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NEW BUTENOLIDES FROM THE GORGONIAN EUPLEXAURA FLAVA(NUTTING)

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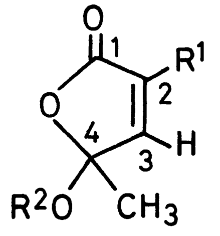
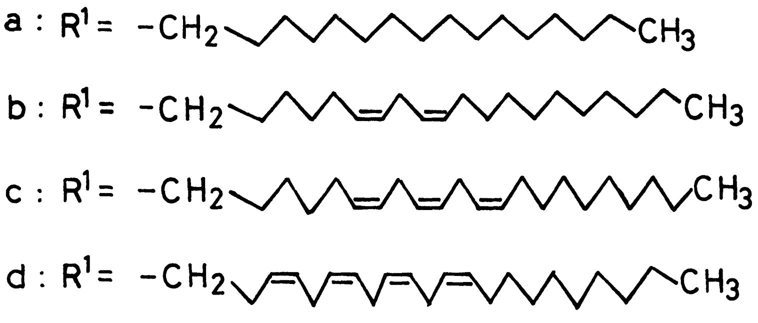
Four new butenolides (1a-d) were isolated from the Japanese gorgonian Euplexaura flava(Nutting). The structures of these compounds were elucidated from spectral data and chemical reactions.

A number of marine natural products such as terpenoids$^{1)}$, steroids$^{2)}$, and fatty acid derivatives$^{3)}$ isolated from coelenterates have received considerable interest because of their unprecedented structures and biological activities. In the course of our investigation$^{4)}$ on the chemical constituents of Japanese coelenterates, we have isolated four new fatty acid derivatives containing a butenolide moiety from a gorgonian Euplexaura flava(Nutting). This paper deals with the isolation and structure elucidation of these butenolides (1a-d) on the basis of spectral properties and chemical reactions. These compounds are the first example of long chain fatty acid derivatives possessing a three carbon-branch at α-position.

Euplexaura flava(Nutting)(wet weight 1.8 kg), collected at the coral reef of Ishigaki Island (Okinawa,Japan), was extracted with methanol and then acetone. The combined MeOH and acetone extracts were suspended in water and extracted with AcOEt. Repeated silica gel column chromatography$^{5)}$ of the AcOEt extract gave a mixture of four compounds (1a-d). High pressure liquid chromatography (Hitachi gel 3010, MeOH) of the mixture gave 1a$^{6)}$(2.38 g, $C_{21}H_{38}O_3$) as colorless needles(mp 67°C) and an oily mixture of 1b-d (2.7 g). Separation of 1b-d was done by an $AgNO_3$-impregnated silica gel column chromatography$^{7)}$ to give 1b (63 mg, colorless oil, $C_{25}H_{42}O_3$), 1c (340 mg, colorless oil, $C_{27}H_{44}O_3$) and 1d (363 mg, colorless oil, $C_{27}H_{42}O_3$).



