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STRUCTURE OF α-FERULENE A SESQUITERPENE HAVING A (+)-ARISTOLANE SKELETON

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The main component of the acidic fraction of the latex of Ferula communis L. (Umbelliferae) was previously described[1].

Steam-distillation of the neutral fraction revealed the presence of a mixture of sesquiterpenoid hydrocarbons. The major constituent, $C_{15}H_{24}$, for which we propose the name α-ferulene[2], had b.p. 110° (8mm); n_D^{18} 1.5041; d_{18} 0.9331; $[\alpha]_D$ +68° (neat); N.M.R. signals at 5.07 (1H broad: olefinic proton), 7.95 (4H broad: two allylic methylene groups), 9.39τ (2 cyclopropane proton multiplet); a multiplet at about 9.0τ (total intensity 12H) may be assigned to four methyl groups.

Dehydrogenation with selenium of α-ferulene afforded eudalene (III), λ_{max} 228, 282 and 320 mμ; picrate m.p. 89-91°[3]. Catalytic hydrogenation gave a saturated dihydroderivative $C_{15}H_{26}$ (II), b.p. 110° (8mm); n_D^{18} 1.4938; d_{18} 0.9183; $[\alpha]_D$ +41,1° (neat), which, by dehydrogenation with palladium-charcoal at 300° produced 1,8-dimethylnaphtha-

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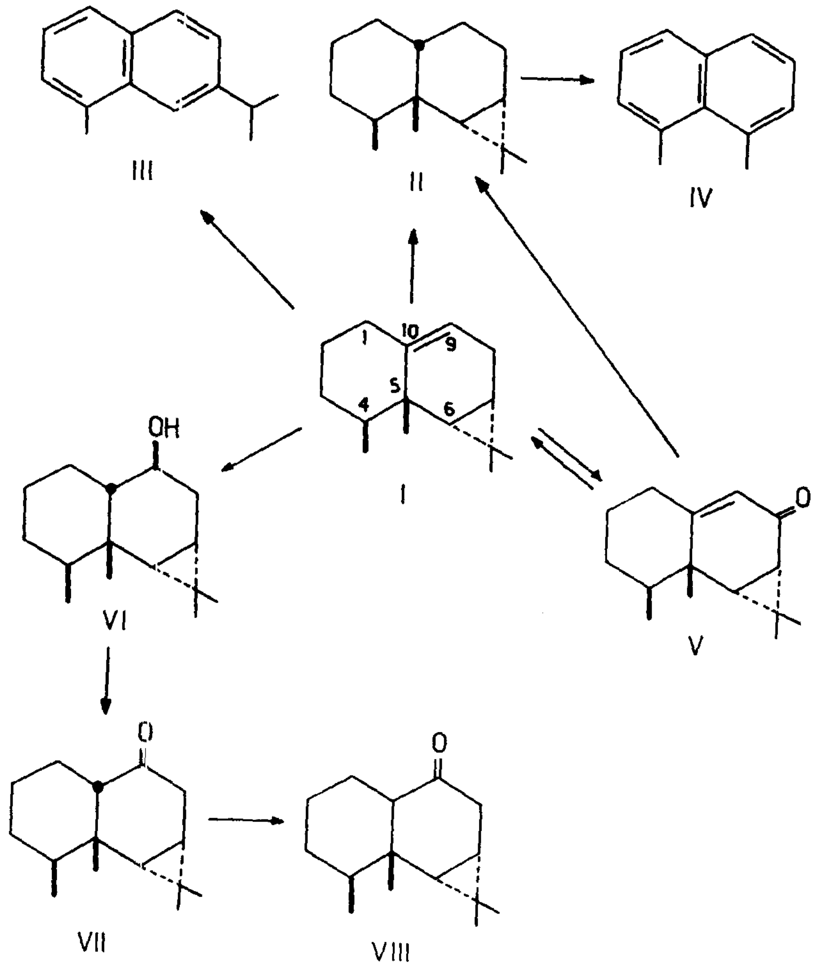
(°). Authors' names are in alphabetical order.


