Suporting information

Synthesis of Stimuli-Responsive Heterofunctional Dendrimer by Passerini Multicomponent Reaction

Naganath G. Patil,[†] Rimesh Augustine,[†] Zhang Yu,[†] Sung Chul Hong,[‡] and Il Kim[*,†]

[†]*Department Polymer Science and Engineering, Pusan National University, Busan 46241, South Korea*

[‡]*Faculty of Nanotechnology and Advanced Materials Engineering, Sejong University, Seoul 05006, South Korea*

Corresponding Author

*E-mail: ilkim@pusan.ac.kr

Table of Contents

1. Experimental section

Materials …… S2

Methods …… S2

2. References …… S3

3. Figure S1−Figure S24 …… S4-S17

Experimental section

Materials

4-Formylbenzeneboronic acid pinacol ester, 5-hydroxy-2-nitrobenzaldehyde, quinolone, ethyl formate, and anhydrous DMF were purchased from Alfa Aesar. Propargyl bromide (80% solution in toluene), 2,2-bis-methylolpropionic acid (bis-MPA), sodium hydride, copper(I) iodide, 2-chloroethanol, sodium azide were purchased from Sigma-Aldrich and used as received. Poly(ethylene glycol) methyl ether (MPEG; M_n = 600), 1,6-diaminohexane, diisopropylamine, phosphoryl chloride, *tert*-butylamine, *p*-toluenesulfonyl chloride, and potassium carbonate were obtained from Duksan Chem. Co. (Seoul, Korea). Common solvents like hexane, ethyl acetate, dichloromethane, and methanol were purchased from Duksan Chem. Co. and distilled prior to use. The starting materials like 2-methyl-3-(prop-2-yn-1-yloxy)-2-((prop-2-yn-1-yloxy)methyl)propanoic acid (BisMPA-dialkyne),[S1] 1,6-diisocyanohexane,[S2] and *tert*-butyl isocyanide,[S3] 5-(2-azidoethoxy)-2-nitrobenzaldehyde,[S4] and tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA)[S5] synthesized as per reported procedure.

Methods

All ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian INOVA 400 NMR spectrometer. The Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectra were recorded at Materials Characterization Lab (MALDI TOF-TOF 5800 System, AB SCIEX, USA) equipped with a nitrogen laser emitting at 337 nm with a 3 ns pulse duration. The instrument was operated in reflector mode and linear mode. The ions were accelerated under a potential of 20 kV. Fourier-transform infrared (FT–IR) spectra were recorded in the range of 4000–500 cm^{-1} by making KBr pallets on Shimadzu IR prestige 21 spectrometer. The UV–vis absorption spectra were recorded on a shimadzu UV-1650 PC. The

fluorescence spectral measurements were carried out on Scinco FS-2 fluorescence spectrometer. The MW and poly-dispersity index (Đ) of the dendrimers measured by using a Waters GPC system, that was equipped with a Waters 1515 pump, Waters 2414 refractive index detector, and three Waters Styragel high-resolution columns at 25 °C using tetrahydrofuran (THF) as eluent at flow rate 1 mL/min. The dynamic light scattering (DLS) measurements were performed on a Nano ZS90 from Malvern Instruments, Ltd, U.K. equipped with a 633 nm wavelength He–Ne laser at angle of 90°. The particle morphology was analyzed by using transmission electron microscopy (TEM), on a JEOL-1299EX electron microscope with an accelerating voltage of 80 keV.

References

(S1) Wu, W.; Driessen, W.; Jiang, and X. Bismpadialkyne Synthesis. *J Am Chem Soc* **2014**, *136*, 3145−3155.

(S2) Sehlinger, A.; Dannecker, P.-K.; Kreye, O.; Meier, M. A. R. Hexyl Diisocyanide Synthesis. *Macromolecules* **2014**, *47*, 2774–2783.

(S3) Nacsa, E. D.; Lambert, T. H. T Bytul Isocyanide Synthesis. *J.Am.Chem.Soc.* **2015**, *137*, 10246 − 10253.

(S4) Matsuo, K.; Kioi, Y.; Yasui, R.; Takaoka, Y.; Miki, T.; Fujishima, S.; Hamachi, I. One-Step Construction of Caged Carbonic Anhydrase I Using a Ligand-Directed Acyl Imidazole-Based Protein Labeling Method. *Chem Sci* **2013**, *4*, 2573 DOI: 10.1039/c3sc50560j.

(S5) Vonhoeren, B.; Dalgleish, S.; Hu, L.; Matsushita, M. M.; Awaga, K.; Ravoo, B. J. TBTA Synthesis. *ACS Appl Mater Interfaces,* **2015**, *7*, 7049–7053.

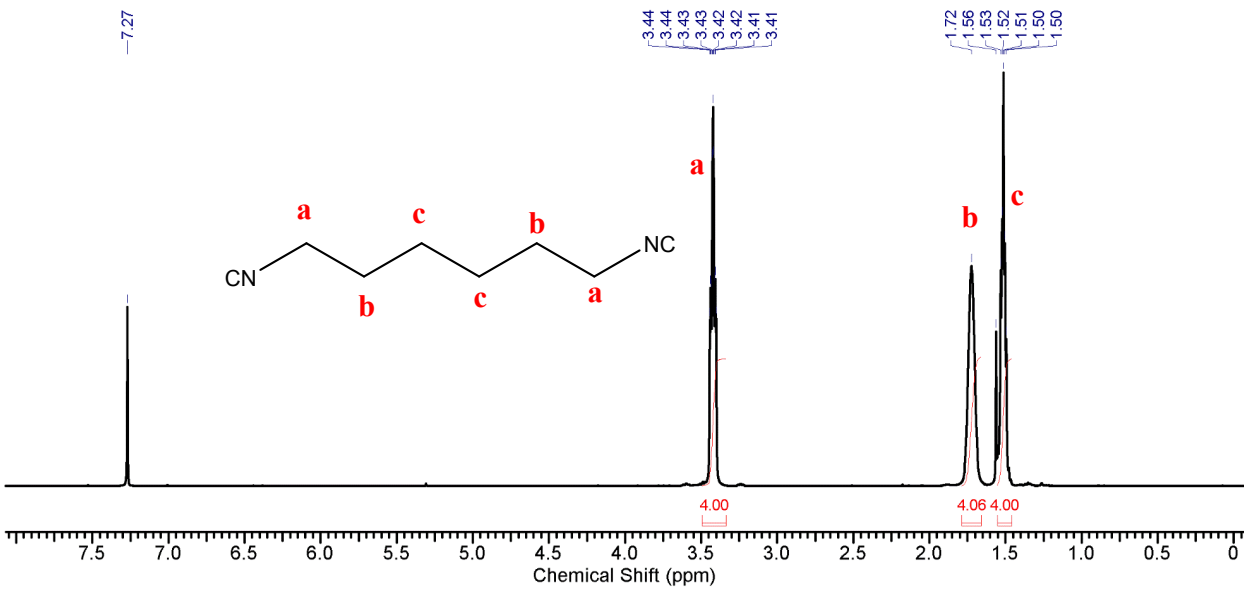

Figure S1: 400 MHz ^{1}H NMR spectrum of 1,6-diisocyanohexane in $CDCl_3$.

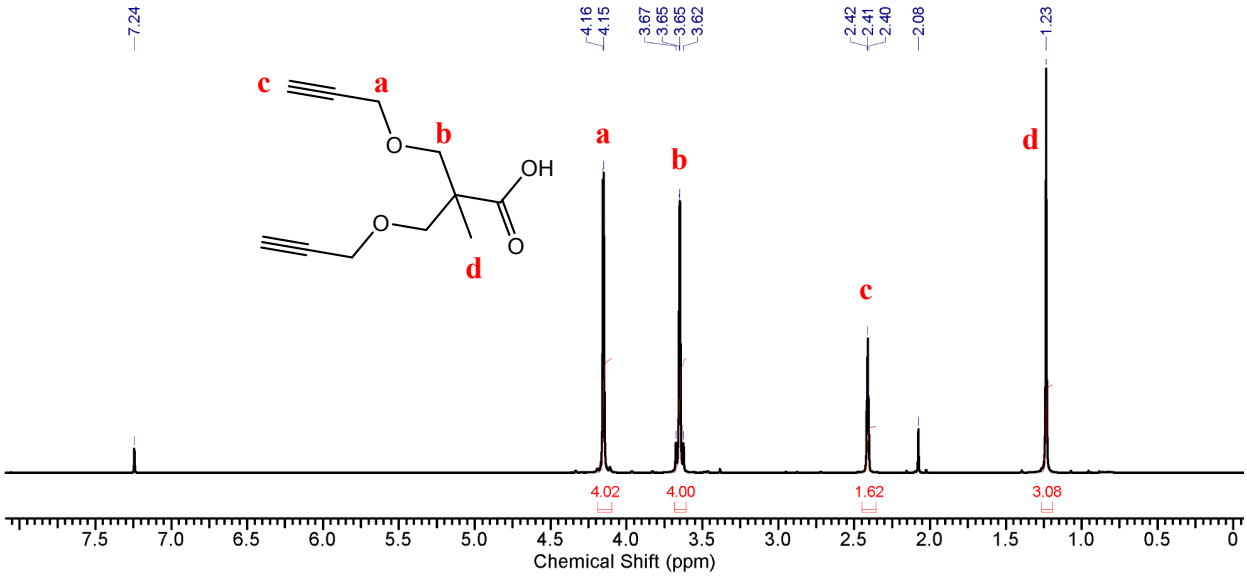

Figure S2: 400 MHz ^{1}H NMR spectrum of BisMPA-dialkyne in $CDCl_3$.

