of the mixture (silica gel, 1:1 hexane–EtOAc).

28a: mp 75–76 °C (hexane); R_f 0.44 (3:1 EtOAc–hexane); $[\alpha]^{18}_D$ +12.5° (*c* 1.4, CH_2Cl_2); ^1H NMR (270 MHz) δ 6.54 (s, 1 H, NH), 4.39 (m, 2 H, H_1), 3.82 (m, 1 H, H_2), 3.66 (br s, 1 H, H_3), 3.29 (br s, 1 H, OH), 1.10–1.48 (m, 28 H), 0.85 (t, *J* = 6.7 Hz, CH_3); IR (melt) 3440, 2910, 2840, 1780, 1460, 1240, 1080, 1030, 720 cm^{-1}; mass spectrum, *m/e* 327 (parent ion). Anal. Calcd for $C_{19}H_{37}NO_3$: 69.68; H, 11.39; N, 4.28. Found: C, 69.57; H, 11.50; N, 4.47.

28b: mp 103–104 °C (hexane–benzene); R_f 0.35 (3:1 EtOAc–hexane); $[\alpha]^{18}_D$ +0.9° (*c* 0.44, EtOH); ^1H NMR (270 MHz) δ 5.60 (s, 1 H, NH), 4.62 (m, 1 H, H_3), 3.82 (m, 1 H, H_2), 3.67 (m, 2 H, H_1), 2.18 (m, 1 H, OH), 1.08–1.74 (m, 28 H), 0.86 (t, *J* = 6.4 Hz, 3 H, CH_3); IR (melt) 3400, 2915, 2845, 1695, 1468, 1073 cm^{-1}; mass spectrum, *m/e* 327 (parent ion), 328 (M^+ + 1); high-resolution mass spectrum, calcd for $C_{19}H_{37}NO_3$ *m/e* 327.2773, found *m/e* 327.2777.

The mixture of crude oxazolidinones **28a** and **28b** (478 mg, 1.46 mmol) was dissolved in 30% aqueous EtOH (20 mL) and treated with LiOH (1.05 g, 43.8 mmol) at reflux overnight. The cooled solutio was diluted with brine (20 mL) and extracted with EtOAc (4 × 20 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford crude dihydrosphingosine **26** (R_f 0.11, 3:1 EtOAc–hexane).

To a solution of this material in CH_2Cl_2 (20 mL) was added pyridine (1.5 mL, 15.4 mmol), (dimethylamino)pyridine (one crystal), and acetyl chloride (1.1 mL, 15 mmol). After being stirred for 1.5 h, the reaction was quenched with MeOH (3 mL), poured into saturated aqueous $NaHCO_3$ (20 mL), and extracted with CH_2Cl_2 (4 × 20 mL). The combined extracts were washed with 1 N HCl (80 mL) and saturated aqueous $NaHCO_3$ (80 mL), filtered through a cotton plug, and concentrated. The crude triacetate was purified by column chromatography (40 × 160 mm silica gel packed column, 1:1 hexane–EtOAc as eluent, R_f 0.56, 3:1 EtOAc–hexane) to afford 564 mg (94%) of pure D-(+)-dihydroxyphingosine triacetate (**29**): mp 93–94 °C (hexane) [lit. mp[13f] 94–96 °C and mp[18a] 97–98 °C]; $[\alpha]^{23}_D$ +17.5° (*c* 1.0, $CHCl_3$) [lit. $[\alpha]^{23}_D$ +17.0° (*c* 1.1, $CHCl_3$)[13f] and $[\alpha]^{19}_D$ +17.4° (*c* 1.4, $CHCl_3$)[18a]]; ^1H NMR (250 MHz) δ 5.83 (d, *J* = 9.0 Hz, 1 H, NH), 4.88 (q, *J* = 5.5 Hz, 1 H, H_3), 4.37 (m, 1 H, H_2), 4.23 (dd, *J* = 11.4, 6.0 Hz, 1 H, H_{1a}), 4.03 (dd, *J* = 11.4, 3.9 Hz, 1 H, H_{1b}), 2.05 (s, 6 H, 2 Ac), 1.98 (s, 3 H, Ac), 1.02–1.37 (m, 28 H), 0.85 (t, *J* = 6.6 Hz, 3 H, CH_3); IR (melt) 3280, 2910, 2845, 1718, 1640, 1540, 1368, 1235, 1040 cm^{-1}; mass spectrum, *m/e* 427 (parent ion), 428 (M^+ + 1). Anal. Calcd for $C_{24}H_{45}NO_5$: C, 67.41; H, 10.61; N, 3.28. Found: C, 67.64; H, 10.34; N, 3.23.

