Unprecedented perspectives in the application of CinNapht fluorophores provided by a "Late-stage" functionalization strategy.

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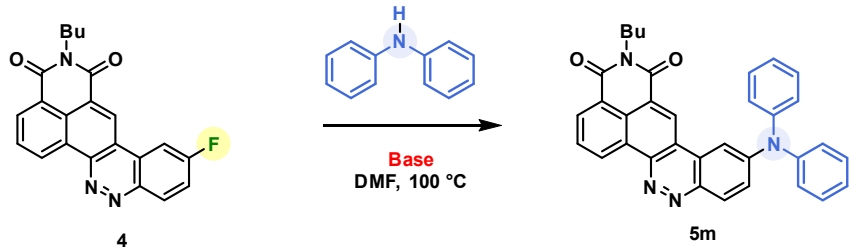
Supporting Information

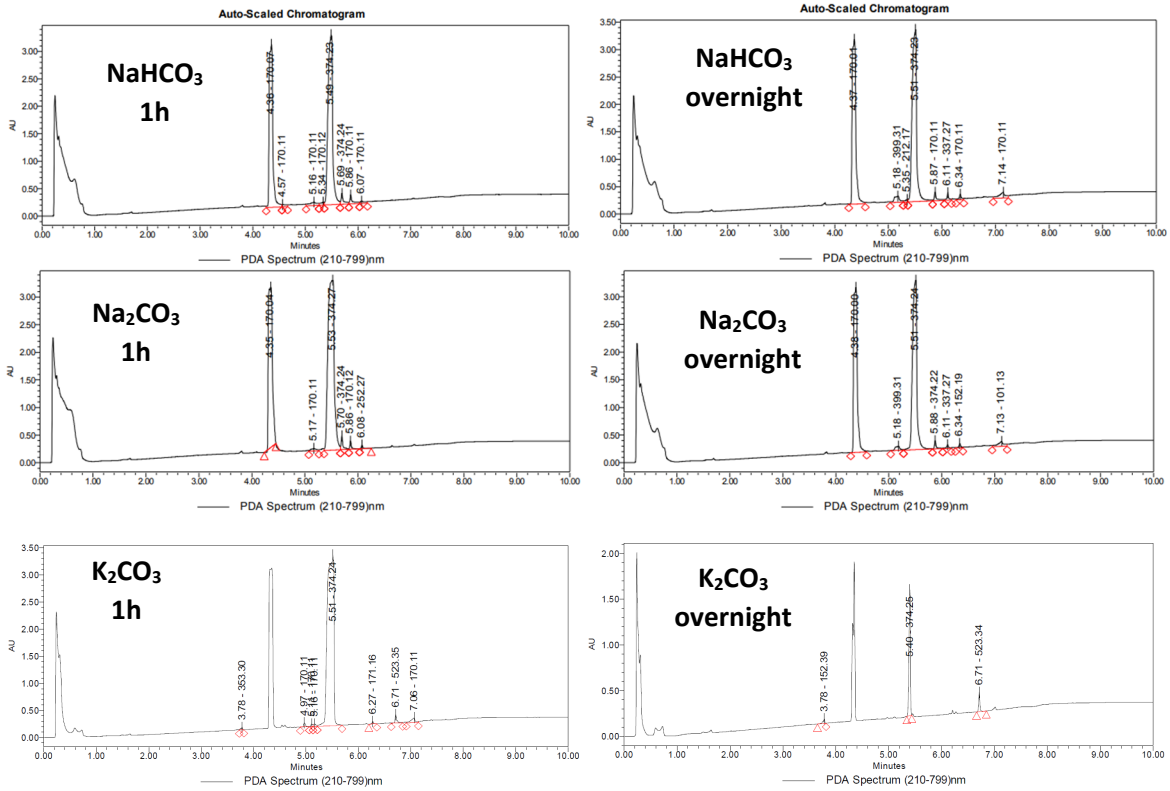
I. Additional figures

Fig S1: Study of caesium contribution in reactivity of aniline



Entry	Base	Conversion	
		1 h	overnight
1	$NaHCO_3$	< 1 %	< 1 %
2	Na_2CO_3	< 1 %	< 1 %
	Na_2CO_3	< 1 %	10 %
3	Cs_2CO_3	37.9 %	**71.6 %**
4	$NaHCO_3$ + CsF	< 1 %	32.4 %
5	Na_2CO_3 + CsF	12.3 %	**78.7 %**
6	Na_2CO_3 + 15-Crown-5	< 1 %	< 1 %

Chromatograms:



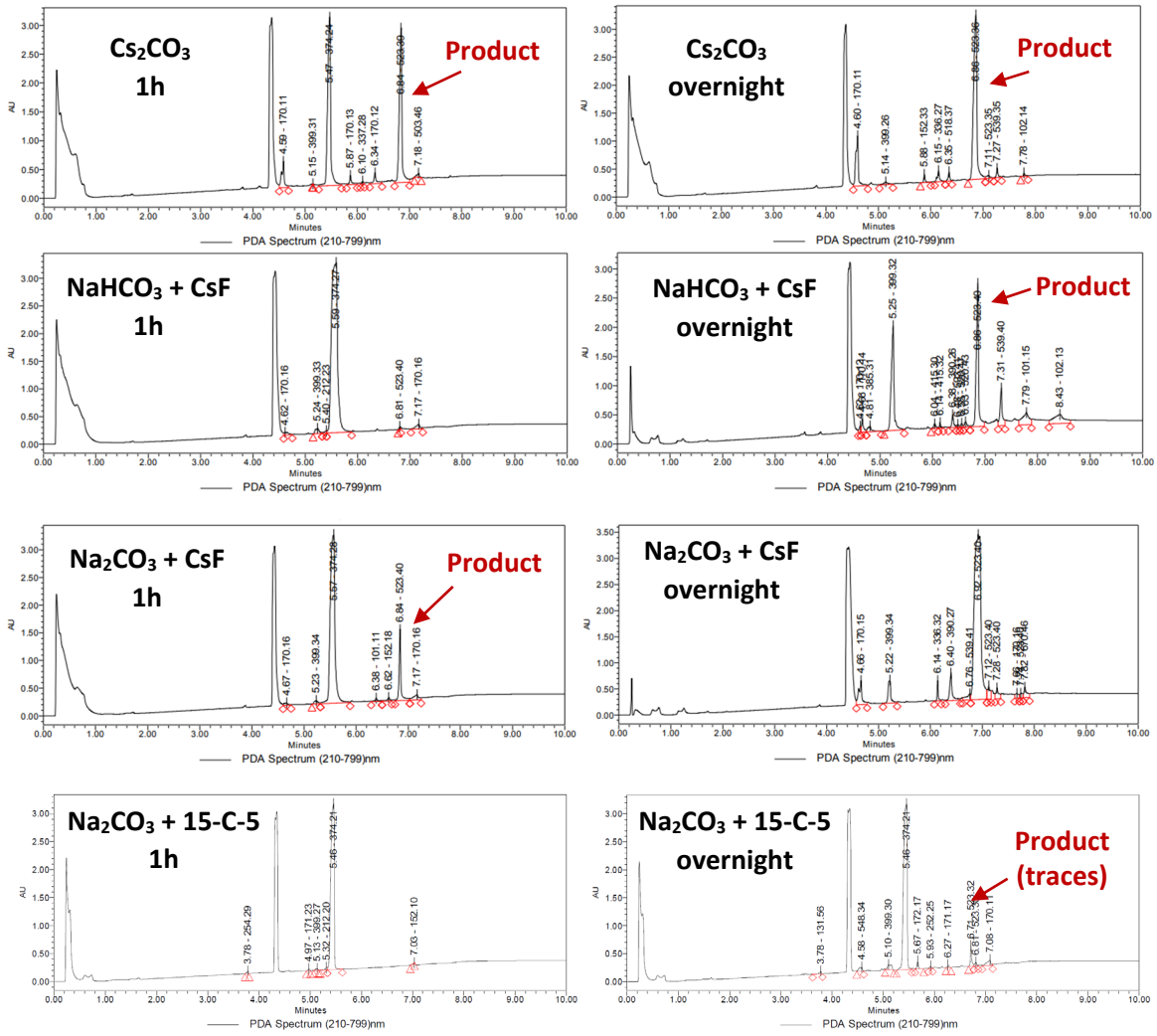


Fig S2: HPLC MaxPlot chromatogram of crude mixture obtained after one night of reaction between CinNapht 4 and *para*-nitroaniline

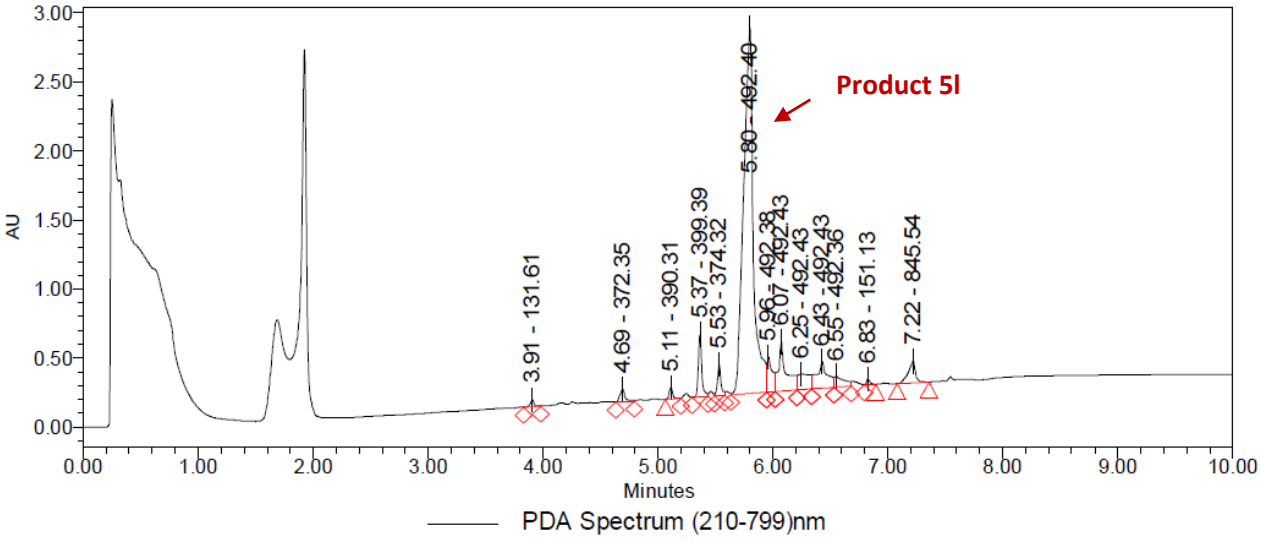


Fig S3: Highlighting the low stability of aryl azide 5n

Top: HPLC MaxPlot chromatogram of crude mixture obtained after incubating CinNapht **5n** at 0.25mM at room temperature in PBS buffer (left) and CH_3CN (right). Bottom: Emission spectrum of the mixture after incubation in PBS buffer with excitation at 440 nm and live A549 cell imaging of CinNaphts **5n** using a 63x oil immersion objective, nucleus was stained with Hoechst 33342, 1µg/mL for 20 min at 37 °C (λ_{Exc}: 405 nm, λ_{Em}: 425 to 500 nm), CinNapht **5n** incubated at 1 µM for 3 h at 37 °C (λ_{Exc}: 470 nm, λ_{Em}: 500 to 700 nm). Scale bar 20 µM.

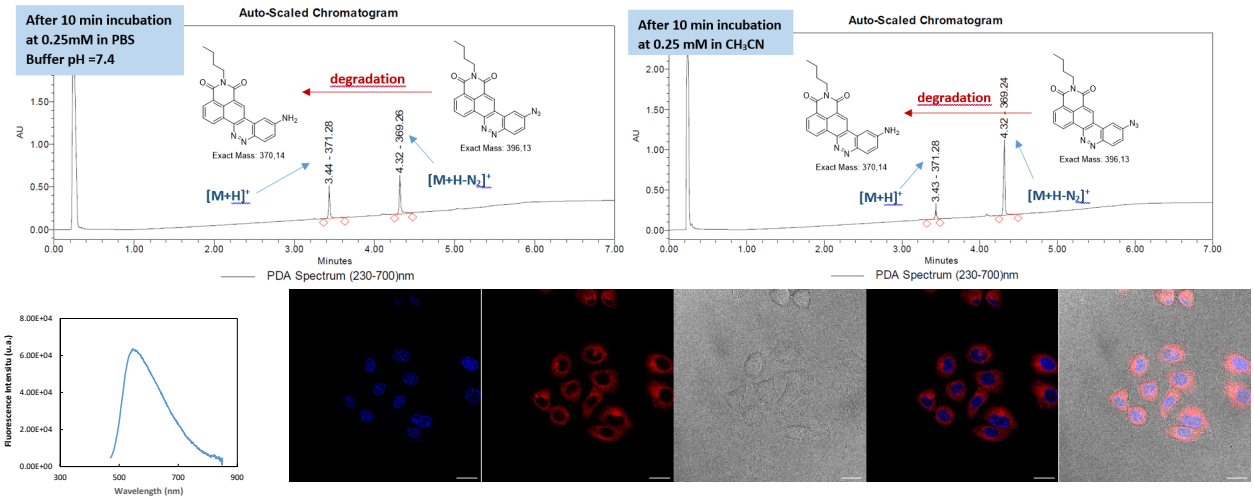
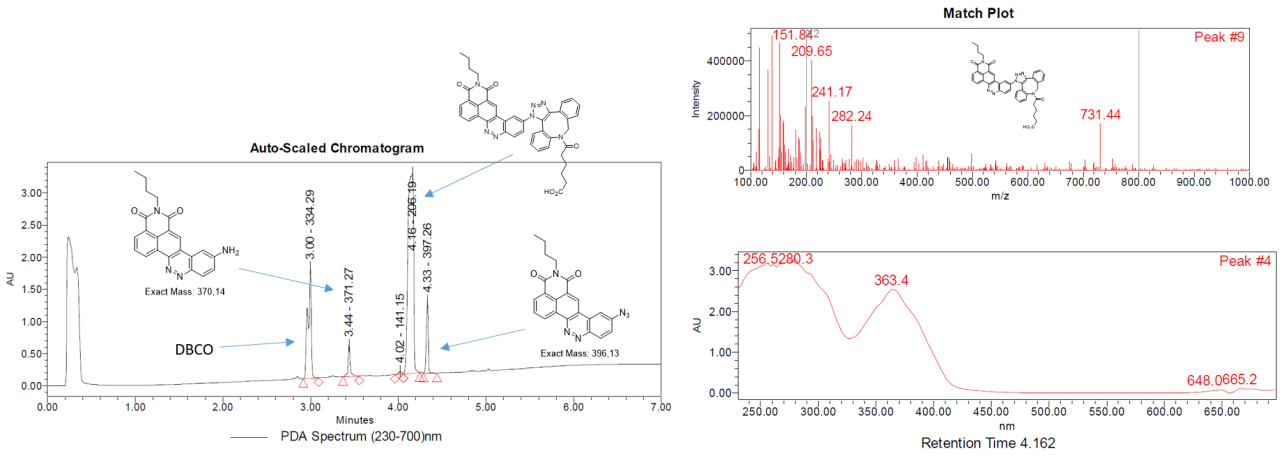
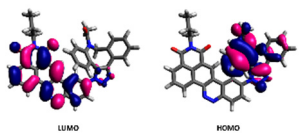


Fig S4: non fluorogenic SPAAC reaction between 5n and DBCO-acid

Top: HPLC MaxPlot chromatogram of crude mixture after 4h of reaction between **5n** and DBCO acid (1.1 equiv.) at 5mM in DMSO (left) and extraction of UV spectrum and MS spectrum of SPAAC click product (right). Bottom: highlighting of separation between HOMO and LUMO with very low oscillator strength that explains the absence of fluorescence of the SPAAC click product.

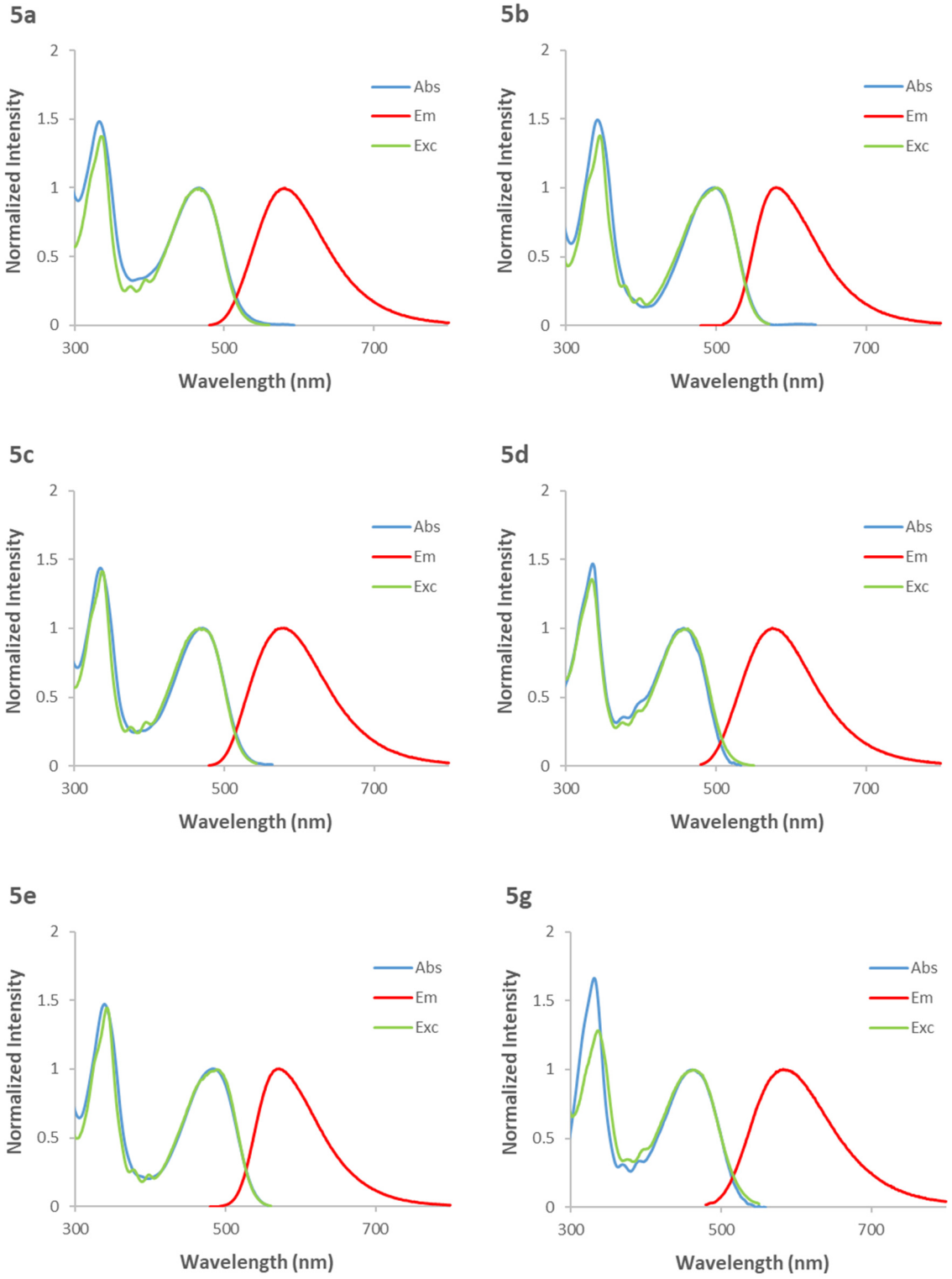




N°	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Symmetry	Major contribs	Minor contribs
1	22013.2900307	454.27103291	0.003	Singlet-A	H-3->LUMO (47%), HOMO->LUMO (45%)	H-3->L+1 (3%)
2	22290.7447543	448.6166842	0.0068	Singlet-A	H-3->LUMO (39%), HOMO->LUMO (54%)	H-3->L+1 (2%), H-1->LUMO (2%)

Fig S5: Absorbance, Emission and excitation spectra of CinNaphts 5a-5q

Spectra were recorded at 25°C in $CHCl_3$ (and DMSO for compound 5o). Emission spectrum was recorded using an excitation at 470 nm (5a, 5c, 5d, 5g and 5p), 480 nm (5e, 5i) or 500 nm (5b, 5k, 5m and 5o). Excitation spectrum was recorded using an emission at 570 nm (5a, 5d, 5e, 5g and 5p), 580nm (5b and 5c), 600 nm (5i and 5k) or 630 nm (5m and 5o).



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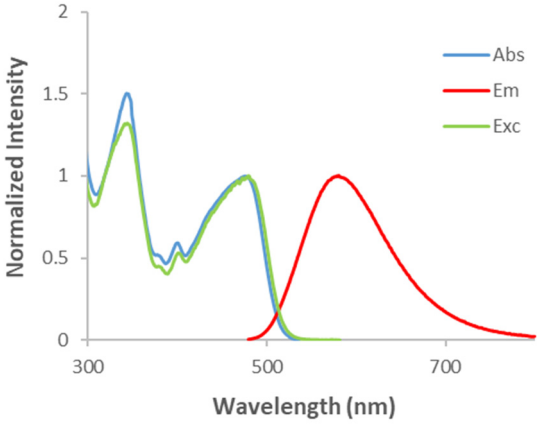
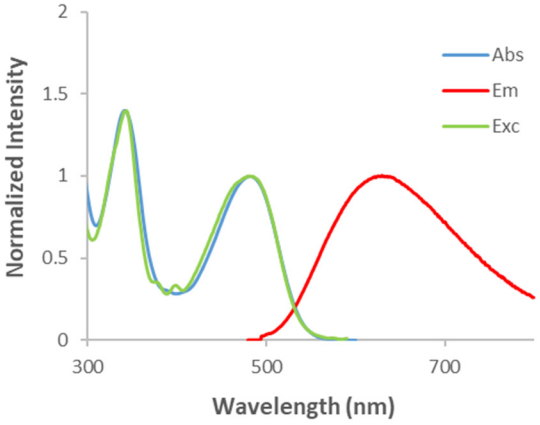
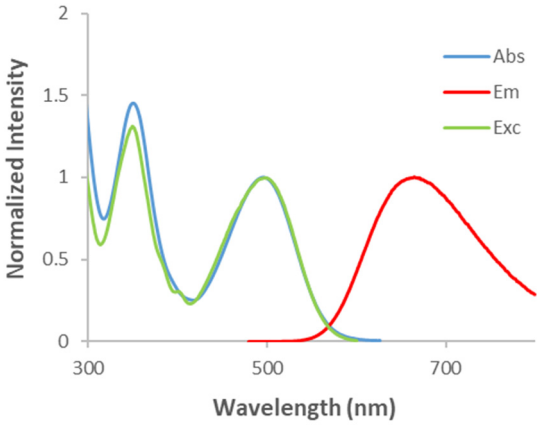


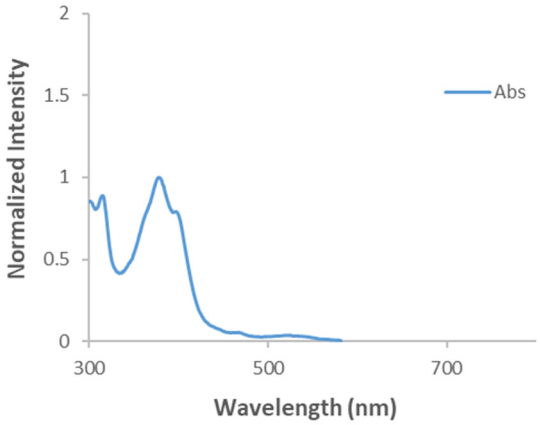
5k



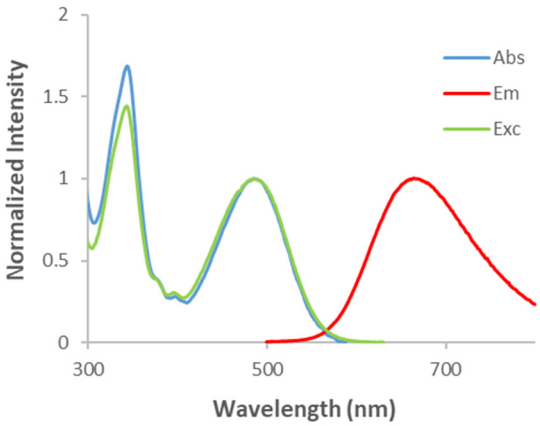
5m



5n



5o



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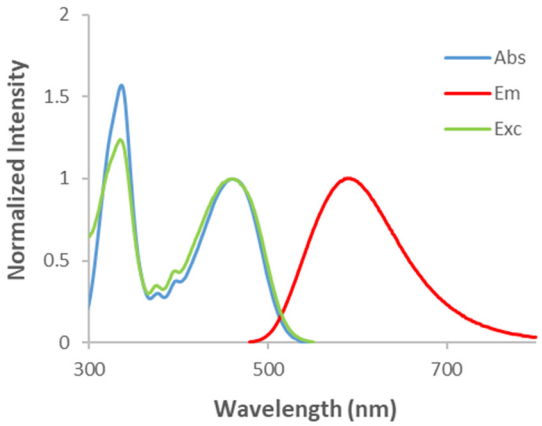

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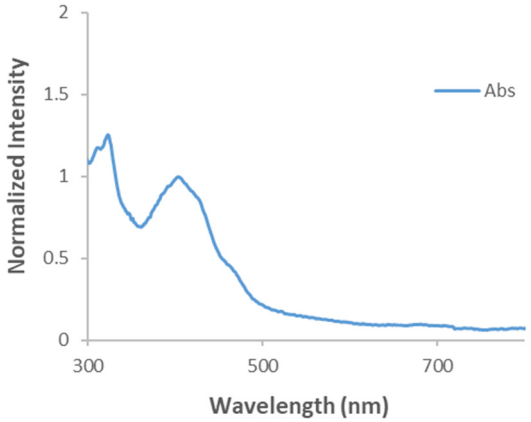
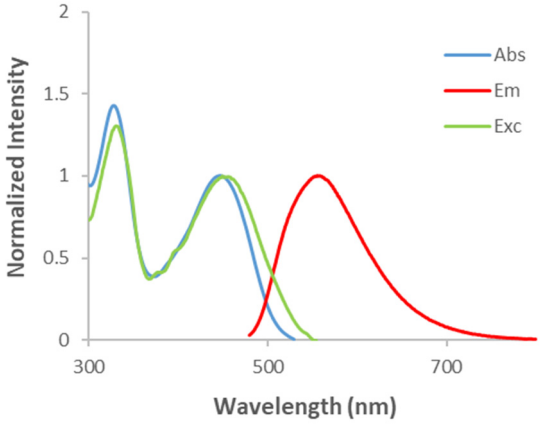


Fig S6: Absorbance, Emission and excitation spectra of CinNaphts 6a-6m and 7a and 7b in Organic Solvents

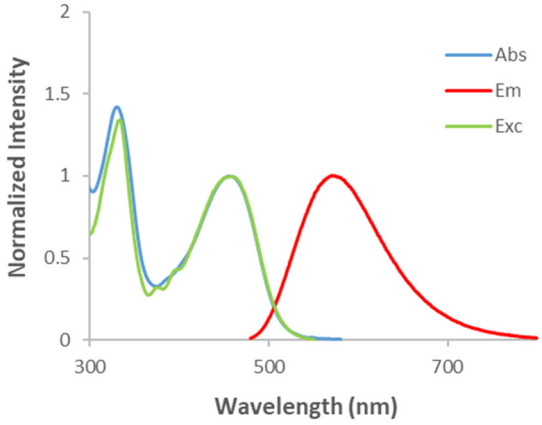
Spectra were recorded at 25°C. Emission spectrum was recorded using an excitation at 450 nm (6a and 6b), 460 nm (6c, 6g, 6j, 6k and 6l), 470 nm (6d, 6e and 6f), 490 nm (6i) and 520 nm (6h). Excitation spectrum was recorded using an emission at 550 nm (6a), 560 nm (6c and 6g), 580 nm (6e and 6f), 600 nm (6b, 6d, 6i, 6j, 6k and 6l) and 620 nm (6h).

Spectra in $CHCl_3$

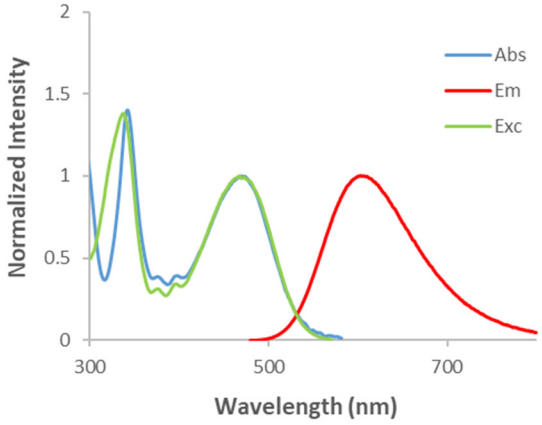
6a



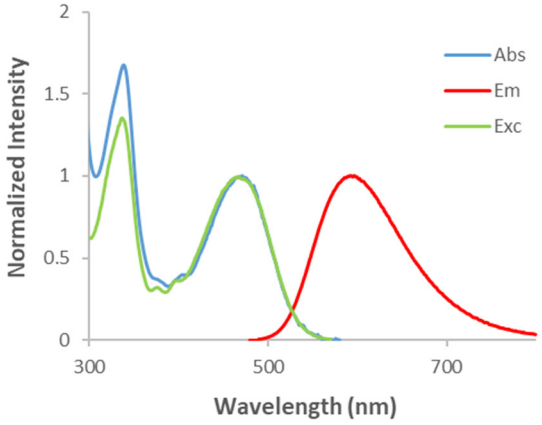
6c



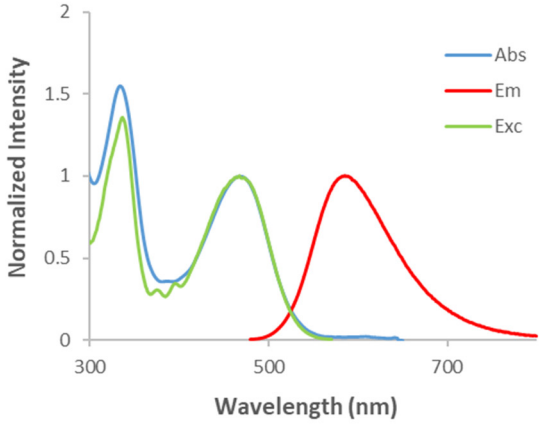
6d



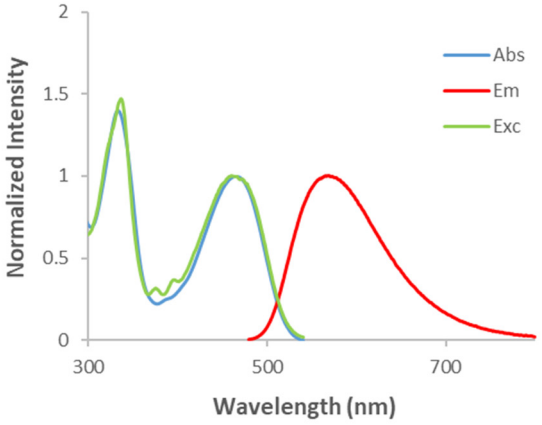
6e

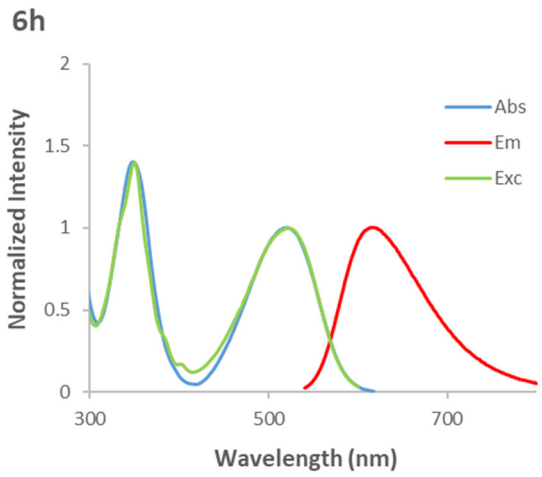


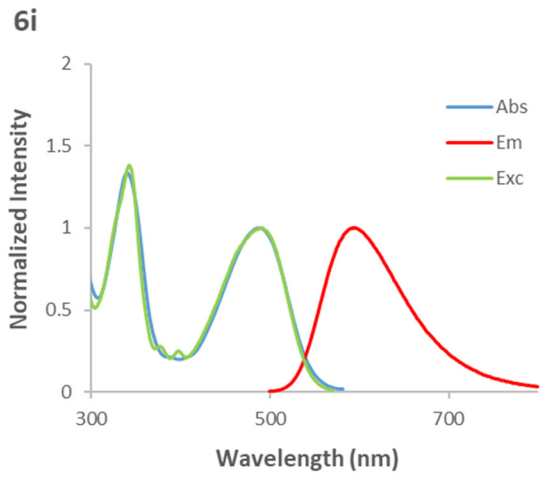
6f

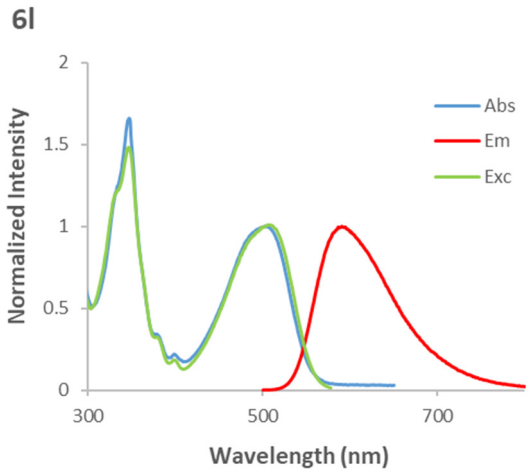


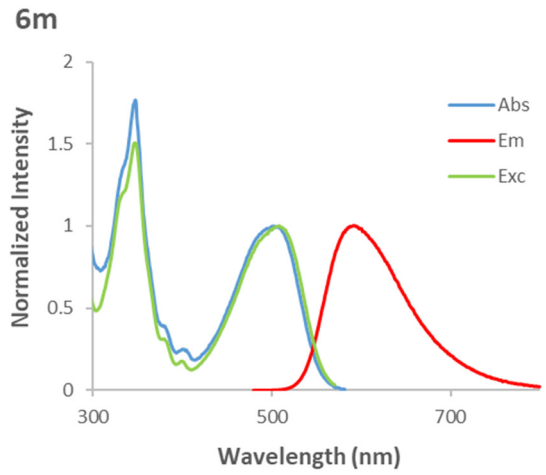
6g

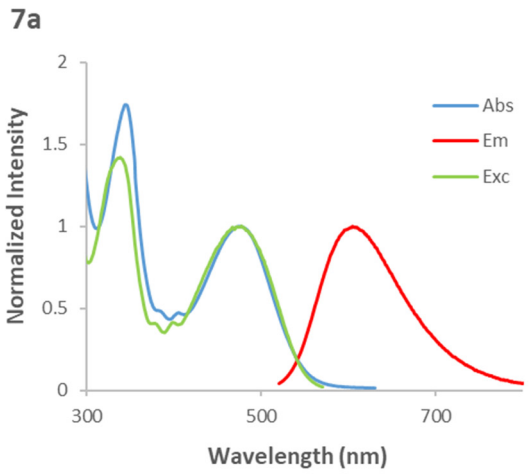


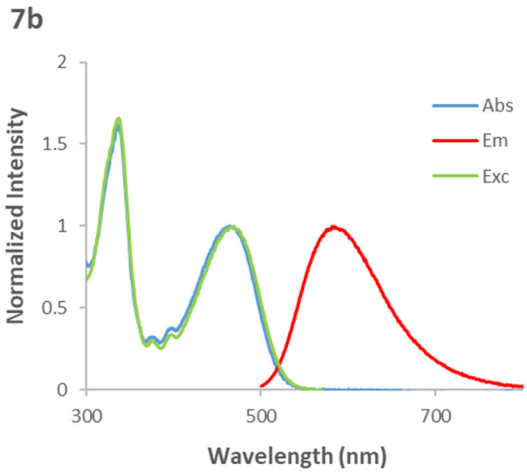






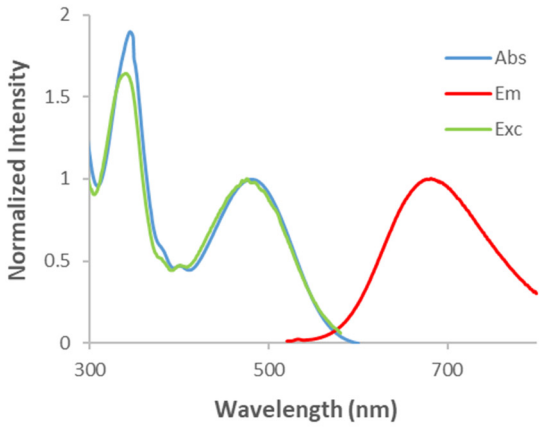




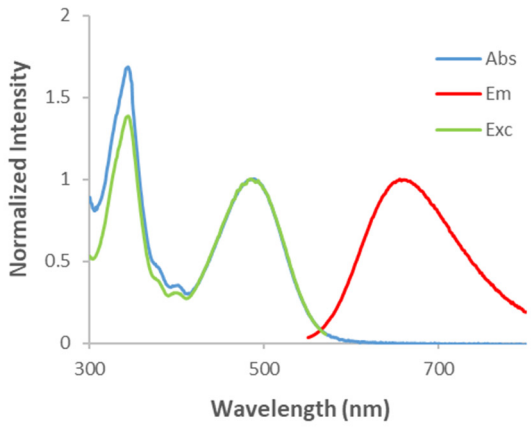


Spectra in DMSO

6b



6e



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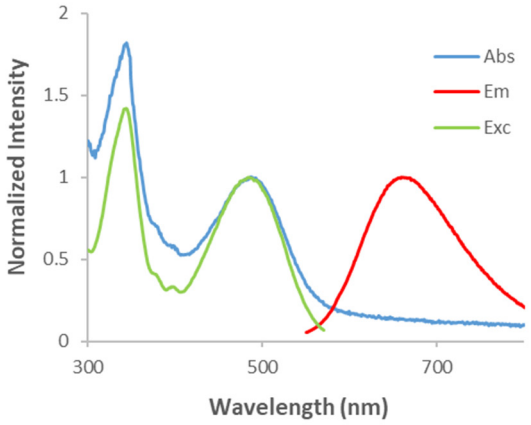
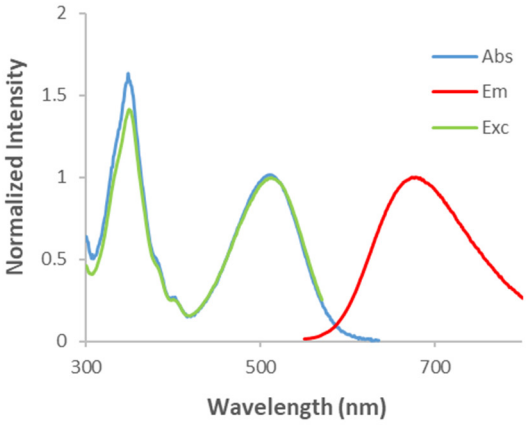
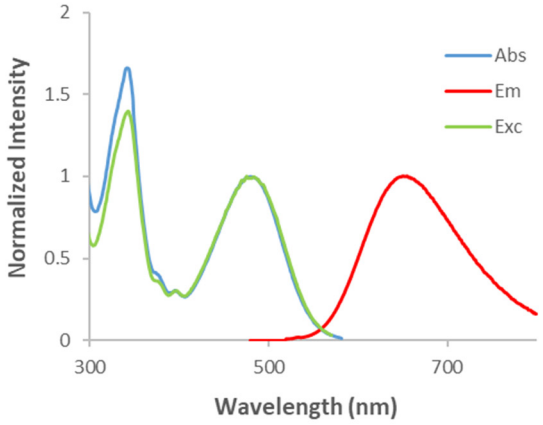


6h



6j



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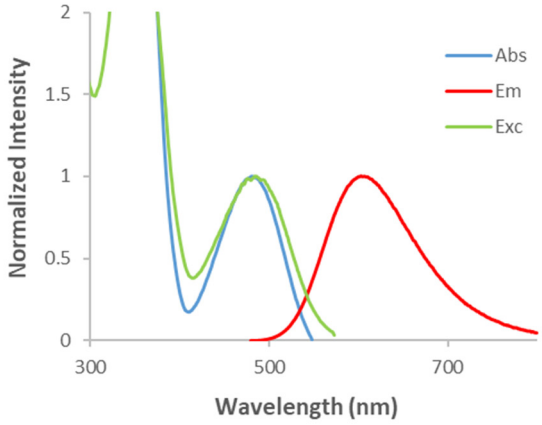


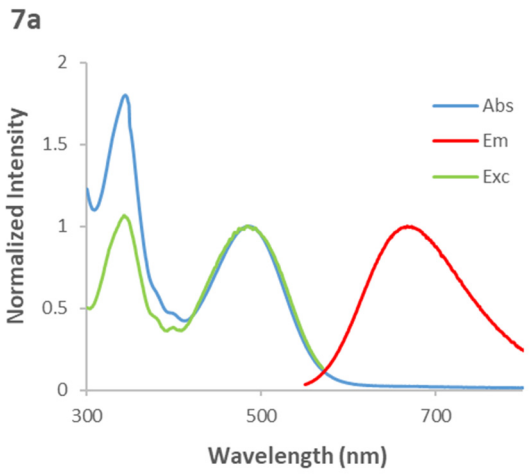
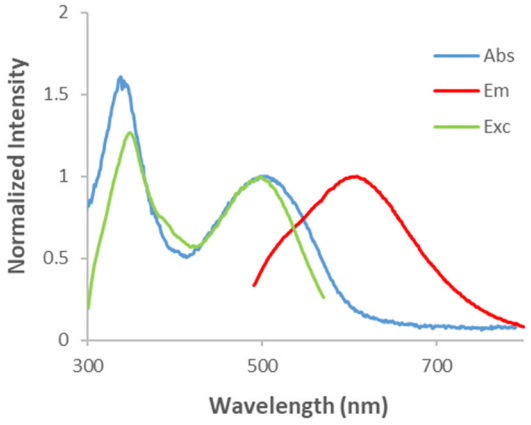


Fig S7: Absorbance, Emission and excitation spectra of CinNaphts 6a-6m in PBS + 5% BSA

Spectras were recorded at 25°C in PBS + 5% BSA. Emission spectrum was recorded using an excitation at 470 nm. Excitation spectrum was recorded using an emission at 570 nm.

6b



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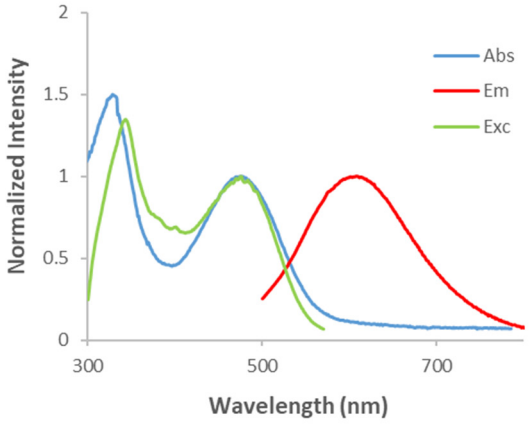

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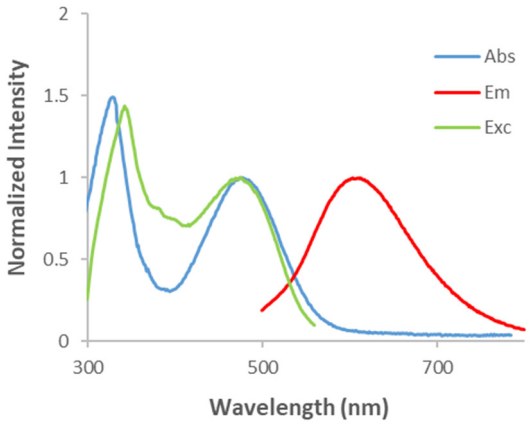

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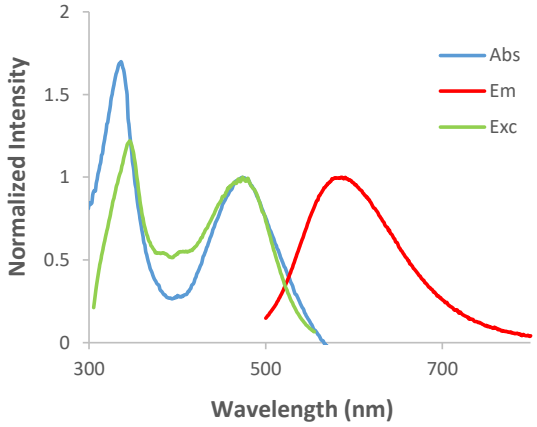

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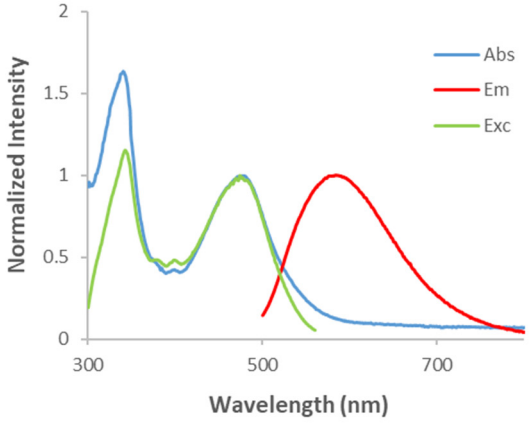

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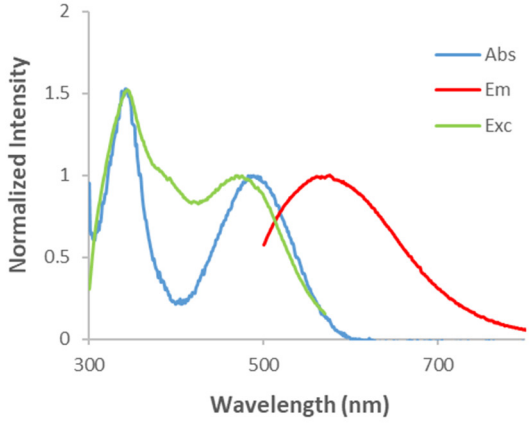


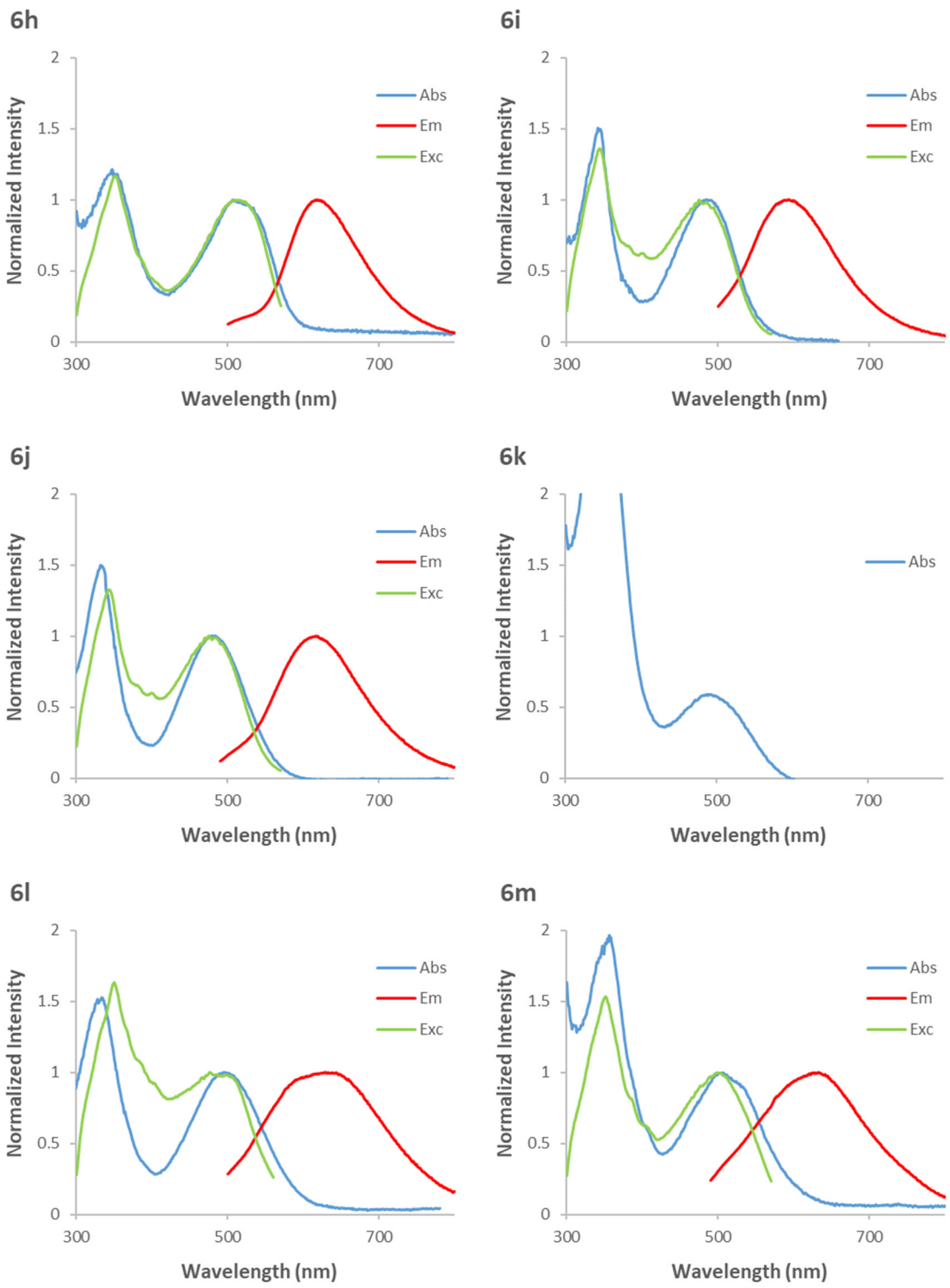
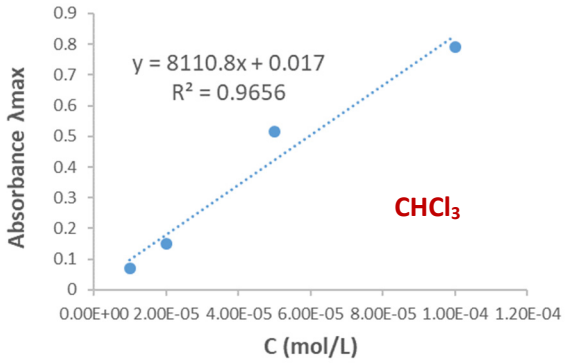


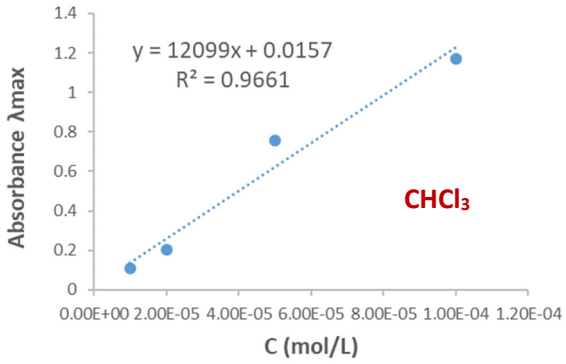
Fig S8: Epsilon Calculation in organic solvents

Absorbance spectra were recorded in at 25°C in $CHCl_3$ (and DMSO for compound 6b, 6j and 6k).

5a



5b



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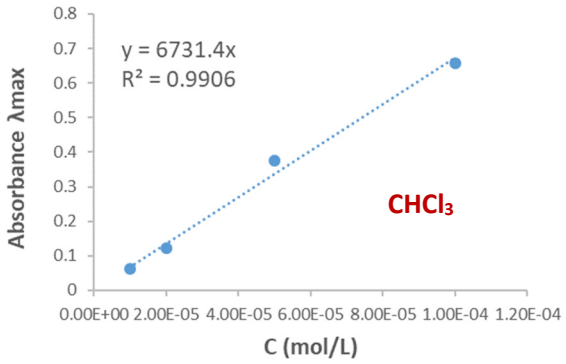

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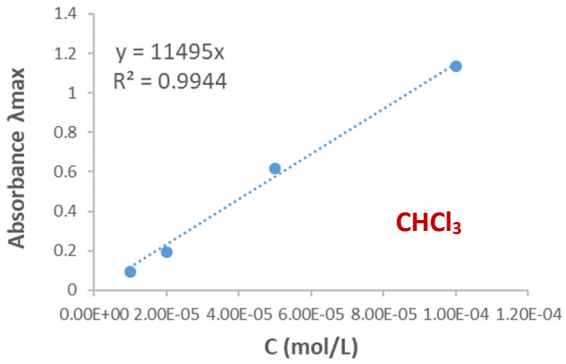

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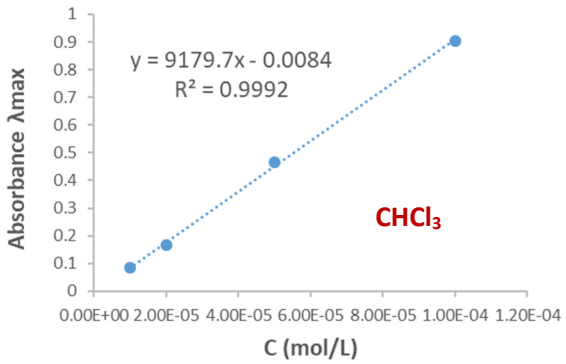

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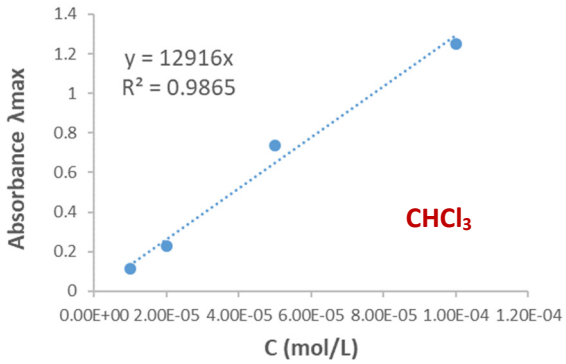

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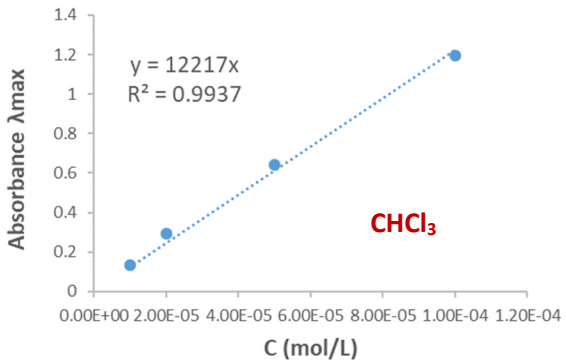

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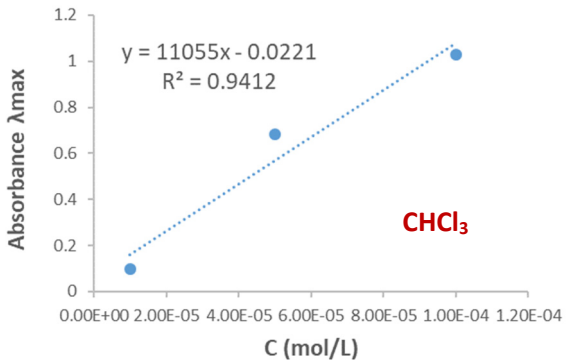

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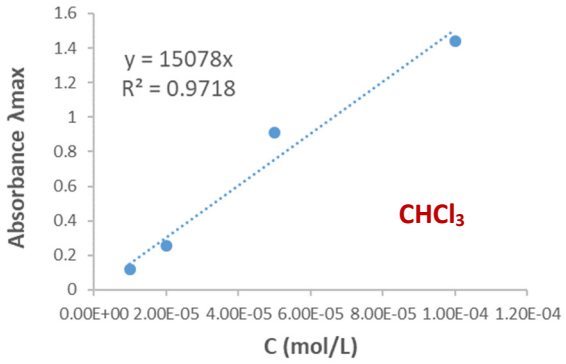
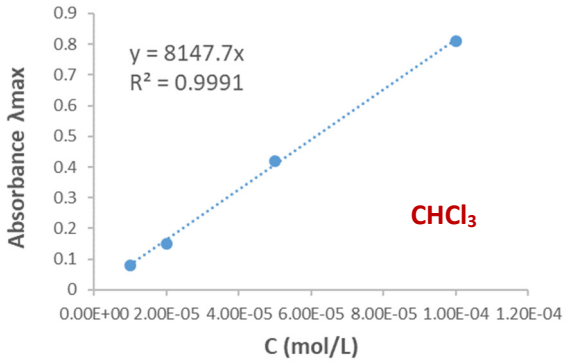
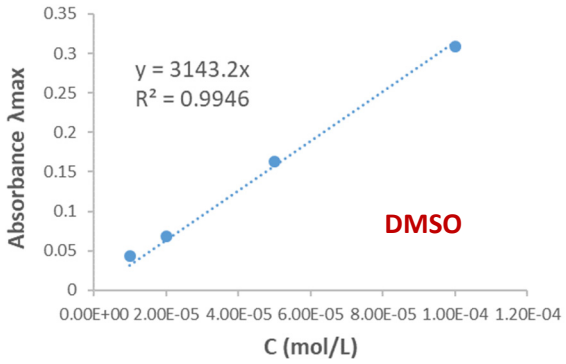


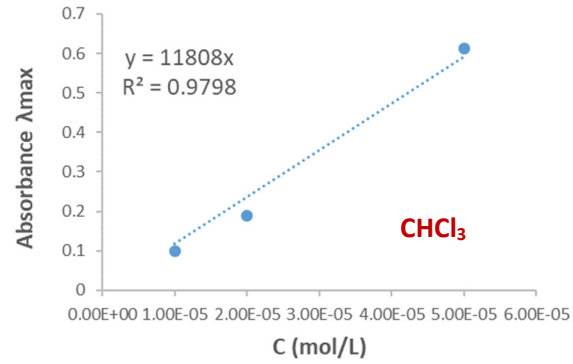
5n



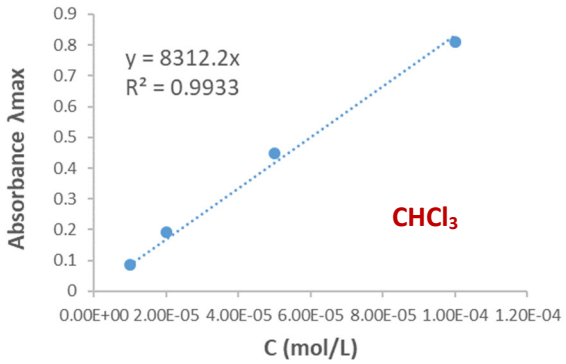
5o



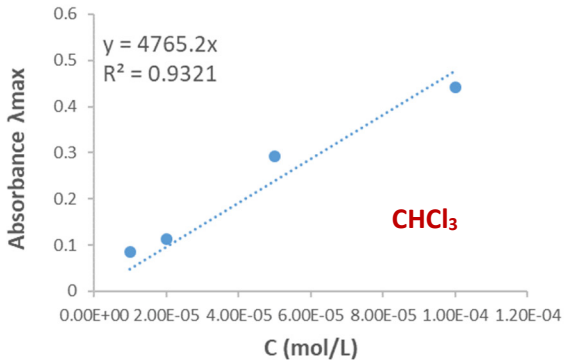
5p



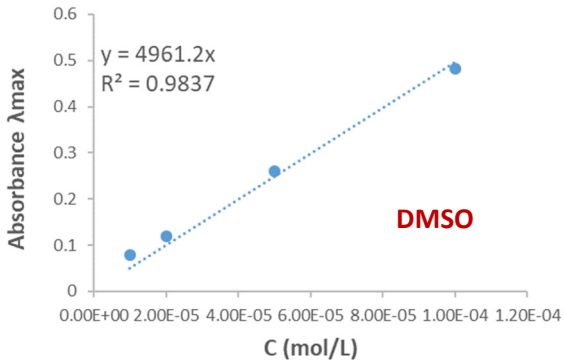
5r



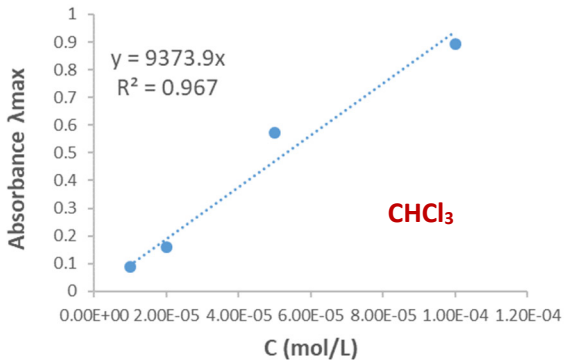
6a



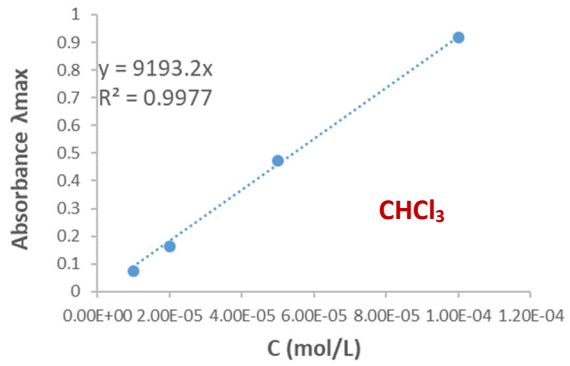
6b



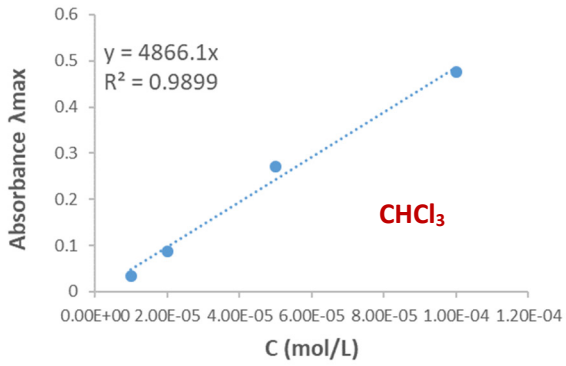
6c



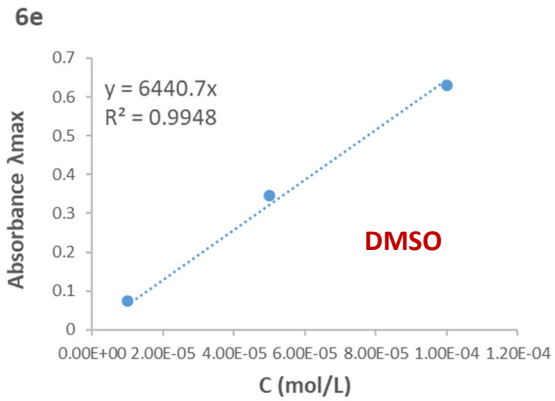
6d



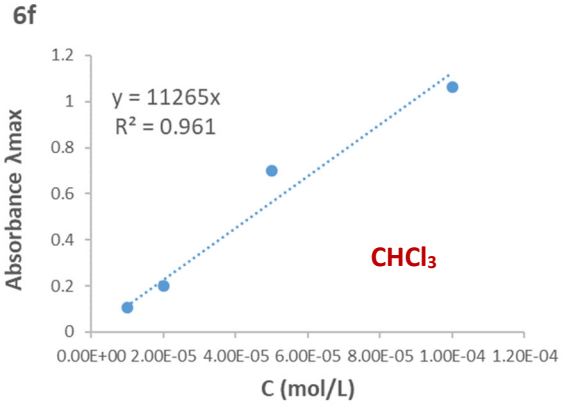
6e



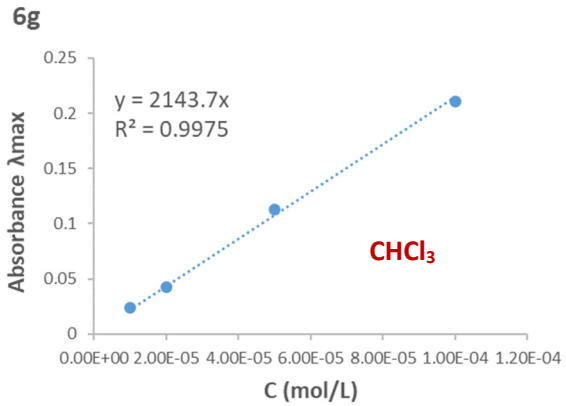
6e



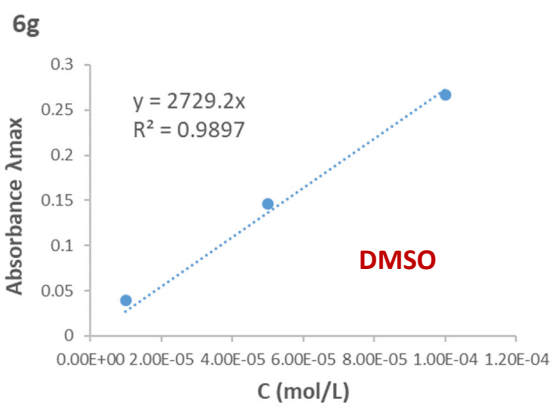
6f



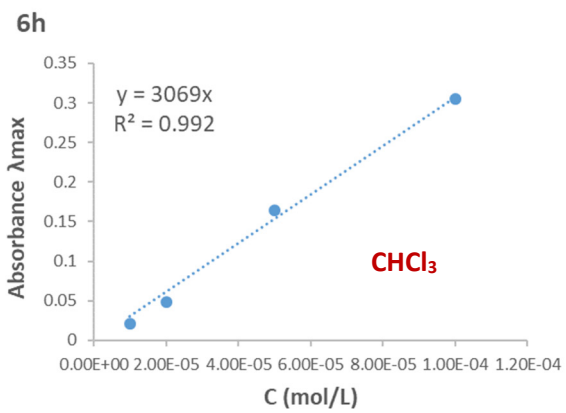
6g



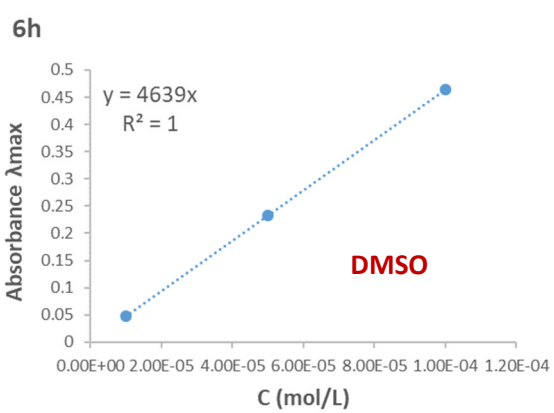
6g



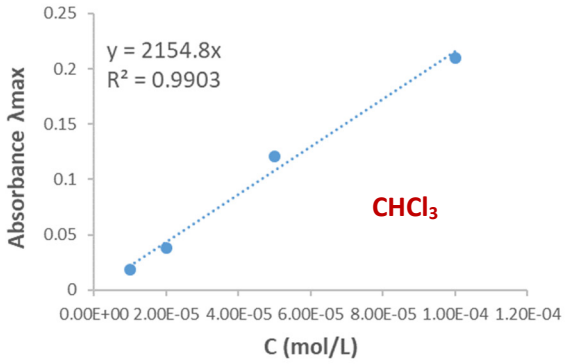
6h



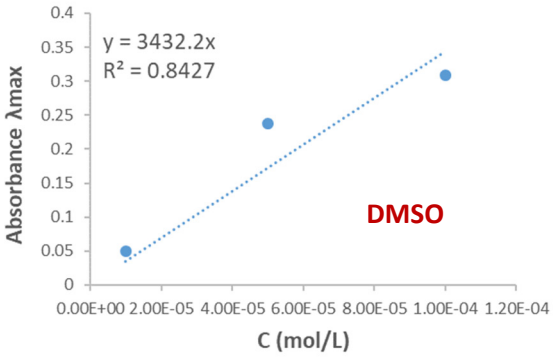
6h



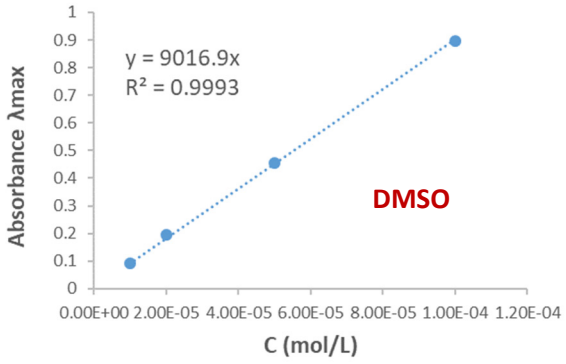
6i


y = 2154.8x
R² = 0.9903
CHCl3
Absorbance λmax
C (mol/L)
0.25
0.2
0.15
0.1
0.05
0
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

