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REDUCTIVE REARRANGEMENT OF ALLYLIC ACETALS (HEX-2-ENOPYRANOSIDES) TO VINYL ETHERS (GLYCALS) BY LAH: GEOMETRY OF THE SUBSTRATE AND REACTION SPECIFICITY[1]

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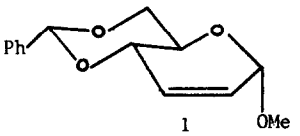
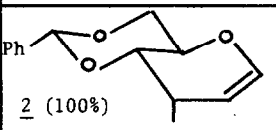
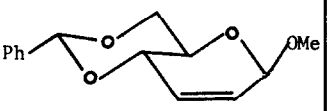
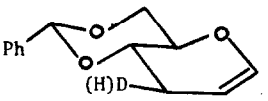
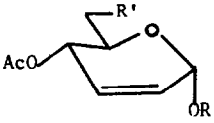
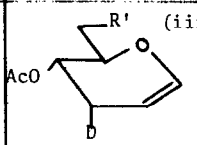
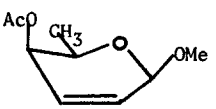
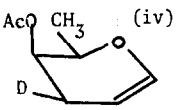
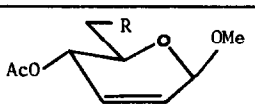
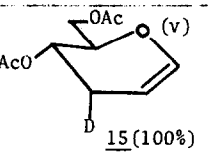
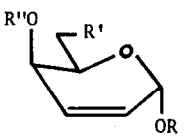
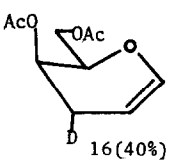
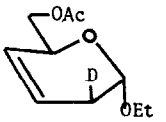
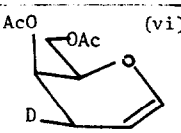
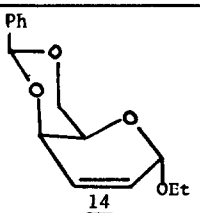
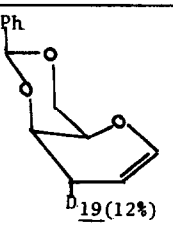
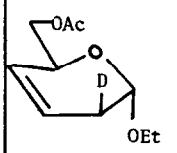
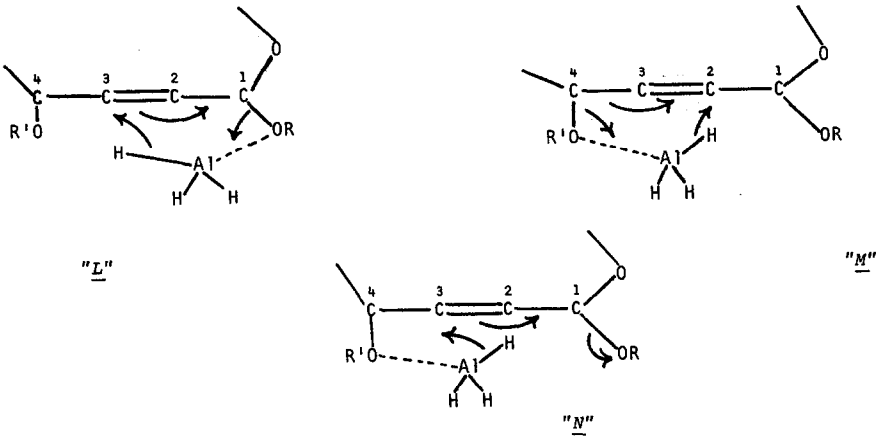
A recent report from this laboratory described the reaction in which unsaturated acetals are reductively rearranged to vinyl ethers by chloride-free LAH in ethereal solvents [2]. The value of this reaction is evident from its use for stereospecific syntheses of the epimeric 2-monodeuterated 2-deoxyriboses [3], which were subsequently employed to establish the stereochemistry of nucleotide deoxygenation [4]. A recent report by Achmatowicz and Szechner [5] offers a valuable extension of our initial observations; however we wish to clarify three aspects of their report which imply (a) that syn-relationship of both allylic oxygens is required for rearrangement, (b) that C-4 control (via "*N*") is preferred, and (c) that the rearrangement is stereospecific only when the C 4 hydroxyl group is free. In addition we report herein the reductive rearrangement of two "ordinary" allylic alcohols, 20 and 21, in which the oxygen lost is not a part of an acetal function.

