TWO NEW ALKALOIDS FROM AN INDIAN SPECIES OF *ZOANTHUS*+

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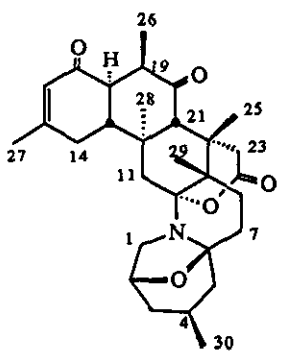
Abstract–A new species of *Zoanthus* from the Bay of Bengal contains a novel group of alkaloids that possess antiinflammatory and analgesic properties. The structures of two new isomeric alkaloids, 28-deoxyzoanthenamine (**4**) and 22-*epi*-28-deoxyzoanthenamine (**5**), were elucidated by interpretation of spectral data.

Previous studies[1,2] of an unidentified colonial zoanthid of the genus *Zoanthus*, which occurs as dense mats on intertidal rocks along the Visakhapatnam coast of India, have resulted in the isolation and identification of three unique alkaloids, zoanthamine (**1**), zoanthenamine (**2**) and zoanthamide (**3**). The alkaloids are of pharmacological interest because they inhibit phorbol myristate acetate (PMA) induced inflammation of the mouse ear. The structure of zoanthamine (**1**) was determined by X-ray analysis[1] and the structures of zoanthenamine (**2**) and zoanthamide (**3**) were proposed on the basis of interpretation of spectral data.[2] In this paper we describe two new isomeric *Zoanthus* alkaloids.



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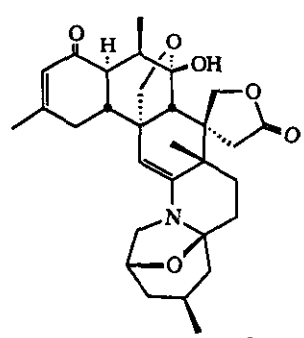

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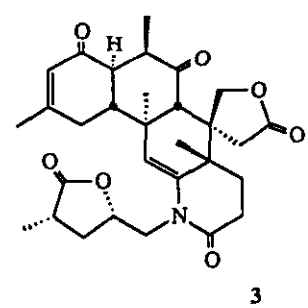

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+Dedicated to Professor Sir Derek H.R. Barton on the occasion of his 70th birthday.

The isomeric alkaloids 28-deoxyzoanthenamine (**4**) and 22-*epi*-28-deoxyzoanthenamine (**5**), which were isolated using the chromatographic procedures described previously,[2] both have the molecular formula $C_{30}H_{39}NO_5$, which corresponds to one less oxygen atom than is present in zoanthenamine (**2**). Comparison of the spectral data of **4** and **5**[3] revealed no major differences, except for the chemical shifts of proton and carbon signals associated with the lactone ring. The infrared spectra of **4** and **5** both contained bands at 1770 (γ-lactone), 1710 (ketone), 1660 and 1635 cm^{-1} (unsaturated ketone). Comparison of the ^{13}C nmr data (Table 1) of **4** and **5**, both of which contained a signal due to a saturated ketone and five methyl signals, with those of zoanthenamine (**2**) strongly suggested that the CH_2O group at C12 and the hemi-ketal group at C20 in **2** were replaced by a methyl group and a ketone in **4** and **5**. The signals assigned to C11 in the spectra of **4** and **5** are downfield of the corresponding signal in the zoanthenamine (**2**) spectrum: this difference is partially due to the γ-effect of the C28 oxygen and may also reflect a change in the geometry of the molecule. Comparison of the ^1H nmr spectra (Table 2) of **4** and **5** with that of zoanthenamine (**2**) also supported this proposal since the H19 and H21 signals were both shifted downfield by the C20 carbonyl group. In addition, the methylene signals at δ 3.95 and 3.51 in zoanthenamine (**2**) are replaced by methyl signals at δ 0.98 and 0.91 in **4** and **5** respectively.

