Electronic Supplementary Information

Chiral and Non chiral Assemblies from Lipdated Serine-Based Pseudopeptidic molecules

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Experimental section

Synthesis and characterization

All reagents were used without further purification. All solvents for the reactions were dried prior to use. Amino acid L-serine was purchased from SRL India. Progress of reactions was monitored by thin layer chromatography (TLC). Purification of compounds was done by silica (100-200) gel column chromatography. Fisher-Scientific melting point apparatus was used for recording melting points. Optical rotations were recorded with a Rudolph Research Analytical Autopol® V Polarimeter; concentration is given in gram/10 mL. IR spectra were recorded on a Nicolet, Protégé 460 spectrometer as KBr pellets. ^{1}H NMR spectra were recorded on Brucker-DPX-300 spectrometer using tetramethylsilane (^{1}H) as an internal standard. Coupling constants are reported in Hz and the ^{1}H NMR data are reported as s (singlet), d (doublet), br (broad), t (triplet) and m (multiplet), dd (double doublet). High Resolution mass spectra (HRMS) were recorded in Bruker MicrO-TOF-QII model using ESI technique. Circular Dichroism (CD) spectra were recorded on JASCO Model J-815 spectropolarimeter equipped with a temperature controller. CD spectra were recorded using 1mm length cell. MD simulations were performed on 320 processors SUN Microsystems clusters at Supercomputing Facility (SCFBio) at IIT Delhi.

Microscopic studies

(a) Scanning Electron Microscopy (SEM)

A 10 µl aliquot of the sample solution was put on a fresh piece of glass, which is attached to a stub via carbon tape. The sample was dried at room temperature and coated with ~10nm of gold. Samples were analyzed using ZEISS EVO 50 SEM.

(b) Field Emission-Scanning Electron Microscopy (FE-SEM)

A 10 µl aliquot of the sample solution was put on a fresh piece of glass, which is attached to a stub via carbon tape. The sample was dried at room temperature and coated with ~10 nm of gold. Samples were analyzed using FEI Quanta 3D FEG High resolution scanning electron microscope (FE-SEM) combined with High-current ion column with Ga liquid-metal ion source.

(c) Atomic Force Microscopy (AFM)

Bruker Dimension Icon atomic force microscope was used for imaging. Tapping mode is used for the analysis. About 10 µl aliquot of the sample solution was transferred onto glass cover slip and allowed to dry and imaged using AFM.

(d) High Resolution-Transmission Electron Microscopy (HR-TEM)

Samples for HR-TEM were prepared by dissolving the compound methanol. A 2µl aliquot of the sample solution was placed on a 200 mesh copper grid and samples were viewed using a TECHNAI G2 (20S-TWIN) electron microscope.

(e) Optical microscopy

Samples for optical microscope were prepared by dissolving compound in methanol. A 5 µL aliquot of the sample solution was placed on a glass slide and allowed to dry in air at room temperature. The glass slide was then covered using a cover slip and analysed using a Nikon T*i* Eclipse inverted optical microscope.

(f) Digital Holographic Microscope

We used an image plane DHM system where a novel optimization based algorithm was used for phase recovery.[1-3] The integrated phase map provided by DHM system may be represented as:

$$\phi(x,y) = \frac{2\pi}{\lambda} \int dz \ [n(x,y,z) - 1],$$

where, λ is the wavelength of laser (670 nm in our system) used in DHM, n(x,y,z) stands for the local refractive index of the cell sample at the location (x,y,z) and the integral has been performed over the z or the cell depth dimension. The lateral magnification achieved in our system is 40X. The phase information is not available in a typical bright field microscope but is measurable with a DHM system.

(g) Powder X-Ray Diffraction

Powder X-ray diffractogram was recorded using Rigaku Ultima IV type II automatic high resolution modulator type X-ray diffractometer system with scintillation detector or on a Bruker D8 Advance diffractometer using radiation αNi-filtered CuK.

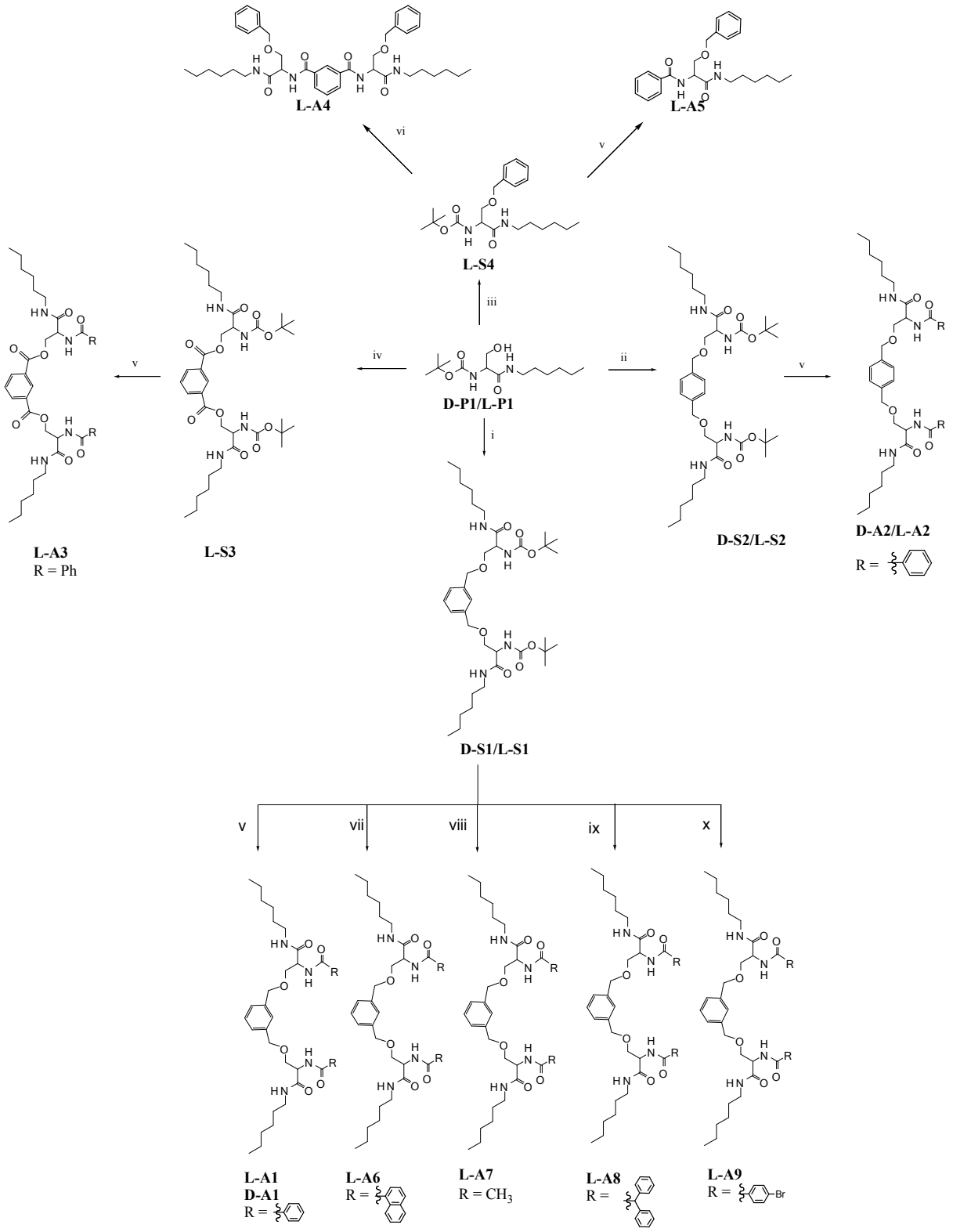
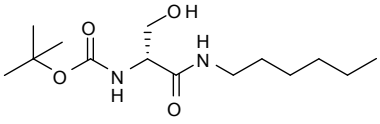
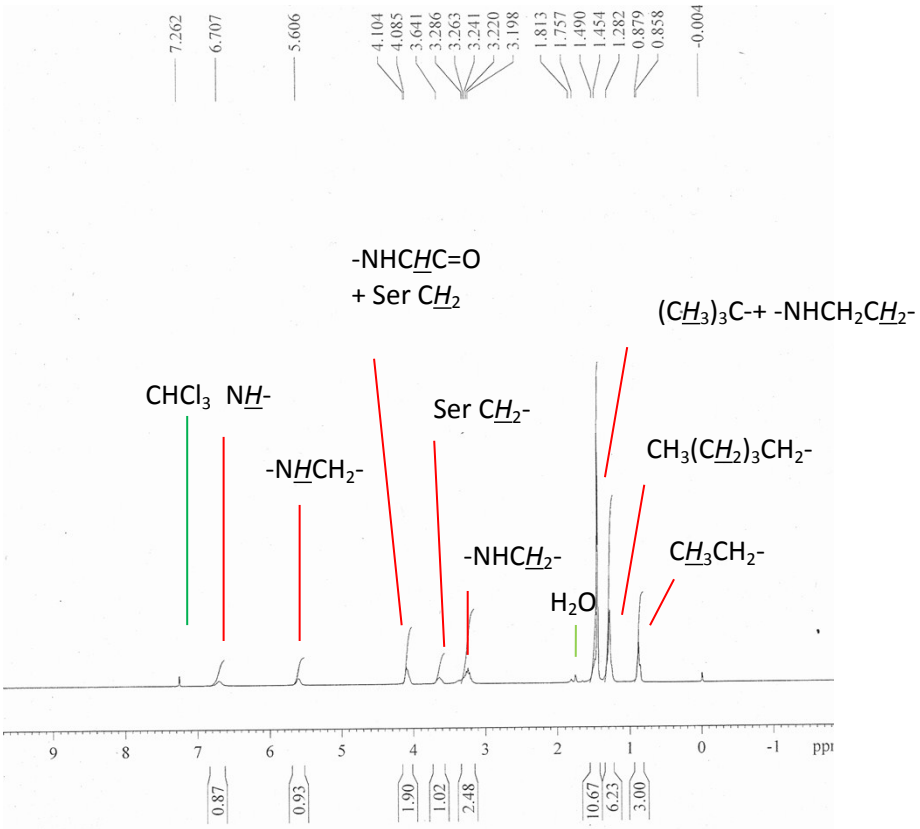

L-A4
L-A5
L-S4
D-P1/L-P1
L-A3
R = Ph
L-S3
D-S2/L-S2
D-A2/L-A2
R =
D-S1/L-S1
L-A1
D-A1
R =
L-A6
R =
L-A7
R = CH3
L-A8
R =
L-A9
R =
Br

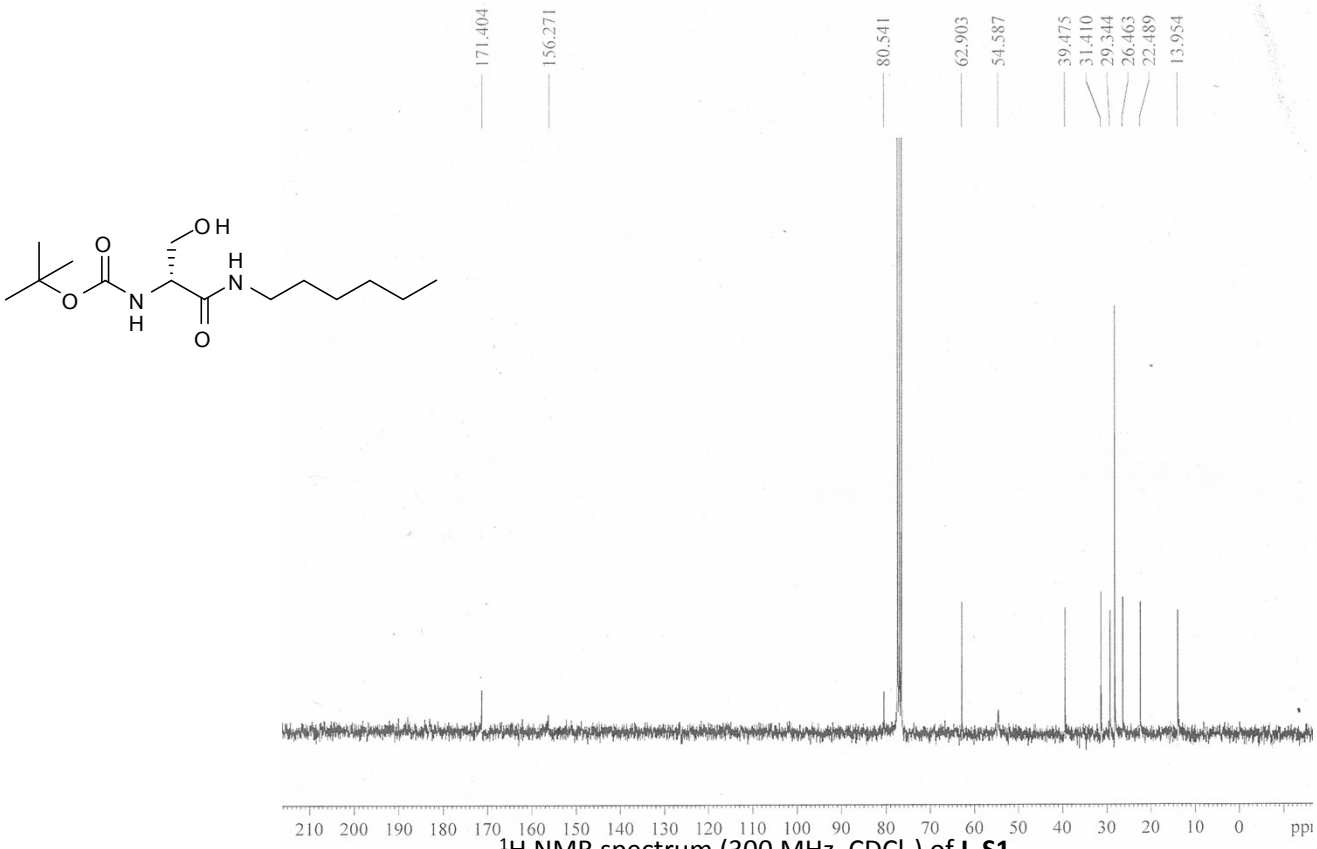
Figure. S1: **Reagents and conditions** i) *m*-xylylene dibromide, TBABr, NaOH, CH_2Cl_2, 18h (ii) *p*-xylylene dibromide, TBABr, NaOH, CH_2Cl_2, 18h (iii) benzyl bromide, TBABr, NaOH, CH_2Cl_2, 12h (iv) benzene 1,3 dicarbonyl dichloride, DMAP, NEt_3, CH_2Cl_2, 24h (v) $HCl_{(g)}$ in EtOAc or TFA/ CH_2Cl_2, 4h; benzoyl chloride, NEt_3, THF/CH_2Cl_2, 24h (vi) TFA/ CH_2Cl_2, 4h; benzene 1,3 dicarbonyl dichloride, NEt_3, CH_2Cl_2, 24h (vii) TFA/ CH_2Cl_2, 4h; 1 naphthoyl chloride, NEt_3, CH_2Cl_2, 24h (viii) TFA/ CH_2Cl_2, 4h; Acetylchloride, NEt_3, CH_2Cl_2, 24h (ix) TFA/ CH_2Cl_2, 4h; diphenylacetyl chloride, NEt_3, CH_2Cl_2, 24h (x) TFA/ CH_2Cl_2, 4h; p bromo benzoyl chloride, NEt_3, CH_2Cl_2, 24h

^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **D-P1**

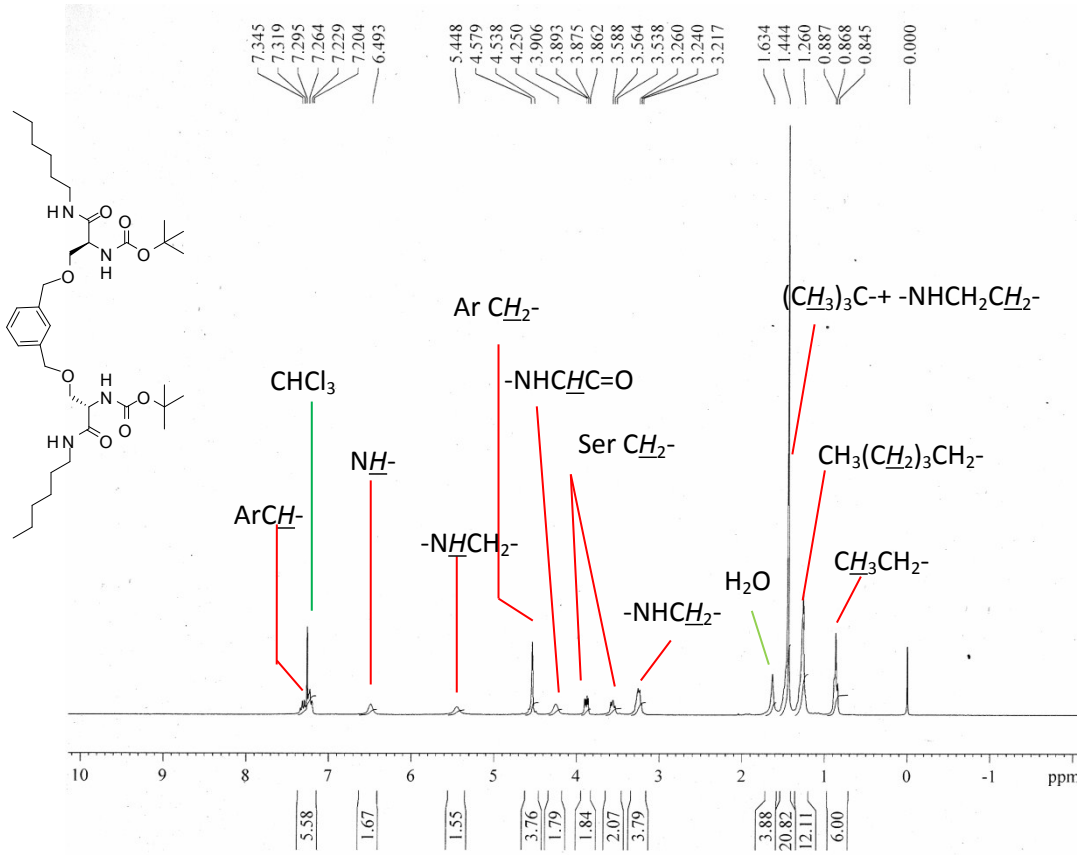




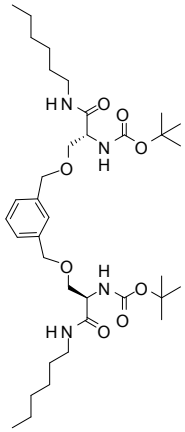
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **D-P1**

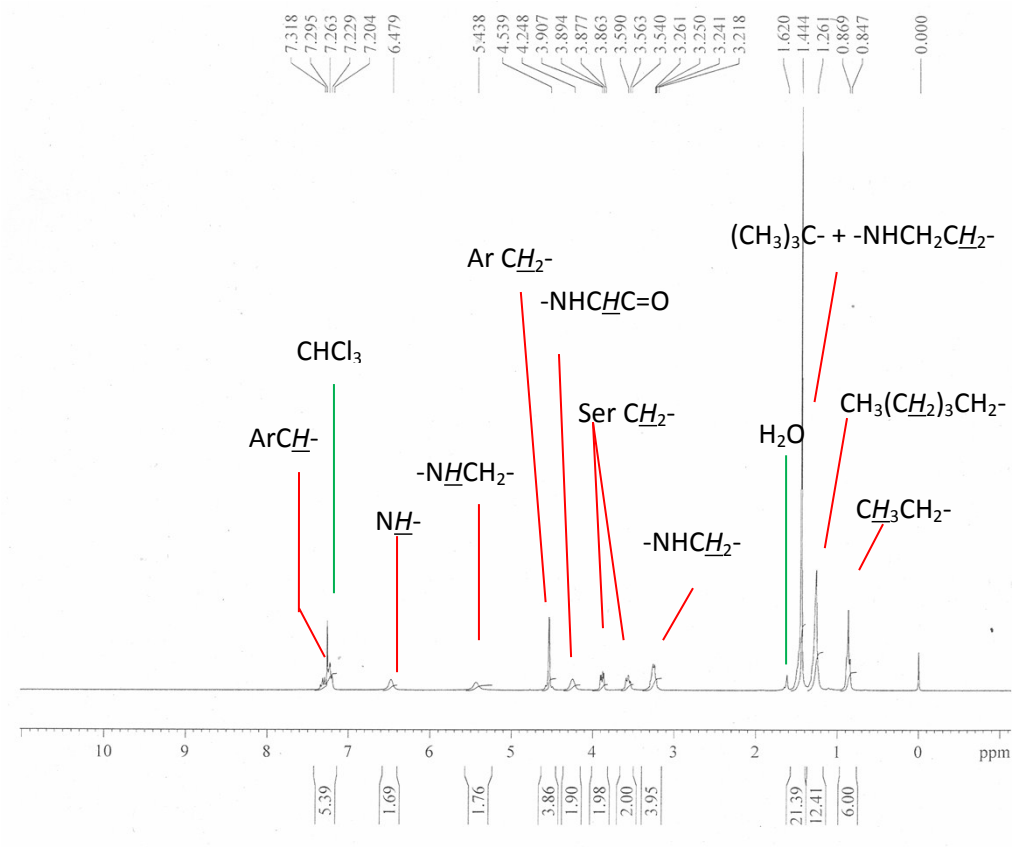


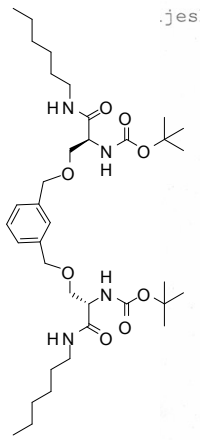
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-S1**