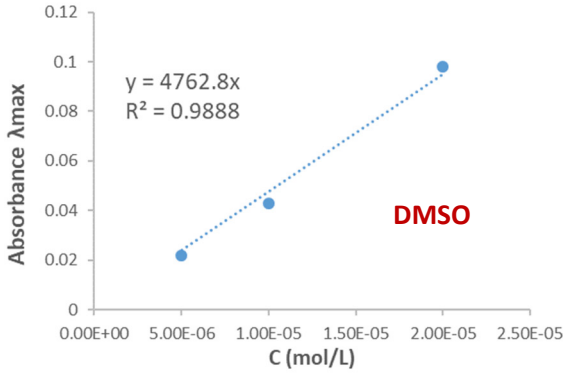
6i


y = 3432.2x
R² = 0.8427
DMSO
Absorbance λmax
C (mol/L)
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

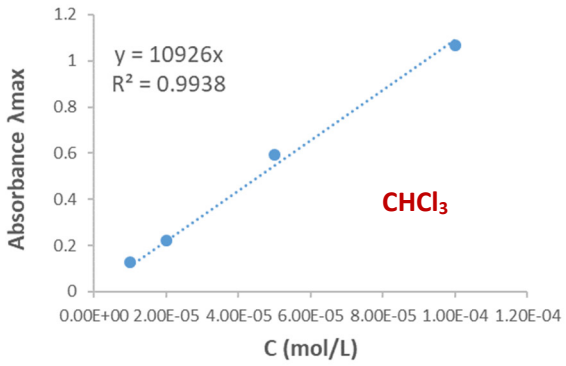
6j


y = 9016.9x
R² = 0.9993
DMSO
Absorbance λmax
C (mol/L)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

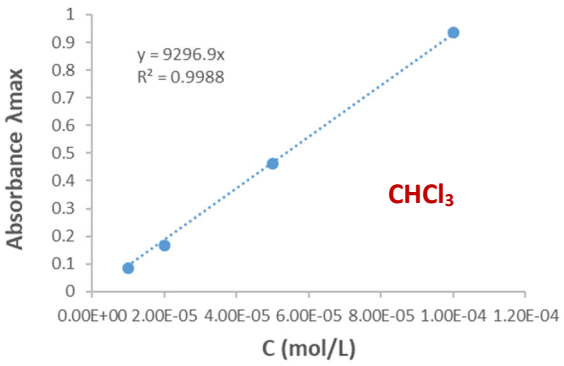
6k


y = 4762.8x
R² = 0.9888
DMSO
Absorbance λmax
C (mol/L)
0.12
0.1
0.08
0.06
0.04
0.02
0
0.00E+00 5.00E-06 1.00E-05 1.50E-05 2.00E-05 2.50E-05

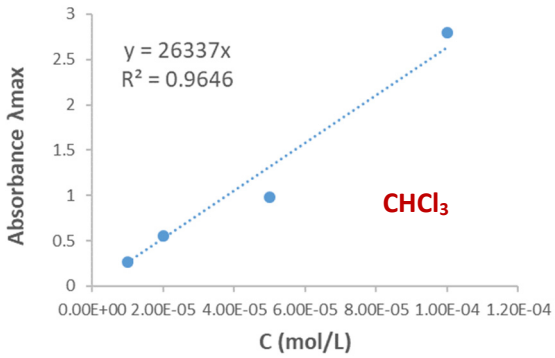
6l


y = 10926x
R² = 0.9938
CHCl3
Absorbance λmax
C (mol/L)
0 0.2 0.4 0.6 0.8 1 1.2
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

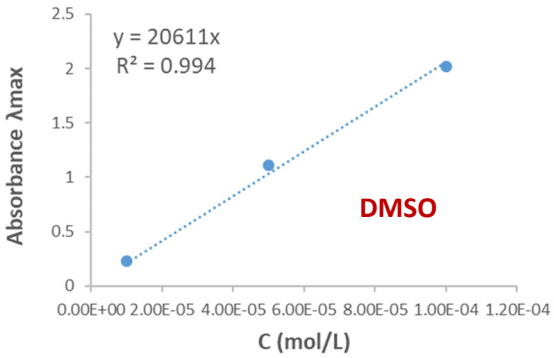
6m


y = 9296.9x
R² = 0.9988
CHCl3
Absorbance λmax
C (mol/L)
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

7a


y = 26337x
R² = 0.9646
CHCl3
Absorbance λmax
C (mol/L)
0 0.5 1 1.5 2 2.5 3
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

7a


y = 20611x
R² = 0.994
DMSO
Absorbance λmax
C (mol/L)
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0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

7b

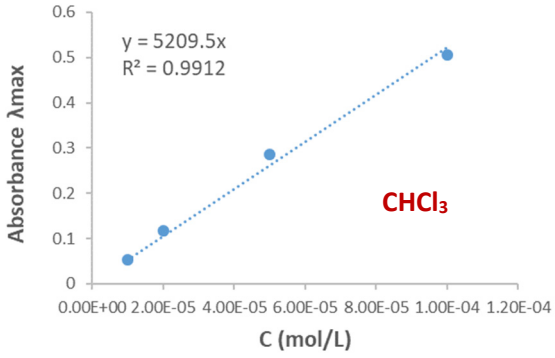
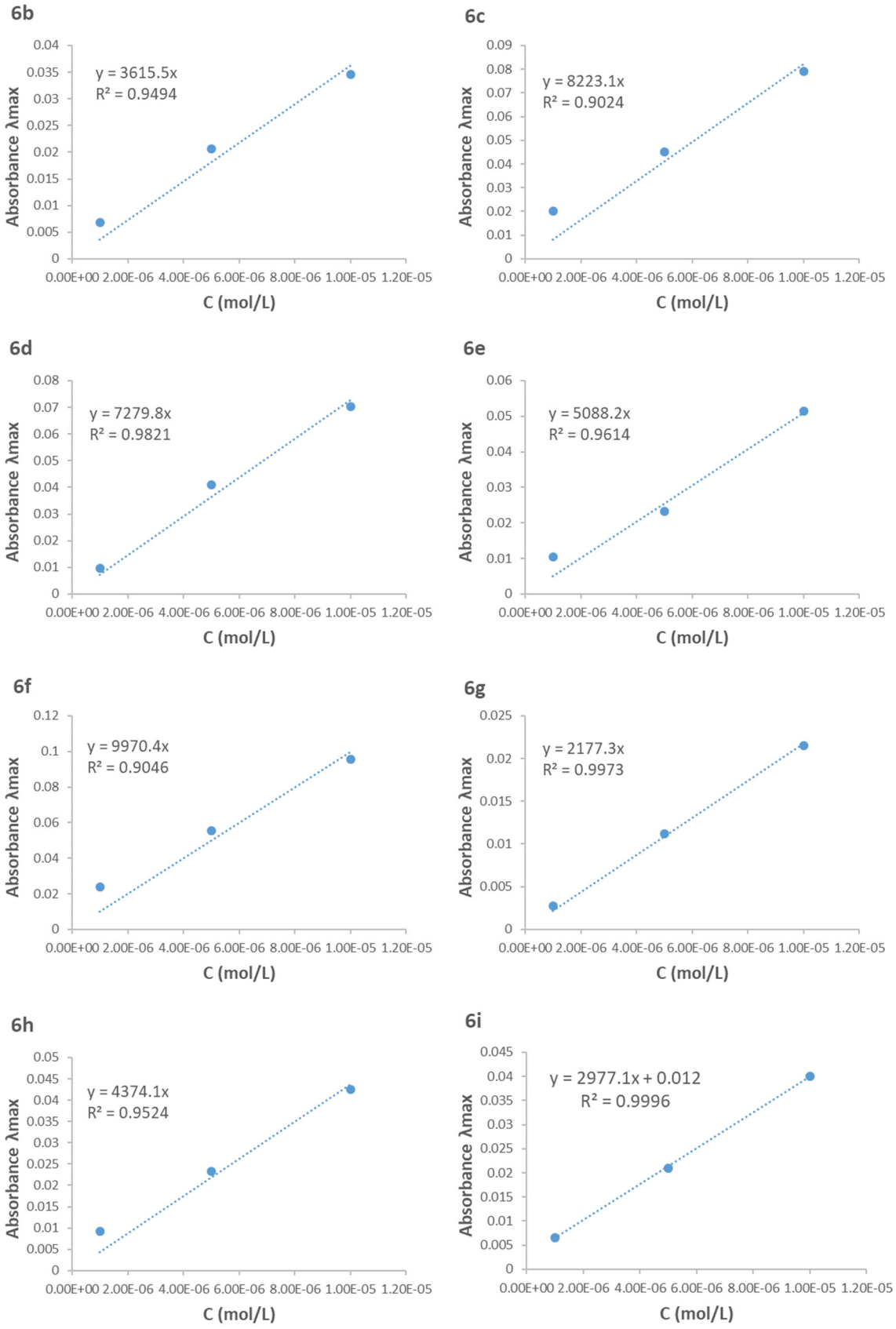

y = 5209.5x
R² = 0.9912
CHCl3
Absorbance λmax
C (mol/L)
0 0.1 0.2 0.3 0.4 0.5 0.6
0.00E+00 2.00E-05 4.00E-05 6.00E-05 8.00E-05 1.00E-04 1.20E-04

Fig S9: Epsilon Calculation in *PBS buffer at pH = 7.4 supplemented with 5% BSA*

Absorbance spectra were recorded in at 25°C in PBS buffer at pH = 7.4 supplemented with 5% BSA.



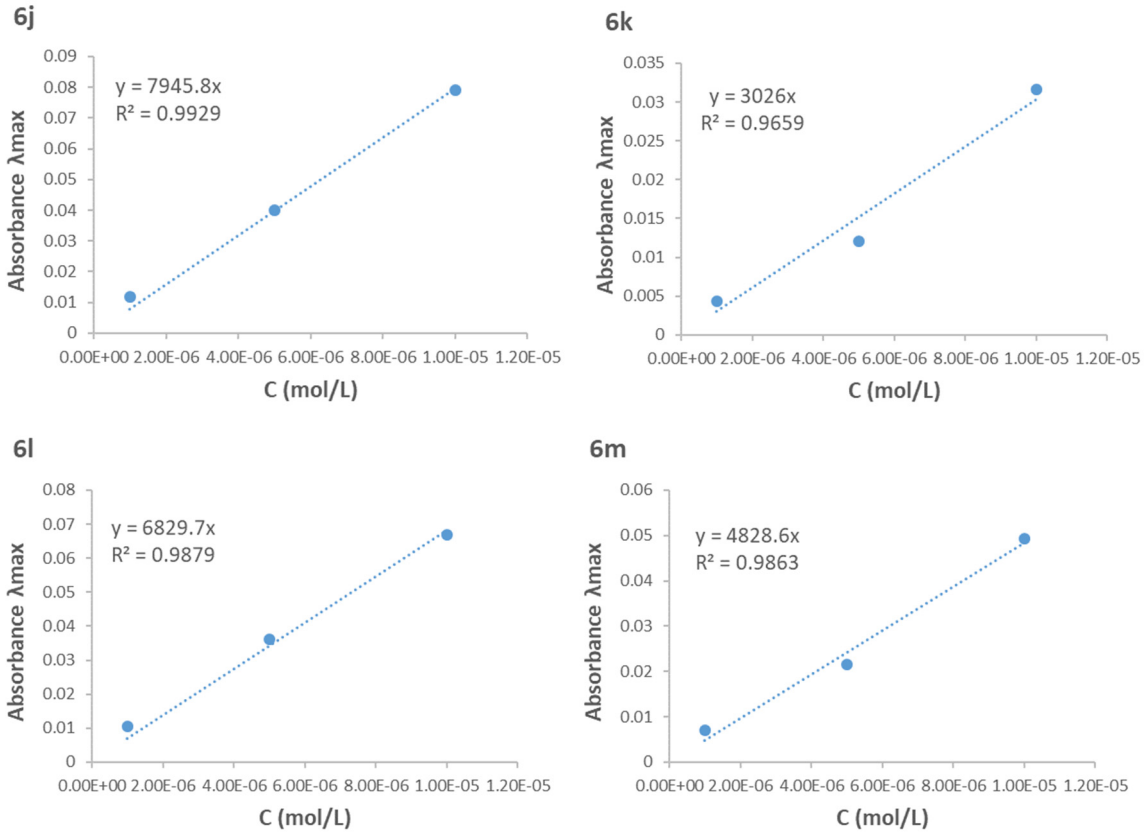


Fig S10: Photobleaching Mechanism

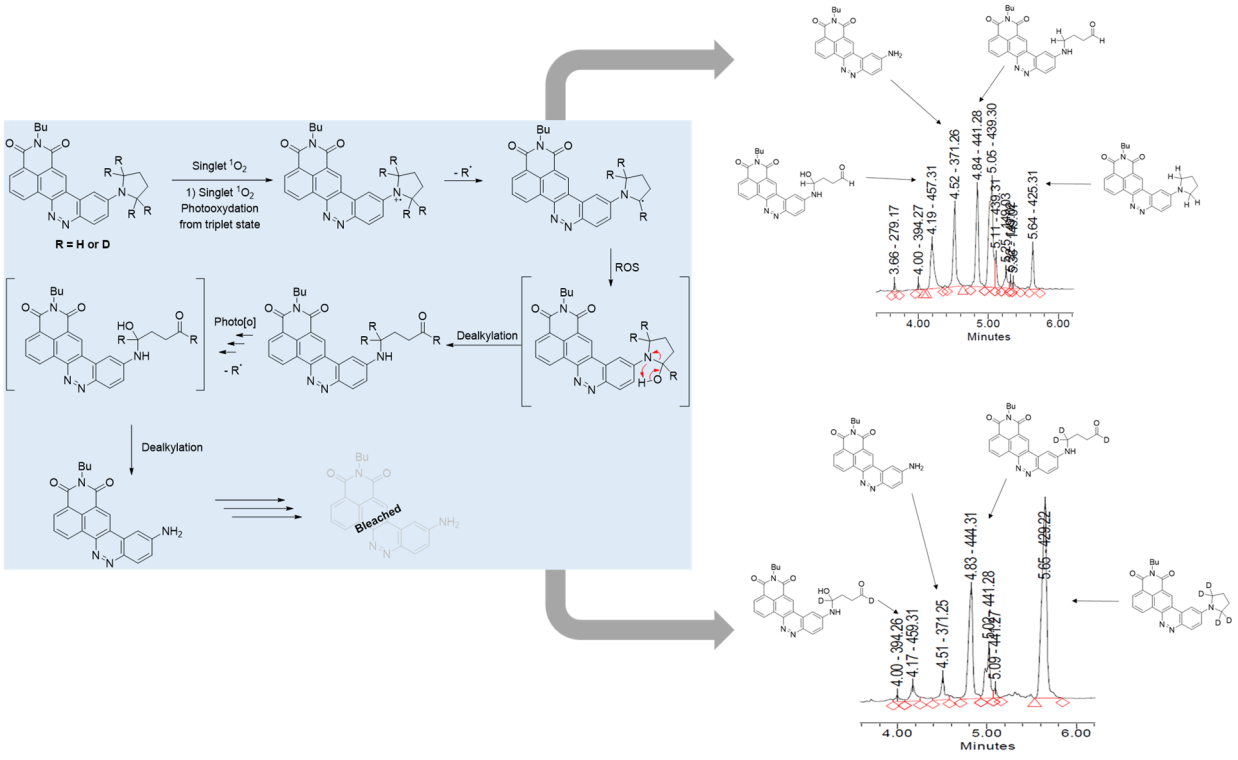


Fig S11: Representative view of mitochondria targeted CinNapht 6i and 6j subcellular localization

For this experiment, CinNapht 6i and 6j were incubated at 5 µM for 3 h at 37 °C, then organelles trackers were added. **6i** and **6j** (λ_{Exc}: 470 nm, λ_{Em}: 550 to 700 nm) MitoView^{TM} 405 (λ_{Exc}: 405 nm, λ_{Em}: 425 to 500 nm), Scale bars 10 µM

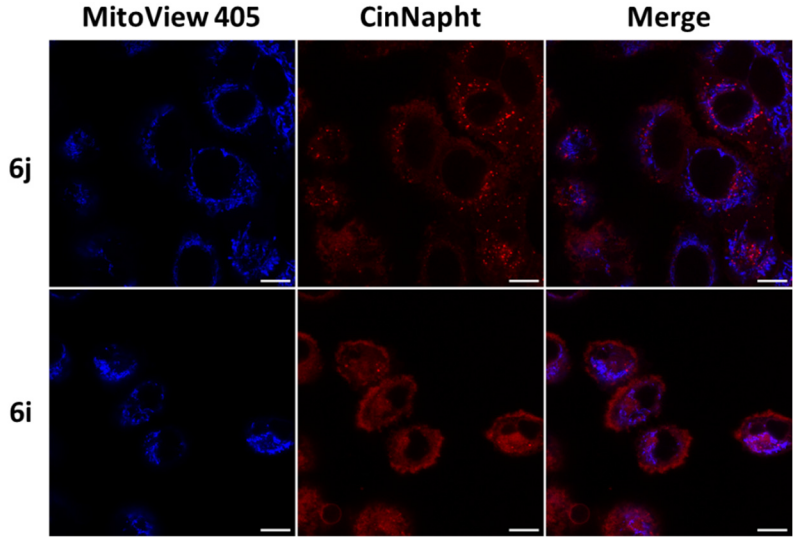


Fig S12: turn on measurment

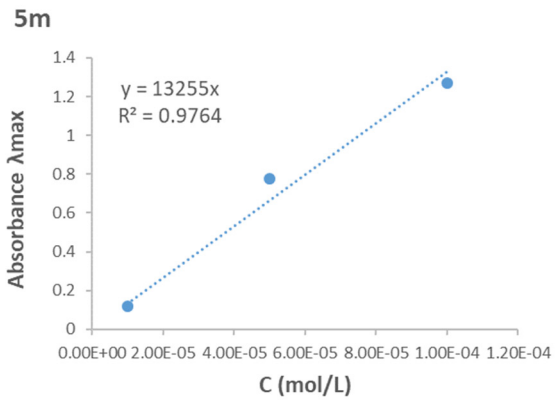
Values obtaineded using ImageJ software measurement tool

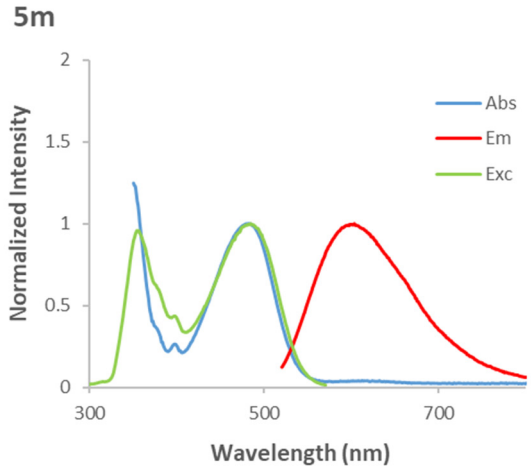
	Lipid Droplet				Cell Cytoplasm	
	Area	Mean			Area	Mean
1	0.593	638.372		1	0.528	27.61
2	0.528	742.295		2	0.528	25.397
3	0.528	404.548		3	0.528	56.336
4	0.528	399.274		4	0.528	19.692
5	0.528	197.082		5	0.528	26.014
6	0.528	337.048		6	0.528	31.151
7	0.528	491.411		7	0.528	21
8	0.528	333.342		8	0.528	22.158
9	0.528	243.062		9	0.528	42.596
10	0.528	1285.377		10	0.528	10.726
11	0.528	559.288		11	0.528	7.11
12	0.528	510.719		12	0.528	6.493
13	0.528	1114.055		13	0.528	5.466
14	0.528	1699.123		14	0.528	14.178
15	0.528	1030.397		15	0.528	11.589
16	0.528	651.075		16	0.528	15.452
17	0.528	394.041		17	0.528	22.801
18	0.528	409.452		18	0.528	16.438
19	0.528	308.603		19	0.528	41.068
20	0.528	376.514		20	0.528	23.267
Average Mean		**606.2539**		**Average Mean**		**22.3271**
		Turn ON factor: 27.1532756				

Fig S13 Photophysical caracterisation of 5n in Oil and Tiacetine

Canola Oil :

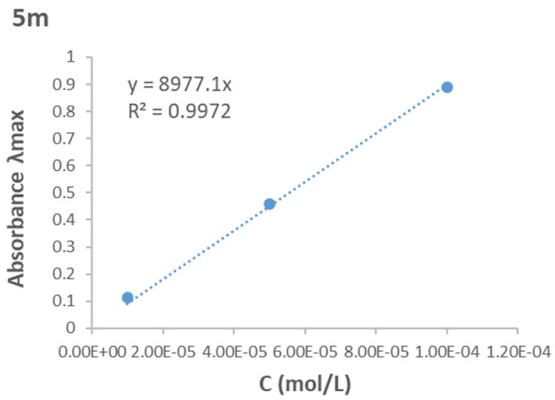
Spectra were recorded at 25°C in Canola oil (mainly composed of unsaturated lipids ~93% from Lesieur, Asnières-sur-Seine, France). Emission spectrum was recorded using an excitation at 480 nm. Excitation spectrum was recorded using an emission at 620 nm.

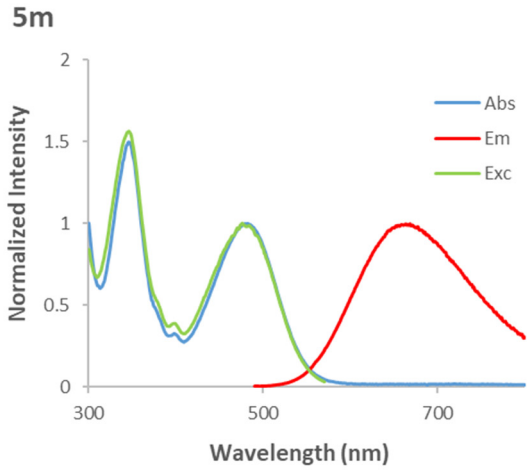




Triacetin

Spectra were recorded at 25°C in Triacetin. Emission spectrum was recorded using an excitation at 480 nm. Excitation spectrum was recorded using an emission at 620 nm.





II. Experimental section

Abbreviations

The following abbreviations are used throughout the text of the ESI file: Abs, absorption; aq., aqueous; Ar, argon; BSA, Bovine Serum Albumin; DCM, dichloromethane; DMF, dimethylformamide; DMSO, dimethylsulfoxide; Em, emission; EtOAc, ethyl acetate; EtOH, ethanol; Ex, excitation; H_2O, water; Hept, heptane; HRMS, High-Resolution Mass Spectrum; IR, infrared; MeCN, acetonitrile; MeOH, methanol; min, minutes; NMR, Nuclear Magnetic Resonance; PBS, phosphate buffered saline; MS, mass spectrometry; RP, reversed phase; RT, room temperature; TFA, trifluoroacetic acid; THF, Tetrahydrofuran; TLC, Thin Layer Chromatography; UV, ultraviolet; Vis, Visible.

General

Unless otherwise noted, all commercially available reagents and solvents were used without further purification. TLC were carried out on silica gel aluminum plates with F-254 indicator; The spots were directly visualized or through illumination with UV lamp (λ = 254/365 nm). Flash-column chromatography purifications were performed on silica gel (40-63 µm) from Macherey-Nagel. Organic solvents for spectroscopy were purchased from Acros Organics or Sigma Aldrich. Absolute EtOH was provided by Carlo Erba. Colza oil (mainly composed of unsaturated lipids ~93% from Lesieur, Asnières-sur-Seine, France).

Instrument and methods

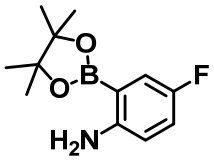
Proton NMR (^{1}H) spectra were recorded on a Bruker Avance 500 or 300 MHz and proton-decoupled carbon ^{13}NMR spectra were recorded at 125 MHz. NMR experiments were carried out in deuteratd solvents and chemical shifts are expressed in parts per million (ppm) from the residual non-deuterated solvent signal. Calibration was made by using residual signals of partially deuterated solvent summarized in 2010 by Fulmer et al. The following abbreviations are used for the multiplicities: s: singlet; d: doublet; t: triplet; q: quadruplet; qt: quintuplet; m: multiplet or overlap of non-equivalent resonances; br s: broad singlet; Coupling constants (J) are reported in hertz (Hz).

High resolution mass spectra were determined on an AEI MS-9 using electrospray ionization (ESI) and a time-offlight (TOF) analyzer. IR spectra were recorded with a PerkinElmer Spectrum BX FT-IR spectrometer directly from the substance via attenuated total reflectance (ATR-IR) and bond vibration frequencies are expressed in reciprocal centimeters (cm^{-1}). HPLC-MS analyses were performed on an Alliance W2690 system (Waters, USA). UV-Visible absorption spectra were recorded on a Varian Cary 100 Series 2 Scan UV-Vis Spectrophotometer using a 10 mm path quartz cell. Emission spectra experiments were performed on an Edimburgh FS-5 spectrofluorimeter with a SC-20 module. Aright angle configuration was used. The relative fluorescence quantum yields were determined using DCM (4-(Dicyanomethylene)-2-methyl-6-(4-dimethylaminostyryl)-4H-pyran) as reference (ϕ_{FL} = 0.43 in EtOH) as reference with the following formula:

$$\Phi_F(x) = \Phi_F(0)\,\frac{1-10^{-A_0}}{1-10^{-A_x}}\,\frac{S_x}{S_0}\left(\frac{n_x}{n_0}\right)^2$$

Synthesis protocols

4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1)

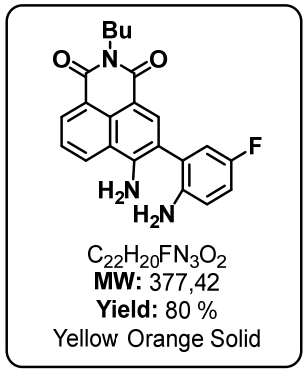


$C_{12}H_{17}BFNO_2$
MW: 237,08
Yield: 84 %
White solid

2-bromo-4-fluoroaniline (3.0 g, 16.0 mmol, 1.0 eq), KOAc (4.71 g, 48.0 mmol, 3.0 eq) and bis(pinacolato)diboron (6.09 g, 24.0 mmol, 1.5 eq) were dissolved in dioxane (85 mL) in a Schlenk tube. The resulting mixture was desoxygenated with freeze-pump-thaw cycling before addition of $Pd(dppf)Cl_2$ (1.17 g, 2.00 mmol, 0.10 eq). The reaction was heated overnight at 90 °C with constant stirring under argon. The mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (Hept/AcOEt 9:1 v/v) to afford compound **1** (3.18 g, 84 %) as a white solid. Analysis were in accordance with previous published work.[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.27 (m, 1H), 6.91 (td, *J* = 8.5, 3.1 Hz, 1H), 6.53 (dd, *J* = 8.8, 4.2 Hz, 1H), 4.57 (s, 2H), 1.34 (s, 12H).

6-amino-5-(2-amino-5-fluorophenyl)-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione (3)

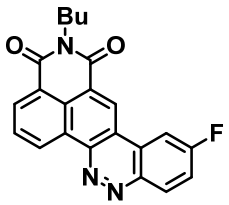


$C_{22}H_{20}FN_3O_2$
MW: 377,42
Yield: 80 %
Yellow Orange Solid

6-amino-5-bromo-2-butyl-1H-benzo[de]isoquinoline-1,3(2H)-dione (2.0 g, 5.76 mmol, 1.0 eq.), 4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (2.05 g, 8.64 mmol, 1.5 eq.), and Na_2CO_3 (1.83 g, 17.3 mmol, 3.0 eq.) were dissolved in a mixture of H_2O, EtOH, and toluene (40 mL, 3:3:10 v/v) in a Schlenk tube. The resulting mixture was deoxygenated with freeze-pump-thaw cycling before addition of $Pd(PPh_3)_4$ (666 mg, 0.576 mmol, 0.1 eq.). The reaction was heated overnight at 80 °C with constant stirring under argon. The mixture was cooled to room temperature, then diluted with DCM and washed with water. The organic layer was collected, dried over $MgSO_4$, and evaporated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (DCM/EtOAc 95:5 to 90:10) to afford compound **3** (1.95 g, 90 %) as a yellow orange solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 7.3 Hz, 1H), 8.36 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 6.98 (td, *J* = 8.5, 2.6 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.80 (dd, *J* = 8.8, 4.8 Hz, 1H), 5.11 (s, 2H), 4.20 – 4.11 (t, 2H), 3.58 (s, 2H), 1.75 – 1.66 (m, 2H), 1.48 – 1.38 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 164.0, 157.4, 155.5, 146.3, 140.5, 135.5, 131.6, 129.5, 127.1, 125.6, 123.4, 120.5, 118.1, 117.7 (d, *J* = 22.2 Hz), 117.1 (d, *J* = 7.8 Hz), 116.7 (d, *J* = 22.3 Hz), 112.4, 40.2, 30.5, 20.5, 14.0.
^{19}F NMR (282 MHz, $CDCl_3$) δ -125.59 (d, *J* = 3.7 Hz).
Rf (DCM/ EtOAc 8:2) = 0.5
IR (neat): ν = 3466, 3358, 3239, 2958, 2876, 1684, 1631, 1586, 1498, 1427, 1393, 1339, 1227, 1146, 777cm^{-1}
ESI-HRMS calculated for $C_{22}H_{21}FN_3O_2$ $[M+H]^+$ 378.1618, found 378.1602

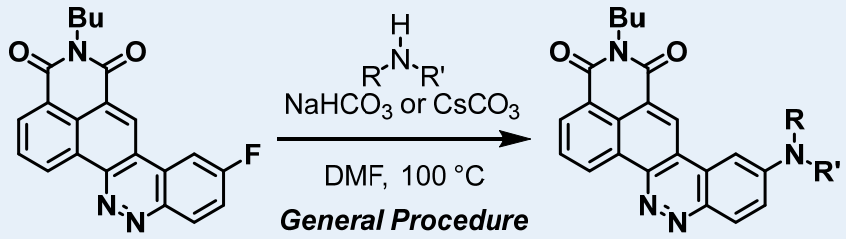
11-butyl-2-fluoro-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (4)



$C_{22}H_{16}FN_3O_2$
MW: 373,39
Yield: 71 %
Yellow Solid

A solution of compound **3** (1.00 g, 2.65 mmol, 1.00 eq.) in CH_3Cl_3 was cooled in an ice bath to 0°C. *m*CPBA (937 mg, 5.43 mmol, 2.05 eq.) was added and the reactring mixture was kept at 0 °C under stirring for 2h after what it was allowed to warm to room temperature. The mixture was then stirred under argon at room temperature 3 days until the reaction was completed. The mixture was washed with a 10% aqueous $Na_2S_2O_3$ solution and extracted with DCM. The organic layer was then washed again with a saturated solution of $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give crude product, which was purified by flash chromatography on silica gel (Hept/EtOAc 95:5 to 85:15, v/v) to afford compound **4** (705 mg, 71 %) as a yellow solid.

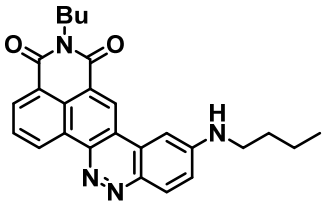
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (d, *J* = 8.2 Hz, 1H), 9.46 (s, 1H), 8.89 (dd, *J* = 8.9, 5.4 Hz, 1H), 8.78 (d, *J* = 7.3 Hz, 1H), 8.34 (d, *J* = 8.8 Hz, 1H), 8.13 (t, *J* = 7.8 Hz, 1H), 7.78 (dd, *J* = 12.2, 4.7 Hz, 1H), 4.32 – 4.18 (m, 2H), 1.86 – 1.71 (m, 2H), 1.56 – 1.41 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 163.9, 163.6, 163.2, 145.2, 141.7, 135.1 (d, *J* = 10.1 Hz), 132.1, 130.8, 129.8, 129.6, 127.8, 125.6, 123.5 (d, *J* = 10.8 Hz), 122.9, 120.7 (d, *J* = 25.5 Hz), 118.8 (d, *J* = 4.9 Hz), 106.7 (d, *J* = 23.6 Hz), 40.8, 30.4, 20.5, 14.0.
^{19}F NMR (282 MHz, $CDCl_3$) δ -100.69 (d, *J* = 5.7 Hz)
Rf (Hept/EtOAc 5:5) = 0.6
IR (neat): ν = 2961, 2873, 1705, 1663, 1622, 1600, 1473, 1418, 1365, 1337, 1230, 1194, 1150, 1127, 1090, 987, 913, 846, 786, 732, 688 cm^{-1}
ESI-HRMS calculated for $C_{22}H_{17}FN_3O_2$ $[M+H]^+$ 374.1305, found 374.1308



General procedure:

CinNapht-F **4** (20 mg, 0.05 mmol, 1 eq), $NaHCO_3$ (18 mg, 0.21 mmol, 4 eq) or Cs_2CO_3 (70 mg, 0.21 mmol, 4 eq) and the corresponding amine (0.11 mmol, 2 eq) were dissolved in DMF (0.50 mL, 0.1 M) and stirred at 100 °C. After the reaction was completed (monitored by TLC using Hept/EtOAc 8:2) the mixture was cooled down to room temperature and diluted in DCM. The mixture was washed with brine and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel or on preparative TLC plate using an appropriate eluting solvent mixture to afford the desired pure product.

11-butyl-2-(butylamino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5a)

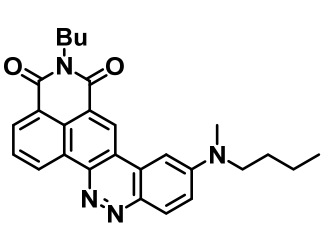


$C_{26}H_{26}N_4O_2$
MW: 426,52
Yield: 92 %
Orange Red Solid

Compound **5a** was prepared according to the general procedure with butylamine (10.5 µL, 0.107 mmol) for 2 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **5a** (21 mg, 92 %) as an orange yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.96 (d, *J* = 8.2 Hz, 1H), 9.46 (s, 1H), 8.72 (d, *J* = 7.2 Hz, 1H), 8.46 (d, *J* = 9.0 Hz, 1H), 8.04 (t, *J* = 7.8 Hz, 1H), 7.38 (s, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 4.72 (s, 1H, CinNapht-NH-CH_2-CH_2-CH_2-CH_3), 4.25 (t, *J* = 7.5 Hz, 2H), 3.41 (q, *J* = 6.6 Hz, 2H, CinNapht-NH-CH_2-CH_2-CH_2-CH_3), 1.85 – 1.71 (m, 4H), 1.58 (qt, 7.4 Hz, 2H), 1.49 (sx, *J* = 7.4 Hz, 2H), 1.04 (m, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 164.0, 151.7, 143.2, 142.2, 133.2, 131.3, 131.1, 129.9, 128.7, 127.6, 126.6, 124.6, 123.1, 122.6, 118.3, 97.1, 52.8, 40.6, 39.3, 30.4, 29.8, 29.6, 20.5, 20.4, 14.0, 13.9.
Rf (DCM/EtOAc 8:2) = 0.4
IR (neat): ν = 2960, 2926, 2868, 1736, 1702, 1654, 1621, 1599, 1538, 1435, 1337, 1224, 1177, 1112, 820, 780, 752, 693 cm^{-1}
ESI-HRMS calculated for $C_{26}H_{27}N_4O_2$ $[M+H]^+$ 427.2134, found 427.2126

11-butyl-2-(butyl(methyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5b)

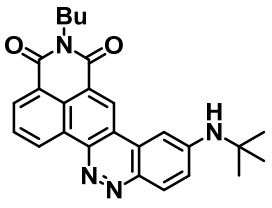


$C_{27}H_{28}N_4O_2$
MW: 440,55
Yield: 95 %
Red Solid

Compound **5b** was prepared according to the general procedure with *N*-methylbutylamine (13.0 µL, 0.11 mmol) for 2 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **5b** (22 mg, 95 %) as a red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.96 (d, *J* = 8.2 Hz, 1H), 9.46 (s, 1H), 8.71 (d, *J* = 7.2 Hz, 1H), 8.52 (d, *J* = 9.0 Hz, 1H), 8.03 (t, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 10.7 Hz, 2H), 4.24 (t, *J* = 7.5 Hz, 2H), 3.63 (t, *J* = 7.4 Hz, 2H), 3.27 (s, 3H, CinNapht-N(CH_3)-Bu, 1.76 (m, 4H), 1.49 (m, 4H), 1.02 (m, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 164.0, 151.7, 143.2, 142.2, 133.2, 131.3, 131.1, 129.9, 128.7, 127.6, 126.6, 124.6, 123.1, 122.6, 118.3, 97.1, 52.8, 40.6, 39.3, 30.4, 29.8, 29.6, 20.5, 20.4, 14.0, 13.9.
Rf (DCM/EtOAc 8:2) = 0.7
IR (neat): ν = 2955, 2929, 2873, 1701, 1663, 1610, 1520, 1492, 1464, 1430, 1385, 1367, 1346, 1270, 1225, 1185, 1118, 920, 867, 814, 788, 752, 693 cm^{-1}
ESI-HRMS calculated for $C_{27}H_{29}N_4O_2$ $[M+H]^+$ 441.2291, found 441.2280

11-butyl-2-(tert-butylamino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5c)

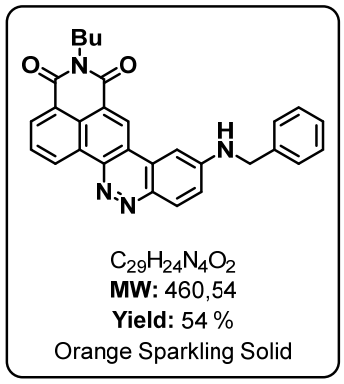


$C_{26}H_{26}N_4O_2$
MW: 426,52
Yield: 47 %
Red Solid

Compound **5c** was prepared according to the general procedure with *tert*-butylamine (22.5 µL, 0.11 mmol) overnight. As the boiling point of tert-butylamine is very low, several equivalents were gradually added to help the completion of the reaction. The crude product was purified by flash chromatography on silica gel (DCM/EtOAc 98:2, v/v) to afford compound **5c** (11 mg, 47 %) as a red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.96 (d, *J* = 8.2 Hz, 1H), 9.43 (d, *J* = 4.4 Hz, 1H), 8.71 (d, *J* = 7.3 Hz, 1H), 8.46 (d, *J* = 7.6 Hz, 1H), 8.03 (t, *J* = 7.8 Hz, 1H), 7.62 (s, 1H), 7.22 (s, 1H), 4.87 (s, 1H, CinNapht-NH-$C(CH_3)_3$), 4.24 (t, *J* = 7.4 Hz, 2H), 1.76 (qt, *J* = 7.4 Hz, 2H), 1.62 (s, 9H, CinNapht-NH-$C(CH_3)_3$), 1.50 (sx, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 163.5, 149.9, 143.2, 142.3, 132.6, 131.0, 130.6, 129.5, 128.4, 127.2, 126.1, 124.4, 122.9, 122.4, 122.3, 117.9, 97.8, 51.8, 40.3, 30.0, 29.3 (3C), 20.2, 13.6.
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2961, 2930, 2870, 1702, 1662, 1619, 1539, 1498, 1472, 1435, 1399, 1368, 1336, 1272, 1226, 1181, 1115, 1078 cm^{-1}
ESI-HRMS calculated for $C_{26}H_{27}N_4O_2$ $[M+H]^+$ 427.2134, found 427.2141

2-(benzylamino)-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5d)

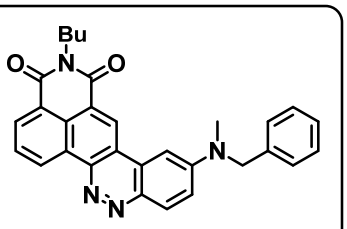


$C_{29}H_{24}N_4O_2$
MW: 460,54
Yield: 54 %
Orange Sparkling Solid

Compound **5d** was prepared according to the general procedure with benzylamine (12.0 µL, 0.11 mmol) for 4 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **5d** (12.0 mg, 54 %) as an orange solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.95 (d, *J* = 7.8 Hz, 1H), 9.44 (s, 1H), 8.69 (d, *J* = 7.0 Hz, 1H), 8.48 (d, *J* = 8.9 Hz, 1H), 8.00 (s, 1H), 7.51 (s, 1H), 7.42 – 7.22 (m, 6H), 5.00 (s, 1H, CinNapht-NH-CH_2-C_6H_5), 4.58 (s, 2H, CinNapht-NH-CH_2-C_6H_5), 4.19 (m, 2H), 1.71 (m, 2H), 1.43 (m, 2H), 0.94 (t, *J* = 7.0 Hz, 3H).
Due to poor solubility, no ^{13}C NMR spectra could be obtained.
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2923, 2853, 1696, 1649, 1610, 1597, 1573, 1555, 1532, 1498, 1464, 1435, 1398, 1367, 1334, 1267, 1222, 1181, 1157, 1109, 1076, 907, 845, 820, 788, 765, 745, 699 cm^{-1}
ESI-HRMS calculated for $C_{29}H_{25}N_4O_2$ $[M+H]^+$ 461.1978, found 461.1972

2-(benzyl(methyl)amino)-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5e)

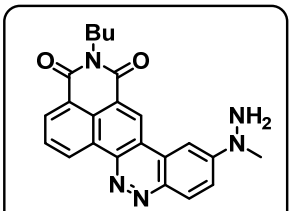


$C_{30}H_{26}N_4O_2$
MW: 474,56
Yield: 83 %
Dark Red Solid

Compound **5e** was prepared according to the general procedure with N-methylbenzylamine (14.0 µL, 0.107 mmol) for 4 h. The crude product was purified by preparative TLC (DCM/EtOAc 7:3, v/v) to afford compound **5e** (20 mg, 83 %) as a dark red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 (d, *J* = 8.2 Hz, 1H), 9.46 (s, 1H), 8.72 (d, *J* = 7.3 Hz, 1H), 8.53 (d, *J* = 9.3 Hz, 1H), 8.04 (t, *J* = 7.8 Hz, 1H), 7.59 (s, 1H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.40 – 7.26 (m, 5H, CinNapht-N(CH_3)-CH_2-C_6H_5), 4.88 (s, 2H, CinNapht-N(CH_3)-CH_2-C_6H_5), 4.24 (t, *J* = 7.4 Hz, 2H), 3.38 (s, 3H, CinNapht-N(CH_3)-CH_2-C_6H_5), 1.77 (qt, *J* = 7.4 Hz, 2H), 1.49 (sx, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 163.9, 152.2, 143.3, 142.2, 136.9, 133.3, 131.4, 131.0, 129.9, 129.2 (2C), 128.8, 127.9, 126.6 (2C), 124.5, 123.3, 122.6, 118.6, 118.4, 97.8, 56.5, 40.7, 39.6, 30.4, 29.8, 29.7, 20.6, 14.0
Rf (DCM/EtOAc 8:2) = 0.7
IR (neat): ν = 2962, 2925, 2854, 1703, 1663, 1612, 1524, 1494, 1434, 1395, 1347, 1227, 1116, 814, 786, 749, 704 cm^{-1}
ESI-HRMS calculated for $C_{30}H_{27}N_4O_2$ $[M+H]^+$ 475.2134, found 475.2121

11-butyl-2-(2-methylhydrazineyl)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5g)

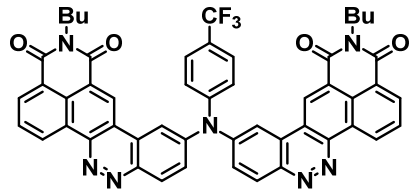


$C_{23}H_{21}N_5O_2$
MW: 399,45
Yield: 80 %
Purple Solid

Compound **5g** was prepared according to the general procedure with methylhydrazine (6.00 µL, 0.11 mmol) for 1 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1, v/v) to afford compound **5g** (17 mg, 80 %) as a purple solid.

^{1}H NMR (300 MHz, DMSO) δ 9.82 (d, *J* = 7.2 Hz, 1H), 9.50 (s, 1H), 8.63 (d, *J* = 6.3 Hz, 1H), 8.42 (d, *J* = 9.4 Hz, 1H), 8.18 – 8.09 (m, 1H), 7.92 (d, *J* = 9.2 Hz, 1H), 7.85 (s, 1H), 5.14 (s, 2H, CinNapht-N(CH_3)-NH_2), 4.19 – 4.06 (m, 2H), 3.49 (s, 3H, CinNapht-N(CH_3)-NH_2), 1.55 – 1.75 (m, *J* = 7.3 Hz, 2H), 1.45 – 1.35 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
Due to poor solubility, no ^{13}C NMR spectras could be obtained.
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2923, 2852, 1698, 1656, 1608, 1491, 1440, 1396, 1376, 1333, 1231, 1180, 1123, 906, 856, 839, 815, 783, 752, 691 cm^{-1}
ESI-HRMS calculated for $C_{23}H_{22}N_5O_2$ $[M+H]^+$ 400.1774, found 400.1762

11-butyl-2-((4-(trifluoromethyl)phenyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5i)

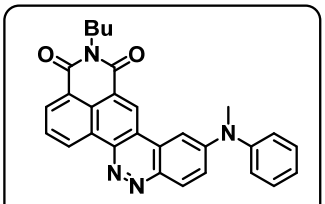


$C_{51}H_{36}F_3N_7O_4$
MW: 867,89
Yield: 45 %
Orange Solid

Compound **5i** was prepared according to the general procedure with 4-nitroaniline (17.0 mg, 0.107 mmol) and Cs_2CO_3 (70 mg, 0.214 mmol) overnight. The crude product was purified by flash chromatography on silica gel (DCM/EtOAc 98:2, v/v) to afford compound **5i** (21 mg, 45 %) as an orange solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.00 (dd, *J* = 8.4, 1.2 Hz, 2H), 9.24 (s, 2H), 8.86 (d, *J* = 9.0 Hz, 2H), 8.74 (dd, *J* = 7.4, 1.2 Hz, 2H), 8.47 (d, *J* = 2.2 Hz, 2H), 8.10 (dd, *J* = 8.4, 7.4 Hz, 2H), 7.88 (dd, *J* = 9.0, 2.3 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 4.11 (t, *J* = 7.5 Hz, 4H), 1.61 (m, 4H), 1.35 (m, 4H), 0.90 (t, *J* = 7.3 Hz, 6H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7 (2C), 163.2 (2C), 149.8 (2C), 148.7, 145.3 (2C), 142.1 (2C), 134.0 (2C), 131.9 (2C), 130.8 (2C), 129.6 (2C), 129.3 (2C), 127.8 (2C), 127.5 (2C), 125.7 (2C), 125.6 (2C), 124.8 (2C), 123.5 (2C), 122.6 (2C), 118.3 (2C), 115.0 (2C), 40.5 (2C), 30.1 (2C), 20.3 (2C), 13.7 (2C).
Despite many efforts, CF_3 signals and Ar near CF_3 signals could not be seen
^{19}F NMR (282 MHz, $CDCl_3$) δ -62.19.
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2958, 2921, 2852, 1703, 1662, 1602, 1515, 1489, 1473, 1455, 1434, 1408, 1380, 1367, 1325, 1261, 1227, 1163, 1116, 1094, 1066, 1014, 938, 908, 862, 843, 815, 787, 751, 735, 699, 691, 667 cm^{-1}
ESI-HRMS calculated for $C_{51}H_{37}F_3N_7O_4$ $[M+H]^+$ 868.2853 found 868.2803

11-butyl-2-(methyl(phenyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5k)

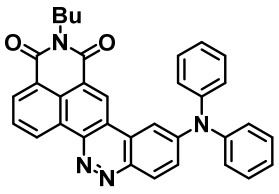


$C_{29}H_{24}N_4O_2$
MW: 460,54
Yield: 12 %
Dark Orange Solid

Compound **5k** was prepared according to the general procedure with N-methylaniline (11.5 µL, 0.11 mmol) and Cs_2CO_3 (70 mg, 0.214 mmol) instead of $NaHCO_3$ overnight. The crude product was purified by flash chromatography on silica gel (DCM/EtOAc 98:2, v/v) to afford compound **5k** (3.0 mg, 12 %) as a dark orange solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (d, *J* = 8.1 Hz, 1H), 9.49 (s, 1H), 8.75 (d, *J* = 7.3 Hz, 1H), 8.44 (d, *J* = 9.2 Hz, 1H), 8.06 (t, *J* = 7.6 Hz, 1H), 7.70 (s, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.25-7.40 (m, 4H), 4.26 (t, *J* = 7.4 Hz, 2H), 3.64 (s, 3H, CinNapht-N($\underline{CH_3}$)-C_6H_5), 1.78 (qt, 2H), 1.50 (sx, *J* = 7.4 Hz, 2H), 1.02 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 163.9, 151.9, 146.7, 143.9, 142.3, 132.5, 131.5, 131.1, 130.5 (2C), 130.0, 128.9, 127.7, 127.2, 126.8 (2C), 126.6, 124.5, 123.6, 122.7, 121.1, 118.5, 99.4, 41.3, 40.7, 30.4, 29.8, 20.6, 14.0.
Rf (DCM/EtOAc 8:2) = 0.7
IR (neat): ν = 2957, 2924, 2854, 1702, 1660, 1614, 1592, 1485, 1466, 1435, 1393, 1333, 1314, 1259, 1227, 1184, 1108, 1025, 908, 843, 821, 783, 751, 731, 702, 693 cm^{-1}
ESI-HRMS calculated for $C_{29}H_{25}N_4O_2$ $[M+H]^+$ 461.1978, found 461.1956

11-butyl-2-(diphenylamino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5m)

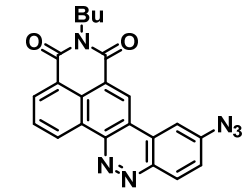


$C_{34}H_{26}N_4O_2$
MW: 522,61
Yield: 76 %
Red Solid

Compound **5m** was prepared according to the general procedure with dibenzylamine (18 mg, 0.107 mmol) and Cs_2CO_3 (70 mg, 0.214 mmol) instead of $NaHCO_3$ overnight. The crude product was purified by flash chromatography on silica gel (DCM/EtOAc 99:1, v/v) to afford compound **5m** (21 mg, 76 %) as a red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (d, *J* = 8.2 Hz, 1H), 9.20 (s, 1H), 8.74 (d, *J* = 7.3 Hz, 1H), 8.55 (d, *J* = 9.2 Hz, 1H), 8.07 (t, *J* = 7.8 Hz, 1H), 8.01 (s, 1H), 7.63 (dd, *J* = 9.2, 1.9 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 4H), 7.30 (dd, *J* = 14.2, 7.5 Hz, 6H), 4.20 (t, *J* = 7.4 Hz, 2H), 1.74 (qt, *J* = 7.4 Hz, 2H), 1.46 (sx, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.2, 163.7, 151.8, 146.0 (2C), 144.6, 142.3, 132.8, 131.6, 131.0, 130.3 (4C), 129.9, 129.0, 127.6, 126.5 (4C), 126.4, 126.2 (2C), 125.0, 124.0, 123.9, 122.7, 118.5, 107.3, 40.7, 30.4, 20.6, 14.0.
Rf (DCM/EtOAc 8:2) = 0.8
IR (neat): ν = 2960, 2926, 2868, 1736, 1702, 1654, 1621, 1538, 1435, 1337, 1224, 1177, 1112, 820, 780, 752, 693 cm^{-1}
ESI-HRMS calculated for $C_{34}H_{27}N_4O_2$ $[M+H]^+$ 523,2134 found 523.2133

2-azido-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5n)

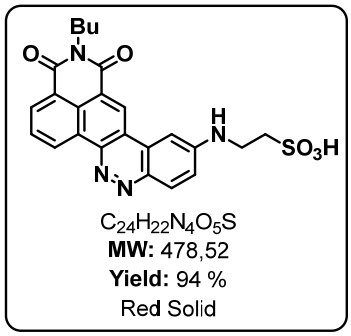


$C_{22}H_{16}N_6O_2$
MW: 396,41
Yield: 86 %
Pale Yellow-Brown Solid

Compound **5n** was prepared according to the general procedure with NaN_3 (7.0 mg, 0.107 mmol) for 20 min, during which a precipitate forms. The mixture was filtered and the residue was washed with water several times. The residue was then redissolved in DCM, and the mixture was dried over $MgSO_4$ and concentrated under reduced pressure to give compound **5n** (18 mg, 86 %) without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (d, *J* = 8.2 Hz, 1H), 9.37 (s, 1H), 8.75 (dd, *J* = 14.4, 8.1 Hz, 2H), 8.14 (s, 1H), 8.08 (t, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 4.23 (t, *J* = 7.4 Hz, 2H), 1.77 (qt, *J* = 7.4 Hz, 2H), 1.49 (sx, *J* = 7.3 Hz, 2H), 1.02 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.1, 163.5, 145.7, 145.3, 142.1, 134.2, 132.2, 131.0, 129.9, 129.7, 127.9, 125.7, 125.5, 123.3, 123.1, 118.3, 110.1, 41.0, 30.6, 30.1, 20.8, 14.2
Rf (DCM/EtOAc 8:2) = 0.7
IR (neat): ν = 2960, 2873, 2118, 1704, 1655, 1613, 1467, 1381, 1330, 1273, 1232, 1096, 844, 786, 752, 689 cm^{-1}
ESI-HRMS calculated for $C_{22}H_{17}N_6O_2$ $[M+H]^+$ 397.1413, found 397.1404

2-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)ethane-1-sulfonic acid (5o)

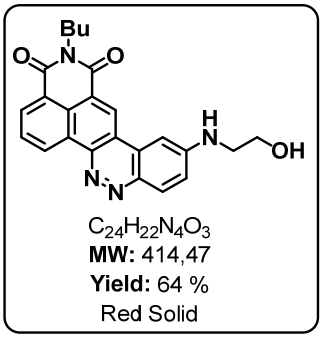


$C_{24}H_{22}N_4O_5S$
MW: 478,52
Yield: 94 %
Red Solid

Compound **5o** was prepared according to the general procedure **A** with taurine (13 mg, 0.107 mmol) overnight. The reaction mixture was redissolved in DCM, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC (DCM/MeOH 8:2, v/v) to afford compound **5o** (24 mg, 94 %) as a red solid.

^{1}H NMR (300 MHz, DMSO) δ 9.72 (d, *J* = 8.1 Hz, 1H), 9.36 (s, 1H), 8.56 (d, *J* = 7.3 Hz, 1H), 8.30 (d, *J* = 9.1 Hz, 1H), 8.09 (t, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 13.0 Hz, 2H), 7.41 (d, *J* = 9.1 Hz, 1H), 4.09 (t, *J* = 7.5 Hz, 2H), 3.67 (q, *J* = 6.5 Hz, 2H, CinNapht-NH-$\underline{CH_2}$-CH_2-SO_3H), 2.88 (t, *J* = 6.9 Hz, 2H, CinNapht-NH-CH_2-$\underline{CH_2}$-SO_3H), 1.67 (qt, *J* = 7.5 Hz, 2H), 1.38 (sx, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, DMSO) δ 163.4, 162.6, 151.9, 143.3, 132.0, 130.4, 129.6, 128.8, 128.6, 126.9, 126.6, 124.6, 124.5, 122.4, 122.2, 121.5, 117.5, 103.0, 102.8, 95.1, 49.5, 29.6, 19.8, 13.7.
Rf (DCM/EtOAc 8:2) = 0.3
IR (neat): ν = 3386, 2960, 1731, 1704, 1659, 1621, 1540, 1501, 1440, 1404, 1339, 1215, 1170, 1129, 1043, 825, 783, 751, 694, 667 cm^{-1}
ESI-HRMS calculated for $C_{24}H_{23}N_4O_5S$ $[M+H]^+$ 479.1389, found 479.1375

11-butyl-2-((2-hydroxyethyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5p)

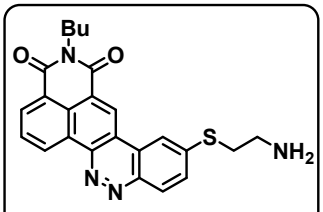


$C_{24}H_{22}N_4O_3$
MW: 414,47
Yield: 64 %
Red Solid

Compound **5p** was prepared according to the general procedure **A** with ethanolamine (6.40 µL, 0.107 mmol) for 1 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 97:3, v/v) to afford compound **5p** (14 mg, 64 %) as a red solid.

^{1}H NMR (500 MHz, DMSO) δ 9.79 (d, *J* = 7.8 Hz, 1H), 9.47 (s, 1H), 8.62 (d, *J* = 7.3 Hz, 1H), 8.34 (d, *J* = 9.1 Hz, 1H), 8.12 (t, *J* = 7.8 Hz, 1H), 7.58 (s, 1H), 7.51 (d, *J* = 9.1 Hz, 2H), 4.93 (t, *J* = 5.2 Hz, 1H), 4.12 (t, *J* = 7.3 Hz, 2H), 3.74 (d, *J* = 5.5 Hz, 2H), 3.56 – 3.49 (m, 2H), 1.67 (qt, *J* = 7.4 Hz, 2H), 1.40 (sx, *J* = 7.4 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).
Due to poor solubility, no ^{13}C NMR spectras could be obtained.
Rf (DCM/EtOAc 8:2) = 0.7
IR (neat): ν = 3379, 2963, 2931, 2484, 1698, 1655, 1615, 1599, 1532, 1499, 1456, 1436, 1401, 1374, 1352, 1336, 1316, 1269, 1223, 1181, 1125, 1081, 1003, 937, 915, 874, 824, 786, 751, 693 cm^{-1}
ESI-HRMS calculated for $C_{24}H_{23}N_4O_3$ $[M+H]^+$ 415.1770 found 415.1759

2-((2-aminoethyl)thio)-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (5r)



$C_{24}H_{22}N_4O_2S$
MW: 430,53
Yield: 49 %
Yellow Solid

Compound **5r** was prepared according to the general procedure **A** with cysteamine hydrochloride (12 mg, 0.107 mmol) for 1 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **5r** (11 mg, 49 %) as a yellow solid.

