Structures and Activities of Tiahuramides A-C, Cyclic Depsipeptides from a Tahitian Collection of the Marine Cyanobacterium *Lyngbya majuscula*

Annabel Levert,[†,□] Rebeca Alvariño,[‡] Louis Bornancin,[†] Eliane Abou Mansour,[†,▽] Adam M. Burja,[§,○] Anne-Marie Genevière,[⊥] Isabelle Bonnard,[†,II] Eva Alonso,[‡] Luis Botana[‡] and Bernard Banaigs*[†,II]

[†] *CRIOBE, USR CNRS-EPHE-UPVD 3278, Université de Perpignan, 66860 Perpignan, France.*

[‡] *Departamento de Farmacología, Facultad de Veterinaria, Universidad de Santiago de Compostela, Lugo 27003, Spain.*

[§] *Heriot-Watt University, Edinburgh, Scotland EH14 4 AS.*

[⊥] *Sorbonne Universités, UPMC Univ Paris 06, CNRS, Biologie Intégrative des Organismes Marins (BIOM), Observatoire Océanologique, F-66650, Banyuls/Mer, France.*

[II] *Laboratoire d'Excellence "CORAIL", France.*

* To whom correspondence should be addressed. Tel: +33 4 68 662074. Fax: +33 4 68 662223. E-mail: banaigs@univ-perp.fr.

□ Present address: SAS AkiNaO, Perpignan, France.

▽ Present address: Universite de Neuchatel, Switzerland.

○ Present address: DSM Nutritional Products, 6480 Dobbin Road, Columbia, MD, 21045, USA.

A.L., R.A. and L.B. contributed equally to this work.

SUPPORTING INFORMATION

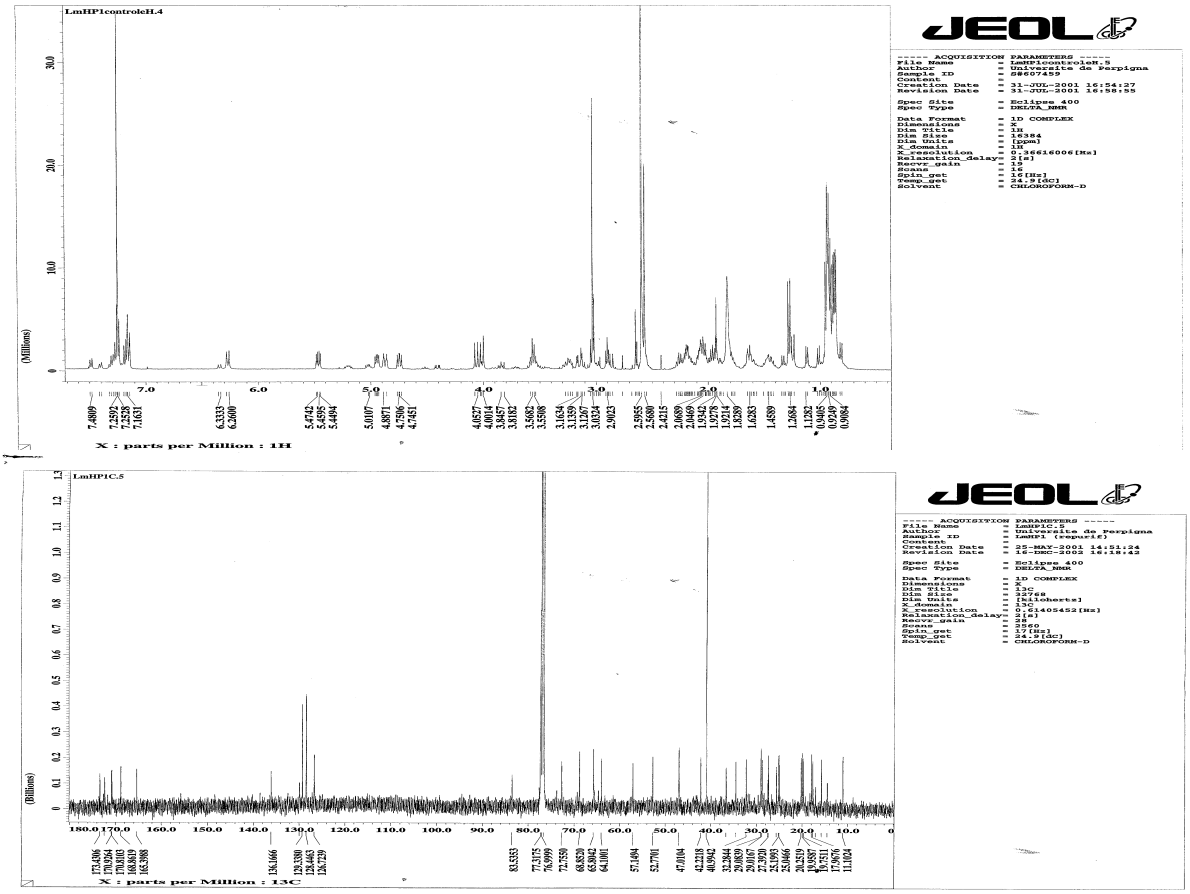
The Supporting Information is available free of charge on the ACS Publications website at DOI:

- NMR Measurement Conditions. All spectra were obtained with a NM-40TH5 dual ^{1}H, ^{13}C probe in a JEOL EX400 operating at 400 MHz for proton and 100.53 MHz for carbon-13 at 298 K. ^{1}H and ^{13}C NMR chemical shifts are referenced to solvent peaks: δ_H 7.24 (residual $CHCl_3$), δ_C 77.0 for $CDCl_3$. Tiahuramide A (7 mg), tiahuramide B (4 mg) and tiahuramide C (3.5 mg) were dissolved in a 5 mm tube in 0.75 ml of $CDCl_3$.