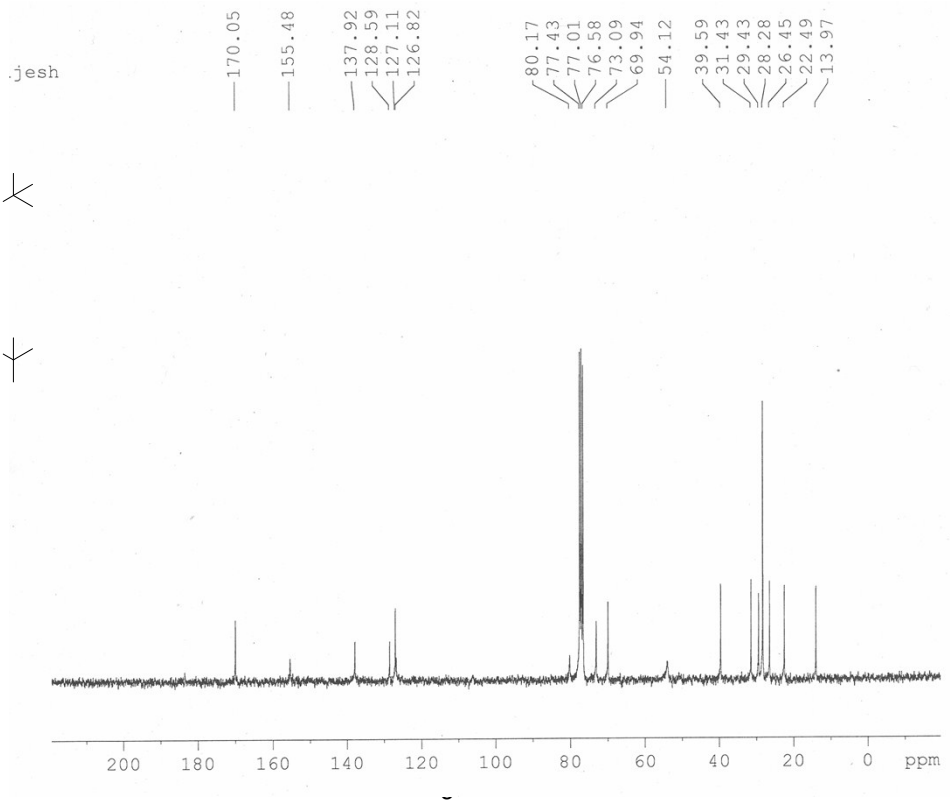


^{1}H NMR Spectrum (300 MHz, $CDCl_3$) of **D-S1**

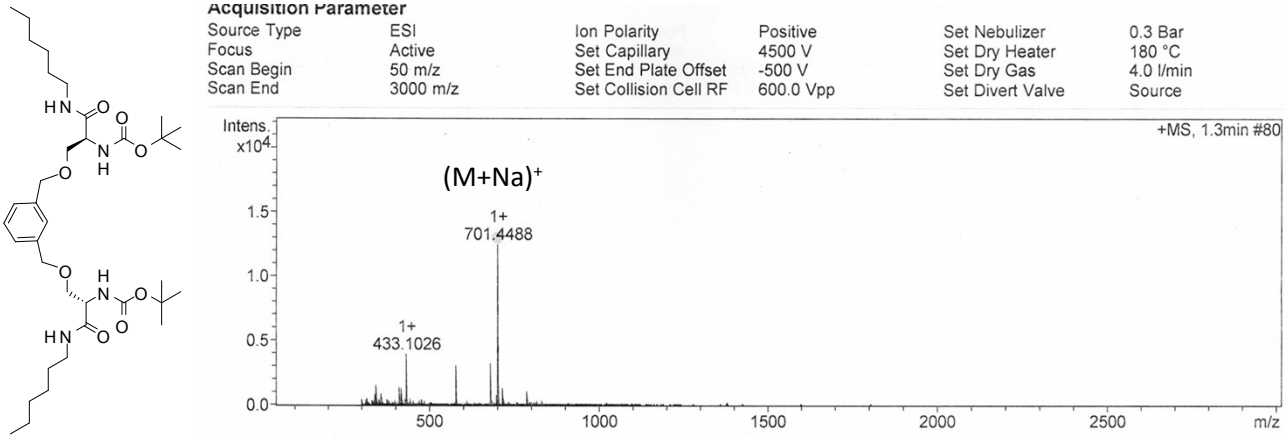




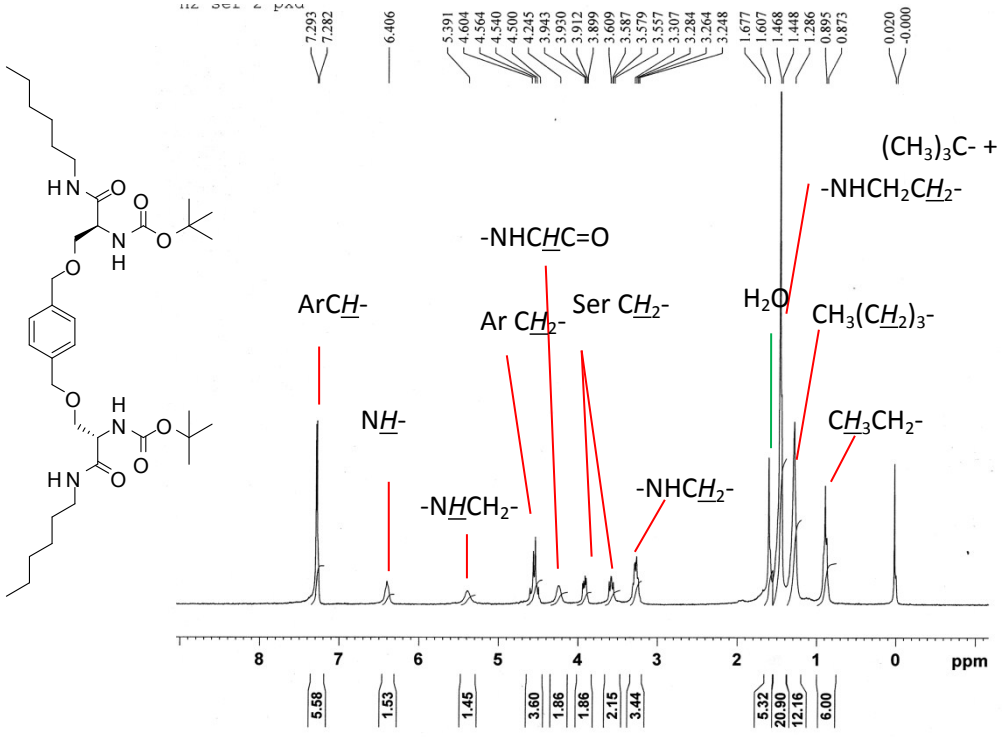




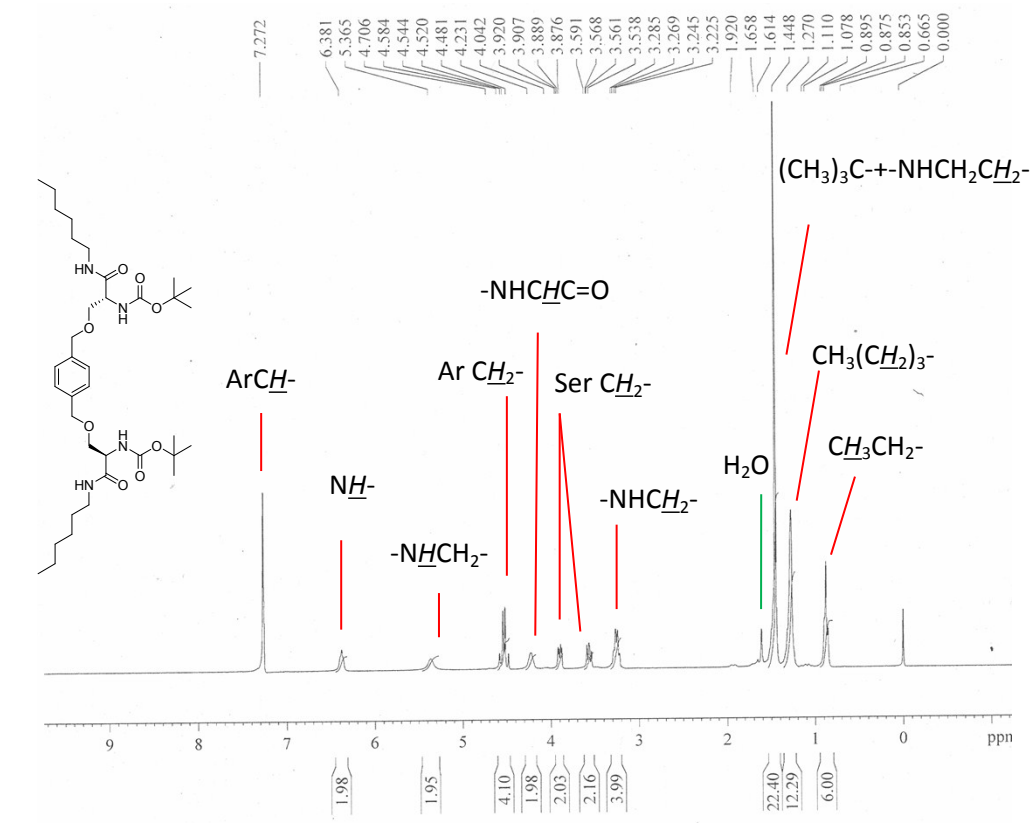
HRMS of **L-S1**



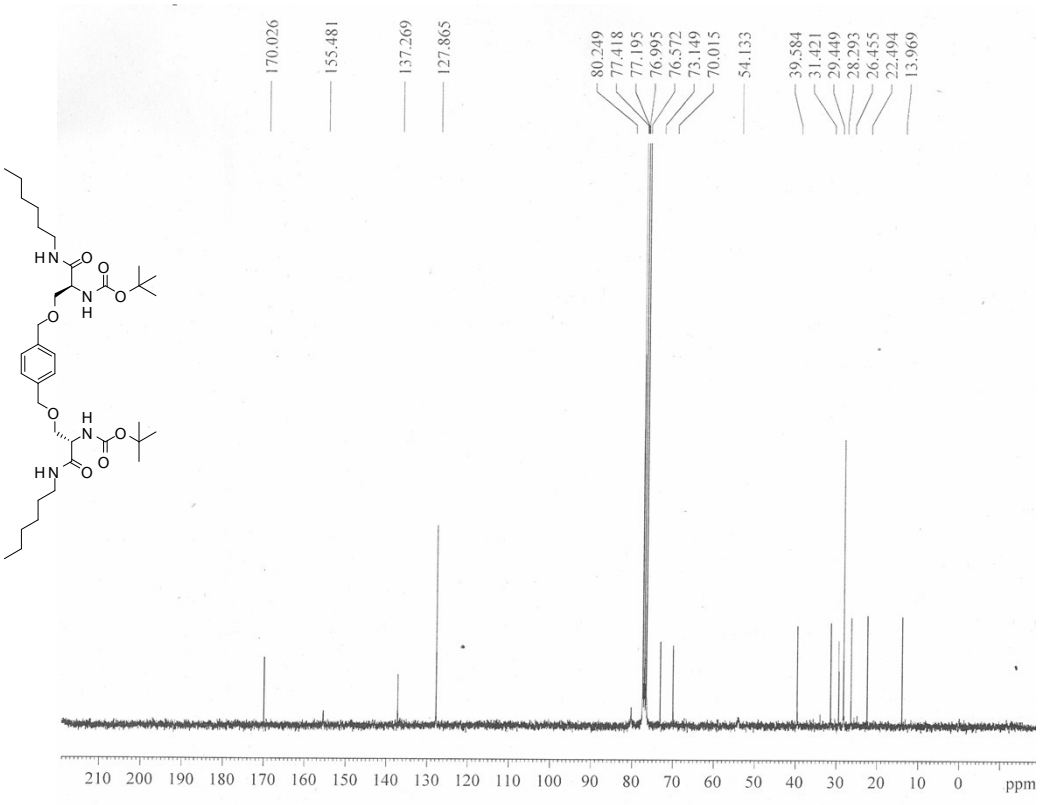
^{1}H NMR Spectrum (300 MHz, $CDCl_3$) of **L-S2**



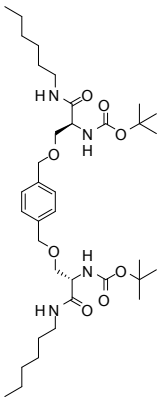
^{1}H NMR Spectrum (300 MHz, $CDCl_3$) of **D-S2**

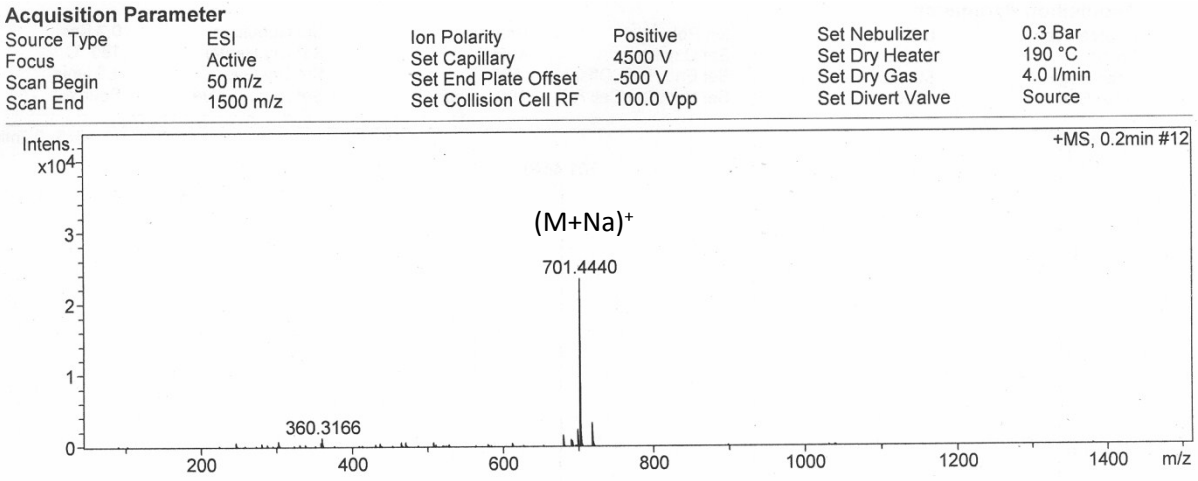


^{13}C NMR Spectrum (75 MHz, $CDCl_3$) of **L-S2**

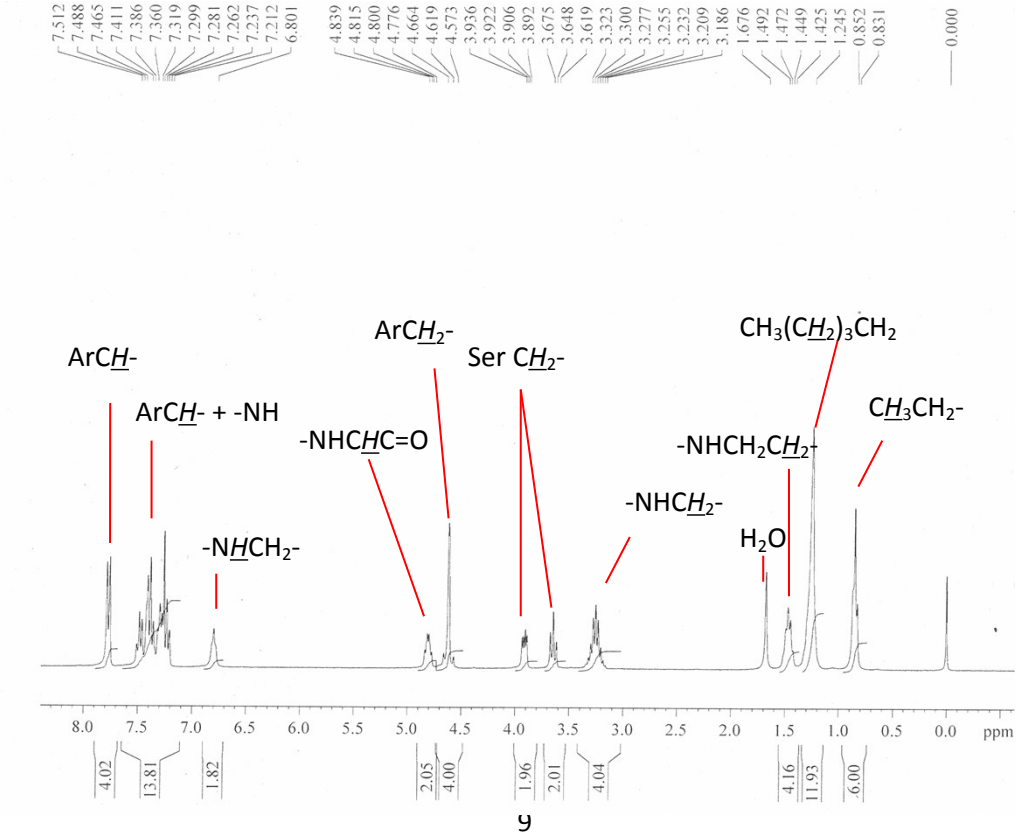


HRMS of **L-S2**

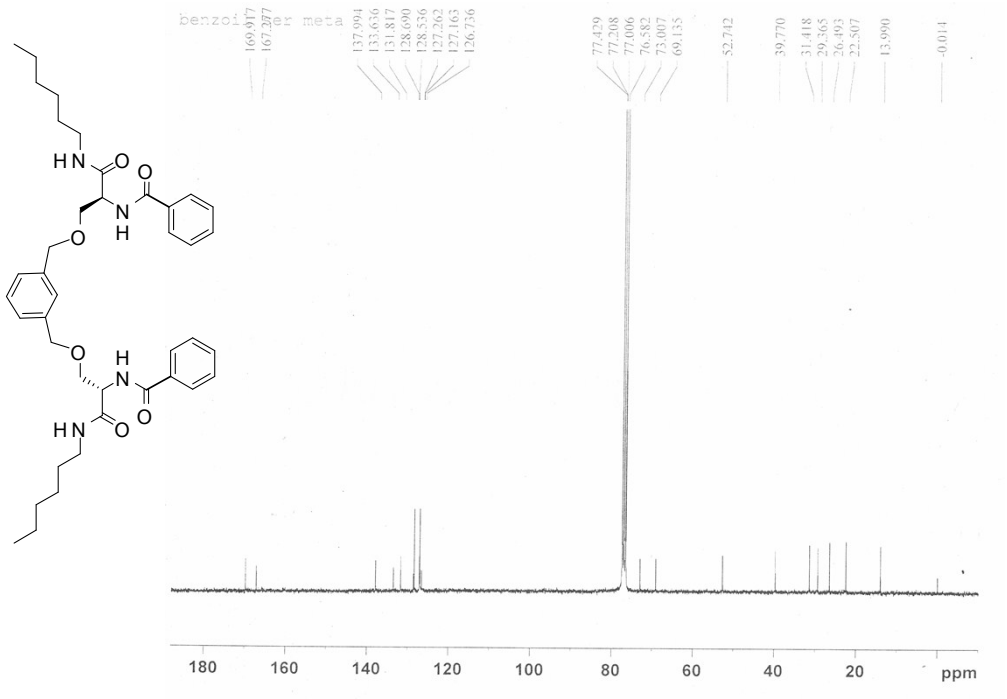




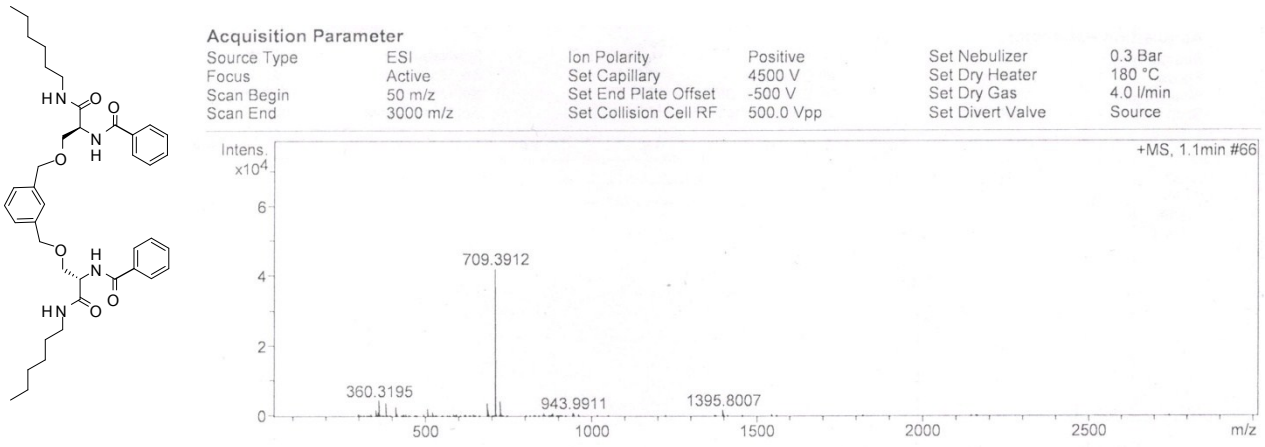
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-A1**



