SESQUITERPENE LACTONES FROM Carpesium eximium

O. A. Konovalova, K. S. Rybalko,
and V. S. Kabanov

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From the epigeal green part of Carpesium eximium C. Winkler we have isolated four sesquiterpene lactones with the composition $C_{15}H_{20}O_3$.

The first lactone with mp 88-89°C (Kofler) $[\alpha]_D^{20}$ + 120° (c 1.5; ethanol) was identical in relation to its constants and IR, UV, and NMR spectra with carabrone – a sesquiterpene lactone from the fruit of Carpesium abratanoides L. [1]..

The second lactone with mp 158-160°C, $[\alpha]_D^{20}$ + 244° (c 5.5; chloroform) was identical with telekin, a sesquiterpene lactone first isolated from Telekia speciosa (Schreb.) Baumg. [2].

The third lactone with mp 130-132°C, $[\alpha]_D^{20}$ + 139.5° (c 4.3; chloroform) gave with acetic anhydride an lactone (taken in the form of a mull in paraffin oil) had, in addition to the absorption band of the carbonyl of a γ-lactone (1765 cm^{-1}) the strong and distinct band of a carbonyl at 1725 cm^{-1} (Fig. 1), but the composition of the lactone, $C_{15}H_{20}O_3$ (molecular weight determined mass spectrometrically), and the presence of a hydroxyl in its excludes the presence of a second carbonyl group. In the IR spectrum of a solution in $CHCl_3$, only one carbonyl absorption band appears, at 1758 cm^{-1}.

From the constants of the initial material and of its acetyl derivative, NMR and UV spectra, and the IR spectrum in $CHCl_3$ the lactone is identical with ivalin – a sesquiterpene lactone from Iva microcephala Nutt. [3].

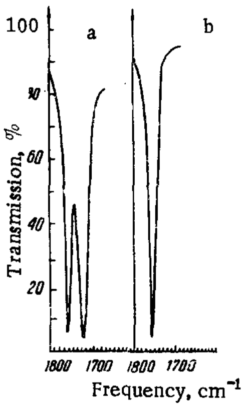

Fig. 1. Absorption bands of the lactone carbonyl in the IR spectrum of lactone C: a) on paraffin oil; b) in chloroform.

It has been observed previously that the carbonyl absorption band of unsaturated lactones splits under certain circumstances of solvent and temperature [4]. This phenomenon has not been described for sesquiterpene lactones. In the present case the splitting of the carbonyl band of a γ-lactone with an exocyclic double bond is observed.

The fourth lactone, with mp 118-120°C (Kofler), $[\alpha]_D^{20}$ + 200° (c 0.8; chloroform), forms an acetate having the composition $C_{17}H_{22}O_4$, mp 161-163°C (ethanol), $[\alpha]_D^{20}$ + 100° (c 3.8; chloroform). The NMR spectrum of this lactone is very similar to that of ivalin: there are differences only in the 1-2.5-ppm region (Fig. 2). The NMR spectra of their acetyl derivatives are also very similar. With ivalin, this lactone gives a melting-point depression of 17°C, and their acetylated derivatives show a depression of 6°C.

As in the case of ivalin, the IR spectrum of this fourth lactone in paraffin oil shows two carbonyl absorption bands while in chloroform solution it shows only one. The IR spectra of ivalin and of this lactone, and also the IR spectra of their acetyl derivatives are not identical, but they are very similar.

The facts given above permit the conclusion that the fourth lactone is a stereoisomer of ivalin. We propose for it the name carpesin. The mass spectrum of carpesin is shown in Fig. 3. The molecular peak has a value of 248; the strongest peak is that with m/e 119; peaks with m/e 230, 215, and 202 are of medium intensity and are probably formed by the elimination of 18 amu (H_2O);

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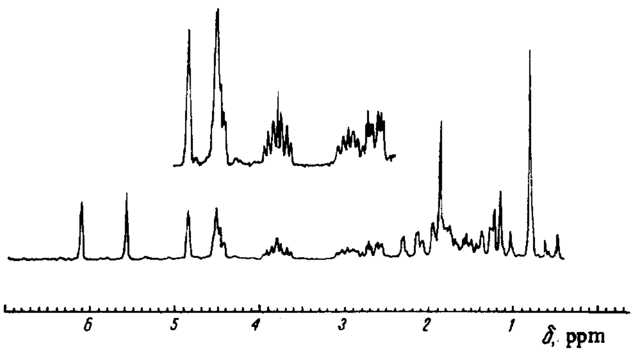

Fig. 2. NMR spectrum of carpesin.

