

CHEMISTRY OF SPONGES, III.¹ MANOALIDE MONOACETATE AND THORECTOLIDE MONOACETATE, TWO NEW SESTERTERPENOIDS FROM *THORECTANDRA EXCAVATUS*

R.C. CAMBIE,* P.A. CRAW,

Department of Chemistry, University of Auckland, Auckland, New Zealand

P.R. BERGQUIST, and P. KARUSO

Department of Zoology, University of Auckland, Auckland, New Zealand

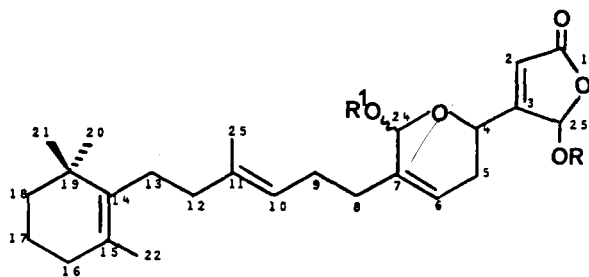
In a continuation of an investigation of the constituents of the Porifera for the purposes of chemotaxonomy (1), we have examined the sponge *Thorectandra excavatus* (Ridley) (order Dictyoceratida). The nomenclature applied to this sponge requires clarification because it represents a new combination in the literature. The species was originally assigned by Ridley to the genus *Stelospongos*. This was a new generic name introduced as a spelling correction (of the earlier *Stelospongos* Schmidt), and it is, thus, a synonym of *Stelospongos*. *Stelospongos* is unrecognizable (2), and, consequently, any species assigned to the genus, other than the type species *Stelospongos friabilis* Hyatt, must be reallocated. *Stelospongos excavatus* belongs in the genus *Thorectandra* Lendenfeld. The original specimen of this species, figured by Ridley, is in the British Museum (BMNH 82.2.23.211), and this specimen from the Arafura Sea is there designated as holotype. One other specimen referred to in Ridley's original description (3) was from Queensland and was interpreted by Ridley to be a juvenile. This small specimen is not *T. excavatus* but is *Dysidea herbacea*.

Chromatography of the light petroleum ether extract of one freeze-dried sponge gave a 0.07% yield of manoalide 25-monoacetate [1], whereas similar treatment of a second freeze-dried sponge gave a 0.15% yield of thorec-

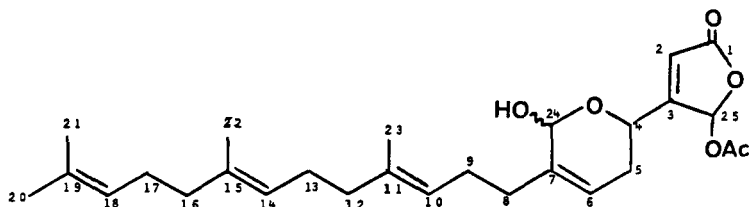
tolide 25-monoacetate [4] and none of compound 1. Extractions of several other individual sponges yielded mixtures of compounds 1 and 4. A similar variation of related constituents has recently been observed by Faulkner *et al.* (4) for the sponge *Luffariella variabilis* (order Dictyoceratida).

Manoalide monoacetate [1] crystallized from CH₂Cl₂/hexanes as flakes, mp 117–119°, [α]_D + 34°. Examination of the spectral data of this compound established that it was closely related to the pharmacologically active (5–7) sesterterpenoid manoalide [2] that has been isolated (8) from the related sponge *L. variabilis*. A molecular formula of C₂₇H₃₈O₆ for compound 1 was suggested by a weak molecular ion peak at *m/z* 458.2672 in the mass spectrum. The base peak at *m/z* 137 and fragment ions at *m/z* 121, 107, and 95 derived from the *m/z* 137 ion were diagnostic for the presence of a C₁₀H₁₇ [(trimethylcyclohexenyl)methyl] end group. The chemical shifts of the C₁₀H₁₇ end group in the ¹³C-nmr spectrum of compound 1 were in good agreement with those of the corresponding resonances for this subunit in the reported spectra of manoalide [2] (8) and also of hydroxymokupalide [5] (9). Furthermore, comparison with the chemical shifts of the α-acetyloxybutenolide terminus in the ¹³C-nmr spectrum of the acetate of mokupalide [6] (9) established that compound 1 corresponded to the monoacetate of manoalide in which the α-hydroxybutenolide rather than the δ-lactol moiety was acetylated (Table 1).

