Supporting Information

Synthesis and structure-mechanical property correlationof an α,β-hybrid peptide containing methyl-3-aminocrotonate

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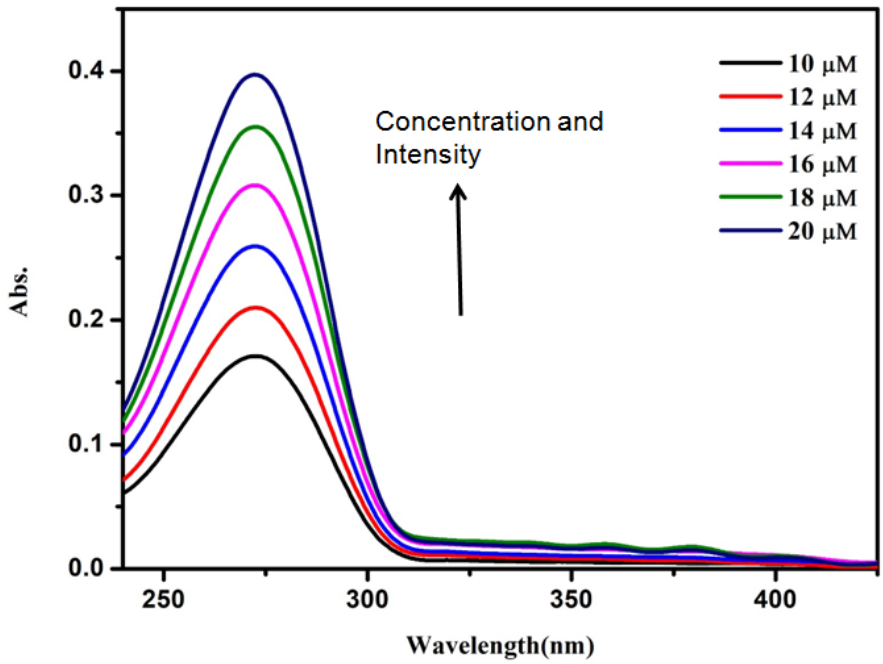
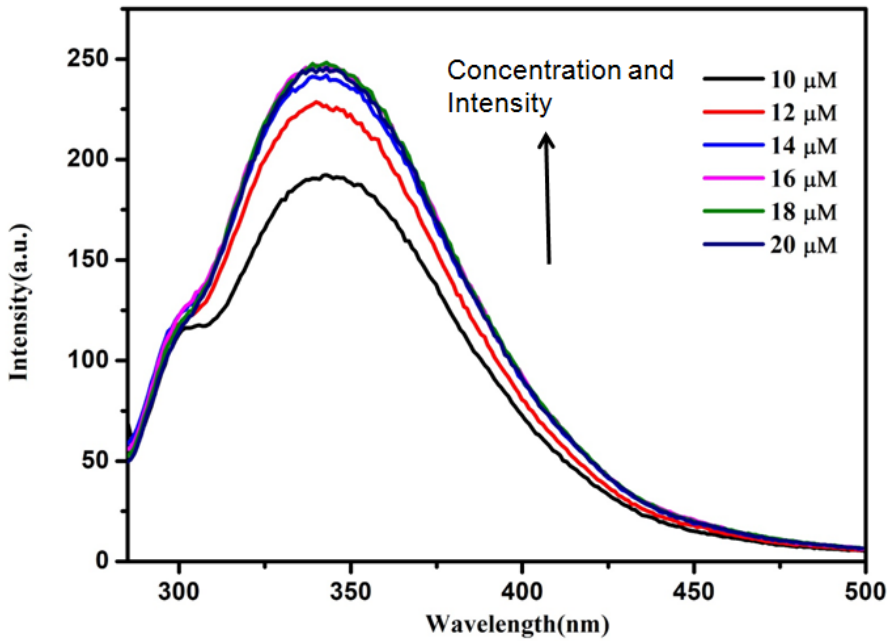
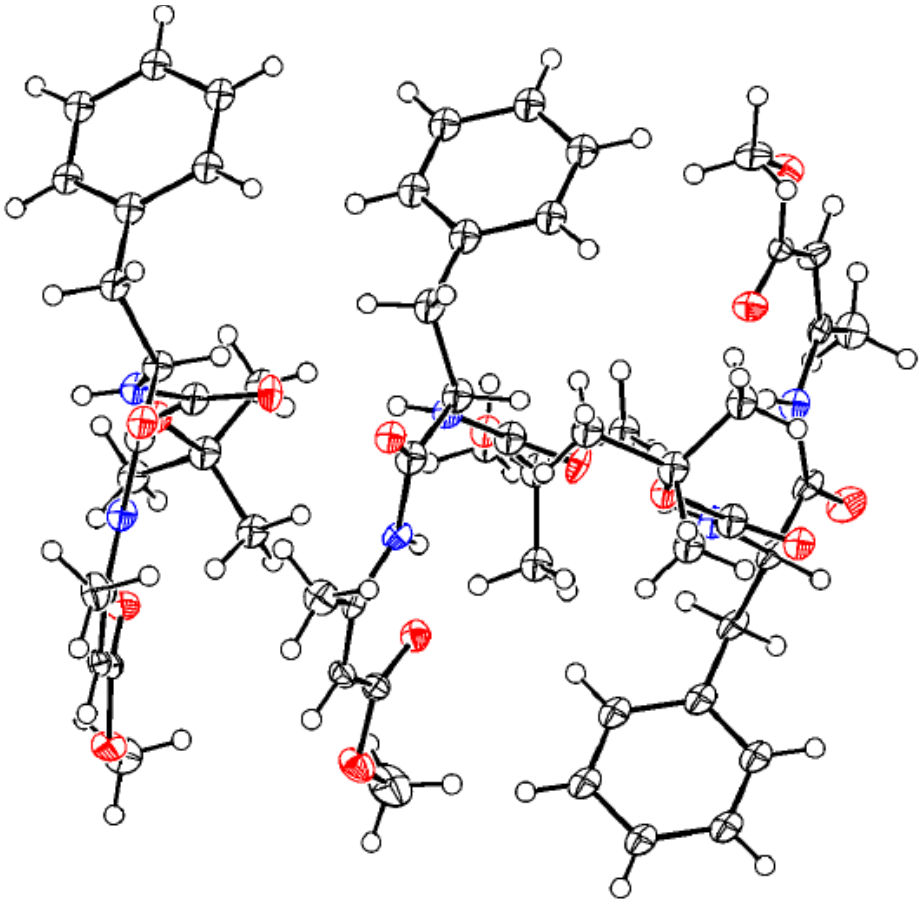


