Poly(phenylacetylene) amines: A general route to water soluble helical polyamines

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Supporting Information

Contents:

1. Materials and Methods

CD measurements were done in a Jasco-720.

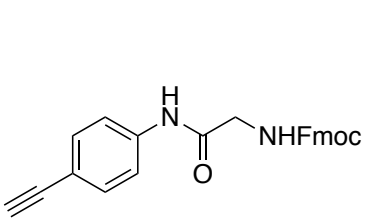
UV spectra were registered in a Jasco V-630.

Raman spectra were carried out in a Renishaw confocal Raman spectrometer (Invia Reflex model), equipped with two lasers (diode laser 785 nm and Ar laser 514 nm).

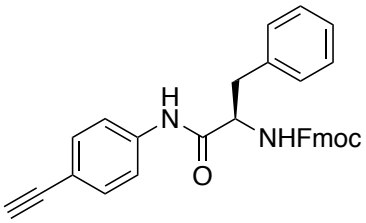
GPC studies were carried out in a Waters Alliance equipped with Phenomenex GPC columns. The amount of polymer used for GPC measurements was 0.5 mg/mL.

NMR experiments were measured in a Varian 300 operating at 300 MHz for proton NMR, 282 MHz for fluorine and 75 MHz for carbon. TMS signal (δ= 0 ppm) was used as internal reference for ^{1}H NMR experiments; $CDCl_3$ signal (δ= 77.2 ppm) or DMSO-d_6 (δ= 39.5 ppm) was used as standard for ^{13}C experiments.

Synthesis of Fmoc protected monomers:



(1)



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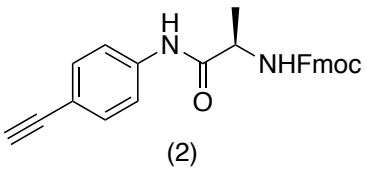

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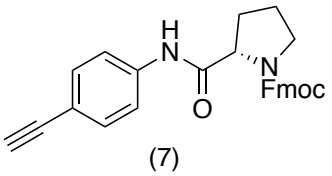

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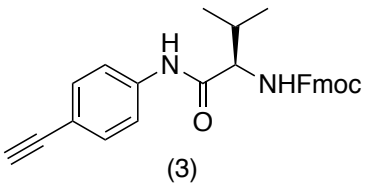

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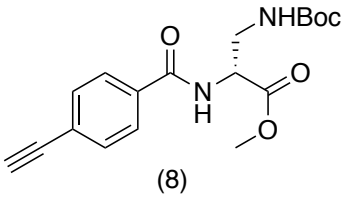

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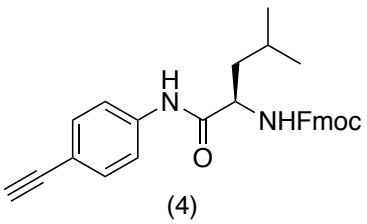

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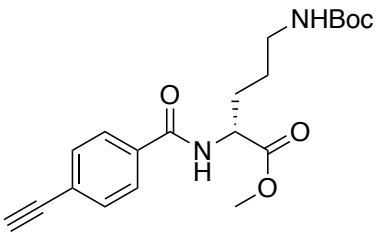

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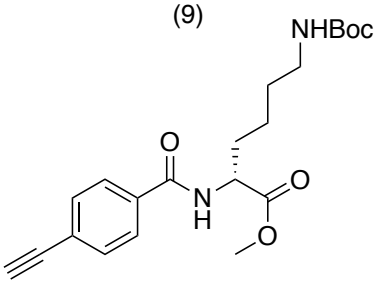

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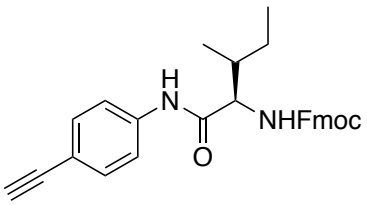

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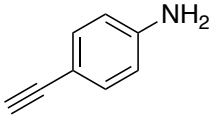


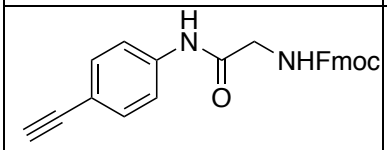
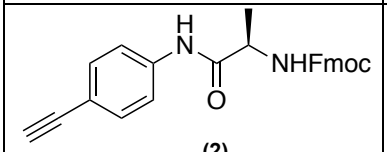
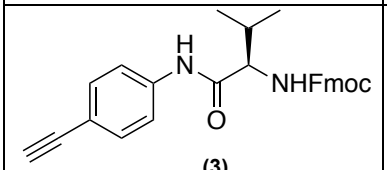
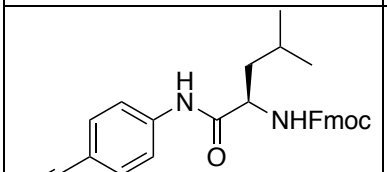
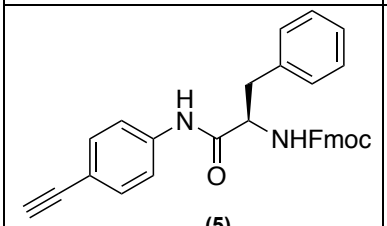
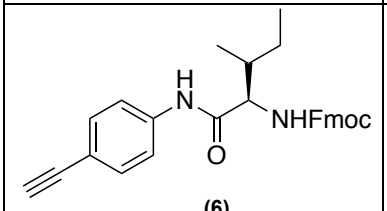
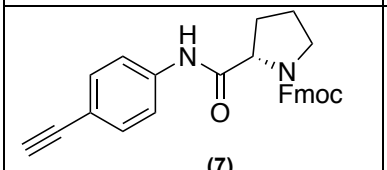
(11)

Figure S1. Structure of Fmoc and Boc protected monomers (1-10), and 4-ethynylaniline (11).

Synthetic procedure of intermediates derivated from 4-ethynylaniline (1, 2, 3, 5, 6, 7).

2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium (HATU, 1.2 equiv.), 1-hydroxy-7-azabenzotriazole (HOAt, 1.2 equiv.), Fmoc-protected aminoacid (1 g, 1.2 equiv.) and diisopropyltriethylamine (DIEA, 1 mL, 1.4 equiv.) were dissolved in dry CH_2Cl_2, and the mixture was stirred for 15 min to activate the acid. Then, 4-ethynylaniline (1.0 equiv.) was added and the reaction mixture was stirred overnight. Then, the organic layer was washed with HCl 1M and brine. The combined organic layers were dried over anhydride Na_2SO_4, filtered and the solvent was evaporated at reduced pressure. The crude product was chromatographed on silica gel (70-230 mesh) with hexane/ethyl acetate (7/3) as eluent.

Table S1. Protected Fmoc compounds (**1**-**7**).

Compound	Fmoc-protected aminoacid	HATU	HOAt	DIEA	4-ethynylaniline	DCM / mL	mg (η %)
 **(1)**	1.00 g	1.28 g (3.36 mmol)	457 mg (3.36 mmol)	0.68 mL (3.39 mmol)	329 mg (2.80 mmol)	28	876 mg (79%)
 **(2)**	1.00 g	1.22 g (3.21 mmol)	437 mg (3.21 mmol)	0.65 mL (3.7474 mmol)	315 mg (2.68 mmol)	27	781 mg (71 %)
 **(3)**	1.00 g	1.12 g (2.95 mmol)	401 mg (2.95 mmol)	0.60 mL (3.44 mmol)	287 mg (2.45 mmol)	25	902 mg (84 %)
 **(4)**	1.00 g	1.08 g (2.83 mmol)	385 mg (2.82 mmol)	0.57 mL (3.30 mmol)	277 mg (2.35 mmol)	24	821 (77%)
 **(5)**	1.00 g	0.98 g (2.58 mmol)	351 mg (2.58 mmol)	0.52 mL (3.01 mmol)	252 mg (2.15 mmol)	22	774 (74%)
 **(6)**	1.00 g	1.08 g (2.83 mmol)	385 mg (2.82 mmol)	0.57 mL (3.30 mmol)	277 mg (2.35 mmol)	24	864 (81%)
 **(7)**	1.00 g	1.13 g (2.96 mmol)	402 mg (2.96 mmol)	0.60 mL (3.45 mmol)	290 mg (2.47 mmol)	25	765 (71%)

(9*H*-fluoren-9-yl)methyl (2-((4-ethynylphenyl)amino)-2-oxoethyl)carbamate (1):

^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 3.80 (d, 2H), 4.05 (s, 1H), 4.2 (m, 1H), 4.28 (m, 2H), 7.32 (m, 5H), 7.60 (m, 3H), 7.72 (d, 2H), 7.87 (d, 2H), 10.14 (s, 1H). ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 49.3, 51.8, 71.0, 85.0, 88.8, 121.3, 124.1, 125.3, 130.4, 132.3, 132.8, 137.6, 144.7, 145.9, 149.0, 161.8, 173.5.

HRMS (ESI) m/z calcd for $C_{25}H_{20}N_2O_3$ [M+H] 396.1474, found 397.1697.

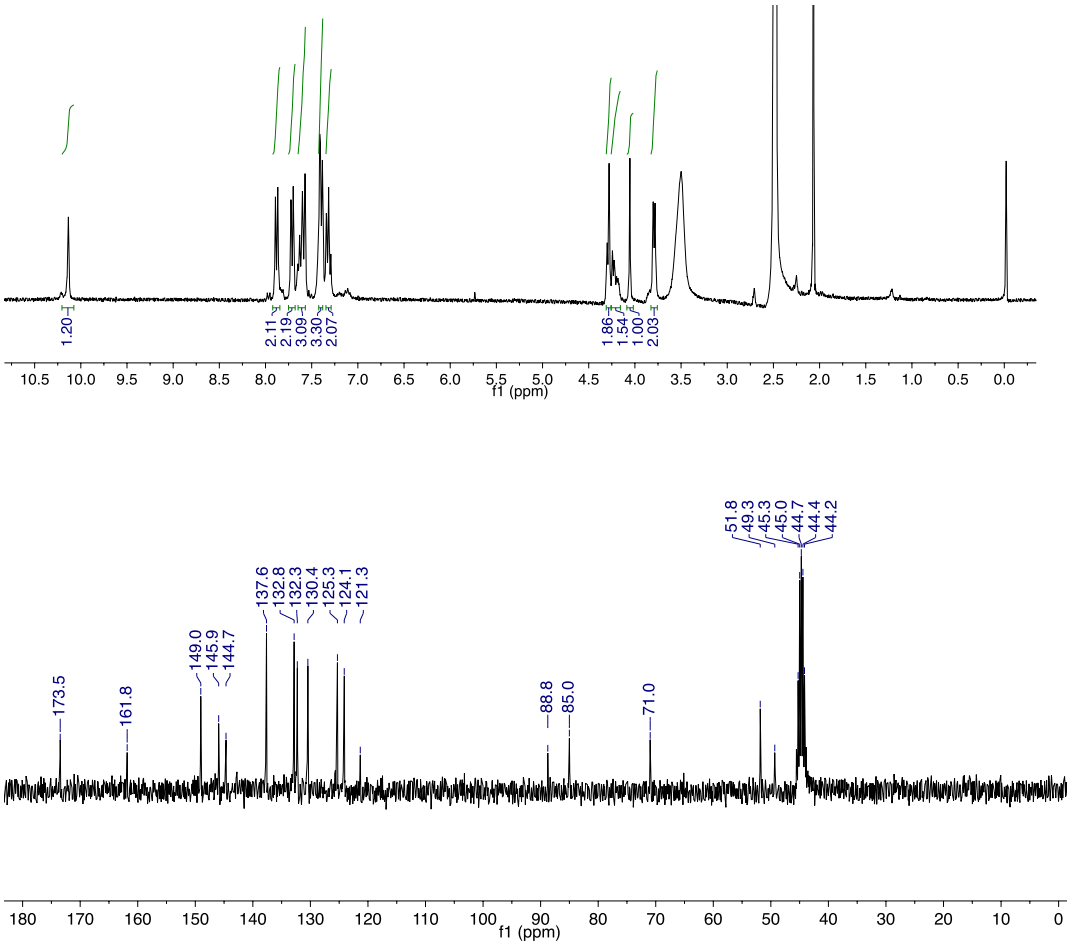


Figure S2. ^{1}H-NMR and ^{13}C-NMR of **1** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl (*S*)-(1-((4-ethynylphenyl)amino)-1-oxopropan-2-yl)carbamate (2):

^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 4.06 (s, 1H), 4.22 (m, 2H), 4.29 (m, 2H), 7.30-7.43 (m, 6H), 7.63 (d, 2H), 7.75 (m, 1H), 7.86 (d, 2H), 10.17 (s, 1H). ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 23.1, 51.9, 55.9, 70.9, 85.0, 88.8, 121.4, 124.1, 125.3, 130.5, 132.3, 132.8, 137.6, 144.7, 145.9, 149.0, 161.0, 177.0.

HRMS (ESI) m/z calcd for $C_{26}H_{22}N_2O_3$ [M+H] 410.1630, found 411.1702.

$[\alpha]_D$= -46 (c= 15 mg/mL, DMSO).

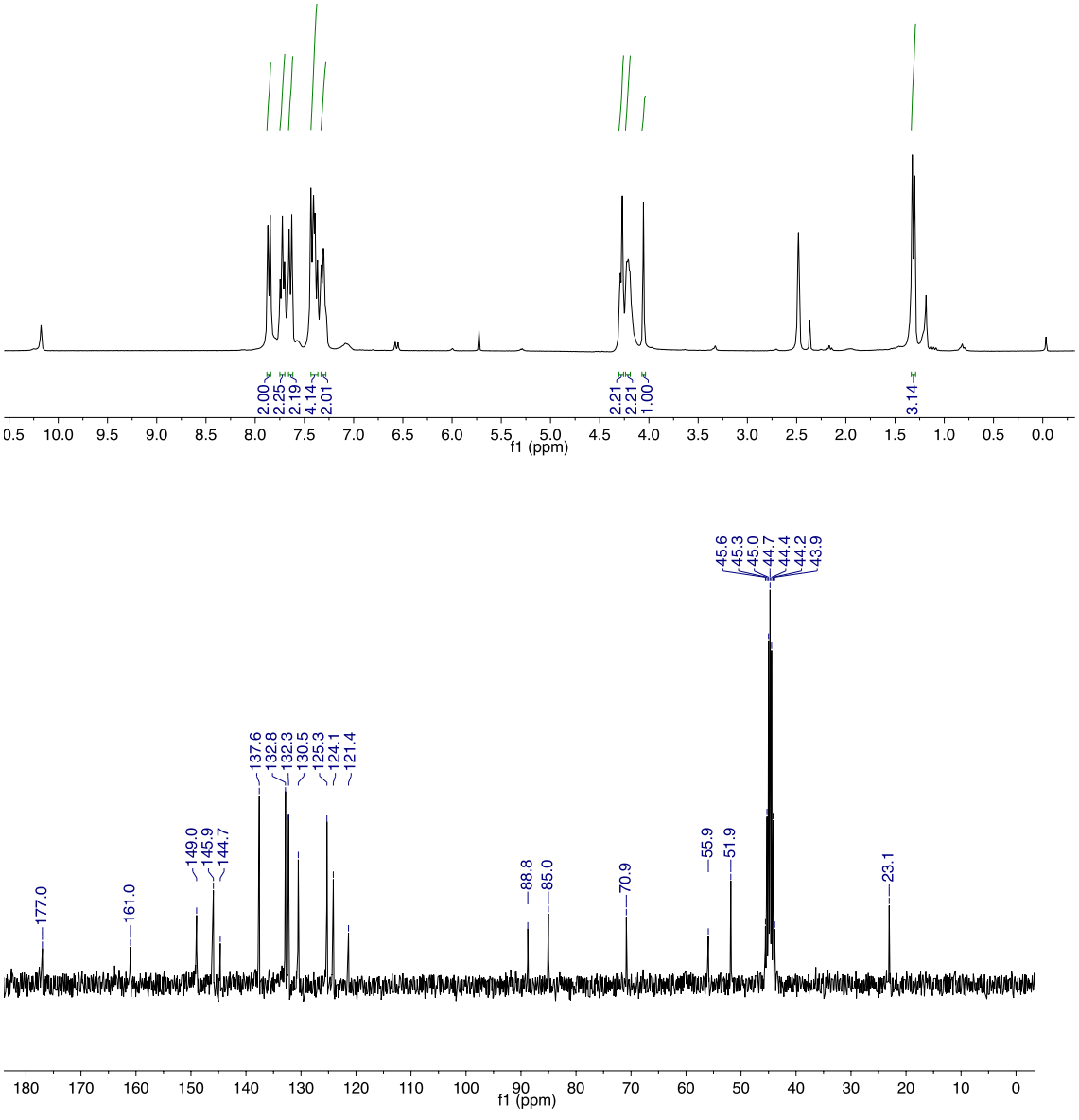


Figure S3. ^{1}H-NMR and ^{13}C-NMR of **2** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl (*S*)-(1-((4-ethynylphenyl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (3):

^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 0.93 (m, 6H), 2.04 (m, 1H), 4.19 (m, 2H), 4.26 (m, 3H). 7.28-7.45 (m, 6H), 7.65-7.86 (m, 7H), 10.26 (s, 1H). ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 23.8, 24.4, 35.5, 51.9, 66.4, 71.0, 85.0, 88.8, 121.5, 124.3, 125.3, 130.6, 132.2, 132.8, 137.6, 144.5, 145.9, 149.0, 161.5, 176.1

HRMS (ESI) m/z calcd for $C_{28}H_{26}N_2O_3$ [M+H] 439.1977, found 439.2015.

$[\alpha]_D$= -23 (c= 15 mg/mL, DMSO).

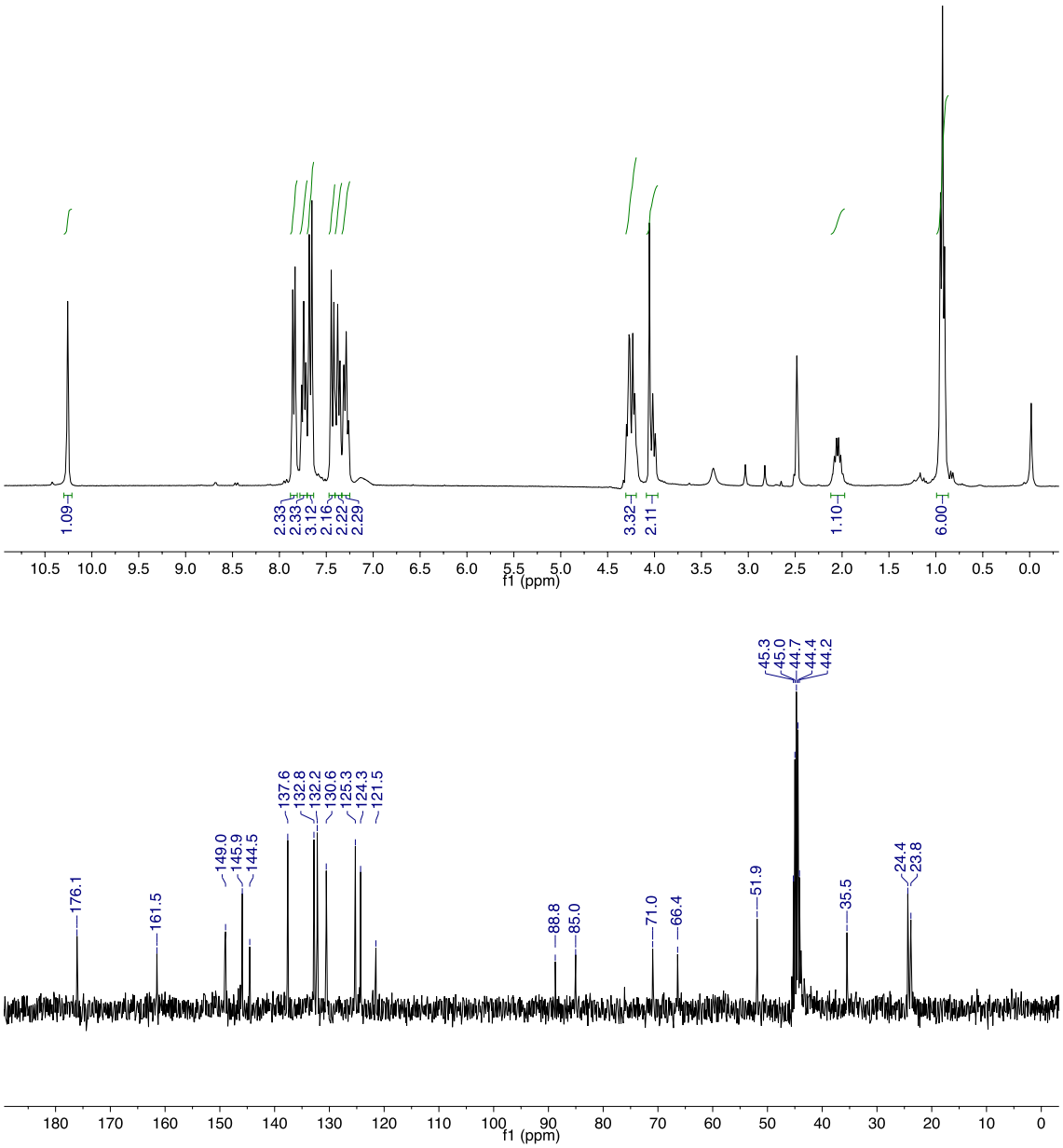


Figure S4. ^{1}H-NMR and ^{13}C-NMR of **3** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl (*S*)-(1-((4-ethynylphenyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (4):

^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 0.91 (m, 6H), 1.70 (m, 3H), 3.04 (s, 1H), 4.15 (m, 1H), 4.34 (m, 3H), 5.72 (m, 1H), 7.25- 7.46 (m, 9H), 7.51-7.74 (m, 3H), 8.81 (s, 1H). ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 54.4, 67.4, 77.5, 83.4, 119.5, 120.0, 124.9, 127.1, 127.8, 130.8, 132.8, 133.2, 141.3, 143.4, 156.9, 171.1.
HRMS (ESI) m/z calcd for $C_{29}H_{28}N_2O_3$ [M+H] 453.2133, found 453.2175.
$[\alpha]_D$= -24 (c= 15 mg/mL, DMSO).

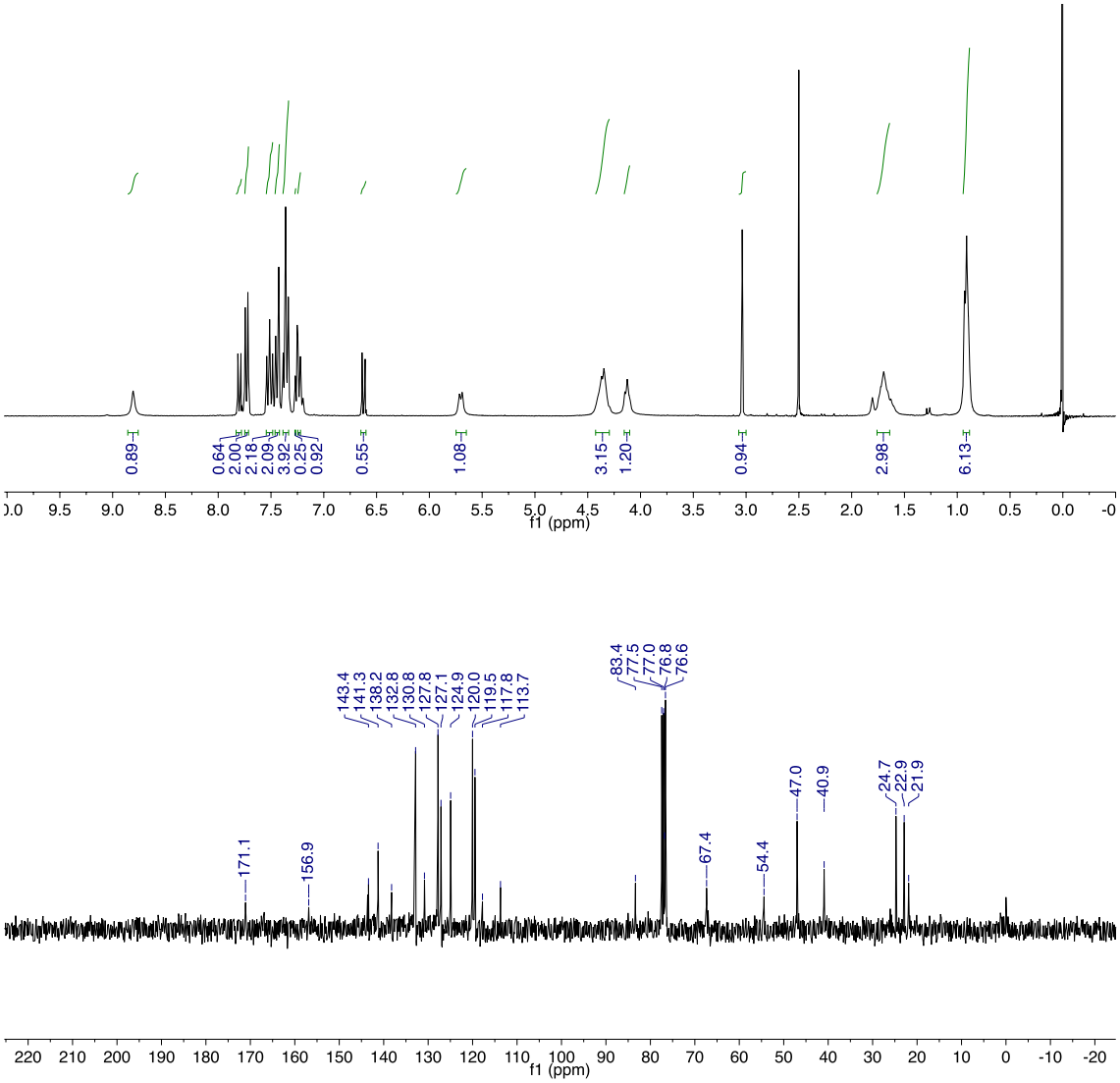


Figure S5. ^{1}H-NMR and ^{13}C-NMR of **4** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl ((2*S*,3*S*)-1-((4-ethynylphenyl)amino)-3-methyl-1-oxopentan-2-yl)carbamate (5)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 0.93 (m, 6H), 1.24 (m, 2H), 1.60-1.97 (m, 1H), 4.17 (m, 2H), 4.40 (m, 2H), 5.62 (m, 1H), 7.23-7.40 (m, 6H), 7.43-7.76 (m, 6H), 8.40 (s, 1H). ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 15.9, 20.5, 29.8, 41.4, 51.9, 65.1, 70.9, 85.0, 88.7, 121.5, 124.3, 125.3, 130.6, 132.2, 132.8, 137.6, 144.5, 145.9, 148.9, 161.4, 176.2

HRMS (ESI) m/z calcd for $C_{29}H_{28}N_2O_3$ [M+H] 453.2133, found 453.2173.

