Supporting information

Peripheral Tailoring of Pentacene: Developing Next-Generation Organic Sonosensitizers for Cancer Sonodynamic Therapy

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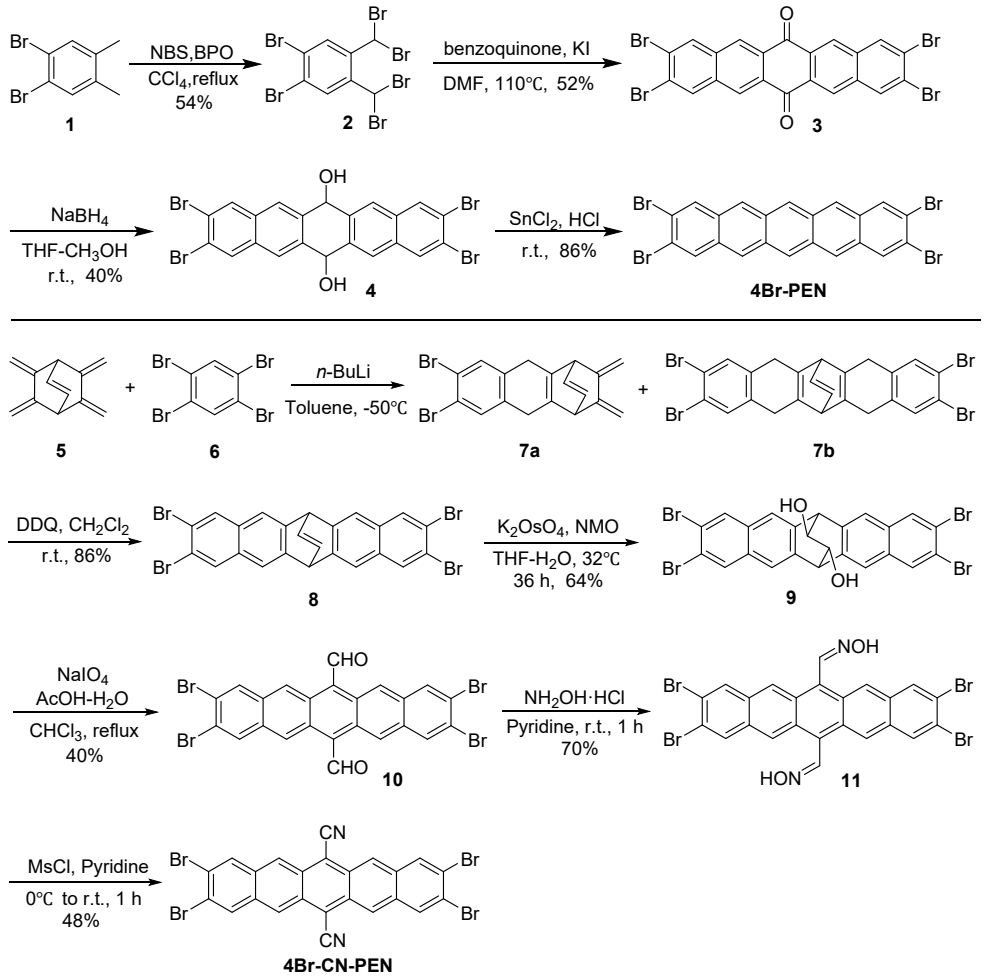
contents:

1. Instruments

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Avance-III DRX spectrometer operating at 500 MHz and 126 MHz respectively. The FTIR analyses were measured by a Thermo-Fisher NICOLETIS20 Fourier transform infrared spectroscopy. The UV-Vis spectra were measured by a Thermo-Fisher Evolution 220 UV-Vis spectrophotometer. The ESR spectra were measured by a Bruker EMXplus-9 electron paramagnetic resonance (EPR) spectrometer. The fluorescence spectra were scanned with an excitation wavelength of 500 nm using a Hamamatsu Quantaurus-Tau fluorescence lifetime spectrometer. MTT assays were performed on a microplate reader (Tecan Group). Fluorescent images were taken by an inverted fluorescence microscope (Nikon Instruments, Japan).

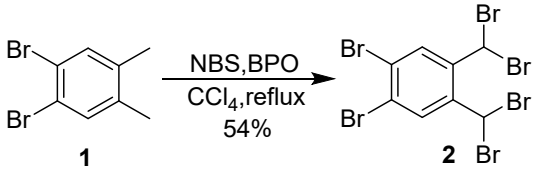
Female BALB/c mice were purchased from Nanjing Qinglongshan Experimental Animal Center. Mice used in experiments were 6-8 weeks old. All animal experiments were performed in accordance with the National Institute of Health Guidelines under the protocols approved by the Animal Ethical and Welfare Committee of Nanjing University of Science and Technology (Approval No: AUCU-NUST2023012).

2. Experimental section



Scheme 1 The synthetic route of 4Br-PEN and 4Br-CN-PEN

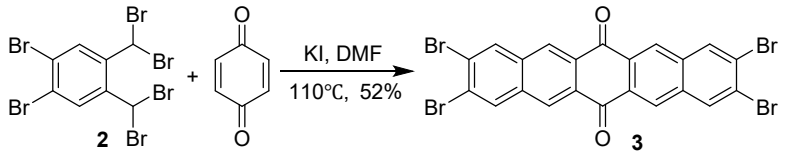
Synthesis of α,α,α', α',4,5-hexabromo-*o*-xylene (2)



To a 500 mL three-necked flask were sequentially added 1,2-dibromo-4,5-dimethylbenzene (2 g, 7.58 mmol), benzoyl peroxide (BPO, 0.06 g, 0.23 mmol), and *N*-bromosuccinimide (NBS, 2.7 g, 15.16 mmol). The system was purged with nitrogen, followed by the addition of 180 mL of anhydrous carbon tetrachloride. The mixture was then gradually heated to reflux under a nitrogen atmosphere and maintained for 4 h. After cooling to room temperature, additional BPO (0.06 g, 0.23 mmol) and NBS (2.7 g, 15.16 mmol) were introduced into the reaction mixture under nitrogen. The mixture was reheated to reflux and stirred for 24 h. Upon completion, the mixture was cooled to room temperature and filtered to remove the generated succinimide byproduct. The filter cake was washed three times with dichloromethane (3×20 mL). The combined filtrate was sequentially washed with saturated sodium thiosulfate solution (3×30 mL) and deionized water (3×30 mL), then

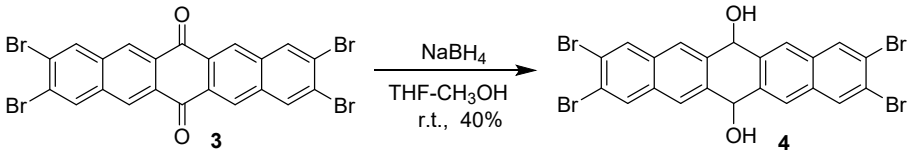
dried over anhydrous sodium sulfate. After filtration, the solution was concentrated under reduced pressure using a rotary evaporator to afford the crude product. Purification by column chromatography (eluent: petroleum ether) yielded 2.38 g of a white solid, corresponding to a 54% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ = 7.92 (s, 2H), 6.97 (s, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ = 140.76, 134.85, 126.60, 34.21.

Synthesis of 2,3,9,10-tetrabromopentacene-6,13-dione (3)



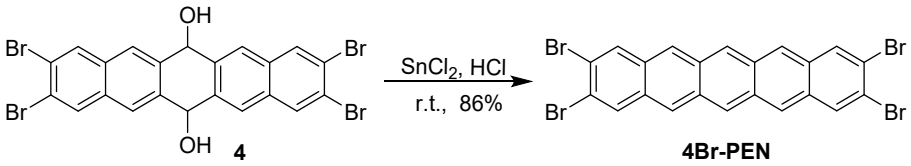
Into a 250 mL reaction flask were sequentially added α,α,α',α',4,5-hexabromo-*o*-xylene (3.5 g, 6.02 mmol), 1,4-anthraquinone (0.66 g, 3.16 mmol), potassium iodide (KI, 7.87 g, 48.16 mmol), and anhydrous *N*,*N*-dimethylformamide (DMF, 70 mL). The reaction mixture was slowly heated to 110 °C under a nitrogen atmosphere and maintained at this temperature for 20 h. After completion, the mixture was cooled to 0 °C and filtered. The filter cake was successively washed with deionized water (3×20 mL), methanol (3×20 mL), and chloroform (3×20 mL) until the filtrate became clear. The collected solid was dried under vacuum to afford 0.98 g of a brown solid (52% yield). However, due to the poor solubility of the product, NMR characterization could not be performed, and the material was directly used in the subsequent reaction. IR (υ cm^{-1}): 3057, 1678, 1595, 1426, 1273, 1095, 989, 940, 728.

Synthesis of 2,3,9,10-tetrabromo-6,13-dihydropentacene-6,13-diol (4)



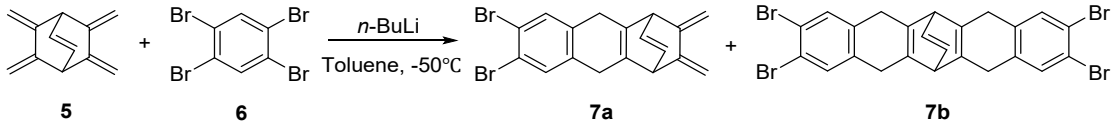
A 250 mL single-necked flask was charged with 2,3,9,10-tetrabromopentacene-6,13-dione (0.5 g, 0.8 mmol), followed by the addition of tetrahydrofuran (THF, 50 mL) and methanol (MeOH, 35 mL). The reaction flask was then cooled in an ice bath, and sodium borohydride ($NaBH_4$, 0.15 g, 4.03 mmol) was added portionwise. After complete addition, the ice bath was removed, and the reaction mixture was stirred at room temperature under a nitrogen atmosphere for 20 h. Upon reaction completion, the mixture was cooled again in an ice bath, and glacial acetic acid was added dropwise to quench the reaction. Gas evolution ceased after approximately 10 min. The resulting suspension was filtered to remove insoluble solids, and the filtrate was washed with saturated sodium bicarbonate solution (3×30 mL). The organic phase was concentrated under reduced pressure using a rotary evaporator to yield the crude product. Purification by column chromatography (eluent: ethyl acetate) afforded 0.2 g of a white solid, corresponding to a 40% yield. ^{1}H NMR (500 MHz, chloroform-*d*) δ = 8.48-8.46 (m, 4H), 8.14-8.10 (m, 4H), 6.31-6.28 (m, 2H), 6.00-5.97 (m, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ = 140.51, 132.66, 132.56, 124.03, 121.48, 69.32.

Synthesis of 2,3,9,10-tetrabromopentacene (4Br-PEN)



A 100 mL single-necked flask was charged with 2,3,9,10-tetrabromo-6,13-dihydropentacene-6,13-diol (0.27 g, 0.44 mmol), followed by the addition of tetrahydrofuran (THF, 40 mL) and methanol (MeOH, 10 mL). Under light exclusion, a saturated solution of stannous chloride ($SnCl_2$) in dilute hydrochloric acid (10 mL) was introduced directly into the reaction flask. The mixture was stirred for 30 min at room temperature. After completion, the reaction mixture was filtered, and the filter cake was successively washed with deionized water (3×20 mL), methanol (3×20 mL), ethanol (3×20 mL), and dichloromethane (DCM, 3×20 mL) until the filtrate became clear. The collected solid was dried under vacuum in the dark, yielding 0.22 g of a bluish-purple solid (86% yield). Due to the poor solubility of the product, solid-state NMR spectroscopy was instead conducted for characterization. ^{13}C (CP-MAS) NMR, δ (ppm): 120-135. IR (υ cm^{-1}): 3130, 1612, 1564, 1465, 1075, 938, 907, 659.