Method B. A mixture of **6a** and **6b** (429 mg, 1.03 mmol) was dissolved in 30% aqueous EtOH (20 mL). LiOH (800 mg, 33.3 mmol) was added and the mixture heated at reflux overnight. The cooled mixture was then diluted with H_2O (25 mL) and extracted with CH_2Cl_2 (4 × 25 mL). The combined organic extracts were filtered through a cotton plug and concentrated to afford 413 mg of crude *N*-benzylamine **30** (R_f 0.19, 2:1 hexane–EtOAc). This material was used immediately in the next reaction without purification.

A solution of crude **30** in MeOH (15 mL) was treated with 10% Pd–C (410 mg), 1 N HCl (1.03 mL, 1.03 mmol), and cyclohexene (0.31 mL, 3.08 mmol).[26] The resulting slurry was heated at reflux for 2 h, then cooled to room temperature, filtered through a pad of Celite, and concentrated to give 315 mg of crude **26**.

A solution of this material in CH_2Cl_2 (10 mL) was treated with pyridine (1.5 mL, 15.4 mmol), acetyl chloride (0.8 mL, 11.1 mmol), and a crystal of 4-DMAP. The resulting solution was stirred for 2 h at room temperature, then quenched with MeOH (5 mL), and diluted with saturated aqueous $NaHCO_3$ (15 mL) and H_2O (10 mL). The organic layer was separated and the aqueous extracted with CH_2Cl_2 (5 × 25 mL). The combined organic extracts were washed with 1 N HCl (100 mL) and saturated aqueous $NaHCO_3$ (100 mL), filtered through a cotton plug, and concentrated to afford crude **29**. This material was purified by chromatography on a 40 × 160 mm silica gel column using 1:1 hexane–EtOAc as eluent to yield 399 mg (91%) of pure dihydrosphingosine triacetate.

***erythro*-2-Benzamido-3-cyclohexyl-1,3-bis(benzoyloxy)propane (31)** was prepared in 78% yield from the mixture of oxazolidinones **9a**/**9b** by using a slightly modified version of the deprotection sequences described for the synthesis of **29** (substitution of benzoyl chloride for acetyl chloride in the final step of methods A and B): mp 63–64 °C; R_f 0.50 (3:1 hexane–EtOAc); ^1H NMR (250 MHz) δ 7.31–8.16 (m, 15 H, Ar), 7.06 (d, *J* = 8.6 Hz, 1 H, NH), 5.22 (dd, *J* = 6.8, 4.1 Hz, 1 H, H_3), 5.04 (ddd, *J* = 10.3, 6.1, 4.2 Hz, 1 H, H_2), 4.58 (m, 2 H, H_1), 1.64–1.94 (m, 6 H), 1.06–1.30 (m, 5 H); IR (melt) 3330, 3060, 2930, 2880, 1790, 1720, 1640, 1600, 1580, 1530, 1490, 1450, 1270, 1070, 1025, 710 cm^{-1}; mass spectrum, *m/e* 485 (parent ion). Anal. Calcd for $C_{30}H_{31}NO_5$: C, 74.20; H, 6.43; N, 2.88. Found: C, 73.93; H, 6.57; N, 2.75.

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Alkaloids from a Marine Zoanthid

C. Bheemasankara Rao, Ammanamanchi S. R. Anjaneyulu, Nittala S. Sarma, and Yenamandra Venkateswarlu

Department of Chemistry, Andhra University, Visakhapatnam 530 003, India

Richard M. Rosser and D. John Faulkner*

Scripps Institution of Oceanography, La Jolla, California 92093

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The colonial zoanthid, *Zoanthus* sp., contains alkaloids of a new structural group. The structure of zoanthamine (**1**) was determined by X-ray crystallographic analysis and has been communicated previously. The structures of zoanthenamine (**2**) and zoanthamide (**3**) were elucidated by comparison of their spectral data with those of zoanthamine (**1**).

