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ISOLATION OF NEW AROMATIC DERIVATIVES FROM A MARINE ALGAL SPECIES *CAULERPA RACEMOSA*

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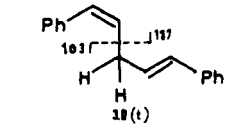
ABSTRACT.—Five new and uncommon aromatic derivatives and the red pigment caulerpin have been reported from the $CHCl_3$ extract of *Caulerpa racemosa*. The structures of the new derivatives have been elucidated as 1,5-diphenyl-1,4-pentadiene [**1**], *trans*-cinnamyl-1-phenyl-2-propenyl ether [**2**], dicinnamyl ether [**3**], cinnamyl-3-phenyl-1-propenyl ether [**4**], and cinnamyl dihydrocinnamate [**5**] on the basis of their analytical and spectral data. The presence of such compounds is unusual in marine algal species, although similar propane dimers are widespread in terrestrial plants.

The genus *Caulerpa* (Caulerpaceae) consists of several green algal species considered as salad delicacies in the Philippines and other countries of the Pacific. *Caulerpa racemosa* (Forsk.) J. Agardh is the most common edible variety. Chemical studies of various *Caulerpa* species have illustrated that they produce acetylenic sesquiterpenoids (1), diterpenoids (2), triterpenoids (3), and nitrogenous compounds (4,5) in addition to the red pigment caulerpin which is commonly present (6). *C. racemosa* collected in Philippine and Sri Lankan waters was reported to yield caulerpin and a colorless toxic substance consisting of a mixture of *N*-acyl sphingosines and sitosterol (7). As a part of our continuing program on the isolation of bioactive metabolites from marine flora and fauna of Indian seas, we undertook the chemical examination of *C. racemosa* collected off the Visakhapatnam coast. We report the presence of five simple aromatics for the first time in nature, except for compound **1** whose synthesis was reported earlier (10). Such derivatives, which are simple C_6-C_3 phenyl propane dimeric ethers or esters with a C_{18} skeleton and may be considered as neolignans (8), are rare in marine alga, but similar compounds are fairly widespread in terrestrial plants. Hormothamnione (9), a novel cytotoxic styryl chromone from the marine cyanophyta *Hormothamnion enteromorphoides*, is in fact a propane dimer and stands out as an isolated example of the presence of such compounds in marine organisms.

The residue from the MeOH extract of dried *C. racemosa* powder (3 kg) was fractionated into hexane, $CHCl_3$, and EtOAc solubles. The residue from the $CHCl_3$ extract on chromatography over a column of Si gel with hexane and hexane/C_6H_6 mixtures furnished the six compounds **1–6**.

Compound **1**, $C_{17}H_{16}$, $[M]^+$ 220, was recognized as a 1,5-diphenyl pentadiene derivative (δ 7.0–7.3, m, 10H). Besides the four olefinic protons, it showed a two-proton methylene triplet at δ 3.0. Its uv spectrum ruled out a conjugated 1,3-pentadiene system favoring a 1,5-diphenyl-1,4-pentadiene [**1**]. A comparison of the spectral characteristics of compound **1** with those of its *E,E*, *E,Z*, and *Z,Z* isomers (10) confirmed it as the *E,Z* derivative. The mass spectrum of the compound, however, showed ions at *m/z* 129 (100), 92 (40), and 91 (40), corresponding to those of 1,5-diphenyl-1,3-pentadiene [**7**], suggesting that the unconjugated diene isomerizes to the conjugated system in the mass spectrometer before fragmentation.

Compound **2**, $C_{18}H_{18}O$, $[M]^+$ 250, also showed two monosubstituted phenyl units at δ 7.0–7.3 (m, 10H), five olefinic protons, a two-proton doublet of $-OCH_2$ group at δ 4.0 ($J = 6$ Hz), and another one-proton doublet for an -OCH- proton at δ 4.75 ($J = 7$ Hz). The two carbons connected to oxygen appeared in



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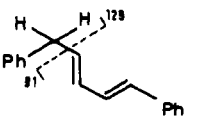

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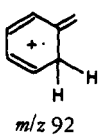
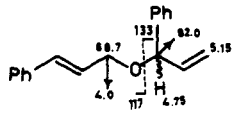


m/z 92



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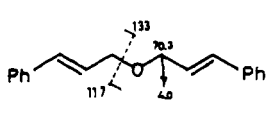

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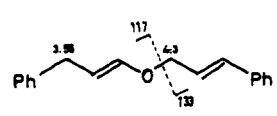

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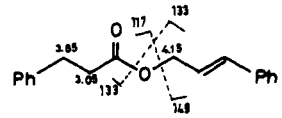

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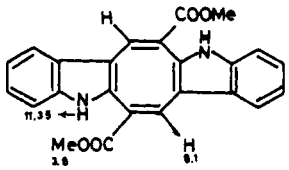

6

its ^{13}C-nmr spectrum at δ 68.7 and 82.0. That the single oxygen present in the compound is present as an ether oxygen is evident from its ir and nmr spectra. From the base peak at *m/z* 117 in its mass spectrum and the chiral nature of the compound, its structure was assigned as *trans*-cinnamyl-1-phenyl-2-propenyl ether [**2**], with the configuration of the chiral center (*R* or *S*) to be decided.

