The *X*-Ray Crystal Structure and Absolute Configuration of Maytenol,† A Reduction Product of the Bis-diterpene Maytenone †

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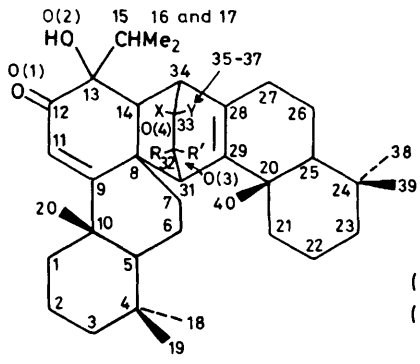
The *X*-ray crystal structure of the bis-diterpene derivative maytenol has been determined. The structure confirms the gross structure previously proposed for maytenone, and in addition the complete absolute configuration of these molecules is now firmly established. Thus maytenone (10) is the *endo* Diels–Alder dimer of (13αH)-13-hydroxyabieta-8(14),9(11)-dien-12-one (10).

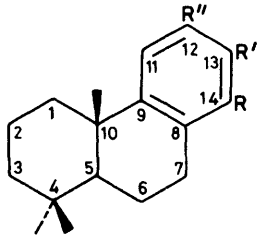
The bis-diterpene maytenone was isolated [1,2] some twenty years ago, together with the pigment pristimerin,[1] from the outer root bark of the tree *Maytenus dispermus*. The constitution (1) for maytenone was established [2] as a result of elucidation of the mechanism of the remarkable thermal fragmentation reaction which maytenone undergoes upon melting. At this temperature (197 °C) maytenone decomposes smoothly to give one molecular proportion of each of the diterpene-related catechols 14-isopropylpodocarpa-8,11,13-triene-12,13-diol (3) and podocarpa-8,11,13-triene-12,13-diol (4) together with propene gas. The structure and indicated absolute stereochemistry of each of these catechols was established by synthesis, thus the C_{20}-catechol (3) was obtained [3] from totarol (5) while podocarpic acid furnished [4] the C_{17} catechol (4).

Attempts to prove the constitution (1) for maytenone based on the oxidation [5] of ferruginol (6) to a hydroxycyclohexa-2,4-dienone and subsequent Diels–Alder dimerisation were unsuccessful. However, model compounds, for example (7), were prepared [5,6] by oxidation of the appropriate phenols with sodium metaperiodate.[7] Qualitatively the model compounds behaved in a similar manner to maytenone on thermolysis, but these reactions did not give (molecular) quantitative proportions of products.[5,6]

While the constitution (1) for maytenone adequately represented the gross structure, the stereochemistry of the central ethano-bridged tetrahydronaphthalene nucleus remained unsettled, as did the stereochemistry of the tertiary alcoholic centres. In view of this we sought to determine the fine stereochemical details of maytenone by *X*-ray crystallography. Unfortunately a sample of maytenone was not available; however, a suitable crystalline specimen of the reduction product maytenol (2) was available from the original study.[2] Maytenol (2) is readily prepared from maytenone by reduction with lithium aluminium hydride in diethyl ether solution, and oxidation of maytenol with chromic acid regenerated maytenone in high yield. Spectroscopy [2] showed that the formation of maytenol involved reduction of just the α,β-saturated ketone.

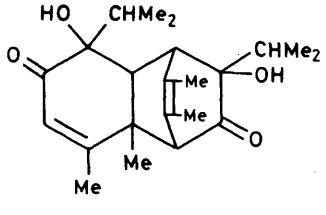


X = OH, Y = CHMe$_2$
(1) R R' = O
(2) R = H, R' = OH



(3) R = CHMe$_2$, R' = R'' = OH
(4) R = H, R' = R'' = OH
(5) R = CHMe$_2$, R' = OH, R'' = H
(6) R = H, R' = CHMe$_2$, R'' = OH

Crystallographic numbering scheme given for compounds (1) and (3). Podocarpane numbering scheme given for compounds (3)—(6)



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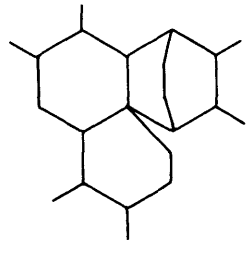


(8)

X-Ray Structure Determination.—Single-crystal *X*-ray diffraction data were collected using an Enraf-Nonius CAD4 diffractometer with Cu-K_α radiation, λ 1.5418 Å. Intensities were measured $0 < \theta < 66°$; 3 595 reflections were scanned and of these 2 621 had $I > 3\sigma(I)$ and were used in the refinement.