Two-dimensional (2D) homonuclear correlated experiments DQF-COSY, HOHAHA and ROESY were all acquired using standard procedures with a spectral width of approximately 4000 Hz in both columns F_1 and F_2. HOHAHA and ROESY were acquired in the phase sensitive mode. The time domain matrix consisted of 256 points in t_1 and 1024-2048 points in t_2 with 64-128 acquisitions for 256 experiments in t_1. Data sets were zero-filled to 512 points in t_1 prior to Fourier transformation to obtain a frequency domain matrix of 512 x 1024-2048 real data points. Squared sine bell apodization functions were used. The HOHAHA spectra were recorded with a mixing time of 100 ms. ROESY spectra were measured with mixing times of 150, 250 and 350 ms. Heteronuclear correlated experiments were performed in ^{1}H-detected mode using the standard pulse programs HSQC and HMBC with a spectral width of approximately 20,000 Hz in F_1 and 4,000 Hz in F_2. The time domain matrix consisted of 256 points in t_1 and 2048 points in t_2 with 128 acquisitions for 256 experiments in t_1. Data sets were zero-filled to 512 points in t_1 prior to Fourier transformation to obtain a frequency domain matrix of 512 x 2048 real data points. The evolution delay was set to optimize 140 Hz couplings for HSQC and 8 Hz couplings for HMBC. Squared sine bell apodization functions were used.

- Figure S1. ^{1}H, ^{13}C, DEPT NMR spectra of tiahuramide A (**1**).