The chemical constituents of an unidentified colonial zoanthid, *Zoanthus* sp.,[1] were investigated as part of a program to study toxic marine organisms from the Visakhapatnam coast of India. The colonial zoanthids, which occur as dense mats on intertidal rocks, can eject jets of water when they are disturbed. If the spray comes in contact with a victim's eyes, it causes tears followed by prolonged redness and pain.[2] An initial investigation of extracts of the whole organism revealed the presence of a series of alkaloids, three of which were isolated and pu-

(1) The animals may be a new species of *Zoanthus*. They were first identified as *Z. sociatus*, but this species is regarded as being restricted to the Caribbean. Specimens are available from either Andhra University or Scripps Institution of Oceanography.

(2) The effects can last up to a week. Several collectors have experienced these irritant effects, and they recommend caution when handling zoanthids from any location.

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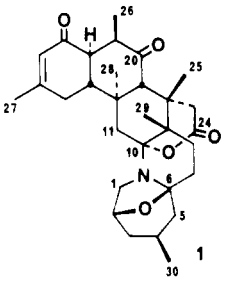
Table I. 360-MHz ^{1}H NMR Spectra of Zoanthamine (1), Zoanthenamine (2), and Zoanthamide (3) [Chemical Shift, Multiplicity, Integration, Coupling Constants]

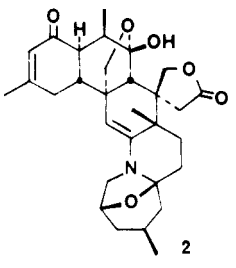
C	1				2				3			
1	3.29	br d	1 H	7	3.15	br s	1 H		4.27	dd	1 H	15, 4
1	3.24	dd	1 H	7, 6	3.14	br d	1 H	7	3.87	dd	1 H	15, 6
2	4.56	m	1 H		4.62	m	1 H		4.74	dddd	1 H	8, 6, 5, 4
3	1.56	dd	1 H	12, 4	1.54	m	1 H		2.36	ddd	1 H	14, 9, 5
3	1.48	ddd	1 H	13, 12, 2	1.49	m	1 H		2.05	ddd	1 H	14, 8, 8
4	2.27	m	1 H		1.74	m	1 H		2.69	m	1 H	
5	2.10	dd	1 H	13, 4	1.87	dd	1 H	13, 5				
5	1.10	t	1 H	13	1.16	t	1 H	13				
7					1.92	m	2 H		2.65	m	2 H	
8	1.55–1.90		4 H		1.75	m	1 H		1.84	m	1 H	
8					1.55	m	1 H		1.64	m	1 H	
11	2.17	d	1 H	14	3.84	s	1 H[b]		5.38	s	1 H	
11	1.92	d	1 H	14								
13	2.42	m	1 H		2.05	m	1 H					
14	2.23	m	2 H		2.33	m	1 H		2.34–2.58		3 H	
14					2.19	m	1 H					
16	5.92	s	1 H		5.88	s	1 H		5.94	s	1 H	
18	2.66	dd	1 H	13, 5	2.59	dd	1 H	13, 5	2.65	dd	1 H	13, 7
19	3.02	dq	1 H	5, 7	2.41	dq	1 H	5, 6	3.14	m	1 H	7
21	3.22	s	1 H		2.26	s	1 H		3.32	s	1 H	
23	3.67	d	1 H	20	3.58	d	1 H	18	3.39	d	1 H	17
23	2.37	d	1 H	20	2.40	d	1 H	18	2.39	d	1 H	17
25	1.00	s	3 H[a]		4.93	d	1 H	9	4.34	d	1 H	10
25					4.22	d	1 H	9	4.29	d	1 H	10
26	1.17	d	3 H	7	1.05	d	3 H	6	1.18	d	3 H	7
27	2.01	s	3 H		1.98	s	3 H		2.05	s	3 H	
28	0.98	s	3 H[a]		3.95	d	1 H	9	1.05	s	3 H[a]	
28					3.51	d	1 H	9				
29	1.20	s	3 H[a]		1.24	s	3 H		1.27	s	3 H[a]	
30	0.92	d	3 H	7	0.92	d	3 H	6	1.29	d	3 H	7
OH					3.35	s	1 H[b]					

[a] Signals may be interchanged. [b] Exchange with D_2O.

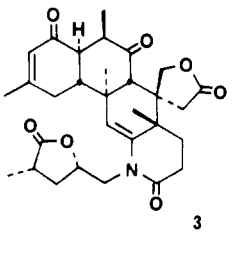
rified. In a preliminary communication[3] we reported the structural determination by X-ray analysis of zoanthamine (1), the first member of the new class of alkaloids. In this paper we report details of the isolation of zoanthamine (1), zoanthenamine (2), and zoanthamide (3) and propose structures for the latter two compounds that are based on interpretation of spectral data.