Synthesis of 6,7-Dibromo-11,12-dimethylene-1,4,9,10-tetrahydro-1,4-ethenoanthracene (7a) and 2,3,9,10-tetrabromo-5,6,7,12,13,14-hexahydro-6,13-ethenopentacene (7b)



5,6,7,8-tetramethylenebicyclo[2.2.2]oct-2-ene was synthesized with a yield of 26% through four steps according to the reference literature [1-4].

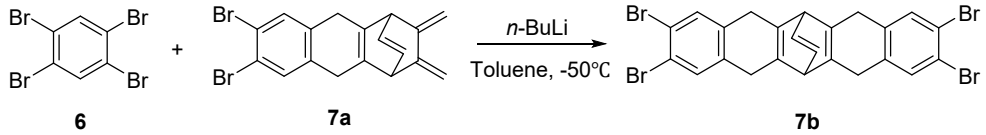
A 250 mL three-necked flask was charged with 5,6,7,8-tetramethylenebicyclo[2.2.2]oct-2-ene (0.6 g, 3.84 mmol) and 3.0 equivalents of 1,2,4,5-tetrabromobenzene (4.54 g, 11.52 mmol). Dry and degassed toluene (80 mL) was added, and the reaction system was purged with nitrogen before being transferred to a cryogenic reactor at −50 °C. A solution of *n*-butyllithium (*n*-BuLi, 1.6 M in hexane, 7.5 mL) was added dropwise to the mixture. After complete addition, the reaction was maintained at low temperature for 3 h. Subsequently, the mixture was allowed to warm gradually to room temperature and stirred overnight. The reaction was quenched by adding water, followed by extraction with ethyl acetate (3×50 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford the crude product. Purification via column chromatography yielded two distinct fractions:

6,7-Dibromo-11,12-dimethylene-1,4,9,10-tetrahydro-1,4-ethenoanthracene (**7a**): Eluted with petroleum ether to give 0.12 g of a white solid (8% yield). ^1H NMR (500 MHz, chloroform-*d*) δ = 7.37 (s, 2H), 6.49-6.47 (m, 2H), 5.09 (s, 2H), 4.87 (s, 2H), 3.95 (t, *J* = 3.8 Hz, 2H), 3.46 (dd, *J* = 4.3, 2.1 Hz, 4H). ^{13}C NMR (126 MHz, chloroform-*d*) δ = 143.63, 135.24, 133.67, 133.47, 133.45, 121.58, 102.06, 52.16, 30.91.

2,3,9,10-Tetrabromo-5,6,7,12,13,14-hexahydro-6,13-ethenopentacene (**7b**): Eluted with petroleum ether/ethyl acetate (300:1, *V*/*V*) to afford 0.91 g of an off-white solid (38% yield). ^1H

NMR (500 MHz, chloroform-*d*) δ = 7.36 (s, 4H), 6.84 (dd, *J* = 4.2, 3.0 Hz, 2H), 4.28 (dd, *J* = 4.1, 3.0 Hz, 2H), 3.51 (d, *J* = 1.4 Hz, 8H). ^{13}C NMR (126 MHz, chloroform-*d*) δ = 139.86, 139.29, 135.42, 133.45, 121.59, 53.84, 32.39.

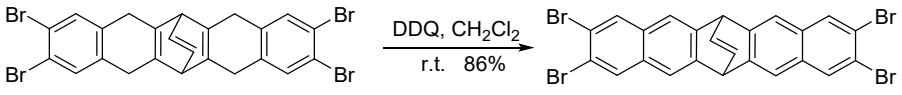
Synthesis of 2,3,9,10-tetrabromo-5,6,7,12,13,14-hexahydro-6,13-ethenopentacene (7b) from 7a



6 **7a** **7b**

A 250 mL three-necked flask was charged with 6,7-dibromo-11,12-dimethylene-1,4,9,10-tetrahydro-1,4-ethenobridged anthracene (**7a**, 0.4 g, 1.03 mmol) and 1,2,4,5-tetrabromobenzene (0.44 g, 1.13 mmol), followed by the addition of dry and degassed toluene (30 mL). The reaction system was purged with nitrogen and transferred to a cryogenic reactor at -50 °C. A solution of *n*-BuLi (1.6 M in hexane, 0.75 mL) was added dropwise to the mixture. After complete addition, the reaction was maintained at low temperature for 3 h, then gradually warmed to room temperature and stirred overnight. The reaction was quenched with water, and the mixture was extracted with ethyl acetate (3×30 mL). The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford the crude product. Purification by column chromatography (eluent: petroleum ether/ethyl acetate, 300:1, *V*/*V*) yielded compound **7b** as an off-white solid (0.27 g, 42% yield).

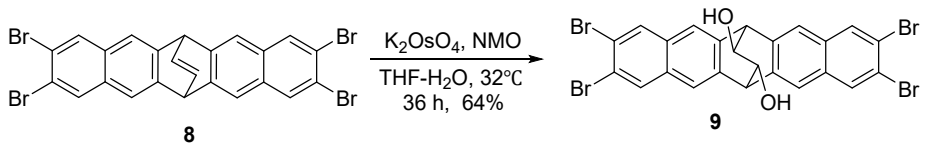
Synthesis of 2,3,9,10-tetrabromo-6,13-dihydro-6,13-ethenopentacene (8)



7b **8**

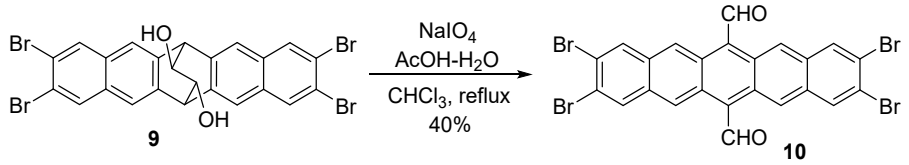
A 100 mL three-necked flask was charged with 2,3,9,10-tetrabromo-5,6,7,12,13,14-hexahydro-6,13-ethenobridged pentacene (**7b**, 0.4 g, 0.64 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.42 g, 1.92 mmol). The mixture was dissolved in dichloromethane (22 mL) and stirred at 28 °C for 24 h under a nitrogen atmosphere. Upon completion, the reaction mixture was filtered, and the filtrate was treated with saturated sodium bicarbonate solution to neutralize residual 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. The aqueous layer was extracted with DCM (3×50 mL), and the combined organic phase was dried over anhydrous sodium sulfate. After filtration, the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (eluent: petroleum ether/ethyl acetate, 200:1, *V*/*V*) yielded compound **8** as an off-white solid (0.34 g, 86% yield). ^{1}H NMR (500 MHz, chloroform-*d*) δ = 7.98 (s, 4H), 7.57 (s, 4H), 7.01 (dd, J = 4.4, 3.0 Hz, 2H), 5.29 (t, J = 3.7 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ = 143.03, 137.90, 131.74, 131.52, 121.63, 120.39, 49.96.

Synthesis of 2,3,9,10-tetrabromo-6,13-dihydro-6,13-ethanopentacene-15,16-diol (9)



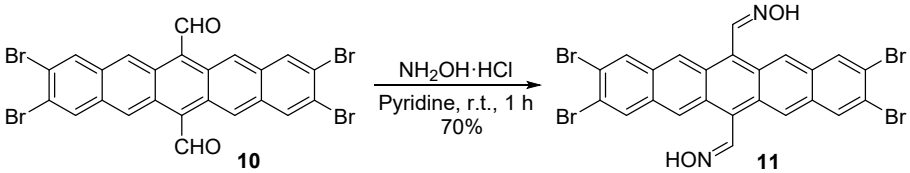
A 100 mL three-necked flask was charged with 2,3,9,10-tetrabromo-6,13-dihydro-6,13-ethenopentacene (0.5 g, 0.81 mmol), followed by the addition of tetrahydrofuran (15 mL) to dissolve the substrate. A solution of 4-methylmorpholine N-oxide (0.57 g, 4.86 mmol) in water (6 mL) was then introduced into the flask, followed by the addition of potassium osmate monohydrate (13 mg, 0.04 mmol) dissolved in water (5 mL). The reaction mixture was purged with nitrogen and stirred at 32 °C for 36 h. Upon completion, saturated sodium thiosulfate solution was added to quench excess oxidant. The mixture was extracted with dichloromethane (3×20 mL), and the combined organic phase was dried over anhydrous sodium sulfate. After filtration, the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (eluent: petroleum ether/ethyl acetate, 2:1, *V*/*V*) yielded 3.14 as an off-white solid (0.29 g, 54% yield).^{1}H NMR (500 MHz, DMSO-d_6) δ = 8.33-8.27 (m, 4H), 7.85 (dt, J = 21.5, 4.2 Hz, 4H), 4.86 (d, J = 6.4 Hz, 2H), 4.61-4.59 (m, 2H), 4.04 (d, J = 6.2 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ = 139.38, 132.36, 132.17, 124.00, 120.57, 67.37, 51.43.

Synthesis of 2,3,9,10-tetrabromopentacene-6,13-dicarbaldehyde (10)



2,3,9,10-Tetrabromo-6,13-dihydro-6,13-ethanopentacene-15,16-diol (0.58 g, 0.89 mmol) was charged into a 500 mL three-necked flask. Chloroform (110 mL) was added, followed by a solution of sodium periodate (0.19 g, 0.89 mmol) dissolved in 40 mL of water and 0.1 mL acetic acid. The reaction system was refluxed at 70 °C under a nitrogen atmosphere for 10 h. After completion, the precipitated green solid was collected by centrifugation and repeatedly washed with water, ethanol, and dichloromethane. The product was vacuum-dried under protection from light to afford 0.23 g of pure green solid (40% yield). Due to poor solubility, NMR characterization was not feasible, and the obtained solid was directly used in subsequent reactions. IR (υ cm^{-1}): 3065, 1673, 1561, 1420, 1277, 1177, 1082, 991, 945, 895, 783.

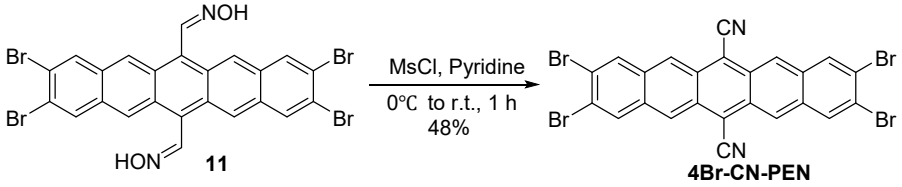
Synthesis of 2,3,9,10-tetrabromopentacene-6,13-dicarbaldehyde dioxime (11)



2,3,9,10-Tetrabromopentacene-6,13-dicarbaldehyde (0.08 g, 0.12 mmol) and hydroxylamine hydrochloride (0.02 g, 0.27 mmol) were added to a 20 mL round-bottom flask. Anhydrous pyridine (4 mL) was introduced, and the reaction mixture was stirred at room temperature for 1 h. The solvent was then removed under reduced pressure using a rotary evaporator, yielding a residue. To this

residue, 4 mL of aqueous HCl (1 M) was added. The precipitated blue solid was collected by centrifugation and repeatedly washed with deionized water and ethanol, affording 0.06 g of pure blue solid (70% yield). Due to the limited solubility of the obtained solid, only the ^{1}H NMR spectrum could be acquired. ^{1}H NMR (500 MHz, DMSO-d_6) δ = 12.07 (s, 2H), 9.25 (s, 2H), 8.81 (s, 4H), 8.32 (s, 4H). IR (υ cm^{-1}): 3365, 3064, 2957, 1597, 1537, 1422, 1275, 991, 940, 897, 752, 675.

