Electronic Supplementary Material (ESI) for Chemical Communications.

Supplementary Information for

Modular synthesis of 4-aminocarbonyl substituted 1,8-naphthalimides and application in single molecule fluorescence detection

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Experimental

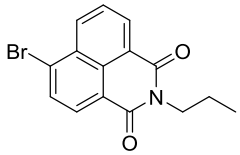
General

All general reagents and solvents were purchased from commercial sources and used as supplied. For the preparation of G3-Xantphos, $[Pd(OAc)_2]_3$ (46-1780) was purchased from Strem Chemicals in accordance with Carole and Colacot.[1] Reactions were monitored using thin-layer chromatography (TLC) with Merck 60 F_{254} silica gel plates and visualised under UV light at 254 nm. Column chromatography was performed using 230–400 Mesh silica gel. All NMR spectra (^{1}H and ^{13}C) were collected on a JEOL Eclipse JNM-Ex 270 MHz, 400 MHz FT-NMR or Bruker Avance 500 MHz spectrometer as specified. Samples were dissolved in $CDCl_3$ or DMSO-d_6 where specified with the residual solvent peak used as the internal reference – $CDCl_3$; 7.26 (^{1}H) and 77.00 (^{13}C), DMSO-d_6; 2.50 (^{1}H) and 39.52 (^{13}C). In instances when either the ^{1}H or ^{13}C resonance was coincidental with the deuterated solvent, the resonance was confirmed by HSQC experiments. All coupling constants are reported in Hertz (Hz). Melting points are uncorrected and were determined using a Bibby Stuart Scientific SMP3 melting point apparatus. High resolution mass spectrometry (ESI) was performed on an Applied Biosystems QTOF-MS. Those reactions that employed microwave irradiation were conducted using a CEM Discover S-Class Microwave reactor, operating at a frequency of 50/60 Hz and continuous irradiation power from 0 to 200 W. All reactions were conducted in a 35 mL microwave vial sealed with a Teflon® crimp cap. UV-visible absorption spectra and molar absorptivity were collected using a Cary 300 Bio UV-Vis spectrophotometer. Emission spectra were collected with a Cary Eclipse fluorescence spectrophotometer. For both UV and fluorescence measurements samples were placed in a 1 cm quartz cuvette.

General Procedure for Cross-coupling

An oven dried flask, equipped with stirrer bar and cooled under N_2 was charged with aryl bromide (0.5 mmol), amide or carbamate (0.60 mmol, 1.2 equiv.), Cs_2CO_3 (0.70 mmol, 1.4 equiv.), G3-Xantphos (1 mol%) and 1,4-dioxane (5 mL per 0.5 mmol of aryl halide). The resultant mixture was heated at 80 or 100 °C as indicated for the indicated time. At the completion of the reaction H_2O (*ca.* 15 mL) was added to give a precipitate which was collected using vacuum filtration and washed using H_2O. In instances where this work up was insufficient further details are provided.

6-Bromo-2-propyl-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (1)



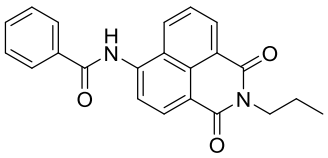
A mixture of 4-bromo-1,8-naphthalic anhydride (3.057 g, 11.03 mmol) and propylamine (950 µL, 11.56 mmol, 1.04 equiv.) in EtOH (15 mL) was heated using microwave irradiation at 100 °C for 1 h. The mixture was then diluted using H_2O and cooled to 0 °C, before the solid was collected using vacuum filtration and washed using H_2O to give the title compound (2.894 g, 82%) as a tan powder.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.64 (dd, *J* = 7.4, 1.0, 1H), 8.59 (dd, *J* = 8.5, 1.0, 1H), 8.42 (d, *J* = 7.9, 1H), 8.04 (d, *J* = 7.9, 1H), 7.80 (dd, *J* = 8.5, 7.4, 1H), 4.16–4.11 (m, 2H), 1.77 (app. sext, J_{app} = 7.5, 2H), 1.01 (t, *J* = 7.4, 3H)

^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 169.8, 163.8, 133.4, 132.2, 131.4, 131.2, 130.8, 130.3, 129.2, 128.3, 123.3, 122.4, 42.2, 21.5, 11.7

Data are in accordance with literature values.[2]

_N_-(1,3-Dioxo-2-propyl-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)benzamide (2)



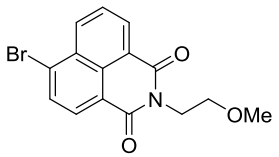
Using the general procedure, **1** (78 mg, 0.246 mmol), benzamide (36 mg, 0.297 mmol, 1.2 equiv.), G3-xantphos (2.5 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (117 mg, 0.361 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 2.5 h. Gives the title compound (82 mg, 93%) as a champagne coloured powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.87 (s, 1H), 8.60–8.58 (m, 1H), 8.54 (d, J = 7.9, 2H), 8.15–8.11 (m, 3H), 7.87 (dd, J = 8.4, 7.4, 1H), 7.67 (t, J = 7.4, 1H), 7.60 (t, J = 7.4, 2H), 4.04–4.01 (m, 2H), 1.71–1.63 (m, 2H), 0.94 (t, J = 7.4, 3H)

^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.0, 164.2, 163.7, 138.6, 134.2, 132.8, 132.4, 131.4, 129.3, 129.1, 127.3, 127.0, 126.2, 124.2, 123.7, 119.7, 119.3, 42.1, 21.5, 11.6.

HRMS (ESI) for $C_{22}H_{18}N_2O_3$ [M + H^+] calcd, 359.1390; found, 359.1395.

6-Bromo-2-(2-methoxyethyl)-1_H_-benzo[_de_]isoquinoline-1,3(2_H_)-dione (3)



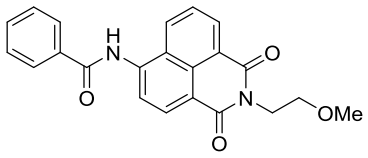
A mixture of 4-bromo-1,8-naphthalic anhydride (1.108 g, 4.000 mmol) and 2-methoxyethylamine (350 μL, 4.054 mmol, 1.01 equiv.) in EtOH (20 mL) was heated at 70 °C for 4.5 h. After this time the mixture was diluted using H_2O and cooled to 0 °C, the resultant solid was collected using vacuum filtration and washed using H_2O to give the title compound (1.194 g, 89%) as an off-white powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.59 (dd, *J* = 7.3, 1.1, 1H), 8.57 (dd, *J* = 8.5, 1.1, 1H), 8.35 (d, *J* = 7.9, 1H), 8.24 (d, *J* = 7.9, 1H), 8.01 (dd, *J* = 8.5, 7.3, 1H), 4.24 (t, *J* = 6.3, 2H), 3.59 (t, *J* = 6.3, 2H), 3.26 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.71, 163.68, 133.3, 132.2, 131.3, 131.1, 130.6, 130.3, 129.0, 128.0, 123.0, 122.1, 69.5, 58.8, 39.4.

Data are in accordance with literature values.[3]

_N_-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)benzamide (4)



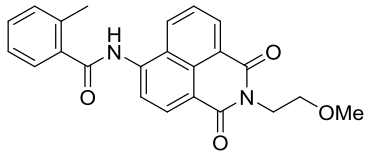
Using the general procedure, **3** (168 mg, 0.503 mmol), benzamide (74 mg, 0.613 mmol, 1.2 equiv.), G3-xantphos (4.8 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (231 mg, 0.709 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 35 mins. Gives the title compound (170 mg, 90%) as a champagne solid.

^{1}H NMR (DMSO-d_6, 270 MHz): δ 10.88 (s, 1H), 8.61 (d, J = 8.6, 1H), 8.54 (d, J = 7.9, 2H), 8.17–8.10 (m, 3H), 7.87 (app. t, J = 8.6, 1H), 7.66–7.56 (m, 3H), 4.27 (t, J = 6.2, 2H), 3.61 (t, J = 6.2, 2H), 3.26 (s, 3H).

^{13}C NMR (DMSO-d_6, 100 MHz) δ 166.5, 163.5, 163.0, 140.7, 134.1, 132.1, 131.3, 131.1, 130.5, 128.5, 128.4, 128.1, 126.6, 126.1, 122.7, 122.2, 118.7, 68.6, 58.0, 38.6.

HRMS (ESI) for $C_{22}H_{18}N_2O_4$ [M + H^+] calcd, 375.1340; found, 375.1330.

_N_-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)-2-methylbenzamide (5)



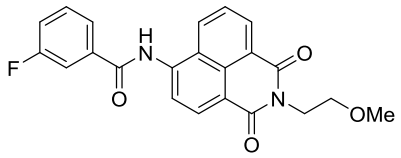
Using the general procedure, **3** (85 mg, 0.253 mmol), *o*-toluamide (**S14**) (42 mg, 0.307 mmol, 1.2 equiv.), G3-xantphos (2.5 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (118 mg, 0.361 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 100 mins. Gives the title compound (93 mg, 95%) as a champagne coloured solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.66–8.60 (m, 3H), 8.23 (s, 1H), 8.18 (d, J = 8.3, 1H), 7.77 (dd, J = 8.3, 7.4, 1H), 7.66 (d, J = 7.3, 1H), 7.48–7.44 (m, 1H), 7.37–7.34 (m, 2H), 4.45 (t, J = 5.9, 2H), 3.74 (t, J = 5.9, 2H), 3.38 (s, 3H), 2.60 (s, 3H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ 168.9, 163.5, 163.0, 140.3, 136.4, 135.6, 131.4, 131.0, 130.6, 130.1, 130.0, 128.4, 127.7, 126.6, 125.7, 125.3, 122.1, 121.5, 118.4, 68.6, 58.0, 38.5, 19.5.

HRMS (ESI) for $C_{23}H_{20}N_2O_4$ [M + H^+] calcd, 389.1496; found, 389.1488.

3-Fluoro-*N*-(2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)benzamide (6)



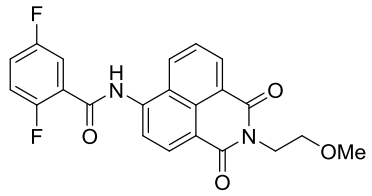
Using the general procedure, **3** (168 mg, 0.510 mmol), 3-fluorobenzamide (86 mg, 0.615 mmol, 1.2 equiv.), G3-xantphos (6.3 mg, 0.007 mmol, 0.01 equiv.), Cs_2CO_3 (226 mg, 0.695 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 55 min. Gives the title compound (184 mg, 92%) as a light ochre powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.94 (s, 1H), 8.62 (d, J = 7.9, 1H), 8.56–8.54 (m, 2H), 8.14 (d, J = 8.0, 1H), 7.97 (d, J = 7.9, 1H), 7.95–7.92 (m, 1H), 7.89 (dd, J = 8.4, 7.4, 1H), 7.67–7.63 (m, 1H), 7.54–7.50 (m, 1H), 4.27 (t, J = 6.2, 2H), 3.61 (t, J = 6.2, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.2 (d, $^4J_{C\text{-}F}$ = 2.0), 163.5, 163.0, 162.0 (d, $^1J_{C\text{-}F}$ = 243.2), 140.2, 136.4 (d, $^3J_{C\text{-}F}$ = 6.9), 131.2, 131.1, 130.7 (d, $^3J_{C\text{-}F}$ = 8.0), 130.5, 128.3, 126.7, 126.1, 124.4 (d, $^4J_{C\text{-}F}$ = 2.4), 122.9, 122.2, 119.1, 119.0 (d, $^2J_{C\text{-}F}$ = 20.9), 115.0 (d, $^2J_{C\text{-}F}$ = 22.9), 68.7, 58.0, 38.6.

HRMS (ESI) for $C_{22}H_{17}FN_2O_4$ [M + H^+] calcd, 393.1245; found, 393.1251.

2,5-Difluoro-*N*-(2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)benzamide (7)



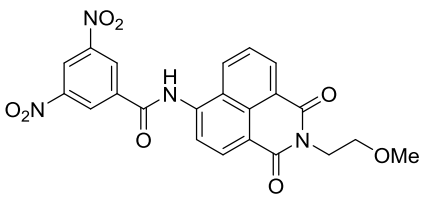
Using the general procedure, **3** (87 mg, 0.251 mmol), 2,5-difluorobenzamide (47 mg, 0.301 mmol, 1.2 equiv.), G3-xantphos (2.4 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (116 mg, 0.358 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 24 mins. Gives the title compound (100 mg, 97%) as a yellow solid.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.04 (s, 1H), 8.65 (d, J = 8.5, 1H), 8.55 (d, J = 7.7, 2H), 8.30 (d, J = 8.5, 1H), 7.91 (t, J = 7.7, 1H), 7.76–7.70 (m, 1H), 7.53–7.48 (m, 2H), 4.26 (t, J = 6.1, 2H), 3.60 (t, J = 6.1, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.5, 163.0, 162.6, 158.4 (dd, $^1J_{C\text{-}F}$ = 163.3, $^4J_{C\text{-}F}$ = 2.0), 154.8 (dd, $^1J_{C\text{-}F}$ = 167.3, $^4J_{C\text{-}F}$ = 2.0), 139.5, 131.4, 131.1, 129.6, 128.3, 126.8, 125.4 (dd, $^2J_{C\text{-}F}$ = 17.6, $^3J_{C\text{-}F}$ = 7.4), 125.1, 122.2, 121.4, 119.5 (dd, $^2J_{C\text{-}F}$ = 24.2, $^3J_{C\text{-}F}$ = 9.0), 118.7, 118.1 (dd, $^2J_{C\text{-}F}$ = 25.1, $^3J_{C\text{-}F}$ = 8.5), 116.6 (dd, $^2J_{C\text{-}F}$ = 25.8, $^3J_{C\text{-}F}$ = 3.3), 68.6, 57.9, 38.7.

HRMS (ESI) for $C_{22}H_{16}F_2N_2O_4$ [M + H^+] calcd, 411.1151; found, 411.1153.

_N_-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)-3,5-dinitrobenzamide (8)



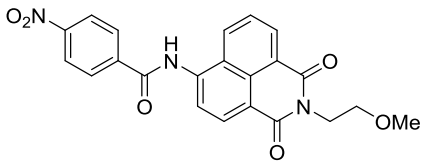
Using the general procedure, **3** (87 mg, 0.249 mmol), 3,5-dinitrobenzamide (**S17**) (65 mg, 0.307 mmol, 1.2 equiv.), G3-xantphos (2.7 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (115 mg, 0.353 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 2.5 h. Gives the title compound (104 mg, 90%) as a yellow solid.

^{1}H NMR (DMSO-d_6, 270 MHz): δ 11.45 (br s, 1H), 9.29 (d, J = 1.9, 2H), 9.03–9.01 (m, 1H), 8.70 (d, J = 8.4, 1H), 8.55 (d, J = 7.7, 2H), 8.17 (d, J = 8.4, 1H), 7.90 (app. t, J_{app} = 7.7, 1H), 4.57 (t, J = 5.7, 2H), 3.61 (t, J = 5.7, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.4, 162.9, 162.7, 148.0, 140.1, 137.1, 131.2, 131.1, 130.4, 128.4, 128.3, 126.7, 126.1, 123.2, 122.2, 121.3, 119.3, 68.6, 57.9, 38.5.

HRMS (ESI) for $C_{22}H_{16}N_4O_8$ [M + H^+] calcd, 465.1041; found, 465.1039.

_N_-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)-4-nitrobenzamide (9)



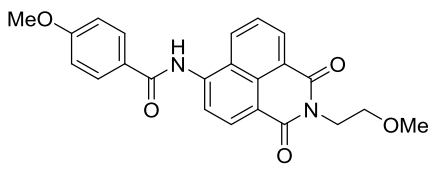
Using the general procedure, **3** (87 mg, 0.259 mmol), 4-nitrobenzamide (83 mg, 0.500 mmol, 1.9 equiv.), G3-xantphos (2.4 mg, 0.0023 mmol, 0.01 equiv.), Cs_2CO_3 (115 mg, 0.352 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 40 mins. Gives the title compound (102 mg, 94%) as a peach solid.

^{1}H NMR (50 °C, DMSO-d_6, 500 MHz): δ 11.18 (s, 1H), 8.64 (dd, J = 8.5, 0.9, 1H), 8.58–8.55 (m, 2H), 8.44–8.42 (m, 2H), 8.35–8.33 (m, 2H), 8.17 (d, J = 8.0, 1H), 7.90 (dd, J = 8.5, 7.3, 1H), 4.27 (t, J = 6.2, 2H), 3.61 (t, J = 6.2, 2H), 3.27 (s, 3H).

^{13}C NMR (50 °C, DMSO-d_6, 125 MHz): δ 164.9, 163.3, 162.8, 149.4, 139.9, 139.8, 131.0, 130.9, 130.1, 129.5, 128.2, 126.5, 126.0, 123.4, 122.7, 122.1, 119.1, 68.6, 57.8, 38.5.

HRMS (ESI) for $C_{22}H_{17}N_3O_6$ [M + H^+] calcd, 420.1190; found, 420.1191.

4-Methoxy-*N*-(2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)benzamide (10)



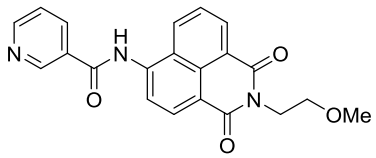
Using the general procedure, **3** (83 mg, 0.249 mmol), 4-methoxybenzamide (**S16**) (76 mg, 0.500 mmol, 2.0 equiv.), G3-xantphos (2.4 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (114 mg, 0.350 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 17 mins. Gives the title compound (84 mg, 83%) as a yellow solid.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.70 (s, 1H), 8.58–8.52 (m, 3H), 8.11 (dd, J = 8.5, 2.8, 3H), 7.85 (dd, J = 8.3, 7.4, 1H), 7.11 (d, J = 8.8 Hz, 2H), 4.26 (t, J = 6.2, 2H), 3.87 (s, 3H), 3.60 (t, J = 6.2, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8, 163.5, 163.0, 162.3, 140.9, 131.2, 131.0, 130.4, 130.1, 128.3, 126.4, 126.1, 126.0, 122.5, 122.1, 118.5, 113.7, 68.6, 57.9, 55.5, 38.5.

HRMS (ESI) for $C_{23}H_{20}N_2O_5$ [M + H^+] calcd, 405.1445; found, 405.1448.

***N*-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)nicotinamide (11)**



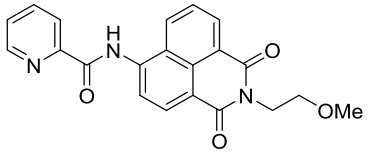
Using the general procedure, **3** (167 mg, 0.500 mmol), 3-nicotinamide (72 mg, 0.591 mmol, 1.2 equiv.), G3-xantphos (4.7 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (231 mg, 0.710 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 55 min. Gives the title compound (156 mg, 83%) as an orange powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.05 (s, 1H), 9.27 (d, J = 1.8, 1H), 8.83 (dd, J = 4.8, 1.4, 1H), 8.67 (d, J = 8.5, 1H), 8.56 (app. d, J_{app} = 8.2, 2H), 8.45 (dt, J = 7.9, 1.8, 1H), 8.18 (d, J = 8.0, 1H), 7.89 (dd, J = 8.5, 7.5, 1H), 7.64 (dd, J = 7.9, 4.8, 1H), 4.27 (t, J = 6.2, 2H), 3.61 (t, J = 6.2, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.2, 163.5, 163.0, 152.6, 149.1, 140.2, 135.9, 131.3, 131.1, 130.4, 129.9, 128.4, 126.7, 126.0, 123.6, 122.7, 122.2, 119.0, 68.7, 58.0, 38.6.

HRMS (ESI) for $C_{21}H_{17}N_3O_4$ [M + H^+] calcd, 376.1292; found, 376.1305.

***N*-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)picolinamide (12)**



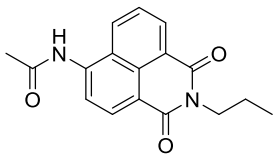
Using the general procedure, **3** (88 mg, 0.254 mmol), 2-picolinamide (**S15**) (37 mg, 0.306 mmol, 1.2 equiv.), G3-xantphos (4.9 mg, 0.005 mmol, 0.02 equiv.), Cs_2CO_3 (122 mg, 0.374 mmol, 1.5 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 24 h. After diluting with H_2O, the precipitate was collected using vacuum filtration and purified by column chromatography, eluting with 50% EtOAc in petroleum spirits to provide the title compound (51 mg, 54%) as a yellow solid.

^{1}H NMR (50 °C, DMSO-d_6, 500 MHz): δ 11.30 (br s, 1H), 8.85–8.83 (m, 1H), 8.57–8.54 (m, 2H), 8.52 (dd, J = 8.5, 0.8, 1H), 8.46 (d, J = 8.1, 1H), 8.26–8.24 (m, 1H), 8.15 (td, J = 7.7, 1.7, 1H), 7.95 (dd, J = 8.4, 7.3, 1H), 7.77–7.74 (m, 1H), 4.29 (t, J = 6.2, 2H), 3.63 (t, J = 6.2, 2H), 3.29 (s, 3H).

^{13}C NMR (50 °C, DMSO-d_6, 125 MHz): δ 163.3, 162.8, 162.7, 149.0, 148.5, 139.4, 138.2, 131.4, 130.8, 128.4, 128.1, 127.3, 126.7, 124.5, 122.4, 122.2, 119.6, 118.1, 68.5, 57.8, 38.4.

HRMS (ESI) for $C_{21}H_{17}N_3O_4$ [M + H^+] calcd, 376.1292; found, 376.1299.

_N_-(1,3-Dioxo-2-propyl-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)acetamide (13)



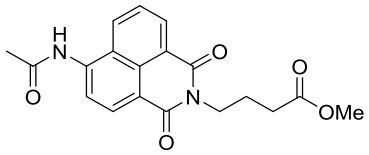
Using the general procedure, **1** (159 mg, 0.498 mmol), acetamide (37 mg, 0.630 mmol, 1.3 equiv.), G3-xantphos (4.6 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (229 mg, 0.702 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 4 h. Gives the title compound (127 mg, 87%) as a champagne powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.38 (s, 1H), 8.69 (dd, J = 8.5, 0.8, 1H), 8.50 (dd, J = 7.3, 0.8, 1H), 8.44 (d, J = 8.2, 1H), 8.30 (d, J = 8.2, 1H), 7.86 (dd, J = 8.5, 7.3, 1H), 4.00–3.97 (m, 2H), 2.28 (s, 3H), 1.68–1.60 (m, 2H), 0.91 (t, J = 7.4, 3H).

^{13}C NMR (DMSO-d_6, MHz): δ169.6, 163.5, 163.0, 140.3, 131.7, 130.9, 129.3, 128.3, 126.4, 124.0, 122.3, 119.4, 117.5, 41.1, 24.1, 20.9, 11.4.

HRMS (ESI) for $C_{17}H_{16}N_2O_3$ [M + H^+] calcd, 297.1234; found, 297.1231.

Methyl 4-(6-acetamido-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)butanoate (14)



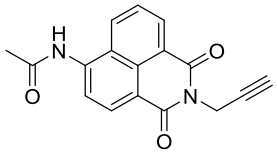
Using the general procedure, **S2** (189 mg, 0.502 mmol), acetamide (36 mg, 0.604 mmol, 1.3 equiv.), G3-xantphos (5.1 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (234 mg, 0.719 mmol, 1.4 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 60 mins. Gives the title compound (162 mg, 91%) as an ochre powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.61 (d, J = 7.2, 1H), 8.58 (d, J = 8.1, 1H), 8.39 (br s, 1H), 8.20 (d, J = 8.4, 1H), 7.89 (br s, 1H), 7.85 (app. t, J_{app} = 7.9, 1H), 4.24 (app. t, J_{app} = 7.1, 2H), 3.65 (s, 3H), 2.45 (t, J = 7.6, 2H), 2.38 (br s, 3H), 2.09 (app. quint, J_{app} = 7.3, 2H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 173.0, 169.6, 163.7, 163.1, 140.3, 131.6, 130.8, 129.2, 128.4, 126.4, 124.0, 122.4, 119.4, 117.5, 51.2, 38.9, 31.0, 24.1, 22.9.

HRMS (ESI) for $C_{19}H_{18}N_2O_5$ [M + H^+] calcd, 355.1288; found, 355.1288.

***N*-(1,3-Dioxo-2-(prop-2-yn-1-yl)-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)acetamide (15)**



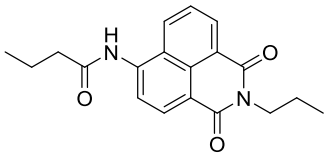
Using the general procedure, **S3** (157 mg, 0.495 mmol), acetamide (36 mg, 0.604 mmol, 1.2 equiv.), G3-xantphos (4.8 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (229 mg, 0.703 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 80 mins. Gives the title compound (142 mg, 97%) as a deep brown powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.44 (s, 1H), 8.75 (dd, *J* = 8.4, 0.8, 1H), 8.56 (dd, *J* = 7.3, 0.8, 1H), 8.51 (d, *J* = 8.2, 1H), 8.34 (d, *J* = 8.2, 1H), 7.91 (dd, *J* = 8.4, 7.3, 1H), 4.77 (d, *J* = 2.4, 2H), 3.14 (t, *J* = 2.4, 1H), 2.29 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 169.6, 162.8, 162.1, 140.8, 132.0, 131.2, 129.7, 128.3, 126.5, 124.0, 121.9, 119.3, 116.9, 79.4, 72.9, 29.0, 24.1.

HRMS (ESI) for $C_{17}H_{12}N_2O_3$ [M + H^+] calcd, 293.0921; found, 293.0943.

***N*-(1,3-Dioxo-2-propyl-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)butyramide (16)**



Using the general procedure, **1** (161 mg, 0.506 mmol), butyramide (53 mg, 0.611 mmol, 1.2 equiv.), G3-xantphos (5.0 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (225 mg, 0.692 mmol,

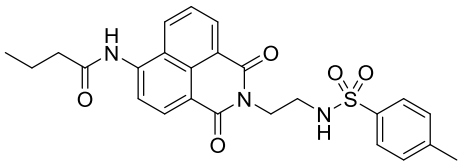
1.4 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 1 h. Gives the title compound (154 mg, 94%) as a tan solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.62 (dd, *J* = 7.3, 0.8 1H), 8.59 (d, *J* = 8.3, 1H), 8.43 (br s, 1H), 8.16 (d, *J* = 8.3, 1H), 7.82 (br s, 1H), 7.77 (dd, *J* = 8.3, 7.3, 1H), 4.15–4.12 (m, 2H), 2.56 (t, *J* = 7.4, 2H), 1.88 (app. sext, *J* = 7.4, 2H), 1.76 (app. sext, *J* = 7.6, 2H), 1.09 (t, *J* = 7.4, 3H), 1.01 (t, *J* = 7.5, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 172.4, 163.5, 163.0, 140.3, 131.6, 130.9, 129.3, 128.3, 126.4, 124.1, 122.3, 119.6, 117.5, 41.1, 38.2, 20.9, 18.6, 13.7, 11.4.

HRMS (ESI) for $C_{19}H_{20}N_2O_3$ [M + H^+] calcd, 325.1547; found, 325.1531.

_N_-(2-(2-((4-Methylphenyl)sulfonamido)ethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)butyramide (17)



Using the general procedure, **S5** (117.6 mg, 0.248 mmol), butyramide (26 mg, 0.301 mmol, 1.2 equiv.), G3-xantphos (2.4 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (116 mg, 0.356 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 1 h. Gives the title compound (107 mg, 90%) as a tan solid.

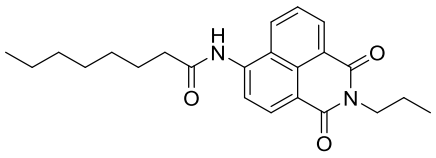
^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.35 (s, 1H), 8.67 (d, *J* = 8.3, 1H), 8.47 (d, *J* = 6.9, 1H), 8.42 (d, *J* = 8.2, 1H), 8.28 (d, *J* = 8.2, 1H), 7.87 (dd, *J* = 8.3, 7.5, 1H), 7.75 (s, 1H), 7.57 (d, *J*

= 8.2, 2H), 7.21 (d, *J* = 8.0, 2H), 4.10 (t, *J* = 6.5, 2H), 3.56 (s, 3H), 3.08 (t, *J* = 6.5, 2H), 2.56 (t, *J* = 7.3, 2H), 1.74–1.66 (m, 2H), 0.99 (t, *J* = 7.3, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 172.8, 164.0, 163.4, 142.9, 140.7, 138.0, 131.9, 131.2, 129.9, 129.6, 128.8, 126.8 (2C), 124.5, 122.8, 120.0, 118.0, 40.3, 39.5, 38.4, 21.3, 19.0, 14.0.

HRMS (ESI) for $C_{25}H_{25}N_3O_5S$ [M + H^+] calcd, 480.1588; found, 480.1589.

_N_-(1,3-Dioxo-2-propyl-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)octanamide (18)



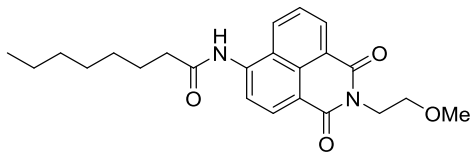
Using the general procedure, **1** (156 mg, 0.489 mmol), octanamide (87 mg, 0.609 mmol, 1.2 equiv.), G3-xantphos (5.2 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (226 mg, 0.694 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 50 mins. Gives the title compound (185 mg, 99%) as a light yellow powder.

^{1}H NMR (50 °C, DMSO-d_6, 500 MHz): δ 10.24 (s, 1H), 8.67 (dd, *J* = 8.5, 0.8, 1H), 8.53 (dd, *J* = 7.3, 0.8, 1H), 8.48 (d, *J* = 8.2, 1H), 8.29 (d, *J* = 8.2, 1H), 7.88 (dd, *J* = 8.5, 7.3, 1H), 4.03 (app. t, J_{app} = 7.5, 2H), 2.58 (t, *J* = 7.4, 2H), 1.72–1.64 (m, 4H), 1.40–1.24 (m, 8H), 0.92 (t, *J* = 7.5, 3H), 0.88 (t, *J* = 6.9, 3H).

^{13}C NMR (50 °C, DMSO-d_6, 125 MHz): δ 172.3, 163.3, 162.8, 140.2, 131.4, 130.6, 129.0, 128.2, 126.1, 124.1, 122.2, 119.5, 117.4, 40.9, 36.1, 31.0, 28.4, 28.2, 24.9, 21.8, 20.7, 13.7, 11.1.

HRMS (ESI) for $C_{23}H_{28}N_2O_3$ [M + H^+] calcd, 381.2173; found, 381.2161.

***N*-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)octanamide (19)**



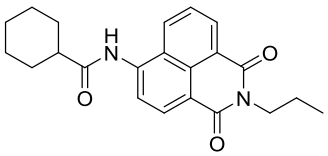
Using the general procedure, **3** (167 mg, 0.500 mmol), octanamide (85 mg, 0.591 mmol, 1.2 equiv.), G3-xantphos (4.3 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (226 mg, 0.694 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 90 mins. Gives the title compound (189 mg, 95%) as an off-white powder.

^{1}H NMR (50 °C, DMSO-d_6, 500 MHz): δ 10.35 (s, 1H), 8.69 (dd, J = 8.5, 0.8, 1H), 8.53 (dd, J = 7.3, 0.8, 1H), 8.47 (d, J = 8.2, 1H), 8.30 (d, J = 8.2, 1H), 7.89 (dd, J = 8.5, 7.3, 1H), 4.24 (t, J = 6.2, 2H), 3.58 (t, J = 6.2, 2H), 3.26 (s, 3H), 2.58 (t, J = 7.5, 2H), 1.68 (app. quint, J_{app} = 7.3, 2H), 1.38–1.27 (m, 8H), 0.87 (t, J = 6.9, 3H).

^{13}C NMR (50 °C, DMSO-d_6, 125 MHz): δ 172.6, 163.5, 163.0, 140.4, 131.7, 131.0, 129.4, 128.4, 126.4, 124.1, 122.2, 119.5, 117.3, 68.7, 58.0, 38.5, 36.2, 31.2, 28.7, 28.5, 25.1, 22.1, 14.0.

HRMS (ESI) for $C_{23}H_{28}N_2O_4$ [M + H^+] calcd, 397.2122; found, 397.2118.

***N*-(1,3-Dioxo-2-propyl-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)cyclohexanecarboxamide (20)**



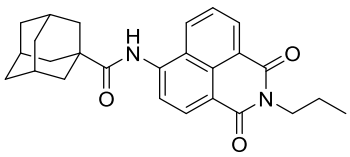
Using the general procedure, **1** (159 mg, 0.498 mmol), cyclohexanecarboxamide (74 mg, 0.584 mmol, 1.2 equiv.), G3-xantphos (5.4 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (227 mg, 0.696 mmol, 1.5 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 80 mins. Gives the title compound (175 mg, 96%) as a light yellow powder.

^{1}H NMR (50 °C, DMSO-d_6, 500 MHz): δ 10.17 (s, 1H), 8.66 (d, J = 8.5, 1H), 8.53 (d, J = 7.3, 1H), 8.47 (d, J = 8.2, 1H), 8.26 (d, J = 8.2, 1H), 7.88 (app. t, J_{app} = 7.9, 1H), 4.03 (t, J = 7.2, 2H), 2.71 (tt, J = 11.5, 3.4, 1H), 1.95 (dd, J = 12.8, 1.6, 2H), 1.81 (dt, J = 13.0, 3.2, 2H), 1.71–1.64 (m, 3H), 1.51 (qd, J = 12.3, 3.2, 2H), 1.35 (qt, J = 12.6, 3.2, 2H), 1.24 (qt, J = 12.0, 2.9, 1H), 0.93 (t, J = 7.5, 3H).

^{13}C NMR (50 °C, DMSO-d_6, 125 MHz): δ 175.2, 163.3, 162.8, 140.3, 131.3, 130.6, 129.1, 128.2, 126.1, 124.3, 122.1, 119.7, 117.4, 44.3, 40.9, 29.0, 25.2, 25.0, 20.7, 11.1.

HRMS (ESI) for $C_{22}H_{24}N_2O_3$ [M + H^+] calcd, 365.1860; found, 365.1860.

(3r,5r,7r)-*N*-(1,3-Dioxo-2-propyl-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)adamantane-1-carboxamide (21)



Using the general procedure, **1** (159 mg, 0.498 mmol), adamantine-1-carboxamide (107 mg, 0.598 mmol, 1.2 equiv.), G3-xantphos (5.1 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (230 mg,

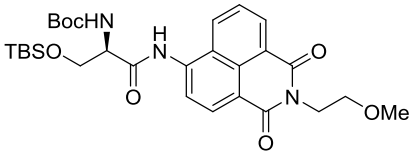
0.705 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 70 mins. Gives the title compound (187 mg, 90%) as a tan powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.83 (s, 1H), 8.52 (dd, J = 7.2, 0.8, 1H), 8.50 (d, J = 8.0, 1H), 8.35 (dd, J = 8.5, 0.8, 1H), 7.89–7.86 (m, 2H), 4.01 (app. t, J_{app} = 7.4, 2H), 2.06 (br s, 9H), 1.75 (s, 6H), 1.66 (app. sext, J_{app} = 7.5, 2H), 0.93 (t, J = 7.5, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.3, 164.1, 163.6, 138.6, 132.4, 131.1, 128.9, 126.7, 125.7, 123.9, 123.5, 119.1, 118.6, 42.3, 41.9, 39.4, 36.3, 28.1, 21.4, 11.5.

HRMS (ESI) for $C_{26}H_{28}N_2O_3$ [M + H^+] calcd, 417.2173; found, 417.2163.

tert-Butyl (_R_)-(3-((_tert_-butyldimethylsilyl)oxy)-1-((2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1_H_-benzo[_de_]isoquinolin-6-yl)amino)-1-oxopropan-2-yl)carbamate (22)



Using the general procedure, **3** (84 mg, 0.250 mmol), **S12** (94 mg, 0.296 mmol, 1.2 equiv.), G3-xantphos (2.4 mg, 0.003 mmol, 0.01 equiv.), Cs_2CO_3 (109 mg, 0.335 mmol, 1.3 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 120 mins. The reaction mixture was diluted using H_2O (*ca*. 20 mL) and extracted using CH_2Cl_2 (3 × 20 mL). The combined organic phase was washed using brine (*ca*. 20 mL), dried ($MgSO_4$), filtered and reduced in vacuo. Column chromatography, eluting with 33% EtOAc in petroleum spirits affords the title compound (117 mg, 82%) as a yellow powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.53 (br s, 1H), 8.65 (m, 2H), 8.50 (d, J = 8.2, 1H), 8.26 (d, J = 8.1, 1H), 7.75 (app. t, J_{app} = 7.9, 1H), 5.54 (br s, 1H), 4.44 (t, J = 5.7, 3H), 4.26 (dd, J = 9.9,

3.2, 1H), 3.90 (dd, *J* = 9.9, 6.9, 1H), 3.73 (t, *J* = 5.7, 2H), 3.38 (s, 3H), 1.52 (s, 9H), 0.92 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H).

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.52 (br s, 1H), 8.65 (d, *J* = 8.6, 1H), 8.54 (d, *J* = 7.2, 1H), 8.51 (d, *J* = 8.1, 1H), 8.19 (d, *J* = 8.1, 1H), 7.87 (dd, *J* = 8.6, 7.2, 1H), 7.00 (d, *J* = 7.8, 1H), 4.56 (app. q, J_{app} = 7.0, 1H), 4.25 (t, *J* = 6.3, 2H), 3.90 (d, *J* = 6.0, 1H), 3.59 (t, *J* = 6.3, 1H), 3.26 (s, 3H), 1.42 (s, 9H), 0.82 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

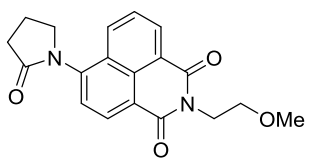
9.53 (br s, 1H), 8.65 (m, 2H), 8.50 (d, *J* = 8.2, 1H), 8.26 (d, *J* = 8.1, 1H), 7.75 (app. t, J_{app} = 7.9, 1H), 5.54 (br s, 1H), 4.44 (t, *J* = 5.7, 3H), 4.26 (dd, *J* = 9.9, 3.2, 1H), 3.90 (dd, *J* = 9.9, 6.9, 1H), 3.73 (t, *J* = 5.7, 2H), 3.38 (s, 3H), 1.52 (s, 9H), 0.92 (s, 9H), 0.18 (s, 3H), 0.17 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.5, 164.3, 163.7, 156.2, 138.6, 132.6, 131.4, 129.9, 126.6, 126.5, 123.6, 123.3, 118.55, 118.50, 81.1, 69.6, 62.8, 58.8, 56.5, 39.2, 28.3, 25.8, 18.4, -5.2, -5.4.

^{13}C NMR (DMSO-d_6, 125 MHz): δ 170.6, 163.5, 163.0, 156.3, 140.0, 131.6, 131.1, 129.6, 128.3, 126.4, 124.6, 122.3, 120.3, 118.1, 78.5, 68.6, 63.3, 58.0, 56.7, 38.5, 28.2, 25.7, 18.0, -5.4, -5.5.

HRMS (ESI) for $C_{29}H_{41}N_3O_7Si$ [M + H^+] calcd, 572.2787; found, 572.2814.

