Supplementary Information

Visible-light-induced cleavege of 4-α-amino acid substituted naphthalimides and its application in DNA photocleavage

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Figures

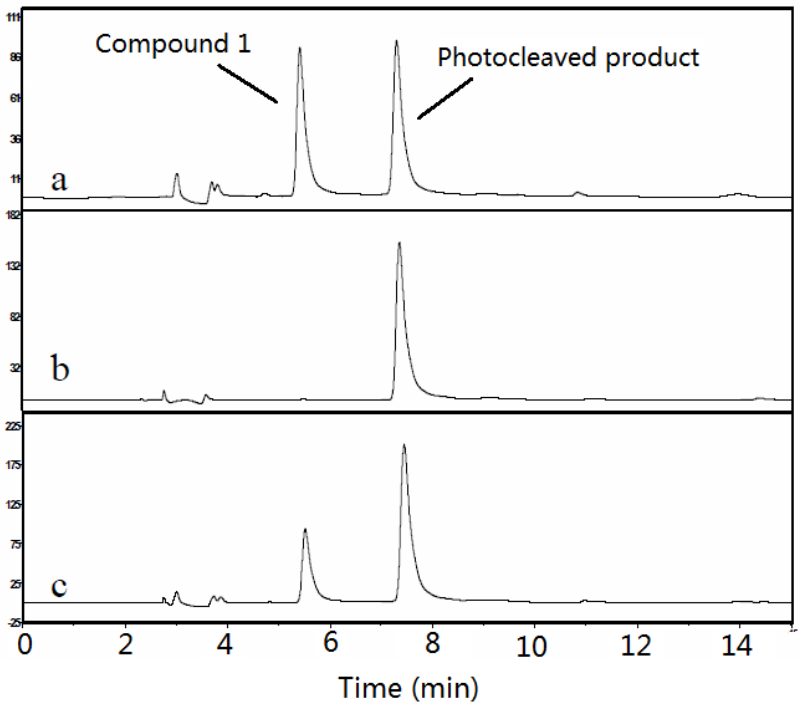


Fig.S1. HPLC analysis of photocleaved products of compounds **1** and **2**. (a) **1** solution after irradiation; (b) purified fluorescent product of compound 2 after photocleavage; (c) mixture of a and b. Gradient elution: 0-15 min, 15% CH_3CN/H_2O(0.1%TFA) to 50% CH_3CN/H_2O (0.1%TFA); detected at 430 nm.

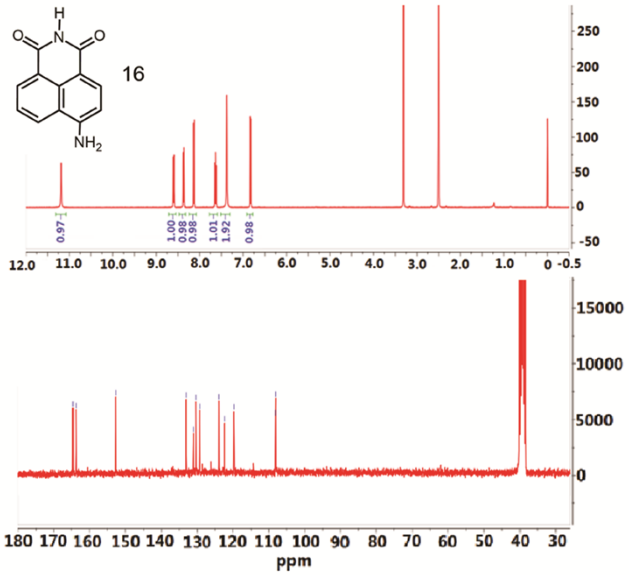


Fig.S2. ^{1}H NMR (top) and ^{13}C NMR (bottom) spectra of photcleaved fluorescent product of 1 and 2. This product was identified to be compound **16.** ^{1}H NMR (400 MHz, DMSO-d6), ^{13}C NMR (75 MHz, DMSO-d6).

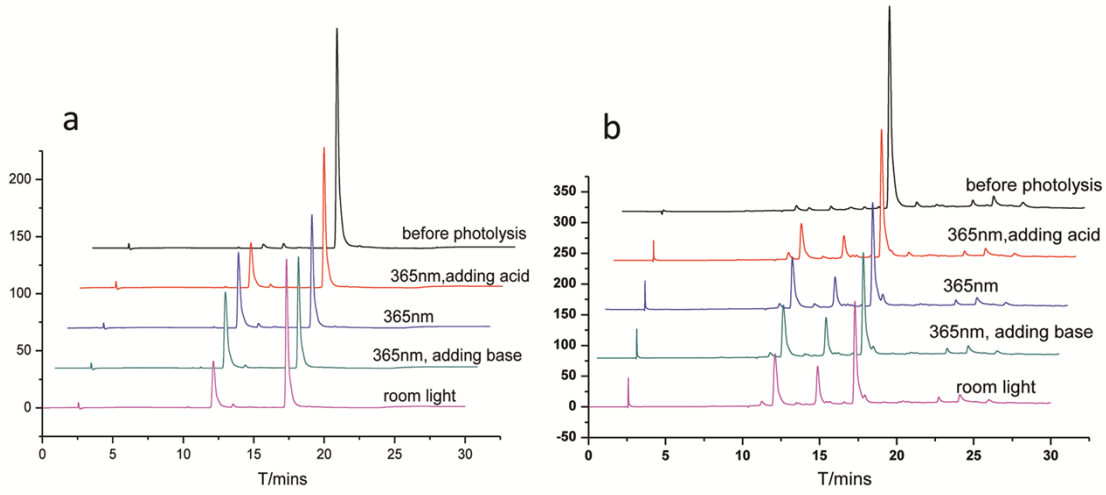


Fig.S3. HPLC analysis of photocleaved products of compound **6**. Detection at 430nm (a) and 270nm (b), Gradient elution: 0–20–30 min, 20% B–90%B–90% B. A: H_2O (0.1%TFA); B: CH_3OH (0.1%TFA). Photocleaved conditions:compound 6 was dissolved in ethanol in the absence or presence of 1% trifluoroacetic acid (TFA) or 1% ammonia, then exposed to 365 nm UV light for 3 hours or room light for 6 hours.