1



2



3

The ether soluble material from an ethanolic extract of *Zoanthus* sp. was fractionated on silica gel. The material eluted with 4:1 benzene–ethyl acetate was further purified by TLC to obtain zoanthamine (1, 9×10^{-4} % wet weight[4]). A more polar, highly colored fraction was rechromatographed on neutral alumina to obtain zoanthamide (3, 2.7×10^{-4} % wet weight) and zoanthenamine (2, 2×10^{-4} % wet weight) which was further purified by silica gel chromatography.

The structure of zoanthamine (1), mp 306–308 °C, was determined by an X-ray diffraction study.[3] The spectral data were fully compatible with the structure. In order to elucidate the structures of zoanthenamine (2) and zoanthamide (3) it was necessary to assign the majority of signals in both the ^{1}H and ^{13}C NMR spectra of zoanthamine (1). Spin decoupling experiments allowed assignment of most of the ^{1}H NMR spectrum (Table I). We were able to assign all the key signals in the ^{13}C NMR spectrum (Table II) by analogy with data from standard compilations. Other signals were assigned by using residual couplings and values derived by applying correction factors to the data of the best available models.

Zoanthenamine (2) was obtained as a white powder, mp 238–240 °C, that slowly decomposed in solution. The molecular formula, $C_{30}H_{39}NO_6$, indicated that zoanthenamine (2) might be a simple oxidation product of zoanthamine (1, $C_{30}H_{41}NO_5$). The presence of the β-methyl enone functionality was deduced from the characteristic signals in the ^{13}C NMR spectrum [δ 199.3 (s), 127.0 (d), 159.8 (s), 23.4 (q)] and ^{1}H NMR signals at δ 5.88 (s, 1 H) and 1.98 (s, 3 H). The ^{1}H NMR signals for protons between C-1 and C-5 were assigned, by means of spin decoupling experiments, to the same bicyclic ether ring system found in zoanthamine. The most noticeable differences between the ^{1}H NMR spectra of 1 and 2 were the replacement of two of the tertiary methyl signals in 1 by signals at δ 3.51 (d, 1 H, J = 9 Hz), 3.95 (d, 1 H, J = 9 Hz),

(3) Rao, C. B.; Anjaneyula, A. S. R.; Sarma, N. S.; Vankateswarlu, Y.; Rosser, R. M.; Faulkner, D. J.; Chen, M. H. M.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 7983.

(4) In ref 3, the recovery was incorrectly recorded as % *dry* weight.

Table II. 50-MHz ^{13}C NMR Data for Zoanthamine (1), Zoanthenamine (2), and Zoanthamide (3)

C	1	2	3
1	47.2 (t)	50.9 (t)	46.4 (t)
2	74.2 (d)	73.8 (d)	76.4 (d)
3	38.8 (t)	38.2 (t)	34.8[a] (t)
4	24.5 (d)	24.4 (d)	33.8 (d)
5	44.4 (t)	44.3 (t)	176.2 (s)
6	89.9 (s)	89.8 (s)	168.7 (s)
7	30.6[a] (t)	32.3[a] (t)	24.8[a] (t)
8	23.7 (t)	24.9 (t)	30.9[a] (t)
9	40.1[b] (s)	41.4[b] (s)	42.7[b] (s)
10	101.6 (s)	144.8 (s)	140.1 (s)
11	41.9 (t)	89.3 (d)	110.9 (d)
12	34.9[b] (s)	48.5 (s)	40.0[b] (s)
13	45.8[c] (d)	43.9[c] (d)	45.6[c] (d)
14	29.9[a] (t)	29.6[a] (t)	28.3[a] (t)
15	159.9 (s)	159.8 (s)	160.6 (s)
16	126.8 (s)	127.0 (d)	126.7 (d)
17	197.2 (s)	199.3 (s)	196.6 (s)
18	48.0[c] (d)	44.3[c] (d)	48.3[c] (d)
19	48.0[c] (d)	44.3[c] (d)	45.6[c] (d)
20	212.0 (s)	111.3 (s)	212.0 (s)
21	53.8 (d)	48.7[c] (d)	48.9[c] (d)
22	39.5[b] (s)	44.4[b] (s)	45.6[b] (s)
23	35.9 (t)	34.4 (t)	33.4[a] (t)
24	172.5 (s)	178.3 (s)	179.0 (s)
25	18.4[d] (q)	72.3[d] (t)	70.9 (t)
26	13.8 (q)	12.8 (q)	14.0 (q)
27	22.9 (q)	23.4 (q)	23.1 (q)
28	20.7[d] (q)	73.8[d] (t)	18.9 (q)
29	18.3[d] (q)	25.6 (q)	24.6 (q)
30	21.8 (q)	21.6 (q)	15.9 (q)

[a-d] Values with identical superscript within a column may be interchanged.