ESI Figure S1: The absorption spectra of α,β-hybrid peptide**1** with increasing concentration.



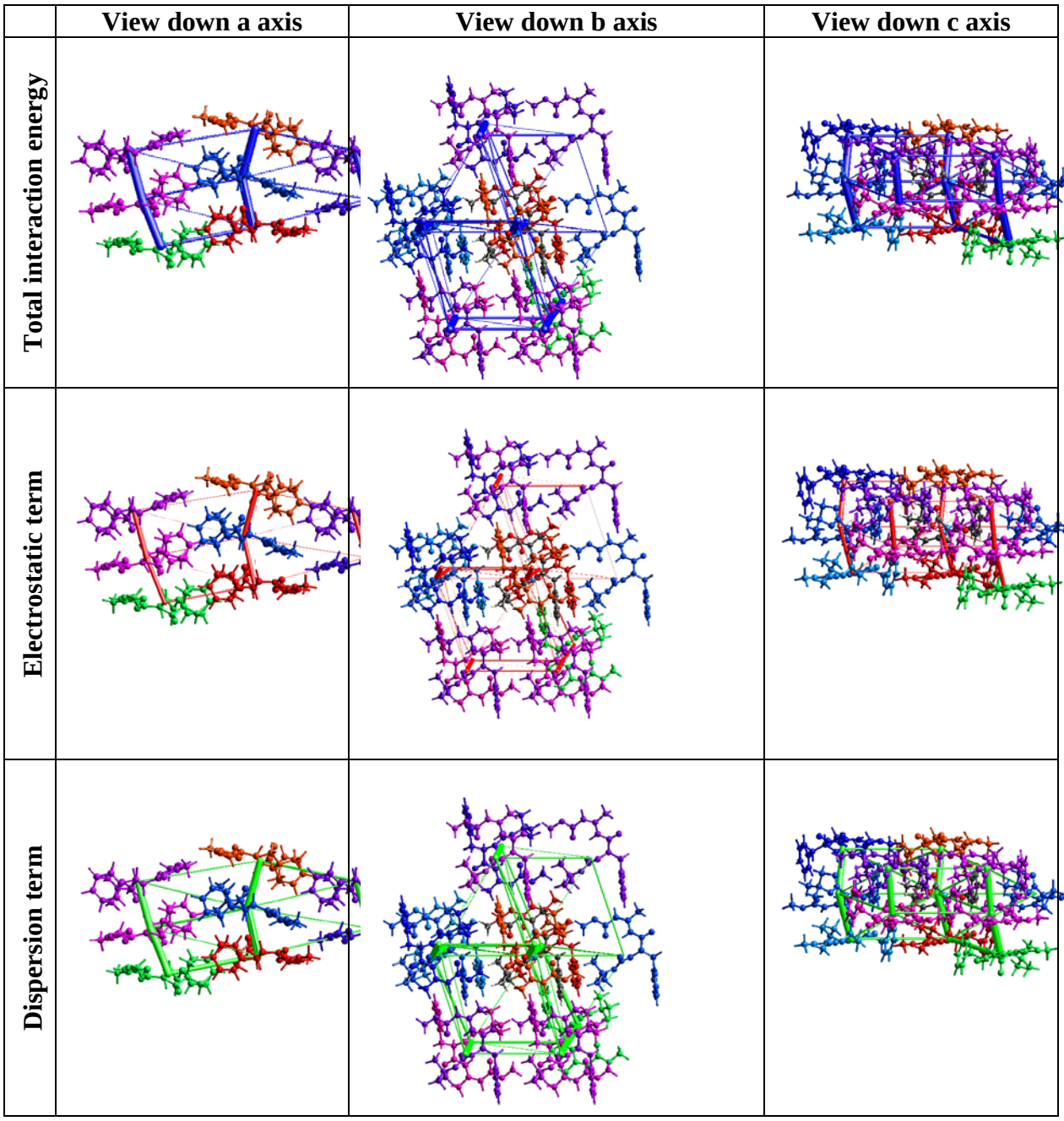
ESI Figure S2: The emission spectra of α,β-hybrid peptide**1** with increasing concentration.