^{1}H NMR (300 MHz, DMSO) δ 9.20 (d, *J* = 8.2 Hz, 1H), 8.70 (s, 1H), 8.22 – 8.14 (m, 2H), 7.93 (s, 1H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.68 (dd, *J* = 8.8, 1.8 Hz, 1H), 3.89 (t, *J* = 7.4 Hz, 2H), 3.31 (t, *J* = 7.2 Hz, 2H, CinNapht-S-$\underline{CH_2}$-CH_2-NH_2), 3.00 (br, 2H, CinNapht-S-CH_2-$\underline{CH_2}$-NH_2), 1.65 – 1.54 (qt, *J* = 7.4 Hz, 2H), 1.38 (sx, *J* = 7.3 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

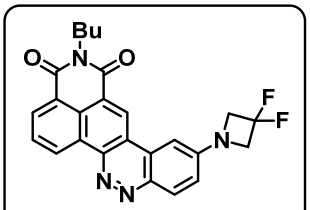
^{13}C NMR (75 MHz, DMSO) δ 162.6, 161.7, 161.2, 145.2, 144.6, 140.1, 130.4, 130.3, 129.1, 129.0, 128.8, 127.9, 125.9, 125.0, 123.5, 121.6, 120.2, 116.4, 116.2, 69.8, 33.7, 29.5, 19.8, 13.7.

Rf (DCM/MeOH 95:5) = 0.6

IR (neat): ν = 2958, 2924, 2851, 1702, 1655, 1616, 1597, 1548, 1505, 1483, 1465, 1433, 1416, 1378, 1364, 1334, 1263, 1229, 1187, 1141, 1090, 1065, 1022, 972, 942, 909, 839, 823, 784, 751, 687, 672 cm^{-1}

ESI-HRMS calculated for $C_{26}H_{23}N_4O_2$ $[M+H+MeCN]^+$ 471.1529, found 471.1535 and $C_{24}H_{23}N_4O_2S$ $[M+H]^+$ 431.1363, found 431.1360

11-butyl-2-(3,3-difluoroazetidin-1-yl)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (6a)

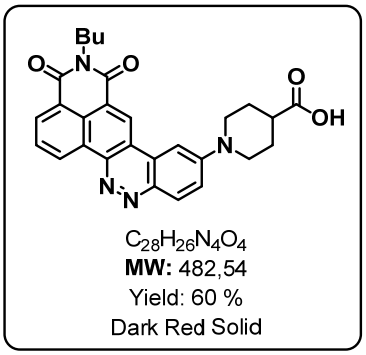


$C_{25}H_{20}F_2N_4O_2$
MW: 446,46
Yield: 75 %
Orange Solid

Compound **6a** was prepared according to the general procedure with 3,3-Difluoroazetidine hydrochloride (14.0 mg, 0.11 mmol) for 4 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **6a** (18 mg, 75 %) as an orange solid.

^{1}H NMR (300 MHz, $CDCl_3$ + 1% TFA*) δ 9.66 (d, *J* = 8.3 Hz, 1H), 9.44 (s, 1H), 8.84 (d, *J* = 7.3 Hz, 1H), 8.71 (d, *J* = 8.8 Hz, 1H), 8.16 (t, *J* = 7.9 Hz, 1H), 7.43 (s, 1H), 7.35 (d, *J* = 9.0 Hz, 1H), 4.80 (t, $J_{(H-F)}$ = 11.1 Hz, 4H, CinNapht-N-($\underline{CH_2}$)$_2$-$\underline{CCF_3}$), 4.17 (t, *J* = 7.4 Hz, 2H), 1.78 (qt, *J* = 7.3 Hz, 2H), 1.38 (sx, *J* = 7.3 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$ + 1% TFA) δ 163.8, 160.0, 139.8, 134.8, 134.1, 131.0, 130.8, 130.2, 130.1, 126.0, 125.5, 125.2, 122.9, 121.9, 120.7, 117.6, 116.6, 98.5, 69.7, 63.8, 41.3, 30.1, 20.3, 13.7.
^{19}F NMR (282 MHz, $CDCl_3$) δ -75.72
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2950, 2918, 2851, 1701, 1660, 1618, 1530, 1510, 1485, 1436, 1392, 1378, 1335, 1231, 1205, 1187, 1112, 905, 840, 750, 694 cm^{-1}
ESI-HRMS calculated for $C_{25}H_{21}F_2N_4O_2$ $[M+H]^+$ 447.1633, found 447.1627
**TFA was added to improve solubility*.

1-(11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)piperidine-4-carboxylic acid (6b)

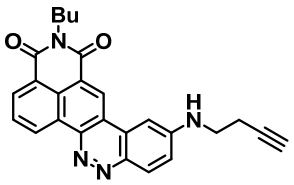


$C_{28}H_{26}N_4O_4$
MW: 482,54
Yield: 60 %
Dark Red Solid

Compound **6b** was prepared according to the general procedure with isonipecotic acid (14.0 mg, 0.11 mmol) overnight. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **6b** (15 mg, 60 %) as a dark red solid.

^{1}H NMR (300 MHz, DMSO) δ 9.48 (d, *J* = 7.3 Hz, 1H), 9.03 (s, 1H), 8.36 (d, *J* = 6.3 Hz, 1H), 8.22 (d, *J* = 9.4 Hz, 1H), 7.92 (t, *J* = 7.8 Hz, 1H), 7.68 (dd, *J* = 9.4, 2.5 Hz, 1H), 7.46 (d, *J* = 2.8 Hz, 1H), 4.17 (d, *J* = 13.2 Hz, 2H), 3.97 (t, *J* = 7.5 Hz, 2H), 3.19 (t, *J* = 10.8 Hz, 2H), 2.65 (m, 1H), 2.03 (m, 2H), 1.68 – 1.80 (m, 2H), 1.68 (qt, *J* = 7.3 Hz, 2H), 1.37 (sx, *J* = 7.3 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, DMSO) δ 175.9, 163.1, 162.2, 152.2, 142.5, 140.6, 131.9, 130.2, 129.4, 128.4, 126.4, 126.2, 123.1, 122.3, 121.9, 120.2, 117.23, 102.7, 99.4, 46.4, 40.1 (overlap with DMSO-d6 signal – 2C), 29.6, 29.0, 27.6 (2C), 19.8, 13.7.
Rf (DCM/MeOH 95:5) = 0.3
IR (neat): ν = 2958, 2920, 2851, 1722, 1699, 1655, 1607, 1516, 1489, 1435, 1400, 1337, 1259, 1229, 1188, 1133, 1114, 1098, 1028, 930,863, 815, 786, 751, 718, 692, 667 cm^{-1}
ESI-HRMS calculated for $C_{28}H_{27}N_4O_4$ $[M+H]^+$ 483.2032, found 483.2051

2-(but-3-yn-1-ylamino)-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (6c)

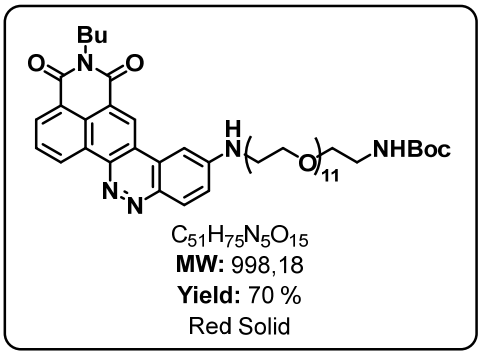


$C_{26}H_{22}N_4O_2$
MW: 422,49
Yield: 62 %
Dark Orange Solid

Compound **6c** was prepared according to the general procedure with But-3-yn-1-amine (9.0 µL, 0.11 mmol) for 4 h. The crude product was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **6c** (14.0 mg, 62 %) as a dark orange solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 9.54 (s, 1H), 8.77 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.56 (d, *J* = 9.0 Hz, 1H), 8.08 (dd, *J* = 8.3, 7.5 Hz, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.31 (dd, *J* = 9.1, 2.4 Hz, 1H), 5.02 (t, *J* = 5.5 Hz, 1H, CinNapht-NH-CH_2-CCH), 4.32 – 4.20 (m, 2H), 3.65 (m, 2H, CinNapht-NH-CH_2-CH_2-CCH), 2.72 (td, *J* = 6.4, 2.6 Hz, 2H, CinNapht-NH-CH_2-CH_2-CCH), 2.18 (t, 1H, *J* = 2.6 Hz, CinNapht-NH-CH_2-CH_2-CCH,), 1.79 (qt, *J* = 7.2 Hz, 2H), 1.49 (sx, 2H, *J* = 7.2 Hz), 1.02 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 164.2, 150.7, 139.8, 133.3, 131.4, 130.9, 129.8, 128.8, 126.5, 124.9, 123.5, 121.0, 118.3, 96.6, 80.7, 71.2, 70.5, 55.5, 42.0, 40.5, 30.3, 29.7, 20.4, 19.1, 13.8
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2958, 2914, 2885, 1699, 1657, 1619, 1607, 1517, 1492, 1459, 1436, 1379, 1328, 1290, 1267, 1230, 1183, 1124, 1068, 943, 905, 831, 824, 786, 753, 693 cm^{-1}
ESI-HRMS calculated for $C_{26}H_{23}N_4O_2$ $[M+H]^+$ 423.1821, found 423.1831

tert-butyl (35-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)-3,6,9,12, 15,18,21,24,27,30,33-undecaoxapentatriacontyl)carbamate (6d')

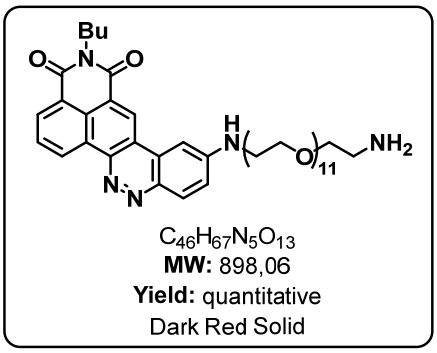


$C_{51}H_{75}N_5O_{15}$
MW: 998,18
Yield: 70 %
Red Solid

Compound **6d'** was prepared according to the general procedure with *O*-(2-Aminoethyl)-*O*'-[2-(Boc-amino) ethyl]decaethylene glycol (69 mg, 0.107 mmol) for 4 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 95:5, v/v) to afford compound **6d'** (35 mg, 70 %) as a red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (d, *J* = 8.2 Hz, 1H), 9.32 (s, 1H), 8.62 (d, *J* = 7.3 Hz, 1H), 8.35 (d, *J* = 8.7 Hz, 1H), 7.94 (t, *J* = 7.8 Hz, 1H), 7.31 – 7.18 (m, 2H), 5.77 (s, 1H), 5.01 (s, 1H), 4.16 (t, *J* = 7.5 Hz, 2H), 3.88 – 3.73 (m, 2H), 3.68 – 3.53 (m, 40H), 3.45 (t, *J* = 4.8 Hz, 2H), 3.23 (d, *J* = 4.1 Hz, 2H), 2.31 (brs, 2H), 1.75 (qt, *J* = 7.4 Hz, 2H), 1.42 (sx, *J* = 7.4 Hz, 2H), 1.36 (s, 9H, CinNapht-PEG11-CH_2-CH_2-NH-C(CH_3)$_3$), 0.94 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 163.5, 151.4, 143.8, 141.9, 132.7, 131.0, 130.6, 129.5, 128.4, 127.2, 126.4, 124.8, 122.8, 122.3, 121.4, 118.0, 95.4, 70.4, 70.3, 70.1, 68.8, 41.3, 40.3, 30.1, 28.3, 20.3, 13.7
Rf (DCM/MeOH 95:5) = 0.4
IR (neat): ν = 2868, 1701, 1661, 1619, 1590, 1541, 1505, 1477, 1455, 1437, 1363, 1344, 1271, 1239, 1221, 1180, 1130, 1107, 1083, 942, 916, 874, 829, 800, 779, 751, 736, 696 cm^{-1}
ESI-HRMS calculated for $C_{51}H_{76}N_5O_{15}$ $[M+H]^+$ 998.5338, found 998.5356

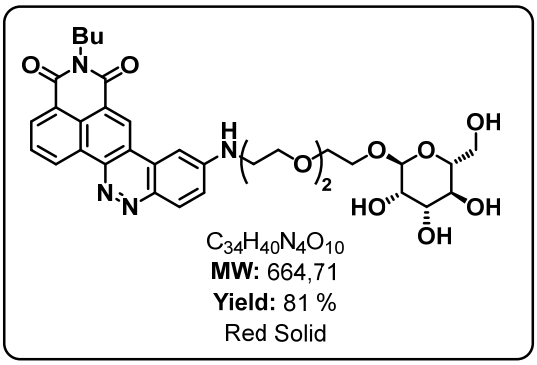
2-((35-amino-3,6,9,12,15,18,21,24,27,30,33-undecaoxapentatriacontyl)amino)-11-butyl-10H-benzo[c]isoquinolino [4,5-gh]cinnoline-10,12(11H)-dione (6d)



Compound **6d** was prepared by dissolving compound **6d'** (35.0 mg, 0.037 mmol) in a mixture of DCM (0.50 mL) and TFA (0.50 mL). After stirring for 1 h, the mixture was evaporated and dried under vacuum, to afford compound **6d** (33.0 mg, quantitative) as a dark red solid without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (d, *J* = 8.0 Hz, 1H), 9.22 (s, 1H), 8.68 (d, *J* = 6.8 Hz, 1H), 8.34 (d, *J* = 9.2 Hz, 1H), 8.00 (t, *J* = 7.9 Hz, 1H), 7.55 - 7.44 (m, 3H), 7.30 (s, 1H), 6.80 (s, 5H), 4.18 (t, *J* = 7.5 Hz, 2H), 3.90 (t, *J* = 4.7 Hz, 2H), 3.78 - 3.61 (m, 40H), 3.18 (br, 2H), 1.82 - 1.67 (m, 2H), 1.55 - 1.40 (m, 2H), 1.00 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 162.8, 153.7, 141.1, 140.4, 131.7, 130.7, 130.0, 128.9, 127.5, 127.3, 127.1, 125.4, 124.0, 123.4, 122.4, 118.9, 95.3, 70.1, 69.9, 69.7, 69.4, 68.5, 66.6, 43.3, 40.3, 39.7, 29.9, 29.4, 20.1, 13.5
Rf (DCM/MeOH 9:1) = 0.2
IR (neat): ν = 2921, 2895, 1665, 1622, 1502, 1438, 1406, 1349, 1290, 1179, 1108, 951, 832, 798, 786, 751, 720, 707, 694 cm^{-1}
ESI-HRMS calculated for $C_{46}H_{68}N_5O_{13}$ $[M+H]^+$ 898.4814, found 898.4799

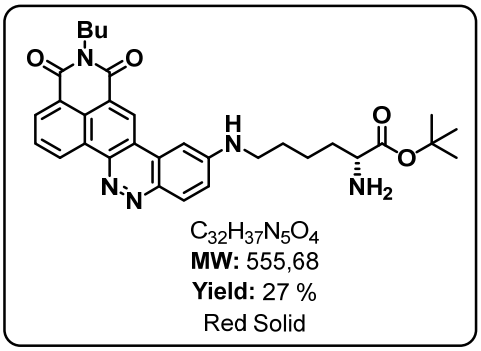
11-butyl-2-((2-(2-(2-(((2S,3S,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)ethoxy)ethoxy)ethyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (6e)



Compound **6e** was prepared according to the general procedure with 2-[2-(2-Aminoethoxy)ethoxy]ethyl α-D-mannopyranoside **9** (49,0 mg, 0.107 mmol) for 4 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 95:5, v/v) to afford compound **6e** (29 mg, 81 %) as a red solid.

^{1}H NMR (699 MHz, MeOD) δ 9.18 (d, *J* = 7.9 Hz, 1H), 8.48 (s, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.17 (dd, *J* = 9.0, 2.2 Hz, 1H), 6.71 (s, 1H), 3.99 (t, *J* = 7.8 Hz, 2H), 3.95 – 3.83 (m, 5H), 3.82 – 3.71 (m, 7H), 3.71 – 3.61 (m, 3H), 3.50 – 3.43 (m, 2H), 1.73 – 1.66 (m, 2H), 1.48 (m, 2H), 1.05 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (176 MHz, MeOD) δ 164.9, 164.1, 153.6, 143.9, 142.2, 132.3, 131.7, 130.7, 129.6, 129.4, 127.7, 126.6, 126.0, 123.2, 118.6, 101.8, 74.7, 72.7, 72.2, 71.8, 71.6, 71.5, 70.4, 68.7, 67.8, 63.0, 44.1, 41.3, 31.2, 30.8, 21.5, 14.3
Rf (DCM/MeOH 8:2) = 0.1
IR (neat): ν = 2957, 2925, 2855, 1733, 1665, 1623, 1460, 1378, 1215, 1082, 1053, 976, 750, 668 cm^{-1}
ESI-HRMS calculated for $C_{34}H_{41}N_4O_{10}$ $[M+H]^+$ 665.2823, found 665.2800

tert-butyl N6-(11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)-L-lysinate (6f)

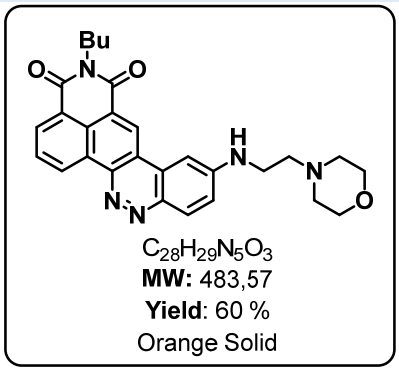


$C_{32}H_{37}N_5O_4$
MW: 555,68
Yield: 27 %
Red Solid

Compound **6f** was prepared according to the general procedure with Fmoc-Lys-OtBu (49.0 mg, 0.11 mmol) for 4 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 95:5, v/v) to afford compound **6f** (12.0 mg, 27 %) as a red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91 (dd, *J* = 8.3, 1.1 Hz, 1H), 9.37 (s, 1H), 8.68 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.01 (dd, *J* = 8.1, 7.6 Hz, 1H), 7.31 (d, *J* = 2.2 Hz, 1H), 7.20 (dd, *J* = 9.1, 2.3 Hz, 1H), 5.01 (t, *J* = 4.8 Hz, 1H, CinNapht-NH-$(CH_2)_4$Lys,), 4.27 – 4.17 (m, 2H), 3.50 – 3.36 (m, 3H, CH_2 + CH(Lys)), 1.86 (br, 4H), 1.78 (m, 2H), 1.65 (m, 2H), 1.48 (s, 9H, $C(CH_3)_3$), 1.24 (br, 4H), 1.01 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 164.2, 163.8, 151.4, 144.0, 142.2, 133.1, 131.3, 130.9, 129.8, 128.7, 127.6, 126.7, 125.1, 123.2, 122.6, 121.1, 118.2, 95.9, 81.3, 55.0, 43.6, 40.6, 34.5, 30.4, 28.8, 28.2 (3C), 23.4, 20.5, 14.0
Rf (DCM/MeOH 95:5) = 0.5
IR (neat): ν = 2957, 2924, 2855, 1728, 1702, 1661, 1621, 1600, 1537, 1501, 1467, 1436, 1401, 1368, 1338, 1255, 1224, 1156, 1119, 1079, 822, 785, 751, 694 cm^{-1}
ESI-HRMS calculated for $C_{32}H_{38}N_5O_4$ $[M+H]^+$ 556.2924, found 556.2906

11-butyl-2-((2-morpholinoethyl)amino)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (6g)

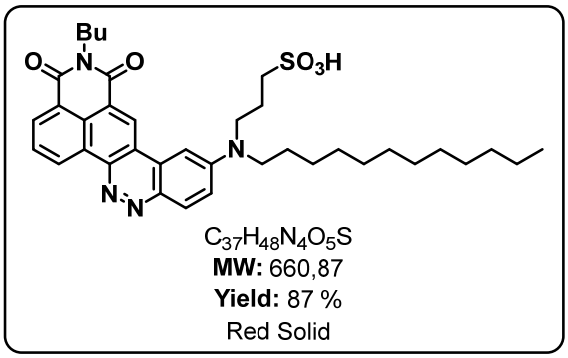


$C_{28}H_{29}N_5O_3$
MW: 483,57
Yield: 60 %
Orange Solid

Compound **6g** was prepared according to the general procedure with 2-morpholin-4-ylethanamine (14.0 µL, 0.11 mmol) for 1 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 95:5, v/v) to afford compound **6g** (16.0 mg, 60 %) as an orange solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (d, *J* = 8.2 Hz, 1H), 9.37 (s, 1H), 8.69 (d, *J* = 7.3 Hz, 1H), 8.45 (d, *J* = 9.0 Hz, 1H), 8.01 (t, *J* = 7.8 Hz, 1H), 7.33 (s, 1H), 7.27 (m, 1H), 5.54 (brs, 1H, CinNapht-NH-CH_2-CH_2-Morpholine), 4.22 (t, *J* = 7.4 Hz, 2H), 3.85 – 3.75 (m, 4H), 3.47 (q, 2H, *J* = 5.6 Hz, CinNapht-NH-CH_2-CH_2-Morpholine), 2.82 (t, *J* = 5.6 Hz, 2H, CinNapht-NH-CH_2-CH_2-Morpholine), 2.59 (brs, 4H), 1.76 (qt, *J* = 7.4 Hz, 2H), 1.48 (sx, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.1, 163.7, 151.1, 143.9, 142.0, 133.0, 131.2, 130.8, 129.7, 128.6, 127.4, 126.5, 124.9, 123.1, 122.5, 121.0, 118.1, 96.1, 66.9, 56.3, 53.3, 40.5, 39.3, 30.2, 20.4, 13.9.
Rf (DCM/MeOH 95:5) = 0.5
IR (neat): ν = 2957, 2829, 2857, 2816, 1699, 1656, 1614, 1577, 1559, 1526, 1500, 1467, 1456, 1435, 1400, 1370, 1335, 1299, 1272, 1223, 1182, 1114, 1079, 1068, 1035, 1009, 939, 914, 870, 823, 782, 751, 732, 694, 670 cm^{-1}
ESI-HRMS calculated for $C_{28}H_{30}N_5O_3$ $[M+H]^+$ 484.2349, found 484.2332

3-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)(dodecyl)amino)propane-1-sulfonic acid (6h)

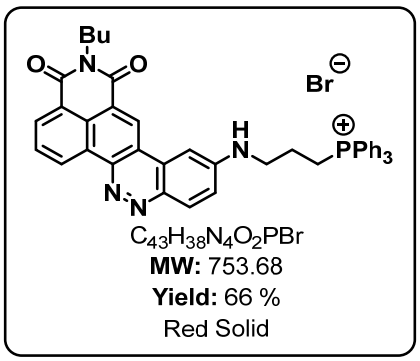


$C_{37}H_{48}N_4O_5S$
MW: 660,87
Yield: 87 %
Red Solid

Compound **6h** was prepared according to the general procedure with 3-(dodecylamino)propane-1-sulfonic acid (33 mg, 0.107 mmol) for 5 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 98:2 to 85:15, v/v) to afford compound **6h** (30 mg, 87 %) as a red solid.

^{1}H NMR (500 MHz, DMSO) δ 9.72 (d, *J* = 8.2 Hz, 1H), 9.39 (s, 1H), 8.56 (d, *J* = 7.3 Hz, 1H), 8.38 (d, *J* = 9.3 Hz, 1H), 8.07 (t, *J* = 7.8 Hz, 1H), 7.67 (dd, *J* = 9.5, 2.5 Hz, 1H), 7.52 (d, *J* = 2.6 Hz, 1H), 4.08 (t, *J* = 7.5 Hz, 2H), 3.78 (t, *J* = 7.7 Hz, 2H), 3.65 (t, *J* = 7.7 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 1.99 (m, 2H), 1.68 (m, 4H), 1.42 (m, 6H), 1.29 (m, 4H), 1.22 (m, 4H), 1.15 (m, 6H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.77 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, DMSO) δ 163.5, 162.7, 150.9, 142.6, 141.3, 132.5, 130.6, 129.9, 129.0, 128.8, 127.1, 126.6, 124.0, 122.6, 122.4, 119.2, 117.6, 96.8, 50.5, 49.7, 48.6, 31.4, 29.8, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 26.6, 26.5, 23.6, 22.2, 20.0, 14.1, 13.9.
Rf (DCM/MeOH 95:5) = 0.1
IR (neat): ν = 2956, 2922, 2853, 1705, 1666, 1610, 1519, 1492, 1466, 1377, 1339, 1229, 1186, 1133, 1044, 787, 722 cm^{-1}
ESI-HRMS calculated for $C_{37}H_{49}N_4O_5S$ $[M+H]^+$ 661.3424, found 661.3414

(3-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)propyl)triphenyl phosphonium (6i)

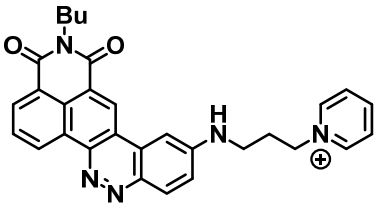


$C_{43}H_{38}N_4O_2PBr$
MW: 753.68
Yield: 66 %
Red Solid

Compound **6i** was prepared according to the general procedure with 3-aminopropyl(triphenyl)phosphanium bromide·HBr (52 mg, 0.11 mmol) for 1 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 to 90:10, v/v) to afford compound **6i** (26 mg, 66 %) as a red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (d, *J* = 8.2 Hz, 1H), 9.17 (s, 1H), 8.84 (s, 1H), 8.63 (d, *J* = 7.3 Hz, 1H), 8.33 (d, *J* = 9.0 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.94 (t, *J* = 7.8 Hz, 1H), 7.82 (dd, *J* = 12.5, 7.8 Hz, 6H, $\underline{CH}_{2Ar}$(TPP)), 7.69 (t, *J* = 7.3 Hz, 3H, $\underline{CH}_{Ar}$(TPP)), 7.60 (td, *J* = 7.4, 2.9 Hz, 6H, $\underline{CH}_{2Ar}$(TPP)), 6.99 (s, 1H, CinNapht-$\underline{NH}$-CH_2-CH_2-CH_2-TPP), 4.17-4.21 (m, 4H), 3.63 (br, 2H), 2.13 (br, 2H), 1.75 (qt, *J* = 7.4 Hz, 2H), 1.46 (sx, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 163.7, 152.0, 144.0, 141.9, 134.9 (d, *J*(C-P) = 2.3 Hz), 133.4 (d, *J*(C-P) = 9.9 Hz), 132.4, 130.9, 130.7, 130.4 (d, *J*(C-P) = 12.5 Hz), 129.5, 128.2, 127.1, 126.6, 124.9, 123.7, 122.2, 118.3 (d, *J*(C-P) = 85.9 Hz), 118.0, 92.9, 42.4 (d, *J*(C-P) = 16.4 Hz), 40.3, 21.4 (d, *J*(C-P) = 32.0 Hz), 21.2 (d, *J* = 16.0 Hz), 24.9, 21.3, 20.5, 13.7
^{31}P NMR (202 MHz, $CDCl_3$) δ 24.77
Rf (DCM/MeOH 95:5) = 0.3
IR (neat): ν = 2959, 2928, 1699, 1657, 1621, 1600, 1541, 1501, 1467, 1437, 1401, 1371, 1338, 1280, 1224, 1181, 1115, 1076, 997, 917, 848, 822, 784, 724, 693 cm^{-1}
ESI-HRMS calculated for $C_{43}H_{38}N_4O_2P$ $[M]^+$ 673.2732, found 673.2710

1-(3-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)propyl)pyridin-1-ium (6j)

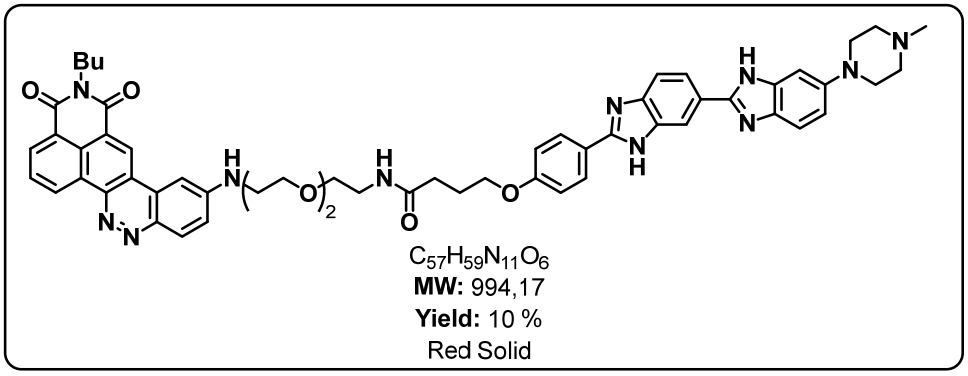


$C_{30}H_{28}N_5O_2^+$
MW: 490,59
Yield: 70 %
Dark Red Solid

Compound **6j** was prepared according to the general procedure with 1-(3-aminopropyl)pyridin-1-ium bromide · HBr (32 mg, 0.107 mmol) for 1 h. The crude product was purified by flash chromatography by RP-HPLC (H_2O + 1% TFA/MeCN + 1% TFA 90:10 to 0:100 in 90 min) to afford compound **6j** (18 mg, 70 %) as a dark red solid.

^{1}H NMR (300 MHz, DMSO) δ 9.71 (dd, *J* = 8.3, 1.2 Hz, 1H), 9.27 (s, 1H), 9.22 – 9.16 (m, 2H), 8.63 (tt, *J* = 7.7, 1.3 Hz, 1H), 8.56 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.31 (d, *J* = 9.7 Hz, 1H), 8.19 (dd, *J* = 7.7, 6.3 Hz, 2H, ($C\underline{H}_{Ar}$)$_2$ (Pyr)), 8.13 – 8.03 (m, 1H, $C\underline{H}_{Ar}$ (Pyr)), 7.55 (d, *J* = 5.9 Hz, 1H, CinNapht-$\underline{NH}$-$(CH_2)_3$-Pyr), 7.43 – 7.34 (m, 2H, ($C\underline{H}_{Ar}$)$_2$ (Pyr)), 4.84 (t, *J* = 7.2 Hz, 2H), 4.08 (t, *J* = 7.4 Hz, 2H), 3.51 (m, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.67 (qt, *J* = 7.3 Hz, 2H), 1.40 (sx, *J* = 7.3 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, DMSO) δ 163.3, 162.6, 151.9, 145.6, 144.9 (2C), 143.2, 132.0, 130.5, 129.6, 128.7, 128.1 (2C), 126.8, 126.5, 124.4, 122.5, 122.2, 117.4, 59.0, 29.7, 29.6, 19.8, 13.7
Rf (DCM/MeOH 95:5) = 0.8
IR (neat): ν = 2964, 1701, 1658, 1618, 1600, 1488, 1471, 1453, 1434, 1406, 1381, 1327, 1271, 1224, 1169, 1111, 1066, 938, 879, 826, 798, 782, 749, 717, 691, 683 cm^{-1}
ESI-HRMS calculated for $C_{30}H_{28}N_5O_2$ $[M]^+$ 490.2243 found 490.2224

N-(2-(2-(2-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)ethoxy)ethoxy)ethyl)-4-(4-(6-(4-methylpiperazin-1-yl)-1H,3'H-[2,5'-bibenzo[d]imidazol]-2'-yl)phenoxy)butanamide (6k)



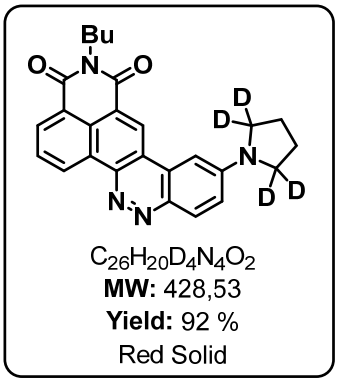
$C_{57}H_{59}N_{11}O_6$
MW: 994,17
Yield: 10 %
Red Solid

Compound **6k** was prepared according to the general procedure with N-(2-(2-(2-aminoethoxy)ethoxy)ethyl)-4-(4-(6-(4-methylpiperazin-1-yl)-1H,3'H-[2,5'-bibenzo[d]imidazol]-2'-yl) phenoxy)butanamide (34 mg, 0.05 mmol) for 1 h. The crude product was purified by flash chromatography by RP-HPLC (H_2O + 1% TFA/MeCN + 1% TFA 90:10 to 0:100 in 90 min) to afford compound **6k** (26 mg, 66 %) as a red solid.

^{1}H NMR (699 MHz, DMSO) δ 9.73 (d, *J* = 8.1 Hz, 1H), 9.39 (s, 1H), 8.52 (d, *J* = 7.2 Hz, 1H), 8.32 (d, *J* = 9.0 Hz, 1H), 8.23 (br, 1H), 8.04 (m, 2H), 7.93 (m, 2H), 7.71 (m, 1H), 7.58 (br, 2H), 7.52 (s, 1H), 7.50 – 7.46 (m, 2H), 7.26 (m, 1H), 7.19 (m, 1H), 7.11 (m, 1H), 7.01 (m, 2H), 4.07 (t, *J* = 7.5 Hz, 2H), 3.99 (t, *J* = 6.5 Hz, 2H), 3.73 (t, *J* = 5.4 Hz, 2H), 3.62 (m, 2H), 3.58 (m, 4H), 3.50 (s, 2H), 3.44 (m, 4H), 3.21 (m, 4H), 2.87 (s, 2H), 2.25 (t, *J* = 7.4 Hz, 2H), 1.93 (m, 2H), 1.65 (m, 2H), 1.38 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (176 MHz, DMSO) δ 171.6, 163.3, 162.7, 160.1, 158.1, 157.9, 157.8, 157.6, 152.3, 143.3, 141.2, 131.9, 130.3, 129.6, 128.8, 128.5, 128.1, 126.9, 126.6, 124.5, 122.4, 122.2, 122.0, 118.1, 117.5, 116.4, 114.7, 69.7, 69.5, 69.1, 68.8, 67.0, 52.6, 47.4, 42.6, 42.1, 38.5, 31.5, 29.6, 24.7, 19.8, 13.7
Rf (DCM/MeOH 95:5) = 0.1
IR (neat): ν = 2964, 2939, 2871, 1697, 1651, 1595, 1506, 1457, 1437, 1382, 1349, 1252, 1225, 1178, 1118, 990, 963, 822, 785, 719 cm^{-1}
ESI-HRMS calculated for $C_{57}H_{59}N_{11}O_6$ $[M]^+$ 994.4728, found 994.4725

11-butyl-2-(pyrrolidin-1-yl-2,2,5,5-d4)-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (6l)

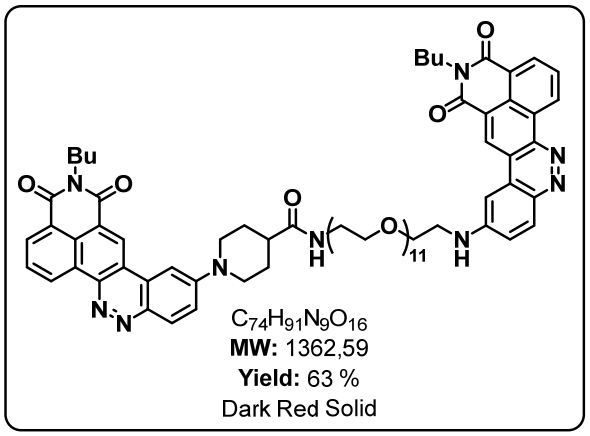


$C_{26}H_{20}D_4N_4O_2$
MW: 428,53
Yield: 92 %
Red Solid

Compound **6l** was prepared according to the general procedure with deuterated pyrrolidine hydrochloride (12.0 mg, 0.11 mmol) for 1 h. The crude product was purified by flash chromatography on silica gel (DCM/MeOH 99:1 v/v) to afford compound **6l** (21.0 mg, 92 %) as a red solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.88 (dd, *J* = 8.2, 1.3 Hz, 1H), 9.24 (s, 1H), 8.65 (dd, *J* = 7.3, 1.3 Hz, 1H), 8.40 (d, *J* = 9.2 Hz, 1H), 7.98 (t, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 1H), 4.20 (t, *J* = 7.6 Hz, 2H), 2.16 (s, 4H, CinNapht-N-$(CD_2)_2$-$(\underline{CH_2})_2$), 1.76 (m, 2H), 1.49 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 164.1, 163.6, 149.8, 143.0, 141.8, 133.0, 131.0, 130.8, 129.6, 128.3, 127.3, 126.4, 124.4, 122.6, 122.4, 118.6, 117.8, 96.8, 40.4, 30.2, 25.4, 25.3, 20.4, 13.9.
^{2}D NMR (61 MHz, $CDCl_3$) δ 3.55 (bs, 4D).
Rf (DCM/MeOH 95:5) = 0.6
IR (neat): ν = 2962, 2923, 2858, 1705, 1668, 1604, 1518, 1484, 1471, 1458, 1433, 1405, 1384, 1372, 1323, 1265, 1231, 1160, 1120, 1095, 1071, 1010, 941, 905, 863, 844, 819, 783, 752, 738, 695, 690, 667 cm^{-1}
ESI-HRMS calculated for $C_{26}H_{20}D_4N_4O_2$ $[M+H]^+$ 429.2150, found 429.2178

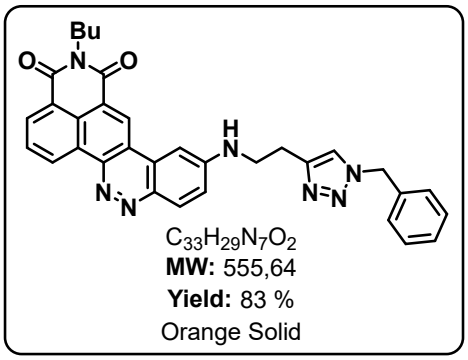
1-(11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)-N-(35-((11-butyl-10,12-dioxo-11,12-dihydro-10H-benzo[c]isoquinolino[4,5-gh]cinnolin-2-yl)amino)-3,6,9,12,15,18,21,24,27,30,33-undecaoxapentatriacontyl)piperidine-4-carboxamide (7a)



To a solution of compound **6d** (5.6 mg, 6.20 µmmol, 1eq) in DMF (62 µL) was added compound **6b** (3 mg, 6.20 µmol, 1eq), BOP (2.9 mg, 6.5 µmol, 1.05 eq). The mixture was cooled down to 0 °C than DIEA (2.1 µL, 0.0124 mmol, 2 eq) was added. The mixture was stirred at room temperature for 1 h. The crude mixture was concentrated *in vacuo* and purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **7a** (5 mg, 63 %) as a dark red solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (d, *J* = 8.4 Hz, 2H), 9.13 (s, 2H), 8.60 (t, *J* = 6.6 Hz, 2H), 8.43 (s, 2H), 7.93 (t, *J* = 7.9 Hz, 2H), 7.52 (d, *J* = 9.4 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.14 (s, 1H), 6.49 (s, 1H), 4.29 – 4.21 (m, 2H), 4.16 (d, *J* = 13.1 Hz, 4H), 3.91 (d, *J* = 5.5 Hz, 2H), 3.75 (d, *J* = 5.0 Hz, 4H), 3.70 – 3.63 (m, 40H), 3.52 (s, 2H), 3.23 – 3.10 (m, 4H), 2.66 (d, *J* = 9.4 Hz, 2H), 2.11 (d, *J* = 12.2 Hz, 2H), 1.96 (s, 2H), 1.74 (d, *J* = 8.1 Hz, 4H), 1.03 – 0.98 (m, 6H).
Rf (DCM/MeOH 95:5) = 0.1
IR (neat): ν = 2962, 2870, 1700, 1655, 1618, 1535, 1490, 1456, 1436, 1400, 1345, 1228, 1095, 1031, 948, 912, 842, 784, 750, 694, 664 cm^{-1}
ESI-HRMS calculated for $C_{74}H_{91}N_9O_{16}$ $[M+H]^+$ 1362.6662, found 1362.6705

2-((2-(1-benzyl-1H-1,2,3-triazol-4-yl)ethyl)amino)-11-butyl-10H-benzo[c]isoquinolino[4,5-gh]cinnoline-10,12(11H)-dione (7b)



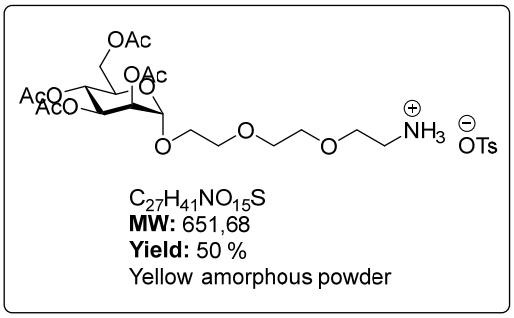
To a solution of compound **6c** (10 mg, 0.024 mmol, 1 eq) in DCM/H_2O (250 µL, 1:1 v/v) was added benzylazide (3.2 mg, 0.024 mmol, 1 eq), $CuSO_4.5H_2O$ (0.6 mg, 0.0024 mmol, 0.1 eq) and sodium ascorbate (1.4 mg, 0.0072 mmol, 0.3 eq). The mixture was stirred under argon atmosphere for 3 h. The crude mixture was washed with H_2O and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (DCM/MeOH 9:1, v/v) to afford compound **7b** (11 mg, 83 %) as an orange solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.96 (dd, *J* = 8.3, 1.3 Hz, 1H), 9.44 (s, 1H), 8.73 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.45 (d, *J* = 8.9 Hz, 1H), 8.04 (dd, *J* = 8.3, 7.4 Hz, 1H), 7.45 – 7.32 (m, 5H, CinNapht-NH-CH_2-CH_2-triazol-CH_2-C_6H_5), 7.29 (m, 2H), 5.67 (s, 1H, CinNapht-NH-CH_2-CH_2-triazol-Bn), 5.54 (s, 2H, CinNapht-NH-CH_2-CH_2-triazol-CH_2-C_6H_5), 4.25 (dd, *J* = 8.5, 6.5 Hz, 2H), 3.75 (m, 2H, CinNapht-NH-CH_2-CH_2-triazol-CH_2-C_6H_5), 3.64 (s, 1H), 3.19 (m, 2H, CinNapht-NH-CH_2-CH_2-triazol-CH_2-C_6H_5), 1.78 (m, 2H), 1.52 – 1.45 (m, 2H), 1.03 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 164.4, 151.7, 148.1, 135.1, 133.6, 131.8, 131.5, 130.3, 129.8, 129.4 (2C), 129.2, 128.7, 127.2 (2C), 125.5, 123.8, 123.1, 121.9, 96.4, 71.2, 54.9, 43.5, 41.1, 32.5, 30.8, 30.3, 25.4, 23.3, 21.0, 14.2, 14.0.
Rf (DCM/MeOH 95:5) = 0.7

IR (neat): ν = 2930, 2918, 2850, 1730, 1698, 1659, 1621, 1599, 1577, 1542, 1499, 1456, 1436, 1402, 1338, 1260, 1224, 1093, 1031, 816, 784, 750, 715, 694 cm^{-1}

ESI-HRMS calculated for $C_{33}H_{29}N_7O_2$ $[M+H]^+$ 556.2057, found 556.2068

1-Ammonium-3,6-dioxaoct-8-yl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside p-toluenesulfonate (8)

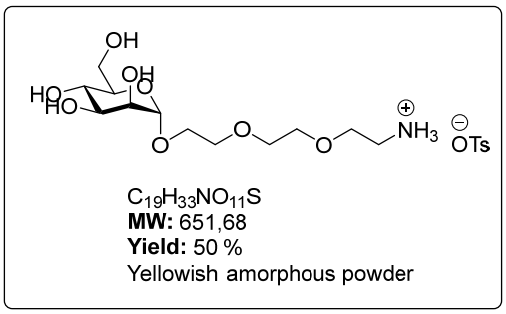


$C_{27}H_{41}NO_{15}S$
MW: 651,68
Yield: 50 %
Yellow amorphous powder

Compound x was synthesized using a procerudre adapted from Yu and coworkers.[2] A suspension of 1-azido-3,6-dioxaoct-8-yl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (1.015 g, 2.01 mmol, 1 eq), Pd/C 10% (100 mg, 10%w) and *p*-toluenesulfonic acid (0.360 g, 2.10 mmol, 1.04 eq) in anhydrous MeOH (75 mL) was stirred under H_2 atmosphere (1 bar). The reaction was monitored by TLC (eluent: Heptane/EtOAc 4:6 v/v) and stirred until completion (1h30). The mixture was filtered on a pad of celite and washed with MeOH (50 mL). The solvent was evaporated off to afford the desired 1-Ammonium-3,6-dioxaoct-8-yl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside *p*-toluenesulfonate (1.144 g, 1.76 mmol, 88%) as a yellow amorphous solid. Analysis were in accordance with the litterature

^{1}H NMR (300 MHz, CD_3OD) : 7.71 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.29-5.23 (m, 3H), 4.90 (bs, 1H), 4.25 (dd, *J* = 12.3, 4.9 Hz, 1H), 4.17-4.04 (m, 3H), 3.83-3.89 (m, 1H), 3.75-3.65 (m, 10H), 3.20-3.08 (m, 2H), 2.37 (s, 3H), 2.15 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H).

1-Ammonium-3,6-dioxaoct-8-yl α-D-mannopyranoside p-toluenesulfonate (9)

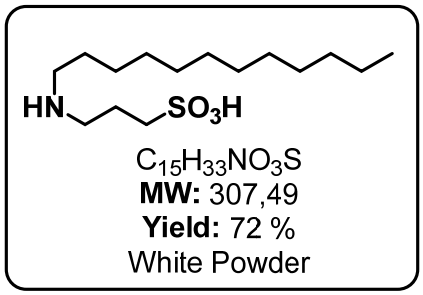


$C_{19}H_{33}NO_{11}S$
MW: 651,68
Yield: 50 %
Yellowish amorphous powder

A solution of 1-ammonium-3,6-dioxaoct-8-yl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside *p*-toluenesulfonate (200 mg, 0.31 mmol) in a mixture of MeOH/H_2O/NEt_3 (4:1:1 v/v/v) was stirred under Ar atmosphere. The reaction was monitored by TLC (eluent: EtOAc/Water/*i*PrOH 8:1:1 v/v/v) and stirred until completion (24h). The solvents were evaporated off then the residue was purified by reversed phase C18 silica gel column chromatography (H_2O/MeCN+0.1% TFA 9:1 to 0:1 v/v). The fractions were collected, concentrated under vacuum to remove acetonitrile and then freeze-dried to afford the desired 1-ammonium-3,6-dioxaoct-8-yl α-D-mannopyranoside *p*-toluenesulfonate as a yellow amorphous powder (80 mg, 0.16 mmol, 50%). Analysis were in accordance with the litterature

^{1}H NMR (300 MHz, D_2O) : 7.72 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 4.92 (s, 1H), 4.02-3.64 (m18H), 2.42 (s, 3H)

3-(dodecylamino)propane-1-sulfonic acid (10)



$C_{15}H_{33}NO_3S$
MW: 307,49
Yield: 72 %
White Powder

The compound was prepared using a synthesis protocol adapted from Masahiko Abea's article.[3] To a solution of dodecylamine (100 mg, 0.539 mmol, 1 eq) in CH_3CN was added 1,3-propane sultone (79 mg, 0.647 mg, 1.2 eq) and refluxed leading to the formation of a white precipitate within 5 min. After 30 min under reflux, the mixture was filtered, and the solid residue was recovered and washed twice with warm CH_3CN. The resulting solid was then dried under vacuum to afford compound the 3-(dodecylamino)propane-1-sulfonic acid (120 mg, 72%) as a white powder. NMR analysis were in accordance with the literature[3]

Photophysical characterization

UV-vis absorption measurements (scan mode) were conducted on a Cary UV 100 spectrophotometer (Varian) using rectangular 10 mm path length quartz cuvettes at 25°C. Fluorescence spectroscopic studies (scan mode) were performed with a Spectrofluorimètre FS 5 (Edinburgh) at 25°C, with rectangular 10 mm path length quartz cuvettes from Hellma. The emission and excitation spectra were recorded with a diluted solution lower than 0.1 absorbance values. For the excitation and emission spectra the slits width were adjusted between 2–5 nm. All fluorescence spectra were corrected from the lamp fluctuations and the apparatus response fluctuations. Fluorescence quantum yields were measured at 25°C, using three diluted solution (A<0.1) and three diluted solution of using DCM (QY = 0.43 in EtOH)[4]. For each QY measurements, slit width, excitation wavelength, scan rate, integration time and emission range were kept the same for the reference and the sample. The fluorescence quantum yield was determined thanks to the following formula:

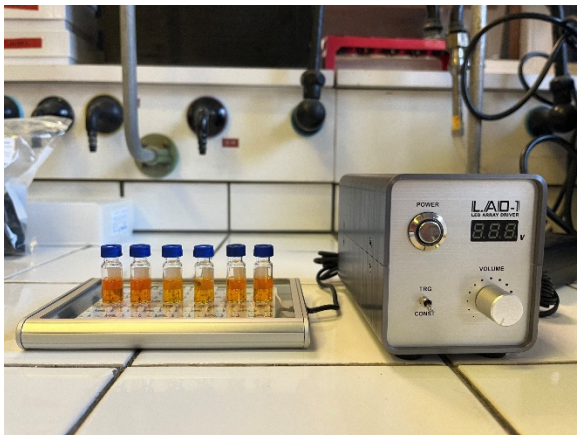
$$\Phi_F(x) = \Phi_F(0)\,\frac{1-10^{-A_0}}{1-10^{-A_x}}\,\frac{S_x}{S_0}\left(\frac{n_x}{n_0}\right)^2$$

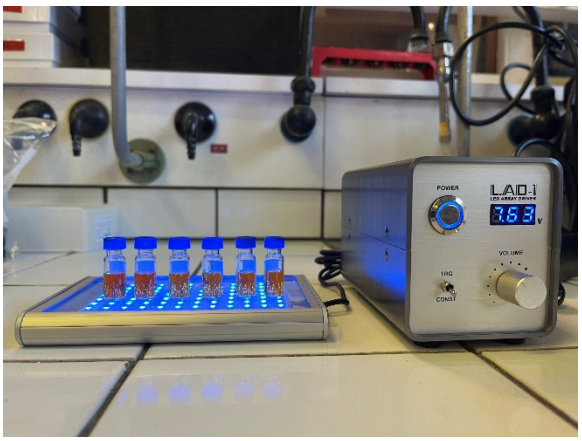
Where S is the slope of the linear plot of the integrated fluorescence intensity in function of the absorbance value, n is the refractive index of the solvents (at 25°C) used in measurements, and the subscripts s and x represent standard and unknown, respectively.

Bleaching experiments:

Bleaching experiments were recorded by using a LED Array Driver (LAD-1 at 10.0 V) and a LED plate (λ=470 nm LED Array LEDA-B). The 10^{-5} M solutions of fluorophores in HPLC vials were put on the LED plate and irradiated at 470 nm for 3h in a black room. Emission spectras and UV-Visible absorption spectras were recorded every 30 minutes during the time of the bleaching. The resulting solutions at t = 0 min and t = 3h were analysed in HPLC-MS.

Experimental set-up:





Cell Culture and Confocal Microscopy

Cell Culture and cell Imaging

Cell lines were obtained from the American type Culture Collection (Rockville, USA) and were cultured according to the supplier's instructions. A459 cells were grown in RPMI 1640 containing 10% FCS and 1% glutamine. Cells were maintained at 37 °C in a humidified atmosphere containing 5% CO2 and were split every 3 or 4 days at a time when enough confluence was obtained. An Ibidi® µ-Slide 8 Well high Glass Bottom plate was seeded with 15 000 cells/well and then maintained at 37 °C in a humidified atmosphere containing 5% CO2 for 24h to 48h. After adequate confluence was obtained, the medium was removed and replaced

by a solution of fluorophore at desired concentration in the appropriate medium, prepared from a stock solution of fluorophore in DMSO, final concentration in DMSO < 1.0%, please note that no solubility issue was noted). The cells were incubated for appropriate amount of time at 37 °C in a humidified atmosphere containing 5% CO2. The fluorophofore solution was then removed and the cells were washed twice with pre-warmed PBS (1X). These wash steps are not required for LD imaging using CinNapht **5n** for which a replacement of the medium is sufficient. Finally, RPMI medium was added before imaging.

Confocal fluorescence microscopy

Fluorescence images were acquired using a Leica SP8-X inverted confocal microscope with a 63× oil immersion objective (HC PL APO CS2 Leica). Excitation was performed using a White laser pulsed at 80MHz set at the desired excitation wavelength or with a Diode 405 nm (Leica, 50 mW). Detection was carried out by using PMT detector (Hamamatsu 6357) or GaAsP Hybrid (Hamamatsu) collecting photons over the appropriate emission wavelength window.

Colocalization experiments:

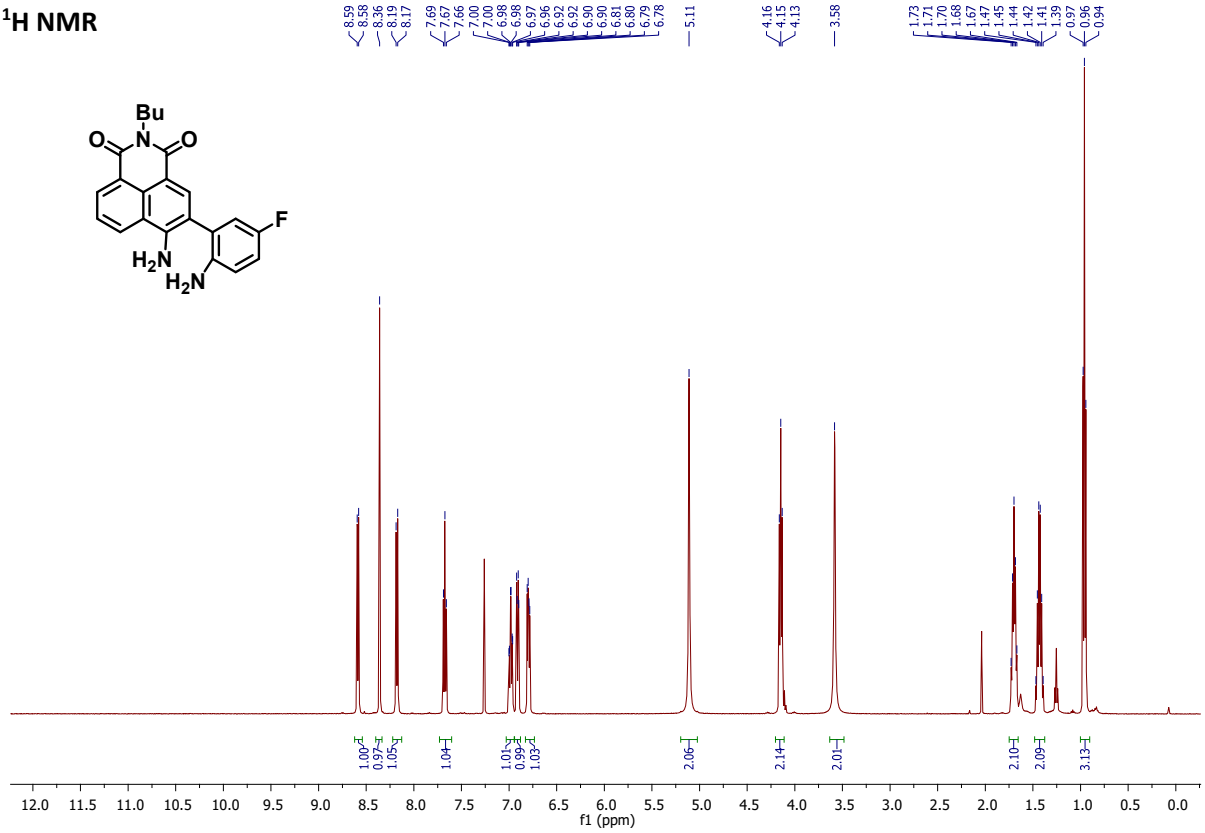
LisoView™405, MitoView™ 405, CellBrite Green® and NucSpot® live 488 were purchased from Biotium.

