Electronic Supplementary Material (ESI)

Supporting Information

A PEGylated photosensitizer-core pH-responsive polymeric nanocarrier for imaging-guided combination chemotherapy and photodynamic therapy

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General Information

Materials

All chemicals and reagents were commercially available and of analytical grade without further purification useless otherwise specified. MPEG (Mn = ~2000) and hydrazine hydrate were purchased from Aladdin Industrial Corporation (China). 2,4-Dimethylpyrrole [22] and MPEG-PhCHO [27] were prepared according to literature respectively. All pH measurements were accomplished by a Model PHS-3C meter. Melting points were measured with a shanghai WRS-1B digital melting point apparatus. 1H NMR (500 MHz) and 13C NMR (125 MHz) were measured on a Bruker Avance III spectrometer. Electrospray mass spectra (ESI-MS) were recorded on a Thermofisher LCQ. Elemental analyses were obtained using a Perkin-Elmer-240C analyzer. Fluorescence spectra were determined on a Perkin Elmer LS-55. UV-vis spectra were measured on a Shimadzu UV-3600. Transmission electron micrographs were obtained using JEOL 2010 transmission electron microscope (TEM) at an accelerating voltage of 200 KV. The sample for TEM measurements was prepared by dropping the solution onto a carbon-coated copper grid. DLS measurements were performed under a Malnern Mastersize 3000 (Malvern Instruments Ltd., UK) equipped with a 10 mW laser light and operating at λ=470 nm.

Synthesis and Characterization of MPEG-Hyd-Br_2-BODIPY

Synthesis of compound hydrazine-Br_2-BODIPY

Compound **A_1** was synthesized according to known procedure in Fig.S1.[S1]

(1) Into a nitrogen-filled 500ml three-necked round-bottom flask were added A_1(4.5g,0.532mol),2,4-dimethylpyrrole(3.8g,3.8mmol) and 300ml Re-steamed DCM. A few drops of trifluoroacetic acid was added as a catalyst .when the solution was changed from colorless to purple-red, the reaction vessel was wrapped with tin foil paper to be protected from light for 12 hours under an argon atmosphere. The above reaction was dissolved in 50 mL of re-distilled methylene chloride under argon atmosphere, and slowly dropped into the reactor with a constant pressure dropping funnel. The reaction was continued for 4 hours after the completion of the dropwise addition. Then, 20 mL of triethylamine was placed in a constant pressure dropping funnel, and added dropwise to a three-necked flask. After the addition was completed, the reaction was further carried out for about one hour, and 20 mL of boron trifluoride was placed in a constant pressure dropping funnel . After the reaction system was further stirred at room temperature for 12 hours , the solution was washed with deionized water several times,the organic layer was combined and washed once with saturated brine. The collected organic layer was dried over anhydrous magnesium sulfate , the resulting solution was evaporated on a rotary evaporator. The crude product was purified in a silica gel column using PE-EA (v/v=10:1-4:1) as an eluent to obtain a dark red solid BODIPY-AcOEt (2.5 g, yield: 29.5%).

M.P.210-212℃, ^{1}H-NMR (500 MHz, $CDCl_3$) δ (TMS, ppm): 7.16 (d, *J* = 8.1 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 5.96 (s, 2H), 4.67 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.53 (s, 6H), 1.40 (s, 6H), 1.33-1.18 (m, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ (TMS, ppm): 167.44, 157.30, 154.28, 142.00, 140.29, 130.63, 128.22, 127.19, 127.02, 126.74, 120.09, 114.22, 64.32, 60.40, 13.46, 13.43, 13.06. ESI-MS: m/z = 427 [M+H^+]. Anal. Calcd. For C23H25BF2N2O3: C, 64.81; H, 5.91; N, 6.57. Found: C, 65.02; H, 5.92; N, 6.75.

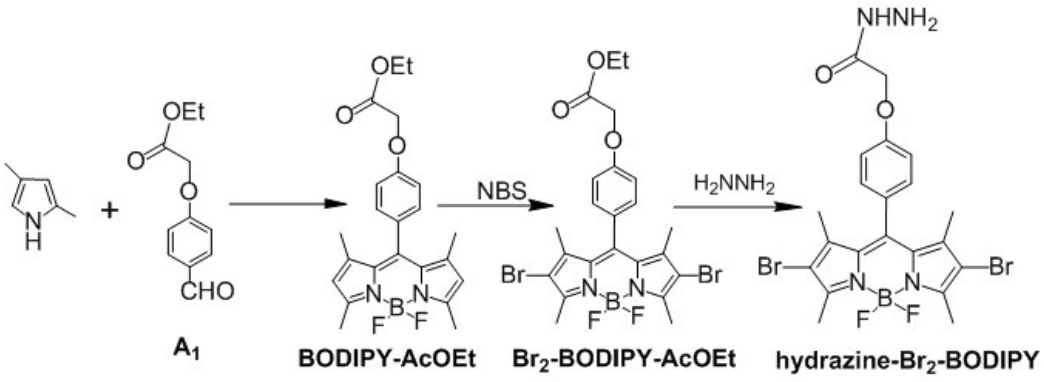


Fig. S1 Synthetic pathway of compound hydrazine-Br_2-BODIPY

(2) Into a 500ml three-necked round-bottom flask were added BODIPY-AcOEt (0.43g, 1 mmol) with 20ml CCl_4. After a drop of DMF was added ,the reaction was heated to 50℃. When the hydrazine-Br_2-BODIPY was completely dissolved, the N-bromosuccinimide (0.43 g, 2.4 mmol) was added portionwise to the reaction system. Then, the temperature of reaction was raised to 85℃ to reflux the reaction for 2 hours. The product was obtained by column chromatography (PE: DCM = 8:1-5:1) to give a red solid Br_2-BODIPY-AcOEt (0.4 g, yield: 68.7%). M.P.271~273℃. ^{1}H-NMR (500 MHz, $CDCl_3$) δ (TMS, ppm): 7.21-7.17 (m, 2H), 7.08 (d, *J* = 8.7 Hz, 2H), 4.73 (s, 2H), 4.32 (d, *J* = 7.1 Hz, 2H), 2.62 (s, 6H), 1.43 (s, 6H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.55, 159.00, 154.12, 142.00, 140.77, 130.92, 129.43, 127.66, 115.80, 111.96, 77.47, 77.22, 76.97, 65.63, 61.77, 14.38, 14.07, 13.88. Anal. Calcd. For C23H23BBr2F2N2O3: C, 47.30; H, 3.97; N, 4.80. Found: C, 47.23; H, 3.89; N, 4.91.

(3) Into a 500ml three-necked round-bottom flask were added Br_2-BODIPY-AcOEt (0.4g,0.69mmol) with 20ml anhydrous methanol,the solution was heated to 50℃.When the Br2-BODIPY-AcOEt was completely dissolved, an excess of 85% hydrazine hydrate was added dropwise to the mixture. After reaction temperature was raised to 90℃ for 2 hours,the solution was poured into water and extracted with dichloromethane several times (3×40 mL). The organic layer was collected, dried over anhydrous sodium sulfate. After filtration and solvent evaporation, the product hydrazine-Br2-BODIPY was obtained as orange red solid. (0.31g, 0.55mmol).

Synthesis and Characterization of PEG polymer M_2 [S2]

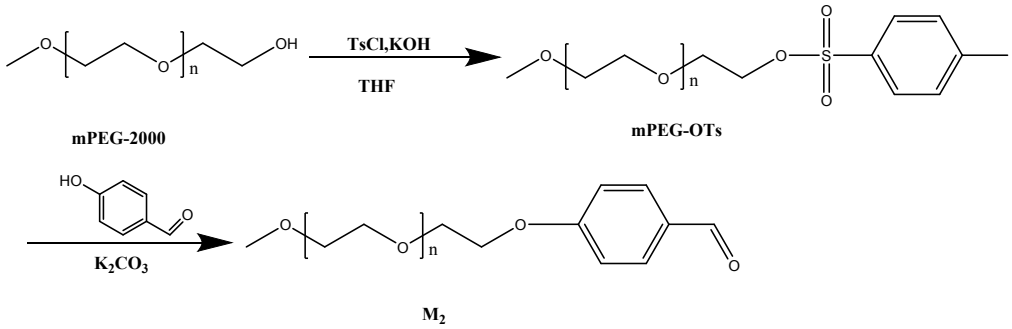


Fig. S2 Synthetic pathway of compound $\mathbf{M_2}$ (MPEG-PhCHO)

(1) In a three-necked flask, mPEG-2000 (20g, 10mmol) was dissolved in 50ml of distilled THF. The solution was cooled to -4℃,and 20g KOH in 50ml of deionized water was slowly added. After stirring for 1 hour, the solution of TsCl(220mg, 0.42mmol) in 50ml of distilled THF with ice-water bath was added dropwise into the mixture with continuous stirring for 2h. After adding,the solution was stirred for 8h under room temperature, the solution was poured into 100ml ice-water and extracted with DGM several times .The organic layer was collected dried over $MgSO_4$ and filtered , the filtrate was concentrated under reduced pressure and the anhydrous ether was added to obtain mPEG-OTs as white solid (15.6g, yield 74.2%).

M.P.35~37℃。

^{1}H-NMR (500 MHz, $CDCl_3$) δ (TMS, ppm): 7.69 (dd, *J* = 8.3, 3.4 Hz, 2H), 7.30-7.20 (m, 2H), 4.05 (s, 2H), 3.71-3.65 (m, 2H), 3.54 (d, *J* = 4.1 Hz, 180H), 3.27 (d, *J* = 3.6 Hz, 3H), 2.35 (d, *J* = 3.0 Hz, 3H).