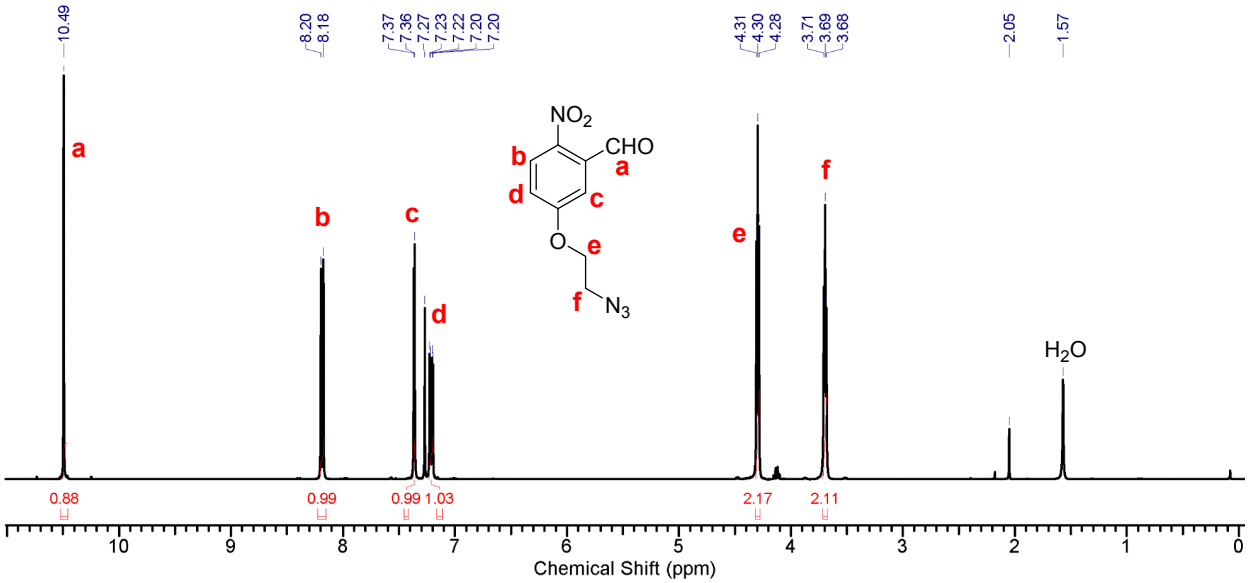

Figure S3: 400 MHz ^{1}H NMR spectrum of 5-(2-azidoethoxy)-2-nitrobenzaldehyde in $CDCl_3$.

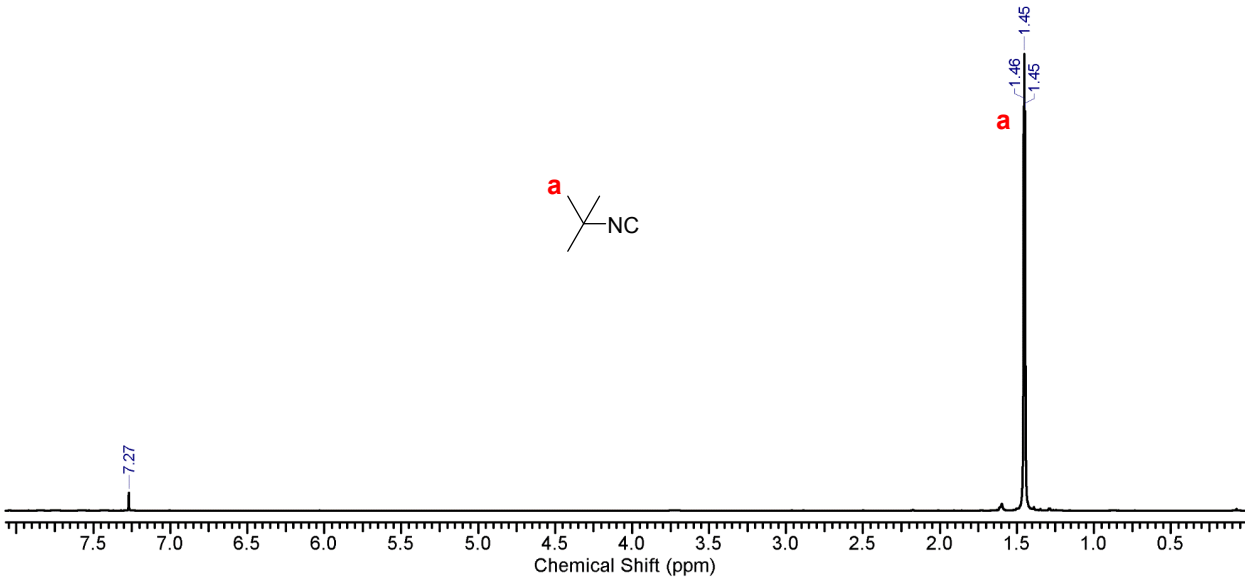

Figure S4: 400 MHz ^{1}H NMR spectrum of t-butyl isocyanide in $CDCl_3$.

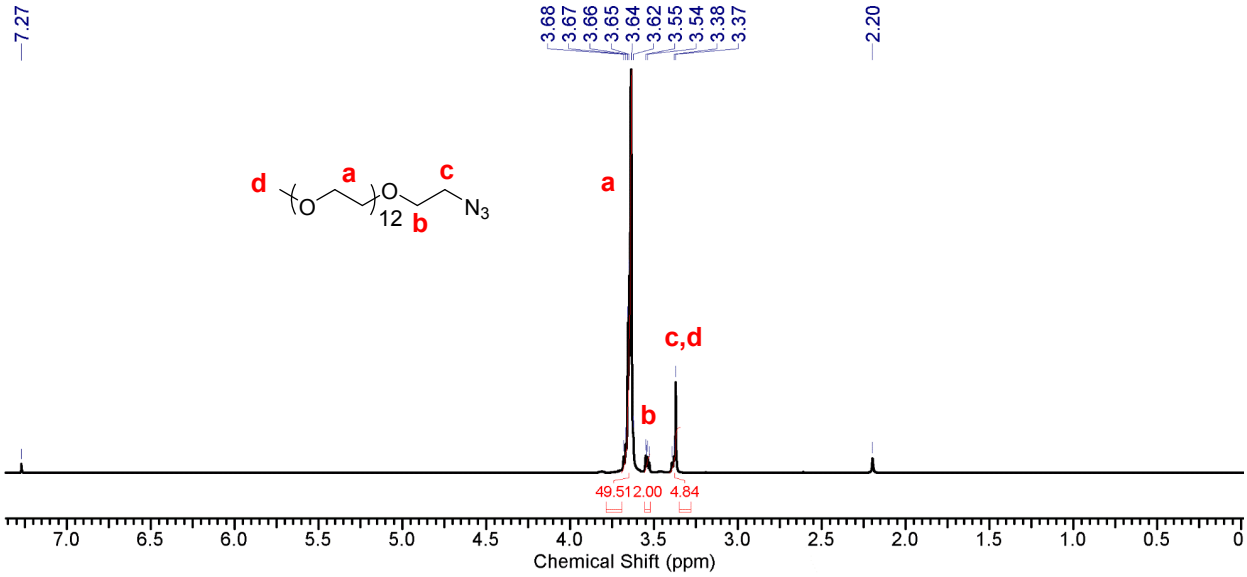

Figure S5: 400 MHz ^{1}H NMR spectrum of MPEG-N_3 in $CDCl_3$.