$[\alpha]_D$= -25 (c= 15 mg/mL, DMSO).

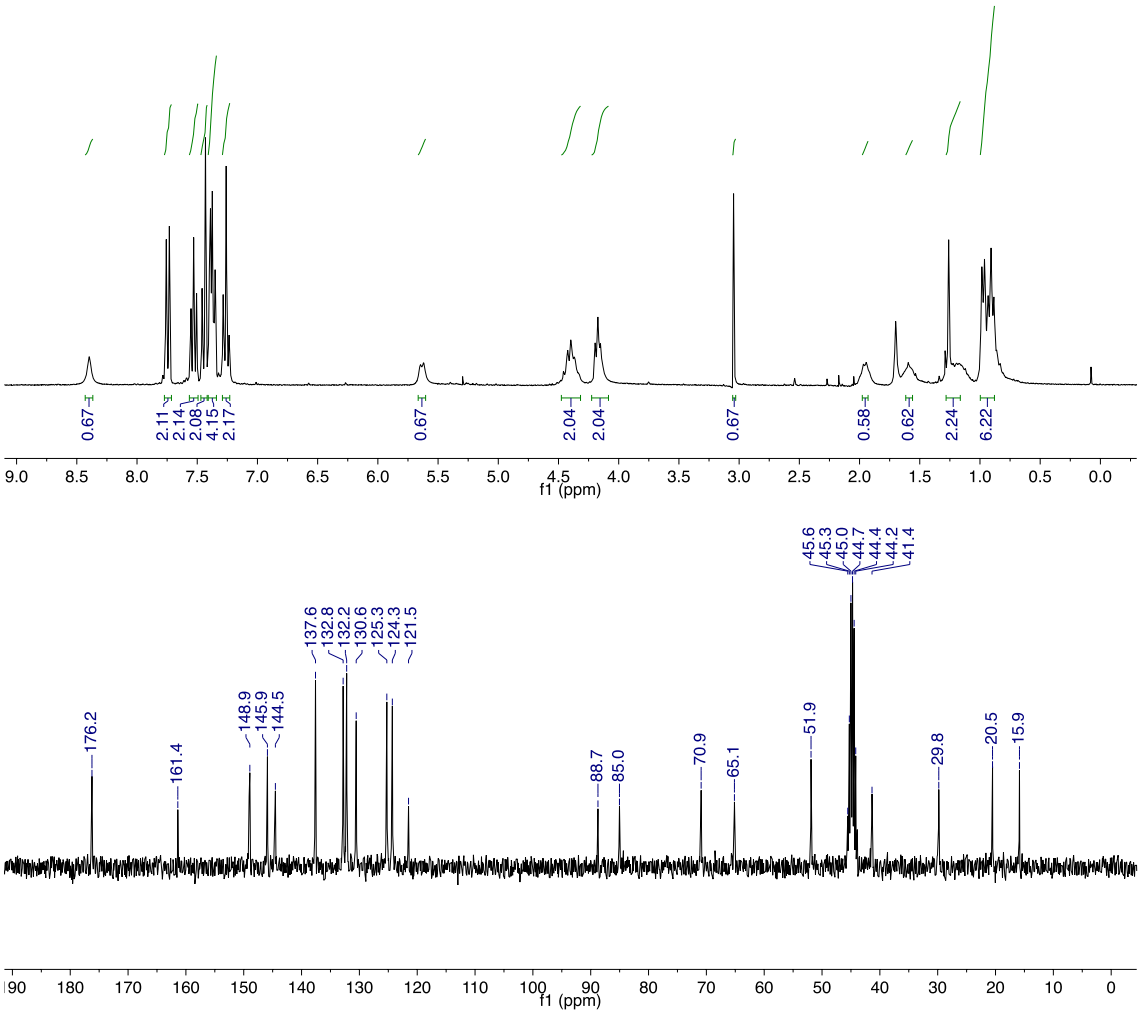


Figure S6. ^{1}H-NMR in $CDCl_3$ and ^{13}C-NMR of **6** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl (*S*)-(1-((4-ethynylphenyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (6):

^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 2.97 (m, 1H), 3.10 (m, 1H), 4.07 (s, 1H), 4.23 (m, 3H), 4.54 (m, 1H) 7.19-7.50 (m, 11H), 7.65-7.93 (m, 6H) 10.37 (s, 1H).
^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 42.7, 51.8, 62.3, 71.0, 85.0, 88.8, 121.6, 124.4, 125.2, 130.5, 131.6, 132.2, 132.8, 133.3, 134.5, 137.6, 143.0, 144.7, 145.9, 149.0, 161.2, 176.1.
HRMS (ESI) m/z calcd for $C_{32}H_{26}N_2O_3$ [M+H] 487.1977, found 487.2016.
$[\alpha]_D$= -24 (c= 15 mg/mL, DMSO).

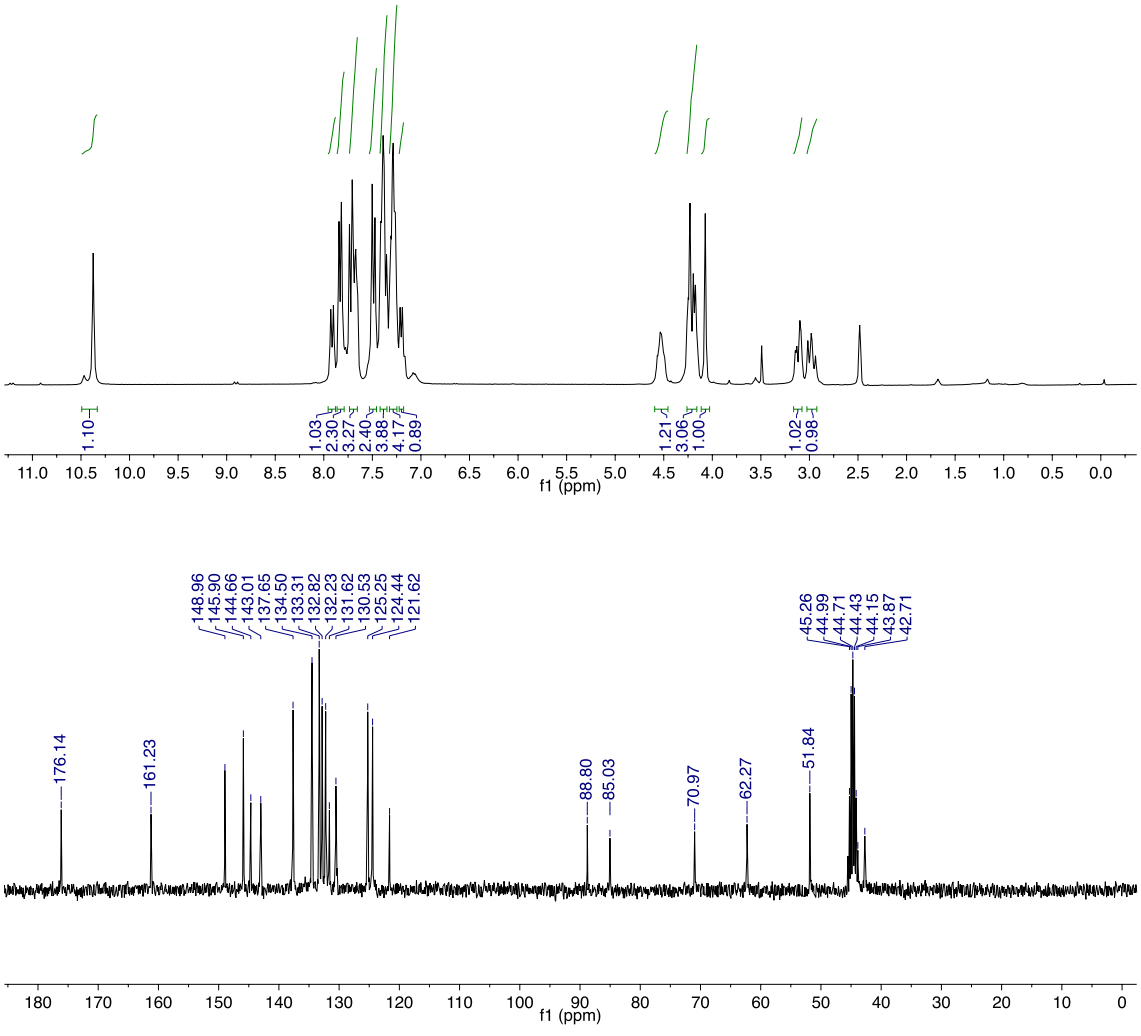


Figure S7. ^{1}H-NMR and ^{13}C-NMR of **5** in DMSO-d_6.

(9*H*-fluoren-9-yl)methyl (*S*)-2-((4-ethynylphenyl)carbamoyl)pyrrolidine-1-carboxylate (7)

^{1}H NMR (300 MHz, DMSO-d6) δ(ppm): 1.89 (m, 3H), 2.20 (m, 1H), 3.49 (m, 1H), 4.06-4.11 (m, 1H), 4.27 (m, 3H), 4.47 (m, 1H), 7.00-7.89 (m, 10H), 10.32 (d, 1H).
^{13}C NMR (62.5 MHz, DMSO-d6) δ (ppm): 28.2, 35.3, 51.9, 65.2, 71.9, 85.1, 88.8, 121.44, 124.33, 130.3, 132.2, 132.9, 137.5, 144.3, 145.9, 149.1
HRMS (ESI) m/z calcd for $C_{29}H_{28}N_2O_3$ [M+H] 437.1820, found 437.1844.
$[\alpha]_D$= -75 (c= 15 mg/mL, DMSO).

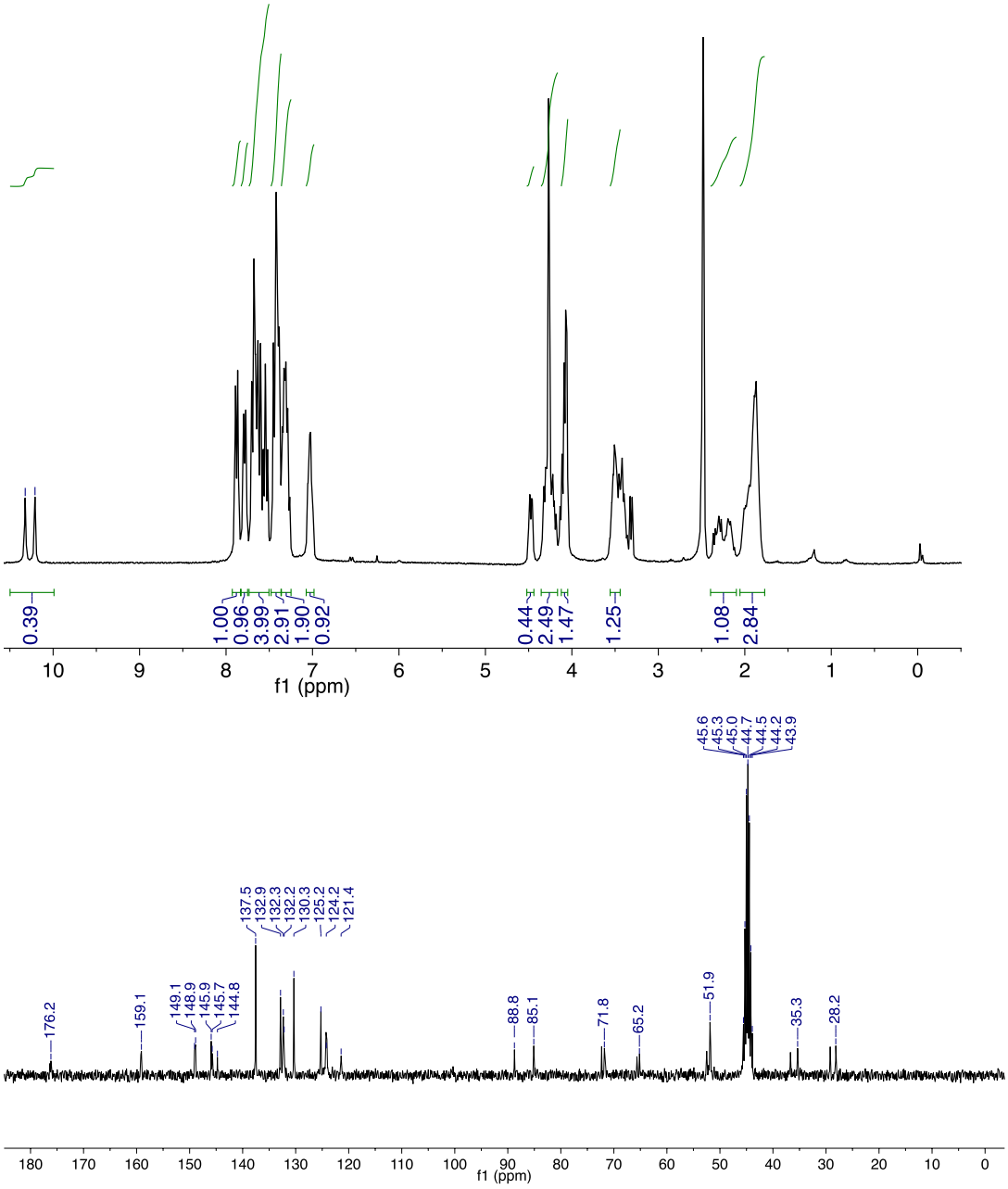


Figure S8. ^{1}H-NMR and ^{13}C-NMR of **7** in DMSO-d_6.

2.2. Amino-phenylacetylenes.

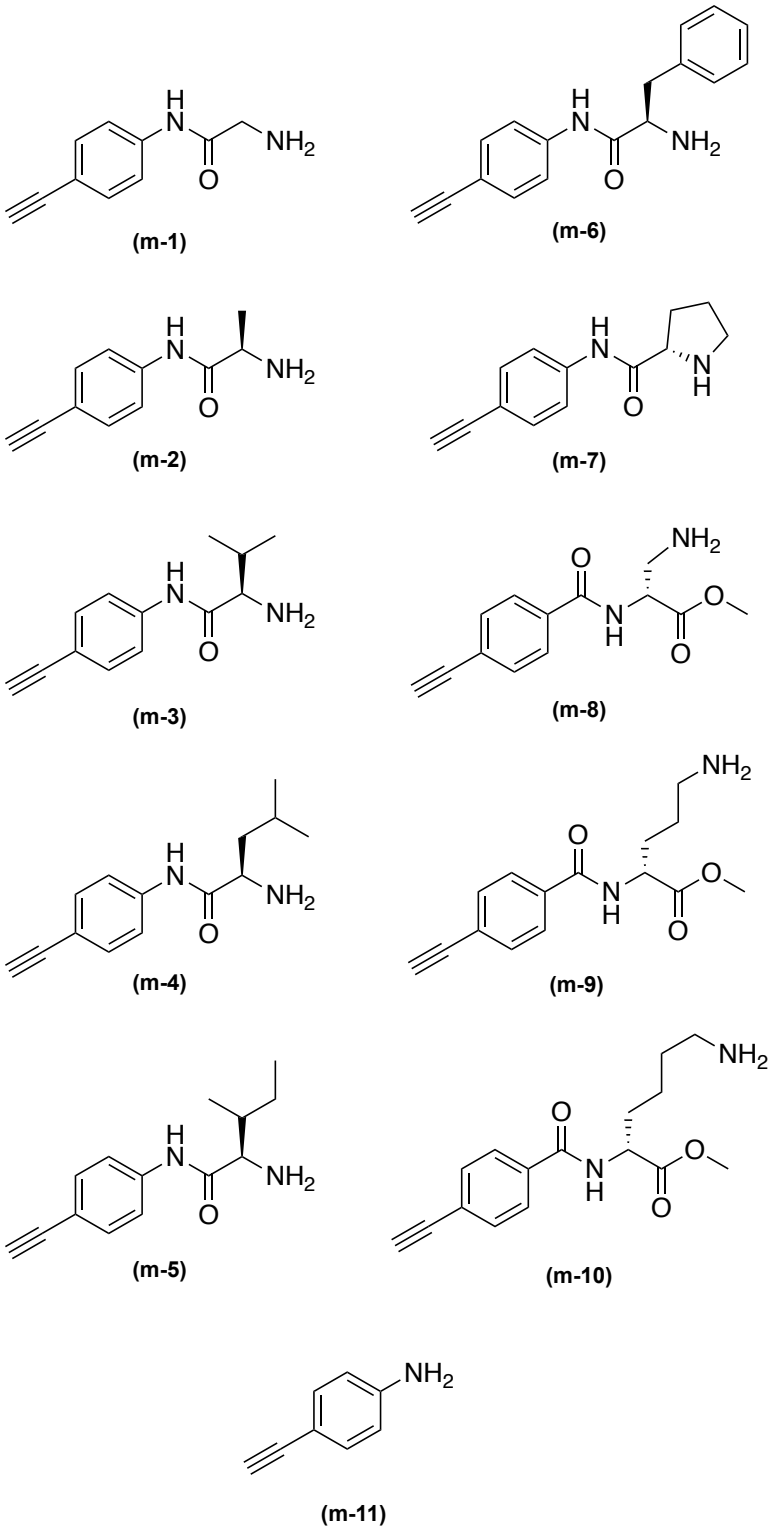
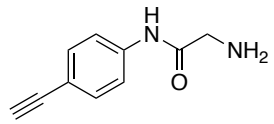
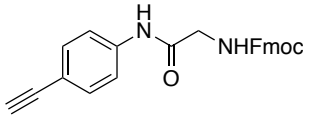
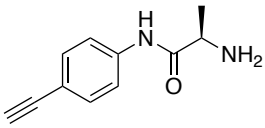
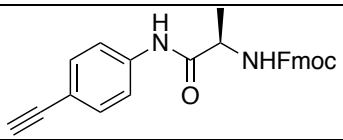
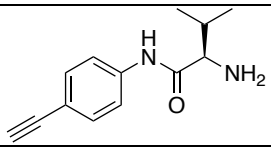
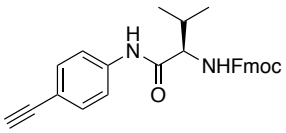
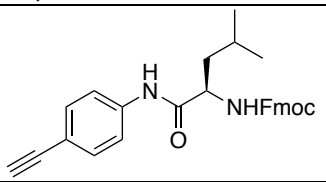
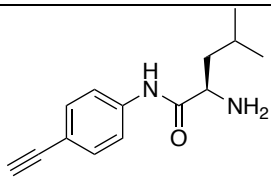
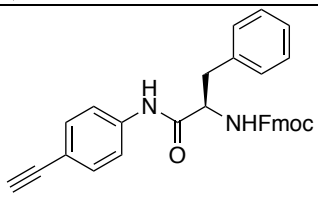
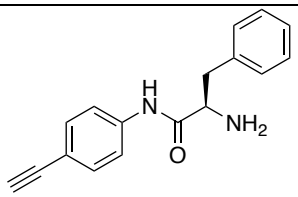
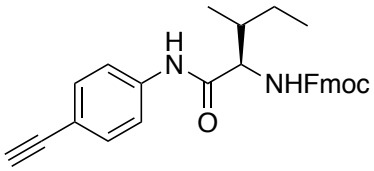
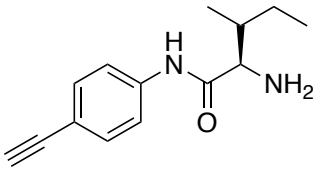
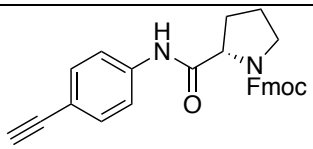
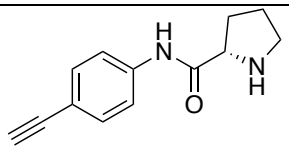


Figure S9. Structure of unprotected monomers (**1-11**).

Deprotection protocol:

The Fmoc group of compounds of **(1), (2), (3), (4), (5), (6)** and **(7)** 700 mg (1.0 equiv.) was removed in a mixture of DCM/piperidine (80/20 v/v) 20% The reaction mixture was stirred at room temperature until the reaction ended (2h). After the completion, the crude products were chromatographed on silica gel (70-230 mesh) with hexane/ethyl acetate (1/1) as eluent.

Table S2. Unprotected Fmoc compounds (m**1**-m**7**).

Product	Starting Material	mg (η %)
		220 (67%)
		221 (69%)
		252 (73%)
		274 (77%)
		334 (88%)
		292 (82%)
		233 (68%)

2-amino-*N*-(4-ethynylphenyl)acetamide (m-1)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 3.39 (s, 2H), 4.77 (s, 2H), 7.34 (d, 2H), 7.54 (d, 2H). ^{13}C NMR (62.5 MHz, d6-DMSO) δ (ppm): 44.3, 76.8, 83.0, 117.5, 119.2, 132.3, 138.7, 172.1.

HRMS (ESI) m/z calcd for $C_{10}H_{10}N_2O$ [M+H] 175.2030, found 175.0867.

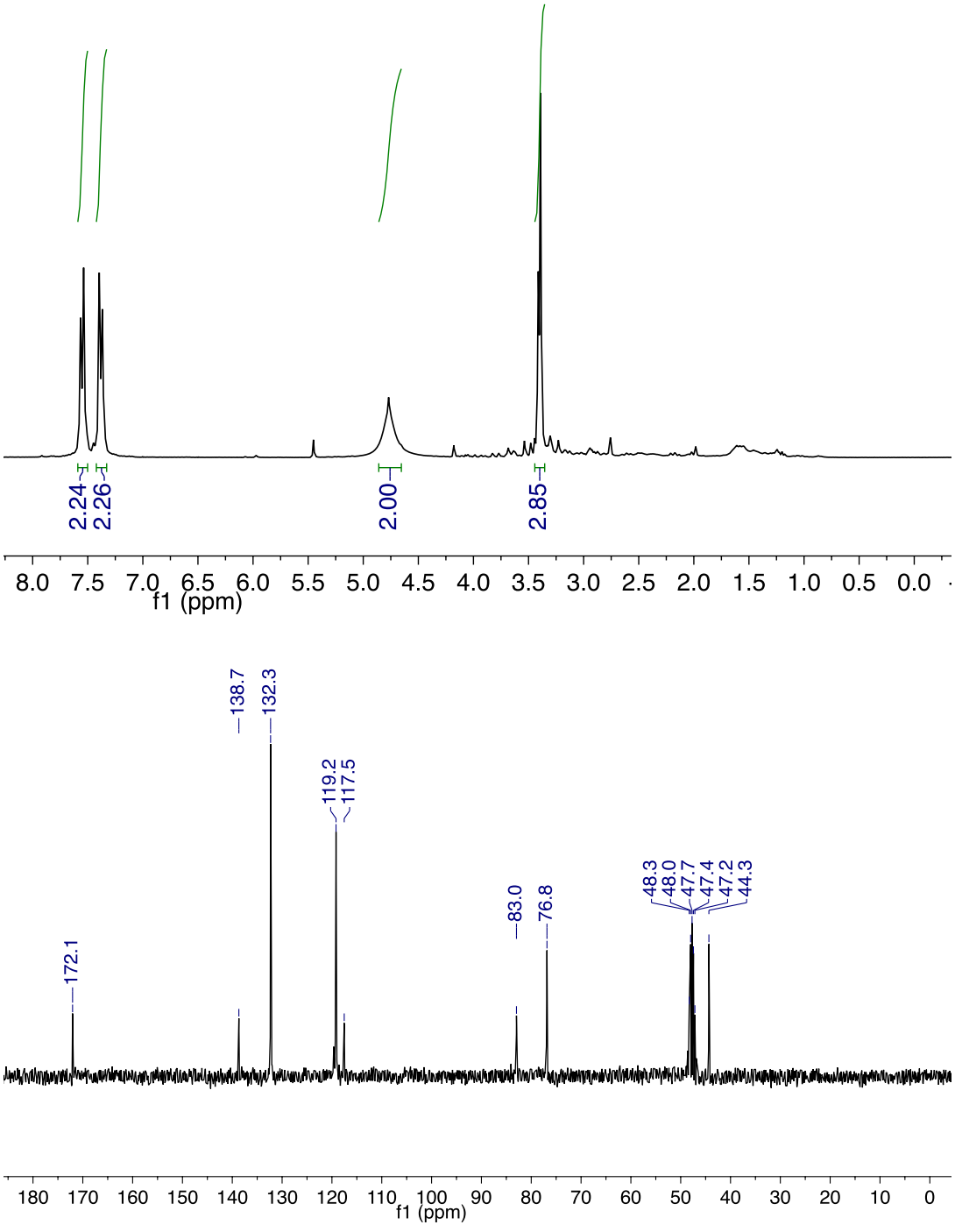


Figure S10. ^{1}H-NMR and ^{13}C-NMR of **m-1** in $CDCl_3$.

(*S*)-2-amino-*N*-(4-ethynylphenyl)propanamide (m-2)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.43 (d, 3H), 1.71 (s, 2H), 3.03 (s, 1H), 3.57 (m, 1H), 7.44 (d, 2H), 7.54 (d, 2H), 9.60 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.5, 51.1, 83.5, 117.3, 118.9, 132.9, 138.3, 173.9.

HRMS (ESI) m/z calcd for $C_{11}H_{12}N_2O$ [M+H] 189.2300, found 189.1023.

$[\alpha]_D$= -25 (c= 15 mg/mL, $CHCl_3$).

