Electronic Supplementary Information for

A modular designed copolymer with anti-thrombotic activity and imaging capability

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Experimental Section

General

All experiments with air- and moisture-sensitive intermediates and compounds were carried out under an inert atmosphere using standard Schlenk techniques. NMR spectra were recorded on a Bruker Advance DPX 400 MHz spectrometer and referenced using the residual proton signal of the solvent. Mass spectra were obtained on either a Bruker APEX II or a Bruker BIFLEX III spectrometer. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. UV-vis spectra were obtained using a Shimadzu 1601PC spectrophotometer. Fluorescence measurements and corresponding lifetime were determined by time-correlated single-photon counting method on an F-900 Edinburgh Analytical Instruments. Gel-permeation chromatography (GPC) analyses were carried out on a multi-angle, digital signal processing light scattering system (Wyatt, USA) using a Shimadzu LC-10A pump coupled to a Dawn Heleos II light scattering detector (equipped with a 100 mW GaAs laser) and a Optilab rEX interferometeric refractometer with THF or DMF (with 25 mM LiBr at 313 K) as eluents on a 10 μm linear MZ-Gel SDplus column, the flow rate used for all measurements was 0.5 mL/min. No calibration standards were used, and dn/dc values were obtained for each injection by assuming 100% mass elution from the columns. M_w, M_n and PDIs were treated using an Astra 5 software package.

Materials and synthesis

Exo-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid was synthesized according to published procedures.[1] 2-Chlorotrityl chloride resin (100 ~ 200 mesh) and Fmoc protected amino acids were purchased from GL Biochem Ltd. (Shanghai, China). Other reagents and solvents were obtained from commercial supplies and used as received without further purification.

***N*-(Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu))-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide (NB-pRGDS monomer).** The peptide monomer was synthesized by standard solid phase peptide chemistry on 2-chlorotrityl chloride resin following the literature procedures.[2] 2-Chlorotrityl chloride resin (2.0 g, predicted loading of 0.8-1.5 mmol/g) was weighed into a 50 mL oven-dried

glass-fritted peptide synthesis flask and allowed to swell in 8 mL of dry DMF for 30 min under gentle agitation with argon. The DMF was drained and a solution of Fmoc-Ser(^{t}Bu)-CO_2H (2.30 g, 6.0 mmol) and ^{i}Pr$_2$EtN (2.1 mL, 12.0 mmol) in DMF (9 mL) was added to the resin and agitated for 2 h. MeOH (3 mL) was then added to the mixture to cap any unreacted 2-chlorotrityl groups and agitated for an additional 10 min. The solution was then drained from the flask and washed with DMF (5 × 15 mL). A 20% solution of piperidine in DMF (15 mL) was added to the resin and agitated for 15 min. The mixture was drained and this procedure was repeated once again. The resin was washed with DMF (5 × 15 mL) and a few beads were removed and tested for complete deprotection with the Kaiser test. Upon positive Kaiser test, a solution of HBTU/HOBt (13.4 mL of a 0.45 M solution in DMF) was added to Fmoc-Asp(O^{t}Bu)-CO_2H (2.48 g, 6.0 mmol) and ^{i}Pr$_2$EtN (2.1 mL, 12.0 mmol) in DMF (3 mL). The solution was added to the resin and agitated for 2 h. The solution was drained from the flask, and the resin was washed with DMF (5 ×15 mL). A few beads were removed and tested for coupling as indicated by a negative Kaiser test. If the coupling was incomplete, the process was repeated with fresh reagents. Deprotection of the Fmoc group followed by coupling with the subsequent amino acid was carried out as described above. After coupling of the Fmoc-6-aminohexanoic acid (Fmoc-ε-Acp-CO_2H) and removal of the Fmoc group, the amino terminus was coupled with *exo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (0.83 g, 6.0 mmol) and confirmed with a negative Kaiser test. The resin was then washed with DMF (5 × 10 mL) and subsequently washed with 10% MeOH/CH_2Cl_2 (5 × 10 mL).

Cleavage of the side-chain protected peptide from the resin was accomplished with the addition of 15 mL of CH_2Cl_2/CF_3CH_2OH/CH_3COOH (7:2:1) to the resin. The resin was agitated briefly under an inert atmosphere and allowed to sit for 1 h with periodic agitation every 15 min. The solution was drained, collected, and repeated once more. The resin was rinsed with 10% MeOH/CH_2Cl_2 (2 × 15 mL). The filtrates were combined and concentrated under reduced pressure. The product was precipitated with cold ether, washed twice with cold ether, and filtered to provide NB-pRGDS monomer as a white powder (1.55 g, 1.50 mmol) that was used without further

purification. MALDI-TOF MS: *m/z* = 1031.2 $[M + H]^+$, 1053.2 $[M + Na]^+$, 1069.1 $[M + K]^+$. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.04 (br, 1H), 7.80 (br, 1H), 7.59 (br, 1H), 7.41 (br, 1H), 6.45 (br, 2H), 6.40 (br, 1H), 6.03 (m, 2H), 4.82 (q, *J* = 6.0 Hz, 1H), 4.49 (m, 2H), 3.94 (m, 2H), 3.78 (m, 1H), 3.59 (m, 1H), 3.19 (m, 4H), 2.93 (m, 2H), 2.86 (m, 2H), 2.74 (m, 2H), 2.54 (s, 3H), 2.47 (s, 3H), 2.25 (m, 2H), 2.07 (s, 3H), 2.02 (m, 1H), 1.80 (m, 2H), 1.63 (m, 6H), 1.50 (m, 2H), 1.44 (s, 6H), 1.40 (s, 9H), 1.29 (m, 4H), 1.14 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 176.55, 175.19, 173.23, 172.46, 171.16, 170.68, 169.45, 158.76, 156.48, 138.27, 137.96, 136.04, 132.56, 132.21, 124.60, 117.47, 86.38, 81.87, 73.78, 61.07, 53.34, 53.02, 49.42, 47.06, 46.22, 44.35, 43.16, 43.09, 41.47, 40.38, 39.48, 37.55, 35.67, 30.41, 29.20, 28.98, 28.51, 27.93, 27.20, 26.21, 25.25, 25.03, 19.19, 17.84, 12.39. Anal. Cacld. for $C_{50}H_{78}N_8O_{13}S$: C, 58.23; H, 7.62; N, 10.87; S, 3.11. Found: C, 58.43; H, 7.50; N, 10.69; S, 2.99.

***N*-(Acp-Arg-Gly-Asp-Ser)-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide (NB-RGDS monomer).** The NB-pRGDS monomer (155 mg, 0.15 mmol) were deprotected in a mixture of 95% TFA, 2.5% H_2O and 2.5 % triisopropylsilane for 20 min, and then precipitated in cold ether. The crude products were filtered and purified on Sephadex-G10 to provide NB-RGDS monomer as a white powder (85 mg, 0.13 mmol, yield 85%). MALDI-TOF MS: *m/z* = 667.5 $[M + H]^+$. ^1H NMR (400 MHz, DMSO-d_6, ppm) δ: 11.71 (br, 2H), 8.33 (m, 2H), 8.03 (m, 1H), 7.80 (m, 1H), 7.64 (m, 1H), 7.21 (br, 4H), 6.12 (m, 2H), 4.55 (q, *J* = 6.8 Hz, 1H), 4.22 (m, 1H), 4.12 (m, 1H), 3.73 (m, 1H), 3.69 (m, 1H), 3.66 (m, 1H), 3.61 (m, 1H), 3.33 (br, 3H), 3.09 (m, 1H), 3.01 (m, 2H), 2.82 (s, 1H), 2.76 (s, 1H), 2.56 (m, 1H), 2.13 (m, 2H), 2.00 (m, 1H), 1.76 (m, 1H), 1.63 (m, 1H), 1.48 (m, 6H). 1.36 (m, 2H), 1.22 (m, 2H), 1.14 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, ppm) δ: 174.41, 172.61, 172.39, 172.35, 172.02, 170.56, 168.70, 156.88, 137.66, 136.29, 61.45, 55.00, 52.31, 49.40, 46.89, 45.62, 42.97, 42.15, 40.95, 40.37, 38.52, 36.40, 35.03, 29.79, 29.00, 28.94, 26.12, 24.89, 24.81. Anal. Cacld. for $C_{29}H_{46}N_8O_{10}$: C, 52.24; H, 6.95; N, 16.81. Found: C, 52.49; H, 6.71; N, 16.97.

5-hydroxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate. A mixture of 1,5-Pentanediol (6.25 g, 60.01 mmol), *exo*-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (2.77 g, 20.05 mmol), DCC

(*N*,*N*-dicyclohexylcarbodiimide, 6.00 g, 29.08 mmol) and DMAP (4-dimethylaminopyridine, 300 mg, 2.46 mmol) was stirred in dry methylene chloride (150 mL) under inert atmosphere for 24 h. After removal of the solvent, the crude product was purified by silica gel column chromatography to give 5-hydroxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate as transparent oil (3.20 g, 14.27 mmol, yield 71%). TLC, R_f=0.35 (petroleum ether:ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.07 (m, 2H), 4.05 (t, 2H, J = 6.6 Hz), 3.60 (t, 2H, J = 6.6 Hz), 2.99 (m, 1H), 2.88 (m, 1H), 2.17 (m, 1H), 2.06 (br, 1H), 1.86 (m, 1H), 1.64 (m, 2H), 1.56 (m, 2H), 1.46 (m, 1H), 1.40 (m, 2H), 1.32 (m, 2H).

5-Rhodamine-B-formyloxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate (NB-RhB monomer). A mixture of 5-hydroxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate (600 mg, 2.67 mmol), Rhodamine B (1.50 g, 3.13 mmol), DCC (1.00 g, 4.85 mmol) and DMAP (300 mg, 2.46 mmol) was stirred in dry methylene chloride (50 mL) under inert atmosphere for 24 h. After removal of the solvent, the crude product was purified by silica gel column chromatography to give 5-rhodamine-B-formyloxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate as deep purple solids (980 mg, 1.51 mmol, yield 57%). TLC, R_f=0.25 (methylene chloride:methanol = 15:1). MALDI-TOF MS: m/z = 649.5 $[M]^+$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.22 (dd, 1H, J = 8.0 and 0.8 Hz), 7.76 (td, 1H, J = 7.6 and 1.2 Hz), 7.68 (td, 1H, J = 7.6 and 1.2 Hz), 7.24 (dd, 1H, J = 7.6 and 0.8 Hz), 7.01 (d, 2H, J = 9.2 Hz), 6.87 (dd, 2H, J = 9.6 and 2.4 Hz), 6.74 (d, 2H, J = 2.4 Hz), 6.04 (m, 2H), 3.98 (t, 2H, J = 6.6 Hz), 3.94 (t, 2H, J = 6.6 Hz), 3.59 (q, 8H, J = 7.2 Hz), 2.93 (m, 1H), 2.84 (m, 1H), 2.12 (m, 1H), 1.81 (m, 1H), 1.52 (m, 2H), 1.44 (m, 3H), 1.27 (m, 14H), 1.20 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 176.09, 164.92, 158.78, 157.61, 155.45, 137.95, 135.54, 133.41, 132.99, 131.21, 131.18, 130.29, 130.12, 129.87, 114.22, 113.41, 96.18, 65.28, 63.80, 46.47, 46.20, 46.07, 43.03, 41.48, 30.19, 28.14, 27.87, 22.21, 12.56. Anal. Cacld. for $C_{41}H_{49}ClN_2O_5$: C, 71.86; H, 7.21; N, 4.09. Found: C, 72.11; H, 6.98; N, 4.34.

Methoxypolyethylene-glycol-350-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate (NB-mPEG monomer). A mixture of methoxypolyethylene glycol 350 (3.50 g, 10.00 mmol), *exo*-

bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (1.38 g, 9.99 mmol), DCC (3.00 g, 14.54 mmol) and DMAP (250 mg, 2.05 mmol) was stirred in dry methylene chloride (60 mL) under inert atmosphere for 24 h. After removal of the solvent, the crude product was purified by silica gel column chromatography to give NB-mPEG monomer as transparent oil (4.10 g, 8.72 mmol, yield 87%). TLC, R_f = 0.10 ~ 0.35 (methylene chloride:methanol = 20:1). MALDI-TOF MS for NB-$COO(CH_2CH_2O)_nCH_3$: *m/z* = 417.2 $[M_{n=7} + H]^+$, 439.2 $[M_{n=7} + Na]^+$, 461.3 $[M_{n=8} + H]^+$, 483.2 $[M_{n=8} + Na]^+$, 505.4 $[M_{n=9} + H]^+$, 527.3 $[M_{n=9} + Na]^+$, 549.4 $[M_{n=10} + H]^+$, 571.4 $[M_{n=10} + Na]^+$, 593.5 $[M_{n=11} + H]^+$, 615.5 $[M_{n=11} + Na]^+$, 637.6 $[M_{n=12} + H]^+$, 659.5 $[M_{n=12} + Na]^+$, 681.6 $[M_{n=13} + H]^+$, 703.4 $[M_{n=13} + Na]^+$, 725.5 $[M_{n=14} + H]^+$, 747.7 $[M_{n=14} + Na]^+$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.01 (m, 2H), 4.14 (m, 2H), 3.60 (m, 2H), 3.55 (m, 22.31H), 3.44 (m, 2H), 3.27 (m, 3H), 2.94 (m, 1H), 2.81 (m, 1H), 2.16 (m, 1H), 1.81 (m, 1H), 1.42 (m, 1H), 1.26 (m, 2H).

