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BIOGENETIC RELATIONSHIPS OF THE VETIVER SESQUITERPENES

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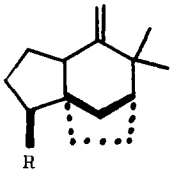
The co-occurrence of the tricyclic vetiver sesquiterpenes, tricyclovetivene[1] (1, R=CH_3), tricyclovetivenol[2] (1, R=CH_2OH) and zizanoic acid[2,3] (1, R=COOH) with α-vetivone[4] (2) and β-vetivone[5] (3a) leads us to postulate a close biogenetic relationship between these widely differing structural types. Experiments to test the following biogenetic pathway to these structures is under current investigation and has, indeed, led to an *in vitro* synthesis of the tricyclovetivane skeleton which will be published shortly.



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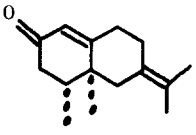

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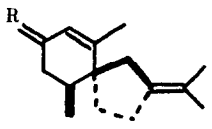
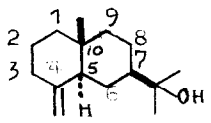


3a; R=O
3b; R=H_2

A possible progenitor of these could belong to the eudesmane class since hinesol (4) and β-eudesmol (5) have both been isolated[6] from *Atractylodes japonica*. One of the two predicted[7] *in vivo* cyclisation processes involving trans-farnesol (6) would yield, after double bond migration, the cyclodeca-1:6--diene derivative which could exist in two forms (7) and (8). The β-configuration of the isopropylol group is assumed since the majority of eudesmane sesquiterpenes have this stereochemistry.[8] Further intramolecular cyclisation of (7) and (8) to give the trans decalin system would yield intermediates of the type (9) and (10) respectively. The former on deprotonation would produce α, β,



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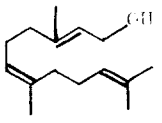

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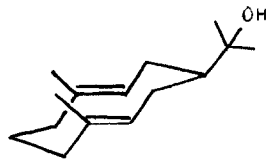

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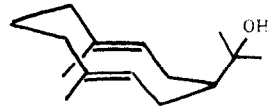

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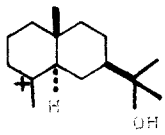

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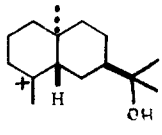

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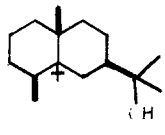

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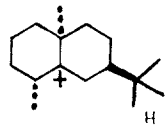

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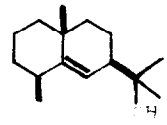

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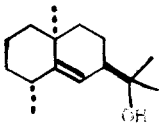

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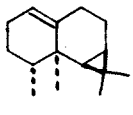

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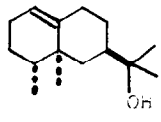

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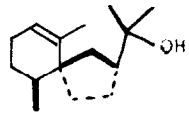

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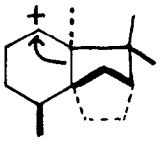

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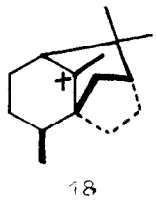

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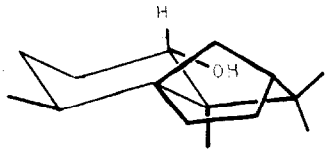

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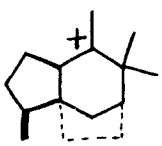

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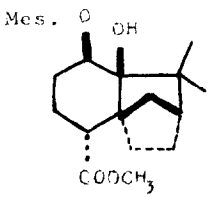

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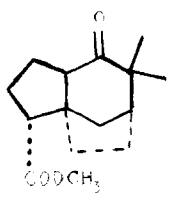

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and γ-eudesmol which have been isolated[9] from Callistris columellaris. A 1-2 hydride shift would rearrange (9) and (10) to the tertiary carbonium ions (11) and (12) respectively. Loss of a proton would then result in the formation of the corresponding $\Delta^{5,6}$ eudesmols (13) and (14).

If it is allowed that all further rearrangements of (13) and (14) in the vetiver plant occur on the α-face of the intermediates, possibly initiated by protonation at the 6β position by an intramolecular process involving the hydroxyl group, then all the complex stereochemical and structural relationships of the vetiver sesquiterpenes can be rationalised. Indeed homoallylic participation of the double bond in the displacement of the tertiary hydroxyl group in (14), with the formation of a cyclopropane ring, could initiate migration of the C-10 methyl group to C-5 leading to the sesquiterpene, calarene[10] (15). Migration of the C-10 methyl group of (14) to C-5 followed by deprotonation would yield (16) which on further elaboration should give α-vetivone (2). On the other hand in (13) migration of C-9 to C-5 with concomitant deprotonation would result in ring contraction with formation of hinesol (4), correct in stereochemical detail. Hinesol (4) is an obvious precursor of β-vetivene (3b) and β-vetivone (3a).

Interaction of the double bond of hinesol (4) with the tertiary hydroxyl group can only lead to the carbonium ion (17); the other alternative (18) being excluded on steric grounds. The α-alcohol (19) formed by nucleophilic attack on (17) has the correct trans coplanar arrangement required for the rearrangement of (19) to the tertiary carbonium ion (20); deprotonation of which would lead to tricyclovetivene (1) having the correct stereochemistry. The feasibility of this rearrangement occurring in vivo is supported by the solvolysis of the mesylate (21) in refluxing pyridine/triethylamine (2:1) to give the ketone (22) possessing the tricyclovetivane ring structure.* Full details of this in vitro transformation leading to a synthesis of the tricyclic vetiver sesquiterpenes will be reported shortly.

* Recently another group has also reported this transformation in a synthesis of epizizanoic acid, F. Kido, H. Uda and A. Yoshikoshi, Chem. Comm., 1969, 1335.

Another biogenetic route to this class of tricyclic sesquiterpenes has been proposed[2,3], however this invoked intermediates of the acorane and cedrane classes[11], neither of which have so far been shown to occur in vetiver oil. A more important criticism[12] of the earlier proposal is that the tricyclic vetiver sesquiterpenes are not related stereochemically to the cedrane class of sesquiterpenes.

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