

(-)-Torreyol ("δ-Cadinol")*

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The major dehydration product of torreyol ("δ-cadinol") is α-muurolene. The known diol (14) obtained via hydroboration of torreyol gives the ether (13) on treatment with brosyl chloride in pyridine. These results, along with others, show that (-)-torreyol possesses the structure and absolute configuration shown in formula (1).

Of the cadalene type sesquiterpene alcohols torreyol (1)¹⁻³ was the first which was isolated in pure state.¹ The dextrorotatory form was obtained from the leaves of *Torreyia nucifera* Sieb et Zucc. (Taxaceae) in 1922.¹ Several compounds, e.g. "(+)-δ-cadinol"⁴ and "sesquigoyol",^{5,6} occurring in some pines,⁴⁻⁶ have been shown to be identical with (+)-torreyol.

"Albicaulol" from *Pinus albicaulis* Engelm.⁷ is identical^{3,6} with (-)-torreyol. It has been isolated from other pine species,⁸⁻¹⁰ as well as from many other conifers^{11,17} and it has been described under various synonyms, such as "pilgerol"¹² and "δ-cadinol".¹³ It also occurs in an angiosperm, *Cedrela odorata*, Meliaceae ("cedrelanol")¹⁴ and in a cryptogam, the alga *Dictyopteris divaricata* (Phaeophyta) ("brown alga cadinol").¹⁵ Lambertol from *Pinus lambertiana* Dougl. is probably either (+)- or (-)-torreyol.⁸

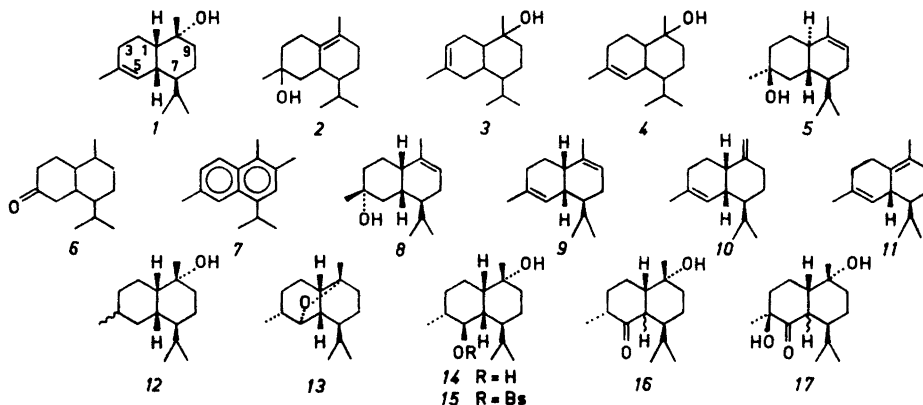
Of the many synonyms, the one most commonly used is δ-cadinol. This name ought to be avoided, however, as it refers to formula (2). In view of its priority, we prefer the use of the name torreyol.

Many different structures have been proposed for torreyol. In 1956 Erdtman *et al.*¹² proposed one of formulas (3), (4), or (5) to represent torreyol. Structure (2), "δ-cadinol", suggested in 1958 by Šorm *et al.*¹³ was excluded by the NMR, ORD, and chemical studies of Dauben *et al.* in 1961.¹⁷ According to the latter authors only structure (5) could account for their results. In 1964 Smolders presented evidence for the location of the double bond in torreyol shown in (5).¹⁴ This was based on quantitative bromination of a dihydronor-

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ketone presumed to have formula (6) as well as on the conversion of torreyol to what was reported to be 2-methylcadalene (7).



In a short communication¹⁸ the present author showed that torreyol was a muurolol (*cis*-fused rings) and that the hydroxyl and isopropyl groups were *trans* oriented. As there appeared to be no reason to doubt Smolders' evidence for the location of the double bond,* structure (8) was proposed. Recently, however, Smolders revised his previous statements and presented conclusive evidence for location of the double bond as in formula (1).²²

In this paper the full details are presented of the work leading to the assignment of the structure and absolute configuration shown in formula (1) to torreyol. The location of the double bond indicated in this formula which is based on the convincing evidence presented by Smolders,²² is confirmed by some of the results which will be described below.

On treatment with hydrogen chloride at -15° torreyol gave a mixture (ratio *ca.* 6:1), as shown by IR spectroscopy,²¹ of cadinene dihydrochloride and muurolene dihydrochloride indicating *cis* ring junction in the alcohol. Previously, (*e.g.* Refs. 12, 13) as in the case of ϵ -muurolene, the formation of muurolene dihydrochloride had been overlooked. Under the same conditions γ -cadinene and α -cadinol (*trans* ring junction) do not give any detectable amount of muurolene dihydrochloride. Torreyol was proved to be a muurolol (a 1-epicadinol) as follows.

Dehydration of torreyol by heating with *p*-bromobenzenesulphonyl (brosyl) chloride in pyridine gave a mixture of α -muurolene (9), γ -muurolene (10),** and δ -cadinene (11) in the approximate ratio 70: 20: 10. The formation of these hydrocarbons on dehydration of torreyol not only proves that the

* The methyl labelling technique for location of double bonds in cadalene type sesquiterpenes has been utilised successfully in a large number of cases (*cf. e.g.* Refs. 13, 19-21).

