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HYDROGENOLYSIS OF THE DIOXOLAN TYPE <u>EXO</u>- AND <u>ENDO</u>- BENZYLIDENE DERIVATIVES OF CARBOHYDRATES WITH THE $LiAlH_4$-$AlCl_3$ REAGENT

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The active AlH_2Cl reagent formed from equimolar quantities of $AlCl_3$ and $LiAlH_4$, exhibits the properties of both Lewis acids and hydride donors[1]. This is the basis if its reactions with acetals to yield hydroxy-ethers[2,3,4].

The direction of the ring cleavage of the 4,6-O-benzylidene acetals of hexosides is determined by the steric requirements of the substituents near the dioxan skeleton[5,6,7].

The secondary cis axial-equatorial hydroxyl groups of pyranosides react with benzaldehyde to give 2-phenyl-1,3-dioxolan derivatives existing in two relatively easily separable diastereomeric forms, absolute configurations of which can be determined by n.m.r.[8,9].

The following four pairs of isomers were synthesized and subjected to hydrogenolysis (in ether-CH_2Cl_2 /1:1/, 1.1 mols of reagent, at 45°). All percentage values show product ratios and not the isolated yields.

Benzyl <u>exo</u>-3,4-O-benzylidene-β-D-arabinopyranoside (<u>1</u>, mp 144-145°;$[\alpha]_D$= -148°; $\delta_{C\underline{H}-Ph}$: 6.18)[10] gave 70 % benzyl 3-O-benzyl-β-D-arabinopyranoside isolated as the diacetate (<u>9</u>, syrup, $[\alpha]_D$=-159°) and 30 % benzyl 4-O-benzyl-β-D-arabinopyranoside, isolated as its crystalline diacetate (<u>10</u>, mp 66-68°; $[\alpha]_D$=-198°). Benzyl <u>endo</u>-3,4-O-benzylidene-β-D-arabinopyranoside (<u>2</u>, mp 96-97°; $[\alpha]_D$=-171°; $\delta_{C\underline{H}-Ph}$: 5.78) yielded, upon hydrogenolysis and acetylation <u>9</u> and <u>10</u> in a ratio of 22:78. Saponification of <u>9</u> and <u>10</u> gave a periodate-resistant and a periodate-oxidizable product, respectively.

Hydrogenolysis of benzyl 2-O-benzyl-<u>exo</u>-3,4-O-benzylidene-β-D-arabinopyranoside (<u>3</u>, mp 85-86°; $[\alpha]_D$=-103°; $\delta_{C\underline{H}-Ph}$: 6.02) gave 81 % benzyl 2,3-di-O-benzyl-β-D-arabinopyranoside (<u>11</u>, syrup, $[\alpha]_D$=-75°) and 19 % benzyl 2,4-

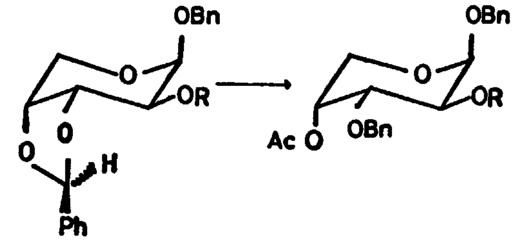
di-O-benzyl-β-D-arabinopyranoside (**12**, mp 73-74°; $[\alpha]_D$=-123°). **11** and **12** were obtained from benzyl 2-O-benzyl-*endo*-3,4-O-benzylidene-β-D-arabinopyranoside (**4**, mp 80-82°; $[\alpha]_D$=-164°; $\delta_{C\underline{H}-Ph}$: 5.89) in a ratio of 16:84.

