Electronic Supporting Information

The effect of amide bond orientation and symmetry on the self-assembly and gelation of discotic tripeptides†

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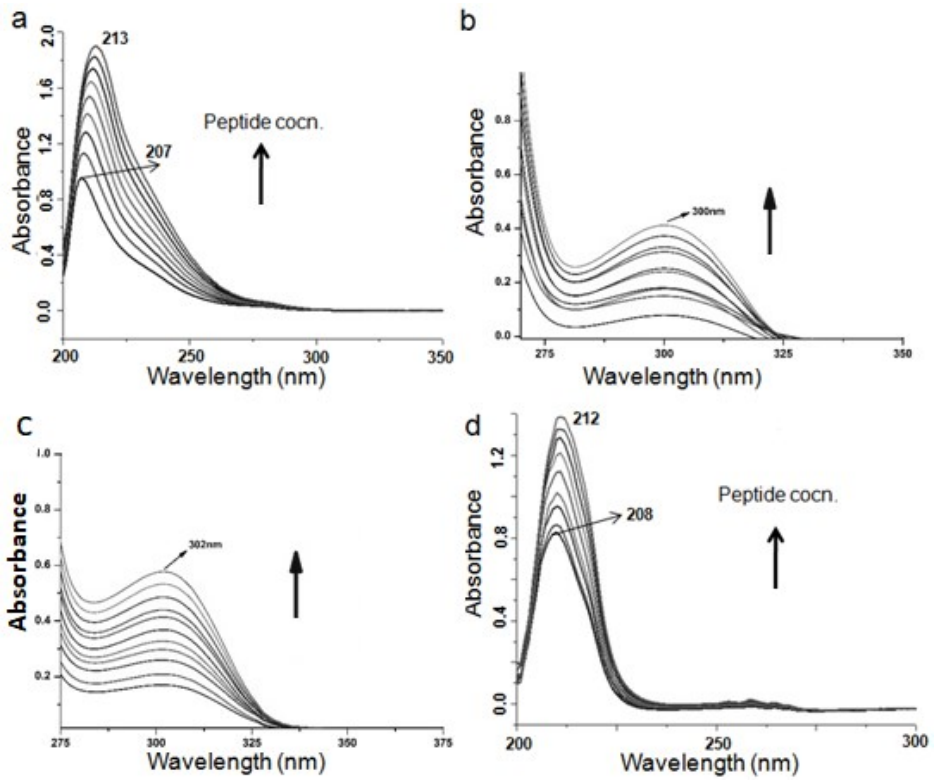
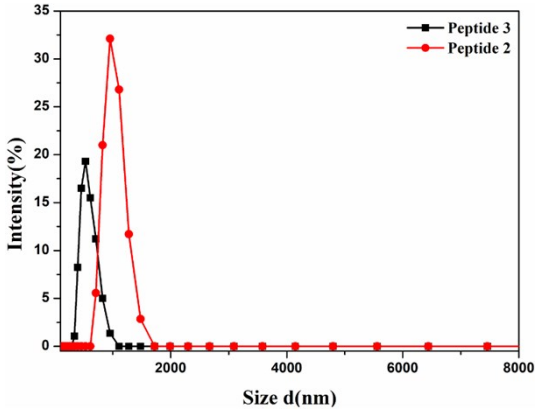
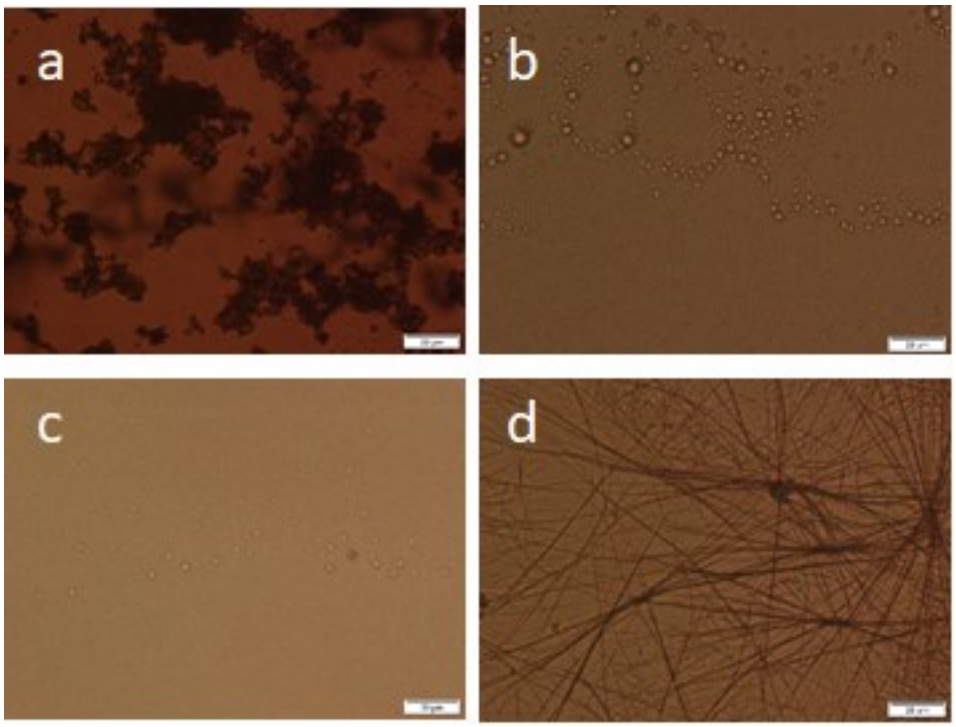


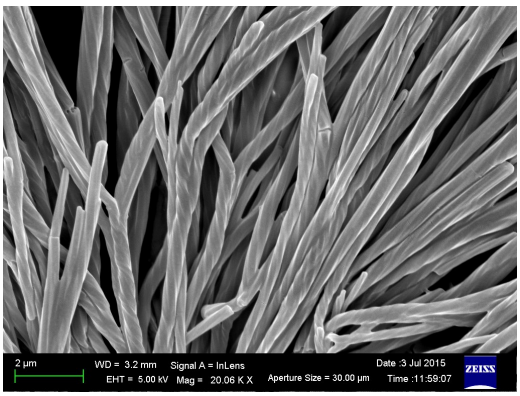
ESI Figure S1. Concentration dependent UV-vis absorption spectra of (a) discotic tripeptide **1**, (b) discotic tripeptide **2**, (c) discotic tripeptide **3** and (d) discotic tripeptide **4** in methanol.



