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ABSOLUTE CONFIGURATION OF CRINITOL. AN ACYCLIC DITERPENE INSECT GROWTH INHIBITOR FROM THE BROWN ALGAE SARGASSUM TORTILE

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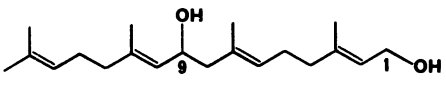
The absolute configuration of the insect growth inhibitor crinitol, isolated from the marine algae Sargassum tortile, has been established by application of the recently developed acyclic allylic benzoate method.

In the course of our search for bioactive natural products, we found that the crude methanol extract of a brown alga Sargassum tortile[1] (Sargassaceae) showed insect growth inhibitory activity with an artificial diet feeding assay.[2] The bioassay directed purification of the methanol extract has led to the isolation of a colorless liquid as the only active principle.[3] The structure of this active compound ($[\alpha]_D$-5°, c 0.43, CH_3OH) was identified as crinitol (1, $[\alpha]_D$-3°), previously isolated from the marine algae Cystoseira crinita (Cystoseiraceae),[4] by the comparison of spectral data.[5] However, the absolute configuration at C-9 remained unknown.

Recently a circular dichroic exciton chirality method for determining the absolute configuration of acyclic allylic alcohols was reported.[6] In order to define the absolute stereochemistry of 1 by this method four derivatives, 2-5,[7] were made and their CD spectra were recorded. Only 2 and 3, whose C-9 hydroxyl group was p-bromobenzoylated, showed the predicted benzoate Cotton effect. The absolute values ($\Delta\varepsilon$) of both of these benzoate Cotton effects were



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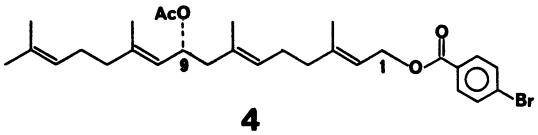

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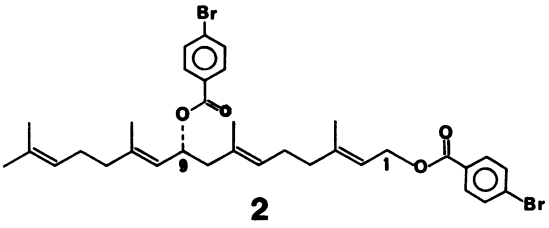

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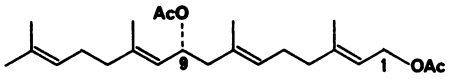

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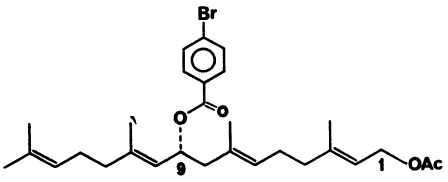

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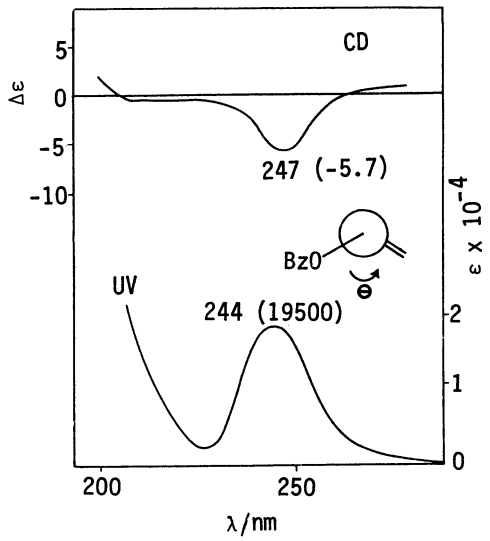

Fig. 1. UV and CD spectra of 3 in EtOH.

almost equal; 2, -5.4 (244 nm) and 3, -5.3 (247 nm). These data clearly indicate that the C-1 benzoate chromophore does not interact with the C-9 benzoate chromophore, unlike dibenzoates of cyclic compounds.[8] The observed negative Cotton effect shown in Fig. 1 is due only to the interaction between the benzoate ^1L_a transition and the double bond π-π^* transition.

