Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Visible light-triggered disruption of micelles of an amphiphilic block copolymer with BODIPY at the junction

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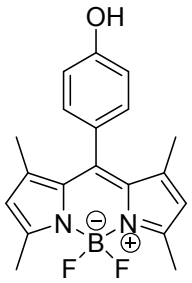
Experimental Section

Materials: 2,4 dimethylpyrrole, 4-hydroxybenzaldehyde, trifluroacetic acid (TFA), 1,4-benzoquinone (DDQ), propargyl bromide, 2- bromoisobutyryl bromide, styrene, copper (I) bromide, 2,2'-bipyridyl were purchased from Aldrich and used without any purification. Boron trifluoride-diethyl etherate (BF_3 etherate) was purchased from Alfa Aesar, potassium carbonate, sodium hydrogen carbonate, sodium sulphate, triethylamine, sodium azide, and Aluminium chloride ($AlCl_3$), were purchased from Spectrochem, sodium borohydride ($NaBH_4$) from Avra chemicals, PEG-N_3 (M_n = 2000 g/mol) was synthesized as per report[1]. Solvents were purchased from local suppliers. THF was dried over sodium and freshly distilled before use. Dichloromethane was dried over calcium hydride and used after distillation; other solvents were used by simple distillation. Deuterated solvents and dialysis tubing with MW-cut-off=12KD were obtained from Aldrich.

All ^1H NMR Spectra were recorded on Bruker 400 or 500MHz spectrometers whereas ^{13}C NMR spectra were recorded on Bruker 100 or 125 MHz spectrometer. HRMS spectra were obtained from ORBITRAP mass analyser Thermoscientific, Q Exactive, GPC analysis was done on T6000M Viscotek Make – 2 using THF as eluent with flow rate 1 mL/min. IR spectra were recorded on Bruker FT-IR Spectrophotometer in the range of 4000-500. Fluorescence emission spectra were recorded on PCI photon counting spectrometer, UV-vis spectra were recorded on SPECORD-210 PLUS Analytikjena spectrophotometer. Blue light LED lamp (470 nm, 150mW.cm^{-2}) from Luxeon Star O-LEDs, Canada was used for irradiation. Dynamic Light Scattering was done on zetasizer ver. 6.01, Serial Number : MAL1033427, Malvern Instruments Ltd. HPLC Chromatograms were recorded on Waters 717 plus Autosampler instrument with Waters 2996 PDA detector connected to Agilent zorbax ODS, 5 µm, 4.6 x 250 mm column.

Synthetic procedures

BODIPY-OH

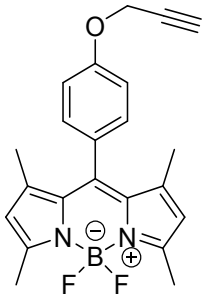


In 500 mL 2 neck round bottom flask 2, 4 dimethyl pyrrole (2 mL, 19.25 mmol) and 150 mL THF were taken this solution was degassed by argon for 30 min. then 4 hydroxy benzaldehyde (1.12 g, 9.171 mmol) was added and again purged by argon for 30 min then few drops of TFA was added and stirred overnight. To this DDQ (2.08 g, 9,171 mmol) in 150 mL THF was added dropwise over 1h and stirred for 5h at room temperature. The colour was changed from orange to dark red to black. To this triethyl amine (51.4 mL, 366.8 mmol) was added dropwise over a time of 40 min then stirred for 30 mins at room temperature and then reaction mixture was cooled in ice bath. BF_3-ethrate (51.8 mL, 412 mmol) was added dropwise. The reaction mixture was stirred for 12h at room temperature. THF was removed under reduced pressure and crude product was dissolved in dichloromethane and washed with

brine solution followed by 0.5N $NaHCO_3$ solution and then several times by water. Organic solvent was dried over Na_2SO_4 and evaporated to dryness. Silica gel column chromatography was carried out with ethyl acetate:Pet ether (1:5) as eluent. *BODIPY-OH* was obtained as red crystals. Yield: 61%

^{1}H NMR (400MHz, $CDCl_3$) δ = 7.22 - 7.08 (m, 2 H), 7.03 - 6.92 (m, 2 H), 6.00 (s, 2 H), 5.27 (br. s., 1 H), 2.57 (s, 6 H), 1.46 (s, 6 H). ^{13}C NMR (100MHz, $CDCl_3$) δ = 156.3, 155.3, 143.2, 141.7, 131.8, 129.4, 127.2, 121.2, 116.1, 14.6; Calcd. $[M]^+$ $C_{19}H_{19}BF_2N_2O$, *m/z*= (340.1559), found: [M+H]= 341.1631.

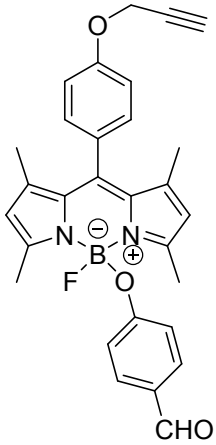
BODIPY-alkyne(1)



BODIPY-Ph-OH (0.9 gm, 2.646 mmol)was dissolved in 50 mL DMF to this K_2CO_3 (0.731 g, 5.291 mmol) was added and stirred for 5 mins, propargyl bromide (0.629 g, 5.291 mmol) was added to reaction mixture and stirred at 70 ^{0}C for 5h. Completion of reaction was checked by TLC. the reaction mixture was concentrated under reduced pressure, dissolved in ethyl acetate and washed two times with brine followed by water. Dried over Na_2SO_4, evaporated and purified by column chromatography using (1:9) ethyl acetate: pet ether to get BODIPY-alkyne as red crystals. Yield: 72%

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.20 (d, *J* = 8.5 Hz, 2 H), 7.10 (d, *J* = 8.5 Hz, 2 H), 5.98 (s, 2 H), 4.77 (d, *J* = 1.8 Hz, 2 H), 2.56 (m, 7 H), 1.43 (s, 6 H). ^{13}C NMR (125MHz, $CDCl_3$) δ = 158.1, 155.4, 143.1, 141.5, 131.8, 129.3, 128.0, 121.2, 115.7, 78.1, 75.9, 56.0, 14.5, Calcd. $[M]^+$ $C_{22}H_{21}BF_2N_2O$ *m/z*= 378.1715, found: [M+H]= 379.1788.

BODIPY-alkyne-CHO (2)

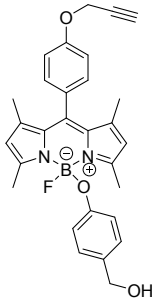


In a two neck flask BODIPY-alkyne (0.6 g, 1.586 mmol) was dissolved in 20 mL dry CH_2Cl_2 under nitrogen flow. To this $AlCl_3$(0.106 g, 0.793 mmol) was added and refluxed for 10 min,

cooled to room temperature and 4-hydroxy benzaldehyde (0.194 g, 1.586 mmol) was added dropwise by dissolving in 20 mL of CH_2Cl_2. After complete addition reaction mixture was refluxed for 30 min, solvents were evaporated, solid reaction mixture re-dissolved in ethyl acetate and passed through neutral aluminium oxide. Orange crystals of BODIPY-alkyne-CHO were obtained by silica gel column chromatography using (1:5) ethyl acetate:pet ether as eluent. Yield: 36%

^{1}H NMR (500MHz , $CDCl_3$) δ = 9.79 (s, 1 H), 7.70 - 7.63 (m, 2 H), 7.26 - 7.20 (m, 2 H), 7.18 - 7.11 (m, 2 H), 6.70 - 6.66 (m, 2 H), 5.95 (s, 2 H), 4.79 (d, *J* = 2.4 Hz, 2 H), 2.58 (t, *J* = 2.4 Hz, 1 H), 2.49 (s, 6 H), 1.46 (s, 6 H) ^{13}C NMR (125MHz , $CDCl_3$) δ = 190.9, 162.5, 162.4, 158.3, 155.9, 143.7, 141.7, 132.0, 129.2, 128.9, 127.7, 121.8, 118.2, 115.9, 115.8, 78.0, 76.0, 56.1, 14.8, 14.7, Calcd. $[M]^+$ $C_{29}H_{26}BFN_2O_3$ *m/z* = 480.2021, found: [M+H] = 481.2093.