^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A1**

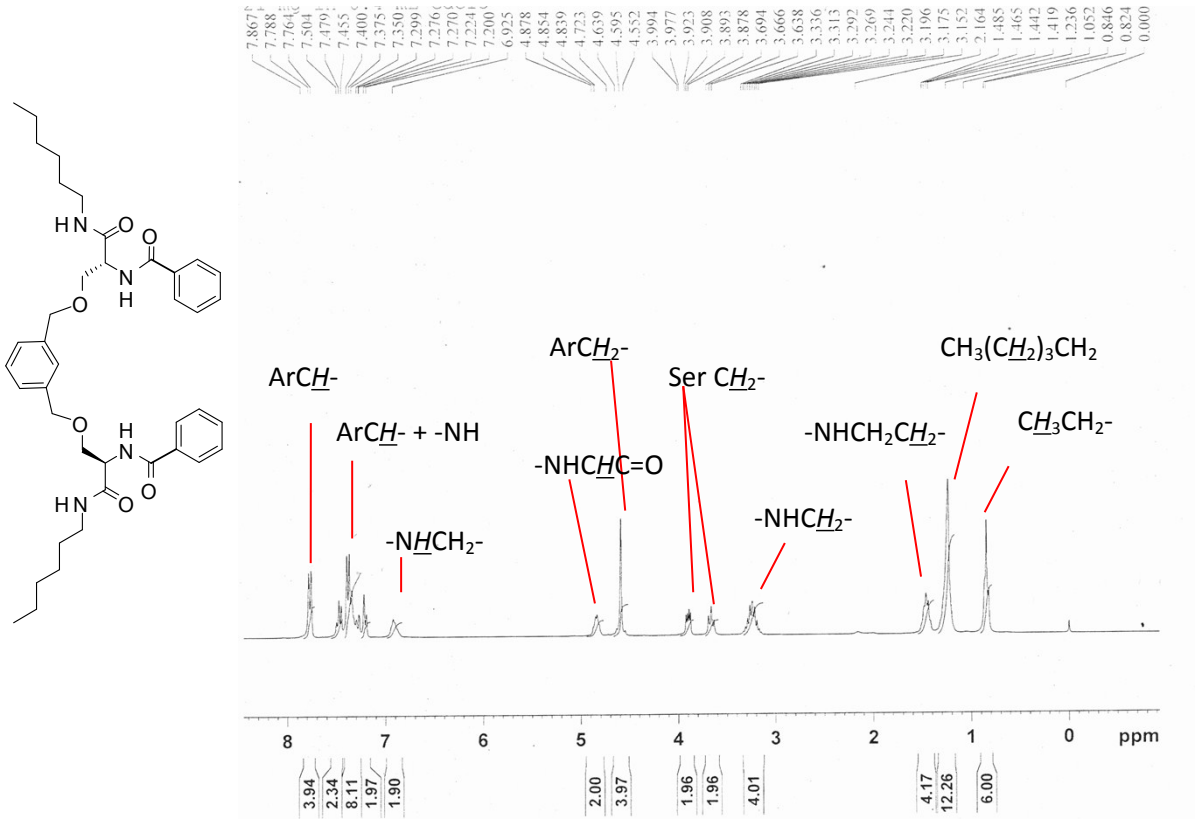


HRMS of **L-A1**

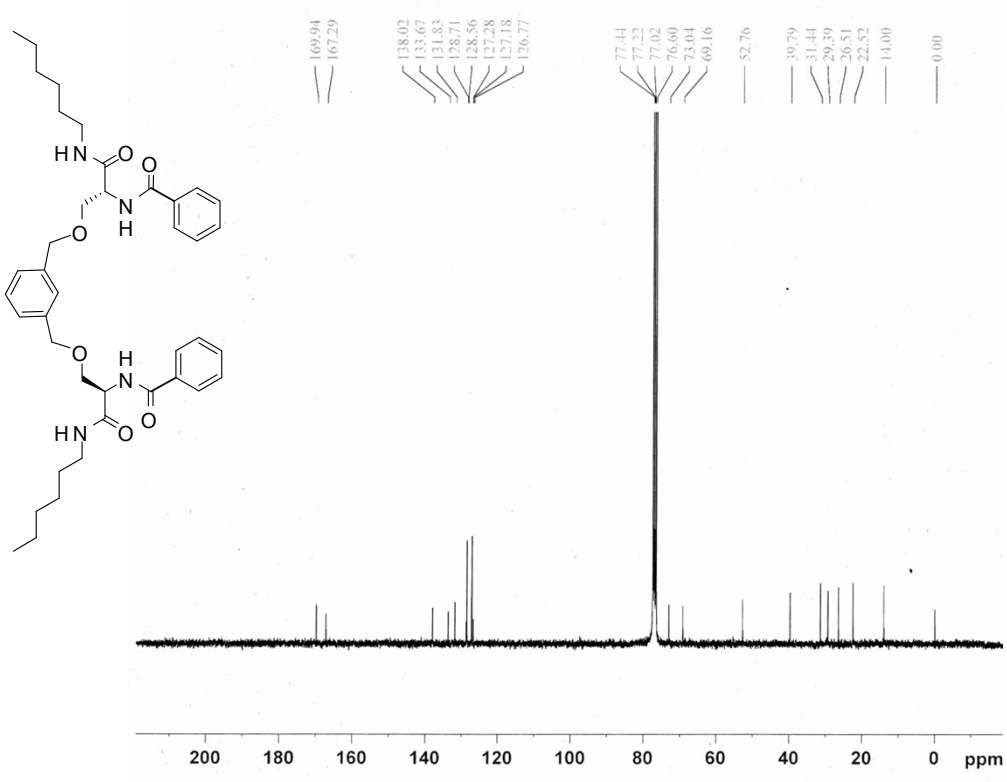


$(M+Na)^+$

^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **D-A1**

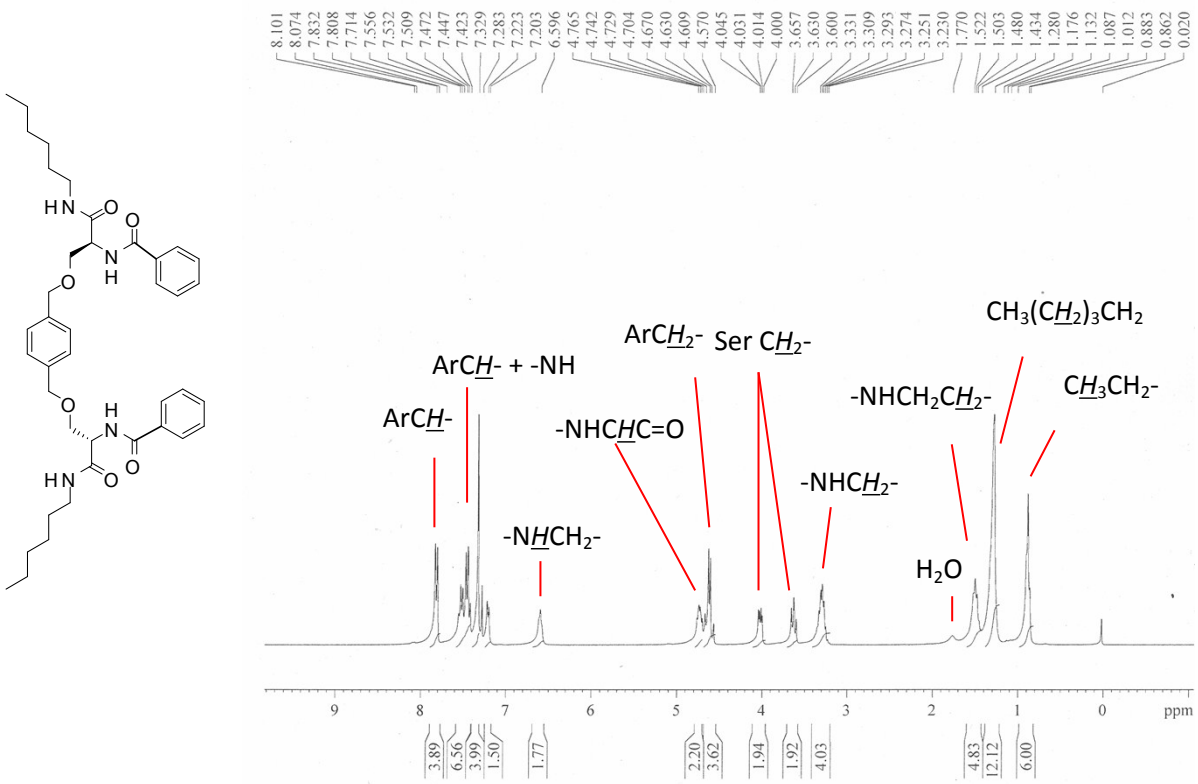


^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **D-A1**

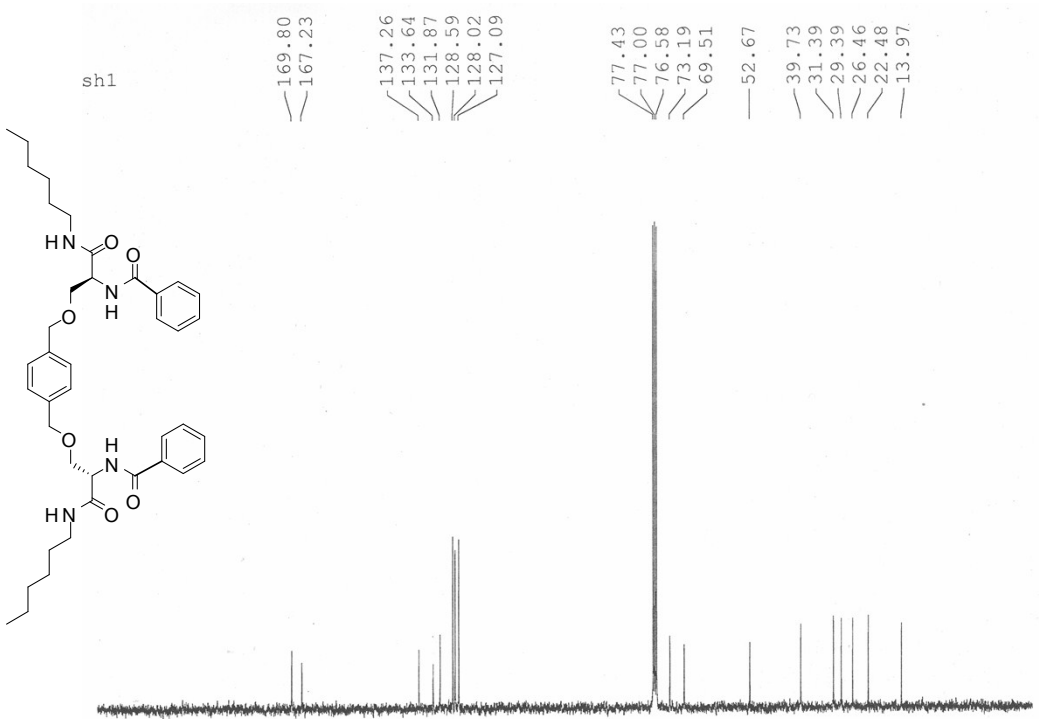


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **L-A2**

^{1}HNMR spectrum (300 MHz, $CDCl_3$) of **L-A2**

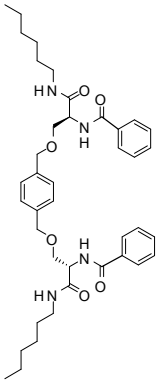


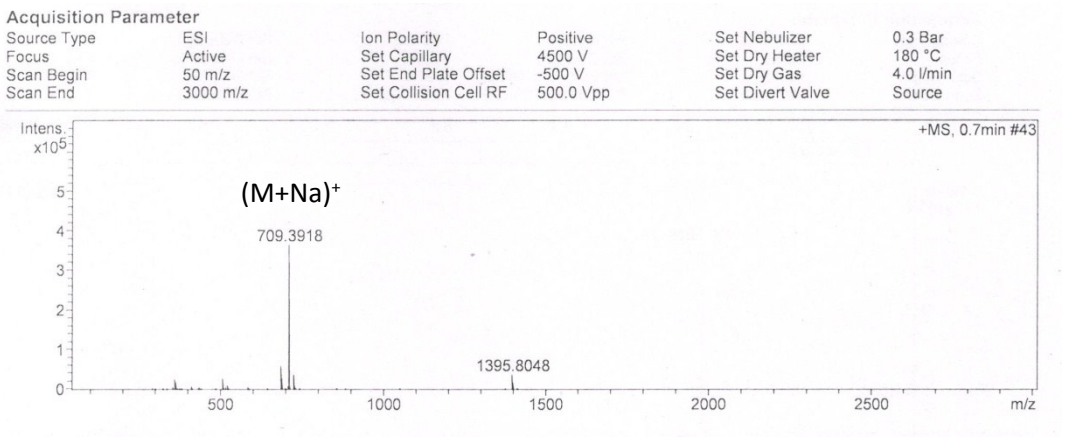
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A2**



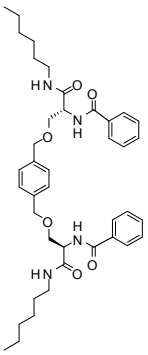
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **D-A2**

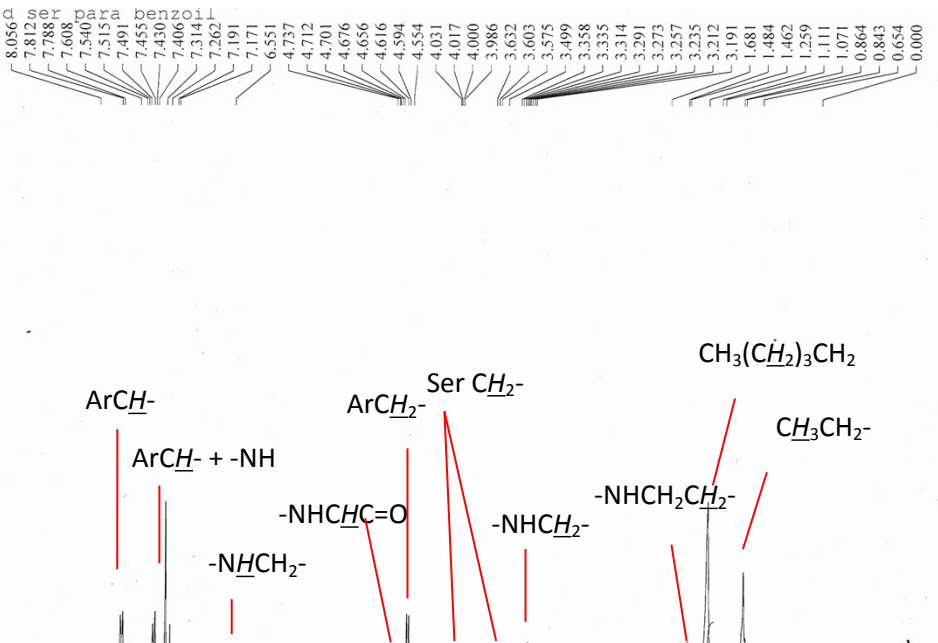
HRMS of **L-A2**



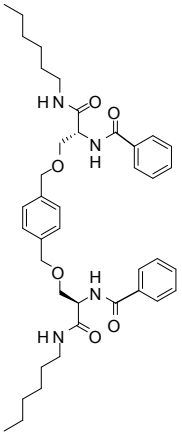


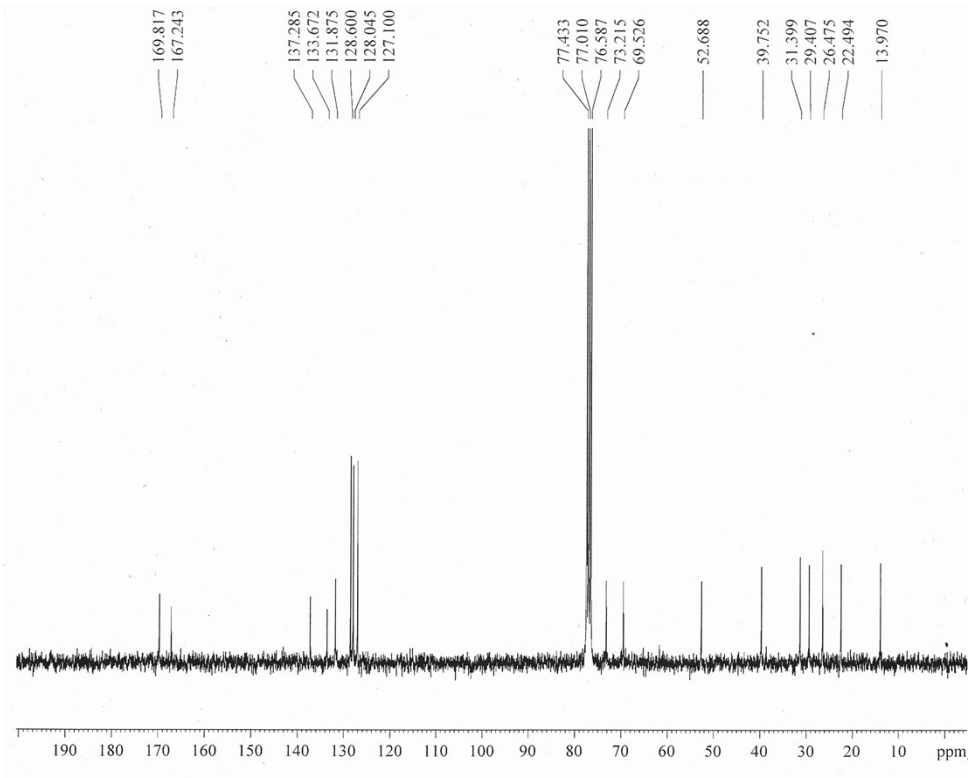
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **D-A2**



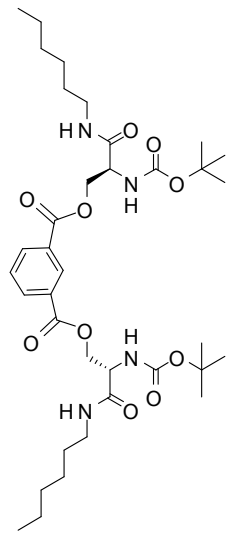


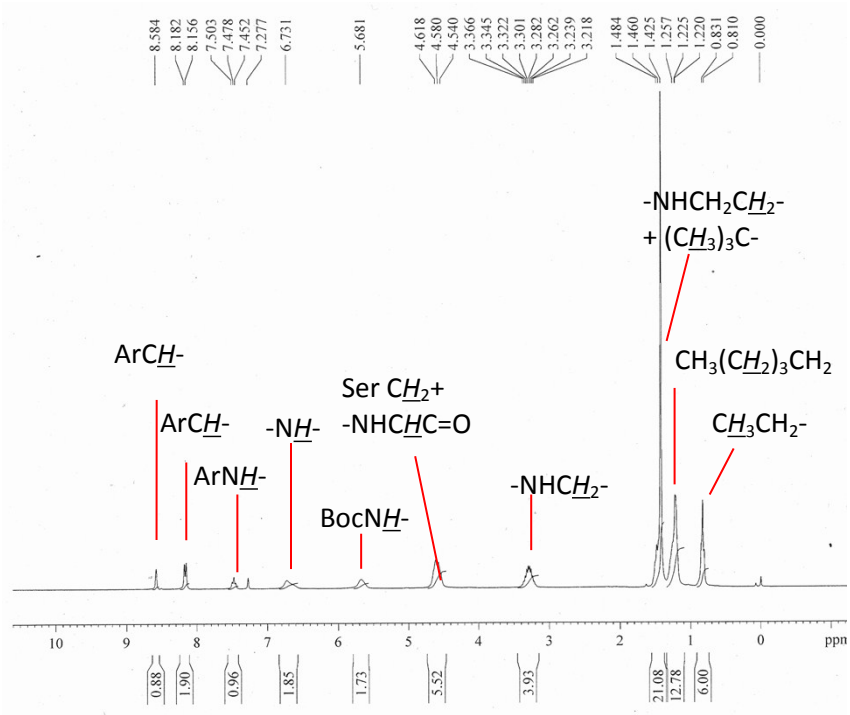
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **D-A2**



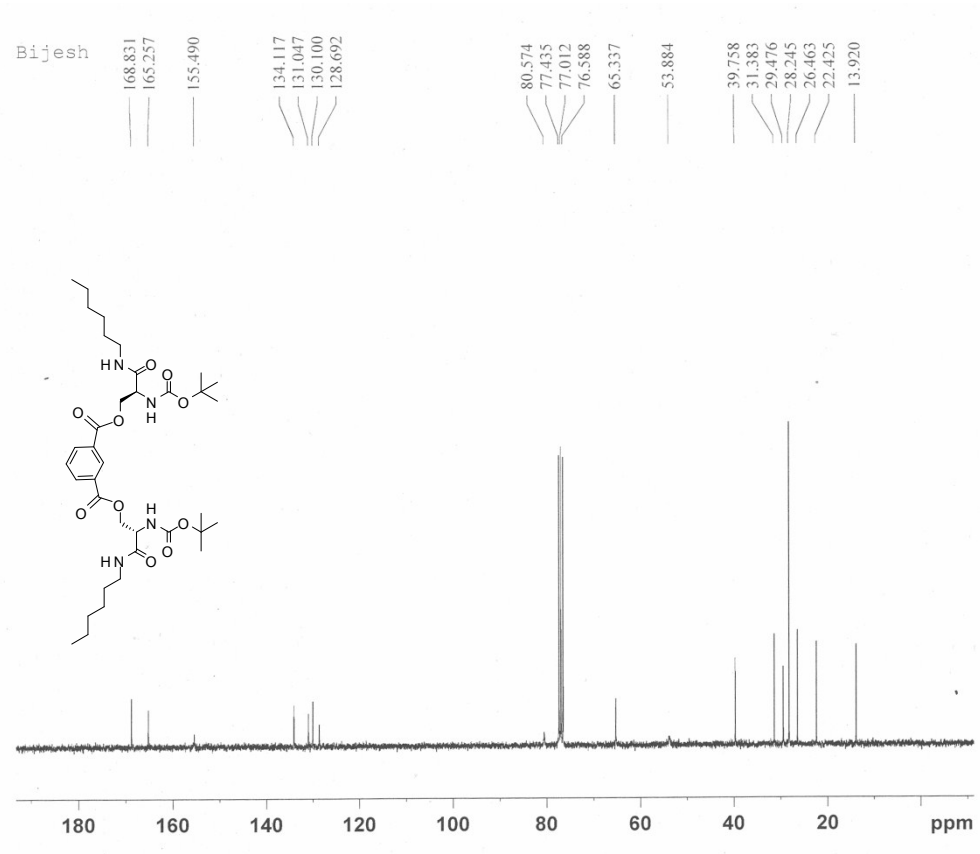


^{1}H NMR (300 MHz, $CDCl_3$) spectrum of **L-S3**

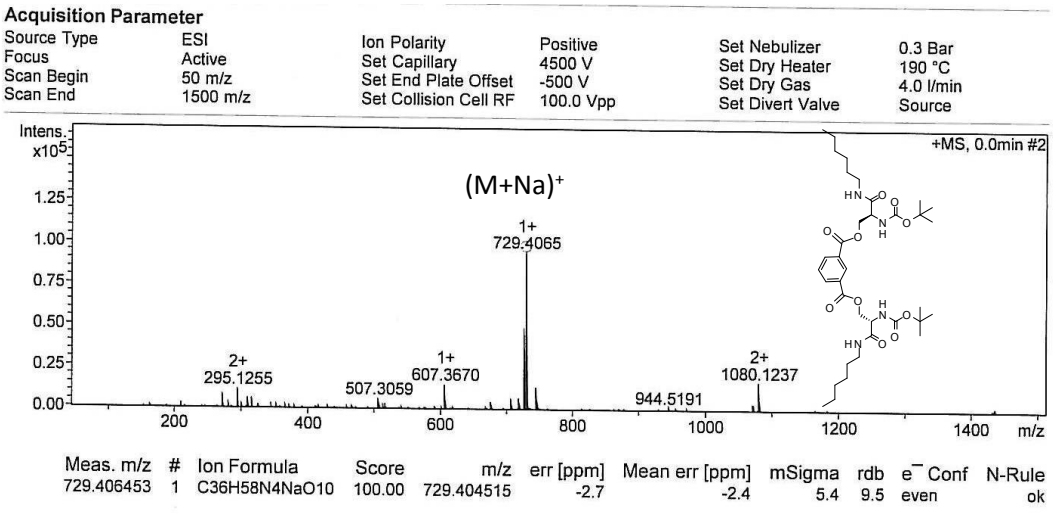




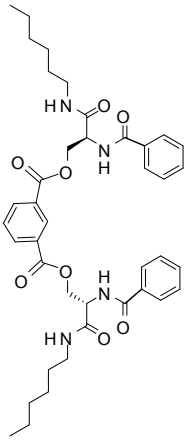
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-S3**

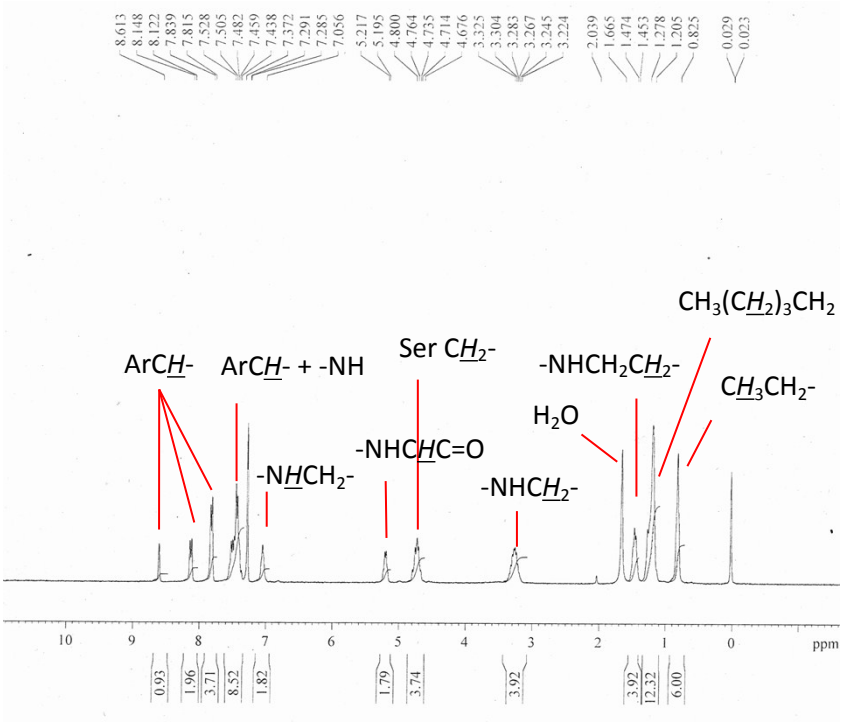


HRMS of **L-S3**

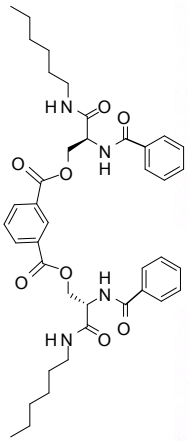


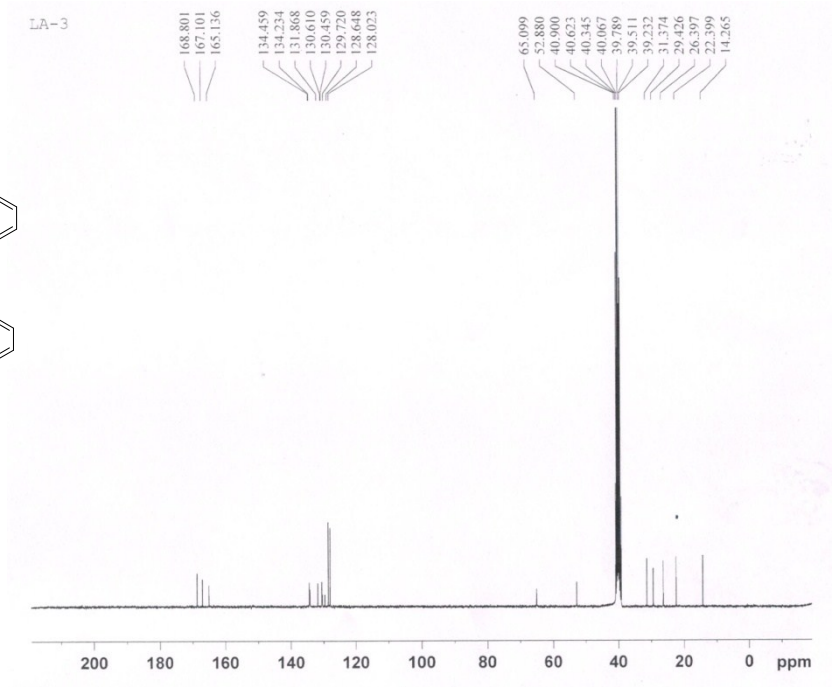
^{1}H NMR spectrum (300MHz, $CDCl_3$) of **L-A3**