4.22 (d, 1 H, J = 9 Hz), and 4.93 (d, 1 H, J = 9 Hz) that were assigned to two isolated -CH_2O- groups in **2**. Furthermore, there were two signals that exchanged with D_2O; a hydroxyl proton signal at δ 3.35 (s, 1 H) that exchanged rapidly and a second signal at δ 3.84 (s, 1 H) that exchanged over a period of days and was assigned to an enamine proton at C-11. The ^{13}C NMR signals at δ 144.8 (s) and 89.3 (d) were assigned to C-10 and C-11 of the enamine. The imposition of an enamine on the zoanthamine structure releases a carboxylic acid functionality which is not present in zoanthenamine (**2**). However, the incorporation of a γ-lactone between the carboxylic acid (C-24) and a methylene group at C-25 accounts for an IR band at 1770 cm^{-1}, ^1H NMR signals at δ 4.93 and 4.22 (C-25 in Table I), and ^{13}C NMR signals at δ 178.3 (C-24) and either 72.3 or 73.8 (C-25). The remaining hydroxymethylene group could be derived in principal from either the C-28 or C-29 methyl groups of zoanthamine (**1**). However, the absence of a ketone carbonyl and the presence in the ^{13}C NMR spectrum of zoanthenamine (**2**) of a ketal or hemiketal carbon signal at δ 111.3 (s) requires the presence of a hydroxymethylene group at C-28 that has cyclized to form a hemiketal at C-20. The signals for protons at C-19 (δ 2.41) and C-21 (δ 2.26) in zoanthenamine (**2**) were upfield of the comparable signals for zoanthamine (**1**) [δ 3.02 (C-19) and 3.22 (C-21)] as expected for the replacement of a carbonyl group by a hemiketal. The structure assigned to zoanthenamine (**2**) is compatible with all spectral data and retains the carbon skeleton and stereochemistry of zoanthamine (**1**).

Zoanthamide (**3**), $[\alpha]_D$ +133° (c 0.83, $CHCl_3$), is a white crystalline solid, mp 278–280 °C. The molecular formula, $C_{30}H_{37}NO_7$, when considered together with an initial analysis of the spectral data, allowed us to propose that zoanthamide (**3**) was an oxidation product of zoanthamine (**1**). Comparison of the spectral data suggested that the C-12 to C-21 portions of **1** and **3** were identical. The ^{13}C NMR spectrum contained signals at δ 179.0 (s, C-24) and 70.9 (t, C-25) that were assigned to a γ-lactone ring, similar to that found in zoanthenamine (**2**). The olefinic carbon signals at 140.1 (s) and 110.9 (d) suggested an enamide instead of the enamine in ring C; this can be accommodated by placing an amide carbonyl [^{13}C NMR, δ 168.7 (s)] at C-6. If it is assumed that oxidative cleavage of the C5–C6 bond to obtain the C-6 amide also produced a carboxylic acid at C-5, then cyclization of the acid to the oxygen at C-2 to form a second γ-lactone provides the rationale for the ^{13}C NMR signal at δ 176.2 (s). The ^1H NMR spectrum of zoanthamide (**3**) supported these assignments. In particular, the C-11 olefinic proton signal was at δ 5.38 (s, 1 H) and did not exchange with D_2O. Spin decoupling experiments confirmed the presence of the γ-lactone ring system attached through a methylene group to the nitrogen atom. The structure assigned to zoanthamide (**3**) is fully compatible with all spectral data and requires the least modification of the zoanthamine carbon skeleton. It should be recognized that the proposed structures for zoanthenamine (**2**) and zoanthamide (**3**) have been arbitrarily assigned the same stereochemistry as zoanthamine (**1**).

