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SELINANE-TYPE SESQUITERPENES. ACOLAMONE AND ISOACOLAMONE

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Isolation of two new selinane-type sesquiterpenes, named acolamone (II) and isoacolamone (III), is described and their structures have also been elucidated in connection with the base catalyzed cyclization of an epoxygermacrone (IV), which has been derived from preisocalamendiol, leading to the formation of a selinane-type α,β-unsaturated ketone (V).

Recently, several new sesquiterpenes have been isolated from the rhizomes of Acorus calamus L (Japanese name "Shyobu") growing in Japan.[1,2] From a biogenetic point of view, most of them must be directly derived from a plausible germacrone-type precursor (I).[1] We further examined sesquiterpenic components of the same plant and could isolate two new selinane-type compounds which may be directly formed from I.

The sliced raw rhizomes of Acorus calamus L were pluverized with a mixer and immersed in n-hexane (room temp., 2 weeks), and then filtered. The filtrates were concentrated under reduced pressure below 35° to leave a brown residue (in ca. 13% yield), which was chromatographed on silica gel (Katayama Chemicals Ltd., 100 - 200 mesh).[3] Elution with pet.ether - ether (9 : 1) gave the sesquiterpenic fraction, which was rechromatographed on silica gel (Kanto Chemicals Ltd., 100 - 200 mesh) and eluted with n-hexane - benzene (1 : 1) to give acolamone (II) and isoacolamone (III) in each ca. 1.6% yield (from the n-hexane extracts).[4] Their physical properties are described below.

Acolamone (II): $C_{15}H_{24}O$ (m/e 220 (M^+)), relative retention 2.70;[5] ν_{max}(film) 1715 and 1645cm^{-1}; δ($CDCl_3$) 0.76 (3H, s), 0.87 (3H, d, J= 6.5Hz), 0.90 (3H, d, J= 6.5Hz), 2.90 (1H, s), 5.00 (1H, br.s) and

5.95ppm (1H, br.s).

Isoacolamone (III): $C_{15}H_{24}O$ (m/e 220 (M^{+})), relative retention 2.30; ν_{max}(film) 1715 and 1645cm^{-1}; δ($CDCl_3$) 0.74 (3H, s), 0.89 (3H, d, J= 6.3Hz), 0.93 (3H, d, J= 6.3Hz), 1.76 (3H, d, J= 1.8Hz), 3.10 (1H, br.s) and 5.42ppm (1H, br.s).

In the comparison of NMR spectra between II and III, the former has two protons attached to an exocyclic double bond (δ 5.00 (1H, br.s) and 5.95ppm (1H, br.s)), whereas III has one proton and the methyl group, both of which are attached to a trisubstituted double bond (δ 5.42 (1H, br.s) and 1.76ppm (3H, d, J= 1.8Hz)). The remaining signals are almost identical in both compounds. Accordingly, these two sesquiterpenes are regarded as double bond isomers. In fact, when heated in a sealed tube (190°, 5hr), II afforded a mixture of two α,β-unsaturated ketones (V (relative retention 2.30) and VI (relative retention 2.79)),[6] whose spectral data were fairly close to each other, in 60 and 27% yields, respectively. The same result was also obtained in the case of III. In connection with a biogenetic type reaction of the epoxygermacrone (IV) the compound (V) was synthesized from IV as follows. When treated with t-BuOK - t-BuOH (room temp., 2hr) under nitrogen, IV has been known to afford a selinane-type compound (VII) in high yield.[7] Further treatment of VII with mesyl chloride - pyridine (room temp., 2hr) afforded a mesylate (VIII) (m/e 218 (M^{+}- 96); δ3.07 (3H, s) and 4.21ppm (1H, t, J= 7.5Hz)) in quantitative yield. Furthermore, VIII reacted with NaI in methyl ethyl ketone (under reflux, 15hr) under nitrogen to give the corresponding iodide (IX) (m/e 346 (M^{+}) and 219 (M^{+}- 127)) in ca. 30% yield. IX was further heated with n-Bu_3SnH in toluene under reflux for 4hr (under nitrogen) to afford an expected reduction product in ca. 95% yield, which was completely identical with V in respect of GLC and IR spectrum. Recently, V has also been formed from ajanol.[8]

Finally, stereostructures of these two selinane-type sesquiterpenes are discussed below. The ORD curve of acolamone showed a weak positive Cotton effect ($[\phi]^{P}_{325nm}+9^{\circ}\times 10^{2}$, $[\phi]^{T}_{280nm}-4^{\circ}\times 10^{2}$, A= +13), whereas that of isoacolamone had a weak negative Cotton effect ($[\phi]^{T}_{314nm}-10^{\circ}\times 10^{2}$, $[\phi]^{P}_{283nm}+7^{\circ}\times 10^{2}$, A= -17).[9] However, the dihydro-compound (X) (relatvie retention 2.32; m/e 222 (M^{+}); ν_{max}(film) 1715cm^{-1}), which was easily obtained from II as well as from III (H_2/PtO_2 in EtOAc), had a positive Cotton effect in its ORD curve ($[\phi]^{P}_{312nm}$