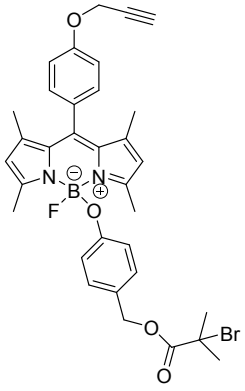
Bodipy-Alkyne-benzyl alcohol (3)



Compound 2 (0.230 g, 0.478 mmol) was dissolved in methanol (50 mL): THF (10 mL). $NaBH_4$ (27.2 mg, 0.718 mmol) was dissolved in 2 mL methanol and added to reaction mixture with constant stirring under inert atmosphere. Stirring was continued for 10 min. The excess $NaBH_4$ was quenched by adding 1 mL of acetone, solvents were evaporated and compound 3 was purified by column chromatography using ethyl acetate: pet ether (3:7) as eluent. Yield: 95%

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.27 - 7.16 (m, 2 H), 7.15 - 7.08 (m, 14 H), 6.56 (d, *J* = 8.5 Hz, 2 H), 5.93 (s, 2 H), 4.78 (d, *J* = 2.1 Hz, 2 H), 4.53 (d, *J* = 4.6 Hz, 2 H), 2.57 (t, *J* = 2.3 Hz, 1 H), 2.52 (s, 6 H), 1.44 (s, 6 H). ^{13}C NMR (125MHz, $CDCl_3$) δ = 158.2, 156.2, 156.1, 155.9, 143.2, 141.5, 132.0, 131.8, 129.3, 129.3, 128.6, 128.0, 121.6, 118.0, 115.8, 115.6, 78.0, 75.9, 65.3, 56.1, 14.8, 14.7; Calcd. $[M+Na]^+$ $C_{29}H_{28}BFN_2O_3Na$ *m/z*= 505.2075, found: [M+Na] =505.2069.

BODIPY-Alkyne-ATRP initiator(4)



Compound 3 (0.2 g, 0.415 mmol) was dissolved in dry dichloromethane (50 mL) to this triethyl amine (0.12 mL, 0.829 mmol) was added and stirred for 10 min at room temperature then reaction mixture was cooled in ice bath and 2 bromoisobutyryl bromide (0.102 mL, 0.829) was added dropwise. Reaction mixture was stirred at room temperature; completion of reaction was followed by TLC. After completion of reaction filtered, and filtrate was washed with water and dried over Na_2SO_4. Compound 4 was obtained as orange crystals after column chromatography with (1:9) ethyl acetate: pet ether as eluent. Yield 80%

^{1}H NMR (500MHz, $CDCl_3$) δ = 7.16 (d, *J* = 1.5 Hz, 2 H), 7.15 - 7.08 (m, 14 H), 6.57 - 6.53 (m, 2 H), 5.94 (s, 2 H), 5.06 (s, 2 H), 4.78 (d, *J* = 2.4 Hz, 2 H), 2.57 (t, *J* = 2.3 Hz, 1 H), 2.52 (s, 6 H), 1.92 (s, 6 H), 1.44 (s, 6 H). ^{13}C NMR (125MHz, $CDCl_3$) δ = 171.6, 158.2, 156.8, 156.7, 155.8, 143.2, 141.5, 132.0, 129.6, 129.3, 128.0, 126.2, 121.6, 118.1, 115.8, 115.6, 78.0, 75.9, 67.8, 56.1, 56.0, 30.8, 14.9, 14.7; Calcd. $[M+Na]^+$ $C_{33}H_{33}BBrFN_2O_4Na$, *m/z*= 653.1599, found: [M+Na] =653.1593.

Polymerization

BODIPY-Alkyne-ATRP initiator (4) (30 mg, 0.0475 mmol) and PEG azide (0.120 g, 0.057 mmol) were dissolved in toluene, purged by argon for 15 min. then styrene (1.08 mL, 9.503 mmol) and Cu(I)Br (6.8 mg, 0.057 mmol) were added. Freeze thaw cycles were repeated three times, filled by argon and 2,2'bipyridyl (22 mg, 1.425 mmol) was added stirred to dissolve again purged by freeze thaw cycles three times finally backfilled by argon and reaction was carried out by inserting schlenk tube in preheated oil bath at 75 ^{0}C for 18 h. The reaction was quenched by cooling in liq. nitrogen and diluted by CH_2Cl_2, passed through neutral alumina to remove catalyst, solvents evaporated and precipitated in pet ether. Finally purification was carried out by dialysis against methanol to remove excess of PEG-N_3.

^{1}H NMR (400MHz, $CDCl_3$) δ= 7.92 (s, 1 H), 7.25 - 6.32 (m,116 H), 5.92 (s, 2 H), 5.25 (s, 2 H), 4.60 (t, 2 H), 4.43 (m, 2 H), 3.91 (t, 2 H), 3.65 (s, 178 H), 3.39 (s, 3 H), 2.50 (br. s., 6 H), 1.86 (br. s., 21 H), 1.69 (br. s., 42 H), 1.44 (br. s., 6 H). IR- 2921.3, 1720.1, 1600.5, 1547.5, 1514.2, 1454.4, 1222.1, 1102.5.

Preparation of Aqueous Solution

P1 (10 mg) was dissolved in 3 mL of THF and stirred for 2h. To this, D.I. water (5mL) was added dropwise over a period of 1h to induce micellization and continued stirring for 2h, this solution was transferred into dialysis tubing and dialysed against D.I. water for 3 days. Finally, the solution was diluted to 10 mL with water to get 0.1wt % aqueous solution of P1. This solution was filtered through 0.45 μm PVDF filters and used for DLS and TEM analysis. 4 mL of 0.1wt % aqueous solution of P1 was irradiated with blue light and from this 10 μL solution was taken, diluted to 3 mL by water and fluorescence spectra were measured. For the measurement of fluorescence emission intensity over irradiation time for P1 in THF, 0.1 wt % P1 in THF with 1 drop of water was irradiated and a fraction of 10 μL was removed, diluted to 3mL by THF and fluorescence spectra were measured.

HPLC Analysis

For verification of formation of 4-hydroxybenzyl alcohol during photocleavage:

a) A solution of compound 4 in THF with one drop of water was irradiated with visible light, then THF was evaporated and mixture was dissolved in methanol for analysis.

b) A solution of P1 in THF was irradiated with visible light and dialysed against water simultaneously for 1h. Outer solution from dialysis was concentrated, redissolved in methanol and analysed.

HPLC analysis was carried out using solvent A - methanol and solvent B - water system with gradient flow rate as per reported procedure[2] with little modifications. Flow rate was maintained at 0.8 mL/min. Gradient system was used as B 95% for 5 mins; B from 95% to 60 % in 1 min; B 60 % from 6-12 min, B from 60% to 20% in 1 min: then B 20 % for 2 min. The chromatograms were extracted at 223 nm.

For Nile red release experiment: Nile red was encapsulated in 0.1wt% polymer P1 in methanol:water (1:1) system and dialysed with same solvent system for 48h with changing outer solvent mixture four times a day to remove untrapped dye. Then, the dye encapsulated solution of P1 was irradiated with dialysis against same solvent mixture (10 mL). After 1h, irradiation was stopped and dialysis tubing was transferred to a fresh 10 mL solution. The older solution was evaporated, redissolved in methanol and used for analysis. HPLC analysis was done using isocratic solvent system with Methanol: water (93:7) with 1mL/min flow rate and chromatograms were extracted at 573 nm.

