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Solvent assisted structural diversity: supramolecular sheet and double helix of a short aromatic γ-peptide

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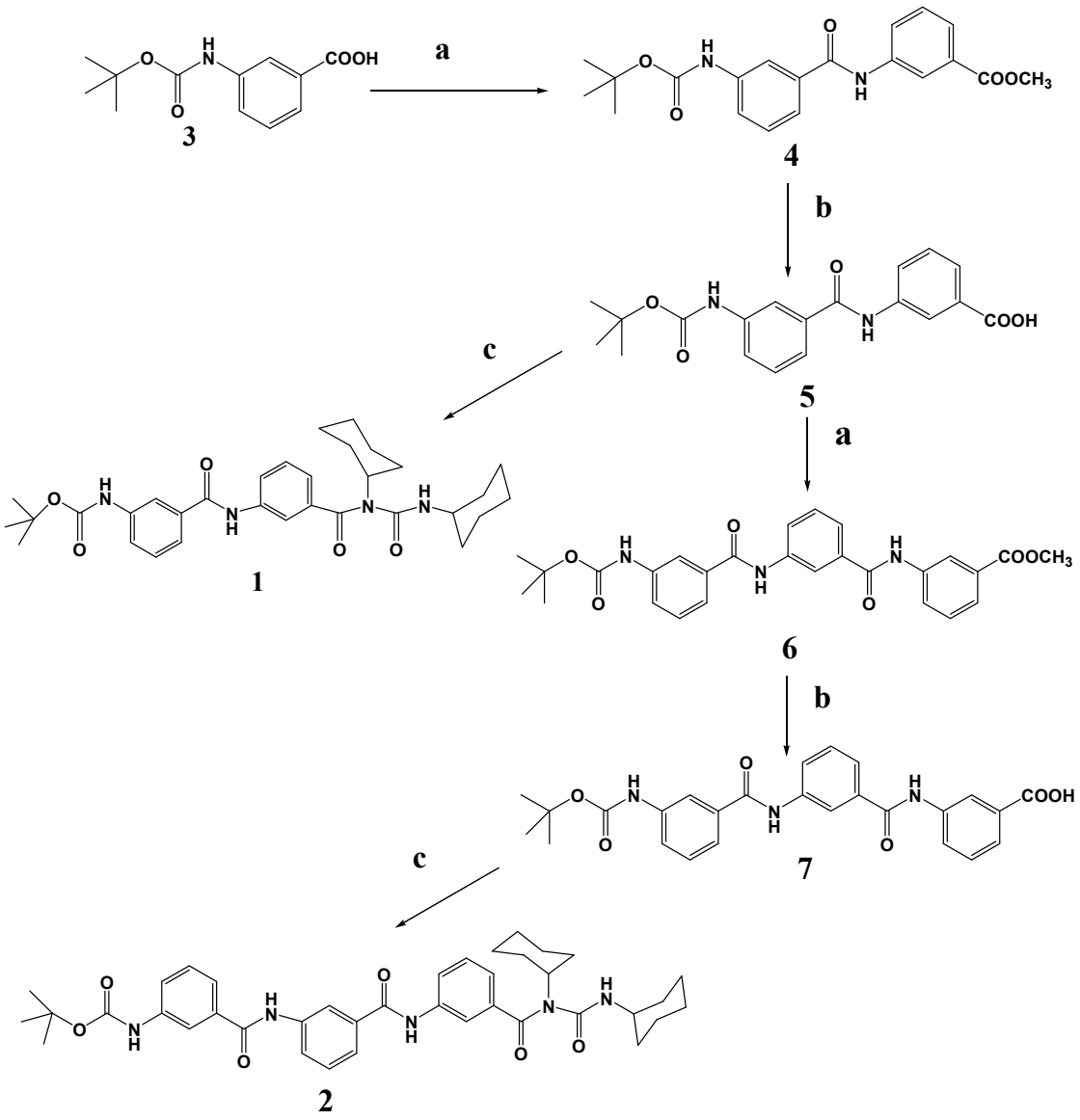


Figure S1 Scheme1: Reagent and condition: (a) Dry DCM, H-*Maba*-OMe, DCC, HOBt, 0^{o}C. (b) MeOH, 2M NaOH. (c) DCU, Et_3N, DCC, HOBt.

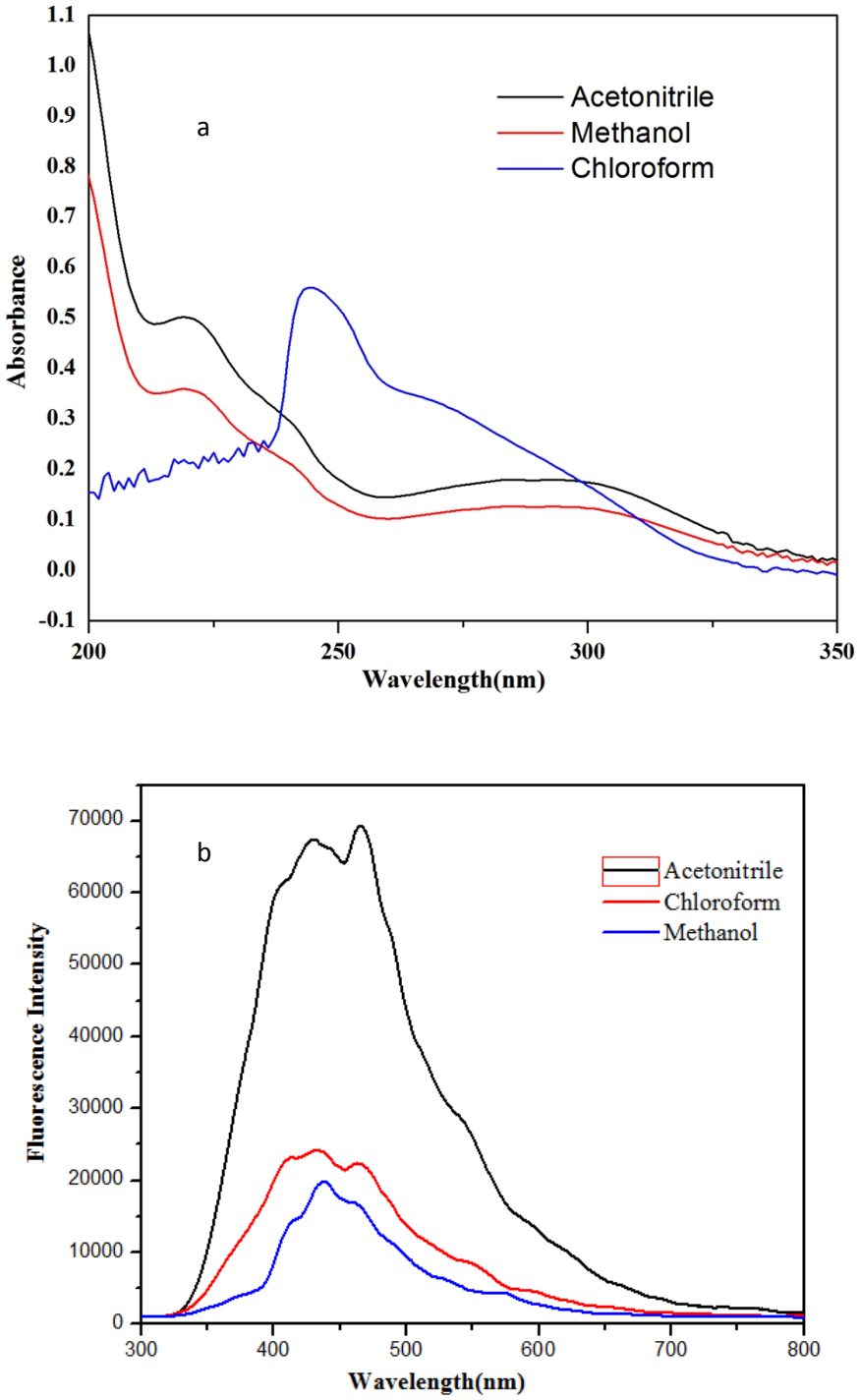


Figure S2. (a) UV-vis spectra of peptide **1**. (b) Fluorescence spectra of peptide **2** in different solvents. Excitation at 220 nm.

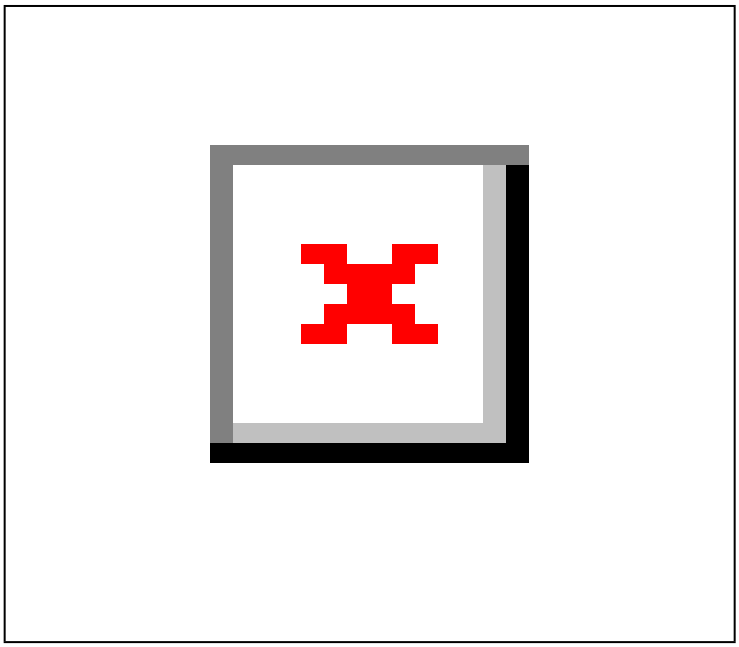
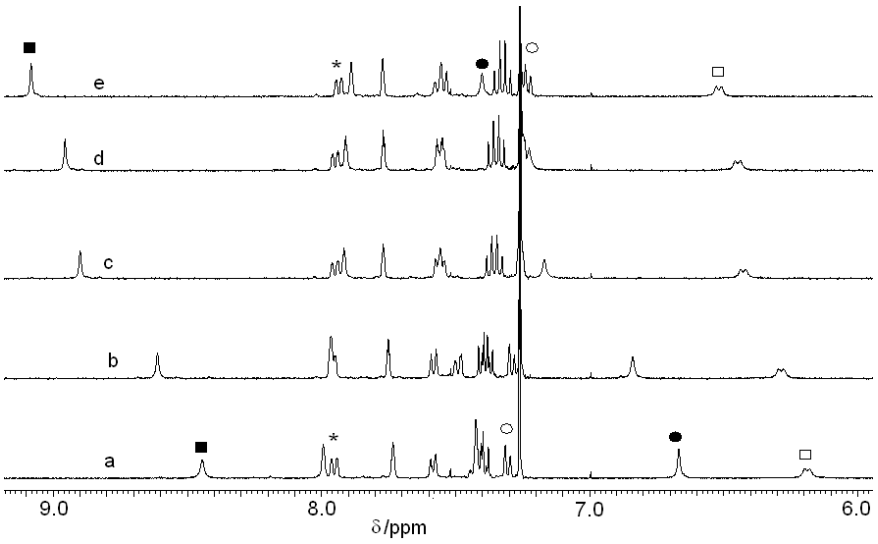
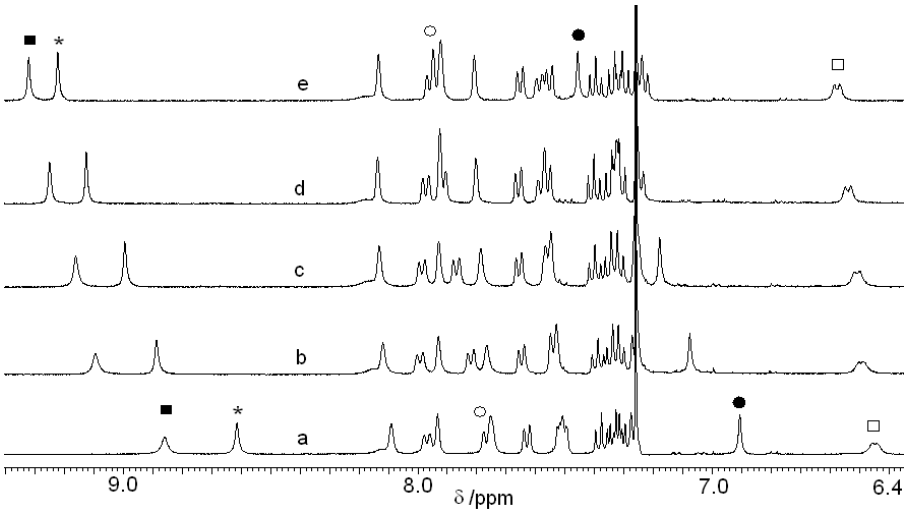


Figure S3: Part of the concentration dependent ^{1}H NMR spectra of peptide **1** in $CDCl_3$ showing downfield shift of the amide protons with increasing concentration. The fill square for Maba 2 NH, fill circle for Maba 1 NH and square for urea NH.



(a)



(b)

Figure S4: (a) Part of 1H NMR solvent tritration spectra of peptide 1 in $CDCl_3$ solution. % of DMSO-d_6 a) 0, b) 2, c) 4, d) 6, e) 10. The fill square for Maba 2 NH, fill circle for Maba 1 NH and square for urea NH. (b) Part of 1H NMR solvent tritration spectra of peptide 1 in $CDCl_3$ solution. % of DMSO-d_6 a) 0, b) 2, c) 4, d) 6, e) 10. The fill square for Maba 3 NH, star for Maba 2 NH, fill circle for Maba 1 NH and square for urea NH.