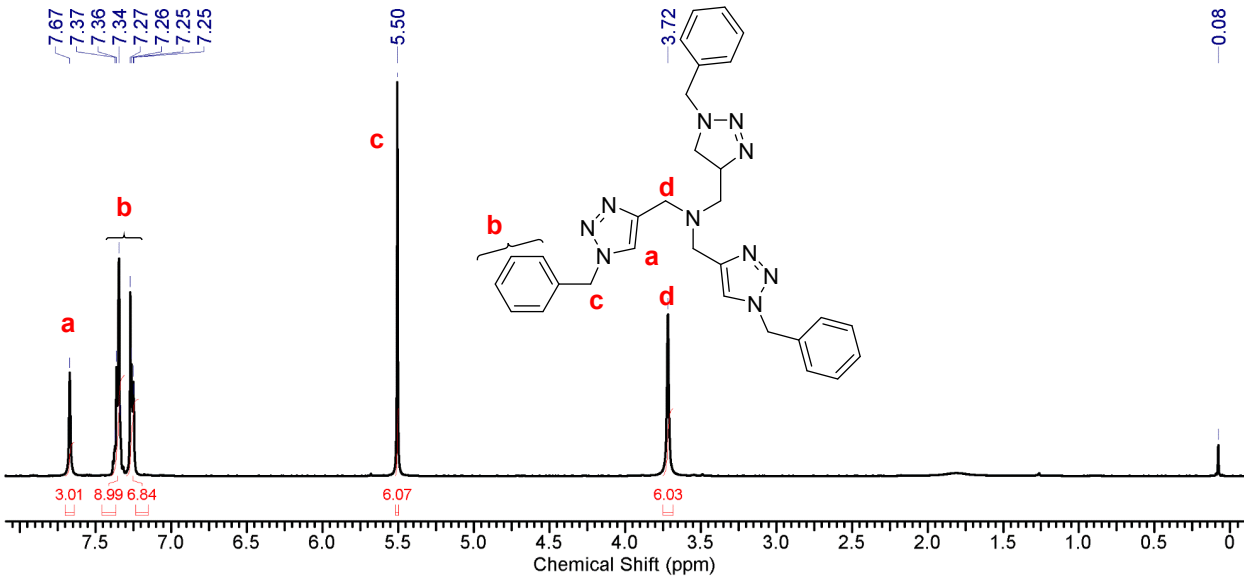

Figure S6: 400 MHz ^{1}H NMR spectrum of TBTA in $CDCl_3$.

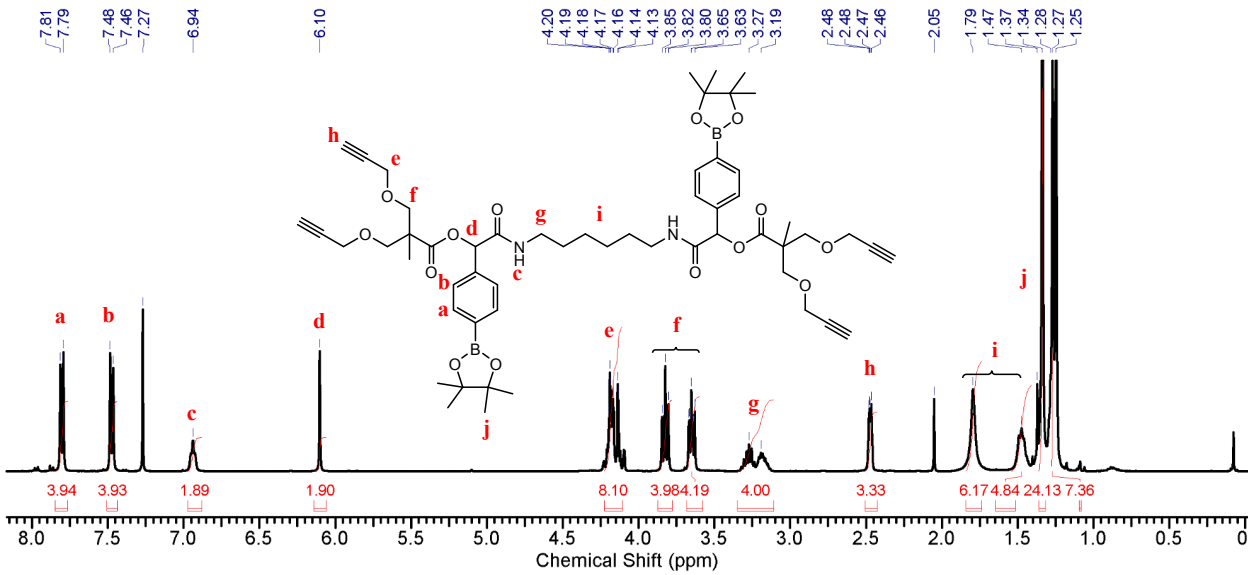

Figure S7: 400 MHz ^{1}H NMR spectrum of G0.5-Alkyne in $CDCl_3$.

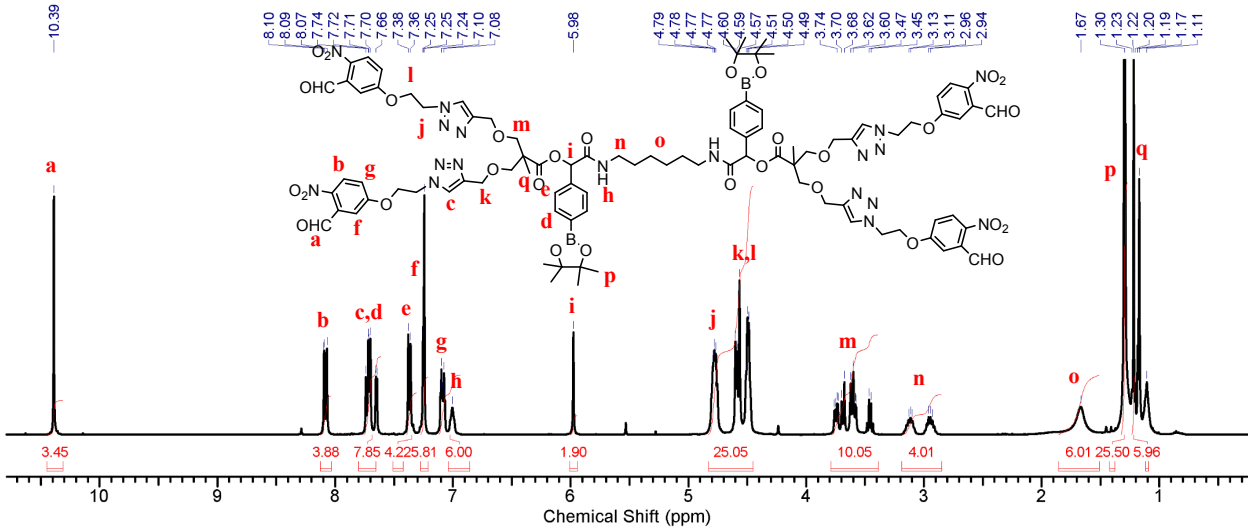

Figure S8: 400 MHz ^{1}H NMR spectrum of G1-Aldehyde in $CDCl_3$.

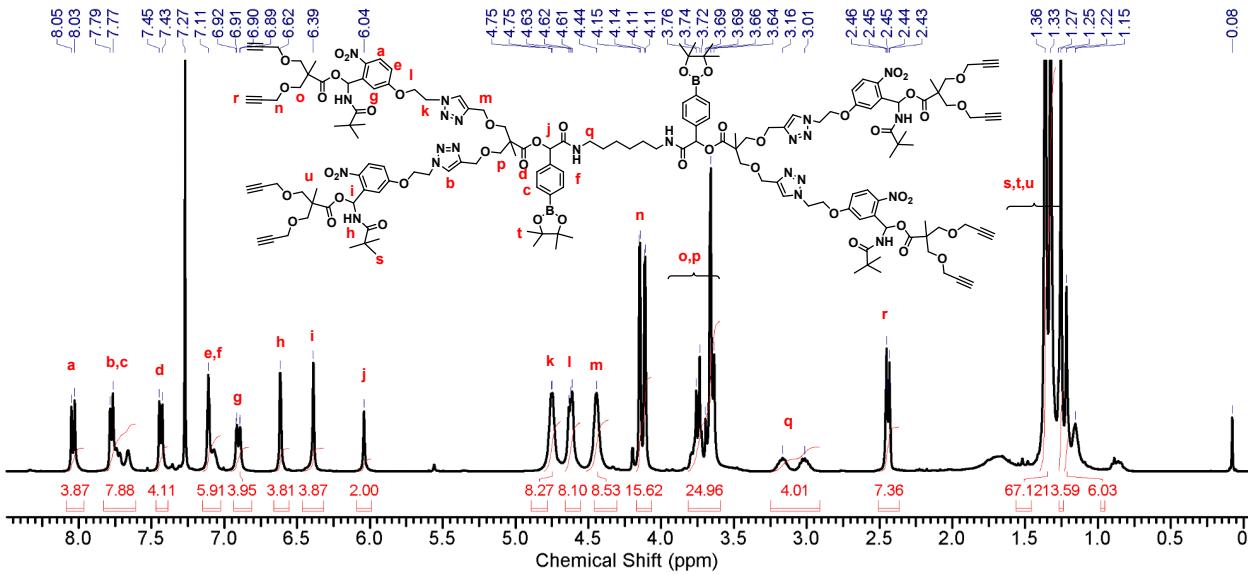

Figure S9: 400 MHz ^{1}H NMR spectrum of G1.5-Aldehyde in $CDCl_3$.

