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THE STRUCTURE OF CHAMAECYNONE
A NOVEL NOR-SESQUITERPENOID FROM *CHAMAECYPARIS FORMOSENSIS* MATSUM.

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A reinvestigation of the terpenoid constituents of the Benihi tree (*Chamaecyparis formosensis* Matsum., Cupressaceae) (1), grown in Formosa, has resulted in the isolation of a novel nor-sesquiterpenoid, chamaecynone (I), which exists in the non-steroid cis-decalin conformation (A) (2,3). This appears to be the first example of a natural acetylenic compound of terpenoid origin (4). Three other closely related nor-sesquiterpenoids, isochamaecynone (II), hydroxyisochamaecynone (III) and dihydroisochamaecynone (IV) were also isolated besides some other C_{14} acetylenic compounds.

Chamaecynone (I), colorless prisms, m.p. 92°C, $[\alpha]_D$ -93.3° (MeOH), $C_{14}H_{18}O$ (M.W. 202 by MS) possesses the following spectroscopic properties: UV, λ_{max}^{MeOH} 230mμ, log ε (4.00); IR, 3330 (C≡CH), 2120 (C≡C), 1675 (C=O) and 1620 (C=C) cm^{-1}, in CCl_4; NMR, 8.99 ($-\overset{|}{C}H-\underset{\sim\sim}{CH_3}$, d, J = 7.0 cps), 8.73 ($-\underset{|}{\overset{|}{C}}-\underset{\sim\sim}{CH_3}$,

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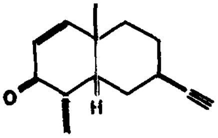
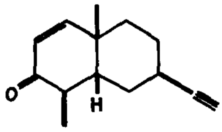


(I)



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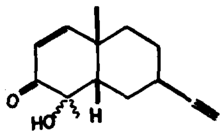

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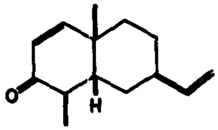

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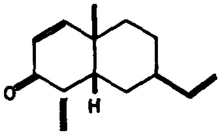

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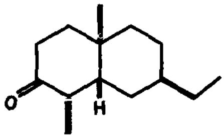

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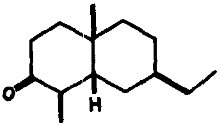
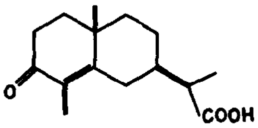
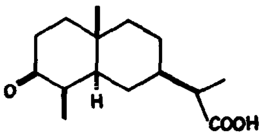


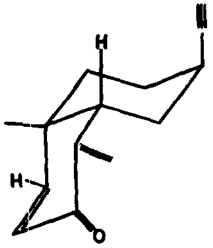
(VII=X)



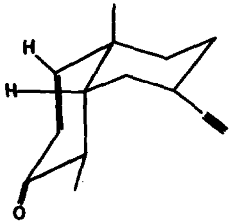
(VIII)



(IX)



(A=I)



(B=II)

s), 8.06 ($-\overset{|}{C}H-C\equiv\underset{\sim\sim}{CH}$, d, J = 2.3 cps), 4.24 ($-CO-\underset{\sim\sim}{CH}=CH-$, d, J = 9.8 cps) and 3.68 ($-CO-CH=\underset{\sim\sim}{CH}-$, d, d, J = 9.8 and 2.2 cps)τ, in CCl_4. Chemical evidences also support the presence of a terminal acetylene group in I, since it afforded a copper complex, m.p. 158° (dec.) and hydrogenation of I over Lindlar catalyst yielded dihydrochamaecynone (V), $C_{14}H_{20}O$, $[\alpha]_D$ -34.6° (MeOH); IR, 3080, 992 and 910 cm^{-1}. The methyl signal at 8.99τ of chamaecynone, I, became a broad singlet when I was treated with sodium deuterium oxide for few hours at room temperature, indicating that the methyl group attached to a carbon atom adjacent to the carbonyl group. Catalytic reduction of I over palladized charcoal gave hexahydrochamaecynone (VI), $C_{14}H_{24}O$, $[\alpha]_D$ -41.98° (MeOH); IR, 1715 cm^{-1}. The above results, when considered along with the known occurrence of selinane type sesquiterpenoids in the Benihi tree (1) and the fact that chamaecynone, I, contains an acetylenic but not an isopropyl group, leads to the conclusion that I is 4,10-dimethyl-7-ethynyl-Δ^1-octalone-3. The following evidences substantiate this structure and also allow one deduce the absolute configuration and conformation.

Hexahydrochamaecynone, VI, was readily isomerized in quantitative yield to hexahydroisochamaecynone (VII), $[\alpha]_D$ $+ 60.3^{\circ}$ (MeOH), (semicarbazone, m.p. 158°), when treated with base for several hours at room temperature. On the other hand, dihydrochamaecynone, V, was isomerized to dihydroisochamaecynone, IV, 90% yield (by NMR) after being allowed to stand overnight, whereas chamaecynone, I, was isomerized to its isomer, II, in only ca 30% yield (by NMR) when allowed to stand for several days.