2-(2-Methoxyethyl)-6-(2-oxopyrrolidin-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (23)



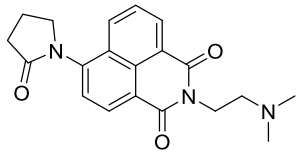
Using the general procedure, **3** (163 mg, 0.488 mmol), 2-pyrrolidinone (50 μL, 0.652 mmol, 1.3 equiv.), G3-xantphos (4.7 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (227 mg, 0.696 mmol, 1.5 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 70 mins. The reaction mixture was diluted using H_2O (*ca.* 25 mL) and extracted using CH_2Cl_2 (*ca*. 25 mL, 2 × 15 mL). The combined organic phase was washed using brine (25 mL), dried ($MgSO_4$), filtered and reduced in vacuo to give the title compound (165 mg, 99%) a light yellow foam.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.63 (dd, *J* = 7.3, 1H), 8.62 (d, *J* = 7.8, 1H), 8.13 (dd, *J* = 8.4, 1.0, 1H), 7.77 (dd, *J* = 8.4, 7.3, 1H), 7.61 (d, *J* = 7.8, 1H), 4.44 (t, *J* = 5.9, 2H), 3.98 (t, *J* = 6.9, 2H), 3.71 (t, *J* = 5.9, 2H), 3.36 (s, 3H), 2.74 (t, *J* = 8.0, 2H), 2.40 (app. quint, J_{app} = 7.1, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.2, 164.1, 163.6, 141.9, 131.8, 131.4, 130.0, 129.3, 127.8, 127.1, 124.1, 123.0, 121.8, 69.5, 58.8, 51.6, 39.3, 31.5, 19.4.

HRMS (ESI) for $C_{19}H_{18}N_2O_4$ [M + H^+] calcd, 339.1339; found, 339.1330.

6-(2-Oxopyrrolidin-1-yl)-2-(2-(dimethylamino)ethyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (24)



Using the general procedure, **S6** (87 mg, 0.249 mmol), pyrrolidinone (23 μL, 0.298 mmol, 1.2 equiv.), G3-xantphos (2.5 mg, 0.0026 mmol, 0.01 equiv.), Cs_2CO_3 (114 mg, 0.351 mmol, 1.4 equiv.) in 1,4-dioxane (2.5 mL) were allowed to react at 100 °C for 2.5 h. The reaction mixture was diluted with H_2O (*ca.* 25 mL) and extracted using CH_2Cl_2 (2 × 15 mL). The combined organic extract was washed using brine (15 mL), dried ($MgSO_4$), filtered and

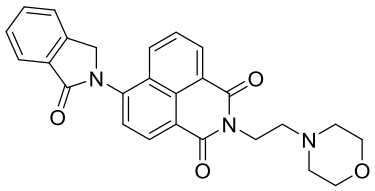
reduced in vacuo to provide the title compound (87 mg, 99%) as a yellow oil that solidified upon standing.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.65–8.60 (m, 2H), 8.14 (dd, *J* = 8.6, 1.0, 1H), 7.77 (dd, *J* = 8.6, 7.3, 1H), 7.61 (d, *J* = 7.9, 1H), 4.32 (t, *J* = 6.9, 2H), 3.98 (t, *J* = 6.9, 2H), 2.75 (t, *J* = 7.6, 2H), 2.64 (t, *J* = 6.9, 2H), 2.46–2.37 (m, 2H), 2.34 (s, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.3, 164.1, 163.7, 142.0, 131.9, 131.4, 130.1, 129.4, 127.9, 127.2, 124.2, 123.3, 122.0, 57.0, 51.8, 45.8, 38.3, 31.7, 19.5.

HRMS (ESI) for $C_{20}H_{21}N_3O_3$ [M + H^+] calcd, 352.1689; found, 352.1659.

2-(2-Morpholinoethyl)-6-(1-oxoisoindolin-2-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (25)



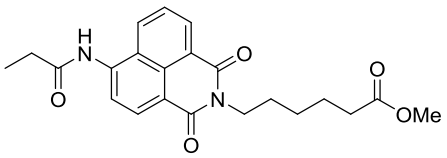
Using the general procedure, **S7** (197 mg, 0.506 mmol), isoindolin-1-one (82 mg, 0.617 mmol, 1.2 equiv.), G3-xantphos (4.2 mg, 0.004 mmol, 0.01 equiv.), Cs_2CO_3 (238 mg, 0.731 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 60 mins. Gives the title compound (208 mg, 93%) a light tan powder.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.69–8.63 (m, 2H), 8.16 (dd, *J* = 8.4, 1.0, 1H), 8.03 (d, *J* = 7.4, 1H), 7.80–7.68 (m, 3H), 7.61 (app. t, J_{app} = 7.2, 2H), 5.02 (s, 2H), 4.37 (t, *J* = 6.9, 2H), 4.46 (t, *J* = 4.6, 4H), 2.72 (t, *J*= 6.9, 2H), 2.60 (t, *J* = 4.6, 4H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.4, 164.0, 163.6, 141.5, 141.4, 132.6, 131.8, 131.5, 131.2, 130.3, 129.4, 128.8, 128.5, 127.4, 125.5, 124.7, 123.2, 123.0, 122.3, 67.1, 56.1, 53.9, 53.8, 37.3.

HRMS (ESI) for $C_{26}H_{23}N_3O_4$ [M + H^+] calcd, 442.1761; found, 442.1775.

Methyl 6-(1,3-dioxo-6-propionamido-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)hexanoate (26)



Using the general procedure, **S9** (610 mg, 1.51 mmol), propionamide (134 mg, 1.83 mmol, 1.21 equiv.), G3-xantphos (14.3 mg, 0.015 mmol, 0.01 equiv.), Cs_2CO_3 (690 mg, 2.11 mmol, 1.40 equiv.) in 1,4-dioxane (15 mL) were allowed to react at 100 °C for 2 h. Gives the title compound (504 mg, 84%) as a yellow solid.

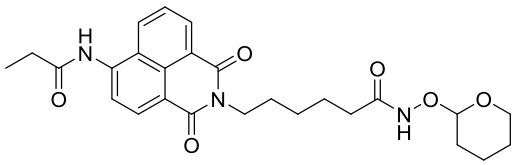
Using the general procedure, **S9** (202 mg, 0.500 mmol), propionamide (44 mg, 0.611 mmol, 1.2 equiv.), G3-xantphos (4.7 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (226 mg, 0.693 mmol, 1.4 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 80 mins. Gives the title compound (175 mg, 88%) as a yellow solid.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.35 (s, 1H), 8.69 (dd, *J* = 8.5, 0.9, 1H), 8.51 (dd, *J* = 7.3, 0.9, 1H), 8.46 (d, *J* = 8.2, 1H), 8.31 (d, *J* = 8.2, 1H), 7.88 (dd, *J* = 8.5, 7.3, 1H), 4.03–4.00 (m, 2H), 3.57 (s, 3H), 2.61 (q, *J* = 7.5, 2H), 2.32 (t, *J* = 7.4, 2H), 1.65–1.54 (m, 4H), 1.37–1.29 (m, 2H), 1.17 (t, *J* = 7.5, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 173.3, 173.2, 163.5, 162.9, 140.4, 131.6, 130.8, 129.3, 128.3, 126.3, 124.0, 122.2, 119.3, 117.3, 51.1, 39.6, 33.0, 29.4, 27.1, 25.9, 24.1, 9.5.

HRMS (ESI) for $C_{22}H_{24}N_2O_5$ [M + H^+] calcd, 397.1758; found, 397.1759.

6-(1,3-Dioxo-6-propionamido-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)-*N*-((tetrahydro-2*H*-pyran-2-yl)oxy)hexanamide (27)



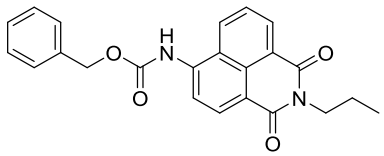
Using the general procedure, **S10** (92 mg, 0.200 mmol), propionamide (29 mg, 0.402 mmol, 2.0 equiv.), G3-xantphos (1.9 mg, 0.002 mmol, 0.01 equiv.), Cs_2CO_3 (93 mg, 0.286 mmol, 1.4 equiv.) in 1,4-dioxane (2.0 mL) were allowed to react at 100 °C for 55 mins. Gives the title compound (65 mg, 67%) as an orange-yellow solid.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 10.88 (s, 1H), 10.39 (s, 1H), 8.70 (dd, *J* = 8.5, 0.9, 1H), 8.52 (dd, *J* = 7.3, 0.9, 1H), 8.47 (d, *J* = 8.2, 1H), 8.31 (d, *J* = 8.2, 1H), 7.88 (dd, *J* = 8.5, 7.3, 1H), 4.74 (t, *J* = 2.8, 1H), 4.02 (t, *J* = 7.2, 2H), 3.89–3.83 (m, 1H). 3.43–3.39 (m, 1H), 2.60 (q, *J* = 7.5, 2H), 1.98 (t, *J* = 7.2, 2H), 1.66–1.44 (m, 10H), 1.34–1.29 (m, 2H), 1.17 (t, *J* = 7.5, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.3, 168.9, 163.5, 162.9, 140.5, 131.6, 130.8, 129.3, 128.3, 126.3, 124.1, 122.3, 119.4, 117.4, 100.8, 61.2, 29.5, 27.7, 27.3, 25.9, 24.7, 24.6, 18.2 (3C), 9.5.

HRMS (ESI) for $C_{26}H_{31}N_3O_6$ [M + Na^+] calcd, 504.2106; found, 504.2109.

Benzyl (1,3-dioxo-2-propyl-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (28)



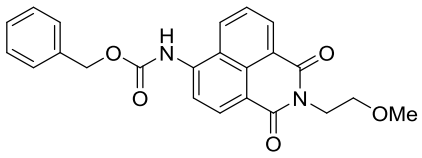
Using the general procedure, **1** (158 mg, 0.495 mmol), benzylcarbamate (91 mg, 0.601 mmol, 1.2 equiv.), G3-xantphos (4.4 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (237 mg, 0.728 mmol, 1.5 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 80 mins. Gives the title compound (167 mg, 87%) as an ochre powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.63 (dd, *J* = 7.3, 0.9, 1H), 8.61 (d, *J* = 8.2, 1H), 8.40 (d, *J* = 8.2, 1H), 8.15 (dd, *J* = 8.5, 0.9, 1H), 7.76 (dd, *J* = 8.5, 7.3, 1H), 7.48–7.39 (m, 6H), 5.31 (s, 2H), 4.15–4.12 (m, 2H), 1.76 (app. sext, J_{app} = 7.5, 2H), 1.01 (t, *J* = 7.5, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.5, 163.0, 154.0, 140.7, 136.2, 131.7, 130.9, 129.3, 128.5, 128.4, 128.3, 128.2, 126.4, 123.9, 122.2, 118.2, 117.1, 66.6, 41.1, 20.9, 11.4.

HRMS (ESI) for $C_{23}H_{20}N_2O_4$ [M + H^+] calcd, 389.1496; found, 389.1476.

Benzyl (2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (29)



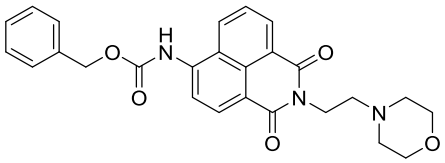
Using the general procedure, **3** (168 mg, 0.504 mmol), benzylcarbamate (92 mg, 0.605 mmol, 1.2 equiv.), G3-xantphos (5.5 mg, 0.006 mmol, 0.01 equiv.), Cs_2CO_3 (231 mg, 0.709 mmol, 1.4 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 105 mins. Gives the title compound (191 mg, 94%) as a burnt yellow powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 10.40 (br s, 1H), 8.72 (d, J = 8.5, 1H), 8.52 (d, J = 7.2, 1H), 8.49 (d, J = 8.3, 1H), 8.22 (d, J = 8.3, 1H), 7.84 (dd, J = 8.5, 7.2, 1H), 7.51–7.36 (m, 5H), 5.28 (s, 2H), 4.24 (t, J = 6.2, 2H), 3.59 (t, J = 6.2, 2H), 3.26 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.6, 163.0, 154.0, 140.8, 136.2, 131.8, 131.1, 129.4, 128.5, 128.4, 128.3, 128.2, 126.4, 123.9, 122.2, 118.2, 117.0, 68.7, 66.6, 58.0, 38.5.

HRMS (ESI) for $C_{23}H_{20}N_2O_5$ [M + H^+] calcd, 405.1445; found, 405.1432.

Benzyl (2-(2-morpholinoethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (30)



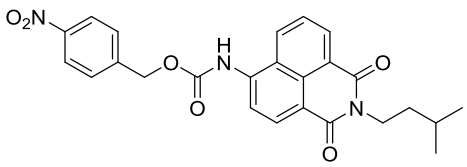
Using the general procedure, **S7** (195 mg, 0.501 mmol), benzylcarbamate (94 mg, 0.620 mmol, 1.2 equiv.), G3-xantphos (4.9 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (244 mg, 0.748 mmol, 1.5 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 110 mins. After this time the reaction mixture was diluted using H_2O (15 mL) but no precipitation occurred. Upon standing the solvent evaporated and the solid residue was reconstituted in H_2O (5 mL) and collected using vacuum filtration. Recrystallisation from EtOH (40 mL) gave the title compound (169 mg, 73%) as a yellow powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.63 (d, J = 7.3, 1H), 8.61 (d, J = 8.2, 1H), 8.41 (d, J = 8.2, 1H), 8.16 (d, J = 8.5, 1H), 7.877 (dd, J = 8.5, 7.3, 1H), 7.48–7.38 (m, 6H), 5.31 (s, 2H), 4.34 (t, J = 7.1, 2H), 3.68 (app. t, J_{app} = 4.5, 4H), 2.70 (t, J = 7.1, 2H), 2.60 (br s, 4H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1, 163.6, 152.9, 138.9, 135.2, 132.6, 131.3, 129.0, 128.80, 128.78, 128.7, 126.7, 125.8, 123.4, 122.8, 117.8, 116.7, 68.0, 67.0, 56.1, 53.8, 37.2.

HRMS (ESI) for $C_{26}H_{25}N_3O_5$ [M + H^+] calcd, 460.1867; found, 460.1857.

4-Nitrobenzyl (2-isopentyl-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (31)



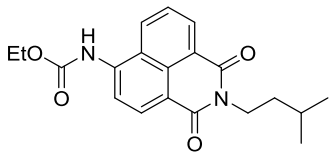
Using the general procedure, **S11** (173 mg, 0.499 mmol), 4-nitrobenzylcarbamate (**S13**) (116 mg, 0.589 mmol, 1.2 equiv.), G3-xantphos (7.4 mg, 0.008 mmol, 0.02 equiv.), Cs_2CO_3 (257 mg, 0.790 mmol, 1.6 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 45 mins. Gives the title compound (209 mg, 91%) as an ochre powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.65 (d, J = 7.3, 1H), 8.61 (d, J = 8.3, 1H), 8.36 (d, J = 8.4, 1H), 8.28 (d, J = 8.6, 2H), 8.18 (dd, J = 8.4, 1H), 7.79 (app. t, J_{app} = 7.9, 1H), 7.62 (d, J = 8.6, 2H), 7.48 (br s, 1H), 5.40 (s, 2H), 4.20–4.17 (m, 2H), 1.72 (app. sept, J_{app} = 6.7, 1H), 1.63–1.58 (m, 2H), 1.01 (d, J = 6.6, 6H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.4, 162.9, 153.8, 147.2, 144.2, 140.5, 131.7, 131.0, 129.3, 128.6, 128.3, 126.5, 124.0, 123.7, 122.3, 118.4, 117.3, 65.3, 38.1, 36.5, 25.9, 22.5.

HRMS (ESI) for $C_{25}H_{23}N_2O_6$ [M + H^+] calcd, 462.1660; found, 462.1681.

Ethyl (2-isopentyl-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (32)



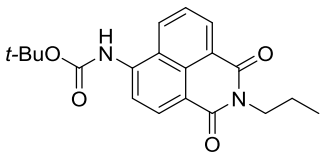
Using the general procedure, **S11** (172 mg, 0.496 mmol), ethylcarbamate (54 mg, 0.605 mmol, 1.2 equiv.), G3-xantphos (4.1 mg, 0.004 mmol, 0.01 equiv.), Cs_2CO_3 (228 mg, 0.701 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 60 mins. Gives the title compound (166 mg, 94%) as an ochre powder.

^{1}H NMR (DMSO-d_6, 270 MHz): δ 10.27 (br s, 1H), 8.72 (d, J = 8.4, 1H), 8.51 (d, J = 7.3, 1H), 8.47 (d, J = 8.3, 1H), 8.19 (d, J = 8.3, 1H), 7.83 (dd, J = 8.4, 7.3, 1H), 4.25 (t, J = 7.1, 2H), 4.05 (app. t, J = 7.4, 2H), 1.68–1.47 (m, 3H), 1.32 (t, J = 7.1, 3H), 0.95 (d, J = 6.4, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.1, 163.6, 153.1, 139.0, 132.5, 131.2, 128.9, 126.6, 125.7, 123.6, 122.8, 117.8, 116.5, 62.2, 39.0, 36.9, 26.5, 22.5, 14.5.

HRMS (ESI) for $C_{20}H_{22}N_2O_4$ [M + H^+] calcd, 355.1652; found, 355.1650.

tert-Butyl (1,3-dioxo-2-propyl-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)carbamate (33)



Using the general procedure, **1** (158 mg, 0.499 mmol), *tert*-butylcarbamate (70 mg, 0.598 mmol, 1.2 equiv.), G3-xantphos (4.7 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (226 mg, 0.695 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 3 h. The reaction mixture was diluted using H_2O (40 mL) and extracted with CH_2Cl_2 (2 × 15 mL). The

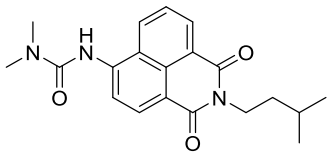
combined organic phase was washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the title compound (95 mg, 55%) as a yellow solid.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.99 (s, 1H), 8.69 (dd, J = 8.5, 0.9, 1H), 8.51 (dd, J = 7.3, 0.9, 1H), 8.46 (d, J = 8.3, 1H), 8.16 (d, J = 8.3, 1H), 7.82 (dd, J = 8.5, 7.3, 1H), 4.01–3.98 (m, 2H), 1.65 (app. sext, J_{app} = 7.5, 2H), 1.54 (s, 9H), 0.92 (t, J = 7.5, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.6, 163.0, 153.1, 141.1, 131.8, 130.9, 129.5, 128.4, 126.2, 123.8, 122.2, 118.1, 116.6, 80.4, 41.1, 28.1, 20.9, 11.4.

HRMS (ESI) for $C_{20}H_{22}N_2O_4$ [M + H^+] calcd, 355.1652; found, 355.1660.

3-(2-Isopentyl-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)-1,1-dimethylurea (34)



Using the general procedure, **S11** (176 mg, 0.509 mmol), 1,1-dimethylurea (54 mg, 0.615 mmol, 1.2 equiv.), G3-xantphos (6.3 mg, 0.007 mmol, 0.015 equiv.), Cs_2CO_3 (230 mg, 0.706 mmol, 1.4 equiv.) in 1,4-dioxane (5.0 mL) were allowed to react at 100 °C for 70 mins. After workup the resultant crude solid was reduced onto Celite and purified using column chromatography, eluting with EtOAc to afford the title compound (128 mg, 71%) as a light yellow powder.

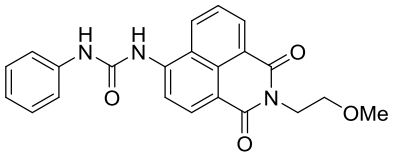
^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.55 (dd, J = 7.3, 1.0, 1H), 8.50 (d, J = 8.2, 1H), 8.18 (d, J = 8.2, 1H), 8.07 (dd, J = 8.5, 1.0, 1H), 7.69 (dd, J = 8.5, 7.3, 1H), 7.13 (br s, 1H), 4.19–4.13 (m, 2H), 3.17 (s, 6H) 1.79–1.56 (m, 3H), 1.00 (d, J = 6.4, 6H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 164.1, 163.6, 154.9, 140.4, 132.4, 130.9, 128.9, 126.3, 126.2, 123.8, 123.4, 118.2, 117.4, 39.0, 36.8, 36.7, 29.7, 26.4, 22.5.

^{13}C NMR ($CDCl_3$, 125 MHz): δ 164.3, 163.8, 155.1, 140.6, 132.5, 131.1, 129.1, 126.4, 126.4, 124.0, 123.5, 118.3, 117.6, 39.1, 37.0, 36.9, 29.8, 26.6, 22.7.

HRMS (ESI) for $C_{20}H_{23}N_3O_3$ [M + H^+] calcd, 354.1812; found 354.1801.

1-(2-(2-Methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)-3-phenylurea (35)



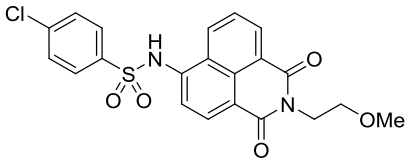
Using the general procedure, **3** (174 mg, 0.521 mmol), *N*-phenylurea (144 mg, 1.058 mmol, 2.0 equiv.), G3-xantphos (4.7 mg, 0.005 mmol, 0.01 equiv.), Cs_2CO_3 (233 mg, 0.715 mmol, 1.4 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 3 h. The reaction mixture was diluted using H_2O (*ca*. 5 mL) and acidified using 2 M HCl to give a precipitate that was collected using vacuum filtration. Trituration using CH_2Cl_2 (*ca*. 2 mL) affords the title compound (87 mg, 43%) as an ochre coloured powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.53 (s, 1H), 9.39 (s, 1H), 8.67 (d, J = 8.5, 1H), 8.57–8.55 (m, 2H), 8.48 (d, J = 8.5, 1H), 7.94 (app. t, J_{app} = 7.9, 1H), 7.55 (d, J = 7.6, 2H), 7.35 (dd, J = 7.6, 7.4, 1H), 7.05 (t, J = 7.4, 1H), 4.25 (t, J = 6.2, 2H), 3.59 (t, J = 6.2, 2H), 3.27 (s, 3H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.5, 162.9, 151.9, 141.7, 139.0, 132.5, 130.9, 129.0, 128.4, 127.7, 126.3, 122.6, 122.3, 122.2, 118.5, 115.0, 114.7, 68.7, 58.0, 38.4.

HRMS (ESI) for $C_{22}H_{19}N_3O_4$ [M + H^+] calcd, 390.1448; found, 390.1447

4-Chloro-*N*-(2-(2-methoxyethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)benzenesulfonamide (36)



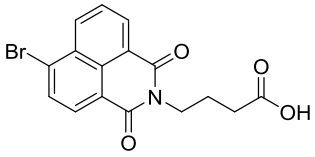
Using the general procedure, **3** (87 mg, 0.251 mmol), 4-chlorobenzene sulfonamide (47 mg, 0.301 mmol, 1.2 equiv.), G3-xantphos (2.4 mg, 0.0025 mmol, 0.01 equiv.), Cs_2CO_3 (116 mg, 0.358 mmol, 1.42 equiv.) in 1,4-dioxane (5 mL) were allowed to react at 100 °C for 2 h. After this time the reaction mixture was diluted using H_2O (*ca.* 15 mL) and acidified to pH 1 using 2M HCl before extracting with CH_2Cl_2 (3 × 10 mL). The combined organic phase was washed with brine (10 mL), dried ($MgSO_4$), filtered and reduced in vacuo to give an orange oil. This oil was taken up in EtOH (*ca.* 5 mL) and H_2O was added to give an opaque mixture which was cooled to 0°C before sonicating at ambient temperature to give a precipitate that was collected using vacuum filtration and washed using H_2O. Gives the title compound (100 mg, 97%) as an off-white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.59 (d, *J* = 7.3, 1H), 8.47 (d, *J* = 8.0, 1H), 8.17 (d, *J* = 8.5, 1H), 7.76–7.72 (m, 3H), 7.61 (d, *J* = 8.0, 1H), 7.42–7.40 (m, 2H), 7.39 (br s, 1H), 4.41 (t, *J* = 5.8, 2H), 3.73 (t, *J* = 5.8, 2H), 3.39 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.9, 163.5, 140.4, 137.4, 137.0, 131.8, 131.6, 129.7, 129.0, 128.7, 127.3, 127.2, 125.5, 123.1, 120.12, 120.09, 69.6, 58.7, 39.2.

HRMS (ESI) for $C_{21}H_{17}{}^{35}ClN_2O_5{}^{32}S$ [M + H^+] calcd, 445.0619; found, 445.0624.

4-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)butanoic acid (S1)

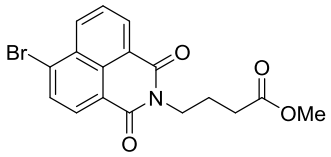


A mixture of 4-bromo-1,8-naphthalic anhydride (277 mg, 1.000 mmol) and 4-aminobutyric acid (123 mg, 1.193 mmol, 1.2 equiv.) was heated in EtOH (3 mL) at 100 °C for 1 h using microwave irradiation. After cooling to ambient temperature the reaction mixture was diluted using H_2O and the solid was collected by vacuum filtration, washing with H_2O to give the title compound (316 mg, 87%) as a tan powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.02 (br s, 1H), 8.53 (d, J = 7.2, 1H), 8.50 (d, J = 8.4, 1H), 8.29 (d, J = 7.8, 1H), 8.19 (d, J = 7.8, 1H), 7.97 (app. t, J_{app} = 7.8, 1H), 4.07 (t, J = 6.7, 2H), 2.31 (br s, 2H), 1.89 (t, J = 6.8, 2H).

Data are in accordance with literature values.[4]

Methyl 4-(6-bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)butanoate (S2)



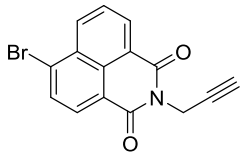
A mixture of **S1** (293 mg, 0.809 mmol) and conc. H_2SO_4 (2 drops) was heated in MeOH (3 mL) at 65 °C for 24 h. After cooling to ambient temperature the reaction mixture was diluted using H_2O and and the solid was collected by vacuum filtration, washing with H_2O to give the title compound (288 mg, 95%) as a beige powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.63 (d, *J* = 7.2, 1H), 8.55 (d, *J* = 8.4, 1H), 8.39 (d, *J* = 7.8, 1H), 8.02 (d, *J* = 7.8, 1H), 7.38 (dd, *J* = 8.4, 7.2, 1H), 4.23 (t, *J* = 6.9, 2H), 3.64 (s, 3H), 2.45 (t, *J* = 7.4, 2H), 2.09 (app. quint, J_{app} = 8.4, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.3, 163.60, 163.57, 133.3, 132.1, 131.2, 131.1, 130.6, 130.3, 128.9, 128.1, 122.9, 122.1, 51.6, 39.6, 31.6, 23.3.

HRMS (ESI) for $C_{17}H_{14}{}^{79}BrNO_4$ [M + H^+] calcd, 376.0179; found, 376.0171.

6-Bromo-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (S3)



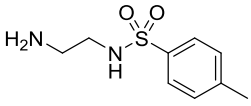
A solution of 4-bromo-1,8-naphthalic anhydride (1.156 g, 4.17 mmol) and propargylamine (325 µL, 5.074 mmol, 1.2 equiv.) in EtOH (10 mL) was heated using microwave irradiation at 100 °C for 1 h. After this time the mixture was diluted using H_2O and cooled to 0 °C, the solid was collected using vacuum filtration and washed using H_2O to give the title compound (1.151 g, 88%) as a brown powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.70 (dd, *J* = 7.3, 1.0, 1H), 8.60 (dd, *J* = 8.5, 1.0, 1H), 8.46 (d, *J* = 7.9, 1H), 8.06 (d, *J* = 7.9, 1H), 7.87 (dd, *J* = 8.5, 7.3, 1H), 4.96 (d, *J* = 2.5, 2H), 2.20 (t, *J* = 2.5, 1H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.0, 162.9, 133.9, 132.6, 131.7, 131.3, 130.9, 130.8, 129.1, 128.3, 122.9, 122.0, 78.4, 70.8, 29.6.

Data are in accordance with literature values.[5]

***N*-(2-Aminoethyl)-4-methylbenzenesulfonamide (S4)**



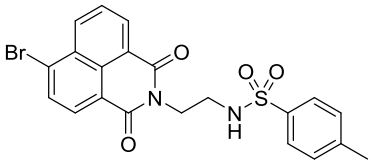
A solution of *p*-toluenesulfonyl chloride (2.04 g, 10.7 mmol) in CH_2Cl_2 (25 mL) was added in a dropwise fashion over 2 h to a stirring solution of ethylenediamine (6.7 mL, 100 mmol, 9.4 equiv.) in CH_2Cl_2 (25 mL). After stirring at ambient temperature for 1 h, the reaction mixture was washed with H_2O (2 × 25 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to provide the title compound (1.71 g, 85%) as a light sienna solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75–7.72 (m, 2H), 7.30–7.28 (m, 2H), 2.95–2.93 (m, 2H), 2.79–2.76 (m, 2H), 2.41 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.4, 136.9, 129.8, 127.1, 45.4, 40.9, 21.6.

Data are in accordance with literature values.[6]

***N*-(2-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)ethyl)-4-methylbenzenesulfonamide (S5)**



A stirring solution of 4-bromo-1,8-naphthalic anhydride (1.050 g, 3.79 mmol) and **S4** (887 mg, 4.13 mmol, 1.09 equiv.) in EtOH was heated at 80 °C for 15 h. After cooling to ambient temperature, the reaction mixture was poured into ice/H_2O (50 mL) and the resultant precipitate

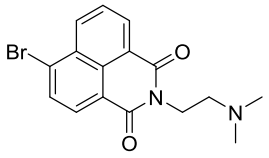
was collected using vacuum filtration, washing H_2O (5 × 5 mL) provides the title compound (1.63 g, 91%) as a tan powder.

^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.57–8.53 (m, 2H), 8.30 (d, *J* = 7.9, 1H), 8.23 (d, *J* = 7.9, 1H), 8.02–7.98 (m, 1H), 7.76 (t, *J* = 6.3, 1H), 7.56 (d, *J* = 8.1, 2H), 7.19 (d, *J* = 8.1, 2H), 4.10 (t, *J* = 6.4, 2H), 3.10 (q, *J* = 6.4, 2H), 2.23 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.2, 164.1, 142.8, 137.2, 133.6, 132.3, 131.4, 131.2, 130.8, 130.6, 129.3, 128.9, 128.2, 126.7, 122.6, 121.7, 42.4, 39.3, 21.2.

Data are in accordance with literature values.[7]

6-Bromo-2-(2-(dimethylamino)ethyl)-1*H*-benzo[*de*]isoquinoline-1,3(*2H*)-dione (S6)



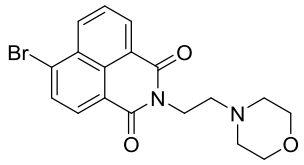
A solution of 4-bromo-1,8-naphthalic anhydride (1.193 g, 4.307 mmol), *N*,*N*-dimethylethylenediamine (515 μL, 4.715 mmol, 1.1 equiv.) in EtOH (45 mL) was heated for 4 h at 80 °C. After cooling to ambient temperature, the reaction mixture was diluted with H_2O and the precipitate was collected using vacuum filtration and washed with H_2O to give the title compound (1.302 g, 87%) as a beige powder.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.66 (dd, *J* = 7.3, 1.0 Hz, 1H), 8.56 (dd, *J* = 8.6, 1.0 Hz, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.84 (dd, *J* = 8.6 Hz, 7.3 Hz, 1H), 4.31 (t, *J* = 6.9 Hz, 2H), 2.67 (t, *J* = 6.9 Hz, 1H), 2.34 (s, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.81, 163.79, 133.4, 132.2, 131.4, 131.2, 130.7, 130.4, 129.1, 128.2, 123.2, 122.3, 57.0, 45.9, 38.4.

Data are in accordance with literature values.[8]

6-Bromo-2-(2-morpholinoethyl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (S7)



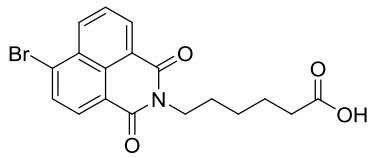
A mixture of 4-bromo-1,8-naphthalic anhydride (1.387 g, 5.006 mmol) and 4-(2-aminoethyl)morpholine (670 μL, 5.105 mmol, 1.02 equiv.) in EtOH (25 mL) was heated at 70 °C for 3.25 h. After cooling to ambient temperature a precipitate formed, the mixture was diluted using H_2O and the solid was collected using vacuum filtration. Washing with H_2O affords the title compound (1.736 g, 89%) as a biege powder.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 8.63 (dd, *J* = 7.3, 1.1, 1H), 8.58 (dd, *J* = 8.5, 1.1, 1H), 8.41 (d, *J* = 7.9, 1H), 8.05 (d, *J* = 7.9, 1H), 7.86 (dd, *J* = 8.5, 7.3, 1H), 4.37 (t, *J* = 6.7, 2H), 3.73 (br s, 4H), 2.78 (br s, 2H), 2.68 (br s, 4H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.62, 163.59, 133.3, 132.0, 131.2, 131.1, 130.6, 130.3, 129.0, 128.1, 123.0, 122.2, 67.0, 56.1, 53.8, 37.3.

Data are in accordance with literature values.[9]

6-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)hexanoic acid (S8)



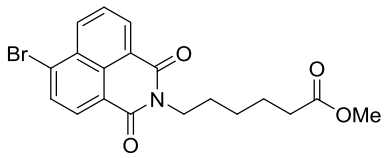
A mixture of 4-bromo-1,8-naphthalic anhydride (1.470 g, 5.30 mmol) and 6-aminohexanoic acid (769 mg, 5.86 mmol, 1.10 equiv.) was heated in EtOH (15 mL) at 100 °C for 1 h using microwave irradiation. After cooling to ambient temperature the reaction mixture was diluted using H_2O to give a precipitate which was collected by vacuum filtration, washing with H_2O gives the title compound (1.96 g, 92%) as a yellow solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.64 (dd, *J* = 7.3, 1.0, 1H), 8.55 (dd, *J* = 8.5, 1.0, 1H), 8.40 (d, *J* = 7.8, 1H), 8.03 (d, *J* = 7.8, 1H), 7.84 (dd, *J* = 8.5, 7.3, 1H), 4.17 (t, *J* = 7.5, 2H), 2.37 (t, *J* = 7.5, 2H), 1.78–1.68 (m, 4H), 1.51–1.44 (m, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 179.5, 163.73, 163.70, 133.3, 132.1, 131.3, 131.2, 130.7, 130.3, 129.0, 128.2, 123.1, 122.3, 40.3, 33.9, 27.7, 26.6, 24.4.

Data are in accordance with literature values.[10]

Methyl 6-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)hexanoate (S9)



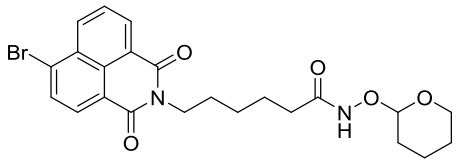
A mixture of **S8** (1.152 g, 2.95 mmol) and conc. H_2SO_4 (14 drops) was heated in MeOH (13 mL) at 65 °C for 48 h. After cooling to ambient temperature the reaction mixture was diluted using H_2O and the solid was collected by vacuum filtration, washing with H_2O to give the title compound (1.127 g, 94%) as a yellow powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.65 (dd, *J* = 7.3, 1.1, 1H), 8.56 (dd, *J* = 8.5, 1.1, 1H), 8.40 (d, *J* = 7.8, 1H), 8.04 (d, *J* = 7.8, 1H), 7.84 (dd, *J* = 8.5, 7.3, 1H), 4.16 (t, *J* = 7.5, 2H), 3.65 (s, 3H), 2.33 (t, *J* = 7.5, 2H), 1.77–1.67 (m, 4H), 1.48–1.42 (m, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.2, 163.7, 163.7, 133.4, 132.2, 131.3, 131.2, 130.7, 130.4, 129.1, 128.3, 123.2, 122.3, 51.6, 40.4, 34.0, 27.8, 26.7, 24.7.

Data are in accordance with literature values.[11]

6-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)-*N*-((tetrahydro-2*H*-pyran-2-yl)oxy)hexanamide (S10)



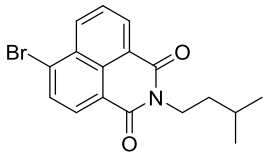
A mixture containing **S8** (472 mg, 1.21 mmol), NH_2OTHP (272 mg, 2.40 mmol, 2.0 equiv.), EDCI·HCl (372 mg, 1.94 mmol, 1.6 equiv.) and HOBt (82 mg, 0.607 mmol, 0.5 equiv.) in MeCN (12 mL) was stirred at ambient temperature for 16 h. After this time, the solvent volume was reduced to one-third and the precipitate was collected using vacuum filtration to provide the title compound (488 mg, 87%) as a pale yellow solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.65 (dd, *J* = 7.3, 0.8, 1H), 8.57 (dd, *J* = 8.4, 0.8, 1H), 8.40 (d, *J* = 7.9, 1H), 8.37 (s, 1H), 8.04 (d, *J* = 7.9, 1H), 7.84 (dd, *J* = 8.4, 7.3, 1H), 4.93 (s, 1H), 4.17–4.14 (m, 2H), 3.96–3.92 (m, 1H), 3.62–3.60 (m, 1H), 2.15 (s, 2H), 1.81–1.72 (m, 8H), 1.63–1.60 (m, 2H), 1.50–1.45 (m, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.4, 163.65, 163.63, 130.3, 132.0, 131.3, 131.1, 130.6, 130.3, 129.0, 128.1, 122.1, 122.2, 102.4, 62.5, 40.2, 33.1, 28.0, 27.4, 26.3, 25.0, 24.9, 18.6.

HRMS (ESI) for $C_{23}H_{25}BrN_2O_5$ [M + H^+] calcd, 489.1025; found, 489.1031.

6-Bromo-2-isopentyl-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (S11)



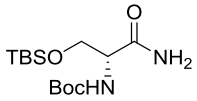
A mixture of 4-bromo-1,8-naphthalic anhydride (1.106 g, 3.992 mmol) and isopentylamine (500 μL, 4.308 mmol, 1.1 equiv.) in EtOH (20 mL) was heated at 70 °C for 19.5 h. After this time the mixture was diluted using H_2O and cooled to 0 °C, the resultant solid was collected using vacuum filtration and washed using H_2O to give the title compound (1.227 g, 89%) as an biege powder.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.66 (d, J = 7.3, 1H), 8.57 (d, J = 8.5, 1H), 8.42 (d, J = 7.9, 1H), 8.04 (d, J = 7.9, 1H), 7.85 (app. t, J_{app} = 7.9, 1H), 4.18 (app. t, J_{app} = 7.8, 2H), 1.72 (sept, J = 6.7, 2H), ~1.61 (m, 2H), 1.01 (d, J = 6.6, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 163.60, 163.58, 133.2, 132.0, 131.2, 131.1, 130.6, 130.2, 129.0, 128.1, 123.2, 122.3, 39.2, 36.8, 26.4, 22.5.

HRMS (ESI) for $C_{17}H_{16}{}^{79}BrNO_2$ [M + H^+] calcd, 346.0437; found, 346.0427.

***tert*-Butyl (*R*)-(1-amino-3-((*tert*-butyldimethylsilyl)oxy)-1-oxopropan-2-yl)carbamate (S12)**



To a stirring solution containing *tert*-butyl (*R*)-(1-amino-3-hydroxy-1-oxopropan-2-yl)carbamate[12] (546 mg, 2.674 mmol), imidazole (364 mg, 5.347 mmol, 2.0 equiv.) and DMAP (4 mg, 0.033 mmol, 0.01 equiv.) in CH_2Cl_2 (25 mL) was added TBSCl (454 mg, 3.012 mmol, 1.1 equiv.) with the aid of CH_2Cl_2 (5 mL). After 21 h the reaction mixture was diluted using CH_2Cl_2 (10 mL), was washed using sat. KH_2PO_4 (25 mL), brine (25 mL), dried ($MgSO_4$), filtered and reduced in vacuo to give a clear oil which solidified on standing. Purification by column chromatography, eluting with EtOAc/petroleum spirits (1:1) afforded the title compound (706 mg, 83%) as a white solid.

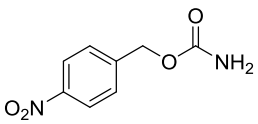
^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.31 (s, 1H), 7.12 (s, 1H), 6.43 (d, J = 8.4, 1H), 4.00–3.96 (m, 1H), 3.74 (dd, J = 10.0, 5.2, 1H), 3.67 (dd, J = 10.0, 5.6, 1H), 1.38 (s, 9H), 0.84 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ 171.7, 155.0, 78.1, 63.5, 56.1, 28.2, 25.8, 18.0, -5.4.