The major differences in the spectral data of **4** and **5** were found in the ^1H nmr spectra, particularly in the chemical shifts (but not coupling constants) of the two pairs of methylene signals assigned to the γ-lactone ring (see Table 1: the signals are assigned α and β with α-hydrogens pointing toward C21). The chemical shift differences indicated that **4** and **5** were isomeric in the vicinity of the γ-lactone ring but they could not be used to pinpoint the isomeric center(s). However, nuclear Overhauser effect difference spectroscopy (NOEDS) clearly

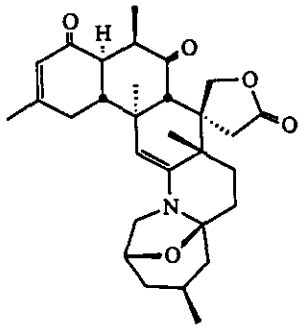
Table 1. 50 MHz ^{13}C nmr data for zoanthenamine (**2**), 28-deoxyzoanthenamine (**4**) and 22-*epi*-deoxyzoanthenamine (**5**).

C#	2	4	5	C#	2	4	5
1	50.9 (t)	50.3 (t)	50.6 (t)	16	127.0 (d)	126.8 (d)	126.8 (d)
2	73.8 (d)	73.8 (d)	73.8 (d)	17	199.3 (s)	197.4 (s)	197.3 (s)
3	38.2 (t)	38.3 (t)	38.3 (t)	18	44.3[c] (d)	46.0[c] (d)	45.7[c] (d)
4	23.4 (d)	23.2 (d)	23.3 (d)	19	44.3[c] (d)	45.6[c] (d)	45.6[c] (d)
5	44.3 (t)	43.9 (t)	43.8 (t)	20	111.3 (s)	213.0 (s)	212.8 (s)
6	89.8 (s)	89.9 (s)	90.0 (s)	21	48.7[c] (d)	49.7[c] (d)	50.6[c] (d)
7	32.3[a] (t)	31.2[a] (t)	31.1[a] (t)	22	44.4[b] (s)	42.7[b] (s)	42.2[b] (s)
8	24.9 (t)	26.0 (t)	26.2 (t)	23	34.4 (t)	35.3 (t)	33.4 (5)
9	41.4[b] (s)	41.0[b] (s)	41.0[b] (s)	24	178.3 (s)	177.2 (s)	176.4 (s)
10	144.8 (s)	142.1 (s)	142.4 (s)	25	72.3[d] (t)	71.4 (t)	71.9 (t)
11	89.3 (d)	99.5 (d)	99.8 (d)	26	12.8 (q)	14.0 (q)	13.9 (q)
12	48.5 (s)	44.5 (s)	45.6 (s)	27	24.4 (q)	24.5 (q)	24.5 (q)
13	43.9[c] (d)	48.7[c] (d)	48.6[c] (d)	28	73.8[d] (d)	20.6 (q)	21.2 (q)
14	29.6[a] (t)	29.6[a] (t)	29.6[a] (t)	29	35.6 (q)	26.0 (q)	25.7 (q)
15	159.8 (s)	160.4 (s)	160.4 (s)	30	21.6 (q)	21.6 (q)	21.7 (q)

a-d For each compound, values with identical superscripts may be interchanged.

Table 2. 360 MHz ^{1}H nmr data for 28-deoxyzoanthenamine (**4**) and 22-*epi*-28-deoxyzoanthenamine (**5**).

H#	**4**		**5**
1	3.23	(d, 1 H, J = 7 Hz)	3.24
1	3.14	(t, 1 H, J = 7 Hz)	3.14
2	4.63	(m, 1 H)	4.63
4	1.78	(m, 1 H)	--
11	4.20	(s, 1 H)	4.24
13	2.42	(m, 1 H)	2.42
14	2.28	(dd, 1 H, J = 17, 13 Hz)	2.28
14	2.44	(m, 1 H)	2.43
16	5.92	(s, 1 H)	5.93
18	2.61	(dd, 1 H, J = 12, 5 Hz)	2.59
19	3.12	(qd, 1 H, J = 7, 5 Hz)	3.12
21	3.40	(s, 1 H)	3.55
23α	3.43	(d, 1 H, J = 18 Hz)	2.83
23β	2.32	(d, 1 H, J = 18 Hz)	2.33
25α	4.25	(d, 1 H, J = 9 Hz)	4.91
25β	4.22	(d, 1 H, J = 9 Hz)	4.15
26	1.18	(d, 3 H, J = 7 Hz)	1.19
27	2.01	(s,3 H)	2.02
28	0.98	(s, 3 H)	0.91
29	1.29	(s, 3 H)	1.27
30	0.91	(d, 3 H, J = 7 Hz)	0.94