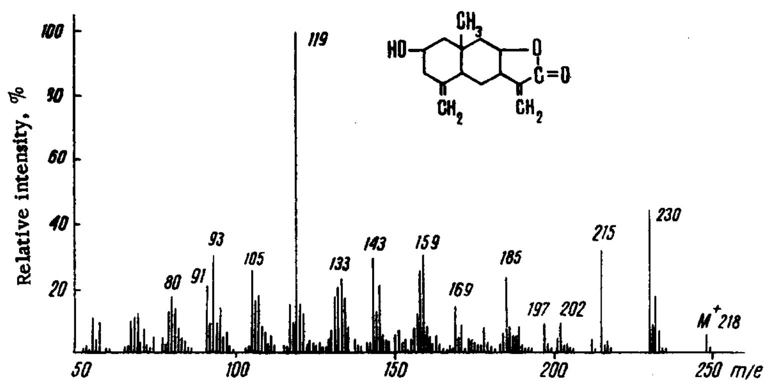

Fig. 3. Mass spectrum of carpesin.

18 + 15 amu ($H_2O + CH_3$), and 18 + 28 amu (H_2O + CO); there is also a series of other peaks which do not contradict the structure proposed for carpesin.

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrometer (mulls in paraffin oil), the UV spectra on a Hitachi EPS-3T instrument, the NMR spectra on a Varian HA-100D (with HMDS as standard), and the mass spectra on an MKh-1306 instrument with the direct introduction of the substance into the source at 70°C and with an ionizing voltage of 30 V. Thin-layer chromatography (TLC) was performed on neutral alumina (activity grade IV) in the benzene–methanol (9 : 1) system with a 0.5% solution of $KMnO_4$ in 0.5% H_2SO_4 as the chromogenic agent. The analyses of the compounds corresponded to the calculated figures.

Isolation of the Lactones. The epigeal part of Carpesium eximium C. Winkler, collected in July, 1964, in the south of the Maritime Territory (1 kg) was steeped in distilled water at 75°C for 1 h three times. The aqueous extract was treated three times with chloroform, and the solvent was distilled off. The resin obtained was chromatographed on a column of neutral alumina (activity grade IV). Elution was performed successively with petroleum ether–benzene (9 : 1, 8 : 2, 1 : 1), benzene, benzene–ether (9 : 1, 8 : 2, 2 : 1), ether, and ether–ethanol (9 : 1, 8 : 2, 1 : 1). The size of the fractions collected was 300-400 ml.

Isolation of Carabrone. The petroleum ether–benzene (9 : 1) fractions deposited acicular crystals showing a single spot with R_f 0.72 on TLC; they were recrystallized from petroleum ether–diethyl ether and dried over P_2O_5 under vacuum for two days. IR spectrum: ν_{max} 1750 cm^{-1} (γ-lactone), 1710 cm^{-1} (C = O), 1660 cm^{-1} (C = C). UV spectrum: λ_{max} 213.5 nm (ε 12,038). NMR spectrum: pair of doublets at 6.0 and 5.4 ppm (J = 3 Hz) (protons of an exocyclic methylene group conjugated with a carbonyl group); multiplet at 4.6 ppm (lactone proton); singlet at 2.0 ppm ($CH_3C = O$); singlet at 1.1 ppm $(CH_3{-}\overset{|}{\underset{|}{C}}{-})$.

Isolation of Telekin. The petroleum ether–benzene (3 : 2) fractions yielded tabular crystals with R_f 0.71, which were recrystallized from the same mixture and were dried over P_2O_5 at 76°C (10 mm Hg).

IR spectrum: ν_{max} 3440 cm^{-1} (OH), 1740 cm^{-1} (α-methylene-substituted γ-lactone), 1665 and 1640 cm^{-1} (C = C). UV spectrum: λ_{max} 201.7 nm (ε 7622). NMR spectrum: pair of doublets at 6.08 and 5.55 ppm (protons of an exocyclic methylene group conjugated with a carbonyl group); singlets at 4.85 and 4.65 ppm (protons of an exocyclic methylene group); sextet at 4.57 ppm (lactone proton); singlet at 0.93 ppm (tertiary methyl group).

