STUDY OF THE STRUCTURE OF SAURIN, A SESQUITERPENE LACTONE FROM SAUSSUREA PULCHELLA

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Saurin, which we have isolated from the plant Saussurea pulchella Fisch. has the composition $C_{15}H_{18} \cdot 0.5\ H_2O$ and contains two hydroxy and two carboxy groups (bands at 1775 and 1720 cm^{-1}). It is an unsaturated substance not containing OCH_3 or CCH_3 groups. The IR spectrum of saurin shows the absence of conjugated double bonds from its molecule.

The hydroxy groups of saurin are acetylated under mild conditions and, consequently, cannot be tertiary. The IR spectrum of diacetylsaurin has bands at 1780, 1758, and 1750 cm^{-1}. The formation of two moles of formaldehyde in the ozonolysis of saurin shows that two double bonds in the molecule of the substance are terminal.

When saurin is catalytically hydrogenated with a platinum catalyst, two double bonds are reduced and the hydrogenolysis of one hydroxy group takes place. In view of this, the latter must be an allyl hydroxy group and belong to the grouping $-C{=}C-C-OH$. The hydrogenation product, tetrahydrodeoxysaurin $C_{15}H_{22}O_4$, has two carbonyl groups (bands at 1768 and 1732 cm^{-1}) and, in contrast to saurin, one hydroxy group and two $C-CH_3$ groups.

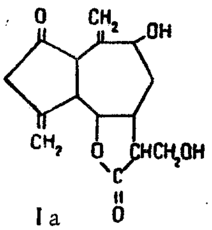
The reduction of tetrahydrodeoxysaurin with sodium borohydride led to a triol $C_{15}H_{26}O_4$ containing, in addition to three hydroxy groups, one carbonyl group (band at 1720 cm^{-1}). This result of reduction shows that tetrahydrodeoxysaurin contains a lactone group capable of being reduced under these conditions which, judging from the position of the absorption band due to it in the spectra of saurin, diacetylsaurin, and tetrahydrosaurin (1775, 1780, and 1768 cm^{-1}, respectively), can only be a γ-lactone group.

The saponification of saurin with aqueous alkali gave a noncrystalline chromatographically homogeneous acid whose IR spectrum has absorption bands of hydroxy groups, a carbonyl group (1750 cm^{-1}), and double bonds.

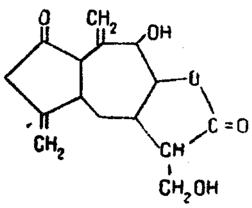
The bromination of saurin gives tetrabromosaurin $C_{15}H_{18}Br_4$; this substance contains two carbonyl groups (bands at 1785 and 1748 cm^{-1}). An excess of bromine leads to a pentabromo derivative, which is due to the presence of mobile hydrogen in the α-position to the carbonyl.

In addition to the γ-lactone carbonyl group, the saurin molecule has another carbonyl group. It can only be a ketonic group, since saurin does not exhibit reactions characteristic for aldehydes. The IR spectrum of saurin has no bands due to the C–H of aldehydes in the 2800 cm^{-1} region. The absorption band of this keto group in the IR spectra of saurin and its conversion products is located in the 1720–1750 cm^{-1} region, which is characteristic for five-membered and not six- or seven-membered encyclic ketones. The saurin molecule lacks groupings that can be oxidized by periodic acid.

The dehydrogenation of tetrahydrodeoxysaurin at 320° C in the presence of selenium led to a mixture of products from which chamazulene, apparently guaiazulene, and a substance $C_{14}H_{16}O_2$ were isolated. The formation of chamazulene on dehydrogenation enables a preliminary conclusion to be drawn about the structure of the carbon skeleton of tetrahydrodeoxysaurin and saurin. If no rearrangement and change in the structure of the nucleus connected with it take place on dehydrogenation, which is not excluded, the structure of saurin may be based on a partially hydrogenated azulene nucleus. In this case, two formulas are probable for saurin, (Ia) and Ib). The position of the terminal methylene double bond is determined by the presence of methyl groups in the corresponding positions of chamazulene. Accordingly, the location of the allyl hydroxy group in the seven-membered ring and of an unconjugated ketone group in the five-membered ring becomes clear. Two possible positions remain for the γ-lactone grouping, both found in sesquiterpene compounds. There can be neither a methyl group nor a terminal methylene group nor an aldehyde group in the α-position to the carbonyl of the lactone group. This position is apparently occupied by the $-CH_2OH$ group.



