Supporting Information

One Small Molecule as Theranostic Agent: Naphthalimide Dye for Subcellular Fluorescent Localization and Photodynamic Therapy *in vivo*

Lei Zhang,[a,‡] KechengLei,[b,‡] JingwenZhang,[a] WenlinSong,[a] YuanhongZheng,[b] Shaoying Tan,[a] Yuwei Gao,[b] YufangXu,[a,*] JianwenLiu,[b,*] XuhongQian[a,*]

[a] State Key Laboratory of Bioreactor Engineering, Shanghai Key Laboratory of Chemical Biology, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China. Fax: +86 21 6425 2603; Tel: +86 21 6425 3589;*E-mail:xhqian@ecsut.edu.cn*;*yfxu@ecust.edu.cn*.

[b] State Key Laboratory of Bioreactor Engineering, Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China

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1. Materials and Instruments

All chemical reagents and solvents are analytic grade and chemicals were purchased from TCI and J&K reagent Co. Ltd without further purification. Compounds were purified through column chromatography with silica gel (HaiYang, Qingdao) 300-400 mesh.

^{1}H NMR and ^{13}C NMR spectra were collected by Bruker AM-400 or AM-500 spectrometer (in $CDCl_3$, CD_3OD and DMSO-d_6, TMS as the internal standard), HRMS was conducted in the Analysis and Test Center of East China University of Science and Technology (ECUST). The purifications of final compounds were tested by HPLC performed on a Hewlett-Packard 1100 system chromatograph with a photodiode array detector using a Zorbax RX-C18, 250 mm × 4.6 mm column. The mobile phase was a gradient of 30-100% acetonitrile (solvent 1) and 10 mMNH_4OAc in water (pH 6.0) (solvent 2) at a flow rate of 1.0 mL/min (0-15.0 min, 30-100% solvent 1). The melting points of compounds were obtained by WRS-1B-digital melting point apparatus. Spectroscopic properties were measured on All Varian Cary 100 UV spectrophotometer and Varian Cary Eclipse FL spectrophotometer and the singlet oxygen quantum yields were accomplished by monochromatic light system composed of CM 110 1/8mmonochromator and ASB-XE-175 Xenon light source from Spectral Products. Optical imaging was performed through fluorescence microscope and confocal microscopy (Nikon, Japan).

2. Synthesis

4-bromo-3-nitro-1,8-naphthalic anhydride (2).

4-bromo-1,8-naphthalic anhydride (5.54 g, 20 mmol) was stirred in 20 mL concentrated sulphuric acid at 0 ^{o}C, sodium nitrate (2.10 g, 24 mmol) was then added slowly within 30 min and the mixture was stirred at room temperature for 3 hours. The mixture was then poured into 200 mL ice water accompanied with stirring fierce and filtrated to get residue. The residue was purified through recrystallization with acetic acid to give out **2**, light yellow solid, yields: 72%. mp> 300 ^{o}C.^{1}H NMR (400 MHz, DMSO-d_6): δ8.91 (s, 1H), 8.82 (d, J = 8.4 Hz, 1H), 8.73 (d, J = 7.2 Hz, 1H), 8.18 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): 160.10, 159.50, 149.83, 135.69, 135.37, 131.40, 130.96, 130.93, 126.03, 122.25, 121.54, 120.90. MS (EI) calcd for $C_{12}H_4BrNO_5$ $[M]^{+}$: 320.9, found: 320.9.

4-((4-bromophenyl)thio)-3-nitro-1,8-naphthalic anhydride (3a).

Compound **2** (2.00 g, 6.21 mmol) was dissolved in 25 mL ethanol, 4-bromobenzenethiol (1.47 g, 7.76 mmol) was then added and the reaction was heated at 80 °C for 5 hours.The mixture was evaporated in vacuum and purified on silica gel chromatography (PE/DCM = 3/1, v/v) to perform**3a**, yellow solid, yield: 82%. mp 194.5-195.4 °C.^{1}H NMR (400 MHz, DMSO-d_6): δ 8.97 (s, 1H), 8.82 (dd, J_1 = 0.8 Hz, J_2 = 8.4 Hz, 1H), 8.67 (dd, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 8.06 (t, J = 7.6 Hz, 1H), 7.51 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 2H), 7.16 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): 160.10, 159.74, 153.44, 134.90, 134.49, 134.10, 133.07, 132.36, 131.39, 131.29, 131.04, 130.97, 125.41, 123.29, 121.47, 121.26. HRMS (ESI) calcd for $C_{18}H_9BrNO_5S$ $[M+H]^+$: 429.9379, found: 429.9384

4-phenylthio-3-nitro-1,8-naphthalic anhydride (3b).[S1]

Compound **2** (2.00 g, 6.21 mmol) was dissolved in 25 mL ethanol, benzenethiol (0.86 g, 7.76 mmol) was then added and the reaction was heated at 80 °C for 5 hours.The mixture was evaporated in vacuum and purified on silica gel chromatography (PE/DCM = 3/1, v/v) to give out **3b**, yellow solid, yield: 75%. mp 177.6-178.9 °C.^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 8.92 (d, J = 8.4 Hz, 1H), 8.82 (s, 1H), 8.73 (d, J = 7.2 Hz, 1H), 7.90 (t, J = 8.0 Hz, 1H), 7.26-7.19 (m, 3H), 7.11 (d, J = 7.6 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): 159.15, 158.88, 152.24, 136.43, 136.19, 135.63, 135.40, 130.62, 130.19, 129.80, 129.70, 129.36, 128.76, 128.34, 127.09, 126.52.

4-((4-bromophenyl)thio)-3-amino-1,8-naphthalic anhydride (4a).

Stannous chloride dihydrate (2.26 g, 10 mmol) was stirred in 15 mL concentrated hydrochloric acid at room temperature for 10 mins, **3a** was added slowly and the reaction was then heated at 85 °C for 3 hours, the mixture was filtered and washed with water until the filtrate was neutral, and residue was dried and purified on silica gel chromatography (PE/DCM = 1/1, v/v) to give out **4a**, yellow green solid, yield: 85%. mp> 300 °C.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, J = 8.4 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 8.15 (s, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.06 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 168.68, 160.55, 149.37, 139.26, 135.63, 133.74, 132.35, 131.72, 129.10, 128.87, 128.04, 123.55, 120.85, 119.87, 118.85, 112.26. HRMS (ESI) calcd for $C_{18}H_{11}BrNO_3S$ $[M+H]^+$: 399.9638, found: 399.9639.

4-phenylthio-3-amino-1,8-naphthalic anhydride (4b). [S1]

Stannous chloride dehydrate (2.26 g, 10 mmol) was stirred in 15 mL concentrated hydrochloric acid at room temperature for 10 mins, **3b** was added slowly and the reaction was then heated at 85 °C for 3 hours, the mixture was filtered and washed with water until the filtrate was neutral, and

residue was dried and purified on silica gel chromatography (PE/DCM = 1/1, v/v) to give out **4b**, yellow green solid, yield: 80%. mp 225.9-226.7 °C.^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ 8.68 (d, J = 8.4 Hz, 1H), 8.36 (d, J = 7.2 Hz, 1H), 8.16 (s, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.22-7.15 (m, 3H), 7.03 (d, J = 7.6 Hz, 2H), 5.09 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): 160.80, 160.74, 149.42, 135.73, 134.47, 132.01, 129.30, 128.94, 128.62, 126.55, 126.12, 124.37, 123.56, 120.40, 118.64, 113.15. MS (ESI) calcd for $C_{18}H_{11}NO_3S$ $[M+H]^+$: 322.0, found: 322.0.

9-bromo-*N*-(2-(2-hydroxyethoxy)ethyl)-benzo[k,l]thioxanthene-3,4-naphthalimide (1a) and 9-bromo-*N*-(2-(2-hydroxyethoxy)ethyl)-benzo[b]furano[2,1-c]naphthalimide (1b).

Sodium nitrite (0.38 g, 5.5 mmol) was added to 32 mL concentrated sulphuric acid and 12 mL acetic acid in three times at -5 °C, **4a**(2.00 g, 5 mmol) was then added slowly within 45 mins, the mixture was stirred for another 1 hour to give out black viscous liquid. At the same time, anhydrous cupric sulfate (34.00 g, 213 mmol) was dissolved in 350 mL deionized water and 45 mL acetic acid, and the blue solution was heated under reflux. Then the black liquid was added dropwise to the blue solution, the mixture was sequentially warmed at 100 °C for another 6 hours, and filtered to give out the brown solid. The solid was then stirred in 10 mL anhydrous ethanol withdiglycolamine (0.22 g, 0.20 mL) at 50 °C for 3 hours.The mixture was evaporated in vacuum and residue was purified on silica gel chromatography (PE/DCM = 1/1, v/v and then DCM/MeOH = 100/1) to give out **1b**, light yellow solid, yield: 70% and **1a**, orange solid, yield: 18%. mp (**1a**) 217.7-218.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 8.0 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.23 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.20 (d, J = 9.0 Hz, 1H), 4.37 (t, J = 5.5 Hz, 2H), 3.79 (t, J = 5.5 Hz, 2H), 3.62 (t, J = 4.5 Hz, 2H), 3.58 (t, J = 4.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 164.15, 163.69, 140.11, 135.53, 132.91, 132.71, 131.08, 130.51, 130.30, 129.65, 128.92, 127.70, 125.35, 121.46, 121.39, 120.69, 119.56, 117.90, 72.50, 68.43, 61.52, 39.80. HPLC purity: 95.3%, Retention time = 13.73 min. HRMS (EI) calcd for $C_{22}H_{16}BrNO_4S$ $[M]^+$: 468.9983, found: 468.9982. mp (**1b**) 201.3-201.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (s, 1H), 8.47 (d, J = 7.2 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 1.6 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.51 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 4.41 (t, J = 5.6 Hz, 2H), 3.91 (t, J = 5.6 Hz, 2H), 3.75~3.73 (m, 4H), 2.36 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 164.12, 163.91, 143.92, 137.13, 137.10, 131.80, 131.02, 130.43, 129.75, 127.50, 126.62, 126.58, 124.81, 124.63, 124.04, 123.25, 119.70, 119.62, 72.38, 68.49, 61.90, 39.72. HPLC purity: 99.5%, Retention time = 14.34 min. HRMS (EI) calcd for $C_{22}H_{16}BrNO_4S$ $[M]^+$: 468.9983, found: 468.9981.