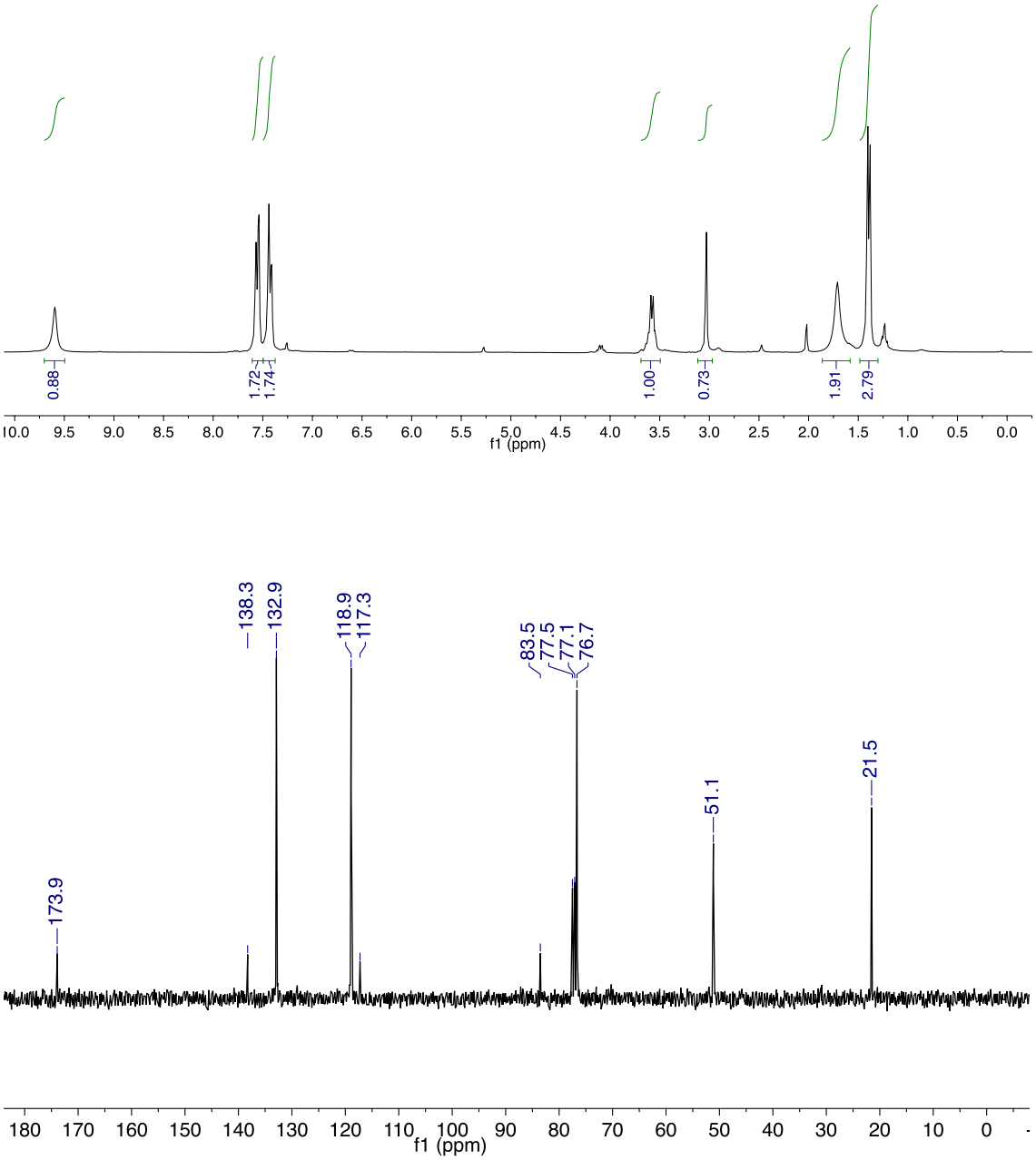


Figure S11. ^{1}H-NMR and ^{13}C-NMR of **m-2** in $CDCl_3$.

(*S*)-2-amino-*N*-(4-ethynylphenyl)-3-methylbutanamide (m-3)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 0.92 (m, 6H), 2.04 (m, 1H), 3.23 (d, 1H), 3.41 (s, 1H), 4.67 (s, 2H), 7.41 (d, 2H), 7.57 (d, 2H). ^{13}C NMR (62.5 MHz, d6-DMSO) δ (ppm): 20.4, 22.6, 36.2, 64.8, 80.9, 86.9, 121.7, 123.4, 136.3, 142.5, 178.1.
HRMS (ESI) m/z calcd for $C_{13}H_{16}N_2O$ [M+H] 217.2840, found 217.1336.
$[\alpha]_D$= -52 (c= 15 mg/mL, $CHCl_3$).

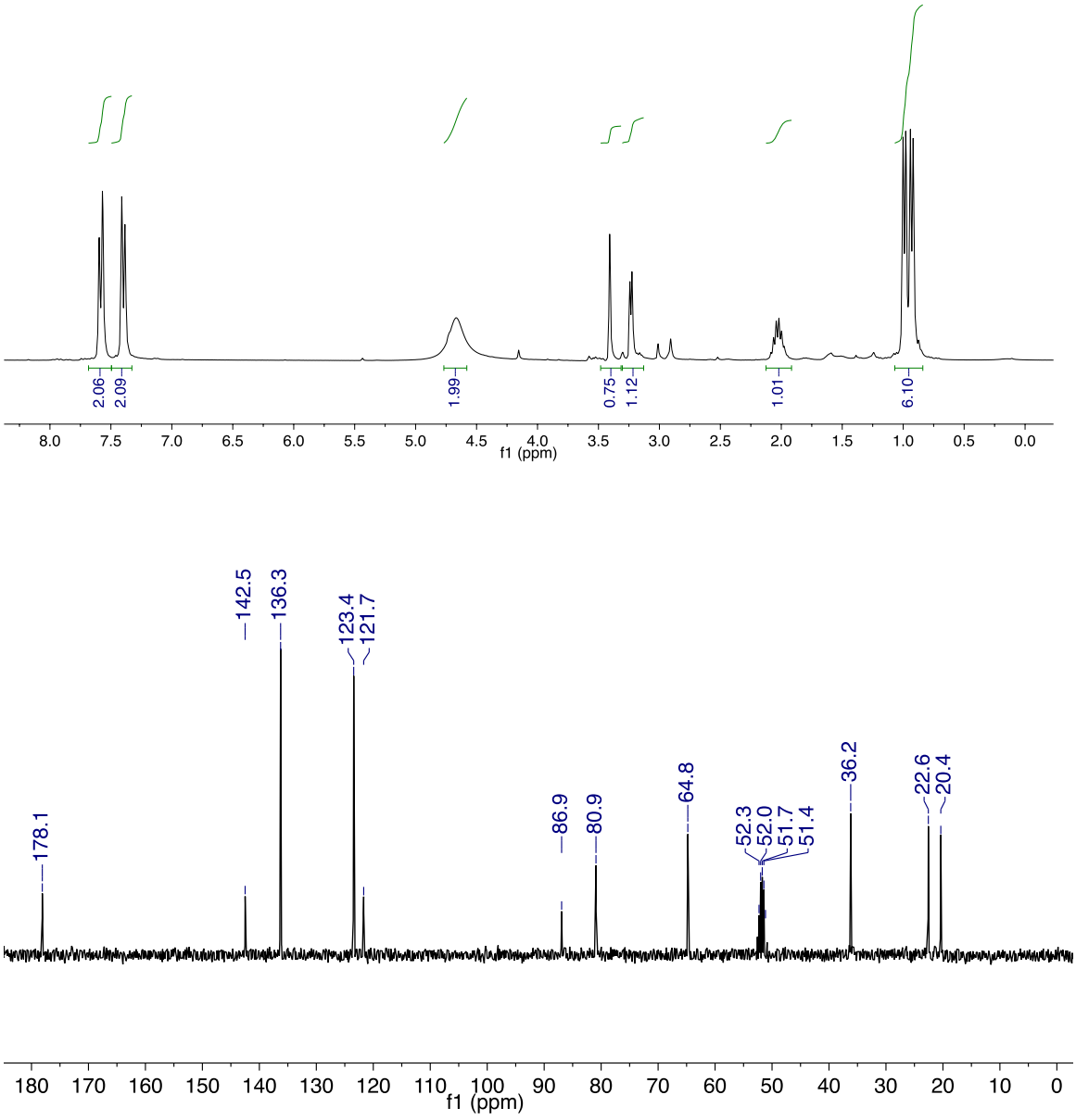


Figure S12. ^{1}H-NMR in $CDCl_3$ and ^{13}C-NMR of **m-3** in DMSO-d_6.

(*S*)-2-amino-*N*-(4-ethynylphenyl)-4-methylpentanamide (m-4)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 0.95 (m, 7H), 1.73 (m, 2H), 3.02 (s, 1H), 3.43 (m, 1H), 4.67 (s, 2H), 7.41 (d, 2H), 7.52 (d, 2H), 9.63 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.3, 23.2, 24.9, 43.4, 53.8, 77.5, 83.5, 117.5, 119.1, 132.9, 138.2, 173.1.

HRMS (ESI) m/z calcd for $C_{14}H_{18}N_2O$ [M+H] 231.3110, found 231.1491.

$[\alpha]_D$= -43 (c= 15 mg/mL, $CHCl_3$).

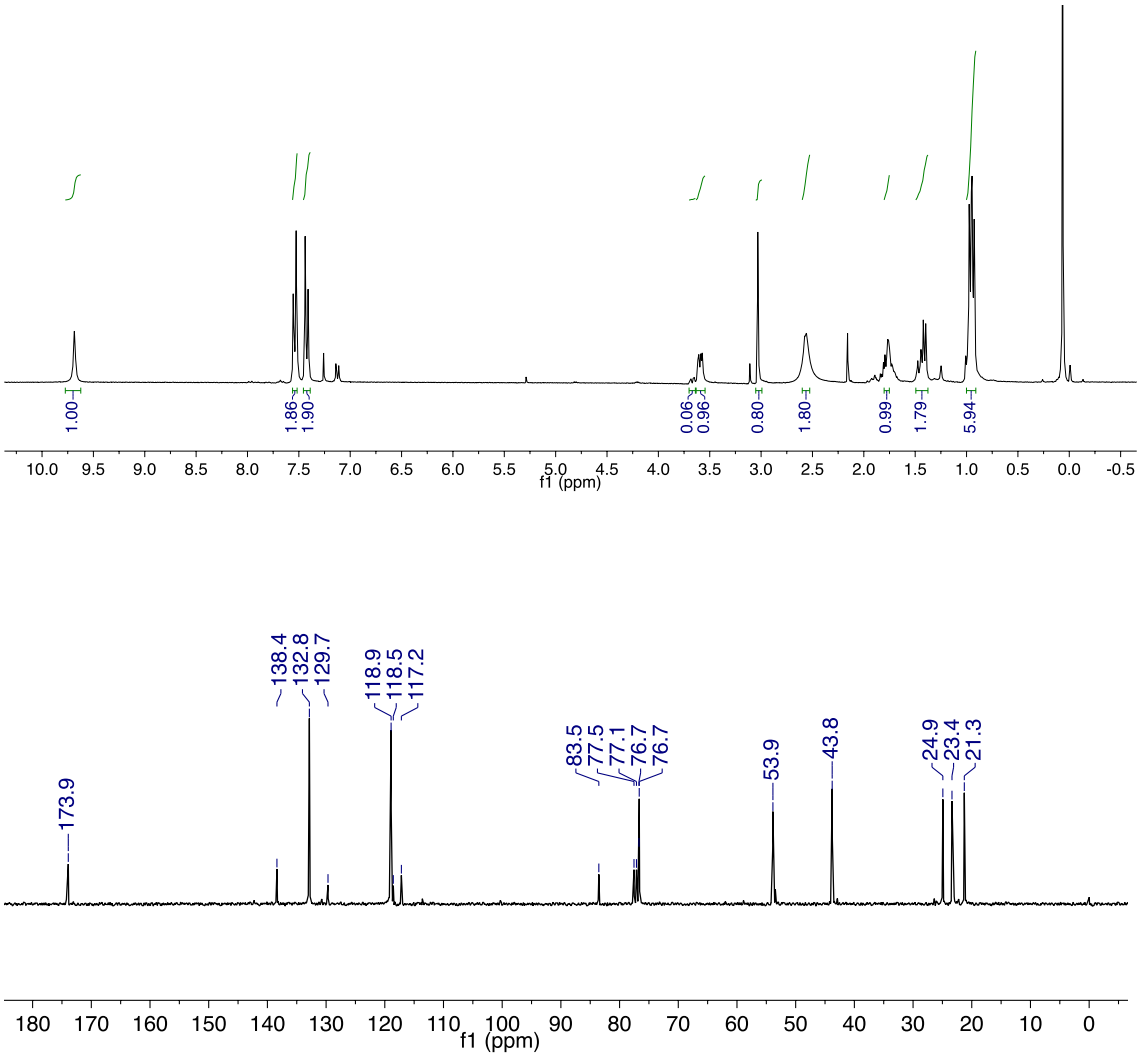


Figure S13. ^{1}H-NMR and ^{13}C-NMR of **m-4** in $CDCl_3$.

(2*S*,3*S*)-2-amino-*N*-(4-ethynylphenyl)-3-methylpentanamide (m-5).

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 0.84-0.96 (m, 6H), 1.07 (m, 1H), 1.34 (m, 1H), 2.05 (m, 1H), 3.00 (s, 1H), 3.34 (m, 1H), 7.39 (d, 2H), 7.51 (d, 2H), 9.64 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 11.9, 16.3, 23.7, 37.9, 60.2, 83.5, 117.2, 119.0, 132.8, 138.2, 172.9.

HRMS (ESI) m/z calcd for $C_{14}H_{18}N_2O$ [M+H] 231.3110, found 231.1492.

$[\alpha]_D$= -65 (c= 15 mg/mL, $CHCl_3$).

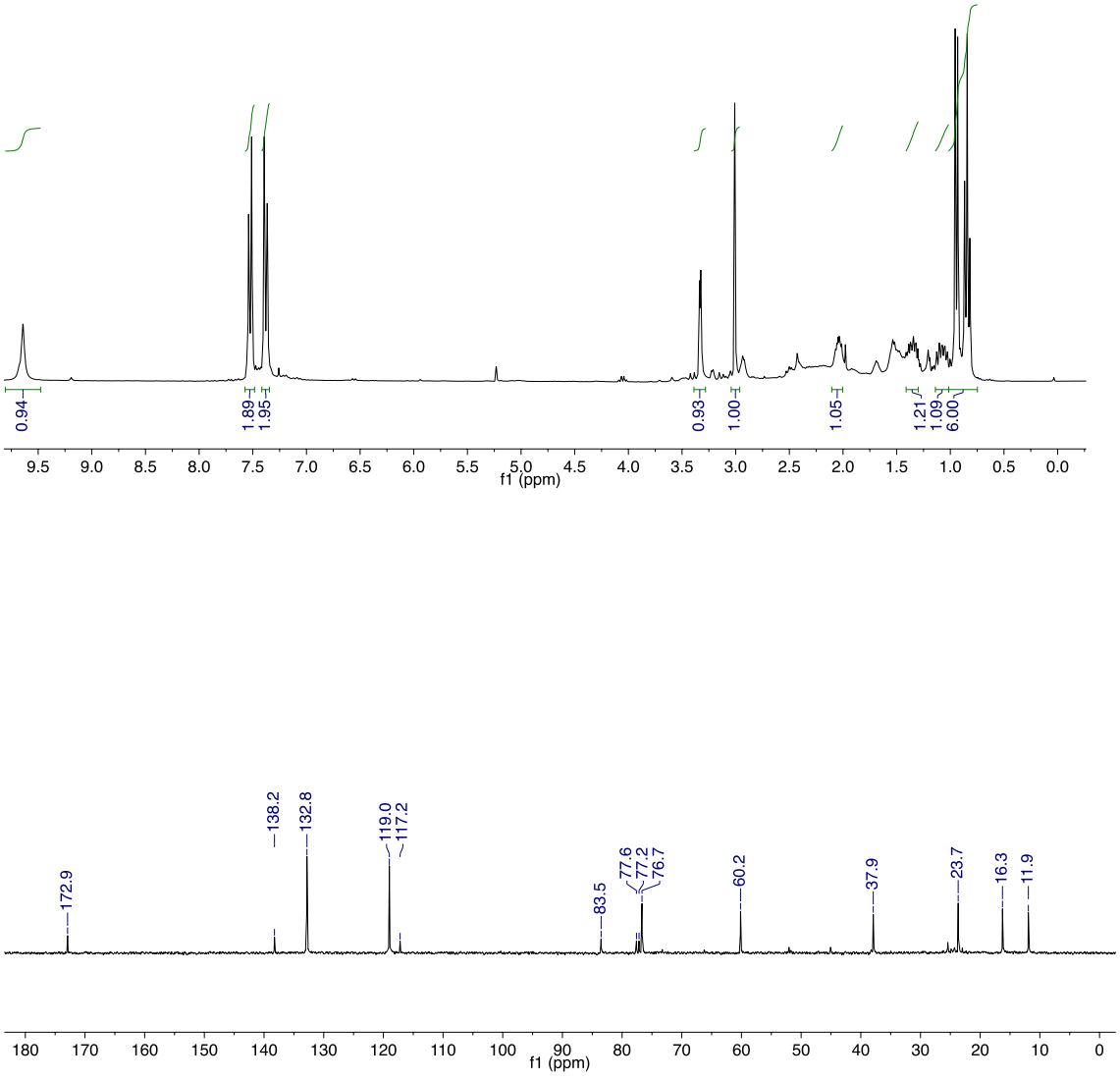


Figure S14. ^{1}H-NMR and ^{13}C-NMR of **m-6** in $CDCl_3$.

(*S*)-2-amino-*N*-(4-ethynylphenyl)-3-phenylpropanamide (m-6)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 2.79 (m, 1H), 3.05 (s, 1H), 3.34 (m, 1H), 3.74 (m, 1H), 7.25 (m, 5H), 7.47 (d, 2H), 7.56 (d, 2H), 9.53 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 40.6, 56.8, 77.5, 83.5, 117.4, 119.0, 127.0, 128.8, 129.3, 132.9, 137.5, 138.1, 172.5.

HRMS (ESI) m/z calcd for $C_{17}H_{16}N_2O$ [M+H] 265.3280, found 265.1334.

$[\alpha]_D$= -114 (c= 15 mg/mL, $CHCl_3$).

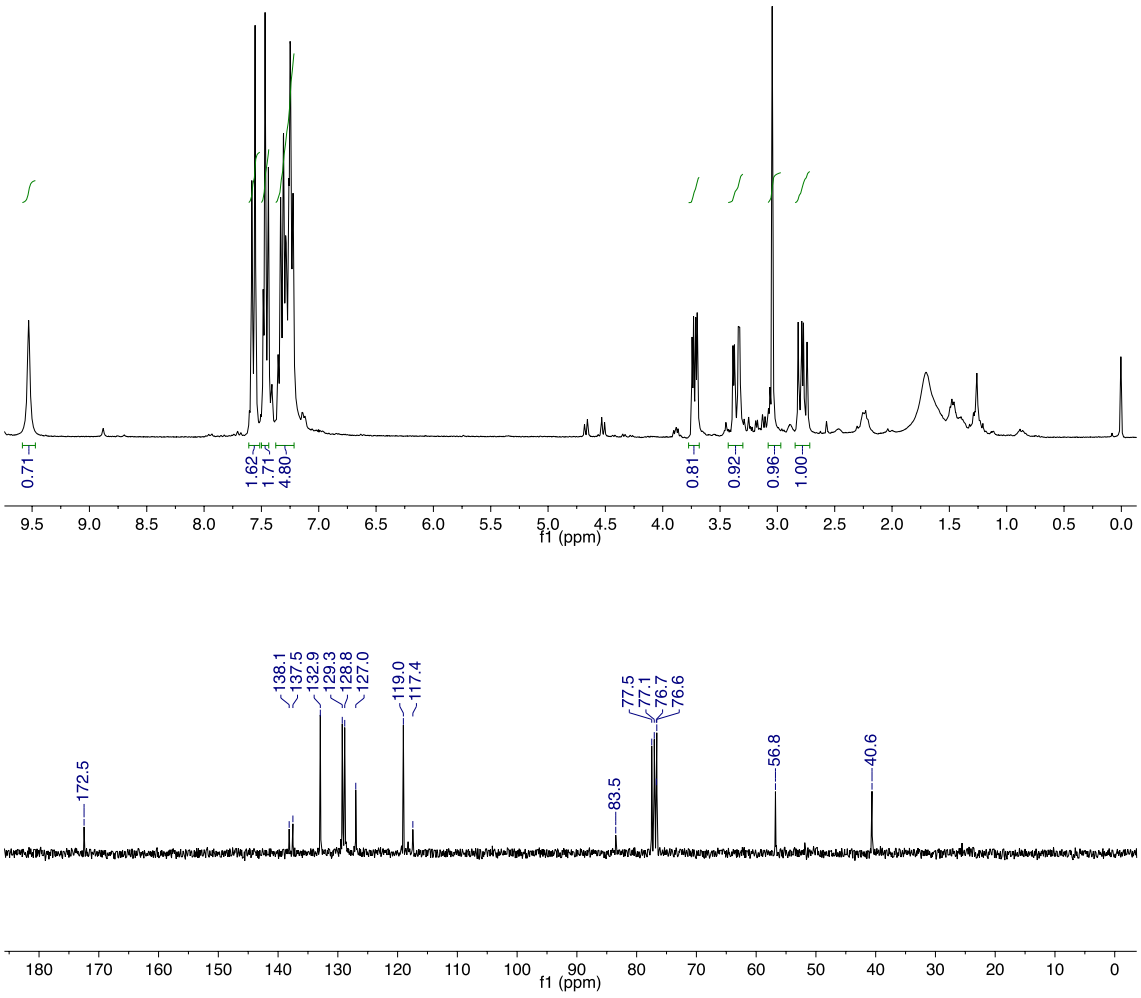


Figure S15. ^{1}H-NMR and ^{13}C-NMR of **m-5** in $CDCl_3$.

(*S*)-*N*-(4-ethynylphenyl)pyrrolidine-2-carboxamide (m-7)

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 0.84-0.96 (m, 6H), 1.07 (m, 1H), 1.34 (m, 1H), 2.05 (m, 1H), 3.00 (s, 1H), 3.34 (m, 1H), 7.39 (d, 2H), 7.51 (d, 2H), 9.64 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 11.9, 16.3, 23.7, 37.9, 60.2, 83.5, 117.2, 119.0, 132.8, 138.2, 172.9.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= -43 (c= 15 mg/mL, $CHCl_3$).

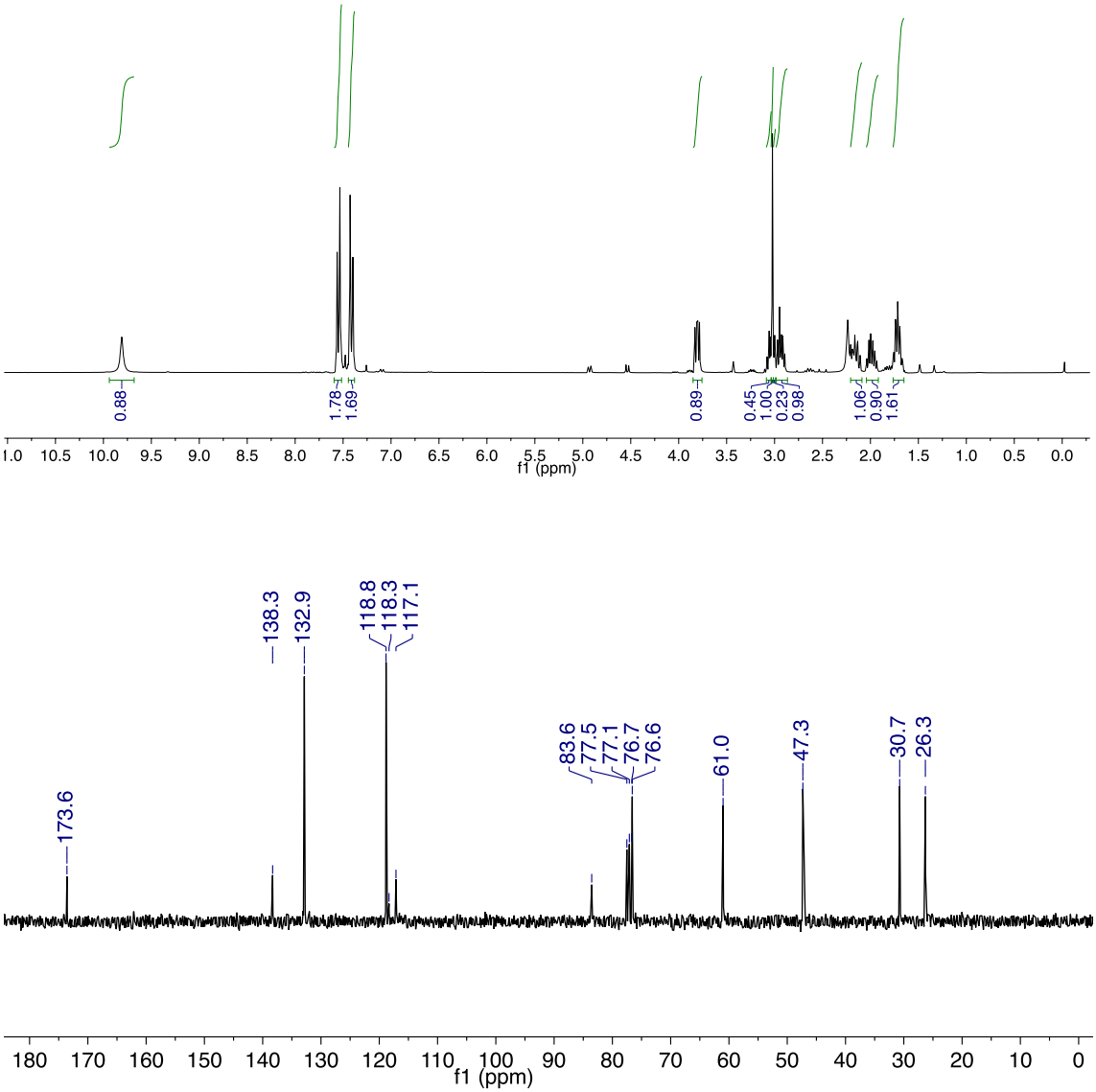


Figure S16. ^{1}H-NMR and ^{13}C-NMR of **m-7** in $CDCl_3$.