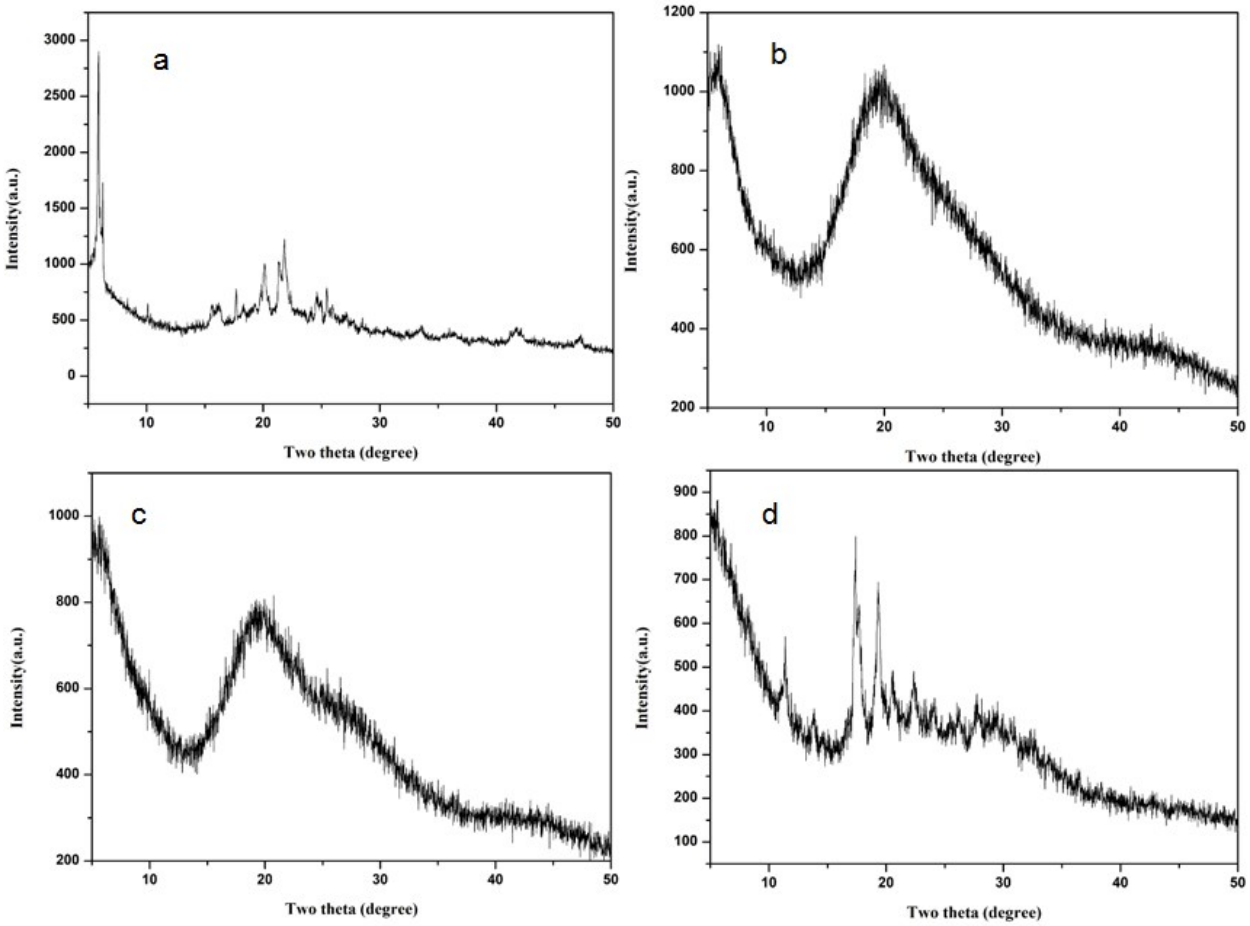
ESI Figure S2. DLS study of discotic tripeptide **2** (d~1008 nm) and discotic tripeptide **3** (d~567 nm) at 298 K.



ESI Figure S3. POM images of (a) discotic tripeptide **1,** (b) discotic tripeptide **2,** (c) discotic tripeptide **3** and (d) discotic tripeptide **4.**



ESI Figure S4. FE-SEM image of twisted fibril of discotic tripeptide **1** in xerogel.



ESI Fig. S5. The PXRD plots of (a) discotic tripeptide **1**, (b) discotic tripeptide **2,** (c) discotic tripeptide **3** and (d) discotic tripeptide **4.**

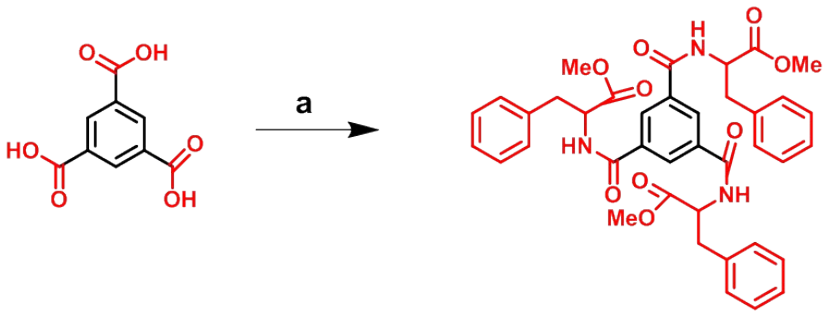
ESI Table S1

Solvent	Peptide 1 (Tgel in °C)	Peptide 2 (Tgel in °C)	Peptide 3 (Tgel in °C)	Peptide 4 (Tgel in °C)
O-xylene	WG	NG	NG	GEL(91 ± 0.5)
m-xylene	WG	NG	NG	GEL(90 ± 0.5)
p-xylene	WG	NG	NG	GEL(95 ± 0.5)
Xylene	WG	NG	NG	GEL(92 ± 0.5)
Toulene	WG	NG	NG	GEL(93 ± 0.5)
Cl-benzene	NG	NG	NG	GEL(46 ± 0.5)
1,2 Dichlorobenzene	NG	NG	NG	GEL(44 ± 0.5)
Benzene	NG	NG	NG	GEL(35 ± 0.5)
Chloroform	NG	NG	NG	NG
Cyclohexane	NG	NG	NG	NG