- *Protocol for* MitoView™ *405 staining:* After 3h of incubation with CinNapht dye, the medium was removed and cells were washed once with prewarmed PBS (1X). A 100 nM MitoView™ 405 solution in appropriate medium was then added, and cells were incubated for 15 minutes at 37 °C. The medium was removed, cells were washed once with prewarmed PBS (1X) then appropriate medium was added before imaging
- *Protocol for LysoView™ 405 staining*: After 3h of incubation with CinNapht dye, the medium was removed and cells were washed once with prewarmed PBS (1X). A 1X LysoView™ 405 solution in a appropriate medium was obtained by dilution of the commercial 1000X solution in DMSO and added to the cells. They were incubated for 30 minutes at 37°C. The medium was removed, cells were washed once with prewarmed PBS (1X) then appropriate medium or a nucleus staining medium solution was added before imaging
- *CellBrite Green® staining:* After 3h of incubation with CinNapht dye, the medium was removed and cells were washed once with prewarmed PBS (1X). A 1:200 CellBrite green solution in a appropriate medium was obtained by dilution of the commercial commercial stock solution and Immediately vortex to mix well. Within 1-2 minutes, cells were incubated with this solution for 30 minutes at 37°C. The medium was removed, cells were washed 3 times for 5 minutes with prewarmed PBS (1X) then appropriate medium or a nucleus staining medium solution was added before imaging
- *Protocol for NucSpot® live 488 staining*: The 1X nucleus staining agent solution was obtained by dilution of the commercial 1000X solution in DMSO supplemented with 50 nm of Verapamil. After incubation with the CinNapht dye, this solution was added to the cells that were then incubated for 30 minutes at 37 °C. The imaging experiments were then directly conducted without washing step
- *Protocol for HOECHST 33342 staining*: A 1µg/mL solution was prepared by dilution of a stock solution of 1mg/mL in DMSO:H_2O (1:1). The solution was centrifuged to avoid eventual solid residue. After incubation with the CinNapht dye, this solution was added to the cells that were then incubated for 15 minutes at 37 °C. Cells were washed once with prewarmed PBS (1X) then appropriate medium was added before imaging

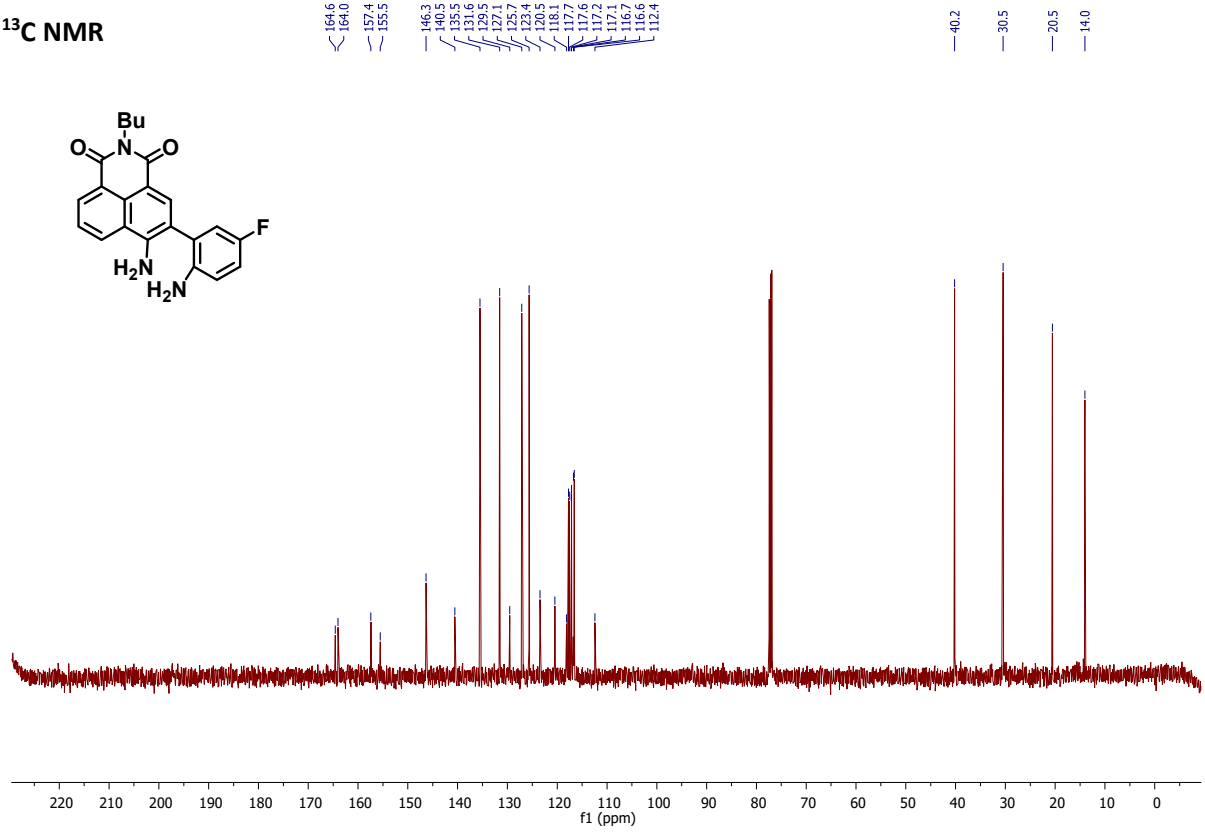
III. NMR and MS Spectra

Compound 3:

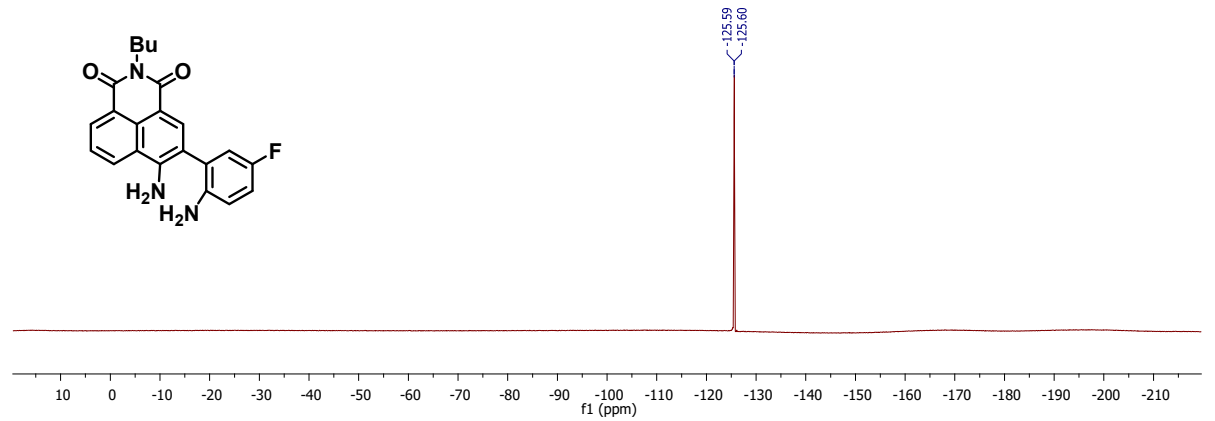
^{1}H NMR



^{13}C NMR



^{19}F NMR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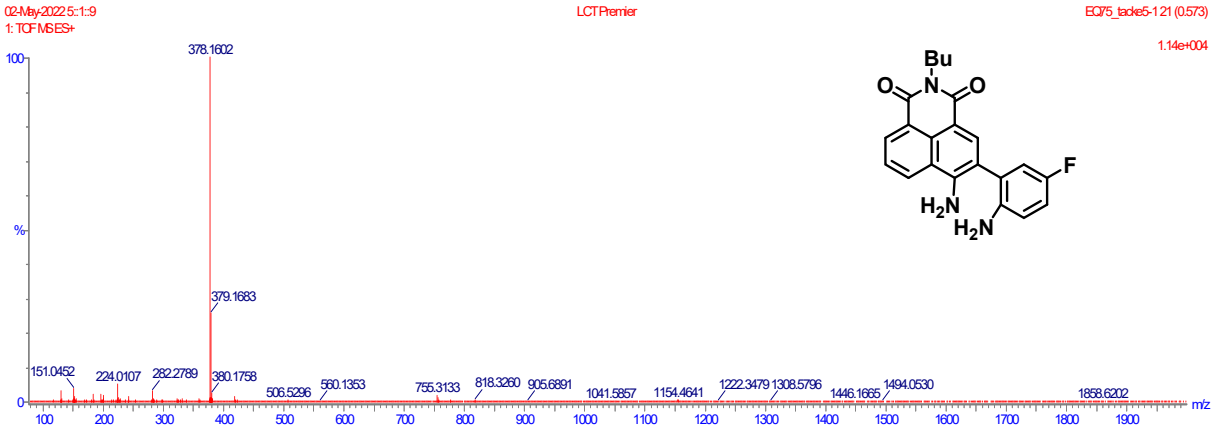
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

HRMS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1858.6202
100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900
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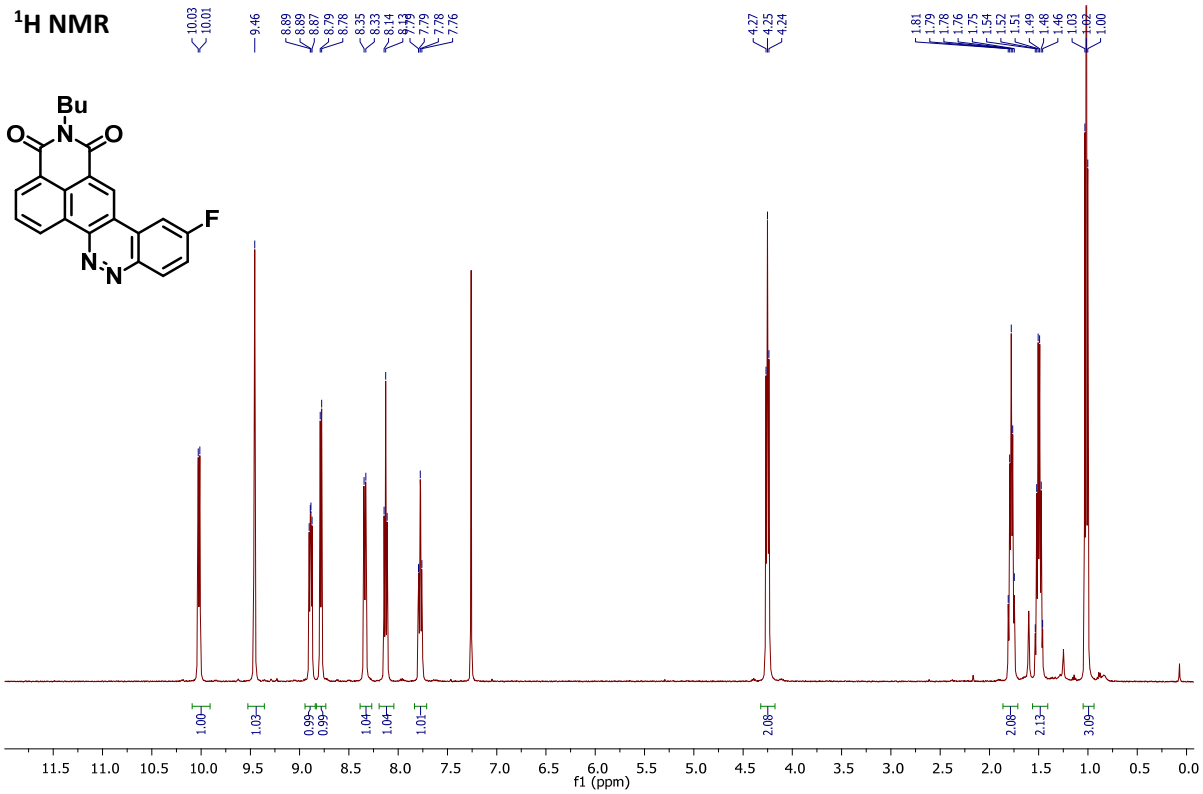
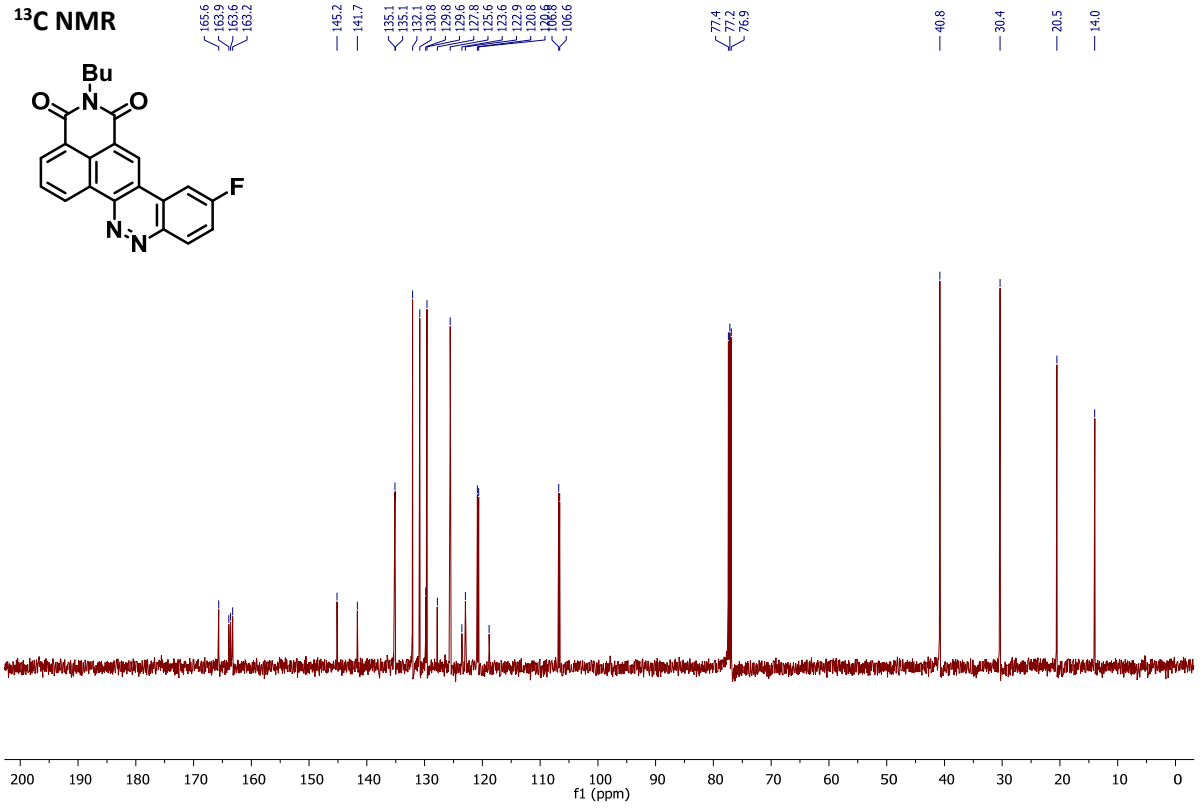
O
F
H2N
H2N

Compound 4:

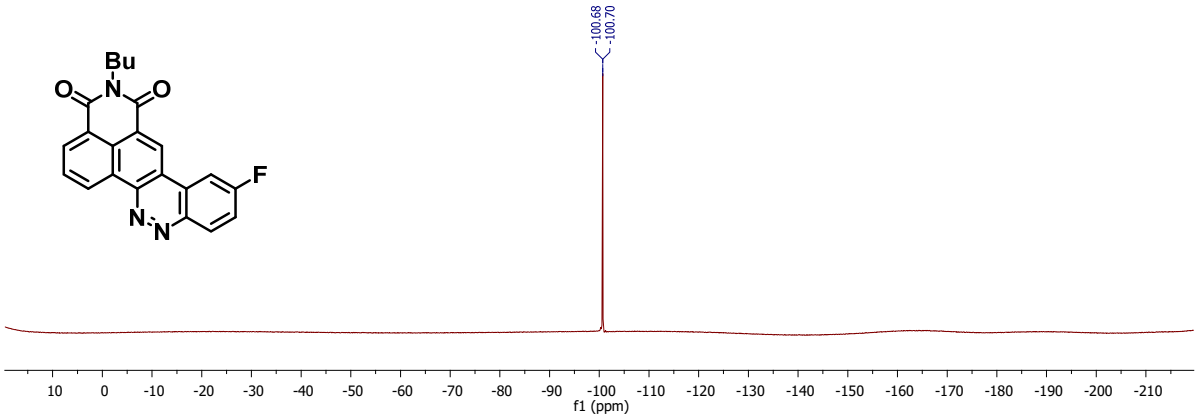
^{1}H NMR



^{13}C NMR



^{19}F NMR


Bu
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N
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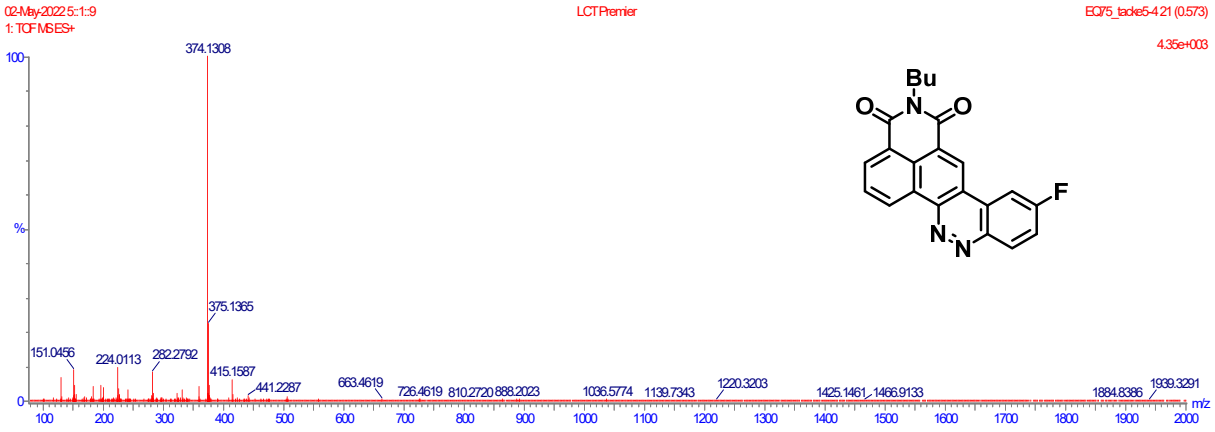
f1 (ppm)

HRMS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1139.7343
1220.3203
1425.1461
1466.9133
1884.8386
1939.3291
Bu
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N
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N
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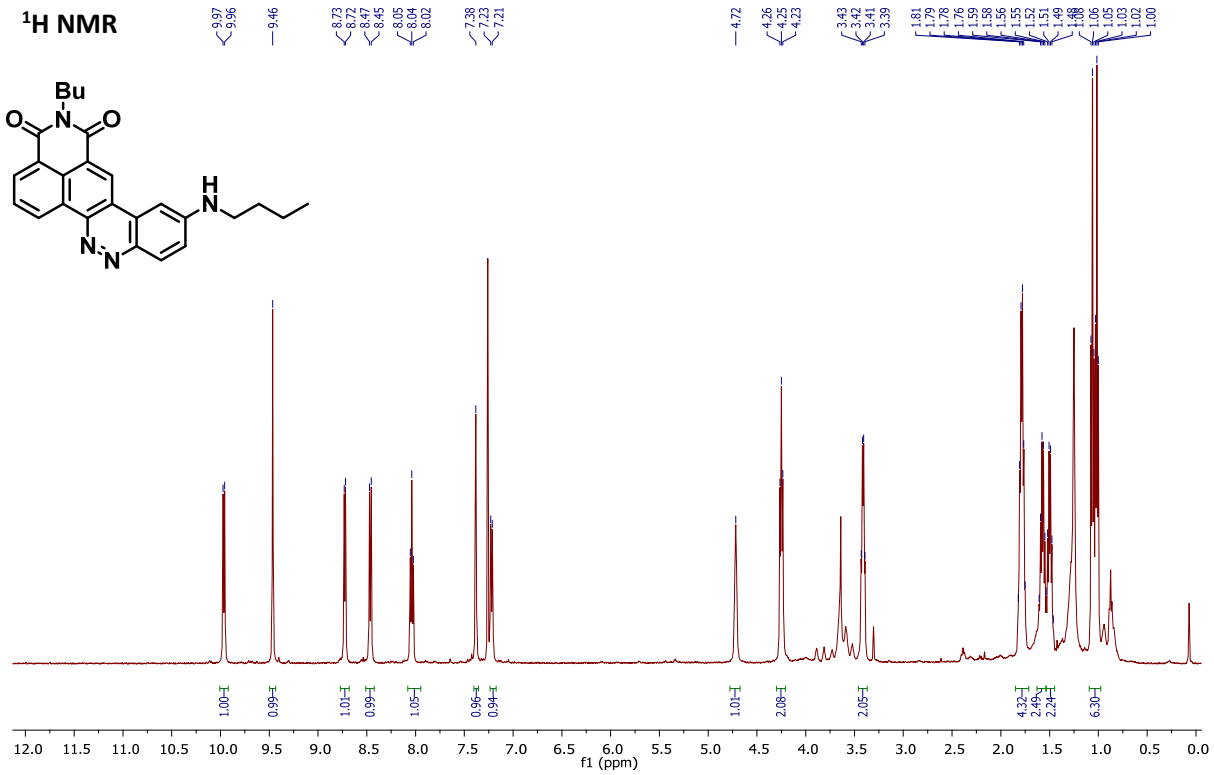
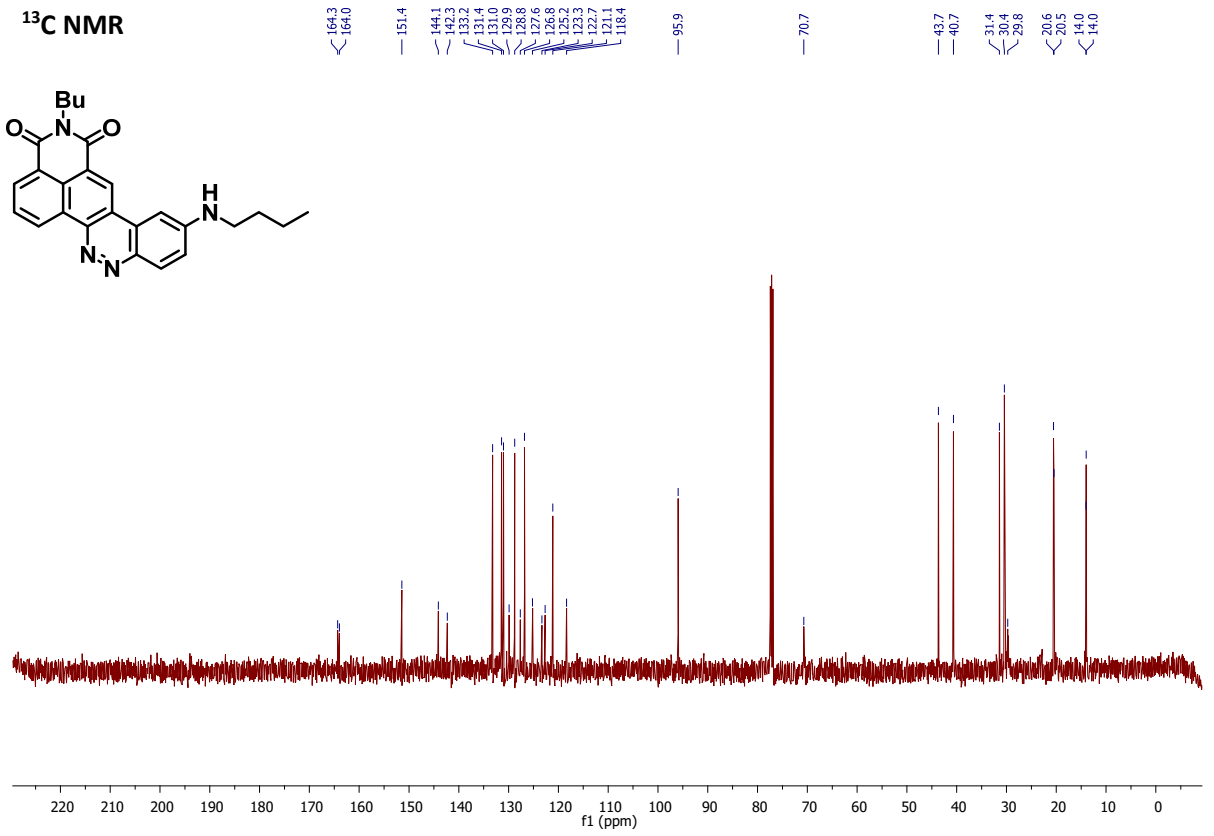
m/z

Compound 5a:

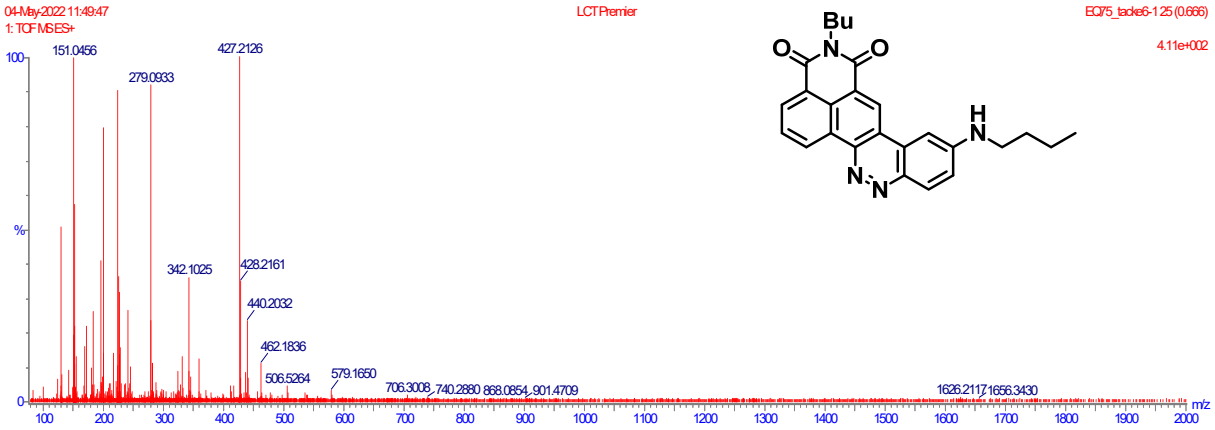
^{1}H NMR



^{13}C NMR



HRMS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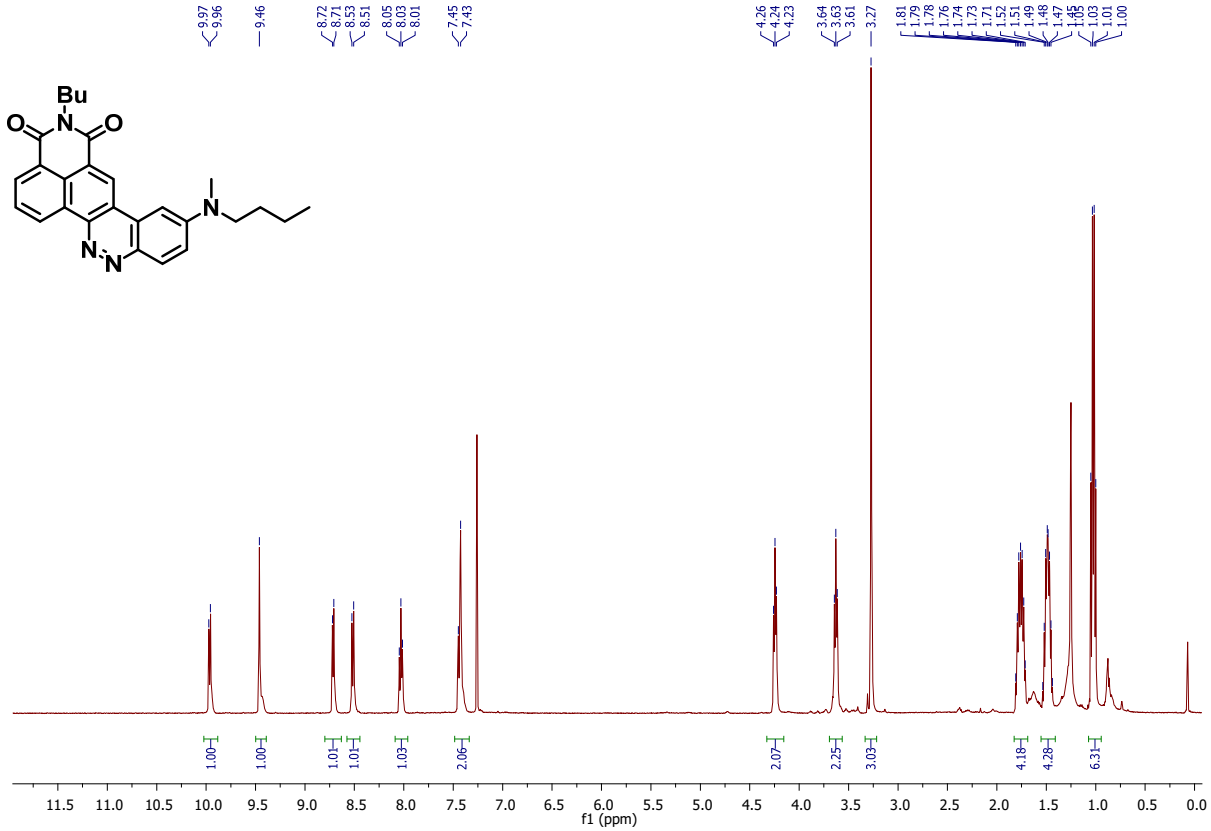
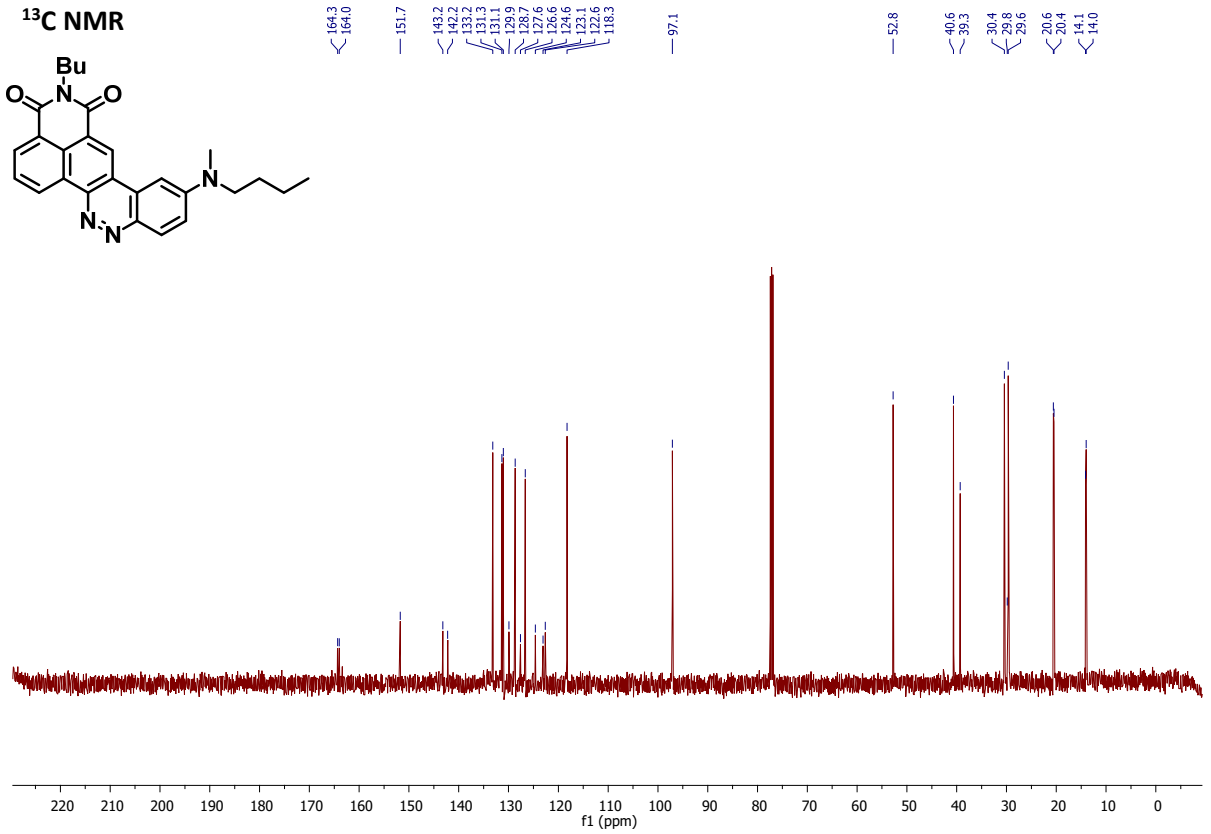
868.0854
901.4709
1626.2117
1656.3430
%
m/z
Bu
O
N
O
H
N
N
N

Compound 5b:

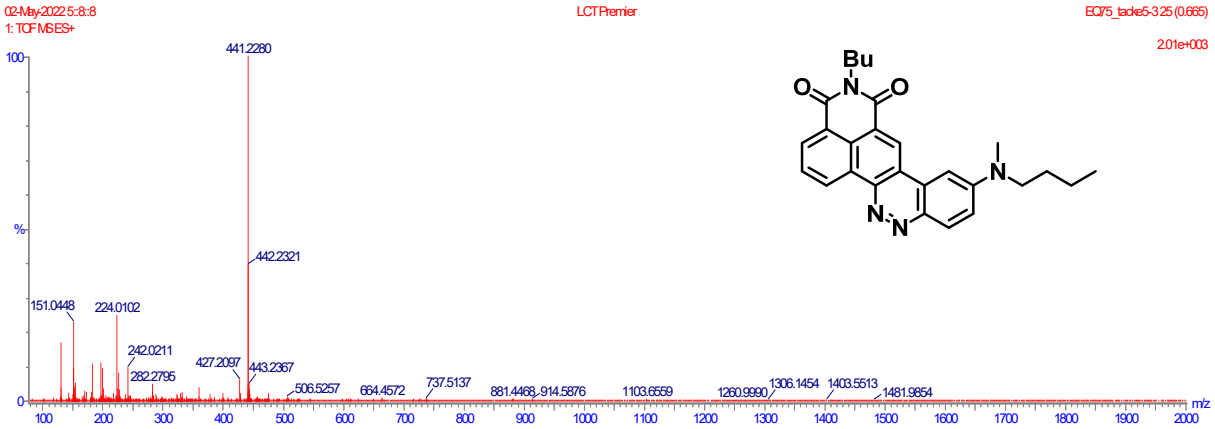
^{1}H NMR



^{13}C NMR

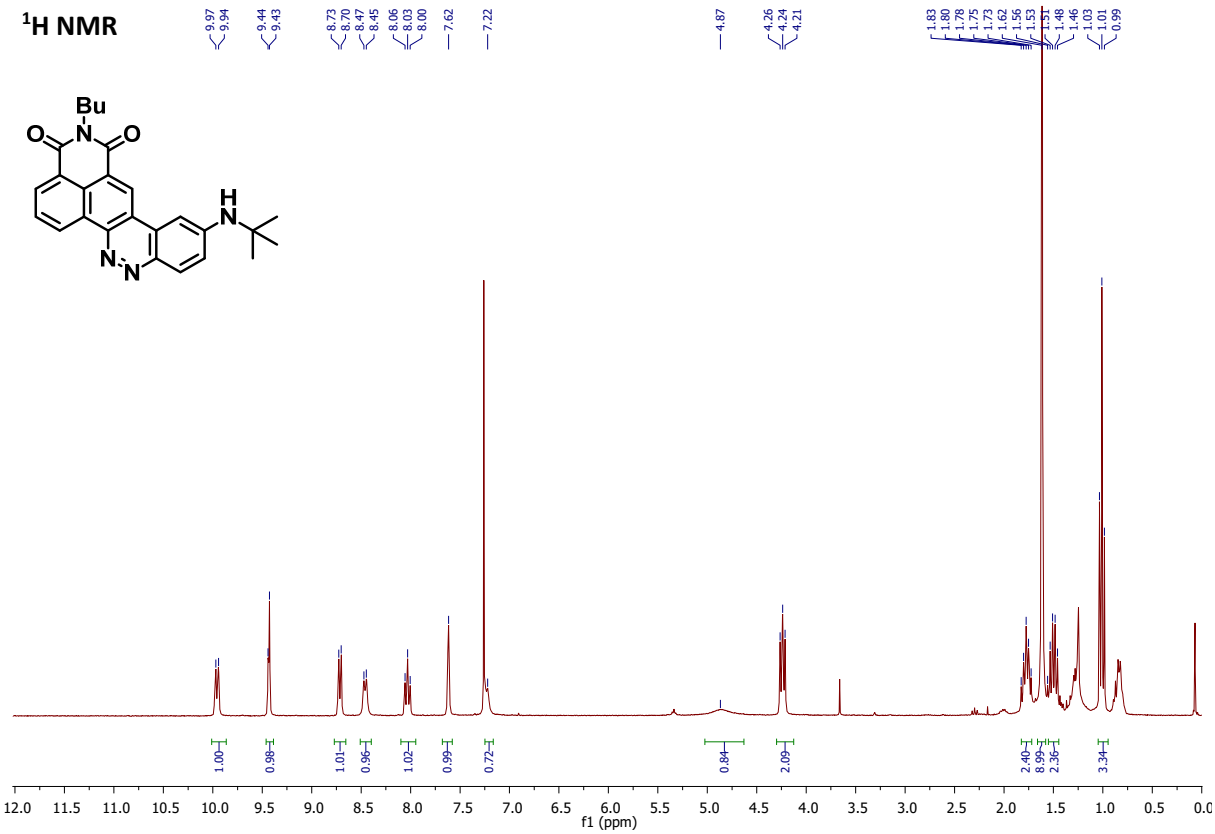


HRMS

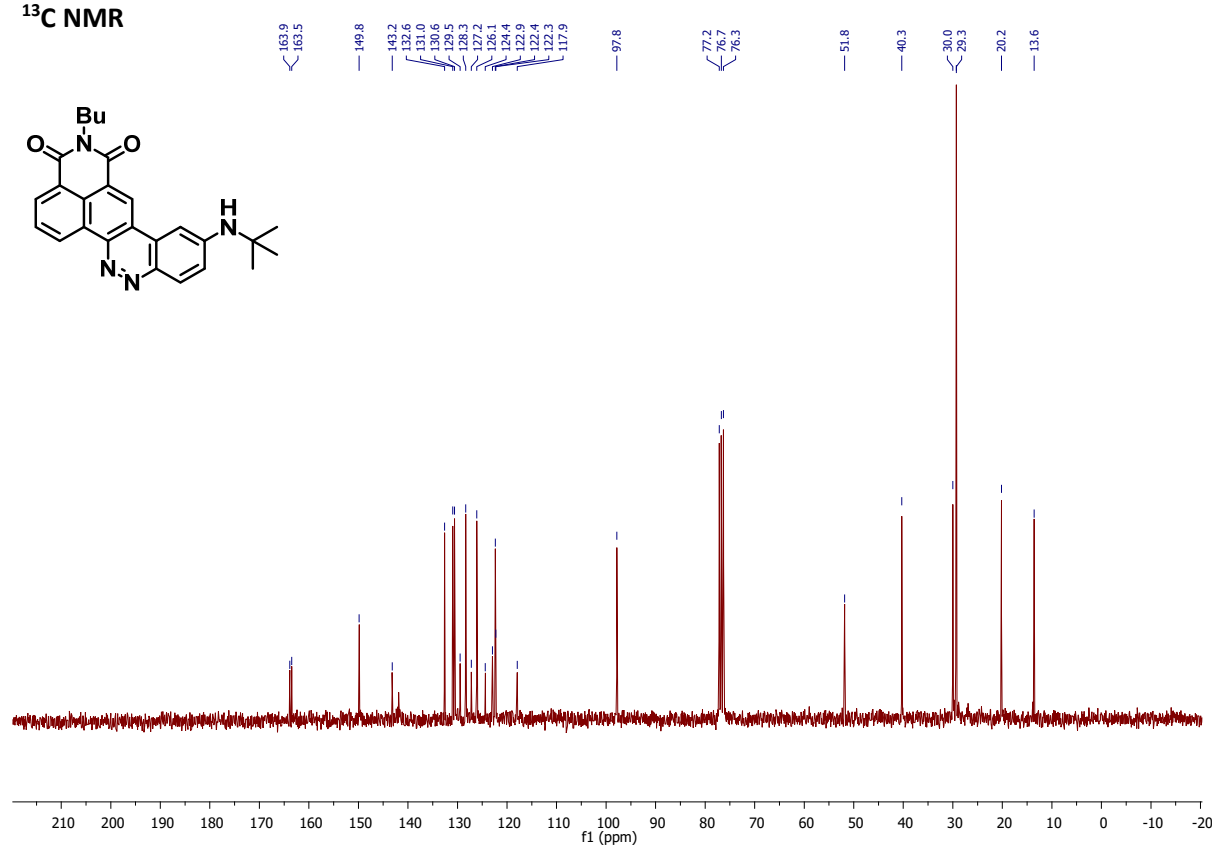

02-May-2022 5::8::8
LCT Premier
EQ75_tacke5-3 25 (0.665)
1: TOF MS ES+
2.01e+003
441.2280
442.2321
151.0448
224.0102
242.0211
282.2795
427.2097
443.2367
506.5257
664.4572
737.5137
881.4468, 914.5876
1103.6559
1260.9990
1306.1454
1403.5513
1481.9854
Bu
O
N
O
N
N
N
%
m/z

Compound 5c:

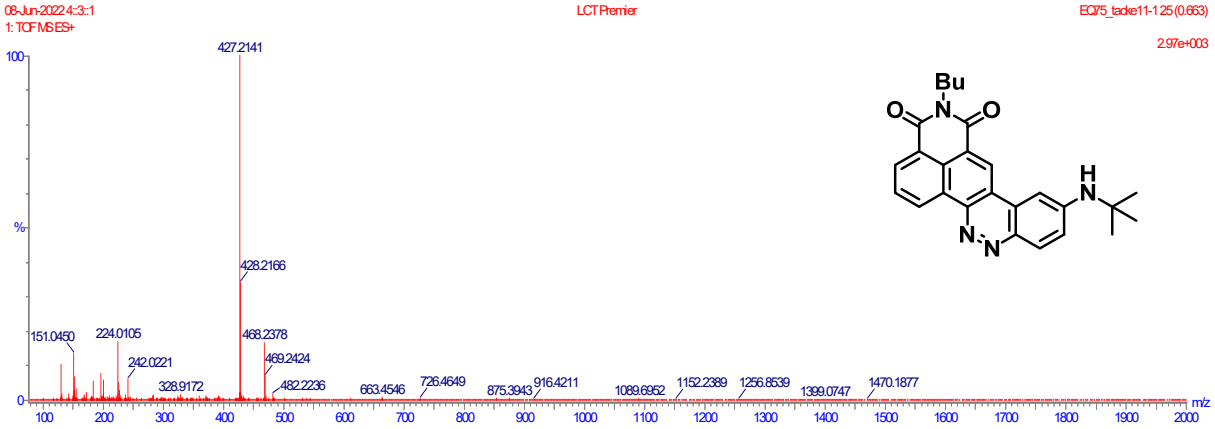
^{1}H NMR



^{13}C NMR

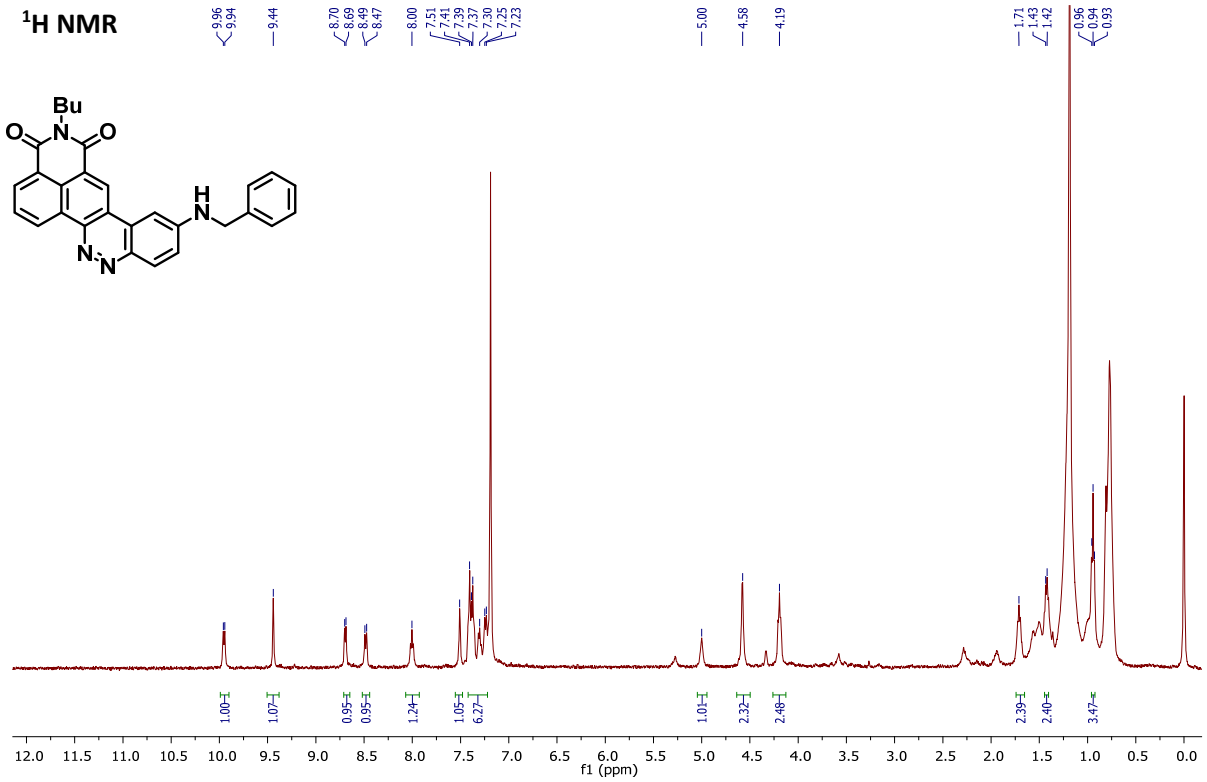


HRMS

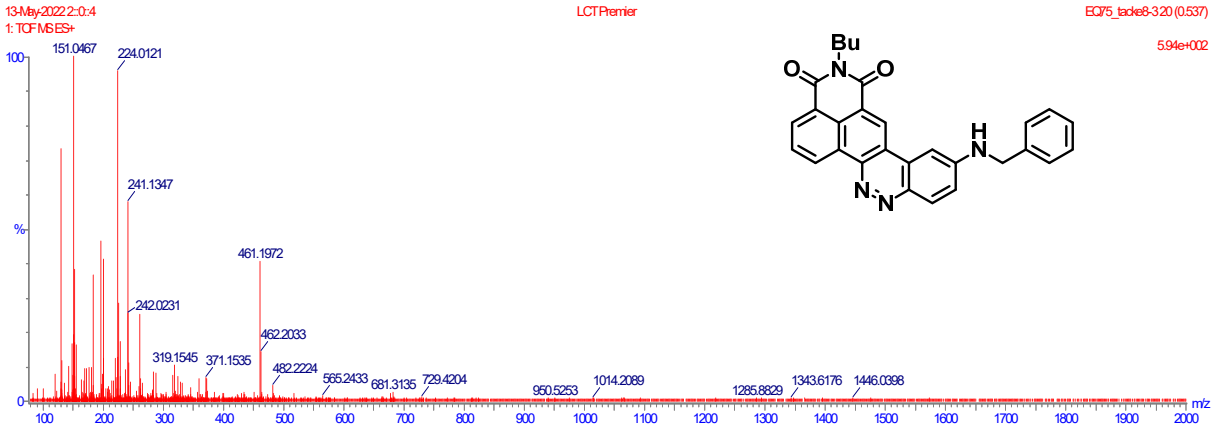

08-Jun-2022 4::3::1
1: TOF MS ES+
LCT Premier
EQ75_tacke11-1 25 (0.663)
2.97e+003
100
%
0
427.2141
428.2166
151.0450
224.0105
242.0221
328.9172
468.2378
469.2424
482.2236
663.4546
726.4649
875.3943
916.4211
1089.6952
1152.2389
1256.8539
1399.0747
1470.1877
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z
Bu
O
N
O
H
N
N
N

Compound 5d:

^{1}H NMR

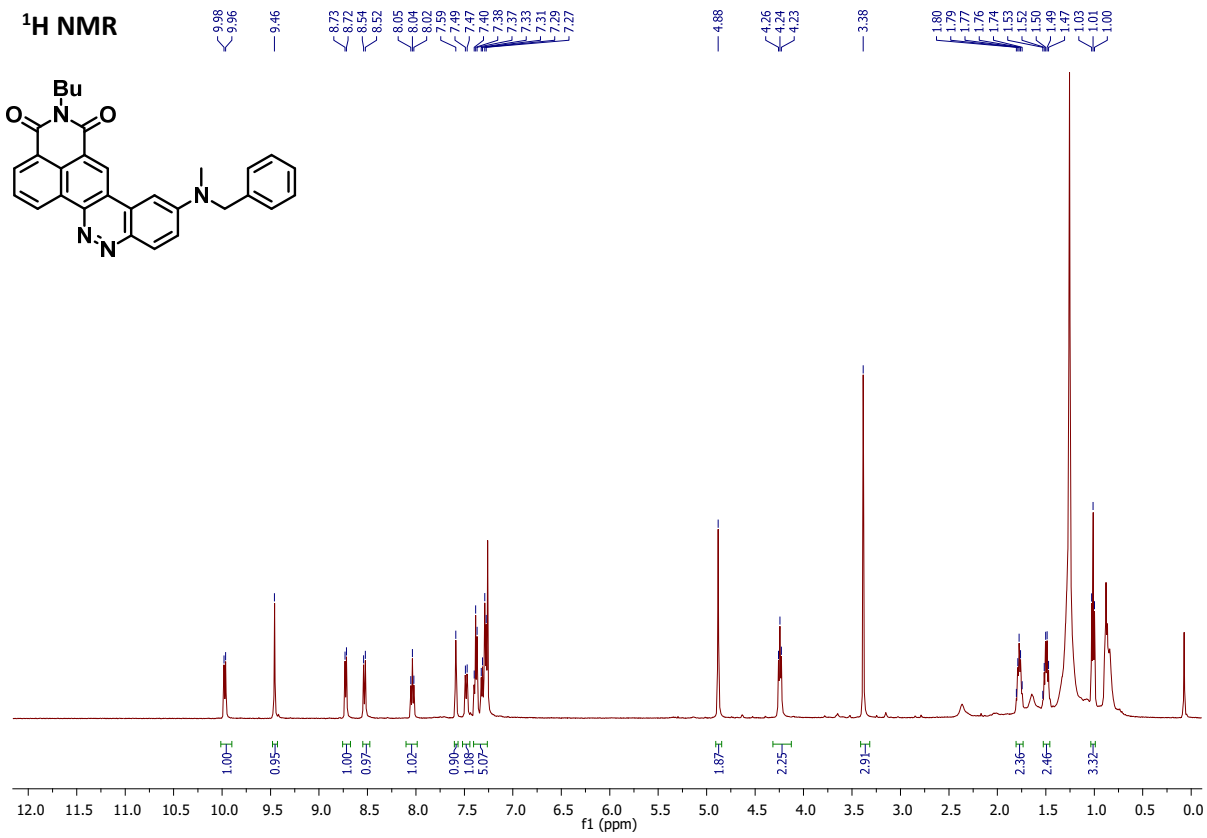


HRMS

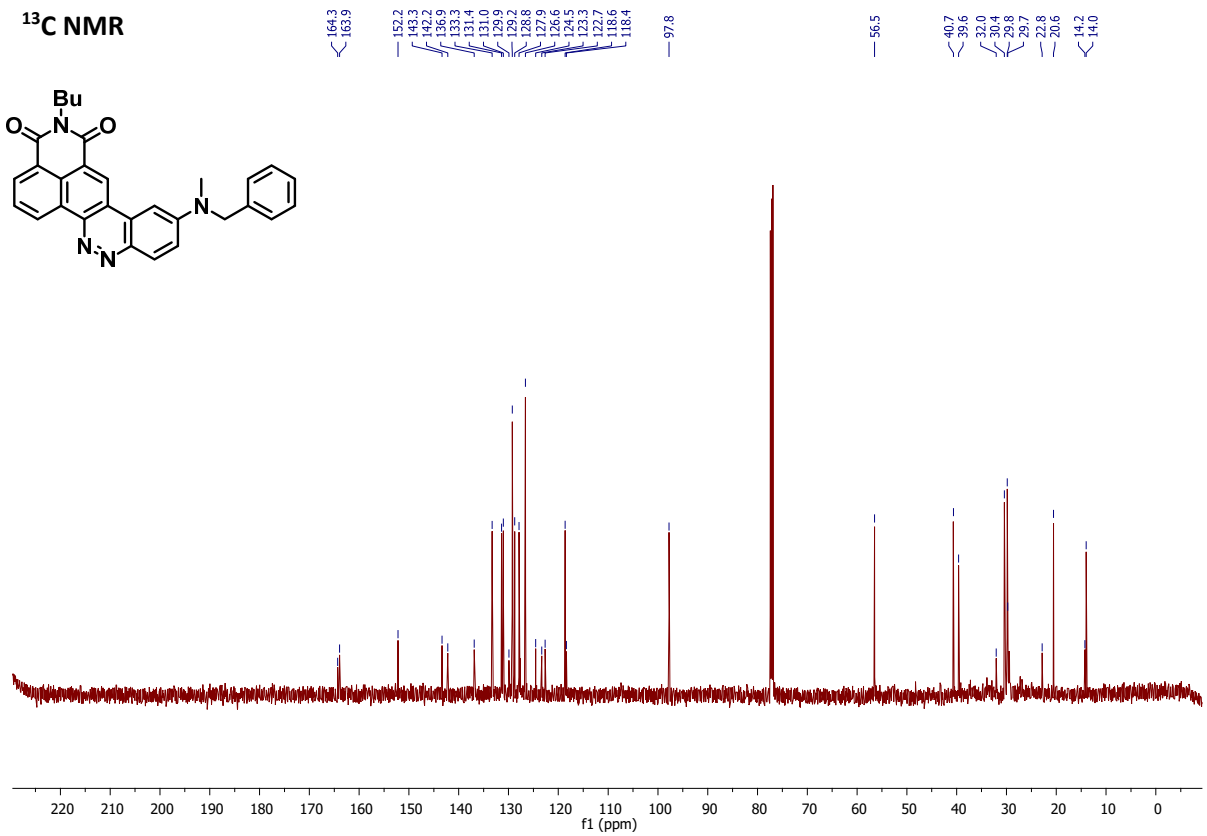


Compound 5e:

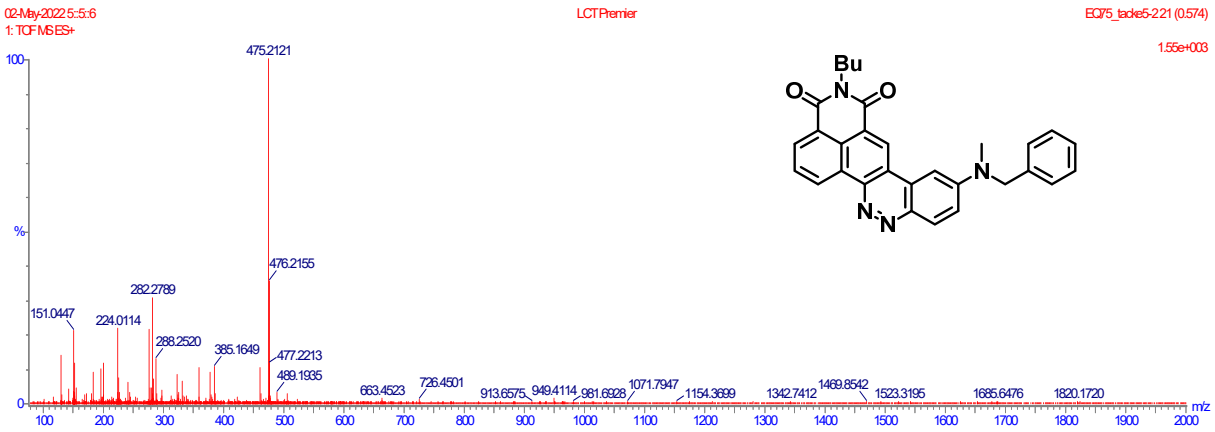
^{1}H NMR



^{13}C NMR

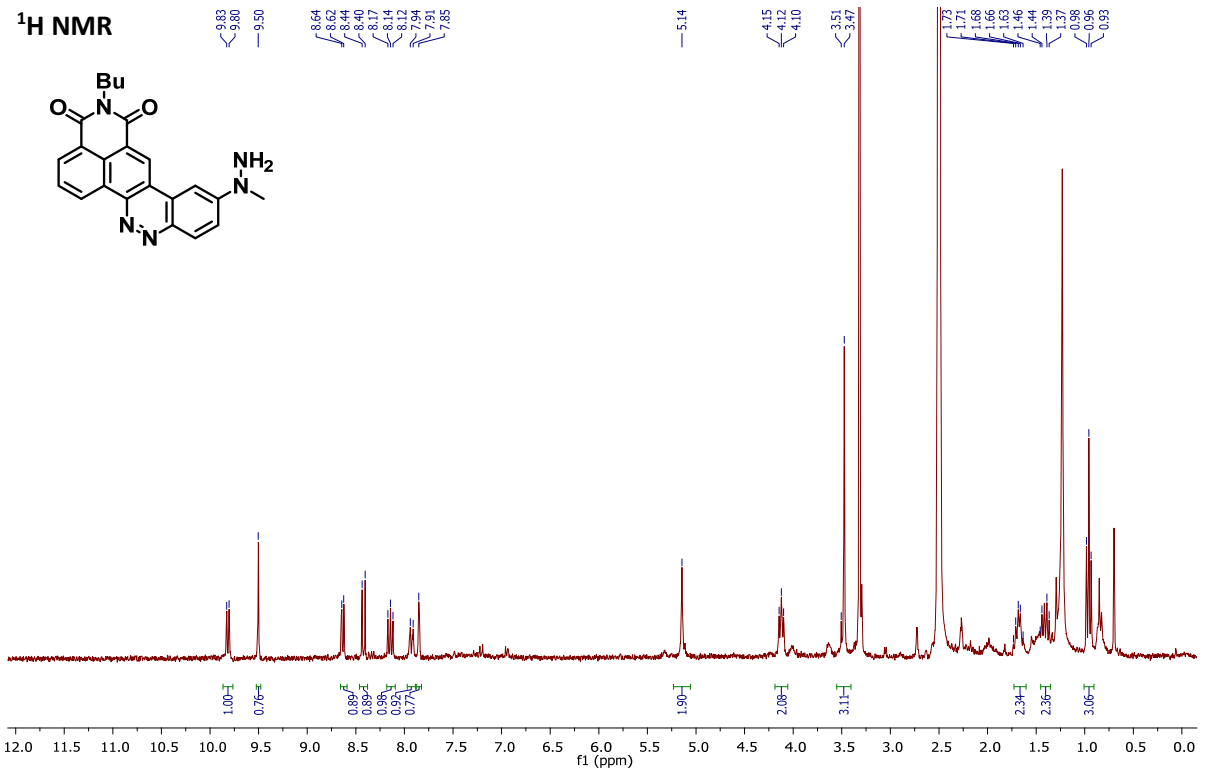


HRMS

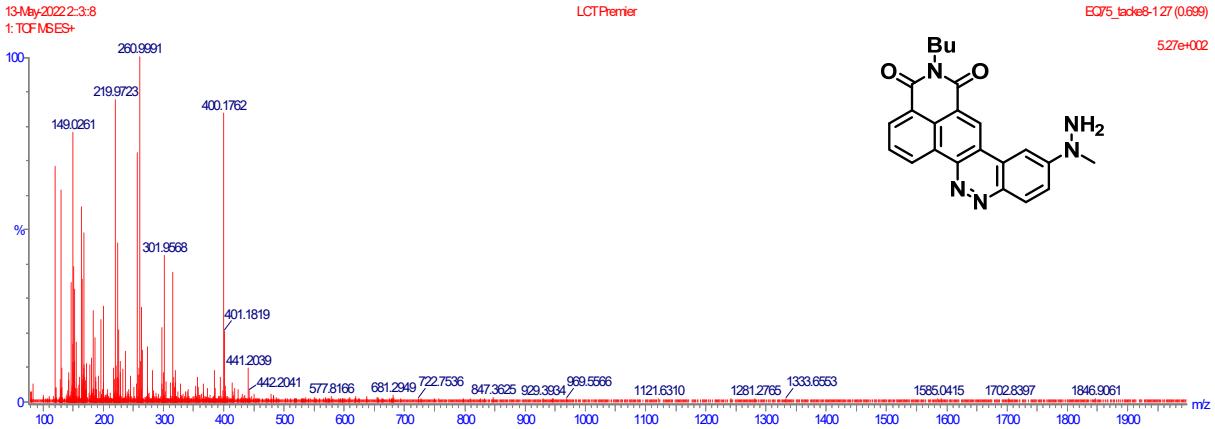

02-May-2022 5::5::6
1: TOF MS ES+
LCT Premier
EQ75_tacke5-2 21 (0.574)
1.55e+003
100
%
0
475.2121
476.2155
282.2789
151.0447
224.0114
288.2520
385.1649
477.2213
489.1935
663.4523
726.4501
913.6575
949.4114
981.6928
1071.7947
1154.3699
1342.7412
1469.8542
1523.3195
1685.6476
1820.1720
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
N
N
N

Compound 5g:

^{1}H NMR

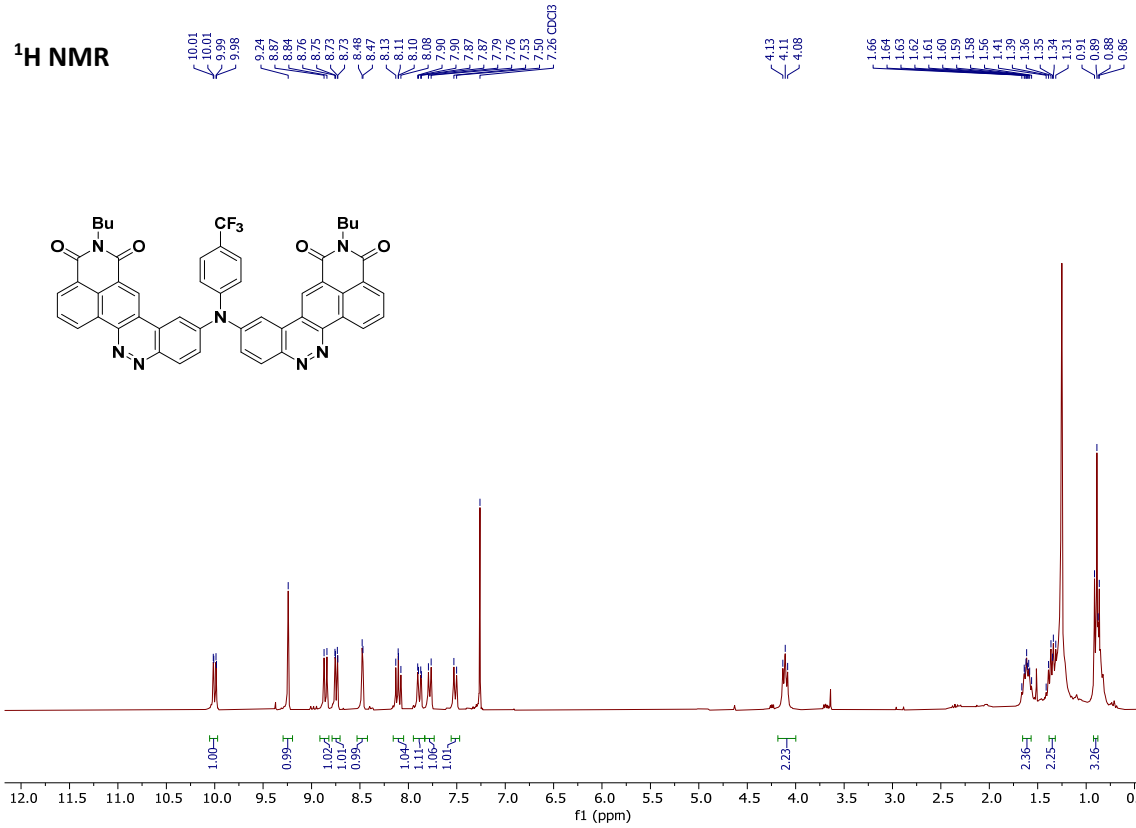


HRMS

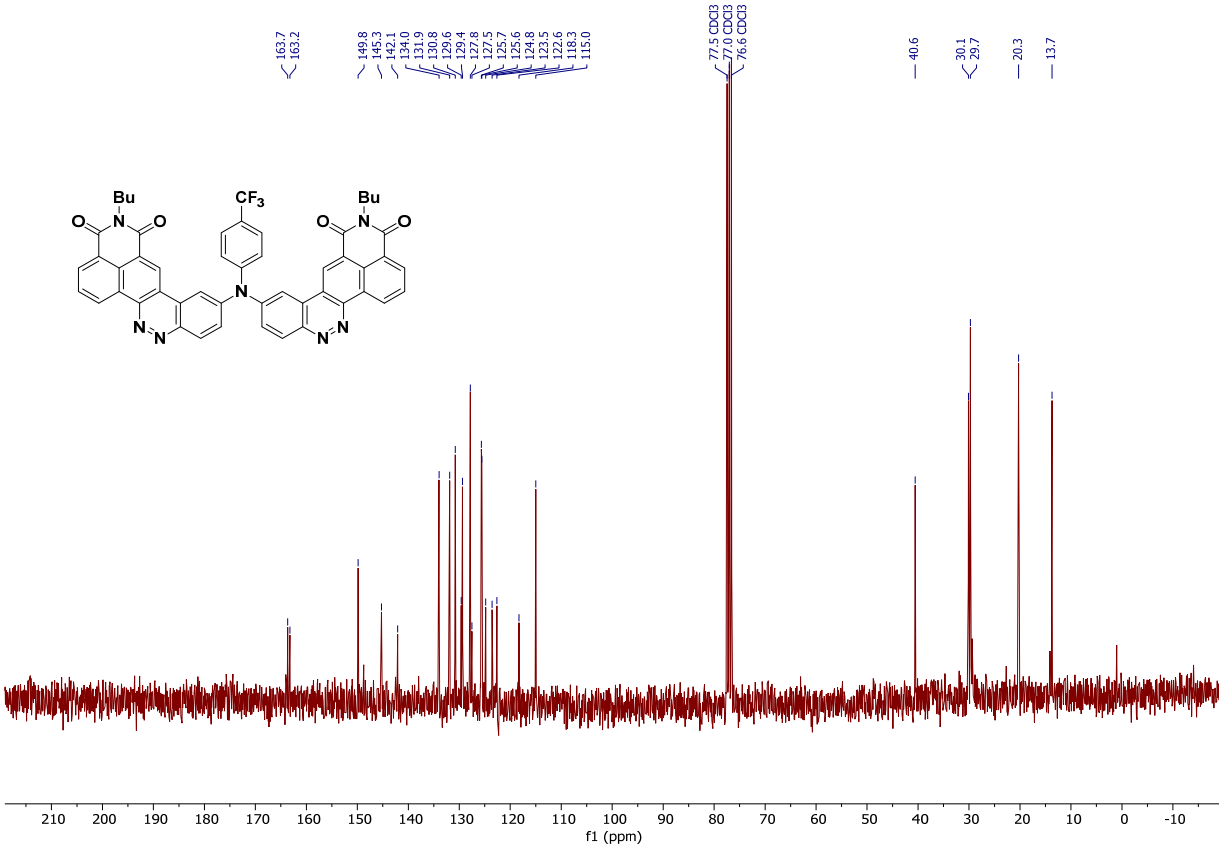


Compound 5i:

