Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary material

(^{1}H, ^{13}C NMR spectra and Mass spectra of synthesized compounds)

Alkylated histidine based short cationic antifungal peptides: synthesis, biological evaluation and mechanistic investigations

Sherry Mittal,[a] Sarabjit Kaur,[a] Anuradha Swami,[b] Indresh K. Maurya,[c] Rahul Jain,[d] Nishima Wangoo*[b] and Rohit K. Sharma*[a]

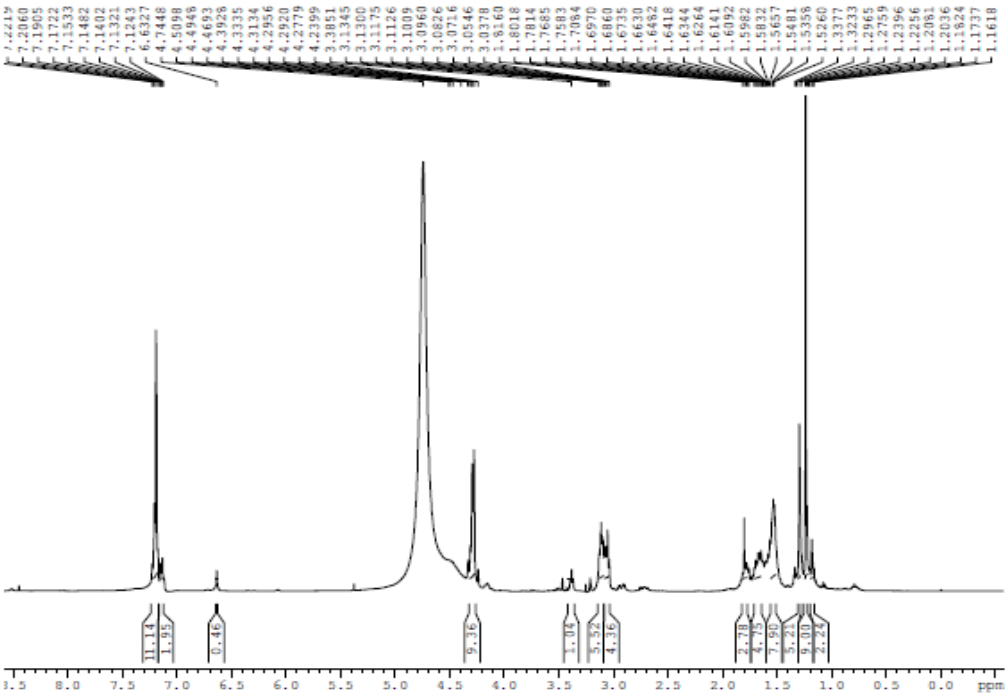
[a]*Department of Chemistry & Centre for Advanced Studies in Chemistry, Panjab University, Sector-14, Chandigarh-160014, India. Email: rohitksg@pu.ac.in; Tel: +91 1722534409; Fax: +91 172 2545074*

[d] *Department of Applied Sciences Division, University Institute of Engineering & Technology (U.I.E.T.), Panjab University, Sector-25, Chandigarh-160014, India. Email: nishima@pu.ac.in*

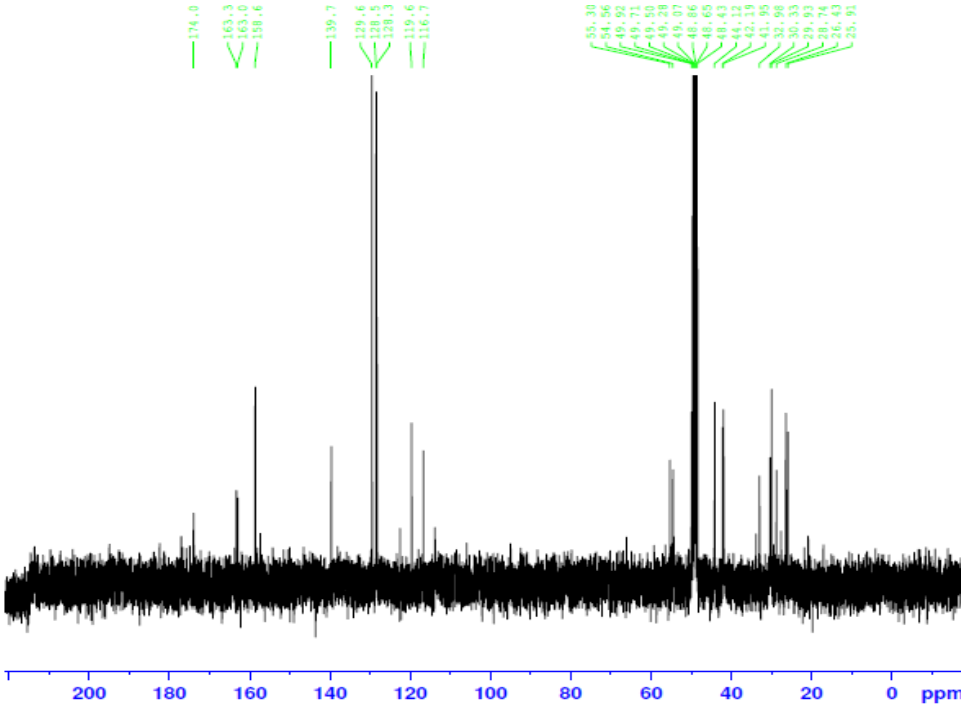
[b]*Department of Microbial Biotechnology, Panjab University, Sector-14, Chandigarh-160014, India*

[c]*Department of Medicinal Chemistry, National Institute of Pharmaceutical Education & Research (NIPER), Sector-67, S.A.S. Nagar, Punjab-160062, India*

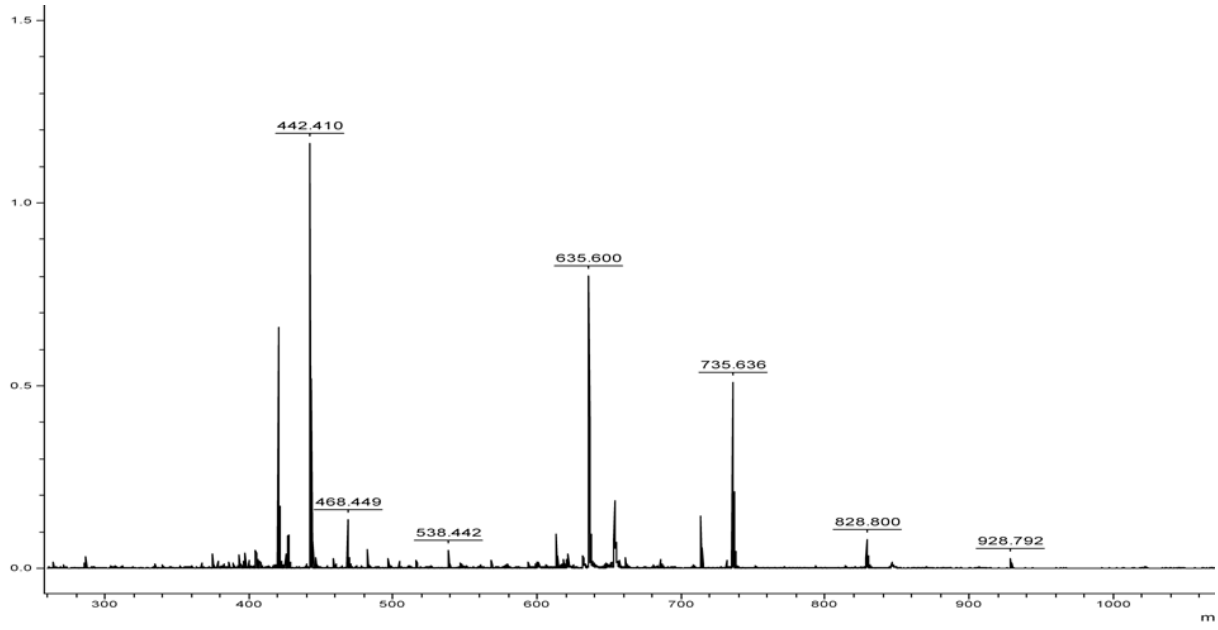
Boc-His(2-t-butyl)-Arg-Arg-NHBzl (14a):



^{1}H-NMR of Boc-His(2-t-butyl)-Arg-Arg-NHBzl (**14a**)

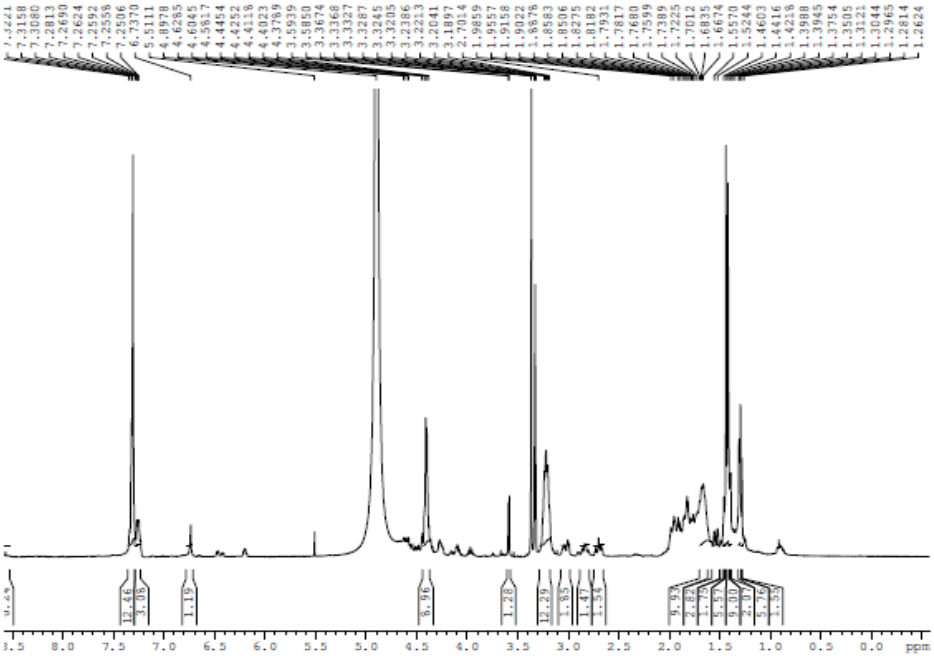


^{13}C-NMR of Boc-His(2-t-butyl)-Arg-Arg-NHBzl (**14a**)