Hexahydroisochamaecynone, VII, exhibits a negative Cotton effect in its ORD curve ($[\phi]_{305}$, -1040, $[\phi]_{267}$, $+ 2995$, A = 40 in MeOH), which is similar to those of β-tetrahydrosantonin (5) and cis-4β,10β-dimethyldecalone-3 (6), having established cis-steroid conformation (as in B).

Therefore, the structure of VII is cis-4β,10β-dimethyl-7β-ethyldecalone-3 in steroid conformation. That this structure is correct was demonstrated as follows: Catalytic reduction of dl-3-oxo-eusantona-4-enoic acid (VIII) (7) over palladized charcoal (8) gave the saturated acid (IX) with the cis ring juncture. The silver salt of IX was treated with bromine under the Hunsdiecker reaction conditions, and the resulting bromide was reduced over palladized charcoal to give racemic saturated ketone (X). IR and NMR spectra (both in CCl_4) of VII and X were identical, as were those of their semicarbazones (m.p. 158° and m.p. 186°, respectively).

The ORD curve of hexahydrochamaecynone, VI, shows a positive Cotton effect ($[\phi]_{304}$, + 178, $[\phi]_{270}$, -1040, A = 28.3 in MeOH) and is similar to those of tetrahydro-epi-α-cyperone (9) and related compounds (10) having established non-steroid conformations, thus indicating that VI is cis-4α,10β-dimethyl-7β-ethyldecalone-3 and that it exists in the non-steroid conformation such as **A**.

The ORD curves of chamaecynone, I, and dihydrochamaecynone, V, show a complex positive Cotton effect, while those of isochamaecynone, II, and dihydroisochamaecynone, IV, exhibit a complex negative Cotton effect. Thus, the compounds belonging to the chamaecynone series exist in the non-steroid conformation such as **A**, whereas those of the isochamaecynone series exist in the steroid conformation such as B.

The results obtained above can be resonably explained from the stereochemical point of view. Namely, the order of rates of alkaline isomerization (change in conformation and inversion of 4α-equatorial methyl groups to 4β-equatorial) parallels the order of bulkiness of the 7β-axial groups in the chamaecynone series and the axial interaction involving this 7β groups provides the driving force for isomerization. Since ethynyl group is smaller than methyl group (11), 1,3-diaxial interaction of 7βethynyl group and two axial hydrogen atoms on C_3 and C_9 in chamaecynone (A) is smaller than those of 10β-methyl group and two axial hydrogen atoms on C_6 and C_8 in isochamaecynone (B). Therefore, (A) should be more favorable conformation than that of (B).

Solvent effects (12) and long range couplings (12, 13) in those compounds also support the conformations assigned to them. In benzene solution, signals due to the 4-methyl groups in I, VI and VII are shifted down-field, 0.03, 0.09 and 0.13 ppm, respectively, from the positions found for carbon tetrachloride solutions. The proton at C-4, however, is shifted 0.19 ppm up-field. Similarly, solvent effects were observed in the case of IV and V. Thus, the 4-methyl groups in those compounds must be equatorial. In the NMR spectrum of II, the ethylenic protons appear as a simple AB quartet at 3.53 and 4.26τ (J = 10 cps), whereas in the case of I, the C_1-proton signal at 3.68τ is further split into a quartet (J = 9.8 and 2.2 cps), the C_2-proton appearing as the expected doublet (J = 9.8 cps) at 4.24τ. This additional coupling, which NMDR at 100 Mc shown to be between H_1 and H_5, is in accord with the non-steroid conformation (A) for I, since Dreiding models indicate that the fragment $H_1\text{-}C_1\text{-}C_{10}\text{-}C_5\text{-}H_5$ would be in the zig-zag coplanar relationship (M or W rule) considered necessary for long range coupling (12, 13), whereas the corresponding fragment in conformation (B) would not. Examples of this particular type of long-range coupling are known but are rather rare (14).

Hydroxy-isochamaecynone (III); colorless prisms, m.p. 162°, $[\alpha]_D$ -39.2° (EtOH), molecular weight 218 (MS), has molecular formula $C_{14}H_{18}O_2$. Spectral data for III are: UV, λ_{max}^{EtOH} 228 mμ (log ε, 3.96); IR, 3460, 3280, 2120, 1675, 1630, 1125, 835, 700 cm^{-1} (KBr pellet); NMR, 8.76 (CH_3, s), 8.68 (CH_3, s), 7.92 ($C\equiv C\text{-}H$, d, J = 2.2 cps), 4.09 (d, J = 10.0 cps), 3.45 (d, J = 10.0 cps)τ. III does not show long range coupling between H_1 and H_5, and shows a negative Cotton effect in its ORD curve. The above suggests that III is 4-hydroxyisochamaecynone.

A new nor-sesquiterpene, $C_{14}H_{20}O$, isolated by gas chromatography, is completely identical with IV from a comparison of their UV, IR and NMR spectra.

Isochamaecynone (II) was also found to occur in the essential oil, but could not be isolated free of chamaecynone; its identity was established by NMR spectra.

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