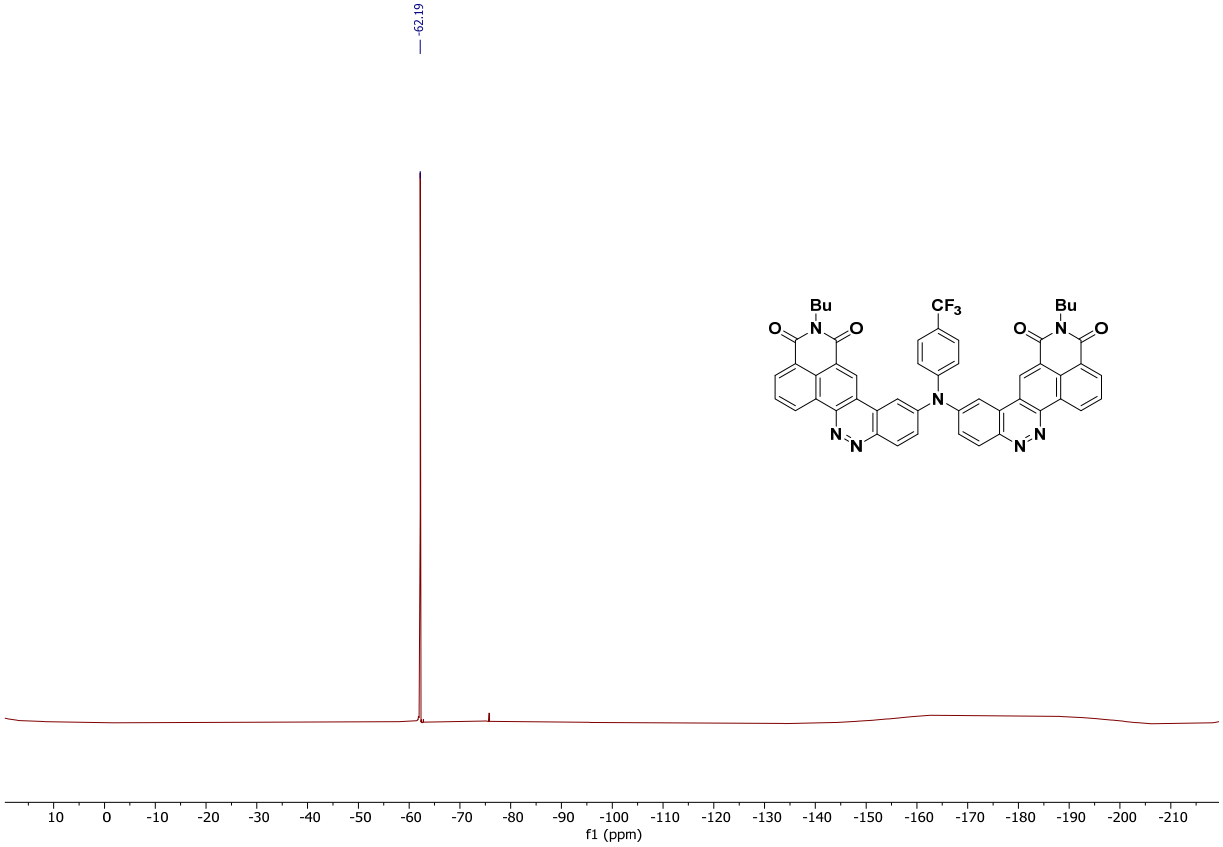
^{1}H NMR



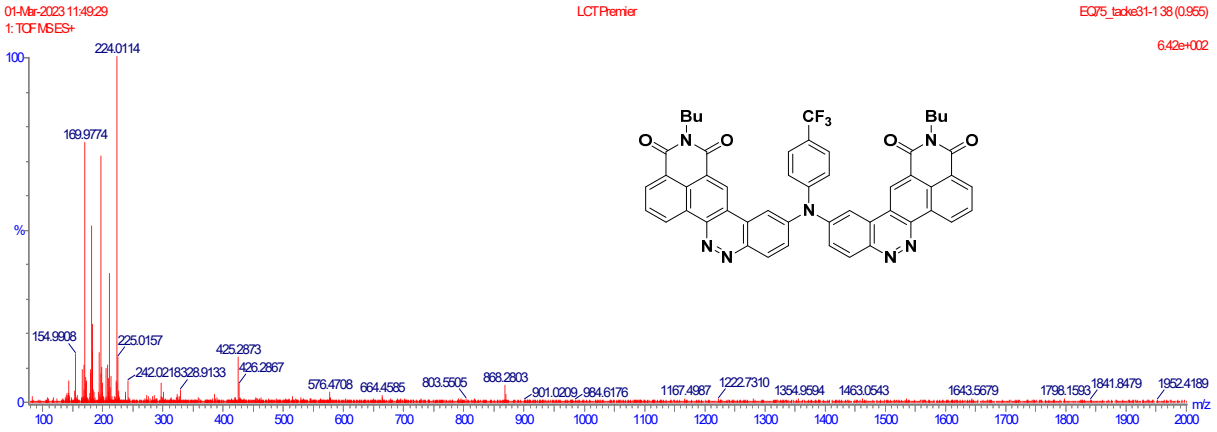
^{13}C NMR



^{19}F NMR

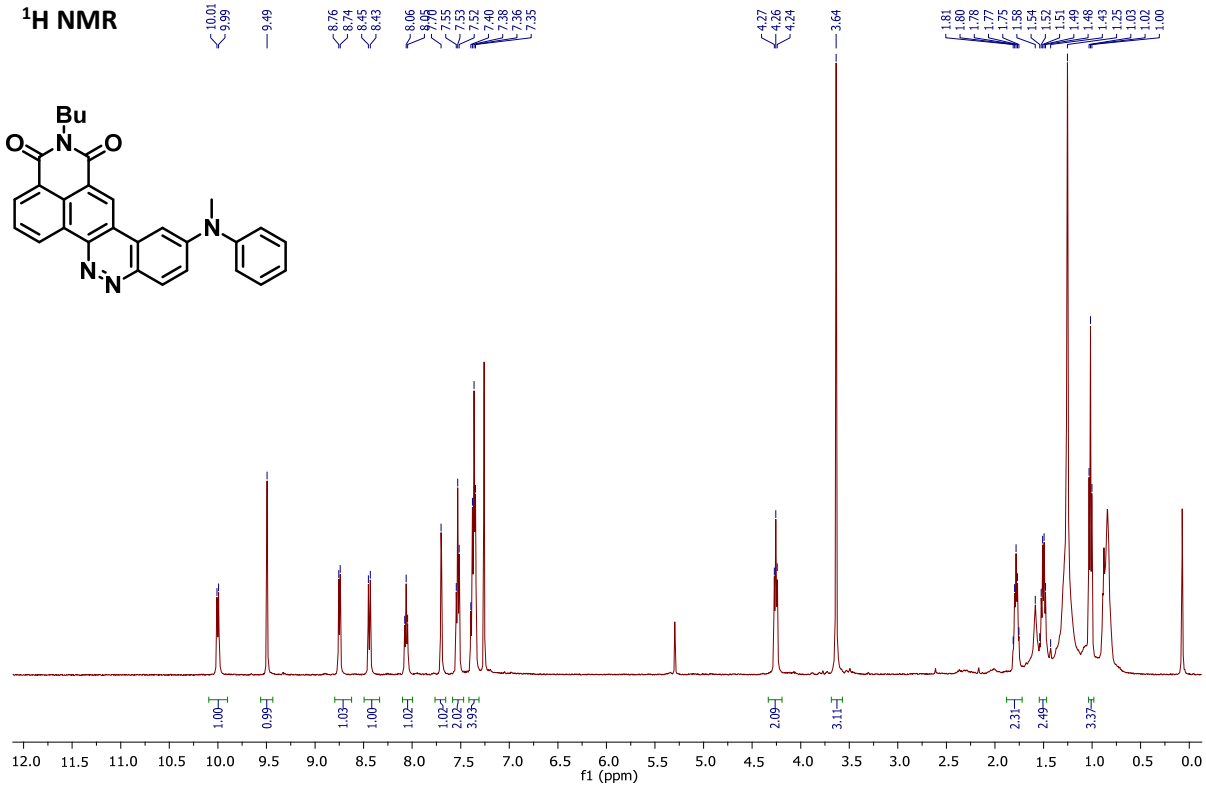

-62.19
Bu
CF3
Bu
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

HRMS

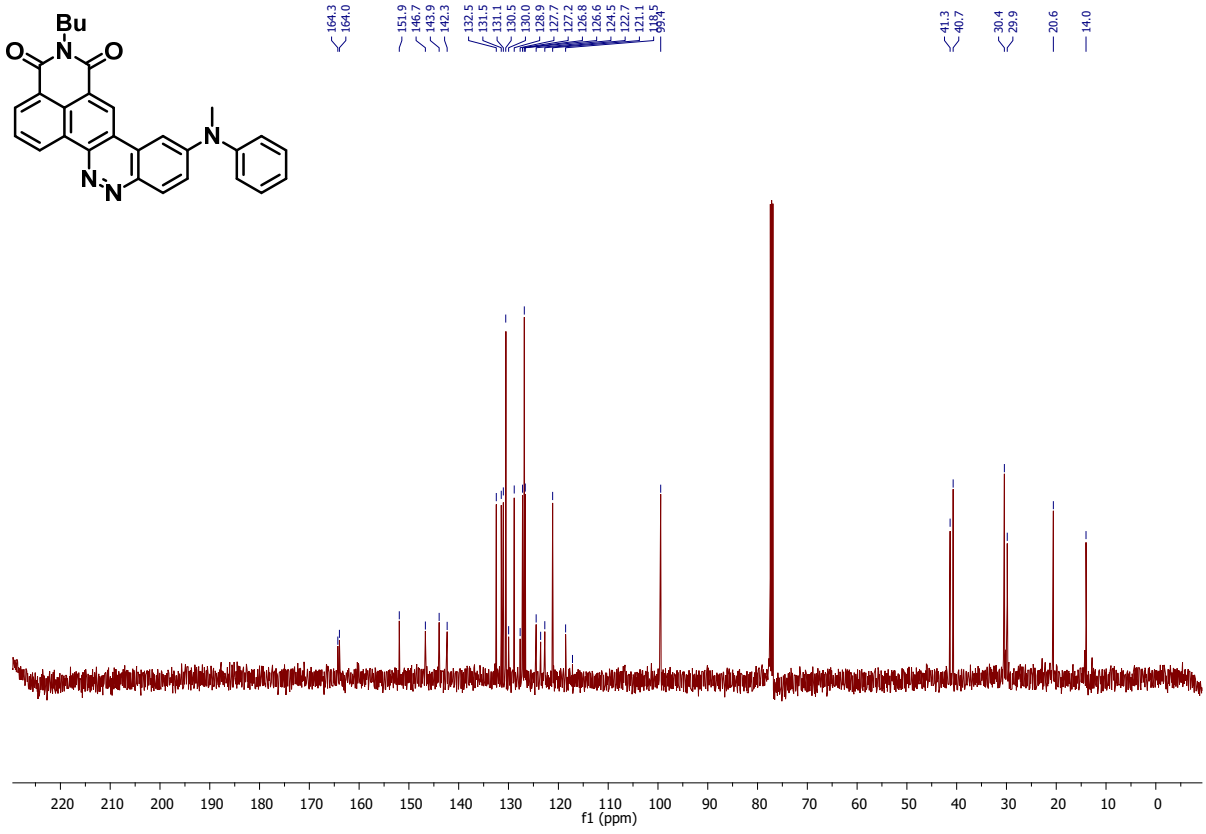

01-Mar-2023 11:49:29
1: TOF MS ES+
LCT Premier
EQ75_tacke31-1 38 (0.955)
6.42e+002
224.0114
169.9774
154.9908
225.0157
242.0218
328.9133
425.2873
426.2867
576.4708
664.4585
803.5505
868.2803
901.0209
984.6176
1167.4987
1222.7310
1354.9594
1463.0543
1643.5679
1798.1593
1841.8479
1952.4189
Bu
CF3
Bu
%
m/z

Compound 5k:

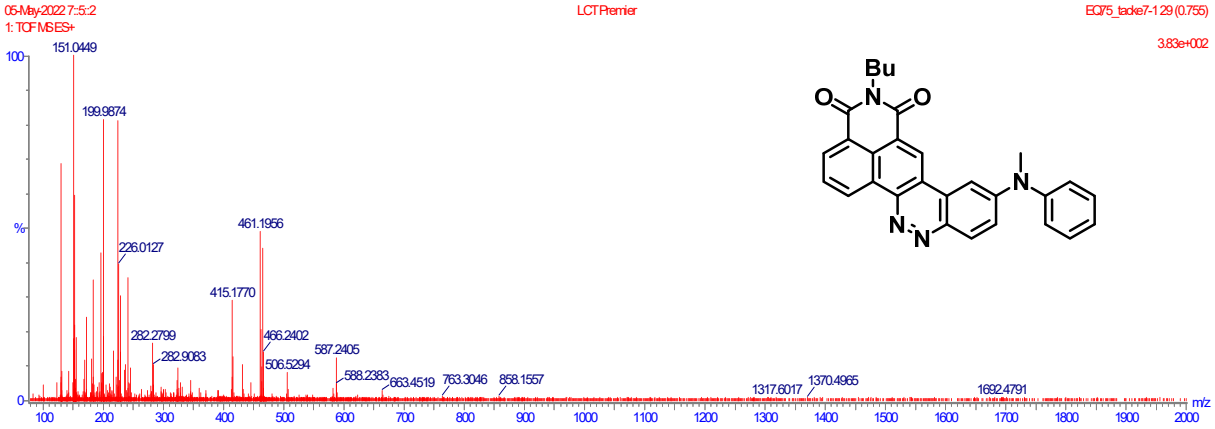
^{1}H NMR



^{13}C NMR

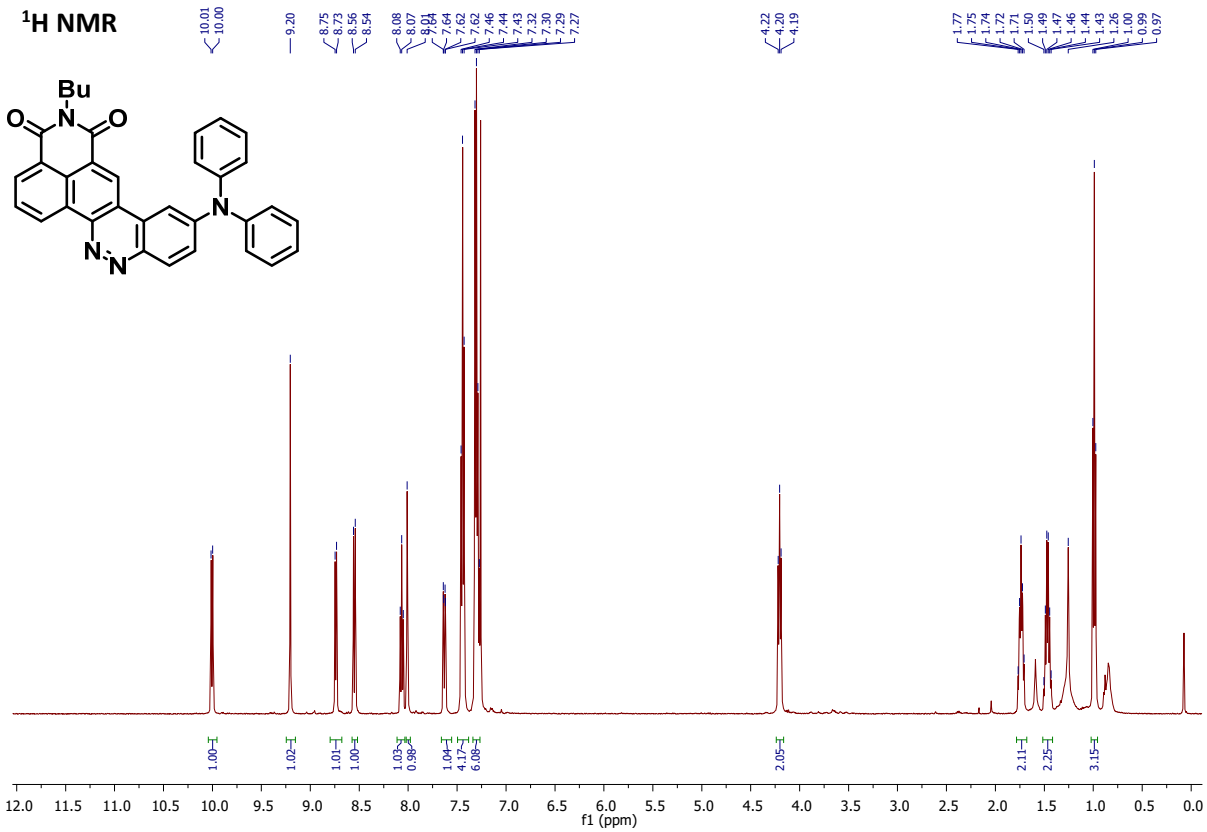


HRMS

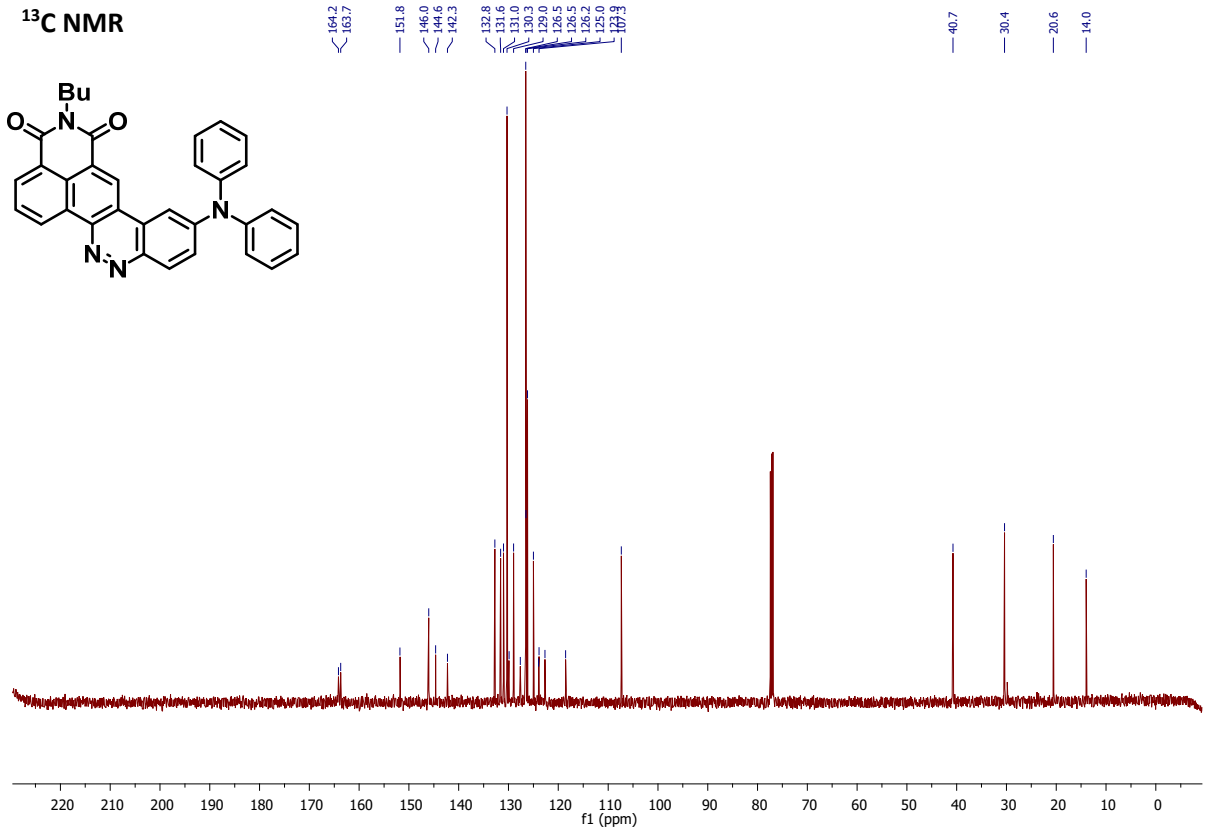

05-May-2022 7::5:2
1: TOF MS ES+
LCT Premier
EQI75_tacke7-1 29 (0.755)
3.83e+002
151.0449
199.9874
226.0127
461.1956
415.1770
282.2799
282.9083
466.2402
506.5294
587.2405
588.2383
663.4519
763.3046
858.1557
1317.6017
1370.4965
1692.4791
Bu
O
N
O
N
N
N
%
m/z

Compound 5m:

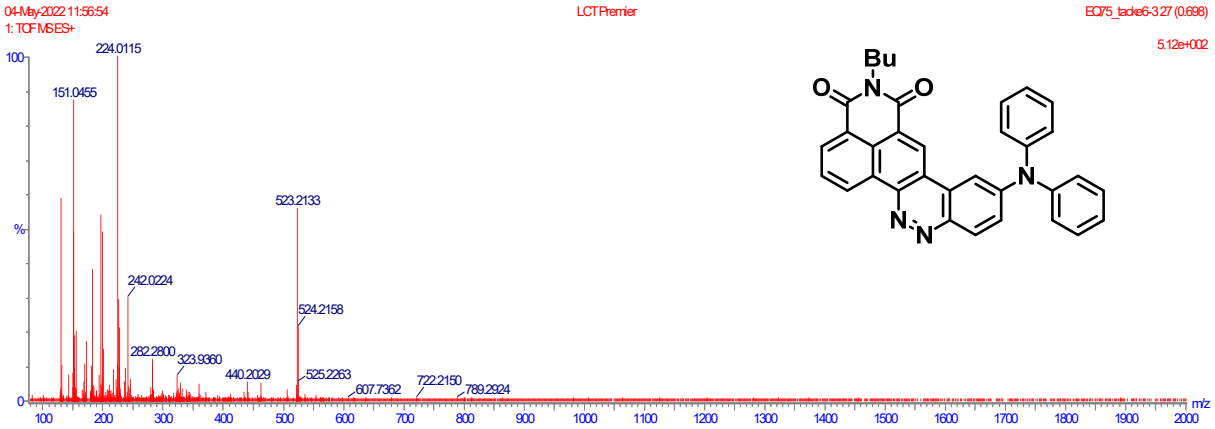
^{1}H NMR



^{13}C NMR

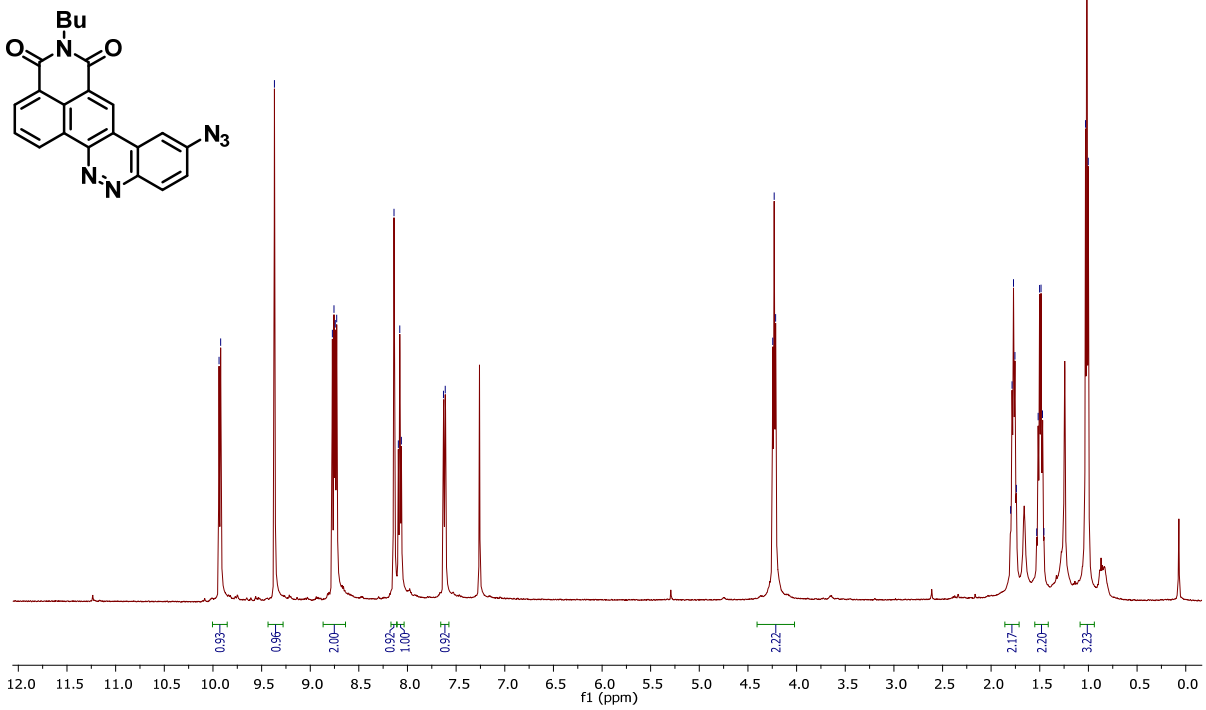


HRMS

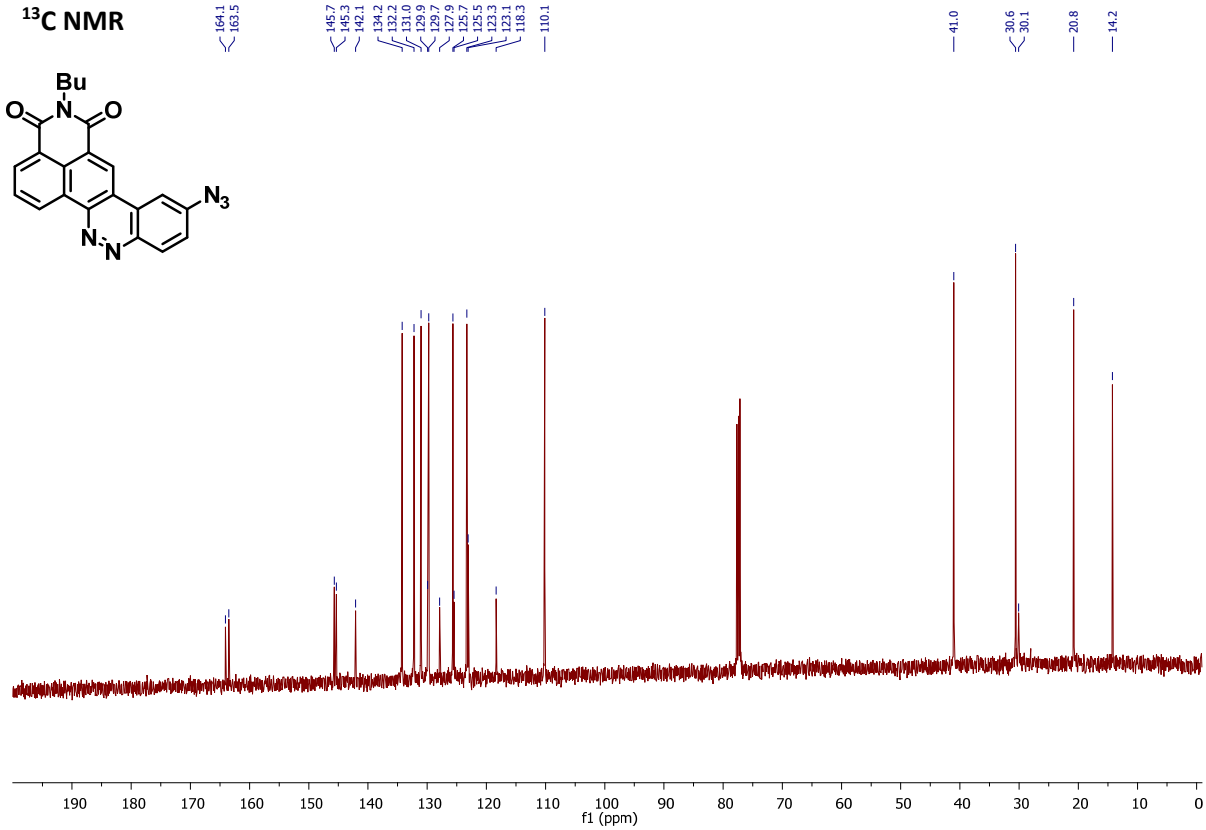

04-May-2022 11:56:54
LCT Premier
EQ75_tacke6-3 27 (0.698)
1: TOF MS ES+
5.12e+002
100
%
0
224.0115
151.0455
523.2133
242.0224
524.2158
282.2800
323.9360
440.2029
525.2263
607.7362
722.2150
789.2924
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
N
N
N

Compound 5n:

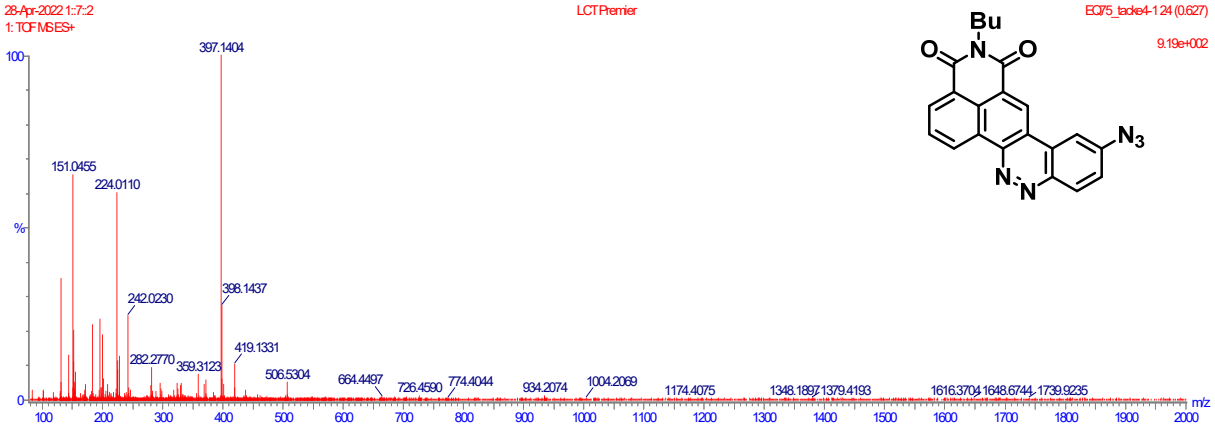
^{1}H NMR



^{13}C NMR

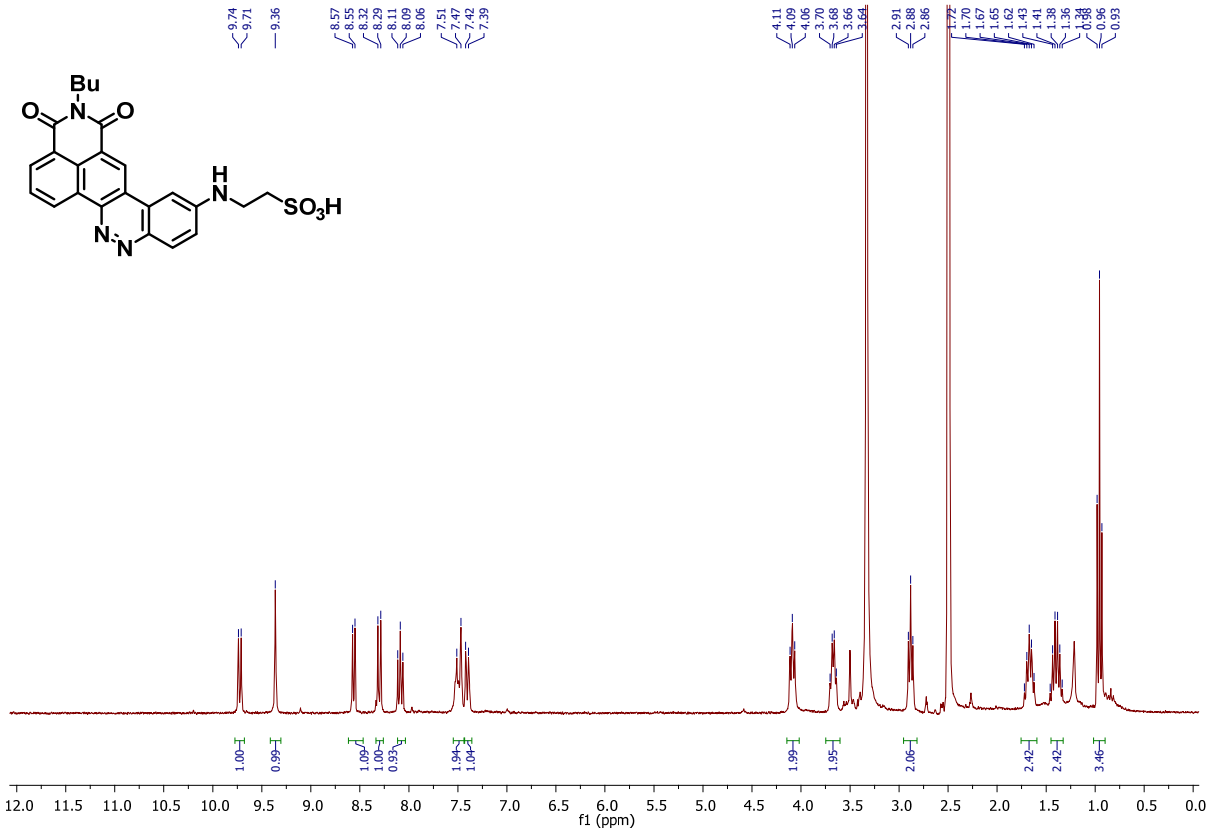


HRMS

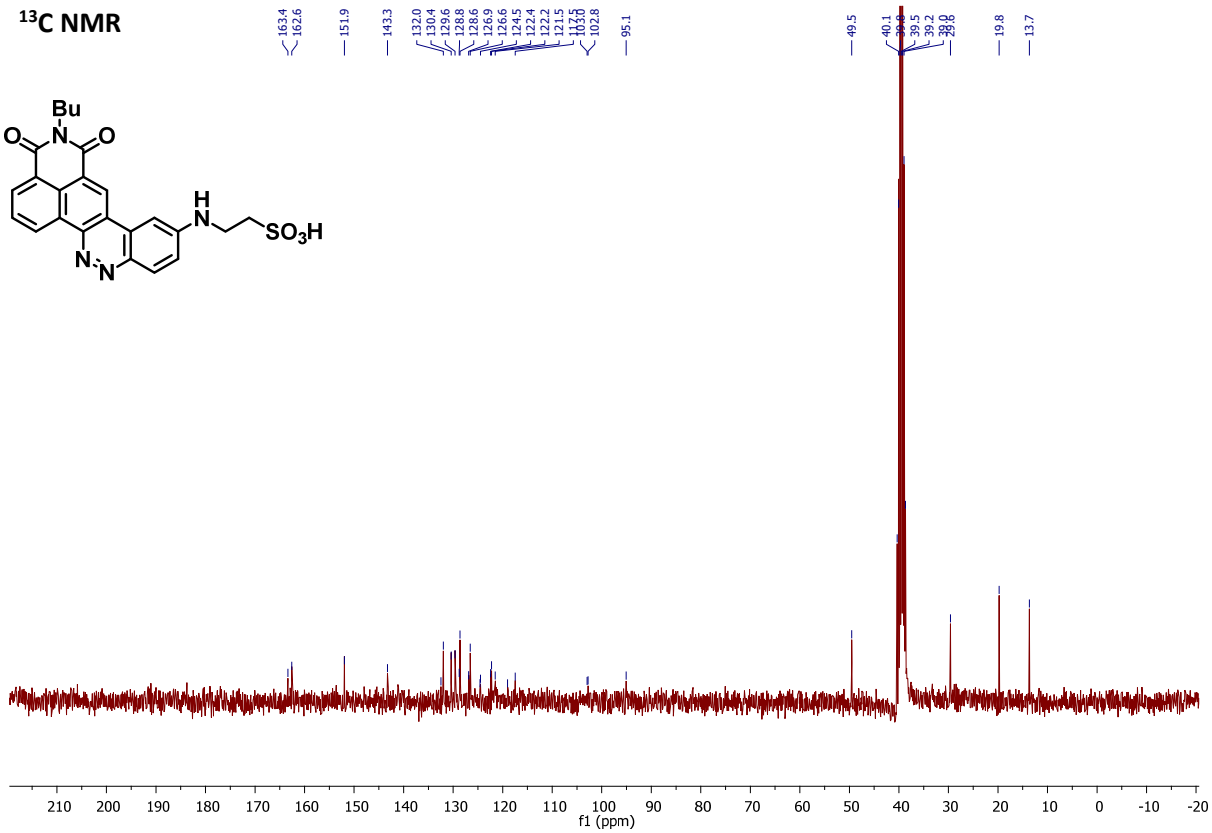

28-Apr-2022 1::7::2
1: TOF MS ES+
LCT Premier
EQ75_tacke4-1 24 (0.627)
9.19e+002
100
%
0
397.1404
151.0455
224.0110
242.0230
398.1437
282.2770
359.3123
419.1331
506.5304
664.4497
726.4590
774.4044
934.2074
1004.2069
1174.4075
1348.1897
1379.4193
1616.3704
1648.6744
1739.9235
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z
Bu
O
N
O
N3
N
N

Compound 5o:

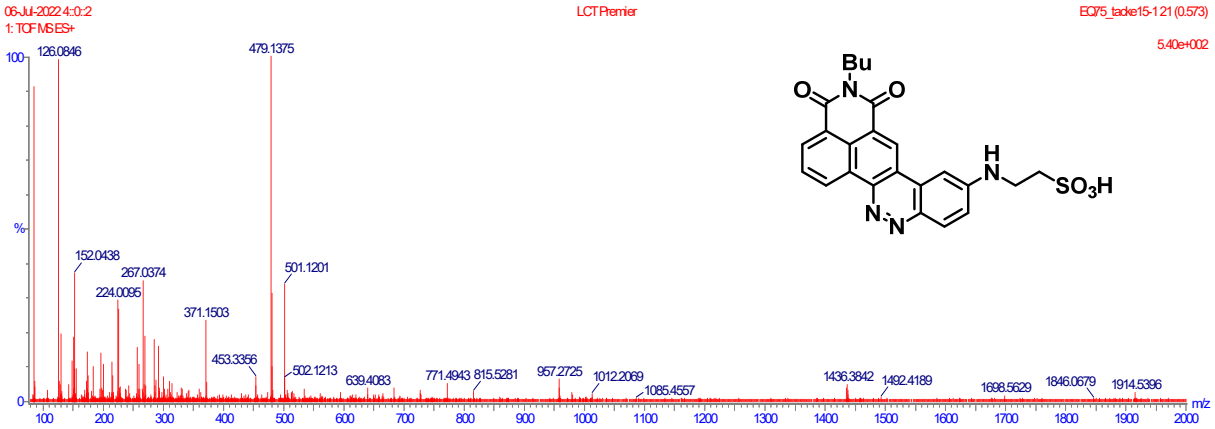
^{1}H NMR



^{13}C NMR

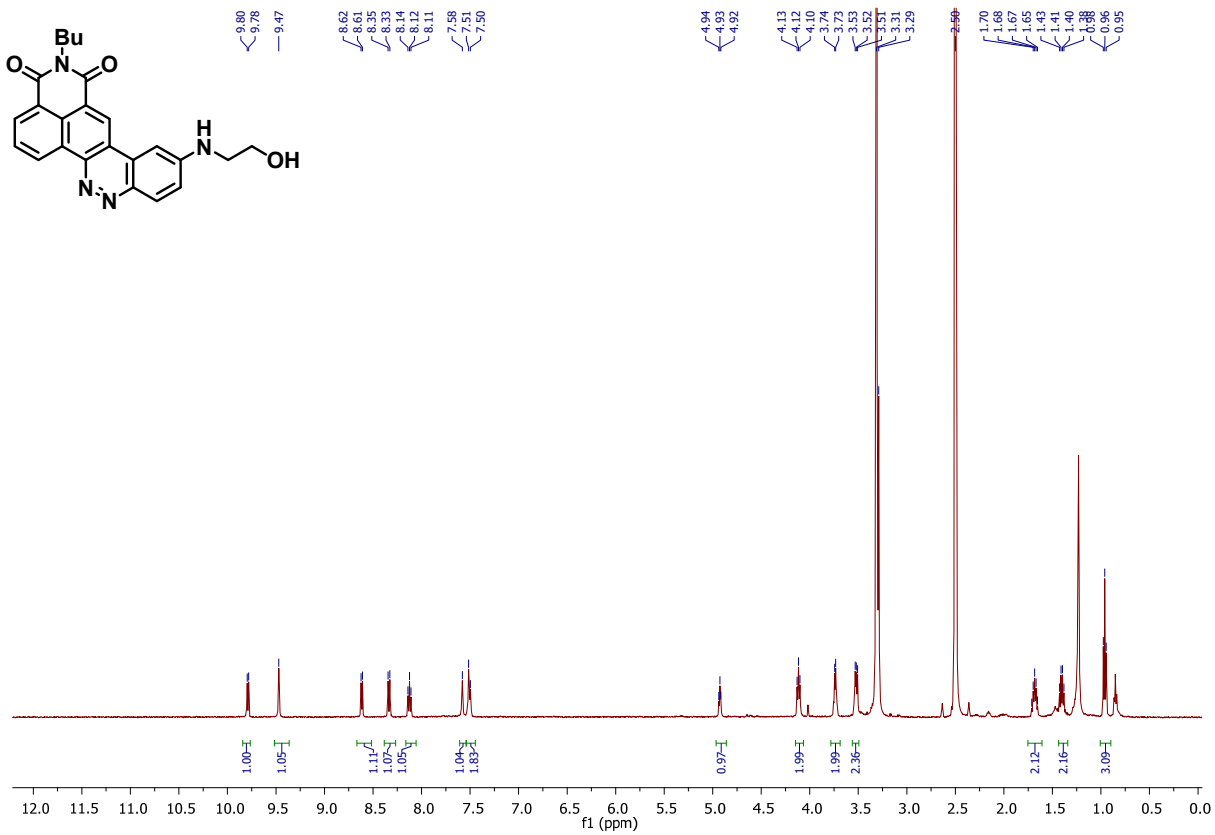


HRMS

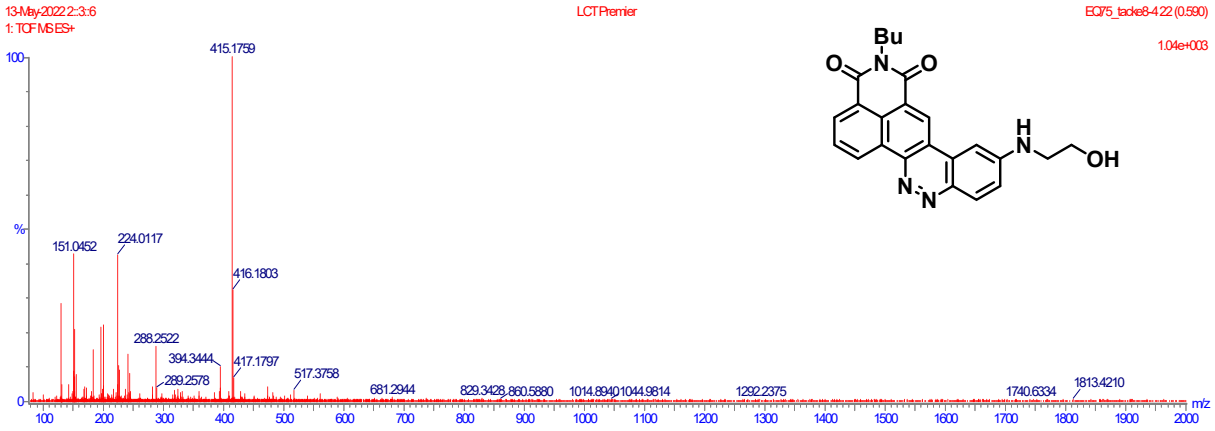

06-Jul-2022 4::0::2
1: TOF MS ES+
LCT Premier
EC75_tacke15-1 21 (0.573)
5.40e+002
100
%
0
126.0846
479.1375
152.0438
267.0374
224.0095
501.1201
371.1503
453.3356
502.1213
639.4083
771.4943
815.5281
957.2725
1012.2069
1085.4557
1436.3842
1492.4189
1698.5629
1846.0679
1914.5396
100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900 2000
m/z
Bu
O
N
O
H
N
SO3H
N
N

Compound 5p:

^{1}H NMR

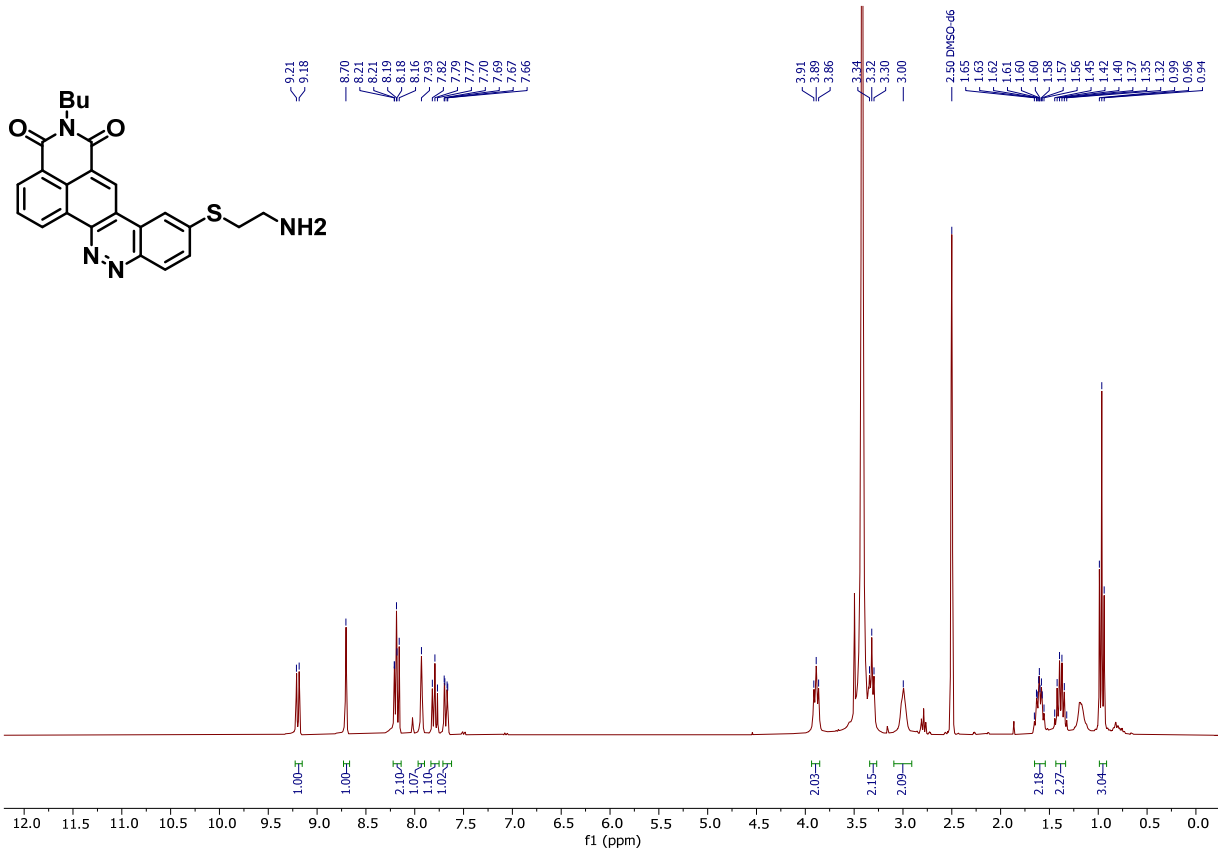


HRMS

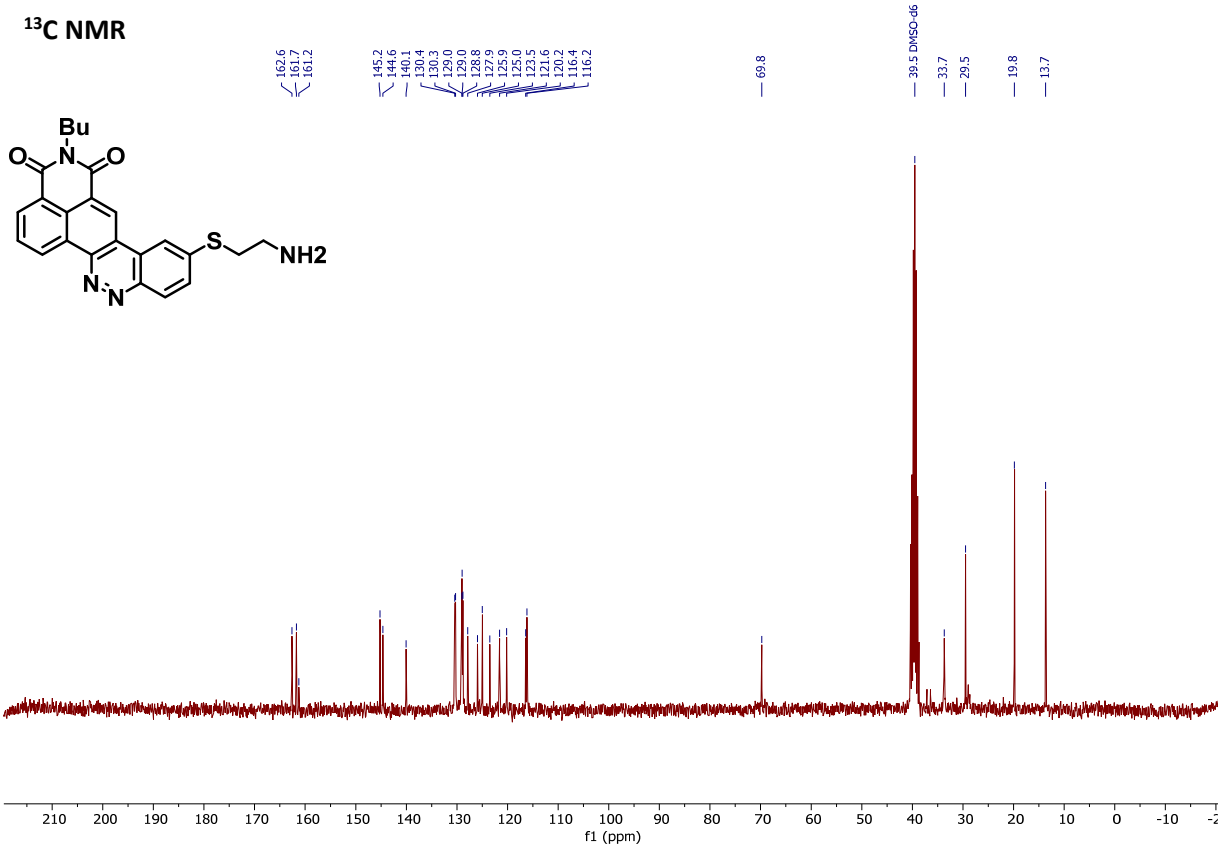


Compound 5r:

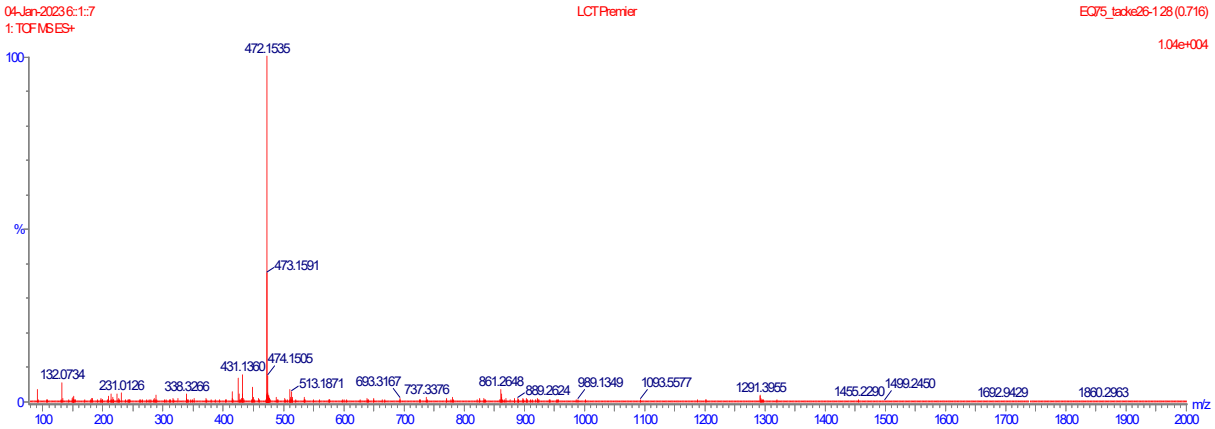
^{1}H NMR



^{13}C NMR

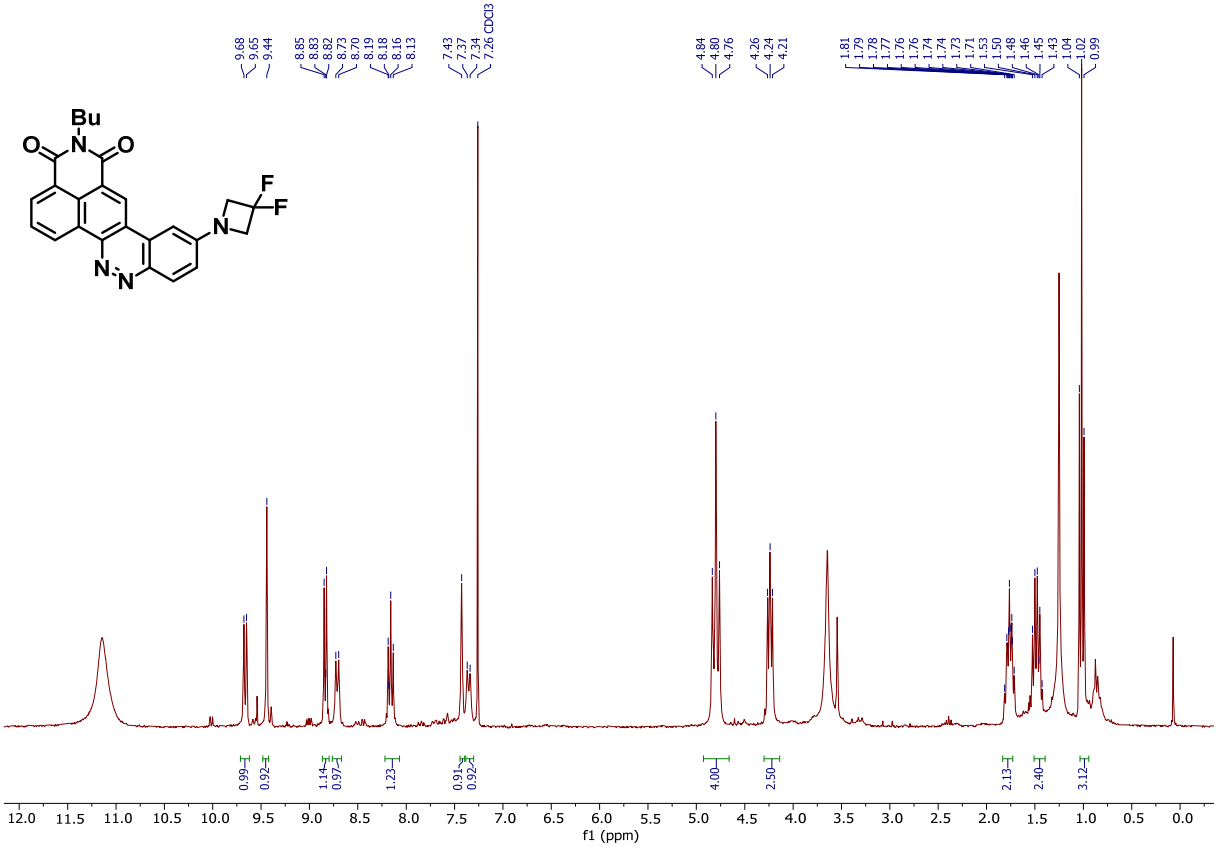


HRMS

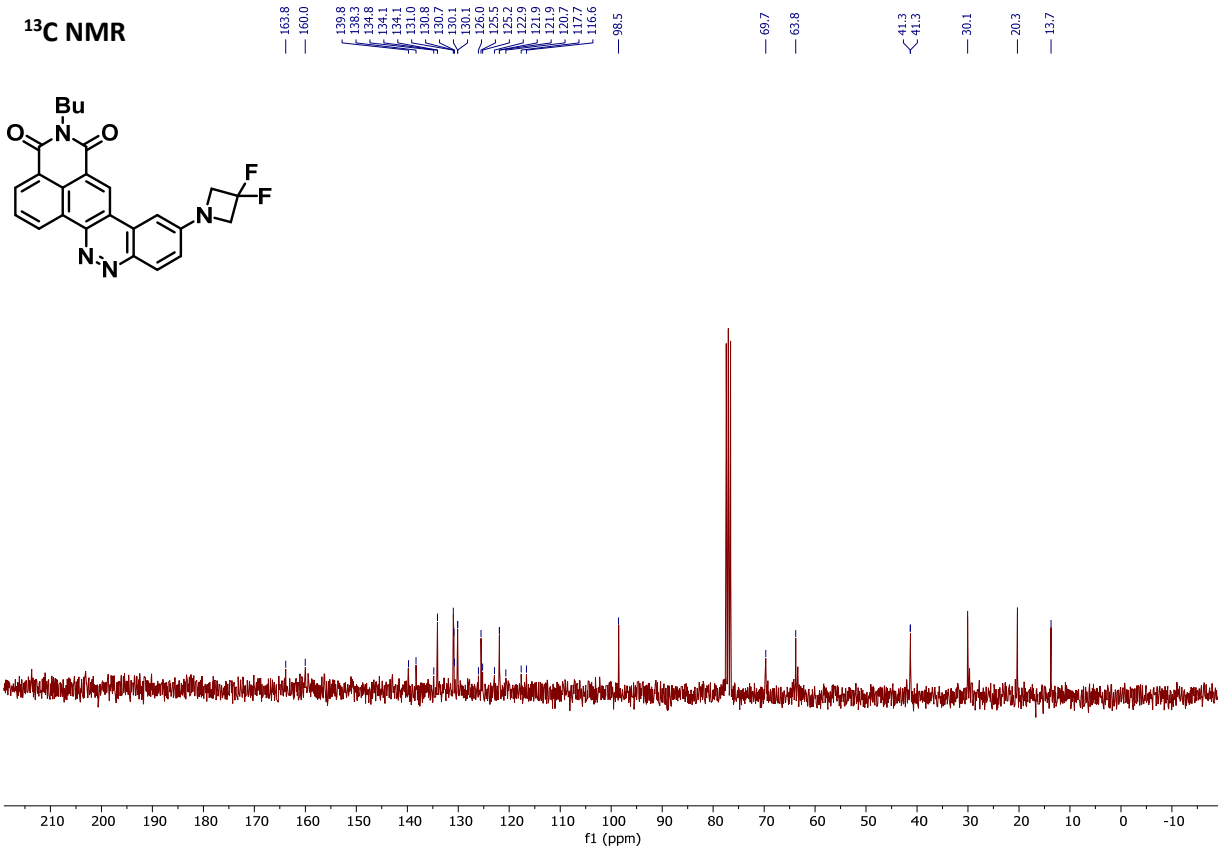

04-Jan-2023 6::1::7
LCT Premier
EC/75_tacke26-1 28 (0.716)
1: TOF MS ES+
1.04e+004
100
%
0
472.1535
473.1591
474.1505
431.1360
132.0734
231.0126
338.3266
513.1871
693.3167
737.3376
861.2648
889.2624
989.1349
1093.5577
1291.3955
1455.2290
1499.2450
1692.9429
1860.2963
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z

Compound 6a:

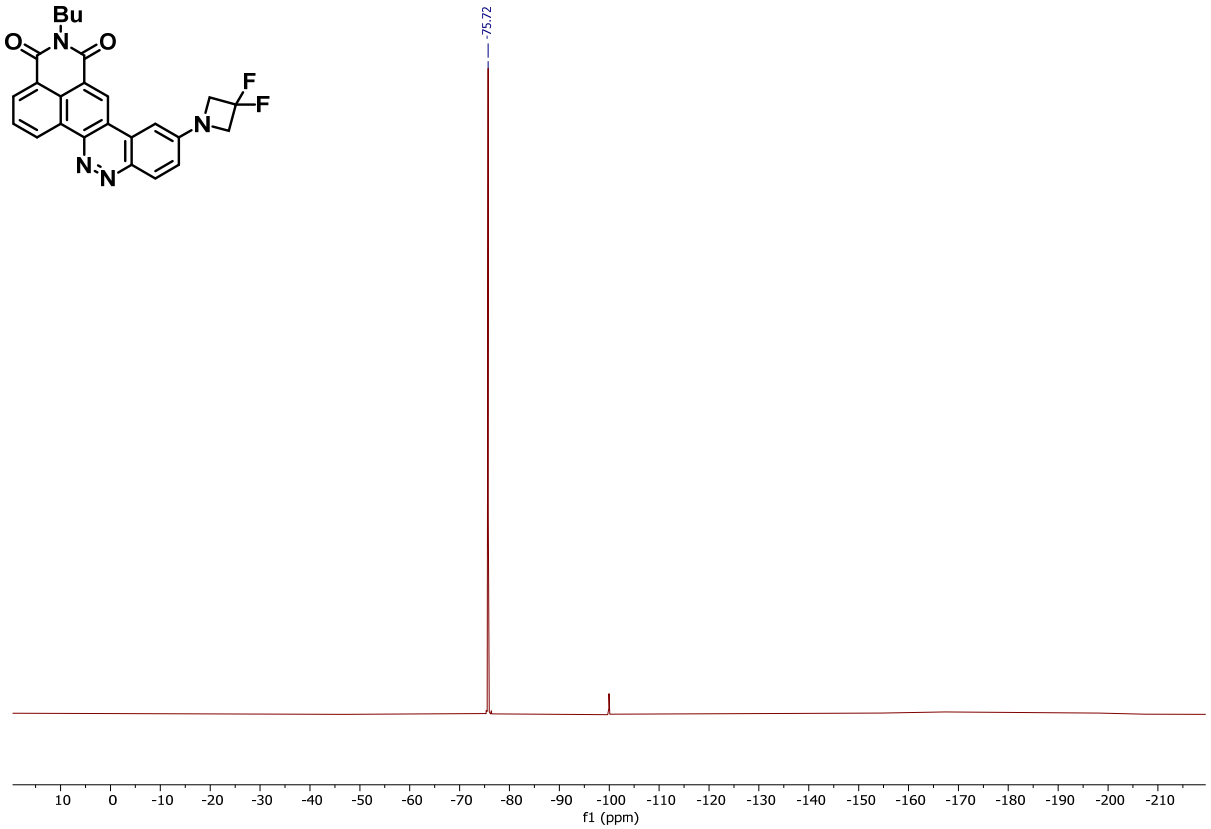
^{1}H NMR



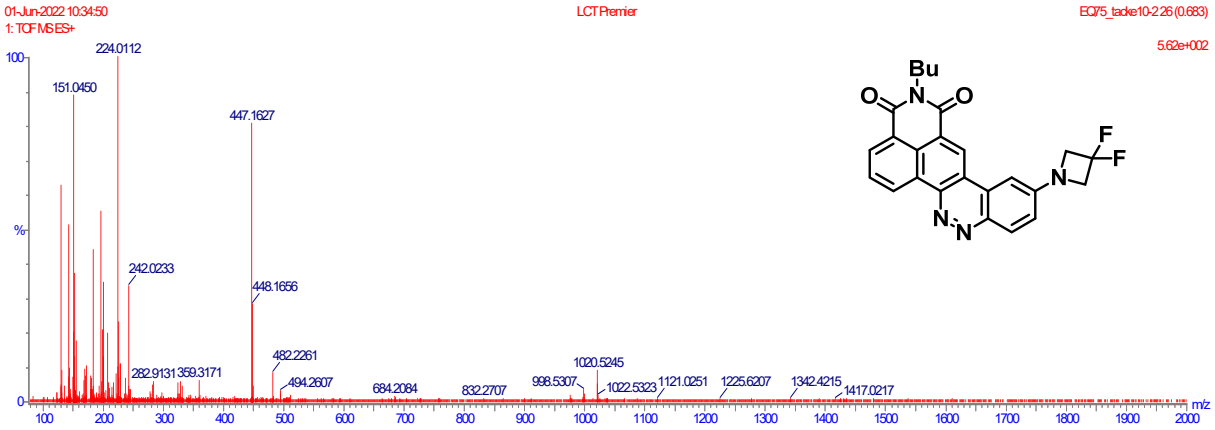
^{13}C NMR



^{19}F NMR

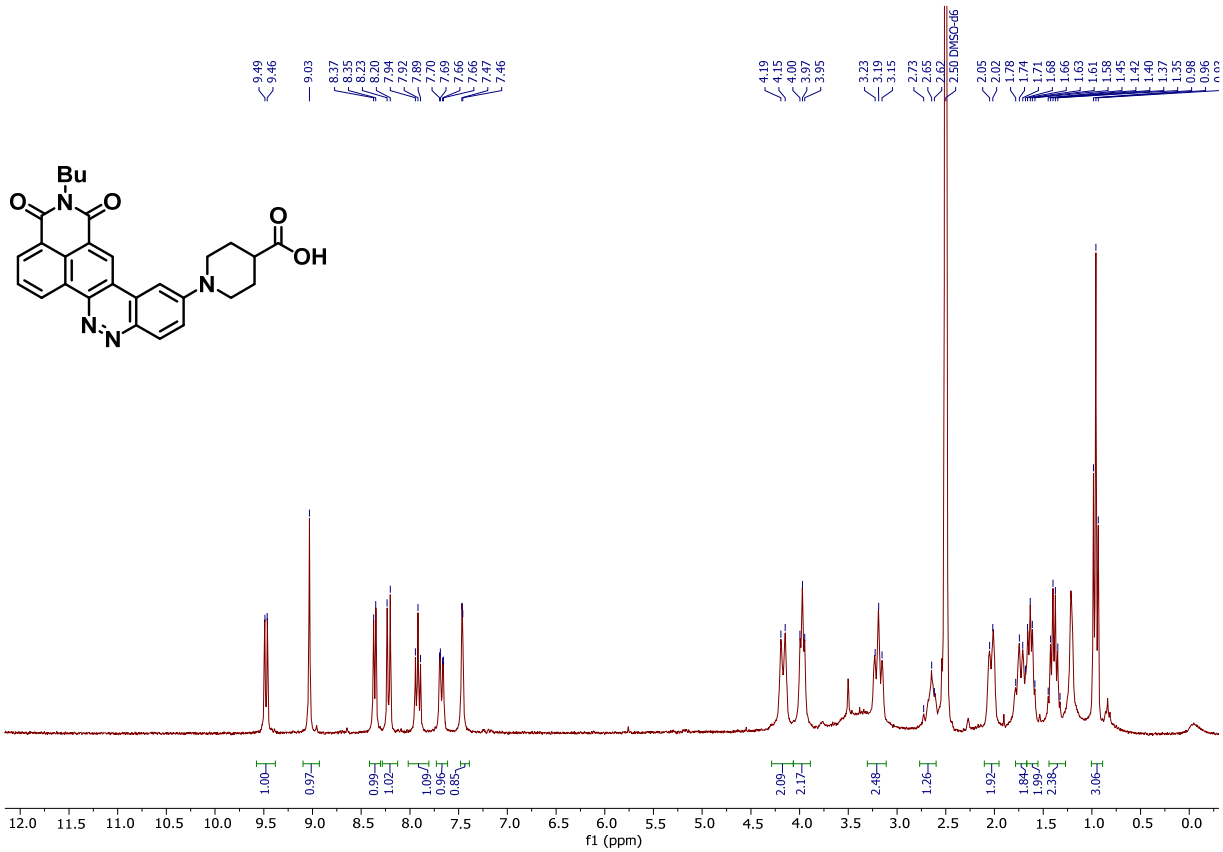

Bu
O
N
O
F
F
N
N
N
-75.72
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

HRMS

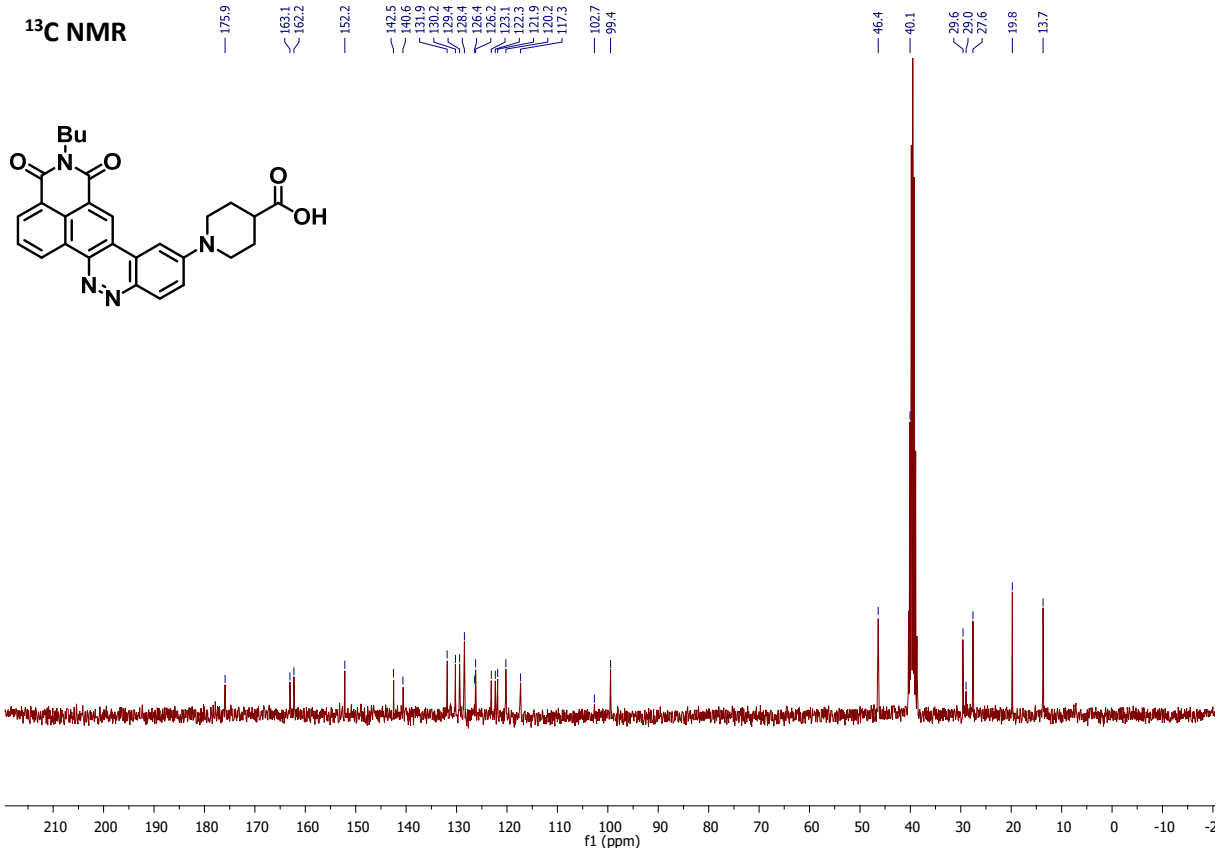

01-Jun-2022 10:34:50
1: TOF MS ES+
LCT Premier
EQ75_tacke10-2 26 (0.683)
5.62e+002
100
%
0
224.0112
151.0450
447.1627
242.0233
448.1656
482.2261
282.9131
359.3171
494.2607
684.2084
832.2707
998.5307
1020.5245
1022.5323
1121.0251
1225.6207
1342.4215
1417.0217
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z
Bu
O
N
O
F
F
N
N
N