** In the preliminary experiments this component was not isolated and it was referred to as "unidentified". At that time the double bond and hydroxyl group of torreyol were thought to be located as shown in formula (8), and hence the alcohol was not anticipated to yield γ -muurolene under the conditions used.

alcohol is a muurolol. The result also confirms that the double bond in torreyol is located between C-4 and C-5 and that the hydroxyl group is attached to C-10.

Contradictory conclusions have been drawn concerning the spatial orientation of the hydroxyl group in torreyol. Smolders considered this group to be equatorial as the major dehydration product (thionyl chloride-pyridine) of dihydrotorreyol (12) had an exocyclic double bond.¹⁴ On the other hand torreyol has been found to be esterified at a comparatively low rate, indicating an axially oriented hydroxyl group.^{13,17} The alcohol has now been converted into the cyclic ether (13), using a reaction sequence which proves that the hydroxyl group is oriented as shown in formula (1). This transformation also confirms the *cis* ring junction in torreyol.

For the conversion of torreyol into the ether (13) it was planned to prepare a monoester of the previously known diol (14) obtained from torreyol by hydration *via* hydroboration.¹⁷ The secondary hydroxyl group of this diol, which has been introduced from the less hindered side of the molecule, would be esterified preferentially. Base treatment of a monoester derived from torreyol in this manner would give either a cyclic ether, hydroxy olefins, or a mixture thereof. Formation of a cyclic ether would only be possible if the tertiary hydroxyl group is on the concave side of the molecule.

When the diol (14) was treated with brosyl chloride in pyridine at room temperature the ether (13) was obtained in high yield. The *trans* relationship between the hydroxyl groups in the diol (14) explains the great ease of formation of the ether (13), presumably *via* the hydroxyester (15).

Being a *cis*-decalin derivative torreyol is conformationally mobile. Even the minor structural change in going from torreyol to dihydrotorreyol may cause a conformational change. Furthermore, the proportions of the various possible conformations may be temperature dependent. Therefore, it is not surprising that dehydration of dihydrotorreyol at 0° predominantly gives an olefin with an exocyclic double bond¹⁴ but torreyol at 120° gives a mixture of olefins in which compounds with endocyclic double bonds predominate (this work).

The Cotton effect curves of two ketones derived from torreyol were found by Dauben *et al.*¹⁷ to favour structure (5) for the alcohol. These ketones should now be represented by formulas (16) and (17). As these ketones are epimerizable at C-6, their configuration at this centre is in doubt. Consequently, a meaningful interpretation of the ORD data is not possible.

The absolute configurations of (+)- and (-)-torreyol follow from their correlation with (+)- and (-)-cadinene dihydrochloride, respectively, which are of known²³ absolute configuration. Formula (1) represents the absolute configuration of (-)-torreyol.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer No. 237 grating instrument (sample as liquid film). For analytical gas-liquid chromatography (GLC) a PYE argon chromatograph (column length 1.2 m, inner diameter 4 mm, 1% Reoplex 470 on Chromosorb W, 80–100 mesh), and for preparative GLC an Aerograph A-700 "Autoprep" (column length 20', outer diameter 3/8", 1% SE 30 on Chromosorb W, 60–80 mesh) were used.

Rotations were taken in chloroform. Light petroleum refers to the fraction b.p. 40–60°.

Hydrochlorination of torreyol. A solution of the alcohol (30 mg) in dry ether (0.3 ml) was saturated with dry hydrogen chloride at –18° and then left in the refrigerator for 15 h. The solvent and excess hydrogen chloride were evaporated off at room temperature under reduced pressure. The residue was crystallised once from a small amount of light petroleum. The crystalline product obtained was a mixture, as shown by its IR spectrum,²¹ of cadinene dihydrochloride and muurolene dihydrochloride (ratio ca. 6:1).

Dehydration of torreyol. A solution of torreyol (80 mg) and brosyl chloride (90 mg) in pyridine (2 ml) was refluxed for 4 h. After cooling the reaction mixture was added to an alumina column (basic, 60 g). Light petroleum (150 ml) eluted a mixture of hydrocarbons (34 mg), and methanol (2%) in ether (150 ml) eluted torreyol (27 mg). According to GLC and thin layer chromatography (TLC) using silver nitrate-silica gel, the hydrocarbon mixture consisted of α -muurolene, γ -muurolene, and δ -cadinene (ratio 70:20:10). The three hydrocarbons isolated by preparative GLC had $[\alpha]_D -91^\circ$ (c 0.3), -3° (c 0.1), and $+89^\circ$ (c 0.1), respectively. Their IR spectra were identical with those of authentic specimens of α -muurolene, γ -muurolene, and δ -cadinene.¹⁰

Hydroboration of torreyol. Torreyol (220 mg) was hydroborated as described by Dauben *et al.*¹⁷ Chromatography on silica gel (eluent ether-hexane 1:1) gave the diol (*14*) (95 mg) m.p. 127°. This diol (90 mg) in pyridine (2 ml) was treated with brosyl chloride (100 mg) at room temperature for 4 h. Without removal of the solvent the reaction mixture was chromatographed on silica gel (60 g, eluent 5% ether in hexane). After 120 ml had been collected the next portion of solvent (180 ml) eluted the cyclic ether (*13*) (59 mg, pure according to TLC and GLC), $[\alpha]_D^{25} +43^\circ$ (c 1.2), ν_{\max} 979 and 952 cm^{-1} . (Found: C 81.0; H 11.7. $\text{C}_{15}\text{H}_{26}\text{O}$ requires C 81.0; H 11.8). MW 222 (mass spec.).

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