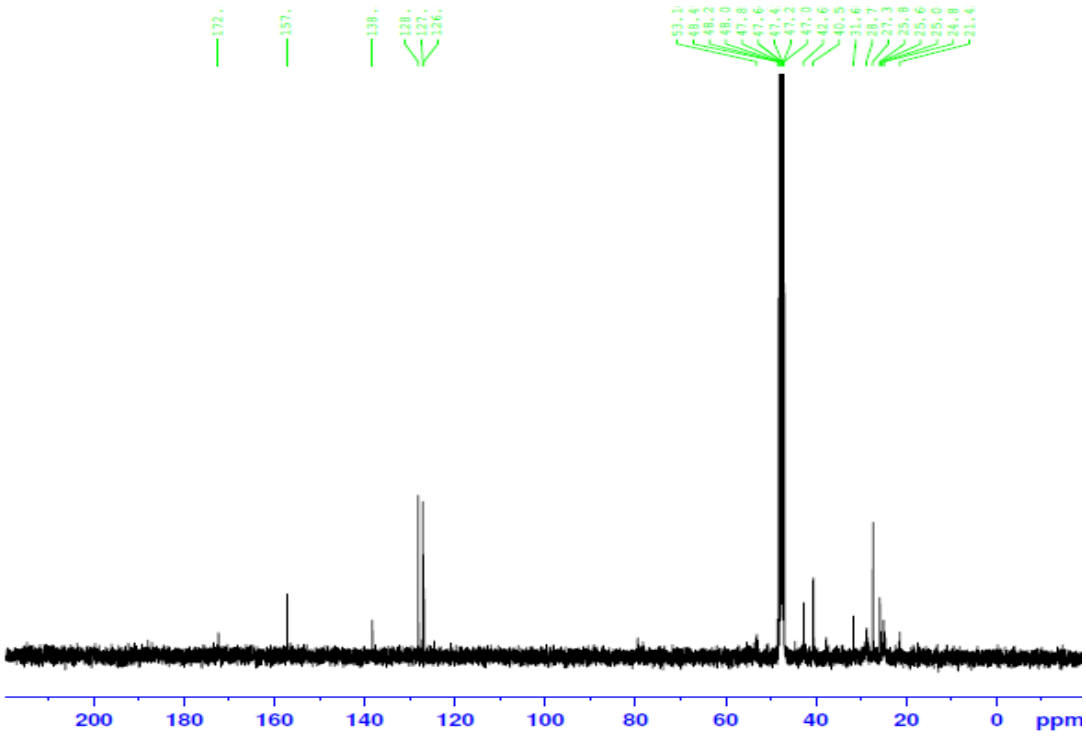


MALDI- MS of Boc-His-(2-t-butyl)-Arg-Arg-NHBzl (**14a**), $[MH]^+$ 713.64

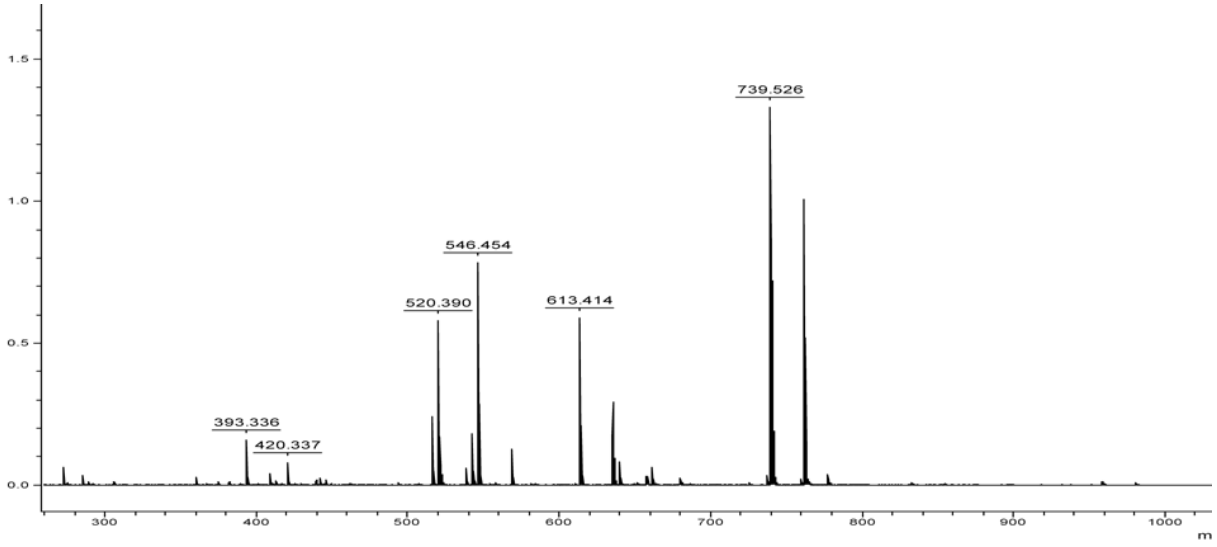
Boc-His(2-cyclohexyl)-Arg-Arg-NHBzl (14b):



^{1}H-NMR of Boc-His(2-cyclohexyl)-Arg-Arg-NHBzl (**14b**)

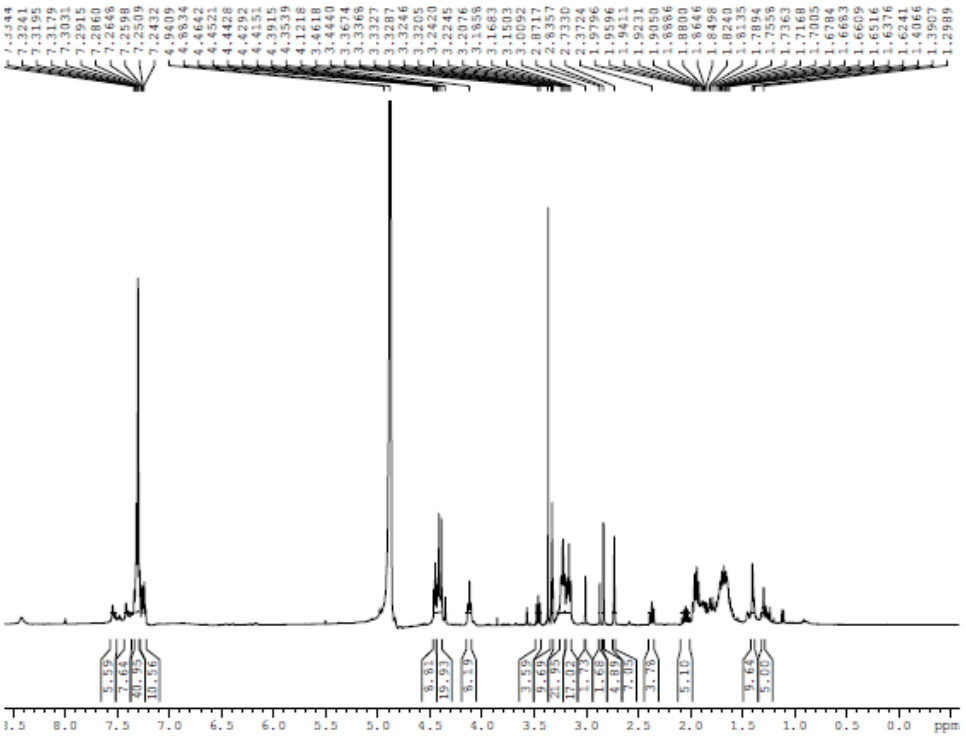


^{13}C-NMR of Boc-His(2-cyclohexyl)-Arg-Arg-NHBzl (**14b**)

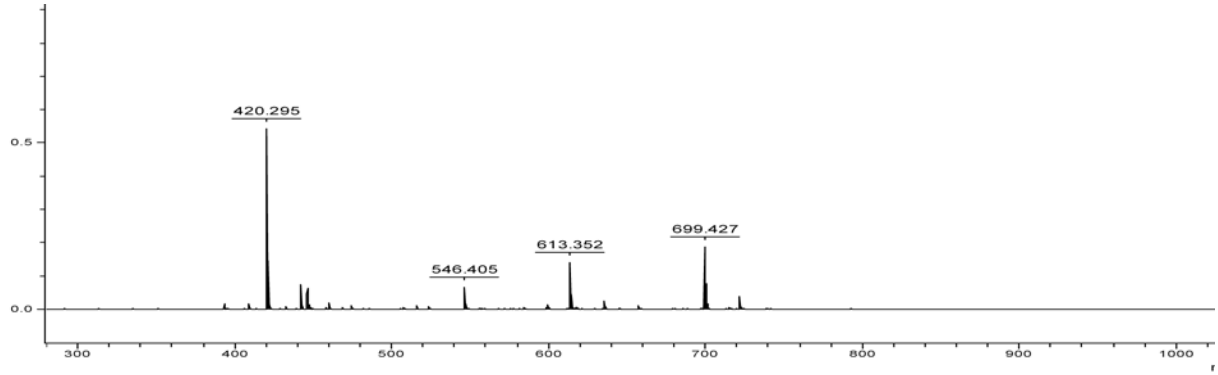


MALDI-MS of Boc-His(2-cyclohexyl)-Arg-Arg-NHBzl (**14b**), $[MH]^+$ 739.52

Boc-His(2-i-propyl)-Arg-Arg-NHBzl (14c):

