Structure and Synthesis of a Phenolic Sesquiterpene, Sesquichamaenol

By MASAYOSHI ANDO, SADAO IBE, SHINZO KAGABU, TORU NAKAGAWA, TOYONOBU ASAO, and KAHEI TAKASE*
(*Department of Chemistry, Faculty of Science, Tohoku University, Katahira-2-chome, Sendai, Japan*)

Summary A new phenolic sesquiterpene, sesquichamaenol, has been isolated and its structure elucidated on the basis of spectroscopic data and total synthesis.

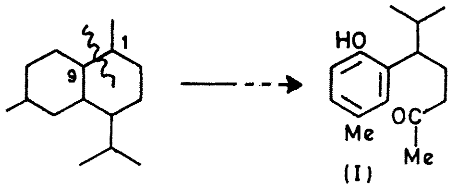
RECENT re-investigations of the constituents of the Benihi tree (*Chamaecyparis formosensis* Matsum. Cupressaceae) have provided novel nor-sesquiterpenoids[1] containing ethynyl groups and also some sesquiterpenoids.[2]

We have now isolated a new phenolic sesquiterpene, containing a novel skeleton, which we call sesquichamaenol.

Sesquichamaenol (I), $C_{15}H_{22}O_2$ (M^+ 234), m.p. 109—110°, $[\alpha]_D$ 0° (MeOH) was isolated as a very minor constituent from column chromatography (silicic acid) of the essential oil of the tree.

The u.v. spectra of (I), λ_{max} (MeOH) 283 nm (log ϵ 3·45) and λ_{max} MeOH–NaOH 290 (3·40) and 305sh (3·18), indicated the presence of a phenolic chromophore. The i.r. spectrum (KBr disc) showed absorption bands at 3430, 1265, 1259, 1205 (phenolic OH), 1695 (C=O), 1613, 1513 (aromatic ring), 890 and 811 cm^{-1} (out-of-plane deformation of 1,2,4-trisubstituted benzene). The n.m.r. spectrum (in $CDCl_3$; 60 MHz) indicated the presence of an isopropyl group (δ 0·73, d, *J* 6·5 Hz and 1·00, d, *J* 6·5 Hz), acetyl group (2·03, s), aromatic methyl (3·24, s), hydroxyl (5·30, bs) aromatic ring protons (6·5—7·0, 3H) and benzylic proton (*ca.* 2·6, m, 1H).

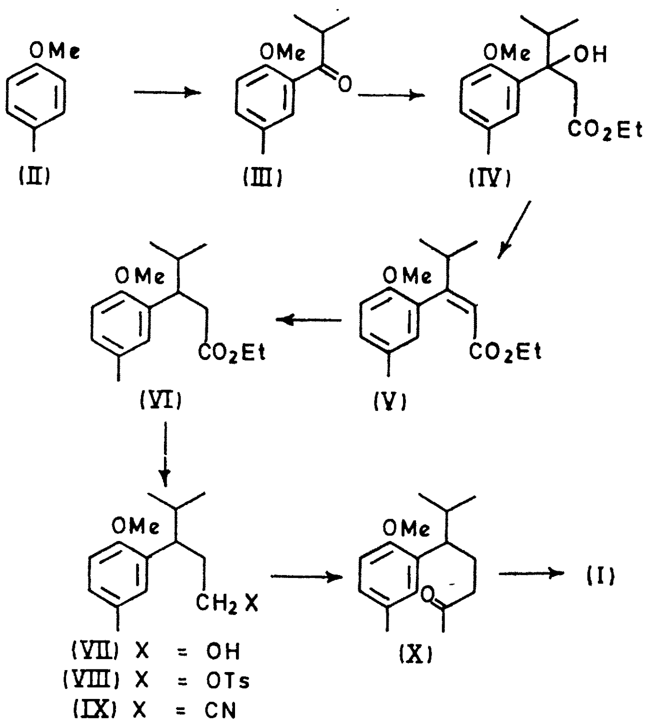
Since the doublet at δ 6·64 (1H) (*J* 9 Hz) may be assigned to a ring proton adjacent to a hydroxy-group, the OH group must be *ortho* to another substituent. If this sesquiterpene originates from cleavage of the cadinane skeleton between C-1 and C-9, sesquichamaenol should have the structure (I).



(I)

In order to confirm the structure, the compound (I) was synthesized, as follows.

Acylation of *p*-methoxytoluene (II) with isobutyroyl chloride in nitrobenzene–tetrachloroethane in the presence of aluminium chloride gave a ketone (III)† (60·8%), b.p 109—110°/0·55 mm Hg. Reformatsky reaction of (III) using ethyl bromoacetate and zinc powder in the presence of iodine afforded a hydroxy-ester (IV) (72·5%), b.p. 170°/0·5 mm Hg. Treatment of (IV) with phosphoryl chloride in pyridine under reflux afforded an unsaturated ester (V) (86%), n.m.r. (CCl_4), 5·78 (olefinic proton, d, *J* 1 Hz). Catalytic hydrogenation of (V) using Pd–C in methanol gave an ester (VI), b.p. 140°/0·2 mm Hg, reduction of which with lithium aluminium hydride afforded an alcohol (VII), b.p. 135° : 0·25 mm Hg in 97% yield from (V).



(II) (III) (IV)

(VI) (V)

(VII) X = OH
(VIII) X = OTs
(IX) X = CN

(X)

The reaction of the tosylate (VIII) with sodium cyanide in dimethylformamide in the presence of a catalytic amount of sodium iodide afforded an oily nitrile (IX) (75%). Grignard reaction of (IX) with methylmagnesium iodide afforded 50% yield of an oily ketone (X), demethylation of which with 48% HBr in refluxing acetic acid under an atmosphere of nitrogen gave the compound (I) (68%), identical with natural sesquichamaenol (m.p., n.m.r., mass spectrum, u.v., and i.r. spectra).

Many cadinane-type sesquiterpenes have been isolated from the same tree,[2–4] and it would be interesting to know whether sesquichamaenol is formed by oxidation of a cadinane-type sesquiterpene or by other biogenesis from another precursor.

(*Received, September 14th,* 1970; *Com.* 1565.)

---

† All new compounds showed satisfactory elemental analyses and spectroscopic data.

[1] T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, **1966**, 3663; T. Asao, S. Ibe, K. Takase, Y. S. Cheng, and T. Nozoe, *ibid.* **1968**, 3639; K. Takase, S. Ibe, T. Asao, T. Nozoe, T. Shimanouchi and Y. Sasada, *Chem. and Ind.*, 1968, 1638.

[2] T. Toda, Y. S. Cheng, and T. Nozoe, *Chem. and Pharm. Bull.* (*Japan*), 1967, **15**, 903.

[3] *cf.* Y. S. Cheng, Dissertation, *Tohoku University*, 1966.

Y. S. Cheng, Y. H. Kuo, and Y. T. Lin, *Chem. Comm.*, 1967, 565.