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SESQUITERPENIC LACTONES OF THE CYNARA SCOLYMUS L. SPECIES+

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In connection with the studies on sesquiterpenic lactones of the Compositae family we resumed the investigation of the Cynara scolymus L. species. Up to the present time only a single sesquiterpenic lactone - cynaropicrin (I) - was reported as the constituent of this species[1]. It was isolated from C. scolymus of Bohemian origin, in the form of a non-crystalline substance of the composition $C_{19}H_{22}O_6$, to which the structural formula I has been assigned[1,2]. Cynaropicrin was also isolated from a related species C. cardunculus L.[2].

During the analysis of the components of the above-ground parts of C. scolymus of Italian origin we isolated two sesquiterpenic lactones. The first was a non-crystalline substance of the composition $C_{19}H_{22}O_6$ (m/e 346) and $[\alpha]_D^{20}$ + 108,6°, which according to its composition and according to a direct comparison of its IR spectrum with the authentic spectrum of cynaropicrin was identical with cynaropicrin. The second lactone was a crystalline substance of m.p. 197°C, $[\alpha]_D^{20}$ + 123°, and the composition $C_{15}H_{18}O_4$, which according to its spectral data and mixture melting point was identical with grosheimin (II). We isolated the latter for comparison according to the original procedure[3] from Grossheimia macrocephala (Muss.-Puschk.) D. Sosn. et Takht.. From the leaves of C. scolymus of Polish origin we also isolated two sesquiterpenic lactones. One of them was again a non-crystalline substance identical, according to its elemental analy-

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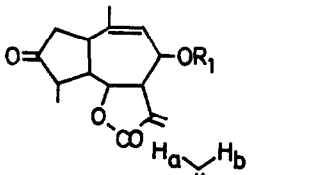
sis and spectral data, with cynaropicrin (I). The second lactone was a crystalline substance of m.p. 126°C, $[\alpha]_D^{20}$ + 60°, and the composition $C_{19}H_{20}O_6$, which was not identical with any of the known lactones. In view of its structural relationship with cynaropicrin we named it dehydrocynaropicrin (III).

The structure of cynaropicrin, expressed by formula I, was proposed originally on the basis of the study of hydrogenation products of cynaropicrin[1,2]. However, our present data, i.e. the IR, mass, and PMR-spectra of the newly isolated cynaropicrin, show that the above structure must be revised and the structure IV assigned to it. According to IR and mass spectra cynaropicrin contains an α,β-unsaturated γ-lactone grouping (1760 cm^{-1}), and α,β-unsaturated ester function (1710 cm^{-1}; m/e 262 (346-84) and 85 ($C_3H_5O.CO^+$)), and two hydroxy groups (3600 and 3500 cm^{-1}; m/e 244 (346-84-18) and 226 (346-84-18-18)). The structure IV was inferred from a detailed analysis of the PMR spectrum of cynaropicrin (HA-100; d_6-DMSO, TMS) using decoupling experiments. The assignments are (first order values, chemical shifts in ppm, splitting in Hz) as follows: $\underline{H}_a$: 6.18 m ($^2J_{a,b}$ = 1.7); $\underline{H}_b$: 5.91 m ($^2J_{b,a}$ = 1.7); $\underline{H}_c$: 4.18 bd (2 H, $J_{c,OH}$ = = 5.5); $\underline{H}_{13}$: 6.02 d ($^4J_{7,13}$ = 3.4); $\underline{H}_{13}'$: 5.52 d ($^4J_{7,13}'$ = 3.0, $^2J_{13,13}' \neq 0 <$ <0.5); $\underline{H}_{14}$: 5.09 bd ($^2J_{14,14}'$ = 2); $\underline{H}_{14}'$: 4.84 bd ($^2J_{14,14}'$ = 2); $\underline{H}_{15}$: 5.23 bs (2 H); $\underline{H}_8$: 5.15 (multiplet overlapped by the signals H_{14}, H_{15}, and OH); $\underline{H}_7$: 3.21 m; $\underline{H}_6$: 4.38 bt ($\Sigma J \approx 18$, multiplet overlapped by the multiplet H_3); $\underline{H}_3$: 4.38 m (multiplet overlapped by the multiplet H_6); $\underline{H}_9$: 2.67 dd ($J_{9,8}$ = 5.5; $^2J_{9,9}'$ = 14); $\underline{H}_9'$: 2.25 dd ($J_{9',8}$ = 3.5; $^2J_{9',9}$ = 14).

