Pergamon

0031-9422(95)00329-0

Phytochemistry, Vol. 40, No. 3, pp. 995–996, 1995

0031-9422/95 $9.50 + 0.00

LONG-CHAIN ALDEHYDES FROM THE RED ALGA, *CORALLINA MEDITERRANEA*

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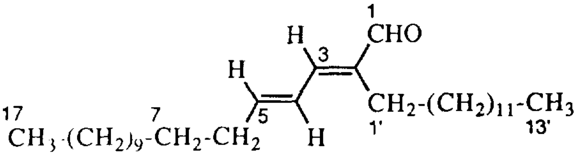
(*Received in revised form* 9 *March* 1995)

Key Word Index—*Corallina mediterranea*; Rhodophyta; red alga; long-chain aldehydes.

Abstract—From the red alga, *Corallina mediterranea*, collected in the Mediterranean Sea, two unusual aldehydes were isolated, (*E*)-2-tridecyl-2-heptadecenal and the new (2*E*,4*E*)-2-tridecyl-2,4-heptadecadienal. The structure of the new metabolite was proposed on the basis of its spectral data.

INTRODUCTION

Marine organisms are a rich source of new metabolites with a wide variety of biological activities, and some of them display significant pharmaceutical potential. Recently, the discovery of new anti-inflammatory agents from marine species has been reported [1, 2]. Continuing our search for biologically active marine natural compounds, we have studied the red alga, *Corallina mediterranea* Aresch (*C. elongata*), collected in Jàvea (Alicante, Spain), whose extract showed anti-inflammatory activity [3] and cytotoxic activity ($LD_{50} = 125\ \mu g\ ml^{-1}$) in the brine shrimp assay [4]. We wish to describe herein the isolation from this alga of two aldehydes, the new (2*E*,4*E*)-2-tridecyl-2,4-heptadecadienal (**1**) and the previously reported (*E*)-2-tridecyl-2-heptadecenal (**2**) [5].



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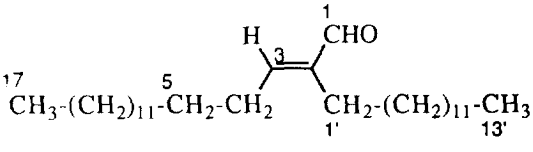

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RESULTS AND DISCUSSION

The dichloromethane extract of dried alga *C. mediterranea* was chromatographed on silica gel, using increasing concentrations of diethyl ether in petrol as the eluent. Along with lipids (fatty acids and triacylglycerols) was isolated a fraction giving a single spot on TLC and a 2,4-dinitrophenylhydrazine positive reaction. Preliminary analysis of the ^1H NMR spectrum showed the presence of two or more components and aldehydic signals. The mixture was resolved by preparative HPLC, leading to the isolation of two pure compounds (*E*)-2-tridecyl-2-heptadecenal (**2**) (0.0008% dry wt) and (2*E*,4*E*)-2-tridecyl-2,4-heptadecadienal (**1**) (0.001%), in order of their polarity.

The spectral data for **2** were in excellent agreement with those for (*E*)-2-tridecyl-2-heptadecenal, previously isolated from the red algae, *Laurencia undulata* and *L. papillosa* [5]. A combination of COSY and HETCOR experiments allowed us to assign the chemical shifts in the ^1H and ^{13}C NMR spectra for both compounds.

Compound **1** had the molecular formula $C_{30}H_{56}O$, from high-resolution mass measurement of the parent ion. The IR bands at 2730, 1680 and 1640 cm^{-1} were characteristic of an α,β-unsaturated aldehyde, while the UV absorption at 280 nm strongly suggested a double-bond extending conjugation. This conjugation was further supported by the ^1H NMR spectrum which showed an aldehyde proton at δ9.38 and three vinyl protons at δ6.77 (H-3, *d*, $J = 11.2$ Hz), 6.50 (H-4, *dd*, $J = 11.2$ and 14.9 Hz) and 6.23 (H-5, *dt*, $J = 14.9$ and 7.5 Hz). The vinyl protons are part of a 1,1,4-trisubstituted 1,3-butadiene. From COSY the doublet at δ6.77 is coupled with the proton at δ6.50, which is coupled with the proton at δ6.23, which in turn is coupled with a methylene at δ2.25 (*m*), which is coupled with another methylene at δ1.48 (*m*). The presence in the ^{13}C NMR spectrum of four doublets at δ194.9 (C-1), 149.5 (C-3), 125.8 (C-4) and 128.9 (C-5) and a singlet at δ144.9 (C-2) confirms the presence of an aldehyde group conjugated with a 1,4-disubstituted 1,3-butadiene. Moreover, the ^{1}H NMR spectrum showed a multiplet at δ2.20 (2H), a strong signal at δ1.26 (40H) and two overlapped triplets at δ0.88 and 0.86 (3H each, $J = 6.8$ Hz). Since the molecular formula of **1** requires three degrees of unsaturation, **1** must therefore have a branched-chain carbon skeleton. The number of methylenes in the two chains of the 1,1,4-trisubstituted 1,3-butadiene system was established by means of mass spectroscopy. The EI mass spectrum of **1** showed two highly diagnostic peaks at *m/z* 249.2222 ($C_{17}H_{29}O$) caused by loss of the chain near the branched carbon (cleavage of C-2, C-1′ bond), and *m/z* 263.2372 ($C_{18}H_{31}O$) produced by allylic cleavage of the side-chain (cleavage of C-1′, C-2′ bond). The stereochemistry of the double bond conjugated with the aldehydic group was established as *E* by NOESY from the presence of NOEs between H-3 (δ6.77), Hs-1′ (δ2.20) and H-4 (δ6.50) and the aldehydic proton (δ9.38). The ^{13}C chemical shift of the allylic methylene group (δ24.1, C-1′) near the branched carbon atom afforded additional proof for the proposed stereochemistry. The large value of the coupling constant between H-4 and H-5 indicates a *trans*-stereochemistry of the double bond; the ^{13}C chemical shift of the second allylic methylene group (δ33.4, C-6), suggests an *E*-configuration for this second double bond.