NG= No Gel, WG= Weak Gel

Experimental

Synthesis of discotic tripeptide 1



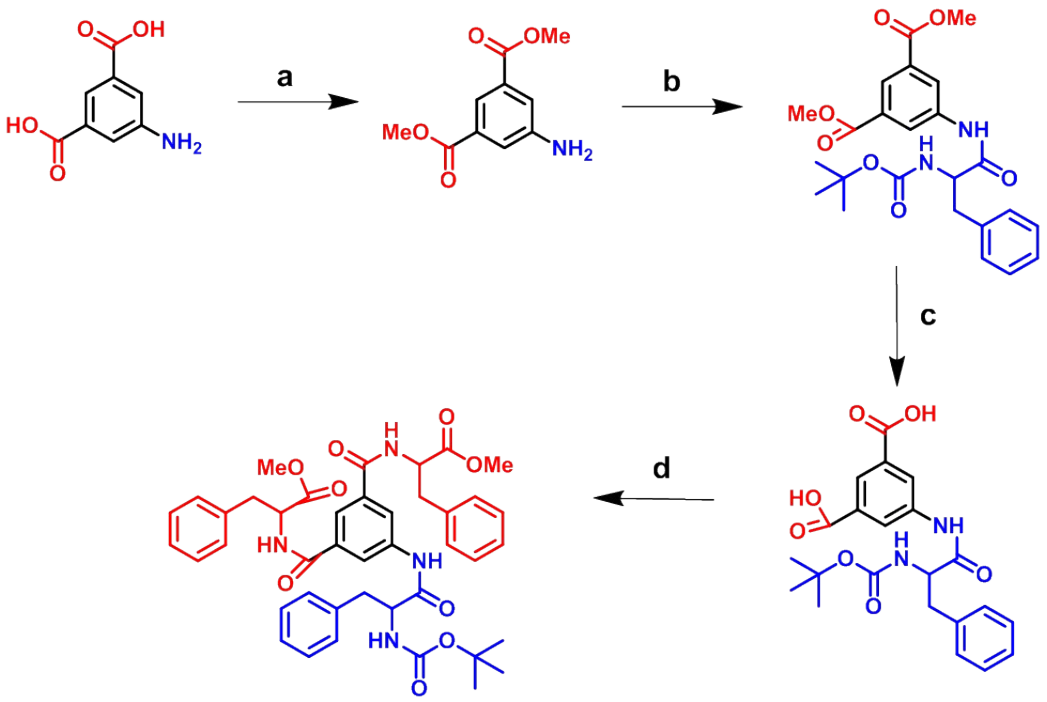
Scheme 1: Synthesis of discotic tripeptide **1**. Reagent and condition: (a) H-Phe-OMe, DCC, HOBt, DMF, 0°C.

500 mg (2.37 mmol) of benzene-1,3,5-tricarboxylic acid was dissolved in a mixture of 10 mL of N,N-dimethylformamide (DMF) and cooled in an ice-water bath. H-Phe-OMe was

isolated from 2.5 g (11.6 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 24 h. DMF 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 1.2 g (1.73 mmol, 72%) of compound **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ in ppm: 8.16-8.15 (d, 3H, NH), 7.26-7.17 (m, 18H, ring H), 5.04-5.02 *(*m, 3H, CαH Tyr), 3.73 (*s*, 9H, OCH3), 3.24-3.17 (m, 6H, CβH Phe). ^{13}C NMR (100MHz, $CDCl_3$ δ in ppm): 172.45, 165.42, 136.02, 134.66, 129.49, 128.85, 127.34, 54.28, 52.72, 37.96. ESI-MS (MeOH): m/z (Calc): $C_{39}H_{39}N_3O_9$ $[M+H]^+$ 694.27; found: 694.2756.

Synthesis of discotic tripeptide 2



Scheme 2: Synthesis of discotic tripeptide **2**. Reagent and condition: (a) $SOCl_2$, MeOH (b) Boc-Phe-OH, DCC, HOBt, DMF, 0°C (c) NaOH, MeOH (d) H-Phe-OMe, DCC, HOBt, DMF, 0°C.

The methyl ester of 5-aminoisophthalic acid was isolated from the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and evaporation. 2.51 g (9.43 mmol) of Boc-Phe-OH was dissolved in 25 ml dry DMF in an ice-water bath. 1.97 g (9.43 mmol) of 5-aminoisophthalic methyl ester was then added to the reaction mixture, followed immediately by 1.946 g (9.43 mmol) dicyclohexylcarbodiimide (DCC) and 1.274 g (9.43 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DMF was evaporated and the residue was dissolved in ethyl acetate (60 mL) and the dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCl (3 x 50 mL), brine (2 x 50 mL), 1 M sodium carbonate (3 x 50 mL) and brine (2 x 50 mL)

and dried over anhydrous sodium sulphate; and evaporated in a vacuum. The product was purified by silica gel (100–200 mesh) using n-hexane–ethyl acetate (3: 1) as eluent. Yield: 3.18 g (6.99 mmol, 75.16%).