(2) Into a 500ml three-necked round-bottom flask were added M**PEG-OTs** (15g, 7.1mmol), **K_2CO_3** (14.28g,120 mmol) and 300ml acetonitrile with stirring for a few minutes, then 4-Hydroxybenzaldehyde (1.3g, 10.65mmol) was added. After refluxing for 3 days under argon protection, the reaction mixture was cooled to room temperature,dissolved in DCM, washed with water and brine several times, dried over MgSO4 and filtered, the filtrate was concentrated under reduced pressure . The residue was poured into excess dry diethyl ether and stirred for a few minutes to give a white solid $\mathbf{M_2}$ (11,6g,yield: 77.3%). M.P.42~44℃。^{1}H-NMR (500 MHz, DMSO-d6) δ (TMS, ppm): 9.80 (s, 1H), 7.75 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 4.14 (t, *J* = 4.8 Hz, 2H), 3.81 (t, *J* = 4.8 Hz, 2H), 3.56 (s, 201H), 3.30 (s, 3H).

Synthesis of compound MPEG-Hyd-Br_2-BODIPY

Into a 500ml three-necked round-bottom flask were added hydrazine-Br2-BODIPY (0.3g, 0.55mmol), **M2**(1.1g,0.52mmol)was dissolved in 20ml of methanol. The solution was heated to 80℃,after the solution was stirred for 8h ,the mixture was poured into 100ml ice-water .Washing the solid three times with anhydrous diethyl ether and petroleum ether several times to obtain a red solid MPEG-Hyd-Br2-BODIPY.

^{1}H NMR (500 MHz, $CDCl_3$): δ (TMS, ppm): 9.59 (s, 1/2H, NH), 9.46 (s, 1/2H, NH), 8.23 (s, 1/2H), 7.85 (s, 1/2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.16 (qd, *J* = 7.4, 6.8, 3.5 Hz, 3H), 7.01- 6.89 (m, 3H), 5.22 (s, 1H), 4.75 (d, *J* = 2.6 Hz, 1H), 4.18 (dt, *J* = 5.0, 3.0 Hz, 2H), 3.88 (q, *J* = 4.2 Hz, 2H), 3.64 (d, *J* = 3.4 Hz, 202H), 3.38 (s, 3H), 2.61 (d, *J* = 2.9 Hz, 6H), 1.43 (d, *J* = 11.5 Hz, 6H).

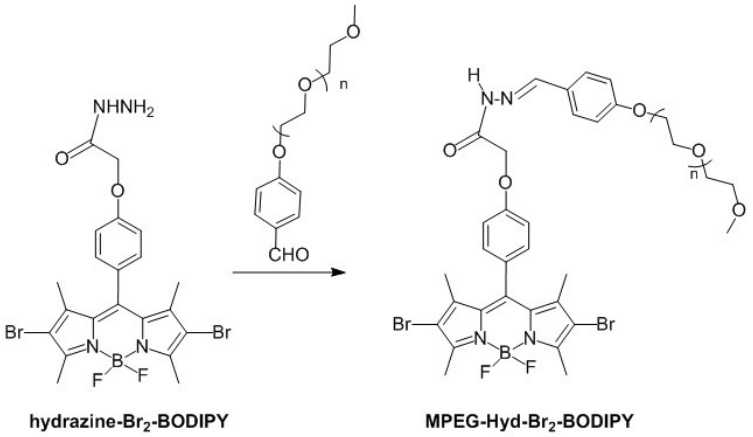


Fig. S3 Synthetic pathway of compound MPEG-Hyd-Br_2-BODIPY

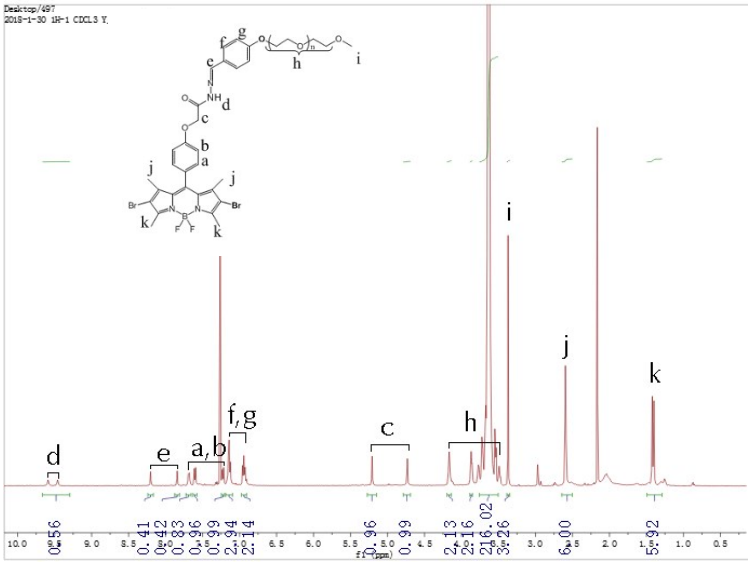


Fig.S4 ^{1}H NMR spectrum of MPEG-Hyd-Br_2-BODIPY in $CDCl_3$

Detection of Singlet Oxygen.

Generation of singlet oxygen can be usually detected by using chemical method using 1,3-diphenylisobenzofuran (DPBF). In our experiment, DPBF was chosen to monitor the release of singlet oxygen into solution. As this reactive species reacts with DPBF through a rapid Diels–Alder reaction, the decrease in DPBF absorbance indicates the decomposition of DPBF and the formation of singlet oxygen. The comparison of the rates of decay of DPBF, as monitored by the time-dependent decrease in absorbance at 417 nm, using DOX loaded MPEG-Hyd-Br_2-BODIPY nano micelles as the sensitizers.

50 µL of DPBF solution (2 mg mL-1) was mixed well with MPEG-hyd-Br_2-BODIPY nano micelles (0.5 mg mL^{-1}, 600 µL) and DOX loaded MPEG-Hyd-Br_2-BODIPY nano micelles (0.5 mg mL^{-1}, 600 µL) respectively and placed in a cuvette, respectively, whereas DPBF only in deionized water was used as control, and then irradiated using a light-emitting diode (LED, 400–450 nm) at a light power

density of 230 mW cm^{-2} for different periods of time. The absorption intensity of DPBF at 417 nm was monitored under different UV illumination periods.

Singlet oxygen yield

$$\phi_{\Delta(T)} = \phi_{\Delta\ (RB)}(S_T / S_{RB})(F_{RB} / F_T)$$

In the formula, the S is the slope of a straight line obtained by linearly fitting the ultraviolet absorption spectroscopy value of the DPBF at 410 nm after the irradiation time to the x-axis, and F is expressed by the irradiation time. The absorption correction factor of the test sample and the reference sample is expressed by the formula $F=1-10^{-OD}$, where OD represents the ultraviolet absorbance value of the compound at the irradiation wavelength. The formula with the subscript T in the formula indicates the relevant data of the test sample; the subscript RB in the formula represents the relevant parameters of the rose bengal and the test data. As can be seen from the related literature, the singlet oxygen yield of rose bengal in aqueous solution is 0.75.

Preparation of blank micelles and DOX-loaded micelles

Micelles were prepared by the dialysis method. 27 mg MPEG-Hyd-Br_2-BODIPY was dissolved in 5 mL aqueous solution (EtOH:H_2O, v:v, 2: 98). Then, water was added until the volume of the solution reached 10 mL to give the blank micelles.

27 mg MPEG-Hyd-Br_2-BODIPY, 7 mg DOX·HCl and 0.15 mL TEA were dissolved in an aqueous solution (EtOH:H_2O, v:v, 2: 98) and stirred for 4 h in the dark. Finally water was added until the volume of the solution reached 10 mL. The ultimate concentrations of DOX and MPEG-Hyd-Br_2-BODIPY were 0.01 mM, respectively. After standing overnight, the solution was dialyzed (molecular weight cut off 8000) against distilled water for 48 h to remove organic solvent and free DOX. The drug loading capacity was calculated according to the literature.[S1]

Drug release of drug loaded micelles in vitro

in vitro DOX release profile of **MPEG-Hyd-Br_2-BODIPY** micelles was studied by dialysis method at pH 5.0, 6.0 and 7.4, respectively. Briefly, 10 mL of DOX-loaded **MPEG-Hyd-Br_2-BODIPY** micelles solution was transferred into a dialysis tube (cutoff MW, 8000) that was immersed into 20 mL of PBS with different pH values. The dialysis tubes were incubated in an air bath with constant shaking at 37 °C. An aliquot (2 mL) of the buffered solutions was collected at the predetermined time points and then supplemented with the same volume of media. The released drug was determined by measuring the UV−vis absorbance of the solutions at 235 nm. All DOX-release experiments were conducted in triplicate and the results were expressed as the average data with standard deviations. 0.1 M tris-HCl (pH = 7.4) and 0.1 M citrate (pH = 6.0, 5.0) buffer solutions were used as dialysis media to simulate normal physiological conditions and the intracellular conditions of tumor.

Cell Uptake and Confocal Fluorescence Imaging.

Human breast cancer cell line (MCF-7 cells), and human cervical cancer cell lines (HeLa cells) were maintained following protocols provided by the American type Tissue Culture Collection. Cells were seeded at a density of 1×10^6 cells mL^{-1} in RPMI 1640 supplemented with 10% FBS, $NaHCO_3$ (2 g L^{-1}), and 1% antibiotics (penicillin/streptomycin, 100 U mL^{-1}). The cells were maintained in a humidified incubator at 37 °C, in 5% CO2/95% air. One day before imaging, cells were passed and plated on 18 mm glass bottom dishes. Cell imaging was carried out after washing cells with PBS for three times. Subsequently, the cells were treated with Hoechst 33342 (10 μg mL^{-1}) for 20 min to stain the nuclei. The cells were washed with PBS to remove extra dye molecules and then sealed

with a microscope glass slide. Observations were performed using a CLSM. The fluorescence signals of Hoechst 33342 (blue), and BODIPY (green) were detected with 405, and 510 nm excitation light, respectively. Confocal fluorescence imaging studies were performed with a ZEISS Laser Scanning Microscope (Zeiss LSM 710).

In Vitro Cytotoxicity Assay.