Polymer Synthesis General Procedure. A solution of Grubbs' third-generation initiator[3] (~0.01 M) was added to a chloroform solution (~0.05 M) containing NB-pRGDS, NB-RhB and NB-mPEG monomers in varied ratios. The reaction mixture was stirred for 15 min at room temperature. After complete conversion of the monomer (>99%, monitored by ^{1}H NMR), the polymerization was quenched by the addition of ethyl vinyl ether and stirred for an additional 15 min. The polymer was precipitated with cold ether, and dried at room temperature under high vacuum. The copolymers were deprotected in a mixture of 95% TFA, 2.5% H_2O and 2.5 % triisopropylsilane for 20 min, and then precipitated in cold ether. The crude products were collected by centrifugation and purified by dialysis (Spectra/Por 3 membrane, MWCO 3500) against water for 5 days at 4°C. After lyophilisation, the resulting copolymers were obtained as red solids. The synthetic details and characterization of monomers and copolymers are provided in the supporting information.

Polymer PNB-Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu)-OH (PNB-pRGDS). ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ: 12.38 (br, 1H), 8.18 (br, 1H), 8.10 (br, 1H), 7.96 (br, 1H), 7.71 (br, 1H), 7.52 (br, 1H), 6.64 (br, 1H), 6.41 (br, 2H), 5.29 (m, 2H), 4.71 (m, 1H), 4.33 (m, 1H), 4.22 (m, 1H), 3.75 (m, 2H), 3.65 (m, 1H), 3.51(m, 1H), 3.06 (m, 4H), 2.96 (m, 4H), 2.69 (m, 2H), 2.52 (s, 3H),

2.44 (s, 3H), 2.14 (m, 2H), 2.02 (s, 3H), 1.88 (m, 1H), 1.67 (m, 2H), 1.49 (m, 8H), 1.42 (s, 6H), 1.38 (s, 11H), 1.22 (m, 2H), 1.12 (s, 9H).

Polymer PNB-RhB. ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ: 8.19 (br, 1H), 7.89 (br, 1H), 7.80 (br, 1H), 7.49 (br, 1H), 7.07 (br, 2H), 6.95 (br, 4H), 5.13 (m, 2H), 3.87 (br, 2H), 3.80 (br, 2H), 3.62 (br, 8H), 2.89 (m, 1H), 2.44 (m, 2H), 1.82 (m, 2H), 1.52 (br, 1H), 1.33 (br, 2H), 1.17 (br, 14H), 0.98 (br, 3H).

Polymer PNB-mPEG. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 5.12 (br, 2H), 4.12 (br, 2H), 3.57 (s, 24.3H), 3.47 (m, 2H), 3.30 (s, 3H), 3.02 (m, 1H), 2.66 (m, 1H), 2.46 (m, 1H), 1.98 (m, 2H), 1.59 (br, 1H), 1.05 (br, 1H).

Copolymer PNB-pRGDS$_{10}$-*co*-mPEG$_{90}$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.10 (br, 0.1H), 7.82 (br, 0.1H), 7.64 (br, 0.1H), 7.44 (br, 0.1H), 6.46 (br, 0.3H), 5.29 (m, 2H), 4.69 (br, 0.1H), 4.31 (br, 0.2H), 4.13 (br, 1.8H), 3.58 (s, 22.3H), 3.48 (m, 1.8H), 3.31 (s, 2.7H), 3.03 (m, 1.7H), 2.66 (m, 2.6H), 2.00 (m, 2.5H), 1.59 (br, 1.7H), 1.38 (s, 1.9H), 1.03 (br, 1.8H).

Copolymer PNB-RGDS$_{10}$-*co*-mPEG$_{90}$. ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ: 12.01 (br, 0.2H), 8.33 (br, 0.2H), 8.01 (br, 0.1H), 7.61 (br, 0.2H), 7.18 (br, 0.4H), 5.37 (m, 2H), 4.54 (br, 0.1H), 4.11 (br, 2H), 3.50 (m, 22.6H), 3.33 (m, 1.8H), 3.23 (s, 2.7H), 3.00 (m, 1.4H), 2.41 (m, 2.1H), 1.92 (m, 2H), 1.58 (m, 1.7H), 1.20 (m, 1.4H).

Copolymer PNB-RhB$_5$-*co*-mPEG$_{95}$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.24 (br, 0.05H), 7.81 (br, 0.05H), 7.71 (br, 0.05H), 7.40 (br, 0.05H), 6.88 (br, 0.1H), 6.74 (br, 0.2H), 5.25 (br, 2H), 4.11 (br, 2.1H), 3.57 (s, 23.5H), 3.46 (m, 1.9H), 3.30 (s, 2.9H), 3.00 (m, 1H), 2.46 (m, 2.1H), 1.98 (m, 2H), 1.58 (br, 1H), 1.27 (br, 0.8H), 1.05 (br, 1.1H).

Copolymer PNB-pRGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.24 (br, 0.05H), 8.11 (br, 0.1H), 7.64 (m, 0.3H), 7.38 (m, 0.15H), 6.87 (br, 0.1H), 6.75 (br, 0.2H), 6.49 (br, 0.3H), 5.28 (br, 2H), 4.67 (br, 0.1H), 4.30 (br, 0.2H), 4.13 (m, 1.9H), 3.58 (s, 21.7H), 3.47 (m, 1.7H), 3.31 (s, 2.6H), 3.03 (m, 1.7H), 2.49 (m, 2.6H), 1.97 (m, 2.5H), 1.59 (br, 1.7H), 1.38 (m, 1.8H), 1.04 (br, 2.8H).

Copolymer PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$. ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ: 11.96 (br, 0.2H), 8.38 (br, 0.3H), 7.62 (br, 0.4H), 7.19 (br, 0.7H), 5.36 (m, 2H), 4.55 (br, 0.1H), 4.11 (br, 1.9H), 3.50 (s, 21.7H), 3.33 (m, 2H), 3.23 (s, 2.6H), 2.99 (m, 1.4H), 2.41 (m, 1.8H), 1.90 (m, 2H), 1.57 (br, 1.7H), 1.20 (br, 1.7H).

Animals

Sprague-Dawley (SD) rats (male, weighing 200±20 g) were purchased from Animal Center of Capital Medical University. The animals were housed in ventilated cages under conventional conditions at a 12 h light and 12 h dark cycle for one day with free access to water and standard laboratory food before being used. The studies were performed based on a protocol reviewed and approved by the ethics committee of Capital Medical University. The committee assured that the welfare of the animals was maintained in accordance with the requirements of the animal welfare act and according to the guide for care and use of laboratory animals.

In vivo antithrombotic assay

This assay was evaluated in a model of artery-vein bypass thrombosis using male SD rats (10 for each group). The normal saline solutions of aspirin, RGD monomer and copolymers were subjected to the rats by oral administration. After 30 min, each rat was anesthetized with urethane (1.5 g/kg, IP), and its right carotid artery and left jugular vein were carefully separated and then connected by polyethylene tubing, which was inserted with a weighted 6-cm thread and filled with heparin sodium (50 IU/mL in NS). The blood was allowed to flow through the tubing for 15 min. The thread was taken out, and the weight of wet thrombus was recorded. Statistical analysis was compared by using ANOVA test. Results were expressed as mean ± SD% and considered to be statistically significant when $p < 0.05$.

In vitro thrombus imaging

Whole blood was obtained from male SD rats and transferred in 1-mL aliquots to lengths of polyethylene tubing. The polyethylene tubing was connected to form a closed loop and the ends were apposed with latex tubing. The rings were rotated at 21 rpm for 30 min on a tube rotator

incubated at 37°C. Clots were prepared by this method to mimic arterial thrombi with a platelet-rich head and a fibrin tail.[4] The clots were then removed, washed with phosphate buffered saline (PBS, pH 7.4) and incubated with non-RGD polymer PNB-RhB_5-*co*-$mPEG_{95}$ (0.025 mg/mL) or RGD containing polymer PNB-$RGDS_x$-*co*-RhB_5-*co*-$mPEG_{95-x}$ (0.025 mg/mL) in PBS buffer. In competitive binding assays, PNB-$RGDS_{10}$-*co*-$mPEG_{90}$ (0.025 mg/mL) or NB-RGDS at 1-fold or 10-fold excess concentration was added 15 min prior to the incubation of PNB-$RGDS_{10}$-*co*-RhB_5-*co*-$mPEG_{85}$ with clots. All incubations were carried out at 37°C in polypropylene tubes for 15 min. After incubation, the clots were collected and washed thoroughly with PBS, and then placed in test tubes for the fluorescence measurements. Clot imaging was performed on a NightOWL LB 983 imaging system (Berthold Technologies, Germany) using 530/20 nm excitation and 600/20 nm emission filters.

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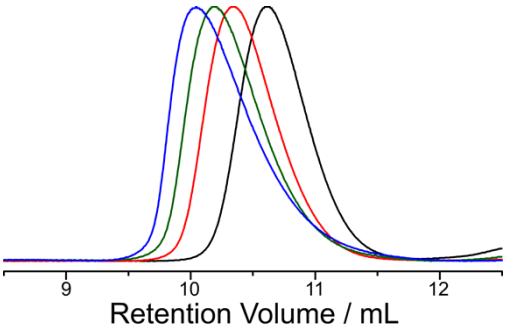

Fig. S1 Normalized GPC curves of PNB-mPEG homopolymers, the degree of polymerization is 25 (black), 50 (red), 75 (green) and 100 (blue), respectively.

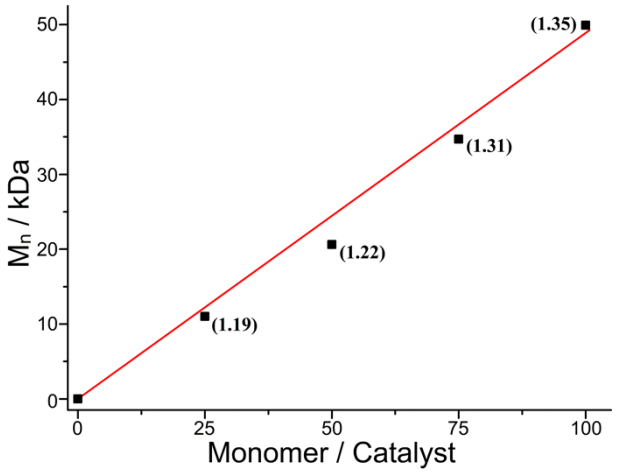

Fig. S2 Plot of M_n *vs* the monomer to initiator ratios for the ROMP of NB-mPEG monomer.

Table S1 GPC data for NB-mPEG homopolymers.

Polymer[a]	[M]/[C]	M_n /kDa	M_w /kDa	PDI
PNB-mPEG$_{25}$	25	11.0	13.1	1.19
PNB-mPEG$_{50}$	50	20.6	25.2	1.22
PNB-mPEG$_{75}$	75	34.7	45.5	1.31
PNB-mPEG$_{100}$	100	49.9	67.5	1.35

[a]Determined by GPC using a LS detector in THF at 298 K.

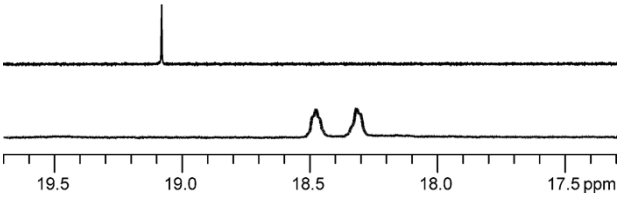

Fig. S3 Carbene ^{1}H NMR signals for Grubbs' third-generation initiator (top), and during the polymerizations of NB-mPEG monomer (bottom) in $CDCl_3$.

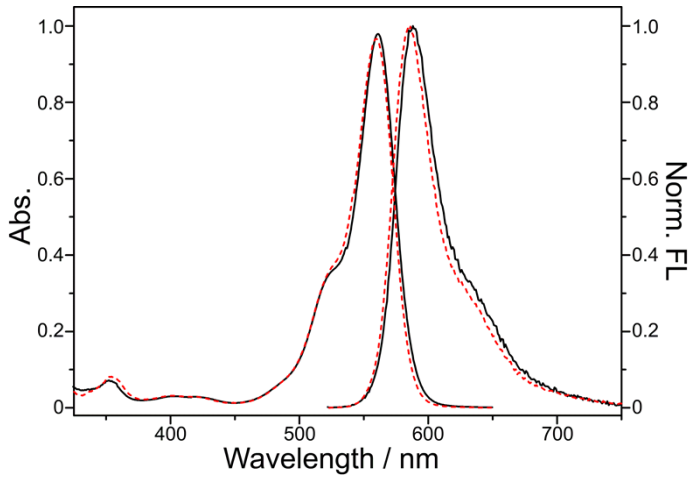

Fig. S4 UV-Vis absorption and normalized fluorescence spectra of NB-RhB (red) with the concentration of 3.41 μg/mL in PBS and PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ (black) with the concentration of 0.048 mg/mL in PBS.

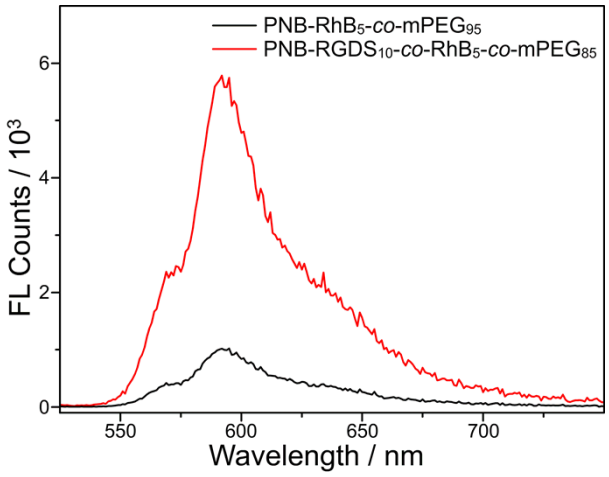

Fig. S5 Fluorescence spectra of PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ (red) and PNB-RhB$_5$-*co*-mPEG$_{95}$ (black) banding with clots.