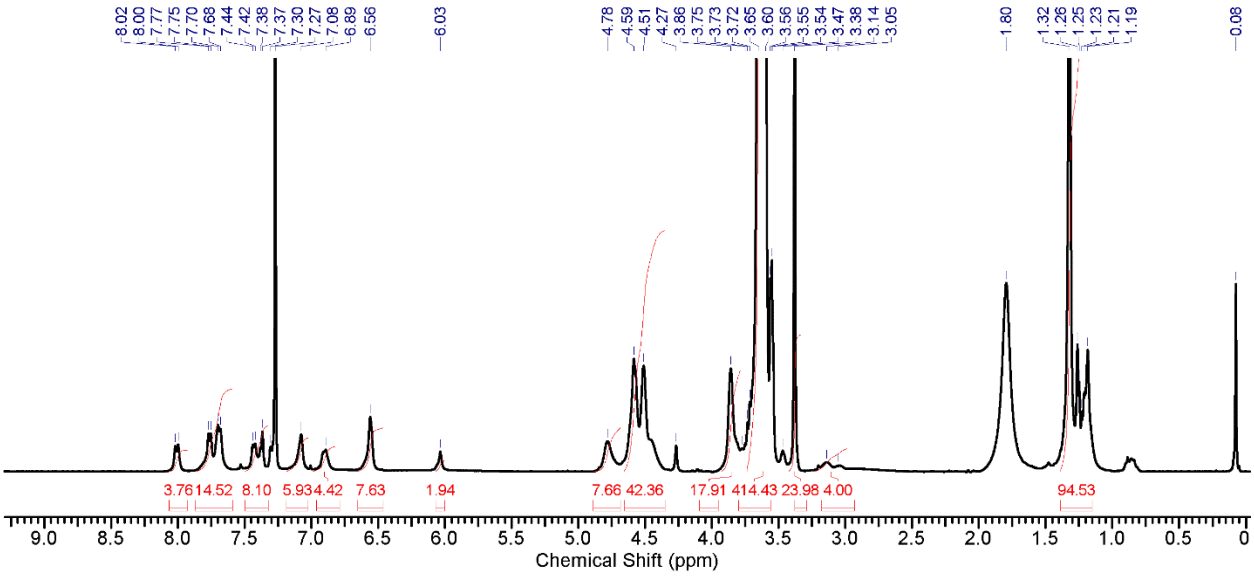

Figure S10: 400 MHz ^{1}H NMR spectrum of G2-PEG in $CDCl_3$.

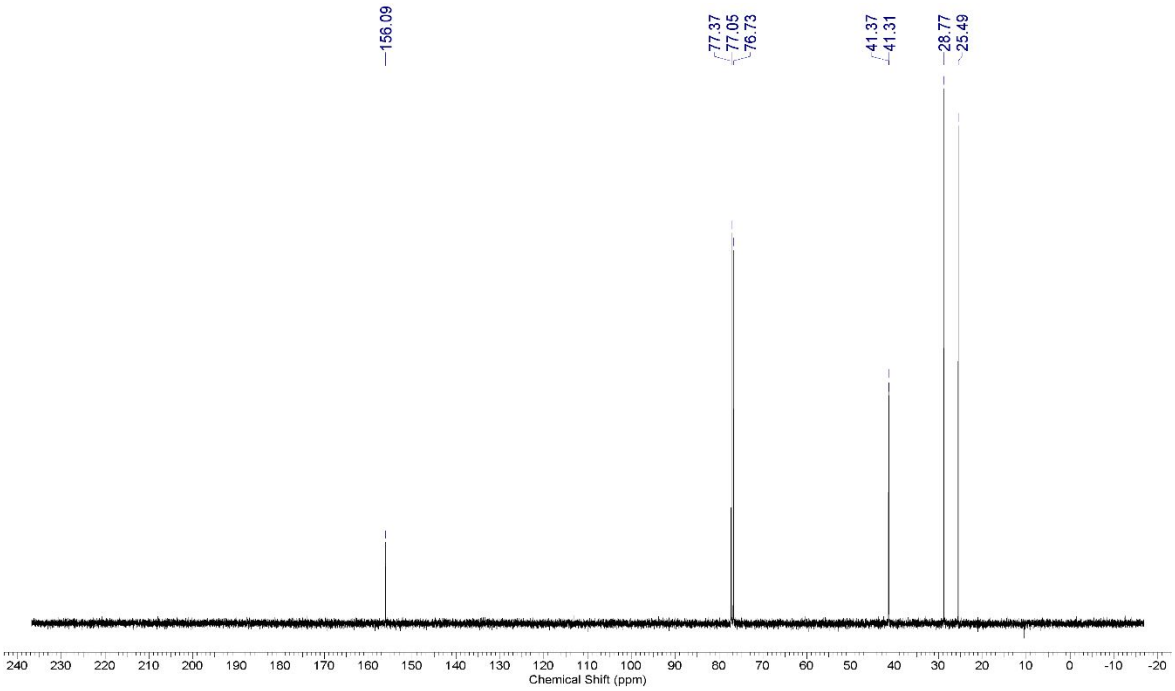

Figure S11: 400 MHz ^{13}C NMR spectrum of 1,6-diisocyanohexane in $CDCl_3$.

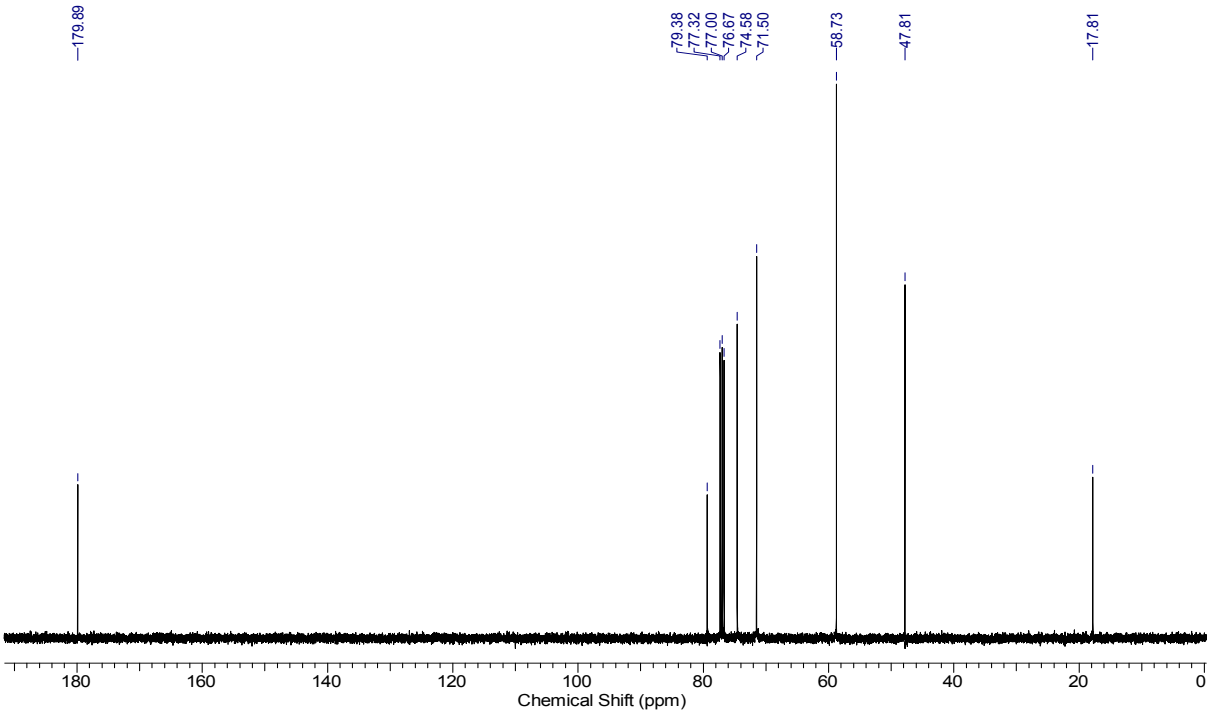

Figure S12: 400 MHz ^{13}C NMR spectrum of BisMPA-dialkyne in $CDCl_3$.

