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# CARDENOLIDE NICOTINATES

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Nicotinic acid and its derivatives are used in medical practice in several diseases, including disturbances of the coronary blood circulation. Consequently, it appeared of definite interest to introduce it as a component part of cardiac glycosides and aglycones and also to study its influence on the biological action of the latter.

| Substance | Empirical formula | Mp, °C | $[\alpha]_D$, deg | Coloration with conc $H_2SO_4$ |
|---|---|---|---|---|
| Strophanthidin 3-mononicotinate | $C_{29}H_{35}O_7N$ | 255—257 | +39.9 ± 3 (in methanol) | Red (0'), yellow (5') |
| Digoxigenin 3,12-dinicotinate | $C_{35}H_{40}O_7N$ | 248—250 | +27.4 ± 3 (in pyridine) | Yellow (0'), orange (80') |
| Cymarin 4'-mononicotinate | — | Amorphous | +31.1 ± 4 (in methanol) | Yellow (0''), green (5''), dark brown (3') |

We have obtained in the form of esters the mononicotinates of strophanthidin and cymarin and the 3, 12-dinicotinate of digoxigenin. Their synthesis was effected in the following way. The cardenolide was dissolved in pyridine and nicotinoyl chloride was added at 0° C. The completeness of the reaction was checked by paper chromatography. After the end of the reaction, ice and a mixture of ethanol and chloroform (1:4) were added to the flask. The alcoholic-chloroformic layer was separated off and treated with sodium carbonate solution and with water, dried with anhydrous sodium sulfate, and evaporated in vacuum. The substances were crystallized from methanol. Their properties are given in the table.

UV spectra of the compounds obtained have a maximum at 263 mμ (log ε 3.22) and two sugars at 257 and 269 mμ which are characteristic for bound nicotinic acid, and also a maximum at 217 mμ (log ε 4.16) corresponding to the butenolide ring of a cardenolide.

The results of biological tests carried out by M. A. Angarskaya and Zh. A. Lyubetskaya unfortunately proved to be negative; the substances synthesized possessed no cardiotonic activity. In view of the fact that the benzoylation of the cardiac glycosides also causes a considerable reduction of their cardiotonic activity (compare the fact that the acetylation of the aglycones raises the activity), it may be assumed that the main cause of this phenomenon is the negative influence of the conjugation of an aromatic system. Attention is drawn to the fact that even a considerable distance of the nicotinic acid residue from the aglycone (the bearer of the action of the cardiac glycosides), as was the case in cymarin nicotinate, did not prevent the loss of cardiotonic activity from the glycoside. It is possible that a cardenolide and nicotinic or benzoic acid bound to it exert opposite biochemical effects.

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# CARDENOLIDES OF CONVALLARIA KEISKEI

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It has previously been reported that desglucocheirotoxin, convallatoxin [1], convallatoxol, convallaside [2], and locundeside [3] have been isolated from C. keiskei Miq. In the present communication we give the results of a study of periplogenin rhamnoside (substance I of [1]) and its identification.

The method of isolating the glycoside was as follows: from the ground Convallaria herb the cardenolides were extracted with 96% ethanol, the extract was evaporated to eliminate the solvent, and the residue was treated with boiling water and the mixture was filtered. The filtrate was purified with a mixture of chloroform and benzene (3:1), after which the glycosides were extracted with chloroform containing 5% of ethanol. Partition chromatography on silica gel (stationary phase water, mobile phase a mixture of benzene and ethyl methyl ketone in various proportions) led to the isolation of the glycoside described, desglucocheirotoxin, and a small amount of convallatoxin.

Periplogenin 3-(O-α-L-rhamnopyranoside) has the composition $C_{29}H_{49}O_9$, mp 170–174° C/219–226° C, $[\alpha]_D^{20}$ – – 20° (c 0.8; methanol). It crystallized from methanol—ether. With 84% sulfuric acid it gives a coloration changing with time: 0 min—red-orange; 1 min—red-orange with a blue border; 5–15 min—light blue; 20 min—gray-green; 30–60 min—gray.

By paper chromatography of the products of acid hydrolysis according to Mannich and Siewert [4], periplogenin and L-rhamnose were detected. The configuration of the glucosidic linkage was determined by Klyne's method [5].

From its physicochemical properties, its coloration with 84% sulfuric acid, its $R_f$ values in various systems, and a mixed melting point, the substance investigated was identical with a synthetic sample [6] of periplogenin (3)-O-α-L-rhamnopyranoside.

This glycoside has previously been isolated from Antiaris toxicaria Lesch. [7]. It has also been detected by paper chromatography in C. majalis L. and C. transcaucasica Utkin.

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# MASS SPECTROMETRY OF THE BISBENZYLISOQUINOLINE ALKALOIDS OF THALICTRUM


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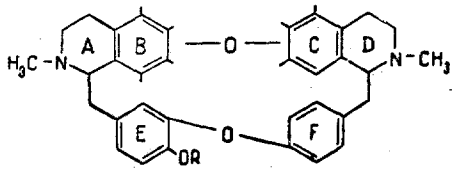
We have studied the mass spectra of the alkaloids hernandezine (I), thalsimine (II), O-methylthalicberine (III), thalmine (IV), and thalfoetidine (V) [1–4]. The spectra were recorded by B. V. Rozynov on a Hitachi RMU-6DS mass spectrometer with the direct introduction of the sample into the ion source (70 eV, 30 μA, 200° C).

All the bases mentioned belong to the group of bisbenzylisoquinoline alkaloids with two ether bridges [(I)–(IV), R = $CH_3$, (V), R = H]. The maximum intensity of the peak of the molecular ion in substance (II) is due to the presence of a 1,2-dehydroisoquinoline ring. The high intensity of the peak of the molecular ion in (V) remains unexplained.




The decomposition of the molecular ions forms the ions $(M - 1)^+$, $(M - 15)^+$, $(M - 31)^+$, *a*, *a'*, b, c, d, and e. The doubly-charged fragment *a* is formed by β-cleavage with the loss of rings E and F. Dimethyl ether splits off from