

NEIGHBORING GROUP EFFECT IN THE β -ELIMINATION-REACTION OF SOME GLUCOPYRANOSYL-(1 \rightarrow 4)-HEXOPYRANOSIDURONATES

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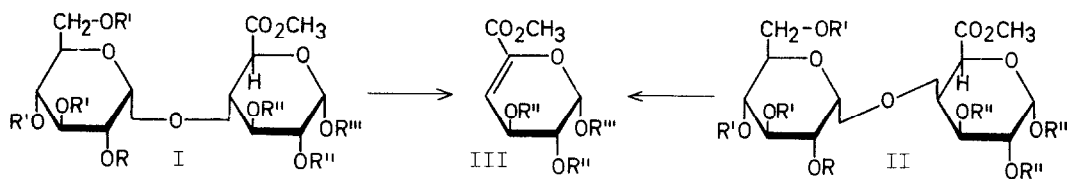
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The enzymic degradation of heparitin sulfate (1), chondroitin sulfates (2), hyaluronic acid (3) led to sulfated or sulfate free oligosaccharides with a terminally linked 4,5-unsaturated-4-deoxy-hexopyranosiduronate unit. These oligosaccharides proved to be similar to the fragmentation-products of lung-, intestines, and omega-heparins, which can be obtained by diazoalkane degradation (4). On the other hand, polyglycosiduronic acids, e.g. pectin (5) or alginic acid (6) give similar products by enzymic or alkaline degradation.

These degradation reactions proved to be β -eliminations in which the "leaving groups" are the C-4 substituted hexopyranosyloxy-residue, together with the C-5 proton, and, with regard to their stereochemistry, can be grouped into two classes: 1. the leaving groups are the C-4 (equatorial) glycopyranosyloxy-residue and the C-5 (axial) proton: cis-elimination. 2. The leaving groups are the C-4 (axial) glycopyranosyloxy-residue and the C-5 (axial)-proton: trans-elimination. Some types of mucopolysaccharides belong to class 1., and pectins to class 2.

In the present short paper we report on the proof of this elimination reaction in synthetic disaccharides, belonging to both types of β -eliminations.



$R = -H, -SO_2CH_3$; $R' = -H, -COCH_3$; $R'' = -CH_2-C_6H_5$; $R''' = -CH_3, -CH_2-C_6H_5$

For studying the cis(e,a)-elimination we synthesized the α -D-glucopyranosyl-(1 \rightarrow 4)- α -D-glucopyranosiduronate derivative-I, and for proving of the trans(a,a)-elimination we choose the corresponding α -D-glucopyranosyl-(1 \rightarrow 4)- α -D-galactopyranosiduronate-derivative-II.

The disaccharide-I was obtained by stereospecific addition of 1,2-anhydro-3,4,6-tri-O-acetyl- α -D-glucopyranoside (Brigl's anhydride \equiv B.A.) to the benzyl-(or methyl)-2,3-di-O-benzyl- α -D-glucopyranosiduronic acid methylester (7). { I: ($R = -H, R' = -COCH_3, R'', R''' = -CH_2-C_6H_5$); $[\alpha]_D^{25} = +118^\circ, c = 0.66$ in ethyl acetate; Anal. Calcd. for $C_{40}H_{46}O_{15}$: C, 62.66; H, 6.05; Found: 62.67; H, 6.25. The corresponding α -D-galactopyranosiduronate-derivative-II: ($R = -H, R' = -COCH_3, R'' = -CH_2-C_6H_5, R''' = -CH_3$), $[\alpha]_D^{25} = +127, c = 0.72$ in $CHCl_3$; Anal. Calcd. for $C_{34}H_{42}O_{15}$: C, 59.12; H, 6.13. Found: C, 58.82; H, 6.13.} was obtained by a similar stereospecific addition of (B.A.) to the methyl-(or benzyl)-2,3-di-O-benzyl- α -D-galactopyranosiduronic acid methylester (m.p. 66-67 $^\circ$, $[\alpha]_D^{25} = +33.3^\circ, c = 0.74$ in $CHCl_3$).

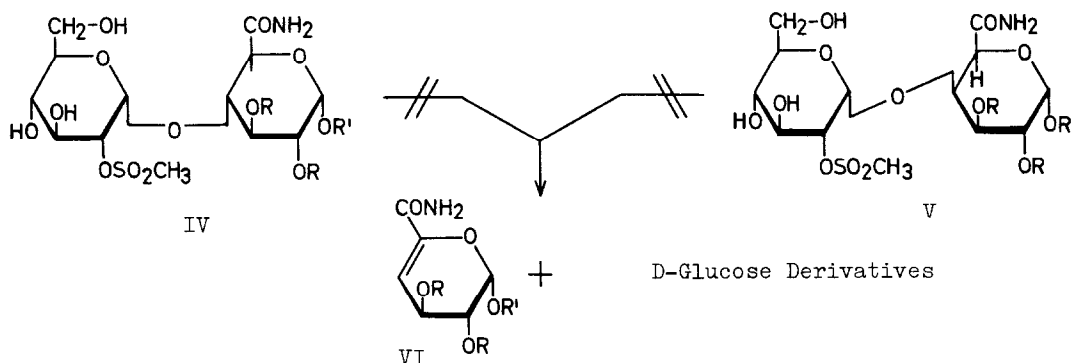
Treating the disaccharide-I and II e.g. with sodium methoxide in a mixture of methanol and benzene at room temperature gives, by splitting off the C-5-proton and the C-4-glucopyranosyloxy residue, the corresponding substituted 4,5-unsaturated-4-deoxyhexopyranosiduronate-III (8). On the basis of our preliminary experiments no stereospecificity can be found regarding the leaving group on the C-4-, and the proton on the C-5-atoms of the hexopyranosiduronate moiety of disaccharides-I and II (9,10). The lack of stereospecificity in these

