Supporting Information

Flavin mononucleotide regulated photochemical isomerization and degradation of zeatin

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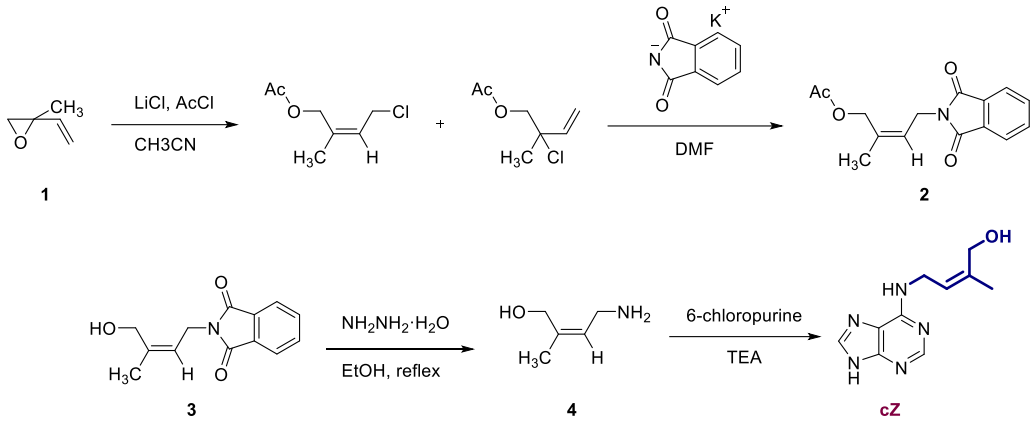
1. General methods and materials

All reagents were commercially available. NMR spectra were recorded on Bruker AVANCE 300 MHz, 400 MHz and 500 MHz. All chemical shifts (δ) are quoted in ppm relative to residual solvent for ^{1}H-NMR and relative to internal resonance for ^{13}C NMR. ESI-MS were recorded on Thermo Fisher Scientific (Exactive). HPLC data was collected with Waters ACQUITY Arc and Agilent Technologies 1260 Infinity, using Agilent Eclipse Plus C18 analysis column (5 μm, 250 × 4.6 mm). Mass spectrometry was collected by Thermo Fisher Scientific (Exactive). The experiment undergoing photolysis was conducted by periodically irradiating the samples using a white LED lamp (56 W) positioned 10 cm (5 mW•cm^{-2}) from the samples. The irradiation intensity of a white LED lamp (400-800 nm) was measured by a radiometer (Photoelectric Instrument Factory of Beijing Normal University).

2. Procedures for the synthesis of compounds

2.1 Synthesis of *cis*- zeatin (cZ)



*(Z)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbut-2-en-1-yl acetate (**2**)*

2-Methyl-2-vinyloxirane (**1**, 1.0 g, 12.0 mmol) and dry LiCl (0.5 g, 12.0 mmol) were suspended in dry acetonitrile (25 mL), acetyl chloride (1.3 mL, 18.0 mmol) was slowly added at 0 °C. After this suspension was stirred at 0 °C for 2 h, warmed to 80 °C and refluxed for 3 h. After cooling, 20 mL of water was added and the mixture was extracted three times with Et_2O (50 mL x 3), the ether extracts were combined and dried over sodium sulfate, filtrated and evaporated to dryness in vacuo to give 2.0 g of crude compound.

To a solution of oily product and potassium phtalimide (2.2 g, 12.0 mmol) in DMF (25 mL) was added NaBr (89 mg, 0.9 mmol) at room temperature, the mixture was warmed to 45 °C for 1 h and then to 60 °C for 3 h. After that, the cooled water (10 mL) was added into mixture and immediately slightly acidified with conc. HCl, then the mixture was added ethyl acetate and placed in a refrigerator (4 °C) overnight, white solids precipitate was removed, after evaporation of the solvent, the crude product was purified by flash chromatography (petroleum ether/ethyl acetate = 10/1, v/v) to afford (Z)-4-(1,3-dioxoisoindolin-2-yl)-2-methylbut-2-en-1-yl acetate as a yellow solid (1.1 g, yield: 32.7% over two steps). ^{1}H NMR (400 MHz, DMSO) δ 7.84 (d, *J* = 4.3 Hz, 4H), 5.44 (t, *J* = 6.5 Hz, 1H), 4.70 (s, 2H), 4.24 (d, *J* = 6.9 Hz, 2H), 2.04 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 170.8 (s), 169.7 (s), 167.9 (s), 134.9 (s), 134.8 (s), 124.2 (s), 123.5 (s), 62.6 (s), 35.1 (s), 21.4 (s), 21.0 (s). HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{15}H_{15}NNaO_4$: 296.08933; found: 296.08923.

*(Z)-2-(4-hydroxy-3-methylbut-2-en-1-yl)isoindoline-1,3-dione (**3**)*

Compound **2** (1.0 g, 3.9 mmol) was dissolved in MeOH (20 mL), t-BuOK (87 mg, 0.8 mmol) was added at room temperature, the solution was then stirred overnight. Then concentrated under reduced pressure, and purified by flash chromatography (petroleum ether/ethyl acetate = 5/1, v/v) to afford (Z)-2-(4-hydroxy-3-methylbut-2-en-1-yl)isoindoline-1,3-dione as a white solid (737 mg, yield: 82.3%). The obtained analytical data matched the literature.[1] ^{1}H NMR (400 MHz, DMSO) δ 7.85 (d, *J* = 3.4 Hz, 4H), 5.23 (t, *J* = 6.5 Hz, 1H), 4.73 (t, *J* = 5.4 Hz, 1H), 4.23 (d, *J* = 6.7 Hz, 2H), 4.09 (d, *J* = 5.2 Hz, 2H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 168.0 (s), 140.3 (s), 134.9 (s), 132.1 (s), 123.5 (s), 120.3 (s), 60.1 (s), 35.2 (s), 21.4 (s). HRMS (ESI): m/z $[M - H]^-$ calcd for $C_{13}H_{12}NO_3$: 230.08227; found: 230.08261.

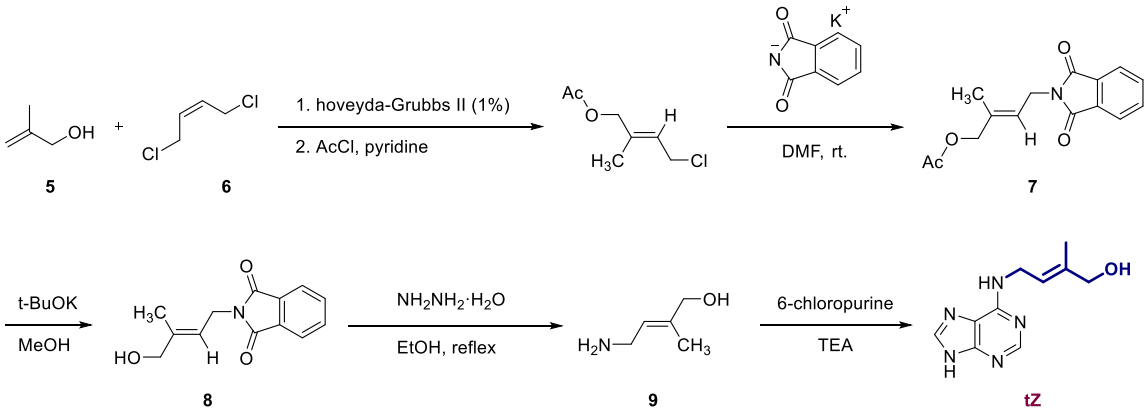
*(Z)-4-amino-2-methylbut-2-en-1-ol (**4**)*

A solution of **3** (737 mg, 3.2 mmol) and hydrazine monohydrate (0.4 mL, 4.8 mmol) in EtOH (10 mL) was stirred, refluxed for 3 h. After cooling, 1 M HCl was added to the reaction solution to pH 3 and the EtOH was evaporated. The pH of the water layer was adjusted to pH 9 with sat. NaOH and extracted with CH_2Cl_2 (10 mL x 3), then organic fractions were combined and dried over sodium sulfate, evaporated to afford (Z)-4-amino-2-methylbut-2-en-1-ol as yellow oil (112 mg, yield: 34.8%). The obtained analytical data matched the literature.[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (s, 1H), 4.01 (s, 2H), 3.26 (d, *J* = 2.8 Hz, 2H), 2.87 (br s, 3H), 1.73 (s, 3H).

*(Z)-4-((9H-purin-6-yl)amino)-2-methylbut-2-en-1-ol (**cZ**)*

6-Chloropurine riboside (287 mg, 1.7 mmol) was added to a stirred solution of compound **4** (112 mg, 1.1 mmol) and triethylamine (609 µL, 4.4 mmol) dissolved in *n*-ppropylalcohol (10 mL). The reaction mixture was refluxed for 5 h, then concentrated under reduced pressure and purified by flash chromatography (methanol/dichloromethane = 1/10, v/v) to afford (Z)-4-((9*H*-purin-6-yl)amino)-2-methylbut-2-en-1-ol as a light yellow solid (241 mg, 51.8%). The obtained analytical data matched the literature.[1] ^{1}H NMR (400 MHz, DMSO) δ 8.17 (s, 1H), 8.08 (s, 1H), 7.62 (s, 1H), 5.35 (s, 1H), 4.14 (s, 2H), 4.03 (s, 2H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 152.7 (s), 139.6 (s), 138.2 (s), 123.8 (s), 60.2 (s), 21.7 (s). HRMS (ESI): m/z [M - H]$^-$ calcd for $C_{10}H_{12}NO_5$: 218.10473; found: 218.10468.

2.2 Synthesis of *trans*- zeatin (tZ)



*(E)-4-chloro-2-methylbut-2-en-1-yl acetate (**7**)*

To a solution of 2-methylprop-2-en-1-ol (**5**, 2.5 mL, 30 mmol) and (Z)-1,4-dichlorobut-2-ene (**6**, 4.7 mL, 30.0 mmol) in CH_2Cl_2 (10 mL) was added Hoveyda-Grubbs catalyst 2nd generation (200 mg, 1 mmol%) at room temperature. The resulting mixture was brought up to 45 °C and stirred for 8 h. After cooling, the mixture was added pyridine (1 mL, 12.3 mmol) and acetyl chloride (2.6 mL, 36.0 mmol) at 0 °C for 30 min, warmed to room temperature and stirred for an additional 4 hour. 10 mL of water was added and the mixture was extracted with Et_2O (40 mL x 3). The organic solvent was removed by reduced pressure to give 4.4 g of crude compound.

To a solution of oily product and potassium phtalimide (2.2 g, 12.0 mmol) in DMF (25 mL) was added NaBr (120 mg, 1.2 mmol) at room temperature, the mixture was warmed to 40 °C for 1 h and then to 60 °C for 11 h. After that, the organic solvent was removed by reduced pressure and crude product was purified by flash chromatography (petroleum ether/ethyl acetate = 5/1, v/v) to afford (E)-4-chloro-2-methylbut-2-en-1-yl acetate as a withe solid (2.6 g, yield: 31.7% over two steps). The obtained analytical data matched the literature.[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 5.4,

3.1 Hz, 2H), 7.67 (dd, *J* = 5.4, 3.1 Hz, 2H), 5.52 (td, *J* = 7.0, 1.2 Hz, 1H), 4.41 (s, 2H), 4.29 (d, *J* = 7.1 Hz, 2H), 2.93 (s, 2H), 2.85 (s, 2H), 2.02 (s, 3H), 1.83 (s, 3H).

*(E)-2-(4-hydroxy-3-methylbut-2-en-1-yl)isoindoline-1,3-dione (**8**)*

Compound **2** (2.0 g, 7.3 mmol) was dissolved in MeOH (20 mL), t-BuOK (174 mg, 1.6 mmol) was added at room temperature, the solution was then stirred overnight. Then concentrated under reduced pressure, and purified by flash chromatography (petroleum ether/ethyl acetate = 5/1, v/v) to afford (E)-2-(4-hydroxy-3-methylbut-2-en-1-yl)isoindoline-1,3-dione as a white solid (1.7 g, yield: 77.5%). The obtained analytical data matched the literature.[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2H), 5.54 (t, *J* = 6.4 Hz, 1H), 4.33 (d, *J* = 7.0 Hz, 2H), 4.01 (s, 2H), 1.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1 (s), 139.8 (s), 133.9 (s), 132.2 (s), 123.2 (s), 118.4 (s), 67.7 (s), 35.3 (s), 13.8 (s). HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{12}NO_5$: 232.09682; found: 232.09689.

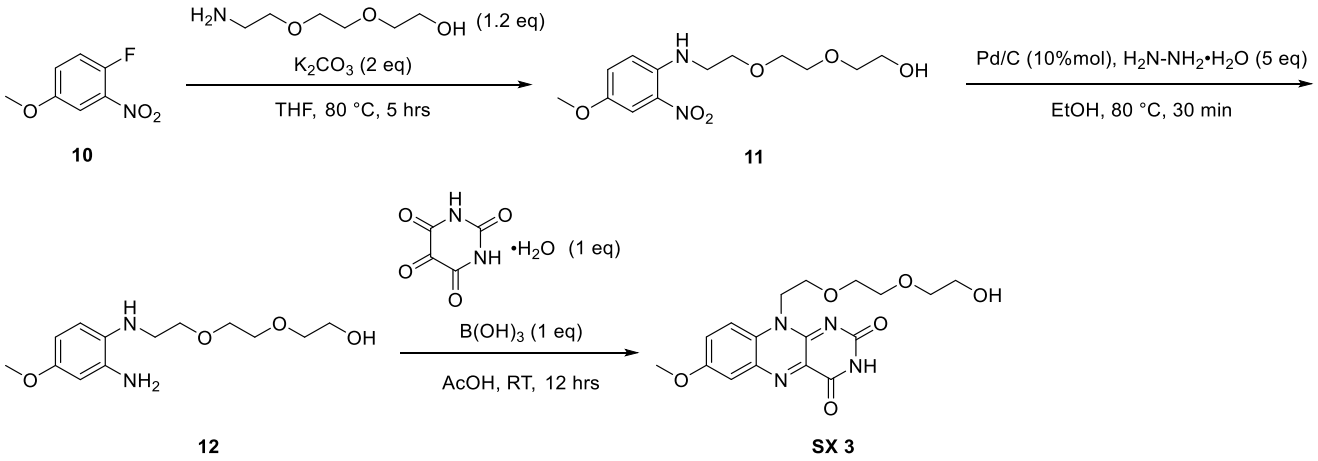
*(E)-4-amino-3-methylbut-2-en-1-ol (**9**)*

A solution of **3** (747 mg, 3.2 mmol) and hydrazine monohydrate (0.4 mL, 4.8 mmol) in EtOH (10 mL) was stirred, refluxed for 3 h. After cooling, 1 M HCl was added to the reaction solution to pH 3 and the EtOH was evaporated. The pH of the water layer was adjusted to pH 9 with sat. NaOH and extracted with CH_2Cl_2 (10 mL x 3), then organic fractions were combined and dried over sodium sulfate, evaporated to afford (E)-4-amino-3-methylbut-2-en-1-ol as yellow oil (130 mg, yield: 40.2%). The obtained analytical data matched the literature.[4] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.50 (d, *J* = 5.4 Hz, 1H), 4.00 (d, *J* = 4.5 Hz, 2H), 3.33 (d, *J* = 6.3 Hz, 2H), 1.68 (d, *J* = 5.7 Hz, 6H). HRMS (ESI): m/z $[M + H]^+$ calcd for $C_5H_{12}NO$: 102.09134; found: 102.09154.