Tiahuramide A /^{1}H & ^{13}C



Tiahuramide A / DEPT

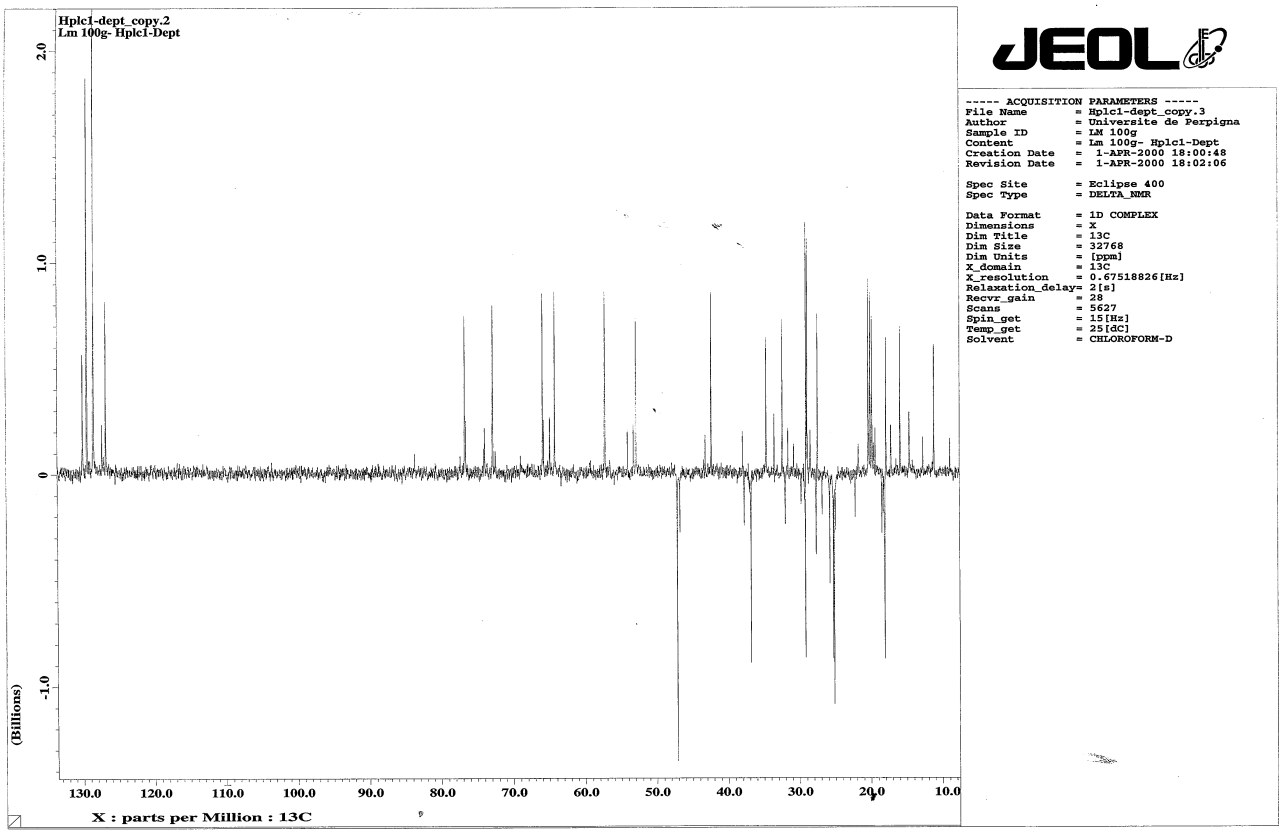
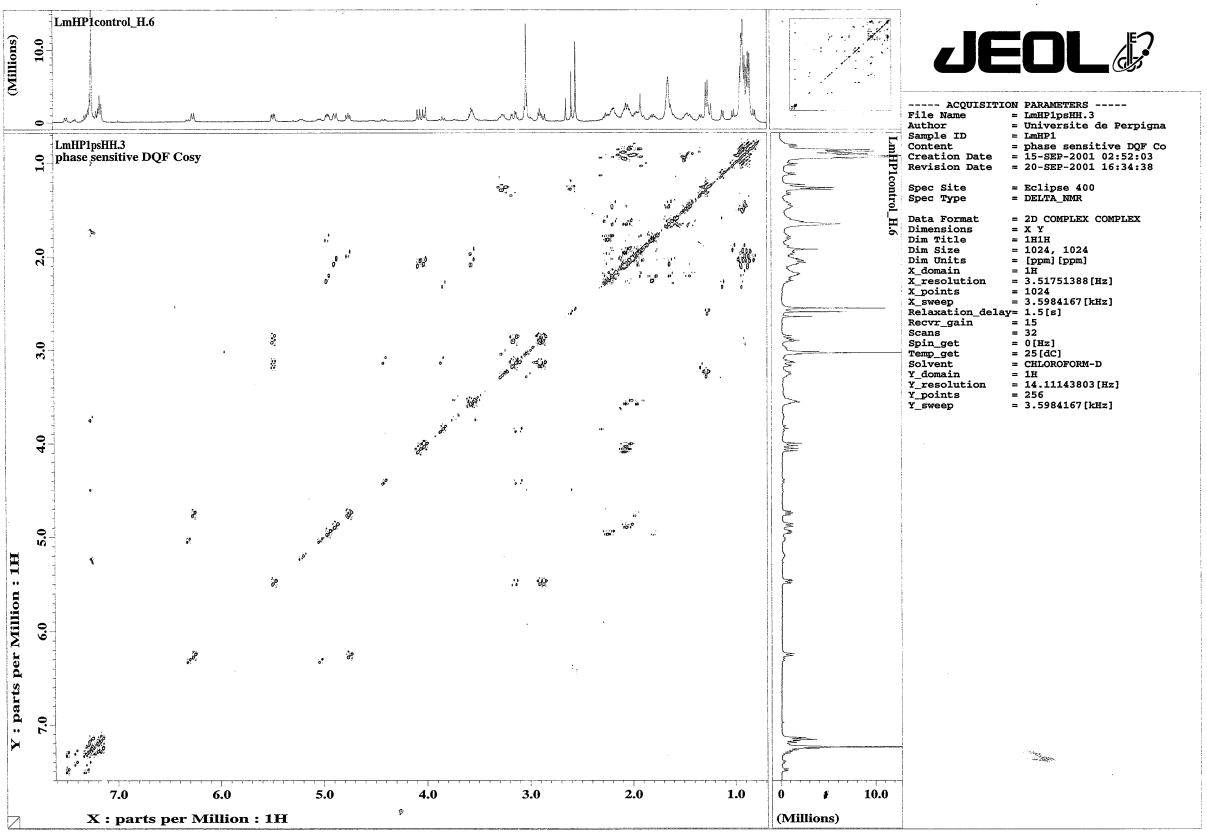


Figure S2. DQF COSY and HOHAHA NMR spectra of tiahuramide A (**1**).