Ia



Ib

Experimental

Isolation of saurin. 1.5 kg of the air-dry epigeal mass of the plant *Saussurea pulchella* was extracted with ether (2 × 10 *l*). The ethereal extracts were evaporated to a volume of 400 ml. The crystals which deposited were separated off and dissolved in a mixture of 180 ml of chloroform and 280 ml of alcohol. The solution was treated with 180 ml of water and 540 ml of petroleum ether. The lower layer was separated off, heated to 70° C, and diluted with 450 ml of hot water (60° –80° C). On cooling, 7 g of saurin was obtained with mp 87° –88° C [from a mixture of alcohol and water (1: 2.5)], $[\alpha]_{589}$ + 60.1°, $[\alpha]_{576}$ + 105.9°, $[\alpha]_{574}$ + 120.0°, $[\alpha]_{486}$ + 205°, $[\alpha]_{405}$ + 246°, $[\alpha]_{368}$ + 333°, $[\alpha]_{334}$ + 426° $[\alpha]_{327}$ + 459°, $[\alpha]_{320}$ + 487°, $[\alpha]_{313}$ + 515°, $[\alpha]_{307}$ + 540°, $[\alpha]_{302}$ + 561°, $[\alpha]_{297}$ + 590°, $[\alpha]_{283}$ +680°, $[\alpha]_{278}$ + 857°, $[\alpha]_{274}$ + 969°, $[\alpha]_{271}$ + 930° (c 0.58; dioxane). IR spectrum (taken on a UR-10 instrument): 3580, 3450, 3280, 2960, 2920, cm^{-1} (in a polyfluorohydrocarbon). 1775, 1720, 1650, 1549, 1410, 1280, 1240, 1150, 1080, 1050, 1035, 995, 970, 960, 920, 800 cm^{-1} (in chloroform).

Found, %: C 62.70, 62.66; H 6.72, 6.85; OH 15.00; H_2O (by the Karl Fischer method) 3.94; mol. wt. 270 (Rast). Calculated for $C_{15}H_{18}O_5 \cdot 0.5\ H_2O$, %: C 62.71; H 6.66; 2.5; OH 14.79; 0.5; H_2O 3.14 mol. wt. 287.

Saurin was chromatographed on Leningrad paper, type "M" in the alcohol – water (3 : 2) system (spots revealed with $KMnO_4$, R_f 0.7). After the crystalline hydrate had been dried (at 150°C and 3 mm, 0.5 hr) an amorphous substance with mp 314°–322°C, insoluble in ether, benzene, dioxane, pyridine, and tetrahydrofuran was formed.

Found, %: C 65.63, 65.13; H 6.78, 6.68. Calculated for $C_{15}H_{18}O_5$, %: C 64.90; H 6.49.

After the amorphous anhydrous substance had been crystallized from a mixture of alcohol and water, a crystalline hydrate with mp 87°–88° C identical with the crystalline hydrate taken for drying was obtained.

Acetylation of saurin. A solution of 0.3 g of saurin in 1 ml of acetic anhydride and 2 ml of pyridine was left overnight at 20° C. The excess of acetic anhydride and the pyridine was distilled off in vacuum, the residue was dissolved in water, and the reaction product was extracted with ether. The extract was washed with 5% hydrochloric acid, with bicarbonate solution, and with water, and was then dried and evaporated. This gave 0.25 g of the noncrystalline diacetylsaurin. IR spectrum: 3045, 1770, 1740, 1648, 1450, 1410, 1380, 1150, 1055, 1035, 1000, 920 cm^{-1} (in chloroform); 1780, 1750 cm^{-1} (in dioxane).