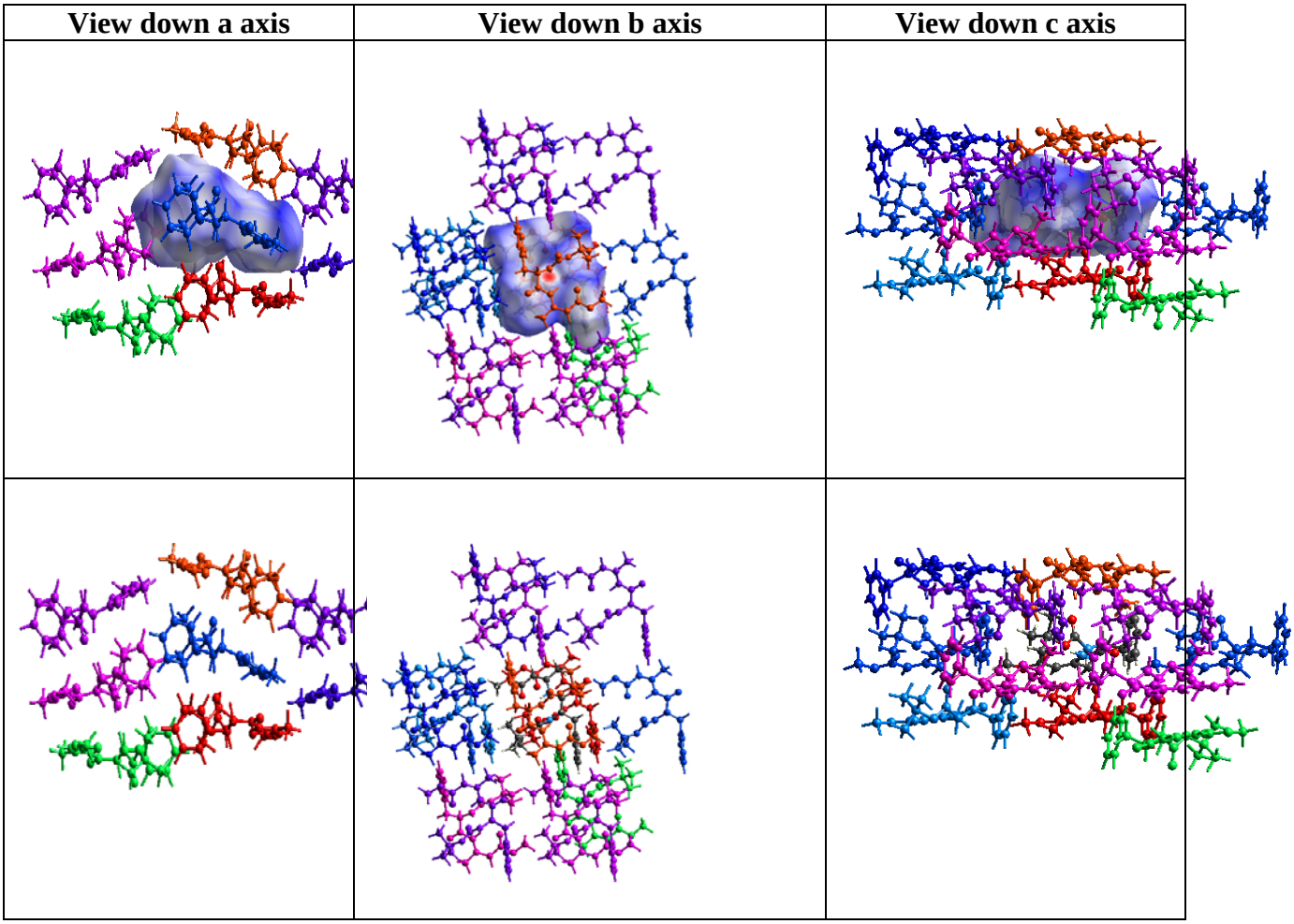
ESI Figure S3: ORTEP diagram of α,β-hybrid peptide **1**. Probability 50%.

ESI Table S1: Crystal data and structure refinement for α,β-hybrid peptide **1.**

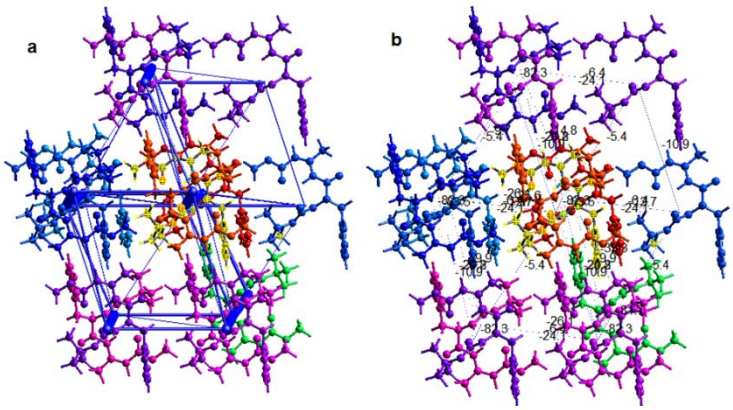
Identification code	haldar_bxphemabpm
Empirical formula	$C_{19}H_{26}N_2O_5$
Formula weight	362.42
Temperature/K	100.00(2)
Crystal system	monoclinic
Space group	P 21/n
a/Å	10.2926(9)
b/Å	27.124(2)
c/Å	21.3576(19
α/°	90
β/°	98.753(2)
γ/°	90
Volume/Å^3	5893.1(9)
Z	12
ρ_{calc}g/cm^3	1.225
μ/mm^{-1}	0.089
F(000)	2328.0
Crystal size/mm^3	0.22× 0.24× 0.26
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	2.2 to 25.4
Index ranges	$-12 \leq h \leq 12$, $-32 \leq k \leq 32$, $-25 \leq l \leq 25$
Reflections collected	31148
Independent reflections	3367
Goodness-of-fit on F^2	1.120
Largest diff. peak/hole / e Å^{-3}	0.34/-0.57
Flack parameter	n/a
R	0.0647
WR2	0.1456



ESI Figure S4: Energy frameworks of α,β-hybrid peptide **1** viewed along different crystallographic directions.