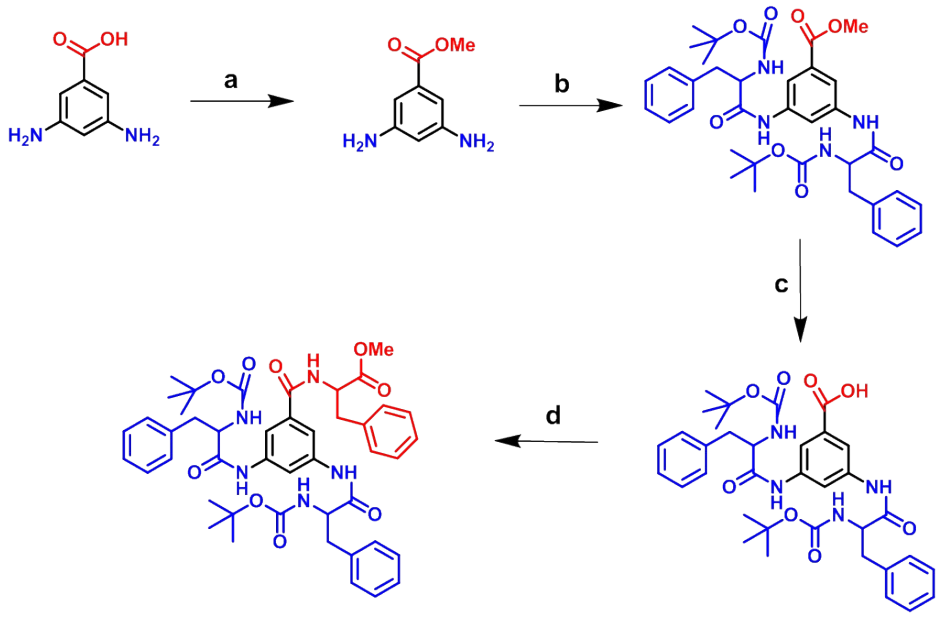
The obtained compound was dissolved in 50 mL of methanol/water mixture (9:1), cooled and 680 mg of NaOH was added and stirred for 6 h. Then methanol was evaporated under reduced pressure, about 20 mL water was added and washed with diethylether. The water portion was acidified with dilute HCL solution, the compound was extracted with ethyl acetate. The organic layer was then dried over anhydrous Na_2SO_4 and dried under reduced pressure. Yield: 2.59 g (6.05 mmol, 86.5%).

Next the compound was dissolved in 25 ml dry DMF in an ice-water bath. H-Phe-OMe was isolated from 3.332 g (15.5 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and the ethyl acetate extract was concentrated to 10 ml. It was then added to the reaction mixture, followed immediately by 2.78 g (13.5 mmol) dicyclohexylcarbodiimide (DCC) and 1.82 g (13.5 mmol) of HOBt. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DMF was evaporated and the residue was dissolved in ethyl acetate (60 mL) and the dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCl (3 x 50 mL), brine (2 x 50 mL), 1 M sodium carbonate (3 x 50 mL)and brine (2 x 50 mL) and dried over anhydrous sodium sulfate; and evaporated in a vacuum to yield BTC 2 as a white solid. The product was purified by silica gel (100–200 mesh) using n-hexane–ethyl acetate (3 : 1) as eluent. Yield: 3.15 g (4.2 mmol, 69.42%).

^{1}H NMR (400 MHz, $CDCl_3$) δ in ppm: 8.52 (s, 1H, NH), 7.29 (s, 3H, NH), 7.25-7.20 (m, 18H, ring H), 5.00-4.98 *(*m, 3H, CαH Phe), 3.73 (*s*, 6H, OCH_3), 3.24-3.23 (m, 6H, CβH

Phe), 1.38 (s, 9H, Boc). ^{13}C NMR (100MHz, $CDCl_3$ δ in ppm): 173.45, 166.23, 137.34, 136.12, 129.35, 128.78, 127.23, 55.87, 54.28, 38.26, 28.42. ESI-MS (MeOH): m/z (Calc): $C_{42}H_{46}N_4O_9$ $[M+Na]^+$ 773.33; found: 773.3165.

Synthesis of discotic tripeptide 3

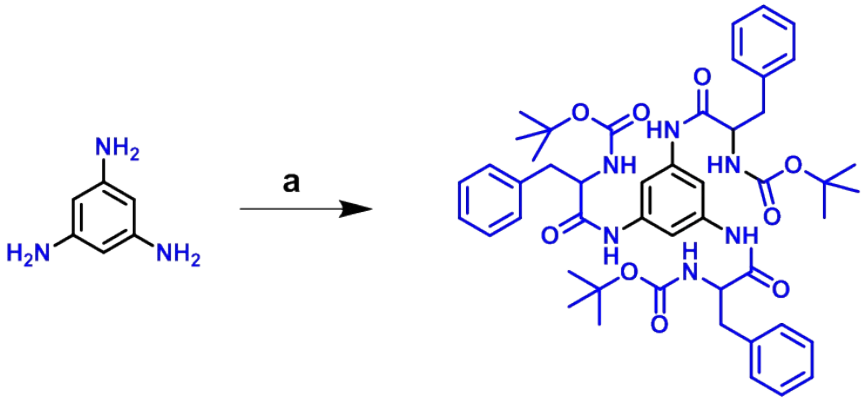


Scheme 3: Synthesis of discotic tripeptide **3**. Reagent and condition: (a) $SOCl_2$, MeOH (b) Boc-Phe-OH, DCC, HOBt, DMF, 0°C (c) NaOH, MeOH (d) H-Phe-OMe, DCC, HOBt, DMF, 0°C.

Similar as the procedure of discotic tripeptide **2** taking 3,5-diaminobenzoic acid instead of 5-aminoisophthalic acid.

^{1}H NMR (400 MHz, $CDCl_3$) δ in ppm: 8.91-8.88 (m, 3H, NH), 7.27-7.23 (m, 20H, ring H and NH), 4.90 *(*m, 3H, CαH Phe), 3.73 (*s*, 3H, OCH_3), 3.14-2.99 (m, 6H, CβH Phe), 1.37 (s, 18H, Boc). ^{13}C NMR (100MHz, $CDCl_3$ δ in ppm): 172.57, 169.34, 138.75, 136.15, 135.73, 129.21, 128.56, 127.11, 126.88, 53.09, 52.33, 37.78, 28.33. ESI-MS (MeOH): m/z (Calc): $C_{45}H_{53}N_5O_9$ $[M+Na]^+$ 830.38; found: 830.3736.

Synthesis of discotic tripeptide 4



Scheme 4: Synthesis of discotic tripeptide **4**. Reagent and condition: (a) Boc-Phe-OH, DCC, HOBt, DMF.

325 mg (2.64 mmol) triaminobenzene was dissolved in 25 mL dry DMF. 2.1 g and (7.91 mmol) Boc-Phe-OH, 1.65 g (8 mmol) DCC and 1.08 g (8 mmol) HOBt were added and stirred for 48 h at room temperature. Then the solution was added to 200 mL water, taken in a separating funnel and shaken for 15 min and 150 mL ethyl acetate was added and shaken for another 10 min. The organic layer was collected and DCU was filtered off. The organic layer was washed with 2 M HCl (3x50 mL), brine (2x50 mL), then 1 M sodium carbonate (3x50 mL) and brine (2x50 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum. Purification was performed by silica gel column (100–200 mesh size) using ethyl acetate and hexane (1 : 5) as eluent. Yield: 1.784 g (2.06 mmol, 78.0%).

