A SESQUITERPENE LACTONE FROM *Acroptilon repens*

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A new sesquiterpene lactone has been isolated from the epigeal part of *Acroptilon repens*, with the composition $C_{19}H_{22}O_6$, mp 199-201°C, M^+ 346, and it has been called acroptin (I). The treatment of (I) with acetic anhydride in pyridine gave a diacetate (II). The structure of (I) has been confirmed by the NMR spectra of (I) and (II). Details of the IR and NMR spectra of (I) and (II) are presented.

From the epigeal part of *Acroptilon repens* (L.) DC., collected in July, 1978, in the botanical garden of the Institute of Botany of the Academy of Sciences of the Azerbaidzhan SSR, a substance with the composition $C_{19}H_{22}O_6$, mp 199–201°C, M^+ 346, has been isolated by chromatography on a column of alumina.

The IR spectrum of the substance has absorption bands of OH groups (3240 and 3400 cm^{-1}), of a γ-lactone ring (1760 cm^{-1}), of an α,β-unsaturated ester group (1715, 1275 cm^{-1}), and of double bonds (1630 cm^{-1}). The intensity of the last-mentioned band is high. This fact and the presence in the IR spectrum of a group of bands in the 885, 900, 915, and 990 cm^{-1} region permits the assumption of the presence of at least three methylenic double bonds in the molecule of the substance, as in the case of a dehydrocostuslactone [1].

The correctness of this point of view was shown by the NMR spectrum of the compound under investigation. This lacks any signals whatever that could characterize methyl groups, and therefore it is possible to assume that the substance is based on a guaiane or germacrane carbon skeleton. Two doublets with centers at 5.66 ppm (J = 3 Hz) and 6.17 ppm (J = 3 Hz), with areas of 1 H each, belong to an exomethylene group at a lactone ring. Two doublets at 4.88 ppm (J = 1.5 Hz, 1 H) and 5.14 ppm (J = 1.5 Hz, 1 H) likewise belong to a $>C=C<^{H}_{H}$ group at C-10. The protons of the third exomethylene group at C-4 give a signal in the spectrum in the form of a singlet at 5.41 ppm with an area of two proton units. In addition, in the weak-field region the spectrum shows two doublets at 6.31 ppm (J = 1.5 Hz, 1 H) and 6.50 ppm (J = 1.5 Hz, 1 H), relating to the two protons of a methylene group at a double bond conjugated with a carbonyl ester group ($O=\underset{|}{C}-\underset{|}{C}=CH_2$), and a singlet at 4.75 ppm (2 H), apparently caused by the presence of a $-CH_2-OH$ group in a side chain. The downfield shift is due, on the one hand to the propinquity of the carbonyl group and, on the other hand, to the double bond.

Thus, according to its elementary composition and molecular weight, three out of the nineteen carbon atoms in the molecule of the lactone under investigation and three out of the six oxygen atoms are included in an ester group, and two oxygen atoms participate in the formation of the lactone ring. The sixth oxygen atom is present in the form of an OH group.

The facts given above show that the ester group is similar to those of muricatin [2], cynaropicrin [3, 4], and saupirin [5].

A comparison of the physicochemical and spectral properties with those of known sesquiterpene lactones showed that the compound under investigation was new, and the name acroptin has been proposed for it.

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The presence of two hydroxy groups was shown by acetylation. On acetylation with acetic anhydride in pyridine, acroptin formed a diacetyl derivative (vitreous substance), with the composition $C_{23}H_{26}O_8$, the IR spectrum of which showed the bands of a γ-lactone ring and of ester groups (strong maximum in the 1775–1710 cm^{-1} region) and of double bonds (1640 cm^{-1}).

The formation of diacetylacroptin was confirmed by its NMR spectrum which revealed a six-proton singlet at 2.0 ppm (CH_3–C=O). It must be mentioned that the singlets of a methylene group at a primary hydroxy group and of the exomethylene group at C-4 in the spectrum of the diacetyl derivative appear in the form of four one-proton singlets in the 4.8–5.2 ppm region.

The signal of the lactone proton in the spectrum of acroptin is masked by the signals of the protons of the exomethylene group at C-10 and of the methylene group at a primary hydroxy group. Only in the spectrum of diacetylacroptin is it possible to consider the structure of the signal. The lactone proton in the NMR spectrum of this derivative appears in the form of a triplet at 4.40 ppm ($J_1 = J_2 = 12$ Hz) and shows an interaction with only two vicinal protons. Thus, the lactone ring in the acroptin molecule is located at C_6–C_7 of a guaiane carbon skeleton.