Tiahuramide A / DQF COSY



Tiahuramide A / HOHAHA 50 ms

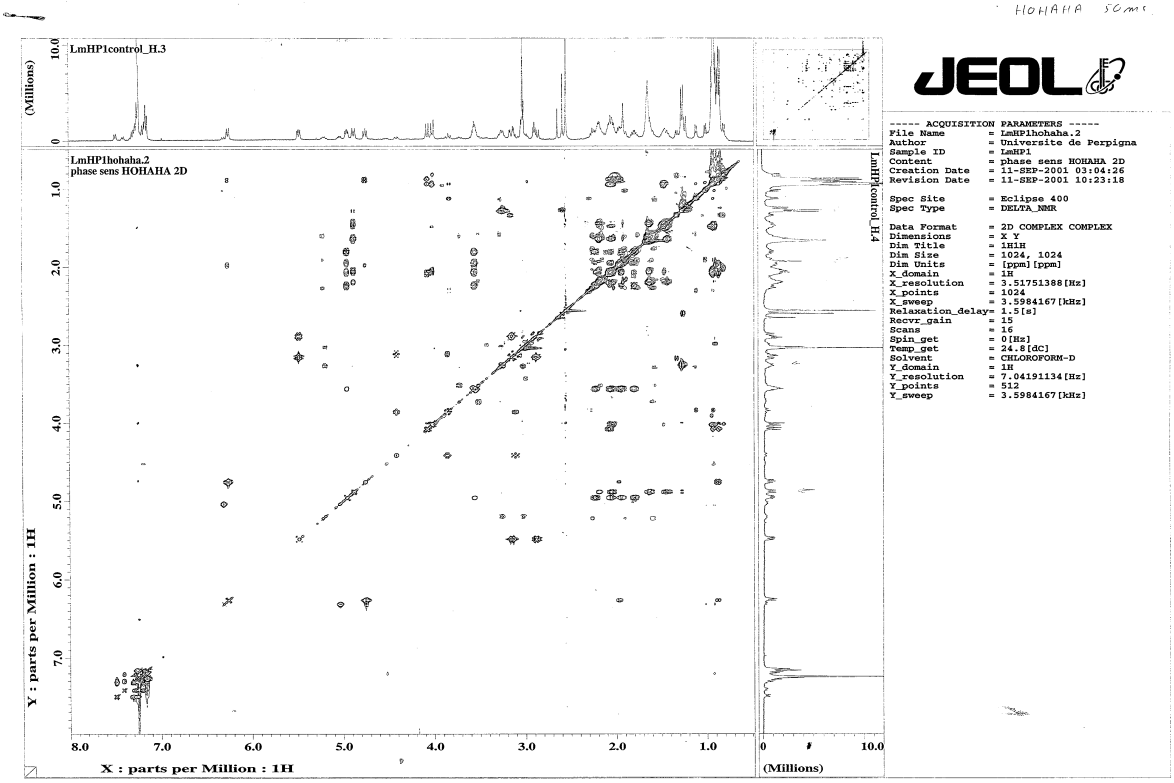
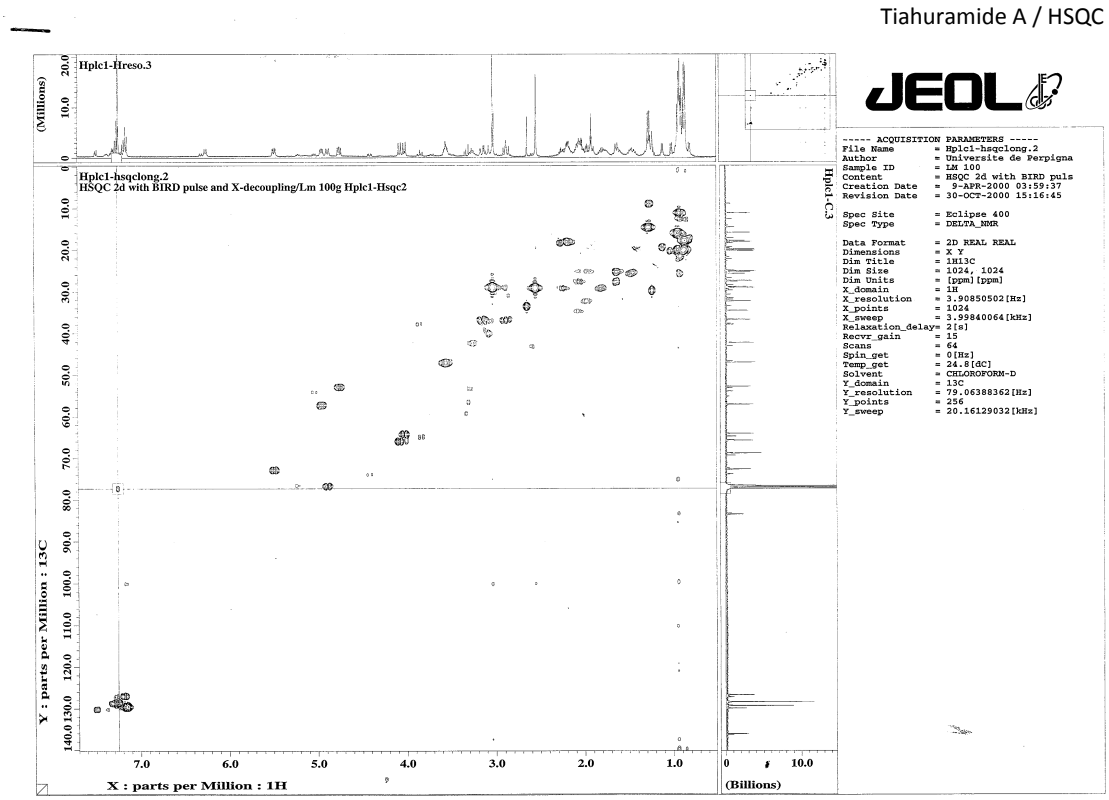
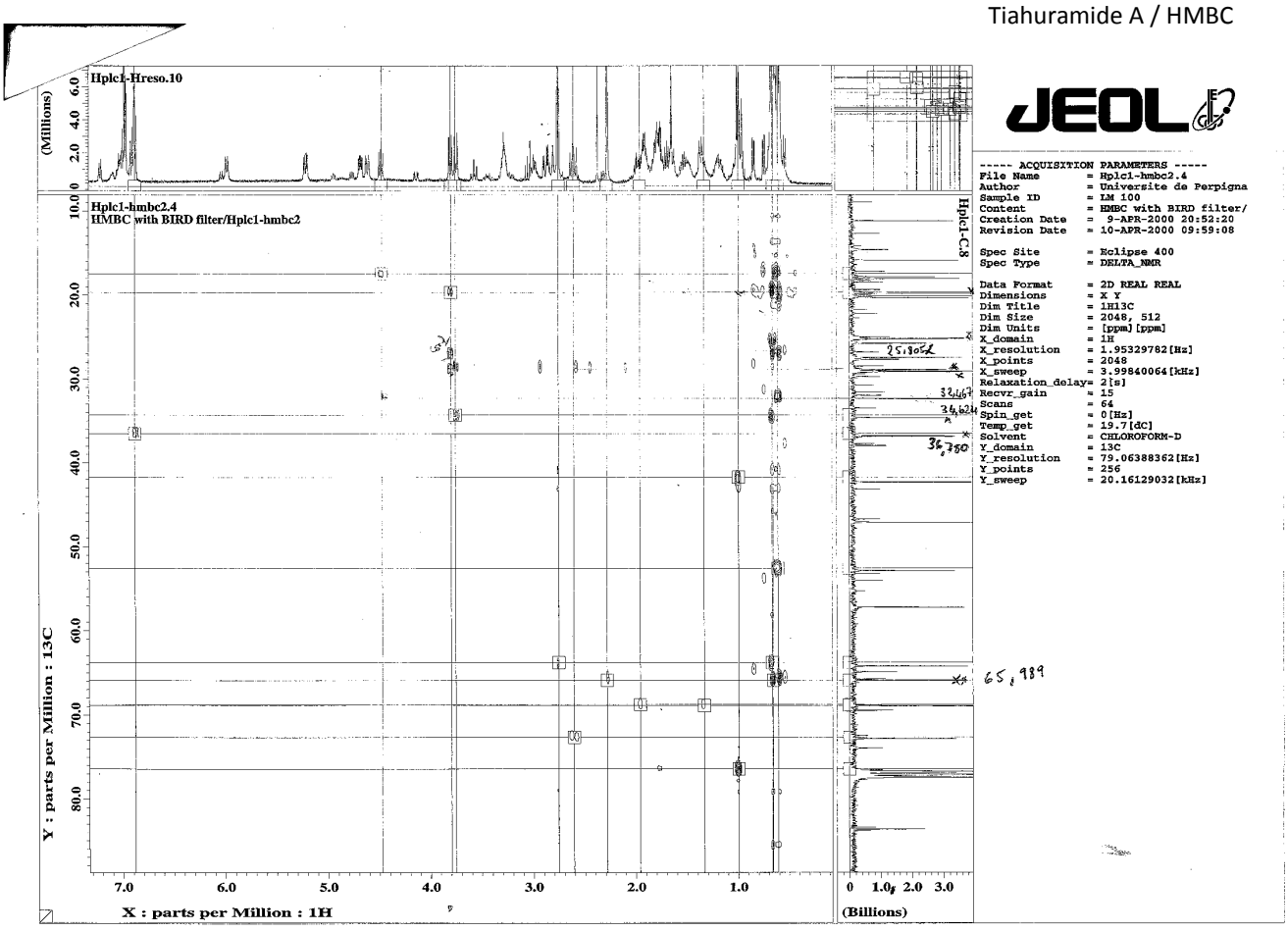