***N*-(2-(2-hydroxyethoxy)ethyl)-benzo[k,l]thioxanthene-3,4-naphthalimide (1c) and *N*-(2-(2-hydroxyethoxy)ethyl)-benzo[b]furano[2,1-c]naphthalimide (1d).** [S1]

Sodium nitrite (0.38 g, 5.5 mmol) was added to 32 mLconcentrated sulphuric acid and 12 mL acetic acid in three times at -5 ^{o}C,**4b** (1.60 g, 5 mmol) was then added slowly within 45 mins, the mixture was stirred for another 1 hour to give out black viscous liquid. At the same time, anhydrous cupric sulfate (34.00 g, 213 mmol) was dissolved in 350 mL deionized water and 45 mL acetic acid, and the blue solution was heated under reflux. Then the black liquid was added dropwise to the blue solution, the mixture was sequentially warmed at 100 ^{o}C for another 6 hours, and filtered to give out the brown solid. The solid was then stirred in 10 mL anhydrous ethanol withdiglycolamine (0.22 g, 0.20 mL) at 50 ^{o}C for 3 hours.The mixture was evaporated in vacuum and residue was purified on silica gel chromatography (PE/DCM = 1/1, v/v and then DCM/MeOH = 100/1) to give out **1d**,, light yellow solid, yield: 55% and **1c**, orange solid, yield: 20%. mp (**1c**) 192.5-193.8 ^{o}C.^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 7.5 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.25~7.34 (m, 4H), 4.39 (t, J = 5.0 Hz, 2H), 3.87 (t, J = 5.0 Hz, 2H), 3.72-3.73 (m, 2H), 3.70-3.71 (m, 2H).^{13}C NMR (125 MHz, $CDCl_3$): 164.12, 163.69, 140.74, 136.77, 132.68, 131.62, 130.88, 130.32, 130.00, 127.84, 127.61, 126.40, 126.10, 125.34, 120.92, 120.35, 119.14, 117.76, 72.30, 68.49, 61.90, 39.58.HPLC purity: 98.3%, Retention time = 11.61 min. HRMS (EI) calcd for $C_{22}H_{17}NO_4S$ $[M]^+$: 391.0878, found: 391.0875. mp (**1d**) 160.0-160.7^{o}C.^{1}H NMR (400 MHz, CDCl3): δ 8.89 (s, 1H), 8.45 (d, J = 7.2 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.09 (dd, J_1 = 2.0 Hz, J_2 = 5.2 Hz, 1H), 7.84 (dd, J_1 = 2.8 Hz, J_2 = 5.2 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.48~7.50 (m, 2H), 4.41 (t, J = 5.2 Hz, 2H), 3.91 (t, J = 5.2 Hz, 2H), 3.72-3.74 (m, 4H), 2.76 (brs, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): 162.78, 162.71, 142.03, 137.75, 134.69, 131.99, 129.75, 129.36, 127.37, 127.34, 125.64, 125.34, 125.23, 123.77, 122.82, 122.24, 122.01, 118.64, 72.08, 66.88, 60.21, 38.71. HPLC purity: 99.5%, Retention time = 12.17 min. HRMS (EI) calcd for $C_{22}H_{17}NO_4S[M]^+$: 391.0878, found: 391.0881.

3. Methods

3.1 Spectroscopic materials and methods

Spectroscopic properties were measured on All Varian Cary 100 UV spectrophotometer and Varian Cary Eclipse FL spectrophotometer and the singlet oxygen quantum yields were accomplished by monochromatic light system composed of CM 110 1/8mmonochromator and ASB-XE-175 Xenon light source from Spectral Products. Optical imaging was performed through fluorescence microscope and confocal microscopy (Nikon, Japan).

3.2 Determination of fluorescent quantum yield

All compounds were dissolved in ethanol at room temperature. Absorbance spectra and relevant fluorescence spectra were collected by a Varian Cary 100 UV-Vis spectrophotometer and a Varian Cary Eclipse Fluorescence spectrophotometer. The molar extinction coefficients were obtained by

Lambert-Beer`s Law and fluorescence quantum yields were calculated as below:

$$\Phi_F = \Phi_R\left(\frac{S}{S_R}\right)\left(\frac{\eta}{\eta_R}\right) \quad (1)$$

where Φ is the fluorescence quantum yield, S is the slope of integrated fluorescence intensity vs. absorbance, η is the relatively refractive index of solvent, subscript $_R$ indicate the reference standard of 4-*N*-butylamide-*N*-butyl-1,8-naphthalimide, whose fluorescent quantum yield (Φ_R) was 0.81 in ethanol.

3.3 Determination of singlet oxygen quantum yield [S2]

To quantify the irradiation-induced singlet oxygen ($^1O_2$), a singlet oxygen trap 1,3-Diphenylisobenzofuran (DPBF) was used in air-saturated acetonitrile. Compounds were dissolved in acetonitrile and added to 100-fold excess DPBF stock solution. After laser irradiation with a monochromator (ASB-XE-175 Xenon light source), the absorbance of DPBF at 410 nm was recorded every half or one minute. Methylene Blue (whose singlet oxygen quantum yield was 0.52 in acetonitrile) was utilized as a contrast. The singlet oxygen quantum yields were determined using the equation:

$$\Phi_{\Delta(T)} = \Phi_{\Delta(MB)}\left(\frac{S_T}{S_{MB}}\right)\left(\frac{F_T}{F_{MB}}\right) \quad (2)$$

Where Φ_Δ is the singlet oxygen quantum yield, S is the slope of absorbance of DBPF vs. irradiation time and F is the absorption correction factor.

3.4 Cell culture

Human cell lines (MCF-7, HCT116, U87, MKN45, A375) were purchased from The Cell Bank of Type Culture Collection of the Chinese Academy of Sciences (Shanghai, China). Cells were cultured in RPMI-1640 or DMEM medium, supplemented with 10% fetal bovine serum (FBS, Hyclone, USA) and 1% antibiotic- antimycotic (ABAM Life Technologies, California, USA) in a humidified atmosphere of 95% air and 5% CO_2.

3.5 Cell viability assay

To evaluate the tumor inhibitory efficacy of **1a-1d**, MCF-7 cells (1×10^4) were suspended in medium and plated in 96 well plates. After treatment with indicated concentrations (0-20 μM) of **1a-1d** for 48 hours, cells were irradiated with the 100-watt quartz-halogen lamp. The fluorescence rate was 240 W/m^2, measured by a photo radiometer (Delta Ohm, Padua, Italy).After 20 mins of PDT treatment and 4 hours of MTT incubation, the cell viability was determined by MTT assay.[S3]As the optimal candidate,**1a** was then solely evaluated in other cell lines including HCT116, U87,

MKN45and A375 cells by the same methods above.

3.6 *In vitro* imaging of 1a

3.6.1 Fluorescence microscopic imaging

With a aim to assess fluorescent imaging results *in vitro*, A375 cells (1×10^5) were treated with **1a** (2.5 μM, 2 mL) for 48 h. After that, cells were exposed to the light of 28.8 J/cm^2 within 20 mins for PDT. 4 hours later, the cells were rinsed with PBS for three times. Images were exposed by excitation at 460 nm and emission at 520 nm under an inverted Fluorescence microscope (Nikon, Japan).

3.6.2 Subcellular localization studies

A375 cells (1×10^5) were seeded on a coverslip and co-incubated with **1a** (2.5 μM, 2 mL) for 48 hours. After 20 mins of PDT treatment, the cells were rinsed with PBS for three times and incubated in culture medium with 100 nMMitoTracker Red (invitrogen, USA) for 20 mins, 100 nM ER-Tracker Red for 20 mins (Beyotime, China), 50 nM Lysosome Tracker Red (Beyotime, China) for 30 mins, 1 μM DAPI (Beyotime, China) for 15 mins, respectively. The stained live cells were observed by confocal microscopy (Nikon, Japan).

3.7 *In vivo* experiments

All six-weeks old nude mice with half males and half females were purchased from Shanghai Slac Laboratory Animal Co. Ltd (The license of experimental animal: SCXK(shanghai) 2012-0002). The mice were maintained under the 12 hour light/dark cycles condition in the specific pathogen free (SPF) cleanroom with fresh air (more than 50%), appropriate temperature (22-26 oC) and humidness (40%-60%). The mice were freely fed with enough sterilized water and food bought from Shanghai Slac Laboratory Animal Co. Ltd. All materials and containers were disinfected and sterilizated before use. After the treatment, the mice were anesthetized and euthanasia in accordance with the international ethical standards. All experimental procedures involving animals in this study were reviewed and approved by the institution of ethics committee in ECUST and strictly conducted according to the guidelines of Care and Use of Laboratory Animals of China (GB14925-2001) for animal experimentation.

Each nude mouse was anesthetized with pelltobarbitalum natricum and subcutaneously inoculated with injection of 1×10^6A375 cells. When the volume of the tumor grew to 100 mm^3 size, mice were randomizedinto three groups: control group，medicine group and PDT group (each group had 6 mice). **1a** (5 mg/kg) was injected into both medicine group and PDT group of mice in situ while saline in the control group. After 8 hours, 600-micron bare fiber was used to give PDT treatment by white light from ASB-XE-175 Xenon light sourceand it was totally irradiated with a light-dose of 259.2 J/cm^{2}within 60 min. All groups were administered the injection twice a week,

total 6 times during the treatment time. Tumor sizes were measured every 3 days using micrometer calipers. 4 hours after the laser treatment, tumor xenografts were removed and measured. During the experiment, tumor sizes were measured every 3 days using micrometer calipers and tumor volume (TV) was calculated using the following formula: TV (mm^3) = D × $d^2/2$, D is the shortest diameters while d is the longest one. Relative tumor volume (RTV) was calculated according to the equation: RTV = V_t /V_0, where V_0 is the tumor volume at day 0 and V_t is the tumor volume at day t.

3.8 H&E staining

Hematoxylin-eosin staining was a conventional method for observing the histological changes of the tissues. After indicated experiments, all of the tumor tissues and several visceral organs tissues were collected and embedded in paraffin. The slices were separately treated with hematoxylin and eosin solution and images were taken with fluorescence microscope (Nikon, Japan).

3.9 Mechanistic study

3.9.1 Measurement of oxidative damage

DCFH-DA method(2',7'-dichlorofluorescein diacetate) was employed to evaluate intracellular reactive oxygen species (ROS) level.[S4]After 20 mins PDT treatment, cells were collected in serum-free medium and co-incubated with 10 μM DCFH-DA at 37 °C for another 20 mins. Cells were then washed three times with PBS and ROS generation was measured using fluorescence intensity of excitation at 488 nm and emission at 525 nm by EnSpire® Multimode Plate Reader (Perkin Elmer, Boston, MA).

3.9.2 Hoechst 33342 staining

A375 cells (1×10^5) were seeded on glass bottom dishes, cultured and treated with **1a** as described above. The cells were stained with Hoechst 33342 (Sigma, USA) for 20 mins at 37 ^oC in the dark condition after rinsed with PBS for twice. The images were exposed by the fluorescence microscope (Nikon, Japan).

