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STRUCTURE OF THE TRITERPENOID ALCOHOL TREMATOL

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INTRODUCTION

The isolation of two isomeric $\Delta^{9(11)}$ pentacyclic triterpenoid alcohols, which were quite difficult to separate from each other, from the stem-bark of the plant *Trema orientalis* was first reported by Ogunkoya *et al.* [1]. In a subsequent communication [2], one of these alcohols was more fully characterized and named trematol. Trematol mp 215–216°, $[\alpha]_D$ −27.8° forms an acetate mp 224–246°, $[\alpha]_D$ −9.1°, a ketone mp 219–220°, $[\alpha]_D$ −55.4° and a ketone-DNP mp 275°. On the basis of available physico-chemical evidence, the authors proposed [2] for trematol a partial structure consisting of a migrated hopane skeleton with a 3β-hydroxyl group and slight structural modifications in rings D and E.

RESULTS AND DISCUSSION

We now provide evidence to show that trematol must be the C-21 epimer of fernenol, and also that the other isomeric alcohol isolated with trematol is fernenol. Positive identification of fernenol has been delayed as a result of inconsistent physical data recorded on the compound in the literature [3]. Identification has now been possible by a careful direct comparison of the MS and IR spectra with those of authentic [4] samples of fernenol.

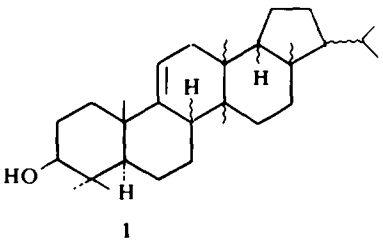
The two most probable partial structures earlier proposed for trematol may be combined to structure (**1**) in which the relative configurations at C-3, C-5 and C-10 are settled. The β-configuration of the C-3 hydroxyl group is now confirmed by the significantly positive (+75)ΔM_1 value of trematol [5]. Thus the hydroxyl group must be β and equatorial. The outstanding problem yet to be resolved consists of determining the relative configurations at C-8, C-13, C-14, C-17, C-18 and C-21.

In the earlier communication [2], the basic molecular skeleton and the position of unsaturation of trematol were determined partly from its NMR and mainly by comparing the MS of trematol, its derived acetate and ketone with the MS data recorded in the literature [3] for known $\Delta^{9(11)}$ and Δ^8 pentacyclic triterpenoids of the arborane and fernane skeletons. A further confirmation of the carbon skeleton has now been obtained from the 100 MHz NMR and high resolution MS of trematol. The NMR showed a total of eight methyl groups two of which were secondary. Furthermore, comparison of MS recorded on a compound with those reported in the literature may not be completely fool-proof, especially when slight structural differences are involved. This is because in the MS fragmentation pattern of a given molecule, the relative abundances of peaks depend very much on the operating conditions, especially temperature [6] and on whether the sample was introduced by direct inlet or heated inlet system [7]. Consequently, the MS of trematol, authentic [4] samples of fernenol, isoarborinol and an unresolved mixture (labelled 'FT') of fernenol and trematol from present work were run on the same machine under identical conditions. All the samples gave virtually an identical fragmentation pattern with significant differences only in the relative abundances of peaks at certain *m/e* values (see Table 1). The close similarity in the MS of compounds with these isomeric skeletons has also been observed [3, 7] for the methyl ethers of arborinol and fernenol. It is therefore difficult, if not impossible, to distinguish between the fernane and arborane isomeric skeletons with the aid of MS. However this MS analysis now firmly confirms the basic skeleton of trematol as a migrated hopane-type and also confirms the location of unsaturation at C-9(11), the possibility of a C-8 unsaturation having been ruled out earlier [2].

In all known [8] triterpenoid types, biogenetic considerations dictate an 'anti' relationship between the C-8 hydrogen and the C-14 hydrogen or methyl. Consequently, if the relative configuration at either of these positions is known, the other is implied. Similarly, in all known pentacylic triterpenoids with a migrated hopane skeleton, biogenetic considerations and a careful examination of Dreiding models dictate an 'anti' relationship between the C-13 methyl and the C-18 hydrogen and a *trans*-fusion of rings D and E also resulting in an 'anti' relationship between the C-17 methyl and the C-18 hydrogen for a thermodynamically favourable conformation [3, 8, 9]. Consequently, a knowledge of the relative configuration of C-13 methyl should most probably fix the relative configurations of the C-18 hydrogen and the C-17 methyl, leaving only the relative configuration of C-21 *iso*propyl group to be determined. There is however one known [10] case of *cis*-fusion of rings D and E in the compounds alangidiol