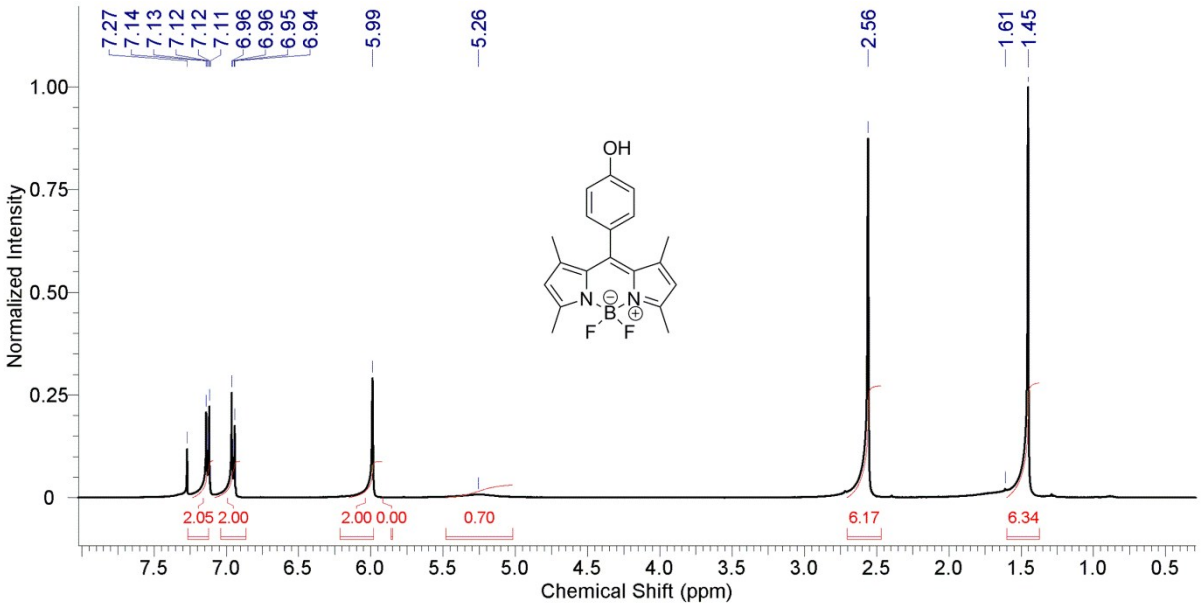


Figure S1: 400MHz ^{1}H NMR spectrum for BODIPY-OH in $CDCl_3$

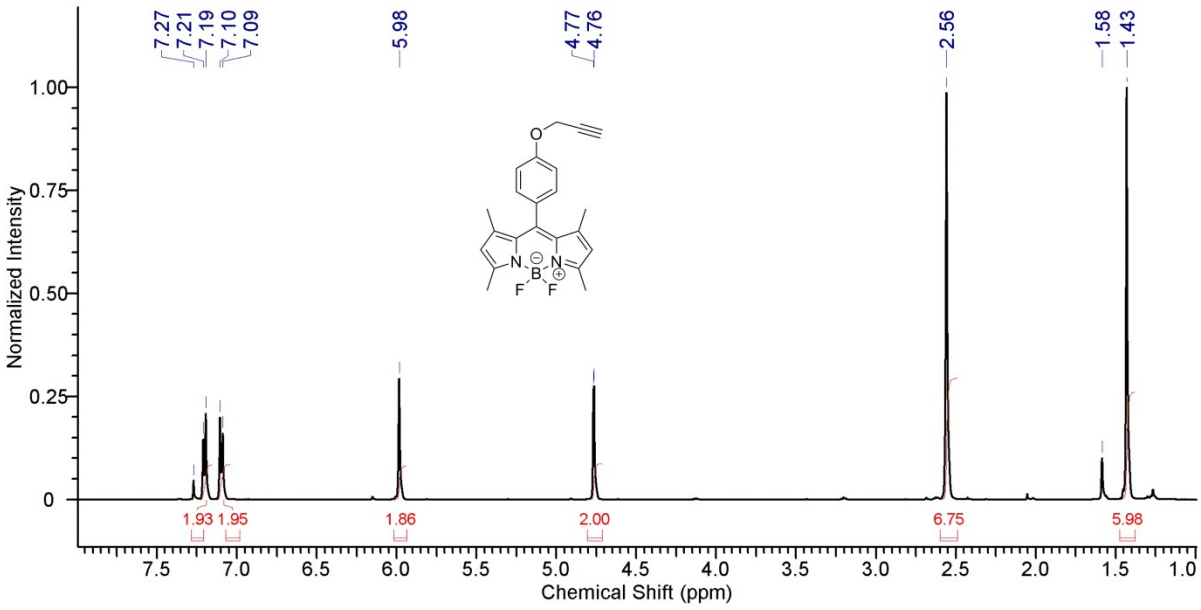


Figure S2: 500MHz ^{1}H NMR spectrum for BODIPY-alkyne in $CDCl_3$

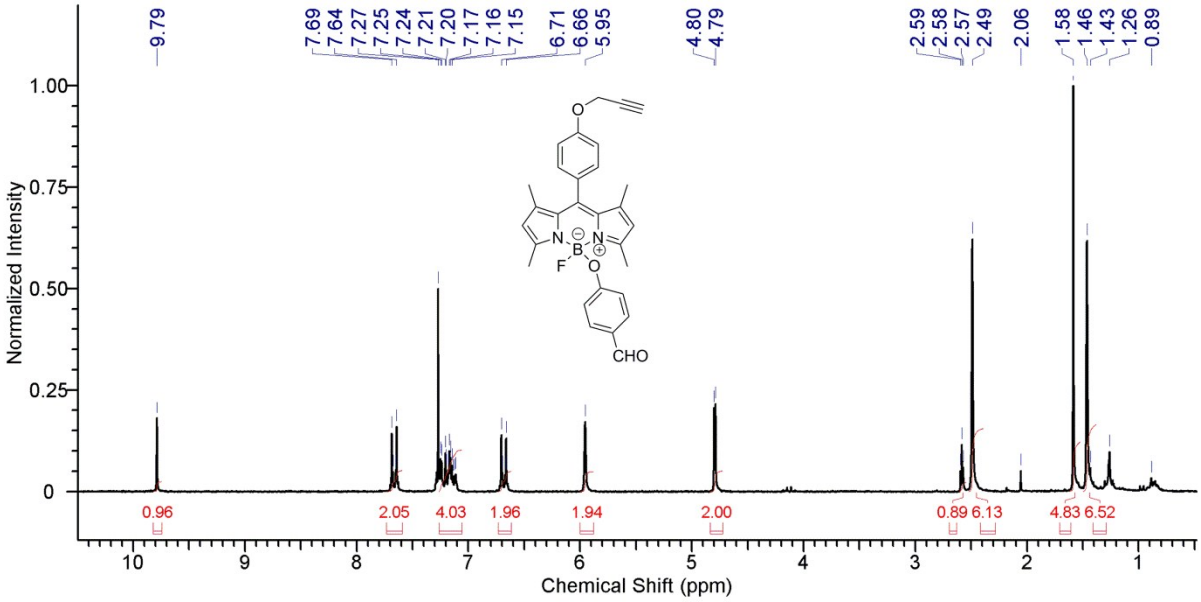


Figure S3: 500MHz ^{1}H NMR spectraum for BODIPY-alkyne-CHO in $CDCl_3$

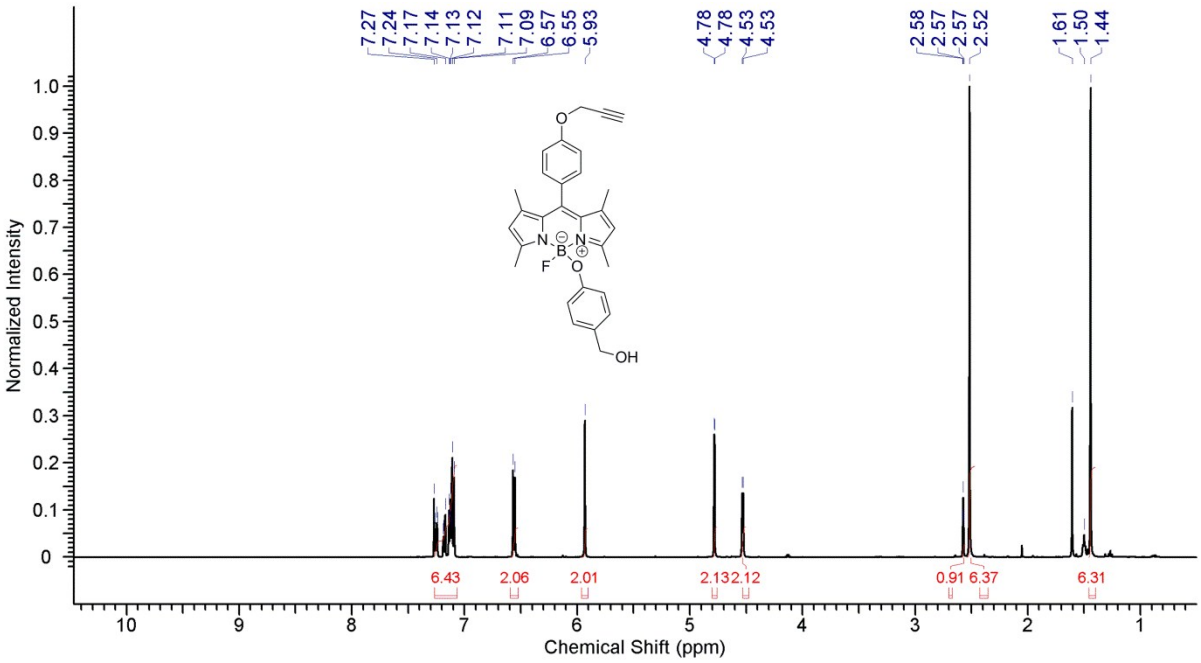


Figure S4: 500MHz ^{1}H NMR spectrum for BODIPY-alkyne-benzyl alcohol in $CDCl_3$