3.9.3 Western blot analysis

After subjected to the indicated treatment, cells were harvested and lysed with cell lysis solution. Total proteins were quantified using the BCA protein assay kit. Equal amount of protein was run on 10% sodium dodecylsulfate (SDS) polyacrylamide gels and then transferred to PVDF membranes. The membranes were blocked in TBS-Tween 20 solution with non-fat dry milk prior to incubated overnight with primary antibodies PARP (SAB, USA), cleaved-PARP (SAB, USA), Caspase 3 (GenTex, USA) and cleaved-Caspase 3 antibodies (GenTex, USA) (1 mg/mL for each antibody). Following three washes with TBS-T, membranes were incubated with HRP conjugated secondary antibody for 2 h at room temperature. Then membranes were washed by TBS-T three times again,

developed in ECL and visualized with X-ray film.β-actin (GenTex, USA) was used as an internal control.

3.9.4 Immunohistochemistry

The expression of Caspase 3 in tumor tissues of nude mice model was assessed by immunohistochemistry assay. The samples were embedded in paraffin and stained by Caspase 3 antibodies (Bioworld, China). [S5] Images were then taken with a fluorescence microscope (Nikon, Japan).

3.9.5 Tunel assay

Tumor apoptosis was performed following the manufacturer's instructions of terminal deoxynucleotidyl transferase Dutp nick end labeling (TUNEL) assay (Roche Applied Science, Germany). The slides were photographed with a fluorescence microscope (Nikon, Japan).

3.10 Statistical analysis

All results shown in the study were obtained in at least three independent experiments and were expressed as mean ± standard deviation (SD). Statistical analysis of data was performed using Excel (Microsoft) and GraphPad Prism 5.0 software (GraphPad Software Inc, CA, USA). Significant differences are considered as *p< 0.05; ** p< 0.01; *** p< 0.001.

4. Data

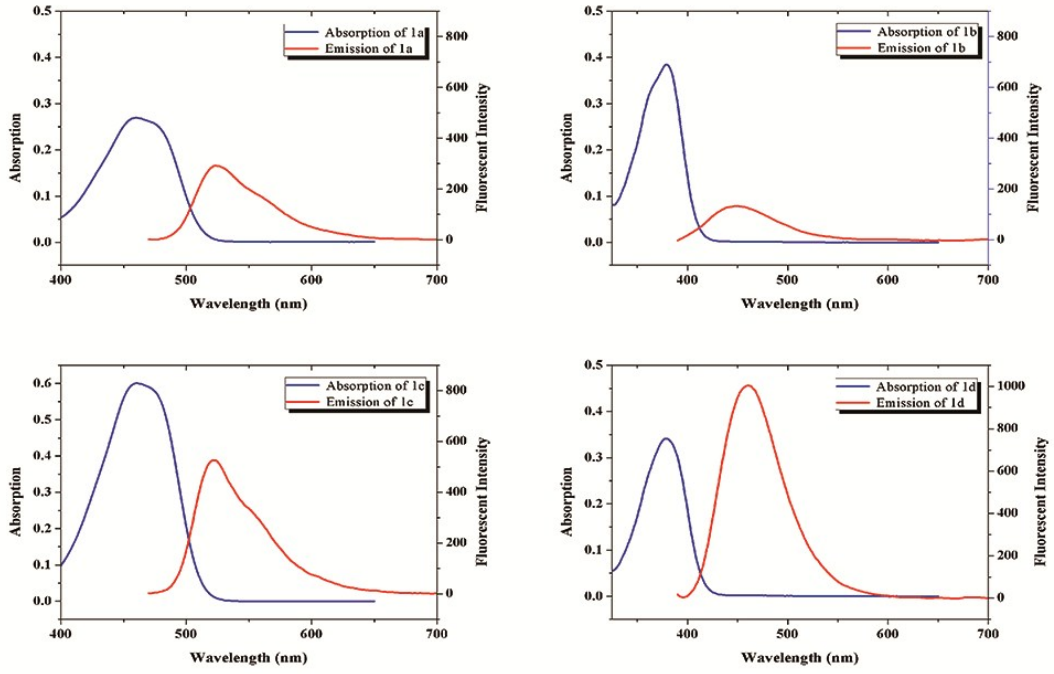


Fig. S1 The UV absorption spectra (blue line) and fluorescent emission spectra (red line)of **1a** (25

μM, slit: 2.5, 2.5), **1b**(25 μM, slit: 5, 5), **1c** (25 μM, slit: 2.5, 2.5) and **1d** (25 μM, slit: 5, 5) in EtOH.

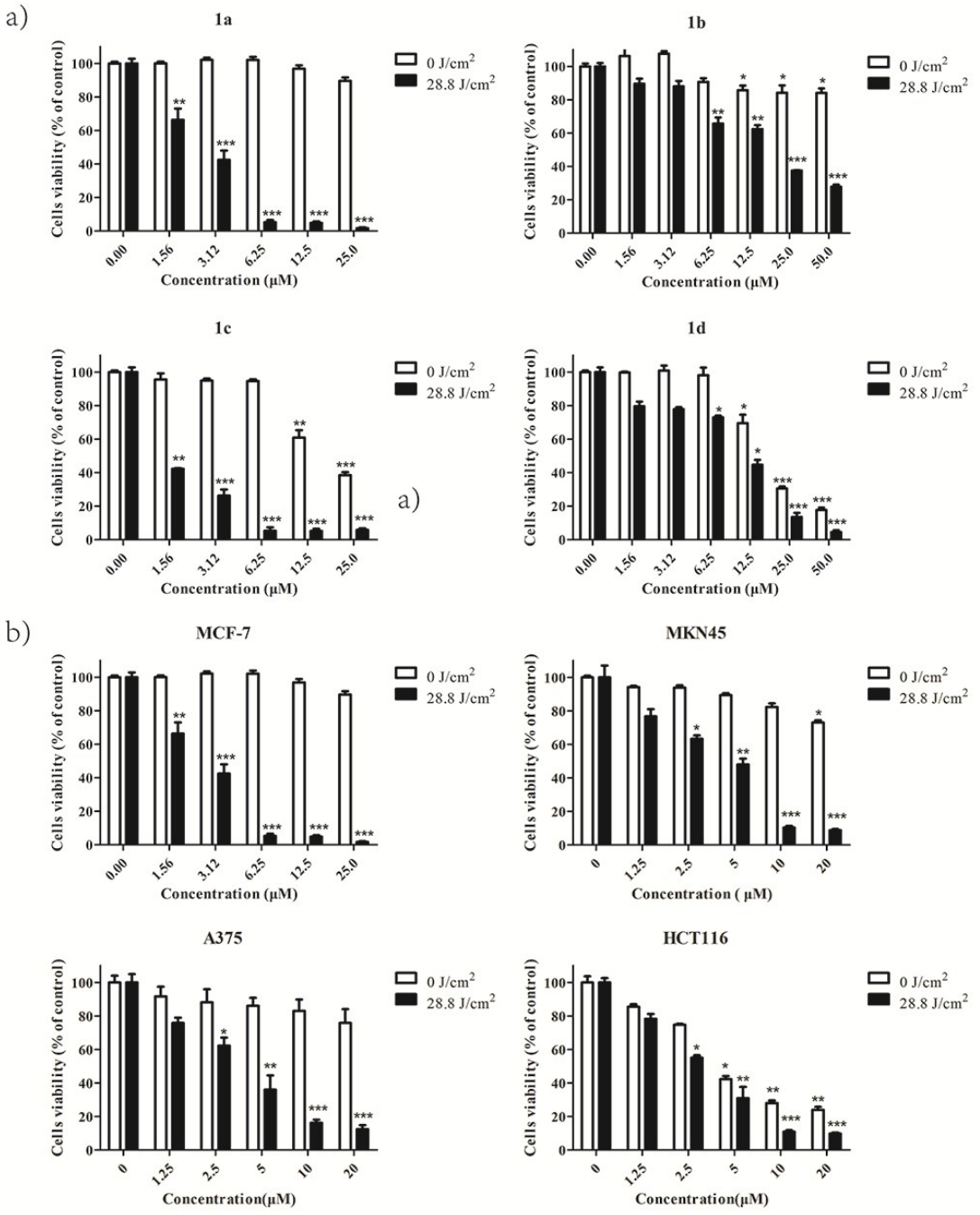


Fig. S2 a) MTT assays of **1a-1d** exposed with laser irradiation of 0 and 28.8 J/cm^2 in MCF-7 cells; b) MTT assays of **1a** exposed with laser irradiation of 0 and 28.8 J/cm^2 light in A375, HCT116, MKN45 and MCF-7 cells.

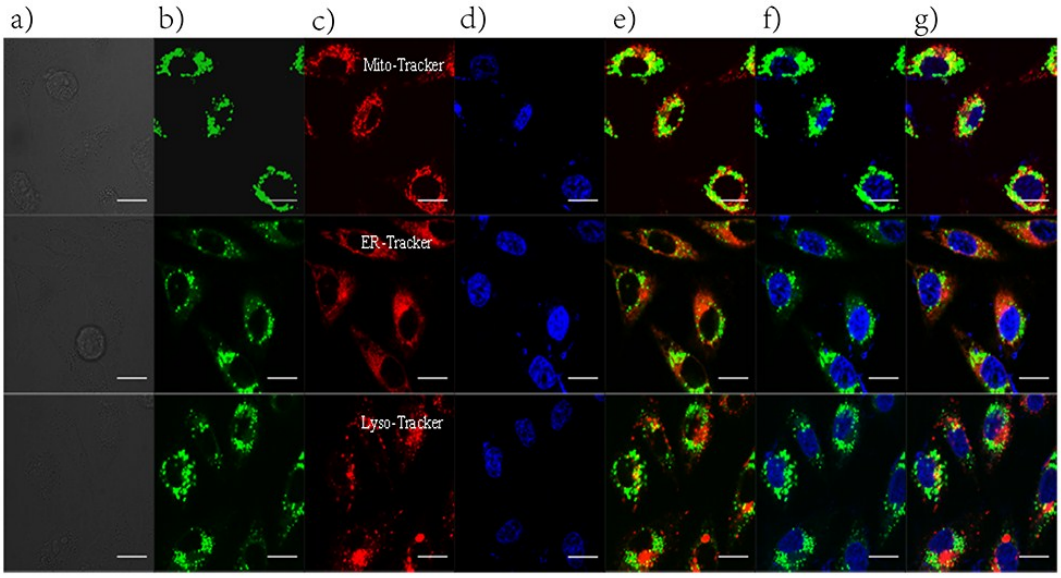


Fig. S3 Fluorescence confocal microscopy imaging of **1a** in A375 cells**.**Co-localizaiton with Mito-Tracker Red, ER-Tracker Red and Lysosome Tracker Red: a) white light; b) **1a**; c) organelles tracker probes; d) blue DAPI; e) the merge results of b and c; f) the merge results of b and d; g) the merge results of b, c and d. Bars: 10 μm