HRMS (ESI) for $C_{14}H_{30}N_2O_4Si$ [M + H^+] calcd, 319.2048; found, 319.2039.

Data are in accordance with literature values.[12]

4-Nitrobenzyl carbamate (S13)



A mixture containing 4-nitrobenzyl alcohol (500 mg, 3.27 mmol) and CDI (577 mg, 3.56 mmol, 1.1 equiv.) in THF (10 mL) under an N_2 atmosphere was stirred at ambient

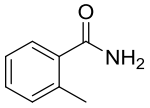
temperature to give an orange mixture. After 4.5 h a further portion of CDI (104 mg, 0.64 mmol, 0.2 equiv.) was added and stirring was continued for a further 25 h. The reaction mixture was reduced in vacuo and ^{1}H NMR analysis of the crude showed no evidence of the benzyl alcohol. The residue was reconstituted in THF (25 mL) before the addition of NH_4OH (28–30%, 5 mL, 38.52 mmol, 11.8 equiv.) to give a red solution which was stirred for 19.5 h. The mixture was concentrated under reduced pressure, taken up in EtOAc (50 mL), washed using 2 M HCl (50 mL), H_2O (50 mL), brine (50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to give a fluffy yellow powder. The solid was triturated in a minimum amount of CH_2Cl_2/MeOH/NH_4OH (90:10:1%) and collected by vacuum filtration, washing with EtOH gives the title compound (453 mg, 71%) as a fluffy pale yellow solid.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.26–8.22 (m, 2H), 7.61–7.58 (m, 2H), 6.85 (br s, 1H), 6.65 (br s, 1H), 5.12 (s, 2H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ 156.3, 146.9, 145.5, 128.1, 123.6, 63.7.

Data are in accordance with literature values.[13]

_o_-Toluamide (S14)



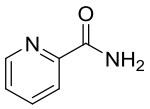
To a stirring solution of *o*-toluic acid (807 mg, 5.90 mmol) in CH_2Cl_2 (55 mL) at ambient temperature, DMF (10 drops) and $SOCl_2$ (1.30 mL, 17.9 mmol, 3.0 equiv.) were sequentially added. After stirring for 1 h, excess solvent was removed *in vacuo* and the residue was suspended in MeCN (55 mL) and cooled to 0 °C before the addition of 28% NH_3 (2.5 mL, 17.97 mmol, 3.0 equiv.). The resultant white slurry was allowed to warm to ambient

temperature and stirred for 2 h, before being diluted with H_2O (15 mL) and extracted into EtOAc (2 × 20 mL). The combined organic phase was washed with sat. $NaHCO_3$ (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed to provide the title compound (533 mg, 67%) as a white solid.

^{1}H NMR ($CDCl_3$, 270 MHz): δ 7.46–7.43 (m, 1H), 7.36–7.30 (m, 1H), 7.25–7.21 (m, 2H), 5.86 (br s, 2H), 2.50 (s, 3H).

^{13}C NMR ($CDCl_3$, 67.5 MHz): δ 172.2, 136.4, 135.2, 131.3, 130.4, 127.0, 125.8, 20.1.

2-Picolinamide (S15)

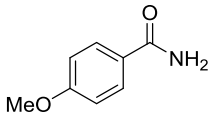


To a stirring solution of 2-picolinic acid (515.6 mg, 4.19 mmol) in CH_2Cl_2 (42 mL) at ambient temperature, DMF (10 drops) and $SOCl_2$ (920 μL, 12.7 mmol, 3.0 equiv.) were sequentially added. After stirring for another 2 h, excess solvent was removed *in vacuo* and the residue was suspended in MeCN (42 mL) and cooled to 0 °C before the addition of NH_4OH (28–30%, 1.75 mL, 12.6 mmol, 3.0 equiv.). The resultant white slurry was allowed to warm to ambient temperature and stirred for 2 h, before being diluted with H_2O (25 mL) and extracted into EtOAc (2 × 25 mL). The combined organic phase was washed with sat. $NaHCO_3$ (30 mL) brine (30 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo* to provide the title compound (286 mg, 56%) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.46–7.43 (m, 1H), 7.36–7.30 (m, 1H), 7.25–7.21 (m, 2H), 5.86 (br s, 2H), 2.50 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.9, 149.6, 148.4, 137.4, 126.6, 122.5.

4-Methoxybenzamide (S16)

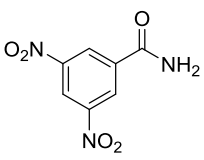


To a stirring solution of *p*-methoxybenzoic acid (210 mg, 1.37 mmol) and CH_2Cl_2 (13 mL) at ambient temperature was added DMF (3 drops) followed by $SOCl_2$ (300 μL, 4.13 mmol, 3.0 equiv.). After stirring for 2 h, excess solvent was removed *in vacuo* and the residue was suspended in MeCN (13 mL) and cooled to 0 °C before the dropwise addition of NH_4OH (28–30%, 580 μL, 4.17 mmol, 3.0 equiv.). The resultant slurry was allowed to warm slowly to ambient temperature and stirred for 1 h before diluting with H_2O (10 mL) and extracted using EtOAc (2 × 15 mL). The combined organic phase was washed using sat. $NaHCO_3$ (15 mL), brine (20 mL), dried ($MgSO_4$), filtered and reduced in vacuo to afford the title compound (126 mg, 61%) as an off white solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79–7.76 (m, 2H), 6.95–6.91 (m, 2H), 5.88 (br s, 2H), 3.85 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.0, 162.7, 129.4, 125.6, 113.9, 55.5.

3,5-Dinitrobenzamide (S17)

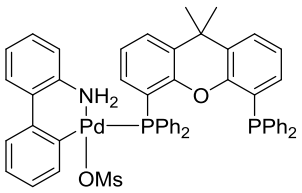


To a stirring solution of 3,5-dinitrobenzoyl chloride (1.06 g, 4.59 mmol) and CH_2Cl_2 (46 mL) at ambient temperature, DMF (12 drops) and $SOCl_2$ (1.00 mL, 13.7 mmol, 3.0 equiv.) were sequentially added. After stirring for 1 h, excess solvent was removed and the residue was taken up in MeCN (46 mL) at 0 °C before the dropwise addition of NH_4OH (28–30%, 1.92 mL, 13.8 mmol, 3.0 equiv.). The resultant slurry was allowed to warm slowly to ambient temperature and stirred for 15 h before the reaction mixture was diluted with 40 mL water and extracted using EtOAc (2 × 30 mL). The combined organic phase was washed sat. $NaHCO_3$ (30 mL), brine (30 mL), dried, filtered and the solvent removed under reduced pressure to afford the title compound (641 mg, 52%) as a yellow powder.

^{1}H NMR (DMSO-*d*6, 500 MHz): δ 9.06 (d, *J* = 2.1, 2H), 8.95 (t, *J* = 2.1, 1H), 8.68 (s, 1H), 8.01 (s, 1H).

^{13}C NMR (DMSO-d_6, 125 MHz): δ 163.8, 148.2, 137.1, 127.8, 120.9.

G3-Xantphos (S18)

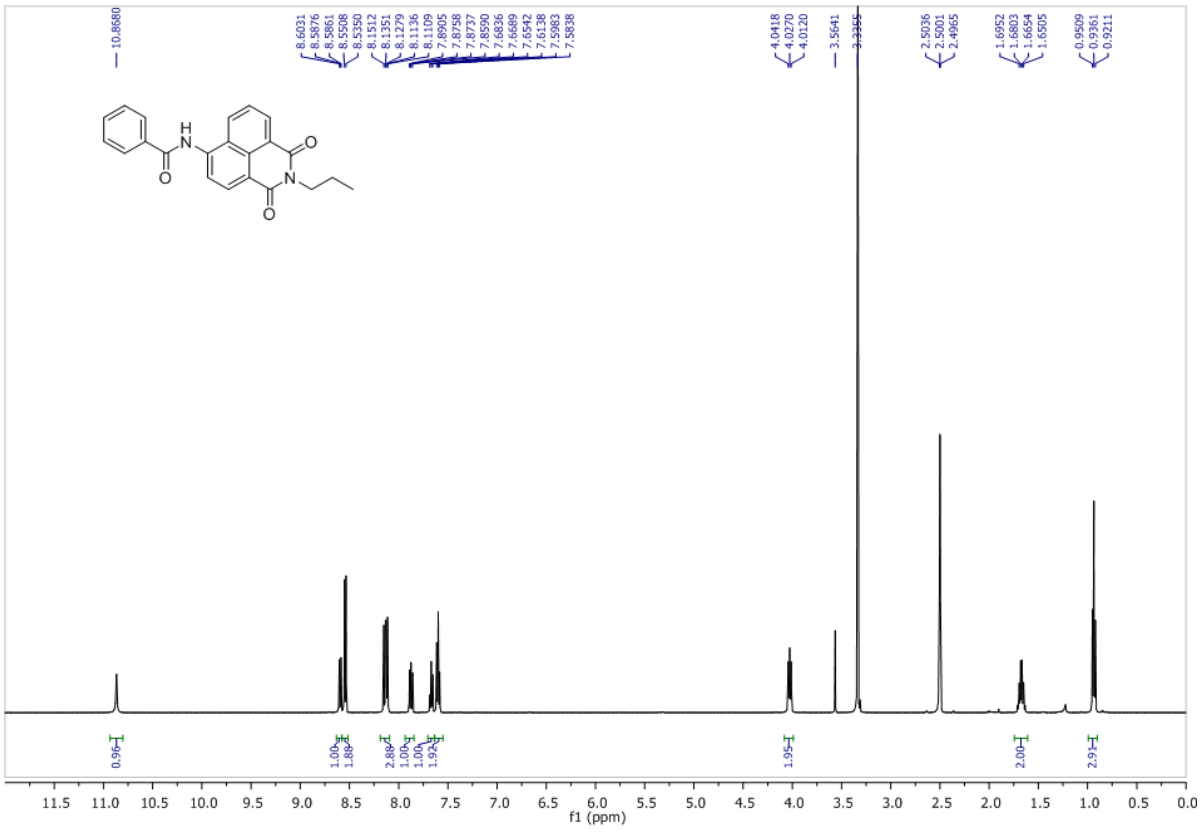


To a stirring solution of μ-OMs dimer[14] (112 mg, 0.151 mmol) in CH_2Cl_2 (1.5 mL) at ambient temperature was added Xantphos (175 mg, 0.302 mmol, 2 equiv.). After 2 h the solvent was removed in vacuo and the solid was triturated with Et_2O to provide the title compound (207 mg, 72%) as an off white solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, *J* = 7.1, 2H), 7.54–7.49 (m, 3H), 7.47–7.39 (m, 4H), 7.37–7.12 (m, 13H), 7.09–6.93 (m, 7H), 6.82 (td. *J* = 7.9, 2.5, 2H), 6.72–6.60 (m, 4H), 6.15 (dd, *J* = 7.7, 1.0, 1H), 2.69 (s, 3H), 1.75 (d, *J* = 5.4, 6H).

Data are in accordance with literature values.[14]

Figure S1 – ^{1}H and ^{13}C NMR of **2**



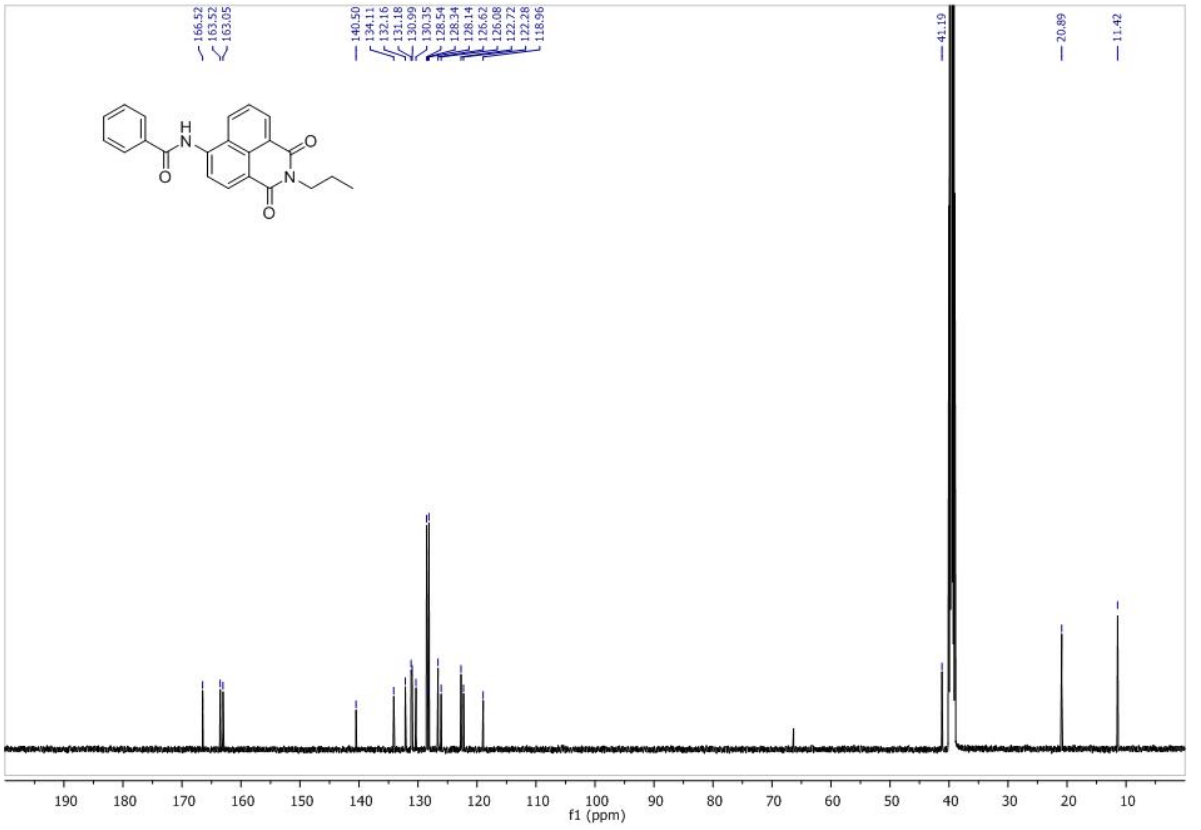
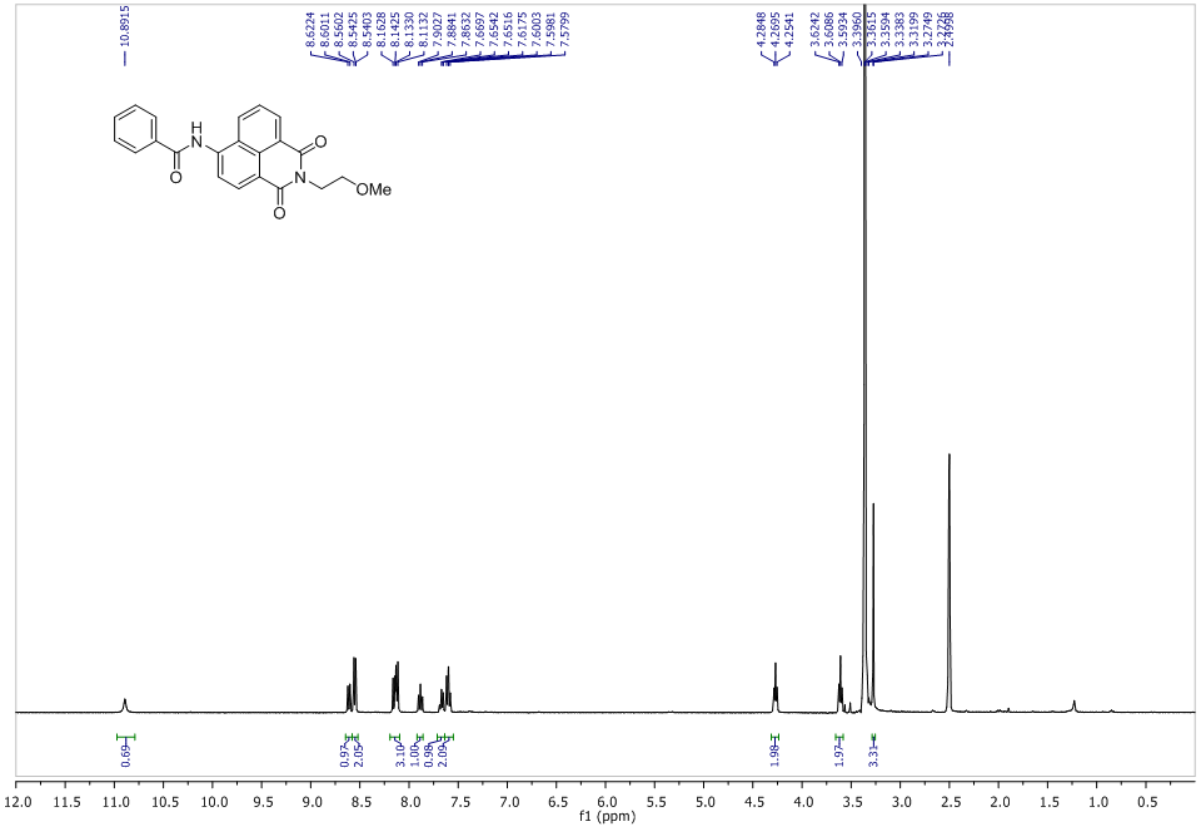


Figure S2 – ^{1}H and ^{13}C NMR of **4**



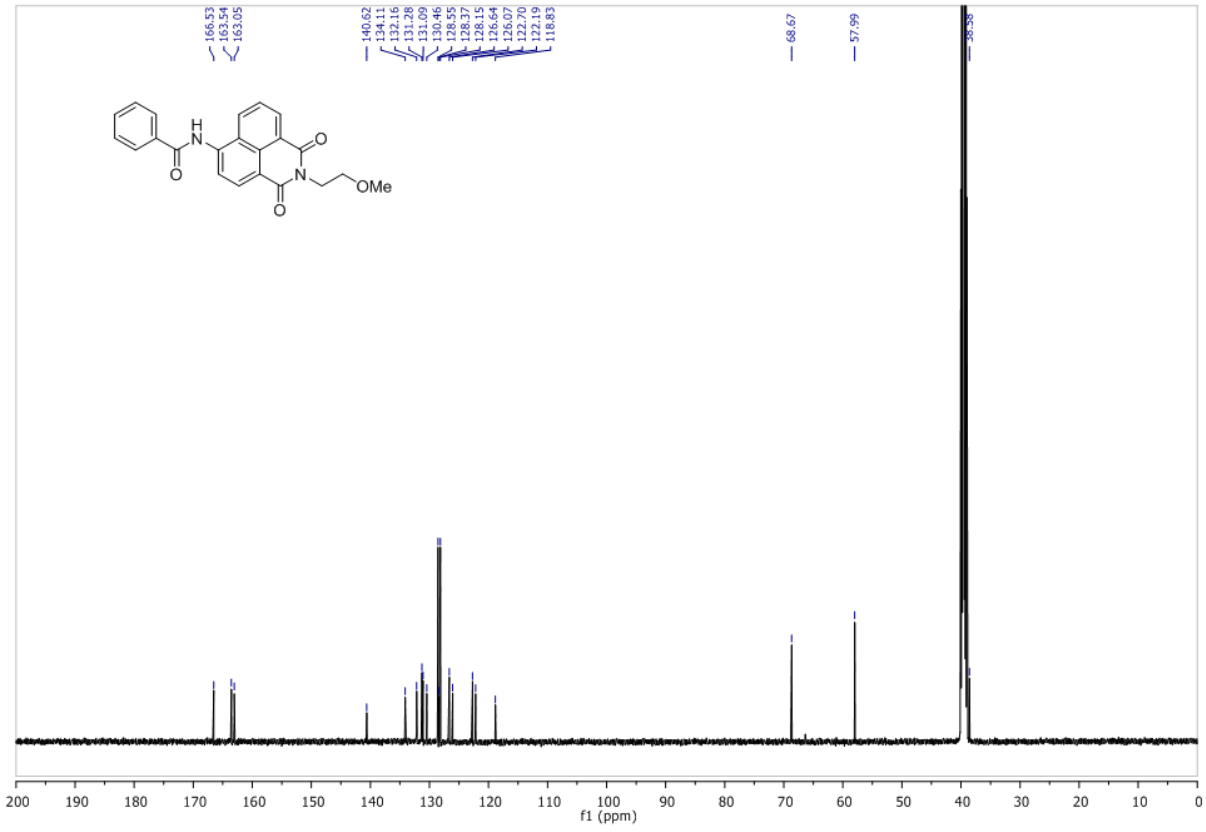
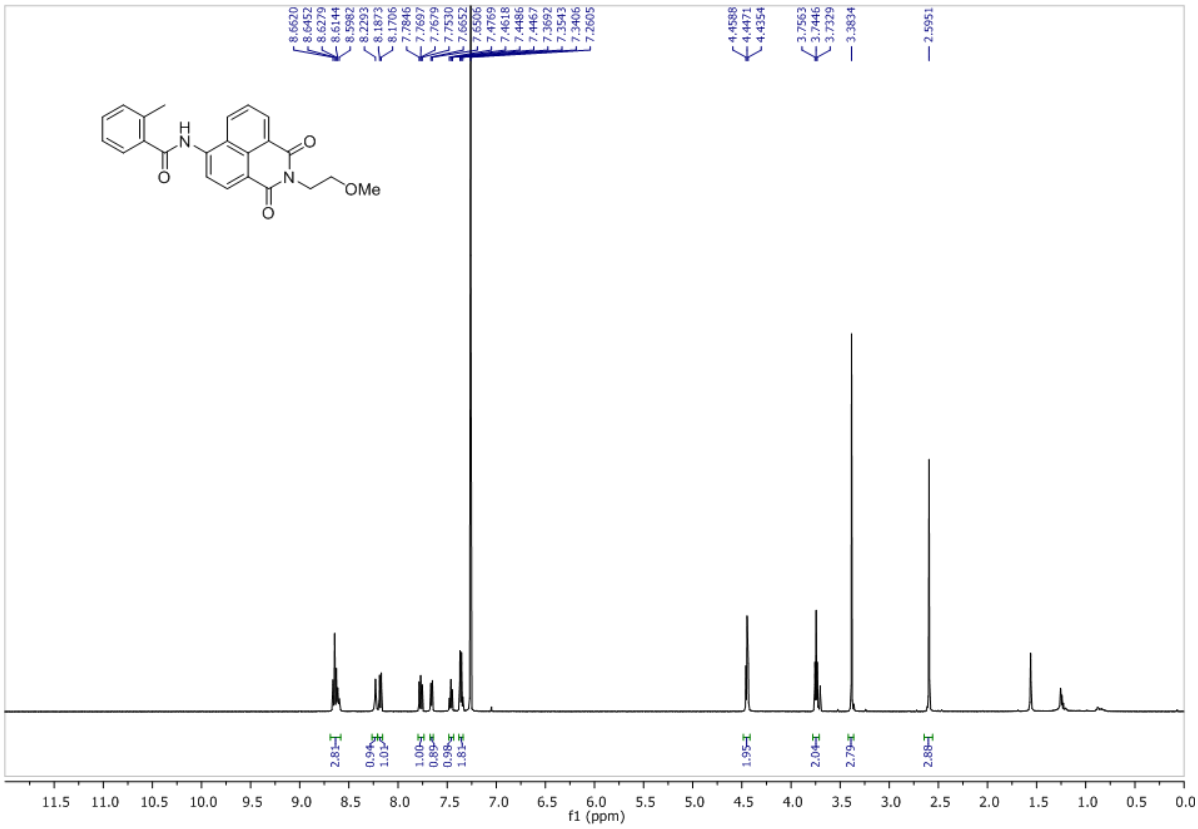


Figure S3 – ^{1}H and ^{13}C NMR of **5**



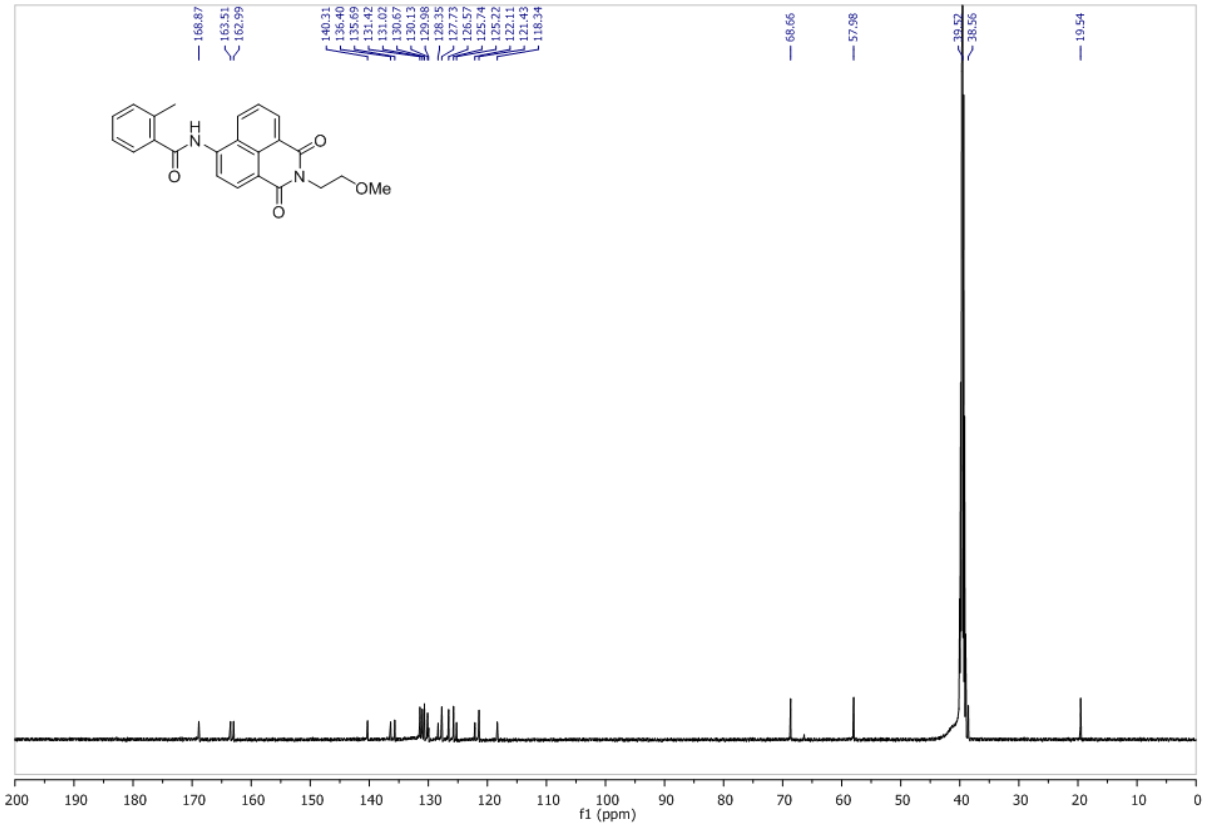


Figure S4 – ^{1}H and ^{13}C NMR of **6**

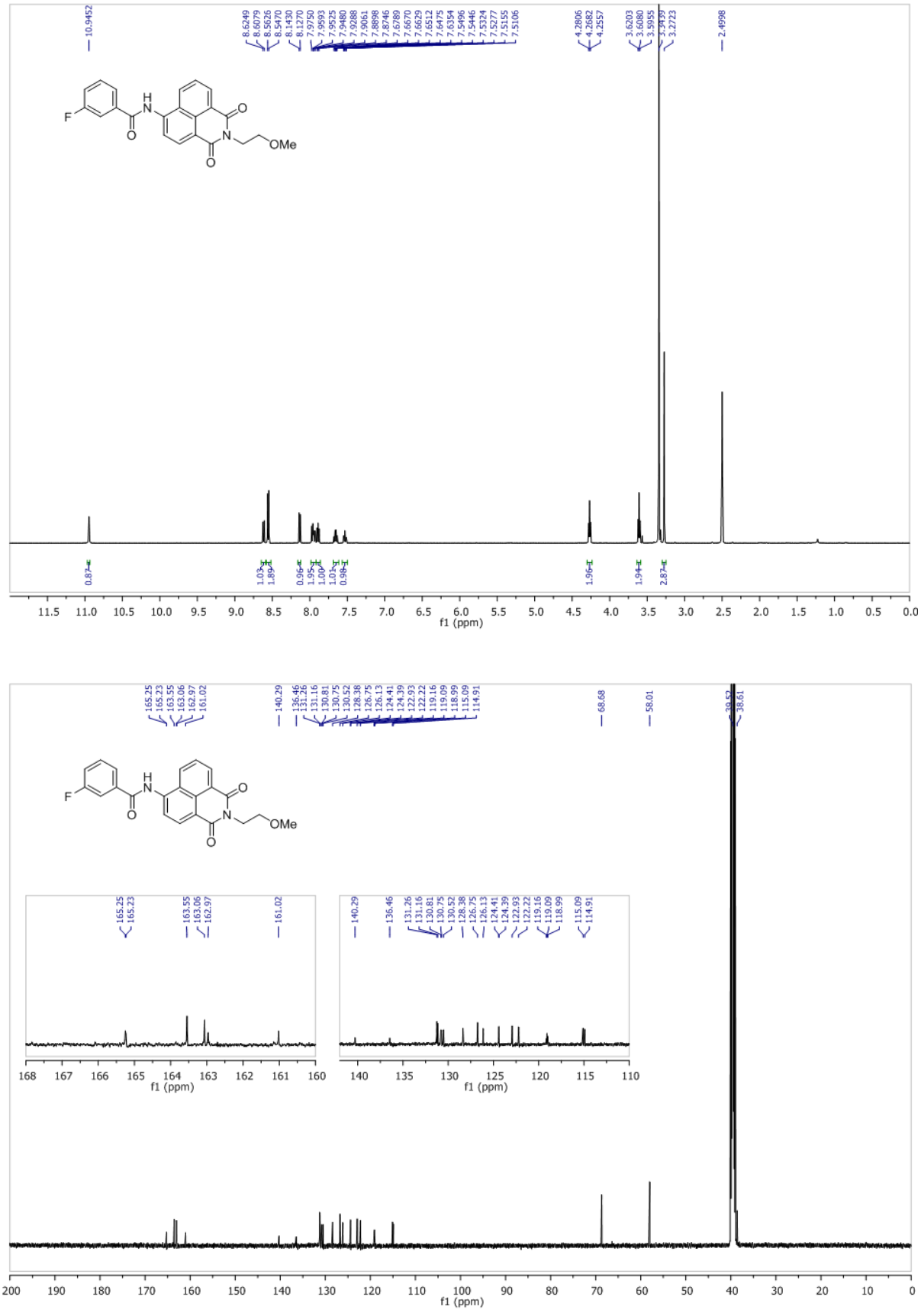
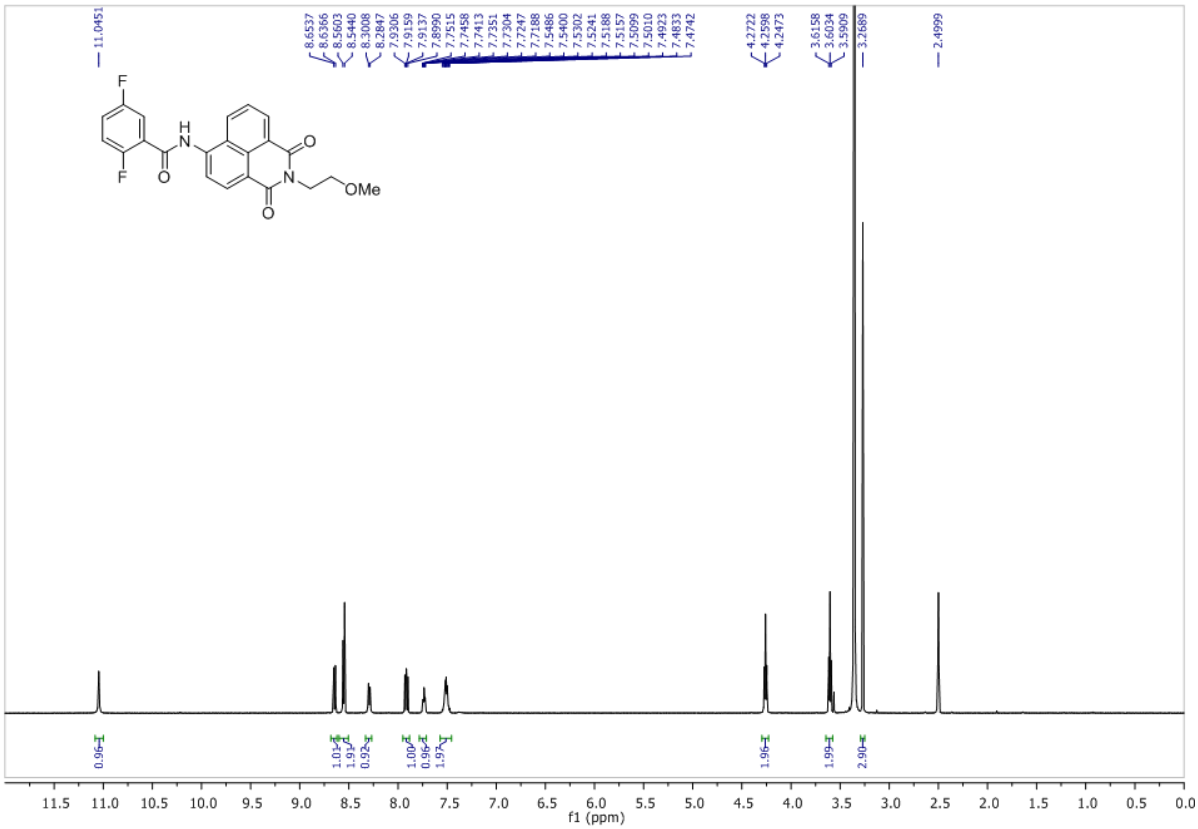


Figure S5 – ^{1}H and ^{13}C NMR of **7**



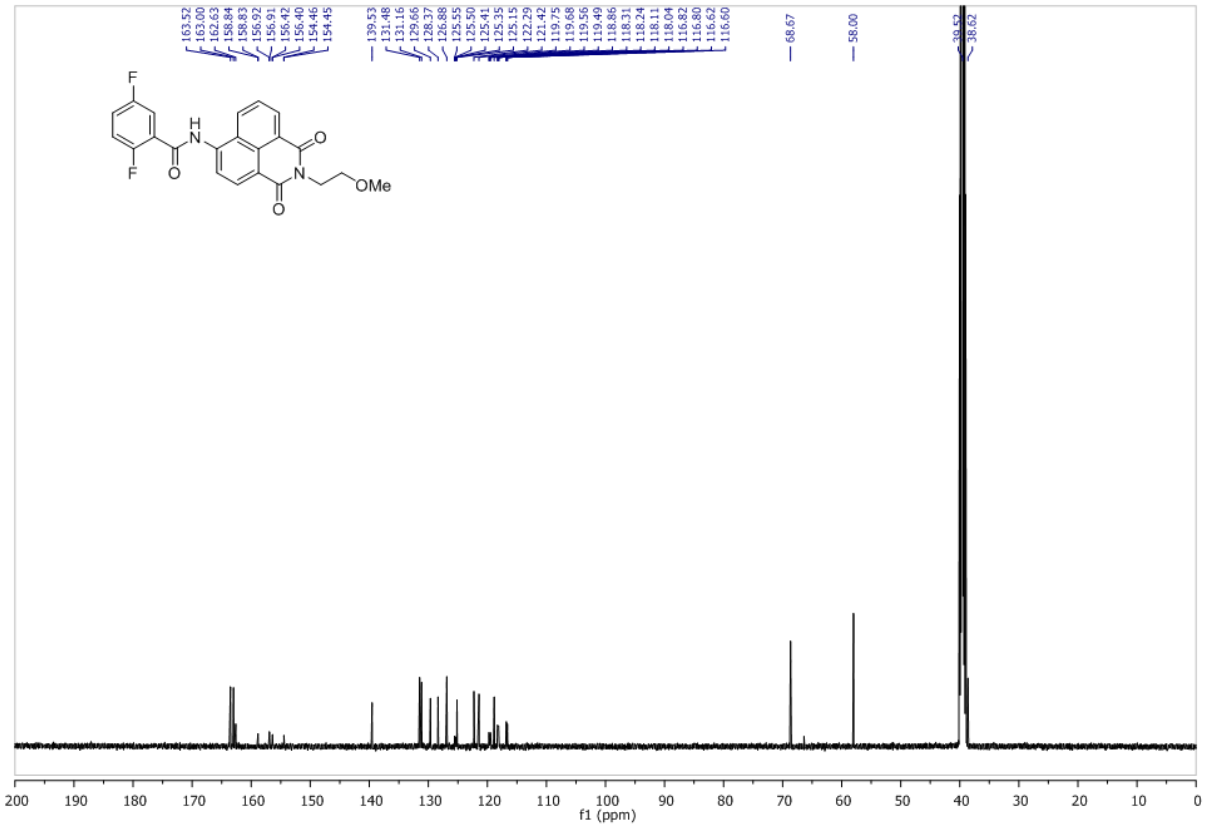
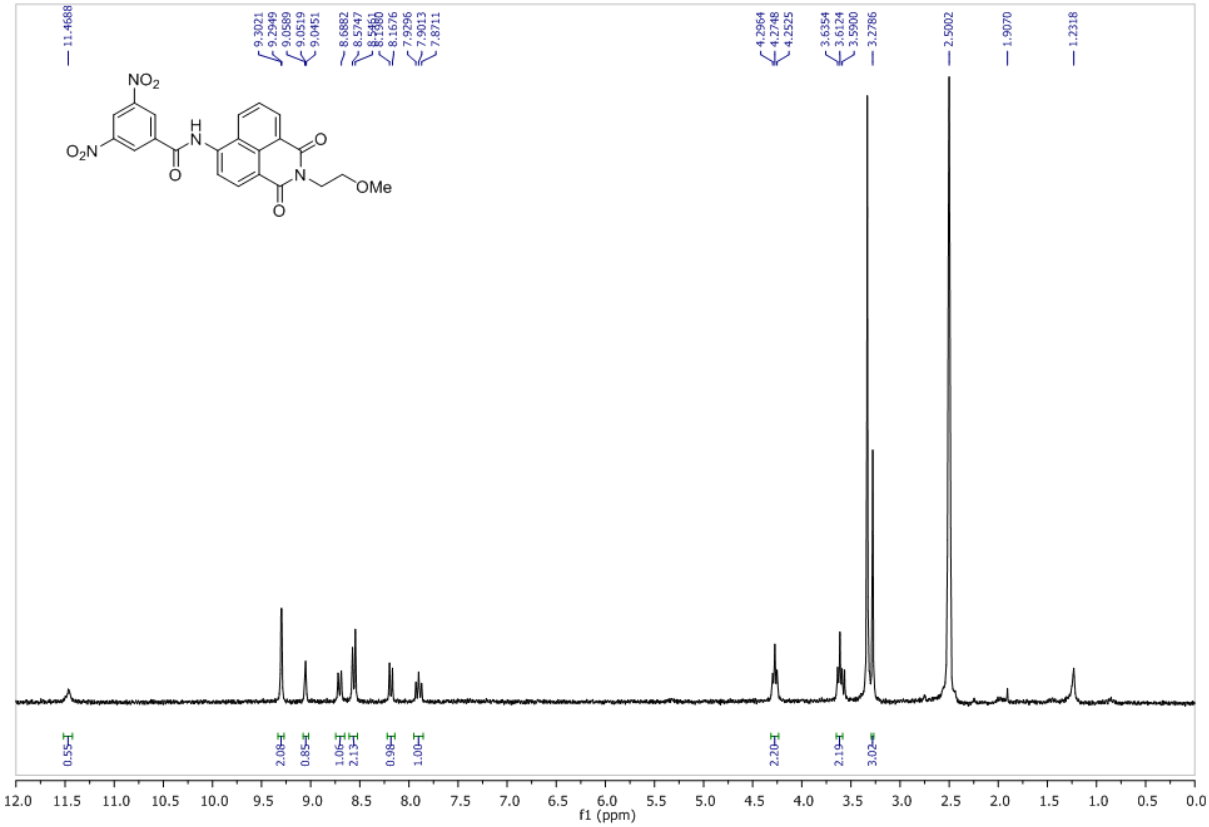


