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REDUCTIVE REARRANGEMENT OF 2,3-UNSATURATED METHYL PYRANOSIDES TO 3-DEOXY GLYCALS

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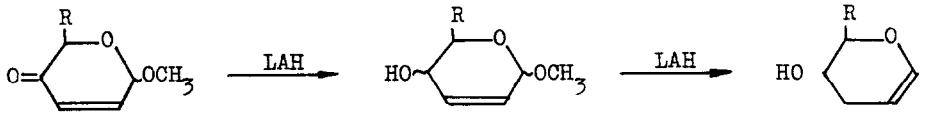
In the course of our studies on a total synthesis of monosaccharides[1)] we have noticed[1c)], during the LAH reduction of methyl 2,3-dideoxy-DL-pent-2-enopyranosid-4-ulose (1) and methyl 2,3-dideoxy-DL-hex-2-enopyranosid-4-ulose (2), that besides the expected 2,3-unsaturated methyl pyranosides 3 and 4, in a consecutive reaction (tlc) 3-deoxy glycals 5 and 6 are formed.



1 R=H
2 R=CH_3

3 R=H
4 R=CH_3

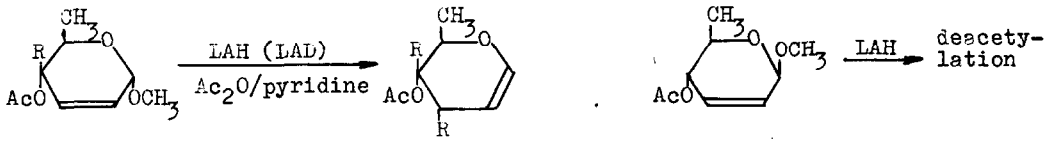
5 R=H
6 R=CH_3

This unusual transformation of 2,3-unsaturated methyl pyranosides into 3-deoxy glycals by LAH treatment was recently described by Fraser-Reid et al.[2)], who have shown its high stereoselectivity and applied this reaction to the elegant synthesis of the stereospecifically deuterated 2-deuterio-2-deoxy-D-ribose[3)]. In this note we report the results of the LAH reduction of acetates[4)] of four diastereomeric methyl 2,3,6-trideoxy-DL-hex-2-enopyranosides 7, 8, 9 and 10, which suggest steric requirements of the above mentioned pseudoglycal ⟶ 3-deoxy glycal rearrangement. Preparation of compounds 7, 8, 9 and 10 has been described before[1a)]. Derivative 11, deuterated at C-4 was obtained analogously to 7 by reduction of 2 with LAD and subsequent acetylation. Stirring of acetate 7 with 3 equiv. of LAH in

ether at room temperature after 10 hrs brought the reaction to completion (tlc) affording 3-deoxy glycal, which was converted into its acetate 12 (acetic anhydride - pyridine mixture and chromatography over silica gel column), bp.$_{15mm}$70° (air bath), yield 70%, (Found:C, 61.76; H, 7.89, $C_8H_{12}O_3$ requires: C, 61.52; H, 7.75%); ir (film) 1735, 1235 (acetate), 1650, 1050 (vinyl ether) cm^{-1}.

In a similar manner to the foregoing (LAH reduction was completed after 3 days) acetate 10 was converted to 4-O-acetyl-3-deoxy glycal 13 with configuration threo, bp.$_{15mm}$70° (air bath), yield 50%, (Found: C, 61.39; H, 7.99, $C_8H_{12}O_3$ requires: C, 61.52; H, 7.75%); ir (film) 1740, 1240 (acetate), 1660, 1070 (vinyl ether)cm^{-1}.

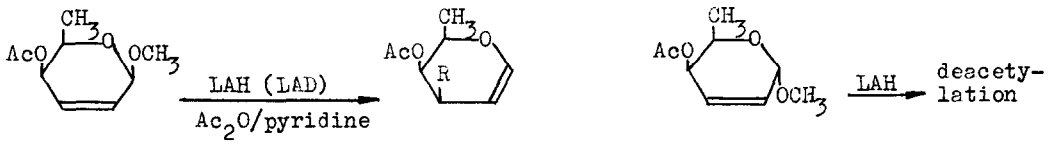
In contrast to the facile pseudoglycal ⟶ 3-deoxy glycal rearrangement of 7 and 10, methyl 4-O-acetyl-2,3,6-trideoxy-DL-hex-2-enopyranosides β-erythro (8) and α-threo (9) after 7 days stirring (3 equiv. LAH, ether, room temperature) gave no trace (tlc) of 3-deoxy glycals, only reduction of an ester group took place.



7 R=H
11 R=D

12 R=H
14 R=D

8

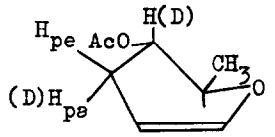


10

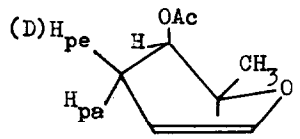
13 R=H
15 R=D

9

From the magnitude of the coupling constant J_{45}=6.6 Hz in 12, and the sum of coupling constants $J_{3pa4} + J_{3pe4}$=9.0 Hz in 13 (Table) it follows that these compounds predominantly exist in the depicted conformations, i.e. with axial H-5 and equatorial H-4 (for H-4 axial the sum of coupling constants amounts to ~13.3 Hz, cf. spectrum of 12) for 13, and with axial H-5 and axial H-4 for 12.