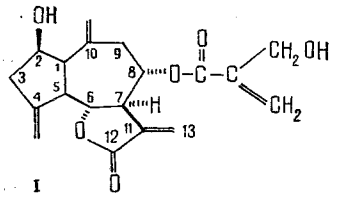
A one-proton quartet with additional splitting at 3.90 ppm ($J_1 = J_2 = J_3 = 8$ Hz) revealed by the NMR spectrum of acroptin belongs to a gem-hydroxylic proton. The additional splitting is due to the fact that the spin–spin coupling constants of the three neighboring protons do not coincide, although they are close. The fact that this signal belongs to a gem-hydroxylic proton is confirmed by the NMR spectrum of diacetylacroptin, where it is shifted downfield by 0.75 ppm (at 4.65 ppm).

Thus, the OH group is secondary and may be located at C-2, C-3, C-8, or C-9. The positions of the hydroxyl at C-3 and C-4 are excluded by the quartet splitting of the signal of the gem-hydroxylic proton, showing its coupling with three vicinal protons. The ratio of the intensities of its components is 1:3:3:1, which also shows coupling only with three vicinal protons, and not with two [6].

As is well known [7], the distance between the signals of an exomethylene group conjugated with a lactone carbonyl is, as a rule, 0.5–0.7 ppm. The presence of an OH group in the β position to it subjects the H_{13} signal to a strong downfield shift, i.e., the distance between the signals of the H_{13} and $H_{13'}$ protons decreases. Yoshioka et al. [8], on analyzing the NMR spectra of a large number of α,β-unsaturated γ-lactones containing a hydroxy group in the β position, showed that such a phenomenon is observed only in the case of the trans linkage of the lactone ring. According to the NMR spectrum of acroptin, the distance between the H_{13} and $H_{13'}$ doublet is 0.51 ppm, and the spin–spin coupling constant (SSCC) of the lactone proton of acroptin diacetate (12 Hz) shows the trans linkage of the lactone ring. Consequently, the presence of the hydroxy group at C-8 is likewise excluded. Hence, the secondary OH group is located at C-2 and, according to the SSCC values, has the β orientation.

So far as concerns the position of the ester group, it may be located at C-8. This is indicated by a partially masked sextet at 5.30 ppm ($J_1 = 4$, $J_2 = J_3 = 10$ Hz) in the NMR spectrum of acroptin. In the NMR spectrum of diacetylacroptin, this signal also appears in the form of a sextet, at 5.47 ppm ($J_1 = 4$, $J_2 = J_3 = 10$ Hz). The SSCCs show the α orientation of the ester group in the acroptin molecule.

Thus, acroptin has the structure (I).



I

As can be seen from the structure (I), acroptin differs from cynaropicrin [9] at least by the position of the OH group in the five-membered ring. Consequently, the necessity arises for comparing some properties of these compounds. Cynaropicrin has been described [3, 9-12] as a noncrystalline substance, while acroptin has mp 199–201°C. In spite of

these differences, for confirmation we compared their IR spectra*: they differ substantially.

It is also necessary to compare synaropicrin with saupirin [5] and muricatin [2, 13]. The structures of these three compounds coincide. Since the configuration of saupirin has not yet been established, it may be assumed that it differs from that of cynaropicrin and muricatin in the stereochemical respect. The configuration of muricatin has been established and agrees completely with that of cynaropicrin [13].

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer in paraffin oil, and NMR spectra on a Varian HA-100D spectrometer, deuterated pyridine being used to dissolve the acroptin and deuterated chloroform for the diacetylacroptin. Chemical shifts are given on the δ scale, with TMS as standard.

Isolation of Acroptin. The material from the extract obtained treating the epigeal part of *Acroptilon repens* with acetone (28 g) was chromatographed on a column (85 × 5 cm) of alumina (activity grade II). The volume of each fraction was 200 ml. Elution was performed with hexane, with hexane–chloroform (1:1) (16 fractions) and (1:2) (six fractions), with chloroform (8 fractions), and with chloroform–ethanol (100:1) (37 fractions). Fractions 33, eluted by chloroform–ethanol, yielded a crystalline substance with the composition $C_{19}H_{22}O_6$, mp 199–201°C (benzene). Yield 0.71% of the weight of the extract. IR spectrum: 3400, 3240, 1760, 1715, 1630 cm^{-1}.

Acetylation of Acroptin. A solution of 50 mg of acroptin in 1 ml of pyridine was treated with 1 ml of acetic anhydride. The mixture was kept at room temperature for 24 h and then the solvent was evaporated off. The residue was dissolved in chloroform and the solution was filtered through a 5-cm layer of alumina. This gave 35 mg of a vitreous substance $C_{23}H_{26}O_8$. IR spectrum: 1775–1710, 1640 cm^{-1}.

SUMMARY

A new guaianolide, $C_{29}H_{22}O_6$, mp 199-201°C, which has been called acroptin, has been isolated from an acetone extract of the epigeal part of *Acroptilon repens* (L.) DC., and its structure has been determined.

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