Residue	NH	Δδ
Peptide 1		
Urea NH	6.14	0.36
Maba (1) NH	6.63	0.71
Maba (2) NH	8.48	0.52
Peptide 2		
Urea NH	6.42	0.12
Maba (1) NH	6.90	0.52
Maba (2) NH	8.61	0.60
Maba(3) NH	8.83	0.48

Table 1: Characteristic ^{1}H NMR parameters for Peptides **1** and **2** (chemical shifts δ).

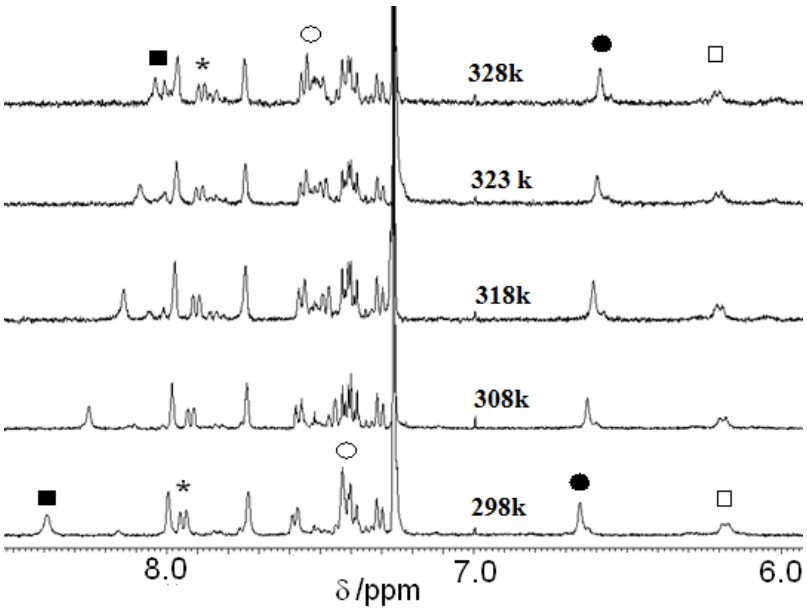


Figure S5: Part of variable temperature 1H NMR spectra of peptide 1 in $CDCl_3$. The fill square for Maba 2 NH, fill circle for Maba 1 NH and square for urea NH.

Residues	NH	Δδ/ΔT
Boc NH	6.63 (6.92)	0.02/10. 0.02/10, 0.01/5, 0.01/5 (10/10, 8/10, 0.2/5, 0.1/5)
Urea NH	6.20 (6.42)	0.06/10, 0.01/10, 0.01/5, 0.01/5 (11/10, 9/10, 0.1/5, 0.1/5)
Maba (1) NH	8.40 (8.61)	0.18/10, 0.11/10, 0.08/5, 0.02/5 (20/10, 11/10, 0.9/5, 0.7/5)
Maba(2) NH	- (8.93)	(21/10, 18/10. 0.4/5, 0.8/5)

Table 2: Characteristic ^{1}H NMR parameters for Peptides **1** and **2** (chemical shifts δ)[a].

[a]Chemical shift values of NH proton resonances for peptides **1** and **2** in $CDCl_3$. Values in parentheses correspond to peptide **2**.

[b]$\Delta\delta/\Delta T$ is the chemical shift difference for NH protons in $CDCl_3$ with temperature for peptide **1** and **2**.

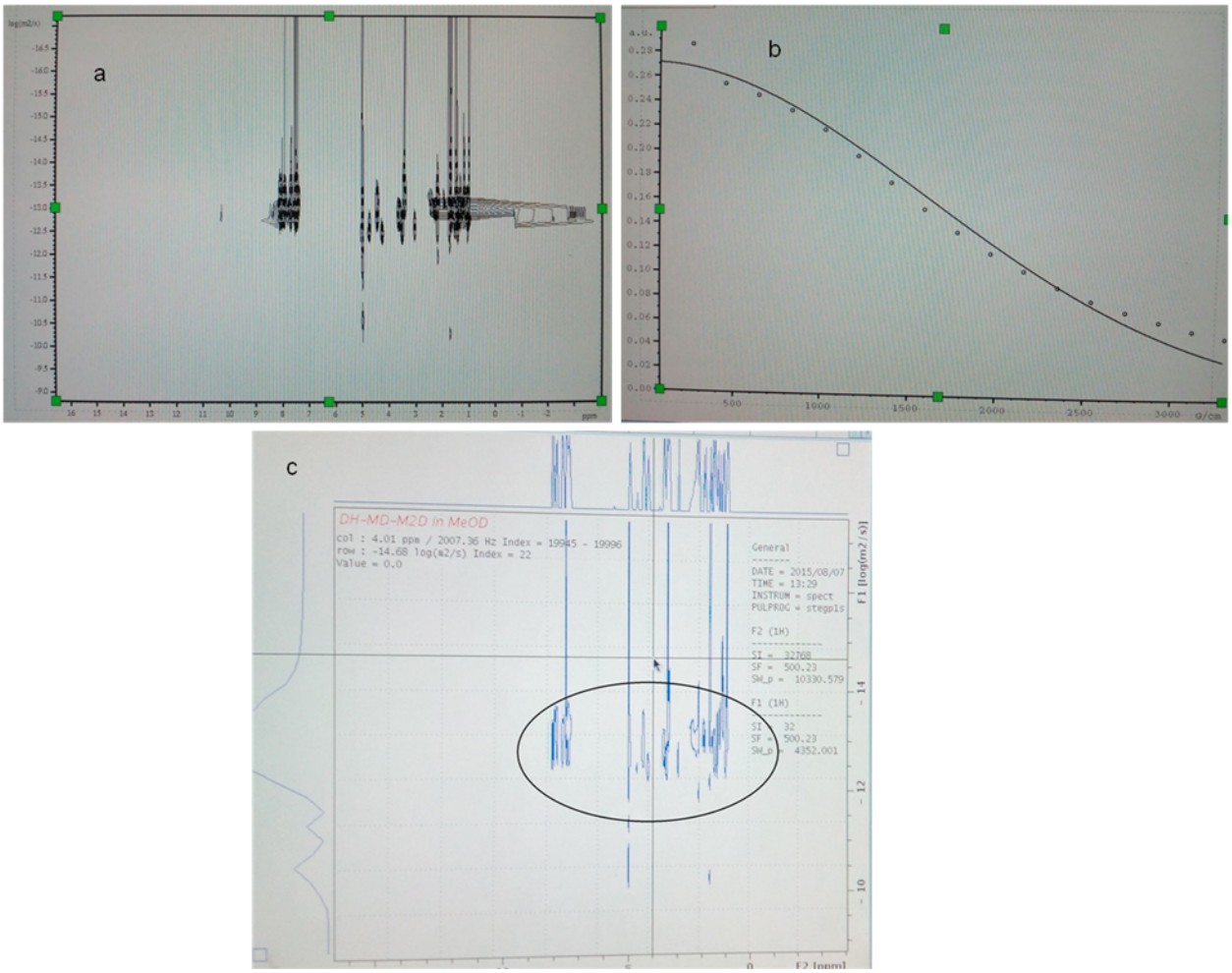


Figure S6: The diffusion coefficients measured by NMR pulsed-gradient spin-echo experiments. The diffusion coefficients are 1.751×10^{-13} m^2/sec for $CDCl_3$ and 1.628×10^{-13} m^2/sec for MeOD. (a) DOSY- NMR spectra of peptide 1 in $CDCl_3$, (b) Diffusion variable gradient of peptide 1 in $CDCl_3$ and (c) DOSY- NMR spectra of peptide 1 in MeOD.

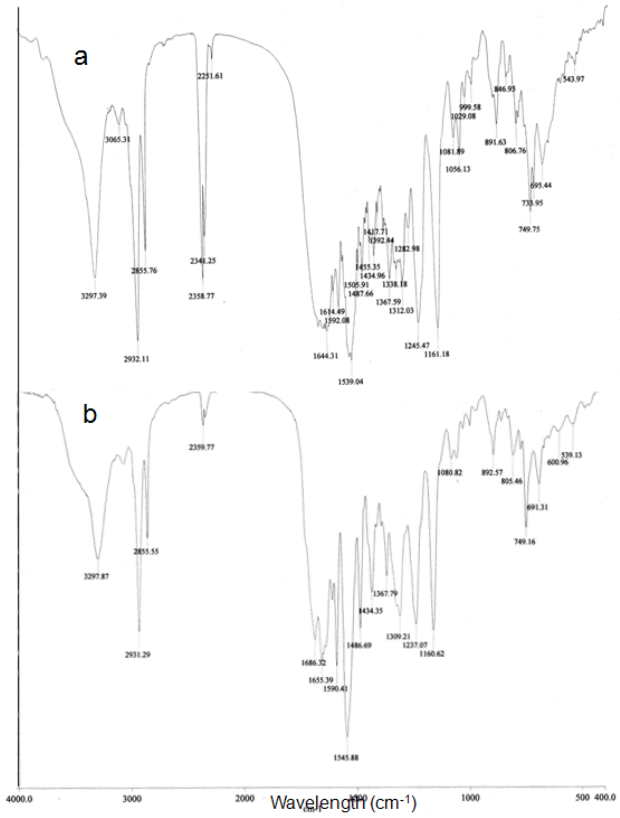


Figure S7. Solid state FT-IR spectra of (a) Peptide 1 and (b) Peptide 2 showing similar backbone conformation.

Experimental Section

General Methods and Materials. Meta-aminobenzoic acid was purchased from Spectochem. HOBt (1-hydroxybenzotriazole) and DCC (dicyclohexylcarbodiimide) were purchased from SRL.

Peptide Synthesis. The peptides were synthesized by conventional solution-phase methods using fragment condensation strategy. The Boc group was used for N-terminal protection and the C-terminus was protected as a methyl ester. Couplings were mediated by dicyclohexylcarbodiimide/1- hydroxybenzotriazole (DCC/HOBt). Methyl ester deprotection was performed via the saponification method. All the intermediates were characterized by 500 MHz or 400 MHz ^{1}H NMR and mass spectrometry. The final compounds were fully characterized by 500 MHz or 400 MHz ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, mass spectrometry, and IR spectroscopy. The peptide **1, 2** were characterized by X-ray crystallography. The products were purified by column chromatography using silica (100-200-mesh size) gel as stationary phase and n-hexane –ethyl acetate mixture as eluent.

(a) Boc-Maba(1)-OH (3). A solution of *m*-aminobenzoic acid (4.1 g, 30 mmol) in a mixture of dioxane (60 mL), water (30 mL) and 1M NaOH (30 mL) was stirred and cooled in an ice-water bath. Di-tert-butylpyrocarbonate (7.0 g, 32 mmol) was added and stirring was continued at room temperature for 6 h. Then the solution was concentrated in vacuum to about 20-30 mL, cooled in an ice-water bath, covered with a layer of ethyl acetate (about 50 mL) and acidified with a dilute solution of $KHSO_4$ to pH 2-3 (Congo red). The aqueous phase was extracted with ethyl acetate and this operation was done repeatedly. The ethyl acetate extracts were pooled, washed with water and drier over anhydrous Na_2SO_4 and evaporated in a vacuum. The pure material was obtained as a white solid.

Yield: 5.42g (22.8 mmol, 76 %).

Melting point: 177^{o}C.

^{1}H NMR (DMSO-d_6, 400 MHz, δ in ppm): 12.87 [1H, s, COOH], 9.54 [1H, s, aromatic proton], 8.14 [1H, s, NH Maba(1)], 7.61-7.60 [1H, d, J = 7.32 Hz aromatic proton],

7.54-7.52 [1H, d, J = 7.32 Hz aromatic proton], 7.38-7.34 [1H, m, aromatic proton], 1.48 [9H, s, Boc protons]; ^{13}C NMR (DMSO-d_6, 125 MHz, δ in ppm): 167.25, 152.73, 139.76, 131.76, 128.77, 122.87, 122.23, 118.74, 79.28, 28.05; FTIR (in cm^{-1}, KBr): 3353, 2972, 2653, 1694, 1594, 1560, 1478, 1452, 1417, 1292, 1243, 1159, 1058.

Anal. Calcd for $C_{12}H_{15}NO_4$ (237.10): C, 60.75; H, 6.37; N, 5.90.

Found: C, 60.80; H, 6.35; N, 5.92.

*(b) Boc-Maba(1)-Maba(2)-OMe (**4**)*: 5.2 g (22.0 mmol) of Boc-Maba-OH was dissolved in 25 mL dry DCM in an ice-water bath. H-Maba-OMe was isolated from 9.3 g (50 mmol) of the corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and ethyl acetate extract was concentrated to 10 mL. It was than added to the reaction mixture, followed immediately by 5.0 g (24 mmol) dicyclohexylcarbodiimide (DCC) and 3.2 g (24 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 dissolved in ethyl acetate (60 mL) and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2M HCl (3 × 50 mL), brine (2 × 50 mL), 1M sodium carbonate (3 × 50 mL) and brine (2 × 50 mL) and dried over anhydrous sodium sulfate; and evaporated in a vacuum to yield compound **2** as a white solid. The product was purified by silica gel (100-200 mesh) using n hexane – ethyl acetate (5:1) as eluent.

Yield: 5.55 g (14.36 mmol, 64%).

Melting point: 140^{o}-141°C.