Synthetic procedure of monomers derivated from 4-ethynylbenzoic acid (m-8, m-9, m-10):

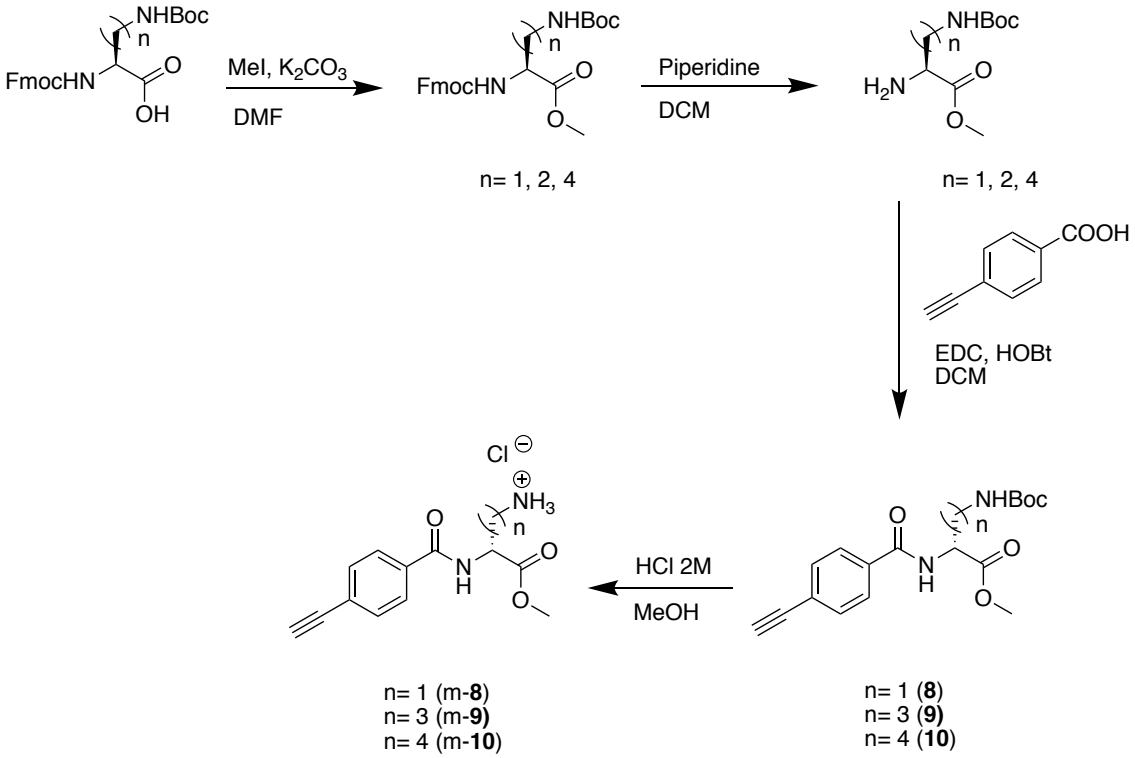


Figure S17. Synthetic procedure for m-(8-10).

N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-beta-t-butyloxycarbonyl-N-beta-methyl-*L*-2,3-diaminopropionic (1000 mg, 1 equiv.) were dissolved in DMF. Then K_2CO_3 (324 mg, 1.0 equiv.) was added following by addition of MeI (146 μL, 1.0 equiv.). Then, the solvent was evaporated at reduced pressure and the crude was diluted in DCM, the organic layer was washed with HCl 1M, saturated solution of NaHCO3 and brine. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated at reduced pressure. The crude product was chromatographed on silica gel (70-230 mesh) with hexane/ethyl acetate (1/1) as eluent, obtaining in 95% yield respectively of pure product.

Then, the FMOC group (800 mg, 1 equiv.) was removed in a mixture of DCM/piperidine (80/20 v/v), when the reaction finished (TLC showed no starting material), solvents were evaporated under reduced pressure and the crude was dried under vacuum. The crude product was chromatographed on

silica gel (70-230 mesh) with hexane/ethyl acetate (1/1) as eluent, obtaining in 76% yield respectively of pure product.

Next, N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (EDC, 1.1equiv.), 1-hydroxbenzotriazole (HOBT, 1.1 equiv.), 4-ethynyl benzoic acid (1.1 equiv.) and diisopropyltriethylamine (DIPEA, 1.4 equiv.) were dissolved in 20 mL of DMF, and the mixture was stirred for 15 min to activate the acid. Then, methyl (*S*)-2-amino-3-((*tert*-butoxycarbonyl)amino)propanoate (1.0 equiv.) was added and the reaction mixture was stirred overnight. The crude product was chromatographed on silica gel (70-230 mesh) with hexane/ethyl acetate (7/3) as eluent, obtaining in 79% the methyl (*S*)-3-((*tert*-butoxycarbonyl)amino)-2-(4-ethynylbenzamido)propanoate.

Finally, methyl (*S*)-3-((*tert*-butoxycarbonyl)amino)-2-(4-ethynylbenzamido)propanoate (250 mg, 1.0 equiv.) were dissolved in HCl (2 M) in MeOH (20 mL). When the reaction finished (TLC showed no starting material), solvents were evaporated under reduced pressure and the crude was dried under vacuum, obtaining in 80% yield of pure product.

The same protocol was used for the preparation of the (*S*)-4-(4-ethynylbenzamido)-5-methoxy-5-oxopentan-1-aminium chloride and (*S*)-5-(4-ethynylbenzamido)-6-methoxy-6-oxohexan-1-aminium chloride in good yields.

Methyl-*N*2-(((9*H*-fluoren-9-yl)methoxy)carbonyl)-*N*6-(*tert*-butoxycarbonyl)-*L*-lysinate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.42 (s, 13H), 1.64 (m, 1H), 3.09 (m, 2H), 3.70 (S, 3H), 4.19 (m, 1H), 4.22 (m, 1H), 4.35 (m, 2H), 4.75 (m, 1H), 5.70 (d, 1H), 7.26 (d, 2H), 7.37 (d, 2H), 7.58 (m, 2H), 7.72 (d, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 22.4, 28.4, 29.6, 31.9, 40.0, 47.1, 52.4, 53.8, 67.0, 79.1,120.0, 125.1, 127.1, 127.7, 141.3, 143.7, 143.9, 156.1, 173.1.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= -17 (c= 15 mg/mL, $CHCl_3$).

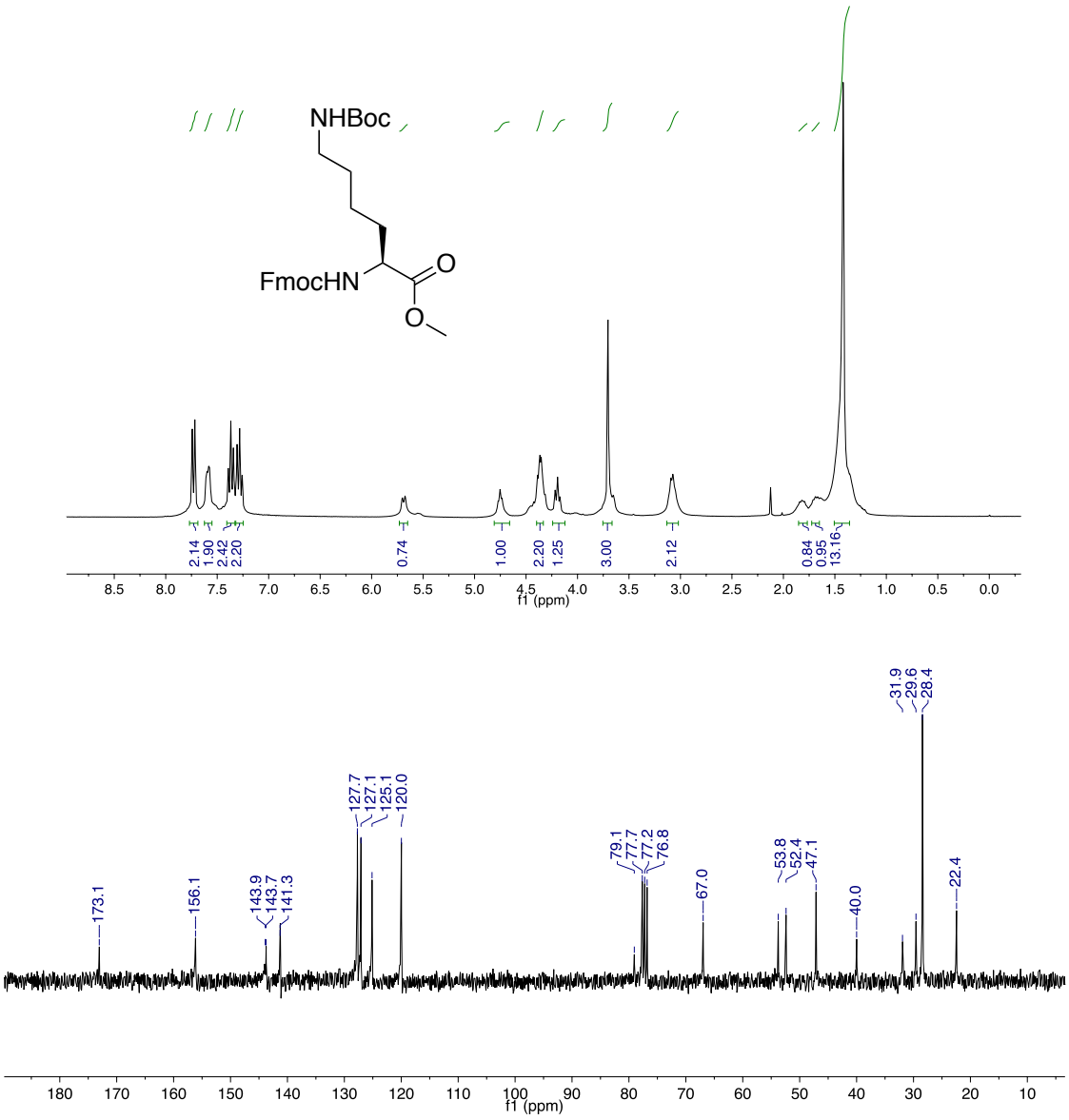


Figure S18. ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$.

Methyl-*N*6-(*tert*-butoxycarbonyl)-*L*-lysinate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.43 (m, 13H), 1.56 (m, 4H), 1.71 (m, 1H), 1.19 (m, 2H), 3.01 (m, 3H), 3.45 (m, 1H), 3.72 (s, 3H), 5.04 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 22,7, 22.9, 28.3, 29.6, 33.1, 34.3, 40.1, 51.5, 51.7, 54.1, 58.3, 62.5, 78.6, 155.9, 176.2.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= -42 (c= 15 mg/mL, $CHCl_3$).

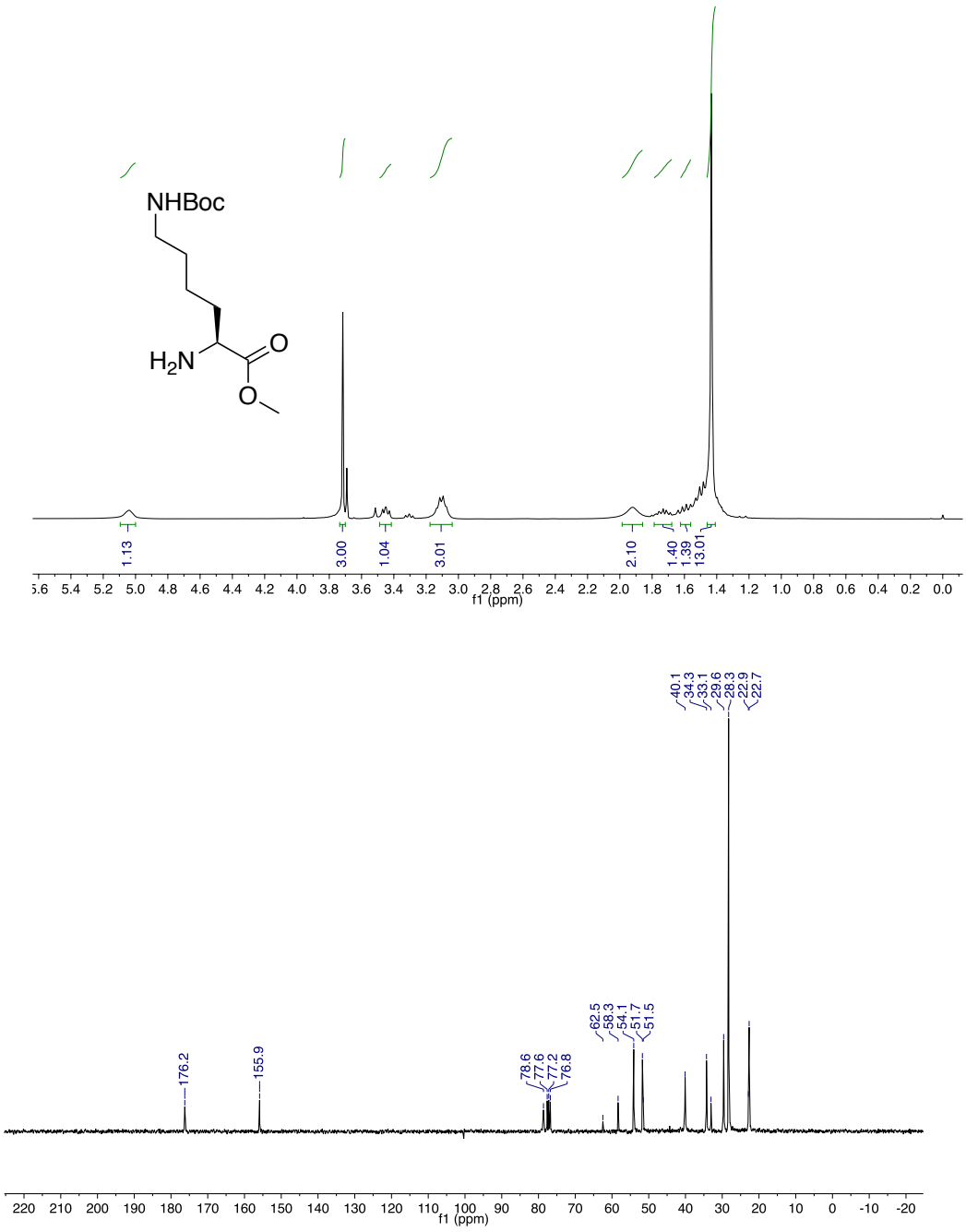


Figure S19. ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$.

Methyl-N^6-(*tert*-butoxycarbonyl)-N^2-(4-ethynylbenzoyl)-*L*-lysinate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.33 (s, 13H), 1.70 (m, 1H), 1.86 (m, 1H), 3.01 (m, 1H), 3.18 (s, 1H), 3.68 (s, 3H), 4.68 (m, 1H), 4.77 (m, 1H), 7.11 (d, 1H), 7.39 (d, 2H), 7.51 (d, 2H), 9.64 (s, 1H). ^{13}C NMR (62.5 MHz, d3-CDCl3) δ (ppm): 22.6, 28.3, 29.5, 31.7, 39.9, 52.4, 52.6, 79.0, 79.7, 82.7, 125.5, 127.2, 132.1, 133.7, 156.1, 166.5, 173.0.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= 24 (c= 15 mg/mL, $CHCl_3$).

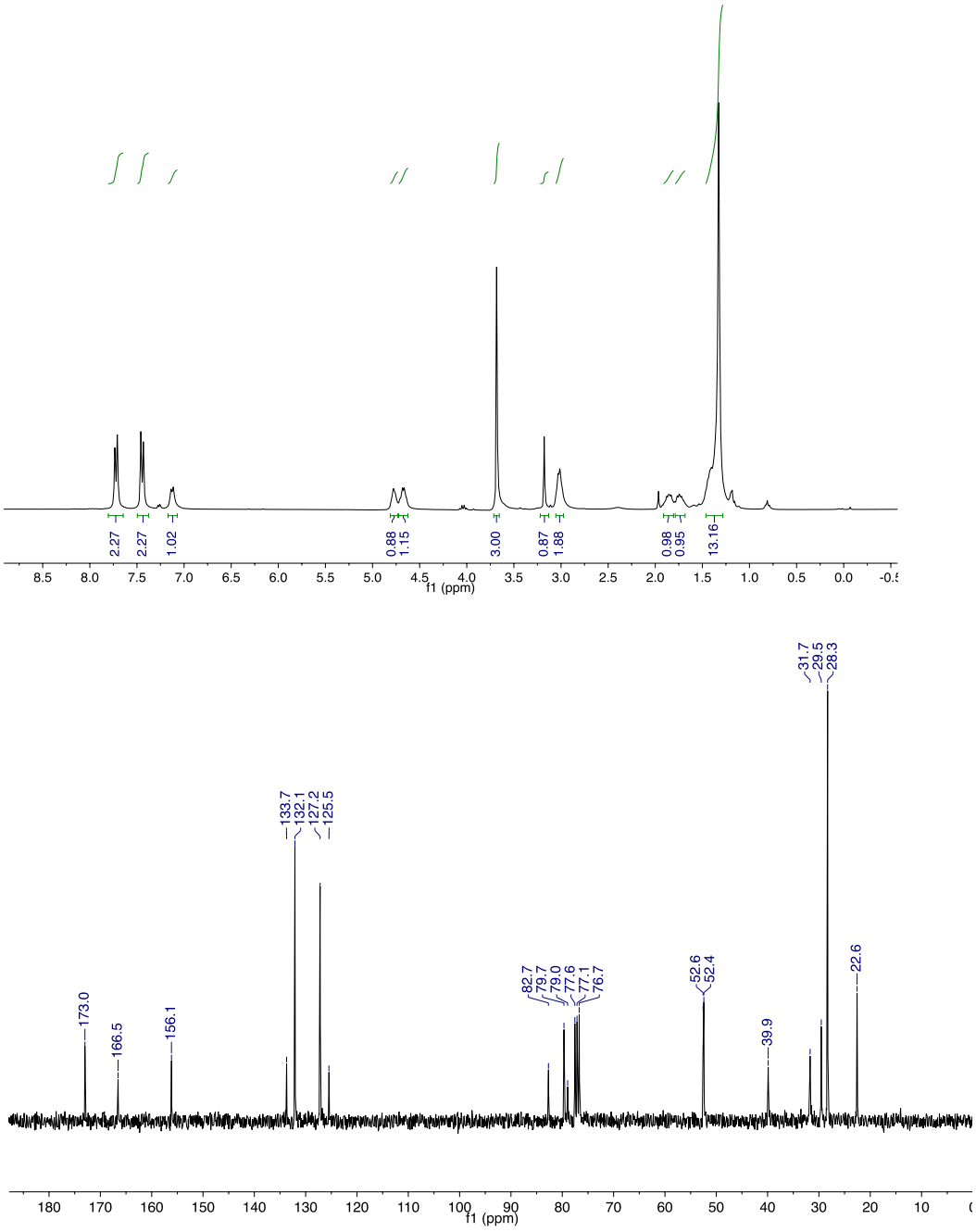


Figure S20. ^{1}H-NMR and ^{13}C-NMR of **10** in $CDCl_3$.

(*S*)-5-(4-ethynylbenzamido)-6-methoxy-6-oxohexan-1-aminium chloride (m-10)

^{1}H NMR (300 MHz, CD_3OD) δ(ppm): 1.04 (m, 6H), 1.07 (m, 1H), 1.34 (m, 1H), 2.05 (m, 1H), 3.00 (s, 1H), 3.34 (m, 1H), 7.26 (d, 2H), 7.53 (d, 2H). ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm): 21.2, 25.1, 28.7, 37.5, 50.0, 51.3, 78.4, 80.6, 124.3, 125.7, 130.2, 132.0, 166.7, 171.1.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= -23 (c= 15 mg/mL, $CHCl_3$).

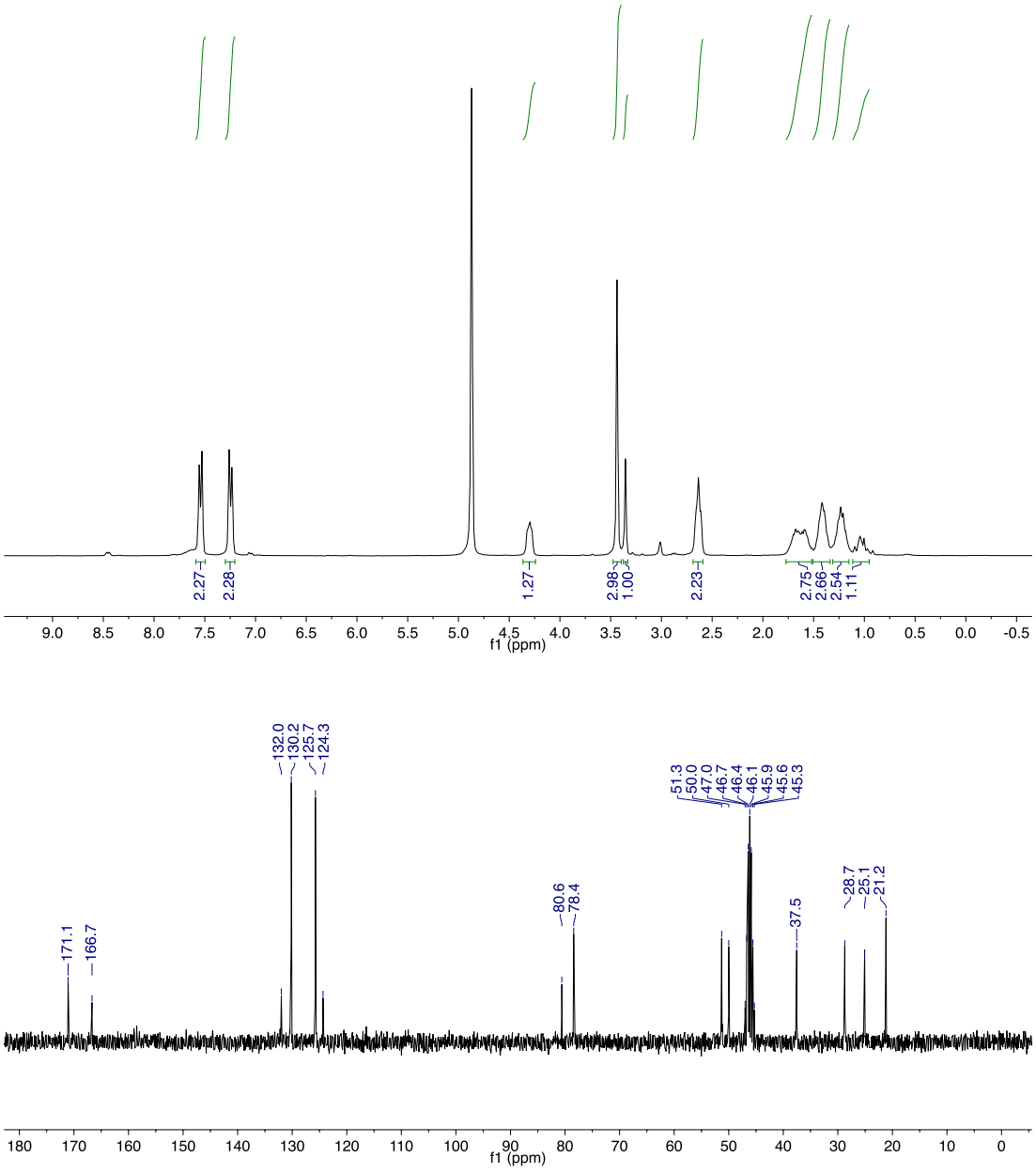


Figure S21. ^{1}H-NMR and ^{13}C-NMR of **m-10** in CD_3OD.

Methyl-(S)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-((tert-butoxycarbonyl)amino)pentanoate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.44 (s, 9H), 1.66 (m, 2H), 1.86 (m, 1H), 3.13 (m, 2H), 3.75 (s, 3H), 4.22 (m, 1H), 4.37 (m, 2H), 4.58 (m, 1H), 5.45 (s, 1H), 7.29-7.34 (t, 2H), 7.37-7.43 (t, 2H), 7.60 (d, 2H), 7.77 (d, 2H), 7.86 (d, 2H), 10.17 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 26.1, 28.4, 29.9, 47.2, 52.5, 53.6, 66.9, 113.6, 120.0, 125.1, 127.1, 127.7, 141.3, 143.7, 160.3, 177.9.

HRMS (ESI) m/z calcd for $C_{26}H_{32}N_2O_6$ [M+H] 469.2294, found 469.2323.

$[\alpha]_D$= -26 (c= 15 mg/mL, DMSO).

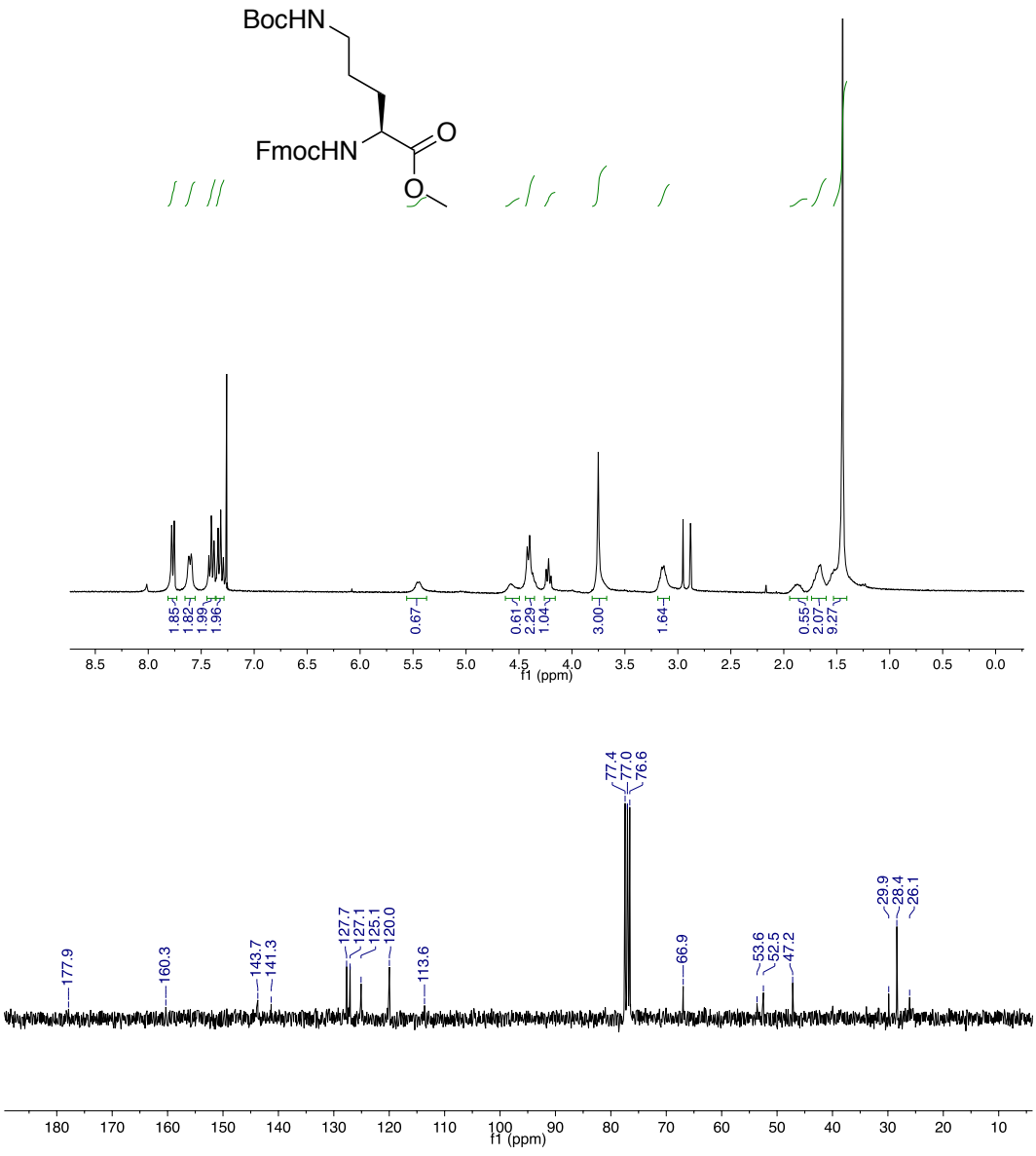


Figure S22. ^{1}H-NMR and ^{13}C-NMR of **9** in $CDCl_3$.