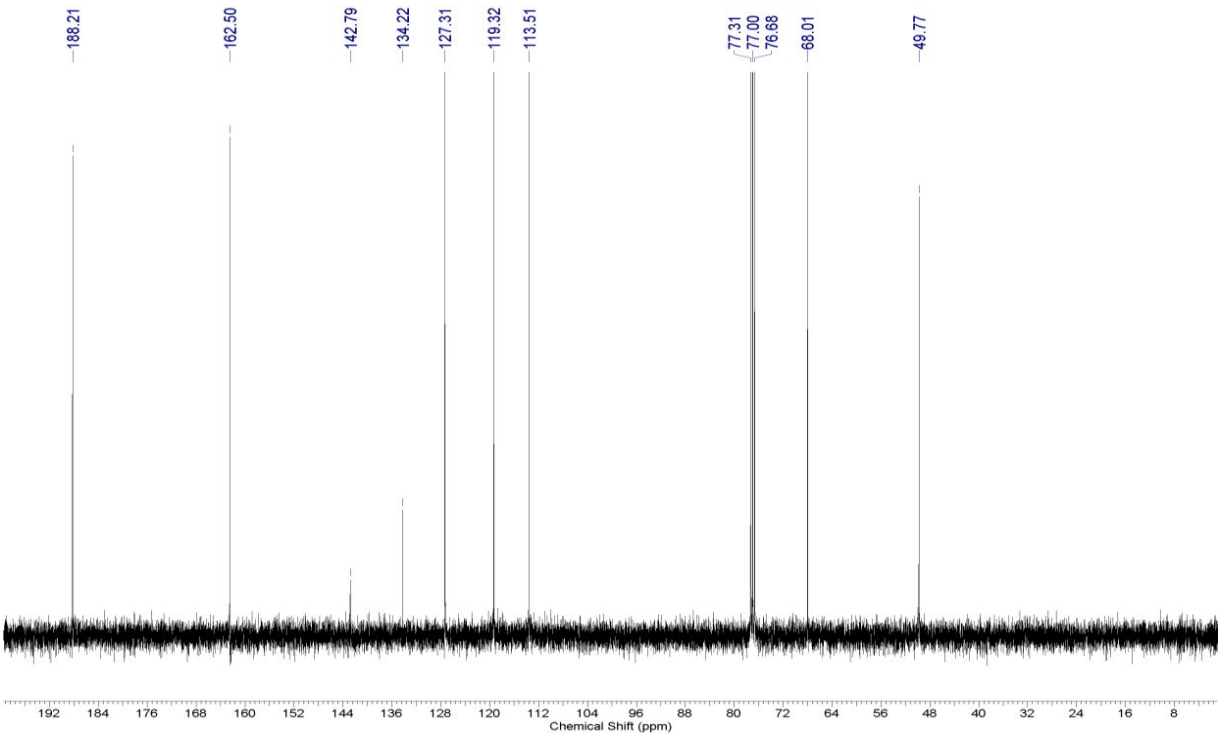

Figure S13: 400 MHz ^{13}C NMR spectrum of 5-(2-azidoethoxy)-2-nitrobenzaldehyde in $CDCl_3$.

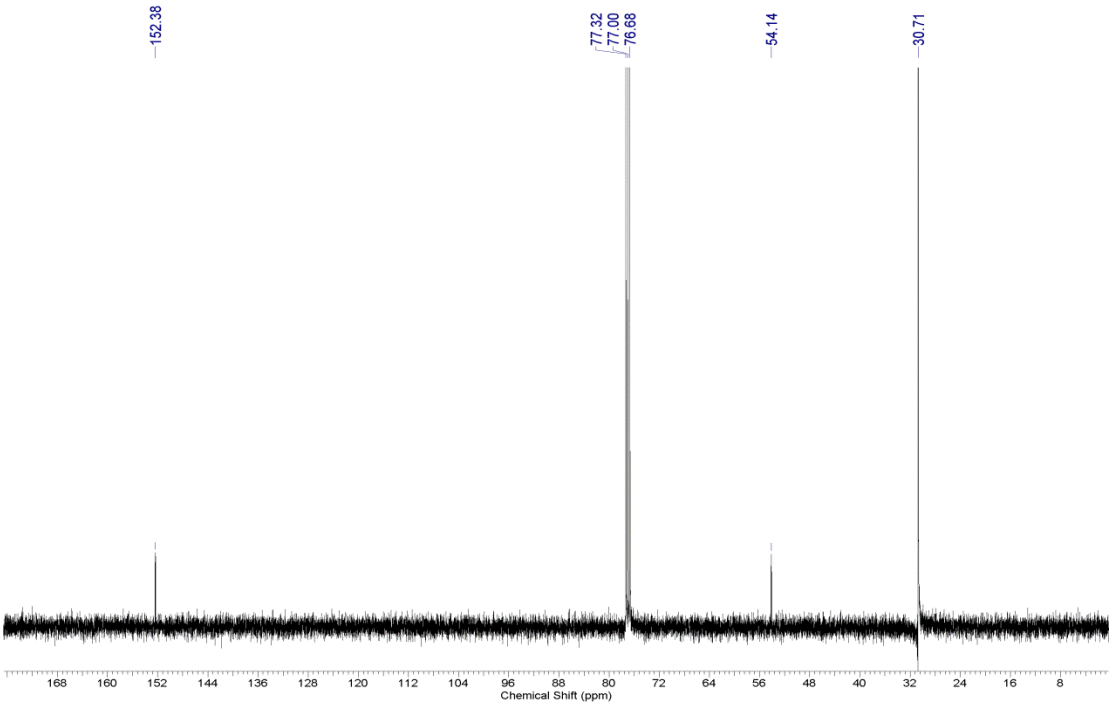

Figure S14: 400 MHz ^{13}C NMR spectrum of t-butyl isocyanide in $CDCl_3$.

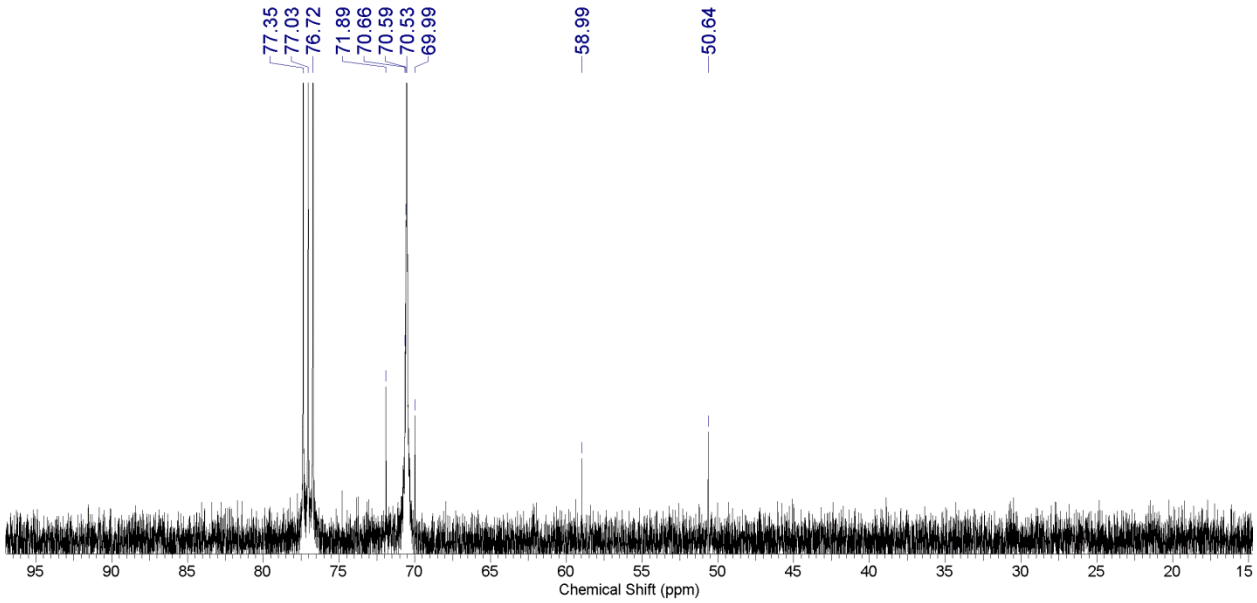

Figure S15: 400 MHz ^{13}C NMR spectrum of MPEG-N_3 in $CDCl_3$.