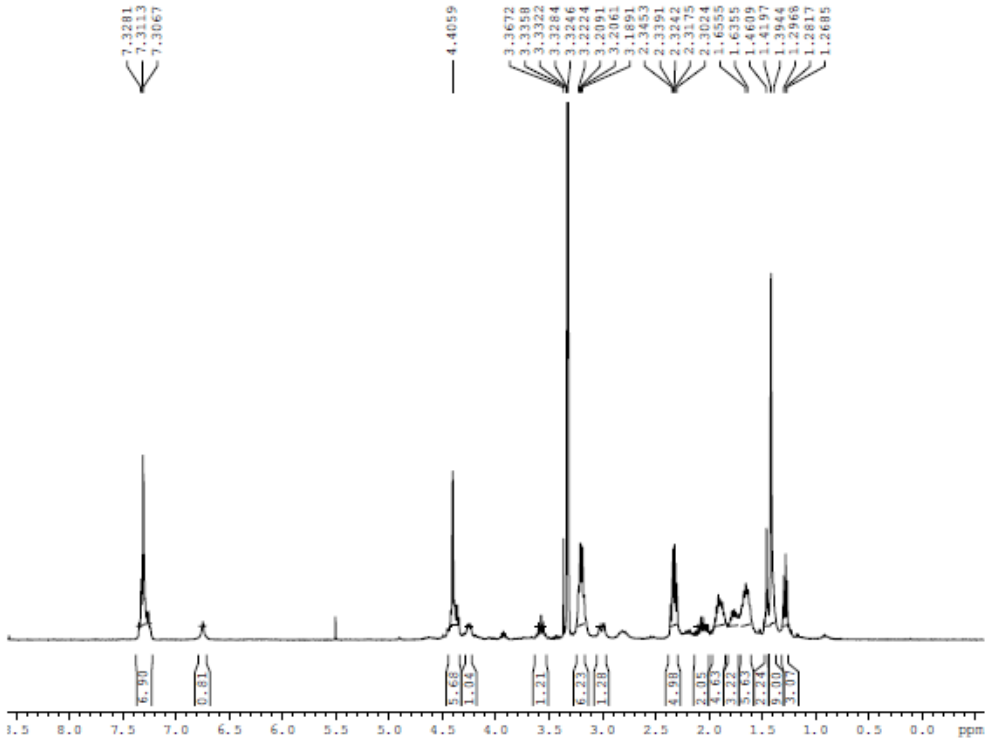


^{1}H-NMR of Boc-His(2-propyl)-Arg-Arg-NHBzl (**14c**)

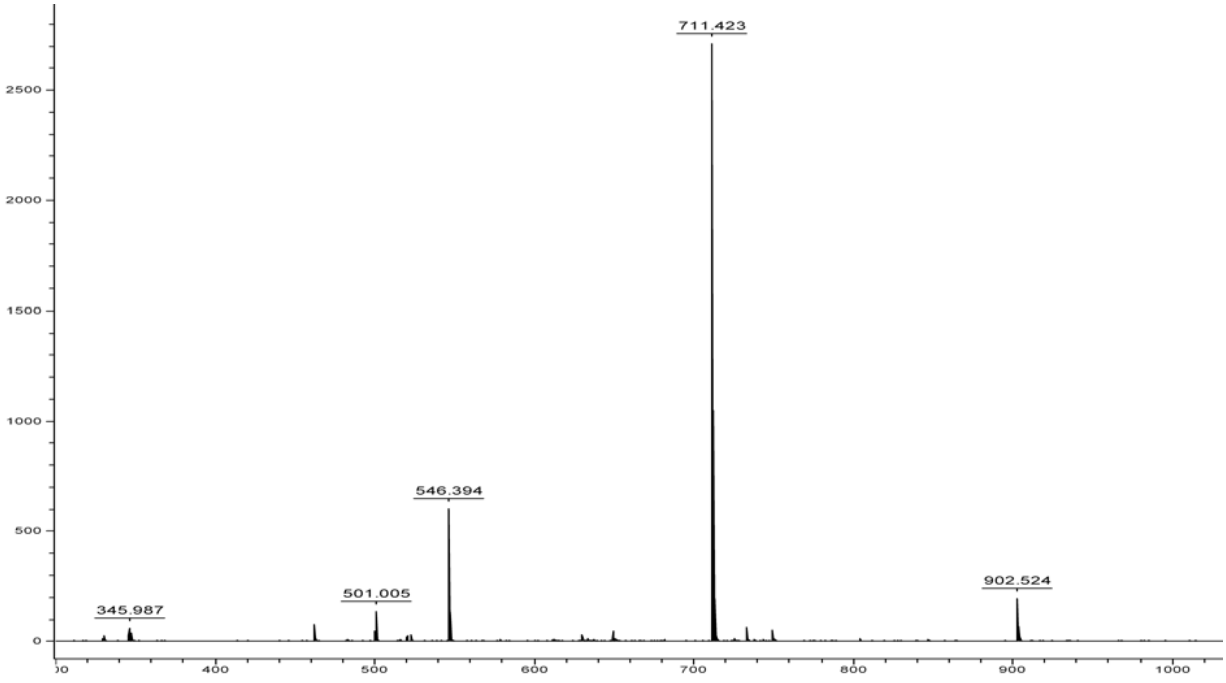


MALDI-MS of Boc-His(2-i-propyl)-Arg-Arg-NHBzl (**14c**), $[MH]^{+}$ 699.42

Boc-His(2-cyclobutyl)-Arg-Arg-NHBzl (14d):

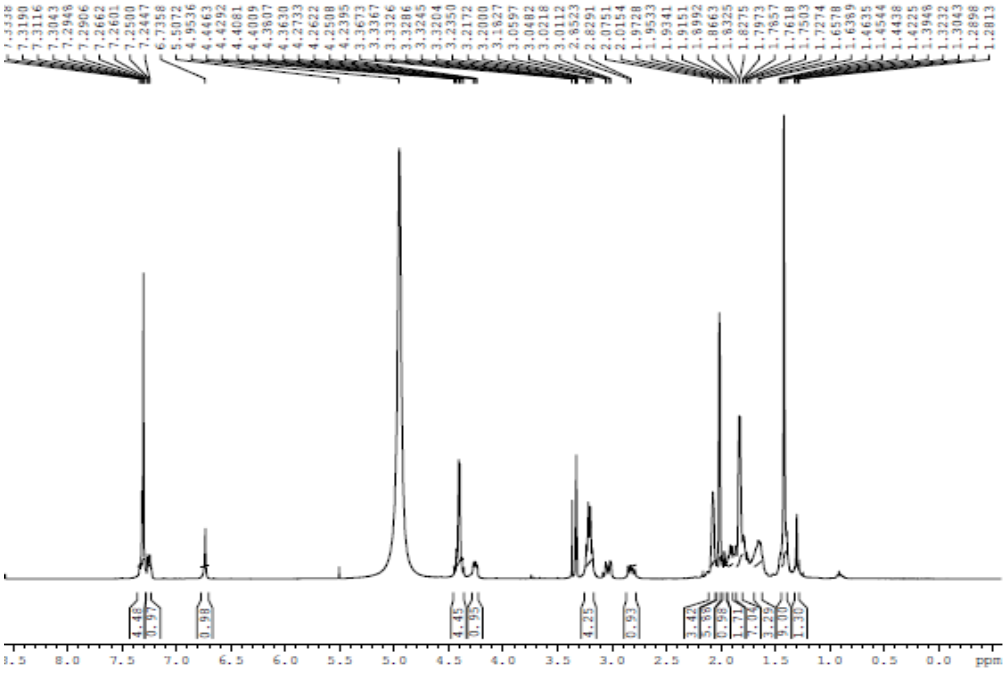


^{1}H-NMR of Boc-His(2-cyclobutyl)-Arg-Arg-NHBzl (**14d**)

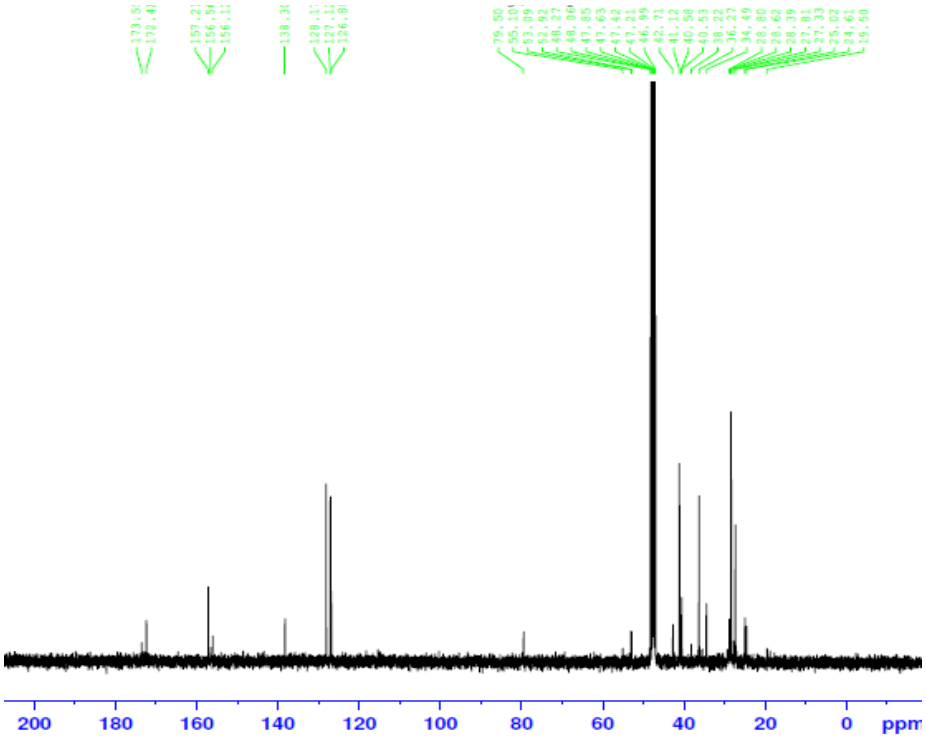


MALDI-MS of Boc-His(2-cyclobutyl)-Arg-Arg-NHBzl (**14d**), $[MH]^{+}$ 711.42

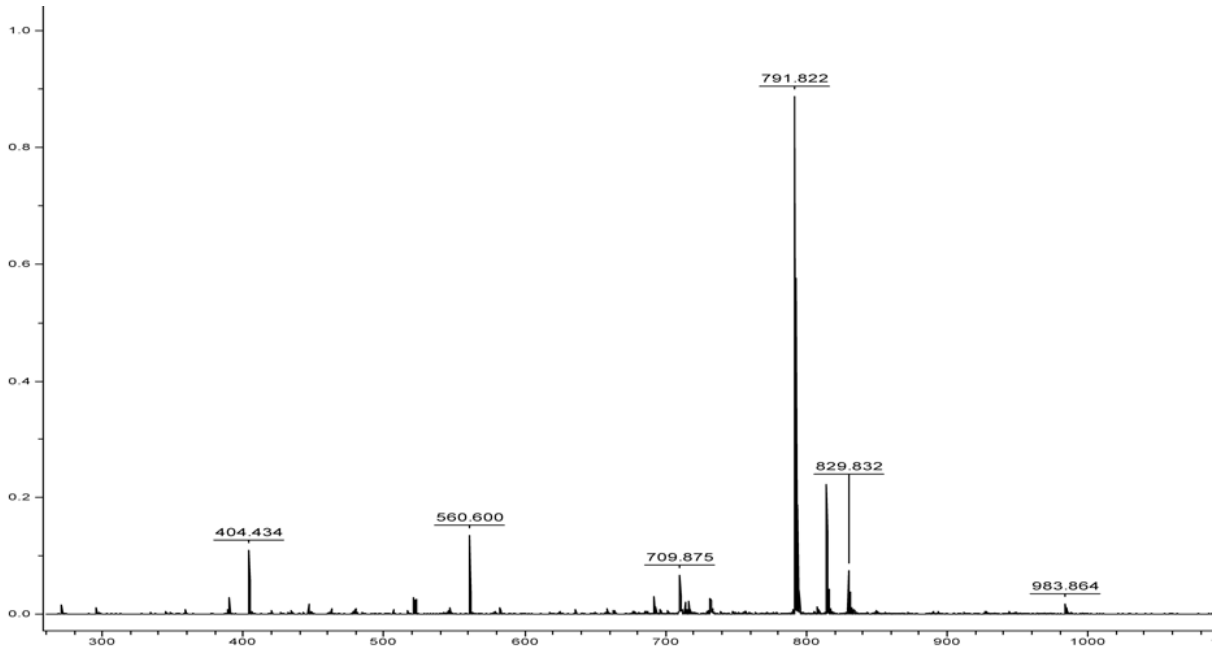
Boc-His(2-adamantyl)-Arg-Arg-NHBzl (14e):