^{1}H NMR ($CDCl_3$, 500 MHz, δ in ppm): 8.17 [1H, s, aromatic proton], 8.14 [1H, s, aromatic proton], 8.06-8.03 [1H, d, J = 8.31 Hz aromatic proton], 7.97 [1H, s, NH Maba(1)], 7.83-7.81 [1H, d, J = 7.50 Hz aromatic proton], 7.57-7.55 [1H, d, J = 8.50 Hz aromatic proton], 7.49-7.41 [3H, m, aromatic proton], 6.68 [1H, s, NH Maba(2)], 3.93 [3H, s, OCH_3] 1.53 [9H, s, Boc protons]; ^{13}C NMR ($CDCl_3$, 125 MHz, δ in ppm): 166.76, 165.76, 152.75, 138.95, 138.19, 135.38, 130.77, 129.38, 129.09, 125.49, 124.91, 121.82, 121.65, 121.32, 117.03, 80.97, 28.27; FTIR (in cm^{-1}, KBr): 3297,2929, 1725, 1697, 1661, 1611, 1592, 1489, 1443, 1367, 1321, 1288, 1263, 1216, 1160, 1100, 1066.

Anal. Calcd for $C_{20}H_{22}N_2O_5$ (370.15): C, 64.85; H, 5.99; N, 7.56.

Found: C, 64.82; H, 6.00; N, 7.60.

TOF MS *m/z* 393.01 [M + Na]+; *M*calcd: 370.15.

(c) Boc-Maba(1)-*Maba*(2)-*OH (**5**):* To 3.7g (10.00 mmol) of compound **2**, 25 mL MeOH and 2M 15 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After 10 h, methanol was removed under vacuum; the residue was dissolve in 50 mL of water, and washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 × 50 mL). The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a white solid.

Yield: 3.1 g (8.6 mmol, 87%).

Melting point: 200^{o}-202°C.

^{1}H NMR (DMSO-d_6, 400 MHz, δ in ppm): 12.98 [1H, br, COOH], 10.41 [1H, s, NH maba(1)], 9.57 [1H, s, NH Maba(2)], 8.42 [1H, s, aromatic proton], 8.06-8.01 (2H, m, aromatic protons], 7.67 [1H, d, aromatic proton], 7.58 [1H, d, aromatic proton], 7.55 [1H, d, aromatic proton], 7.49-7.41 [2H, m, aromatic protons], 1.49 [9H, s, Boc protons]; ^{13}C NMR (DMSO-d_6, 125 MHz, δ in ppm): 167.21, 165.92, 152.81, 139.77, 139.44 135.50, 131.21, 121.86, 128.64, 124.41, 124.36, 121.29, 121.07, 117.65, 79.30, 28.11. FTIR (in cm^{-1}, KBr): 3354, 2977, 2361, 1702, 1649, 1590, 1542, 1489, 1409, 1304, 1243, 1172, 1065.

Anal. Calcd for $C_{19}H_{20}N_2O_5$ (356.14): C, 64.04; H, 5.66; N, 7.86.

Found: C, 64.00; H, 5.68; N, 7.87.

(d) Boc-Maba(1)-*Maba*(2)-*Maba*(3)*–OMe (**6**):* 1.81 g (5.0 mmol) Boc-Maba-Maba-OH was dissolved in 15mL dry DCM in an ice-water bath. H-Maba-OMe 1.8 g (10 mmol) was isolated from corresponding methyl ester hydrochloride by neutralization, subsequent extraction with ethyl acetate and concentrated to 4 mL. Then it was added to the reaction mixture, followed immediately by 1.23 g (6.0 mmol)

dicyclohexylcarbodiimide (DCC) and 0.810 g (6.0 mmol) HOBt. The reaction mixture was allowed to come to room temperature and stirred for 72 h. The residue was taken in 30 mL ethyl acetate and dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the tripeptide (7) as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane (1:6) as eluent.

Yeild: 1.767 g (3.60 mmol, 72%).

Melting point: 188°-189°C.

^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm): 8.37 [1H, s, NH Maba(1)], 8.28 [1H, s, NH Maba(2)], 8.22-8.21 [2H, m, aromatic protons], 8.08-8.02 [2H, m, aromatic protons], 7.84-7.79 [2H, m, aromatic protons], 7.68-7.66 [1H, d, aromatic proton], 7.57-7.55 [1H, d, aromatic proton], 7.50-7.39 [4H, m, aromatic protons], 6.748 [1H, s, NH Maba(3)], 3.92 [3H, s, OCH_3], 1.53 [9H, s, Boc protons]; ^{13}C NMR (DMSO-d_6, 125 MHz, δ in ppm): 166.13 165.94, 165.77, 152.81, 139.79, 139.59, 139.40, 135.52, 135.25, 130.04, 129.12, 128.69, 128.65, 124.73, 124.25, 123.48, 122.66, 121.28, 121.06, 120.81, 119.93, 117.64, 79.30, 52.20, 28.10; FTIR (in cm^{-1}, KBr): 3369, 3285, 2924, 2853, 2343, 1732, 1705, 1651, 1609, 1589, 1566, 1540, 1488, 1366, 1308, 1292, 1233, 1170, 1058.

Anal. Calcd for $C_{27}H_{27}N_3O_6$ (489.19): C, 66.25; H, 5.56; N, 8.58.

Found: C, 66.30; H, 5.54; N, 8.60.

TOF MS *m/z* 512.05 [M + Na]+; *M*calcd: 489.19.

(e) Boc-Maba(1)-*Maba*(2)-*Maba*(3)-*OH (7):* To 1.5 g (3.06 mmol) of compound **7**, 25 mL MeOH and 2M 15 mL NaOH were added and the progress of saponification was monitored by thin layer chromatography (TLC). The reaction mixture was stirred. After 10 h, methanol was removed under vacuum; the residue was dissolve in 50 mL of water, and washed with diethyl ether (2 × 50 mL). Then the pH of the aqueous layer was adjusted to 2 using 1M HCl and it was extracted with ethyl acetate (3 × 50 mL).

The extracts were pooled, dried over anhydrous sodium sulfate, and evaporated under vacuum to obtained compound as a white solid.

Yeild: 1.17 g (2.47 mM, 81%).

Melting point: 270^{o}-272°C.

^{1}H NMR ($CDCl_3$, 400 MHz, δ in ppm): 12.95 [1H, b, COOH], 10.46-10.45 [2H, d, aromatic protons], 9.58 [1H, s, NH Maba(1)], 8.43 [1H, s, NH Maba(2)], 8.32 [1H, s, NH Maba(3)], 8.07-7.99 [3H, m, aromatic protons], 7.71-7.41 [7H, m, aromatic protons], 1.49 [9H, s, Boc protons]; ^{13}C NMR (DMSO-d_6, 125 MHz, δ in ppm): 167.20, 165.93, 175.73, 152.81, 139.77, 139.42, 139.38, 135.51, 135.32, 131.23, 128.88, 128.67, 128.65, 124.45, 124.39, 123.44, 122.66, 121.28, 121.08, 119.94, 117.65, 79.30, 28.11. FTIR (in cm^{-1}, KBr): 3316, 2979, 2926, 2359, 2343, 1698, 1645, 1590, 1543, 1487, 1406, 1304, 1245, 1169, 1066.

Anal. Calcd for $C_{26}H_{25}N_3O_6$ (475.17): C, 65.67; H, 5.30; N, 8.84.

Found: C, 65.63; H, 5.35; N, 8.86.

(f) Boc-Maba(1)-*Maba*(2)-*DCU (1):* 0.46 g (1.29 mmol) compound Boc-Maba-Maba-OH was dissolved in 15 mL dry DCM on an ice-water bath. 0.226 g (1.29 mmol) DCC was added to the solution. 0.18 mL (1.29 mmol) of triethyl amine was added to 0.29 g (1.29 mmol) dicyclohexylureain 15 mL dry DCM. This solution was added to the previous solution. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DCM was evaporeted under vacuum and ethyl acetate was added to the solid mass. Dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the desired compound as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane (1:3) as eluent.

Yield: 0.6 g (1.06 mmol, 82%).

Melting point: 196^{o}-197^{o}C.

^{1}H NMR ($CDCl_3$, 500 MHz, δ in ppm): 8.33 [1H, s, NH Maba(1)], 7.98 [1H, s, aromatic proton], 7.94-7.93 [1H, d, aromatic proton], 7.74 [1H, s, aromatic proton], 7.47-7.38 [3H, d, aromatic protons], 7.31-7.30 [1H, d, aromatic proton], 6.65 (1H, s, NH Maba(2)], 6.20 (1H, b, NH DCU), 4.12-4.3 [1H, m,CαH cyh], 3.49 [1H, m, CαH cyh], 2.01-1.99 [2H, m, cyh] , 1.85-1.77 [5H, m, cyh], 1.53 [9H, s, Boc protons], 1.33-1.16 [8H, m, cyh], 0.91-0.87 [4H, m, cyh]; ^{13}C NMR ($CDCl_3$, 125 MHz, δ in ppm): 169.87, 165.84, 154.25, 152.87, 138.75, 138.56, 137.34, 135.47, 129.29, 129.00, 122.39, 122.31, 122.01, 121.88, 118.80, 117.18, 56.29, 49.90, 32.02, 31.87, 30.66, 29.64, 29.60, 29.30, 28.26, 26.05, 25.36, 25.22, 24.71, 24.59, 22.64, 14.06; FTIR (in cm^{-1}, KBr): 3297, 2932, 2855, 2358, 2341, 1644, 1614, 1539, 1338, 1312, 1245, 1161, 1081, 1056.

Anal. Calcd for $C_{32}H_{42}N_4O_5$ (562.32): C, 68.30; H, 7.52; N, 9.96.

Found: C, 68.32; H, 7.54; N, 9.95.

TOF MS *m/z* 585.12 [M + Na]+; *M*calcd: 562.32.

(g) Boc-Maba(1)-*Maba*(2)-*Maba*(3)-*DCU* ***(2)****:* 0.39g (0.82mmol) compound Boc-Maba-Maba-Maba-OH was dissolved in 15 mL dry DCM on an ice-water bath. 0.169g (0.82mmol) DCC was added to the solution. 0.11 mL (0.82mmol) of triethyl amine was added to 0.18 g (0.82mmol) dicyclohexylurea in 15 mL dry DCM. This solution was added to the previous solution. The reaction mixture was allowed to come to room temperature and stirred for 48 h. DCM was evaporeted under vacuum and ethyl acetate was added to the solid mass. Dicyclohexylurea (DCU) was filtered off. The organic layer was washed with 2 M HCL (3 × 50 mL), brine (2 × 50 mL), then 1 M sodium carbonate (3 × 30 mL) and brine (2 × 30 mL) and dried over anhydrous sodium sulfate and evaporated under vacuum to yield the desired compound as a white solid. Purification was done by silica gel column (100-200 mesh size) and ethyl acetate and hexane (1:3) as eluent.

Yield: 0.47 g (0.7 mmol, 85%).

Melting point: 225^{o}-227^{o}C.

^{1}H NMR ($CDCl_3$, 500 MHz, δ in ppm): 9.02 [1H, s, NH Maba(1)], 8.77 (1H, s, NH Maba(2)], 8.04 [1H, s, aromatic proton], 7.97-7.96 [1H, d, aromatic proton], 7.91 [1H, s, aromatic proton], 7.74-7.73 [2H, d, aromatic protons], 7.62-7.60 [1H, d, aromatic proton], 7.50-7.47 [2H, d, aromatic protons], 7.36-7.22 [3H, m, aromatic protons], 7.18-7.16 [1H, m, aromatic proton], 6.98 [1H, s, NH Maba(3)], 6.53 (1H, b, NH DCU), 4.13-4.07 [1H, m, CαH cyh], 3.43-3.41 [1H, s, CαH cyh], 1.82-1.73[8H, m, cyh], 1.53 [9H, s, Boc prptons], 1.21-1.09 [8H, m, cyh], 0.97 [1H, m, cyh], 0.87-0.83 [2H, m, cyh]; ^{13}C NMR ($CDCl_3$, 125 MHz, δ in ppm): 169.48, 166.41, 165.99, 154.06, 153.05, 138.78, 138.66, 137.96, 136.85, 135.13, 134.85, 129.10, 128.95, 128.67, 128.17, 124.53, 123.91, 122.61, 122.16, 122.09, 121.84, 119.95, 119.42, 117.66, 80.80, 55.79, 50.07, 33.14, 31.89, 30.56, 29.64, 28.26, 25.96, 25.18, 24.69, 13.92; FTIR (in cm^{-1}, KBr): 3297, 2931, 2855, 2359, 1686, 1655, 1590, 1545, 1486, 1434, 1367, 1309, 1237, 1160, 1080.

Anal. Calcd for $C_{39}H_{47}N_5O_6$ (681.35): C, 68.70; H, 6.95; N, 10.27.

Found: C, 68.75; H, 6.93; N, 10.28.

TOF MS *m/z* 704.08 [M + Na]+; *M*calcd: 681.35.

Abbreviation we used:

Cyh= cyclohexane.

Figure S8: ^{1}H NMR (400 MHz, DMSO-d_6) spectra of Boc-Maba(1)-OH.