Methyl (S)-2-amino-5-((tert-butoxycarbonyl)amino)pentanoate

^{1}H NMR (300 MHz, $CDCl_3$.) δ(ppm): 1.44 (s, 9H), 1.66 (m, 3H), 1.86 (m, 1H), 3.05 (m, 3H), 3.45 (m, 1H), 3.75 (s, 3H), 4.22 (m, 1H), 4.37 (m, 2H), 4.58 (m, 1H), 5.45 (s, 1H), 7.29-7.34 (t, 2H), 7.37-7.43 (t, 2H), 7.60 (d, 2H), 7.77 (d, 2H), 10.17 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$.) δ (ppm): 29.0, 31.3, 35.1, 43.5, 57.3, 58.3, 82.5, 161.0, 172.9.

HRMS (ESI) m/z calcd for $C_{11}H_{22}N_2O_4$ [M+H] 247,1613, found 247.1651.

$[\alpha]_D$= -34 (c= 15 mg/mL, DMSO).

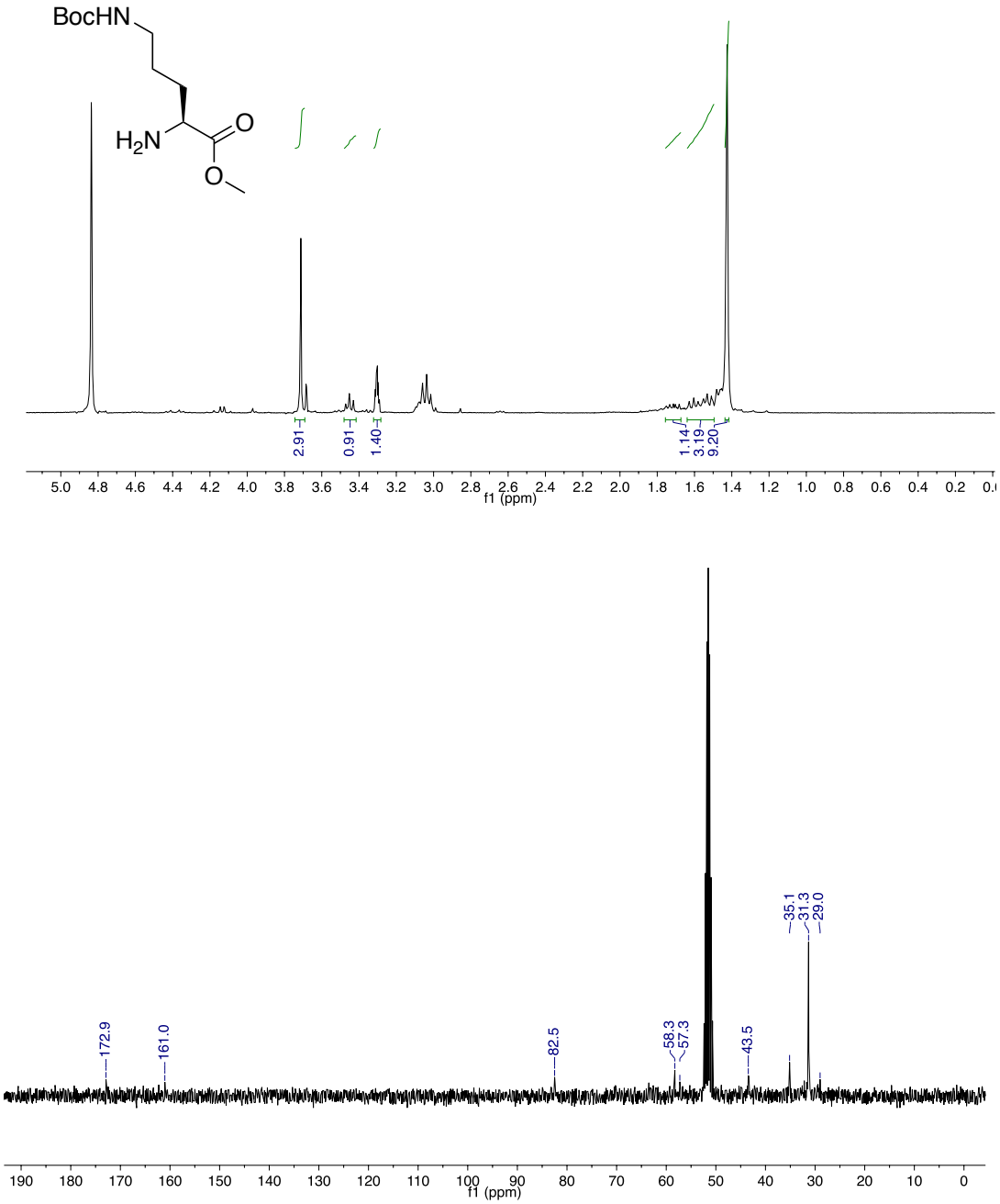


Figure S23. ^{1}H-NMR and ^{13}C-NMR of m-**9** in $CDCl_3$.

Methyl-(S)-5-((tert-butoxycarbonyl)amino)-2-(4-ethynylbenzamido)pentanoate

^{1}H NMR (300 MHz, $CDCl_3$.) δ(ppm): 1.46 (s, 9H), 1.58 (m, 2H), 1.80 (m, 1H), 1.97 (m, 1H), 3.14 (m, 2H), 3.20 (s, 1H), 3.78 (s, 3H), 4.76 (m, 1H), 4.81 (m, 1H), 7.06 (s, 1H), 5.45 (s, 1H), 7.53-7.81 (m, 4H).^{13}C NMR (62.5 MHz, $CDCl_3$.) δ (ppm): 14.1, 26.5, 28.3, 29.1, 31.5, 39.9, 52.5, 52.7, 79.3, 79.6, 82.7, 125.5, 127.2, 132.1, 133.6, 156.2, 166.5, 172.9.

HRMS (ESI) m/z calcd for $C_{20}H_{26}N_2O_5$ [M+H] 375.1875 , found 375.1920.

$[\alpha]_D$= 8 (c= 15 mg/mL, DMSO).

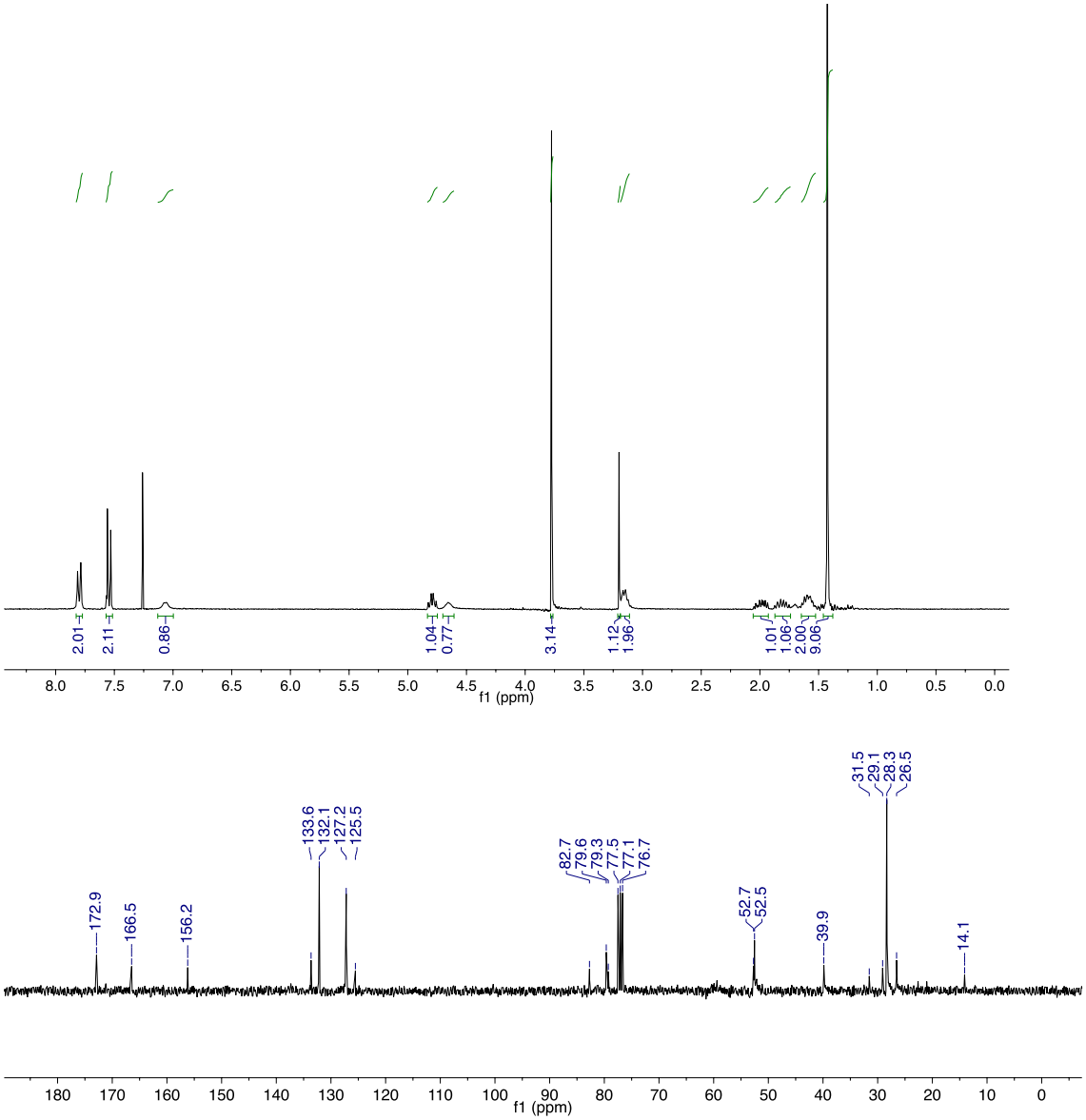


Figure S24. ^{1}H-NMR and ^{13}C-NMR of m-**9** in $CDCl_3$.

(S)-4-(4-ethynylbenzamido)-5-methoxy-5-oxopentan-1-aminium chloride (m-9)

^{1}H NMR (300 MHz, d6-DMSO) δ(ppm): 1.85 (m, 2H), 1.97 (m, 2H), 1.97 (m, 2H), 3.02 (m, 2H), 3.20 (s, 1H), 3.78 (s, 3H), 4.76 (m, 1H), 4.81 (m, 1H), 7.06 (s, 1H), 5.45 (s, 1H), 7.53-7.81 (m, 4H).^{13}C NMR (62.5 MHz, d6-DMSO) δ (ppm): 28.0, 31.8, 43.0, 55.8, 56.5, 84.1, 86.1, 100.3, 129.9, 131.3, 135.7, 137.4, 172.0, 176.1.

HRMS (ESI) m/z calcd for $C_{15}H_{19}ClN_2O_3$ [M+] 275,.412, found 275.1390.

$[\alpha]_D$= -16 (c= 15 mg/mL, DMSO).

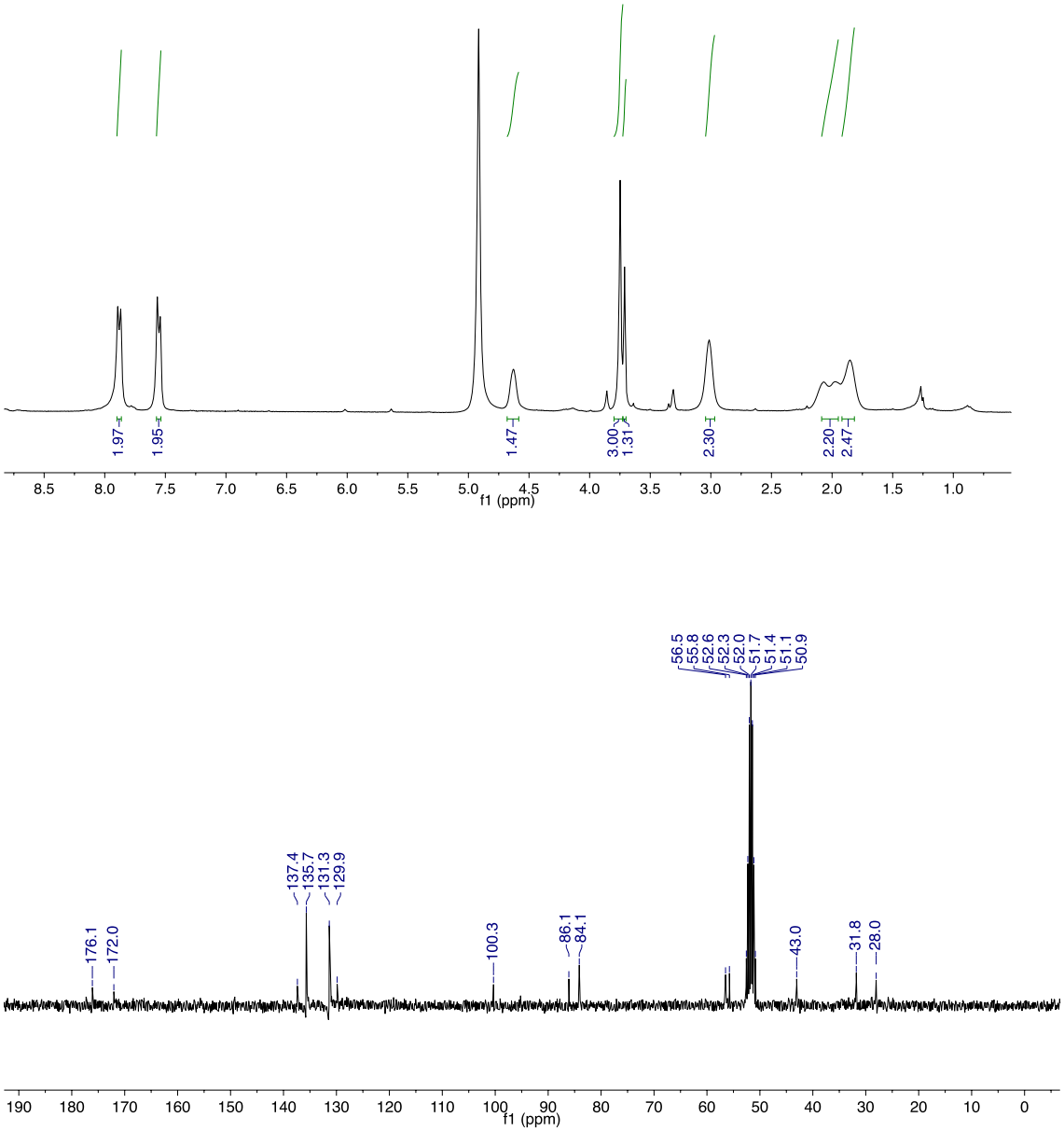


Figure S25. ^{1}H-NMR and ^{13}C-NMR of m-**9** in d6-DMSO.

Methyl(*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-3-((*tert*-butoxycarbonyl)amino)propanoate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.45 (s, 9H), 2.99 (m, 1H), 1.34 (m, 1H), 3.38 (m, 1H), 3.76 (s, 3H), 4.22 (m, 1H), 4.43 (m, 3H), 4.99 (m, 1H), 5.63 (m, 1H), 7.31 (t, 2H), 7.40 (t, 2H), 7.60 (d, 2H), 7.77 (d, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 28.4, 36.5, 47.2, 51.4, 52.7, 67.0, 120.0, 125.1, 127.1, 127.7, 141.3, 143.6, 156.0, 177.5.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= 19 (c= 15 mg/mL, $CHCl_3$).

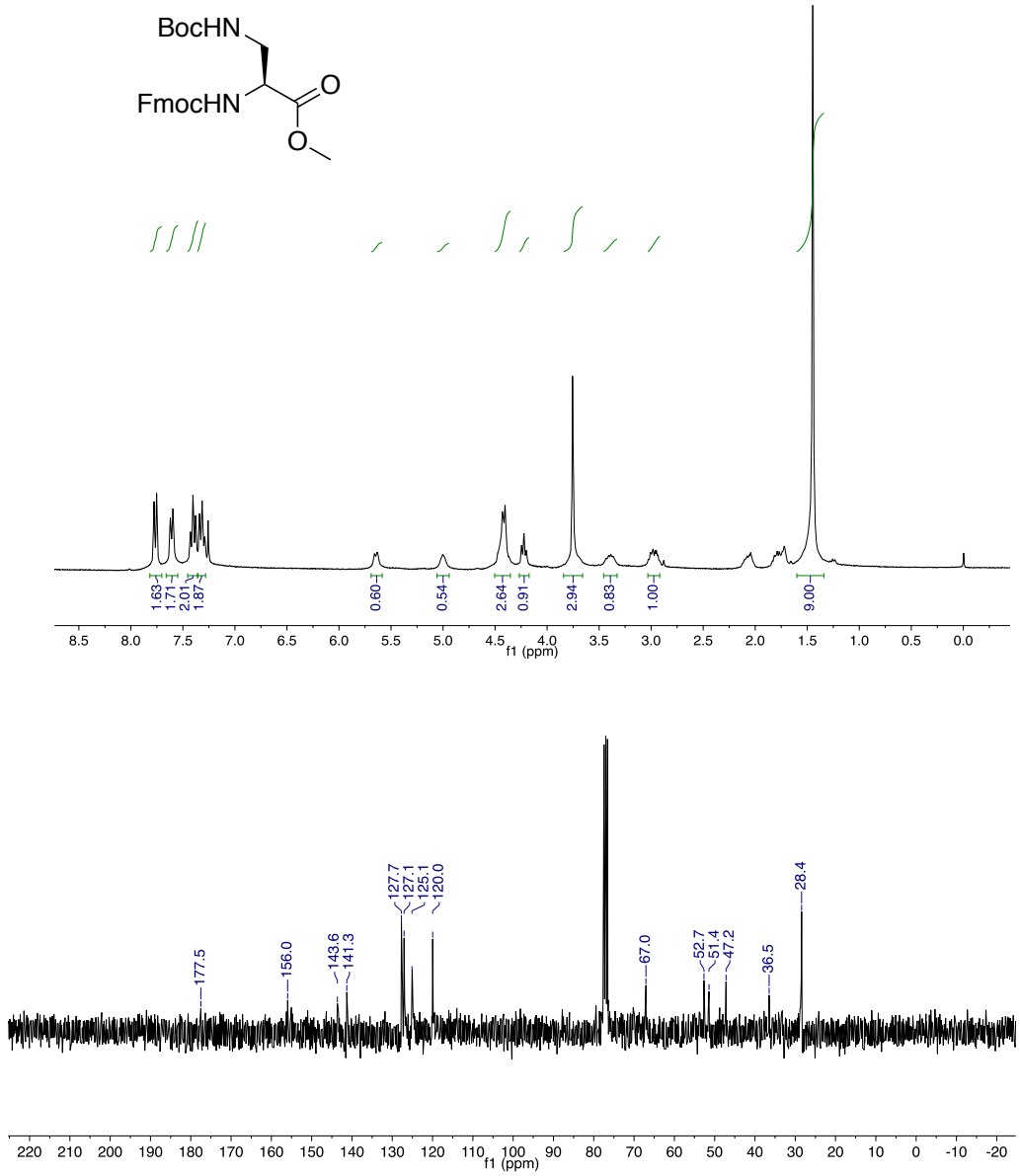


Figure S26. ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$.

Methyl (*S*)-2-amino-3-((*tert*-butoxycarbonyl)amino)propanoate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.45 (s, 9H), 2.02 (m, 2H), 1.34 (m, 1H), 3.30 (m, 1H), 3.56 (m, 1H), 3.74 (s, 1H), 4.94-5.14 (m, 1H), 7.63 (s, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 28.4, 34.4, 37.8, 52.2, 52.9, 146.0, 175.6.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= 22 (c= 15 mg/mL, $CHCl_3$).

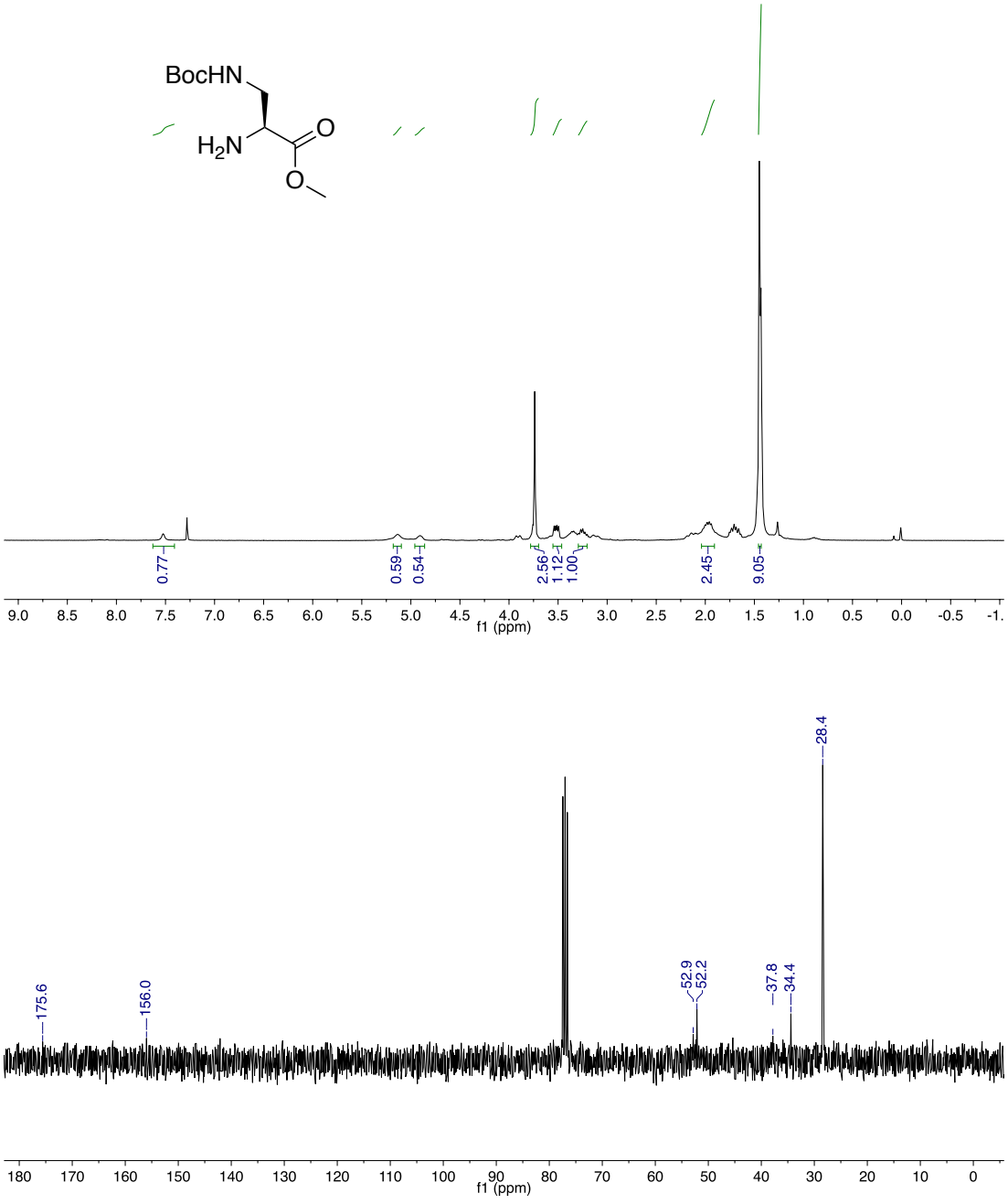


Figure S27. ^{1}H-NMR and ^{13}C-NMR in $CDCl_3$.

Methyl(*S*)-3-((*tert*-butoxycarbonyl)amino)-2-(4-ethynylbenzamido)propanoate

^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm): 1.43 (m, 6H), 3.01 (m, 1H), 3.20 (m, 1H), 3.48 (m, 1H), 3.77 (s, 3H), 4.88 (m, 1H), 5.13 (m, 1H), 7.39 (d, 1H), 7.56 (d, 2H), 7.85 (d, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 28.4, 32.6, 36.4, 50.1, 52.7, 79.7, 82.7, 125.7, 127.2, 132.3, 133.5, 156.3, 166.6, 172.9.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580. $[\alpha]_D$= 13 (c= 15 mg/mL, $CHCl_3$).