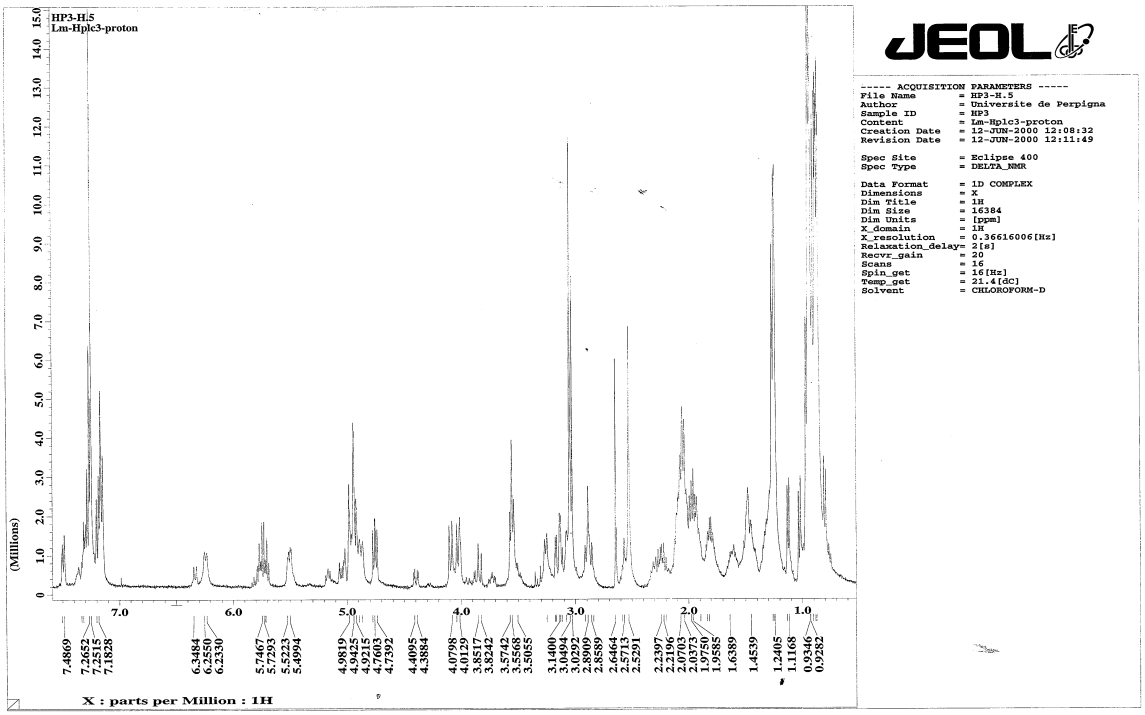
Figure S3. HSQC and HMBC NMR spectra of tiahuramide A (**1**).