Synthesis of 2,3,9,10-tetrabromopentacene-6,13-dicarbonitrile (4Br-CN-PEN)



2,3,9,10-Tetrabromopentacene-6,13-dicarbaldehyde dioxime (0.06 g, 0.09 mmol) was dissolved in pyridine (6 mL) in a reaction flask. The system was cooled in an ice bath, and methanesulfonyl chloride (0.26 mL, 3.33 mmol) was added under nitrogen protection. After complete addition, the reaction was allowed to warm to room temperature and stirred for 90 min. The mixture was quenched with methanol, and the precipitated green solid was collected by centrifugation. The product was thoroughly washed with deionized water, ethanol, and dichloromethane, yielding 0.03 g of pure green solid (48% yield). Due to the poor solubility of the product, solid-state NMR spectroscopy was instead performed. ^{13}C (CP-MAS) NMR, δ (ppm): 113, 125-135. IR (υ cm^{-1}): 3053, 2212, 1616, 1564, 1415, 1207, 1150, 1078, 991, 944, 893, 770, 669, 632.

3. DFT Calculations

The Gaussian 16 program was used for all the DFT calculations [5]. The ground-state (S_0) geometry of the complexes was using restricted DFT at M06-2X/def2-SVP level. For all the vertical excitation (S_1) energy was performed with TDDFT method with M06-2X/def2-SVP level.

Table S1. Cartesian coordinates for all optimized geometries of 4Br-PEN.

The excitation energy of 4Br-PEN is 2.2893 eV.

C	1.22037800	0.72482600	0.00000000
C	0.00008200	1.40587000	0.00000000
C	-1.22074400	0.72472800	0.00000000
C	-1.22074400	-0.72472800	0.00000000
C	0.00008200	-1.40587000	0.00000000
C	1.22037800	-0.72482600	0.00000000
C	-2.45941400	1.40745600	0.00000000
C	-2.45941400	-1.40745600	0.00000000
C	-3.65886500	-0.72293500	0.00000000
C	-3.65886500	0.72293500	0.00000000
C	-4.92135000	1.40487400	0.00000000
H	-4.93241200	2.49003700	0.00000000

C	-6.09373400	0.72144300	0.00000000
C	-6.09373400	-0.72144300	0.00000000
C	-4.92135000	-1.40487400	0.00000000
H	-2.46097400	2.49509000	0.00000000
H	-0.00010300	2.49366000	0.00000000
H	-0.00010300	-2.49366000	0.00000000
H	-2.46097400	-2.49509000	0.00000000
H	-4.93241200	-2.49003700	0.00000000
C	6.09378200	0.72171700	0.00000000
C	4.92164700	1.40510800	0.00000000
C	3.65862800	0.72322400	0.00000000
C	3.65862800	-0.72322400	0.00000000
C	4.92164700	-1.40510800	0.00000000
C	6.09378200	-0.72171700	0.00000000
H	2.46067800	2.49518200	0.00000000
H	4.93234600	2.49030000	0.00000000
C	2.45961400	1.40751400	0.00000000
C	2.45961400	-1.40751400	0.00000000
H	4.93234600	-2.49030000	0.00000000
H	2.46067800	-2.49518200	0.00000000
Br	-7.71217500	-1.68264500	0.00000000
Br	-7.71217500	1.68264500	0.00000000
Br	7.71218400	-1.68256900	0.00000000
Br	7.71218400	1.68256900	0.00000000

Table S2. Cartesian coordinates for all optimized geometries of 4Br-CN-PEN. The excitation energy of 4Br-CN-PEN is 2.0437 eV.

C	-1.23557000	-0.72232100	0.00000000
C	-0.00004100	-1.40073600	0.00000000
C	1.23588900	-0.72233300	0.00000000
C	1.23588900	0.72233300	0.00000000
C	-0.00004100	1.40073600	0.00000000
C	-1.23557000	0.72232100	0.00000000
C	2.46890400	-1.40865800	0.00000000
C	2.46890400	1.40865800	0.00000000
C	3.66829500	0.72152100	0.00000000
C	3.66829500	-0.72152100	0.00000000
C	4.92759200	-1.40642700	0.00000000
H	4.93629000	-2.49136100	0.00000000
C	6.10011800	-0.72177800	0.00000000
C	6.10011800	0.72177800	0.00000000
C	4.92759200	1.40642700	0.00000000
H	2.47019500	-2.49536300	0.00000000

H	2.47019500	2.49536300	0.00000000
H	4.93629000	2.49136100	0.00000000
C	-6.10006300	-0.72197600	0.00000000
C	-4.92762800	-1.40655700	0.00000000
C	-3.66802500	-0.72165700	0.00000000
C	-3.66802500	0.72165700	0.00000000
C	-4.92762800	1.40655700	0.00000000
C	-6.10006300	0.72197600	0.00000000
H	-2.46991900	-2.49543600	0.00000000
H	-4.93601800	-2.49149400	0.00000000
C	-2.46894700	-1.40871800	0.00000000
C	-2.46894700	1.40871800	0.00000000
H	-4.93601800	2.49149400	0.00000000
H	-2.46991900	2.49543600	0.00000000
Br	7.71599700	1.68057000	0.00000000
Br	7.71599700	-1.68057000	0.00000000
Br	-7.71607600	1.68044100	0.00000000
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C	-0.00005400	2.83527800	0.00000000
C	-0.00005400	-2.83527800	0.00000000
N	-0.00008400	3.99347800	0.00000000
N	-0.00008400	-3.99347800	0.00000000

4. Identification and Testing Spectra of Compounds

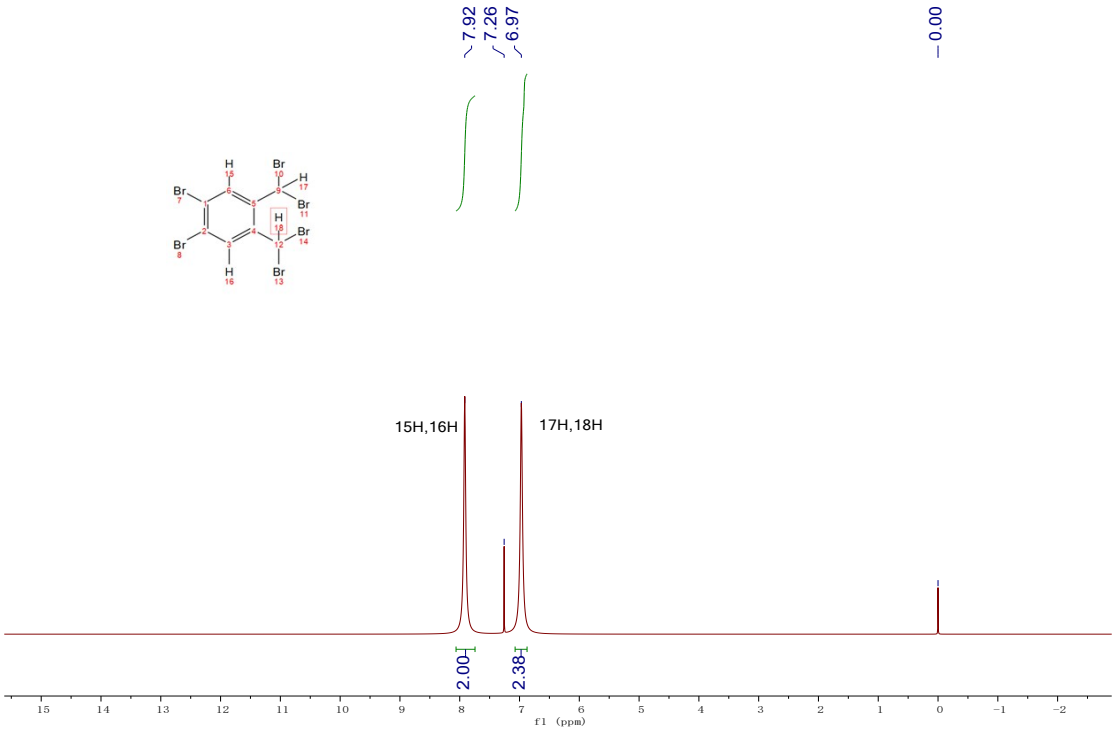

Fig. S1. [1]H NMR (CDCl3, 500 MHz) spectrum of compound **2**.

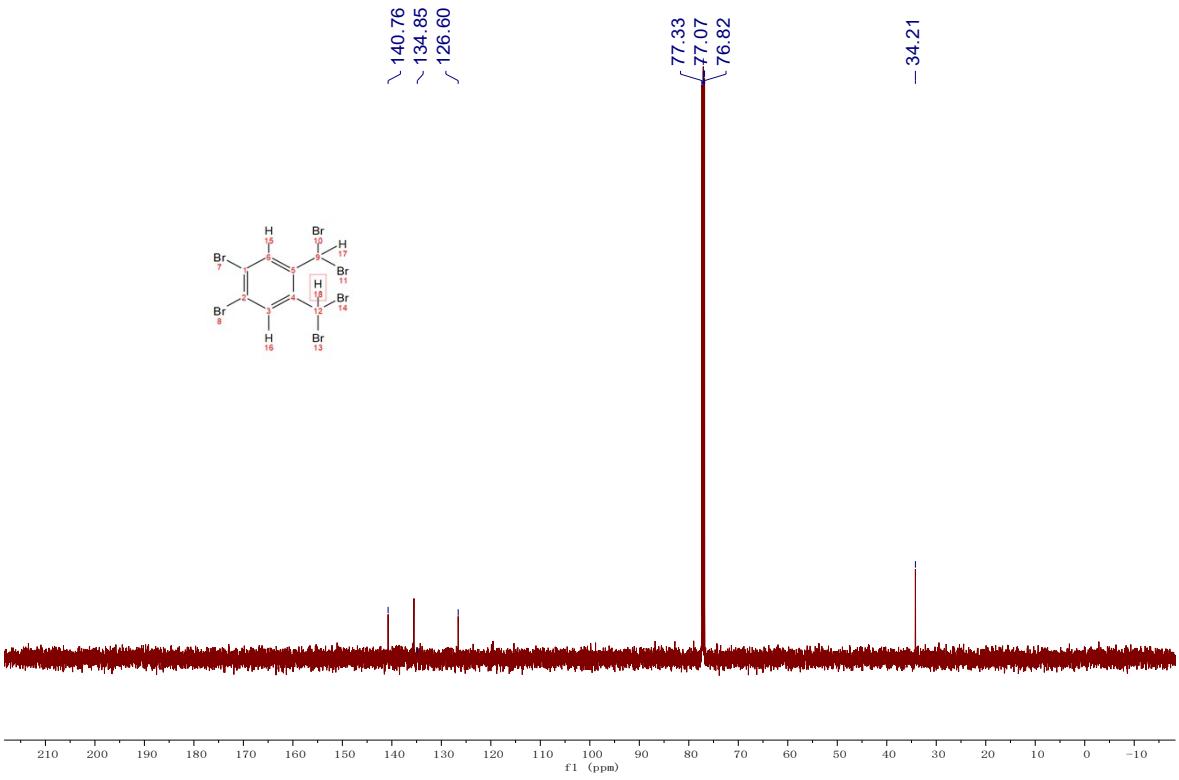

Fig. S2. [13]C NMR (CDCl3, 126 MHz) spectrum of compound **2**.

