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TERPENOIDS—LXXII[1]

CHEMICAL STUDIES OF MARINE INVERTEBRATES—XXVI[2] $\Delta^{9(12)}$-CAPNELLENE-3β,8β,10α,14-TETROL, A NOVEL POLYOXYGENATED SESQUITERPENE FROM THE ALCYONARIAN *CAPNELLA IMBRICATA*

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Abstract—The structure determination of the new sesquiterpene, $\Delta^{9(12)}$-capnellene-3β,8β,10α,14-tetrol 1, is described.

In previous publications,[1,3] we described the isolation and structure determination of four representatives of the hitherto unknown capnellane skeleton from the soft coral *Capnella imbricata*. We wish now to report the structure determination of a fifth highly oxygenated member of this class of sesquiterpenes, the tetrol 1 so far only found in samples collected at Leti, Province of Maluku, Indonesia, and absent in *Capnella* collected from many other localities.[1]

The NMR spectrum (1:1 mixture of d_5-pyridine and D_2O) of tetrol 1 ($C_{15}H_{24}O_4$; IR 3400 (OH), 905 cm^{-1} (C=CH$_2$)) suggests the presence of two tertiary methyl groups (s, 3H each at 1.42 and 1.68), one primary (dd, 2H at 3.82), one allylic secondary (m, 1H at 5.33), one secondary non-allylic hydroxyl groups (m, 1H at 4.6) and one vinylic methylene (m, 2H at 5.40).

Acetylation of 1 furnished the triacetate 2 whose IR spectrum (ν_{OH} at 3.500 cm^{-1}) implies the presence of a tertiary alcohol. Its NMR is similar to that of $\Delta^{9(12)}$-capnellene-3β,8β,10α-triol diacetate 3[1] but shows clearly that hydroxylation of one of the tertiary methyl groups of 3 had occurred (AB system centered at 4.1 ppm). This was further substantiated by the ^{13}C NMR spectrum of 1 wherein one of the three tertiary methyl group signals of the capnellane skeleton is lacking and replaced by one triplet at 73.84 ppm. Oxidation of 1 with manganese dioxide furnished the oily α,β-unsaturated ketone 4, thus confirming the presence of an allylic secondary alcohol. The capnellane skeleton of 1 was established by the following reaction sequence: Li/NH$_3$ reduction of 4 afforded the keto-triol 5 which, without preliminary purification, was dehydrated to the α,β-unsaturated ketone 6. Li/NH$_3$ reduction of 6 yielded the saturated keto-diol 7 (IR 1720 cm^{-1}) which upon tosylation (*p*-TsCl/pyridine) to the ditosylate 8 and immediate reduction with LiAlH$_4$ in THF under reflux, led to capnellane-8β-ol 9. Jones oxidation of 9 yielded the monoketone 10 identical (IR, GC and MS) with the ketone derived from the previously described $\Delta^{9(12)}$-capnellene-8β,10α-diol 11.[1] This established the nature of the skeleton of 1 and also the position of unsaturation at 9(12), a secondary hydroxyl at C-8 and a tertiary hydroxyl at C-10.

There remained only the location of the secondary non-allylic and primary alcohols. The primary hydroxyl function in 1 could only be attached to carbon atoms C-13, C-14 or C-15. The presence of a primary hydroxyl group at either C-14 or C-15 rather than C-13 was indicated as follows: Jones oxidation of 7 afforded the diketo-acid 12 (M$^+$ 264) which could not be decarboxylated under acidic conditions (*p*-toluenesulfonic acid; 2N HCl) thus excluding C-13 as the site of the primary hydroxyl group. This conclusion could be further substantiated by Fetizon oxidation of 7 to the diketo-aldehyde 13 (M$^+$ 246) which could not be deformylated under either acidic or basic conditions.