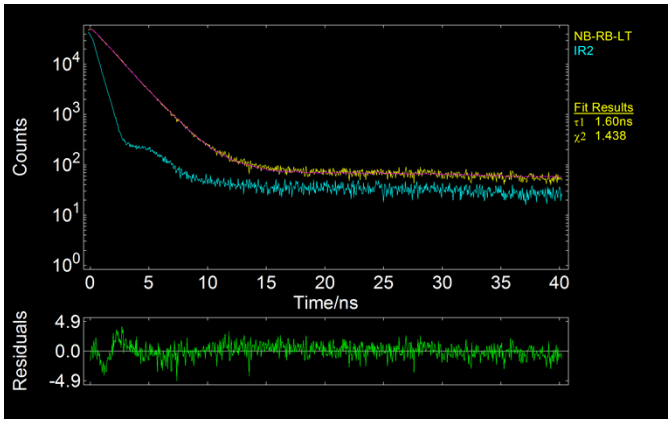

Fig. S6 The decay profile of fluorescence @ 590 nm for NB-RhB monomer with the concentration of 3.41 μg/mL in PBS, it gives the lifetime of 1.60 ns.

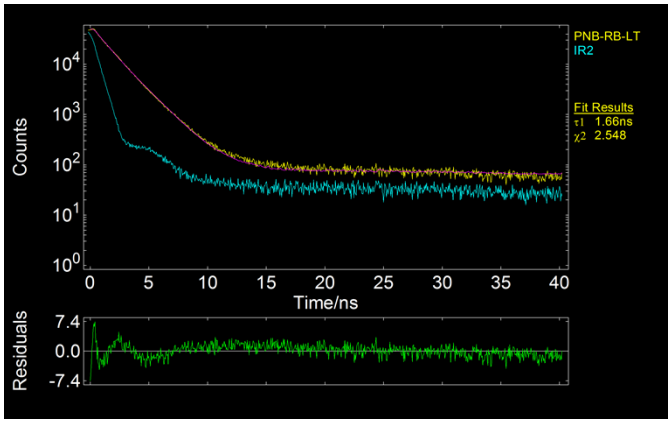

Fig. S7 The decay profile of fluorescence @ 592 nm for PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ copolymer with the concentration of 0.048 mg/mL in PBS, it gives the lifetime of 1.66 ns.

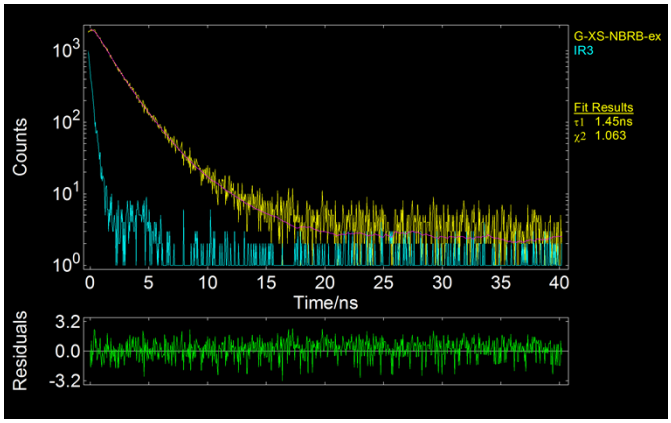

Fig. S8 The decay profile of fluorescence @ 592 nm for PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ copolymer banding with clot, it gives the lifetime of 1.45 ns.

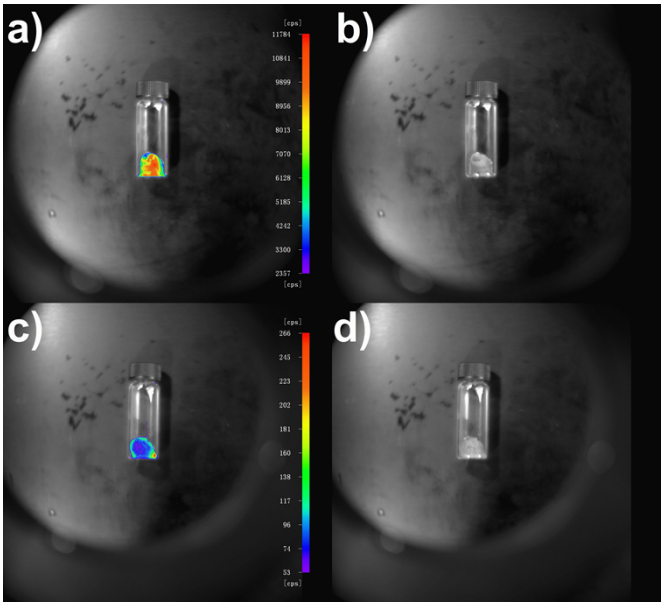

Fig. S9 Clot fluorescence images after the binding with PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ (a,b) and PNB-RhB$_5$-*co*-mPEG$_{95}$ (c,d) copolymers.

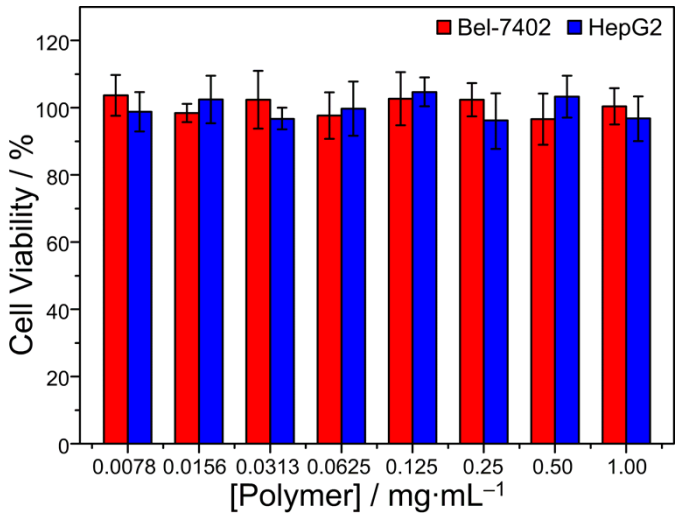

Fig. S10 Relative viability of Bel-7402 (red) and HepG2 (blue) cells after incubation with the PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ copolymer at various concentrations for 24 h assessed by MTT assay.

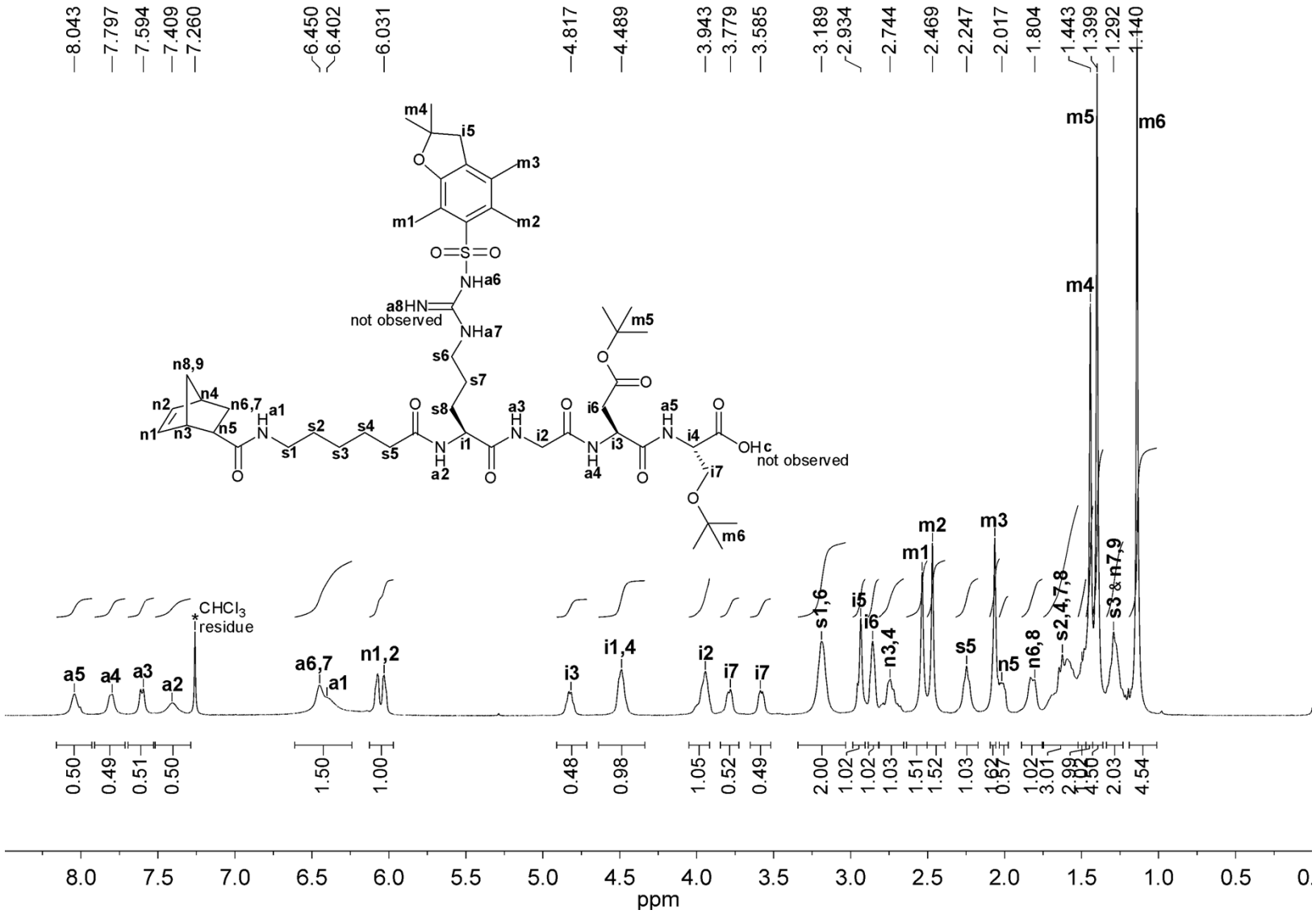

Fig. S11 ^{1}H NMR spectrum for *N*-(Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu))-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide in $CDCl_3$.

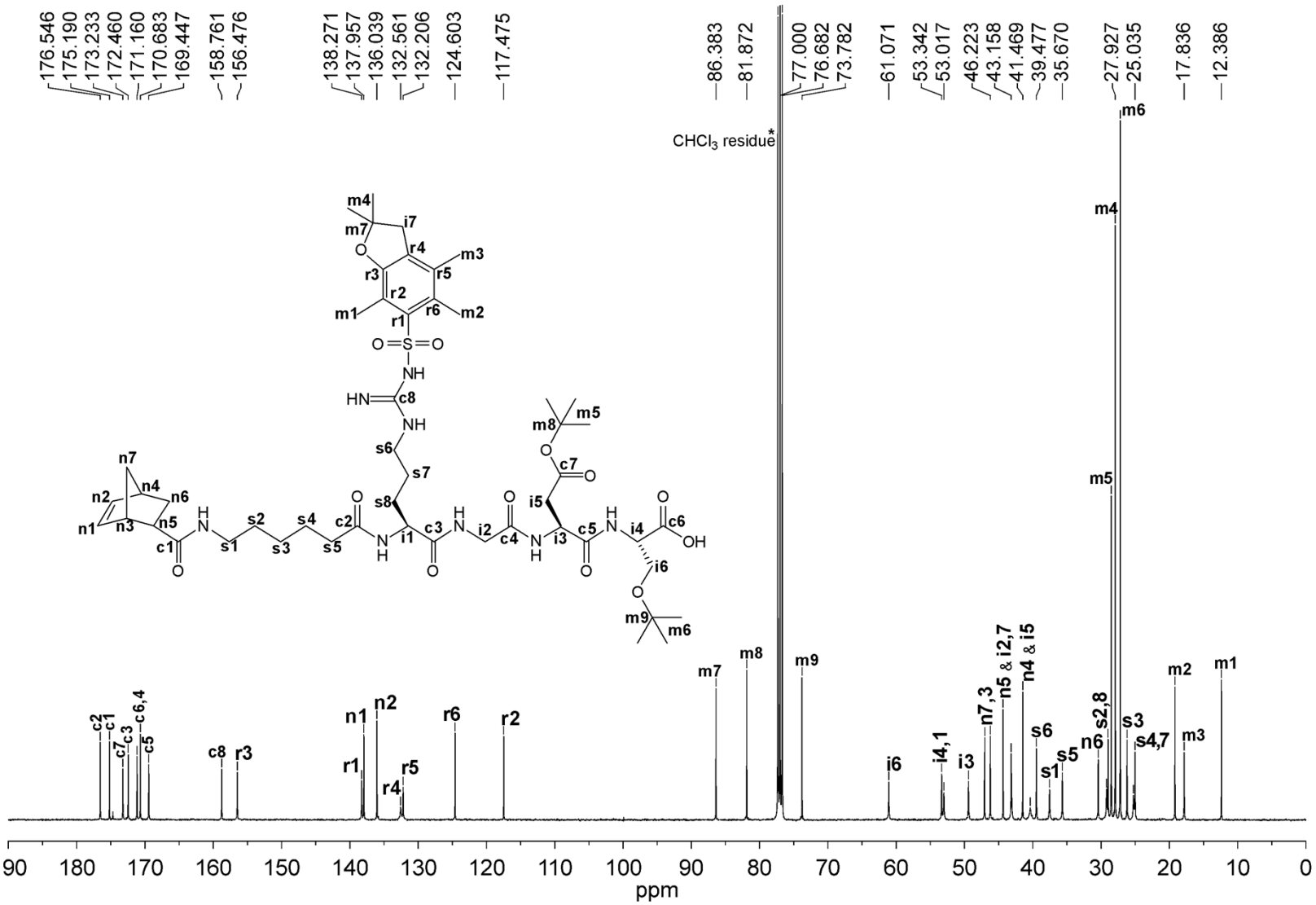

Fig. S12 ^{13}C NMR spectrum for *N*-(Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu))-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide in $CDCl_3$.

