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THE STRUCTURE OF ACTINIDIOLIDE, DIHYDROACTINIDIOLIDE AND ACTINIDOL*

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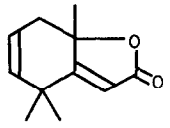
Previously, T. Sakan and coworkers (1) reported on the phisiologically active components of Actinidia polygama for Felidae animals and Chrysopidae.

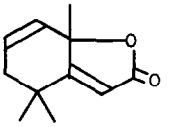
From the essential oil of the leaves of Actinidia polygama, after removal of the matatabilactone (2) by dissolving it in hot alkali, three new terpenes (actinidiolide, dihydroactinidiolide and actinidol) were isolated by fractional distillation and repeated column chromatography on alumina and silica gel. The former two terpenes have been found to be effective for Felidae animals in lower order.

In this communication we wish to present the structure elucidations of these terpenes. The UV spectra of both actinidiolide (I) ($C_{11}H_{14}O_2$, $[\alpha]_D^{12}$ +7.7°) and dihydroactinidiolide (II) ($C_{11}H_{16}O_2$, m.p.40-41°, $[\alpha]_D^{15}$ +7.1°) showed the maximum absorption at 241mμ(ε=10000) and the IR spectra of both compounds showed bands at 1745cm^{-1}(C=O), 1630cm^{-1}(C=C) and 1360, 1380cm^{-1}(gem-dimethyl). On hydrogenation with 10% Pd/C, actinidiolide (I) absorbed one mole of hydrogen to give a dihydroactinidiolide (II), which resisted to further hydrogenation and alkaline hydrolysis. However, on hydrogenation with Adams catalyst dihydroactinidiolide (II) absorbed another one mole of hydrogen to give tetrahydroactinidiolide (III), which was hydrolyzed with potassium hydroxide. The IR spectrum of tetrahydroactinidiolide showed band at 1770cm^{-1} indicative of the presence of γ-lactone. From these findings, the presence of α,β-unsaturated butenolide ring was suggested in both actinidiolide and dihydroactinidiolide. The nmr spectrum of dihydroactinidiolide (II) showed signals at 8.79τ, 8.72τ, 8.47τ due to three quarternary methyl groups. A singlet at 4.38τ(1H) should be ascribed to the α-vinyl proton of an α,β-unsaturated γ-lactone. The remaining six protons exhibited in the region 8-8.7τ. The nmr spectrum of actinidiolide (I) is similar to that of dihydroactinidiolide (II), except that the signals of two protons appeared at 4.28τ,

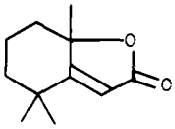
instead of the disappearance of signals of four protons in the region 7.8τ. The nmr spectrum of tetrahydroactinidiolide (III) showed signals at 9.1, 8.95 and 8.47τ due to three quarternary methyl groups. There are no signals in the region 4.2-4.7τ. From these results, the structure of dihydroactinidiolide was deduced to be (II) and the possible structure of actinidiolide is represented by (Ia) or (Ib).



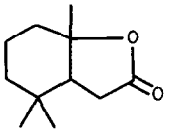
(Ia)



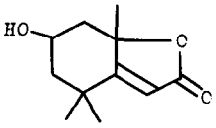
(Ib)



(II)



(III)

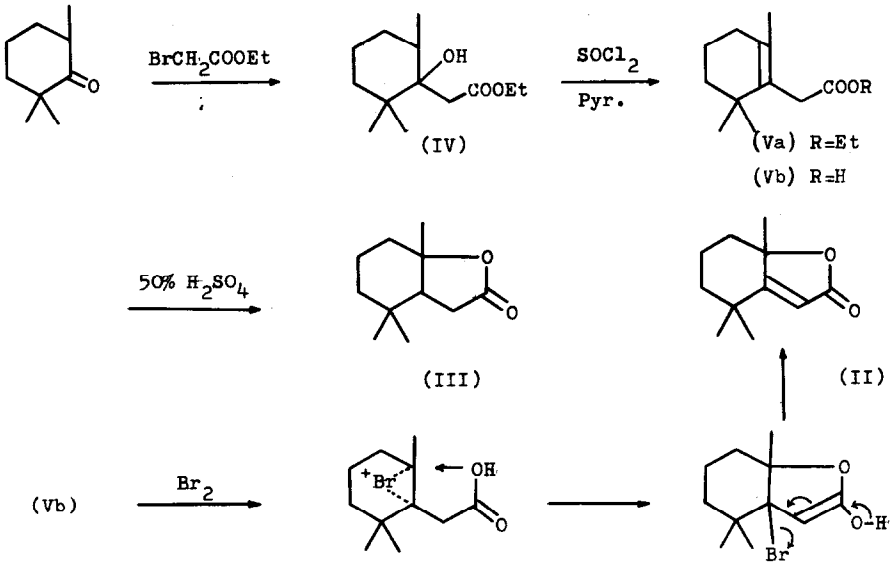


(VI)

