CHEMISTRY LETTERS, pp. 2183-2186, 1990.

Litophynin D and E, Two New Diterpenoids from a Soft Coral Litophyton sp.

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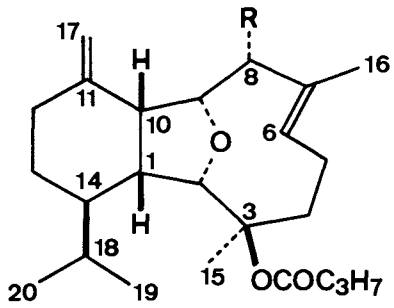
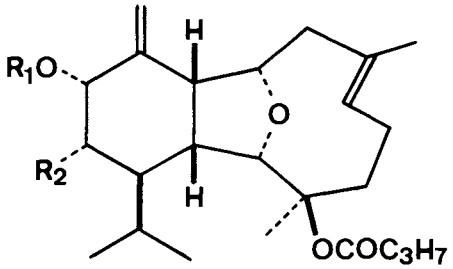
The structures of litophynin D and E, two new diterpenoids isolated from a soft coral Litophyton sp., have been established on the basis of spectral and chemical evidence.

Recently, we reported the structures of three insect growth inhibitory diterpenoids, litophynin A (**1**), B (**2**), and C (**3**), isolated from the soft coral Litophyton sp.[1] Our continuing search for the biologically active constituents of the same animal has led to the isolation of two additional congeners, named litophynin D and E. In this paper, we wish to report the structures of these new compounds. Litophynin D exhibits significant brine shrimp lethalty (LD_{50} 0.9 ppm).[2]

Litophynin D (**4**) was isolated as an optically active colorless oil[3] (0.00033%, wet weight), $[\alpha]_D^{22.5}$ -32.5° (c 0.14, $CHCl_3$), from the dichloromethane soluble fraction of the methanol extract of frozen specimens through Sephadex LH-20 (MeOH) and silica gel (hexane/EtOAc) column chromatography, followed by reverse phase HPLC (ODS column, MeOH/H_2O). The molecular formula $C_{28}H_{42}O_7$ was established by EIMS (m/z 490, M^+) and ^{13}C NMR data. It showed IR absorptions attributable to ester (1735) and exo methylene (3080, 1640, and 910 cm^{-1}) groups. The close similarity between **4** and litophynin C acetate (**6**)[1b] was revealed by the comparison of their spectral data. The ^{13}C NMR data of **4** included twenty signals compatible with the carbon frame work of **6**. Variances noted were in observations of signals due to two secondary acetoxyl groups in **4**, one more than that of **6**. A combination of the ^1H-^1H and ^1H-^{13}C COSY spectra together with partial spin decoupling studies allowed a complete assignment of all the proton and carbon resonances,[3] leading to a gross structure **1** for litophynin D except the positions of three acyl groups. Though there is no evidence to determine the positions of these three acyl groups, we assigned tentatively the location of butyrate group at C_3, and hence two acetate groups at C_{12} and



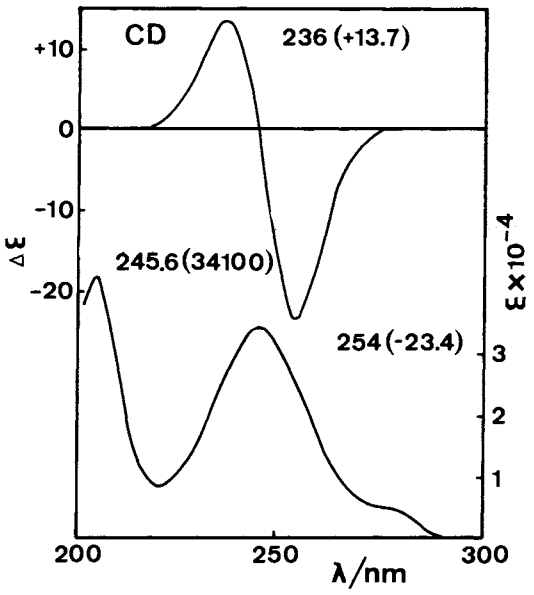


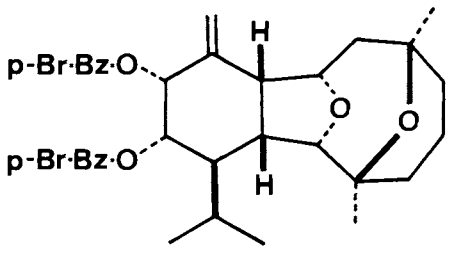
1 R=H
2 R=OCOC$_3$H$_7$

3 $R_1=R_2=H$
4 R_1= Ac, R_2=OAc
6 R_1= Ac, R_2=H
7 R_1= p-BrC$_6$H$_4$CO, R_2=H

C_{13}, from the fact that most of the congeners isolated from the same animal have the butyrate group at C_3. The relative stereochemistry at C_{12} and C_{13} was deduced from the J-values between 12-H and 13-H (2.9 Hz) and between 13-H and 14-H (10.3 Hz) as shown in structure **4**.

