Supporting information for

Controlled Micellar Disassembly of Photo- and pH-cleavable Linear-Dendritic Block Copolymers

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Synthesis:

ONB-acetonide-bisMPAG1-alkyne (1): 5-propargylether-2-nitrobenzyl alcohol (0.2g, 0.96 mmol), bis-MPA anhydride (0.382g, 1.15 mmol), DMAP (0.017g, 0.013 mmol) and pyridine (155µl, 1.9 mmol) were added to dry CH_2Cl_2 in a reaction flask under argon flow and reaction mixture was stirred at room temperature for 15 h. After completion of the reaction excess anhydride was quenched with addition of 2 ml of water under vigorous stirring, followed of dilution with 300 ml of CH_2Cl_2 and the solution was washed with 10 % of $NaHSO_4$ (3 × 500 ml), and 10 % of Na_2CO_3 (3×500 ml). The organic phase was dried over Na_2SO_4, concentrated and purified by column chromatography on silica gel, eluting with hexane and gradually increasing the polarity to ethyl acetate and pet ether (30:70) to give white colour solid. Yield: 92%. ^{1}H NMR ($CDCl_3$, 200 MHz): 1.22(s, 3H), 1.41(s, 3H), 1.48 (s, 3H), 2.57(t, J=2Hz, 1H), 3.71(d, J=12Hz, 2H), 4.29(d, J=12Hz, 2H), 4.80(d, J=4Hz, 2H), 5.67(s, 2H), 6.98(dd, 4Hz, 1H), 7.29(s, 1H), 8.20(d, J=8Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 50MHz): 18.40, 21.07, 26.22, 29.66, 42.33, 56.23, 61.65, 63.40, 66.19, 79.15, 98.29, 114.18, 127.81, 135.78, 140.57, 161.75, 173.56 ppm.

ONB-bisMPAG1-alkyne (2): ONB-bis-MPAG1 alkyne (3.5g, 9.6mmol) was dissolved in 200 ml MeOH and 30ml DCM. Concentrated sulphuric acid (1.7ml) was added drop wise at room temperature and then stirred the reaction mixture additional 2 hrs in the dark. The reaction was monitored by the TLC after completion of the reaction the reaction mixture was concentrated to one-third of its initial volume. Ethyl acetate was added to the reaction mixture and washed with 1M Na_2CO_3 and brine solution. The organic layer was dried over Na_2SO_4 and evaporated the ethyl acetate to get yellow colour solid without any further purification. Yield 85%. ^{1}H NMR (CDCl3, 200 MHz): 1.15(s, 3H), 2.58(t, J=2Hz, 1H), 3.78(d, J=10Hz, 2H), 4.03(d, J=10Hz, 2H), 4.84 (d, J=2Hz, 2H), 5.69(s, 2H), 6.98(dd, 2Hz, 1H), 7.29(s, 1H), 8.19(d, J=8Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 50MHz): 17.25, 49.53, 56.34, 61.56, 63.72, 64.80, 68.96, 105.25, 113.40, 114.87, 127.86, 135.57, 161.87 ppm.

ONB-acetonide-bisMPAG2-alkyne (3) : ONB-bis-MPAG1 alkyne (2OH) (2.7g, 8.3mmol), bis-MPA anhydride (6.8g, 20.8 mmol), DMAP (0.305g, 2.5 mmol) and pyridine (1.68ml, 20.8 mmol) were added to dry CH_2Cl_2 in a reaction flask under argon flow and reaction mixture was stirred at room temperature for 15 h. After completion of the reaction excess anhydride was quenched with addition of 2 ml of water under vigorous stirring, followed of dilution with 300 ml of CH_2Cl_2 and the solution was washed with 10 % of $NaHSO_4$ (3 × 500 ml), and 10 % of Na_2CO_3 (3×500 ml). The organic phase was dried over Na_2SO_4, concentrated and purified by column chromatography on silica gel, eluting with hexane and gradually increasing the polarity to ethyl acetate and pet ether (30:70) to give yellow colour solid (4.9 g). Yield 92%. ^{1}H NMR ($CDCl_3$, 200 MHz): 1.13(s, 6H), 1.33(s, 6H), 1.39 (s, 3H), 1.41(s, 6H), 2.64(t, J=2Hz, 1H), 3.59(d, J=12Hz, 4H), 4.12(d, J=12Hz, 4H), 4.41(s, 4H), 4.82(d, J=2Hz, 2H), 5.59(s, 2H), 7.00(dd, 4Hz, 1H), 7.17(d, J=4Hz, 1H), 8.20(d, J=8Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$, 50MHz): 18.39, 19.05, 22.37, 26.02, 42.72, 47.73, 56.92, 64.65, 65.91, 66.62, 98.75, 114.72, 115.22, 128.55, 135.36, 141.41, 162.21, 172.47, 174.27 ppm.

ONB-bisMPAG2-alkyne (4): ONB-bis-MPAG2 alkyne (4.4g, 6.92mmol) was dissolved in 300 mL MeOH and 30ml DCM. Concentrated sulphuric acid (7ml) was added drop wise at room temperature and then stirred the reaction mixture additional 2 hrs in the dark. The reaction was monitored by the TLC after completion of the reaction the reaction mixture was concentrated to one-third of its initial volume. Ethyl acetate was added to the

reaction mixture and washed with 1M Na_2CO_3 and brine solution. The organic layer was dried over Na_2SO_4 and evaporated the ethyl acetate to get yellow colour solid without any further purification. Yield 85%. ^{1}H NMR (CD_3OD, 200 MHz): 1.12(s, 6H), 1.37(s, 3H), 3.09(t, J=2Hz, 1H), 3.55-3.69(m, 8H), 4.35(m, 4H), 4.93 (d, J=2Hz, 2H), 5.55(s, 2H), 7.09(dd, 2Hz, 1H), 7.27(s, 1H), 8.18(d, J=8Hz, 1H) ppm.

ONB-C9-bisMPAG2-alkyne (5): ONB-bis-MPAG2 4(OH) (6) (1g, 1.8 mmol), DMAP (0.021g, 0.17 mmol) was dissolved in dry DCM and added triethylamine (1.5 ml, 10.7 mmol) at 0˚C. Decanoyl chloride (2.06ml, 10.7mmol) was added drop by drop for 15 min and allowed to stir for 12 h. After completion, reaction mixture was washed with sodium bicarbonate and brine solution. Crude product was purified by column chromatography by eluting with 20% ethyl acetate and pet ether to obtain yellow colour liquid. Yield 75%. ^{1}H NMR ($CDCl_3$ 200 MHz) δ: 0.88(t, J=6Hz, 12H), 1.12-1.44(m, 54H), 1.48-1.75(m, 11H), 2.28(t, J=6, 8H), 2.62(t, J=2Hz, 1H), 4.14-4.40(m, 12H), 4.84(d, J=2Hz, 2H), 5.56(s, 2H), 7.02(dd, J=2Hz, 1H), 7.15(d, J=2Hz, 1H), 8.19(d, J=10Hz, 1H).^{13}C NMR (CDCl3, 50MHz) 14.13, 17.77, 22.68, 24.87, 29.29, 31.88, 34.04, 46.44, 62.76, 65.01, 65.65, 114.14, 115.28, 127.99, 134.34, 161.50, 172.14, 173.25. MALDI-TOF MS: Calcd. 1171.74 Found 1194.77 for $[M+Na]^+$

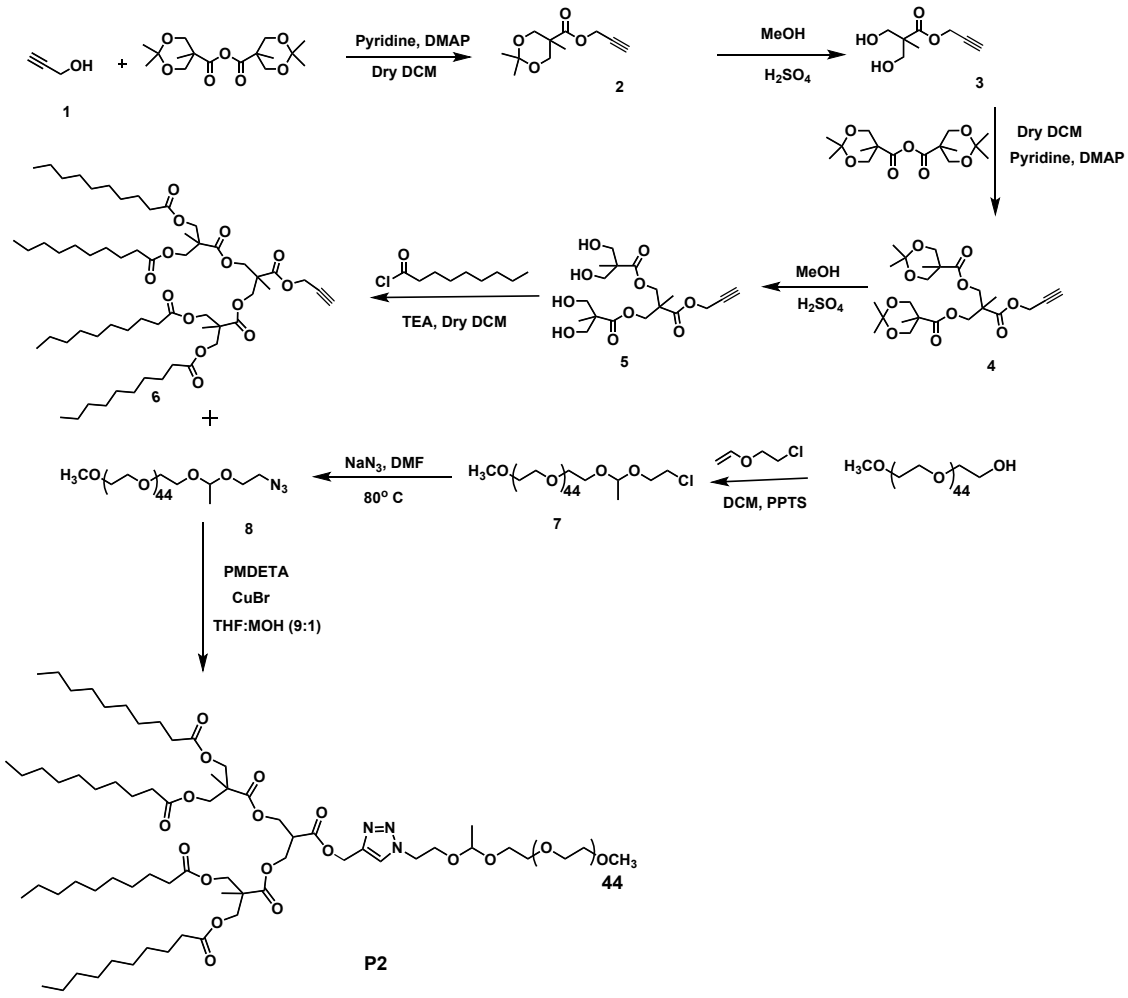
PEG2K-*Ace*-Cl (6): Polyethylene glycol monomethylether (M_n = 2000 g/mol) (5g, 2.5 mmol) and pyridine p-toluene sulphonate (PPTS) (0.125g, 0.49mmol) were dried by azeotropic distillation with toluene just before start the reaction. Then the reaction mixture was dissolved in the 50 mL dry DCM and chloro ethyl vinyl ether (CEVE) (2.56g, 25mmol)was added by dissolving in 10 ml dry DCM drop wise over 15 min under argon atmosphere at 0^{o}C. After one hour 20 ml of 5Wt% Na_2CO_3 solution was added to quench the reaction and to avoid the cleavage of the acetal linkage. Then the reaction mixture was diluted with 100ml DCM and washed with brine solution. Finally the reaction mixture was precipitated into cold hexane and the filtrate was dried under vaccum. ^{1}H NMR ($CDCl_3$ 200 MHz) δ: 1.31(d, J=6Hz, 3H), 3.36(s, 3H), 3.63(m, 174H), 4.80(q, J=6Hz, 1H) ppm.