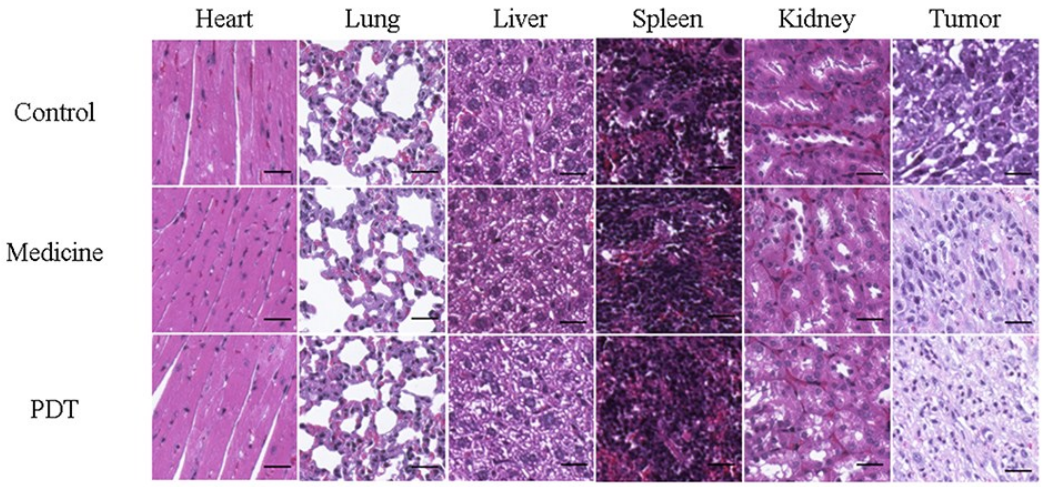


Fig. S4 Pathological changes of major organs (including kidney, liver, spleen, heart and lung) and tumor tissues by H&E stained images. Bars: 50 μm.

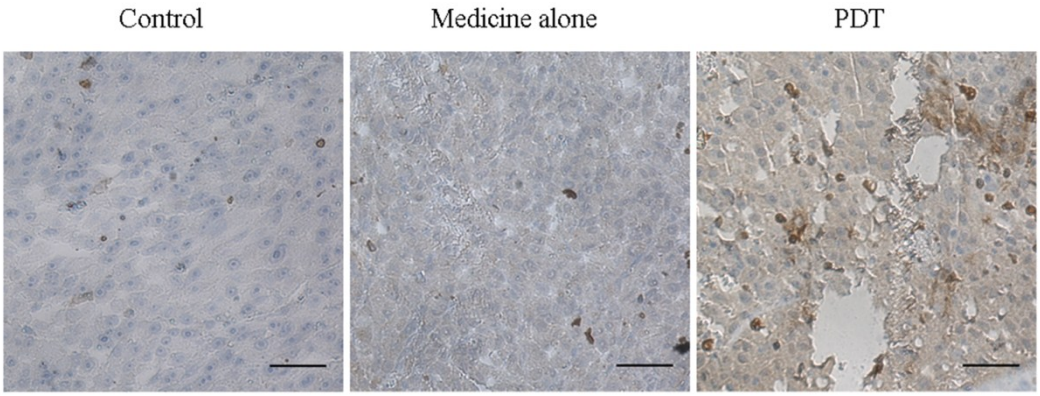


Fig. S5 Immunohistochemical assessment of cleaved-Caspase 3 expression of tumor cells after **1a**-induced PDT treatment. Scale bars: 50 μm;

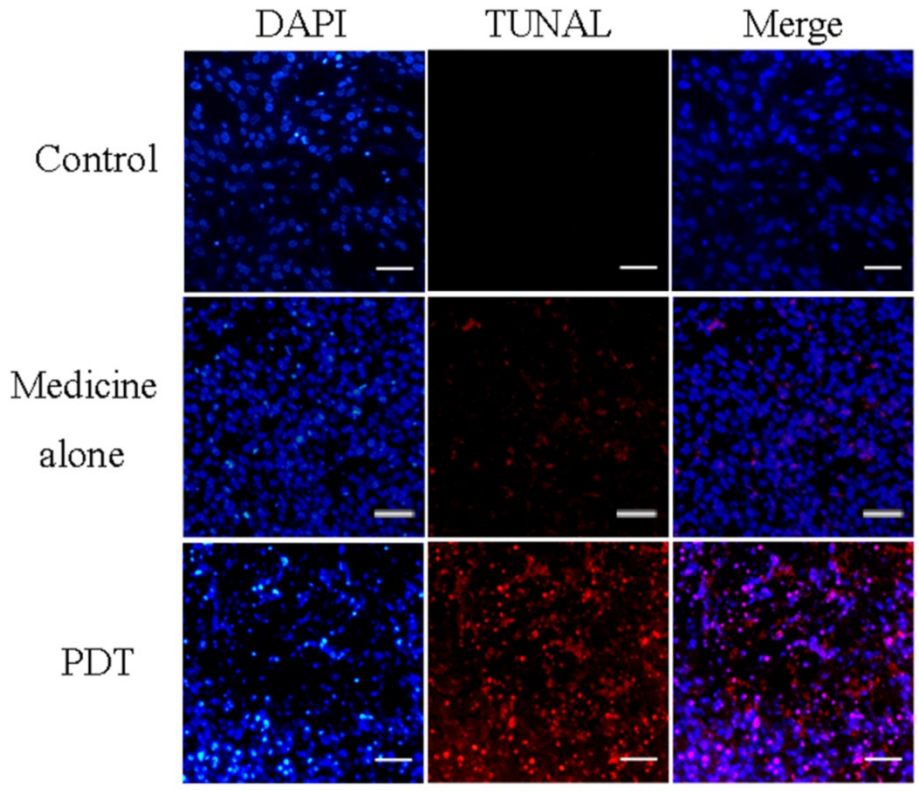


Fig. S6 TUNEL assays of apoptotic cells in the tumor tissues. The nuclei stained with DAPI (bright blue) and apoptotic cells (bright red) were observed using fluorescent microscopy. Bars: 50 μm

5. NMR spectra

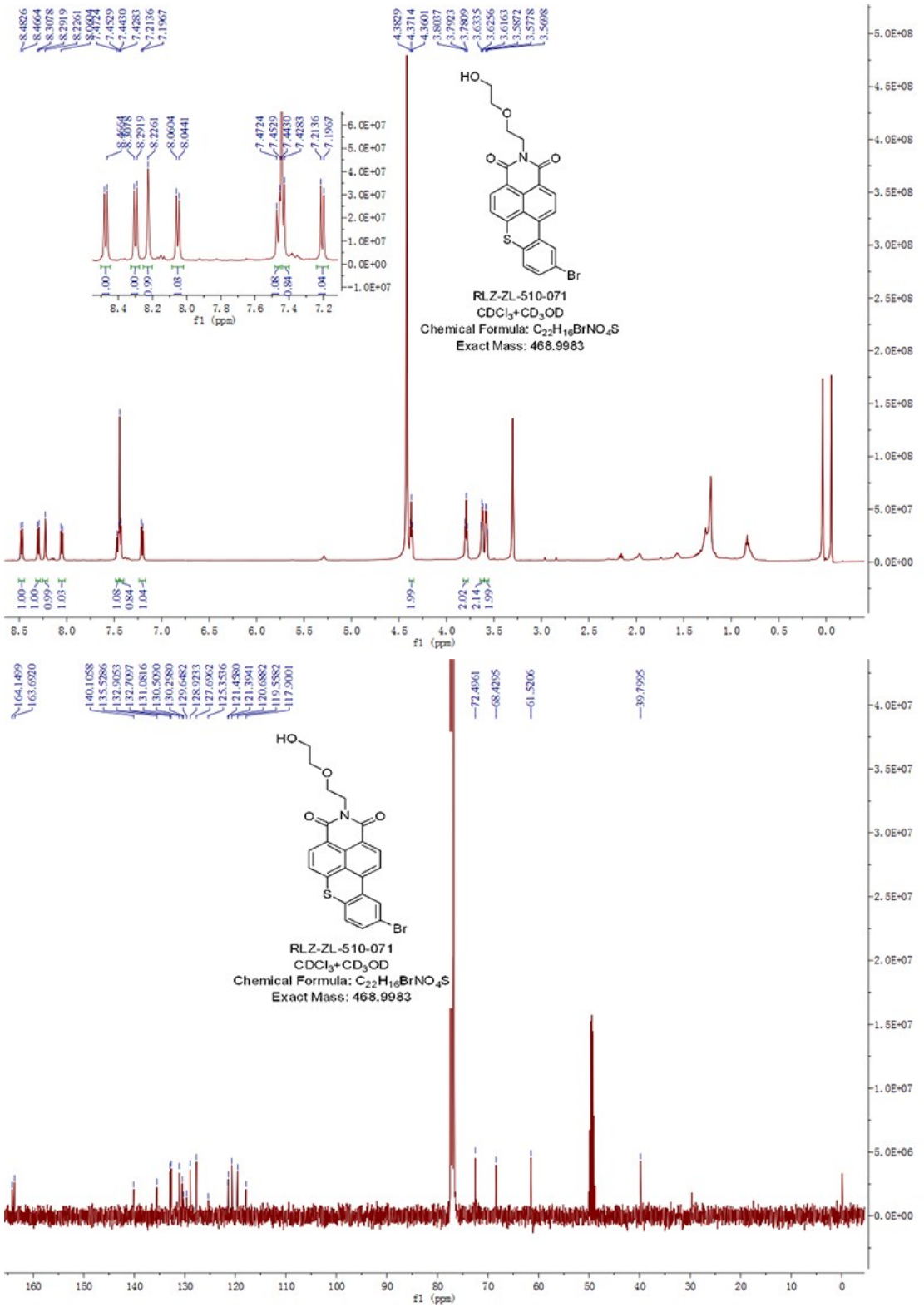


Fig. S7 The ^{1}H-NMR and ^{13}C-NMR spectrum of **1a**

Elemental Composition Report **Page 1**

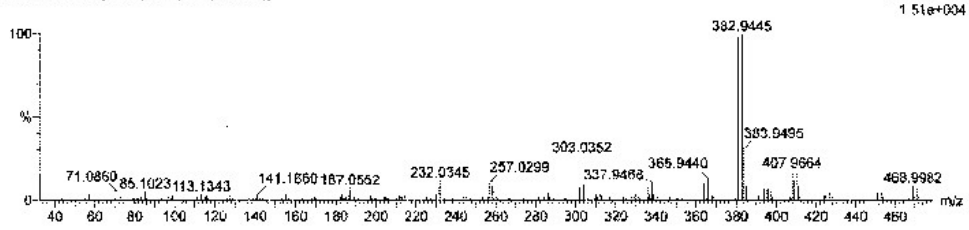
Multiple Mass Analysis: 53 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
6263 formula(e) evaluated with 255 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-24 H: 0-18 N: 0-1 O: 0-5 S: 0-1 79Br: 0-1 81Br: 0-1