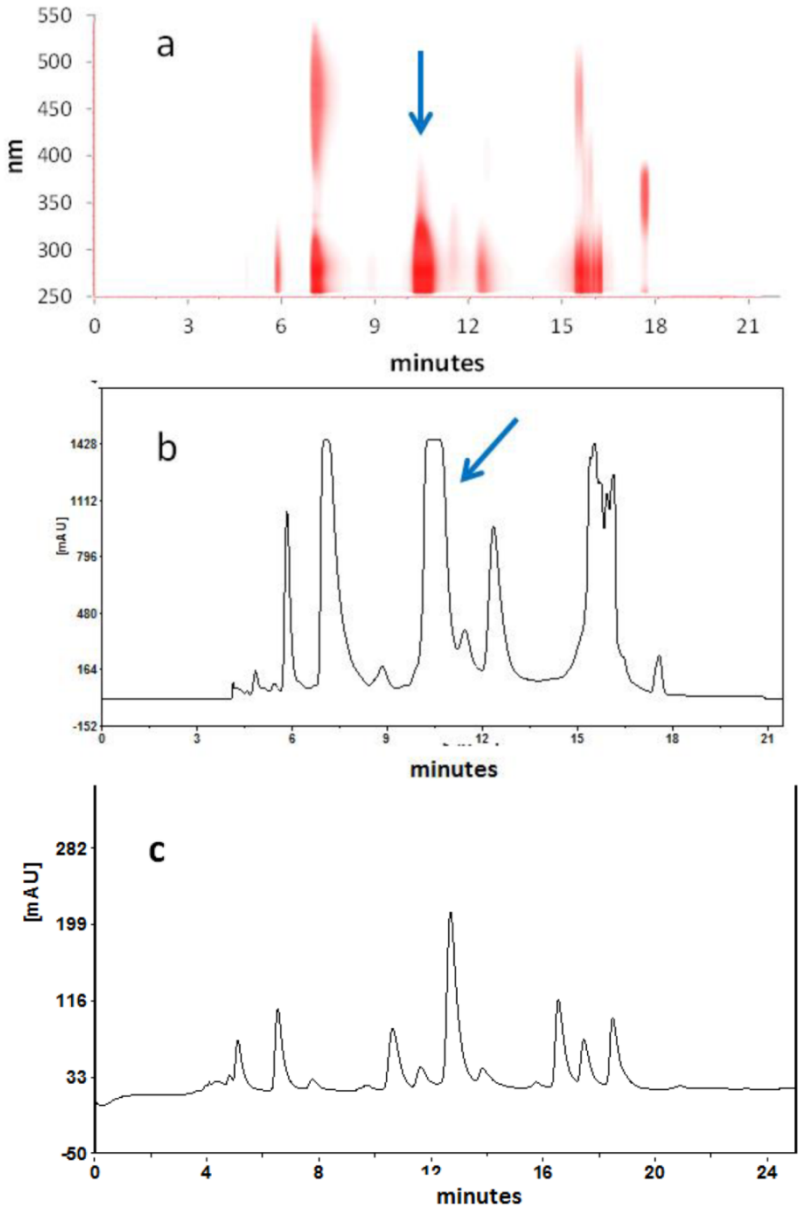


Fig.S4 HPLC analysis of photocleaved products of compound 6. (a) 2D-DAD chromatogram of the preprtation-HPLC of compound 6 after irradiation. (b) Extracted chromatogram at 270 nm from a. Gradient elution: 0-9-12 min, 50% B-50% B-90% B. A: H_2O (0.1%TFA); B: CH_3OH (0.1% TFA), 3 ml/min. (c) HPLC analysis of the collected product (the peak pointed by arrow in above chromatogram) after standing for two days in dark, Gradient elution:0-20 min, 50% CH_3OH/H_2O (0.1%TFA)-90% CH_3OH/H_2O (0.1%TFA), 0.8 ml/min, 270 nm).

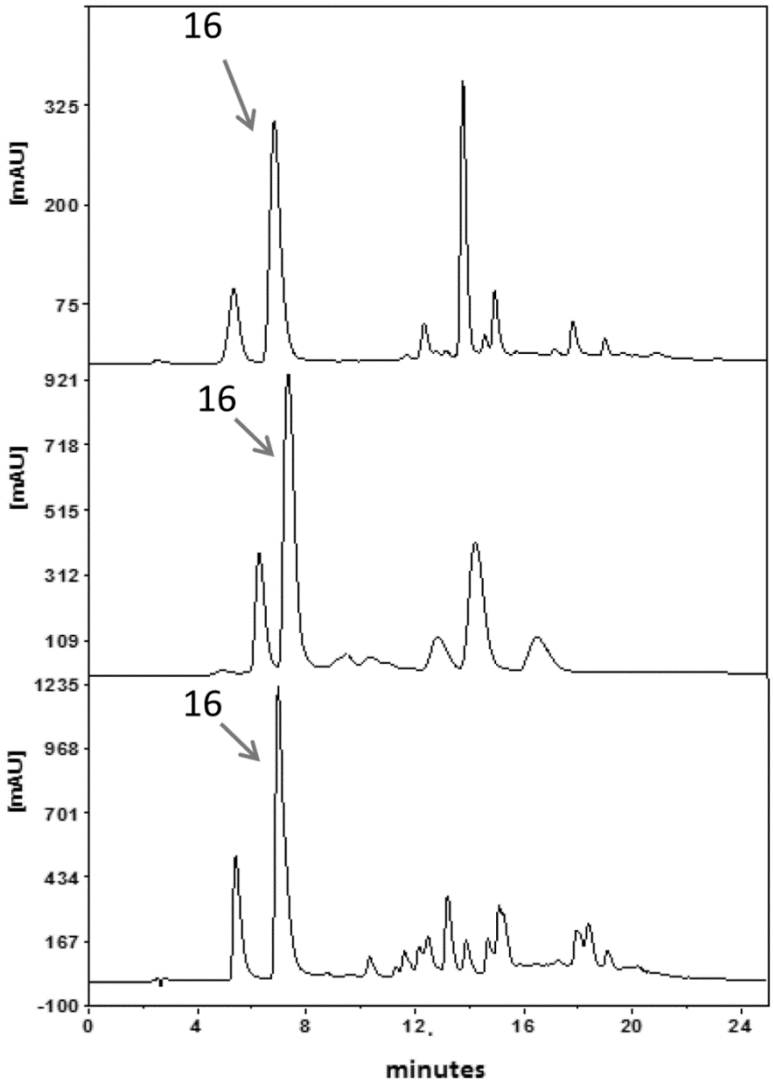


Fig.S5 HPLC analysis of photocleaved compound 6 before (a) and after concentrated by rotary evaporation at 10°C (b) or at 35 °C (c) HPLC program:0-20 min, 50% CH3OH/H2O (0.1% TFA)-90% CH3OH/H2O (0.1% TFA), 0.8 ml/min, detected at 270 nm.