PEG_{2K}-*Ace*-N_3 (7): PEG_{2K}-*Ace*-Cl (8) (5g, 2.3 mmol), NaN_3 (1.54g, 23.6 mmol) were dissolved in DMF and stirred at 60^{o}C for 24hr. After completion of the reaction DMF was removed under reduced pressure. The crude product was precipitated in cold diethyl ether, the obtained white product was dried under vacuum. Yield 90%. ^{1}H NMR ($CDCl_3$ 200 MHz) δ: 1.31(d, J=6Hz, 3H), 3.36(s, 3H), 3.48-3.77(m, 178H), 4.79(q, J=6Hz, 1H) ppm.^{13}C NMR ($CDCl_3$, 100MHz) 19.37, 43.23, 64.03, 64.96, 70.49, 99.73, 125.21, 128.14, 128.94 ppm. MALDI-TOF MS: Calcd. 2106.35 Found 2106.2 for [M+].

Click reaction between ONB-C9-bisMPAG2-alkyne dendron and PEG_{2K}-*Ace*-N_3 (P1):

Alkyne functionalised ONB-bis-MPAG2 $(C10)_4$ dendron (0.7g, 0.4 mmol) and PEG_{2K}-*Ace*-N_3 (0.7g 0.33 mmol) were dissolved in dry THF, and resultant mixture was degassed for 15 min. CuBr (0.048g, 0.033 mmol), and PMDETA (69 µl, 0.33 mmol) were then added and allowed to stir for 24 hr under argon atmosphere. After completion of the reaction, the reaction mixture was passed through the neutral alumina to remove the copper salts and finally precipitated in the cold hexane to remove the excess dendron and final click product was dried under vacuum. Yield 75%. ^{1}H NMR ($CDCl_3$ 200 MHz) δ: 0.88(t, J=8Hz, 12H), 1.14-1.37(m, 60H), 1.48-

1.67(m, 8H), 2.28(t, J=8Hz, 8H), 3.38(s, 3H), 3.49-3.70(m, 174H), 3.99(t, J=4Hz, 2H), 4.18(m, 8H), 4.32(m, 4H), 4.57(t, J=4Hz, 2H), 4.72(q, J=6Hz, 1H), 5.52(s, 2H), 7.07(dd, J=2Hz, 1H), 7.17(d, J=2Hz, 1H), 7.85(s, 1H), 8.16(d, J=8Hz, 1H) ppm.^{13}C NMR (CDCl3, 50MHz) 14.06, 17.70, 19.35, 22.61, 24.78, 29.21, 31.80, 33.95, 46.33, 46.84, 58.99, 63.05, 64.91, 70.50, 99.93, 108.59, 120.58, 124.50, 142.23, 162.28, 172.06, 173.18 ppm. MALDI-TOF MS: Calcd. 3277.99 Found 3277.76 for [M+].



Scheme S1. Synthesis of polymer P2.

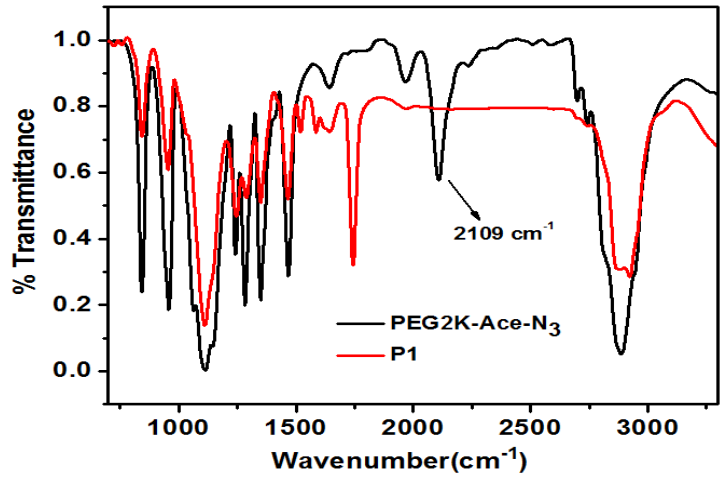


Figure S1. FT-IR spectra of linear-dendritic copolymer after the click reaction.

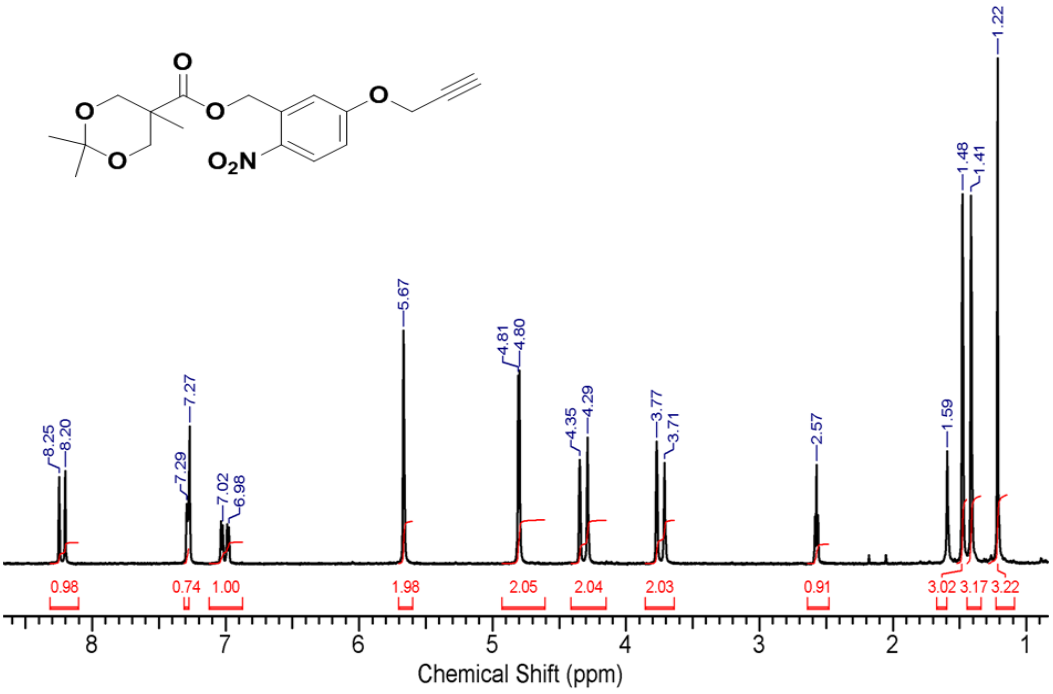


Figure S2. 200 MHz ^{1}H NMR spectrum of ONB-acetonide-bisMPAG1-alkyne in $CDCl_3$.