ESI Figure S5: Graphical representation of calculated aggregate total interaction energies of molecule within 3.8 Å (first row hirshfeld surface mode and second row normal mode).

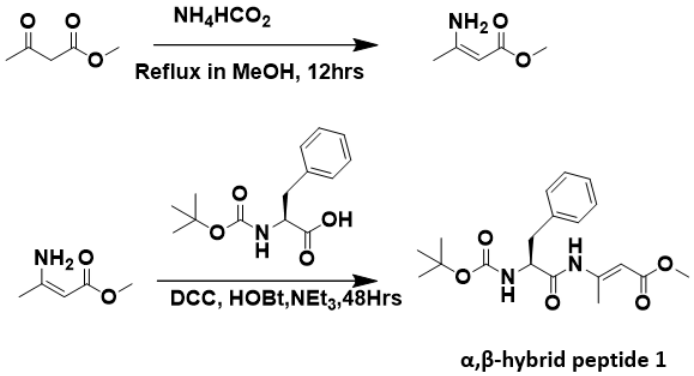


ESI Figure S6: (a) and (b) Energy with respect to different tubes is shown below along crystallographic b-direction.

ESI Table S2: Intermolecular interaction energies (kJ/mol) for the α,β-hybrid peptide **1,** calculated using B3LYP/6-31G(d,p) dispersion corrected DFT model, with X–H bond lengths normalized to standard neutron diffraction values. The total energy (E_{tot}), electrostatic (E_{ele}), polarization (E_{pol}), dispersion (E_{dis}), and exchange-repulsion (E_{rep}) components of the energy are listed below. R indicates the distance between molecular centroids (mean atomic position) in Å.

	N	Symop	R	E_ele	E_pol	E_dis	E_rep	E_tot
	1	x,y,z	4.92	-40.8	-12.2	-89.6	75.6	-83.5
	1	x,y,z	4.74	-49.3	-11.1	-79.0	75.8	-82.3
	1	-1+x,y,z	11.35	0.6	-0.1	-4.9	0.7	-3.3
	1	-1/2+x,1.5-y,-1/2+z	10.0	-3.0	-1.1	-16.7	9.5	-12.7
	2	x,y,z	10.29	-8.9	-2.3	-24.2	13.1	-24.1
	1	-1+x,y,z	11.20	-0.7	-0.3	-6.7	0.7	-6.4
	1	1/2+x,1.5-y,1/2+z	12.04	-5.3	-0.9	-16.0	0.0	-20.2
	2	X+1/2,-y+1/2,z+1/2	12.81	0.3	-0.1	-2.5	0.0	-1.8
	2	X+1/2,-y+1/2,z+1/2	11.43	-2.1	-0.3	-18.0	11.6	-10.9
	1	1/2+x,1.5-y,1/2+z	10.60	-6.8	-1.2	-31.3	21.8	-21.8
	1	-1/2+x,1.5-y,-1/2+z	11.95	-0.7	0.0	-7.5	3.1	-5.4