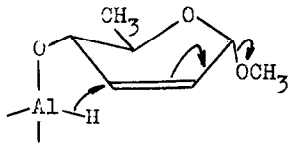
12 (14)



13 (15)

In the pmr spectrum of 12 the signal at δ 2.00 with larger J_{34} splitting have been assigned to the pseudoaxial hydrogen and at δ 2.38 with smaller J_{34} to pseudoequatorial[5]. For compound 13 applying qualitatively the relation developed by Garbisch[6], on the basis of magnitudes of vicinal and allylic couplings with olefinic protons the signal at δ 2.35 and 2.04 have been assigned to pseudoaxial and pseudoequatorial hydrogens respectively. With the aid of the foregoing assignments the steric course of an approach of the incoming hydride ion have been demonstrated by examining the pmr spectra of LAD reduction and subsequent acetylation products of 10 and 11. Configuration of deuterium on C-3 in compounds 14 and 15 followed from the disappearance of signals corresponding to $H\text{-}3_{pa}$ and $H\text{-}3_{pe}$ respectively.

High stereoselectivity and stereospecificity[7] of the studied reaction may be rationalized as follows. After reduction of an ester group alkoxyaluminum hydride derivative is formed, which in case of compounds 7 and 10 undergoes an intramolecular hydride displacement of methoxyl group in a concerted process according to the abnormal bimolecular mechanism[8] (S_N2'), i.e. hydride ion comes in and the leaving methoxyl group departs from the same side of the ring. This explains stereoselectivity of the reaction, and at the same time accounts for its stereospecificity[9], since alkoxyaluminum hydride derivatives of compounds 8 and 9 do not fulfil stereoelectronic requirements of S_N2' reaction and can not undergo rearrangement. Our findings in principal corroborate the results reported by Fraser-Reid et al.[2,3], however with supplement that the pseudoglycal ⟶ 3-deoxy glycal rearrangement of 2,3-unsaturated pyranosides with free C-4 hydroxyl group is stereospecific and its course is go-



verned by the steric relationship (cis-trans) of C-4 hydroxyl and C-1 methoxyl groups.

Table. Pmr data[a] of 4-O-acetyl-3-deoxy glycals 12 and 13.

Comp.	Chemical shifts (ppm, δ) and coupling constants[b] (Hz)							
	H-1	H-2	H-3_{pa}	H-3_{pe}	H-4	H-5	OAc	CH_3
12	6.25 J_{12}=6.2 J_{13pa}=-1.95 J_{13pe}=-1.95	4.56 J_{23pa}=3.3 J_{23pe}=4.2	2.00 J_{3pa3pe}=-17.5 J_{3pa4}=7.1	2.38 J_{3pe4}=6.2	4.75 J_{45}=6.6	3.92 J_{56}=6.7	2.07	1.25
13	6.35 J_{12}=6.2 J_{13pa}=-2.5 J_{13pe}=-1.5	4.56 J_{23pa}=3.0 J_{23pe}=4.5 J_{24}=1.1	2.35 $J_{3pa4}+J_{3pe4}$=9.0	2.04	5.03 J_{45}=1.0	4.01 J_{56}=6.6	2.09	1.22

[a]Pmr spectra were measured on Jeol JNM-4H-100 spectrometer for $CDCl_3$ solutions with TMS as internal reference. [b]Coupling constants have been evaluated on the basis of the first order treatment and have been confirmed by decoupling experiments.

References and footnotes

1.a)O.Achmatowicz Jr.,P.Bukowski,B.Szechner,Z.Zwierzchowska and A.Zamojski, Tetrahedron,27,1973(1971). b)O.Achmatowicz Jr. and B.Szechner, Bull.Acad.Polon. Sci.,sér.sci.chim.,19,309(1971). c)P.Bukowski, Ph.D.Dissertation, Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, 1971.

2.B.Fraser-Reid and B.Radatus,J.Amer.Chem.Soc.,92,6661(1970).

3.B.Radatus,M.Yunker and B.Fraser-Reid,J.Amer.Chem.Soc.,93,3086(1971).

4.We have employed acetates for reduction since they have been previously[1a)] characterized, and the outcome of LAH reduction is the same as for free carbinols (tlc).

5.This assignment is supported by consideration of H-3 and H-2 hydrogens couplings.

6.E.W.Garbisch,J.Amer.Chem.Soc.,86,5561(1964).

7.We use terms "stereoselective" and "stereospecific" in the sence proposed by H.Zimmerman et al.(see E.L.Eliel. "Stereochemistry of Carbon Compounds",McGraw Hill Book Comp.,Inc.1962,p.436) and therefor Fraser-Reid's et al.[2)] "stereospecificity" corresponds to "stereoselectivity".

8.P.B.D.de la Mare in "Molecular Rearrangements" Part I,ed.p.de Mayo,Interscience Publishers,N.Y.1963,ch.2.

9.At least reactions carried out at room temperature (cf. ref.2).