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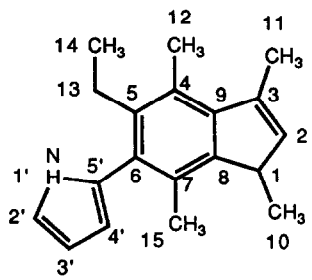
TRIKENTRAMINE, AN UNUSUAL PYRROLE DERIVATIVE FROM THE SPONGE *TRIKENTRION LOEVE* CARTER

Maurice Aknin+, Joseph Miralles++, Jean-Michel Kornprobst+,*, Robert Faure•, Emile-Marcel Gaydou••, Nicole Boury-Esnault§, Yoko Kato# and Jon Clardy#,*

+ Département de Chimie and ++ Département de Biologie Végétale
Université Cheikh Anta Diop de Dakar, SENEGAL
• Laboratoire de Chimie Organique Physique and •• Laboratoire de Phytochimie
Faculté des Sciences et Techniques de Saint Jérôme, 13397 Marseille Cedex, FRANCE
§ Centre d'Océanologie de Marseille, Station Marine d'Endoume
13007 Marseille, FRANCE
Department of Chemistry - Baker Laboratory, Cornell University
Ithaca, NY 14853-1301, U.S.A.

Summary: Trikentramine, an unusual pyrrole, has been isolated from the Senegalese sponge *Trikentrion loeve* and characterized by spectroscopic and X-ray diffraction techniques.

As part of our continuing investigation of marine natural products from the Senegalese coast, we have studied the sponge *Trikentrion loeve* Carter (Axinellidae, family Euryponidae). The chemistry of two other species of *Trikentrion* has been studied: *T. helium* which contains trikentriorhodin, a cyclopentane containing carotenoid[1], and the Australian species *T. flabelliforme* which contains the trikentrins, a series of six closely related cyclopentanoindoles[2]. In this paper we describe the isolation and structural elucidation of trikentramine, **1**, an intriguing pyrrole containing compound.



1

Specimens of *T.loeve* were collected by hand (SCUBA) at Thiouri-ba (40-45 m depth, off Dakar). Air dried sponges were continuously extracted with MeOH/$CHCl_3$ (3/1, v/v) and the

crude extract chromatographed on silica gel with eluants of increasing polarity. Trikentramine, **1** eluted with benzene and was recrystallized from hexane: m.p. 145 °C, $[\alpha]_D^{27}$ = +175° (*c* 0.81 $CHCl_3$).

The mass spectrum (EI, 12 and 70 eV) showed three peaks: m/z 265 (100%, M^+), 266 (20.6%, M^+ + 1) and 267 (2.0%, M^+ + 2) and suggested the empirical formula $C_{19}H_{23}N$ which required nine degrees of unsaturation. The presence of twelve deshielded carbons in the ^{13}C NMR spectra implied six double bonds and a tricyclic structure. An sharp and intense N-H absorption at 3350 cm^{-1} and a large band at 720 cm^{-1} in the IR spectrum were consistent with a deshielded N-H resonance (δ 7.78 ppm) in the ^1H NMR spectrum. This latter signal was observed by double resonance and 2D-homonuclear correlated[3,4] experiments (COSY) to be coupled to an isolated spin system consisting of three mutually coupled deshielded protons (δ 6.06, 6.30 and 6.84 ppm). These observations, together with UV absorptions (EtOH) at 209 nm (21300), 222 nm (39700) and 271 nm (10700) were consistent with a 2-monosubstituted pyrrole bound to an indene (see NMR discussion below).

Values of chemical shifts and coupling constants for ^1H NMR and ^{13}C NMR ($CDCl_3$, TMS) are given in Table 1. Carbon-proton correlations were established by heteronuclear correlation spectroscopy with decoupling in the F_1 dimension, and quaternary carbon resonances were assigned by comparison with known analog structures[5,6]. The following alkyl groups were identified in **1**: one ethyl group (δ 2.45 ppm, 2 H and 1.04 ppm, 3 H), three tertiary methyl groups (δ 2.07, 2.36, and 2.54 ppm) and a secondary methyl group (δ 1.24 ppm) coupled to a methine proton (δ 3.36 ppm). A long range coupling (1.7 Hz) was observed between the CH_3-11 (δ 2.36 ppm) and the H-1 methine proton (δ 3.36 ppm). Furthermore in the COSY spectrum cross correlation signals were observed between H-1 and both CH_3-10 (δ 1.24 ppm) and CH_3-11 (δ 2.36 ppm). These latter observations were consistent with the sequence CH_3-CH-CH=C-CH_3 of the cyclopentenyl moiety of an indene. The four remaining groups, two methyls, one ethyl and the pyrrole were therefore substituents on the benzene ring.