MTT (Tetrazolium-based standard 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay was carried out to investigate the dark toxicity and phototoxicity of MPEG-Hyd-Br_2-BODIPY nano micelles. MCF-7 cells and HeLa cells were first respectively seeded to two 96-well plates at a seeding density of 1×10^4 cells per well in 200 μL complete medium, which was incubated at 37 °C for 24 h. After rinsing with PBS, MCF-7 or HeLa cells were incubated with 200 μL culture media containing serial concentrations of MPEG-Hyd-Br_2-BODIPY nano micelles for 24 h. One plate was kept in the dark for studying dark toxicity, and another plate was irradiated using a 635 nm laser (Changchun Laser Optoelectronics Technology Co., Ltd., China) at a power of 230 mW cm^{-2} for 5 min. Afterward, the cells were grown for another 24 h. Then, 20 μL of 5 mg mL^{-1} MTT solution in pH 7.4 PBS was added to each well. After a 4 h incubation, the medium containing unreacted MTT was removed carefully, and 150 μL of DMSO was added to each well to dissolve the formazan crystals. After 1 h the absorbance (abs.) was measured at 490 nm in a TRITURUS microplate reader. The cell viability was then determined by the following equation: cell viability (%) = (mean of abs. value of treatment group/mean abs. value of control) × 100%. Calculation of the half lethal dose (IC50) values was done according to Huber and Koella.[S2]

General Procedure for UV-Vis and Fluorescence Studies

Stock solutions of metal ions were prepared (1×10^{-2} mol/L) in deionized water, A stock solution of compound **MPEG-Hyd-Br_2-BODIPY** were prepared (1×10^{-2} mol/L) in CH_3CH_2OH/H_2O (2:98, v/v) . A stock solution of compounds **MPEG-Hyd-Br_2-BODIPY,** Doxorubicin wrapped MPEG-Hyd-Br2-BODIPY and Adding acid doxorubicin to wrap **MPEG-Hyd-Br_2-BODIPY** (1×10^{-5} mol·L^{-1}) was prepared in H_2O immediately before the experiments. In experiments, each time a 2 mL solution of **MPEG-Hyd-Br_2-BODIPY** (10 μM) was filled in a quartz optical cell of 1 cm optical path length.

References

(S1) H. Wang, G. Liu, S. Dong, J. Xiong, Z. Dua and X. Cheng, *J. Mater. Chem. B*, 2015, **3**, 7401-7407.

(S2) Huber, W. Koella, J. C. *Acta Trop.* 1993, **55**, 257−261.

(S3) S. Intagliata, M. N. Modica, V. Pittalà, et al. *Bioorg. Med. Chem*., 2017, **25**(3):1250-1259.

(S4) H. Wang, G. Liu, S. Dong, J. Xiong, Z. Dua and X. Cheng, *J. Mater. Chem. B*, 2015, **3**, 7401-7407.

Drug loading efficiency

DLE (wt%)= (amount of loaded drug/total amount of miscelles) $\times$ 100%

Drug loading content

DLC (wt%)= (amount of loaded drug/total amount of feeding drug) $\times$ 100%

Absorption and Emission Spectra of compound MPEG-Hyd-Br_2-BODIPY

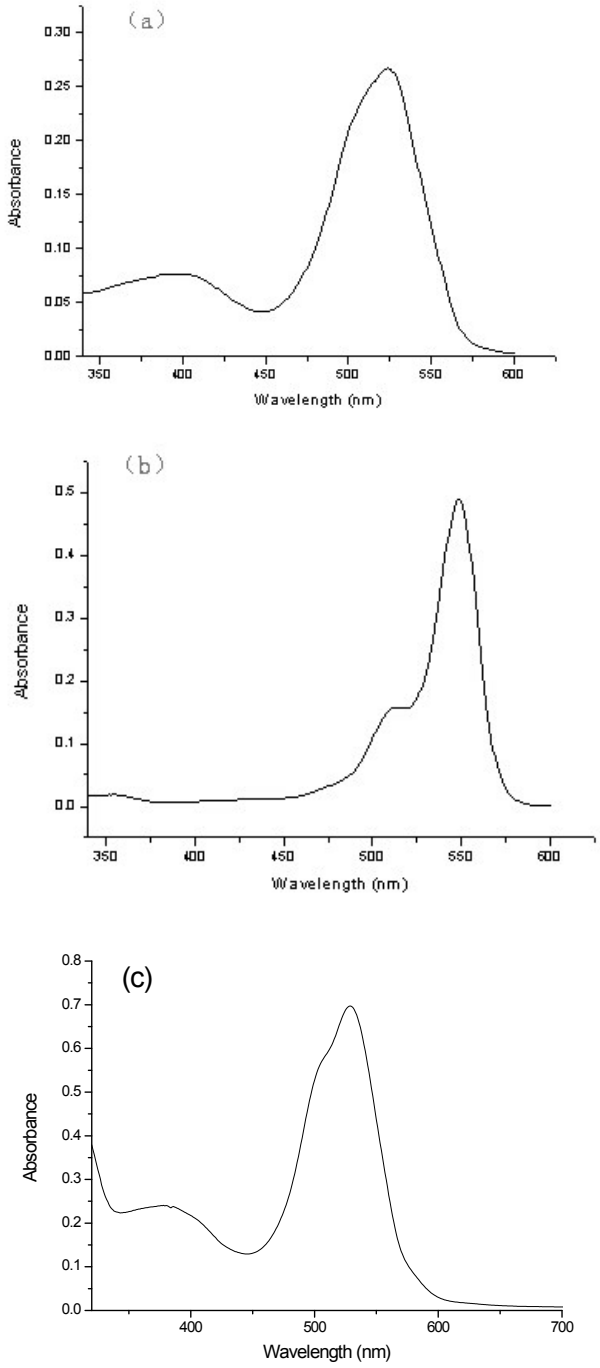


Fig. S5: (a) Absorbance of MPEG-Hyd-Br_2-BODIPY (10μM), (b) Absorbance of compound Rose Bengale (10μM) in CH_3CH_2OH/H_2O (2:98, v/v), (c) Absorbance of Doxorubicin wrapped MPEG-Hyd-Br_2-BODIPY (10μM) in CH_3CH_2OH/H_2O (2:98, v/v).

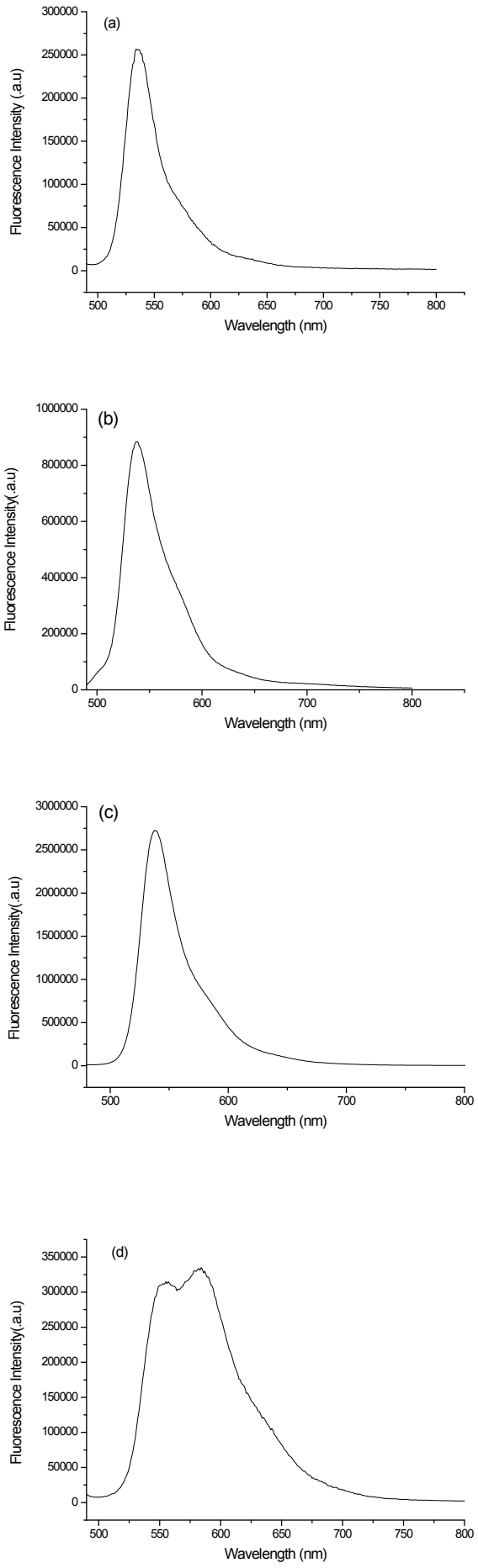
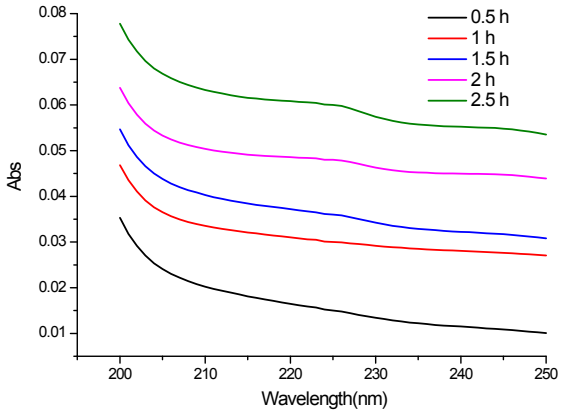


Fig. S6: (a) Fluorescence spectrum of MPEG-Hyd-Br_2-BODIPY(10 μ M), (b) Fluorescence spectrum of DOX-loaded MPEG-Hyd-Br_2-BODIPY(10 μ M), (c) Fluorescence spectra of DOX-loaded MPEG-Hyd-Br_2-BODIPY(10 μ M)(pH = 5.0), (d) Fluorescence spectra of DOX(10 μ M),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2.5 h
Abs
Wavelength(nm)