1a-d R^2= H
3a-d R^2= $COCH_3$



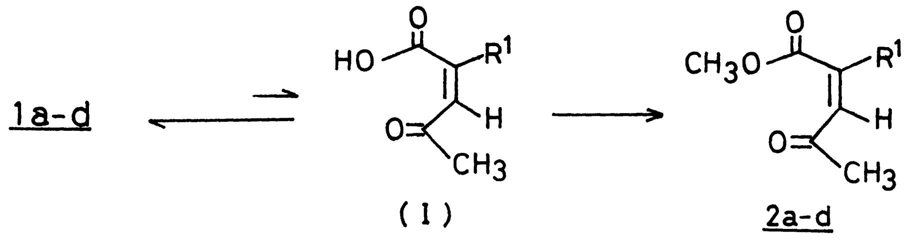
The IR, ^1H-NMR and ^{13}C-NMR spectra of 1a-d as shown in the Table suggest that all these compounds possess an α,β-unsaturated γ-lactone (butenolide) moiety to which a hydroxyl group, a methyl group, and a saturated or unsaturated straight-chain hydrocarbon group ($C_{16}H_{33}$- for 1a, $C_{20}H_{37}$- for 1b, $C_{22}H_{39}$- for 1c and $C_{22}H_{37}$- for 1d) are attached. In each compound, the ^1H-NMR signal at δ 6.76-6.78 ppm assignable to an olefinic proton at the β-position (C-3) of the α,β-unsaturated carbonyl system reveals that the above-mentioned groups are located at C-2 and C-4 positions on the butenolide ring. The ^{13}C-NMR signals at δ 104-5 ppm (s) assignable to a quarternary carbon bearing two oxygen atoms indicate that the hydroxyl group and either of the methyl or long chain hydrocarbon group are attached at C-4 position. The location of these groups are determined by the following chemical reaction. Treatment of 1a-d with diazomethane gave the methylketones (2a-d)[8]. This result established the position of the methyl group at C-4 as well as the long chain hydrocarbon group at C-2. The formation of 2a-d was explained by the presence of an equilibrium between the lactol (1a-d) and their corresponding keto carboxylic acid (I)[9] (Scheme).

Acetylation of the lactol (1a-d) with acetic anhydride in pyridine gave the corresponding acetates (3a-d)[10] which showed an acetylation shift[11] in the ^{13}C-NMR spectra, providing a further evidence for the arrangement of the substituents on the lactol moiety. On going from 1b to 3b, for example, the signals of both C-4 (104.7 ppm) and C-2 (136.3 ppm) of 1b shifted to lower field by +1.0 and 0.3 ppm, respectively, while the olefinic carbon signal at C-3 (146.6 ppm) of 1b appeared at higher field by -1.9 ppm in 3b.

With respect to the unsaturated long chain hydrocarbon moiety of 1b-d, the presence of $-CH=CH-CH_2-CH=CH-$ for 1b, $-CH=CH-CH_2-CH=CH-CH_2-CH=CH-$ for 1c and $(-CH=CH-CH_2-CH=CH-)_2CH_2$ for 1d was shown by the ^1H-NMR signals at δ 2.76 (2H) of

Table. Spectral data of 1a-d

	1a	1b	1c	1d
IR($CHCl_3$) cm^{-1}	3560, 1760, 1655	3560, 1760, 1655	3565, 1765, 1655	3565, 1765, 1655
^{1}H-NMR($CDCl_3$) δ ppm	0.88(3H,t)	0.89(3H,t)	0.86(3H,t)	0.89(3H,t)
	1.25(28H,brs)	1.28(22H,brs)	1.30(20H,brs)	1.30, 1.35(14H,brs)
	1.68(3H,s)	1.68(3H,s)	1.69(3H,s)	1.69(3H,s)
		2.05(4H,brd)	2.05(4H,brd)	2.05(4H,brd)
	2.20(2H,brt)	2.25(2H,brt)	2.25(2H,brt)	2.25(2H,brt)
		2.76(2H,t)	2.80(4H,t)	2.80(6H,brt)
		5.35(4H,m)	5.35(6H,m)	5.35(8H,m)
	6.78(1H,t,J=2 Hz)	6.77(1H,t,J=2 Hz)	6.76(1H,t,J=2 Hz)	6.78(1H,t,J=2 Hz)
^{13}C-NMR($CDCl_3$) δ ppm	14.1(q), 24.7(q) 31.9(t),105.0(s) 135.8(s),147.3(d) 172.4(s)	14.1(q), 24.9(q) 25.7(t), 31.5(t) 104.7(s) 127.9(d,2C) 130.1(d,2C) 136.3(s),146.6(d) 171.4(s)	14.1(q), 24.9(q) 25.7(t,2C) 31.5(t) 105.1(s) 127.7(d,2C) 128.2(d,2C) 130.3(d,2C) 136.1(s),146.9(d) 171.8(s)	14.1(q), 24.9(q) 25.7(t,3C) 31.5(t) 104.8(s),127.5(d) 127.8(d),127.9(d) 128.3(d),128.5(d,2C) 130.1(d),130.4(d) 136.1(s),146.8(d) 171.6(s)