Long-chain aldehydes, such as (8*Z*)-heptadecenal, (8*Z*,11*Z*)-heptadecadienal and (8*Z*,11*Z*,14*Z*)-heptadecatrienal, identified in green algae [6], having the characteristic odour of the essential oils from marine green algae, are peculiar to the Ulvacea. The finding of these unusual aldehydes, from a different genus of Rhodophyta, could be a peculiarity of this class of seaweeds.

EXPERIMENTAL

^{1}H and ^{13}C NMR were recorded at 500 and 125 MHz, respectively, in $CDCl_3$ with TMS as int. standard. 2D NMR were obtained using Bruker microprograms. Silica gel chromatography was performed using precoated Merck F_{254} plates and Merck Kieselgel 60 powder. Prep. HPLC purifications were carried out on a Spherisorb S5W column (25 cm × 4.6 mm i.d.) using a RI detector.

Extraction and isolation of compounds. The alga was collected at Jàvea (Alicante, Spain) and air-dried. A voucher specimen is deposited in the herbarium of the Plant Biology Department, Faculty of Biology, Valencia. Dried alga (5.2 kg) was extracted with CH_2Cl_2 in a Soxhlet apparatus. The extract was evapd *in vacuo* to obtain a brown oil (13.6 g), which was applied to a column of silica gel. The column was eluted with a solvent gradient system from petrol (40–70) to Et_2O. Frs exhibiting a similar TLC profile (R_f 0.5 in petrol–Et_2O, 49:1) were combined to obtain a mixt. of **1** and **2**, which gave a 2,4-dinitrophenylhydrazine positive reaction. The mixture was resolved by prep. HPLC (*n*-hexane–EtOAc, 19.9:0.1).

(2E,4E)-2-*Tridecyl*-2,4-*heptadecadienal* (**1**). Yield 55 mg. UV λ_{max} (MeOH) nm (log ε): 280 (4.33). IR ν_{max} ($CHCl_3$) cm^{-1}: 2730, 1680, 1640. EIMS *m/z* (rel. int.): 432.4328 $[M]^+$ ($C_{30}H_{56}O$, requires 432.4331) (9), 431 (4), 403 (5.5), 264 (59), 263.2372 ($C_{18}H_{31}O$, requires 263.2375) (100), 249.2222 ($C_{17}H_{29}O$, requires 249.2218) (11), 211 (65). ^{1}H NMR: δ0.86 (3H, *t*, $J = 6.8$ Hz, H-17 or H-13′), 0.88 (3H, *t*, $J = 6.8$ Hz, H-17 or H-13′), 1.26 (40H), 1.48 (2H, *m*, H-7), 2.20 (2H, *m*, H-1′), 2.25 (2H, *m*, H-6), 6.23 (1H, *dt*, $J = 14.9$ and 7.5 Hz, H-5), 6.50 (1H, *dd*, $J = 14.9$ and 11.2 Hz, H-4), 6.77 (1H, *d*, $J = 11.2$ Hz, H-3), 9.38 (1H, *s*, H-1). ^{13}C NMR: δ194.9 (*s*, C-1), 149.5 (*d*, C-3), 144.9 (*s*, C-2), 128.9 (*d*, C-5), 125.8 (*d*, C-4), 33.4 (*t*, C-6), 31.9 (*t*, C-15 and C-11′), 29.7 (*t*), 29.5 (*t*), 29.4 (*t*), 29.3 (*t*), 28.9 (*t*), 28.8 (*t*), 28.7 (*t*), 24.1 (*t*, C-1′), 22.7 (*t*, C-16 and C-12′), 14.1 (*q*, C-17 and C-13′).

(E)-2-*Tridecyl*-2-*heptadecenal* (**2**). Yield 40 mg. UV λ_{max} (MeOH) nm (log ε): 231 (4.02). IR ν_{max} ($CHCl_3$) cm^{-1}: 2730, 1680, 1640; EIMS *m/z* (rel. int.): 434 $[M]^+$ (23), 433 (12), 405 (7), 265 (30), 251 (33), 237 (55), 223 (15), 95 (100). ^{1}H NMR: δ0.88 (6H, *t*, $J = 6.8$ Hz), 1.26 (44H), 1.48 (2H, *m*), 2.21 (2H, *m*), 2.34 (2H, *m*), 6.43 (1H, *t*, $J = 7.4$ Hz), 9.36 (1H, *s*). ^{13}C NMR: δ195.3 (*s*, C-1), 155.2 (*d*, C-3), 143.9 (*s*, C-2), 31.9 (*t*, C-15 and C-11′), 29.7 (*t*), 29.5 (*t*), 29.4 (*t*), 29.3 (*t*), 28.9 (*t*), 28.8 (*t*), 28.7 (*t*, C-4), 24.1 (*t*, C-1′), 22.7 (*t*, C-16 and C-12′), 14.1 (*q*, C-17 and C-13′).

Acknowledgements—This research was supported by the Progetto Strategico 'Tecnologie Chimiche Innovative' C.N.R., Rome, Italy and by grant PM92-0145 from DGICYT, Spanish Ministerio de Educacion y Ciencia. We thank Dr Boisset, Department of Plant Biology, University of Valencia, and Dr N. Zavodnik, 'R. Boskovic' Institute of Rovinj (HR) for identification of the alga.

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