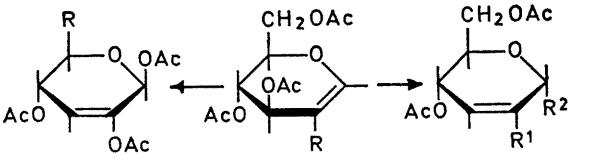
Allylic Isomerisations of Unsaturated Carbohydrate Derivatives. A New Approach to the Synthesis of Amino, Thio, and Branched-chain Sugars

By R. J. FERRIER*† and N. VETHAVIYASAR

(*Department of Chemistry, Birkbeck College, University of London, Malet Street, London* WC1E 7HX)

Summary 2,3-Unsaturated hexopyranoside derivatives with azido-, thiocyanato-, vinyloxy-, and (methylthio)-thiocarbonyloxy-groups at C-4 rearrange thermally to give 3,4-unsaturated isomers with azido-, isothiocyanato-, acetaldehydo-, and (methylthio)carbonylthio-groups attached to C-2; the asymmetry of C-4 in the initial compounds is transmitted to C-2 during the isomerisations.

1,2-UNSATURATED cyclic carbohydrates, *e.g.* tri-*O*-acetyl-D-glucal (I) and its 2-acetoxy-derivative (II), in the presence of acid catalysts, can be converted into 2,3-unsaturated glycosyl compounds (III), *e.g.* glycosides[1] and nucleosides,[2] with high stereospecificity in reactions which offer a novel approach to the synthesis of saturated compounds of biochemical significance. In addition, for example, the 1,2-unsaturated compound (II) can be caused to isomerise thermally to the 2,3-unsaturated ester (IV) in a reaction believed to proceed by the S_Ni' mechanism.[3] Such allylic isomerisations at other sites of carbohydrates are not well known, although 1,2,4-tri-*O*-acetyl-3-deoxy-β-D-*glycero*-pent-2-enopyranose (V) apparently rearranges to a 3,4-unsaturated compound prior to fragmentation in the mass

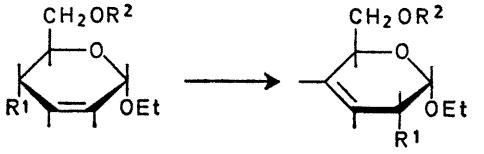


(IV) R = CH_2OAc (I) R = H (III) R^1 = H or OAc;
(V) R = H (II) R = OAc R^2 = alkoxy, acyloxy, purinyl *etc.*

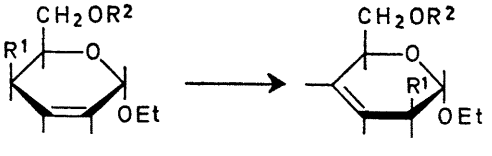
spectrometer,[4] and we report here the isomerisation of several 2,3-unsaturated glycoside derivatives bearing various allylic groups which contain the general structural feature C-4–X–Y=Z and which can take part in allylic rearrangements involving six-membered cyclic transition

† Present address: Department of Chemistry, Victoria University of Wellington, New Zealand.

states or intermediates.[5] By this means, 2,3-unsaturated derivatives [(VI)—(IX) and (XIV)—(XVII)] obtained from the readily available tri-*O*-acetyl-D-glucal have been converted into 3,4-unsaturated isomers [(X)—(XIII) and (XVIII)—(XXI)], new functionality has been introduced at C-2, and the potential of unsaturated carbohydrate compounds as intermediates in the synthesis of saturated analogues has been extended.