Crystal Data.—$C_{40}H_{62}O_4$, $M = 606.92$, orthorhombic, $a = 11.383(1)$, $b = 16.780(1)$, $c = 19.124(1)$ Å, $U = 3652.7$ Å^3, $D_c = 1.10$ g cm^{-3}, $Z = 4$, $\mu = 1.25$ cm^{-1}, space group $P2_12_12_1$.

The structure was solved, after some initial difficulty, using the direct methods MULTAN programme.[8] Using default values, MULTAN found the twenty-two-atom fragment (8)

† Maytenol is a 1,3,4,4a,6,7,7a,8,9,10a,10,11,12,13,14,14a,15,16,17,-17a-icosahydro-7,18,19-trihydroxy-7,19-di-isopropyl-1,1,4a,11,11,-14a-hexamethyl-8,15-ethano-2*H*-benzo[*a*]naphtho[1,2-*k*]anthracen-6-one and maytenone is the corresponding 7,19-dihydroxy-6,18-dione.

‡ Deceased 12th April, 1983.

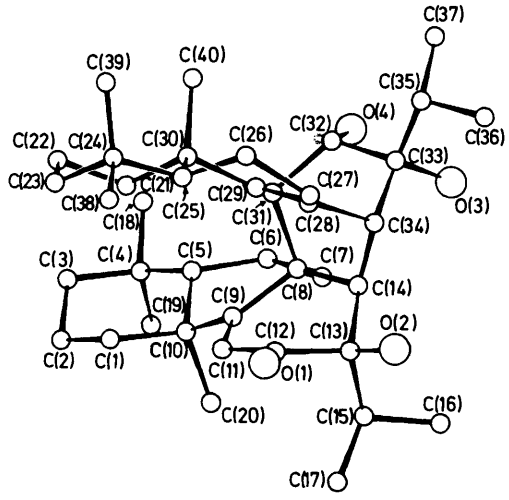


Figure 1. Molecular structure of maytenol (2) with crystallographic numbering scheme

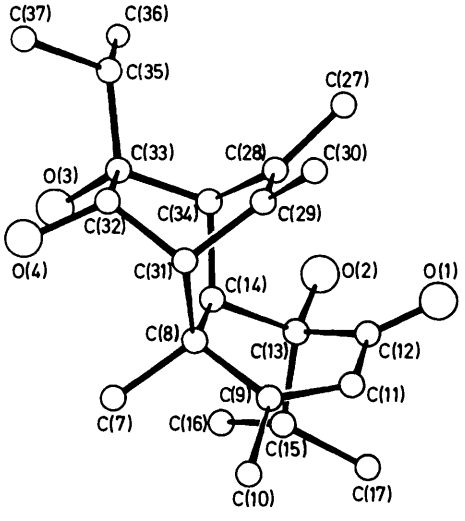


Figure 2. Alternative perspective view of the molecular structure of the central chromophore of maytenol (2), with peripheral atoms removed for clarity

the co-ordinates of whose atoms were then re-cycled whence all but three of the heavy atoms were located. The trial structure was refined using the CRYSTALS package, the missing atoms then being readily located by a Fourier synthesis. Further refinement by least-squares was then carried out using firstly isotropic and then anisotropic temperature factors, the structure being treated in two blocks. This process produced a convergent result with an *R*-value of 9.72%; all the hydrogen atoms were then located from a Fourier difference map. Hydroxy group hydrogen atoms were placed in their found positions but all the other hydrogens were located in their calculated positions. Further refinement was then carried out, hydrogen atoms not being refined, and the final *R*-value obtained was 5.41%.