*(E)-4-((9H-purin-6-yl)amino)-2-methylbut-2-en-1-ol (**tZ**)*

6-Chloropurine riboside (300 mg, 1.9 mmol) was added to a stirred solution of compound **4** (130 mg, 1.3 mmol) and triethylamine (710 μL, 5.1 mmol) dissolved in *n*-ppropylalcohol (10 mL). The reaction mixture was refluxed for 5 h, then concentrated under reduced pressure and purified by flash chromatography (methanol/dichloromethane = 1/10, v/v) to afford (E)-4-((9*H*-purin-6-yl)amino)-2-methylbut-2-en-1-ol as a light yellow solid (280 mg, 79.2%). The obtained analytical data matched the literature.[4] ^{1}H NMR (300 MHz, DMSO) δ 12.86 (s, 1H), 8.16 (s, 1H), 8.05 (s, 1H), 7.66 (s, 1H), 5.52 (s, 1H), 4.70 (t, *J* = 5.6 Hz, 1H), 4.13 (s, 2H), 3.78 (d, *J* = 4.9 Hz, 2H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 154.2 (s), 152.4 (s), 149.4 (s), 138.6 (s), 137.0 (s), 121.0 (s), 118.8 (s), 65.9 (s), 37.2 (s), 13.7 (s). HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{10}H_{14}NO_5$: 220.11929; found: 220.11905.

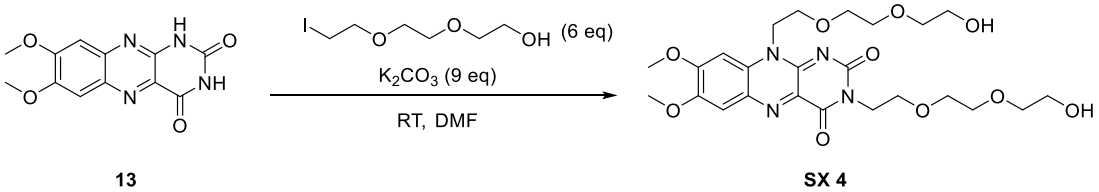
3. Synthesis of Flavin derivatives photocatalysts



To a solution of **10** (513 mg, 3.0 mmol) in THF (10 mL) was added K_2CO_3 (829 mg, 6.0 mmol) and 2-(2-(2-aminoethoxy)ethoxy)ethan-1-ol (537 mg, 3.6 mmol). The reaction was stirred at 80 °C for 5 hours, after which the reaction mixture was diluted with ethyl acetate (15 mL x 3) and extracted with water (15 mL x 3). The organic layer was dried with Na_2SO_4, concentrated under reduced pressure to give 2-(2-(2-((4-methoxy-2-nitrophenyl)amino)ethoxy)ethoxy)ethan-1-ol as Orange yellow liquid (307 mg, yield 34.1%), which was directly used in the next step.

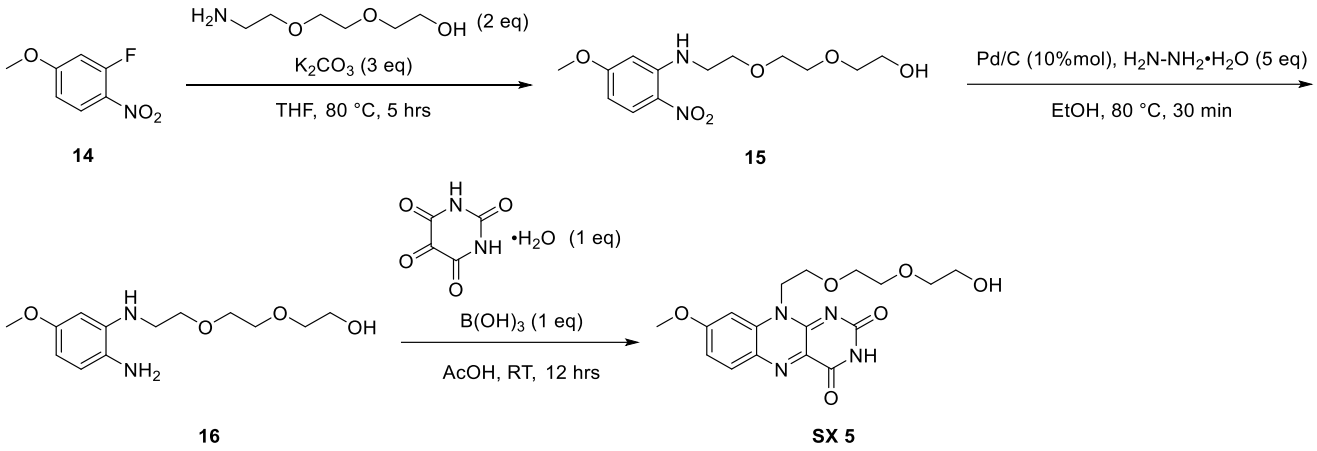
To a solution of **11** (300 mg, 1.0 mmol) and Pd/C (300 mg) in EtOH (20 mL) being cooled to 0 °C was dropped in hydrazinium hydroxide solution (400 μL, 5.0 mmol). Then the reaction was stirred at 80 ºC for 30 minutes, after which the mixture was filtered. The organic layer was concentrated under reduced pressure to give 2-(2-(2-((2-amino-4-methoxyphenyl)amino)ethoxy)ethoxy)ethan-1-ol as a colorless liquid, which was directly used in the next step.

To a solution of **12** (300 mg, 1.0 mmol) in AcOH (16 mL) was added alloxan monohydrate (160 mg, 1.0 mmol) and $B(OH)_3$ (62 mg, 1.0 mmol). The reaction was stirred at room temperature for 12 hours, after which the mixture was evaporated to remove the AcOH. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 30/1) to give 10-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-7-methoxybenzo*[g]*pteridine-2,4*(3H,10H)*-dione as a red solid (201 mg, yield 53.5%). ^{1}H NMR (400 MHz, DMSO) δ 11.33 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.57 (s, 2H), 4.79 (s, 2H), 4.54 (s, 1H), 3.91 (s, 3H), 3.83 (s, 2H), 3.53 (s, 2H), 3.42 (d, *J* = 3.7 Hz, 2H), 3.31 (d, *J* = 4.4 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 160.2 (s), 157.5 (s), 155.9 (s), 150.2 (s), 139.0 (s), 136.5 (s), 128.4 (s), 125.5 (s), 118.9 (s), 111.6 (s), 96.1 (s), 72.8 (s), 70.6 (s), 70.2 (s), 67.4 (s), 60.6 (s), 56.5 (s), 45.1 (s). HRMS (ESI): Cacld. for $[M+H]^+$ $C_{17}H_{21}N_4O_6$: 377.14556, found: 377.14755.



To a solution of **13** (274 mg, 0.2 mmol) in DMF (2 mL) was added K_2CO_3 (414 mg, 1.8 mmol) and 2-(2-(2-iodoethoxy)ethoxy)ethan-1-ol (520 mg, 1.2 mmol). The reaction was stirred at room temperature for 12 hours,it was quenched with water (20mL) and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 4). The organic layer was

dried with Na_2SO_4, concentrated under reduced pressure to give 3,10-bis(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-7,8-dimethoxybenzo*[g]*pteridine-2,4*(3H,10H)*-dione as yellow liquid (29 mg, yield 27.0%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.27 (s, 1H), 4.69 (t, *J* = 6.0 Hz, 2H), 4.43 (t, *J* = 5.6 Hz, 2H), 4.12 (s, 3H), 4.05 (s, 3H), 3.90 (dt, *J* = 12.9, 5.8 Hz, 4H), 3.79 – 3.49 (m, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2 (s), 156.7 (s), 152.7 (s), 150.6 (s), 144.5 (s), 141.7 (s), 137.6 (s), 126.5 (s), 107.4 (s), 105.0 (s), 72.6 (s), 70.4 (d, *J* = 4.6 Hz), 70.0 (s), 67.7 (d, *J* = 4.6 Hz), 61.7 (s), 56.8 (s), 56.5 (s), 41.5 – 41.4 (m), 41.1 (d, *J* = 29.0 Hz). HRMS (ESI): Cacld. for $[M+Na]^+$ $C_{24}H_{34}N_4O_{10}Na$: 561.21671, found: 561.21722.



To a solution of **14** (855 mg, 5.0 mmol) in THF (20 mL) was added K_2CO_3 (2.1 g, 15.0 mmol) and 2-(2-(2-aminoethoxy)ethoxy)ethan-1-ol (1.5 g, 10.0 mmol). The reaction was stirred at 80 °C for 5 hours, after which the reaction mixture was diluted with ethyl acetate (50 mL) and extracted with water (50 mL). The organic layer was dried (Na_2SO_4), concentrated under reduced pressure to give 2-(2-(2-((5-methoxy-2-nitrophenyl)amino)ethoxy)ethoxy)ethan-1-ol as yellow liquid (1.35 g, yield 90.2%), which was directly used in the next step. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.13 (d, *J* = 9.5 Hz, 1H), 6.23 (dd, *J* = 9.5, 2.4 Hz, 1H), 6.16 (d, *J* = 2.0 Hz, 1H), 3.85 (s, 3H), 3.80 (t, *J* = 5.4 Hz, 2H), 3.73 (d, *J* = 2.9 Hz, 2H), 3.70 (s, 4H), 3.65 – 3.56 (m, 2H), 3.47 (dd, *J* = 10.4, 5.2 Hz, 2H), 2.45 (s, 1H).

To a solution of **15** (1.4 g, 4.5 mmol) and Pd/C (500 mg) in EtOH (20 mL) being cooled to 0 °C was dropped in hydrazinium hydroxide solution (1.1 mL, 22.5 mmol). Then the reaction was stirred at 80 ºC for 30 minutes, after which the mixture was filtered. The organic layer was concentrated under reduced pressure to give 2-(2-(2-((2-amino-5-methoxyphenyl)amino)ethoxy)ethoxy)ethan-1-ol as a colorless solid, which was directly used in the next step.

To a solution of **16** (1.2 g, 4.5 mmol) in AcOH (16 mL) was added alloxan monohydrate (720 mg, 4.5 mmol) and $B(OH)_3$ (278 mg, 4.5 mmol). The reaction was stirred at room temperature for 12 hours, after which the mixture was evaporated to remove the AcOH. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 30/1) to give 10-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-8-methoxybenzo*[g]*pteridine-2,4*(3H,10H)*-dione as a yellow solid (864 mg, yield 51%). ^{1}H NMR (300 MHz, DMSO) δ 11.28 (s, 1H), 8.02 (d, *J* = 9.1 Hz, 1H), 7.42 (s, 1H), 7.38 – 7.14 (m, 1H), 4.82 (s, 2H), 4.51 (t, *J* = 5.4 Hz, 1H), 4.02 (s, 3H), 3.86 (d, *J* = 5.2 Hz, 2H), 3.63 – 3.51 (m, 2H), 3.50 – 3.42 (m, 2H), 3.42 – 3.36 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 165.1 (s), 160.5 (s), 156.1 (s), 151.2 (s), 136.0 (s), 135.0 (s), 133.8 (s), 131.0 (s), 116.8 (s), 99.7 (s), 72.8 (s), 70.6 (s), 70.2 (s), 67.6 (s), 60.6 (s), 57.0 (s), 45.1 (s). HRMS (ESI): Cacld. for $[M+Na]^+$ $C_{17}H_{20}N_4O_6Na$: 399.12751, found: 399.12766.

4. Optimization of photoisomerization of zeatin

4.1 Screening of photosensitizer

A 2 mL HPLC vial was charged with H_2O (978 µL), cZ (50 mM in DMSO, 2 µL) and dyes photosensitizer (1 mM in H_2O, 20 µL). After all components were fully dissolved, the vial was irradiated with LED (530nm, 470nm or 620 nm) for 2 h. Then adenosine (internal standard, 50 mM in DMSO, 2 µL) was added to the mixture and the vial was analysed by HPLC.

An Agilent HPLC system equipped with an Agilent ZORBAX SB-C18 column (250 × 4.6 mm, 5 µm) was used with the following gradient program with mobile phases A (water) and B (methanol): 0−8 min 35−55% B, 8−15 min 85% B, 15−20 min 35% B. The detection wavelength was set at 260 nm.

