INTENSIFICATION OF THE HYDROLYSIS OF THE MONOAMMONIUM SALT OF GLYCYRRHIZIC ACID

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Salts of glycyrrhizic acid serve as a source for the preparation of its aglycone — glycyrrhetinic acid— the sodium salt of which (glitsirenat) has been approved for medical use. Among other methods, the hydrolysis of the potassium [1, 2] and ammonium [3] salts of glycyrrhizic acid is carried out with 5% H_2SO_4 for 10 h. The yields of glycyrrhetinic acid by these methods are not very high and the possibility of its undesirable isomerization is not excluded.

The results of our investigations on the hydrolysis of the monoammonium salt of glycyrrhizic acid with 5-10% hydrochloric acid performed in comparison with hydrolysis with 5% H_2SO_4 have shown that under the same temperature conditions the use of 7% HCL is the optimum for 100% hydrolysis. In this case, hydrolysis takes place quantitatively in 3 h, and even after the first 5 min the yield of glycyrrhetinic acid amounted to 73%.

To determine the rate constants of hydrolysis, a 0.5-g sample of glitsiram containing 97.2% of glycyrrhizic acid was dissolved in 42 ml of distilled water, 8.2 ml of concentrated HCl was added, and the mixture was heated at 100°C for 5, 10, 20, 40, 80, and 120 min. The precipitate after hydrolysis was washed, dried, and extracted with chloroform. Then the chloroform was distilled off and, after drying, the residue was weighed. The figures obtained showed the amount of unchanged glycyrrhizic acid after the corresponding time interval.

The hydrolysis rate constant was calculated from the formula

$$K = \frac{2.303 \log \frac{C}{C_0}}{t}$$

where C_0 is the initial amount of glycyrrhizic acid, C is the amount of glycyrrhizic acid not having undergone hydrolysis after time t, and t is the time of hydrolysis.

The rate constants for the hydrolysis of glitsiram using 7% HCl for various values of the time are given below:

C_0	C	t, min	$\frac{C}{C_0}$	$\log \frac{C}{C_0}$	K
0.486	0.1284	5	0.264	−0.5784	0.266
	0.0924	10	0.190	−0.7212	0.162
	0.0919	20	0.189	−0.7235	0.083
	0.0714	40	0.147	−0.8327	0.048
	0.0496	80	0.102	−0.9940	0.028
	0.0048	120	0.01	−2.0	0.029

The mean value of the rate constant of the hydrolysis of glitsiram with 7% HCl is 0.103, while in the case of 5% H_2SO_4 it is no higher than 0.015.

The precipitate of glycyrrhetinic acid obtained after hydrolysis dissolved almost completely in chloroform, which also shows the completeness of hydrolysis. The chloroform extract was purified by activated carbon. After filtration and the distillation of the chloroform, the residue was dried at 80°C and was dissolved in hot 95% ethanol. By lowering the concentration of ethanol to 40% by the addition of hot water, pure glycyrrhetinic acid separated out in the form of a microcrystalline precipitate, which was separated off by centrifuging.

The glycyrrhetinic acid was a white powder with mp 265-268°C. The UV, IR, and NMR spectra of the samples obtained were recorded and proved to be identical with the spectra of a

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standard sample (β-glycyrrhetinic acid).

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STEROID SAPONINS AND SAPOGENINS OF *Allium*.

XIII. TUROSIDE A 6-O-BENZOATE FROM *Allium turcomanicum*

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We have continued the study of the total extractive substances obtained previously [1] from the bulbs of *Allium turcomanicum* Rgl. By chromatographing the extract on a column of SiO_2 [elution with chloroform–methanol (7:1)] we isolated 0.24% (calculated on the air-dry raw material) of a glycoside (I), $C_{57}H_{86}O_{25}$ with mp 242-245°C (methanol–chloroform); $[\alpha]_D^{23}$ −108.7±2° [c 0.92; chloroform–methanol (10:1)]; ν_{max}^{KBr}, cm^{-1}: 3500-3300 (OH); 1720, 1280 (ester group); 1605, 1590, 725 (benzene ring); 990, 930 > 900, 860 (spiroketal chain of the 25S series) [2, 3].

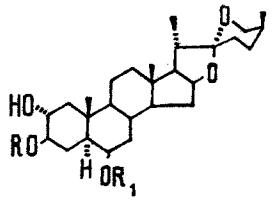
In a hydrolyzate of compound (I) by the GLC method [4, 5] we detected galactose, glucose, and xylose in a ratio of 1:2:1.

The acid hydrolysis of 200 mg of the glycoside (I) with 5% methanolic HCl at the boil for 5 h led to 48 mg of a mixture of genins (II) and (III). They were separated chromatographically on SiO_2. When the column was eluted with the chloroform–methanol (50:1) system, 12 mg of compound (II) was isolated [mp 137-138°C (ether–hexane); $[\alpha]_D^{23}$ −60.8±3° (c 0.67; chloroform)], which was identified as neoapigenin 6-O-benzoate [6]. On continuing elution with chloroform–methanol (20:1) we isolated 18 mg of a genin (III) [mp 266-267°C (methanol); $[\alpha]_D^{23}$ −70.5±3° (c 0.92; chloroform–methanol (10:1))], identified as neoapigenin [7].

Compound (I) (200 mg) was dissolved in 50 ml of 2% KOH solution and the mixture was left at 0°C for 16 h, after which it was poured into water, the methanol was distilled off, and the product was extracted with butanol. This gave 70 mg of the glycoside (IV) which, by its physicochemical constants [mp 281-283°C (methanol), $[\alpha]_D^{23}$ −62.3±3° (c 0.76; chloroform–methanol (10:1))] and by a comparison of IR spectra and R_f values on TLC [SiO_2, chloroform–methanol–water (65:35:8)] was identified as turoside A [1].

The aqueous residue was acidified (HCl) and treated with chloroform. Benzoic acid was found in the extract with the aid of TLC [SiO_2, ethanol–ammonia–water (10:1.4:1.2)].

From an analysis of the PMR spectrum (HMDS, δ, ppm, C_5D_5N) of compound (I) it follows that it contains only one benzoate group, the protons of which appear at 7.94 ppm (2 H, doublet with fine splitting of the protons in the ortho position to the ester group)[8]) and at 7.27 ppm (3 H, multiplet – the remaining protons of the benzoate group, the signal of which



I. R = lycotetraose, $R_1 = C_6H_5CO$;
II. R = H, $R_1 = C_6H_5CO$
III. $R = R_1 = H$;
IV. R = lycotetraose, $R_1 = H$;

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