Discussion

The molecular structure of maytenol is shown in Figure 1, while Figure 2 shows a view of the central chromophore of the molecule with many atoms removed for clarity. Final atomic co-ordinates, bond lengths, and bond angles are listed in Tables 1, 2, and 3, respectively. Observed and calculated structure factors and thermal parameters are listed in Supplementary Publication No. SUP 23644 (26 pp).* Comparison of Figure 1 with the structures of the two maytenone thermolysis products (3) and (4), the absolute configurations of which having already been established,[3,4] shows that Figure 1 represents the complete absolute configuration of maytenol. It follows that maytenone should now be represented by the stereostructure (9), and several important features regarding the biosynthesis of maytenone can now be discussed. First, oxidation of the precursor ferruginol (6) must occur at the less hindered α face to give the hydroxycyclohexadienone (10). Diels–Alder dimerisation of (10) then proceeds with union of the two α faces of the monomers according to the normal *endo* rule to give mayte-

Table 1. Refined fractional atomic co-ordinates ($\times 10^4$) with standard deviations in parentheses

Atom [a]	*x/a*	*y/b*	*z/c*
C(9)	7 965(7)	3 619(4)	2 376(3)
O(1)	9 602(6)	1 831(3)	2 133(3)
C(14)	9 481(7)	3 699(4)	1 328(3)
C(7)	7 939(6)	4 772(4)	1 563(3)
C(1)	6 620(8)	3 592(5)	3 447(4)
C(8)	8 761(7)	4 155(4)	1 908(3)
O(2)	10 080(6)	2 390(3)	891(3)
C(13)	9 180(8)	2 793(4)	1 254(4)
C(11)	8 256(8)	2 839(4)	2 449(4)
C(6)	7 249(7)	5 286(4)	2 080(4)
C(5)	6 966(6)	4 889(4)	2 795(4)
C(4)	6 009(7)	5 323(6)	3 222(4)
C(10)	6 848(7)	3 960(4)	2 706(4)
C(12)	9 080(8)	2 446(4)	1 988(4)
C(2)	5 655(7)	4 015(6)	3 846(5)
C(3)	5 884(8)	4 897(6)	3 937(4)
C(18)	6 432(8)	6 177(6)	3 367(5)
C(16)	8 100(10)	2 890(6)	95(4)
C(15)	7 982(9)	2 681(5)	870(4)
C(20)	5 817(8)	3 704(5)	2 216(4)
C(19)	4 809(8)	5 379(6)	2 870(5)
C(17)	7 490(10)	1 839(6)	946(5)
C(31)	9 728(6)	4 560(3)	2 406(3)
C(33)	11 122(7)	4 722(4)	1 355(3)
C(29)	10 587(6)	3 932(3)	2 671(3)
O(4)	9 949(4)	5 857(2)	1 753(2)
C(28)	11 162(7)	3 563(4)	2 161(3)
O(3)	10 650(5)	5 006(3)	713(2)
C(32)	10 531(6)	5 148(4)	1 994(3)
C(34)	10 802(7)	3 822(4)	1 423(3)
C(25)	11 525(6)	3 022(4)	3 534(3)
C(30)	10 901(6)	3 845(4)	3 456(3)
C(21)	9 804(6)	3 854(4)	3 918(3)
C(37)	12 763(8)	5 754(5)	1 375(4)
C(40)	11 669(7)	4 582(4)	3 641(4)
C(35)	12 459(7)	4 864(4)	1 364(4)
C(27)	12 126(7)	2 956(4)	2 268(3)
C(24)	11 801(6)	2 752(4)	4 301(3)
C(22)	10 112(7)	3 665(5)	4 687(3)
C(26)	12 555(6)	2 946(4)	3 028(3)
C(36)	13 076(8)	4 465(5)	747(4)
C(38)	12 097(8)	1 849(4)	4 291(4)
C(23)	10 687(7)	2 858(5)	4 744(4)
C(39)	12 853(6)	3 179(5)	4 629(4)

[a] Crystallographic numbering scheme used in Tables 1—3.

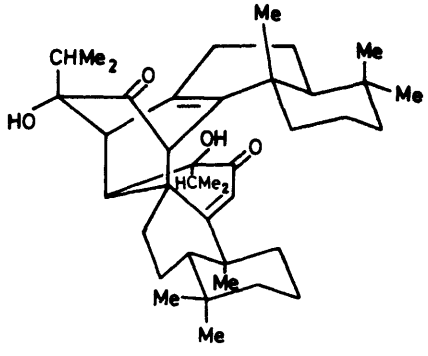
* For details of the Supplementary Publications scheme, see Instructions for Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