- Figure S4. ^{1}H spectra of tiahuramides B (**2**) and C (**3**).

Tiahuramide B / ^{1}H



Tiahuramide C / ^{1}H

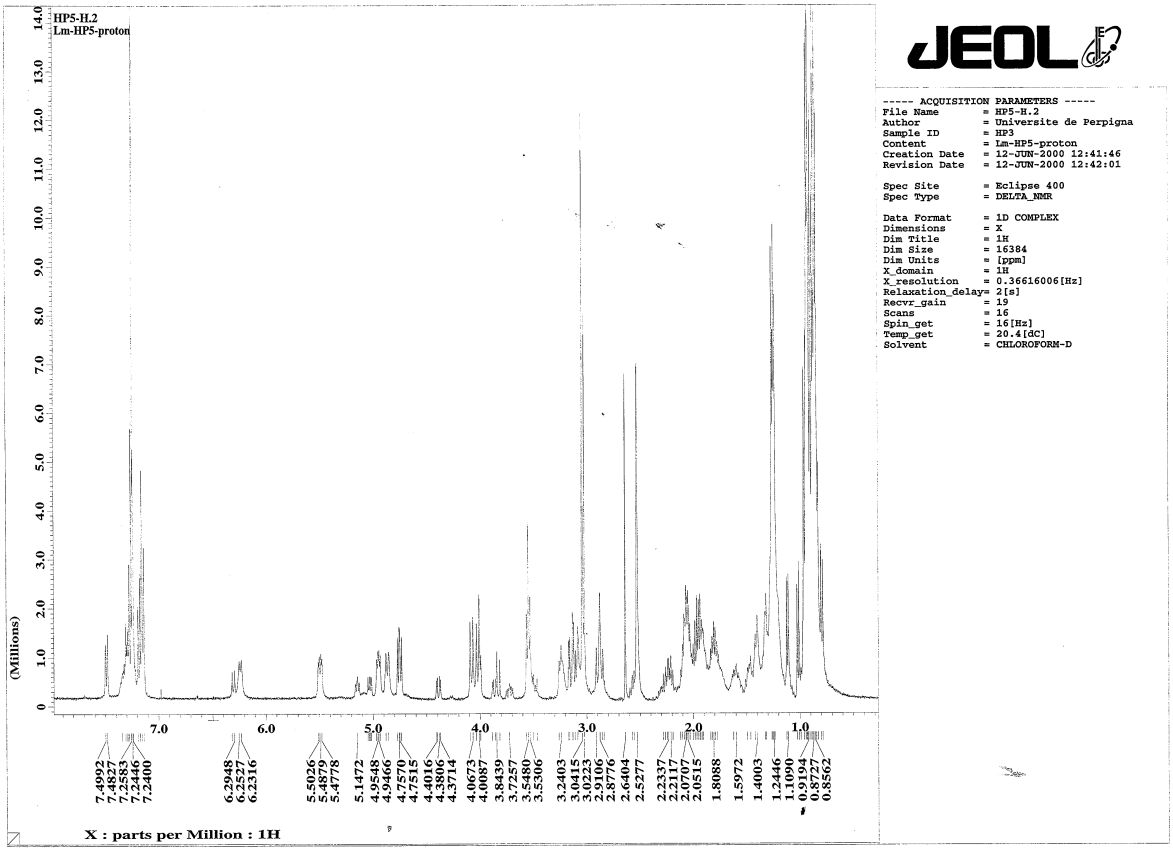
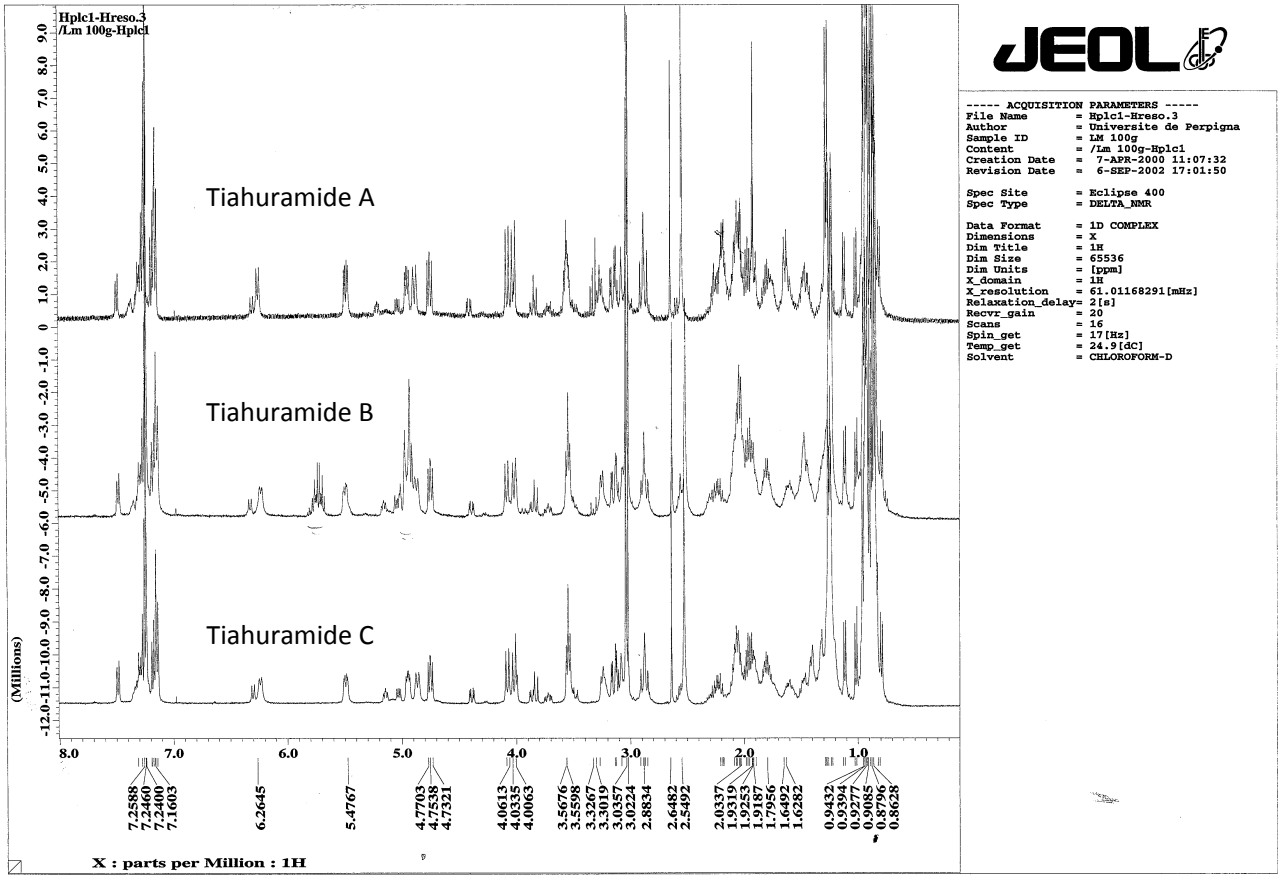


