SESQUITERPENES OF THE ROOTS OF Inula grandis

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We have previously reported the isolation from the roots of Inula grandis Schrenk of the total sesquiterpene lactones which, according to TLC, consisted of eight substances. From this mixture two components were isolated to which the names grandin [1] and igalan [2] were given. Continuing a study of the lactones, by repeated column and thin-layer chromatography we have isolated another four substances.

When the column was washed with benzene containing methanol, a substance $C_{15}H_{20}O_3$ with mp 270°C (decomp.), R_f 0.58 (cherry-red spot), readily soluble in methanol, ethanol, and benzene, and sparingly soluble in aqueous ethanol, was obtained. Its IR spectrum (Fig. 1a) exhibited bands at 1770 cm^{-1} (carbonyl of a γ-lactone), 1670, 1419, 1440, and 1140 cm^{-1} (exocyclic methylene group in conjugation with a lactone carbonyl), 896, 830, and 850 cm^{-1} (primary-tertiary double bond), 3400 cm^{-1} (hydroxy group), and 2945, 2840, and 2880 cm^{-1} (C-methyl groups). There were no absorption maxima in the 210-360 nm region of the UV spectrum, which shows the absence of conjugation. The substance is neutral and possesses the properties of a lactone: it dissolves in alkalis on heating and is reprecipitated unchanged on acidification. The chemical properties and the spectral characteristics show that this substance is a sesquiterpene lactone, and we have provisionally called it igalin.

The same fractions yielded a second substance with the composition $C_{15}H_{26}O_2$, mp 102-102.5°C (aqueous ethanol), R_f 0.20 (bright crimson coloration), which we have called igalol. Its IR spectrum (Fig. 1c) shows strong absorption bands at 1640, 1440, and 890 cm^{-1}, which are characteristic for a primary-tertiary double bond, and a broad band in the 3200-3400 cm^{-1} region (hydroxy group). On comparing the spectral characteristics (IR and mass spectra), it can be seen that igalol is identical with the diol which we obtained by the reduction of igalan with sodium borohydride and, consequently, has the structure I (see Fig. 1c). The difference in the melting points of the natural and synthetic products is probably due to the fact that the latter consists of a mixture of epimers.

The washing of the chromatographic column with methanol yielded a compound $C_{15}H_{28}O_5$, mp 320° (from ethanol), readily soluble in water, and soluble in cold ethanol, ether, benzene, and chloroform. It is neutral and does not react with carbonyl reagents. Its IR spectrum (see Fig. 1b) has bands at 3280-3250 and 1080, 1170 cm^{-1} (hydroxy groups), 1345, 1370, and 1170 cm^{-1} (gem-dimethyl groups), 2974, 2945, and 2850 cm^{-1} (C-methyl groups), and 1645 cm^{-1} (C=C bond). There is no absorption in the 210-260 nm region of the UV spectrum. These facts show that this substance, which has been called provisionally grandol, is a sesquiterpene alcohol.

According to TLC, the filtrate from the separation of the igalan contained two substances with R_f 0.84 (igalan) and 0.9 (bright crimson coloration). After repeated rechromatography of this fraction, we obtained a yellowish syrupy mass with a characteristic odor readily soluble in petroleum ether, benzene, chloroform, and ethanol. The main component of this mixture (R_f 0.9) did not react with carbonyl reagents and, from its behavior with alkalis, is a lactone ("lactone No. 8"). It was impossible to isolate it in the crystalline state. Its UV spectrum showed no absorption maxima in the region indicated above, and the IR spectrum (see Fig. 1d) showed strong bands at 1750-1780 cm^{-1} (carbonyl of a γ-lactone), 1670 and 1642 cm^{-1} (double bond), 2940 and 2880 cm^{-1} (C-methyl group), and 3500-3300 cm^{-1} (hydroxy group). The broad carbonyl band in the 1750 cm^{-1} region and also absorption in the 1250 and 1270 cm^{-1} regions give grounds for assuming the presence of an unsaturated ester grouping in this lactone. The strong absorption at 1110-1160 cm^{-1}