^{1}H NMR ($CDCl_3$, 400 MHz), δ in ppm: 7.216–7.165 (m, 15H, aromatic protons Phe), 5.742 (s, 3H, TAB), 5.371 (s, 3H, NH TAB), 4.994 (s, 3H, NH Boc), 4.313–4.298 (m, 3H, CαH Phe), 3.009 (s, 6H, CβH Phe), 1.340 (s, 27H, Boc). ^{13}C NMR ($CDCl_3$, 100 MHz, δ in ppm): 174.25, 155.89, 136.72, 129.32, 128.72, 127.24, 80.71, 55.59, 38.73, 28.15. ESI-MS (MeOH): m/z (Calc): $C_{48}H_{60}N_6O_9$ $[M+Na]^+$ 886.43; found: 886.26.

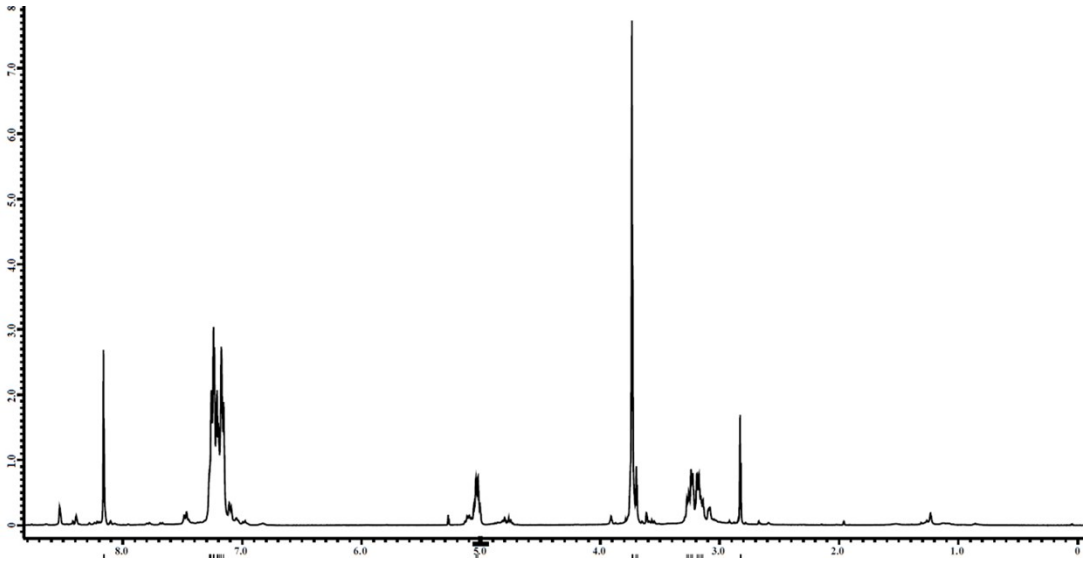


Fig. S6. ^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm}) of discotic tripeptide **1.**

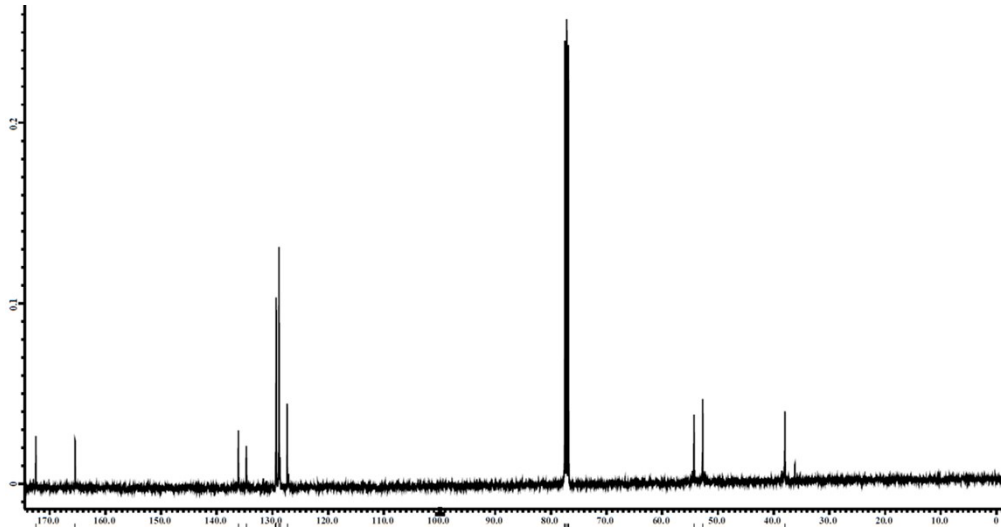


Fig. S7. ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm}) of discotic tripeptide **1.**