^{1}H-NMR of Boc-His(2-adamantyl)-Arg-Arg-NHBzl (**14e**)

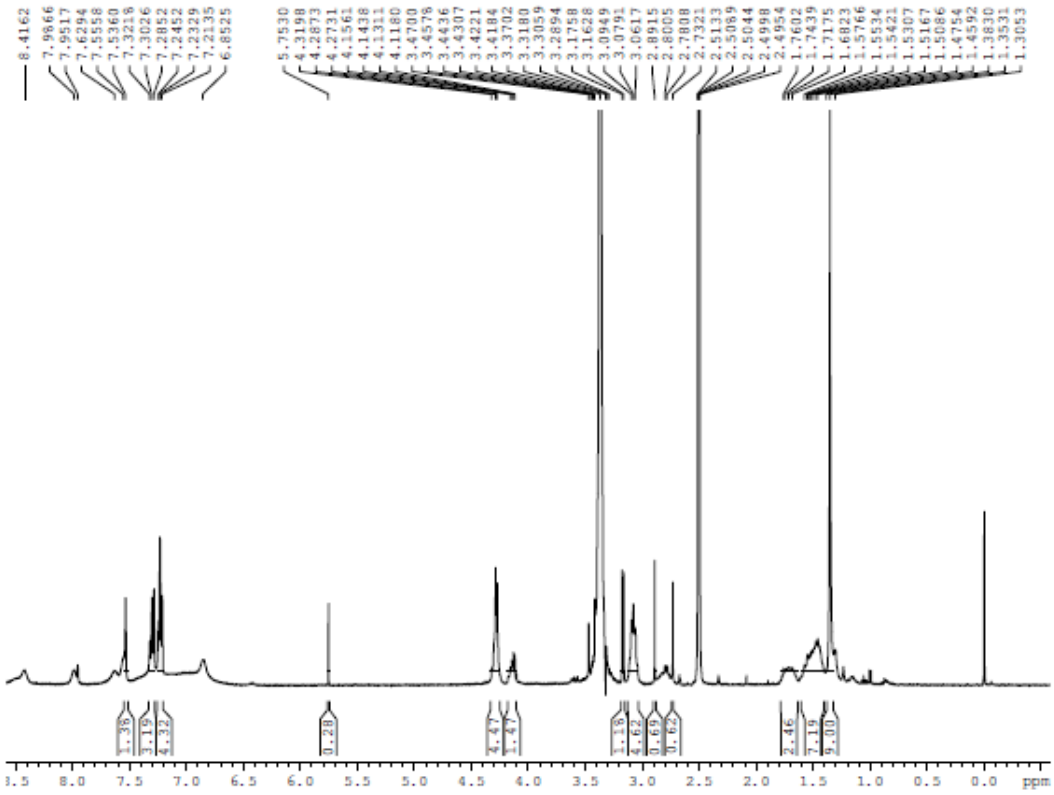


^{13}C-NMR of Boc-His(2-adamantyl)-Arg-Arg-NHBzl (**14e**)

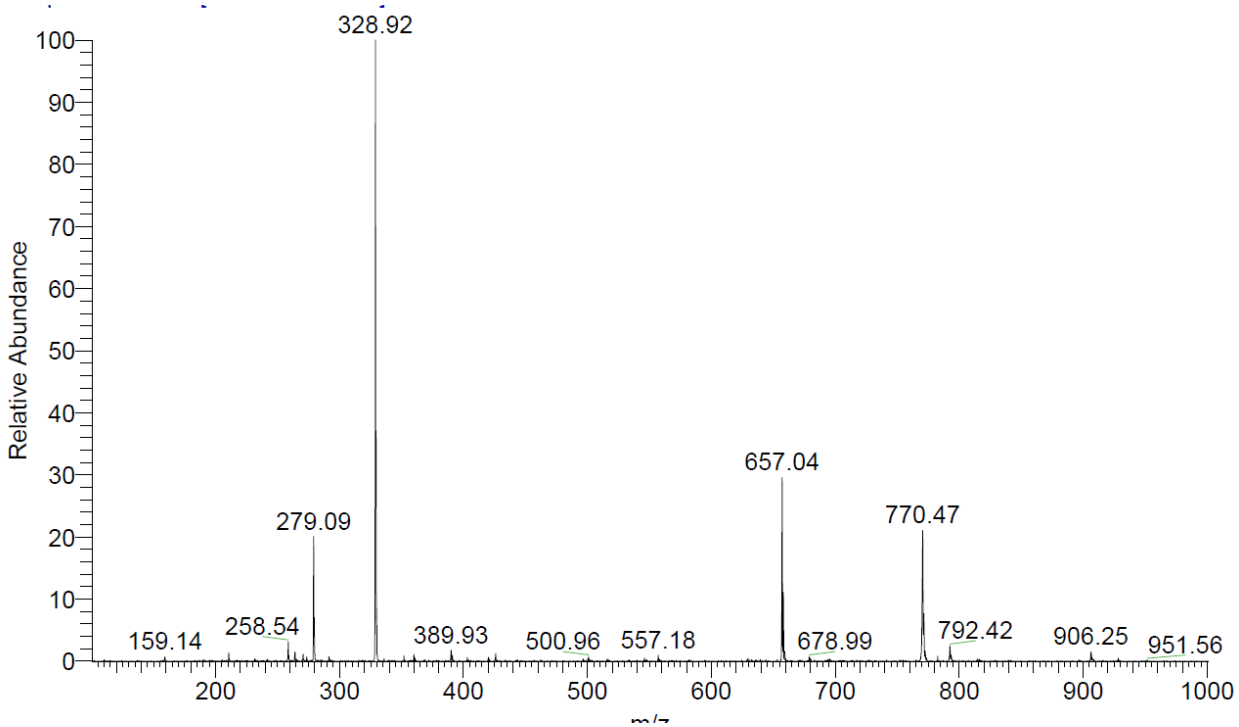


MALDI-MS of Boc-His(2-adamantyl)-Arg-Arg-NHBzl (**14e**), $[MH]^+$ 791.82

Boc-His-Arg-Arg-NHBzl (14f):

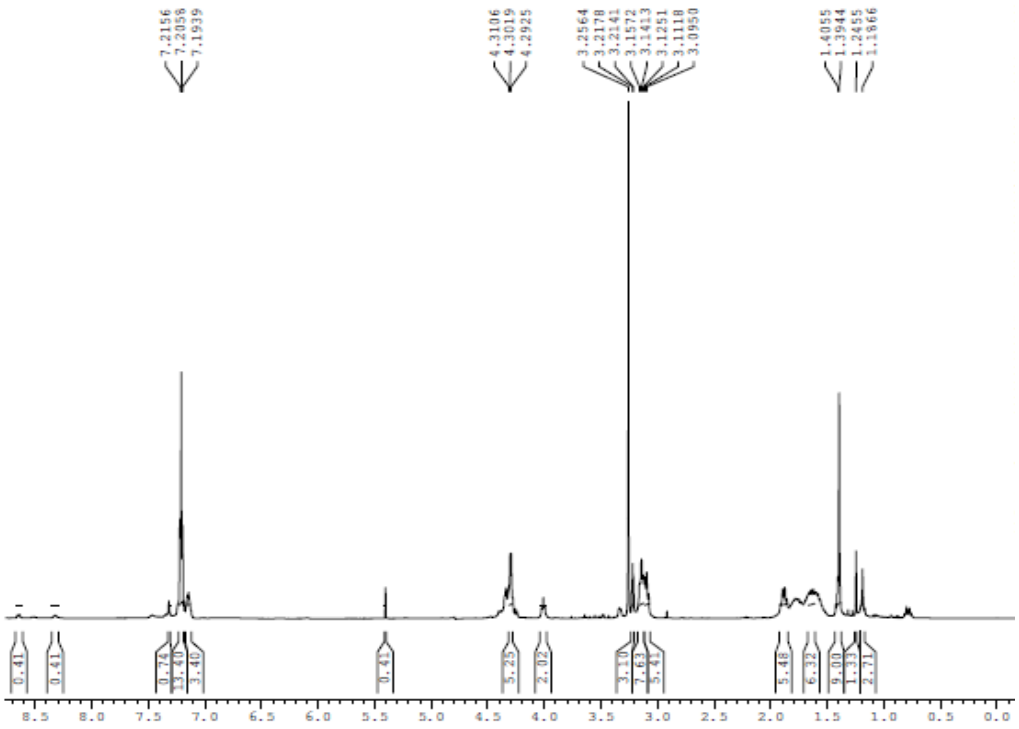


^{1}H-NMR of Boc-His-Arg-Arg-NHBzl (**14f**)