Figure S6 – ^{1}H and ^{13}C NMR of **8**



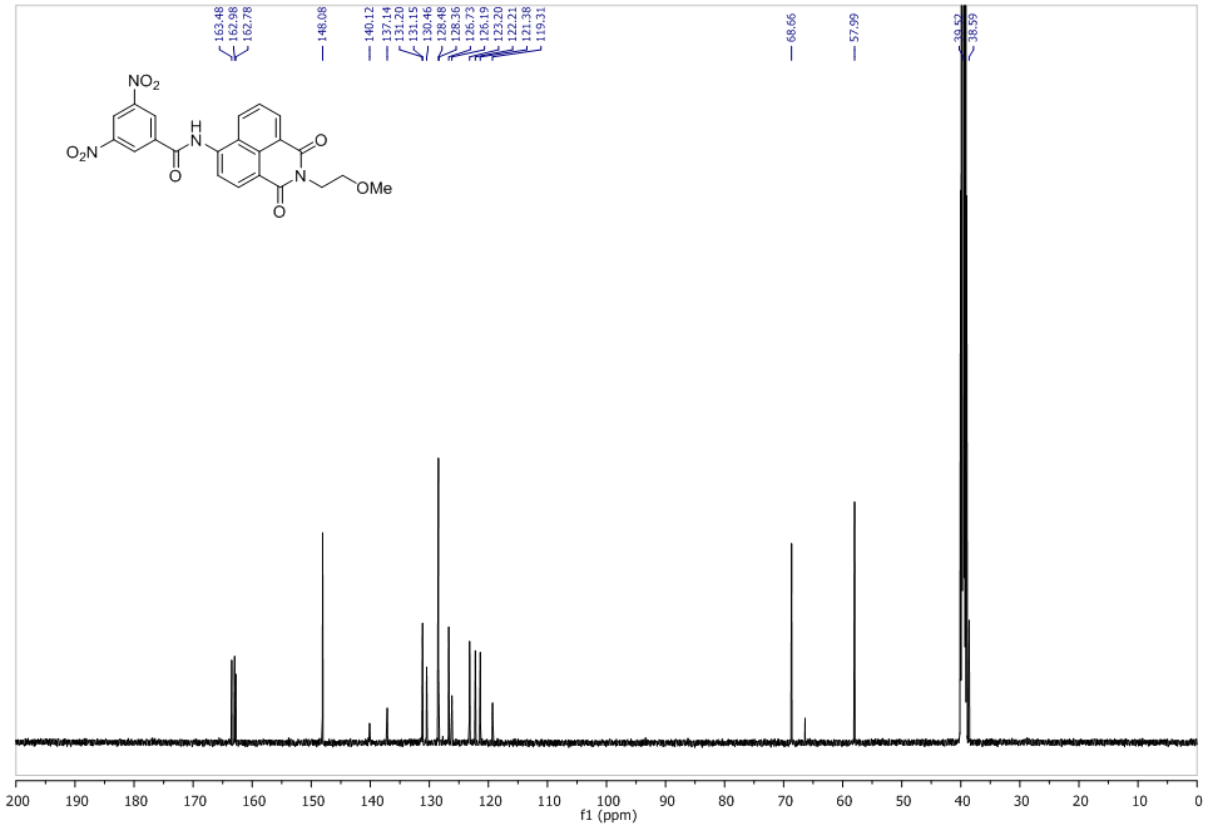
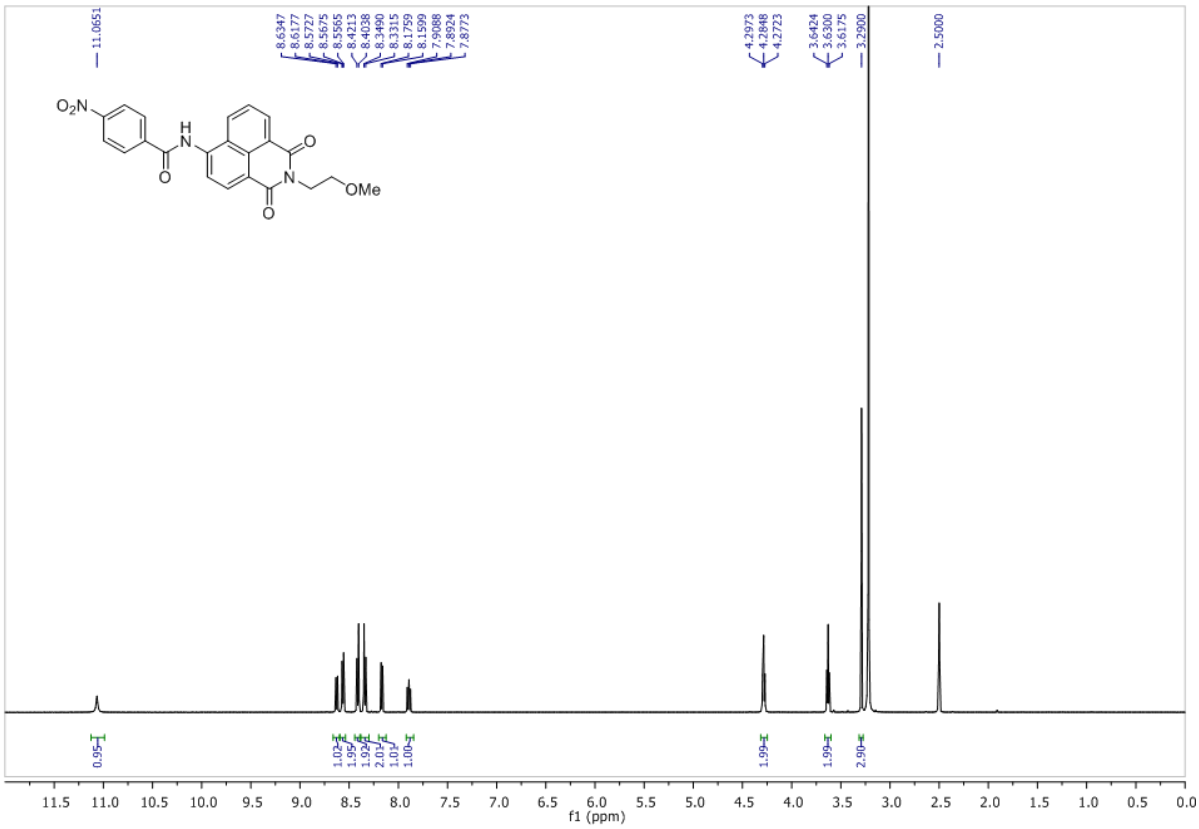


Figure S7 – ^{1}H and ^{13}C NMR of **9**



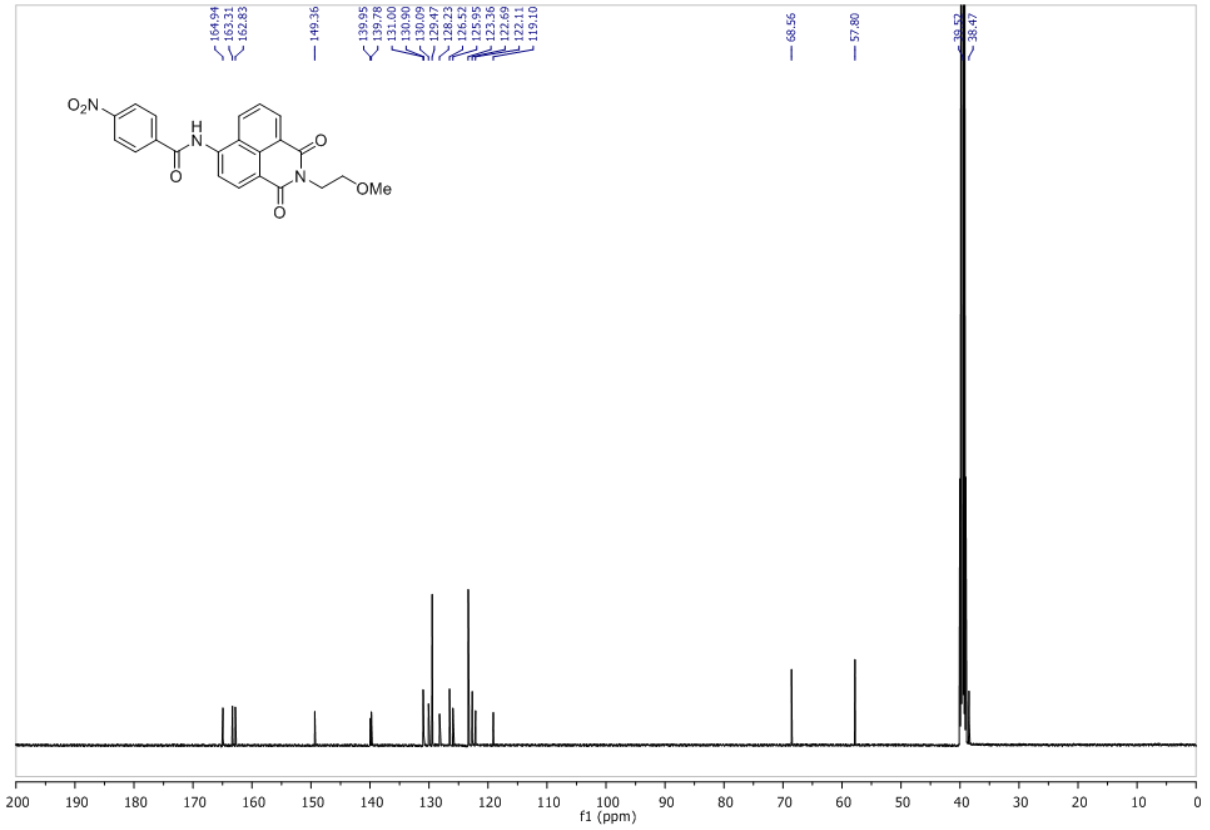
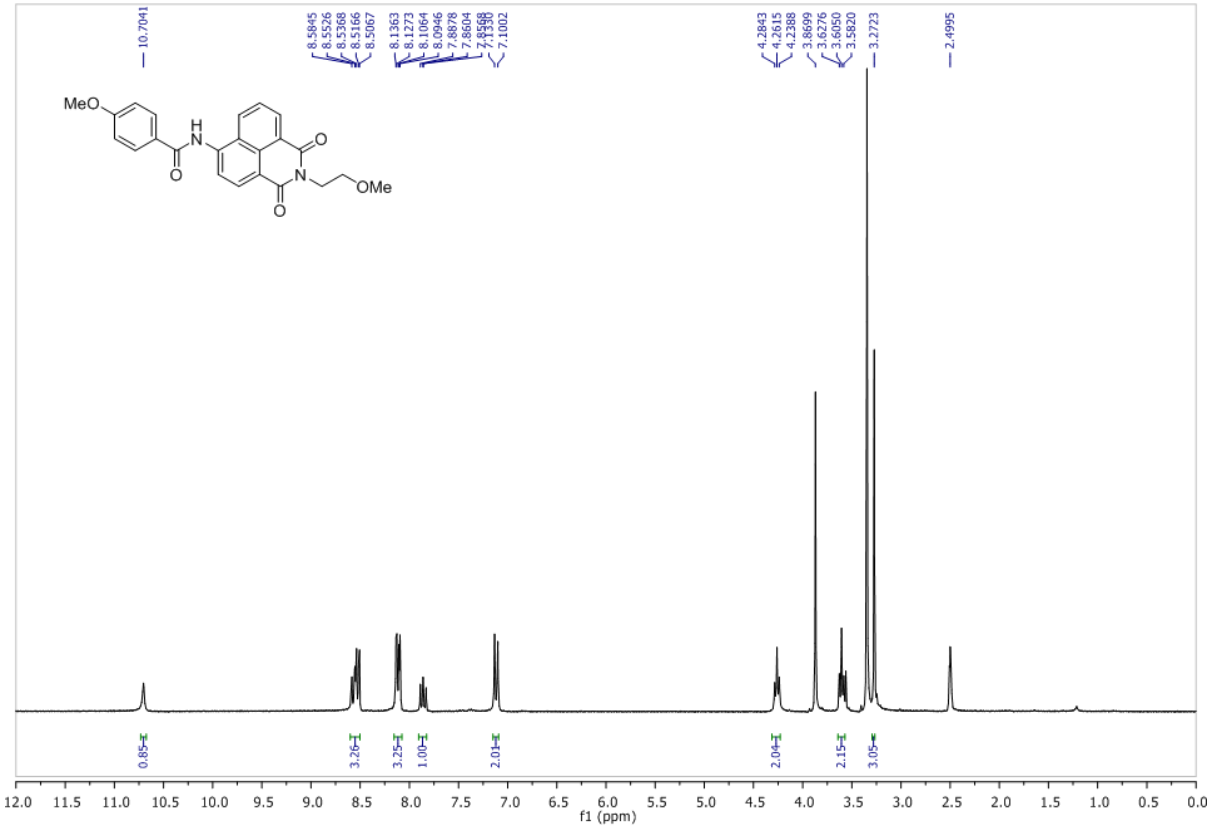


Figure S8 – ^{1}H and ^{13}C NMR of **10**



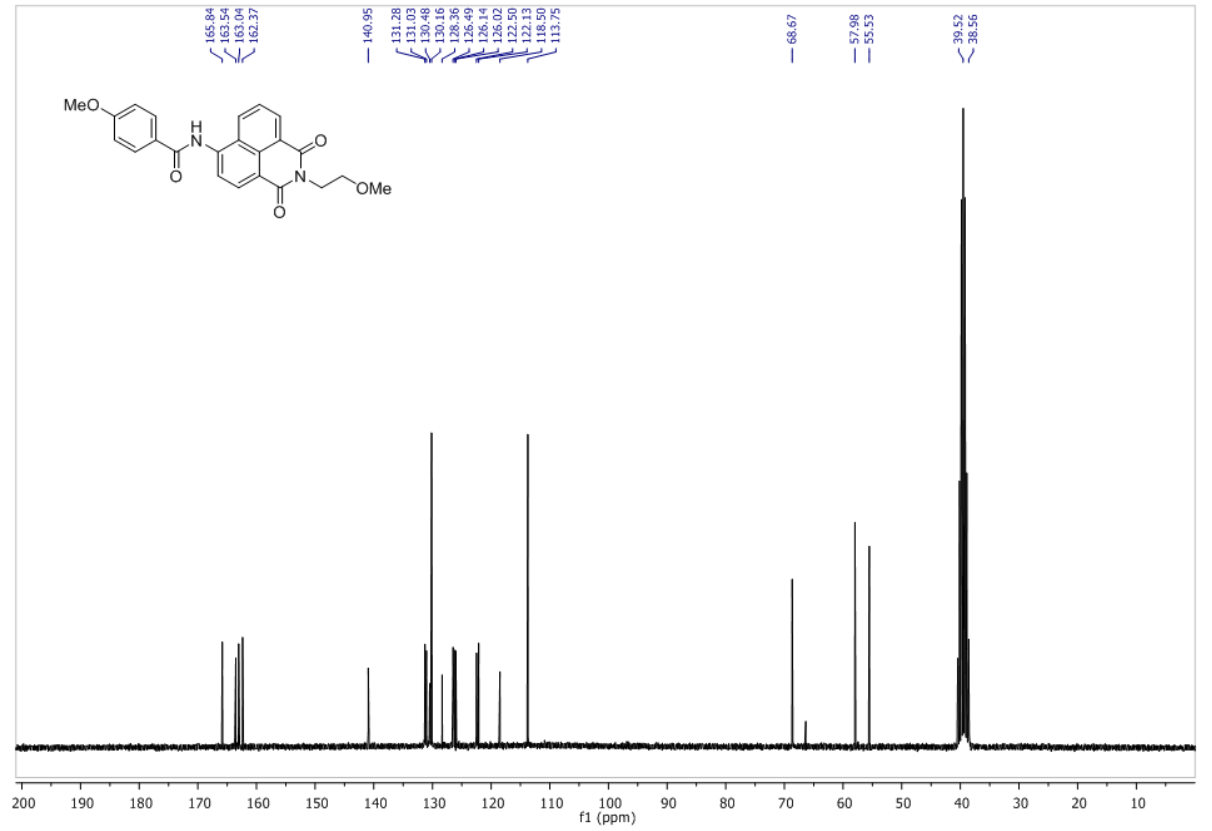


Figure S9 – ^{1}H and ^{13}C NMR of **11**

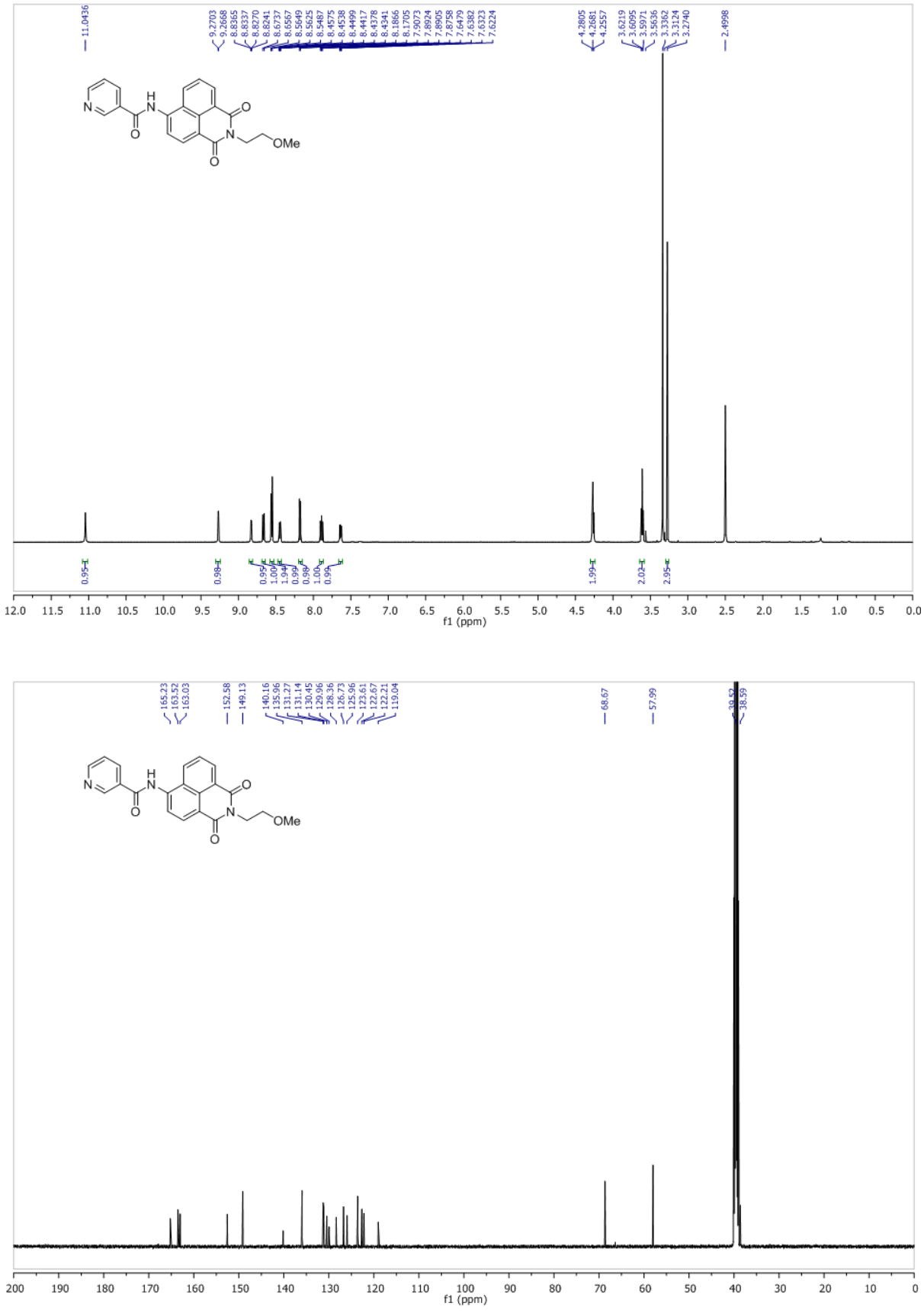
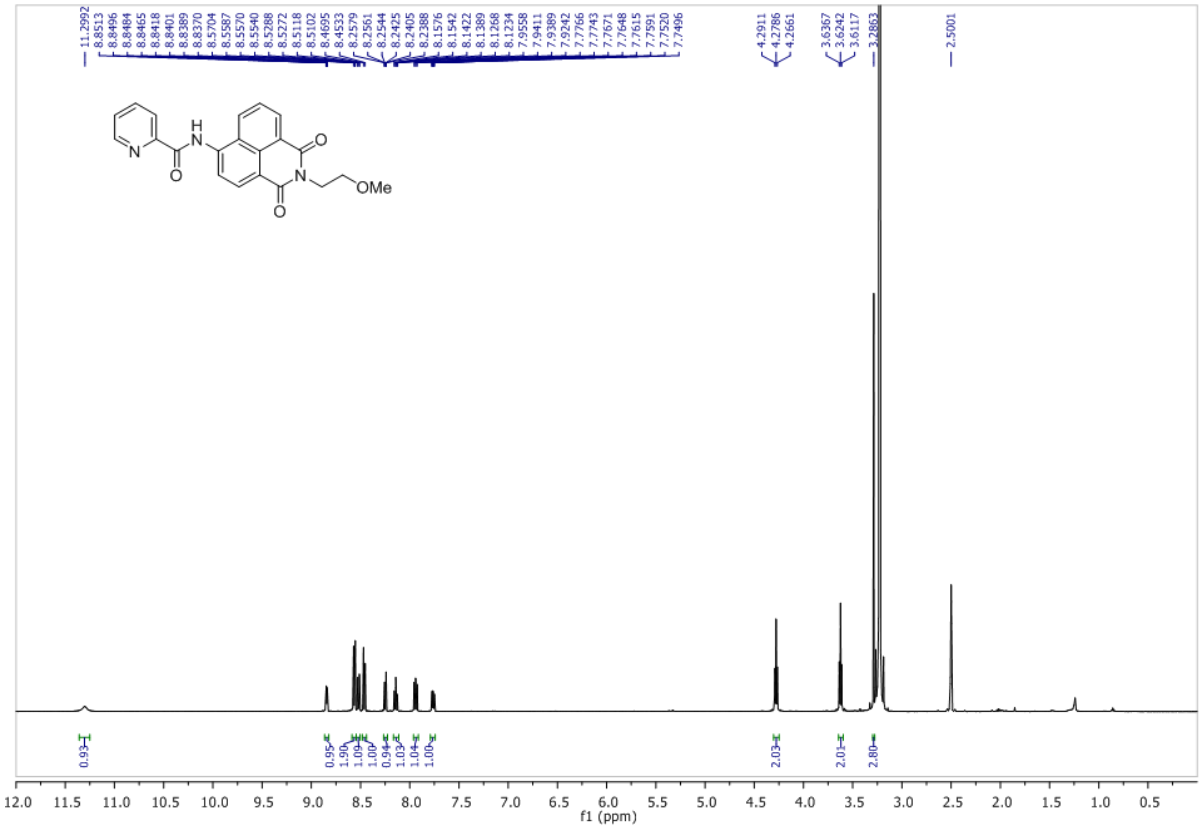


Figure S10 – ^{1}H and ^{13}C NMR of **12**



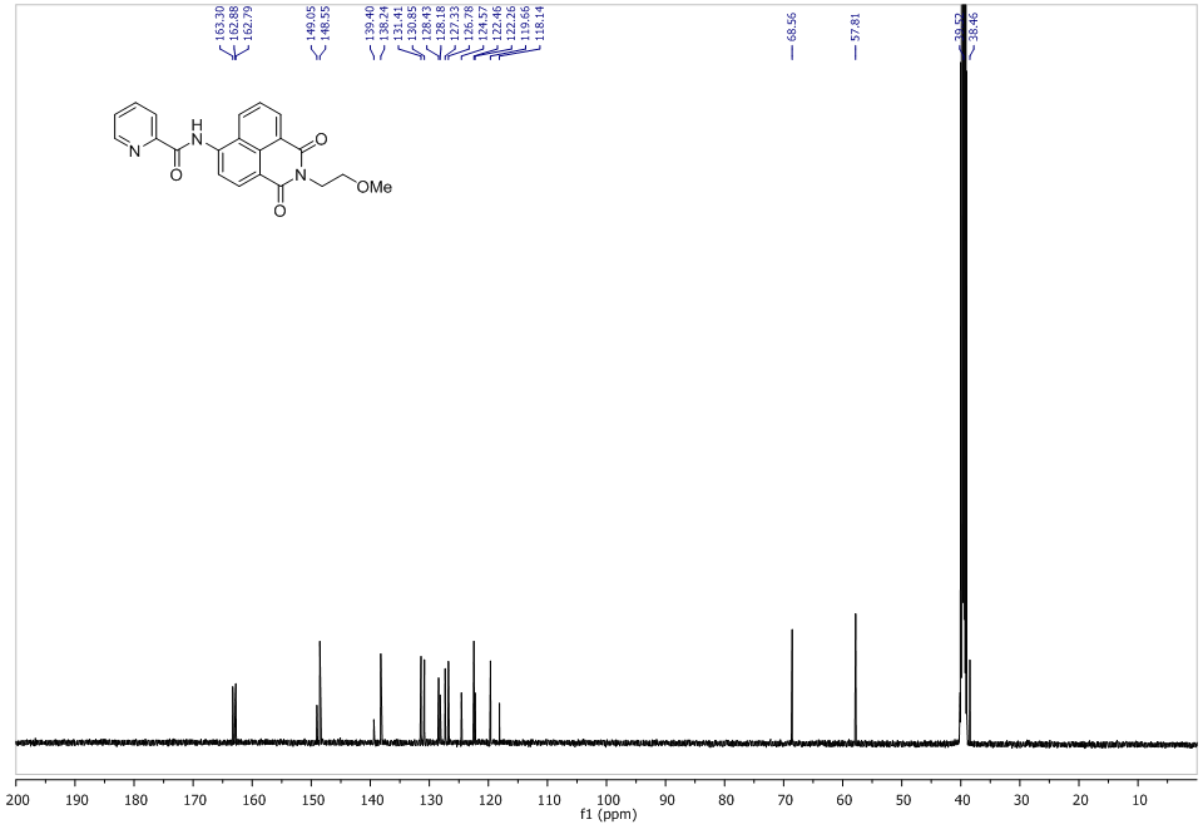
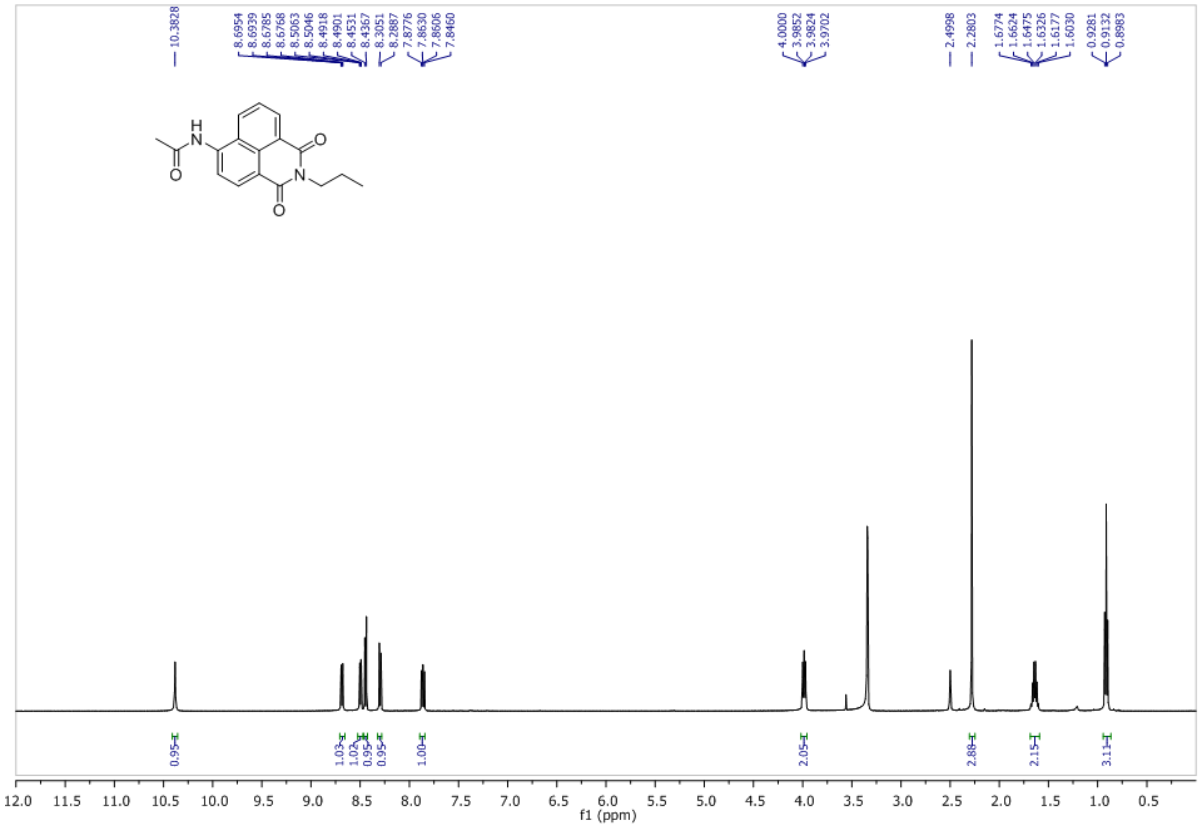


Figure S11– ^{1}H and ^{13}C NMR of **13**



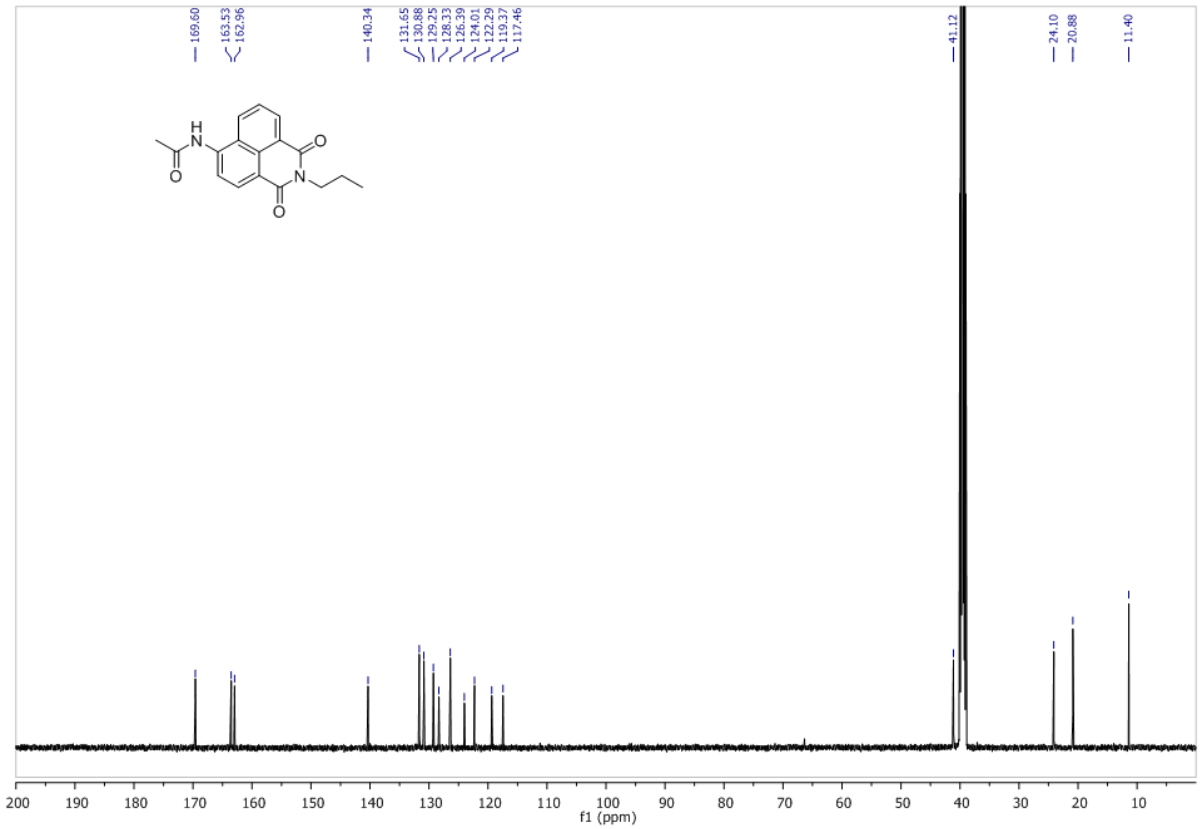
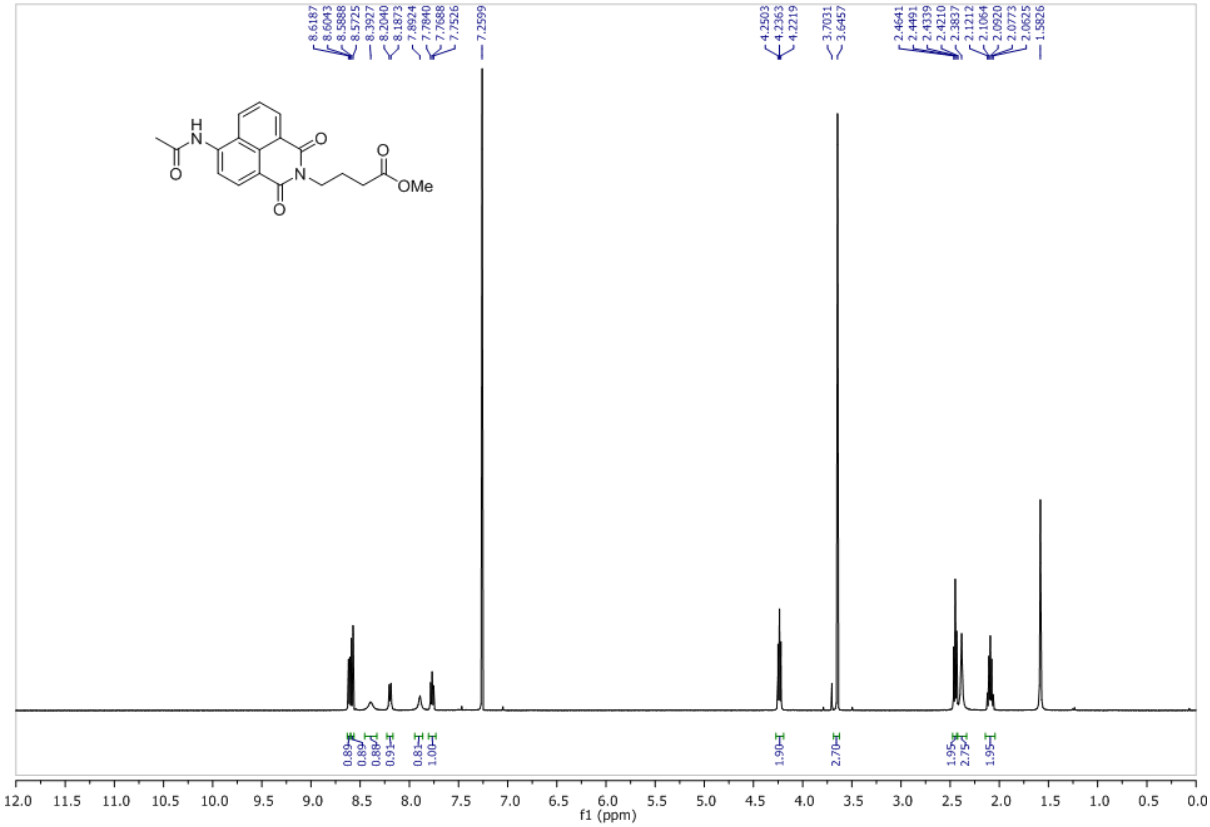


Figure S12 – ^{1}H and ^{13}C NMR of **14**



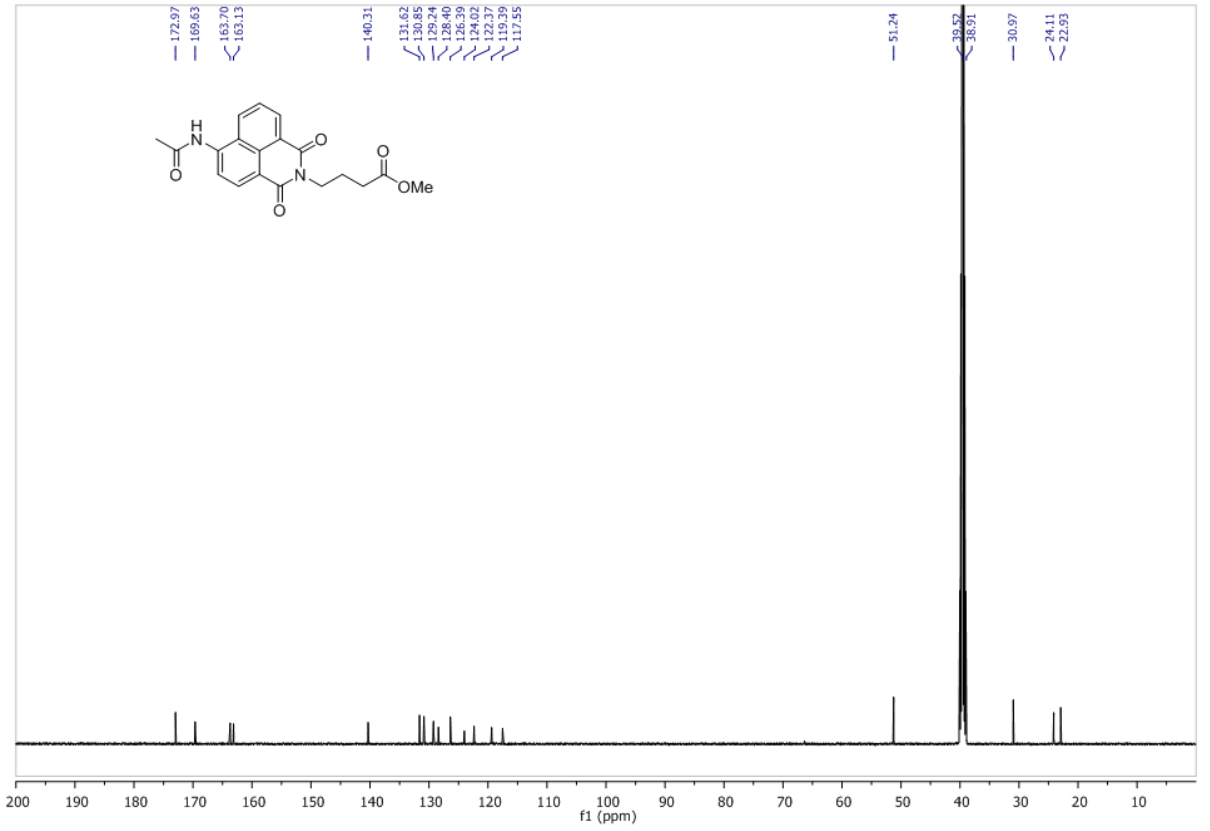
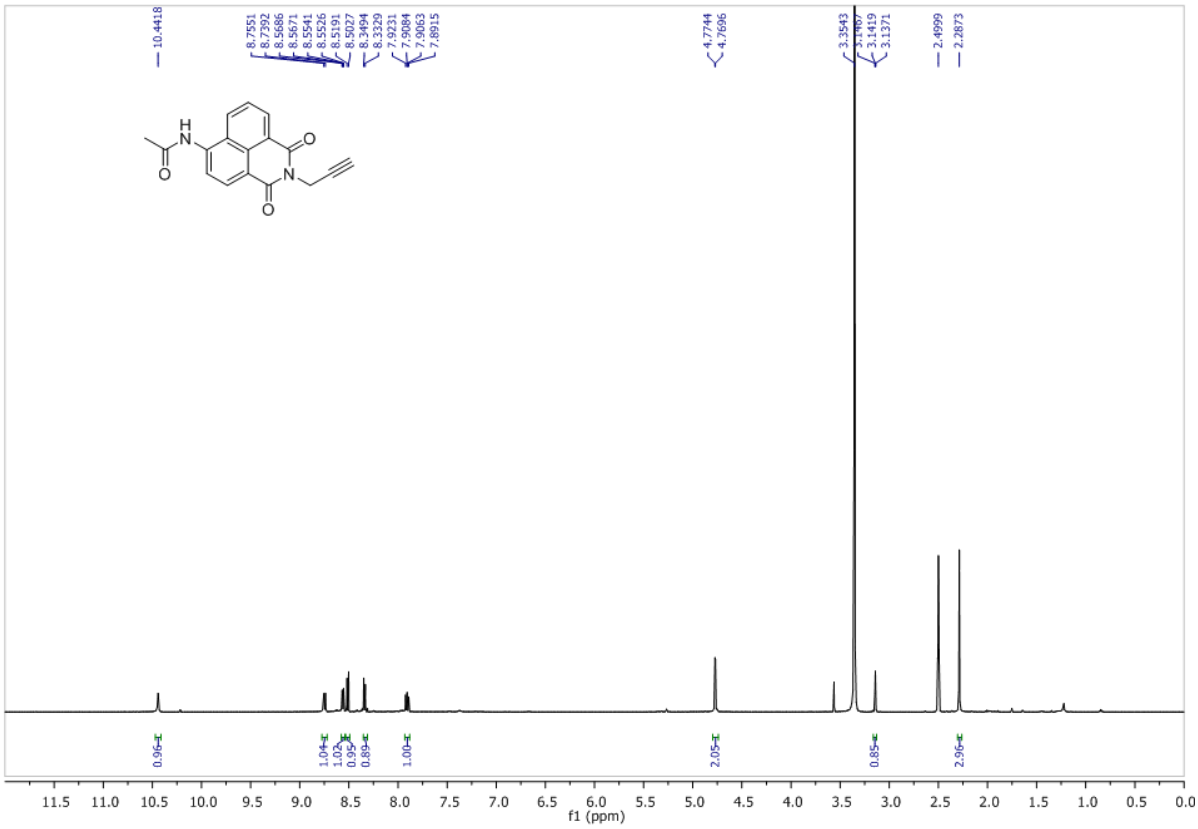