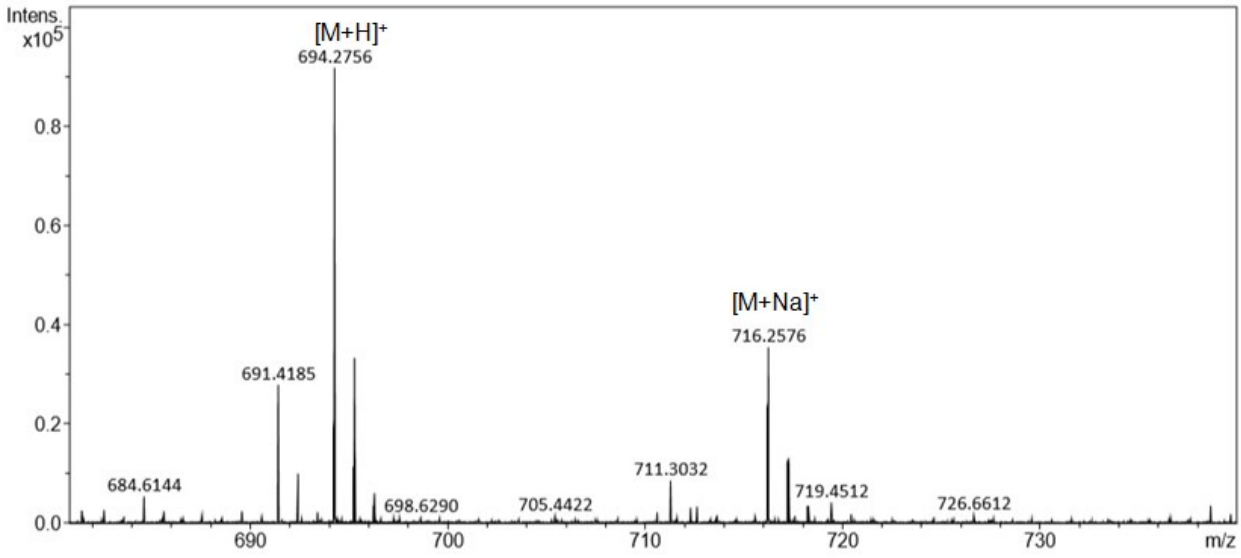


Fig. S8. MS spectra of discotic tripeptide **1.**

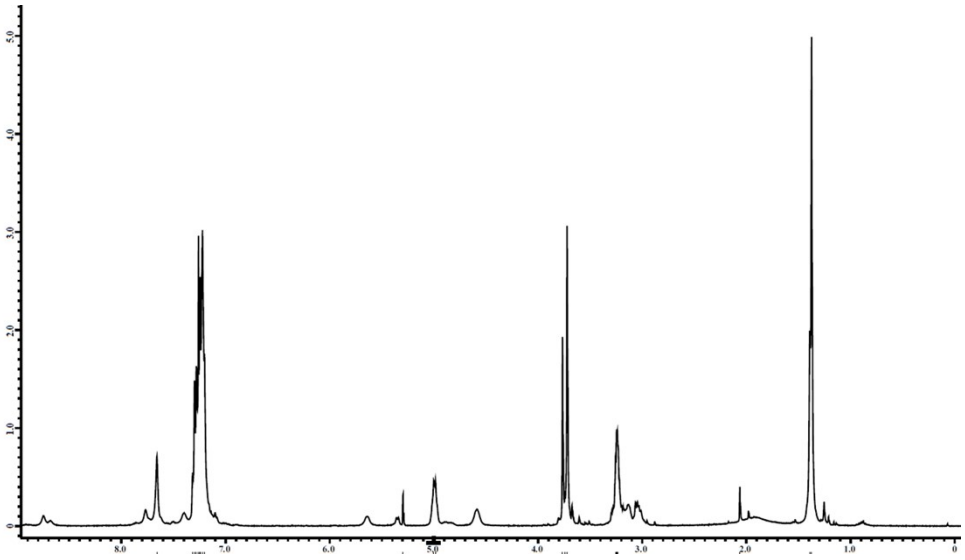


Fig. S9. ^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm}) of discotic tripeptide **2.**

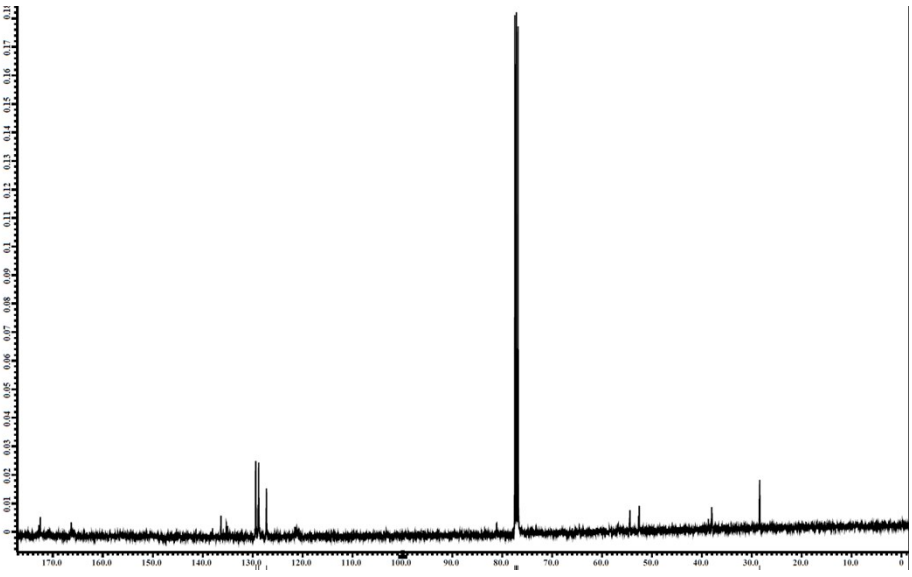


Fig. S10. ^{13}C NMR ($CDCl_3$, 100 MHz, $\delta_{ppm)}$ of discotic tripeptide **2.**