If all possible rotomers were equally present the sum of the Cotton effects should cancel. However, it has been shown for a large number of secondary allyic benzoates the rotomer having the carbinyl hydrogen and the double bond eclipsed is favored. The presence of a large J_{vic} of 9.0 Hz between the olefinic and C-9 carbinyl protons in 2 and 3 is consistent with such a preferred conformer, as the size of the coupling is dependent on the dihedral angle. Thus, the absolute configuration of crinitol, 1, was determined to be 9-R. This is the first actual application of the allylic benzoate method to a natural acyclic allylic alcohol.

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References

1) Plant material was collected near Osaka, Japan by one of the authors (N.I.).

2) I. Kubo and J. A. Klocke, "Plant Resistance to Insect," ed by P. Hedin, ACS Symposium Series 208, American Chemical Society, Washington, D. C., (1983), p. 329.

3) The effective dose (ED_{50}) for 50% growth inhibition of Pectinophora gossypiella was 500 ppm. The same compound also exhibited a specific antimicrobial activity against gram negative bacteria. The growth of Escherichia coli was completely inhibited at a concentration of 50 μg/ml (MIC). This specific antimicrobial activity may be explained by the possibility that crinitol inhibits KDO transferase since KDO is unique to gram negative bacteria.

4) E. Fattorusso, S. Magno, L. Mayol, C. Santacroce, and D. Sica, Tetrahedron Lett., 1976, 937.

5) CI-MS (NH_3) 289 (MH^+-H_2O) and 271 (MH^+-2H_2O), ^1H NMR ($CDCl_3$) 5.41 (1H, brt, J=9.7 Hz), 5.05-5.25 (3H, m), 4.40 (1H, ddd, J=7.5, 12.0, 12.0), 4.12 (2H, m), 1.68 (3H, s), 1.67 (3H, s), 1.66 (3H, s) and 1.60 (3H, s) ppm, ^{13}C NMR ($CDCl_3$) 138.9(s), 138.2(s), 132.2(s), 131.6(s), 128.2(d), 127.0(d), 124.6(d), 123.9(d), 65.4(d), 59.2(t), 48.1(t), 39.5(t), 39.2(t), 26.4(t), 25.8(t), 25.6(q), 17.7(q), 16.6(q), 16.1(q) and 15.9(q) ppm. The position of the secondary hydroxyl group was readily resolved to be at C-9 by 2D NMR.

6) N. C. Gonnella, K. Nakanishi, V. S. Martin, and K. B. Sharpless, J. Am. Chem. Soc., 104, 3775 (1982).

7) 2 EI-MS m/z 672 (M^+), 670 (M^+), 472, 470, 270: 3 EI-MS m/z 532 (M^+), 530 (M^+), 330, 270, ^1H NMR ($CDCl_3$) 7.88 (2H, d, J=9.0), 7.56 (2H, d, J=9.0), 5.85 (1H, ddd, J=5.6, 7.8 9.0, 9-H), 5.27 (1H, tq, J=7.5, 1.3, 2-H), 5.21 (1H, dq, J=9.0, 1.2, 10-H) 5.17 (1H, brt, J=7.0, 6-H), 5.06 (1H, m, 14-H), 4.55 (2H, brd, J=7.5, 1-H), 2.45 (1H, dd, J=7.8, 13.5, 8-H), 2.24 (1H, dd, J=5.6, 13.5, 8-H), 2.05 (3H, s, Ac), 1.9-2.1 (8H, m), 1.76 (3H, d, J=1.2, 11-Me), 1.67 (3H, brs, 7-Me), 1.66 (3H, brs, 15-Me), 1.64 (3H, d, J=1.3, 3-Me), 1.58 (3H, brs, 15-Me); 4 EI-MS m/z 532 (M^+), 530 (M^+), 472, 470, 270; 5 EI-MS m/z 390 (M^+), 330, 270.

8) H. Liu and K. Nakanishi, J. Am. Chem. Soc., 103, 5591 (1981).

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