Supporting Information

Toward the Synthesis and Improved Biopotential of an *N*-methylated Analog of a Proline-Rich Cyclic Tetrapeptide from Marine Bacteria

Rajiv Dahiya[1]*, Suresh Kumar[2]*, Sukhbir Lal Khokra[2] , Sheeba Varghese Gupta[3], Vijaykumar B. Sutariya[3], Deepak Bhatia[4], Ajay Sharma[5], Shamjeet Singh[1] and Sandeep Maharaj[1]

[1]*Laboratory of Peptide Research and Development, School of Pharmacy, Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Trinidad & Tobago, West Indies; Rajiv.Dahiya@sta.uwi.edu; Shamjeet.Singh@sta.uwi.edu; Sandeep.Maharaj@sta.uwi.edu*
[2]*Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra 136119, Haryana, India; sureshmpharma@rediffmail.com; slkhokra@kuk.ac.in*
[3]*Department of Pharmaceutical Sciences, USF College of Pharmacy, University of South Florida, Tampa, FL 33612-4749, USA; svarghes@health.usf.edu; vsutariy@health.usf.edu*
[4]*Department of Pharmacogenomics, Bernard J. Dunn School of Pharmacy, Shenandoah University- ICPH Fairfax, Fairfax, VA 22031, USA; dbhatia@su.edu*
[5]*Department of Pharmacognosy, Amity Institute of Pharmacy, Amity University, Gwalior 474020, Madhya Pradesh, India; asharma5@gwa.amity.edu*

Content	*Page*

ppm

Current Data Parameters
NAME   proton
EXPNO   72
PROCNO   5

F2 - Acquisition Parameters
Date_   500000
Time   13.27
INSTRUM   dpx300
PROBHD   5mm Dual Z5
PULPROG   zg
TD   32768
SOLVENT   CDCl3
NS   8
DS   0
SWH   8992.806 Hz
FIDRES   0.274439 Hz
AQ   1.8219508 sec
RG   114
DW   55.600 usec
DE   4.50 usec
TE   300.0 K
D1   5.00000000 sec
P1   11.00 usec
DE   4.50 usec
SFO1   300.1342018 MHz
NUC1   1H
PL1   0.00 dB

F2 - Processing parameters
SI   32768
SF   300.1300056 MHz
WDW   EM
SSB   0
LB   0.80 Hz
GB   0
PC   0.50

1D NMR plot parameters
CX   21.00 cm
F1P   10.000 ppm
F1   3001.30 Hz
F2P   -0.500 ppm
F2   -150.07 Hz
PPMCM   0.50000 ppm/cm
HZCM   150.06500 Hz/cm

Integral

Figure S1. ^{1}H NMR spectrum for proline-rich N-methylated tetracyclopeptide **4**

ppm

Current Data Parameters
NAME   41
EXPNO   360
PROCNO   1

F2 - Acquisition Parameters
Date_   500000
Time   11.27
INSTRUM   dpx300
PROBHD   5mm Dual Z5
PULPROG   zgdc
TD   16384
SOLVENT   CDCl3
NS   5276
DS   0
SWH   18632.393 Hz
IDRES   1.149438 Hz
AQ   0.4350452 sec
RG   9195.2
DW   26.550 usec
DE   4.50 usec
TE   300.0 K
d11   0.0300000 sec
PL12   17.80 dB
CPDPRG2   waltz16
PCPD2   90.00 usec
SFO2   300.1330013 MHz
NUC2   1H
PL2   0.00 dB
D1   1.00000000 sec
P1   9.40 usec
DE   4.50 usec
SFO1   75.4767751 MHz
NUC1   13C
PL1   0.00 dB

F2 - Processing parameters
SI   16384
SF   75.4677572 MHz
WDW   EM
SSB   0
LB   5.00 Hz
GB   0
PC   1.40

1D NMR plot parameters
CX   20.00 cm
F1P   200.000 ppm
F1   15093.55 Hz
F2P   0.000 ppm
F2   0.00 Hz
PPMCM   10.00000 ppm/cm
HZCM   754.67761 Hz/cm

Figure S2. ^{13}C NMR spectrum for proline-rich N-methylated tetracyclopeptide **4**