Compound 6b:

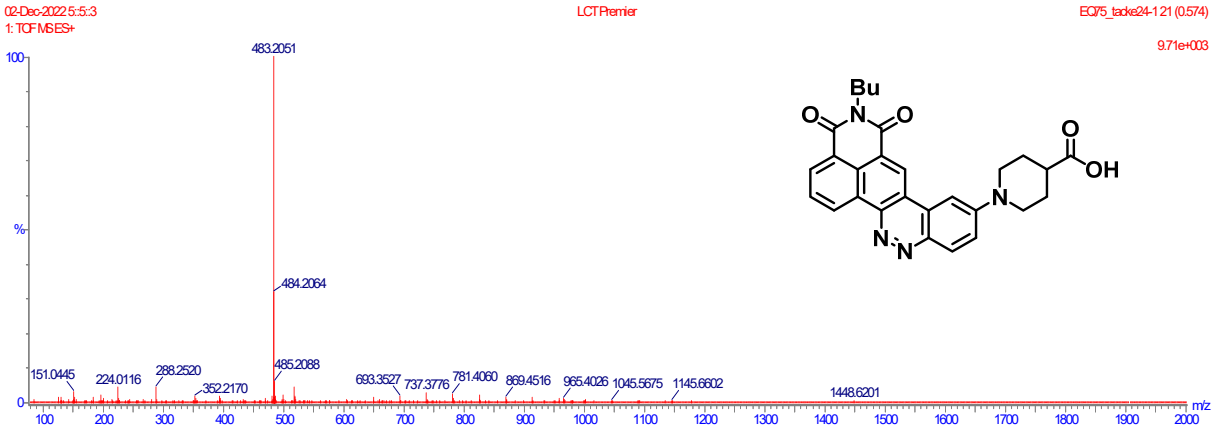
^{1}H NMR



^{13}C NMR

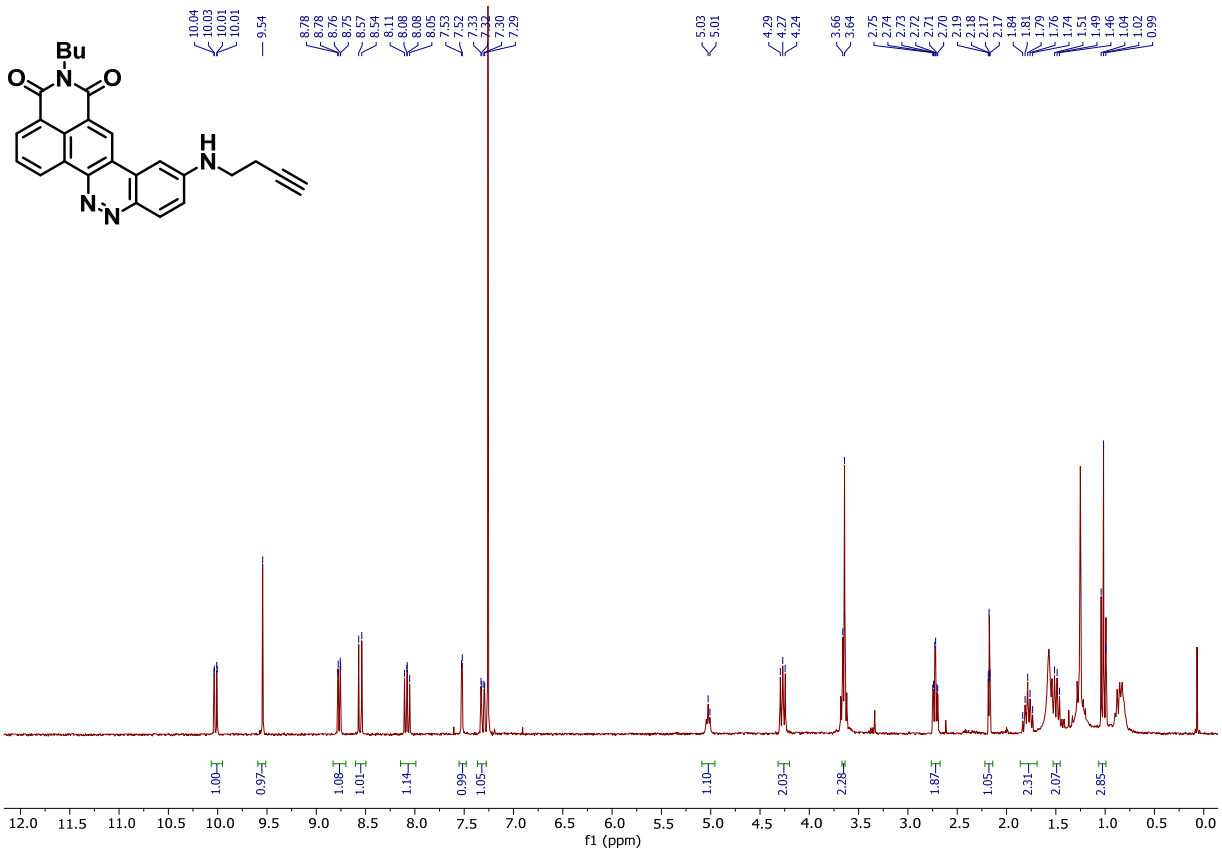


HRMS

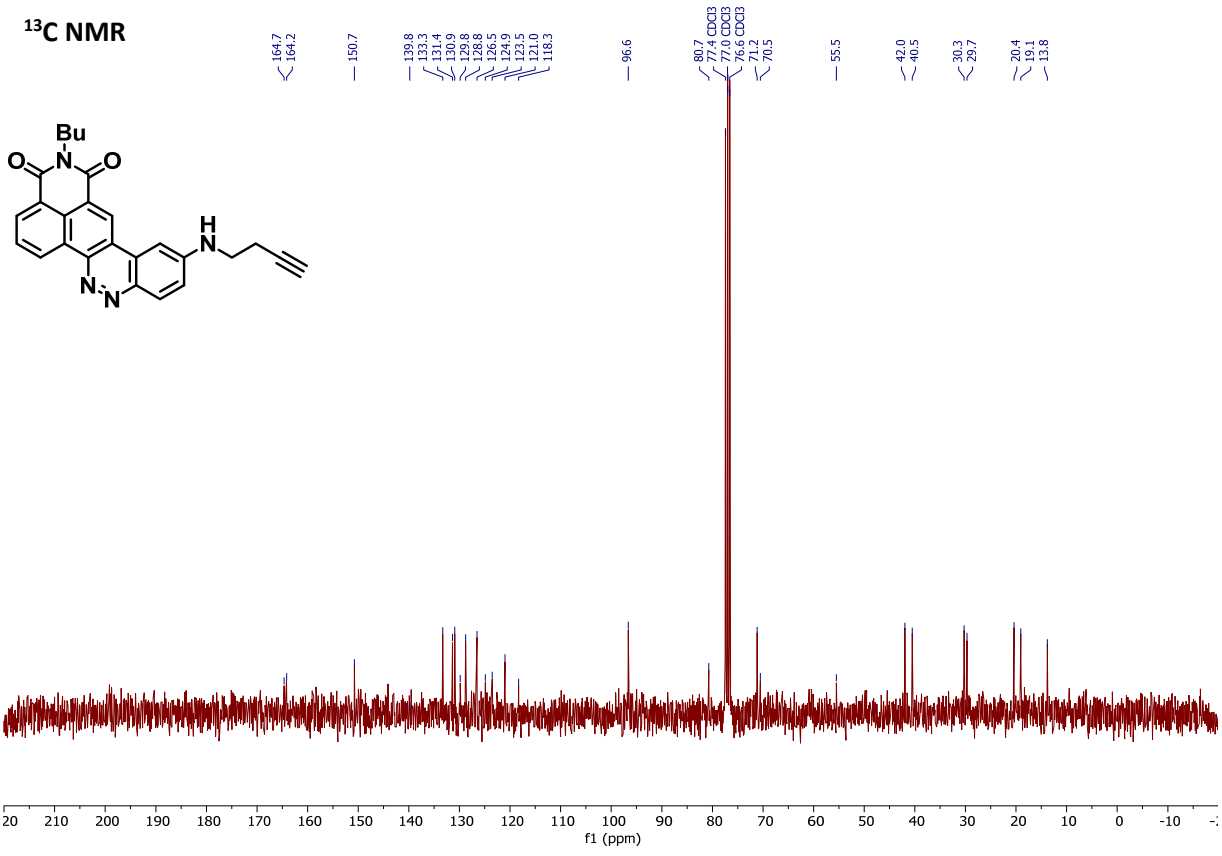

02-Dec-2022 5::5::3
LCT Premier
EC75_tacke24-1 21 (0.574)
1: TOF MS ES+
9.71e+003
100
%
0
483.2051
484.2064
485.2088
151.0445
224.0116
288.2520
352.2170
693.3527
737.3776
781.4060
869.4516
965.4026
1045.5675
1145.6602
1448.6201
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
N
O
O
O
OH
N
N
N

Compound 6c:

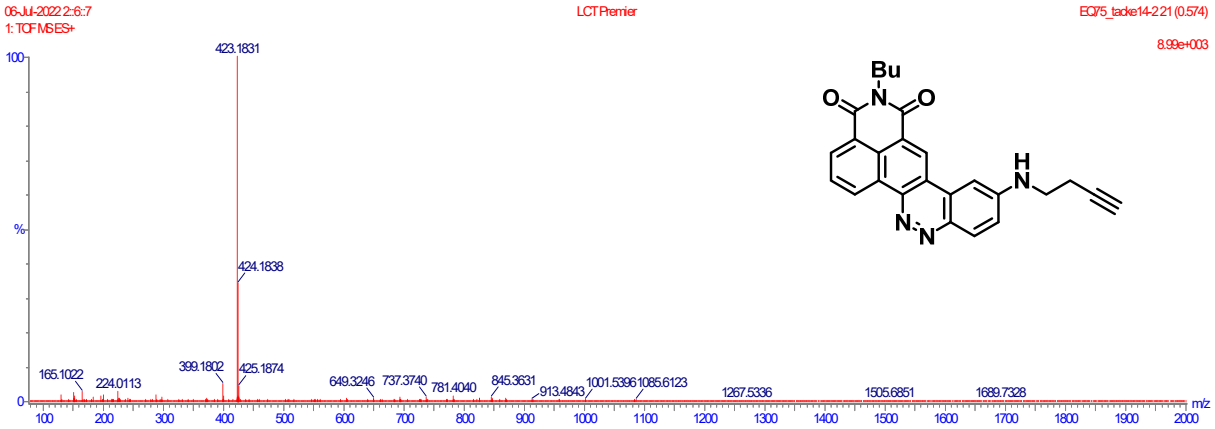
^{1}H NMR



^{13}C NMR

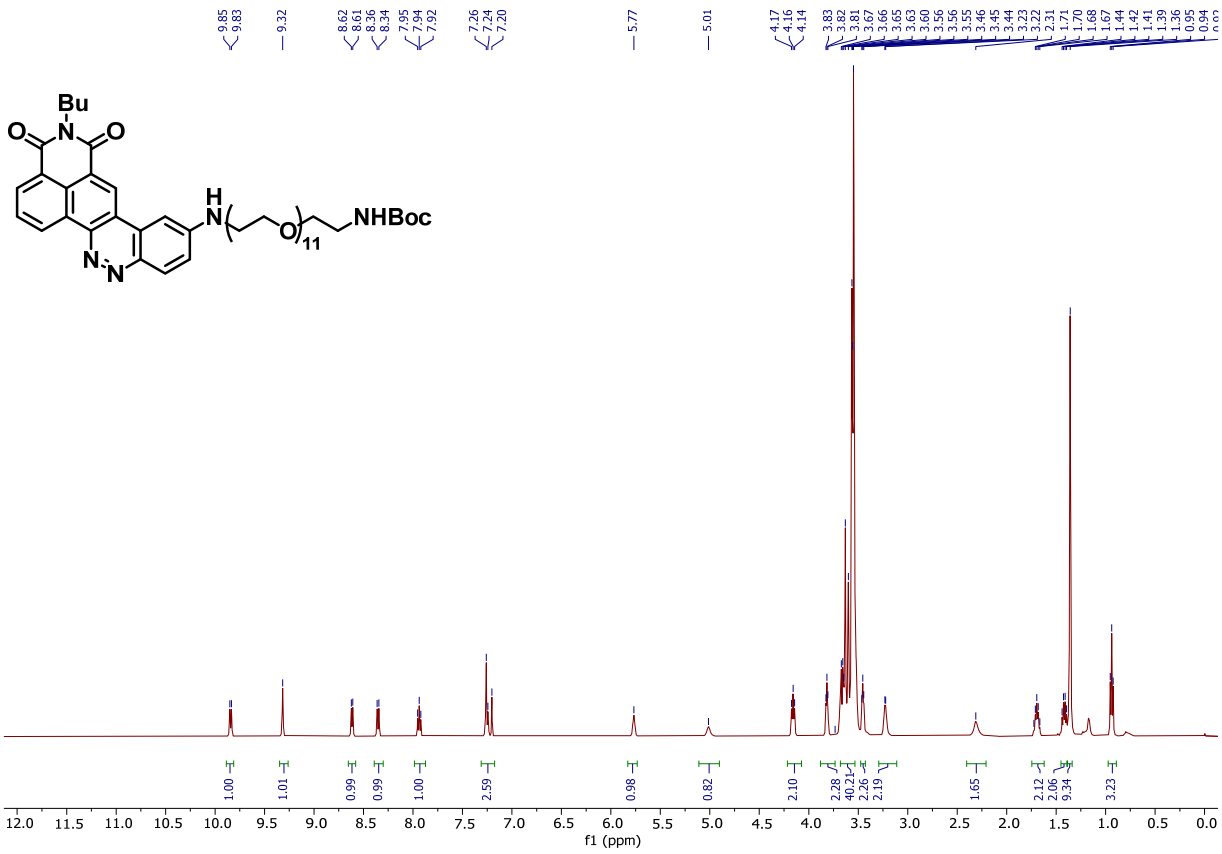


HRMS

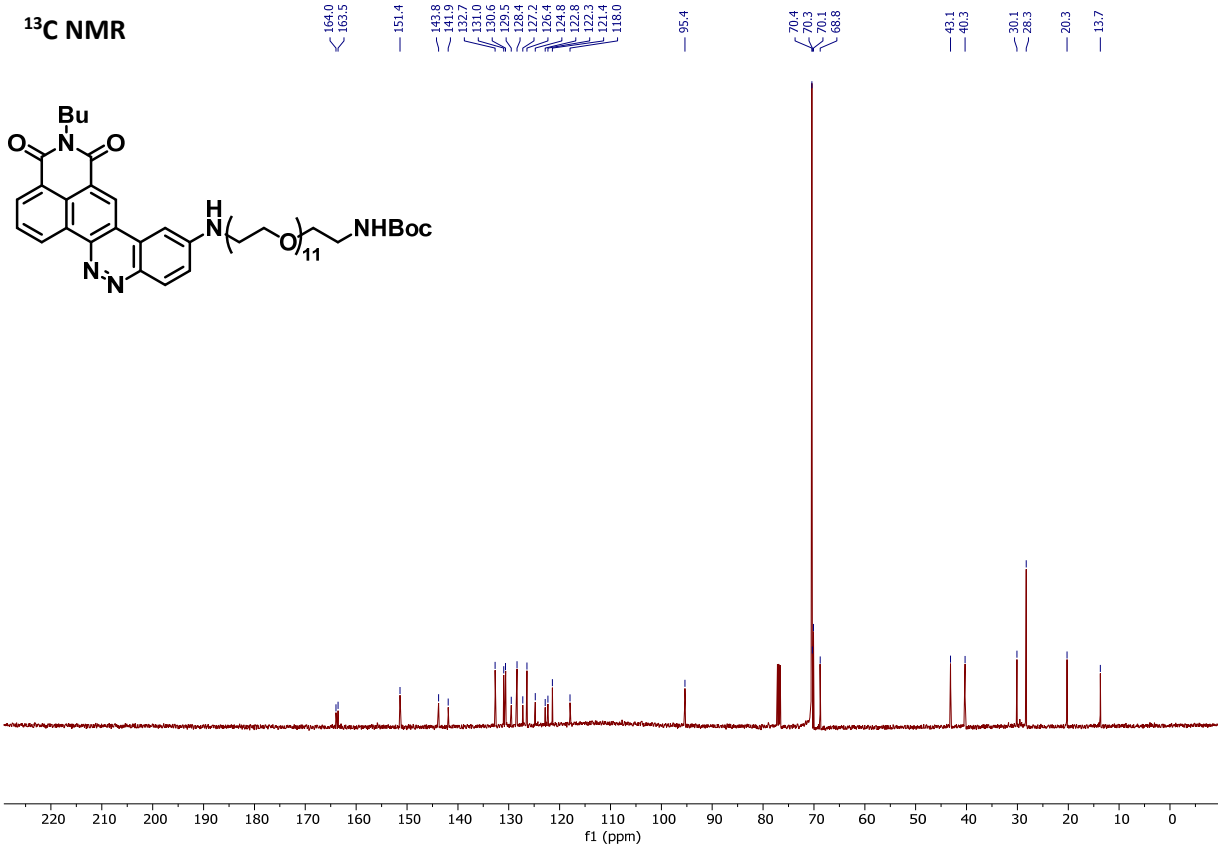

06-Jul-2022 2::6::7
LCT Premier
EC75_tacke14-2 21 (0.574)
1: TOF MS ES+
8.99e+003
423.1831
424.1838
425.1874
399.1802
165.1022
224.0113
649.3246
737.3740
781.4040
845.3631
913.4843
1001.5396
1085.6123
1267.5336
1505.6851
1689.7328
Bu
O
N
O
H
N
N
N
%
m/z

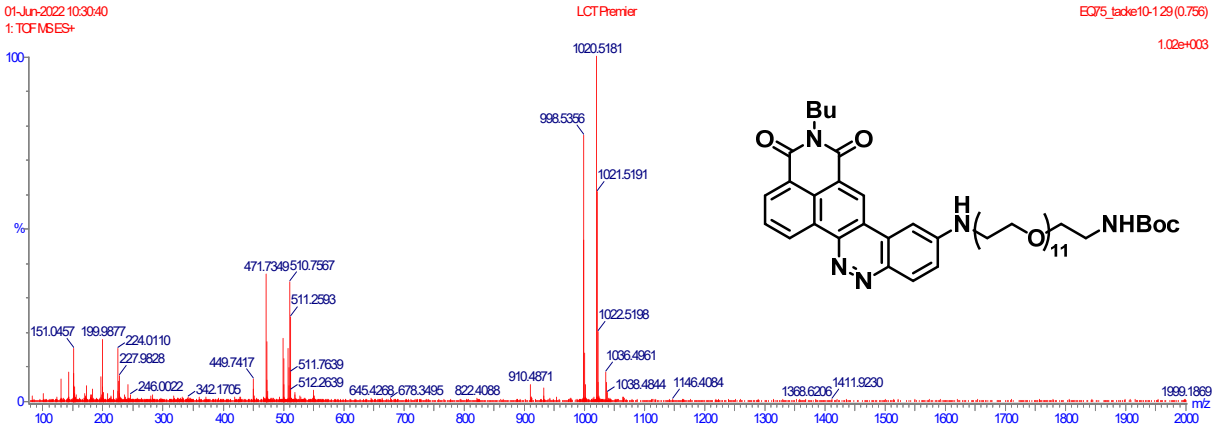
Compound X:

^{1}H NMR



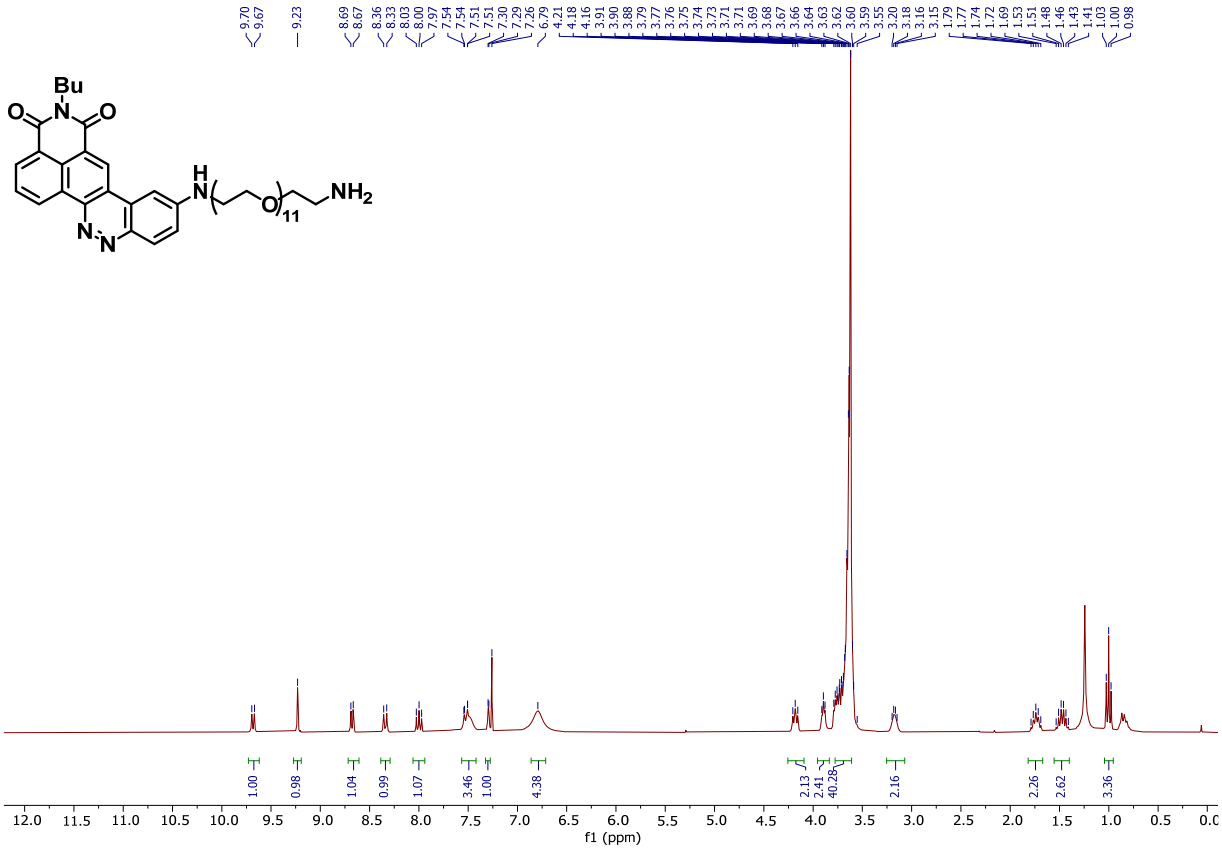
^{13}C NMR



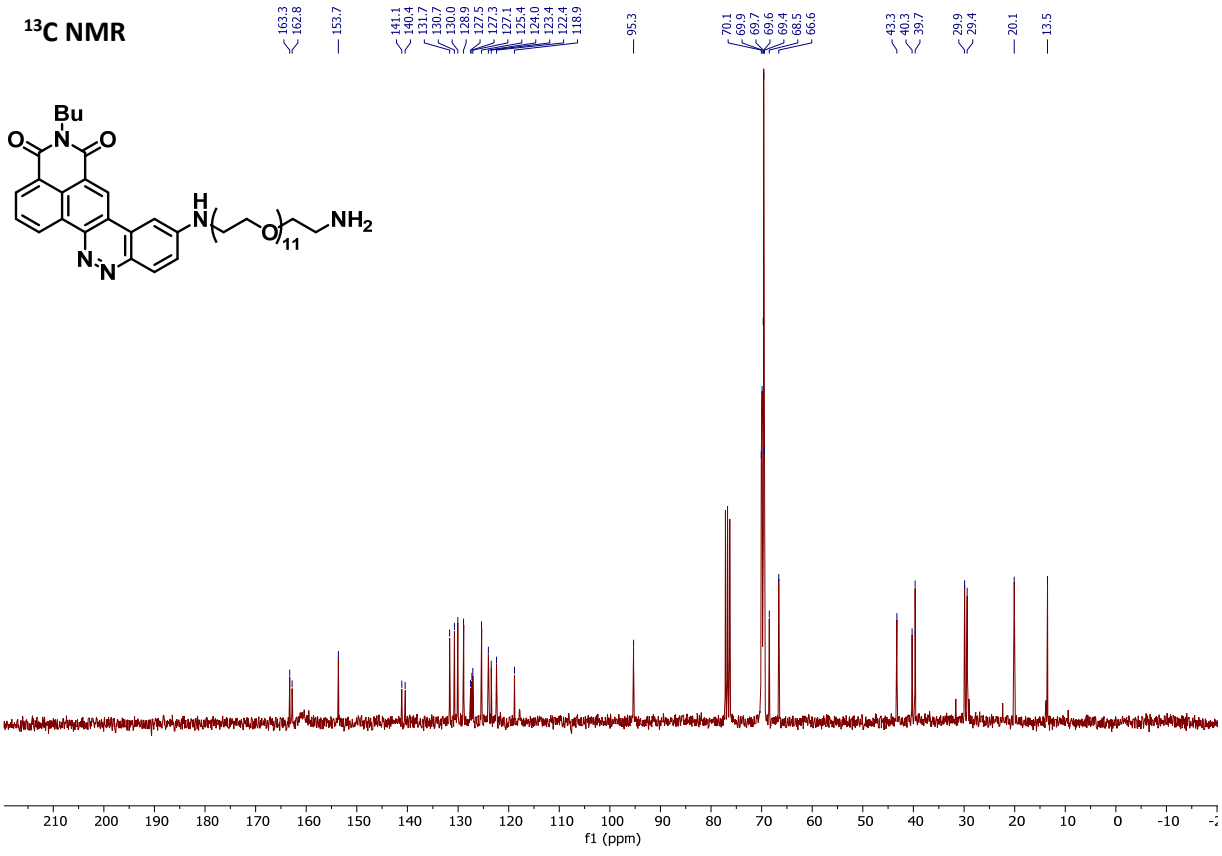

01-Jun-2022 10:30:40
1: TOF MS ES+
LCT Premier
EC75_tacke10-1 29 (0.756)
1.02e+003
100
%
0
1020.5181
998.5356
1021.5191
471.7349
510.7567
511.2593
1022.5198
151.0457
199.9877
224.0110
227.9828
449.7417
511.7639
512.2639
1036.4961
246.0022
342.1705
645.4268
678.3495
822.4088
910.4871
1038.4844
1146.4084
1368.6206
1411.9230
1999.1869
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
N
O
O
H
N
O
11
NHBoc
N
N

Compound 6d:

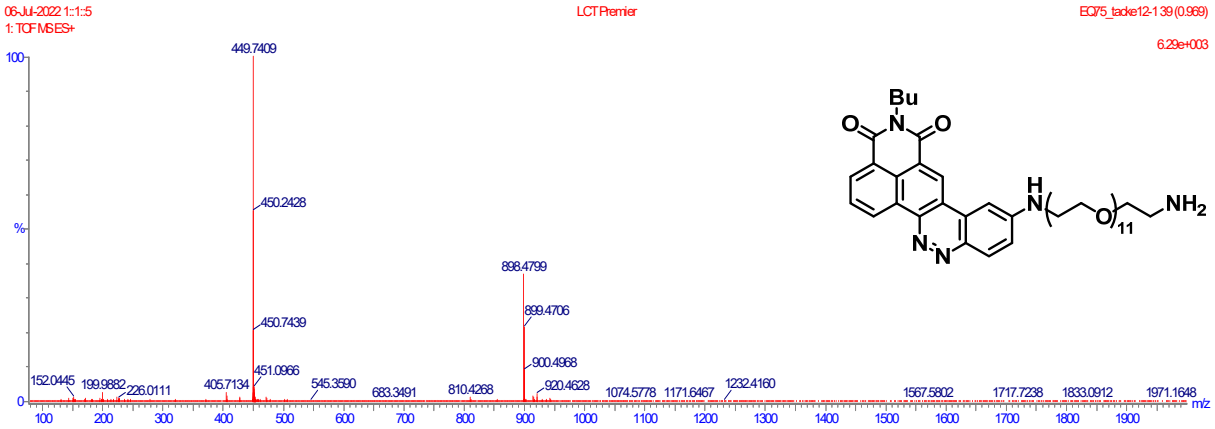
^{1}H NMR



^{13}C NMR

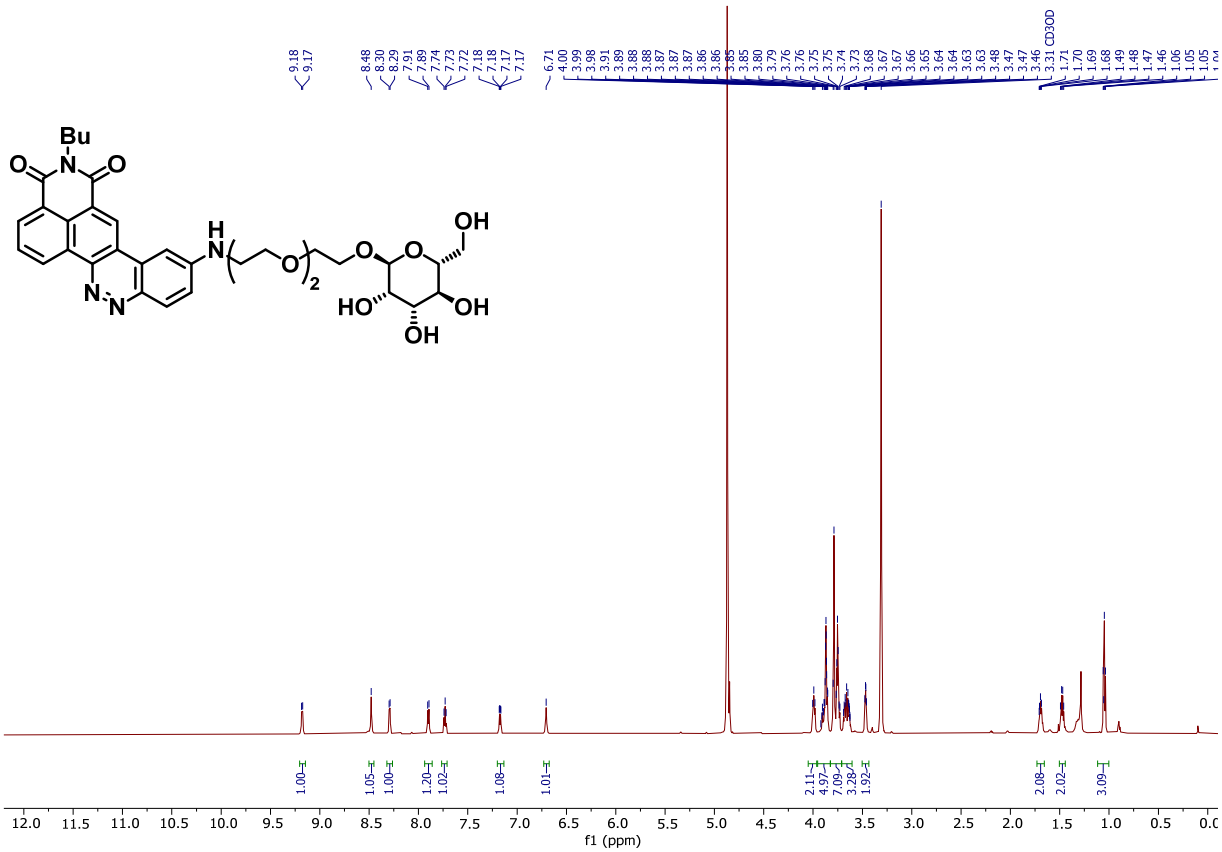


HRMS

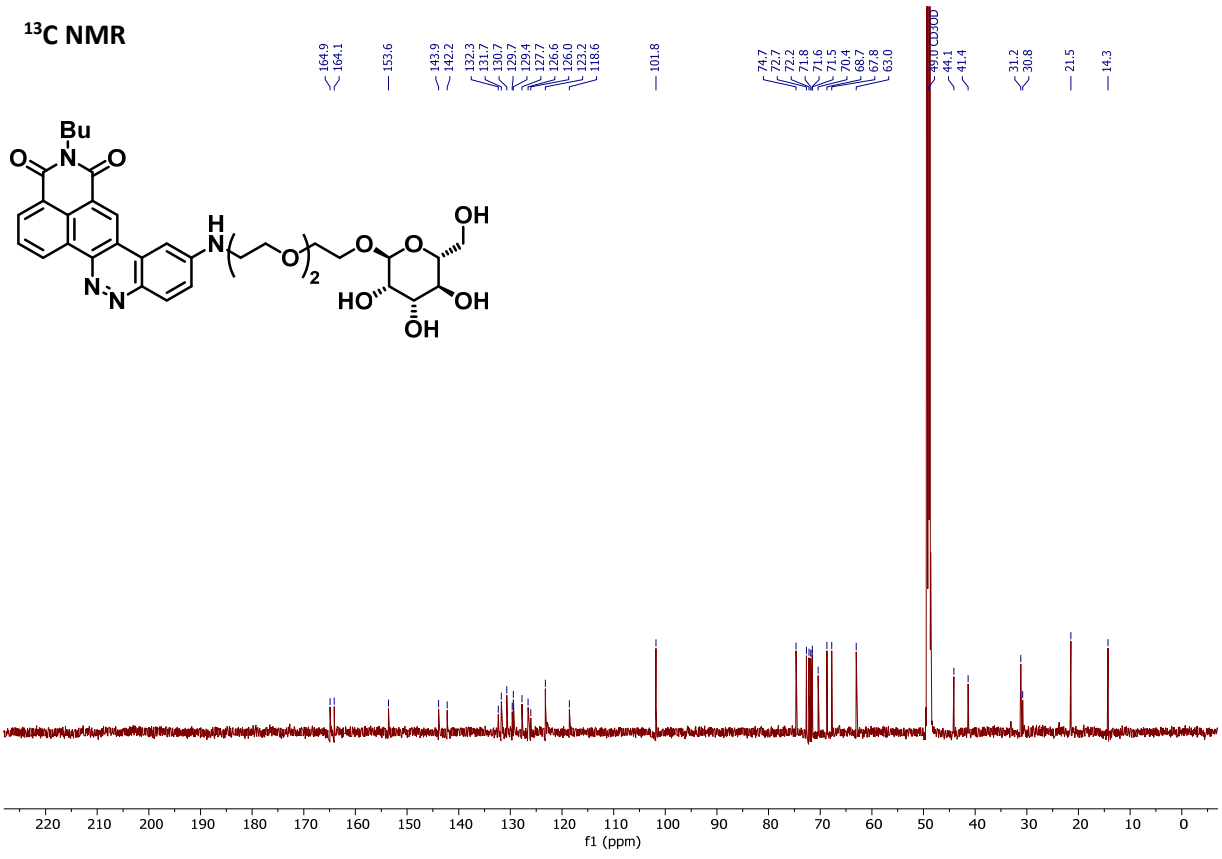

06-Jul-2022 1::1::5
LCT Premier
EC75_tacke12-1 39 (0.969)
1: TOF MS ES+
6.29e+003
449.7409
450.2428
898.4799
899.4706
450.7439
900.4968
451.0966
152.0445
199.9882
226.0111
405.7134
545.3590
683.3491
810.4268
920.4628
1074.5778
1171.6467
1232.4160
1567.5802
1717.7238
1833.0912
1971.1648
%
m/z
Bu
H
NH2
11

Compound 6e:

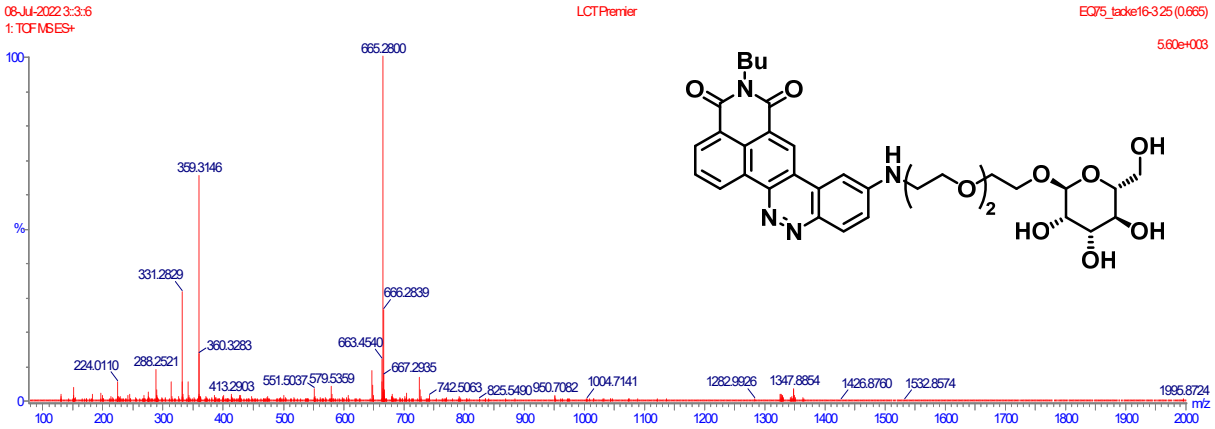
^{1}H NMR



^{13}C NMR

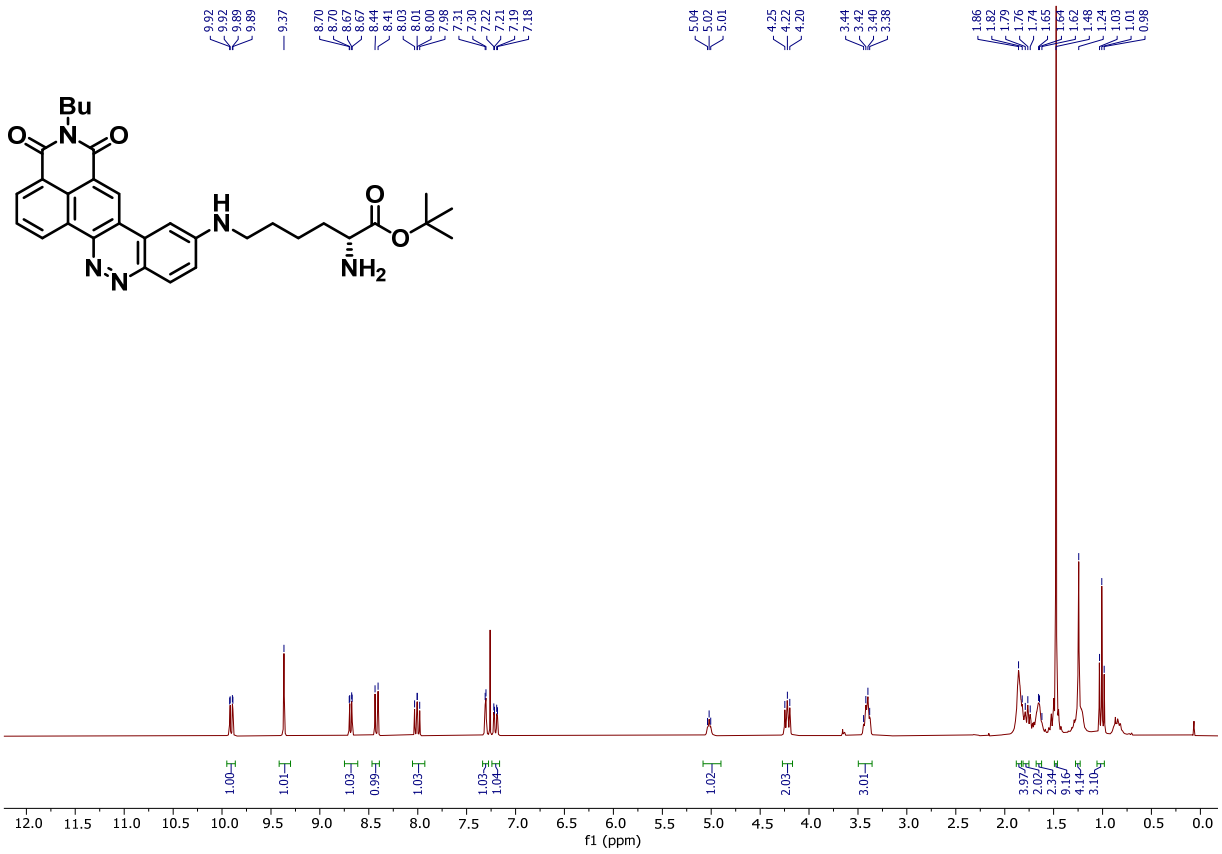


HRMS

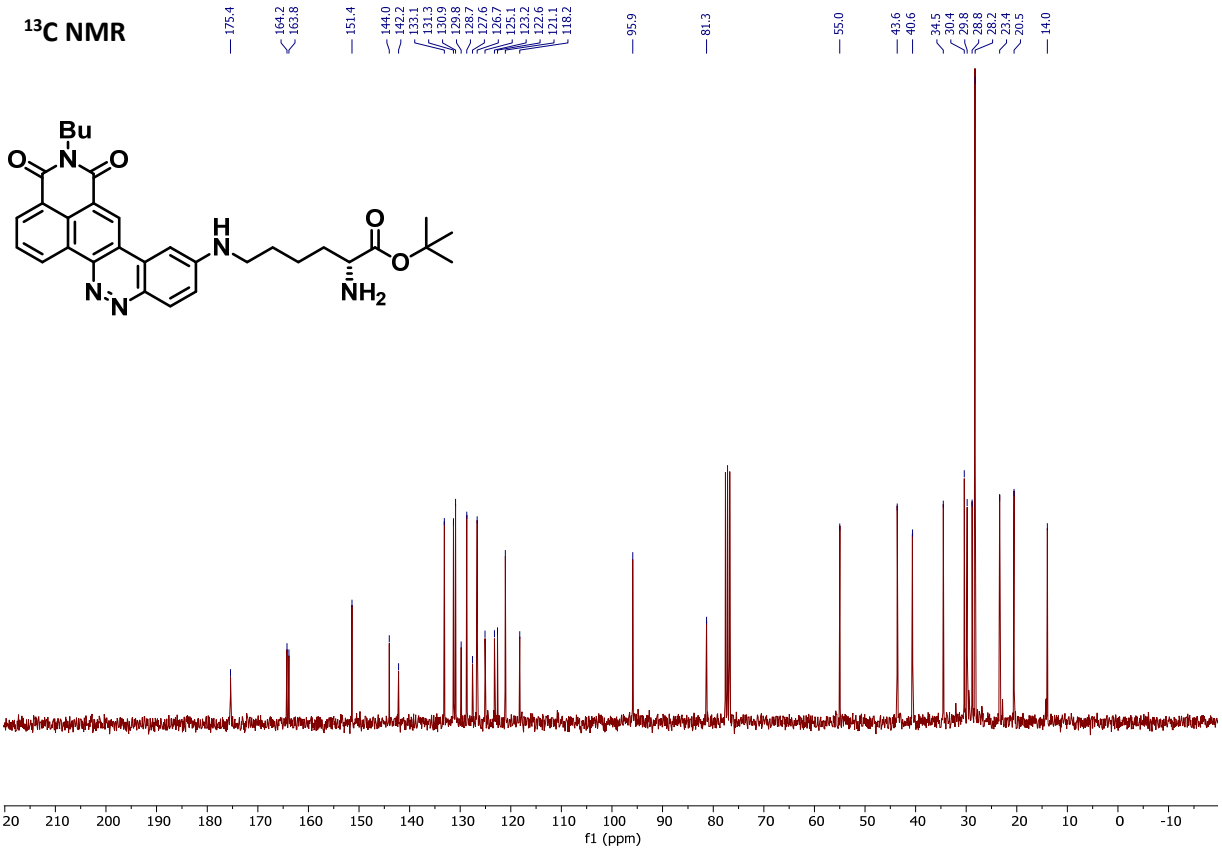

08-Jul-2022 3::3:6
1: TOF MS ES+
LCT Premier
EQ75_tacke16-3 25 (0.665)
5.60e+003
100
%
0
665.2800
359.3146
331.2829
666.2839
360.3283
663.4540
667.2935
224.0110
288.2521
413.2903
551.5037
579.5359
742.5063
825.5490
950.7082
1004.7141
1282.9926
1347.8854
1426.8760
1532.8574
1995.8724
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
H
N
N
N
O
2
O
O
OH
HO
OH
OH

Compound 6f:

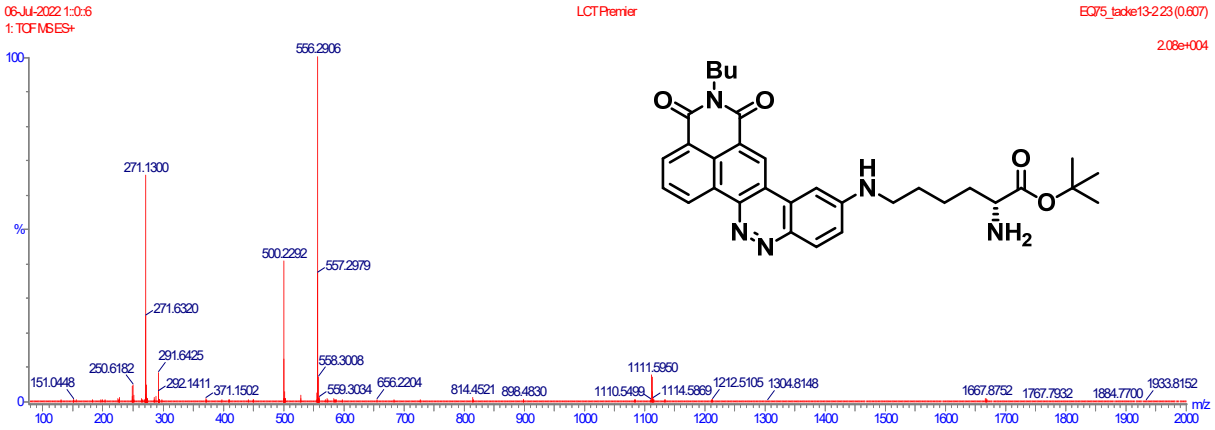
^{1}H NMR



^{13}C NMR

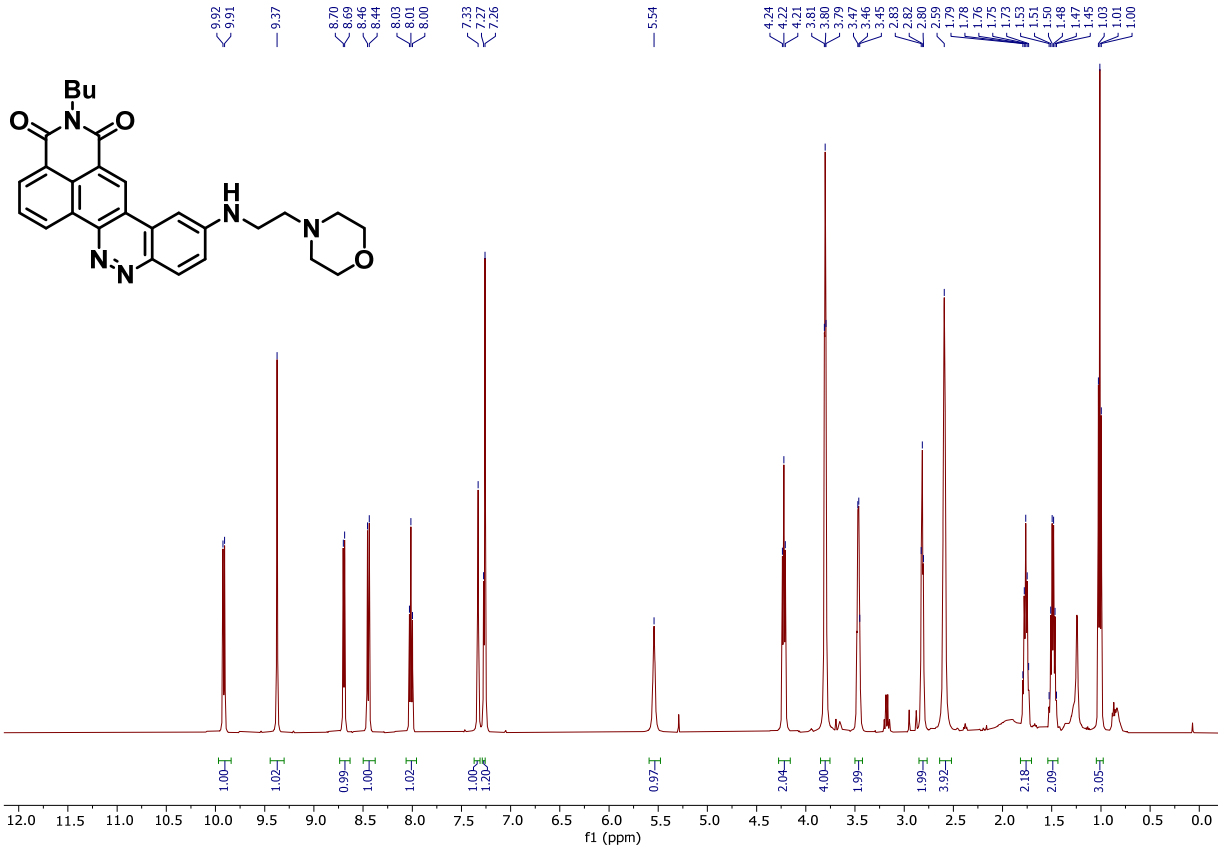


HRMS

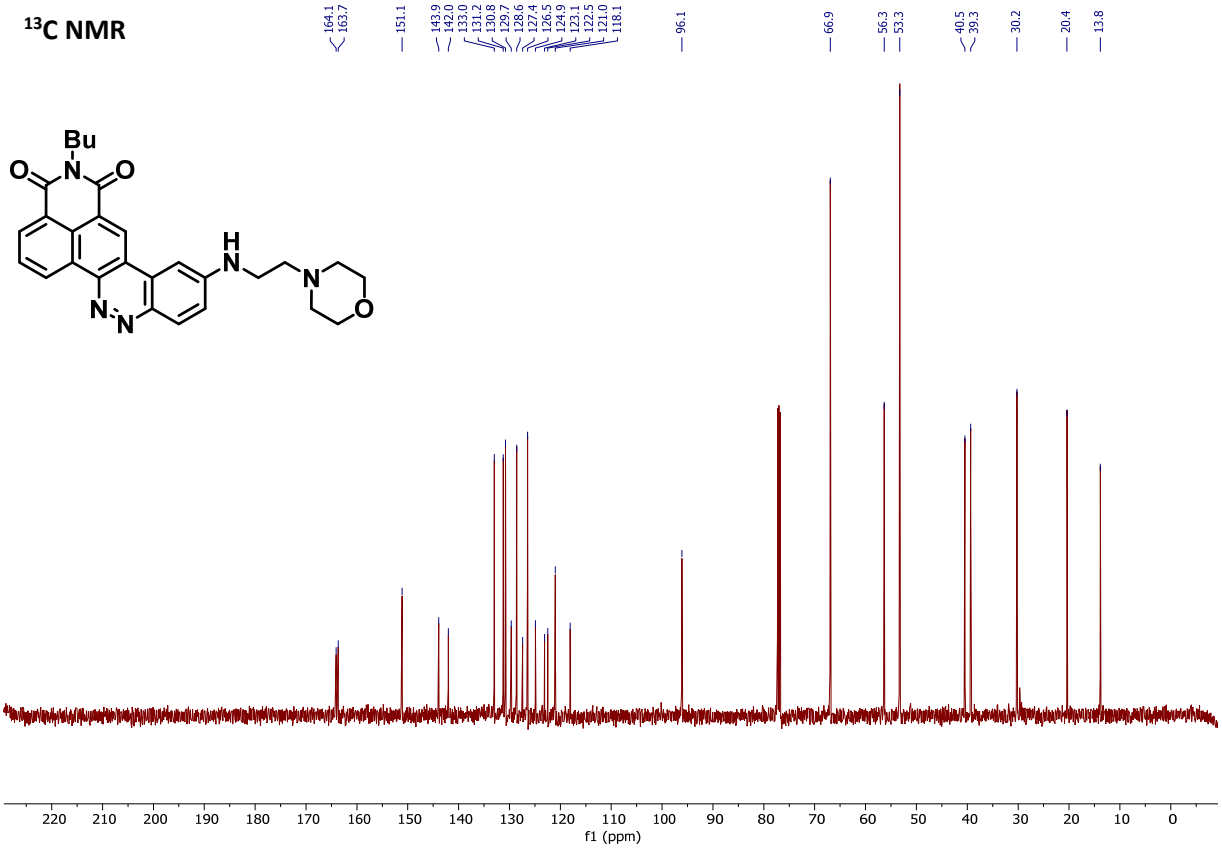

06-Jul-2022 1::0:6
1: TOF MS ES+
LCT Premier
EO75_tadke13-2 23 (0.607)
2.08e+004
100
%
0
556.2906
271.1300
500.2292
557.2979
271.6320
291.6425
558.3008
250.6182
292.1411
151.0448
371.1502
559.3034
656.2204
814.4521
898.4830
1111.5950
1110.5499
1114.5869
1212.5105
1304.8148
1667.8752
1767.7932
1884.7700
1933.8152
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
H
N
O
O
NH2
N
N

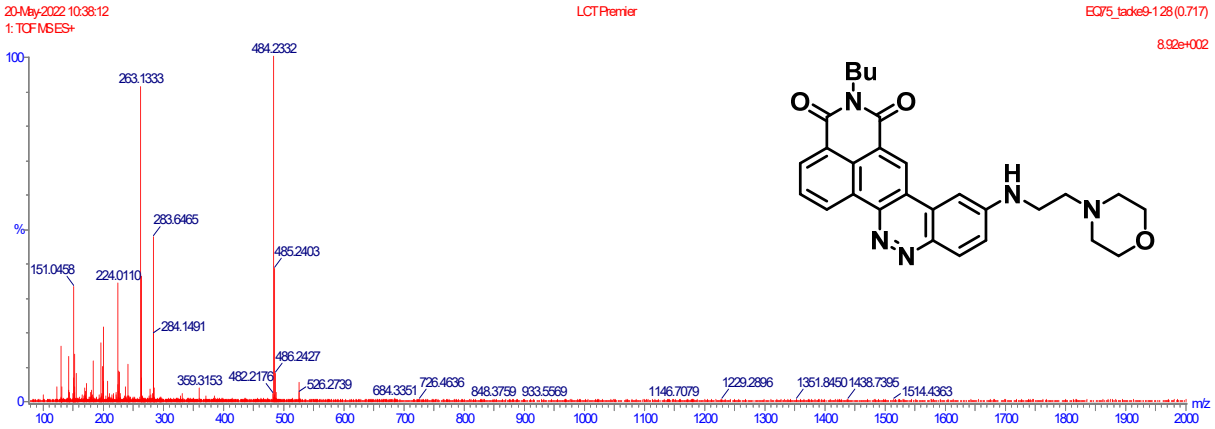
Compound 6g:

^{1}H NMR



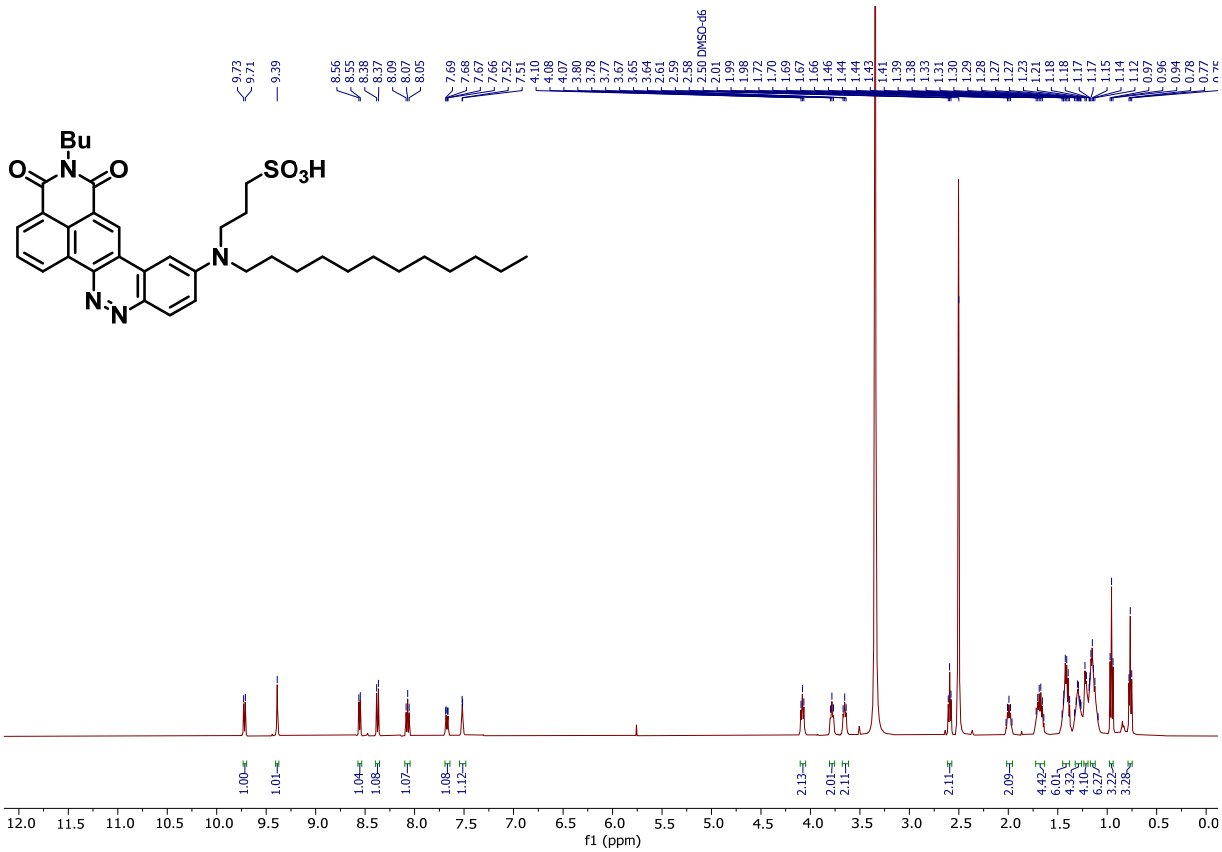
^{13}C NMR



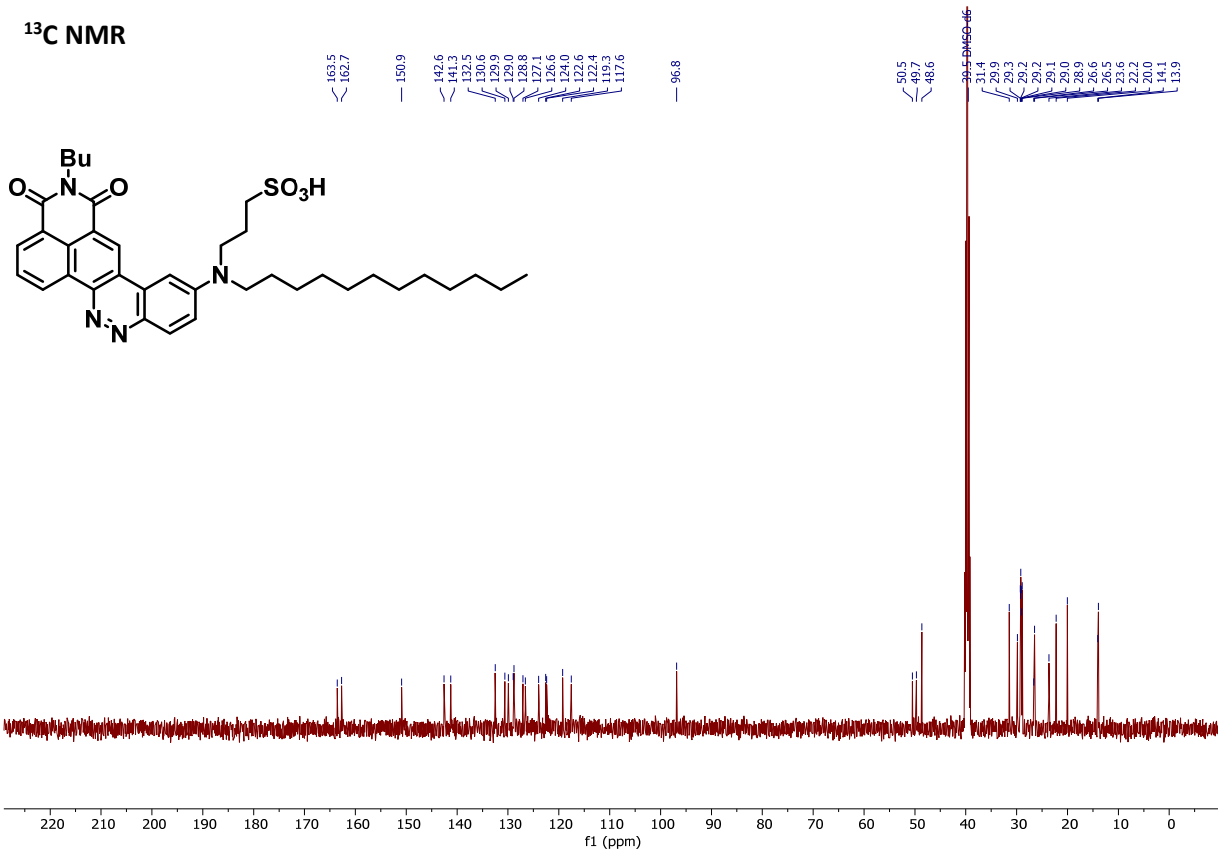

20-May-2022 10:38:12
LCT Premier
EQ75_tacke9-1 28 (0.717)
1: TOF MS ES+
8.92e+002
100
%
0
484.2332
263.1333
283.6465
485.2403
151.0458
224.0110
284.1491
486.2427
359.3153
482.2176
526.2739
684.3351
726.4636
848.3759
933.5569
1146.7079
1229.2896
1351.8450
1438.7395
1514.4363
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
H
N
N
N
N
O