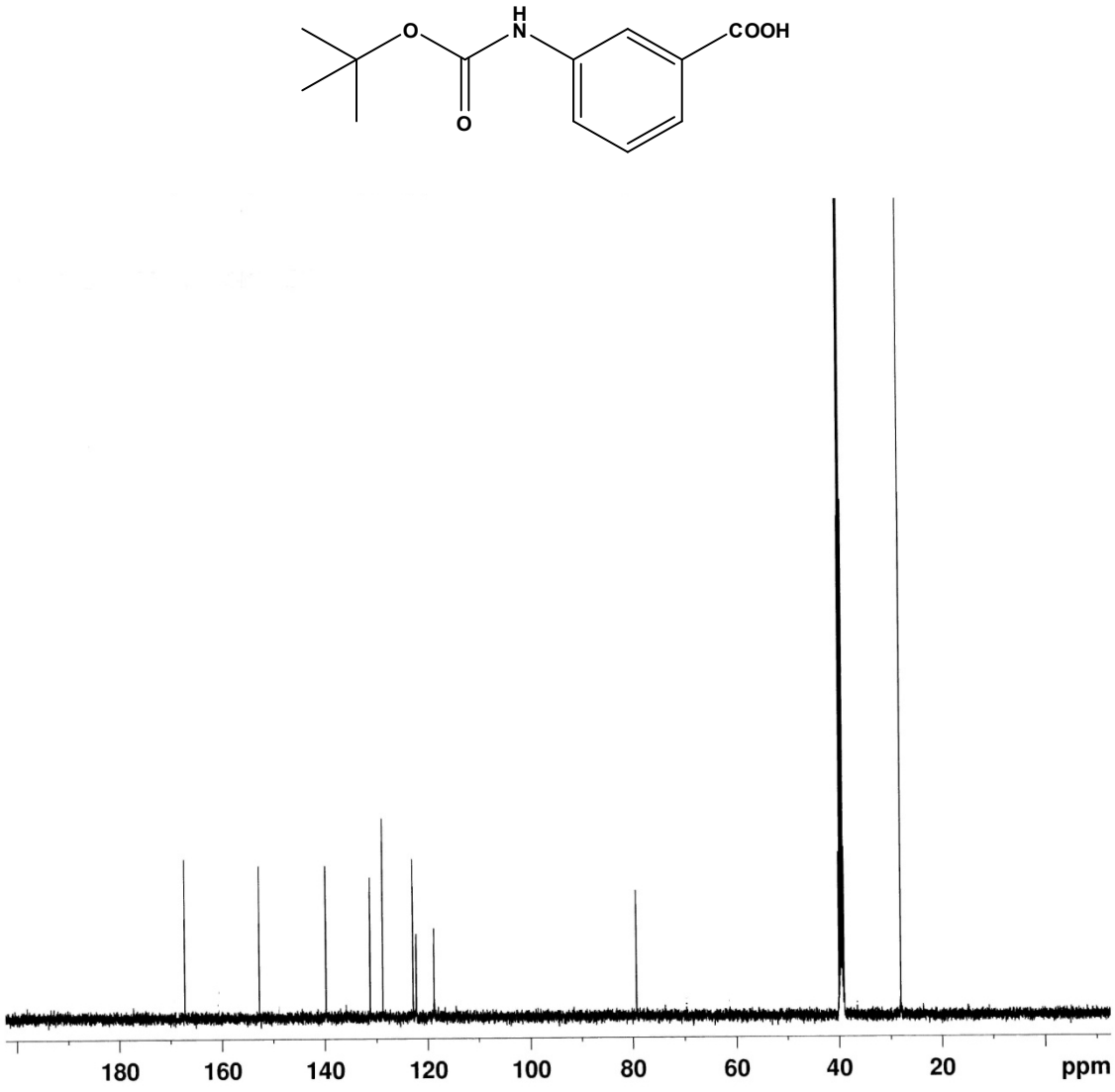


Figure S9: ^{13}C NMR (125 MHz, DMSO-d_6) spectra of Boc-Maba(1)-OH.

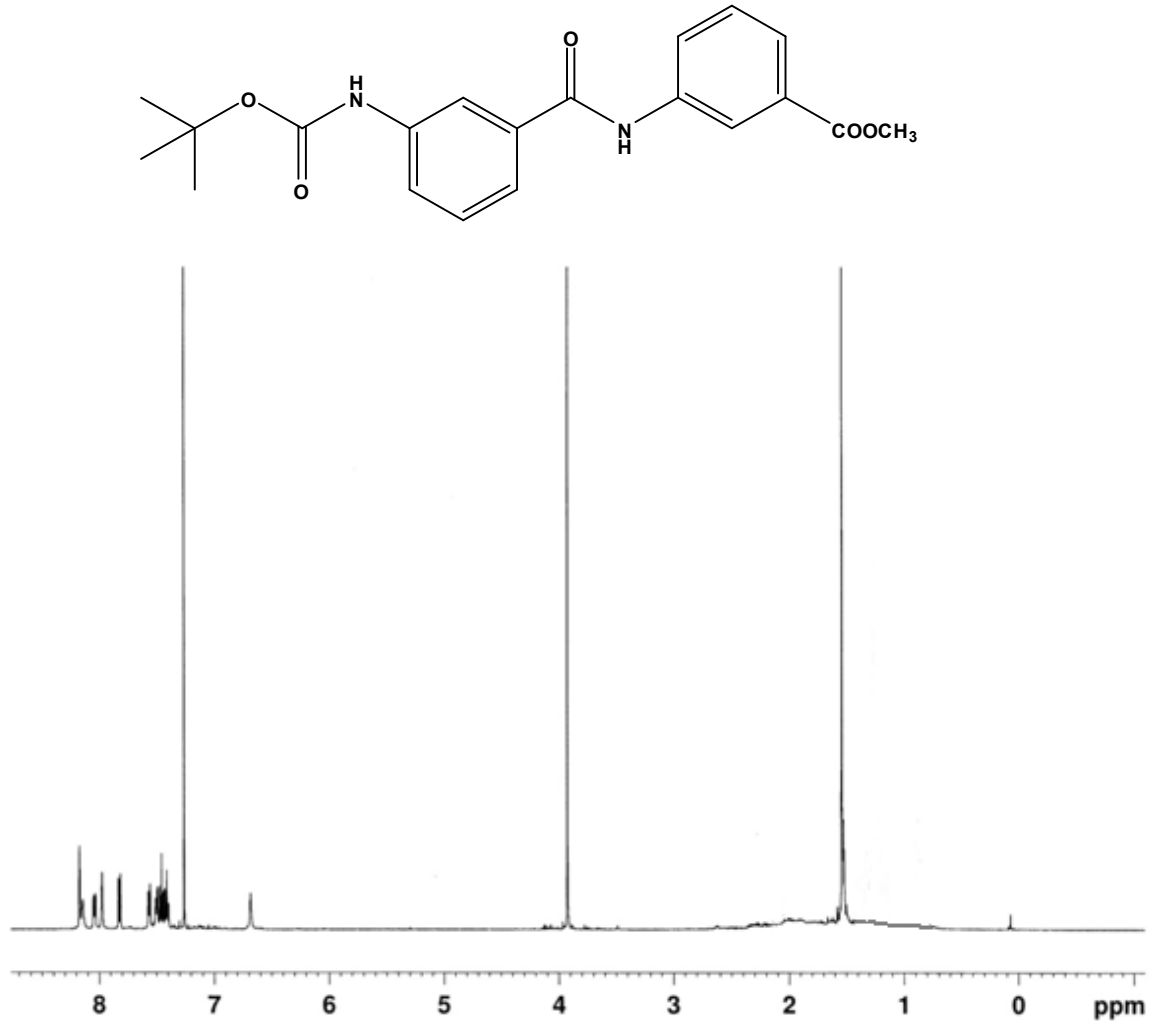


Figure S10: ^{1}H NMR (500 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-$COOCH_3$.

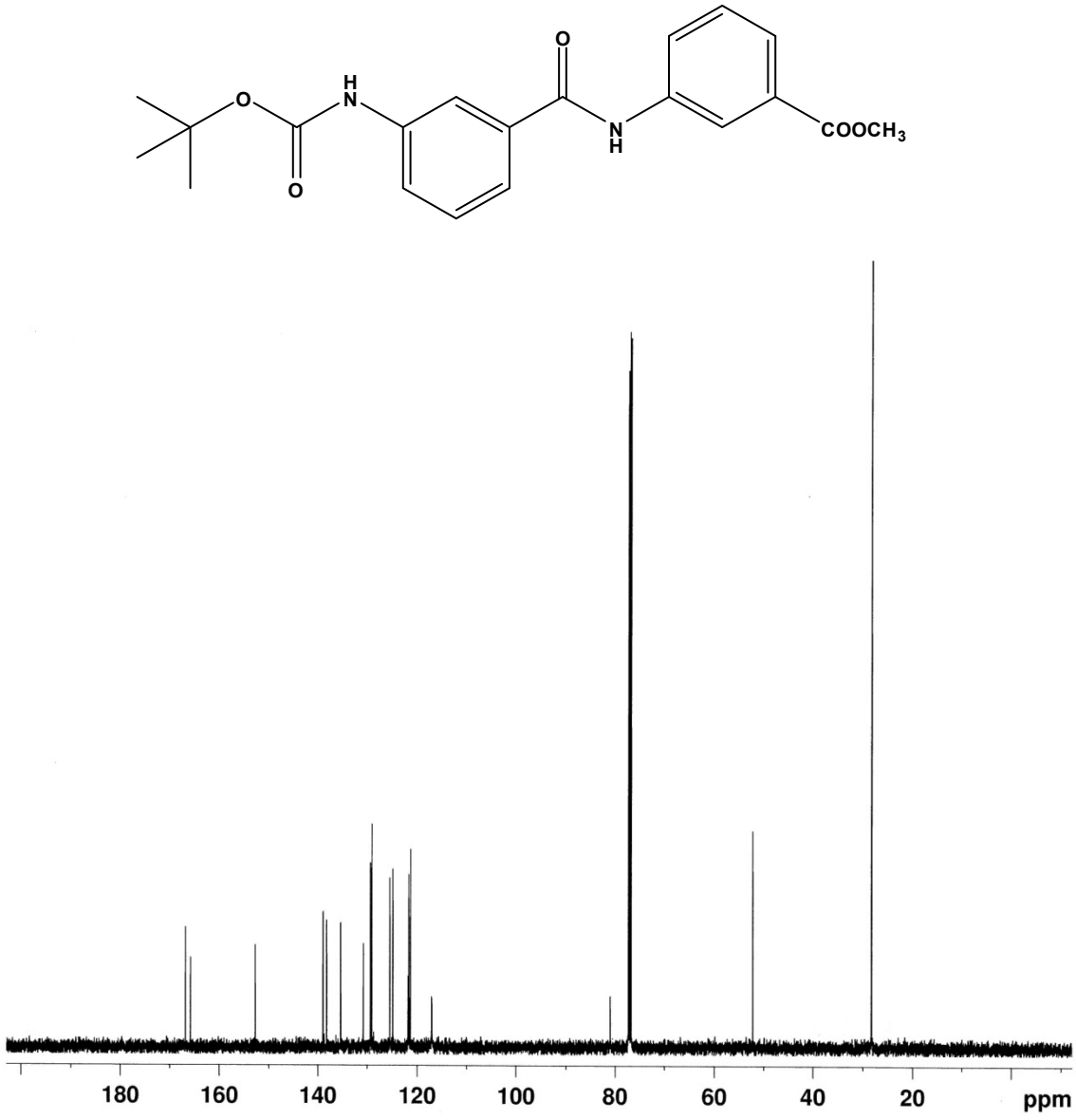


Figure S11: ^{13}C NMR (125 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-$COOCH_3$.

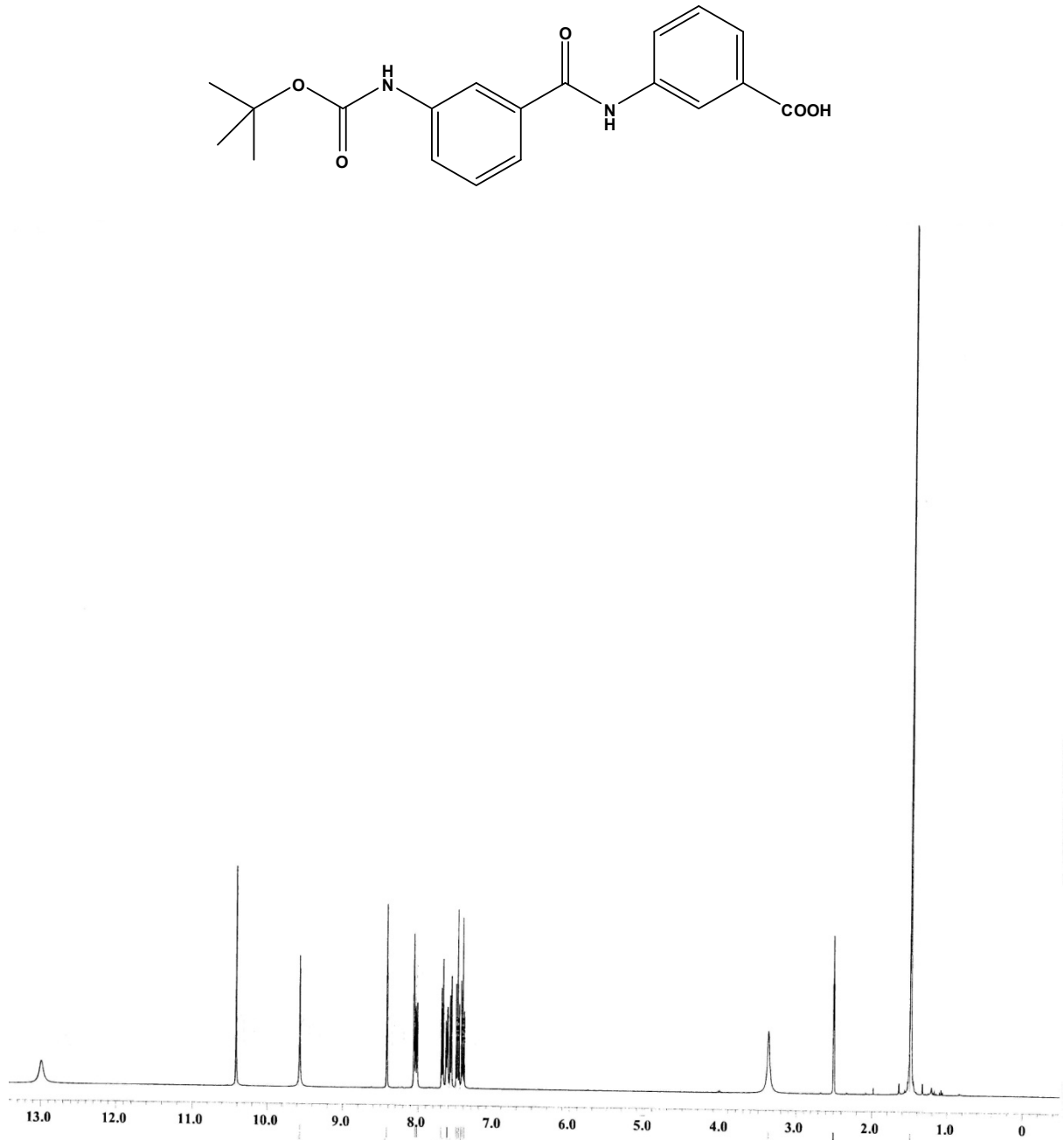


Figure S12: ^{1}H NMR (400 MHz, DMSO-d_6) spectra of Boc-Maba(1)-Maba(2)-COOH.