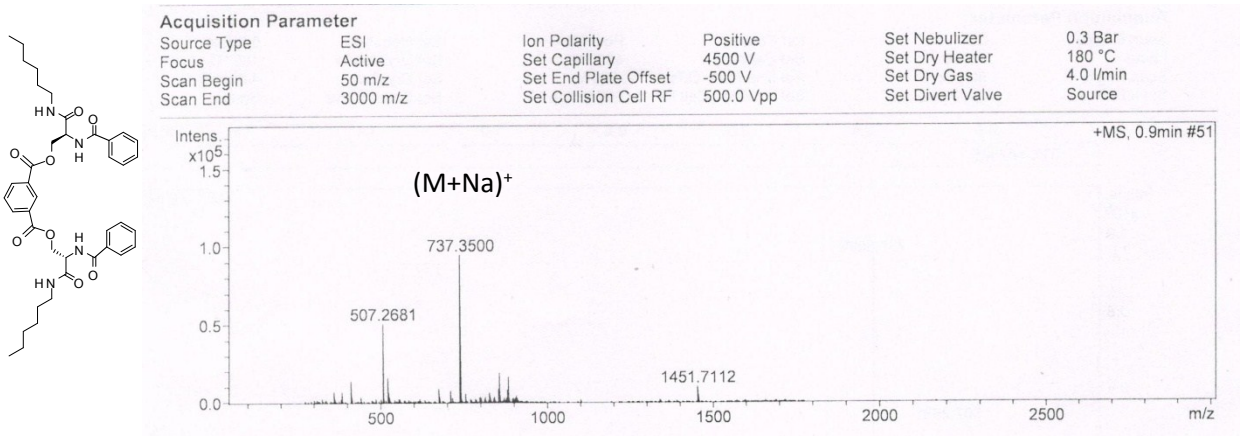


^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **L-A3**

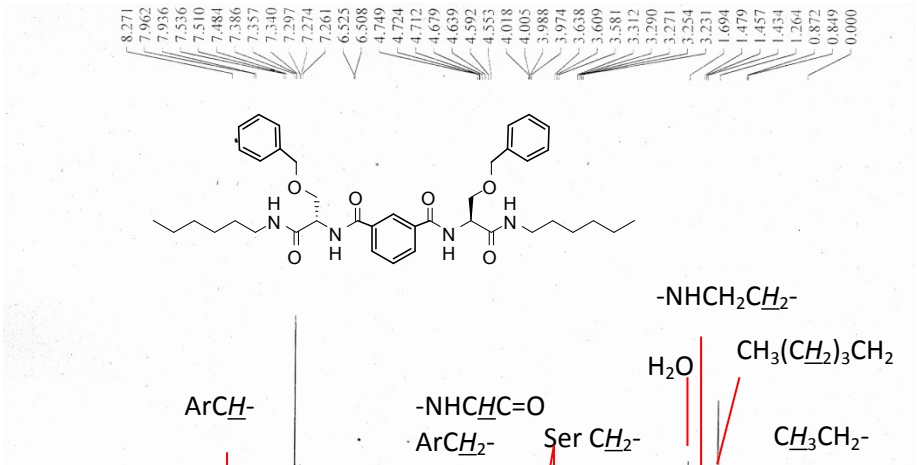




HRMS of **L-A3**

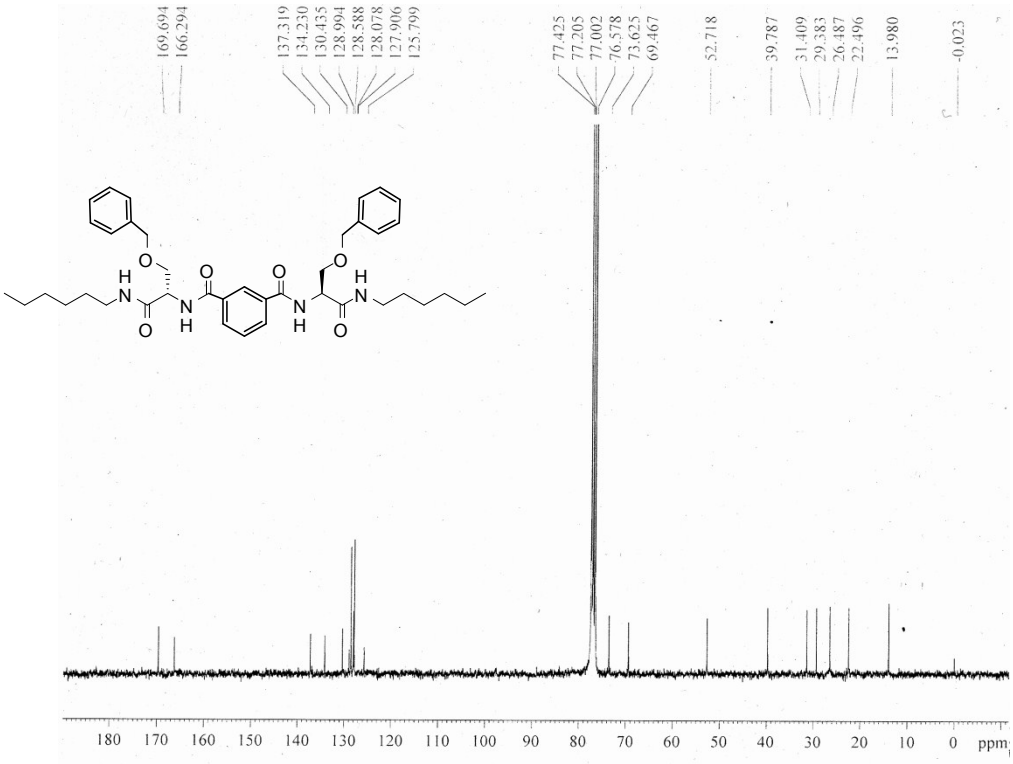


^{1}H NMR spectrum (300MHz, $CDCl_3$) of **L-A4**

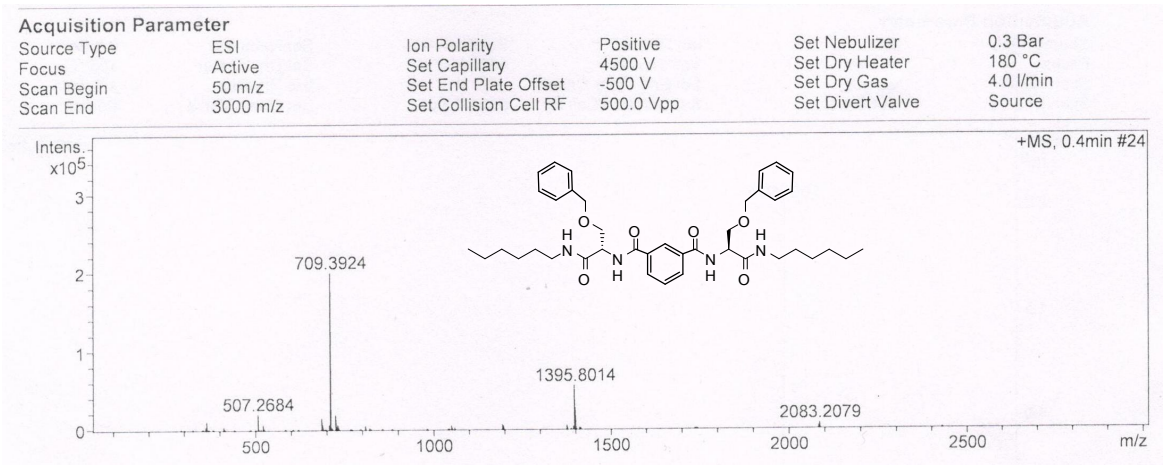


ArC*H*-+ NH

^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A4**

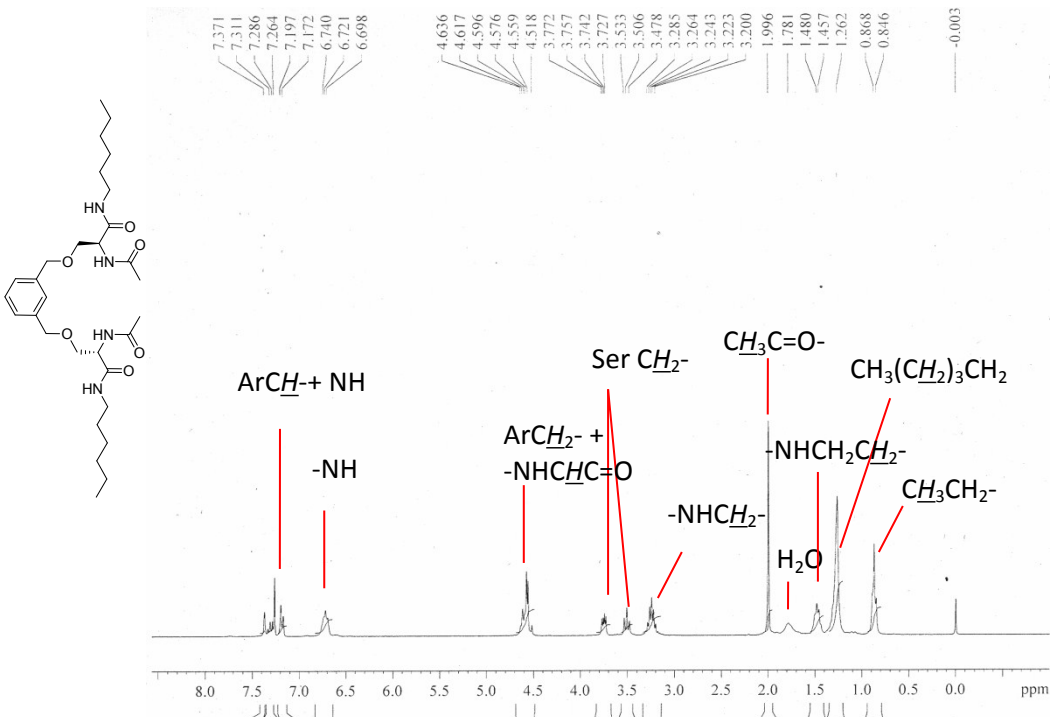


HRMS of **L-A4**

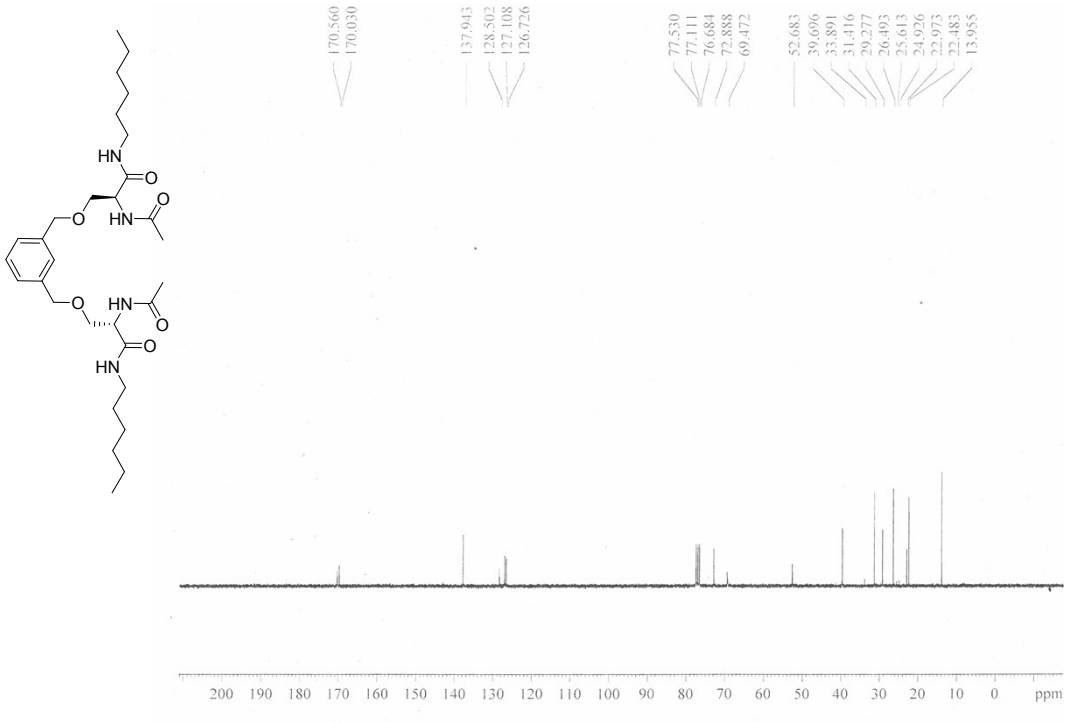


$(M+Na)^+$

^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-A7**



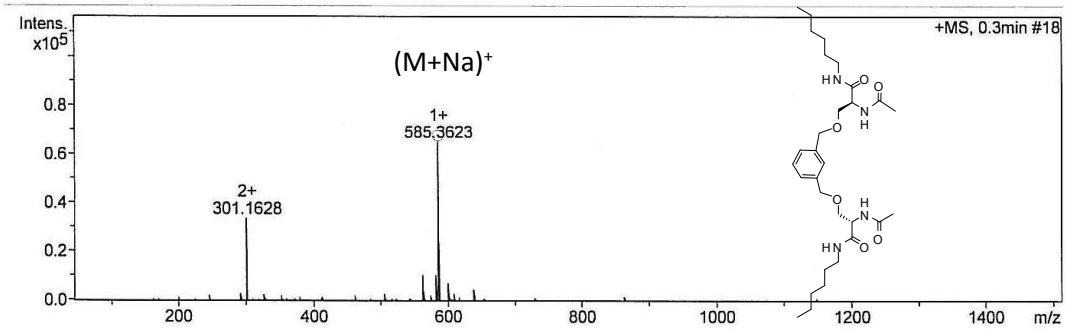
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A7**



HRMS of L-A7

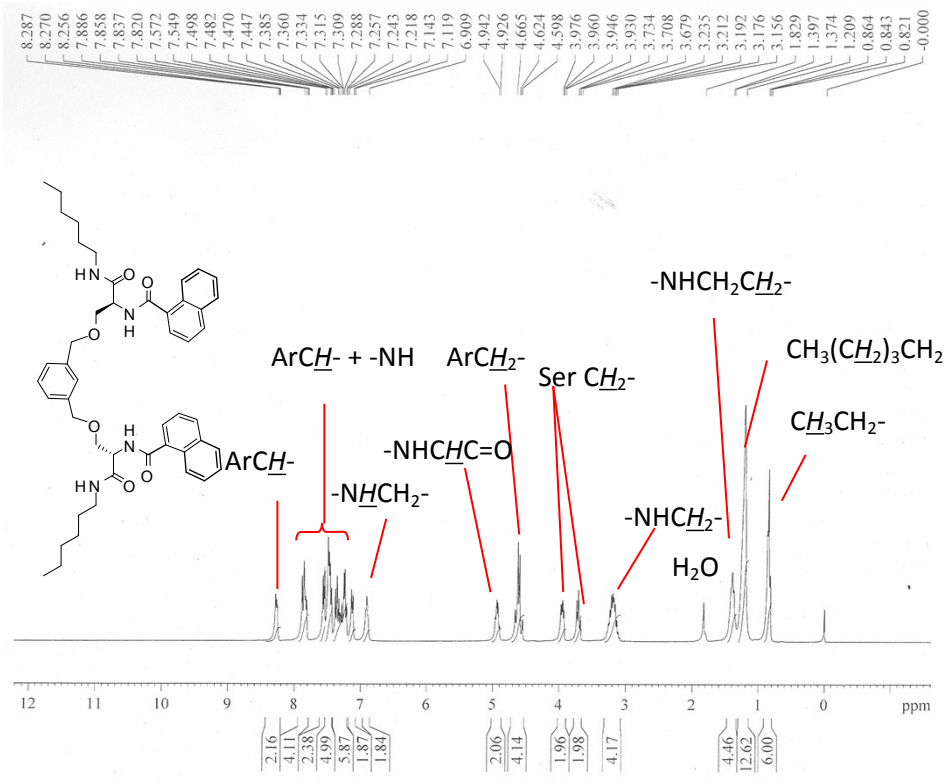
Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	190 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Source

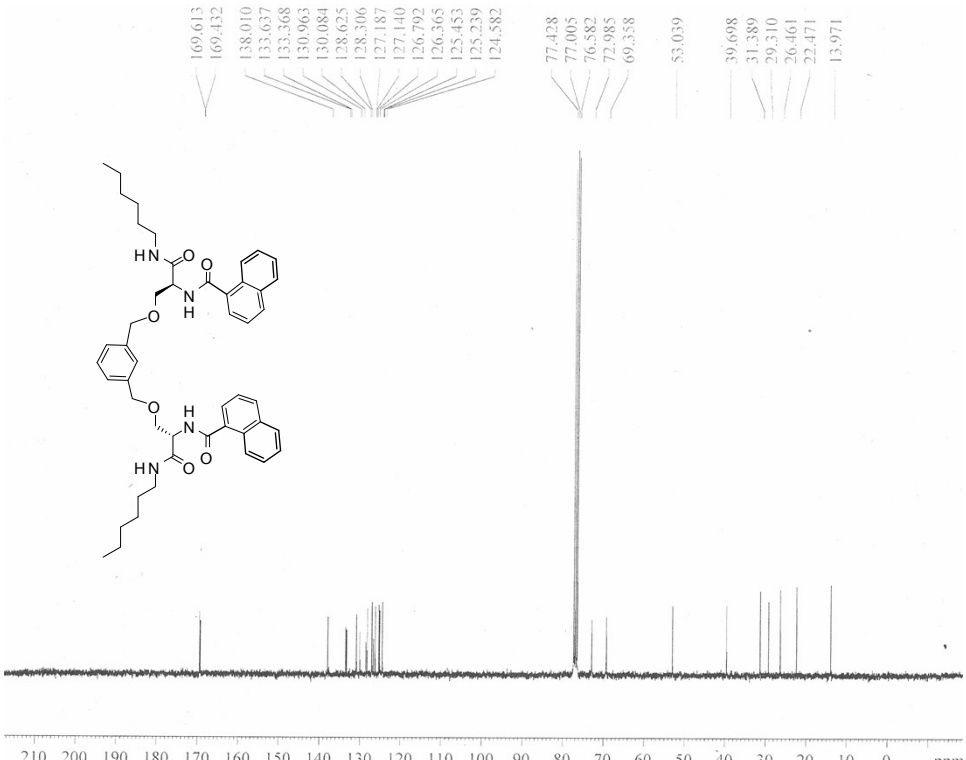


Meas. m/z	#	Ion Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e¯ Conf	N-Rule
585.362333	1	C30H50N4NaO6	100.00	585.362256	0.1	0.6	8.6	7.5	even	ok

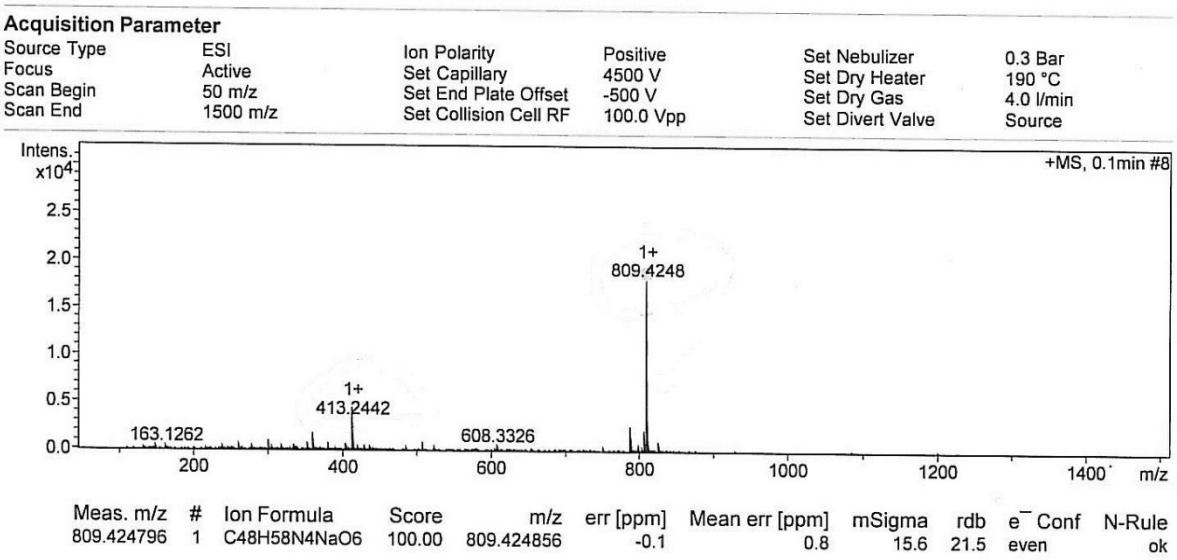
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-A6**



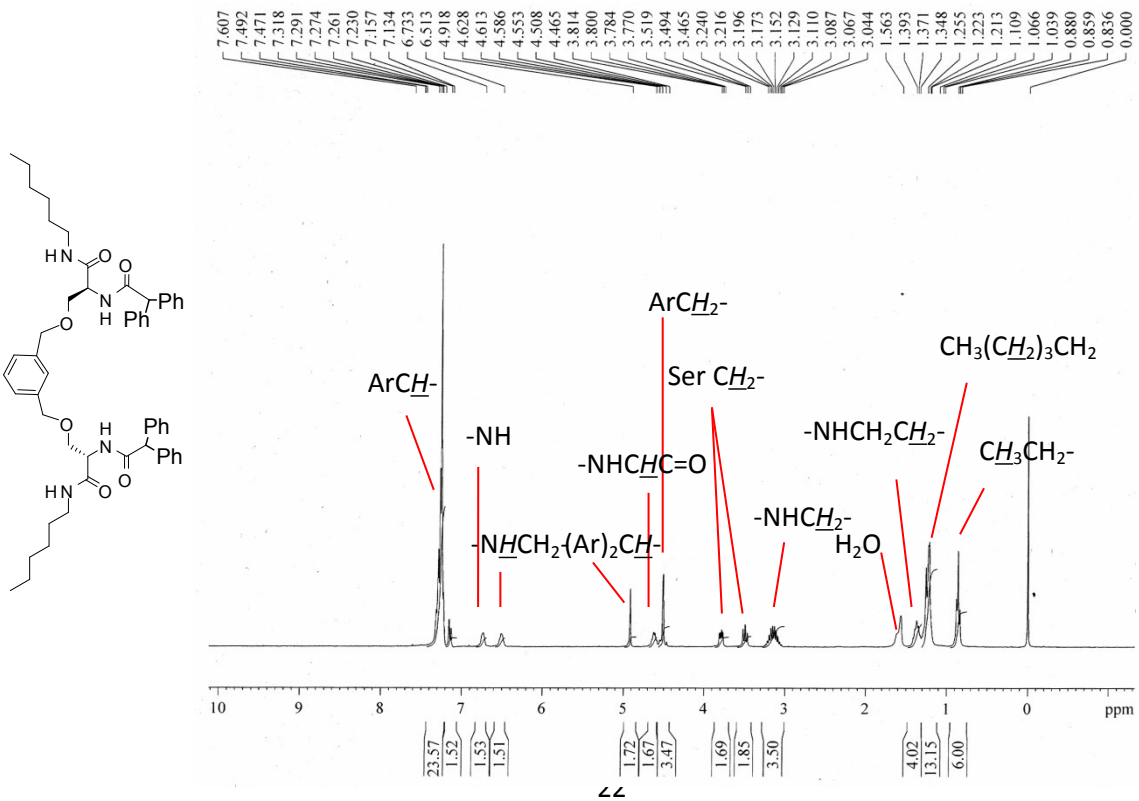
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A6**