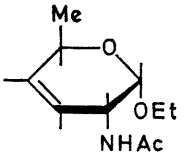
	R^1	R^2			R^1	R^2
(VI)	N_3	$MeSO_2$	⟶	(X)	N_3	$MeSO_2$
(VII)	SCN	$MeSO_2$	⟶	(XI)	NCS	$MeSO_2$
(VIII)	O·CH=CH_2	CO·C_6H_4·NO_2	⟶	(XII)	CH_2·CHO	CO·C_6H_4·NO_2
(IX)	O·CS·SMe	O·CS·SMe	⟶	(XIII)	S·CO·SMe	O·CS·SMe



	R^1	R^2			R^1	R^2
(XIV)	N_3	$MeSO_2$	⟶	(XVIII)	N_3	$MeSO_2$
(XV)	SCN	$MeSO_2$	⟶	(XIX)	NCS	$MeSO_2$
(XVI)	O·CH=CH_2	Bz	⟶	(XX)	CH_2·CHO	Bz
(XVII)	O·CS·SMe	O·CS·SMe	⟶	(XXI)	S·CO·SMe	O·CS·SMe

The azides (VI) and (XIV) and the thiocyanates (VII) and (XV) were prepared from the corresponding 4,6-dimethanesulphonates by nucleophilic displacements using sodium azide and potassium thiocyanate in *NN*-dimethylformamide at, or close to, room temperature. Reactions occurred preferentially at the secondary, allylic positions (4-H resonances affected specifically), without rearrangement of the double bonds (1-H coupled to the vinylic protons, and m.s. fragmentations caused loss of the O_R, C-5, and C-6 sections of the molecules[4]), and with configurational inversion at C-4 (change in signs of optical rotations; consistent $J_{4,5}$ values).[6] Direct substitutions were used in the preparations of the vinyl ethers (VIII) and (XVI)[7] and the xanthate esters (IX) and (XVII).[8]

in products (XI) and (XIX) were identified by their broad absorptions near 2100 cm^{-1} (thiocyanates give sharp absorptions near 2160 cm^{-1}), the substituted acetaldehyde groups in compounds (XII) and (XX) by appropriate n.m.r. signals and by the reducing properties, and the (methylthio)-carbonylthio-groups in the esters (XIII) and (XXI) by the upfield shifts [1·65 and 1·8 p.p.m. relative to 4-H in compounds (IX) and (XVII)] of the ester (2-H) protons. Furthermore, the products fragmented by loss of ethyl formate in the mass spectrometer, indicating that the double bonds were at position 3,4.[4]



(XXII)

As is to be expected from the symmetry of the azido-group, the azide reactions did not proceed to completion. Nevertheless, from the equilibrium mixture of compounds (VI) and (X) the 3,4-unsaturated acetamido-derivative (XXII) was isolated following lithium aluminium hydride reduction and acetylation; it was also obtained from the isothiocyanate (XI) by treatment with boiling acetic anhydride in the presence of sodium acetate followed by

The isomerisation of hex-2-enopyranosides to hex-3-enopyranosides

Compound	Conditions for reaction: Temperature (°)	Time (h)	Solvent	Product	Yield (% isolated)
(VI)	140	4	$HCONMe_2$	(X)	—
(VII)	140	6	$HCONMe_2$	(XI)	52
(VIII)	185	3·5	$PhNO_2$	(XII)	75
(IX)	140	2	$HCONMe_2$	(XIII)	37
(XIV)	100	1·5	PhMe	(XVIII)	—
(XV)	100	1·0	PhMe	(XIX)	>83
(XVI)	180	0·6	$PhNO_2$	(XX)	70
(XVII)	120	1	PhMe	(XXI)	100

The isomerisations were effected under the conditions given in the Table, were followed by t.l.c., and were all characterised by changes in the signs of the optical rotations: this is consistent with expectations for such suprafacial allylic rearrangements.[9] The isothiocyanate groups

reductive removal of the methanesulphonyloxy-group. On the other hand, the thiocyanate–isothiocyanate isomerisations and the Claisen rearrangements proceeded cleanly and apparently to completion; in the same way, the *threo*-bis-xanthate (XVII) reacted smoothly but the *erythro*-isomer (IX) gave two products, the second having apparently been formed by attack of the thiomethyl sulphur atom at C-2 and loss of carbon oxysulphide.

Presumably the greater reactivity of the *threo*-compounds (XIV—XVII) in reactions of this type (Table) follows from the *quasi*-axial orientation of their C-4 substituents and the consequent relative ease with which cyclic transition states such as are involved in the [3,3]-sigmatropic shift reactions can be formed.

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