$+19^{\circ} \times 10^{2}$, $[\phi]^{T}_{274nm} -13^{\circ} \times 10^{2}$, A= +32),[10] indicating that acolamone and isoacolamone should have the stereostructures (II) and (III), respectively. Structurally, the former is regarded as the higher oxidation substance of junenol (XI).[11, 12] At present, it is not clear whether two selinane-type sesquiterpenes (II and III) are directly formed from I enzymatically or nonenzymatically in vivo. However, the isolation of these sesquiterpenes strongly suggests the occurrence of the plausible germacrone-type precursor (I) in the plant.

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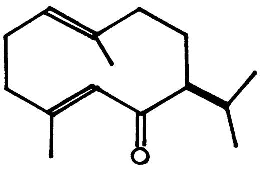
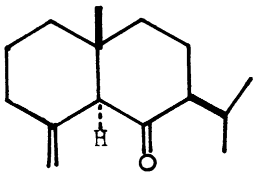
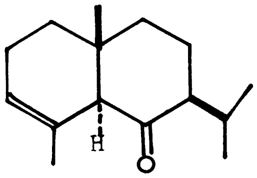


(I)



(II)



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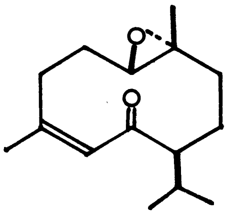
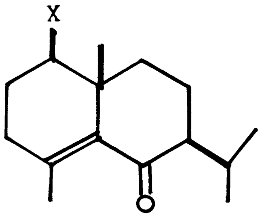


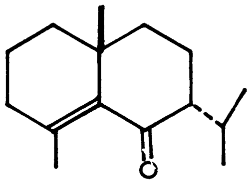
(IV)



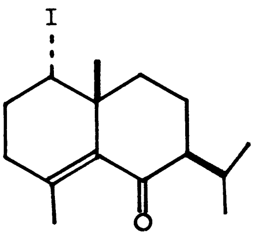
(V) X = H

(VII) X = OH

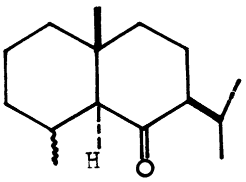
(VIII) X = OMs



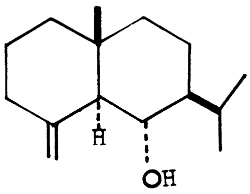
(VI)



(IX)



(X)



(XI)

REFERENCES AND FOOTNOTES

1. S. Yamamura, M. Iguchi, A. Nishiyama, M. Niwa, H. Koyama and Y. Hirata, Tetrahedron, **27**, 5419 (1971) and references cited therein.
2. H. Minato, R. Fujioka and K. Takeda, Chem. Pharm. Bull. Japan, **19**, 638 (1971).
3. Attempted separation of sesquiterpenes such as I is in progress by using cellulose powder and florisil instead of silica gel as well as alumina.
4. Shyobunone and its isomers could be obtained after elution of acolamone and isoacolamone.
5. Relative retention was recorded vs. calamenene as an internal standard (Stationary phase: 5% PEG 20M on Celite 545 (stainless steel ϕ3mm x 1.5m); Column temp., 90°; Carrier gas: Nitrogen, 1.2Kg/cm^2, 85ml/min; Detector: Flame ionizer).
6. D. W. Theobald, Tetrahedron, **20**, 2593 (1964).
7. M. Iguchi, M. Niwa and S. Yamamura, Chem. Commun., in press (1972).
8. V. A. Babkin, Z. V. Dubovenko and V. A. Pentegova, Khim. Prir. Soedin, 736 (1971).
9. It seems to be pretty dangerous to apply the octant rule to such α,β-unsaturated ketones as II and III. Therefore, the stereochemistry at C_5-position should be discussed in the case of the corresponding dihydro-compound (X).
10. The direct comparison of physical data between X and the oxidation product of dihydrojunenol has not been carried out, but these two compounds seem to be identical (see references 6 and 11).
11. V. Herout, O. Motl and F. Šorm, Coll. Czech. Chem. Commun., **22**, 785 (1957); S. C. Bhattacharyya, A. S. Rao and A. M. Shaligram, Chem. and Ind., 469 (1960).
12. Probably, II is not produced by the oxidation of junenol (XI) in vivo, but directly derived from the germacrone (I).

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