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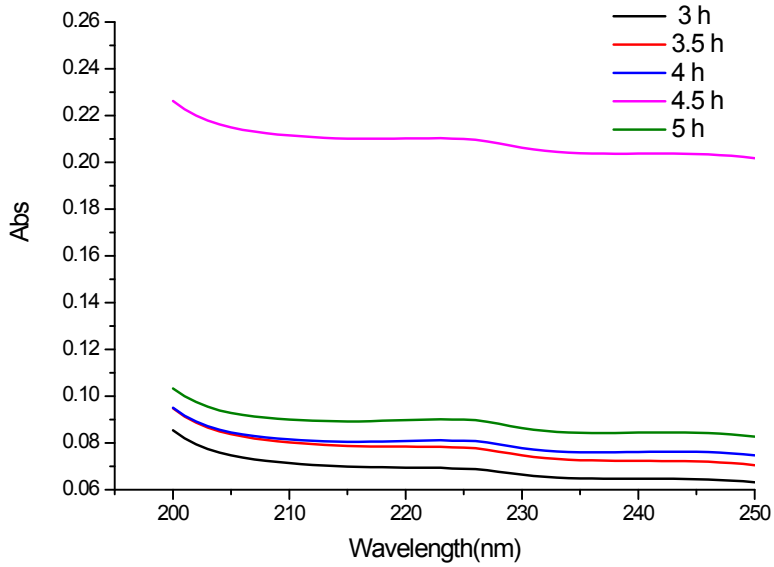
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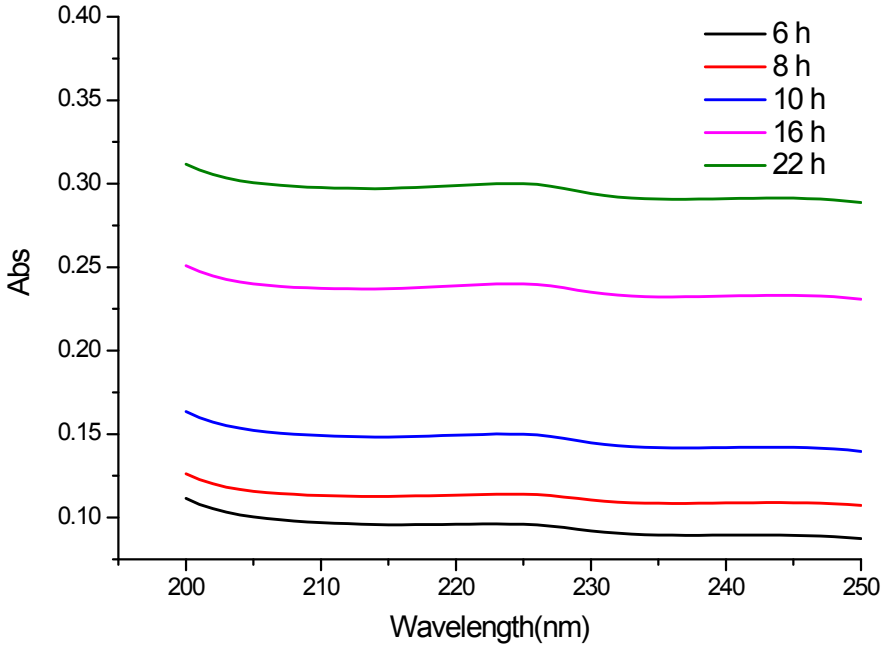
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10 h
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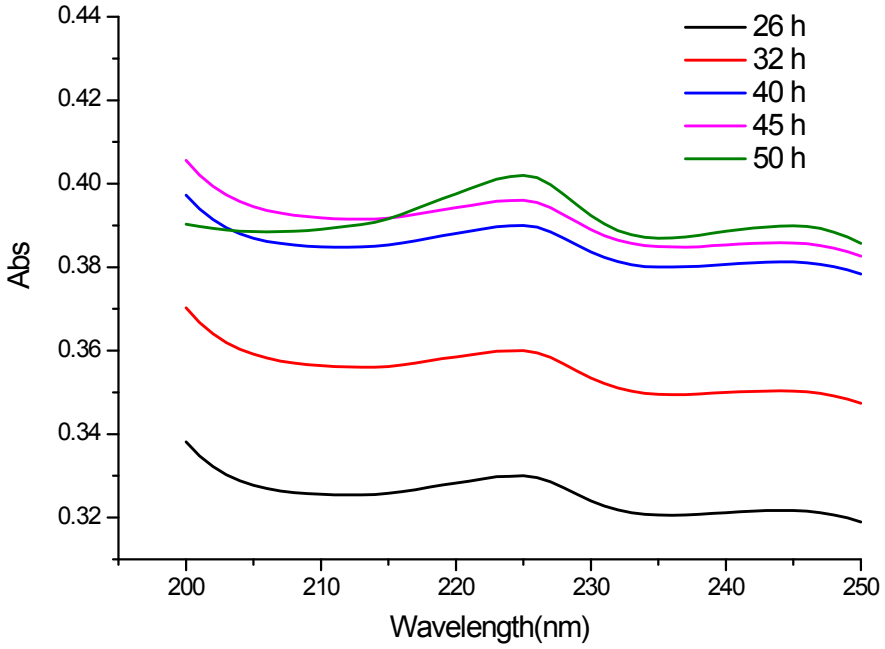
(c)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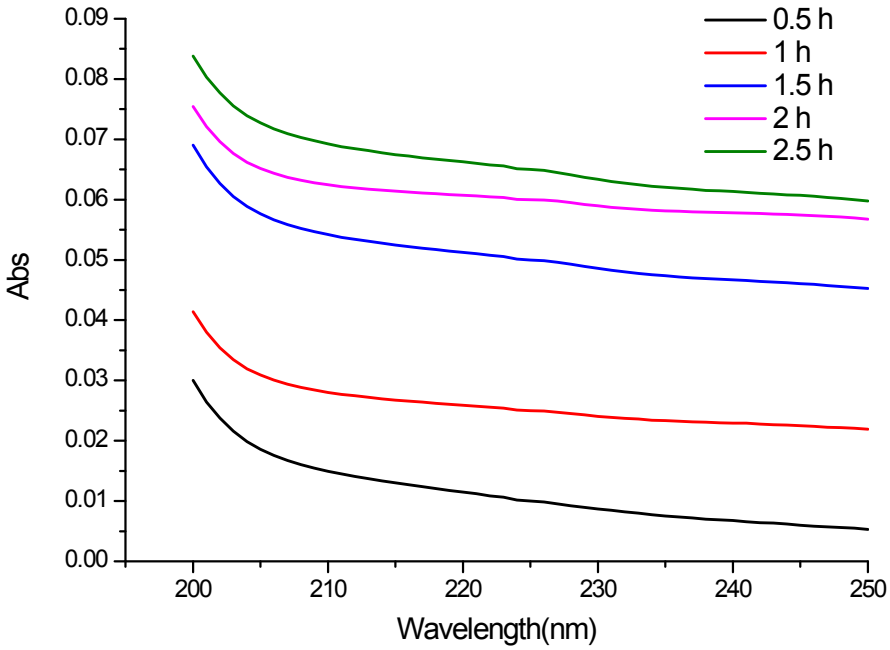
(d)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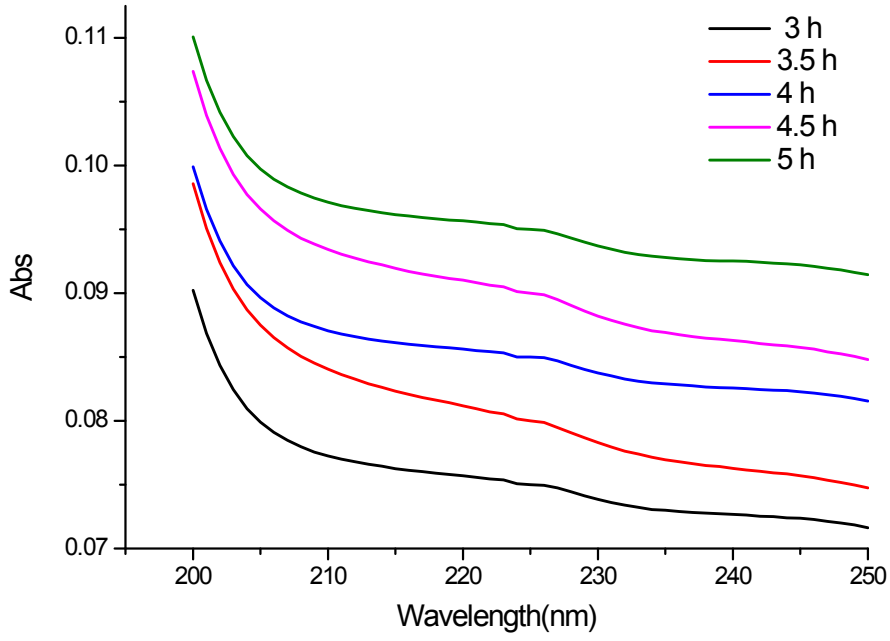
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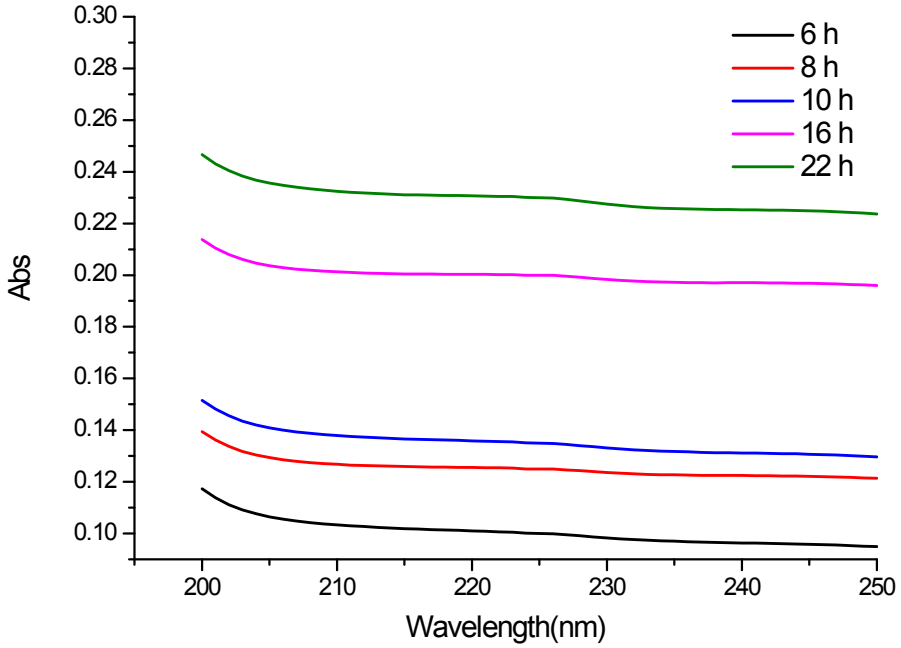
Wavelength(nm)

