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SHORT COMMUNICATION

THE STRUCTURE OF CASCARILLIC ACID FROM CASCARILLA ESSENTIAL OIL

O MOTL, MAHASEN AMIN and P SEDMERA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague-6,
Czechoslovakia

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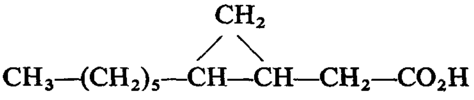
Abstract—On the basis of physico-chemical data and chemical reactions it was established that cascarillic acid, $C_{11}H_{20}O_2$, present in cascarilla essential oil, is the cyclopropanecarboxylic acid (I)

INTRODUCTION

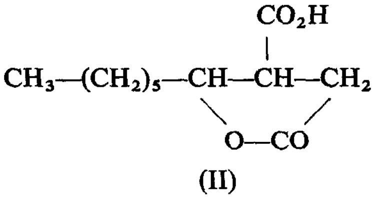
CASCARILLIC acid, $C_{11}H_{20}O_2$, is the main component of the acid fraction of cascarilla essential oil[1,2] obtained mainly from the bark of *Croton eluteria* Benett by steam distillation Although some of its chemical properties have been known for more than 70 years,[1,3] its structure has not yet been determined During study of the composition of this essential oil, we isolated the acid $C_{11}H_{20}O_2$ as the main component of the acid fraction The mixture of acids (acid fraction) was converted to methyl esters which were separated by fractional distillation and chromatography on silica gel, being monitored by GLC The main product was a methyl ester $C_{12}H_{22}O_2$ (high resolution MS) corresponding in its composition to the methyl ester of the original cascarillic acid The melting points of its crystalline derivatives, such as amide, and the oxidation product with nitric acid, were in agreement with the literature data [1,3]

The NMR spectrum of the methyl ester of the mentioned acid (100 MHz, $CDCl_3$) contains the multiplets of four cyclopropane protons in the characteristic region 0 2–1 0 ppm, a deformed triplet of the terminal methyl group at 0 97 ppm, a ten-proton multiplet at 1 28 ppm, a two-proton doublet ($J = 7{\cdot}2$ Hz) at 3 21 ppm, and a singlet of a methyl ester group at 3 67 ppm The doublet at 3 21 ppm may be assigned to two equivalent protons of the methylene group in α-position to the carbonyl, neighbouring with the carbon atom substituted by a single proton The presence of the ester group and the cyclopropane ring is also indicated by the 1744 and 3070 cm^{-1} frequencies in the IR spectrum. From the data given structure (I) follows for cascarillic acid.



$CH_3\text{—}(CH_2)_5\text{—}CH\text{—}CH\text{—}CH_2\text{—}CO_2H$ (with CH_2 bridging the two CH)

Cascarillic acid (I)



$CH_3\text{—}(CH_2)_5\text{—}CH\text{—}CH(CO_2H)\text{—}CH_2$, $O\text{—}CO$

(II)

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[1] H THOMS and G FENDLER, *Arch Pharm* **238**, 671 (1900)

[2] E. GILDEMEISTER and F HOFFMANN, *Die Ätherischen Öle*, Vol. IIId, p 186, Akademie Verlag, Berlin (1966)

[3] *Beilsteins Handbuch der Organischen Chemie*, IV Edn, Vol 2, p 460, Springer–Verlag, Berlin (1920).

In agreement with the literature data[1] the oxidation of the free acid with nitric acid gave a crystalline product, m.p. 111°, which was further methylated with CH_2N_2. The NMR spectrum of this substance (100 MHz, $CDCl_3$) contains a triplet of the terminal methyl group at 0·83 ppm ($J = 6·5$ Hz), a multiplet of aliphatic protons at 1·25 ppm (8H) and 2·16 ppm (2H), a three proton multiplet of strongly coupled protons at 3·1–3·65 ppm, singlet of an ester methyl at 4·21 ppm, and a one proton multiplet at 5·00 ppm (—CHO—CO—). The IR spectrum contains bands of the ester group (1742 cm^{-1}) and five-membered lactone (1789 cm^{-1}). Therefore, it cannot be a dicarboxylic acid, as described in the literature,[1] but a substance with the probable structure (II).

EXPERIMENTAL

The NMR spectra were measured in $CDCl_3$ on a Varian HA-100 apparatus, using TMS as internal standard. The IR spectra were measured in $CHCl_3$, and the mass spectra on a AEI MS 902 spectrograph. The m.ps were determined on a Kofler block and they are not corrected. The b.ps were also not corrected. GLC analyses were performed on a Perkin–Elmer F 11 apparatus. For column chromatography silica gel according to Pitra and Štěrba[4] was employed (30–60 μ), which was deactivated by the addition of 11% of water before use. For TLC silica gel G Merck according to Stahl was used.

Isolation of cascarillic acid. Cascarilla essential oil (454 g, a product of Fritzsche Dodge and Olcott Inc., New York) was diluted with the same volume of pentane and extracted three times with 2 N aq. Na_2CO_3. The combined extracts were acidified with dilute H_2SO_4 and extracted with ether. The residue after the evaporation of ether weighed 9·7 g. The mixture of acids (9 g) was dissolved in ether (15 ml) and a solution of CH_2N_2 was added to the solution until the yellow colour persisted. After the evaporation of ether, the mixture of methyl esters was submitted to fractional distillation on a 9 TP column at 100 torr. The main fraction of b.p. 115° (3·5 g) contained according to GLC analysis (capillary column 50 m long, i.d. 0·2 mm, wetted with Carbowax 20 M, carrier gas N_2) only one component. The subsequent fraction of b.p. 115–120° (2·2 g) was composed of the same main component with admixture of traces of impurities. Chromatography of 400 mg of the main fraction on silica gel (40 g) with pentane gave a liquid of $[\alpha]_D^{20}$ $-10·5°$ ($c = 0·5530$, $CHCl_3$)and n_D^{21} 1·4361. Its mol. wt. determined by high-resolution mass spectrometry 198·158 corresponds to the composition $C_{12}H_{22}O_2$. The saponification of the methyl ester (2·2 g) was carried out in the conventional manner with 0·5 N ethanolic KOH.

From cascarillic acid its amide, m.p. 78° (aq. EtOH) was prepared in the manner[1] described, mol. wt. 183 (determined by mass spectrometry).

Oxidation of cascarillic acid with nitric acid. Cascarillic acid (1·5 g) was added dropwise to 6 ml of conc. HNO_3 heated to 60° and this mixture was heated until the evolution of nitrous gases stopped. The reaction mixture was poured into water and the heavy oil was separated and crystallized from water to give leaflets of m.p. 111°. The methyl ester of this product was prepared using CH_2N_2, yield 120 mg, b.p. 190° (bath temperature) at 2 torr.

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[4] J. PITRA and J. ŠTĚRBA, *Chem. Listy* **57**, 389 (1963).

Key Word Index—Croton eluteria, Euphorbiaceae, cascarilla oil, cascarillic acid; cyclopropanecarboxylic acid.