The ring cleavage of phenyl 2-O-benzyl-*exo*-3,4-O-benzylidene-β-D-fucopyranoside (**5**, mp 93-94°; $[\alpha]_D$=+13°; $\delta_{C\underline{H}-Ph}$: 6.00) yielded 71 % phenyl 2,3-di-O-benzyl-β-D-fucopyranoside (**13**, mp 89-90°; $[\alpha]_D$=+12°) and 29 % phenyl 2,4-di-O-benzyl-β-D-fucopyranoside (**14**, mp 51-53°; $[\alpha]_D$=+9°). Phenyl 2-O-benzyl-*endo*-3,4-O-benzylidene-β-D-fucopyranoside (**6**, mp 103-106°; $[\alpha]_D$= +46°; $\delta_{C\underline{H}-Ph}$: 5.90) gave, in quantitative yield, **14**, only. The only product from benzyl 2,6-di-O-benzyl-*exo*-3,4-O-benzylidene-β-D-galactopyranoside (**7**, mp 132-133°; $[\alpha]_D$=-2.6°; $\delta_{C\underline{H}-Ph}$: 5.95) was benzyl 2,3,6-tri-O-benzyl-β-D-galactopyranoside (**15**, syrup, $[\alpha]_D$=-14°). The cleavage of the dioxolan ring of benzyl 2,6-di-O-benzyl-*endo*-3,4-O-benzylidene-β-D-galactopyranoside (**8**, mp 65-66°; $[\alpha]_D$=+12°; $\delta_{C\underline{H}-Ph}$: 5.85) gave benzyl 2,4,6-tri-O-benzyl-β-D-galactopyranoside (**16**, mp 60-63°; $[\alpha]_D$=-16°). The reactions of both **7** and **8** are highly stereoselective, i.e. in **7** the only site of the attack by the reagent is the axial C_4-oxygen atom of the galactopyranoside which also participates in the the dioxolan ring. However, in the case of **8** the reagent attacks only the equatorial C_3-oxygen atom.

The structure of the products of the cleavage reactions was proved by the methyl ethers obtained upon successive methylation, catalytic hydrogenation and acid hydrolysis of them.

These reactions prove that the hydrogenolytic ring cleavages of 3,4-O-benzylidene pyranosides proceed via different routes. In the *exo* isomers the reagent attacks the axial oxygen atom forming an axial hydroxyl-equatorial benzyl derivative. On the contrary, in the *endo* isomers the equatorial oxygen atom is attacked leading to a product with the hydroxyl group in the equatorial and the O-benzyl group in the axial position, respectively.

Our results suggest that both **1** and **2** are $^1C_4$ conformers. **9** can be derived from **1**, after hydrogenolysis and acetylation, if the C_4-O in **1** is axial and **10** from **2** if the C_3-O is equatorial. The n.m.r. spectra of both **1** and **2** show that they are strongly deformed $^1C_4$ conformers ($J_{4,5a} \approx J_{4,5e} \approx 1.8$ Hz)

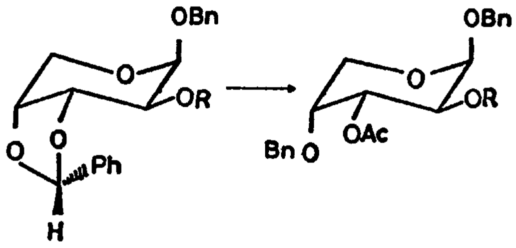


<u>1</u> R = H

<u>3</u> R = Bn

<u>9</u> R = Ac

<u>11</u> R = Bn

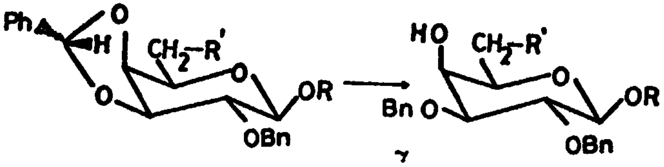


<u>2</u> R = H

<u>4</u> R = Bn

<u>10</u> R = Ac

<u>12</u> R = Bn

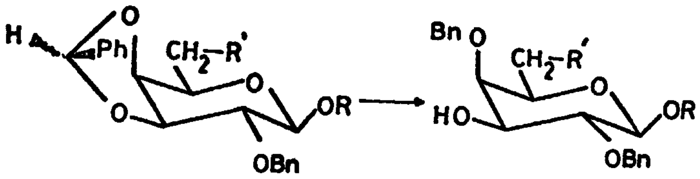


<u>5</u> R = Ph; R'= H

<u>7</u> R = Bn; R'= OBn

<u>13</u> R = Ph; R'= H

<u>15</u> R = Bn; R'= OBn



<u>6</u> R = Ph; R'= H

<u>8</u> R = Bn; R'= OBn

<u>14</u> R = Ph; R'= H

<u>16</u> R = Bn; R'= OBn

Bn = Benzyl

Ac = Acetyl

and this finding is confirmed by other authors[9], too.

This procedure, offers a new method for the selective protection of cis axial-equatorial hydroxyl groups of hexo- and pentopyranosides, in form of benzyl ether.

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