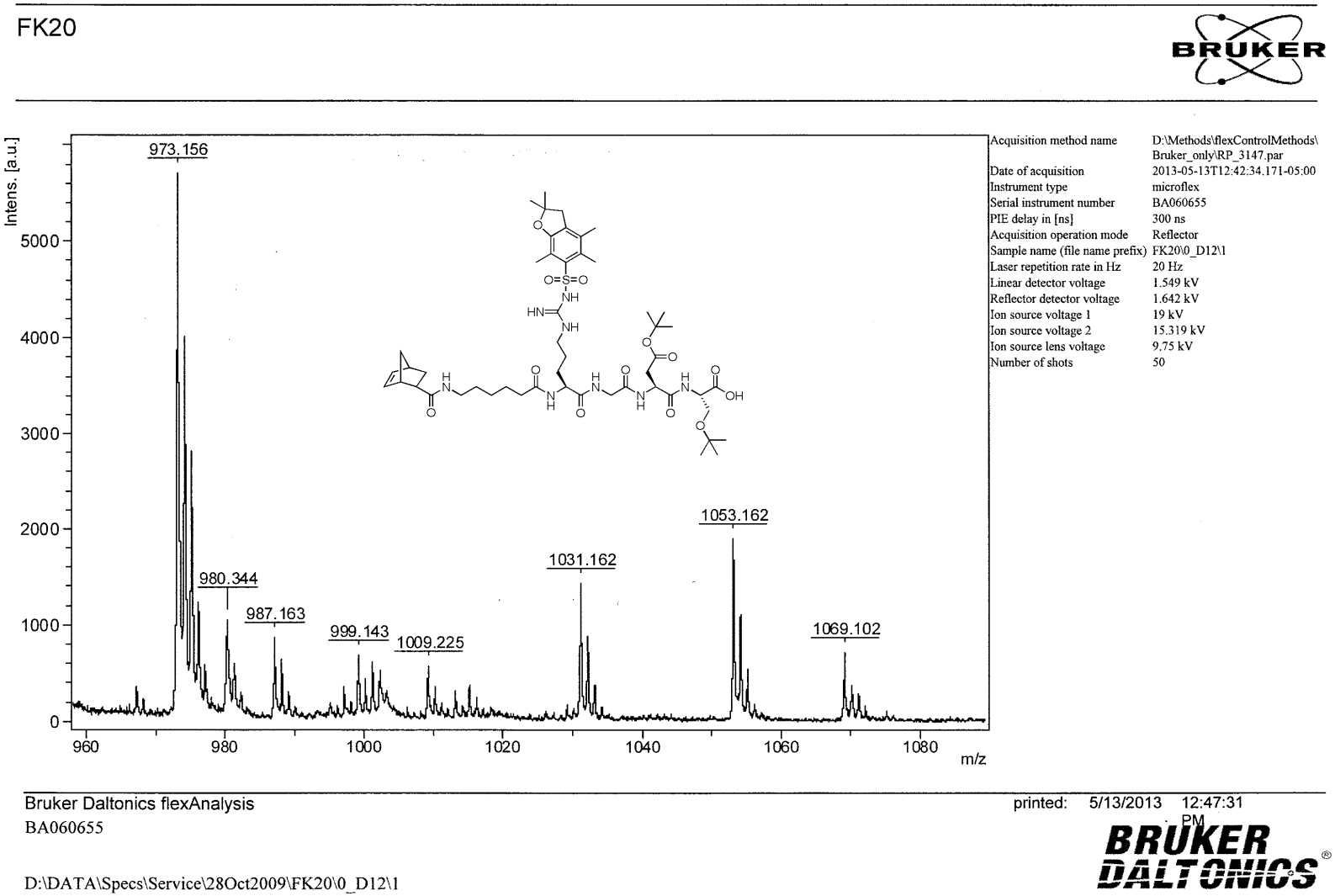

Fig. S13 MALDI-TOF MS spectrum for *N*-(Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu))-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide.

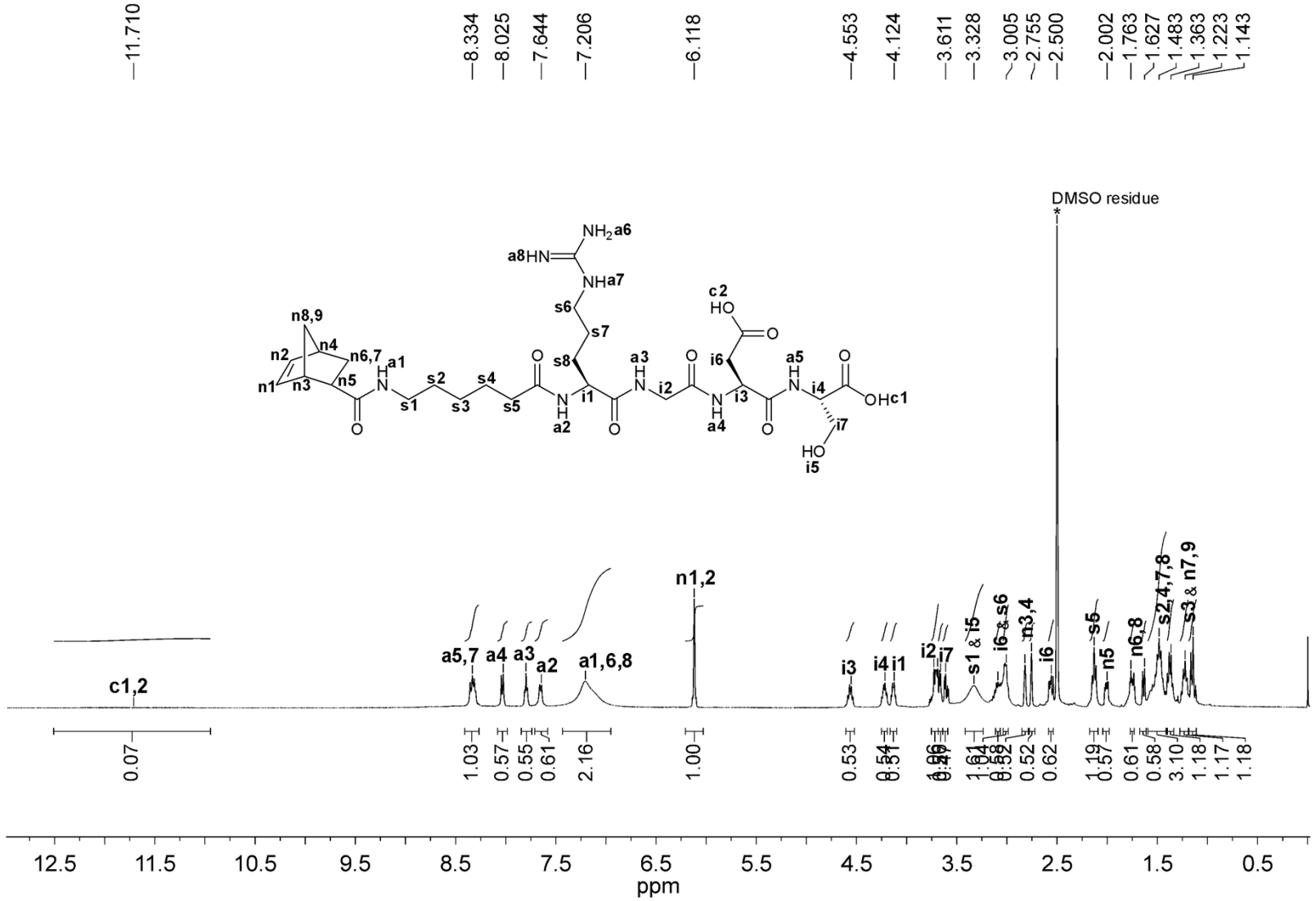

Fig. S14 ^{1}H NMR spectrum for *N*-(Acp-Arg-Gly-Asp-Ser)-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide in DMSO-d_6.

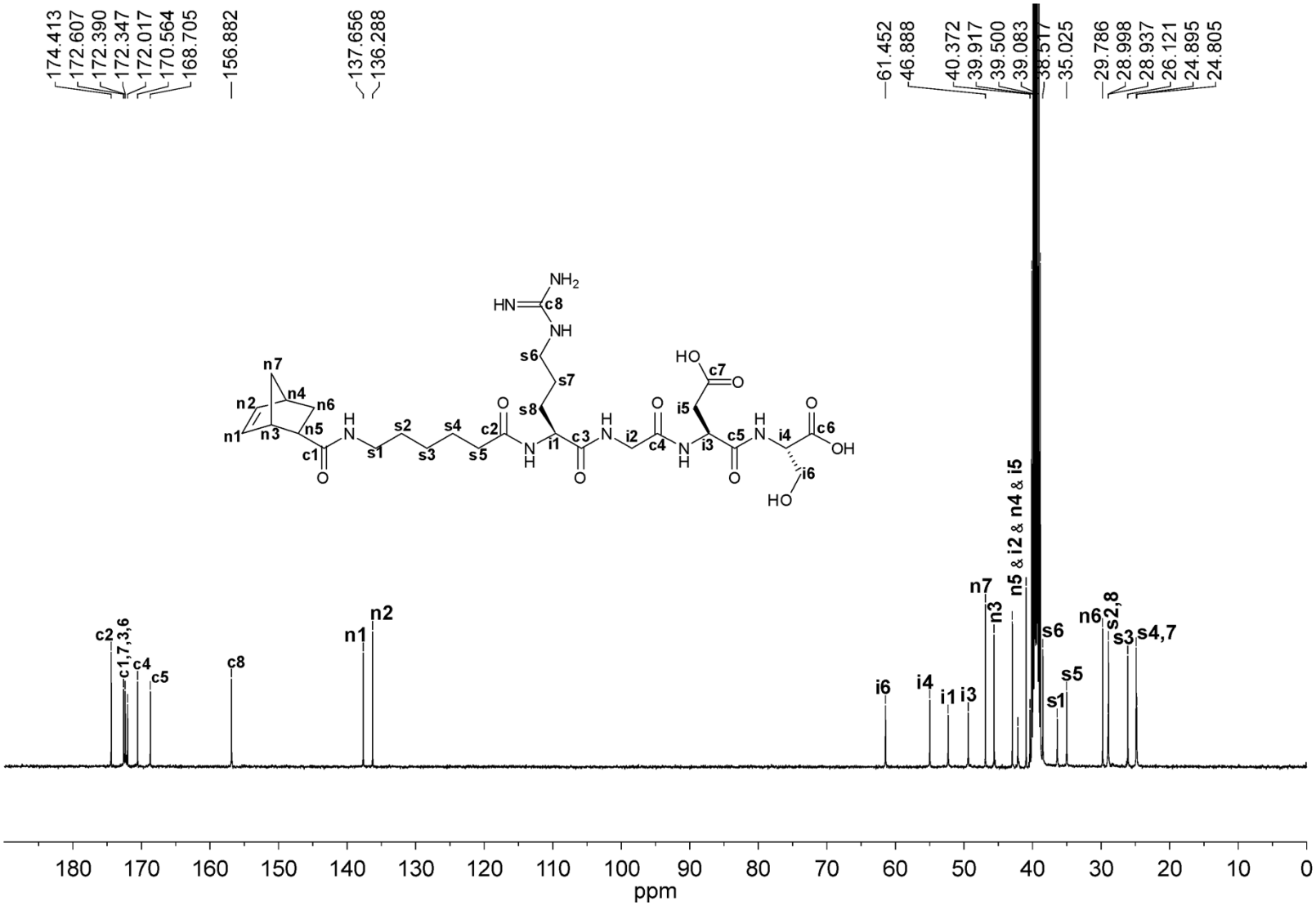

Fig. S15 ^{13}C NMR spectrum for *N*-(Acp-Arg-Gly-Asp-Ser)-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide in DMSO-d_6.