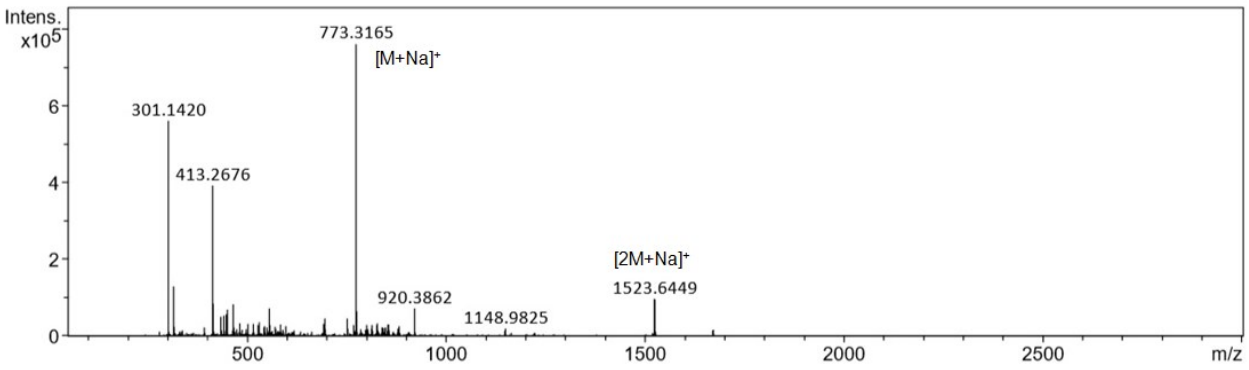


Fig. S11. MS spectra of discotic tripeptide **2.**

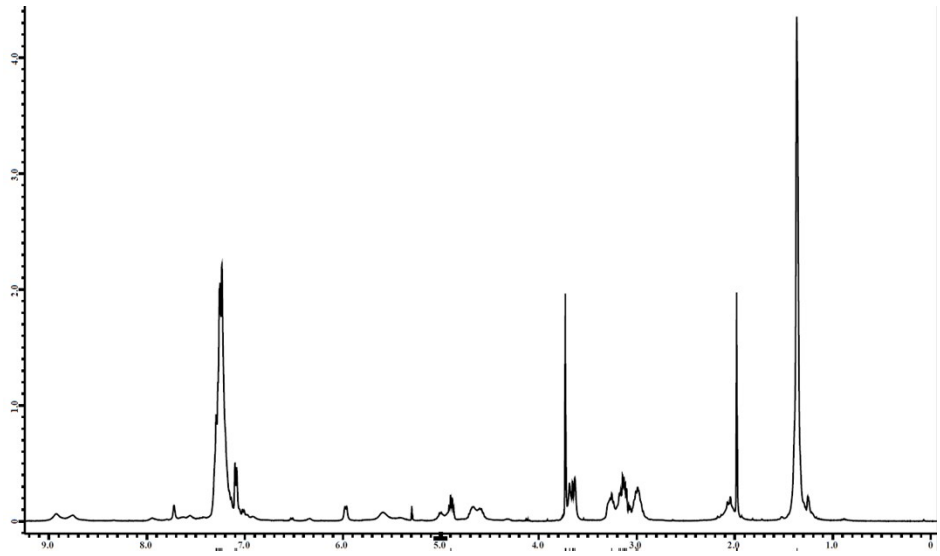


Fig. S12. ^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm}) of discotic tripeptide **3.**

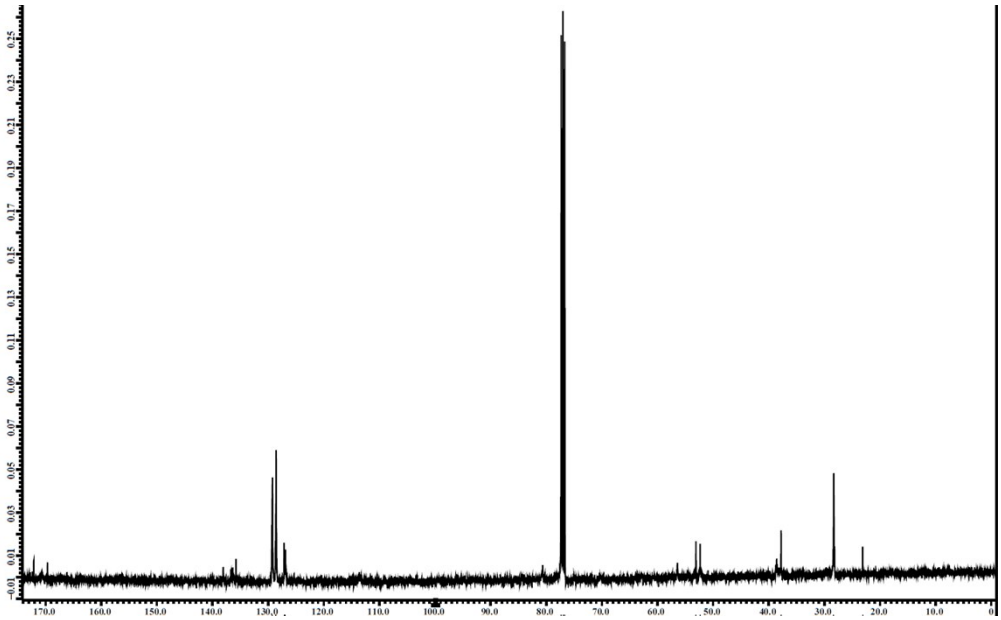


Fig. S13. ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm}) of discotic tripeptide **3.**