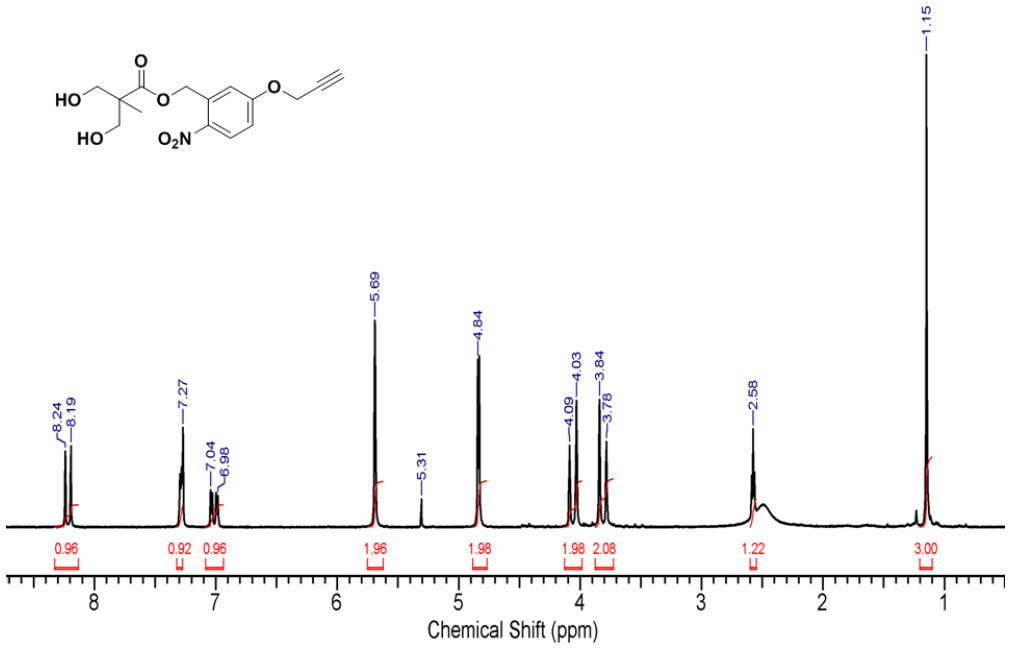


Figure S3. 200 MHz ^{1}H NMR spectrum of ONB-bisMPAG1-alkyne in $CDCl_3$.

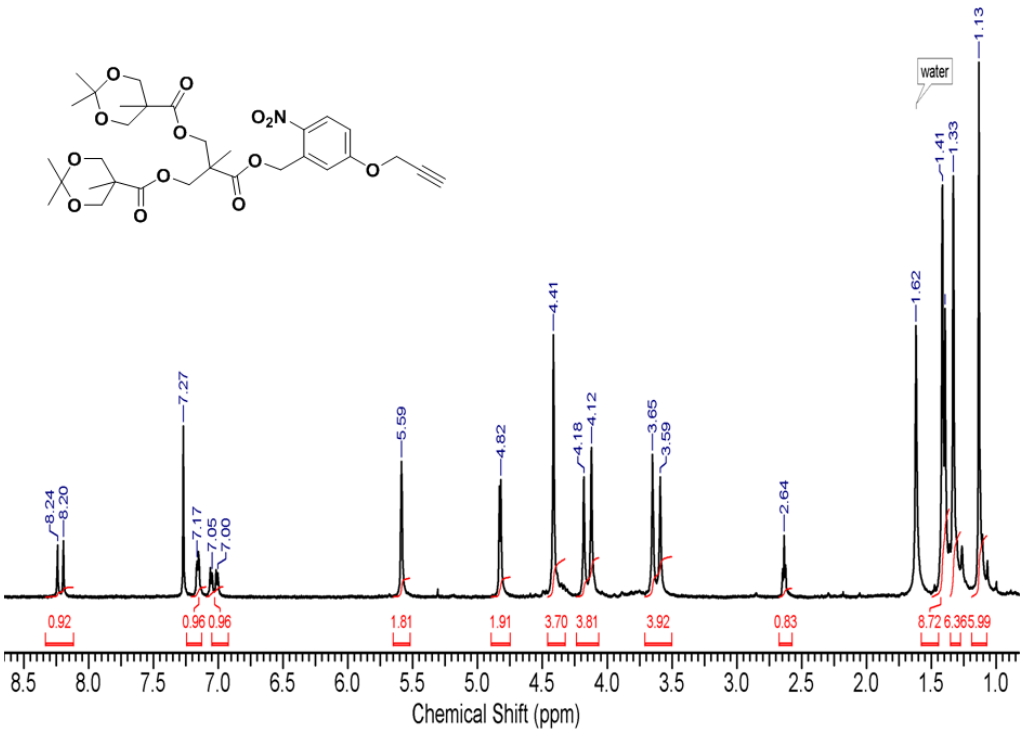


Figure S4. 200 MHz ^{1}H NMR spectrum of ONB-acetonide-bisMPAG2-alkyne in $CDCl_3$.

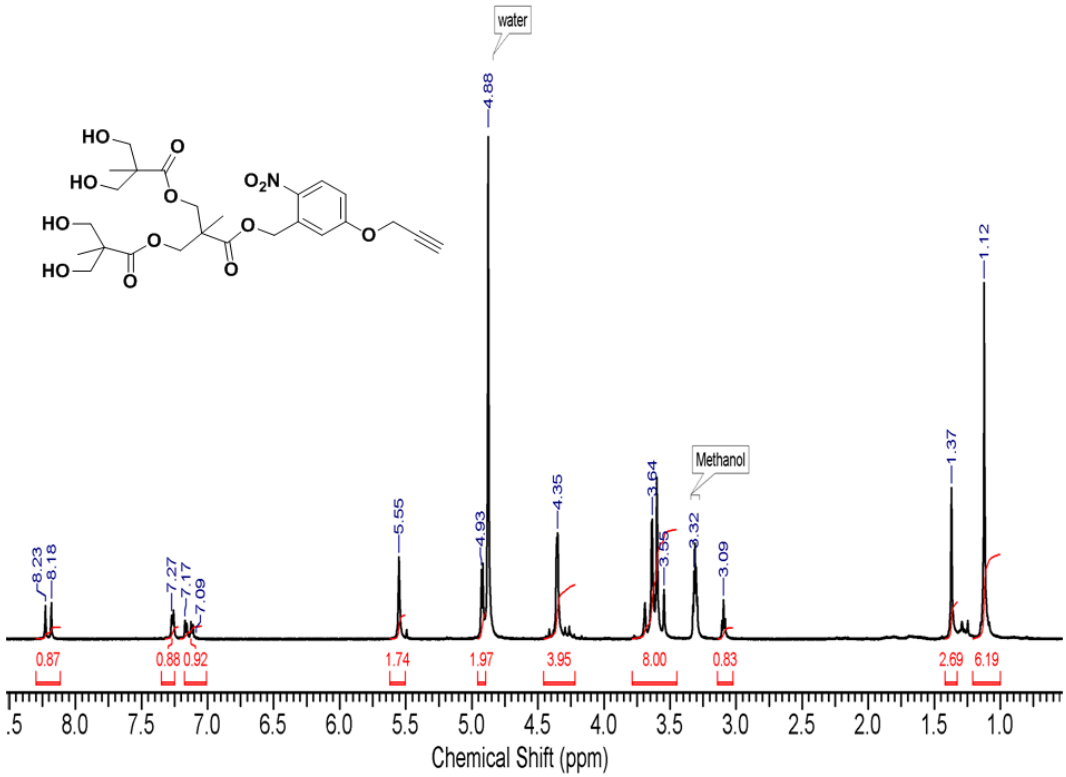


Figure S5. 200 MHz ^{1}H NMR spectrum of ONB-bisMPAG2-alkyne in $CDCl_3$.

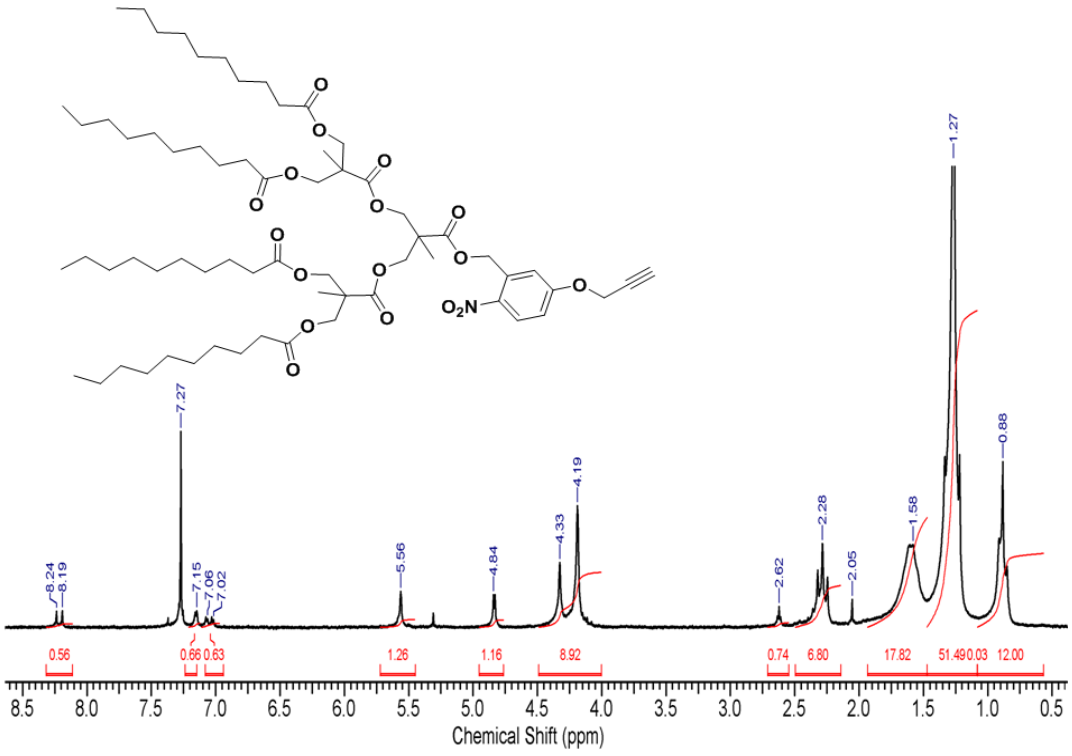


Figure S6. 200 MHz ^{1}H NMR spectrum of ONB-C9-bisMPAG2-alkyne in $CDCl_3$.