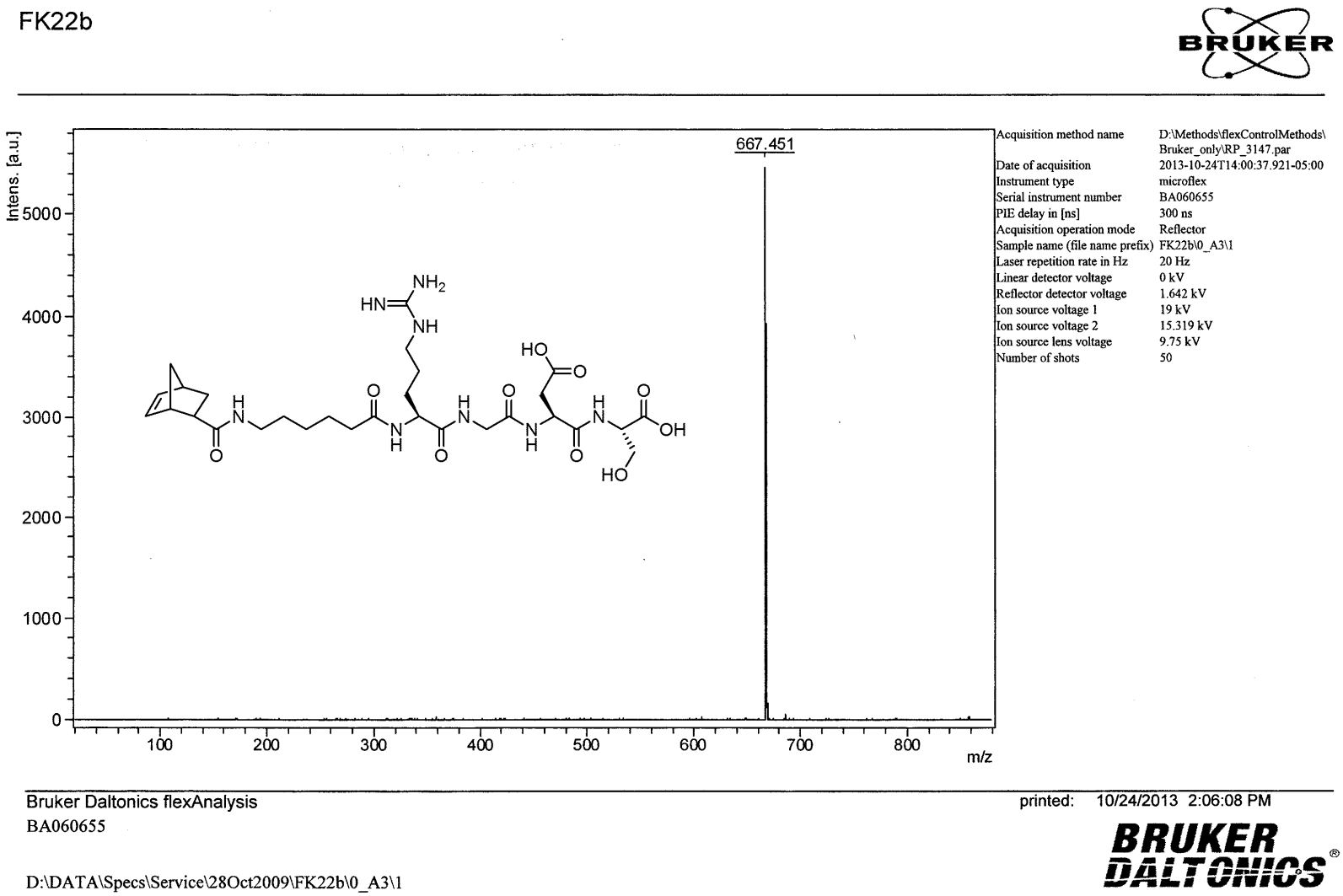

Fig. S16 MALDI-TOF MS spectrum for *N*-(Acp-Arg-Gly-Asp-Ser)-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxamide.

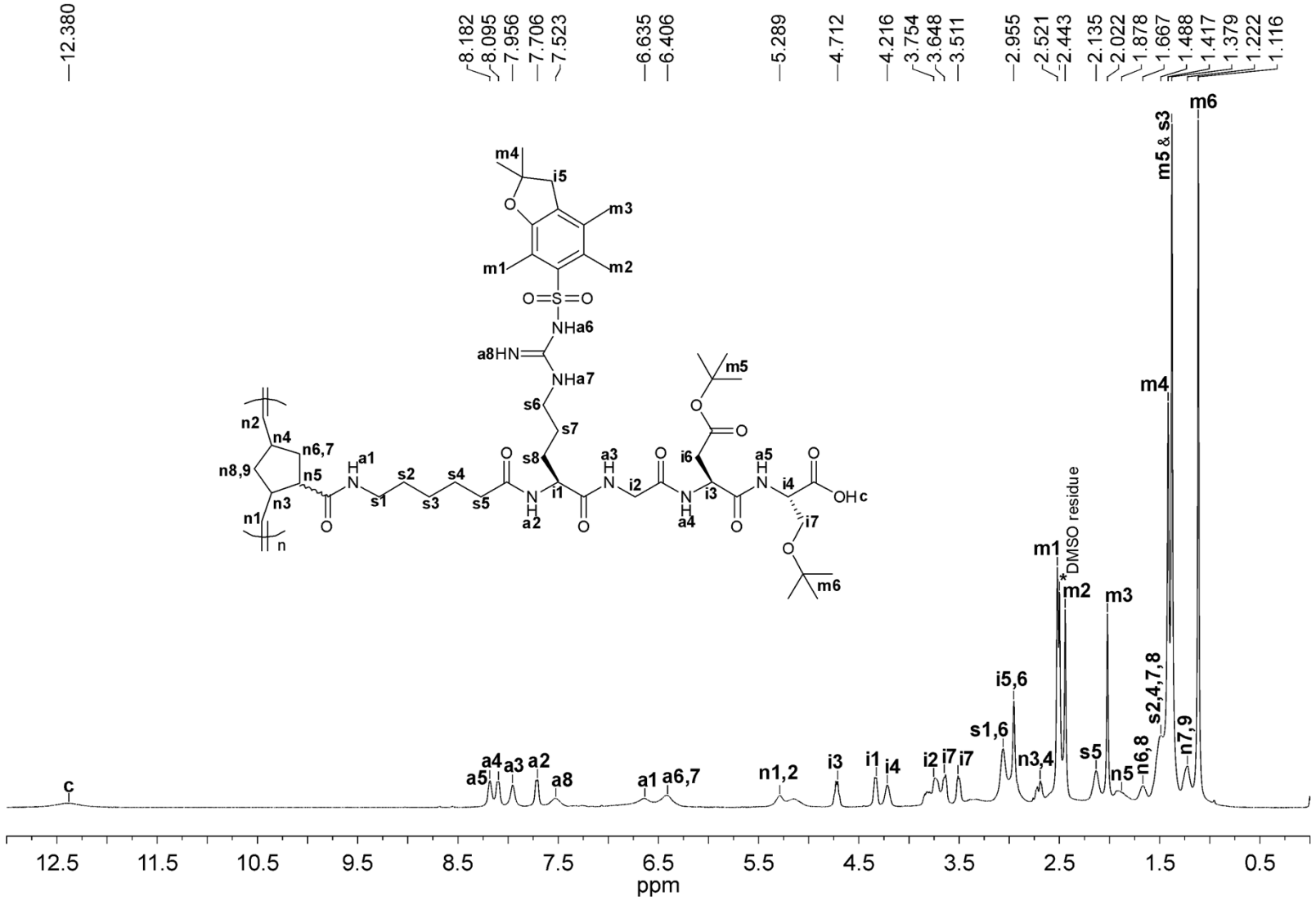

Fig. S17 ^{1}H NMR spectrum for PNB-Acp-Arg(Pbf)-Gly-Asp(O^{t}Bu)-Ser(^{t}Bu)-OH in DMSO-d_6.

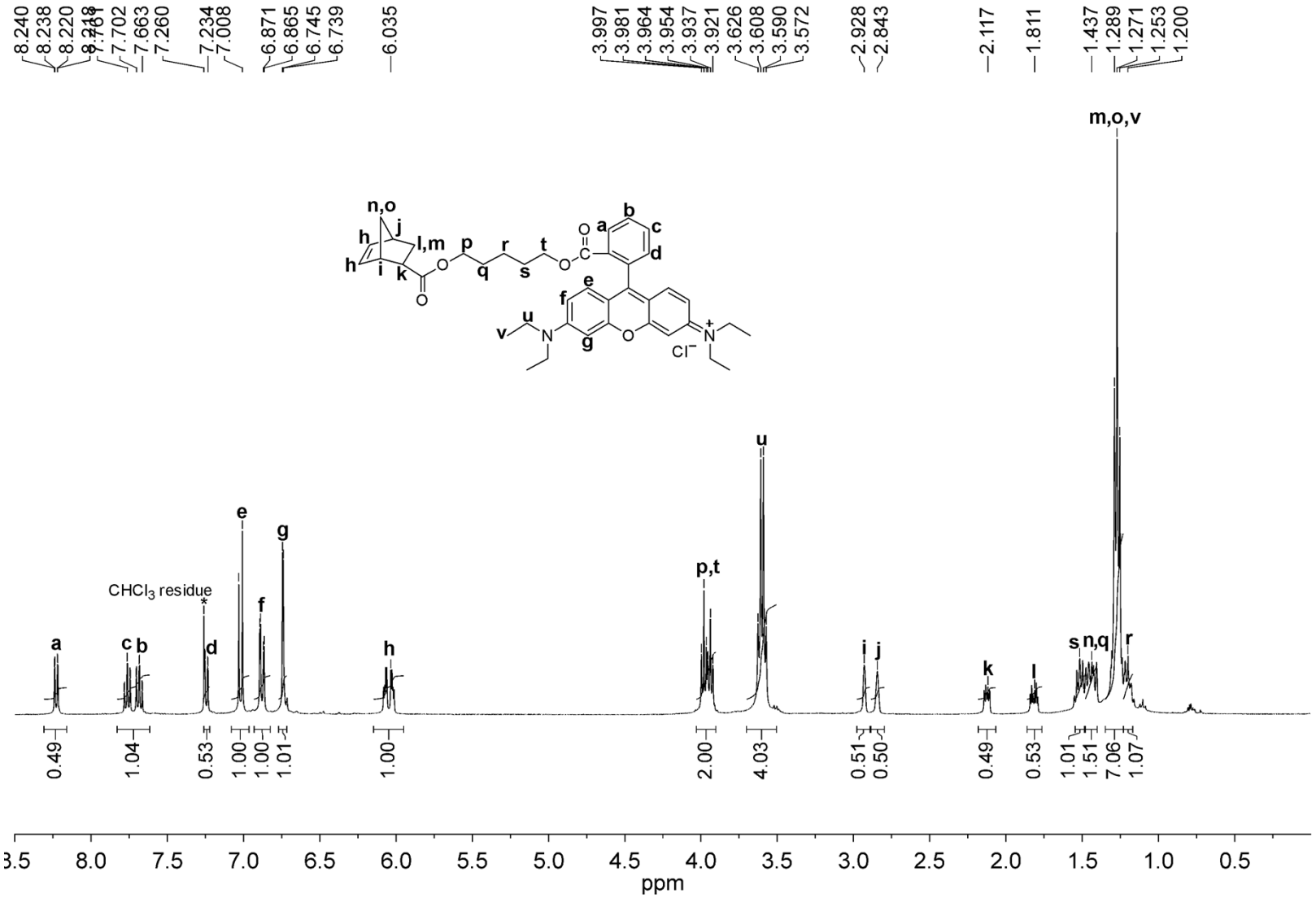

Fig. S18 ^{1}H NMR spectrum for 5-rhodamine-B-formyloxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate in $CDCl_3$.

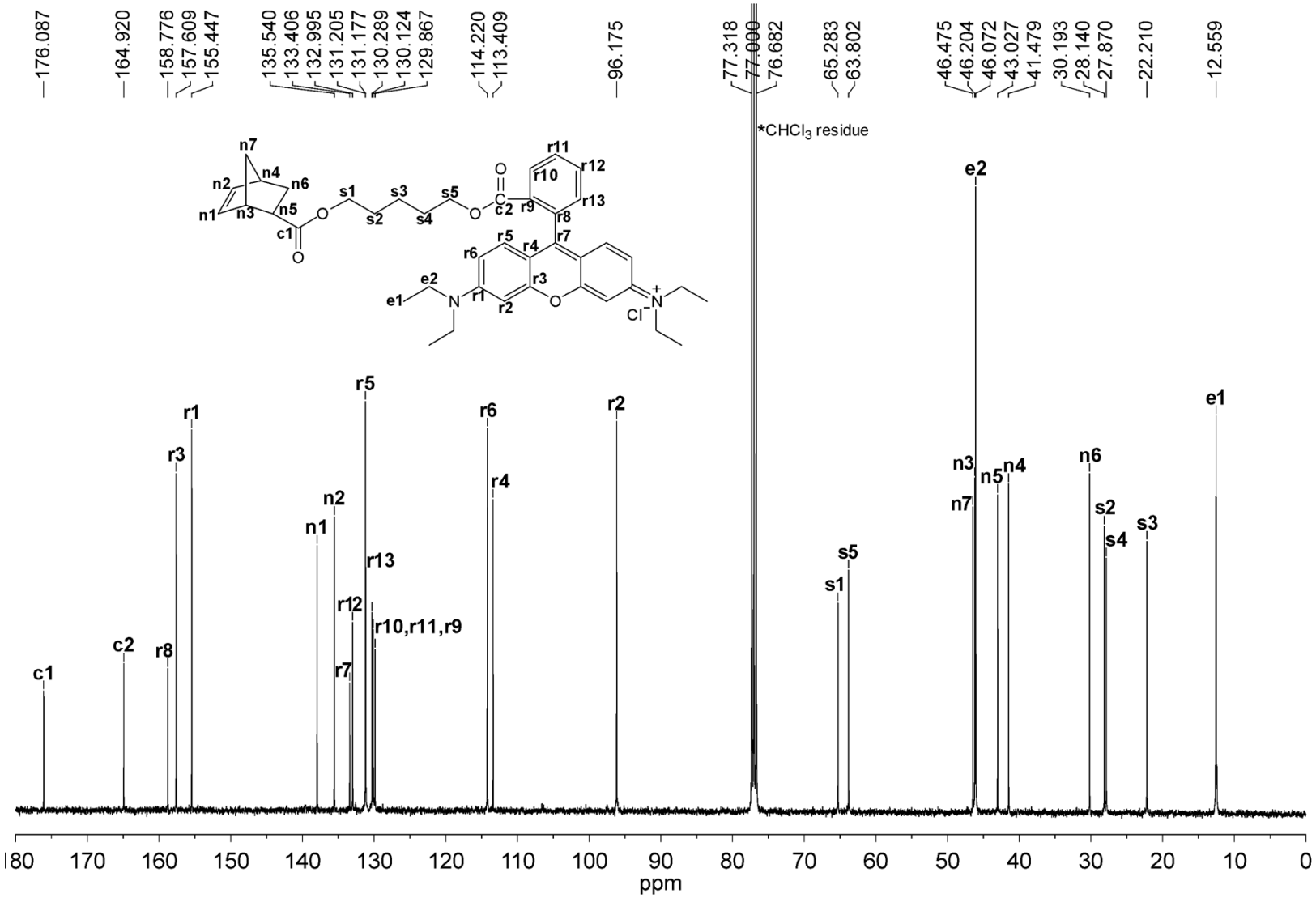

Fig. S19 ^{13}C NMR spectrum for 5-rhodamine-B-formyloxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate in $CDCl_3$.