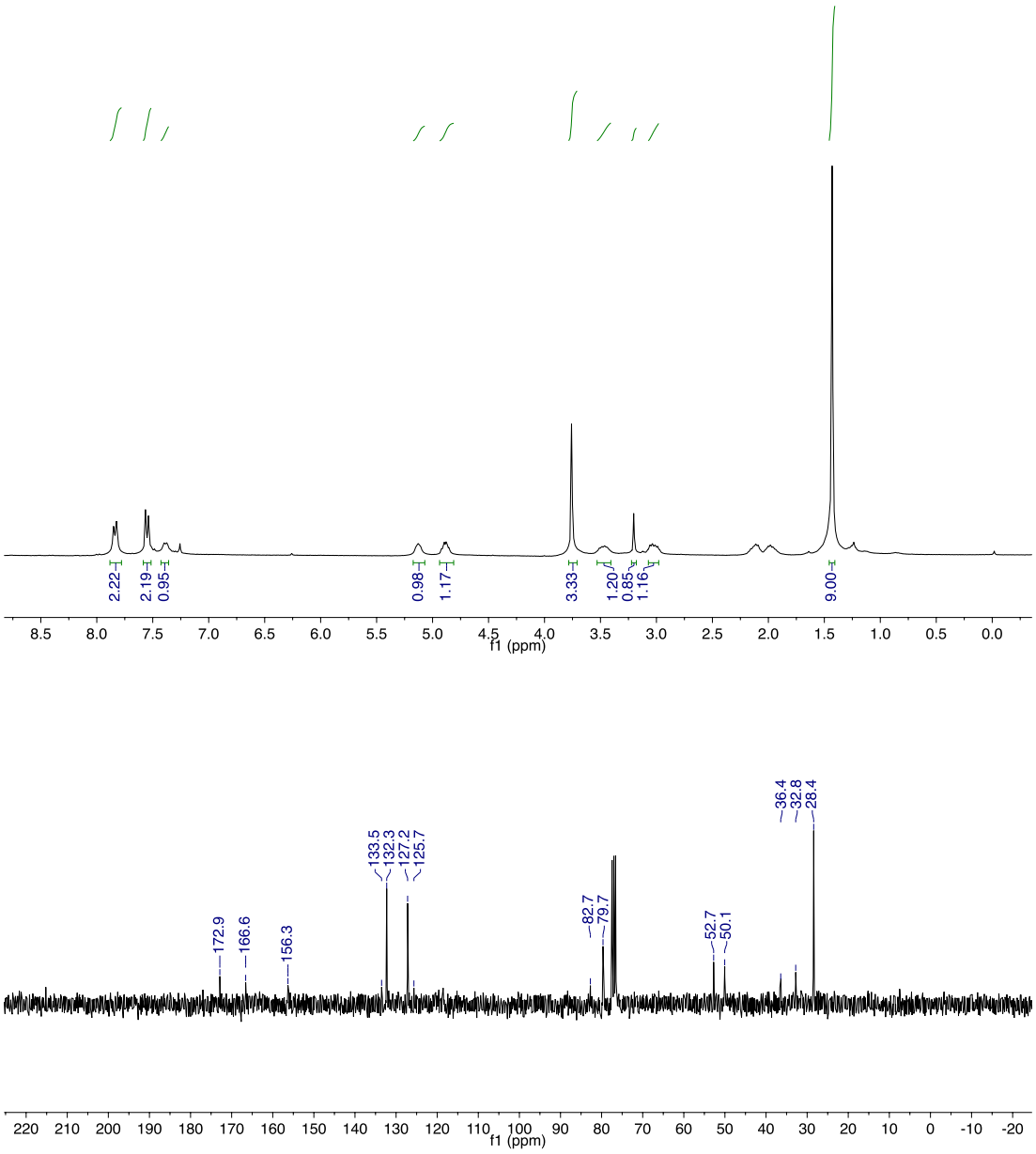


Figure S28. ^{1}H-NMR and ^{13}C-NMR of **8** in $CDCl_3$.

(*S*)-2-(4-ethynylbenzamido)-3-methoxy-3-oxopropan-1-aminium (m-8)

^{1}H NMR (300 MHz, CD_3OD) δ(ppm): 1.77 (m, 2H), 1.93 (m, 2H), 2.66 (s, 4H), 3.20 (s, 1H), 3.32 (s, 3H), 4.31 (m, 2H), 7.11 (d, 2H), 7.39 (d, 2H). ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm): 27.3, 34.9, 48.9, 50.3, 78.5, 80.5, 124.5, 125.7, 130.2, 131.5, 166.7, 169.8, 171.0.

HRMS (ESI) m/z calcd for $C_{13}H_{14}N_2O$ [M+H] 215.2680, found 265.1580.

$[\alpha]_D$= -27 (c= 15 mg/mL, $CHCl_3$).

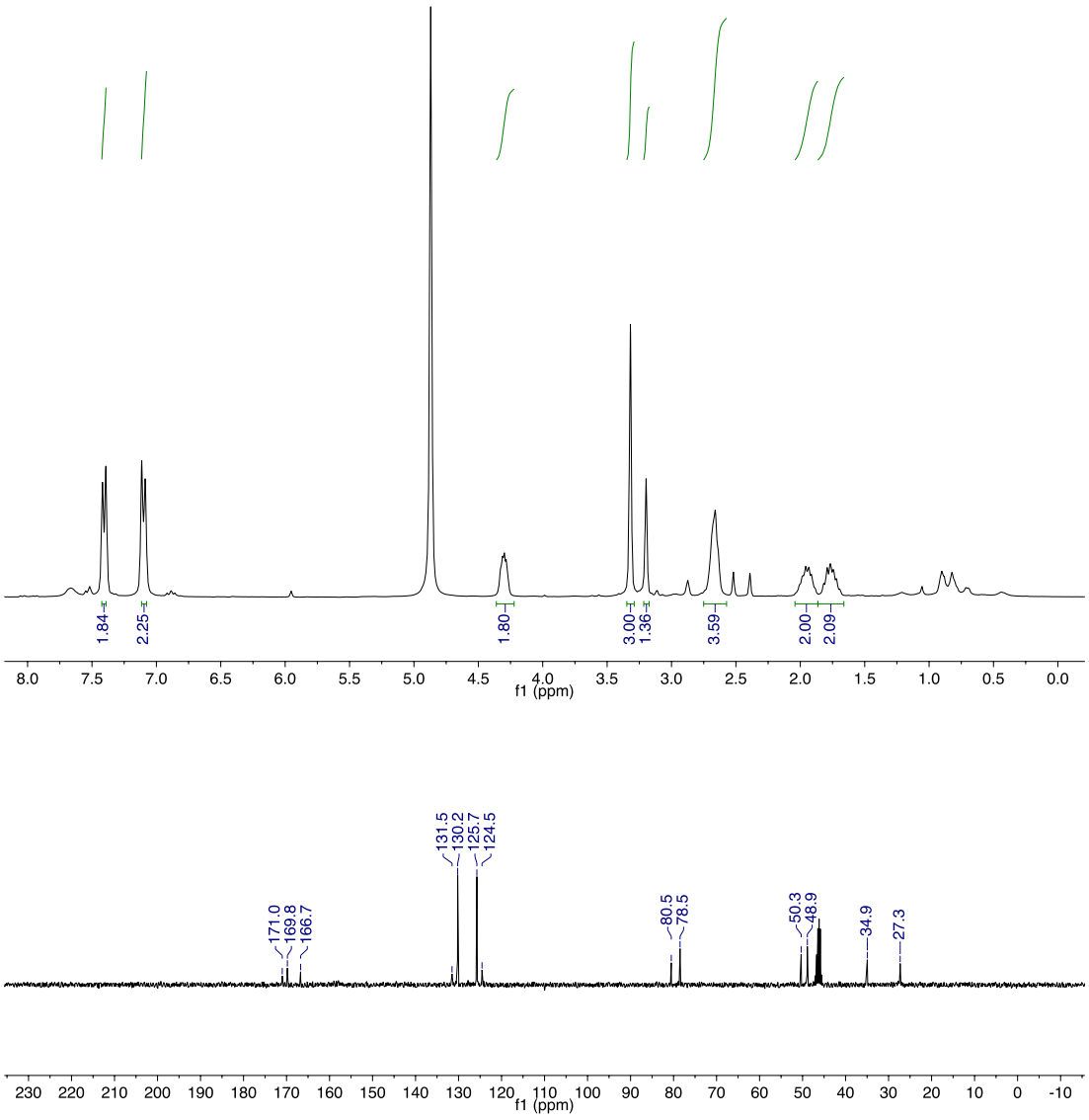


Figure S29. ^{1}H-NMR and ^{13}C-NMR of **m-8** in CD_3OD.

Polymer synthesis

General procedure for polymerization

Firstly, in a general way, the synthesized monomers were dissolved in water and DMF, adding as catalysts $Rh(nbd)BPh_4$, $[Rh(cod)_2]BF_4$, and $[Rh(nbd)Cl]_2$. The reaction mixture was stirred at r.t. for 36h without obtaining any polymer. The problem is that the Rh (I) catalyst is poisoned with the presence of free amines. (Table S3).

To solve this problem, monomers (**1-11**) were added as a solid in a flask. Water and HCl (11 M, 1.0 eq.) were added in order to protonate the amino group and avoid the catalyst poisoning. Next, a solution of $[Rh(cod)_2]BF_4$ in water at r.t. (Table S4) The reaction mixture was stirred at r.t. for 36h. Next, the resulting polymers were diluted in water and lyophilized. After that, the polymers were dissolved in MeOH and precipitated in large amount of ethyl acetate and centrifuged (twice).

Table S3. Catalysts poisoned with monomers (**1-11**).

Catalyst	mol/L catalyst	monomer	mol/L monomer
$Rh(nbd)BPh_4$	0.005 – 0,01	m(1-11)	0.5
$[Rh(cod)_2]BF_4$	0.005 – 0,01	m(1-11)	0.5
$[Rh(nbd)Cl]_2$	0.005 – 0,01	m(1-11)	0.5

Table S4. Polymerization conditions of Poly (**1-11**).

Monomer	Mass (mg)	Water (µL)	Catalyst (mg)	HCl (µL)	Yield (mg)
m-**1**	80	810	0.92	43	73% (58 mg)
m-**2**	80	748	0.86	40	81% (65 mg)
m-**3**	80	652	0.75	31	76% (61 mg)
m-**4**	80	612	0.70	29	85% (68 mg)
m-**5**	80	612	0.70	29	78 % (62 mg)
m-**6**	80	534	0.64	25	80 % (64 mg)
m-**7**	80	658	0.76	31	88% (70 mg)
m-**8**	80	392	0.45	19	61% (49 mg)
m-**9**	80	714	0.67	17	65% (52 mg)
m-**10**	80	610	0.56	75	70% (56 mg)
m-**11**	80	1500	1.39	64	59% (56 mg)

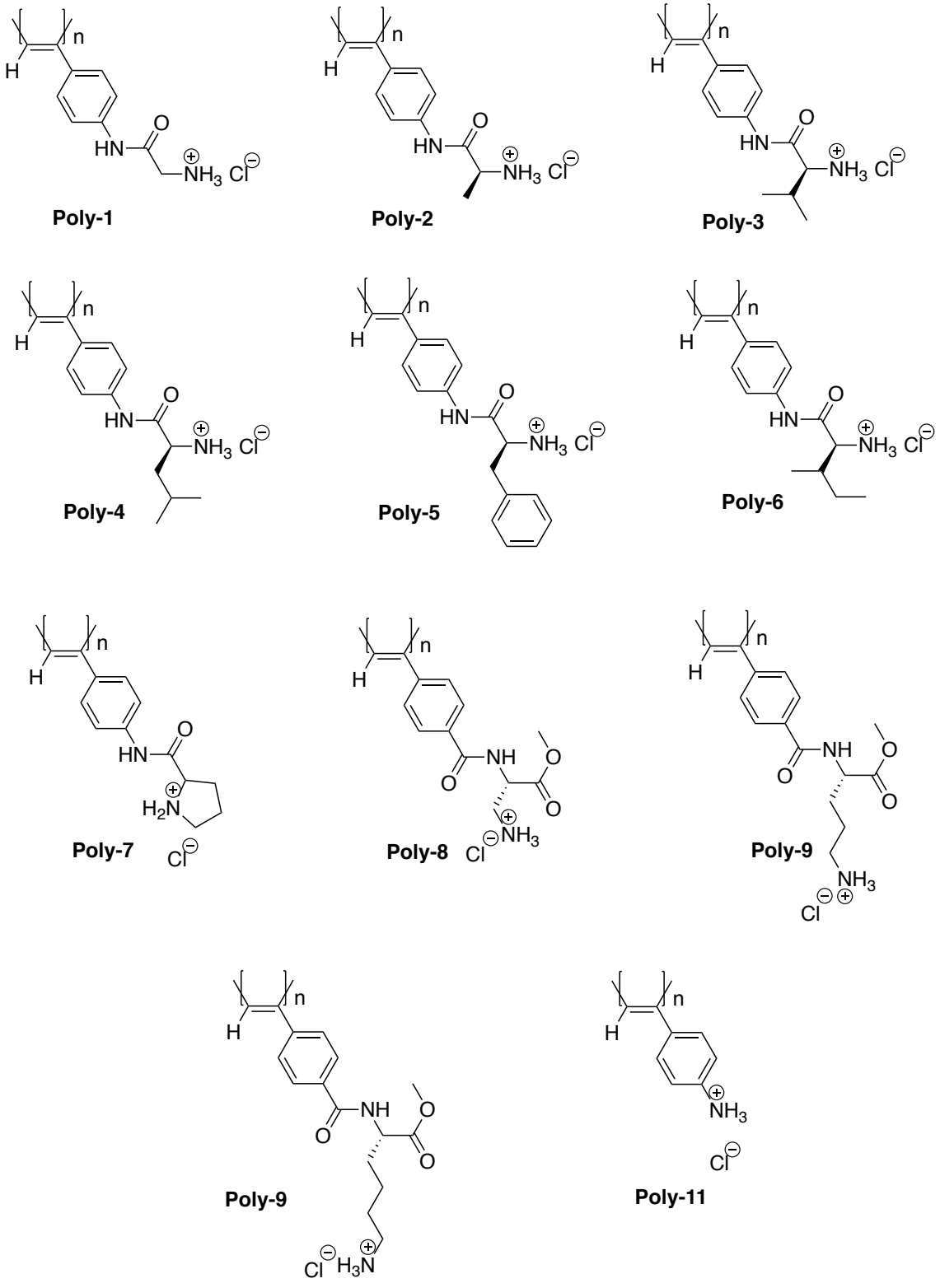


Figure S30. Structure polymers (**1-11**).

GPC Experiments

The molecular weight (Mn) of all polymers was estimated by GPC with water 0.05 M solution of $NaNO_3$ as eluent at flow rate 1 mL/mn at concentration 0.5 mg/mL, using narrow poly(styrene sulfonate) sodium salt standards (PSS) as calibrants.

Table S5. GPC data of poly **1-11.**

Polymer	Mn	Mw	Mp	Mz	PDI
Poly-**1**	9023	79780	177270	208956	2.84
Poly-**2**	75210	177969	199247	385492	2.36
Poly-**3**	31336	111279	128535	229286	3.55
Poly-**4**	67796	217186	236216	330460	3.20
Poly-**5**	72385	119688	133359	166334	1.65
Poly-**6**	62895	163210	194796	271561	2.91
Poly-**7**	62672	149420	171588	232734	2.38
Poly-**8**	58835	138218	167152	192114	1.78
Poly-**9**	61232	145023	168445	209865	2.08
Poly-**10**	67855	176564	195133	176950	1.53
Poly-**11**	4764	5779	5344	6950	1.21

NMR Experiments

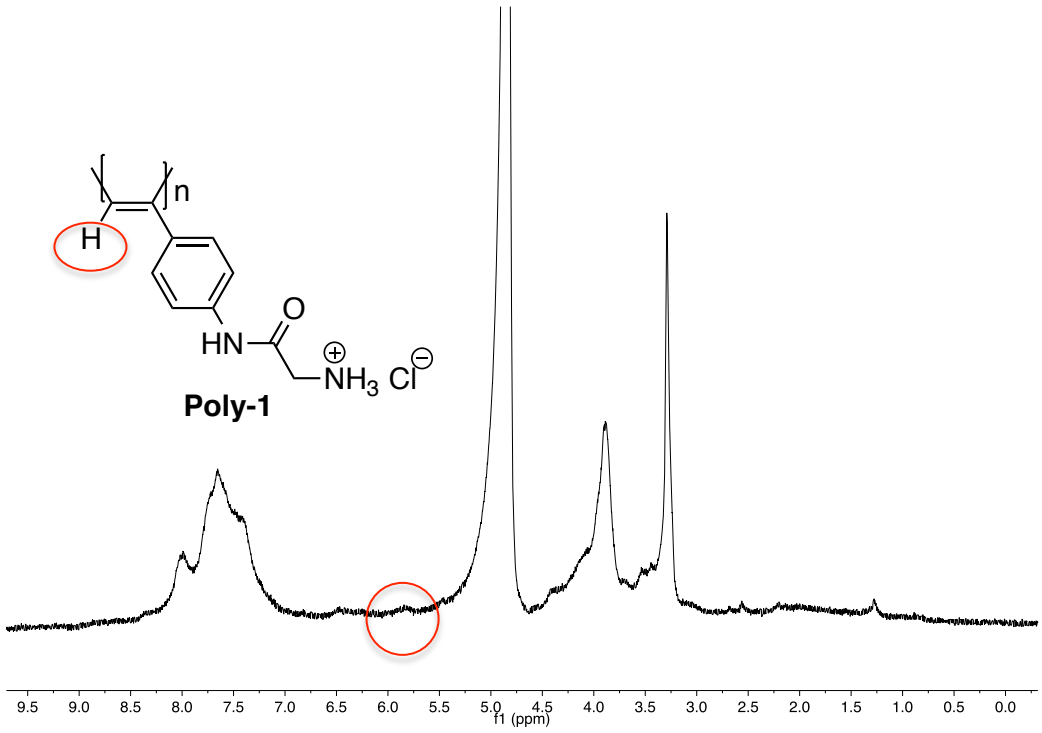


Figure S31. ^{1}H-NMR of poly-**1** in CD_3OD.

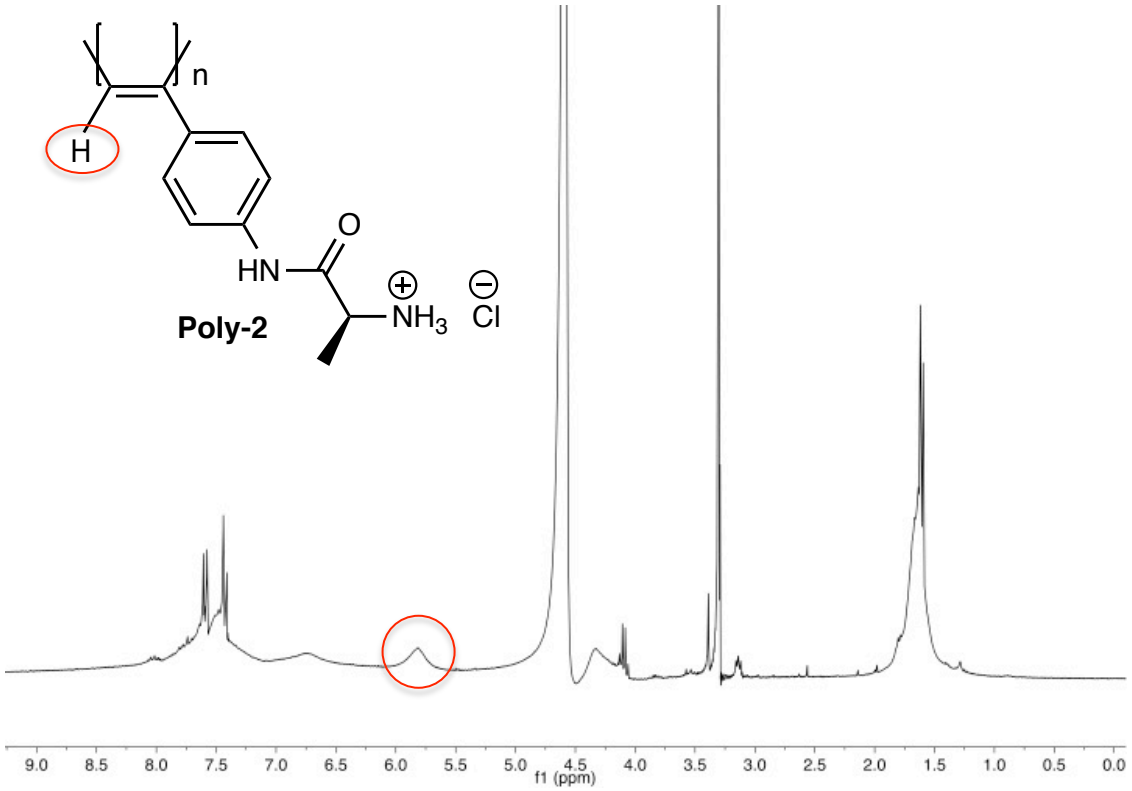


Figure S32. ^{1}H-NMR of poly-**2** in CD_3OD.

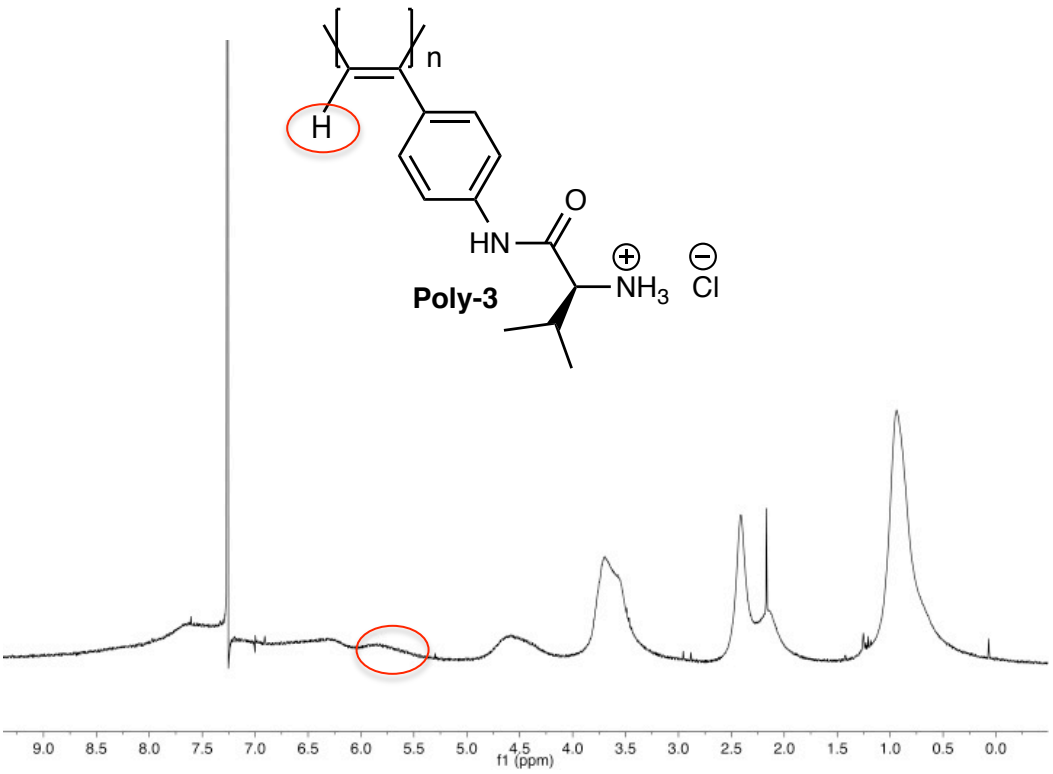


Figure S33. ^{1}H-NMR of poly-**3** in CD_3OD.

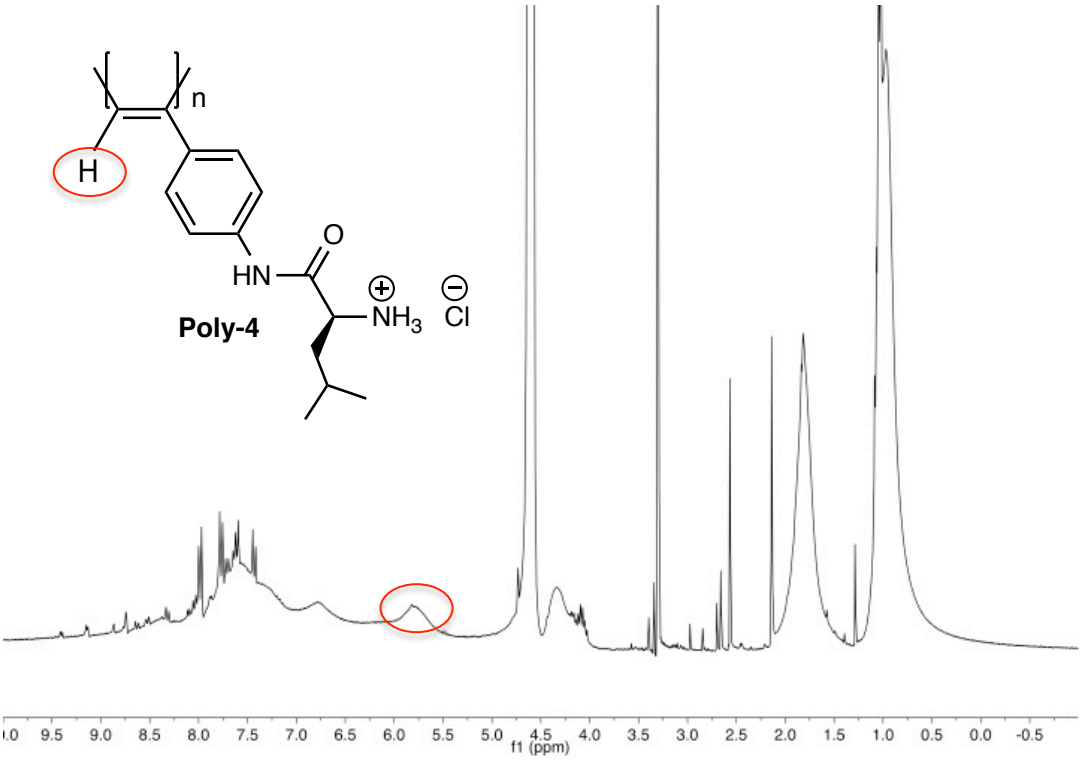


Figure S34. ^{1}H-NMR poly-**4** in CD_3OD.

