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ISOLATION AND STRUCTURE DETERMINATION OF FLOURENSIC ACID, A NEW SESQUITERPENE OF THE EREMOPHILANE TYPE.[1]

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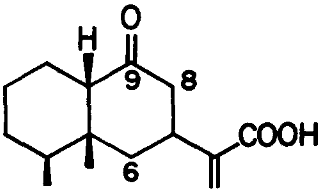
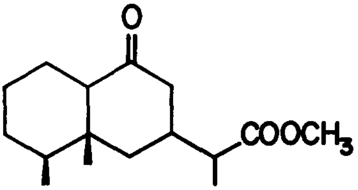
The eremophilane group of sesquiterpenes is characterised by a carbon skeleton which does not obey the well-known isoprene rule, and although a number of examples have been discovered recently[2] there are still relatively few known members of this group. We wish to report the isolation and structure elucidation of flourensic acid, the first example of a naturally-occurring carboxylic acid in this group.

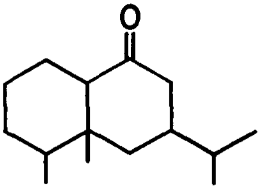
Flourensia cernua DC. (compositae) is a shrub native to Mexico and the southwestern U.S.A.; the present sample was collected near Sul Ross, Texas in March 1968. Extraction of the flowering heads with ethanol followed by chromatography on silicic acid yielded a new sesquiterpene of composition[3] $C_{15}H_{22}O_3$ which we name flourensic acid and for which we propose structure I. Flourensic acid is soluble in dilute aqueous sodium bicarbonate and gives an nmr spectrum ($\delta(CDCl_3)$; 0.82 (3H, d, J = 5Hz), 1.02 (3H, s), 1.4 (7H, m), 2.2 (6H, m), 5.60 (1H, s), 6.32 (1H, s)) consistent with the presence of secondary and tertiary methyl groups and a terminal methylene group. The ultraviolet absorption spectrum (λmax 203 nm; ε 8450) supports its formulation as an αβ-unsaturated acid.



I



II



IV

Hydrogenation of flourensic acid proceeded with the uptake of one mole of hydrogen to yield a carboxylic acid which gave the ester II on methylation. The infrared spectrum of II ($\nu_{max}^{CCl_4}$ 1736 and 1706 cm^{-1}) confirmed the presence of a carboxylic ester and an acyclic or

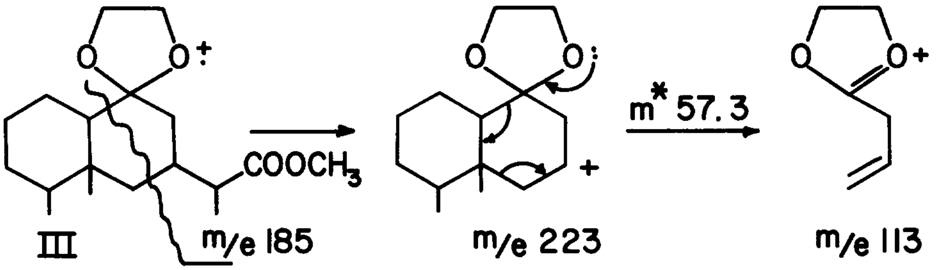
6 or 7 membered ring ketone. On electron impact II yielded a McLafferty rearrangement ion of moderate intensity at $^m/e$ 74 corresponding to hydrogen transfer from the ring to the carbonyl group of the ester, an intense ion at $^m/e$ 179 due to cleavage of the isopropionate side-chain, but <u>no</u> ion at $^m/e$ 180 corresponding to McLafferty rearrangement to a carbonyl group located in the 6- or 8-position. These facts confirm the nature of the side-chain in II.