(f)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240
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Wavelength(nm)
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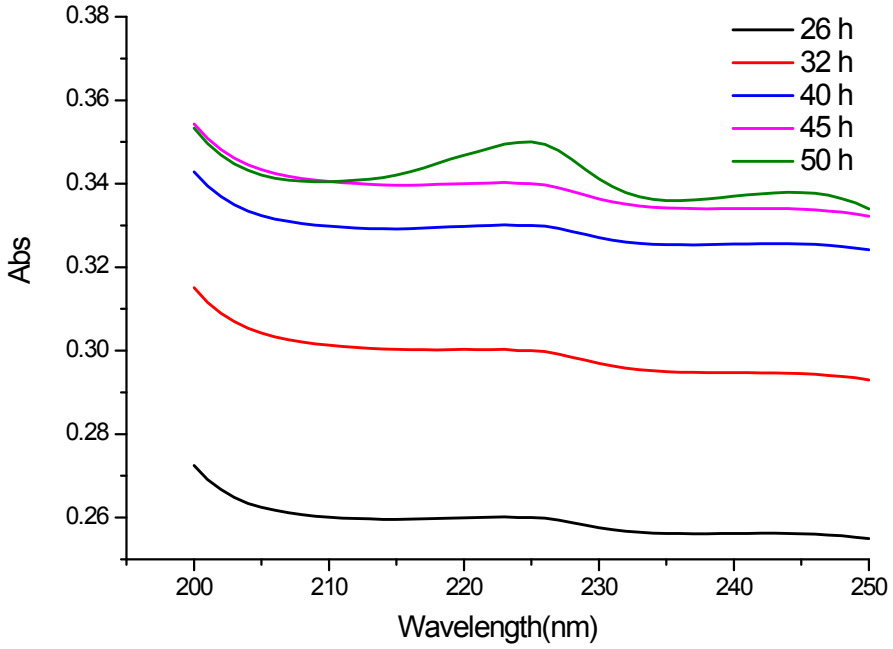
8 h
10 h
16 h
22 h

(g)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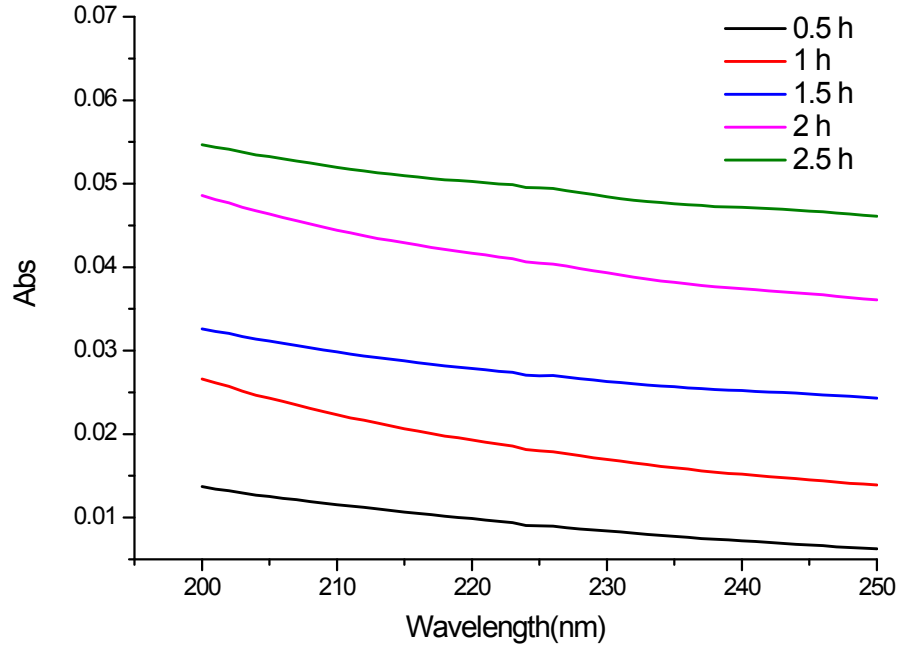
50 h

(h)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0.05
0.04
0.03
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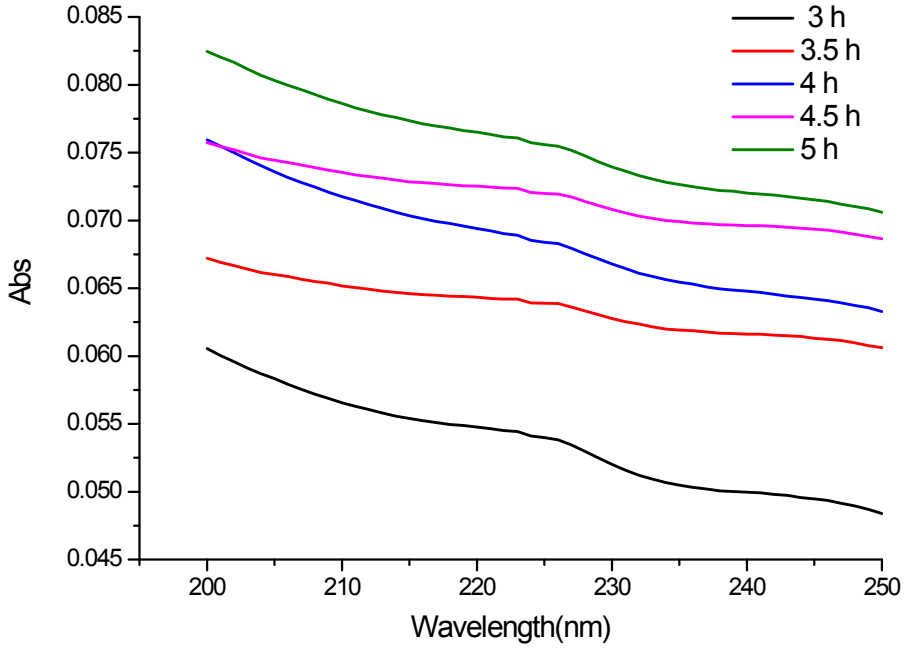
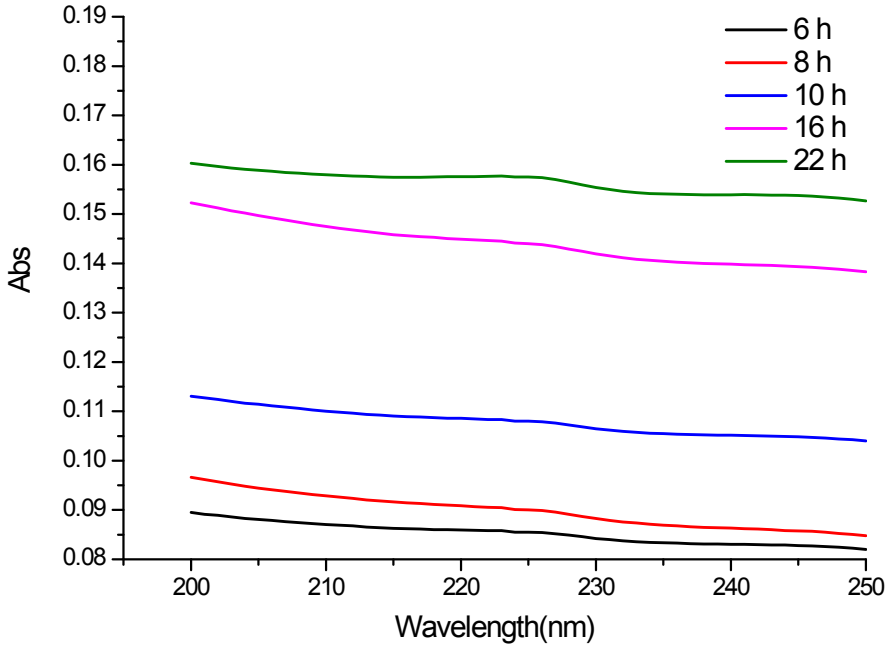
0.01
Abs
200
210
220
230
240
250
Wavelength(nm)
0.5 h
1 h
1.5 h
2 h
2.5 h

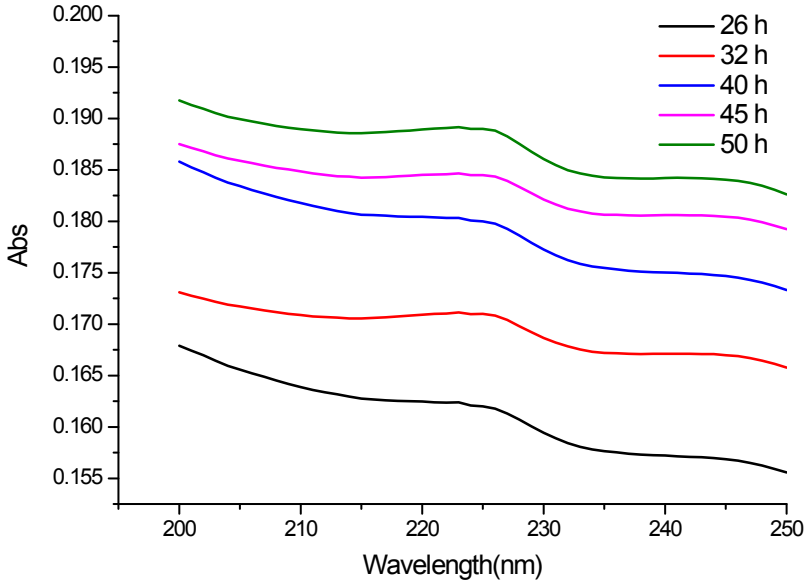
(i)