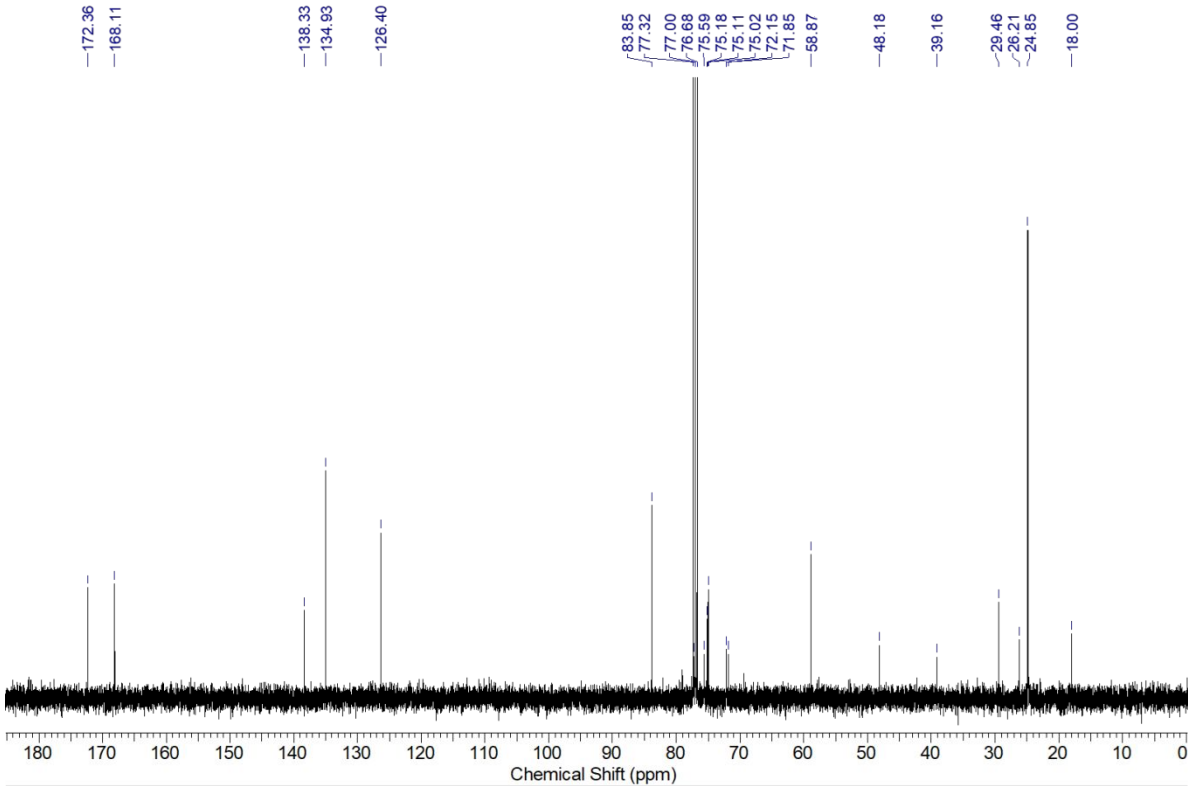

Figure S16: 400 MHz ^{13}C NMR spectrum of G0.5-Alkyne in $CDCl_3$.

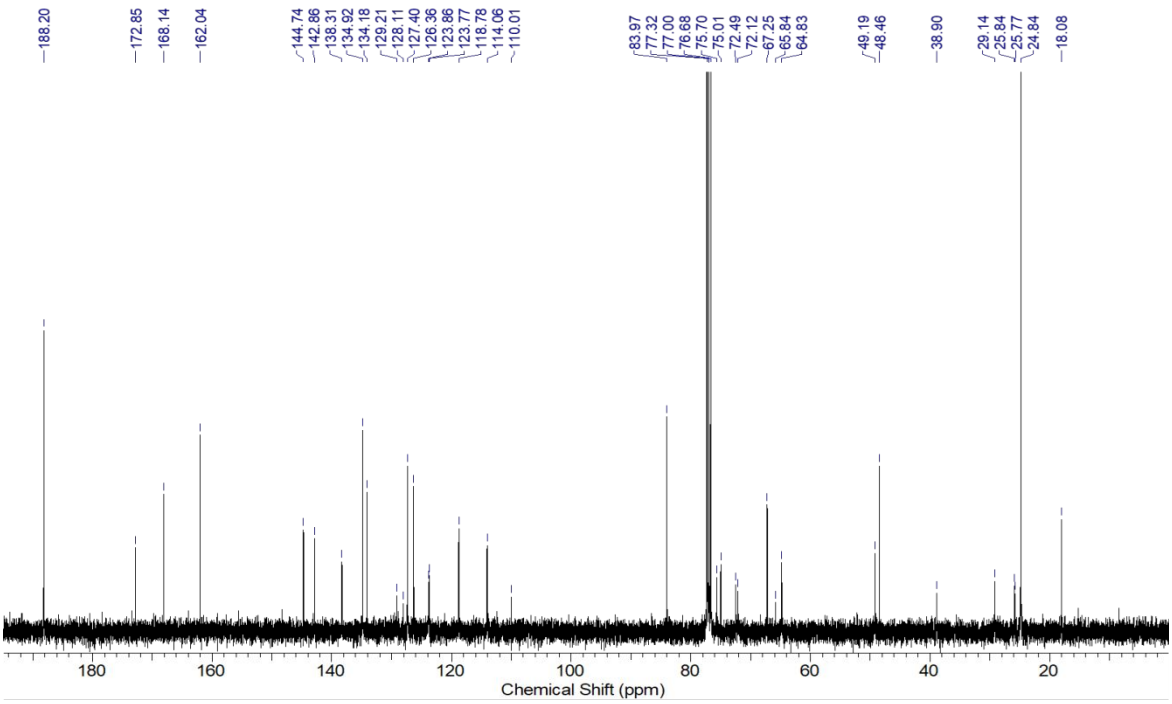

Figure S17: 400 MHz ^{13}C NMR spectrum of G1-Aldehyde in $CDCl_3$.

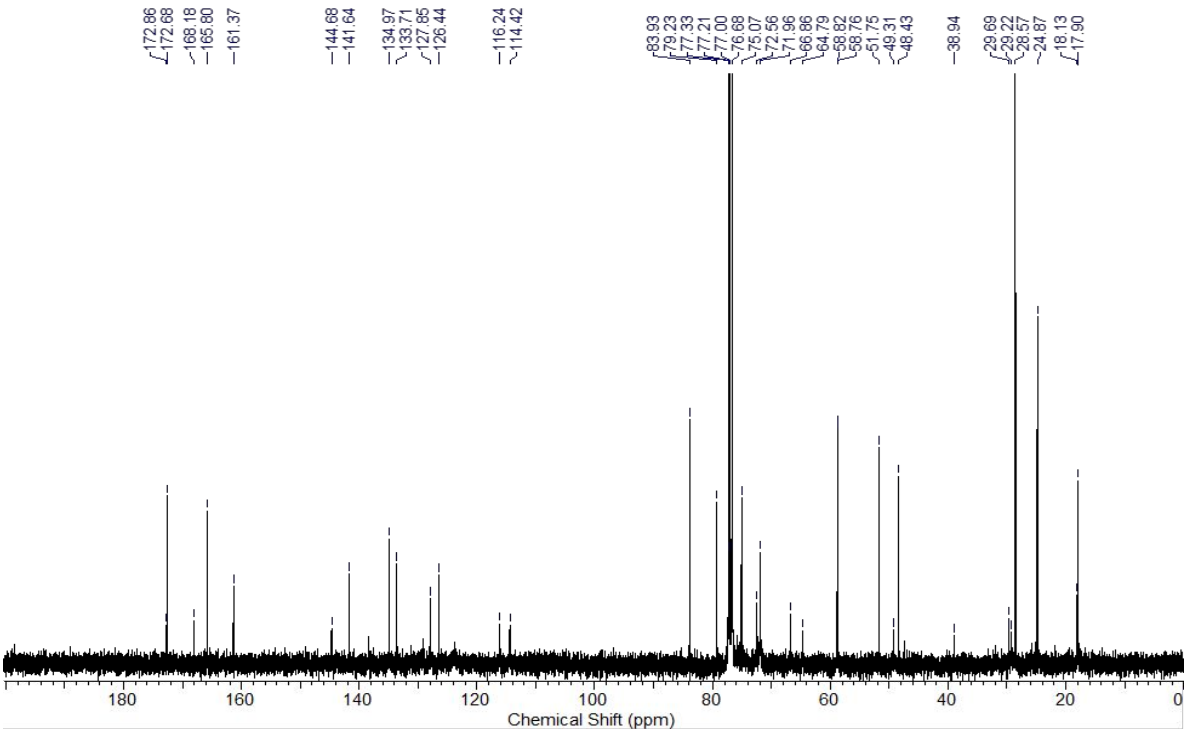

Figure S18: 400 MHz ^{13}C NMR spectrum of G1.5-Alkyne in $CDCl_3$.