In the previous paper,[1b] we reported the determination of the absolute configuration of **3** by an application of the CD allylic benzoate method to its p-bromobenzoate (**7**). However, the CD spectrum of **7** exhibited only a weak Cotton effect ($\Delta\varepsilon$ +1.6) in the region of the p-bromobenzoate $\pi \rightarrow \pi^*$ transition owing to the twisted trans-olefin. Therefore, we reexamined the absolute configuration of Litophyton diterpenoids by an application of the





8

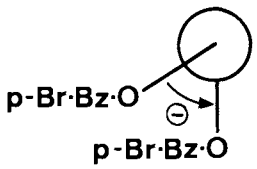
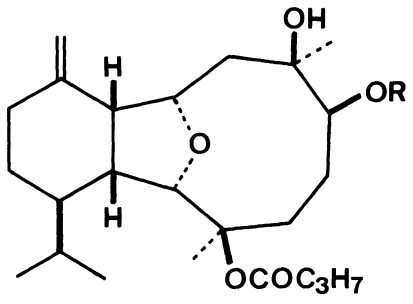
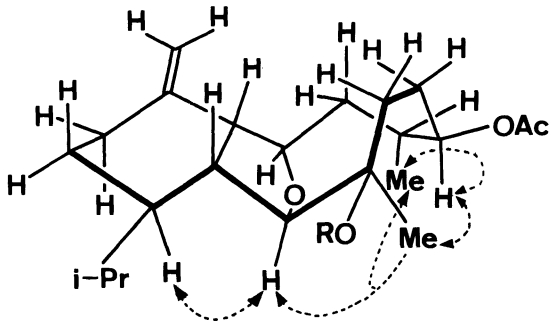


Fig. 1. CD and UV spectra of **8**.



5 R=H
9 R=Ac



←···→ NOE R=COCH3
9a

dibenzoate chirality rule[4] to **8**,[5] which was derived from **4** by reduction with $LiAlH_4$, followed by treatment with p-bromobenzoyl chloride/pyridine. The UV and CD spectra of **8** are presented in Fig. 1, the CD spectrum showing the two split Cotton effects at 254 nm ($\Delta\varepsilon$ -23.4) and 236 nm ($\Delta\varepsilon$ +13.7). Taking account of this result and the J-values between 12-H and 13-H (2.5 Hz) in **8**, the negative chirality between the vicinal p-bromobenzoyl groups was designated as shown in Fig. 1. Thus, the absolute configuration of litophynin D was established as shown in structure **4**.

Litophynin E (**5**) was obtained as a colorless viscous oil (0.00031%, wet weight), $C_{24}H_{40}O_5$, $[\alpha]_D^{20}$ -13.1° (c 0.21, $CHCl_3$), from the more polar fraction. It had IR absorptions indicative of hydroxyl (3400), ester (1735), and exocyclic methylene (1640 and 895 cm^{-1}) groups, and formed a monoacetate (**9**), $C_{26}H_{42}O_6$, colorless oil,[6] the IR spectrum of which still showed hydroxylic absorptions at 3600 and 3450 cm^{-1}, on acetylation with acetic anhydride-pyridine. **9** showed spectral data quite similar to those of litophynin A (**1**) except for the following observation. The ^1H and ^{13}C NMR spectra of **9**, which were completely assigned by the same techniques described above, did not show the presence of the trisubstituted double bond present in **1** but, instead, showed the presence of a monoacetylated 1,2-glycol moiety [δ_H 5.64 (1H, brd, J=5.5 Hz); δ_C 75.67 and 84.85], suggesting the presence of a glycol system at C_6-C_7 in **5**. The stereochemistry at C_6 and C_7 positions was deduced from the scrutiny of the NOESY spectrum of **9**. Namely, observations of NOEs among 15-Me, 6-H, and 16-Me defined the configuration of both hydroxyl groups as β. From the evidence outlined above, we proposed the structure **5** for litophynin E.

The present work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture (No. 63470022 to M. O.).