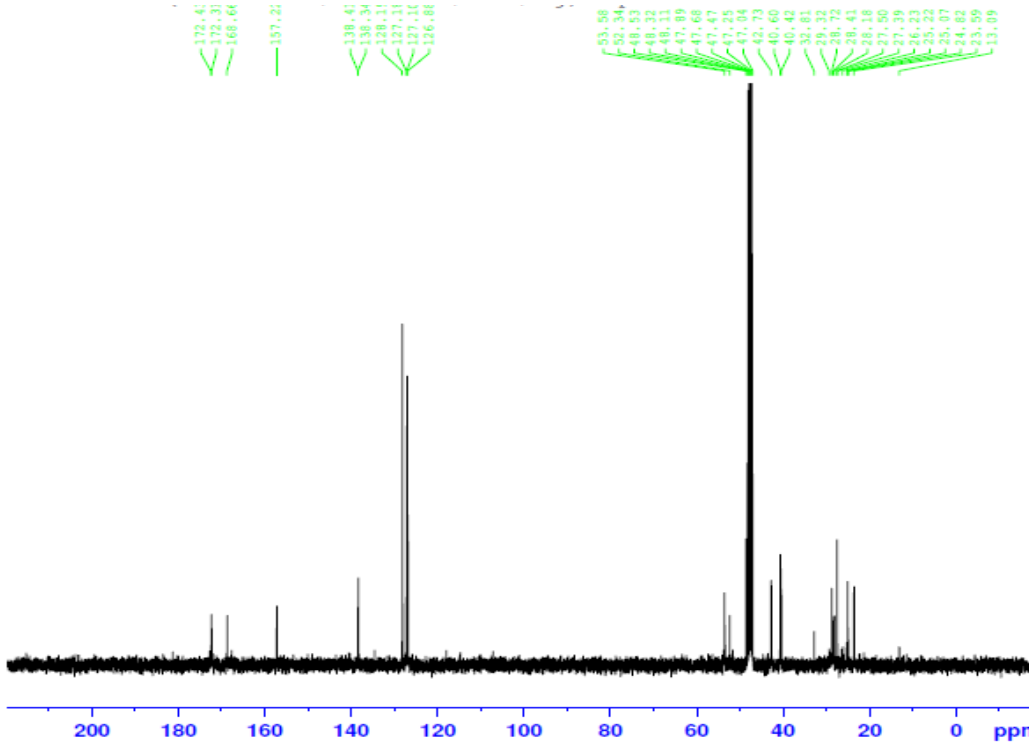


MS of Boc-His-Arg-Arg-NHBzl (**14f**), $[MH]^+$657.04

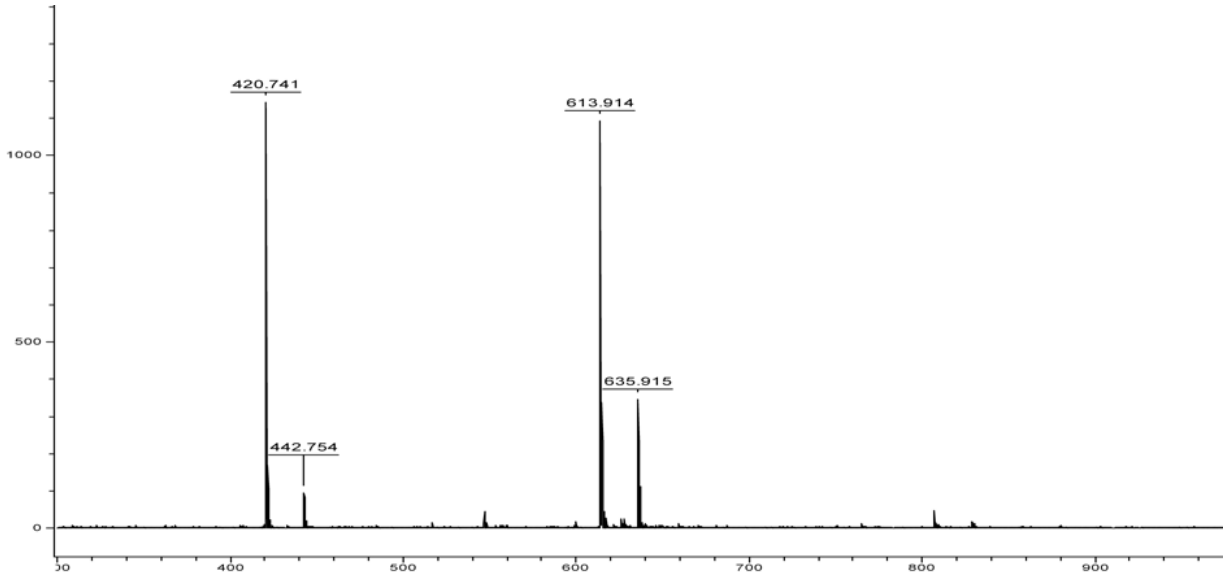
His(2-t-butyl)-Arg-Arg-NHBzl (15a):



^{1}H-NMR of His(2-t-butyl)-Arg-Arg-NHBzl (**15a**)

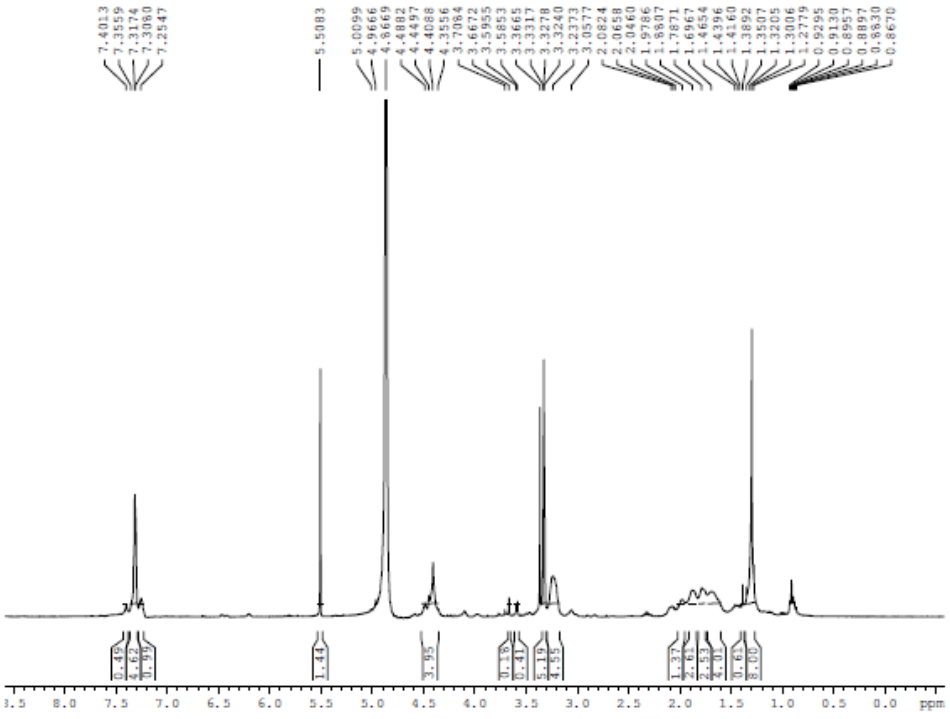


^{13}C-NMR of His(2-t-butyl)-Arg-Arg-NHBzl (**15a**)

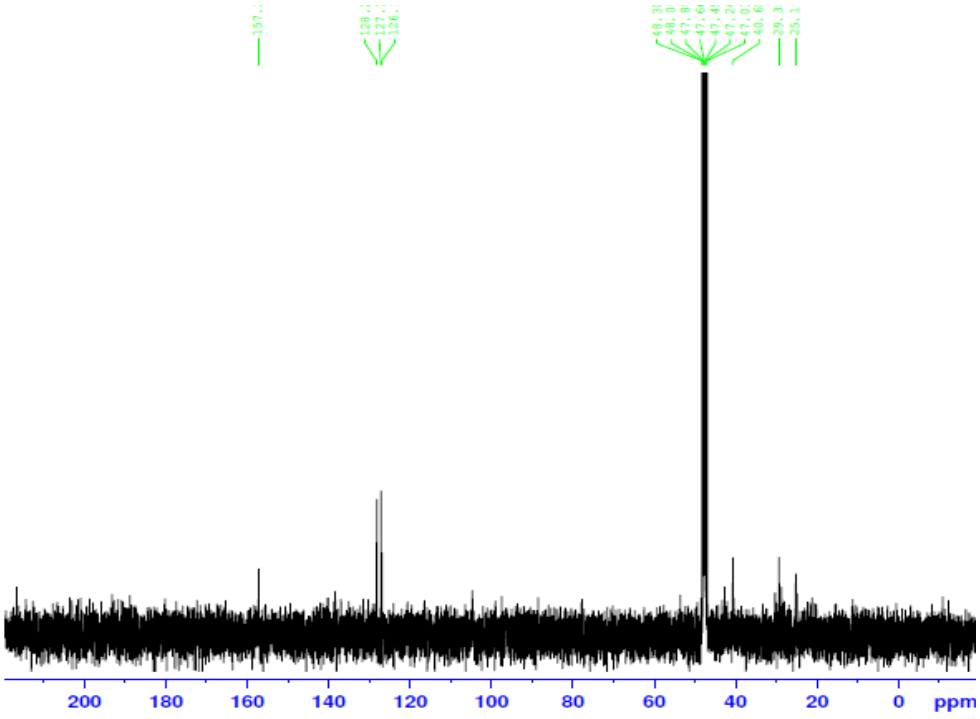


MALDI- MS of His-(2-t-butyl)-Arg-Arg-NHBzl (**15a**), $[MH]^+$ 613.91

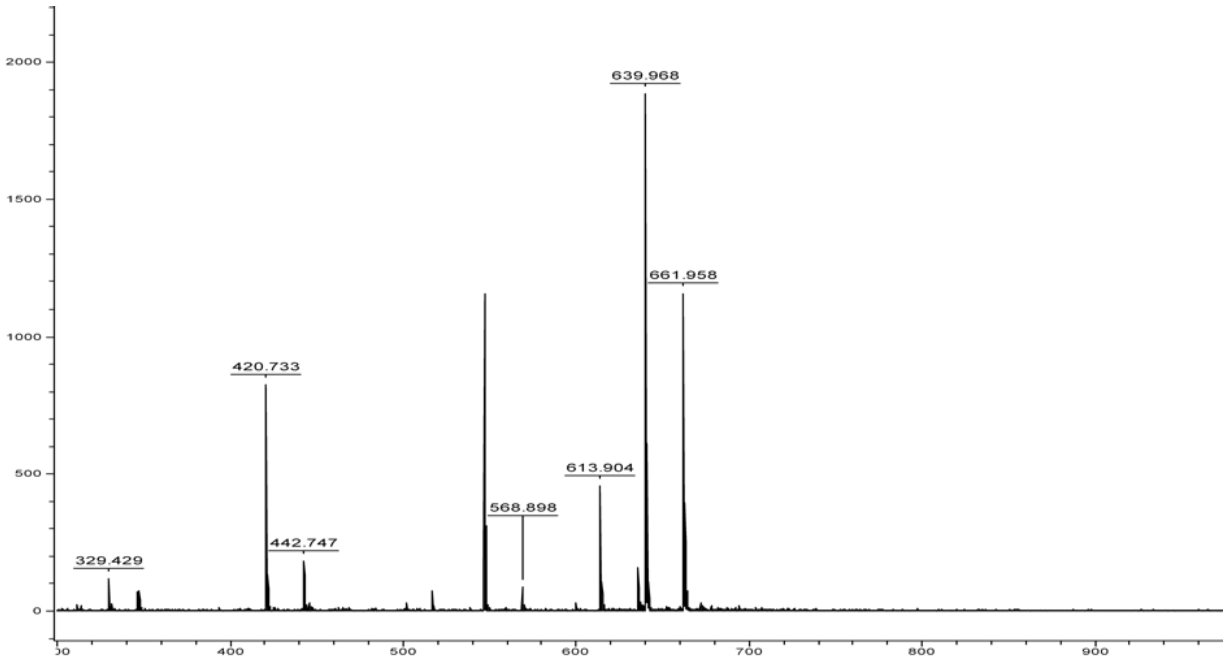
His(2-cyclohexyl)-Arg-Arg-NHBzl (15b):