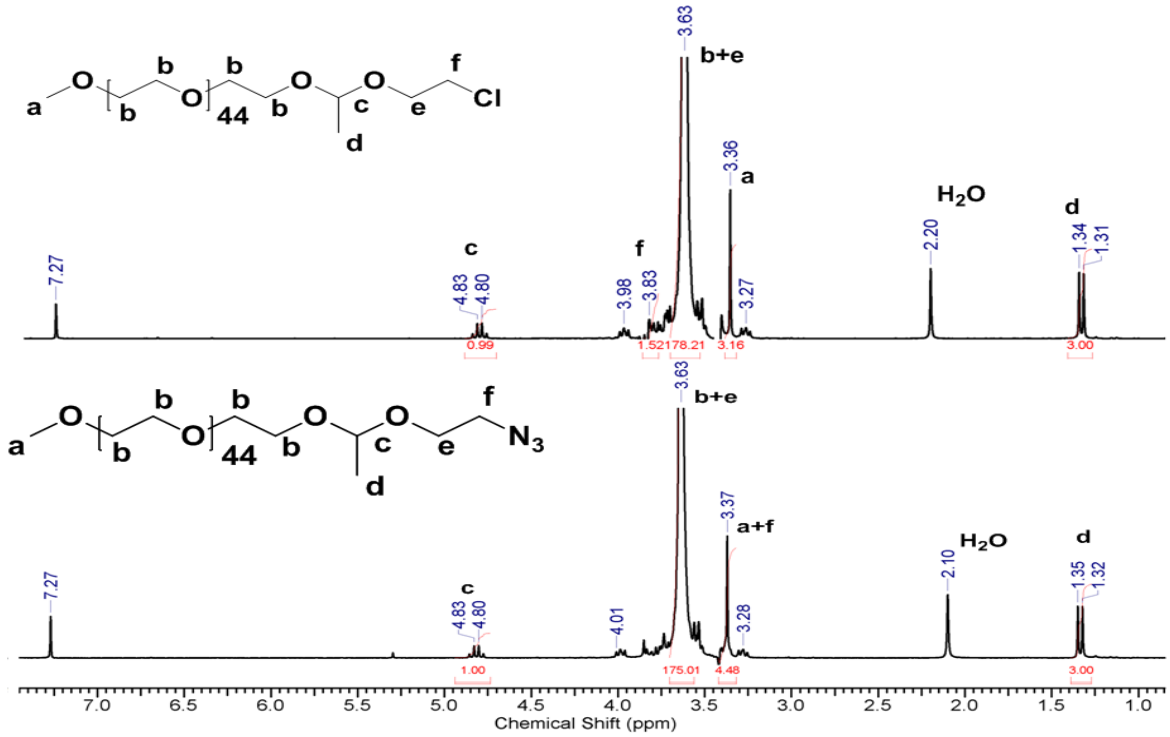


Figure S7. 200 MHz ^{1}H NMR spectrum of PEG_{2K}-*Ace*-N_3 (upper) and PEG_{2K}-*Ace*-N_3 in $CDCl_3$.

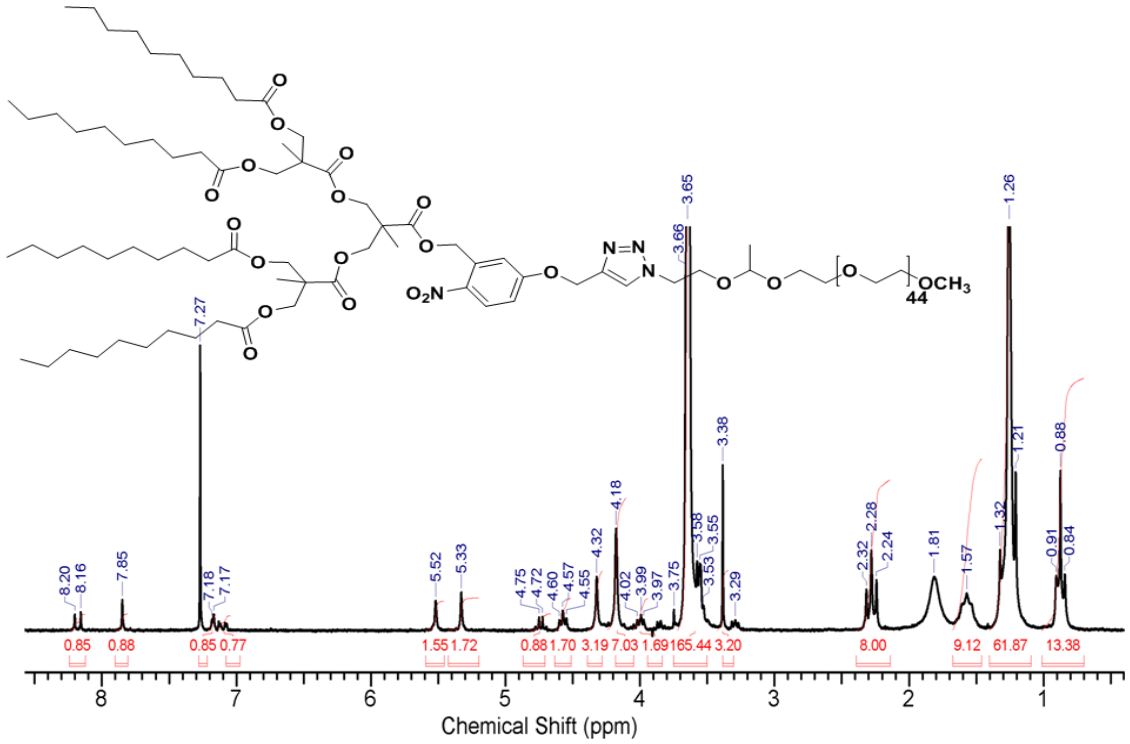


Figure S8. 200 MHz ^{1}H NMR spectrum of ONB-C9-bisMPAG2-*Ace*-PEG_{2K} in $CDCl_3$.

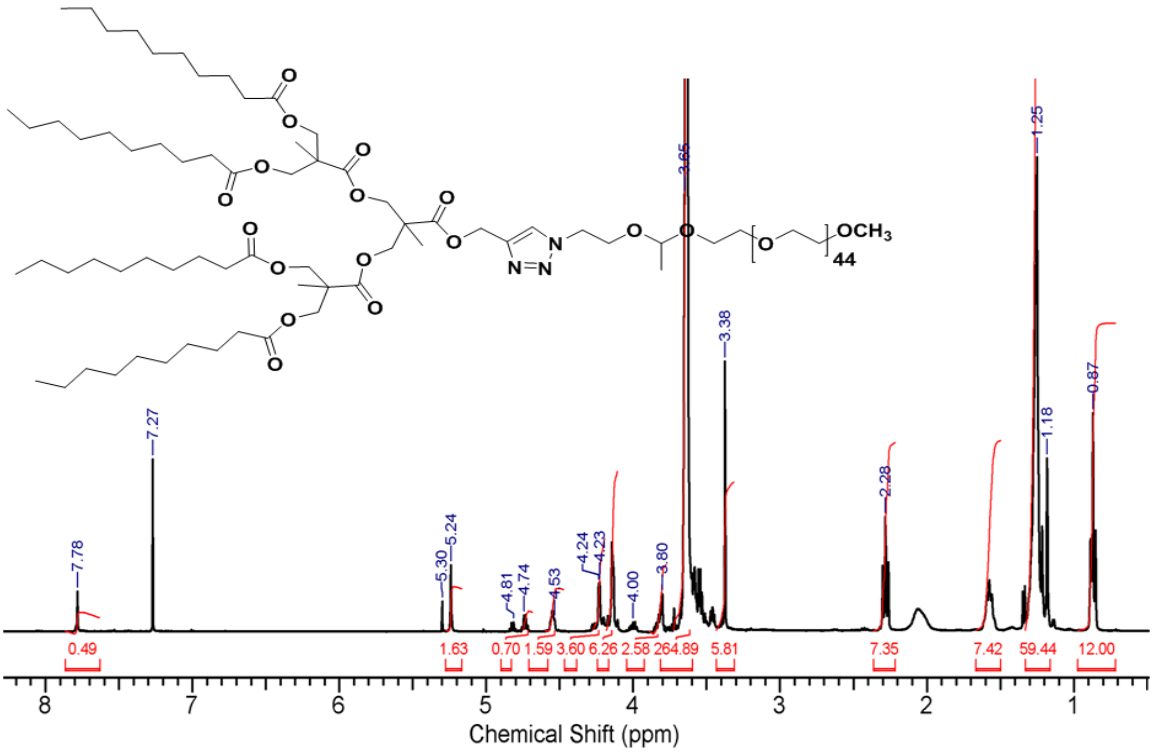


Figure S9. 200 MHz ^{1}H NMR spectrum of C9-BisMPAG2-*Ace*-PEG$_{2K}$ in $CDCl_3$.