Scheme

1b, 2.80 (4H) of 1c and 2.80 (6H) of 1d which are assignable to the methylene protons deshielded by two allylic double bonds. The position of the double bonds as shown in the structures 1b-d was elucidated by chemical degradation of 1b-d. Ozonolysis of 1b followed by methylation with diazomethane yielded methyl n-undecanoate as checked by GC-MS. On similar experiments methyl n-caprate was obtained from both 1c and 1d. The Z-type geometry of all carbon-carbon double bonds in the hydrocarbon chain of 1b-d was deduced from the ^{13}C-NMR spectra. The resonance at 25.7 ppm, integrating a carbon atom for 1b, two carbon atoms for 1c and three carbon atoms for 1d (Table), are characteristic for methylene carbons shielded by two allylic Z-double bonds.[12)]

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5) Column chromatography was repeated three times by using the following eluting solvent systems; 1) hexane-AcOEt (10:1 then 3:1), 2) C_6H_6-AcOEt(15:1) and 3) C_6H_6-AcOEt (10:1).

6) All new compounds gave satisfactory high resolution mass measurements, and the $[\alpha]_D$ value of these compounds was zero.

7) Silica gel (300 g) was suspended in 600 ml of 10 % aqueous $AgNO_3$ solution, and activated at 180°C for 3 h. Hexane-acetone mixture (6:1, 4:1 and then 3:1) was used as an eluting solvent.

8) 2a: colorless rods (mp 49-53°C); IR($CHCl_3$) 1720, 1690, 1620 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.84(3H,t) 2.23(3H,s), 2.32(2H,brt), 3.79(3H,s), 6.12(1H,t,J=1.8 Hz).
   2b: colorless oil: IR($CHCl_3$) 1720, 1685, 1610 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.89(3H,t), 2.21(3H,s) 2.76(2H,t,J=6 Hz), 3.75(3H,s), 5.29(4H,m), 6.09(1H,t,J=1.5 Hz).
   2c: colorless oil; IR($CHCl_3$) 1720, 1685, 1610 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.89(3H,t), 2.22(3H,s) 2.81(4H,t,J=6 Hz), 3.78(3H,s), 5.36(6H,m), 6.11(1H,t,J=2 Hz).
   2d: colorless oil; IR($CHCl_3$) 1720, 1685, 1610 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.86(3H,t), 2.22(3H,s) 2.81(6H,brt), 3.78(3H,s), 5.37(8H,m), 6.11(1H,t,J=1.5 Hz).

9) The compounds (1a-d) almost exist as a lactol form in a $CHCl_3$ or $CDCl_3$ solution.

10) 3a: colorless rods (mp 48-53°C); IR($CHCl_3$) 1765, 1730 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.86(3H,t) 1.80(3H,s), 2.05(3H,s), 2.28(2H,brt), 7.15(1H,t,J=2 Hz).
   3b: colorless oil; IR($CHCl_3$) 1770, 1730 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.89(3H,t), 1.80(3H,s), 2.03 (3H,s), 2.75(2H,t,J=6 Hz), 5.34(4H,m), 7.14(1H,t,J=2 Hz).
   3c: colorless oil; IR($CHCl_3$) 1775, 1735 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.89(3H,t), 1.79(3H,s), 2.02 (3H,s), 2.79(4H,t,J=6 Hz), 5.35(6H,m), 7.15(1H,t,J=2 Hz).
   3d: colorless oil; IR($CHCl_3$) 1770, 1730 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ_{ppm} 0.89(3H,t), 1.79(3H,s), 2.05 (3H,s), 2.82(6H,brt), 5.36(8H,m), 7.15(1H,t,J=2 Hz).

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