Experimental



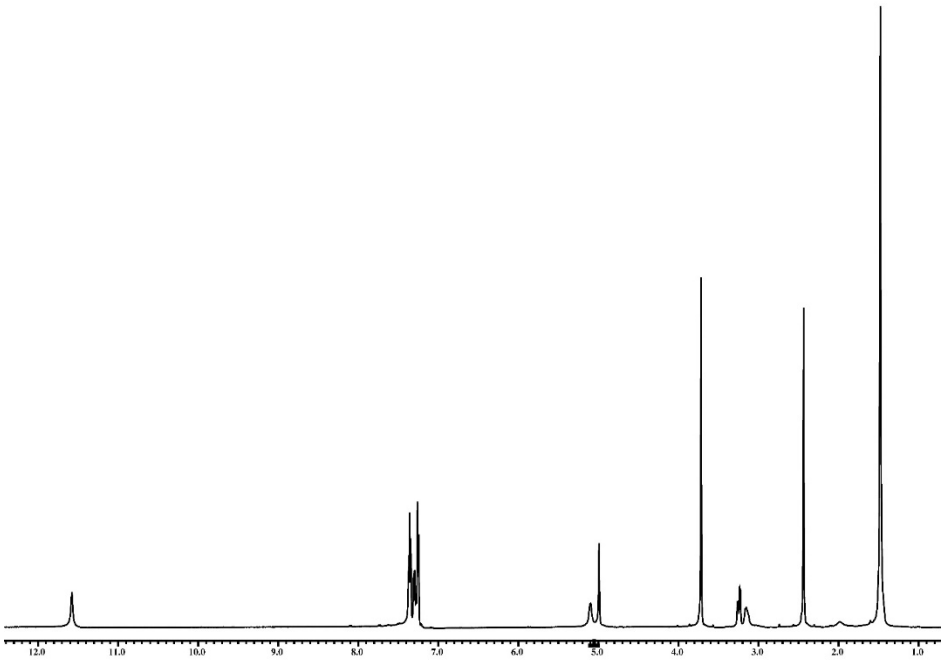
Scheme 1: Synthesis of α,β-hybrid peptide **1.**

Synthesis: In a 250 mL round bottom flask (RBF) with a magnetic stir bar, methanol (10 mL) was poured into the RBF along with solid ammonium formate(300 mmol) 18.9 g. 12 mL (100 mmol) of ethyl acetoacetate was added into the flask. The flask was placed over a magnetic spinner and stirred and refluxed for 12 hrs. The flask was then placed on a rotary evaporator to evaporate excess solvent. The product was then diluted with 200 mL of ethyl acetate and then workup is done and washed first with distilled water and then with brine. The organic layer was collected in an Erlenmeyer flask and dried over anhydrous sodium sulphate. The product was then vacuum filtered again, and then concentrated in a 250 mL RBF using a rotary evaporator. After the solvent had evaporated, the yield (68%) of the (E)-methyl 3-aminobut-2-enoate was 7.8 g.

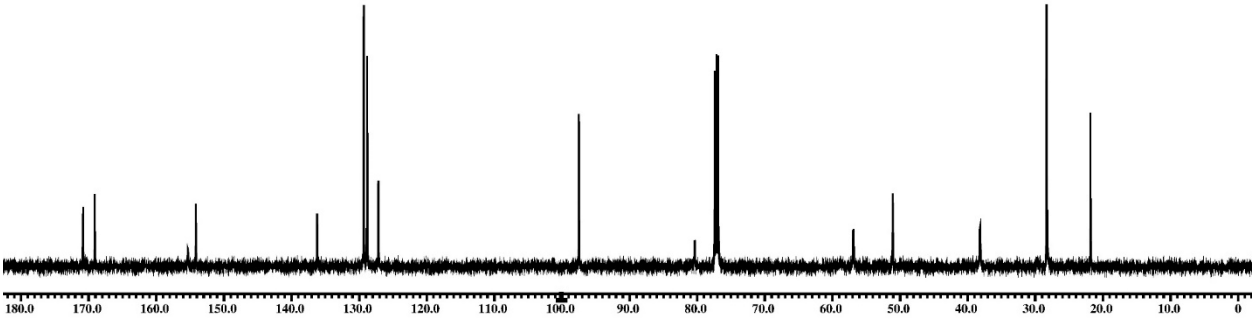
Synthesis of α,β-hybrid peptide 1: 1.1 g (10 mmol) of (E)-methyl 3-aminobut-2-enoate was dissolved in a mixture of 10 mL of dichloromethane(DCM) and cooled in an ice-water bath. H-Phe-OMe was isolated from 2.5 g (11 mmol) of the corresponding methyl ester hydrochloride by neutralization with saturated sodium carbonate, subsequent extraction with ethyl acetate, and concentration (10 mL), and this was added to the reaction mixture, followed immediately by 1.85g (9 mmol) of dicyclohexylcarbodiimide (DCC) and 1.21g (9 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DCM was evaporated, and the

residue was taken in ethyl acetate (60 mL); dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCl (3 X 50 mL), brine, 1 M sodium carbonate (3 X 50 mL), and brine (2 X 50 mL), dried over anhydrous sodium sulphate, and evaporated under vacuum to yield 2.6 g (72%) of α,β-hybrid peptide **1** after column chromatography (1:4 Ethylacetate:hexane column solvent). The compounds was characterized by 500 MHz ^{1}H NMR spectroscopy, 125 MHz ^{13}C NMR spectroscopy, Mass spectrometry, etc.

