STRUCTURE OF GLABRIC ACID

N. P. Kir'yalov and V. F. Bogatkina

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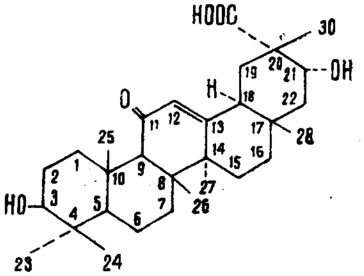
From the methyl esters of the triterpenoids obtained in the methanolysis of the saponins of the roots of *Glycyrrhiza glabra* we have isolated methyl glycyrrhetate by crystallization from ethanol. The mother liquor was chromatographed on a column of alumina (activity grade II). Elution with diethyl ether–benzene (9:1) gave more methyl glycyrrhetate (R_f 0.5) and a substance $C_{31}H_{48}O_5$ with mp 274-276°C, R_f 0.22, M^+ 584; IR spectrum, cm^{-1}: 1620, 1665, 1703, 1720, 3450, 3580. Yield about 1% of the weight of the methanolysis products. In its composition and in the properties of derivatives (Table 1), the compound isolated was identical with methyl glabrate [1]. The mass spectrum of the diacetate of methyl glabrate that we obtained agreed completely with that published by Elgamal and Fayez [2].



There is contradictory information in the literature on the structure of glabric acid. Some authors [1] consider that this acid is a hydroxy-18α-glycyrrhetic acid in which the second hydroxy group is secondary and is probably present in ring E. However, others state that this acid is 26-hydroxyglycyrrhetic acid [2], basing this statement on an interpretation of the mass spectrum of the diacetate of methyl glabrate.

In the NMR spectrum of methyl glabrate that we obtained, signals at δ 3.2 (triplet, 1 H) and δ 3.49 (1 H) correspond to the protons of the OH groups; in the NMR spectrum of the diacetate of the methyl ester (Fig. 1) these protons are found at δ 4.5 and 4.9 (quartet, J_1 = 5, J_2 = 11), respectively [3]. This shows that glabric acid has two secondary hydroxy groups. In order to refine the structure of glabric acid, the methyl ester was hydrogenated (PtO_2, acetic acid). A deoxo compound was obtained [4]: $C_{31}H_{50}O_4$, mp 242°C, $[\alpha]_D^{20}$ −19.1° (c 0.42; $CHCl_3$), IR spectrum, cm^{-1}: 1720, 3430, 3580. When the diacetate of methyl deoxyglabrate was heated in glacial acetic acid with selenium dioxide (1 h, boiling-water bath), it formed a dehydro derivative with mp 234-236°C, $[\alpha]_D^{20}$ −80°, identical in respect of melting point, R_f value, and IR and NMR spectra with the diacetate of methyl macedonate [5]. Furthermore, the oxidation of glabric acid diacetate with chromium trioxide in acetic acid (12 h, room temperature) also gave a known compound with mp 333-335°C, corresponding in respect of R_f value, UV spectrum (λ_{max} 235 nm) and IR spectrum (1660, 1730, 1780 cm^{-1}) to the diacetate of 21α-hydroxyisoglabrolide [6].

On the basis of these facts, we have concluded that glabric acid is probably 21-hydroxy-18α-glycyrrhetic or an isomeric acid. Taking into account the proposed structure for macedonic acid [7], glabric acid can be regarded as 3,21-dihydroxy-11-oxoolean-12-en-29-oic acid.

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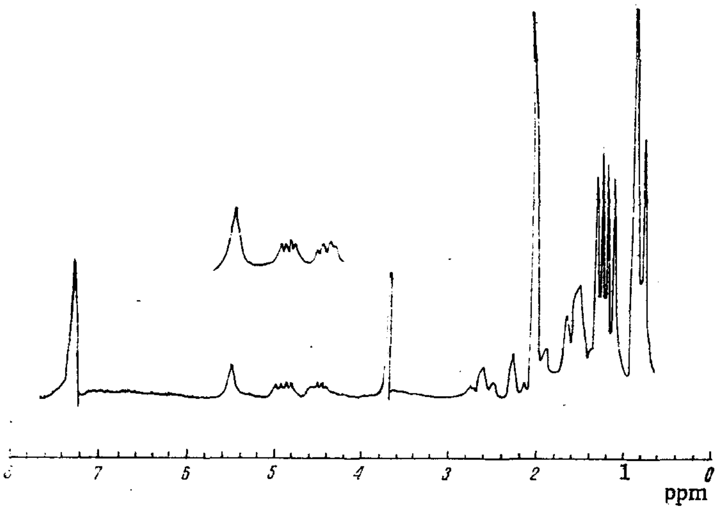

Fig. 1. NMR spectrum of the diacetate of methyl glabrate ($CDCl_3$, Varian-HA-100).

TABLE 1. Properties of Glabric Acid and Its Derivatives

Substance	mp, °C	$[\alpha]_D^{20}$, deg	UV spectrum, nm	Literature data		
				mp, °C	$[\alpha]_D^{20}$, deg	UV spectrum, nm
Glabric acid	325–328	+23 (ethanol)	243	329–333	−26 (pyridine)	242
Methyl glabrate	274–276	+20	243	277–280	+16	242
Diacetate of methyl glabrate	314–316	+33	243	315–320	+42	242
Diacetate of glabric acid	308–309	+22	243	308–309	+38	242

The fragments with m/e 246, 277, 306, 307, and 389 observed in the mass spectrum of the diacetate of methyl glabrate and showing, according to Elgamal and Fayez [2], the presence of a primary OH group at C_{26} have apparently been interpreted incorrectly.

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