \approx 10$, $J_{2,1} = 3·2$, $J_{2,4e} = 1·2$, $J_{2,4ax} \neq 0 < 1$), 5·72 (H_3, $J_{3,2} \approx 10$, $J_{3,4ax} = 4·2$, $J_{3,4e} = 4·0$, $J_{3,1} \neq 0 < 1$), 5·48 (H_1, $J_{1,2} = 3·2$, $J_{1,3} \neq 0 < 1$), 4·64 (H_5, $J_{5,4ax} = 4·2$, $J_{5,4e} = 1·0$, $J_{5,6endo} = 2·05$, $J_{5,6exo} = 5·9$), 3·97 (H_{6exo}, $J_{6exo,6endo} = 7·2$, $J_{6exo,5} = 5·9$,

$J_{6exo,4ax} = 2{\cdot}0$, $J_{6exo,1} \neq 0 < 1$), 3·70 (H_{6endo}, $J_{6endo,6exo} = 7{\cdot}2$, $J_{6endo,5} = 2{\cdot}05$, $J_{6endo,1} \approx \approx 0$), 2·78 ($H_{4ax,4e} = 17{\cdot}7$, $J_{4ax,5} = 4{\cdot}2$, $J_{4ax,3} = 4{\cdot}2$), 1·87 (H_{4e}, $J_{4e,4ax} = 17{\cdot}7$, $J_{4e,3} = = 4{\cdot}0$, $J_{4e,5} = 1{\cdot}0$, $J_{4e,2} = 1{\cdot}2$). The residue from distillation over the column was extracted continuously with chloroform, the extract dried over anhydrous magnesium sulphate, freed from the solvent, and the residue crystallised from ether–light petroleum to give 0·6 g (42%) of compound *XIV*.

Isomerisation of Compounds *X* and *XVI*

To 1·5 ml of a 1-molar solution of potassium tert-butoxide in tert-butyl alcohol was added at 50°C compound *X* or *XVI* (15 mg), and at intervals were withdrawn samples of the reaction mixture (with compound *X* after 60 min, with compound *XVI* after 30 min). 0·1 ml of the sample of the reaction mixture was diluted with 0·2 ml of water and extracted three times with 0·1 ml of dichloromethane. The extract was dried over anhydrous magnesium sulphate and analysed by gas chromatography. The ratio of the concentrations of the isomer and the starting compound was determined as a function of time; it was verified that within the experimental error, the extracting procedure is without any effect upon the ratio of concentrations of the two compounds. The reaction was performed to a conversion of 2–6%.

Hydrogenation of Compounds *X* and *XVI*

Approximately 15 mg of each compound (*X* and *XVI*) were dissolved in 1 ml of ether, then was added 5% platinum on charcoal (10 mg), and hydrogenated at room temperature and atmospheric pressure. At intervals (after c. 3 min) were from the mixture withdrawn samples and these gas chromatographically analysed. The reaction was performed up to 95% conversion of the mixture into compound *III*. The evaluation was carried out by using the relation:

$$K = k_{XVI}/k_X = \frac{\log (1 + x_0^{-1}) - \log (1 + x^{-1} + x_1)}{\log (1 + x_0) - \log (1 + x + x_2)},$$

where K is the ratio of the rate constants, $x = c_1/c_2$, $x_0 = c_{10}/c_{20}$, $x_1 = c/c_1$, $x_2 = c/c_2$, and c_1 and c_2 are the momentary and c_{10} and c_{20} the initial concentrations of the substances *XVI* and *X*, and c the concentration of substance *III*. The ratio of the rate constants, K, is 1·47 and is independent of the degree of conversion.

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