Moreover, the mass spectra of 7, 12, 14 and 13 displayed peaks at *m/e* 101 ($C_5H_9O_2$, 13%); 114 ($C_5H_6O_3$, 70%) 128 ($C_6H_8O_3$, 100%) and 98 ($C_5H_6O_2$, 63%), respectively. The generation of such ions is only consistent with the cleavage of the C_1–C_{11} and C_7–C_8 bonds, thereby strongly suggesting the presence of a primary hydroxyl group at C-14 or C-15, and a secondary hydroxyl group at C-3.

The existence of a secondary hydroxyl group in ring A at position 3 was reinforced by the following considerations: ^{1}H-NMR spectra of 1 and 2 depicted the presence of a non-allylic secondary carbinol group (m at

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4.6† and 5.15 ppm, respectively). These chemical shifts are comparable with those of compounds **15** and **3** (4.13 and 1.50 ppm), and different from those of compounds **16** and **17** (3.86 and 4.63 ppm).[1] The ^{13}C NMR spectrum of **1** also agrees with these assignments (C-3: 81.01 ppm in **1** and 81.4 ppm in **15**).

The complete structure of **1** was established by single crystal X-ray diffraction analysis. Crystals of **1** belong to the space group $p2_12_12_1$ with $a = 18.44$, $b = 13.20$, $c = 6.51$ Å, $Z = 4$. There are also eight water molecules in the unit cell. A total of 979 independent X-ray intensities with $\theta < 50°$ were collected with Cu K_α radiation on a diffractometer. The structure was solved by direct methods and refined with isotropic thermal parameters (Table 1) by full-matrix least-squares to the conventional residual $R = 0.12$. The tetrol, given the same absolute configuration as $\Delta^{9(12)}$-capnellene-3β,8β,10α-triol **15**,[4] has similar conformation angles as one of the two independent molecules in the crystal structure of **15** (Fig. 1). There is one intramolecular hydrogen bond, O(4)–H···O(3), of 2.762(4) Å and seven other hydrogen bonds ranging from 2.73 to 2.81 Å. Thus all OH hydrogens are involved in hydrogen bonds.

Several other representatives of the capnellane class of sesquiterpenes are currently being investigated.

Table 1. Atomic coordinates (×10⁴) and thermal parameters (×10 Å²) with e.s.d.'s in parentheses

	X	Y	Z	B
C(1)	3681(7)	5624(10)	28(2)	34(3)
C(2)	3066(6)	6400(9)	−6(2)	28(3)
C(3)	3491(6)	7402(9)	19(2)	25(2)
C(4)	4192(7)	7281(10)	−112(2)	31(3)
C(5)	4863(7)	7789(10)	−13(2)	31(3)
C(6)	5318(6)	6939(9)	91(2)	24(3)
C(7)	6144(7)	7094(11)	69(3)	43(3)
C(8)	6341(7)	6566(10)	−135(2)	33(3)
C(9)	5659(7)	5986(10)	−209(2)	29(2)
C(10)	5107(6)	5969(9)	−36(2)	26(3)
C(11)	4318(6)	6098(9)	−105(2)	22(2)
C(12)	5562(8)	5613(12)	−393(2)	43(3)
C(13)	4088(8)	7641(12)	333(2)	38(3)
C(14)	3472(7)	4593(10)	−57(2)	33(3)
C(15)	3824(7)	5516(10)	271(2)	35(3)
O(1)	3058(4)	8264(6)	−51(1)	36(2)
O(2)	6594(5)	7261(7)	−293(1)	38(2)
O(3)	5250(4)	5052(6)	88(1)	34(2)
O(4)	4082(4)	3902(6)	−38(1)	40(2)
O(W1)	1644(4)	421(6)	−223(1)	32(2)
O(W2)	2456(4)	8897(6)	413(1)	35(2)

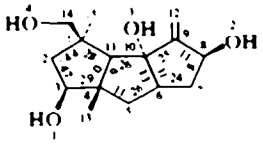
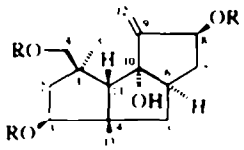
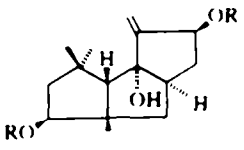


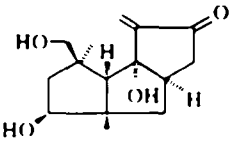
Fig. 1. Torsion angles for compound **1**.