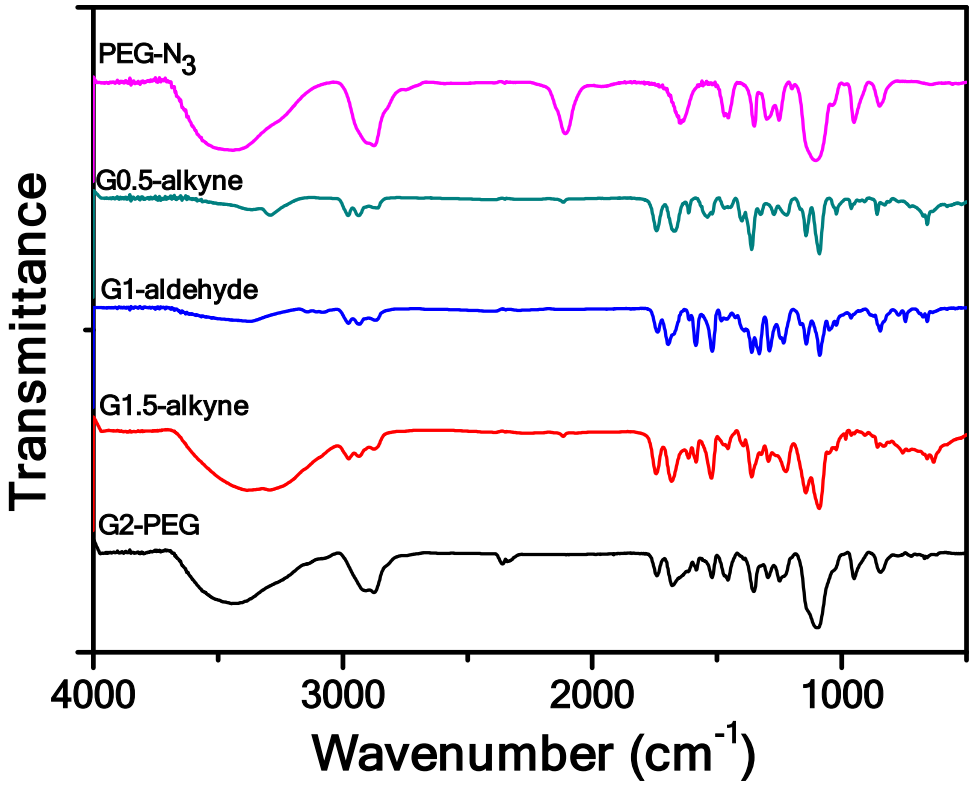

Figure S19: IR spectra for PEG azide, G0.5 alkyne, G1 aldehyde, G1.5 alkyne and G2-PEG.

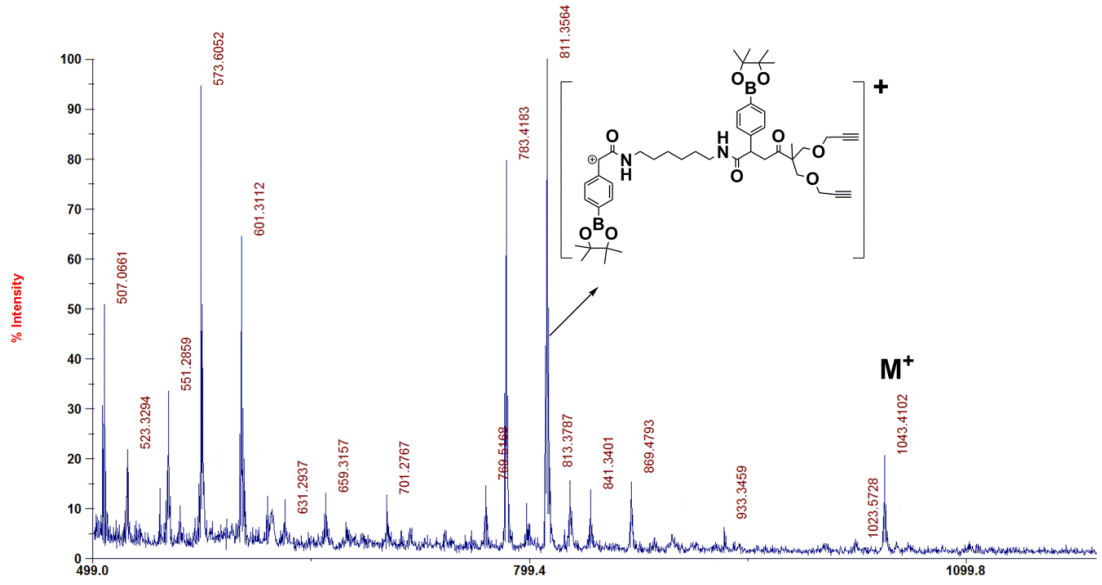

Figure S20: MALDI-TOF spectrum for G0.5-alkyne.

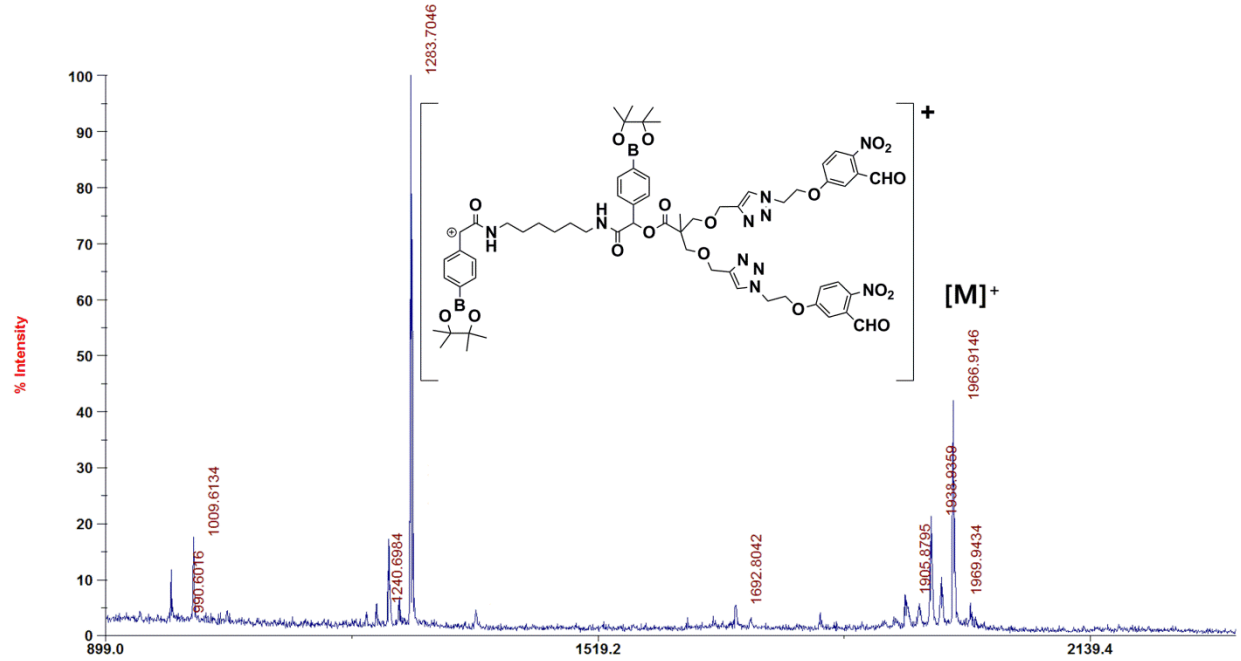

Figure S21: MALDI-TOF spectrum for G1-aldehyde.