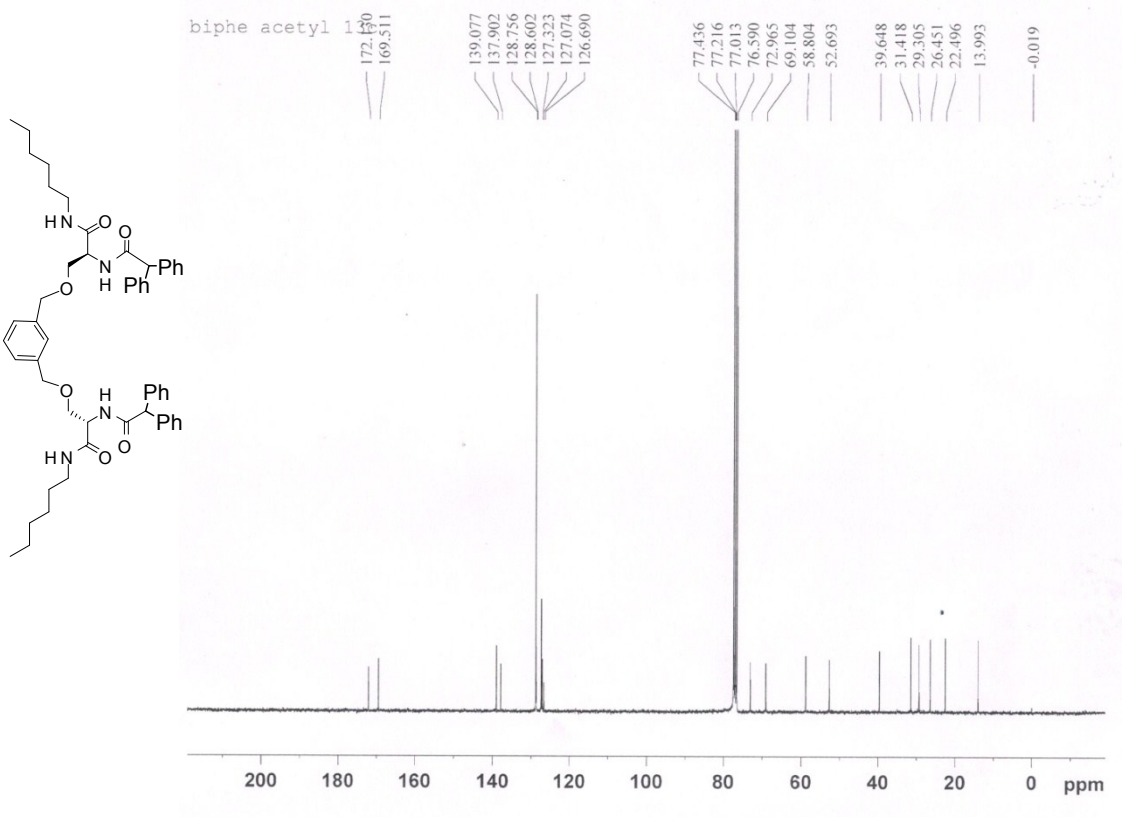
HRMS of **L-A6**



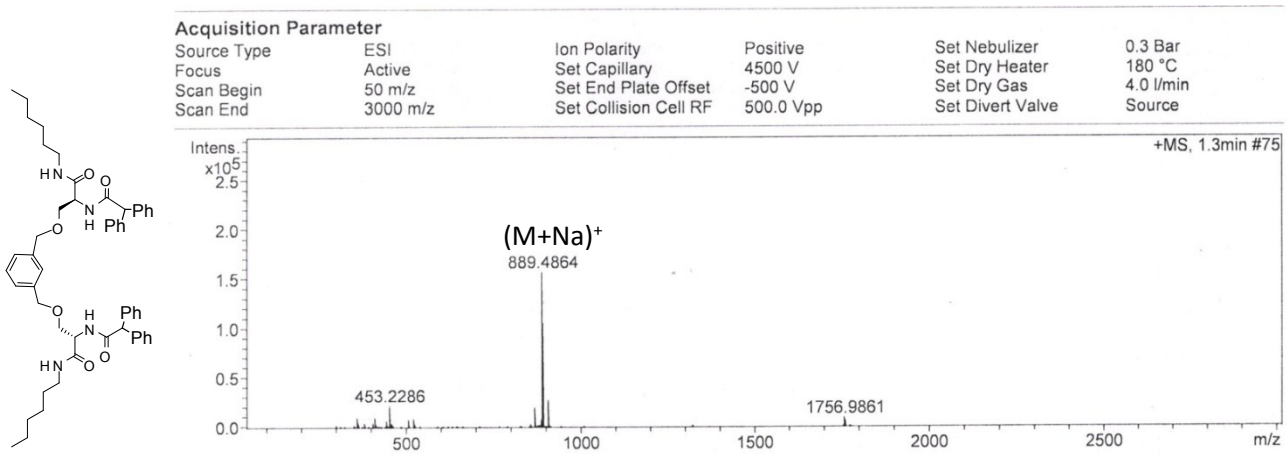
^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-A8**



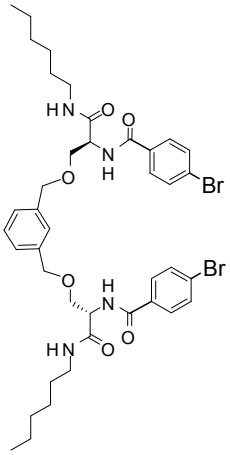
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A8**

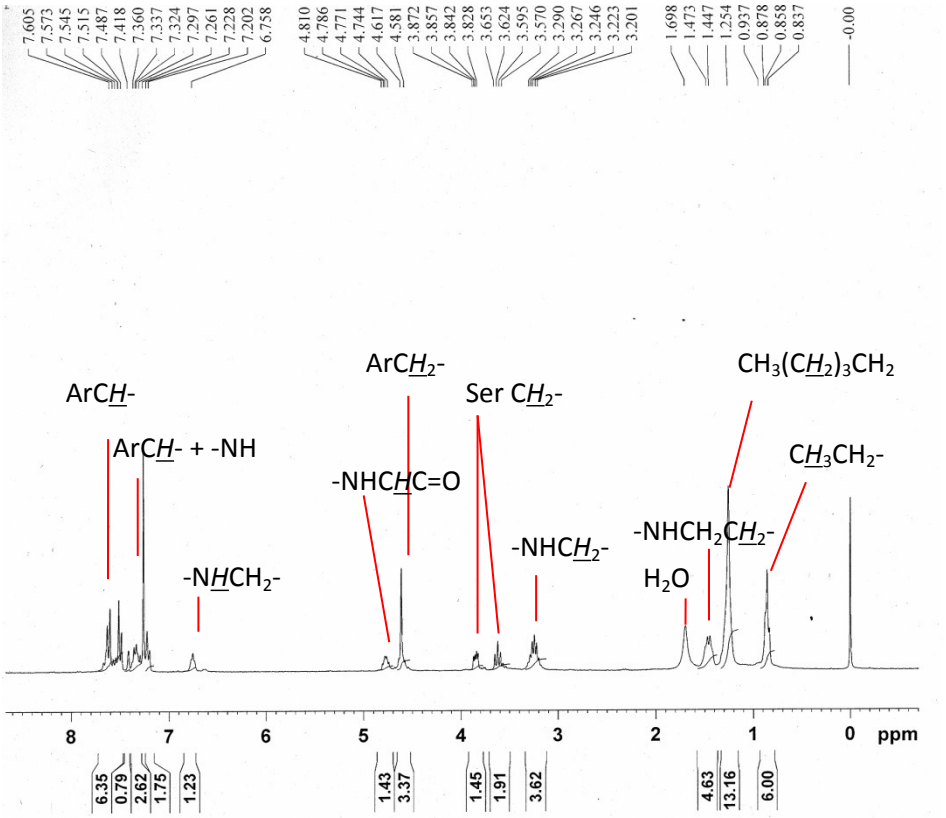


HRMS of **L-A8**

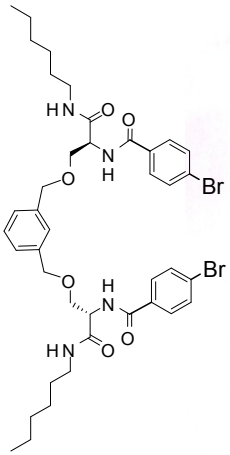


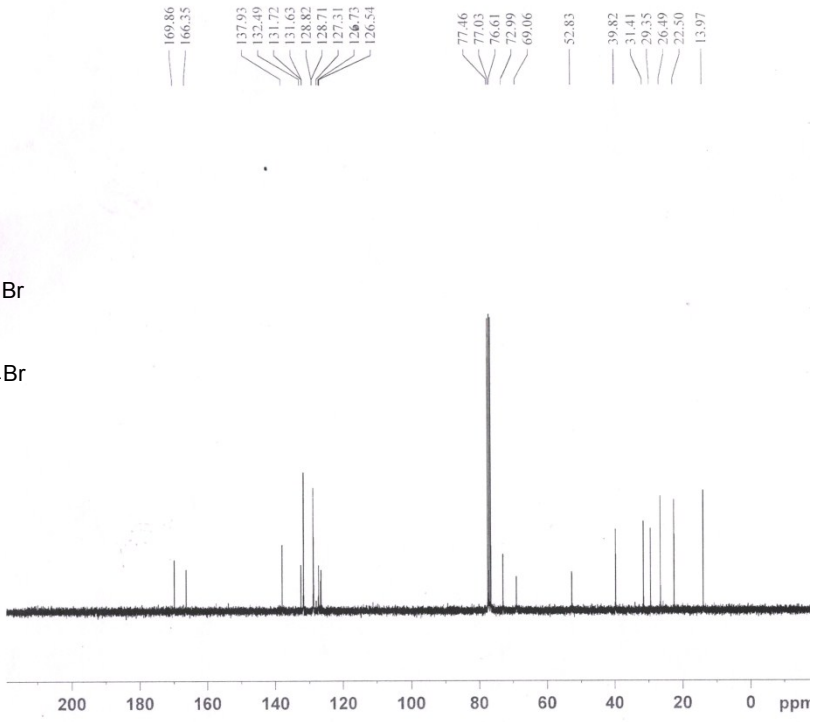
^{1}H NMR (300MHz, $CDCl_3$) of **L-A9**



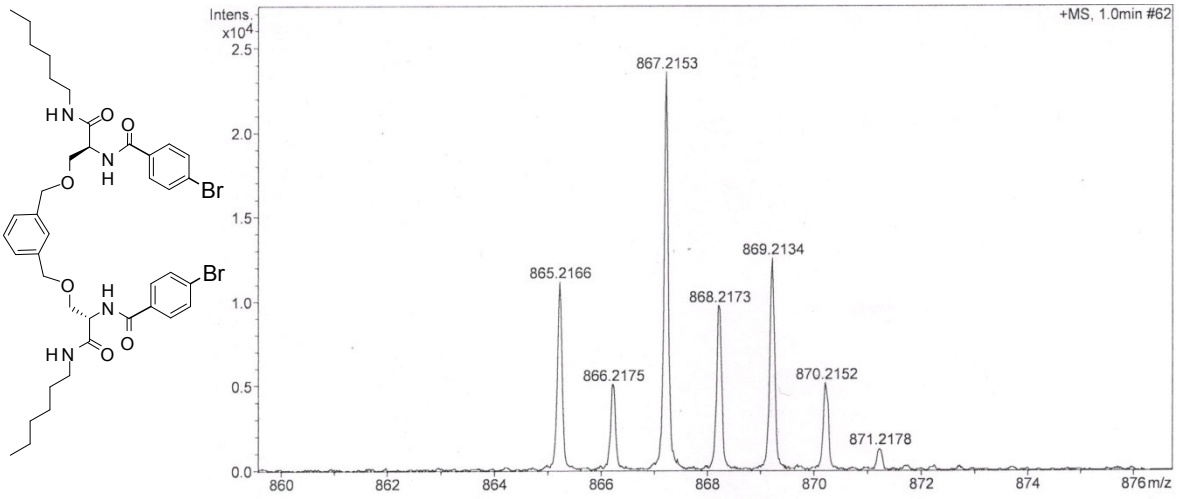


^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A9**



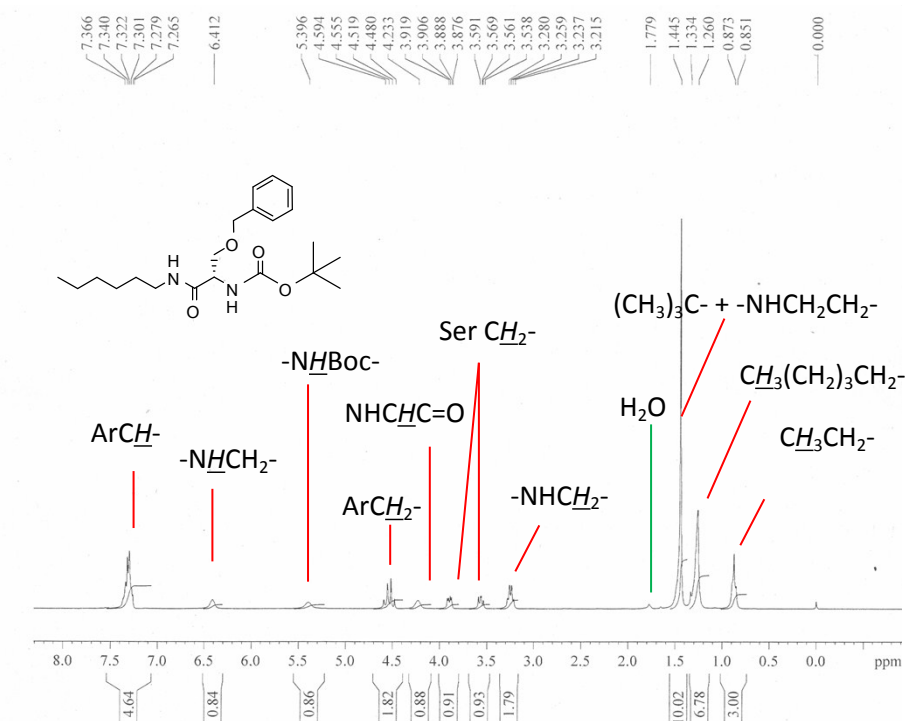


HRMS of **L-A9**

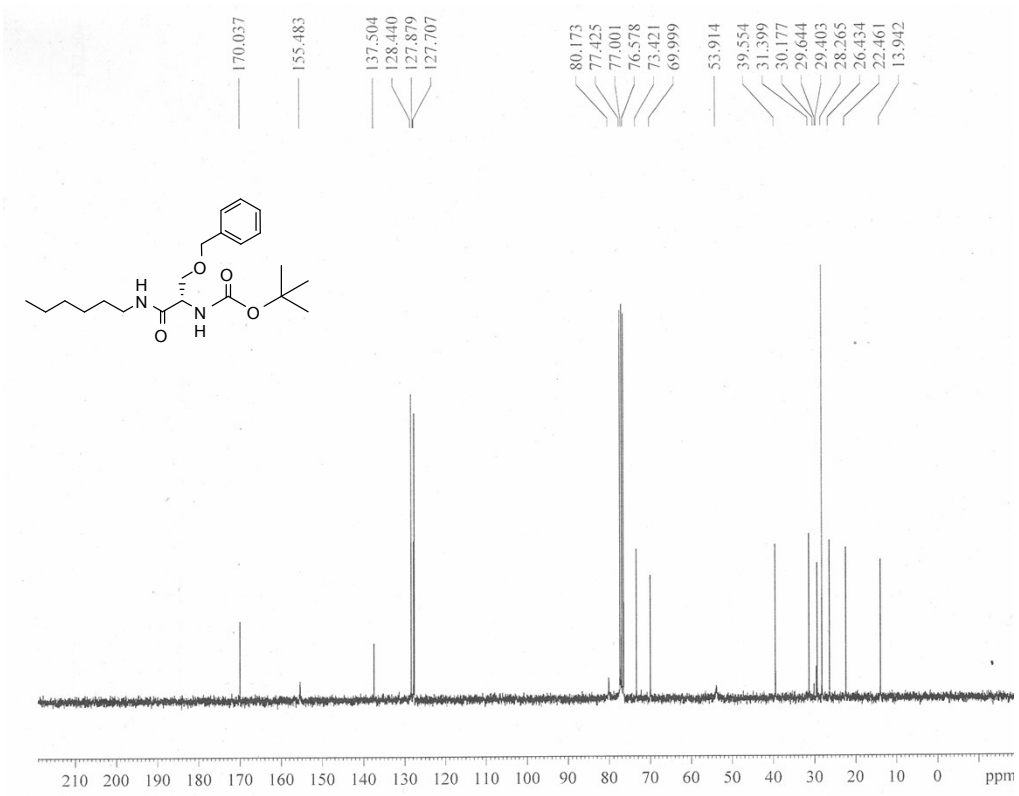


$(M+Na)^+$

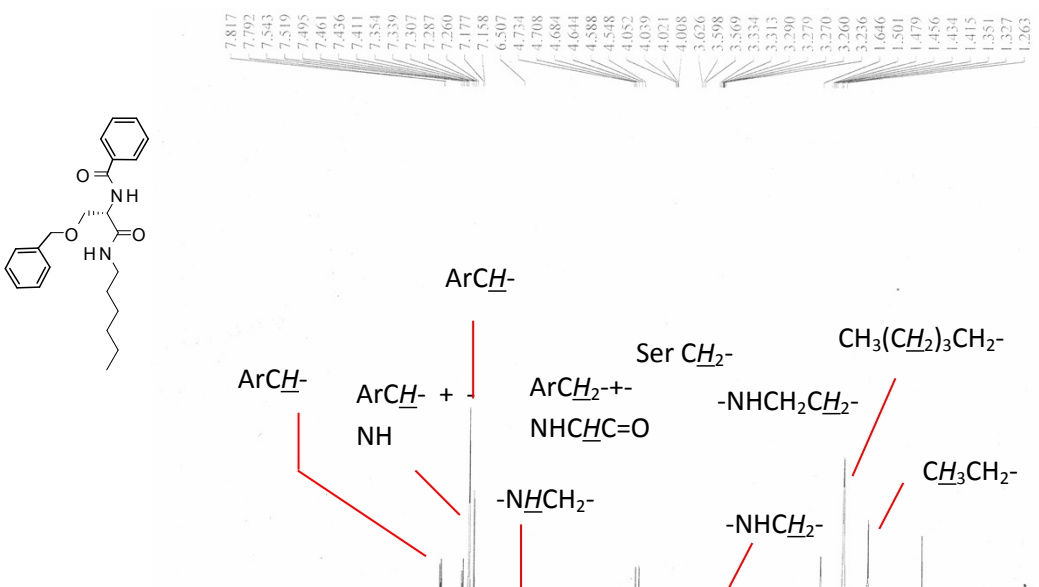
^{1}H NMR (300MHz, $CDCl_3$) of **L-S4**



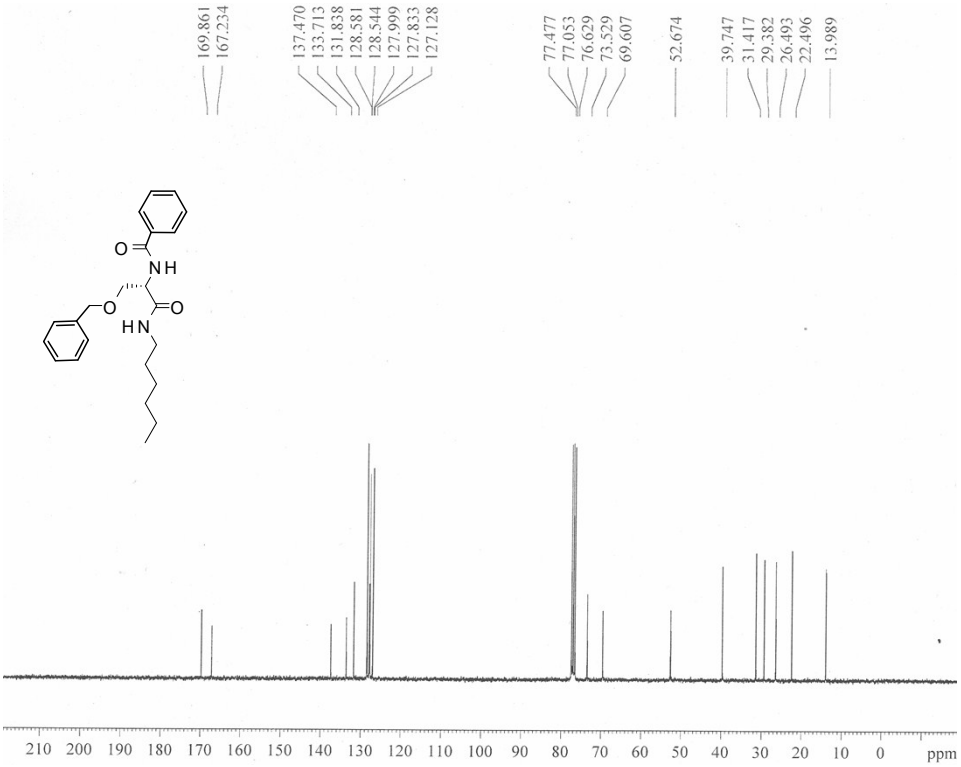
^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-S4**



^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **L-A5**



^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **L-A5**



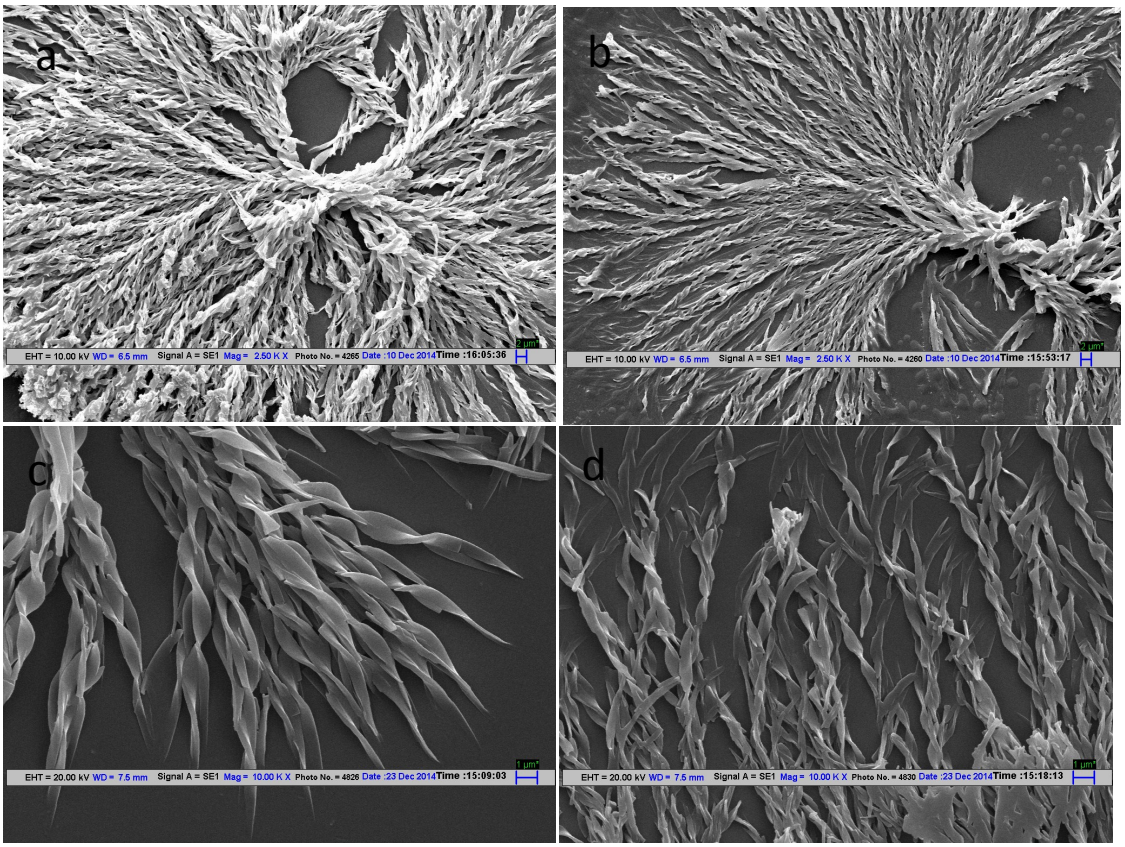

a
EHT = 10.00 kV WD = 6.5 mm Signal A = SE1 Mag = 2.50 K X Photo No. = 4265 Date :10 Dec 2014 Time :16:05:36
b
EHT = 10.00 kV WD = 6.5 mm Signal A = SE1 Mag = 2.50 K X Photo No. = 4260 Date :10 Dec 2014 Time :15:53:17
c
EHT = 20.00 kV WD = 7.5 mm Signal A = SE1 Mag = 10.00 K X Photo No. = 4826 Date :23 Dec 2014 Time :15:09:03
d
EHT = 20.00 kV WD = 7.5 mm Signal A = SE1 Mag = 10.00 K X Photo No. = 4830 Date :23 Dec 2014 Time :15:18:13