Although the zoanthamine alkaloids **1–3** were isolated during a search for the inflammatory agents in *Zoanthus* sp., initial studies indicated that all three compounds inhibit phorbol myristate acetate (PMA) induced inflammation of the mouse ear.[5]

The zoanthamine alkaloids **1–3** are a new class of alkaloids of unknown biosynthetic origin. Although the structures contain isoprenoid elements, there is no clear sequence of head-to-tail linkages that would suggest an obvious triterpenoid origin.

Experimental Section

Specimens of *Zoanthus* sp. were collected by hand from intertidal rocks along the Visakhapatnam coast (17°N, 83°E). The animals (10 kg wet weight) were rinsed with fresh water, separated from contaminants and immediately homogenized in ethanol (5 L). After 72 h at room temperature the suspension was filtered and the extraction repeated three times. The combined extracts were concentrated under reduced pressure to obtain an aqueous suspension (1.5 L). The suspension was extracted with ether (12 × 250 mL) and the combined extracts evaporated to obtain a dark green gum (25 g). The oil was chromatographed on silica gel (100–200 mesh, 150 g) with eluants of increasing polarity from petroleum ether (40–60 °C) through benzene to ethyl acetate. Fractions eluted with 20% ethyl acetate in benzene contained zoanthamine (**1**) that was further purified by preparative TLC on silica gel (R_f 0.58, ethyl acetate) and crystallized from methanol to obtain white crystals (90 mg). Since more polar fractions were highly colored due to chlorophylls, the column was washed with ethyl acetate. This material (3 g) was rechromatographed on neutral alumina (40 g). Material eluted with 5% methanol in chloroform gave crystals of zoanthamide (**3**, 27 mg) from methanol. Material eluted with 10% methanol in chloroform gave a mixture of metabolites (200 mg) that was again chromatographed on silica gel (100–200 mesh, 10 g). The material eluted with 30% ethyl acetate in benzene gave zoanthenamine (**2**, 20 mg) as crystals from benzene.

Zoanthamine (1): mp 306–308 °C; $[\alpha]_D$ +18° (c 0.4, $CHCl_3$); IR ($CHCl_3$) 1720 (br), 1660 cm^{-1}; UV (CH_3CN) 233 nm (ϵ 11 000); ^1H NMR ($CDCl_3$) see Table I; ^{13}C NMR ($CDCl_3$) see Table II; HRMS, obsd m/z 495.2969, $C_{30}H_{41}NO_5$ requires 495.2985.

Zoanthenamine (2): mp 238–240 °C; IR ($CHCl_3$) 3300–3600 (br), 1770, 1660, 1640 cm^{-1}; UV (CH_3CN) 234 nm; ^1H NMR ($CDCl_3$) see Table I; ^{13}C NMR ($CDCl_3$) see Table II; HRMS, obsd m/z 509.2782, $C_{30}H_{39}NO_6$ requires 509.2777.

(5) Van Arman, C. G. *Clin. Pharmacol. Ther.* **1974**, *16*, 900.

Zoanthamide (3): mp 278–280 °C; $[\alpha]_D$ +133° (*c* 0.83, $CHCl_3$); IR ($CHCl_3$) 1770, 1715, 1670, 1660, 1640 cm^{-1}; UV (CH_3CN) 235 nm (ε 23 900); ^1H NMR ($CDCl_3$) see Table I; ^{13}C NMR ($CDCl_3$) see Table II; HRMS, obsd *m/z* 523.2549, $C_{30}H_{37}NO_7$ requires 523.2570.

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Registry No. 1, 93426-90-5; 2, 97877-69-5; 3, 97877-70-8.

Synthesis of Vinca Alkaloids and Related Compounds. 21.[1] Preparation of (±)-Eburnamonine, (±)-3-Epieburnamonine, and (±)-*C*-Norquebrachamine from a Common Intermediate

György Kalaus,[†] Numan Malkieh,[†] Ildikó Katona,[†] Mária Kajtár-Peredy,[‡] Tibor Koritsánszky,[‡] Alajos Kálmán, Lajos Szabó,[†] and Csaba Szántay*[†]

Department of Organic Chemistry, Technical University, Budapest Gellért tér 4, H-1521, Budapest, Hungary, and Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, Pusztaszeri út 59-67, H-1525, Budapest, Hungary

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The pentacyclic indole derivatives (±)-eburnamonine (**8b**) and (±)-3-epieburnamonine (**17b**) and the tetracyclic (±)-*C*-norquebrachamine (**10**) have been synthesized from the easily available common intermediate **2a**. In the course of the syntheses some unexpected transformations were observed. Structure elucidations of new products were performed partly by X-ray analysis.