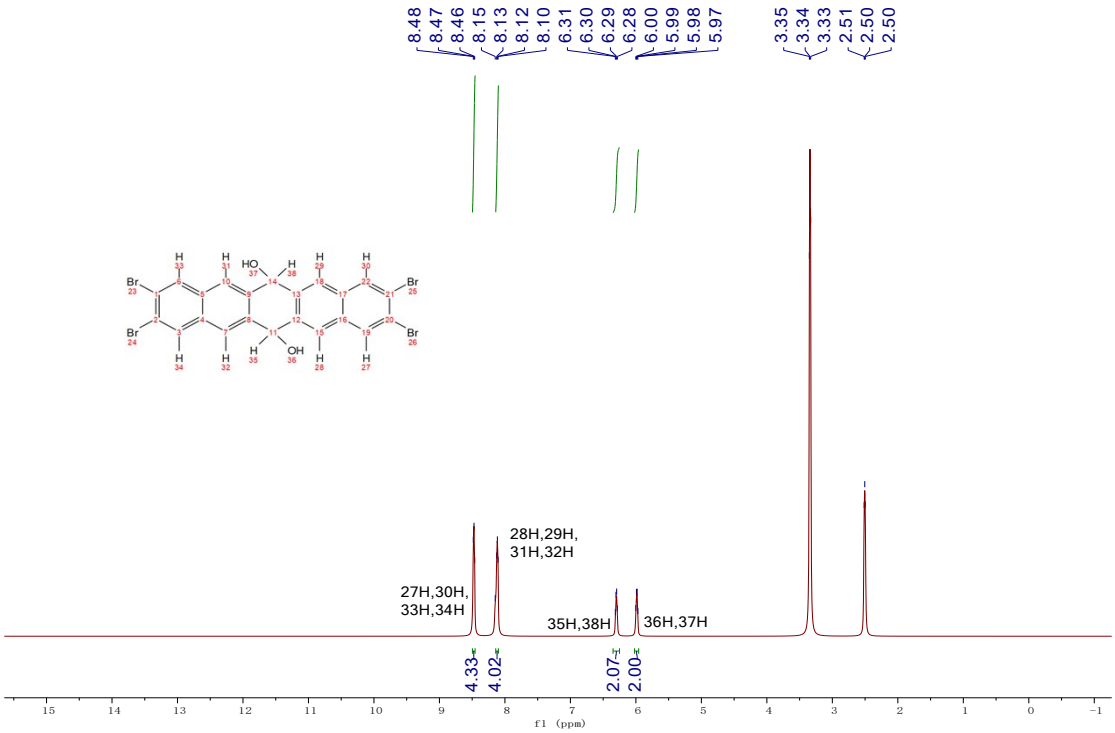

Fig. S3. [1]H NMR (DMSO, 500 MHz) spectrum of compound **4**.

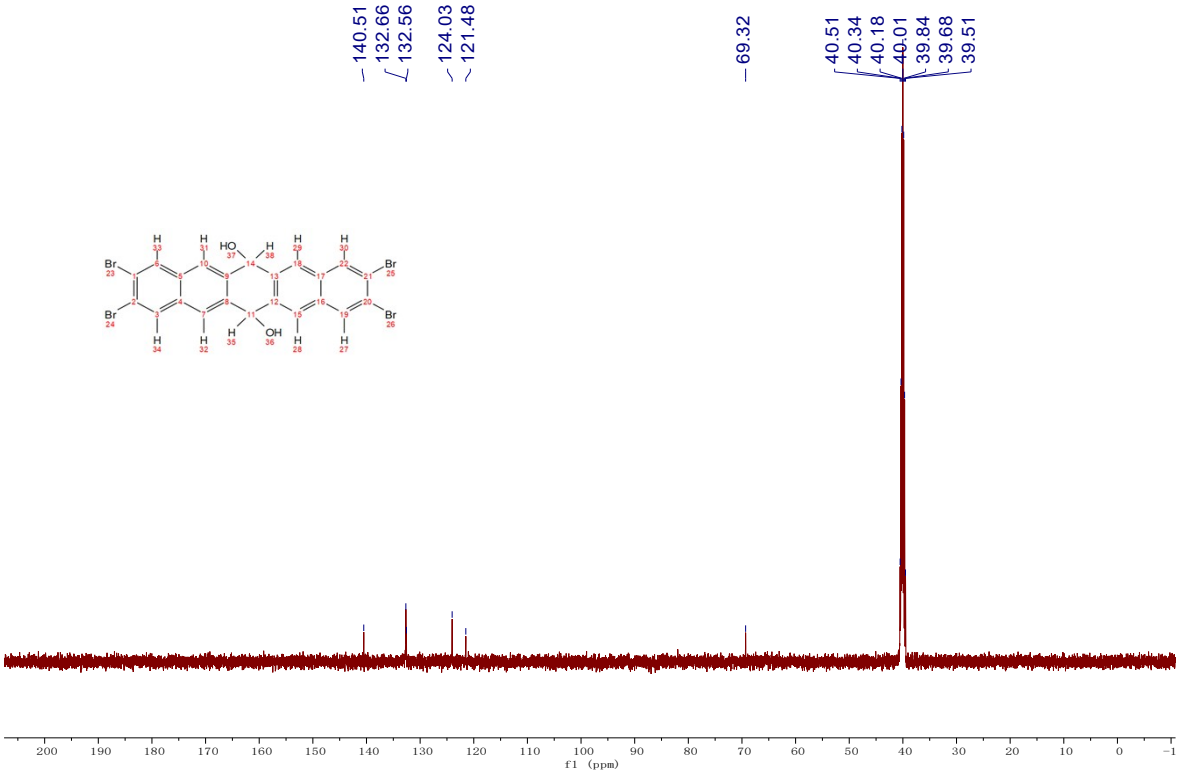

Fig. S4. [13]C NMR (DMSO, 126 MHz) spectrum of compound **4**.

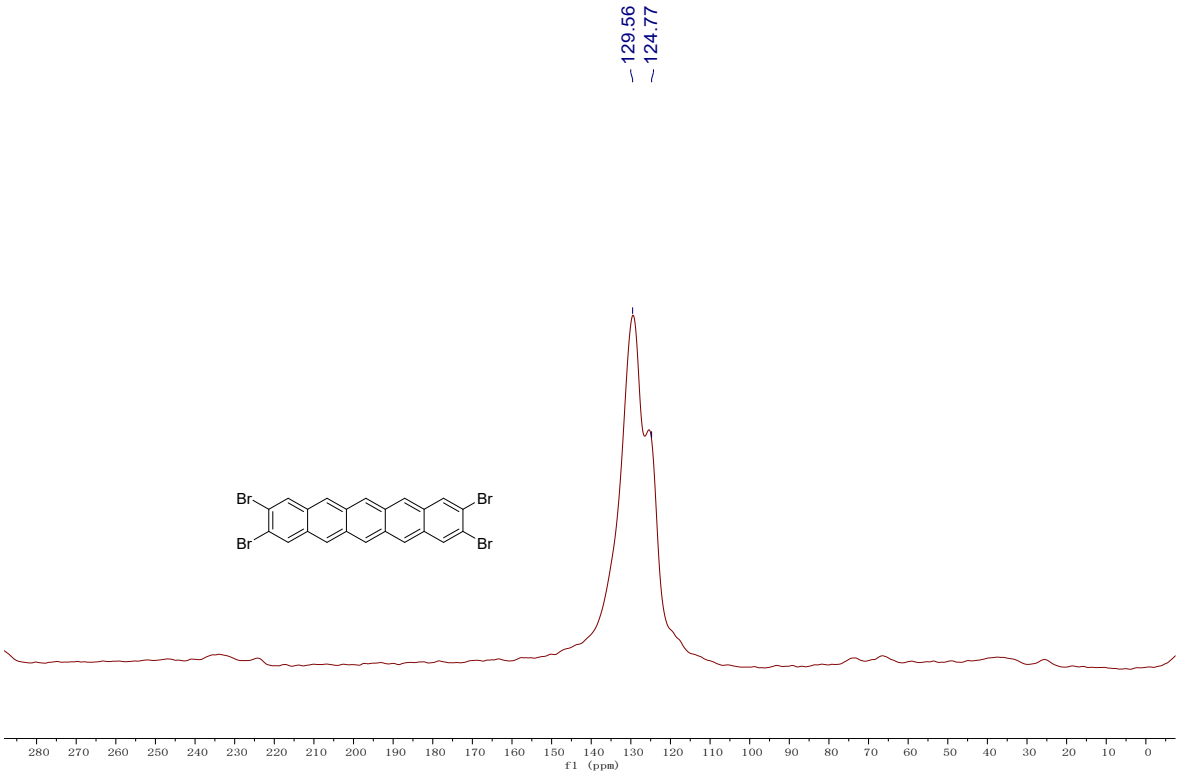

Fig. S5. ^{13}C NMR(CP-MAS) spectrum of 4Br-PEN.

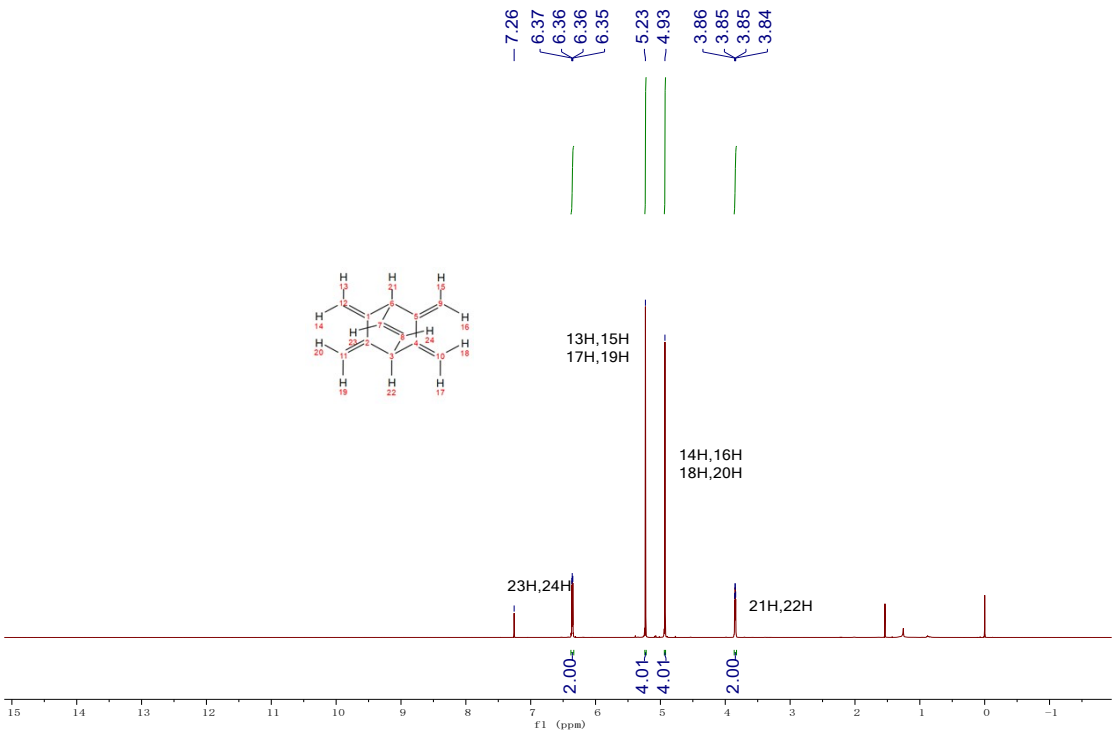

Fig. S6. ^{1}H NMR (CDCl3, 500 MHz) spectrum of compound **5**.