Figure S2: SEM image of **L-A1** (1 mM in methanol) (a-b) Different parts of dendrites showing left handed twisted-ribbons (c) Zoomed image of **L-A1** showing the presence of intertwining at the end of ribbons. (d) Co-existence of flat ribbons and twisted-ribbons. Scale bar (a-b) 2 μm (c-d) 1 μm

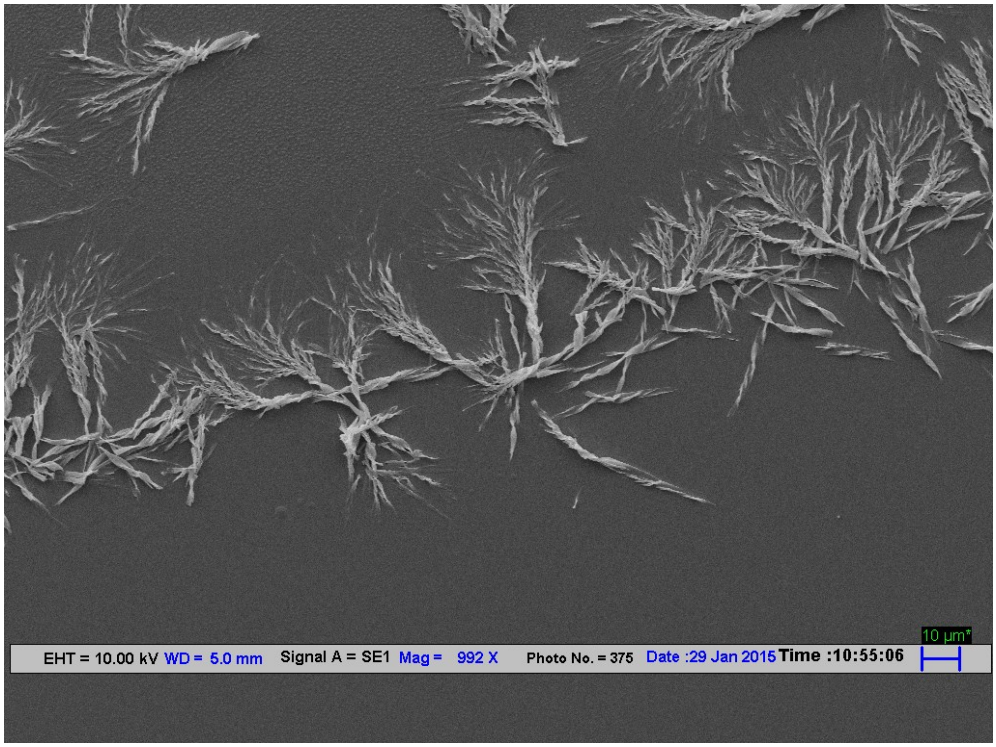


Figure S3: SEM image of **L-A1** showing the partially formed dendritic structures.

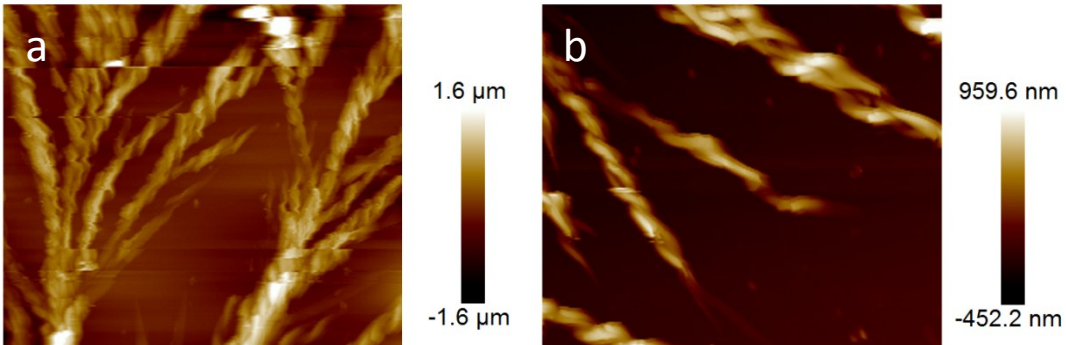


Figure S4: AFM image of **L-A1** a) part of a dendrite b) zoomed image of twisted-ribbons (c) AFM cross sectional analysis of **L-A1**

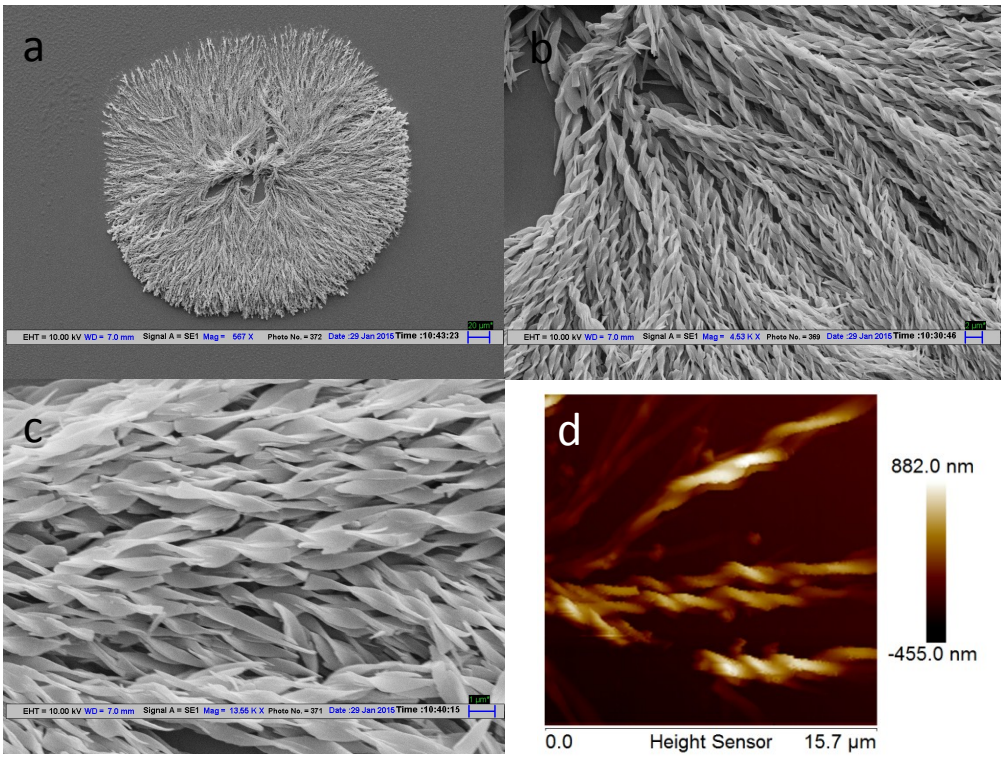


Figure S5: SEM image of **D-A1** (1 mM in methanol) (a) zoomed out image of a part of dendritic structure (b-c) magnified image of a dendritic structure showing intertwined twisted-ribbons. d) AFM image of **D-A1** showing the right handed twisted-ribbons. Scale bar (a) 20 µm (b) 2 µm (c) 1 µm

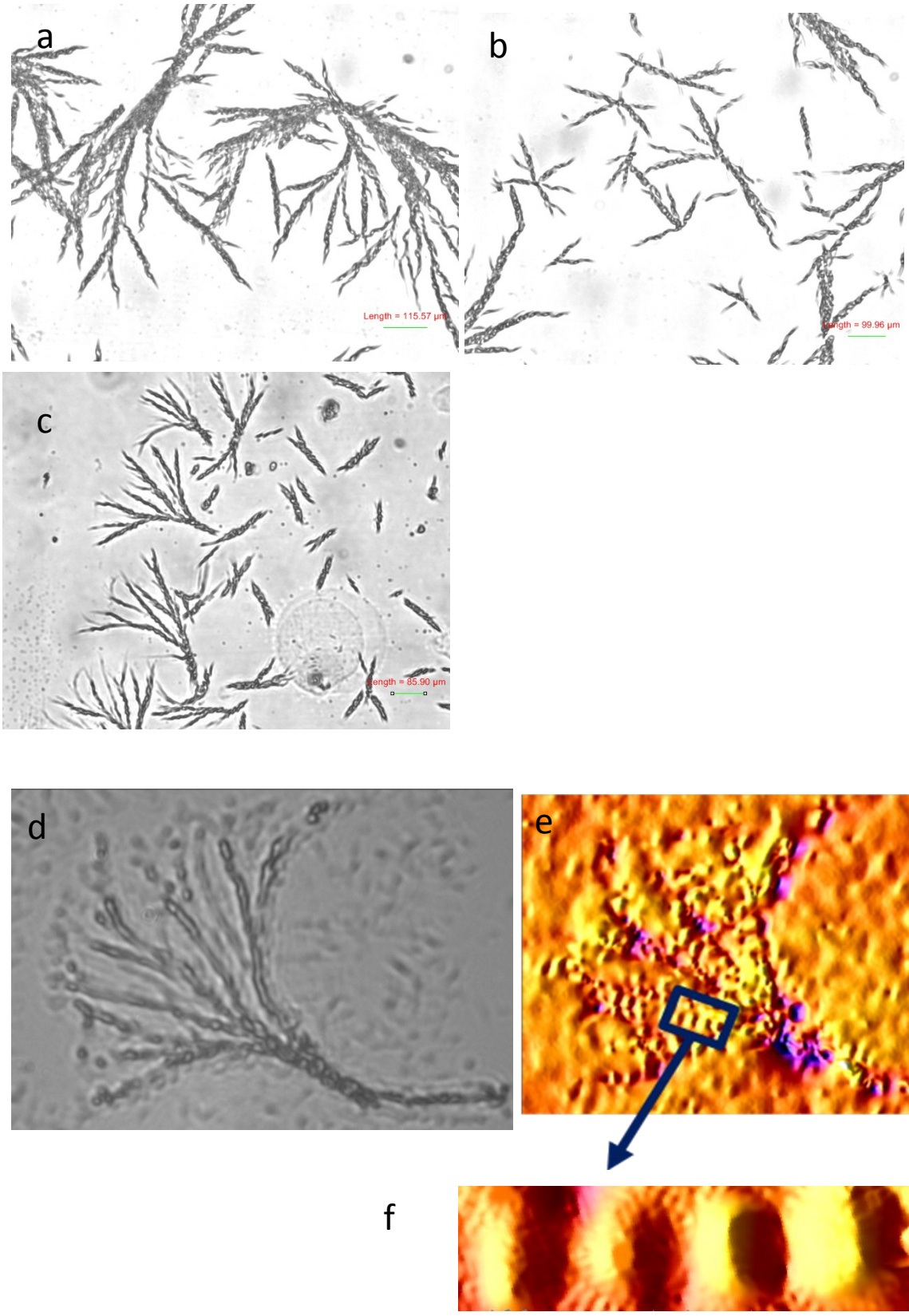


Figure S6: Optical microscopic (magnigication 100x) images of (a-b) **L-A1** (c) **D-A1** (d) Optical microscopic (40x) and (e) corresponding DHM micrographs of **L-A1** (f) zoomed view of (e)

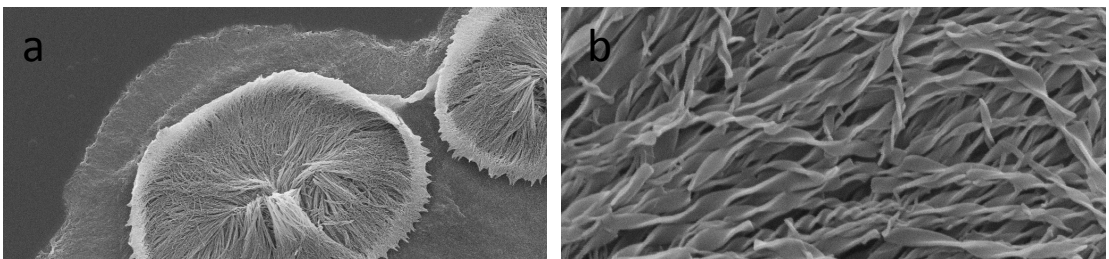


Figure S7: SEM image of **L-A2** (1 mM, Methanol) (a) Lower magnified image showing two distinct regions; Region 1 and region 2 (b) magnified image of region 1 (c) magnified image of **L-A2 (**region 2) (d) SEM image of **D-A2** (region 1) in methanol (e) magnified image of **L-A2 (**region 2) (1 mM) Scale bar (a) 3 µm (b) 300 nm (c) 200 nm (d) 1 µm (e) 300 nm

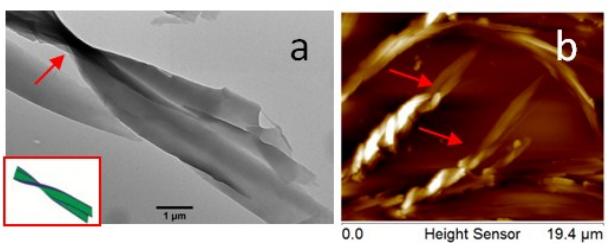


Figure S8: (a) HR-TEM image and (b) AFM image of peripheral regions of dendrite from **L-A1**, showing the coexistence of flat-ribbons and twisted-ribbons with left-handed helical sense. The arrow indicates the region where two flat ribbons fuse together. Inset shows a pictorial representation of twisted ribbon. (c) Height image showing the twisted region (green) and flat region (red)

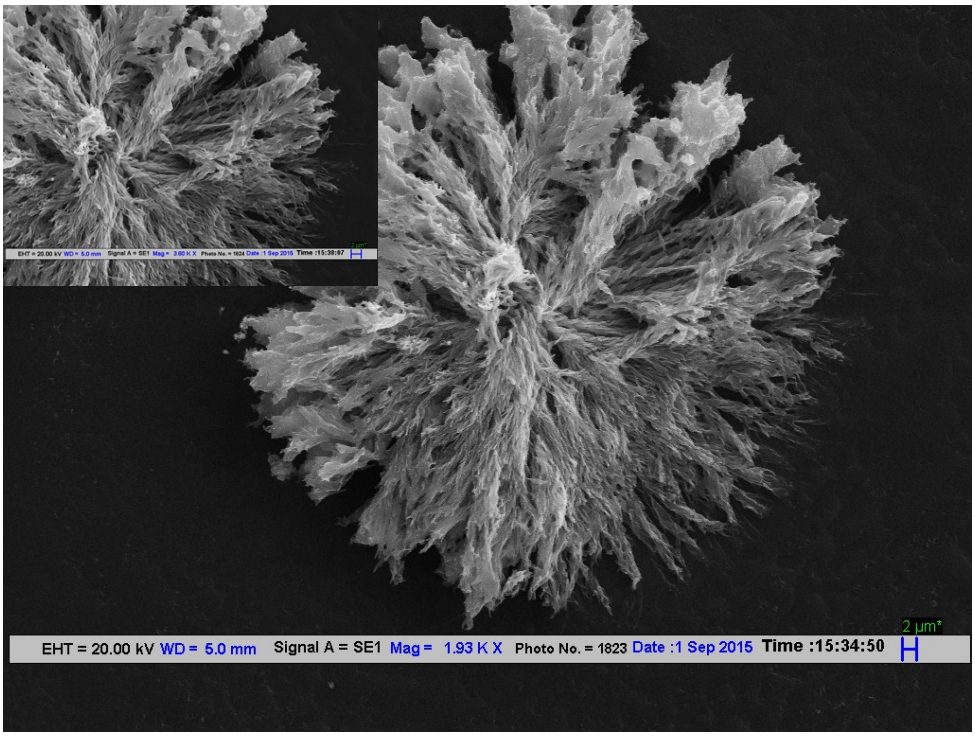


Figure S9: Dendritic structure obtained from an aged methanolic solution (8 months) of **L-A1**. Inset shows the magnified image of the dendritic structure, showing left-handed twisted ribbons (Scale bar 2 µm).

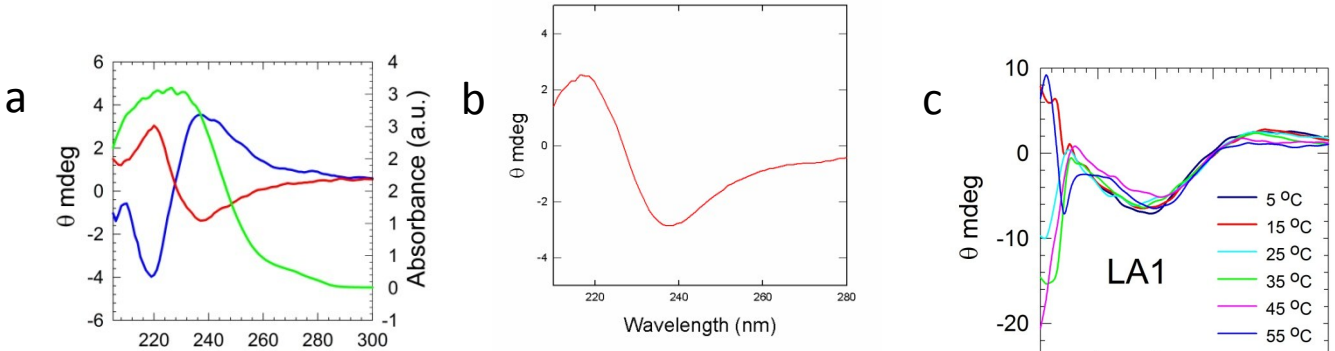


Figure S10: (a) UV (green) and CD spectra of **L-A1** (blue) and CD spectrum of **D-A1** (red) (b) CD spectrum of **D-A2** (c) Temperature-dependent CD spectrum of **L-A1**.

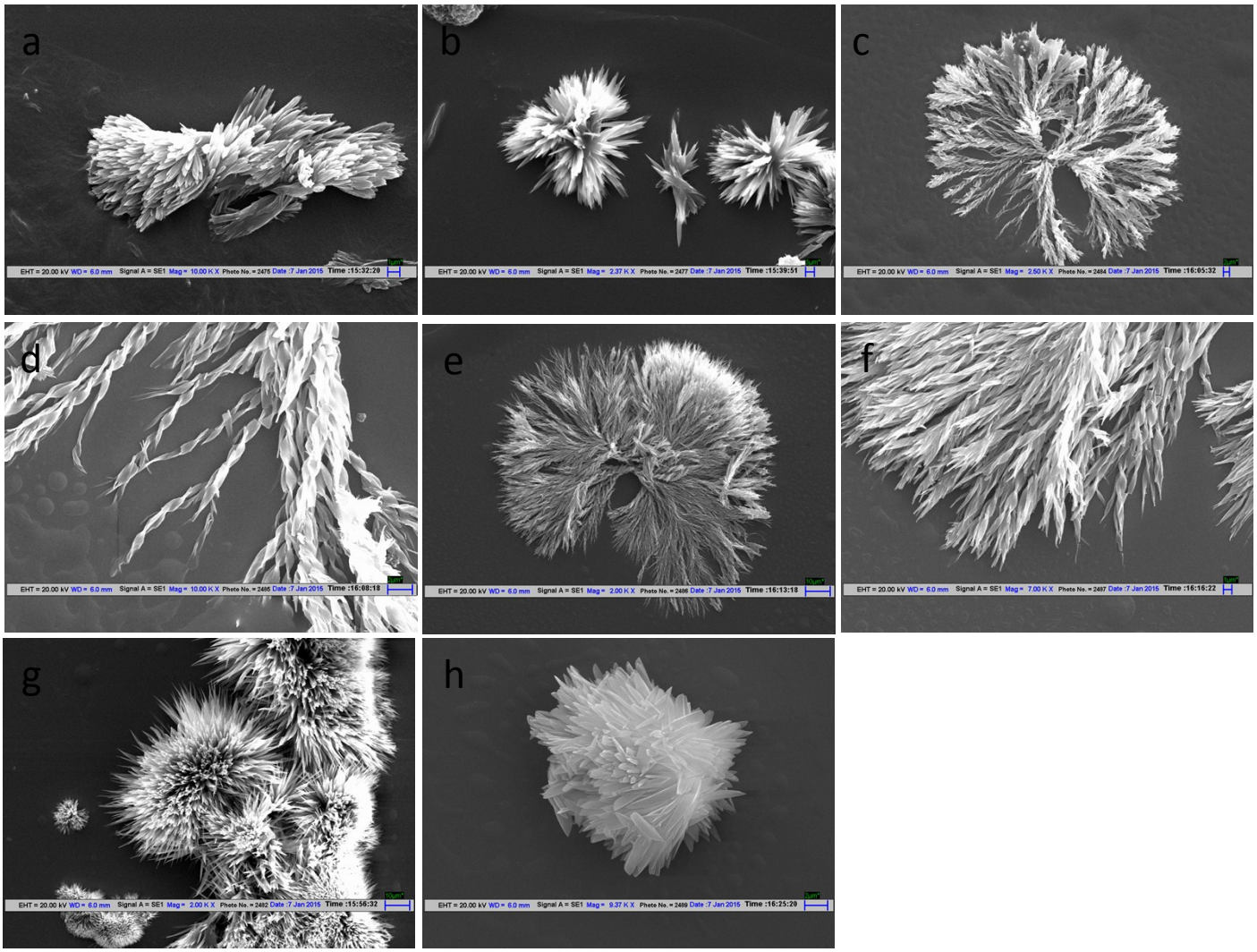


Figure S11: SEM images of (a) **L-A1** in THF (Scale bar 1μm) (b) **L-A1** in EtOAc (Scale bar 3 μm) (c-d) **L-A1** in $CHCl_3$:CH_3OH at low (c) and high (d) magnification; (Scale bar 2 μm) (e-f) **L-A1** in ethanol; (Scale bar for (e) 10 μm and (f) 1 μm) (g) **L-A1** in CH_3CN; (Scale bar 10 μm) (h) **L-A1** in isopropanol; (Scale bar 2 μm)

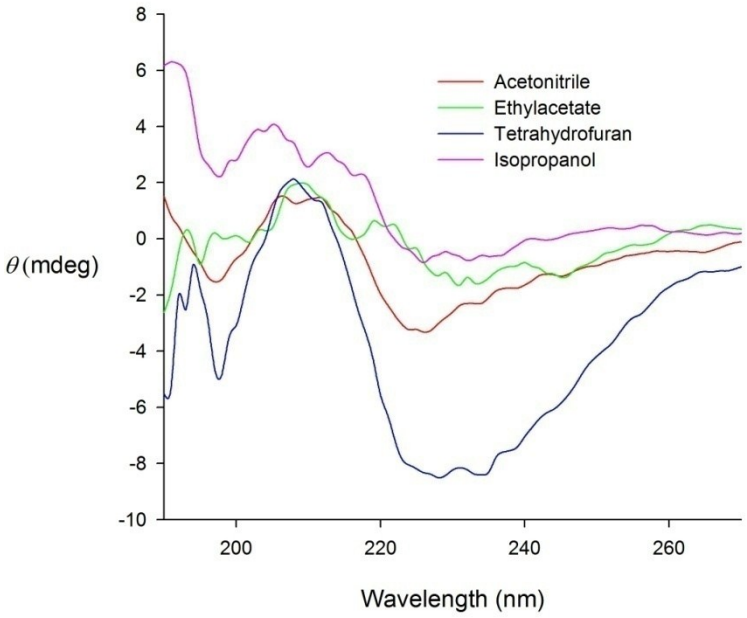


Figure S12: CD spectra of **L-A1** in various solvents.

