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STRUCTURE AND SYNTHESIS OF ACTIVE COMPONENT FROM A MARINE ALGA, SARGASSUM TORTILE, WHICH INDUCES THE SETTLING OF SWIMMING LARVAE OF CORYNE UCHIDAI

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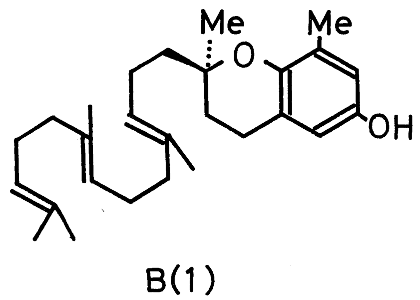
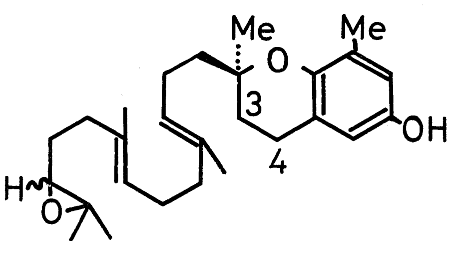
Based on the observation that the juice of yoremoku induces the settling of swimming larvae of Coryne Uchidai, we searched the active component in the alga by means of bioassay using the swimming larvae and elucidated the structure of the active principle to be 1 and 2. The structure was unequivocally confirmed by synthesis and (±)-epoxide (2) exhibited the clear activity toward the settling of swimming larvae.

It is well known biologically that most of epiphytic hydroid have their own preferable alga and this particular associative relation is formed by settling of swimming hydrozoan larvae onto the associated algal thallus. One of us (Y. Kakinuma) has observed recently that the settling of swimming larvae of Coryne Uchidai, a kind of hydrozoa, was clearly induced by adding the juice of Sargassum tortile (Japanese name; yoremoku), a kind of algae to which the larvae settle specifically.[1] This finding has prompted us to search the active substance in the alga and this paper is concerned with the structural elucidation including the



B(1)

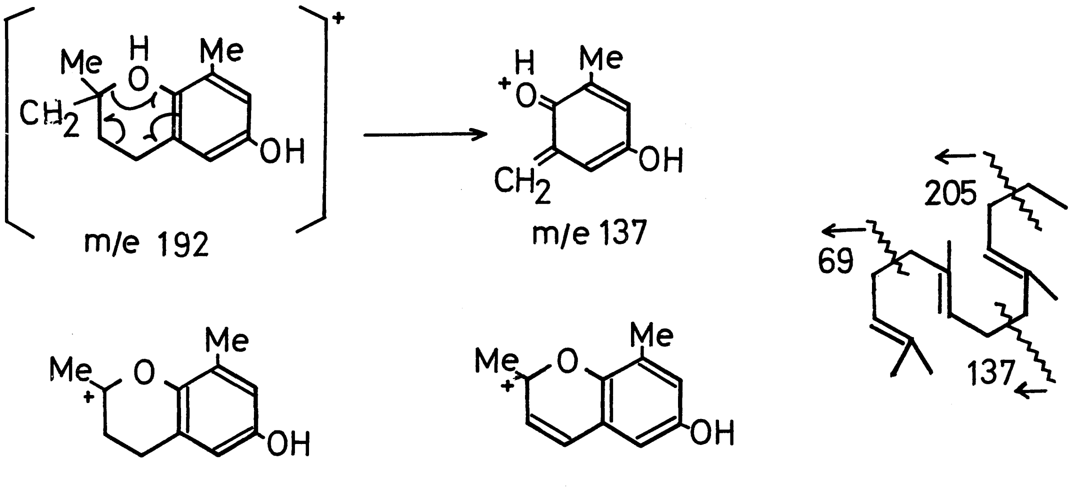


A(2)
(3) 3,4-dehydro

synthesis of the compounds which induce the settling of the swimming larvae.

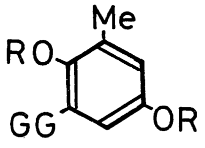
The neutral part (22 g) of n-hexane extracts of the dried alga (3.5 kg) was fractionated by the aids of column and thin layer chromatographies on SiO_2 into 20 fractions. By screening of the even numbered fractions for the activity against the induction of settling of the swimming larvae of Coryne Uchidai, we obtained 302 mg of active portion which causes the swimming larvae to settle within a few hours after treatment. The active portion consisted of six compounds, which were separated by repeat of preparative TLC into A (22 mg, $C_{27}H_{40}O_3$), B (89 mg, $C_{27}H_{40}O_2$) and others ($C\sim F$). On catalytic hydrogenation, B λ_{max}^{EtOH} 300 nm (ε=2900), afforded a hexahydro derivative, λ_{max}^{EtOH} 300 nm (ε=3500), which gave a monoacetate on acetylation. These as well as physical evidence, especially mass spectra, suggests that B is δ-tocotrienol (1), already isolated from Hevea latex by Pennock et al.[2] High resolution mass spectra of both B and its hexahydro derivative showed prominent peaks at m/e 192 $(C_{12}H_{16}O_2)^+$, 177 $(C_{11}H_{13}O_2)^+$, and 137 $(C_8H_9O_2)^+$ due to chromane nucleus, while farnesyl group in B was deduced from the observation[3] of relatively strong peaks at m/e 69 $(C_5H_9)^+$, 137 $(C_{10}H_{17})^+$, and 205 $(C_{15}H_{25})^+$ in the spectrum of B. The possible structure of these fragment ions were shown in the figure.[4]

Spectral data of A are alike with those of B (1) and comparison of physical evidence of these two compounds leads to the postulation that A is epoxy-δ-tocotrienol (2), which was confirmed by synthesis in the following manner.