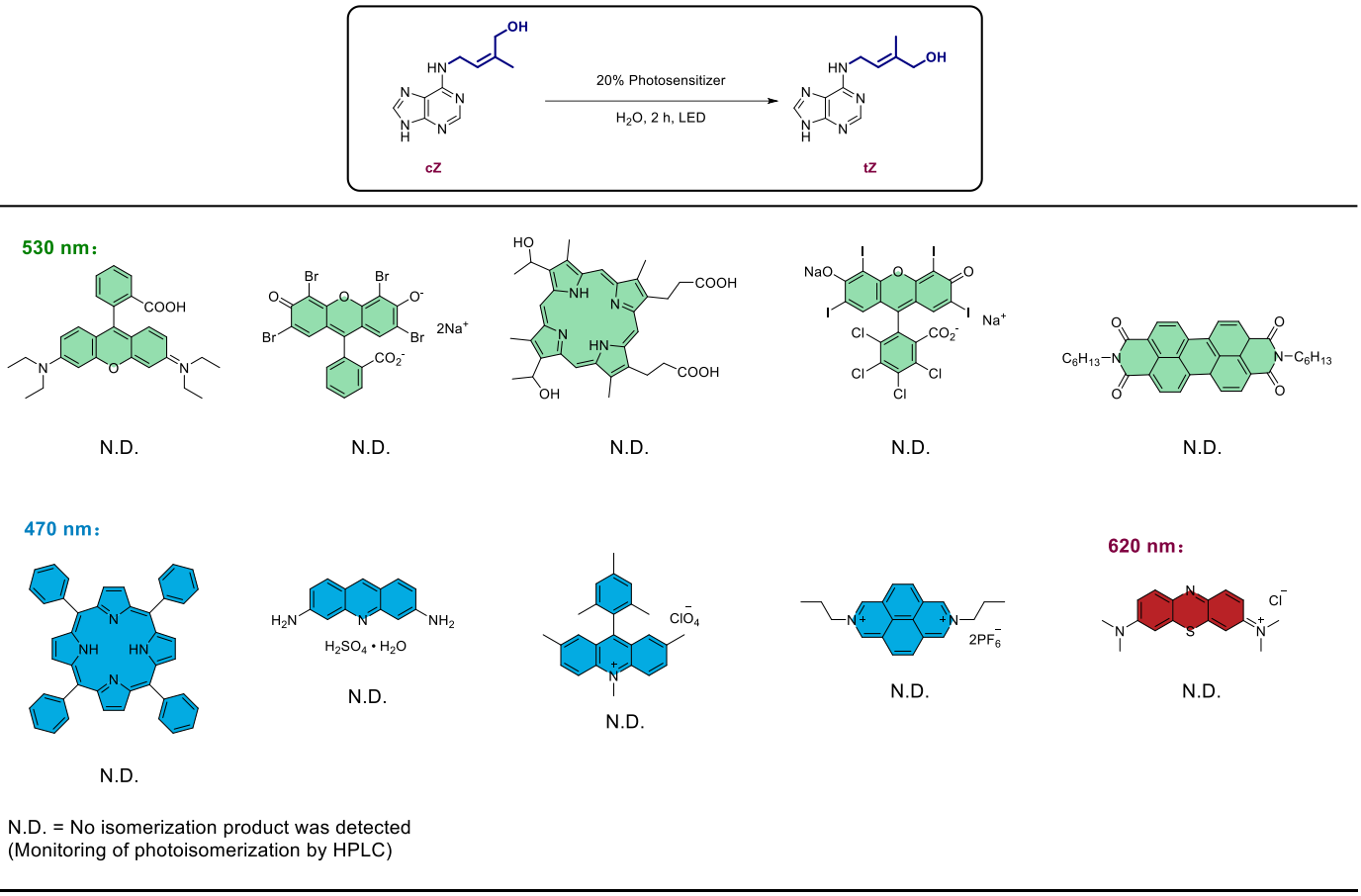


Figure S1. Screening of dyes photosensitizers

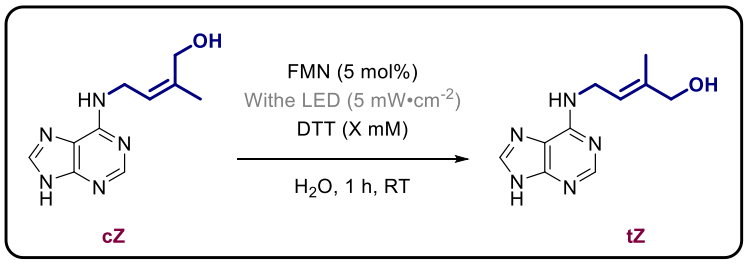
4.2 Isomerization and degradation of zeatin

A 2 mL HPLC vial was charged with H_2O (946 µL), zeatin (50 mM in DMSO, 4 µL), DTT (50 mM in H_2O, 40 µL) and FMN (1 mM in H_2O, 10 µL). After all components were fully dissolved, the vial was irradiated with white LED (5 $mW•cm^{-2}$) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC. For the control experiments, the mixture was treated without DTT, photosensitizer or illumination.

A Waters HPLC system equipped with an Agilent ZORBAX SB-C18 column (250 × 4.6 mm, 5 µm) was used with thefollowing gradient program with mobile phases A (water) and B (methanol): 0−8 min 35−55% B, 8−15 min 85% B, 15−20 min 35% B. The detection wavelength was set at 270 nm.

4.3 Optimization of isomerization conditions

A 2 mL HPLC vial was charged with H_2O (986 µL), **cZ** (50 mM in DMSO, 4 µL), and FMN (1 mM in H_2O, 10 µL), then DTT was added to the mixture until the final concentration of 6/30/120/240/300 mM. After all components were fully dissolved, the vial was irradiated with white LED (5 $mW•cm^{-2}$) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC.



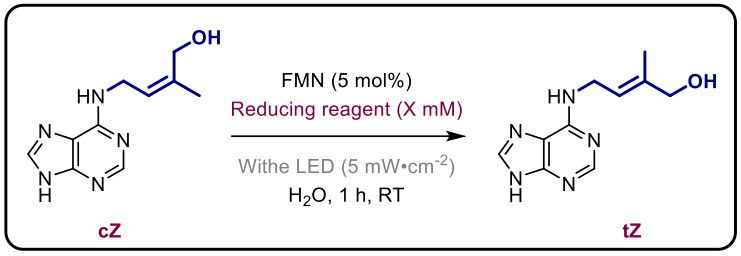
Entry	Substrate	X	trans [%][a]
1	*cis*-zeatine	6	46
2	*cis*-zeatine	30	62
3	*cis*-zeatine	120	64
4	*cis*-zeatine	240	64
5	*cis*-zeatine	300	63

[a] HPLC yields of **tZ** based on peak area ratio

Table S1. Optimization of isomerization conditions

4.4 Optimization of reducing agents

A 2 mL HPLC vial was charged with H_2O (986 µL), **cZ** (50 mM in DMSO, 4 µL), and FMN (10 mM in H_2O, 1 µL), then reducing reagent was added to the mixture. After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC.



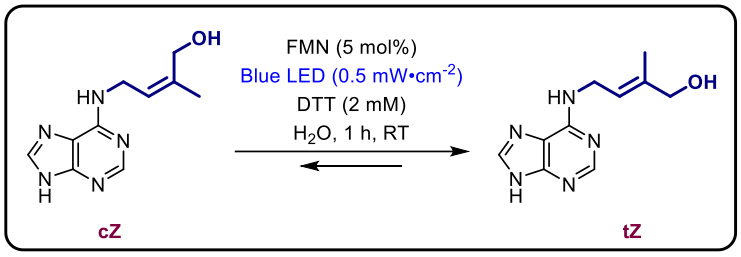
Entry	Substrate	Reducing reagent	X	trans [%][a]	cis [%][a]
1	*cis*-zeatin	cysteine	10	59	10
2	*cis*-zeatin	cysteine	25	66	14
3	*cis*-zeatin	cysteine	50	66	29
4	*cis*-zeatin	vitamin C	6	N.D.	>99
5	*cis*-zeatin	vitamin C	300	N.D.	>99

[a] HPLC yields of **tZ** or **cZ** based on peak area ratio

Table S2. Optimization of reducing agents

4.5 Isomerization and degradation of zeatin under blue LED

A 2 mL HPLC vial was charged with H_2O (955 µL), zeatin (50 mM in DMSO, 4 µL), DTT (50 mM in H_2O, 40 µL) and FMN (10 mM in H_2O, 1 µL). After all components were fully dissolved, the vial was irradiated with blue LED (0.5 mW•cm^{-2}) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC. For the degradation experiments, the mixture was treated without DTT.



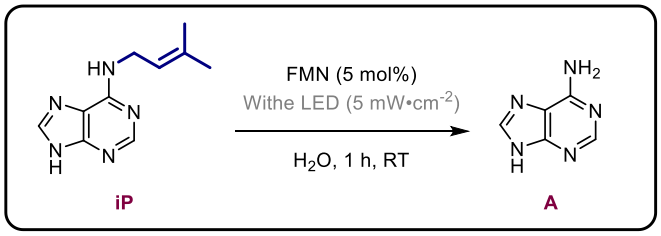
Entry	Substrate	Conditions	trans [%][a]	cis [%][a]	A [%][a]
1	*cis*-zeatin	Standard	**30**	51	8
2	*cis*-zeatin	No DTT	N.D.	29	17
5	*trans*-zeatin	Standard	76	**3**	8
6	*trans*-zeatin	No DTT	N.D.	N.D.	56

[a] HPLC yields of **tZ/cZ/A** based on peak area ratio

Table S3. Isomerization and degradation of zeatin under blue LED

4.6 Effect of degradation conditions on iP or iPR

A 2 mL HPLC vial was charged with H_2O (995 μL), iP or iPR (50 mM in DMSO, 4 μL), and FMN (10 mM in H_2O, 1 μL). After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. Then std. (internal standard, 50 mM in DMSO, 4 μL) was added to the mixture and the vial was analysed by HPLC.



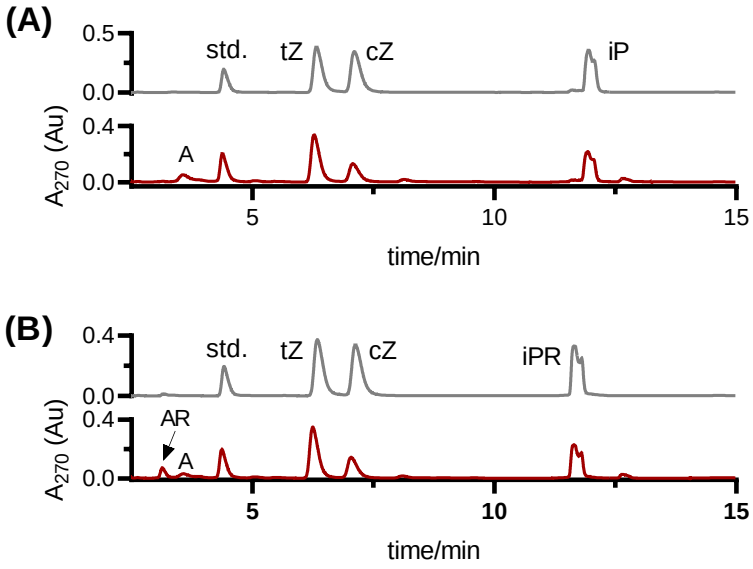
Entry	Substrate	Conditions	Remaining [%][a]	A [%][a]
1	iP	Standard	N.D.	42
2	iP	12 mM DTT	80	13
3	iPR	Standard	N.D.	61
4	iPR	12 mM DTT	82	17

[a] HPLC yields of **iP/iPR** or **A/AR** based on peak area ratio

Table S4. Effect of degradation conditions on iP or iPR

4.7 Competitive degradation of cZ/tZ/iP/iPR

A 2 mL HPLC vial was charged with H_2O (987 μL), cZ (50 mM in DMSO, 4 μL), tZ (50 mM in DMSO, 4 μL), iP or iPR (50 mM in DMSO, 4 μL) and FMN (10 mM in H_2O, 1 μL). After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 μL) was added to the mixture and the vial was analysed by HPLC.



Remaining(%)		
tZ	cZ	iP
73%	32%	56%

Remaining(%)		
tZ	cZ	iPR
80%	36%	65%

Figure S2. Competitive degradation of cZ/tZ/iP/iPR. HPLC analysis of cZ/tZ/iP (A) or cZ/tZ/iPR (B) under black (Grey) or treatment whith FMN and then light for 1 h under white LED (red).

4.8 Effect of isomerization conditions on m^6A or tZ-CO

A 2 mL HPLC vial was charged with H_2O (995 µL), tZ-CO or m^6A (50 mM in DMSO, 4 µL), and FMN (10 mM in H_2O, 1 µL), then DTT was added to the mixture until the final concentration of 2 mM. After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. Then std. (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC.

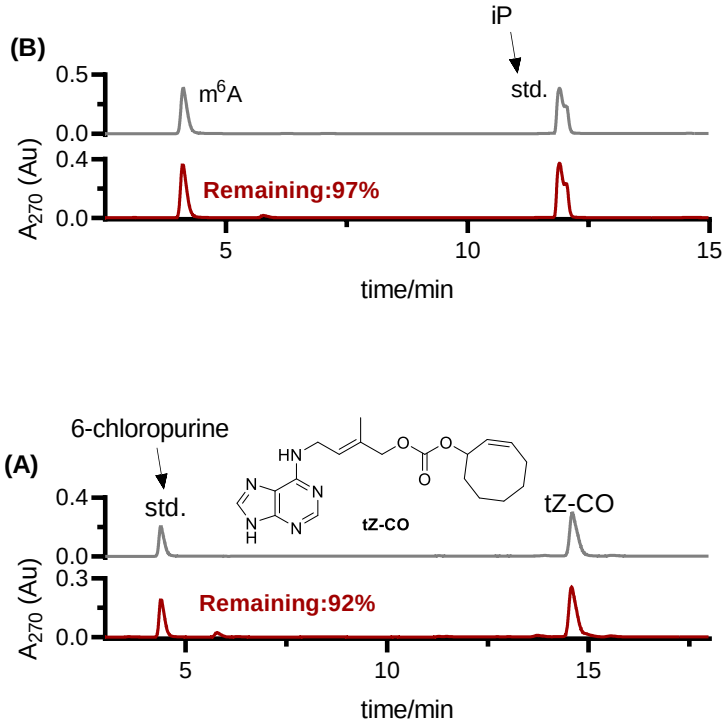


Figure S3. Effect of isomerization conditions on m^6A or tZ-CO. A) HPLC analysis of tZ-CO (A) or m^6A (B) treatment with FMN and DTT under white LED light for 1 h. From the top down: mixture of standard, tZ-CO (200 µM, A) or m^6A (200 µM, B) (Grey); incubation of tZ-CO (200 µM, A) or m^6A (200 µM, B) with FMN (5 mol%) and DTT (2 mM), No product peak was observed.

4.9 Screening of Flavin photosensitizers

A 2 mL HPLC vial was charged with **cZ** (50 mM in DMSO, 4 µL), DTT (300 mM in H_2O, 986 µL) and flavin photosensitizers (1 mM in H_2O, 10 µL) After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. Then 6-chloropurine (internal standard, 50 mM in DMSO, 4 µL) was added to the mixture and the vial was analysed by HPLC.