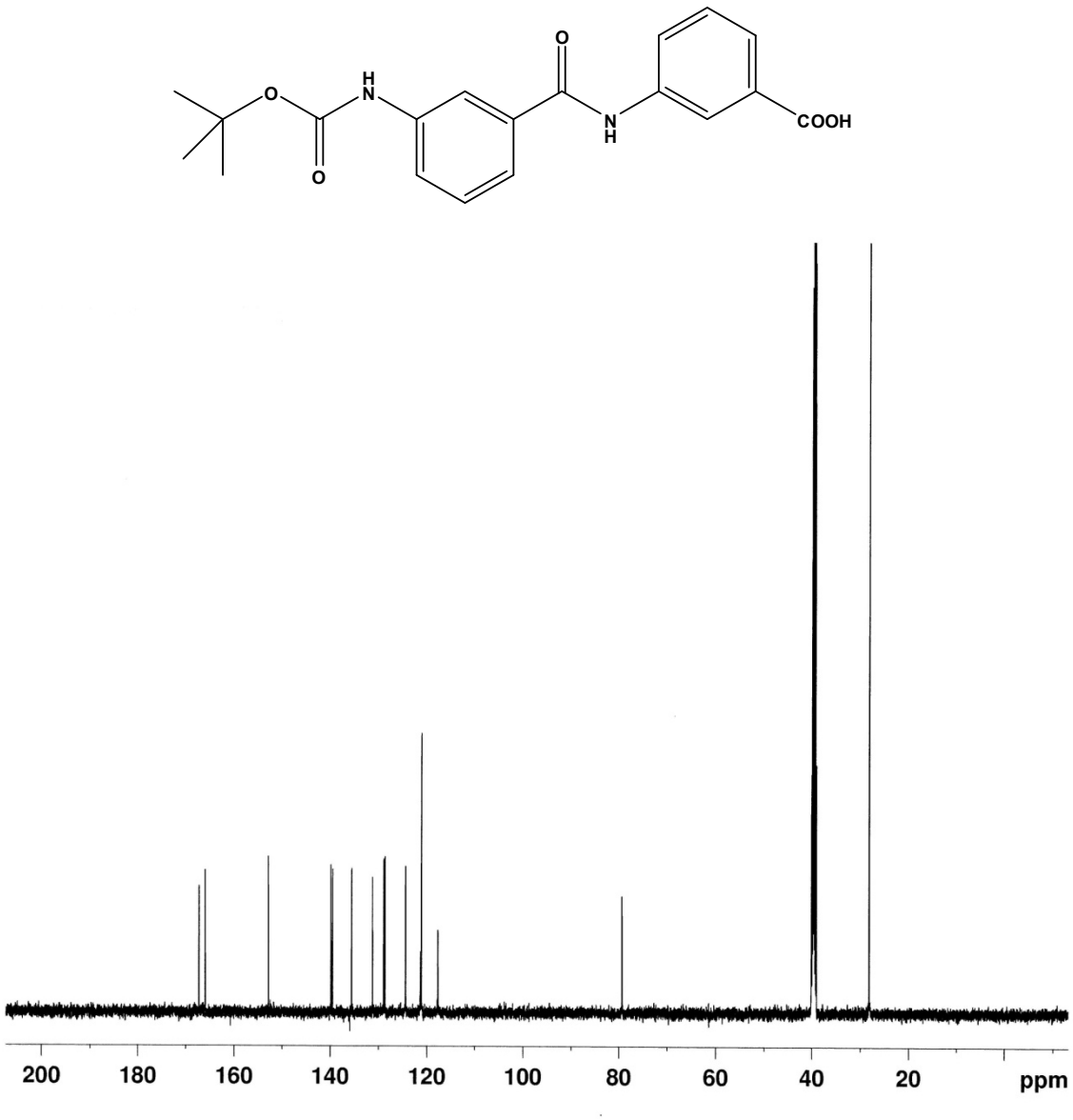


Figure S13: ^{13}C NMR (125 MHz, DMSO-d_6) spectra of Boc-Maba(1)-Maba(2)-COOH.

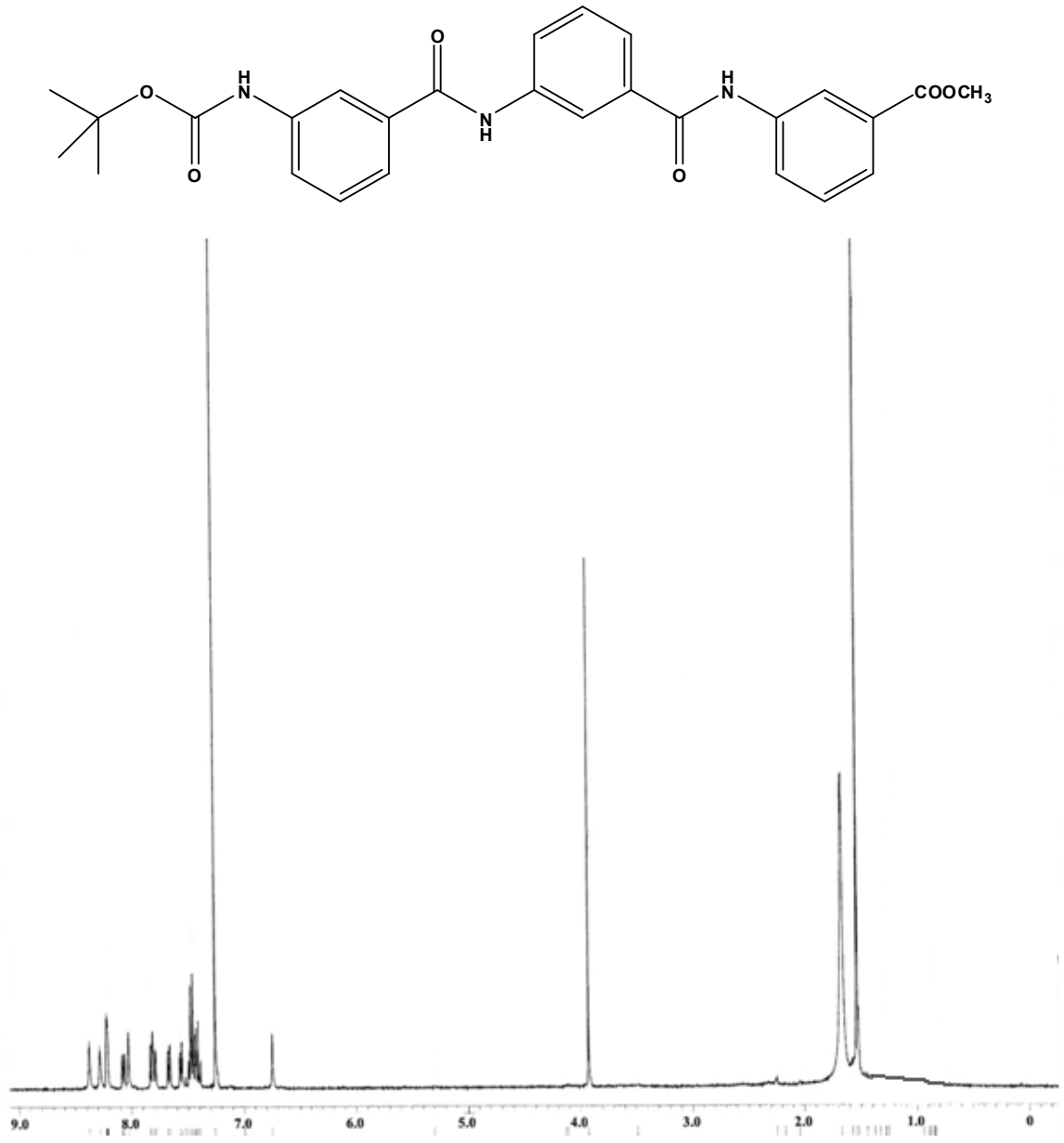


Figure S14: ^{1}H NMR (400 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-Maba(3)-OCH_3.

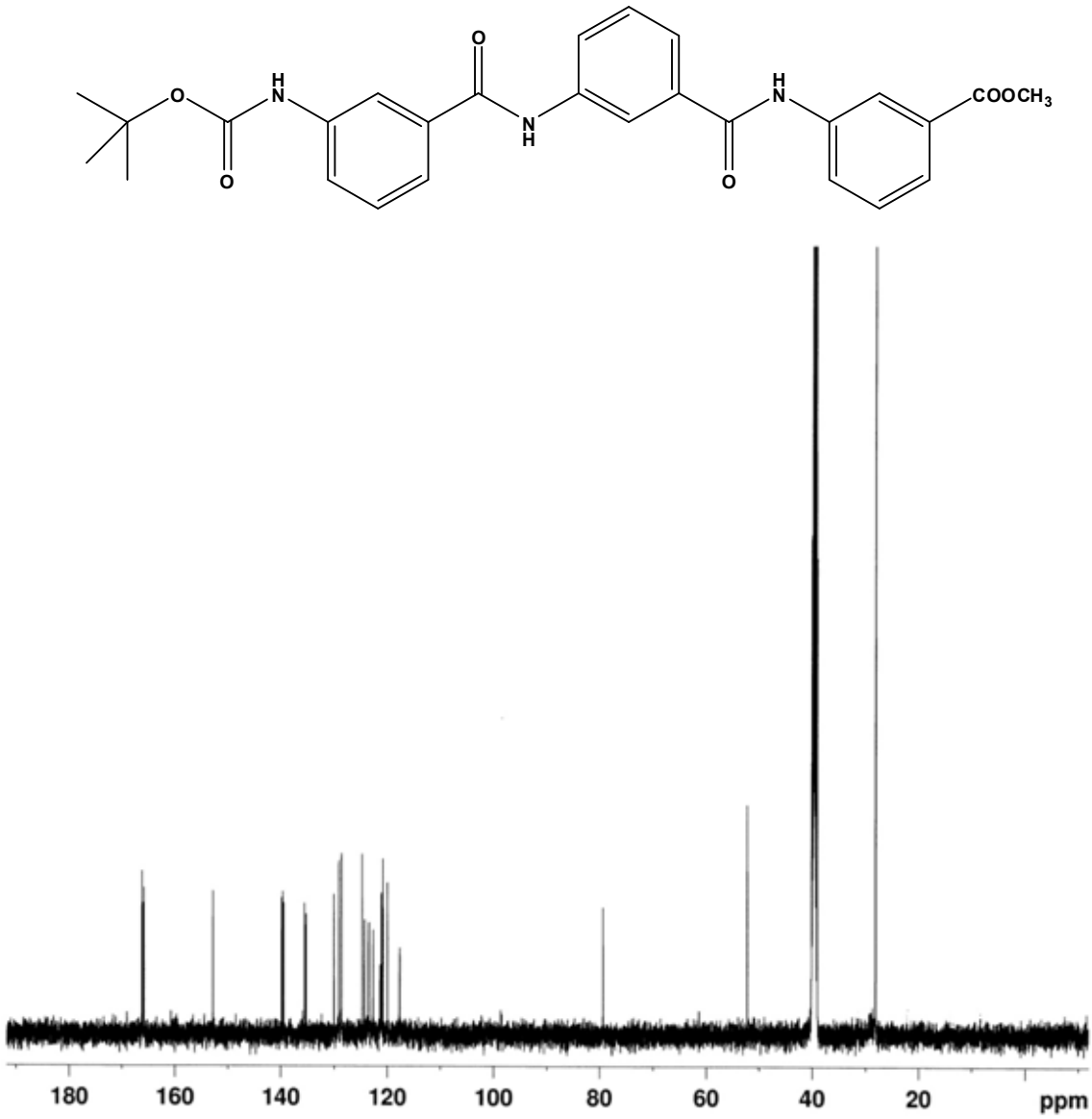
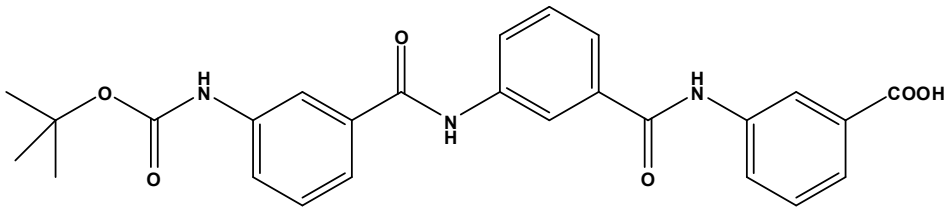


Figure S15: ^{13}C NMR (125 MHz, DMSO-d_6) spectra of Boc-Maba(1)-Maba(2)-Maba(3)-OCH_3.



