Biogenetic Model Reactions of Germacrone-type Sesquiterpenes

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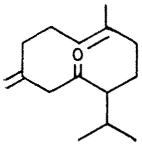
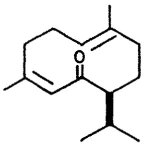
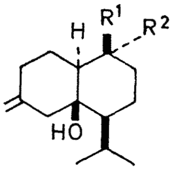
Summary Acid catalysed conversion of germacrone-type sesquiterpenes into cadinene-type compounds has been carried out by using 80% aq. AcOH or $AlCl_3$ in dry ether, and ε-cadinene has been synthesized from preisocalamendiol in two steps.

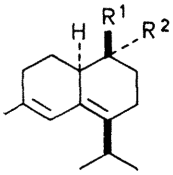
Preisocalamendiol (I) has already been synthesized from (−)-santonin.[1] We describe here some biogenetic model reactions, which are novel and significant for the formation of cadinene-type sesquiterpenes, using germacrone-type sesquiterpenes, preisocalamendiol (I) and a ten-membered-ring compound (II) [which has been synthesized in three steps from isocalamendiol (III)] as well as shyobunone.[2]


(I)

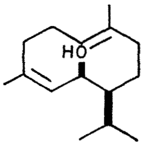

(II)



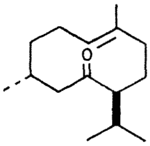
(III) R^1 = Me, R^2 = OH
(IV) R^1 = OH, R^2 = Me
(V) R^1, R^2 > = CH_2

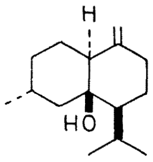


(VI) R^1 = Me, R^2 = OH
(VII) R^1 = Me, R^2 = OAc
(VIII) R^1 = OH, R^2 = Me

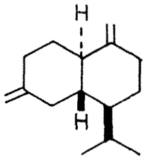


(IX)

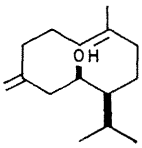

(X)



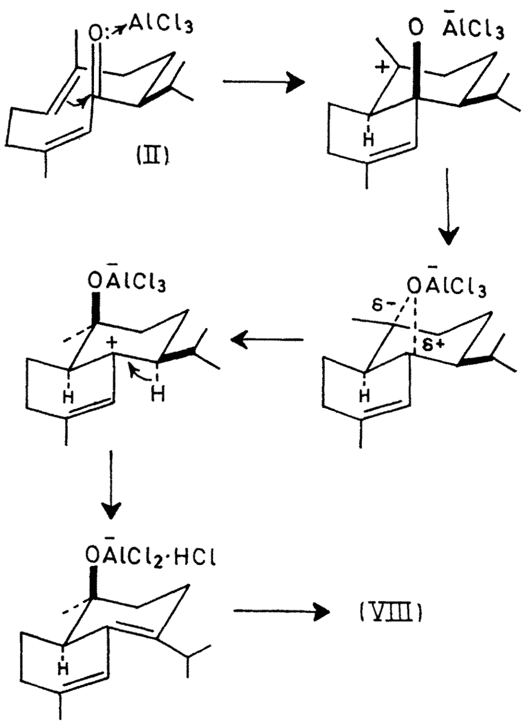
(XI)



(XIII)



(XII)



When treated with 80% aq. AcOH (room temp., 5 min.), preisocalamendiol (I),[3] which co-occurs with isocalamendiol (III), was readily converted into (III) in 47% yield, whereas calamendiol (IV)[4] was not detected in the reaction mixture. This result indicates that (III) may be formed non-enzymatically from (I), by a concerted mechanism, in the plant. When $AlCl_3$ in dry ether (0°, 10 min.) was used instead of 80% aq. AcOH, the dienol (V), a known compound,[5] was obtained from (I) in 54% yield.

Acid catalysed reactions of the αβ-unsaturated ketone (II) were also carried out under essentially the same conditions. It reacted with 80% aq. AcOH to afford (in 45 and 21% yields, respectively) a mixture of two conjugated dienes [(VI) and (VII)], the structures of which were confirmed by i.r., u.v., n.m r., and mass-spectrometric data. Treatment of (VII) with $LiAlH_4$ afforded (VI) in high yield. On the basis of a concerted cyclization mechanism, these compounds [(VI) and (VII)] must have the same configuration as isocalamendiol (III). On the other hand, in the case of $AlCl_3$ in dry ether (0°, 10 min.) a new conjugated diene (VIII), a configurational isomer of (VI), was isolated in 72% yield. Its spectral data are almost identical with those of (VI) except for an n.m.r. signal due to a methyl group attached to a carbon atom bearing a hydroxy-group: (VI) exhibits a methyl singlet at δ 1·06, whereas that in (VIII) appears at δ 1·28. An axial methyl signal is observed at higher field than the corresponding equatorial methyl signal in cyclohexane systems.[6] If it is true in the cyclohexene system, (VI) must have an axial methyl group. This is in agreement with the structure (VI) being formed by a concerted cyclization mechanism analogous to that by which preisocalamendiol (I) gives isocalamendiol (III). The formation of (VIII) from (II) in the presence of $AlCl_3$ appears to take place in a stepwise mechanism, as described below.

We have further examined the acid-catalysed cyclization reactions of the reduction products corresponding to germacrones (I and II). Reduction of (II) with di-isobutylaluminium hydride (0—5°, 2 h) did not afford the desired dienol (IX), but a saturated ketone (X) (72% yield) which could be converted into the known compound (XI),[5] in 20% yield, when treated with 80% aq. AcOH (room temp.).

Finally, ϵ-cadinene was synthesized from (I) as follows. Preisocalamendiol (I) was treated with $LiAlH_4$ in ether (room temp., 30 h) to give, in quantitative yield, the corresponding reduction product (XII), which was fairly stable in 80% aq. AcOH at room temp. However, (XII) reacted with mesyl chloride–pyridine (room temp., 7 h) to give in 35% yield an ϵ-cadinene (XIII), the structure of which was confirmed by catalytic reduction on PtO_2 to give a tetrahydro-derivative which had an i.r. spectrum completely identical with that of an authentic sample of tetrahydrocadinene.

All compounds gave satisfactory physical data.

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