Table 1. Comparison of the mass spectra (relative abundance %) of selected 9(11) pentacyclic triterpenes

m/e	241	243	247	255	259	273	323	341	393	411	M^+
Fernenol (F)	34	14	10	13	100	16	3	4	23	94	38
Isoarborinol	27	12	10	13	73	22	6	12	21	100	61
Trematol (T)	33	18	10	16	86	17	2	2	17	100	35
'FT' mixture	33	16	10	14	100	15	2	2	20	100	37



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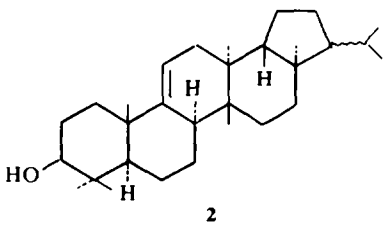

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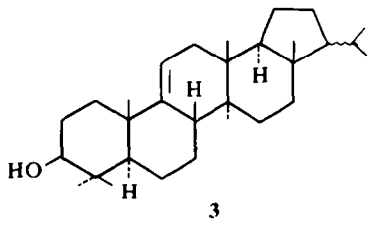

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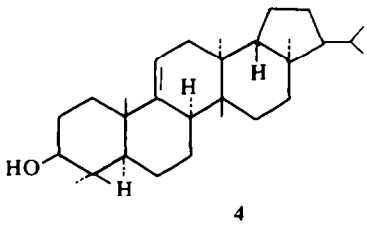

4

and isoalangidiol. In these two compounds, hydroxylation at C-18 must involve a biogenetic route somewhat different from normal resulting in structures in which the C-18 hydroxyl, unlike the C-17 methyl, group assumes an axial rather than the usual equatorial disposition.

In the light of the above considerations, the structure of trematol may be narrowed down to only two possibilities: fernane skeleton (**2**) and arborane skeleton (**3**). Attempts to assign one of these possibilities to trematol by the method of molecular rotation differences [5] were unsuccessful due to a scarcity of appropriate reference compounds with the euphane/fernane (unlike lanostane/arborane) skeletons in the literature. The oxidation [3] (monitored by TLC, IR and NMR), of a colourless well-crystalline unresolved mixture of trematol and fernenol, with perbenzoic acid followed by an acid-catalysed cleavage of the resulting epoxides and column chromatographic purification gave a colourless crystalline mixture of 7,9(11) heteroannular dienols which was also not resolvable chromatographically. The derived crystalline dienyl acetates were similarly unresolvable. However the UV spectrum of the unresolved acetates showed absorptions at λ_{max}^{Hexane} 232 (ε_{max} 13050), 239.5 (ε_{max} 14910) and 247.5 (ε_{max} 11 180) which are characteristic of 7,9(11)-dienes with 13α and 14β-methyl groups and 1(10),5-dienes [3]. Significantly, no absorption bands indicative of 13β and 14α-methyl groups of 7,9(11)-diene skeleton [11] were observed in the UV spectrum of either the dienol or the dienyl acetate. These UV data clearly indicate that each of the component dienes of the resolved mixture must have C-13α and C-14β-methyl groups.

Following the biogenetic arguments earlier advanced, the skeleton of trematol is almost certainly of the fernane type and presumably differs from that of fernenol only in the relative configuration of the C-21 *iso*-propyl group. Trematol may thus be formulated as the C-21 epimer of fernenol. This structure **4** represents the first known example of a migrated hopane structure in which the C-17 methyl and the C-21 *iso*-propyl groups are *trans*.

EXPERIMENTAL

NMR spectra were run in $CDCl_3$ with TMS as internal standard. MS were run on a Vacuum Generators 7070F spectrometer operating at 70 eV by the direct inlet system at 180° calibrated against perfluorokersone. Optical rotations were determined in $CHCl_3$ at room temp. TLC was carried out on Si gel Merk Type 60 and visualized in I_2 vapour while CC was carried out on neutral alumina Fluka Type 507c. The conversions of $\Delta^{9(11)}$ into $\Delta^{7,9(11)}$-dienes were carried out according to the procedure of ref. [3].

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