STRUCTURE OF THE SESQUITERPENE LACTONES FROM CYCLACHAENA XANTHIFOLIA

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We have studied the total sesquiterpene lactones obtained from a chloroform extract of the racemes of *C. xanthifolia* Fresen. (*Iva xanthifolia* Nutt.), family *Compositae* and consisting of four substances.

A ketolactone $C_{15}H_{20}O_4$ (I) was identified as coronopilin [1]. An optically active substance, $C_{15}H_{20}O_4$, (II) with mp 164–166° C has no maxima in the UV spectrum characteristic for conjugated double bonds. We have called it ivoxanthin. Its IR spectrum has absorption bands at 3490 cm^{-1} (hydroxyl group), 1660 and 820 cm^{-1} (exocylic double bond) and 1745 cm^{-1} (γ-lactone and cyclopentanone). With 2,4-dinitrophenylhydrazine it readily forms a hydrazone with mp 130–132° C, which confirms the presence of a ketonic group in the molecule of this compound.

The IR spectrum of the product of the dehydration of substance II with thionyl chloride, having mp 144–146° C, exhibits absorption bands at 1710 and 1585 cm^{-1} due to a carbonyl group in conjugation with a symmetrically disubstituted double bond. In the IR spectra of ivoxanthin and the product of its dehydration, the absorption band of this keto group is in the 1745–1710 cm^{-1} region, which is characteristic for five-membered ketones and not for six- or seven-membered ketones.

When the ketolactone II was oxidized with chromic anhydride in acetonic solution or was acetylated with acetic anhydride in the presence of pyridine, it underwent dehydration, forming an unsaturated product $C_{15}H_{18}O_3$ (III). We obtained a substance of the same composition from the plant. Its IR spectrum coincided with the IR spectra of the product of the dehydration of ivoxanthin with mp 144–146° C and with that of the sesquiterpene lactone ambrosin [2,3]. Mixtures of the products of the dehydration of ivoxanthin and of the native substance from the plant with an authentic sample of ambrosin gave no depression of the melting point.

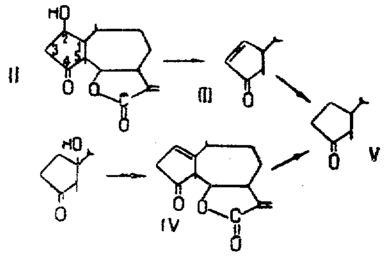
The hydrogenation of one double bond of substance III over $Pd/SrCO_3$ gave a crystalline product, V, with mp 162–164° C, the IR spectrum of which had absorption bands at 1750 cm^{-1} (γ-lactone and cyclopentanone) and 1680 cm^{-1} (double bond). The IR spectra had maxima characteristic for a lactone carbonyl and a nonconjugated ketonic CO group: 270 and 290 mμ (log ε 4.15 and 1.47, respectively). These properties of the hydrogenation product correspond to literature data for dihydroambrosin [4].

The dehydrogenation of substance III after its preliminary saturation with hydrogen at 300–320° C in the presence of selenium gave a mixture of products. From them we isolated artemazulene, obtained from ambrosin previously by other workers [4].

On the basis of what has been stated above, it may be assumed that the hydroxyl group in the molecule of ivoxanthin is located in a five-membered ring in the β position with respect to a ketonic carbonyl group.

A ketolactone $C_{15}H_{18}O_3$ with $[\alpha]_D^{20}$ −60° (chloroform) which we isolated from the plant, was identical according to a mixed melting point and its IR spectrum with the product of the dehydration of coronopilin (IV). Its IR spectrum had bands at 1760 cm^{-1} (γ-lactone group and cyclopentanone) and 1655 and 820 cm^{-1} (trisubstituted double bond). The partial hydrogenation of IV over platinum (Adams) in ethyl acetate gave a saturated compound the IR spectrum of which coincided with that of dihydroambrosin and which exhibited no depression of the melting point in admixture with a sample of dihydroambrosin obtained by the hydrogenation of III.

The facts presented permit the assumption that substance IV has the structure of 1,2-anhydrocoronopilin.



EXPERIMENTAL

We studied the racemes of C. xanthifolia Fresen., collected in September 1967, in the Ukraine (Zaporozh'e region). The IR spectra were recorded on a UR-10 instrument in samples molded with KBr and the UV spectra on an SF-4 spectrophotometer in ethanol.

Isolation of the sesquilactones. The air-dry racemes (12 kg) were extracted with chloroform (60 *l*). The extract was evaporated to a volume of 5 *l* and dried with sodium sulfate and the solvent was distilled off. 80 g of the extract was treated with 500 ml of 50% aqueous acetone. The residue was filtered off and the filtrate was evaporated; 50 g of the combined lactones (0.41%) was dissolved in 250 ml of benzene and the solution was treated with 250 ml of ether. This gave 38 g of a crystalline substance identical with the sesquiterpene lactone coronopilin.

The mother liquor from which the coronopilin was isolated was evaporated. The residue was dissolved in 70 ml of methanol and the solution was poured into 0.5 *l* of petroleum ether. The crystals that precipitated were purified by crystallization from benzene. This gave 3.5 g of ivoxanthin with mp 164–166° C (vacuum sublimation), $[\alpha]_D^{20}$ +47.7° (c 6.5; chloroform). IR spectrum, cm^{-1}: 3490 (—OH), 1745 (γ-lactone and cyclopentanone), 1660 and 820 ($>C{=}CH_2$).

