Biogenetic Model Reactions of Epoxygermacrone

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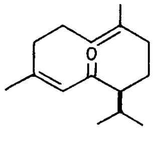
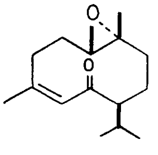
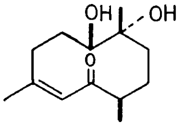
Summary Treatment of the epoxygermacrone (II) with 80% HCO_2H, $AlCl_3$, Bu^tOK, or basic alumina afforded various cyclization products; in particular, (II) gave a *cis*-selinane sesquiterpene (IV) with 80% HCO_2H.



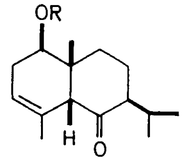
(I)



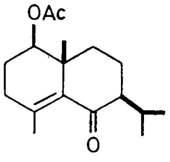
(II)



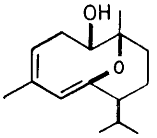
(III)



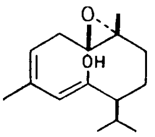
(IV) R = H
(V) R = Ac



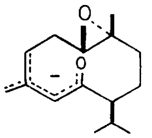
(VI)



(VII)



(A)



(B)

Epoxidation of the $\alpha\beta$-unsaturated germacrone (I)[1] with *m*-chloroperoxybenzoic acid (1·06 equiv.; 0°; 20 h) gave in quantiative yield the expected mono-epoxide (II) [m.p. 55°; *m/e* 236 (M^+); ν_{max} (KBr) 1675 and 1620 cm^{-1}; λ_{max} (MeOH) 243 nm (ϵ, 6460)], which was used for biogenetic model reactions, as follows.

When treated with 80% HCO_2H (−18 to −20°; 10 min), (II) afforded a dihydroxyketone (III), m.p. 155—157°, and a cyclic compound (IV) in 47·5 and 34·2% yields, respectively. The structure (IV) was based on its spectral data [*m/e* 236 (M^+); ν_{max} (film) 3430br and 1705 cm^{-1}; δ ($CDCl_3$) 0·91 (6H, d, *J* 5·0 Hz), 1·02 (3H, s), 1·58br (3H, s), 3·53 (1H, t, *J* 5·0 Hz), and 5·44br (1H) p.p.m.] and chemical evidence. Acetylation of (IV) with Ac_2O–pyridine (room temp.; overnight) gave the corresponding acetoxy-compound (V). In its n.m.r. spectrum, the triplet at δ 3·53 in (IV) is observed at δ 4·80 (1H, t, *J* 4·5 Hz) p.p.m. The remaining signals are nearly identical in both compounds except for an Me singlet at δ 2·03 p.p.m. in (V). The o.r.d. curve of (V) showed a negative Cotton effect ($[\Phi]^{T}_{318}$ −72° × 10^2, $[\Phi]^{P}_{276}$ +63° × 10^2, A = −135). When treated with 100% HCO_2H under reflux, (V) was converted into a fully substituted $\alpha\beta$-unsaturated ketone (VI), *m/e* 278 (M^+). In its n.m.r. spectrum, the coupling constant for the proton attached to the carbon atom bearing the acetoxy-group is different from that in (V); the configuration of the acetoxy-group should be axial in (V) and equatorial in (VI). In addition, the o.r.d. curve of (VI) has a strong positive peak ($[\Phi]^{P}_{264}$ +150° × 10^2).† The stereostructures of the cyclization product and the acid isomerization compound can thus be represented by (IV) and (VI), respectively. (VI) was also obtained in 75% yield when (II) was treated with Bu^tOK–Bu^tOH (1·1 equiv.; room temp.; 2 h; under

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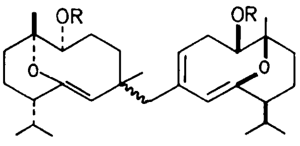
† The o.r.d. curve of cholest-4-en-6-one also has a strong positive peak in the same region.

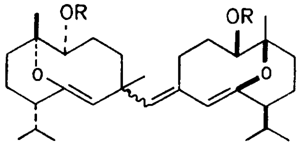
N_2) followed by acetylation with Ac_2O–pyridine. In the above cyclizations (80% HCO_2H and Bu^tOK), (A) and (B) respectively are possible intermediates and the stereochemistry of the cyclization products is determined by the corresponding conformations of (A) and (B). It should be noted that this is the first example of the formation of *cis*-selinane in intramolecular cyclizations of ten-membered ring sesquiterpenes, which usually afford *trans*-selinanes.

We have further examined the cyclizations of (II) with $AlCl_3$.[2] When treated with $AlCl_3$ in dry ether (−18°; 20 min), (II) gave three different products [(VII), (VIII) and (IX)] in 18, 47, and 33% yield, respectively. The last two [(VIII), m.p. 159·5—160·5° and (IX), m.p. 143·5—144·5°] are dimeric [*m/e* 472 M^+)] and regarded as double bond isomers, which are converted into the corresponding acetates (X) and (XI), respectively, on acetylation with Ac_2O–pyridine.

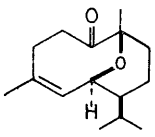
Finally, (II) was absorbed on basic alumina (150—250 mesh), and then eluted with benzene–n-hexane (3:1) to give an isomer (XII) (34%), catalytic reduction (5% Pd–C in MeOH) of which afforded a dihydro-derivative (XIII), m.p. 37—40°. Further elution with ether gave another fairly unstable isomer (XIV) (46%).



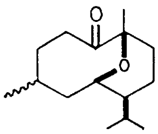
(VIII) R = H
(X) R = Ac



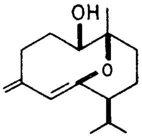
(IX) R = H
(XI) R = Ac



(XII)



(XIII)



(XIV)

All compounds gave satisfactory physical data, and their structures were confirmed by i.r., u.v., n.m.r., and mass-spectrometric data.

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[1] M. Iguchi, A. Nishiyama, S. Yamamura, and Y. Hirata, *Tetrahedron Letters*, **4295**, **1969**.

[2] M. Iguchi, M. Niwa, and S. Yamamura, *Chem. Comm.*, **1971**, **974**.