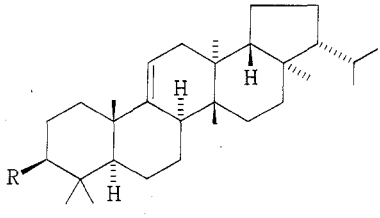
ISOLATION OF FERNENOL FROM *ARTEMISIA VULGARIS* L.*

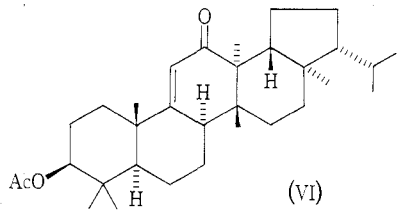
By S. K. Kundu,† A. Chatterjee,† and A. S. Rao‡

The plant *Artemisia vulgaris* L. (family Compositae) enjoys a great reputation as a drug for stomachic, deobstruent, antispasmodic, and anthelmintic properties. It is used as a tonic for asthma by tribal people in the Himalayan region.[1] The volatile oil of the plant is said to be a good larvicide and a feeble insecticide.[2]

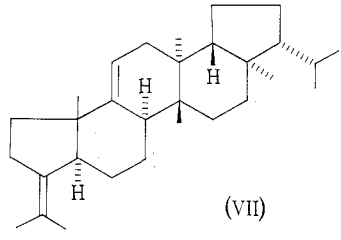
In a preliminary communication[3] we have described the reactions which have enabled us to assign the structure (I) for fernenol,[4] a pentacyclic triterpene alcohol isolated from *Artemisia vulgaris* L. Details of the isolation procedure and preparation of the derivatives (II)–(VII) of fernenol are given in the Experimental section.



(I) R = OH
(II) R = OAc
(III) R = OBz
(IV) R = O
(V) R = OMe



(VI)



(VII)

Experimental

M.p.'s are uncorrected. Rotations were taken in chloroform solution. N.m.r. spectra were run on a 60-Mc/s Varian instrument in CCl_4 using tetramethylsilane as internal standard. The plant material was obtained through the courtesy of the Director, Medicinal Plants, West Bengal, who had collected it from Darjeeling and Siliguri Districts, North Bengal.

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† Department of Chemistry, University College of Science and Technology, Calcutta-9, India.

‡ National Chemical Laboratory, Poona-8, India.

[1] Chopra, R. N., Nayar, S. L., and Chopra, I. R., "Glossary of Indian Medicinal Plants." p. 26. (Council of Scientific and Industrial Research: India 1956.)

[2] Chopra, R. N., Roy, D. N., and Ghosh, S. M., *J. Malar. Inst. India*, 1940, **3**, 495.

[3] Kundu, S. K., Chatterjee, A., and Rao, A. S., *Tetrahedron Lett.*, 1966, 1043.

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Isolation of Fernenol (I)

Dried, powdered plant (40 kg) of *Artemisia vulgaris* L. was extracted with light petroleum at room temperature. The resinous mass obtained after removal of solvent at 40° was treated with methanol and the waxy solid which separated out was removed. The mother liquor, on removal of methanol at 40°, afforded a viscous oil (1 kg) which was chromatographed in 3 batches over neutral alumina (grade III, 6 kg) and eluted successively with light petroleum, light petroleum–benzene (1 : 1) mixture, benzene, and ethanol. The product obtained in the light petroleum–benzene eluate on repeated chromatography over neutral alumina (grade II) afforded fernenol in the light petroleum–benzene (1 : 2) eluate as a solid, m.p. 135–155°. Final purification was done by repeated chromatography and crystallization from absolute methanol to afford long stout needles (350 mg), m.p. 194°, $[\alpha]_D$ −24° (*c*, 0·64); ν_{max} ($CHCl_3$): 3650, 2967, 1471, 1465, 1374, 1316, 1274, 1248, 1205, 1174, 1136, 1081, 1053, 1020, 980, 960, 950, 938, and 880 cm^{-1}. N.m.r. spectrum: signals at 4·75 τ (1H, broad, vinyl proton; trisubstituted double bond), 6·90 τ (1H, broad, H–C–OH), and 8·95, 9·05, 9·11, 9·15, 9·17, 9·25, 9·28 τ (24H, eight CH_3 groups); mass spectrum: M^+ 426 ($C_{30}H_{50}O$, 426); *m/e* 411, 393, 273, 259, 246, 241 (Found: C, 84·4; H, 11·8. Calc. for $C_{30}H_{50}O$: C, 84·2; H, 11·8%).