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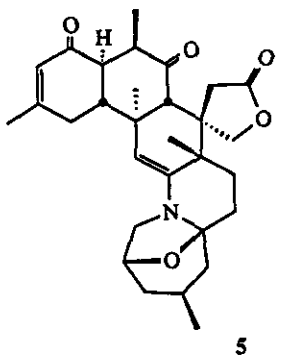

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showed that **4** and **5** were isomeric at C22 (Table 3). For both compounds, irradiation of the H21 signal caused enhancements of the $CH_3$26, $CH_3$29 and H13 signals, confirming the same geometry about the two adjacent rings, but caused a small enhancement of the H25α signal in **4** and the H23α signal in **5**, suggesting that the alkaloids **4** and **5** were isomeric at C22. Irradiation of the $CH_3$29 signal gave enhancements of the H21 signal in both **4** and **5**, the H25β signal in **4** and the H23β signal in **5**. Furthermore, irradiation of the $CH_3$28(+$CH_3$30) signal produced enhancements of the H18 signal in both **4** and **5**, the H23α and H23β signals in **4** and the H25α and H25β signals in **5**,

Table 3. Comparison of nuclear Overhauser effect difference spectroscopy (NOEDS) data.

Signal Irradiated	*Signals Enhanced*	
	4	**5**
H18	H19, H28	H19, H28
H21	H29, H26, H13, H25α	H29, H26, H13, H23α
H23α	H23β	H23β
H25α	H21	not done
H28 (H30)	H18, H23α, H23β, H11 (H4)	H18, H25α, H25β, H11 (H4)
H29	H21, H25β	H21, H23

confirming the proposed geometries.[4] The two epimers **4** and **5** can be formed by cyclization of a putative intermediate **6** in which rotation about the 9,22 bond can occur.

28-Deoxyzoanthenamine (**4**) is a potent antiinflammatory and analgesic agent.[5]

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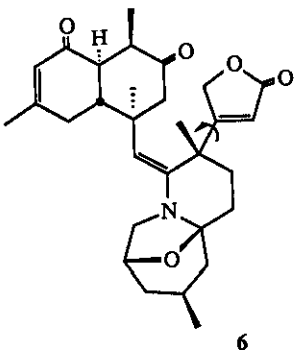
2. C.B. Rao, A.S.R. Anjaneyulu, N.S. Sarma, Y. Venkateswarlu, R.M. Rosser, and D.J. Faulkner, *J. Org. Chem.*, 1985, *50*, 3757.
3. **28-Deoxyzoanthenamine (4)**: mp 305-307°C; $[\alpha]_D$ 216° (c 3.7, $CHCl_3$); ir ($CHCl_3$) 1770, 1710, 1660, 1635 cm^{-1}; uv (MeOH) 238 nm (ε 16,250); ^1H nmr ($CDCl_3$) see Table 2; ^{13}C nmr ($CDCl_3$) see Table 1; HRMS, *m/z* 493.2826, $C_{30}H_{39}NO_5$ requires 493.2823, 478.2585 ($C_{29}H_{36}NO_5$), 328.1914 ($C_{20}H_{26}NO_3$).
22-*epi*-28-Deoxyzoanthenamine (5): oil; $[\alpha]_D$ +85° (c 2.36, $CHCl_3$); ir ($CHCl_3$) 1770, 1710, 1660, 1635 cm^{-1}; uv (MeOH) 237 nm (ε 14,200); ^1H nmr ($CDCl_3$) see Table 1; ^{13}C nmr ($CDCl_3$) see Table 2; HRMS, *m/z* 493.2839, $C_{30}H_{39}NO_5$ requires 493.2828, 478.2583 ($C_{29}H_{36}NO_5$), 328.1930 ($C_{20}H_{36}NO_3$).
4. Having shown that isomers at C22 can exist, we had to determine the stereochemistry at C22 in zoanthenamine (**2**) which had been assumed to be the same as that in zoanthamine (**1**). Fortunately, n.O.e. measurements indicated that the proposed stereochemistry at C22 of zoanthamine (**2**) is correct.
5. 28-Deoxyzoanthenamine (**4**) inhibits phorbol myristate acetate (PMA) induced inflammation of the mouse ear (ED_{50} = 9 μg/ear; cf. manoalide ED_{50} = 85 μg/ear) and is active at 50 mg/Kg in the phenylquinone assay for analgesia.



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