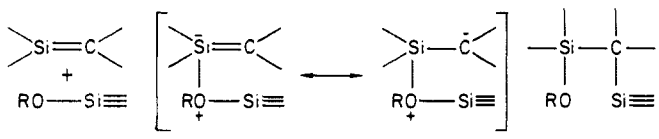

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species such as **4** may exist on the potential surface for the addition of alkoxysilanes to silenes, they are apparently not chemically significant.

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Supplementary Material Available: Details of the X-ray structure determination of **3**, including tables of bond lengths, bond angles, fractional coordinates, and thermal parameters (10 pages). Ordering information is given on any current masthead page.

Jaspamide, a Modified Peptide from a *Jaspis* Sponge, with Insecticidal and Antifungal Activity

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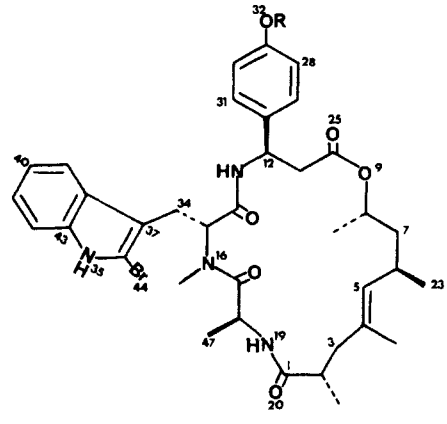
Sponges of the genus *Jaspis* have received limited attention from marine natural products chemists with only one group of metabolites, the isomalabaricane triterpenes, being previously reported.[2] We now wish to report the isolation of a novel metabolite, jaspamide (*1*), of mixed peptide/polyketide biosynthesis from a



1 R = H

3 R = Ac

Jaspis sp. collected both at Suva Harbor, Fiji, and a marine lake in Palau.[3] Jaspamide exhibited potent insecticidal activity against

Table I. ^1H and ^{13}C NMR Data ($CDCl_3$) for Jaspamide (**1**)

C	^{13}C,[b] ppm	^1H (mult, J, Hz),[c] δ	^1H–^1H connections
1	175.1[a]		
2	40.1	2.50 (m)	H-3 (A & B), Me-21
3	40.7	2.38 (A) (dd, 15.7, 10.8), 1.89 (B) (d, 15.7)	H-3B, H-2, H-5[d] (A); H-3A, H-5[d] (B)
4	131.1		
5	127.8	4.75 (d, 7.1)	H-6, H-3 (A & B)[d]
6	29.2	2.23 (m)	H-5, H-7, Me-23
7	43.3	1.32 (m)	H-6, H-8
8	70.8	4.62 (m)	H-7, Me-24
10	174.4[a]		
11	39.7	2.65 (A) (dd, 4.7, 15.0), (B) 2.65 (dd, 5.5, 15.0)	H-11B, H-12 (A); H-11A, H-12 (B)
12	49.0	5.26 (dd, 4.7, 8.4)	H-11 (A & B), H-13 H-27,[d] H-31[d]
13		7.65 (d, 8.4)	H-12
14	170.5[a]		
15	55.5	5.85 (dd, 6.4, 10.2)	H-34 (A & B)
17	168.9[a]		
18	45.8	4.75 (m)	Me-47, H-19
19		6.63 (bs)	H-18[d]
21	20.3	1.12 (d, 6.8)	H-2
22	18.5	1.56 (s)	
23	21.9	0.81 (d, 6.5)	H-6
24	19.0	1.05 (d, 6.3)	H-8
26	133.6		
27	127.1	6.94 (d, 8.3)	H-28, H-12[d]
28	115.6	6.66 (d, 8.3)	H-27
29	155.7		
30	115.6	6.66 (d, 8.3)	H-31
31	127.1	6.94 (d, 8.3)	H-30, H-12[d]
34	23.2	3.38 (A) (dd, 6.3, 15.2), 3.24 (B) (dd, 10.5, 15.2)	H-34B, H-15 (A); H-34A, H-15 (B)
35		8.70 (br s)	
36	109.0		
37	111.1		
38	131.3		
39	118.1	7.24 (d, 7.3)	H-40
40	122.3	7.13 (dd, 7.3, 7.7)	H-39, H-41
41	120.9	7.10 (dd, 7.3, 7.7)	H-40, H-42
42	110.6	7.56 (br d, 7.3)	H-41, H-35[d]
43	136.1		
45	30.8	2.98 (s)	
47	17.8	0.70 (d, 6.9)	H-18, H-19*d*

[a] Interchangeable. [b] Measured at 100 MHz. [c] Measured at 300 MHz. [d] Proton connectivities observed in the COSY spectrum.