0.085
0.080
0.075
0.070
0.065
0.060
0.055
0.050
0.045
Abs
200
210
220
230
240
250
Wavelength(nm)
3 h
3.5 h
4 h
4.5 h
5 h

(j)



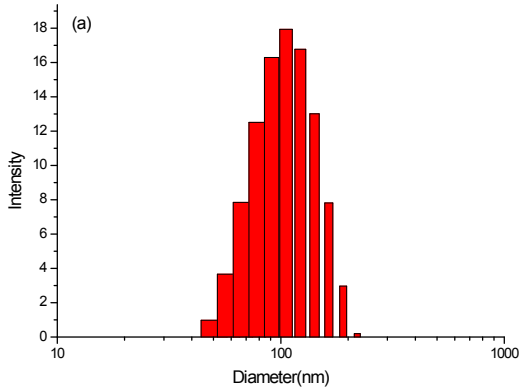
(k)

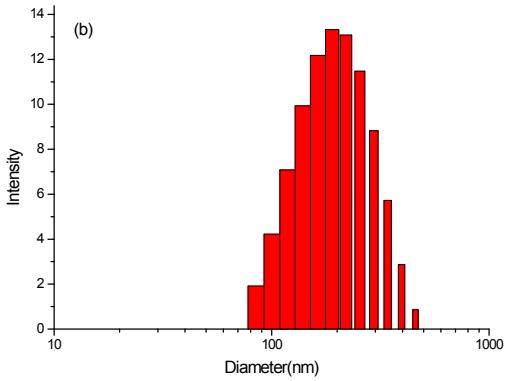


(l)

Figure S7. The UV-vis absorption spectra for the DOX release from DOX-loaded MPEG-Hyd-Br2-BODIPY micelles at ph =5.0(**a-d**), 6.0(**e-h**), and 7.4(**i-l**).

Diameter of MPEG-Hyd-Br2-BODIPY micelles &DOX-loaded MPEG-Hyd-Br_2-BODIPY micelles & DOX-loaded MPEG-Hyd-Br_2-BODIPY micelles at ph =5.0.





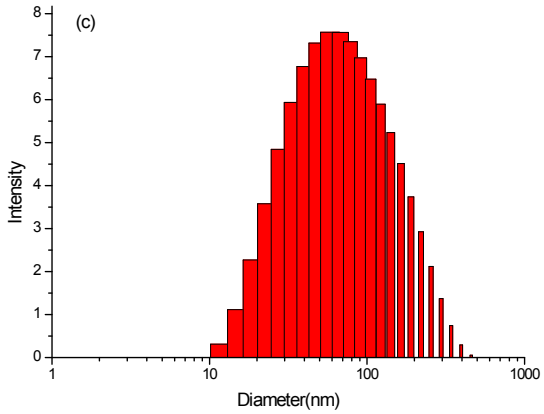
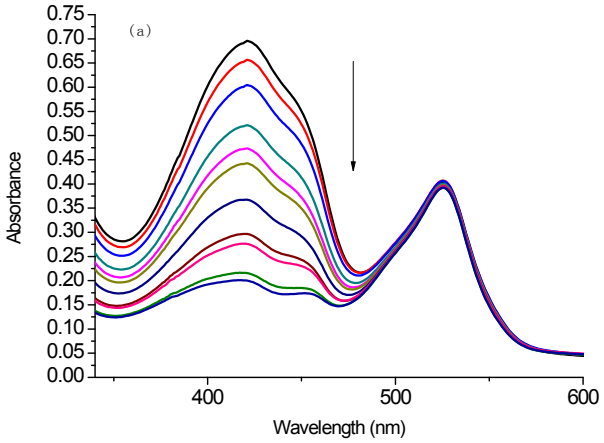
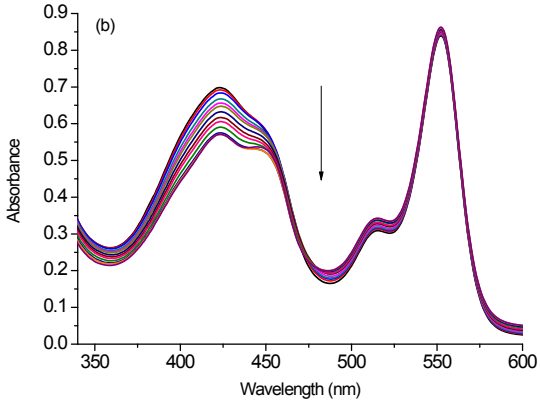
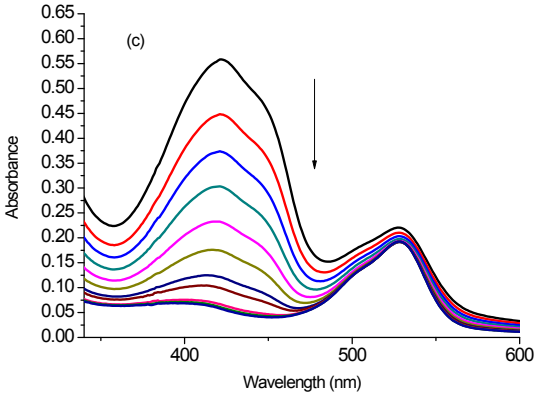


Figure S8. DLS data of the Diameter of, (a)MPEG-Hyd-Br_2-BODIPY,(b)Doxorubicin wrapped MPEG-Hyd-Br_2-BODIPY,(c)Adding acid doxorubicin to wrap MPEG-Hyd-Br_2-BODIPY aggregated practicle .

Singlet oxygen generation curve of photosensitizer in aqueous solution


(a)
Absorbance
Wavelength (nm)


(b)
Absorbance
Wavelength (nm)


(c)
Absorbance
Wavelength (nm)

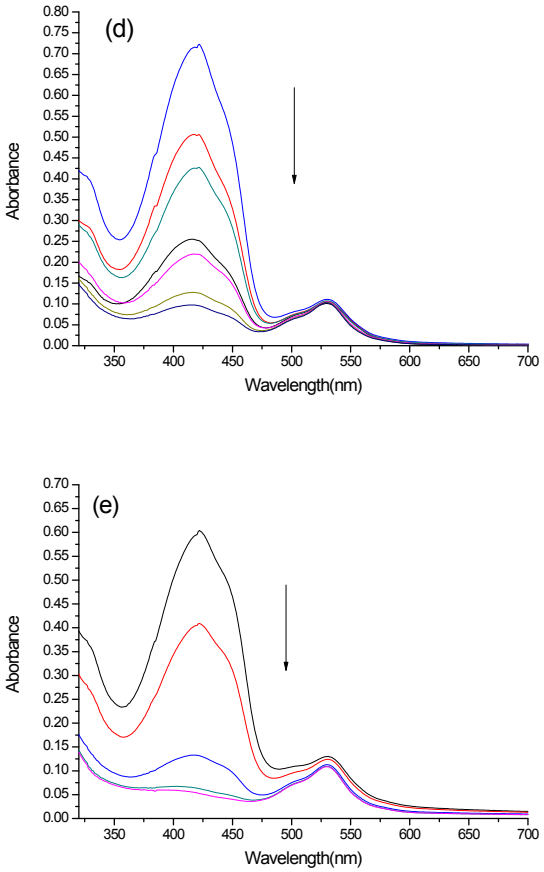
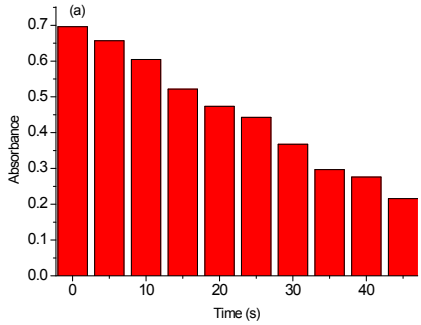
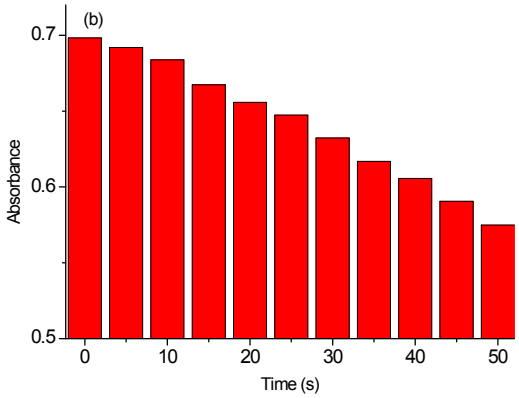
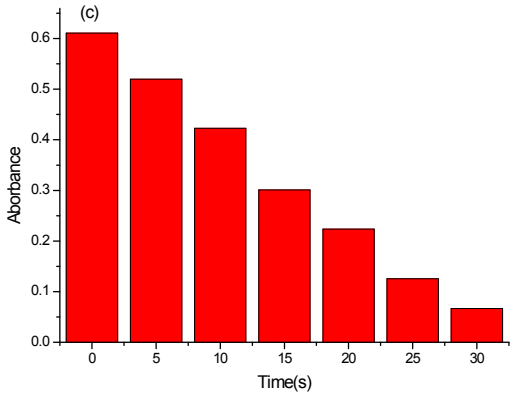


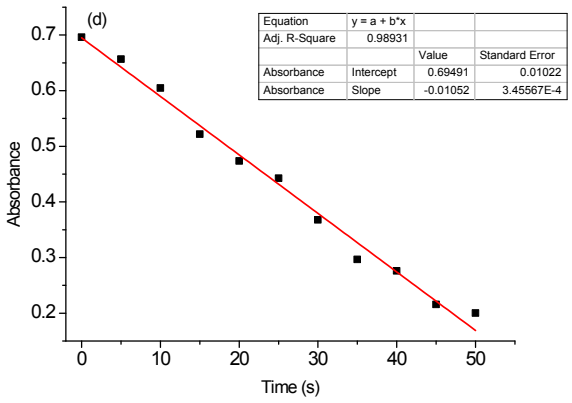
Fig. S9: (a) Time-dependent decrease of absorbance of DPBF(10 μ M) with MPEG-Hyd-Br_2-BODIPY (10 μ M) under 450 nm irradiation in CH_3CH_20H/H_2O (2:98, v/v), (b) Time-dependent decrease of absorbance of DPBF(10 μ M) with Rose Bengale (10μM) under 450 nm irradiation in CH_3CH_20H/H_2O (2:98, v/v), (c) Time-dependent decrease of absorbance of DPBF(10 μ M) with MPEG-Hyd-Br_2-BODIPY (10μM) under 450 nm irradiation in CH_3CH_20H/H_2O (2:98, v/v)(pH = 5.0), (d) Time-dependent decrease of absorbance of DPBF(10 μ M) with DOX-loaded MPEG-Hyd-Br_2-BODIPY (10μM) under 450 nm irradiation in CH_3CH_20H/H_2O (2:98, v/v) , (e) Time-dependent decrease of absorbance of DPBF(10 μ M) with DOX-loaded MPEG-Hyd-Br_2-BODIPY (10μM) under 450 nm irradiation in CH_3CH_20H/H_2O (2:98, v/v) (pH = 5.0) ,the irradiation wavelength was 450 nm, the irradiation time was 5 s, and the interval was 2 min.