Compound **3**, $C_{18}H_{18}O$, $[M]^+$ 250, was also found to be an ether with two monosubstituted phenyl units at δ 7.1–7.3 (m, 10H). In addition to four olefinic protons, it showed two -OCH_2 groups at δ 4.0 (d, 4H, $J = 7$ Hz). Its ^{13}C-nmr spectrum was symmetrical, showing only nine peaks, the -OCH_2- carbons coming at δ 70.3. It could be readily characterized as dicinnamyl ether [**3**] (12).

Compound **4**, $C_{18}H_{18}O$, $[M]^+$ 250, was recognized from its spectral characteristics as an ether isomeric to compound **3**. It showed two broad doublets at δ 4.3 ($J = 7$ Hz) and 3.55 ($J = 7$ Hz) for an -OCH_2- group and a benzylic methylene, respectively, instead of the two -OCH_2 groups of compound **3**. It could be assigned the structure cinnamyl-3-phenyl-1-propenyl ether [**4**], which was supported by the base peak at *m/z* 117 in its mass spectrum. The ir absorption at 960 cm^{-1} and the coupling constant $J = 16$ Hz for the deshielded olefinic protons suggested the *E,E* configuration at the double bonds.

Compound **5**, $C_{18}H_{18}O_2$, $[M]^+$ 266, indicated the presence of an ester function (1720 cm^{-1}). In addition to two olefinic protons, it showed a two-proton doublet of an -OCH_2- group at δ 4.15 ($J = 6$ Hz), a benzylic methylene triplet at δ 3.65 ($J = 5$ Hz), and another methylene proton triplet at δ 3.05 ($J = 5$ Hz). It could thus be assigned as cinnamyl dihydrocinnamate [**5**], and this

was further supported by the abundant fragment ions at *m/z* 133 and 117.

Compound **6**, $C_{24}H_{18}O_4N_2$, $[M]^+$ 398, the orange red crystalline compound, was found to be identical with caulerpin [**6**] in every respect (11).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were uncorrected. ^1H nmr (90 MHz) and ^{13}C nmr (25.5 MHz) were recorded in $CDCl_3$ with TMS as internal standard; uv MeOH; ir $CHCl_3$ or neat; cc Si gel (100–200 mesh) tlc Si gel G (Acme); the spots were identified by spraying with 10% H_2SO_4 in MeOH.

COLLECTION, EXTRACTION, AND PURIFICATION.—The green algal material (wet wt 15 kg) of *C. racemosa* collected off the Visakhapatnam coast February 10–15, 1989 (with the voucher specimen deposited in the Department of Botany, Andhra University, Visakhapatnam) was made free from contaminants and dried in the shade. The air-dried and powdered material (3 kg) was exhaustively extracted with MeOH. The MeOH extract was concentrated under reduced pressure to yield a mostly aqueous residue (2 liters). This was fractionated into hexane, $CHCl_3$ and EtOAc solubles. On concentration, the $CHCl_3$ extract afforded a dark brown gum (6 gm) which was chromatographed over a column of Si gel with solvents of increasing polarity from petroleum ether (bp 60–80°) through C_6H_6 to EtOAc. The selected fractions were purified further by passing over a Si gel column to yield the following pure compounds: 1,5-diphenyl-1,4-pentadiene [**1**], *trans*-cinnamyl-1-phenyl-2-propenyl ether [**2**], dicinnamyl ether [**3**], cinnamyl-3-phenyl-1-propenyl ether [**4**], cinnamyl dihydrocinnamate [**5**], and caulerpin [**6**].

1,5-Diphenyl-1,4-pentadiene [**1**].—Compound 1 (25 mg): oil; R_f 0.7 [hexane-C_6H_6 (7:3)]; found C 92.8, H 7.2 ($C_{17}H_{16}$ requires C 92.7, H 7.2%); uv λ max nm 203.7, 258.6, 293.3; ir ν max cm^{-1} 3050, 2950, 1600, 1500, 1450, 960, 750, 690; ^1H nmr ($CDCl_3$) δ 3.0 (t, 2H, $-CH_2-$, $J=5.6$ Hz), 5.9–6.5 (m, 4H, =CH-), 7.0–7.3 (m, 10H, Ar-H); ms *m/z* (rel. int.) $[M]^+$ 220 (68), 143 (7), 129 (100), 127 (8), 115 (30), 103 (8), 93 (5), 92 (40), 91 (40), 77 (12).