A combined analysis of the NOESY and COSY results revealed the substituent pattern. The NOESY spectrum cross peak observed between CH_3-10 (δ 1.24 ppm) and CH_3-15 (δ 2.07) suggested that CH_3-15 was attached to C7. The absence of diagonal signals in the COSY spectrum between CH_2-13 (δ 2.45 ppm) and the CH_3-12 (δ 2.54 ppm) together with a cross peak in the NOESY spectrum between CH_3-12 and CH_3-11 (δ 2.36 ppm) required CH_3-12 to be at C-4 and the ethyl group to be at C-5. Thus the pyrrole substituent had to occupy the last available position, C-6.

A single crystal X-ray diffraction analysis unambiguously defined the structure. Crystals formed in the orthorhombic space group $P2_12_12_1$, and accurate lattice constants of a = 7.002(2), b = 11.779(2), and c = 19.186(6) Å were determined from a least-squares fit of diffractometer measured 2θ-values. One molecule of composition $C_{19}H_{23}N$ formed the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected using 2θ:θ scans and Cu Kα radiation. Of the 1261 reflections measured in this fashion, 1046 (83%) were judged observed ($|F_o| \geq 4\sigma(|F_o|)$) and used in subsequent calculations. The structure was phased using direct methods and refined

using full-matrix least-squares with anisotropic heavy atoms and fixed isotropic riding hydrogens to a conventional discrepancy index of 5.7%.[7]

A computer generated perspective drawing of the final X-ray model of trikentramine is given in Figure 1. The X-ray experiment did not define the absolute stereochemistry at C-1, so the enantiomer shown represents an arbitrary choice. The substituents on the fully substituted aromatic ring are oriented so as to minimize steric congestion with the planes of the pyrrole and ethyl group essentially perpendicular to the plane of the indene.

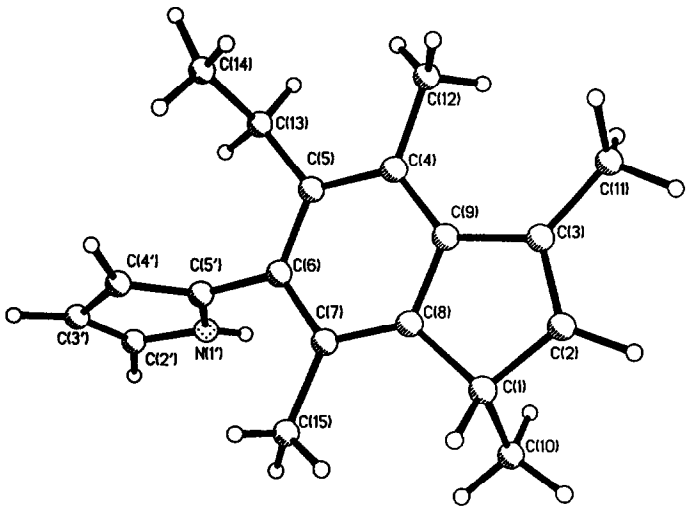


Figure 1. A computer generated perspective drawing of the final X-ray model of trikentramine (1). No absolute configuration is implied.

The structure of trikentramine 1 seems to be completely new, and to our knowledge, no natural product, of either terrestrial or marine origin, has such a skeleton. The biosynthesis of trikentramine is thus an intriguing question, and our ongoing work on additional, closely related compounds from *T. loeve* may provide some clues.

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Notes and References

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Table 1. ^{1}H and ^{13}C NMR data for trikentramine (1).

C/H	δ ppm	Intensity	^{1}H NMR Multiplicity	J (Hz)	^{13}C NMR
1'	7.78	1H			
2'	6.84	1H	ddd	2.9, 2.7, 1.5	116.49
3'	6.30	1H	ddd	2.9, 2.9, 2.9	108.25[a]
4'	6.06	1H	ddd	2.9, 2.7, 1.5	108.98[a]
5'					126.90
1	3.36	1H	q. quint.	7.3, 1.7, 1.7	42.36
2	6.12	1H	quint.	1.7, 1.7	139.37
3					142.98b
4					131.68
5					142.58b
6					139.20
7					130.71
8					150.70
9					146.20
10	1.24	3H	d	7.3	16.50
11	2.36	3H	t	1.7	18.70
12	2.54	3H	s		15.84
13	2.45	2H	mult.	7.3	24.25
14	1.04	3H	t.	7.3	16.32
15	2.07	3H	s.		16.84

^{1}H NMR (200 MHz, $CDCl_3$, TMS); ^{13}C NMR (50.3 MHz, $CDCl_3$, TMS).

[a,b] These assignments may be reversed

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