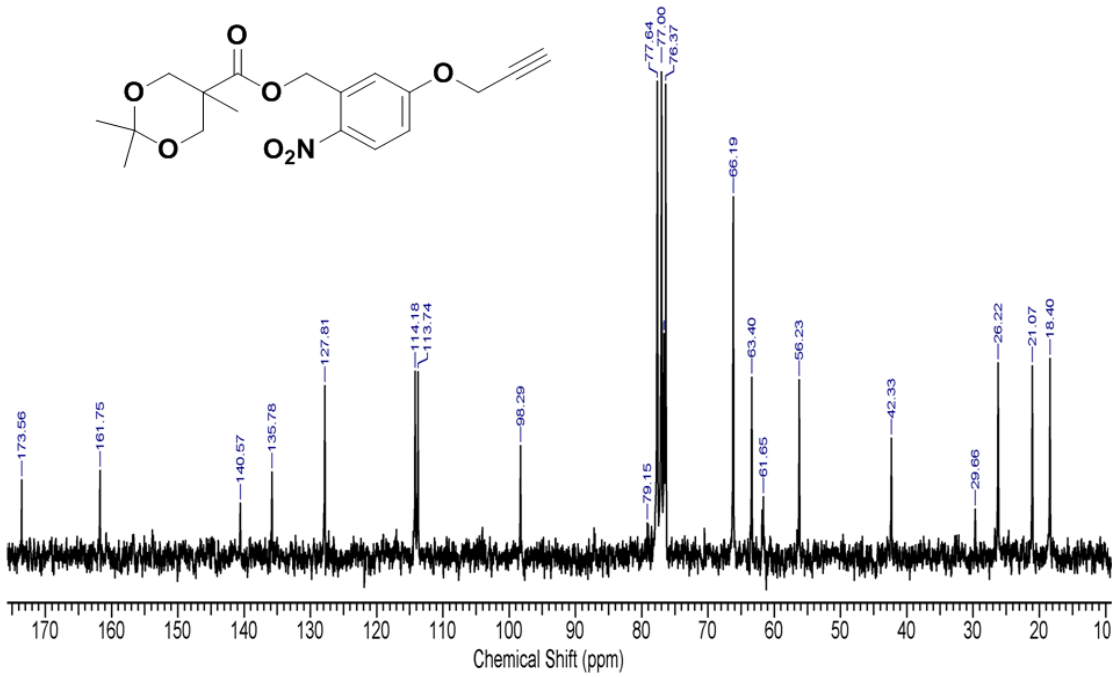


Figure S10. 50 MHz ^{13}C NMR spectrum of ONB-acetonide-bisMPAG1-alkyne in $CDCl_3$.

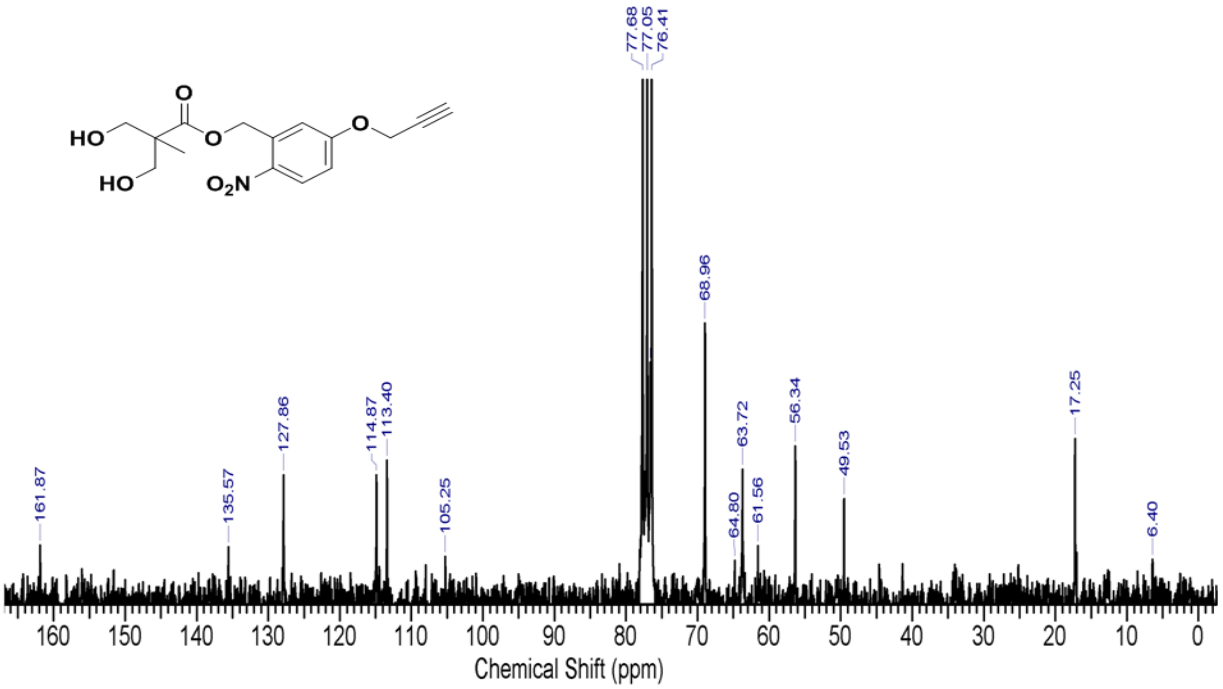


Figure S11. 50 MHz ^{13}C NMR spectrum of ONB-bisMPAG1-alkyne in $CDCl_3$.

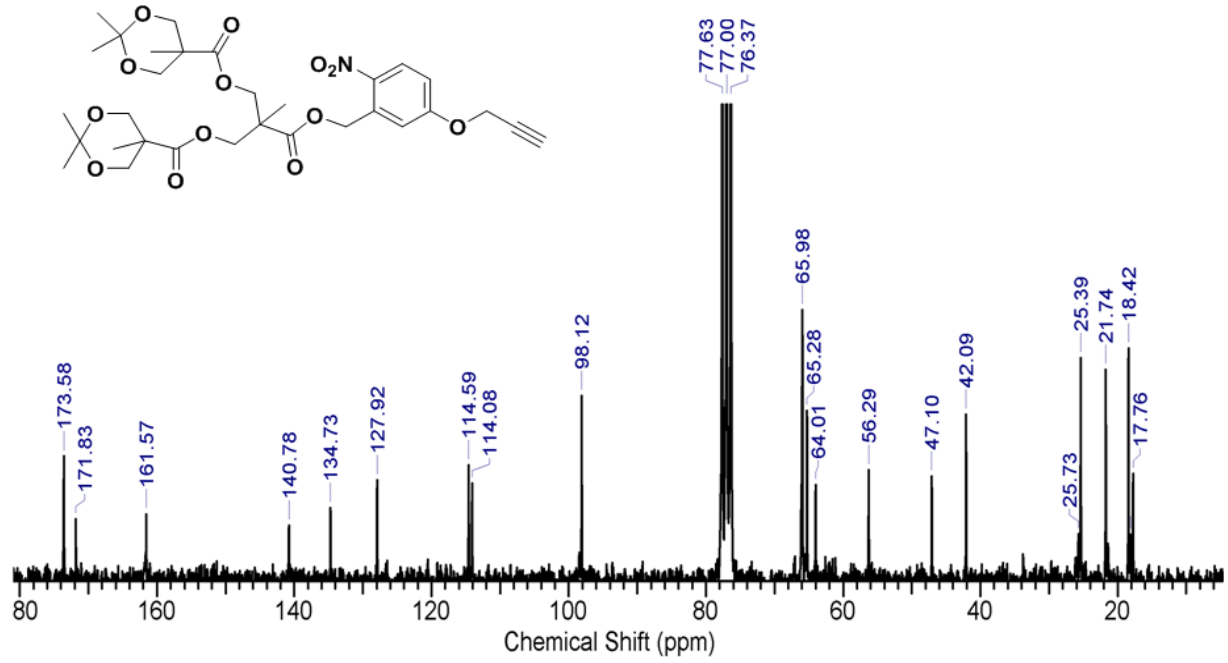


Figure S12. 50 MHz ^{13}C NMR spectrum of ONB-acetonide-bisMPAG2-alkyne in $CDCl_3$.

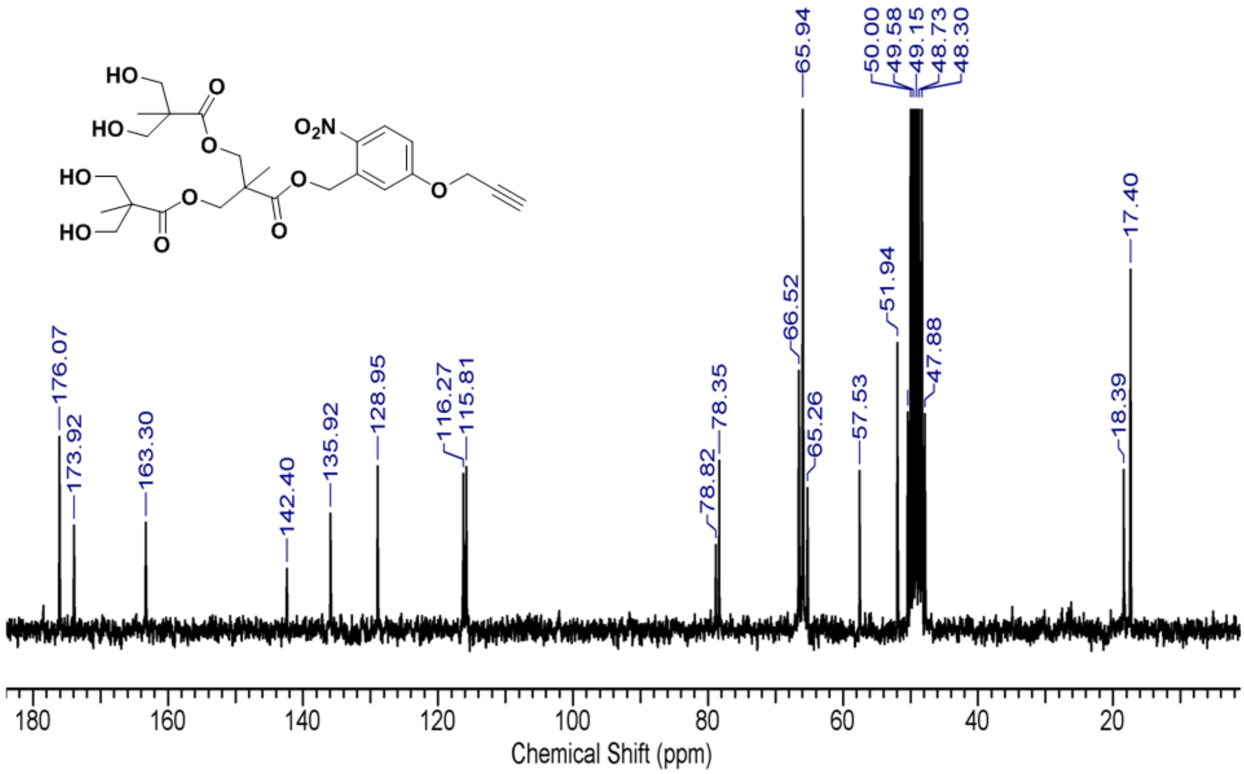


Figure S13. 50 MHz ^{13}C NMR spectrum of ONB-bisMPAG2-alkyne in $CDCl_3$.