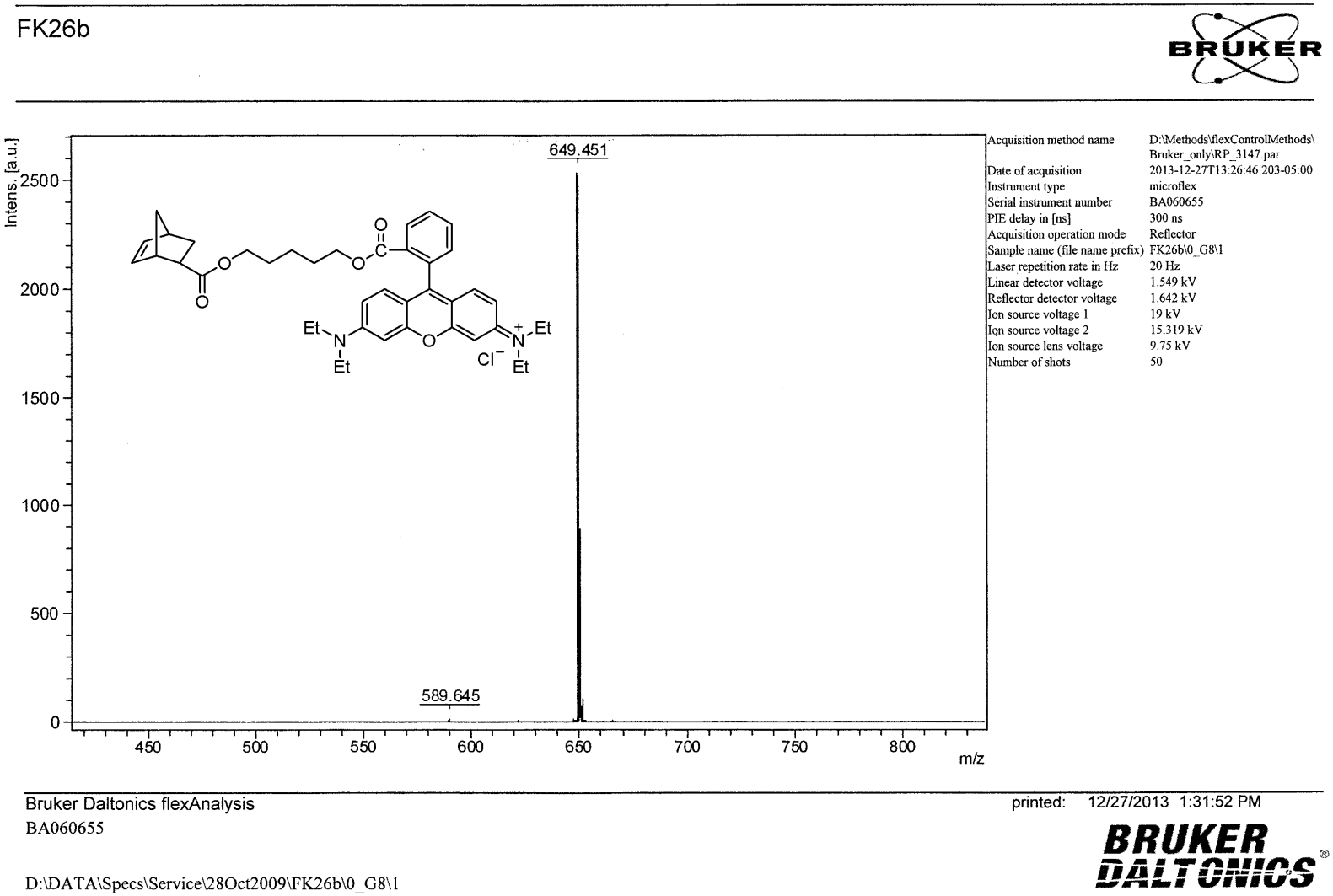

Fig. S20 MALDI-TOF MS spectrum for 5-rhodamine-B-formyloxypentyl-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate.

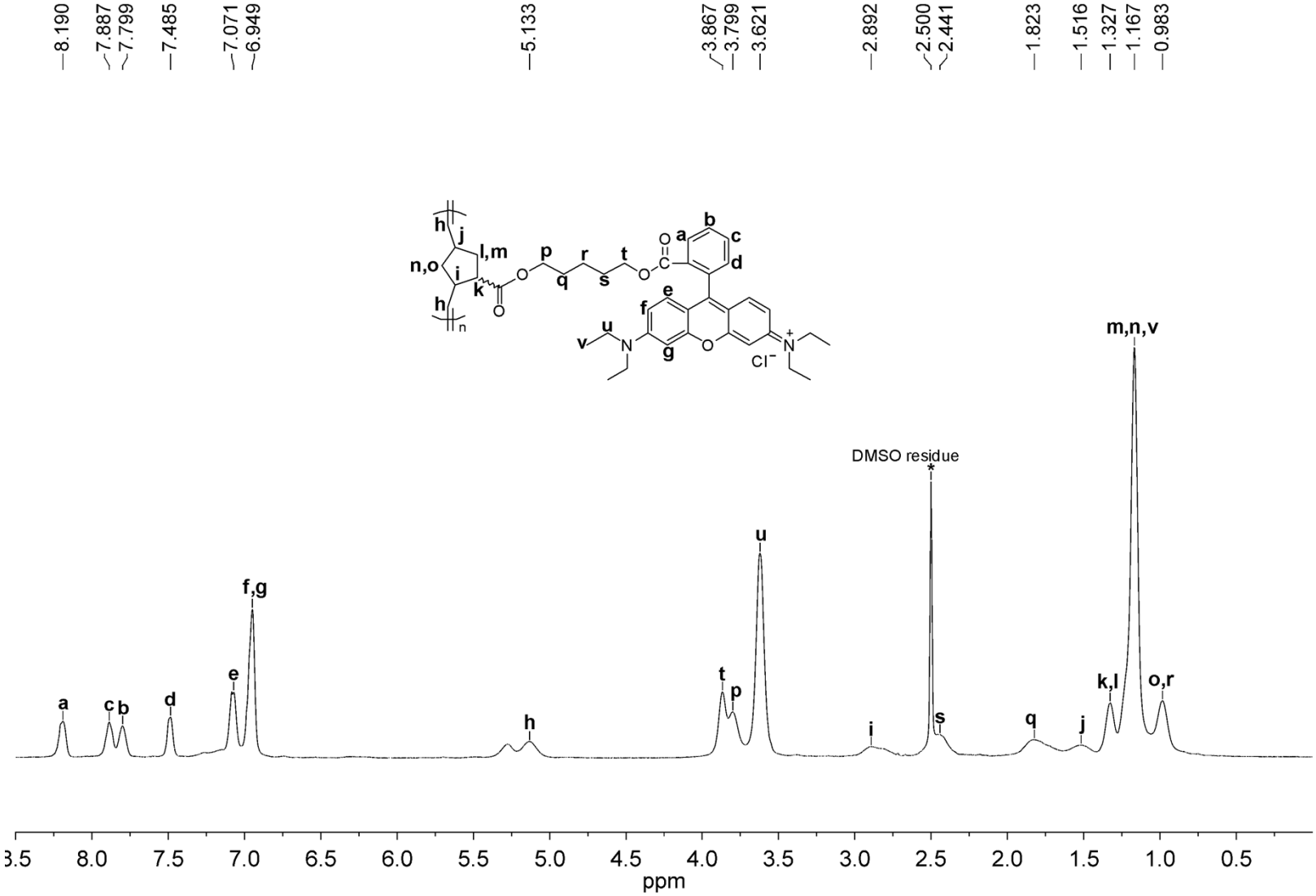

Fig. S21 ^{1}H NMR spectrum for PNB-RhB in DMSO-d_6.

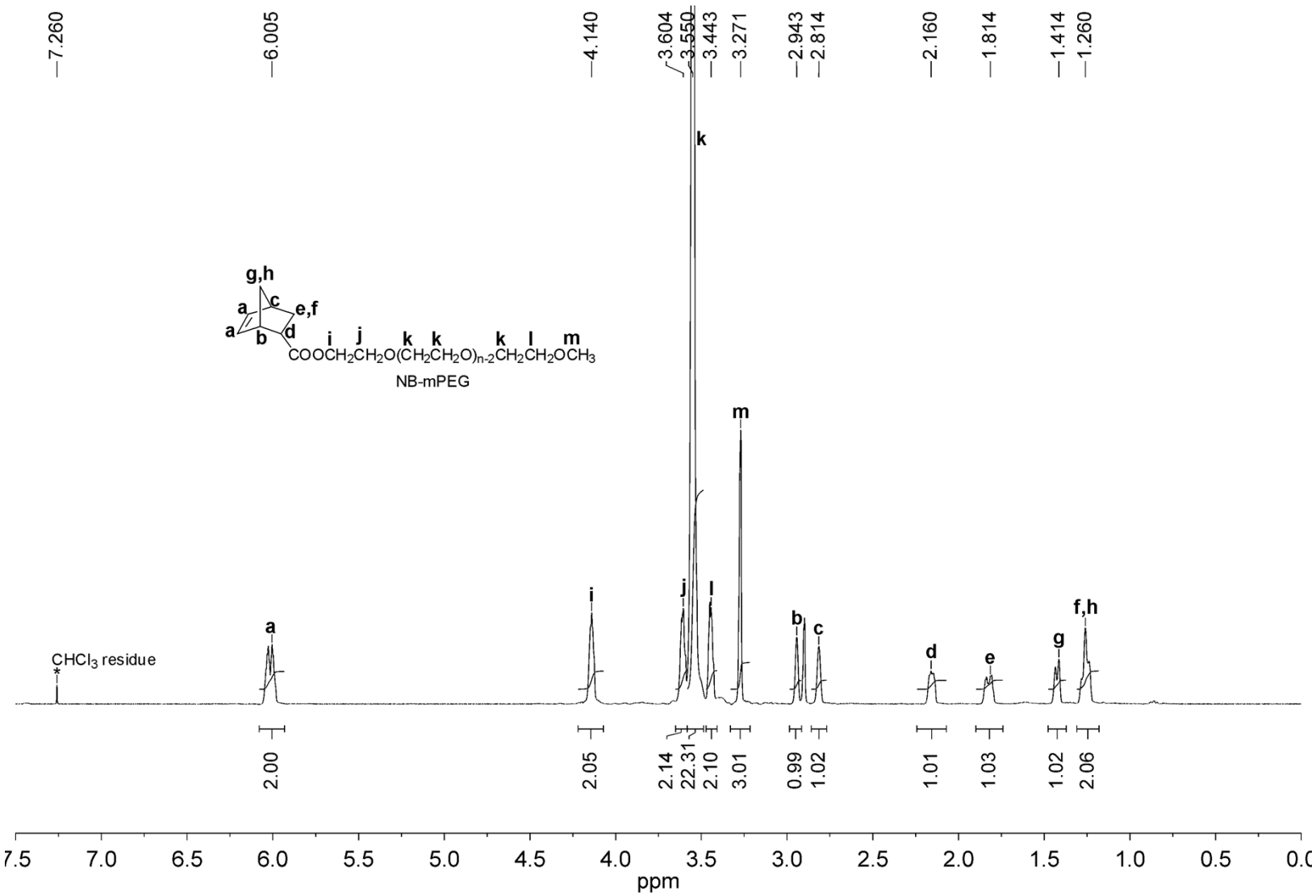

Fig. S22 ^{1}H NMR spectrum for methoxypolyethylene-glycol-350-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate in $CDCl_3$.