Found, %: C 68.13, 68.14; H 7.74, 7.62; mol. wt. 264 (mass spectrometry). Calculated for $C_{15}H_{20}O_4$, %: C 68.16; H 7.63. Mol. wt. 264.

Melting point of the 2,4-dinitrophenylhydrazone 130–132° C (from ethanol).

The mixture of petroleum ether and methanol after the separation of substance II was evaporated and the residue was chromatographed on 250 g of alumina (activity grade III) in the petroleum ether–chloroform (7 : 3) system. The evaporated eluates gave a crystalline substance III. After two recrystallizations from benzene–ether (1 : 1), mp 144–146° C (no depression of the melting point was found in a mixture with authentic ambrosin), $[\alpha]_D^{20}$ −122° (c 8.8; chloroform). IR spectrum, cm^{-1}: 1770 (γ-lactone), 1710 (α, β-unsaturated ketone in a five-membered ring), 1660 and 820 ($>C{=}CH_2$), and 1585 (conjugated $—HC{=}C—$ in a five-membered ring). UV spectrum: 219, 320 mμ (log ε 4.18, 1.70, respectively).

Then the column was eluted in the petroleum ether–benzene (1 : 1) system. Evaporation of the eluate yielded a crystalline substance, IV, with mp 85–87°°C. After three recrystallizations from ether, mp 120–122° C, $[\alpha]_D^{20}$ −60° (c 7.5; chloroform). IR spectrum: 1760, 1655, 820 cm^{-1}.

Found, %: 72.95, 73.10; H 7.41, 7.28. Calculated for, $C_{15}H_{18}O_3$, %: C 73.15; H 7.37.

Dehydration of coronopilin. A solution of 1 g of coronopilin in 5 ml of dry pyridine was cooled to 0° C, and 1.5 ml of thionyl chloride was added dropwise. After 15 min, ice water was added to the mixture and it was treated with chloroform. The chloroform extract was washed with 5% HCl and then with water and was dried with sodium sulfate. After the solvent had been distilled off, the residue was crystallized from ether, which gave 0.7 g of anhydrocoronopilin with mp 120–122° C, $[\alpha]_D^{20}$ −58° (c 7; chloroform). The IR spectrum of this compound was identical with that of compound IV from the plant; a mixture gave no depression of the melting point.

Treatment of ivoxanthin with acetic anhydride. To a solution of 1.5 g of substance II in 5 ml of pyridine was added 5 ml of acetic anhydride. The mixture was left at 20° C for 15 hr. After the usual working up, crystallization from benzene–petroleum ether (1 : 1) gave 1.2 g of substance III with mp 144–146° C, $[\alpha]_D^{20}$ −128° (c 6.7; chloroform). Its IR and UV spectra coincided with those of ambrosin, and a mixture with ambrosin gave no depression of the melting point.

Products with the same compositions were obtained by the oxidation of II with chromic anhydride in acetone and by the dehydration of II with $SOCl_2$ in pyridine.

Hydrogenation of substance III. The hydrogenation of 123 mg of the ketolactone III was carried out in 5 ml of ethyl acetate in the presence of 20 mg of 5% $Pd/SrCO_3$. At 25° C and 755 mm, 15 ml of hydrogen was absorbed, which corresponds to one double bond. After the usual working up, crystallization from ether yielded 100 mg of substance V. By purification on 8 g of silica gel with a mixture of benzene and acetone (9 : 1) the melting point was raised to 162–164° C. IR spectrum, cm^{-1}: 1750 (unsaturated γ-lactone and cyclopentanone) and 1680 ($>C=C<$). UV spectrum: λ_{max} 270, 290 mμ (logε 4.15, 1.47). Literature data for dihydroambrosin: mp 165° C. The UV and IR spectra coincided [4].

Hydrogenation of the ketolactone (IV). The hydrogenation of 116 mg of substance IV was carried out in 5 ml of ethyl acetate over 23 mg of platinum oxide (Adams). At 24° C and 755 mm, 20 ml of hydrogen was absorbed, which corresponds to 1.2 equivalent. After the usual working up, the hydrogenation product was purified on 8 g of silica gel in the benzene–acetone (9 : 1) system. Evaporation of the eluates yielded 98 mg of dihydroambrosin with mp 163–164° C (from ether). A mixture with the dihydroambrosin described above gave no depression of the melting point, and their IR spectra coincided.

Dehydrogenation of substance III. The lactone III (0.5 g) was saturated with hydrogen as described above. The hydrogenation product was heated with 1 g of selenium at 300–320° C for 10 min. The reaction mixture was extracted with petroleum ether and chromatographed on alumina (activity grade II). Evaporation of an eluate of the middle zone gave a blue oil forming a trinitrobenzene derivative with mp 187–189° C (from ethanol), which corresponds to the trinitrobenzene derivative of artemazulene. Literature data: mp of the trinitrobenzene derivative of artemazulene 188–189° C [4].

CONCLUSIONS

The racemes of Cyclachaena xanthifolia Fresen. have yielded four sesquiterpene lactones, two of which are new, not having been described in the literature previously, and these have been called ivoxanthin and 1,2-anhydrocoronopilin. Structures II and IV have been proposed for these.

The plant also contains the sesquiterpene lactones coronopilin and ambrosin.

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