RLZ-ZL-510-071
20150095 448 (7.467) Cm (448-(70+659))

Waters GCT Premier

TOF MS EI+
1.51e+004



Minimum:	3.00				-1.5		
Maximum:	100.00		5.0	10.0	50.0		
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
57.0709	3.52	57.0704	0.4	7.0	0.5	2773012.9	C4 H9
71.0860	4.58	71.0861	-0.1	-1.4	0.5	654.3	C5 H11
85.1023	5.05	85.1017	0.6	7.1	0.5	213.5	C6 H13
99.1175	3.26	99.1174	0.1	1.0	0.5	2773016.3	C7 H15
113.1343	3.35	113.1330	1.3	11.5	0.5	57.3	C8 H17
127.1492	3.09	---					
141.1660	3.24	---					
155.1798	3.00						
182.9687	3.18	182.9684	0.3	1.6	5.0	156.5	C7 H6 N 79Br
		182.9666	2.1	11.5	0.5	213.8	C5 H10 S 81Br
		182.9657	3.0	16.4	0.5	172.7	C4 H8 O3 79Br
		182.9717	-3.0	-16.4	0.0	159.3	C4 H10 N S 79Br
		182.9718	-3.1	-16.9	1.0	202.0	C4 H8 N O2 81Br
187.0552	7.21	187.0548	0.4	2.1	12.5	149.4	C15 H7
		187.0581	-2.9	-15.5	7.5	130.6	C12 H11 S
		187.0514	3.8	20.3	-1.0	205.6	C4 H13 N O5 S
214.0659	3.37	214.0657	0.2	0.9	13.5	2773034.5	C16 H8 N
		214.0664	-0.5	-2.3	4.0	2773176.8	C10 H14 O3 S
		214.0630	2.9	13.5	9.0	2773036.0	C13 H10 O3
		214.0690	-3.1	-14.5	8.5	2773169.3	C13 H12 N S
230.0181	3.53	230.0181	0.0	0.0	3.5	950.7	C9 H13 N O 79Br
		230.0190	-0.9	-3.9	14.0	1333.2	C16 H6 S
		230.0163	1.8	7.8	-1.0	1417.7	C7 H17 O S 81Br
		230.0157	2.4	10.4	19.0	1335.5	C19 H2
		230.0154	2.7	11.7	-1.0	589.1	C6 H15 O4 79Br
		230.0214	-3.3	-14.3	-1.5	841.2	C6 H17 N O S 79Br
		230.0215	-3.4	-14.3	10.0	1369.5	C12 H6 O5
		230.0215	-3.4	-14.8	-0.5	1411.4	C6 H15 N O3 81Br
231.0253	7.37	231.0259	-0.6	-2.6	3.0	939.2	C9 H14 N O 79Br
		231.0241	1.2	5.2	-1.5	997.2	C7 H18 O S 81Br
		231.0268	-1.5	-6.5	13.5	861.7	C16 H7 S
		231.0235	1.8	7.8	18.5	862.1	C15 H3
		231.0232	2.1	9.1	-1.5	969.9	C6 H16 O4 79Br
		231.0293	-4.0	-17.3	-1.0	1049.8	C6 H16 N O3 81Br
		231.0293	-4.0	-17.3	9.5	965.0	C12 H7 O5
		231.0208	4.5	19.5	3.5	1017.0	C10 H18 O 81Br
232.0345	11.86	232.0347	-0.2	-0.9	13.0	23.2	C16 H8 S
		232.0337	0.8	3.4	2.5	948.2	C9 H15 N O 79Br
		232.0371	-2.6	-11.2	-1.5	176.3	C6 H17 N O3 81Br
		232.0372	-2.7	-11.6	9.0	90.8	C12 H8 O5
		232.0313	3.2	13.8	18.0	39.3	C19 H4
233.0357	3.28	233.0358	-0.1	-0.4	4.0	2773199.8	C8 H11 N O5 S

Fig. S8 The HR-MS spectrum of **1a**

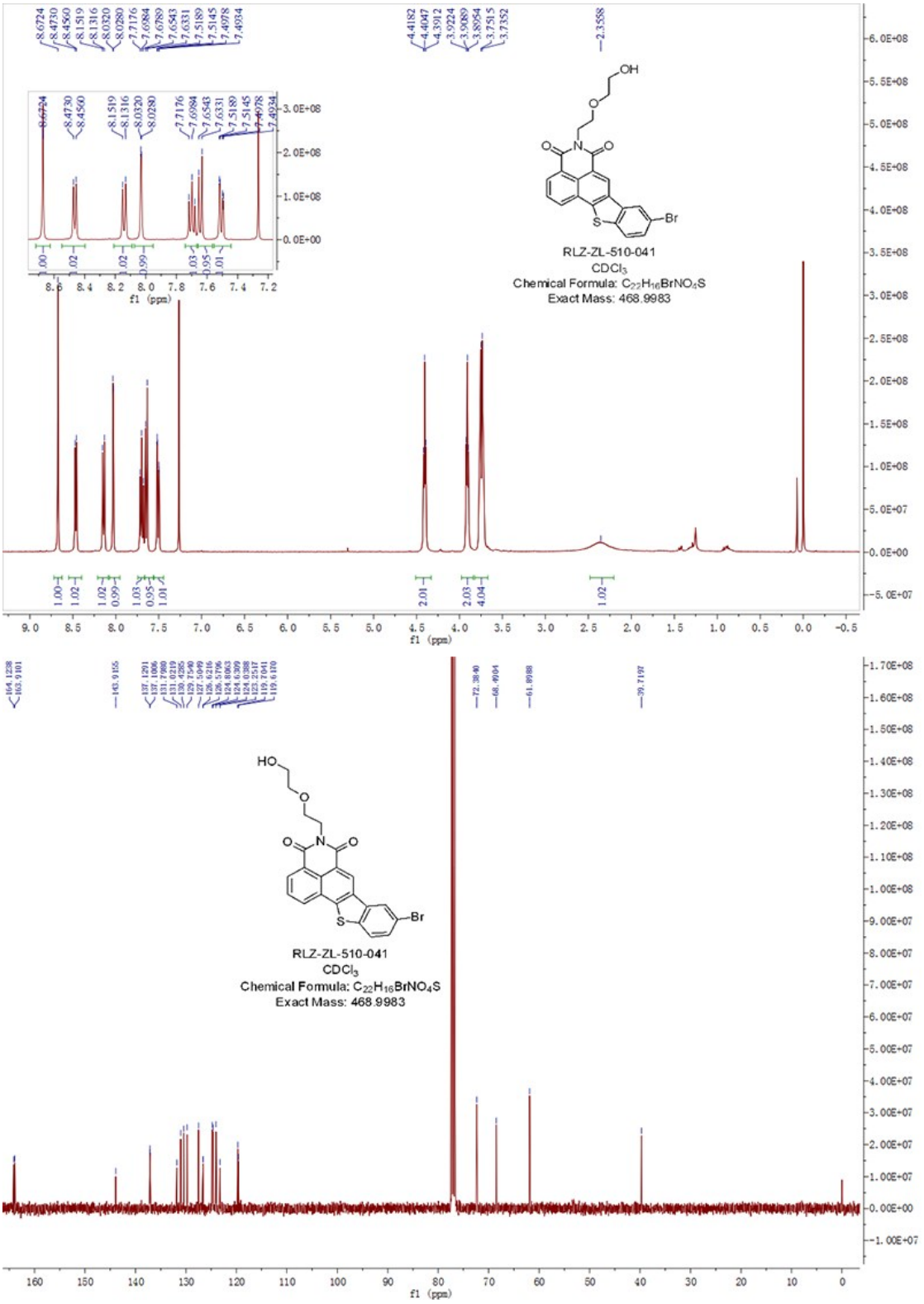


Fig. S9 The ^{1}H-NMR and ^{13}C-NMR spectrum of **1b**

Elemental Composition Report Page 1

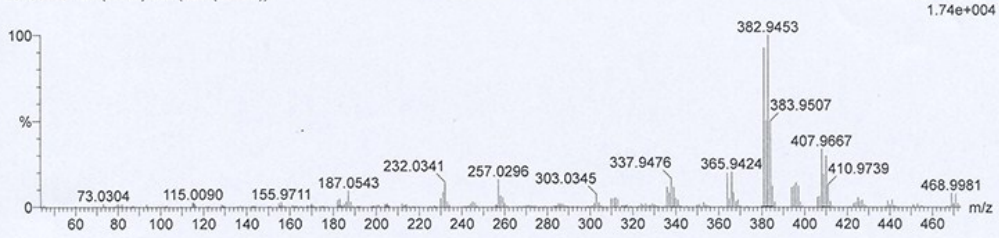
Multiple Mass Analysis: 50 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
4707 formula(e) evaluated with 202 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-22 H: 0-16 N: 0-1 O: 0-4 S: 0-1 79Br: 0-1 81Br: 0-1

RLZ-ZL-510-041
20160115 427 (7.117) Cm (427-(87+93))