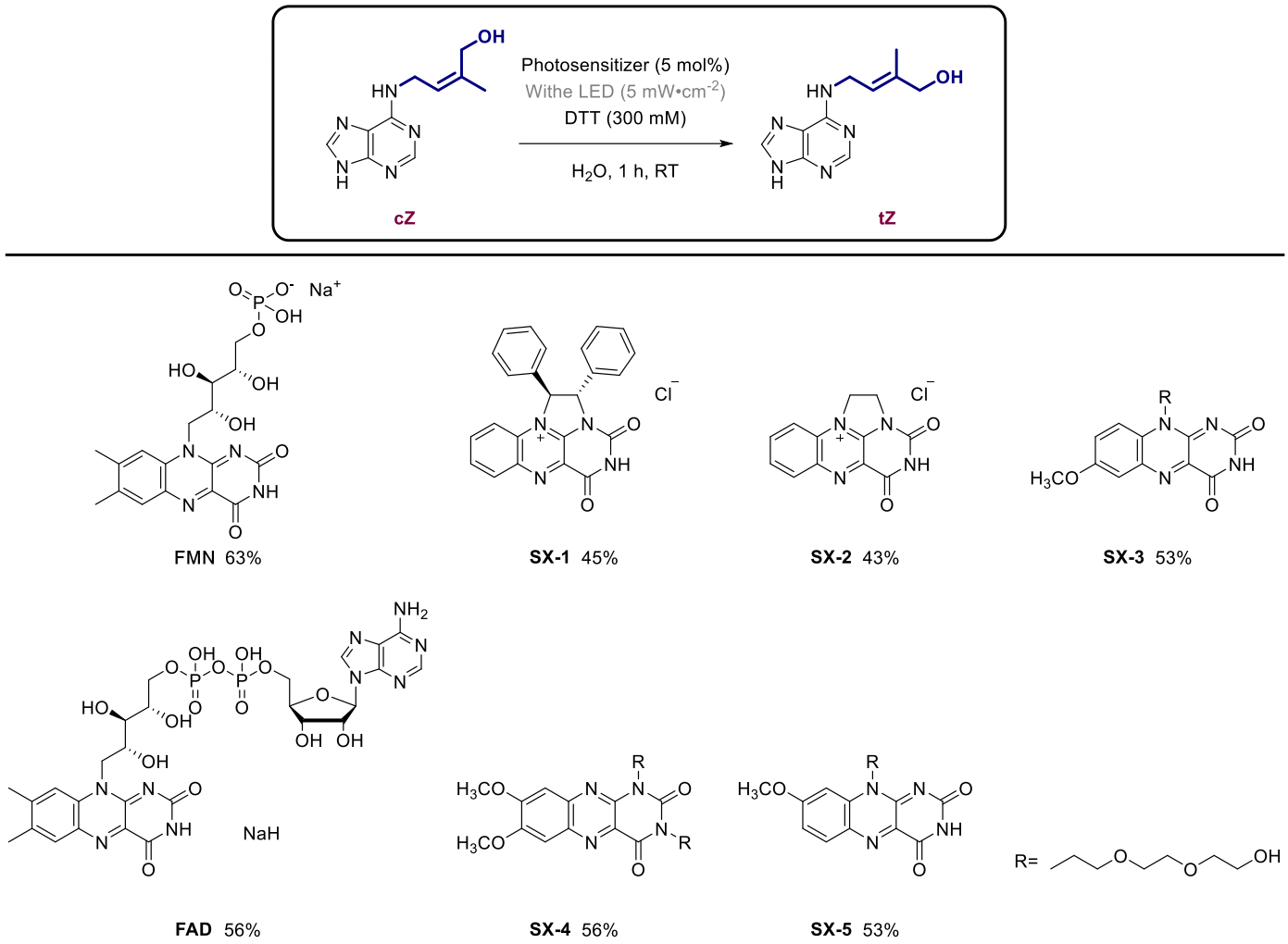


Figure S4. Screening of Flavin photosensitizers

5. Isomerization of cZ in Hela cells

5.1 Cell Lines and Cell Culture

HeLa cell used in this study was purchase from National Infrastructure of Cell Line Resource, China and was cultured in high-glucose dulbecco's modified eagle medium (DMEM) supplemented with 10% (v/v) fetal bovine serum (FBS) and 1% penicillin-streptomycin at 37 °C in an atmosphere of 5% CO_2. DMEM, FBS and penicillin/streptomycin are purchased from Gibco (NY, USA).

5.2 The CCK-8 Assay

Cell suspension of 100 µl was dispensed (1×10^4 cells/ well) in 96-well plates. The plates were pre-incubated for 24 h, followed by the treatments of either DMSO (0.5%, control) or various concentrations of compounds for 12 h, the mixtures were replaced with fresh cell culture medium and added 10 µl of CCK-8 solution (#CA1210, Solarbio) to each well of the plate. The absorbance was measured at 450 nm using a multimode microplate reader (Bio-Tek Synergy H1m). For the samples undergoing irradiation, cells were radiated under white LED (5 mW•cm^{-2}) for either 1 h or 3 h before CCK-8 was added.

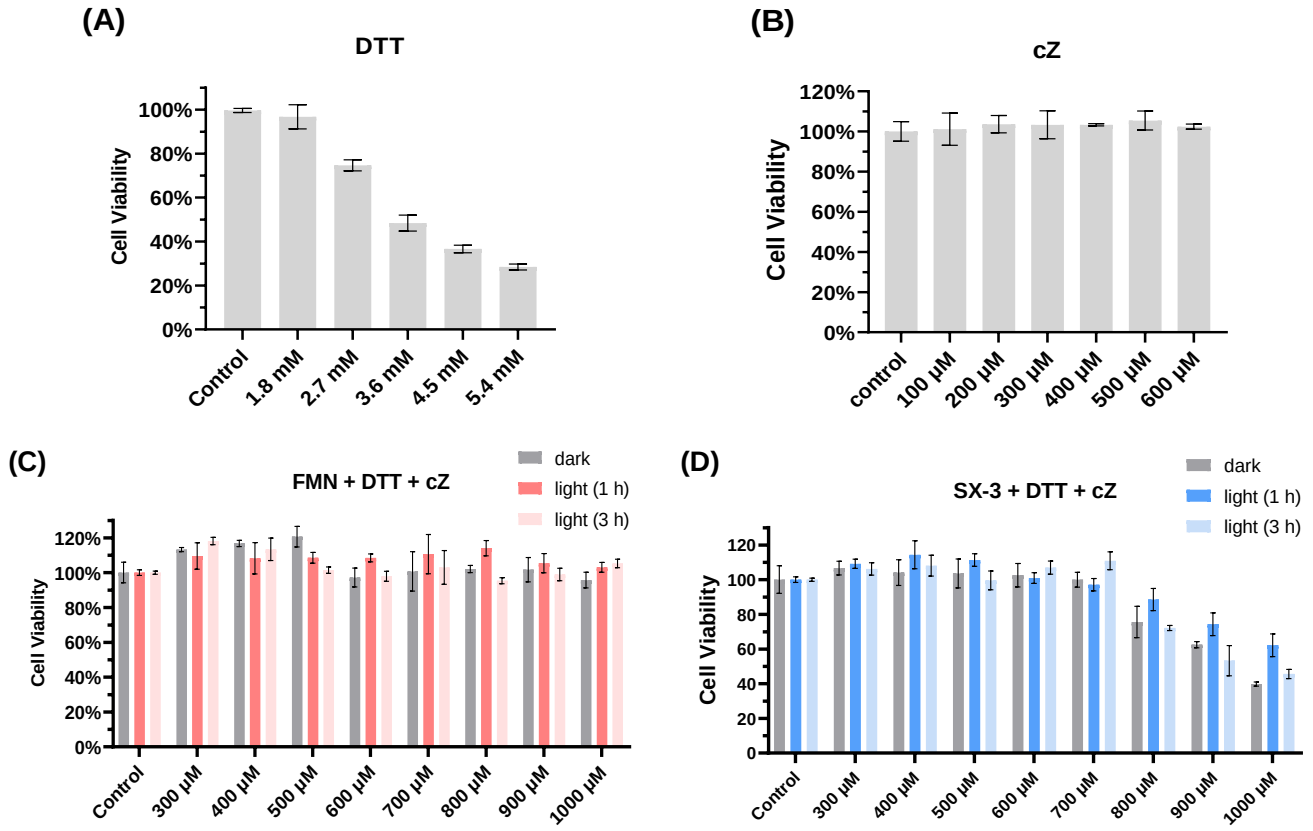


Figure S5. Measurement of HeLa cell's viability using CCK-8 assay. (A) Viabilities of HeLa cells incubated with **DTT** at varied concentrations for 12 h, control sample upon treatment with 0.5 % DMSO. (B) Viabilities of HeLa cells incubated with **cZ** at varied concentrations for 12 h, control sample upon treatment with 0.5 % DMSO. (C) Viabilities of HeLa cells after 12 h incubation with (pink blocks) or without (gray blocks, control) **DTT** (1.8 mM), **cZ** (600 µM) and varied concentrations of **FMN**. (D) Viabilities of HeLa cells after 12 h incubation with (blue blocks) or without (gray blocks, control) **DTT** (1.8 mM), **cZ** (600 µM) and varied concentrations of **SX-3**. Normalized to DMSO-treated samples for each sample, LED irradiation was applied (1 h or 3 h, 5 mW•cm^{-2}), error bars indicate mean ± SEM (n = 3).

5.3 Standard procedure for in vitro experiments

HeLa cells were cultured in DMEM medium supplemented with 10% FBS at 37 °C under atmosphere containing 5% CO_2. HeLa cells were seeded at a density of 9×10^6 cells into 10 cm cell culture dishes (Corning, #430167). 24 h after plating, solutions of DTT (1.8 mM), cZ (0.6 mM) and FMN (1.0 mM) were prepared in the DMEM medium. HeLa cells were incubated with each of the above solutions at 37 °C for 12 h and washed three times with phosphate buffered saline (PBS), fresh cell culture medium (10 mL) was added and the cells were irradiated under white LED light (5 $mW•cm^{-2}$) for 1 h or 3 h, respectively. Then, cell culture medium was decanted, the cells were washed twice with PBS and were pelleted following trypsinization, 500 μL of Cell lysates (Beyotime, #P0013K) was added to each collection tube and incubated at 4 °C for 1 h. CKs was extracted and detected by UHPLC-MS/MS.

5.4 Extraction and detection of CKs

A modified protocol of hormone extraction and purification utilizing conditions as described for processing samples.[5] 800 μL of extraction buffer (CH_3OH:H_2O:HCO_2H [15:4:1, v/v/v]) was added to each liquid sample and were allowed to passively extract overnight at -20 °C. Then, insoluble proteins were precipitated by centrifugation (3000 rpm, 1 h), and the supernatant was collected, dried down by N_2, and resuspended in 400 μL of CH_3CN:H_2O:formic acid [5:949:1] for mass spectrometric analysis. UHPLC-MS/MS were collected by UPLC-QqQ-MS/MS (Waters ACQUITY UPLC H-Class, Xevo TQ-S, Positive ion, ESI, MRM detection) using Column: Waters ACQUITY UPLC HSS T3, 1.7 μm, 100 × 2.1 mm (Flow rate: 0.3 mL·min-1, Retention time: cZ 4.31 min, tZ 3.94 min). 0.1% formic acid in H_2O (buffer A) and 0.1% formic acid in CH_3CN (buffer B) were applied as mobile phase. Gradient elution: 0−2 min 10% B, 2−4 min 10−20% B, 4−6 min 20−40% B, 6−8 min 40−50% B, 8−10 min 50−60% B, 10−11 min 60−70% B, 11−12 min 70−80% B, 12−14 min 80−85% B, 14−18 min 85−10% B, 18−20 min 10% B. The mass spectrometer parameters of cZ and tZ are 3.0 kV capillary voltage, 10 V cone voltage, and 22 collision voltage. Quantitative data were processed by the Masslynx V4.1 software, the Precursor ion (m/z) is 219.24^+ and Product ion (m/z) is 135.92^+.

6. In vivo experimental details

6.1 Endogenous cytokinins (CKs) content analysis

Rice (O. sativa L.) ssp. Japonica (cv. Nipponbare) was used for FMN and DTT treatment. Plant seeds germinated in water at 37℃ in the dark for 3 days and transferred to 96-well plates in the water under a 14-h light (28℃)/10-h dark (22℃) photoperiod at 400-500 μmol $m^{-2}s^{-1}$ light intensity and 65% humidity. After 3 days, the rice seedlings were transferred to Yoshida's nutrient solution for hydroponic culture. After 10 days, the seedlings were treatment with Yoshida's nutrient solution (Control), nutrient solution containing 2mM FMN and 3mM DTT, 3mM FMN and 5mM DTT, 3mM FMN for 30 hours, respectively. Then the roots were harvested for hormone extracted.

CKs were extracted, quantified, and analyzed using a previously described method.[6] In brief, the hormones were extracted using 80% methanol with internal standards (i.e., 45 pg [$^2H_5$]tZ, [$^2H_5$]tZR, [$^2H_6$]iP and [$^2H_6$]iPR); after drying with nitrogen gas, the pellet was dissolved in 300 μL 30% (v/v) methanol. After centrifugation, the supernatant was passed through a 0.22-mm membrane filter and used for CK quantification. The CKs were separated with the LC (ExionLCTM,AB SCIEX) and analyzed with the triple quadruple MS QTRAP 5500 system (AB SCIEX). The data were processed using MultiQuant software (version 3.0.2, AB SCIEX).

6.2 Effect of FMN on the development of rice seedlings.

Rice (O. sativa L.) ssp. Japonica (cv. Nipponbare) was used for FMN and DTT treatment. Plant seeds germinated in water at 37℃ in the dark for 3 days and transferred to 96-well plates in the water, 0.5mM FMN, 1.0 mM FMN and 3.0 mM FMN, respectively. After 3 days, the seedlings were treatment with Yoshida's nutrient solution (Control), nutrient solution containing 0.5 mM FMN, 1.0 mM FMN 3mM FMN for 12 days, respectively. Then the roots were harvested for hormone extracted. CKs were extracted, quantified, and analyzed using a previously described method.[6]

7. Proposed mechanism

A 2 mL HPLC vial was charged with H_2O (946 µL), cZ (50 mM in DMSO, 4 µL) and FMN (1 mM in H_2O, 10 µL) After all components were fully dissolved, the vial was irradiated with white LED (5 mW•cm^{-2}) for 1 h. The reaction mixtureis separated for mass spectrometry analysis.[7]