Compound 6h:

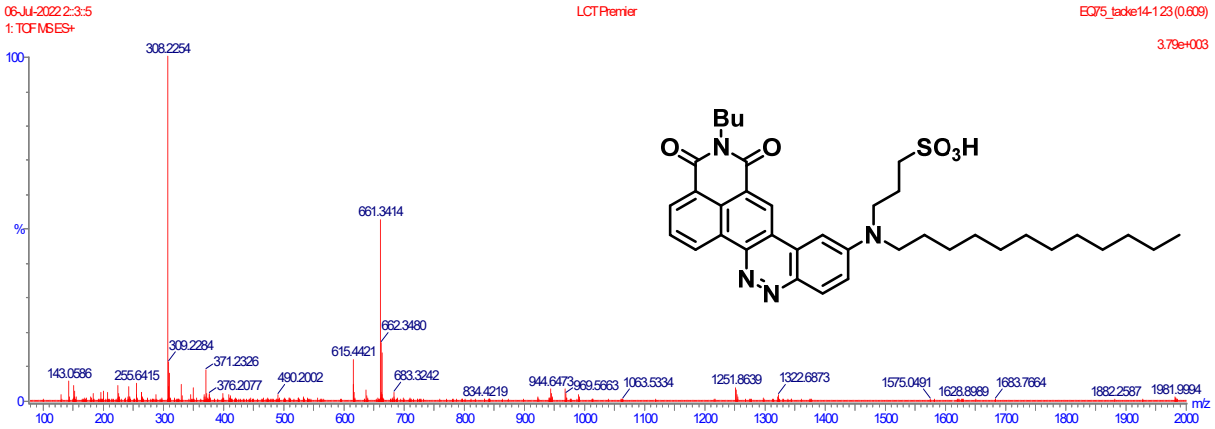
^{1}H NMR



^{13}C NMR

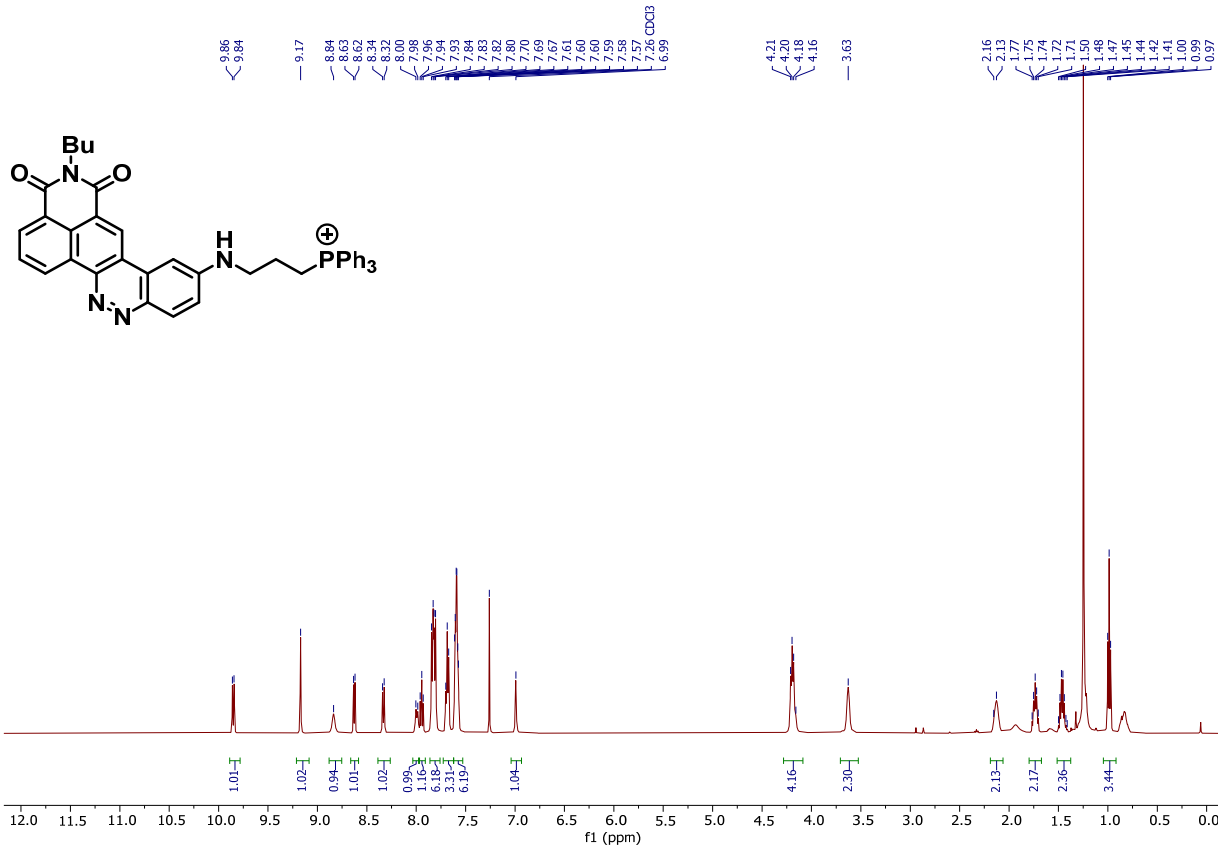


HRMS

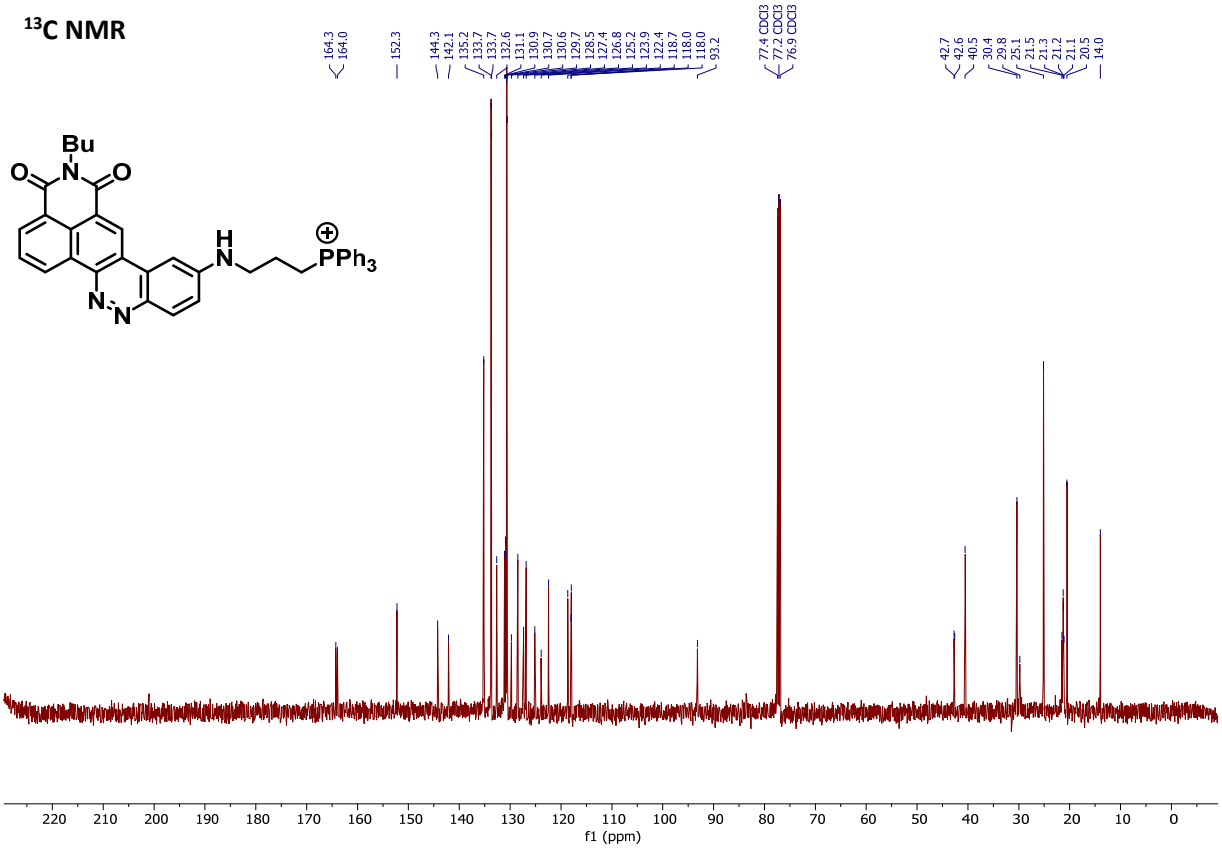

06-Jul-2022 2::3:5
LCT Premier
EC75_tacke14-1 23 (0.609)
1: TOF MS ES+
3.79e+003
100
%
0
308.2254
661.3414
662.3480
309.2284
615.4421
371.2326
376.2077
490.2002
683.3242
143.0586
255.6415
834.4219
944.6473
969.5663
1063.5334
1251.8639
1322.6873
1575.0491
1628.8989
1683.7664
1882.2587
1981.9994
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
SO3H
N
N
N

Compound 6i:

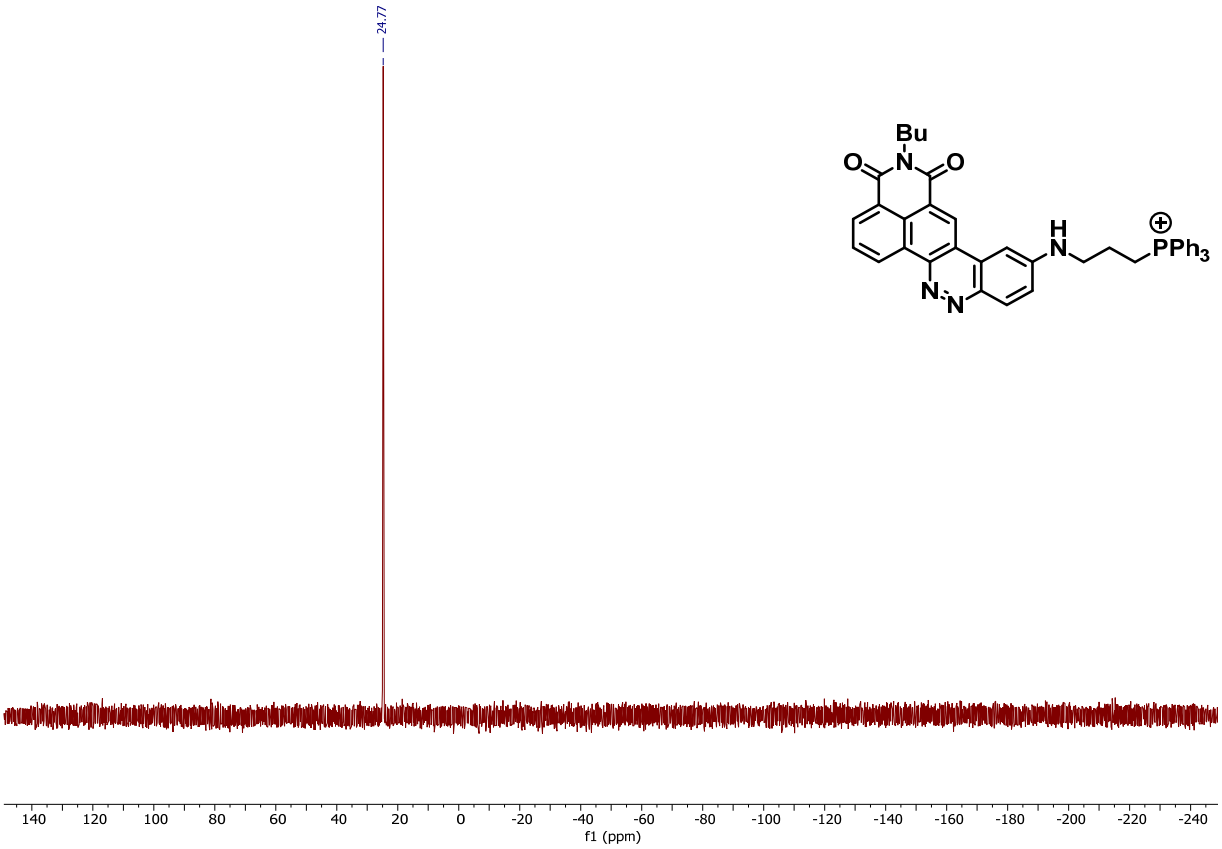
^{1}H NMR



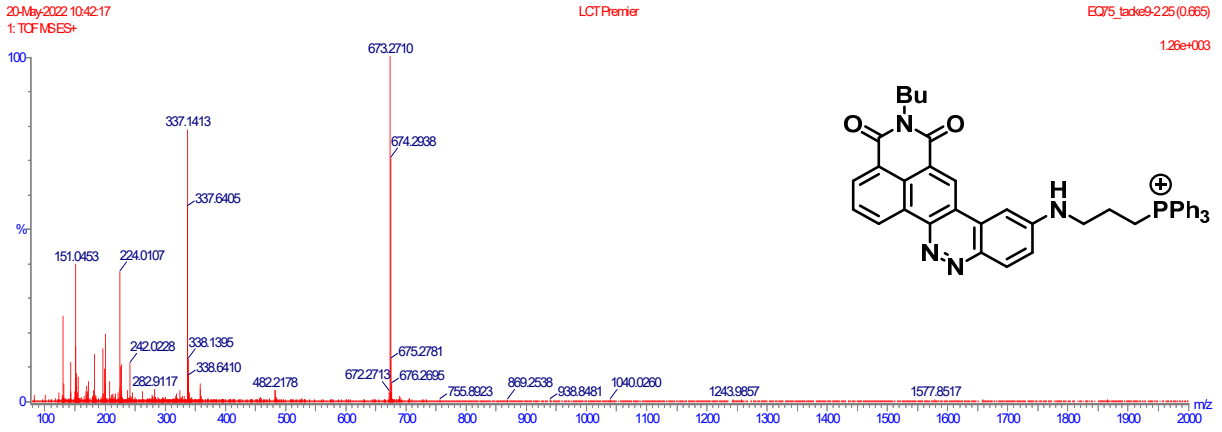
^{13}C NMR



^{31}P NMR

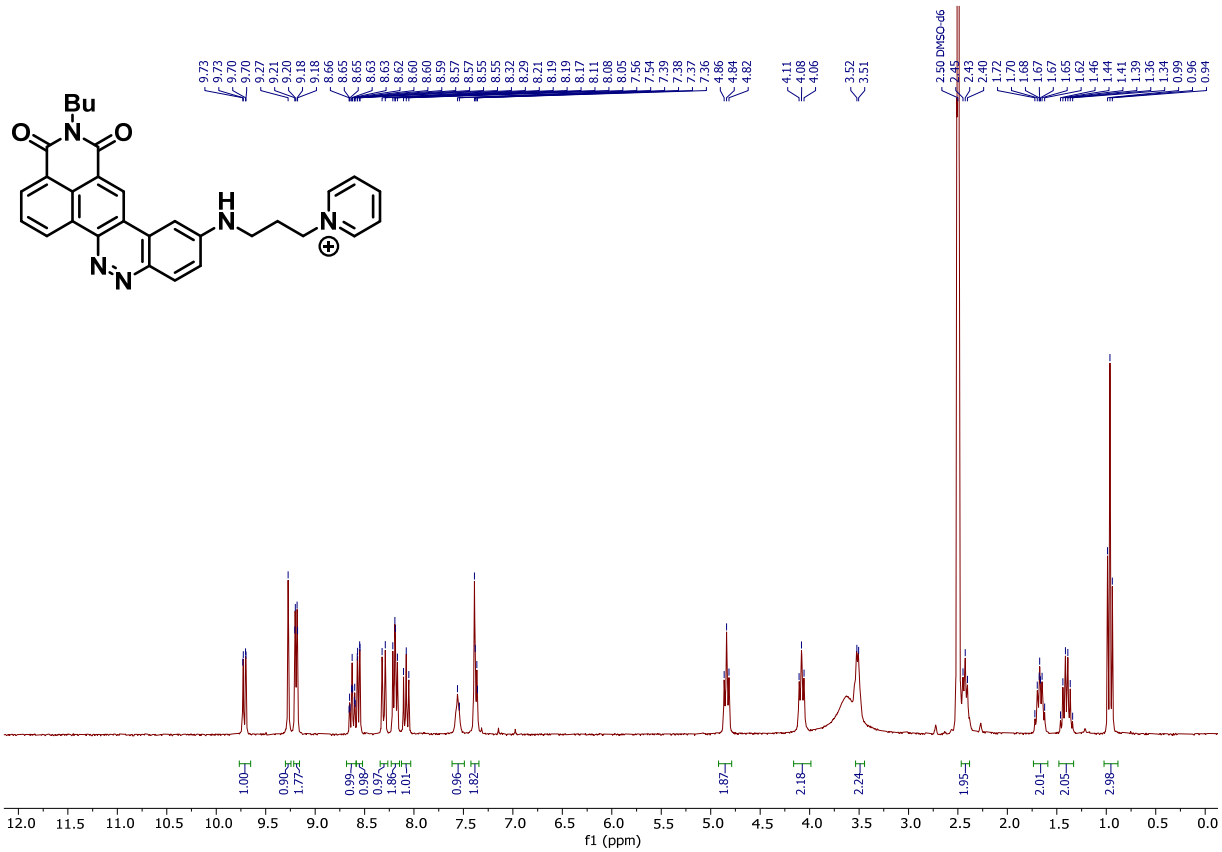

24.77
Bu
O
N
O
H
N
PPh3
N
N
140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

HRMS

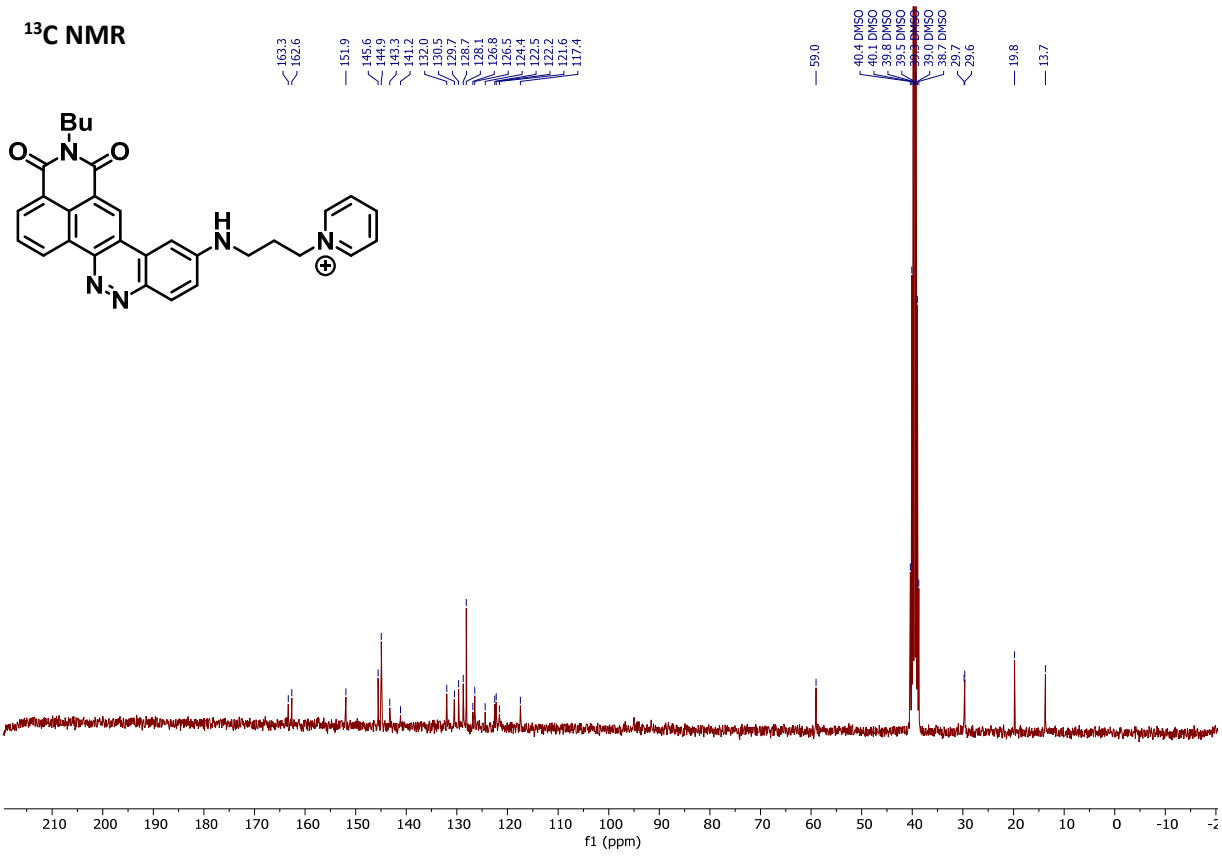

20-May-2022 10:42:17
1: TOF MS ES+
LCT Premier
EQ75_tacke9-2 25 (0.665)
1.26e+003
100
%
0
673.2710
337.1413
674.2938
337.6405
151.0453
224.0107
242.0228
338.1395
338.6410
282.9117
482.2178
672.2713
676.2695
675.2781
755.8923
869.2538
938.8481
1040.0260
1243.9857
1577.8517
Bu
O
N
O
H
N
PPh3
N
N
100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900 2000
m/z

Compound 6j:

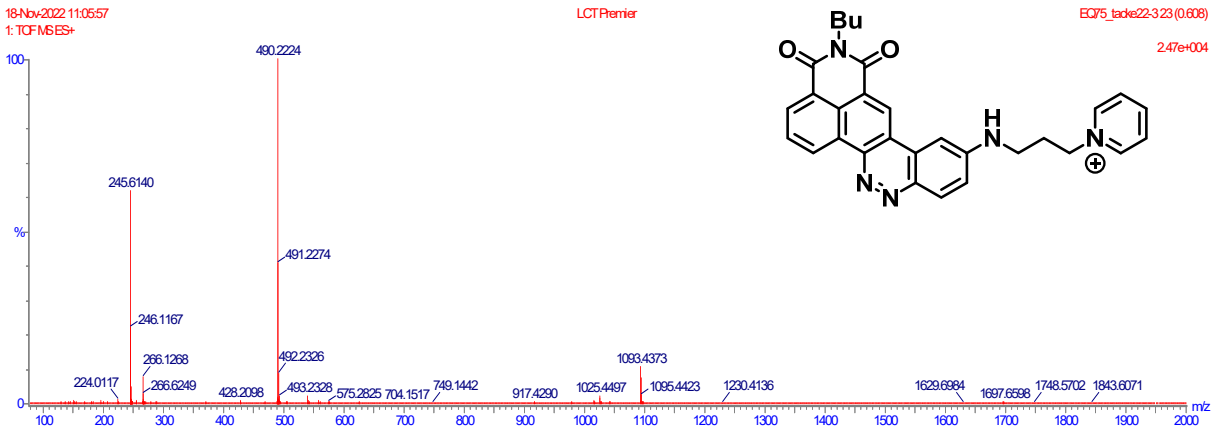
^{1}H NMR



^{13}C NMR

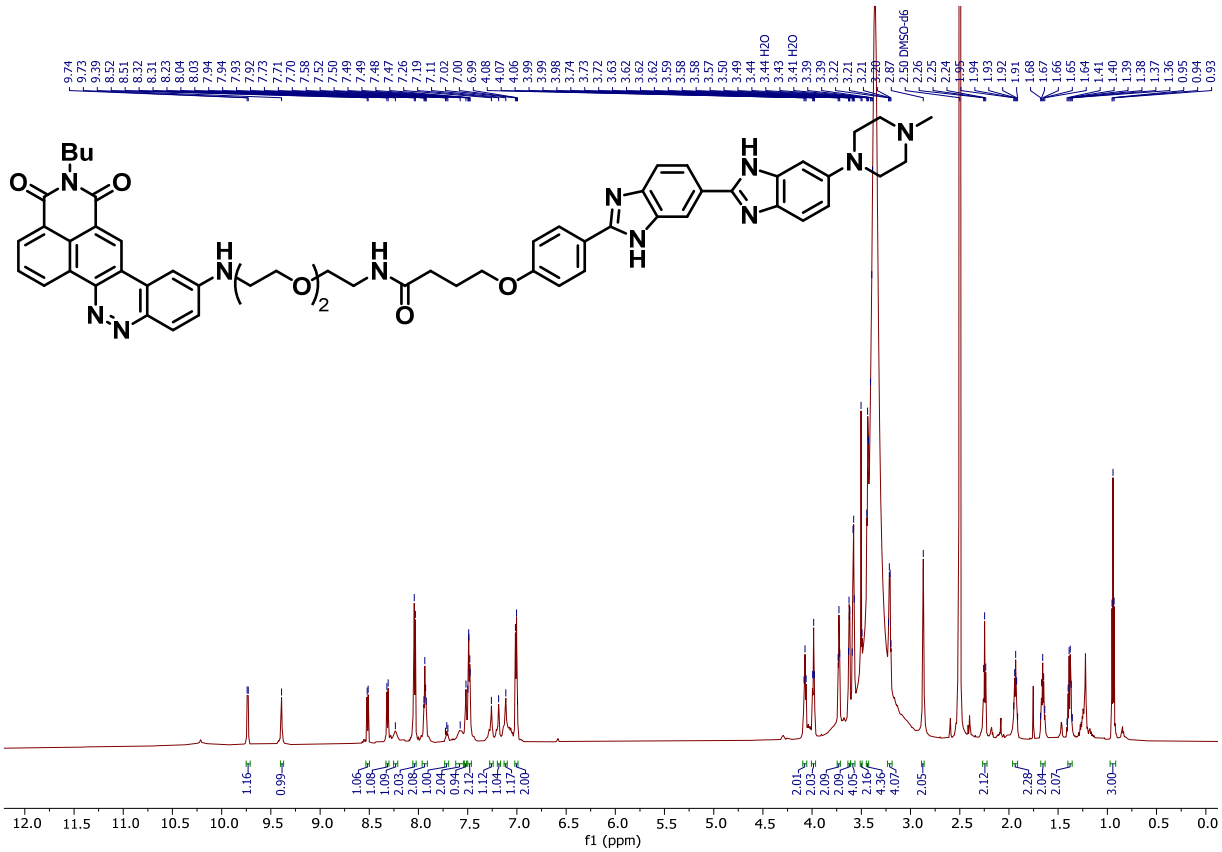


HRMS

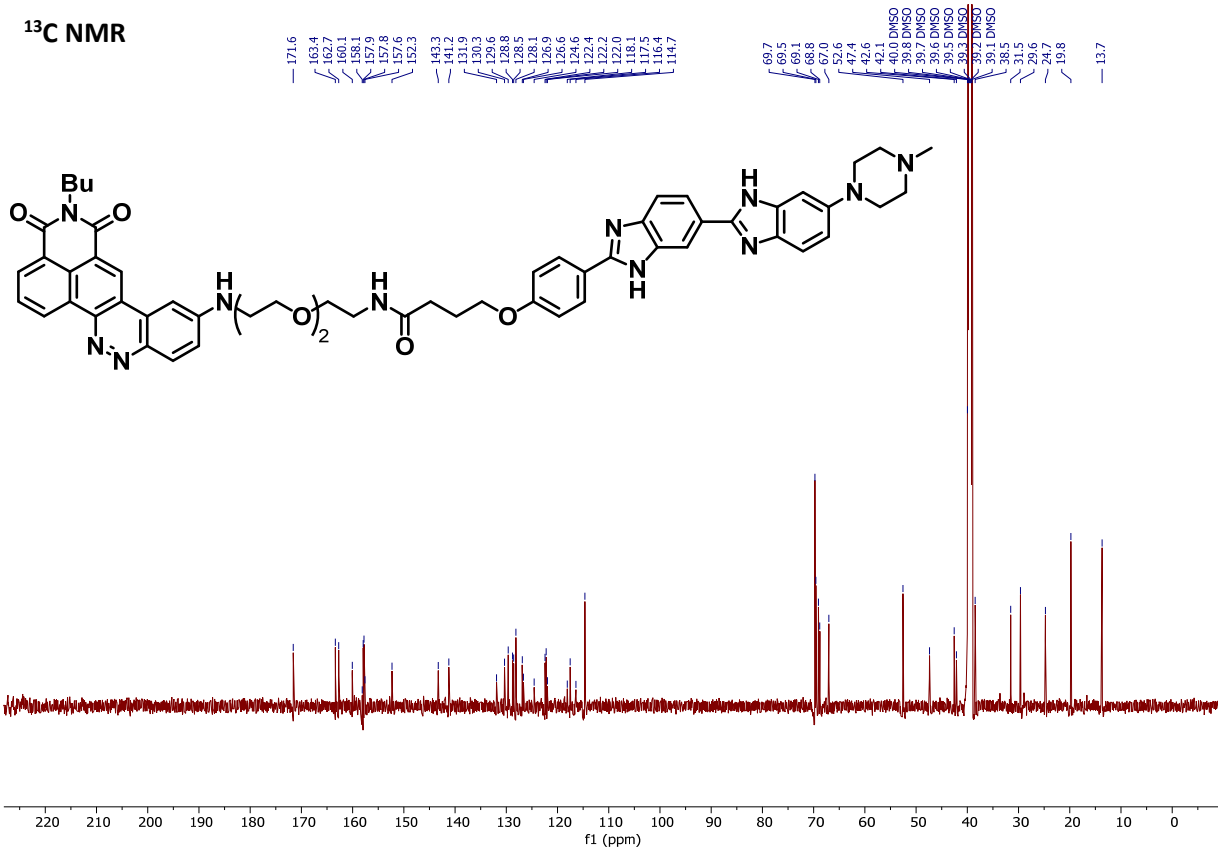

18-Nov-2022 11:05:57
1: TOF MS ES+
LCT Premier
EO75_tadke22-3 23 (0.608)
2.47e+004
100
%
0
490.2224
245.6140
491.2274
246.1167
266.1268
492.2326
224.0117
266.6249
428.2098
493.2328
575.2825
704.1517
749.1442
917.4290
1025.4497
1093.4373
1095.4423
1230.4136
1629.6984
1697.6598
1748.5702
1843.6071
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z
Bu
O
N
O
H
N
N
N
N
⊕

Compound 6k:

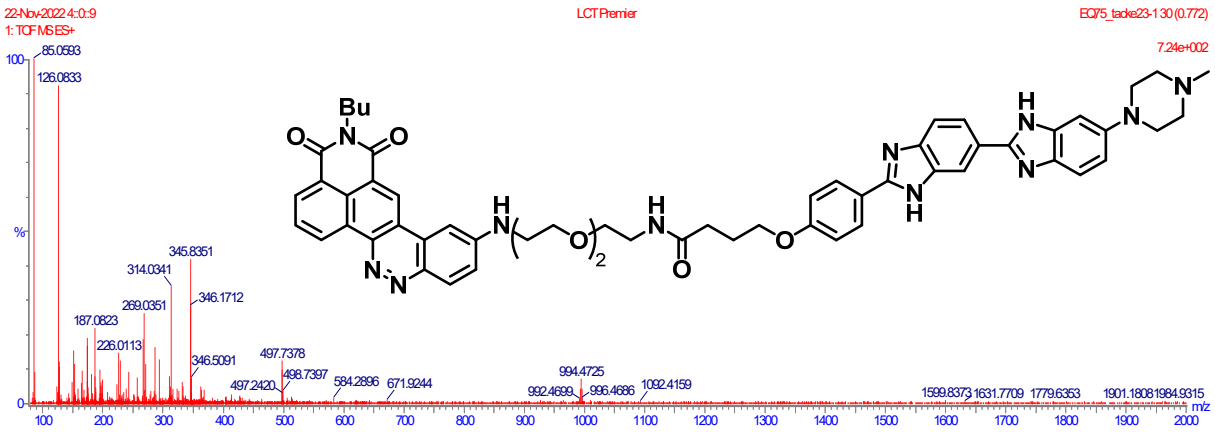
^{1}H NMR



^{13}C NMR

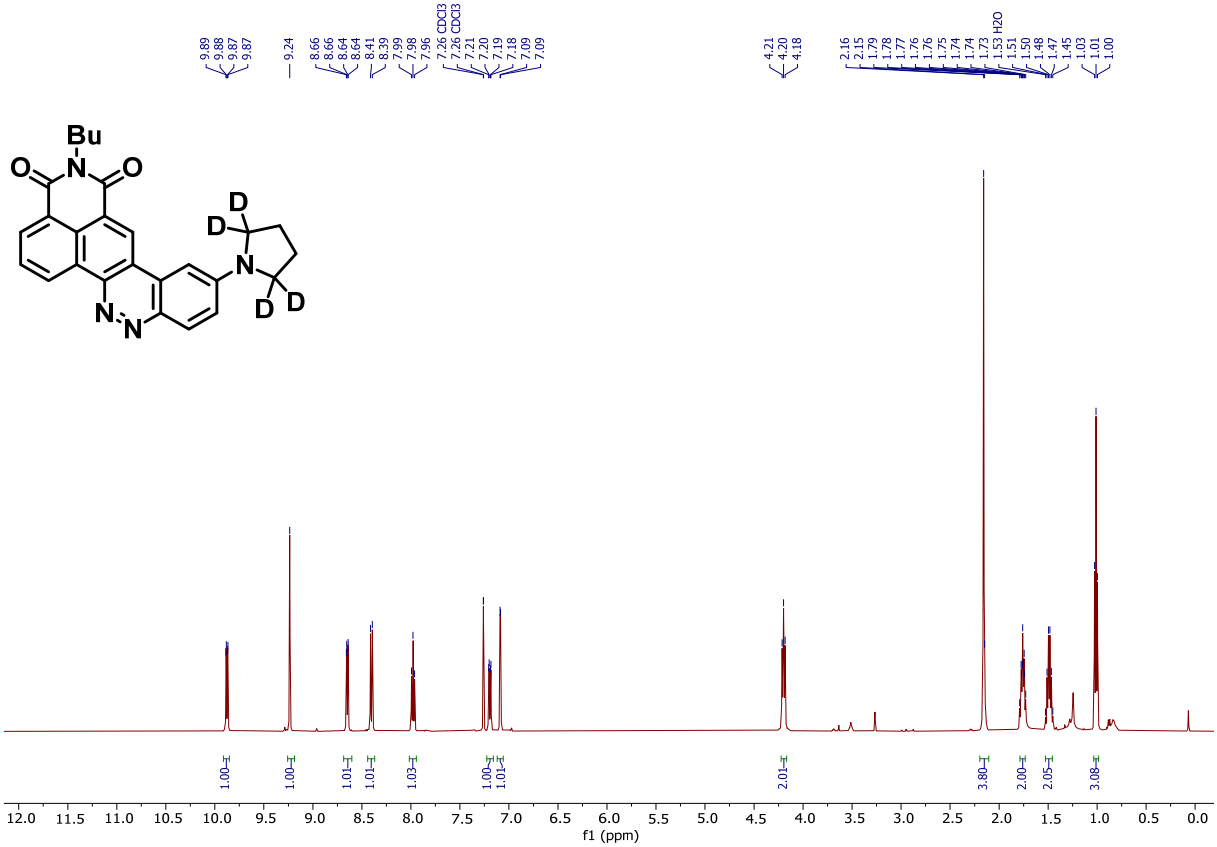


HRMS

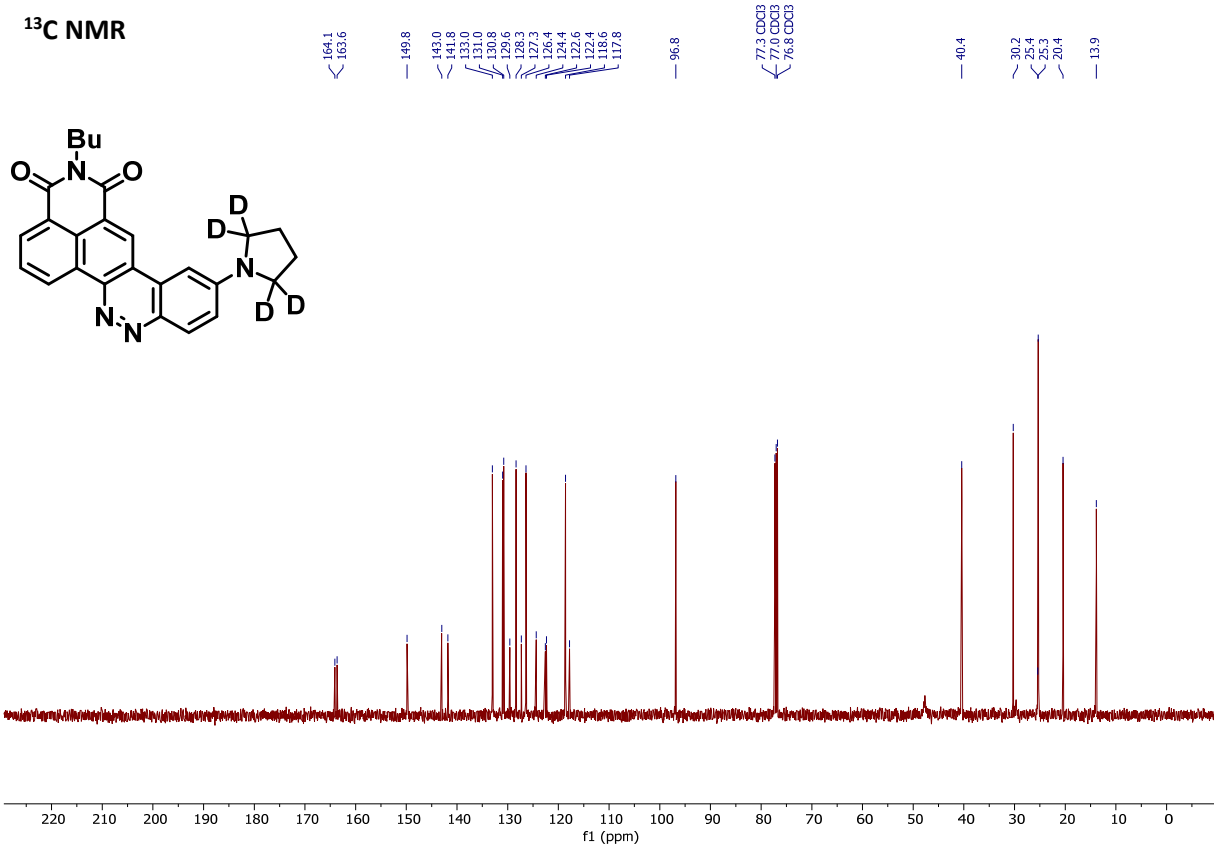

22-Nov-2022 4::0::9
1: TOF MS ES+
LCT Premier
EQ75_tadke23-1 30 (0.772)
7.24e+002
100
%
0
85.0593
126.0833
345.8351
314.0341
346.1712
269.0351
187.0823
226.0113
346.5091
497.7378
498.7397
497.2420
584.2896
671.9244
994.4725
992.4699
996.4686
1092.4159
1599.8373
1631.7709
1779.6353
1901.1808
1984.9315
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000

Compound 6l:

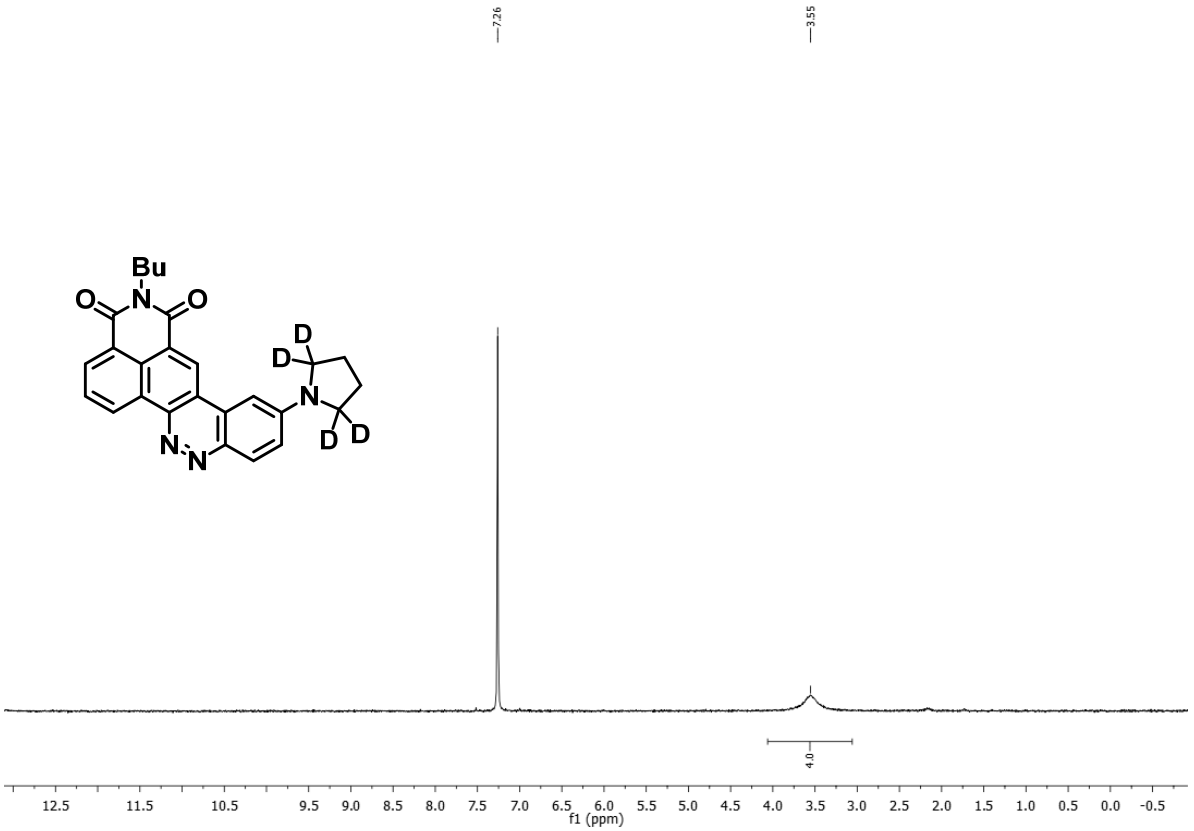
^{1}H NMR



^{13}C NMR



^{2}H NMR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3.55
Bu
O
N
O
D
D
N
D
D
N
N
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12.5
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10.5
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
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2.5
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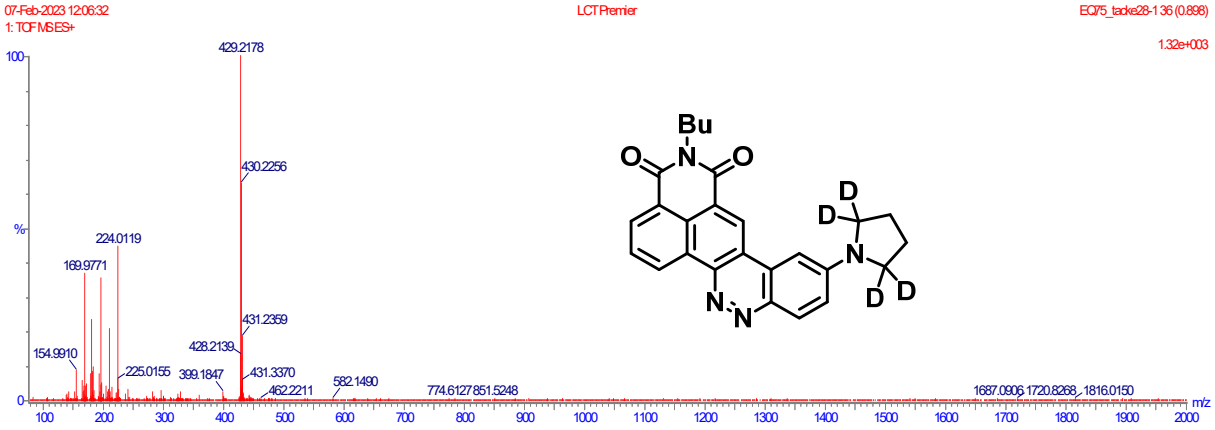
0.5
0.0
-0.5
f1 (ppm)

HRMS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%
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430.2256
224.0119
169.9771
431.2359
428.2139
154.9910
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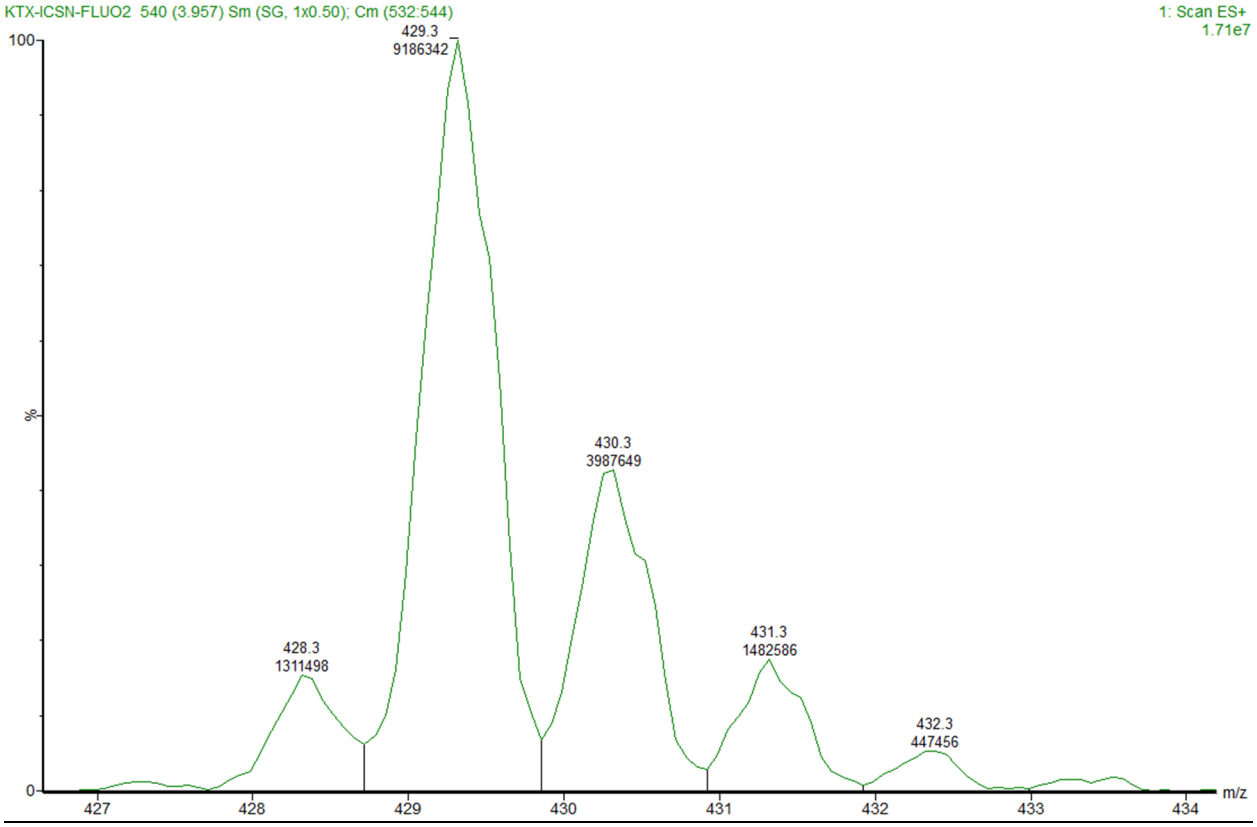
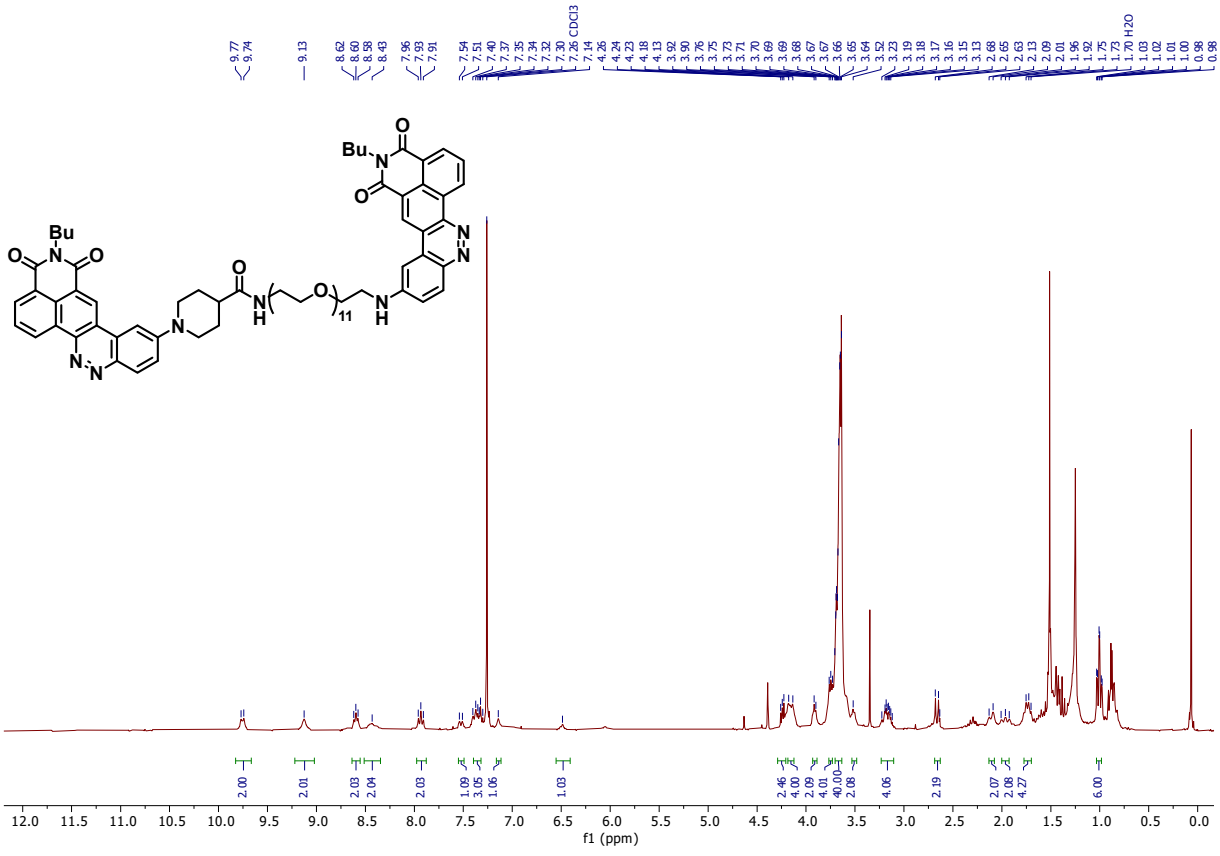
399.1847
431.3370
462.2211
582.1490
774.6127
851.5248
1687.0906
1720.8268
1816.0150
m/z
100
200
300
400
500
600
700
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
Bu
O
N
O
D
D
N
D
D
N
N

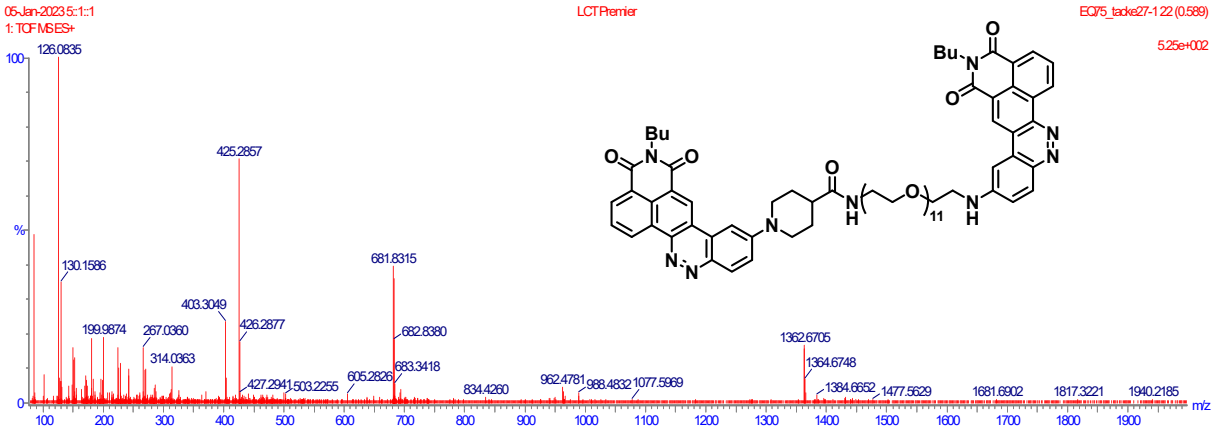


Compound 7a:

^{1}H NMR



HRMS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682.8380
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503.2255
605.2826
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1077.5969
1362.6705
1364.6748
1384.6652
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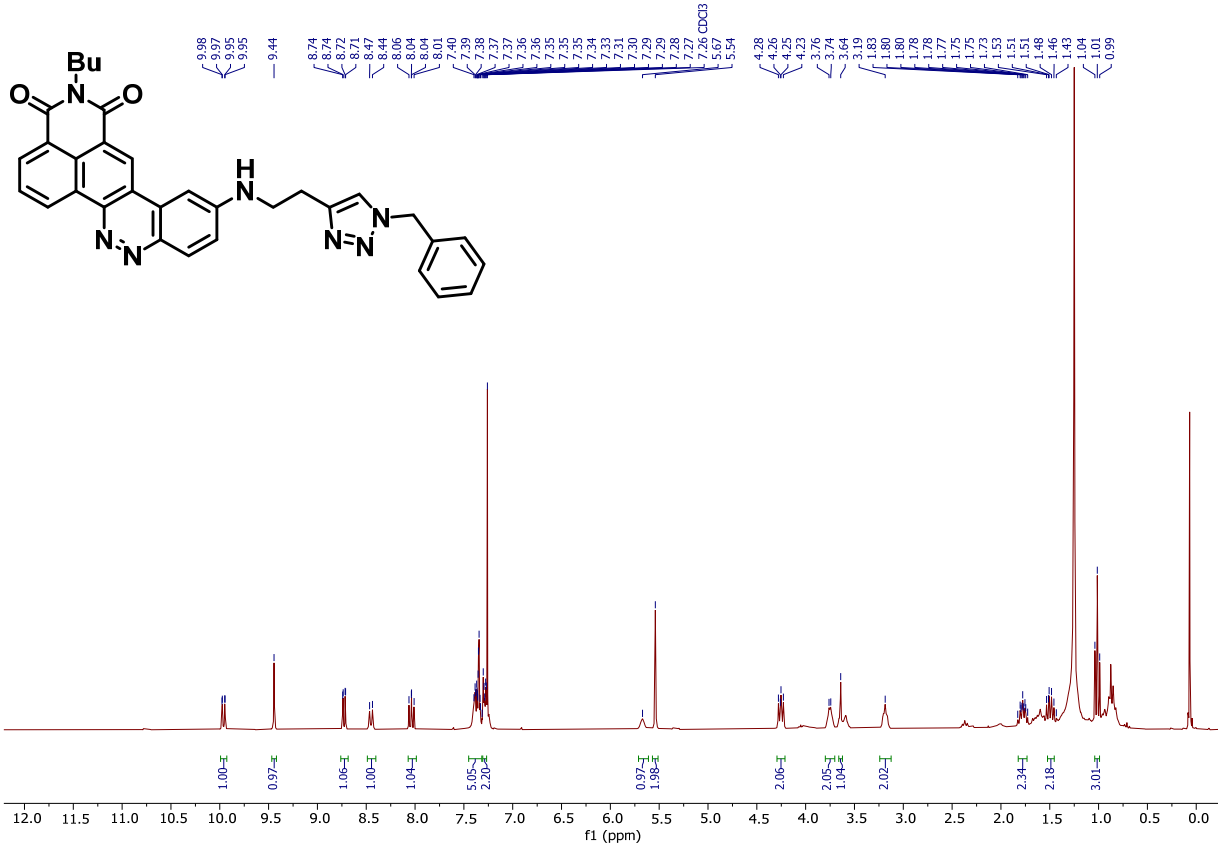
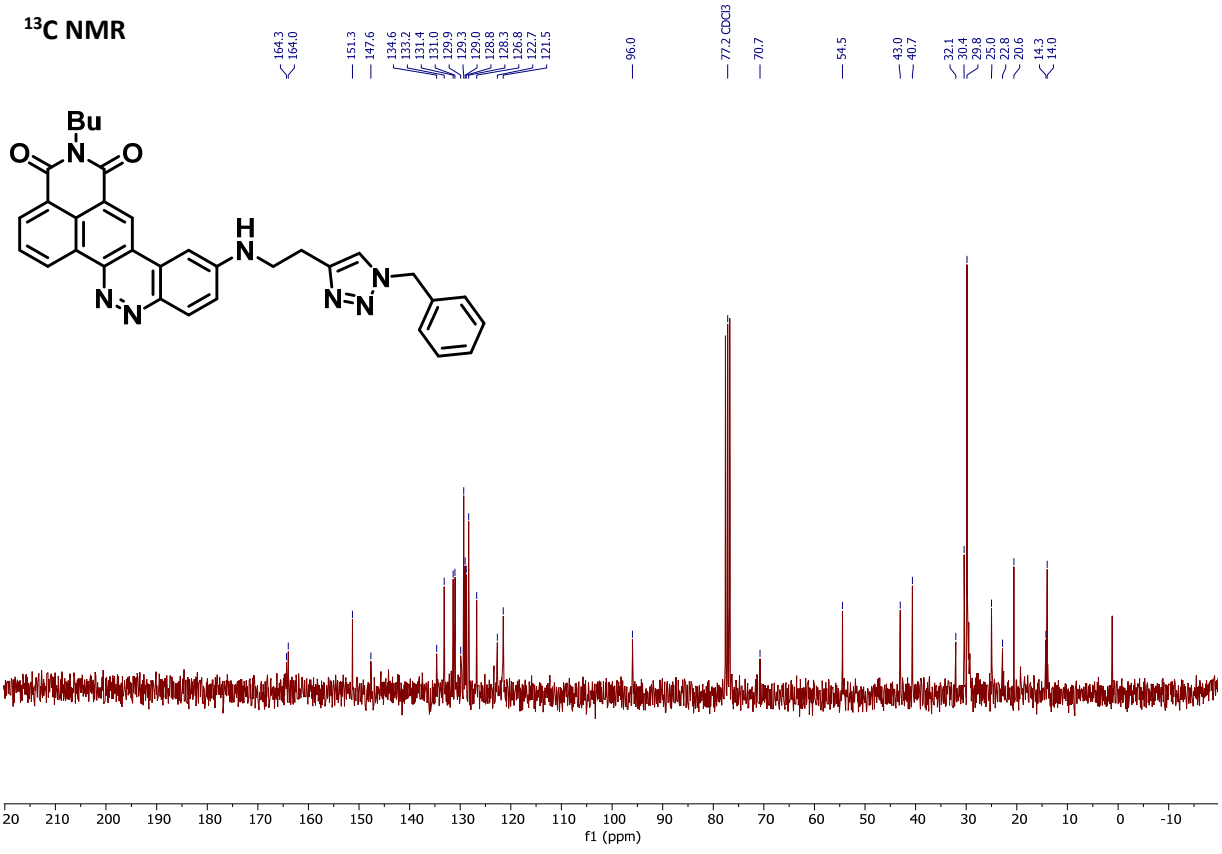
1817.3221
1940.2185
m/z
Bu
O
N
H
11

Compound 7b:

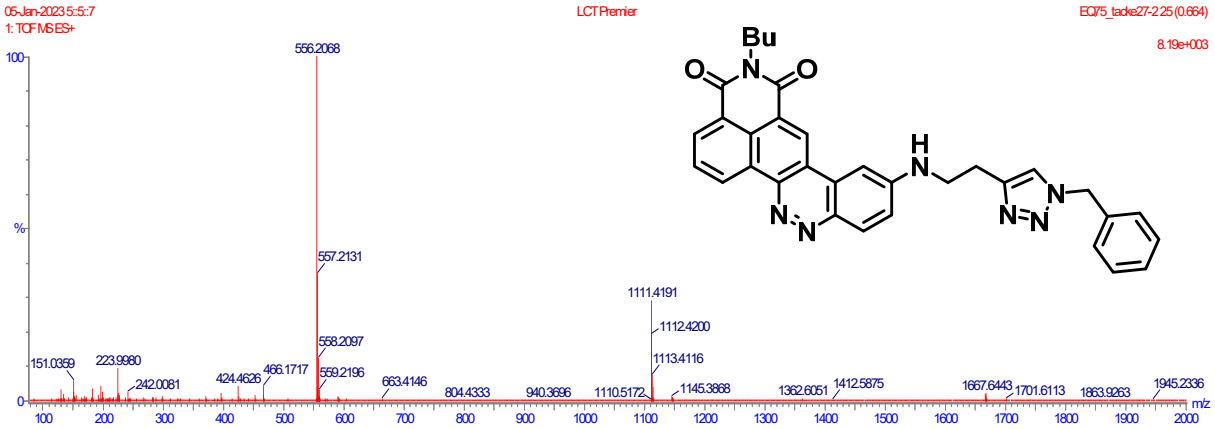
^{1}H NMR



^{13}C NMR



HRMS



1. F. Zhou and T. G. Driver, *Org. Lett.*, 2014, **16**, 2916-2919.
2. L. Yu, Y. Hou, C. Cheng, C. Schlaich, P.-L. M. Noeske, Q. Wei and R. Haag, *ACS App. Mat. Int.*, 2017, **9**, 44281-44292.
3. K. Sakai, M. Kaji, Y. Takamatsu, K. Tsuchiya, K. Torigoe, K. Tsubone, T. Yoshimura, K. Esumi, H. Sakai and M. Abe, *Colloids Surf. A Physicochem. Eng. Asp.*, 2009, **333**, 26-31.
4. K. Rurack and M. Spieles, *Anal. Chem.*, 2011, **83**, 1232-1242.