Waters GCT Premier

TOF MS EI+
1.74e+004



Minimum:	3.00				-1.5		
Maximum:	100.00		5.0	10.0	50.0		
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
181.9706	3.88	181.9701	0.5	2.7	11.5	346.1	C10 N O S
		181.9731	-2.5	-13.7	5.0	601.6	C8 H7 79Br
		181.9674	3.2	17.6	7.0	369.2	C7 H2 O4 S
182.9697	4.70	182.9684	1.3	7.1	5.0	271.5	C7 H6 N 79Br
		182.9717	-2.0	-10.9	0.0	278.4	C4 H10 N S 79Br
		182.9718	-2.1	-11.5	1.0	249.6	C4 H8 N O2 81Br
		182.9666	3.1	16.9	0.5	255.2	C5 H10 S 81Br
		182.9657	4.0	21.9	0.5	293.4	C4 H8 O3 79Br
187.0543	9.25	187.0548	-0.5	-2.7	12.5	72.1	C15 H7
		187.0581	-3.8	-20.3	7.5	75.9	C12 H11 S
230.0202	4.93	230.0190	1.2	5.2	14.0	1788.5	C16 H6 S
		230.0215	-1.3	-5.7	-0.5	1913.8	C6 H15 N O3 81Br
		230.0181	2.1	9.1	3.5	1055.2	C9 H13 N O 79Br
		230.0242	-4.0	-17.4	14.5	1812.5	C15 H4 N O2
		230.0157	4.5	19.6	19.0	1793.0	C19 H2
		230.0154	4.8	20.9	-1.0	1113.0	C6 H15 O4 79Br
231.0257	8.47	231.0259	-0.2	-0.9	3.0	1365.0	C9 H14 N O 79Br
		231.0268	-1.1	-4.8	13.5	1144.6	C16 H7 S
		231.0235	2.2	9.5	18.5	1170.3	C19 H3
		231.0232	2.5	10.8	-1.5	1401.8	C6 H16 O4 79Br
		231.0293	-3.6	-15.6	-1.0	1393.7	C6 H16 N O3 81Br
		231.0208	4.9	21.2	3.5	1349.9	C10 H14 O 81Br
232.0341	14.27	232.0337	0.4	1.7	2.5	1253.4	C9 H15 N O 79Br
		232.0347	-0.6	-2.6	13.0	6.0	C16 H8 S
		232.0313	2.8	12.1	18.0	37.9	C19 H4
233.0358	3.15	233.0364	-0.6	-2.6	2.5	2773048.3	C10 H16 O 81Br
		233.0391	-3.3	-14.2	17.5	2773071.3	C19 H5
257.0296	15.96	257.0299	-0.3	-1.2	15.0	441.9	C17 H7 N S
		257.0272	2.4	9.3	10.5	502.6	C14 H9 O3 S
		257.0265	3.1	12.1	20.0	513.4	C20 H3 N
		257.0263	3.3	12.8	0.0	893.6	C7 H16 N O4 79Br
258.0358	6.52	258.0351	0.7	2.7	10.0	417.8	C14 H10 O3 S
		258.0344	1.4	5.4	19.5	403.2	C20 H4 N
		258.0377	-1.9	-7.4	14.5	381.5	C17 H8 N S
		258.0317	4.1	15.9	15.0	439.9	C17 H6 O3
		258.0317	4.1	15.9	4.5	520.8	C11 H15 N O 81Br
259.0420	5.52	259.0422	-0.2	-0.8	19.0	61.0	C20 H5 N
		259.0429	-0.9	-3.5	9.5	67.6	C14 H11 O3 S
		259.0395	2.5	9.7	14.5	77.2	C17 H7 O3
		259.0395	2.5	9.7	4.0	126.4	C11 H16 N O 81Br
		259.0456	-3.6	-13.9	14.0	50.4	C17 H9 N S
303.0345	7.09	303.0354	-0.9	-3.0	15.0	34.1	C18 H9 N O2 S

Fig. S10 The HR-MS spectrum of **1b**

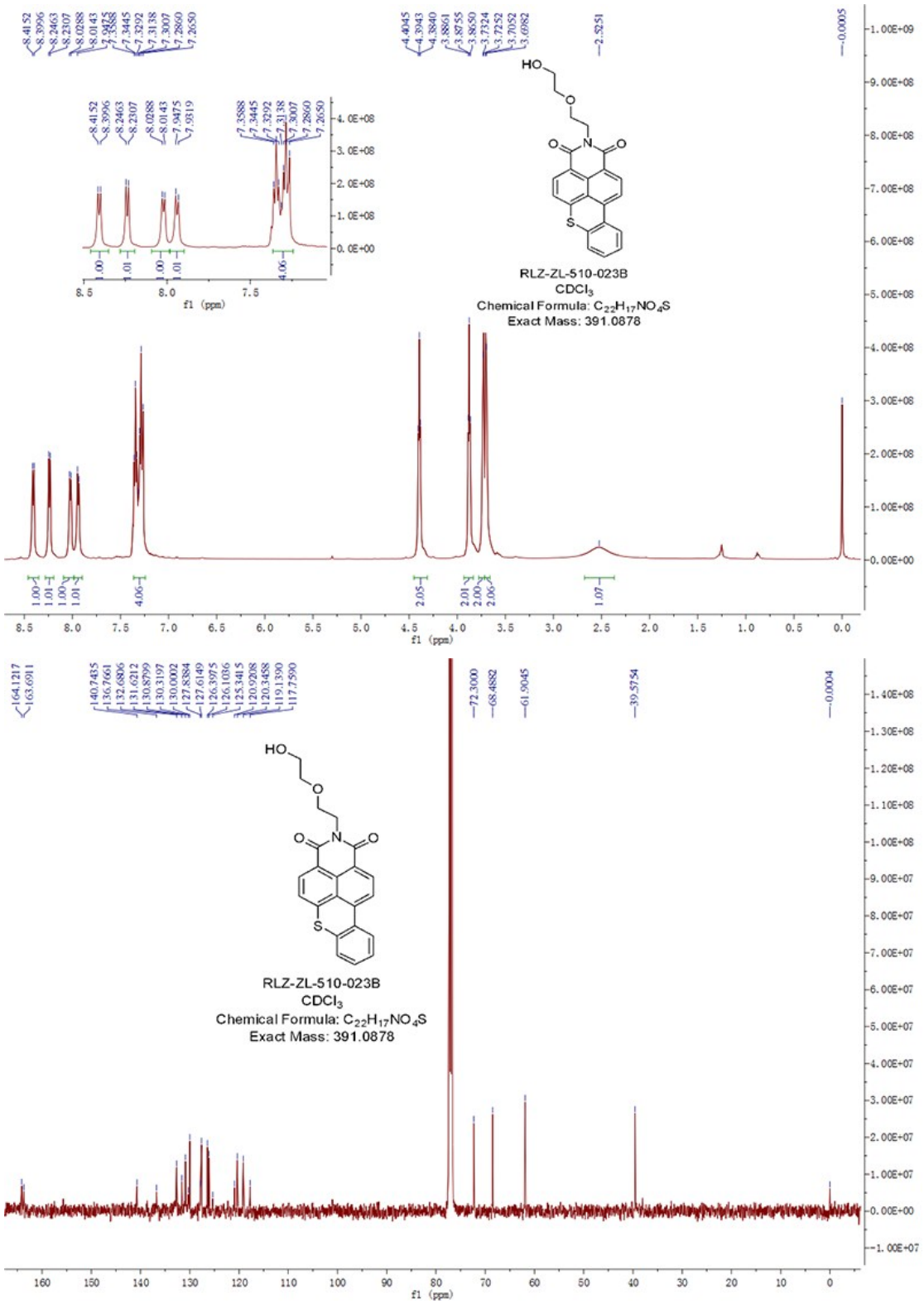
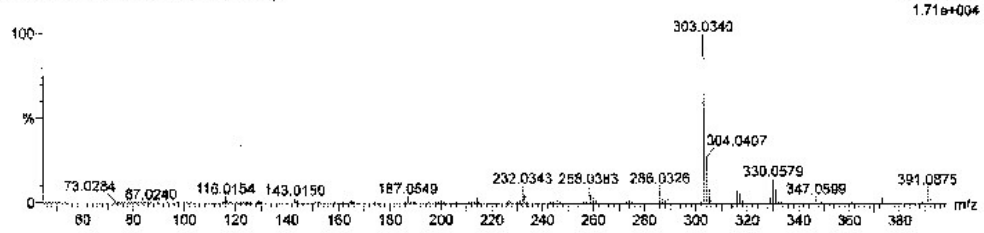


Fig. S11 The ^{1}H-NMR and ^{13}C-NMR spectrum of **1c**

Elemental Composition Report Page 1

Multiple Mass Analysis: 22 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
552 formula(e) evaluated with 43 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-22 H: 0-17 N: 0-1 O: 0-4 S: 0-1
RLZ-ZL-600-023b GCT Premier TOF MS EI+ 1.71e+004
20141038 614 (10.234) Cm (614-(5+626))



Minimum:	3.00				-1.5		
Maximum:	100.00		5.0	10.0	50.0		
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
116.0154	3.46	116.0170	-1.6	-13.8	2.5	2773175.0	C4 H6 N O S
		116.0136	1.8	15.5	7.5	2773019.0	C7 H2 N O
		116.0110	4.4	37.9	3.0	2773023.8	C8 H4 O4
187.0549	3.76	187.0548	0.1	0.5	12.5	314.4	C15 H7
		187.0581	-3.2	-17.1	7.5	303.7	C12 H11 S
214.0656	3.12	214.0657	-0.1	-0.5	13.5	4.8	C16 H8 N
		214.0664	-0.8	-3.7	4.0	13.3	C10 H14 O3 S
		214.0630	2.6	12.1	9.0	9.1	C13 H10 O3
		214.0690	-3.4	-15.9	8.5	6.6	C13 H12 N S
232.0343	9.87	232.0347	-0.4	-1.7	13.0	161.1	C15 H8 S
		232.0313	3.0	12.9	18.0	180.7	C19 H4
233.0405	1.82	233.0391	1.4	6.0	17.5	1.5	C19 H5
		233.0425	-2.0	-8.6	12.5	16.8	C15 H9 S
246.0383	3.16	246.0377	0.6	2.4	13.5	2773211.5	C16 H8 N S
		246.0351	3.2	13.0	9.0	2773217.5	C13 H10 O3 S
		246.0344	3.9	15.9	18.5	2773062.8	C19 H4 N
258.0383	9.81	258.0377	0.6	2.3	14.5	429.6	C17 H8 N S
		258.0351	3.2	12.4	10.0	475.3	C14 H10 O3 S
		258.0344	3.9	15.1	19.5	472.3	C20 H4 N
259.0448	5.52	259.0456	-0.8	-3.1	14.0	289.0	C17 H9 N S
		259.0429	1.9	7.3	9.5	315.8	C14 H11 O3 S
		259.0422	2.6	10.0	19.0	306.7	C20 H5 N
260.0371	4.21	260.0391	-1.0	-3.8	9.5	87.0	C13 H10 N O3 S
		260.0348	2.3	8.8	14.5	50.4	C16 H6 N O3
286.0326	10.16	286.0327	-0.1	-0.3	15.5	73.3	C18 H8 N O S
		286.0300	2.6	9.1	11.0	84.0	C15 H10 O4 S
		286.0293	3.3	11.5	20.5	124.7	C21 H4 N O
303.0340	100.00	303.0356	-1.4	-4.6	15.0	113.8	C18 H5 N O2 S
		303.0323	2.0	6.6	20.0	285.3	C21 H5 N O2
304.0407	27.74	304.0399	0.8	2.6	19.5	43.8	C21 H6 N O2
		304.0432	-2.5	-8.2	14.5	50.2	C18 H10 N O2 S
305.0390	7.97	305.0425	-3.5	-11.5	18.5	85.9	C22 H9 S
316.0435	7.31	316.0432	0.3	0.9	15.5	308.8	C19 H10 N O2 S
		316.0399	3.6	11.4	20.5	326.6	C22 H6 N O2
317.0514	6.02	317.0511	0.3	0.9	15.0	3.7	C19 H11 N O2 S
		317.0477	3.7	11.7	20.0	8.1	C22 H7 N O2
328.0451	3.22	328.0432	1.9	5.8	16.5	1336.2	C20 H10 N O2 S
329.0514	3.22	329.0511	0.3	0.9	16.0	1706.8	C20 H11 N O2 S
330.0579	14.27	330.0589	-1.0	-3.0	15.5	220.7	C20 H12 N O2 S
331.0650	7.83	331.0667	-1.7	-5.1	15.0	19.5	C20 H13 N O2 S
347.0599	3.87	347.0616	-1.7	-4.9	15.0	12.0	C20 H13 N O3 S
373.0806	3.47	373.0773	3.3	8.8	16.0	16.4	C22 H15 N O3 S
391.0875	9.78	391.0879	-0.3	-0.8	15.0	0.4	C22 H17 N O4 S