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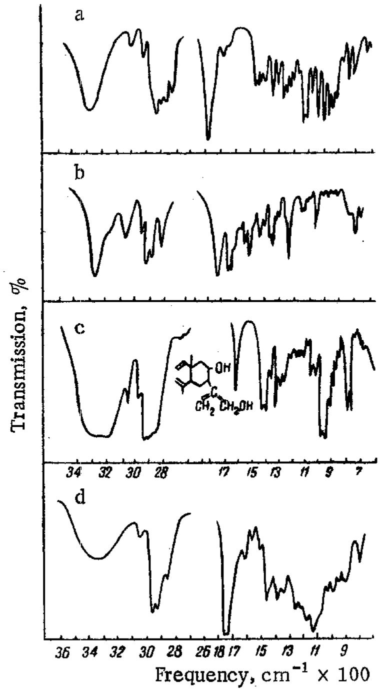

Fig. 1. IR spectra of igalin (a), grandol (b), igalol (c), and lactone No. 8 (d).

and the bands at 1670 and 1410 cm^{-1}, together with the absence of absorption at 1690 cm^{-1}, show the presence of an exocyclic methylene group and the absence of a double bond in the lactone ring. The NMR spectrum (solution of the substance in CCl$_4$) exhibited the signals of methyl groups: on a tertiary carbon atom – doublets at 1.26, J = 7 Hz, and 1.06 ppm, J = 7 Hz (exocyclic methylene group attached to a lactone ring); doublets at 5.50 and 6.00 ppm, J = 2.5 Hz (lactone proton); multiplets in the 4.6-5.1 ppm region (protons at a double bond); and doublets at 6.95 and 7.27 ppm, J = 7 Hz. The chemical study of the hydroxy lactone No. 8 is continuing.

EXPERIMENTAL

The NMR spectra were taken on a JNM-4N-100/100 MHz instrument, the IR spectra on a UR-20 spectrophotometer, the UV spectra on a "Hitachi" spectrophotometer, and the mass spectra on an MKh-1303 instrument. TLC was performed in a fixed layer of alumina in the benzene–methanol–ethyl acetate (94 : 3 : 3) system. The spots were revealed by spraying the plates with a 1% solution of vanillin in conc. H$_2$SO$_4$ and methanol.

Igalin. After elution of the igalan, the chromatographic column was washed with benzene and then with benzene containing 1-5% of methanol, fractions 13-21 (0.5 liter each) being collected. When the eluate was concentrated in vacuum, a substance (grandin) crystallized out which was filtered off and washed with methanol. The methanolic filtrate was distilled off. This gave 0.06 g of a mixture with R$_f$ 0.58 and 0.20; it was dissolved in hot 30% methanol. On cooling, the solution deposited 0.05 g of a substance C$_{15}$H$_{20}$O$_3$ in the form of colorless acicular crystals with mp 134-135°C and 270°C, mol. wt. 248 (mass-spectrometrically).

Igalol. The filtrate from the separation of the igalin was diluted with a threefold volume of hot water. A precipitate of igalol with the composition C$_{15}$H$_{26}$O$_2$ and mp 102-102.5°C (from aqueous ethanol) was formed, mol. wt. 238.

Grandol. When the chromatographic column was eluted with methanol (fractions 22-34), and the solvent was distilled off, a precipitate was obtained which was filtered off and washed with benzene. The insoluble part was recrystallized from ethanol. In this way, 0.25 g of colorless crystals C$_{15}$H$_{28}$O$_5$, mp 320°C (decomp.), mol. wt. 288, was obtained.

The Hydroxy Lactone No. 8. The filtrate from the separation of the igalan [2] was diluted with 50% aqueous methanol and the precipitate was filtered off. The filtrate was rechromatographed on a column of alumina, being eluted subsequently with 80% methanol. The eluate was concentrated in vacuum and was treated repeatedly with petroleum ether. The extract was rechromatographed on alumina, then eluted with petroleum ether. Concentration of the eluate gave a yellowish syrupy mass with R$_f$ 0.9.

SUMMARY

The roots of Inula grandis Schrenk has yielded a sesquiterpene lactone C$_{15}$H$_{20}$O$_3$, mp 134-135°C and 270°C, which has been called igalin, and two diols – C$_{15}$H$_{26}$O$_2$ with mp 102-102.5°C and C$_{15}$H$_{28}$O$_5$ with mp 320°C – which have been called igalol and grandol, respectively.

Igalol is identical with the diol obtained by the reduction of igalan with sodium borohydride, and has the structure elemane-8,12-diol.

The sesquiterpene hydroxy lactone "lactone No. 8" has been isolated in the form of an oil and it is now being studied.

LITERATURE CITED

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