IV. Single Crystal X-ray Crystallography (SC-XRD)

Crystal data for ET_I_047**:**

$C_{22}H_{16}FN_3O_2$, M_r = 375.39, monoclinic, $P2_1/n$ (No. 14), a = 4.8187(4) Å, b = 15.7239(18) Å, c = 22.4752(16) Å, $\alpha = \gamma = 90^{\circ}$, $\beta = 91.507^{\circ}$ V = 1702.3(3)Å^3, T = 173.00(10) K, Z = 4, μ (Cu K_α) = 0.849, 11107 reflections measured, 2878 unique (R_{int} = 0.0554) which were used in all calculations. The final wR_2 was 0.3593 (all data) and R_1 was 0.0934 (I≥2 σ(I)). The goodness of fit on F2 was 0.933.

Experimental

Crystals of compound **4** were obtained by slow evaporation of Heptane/Ethyl Acetate mixture.

Single crystals suitable to X-ray diffraction structural analyses were transferred upon a microscope slide and one of them selected under a binocular, mounted on a nylon loop and fixed with Paratone® oil. Then, X-ray diffraction and crystallographic data were collected at 273 K using redundant ω scans on Rigaku Rapid II (IP area detector system) diffractometer equipped with a rotating anode mm007 HF generator and Osmic mirrors (Cu Kα radiation, λ = 1.54187 Å). Data were indexed, integrated and scaled using *FS_Process* from the *CrystalClear* [1] software suite.

Using Olex2 [2], the structure was readily solved by intrinsic phasing methods (SHELXT [3]), and by full-matrix least-squares methods on F^2 using SHELXL [4]. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms have been added geometrically and treated as riding on their parent atoms.

The molecular graphics presented here were computed with Mercury 2020.3.0 [5].

Crystallographic data have been deposited in the Cambridge Crystallographic Data Centre database (the deposition number is CCDC 2221167). Copies of the data can be obtained free of charge from the CCDC at www.ccdc.cam.ac.uk.

[1] Rigaku CrystalClear-SM Expert 2.0 r4. **2009**

[2] Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. *J. Appl. Cryst*. **2009**, 42, 339-341.

[3] Sheldrick, G.M. *Acta Cryst*. **2015**, A71, 3-8.

[4] Sheldrick, G.M. *Acta Cryst*. **2015,** C71, 3-8.

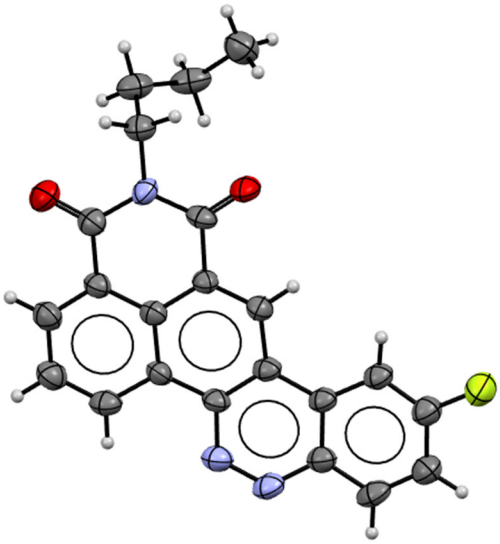
[5] Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. J. *Appl. Cryst*. **2006**, 39, 453-457.

Table 1: Crystal data and structure refinement

Identification code		**ET_I_047**
		A. Crystal Data
Empirical Formula		$C_{22}H_{16}FN_3O_2$
Formula Weight		375.39
Crystal Color, Habit		[light yellow, rect.Prism]
Crystal Dimensions (mm^3)		0.50 × 0.02 × 0.01
Crystal System		monoclinic
Space Group		$P2_1/n$
Unit cell dimensions	*a* (Å)	4.8187(4)
	b (Å)	15.7239(18)
	c (Å)	22.4752(16)
	α (°)	90
	β (°)	91.507
	γ (°)	90
Volume (Å3)		2901.98(10)
Z value		4
Calculated density $D_{calc.}$ ($g.cm^{-3}$)		1.465
Absorption coefficient μ (mm^{-1})		0.849
F (000)		784.0
		B. Intensity Measurements
Diffractometer		Rigaku Rapid II
Radiation type		Cu K_α
Wavelength (Å)		1.54187
Voltage, Current (kV, mA)		(40, 30)
***T* (K)**		273.00 (10)
2θ range for data collection (°)		6.862 to 130.17
Limiting indices		-4 ≤ h ≤ 5, -18 ≤ k ≤ 12, -26 ≤ l ≤ 26
Reflections collected/unique		11107/2878
Completeness to θ full (%)		98.8
		C. Structure Solution and Refinement
R_{int}		0.0554
Absorption correction		Semi-empirical from equivalents
Refinement method		Full-matrix least-squares on F^2
Data/restraints/parameters		2878/0/254
Goodness-of-fit on F^2		0.933
Final R indices [*I*>2σ(*I*)]	R_1 wR_2	0.0934 0.2397
R indices (all data)	R_1 wR_2	0.2014 0.9593

Largest Δ peak and hole (e.Å^{-3})	0.45/-0.27

Figure 1: (left) ORTEP drawing of ***compound 4*** *with thermal ellipsoids drawn at the 30% probability level; (right) Labelling scheme of the structure.*



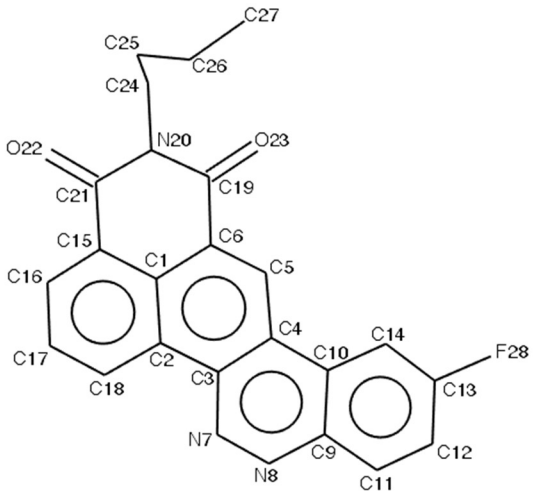


Table 2: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for compound 4. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U_{eq}
O23	8262(8)	5682(3)	7714.4(18)	87.5(15)
F28	1332(8)	8092(3)	5555.4(17)	108.4(14)
O22	8296(9)	2918(3)	8294(2)	94.4(16)
N20	8154(9)	4307(4)	8030(2)	68.0(15)
N7	-1302(10)	4231(3)	5966(2)	77.7(16)
N8	-2331(10)	4821(4)	5616(2)	80.6(16)
C6	5079(10)	4769(4)	7203(2)	59.9(16)
C1	4017(11)	3937(4)	7152(3)	62.0(15)
C4	1956(11)	5263(4)	6404(2)	64.2(17)
C2	1882(11)	3778(4)	6722(2)	62.6(16)
C19	7280(11)	4975(5)	7665(3)	69.1(19)
C15	5065(11)	3284(4)	7519(3)	65.8(17)
C5	4125(11)	5405(4)	6843(3)	65.2(16)
C3	846(11)	4447(4)	6356(3)	65.4(17)
C10	829(12)	5901(4)	6014(3)	66.0(17)

Atom	x	y	z	U_{eq}
C21	7264(11)	3460(5)	7977(3)	71.9(18)
C14	1741(11)	6752(4)	5986(3)	72.5(18)
C18	895(12)	2928(5)	6686(3)	77.4(19)
C9	-1339(13)	5649(5)	5618(3)	73.3(18)
C16	4045(13)	2480(4)	7464(3)	80.9(19)
C24	10285(13)	4493(4)	8497(3)	84(2)
C11	-2561(12)	6222(5)	5216(3)	85(2)
C13	468(14)	7275(5)	5593(3)	82(2)
C17	1943(14)	2302(5)	7045(3)	85(2)
C12	-1671(14)	7039(5)	5199(3)	88(2)
C25	9113(14)	4604(5)	9108(3)	93(2)
C26	7349(14)	5396(5)	9198(3)	96(2)
C27	8994(16)	6218(5)	9199(3)	111(3)

Table 3: Anisotropic Displacement Parameters (×10^4) for compound 4. The anisotropic displacement factor exponent takes the form: -2π^2[h^{2}a^2 × U_{11}+2hka* × b* × U_{12}+ ...].*

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O23	79(3)	89(4)	92(3)	11(3)	-36(2)	-15(3)
F28	112(3)	98(3)	114(3)	19(2)	-18(2)	-1(3)
O22	90(3)	94(4)	98(3)	6(3)	-20(3)	20(3)
N20	64(3)	70(4)	69(3)	12(3)	-11(3)	8(3)
N7	72(3)	86(4)	74(4)	-13(3)	-13(3)	-3(3)
N8	66(3)	99(5)	76(4)	-2(4)	-21(3)	15(3)
C6	54(3)	58(4)	66(4)	-5(3)	-11(3)	0(3)
C1	59(3)	63(4)	64(4)	-10(3)	0(3)	1(3)
C4	52(3)	74(5)	66(4)	-10(4)	-11(3)	9(3)
C2	65(3)	56(4)	66(4)	-12(3)	-4(3)	-5(3)
C19	54(3)	79(5)	74(4)	-18(4)	-10(3)	-9(4)
C15	60(4)	62(5)	75(4)	-11(4)	-8(3)	0(4)
C5	62(3)	64(4)	69(4)	1(3)	-7(3)	-8(3)
C3	57(3)	68(5)	70(4)	-10(4)	-13(3)	-8(3)
C10	56(3)	76(5)	65(4)	-3(4)	-10(3)	9(3)
C21	57(4)	72(5)	86(5)	-9(4)	-3(3)	7(4)
C14	62(4)	83(6)	72(4)	1(4)	-12(3)	9(4)
C18	62(4)	93(6)	76(4)	-13(4)	-13(3)	-1(4)
C9	71(4)	79(6)	69(4)	-10(4)	-9(3)	8(4)
C16	85(5)	70(5)	87(5)	-16(4)	-2(4)	4(4)
C24	82(4)	89(5)	79(5)	-1(4)	-17(4)	-5(4)
C11	68(4)	115(7)	70(4)	2(5)	-17(3)	24(5)
C13	77(4)	88(6)	81(5)	7(4)	-7(4)	-1(4)
C17	85(4)	79(5)	90(5)	-5(4)	-4(4)	-18(4)
C12	87(5)	88(6)	89(5)	2(5)	-19(4)	10(4)
C25	84(5)	123(7)	71(5)	-2(4)	-16(4)	-14(5)
C26	70(4)	152(8)	65(4)	-13(5)	-9(3)	3(5)
C27	123(6)	101(6)	108(6)	-20(5)	-6(5)	0(5)

Table 4: Bond Lengths in Å for compound 4

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O23	C19	1.212(7)	C4	C10	1.430(7)
F28	C13	1.355(7)	C2	C3	1.419(7)
O22	C21	1.209(7)	C2	C18	1.419(8)
N20	C19	1.392(7)	C15	C21	1.485(8)
N20	C21	1.403(7)	C15	C16	1.361(7)
N20	C24	1.478(7)	C10	C14	1.410(7)
N7	N8	1.305(6)	C10	C9	1.412(8)
N7	C3	1.381(7)	C14	C13	1.344(8)
N8	C9	1.387(7)	C18	C17	1.362(8)
C6	C1	1.409(7)	C9	C11	1.395(8)
C6	C19	1.500(7)	C16	C17	1.392(9)
C6	C5	1.359(7)	C24	C25	1.509(8)
C1	C2	1.415(7)	C11	C12	1.355(8)
C1	C15	1.402(7)	C13	C12	1.392(8)
C4	C5	1.435(7)	C25	C26	1.525(8)
C4	C3	1.393(7)	C26	C27	1.515(8)

Table 5: Bond Angles in ˚ for compound 4.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C19	N20	C21	125.5(6)	N7	C3	C4	123.7(6)
C19	N20	C24	117.6(5)	N7	C3	C2	115.7(6)
C21	N20	C24	116.9(5)	C4	C3	C2	120.6(5)
N8	N7	C3	118.3(6)	C14	C10	C4	125.4(6)
N7	N8	C9	122.7(5)	C9	C10	C4	116.9(6)
C1	C6	C19	120.3(6)	C9	C10	C14	117.6(6)
C5	C6	C1	121.3(5)	O22	C21	N20	120.0(6)
C5	C6	C19	118.3(6)	O22	C21	C15	123.5(7)
C6	C1	C2	118.4(6)	N20	C21	C15	116.5(6)
C15	C1	C6	120.6(5)	C13	C14	C10	118.2(6)
C15	C1	C2	121.1(6)	C17	C18	C2	121.9(6)
C5	C4	C10	124.7(6)	N8	C9	C10	120.9(6)
C3	C4	C5	117.9(6)	N8	C9	C11	117.7(7)
C3	C4	C10	117.4(5)	C11	C9	C10	121.4(7)
C1	C2	C3	120.3(6)	C15	C16	C17	120.2(6)
C1	C2	C18	116.2(6)	N20	C24	C25	113.6(5)
C3	C2	C18	123.5(6)	C12	C11	C9	120.1(7)
O23	C19	N20	121.7(5)	F28	C13	C12	115.9(7)
O23	C19	C6	122.0(6)	C14	C13	F28	119.1(6)
N20	C19	C6	116.3(6)	C14	C13	C12	125.0(7)
C1	C15	C21	120.7(6)	C18	C17	C16	120.4(6)
C16	C15	C1	120.2(6)	C11	C12	C13	117.7(7)
C16	C15	C21	119.1(6)	C24	C25	C26	116.0(6)
C6	C5	C4	121.5(5)	C27	C26	C25	113.8(6)

Table 6: Torsion Angles in ˚ for compound 4.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
F28	C13	C12	C11	178.9(5)	C5	C6	C1	C15	178.6(5)
N20	C24	C25	C26	-68.8(7)	C5	C6	C19	O23	-1.8(9)
N7	N8	C9	C10	-1.4(9)	C5	C6	C19	N20	178.9(5)
N7	N8	C9	C11	178.7(5)	C5	C4	C3	N7	178.0(5)
N8	N7	C3	C4	0.9(9)	C5	C4	C3	C2	-1.3(8)
N8	N7	C3	C2	-179.8(5)	C5	C4	C10	C14	2.5(9)
N8	C9	C11	C12	180.0(6)	C5	C4	C10	C9	-178.8(5)
C6	C1	C2	C3	-0.3(8)	C3	N7	N8	C9	0.6(9)
C6	C1	C2	C18	179.6(5)	C3	C4	C5	C6	-0.1(8)
C6	C1	C15	C21	1.5(8)	C3	C4	C10	C14	-178.0(5)
C6	C1	C15	C16	-179.4(5)	C3	C4	C10	C9	0.7(8)
C1	C6	C19	O23	179.0(5)	C3	C2	C18	C17	179.9(6)
C1	C6	C19	N20	-0.3(7)	C10	C4	C5	C6	179.4(5)
C1	C6	C5	C4	1.4(8)	C10	C4	C3	N7	-1.6(9)
C1	C2	C3	N7	-177.8(5)	C10	C4	C3	C2	179.2(5)
C1	C2	C3	C4	1.5(9)	C10	C14	C13	F28	-179.4(5)
C1	C2	C18	C17	0.1(9)	C10	C14	C13	C12	-1.2(10)
C1	C15	C21	O22	-177.9(6)	C10	C9	C11	C12	0.1(10)
C1	C15	C21	N20	1.6(8)	C21	N20	C19	O23	-175.6(5)
C1	C15	C16	C17	-0.4(9)	C21	N20	C19	C6	3.8(8)
C4	C10	C14	C13	179.8(5)	C21	N20	C24	C25	-81.9(7)
C4	C10	C9	N8	0.7(8)	C21	C15	C16	C17	178.7(6)
C4	C10	C9	C11	-179.4(5)	C14	C10	C9	N8	179.5(5)
C2	C1	C15	C21	-178.7(5)	C14	C10	C9	C11	-0.6(9)
C2	C1	C15	C16	0.4(9)	C14	C13	C12	C11	0.7(10)
C2	C18	C17	C16	-0.1(10)	C18	C2	C3	N7	2.3(8)
C19	N20	C21	O22	175.1(5)	C18	C2	C3	C4	-178.4(5)
C19	N20	C21	C15	-4.4(8)	C9	C10	C14	C13	1.1(8)
C19	N20	C24	C25	100.6(6)	C9	C11	C12	C13	-0.1(10)

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
C19	C6	C1	C2	178.0(5)	C16	C15	C21	O22	3.0(9)
C19	C6	C1	C15	-2.2(8)	C16	C15	C21	N20	-177.5(5)
C19	C6	C5	C4	-177.8(5)	C24	N20	C19	O23	1.7(8)
C15	C1	C2	C3	179.9(5)	C24	N20	C19	C6	-178.9(5)
C15	C1	C2	C18	-0.2(8)	C24	N20	C21	O22	-2.2(8)
C15	C16	C17	C18	0.2(10)	C24	N20	C21	C15	178.3(5)
C5	C6	C1	C2	-1.2(8)	C24	C25	C26	C27	-69.7(7)

*Table 7: Hydrogen Bonds for **compound 4**.*

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
C14	H14	O22[1]	0.93	2.50	3.391(8)	160.5
C11	H11	N8[2]	0.93	2.56	3.465(9)	165.1

[1]3/2-X,1/2+Y,3/2-Z; [2]-1-X,1-Y,1-Z

Table 8: Hydrogen Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for compound 4.

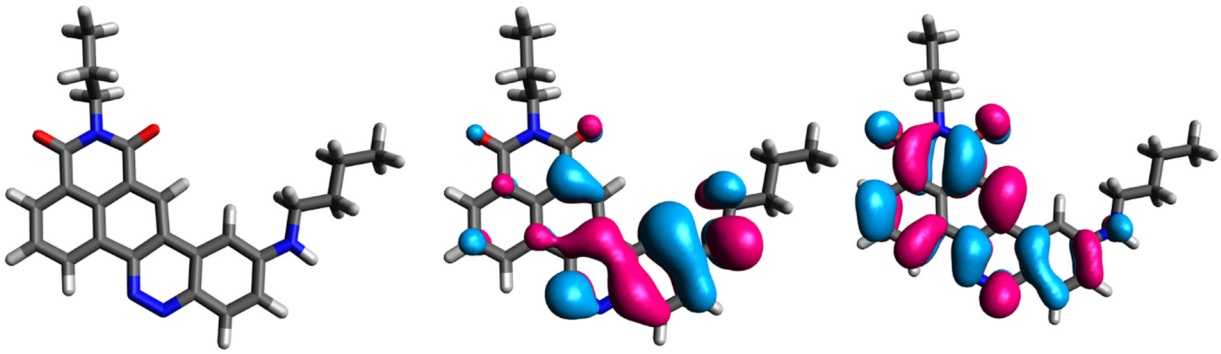
Atom	x	y	z	*U(eq)*
H5	4896.17	5945.04	6881.21	78
H14	3184.43	6945.31	6233.47	87
H18	-506.35	2795.92	6409.28	93
H16	4753.18	2047.99	7706.05	97
H24A	11261.26	5008.61	8390.49	100
H24B	11624.47	4032.85	8509.78	100
H11	-3988.66	6042.69	4959.12	102
H17	1249	1751.58	7010.79	102
H12	-2462.08	7428.34	4933.17	106
H25A	10646.44	4615.43	9396.21	112
H25B	7992.66	4108.99	9194.54	112

Atom	x	y	z	*U(eq)*
H26A	5932.65	5422.73	8883.83	115
H26B	6415.59	5346.27	9573.63	115
H27C	9598.82	6334.49	8803.7	166
H27B	10580.98	6163.54	9463.39	166
H27A	7842.94	6675.59	9330.41	166

V. DFT calculations

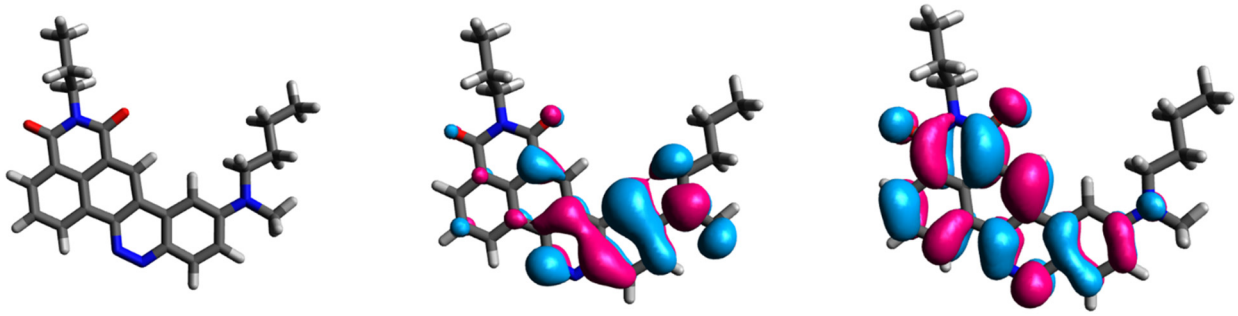
Ground state geometries and frontiers molecular orbitals distributions:

5a:



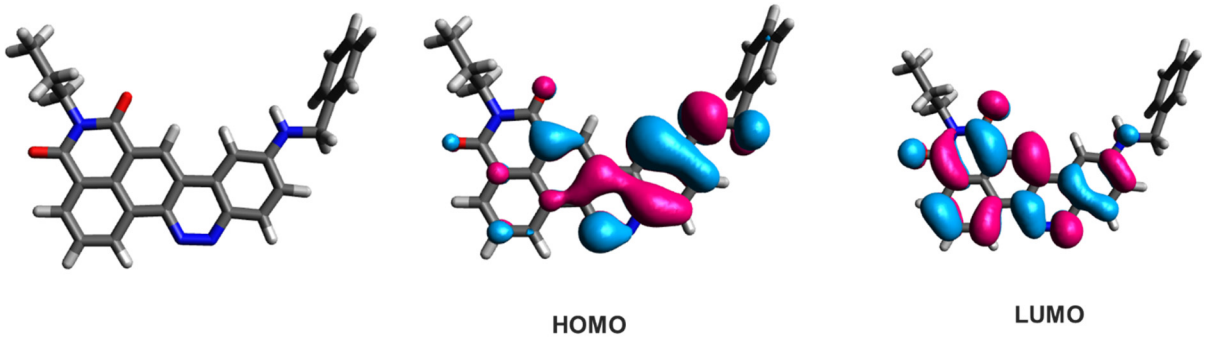
HOMO LUMO

5b:



HOMO LUMO

5d:



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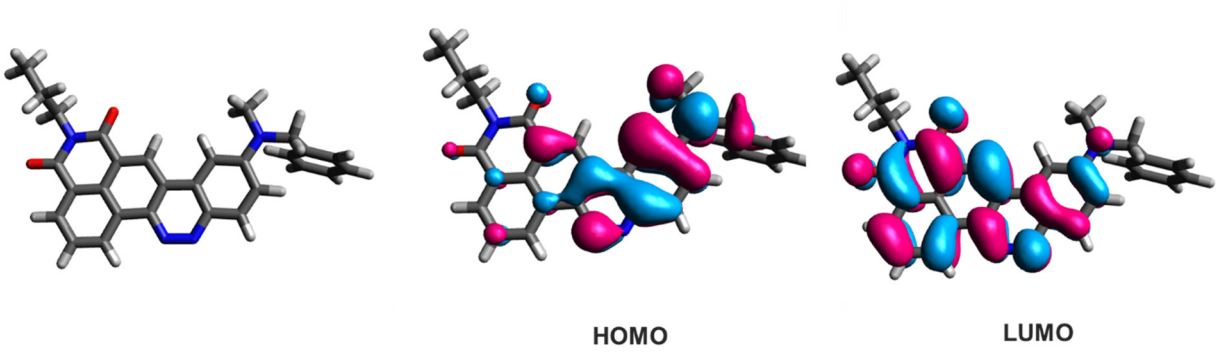

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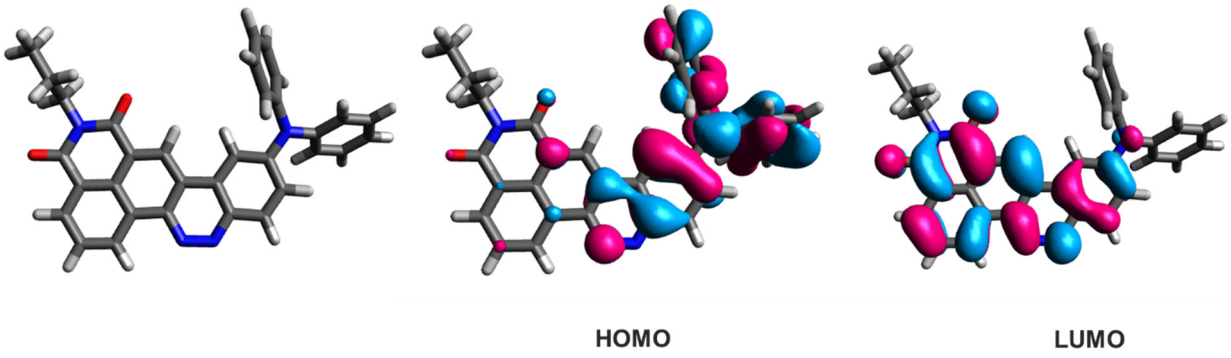

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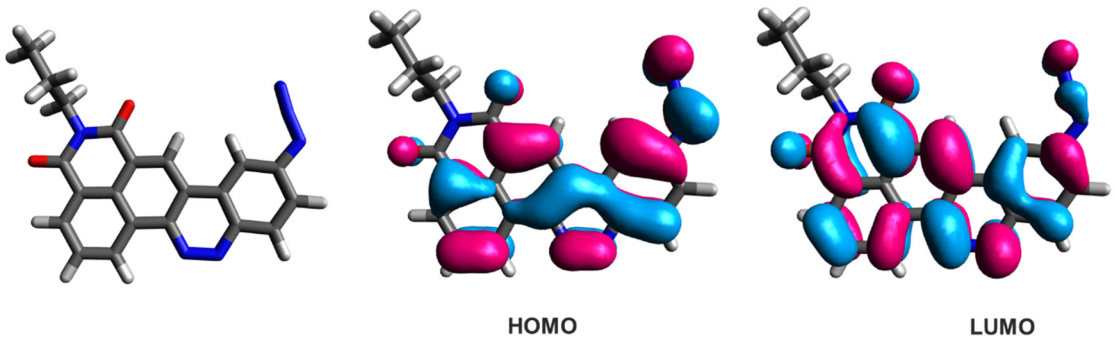
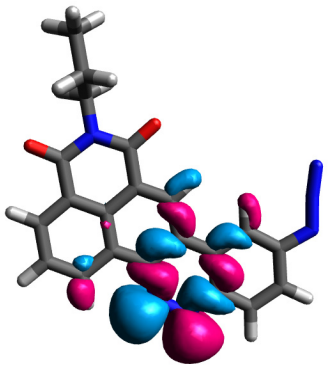
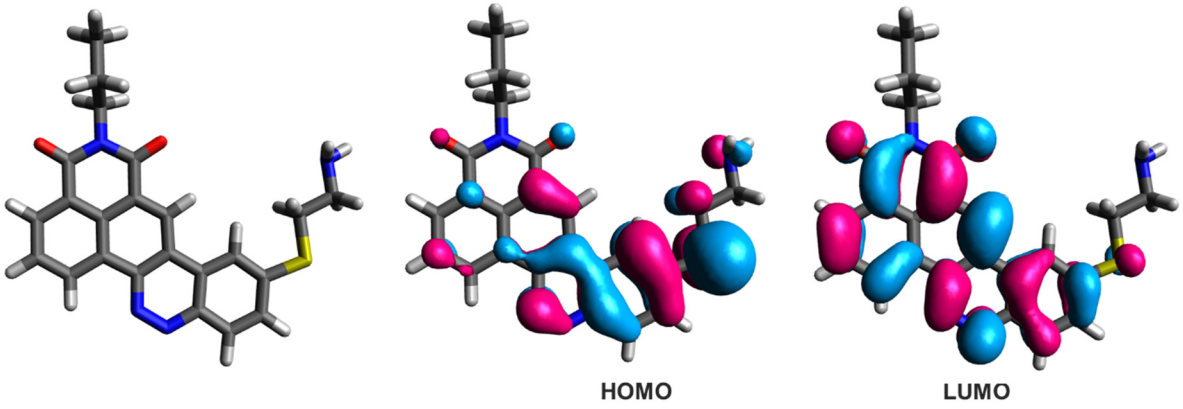
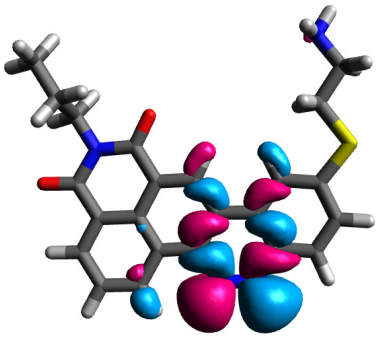




HOMO-1

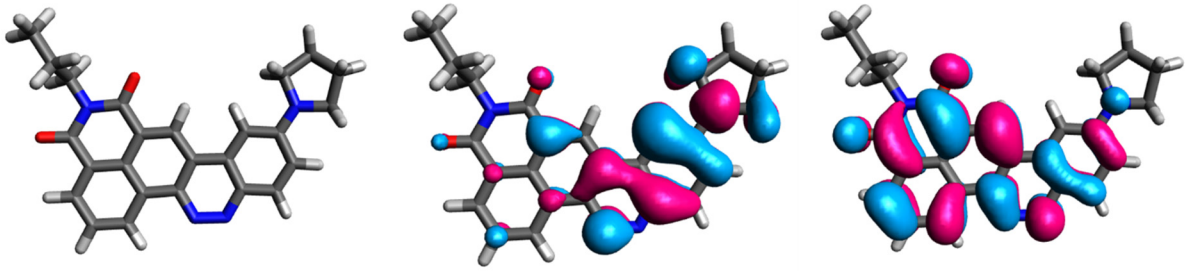
5r:





HOMO-1

6l:


HOMO
LUMO

Simulated UV spectra (blue lines) and oscillator strengths (green bars):

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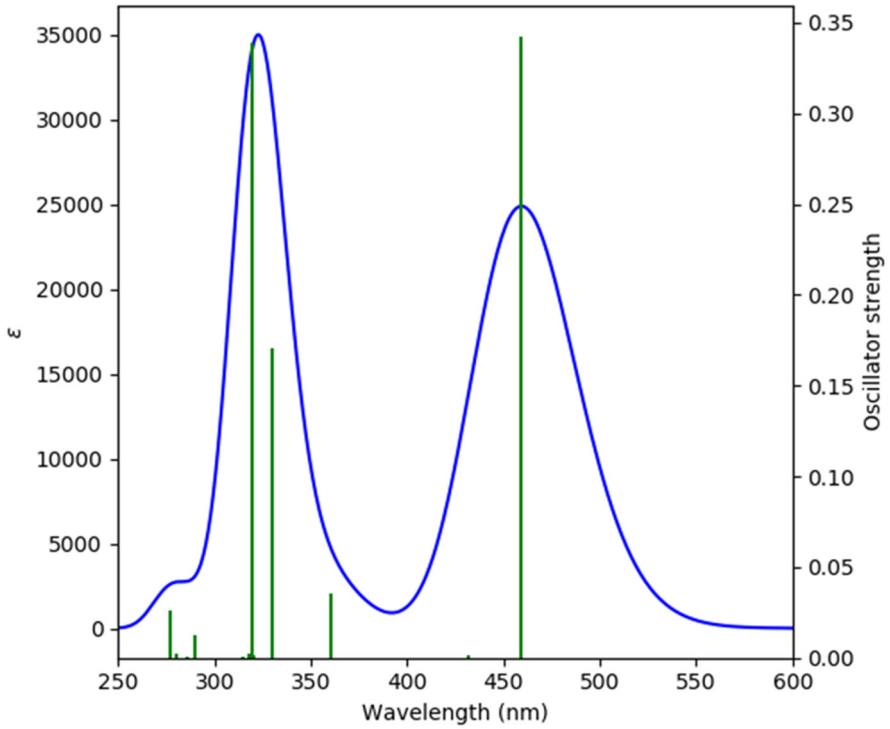
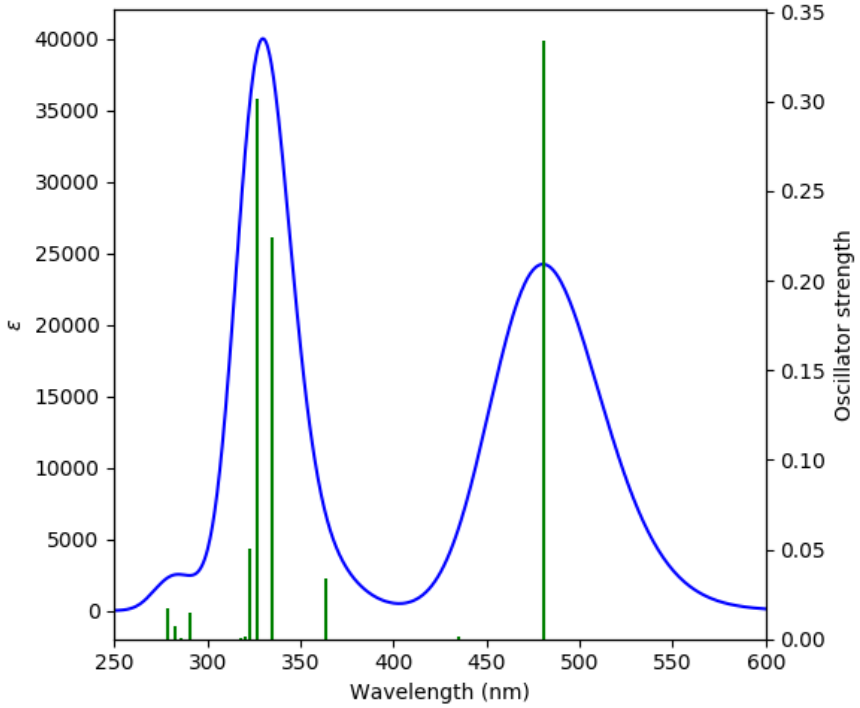


5b:



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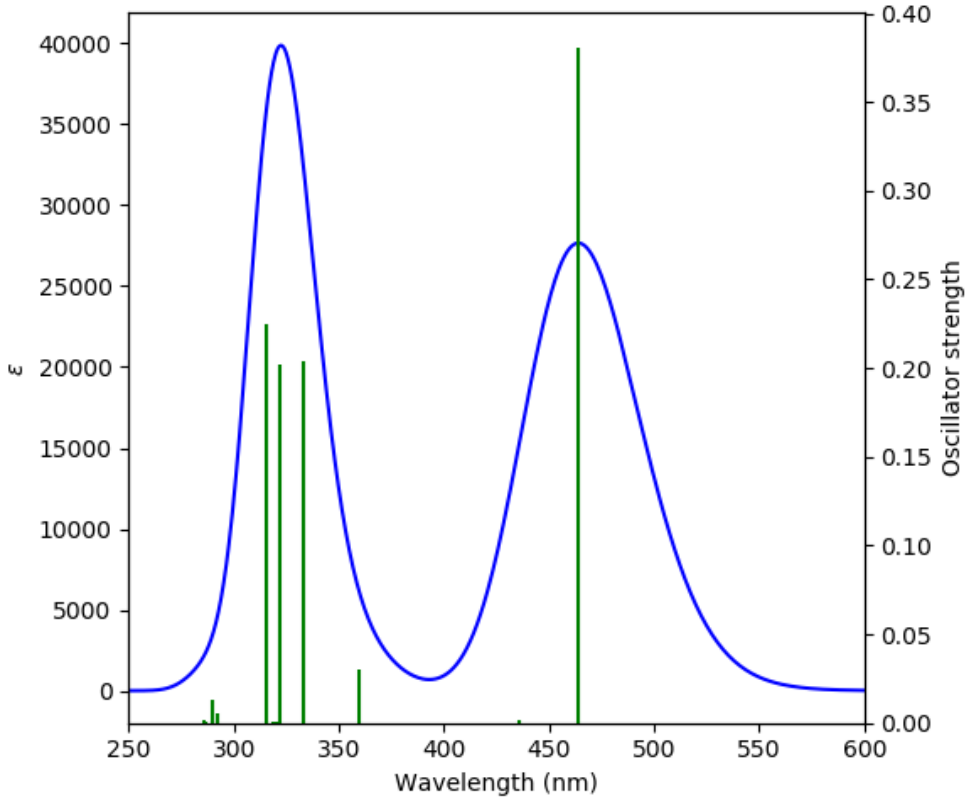
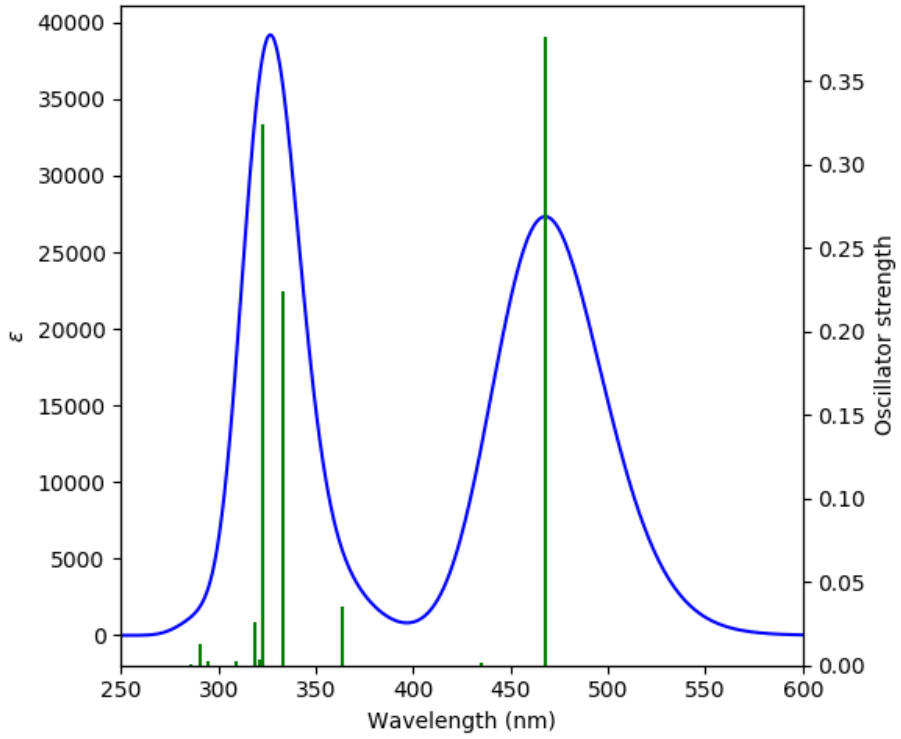
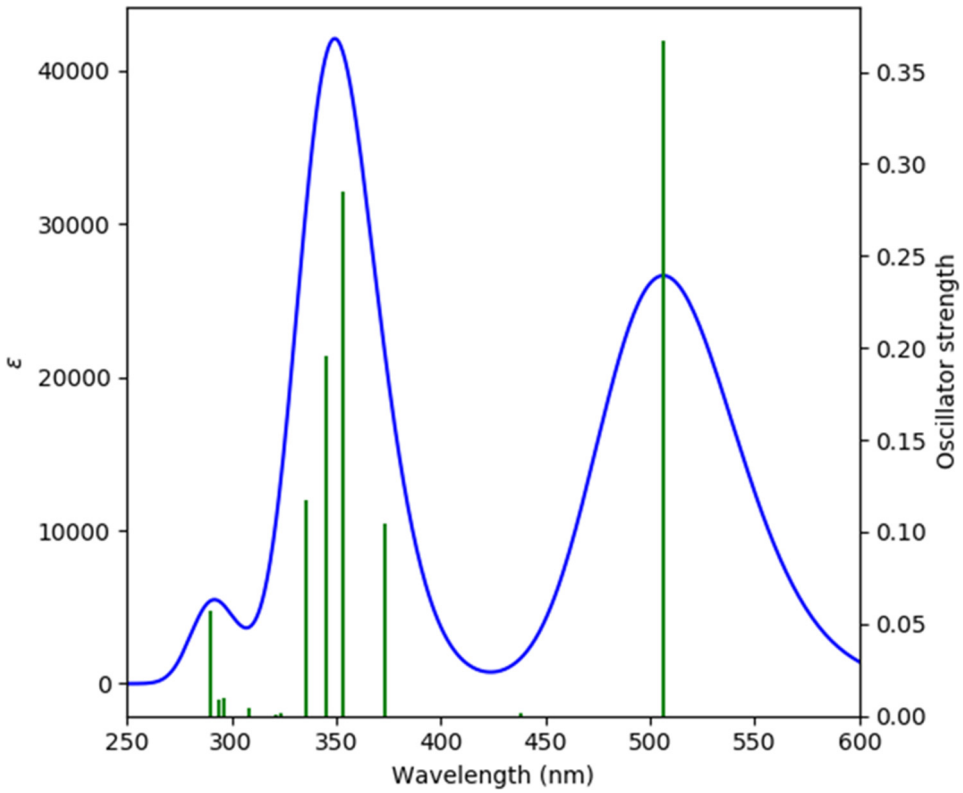

40000
35000
30000
25000
20000
15000
10000
5000
0
ε
250
300
350
400
450
500
550
600
Wavelength (nm)
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Oscillator strength

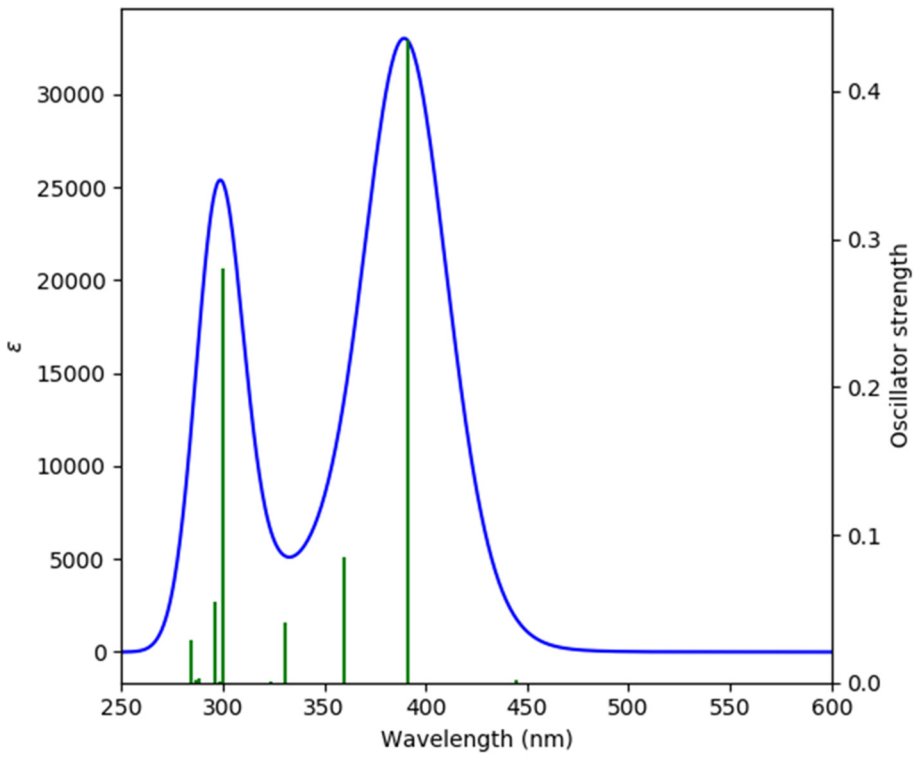
5e:


40000
35000
30000
25000
20000
15000
10000
5000
0
ε
250
300
350
400
450
500
550
600
Wavelength (nm)
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Oscillator strength

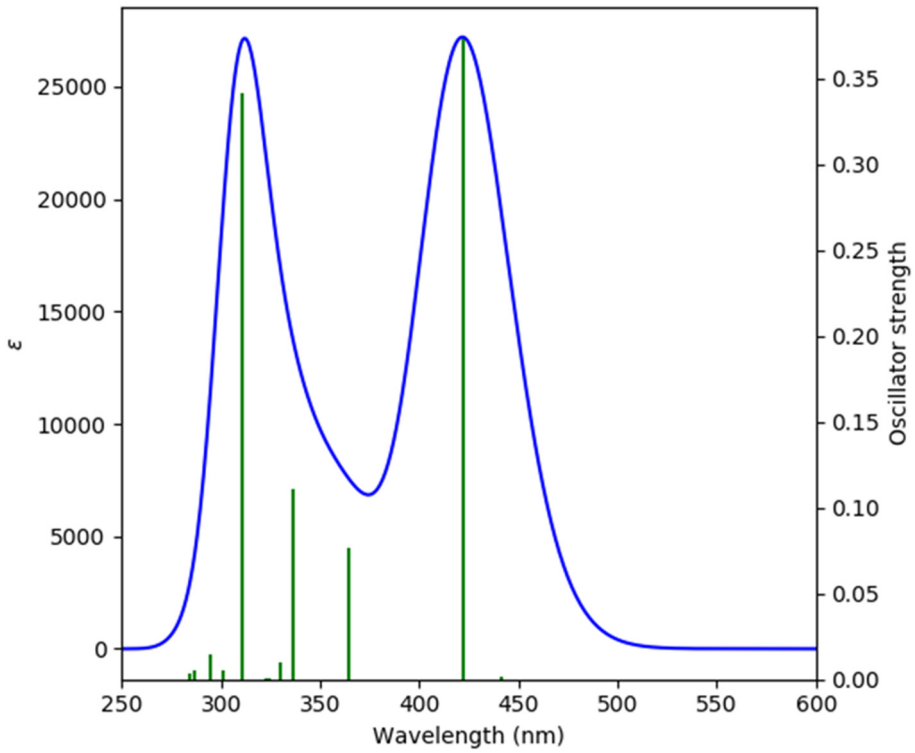
5m:


40000
30000
20000
10000
0
ε
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Oscillator strength
250
300
350
400
450
500
550
600
Wavelength (nm)

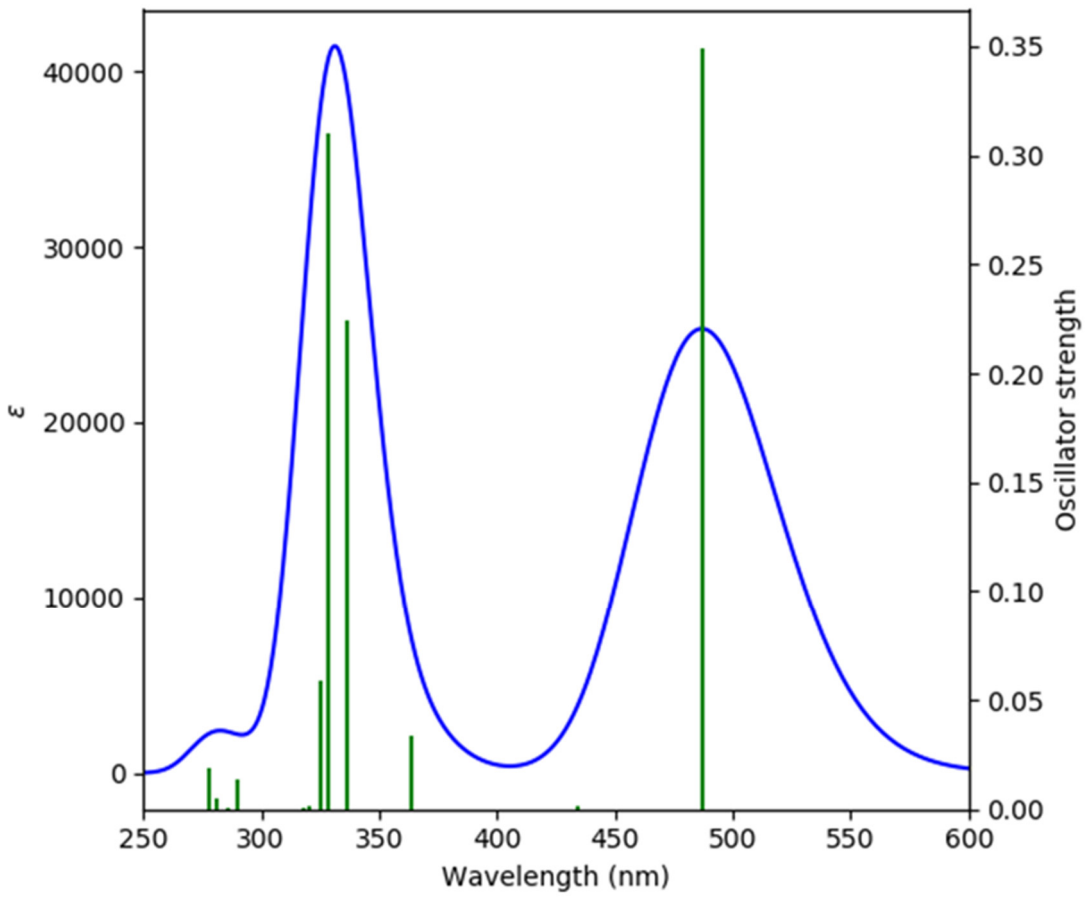
5n:


30000
25000
20000
15000
10000
5000
0
ε
0.4
0.3
0.2
0.1
0.0
Oscillator strength
250
300
350
400
450
500
550
600
Wavelength (nm)

5r:


25000
20000
15000
10000
5000
0
ε
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Oscillator strength
250
300
350
400
450
500
550
600
Wavelength (nm)

6l:



Simulated UV data (excitation number, energy, wavelength, oscilator strenghs and transition involved):

5a:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	21768.90404	459.3708522	0.3426	HOMO->LUMO (99%)
2	23166.66286	431.6547471	0.0013	H-1->LUMO (91%)
3	27743.85925	360.4401216	0.0354	H-2->LUMO (69%), HOMO->L+1 (15%)
4	30304.66956	329.9821494	0.1705	H-3->LUMO (72%), H-2->LUMO (11%), HOMO->L+2 (11%)
5	31189.45977	320.6211353	0.0013	H-1->L+1 (84%)
6	31295.1184	319.5386537	0.3387	H-2->LUMO (16%), HOMO->L+1 (76%)
7	31468.5276	317.7778168	0.0027	H-4->LUMO (81%)
8	31775.82484	314.7046552	0.0008	H-3->LUMO (14%), HOMO->L+2 (77%)
9	34529.40166	289.6082619	0.0129	H-7->LUMO (35%), H-5->LUMO (45%)
10	35008.49499	285.6449557	0.0007	H-1->L+2 (93%)
11	35662.61063	280.4057197	0.0027	H-7->LUMO (39%), H-6->LUMO (14%), H-5->LUMO (22%)
12	36132.83186	276.7566084	0.0265	H-6->LUMO (47%), H-5->LUMO (12%), H-3->L+1 (21%)

5b:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	20819.58948	480.3168675	0.3342	HOMO->LUMO (99%)
2	22973.0898	435.291904	0.0013	H-1->LUMO (91%)
3	27474.47007	363.9742632	0.0339	H-2->LUMO (65%), HOMO->L+1 (16%)
4	29844.93354	335.0652461	0.2238	H-3->LUMO (55%), HOMO->L+1 (11%), HOMO->L+2 (24%)
5	30575.67185	327.0574086	0.3012	H-2->LUMO (22%), HOMO->L+1 (69%)
6	30975.72285	322.833467	0.0502	H-3->LUMO (28%), HOMO->L+2 (64%)
7	31183.81389	320.6791843	0.0014	H-1->L+1 (82%)
8	31438.68509	318.0794608	0.0006	H-4->LUMO (74%)
9	34416.48404	290.5584425	0.0146	H-7->LUMO (29%), H-5->LUMO (47%)
10	34993.17046	285.770048	0.0007	H-1->L+2 (93%)
11	35419.0312	282.3340917	0.0071	H-7->LUMO (32%), H-6->LUMO (31%), H-5->LUMO (11%)
12	35908.60973	278.4847443	0.017	H-7->LUMO (21%), H-6->LUMO (37%), H-5->LUMO (15%), H-3->L+1 (15%)

5d:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	21551.13434	464.0126984	0.381	HOMO->LUMO (99%)
2	22937.60141	435.9653751	0.0013	H-1->LUMO (91%)
3	27810.80327	359.5724979	0.0305	H-2->LUMO (67%), HOMO->L+1 (12%)
4	30019.95585	333.1117491	0.2035	H-3->LUMO (65%), H-2->LUMO (11%), HOMO->L+2 (12%)
5	31093.47979	321.610835	0.2019	HOMO->L+1 (64%), HOMO->L+2 (15%)
6	31255.59723	319.9426946	0.0008	H-6->LUMO (25%), H-1->L+1 (63%)
7	31404.8098	318.4225621	0.001	H-6->LUMO (60%), H-1->L+1 (25%)
8	31692.74973	315.5295796	0.2248	H-3->LUMO (11%), H-2->LUMO (10%), HOMO->L+1 (13%), HOMO->L+2 (59%)
9	34208.393	292.3259213	0.0059	H-7->LUMO (14%), H-4->LUMO (70%)
10	34500.3657	289.852	0.0126	H-9->LUMO (26%), H-7->LUMO (32%), H-4->LUMO (27%)
11	34885.89872	286.6487712	0.0011	H-1->L+2 (92%)
12	35008.49499	285.6449557	0.0019	H-5->LUMO (94%)

5e:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	21375.30548	467.8295714	0.3766	HOMO->LUMO (99%)

2	22972.28325	435.307187	0.0013	H-1->LUMO (91%)
3	27530.92888	363.2278462	0.0354	H-2->LUMO (70%), HOMO->L+1 (13%)
4	30001.4051	333.3177219	0.2238	H-4->LUMO (37%), H-3->LUMO (34%), HOMO->L+2 (12%)
5	30951.52621	323.085845	0.3238	H-2->LUMO (16%), HOMO->L+1 (77%)
6	31158.00415	320.944819	0.0031	H-1->L+1 (81%)
7	31357.22309	318.9057899	0.0263	H-3->LUMO (13%), HOMO->L+2 (75%)
8	31403.19669	318.4389187	0.0007	H-6->LUMO (76%)
9	32315.40975	309.4498902	0.0026	H-4->LUMO (44%), H-3->LUMO (50%)
10	33943.84314	294.6042367	0.0021	H-5->LUMO (95%)
11	34422.93648	290.5039786	0.0127	H-9->LUMO (32%), H-7->LUMO (47%)
12	34965.74761	285.994171	0.0004	H-1->L+2 (94%)

5m:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	19749.29175	506.347272	0.3672	HOMO->LUMO (99%)
2	22827.91	438.0602516	0.002	H-2->LUMO (75%), H-1->LUMO (16%)
3	26782.44637	373.3788864	0.1044	H-1->LUMO (38%), HOMO->L+1 (36%)
4	28310.06046	353.2313191	0.2847	H-3->LUMO (13%), HOMO->L+1 (44%), HOMO->L+2 (35%)
5	28955.304	345.3598691	0.1957	H-1->LUMO (38%), HOMO->L+1 (16%), HOMO->L+2 (29%)
6	29777.98952	335.8185076	0.1176	H-3->LUMO (65%), HOMO->L+2 (24%)
7	30893.45429	323.6931651	0.0017	H-2->L+1 (67%), H-1->L+1 (14%)
8	31133.00096	321.2025726	0.0005	H-8->LUMO (80%)
9	32440.42569	308.2573606	0.004	H-6->LUMO (14%), H-4->LUMO (74%)
10	33738.97832	296.3930889	0.0096	H-6->LUMO (55%), H-4->LUMO (20%)
11	34008.3675	294.0452817	0.0085	H-5->LUMO (71%)
12	34453.58554	290.2455533	0.0573	H-11->LUMO (27%), H-9->LUMO (25%), H-6->LUMO (13%), HOMO->L+4 (15%)

5n:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	22471.41295	445.0098453	0.0016	H-1->LUMO (91%)
2	25575.84094	390.9939862	0.4349	HOMO->LUMO (98%)
3	27780.96075	359.9587534	0.0851	H-2->LUMO (81%)
4	30244.17798	330.6421489	0.0411	H-3->LUMO (88%)
5	30661.97317	326.1368713	0	H-4->LUMO (69%), H-1->L+1 (12%)
6	30880.54942	323.8284353	0.001	H-4->LUMO (11%), H-1->L+1 (74%)
7	33354.25186	299.8118514	0.2807	H-5->LUMO (12%), HOMO->L+1 (73%)
8	33498.6251	298.5197145	0.0003	H-3->L+3 (10%), H-2->L+3 (14%), HOMO->L+3 (68%)
9	33724.46034	296.5206826	0.0543	H-7->LUMO (20%), H-5->LUMO (40%), HOMO->L+1 (12%)
10	34656.03071	288.5500675	0.0028	H-7->LUMO (38%), H-2->L+1 (13%), HOMO->L+2 (12%)
11	34914.93468	286.4103883	0.0022	H-1->L+2 (82%)
12	35135.93059	284.6089411	0.0292	H-7->LUMO (18%), H-5->LUMO (17%), H-3->L+1 (11%), H-2->L+1 (16%), H-2->L+2 (13%)

5r:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	22670.63189	441.0993063	0.0015	H-1->LUMO (88%)
2	23703.82811	421.8727858	0.3734	HOMO->LUMO (98%)
3	27455.91932	364.2201845	0.077	H-2->LUMO (75%)
4	29752.98633	336.1007157	0.1106	H-4->LUMO (61%), H-3->LUMO (19%), H-2->LUMO (12%)
5	30337.73829	329.6224624	0.0097	H-4->LUMO (22%), H-3->LUMO (75%)
6	30820.05784	324.4640244	0.0004	H-5->LUMO (26%), H-1->L+1 (54%)
7	30964.43108	322.9511943	0.0008	H-6->LUMO (13%), H-5->LUMO (42%), H-1->L+1 (32%)
8	32181.52172	310.7373258	0.3414	HOMO->L+1 (85%)
9	33235.68836	300.8813867	0.0049	HOMO->L+2 (69%)
10	33955.94146	294.4992708	0.0144	H-8->LUMO (25%), H-6->LUMO (35%), H-5->LUMO (14%)
11	34848.79721	286.9539496	0.0049	H-8->LUMO (35%), H-7->LUMO (26%), H-6->LUMO (10%)
12	35154.48134	284.4587551	0.0033	H-1->L+2 (84%)

6l:

No.	Energy (cm-1)	Wavelength (nm)	Osc. Strength	Major contribs
1	20537.29543	486.9190316	0.3494	HOMO->LUMO (99%)
2	23039.22726	434.0423351	0.0012	H-1->LUMO (91%)
3	27491.40771	363.7500162	0.0335	H-2->LUMO (61%), HOMO->L+1 (20%)
4	29731.20936	336.3468966	0.2243	H-3->LUMO (39%), HOMO->L+1 (17%), HOMO->L+2 (37%)
5	30427.26583	328.6525991	0.3097	H-2->LUMO (30%), HOMO->L+1 (60%)
6	30782.95634	324.8550883	0.0585	H-3->LUMO (44%), HOMO->L+2 (50%)
7	31210.43018	320.4057086	0.0014	H-1->L+1 (83%)
8	31479.01281	317.6719696	0.0005	H-4->LUMO (78%)
9	34475.36251	290.0622146	0.014	H-7->LUMO (30%), H-5->LUMO (48%)
10	34956.87551	286.0667567	0.0006	H-1->L+2 (94%)
11	35526.30293	281.4815833	0.0047	H-7->LUMO (36%), H-6->LUMO (23%), H-5->LUMO (15%)
12	36015.07492	277.6615077	0.019	H-7->LUMO (16%), H-6->LUMO (41%), H-5->LUMO (14%), H-3->L+1 (18%)

Cartesian coordinates of the optimized geometries:

5a:

C -4.40414 0.66568 -0.28835
C -3.88616 -0.71547 -0.17749
C -2.49764 -0.95553 -0.11960
C -1.57956 0.13331 -0.16275
C -2.07446 1.52556 -0.27207
N -3.45778 1.69754 -0.35801
C -4.77744 -1.77457 -0.13086
C -4.30196 -3.08878 -0.02728
C -2.94451 -3.34222 0.03128
C -2.01513 -2.28309 -0.01252
C -0.58849 -2.50111 0.04712
C 0.29524 -1.40349 -0.00024
C -0.22993 -0.08928 -0.10441
N -0.16588 -3.79929 0.14961
N 1.10138 -4.06805 0.20767
C 2.02927 -3.07451 0.16734
C 1.69964 -1.69359 0.06171
C 3.39548 -3.45618 0.23527
C 4.38091 -2.51653 0.19906
C 4.06309 -1.12343 0.09115
C 2.72041 -0.73525 0.02495

N 5.07774 -0.22473 0.05665
C 4.90503 1.21508 -0.04786
C 6.25696 1.91999 -0.05102
C 6.12581 3.44050 -0.15782
C 7.48139 4.14871 -0.15960
C -3.96484 3.07660 -0.46704
C -4.20531 3.71450 0.90134
C -4.72971 5.14443 0.76843
O -1.32414 2.48860 -0.29025
O -5.59673 0.91983 -0.32134
H -5.83807 -1.56536 -0.17638
H -5.00574 -3.91110 0.00735
H -2.56750 -4.35217 0.11165
H 0.42821 0.76784 -0.13975
H 3.62101 -4.51208 0.31605
H 5.42338 -2.81007 0.25177
H 2.47425 0.31270 -0.05621
H 6.02001 -0.57825 0.10826
H 4.35655 1.45718 -0.96703
H 4.29896 1.57732 0.79215
H 6.79703 1.66222 0.86760
H 6.85555 1.54414 -0.88914
H 5.57836 3.69211 -1.07298
H 5.51911 3.80981 0.67646
H 7.36249 5.23210 -0.23694
H 8.03603 3.93768 0.75955
H 8.09596 3.81843 -1.00234
H -3.22523 3.64496 -1.02771
H -4.89221 3.03114 -1.03449
H -4.92174 3.10140 1.45528
H -3.26701 3.70891 1.46312
H -4.89952 5.59263 1.75001
H -4.01751 5.77723 0.23061
H -5.67717 5.16755 0.22198

5b:

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C -4.01343 -0.82379 -0.22017
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H 6.25406 2.01225 -1.02380
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C 1.18423 0.26079 -0.12027
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C 6.88499 4.22762 -0.47418
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O 6.57239 -0.04344 0.74191
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5m:
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C 3.48553 -1.25032 0.10661
C 2.67702 -0.08355 0.22795
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C 5.07576 -3.53578 -0.14220
C 3.70324 -3.64651 -0.25782
C 2.88038 -2.50802 -0.13691
C 1.44306 -2.57362 -0.25194
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H -1.33973 0.49747 0.09544

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5r:

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6l:

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