Figure S13 – ^{1}H and ^{13}C NMR of **15**



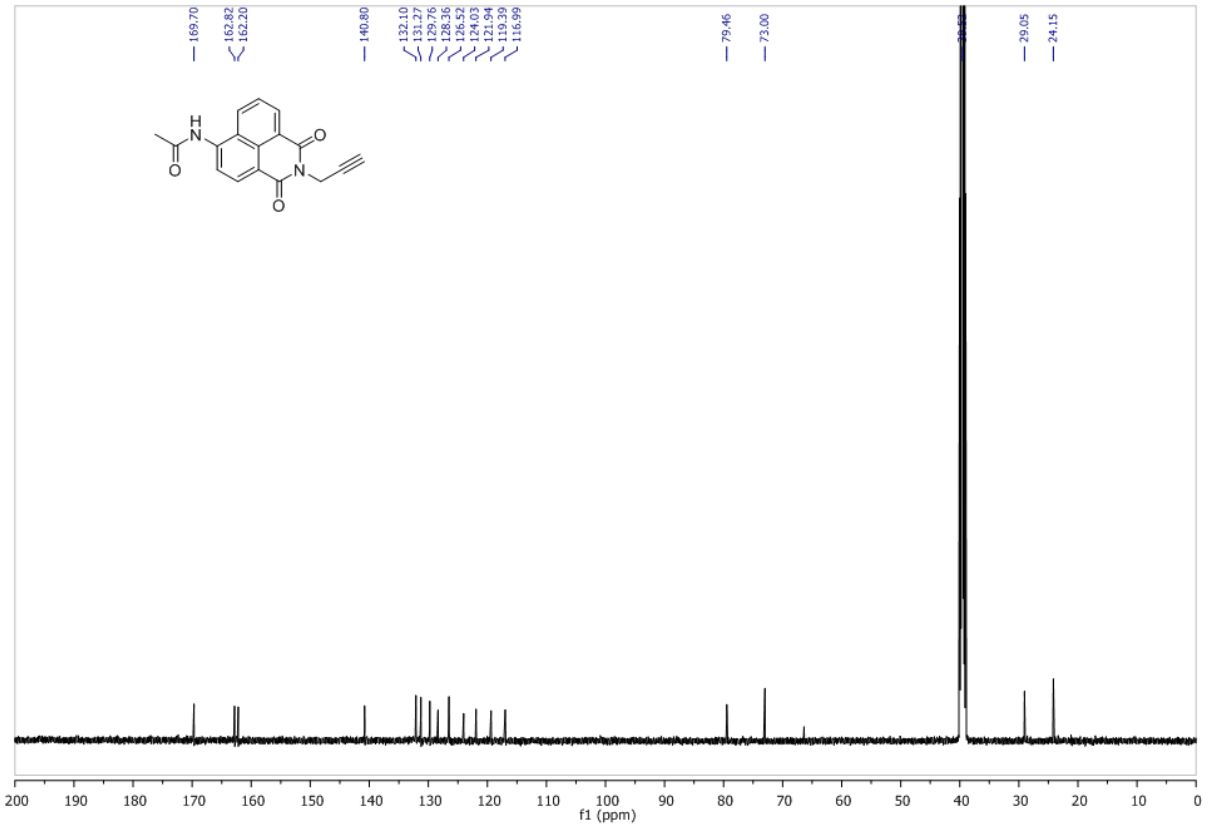
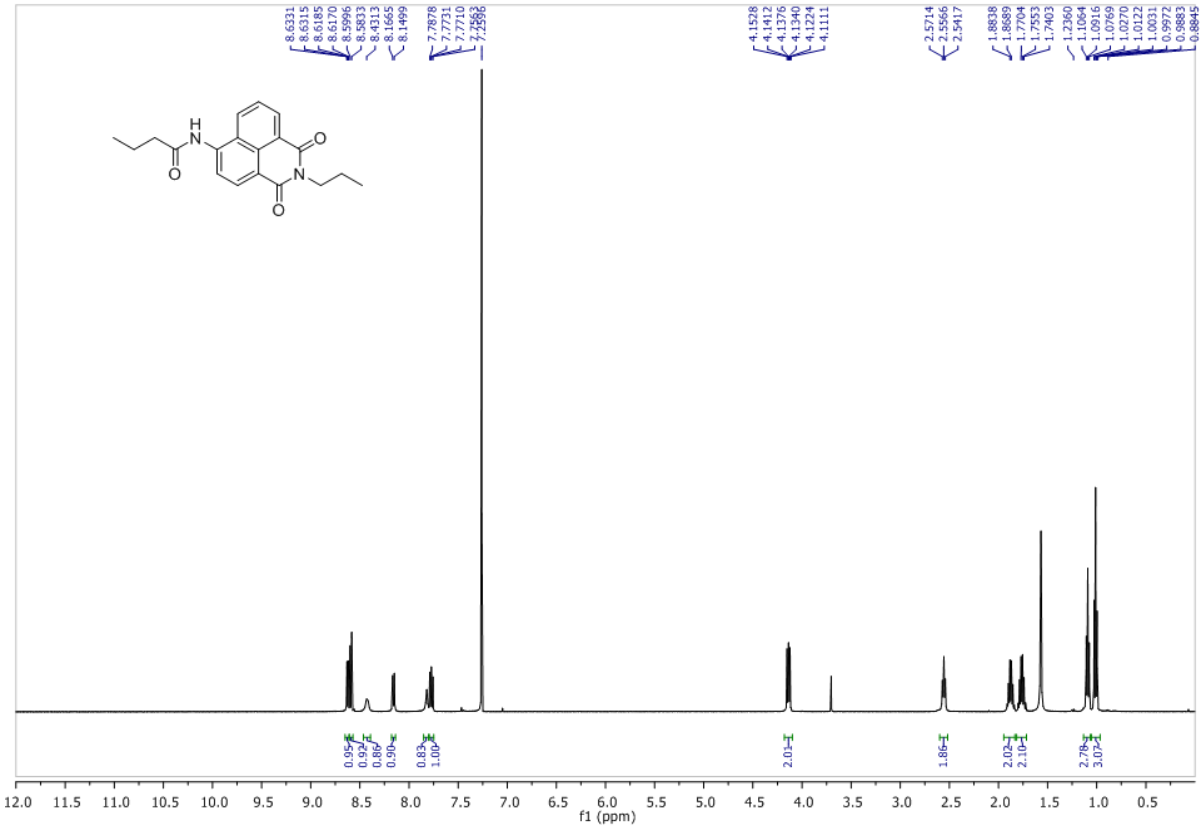


Figure S14 – ^{1}H and ^{13}C NMR of **16**



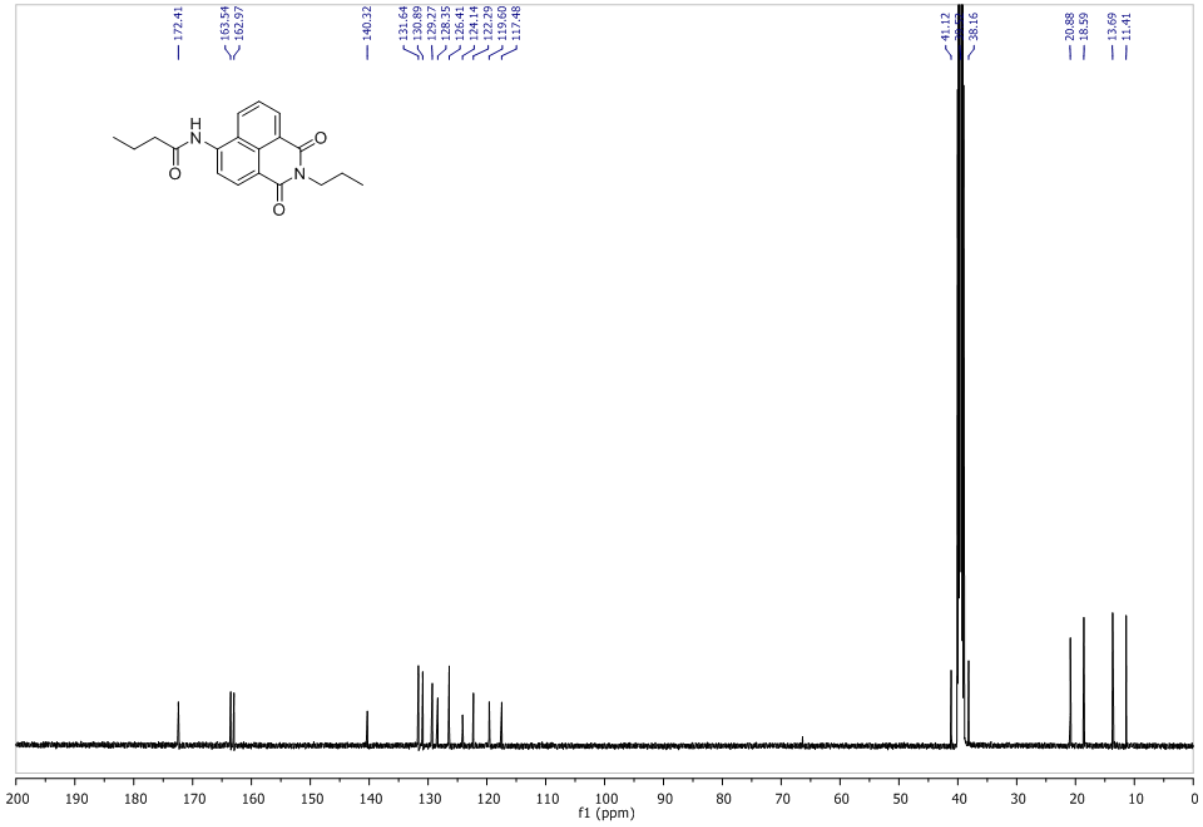
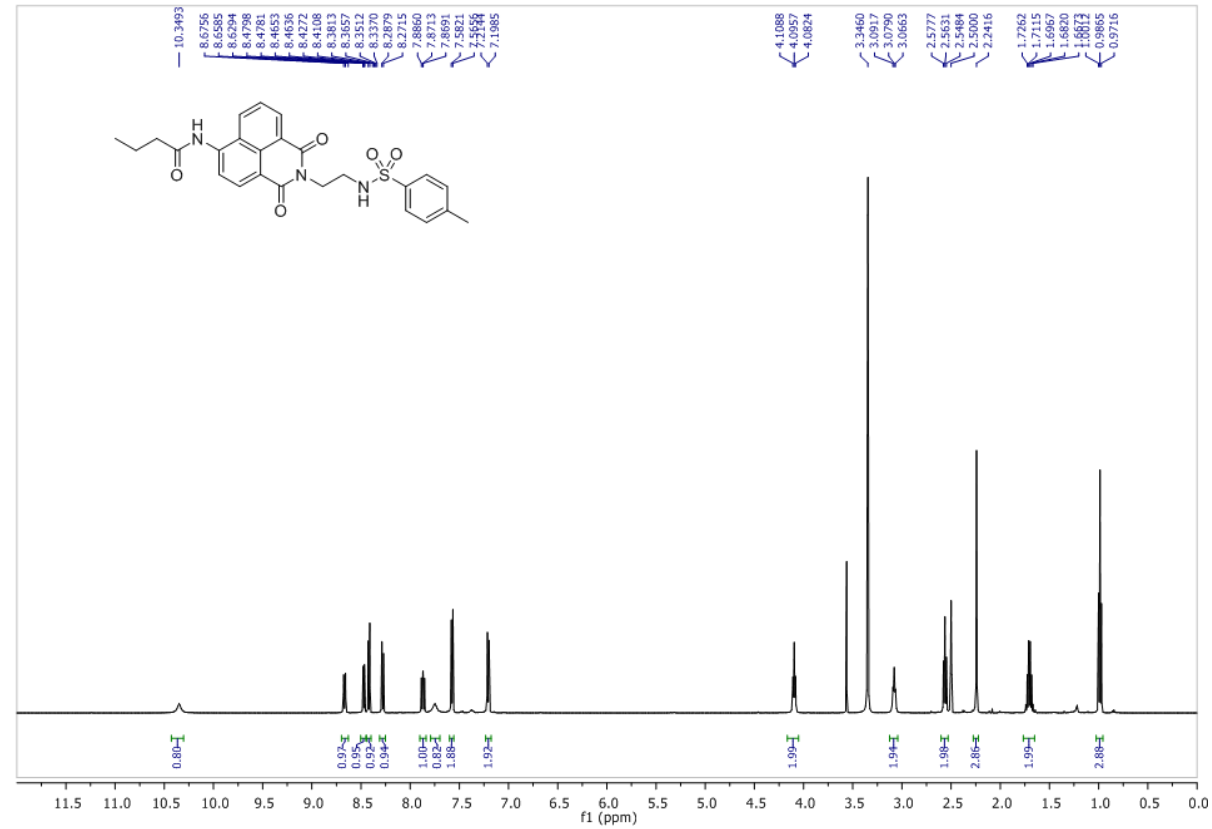


Figure S15 – ^{1}H and ^{13}C NMR of **17**



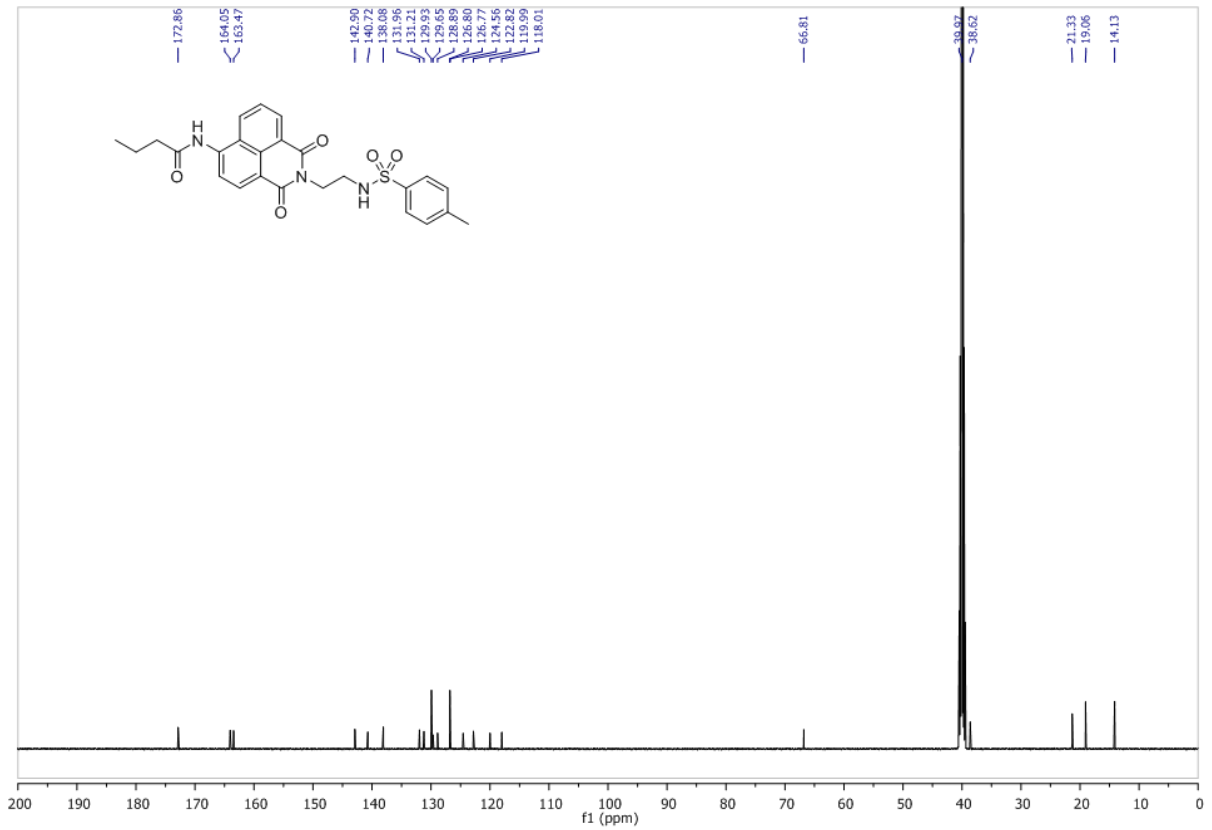
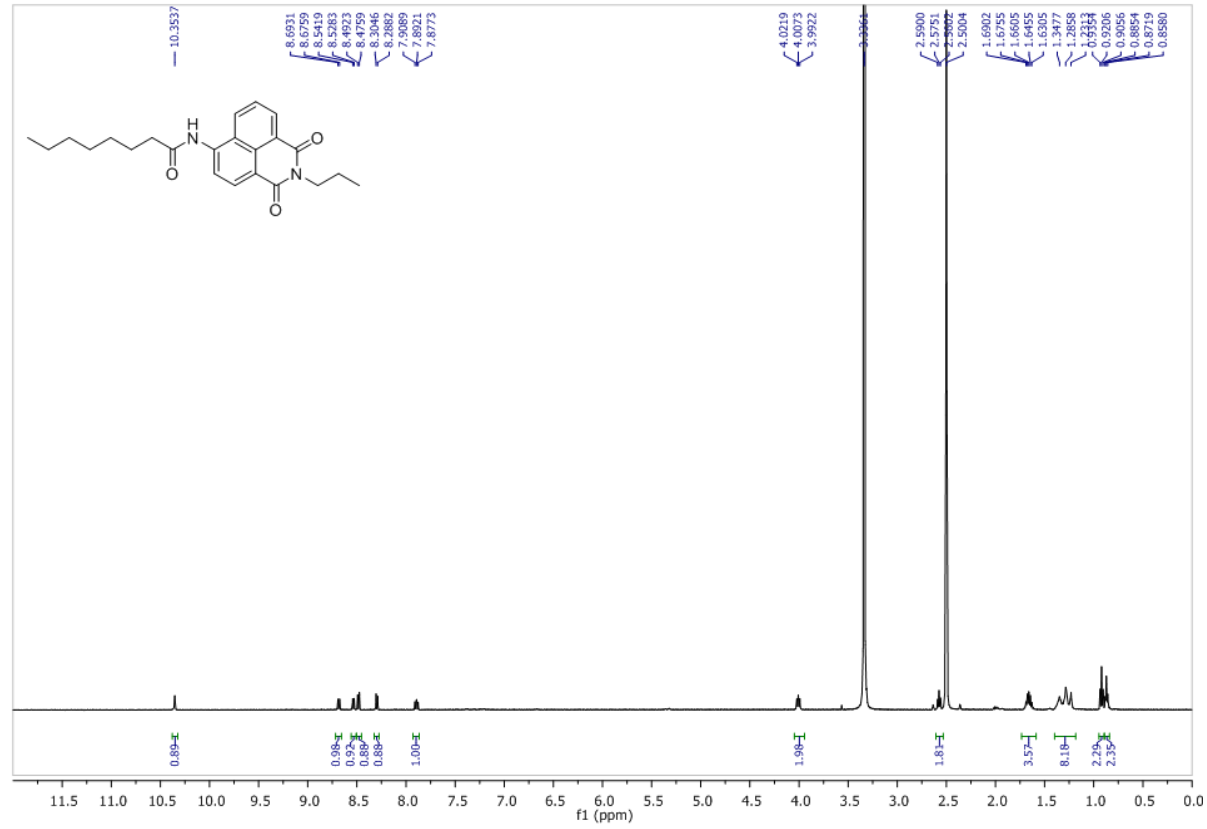


Figure S16 – ^{1}H and ^{13}C NMR of **18**



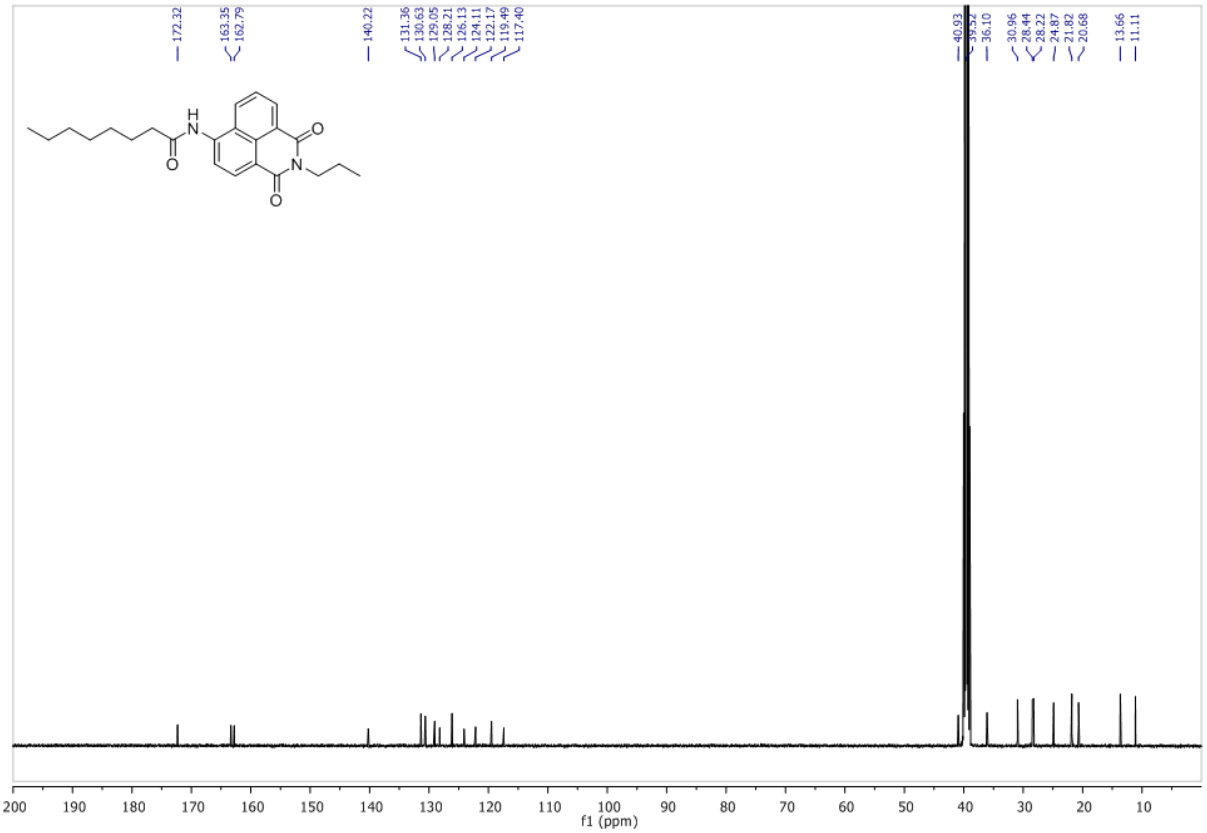
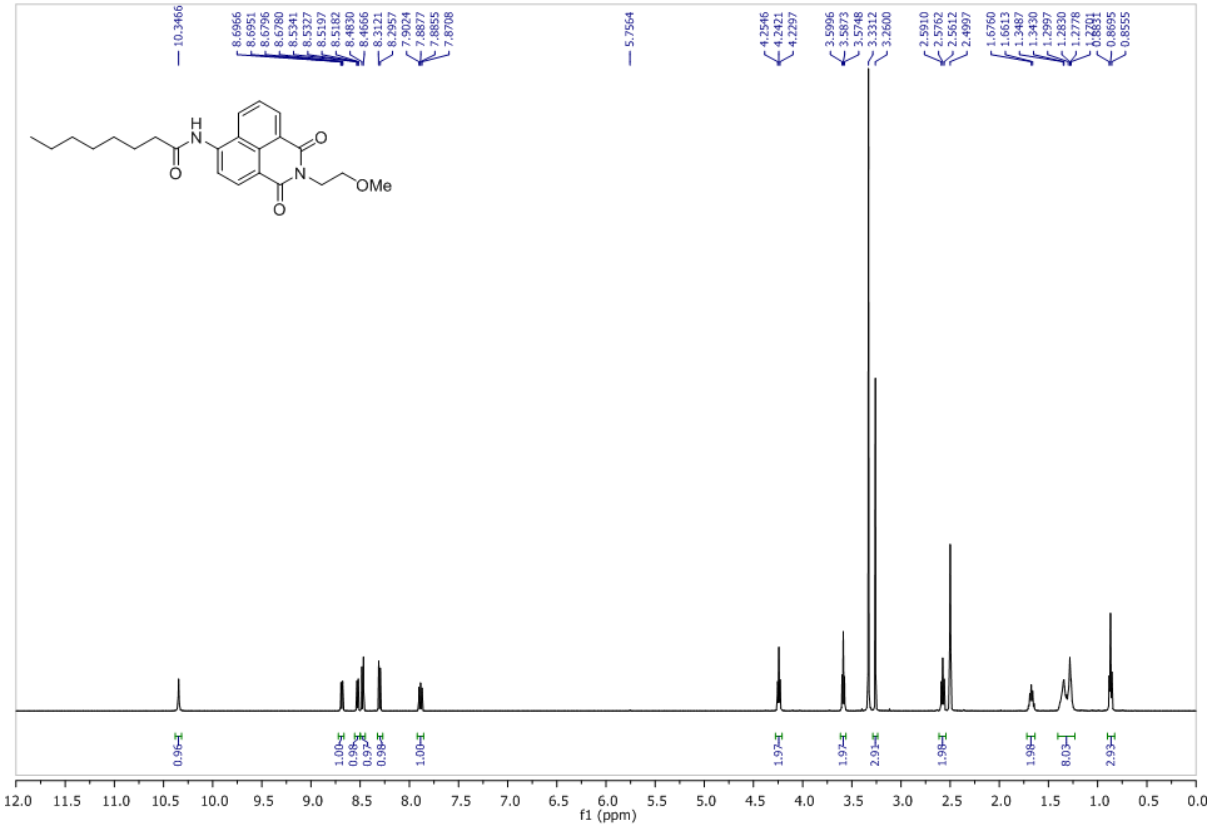


Figure S17 – ^{1}H and ^{13}C NMR of **19**



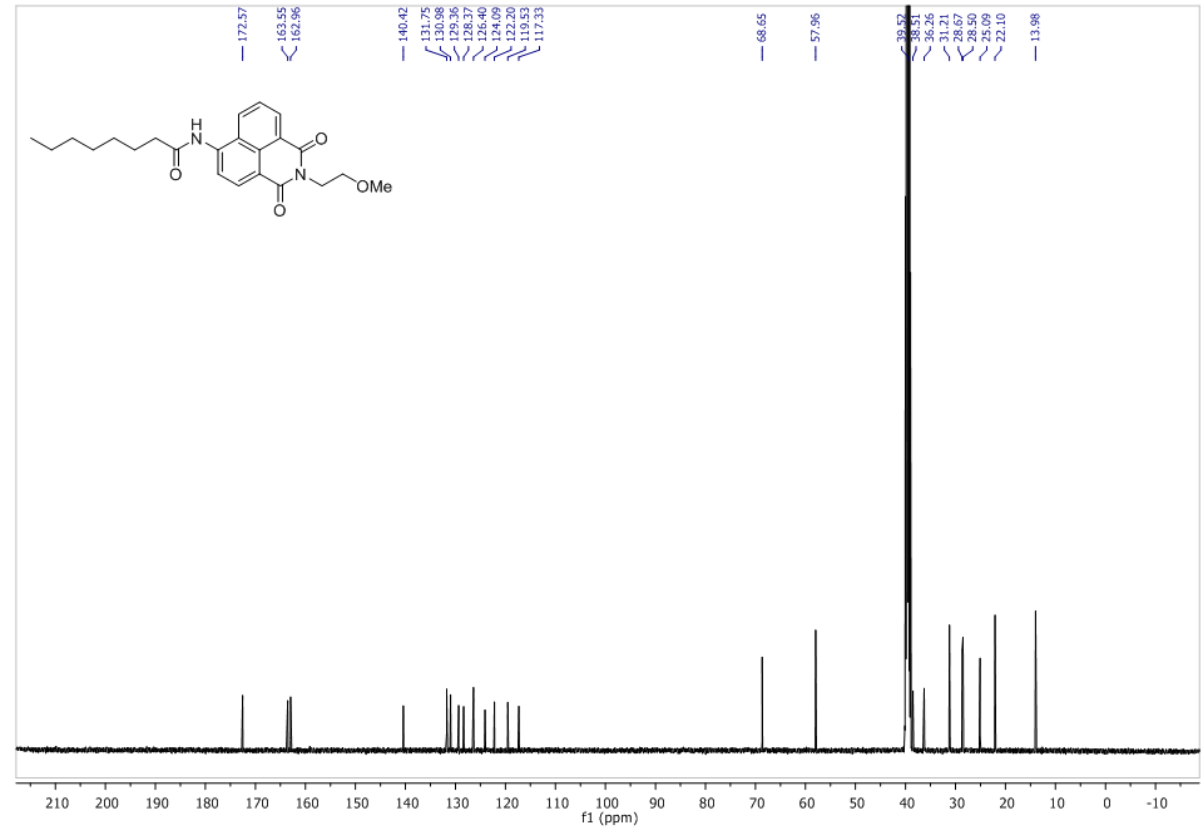
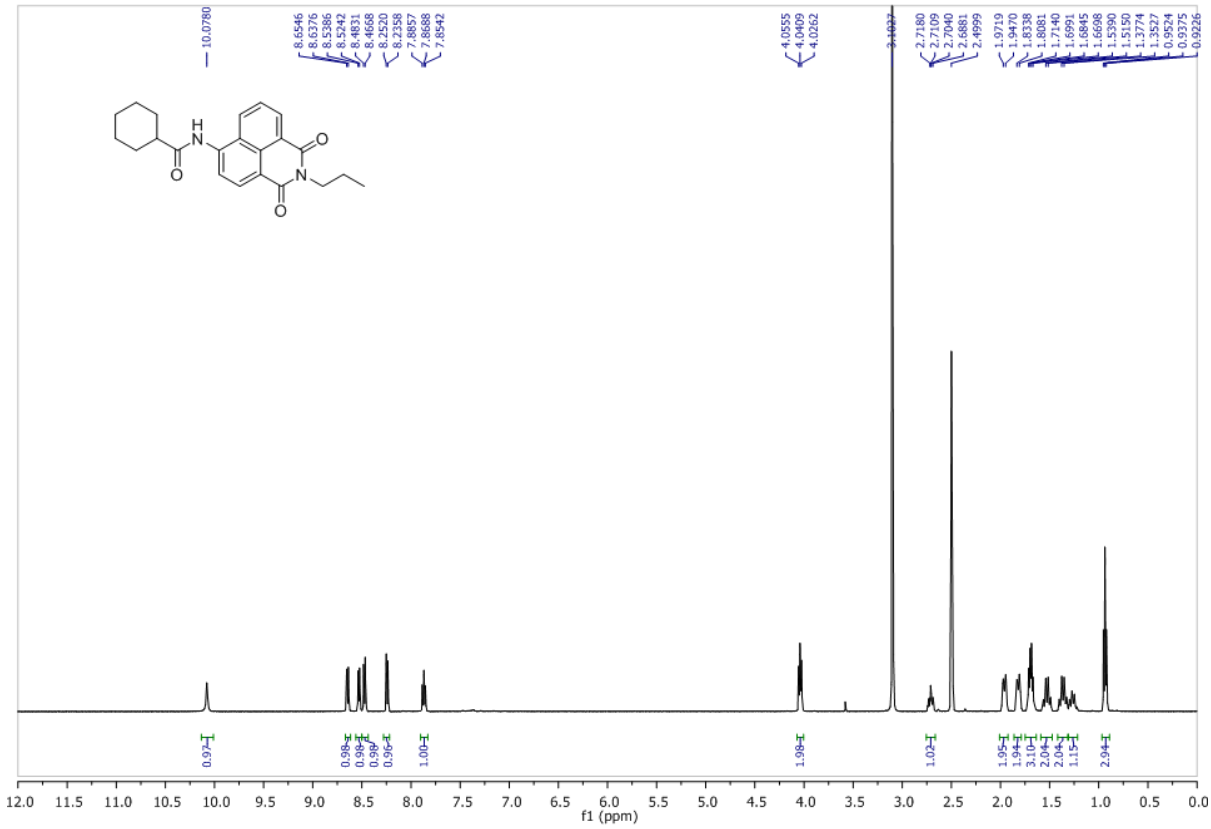


Figure S18 – ^{1}H and ^{13}C NMR of **20**



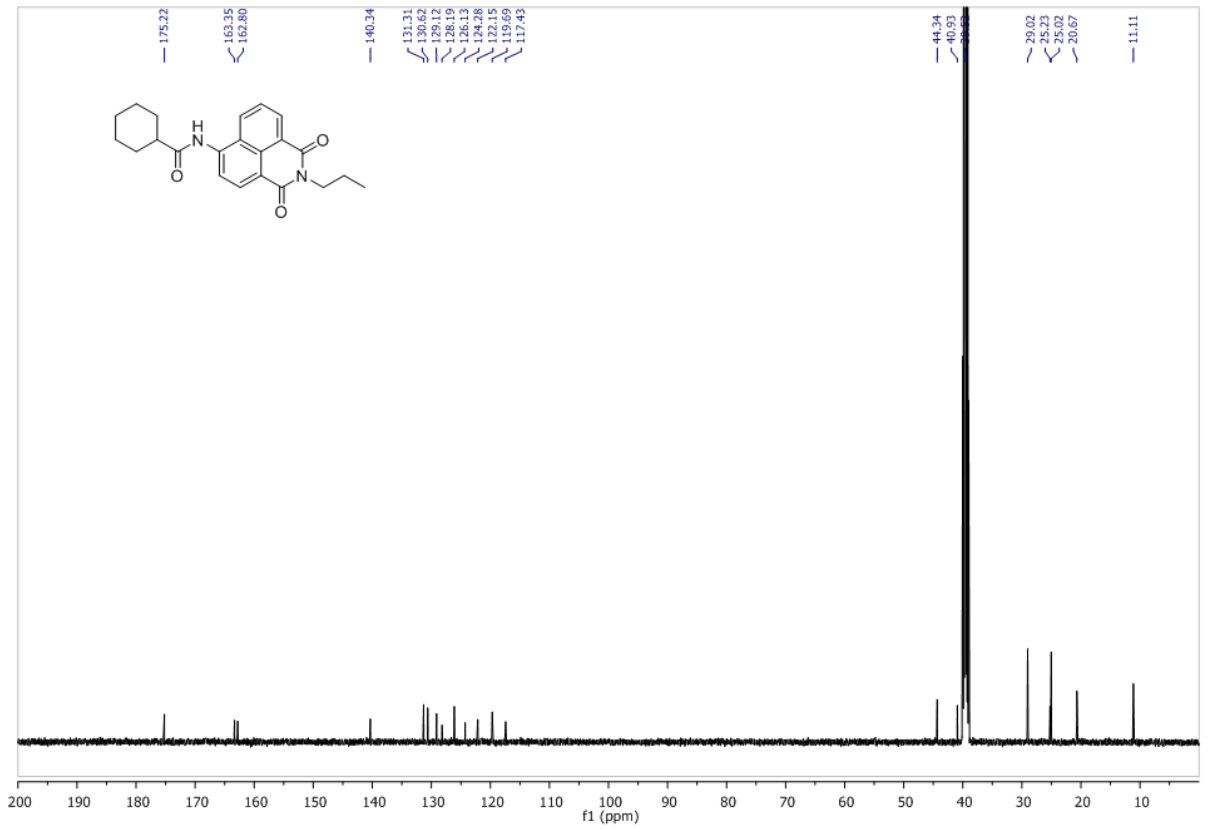
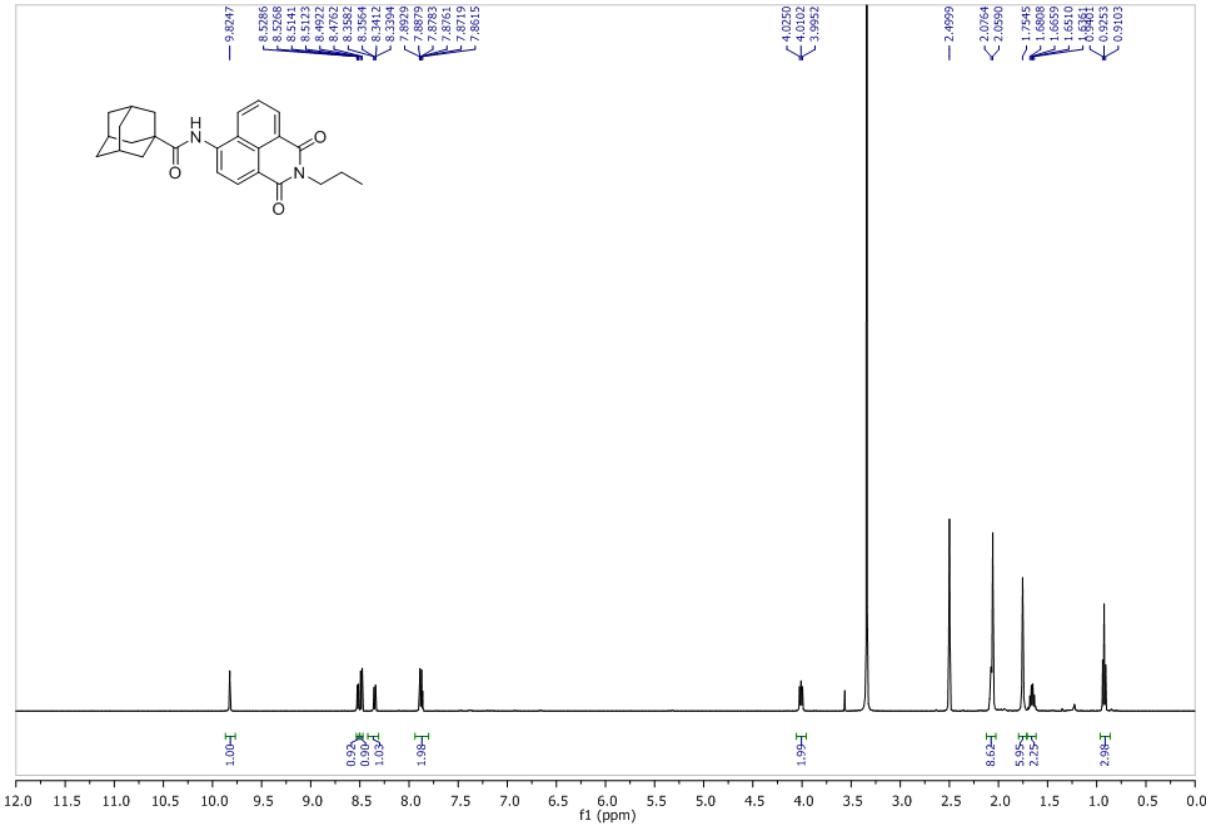