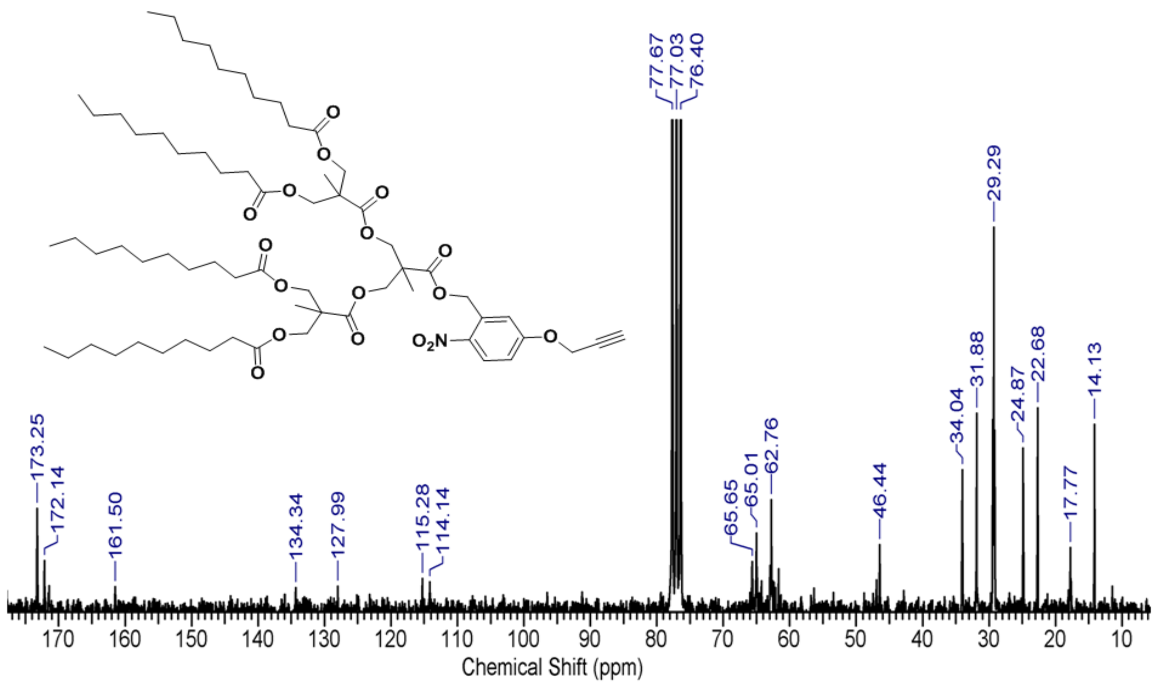


Figure S14. 50 MHz ^{13}C NMR spectrum of ONB-C9-bisMPAG2-alkyne in $CDCl_3$.

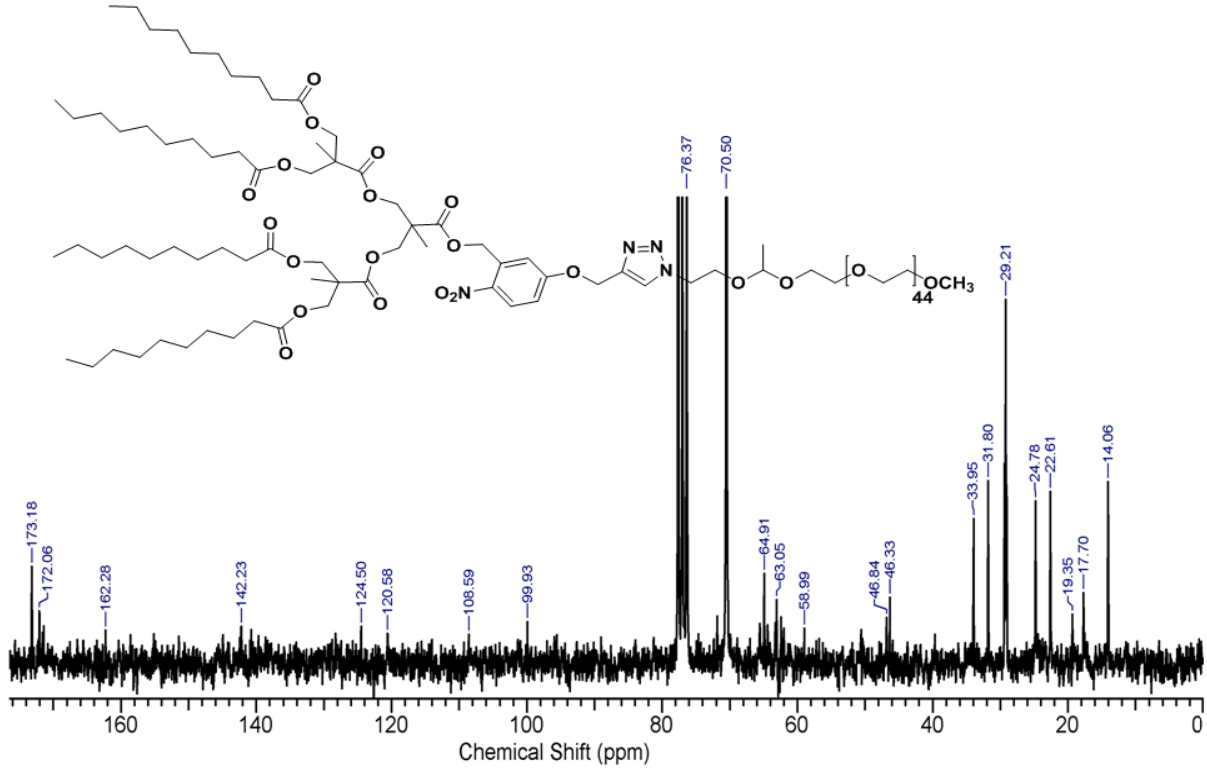


Figure S15. 50 MHz ^{13}C NMR spectrum ONB-C9-bisMPAG2-*Ace*-PEG$_{2K}$ (P1) in $CDCl_3$.

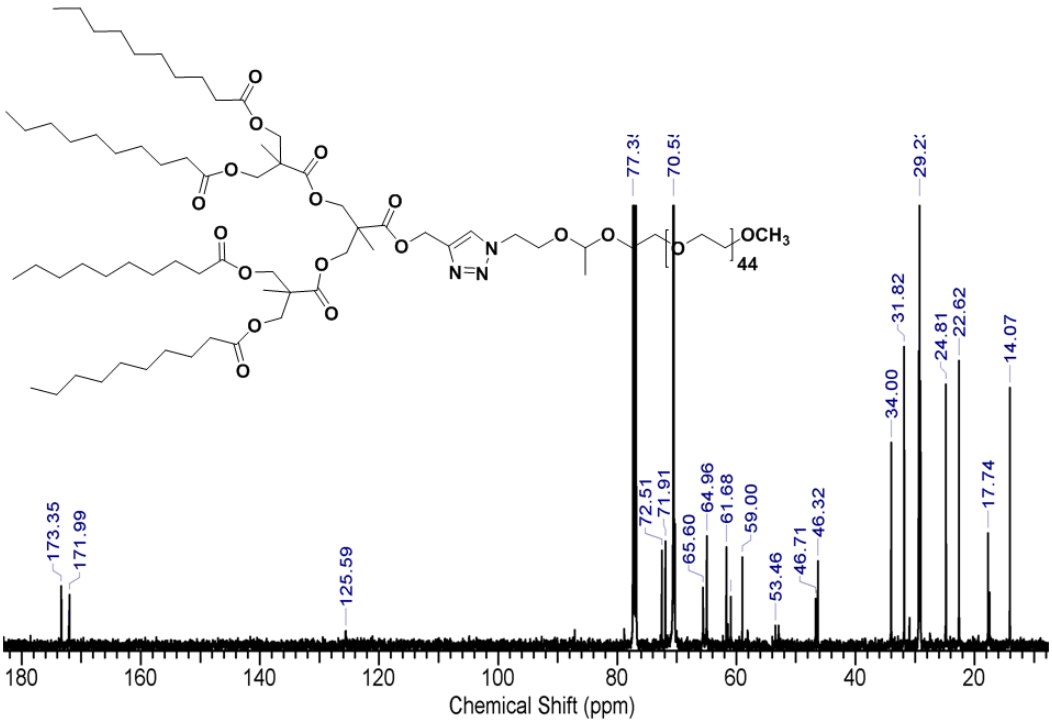


Figure S16. 100 MHz ^{13}C NMR spectrum C9-BisMPAG2-*Ace*-PEG$_{2K}$ (P2) in $CDCl_3$.