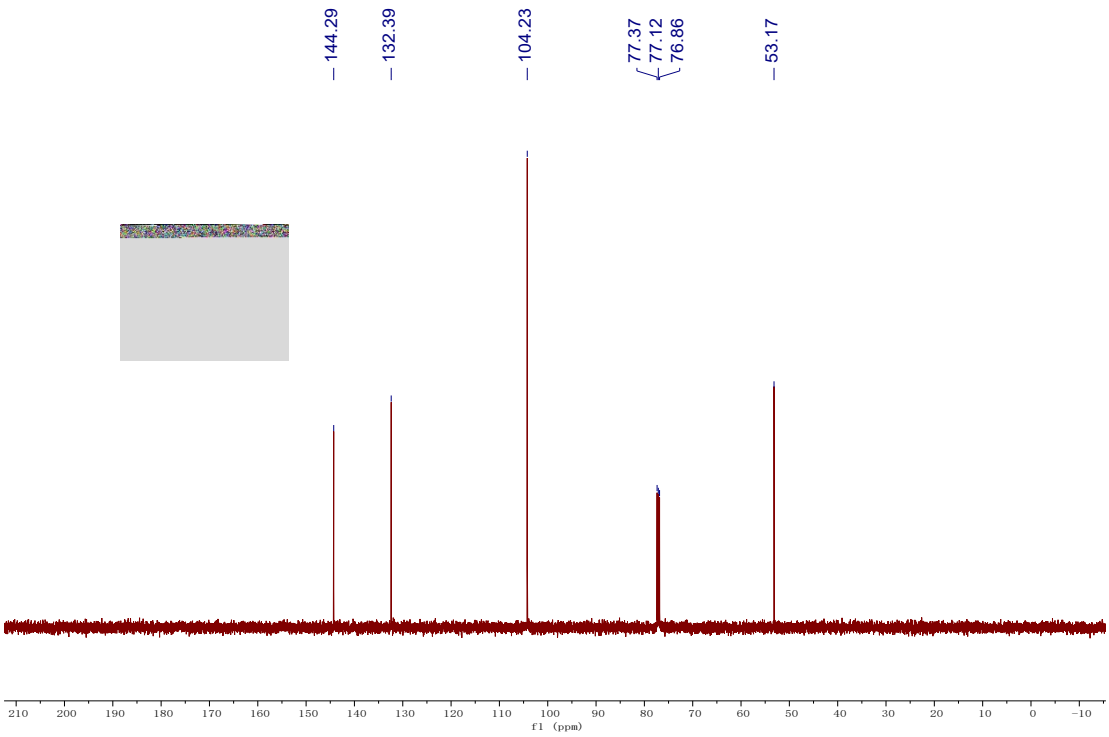

Fig. S7. ^{13}C NMR (CDCl3, 126 MHz) spectrum of compound **5**.

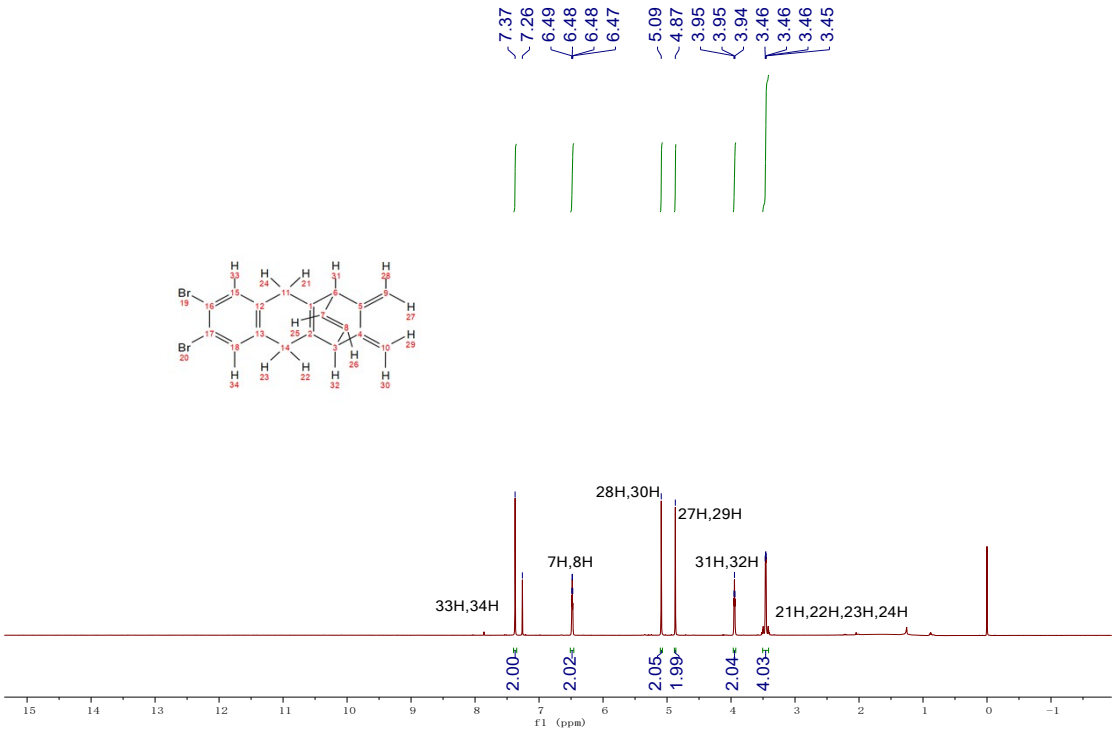

Fig. S8. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **7a**.

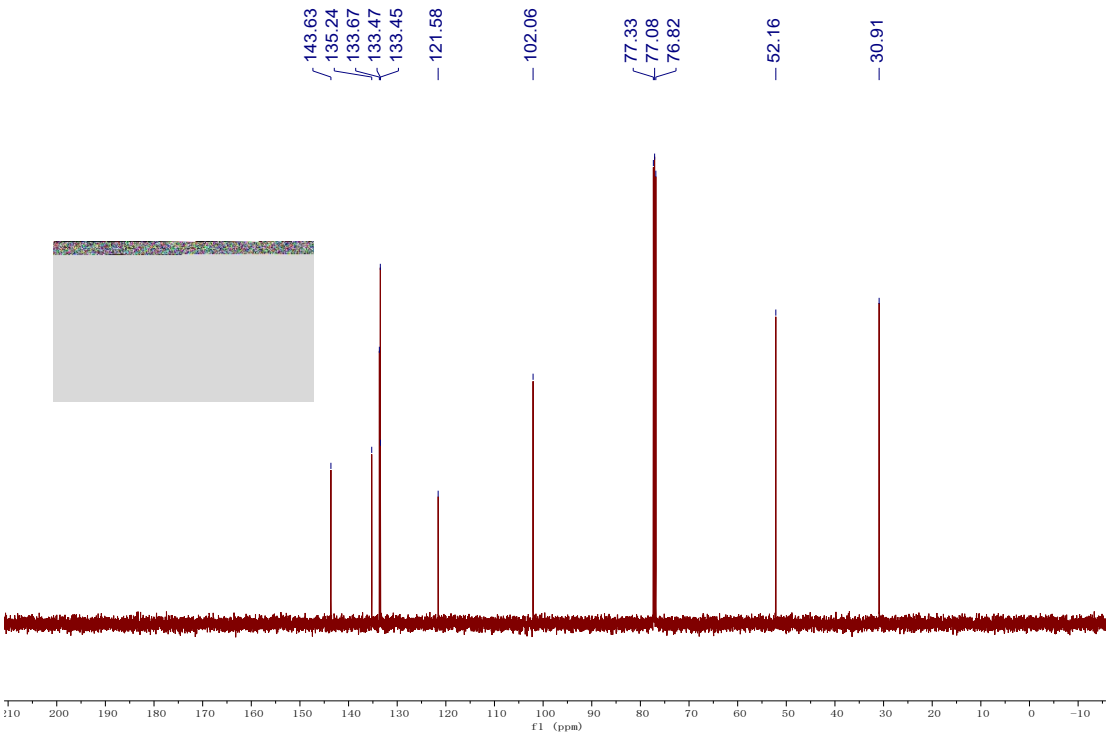

Fig. S9. ^{13}C NMR (CDCl3, 126 MHz) spectrum of compound **7a**.

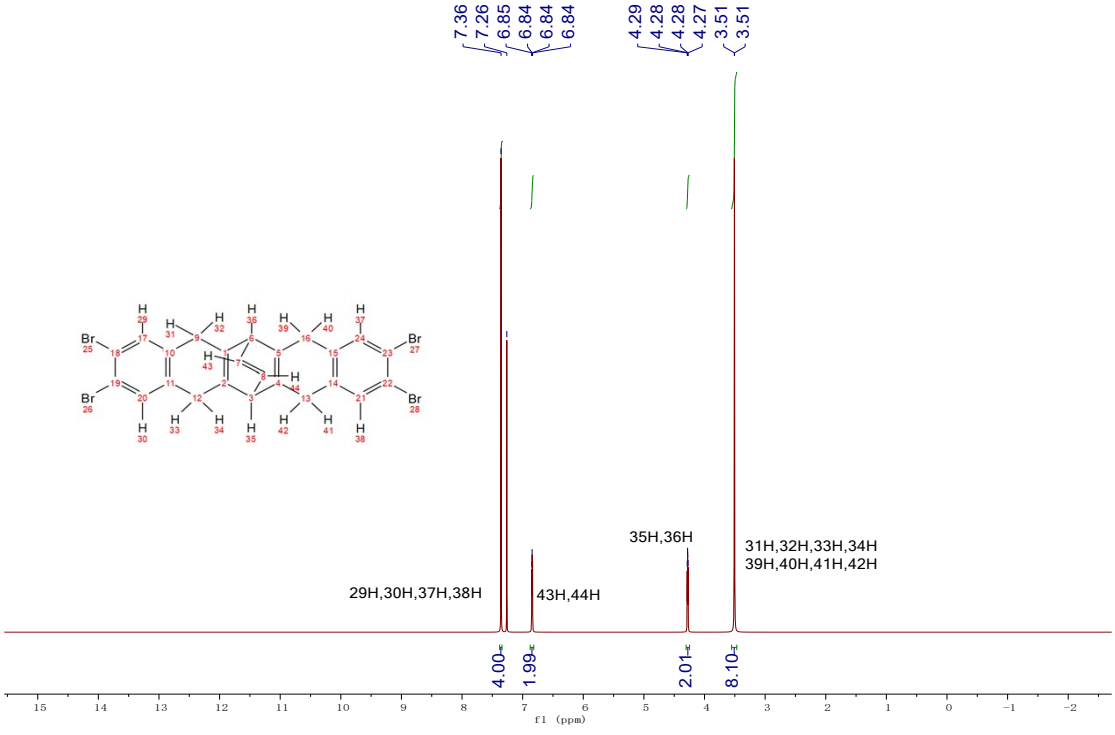

Fig. S10. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **7b**.

