164. Sarcodictyenone, a Ring-Reduced, Optically Active Linear Tetraprenylquinone from the Mediterranean Stolonifer *Sarcodictyon roseum* (= *Rolandia rosea*)

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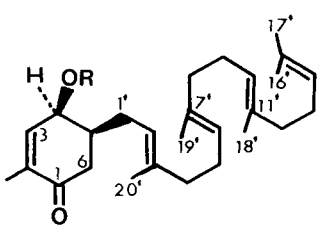
The Mediterranean stolonifer *Sarcodictyon roseum* (= *Rolandia rosea*) (Cnidaria, Anthozoa, Alcyonaria, Stolonifera, Clavulariidae) contains the first example of a chiral, optically active prenyl derivative of a reduced benzoquinone, sarcodictyenone (= (+)-(4*R**,5*R**)-5-geranylgeranyl-4-hydroxy-2-methylcyclohex-2-en-1-one; (+)-**1a**).

1. Introduction. – Amongst the various marine terpenoids of mixed biogenesis [1], polyprenylquinones and hydroquinones occupy a large area. Most such compounds have been isolated from either marine plants of the class Phaeophyceae, order Fucales [1b] [1d], or marine sponges of the class Demospongiae, order Dictyoceratida [1a]. A few such compounds have also been isolated from marine, tropical cnidarians of the class Anthozoa, orders Alcyonacea (*Nephthea* sp.) [2a] and Gorgonacea (*Plexaura flava*) [2b] or Tunicata of the class Ascidiacea, order Aplousobranchia (*Aplidium californicum* [3a] and *A. cavernosa* [3b]).

Here, we report on the tetraprenylated cyclohexenone sarcodictyenone ((+)-**1a**) isolated from *Sarcodictyon roseum* (= *Rolandia rosea* (PHILIPPI)), phylum Coelenterata (*Frey* and *Leuckart*, 1847), order Stolonifera (*Hickson*, 1883), family Clavulariidae (*Hickson*, 1894) [4], of temperate waters. This is the first example, at least as regards the marine environment, of a natural product of formal reduction of a prenylated hydroquinone (or quinone) which, because of this, is optically active.

2. Results and Discussion. – The high-resolution MS of sarcodictyenone gives the formula $C_{27}H_{42}O_2$, implying seven unsaturations, whilst at low-resolution, there is evidence (MS MS B/E linked scans [5]) for the primary loss of a H_2O molecule from the



(+)-**1a** R = H
1b R = *p*-CN-C_6H_5CO

molecular ion. The presence of an OH function is confirmed by a 3420-cm^{-1} absorption band in the IR spectrum which also suggests an α,β-unsaturated ketone CO group (1650 cm^{-1}). The latter system is clearly seen in the ^{13}C-NMR spectrum (*s* at 199.60 for CO, *d* at 143.30 for C(β), which must, therefore, bear a H-atom). Such functionalities can be put together in a γ-hydroxylated cyclohexenone ring bearing a side chain as shown in structure (+)-**1a**, on the basis of three series of ^{1}H-NMR observations, *i.e.* double irradiations, NOE effects, and shift-reagent effects.

First of all, there are some informative double irradiations in the ^{1}H-NMR. Thus, on irradiation at H–C(3), the br. *s* at 1.80 ppm for Me-C(2) becomes a *d* with J(Me,4) = 1.0 Hz whilst the br. *s* at 4.36 ppm for H–C(4) sharpens. Irradiation at H–C(4) results in the three following events: (*i*) br. *s* of Me-C(2) becomes a *d* with J(Me,3) = 1.3 Hz, (*ii*) a coupling (J(5,4) = 3.5 Hz) disappears from the partially emerging *m* at 2.16 ppm for H–C(5), and (*iii*) the *dq* at 6.70 ppm for H–C(3) becomes a *q* with J(3,Me) = 1.3 Hz. On irradiation at Me–C(2), the *dq* at 6.70 ppm (H–C(3)) becomes a *d* with J(3,4) = 5.2 Hz, whilst the br. *s* at 4.36 ppm (H–C(4)) becomes a *dd* with J(4,3) = 5.2 and J(4,5) = 3.5 Hz. Finally, on irradiation at H–C(5), the br. *s* at 4.36 ppm for H–C(4) becomes a *dq* (J(4,3) = 5.2, J(4,7) = 1.0 Hz), whilst the two *dd* for the CH_2(6) give origin to an *AB* system with J_{gem} = 16.5 Hz.