Heliothis virescens (LC_{50} 4 ppm, azadirachtin exhibited an LC_{50} of 1 ppm in this assay)[4] and antimicrobial activity against *Candida albicans* (11-mm zone of inhibition around a 7.6-mm disk impregnated with 1 μg of jaspamide). Jaspamide is one of the most potent metabolites against *Candida albicans* encountered in this program; however, it was completely inactive against a variety of Gram positive and Gram negative bacteria.

A MeOH extract of *Jaspis* obtained by soaking 73 g of pulverized freeze-dried tissue was subjected to a solvent partition to give 500 mg of combined CCl_4- and $CHCl_3$-soluble material. Filtration of this material through a silica gel 60 column (2.4 cm × 10 cm, EtOAc) followed by HPLC (Partisil 10, 4.6 mm × 25 cm; EtOAc/Hexane, 8:2) gave jaspamide (**1**) as a colorless oil (80 mg, 0.10% yield): $[\alpha]_D$ + 65.8° (*c* 1.535, CH_2Cl_2), $C_{36}H_{45}N_4O_6Br$ (HRFABMS, MH^+ 709.2596; requries 709.2602).

The depsipeptide nature of jaspamide was evident from IR bands at 1715, 1684, 1674, and 1638 cm^{-1} and ^{13}C NMR signals at 175.1, 174.4, 170.5, and 168.9 ppm indicating the presence of four units. An alanine unit was readily assigned from NMR spectral data including ^1H–^1H and ^1H–^{13}C 2D COSY experiments (see Table I). A 2-bromoabrine (*N*-methyltryptophan) unit was

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(1) Alfred P. Sloan Foundation Fellow, 1985–1987.
(2) (a) Ravi, B. N.; Wells, R. J.; Croft, K. D. *J. Org. Chem.* **1981**, *46*, 1998. (b) Ravi, B. N.; Wells, R. J. *Aust. J. Chem.* **1982**, *35*, 39.
(3) The specimen collected at Suva, Fiji, was identified as a *Jaspis* sp. by Dr. Avril Ayling, Sea Research, Daintree, Queensland 4873, Australia.
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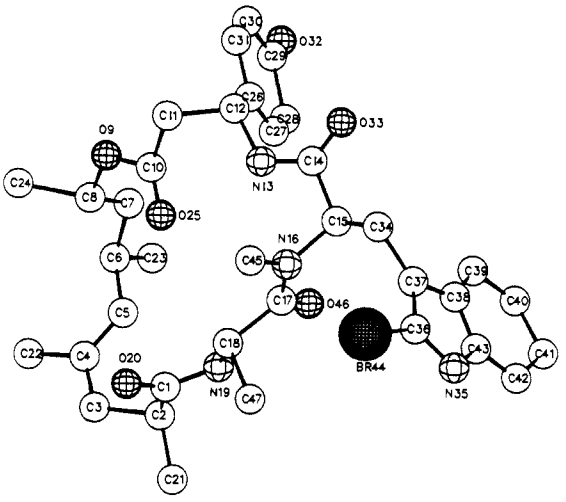
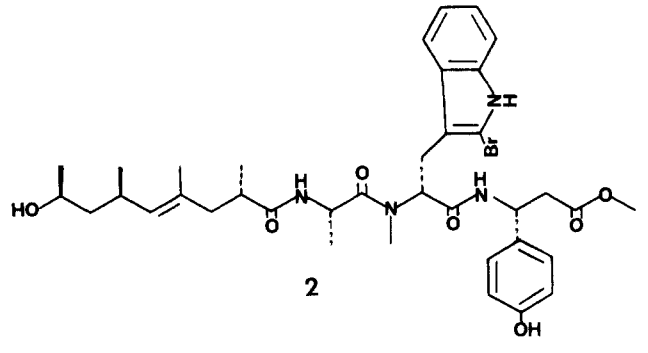


Figure 1. Computer-generated perspective drawing of the current X-ray model of jaspamide acetate. Hydrogens are omitted for clarity. The acetate at O32 is extensively disordered and not shown.

assigned on the basis of ^{1}H NMR data for a 2,3-disubstituted indole [δ 8.70 (br s, 1 H), 7.56 (br d, 1 H, J = 7.3 Hz), 7.24 (d, 1 H, J = 7.3 Hz), 7.13 (dd, 1 H, J = 7.3, 7.7 Hz), 7.10 (dd, 1 H, J = 7.3, 7.7 Hz)] and ^{13}C NMR data that correlated very closely with values recorded for the sodium salt of abrine.[5] The only notable difference observed was at the 2-position of the indole (C-36) which shows a 10 ppm upfield shift relative to abrine, consistent with a bromine at that position. The *N*-methyl was assigned to the bromoabrine unit because the α-proton at δ 5.85 (dd, J = 10.2, 6.4 Hz) did not show connectivity to an NH proton in the COSY spectrum. The remaining amino acid β-tyrosine is isomeric with tyrosine and exhibited ^{1}H and ^{13}C NMR data compatible with either structure, based on chemical shift analysis and proton decoupling studies. However, careful inspection of the COSY spectrum revealed allylic coupling between the methine proton H-12 and the ortho protons of the phenyl ring H-27 and H-31. The presence of this coupling is most consistent with a structure where the phenyl ring is attached directly to a methine carbon.