eliminations give similar results as the eliminations-studies on synthetic D-gluco- and D-galactopyranosiduronate-4-O-sulfonate derivatives (4b), where the leaving groups are the methanesulfonate-residue together with the C-5-proton.

As we furthermore found, the introduction of a methanesulfonylester function into the hydroxyl-group-2 of the glucopyranoside leaving group of disaccharide-I and -II, facilitates the β -elimination. I: (R = $-\text{SO}_2\text{CH}_3$, R' = $-\text{COCH}_3$, R'', R''' = $-\text{CH}_2-\text{C}_6\text{H}_5$), $[\alpha]_D^{25} = +108.5^\circ$, c = 0.8 in CHCl_3 ; Anal. Calcd. for $\text{C}_{41}\text{H}_{48}\text{O}_{17}\text{S}$: C, 58.28; H, 5.72; S, 3.79. Found: C, 58.32; H, 5.80; S, 3.67. II: (R = $-\text{SO}_2\text{CH}_3$, R' = $-\text{COCH}_3$, R'' = $-\text{CH}_2-\text{C}_6\text{H}_5$, R''' = $-\text{CH}_3$), $[\alpha]_D^{25} = +127^\circ$, c = 0.68 in CH_3OH . Anal. Calcd. for $\text{C}_{35}\text{H}_{44}\text{O}_{17}\text{S}$: C, 54.68; H, 5.78; S, 4.17. Found: C, 54.79; H, 5.70; S, 4.05.

Quantitative measurements regarding the rate of the above mentioned β -elimination reactions will be published later.

Furthermore, we carried out some experiments in order to establish the role of the carboxylate-function in the β -elimination of both disaccharides-I and II.



Compound-IV (R, R' = $-\text{CH}_2-\text{C}_6\text{H}_5$), m.p. 144-145 $^\circ$, $[\alpha]_D^{25} = +134^\circ$, c = 0.29 in CH_3OH . Anal. Calcd. for $\text{C}_{34}\text{H}_{41}\text{O}_{13}\text{NS}$: C, 58.03; H, 5.78; N, 1.99; S, 4.56. Found: C, 57.81; H, 5.80; N, 1.94; S, 4.62. was obtained by ammonolytical cleavage of the disaccharide-I (R = $-\text{SO}_2\text{CH}_3$, R' = $-\text{COCH}_3$, R'', R''' = $-\text{CH}_2-\text{C}_6\text{H}_5$). The correspon-

ding D-galactopyranosiduronamide-disaccharide derivative-V ($R = -CH_2-C_6H_5$, $R' = -CH_3$), m.p. 136-138°, $[\alpha]_D^{25} = +126^\circ$, $c = 0.38$ in CH_3OH), Anal. Calcd. for $C_{28}H_{37}NO_{13}S$: C, 53.58; H, 5.94; N, 2.23; S, 5.11. Found: C, 53.49; H, 6.03; N, 2.41; S, 5.28). was obtained on similar way (by ammonolysis) starting from disaccharide II ($R = -SO_2CH_3$, $R' = -COCH_3$, $R'' = -CH_2-C_6H_5$, $R''' = -CH_3$).

We found that compound IV and V give no 4,5-unsaturated-4-deoxyhexopyranosiduronamide VI using similar conditions, which was used for the mild β -elimination reaction of the corresponding methyluronate disaccharides I and II. Even after treating the compounds IV and V for 10 days under the above-mentioned conditions only very small amount of unsaturated uronamide VI could be detected by thin-layer chromatography on Silica Gel. (The reference substances VI were obtained by ammonolytical cleavage of the corresponding 4,5-unsaturated-deoxyhexopyranosiduronate (8). VI: $R = -CH_2-C_6H_5$, $R' = -CH_3$, m.p. 56-57°, $[\alpha]_D^{25} = +143.5^\circ$, $c = 1.06$ in $CHCl_3$. Anal. Calcd. for $C_{21}H_{23}O_5N$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.40; H, 6.43; N, 3.91. VI: $R, R' = -CH_2-C_6H_5$, m.p. 81-82°, Anal. Calcd. for $C_{27}H_{27}O_5N$: C, 72.79; H, 6.11; N, 3.14. Found: C, 72.77; H, 6.04; N, 2.08).

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