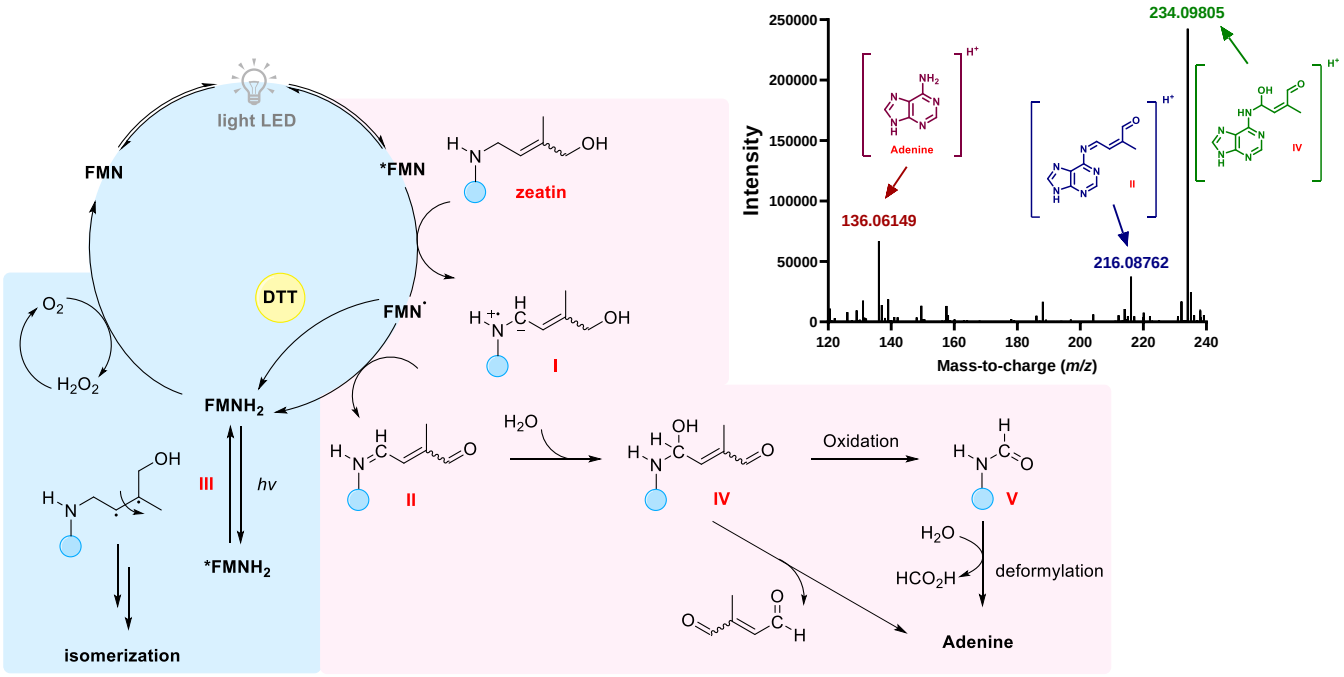
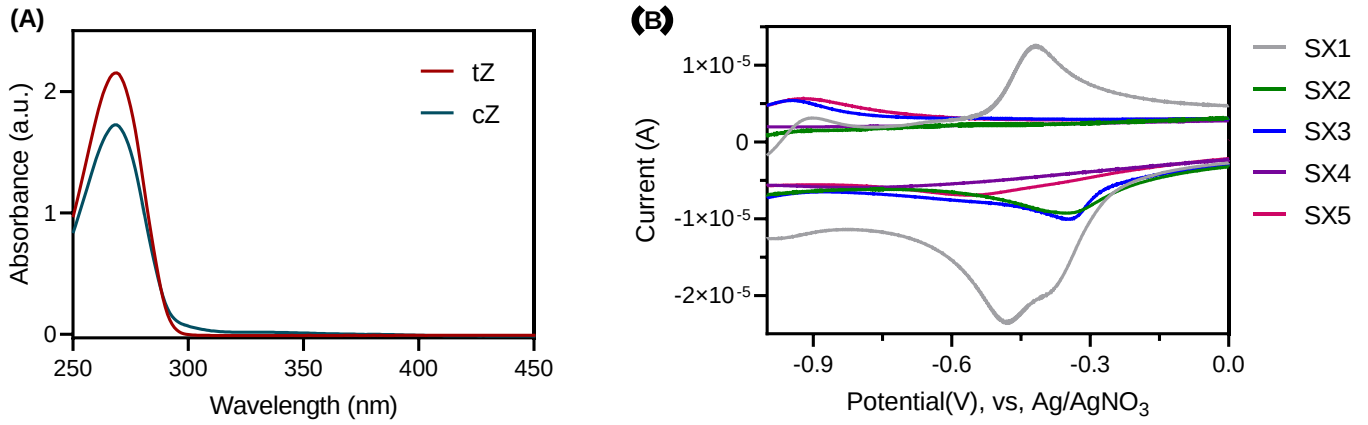


Figure S6. The MS spectrogram of the reaction mixture. The m/z at 136.06149, 216.08762, and 234.09805, correspond to A, II, and IV, respectively.

8. Properties of compounds

Cyclic voltammetry (CV) determination: Photosensitizer (1 mmol) was dissolved in Acetonitrile (10 mL). Tetrabutylammonium tetrafluoroborate (0.1 M concentration) was used as the supporting electrolyte for the voltammetry, CV studies were performed in a 10 mL glass vial fitted with a glassy carbon working electrode (3.0 mm in diameter), a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode. The solution of interest was sparged with nitrogen for 5 minutes before data collection. Scan rate: 0.1 V/s.

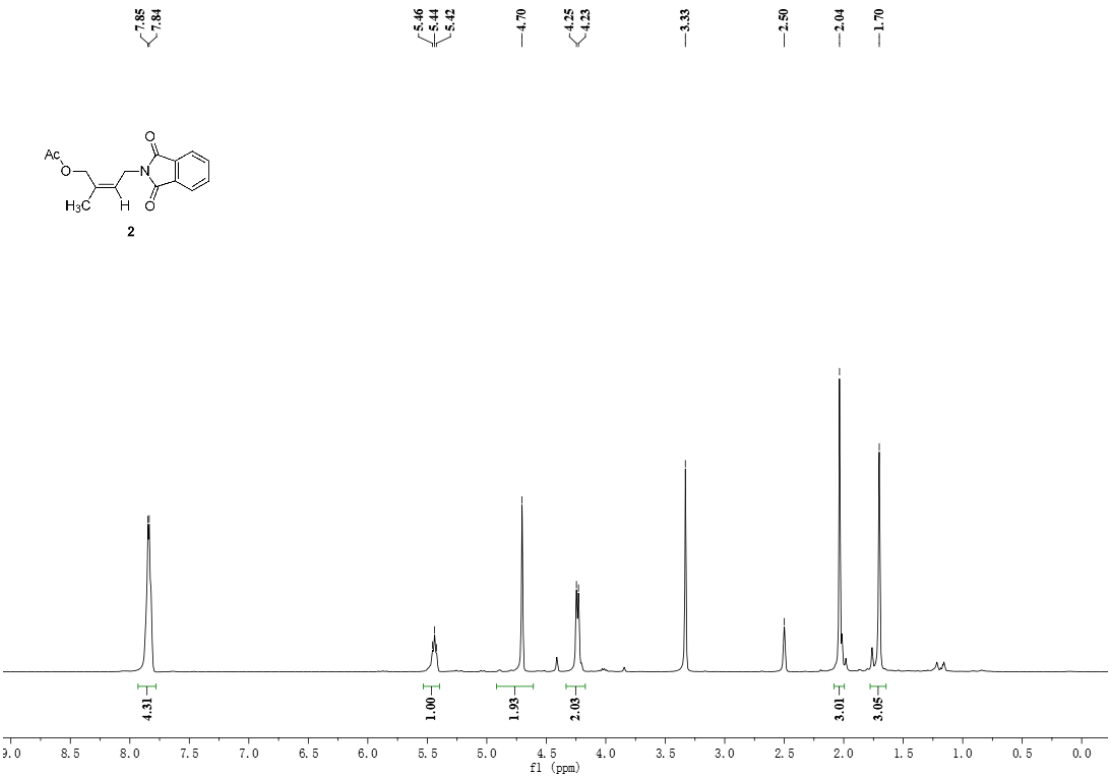


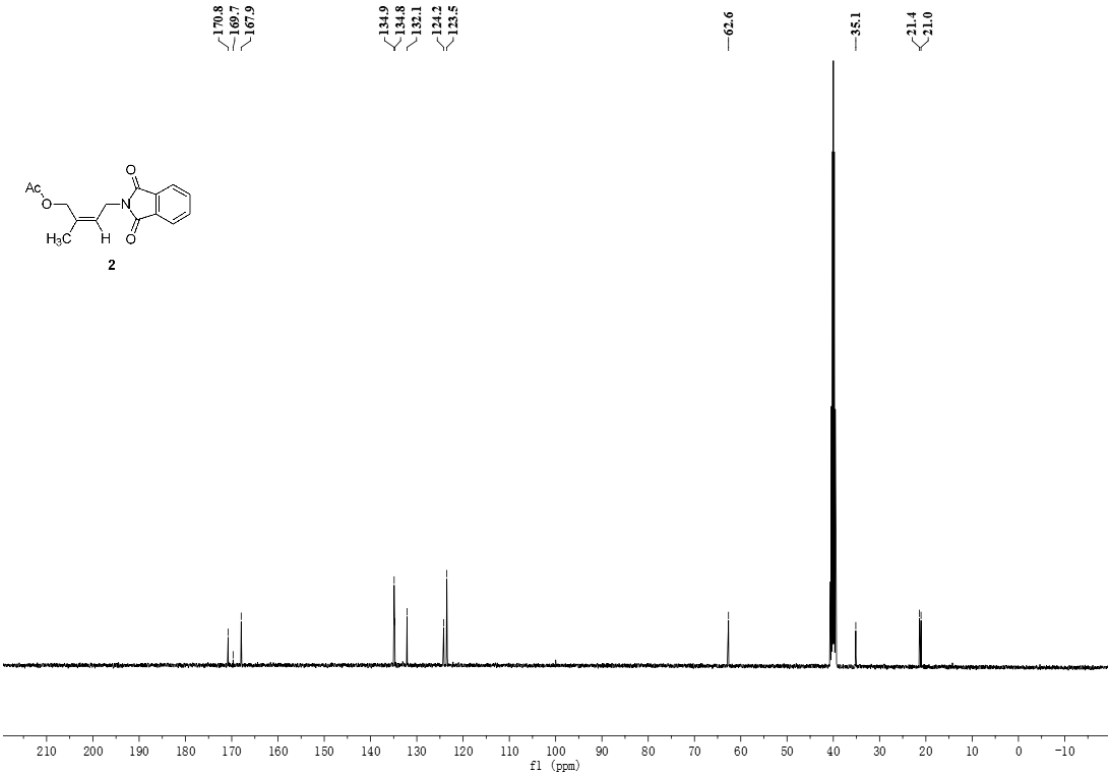
Compound	Potential (V), vs, $Ag/AgNO_3$	Compound	Potential (V), vs, $Ag/AgNO_3$
SX1	-0.42	SX3	-0.95
SX2	-0.93	SX5	-0.92

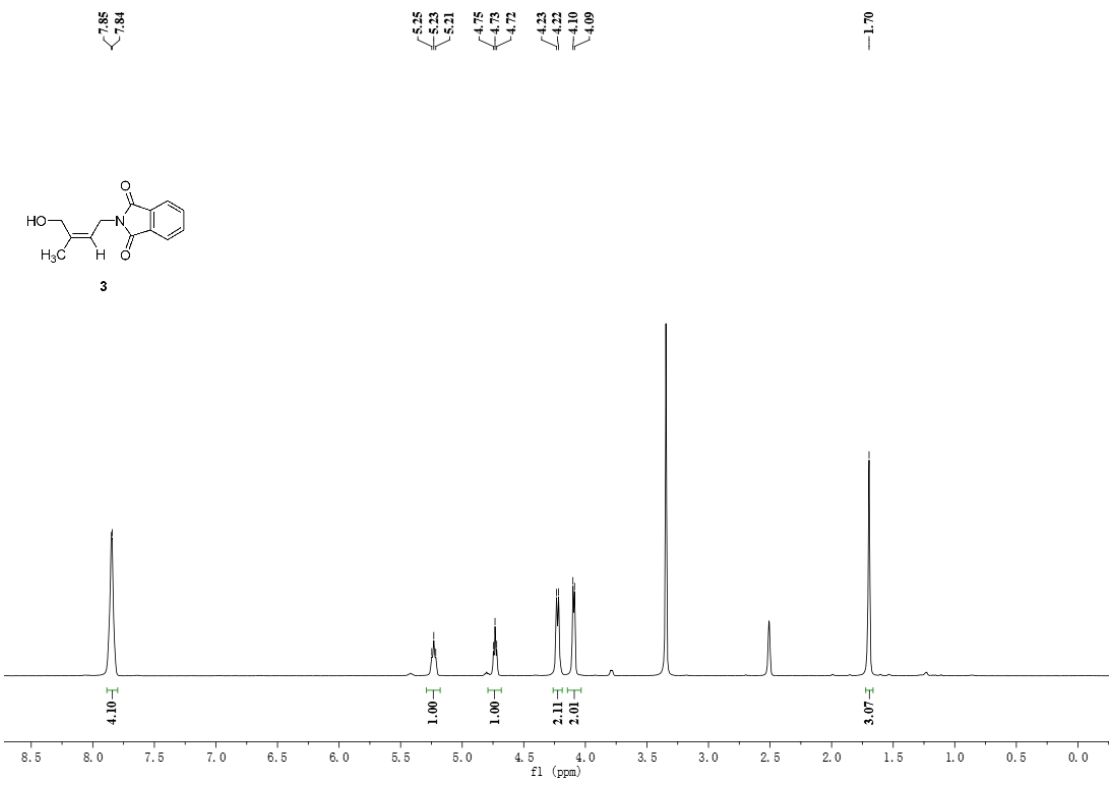
(C)

Figure S7. Properties of compounds. (A) The UV-vis absorption spectrum of reaction mixture containing 0.1 mM cZ or tZ (0.2% DMSO, 3 mL). (B) CV voltammograms of **SX1-5**. (C) Redox potential for photosensitizers derivatives.