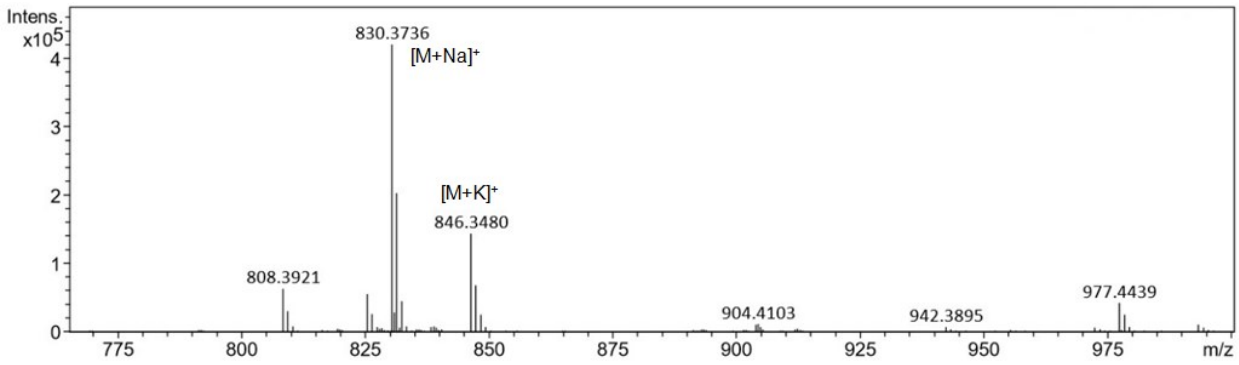


Fig. S14. MS spectra of discotic tripeptide **3.**

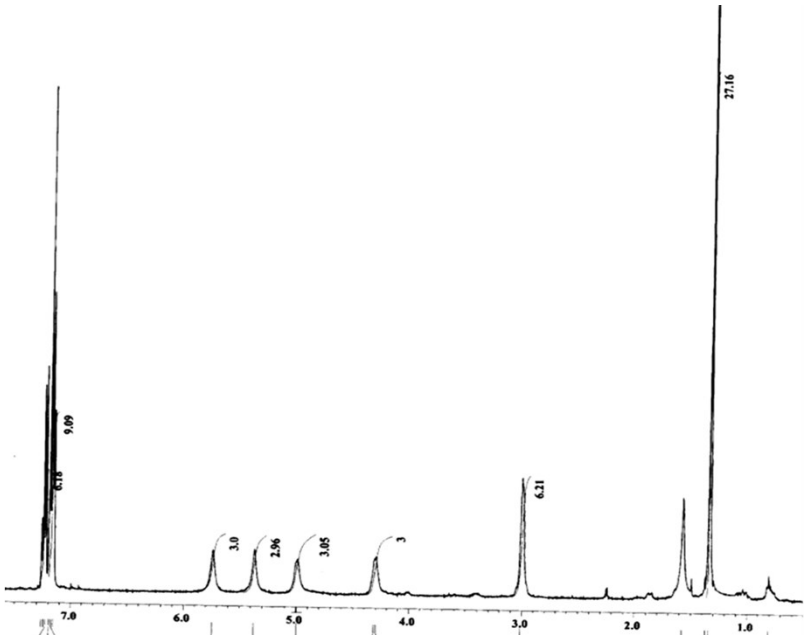


Fig. S15. ^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm}) of discotic tripeptide **4.**

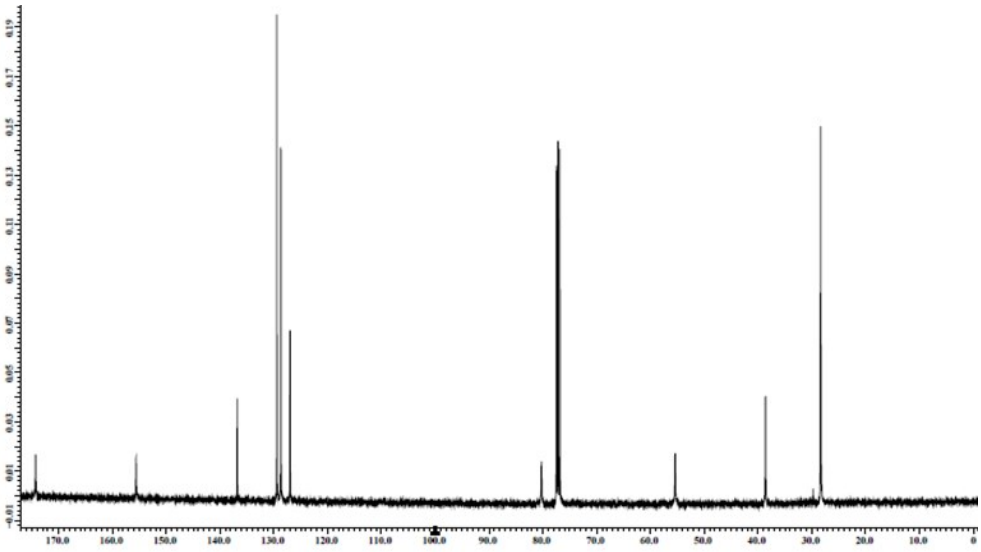


Fig. S16. ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm}) of discotic tripeptide **4.**

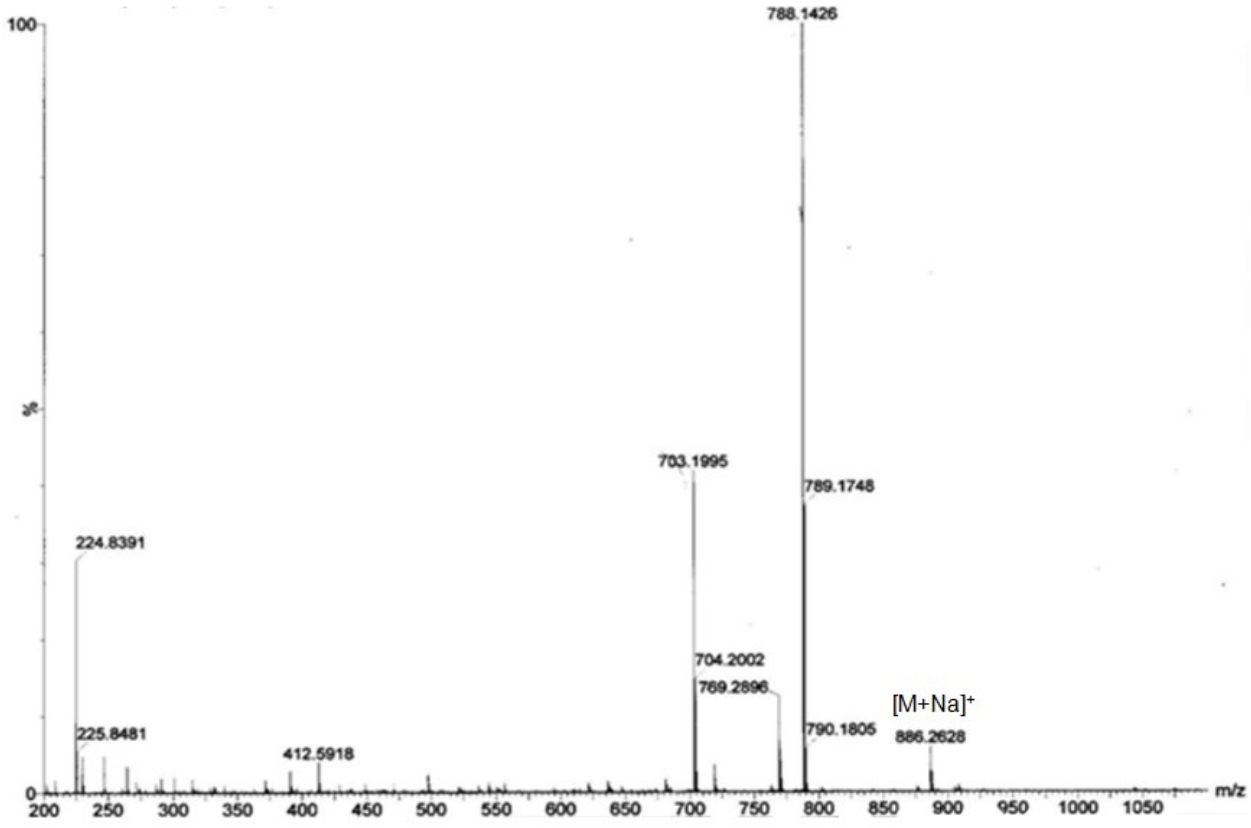


Fig. S17. MS spectra of discotic tripeptide **4.**