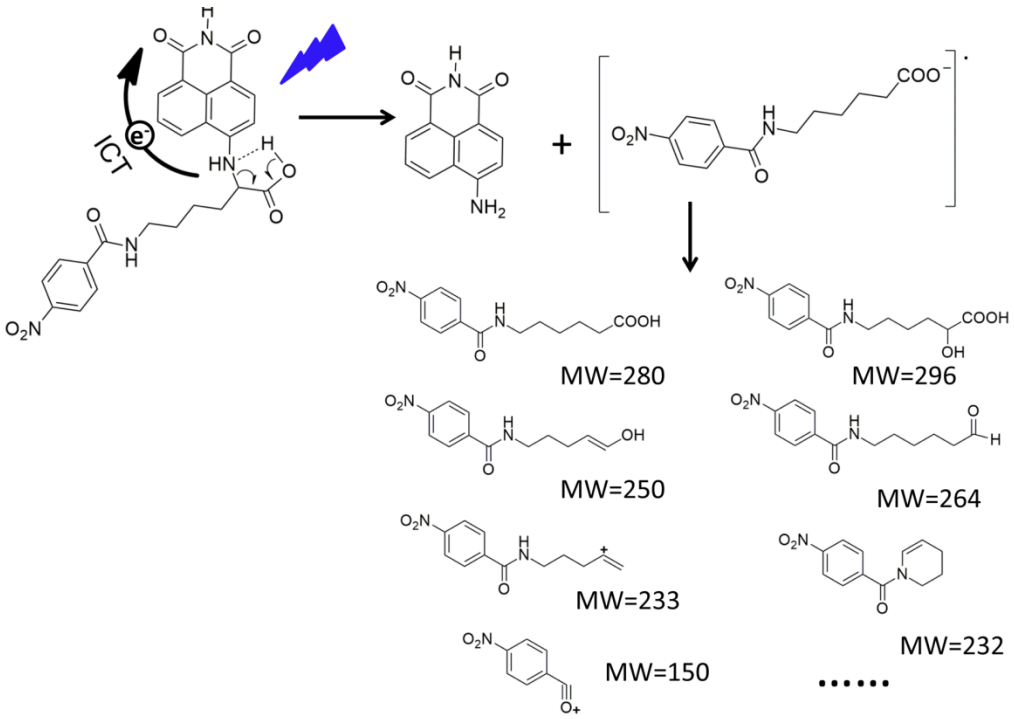


Fig. S6 Potential structures of some photocleaved compounds of compound 6

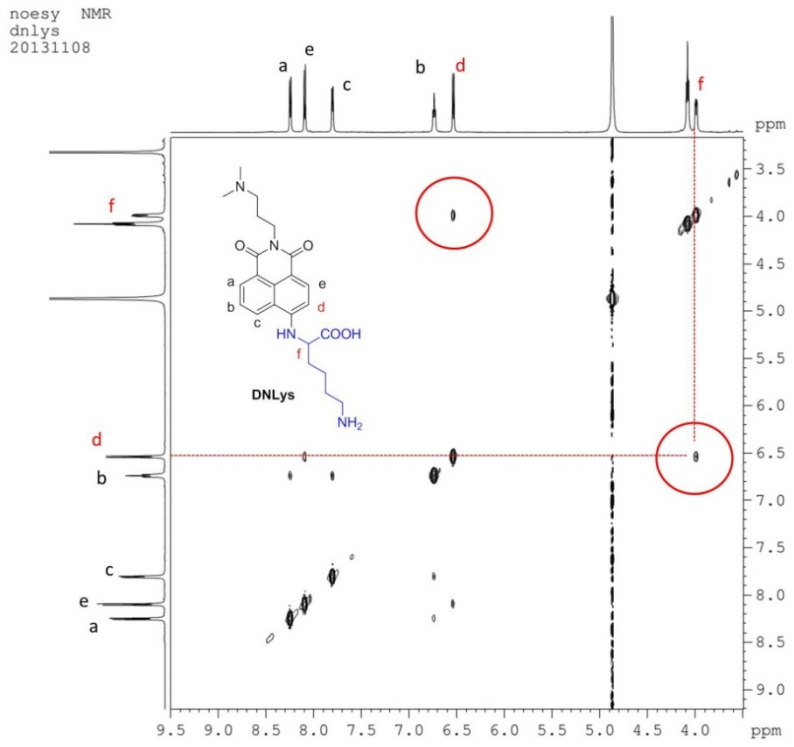


Fig.S7. The Partial NOESY NMR spectrum of DNLys (600 MHz, MeOD)

Absorption and emission spectra measurement

The stoke solutions (1 mM and 10 mM) of compounds used in the experiment were

prepared in DMSO, and stored at 4°C. CT-DNA stock solution was prepared in Tris-HCl buffer (25 mM in base pair, pH 7.6), and stored at -20°C. For absorption Spectra measurement, 1 μL of stock solutions (10 mM) of compounds were added into 200 μL of PBS buffer (pH 7.4). For emission spectra measurement, 2 μL of stock solutions (1mM) of compounds was added into 1 mL of PBS buffer (pH 7.4). The absorption spectra were recorded on a Hitachi U-2550 UV/vis spectrophotometer (Kyoto, Japan). Fluorescence emission spectra were recorded on a Hitachi F-4600 fluorescence spectrofluorometer (Kyoto, Japan). The absorption and fluorescence spectra were recorded in a 1.0-cm quartz cuvette.

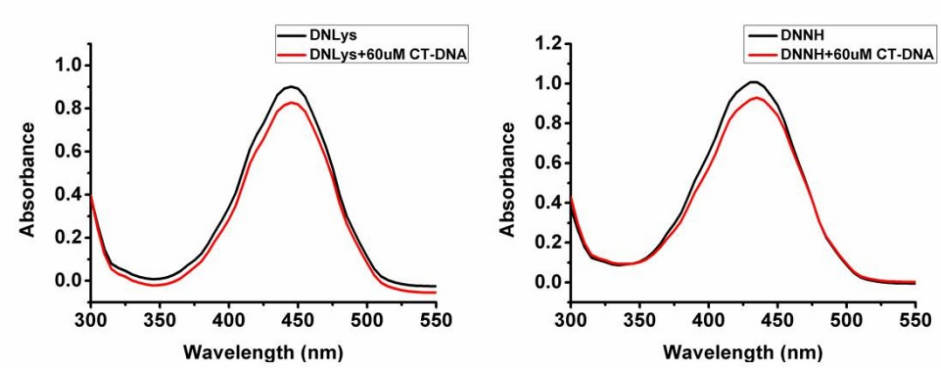


Fig.S8. Absorption spectra of DNLys, DNNH (0 μM) in the absence and presence of 60 μM CT-DNA (in base pair) in pH 7.4 PBS buffer.

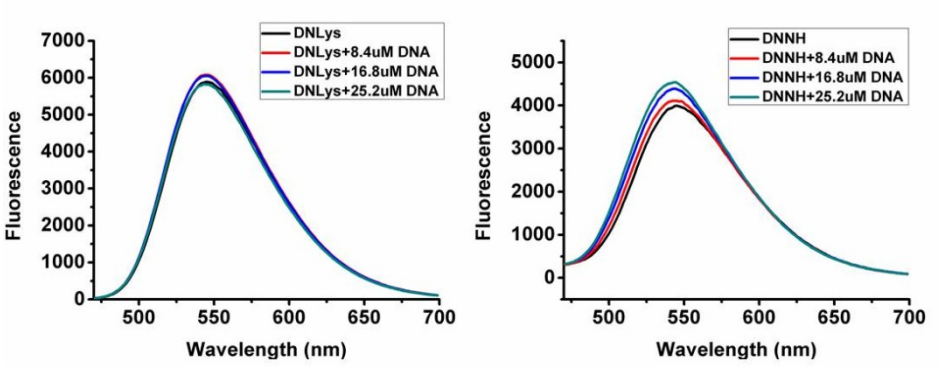


Fig.S9. Fluorescence spectra of DNLys, DNNH (2 μM) in the absence and presence of different concentration of CT-DNA (in base pair). in pH 7.4 PBS buffer. [CT-DNA]: 0 μM, 8.4 μM, 16.8 μM, 25.2 μM), exicited at 445 nm.

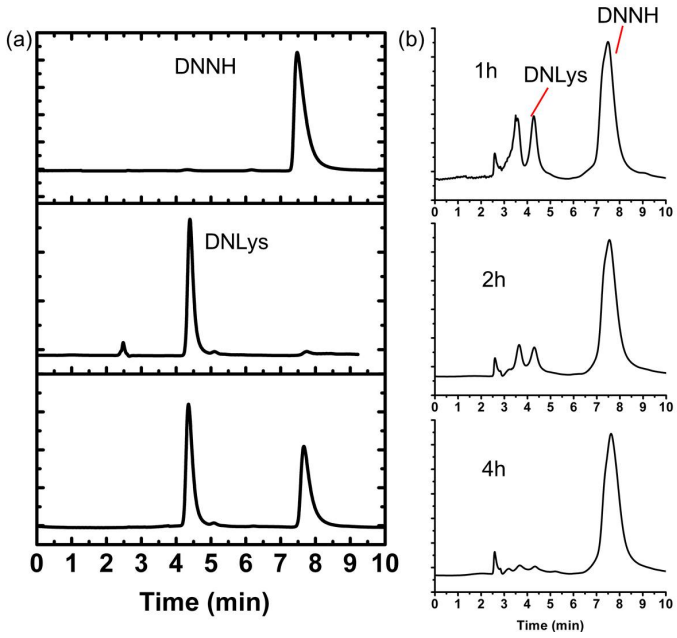


Fig.S10. (a) HPLC chromatograms of DNNH, DNLys and mixture of DNNH and DNLys. (b) HPLC analysis of DNLys in methanol solution after irradiated under 465-470 nm LED light for 1, 2, 4 h at room temperature. Mobile phase: methanol : H_2O (0.1%TFA), 4 : 6, detected at 245 nm.

Experimental section

Materials

4-bromo-1,8-naphthalic anhydride was purchased from Liaoning Dye Chemical Co.,LTD (Liaoyang,china). α-amino acids were purchased from Beijing xinjinke biological technology Co., LTD. Other chmicals were were obtained from JK-chemical company (Beijing). CT-DNA and PBR322 DNA were purchased from Takra Biotechnology (Dalian) Co.,LTD. Counting Kit-8 (CCK-8) was purchased from DojindoLaboratorise (Shanghai) Co., LTD. All solvents were purchased from Beijing Chemical Plant, China. All chemical reagents were used without further purification. Deionized water was purified by a UPHW-III-90T water purification system (chengdu,china) and was used throughout this work.

Instruments.