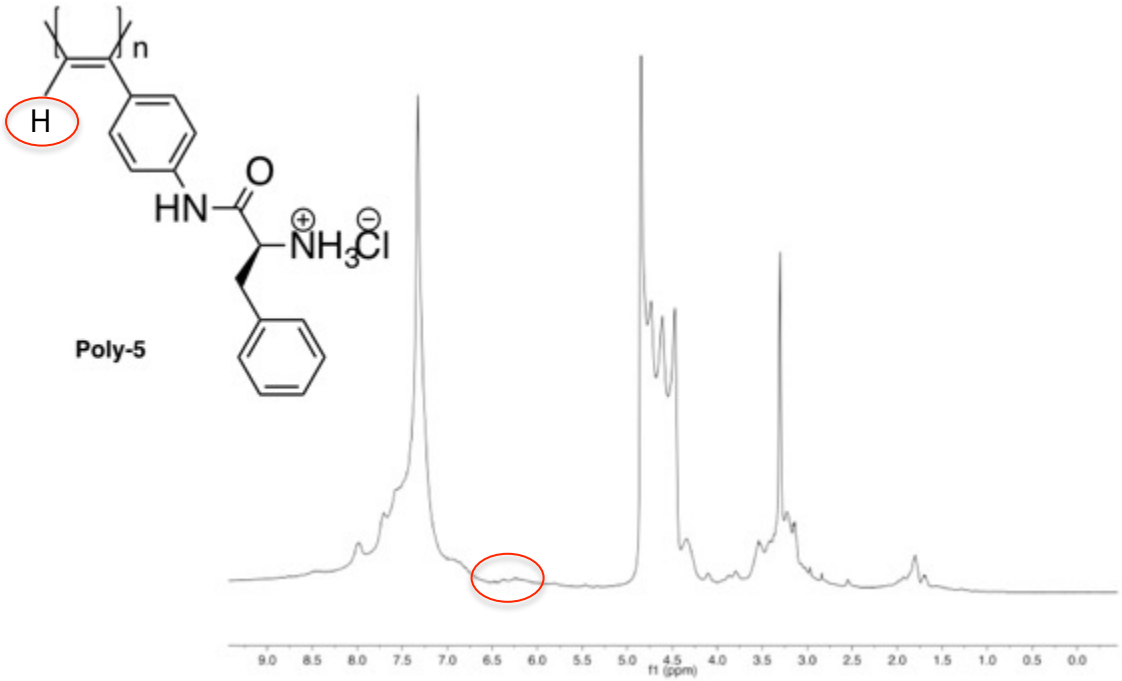


Figure S35. ^{1}H-NMR of poly-**5** in CD_3OD.

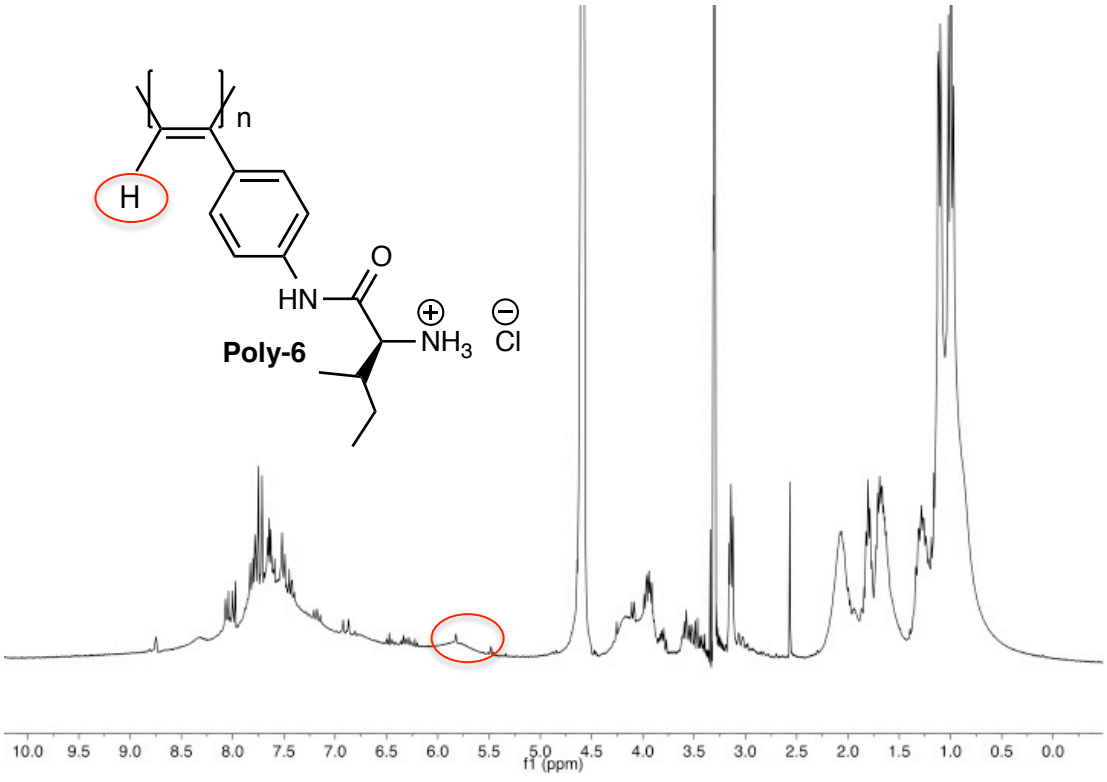


Figure S36. ^{1}H-NMR of poly-**6** in CD_3OD.

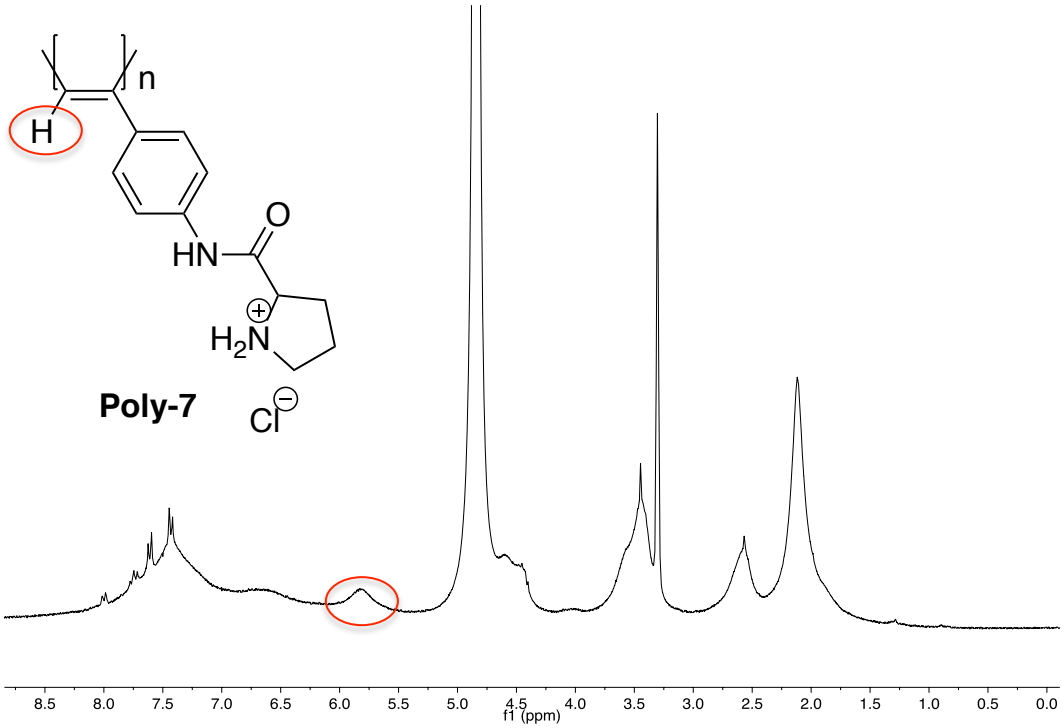


Figure S37. ^{1}H-NMR of poly-**7** in CD_3OD.

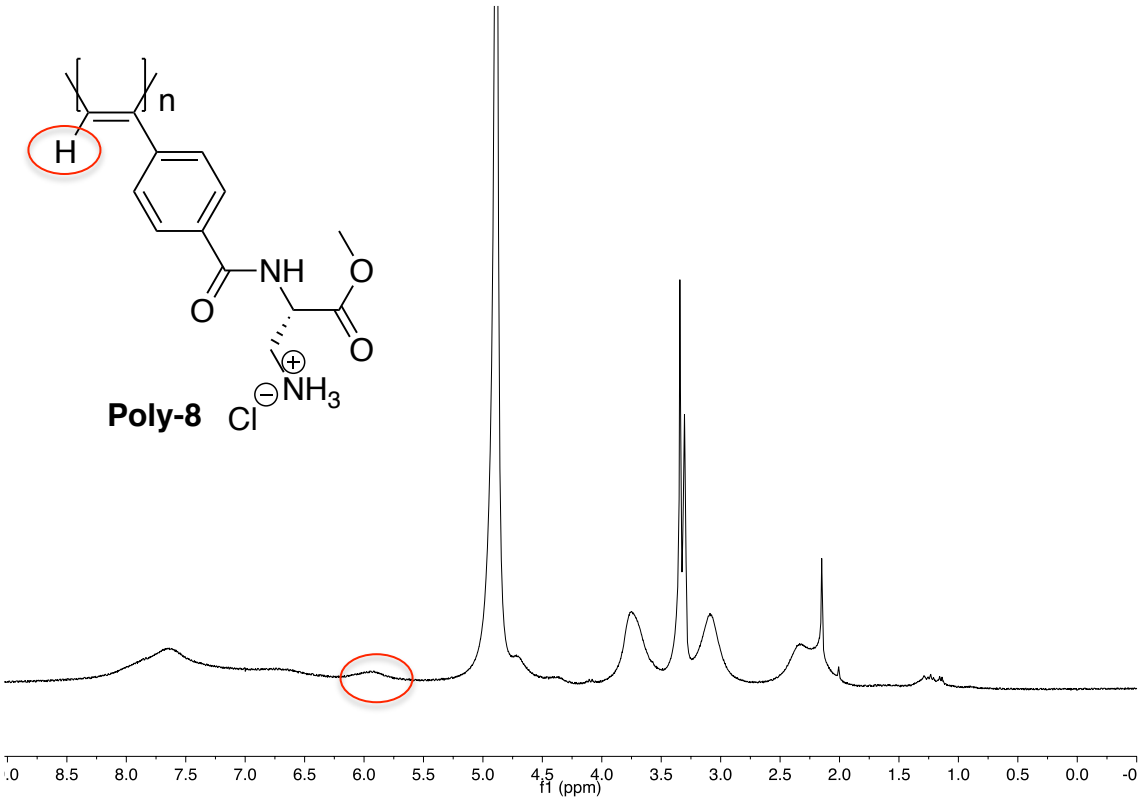


Figure S38. ^{1}H-NMR of poly-**8** in CD_3OD.

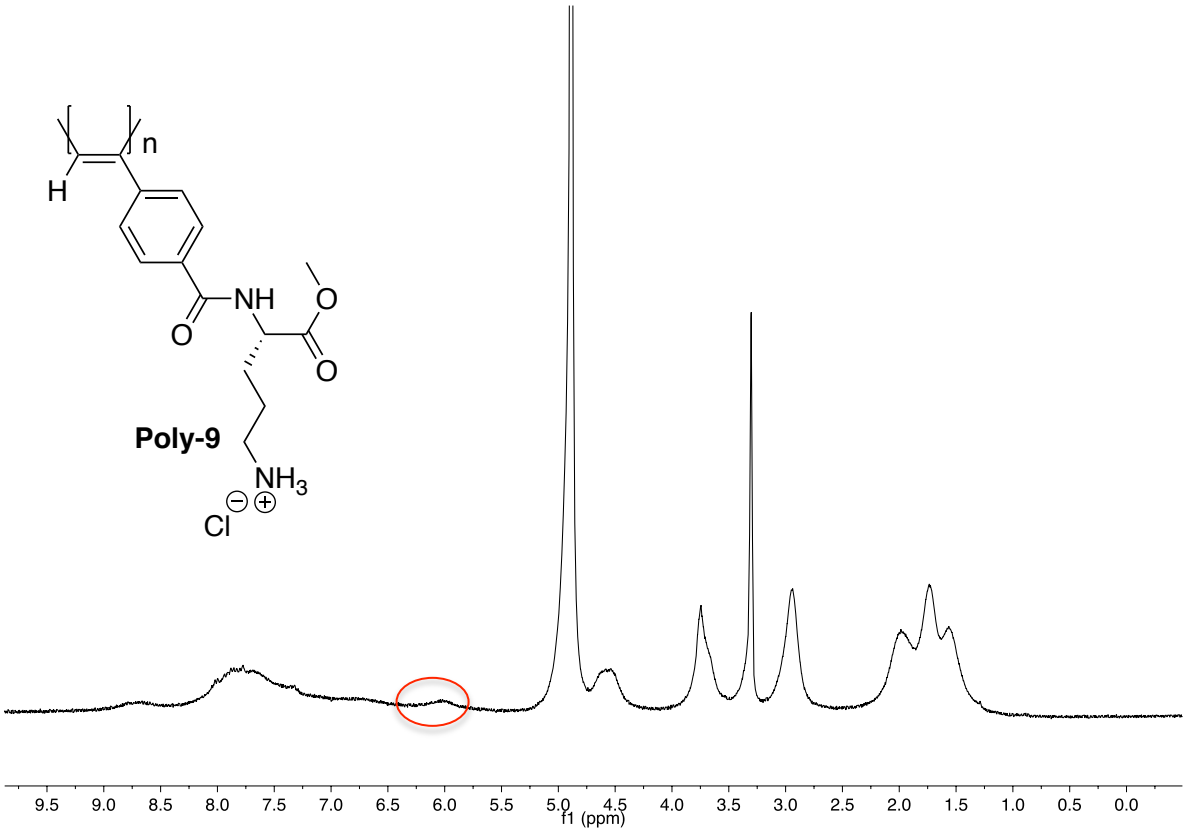


Figure S39. ^{1}H-NMR of poly-**9** in CD_3OD.

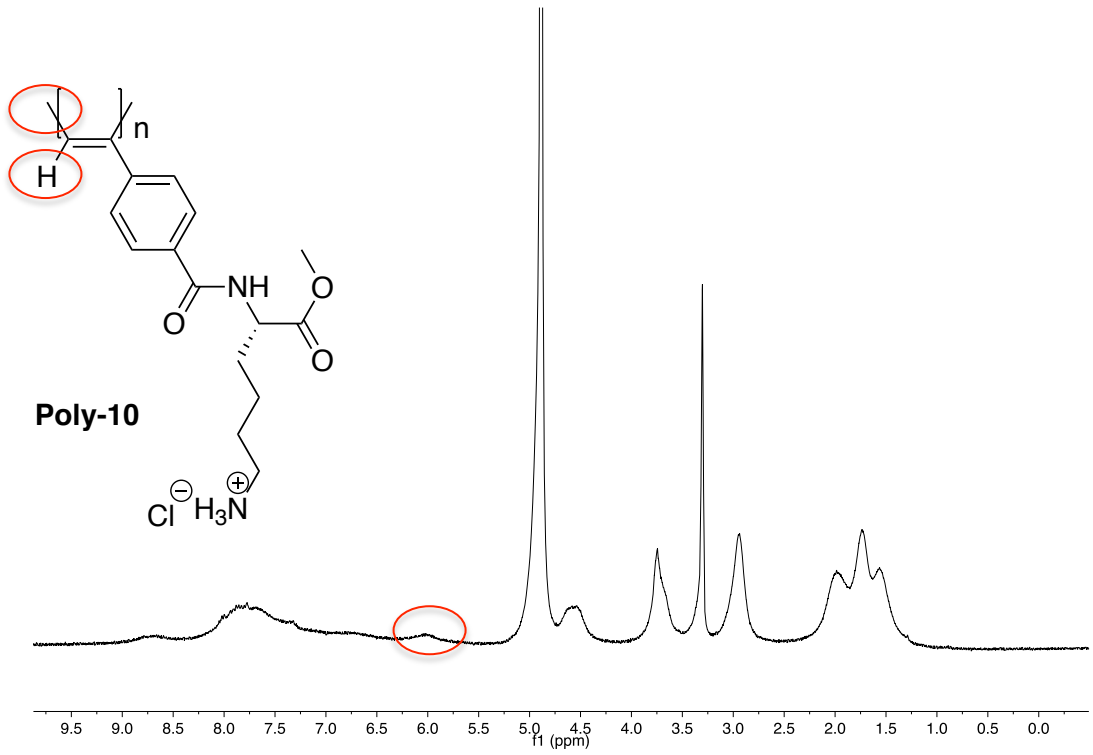


Figure S40. ^{1}H-NMR of poly-**10** in CD_3OD.

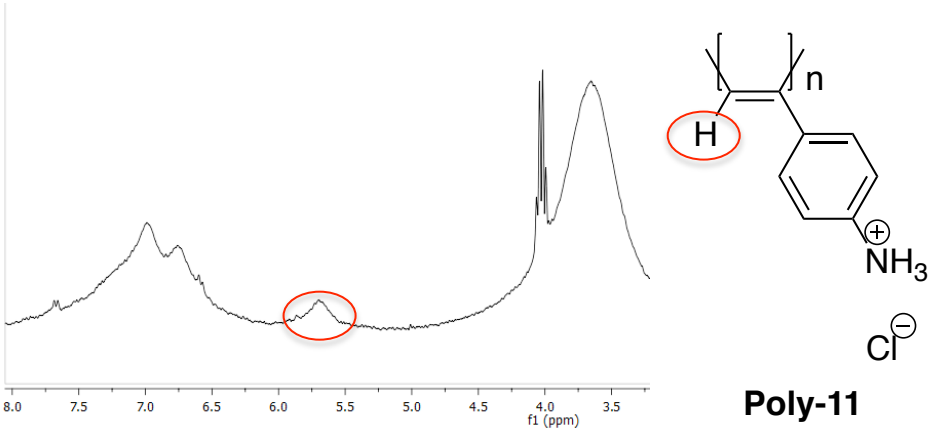


Figure S41. ^{1}H-NMR of poly-**11** in CD_3OD.

Raman Spectroscopy

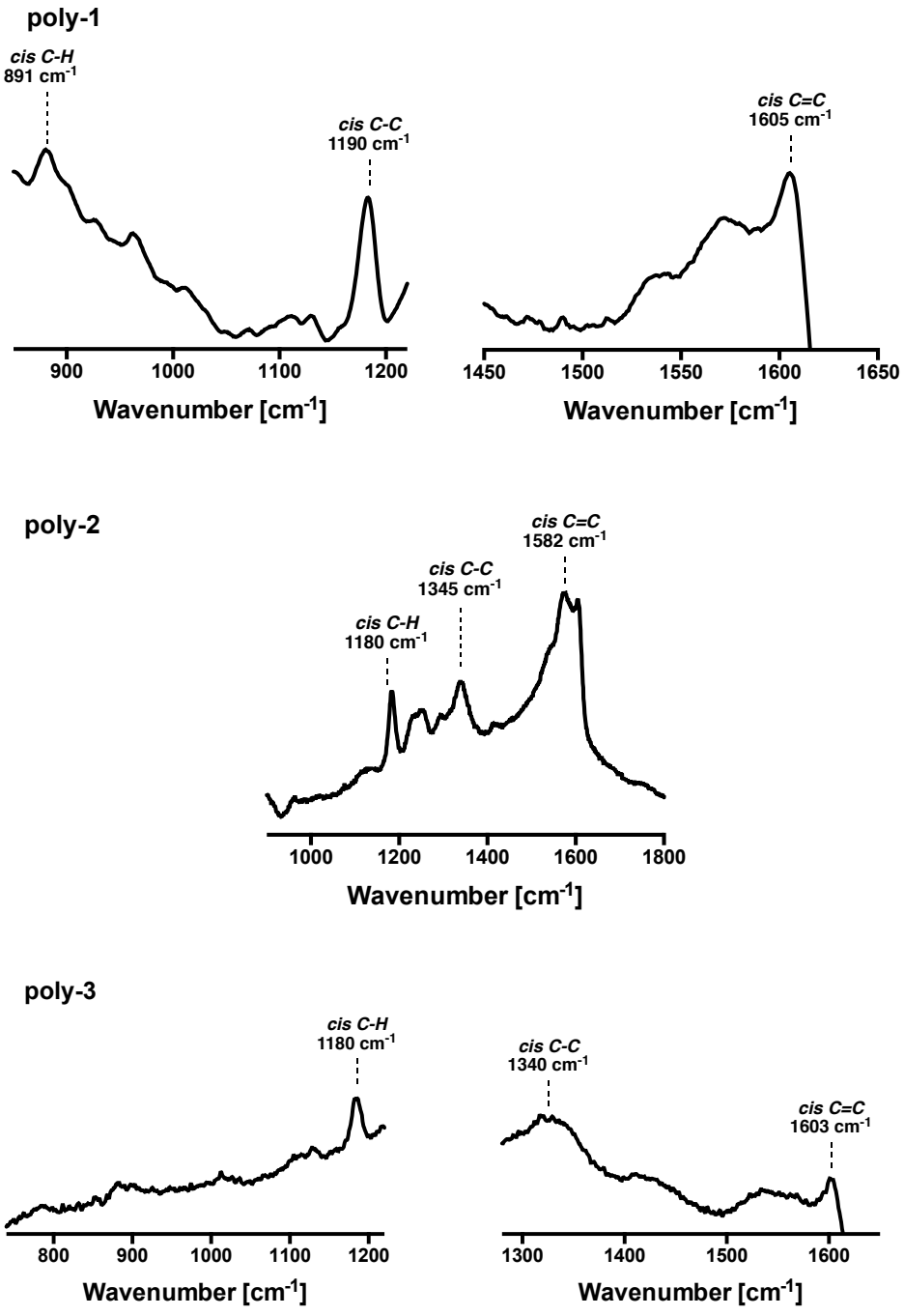


Figure S42. Raman spectra of poly **1-3**, showing the characteristic bands of a cis-polyene backbone.

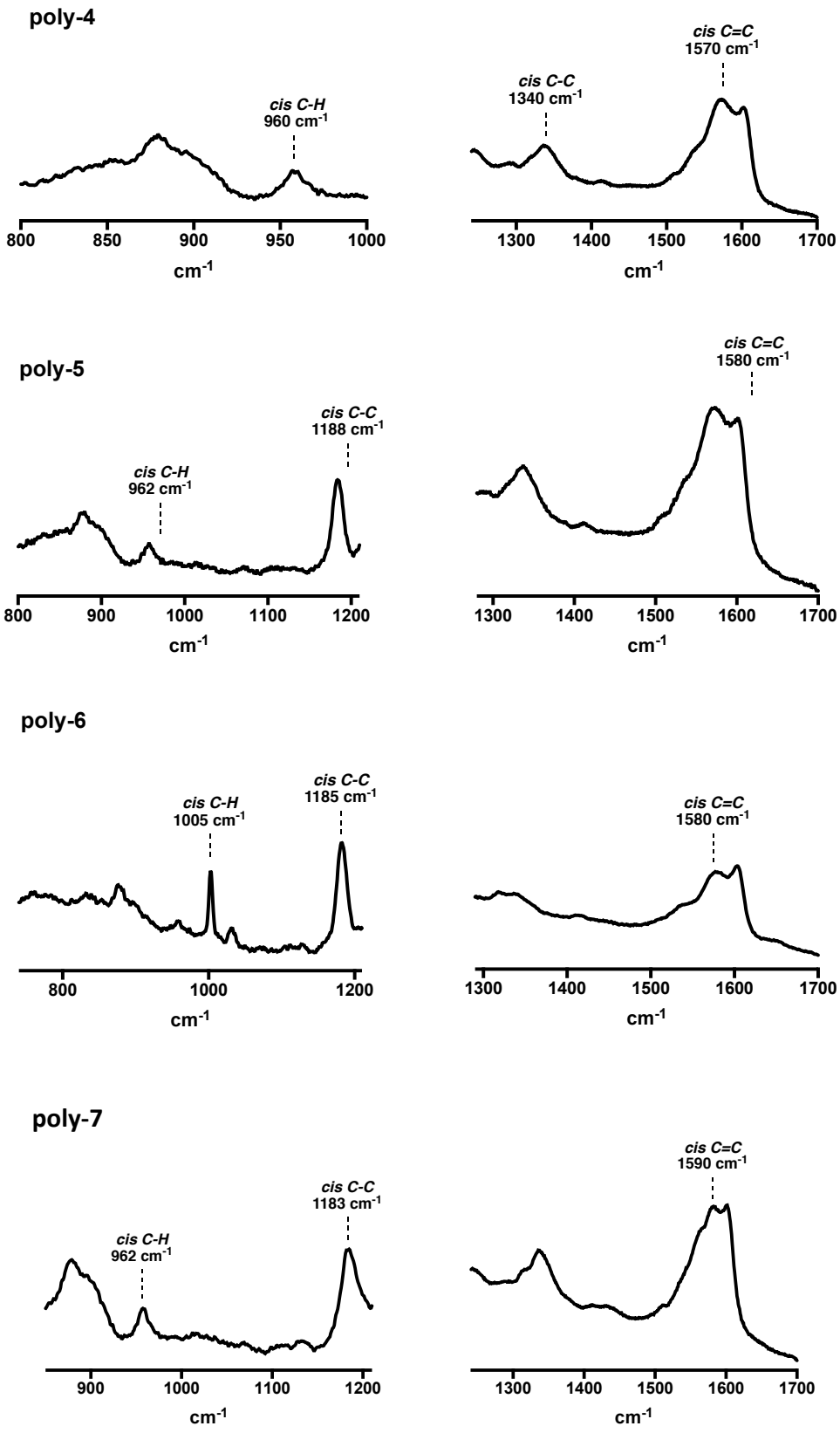


Figure S43. Raman spectra of poly **4-7**, showing the characteristic bands of a cis-polyene backbone.