Figure S5. Comparison of ^{1}H and ^{13}C NMR NMR spectra of tiahuramides A-C (**1-3**).

Tiahuramides A-C / ^{1}H comparison



Tiahuramides A-C / ^{13}C comparison

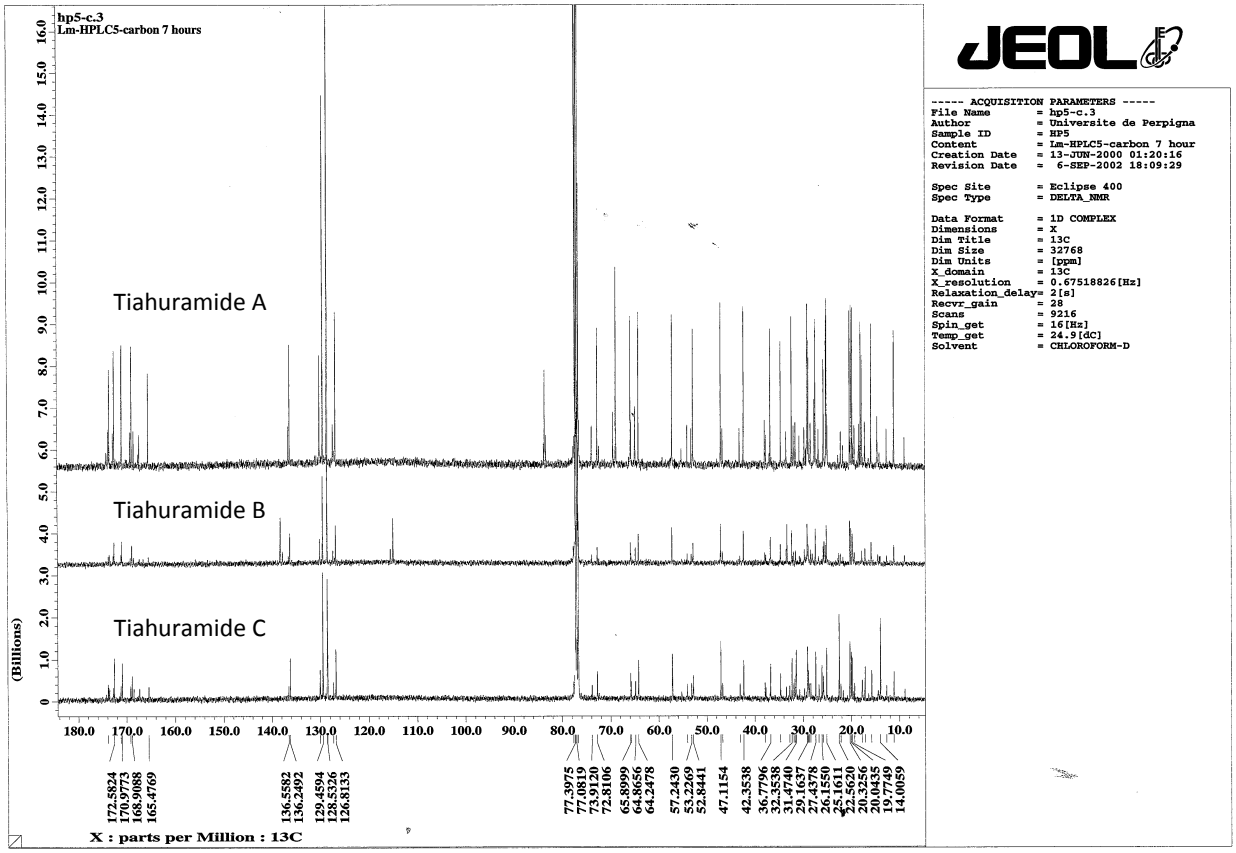


Figure S6. HPLC chromatograms of the Marfey's analysis.