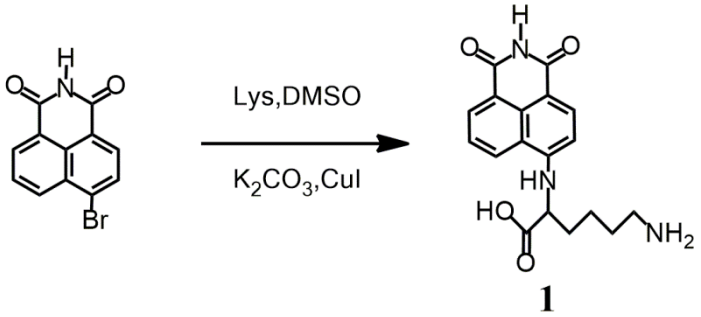
^{1}H NMR spectra were recorded at 300 MHz, and ^{13}C NMR spectra were recorded at 75 MHz on a Brucker AM 300 spectrometer with tetramethylsilane (TMS) as the internal standard. J values were given in hertz. Low-resolution mass spectra

(MS) were recorded on a LC-MS 2010A (Shimadzu) instrument using standard conditions. High-resolution MS were obtained on a BrukerDaltonics flex-Analysis.

Synthesis and characterization

4-Bromo-1,8-naphthalimide. 4-Bromo-1,8-naphthalic anhydride (2.7 g, 10 mmol) was suspended in 300 mL of absolute ethanol and heated to 75 °C under stirring. Ammonia (5 mL) was then dropped into the reaction solution. After 1 hour's refluxing, the mixture was cooled to room temperature. Then the solid was filtered and washed with absolute ethanol, then dried under vacuum at 40°C. ^{1}HNMR (400 MHz, DMSO-*d6*) (δ, ppm) 7.94 (t, J = 7.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 8.23 (d, J = 7.6 Hz, 1H), 8.48 (m, 2H), 11.80(s, 1H). EI-MS m/z 275$(M)^+$.

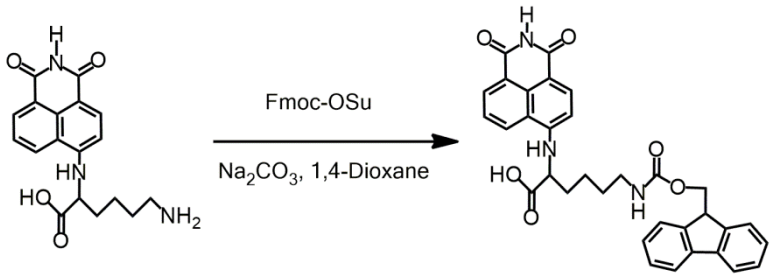
Compound 1, 4-(1-carboxyl-5-amino-amylamino)-1,8-naphthalimide.



1

4-Bromo-1,8-naphthalimide (2.2g, 8mmol, 1 equiv), CuI (1 equiv), K_2CO_3 (1.25 equiv), L-lysine (2 equiv) were added in 100 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, the supernatant was added with 200 mL of chloroform. The obtained precipitate was washed repetively with chloroform and water to yield the crude product. The crude product was purified by silica gel chromatography (ethyl acetate/MeOH/glacial acetic acid, 1:1:0.1) to yield compound 1 as yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 8.68 (d, J = 6.1 Hz), 8.36 (d, J = 8.5 Hz), 8.01 (d, J = 8.5 Hz), 7.80 (d, J = 7.2 Hz), 6.79 (t, J = 7.6 Hz), 6.45 (d, J = 8.7 Hz), 3.76 (t, J = 9.6 Hz), 3.63 – 2.96 (m), 2.79 (s), 2.23 – 2.06 (m), 1.83 (s), 1.68 (d, J=1.7 Hz), 1.61-1.47 (m), 1.37 (d, J=3.3 Hz). ESI-MS 342.2$(M+H)^+$

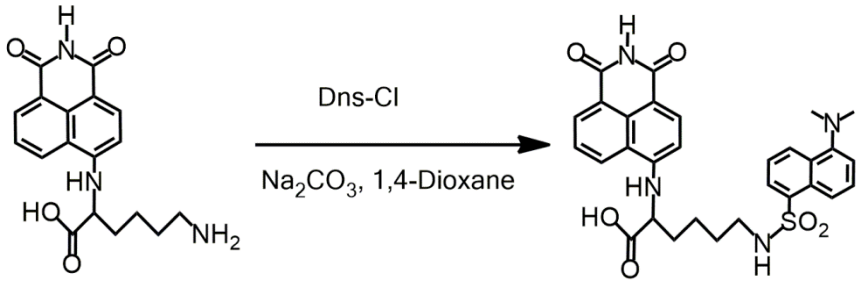
Compund 5, 4-[1-carboxyl-5-(9-fluorenylmethoxycarbonylamino)-amylamino]-1,8-naphthalimide



1 **5**

The crude product of compound 1 (50 mg) was disoved in HCl solution (2 %) and added with $CuSO_4$ (200mg), then the pH of solution was adjusted to 8 with Na_2CO_3. Fmoc-OSu (1 equiv) dissolved in 1,4- dioxane was added dropwise to the mixture with stirring and reacted for 3 h. The reaction mixture was washed with dichloromethane twice. The pH of solution was adjusted to 5 with HCl, the generated precipitate was purified by silica gel chromatography (ethyl acetate/MeOH/glacial acetic acid, 1:1:0.1) to yield compound 5 as yellow solid., 586.2 (M+Na) . ^{1}H NMR (400 MHz, DMSO) δ 11.19(s), 8.30 (d, *J* = 9.2 Hz), 8.15 (d, *J* = 10.4 Hz), 7.90–7.84 (m), 7.68-7.62 (m), 7.50–7.26 (m),6.65 (d, *J* = 9.2 Hz), 4.2–4.15 (m), 3.81 (s), 2.94 (s), 1.89 – 1.84 (m), 1.38 – 1.16 (m),0.94 – 0.86 (m). ESI-MS 564.2 $(M+H)^+$, 586.2 $(M+Na)^+$

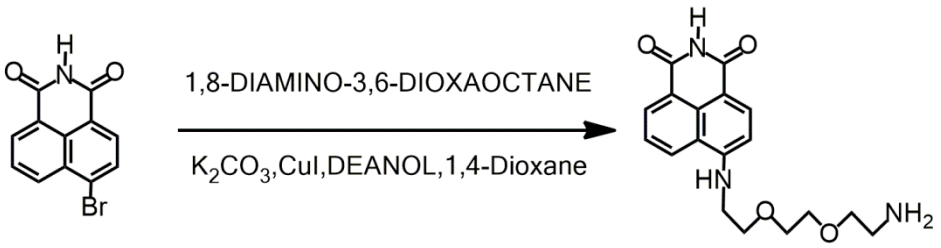
Compound 7, 4-(1-carboxyl-5-dansylamino amylamino)-1,8-naphthalimide



1 **7**

Compound 1 (50 mg) was disoved in DMSO and mixed with 200 μL of 10% Na_2CO_3. Dansyl-Cl (40 mg) dissolved in 1,4 - dioxane (800 μL) was added dropwise to the mixture with stirring and reacted for 2 h. Te product was purified by RP-HPLC to yield 20 mg compound 7 as yellow solid. ESI-MS 573.1$(M-H)^-$

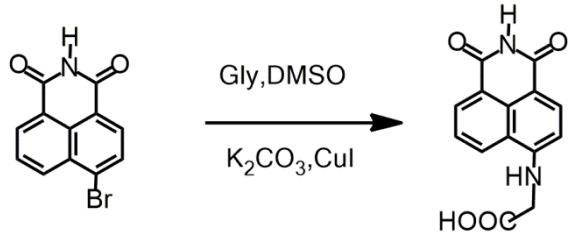
Compound 11, 4-(8-amino-3,6-dioxaoctanoylamino)-1,8-naphthalimide



11

4-Bromo-1,8-naphthalimide (0.54g, 1 equiv，2mmol)，CuI (0.5 equiv), K_2CO_3 (1.5 equiv), 1.5 mL of 1,8-diamino-3,6-dioxaoctane (5 equiv) and 120 μL of DEANOL were added to 5 mL of 1,4-dioxane. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and washed with water, and further purified by silica gel chromatography (ethyl acetate/MeOH/glacial acetic acid, 50:50:0.5) to yield compound 11 (0.3g) as yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 8.68 (d, J = 8.4 Hz, 1H), 8.38 (d, J = 7.2 Hz, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.74 (m, 4H), 7.67 (t, J = 8.0 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 3.72 (t, J = 6.0 Hz, 2H), 3.56 (m, 8H), 2.91 (q, J = 5. 2 Hz, 2H). ESI-MS 344.1 $(M+H)^+$, 366.1 $(M+Na)^+$.

