BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 2920—2921 (1973)

Stereostructure of Zonarene

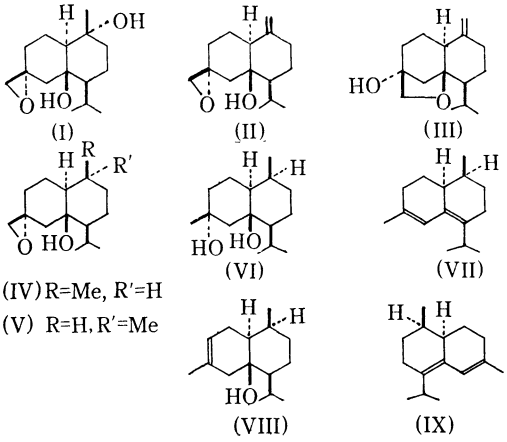
Masanobu IGUCHI, Masatake NIWA, and Shosuke YAMAMURA*

Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya 468

(Received May 1, 1973)

Zonarene, a cadinane-type sesquiterpene, has been isolated from the brown seaweed (*Dictyopteris zonarioides*), and the structure of this hydrocarbon also been established by Fenical and his co-workers except for its stereostructure.[1] In the present paper, we wish to describe the stereostructure of zonarene including the absolute configuration by means of chemical transformation from preisocalamendiol, which has been synthesized from *l*-santonin,[2] to (+)-zonarene.

As described in the previous papers,[3,4] the epoxy-diol (I) was obtained from isocalamendiol, an acid-catalyzed cyclization product of preisocalamendiol, the absolute configuration of which had been already established. Further treatment of I with $POCl_3$–pyridine afforded the known dehydration product (II)[4] and a hydroxy-olefin (III)[5] in 40 and 27% yields, respectively. The structure of the latter was confirmed by its spectral data, in particular by the NMR signal at δ 3.46 ppm (2H, s) assigned to two protons attached to the carbon atom bearing the ether-oxygen atom. Catalytic hydrogenation of II on PtO_2 in AcOEt (room temp., 1.5 hr) afforded a mixture of two dihydro-compounds [IV (mp 69—70 °C) and V (mp 77—80 °C) in 82 and 6% yields, respectively]. On the basis of the comparison of the NMR spectra between IV and V, the newly formed secondary methyl group in the main product (IV) must be in an axial configuration (δ 1.05 ppm), whereas the corresponding methyl group in the latter is in an equatorial configuration (δ 0.85 or 0.87 ppm).[6] When treated with $LiAlH_4$ in ether (room temp., 2 hr), IV was converted into the corresponding diol (VI, mp 104—105 °C) in 92% yield. Finally, action of $POCl_3$–pyridine (room temp., overnight, and then 40 °C, 2 hr) on VI converted it to a mixture of two dehydration products (VII and VIII in 30 and 38% yields, respectively). The former was completely identical with an authentic sample of zonarene (glc and IR spectrum) except for the sign of the optical rotation cited in the literature.[1] The structure of the latter was characterized by its physical data [ν_{max}(film) 3550 cm^{-1}; $\delta(CCl_4)$ 1.63 (3H, br.s) and 5.48 ppm (1H, br.s)]. In conclusion, the stereostructure of zonarene including the absolute configuration should be represented by IX. Recently, the same result has also been obtained by Andersen and his co-workers.[7]



Experimental

All the melting-points are uncorrected. The IR spectra were recorded on a Hitachi-215 spectrophotometer. The NMR spectra were taken on Varian A-60 and Nihondenshi JNM-60H (60 MHz) spectrometers, using $CDCl_3$ as the solvent, unless otherwise stated. Only prominent peaks are cited. The chemical shifts are given in ppm relative to the internal TMS. The coupling constants are given in Hz (s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet). The mass spectra were obtained on a Hitachi RMU-6D mass spectrometer operating with an ionization energy of 70 eV. Optical rotation was measured on a JASCO ORD/UV-5 spectrometer using MeOH as a solvent.

Dehydration of the Epoxy-diol (I). According to essentially the same condition as previously reported,[4] dehydration of the epoxy-diol (560 mg) in pyridine (10 ml) with $POCl_3$ (2 ml) in pyridine (4 ml) was carried out to give a pale brown oil (500 mg), which was chromatographed on alumina (Katayama Co. Ltd., 150—250 mesh; 10 g) and eluted with *n*-hexane–ether (1:1) to give the known colorless liquid (208 mg) of II[4] as the first fraction. After elution of II, a colorless liquid (140 mg) of III was isolated; ν_{max}^{film} 3460 br., 3080, 1645, 900, and 885 cm^{-1}; δ 0.91 (3H, d, J=7.0 Hz), 0.94 (3H, d, J=7.0 Hz), 3.46 (2H, s), 4.80 (1H, br.s), and 4.98 ppm (1H, br.s). Found: *m/e* 236.1785. Calcd for $C_{15}H_{24}O_2$: *m/e* 236.1776.

Catalytic Hydrogenation of the Epoxy-olefin (II). Catalytic hydrogenation of the epoxy-olefin (220 mg) in AcOEt (5 ml) over PtO_2 (5 mg) was carried out at room temp. for 1.5 hr, and then filtered to remove the catalyst. The filtrate was concentrated under reduced pressure to give a colorless liquid (220 mg), from which two reduction products were separated by preparative tlc (neutral alumina (E. Merck,

* To whom inquires should be addressed.

