Biogenetic-type Synthesis of α- and β-Levantenolides

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Summary C_{20}-Butenolide (IV), which was derived from the reaction of monocyclofarnesyl bromide (VIII) and 2,2′-di-3-methylfurylmercury followed by photo-oxidation, afforded α- and β-levantenolides [(I) and (II)] by treatment with anhydrous stannic chloride.

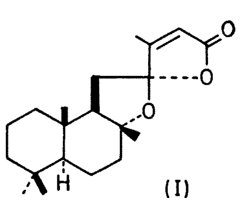
WE report the biogenetic-type synthesis of α- and β-levantenolides [(I) and (II)], diterpene lactones isolated from Turkish tobacco.[1]

The possible biogenesis of levantenolides might involve the cyclization of the hypothetical precursor (III) which would *in vivo* be derived from geranylgeraniol. The analogous compound (IV) was chosen instead of the precursor (III) for the cyclization since the acid-catalysed partial cyclization of farnesic acid (V) to monocyclofarnesic acid (VI) and its easy preparation from dihydroionone are known.[2,3]

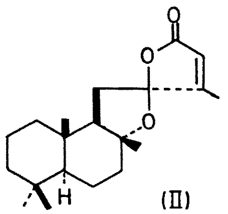
Monocyclofarnesol (VII) was treated with PBr_3 to give the corresponding bromo-derivative (VIII), which was stirred with 2,2′-di-3-methylfurylmercury[4] (room temp., C_6H_6) to give the furano-derivative (IX) [50%; n.m.r.,† δ 7·16 and 6·1 (1-H and 2-H), 3·26 (d, 5-H J = 7·2 Hz), and 5·27 p.p.m. (t, 6-H, J = 7·2 Hz)].

The compound (IX) was photo-oxidized with oxygen in the presence of eosine[5] in methanol to give the butenolide derivative (IV) (50%, after purification on short silica gel column: i.r.; 1770 and 1658 cm^{-1}; n.m.r.; δ 5·75 and 4·88 (br s and br t, 2-H and 6-H) and 2·52 p.p.m. (m, 5-H).

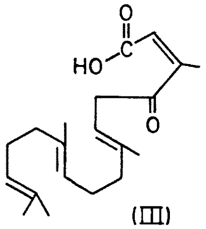
A stirred benzene solution (20 ml.) of (IV) (170 mg.) with 0·2 ml. of anhydrous stannic chloride[6] (10°, 4 hr.) gave, after recrystallization, white needles (I), m.p. 192—194°. After removal of (I), the remaining mixture was purified by silica gel column chromatography to give a further yield of (I) (total yield, 30%) and another crystalline compound (II), m.p. 171—173° (12%). I.r. ($CHCl_3$) and n.m.r. spectra as well as t.l.c. with different solvents of white crystalline, (I) and (II), were completely superimposable upon those of natural α- and β-levantenolide, respectively.



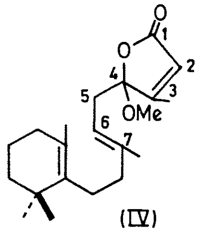
(I)



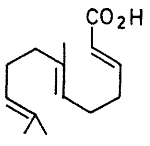
(II)



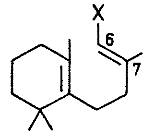
(III)



(IV)

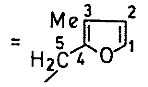


(V)



(VI) X = CO_2H
(VII) X = CH_2OH
(VIII) X = CH_2Br

(IX) =



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† Varian T-60 spectrometer, Me_4Si as internal standard.

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