Compound 2, 4-carboxymethylamino-1,8-naphthalimide

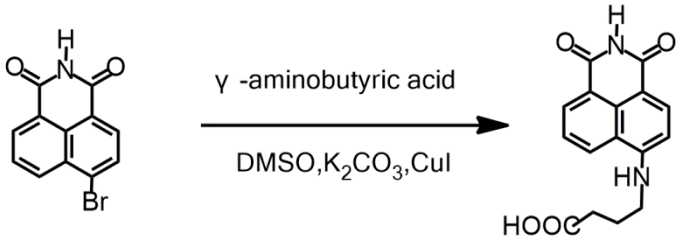


2

4-Bromo-1,8-naphthalimide (0.11g, 0.4 mmol, 1 equiv), CuI (0.25 equiv), K_2CO_3 (0.4 equiv), Glycine (0.3 g, 10 equiv) were added in 4 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and added with alkaline water and washed with dichloromethane twice. Then the solution was acidified with HCl to obtain precipitate. The solution was extracted with chloroform. The precipitate and chloroform extract were dried to obtain compound 2 (50mg) as yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 12.91 (s, 1H), 11.29 (s, 1H), 8.65 (d, J =

8.4 Hz, 1H), 8.40 (d, J = 7.1 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.03 (s, 1H), 7.71 (t, J = 7.7 Hz, 1H), 6.64 (d, J = 8.3 Hz, 1H), 4.17 (d, J = 5.6 Hz, 2H). ESI-MS 269.1 $(M-H)^-$. HRMS (ESI): m/z Calcd for $C_{14}H_{11}N_2O_4$ $(M+H)^+$, 271.0713, found, 271.0714.

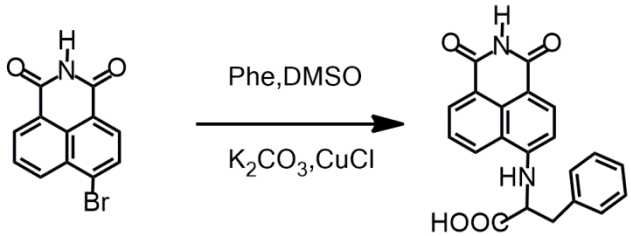
Compound 13, 4-carboxypropylamino -1,8-naphthalimide



13

4-Bromo-1,8-naphthalimide (0.11g, 0.4mmol, 1equiv), CuI (0.25 equiv), K_2CO_3 (0.4 equiv), **4-Aminobutyric acid** (0.41 g 10 equiv) were added in 4 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and added with dichloromethane to obtained precipitate. The precipitate was washed with dichloromethane twice, suspended in HCl solution, and extracted with chloroform. The chloroform extract was dried to obtain compound 13 (61 mg) as yellow solid. ESI-MS 297.1 $(M-H)^-$.

Compound 3, 4-(1-carboxyl-phenylethylamino)-1,8-naphthalimide

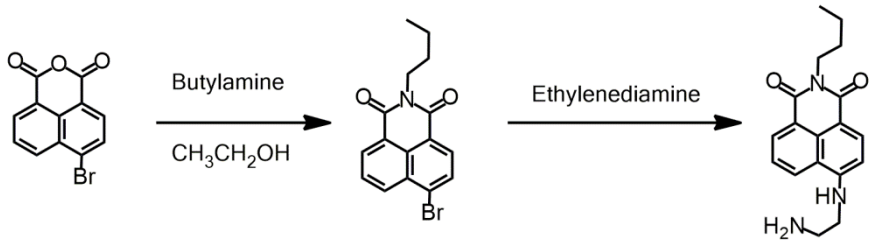


3

4-Bromo-1,8-naphthalimide（1 g, 4 mmol, 1 equiv), CuCl (0.25 equiv), K_2CO_3 (2.5 equiv), phenylalanine (2.5 equiv) were added to 22 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and added with dichloromethane to obtained precipitate. The precipitate was washed repeatively

with dichloromethane and further purified by silica gel chromatography (CH_2Cl_2/MeOH, 100:4 v/ v) to yield compound 3 (0.5 g) as yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 13.71 – 12.24 (m, 1H), 11.31 (s, 1H), 8.79 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 7.2 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.16 (t, *J* = 7.3 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 4.56 (d, *J* = 7.5 Hz, 1H), 3.34 (s, 2H). ESI-MS 359.2 $(M-H)^-$. HRMS (ESI): m/z Calcd for $C_{21}H_{15}N_2O_4$ $(M-H)^-$, 359.1037, found, 359.1034.

Compound 15, 4-(2-aminoethylamino)-N-n-butyl-1,8-naphthalimide

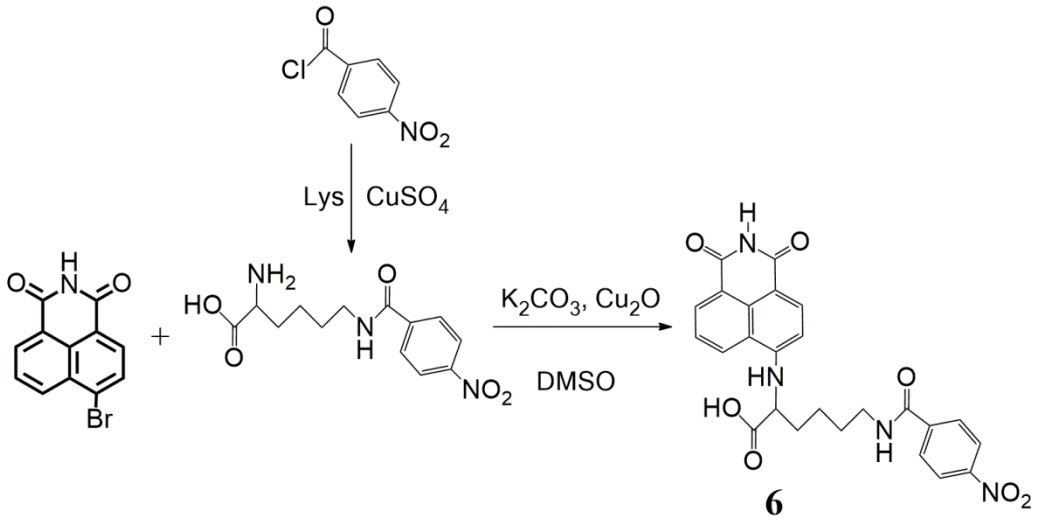


15

4-Bromo-1,8-naphthalic anhydride (4 g, 10 mmol) was suspended in 400 mL of absolute ethanol and heated to 75 °C under stirring. 6 mL of n-Butylamine was added dropwise to the mixture and refluxed with stirring for 1 h. The reaction mixture was cooled to room temperature. The precipitate was filtered and washed with absolute ethanol for three times. The solid was dried under vacuum at 45°C to obtain 4-Bromo -N-n-butyl-1,8-naphthalimide 4.1 g.