Second, there are revealing NOE effects. In fact, on irradiation at H–C(3), there are 8 and 3% positive enhancements on H–C(4) and Me–C(2), respectively, which further prove the connectivities suggested above. Most important, on irradiation at H–C(4), there are 13 and 6% positive enhancements at H–C(3) and H–C(5), respectively, in accordance with the relative configurations at C(4) and C(5) in (+)-**1a**. This is confirmed by shift-reagent effects at a Eu(fod)$_3$/sarcodictyenone ((+)-**1a**) molar ratio of 0.2 as follows: $\Delta\delta$ = 0.60 on both H–C(4) and H$_\beta$–C(6), 0.50 on H$_\alpha$–C(6), 0.37 on H–C(3), 0.30 on both Me–C(2) and 2H–C(1'), 0.15 on H–C(2'), and 0.08 ppm on Me–C(3'). The fact that H$_\beta$–C(6) undergoes a larger deshielding than H–C(3) indicates the pseudoaxial position for the OH group, in accordance with the above NOE effects on irradiation at H–C(4). These shift-reagent effects allow us to extend the side chain up to C(3'). The side chain can then be completed as shown in structure (+)-**1a** on the close analogy of the relevant ^{13}C-NMR resonances with those for geranylgeraniol.

All these assignments were further supported by an unambiguous relation of every C-atom to the directly bound H-atoms as shown *via* ^1J(C,H)-HETCOR experiments [6].

In an unsuccessful attempt to define the absolute configuration of (+)-**1a** by CD spectroscopy *via* exciton coupling [7] on the basis of a suitable enone model [8], we have transformed (+)-**1a** to the *p*-cyanobenzoate **1b**. However, the CD of **1b** (see *Exper. Part*) fails to show the expected exciton coupling, as two CD bands of extremely different intensity are observed in the relevant region (241 and 222 nm). This does not allow any safe conclusion about the absolute configuration of (+)-**1a**.

Among the Stolonifera, the only genus so far investigated has been *Clavularia* of either tropical [9] or Japanese [10] waters. These animals were found to contain two classes of natural products. One class comprises terpenoids such as aromadendrane and copaane sesquiterpenoids [9a], degraded sesquiterpenoids of trinor-guaiane type [10a], which have also been synthesized [10b], dolastane [9b] and methyl-migrated dolabellane [9c] diterpenoids, and a 22,23-cyclopropano-5b,6β-epoxy-18-nor-2-en-1-on steroid [10c]. New eicosanoids (clavulones = claviredones [10d] or chloroclavulones, *i.e.* clavulones bearing an α-Cl-atom on the cyclopentenone moiety [10e]) constitute the other class of compounds. Interestingly, some new clavulones have been isolated in the course of biosynthetic experiments with cell-free extracts [11]. The hydrocarbon inflatene has finally to be mentioned, having also been isolated from a tropical animal of this genus [12].

Neither a metabolite similar to (+)-**1a** nor one of the common [1–3] prenylquinones or -hydroquinones, which might be thought as precursors of (+)-**1a**, have been previously

isolated from Stolonifera. As achiral prenylquinones and -hydroquinones frequently display interesting bioactivities [1–3], one wonders whether the chirality introduced in (+)-**1a** serves a particular biological role. Actually, in our hands, raw extracts of *S. roseum* proved inactive against phytopathogenic fungi and bacteria. However, no other biotest has been carried out.

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Experimental Part

1. *General.* Column and flash chromatography: *Merck* silica gel *60* (70–230 mesh) and *Merck-LiChrosorb RP18* (40–65 μm), respectively. HPLC: 25 × 1 cm *Merck-LiChrosorb RP8* (7 μm) column, 5 ml/min solvent flux, monitoring by UV at 254 nm. [α]: *JASCO-DP-181* polarimeter. UV (λ_{max} in nm, ε in mol^{-1} l cm^{-1}) and IR ($\tilde{\nu}_{max}$ in cm^{-1}): *Perkin-Elmer-Lambda-3* and *Pye-Unicam-SP3-100* spectrometer, respectively. MS (EI; *m/z* (%)): home-built spectrometer based on the *ELFS-4-162-8-Extranuclear* quadrupole (low-resolution experiments) or *VG ZAB2F* (high-resolution and MS MS B/E linked scan experiments [5]). NMR: *Varian XL-300* (^{13}C-NMR at 75.43 MHz, ^{1}H-NMR at 300 MHz); δ (ppm) relative to internal Me_4Si (= 0 ppm) and *J* in Hz.

2. *Isolation. S. roseum* was collected by scuba diving in the East Pyrenean area at depths of 20–35 m in August 1985. The animal and the gorgonian skeleton on which it grows, pushing the gorgonian away, were cut into small pieces so as to fill a 5-l flask and then extracted with EtOH. Evaporation and extraction with petroleum ether gave a dark oil (5 g) which was chromatographed on silica gel (gradient elution: petroleum ether/AcOEt). Central fractions were flash chromatographed with acetone in order to eliminate sterols. HPLC with CH_3CN/H_2O 8:2 gave sarcodictyenone ((+)-**1a**; 0.007 g).