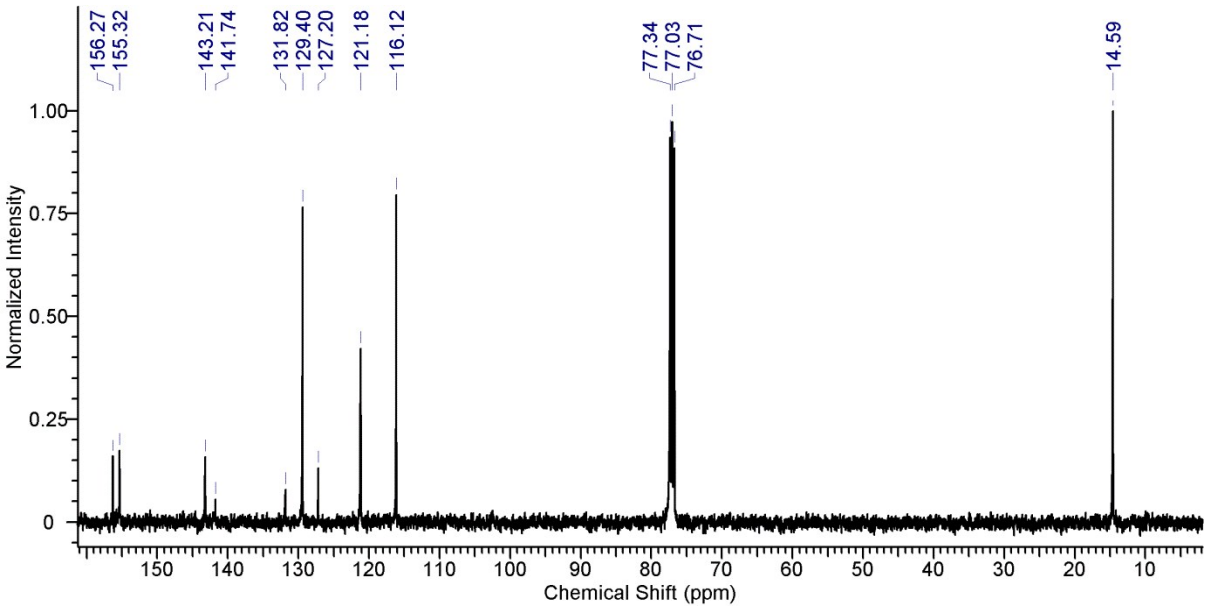


Figure S5: 100MHz ^{13}C NMR spectrum for BODIPY-OH in $CDCl_3$

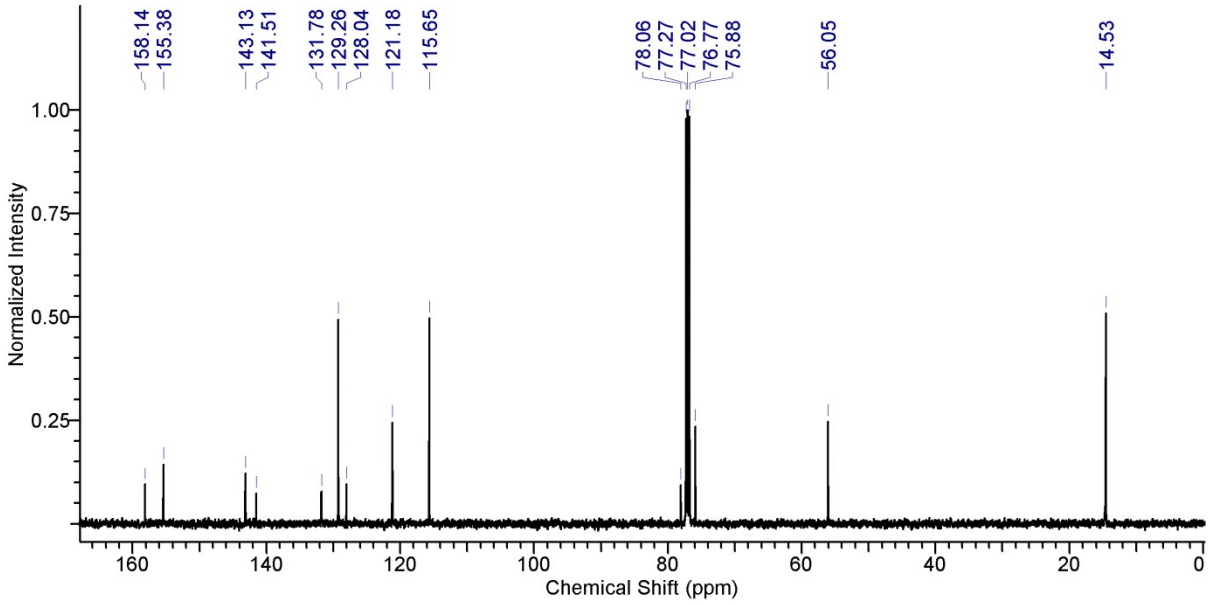


Figure S6: 125MHz ^{13}C NMR spectrum for BODIPY-alkyne in $CDCl_3$

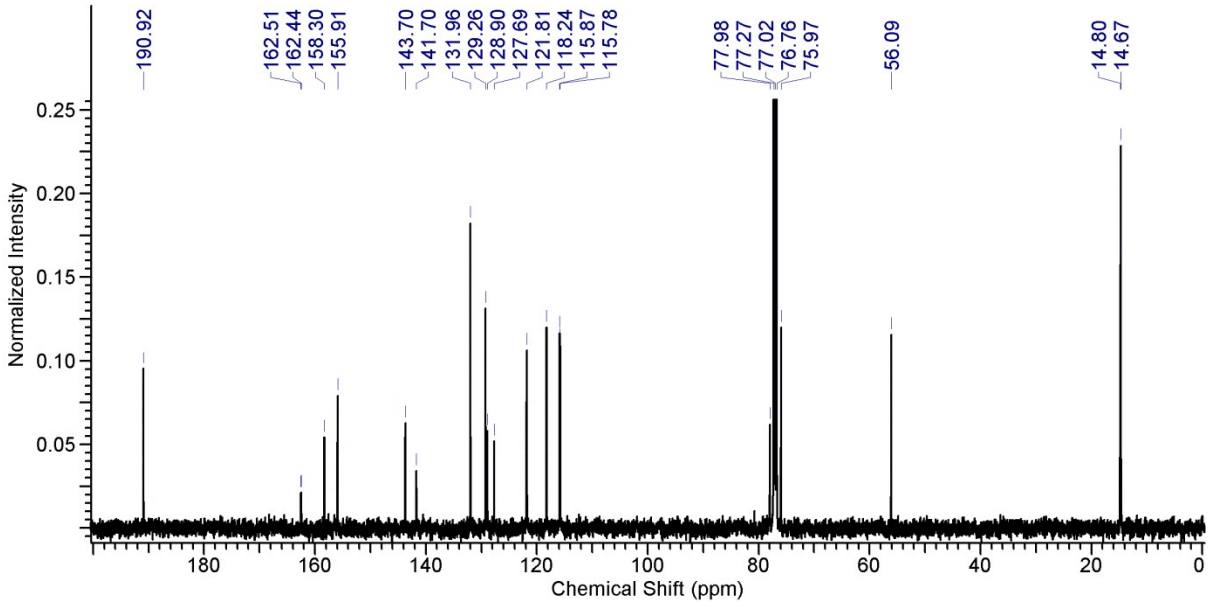


Figure S7: 125MHz ^{13}C NMR spectrum for BODIPY-alkyne-CHO in $CDCl_3$

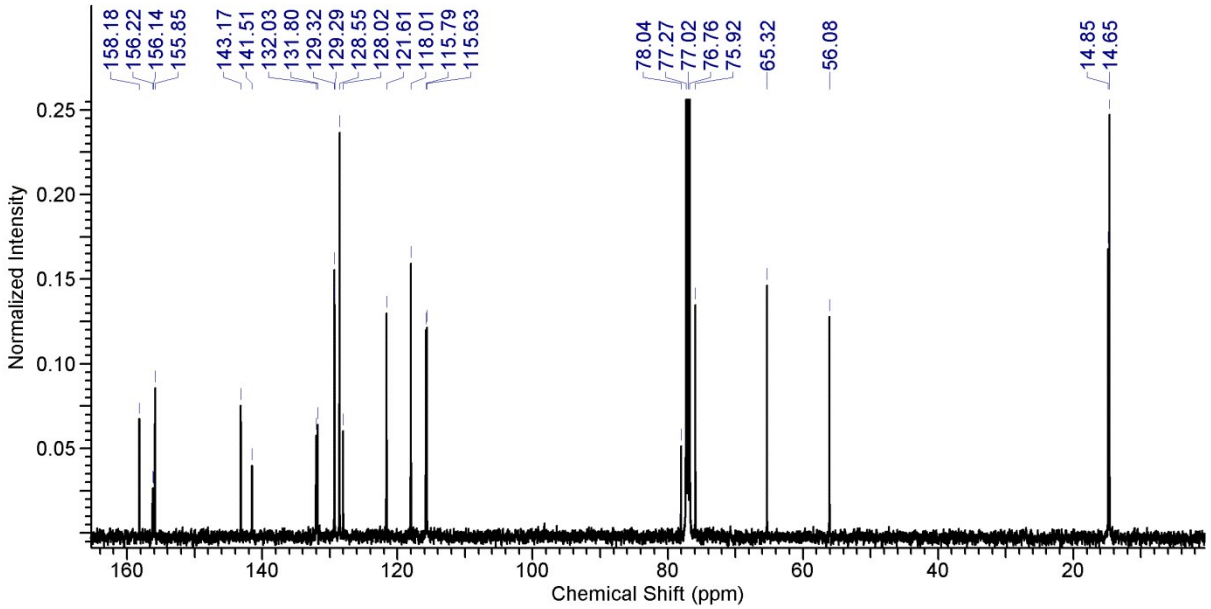


Figure S8: 125MHz ^{13}C NMR spectrum for BODIPY-alkyne-benzyl alcohol in $CDCl_3$

