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SYNTHESIS OF LEVANTENOLIDES FROM ACYCLIC PROGENITOR

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The unique and interesting structure of α- and β-levantenolides (I, and II), diterpene lactones isolated from Turkish tobacco[1], have prompted us to study the total synthesis based on biogenetical consideration.

A possible biogenesis of levantenolides might be the cyclization of a hypothetical precursor (III) which would be in vivo derived from geranyl geraniol. In a previous communication we have reported[2] the synthesis of I and II by cyclization of the analogous compound (IV). From a biogenetical point of view it is, however, more desirable to attempt the cyclization of acyclic progenitor (V), which is synthesized as follows.

Trans, trans-farnesol[3] (VI) was treated with phosphorous tribromide to afford the corresponding bromo derivative[4] (VII), which was stirred with 2,2'-di-3-methylfuryl mercury[5] at room temperature in benzene solution to give the furano derivative (VIII) with 50 % yield. VIII: NMR[6] ; 1.58(6H, s), 1.93(3H, s), 2.00(6H, s), 3.32(d, 7 Hz, C_5-H), 5.08(m, olefin-protons), 6.03 (d, 2 Hz, C_2-H), and 7.10(d, 2 Hz, C_1-H).

The furano derivative (VIII) was subjected to photo-oxidation with three 20 w-fluorescent lamps under oxygen atmosphere in the presence of eosine in methanol[7] and subsequent treatment of the reaction mixture (V and IX) with chromic anhydride-pyridine complex[8] to give the acyclic butenolide progenitor (V) with 30 % from VIII after purification with short silica gel column. V : IR (film) ; 1773, and 1658 cm^{-1}, NMR ; 1.58(6H, s), 1.64(6H, s), 1.93(3H, s) 3.13(3H, s), 4.93(m, olefin protons), and 5.80(s, C_2-H).

The mass spectra of IV and V show, in addition to the molecular ion at 332, the strong peaks at m/e $205(M-a)^+$ and $127\ (a)^+$, which are derived from cleavage at C_4-C_5 bond respectively. The peak at m/e 205 in each compound corresponds to monocyclo- and acyclic-farnesyl fragment cation.

Cyclization of V was carried out by treatment with anhydrous stannic chloride (0.2 mol equivalent) in benzene solution at room temperature for 24 hours. The crude cyclized products were purified by passing through a silica gel column to afford white needles (I), mp 192-194° (13 % yield) and II, mp 171-173° (Ca 4 %). IR in chloroform and NMR spectra of white crystalline, (I) and (II), were completely superimposable with natural α-and β-levantenolides respectively. Yield and rate of the cyclization of V are somewhat lower and slower than the analogous compound (IV), which was transformed into levantenolides in 42 % yield after 4 hours.

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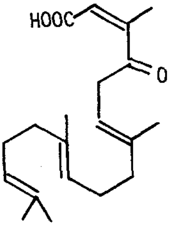
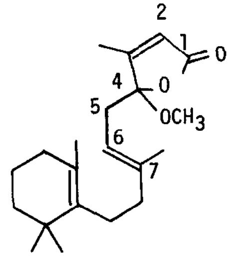
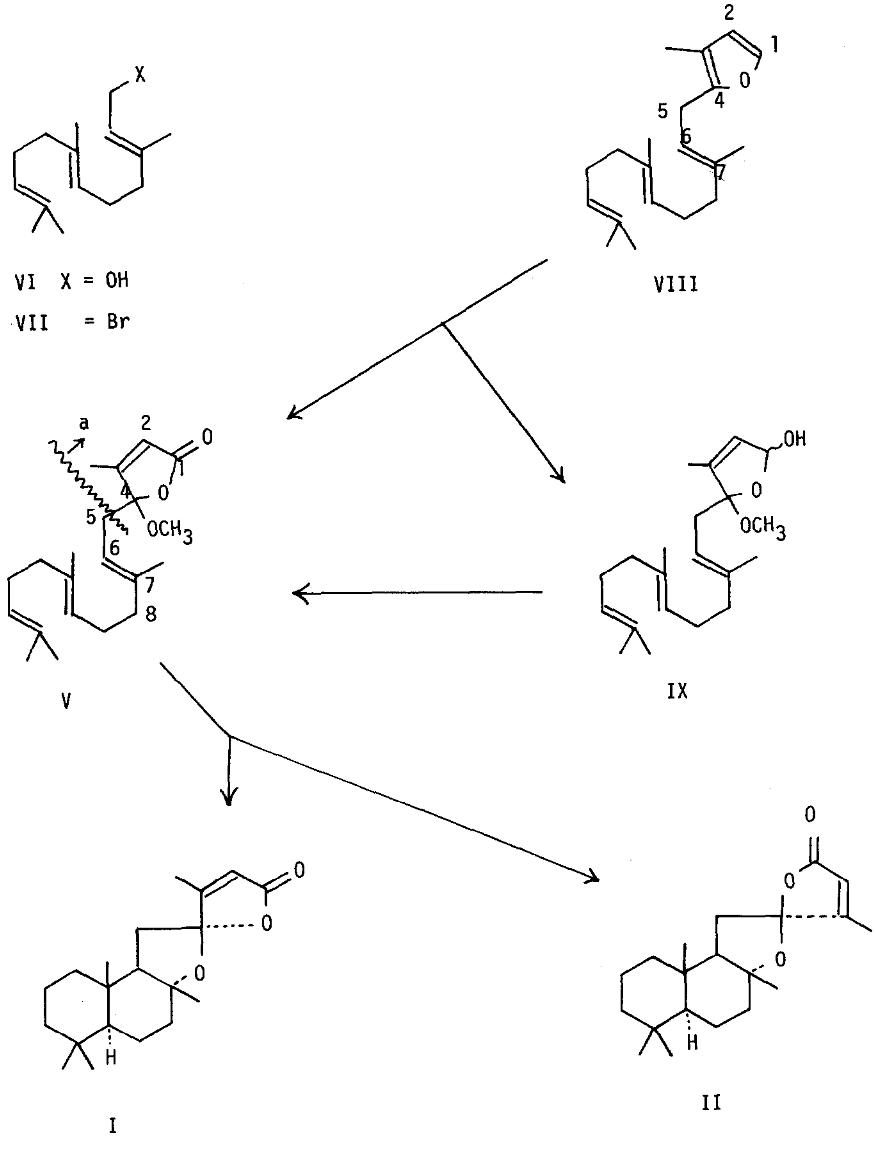

HOOC
O

III


2
1
O
4
O
OCH3
5
6
7

IV


X
VI X = OH
VII = Br
2
1
O
4
5
6
7
VIII
a
2
O
4
O
5
OCH3
6
7
8
V
OH
O
OCH3
IX
O
O
O
H
I
O
O
O
H
II