Reduction of the keto-ester II with lithium aluminum hydride followed by selenium dehydrogenation yielded a hydrocarbon whose ultraviolet absorption spectrum (λmax 320, 275 228 nm) indicated it to be a naphthalene derivative, thus establishing flourensic acid as a eudesmane, an eremophilane, or a valencane derivative. On mass spectrometric examination the ketal III obtained by ketalisation of the keto-ester II gave an ion $C_9H_{13}O_4^+$ at $^m/e$ 185, demanding that the ketal group and the ester side-chain be located in the same ring. Since the absence of McLafferty rearrangement previously noted precludes location of the carbonyl group at C-6 or C-8, this evidence fixes the carbonyl group at C-9.

Conversion of the carbomethoxy group of the ketal III to a methyl group was effected by treatment with lithium aluminum hydride followed by conversion of the alcohol to its methane sulfonate ester and further treatment with lithium aluminum hydride. Hydrolysis then yielded the ketone IV, which exchanged three hydrogens for deuterium on treatment with D_2O and base. Treatment with 2,4-dinitrophenylhydrazine yielded a crystalline 2,4-dinitrophenylhydrazone, m.p. 180-181° (lit.[4] 179-181°), while the optical rotatory dispersion of IV was identical to that previously published for <u>cis</u>-tetrahydroeremophilone.[5]

The possibility of epimerisation of the C-10 bridgehead during the chemical conversions is excluded by the fact that the ORD curve of flourensic acid is similar to that of <u>cis</u>-tetrahydroeremophilone, and these experiments thus establish the structure and stereochemistry I for flourensic acid.

One additional fragmentation of the ketal III on electron impact proved to be of interest. In addition to the expected[6] ion at $^m/e$ 185 an intense ion at $^m/e$ 113 was noted.



Since an ion of this $^{m}/e$ is usually indicative of an α-methylcyclohexanone ring its formation in this instance was surprising. A metastable ion at $^{m}/e$ 57.3 supported its formation as indicated (arrows) from the intense cleavage ion at $^{m}/e$ 223, indicating that cyclic ketals can sometimes fragment via misleading pathways.

Acknowledgements

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References

1. Constituents of American Poisonous Plants II. Part I: Flavonoids from Flourensia Cernua, M. M. Rao, D. G. I. Kingston and T. D. Spittler, Phytochem., 9 227 (1970).

2. A. R. Pinder, Perfumery and Essential Oil Record, London, April 1968 and September 1968; see also C. J. W. Brooks and G. H. Draffan, Tetrahedron 25, 2865 (1969); G. L. Chetty, L. H. Zalkow, and R. A. Massy-Westropp, Tetrahedron Letters, 307 (1969); H. Fuhrer, A. K. Ganguly, K. W. Gopinath, T. R. Govindachari, K, Nagarajan, B. R. Pai and P. C. Parthasarathy, Tetrahedron, 26, 2371 (1970); T. R. Govindachari, P. A. Mohamed and P. C. Parthasarathy, Tetrahedron, 26, 615 (1970); A. R. Pinder, Tetrahedron Letters, 413 (1970); G. A. Eagle, D. E. A. Rivett, D. H. Williams and R. G. Wilson, Tetrahedron, 25, 5227 (1969); K. Naya and I. Takagi, Tetrahedron Letters, 629 (1968); Y. Tanahashi, Y. Ishizaki, T. Takahashi and K. Tori, Tetrahedron Letters, 3739 (1968); J. Harmatha, Z. Samek, L. Novotny, V. Herout and F. Sorm, Coll. Czech. Chem. Comm., 34, 1739 (1969).

3. All new compounds gave elemental analyses or exact mass measurements of their parent ion in agreement with their stated compositions.

4. C. Djerassi, R. Mauli, and L. H. Zalkow, *J. Am. Chem. Soc.*, *81*, 3424 (1959).

5. C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, *78*, 6362 (1956). The isomer designated *trans* in this paper was later shown to be the *cis* isomer; D. F. Grant and D. Rogers, *Chemistry and Industry*, 278 (1956); C. Djerassi, R. Mauli and L. H. Zalkow, *J. Am. Chem. Soc.*, *87*, 3424 (1959).

6. C. Djerassi, H. Budzikiewicz and D. H. Williams, "Structure Determination of Natural Products by Mass Spectrometry" Vol. II, Holden-Day, Inc., San Francisco, 1966.