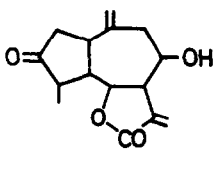
On saponification of cynaropicrin crystalline dihydroxy lactone V was obtained of m.p. 150-151.5°C, $[\alpha]_D^{20}$ + 119.7°, and the composition $C_{15}H_{18}O_4$ (m/e 262) the structure of which, expressed by formula V, was also in agreement with the IR, mass, and PMR spectra, and with the formula IV for cynaropicrin. Characteristic parameters of the PMR spectrum of compound V are the following (HA-100; d_6-DMSO + trace of $CDCl_3$; TMS): $\underline{H}_{13}$: 6.12 q ($^4J_{7,13}$ = 3.0; $^2J_{13,13}'$ = 1.5); $\underline{H}_{13}'$: 6.06 q ($^4J_{7,13}'$ = 3.4; $^2J_{13,13}'$ = 1.5); $\underline{H}_{15}$: 5.20 bs (2 H); $\underline{H}_{14}$: 4.98 bd ($^2J_{14,14}'$ = 2); $\underline{H}_{14}'$: 4.88 bd ($^2J_{14,14}'$ = 2); $\underline{H}_3$: 4.35 m (after exchange bt; $^4J_{3,15} \neq 0$); C_3-O$\underline{H}$: 5.03 d ($J_{3,OH}$ = 6); $\underline{H}_6$: 4.07 dd (ΣJ= = 18.5; J_1 = 8.5; J_2 = 10); $\underline{H}_7$: 2.85 m (multiplet completely overlapped by

signals of other protons); $\underline{H}_8$: 3.76 m (after exchange dt; J_1 = 9.5; $J_2 = J_3$ = = 4.5-5); C_8-O$\underline{H}$: 5.13 d ($J_{8,OH}$ = 5); $\underline{H}_{9'}$: 2.13 dd ($J_{9',8}$ = 5; $^2J_{9,9'}$ = 13).

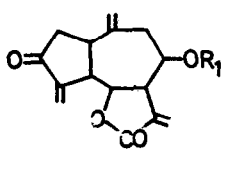
Dehydrocynaropicrin (III) had in its IR spectrum maxima characteristic of the following groups: Hydroxyl (3600 cm^{-1}), two carbonyl groups (1720 cm^{-1} with an inflexion at 1710 cm^{-1}), an α,β-unsaturated γ-lactone (1765 cm^{-1}), and a double bond (1637 cm^{-1}). From a detailed analysis of its PMR spectrum it followed that its structure is expressed by formula III. The characteristic parameters of the PMR spectrum of dehydrocynaropicrin (HA-100; $CDCl_3$ + trace of d_6-DMSO; TMS) are the following: $\underline{H}_a$: 6.33 m; $\underline{H}_b$: 6.01 m (ΣJ = 4; $^2J_{b,a}$ = = 1.2; $|J_{b,c} + J_{b,c'}|$ = 2.90); 4.38 q (2 H; $|1/2\ J_{a,c} + J_{a,c'}|$ = 0.8; $1/2|J_{b,c} +$ + $J_{b,c'}|$ = 1.5); $\underline{H}_{13}$: 6.30 d ($^4J_{7,13}$ = 3.5); $\underline{H}_{13'}$: 5.80 d ($^4J_{7,13'}$ = 2.9; $^2J_{13,13'} \neq 0 < 0.5$); $\underline{H}_{15}$: 6.28 m; $\underline{H}_{15'}$: 5.88 bq ($^2J_{15,15'}$ = 1; $^4J_{5,15'}$ = 2); $\underline{H}_{14}$: 5.08 bs; $\underline{H}_{14'}$: 4.89 bs ($^2J_{14,14'} \neq 0$); $\underline{H}_6$: 4.11 dd (ΣJ = 18; J_1 = 8.5; J_2 = 9.4); $\underline{H}_8$: 5.12 m (ΣJ = 22.8; J_1 = 5.6; J_2 = 7.2; J_3 = 10.0); $\underline{H}_7$: 3.41 m ($\Sigma\ ^3J$ = 19; $^3J_1$ = 8.8; $^3J_2$ = 10); $\underline{H}_9$: 2.91 dd ($J_{9,8}$ = 5.8; $^2J_{9,9'}$ = 13.5); $\underline{H}_{9'}$: 2.38 dd ($J_{9',8}$ = 7.5; $^2J_{9',9}$ = 13.5; $^4J_{9',14'} \neq 0 < 0.5$); $\underline{H}_5$: 3.31; $\underline{H}_1$: 3.20; 2 $\underline{H}_2$: 2.55 (complex multiplet). The analysis of the PMR-spectrum of dehydro-cynaropicrin (III) was confirmed by the analysis of the PMR spectrum of its adduct with trichloroacetylisocyanate which was prepared by a reaction in situ in a conventional manner[4].



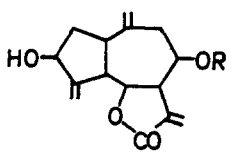
I : R_1 = -CO-C(=H_a)-$CH_{2(c)}$OH



II

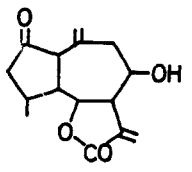


III

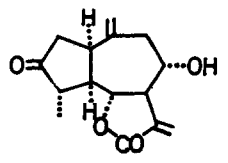


IV : R = R_1

V : R = H



VI



VII

The structure of grosheimin (II) was investigated by Rybalko and co-workers[3,5] and in their last paper they proposed the formula VI for it[6]. However, the work of Spanish authors[7-10] who isolated grosheimin from Amberboa lippii D.C. shows that grosheimin has the constitution II and the stereostructure VII. The formula VII has also been proposed for grosheimin in our study[11].

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