Figure S19 – ^{1}H and ^{13}C NMR of **21**



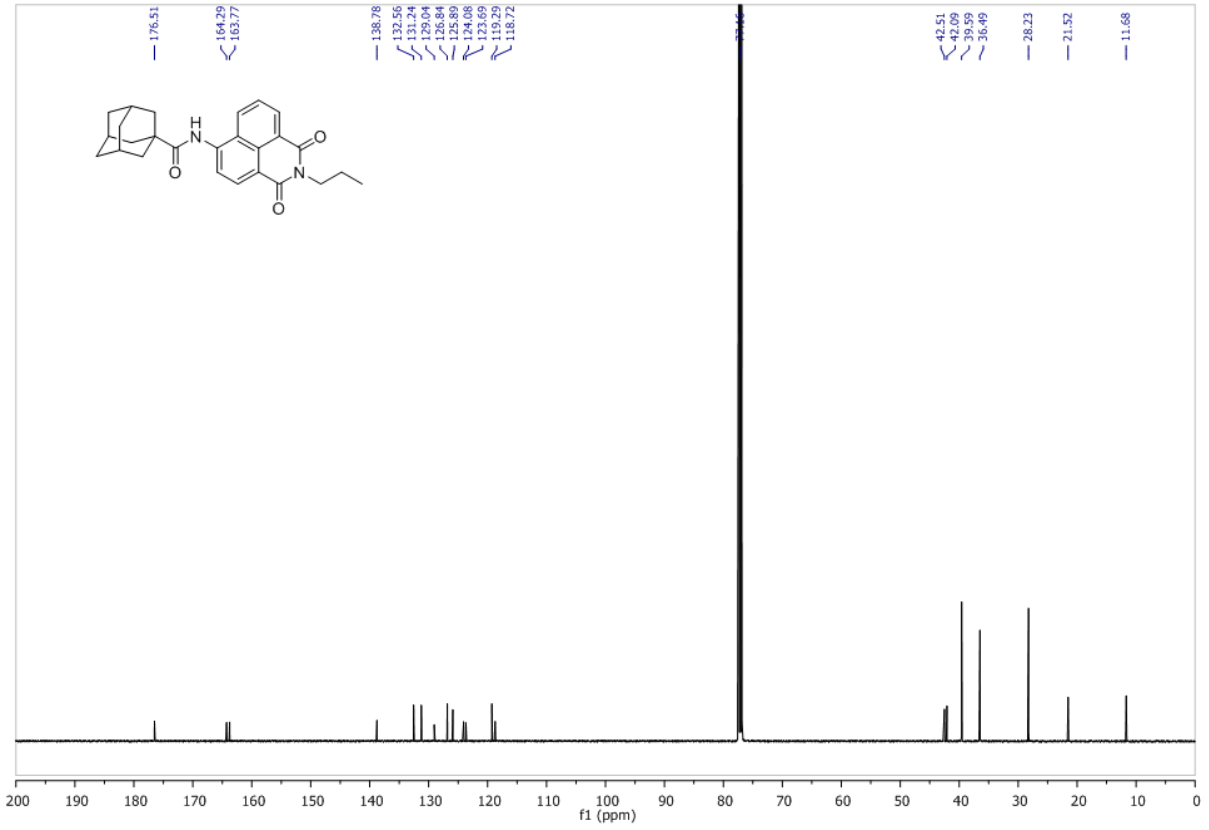
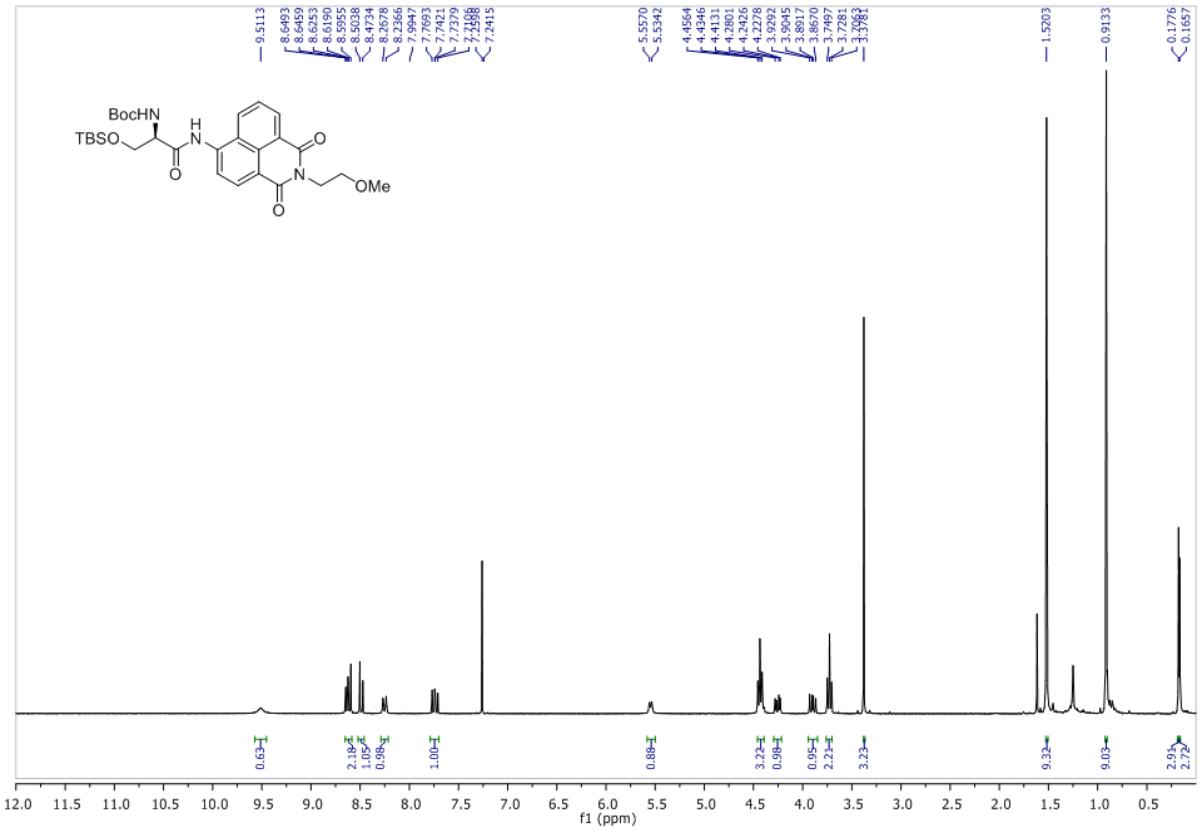


Figure S20 – ^{1}H and ^{13}C NMR of **22**



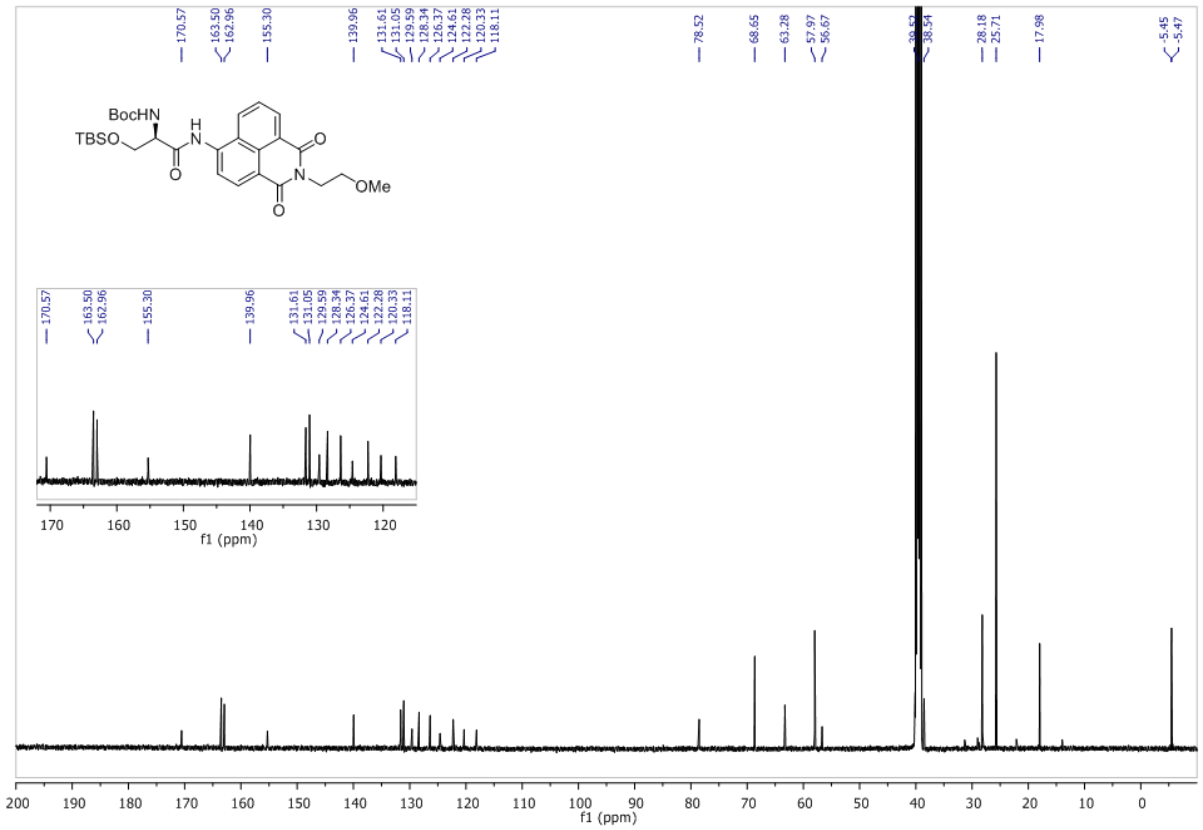
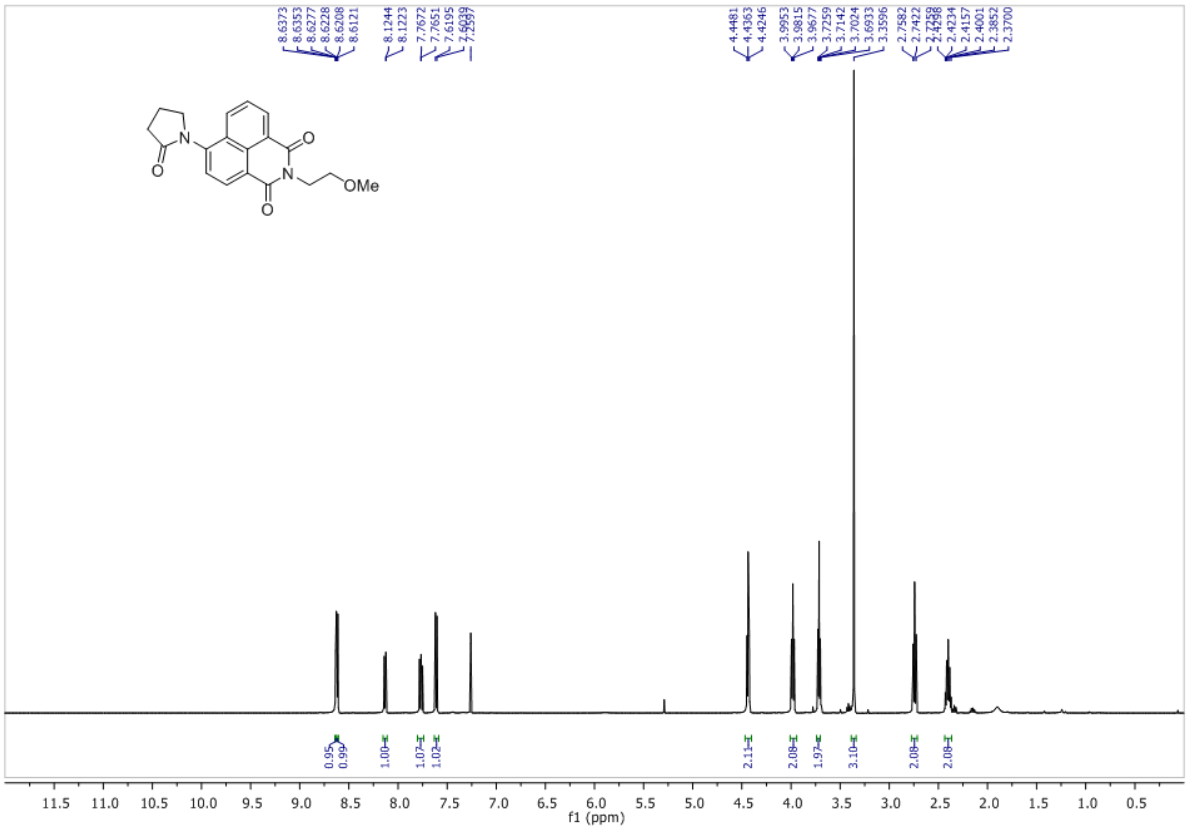


Figure S21 – ^{1}H and ^{13}C NMR of **23**



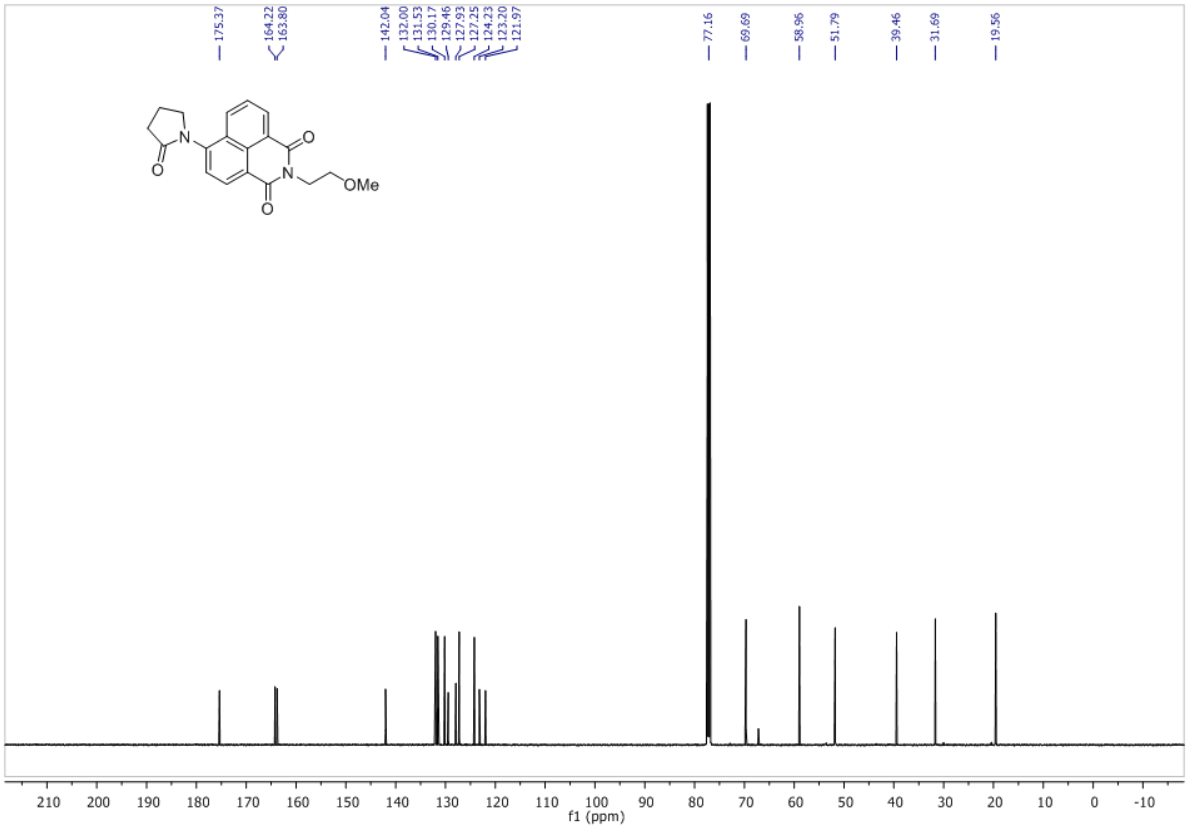
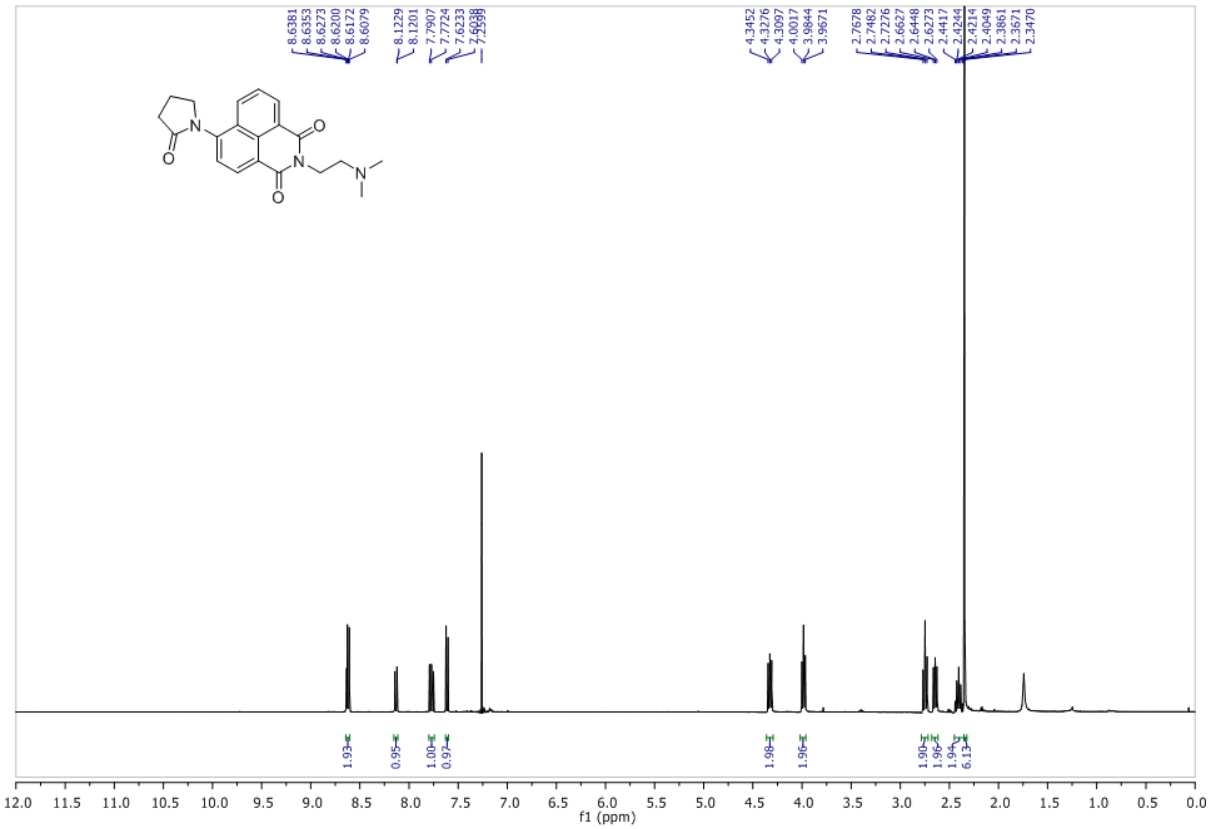


Figure S22 – ^{1}H and ^{13}C NMR of **24**



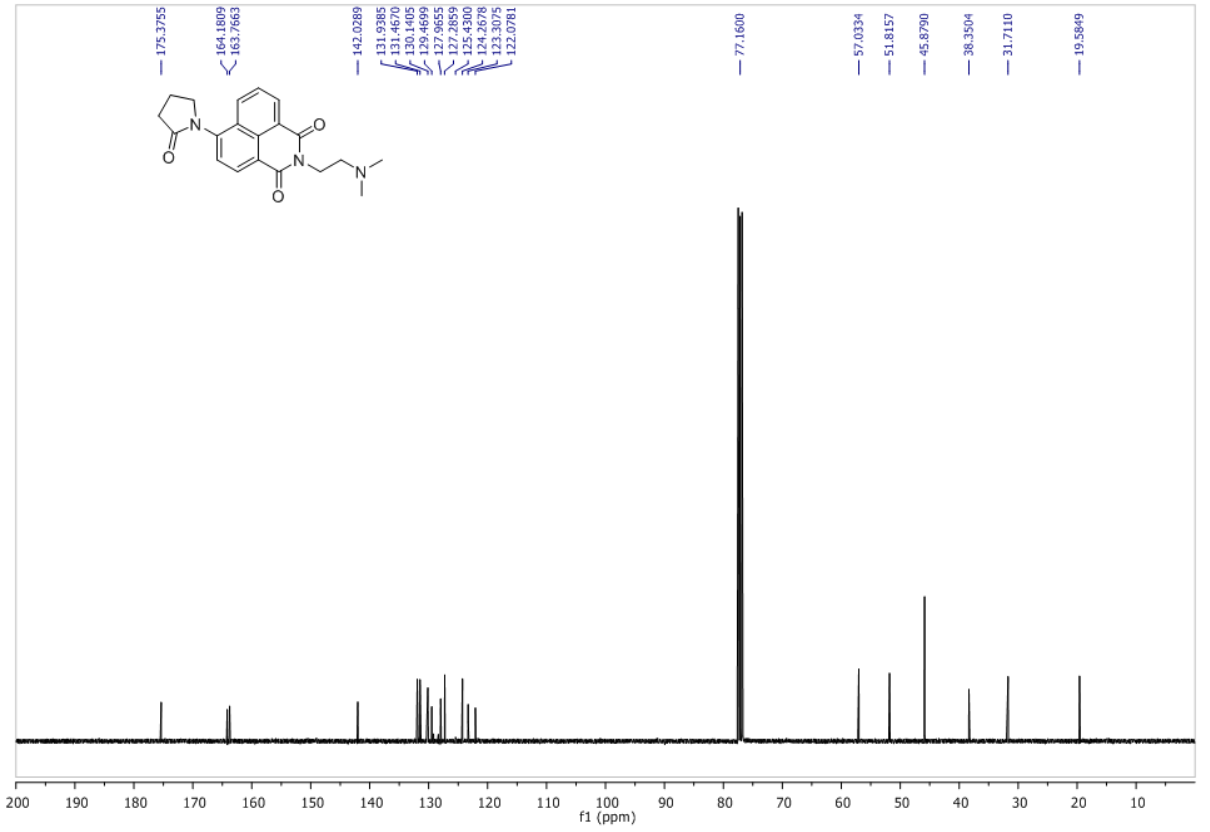
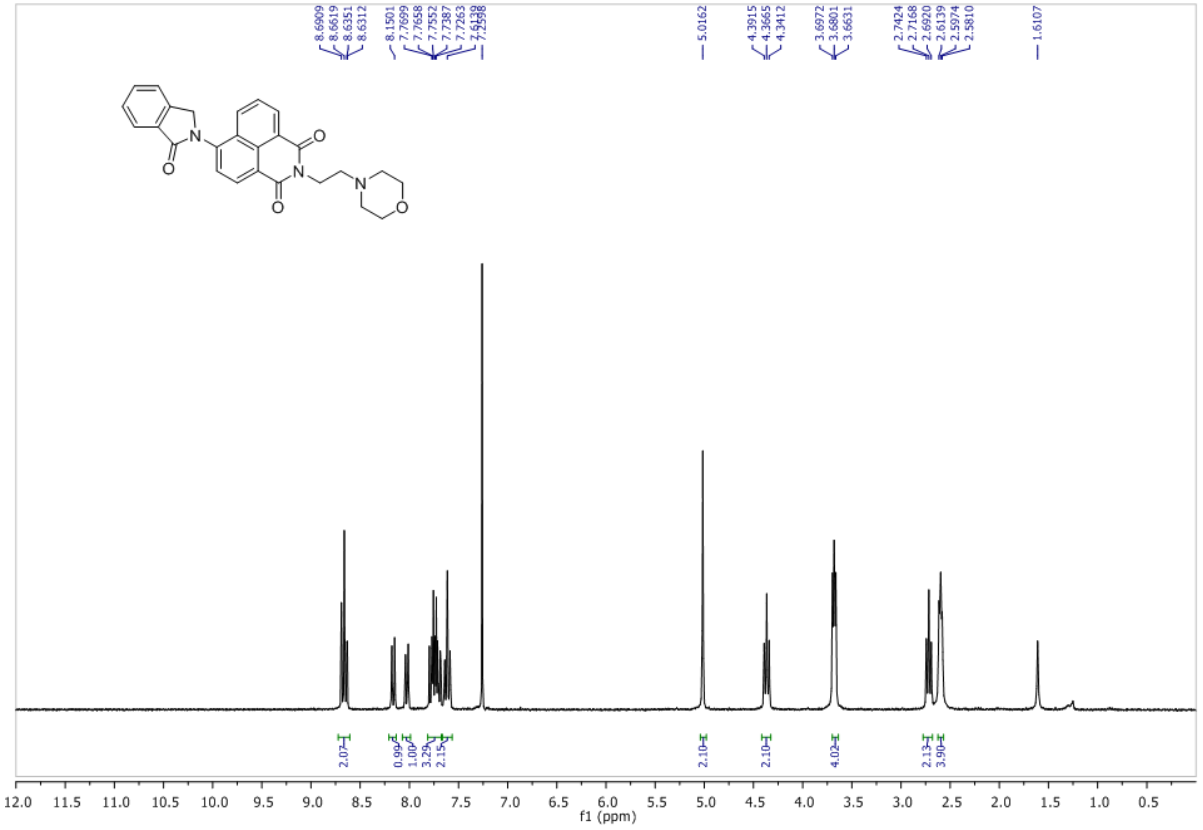


Figure S23 – ^{1}H and ^{13}C NMR of **25**



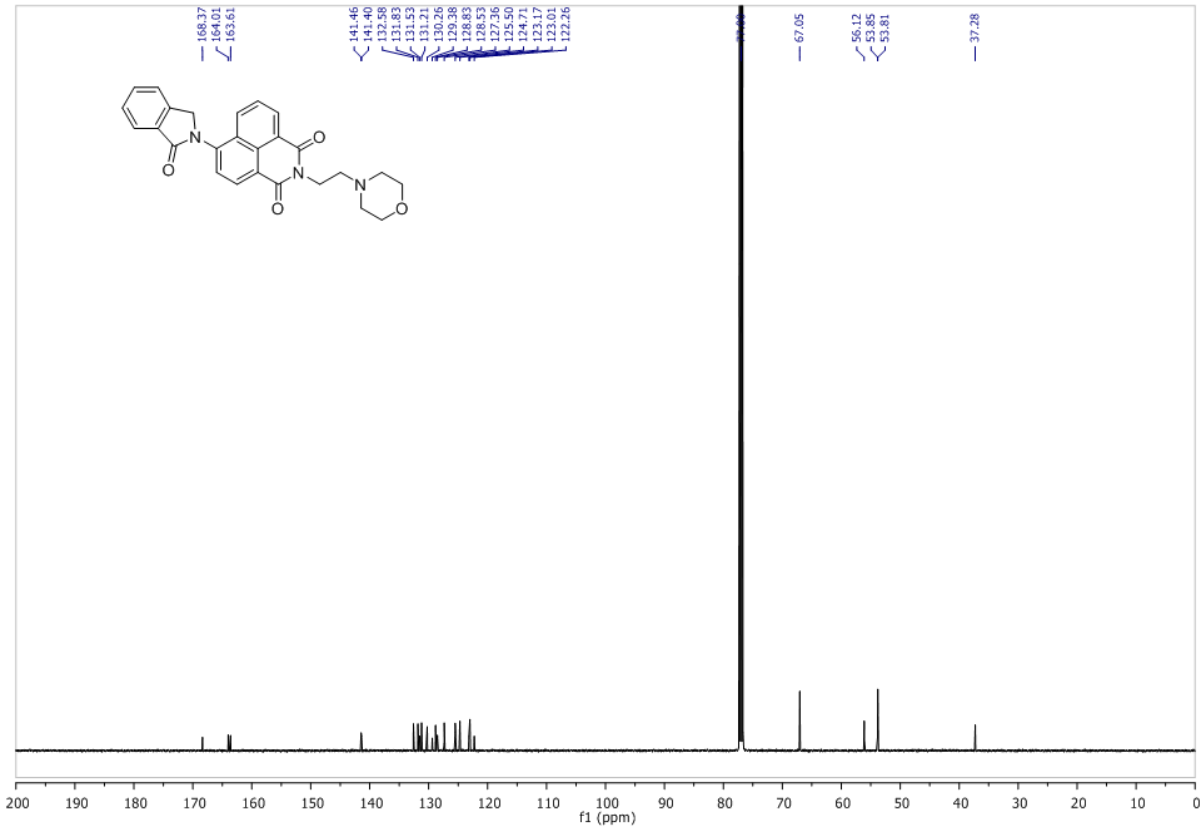
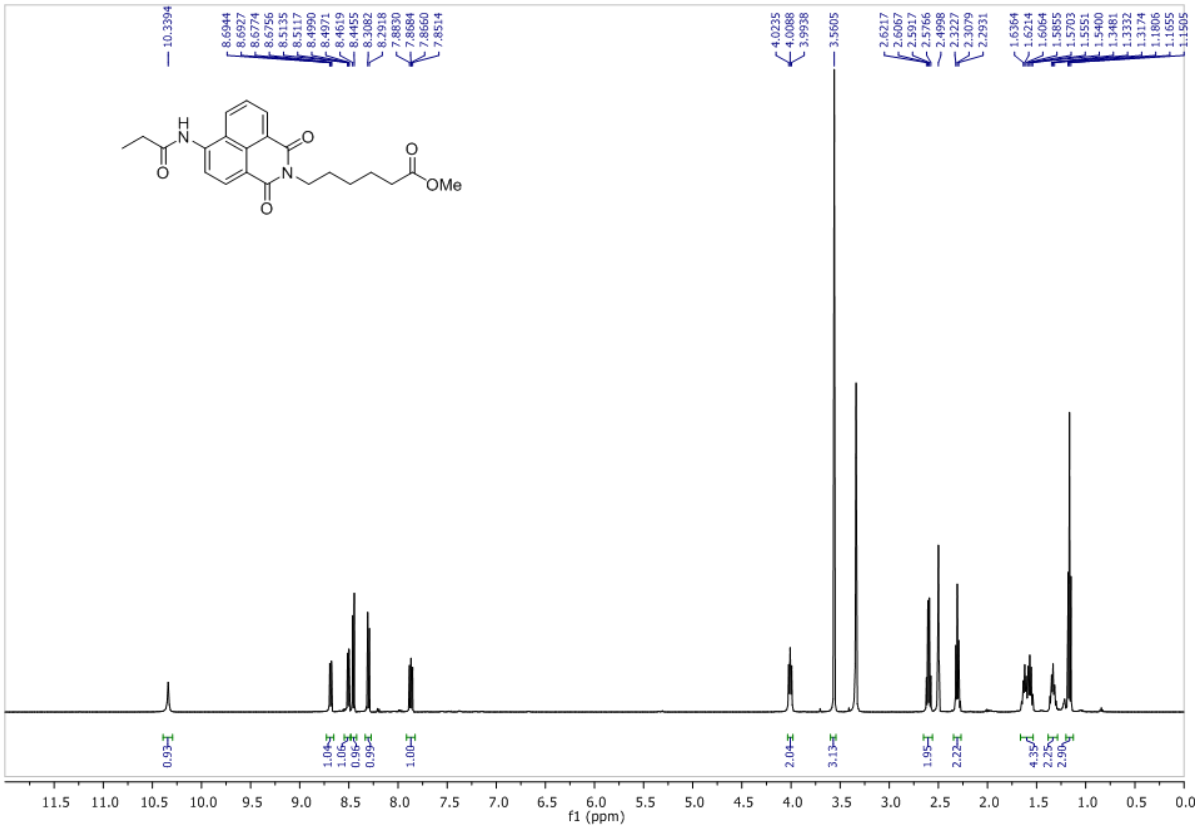


Figure S24 – ^{1}H and ^{13}C NMR of **26**



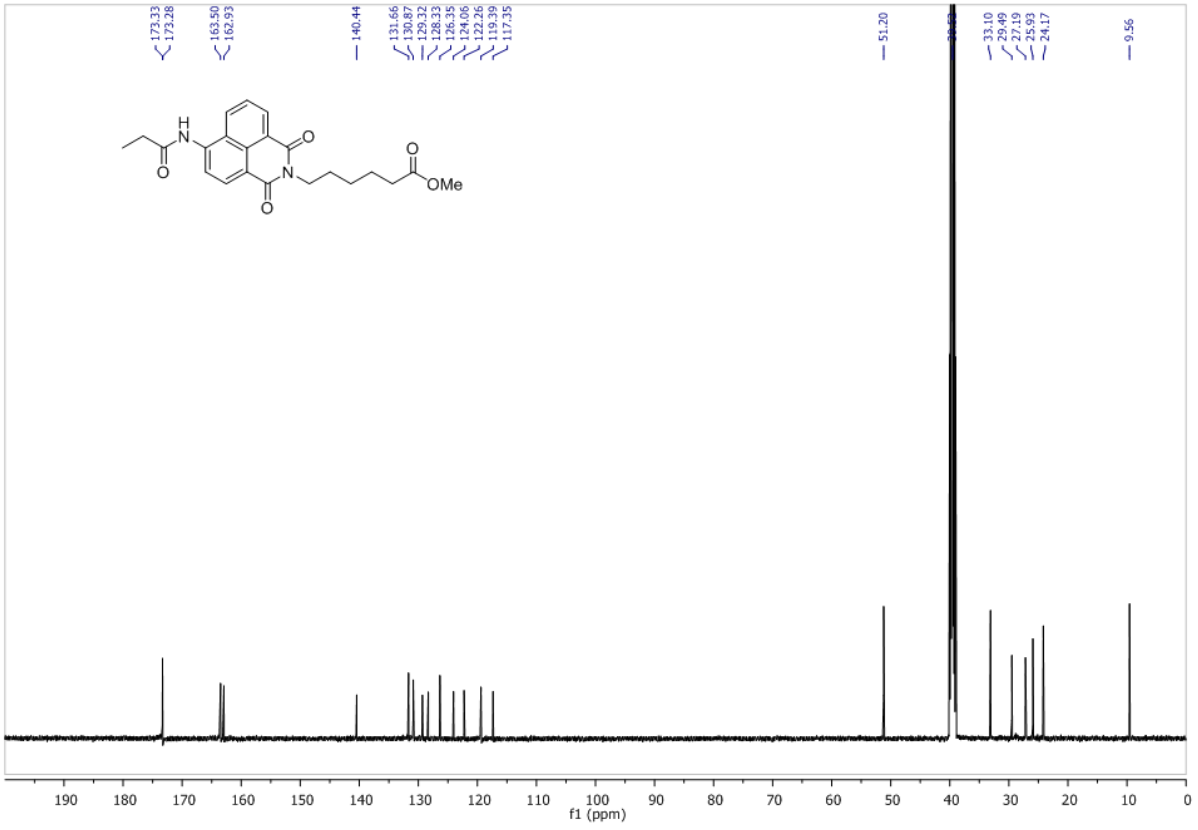
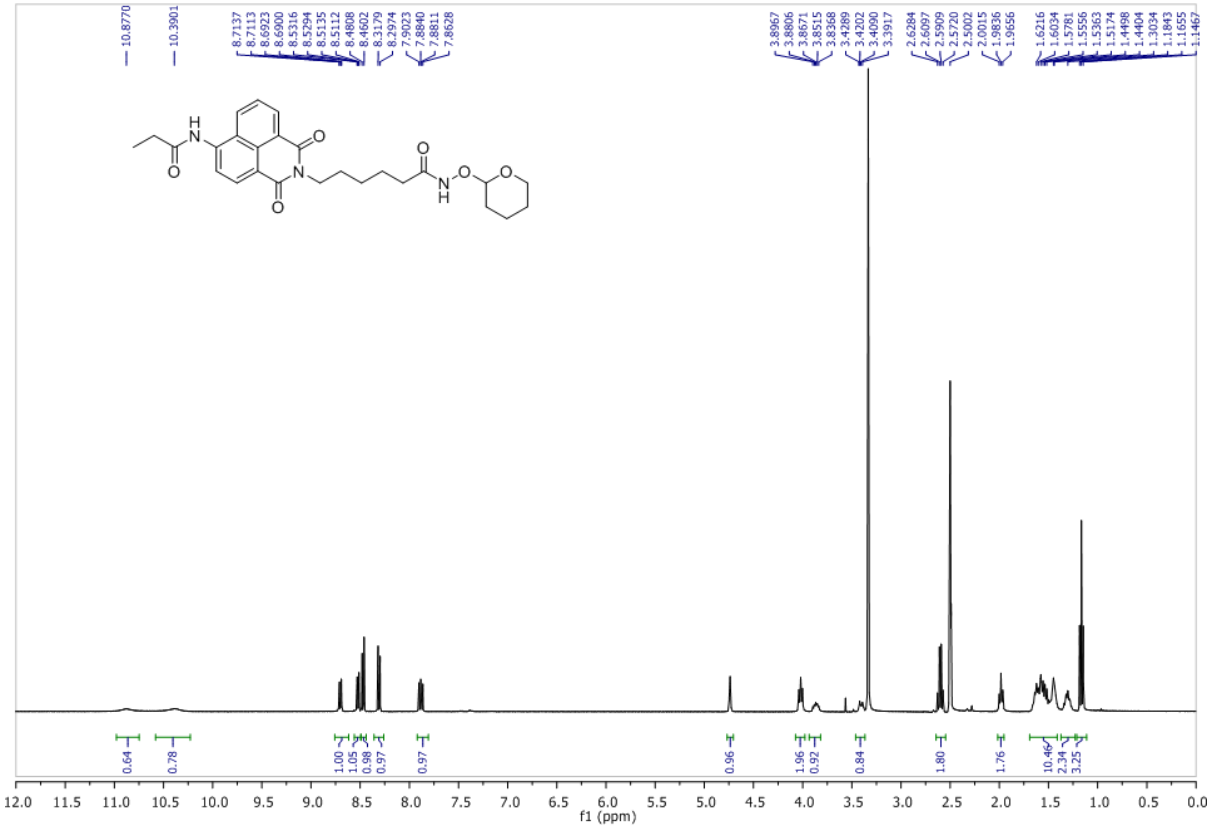