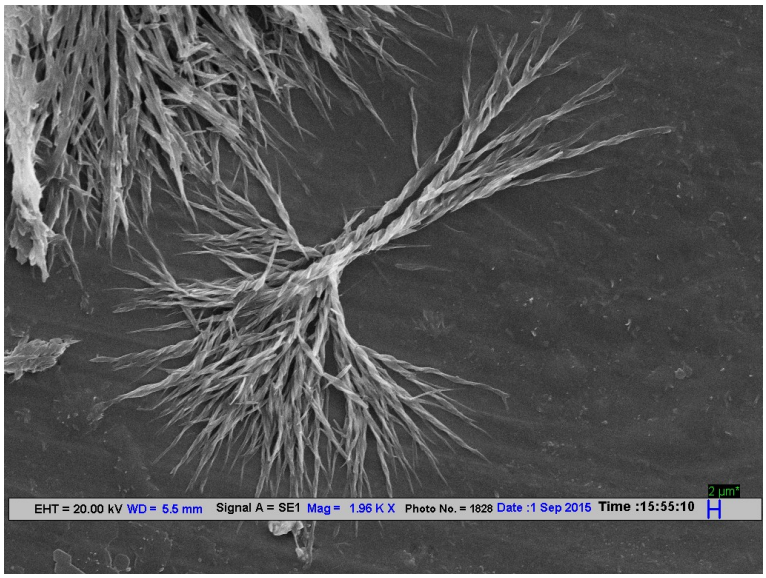


Figure S13: SEM image **L-A1** (1 mM, Methanol) on aluminium sheet showing of dendritic structure.

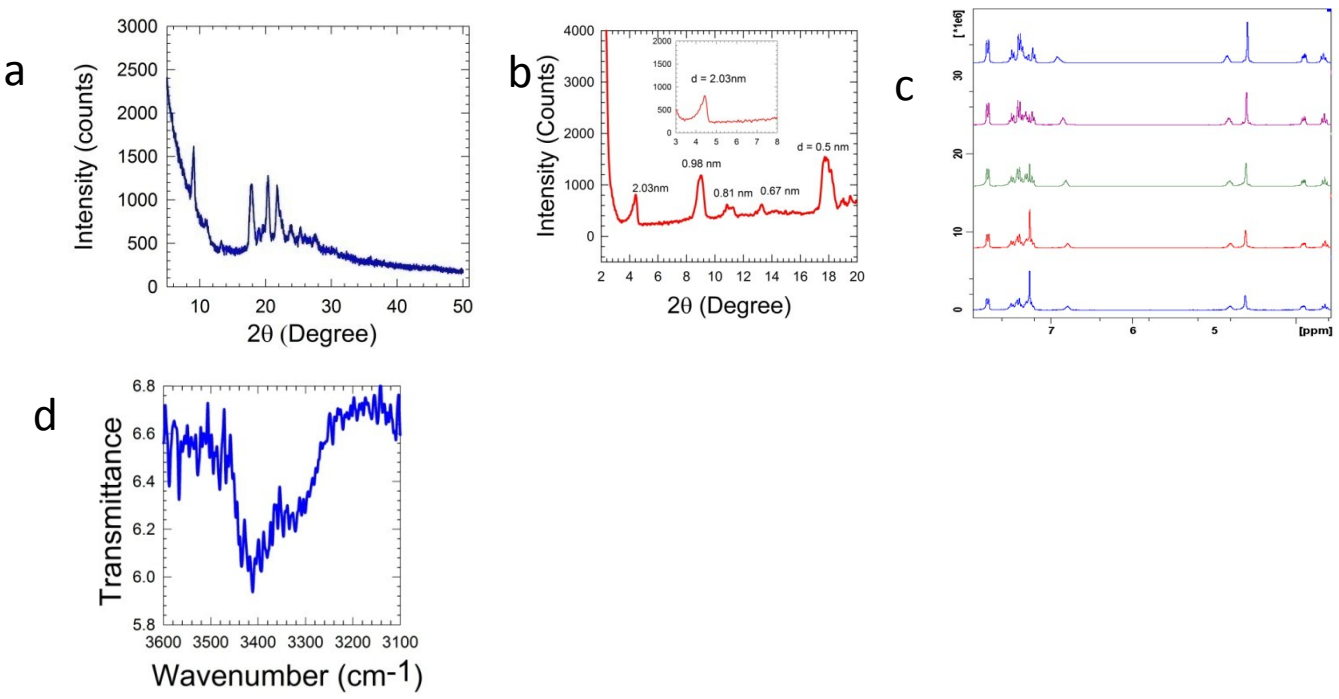


Figure S14: (a) PXRD profile of **L-A1** (b) Low angle PXRD profile of **L-A1** (c) Concentration-dependent ^{1}H NMR spectra of **L-A1** (6.5 mM, 7.6 mM, 21.8 mM, 51 mM, 76.5 mM from bottom to top) (d) Solution IR spectrum of **L-A1** in $CHCl_3$

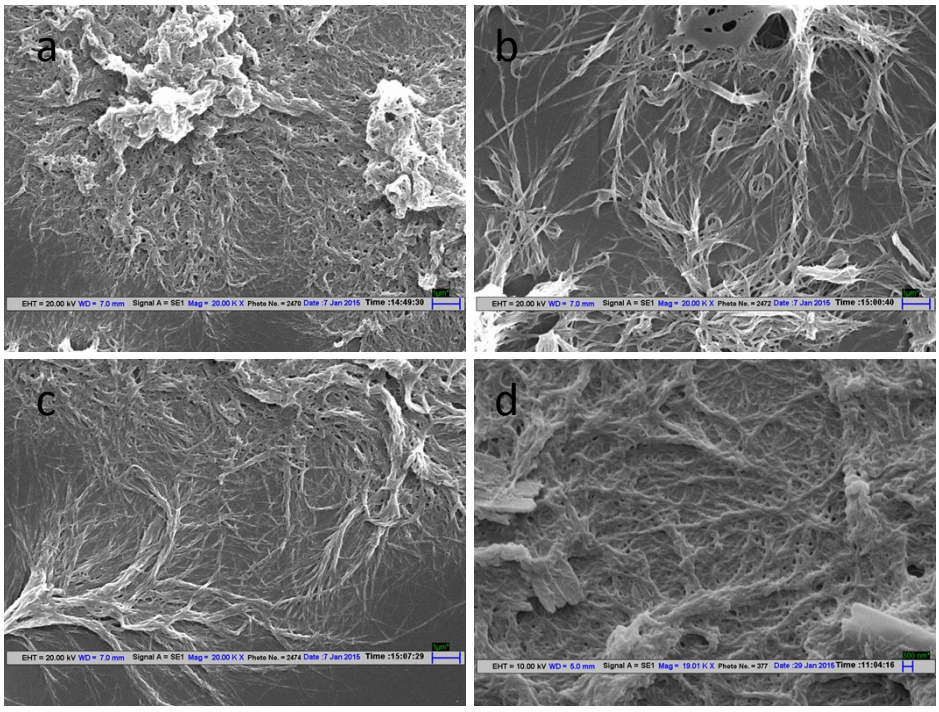


Figure S15: (a) **L-A6** in CH_3OH; (Scale bar 1μm) (b) **L-A7** in CH_3OH; (Scale bar 1 μm) (c) **L-A8** in CH_3OH; (Scale bar 1 μm) (d) **L-A9** in CH_3OH; (Scale bar 300 nm)

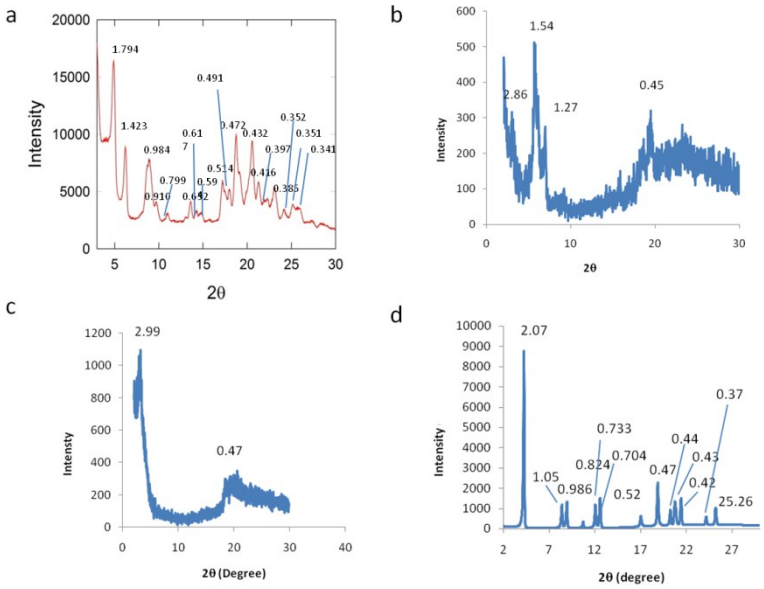


Figure S16: Powder xrd patterns of (a) **L-A2** (c) **L-A3** (c) **L-A4** (d) **L-A5**

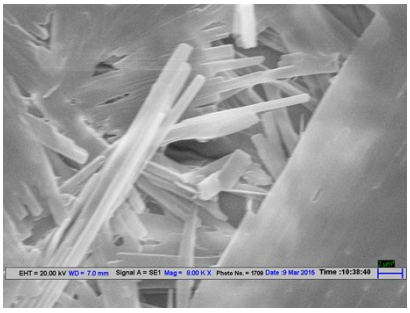
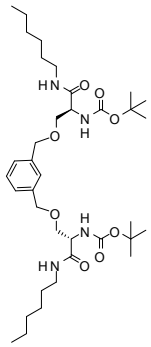


Figure S17: SEM image of 1mM solution of **L-A5** in methanol. Scale bar 2 μm.

Synthesis and characterization of compounds

Compound **L-S1**



To an ice cooled and well stirred solution of **L-P1** (1.03 g, 3.57 mmol) in CH_2Cl_2 (150 mL), added $NaOH_{(aq)}$ (8 mL), and TBABr (0.20 g, 0.62 mmol). *m*-Xylylene dibromide (0.47 g, 1.78 mmol) was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was washed several times with water and the organic layer was dried over anhyd. Na_2SO_4 and evaporated to yield crude product. The crude mixture was chromatographed over a short column of silicagel (230-400 mesh) using EtOAc: Hexane (1:3) to yield 0.4 g of **L-S1**.

% Yield: 33 %

Appearance: White solid

Melting point: 105 ^oC

$[\alpha]_D$: 2.97 (c = 0.010)

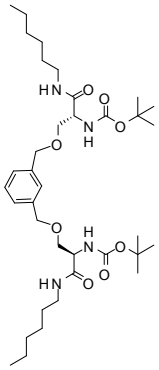
^{1}H NMR (300MHz, $CDCl_3$): δ 0.87 (br t, 6H, C*H*$_3$CH$_2$-), 1.26 (br m, 12H, CH$_3$(C*H*$_2$)$_3$-), 1.44 (s + m, 22H, -C(C*H*$_3$)$_3$+ -NHCH$_2$C*H*$_2$-), 3.24 (m, 4H, -NHC*H*$_2$CH$_2$-), 3.56 (m, 2H, Ser C*H*$_2$-), 3.89 (dd, J_1 = 3.9 Hz, J_2 = 9.3 Hz, 2H, Ser C*H*$_2$-), 4.25 (br s, 2H, -NHC*H*C=O), 4.56 (m, 4H, ArC*H*$_2$-), 5.45 (s, 2H, -N*H*Boc), 6.49 (br s, 2H, -N*H*CH$_2$),7.20-7.35 (m, 4H, Ar*H*).

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 28.3, 29.4, 31.4, 39.6, 54.1, 69.9, 73.1, 80.2, 126.8, 127.1, 128.6, 137.9, 155.5, 170.1

IR (KBr): 3333, 2929, 2859, 1691, 1654, 1529, 1460, 1367, 1304, 1244, 1169, 1121, 1055 cm^{-1}

HRMS calcd for $C_{36}H_{62}N_4NaO_8Na$ m/z = 701.4465, obtained m/z = 701.4488.

Compound **D-S1**



To an ice cooled and well stirred solution of **D-P1** (2.63 g, 9.13 mmol) in CH_2Cl_2 (100 mL), added $NaOH_{(aq)}$ (8 mL), and TBABr (0.400 g, 1.24 mmol). *m*-Xylylene dibromide (1.20 g, 4.55 mmol) was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was washed several times with water and the organic layer was dried over anhyd. Na_2SO_4 and evaporated to yield 3.2 g of crude mixture. The crude mixture was chromatographed over a short column of silicagel (230-400 mesh) using EtOAc: Hexane (2:3) to yield 1.2 g of **D-S1**.

% Yield: 39 %

Appearance: White solid

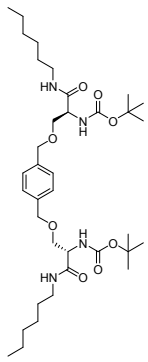
Melting point: 106 ^{o}C

$[\alpha]_D$: -4.9 (c = 0.0103)

^{1}H NMR (300MHz, $CDCl_3$): δ 0.86 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.26 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.44 (s + m, 22 H, -C(C$\underline{H}_3$)$_3$ + -NHCH$_2$C$\underline{H}_2$-), 3.25 (m, 4H, -NHC$\underline{H}_2$CH$_2$-), 3.56 (m, 2H, Ser C$\underline{H}_2$-), 3.89 (dd, J_1 = 3.9 Hz, J_2 = 9.2 Hz, 2H, Ser C$\underline{H}_2$-), 4.25 (br s, 2H, -NHC$\underline{H}$C=O), 4.54 (m, 4H, ArC$\underline{H}_2$-), 5.44 (s, 2H, -N$\underline{H}$Boc), 6.48 (br s, 2H, -N$\underline{H}$CH$_2$),7.15-7.4 (m, 4H, Ar$\underline{H}$).

IR (KBr): 3335, 3071, 2960, 2930, 2859, 1690, 1654, 1527, 1464, 1365, 1303, 1274, 1242, 1170, 1121, 1054, 1025 cm^{-1}

Compound **L-S2**



To an ice cooled and well stirred solution of **L-P1** (2.02 g, 7.01 mmol) in CH_2Cl_2 (100 mL), added $NaOH_{(aq)}$ (6 mL), and TBABr (0.3 g, 0.93 mmol). *p*-Xylylene dibromide (0.925 g, 3.5 mmol) was added and the reaction mixture was stirred at room temperature for 18h. The reaction mixture was washed several times with water and the organic layer was dried over anhyd. Na_2SO_4 and evaporated to yield 1.7 g of the crude product. The crude mixture was chromatographed over a short column of silicagel (100-200 mesh) using EtOAc: Hexane (1:3) to yield 0.469 g of **L-S2**.

% Yield: 19.7 %

Appearance: White solid

Melting point: 101-102 ^{o}C

$[\alpha]_D$: 2.86 (c = 0.0105)

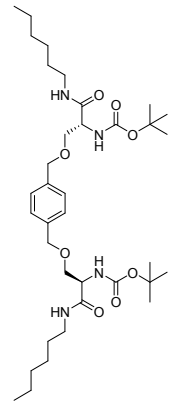
^{1}H NMR (300MHz, $CDCl_3$): δ 0.88 (m, 6H, C$\underline{H}_3$CH$_2$-), 1.29 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.46 (s + m, 22H, -C(C$\underline{H}_3$)$_3$ + -NHCH$_2$C$\underline{H}_2$-), 3.27 (m, 4H, -NHC$\underline{H}_2$CH$_2$-), 3.58 (dd, J_1 = 6.6 Hz, J_2 = 9 Hz, 2H, Ser C$\underline{H}_2$-), 3.92 (dd, J_1 = 3.9 Hz, J_2 = 9.3 Hz, 2H, Ser C$\underline{H}_2$-), 4.25 (br s, 2H, -NHC$\underline{H}$C=O), 4.55 (q, 4H, J = 7.2 Hz, ArC$\underline{H}_2$-), 5.39 (br s, 2H, -N$\underline{H}$ Boc), 6.41 (br s, 2H, -N$\underline{H}$CH$_2$), 7.28 (s, 4H, Ar$\underline{H}$)

^{13}CNMR (75MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 28.3, 29.5, 31.4, 39.6, 54.1, 70.0, 73.2, 80.3, 127.9, 137.3, 155.5, 170.0

IR (KBr): 3333, 2928, 2854, 1688, 1659, 1627, 1574, 1530, 1459, 1367, 1306, 1243, 1169, 1112, 1048 cm^{-1}

HRMS calcd for $C_{36}H_{62}N_4O_8Na$ m/z = 701.4465, obtained m/z = 701.4440.

Compound **D-S2**



To an ice cooled and well stirred solution of **D-P1** (1.47 g, 5.10 mmol) in CH_2Cl_2 (75 mL), added $NaOH_{(aq)}$ (4 mL), and TBABr (0.32 g, 1 mmol). *p*-Xylylene dibromide (0.673 g, 2.55 mmol) was added and the reaction mixture was stirred at room temperature for 18h. The reaction mixture was washed several times with water and the organic layer was dried over anhyd. Na_2SO_4 and evaporated to yield 1.76 g of the crude product. The crude mixture was chromatographed over a short column of silicagel (100-200 mesh) using EtOAc: Hexane (1:3) to yield 0.374 g of **D-S2**.

% Yield: 22 %

Appearance: White solid

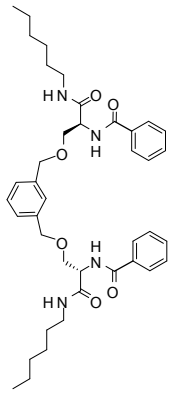
Melting point: 101-102 ^oC

$[\alpha]_D$: - 2.08 (c = 0.0144)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.27 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.45 (s + m, 22H, -NHCH$_2$C$\underline{H}_2$- + -C(C$\underline{H}_3$)$_3$), 3.26 (m, 4H, -NHC$\underline{H}_2$CH$_2$-), 3.57 (dd, J_1 = 6.9 Hz, J_2 = 9 Hz, 2H, Ser C$\underline{H}_2$-), 3.90 (dd, J_1 = 3.9 Hz, J_2 = 9.3 Hz, 2H, Ser C$\underline{H}_2$-), 4.23 (br s, 2H, -NHC$\underline{H}$C=O), 4.53 (q, 4H, J = 7.2 Hz, ArC$\underline{H}_2$-), 5.37 (br s, 2H, -N$\underline{H}$ Boc), 6.38 (br s, 2H, -N$\underline{H}$CH$_2$), 7.27 (s, 4H, Ar$\underline{H}$)

IR (KBr): 3326, 3103, 2927, 2859, 1712, 1657, 1525, 1459, 1365, 1304, 1247, 1168, 1105, 1052 cm^{-1}

Compound **L-A1**



To an ice cooled solution of **L-S1** (0.118 g, 0.173 mmol) in CH_2Cl_2 (0.20 mL), added TFA (0.19 mL, 2.5 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.12 mL, 0.86 mmol) and benzoyl chloride (0.49 g, 0.346 mmol), and left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over anhyd. Na_2SO_4 and evaporated to yield 0.17 g of the crude product. It was then chromatographed over silica gel (60-120 mesh) using EtOAc: Hexane (1:1) to yield 0.05 g of the pure product.

% Yield: 42 %

Appearance: White solid

Melting point: 180 ^oC

$[\alpha]_D$: 15.9 (c = 0.0107)

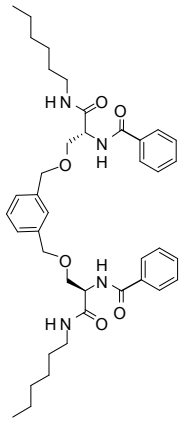
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.25 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.46 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 3.28 (m, 4H, -NHC$\underline{H}_2$-), 3.65 (m, 2H, SerC$\underline{H}_2$-), 3.92 (dd, J_1 = 4.2 Hz, J_2 = 9 Hz, 2H, SerC$\underline{H}_2$-), 4.62 (m, 4H, ArC$\underline{H}_2$-), 4.81 (m, 2H, -NHC$\underline{H}$C=O), 6.80 (br s, 2H, -N$\underline{H}$CH$_2$-), 7.15-7.55 (m, 12H, Ar$\underline{H}$+N$\underline{H}$-), 7.78 (d, J = 7.8 Hz, 4H, Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.7, 69.1, 73.0, 126.7, 127.2, 127.3, 128.5, 128.7, 131.8, 133.6, 138.0, 167.3, 169.9

IR (KBr): 3289, 2928, 2861, 1661, 1637, 1532, 1459, 1352, 1320, 1256, 1156, 1111 cm^{-1}

HRMS calcd for $C_{40}H_{54}N_4O_6Na$ m/z = 709.3941, obtained m/z = 709.3912.

Compound **D-A1**



To an ice cooled solution of **D-S1** (0.20 g, 0.295 mmol) in CH_2Cl_2 (0.3 mL), added TFA (0.3 mL, 4.48 mmol) and left stirred for 4 h. The raction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.21 mL, 1.47 mmol) and benzoyl chloride (0.0829 g, 0.59 mmol), and left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over anhyd. Na_2SO_4 and evaporated to yield 0.150 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: Hexane (3:1) to yield 0.075 g of the pure product.

% Yield: 37 %

Appearance: White solid

Melting point: 180 ^{o}C

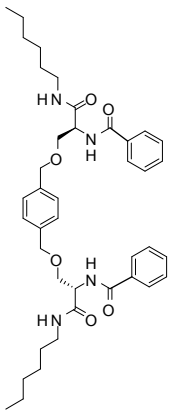
$[\alpha]_D$: -19.38 (c = 0.0108)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.24 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.45 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 3.24 (m, 4H, -NHC$\underline{H}_2$-), 3.67 (m, 2H, SerC$\underline{H}_2$-), 3.90 (dd, J_1 = 4.5 Hz, J_2 = 9 Hz, 2H, SerC$\underline{H}_2$-), 4.60 (m, 4H, ArC$\underline{H}_2$-), 4.85 (br m, 2H, -NHC$\underline{H}$C=O), 6.93 (br s, 2H, -N$\underline{H}$CH$_2$-), 7.15-7.50 (m, 12H, Ar$\underline{H}$+N$\underline{H}$-), 7.78 (d, J = 7.2 Hz, 4H, Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.8, 69.2, 73.0, 126.8, 127.2, 127.3, 128.6, 128.7, 131.8, 133.7, 138.0, 167.3, 169.9

IR (KBr): 3288, 3084, 2928, 2862, 1661, 1637, 1531, 1489, 1459, 1379, 1352, 1320, 1256, 1156, 1111, 1085 cm^{-1}

Compound **L-A2**



To an ice cooled solution of **L-S2** (0.3 g, 0.442 mmol) in CH_2Cl_2 (0.5 mL), added TFA (0.5 mL, 6.52 mmol) and left stirred for 4 h. The reaction mixture then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.19 mL, 1.33 mmol) and benzoyl chloride (0.124 g, 0.88 mmol), and left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected, dried over anhyd. Na_2SO_4 and evaporated to yield 0.187 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: $CHCl_3$ (1:1) to yield 0.137 g of the pure product.

