Synthesis of Unsaturated Sugars containing Vinylic Substituents

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WE report the synthesis of novel unsaturated sugar derivatives of the vinyl thioether and vinyl azide types by elimination reactions. Reaction of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside[1] (I) with sodium thiophenoxide in refluxing methylcellosolve for 1½ hr. afforded the syrupy phenyl thioether derivative (IIa) as the main product. The position of attachment and hence the expected D-*altro* configuration was established by reductive desulphurization of the corresponding syrupy 3-*O*-methyl ether (IIc), which gave crystalline methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-α-D-*ribo*-hexopyranoside, m.p. 88—90°, $[\alpha]_D^{25}$ 111° (*c*, 1·05, $CHCl_3$).† This

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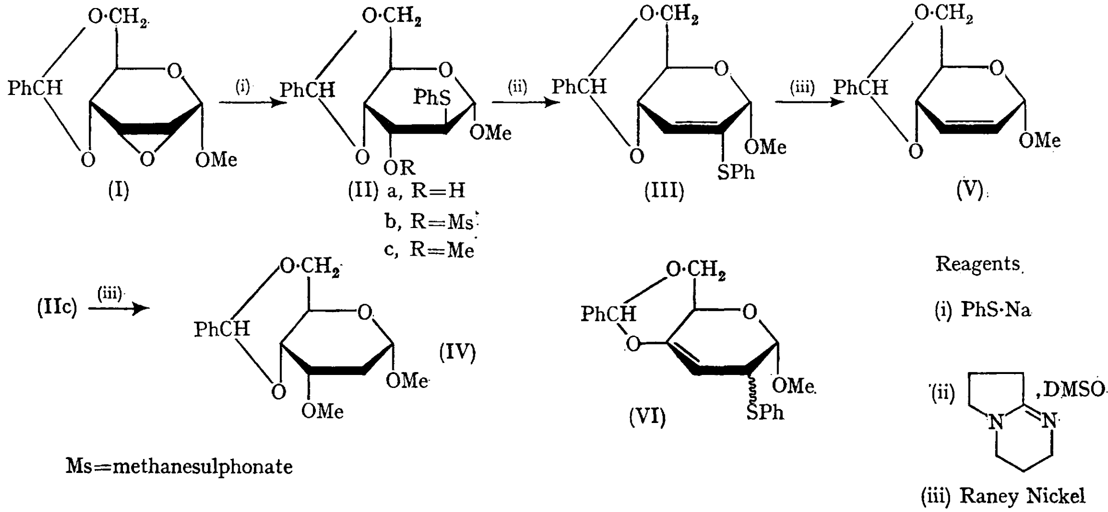
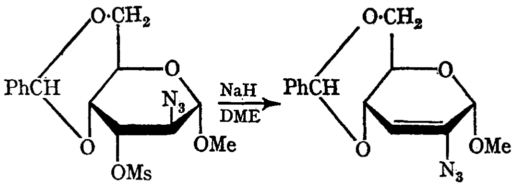
† Melting points are uncorrected. Crystalline compounds gave correct elemental analyses and had spectral properties (i.r., n.m.r., mass) consistent with their structures. V.p.c. analyses were performed using a 3% OV-17 column packing (Applied Science Laboratories, State College, Pennsylvania). Mass spectra were obtained by courtesy of Dr. D. C. DeJongh, Wayne State University, Detroit, Michigan [compounds (III), (V), (X)].



Ms=methanesulphonate

apparently represents the first example of the opening of an epoxide in a cyclic sugar derivative with thiophenoxide ion. Treatment of the crystalline methanesulphonate (IIb), m.p. 130—131°, $[\alpha]_D^{25}$ 79·5° (*c*, 0·994, $CHCl_3$) with 1,5-diazabicyclo-[4,3,0]-5-nonene[2] in dry dimethyl sulphoxide (DMSO) (65—70°, 2·5 hr.) afforded a > 90% yield of crystalline methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-phenylthio-α-D-*erythro*-hex-2-enopyranoside (III), m.p. 145°, $[\alpha]_D$ − 84·5° (*c*, 1·04, $CHCl_3$); λ_{max} 246 mμ (EtOH, ϵ 7·4 × 10^3), τ 4·18 (vinyl H, apparent s), 5·2 (C-1 H, s), 6·57 (OMe). The structure of (III) was evident from n.m.r. and mass spectral data; M^+ 356, m/e 325 (M − OMe), *etc.* Reductive desulphurization of (III) afforded a crystalline mixture which was separated by chromatography into compound (V),[3,4] m.p. 116—117°, and starting material. A plausible mechanism for the formation of (III) involves a C-2 carbanion intermediate stabilized by the phenylthio-group. The elimination reaction could be effected even in the presence of sodium hydrogen carbonate in refluxing benzene. However, this required entended reaction periods and the yields were much lower (15%). A crystalline by-product in this reaction was identified as (V) which indicates the possibility of mixed mechanisms, since both C-2 and C-3 substituents are lost. Trace amounts of (V) were also detected in the diazabicyclononene reactions. The effectiveness of this base in this type of elimination is especially significant when one considers that in the presence of sodium hydride in refluxing 1,2-dimethoxyethane (DME), the product of elimination was invariably a mixture of (III) and the isomeric (VI) (τ 4·18 vinyl H, 6·47 OMe) presumably formed by allylic rearrangement. Both types of unsaturated sugar derivatives (containing SMe or SCH_2Ph groups at C-2) are formed in such base-catalysed elimination reactions.[5]

