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SYNTHESIS OF RHAMNOSIDES FROM ERYSIMIN AND HELVETICOSOL

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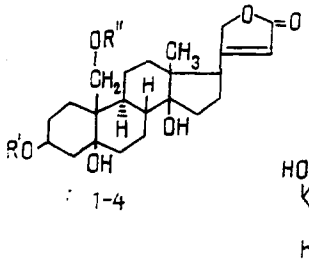
With the aim of obtaining model compounds of interest in the elucidation of the "structure-biological activity" question we have synthesized L-rhamnosides from two glycosidic cardenolides – erysimin and helveticosol – by the Koenigs–Knorre method in V. T. Chernobai's modification [1] .

The performance of the glycosylation reaction was complicated by the fact that both the initial glycosides contain a readily hydrolyzable 2-deoxysugar (D-digitoxose) and erysimin, in addition, contains an angular group that, in solutions, undergoes autooxidation by atmospheric oxygen. Thus, after the glycosylation of helveticosol we obtained strophanthidol (1) and convallotoxin (2), identified by comparison with authentic specimens, and also strophanthidol 19-O-α-L-rhamnoside (3), mp 167-171°C, $[\alpha]_D^{20}$ −3.20 ± 3° (MeOH) and strophanthidol 19-O-(3′,4′-di-O-acetyl−α-L-rhamnoside) (4), a new compound with the composition $C_{33}H_{48}O_{12}$, $[\alpha]_D^{20}$ −18.70 ± 4°; MeOH). In establishing the structures of substances (3) and (4), in addition to the usual methods – elemental analysis, hydrolysis, reactions for the absence of 2-deoxysugars, and molecular rotation increments – we used a known kinetic method [2] of determining axial and equatorial OH groups by means of the acetylation reaction. For compound (4), this revealed the presence of two typical axial OH groups, one of which was in the steroid moiety at C-3 and the other in the L-rhamnose unit at C-2′. This showed that the L-rhamnose residue was present at C-19.

The saponification of substance (4) gave strophanthidol 19-O-α-L-rhamnoside (3), identical, according to its properties and the results of investigations, with that described by Chernobai [3].

The glycosylation of erysimin was carried out analogously, but at room temperature (22-24°C) for 5 h.

After deacetylation and the removal of the α-L-rhamnose, the cardenolides were separated into neutral and acid fractions by treatment with a 2 N alcohlic–chloroform solution of Na_2CO_3. Separation of the neutral glycosides and the cardenolidecarboxylic acids was achieved by chromatographing each of the corresponding fractions on cellulose in the toluene–butan-1-ol (1.5:1)/water system. The neutral fraction yielded the initial erysimin and the desired new glycoside (5) – with the composition $C_{33}H_{52}O_{13}$, $[\alpha]_D^{20}$ −19.3 ± 4° (c 0.27; MeOH).From the acid fraction we obtained erysimin-19–carboxylic acid and the new glycoside (6), composition $C_{35}H_{52}O_{14}$; bp 172-175°, $[\alpha]_D^{20}$ −11.2 ± 3° (c 0.45; MeOH). The two new glycosides (5) and (6) differed by their substituents at C-10, as was shown by the conversion of (5) into (6) on oxidation with potassium permanganate.



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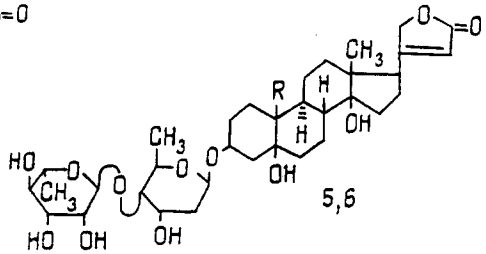

5,6

1. R′=R″=H
2. R′=α-*L*-Rha; R″=H
3. R′=H; R″=α-*L*-Rha
4. R′=H; R″=3′,4′-di-O-Ac-α-*L*-Rha
5. R=CHO
6. R=COOH

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The molecular rotation increment of the L-rhamnose unit ($\Delta[M] = -280°$) for compound (5) showed that the L-rhamnose was attached by an α-glycosidic bond and was present in the pyranose form

The site of attachment of the L-rhamnose residue at C-4′ of the D-digitoxose residue was taken as the most probable in the light of the following circumstances. The hydroxyl at C-4′ of erysimin is equatorial, most spatially accessible, and therefore most reactive. Literature reports of the synthesis of erysimin 4′-D-xyloside [4] likewise confirm the hypothesis that glycosylatiuon takes place mainly at C-4′.

Thus, the new glycosides were strophanthidol 19-O-(3′,4′-di-O-acetyl-α-L-rhamnoside) (4), erysimin 4′-O-α-L-rhamnopyranoside (5), and 19-(formyl→carboxy)erysimin 4′-O-α-L-rhamnopyranoside (6)

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