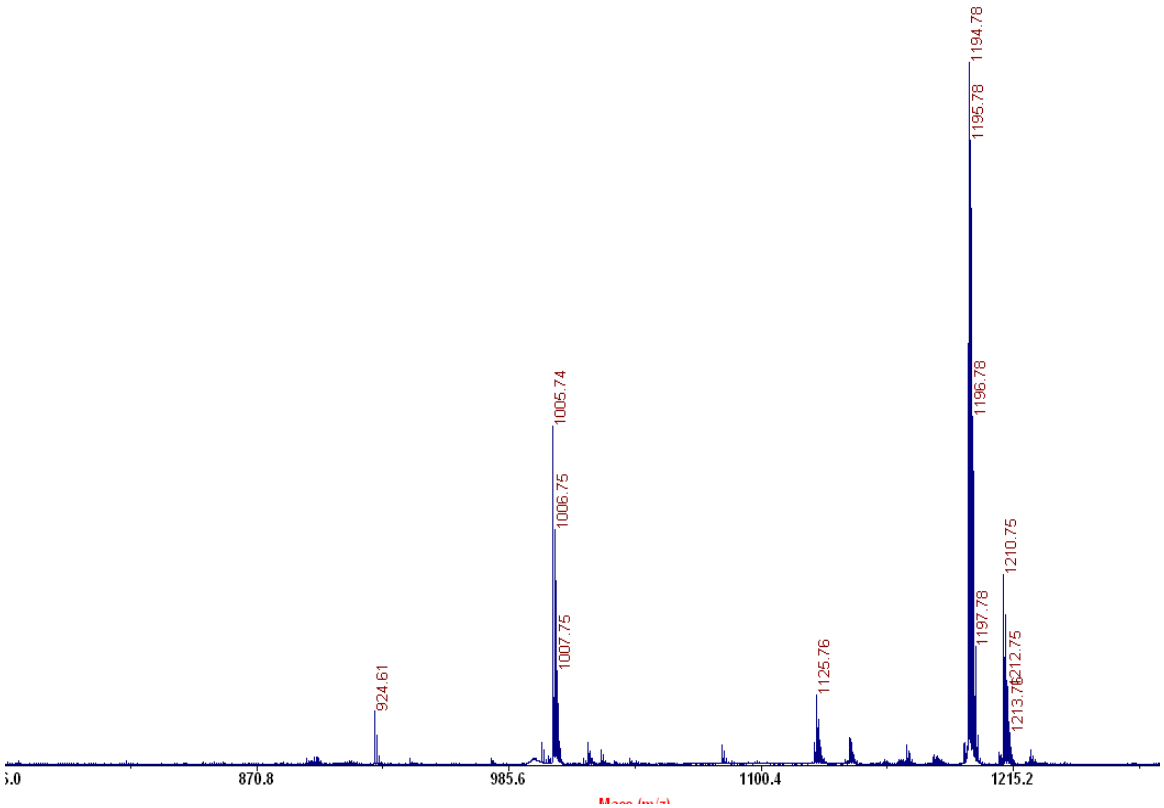


Figure S17. MALDI-TOF spectrum of C9-bisMPAG2-ONB-alkyne.

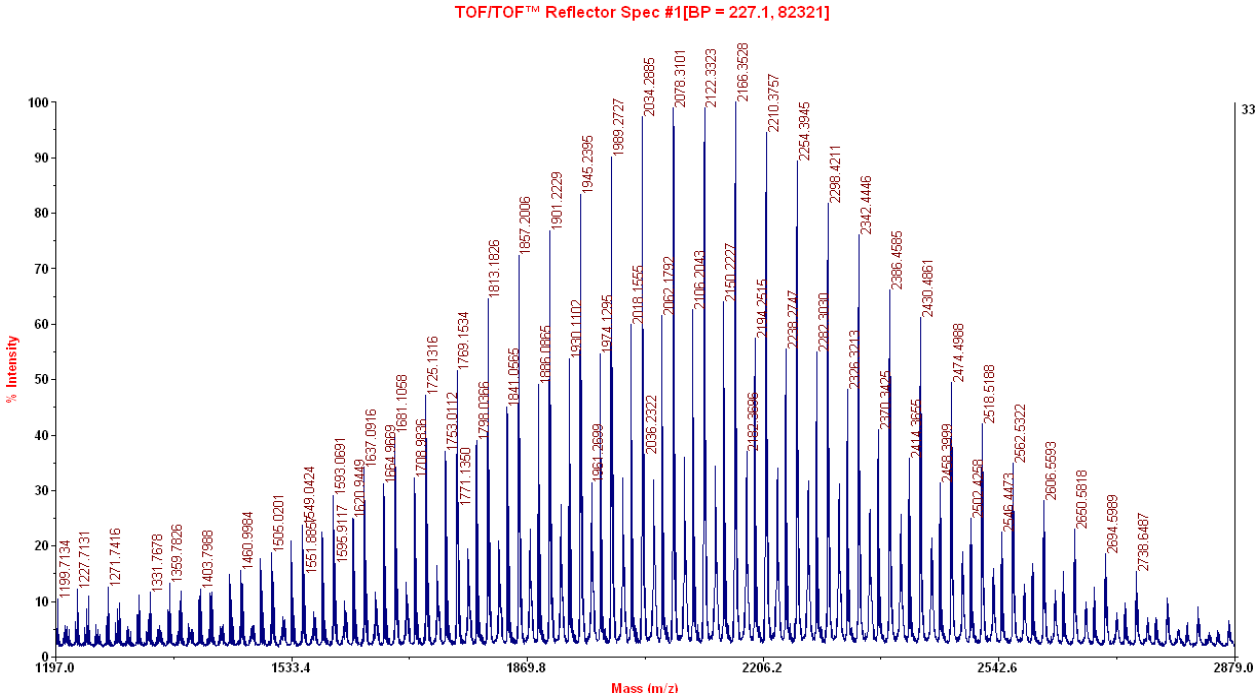


Figure S18. MALDI-TOF spectrum of PEG_{2K}-*Ace*-azide.

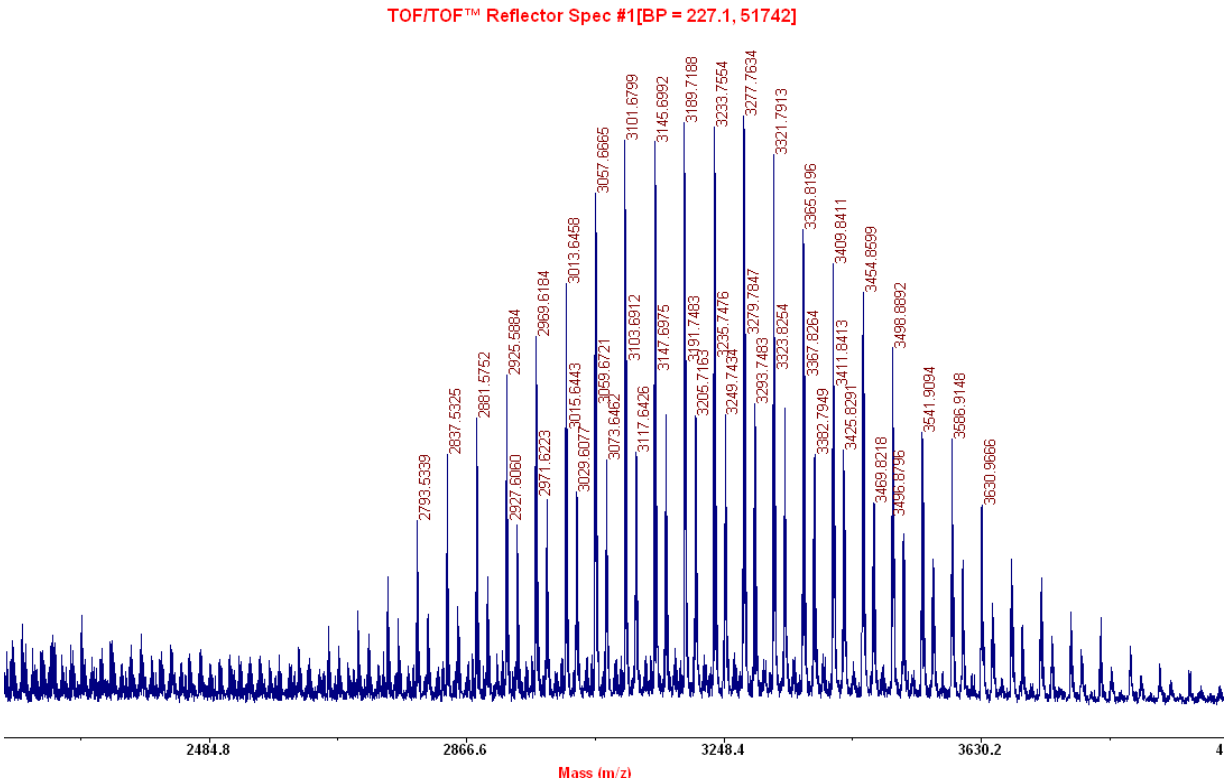


Figure S19. MALDI-TOF spectrum of P1.

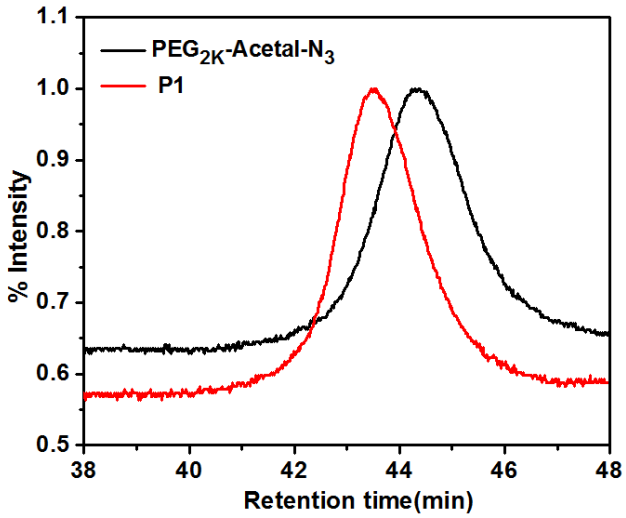


Figure S20. GPC chromatograms of PEG-acetal-N_3 and final linear dendritic copolymer **P1**.