The structure of dihydroactinidiolide (II) was fully confirmed by the total synthesis. The Reformatsky reaction of 2,2,6-trimethylcyclohexanone (3) with ethylbromoacetate yielded the hydroxyester (IV) which was dehydrated with thionyl chrolide in pyridine to give a mixture of olefinic ester (V, R=Et). Alkaline hydrolysis of the olefinic ester, followed by treatment with hot 50% H_2SO_4 (4) gave a tetrahydroactinidiolide (III), while the addition of bromine to olefinic acid (V, R=H) gave dihydroactinidiolide (II) with simultaneous dehydrobromination (5). The purification of dihydroactinidiolide (II) was effected by heating with 25% KOH to remove acidic impurities. The synthetic dihydroactinidiolide and tetrahydroactinidiolide were identified respectively with natural specimens by comparison of their richly detailed IR spectra. Additional confirmation of identity was provided by gas chromatographic retention time.

Recently, Hodges and Porte (6) reported the structure of loliolide (VI), the C_{11} terpene from Lolium pelenne and they assigned the structure (VI) for this lactone. While, Wada and Satoh (7) gave independently the same structure for digiprolactone, the terpene from Digitalis purpurea. The biogenesis of these odd terpenes has never been discussed in the literature. Fortunately, we have succeeded in the isolation of

very small amount of actinidol, which is seemed to be a biogenetic precursor of C_{11} terpenes.

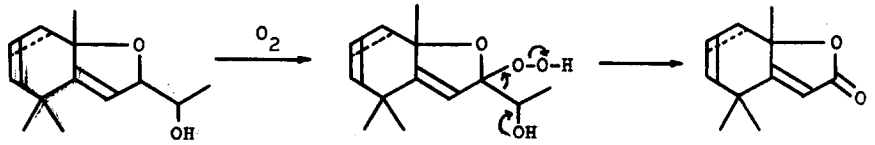


Actinidol is a very unstable liquid and is subjected to air oxidation to give actinidiolide (I). Therefore the structure of actinidol is seemed to have the similar structure to actinidiolide (I). However, the elementary analysis of actinidol was in agreement with the molecular formula $C_{13}H_{20}O_2$, which was further supported by mass spectrum. The IR spectrum of actinidol showed bands at 3452cm^{-1}(OH), 1640 and 1660cm^{-1} (C=C). The nmr spectrum of actinidol showed signals at 8.85, 8.75 and 8.60τ due to three quarternarymethyl groups. A doublet at 7.95τ(2H) was assigned to methylene protons and multiplet signals at 4.25τ(2H) were assigned to vinyl protons.

Keeping in mind the structure of actinidiolide (I), these data for actinidol led to its formulation as (VII). The mass spectrum of actinidol is consistent with the structure (VII). The base peak at m/e 163 formed by loss of 45 from the molecular ion m/e 208 is good accounted with the fission illustrated below. This fragmentation is supported with the presence of metastable peak m/e 128 (calculated value is 127.7).

m/e 208 m/e 163

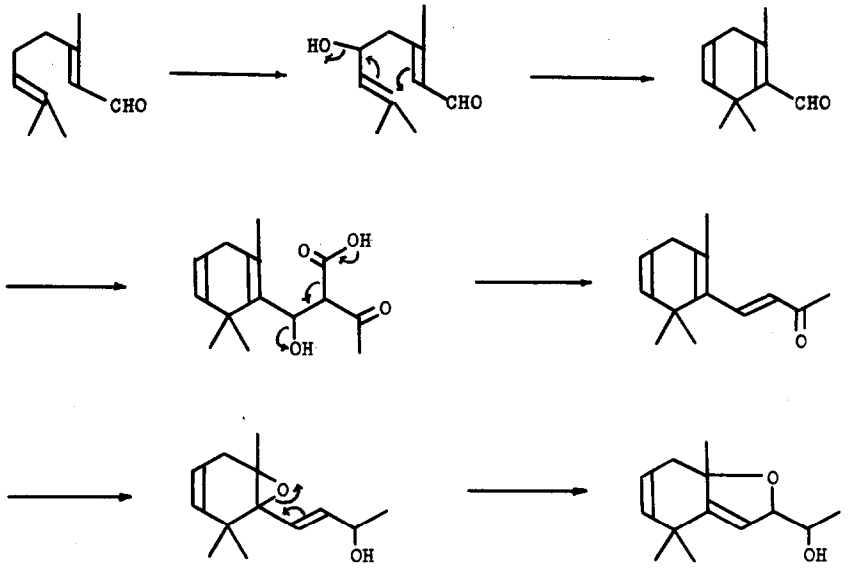
The mechanism of air oxidation of actinidol to actinidiolide is illustrated as follows.



(VII) (I)

The biogenesis of actinidol:

Although the experimental evidence is not available, a possible biogenetic route to actinidol may be illustrated below.



(VII)

The enzymatic oxidative cyclization of citral, followed by condensation with acetoacetic acid and decarbonylation would afford unsaturated ketone. Enzymatic reduction of the carbonyl group, followed by epoxidation and cleavage of epoxide would give actinidol.

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