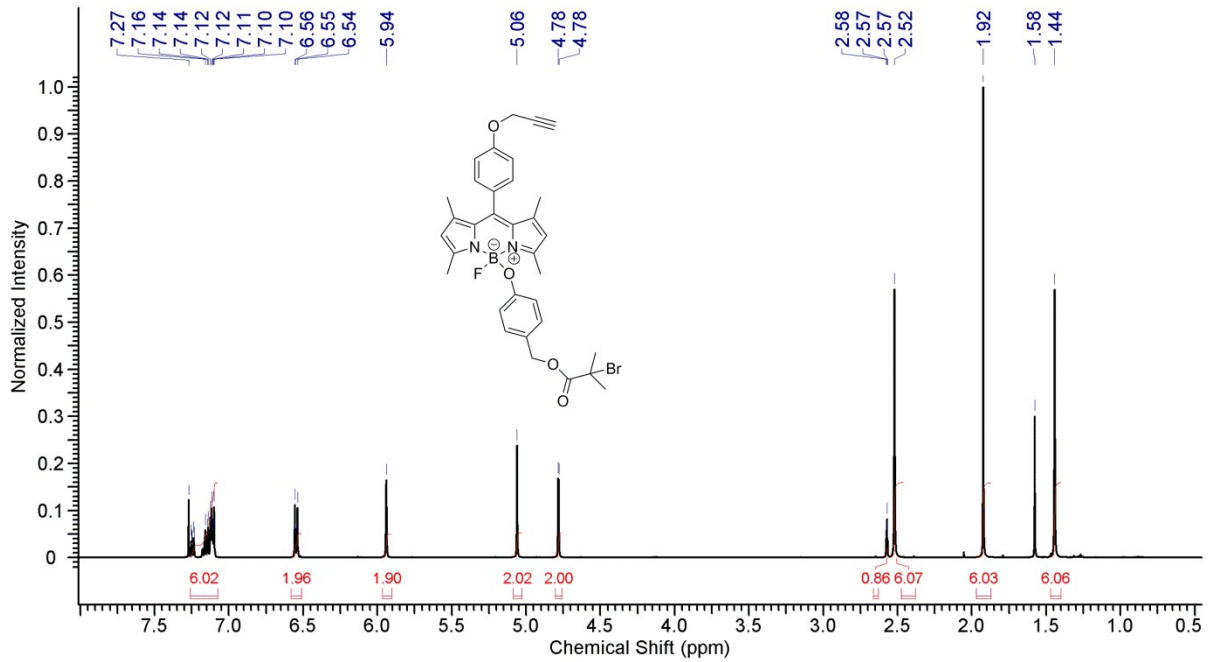


Figure S9: 500MHz ^{1}H NMR spectrum for BODIPY-alkyne ATRP in $CDCl_3$

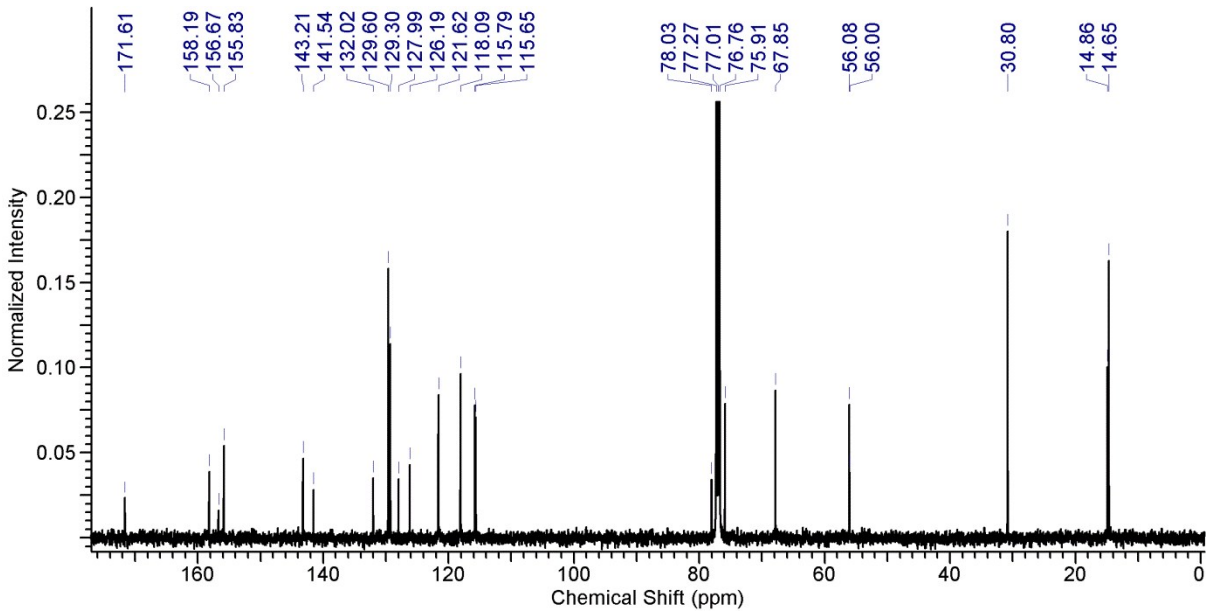


Figure S10: 125MHz ^{13}C NMR spectrum for BODIPY-alkyne-ATRP initiator in $CDCl_3$

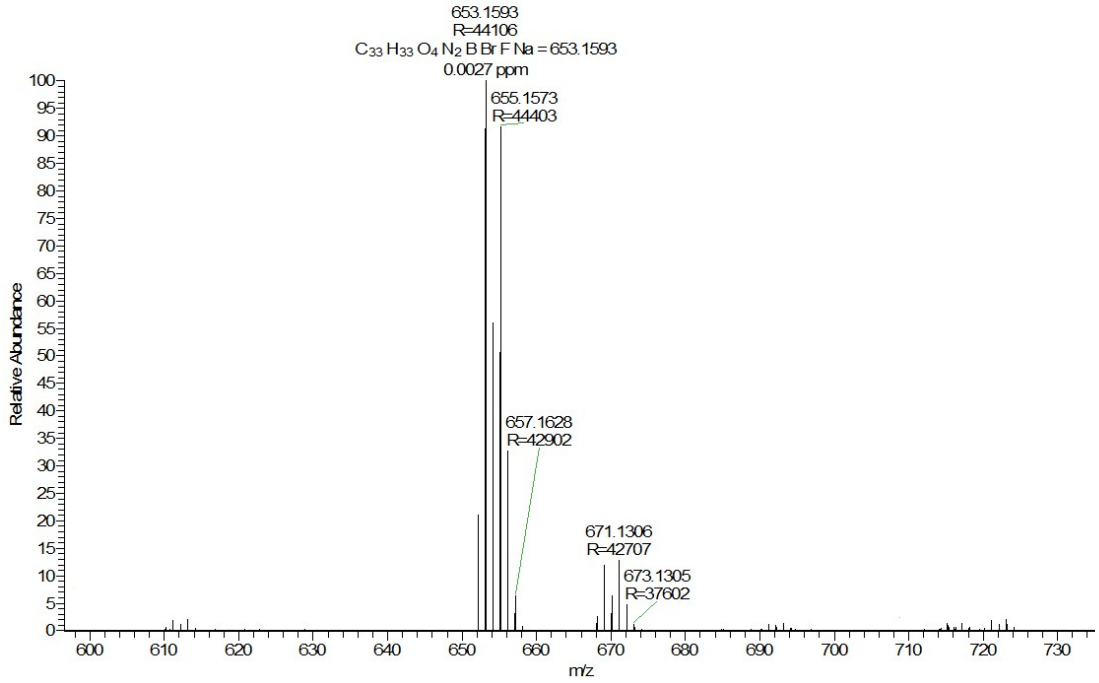


Figure S11: HRMS spectra for BODIPY-Alkyne-ATRP initiator (4).