Fig. S12 The HR-MS spectrum of **1c**

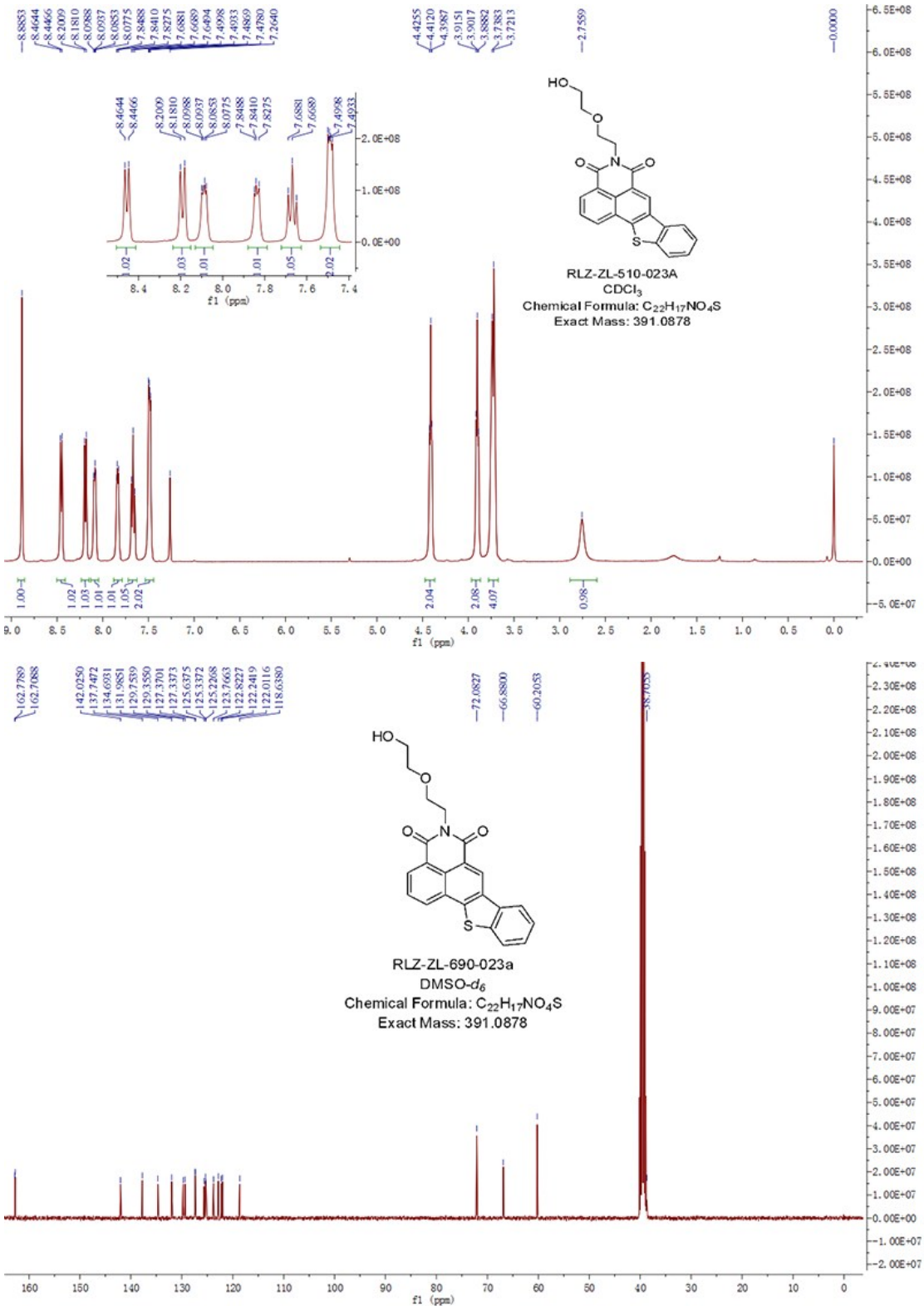


Fig. S13 The ^{1}H-NMR and ^{13}C-NMR spectrum of **1d**

Elemental Composition Report Page 1

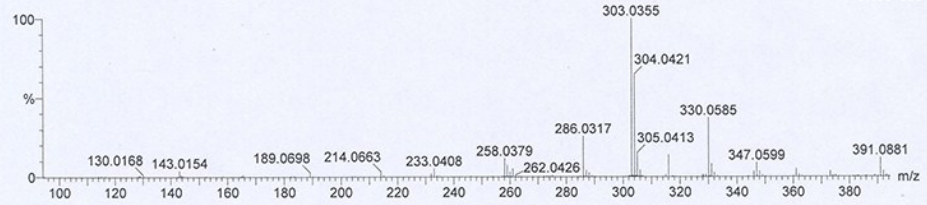
Multiple Mass Analysis: 22 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
508 formula(e) evaluated with 39 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-22 H: 0-17 N: 0-1 O: 0-4 S: 0-1

RLZ-ZL-510-023A
20160116 622 (10.374) Cm (622-54:67)

Waters GCT Premier

TOF MS EI+
9.18e+003



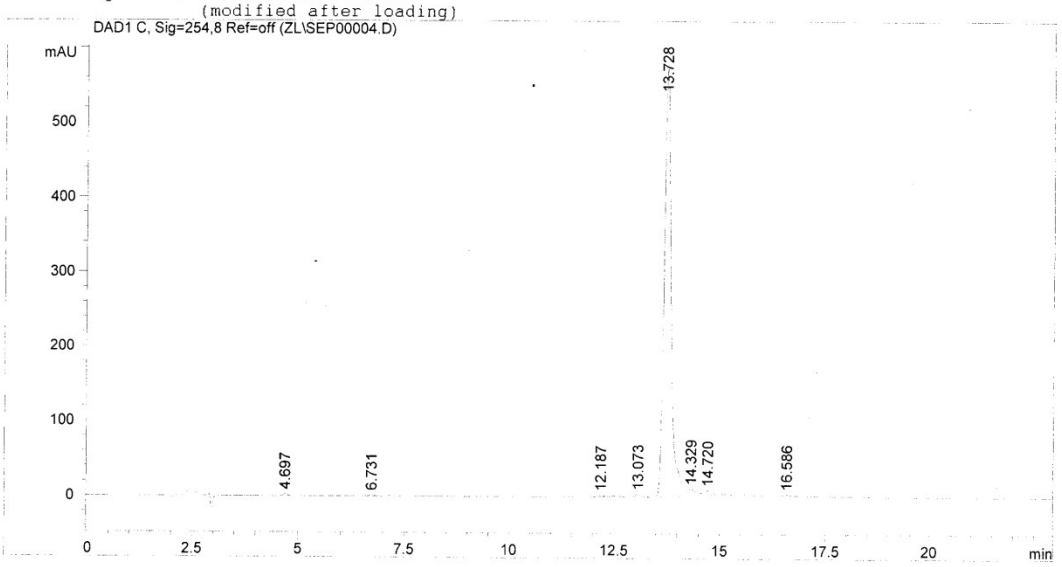
Minimum:	3.00				-1.5		
Maximum:	100.00		5.0	10.0	50.0		
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
143.0154	3.78	143.0167	-1.3	-9.1	3.5	2773097.0	C6 H7 O2 S
		143.0133	2.1	14.7	8.5	2773016.5	C9 H3 O2
214.0663	3.13	214.0664	-0.1	-0.5	4.0	2773091.8	C10 H14 O3 S
		214.0657	0.6	2.8	13.5	2773021.0	C16 H8 N
		214.0690	-2.7	-12.6	8.5	2773086.3	C13 H12 N S
		214.0630	3.3	15.4	9.0	2773024.8	C13 H10 O3
233.0408	5.09	233.0391	1.7	7.3	17.5	15.0	C19 H5
		233.0425	-1.7	-7.3	12.5	4.5	C16 H9 S
258.0379	11.31	258.0377	0.2	0.8	14.5	212.5	C17 H8 N S
		258.0351	2.8	10.9	10.0	242.6	C14 H10 O3 S
		258.0344	3.5	13.6	19.5	233.6	C20 H4 N
259.0448	7.16	259.0456	-0.8	-3.1	14.0	221.4	C17 H9 N S
		259.0429	1.9	7.3	9.5	233.9	C14 H11 O3 S
		259.0422	2.6	10.0	19.0	241.6	C20 H5 N
261.0396	5.08	261.0374	2.2	8.4	13.5	5.8	C17 H9 O S
		261.0426	-3.0	-11.5	14.0	2.0	C16 H7 N O3
286.0317	25.43	286.0327	-1.0	-3.5	15.5	28.5	C18 H8 N O S
		286.0300	1.7	5.9	11.0	11.1	C15 H10 O4 S
		286.0293	2.4	8.4	20.5	89.6	C21 H4 N O
287.0367	3.92	287.0371	-0.4	-1.4	20.0	50.3	C21 H5 N O
		287.0378	-1.1	-3.8	10.5	54.2	C15 H11 O4 S
		287.0344	2.3	8.0	15.5	59.1	C18 H7 O4
		287.0405	-3.8	-13.2	15.0	45.3	C18 H9 N O S
303.0355	100.00	303.0354	0.1	0.3	15.0	1379.0	C18 H9 N O2 S
		303.0320	3.5	11.5	20.0	1479.5	C21 H5 N O2
304.0421	64.47	304.0432	-1.1	-3.6	14.5	6.1	C18 H10 N O2 S
		304.0399	2.2	7.2	19.5	51.5	C21 H6 N O2
305.0413	14.80	305.0425	-1.2	-3.9	18.5	32.9	C22 H9 S
306.0412	4.12	306.0377	3.5	11.4	18.5	2773132.0	C21 H8 N S
316.0435	13.74	316.0432	0.3	0.9	15.5	5546641.5	C19 H10 N O2 S
		316.0399	3.6	11.4	20.5	5546644.0	C22 H6 N O2
330.0585	36.99	330.0589	-0.4	-1.2	15.5	6.6	C20 H12 N O2 S
331.0642	7.83	331.0667	-2.5	-7.6	15.0	7.4	C20 H13 N O2 S
346.0541	3.26	346.0538	0.3	0.9	15.5	444.3	C20 H12 N O3 S
347.0599	8.70	347.0616	-1.7	-4.9	15.0	15.8	C20 H13 N O3 S
348.0653	3.18	348.0694	-4.1	-11.8	14.5	0.9	C20 H14 N O3 S
361.0777	4.86	361.0773	0.4	1.1	15.0	0.7	C21 H15 N O3 S
373.0772	3.35	373.0773	-0.1	-0.3	16.0	19.2	C22 H15 N O3 S
391.0881	11.80	391.0878	0.3	0.8	15.0	0.7	C22 H17 N O4 S
392.0914	3.29	---					