% Yield: 45 %

Apperence: White Solid

Melting point: 190 ^oC

$[\alpha]_D$: 15 (c = 0.006)

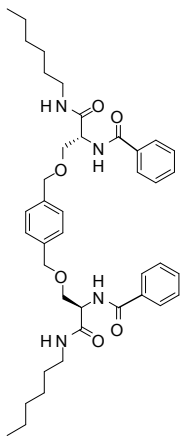
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.28 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.49 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 3.27 (m, 4H, -NHC$\underline{H}_2$-), 3.63 (m, 2H, SerC$\underline{H}_2$-), 4.02 (dd, J_1 = 4.2 Hz, J_2 = 9.3 Hz, 2H, SerC$\underline{H}_2$-), 4.62 (q, J = 6.3 Hz, 4H, ArC$\underline{H}_2$-), 4.74 (m, 2H, -NHC$\underline{H}$C=O), 6.48 (br t, 2H, -N$\underline{H}$CH$_2$-), 7.21 (d, J = 6 Hz, 2H, -N$\underline{H}$-), 7.33 (s, 4H, Ar$\underline{H}$), 7.41-7.6 (m, 6H, Ar$\underline{H}$), 7.82 (d, J = 7.2 Hz, 4H, Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.7, 52.7, 69.5, 73.2, 127.1, 128.0, 128.6, 131.9, 133.6, 137.3, 167.2, 169.8

IR (KBr): 3296, 3091, 2927, 2859, 1661, 1636, 1532, 1463, 1359, 1320, 1252, 1153, 1108 cm^{-1}

HRMS calcd for $C_{40}H_{54}N_4O_6Na$ m/z = 709.3941, obtained m/z = 709.3918.

Compound **D-A2**



To an ice cooled solution of **D-S2** (0.274 g, 0.404 mmol) in CH_2Cl_2 (0.5 mL), added TFA (0.5 mL, 6.52 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.17 mL, 1.213 mmol) and benzoyl chloride (0.113 g, 0.81 mmol), and was left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 0.15 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: $CHCl_3$ (1:1) to yield 0.123 g of the pure product.

% Yield: 44 %

Appearance: White solid

Melting point: 190 ^{o}C

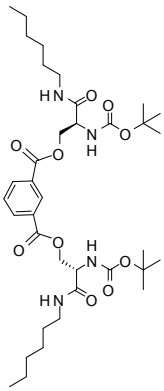
$[\alpha]_D$: -21.69 (c = 0.0083)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.85 (br t, 6H, C<u>*H*</u>$_3$CH$_2$-), 1.26 (br m, 12H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.47 (m, 4H, -NHCH$_2$C<u>*H*</u>$_2$-), 3.27 (m, 4H, -NHC<u>*H*</u>$_2$-), 3.60 (m, 2H, SerC<u>*H*</u>$_2$-), 4.01 (dd, J_1 = 4.2 Hz, J_2 = 9.3 Hz, 2H, SerC<u>*H*</u>$_2$-), 4.61 (q, J = 6.6 Hz, 4H, ArC<u>*H*</u>$_2$-), 4.71 (m, 2H, -NHC<u>*H*</u>C=O), 6.55 (br s, 2H, -N<u>*H*</u>CH$_2$-), 7.18 (d, J = 6 Hz, 2H, N<u>*H*</u>-), 7.31 (s, 4H, Ar<u>*H*</u>), 7.40-7.55 (m, 6H, Ar<u>*H*</u>), 7.8 (d, J = 7.2 Hz, 4H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.7, 69.5, 73.2, 127.1, 128.1, 128.6, 131.9, 133.7, 137.3, 167.2, 169.8

IR (KBr): 3296, 3099, 2927, 2860, 1634, 1532, 1465, 1361, 1319, 1252, 1154, 1108, 1027cm^{-1}

Compound **L-S3**



To an ice cooled solution of **L-P1** (1.24 g, 4.296 mmol), in dry CH_2Cl_2 (50 mL), added DMAP (0.20 g, 1.64 mmol), benzene 1,3 dicarbonyldichloride (0.436 g, 2.148 mmol) and left stirred for 24 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 1.10 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using $CHCl_3$:Methanol (9:1) to yield 0.70 g of the pure product.

% Yield: 46 %

Appearance: White solid

Melting point: 140 ^{o}C

$[\alpha]_D$: 1.65 (c = 0.0121)

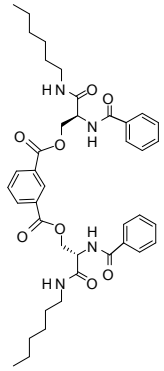
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (br t, 6H, C<u>*H*</u>$_3$CH$_2$-), 1.23 (br m, 12H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.43 (s, 18H, (CH$_3$)$_3$C-), 1.47 (m, 4H, -NHCH$_2$C<u>*H*</u>$_2$-), 3.29 (m, 4H, -NHC<u>*H*</u>$_2$-), 4.58 (m, 6H, SerC<u>*H*</u>$_2$- + -NHC<u>*H*</u>C=O), 5.68 (br s, 2H, -N<u>*H*</u>Boc), 6.73 (br s, 2H, -N<u>*H*</u>CH$_2$-), 7.48 (t, J = 7.5 Hz, 1H, Ar<u>*H*</u>), 8.17 (d, J = 7.8 Hz, 2H, Ar<u>*H*</u>), 8.58 (s, 1H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 22.4, 26.5, 28.3, 29.5, 31.4, 39.8, 53.9, 65.3, 80.6, 128.7, 130.1, 131.1, 134.1, 155.5, 165.3, 168.8

IR (KBr): 3327, 3100, 2930, 2861, 1733, 1655, 1528, 1459, 1368, 1306, 1244, 1168, 1100, 1057 cm^{-1}

HRMS calcd for $C_{36}H_{58}N_4O_{10}Na$ m/z = 729.4051, obtained m/z = 729.4065

Compound **L-A3**



To an ice cooled solution of **L-S3** (0.20 g, 0.28 mmol), added $HCl_{(g)}$ in EtOAc (5 mL) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry THF (50 mL), added DIEA (0.1 mL, 0.577) and benzoyl chloride (0.079g, 0.57 mmol), and was left stirred for 12 h. The precipitated reaction mixture was filtered and washed several times with acetonitrile, ethanol and THF. The resulting residue was dried to yield 0.20 g of the pure product.

% Yield: 99 %

Appearance: White solid

Melting point: 210 ^oC

$[\alpha]_D$: 3.80 (c = 0.0079)

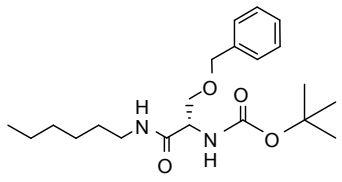
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83 (br t, 6H, C<u>*H*</u>$_3$CH$_2$-), 1.21 (br m, 12H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.46 (m, 4H, -NHCH$_2$C<u>*H*</u>$_2$-), 3.28 (m, 4H, -NHC<u>*H*</u>$_2$-), 4.75 (m, 4H, SerC<u>*H*</u>$_2$-), 5.21 (m, 2H, -NHC<u>*H*</u>C=O), 7.06 (br s, 2H, -N<u>*H*</u>CH$_2$-), 7.35-7.58 (m, 9H, NH + Ar<u>*H*</u>), 7.83 (d, J = 7.2 Hz, 4H, Ar<u>*H*</u>), 8.14 (d, J = 7.8 Hz, 2H, -Ar<u>*H*</u>), 8.61 (s, 1H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, DMSO-*d6*): δ 14.3, 22.4, 26.4, 29.4, 31.4, 52.9, 65.1, 128.0, 128.7, 129.7, 130.5, 130.6, 131.9, 134.2, 134.5, 165.1, 167.1, 168.8.

IR (KBr): 3298, 3072, 2929, 2860, 1732, 1638, 1537, 1487, 1460, 1364, 1297, 1246, 1162, 1100, 1005 cm^{-1}

HRMS calcd for $C_{36}H_{58}N_4O_{10}Na$ m/z = 737.3526, obtained m/z = 737.3500

Compound **L-S4**



To an ice cooled solution of **L-P1** (0.2 g, 0.69 mmol) in CH_2Cl_2 (50 mL), added NaOH solution (6 mL), followed by benzyl bromide and TBABr (0.1 g, 0.31 mmol) and stirred for 12h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 0.5 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: Hexane (1:4) to yield 0.206 g of the pure product.

% Yield: 78 %

Appearance: Viscous liquid

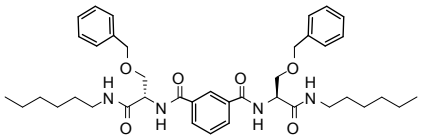
$[\alpha]_D$: 3.42 (c = 0.0117)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (br t, 3H, C<u>*H*</u>$_3$CH$_2$-), 1.26 (br m, 6H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.45 (s+m, 11 H, (CH$_3$)$_3$C- + -NHCH$_2$C<u>*H*</u>$_2$-), 3.25 (m, 2H, -NHC<u>*H*</u>$_2$-), 3.57 (dd, J_1 = 6.6 Hz, J_2 = 9.2 Hz, 1H, SerC<u>*H*</u>$_2$-), 3.90 (dd, J_1 = 3.9 Hz, J_2 = 9.2 Hz, 1H, Ser C<u>*H*</u>$_2$-), 4.23 (br s, 1H, NHC<u>*H*</u>C=O), 4.54 (q, J = 10.8 Hz, 2H, ArC<u>*H*</u>$_2$-), 5.40 (br s, 1H, -N<u>*H*</u>Boc), 6.41 (br s, 1H, -N<u>*H*</u>CH$_2$-), 7.31 (m, 5H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 22.5, 26.4, 28.3, 29.4, 31.4, 39.6, 53.9, 70.0, 73.4, 80.2, 127.7, 127.9, 128.4, 137.5, 155.5, 170.0

IR (KBr): 3341, 3009, 2927, 2858, 2361, 1711, 1662, 1497, 1460, 1367, 1245, 1169, 1111 cm^{-1}

Compound **L-A4**



To an ice cooled solution of **L-S4** (0.274 g, 0.724 mmol) in CH_2Cl_2 (1 mL), added TFA (1 mL, 13.04 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2, added NEt_3 (0.17 mL, 1.213 mmol) and benzene 1,3 dicarbonyldichloride (0.055 g, 0.274 mmol), and left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over anhyd. Na_2SO_4 and evaporated to yield 0.155 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: Hexane (4:2) to yield 0.084 g of the pure product.

% Yield: 45 %

Apperence: White solid

Melting point: 184 ^{o}C

$[\alpha]_D$: 21.84 (c = 0.0087)

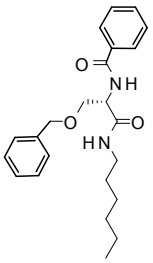
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (br t, 6H, C<u>*H*</u>$_3$CH$_2$-), 1.26 (br m, 12H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.46 (m, 4H, -NHCH$_2$C<u>*H*</u>$_2$-), 3.27 (m, 4H, -NHC<u>*H*</u>$_2$-), 3.61 (m, 2H, SerC<u>*H*</u>$_2$-), 4.00 (dd, J_1 = 3.9 Hz, J_2 = 9.2 Hz, 2H, Ser CH$_2$-) 4.62 (q, J = 14.2 Hz, 4H, ArC<u>*H*</u>$_2$-), 4.72 (m, 2H, -NHC<u>*H*</u>C=O), 6.52 (br t, 2H, -N<u>*H*</u>CH$_2$-), 7.38-7.41 (m, 12H, -N<u>*H*</u> + Ar<u>*H*</u>), 7.51 (t, J = 7.8 Hz, 1H, Ar<u>*H*</u>), 7.95 (d, J = 7.8 Hz, 2H, -Ar<u>*H*</u>), 8.27 (s, 1H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.7, 69.5, 73.6, 125.8, 127.9, 128.1, 128.6, 129.0, 130.4, 134.2, 137.3, 166.3, 169.7

IR (KBr): 3288, 3094, 3036, 2928, 2859, 1642, 1530, 1459, 1361, 1301, 1250, 1114, 1025 cm^{-1}

HRMS calcd for $C_{40}H_{54}N_4O_6Na$ m/z = 709.3941, obtained m/z = 709.3924.

Compound **L-A5**



To an ice cooled solution of **L-S4** (0.208 g, 0.5499 mmol) in CH_2Cl_2 (1mL), added TFA (1mL, 13.04 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.5 mL, 3.59 mmol) and benzoyl chloride (0.077 g, 0.5499 mmol), and reaction mixture was left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 0.250 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: Hexane (1:1) to yield 0.18 g of the pure product.

% Yield: 86 %

Apperence: White solid

Melting point: 116 ^oC

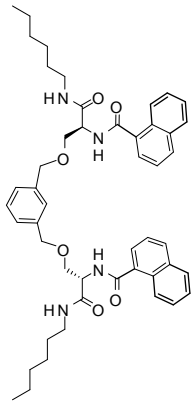
$[\alpha]_D$: 15 (c = 0.010)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (br t, 3H, C$\underline{H}_3$CH$_2$-), 1.26 (br m, 6H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.46 (m, 2H, -NHCH$_2$C$\underline{H}_2$-), 3.30 (m, 2H, -NHC$\underline{H}_2$-), 3.60 (m, 1H, SerC$\underline{H}_2$-), 4.03 (dd, J_1 = 3.9 Hz, J_2 = 9.3 Hz, 1H, Ser C$\underline{H}_2$-), 4.62 (q, J = 16.8, 2H, ArC$\underline{H}_2$-), 4.72 (m, 1H, -NHC$\underline{H}$C=O), 6.51 (br s, 1H, -N$\underline{H}$CH$_2$-), 7.17 (d, J = 5.7 Hz, 1H, ArCON$\underline{H}$), 7.30-7.60 (m, 8H, Ar$\underline{H}$), 7.80 (d, J = 7.5 Hz, 2H, -Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.7, 69.6, 73.5, 127.1, 127.8, 128.0, 128.5, 128.6, 131.8, 133.7, 137.5, 167.2, 169.9

IR (KBr): 3294, 3063, 3036, 2928, 2861, 1952, 1639, 1532, 1457, 1361, 1319, 1252, 1114, 1078, 1027 cm^{-1}

Compound **L-A6**



To an ice cooled solution of **L-S1** (0.20 g, 0.295 mmol) in CH_2Cl_2 (0.3 mL), added TFA (0.3 mL, 3.91 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.12 mL, 0.884 mmol) and 1-naphthoyl chloride (0.112 g, 0.59 mmol), and was left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 0.237 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: $CHCl_3$ (1:1) to yield 0.077 g of the pure product.

% Yield: 33 %

Apperence: White solid

Melting point: 194 ^{o}C

$[\alpha]_D$: 2.08 (c = 0.0098)

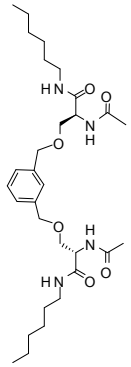
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.21 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.39 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 3.18 (m, 4H, -NHC$\underline{H}_2$-), 3.71 (m, 2H, SerC$\underline{H}_2$-), 3.96 (dd, J_1 = 4.8 Hz, J_2 = 9 Hz, 2H, Ser C$\underline{H}_2$-), 4.61 (q, J = 7.8 Hz, 4H, ArC$\underline{H}_2$-), 4.93 (m, 2H, -NHC$\underline{H}$C=O), 6.91 (br m, 2H, -N$\underline{H}$-), 7.13 (d, J = 7.2 Hz, 2H, -N$\underline{H}$), 7.20-7.63 (m, 12H, Ar$\underline{H}$), 7.85 (m, 4H, Ar$\underline{H}$), 8.27 (m, 2H, Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.3, 31.4, 39.7, 53.0, 69.4, 73.0, 124.6, 125.2, 125.5, 126.4, 126.8, 127.1, 127.2, 128.3, 128.6, 130.1, 131.0, 133.4, 133.6, 138.0, 169.4, 169.6

IR (KBr): 3292, 3050, 2926, 2857, 1938, 1636, 1531, 1462, 1369, 1315, 1253, 1157, 1111, 1023 cm^{-1}

HRMS calcd for $C_{48}H_{58}N_4O_6Na$ m/z = 809.4254, obtained m/z = 809.4248.

Compound **L-A7**



To an ice cooled solution of **L-S1** (0.20 g, 0.295 mmol), in dry in CH_2Cl_2 (0.3 mL) added TFA (0.3 mL, 3.9 mmol) and left stirred for 4 h. The reaction mixture then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.12 mL, 0.884 mmol) and acetyl chloride (0.05 mL, 0.70 mmol), and left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over Anhyd. Na_2SO_4 and evaporated to yield 0.170 g of the crude product. It was then precipitated with acetonitrile to yield 0.135 g of pure product.

% Yield: 81 %

Apperence: White solid

Melting point: 164 ^{o}C

$[\alpha]_D$: 1.00 (c = 0.010)

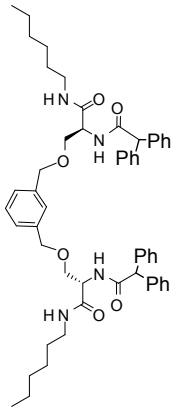
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.26 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.47 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 2.00 (s, 6H, C$\underline{H}_3$C=O), 3.24 (m, 4H, -NHC$\underline{H}_2$-), 3.51 (m, 2H, SerC$\underline{H}_2$-), 3.75 (dd, J_1 = 4.5 Hz, J_2 = 9 Hz, 2H, Ser C$\underline{H}_2$-), 4.50-4.65 (m, 6H, ArC$\underline{H}_2$-+ -NHC$\underline{H}$C=O), 6.72 (br m, 4H, -N$\underline{H}$-), 7.15-7.38 (m, 4H, Ar$\underline{H}$)

^{13}C NMR (75MHz, $CDCl_3$): δ 14.0, 22.5, 23.0, 26.5, 29.3, 31.4, 39.7, 52.7, 69.5, 72.9, 126.7, 127.1, 128.5, 137.9, 170.0, 170.6

IR (KBr): 3290, 3103, 2956, 2928, 2858, 2363, 1640, 1548, 1461, 1376, 1302, 1252, 1158, 1124, 1036 cm^{-1}

HRMS calcd for $C_{30}H_{50}N_4O_6Na$ m/z = 585.3628, obtained m/z = 585.3623.

Compound **L-A8**



To an ice cooled solution of **L-S1** (0.20 g, 0.295 mmol) in CH_2Cl_2 (0.3 mL), added TFA (0.3 mL, 0.39 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (0.12 mL, 0.884 mmol) and diphenylacetyl chloride (0.136g, 0.5896 mmol), and was left stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2, washed with 0.2 N H_2SO_4, saturated $NaHCO_3$ and water. The organic layer was collected dried over anhyd. Na_2SO_4 and evaporated to yield 0.178 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using $CHCl_3$: CH_3OH (95:5) to yield 0.12 g of the pure product.

% Yield: 47 %

Apperence: White solid

Melting point: 194 ^oC

$[\alpha]_D$: -11.34 (c = 0.0097)

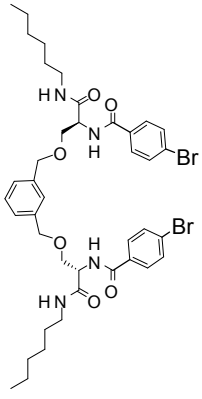
^{1}H NMR (300 MHz, $CDCl_3$):): δ 0.86 (br t, 6H, C<u>*H*</u>$_3$CH$_2$-), 1.24 (br m, 12H, CH$_3$(C<u>*H*</u>$_2$)$_3$-), 1.35 (m, 4H, -NHCH$_2$C<u>*H*</u>$_2$-), 3.15 (m, 4H, -NHC<u>*H*</u>$_2$-), 3.50 (m, 2H, SerC<u>*H*</u>$_2$-), 3.79 (dd, J_1 = 4.8 Hz, J_2 = 8.9 Hz, 2H, Ser CH$_2$-), 4.50 (m, 4H, ArC<u>*H*</u>$_2$-), 4.62 (m, 2H, -NHC<u>*H*</u>C=O), 4.92 (s, 2H, Ar$_2$ C*H*-), 6.51 (br s, 2H, -N<u>*H*</u>CH$_2$-), 6.73 (d, J = 6.6 Hz, 2H, ArCON<u>*H*</u>-), 7.14 (d, J = 7.5 Hz, 2H, Ar<u>*H*</u>), 7.27 (m, 22H, Ar<u>*H*</u>)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.3, 31.4, 39.7, 52.7, 58.8, 69.1, 73.0, 76.6, 126.7, 127.1, 127.3, 128.6, 128.8, 137.9, 139.1, 169.5, 172.1

IR (KBr): 3295, 3063, 2927, 2858, 1641, 1541, 1496, 1455, 1373, 1216, 1159, 1114, 1032 cm^{-1}

HRMS calcd for $C_{54}H_{66}N_4O_6Na$ m/z = 889.4880, obtained m/z = 889.4864.

Compound **L-A9**



To an ice cooled solution of **L-S1** (0.3 g, 0.442 mmol) in CH_2Cl_2 (0.3 mL), added TFA (0.3 mL, 0.39 mmol) and left stirred for 4 h. The reaction mixture was then evaporated and the resulting amine was dissolved in dry CH_2Cl_2 (50 mL), added NEt_3 (1.23 mL, 8.84 mmol) and freshly prepared p-bromobenzoyl chloride (0.192 g, 0.8844 mmol), and was left stirred for 12 h. The reaction mixture was diluted, washed with

0.2 N H_2SO_4, $NaHCO_3$ and water. The organic layer was collected dried over anhyd. Na_2SO_4 and evaporated to yield 0.47 g of the crude product. It was then chromatographed over silica gel (100-200 mesh) using EtOAc: Hexane (3:2) to yield 0.17 g of the pure product.

% Yield: 46 %

Appearance: White solid

Melting point: 190 ^oC

$[\alpha]_D$: 17.14 (c = 0.0105)

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (br t, 6H, C$\underline{H}_3$CH$_2$-), 1.25 (br m, 12H, CH$_3$(C$\underline{H}_2$)$_3$-), 1.46 (m, 4H, -NHCH$_2$C$\underline{H}_2$-), 3.25 (m, 4H, -NHC$\underline{H}_2$-), 3.62 (m, 2H, SerC$\underline{H}_2$-), 3.85 (dd, J_1 = 4.5 Hz, J_2 = 8.9 Hz, 2H, Ser C$\underline{H}_2$-), 4.62 (m, 4H, ArC$\underline{H}_2$-), 4.78 (m, 2H, -NHC$\underline{H}$C=O), 6.76 (br m, 2H, -N$\underline{H}$-), 7.15-7.7 (m, 14H, -N$\underline{H}$+ Ar$\underline{H}$)

^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 22.5, 26.5, 29.4, 31.4, 39.8, 52.8, 69.1, 73.0, 126.5, 126.7, 127.3, 128.7, 128.8, 131.7, 132.5, 137.9, 166.4, 169.9

IR (KBr): 3296, 2928, 2860, 1635, 1593, 1539, 1479, 1364, 1160, 1115, 1012 cm^{-1}

HRMS calcd for $C_{40}H_{52}Br_2N_4O_6Na$ m/z = 865.2151, obtained m/z = 865.2166.

MD simulations

Molecular dynamics simulations

We generated several initial conformations of **L-A1**, **L-A2** and **L-A3** using Accelerys Discovery suite software and performed MD on energetically best structures. MD simulations were performed at Supercomputing Facility (SCFBio) at Indian Institute of technology Delhi. The AMBER 12 package was used for performing Molecular Dynamics (MD) simulations. Molecules were solvated in CH_3OH in an octahedron box of solvent. The energy minimization and MD simulations of **L-A1-L-A3** were carried out with the aid of the SANDER module of the AMBER 12 program.[4] The simulation was first affected with 1000 step minimization using the steepest descent algorithm followed by a 2000 step minimization using conjugate gradient to remove bad steric contacts. Topology and parameter files for the **L-A1–L-A3** were prepared using the model developed by Cornell et al.[5] Then the system was allowed to equilibrate with methanol molecules at 300 K followed by the equilibration of **L-A1–L-A3** and slowly heating from T = 10 to 300 K for 1ns. The system was then equilibrated at 300 K for 300 ps.

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