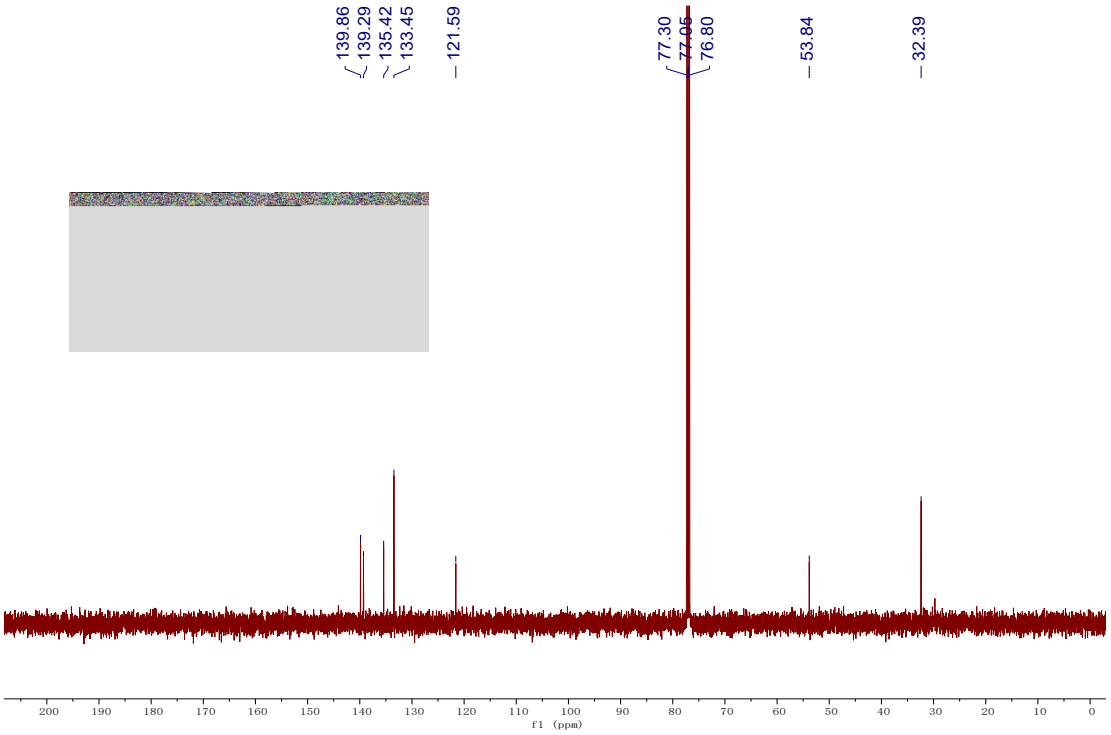

Fig. S11. ^{13}C NMR (CDCl3, 126 MHz) spectrum of compound **7b**.

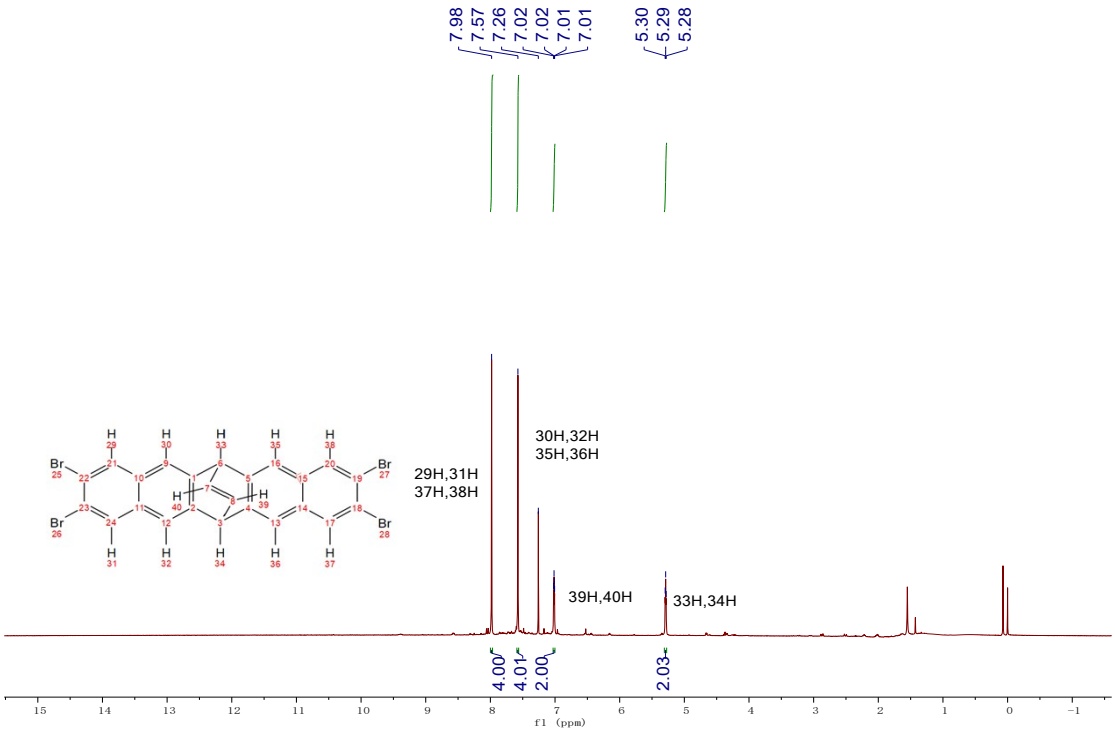

Fig. S12. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **8**.

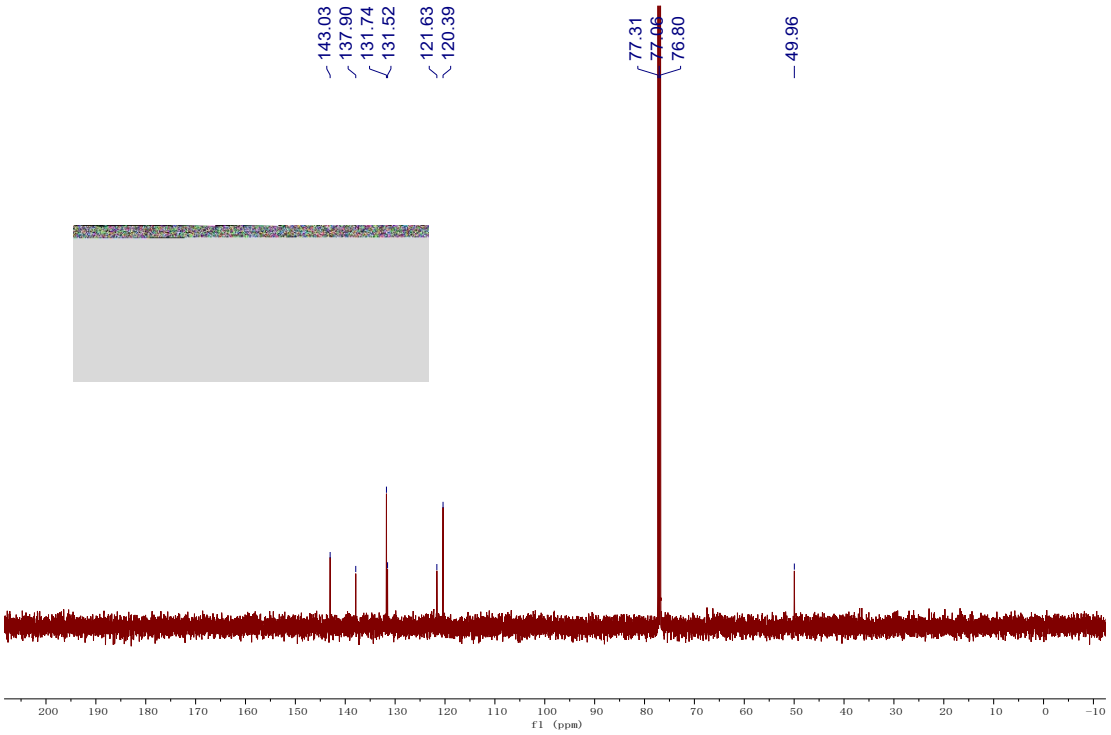

Fig. S13. ^{13}C NMR (CDCl3, 126 MHz) spectrum of compound **8**.

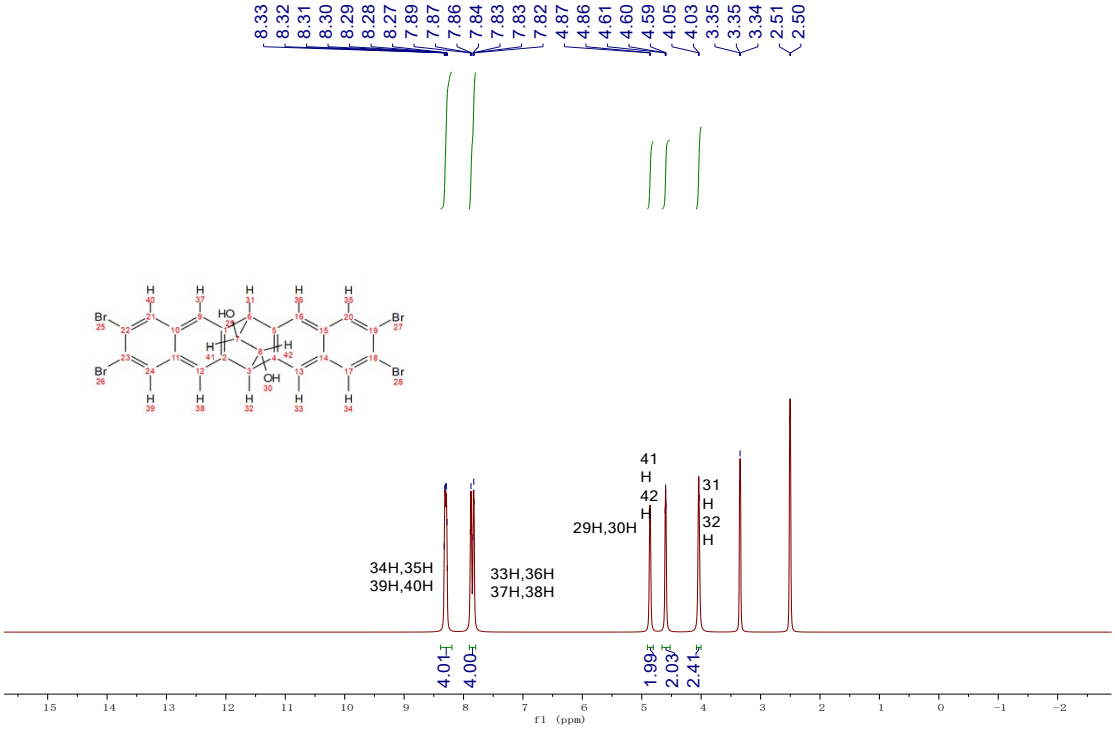

Fig. S14. ^{1}H NMR (DMSO, 500 MHz) spectrum of compound **9**.