In the synthesis of therapeutically important Vinca alkaloids, the enamine 1,[2] serving as key intermediate, was made to react with paraformaldehyde.[3] If the reaction is effected in the melt, a product of structure **3** was isolated in addition to the hydroxymethyl derivative **2a** (Scheme I). The latter, which contains the C1 ethyl and the C12 hydrogen in the trans relationship, is formed with high stereoselectivity. At the boiling point of dichloromethane, pure **2a** is obtained in high yield.

Derivatives with the eburnane skeleton[4] can be prepared through the aldehyde obtained by oxidation of **2a**. In the present work, however, another approach was realized.

The natural compounds are mostly derived from the 1-ethyl, 12b-H cis epimers; therefore, the possibility that compounds of type **2** might be epimerized to the cis isomers was investigated. **2a** was converted with phosphoryl chloride to the chloride **2e**, which was oxidized in glacial acetic acid with $Na_2Cr_2O_7$.[5] The resulting iminium salt **4e** was reduced catalytically (H_2/Pd/C) or with $NaBH_4$. In the first case the **2e**:**5e** ratio was 1.6:1 and in the second 5:1. Thus, when the reducing agent is hydride ion, the trans epimer strongly predominates in the reaction mixture.

Because it was assumed on the basis of our earlier experiences[2b] that an increase in the bulk of the C1 substituent would favor the formation of the cis epimer, the acetyl **2b** and benzoyl **2c** derivatives were oxidized to the iminium salts **4b,c**. In fact, reduction of the latter compounds gave a higher proportion of the cis epimers **5b,c** than saturation of **4e**. As **2b,c** are hydrolyzed considerably more easily in alkaline medium than **5b,c**, separation of the two isomers becomes facile.

The results are summarized in Table I. Further hydrolysis of the esters **5b,c** yields the alcohol **5a**, and from this the derivative **5d** could be obtained by mesylation.

As we have previously shown,[6] the (−)-nitrile **5f** can be converted into (−)-eburnamonine in very good yield. Consequently the preparation of the nitrile from **5e** by a simple displacement reaction was attempted (Me_2SO at 100 °C, sodium cyanide for 1 h). However, the expected

Scheme I

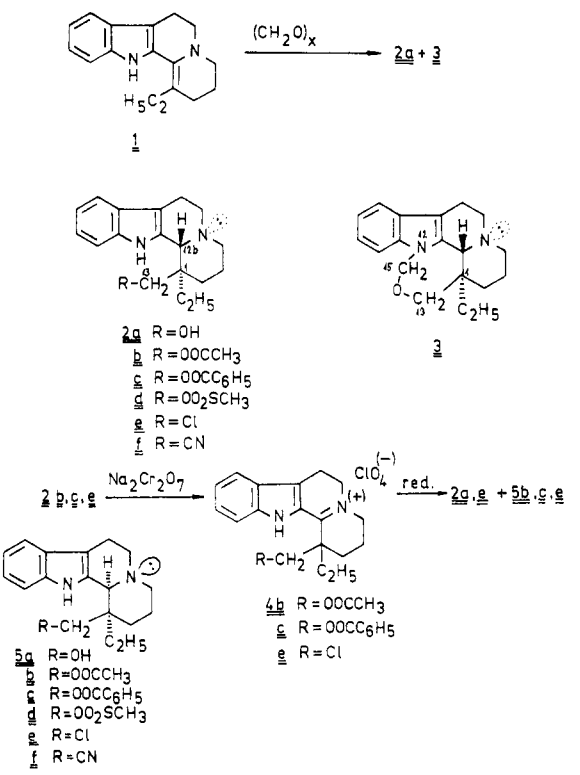

Table I. Reduction of Esters 4b and 4c

starting material	reacn conditions	product ratio[a] 2a, %	5b or 5c, %
4b	$NaBH_4$ (ethanol), 0 °C	44.8	53.4
	Pd/C/H_2, room temp	32.4	38.3
4c	$NaBH_4$ (ethanol), 0 °C	13.8	65.2
	Pd/C/H_2, room temp	16.6[b]	33.8

[a] After selective hydrolysis. [b] Unchanged starting material was also contained in the reaction mixture.

[†] Technical University.
[‡] Hungarian Academy of Sciences.