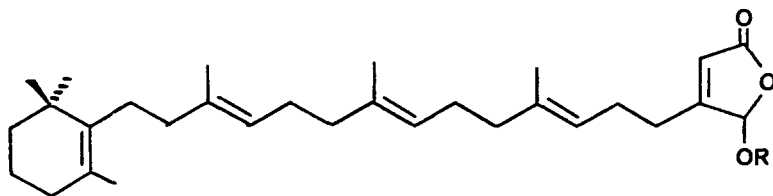
¹For Part II, see R.C. Cambie, P.A. Craw, P.R. Bergquist, and P. Karuso, *J. Nat. Prod.*, **50**, 948 (1987).



- 1** R = Ac, R¹ = H
2 R = R¹ = H
3 R = R¹ = Ac



4



- 5** R = H
6 R = Ac

The remaining ¹³C-nmr signals of compound **1** were in good agreement with those reported for manolide **2** (9). Finally, direct comparison of the ¹H-nmr (in C₆D₆),² ir, and mass spectra of the compound from *T. excavatus* with those of the two C-25 epimeric monoacetates prepared from manolide [**2**] (8) unequivocally established that it has the structure **1** and that it corresponded with the monoacetate "3b" of de Silva

and Scheuer (8). Lack of a recorded optical rotation for de Silva and Scheuer's monoacetate does not permit comment on whether or not the respective samples have the same absolute stereochemistry. Acetylation of manolide monoacetate [**1**] gave a diacetate [**3**]. Small differences in the ¹H-nmr spectrum from those recorded for the epimeric diacetates of manolide (9) can be accounted for by the use of different solvents for the respective determinations. Faulkner *et al.* (4) have commented on the high solvent dependency of the ¹H-nmr spectrum of manolide itself.

Thorectolide monoacetate [**4**] was isolated as an unstable waxy solid, [α]_D + 33°. A weak molecular ion at *m/z* 458.2662 in the mass spectrum of com-

²With the exception of the concentration-dependent hydroxyl proton, chemical shifts of all signals were at ca. 0.1 ppm higher field than those reported in Yunker and Scheuer (9). However, direct comparison with values from a figure of the ¹H-nmr spectrum of **1** from the Ph.D. thesis of D. de Silva (11) showed exact identity.

TABLE 1. Partial ^{13}C -nmr Resonances of Manoalide Monoacetate [1], Thorectolide Monoacetate [4], and Related Compounds.

Carbon	Compound					
	1	2(8)	3	4	5(9)	6(9)
1	169.5	172.3	169.6	169.6	172.1	169.6
2	118.8	117.7	119.2	118.5	117.1	118.3
3	165.8	169.1	164.6	165.9	169.9	166.6
25(30)	92.9	99.1	92.7	92.8	99.3	93.8
4	61.7	63.3	64.2	61.6		
5	32.6	33.1	32.8	32.4		
6	120.4	121.1	122.1	120.2		
7	137.0	137.3	137.3	137.5		
24	91.6	91.7	89.8	91.4		
OCOCH ₃	169.1		168.3	169.1		
			169.0			

compound **4** suggested a molecular formula of $\text{C}_{27}\text{H}_{38}\text{O}_6$, and, thus, it was isomeric with manoalide 25-monoacetate [**1**]. However, the absence of the characteristic fragment ions at m/z 137, 121, 107, and 95 in the mass spectrum of **4** indicated that thorectolide monoacetate did not contain a (trimethylcyclohexenyl)-methyl end group. As the ^1H -nmr spectrum of compound **4** contained resonances attributable to three similar olefinic methyl groups (δ 1.60, s, 9H) and one dissimilar olefinic methyl group (δ 1.69, s, 3H), it was concluded that compound **4** contained a farnesane end group. This was confirmed by the ^{13}C -nmr spectrum, which exhibited upfield quartets at δ 15.9, 16.9, and 17.6 due to the three methyl groups (C-21, C-22, C-23) on double bonds with *E* stereochemistry and another quartet at δ 25.5 due to the other terminal methyl group (C-20) (10). The positions of the resonances due to the δ -lactol and α -acetyloxybutenolide moieties in the ^1H - and ^{13}C -nmr spectra of thorectolide monoacetate [**4**] closely resembled those

of manoalide monoacetate [**1**] (Table 1), thereby confirming that both compounds have the same functionalized end group. The above data indicated that thorectolide monoacetate must have structure **4**. The stereochemistry at C-4 and C-25 remains unassigned.