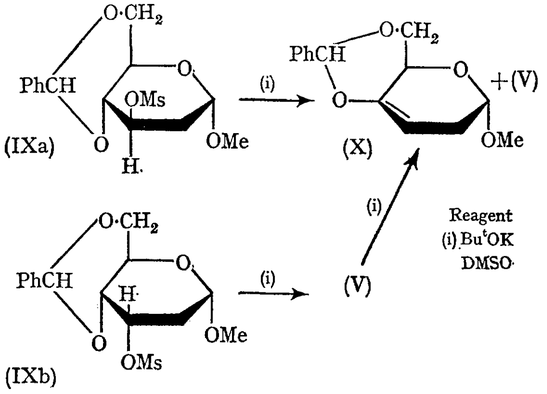
Treatment of methyl 2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulphonyl-α-D-altropyranoside[6] (VII) with excess of sodium hydride in refluxing DME (2·5—3 hr.) afforded a 35% yield of the highly crystalline methyl 2-azido-4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (VIII), m.p. 143—144°; $[\alpha]_D^{25}$ 88° (*c*, 0·826, $CHCl_3$); λ_{KBr} 2120 cm.$^{-1}$, azide; 1652 cm.$^{-1}$, C=C; τ 4·3 (vinyl H, unresolved), 5·2 (OMe). Other products were demesylated starting material, unchanged reactants, and a small amount of (V). In the presence of diazabicyclononene in dimethyl sulphoxide at 70° (or at 115°) (18 hr.), compound (VII) afforded a larger proportion of (V) in addition to some of the expected (VIII) and unreacted (VII). The formation of the vinyl azide (VIII) is in itself interesting from a mechanistic viewpoint especially if a carbanion intermediate is postulated. The loss of both azide and methanesulphonyloxyl groups in these base-catalysed eliminations implies



(VII) (VIII)

the possibility of mixed mechanisms. The formation of (V) is reminiscent of a similar observation made by Guthrie and Murphy[7] when compound (VII) was treated with hydrazine. It is of interest to comment briefly on the spectral properties of compound (VIII). Alkyl azides [such as (VII), *etc.*] have a weak absorption at *ca.* 287 mμ attributed to the $\pi \rightarrow \pi^*$ transition, and a stronger absorption band below 220 mμ. The spectrum of (VIII) in ethanol exhibits a strong absorption band at 243 mμ (ϵ 1×10^4), which is a manifestation of the possible activating effect of the double bond. It is also interesting to note that the vinyl azide (VIII) appears to be the first example of its kind in a six-membered ring, since efforts to prepare 1-azidocyclohexane have been unsuccessful.[8] With the objective of isolating an azirine derivative, solutions of (VIII) were irradiated at 3000 Å in a variety of solvents. Unfortunately the major product was an unidentifiable amorphous solid. Two crystalline substances were also isolated (< 1% yield) and are being presently investigated. The unsaturated sugars (III) and (V) are also photochemically unstable (3000 Å).

In the demethanesulphonyloxylation of the epimeric methanesulphonates (IXa)[9] and (IXb),[9,10] in the presence of potassium t-butoxide in dimethyl sulphoxide, in both cases elimination was complete at room temperature within 3 hr. In the case of (IXa) the product was a crystalline mixture which consisted of (X)[11] and (V) (2 : 1 ratio, by v.p.c. analysis). However, in the case of (IXb) where a *trans*-diaxial arrangement prevails between one of the C-2 protons and the C-3 substituent, the product was almost exclusively (V) [79% yield, 98% of (V) and 2% (X) by v.p.c. analysis].



Almost complete isomerization of (V) to (X) could be effected in the presence of Bu^{t}OK (2 days, room temperature). Compound (V), however, remained unaffected in the presence of the diazabicyclononene in dimethyl sulphoxide and was recovered unchanged after 1 hr. at 125°.

(*Received, April 16th,* 1968; *Com.* 465.)

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