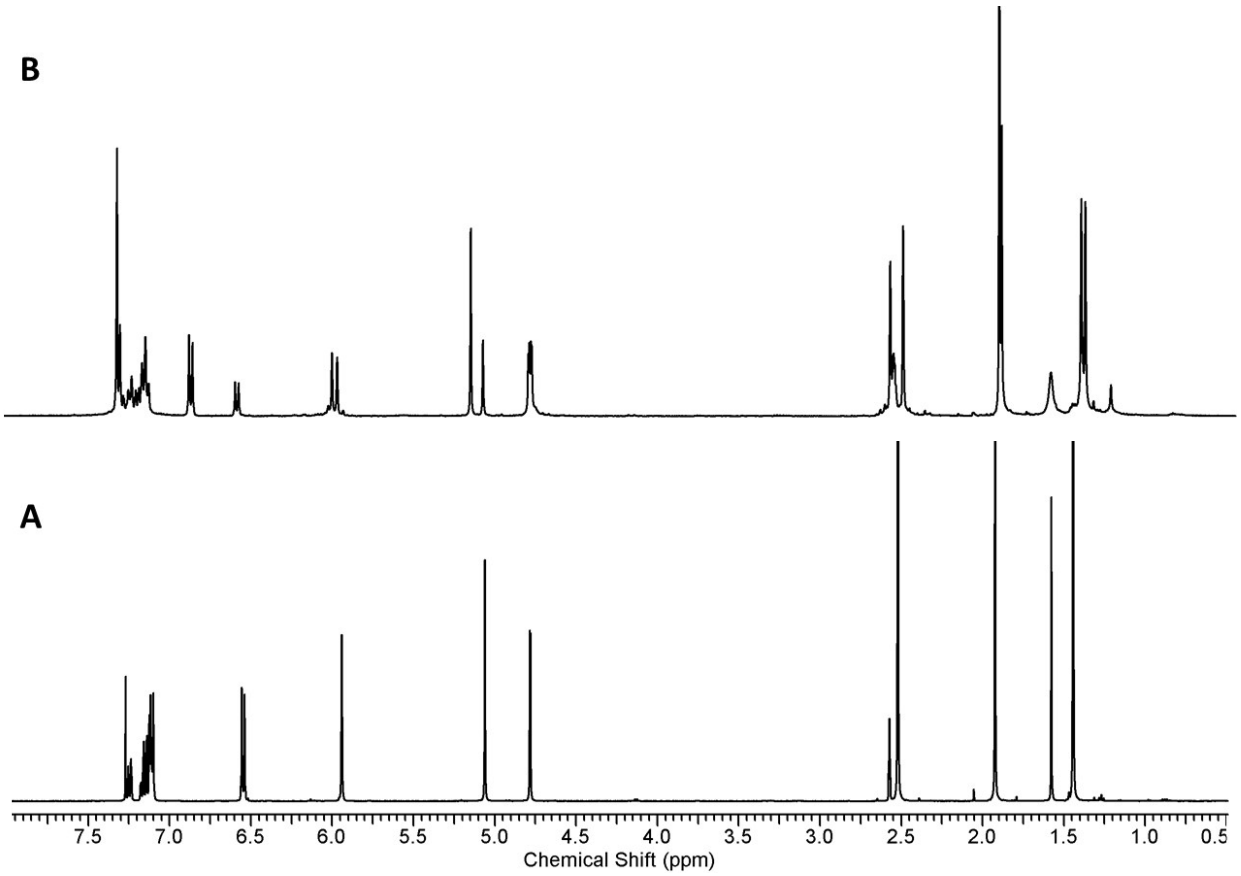


Figure S12: ^{1}H NMR spectrum in $CDCl_3$ of BODIPY-Alkyne-ATRP initiator (4) A) before irradiation B) after irradiation with visible light (470 nm).

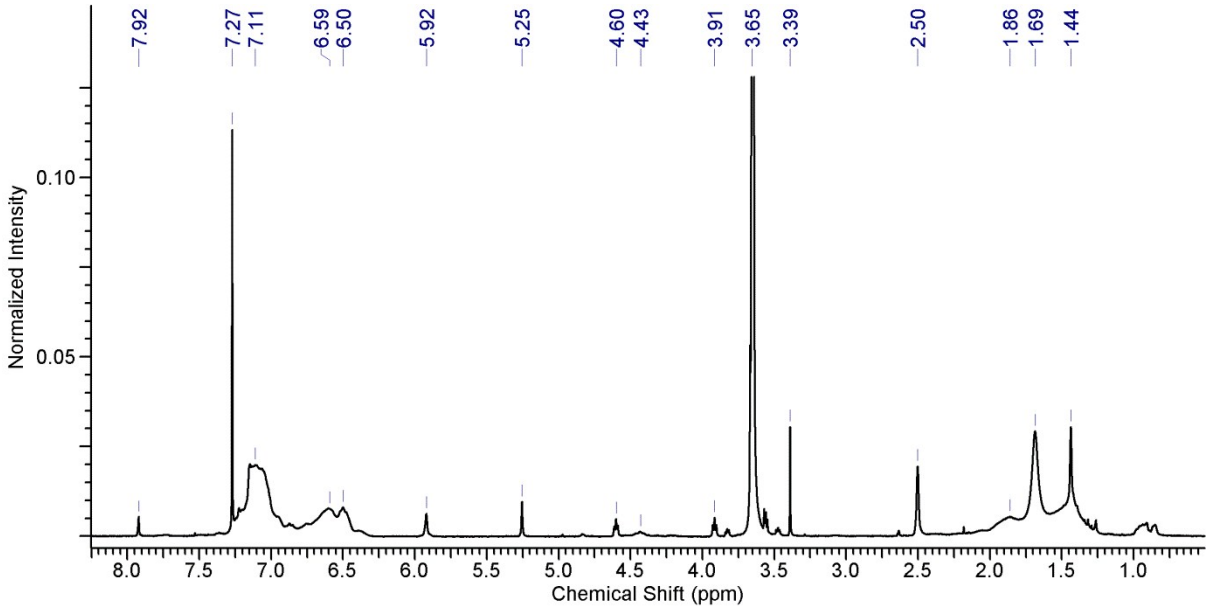


Figure S13: 400MHz ^{1}H NMR spectrum for P1 in $CDCl_3$

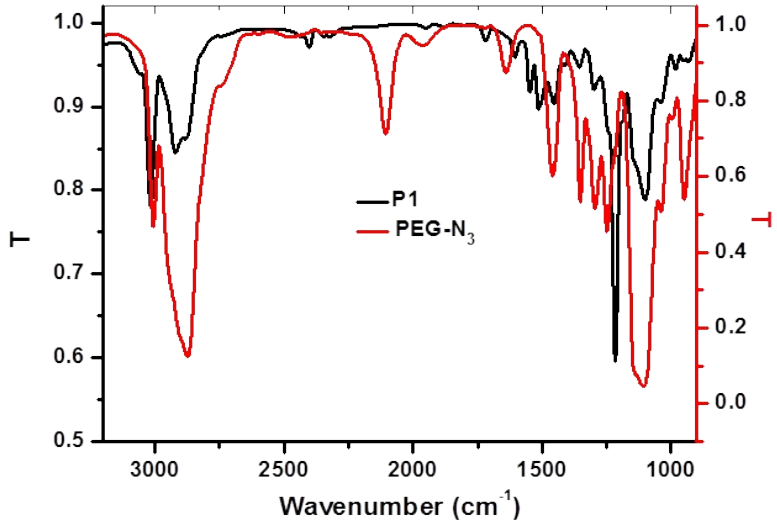


Figure S14: FTIR spectra overlay for PEG-N_3 and P1

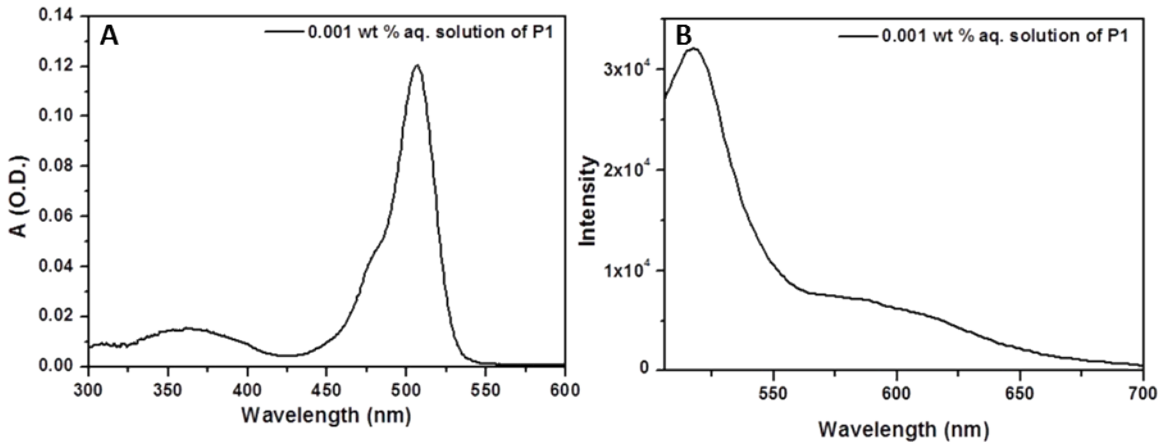


Figure S15: A) UV spectrum B) fluorescence emission spectrum for 0.001 wt% P1 in aqueous solution.