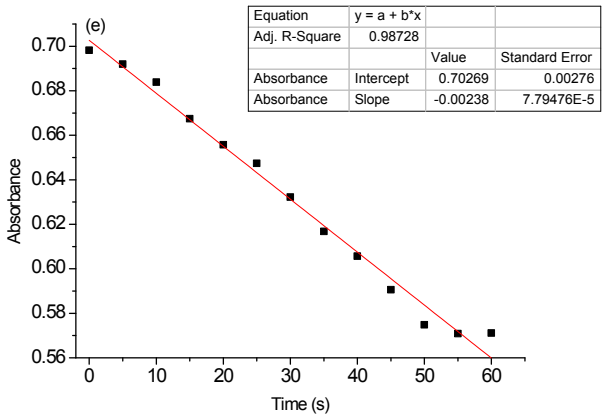
UV maximum absorption value change of DPBF chart of MPEG-Hyd-Br_2-BODIPY and Rose Bengale under light irradiation.




(b)
Absorbance
0.7
0.6
0.5
0
10
20
30
40
50
Time (s)


(c)
Aborbance
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
5
10
15
20
25
30
Time(s)


(d)
Equation y = a + b*x
Adj. R-Square 0.98931
Value Standard Error
Absorbance Intercept 0.69491 0.01022
Absorbance Slope -0.01052 3.45567E-4
Absorbance
0.7
0.6
0.5
0.4
0.3
0.2
0
10
20
30
40
50
Time (s)


(e)
Equation y = a + b*x
Adj. R-Square 0.98728
Value Standard Error
Absorbance Intercept 0.70269 0.00276
Absorbance Slope -0.00238 7.79476E-5
Absorbance
0.70
0.68
0.66
0.64
0.62
0.60
0.58
0.56
0
10
20
30
40
50
60
Time (s)

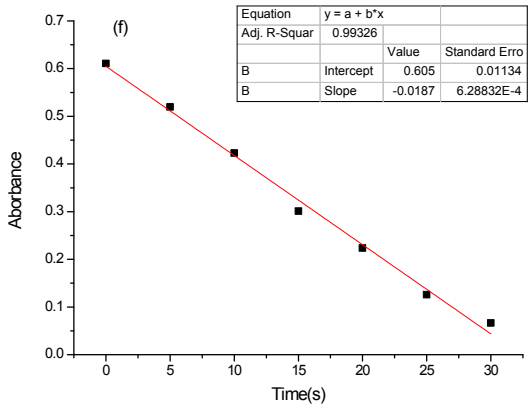


Fig. S10: (a)-(c) Time dependent decrease in DPBF absorption as a function of illumination time, corresponding to (a), (b) and (d) in Fig. S6 respectively. (d)-(f) Decay curves of DPBF absorption at 410 nm as a function of illumination time, corresponding to (a), (b) and (d) in Fig. S6 respectively.