A mixture of this substance with a sample of telekin gave no depression of the melting point. A lactone that we had isolated previously from this species [5] also proved to be identical with telekin.

Isolation of Ivalin. The benzene fractions yielded crystals of ivalin, which were recrystallized from ether, R_f 0.44. IR spectrum: ν_{max} 3440 and 3400 cm^{-1} (OH), 1765 and 1725 cm^{-1} (C = O), and 1665 and 1650 cm^{-1} (C = C); ν_{max} ($CHCl_3$): 3500 and 1758 cm^{-1}. UV spectrum: λ_{max} 200.5 nm (ε 11,487). NMR spectrum: singlets at 6.15 and 5.62 ppm (exocyclic methylene in a γ-lactone ring; feebly resolved doublets at 4.88 and 4.56 ppm (protons of a second exocyclic methylene group), multiplet at 4.50 ppm (lactone proton), multiplet at 3.82 ppm (hemihydroxyl proton), singlet at 0.82 ppm (protons of a tertiary methyl group).

Acetylivalin. To a solution of 0.1 g of ivalin in 2 ml of pyridine was added 1 ml of acetic anhydride, and the mixture was heated in the water bath at 50°C for 1 h. After cooling, the reaction mixture was treated with 15 volumes of water and the reaction product was extracted with chloroform. The chloroform extract was washed with a 5% solution of HCl and then with water to neutrality, and the chloroform was distilled off. The white crystals that deposited were recrystallized from ethanol and were dried in vacuum over P_2O_5; composition $C_{17}H_{22}O_4$, mp 148.5-150°C (Kofler), $[\alpha]_D^{20}$ + 110° (c 4.0; chloroform). IR spectrum: ν_{max} 1765 cm^{-1} (γ-lactone), 1730 cm^{-1} (OCO), 1668 and 1650 cm^{-1} (C = C). NMR spectrum: pair of singlets at 6.10 and 5.58 ppm (protons of an α-methylene group in a γ-lactone), feebly resolved doublets at 4.90 and 4.56 ppm (protons of an exocyclic methylene group), multiplet at 4.49 ppm (lactone proton), multiplet at 4.82 ppm (hemiacetyl proton), singlet at 1.99 ppm (acetyl methyl group), singlet at 0.85 ppm (tertiary methyl group).

Isolation of Carpesin. The mother liquors after the isolation of ivalin yielded white crystals with mp 115-128°C, which were fractionally crystallized from ether. IR spectrum: ν_{max} 3530, 3440, and 3400 cm^{-1} (OH), 1762 and 1728 cm^{-1} (C = O), and 1666 and 1650 cm^{-1} (C = C); ν_{max} ($CHCl_3$): 3600, 1760, 1670, and 1648 cm^{-1}. UV spectrum: λ_{max} 201 nm (ε 11,419). NMR spectrum: pair of singlets at 6.11and 5.53 ppm (protons of an α-methylene group in a γ-lactone), feebly resolved doublets at 4.86 and 4.52 ppm (protons of a second exocyclic methylene group), multiplet at 3.80 ppm (lactone proton), and singlet at 0.80 ppm (protons of a tertiary methyl group).

Carpesin acetate was obtained by the method described above.

IR spectrum: ν_{max} 1750 cm^{-1} (γ-lactone), 1728 (OCO), 1665 and 1648 cm^{-1} (C = C). NMR spectrum: feebly resolved doublets at 6.09 and 5.53 ppm (signals of the protons of an α-methylene group of a γ-lactone), broadened singlets at 4.85 and 4.56 ppm (exocyclic methylene group), multiplet at 4.88 ppm (hemiacetyl proton), multiplet at 4.45 ppm (lactone proton).

SUMMARY

From the epigeal part of Carpesium eximium C. Winkler four sesquiterpene lactones with the composition $C_{15}H_{20}O_3$ have been isolated: carabrone, telekin, ivalin, and a new sesquiterpene lactone, a stereoisomer of ivalin, which has been called carpesin.

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