Biogenetic-type Synthesis of (±)-Drimenin

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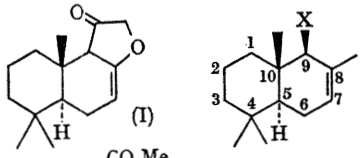
DRIMAN-type sesquiterpenes are of biogenetic interest since their structural relationship with the steroids and triterpenes suggests a close biosynthetic kinship with the higher terpenes.[1] Further, the γ-lactone group of drimenin (I) might be expected to arise from oxidation at C(12) of drimenol (II) which occurs with (I) in the same plant.[2]

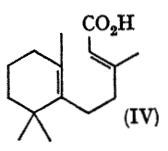
Drimenin (I) has been synthesized,[3] and biogenetic-type syntheses of drimenol have been carried out.[4] Drimenic acid (III) is reported to be derived from farnesic or monocyclofarnesic acid by acid catalysed cyclization.[5] We have improved the latter reaction and increased the yield of (III) from monocyclofarnesic acid (IV)[6] by up to 55% by treatment of (IV) with a BF_3-saturated solution[7] Et_2O–C_6H_6 (1 : 5) (30°, 24 hr.).

The methyl ester (V) of (III) was photo-oxidised[8] [three 20-w fluorescent lamps, hematoporphyrin or Rose Bengal as sensitizer, in pyridine or xylene–isopropyl alcohol (1 : 1)] and the peroxides, without purification, were reduced with potassium iodide to afford the mixture of hydroxy-esters (VI) (33%, m.p. 108°), and (VII; R = Me) (23%, m.p. 100°) and oxo-ester (VIII) (33%, m.p. 81°) which were separated by silica gel chromatography.

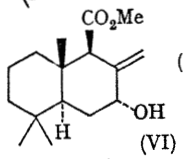


(I)

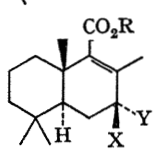
(II) X=CH_2OH
(III) X=CO_2H
(V) X=CO_2Me



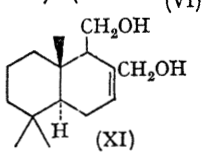
(IV)



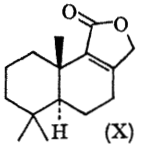
(VI)



(VII) X=H, Y=OH
(VIII) X, Y=O, R=Me
(IX) X=OH, Y=H, R=Me



(XI)



(X)

Photo-oxidation with hematoporphyrin in pyridine solution gave the same products directly in similar yields.

The structures of (VI), (VII), and (VIII) were assigned on the basis of chemical and physical evidence. On treatment with potassium hydroxide in refluxing dioxan, (VI) was converted into (VII; R = H). Oxidation of (VII) with manganese dioxide afforded (VIII) (quantitative yield) and reduction of (VIII) with sodium borohydride gave the epimeric alcohol (IX) as a major product.

Hydrolysis and simultaneous lactonization of (VI) (dioxan–6N-sulphuric acid (13 : 1) 90°, 24 hr.) gave the mixture of two lactones, (I) (69%) and (X) (11%), which were separated by silica gel chromatography. They were proved to be identical with (±)-drimenin (I) and (±)-isodrimenin (X) as follows: reduction of (I) with lithium aluminium hydride afforded the corresponding diol (XI), m.p. 75·5—77°, the i.r. spectrum of which in carbon tetrachloride was completely identical with that obtained from natural drimenin by the same treatment.[2b,9]

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