Found, %: C 62.09, 62.70; H 5.81, 5.82. Calculated for $C_{19}H_{22}O_7$, %: C 62.98; H 6.07.

The diacetylsaurin was chromatographed under the same conditons as saurin, R_f 0.56.

Catalytic hydrogenation of saurin. One gram of saurin in 30 ml of glacial acetic acid was hydrogenated over platinum (from 0.3 g of PtO_2); 350 ml of hydrogen was absorbed. The residue after the acetic acid had been distilled off was dissolved in ether. The solution was washed with water, dried, and evaporated. This gave 1 g of noncrystalline substance, the chromatography of which on plates with a fixed layer of silica gel showed the presence of three substances, with R_f 0.84, 0.58, and 0.21 [KSK silica gel with 5% of calcium sulphate; solvent: ether–petroleum ether (1 : 1); spots revealed with conc. H_2SO_4]. On standing, the mass partially crystallized, and tetrahydrodeoxysaurin was isolated with mp 134°–136° C (from ether), $[\alpha]_{389}$ + 41.3°, $[\alpha]_{578}$ +41.0°, $[\alpha]_{546}$ +46.1°, $[\alpha]_{436}$ + 70.6°, $[\alpha]_{405}$ +79.7°, $[\alpha]_{394}$ +85.1°, $[\alpha]_{382}$ +90.5°, $[\alpha]_{371}$ +98.1°, $[\alpha]_{365}$ 100°, $[\alpha]_{351}$ +106°, $[\alpha]_{342}$ +116°, $[\alpha]_{334}$ +125°, $[\alpha]_{327}$ +127°, $[\alpha]_{313}$ + 124°, $[\alpha]_{302}$ +138°, $[\alpha]_{297}$ +150° (c 0.56; dioxane), R_f 0.58: IR spectrum: 3450, 1767, 1732, 1745, 1390, 1355, 1300, 1265, 1235, 1200, 1162, 1100, 1072, 1025, 1015, 965, 855, 735 cm^{-1} (in chloroform).

Found, %: C 67.43; H 8.67; CCH_3 11.09. Calculated for $C_{15}H_{22}O_4$, %: C 67.64; H 8.32; 2 CCH_3 11.2.

Acetylation of tetrahydrodeoxysaurin. 0.3 g of the substance was acetylated with a mixture of 1 ml of acetic anhydride and 2 ml of pyridine. The reaction product was treated by the method described above. This gave 0.2 g of acetyltetrahydrodeoxysaurin.

Found, %: C 66.72; H 8.04. Calculated for $C_{17}H_{24}O_5$, %: C 66.21; H 7.84.

Bromination of saurin. A solution of 0.051 g (0.17 mmole) of saurin in 2 ml of CH_3COOH was treated with 8.3 ml of a solution of 0.31 g (0.93 mmole) of $C_5H_5N \cdot HBr \cdot Br_2$ in 15 ml of CH_3COOH. After an hour, the solution had become decolorized. On dilution with water, a white amorphous substance deposited which was insoluble in water and readily soluble in alcohol and ether. An ethereal solution of the substance was washed successively with a solution of bicarbonate and water and was dried and evaporated. This gave 0.08 g of an amorphous substance with mp 123°–128° C. IR spectrum: 3450, 1785, 1743 cm^{-1} (in paraffin oil).

Found, %: C 30.26; H 3.22; Br 53.43. Calculated for $C_{15}H_{18}O_5Br_4$, %: C 30.10; H 3.01; Br 53.50.

Ozonolysis of saurin. A current of ozonized oxygen was passed through a solution of 0.89 g (3 mmole) of saurin in 100 ml of chloroform at 0° C for an hour; about 7 mmole of ozone was absorbed. The solution was evaporated in vacuum at 25° C. With dimedone, the distillate yielded 1.9 g of formaldehyde-dimedone with mp 183°–184° C

(6.5 mmole).