EXPERIMENTAL

General experimental details are given in Karuso *et al.* (1). A voucher specimen of *T. excavatus* is preserved in the Department of Zoology, University of Auckland, register number PRB8415.

MANOALIDE 25-MONOACETATE [1].—A freeze-dried specimen (67 g) of *T. excavatus*, collected at 10-m depth off Darwin, Australia, was broken into small pieces and extracted (Soxhlet) with *n*-pentane for 9 h. Removal of solvent gave a brown oil that was chromatographed on Si gel (50 g). Successive elution with CH_2Cl_2 containing increasing amounts of Et_2O gave a fraction (0.26 g) enriched in the desired material. Further chromatography of this material (preparative tlc, 25% EtOAc /hexanes) gave manoalide monoacetate that crystallized from CH_2Cl_2 /hexanes as flakes (45 mg, 0.07% of sponge dry weight), mp 117–119°, $[\alpha]^{17}_D +34^\circ$ ($c=1.0$, CHCl_3), (Found: $[\text{M}]^+$ 458.2672, $\text{C}_{17}\text{H}_{38}\text{O}_6$ requires 458.2668); $\text{ir } \nu$ max (KBr) 3450 (OH), 1787 (γ -

lactone), 1770, 1746 (OAc), 1650 (C=C), 1225, 1195, 1050, 985, 885 cm^{-1} ; $\text{uv } \lambda \text{ max (CHCl}_3\text{)}$ 239 nm (ϵ 1600); $^1\text{H nmr } \delta$ (CDCl_3) 0.99, s, 6H, H-20, 21; 1.60, br s, 3H, H-22; 1.28–2.50, m, 14H; 1.64, br s, 3H, H-23; 2.17, s, OAc; 3.12, s, exchanged with D_2O , OH; 4.76, ddd, $J=10$, 4, 2 Hz, H-4; 5.14, dd, $J=5$, 5 Hz, H-10; 5.31, s, H-24; 5.71, dd, $J=4.7$, 3.7 Hz, H-6; 6.11, dd, $J=2$, 1 Hz, H-2; 7.10, d, $J=0.5$ Hz, H-25; δ_{H} (C_6D_6) 1.07, s, 6H, H-20, 21; 1.57, s, 3H, H-22; 1.54–1.69, m, 14H; 1.64, s, 3H, H-23; 2.22, s, OAc; 3.15 br d, exchanged with D_2O , OH; 4.53, ddd, $J=10$, 4, 2 Hz, H-4; 5.12, d, $J=4$ Hz, H-24; 5.30, m, 2H, H-6, 10; 5.59, dd, $J=2$, 1 Hz, H-2; 7.10, d, $J < 1$ Hz, H-25; $^{13}\text{C nmr } \delta$ (CDCl_3) 16.1, C-23; 19.6, C-17; 19.8, C-22; 20.7, OCOCH_3 ; 25.9, C-13; 27.9, C-9; 28.6 (2), C-20, 21, 32.6, 32.8, C-5, 16; 35.0, C-19; 39.7, 39.8, 40.3, C-8, 12, 18; 6.17, C-4; 91.6, C-24; 92.9, C-25; 118.8, C-2; 120.4, 122.8, C-6, 10; 126.9, C-15; 136.9, C-14; 137.0, 137.5, C-7, 11; 165.8, C-3; 169.1, OCOCH_3 ; 169.5, C-1; $\text{ms } m/z$ [M^+] 458 (<0.1%), [$\text{M}-\text{HOAc}-\text{H}_2\text{O}$] 380 (0.2), 352 (0.15), [$\text{C}_{10}\text{H}_{17}$] 137 (100), [C_9H_{13}] 121 (20), [C_8H_{11}] 107 (15), [C_7H_9] 95 (74), 81 (67), 43 (50).

MANOALIDE DIACETATE [3].—Acetylation of compound **1** with Ac_2O /pyridine gave manoalide diacetate as an unstable waxy solid; $^1\text{H nmr } \delta$ (CDCl_3) 1.00, s, 6H, H-20, 21; 1.62, br s, 3H, H-22; 1.3–2.4, m, 14H; 1.70, br s, 3H, H-23; 2.10, 2.15, 2 s, OAc; 4.72, ddd, $J=10$, 4, 2 Hz, H-4; 5.13, m, H-10; 5.85, dd, $J=5.7$, 3.7 Hz, H-6; 6.15, dd, $J=2$, 0.8 Hz, H-2; 6.30, s, H-24; 7.06, s, H-25; $^{13}\text{C nmr } \delta$ (CDCl_3) 16.1, 19.6, 19.8, 20.5, 21.1, 25.8, 27.9, 28.6 (2), 31.9, 32.8, 35.0, 39.8, 40.3, 64.2, 89.8, 92.7, 119.2, 122.1, 122.2, 127.0, 135.0, 137.0, 137.3, 164.6, 168.3, 169.0, 169.6.