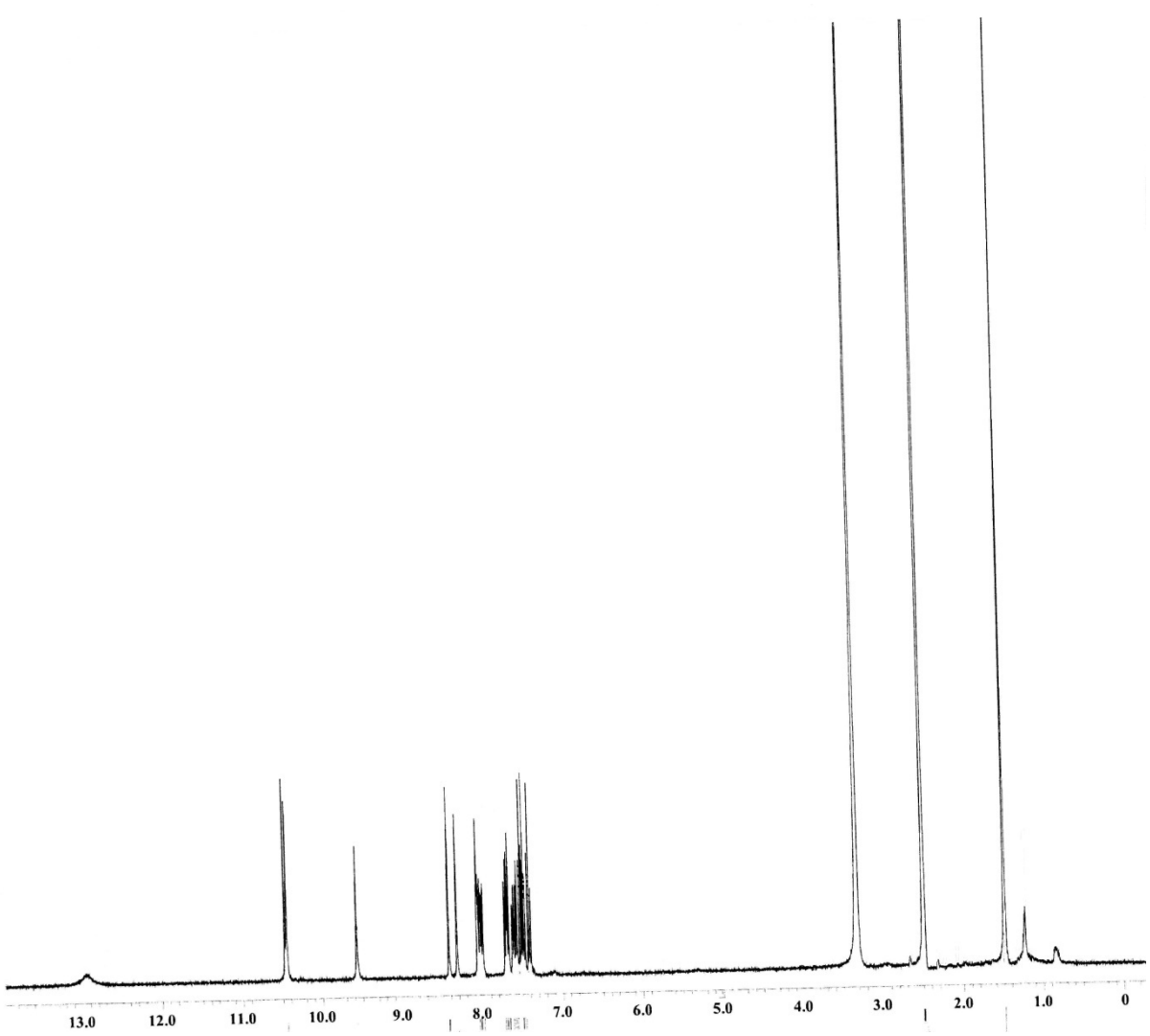


Figure S16: ^{1}H NMR (400 MHz, DMSO-d_6) spectra of Boc-Maba(1)-Maba(2)-Maba(3)-OH.

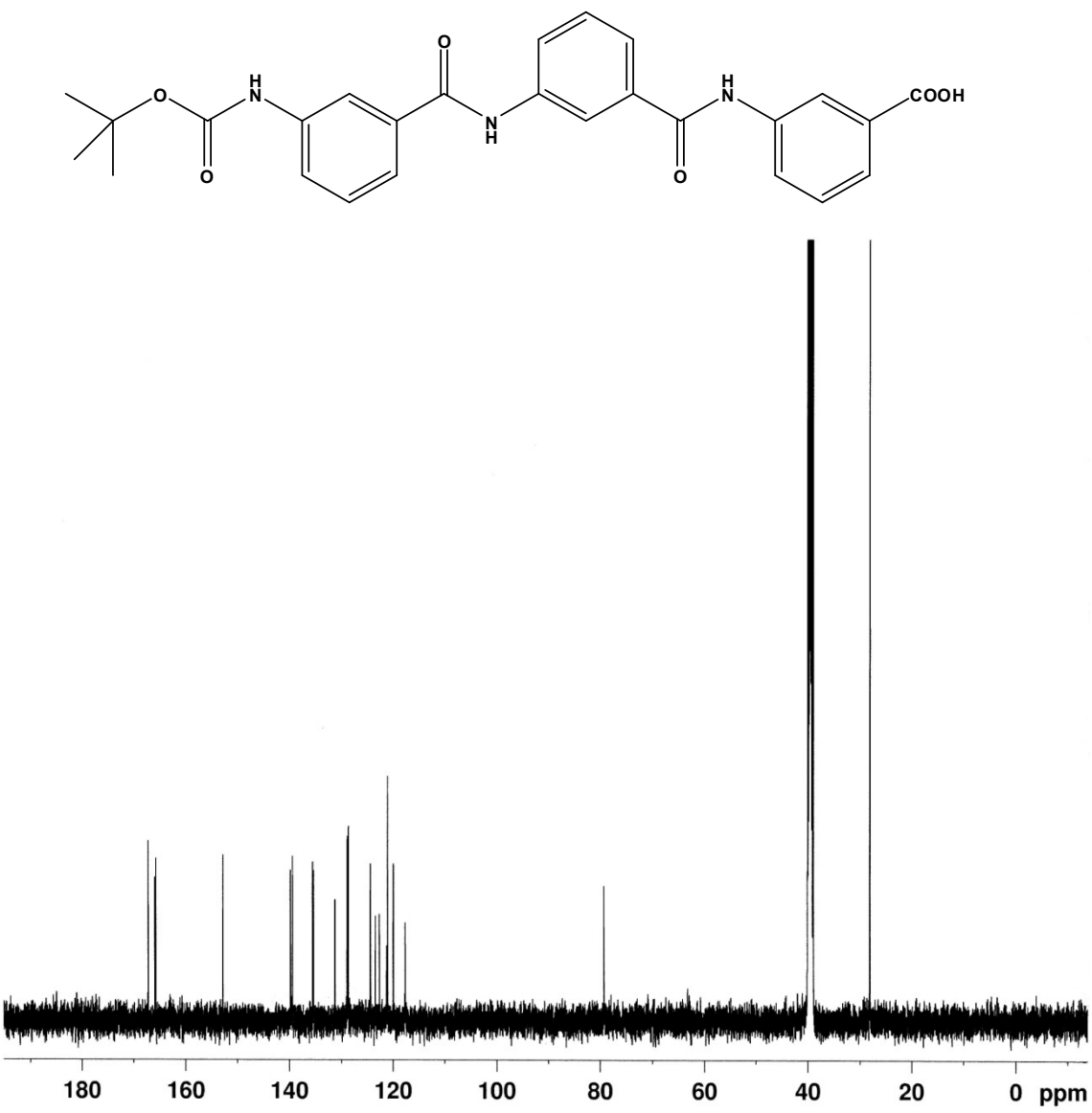


Figure S17: ^{13}C NMR (125 MHz, DMSO-d_6) spectra of Boc-Maba(1)-Maba(2)-Maba(3)-OH.

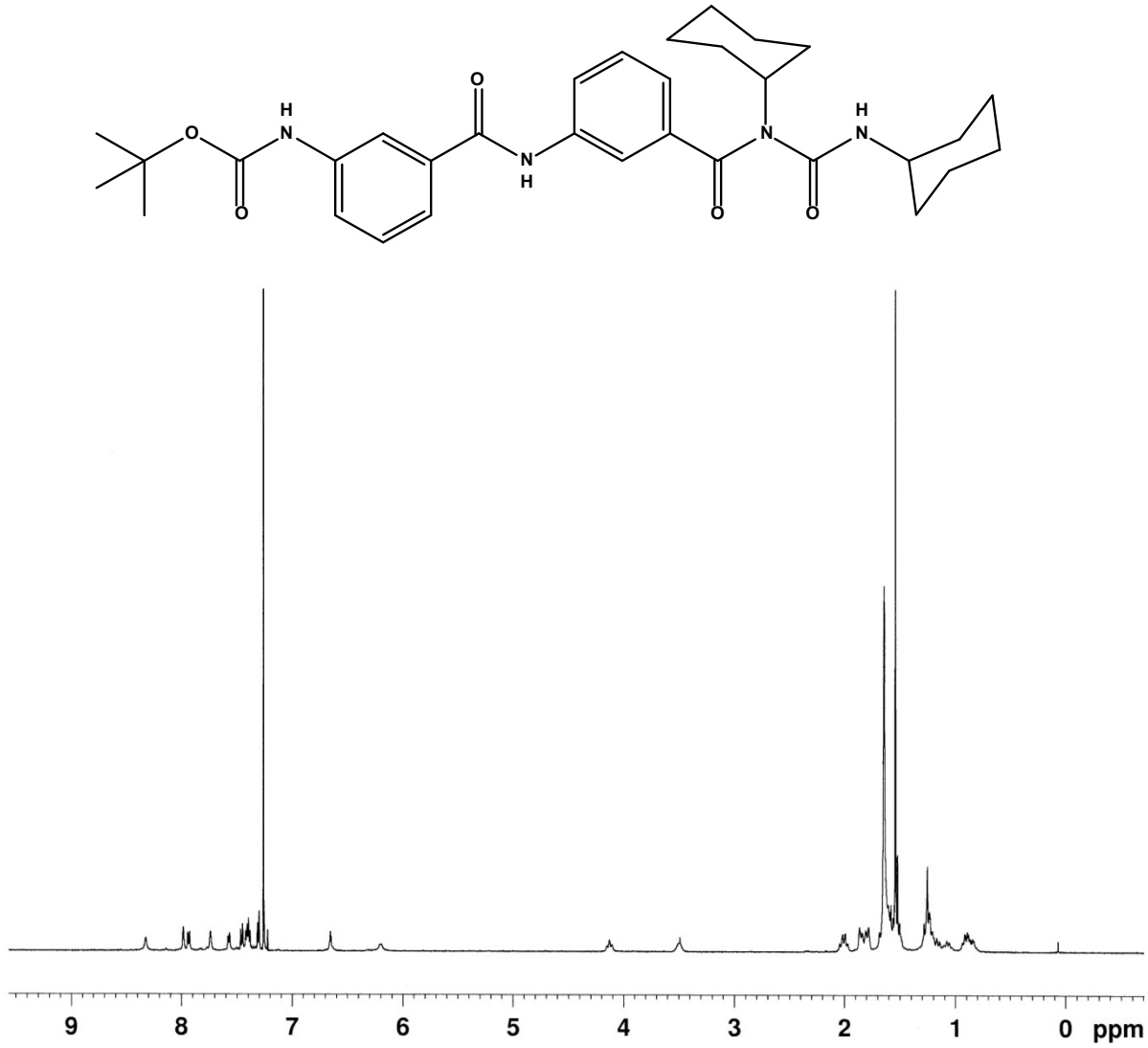


Figure S18: ^{1}H NMR (500 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-DCU 1.

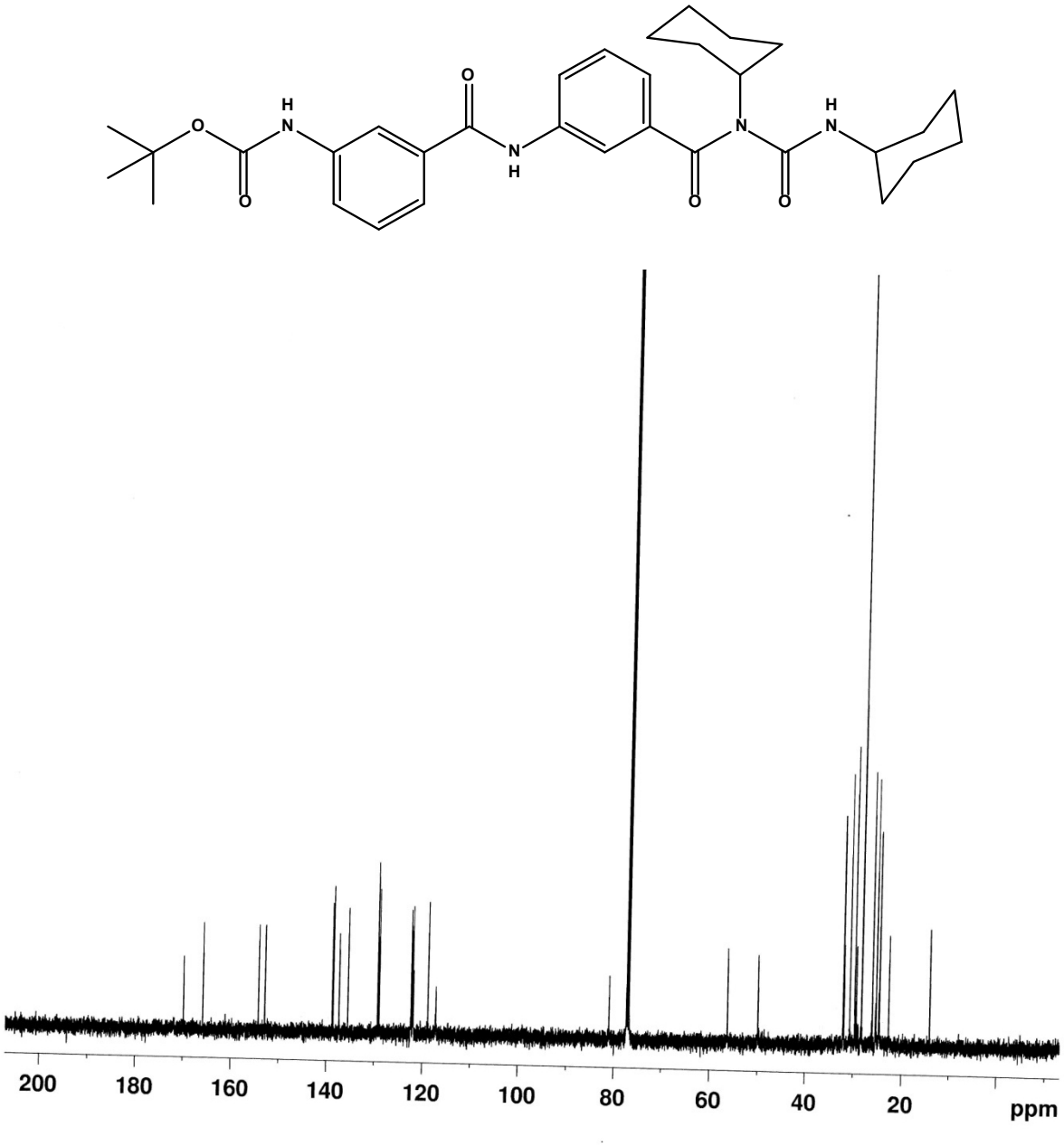


Figure S19: ^{13}C NMR (125 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-DCU 1.