Figure S3. Mass spectrum for proline-rich *N*-methylated tetracyclopeptide **4**

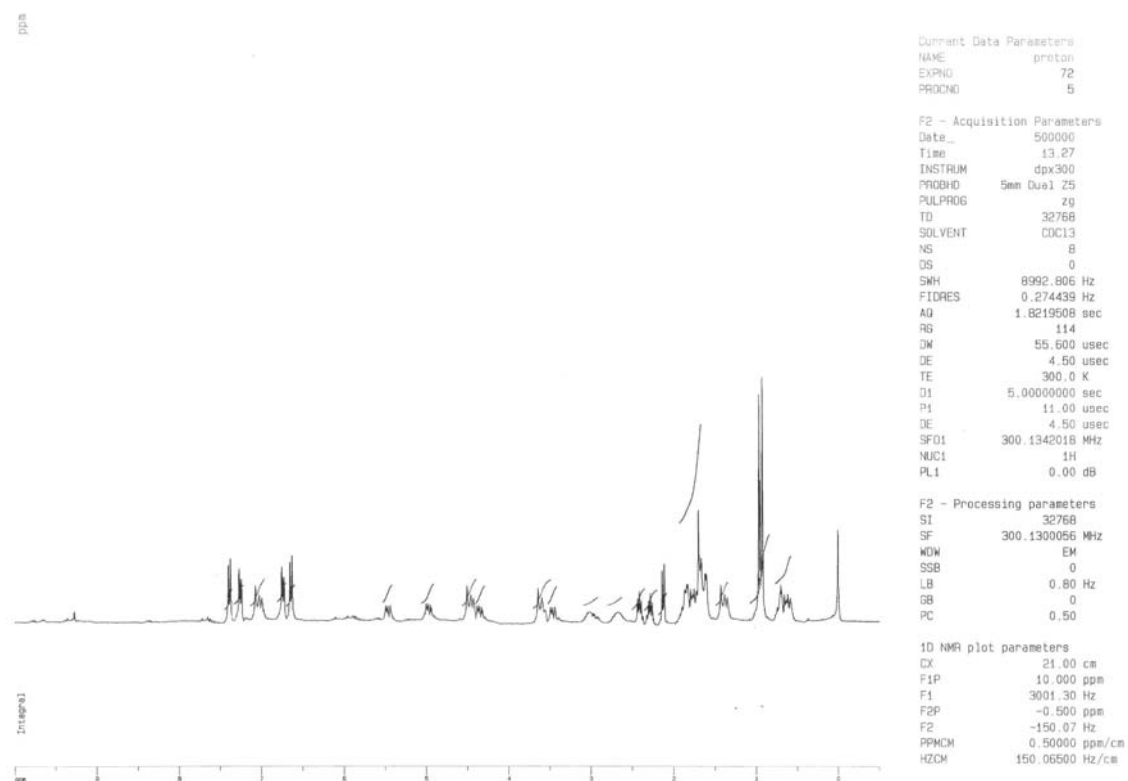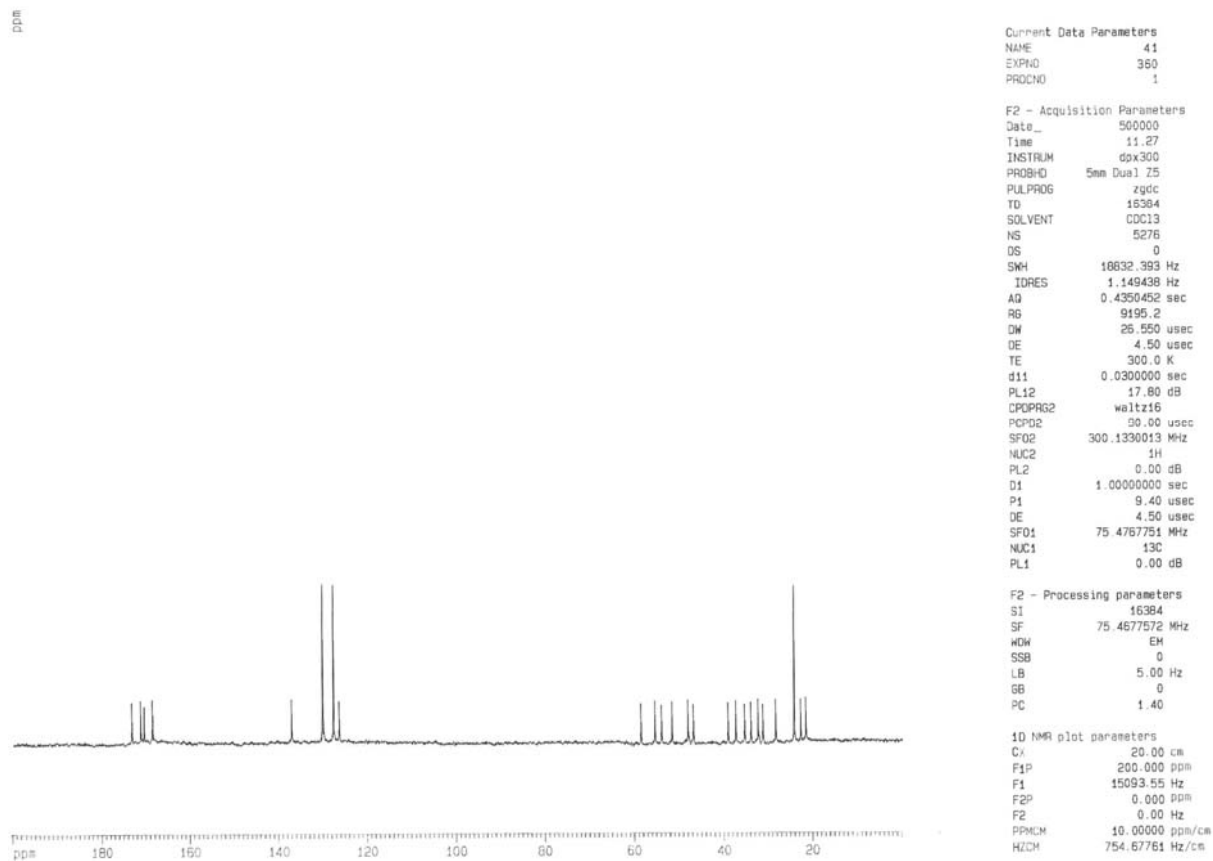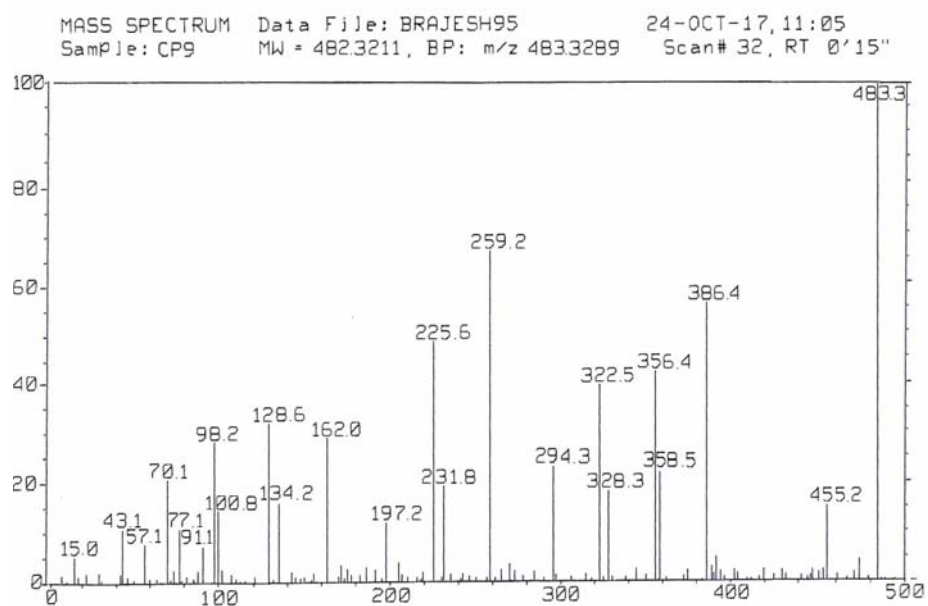**Table S1.** Various steric and lipophilicity parameters for linear and cyclotetrapeptide (**3**, **4**)

Parameter	*Calculated value for	
	Compound 3	Compound 4
Molar Refractivity (MR[20])	165.05 ± 0.3 cm^3	133.74 ± 0.4 cm^3
Molar Volume (MV[20])	523.8 ± 3.0 cm^3	391.9 ± 5.0 cm^3
Parachor (P$_r$)	1384.4 ± 6.0 cm^3	1072.4 ± 6.0 cm^3
Refractive Index (n[20])	1.542 ± 0.02	1.598 ± 0.03
Surface Tension (γ[20])	48.7 ± 3.0 dyne/cm	56.0 ± 5.0 dyne/cm
Density (d[20])	1.173 ± 0.06 g cm^{-3}	1.23 ± 0.1 g cm^{-3}
Polarizability (α)	$65.43 \pm 0.5 \ 10^{-24}$ cm^3	$53.02 \pm 0.5 \ 10^{-24}$ cm^3
log P (n-Octanol/water)	4.19 ± 0.78	3.86 ± 0.89

*Values were calculated using ACD/ChemSketch 2.0 software