III
II
IV
1
10
9
5
4
6
I
OH
VI
O
V
O
VII
O
VIII

lene (IV), m.p. 63°, identified by comparison with an authentic sample[4]. α-Ferulene is readily oxidized by air: chromatography over alumina of the auto-oxidation mixture gave a ketone (V), $C_{15}H_{22}O$; m.w. 218 (mass spec.); m.p.101-102° (2,4-dinitrophenylhydrazone m.p. 170-172°); $[\alpha]_D^{CHCl_3}$ +369°; ν_{CO} 1660 cm^{-1}; λ_{max} 240, 310 mμ, log ε_{max} 4.10, 2.11. This gave α-ferulene by Wolff-Kishner reduction and the dihydroderivative II by catalytic hydrogenation. The I.R. spectrum of the ketone is exactly superimposable on that of aristolone[5]. The physical constants of these two ketones are identical; only their rotatory powers are opposite in sign: therefore aristolone and ketone V must be enantiomers.Furthermore, the I.R. spectra of α-ferulene and of II are superimposable, respectively, on those of 9-aristolene and of aristolane (calarane).[6]

From these data it is possible to propose for α-ferulene the structure I.

The different courses of the aromatizations of I and II may be explained as follows: The formation of eudalene from I probably involves opening of the cyclopropane ring after 1,2-shift of the angular methyl group caused by the presence of the double bond. A similar transformation is not possible for the saturated compound II, in which the primary cleavage is likely to involve the cyclopropane ring with subsequent shift of the angular methyl group to the 6 position, and elimination of the more bulky isopropyl group.

A further proof of the position of the double bond in α-ferulene and of its stereochemistry was obtained as follows: Hydroboration-oxidation of I gave an alcohol (VI), m.p. 142-143°; $[\alpha]_D^{CHCl_3}$ +68°, in which the hydroxyl group should be equatorially oriented (it was not possible to demonstrate this point on the basis of the I.R. spectra of VI and of the corresponding acetate[7], as both had complex C-O bending absorption). Oxidation of VI with CrO_3[8] afforded the <u>cis</u>-ketone VII, m.p. 45-47°; $[\alpha]_D^{CHCl_3}$ +160°, whose O.R.D. curve, in agreement with the octant rule[9] showed a strongly positive Cotton effect. This ketone was converted by alkali to the <u>trans</u>-form VIII, m.p. 36-39°; $[\alpha]_D^{CHCl_3}$ -18°, with a negative Cotton effect curve.

Since α-ferulene is enantiomer of 9-aristolene and ketone V of aristolone, structure and stereochemistry suggested should be correct. They are rather striking examples of enantiomerism in sesquiterpenes of such complex structures.

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REFERENCES

1. S.Carboni, V.Malaguzzi and A.Marsili, <u>Tetrahedron Letters</u>, 2783 (1964).
2. F.W.Semmler, K.G.Jonas and P.Roenisch (<u>Ber. dtsch. chem.</u>

Ges. **50**, 1823 (1917)) have called ferulene a monocyclic sesquiterpene of formula $C_{15}H_{26}$, isolated from *Dorema ammoniacum* Don.

Following the suggestion of G.Büchi, M.S.v.Vittenau and D.H.White (*J.Amer. Chem. Soc*. **81**, 1968 (1959)), we have adopted the ionone-irone nomenclature for the designation of our sesquiterpene.

3. L.Ruzicka, J.Meyer and M.Mingazzini, *Helv. Chim. Acta* **5**,345 (1922); J.Plìva, M.Horàk, V.Herout and F.Šorm, *Die Terpene*, Teil I, S79. Akademie Verlag, Berlin (1960).
4. W.J.Mitchell, R.D.Topson and J.Vaugham, *J. Chem.Soc*. 2526 (1962).
5. S.Furukawa and N.Soma, *J. Pharm. Soc. Japan*, **81**, 559 (1961); S.Furukawa, K.Oyamada and N.Soma, *Ibid*. **81**, 565 (1961); S.Furukawa, *Ibid*. **81**, 570 (1961).
6. G.Büchi, F.Greuter and Takashi Tokoroyama, *Tetrahedron Letters*, 827 (1962); J.Streith, P.Pesnelle and G.Ourisson, *Bull. soc. chim. France*, **1963**, 518; J.Vrkoč, J.Křepinský, V.Herout and F.Šorm, *Coll. Czech. Chem. Commun*. **29**, 795(1964).
7. A.E.Braude and E.S.Waight in "*W.Klyne, Progress in Stereochemistry*", Vol. I, p. 166. Butterworths, London (1954).
8. H.C.Brown and C.P.Garg, *J.Amer. Chem. Soc*. **83**, 2952 (1961).
9. W.Moffitt, R.B.Woodward, A.Moscowitz, W.Klyne and C.Djerassi, *J.Amer. Chem. Soc*. **83**, 4013 (1961).