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THE ABSOLUTE CONFIGURATION OF CYCLOEUDESMOL FROM THE RED ALGA *LAURENCIA NIPPONICA* YAMADA[1)]

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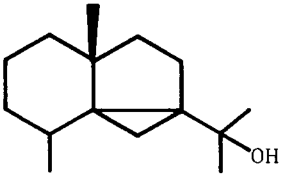
Summary: The absolute configuration of cycloeudesmol, isolated from the red alga *Laurencia nipponica* Yamada and *Chondria oppositiclada* Dawson, is determined by the crystallographic study.

In our previous report[2)], the structure of isocycloeudesmol, $C_{15}H_{26}O$, isolated from *L. nipponica* Yamada, has been proposed as the formula 1 by the spectral and chemical evidences. On the other hand, cycloeudesmol, $C_{15}H_{26}O$, was isolated from the red alga *C. oppositiclada* Dawson by Fenical and Sims[3)] and its structure was proposed as shown in the formula 2 and the syntheses of four possible stereoisomers of 2 have been attempted in three laboratories[4)]. Recently, the total syntheses of the stereoisomers of 2 have been completed and they were found to be different from the natural cycloeudesmol and it was concluded that the structure (2) of cycloeudesmol, proposed by Fenical and Sims, should be revised[4b)]. Meanwhile, the cautious comparison of IR and ^1H NMR spectra and the optical rotation[5)] came to the conclusion that isocyclo-



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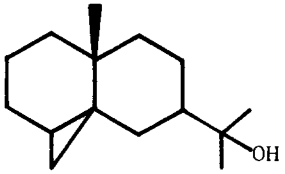

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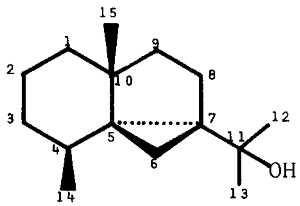
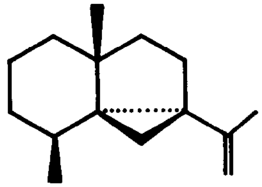


3

eudesmol (1) was identical with cycloeudesmol[6)]. Herein we wish to report the absolute stereostructure (3) of cycloeudesmol by the X-ray crystallographic study.



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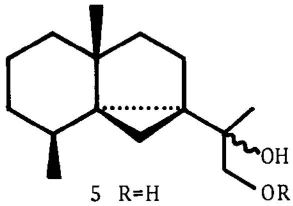
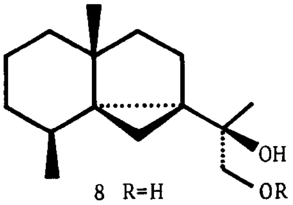


5 R=H

6 R=Ts

7 R=Bz



8 R=H

9 R=Ac

In spite of the repeated measurements, the crystals of cycloeudesmol (3) were not satisfactory for X-ray crystallographic study because of its easily volatile nature on the measuring conditions. And thus, the preparation of the derivative from 3 was required without skeletal conversion for this study. Treatment of 3 with $SOCl_2$-Py in CH_2Cl_2 at 0°C for 20 h resulted in nearly quantitative dehydration to cycloeudesmene (4)[3)]; colorless oil, $[\alpha]_D$ +23.6° (c; 1.0, $CHCl_3$), $C_{15}H_{24}$ *m/e* 204 (M^+); ν_{max}^{film} 3080, 3050, 1640 and 885 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.39 (1H, dd, J=5, 1 Hz), 0.61 (1H, d, J=5), 1.03 (3H, d, J=7), 1.04 (3H, s), 1.1-2.2 (11H), 1.87 (3H, br. d, J=1), 4.67 (1H, d, J=2) and 4.85 (1H, dq, J=2, 1). OsO_4 oxidation of 4 in Py gave glycol (5), which was the inseparable epimeric mixture on TLC. Tosylation of this mixture (5) and successive reduction of the resulting monotosylate (6) with LAH regenerated cycloeudesmol (3) and thus, it was clarified that the skeletal conversion did not occur during the above dehydration and oxidation reactions. Separation of the inseparable mixture of glycol (5) has been achieved by benzoylation of 5 and successive separation of the resulting monobenzoate (7) on TLC (silica gel). Less polar monobenzoate of 7 on TLC (70% of the mixture) was hydrolyzed with K_2CO_3 in MeOH to glycol (8) and successive treatment of 8 with Ac_2O in Py gave monoacetate (9); mp, 102-103°C (hexane-isopropyl ether), $[\alpha]_D$ -5.6° (c; 1.3, $CHCl_3$), $C_{17}H_{28}O_3$ *m/e* 280 (M^+), ν_{max}^{nujol} 3480, 1715, 1268, 1165, 1030, 1020 and 942 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.48 (1H, d, J=5 Hz), 0.64 (1H, d, J=5), 1.03 (3H, s), 1.06 (3H, d, J=7), ca. 1.1-2.3 (12H), 1.30 (3H, s), 2.11 (3H, s), 4.13 (1H, d, J=12) and 4.39 (1H, d, J=12), which was submitted to the X-ray crystallographic study.