Saponification of saurin. One gram of saurin was heated for 1 hr with 75 ml of 0.1 N caustic potash. After evaporation to small bulk, the solution was acidified with 10% hydrochloric acid. The reaction product was extracted with ether. This gave 0.8 g of a noncrystalline substance. Chromatography was carried out on Leningrad paper, type "M" (paper previously washed with 1 N citric acid and then with water) in the propan-1-ol–conc. NH_4OH (6:4) system (spots revealed with Bromophenol Blue, R_f 0.52). IR spectrum: 3400, 1750, 1650 cm^{-1} (in paraffin oil).

Equiv. wt. found: 290. Calculated for $C_{15}H_{20}O_6$: 296.

Reduction of tetrahydrodeoxysaurin. A mixture of 0.5 g of tetrahydrodeoxysaurin and 0.5 g of sodium borohydride was dissolved in 50 ml of 50% methanol. The solution was left at 20° C for 18 hr and was then evaporated in vacuum to small bulk, leading to the deposition of 0.45 g of a substance which was crystallized by the addition of ether. This gave 0.2 g of a triol with mp 183.5°–185.5° C (from ether). IR spectrum: 3620, 3030, 1720 cm^{-1} (in chloroform).

Found, %: C 66.74; H 9.46; CCH_3 11.46; H_{labile} 1.11. Calculated for $C_{15}H_{26}O_4$, %: C 66.70; H 9.60; 2 CCH_3 11.1; 3H 1.02.

Oxidation of saurin with periodic acid. 0.068 g of saurin in 15 ml of methanol was oxidized with 0.15 g of sodium periodate. After 16 hr, 0.13 g of periodate was found in the solution.

Dehydrogenation of tetrahydrodeoxysaurin. A mixture of 1.6 g of the substance and 2 g of selenium was heated at 320° C for 10 min. The reaction products were extracted with ether and were then chromatographed on alumina from petroleum ether (bp 40–60° C) Elution of the column gave three fractions corresponding to the three separate zones on the column: 0.4 g of a blue liquid (fraction 1), 0.07 g of a blue product (fraction 2), and 0.1 g of an orange crystalline substance (fraction 3). Fractions 1 and 2 were chromatographed on Whatman No. 1 paper impregnated with a 10% solution of silicone oil in petroleum ether (bp 40°–60° C). Each fraction gave a single spot on the chromatograms: fraction 1 – R_f 0.63; fraction 2 – R_f 0.40. These values correspond to the R_f values for chamazulene and guaiazulene, respectively [1]. The IR spectrum of fraction 1 coincided with that of chamazulene [2]. By a known method, the trinitrobenzene derivative with mp 130° C was obtained from fraction 1. A mixture with the authentic trinitrobenzene derivative of chamazulene melted at the same temperature. The substance of fraction 3 was recrystallized from ether and had mp 127°–130° C, IR spectrum: 1730, 1604, 1551, 1510 cm^{-1} (in $CHCl_3$). UV spectrum (taken on an SF-4 instrument in alcohol): 237, 265, 386, 403 mμ (log ε 4.29, 4.33, 4.29, 4.35).

Found, %: C 78.47, 78.12; H 7.47, 7.54. Calculated for $C_{14}H_{16}O_2$, %: C 77.90; H 7.43.

Summary

Saurin, a sesquiterpene isolated from Saussurea pulchella Fisch., has the composition $C_{15}H_{15}O_5 \cdot 0.5\ H_2O$. It It contains a γ-lactone ring, two hydroxy groups, two terminal methylene groups, and a keto group in a five-membered ring. Dehydrogenation with selenium gives chamazulene and, apparently, guaiazulene. Two possible structural formulas of saurin, (Ia) and (Ib), are proposed.

REFERENCES

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