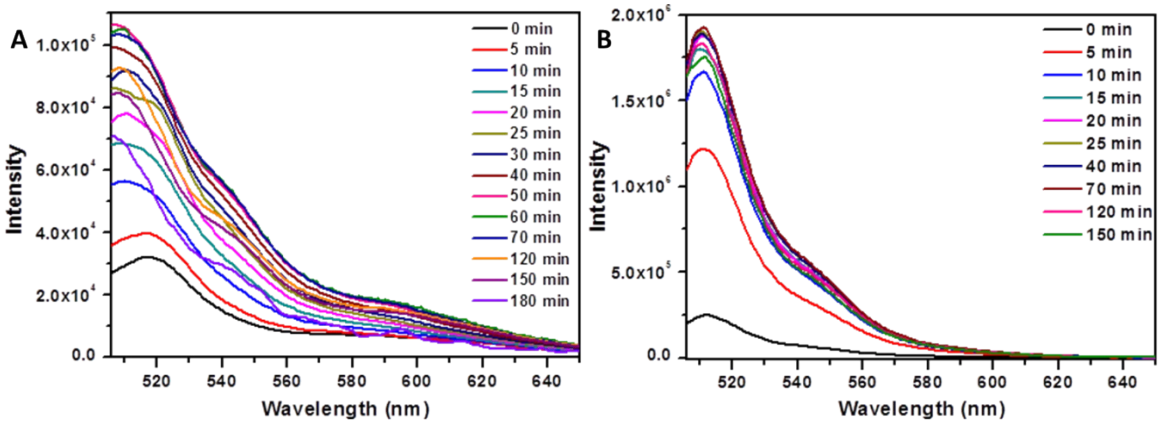


Figure S16: Fluorescence emission spectra for 0.001wt% P1 with blue light irradiation time A) in water B) in THF

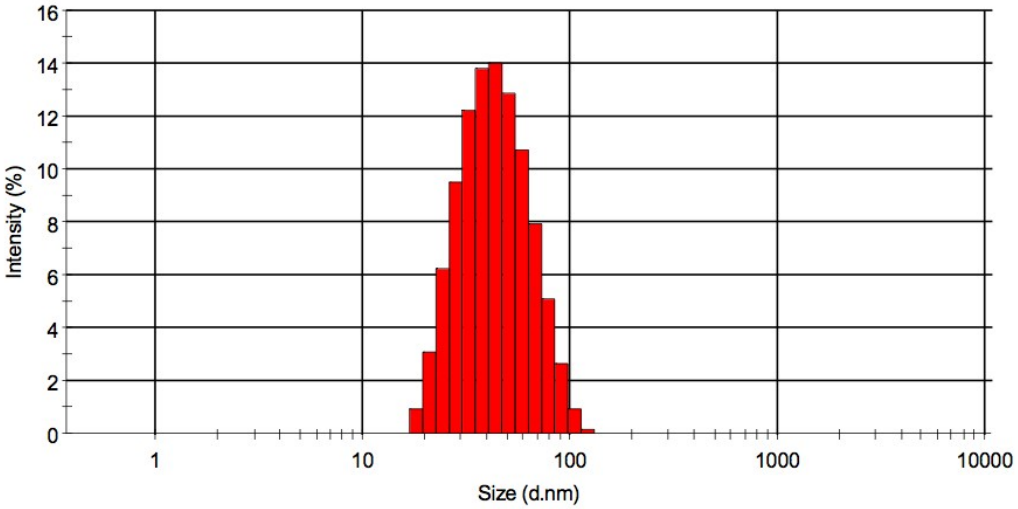


Figure S17: DLS size distribution curve for 0.1wt% solution of P1 in THF:water (1:1)

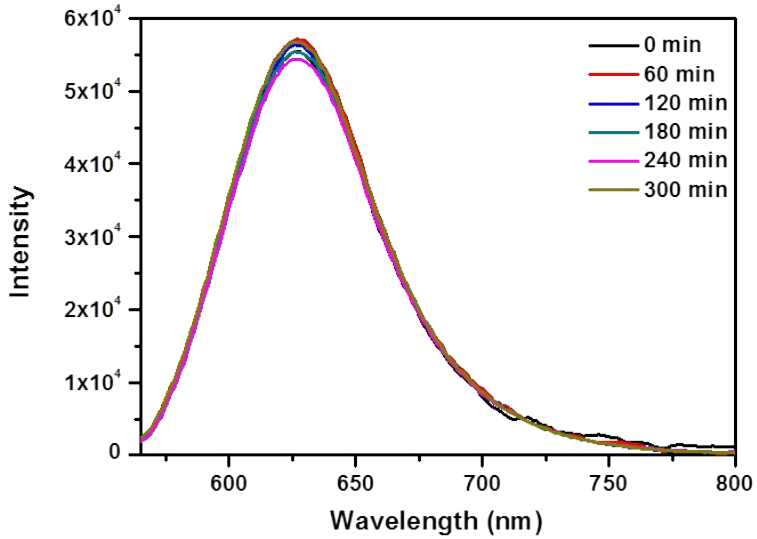


Figure S18: Fluorescence emission spectra of Nile red for 0.1 wt. % P1 solution without irradiation

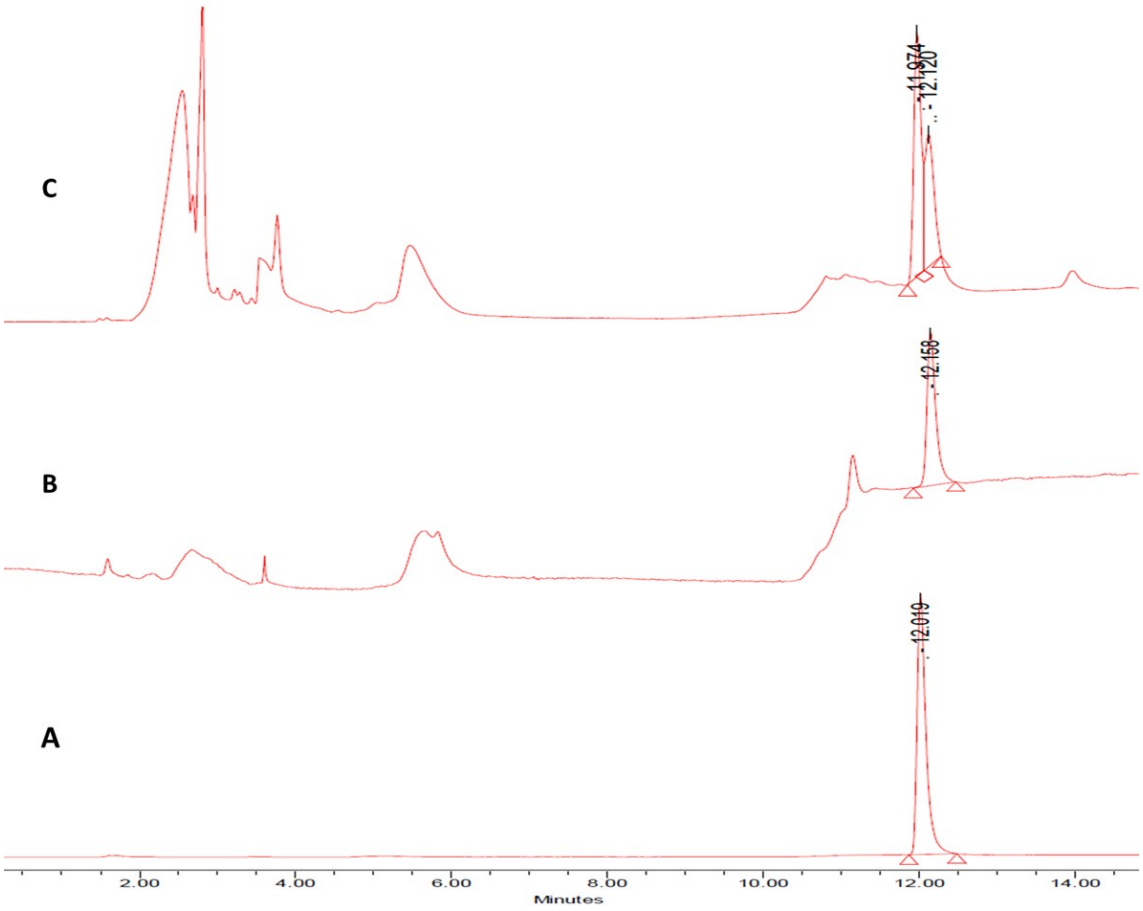


Figure S19: HPLC chromatograms for A) 4-hydroxybenzyl alcohol, B) compound 4 after photoirradiation and C) P1 after photoirradiation

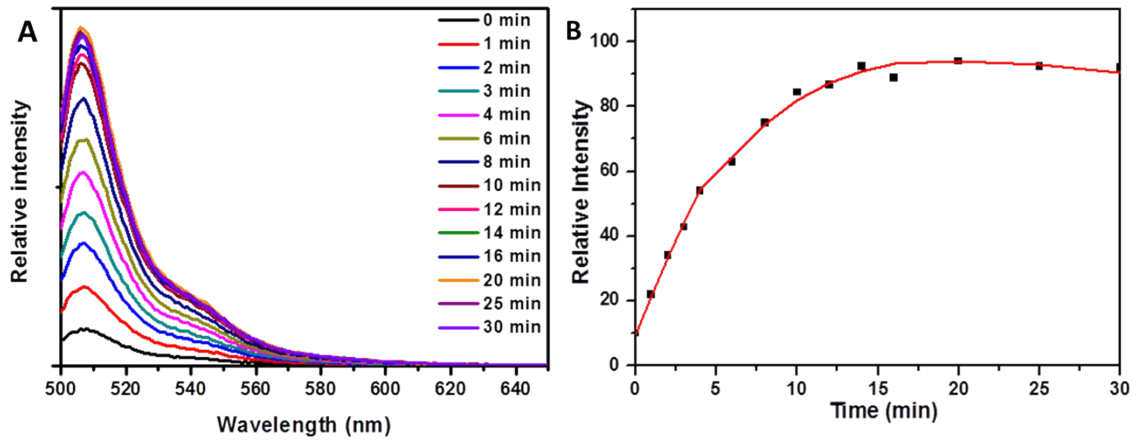


Figure S20: A) Fluorescence emission spectra of Compound 4 in THF with 1 drop of water after photoirradiation and B) corresponding profile for increase in fluorescence intensity with time