^{1}H-NMR of His(2-cyclohexyl)-Arg-Arg-NHBzl (**15b**)

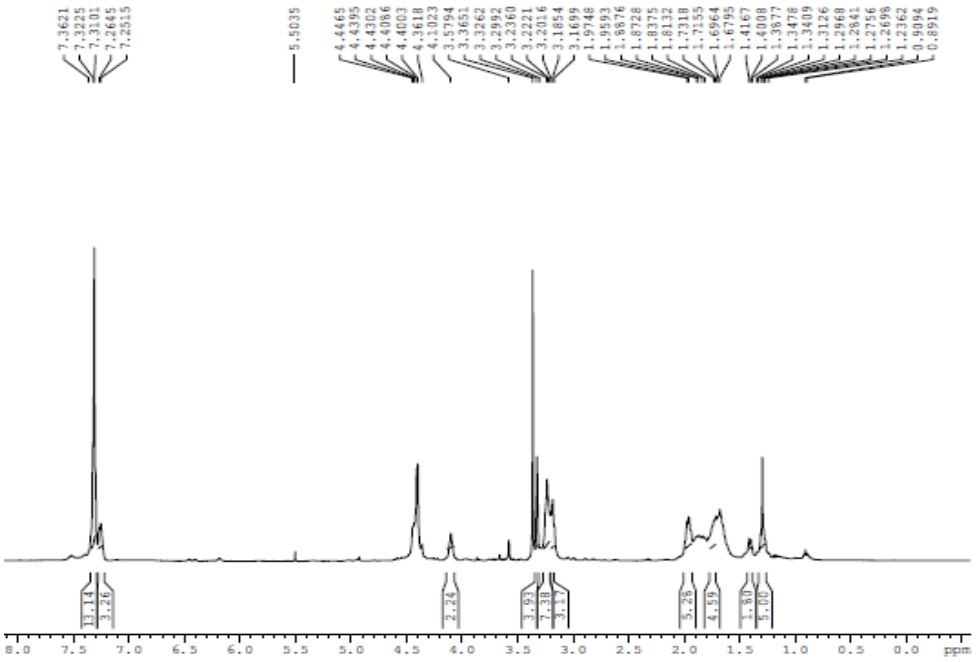


^{13}C-NMR of His(2-cyclohexyl)-Arg-Arg-NHBzl (**15b**)

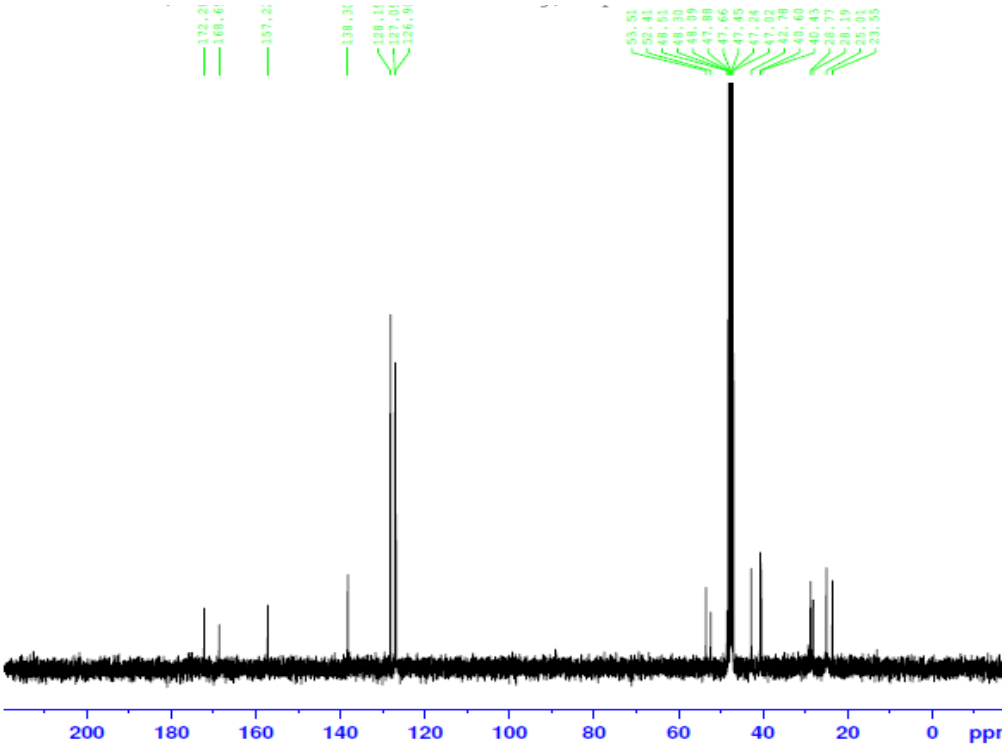


MALDI-MS of His(2-cyclohexyl)-Arg-Arg-NHBzl (**15b**), $[MH]^+$ 639.96

His(2-i-propyl)-Arg-Arg-NHBzl (15c):

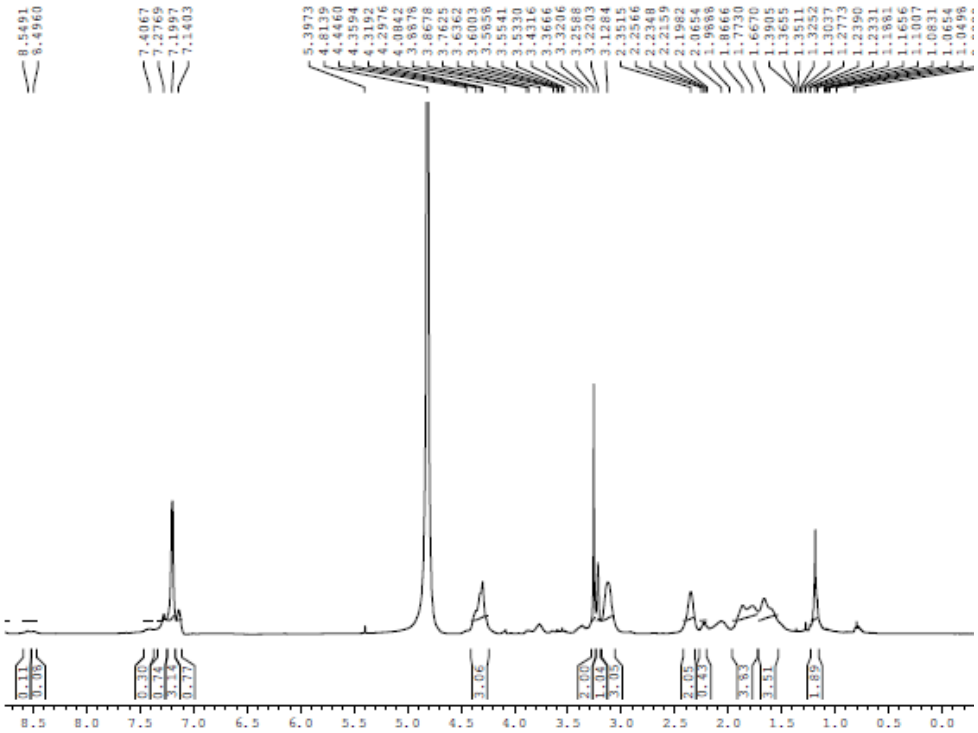


^{1}H-NMR of His(2-i-propyl)-Arg-Arg-NHBzl (**15c**)

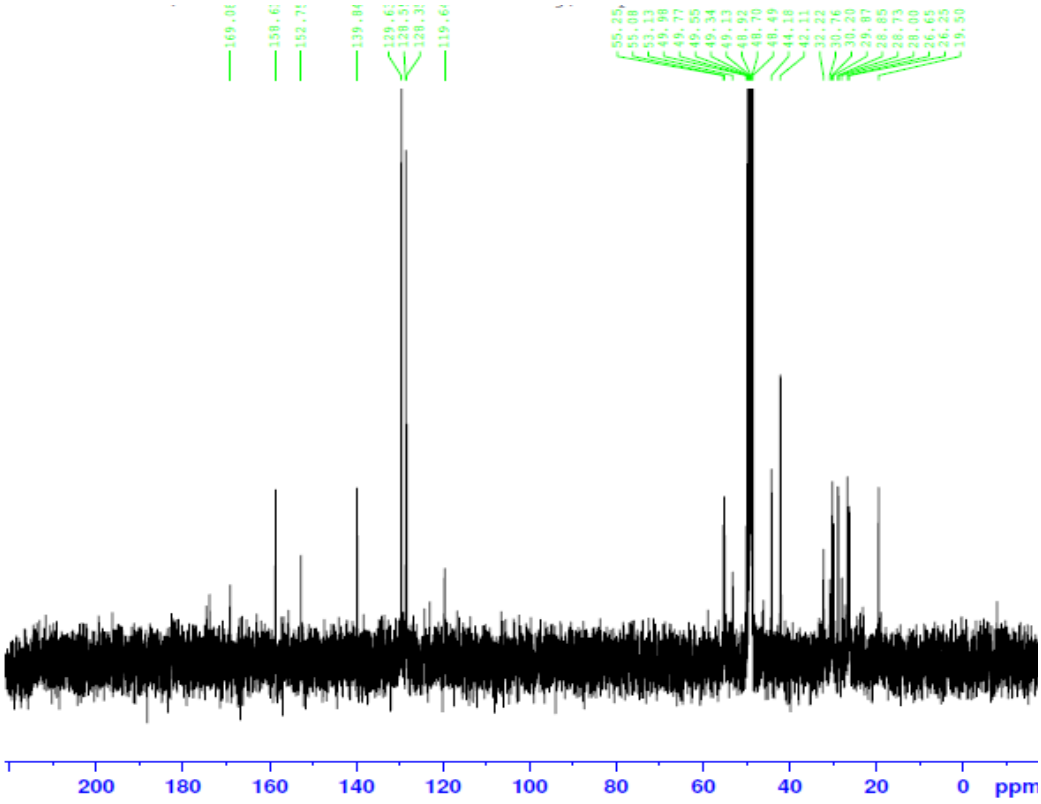


^{13}C-NMR of His(2-i-propyl)-Arg-Arg-NHBzl (**15c**)