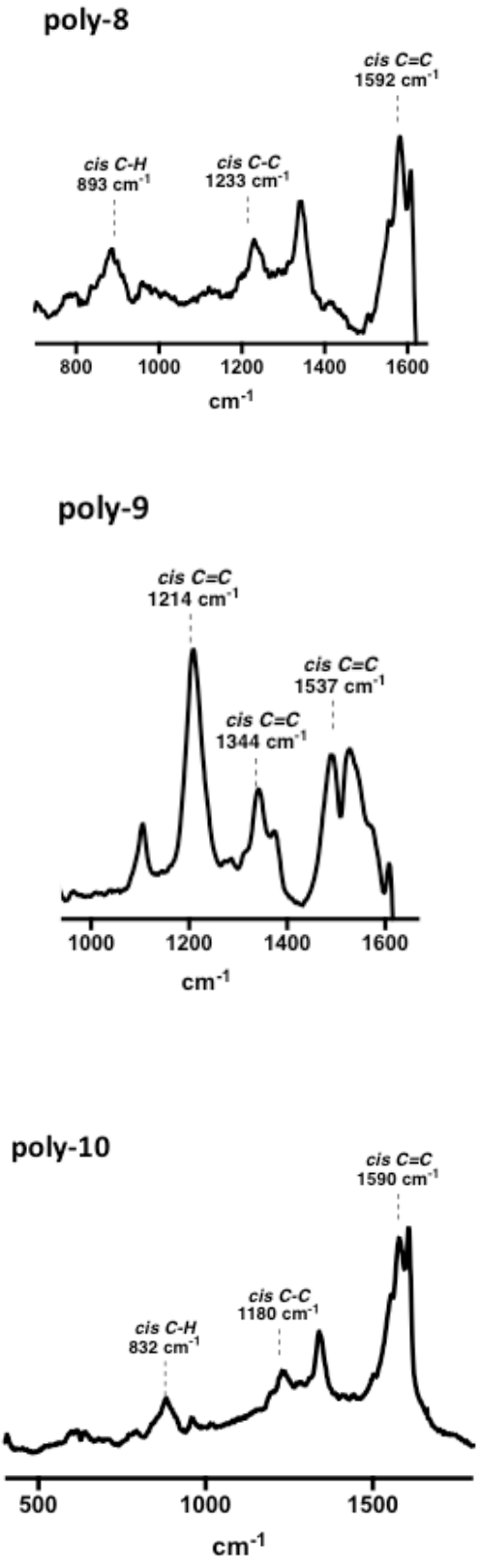


Figure S44. Raman spectra of poly **8-10** showing the characteristic bands of a cis-polyene backbone.

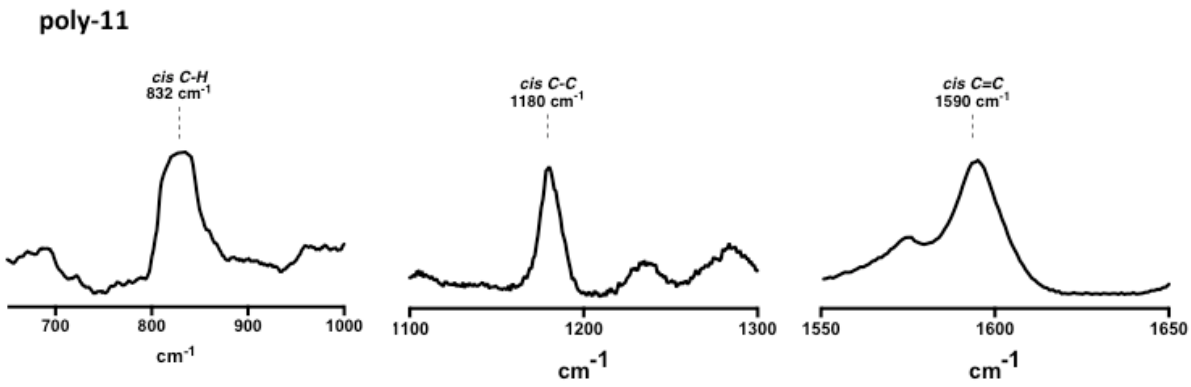


Figure S45. Raman spectra of poly **11**, showing the characteristic bands of a cis-polyene backbone.

CD and UV experiments

CD studies of solutions of poly-**2**, poly-**7**, poly-**8** and poly-**9** (0.5 mg/mL) were carried out in water and in organic polar solvents such as MeOH and DMSO.

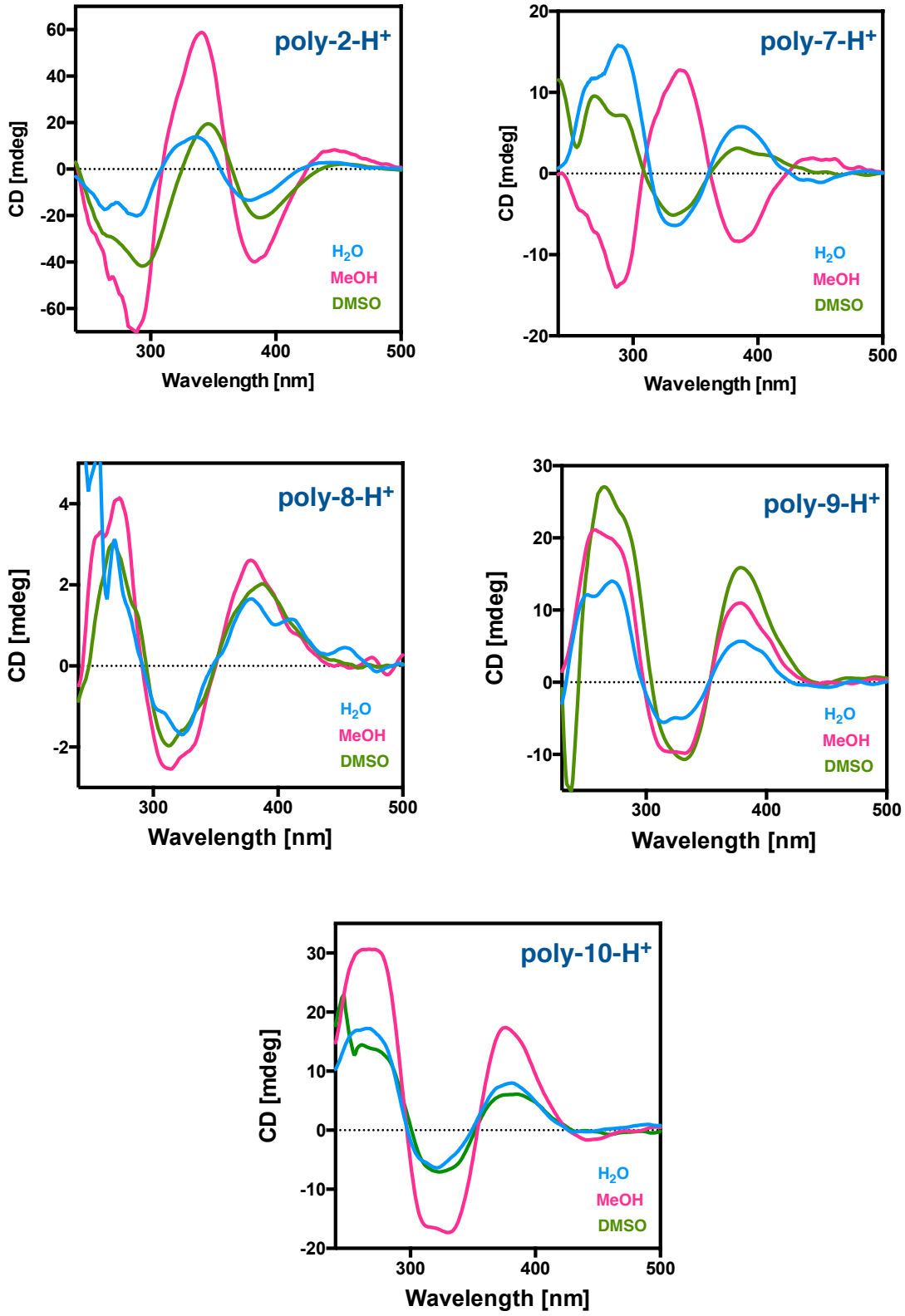


Figure S46. CD spectra of poly-**2,** poly-**7**, poly-**8** and poly-**9** in H_2O, MeOH, DMSO (0.5 mg/mL).

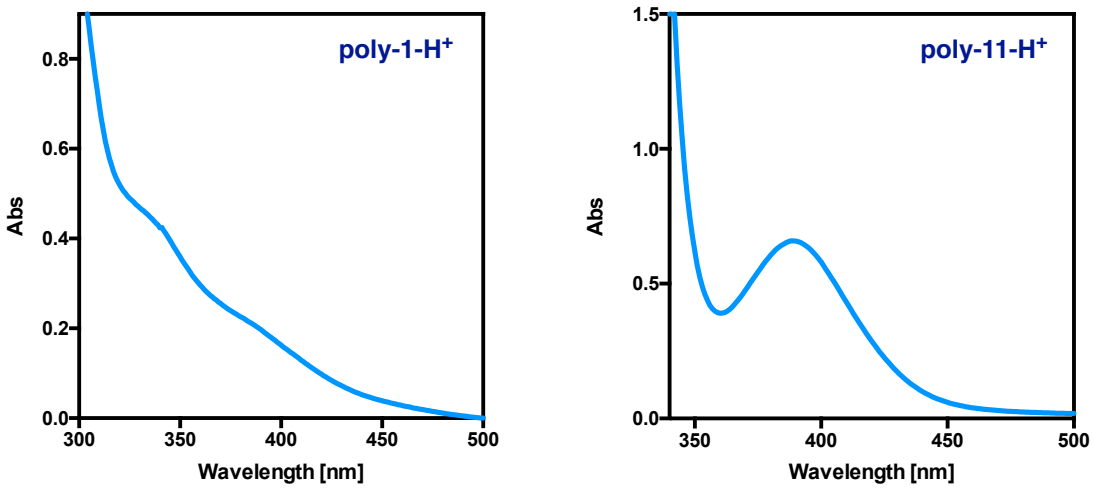


Figure S47. UV-vis spectra of poly-**1** and poly-**10** in water (1.0 mg/mL).

CD studies: pH dependence

Titrations of polymers (poly-**3**, poly-**4**, poly-**5**, poly-**7** and poly-**9**) were carried out at different pHs in water (0.5 mg/mL).

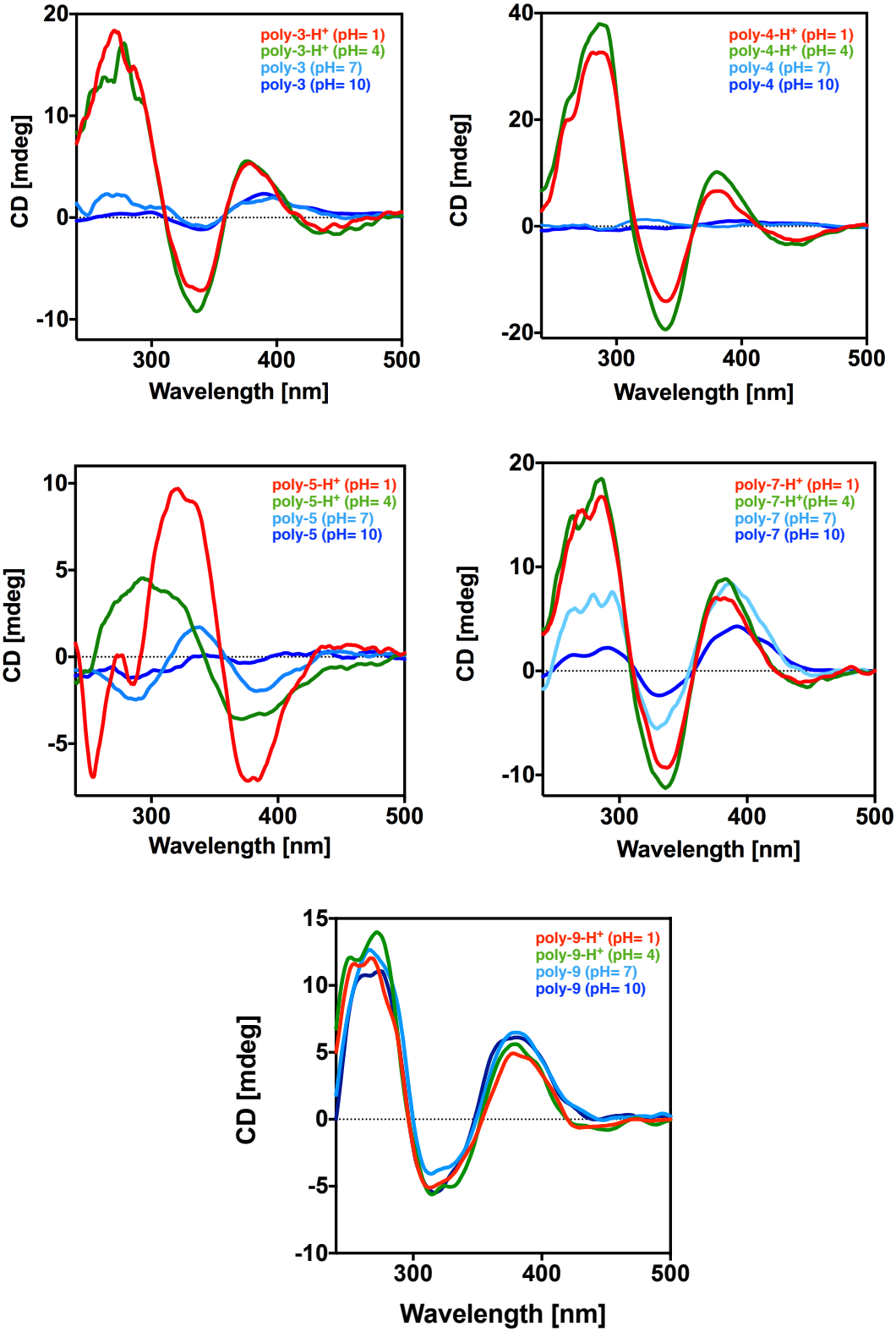
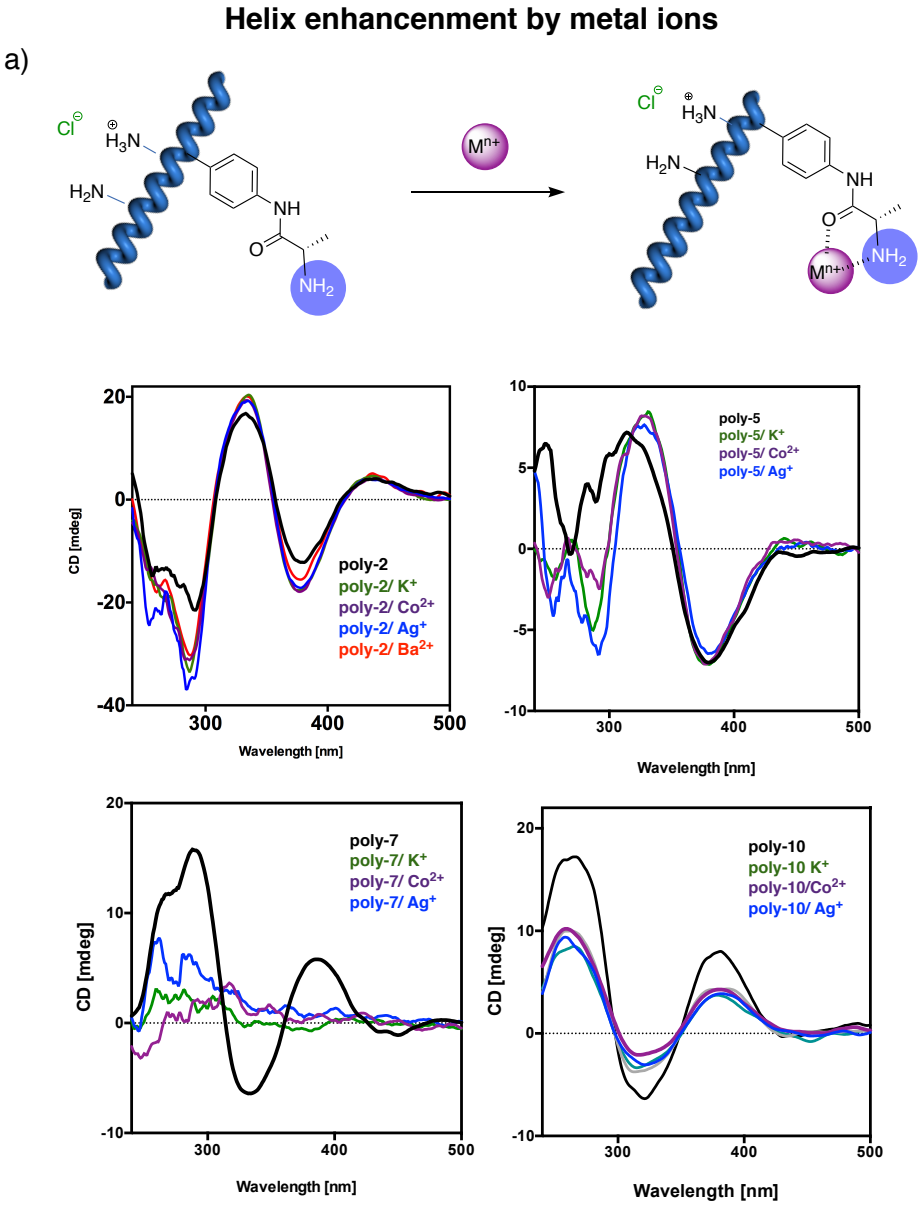


Figure S48. CD spectra of poly-**3**, poly-**4**, poly-**5,** poly-**7** and poly-**9** at different pHs in water (0.5 mg/mL).

Interaction with metals:

Helix enhancement of poly-**2**, and poly-(**5-10**) by metal ions used as external stimuli. This experiment corroborates the presence of a syn conformation for the carbonyl and amino group at the pendant (Figure S49a).
Helix inversion of poly-**3** and poly-**4** by metal ions used as external stimuli. Tis experiment confirm the presence of and anti conformation between the carbonyl and the amino group at the pendant (figure S49b).



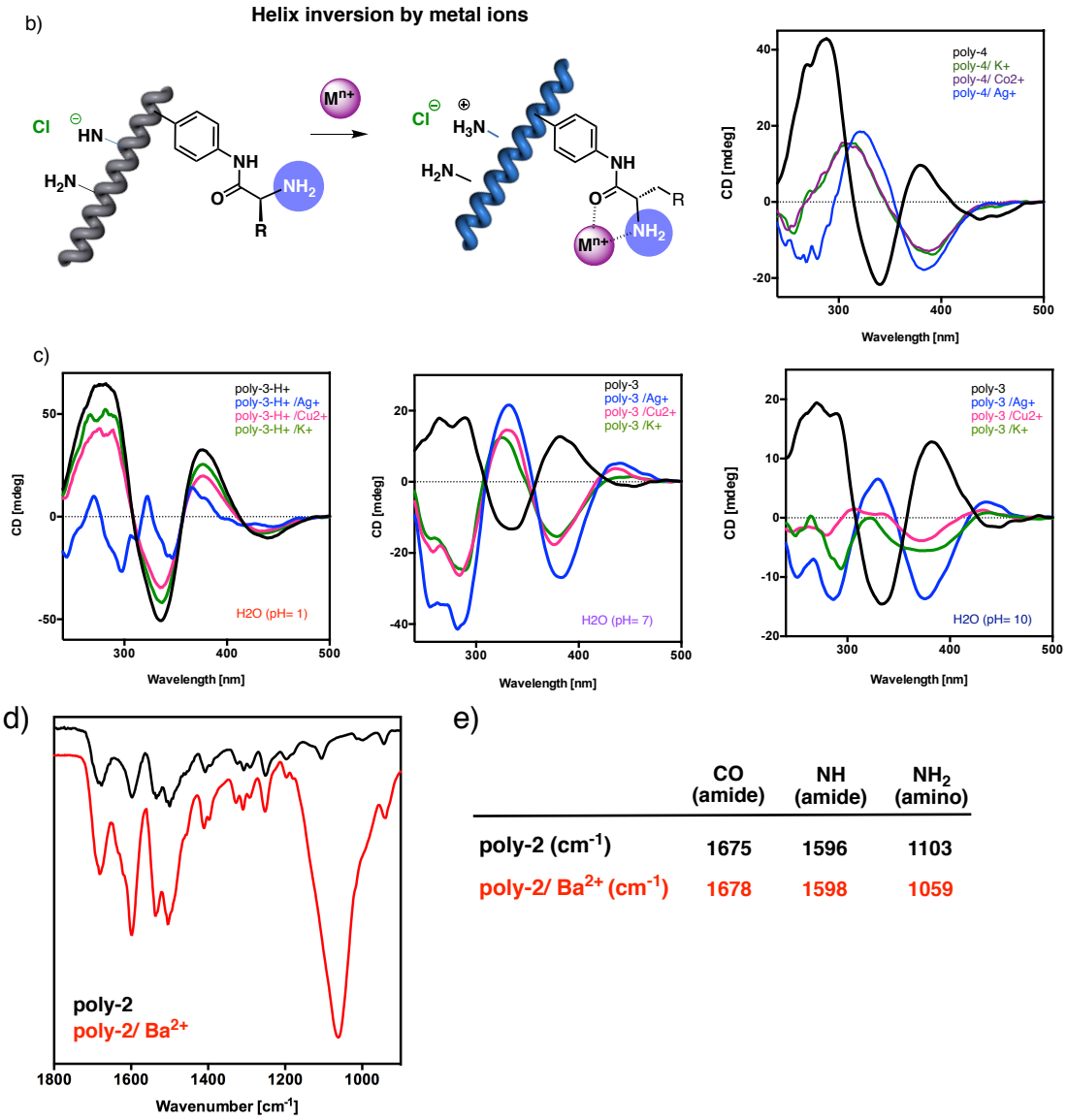


Figure S49. Schematic illustration of the chelation process mediated by metal ions showing a (a) helical enhancement in poly-**2,** poly-**5,** poly-**7** and poly-**10** in H_2O (pH=4.5) or (b) a helix inversion for poly 4 or (c) poly-**3** at different pH. d) IR spectra of poly-**2** and poly-**2**/Ba^{2+} complex. e) Wavenumber shifting of the vibration bands related with the carbonyl and amino groups.

Thermal Studies

TGA studies were carried out in order to determine the thermal stability of the polymers. As a general protocol a polymer simple was kept in a platinum pan and heated from 40 ºC to 800 ºC with a heating rate of 10 ºC/min.

Polymers loose weight around 100ºC as consequence of water evaporation during the heating process.

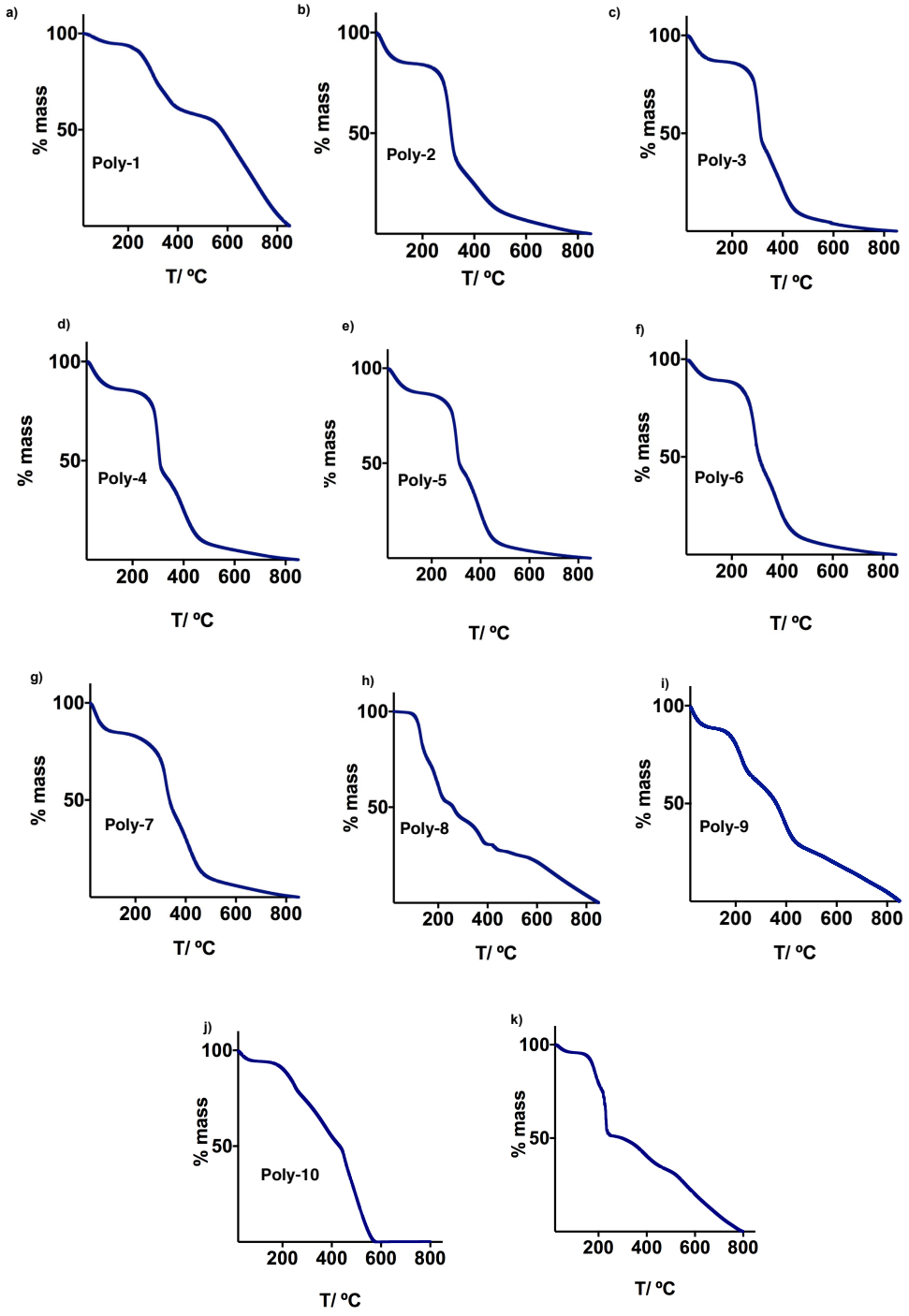


Figure S50. TGA thermograms of a) Poly-**1**, b) Poly-**2**, c) Poly-**3**, d) Poly-**4**, e) Poly-**5**, f) Poly-**6**, g) Poly-**7**, h) Poly-**8**, i) Poly-**9**, j) Poly-**10**, k) Poly-**11**.