The items (a), (b) and (c) above, fall within the purview of three mechanistic headings: Substrate Geometry, Transition State Geometry and Reaction Specificity respectively, and we will examine these below.

Substrate Geometry: Achmatowicz and Szechner report that the syn-isomers 5 and 6 are arranged to 9 and 10 respectively in ether and LAH at room temperature, whereas anti-isomers 7 and 8 are not rearranged. In our experience[2], syn-isomer 1 is rearranged readily to 2 in ether, but the anti-isomer 3 requires refluxing dioxan as solvent before the rearrangement-proceeds at a useful rate. Accordingly we examined the anti-isomers 12, 13[6] and 14[6] in refluxing dioxan. All three were rearranged in 30h, 4h and 4h respectively (Chart) thereby indicating that 1,4-anti-relationship is not a barrier to the process. The products were readily identifiable[6] and the difference in rate will be commented upon below.

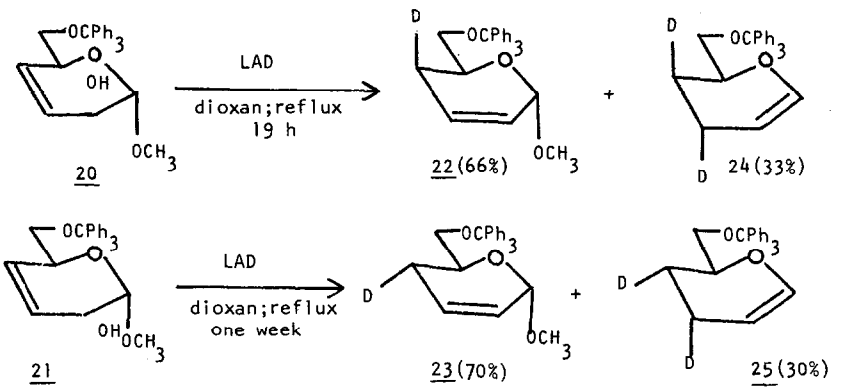
Transition-State Geometry: The orientation of deuterium in the products from LAD reactions, provides a clue to the allylic oxygen (C-1 or C-4) exercising control via transition state "L", "*N*" or "*N*". For this purpose, compounds 1,5 and 6 are unhelpful since both oxygens are syn-

SUBSTRATE	Time[13] (hrs)	PRODUCTS[6,12] C - 1 Control "L"	C - 4 Control "M"	C - 4 Control "N"
 1	0.5	 2 (100%)		(i)[2]
 3	20	 4 (100%)		(ii)[2]
 5 R = Me;R' = H 11 R = Et;R' = OAc	2.5			 (iii)[2,5] 9 R = H 15 R = OAc (100%)
 6				 (iv)[5] 10
 7 R = H 12 R = OAc	30			 (v) 15 (100%)
 8 R = Me; R' = H; R'' = OAc 13 R = Et; R' = R'' = OH	4	 16 (40%)	 17 (20%)	 (vi) 18 (40%)
 14	4	 19 (12%)	 17 (88%)	(vii)



related. However, the anti-isomers 3, 12, and 13 allow discrete diagnosis, as the results in the Chart indicate. The results from 13 and 14 show that several modes of control are operable in a given substrate. Thus products 16 and 19 are formed by C-1 control via transition state *"L"* however products 17 and 18 are both formed by C-4 control, but by different transition states - *"M" and "N"* respectively.