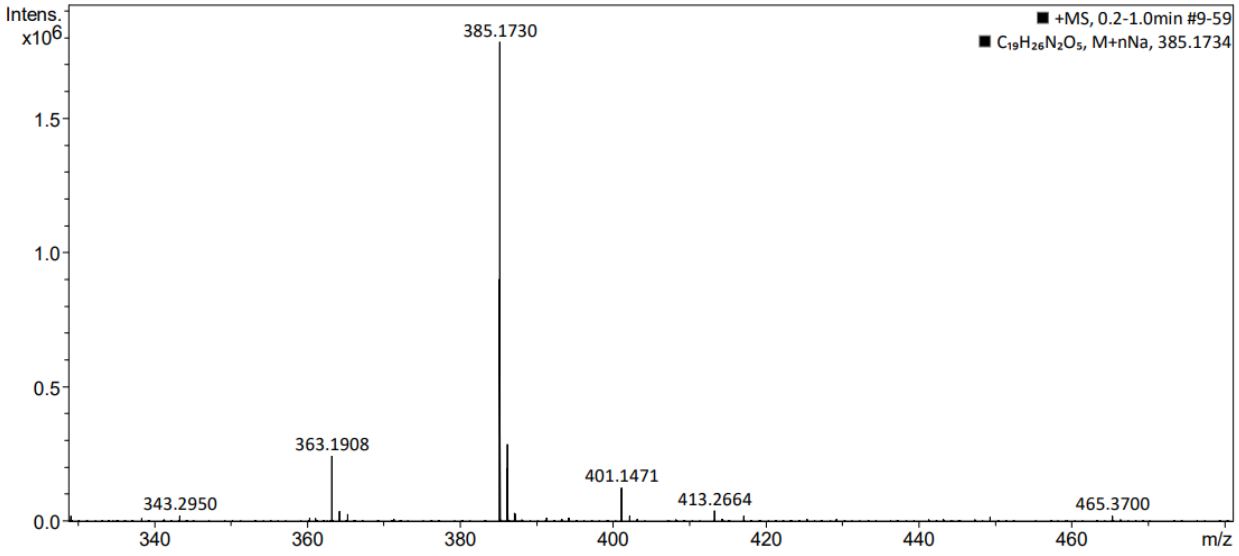
^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm, 298 K): 11.64-11.56 (1H, NH between double bond and C=O), 7.47–7.25 (m, 6H, 5H aromatic protons & 1H NH), 5.16-5.08 (m, 1H, Phe C^{α} H), 5.05-4.97 (m, 1H, double bond H) 3.72-3.75 (s, 3H, OCH_3), 3.22-3.12 (m, 2H, Phe C^{β} H), 2.48-2.42 (s, 3H, Double bond-CH_3), 1.50-1.45 (s, 9H, BOC-CH_3) (ESI Figure S6). ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm, 298 K): 170.93, 169.07, 155.34, 154.16, 136.14, 129.31,128.75, 127.15, 97.40, 80.52, 56.90, 51.07, 38.31, 28.48, 21.87 (ESI Figure S7). Mass spectra, ESI-MS: $C_{19}H_{26}N_2O_5Na$, found *m*/*z*: 385.1730 $[M + Na]^+$, calculated for $C_{19}H_{26}N_2O_5Na$ 385.1734 (ESI Figure S8).



ESI Figure S7: ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of α,β-hybrid peptide **1**.



ESI Figure S8: ^{13}C NMR (125 MHz, $CDCl_3$, δ in ppm, 298K) spectrum of α,β-hybrid peptide **1**.



ESI Figure S9: Mass spectra of α,β-hybrid peptide **1**.