3. *Sarcodictyenone* (= *(+)-(4R*,5R*)-4-Hydroxy-2-methyl-5-[(2E,6E,10E)-3,7,11,15-tetramethylhexadeca-2,6,10,14-tetraenyl]cyclohex-2-en-1-one;* (+)-**1a**). Colourless semisolid. $[\alpha]_D = +52.0°$, $[\alpha]_{577} = +55.0°$, $[\alpha]_{546} = +65.7°$, $[\alpha]_{435} = +103.4°$ (23°, *c* = 0.17, EtOH). UV (EtOH): 203 (25000), 229 (8500). IR (film): 3420*s*, 1650*s*, 1430*m*. ^{1}H-NMR ($CDCl_3$): 1.60 (br. *s*, 3 H–C(16′), 3 H–C(18′), 3 H–C(19′)); 1.63 (br. *s*, 3 H–C(20′)); 1.68 (br. *s*, 3 H–C(17′)); 1.80 (br. *s*, CH_3–C(2)); 1.93–2.13 (series of *m*, 1 H–C(1′), 2 H–C(4′), 2 H–C(5′), 2 H–C(8′), 2 H–C(9′), 2 H–C(12′), 2 H–C(13′)); 2.16 (partially emerging *m*, H–C(5)); 2.26 (br. *ddd*, $J_{gem} = 13.5$, $J(1',5) = J(1',2') = 6.5$, 1 H–C(1′)); 2.37 (*dd*, $J_{gem} = 16.5$, $J(6\alpha,5) = 3.9$, H_α–C(6)); 2.51 (*dd*, $J_{gem} = 16.5$, $J(6\beta,5) = 10.4$, H_β–C(6)); 4.36 (br. *s*, H–C(4)); 5.10 (*m*, H–C(6′), H–C(10′), H–C(14′)); 5.14 (br. *t*, $J(2',1') = 6.5$, partially submerged by the previous signal, H–C(2′)); 6.70 (*dq*, $J(3,4) = 5.2$, $J(3,Me) = 1.3$). ^{13}C-NMR ($CDCl_3$; multiplicities from APT [13] experiments): 15.72 (*q*, CH_3–C(2)); 16.07, 16.03 (2 *q*, C(18′), C(19′)); 16.22 (*q*, C(20′)); 17.71 (*q*, C(16′)); 25.73 (*q*, C(17′)); 26.50, 26.62, 26.77 (3 *t*, C(5′), C(9′), C(13′)); 28.92 (*t*, C(1′)); 39.13 (*t*, C(6)); 39.69, 39.76, 39.81 (3 *t*, C(4′), C(8′), C(12′)); 40.20 (*d*, C(5)); 66.31 (*d*, C(4)); 121.03 (*d*, C(2′)); 123.94, 124.18, 124.38 (3 *d*, C(6′), C(10′), C(14′)); 131.33 (*s*, C(15′)); 135.00, 135.31, 137.07, 137.86 (4 *s*, C(2), C(3′), C(7′), C(11′)); 143.30 (*d*, C(3)); 199.60 (*s*, C(1)). MS: 398 (11, M^+), 380 (2, $M^+ - H_2O$), 355 (2), 329 (4), 175 (27), 161 (25), 121 (75), 95 (72), 93 (78), 69 (100). B/E on M^+: 380 and 355. HR-MS: 398.3198 ± 0.01 ($C_{27}H_{42}O_2$, calc. 398.3185).

4. *Sarcodictyenone* p-*Cyanobenzoate* (= *(1R*,6R*)-3-Methyl-4-oxo-6-[(2E,6E,10E)-3,7,11,15-tetramethylhexadeca-2,6,10,14-tetraenyl]cyclohex-2-enyl* p-*Cyanobenzoate;* **1b**). Colourless oil. CD (EtOH, $4.45 \cdot 10^{-5}$ M; $\Delta\varepsilon$ [mol^{-1} lcm^{-1}]: 222 (−0.09), 241 (+2.02, max.), 323 (−0.03). UV (EtOH): 203.8 (36500), 240 (26200). ^{1}H-NMR ($CDCl_3$): 1.48 (br. *s*, 3 H–C(20′)); 1.59 (br. *s*, 3 H–C(16′), 3 H–C(18′), 3 H–C(19′)); 1.68 (br. *s*, 3 H–C(17′)); 1.83 (br. *s*, CH_3–C(2)); 1.92–2.10 (series of *m*, 2 H–C(4′), 2 H–C(5′), 2 H–C(8′), 2 H–C(9′), 2 H–C(12′), 2 H–C(13′)); 2.12 (partially submerged) and 2.28 (2 *ddd*, $J_{gem} = 14.3$, $J(1',2') = J(1',5) = 7.0$, 2 H–C(1′)); 2.42 (*m*, H–C(5)); 2.58 (*dd*, $J_{gem} = 16.3$, $J(6\alpha,5) = 4.5$, H_α–C(6)); 2.64 (*dd*, $J_{gem} = 16.3$, $J(6\beta,5) = 10.3$, H_β–C(6)); 5.10 (*m*, H–C(2′), H–C(6′), H–C(10′), H–C(14′)); 5.61 (br. *dd*, $J(4,3) = 4.9$, $J(4,5) = 3.0$, H–C(4)); 6.87 (*dq*, $J(3,4) = 4.9$, $J(3,Me) = 1.4$, H–C(3)); 7.77, 8.14 (*AB*, $J_o = 8.3$, arom. H).

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