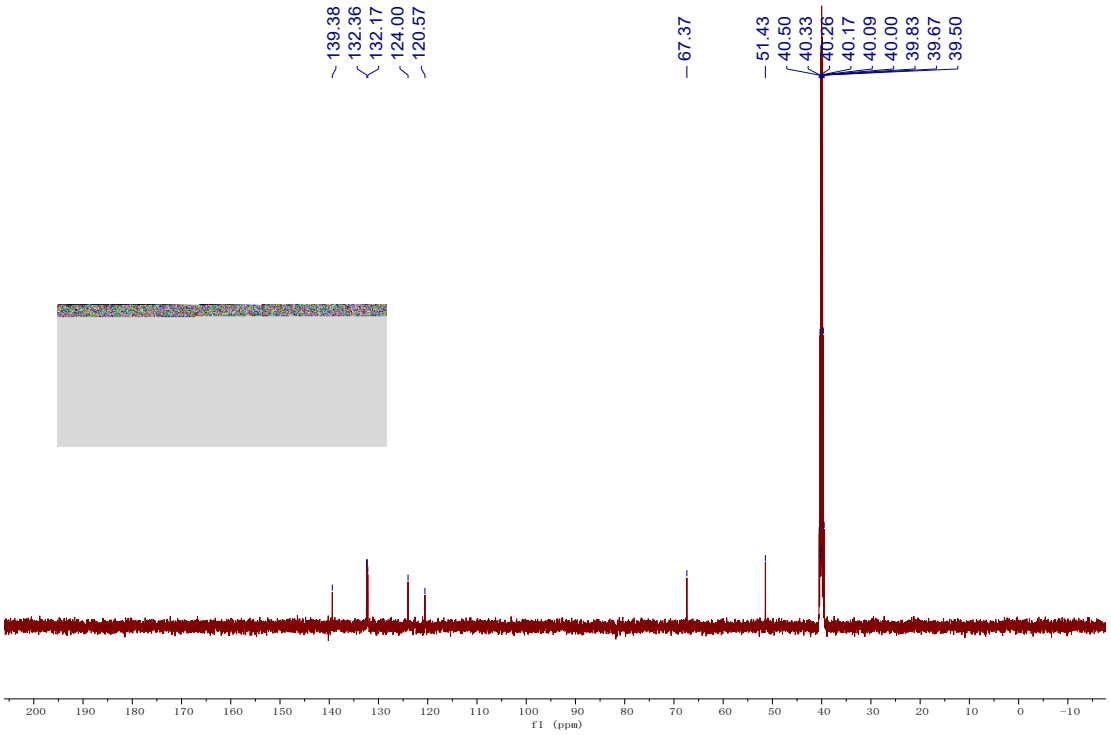

Fig. S15. ^{13}C NMR (DMSO, 126 MHz) spectrum of compound **9**.

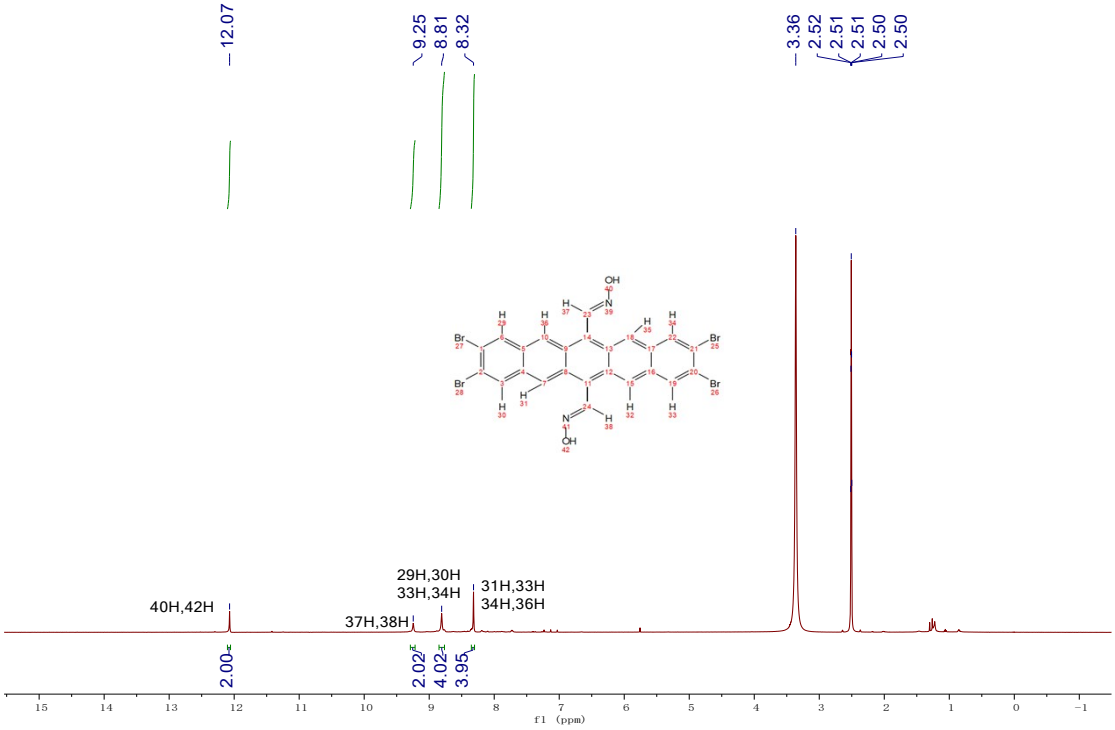

Fig. S16. ^{1}H NMR (DMSO, 500 MHz) spectrum of compound **11**.

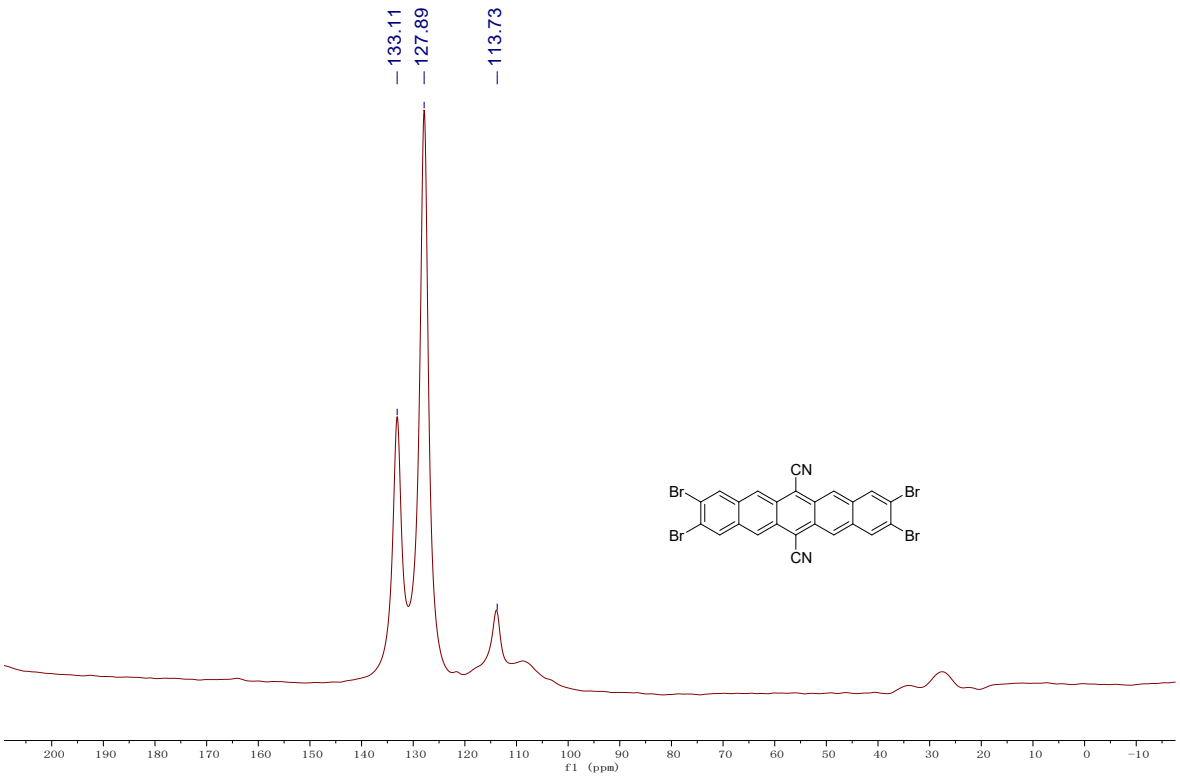

Fig. S17. ^{13}C NMR(CP-MAS) spectrum of 4Br-CN-PEN.

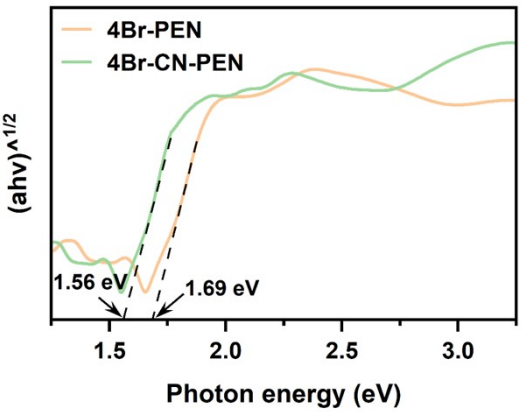

Fig. S18. Optical bandgap of 4Br-PEN and 4Br-CN-PEN calculated by tauc plot method.

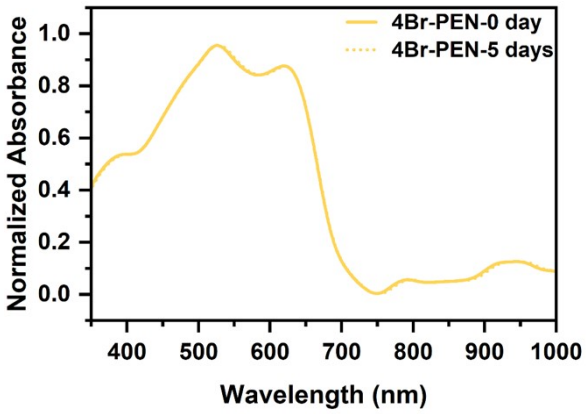

Fig. S19. UV-Vis absorption spectra of 4Br-PEN, freshly prepared and after 5 days respectively.

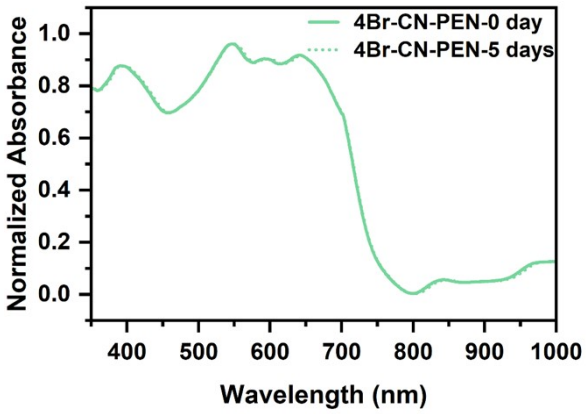

Fig. S20. UV-Vis absorption spectra of 4Br-CN-PEN, freshly prepared and after 5 days respectively.

Table S3 Photophysical properties and computational results for 4Br-PEN and 4Br-CN-PEN.

compound	$\lambda_{abs,max}$ (nm)	$\lambda_{em,max}$ (nm)	λ_{onset} (nm)	τ (ns) [a]	$E_{g,DFT}$ (eV) [b]	ΔE_{ST} (eV) [c]
4Br-PEN	622	579	705	0.61	2.143	2.218
4Br-CN-PEN	643	579	756	0.64	1.898	1.978

[a] Fluorescence lifetimes excited at 500 nm.

[c] $E_{g,DFT}$ from DFT calculations with B3LYP/6-31G* level.

[d] ΔE_{ST} from TD-DFT calculations with M06-2X/def2-SVP level.