THORECTOLIDE MONOACETATE [4].—The freeze-dried sponge (232 g) collected off Darwin was extracted (Soxhlet) with light petroleum ether (bp 35–45°) as above for 8 h. Removal of the solvent gave a brown oil (1.62 g) that was chromatographed on Si gel (50 g). Successive elution with hexane containing increasing proportions of EtOAc gave a fraction (eluted with 10% EtOAc) enriched in the desired material. Further chromatography of this material on Si gel (EtOAc/ CH_2Cl_2) followed by hplc (Si; 10% EtOAc/hexanes) yielded pure thorectolide monoacetate as an unstable waxy solid (0.35 g, 0.15% of sponge dry weight), $[\alpha]^{23+33^\circ}$ ($c=1.0$, CHCl_3), (Found: [M^+] 458.2662, $\text{C}_{27}\text{H}_{38}\text{O}_6$ requires 458.2668); $\text{uv } \lambda \text{ max (MeOH)}$ 225 (ϵ 4500); $\text{ir } \nu \text{ max (CCl}_4\text{)}$ 3500 (OH), 1801 (γ -lactone), 1762 (OAc), 1660 (C=C), 1440, 1370, 1205, 1145, 1063, 1030, 995, 830, 760 cm^{-1} ; $^1\text{H nmr } \delta$ (CDCl_3) 1.60, s,

9H, H-21, 22, 23; 1.69, s, 3H, H-20; 1.20–2.40, m, 14H; 2.17, s, OAc; 3.15, br s, OH; 4.78, ddd, $J=8$, 6, 1.2 Hz, H-4; 5.14, dd, $J=5$, 5 Hz, H-10, 14, 18; 5.31, br s, H-24; 5.71, dd, $J=4.7$, 3.7 Hz, H-6; 6.11, dd, $J=2.0$, 1.0 Hz, H-2; 7.10, d, $J=0.5$ Hz, H-25; $^{13}\text{C nmr } \delta$ (CDCl_3) 15.9, q, $^1J_{\text{CH}}=124$ Hz, C-23; 16.9, q, $^1J_{\text{CH}}=124$ Hz, C-22; 17.6, q, $^1J_{\text{CH}}=123$ Hz, C-21; 20.5, q, $^1J_{\text{CH}}=130$ Hz, OCOCH_3 ; 25.5, q, $^1J_{\text{CH}}=123$ Hz, C-20; 25.8, t, $^1J_{\text{CH}}=124$ Hz, C-13; 26.5, t, $^1J_{\text{CH}}=124$ Hz, C-17; 26.6, t, $^1J_{\text{CH}}=124$ Hz, C-9; 28.3, t, $^1J_{\text{CH}}=125$ Hz, CH_2 ; 32.4, t, $^1J_{\text{CH}}=125$ Hz, C-5; 39.6, 2t, $^1J_{\text{CH}}=125$ Hz, 2CH_2 ; 61.6, d, $^1J_{\text{CH}}=141$ Hz, C-4; 91.4, d, $^1J_{\text{CH}}=162$ Hz, C-24; 92.8, dd, $^1J_{\text{CH}}=180$ Hz, $^2J_{\text{CH}}=9.7$ Hz, C-25; 118.5, d, $^1J_{\text{CH}}=182$ Hz, C-2; 120.2, d, $^1J_{\text{CH}}=157$ Hz, C-6; 123.3, 123.9, 124.2, 3 d, $^1J_{\text{CH}}=150$ Hz, C-10, 14, 18; 131.0, s, C-19; 134.8, 135.6, 2 s, C-11, 15; 137.5, s, C-7; 165.9, s, C-3; 169.1, s, OCOCH_3 ; 169.6, s, C-1; $\text{ms } m/z$ [M^+] 458 (<0.1%), 352 (<0.1), 267 (1), 253 (1), 239 (2), 225 (2), 211 (3), 197 (3), 183 (4), 169 (5), 155 (6), 149 (15), 141 (8), 113 (15), 99 (21), 97 (15), 85 (48), 71 (69), 57 (100).

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