4-Bromo -N-n-butyl-1,8-naphthalimide (4.1 g, 12 mmol) was added into 45 mL of ethylenediamine and reacted at 65°C with stirring overnight. The reaction mixture was dried by rotary evaporation, then washed repeatively with water and CH_2CI_2, dried under vacuum at 45°C to obtain 3.1 g compound 15 as yello solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 7.2 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 6.14 (s, 1H), 4.29 – 4.06 (m, 2H), 3.41 (d, *J* = 5.2 Hz, 2H), 3.18 (t, *J* = 5.4 Hz, 2H), 1.70 (dd, *J* = 14.8, 7.6 Hz, 2H), 1.44 (dt, *J* = 15.1, 7.6 Hz, 5H), 0.97 (t, *J* = 7.3 Hz, 3H). ESI-MS 312.2. $(M+H)^+$

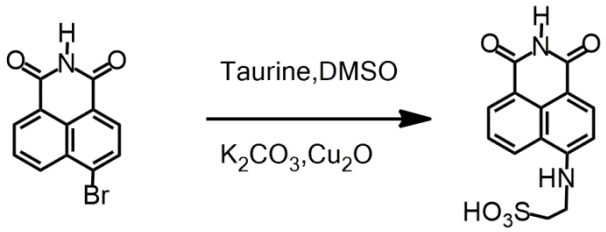
Compound 6, 4-[1-carboxyl-5-(4-benzoylamino)amylamino)-1,8-naphthalimide



L-Lys (3.2g, 22 mmol, 1 equiv) and $CuSO_4$ (11 mmol 0.5 equiv) dissolved in 200 mL of water, then added dropwse with p-nitrobenzoyl chloride (22 mmol, 1 equiv) dissolved in 1,4-dioxane in ice bath, and reacted at room temperature for 3 h. After centrifuge, the residue was washed with water and ethyl ether twice. Then the residue dissolved in HCl solution (pH = 1), and added with Na_2S (0.6 equiv). after filtration, the filtrate washed with ethyl ether, and adjusted pH to 6～7 to obtained precipitate. The precipitate was washed with water and dried under vacuum at 45°C to obtain 5-(4-benzoylamino)-lusine (3 g) as white powder. ^{1}H NMR (400 MHz, DMSO) δ 8.68 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 7.3 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.83 – 7.48 (m, 2H), 6.80 (d, *J* = 8.6 Hz, 1H), 4.87 (t, *J* = 5.5 Hz, 1H), 4.76 (t, *J* = 5.8 Hz, 1H), 4.11 (t, *J* = 6.6 Hz, 2H), 3.69 (q, *J* = 5.8 Hz, 2H), 3.57 (q, *J* = 6.3 Hz, 2H), 3.46 (q, *J* = 5.5 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 171.42, 165.03, 149.40, 140.71, 129.26, 123.92, 52.35, 30.07, 28.78, 22.22.

4-Bromo-1,8-naphthalimide（1 mmol, 1 equiv, 0.275 g), Cu_2O (0.2 equiv), K_2CO_3 (1 equiv) and 5-(4-benzoylamino)-lusine (1 equiv) were added in 5 mL DMSO, Under a nitrogen atmosphere, the mixture was heated to 95 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and added with dichloromethane to obtained precipitate. The precipitate was washed repeatively with dichloromethane and acidic water to obtain compound 6 (0.3 g) a yellow powder. ESI-MS 489.2 $(M-H)^-$.

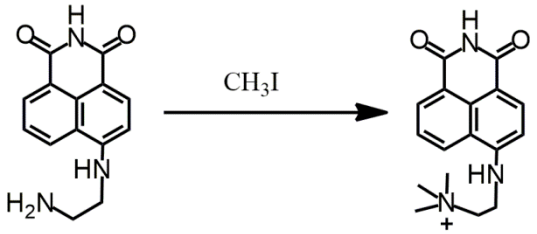
Compound 10, 4-(**2-sulfonylethylamino**)-1,8-naphthalimide



10

4-Bromo-1,8-naphthalimide（27 mg, 0.1 mmol, 1 equiv), Cu_2O (1 equiv), K_2CO_3 (10 equiv), **taurine** (5 equiv) were added to 3 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted overnight with stirring. Then the heterogeneous mixture was cooled to room temperature, and added with dichloromethane to obtained precipitate. The precipitate was washed with dichloromethane and ethyl acetate, then further purified by RP-HPLC to yield compound 10 (25 mg) as yellow powder. ^{1}H NMR (400 MHz, DMSO) δ 11.27 (s, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 8.39 (d, *J* = 7.2 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 3.62 (t, *J* = 6.8 Hz, 2H), 2.89 (t, *J* = 6.8 Hz, 2H). ESI-MS 319.0$(M\text{-}H)^-$.

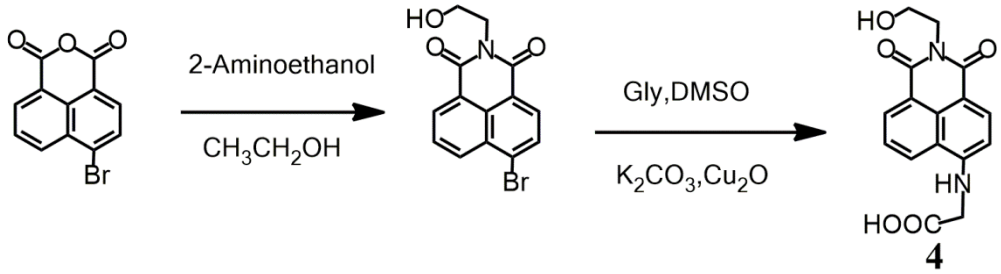
Compound 12, 4-(2- trimethylaminoethylamino)-1,8-naphthalimide



8 **12**

Compound 8 **(**0.1 g), K_2CO_3 (0.1 g) and CH_3I (0.2 g) dissolved in 20 mL methanol and reacted at room temperature overnight. The reaction solution was by RP-HPLC to yield compound 12 (20 mg) as yellow powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 7.9 Hz, 1H), 8.38 (d, *J* = 7.3 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 1H), 3.88 (s, 2H), 3.66 (s, 2H), 3.18 (s, 9H). ESI-MS, 298.1M^+.

Compound 4, 4-carboxymethylamino- N-(2-hydroxyethyl)-1,8-naphthalimide

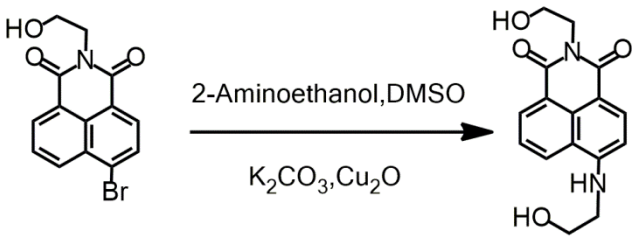


4-Bromo-N-(2-hydroxyethyl)-1,8-naphthalimide.

4-Bromo-1,8-naphthalic anhydride (0.56 g, 2 mmol) was suspended in 50 mL of absolute ethanol and heated to 75 °C under stirring. Ethanolamine (3.6 mL) was added dropwise to the reaction mixture. After 1 hour's refluxing, the mixture was cooled to room temperature. Then the solid was filtered and washed with absolute ethanol, then dried under vacuum at 40°C to obtain 4-Bromo-N-(2-hydroxyethyl)-1,8-naphthalimide (0.5 g) as white powder. ^{1}H NMR (400 MHz, DMSO-*d6*) (δ, ppm) 3.60 (q, J = 6.0Hz 2H), 4.13 (t, J = 6.4Hz 2H), 4.78(t, J = 6.0Hz 1H), 7.98 (t, J = 7.6 Hz, 2H), 8.20 (d, J = 7.6 Hz, 1H), 8.32 (d, J = 7.6 Hz, 1H), 8.55 (t, 2H). ^{13}C NMR (400 MHz, DMSO-*d6*) (δ, ppm) 42.4, 58.2, 122.2, 123.1, 128.5, 129.1, 130.0, 130.1, 131.3, 131.7, 131.9, 132.9, 163.38, 163.43. EI-MS m/z 319 $(M)^+$.

4-Bromo-N-(2-hydroxyethyl)-1, 8-naphthalimide (0.4 mM, 1 equiv), Cu_2O (0.2 equiv), K_2CO_3 (0.5 equiv), glycine (10 equiv) were added to 4 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted with stirring for 10 h. the heterogeneous mixture was cooled to room temperature and added with dichloromethane to obtain precipitate. The precipitate was washed three times with water and dichloromethane and further purified by silica gel chromatography (4:1 ethyl acetate/ MeOH) to yield compound 4 (91 mg) as yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) (δ, ppm) 3.57 (q, J = 6.0Hz 2H), 4.10(t, J = 6.4Hz 2H), 4.16 (d, J = 5.6Hz 2H), 4.76(t, J = 5.6Hz 1H), 6.64 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 7.6 Hz,1H), 8.03 (t, J = 5.6 Hz,1H), 8.25 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 7.2 Hz, 1H), 8.63 (d, J = 8.4 Hz, 1H), 12.40(s, 1H). ^{13}C NMR (400 MHz, DMSO-*d6*) (δ, ppm) 40.8, 41.9, 58.5, 104.8, 109.2, 120.6, 122.5, 125.1, 128.8, 129.8, 131.2, 134.4, 150.9, 163.6, 164.4.171.8. ESI-MS m/z 313.1$(M-H)^-$.