References

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2) B. N. Meyer, N. R. Ferrigin, J. E. Putnam, L. B. Jacobsen, D. E. Nichols, and J. L. McLaughlin, Planta Med., **45**, 31 (1982).

3) **4**: MS m/z (rel intensty) 490 (M^+, 5), 430 (11), 402 (24), and 71 (100); ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 and 1.09 (3H each, d, J=7.1 Hz, 19- and 20-H), 0.93 (3H, t, J=7.4 Hz, 4'-H), 1.59 (2H, sext, J=7.4 Hz, 3'-H), 1.60 (3H, brs, 15-H), 1.80 (3H, d, J=1.0 Hz, 16-H), 2.18 (2H, t, J=7.4 Hz, 2'-H), 2.19 (1H, td, J=8.6 and 2.0 Hz, 1-H), 2.80 (1H, brt, J=8.6 Hz, 10-H), 3.89 (1H, brs, 2-H), 4.44 (1H, dd, J=8.6 and 5.2 Hz, 9-H), 4.87 (1H, dd, J=10.3 and 2.9 Hz, 13-H), 5.15 and 5.27 (1H each, s, 17-H), 5.56 (1H, brd, J=10.5 Hz, 6-H), and 5.62 (1H, d, J=2.9 Hz, 12-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.60 (4'), 15.92 (19), 18.65 (3'), 20.74 (16), 21.19 and 21.22 (2Ac), 23.87 (20), 23.93 (15), 24.65 (5), 28.41 (18), 37.65 (4 and 2'), 38.65 (8), 40.21 (1), 44.99 (14), 45.80 (10), 73.41 (12), 73.50 (13), 81.53 (9), 87.36 (3), 91.52 (2), 118.50 (17), 125.05 (7), 131.62 (6), 139.70 (11), 169.89 and 169.96 (2Ac), and 172.40 (1').

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5) **8**: IR (CCl_4) 3100, 1730, 1645, 1595, and 1495 cm^{-1}; HRMS m/z 704.0995/702.1003/700.0912 (M^+, $C_{34}H_{38}O_6Br_2$, ΔM 0.0/-1.2/+5.2 mmu); ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (3H, s, 15-H), 1.32 (3H, s, 16-H), 5.16 (1H, dd, J=11.6 and 2.5 Hz, 13-H), 5.94 (1H, d, J=2.5 Hz, 12-H), and 7.50, 7.62, 7.74, and 7.90 (2H each, d, J=8.7 Hz, aromatic H); ^{13}C NMR (100 MHz, $CDCl_3$) 29.96 (16), 35.76 (15), 36.13 (6), 74.42 (12), 74.53 (13), 75.59 (3), 76.88 (7), and 128.26, 128.30, 129.15, 129.34, 131.24, 131.37, 131.81, 132.08, 164.72, and 164.79 (p-bromobenzoyl).

6) **9**: HRMS m/z 432.2933 (M^+-H_2O, $C_{26}H_{42}O_6-H_2O$, ΔM +5.7 mmu); ^1H NMR (400 MHz, $CDCl_3$) δ 0.78 and 0.97 (3H each, d, J=7.0 Hz, 19- and 20-H), 0.99 (3H, t, J=7.5 Hz, 4'-H), 1.19 (3H, s, 16-H), 1.38 (3H, s, 15-H), 1.70 and 1.71 (1H each, sext, J=7.5 Hz, 3'-H), 2.06 (3H, s, Ac), 2.18 (1H, dd, J=11.3 and 7.6 Hz, 1-H), 2.29 and 2.34 (1H each, t, J=7.5 Hz, 2'-H), 3.01 (1H, t, J=7.5 Hz, 10-H), 3.63 (1H, s, 2-H), 4.16 (1H, ddd, J=10.7, 7.5, and 4.6 Hz, 9-H), 4.63 and 4.68 (1H each, s, 17-H), and 5.64 (1H, brd, J=5.5 Hz, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.70 (4'), 15.48 (19), 18.47 (3'), 21.38 (Ac), 21.93 (20), 23.12 (15), 23.76 (16), 24.76 (13), 29.07 (18), 29.30 (5), 31.57 (12), 36.00 (4), 37.51 (2'), 43.97 (14), 45.93 (1), 46.09 (8), 53.90 (10), 75.67 (7), 78.18 (9), 84.85 (6), 86.56 (3), 92.30 (2), 109.43 (17), 147.73 (11), 171.80 (Ac), and 172.26 (1').

(Received September 7, 1990)