9. NMR spectra



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1.70
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N
O
O
H3C
H
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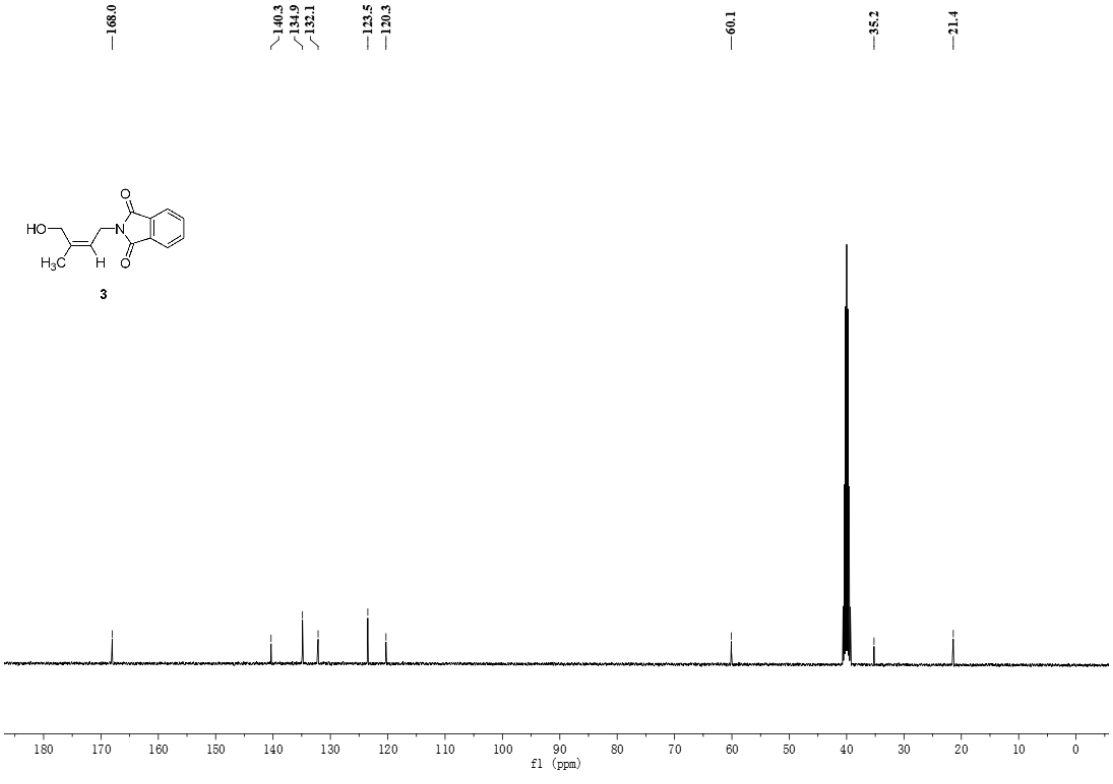
4.10
1.00
1.00
2.11
2.01
3.07
f1 (ppm)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H
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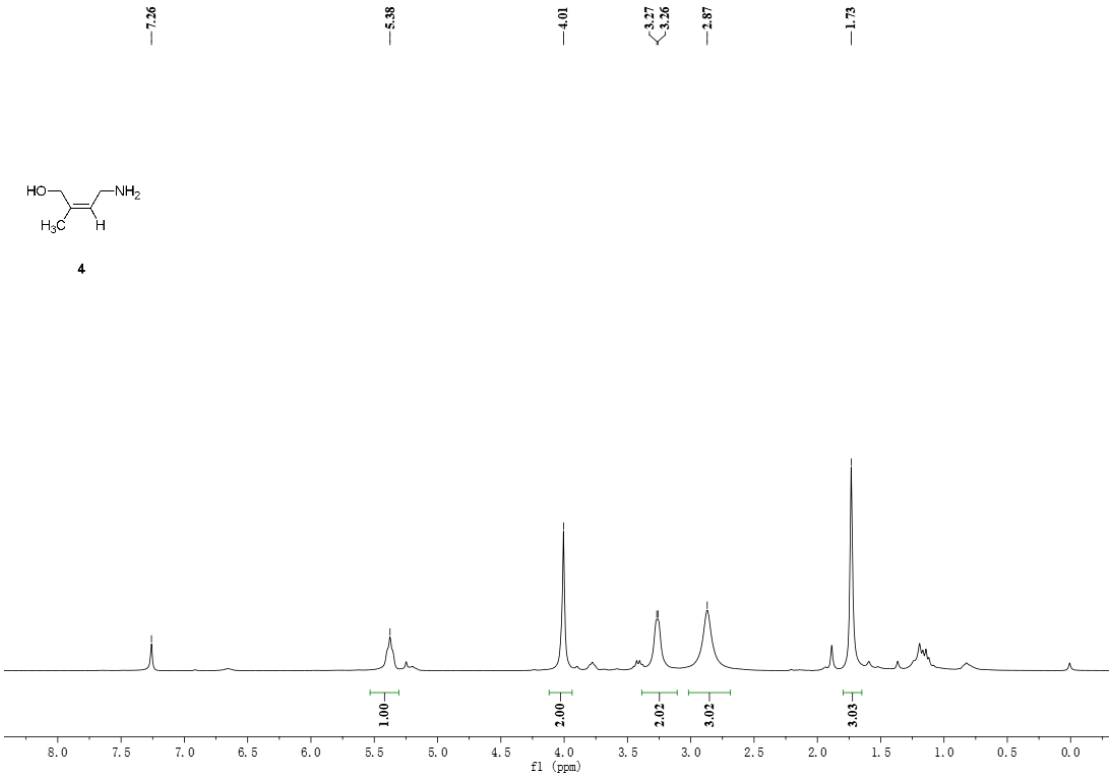
f1 (ppm)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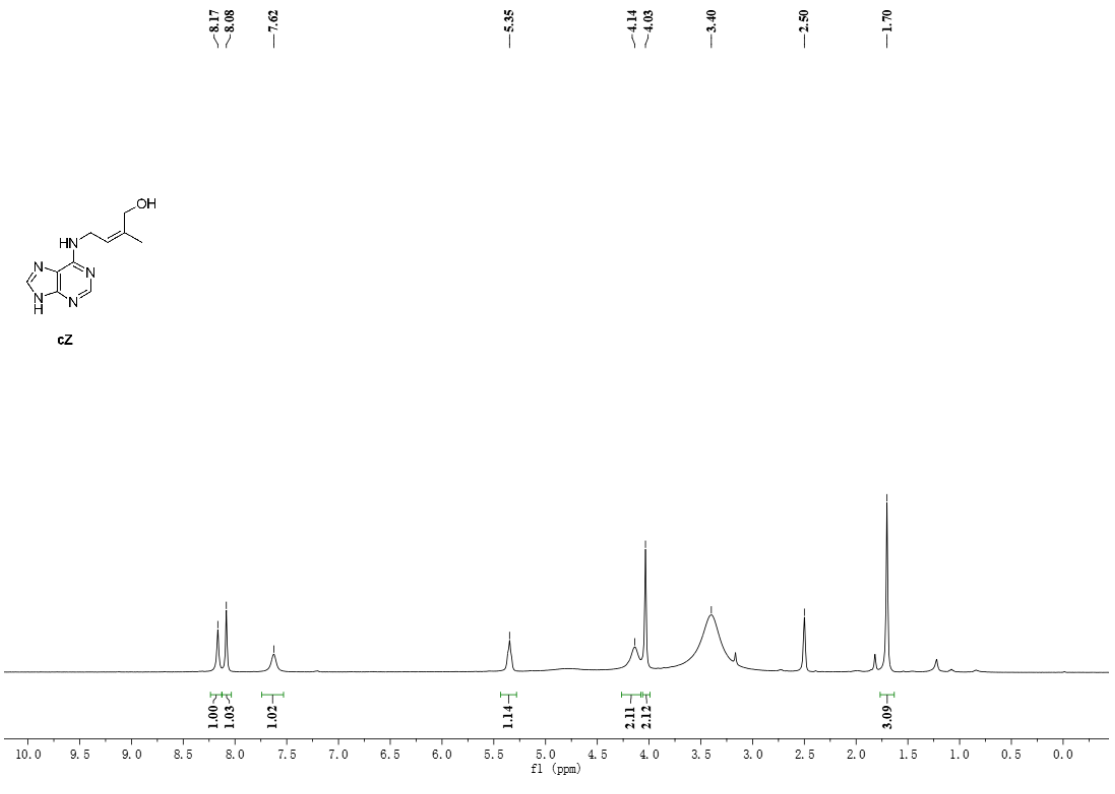
f1 (ppm)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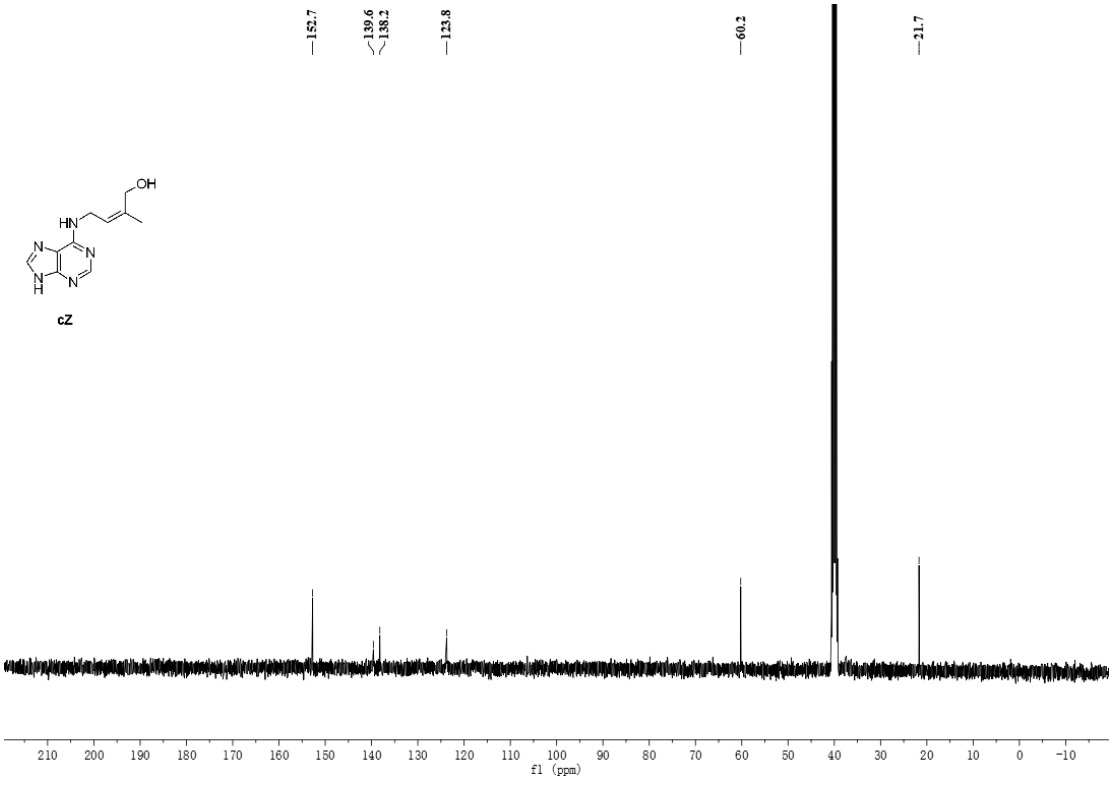
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H
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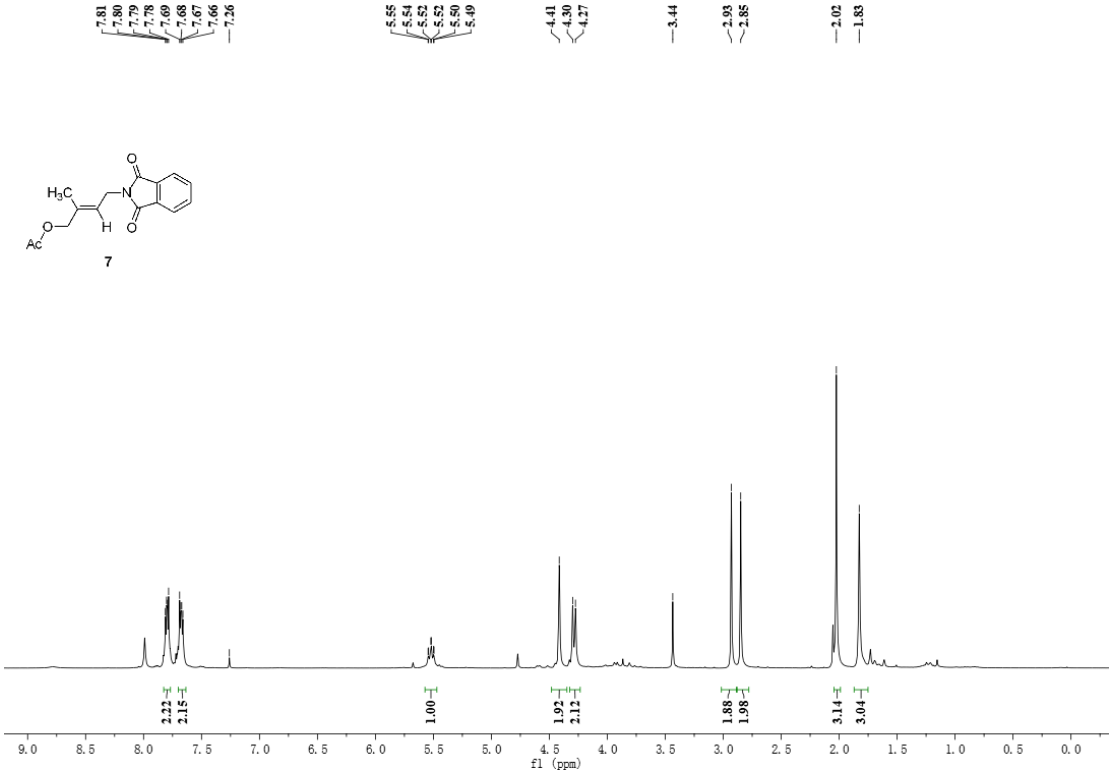
f1 (ppm)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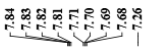
f1 (ppm)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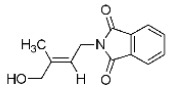
4.01
1.85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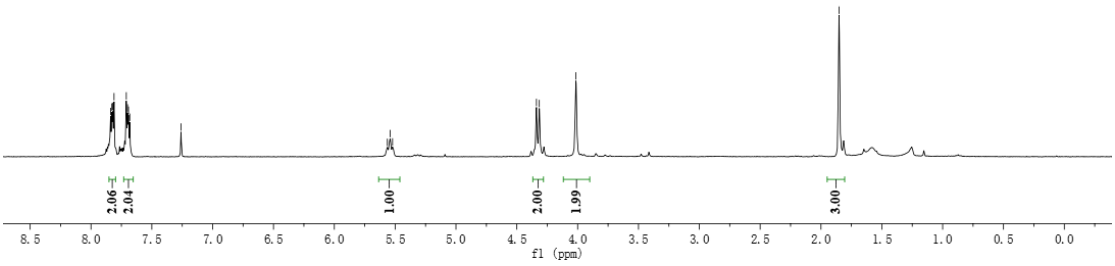
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3.5
3.0
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1.5
1.0
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0.0
f1 (ppm)


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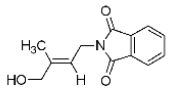
13.8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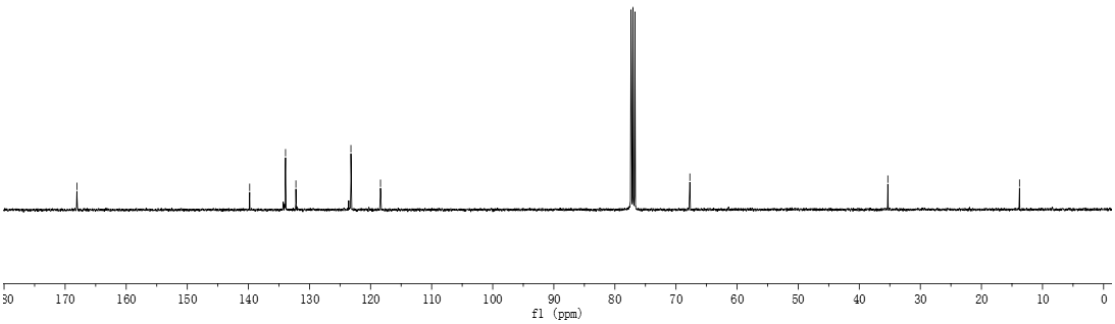
H
N
O
O