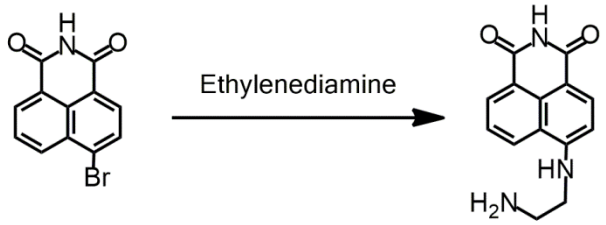
Compound 14, 4-(2-hydroxyethyl)amino- N-(2-hydroxyethyl)-1,8-naphthalimide



14

4-Bromo-N-(2-hydroxyethyl)-1, 8-naphthalimide (0.6 mM, 1 equiv), Cu_2O (0.2 equiv), K_2CO_3 (0.5 equiv), ethanolamine (10 equiv) were added in 6 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted with stirring for 10 h. the heterogeneous mixture was cooled to room temperature and added with dichloromethane to obtain precipitate. The precipitate was washed three times with water and dichloromethane and further purified by silica gel chromatography (4:1 ethyl acetate/ MeOH) to yield compound 14 (140 mg) as yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) (δ, ppm) 3.45 (q, J = 5.6Hz 2H), 3.57 (q, J = 6.4Hz 2H), 3.68 (q, J = 5.6Hz 2H), 4.10(t, J = 6.4Hz 2H), 4.76(t, J = 5.6Hz 1H), 4.86(t, J = 5.6Hz 1H), 6.80 (d, J = 8.4 Hz, 1H), 7.66 (m, 2H), 8.25 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 7.2 Hz, 1H), 8.69 (d, J = 8.4 Hz, 1H). ^{13}C NMR (400 MHz, DMSO-*d6*) (δ, ppm) 41.9, 46.0, 58.5, 59.3, 104.3, 108.2, 120.6, 122.4, 124.7, 129.0, 130.0, 131.1, 134.7, 151.3, 163.6, 164.4. ESI-MS m/z 301.2$(M+H)^+$, 323.1$(M+Na)^+$, 339.1$(M+K)^+$.

Compound 8, 4-(2-aminoethylamino)-1,8-naphthalimide

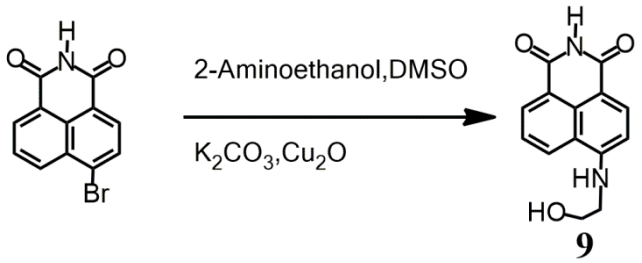


8

4-Bromo-1, 8-naphthalimide (4 mM, 1 equiv) was added to 11 mL of 1,2-Diaminoethane (10 equiv), and reacted at 70°C with stirring for 10 h. The reaction mixture was dried by rotary evaporation, then washed repeatively with CH_2CI_2 and water, and further purified by silica gel chromatography (4:1 ethyl acetate/ MeOH) to

yield compound 8 (0.52 g) as yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) (δ, ppm) 2.86 (t, *J* = 6.4Hz 2H), 3. 38(t, *J* = 6.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 7.66 (m, 2H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 7.2 Hz, 1H), 8.69 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (400 MHz, DMSO-*d6*) (δ, ppm) 46.1, 62.6, 104.2, 108.6, 121.0, 122.8, 124.7, 129.2, 130.5, 131.2, 133.9, 151.3, 164.3, 165.0. EI-MS m/z 255(M)$^{+}$.

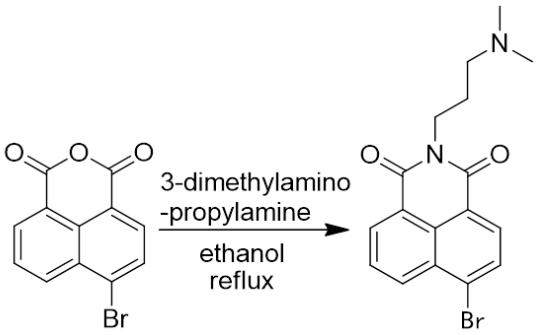
Compound 9, 4-(2-hydroxyethyl)amino-1,8-naphthalimide



9

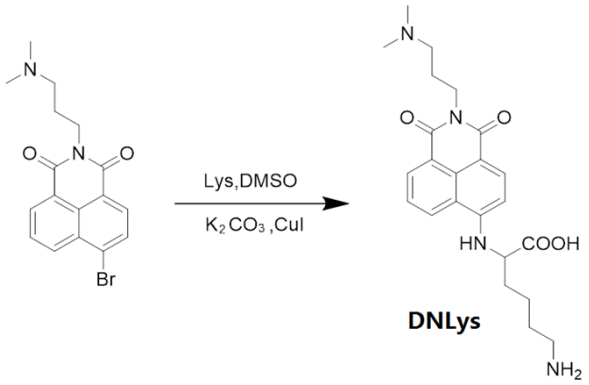
4-Bromo-1, 8-naphthalimide (1.1 g, 4 mM, 1 equiv), Cu_2O (0.2 equiv), K_2CO_3 (0.5 equiv) and ethanolamine (10 equiv) were added in 30 mL of DMSO. Under a nitrogen atmosphere, the mixture was heated to 90 °C and reacted with stirring for 10 h. The heterogeneous mixture was cooled to room temperature and added with dichloromethane to obtain precipitate. The precipitate was washed three times with water and dichloromethane and further purified by silica gel chromatography (4:1 ethyl acetate/ methanol) to yield compound 9 (800 mg) as yellow solid.. ^{1}H NMR (400 MHz, DMSO-*d6*) (δ, ppm) 3.47 (q, *J* = 5.6Hz 2H), 3.70 (q, *J* = 5.2Hz 2H), 4.87(t, *J* = 5.2Hz 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 7.66 (m, 2H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 7.2 Hz, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 11.22(s, 1H). ^{13}C NMR (400 MHz, DMSO-*d6*) (δ, ppm) 46.6, 59.9, 104.7, 109.2, 121.6, 123.5, 124.9, 129.6, 131.0, 131.9, 134.4, 151.9, 164.8, 165.6. EI-MS m/z 256 (M)$^{+}$

N-dimethylaminopropyl-4-bromine-1,8-naphthalimide.



3.5 g (12.6 mmol) 4-bromine-1,8-naphthalic anhydride was dissolved in ethanol (300 mL) and heated to reflux. Then 1.7 mL of 3-dimethylaminopropylamine (13.3 mmol) was added dropwise to the mixture. The resulted mixture was refluxed with stirring for 1 h. The reaction was stopped after the solution became clear. After cooling down to room temperature, water was added to the reaction mixture precipitate the crude product. The precipitate was collected by vacuum filtration, and washed with water and ethanol for three times respectively, and finally dried under vacuum (yield 95%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.59 (d, J = 6.0 Hz, 1H), 8.49 (d, J = 9.0 Hz, 1H), 8.34 (d, J = 6.0 Hz, 1H), 7.97 (d, J = 6.0 Hz, 1H), 7.89 (t, J = 7.5 Hz, 1H), 4.19 (t, J = 7.5 Hz, 2H), 2.23 (s, 6H), 1.94-1.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 163.58, 163.56, 133.20, 132.00, 131.18, 131.10, 130.60, 130.20, 128.97, 128.09, 123.15, 122.29, 57.33, 45.46, 39.20, 26.11; MS (ESI): m/z 361.2 $(M+H)^+$.