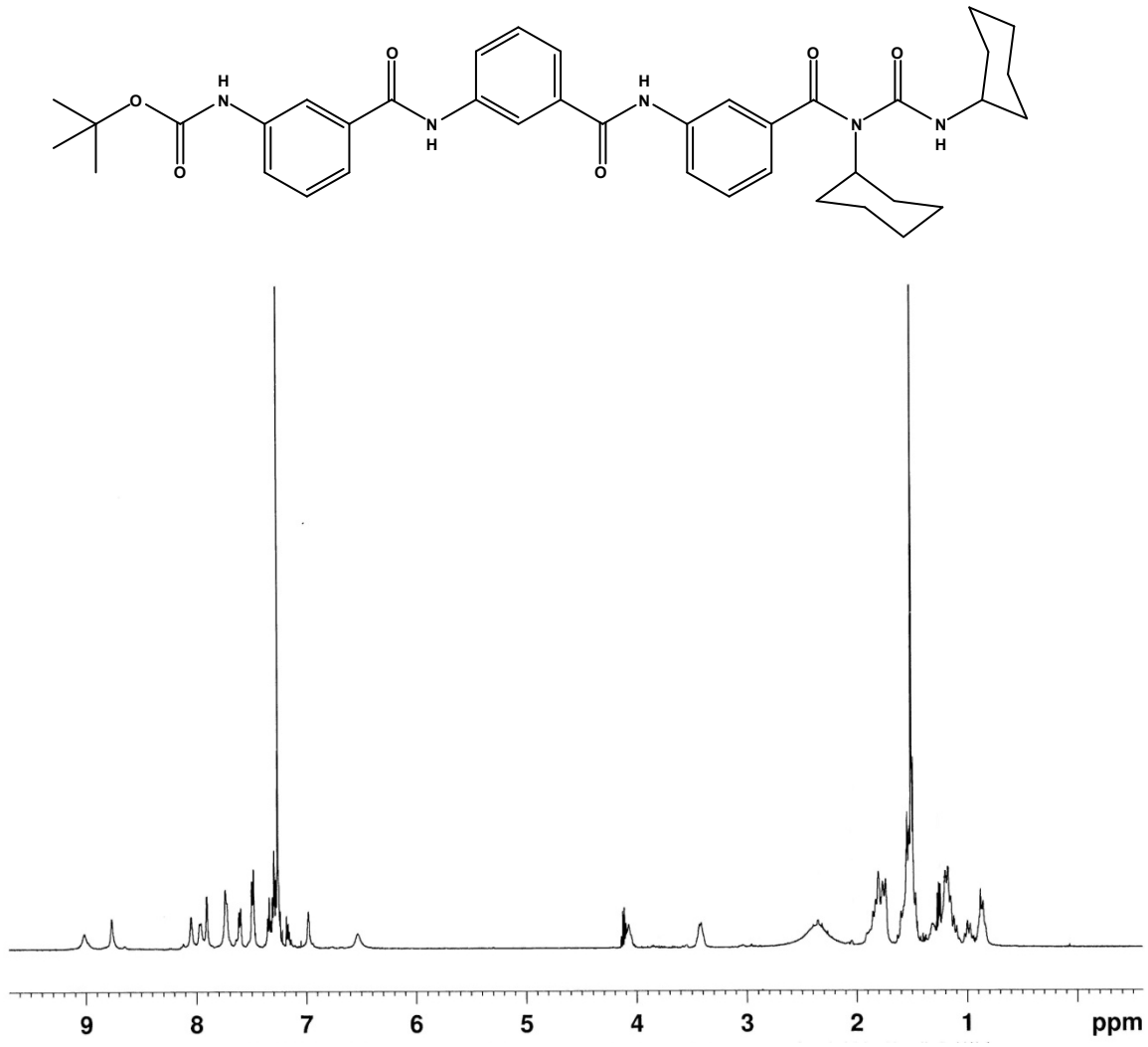


Figure S20: ^{1}H NMR (500 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-Maba-DCU.

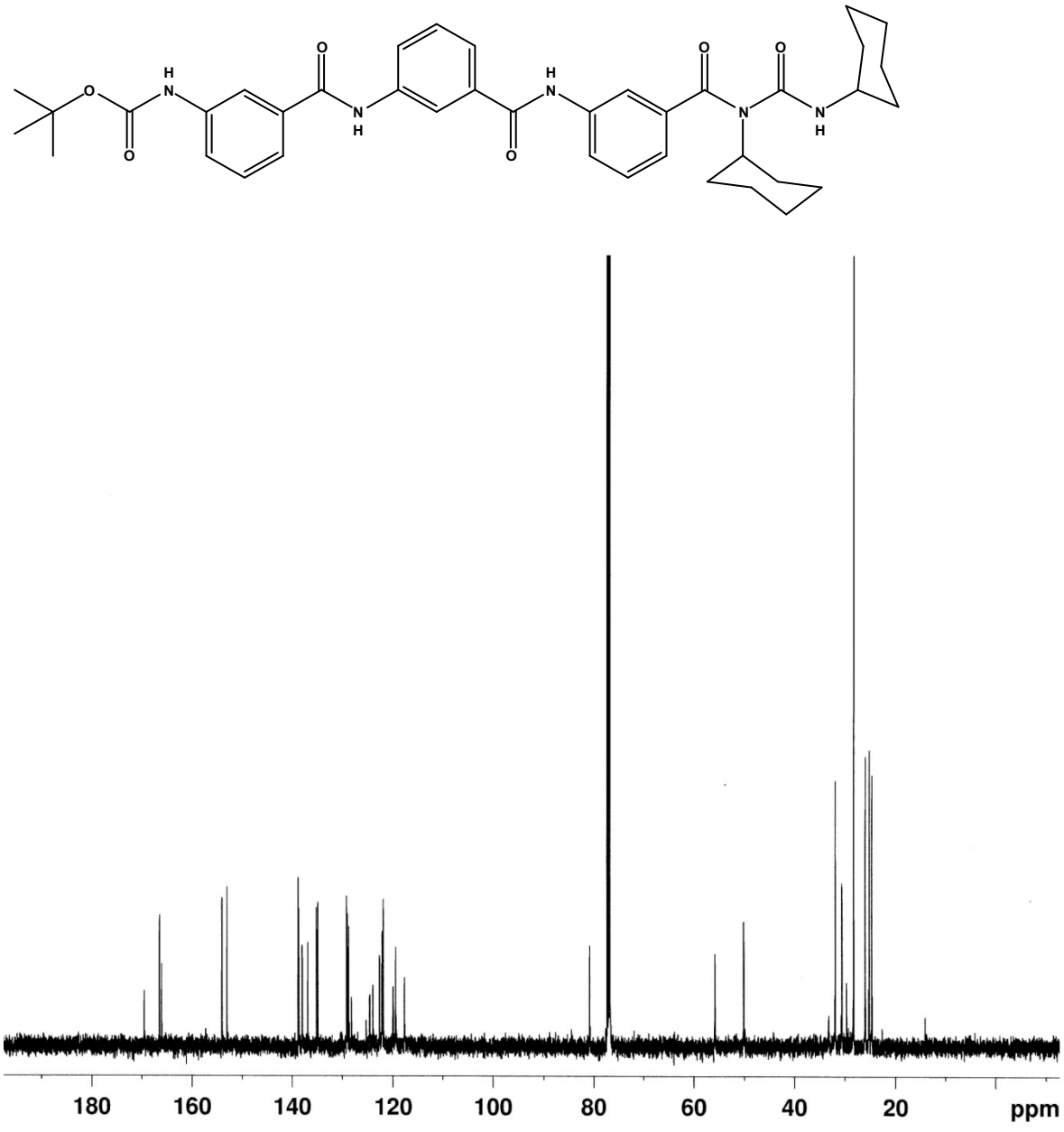


Figure S21: ^{13}C NMR (125 MHz, $CDCl_3$) spectra of Boc-Maba(1)-Maba(2)-Maba-DCU.