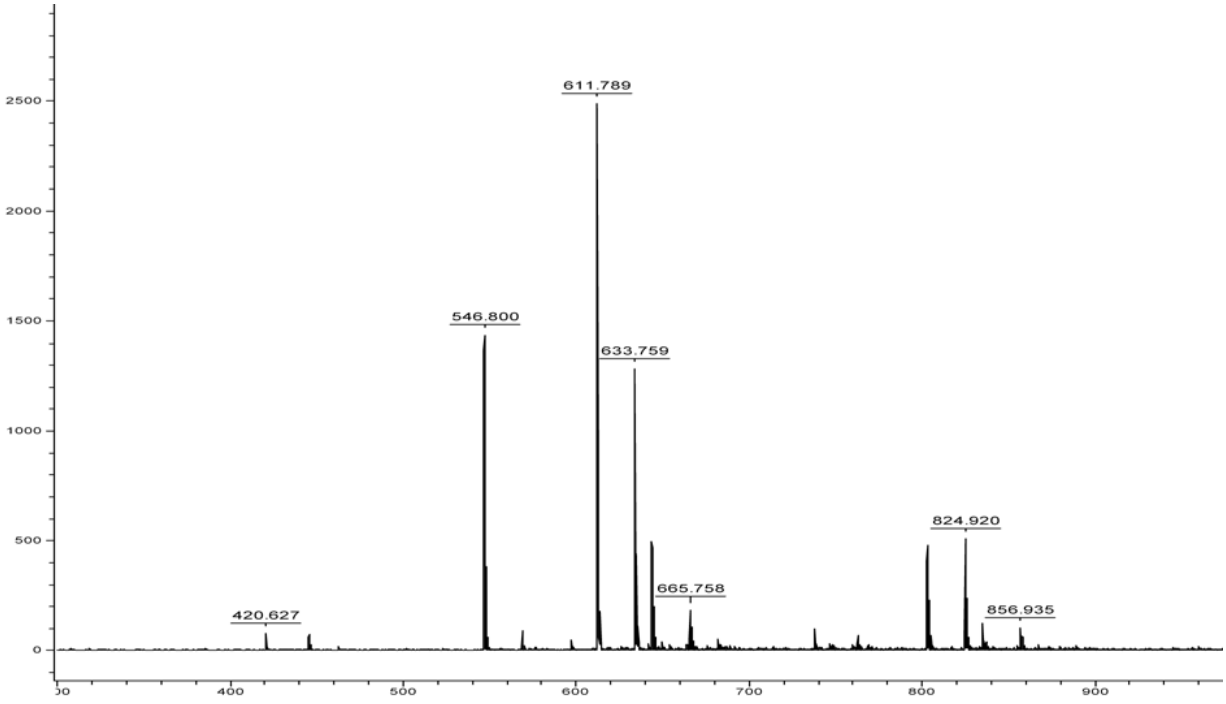
His(2-cyclobutyl)-Arg-Arg-NHBzl (15d):



^{1}H-NMR of His(2-cyclobutyl)-Arg-Arg-NHBzl (**15d**)

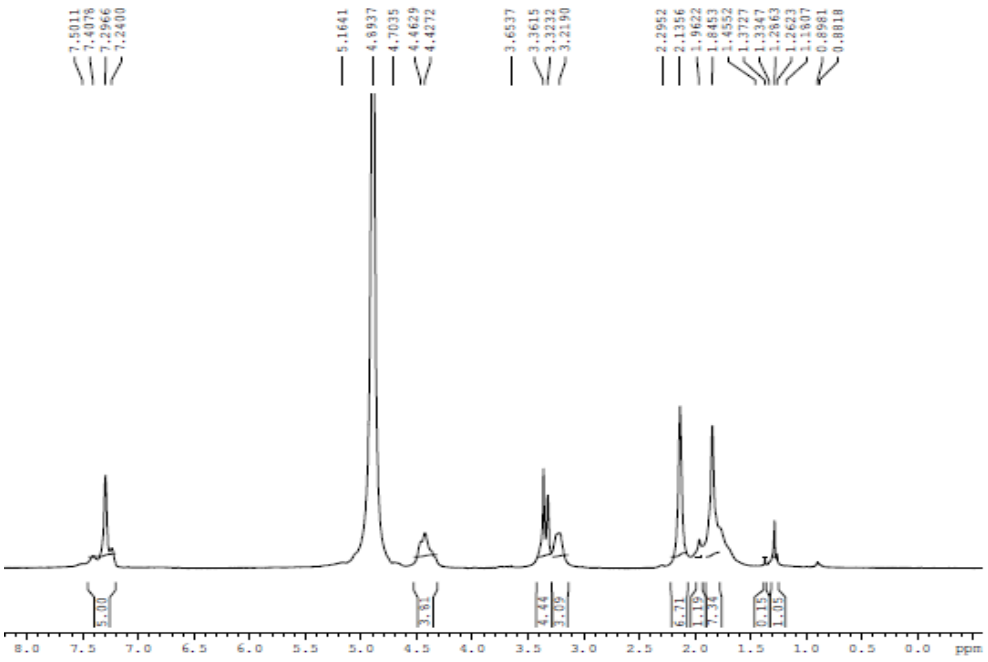


^{13}C-NMR of His(2-cyclobutyl)-Arg-Arg-NHBzl (**15d**)

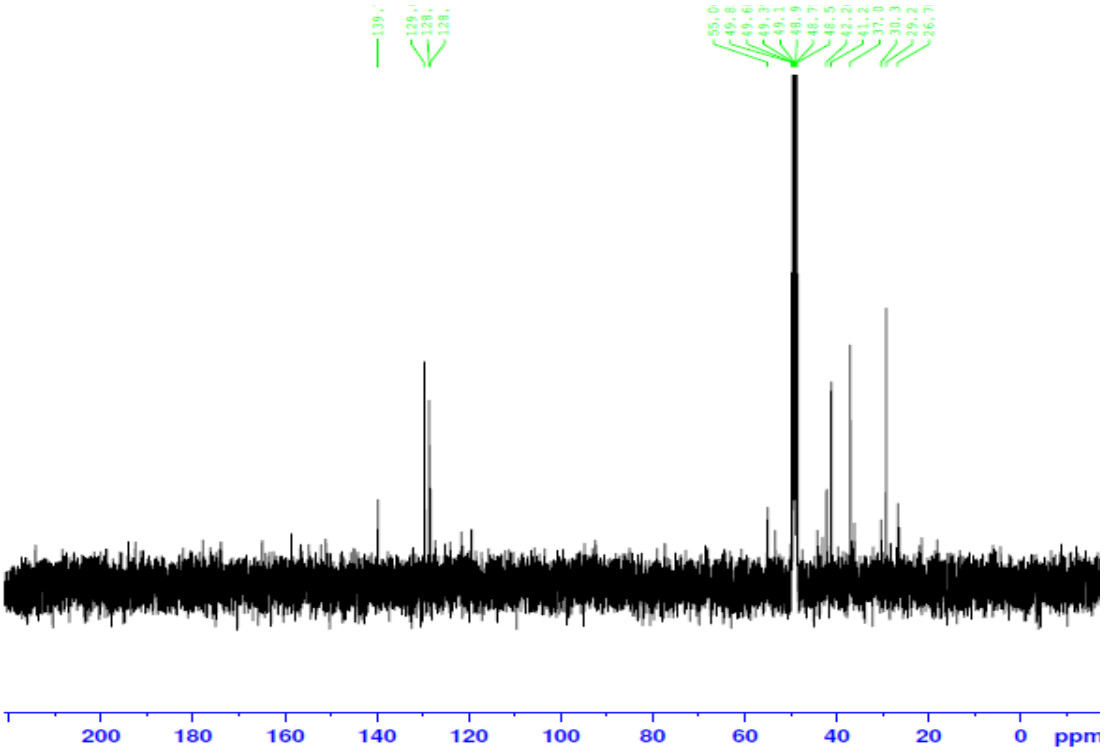


MALDI-MS of His(2-cyclobutyl)-Arg-Arg-NHBzl (**15d**), $[MH]^+$ 611.78

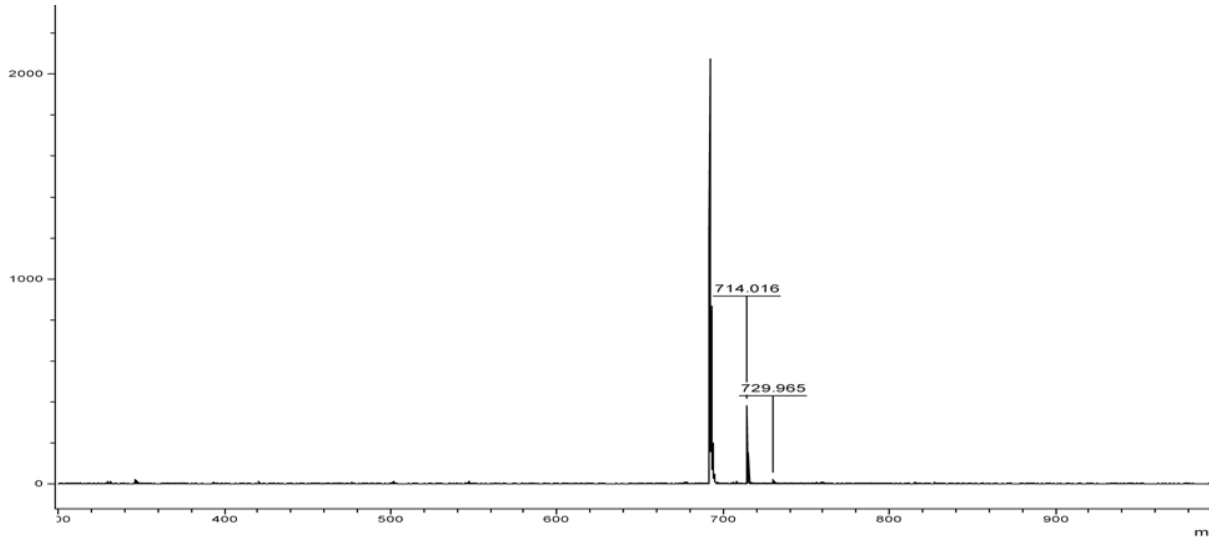
His(2-adamantyl)-Arg-Arg-NHBzl (15e):