Table 2. Bond lengths (Å) with standard deviations in parentheses

C(1)–C(2)	1.51(1)	C(8)–C(31)	1.61(1)	C(14)–C(34)	1.53(1)	C(29)–C(30)	1.55(1)
C(1)–C(10)	1.57(1)	C(9)–C(11)	1.36(1)	C(21)–C(22)	1.55(1)	C(30)–C(40)	1.56(1)
C(2)–C(3)	1.51(1)	C(9)–C(10)	1.53(1)	C(21)–C(30)	1.53(1)	C(29)–C(31)	1.52(1)
C(3)–C(4)	1.55(1)	C(10)–C(20)	1.56(1)	C(22)–C(23)	1.51(1)	C(31)–C(32)	1.56(1)
C(4)–C(5)	1.54(1)	C(11)–C(12)	1.45(1)	C(23)–C(24)	1.54(1)	C(32)–O(4)	1.44(1)
C(4)–C(18)	1.54(1)	C(12)–O(1)	1.22(1)	C(24)–C(25)	1.57(1)	C(32)–C(33)	1.57(1)
C(4)–C(19)	1.53(1)	C(12)–C(13)	1.52(1)	C(24)–C(38)	1.55(1)	C(33)–O(3)	1.42(1)
C(5)–C(6)	1.56(1)	C(13)–O(2)	1.41(1)	C(24)–C(39)	1.53(1)	C(33)–C(35)	1.54(1)
C(5)–C(10)	1.57(1)	C(13)–C(15)	1.56(1)	C(25)–C(26)	1.53(1)	C(33)–C(34)	1.56(1)
C(6)–C(7)	1.53(1)	C(13)–C(14)	1.56(1)	C(25)–C(30)	1.56(1)	C(35)–C(37)	1.53(1)
C(7)–C(8)	1.55(1)	C(15)–C(16)	1.52(1)	C(26)–C(27)	1.53(1)	C(35)–C(36)	1.53(1)
C(8)–C(9)	1.56(1)	C(15)–C(17)	1.53(1)	C(27)–C(28)	1.51(1)	C(34)–C(28)	1.53(1)
C(8)–C(14)	1.58(1)			C(28)–C(29)	1.33(1)		