^{1}H NMR、^{13}C NMR and MS spectrum

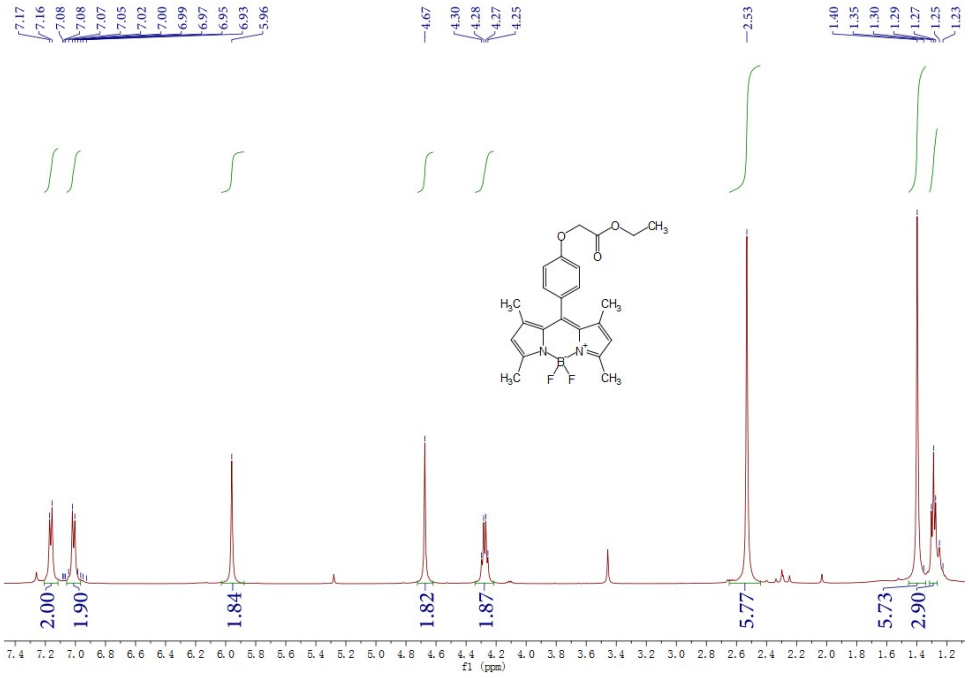


Figure S11: ^{1}H NMR spectrum of compound BODIPY-AcOEt in $CDCl_3$

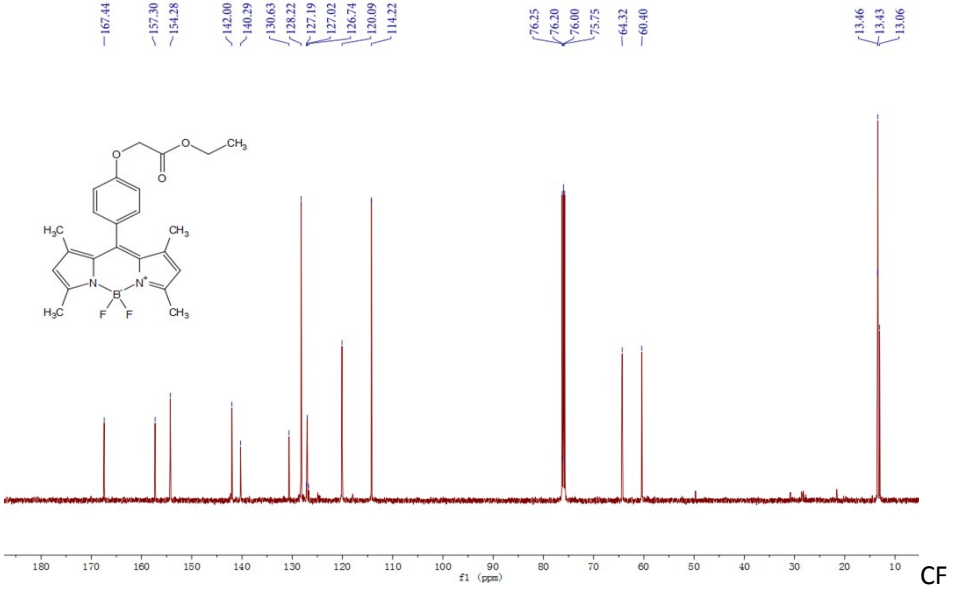


Figure S12:^{13}C NMR spectrum of compound BODIPY-AcOEt in $CDCl_3$

Br2-BODIPY-AcOEt

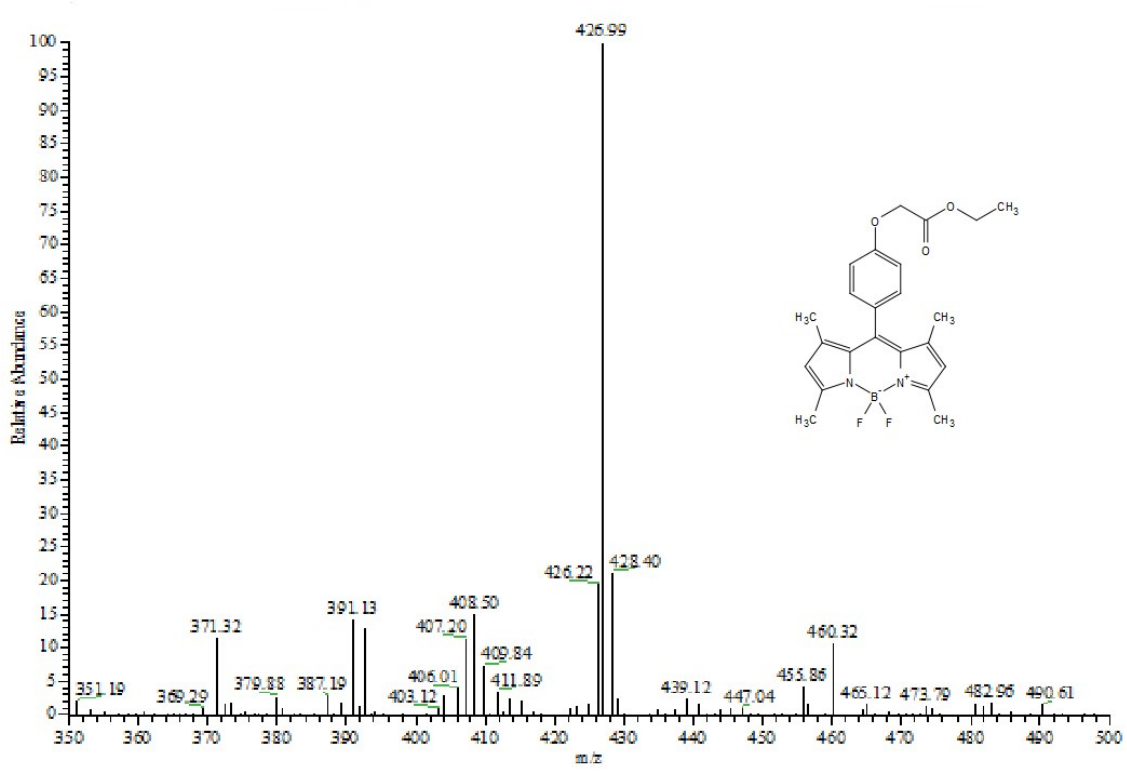


Figure S13:MS spectrum of compound BODIPY-AcOEt

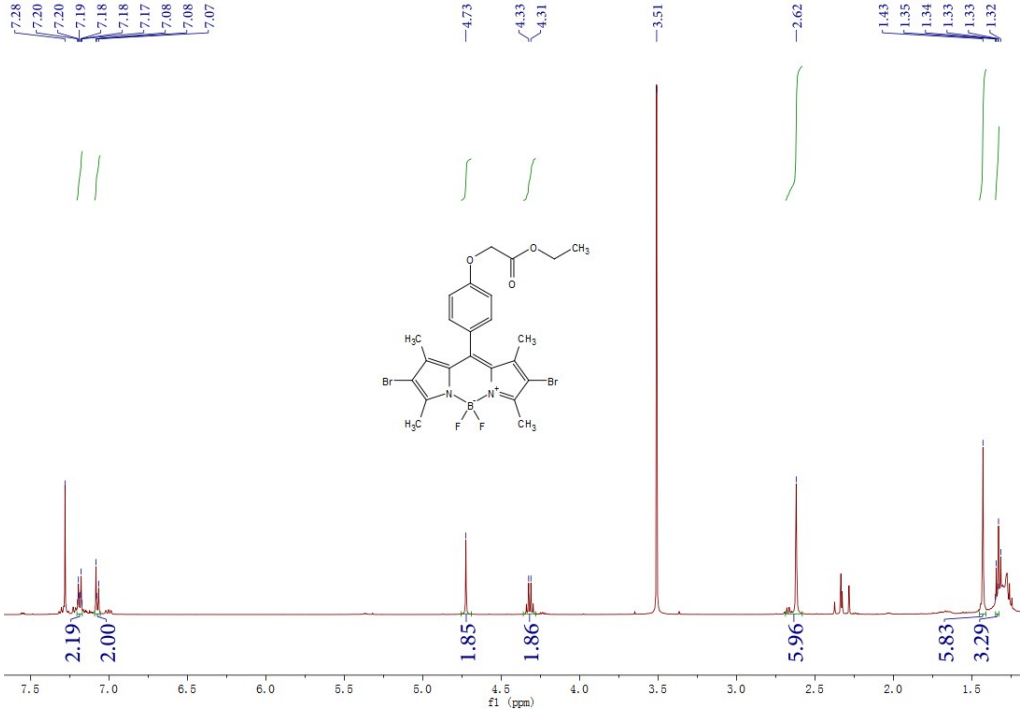


Figure S14:^{1}H NMR spectrum of compound Br_2-BODIPY-AcOEt in DMSO

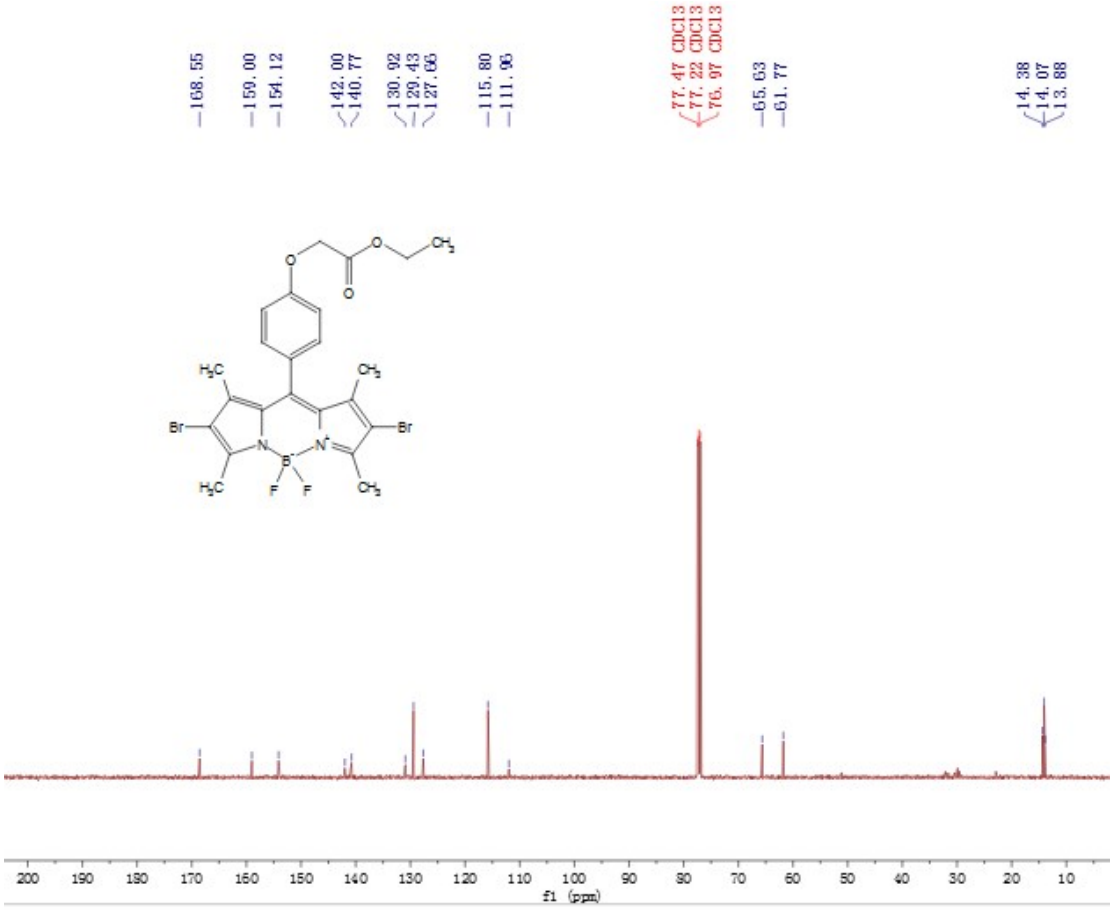


Figure S15:^{13}C NMR spectrum of compound Br_2-BODIPY-AcOEt in $CDCl_3$

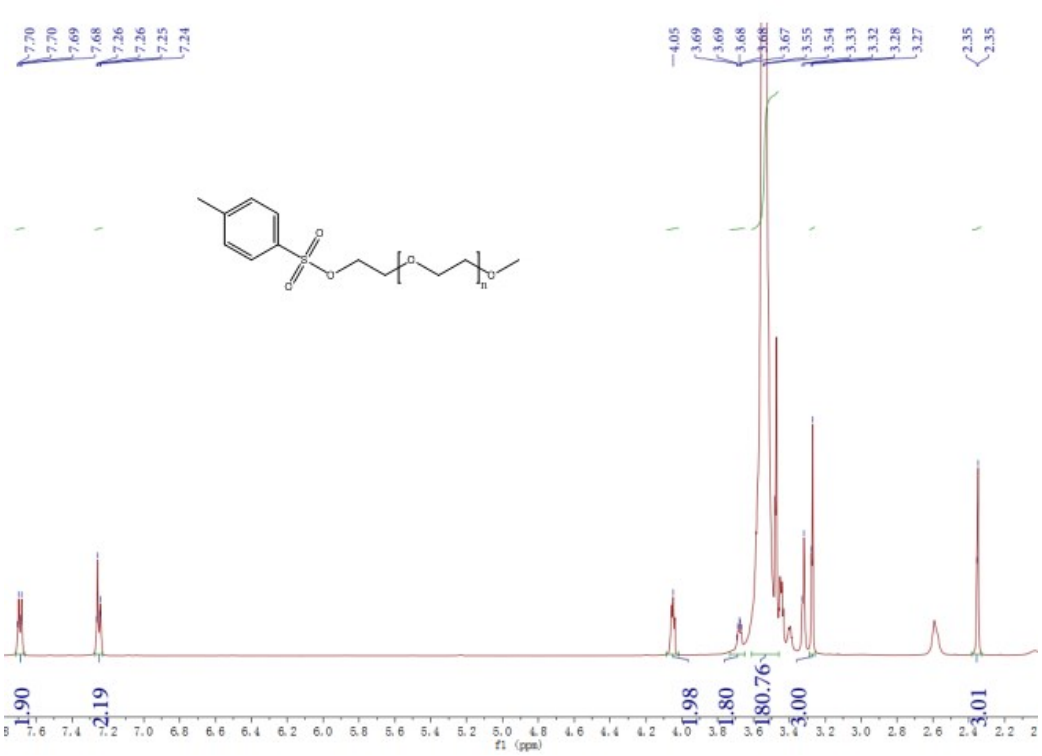


Figure S16:[1H] NMR spectrum of compound oPEG-OTs in $CDCl_3$

Figure S17:[1]H NMR spectrum of compound M_2 in $CDCl_3$