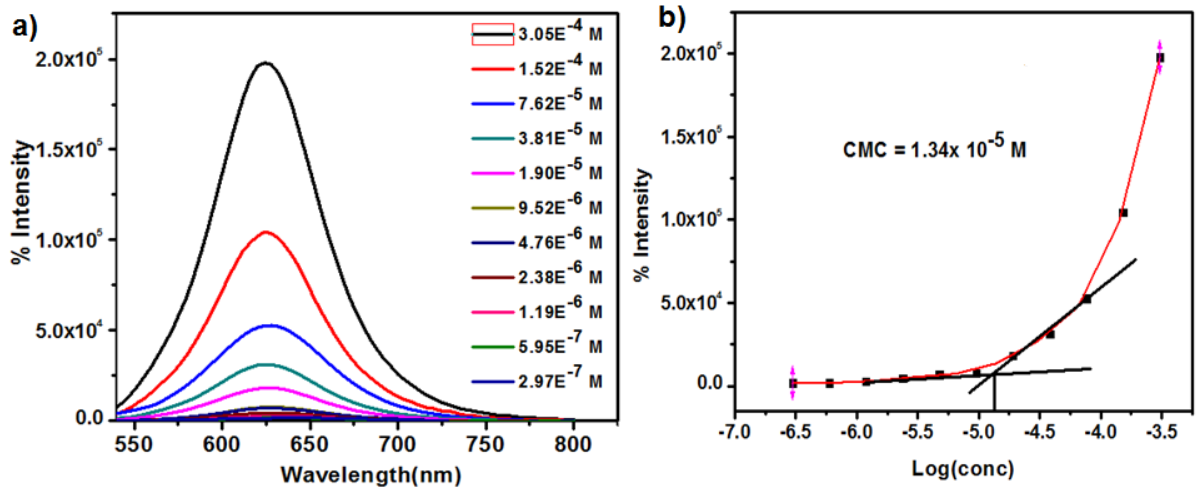


Figure S21. a) Fluorescence emission spectra of Nile red with varying concentration of P1in water and b) plot of emission intensity versus log (conc.) for CMC determination of P1.

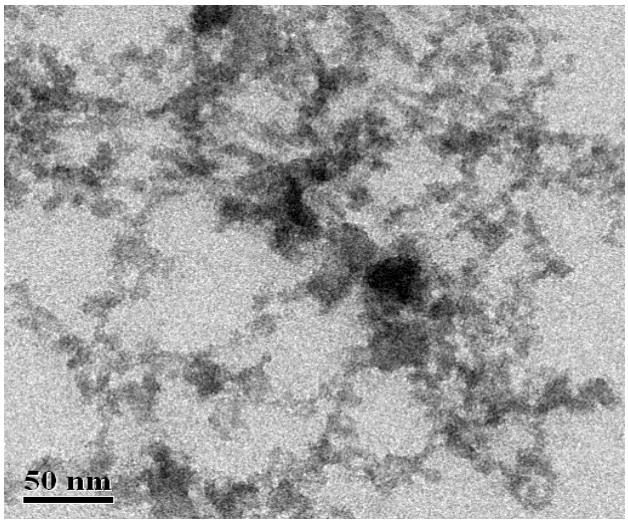


Figure S22. TEM image of P1 (0.1wt % in water) at pH 7.

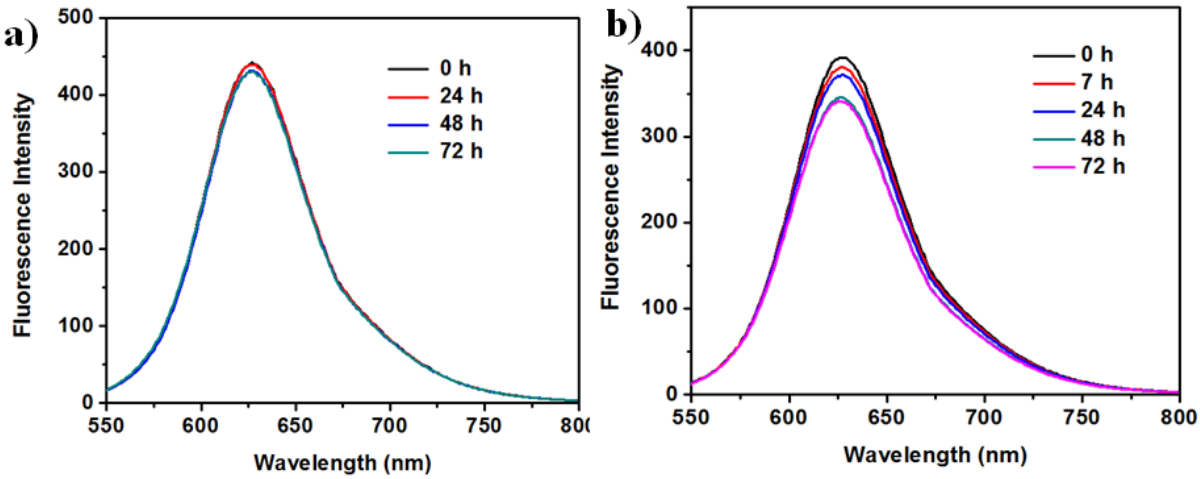


Figure S23. Fluorescence emission spectra of Nile Red in P1 (0.1wt% aqueous solution) at a) pH 7.4 and b) pH 5.0.

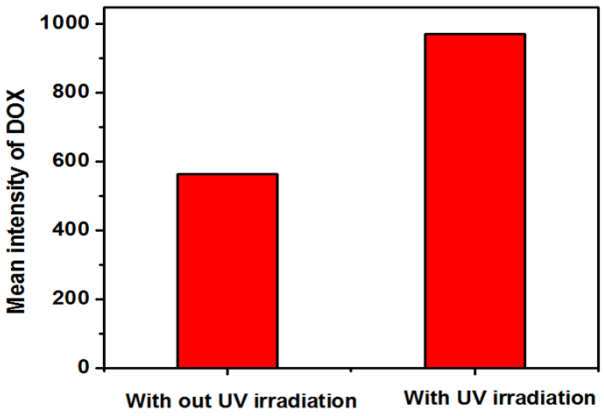
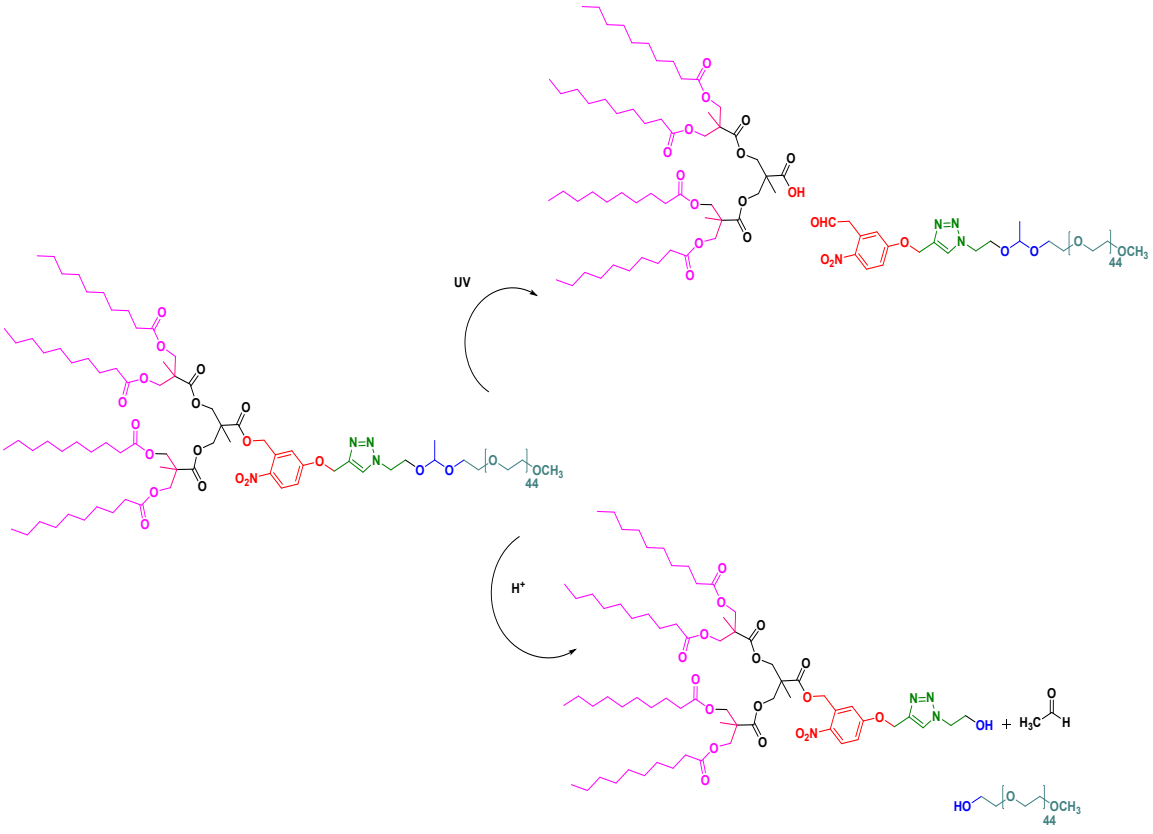


Figure S24. Mean fluorescence intensity of DOX quantified by Imaging Software ZEN PRO 2012 (From Carl ZEISS). Total number of cells counted =10.



Scheme S2: Proposed photo and pH cleavable products of **P1**.

References:

1) M. Kang and B. Moon, *Macromolecules* 2009, **42**, 455-458.

2) J. M. Schumers, J. F. Gohy and C. A. Fustin, *Polym. Chem.,* 2010, **1**, 161.