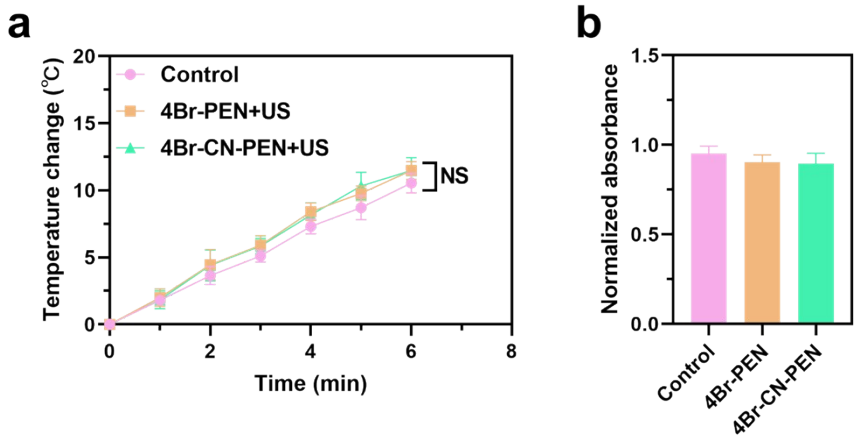

Fig. S21. (a) Temperature changes of Control, 4Br-PEN and 4Br-CN-PEN under US irradiation (1.0 W/cm^2, 1.0 MHz, 50% duty cycle) for different time intervals. NS: no significance. (b) Absorbance changes of DPBF at 410 nm in the presence of 4Br-PEN and 4Br-CN-PEN after heating at 80 ℃ for 30 min.

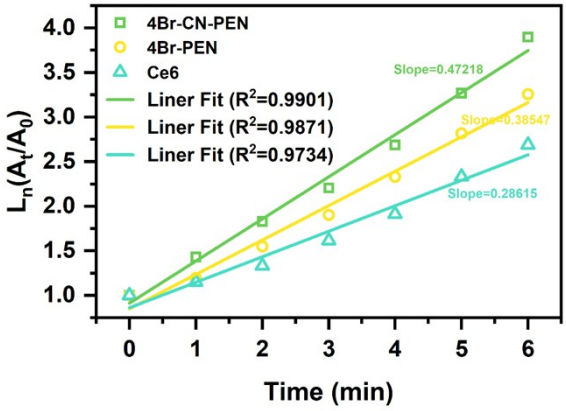

Fig. S22. Fluorescence Intensity at 525 nm for Ce6, 4Br-PEN, and 4Br-CN-PEN with Fitting Lines.

"Aqueous solutions of Ce6, 4Br-PEN, and 4Br-CN-PEN (0.5 mg·mL-1) were prepared, mixed with an equal volume of 5 μM SOSG, and subjected to identical ultrasound treatment (1 MHz, 1 W·cm^{-2}, 50% duty cycle). The fluorescence intensity at 525 nm was subsequently measured for all three groups. The fluorescence intensity of the three sample groups was monitored over time. The singlet oxygen generation rate (R) was determined from the slope of the fitted line.

Formula：

$$\Phi_{4Br\text{-}PEN} = \Phi_{Ce6} * (R_{4Br\text{-}PEN}/R_{Ce6})$$

$$\Phi_{4Br\text{-}CN\text{-}PEN} = \Phi_{Ce6} * (R_{4Br\text{-}CN\text{-}PEN}/R_{Ce6})$$

The singlet oxygen yield of Ce6 was normalized to 1 for quantitative comparison. Accordingly, under the given ultrasonic conditions (1 W·cm^{-2}, 1 MHz, 50% duty cycle), 4Br-PEN and 4Br-CN-PEN exhibited singlet oxygen yields 1.35 and 1.65 times that of Ce6, respectively."

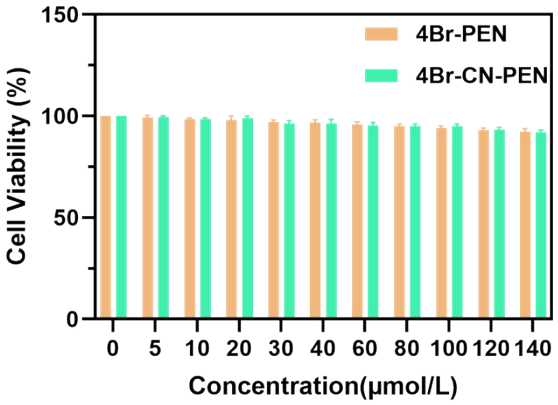

Fig. S23. Cytotoxicity of 4Br-PEN and 4Br-CN-PEN against NCTC 1469 cells.

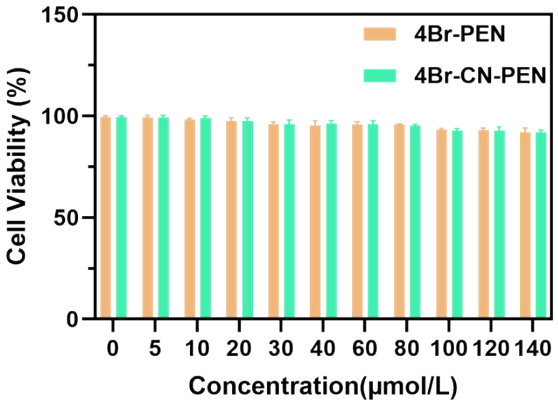

Fig. S24. Cytotoxicity of 4Br-PEN and 4Br-CN-PEN against L02 cells.

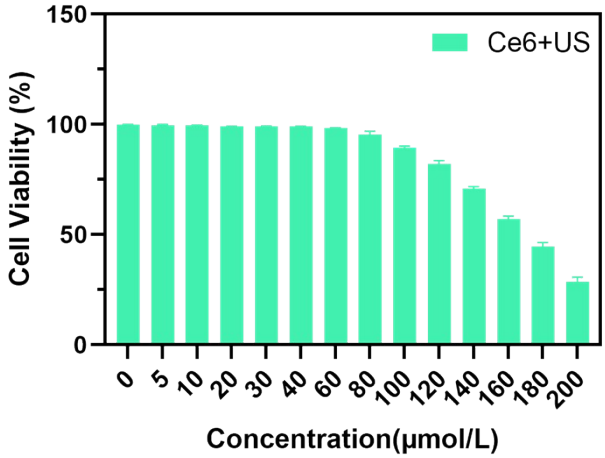

Fig. S25. Cell viability of 4T1 cells after incubation with various concentrations of Ce6.

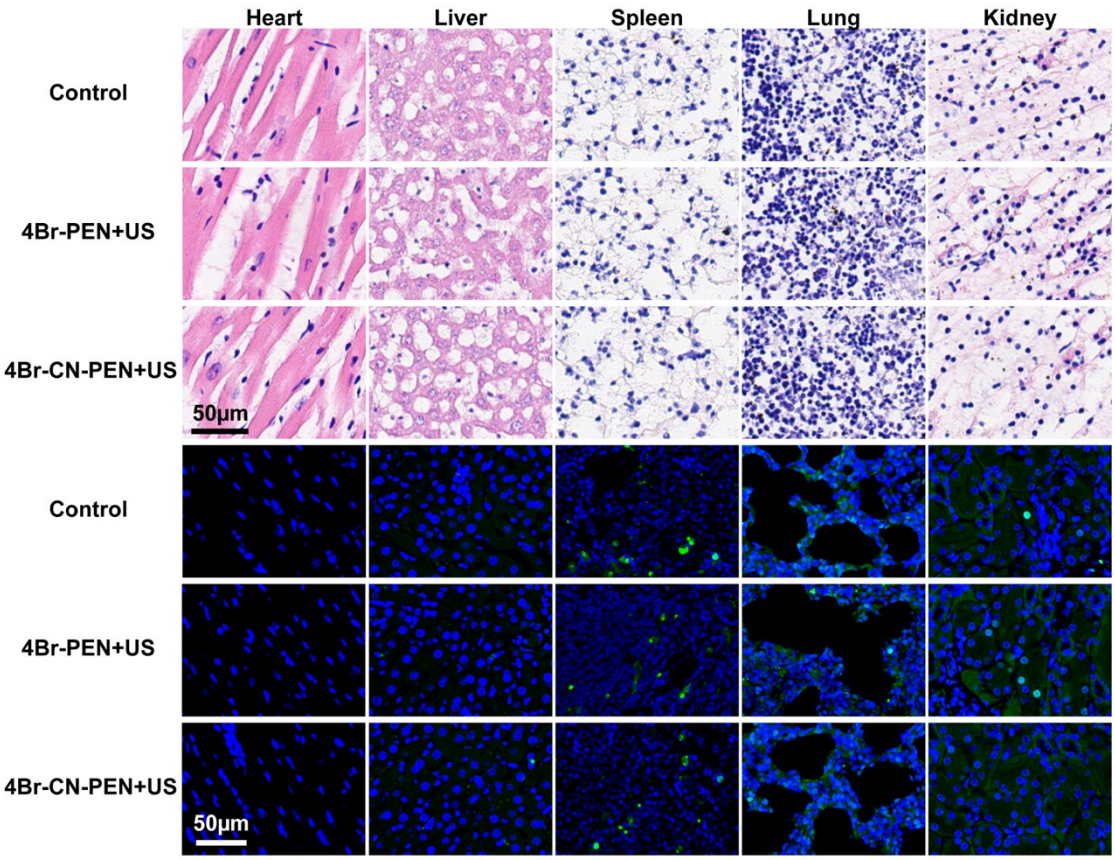

Fig. S26. H&E and TUNEL staining major organ tissues (heart, liver, spleen, lung, and kidney) of mice after 14 days of treament.

5. References

[1] H. Uno, H. Watanabe, Y. Yamashita and N. Ono, *Org. Biomol. Chem.* **2005**, *3*, 448-453.

[2] K. Hermann, S. Sardini, Y. Ruan, R. J. Yoder, M. Chakraborty, S. Vyas, C. M. Hadad, J. D. Badjić, *J. Org. Chem.* **2013**, *78*, 2984-2991.

[3] C. T. Lin, T. C. Chou, *J. Org. Chem.* **1990**, *55*, 2252-2254.

[4] R. Gabioud, P. Vogel, *Helv. Chim. Acta*, **1983**, *66*, 1134-1147.

[5] M. J. Frisch; G. W. Trucks; H. B. Schlegel; G. E. Scuseria; M. A. Robb; J. R. Cheeseman; G. Scalmani; V. Barone; G. A. Petersson; H. Nakatsuji; X. Li; M. Caricato; A. Marenich; Bloino; J. B. Janesko; G. R. Gomperts; B. Mennucci; H. P. Hratchian; J. V. Ortiz; A. F. Izmaylov; J. L. Sonnenberg; D. Williams-Young; F. Ding; F. Lipparini; F. Egidi; J. Goings; B. Peng; A. Petrone; T. Henderson; D. Ranasinghe; V. G. Zakrzewski; J. Gao; N. Rega; G. Zheng; W. Liang; M. Hada; M. Ehara; K. Toyota; R. Fukuda; J. Hasegawa; M. Ishida; T. Nakajima; Y. Honda; O. Kitao; H. Nakai; T. Vreven; K. Throssell; J. A. Montgomery; Jr.; J. E. Peralta; F. Ogliaro; M. Bearpark; J. J. Heyd; E. K. Brothers; N. Kudin; V. N. Staroverov; T. Keith; R. Kobayashi; J. Normand; K. Raghavachari; A. Rendell; J. C. Burant; S. S. Iyengar; J. Tomasi; M. Cossi; J. M. Millam; M. Klene; C. Adamo; R. Cammi; J. W. Ochterski; R. L. Martin; K. Morokuma; O. Farkas; J. B. Foresman and D. J. Fox, Gaussian, Inc., Wallingford, CT, 2016.