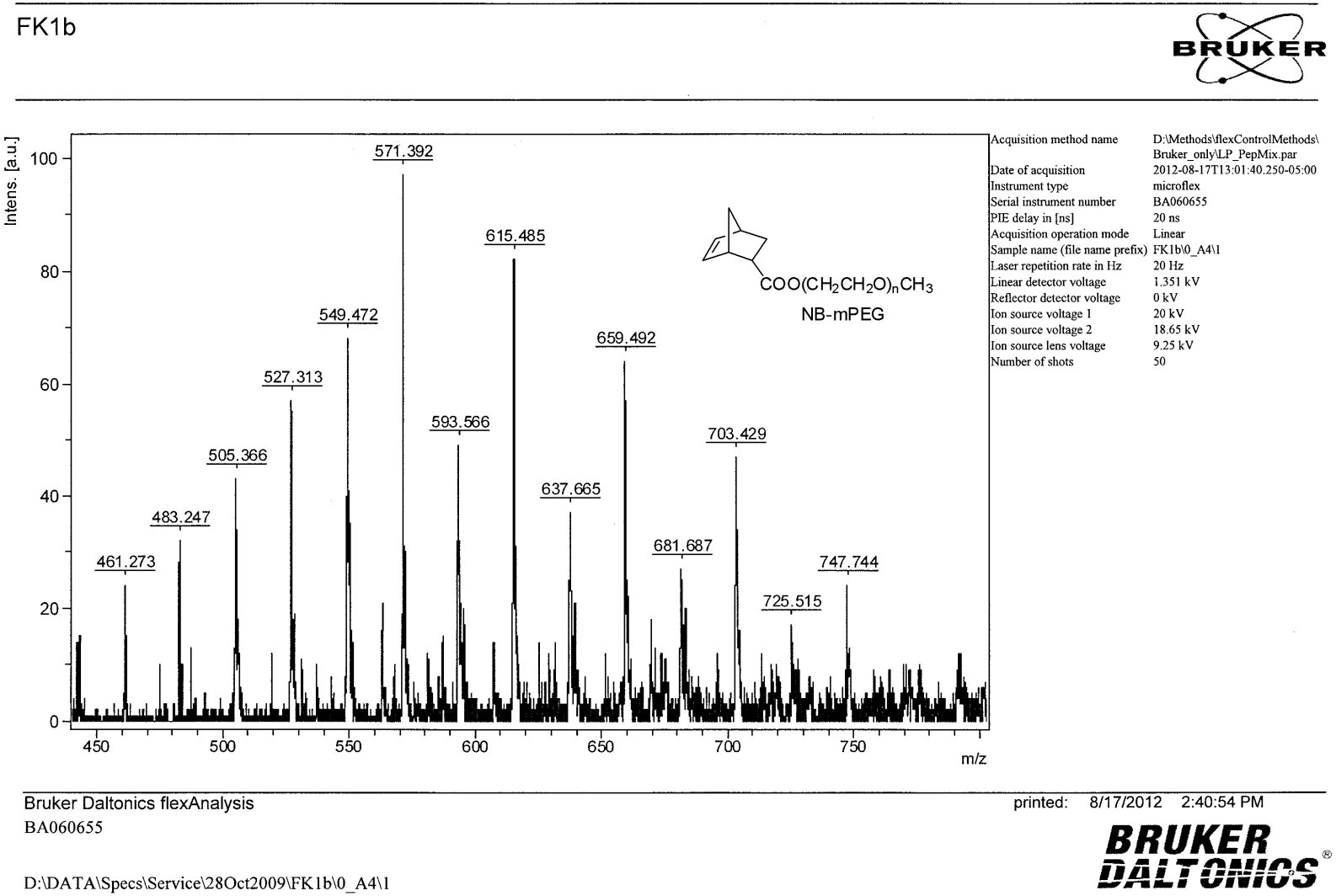

Fig. S23 MALDI-TOF MS spectrum for methoxypolyethylene-glycol-350-*exo*-bicyclo[2.2.1]-hept-5-ene-2-carboxylate.

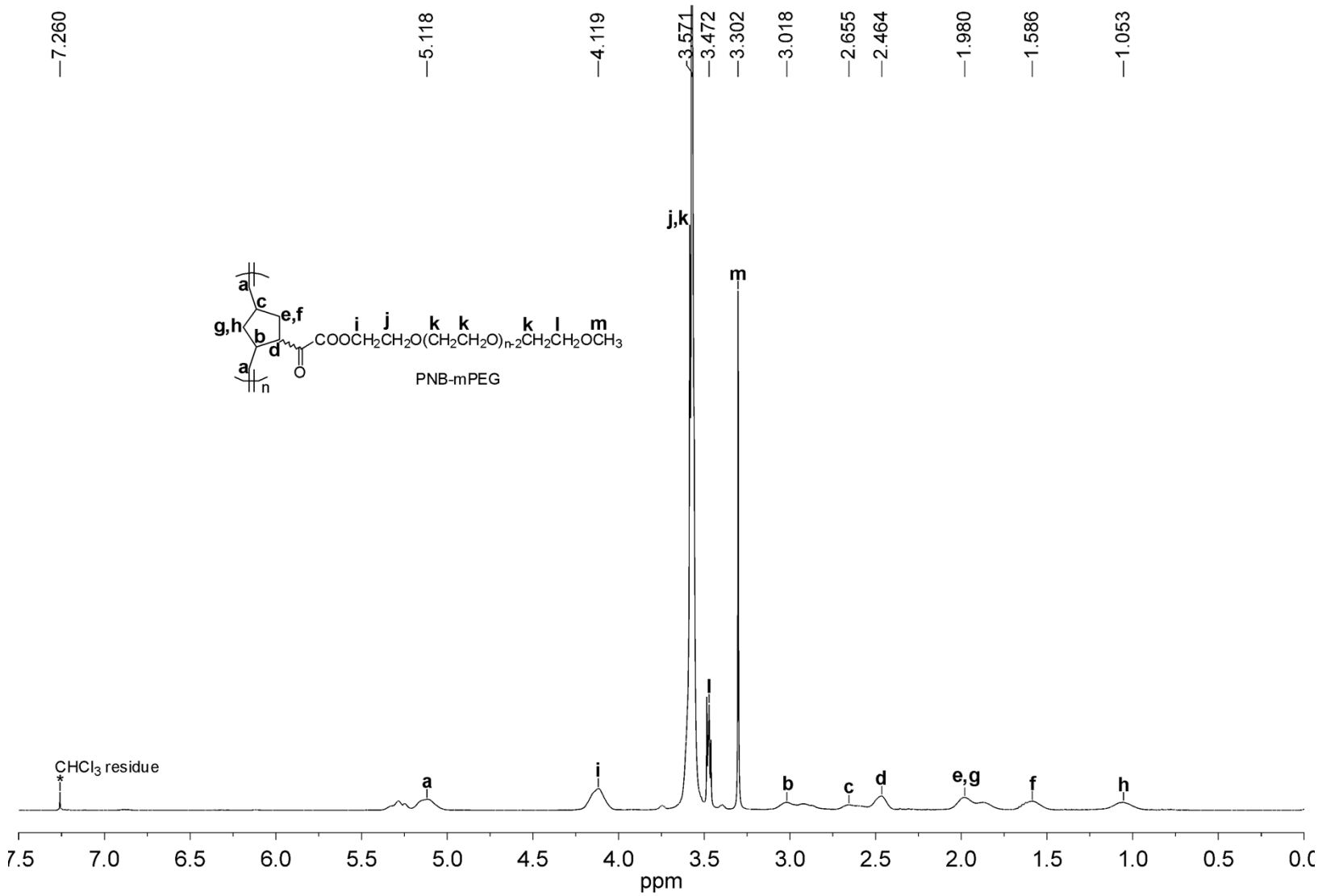

Fig. S24 ^{1}H NMR spectrum for PNB-mPEG in $CDCl_3$.

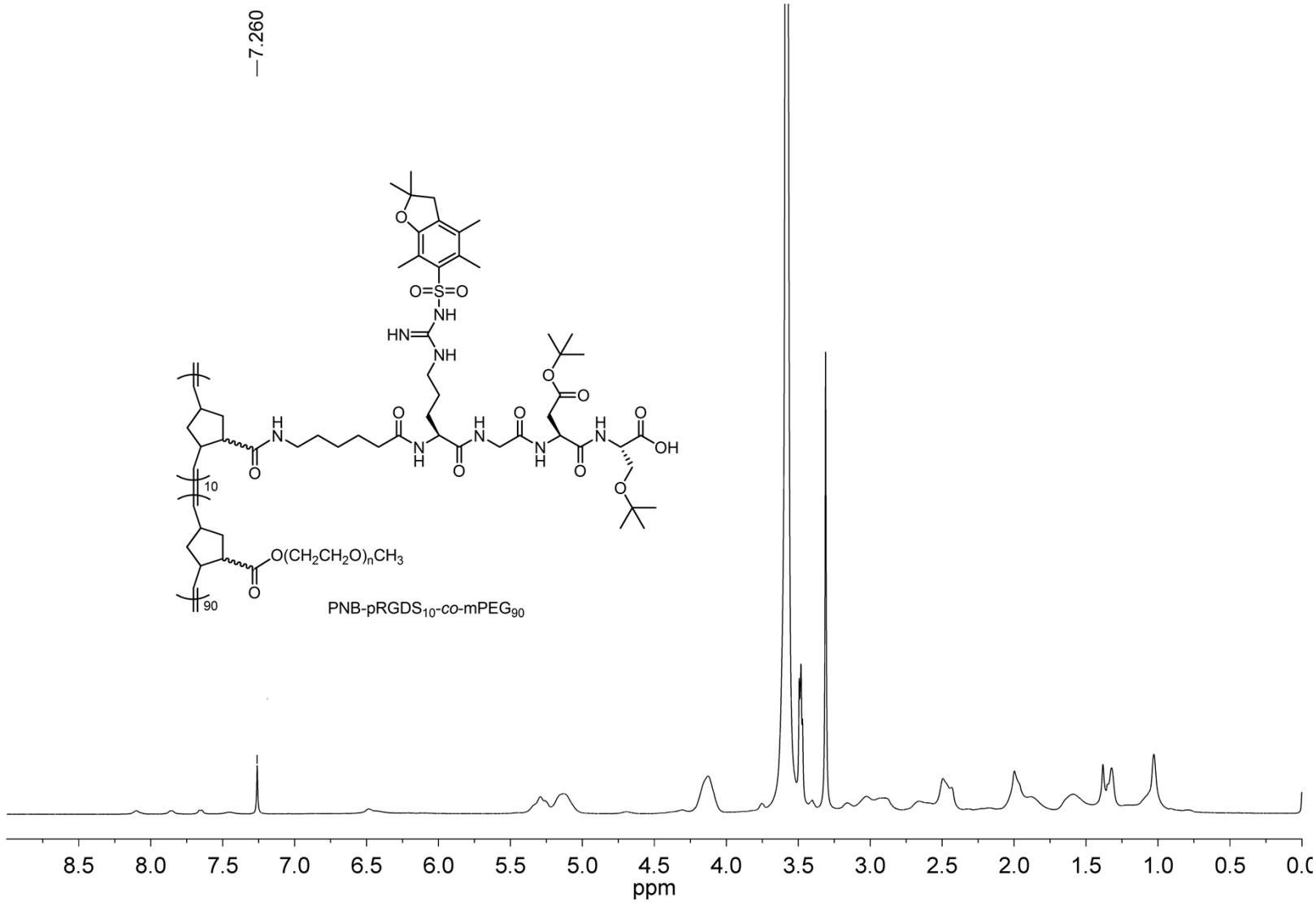

Fig. S25 ^{1}H NMR spectrum for PNB-pRGDS$_{10}$-*co*-mPEG$_{90}$ in $CDCl_3$.

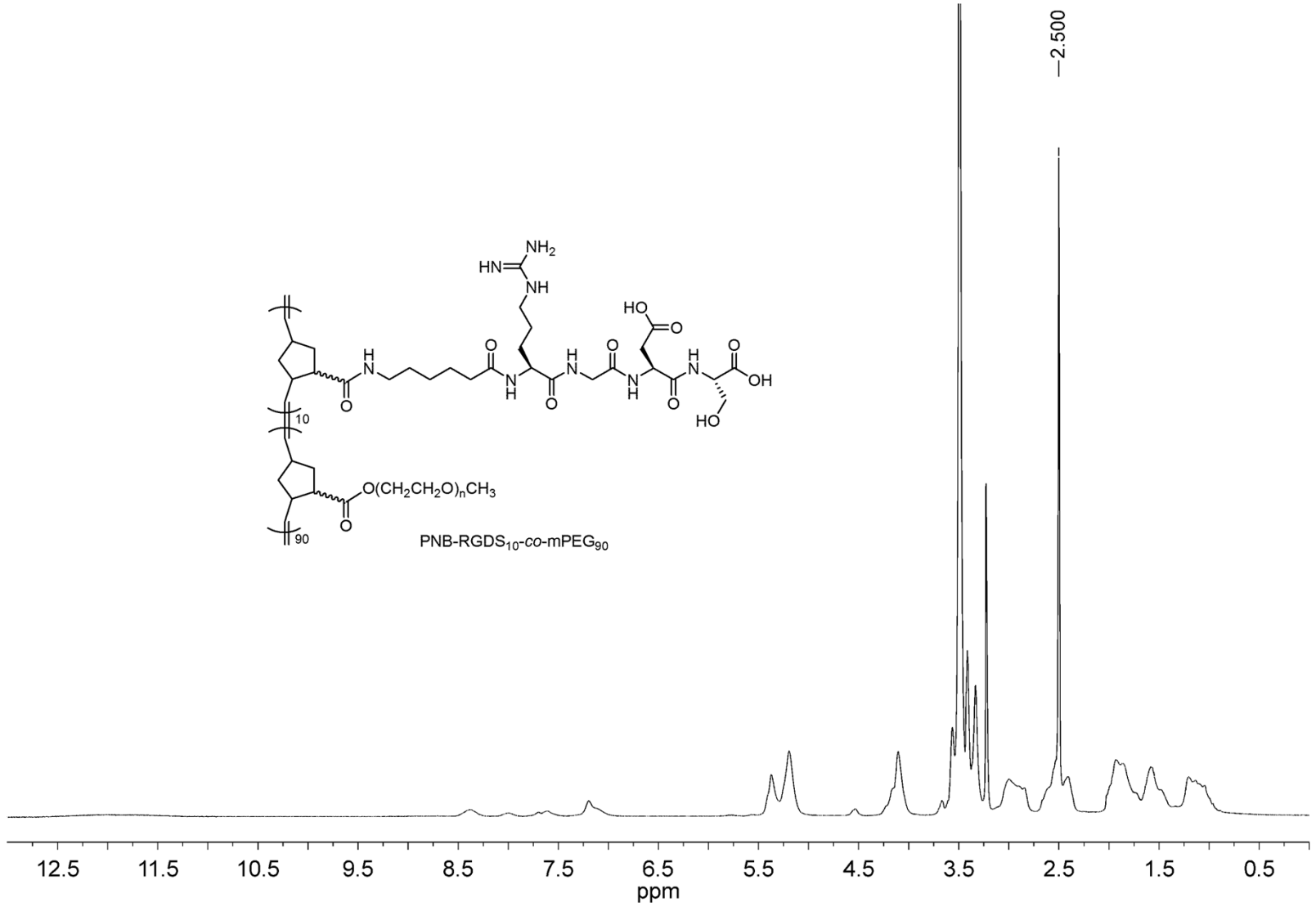

Fig. S26 ^{1}H NMR spectrum for PNB-RGDS$_{10}$-*co*-mPEG$_{90}$ in DMSO-d_6.