8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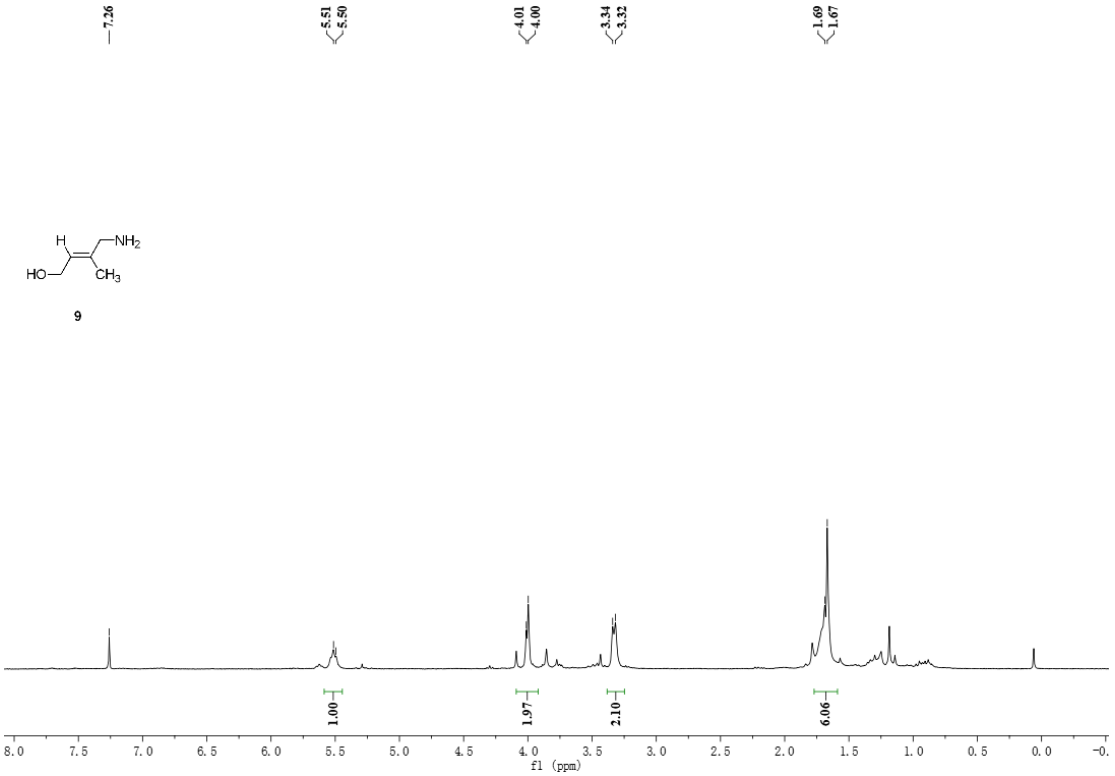
f1 (ppm)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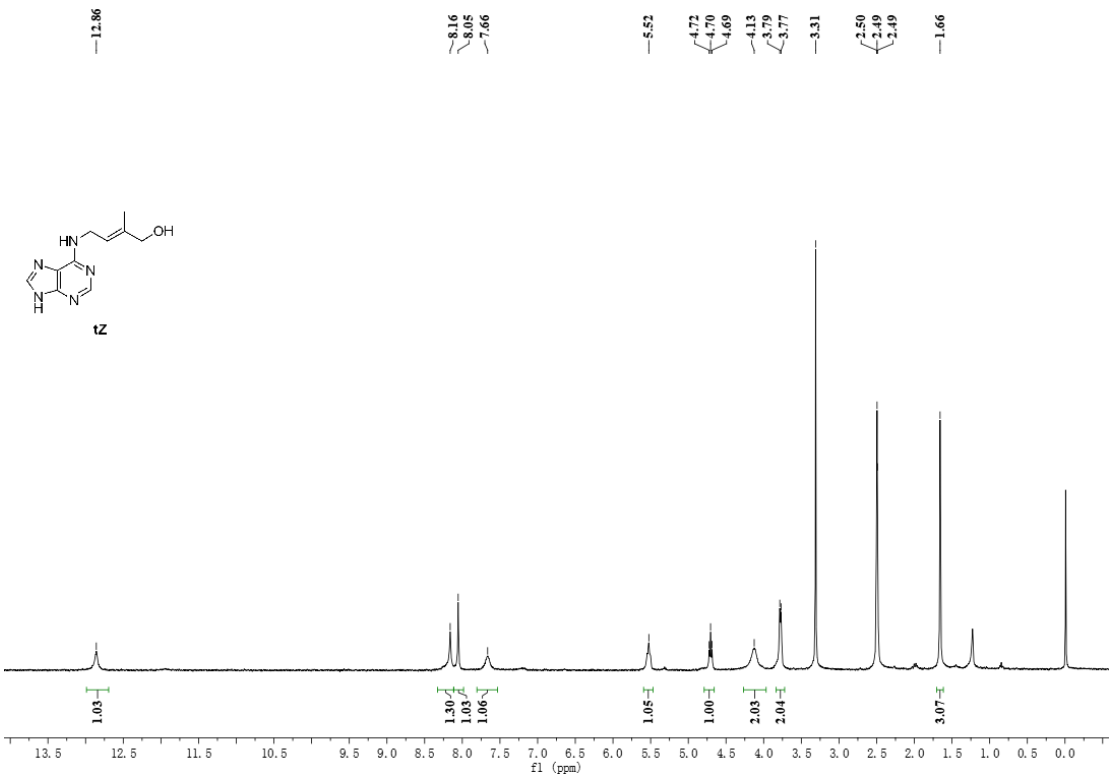
9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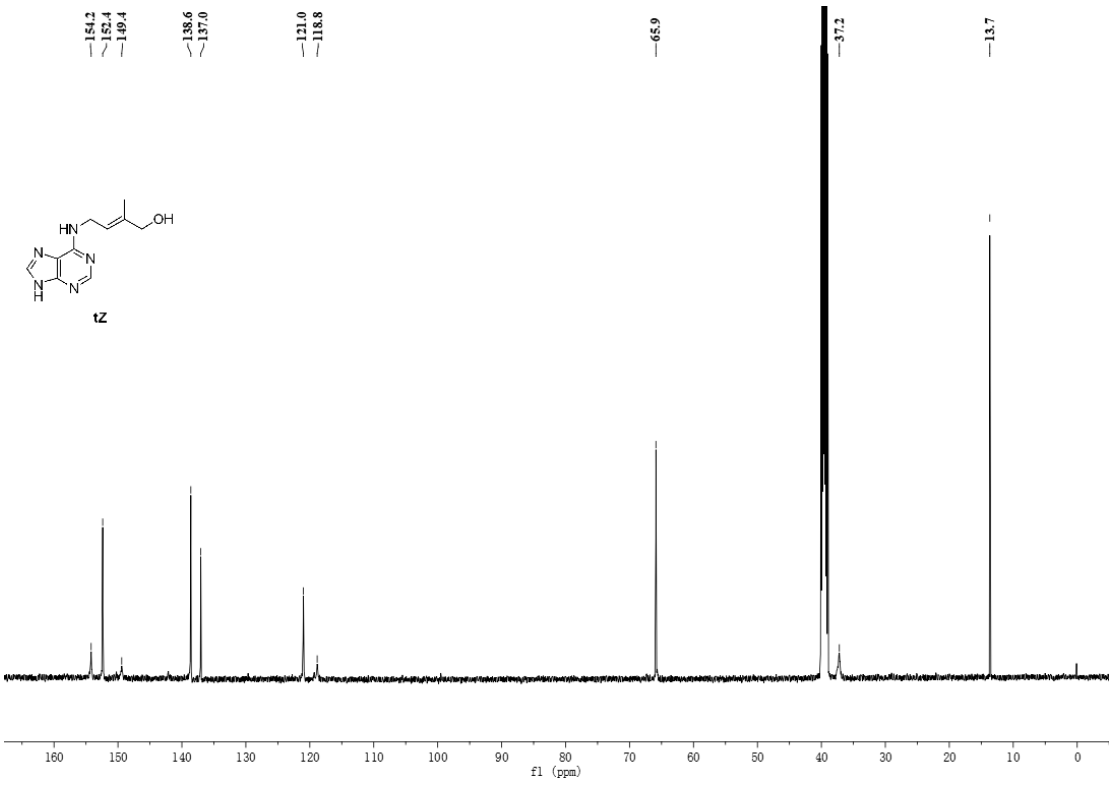
f1 (ppm)

tZ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tZ
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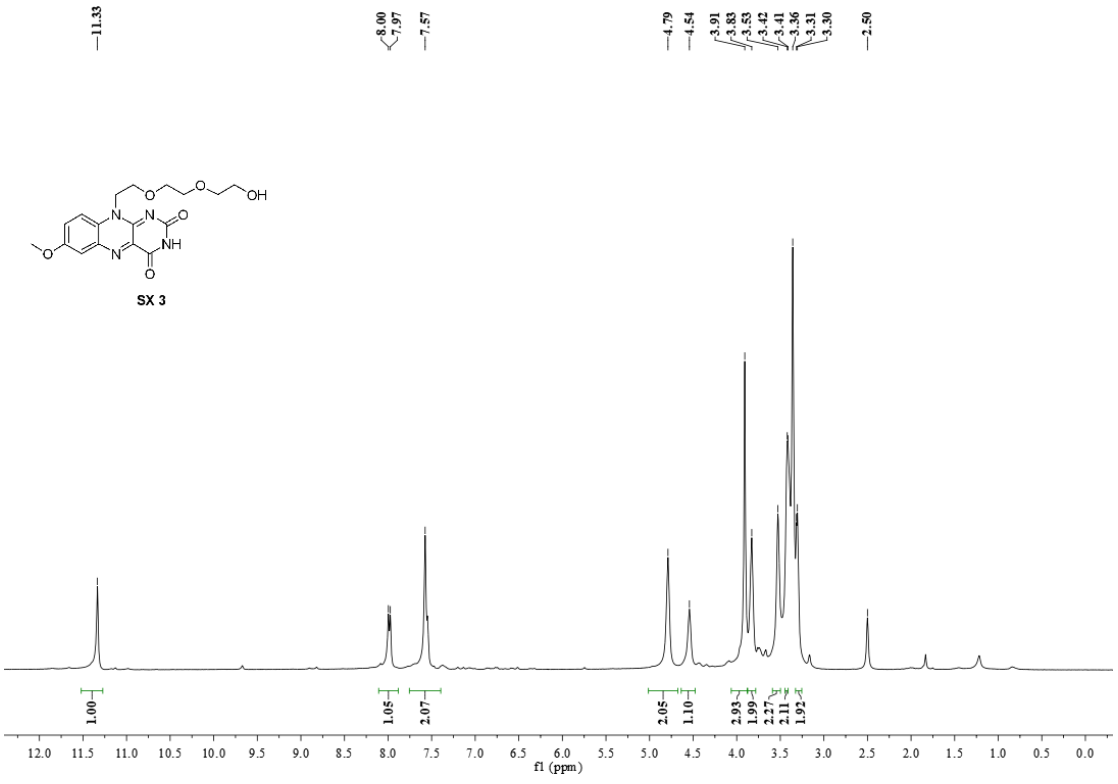
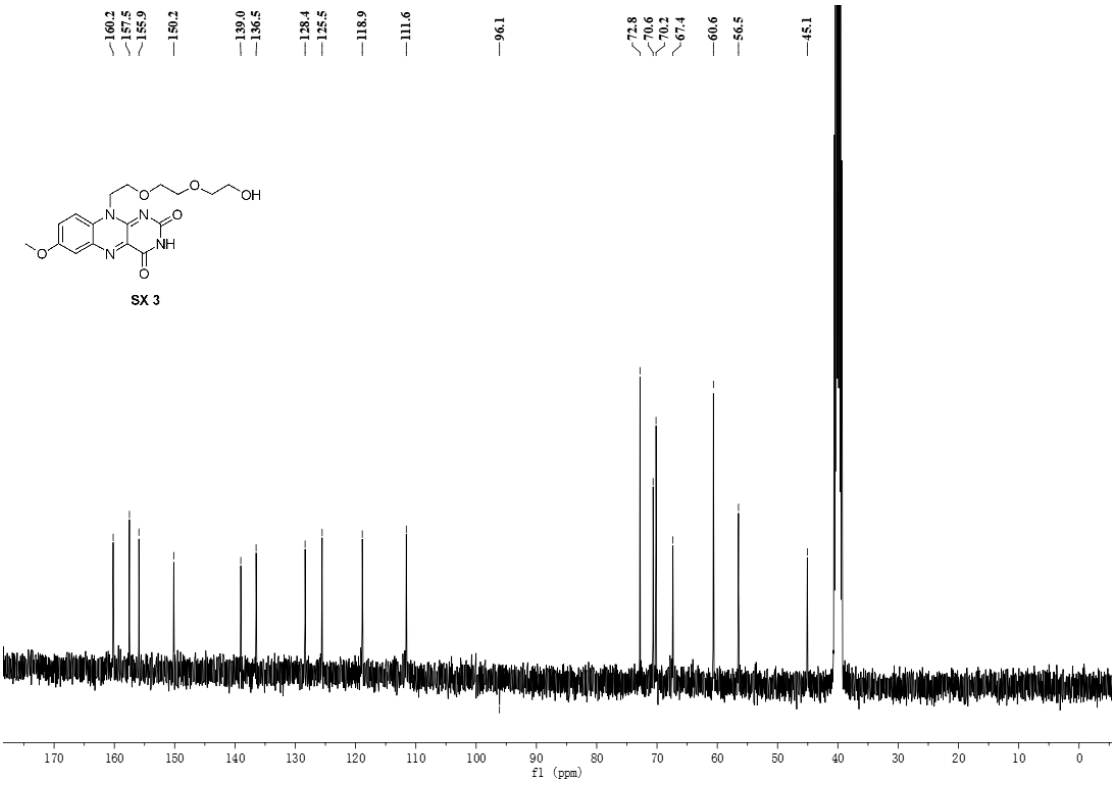
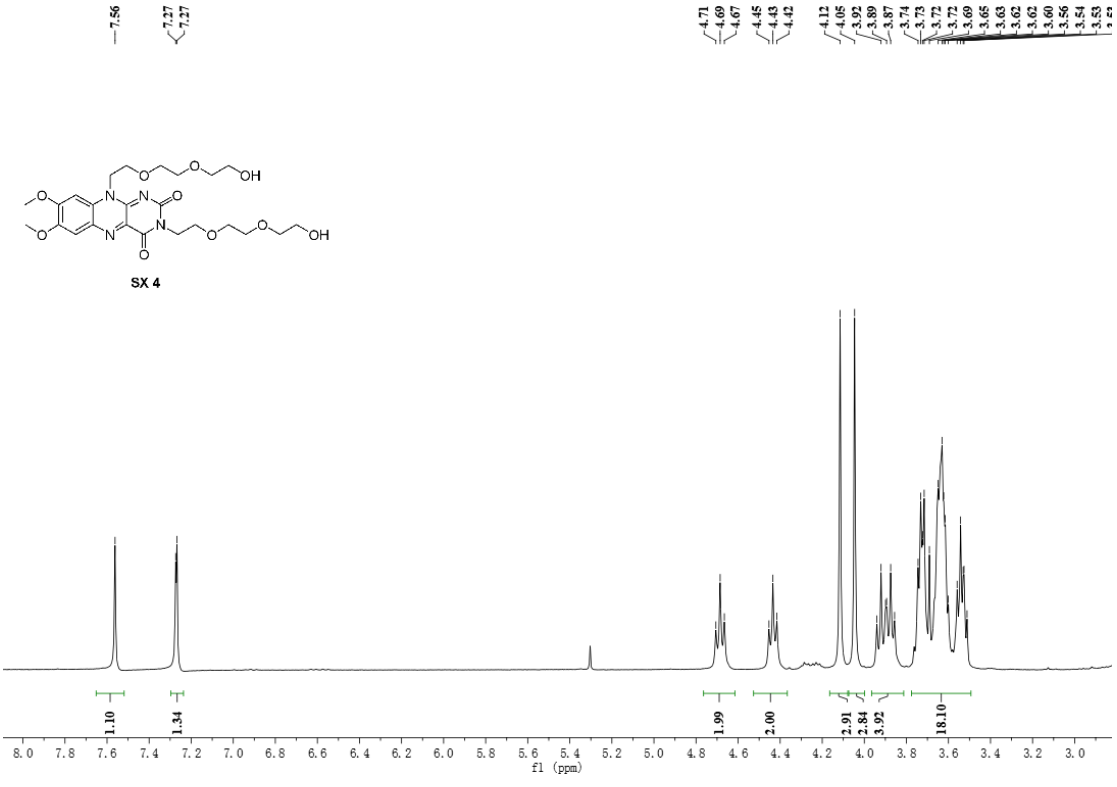
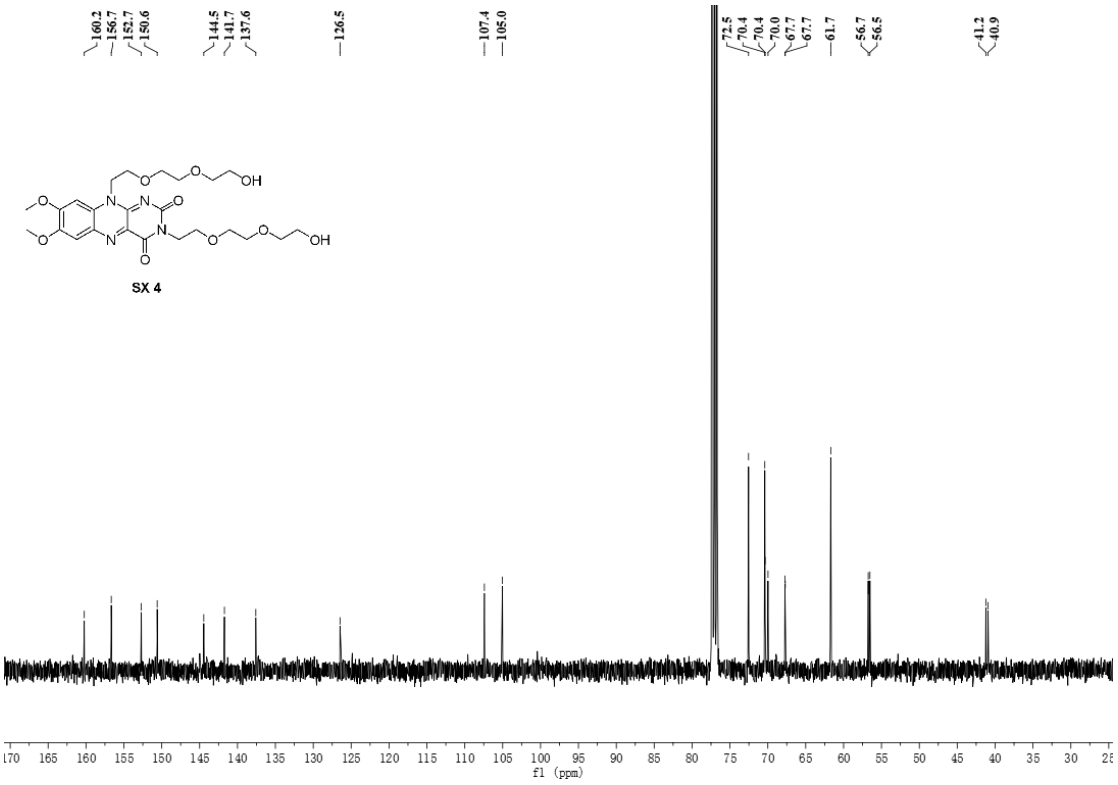
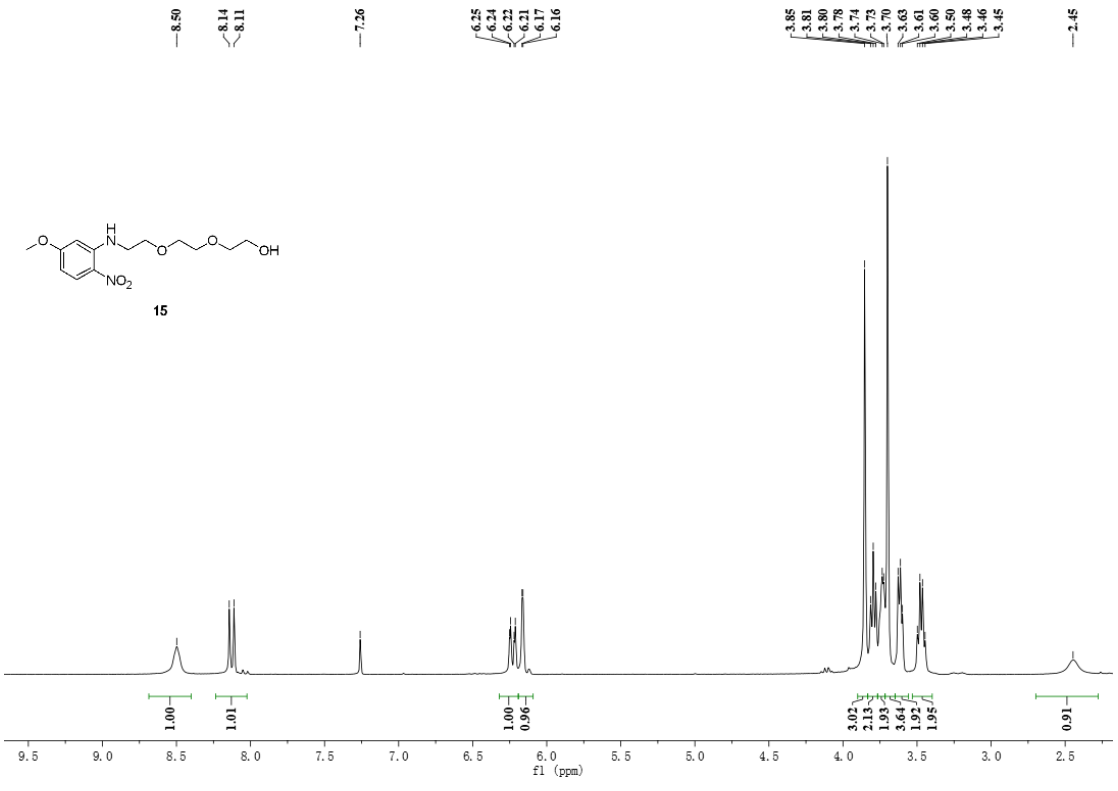
70
60
50
40
30
20
10
0
f1 (ppm)