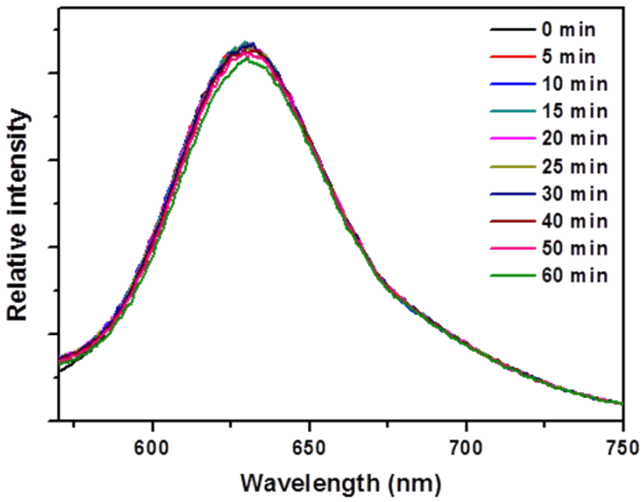


Figure S21: Fluorescence spectra of Nile red loaded 0.1 wt % P1 micelles in THF: water (2:1, v/v) upon photoirradiation

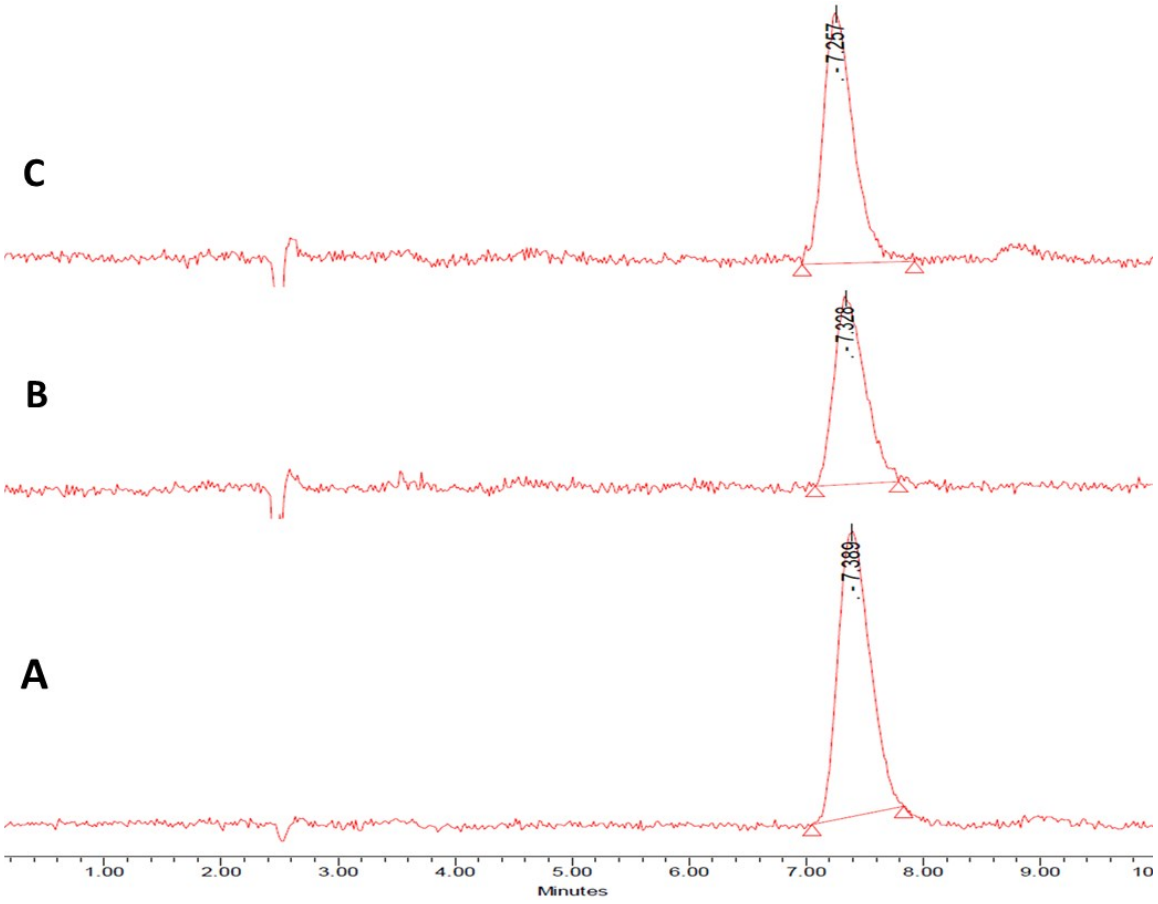


Figure S22: HPLC chromatogram of A) Nile red; and of outer solution from dialysis of Nile red encapsulated P1 micelles B) after 1h of photoirradiation, and C) 5h after photoirradiation

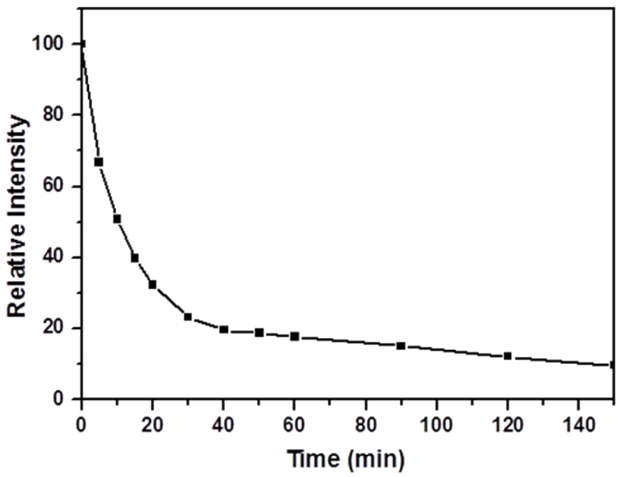


Figure S23: Fluorescence intensity profile for Nile red from P1 micelles in THF: water (10:90) with photoirradiation

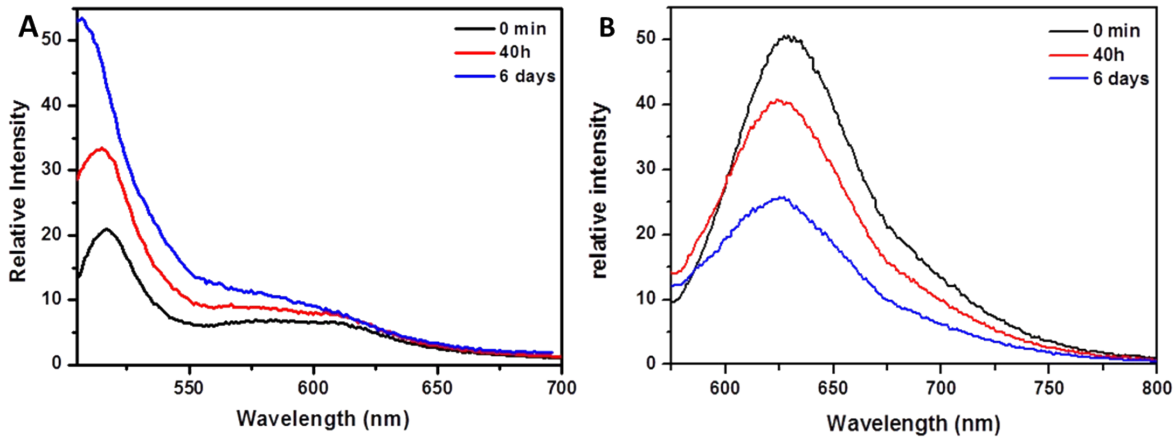


Figure S24: Fluorescence emission spectra of A) 0.1wt% aqueous solution of P1 and B) Nile red encapsulated in 0.1wt% aqueous solution of P1 under ambient light

References

1. N. Kalva, V. K. Aswal, A. V. Ambade, *Macromol. Chem. Phys.,* 2014, **215**, 1456.
2. Y. Xu, J. Chen, Y. Li, S, Peng, X. Gu, M. Sun, K. Gao, J. Fang, *Org. Biomol. Chem.*, 2015, **13**, 2634.