1: R = H
2: R = OCOCH₃



3: R = OCOCH₃
15: R = H



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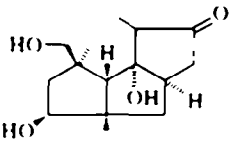

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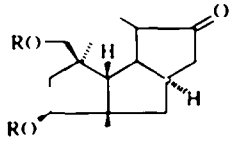
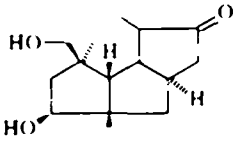


7: R = H
8: R = Ts



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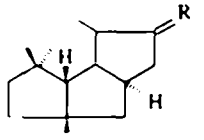
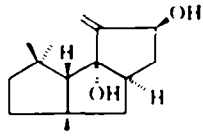


9: R = 
10: R = =O



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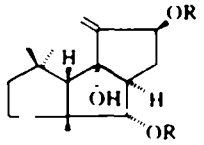
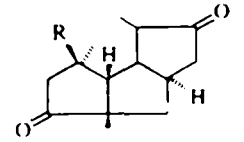


16: R = H
17: R = OCOCH₃



12: R = COOH
13: R = CHO
14: R = COOCH₃

Varian XL 100 spectrometer operating at 25.5 MHz. Mass spectra (direct inlet system) were obtained by Mr. R. Ross with an AEI MS-9 or an Atlas CH-4 spectrometer and all peaks of relative intensity greater than 5% are reported. Mass spectral high resolution measurements were made by Miss Annemarie Wegmann using a Varian MAT 711 spectrometer. All GC analyses were carried out at oven temp. of 150–200° using a Hewlett-Packard 402 high efficiency gas chromatograph equipped with all-glass U-tube columns packed with 3% OV25, OV17 or OV3 stationary phases coated over Gas-Chrom Q (100–120 mesh). All TLC was performed using Merck silica gel F_{254}, compounds were visualized with ceric sulfate 2% in $H_2SO_4$2N. All compounds were found to be homogeneous by TLC and GC.

The general procedure for the isolation of the sesquiterpene of *Capnella imbricata* has been described.[1]

$\Delta^{9(12)}$-*Capnellene*-3β,8β,10α,14-*tetrol* **1**: m.p. 192–5°; $[\alpha]_D^{20}$ + 70° (MeOH, $c = 0.32$) IR 3400 cm⁻¹; NMR (pyridine d_5/D_2O) 1.42, 1.68 (s, 3H each CH_3–C(CH₃)–), 3.82 (dd, 2H, CH_2OH), 4.60 (m, 1H, CHOH), 5.33 (m, 1H, =C–CHO), 5.40 (m, 2H, CH_2=); MS: *m/e* 250 (5%, M–H_2O), 232(6), 219(18), 211(4), 202(17), 201(12), 199(10), 198(40), 149(27), 139(20), 131(13), 125(40), 123(17), 121(22), 112(37), 108(57), 107(100), 96(25), 95(43), 91(20), 81(17), 79(20), 69(17), 55(30). ^{13}C NMR (TMS, MeOH): C-1(44.10), C-2(46.66), C-3(81.01), C-4(52.42), C-5(45.95), C-6(50.10), C-7(38.44), C-

EXPERIMENTAL

M.ps (Kofler) are uncorrected. All rotations and IR spectra were determined in chloroform solution. CD spectra were measured in MeOH. All NMR spectra were recorded ($CDCl_3$, unless otherwise mentioned, with TMS as internal standard) on a Varian T-60 or XL-100 spectrometer; all chemical shifts are reported in δ values. ^{13}C NMR spectra were recorded using a

†This spectrum was recorded in 1:1 pyridine d_5-D_2O solution.