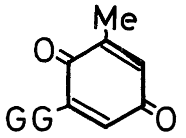
The methoxymethyl group of geranylgeranyl toluquinol bis ether (4), which was synthesized in fairly good yields as described previously,[5] can be removed by treatment with aqueous hydrochloric acid. During the hydrolysis, a part of hydroquinone

(5) was air-oxidized to quinone (6) and hence the mixture was treated, without separation, with silver oxide to convert the former to the latter. Terminal double bond of 6 was changed into the corresponding bromohydrin in 34% yield by treatment with NBS in aqueous dimethoxyethane, and pyridine solution of the latter compound was warmed at 50°C for 48 hr[6] to be transformed selectively into the chromene derivative (7), which was treated with cold methanolic 2N-KOH to afford 3 in high yield. 3, λ_{max}^{MeOH} 332 nm (ε=2540), Mass, 410 (M^+), 175 ($C_{11}H_{11}O_2$, base peak), and three strong peaks at m/e 121, 119 and 117, NMR (CCl_4) 1.23, 1.27 and 1.32 (each 3H, s, -O-C-Me x 3), 1.57 (bs. C=C-Me x 2), 2.08 (3H, aromatic Me), 2.62 (1H, t, 6 Hz, HC-O-C), 5.07 (2H, m, C=C-H), 5.45 and 6.15 (each 1H, d, 10 Hz, C_3- and C_4-H), 6.20 and 6.37 (each 1H, d, 2 Hz, aromatic H). The C_3-C_4 double bond of 3 is selectively reduced by Na-EtOH to afford 2. 2 λ_{max}^{MeOH} 295 nm (ε=2090), Mass, 412 (M^+), 410 $(M-2)^+$, 177 $(C_{11}H_{13}O_2)^+$, 175 $(C_{11}H_{11}O_2{}^+$, base peak), and 137 $(C_8H_9O_2)^+$. NMR 1.22 (6H, s) and 1.25 (3H, s) [OCMe x 3], 1.58 (bs, C=C-Me x 2), 2.06 (aromatic Me), 2.58 (3H, m, C_4-H_2 plus HC-O-C), 5.07 (2H, m, C=C-H), 6.20 and 6.34 (each 1H, aromatic H).



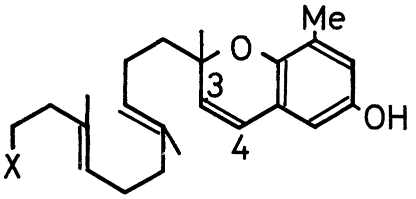
(4) R = CH_2OMe

(5) R = H



(6)

GG = geranylgeranyl



(7) X = $CHBr\cdot\overset{OH}{C}Me_2$

(8) X = $CHOH\cdot CMe=CH_2$

(9) X = $CO\cdot CHMe_2$

Similarly, quinone (6) was converted to (±)-δ-tocotrienol (1) by successive treatments with refluxing pyridine and then with Na-EtOH.[7] 1, NMR 1.22 (3H, s, C_2-Me), 1.56 and 1.64 (9H and 3H, bs, C=C-Me, cis and trans, respectively), 1.71 (2H, t, 7 Hz, C_3-H_2), 2.05 (3H, s, C_8-Me), 2.63 (2H, t, 7 Hz, C_4-H_2), 5.02 (3H, bm, C=C-H), 6.20 and 6.32 (each 1H, d, 3 Hz, C_5- and C_7-protons). Physical evidence (NMR and Mass) of our synthetic materials (1 and 2) are identical with that isolated from Sargassum tortile and synthetic epoxides (2 and 3) showed the clear activity toward the settling of swimming larvae of Coryne Uchidai. For example, addition of ca 50 ppm of synthetic material (2) caused the swimming larvae to settle completely after two days while those in control experiment remained unchanged at the same conditions.[8]

Since B (1) shows positive optical rotation of $[\alpha]_D$ + 22.15°, our natural δ-tocotrienol is deduced[9] to have an α-configuration concerning C_2- methyl. On the other hand, epoxide (2) possesses two asymmetric centers and the synthetic epoxide consists obviously of four stereoisomers. Although methyl group at C_2 is assumed to be α as in the case of 1, we have at present no evidence concerning the stereochemistry of the active form of the epoxides (2).

Determination of absolute configuration of natural epoxide and structural elucidation of other compounds (C ∿ F) are now in progress.

References

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1. Y. Kakinuma, Bull. Mar. Bio. Stat., Asamushi, Tohoku Univ., 10, 37 (1960); M. Nishihira, ibid., 13, 83 (1968).
2. K. J. Whittle, P. J. Dunphy, J. F. Pennock, Biochem. J., 100, 138 (1966).
3. C. R. Enzell, B. Kimland, L. E. Gunnarson, Tetrahedron Letts., 1971, 1983; U. T. Bhalerao, H. Rapoport, J. Am. Chem. Soc., 93, 105 (1971).
4. A. G. Gonzalez, J. Darias, J. D. Martin, C. Pascual, Tetrahedron, 29; 1605 (1973).
5. A. S. Kumanireng, T. Kato, Y. Kitahara, Chem. Letts., 1973, 1045.
6. This condition is serious since a mixture of allyl alcohol (8) and ketone (9), probably derived from epoxide cleavage of 3 by the action of pyridine-HBr, was obtained when the pyridine solution of bromohydrin was refluxed.
7. H. Mayer, J. Metzger, O. Isler, Helv. Chem. Acta, 50, 1375 (1967), and references therein.
8. T. Kato, A. S. Kumanireng, I. Ichinose, Y. Kitahara, Y. Kakinuma, M. Nishihira, M. Kato, Experientia, in press.
9. O. Isler, M. Montavon, Bull. Soc. Chim. Fr., 1965, 2403.

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