Fernenyl Acetate (II)

Fernenol (100 mg) in pyridine (10 ml) was treated with acetic anhydride (1 ml) and kept for 16 hr at room temperature. It was then poured into crushed ice, and extracted with ether; the ether solution was washed with dil. HCl (4 times), then with water, and dried (Na_2SO_4). The residual solid (108 mg), after removal of ether, was chromatographed over alumina (grade III, 10 g). The light petroleum-eluted material on repeated crystallization from methanol–ethyl acetate afforded fine needles, m.p. 215–216°, $[\alpha]_D$ −10° (*c*, 0·69); ν_{max} (Nujol): 2976, 1748, 1471, 1379, 1325, 1307, 1176, 1156, 1110, 1075, 1042, 1031, 1018, 995, 985, 965, 952, 910, 885, 875, 826, 798, and 722 cm^{-1}; mass spectrum: M^+ 468 ($C_{32}H_{52}O_2$, 468); *m/e* 453, 408, 393, 315, 301, 241 (Found: C, 82·0; H, 11·25. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%).

Saponification of Fernenyl Acetate

The acetate (50 mg) was refluxed with alcoholic KOH (10%, 20 ml) on a steam-bath for 4 hr, cooled, diluted with water, extracted with ether, washed with water, and dried (Na_2SO_4). Removal of ether gave a solid mass (48 mg) which was chromatographed over alumina (grade II, 5 g). The light petroleum–benzene (1 : 1) mixture eluted a solid which on crystallization from absolute methanol afforded fernenol, m.p. 194°, $[\alpha]_D$ −24° (*c*, 1·02).

Fernenyl Benzoate (III)

Fernenol (28 mg) in pyridine (10 ml) was treated with benzoyl chloride (1 ml) and kept for 36 hr at room temperature. It was then poured onto crushed ice, extracted with ether, washed with dil. HCl (5 times), then with water. Removal of solvent afforded a semi-solid mass which was warmed on steam-bath for 1 hr with water (25 ml), cooled, extracted with ether, washed with $NaHCO_3$, then with water, dried (Na_2SO_4), and the solvent evaporated to give a semi-solid mass (38 mg). The chromatography of this mass over a column of alumina (grade III, 10 g) using light petroleum as eluent gave a solid which crystallized from methanol–chloroform as long stout crystals, m.p. 215°; ν_{max} (Nujol): 2924, 1704, 1647, 1600, 1575, 1453, 1370, 1334, 1307, 1270, 1200, 1170, 1110, 1093, 1064, 1036, 1020, 990, 955, 935, 870, 818, 795, and 710 cm^{-1} (Found: C, 83·9; H, 10·15. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·25%).

Saponification of the benzoate (15 mg) with alcoholic KOH (10%; 5 ml) and working up as in the case of acetate gave fernenol (8 mg), m.p. 194°, $[\alpha]_D$ −24° (*c*, 0·46).

Methyl Ether of Fernenol (V)

Fernenol (25 mg) was dissolved in dry benzene (2 ml), potassium metal (25 mg) was added, and the mixture refluxed for 3 hr with vigorous shaking at intervals to disperse the molten potassium into small globulets. Methyl iodide (1 ml) was then added, refluxing was continued

for 3 hr more; the mixture was cooled and methanol was added. The solvents were removed under vacuum and the residue was extracted with ether, washed with water, and dried (Na_2SO_4). The residual solid obtained after the evaporation of ether was chromatographed over alumina (grade II, 2 g) and eluted with light petroleum. The solid obtained was crystallized from methanol–acetone as fine needles, m.p. 234–235°; mixed m.p. with a sample of arundoin (m.p. 236–237°) kindly supplied by Dr S. Natori showed no depression. T.l.c.: the above methylation product as well as arundoin had R_F 0·55 with benzene as a solvent phase.

Gas chromatography: 0·5% Apiezon L on gas-chrom Z (100–200 mesh); column temperature 240±1°; detector temperature 248±1° (Loveloch Argon ionization type with ^{90}Sr source); inlet pressure: 10–12 lb/sq in. Methyl ether of fernenol had the same relative R_T (4·28) as arundoin (4·28) (standard: 5α-cholestane = 1).

I.r. spectrum (in KCl): bands at 3030, 2986, 2955, 2930, 2880, 2845, 1470, 1455, 1435, 1395, 1385, 1375, 1365, 1238, 1200, 1180, 1110, 1000, 990, 970, 960, 948, 910, 862, 820, and 795 cm^{-1}. The infrared spectrum of arundoin was superimposable with the above spectrum.

Acknowledgments

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