GRANDULIN AND GRANDICIN—NEW SESQUITERPENE LACTONES FROM INULA GRANDIS

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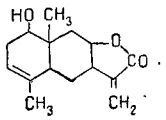
From the leaves of Inula grandis Schrenk (Compositae) collected in the Tashkent region in April, by extraction with chloroform and subsequent chromatography on alumina, we have isolated two new sesquiterpene lactones with the composition $C_{15}H_{20}O_3$, mol. wt. 248 (by mass spectrometry), which we have called "grandulin" and "grandicin." The lactone properties of the substances were confirmed by their dissolution in caustic alkalis on heating and by their recovery in the unchanged state on subsequent acidification. On titration, the lactones each consumed one mole of alkali, which showed the presence of a single lactone grouping in each of them.

Grandulin is a hydroxylactone, mp 130° C (from chloroform), $[\alpha]_D^{18}$ +125° (c 1.00; ethanol), R_f 0.7 [in the n-hexane–benzene–methanol (5 : 4 : 1) system, on paper impregnated with a 10% solution of formamide in methanol]. IR spectrum, cm^{-1}: 3395 and 3440 (OH group), 1753 (carbonyl of a γ-lactone), 1716, and 1640, 896, and 830 (primary-tertiary double bond). UV spectrum: λ_{max} 209 mμ, log ε 3.72 (exocyclic methylene grouping conjugated with the carbonyl of a lactone).

The NMR spectrum (100 MHz) of grandulin has the signal of a methyl group attached to a quaternary carbon atom (singlet, δ 1.00 ppm), a methyl group on a double bond (singlet, 2.05 ppm), an exocyclic methylene group conjugated with a lactone carbonyl (doublets, 5.45 and 6.03 ppm, J = 3.5 Hz), a lactone proton (octet, 4.63 ppm), and a proton attached to a tertiary carbon atom (octet, 3.06 ppm). Catalytic hydrogenation over Pt (Adams) gave a tetrahydro derivative with mp 148–149° C (from petroleum ether), the IR spectrum of which lacked the absorption bands at 1640 and 823 cm^{-1} and at 1716 cm^{-1}.

Taking into account the features of the NMR spectrum and the phylogenetic closeness of I. grandis to I. helenium L. and to Telekia speciosa (Schreib) Baumg., which comprise one section of Corvisartia, it may be concluded that grandulin is a lactone of the eudesmane series. On considering its physicochemical properties and comparing them with literature data for farinosin [1], ivelin [2], ivangustin [3], asperilin [4], santamarin [5], and 3-epiisotelekin [6], and their derivatives, it can be seen that the most probable structure for grandulin is



The melting point of the tetrahydro derivative was identical with that for tetrahydroasperilin.

Grandicin is a ketolactone with mp 88–90° C, $[\alpha]_D^{18}$ +111° (c 1.02; ethanol), R_f 0.93 (2,4-dinitrophenylhydrazone with mp 189–190° C). IR spectrum, cm^{-1}: 1750 (carbonyl of a γ-lactone), 1710 (carbonyl of a ketone), 1660 and 823 (double bond); UV spectrum: λ_{max} 205–210 mμ (log ε 3.78).

Its NMR spectrum has the signals of a quaternary methyl group (singlet, 0.75 ppm), and a tertiary methyl group (complex multiplet in the 1.2–1.71 ppm) each with an intensity of 3 H, and also signals of a lactone proton (multiplet, 3.68 ppm) and an exocyclic methylene group (singlets, 5.52 and 6.02 ppm). As observed previously, in alanto- and isoalantolactones there is no spin-spin coupling between H_{13} and H_{13a} [7]. The hydrogenation of grandicin gave a dihydro derivative with mp 46–47° C (from petroleum ether) (2,4-dinitrophenylhydrazone with mp 178° C). In its IR spectrum the absorption bands of the double bonds have disappeared and the carbonyl band has shifted to about 1780 cm^{-1}. In the NMR spectrum of the dihydro derivative there are three signals of methyl groups, at 1.00, 1.07, and 2.07 ppm, and the signal of a lactone proton, multiplet, 4.73 ppm; there are no signals of an exocyclic methylene group.

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