8(73.84), C-9(161.90), C-10(89.11), C-11(63.54), C-12(109.09), C-13(24.80), C-14(73.84), C-15(21.96). On acetylation compound 1 furnished the triacetate 2: m.p. 122°; IR 1740 cm^{-1}; NMR: 0.95, 1.35 (s, 3H each, CH_3–C), 2.05 (s, 6H, 2x CH_3COO), 2.10 (s, 3H, CH_3COO), 4.10 (dd, 2H, CH_2OAc), 5.15 (m, 1H, CHOAc), 5.40 (bs, 2H, CH_2=), 5.83 (m, 1H, =C–CHOAc); MS: *m/e* 376 (1%, M–H_2O), 334 (13, M–CH_3COOH), 292(3), 274(27), 261(5), 214(13), 201(10), 181(7), 167(21), 121(4), 120(30), 108(55), 107(88), 94(49), 43(100).

$\Delta^{9(12)}$-Capnellene-3β,10α,14-triol-8-one **4**. To compound **1** (100 mg) dissolved in warm chloroform (200 ml) was added 1 g of active manganese dioxide, and the mixture stirred at room temp. in the dark overnight. After filtration and evaporation of the solvent, the residue was purified by preparative TLC to give oily **4**: IR: 1700 cm^{-1} (C=O); CD: $[\theta]_{360}$ + 375, $[\theta]_{317}$ – 3718, $[\theta]_{290}$ + 8880; NMR ($CDCl_3$-acetone d_6): 0.90, 1.42 (s, 3H each, CH_3–C), 3.30 (dd, 2H, CH_2OH), 4.26 (m, 1H, CHOH), 5.58, 6.16 (s, 1H each, CH_2=C); MS: *m/e* 266 (2%, M⁺), 248(3), 149(9), 143(5), 101(5), 91(6), 83(6), 81(3), 74(4), 71(5), 69(5), 59(55), 58(11), 57(10), 56(5), 55(10), 43(100).

On acetylation compound **4** furnished a diacetate: oil, IR: 1715 cm^{-1} (C=O); NMR: 0.80, 1.40 (s, 3H each, CH_3–C), 2.03, 2.10 (s, 3H each, CH_3COO), 4.28 (dd, J = 11, 14 Hz, 2H, CH_2OAc), 5.13 (m, 1H, CHOAc), 5.50, 6.20 (s, 1H each, CH_2=C).

Δ^{9}-Capnellene-3β,14-diol-8-one **6**. To a soln of Li (100–150 mg) in 100 ml of liquid ammonia was added a soln of **4** (100 mg) in tetrahydrofurane (25–40 ml). After 30 min., solid ammonium chloride was slowly added until the blue soln decolorized. The ammonia was allowed to evaporate; water (50 ml) and ether (100 ml) were added and the mixture stirred vigorously for 10 min. After separation and drying over Na_2SO_4, the ether layer was evaporated to an oily residue. Crude **5** was dissolved in methanol (15 ml) to which five drops of 10% KOH were added, and the mixture stirred at room temp. for 6 h. The soln was then poured into equal volume of water and extracted twice with ethyl acetate (2 × 50 ml), washed with water, dried over Na_2SO_4, and evaporated to a gum which was purified by preparative TLC, to yield oily **6**: IR: 1715 cm^{-1} (C=O); NMR: 0.86, 1.10 (s, 3H each, CH_3–C), 1.66 (d, J = 1.5 Hz, 3H, CH_3–C=C), 3.50 (m, 2H, CH_2OH), 4.0 (m, 1H, CHOH); MS: *m/e* 250 (23%, M⁺), 233(4), 232(20), 202(22), 179(12), 178(17), 175(11), 174(12), 161(17), 160(15), 159(11), 150(18), 149(20), 135(15), 133(14), 111(20), 109(24), 107(19), 105(22), . . . 43(100).