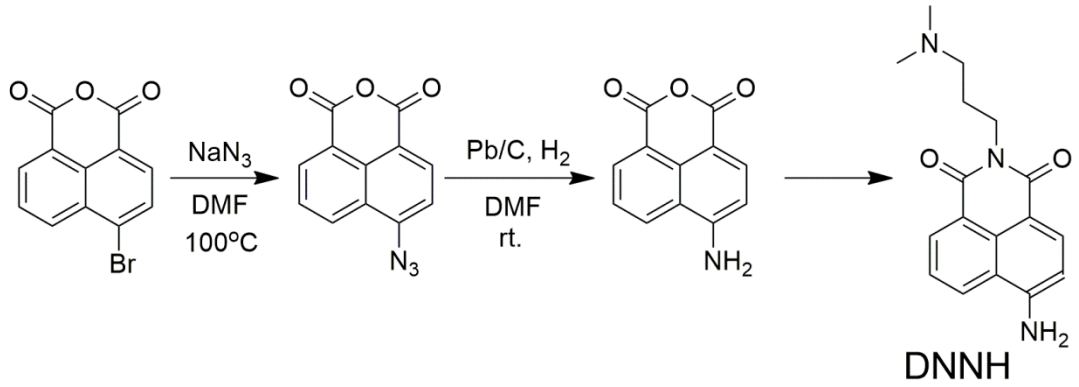
Compound DNLys, 4-(1-carboxyl-5-amino-amylamino)-N-dimethylaminopropyl-1,8-naphthalimide



550 mg (3.02 mmol) lysine was dissolved in 3 mL of NaOH (2 M) solution to obtain solution 1. 500 mg (1.39 mmol) N-dimethylaminopropyl-4-bromine-1,8-

naphthalimide, CuI (150 mg, 1.61 mmol) and K_2CO_3 (200 mg, 1.45 mmol) were added into10 mL of DMSO and heated to 50°C with stirring to obtain solution 2. After half an hour, solution 1 was added dropwise to solution 2. The mixture was heated to 90 °C and reacted for 24 h with stirring. After cooled to room temperature, DMSO was evaporated under reduced pressure. The residue was purified by silica-gel (100-200 mesh) column chromatography (Dichloromethane/methanol/ammonia, 4:1:0, 4:1:0.2, 2:1:0.2, V/V/V) to yield DNLys as yellow solid (230 mg, 31.9% yield). ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm): 8.92 (d, *J* = 6.0 Hz, 1H), 8.26 (d, *J* = 9.0 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.56 (d, *J* = 6.0 Hz, 1H), 6.50 (t, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 9.0 Hz, 1H), 3.92 (s, 2H), 3.75 (s, 1H), 2.86 (s, 2H), 2.50 (t, *J* = 3.0 Hz, 2H), 2.37 (t, *J* = 12 Hz, 6H), 1.9-1.78 (m, 2H), 1.76-1.60 (m, 2H),1.50-1.39 (m, 2H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 177.56, 163.56, 163.25, 151.92, 133.70, 128.68, 128.68, 128.47, 127.53, 123.65, 120.50, 120.02, 107.72, 104.06, 60.30, 57.37, 45.38, 38.14, 36.73, 30.10, 26.55, 25.87, 22.64. MS (ESI): m/z 427.3, $(M+H)^+$; HRMS (ESI): m/z Calcd for $C_{23}H_{31}N_4O_4$ $(M+H)^+$, 427.2340, found,427.2338.

Compound DNNH, N-dimethylaminopropyl-4-amino-1,8-naphthalimide



13 g (46.9 mmol) 4-bromine-1,8-naphthalic anhydride was added into 50 mL of DMF and stirred for 0.5 h. 3.5 g NaN_3 (53.8 mmol) was dissolved in 1 mL of water and then added into the DMF solution. The mix solution was heated to 100 °C and the color of solution changed from white turbid liquid to brown clear solution. The reaction was stopped after 15 min and the reaction was added with water to to obtain yellow precipitate. The precipitate was collected by vacuum filtration, washed with water and ethanol for three times, and finally dried under vacuum to yield 4-azido-1,8-naphthalic anhydride (10.3 g, 92% yield).

4-azido-1,8-naphthalic anhydride (9 g, 37.5 mmol) and 10% Pd/C as catalyst (463 mg) was added to 100 mL of DMF. Then, the mixture was stirred under H_2 pressure at room temperature for 36 h. After filtration, the solution was added water to obtain yellow precipitate. The precipitate was washed with water and ethanol for three times respectively, and finally dried under vacuum to yield 4-amino-1,8-naphthalic anhydride (6.5 g, 81.4% yield)

4-amino-1,8-naphthalic anhydride 2 g (9.39 mmol) was dissolved in ethanol (160 mL) and heated to reflux. Then 1 mL of 3-dimethylaminopropylamine (7.8 mmol) was added to the mixture dropewise. The resulted mixture was heated to reflux with stirring for 1 h. The reaction was stopped after the solution became clear. After cooling down to room temperature, the reaction mixture was added with water to obtain precipitate. The precipitate was collected by vacuum filtration, and then washed with water and ethanol for three times respectively, and finally dried under vacuum to yield DNNH (2.6 g, yield 93.2%). ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm): 8.60 (d, *J* = 9.0 Hz, 1H), 8.41 (d, *J* = 6.0 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.42 (s, 2H), 6.50 (t, *J* = 7.5 Hz, 1H), 7.42 (s, 1H), 6.83 (d, *J* = 6.0 Hz, 1H), 4.01 (t, *J* = 7.5 Hz, 2H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.12 (s, 6H), 1.75-1.66 (m, 2H); ^{13}C NMR (DMSO, 75 MHz) δ (ppm): 163.76, 162.89, 152.66, 133.90, 130.90, 129.66, 129.24, 123.94, 121.80, 119.36, 108.13, 107.59, 56.83, 45.08, 25.82. MS (ESI): m/z 298.1, $(M+H)^+$; HRMS (ESI): m/z Calcd for $C_{17}H_{20}N_3O_2$ $(M+H)^+$, 298.1550, found, 298.1550.

Photoclevage experiments

Photoclevage experiments were performed under daylight, UV light (365 nm) or blue light (465-470 nm) as indicated in text. Samples were irradiated in glass vials. For blue light irradiation, samples were irradiated by an LED array of twelve blue 5630 SMD LEDs. Output power, 3W; wavelength, 465-470 nm. The illuminance of sample points was 1700 lm/m^2 measured by illuminometer YF2006 professional pocket.

Thin layer chromatography (TLC) analysis of photoclevage of 4-amino-1,8-naphthalimides

The photoclevage of compounds 1-15 of was detected by TLC. After photoclevage, the reaction solutions were applied on the precoated silica gel 60 GF254TLC plate. Mobile phase: Ethyl acetate/methanol/ammonia, v/v/v, 3/1/0.2 (the ratio was adjusted based on the polarity of tese compounds). Saturation time : 20 min. Detection : under UV light at 366 nm.

HPLC analysis and preparation of photocleaved products of 4-amino-1,8-naphthalimides

For analysis: After photoclevage, the reaction solution was applied for reversed phase-HPLC assay. Condition：C_{18} column: Agela, 5 μm, 100Å, 4.6×250 mm; mobile phase A: Water with 0.1% trifluoroacetic acid (TFA); B: methanol or Acetonitrile with 0.1% TFA; gradient elution; flow rate: 1 mL/min, Detected on diode-array detector from 220 - 500 nm.

For preparation: After photocleavage, the reaction solution was concentrated by rotary evaporation and applied for preparation by RP-HPLC. Condition: C_{18} column (5μ 250×10mm I.D), mobile phase A: Water with 0.1% TFA; B: methanol with 0.1% TFA 220nm-500nm; gradient elution; flow rate: 3 mL/min, Detected on diode-array detector from 220-500 nm. The eluate of the peak of photocleaved products was collected for identification.

Gel Electrophoresis

4 μLof DNA samples were loaded onto 1% agarose gel. The running buffer was 1X trisborate-ethylenediaminetetraacetic acid buffer (TBE, pH 8.05). The gel was balanced for 10 min at 110 V, and then the electrophoresis was performed for about 40 min at 110 V. Finally, The gel was stained with ethidium bromide, exposed to UV light and photographed.