The operation of transition state *"L"* in the reactions of 1 and 3 also provides a rationalization for the slowness of 3, since 3 would have to assume a boat conformation for the methoxy-allane complex to be optimally poised for delivery of the hydride ion to carbon-3. The failure of C-4 control via *"N"* in 3 (which would have produced some 2) is understandable, since the trans-fused benzylidene ring would not readily accommodate such a transition state. Similar reasoning accounts for the sluggishness of 12 as compared with 13 and 14.



Reaction Specificity: This aspect must be considered with respect to the transition state involved "*L*", "*M*", *or* "*N*". In equations (i) and (ii), the products (2 and 4) indicate that the reactions are both stereo- and regio-specific. Similarly in equation (vii), the reactions giving 19 and 17 are both stereo-and regio-specific for the oxygen exercising control in the transition state, C-1 and C-4 respectively. The dilemma of the epimers 16 and 18 (equation (vi) arises because C-4 control of 13 while being stereospecific is not regiospecific. The data in the chart indicate that allylic hydroxyl groups (generated in situ) show a predilection for a 5-centre.

The formation of 17 from 13 implied that an "ordinary" allylic alcohol would give the rearranged olefin under the reaction conditions. Indeed the "ordinary" allylic alcohols 20 and 21 readily gave the rearranged olefins 22[6] and 23[6]. As expected these substances were further transformed under the reaction conditions to the glycals 24[6] and 25[6]. These results indicate that for 20 and 21 (at least) the 2-phenyl substituent found necessary for comparable rearrangement of acylic allylic systems is not required.[11] Experiments are underway to see what other systems may be prone to this reductive rearrangement.

[1] Supported by grants from the National Research Council of Canada and Bristol Laboratories.

[2] B. Fraser-Reid and B. Radatus, J.Amer. Chem. Soc., 92, 66661 (1970).

[3] B. Radatus, M. Yunker and B. Fraser-Reid, ibid., 93 3086 (1971).

[4] B. Fraser-Reid and B. Radatus, ibid., 93, 6342 (1971).

[5] O. Achmatowicz and B. Szechner, Tetrahedron Letters., 1205 (1972).

[6] All new compounds satisfactory elemental and/or mass spectral analysis and their spectroscopic parameters were in complete agreement with those of suitable models [2,5]

[7] G. Stork and W.N. White, J. Amer. Chem. Soc., 78 4609 (1956); C.W. Jefford, S.N. Mahajan and J. Gunsher, Tetrahedron, 24, 2921 (1968).

[8] A close parallel exists with photosensitised oxygenation of allylic systems, where the hydrogen being ejected is preferably axial [9]

[9] A. Nickon, V.T. Thuang, P.J.L. Daniels, R.W. Denny, T.B. Di Giorgio, J. Tsunetsuga, H.G. Vilhuber and E. Werstiuk, J. Amer. Chem. Soc., 94, 5517 (1972); A. Nickon and W. Mendelson, Can. J. Chem., 43 1419 (1956).

[10] PhCHDOH was isolated from the reaction with 14 and LAD.

[11] W.T. Borden and M. Scott, Chem. Comm., 381 (1971); W.T. Borden, J. Amer. Chem. Soc., 92, 4898 (1970)

[12] With exception of 5 and 6 [5] all compounds were rearranged in refluxing dioxan with LAD. Only the cyclic rearrangement products are shown. Acyclic vinyl ethers are sometimes produced [2] but are usually very minor products. The percentages are referred to the total cyclic glycals isolated by column chromatography. In equations (iii) to (vii), the reduction products were acetylated prior to isolation.

[13] Reactions with LAD are usually much slower than with LAH [2]; see also E.L. Eliel , B.E. Nowak, R.A. Daignault and V.G. Badding, J. Org. Chem., 30, 2441, 2448 (1965).