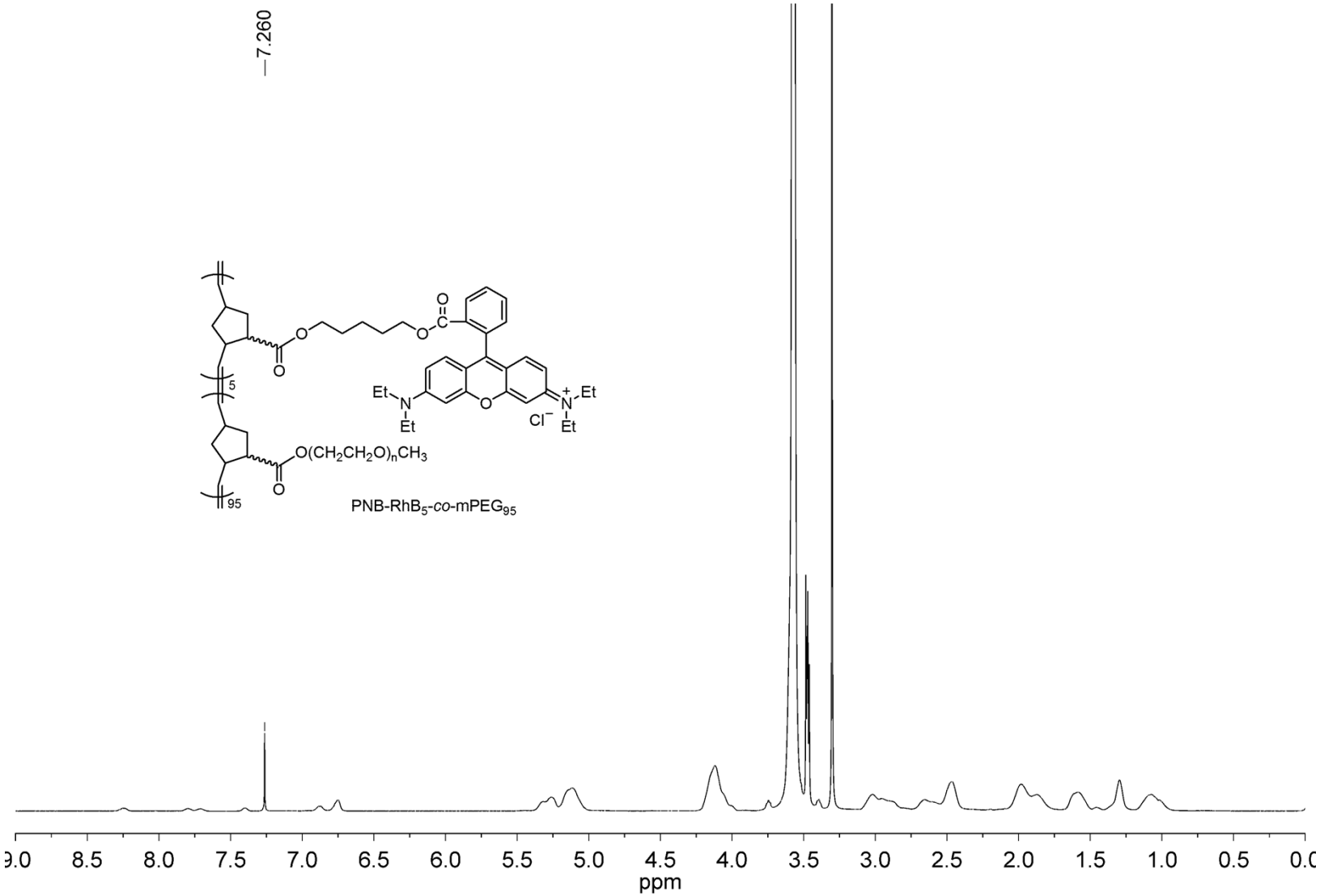

Fig. S27 ^{1}H NMR spectrum for PNB-RhB$_5$-*co*-mPEG$_{95}$ in CDCl$_3$.

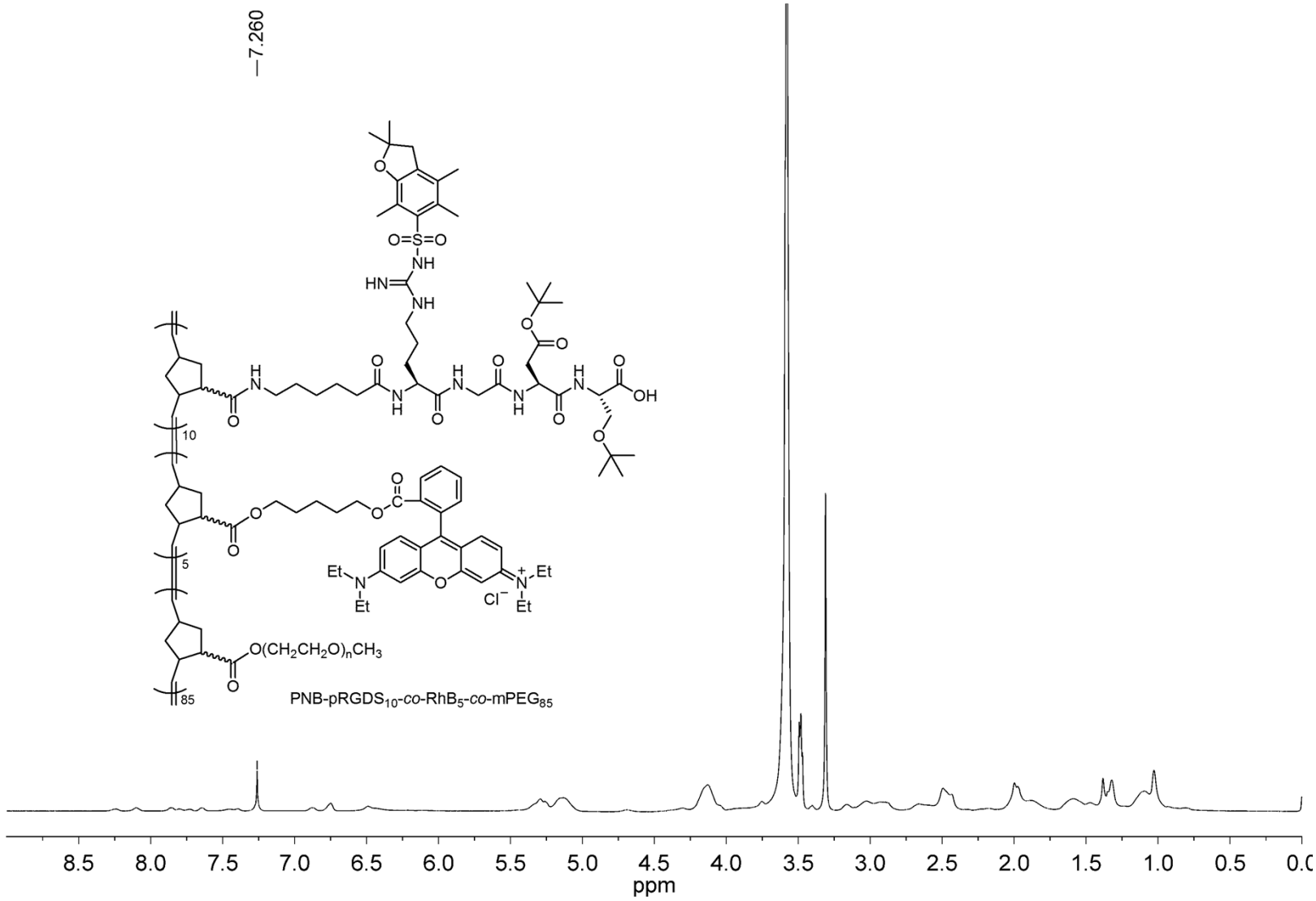

Fig. S28 ^{1}H NMR spectrum for PNB-pRGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ in $CDCl_3$.

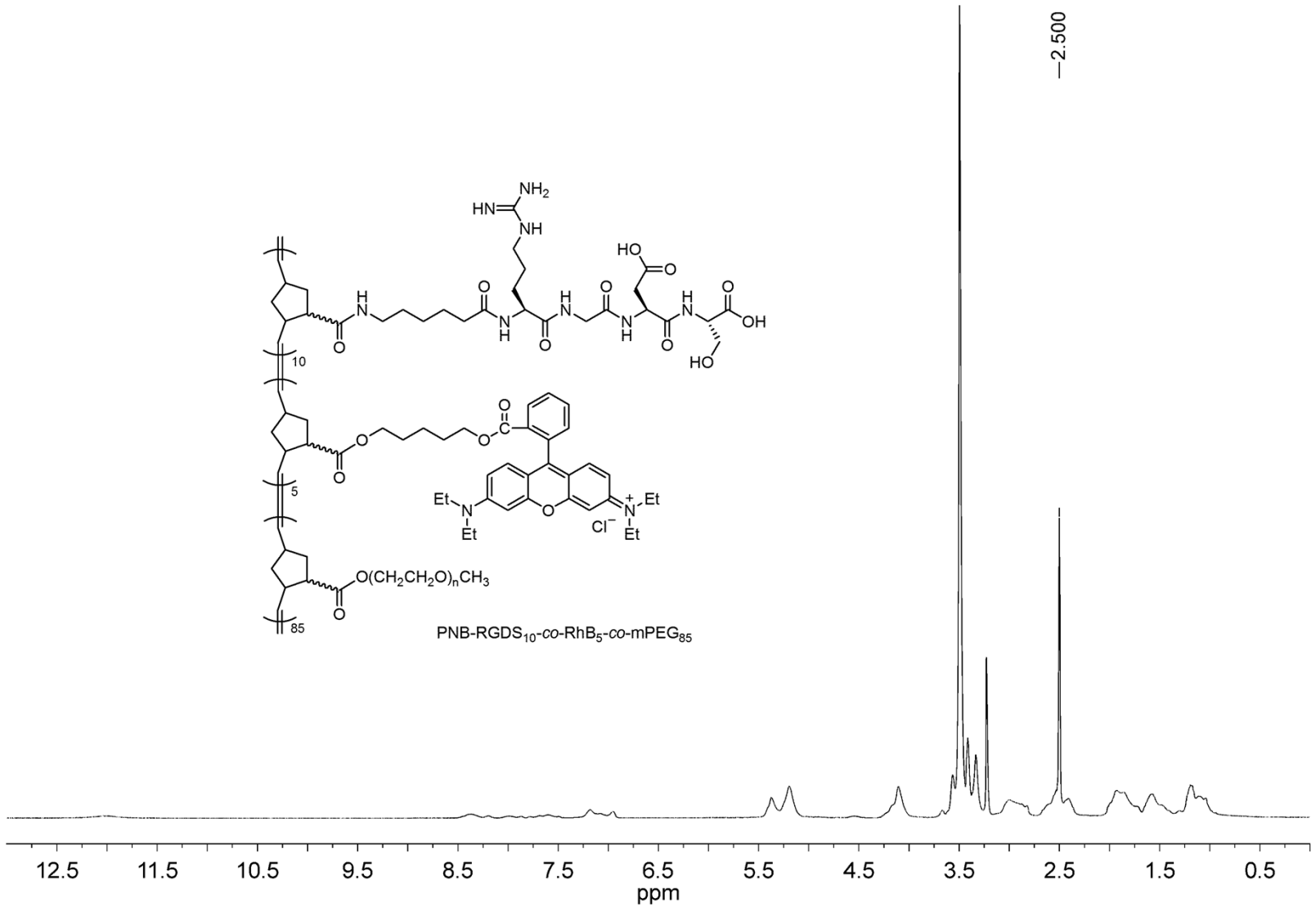

Fig. S29 ^{1}H NMR spectrum for PNB-RGDS$_{10}$-*co*-RhB$_5$-*co*-mPEG$_{85}$ in DMSO-d_6.