trans-*Cinnamyl-1-phenyl-2-propenyl ether* [**2**].—Compound **2** (30 mg): oil; R_f 0.5 [hexane-C_6H_6 (7:3)]; $[\alpha]^{32.4}D$ +1.67° ($c=0.06$, $CHCl_3$); found C 86.3, H 7.2 ($C_{18}H_{18}O$ requires C 86.4, H 7.2%); uv λ max nm 206, 250, 283, 292; ir ν max cm^{-1} 3050, 2900, 1490, 1450, 1100, 1050, 960, 740, 680; ^1H nmr ($CDCl_3$) δ 4.0 (d, 2H, $-OCH_2-$, $J=6$ Hz), 4.75 (d, 1H, -OCH-, $J=7$ Hz), 5.15 (m, 2H, =CH-), 5.6–5.8 (m, 3H, -CH=CH-), 7.0–7.3 (m, 10H, Ar-H); ^{13}C nmr ($CDCl_3$) δ 141.0, 138.9, 136.8, 132.1, 128.5, 127.6, 126.9, 126.4, 126.2, 116.3, 82.0, 68.7; ms *m/z* (rel. int.) $[M]^+$ 250 (5), 133 (10), 117 (100), 115 (98), 105 (65), 91 (75), 77 (40).

Dicinnamyl ether [**3**].—Compound **3** (200 mg): oil; R_f 0.4 [hexane-C_6H_6 (7:3)]; found C 86.3, H 7.2 ($C_{18}H_{18}O$ requires C 86.4, H 7.2%); uv λ max nm 205, 254, 282.2, 292.5: ir ν max cm^{-1} 3050, 2850, 1590, 1490, 1450, 1350, 1110, 1050, 960, 740, 680; ^1H nmr δ 4.0 (d, 4H, $J=7$ Hz, $-OCH_2-$), 6.0–6.5 (m, 4H, -CH=CH-), 7.1–7.3 (m, 10H, Ar-H); ^{13}C nmr ($CDCl_3$) δ 136.5, 132.1, 128.4, 127.4, 126.7, 125.8, 70.3; ms *m/z* (rel. int.) $[M]^+$ 250 (5), 133 (10), 117 (98), 91 (100).

Cinnamyl-3-phenyl-1-propenyl ether [**4**].—Compound **4** (35 mg): oil; R_f 0.38 [hexane-C_6H_6 (7:3)]; found C 86.3, H 7.2 ($C_{18}H_{18}O$ requires C 86.4, H 7.2%); uv λ max nm 207, 252, 292; ir ν max cm^{-1} 2900, 1660, 1590, 1490, 1450, 1360, 1120, 1000, 960; ^1H nmr ($CDCl_3$) δ 3.55 (br d, 2H, $-CH_2-$, $J=7$ Hz), 4.3 (br d, 2H, $-OCH_2$, $J=7$ Hz), 5.2 (d, t, 1H, =CH-, $J=16$ Hz, 7 Hz), 5.95 (d, t, 1H, $-O-CH_2-CH=$, $J=16$ Hz, 7 Hz), 6.35 (d, 1H, $=CH-Ar$, $J=16$ Hz), 6.7 (d, 1H, $J=16$ Hz, =CH-O-), 7.15–7.30 (m, 10H, Ar-H); ms *m/z* (rel. int.) $[M]^+$ 250 (5), 133 (15), 117 (100), 105 (30), 91 (35).

Cinnamyl dihydrocinnamate [**5**].—Compound **5** (25 mg): oil; R_f 0.3 [hexane-C_6H_6 (7:3)]; found C 81.2, H 6.7 ($C_{18}H_{18}O_2$ requires C 81.2, H 6.7%); uv λ max nm 210, 254, 282; ir ν max cm^{-1} 2950, 1720, 1680, 1360, 1110, 960; ^1H nmr ($CDCl_3$) δ 3.05 (t, 2H, $-CH_2-$, $J=5$ Hz), 3.65 (t, 2H, $-CH_2-$, $J=5$ Hz), 4.15 (d, 2H, $-OCH_2-$, $J=5.5$ Hz), 6.15 (d, t, 1H, $-CH_2-CH=$, $J=16$ Hz, 7 Hz), 6.55 (d, 1H, =CH-Ar, $J=16$ Hz), 7.2 (br s, 10H, Ar-H); ms *m/z* (rel. int.) $[M]^+$ 266 (7), 149 (8), 133 (90), 131 (100), 117 (78), 105 (38), 91 (45), 77 (35).

Caulerpin [**6**].—Caulerpin (300 mg): orange red prisms; mp 316–318°; R_f 0.3 (C_6H_6); found C 72.2, H 4.5 ($C_{24}H_{18}O_4N_2$ requires C 72.3, H 4.5%); uv λ max nm 220, 270, 290, 317; ir ν max cm^{-1} 3400 (br), 1690, 1260; ^1H nmr (DMSO-d_6) δ 3.8 (s, 6H, 2×-COOMe), 7.0–7.4 (m, 8H, Ar-H), 8.1 (s, 2H, 2×=CH-), 11.35 (s, 2H, 2×-NH-); ms *m/z* (rel. int.) $[M]^+$ 398 (100), 366 (22), 338 (20), 306 (25), 279 (50), 278 (45), 139 (25).

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