1) W. Fenical, J. J. Sims, R. M. Wing and P. C. Radlick, *Phytochemistry*, **11**, 1161 (1972).

2) K. Kato, Y. Hirata, and S. Yamamura, *Tetrahedron*, **27**, 5987 (1971).

3) S. Yamamura, M. Iguchi, A. Nishiyama, M. Niwa, H. Koyama, and Y. Hirata, *ibid.*, **27**, 5419 (1971); M. Iguchi, M. Niwa, and S. Yamamura, *Chem. Commun.*, **1971**, 974.

4) S. Yamamura, M. Iguchi, M. Niwa and Y. Hirata, This Bulletin, **45**, 266 (1972).

5) This compound had not been detected in the previous experiment (see Ref.4).

6) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962); R. F. Zurcher, *Helv. Chim. Acta*, **46**, 2054 (1963).

7) N. H. Andersen, D. D. Syrdal, B. M. Lawernce, S. J. Terhune and J. W. Hogg, *Phytochemistry*, **12**, 827 (1973).

A. G., Germany)) using *n*-hexane–benzene (1:1). The upper fraction gave white crystals (181 mg) of IV; mp 69—70 °C (from *n*-hexane); ν_{max}^{KBr} 3570 cm^{-1}; δ (CCl_4) 0.87 (3H, d, J=6.9 Hz), 0.90 (3H, d, J=6.9 Hz), 1.05 (3H, d, J=7.0 Hz), and 2.46 ppm (2H, s). Found: *m/e* 238.1940. Calcd for $C_{15}H_{26}O_2$: *m/e* 238.1933. From the lower fraction, a colorless liquid (31 mg) was obtained, which was further purified by preparative tlc (Kieselgel GF_{254}) using *n*-hexane–ether (2:1) to give white crystals (14 mg) of V; mp 77—80 °C (from *n*-hexane); ν_{max}^{film} 3570 cm^{-1}; δ (CCl_4) 0.85 and 0.87 (9H, each br.d, $J\simeq$6.3 Hz), and 2.48 ppm (2H, s). Found: *m/e* 238.1901. Calcd for $C_{15}H_{26}O_2$: *m/e* 238.1933.

Reduction of Dihydro-epoxide (IV) with $LiAlH_4$. $LiAlH_4$ (10 mg) was added to a solution of IV (130 mg) in anhyd. ether (10 ml), and then the mixture was stirred at room temp. for 2 hr. After the decomposition of the excess reagent with three drops of water, the reaction solution was filtered. The filtrate was concentrated under reduced pressure to give white crystals, which was purified by preparative tlc (Wakogel B5-F) using *n*-hexane–ether (2:1) to give white crystals (120 mg) of the diol (VI); mp 104—105 °C; ν_{max}^{KBr} 3340 br. cm^{-1}; δ 0.93 (6H, d, J=7.0 Hz), 1.05 (3H, d, J=7.0 Hz), 1.20 (3H, s), and 2.85 ppm (2H, s, OH); *m/e* 240 (M^+). Found: C, 74.70; H, 12.01%. Calcd for $C_{15}H_{28}O_2$: C, 74.95; H, 11.74%.

Dehydration of the Diol (VI). Into a solution of the diol (110 mg) in anhyd. pyridine (10 ml) was slowly stirred a solution of $POCl_3$ (2 ml) in anhyd. pyridine (2 ml) at −15 °C. The reaction solution was further stirred at room temp. overnight, and then at 40 °C for 2 hr. The reaction solution was then poured into large amounts of ice and extracted with ether. The ether extract was washed successively with 5% hydrochloric acid and with water, and then dried over anhydrous Na_2SO_4. The subsequent removal of the solvent gave a pale yellow oil (100 mg), from which two dehydration products were obtained by preparative tlc (Wakogel B5-F) using *n*-hexane–benzene (2:1). The upper fraction afforded a colorless oil (33 mg), which was further purified by preparative tlc (10% $AgNO_3$-Wakogel B5-F) using *n*-hexane–benzene (2:1) to give a colorless liquid (28 mg) of (+)-zonarene (VII, $[\alpha]_D^{25}$ +322°) (glc, tlc, and IR spectrum). On the other hand, the lower fraction afforded a colorless oil (42 mg), which was also purified by preparative tlc (Wakogel B5-F) using *n*-hexane–benzene (1:1) to give a colorless liquid (39 mg) of VIII; ν_{max}^{film} 3550 cm^{-1}; δ (CCl_4) 0.94 (6H, d, J=6.4 Hz), 1.04 (3H, d, J=6.0 Hz), 1.63 (3H, br.s), and 5.48 ppm (1H, br.s). Found: *m/e* 222.1975. Calcd for $C_{15}H_{26}O$: *m/e* 222.1984).

The authors wish to thank Dr. W. Fenical (University of California, U.S.A.) for an authentic sample of zonarene. They are also indebted to Professor Akira Tatematsu and Mr. Hiroshi Sakurai (Meijo University) for measurements of high resolution mass spectra.