The crystal data for 9 were as follows: $C_{17}H_{28}O_3$, orthorhombic, space group $P2_12_12_1$, $a = 12.228(4)$, $b = 18.095(8)$, $c = 7.246(7)$ Å, $Z = 4$, $D_c = 1.162$ g cm^{-3}. 1536 unique intensity data for $2\theta < 128°$ were collected on an automatic, four-circle diffractometer with graphite-monochromated CuKα radiation. The structure was elucidated by the Monte Carlo direct method[7)], using the 20 strongest reflections as the starting set. The 39th random phase set led to the correct solution; an E-map calculated with 357 phases revealed the locations of all the non-hydrogen atoms. The structure obtained was refined by the block-diagonal least-squares method with anisotropic temperature factors. After all the hydrogen atoms, except those of the acetyl group, had been located in a difference Fourier map, a further least-squares refinement was repeated including the hydrogen atoms with isotropic temperature factors. The final R value was 0.048. The absolute configuration was determined by using the anomalous dispersion of oxygen and carbon atoms for CuKα radiation[8)]. For the application of the Bijvoet method[9)], 15 sets of hkl, $\bar{h}\bar{k}l$, $\bar{h}kl$, and $h\bar{k}l$ reflections with large values of $|\Delta F_c|/\bar{F}_c$ were selected. The results are summarized in Table 1. The signs of the corresponding ΔF_o and ΔF_c values are in

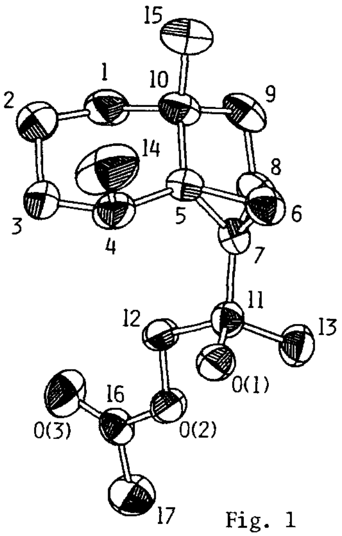


Fig. 1

Table 1. Bijvoet inequalities

h	k	l	$\bar{F}_o$[a)]	$\bar{F}_c$[a)]	ΔF_o[b)]	ΔF_c[b)]	h	k	l	$\bar{F}_o$	$\bar{F}_c$	ΔF_o	ΔF_c
5	8	2	4.23	4.30	-0.20(6)	-0.10	2	5	4	9.21	9.24	-0.09(6)	-0.11
3	4	7	5.05	5.52	0.18(6)	0.10	3	5	2	10.82	11.57	0.26(5)	0.14
9	5	5	5.15	5.20	0.16(6)	0.08	2	4	1	11.51	9.77	0.22(2)	0.12
2	10	1	7.51	7.14	0.13(4)	0.09	1	6	3	6.81	6.69	0.06(5)	0.08
6	5	3	5.50	5.14	-0.04(2)	-0.07	4	7	2	11.68	11.70	-0.06(2)	-0.14
10	3	4	5.23	5.63	-0.10(7)	-0.07	11	7	2	5.16	5.51	-0.07(4)	-0.06
7	1	1	5.03	4.83	0.08(5)	0.06	8	9	1	5.16	5.80	0.13(4)	0.06
7	10	4	5.73	5.74	-0.09(6)	-0.07							

a) $\bar{F} = \{|F(hkl)|+|F(\bar{h}\bar{k}l)|+|F(\bar{h}kl)|+|F(h\bar{k}l)|\}/4$

b) $\Delta F = \{|F(hkl)|+|F(\bar{h}\bar{k}l)|-|F(\bar{h}kl)|-|F(h\bar{k}l)|\}/2$

agreement with each other for all the 15 sets of reflections; this indicates that the actual absolute configuration corresponds to that shown in Fig. 1. Thus, the complete structure of 9 including the absolute configuration has been established as shown in the formula 9 and consequently, the structure of cycloeudesmol including the absolute configuration should be represented as the formula 3$^{10)}$.

References and Notes

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5) The optical rotation of isocycloeudesmol, given as $[\alpha]_D$ +21.5° (c; 2.10, $CHCl_3$) in ref. 2), was corrected to $[\alpha]_D$ -32.3° (c; 1.67, $CHCl_3$), T. Suzuki, H. Kikuchi, and E. Kurosawa, *Chem. Lett.*, 1981, 441.

6) Our compound, isolated from *L. nipponica*, showed the presence of three tertiary methyls and one secondary methyl in ^{1}H NMR spectrum (100 MHz)$^{2)}$. On the other hand, Fenical and Sims reported$^{3)}$ that cycloeudesmol, isolated from *C. oppositiclada*, exhibited the presence of three methyl singlets, missing the recognition of a secondary methyl group at C-4 in ^{1}H NMR spectrum (220 MHz). From the above NMR spectral data, our compound was obviously found to be different from cycloeudesmol and so, previously designated as isocycloeudesmol. Dr. W. Fenical also clearly saw that isocycloeudesmol and cycloeudesmol were identical from a comparison of both spectral data; private communication.

7) A. Furusaki, *Acta Crystallogr.*, A35, 220 (1979).

8) International Tables for X-ray Crystallography, Vol. IV, p. 149, The Kynoch Press, Birmingham, England (1974).

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10) The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratories, Lensfield Road, Cambridge CB2 1EW.

(Structure factors have been deposited with the British Library at Boston Spa,

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