Figure S25 – ^{1}H and ^{13}C NMR of **27**



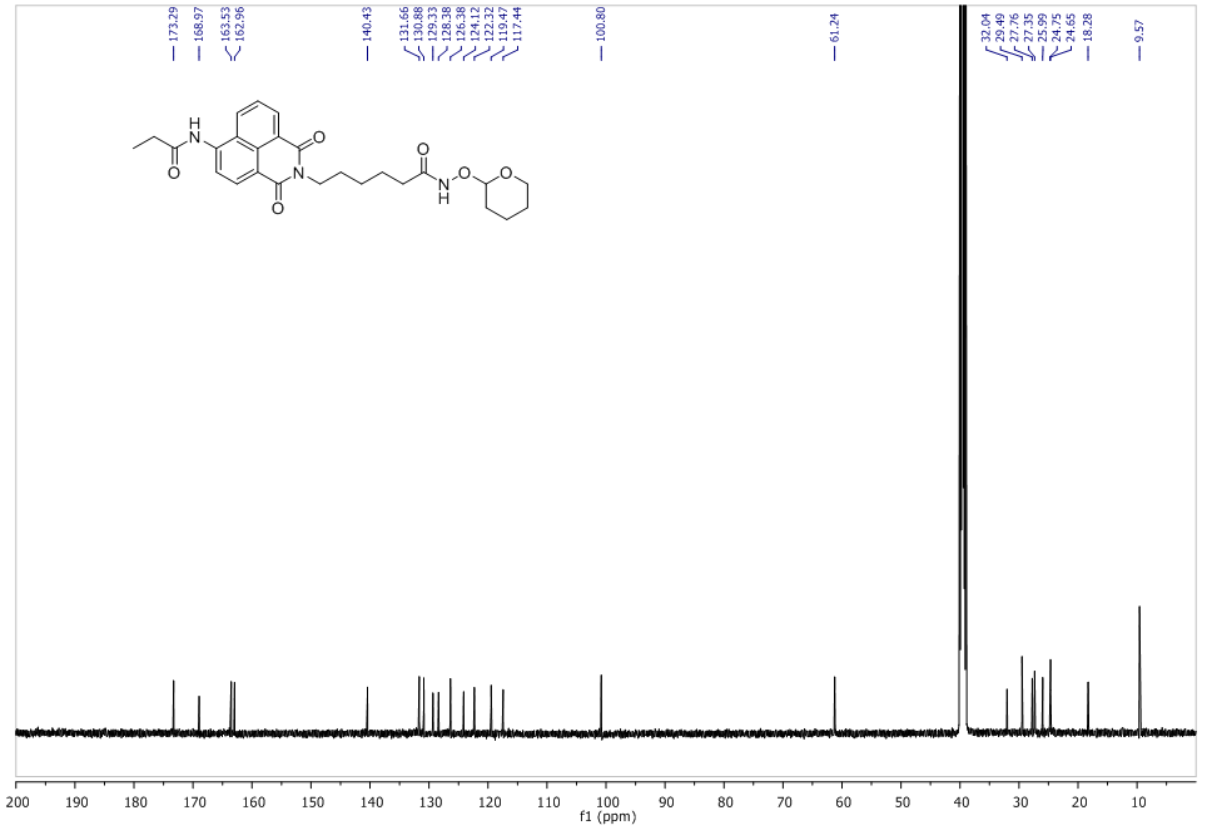
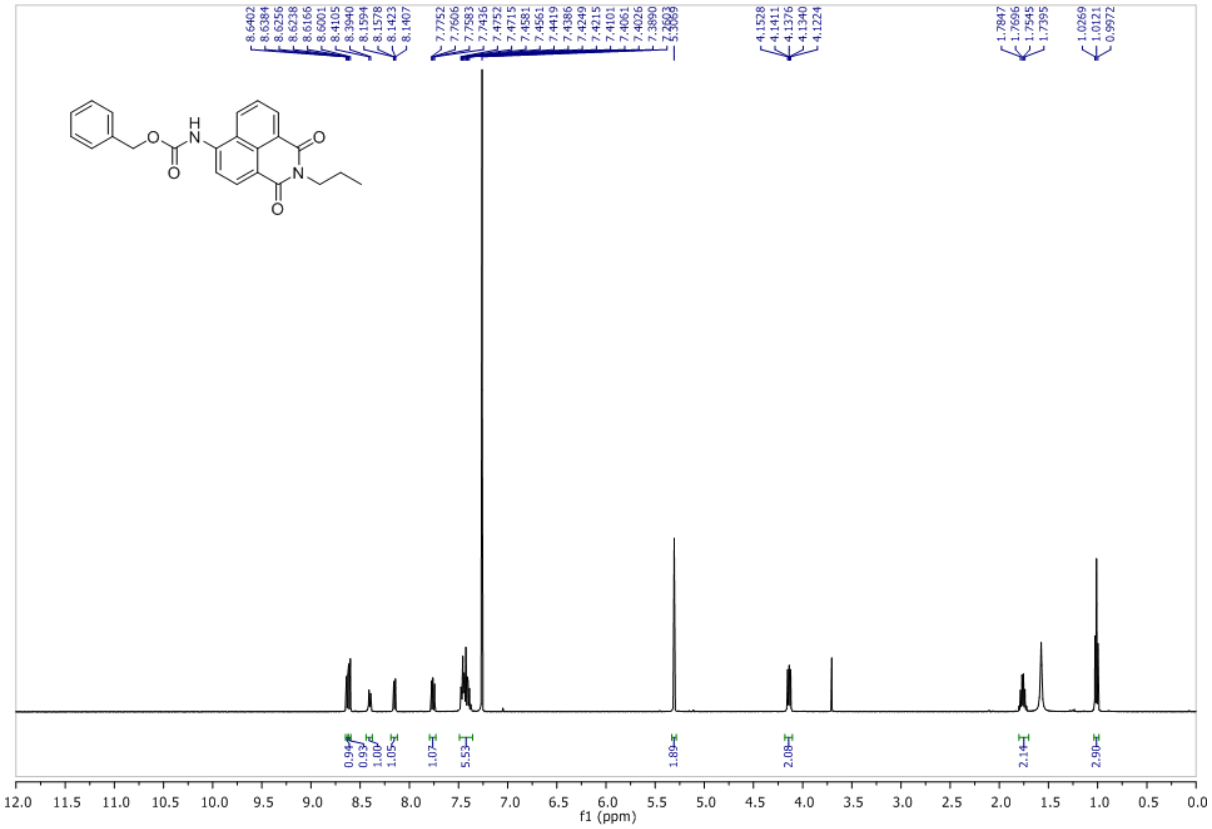


Figure S26 – ^{1}H and ^{13}C NMR of **28**



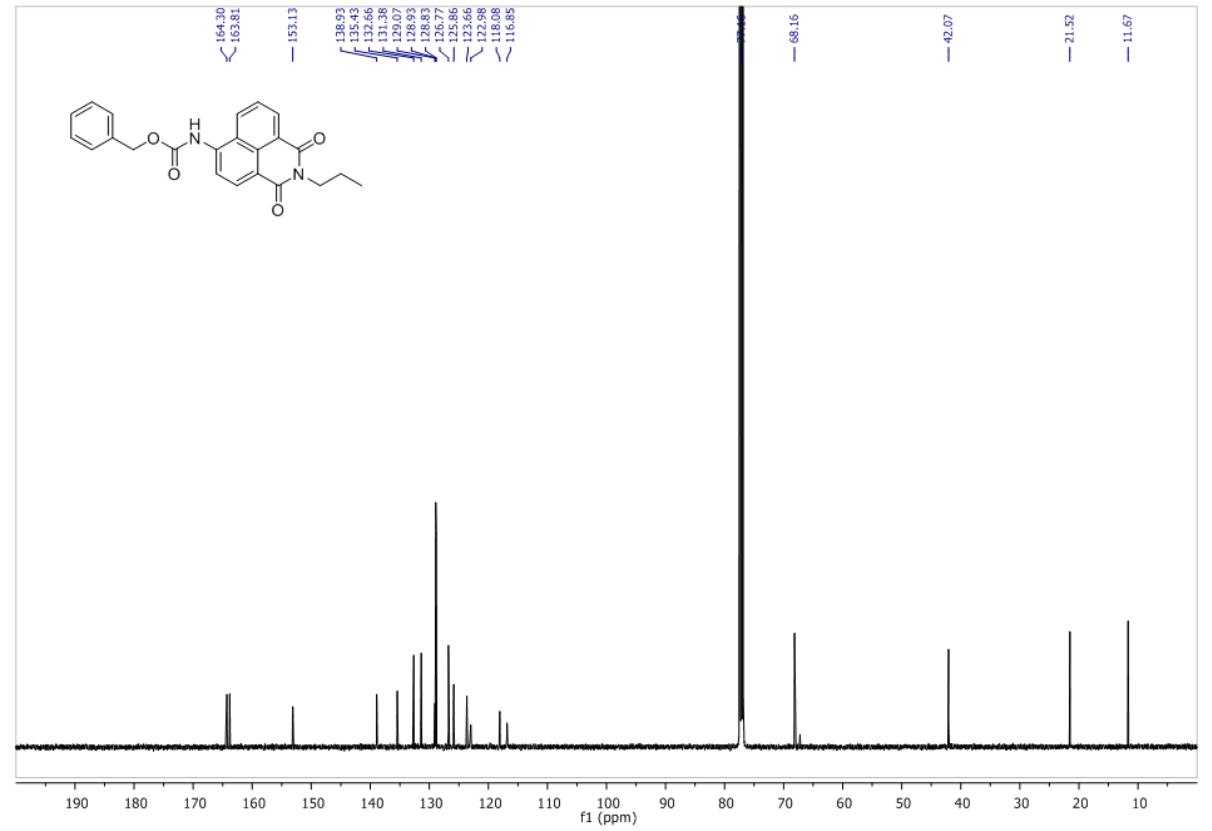
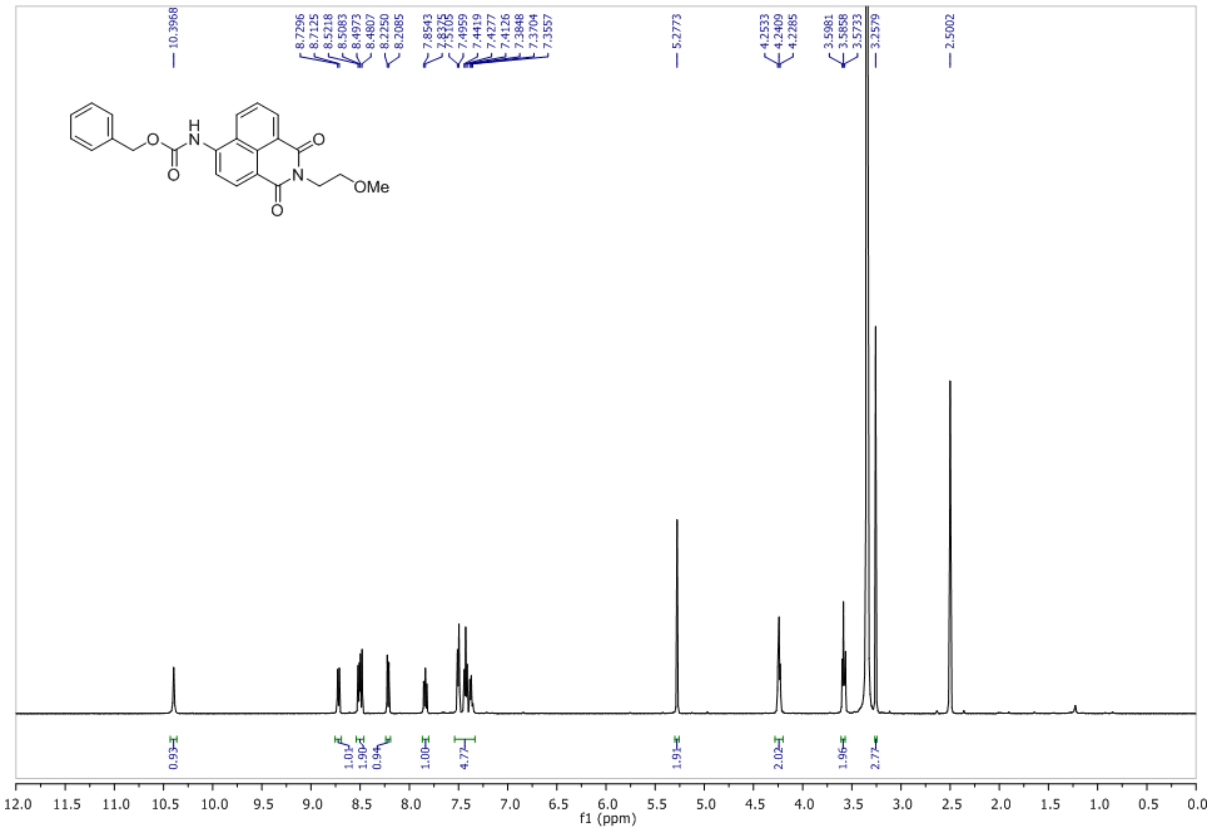


Figure S27 – ^{1}H and ^{13}C NMR of **29**



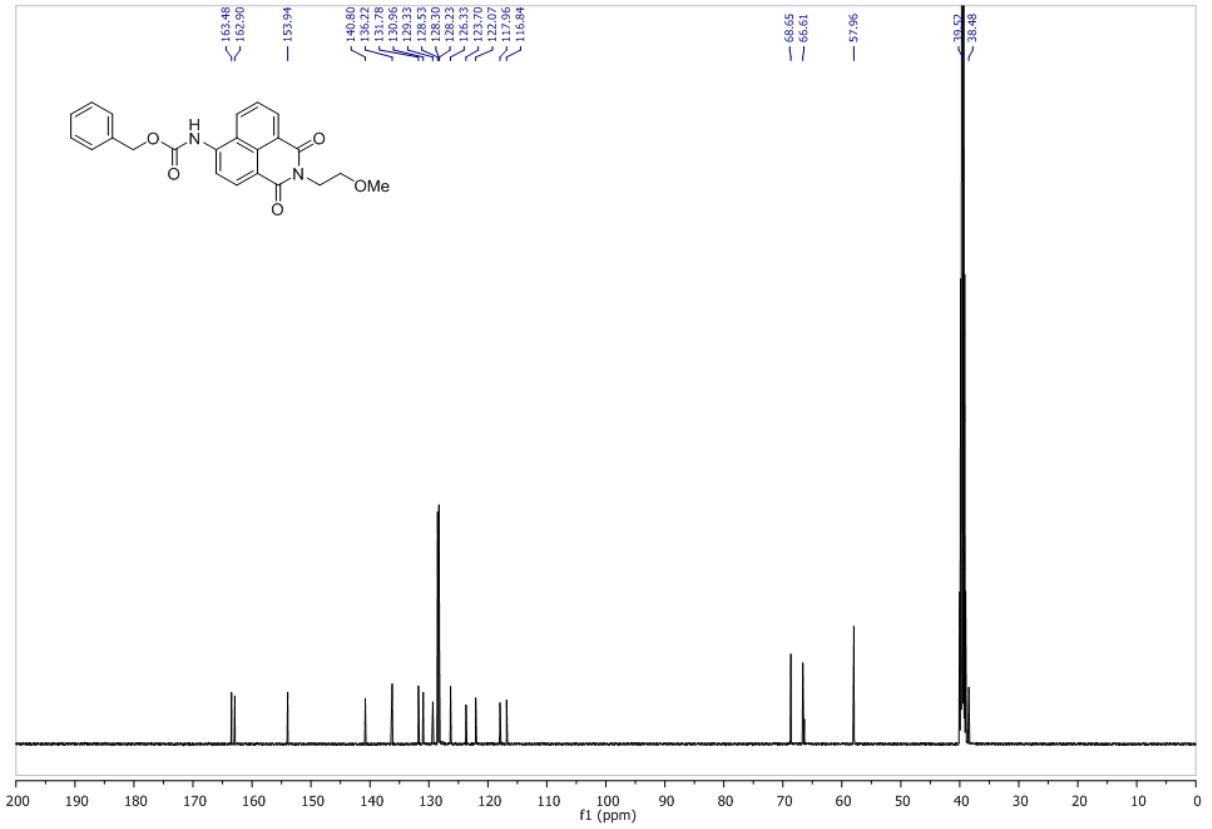
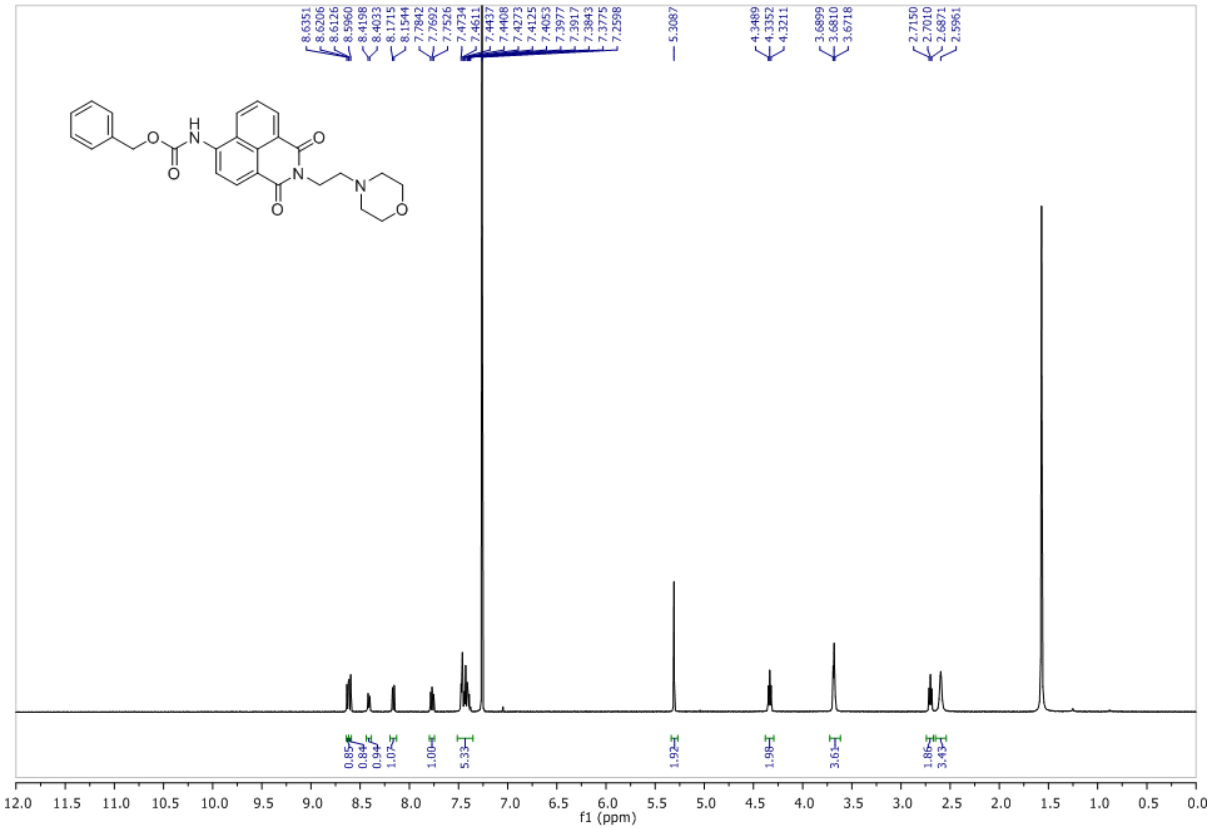


Figure S28 – ^{1}H and ^{13}C NMR of **30**



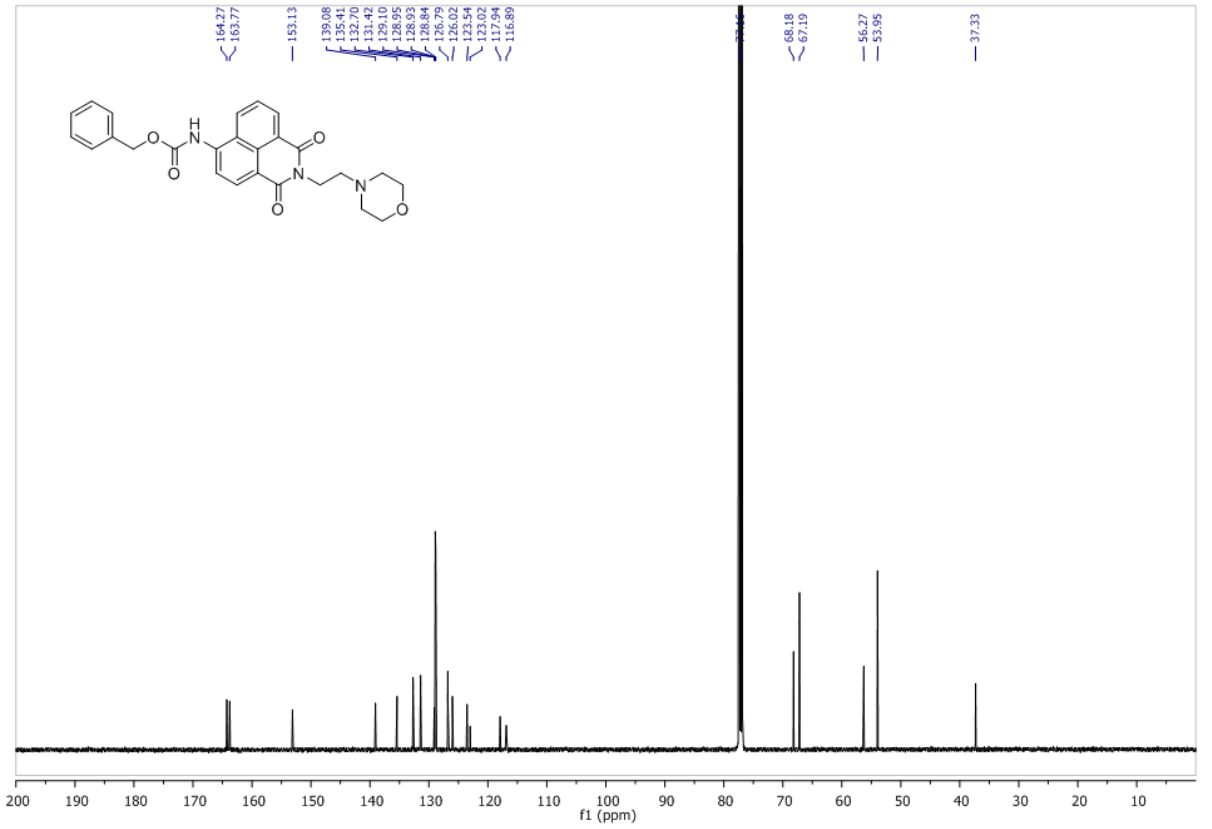
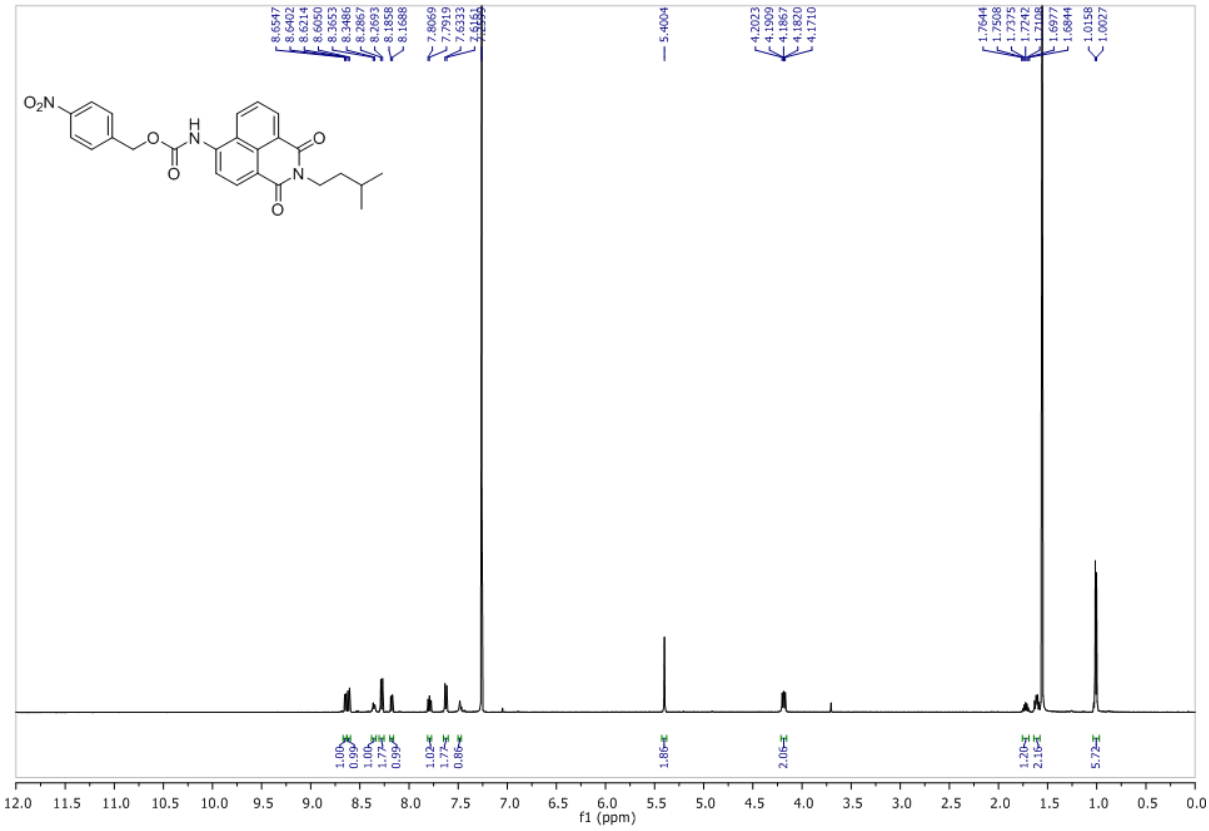


Figure S29 – ^{1}H and ^{13}C NMR of **31**



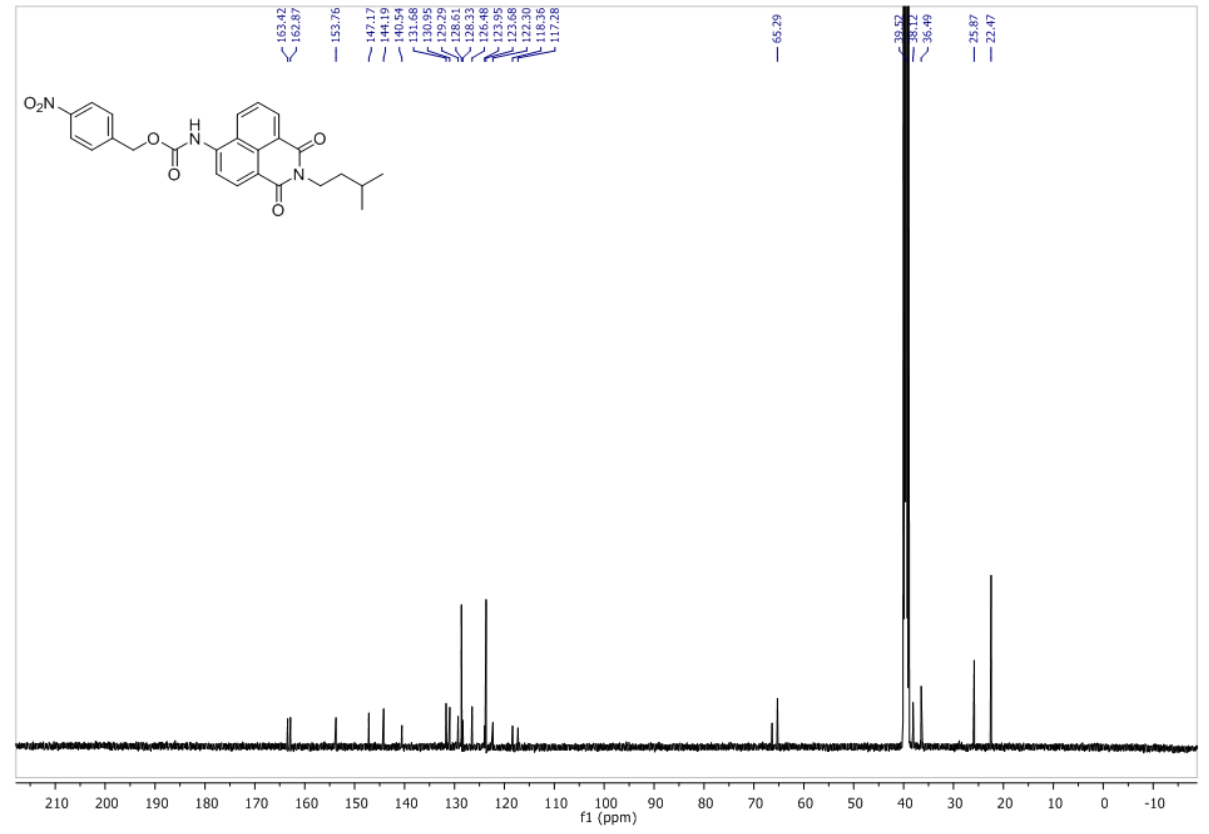
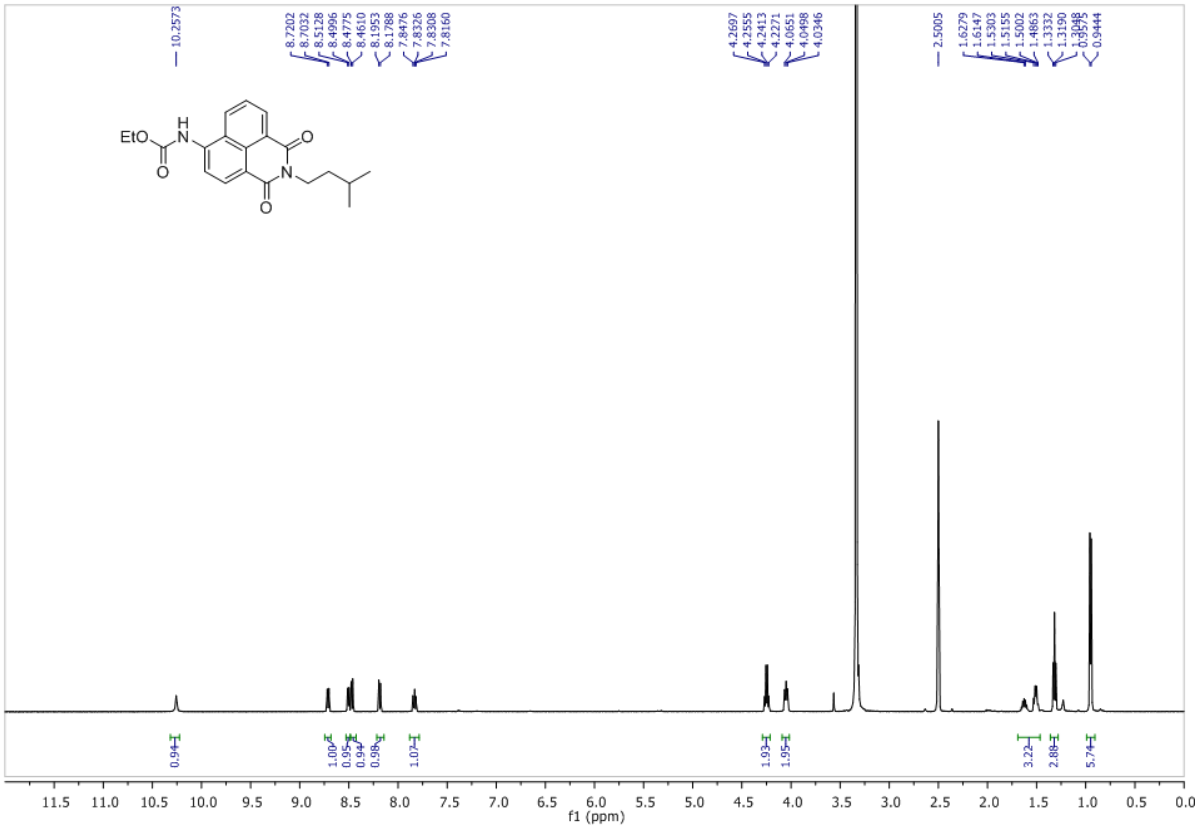


Figure S30 – ^{1}H and ^{13}C NMR of **32**



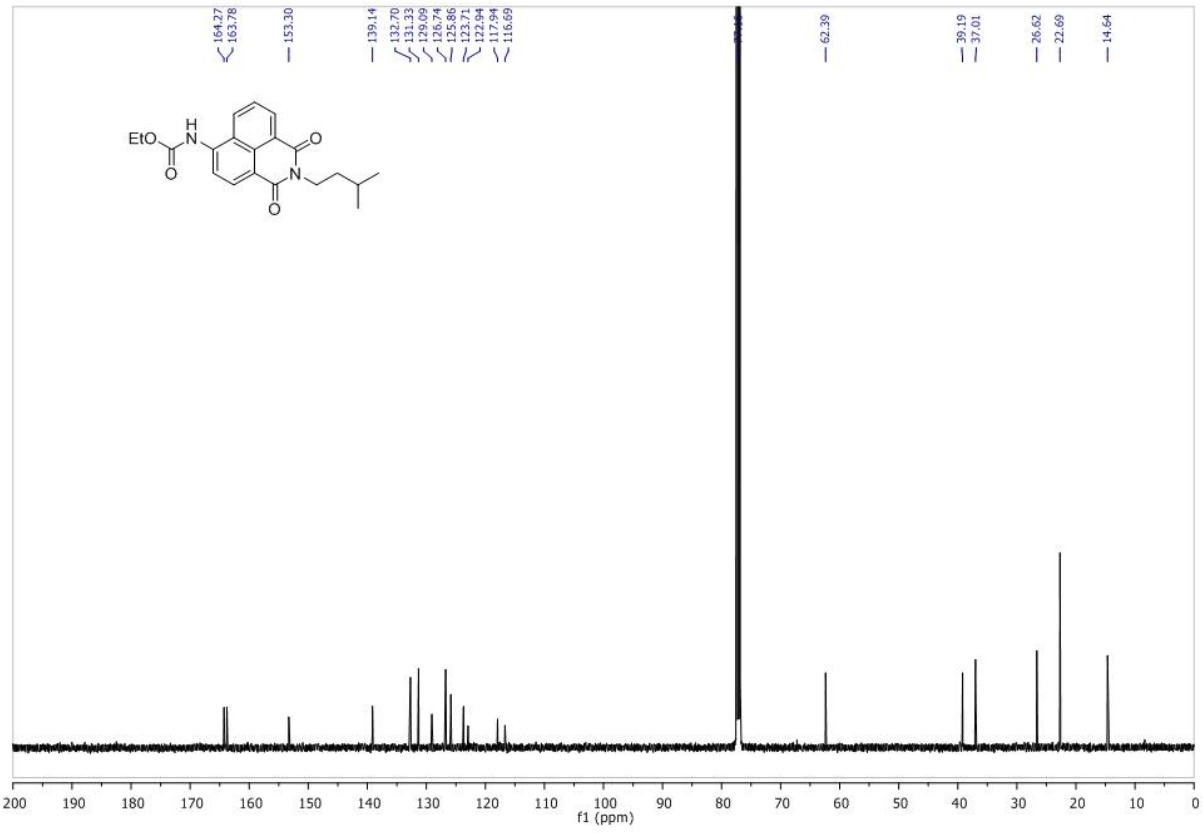
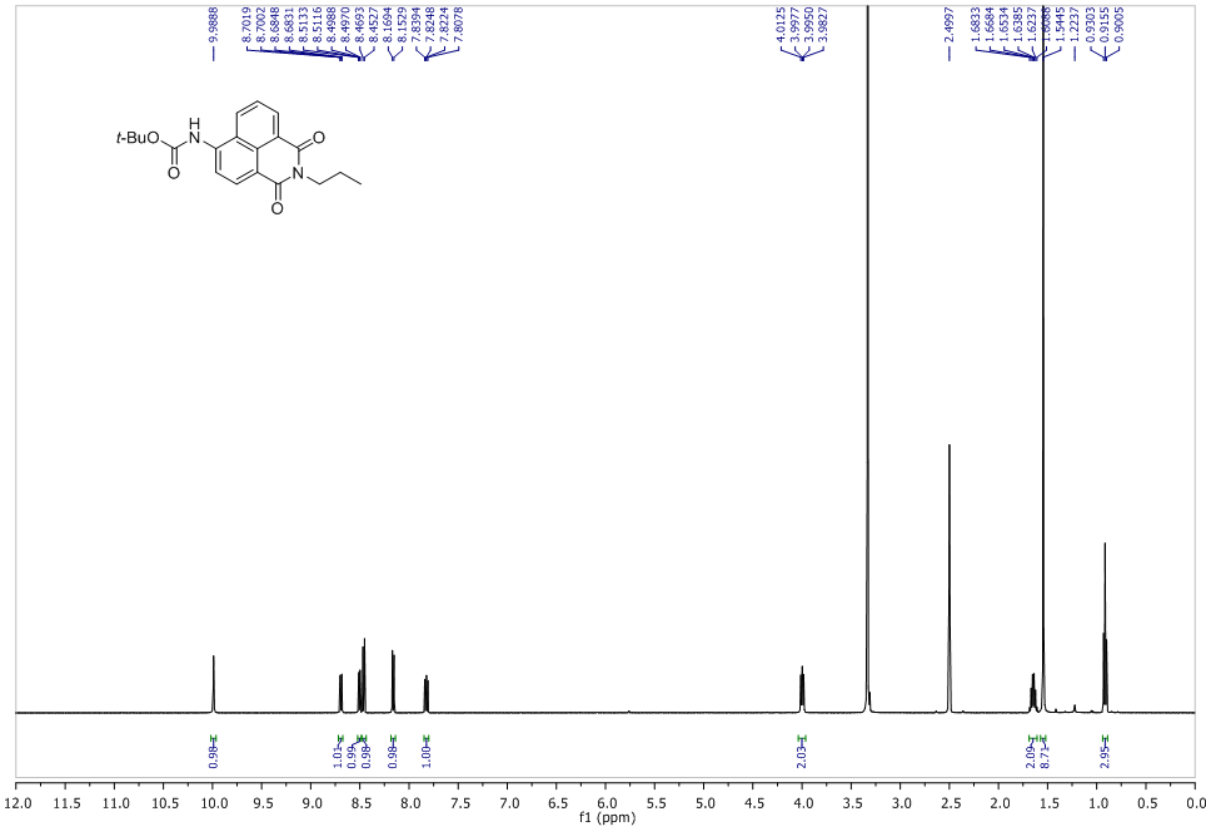