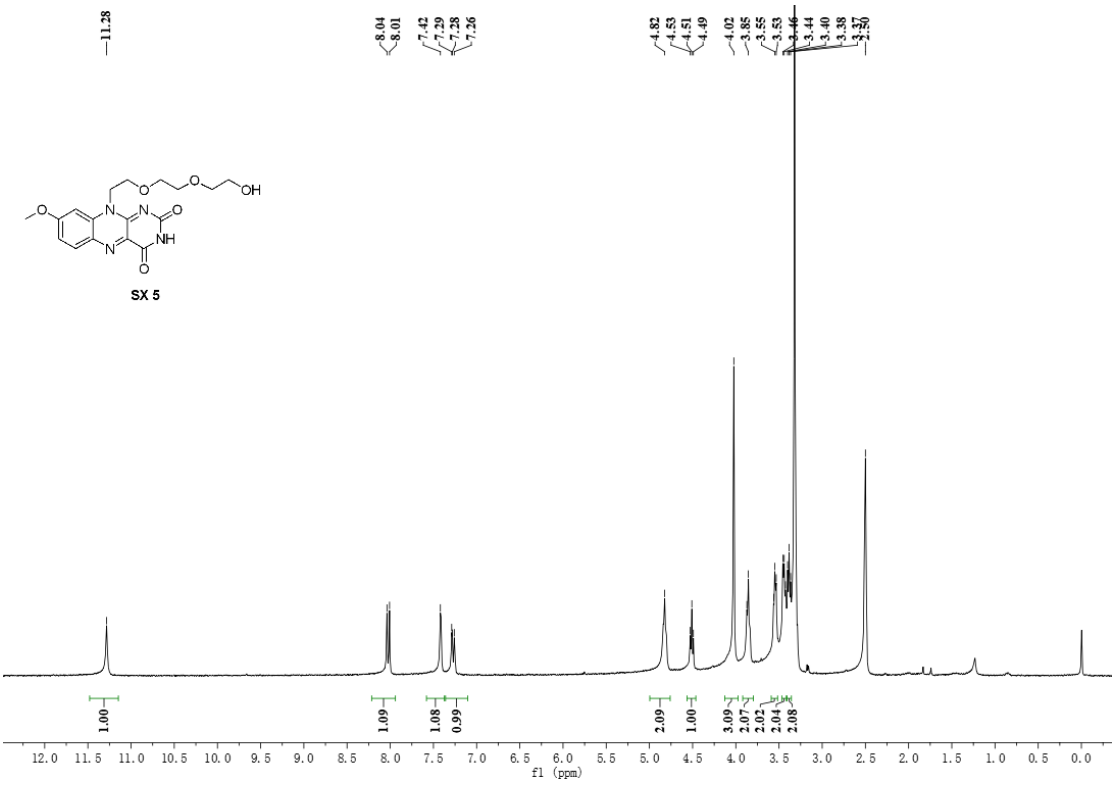

11.33
8.00
7.97
7.57
4.79
4.54
3.91
3.83
3.55
3.42
3.41
3.36
3.31
3.30
2.50
O
O
OH
N
N
O
O
NH
N
O
SX 3
1.00
1.05
2.07
2.05
1.10
2.93
1.99
2.27
2.11
1.92
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

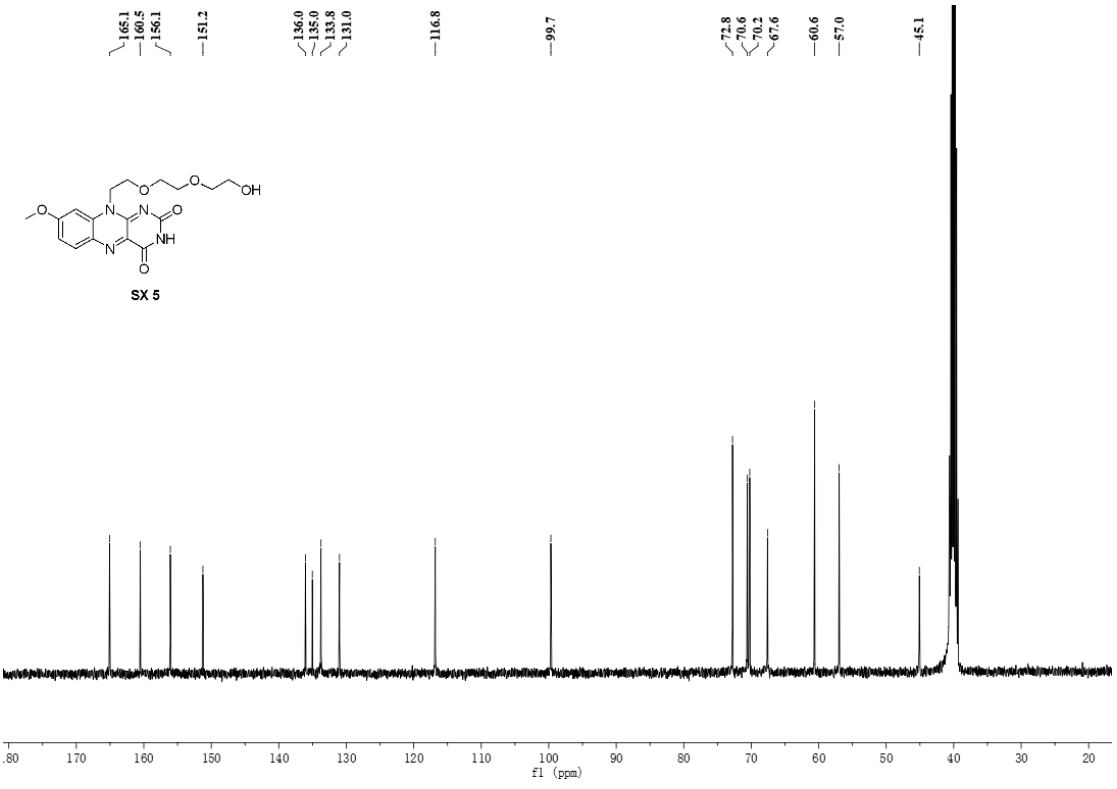

160.2
157.5
155.9
150.2
139.0
136.5
128.4
125.5
118.9
111.6
96.1
72.8
70.6
70.2
67.4
60.6
56.5
45.1
OH
O
N
NH
SX 3
f1 (ppm)


7.56
7.27
7.27
4.71
4.69
4.67
4.45
4.43
4.42
4.12
4.05
3.92
3.89
3.87
3.74
3.73
3.72
3.72
3.69
3.65
3.63
3.62
3.62
3.60
3.56
3.54
3.53
OH
O
N
SX 4
1.10
1.34
1.99
2.00
2.91
2.84
3.92
18.10
f1 (ppm)


160.2
156.7
152.7
150.6
144.5
141.7
137.6
126.5
107.4
105.0
72.5
70.4
70.4
70.0
67.7
67.7
61.7
56.7
56.5
41.2
40.9
OH
OH
SX 4
f1 (ppm)


8.50
8.14
8.11
7.26
6.25
6.24
6.22
6.21
6.17
6.16
3.85
3.81
3.80
3.78
3.74
3.73
3.70
3.63
3.61
3.60
3.50
3.48
3.46
3.45
2.45
OH
NO2
15
1.00
1.01
1.00
0.96
3.02
2.13
1.93
3.64
1.92
1.95
0.91
f1 (ppm)


11.28
8.04
8.01
7.42
7.29
7.28
7.26
4.82
4.53
4.51
4.49
4.02
3.85
3.55
3.53
3.46
3.44
3.40
3.38
3.37
2.50
OH
O
N
NH
SX 5
1.00
1.09
1.08
0.99
2.09
1.00
3.09
2.07
2.02
2.04
2.08
f1 (ppm)


165.1
160.5
156.1
151.2
136.0
135.0
133.8
131.0
116.8
99.7
72.8
70.6
70.2
67.6
60.6
57.0
45.1
OH
O
N
NH
SX 5
f1 (ppm)

10. References

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