Conversion of Δ^{9}-capnellene-3β,14-diol-8-one **6** *to capnellan-8-one* **10**. Li/NH_3 reduction of **6** (see above for experimental procedure) furnished oily capnellane-3β,14-diol-8-one **7**: IR: 1720 cm^{-1}; MS: *m/e* 252.17384 (17%, M⁺ calculated for $C_{15}H_{24}O_3$: 252.17253) 234(9), 204(100), 177(39), 161(15), 135(15), 133(20), 121(24), 119(15), 109(42), 101(13), 94(40), 93(41), 91(29), 83(28), 79(31), 77(21), ...

On tosylation (*p*-TsCl/pyridine) compound **7** furnished a ditosylate **8**, which was reduced directly with $LiAlH_4$ in THF under reflux for 6 h to provide **9**, which was oxidized with Jones reagent to **10** identical (GC, MS and IR) with the ketone derived from $\Delta^{9(12)}$-capnellane-8β,10α-diol **15**.[1]

Jones oxidation of **7**. To a solution of the keto-diol **7** (5 mg) in acetone (5 ml) was added Jones reagent dropwise at room temp. for 15 min. The mixture was poured into water, extracted with ethyl acetate, washed with water, dried over Na_2SO_4 and evaporated to a gum. The analysis of this gum by TLC depicted one broad spot typical of a free carboxylic acid. To the gum were added methanol (40 ml) and HCl (10N, 1 ml). The mixture was refluxed for 24 h, poured into ice and extracted with ethyl acetate. Preparative TLC furnished the more mobile diketo-ester **14** and the less mobile diketo-acid **12**.

3,8-Dioxocapnellan-14-oic acid **12**. IR: 1710–1730 cm^{-1} (C=O); MS: *m/e* 264 (5%, M⁺), 151(100), 128(10), 114(70), 109(17), 107(25), 95(15), 94(14), 93(20), 91(9), 86(46), 81(7), 79(14), 77(8), 69(10). . . .

Methyl 3,8-dioxocapnellan-14-oate **14**. IR: 1735 cm^{-1} (C=O); MS: *m/e* 278.15039 (M⁺, calculated for $C_{16}H_{22}O_4$: 278.15179), 128.04734 ($C_6H_8O_3$), 107(11), 100(24), 73(10), 69(17), 61(26), 45(27), 43(33).

The decarboxylation of **12** with *p*-TsOH and 2N HCl was attempted but in every case **12** was recovered unchanged.

Fetizon oxidation[3] of the keto-diol **7**. A mixture of **7** (5 mg), Fetizon reagent (300 mg) and benzene (50 ml) was heated under reflux for 7 h. A portion (10 ml) of the benzene was distilled, but the remaining solution, when checked by TLC, depicted much unreacted starting material. The mixture was then refluxed for additional 72 h during which period almost all benzene was distilled. Preparative TLC of the residue furnished the oily 3,8-dioxo-capnellan-14-al **13**: IR: 1725 cm^{-1} (C=O); MS: *m/e* 248.14102 (6%, M⁺, calculated for $C_{15}H_{20}O_3$: 248.14123); 204(22), 151(31), 133(10), 108(28), 107(100), 98(63), 95(22), 94(49), 93(29), 91(18), 79(23), 77(15), 69(53).

This aldehyde could not be deformylated by heating with *p*-TsOH (in benzene) or aq KOH (in methanol).

Gas chromatographic retention times† relative to compound **1**, of compounds **7**, **10**, **12** and **14**

Compound No.	Relative retention time
1	1.00
4	1.10
10	0.20
12	0.65
14	0.41

†Over OV-3 3% on gas chrom Q (100–120), oven temp. 190° det. 290 inj. 260.

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