The fourth unit of jaspamide is an 11-carbon hydroxy acid containing four methyl groups on alternating carbons, characteristic of a polypropionate unit. The proton connectivities in this unit were defined as shown in Table I by a combination of proton decoupling and COSY data. The diastereotopic protons at C-3 (δ 2.38 and 1.89) both showed allylic coupling to the olefinic proton at C-5 allowing connection across the double bond. However, only one of the C-3 protons (downfield) showed coupling to the adjacent H-2, indicating there is some rigidity in the 19-membered ring.

Saponification and workup of jaspamide yielded a linear derivative **2**. The high-resolution FAB spectrum of **2** was consistent



2

with the amino acid sequence shown, exhibiting intense ions corresponding to cleavage of the amide bond between β-tyrosine and 2-bromoabrine [m/z 546.1963, $C_{27}H_{37}N_3O_4Br$ (-0.6 mmu)] and cleavage of the amide bond between 2-bromoabrine and alanine [m/z 474.1031, $C_{22}H_{23}N_3O_4Br$ + $2H^+$ (0.1 mmu); 268.1925, $C_{15}H_{26}NO_3$ (1.1 mmu)].

Hydrolysis of jaspamide (**1**) with 4 N $MeSO_3H$, 0.2% 3-(2-aminoethyl)indole as catalyst, followed by derivatization with dansyl chloride and diazomethane yielded 1 equiv of (*S*)-alanine as determined by chiral HPLC [Pirkle type, (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine, 75:25 hexane/EtOAc] but failed to give significant amounts of the other three expected products. Since these attempts to assign stereochemistry were largely unsuccessful and some question remained about the β-tyrosine unit, an x-ray analysis was performed on a crystalline acetate derivative **3**, mp 145-47 °C. A computer-generated perspective drawing is presented in Figure 1. The acetate group is extensively disordered. The absolute configuration was determined from the known configuration of alanine and is 2*S*,6*R*,8*S*, 12*R*,15*R*,18*S*. Efforts to improve the model are continuing and will be reported in a subsequent publication.

Jaspamide represents a new class of cyclic depsipeptides. It contains a propionate unit and two rare amino acids, β-tyrosine previously reported in the edeine peptides[6] and 2-bromoabrine which is apparently a new amino acid. Furthermore, both 2-bromoabrine and β-tyrosine have the unnatural D configuration.

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(5) ^{13}C NMR assignments for abrine Na salt recorded in D_2O: δ 182.1 (C-1'), 136.4 (C-7a), 127.5 (C-3a), 124.3 (C-5), 121.8 (C-6), 119.2 (C-4), 119.0 (C-2), 112.0 (C-7), 111.3 (C-3), 66.4 (C-2'), 33.6 (NCH_3), 28.8 (C-3').

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Classical (M = Os) and Nonclassical (M = Fe, Ru) Polyhydride Structures for the Complexes $MH_4(PR_3)_3$

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Recent developments in the coordination chemistry of molecular hydrogen have been very rapid.[1-4] In particular we have described a method of detecting these species using the fact that $M(H_2)$ resonances for a dihydrogen complex have T_1's more than an order of magnitude shorter than those for classical hydrides containing only terminal M-H bonds.[4b,c] We have recently shown by this method that IrH_5L_2 (L = $P(C_6H_{11})_3$) has a classical structure but its protonation product $[IrH_2(H_2)_2L_2]^+$ is a nonclassical bis-dihydrogen dihydride.

The complexes $MH_4(PR_3)_3$ of the iron triad constitute one of the best known examples of polyhydride complexes and are often cited as examples of the M(IV) oxidation state. Recently, Morris

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(4) Crabtree, R. H.; Lavin, M. (a) *J. Chem. Soc., Chem. Commun.* **1985**, 794; (b) **1985**, 1661; (c) *J. Am. Chem. Soc.*, in press. (d) T_1 values are ±10%. (e) The T_1 of free H_2 in toluene at 205 K is much longer (1.6 s) than those of complexed H_2 in **1** and **2** because the rotational correlation time is so much shorter in the free state.[4c] This further rules out exchange with free H_2 as the source of the short T_1 in **1** and **2**.

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