^{1}H-NMR of His(2-adamantyl)-Arg-Arg-NHBzl (**15e**)

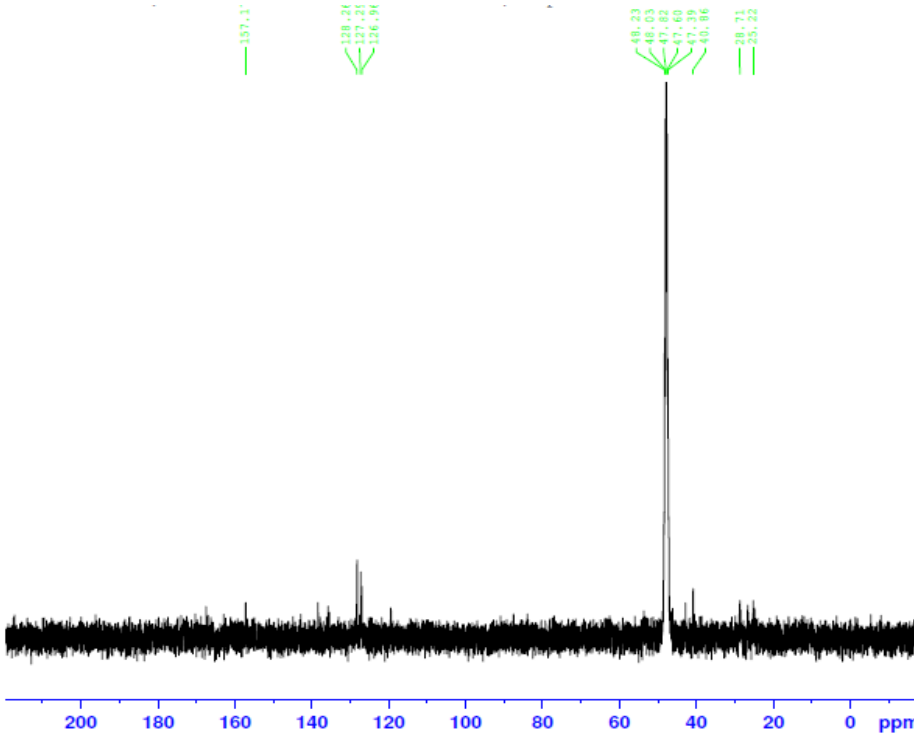


^{13}C-NMR of His(2-adamantyl)-Arg-Arg-NHBzl (**15e**)

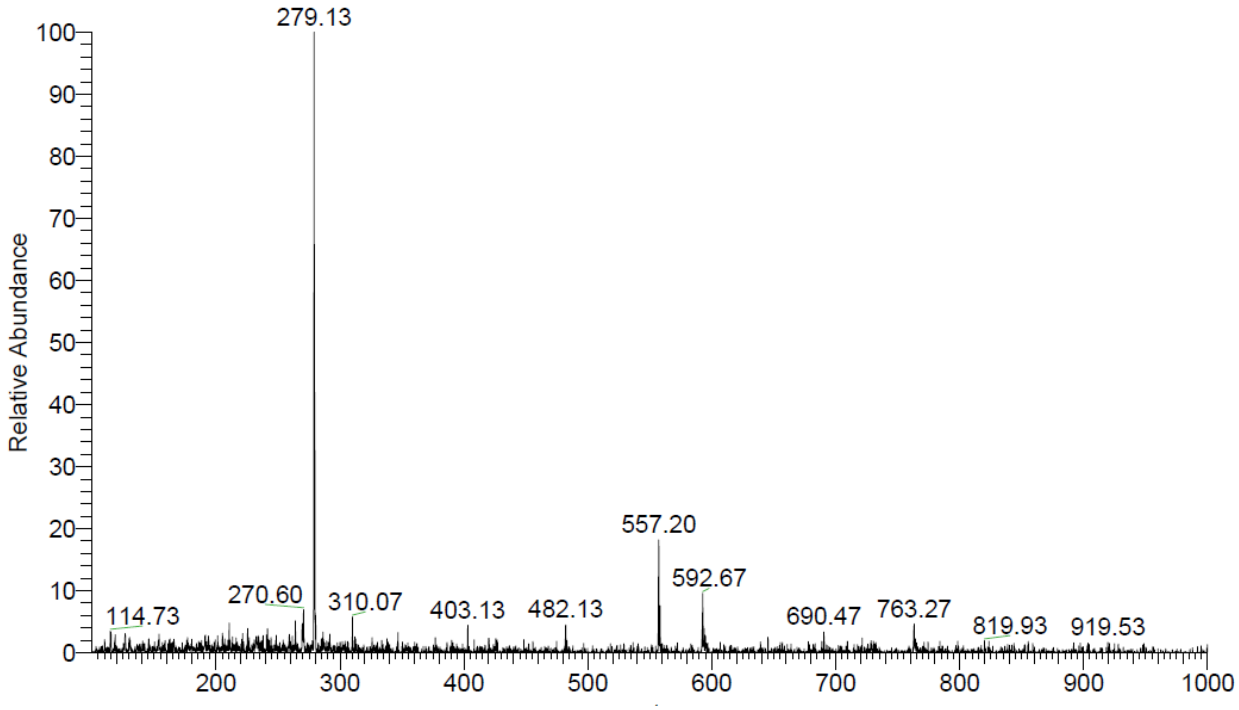


MALDI-MS of His(2-adamantyl)-Arg-Arg-NHBzl (**15e**), $[MH]^+$ 691.02

His-Arg-Arg-NHBzl (15f):



^{13}C-NMR of His-Arg-Arg-NHBzl (**15f**)



MS of His-Arg-Arg-NHBzl (**15f**), $[MH]^+$ 557.20

Table S1. Antifungal activity of synthesized tripeptides (series I and II), MIC values along with standard deviation values of active compounds (Antifungal assay was carried out in three replicates and data expressed as mean ± standard deviation).

No.	R	R_1[a]	*C. albicans* MIC[b]	*C. kyfer* MIC	*C. neoformans* MIC	*A. niger* MIC	*N. crassa* MIC
			Series I				
9a	t-butyl	Boc	>250	>250	>250	>250	>250
9b	Cyclohexyl	Boc	>250	>250	>250	>250	>250
9c	i-propyl	Boc	>250	>250	>250	>250	>250
9d	Cyclobutyl	Boc	>250	>250	>250	>250	>250
9e	Adamantyl	Boc	>250	>250	**112.2 ± 1.32 (125 ± 1.48)**	>250	**112.2 ± 0.30 (125 ± 0.34)**
9f	H	Boc	>250	>250	>250	>250	>250
10a	t-butyl	H	>250	>250	>250	>250	250
10b	Cyclohexyl	H	>250	>250	>250	>250	>250
10c	i-propyl	H	>250	>250	>250	>250	>250
10d	Cyclobutyl	H	>250	>250	**18.2 ± 0.97 (31.25 ± 1.68)**	>250	>250
10e	Adamantyl	H	>250	>250	>250	>250	>250
10f	H	H	>250	>250	>250	>250	>250
			Series II				
14a	t-butyl	Boc	>250	>250	**44.6 ± 0.43 (62.5 ± 0.61)**	>250	>250
14b	Cyclohexyl	Boc	**18.5 ± 0.96 (25 ± 1.29)**	>250	**46.2 ± 1.24 (62.5 ± 1.68)**	>250	>250
14c	i-propyl	Boc	>250	>250	**10.9 ± 1.63 (15.62 ± 2.35)**	>250	>250
14d	Cyclobutyl	Boc	>250	>250	**11.1 ± 0.22 (15.62 ± 0.31)**	**177.8 ± 0.24 (250 ± 0.34)**	**177.8 ± 0.34 (250 ± 0.48)**
14e	Adamantyl	Boc	**98.9 ± 2.65 (125 ± 3.34)**	>250	**24.7 ± 0.19 (31.25 ± 0.25)**	**98.9 ± 3.33 (125 ± 4.21)**	**19.8 ± 0.18 (25 ± 0.22)**
14f	H	Boc	>250	>250	**82.1 ± 0.25 (125 ± 0.39)**	>250	>250
15a	t-butyl	H	>250	>250	**9.6 ± 1.25 (15.62 ± 2.03)**	>250	>250
15b	Cyclohexyl	H	>250	>250	**1.25 ± 0.44 (1.95 ± 0.68)**	>250	>250

15c	i-propyl	H	>250	>250	**74.8 ± 1.26 (125 ± 2.12)**	>250	>250
15d	Cyclobutyl	H	>250	>250	**76.4 ± 0.29 (125 ± 0.48)**	>250	>250
15e	Adamantyl	H	**86.3 ± 0.30 (125 ± 0.44)**	**86.3 ± 0.22 (125 ± 0.31)**	**86.3 ± 0.67 (125 ± 0.98)**	**86.3 ± 0.62 (125 ± 0.91)**	>250
15f	H	H	>250	>250	**34.8 ± 1.26 (62.5 ± 2.28)**	>250	>250
	Amphotericin B	control	0.72 ± 0.06 (0.78 ± 0.07)	11.5 ± 0.11 (12.5 ± 0.12)	< 0.18 ± 0.16 (0.20 ± 0.18)	0.36 ± 0.11 (0.39 ± 0.12)	0.36 ± 0.14 (0.39 ± 0.16)

[a] Refer Figure 1; [b] MIC: Minimum Inhibitory Concentration [in μg/mL (μM)]