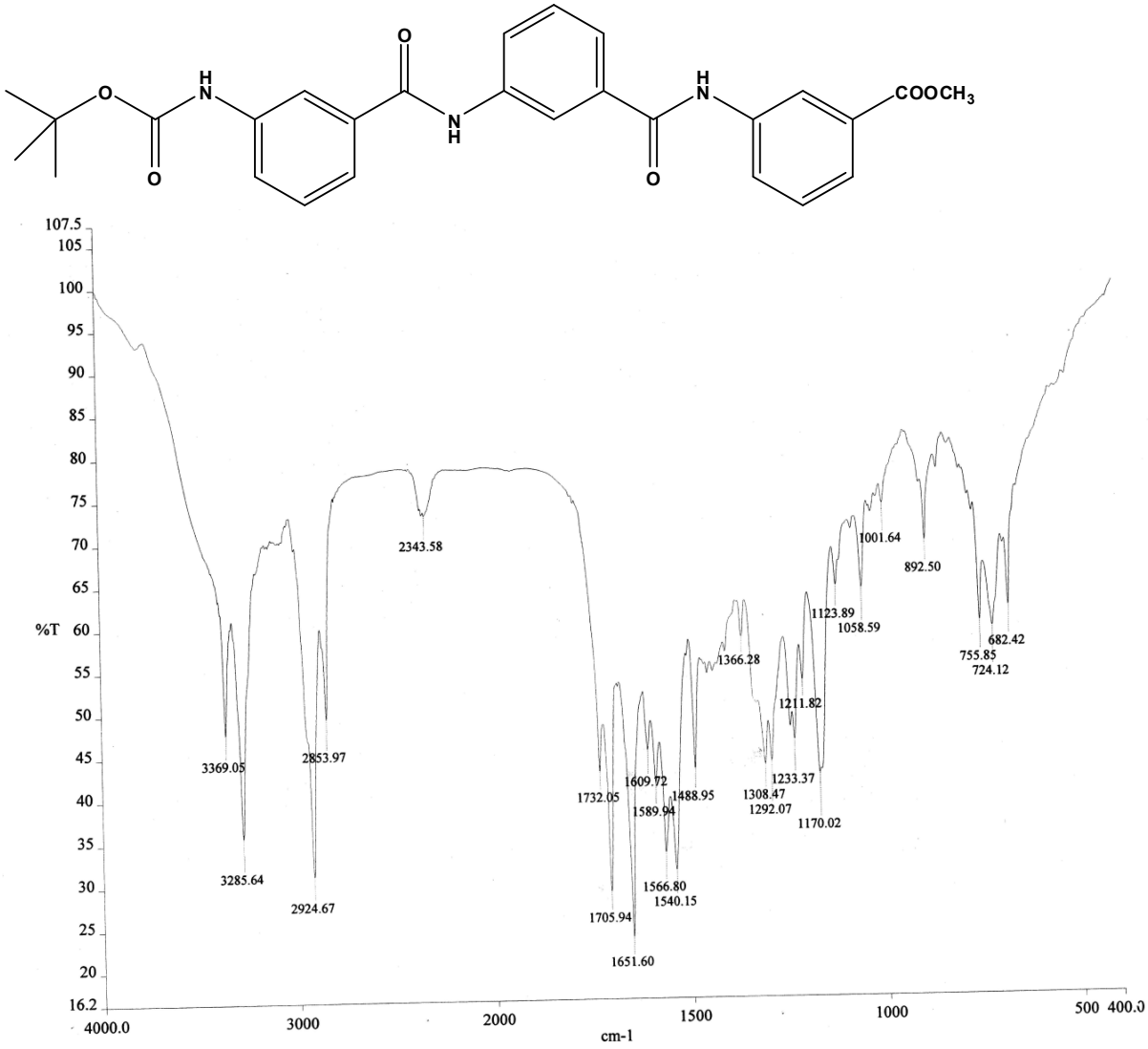


Figure S22: FTIR spectra of Boc-Maba(1)-Maba(2)-Maba(3)-COOMe in solid state

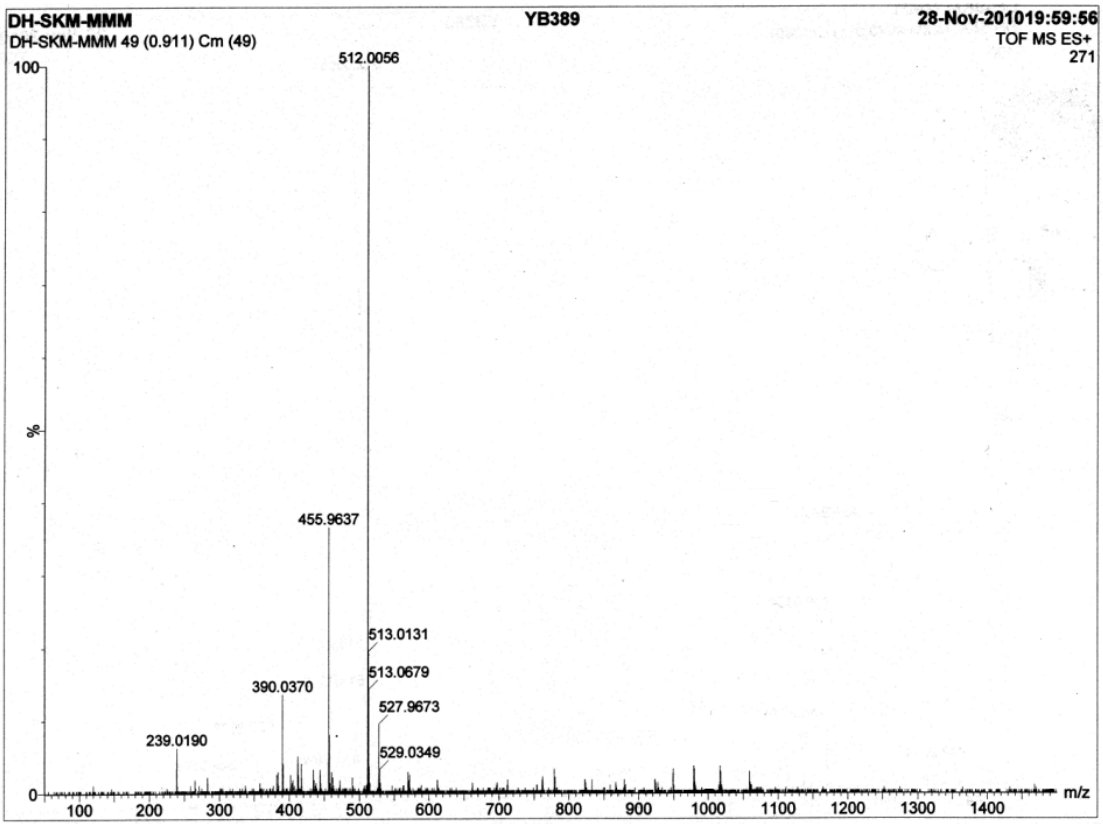


Figure S23: Mass spectra of Boc-Maba(1)-Maba(2)-Maba(3)-COOMe.

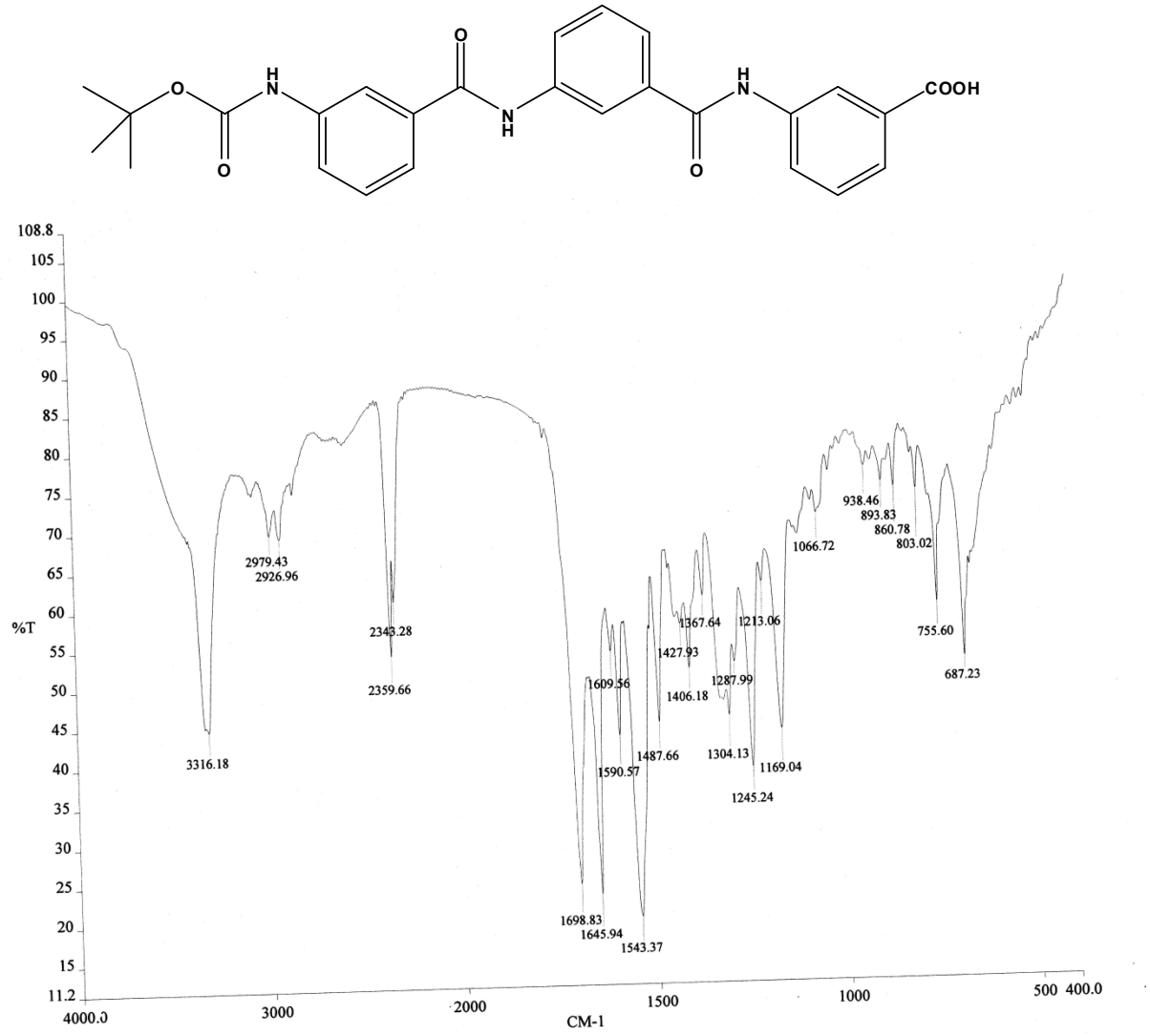


Figure S24: FTIR spectra of Boc-Maba(1)-Maba(2)-Maba(3)-COOH in solid state.

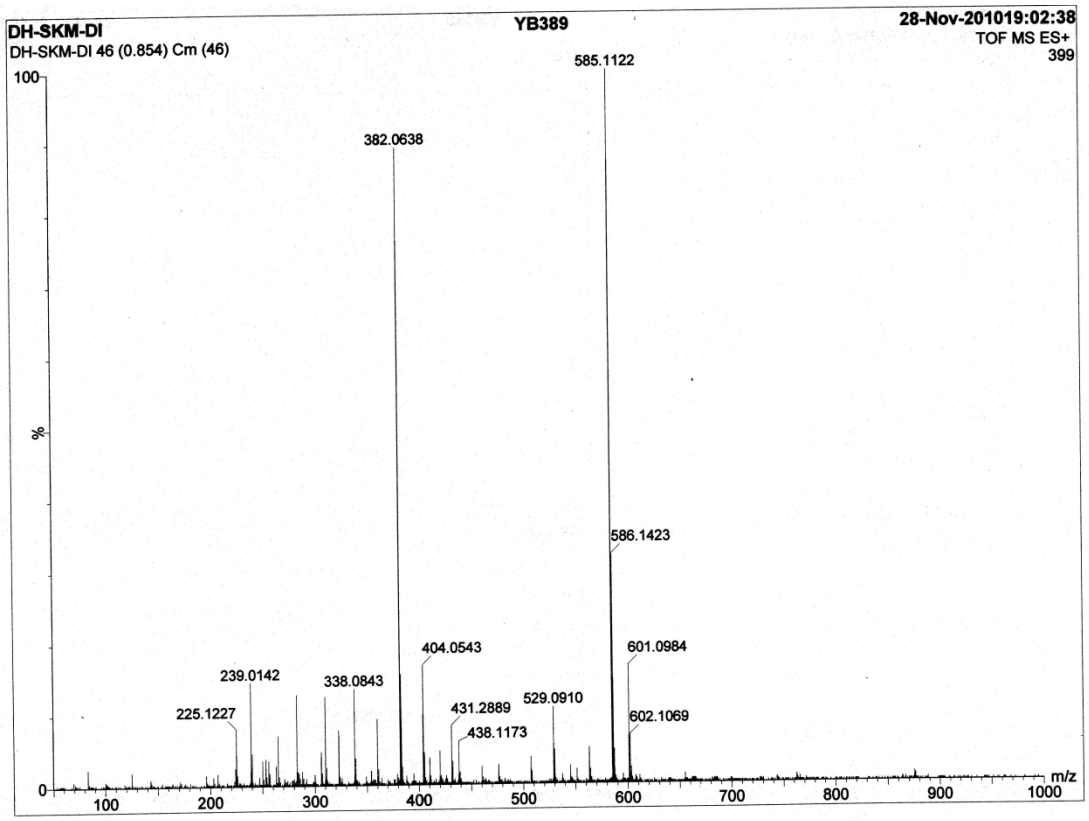


Figure S25: Mass spectra of Boc-Maba(1)-Maba(2)-DCU **1**.

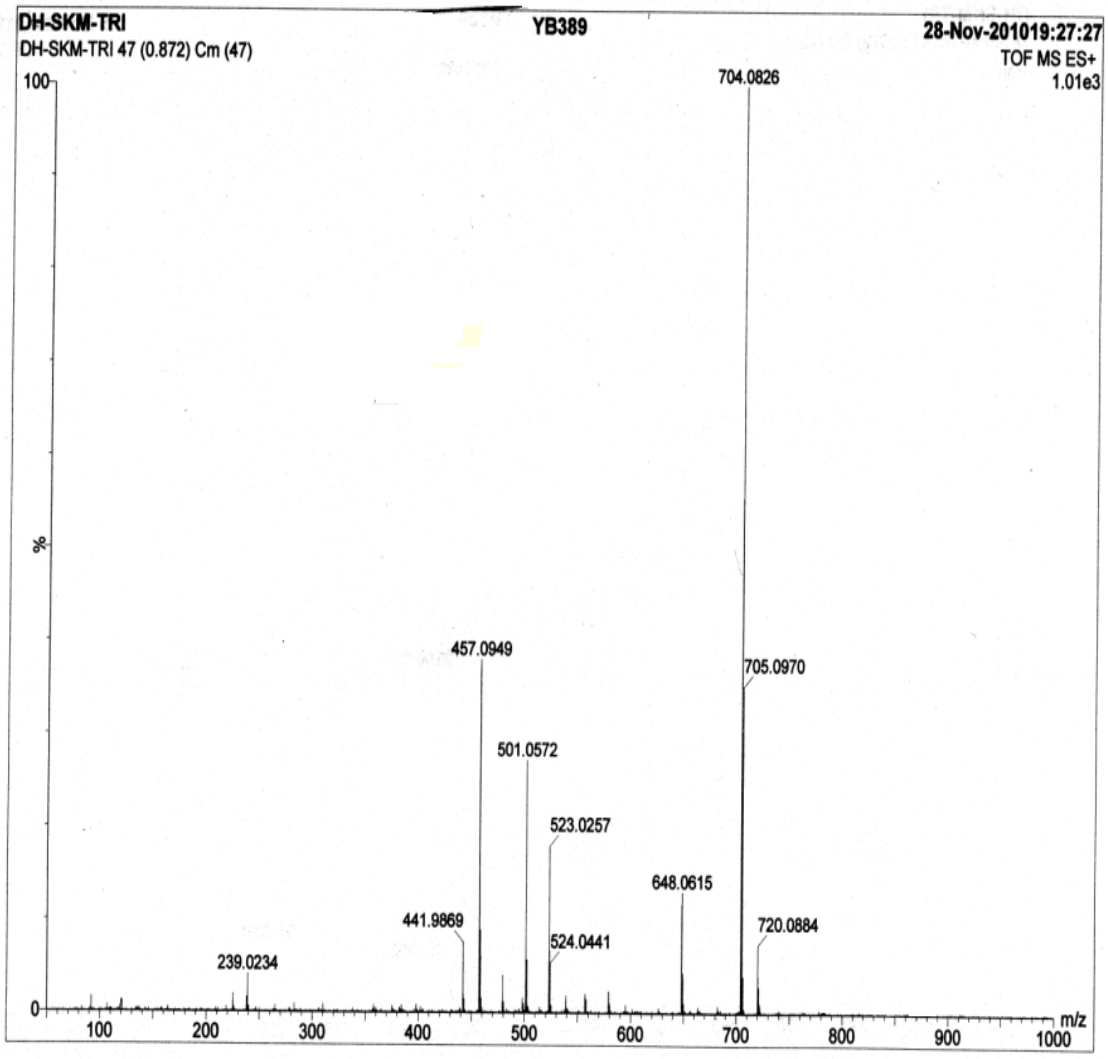


Figure S26: Mass spectra of Boc-Maba(1)-Maba(2)-Maba(3)-Maba(3)-DCU **2**.