Table 3. Bond angles (°) with standard deviations in parentheses

C(10)–C(1)–C(2)	112.9(7)	C(9)–C(10)–C(20)	105.8(6)	C(12)–C(13)–O(2)	108.9(7)	C(24)–C(25)–C(30)	115.9(5)
C(1)–C(2)–C(3)	113.1(7)	C(9)–C(10)–C(1)	111.3(6)	C(12)–C(13)–C(15)	108.8(7)	C(24)–C(25)–C(26)	114.6(6)
C(2)–C(3)–C(4)	111.5(8)	C(9)–C(10)–C(5)	110.1(6)	C(12)–C(13)–C(14)	107.7(6)	C(26)–C(25)–C(30)	111.3(5)
C(3)–C(4)–C(5)	108.3(8)	C(1)–C(10)–C(5)	107.9(6)	O(2)–C(13)–C(14)	110.5(7)	C(25)–C(26)–C(27)	110.9(6)
C(3)–C(4)–C(19)	109.6(7)	C(1)–C(10)–C(20)	108.0(6)	O(2)–C(13)–C(15)	110.3(6)	C(26)–C(27)–C(28)	111.5(6)
C(3)–C(4)–C(18)	107.4(7)	C(20)–C(10)–C(5)	113.7(6)	C(15)–C(13)–C(14)	110.6(7)	C(27)–C(28)–C(29)	125.0(6)
C(18)–C(4)–C(19)	107.6(8)	C(9)–C(11)–C(12)	122.3(7)	C(13)–C(14)–C(34)	111.0(6)	C(27)–C(28)–C(34)	120.6(6)
C(18)–C(4)–C(5)	108.3(7)	C(11)–C(12)–O(1)	124.1(7)	C(13)–C(14)–C(8)	114.9(6)	C(34)–C(28)–C(29)	114.4(6)
C(19)–C(4)–C(5)	115.3(7)	C(11)–C(12)–C(13)	115.9(7)	C(8)–C(14)–C(34)	111.2(5)	C(28)–C(29)–C(30)	123.6(6)
C(4)–C(5)–C(6)	114.2(6)	O(1)–C(12)–C(13)	119.7(8)	C(14)–C(34)–C(28)	109.5(5)	C(28)–C(29)–C(31)	113.3(5)
C(4)–C(5)–C(10)	117.6(7)	C(30)–C(29)–C(31)	122.4(5)	C(14)–C(34)–C(33)	110.5(6)	C(31)–C(32)–C(33)	110.9(5)
C(6)–C(5)–C(10)	110.4(6)	C(29)–C(30)–C(21)	111.7(5)	C(33)–C(34)–C(28)	106.8(5)	O(3)–C(32)–C(33)	109.0(5)
C(5)–C(6)–C(7)	115.7(6)	C(29)–C(30)–C(25)	106.4(5)	C(30)–C(21)–C(22)	111.2(6)	C(32)–C(33)–O(4)	111.0(5)
C(6)–C(7)–C(8)	114.4(5)	C(29)–C(30)–C(40)	105.9(5)	C(21)–C(22)–C(23)	110.6(6)	C(32)–C(33)–C(34)	106.1(5)
C(7)–C(8)–C(31)	112.6(5)	C(40)–C(30)–C(21)	108.6(6)	C(22)–C(23)–C(24)	115.9(6)	C(32)–C(33)–C(35)	110.2(6)
C(7)–C(8)–C(14)	109.9(5)	C(40)–C(30)–C(25)	115.3(5)	C(23)–C(24)–C(38)	107.4(6)	O(4)–C(33)–C(34)	107.9(5)
C(7)–C(8)–C(9)	106.3(6)	C(21)–C(30)–C(25)	109.0(5)	C(23)–C(24)–C(39)	111.5(6)	O(4)–C(33)–C(35)	109.3(6)
C(14)–C(8)–C(9)	115.2(5)	C(29)–C(31)–C(32)	103.2(5)	C(23)–C(24)–C(25)	108.6(6)	C(35)–C(33)–C(34)	112.3(6)
C(31)–C(8)–C(9)	107.6(5)	C(29)–C(31)–C(8)	110.1(5)	C(38)–C(24)–C(39)	106.9(6)	C(33)–C(35)–C(36)	111.9(7)
C(8)–C(9)–C(10)	120.3(6)	C(32)–C(31)–C(8)	111.8(5)	C(38)–C(24)–C(25)	108.3(6)	C(33)–C(35)–C(37)	112.2(7)
C(8)–C(9)–C(11)	118.3(7)	C(31)–C(32)–O(3)	114.5(5)	C(39)–C(24)–C(25)	113.9(6)	C(36)–C(35)–C(37)	109.5(6)
C(17)–C(15)–C(16)	109.4(6)	C(16)–C(15)–C(13)	110.7(5)	C(16)–C(15)–C(13)	112.7(7)		



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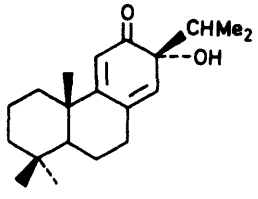

(10)

none. This mode of dimerisation has the important consequence that the hydroxy functions are directed towards both one another and the 'inside' of the molecule. The structures of several simple dimeric cyclohexa-2,4-dienones have been determined previously [9,10] by *X*-ray diffraction. Where these dimers involve hydroxycyclohexa-2,4-dienones [9] the stereochemistry at the tertiary alcoholic centres is the same as that now found in maytenol. These dimers show a lengthening of the bonds corresponding to C(8)–C(31) and C(8)–C(14) * in maytenol, maximum values found [9] for these bonds being 1.589(3) and 1.567(3) Å, respectively. The increased length of the C(8)–C(31) * bond in maytenol, 1.61(1) Å, must reflect the added internal strain due to the additional alicyclic rings substituent upon the central nucleus.

Comparing Figure 1 and the stereostructure (9) of maytenone, it can be seen that the maytenone ⟶ maytenol reduction involves attack of the reagent from the α face of the α,β-saturated ketone. Inspection of a model of maytenone shows that the alternative β face is more hindered by the CH_2 group at C(7).*

* Crystallographic numbering.

Acknowledgements

We thank Professor A. W. Johnson for a sample of maytenol and one of us (C. P. F.) thanks the University of Sheffield Research Fund for financial support.

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Received 13*th December* 1982; *Paper* 2/2071