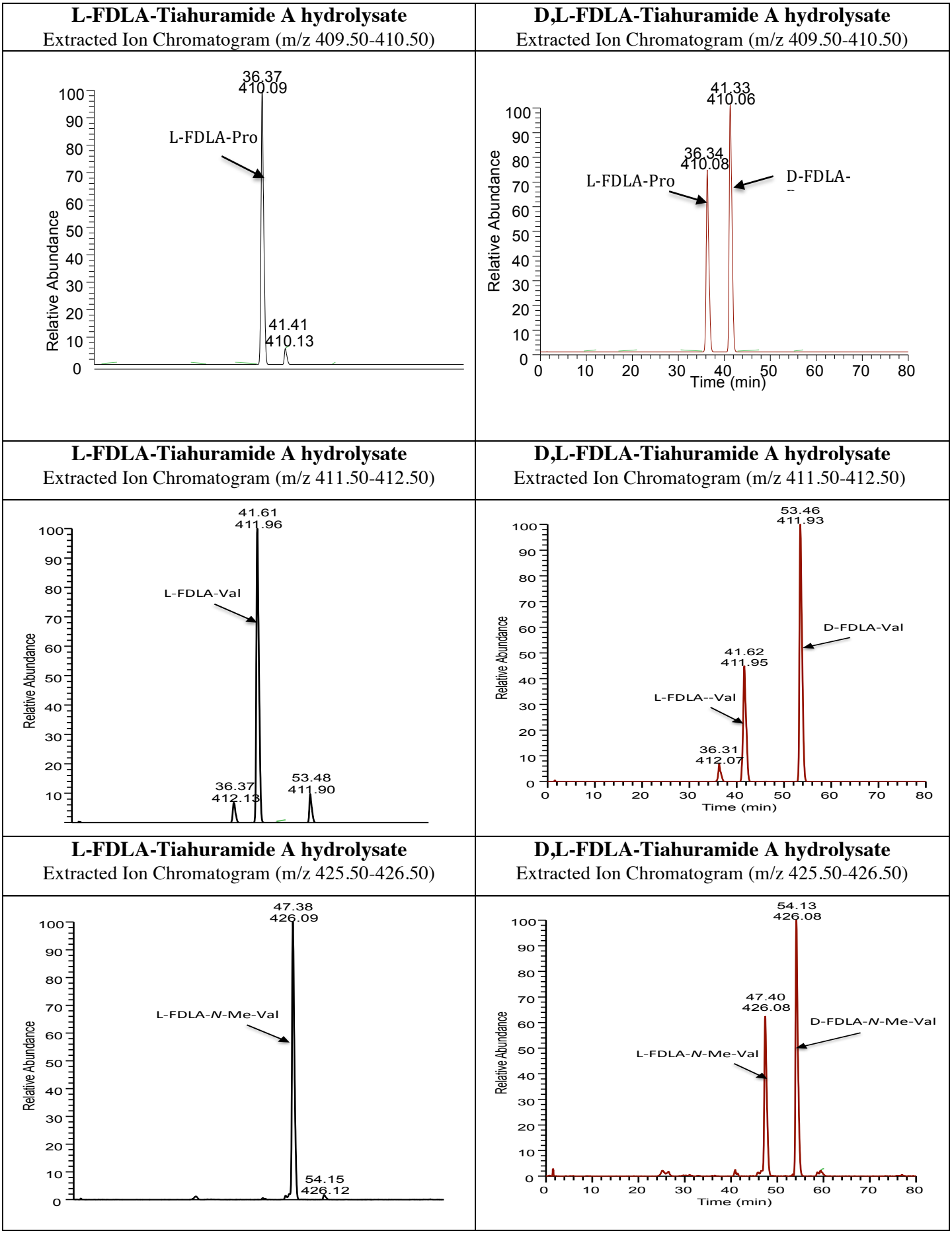


Table S1: Retention times (min) of standard and natural Marfey's *N*-Me-Ile derivatives

	Standard *N*-Me-Ile		***N*-Me-Ile from Tiahuramide A hydrolysate**
	N-Me-L-*allo*-Ile (2S,3R)-Ile	*N*-Me-L-Ile (2S,3S)-Ile	*N*-Me-L-Ile (2S,3S)-Ile
L-FDLA	52.12	51.78	51.78
D-FDLA	59.26	59.08	59.10

Gradient : from 10% CH_3CN-90% 0.01 M formic acid to 50%-50% at 0.3 mL/min over 70 min, then to 80%-20% over 10 min

Figure S7. HPLC chromatograms of the Marfey's analysis of standard and natural Marfey's *N*-Me-Ile derivatives