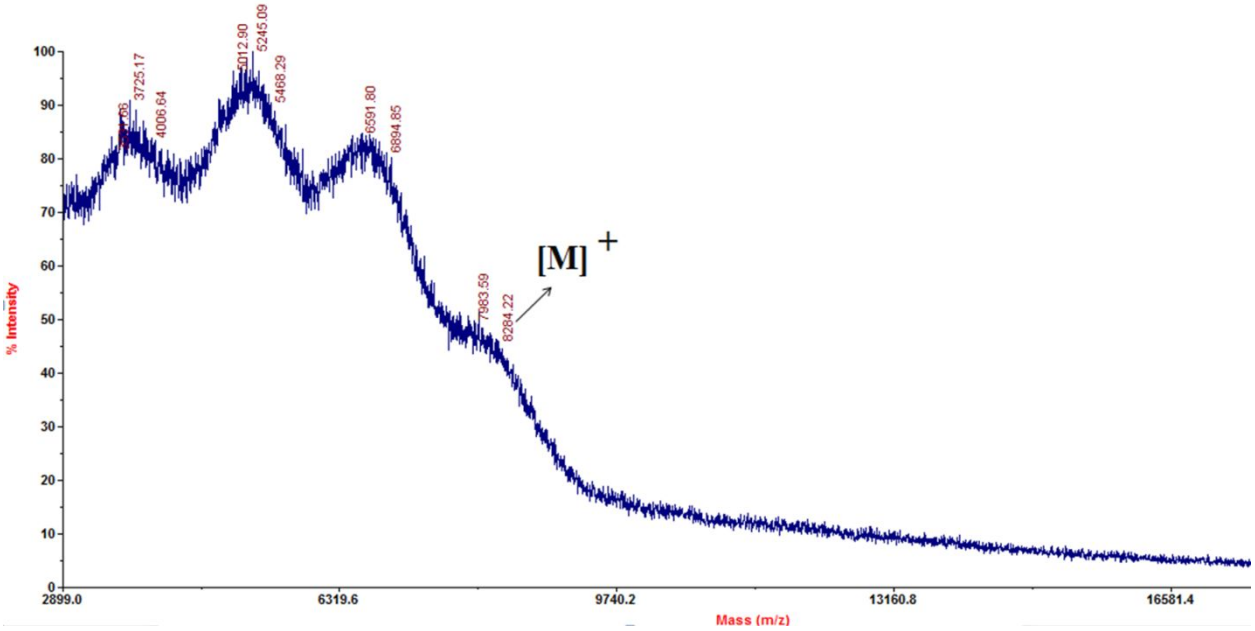

Figure S22: MALDI-TOF spectrum for G2-PEG.

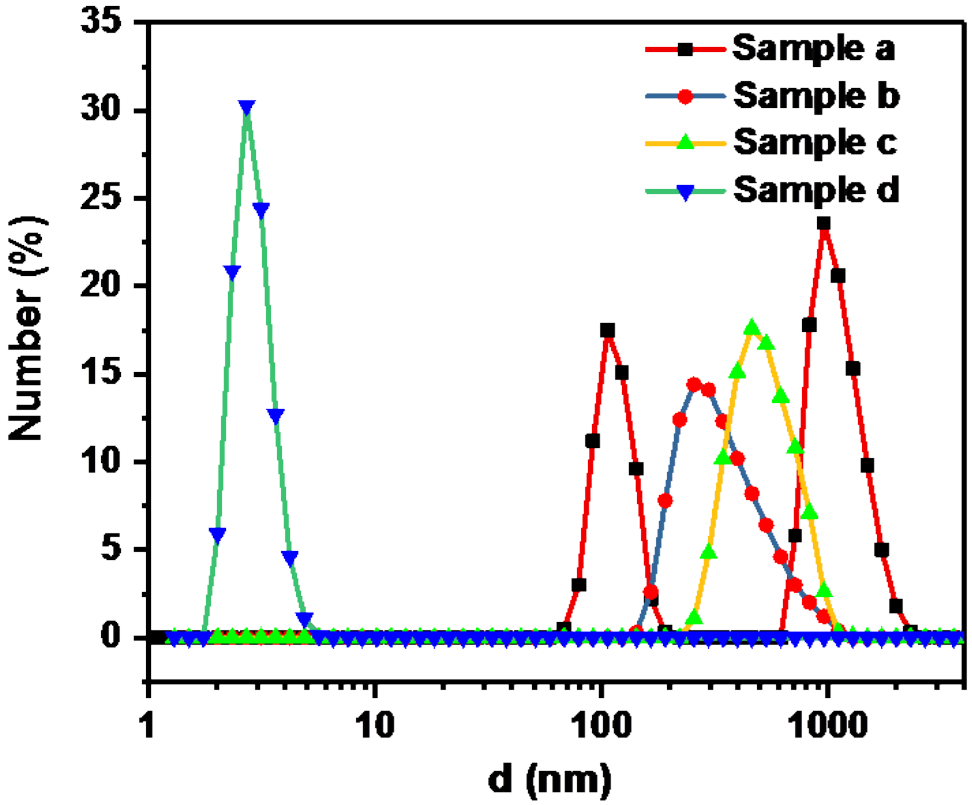

Figure S23: DLS size distribution curve for 0.5 wt. % G2-PEG dendrimer at sample a) water/DMF (9/1 *v/v*) prepared by stirring at room temperature, Sample b) water/DMF (7/3 *v/v*) annealed at 80 ºC, Sample c) water/DMF (5/5 *v/v*) annealed at 80 ºC, Sample d) in DMF

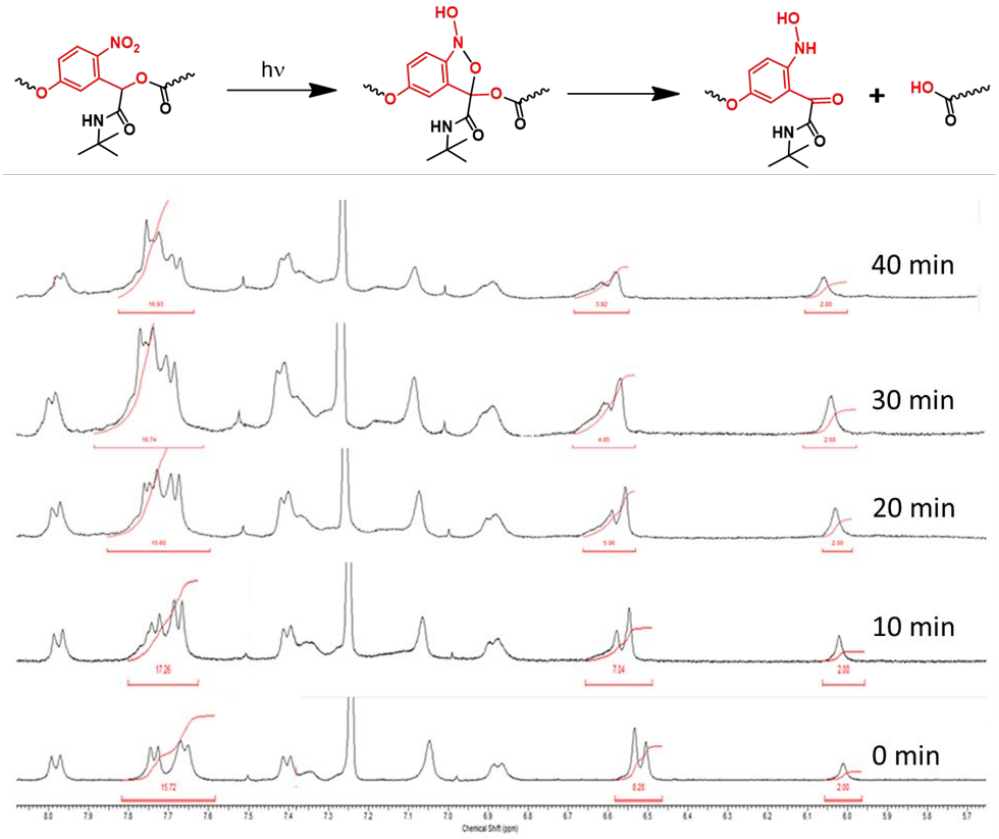

Figure S24: Time dependent UV-responsive degradation of dendrimer followed by 400 MHz ^{1}H NMR spectroscopy.