Fig. S14 The HR-MS spectrum of **1d**

Data File C:\HPCHEM\1\DATA\ZL\SEP00004.D Sample Name: ZL09-1-071

RX C-18 4.6mm*250 Flow=1ml/min 132bar buffer

```
Injection Date  : 9/1/2015 3:56:38 PM
Sample Name     : ZL09-1-071                    Vial :  -
Acq. Operator   :
Method          : C:\HPCHEM\1\METHODS\ZL-1.M
Last changed    : 9/1/2015 2:23:57 PM
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
```

Signal 1: DAD1 C, Sig=254,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.697	BB	0.1126	19.95954	2.75191	0.2867
2	6.731	BP	0.1602	24.49353	2.19506	0.3518
3	12.187	BB	0.1350	16.66508	1.81653	0.2394
4	13.073	BP	0.1430	31.62502	3.44885	0.4543
5	13.728	BV	0.1752	6632.81689	572.54071	95.2725
6	14.329	VV	0.1864	120.27122	8.96936	1.7276
7	14.720	VB	0.2115	100.59117	6.39537	1.4449
8	16.586	PB	0.1492	15.52197	1.62920	0.2230
Totals :				6961.94443	599.74699	

Results obtained with enhanced integrator!

*** End of Report ***

nstrument 1 9/1/2015 4:22:10 PM Page 1 of 1

Fig. S15 The HPLC report of **1a**

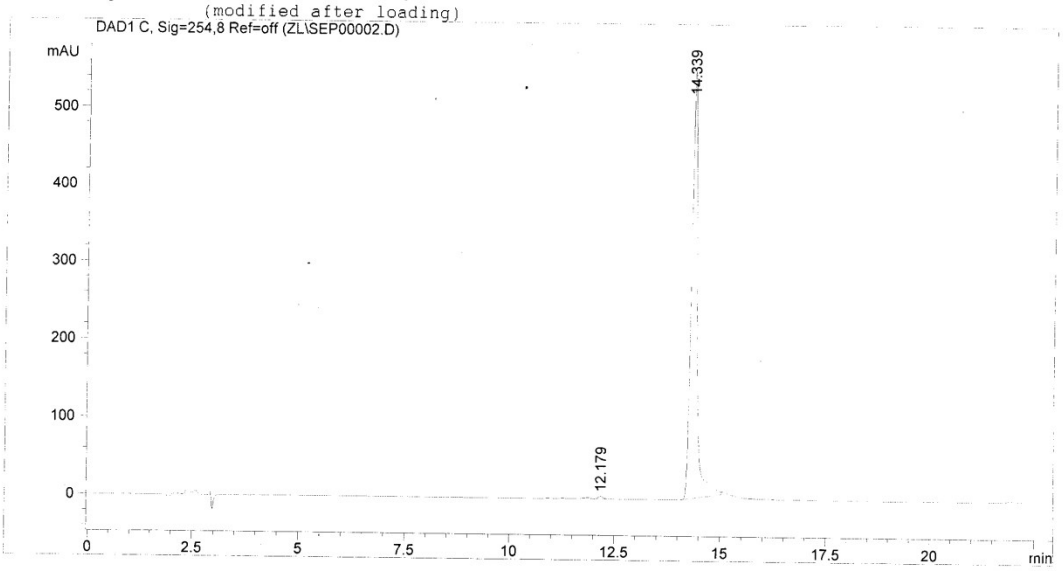
Data File C:\HPCHEM\1\DATA\ZL\SEP00002.D

Sample Name: ZL09-1-041

RX C-18 4.6mm*250 Flow=1ml/min 132bar buffer

1b

```
Injection Date   : 9/1/2015 2:33:18 PM
Sample Name      : ZL09-1-041                    Vial :  -
Acq. Operator    :
Method           : C:\HPCHEM\1\METHODS\ZL-1.M
Last changed     : 9/1/2015 2:23:57 PM
                   (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 C, Sig=254,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.179 BP    0.1189   25.84955    3.39254   0.4675
   2  14.339 PB    0.1507 5503.07031  550.21826  99.5325

Totals :                  5528.91986  553.61080

 Results obtained with enhanced integrator!
```

*** End of Report ***

nstrument 1 9/1/2015 3:43:20 PM

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Fig. S16 The HPLC report of **1b**

Data File C:\HPCHEM\1\DATA\ZL\MAR00098.D Sample Name: ZL03-17-023b

XDB 4.6mm*250 Flow=1.0ml/min 124bar (buffer)

```
==========================================================================
Injection Date  : 3/17/2016 9:45:39 AM
Sample Name     : ZL03-17-023b                    Vial :   -
Acq. Operator   :
Method          : C:\HPCHEM\1\METHODS\ZL-1.M
Last changed    : 3/17/2016 8:29:00 AM
                  (modified after loading)
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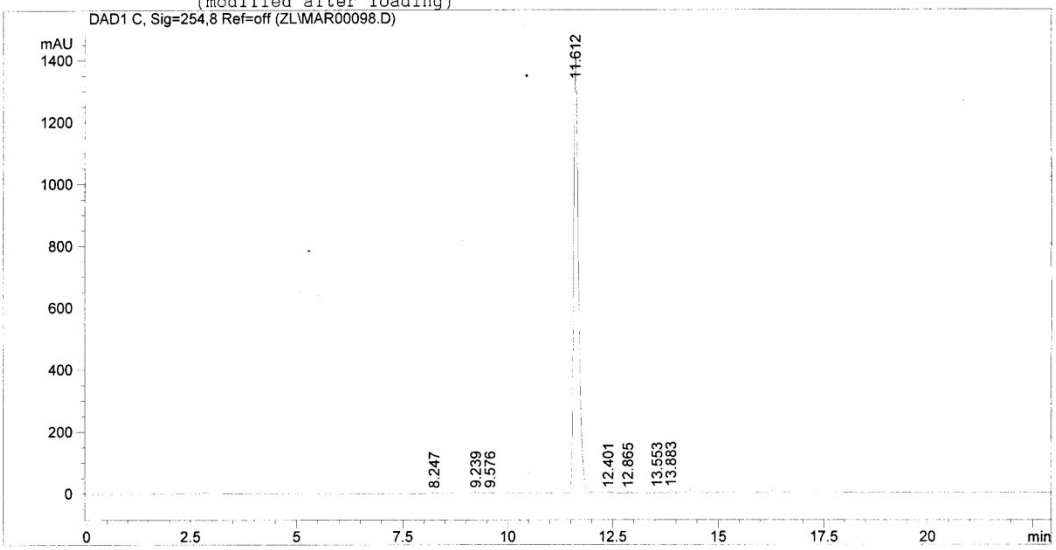


```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 C, Sig=254,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.247 BP    0.0965   19.55952    3.06262   0.1691
   2   9.239 BB    0.0937   24.38282    3.85981   0.2108
   3   9.576 BB    0.0956   26.75882    4.23897   0.2314
   4  11.612 BB    0.1220 1.13723e4  1411.86841  98.3392
   5  12.401 BB    0.1337   16.01753    1.64295   0.1385
   6  12.865 PP    0.1158   23.30769    3.02792   0.2015
   7  13.553 BB    0.1245   33.98743    3.86789   0.2939
   8  13.883 BP    0.1109   48.04242    6.60427   0.4154

Totals :                  1.15643e4  1438.17283

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```

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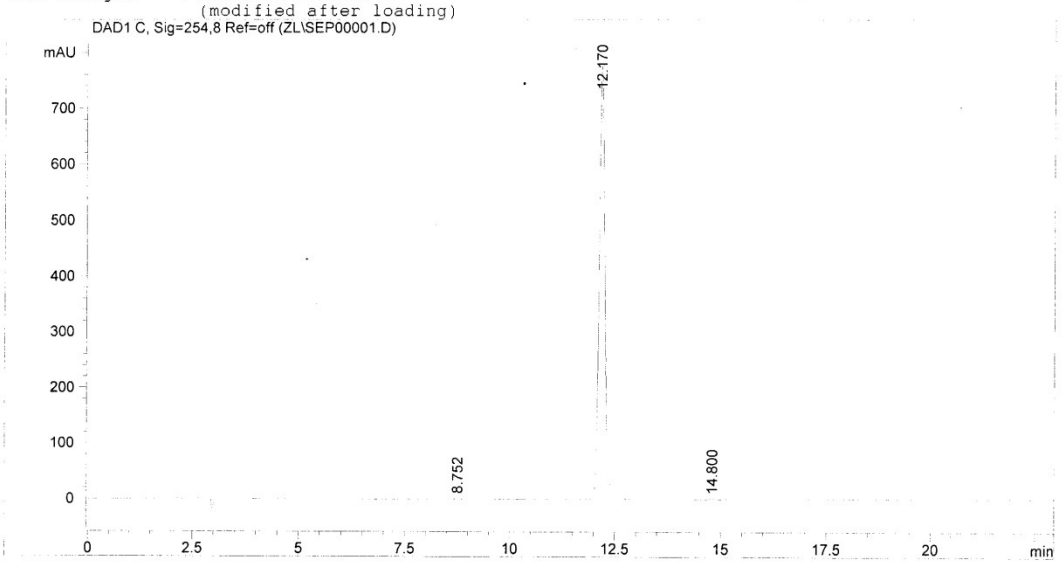
Fig. S17 The HPLC report of **1c**

Data File C:\HPCHEM\1\DATA\ZL\SEP00001.D Sample Name: ZL09-1-023a

RX C-18 4.6mm*250 Flow=1ml/min 132bar buffer

1d

```
Injection Date  : 9/1/2015 2:03:58 PM
Sample Name     : ZL09-1-023a                    Vial :  -
Acq. Operator   :
Method          : C:\HPCHEM\1\METHODS\ZL-1.M
Last changed    : 9/1/2015 2:23:57 PM
                  (modified after loading)
```



Area Percent Report

```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 C, Sig=254,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.752 BB    0.1288   20.05272    2.36865   0.2699
   2  12.170 BB    0.1452 7391.17627  775.62482  99.4861
   3  14.800 BB    0.1798   18.12612    1.60395   0.2440

Totals :                  7429.35511  779.59742

 Results obtained with enhanced integrator!

                  *** End of Report ***
```

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Fig. S18 The HPLC report of **1d**

6. References

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