Figure S31 – ^{1}H and ^{13}C NMR of **33**



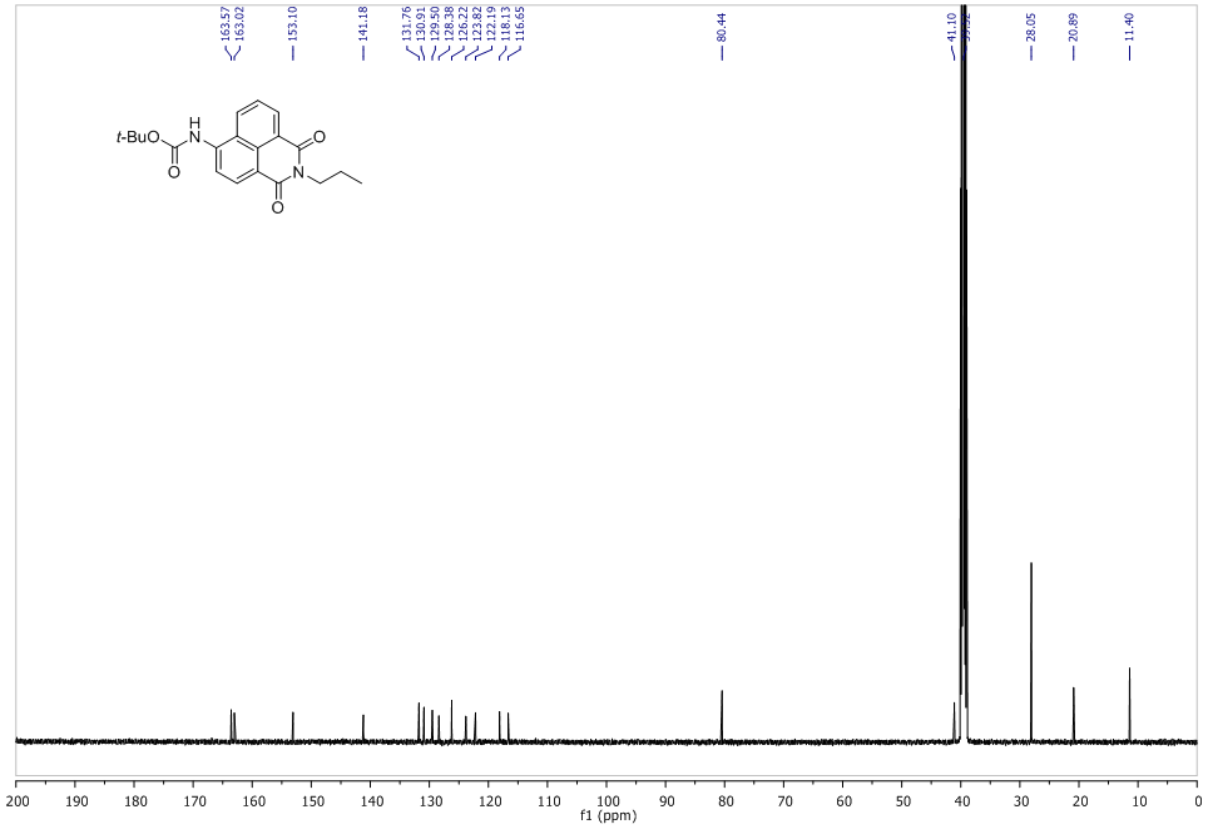
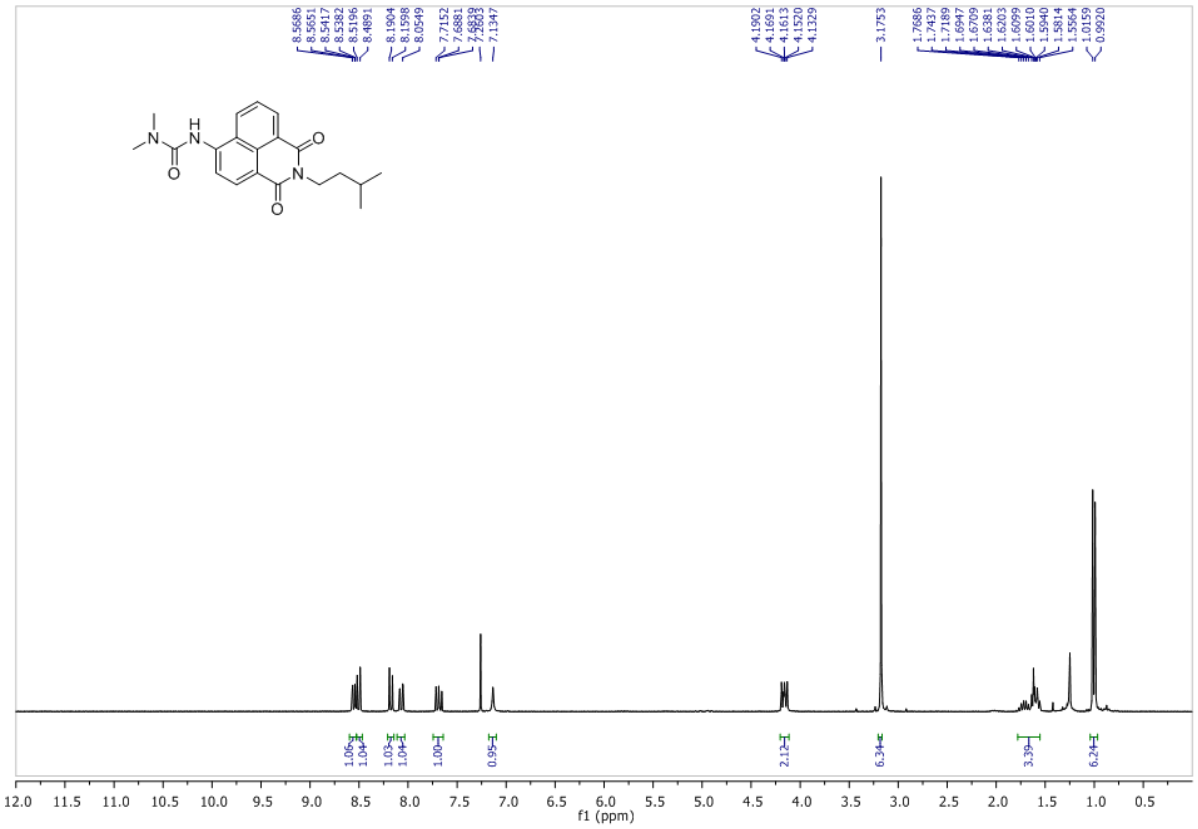


Figure S32 – ^{1}H and ^{13}C NMR of **34**



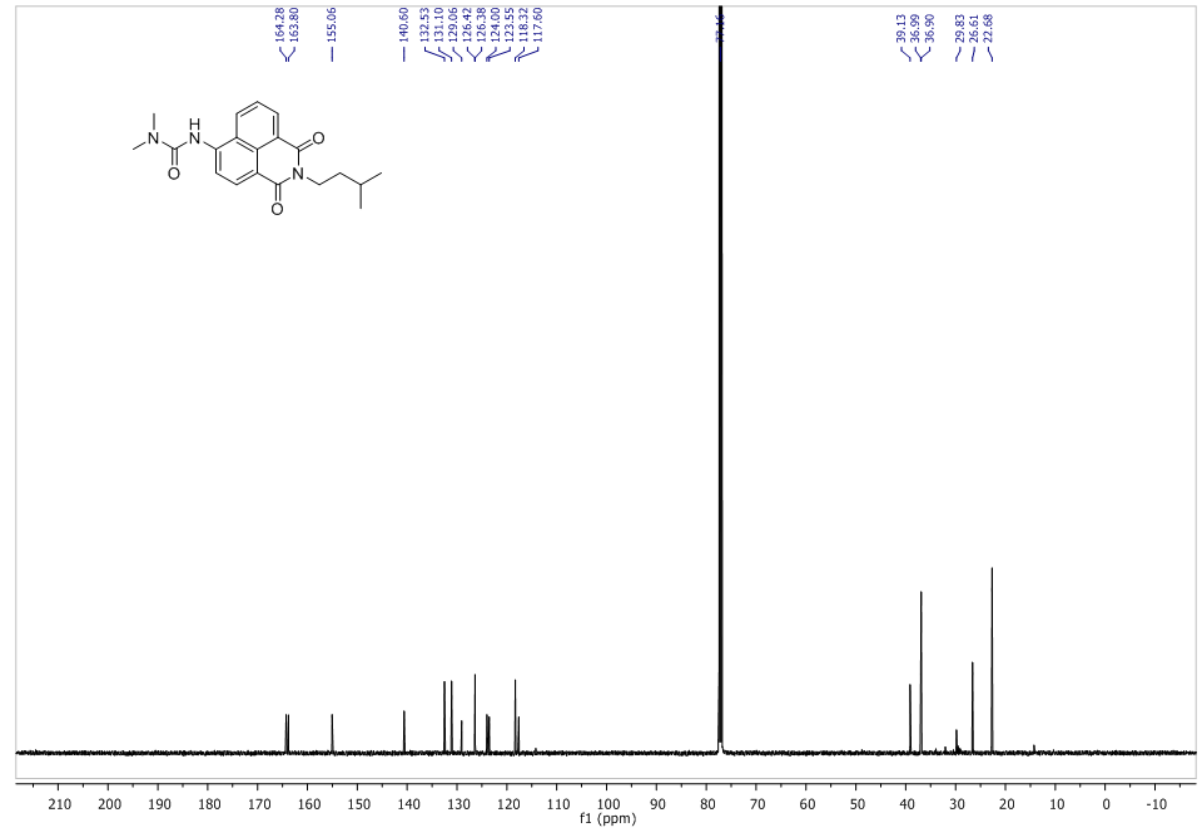
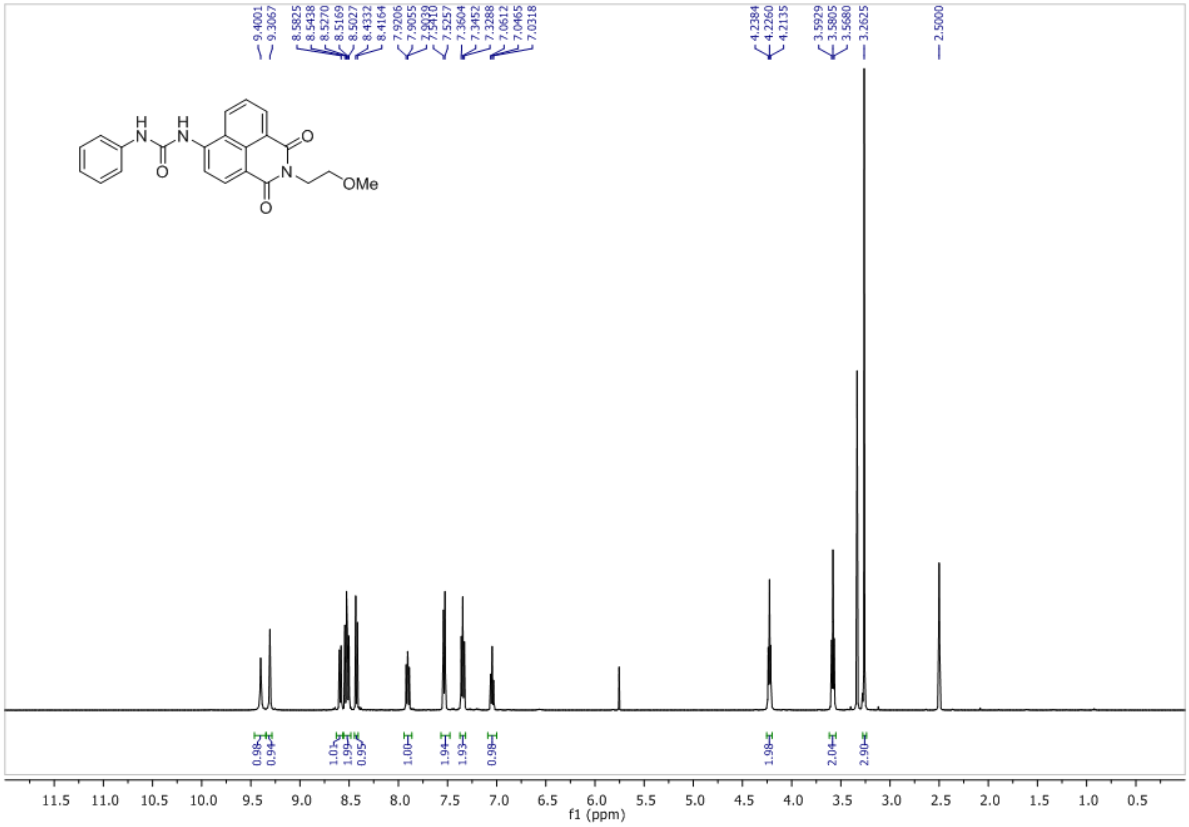


Figure S33 – ^{1}H and ^{13}C NMR of **35**



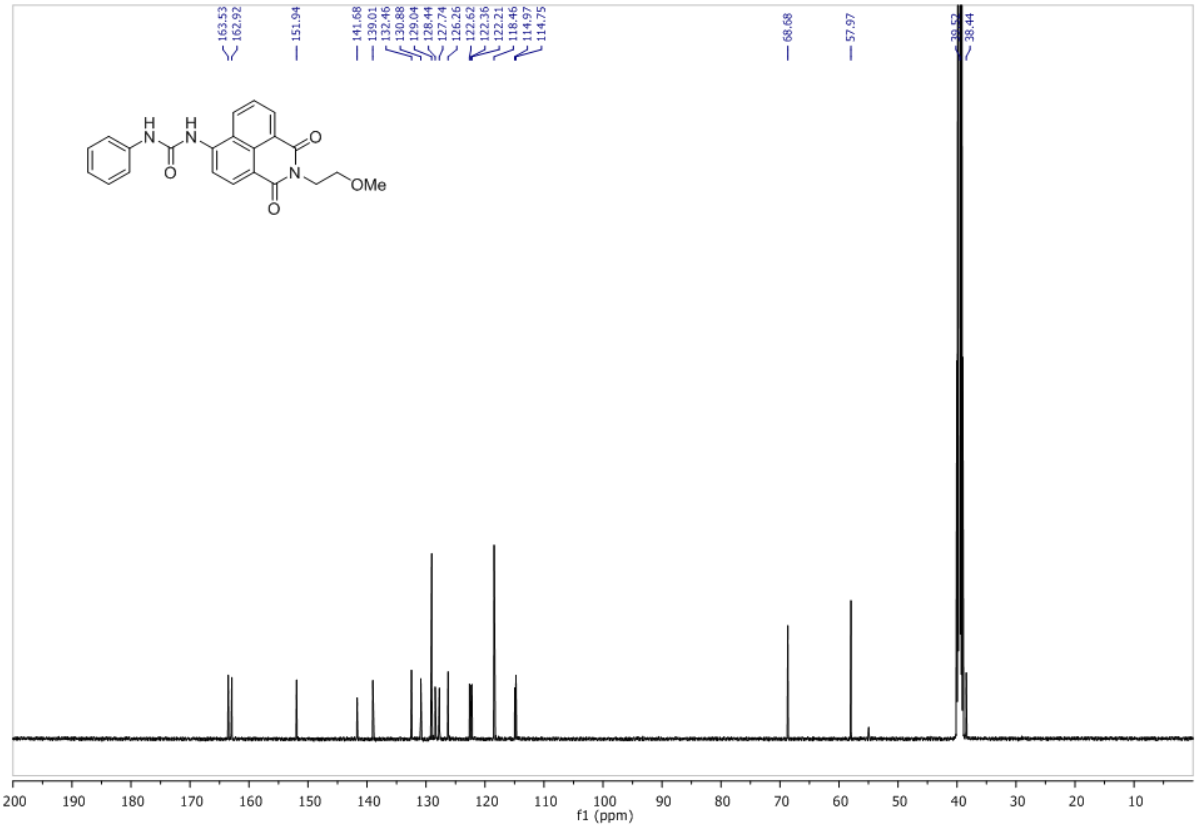
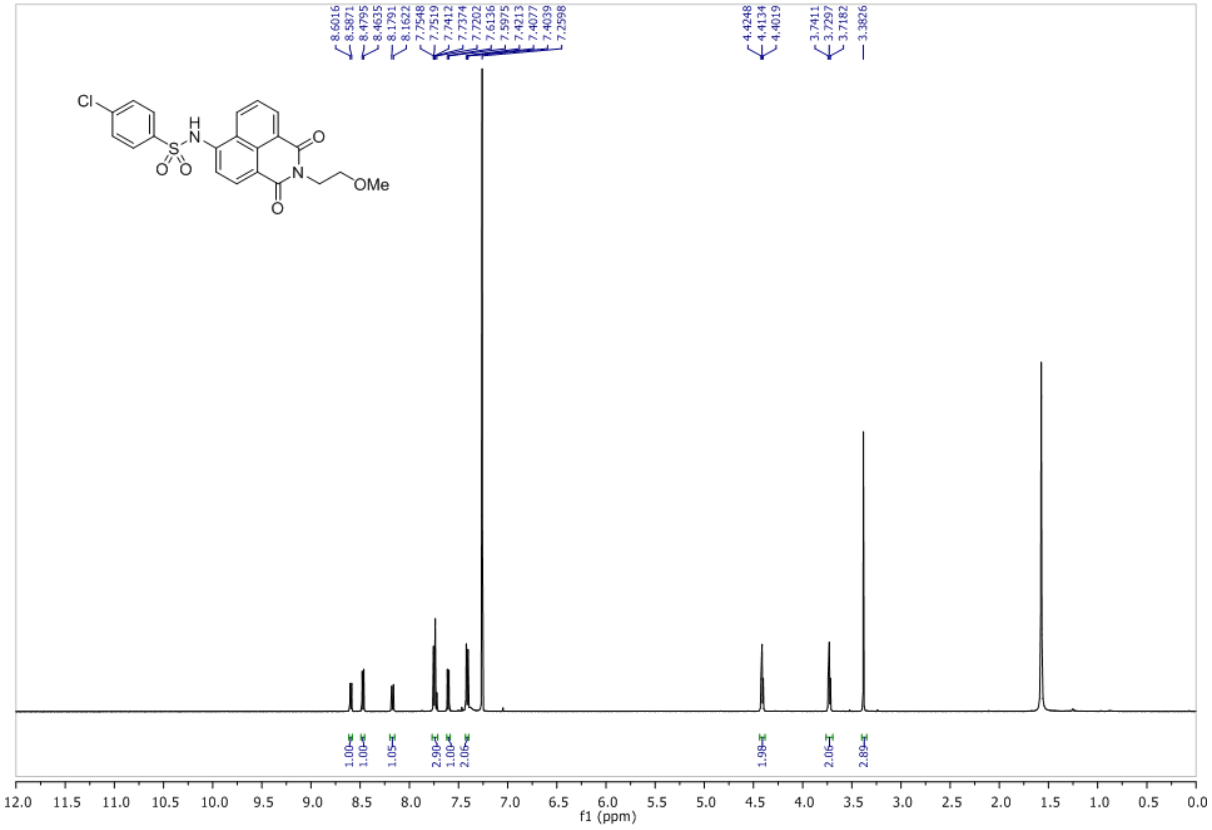


Figure S34 – ^{1}H and ^{13}C (APT) NMR of **36**



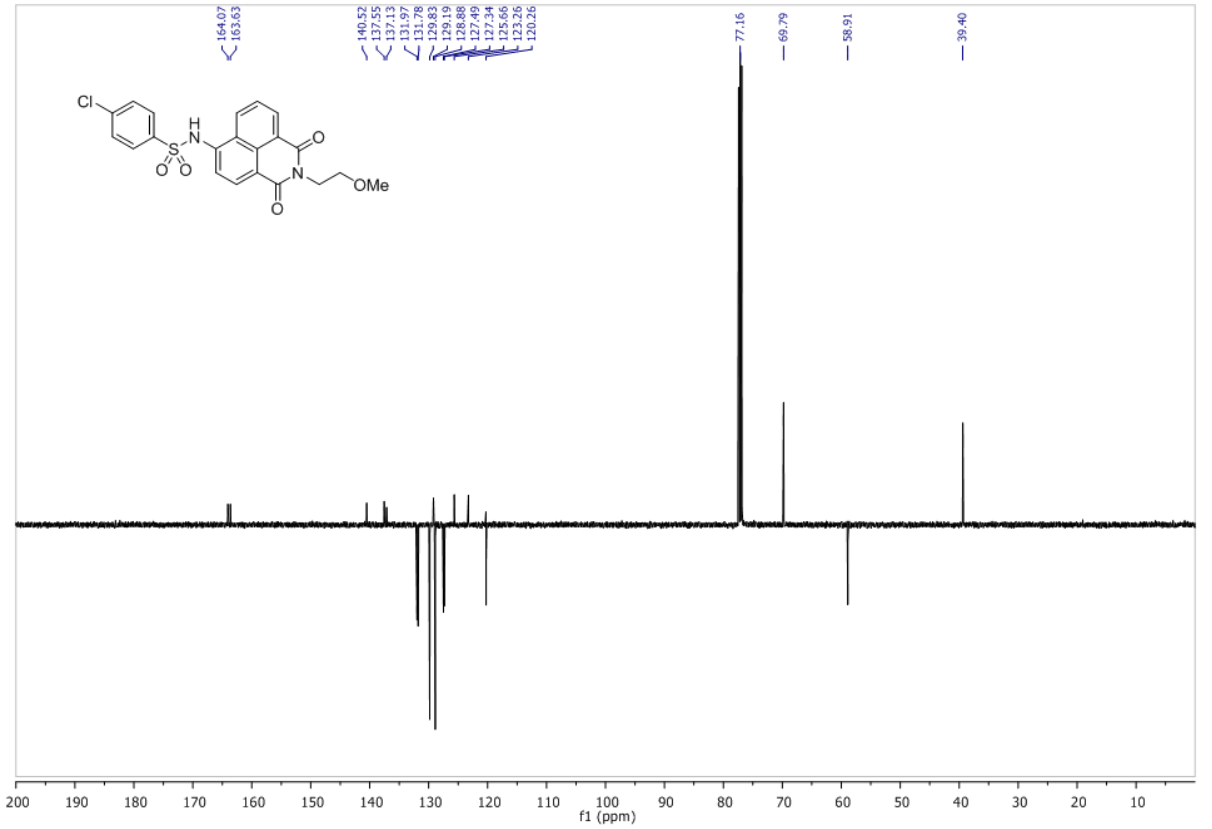
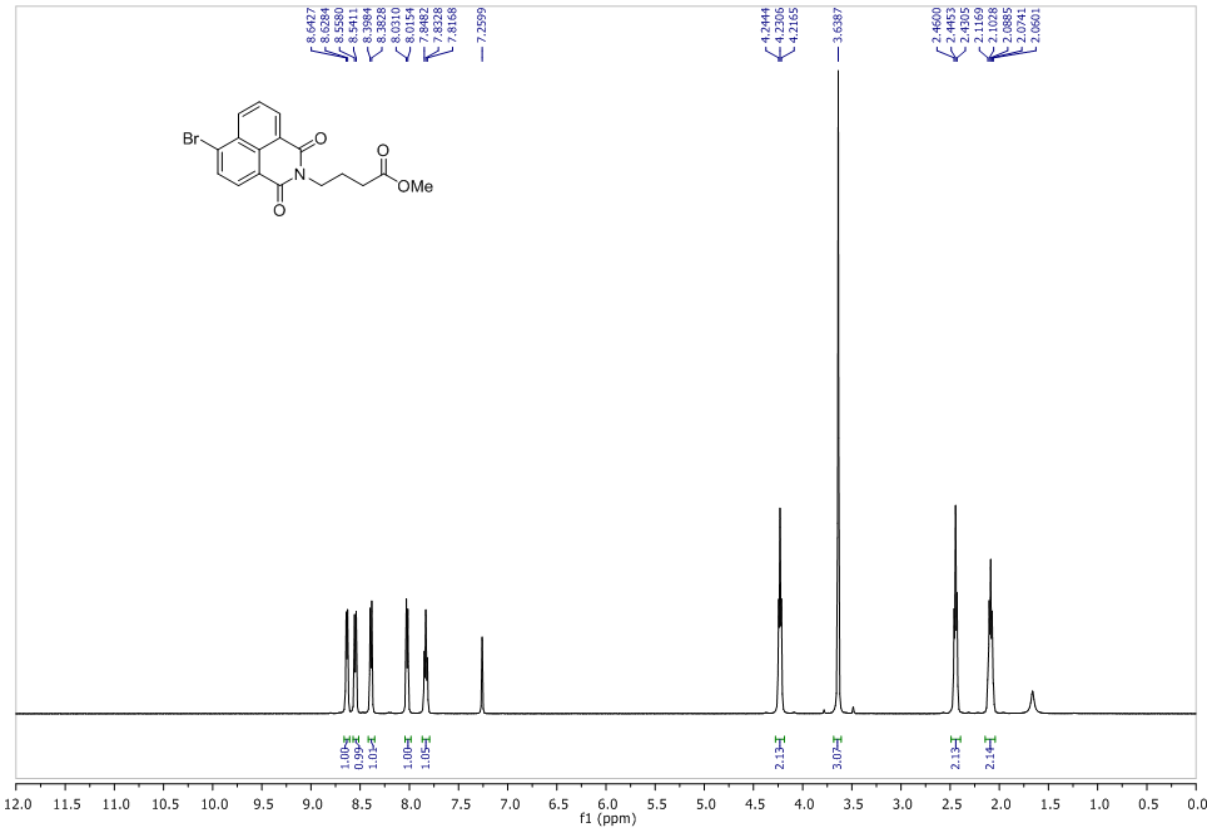


Figure S35 – ^{1}H and ^{13}C NMR of **S2**



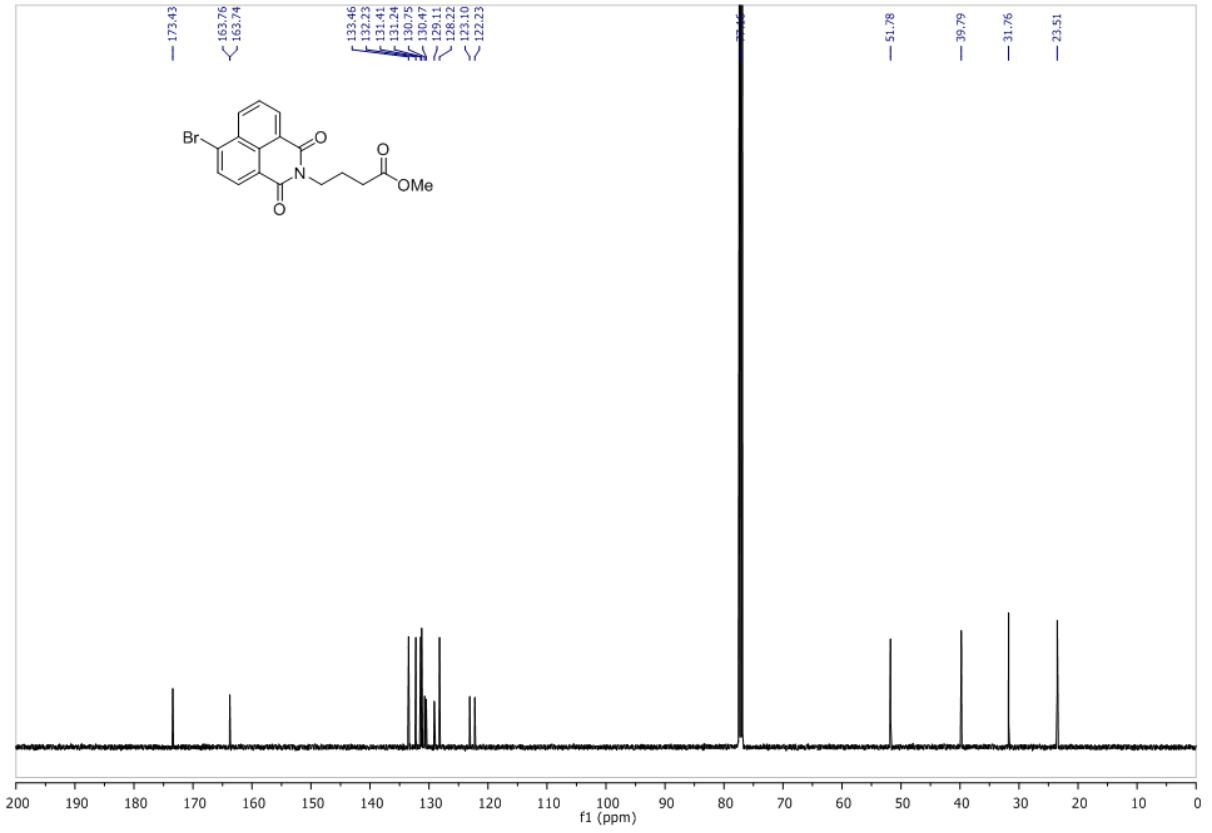
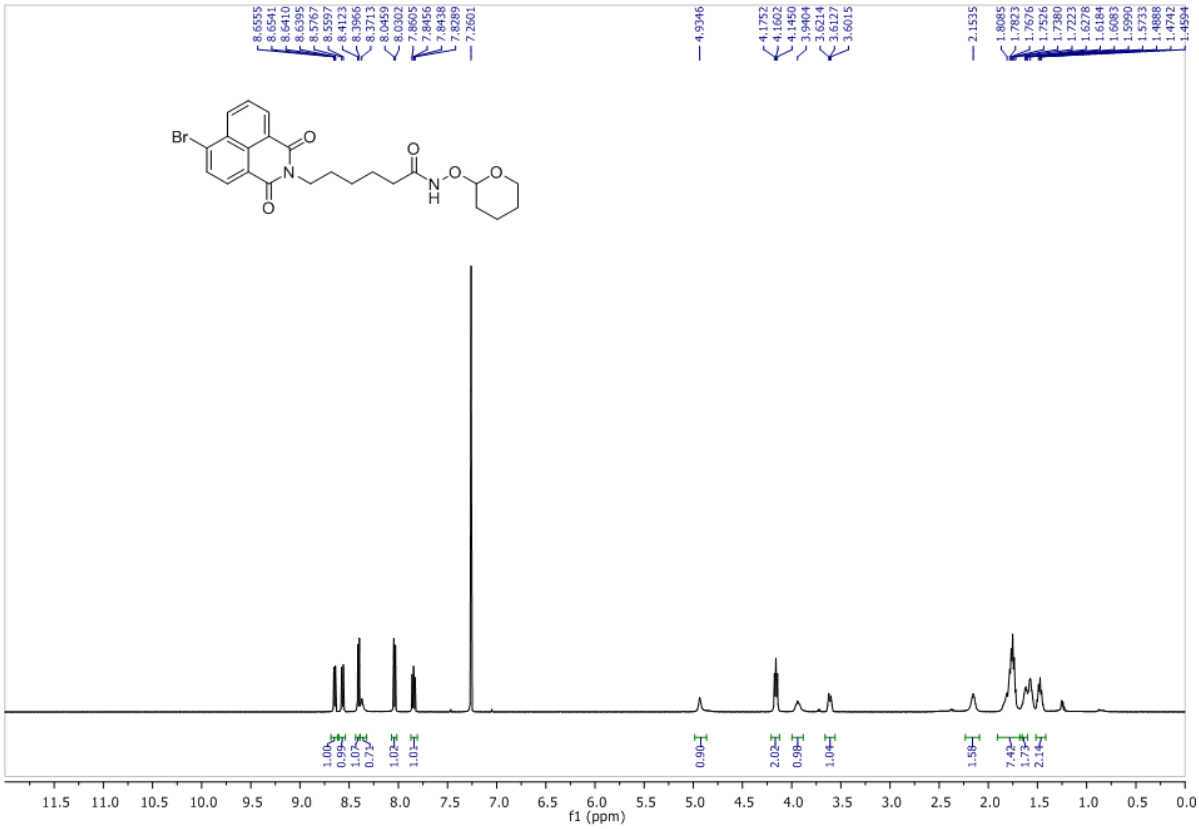


Figure S36 – ^{1}H and ^{13}C NMR of **S10**



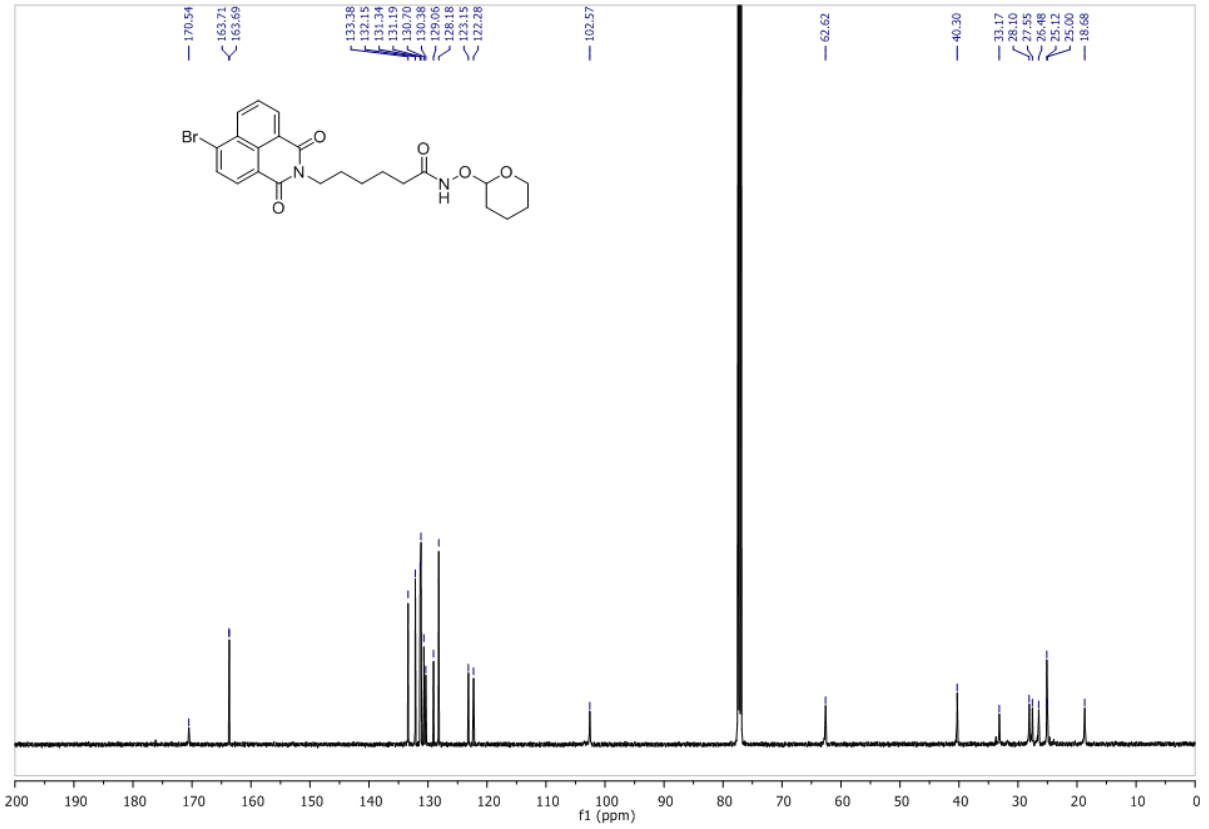
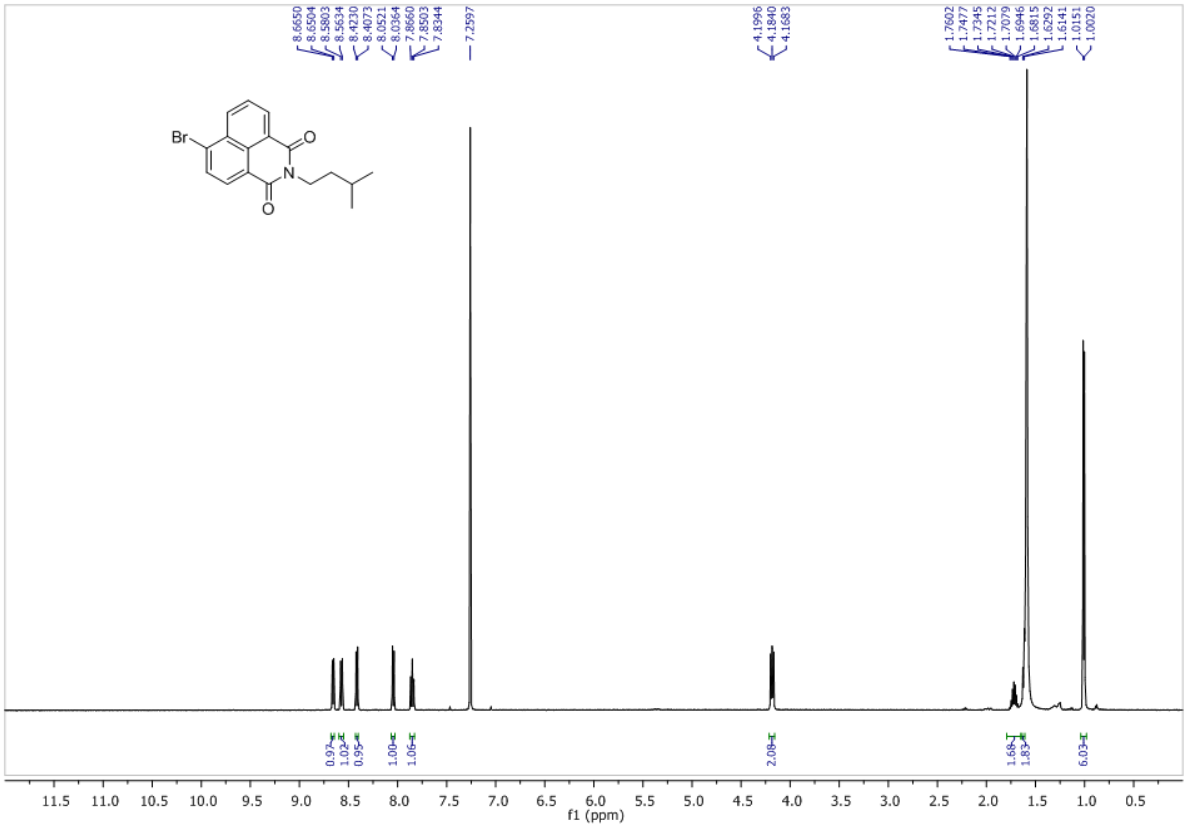


Figure S37 – ^{1}H and ^{13}C NMR of **S11**



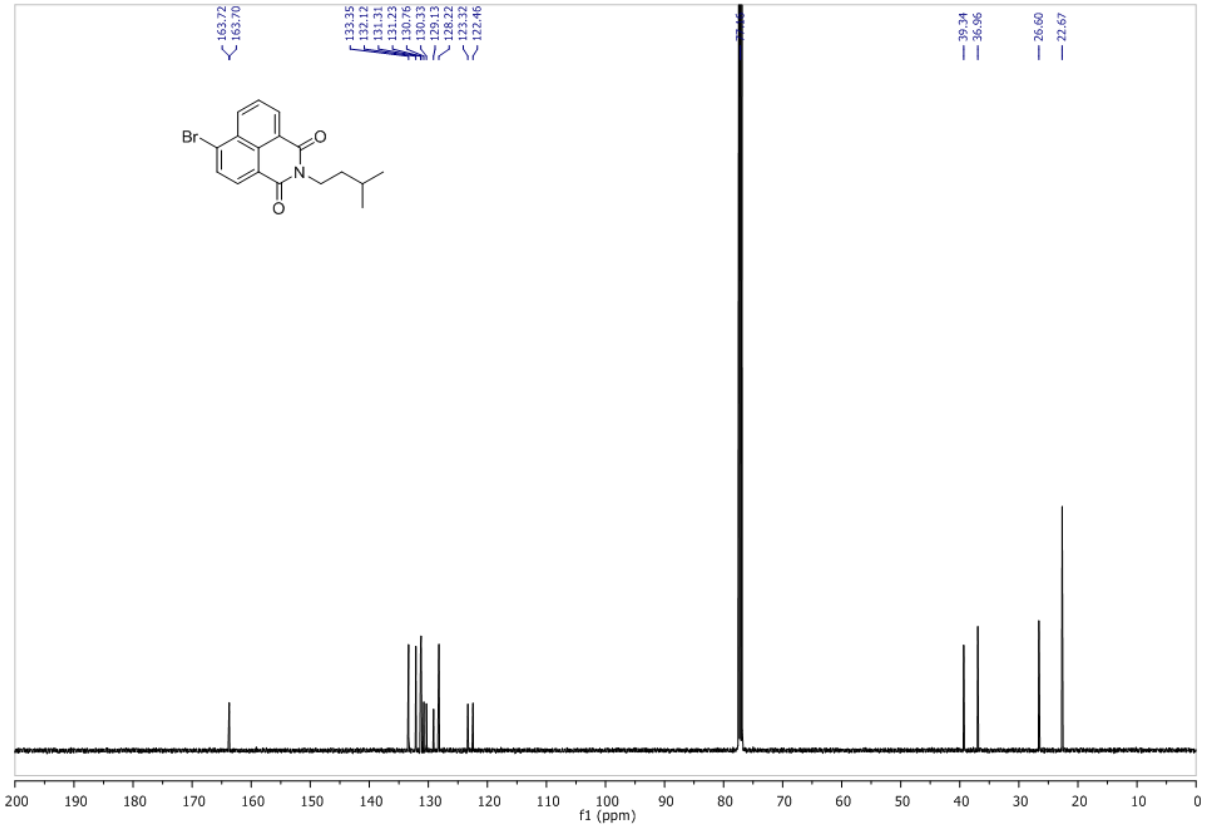


Table S1. Photophysical properties of selected examples.

Entry	Compound	Solvent	Additive	Absorption Properties		Emission Properties					
				λ_{abs} (nm)	ε_M (M^{-1} cm^{-1})	λ_{em} (nm)	Stokes shift (nm)	Stokes shift (cm^{-1})	Φ_F	Brightness[a] (M^{-1} cm^{-1})	Lifetime[b] (ns)
1	**4**	DMSO	-	364	17,800	469	105	6,151	0.33	5,900	-
2	"	DMSO	NaOH	489	24,800	583	94	3,297	0.44	10,900	-
3	**6**	DMSO	-	366	15,500	462	96	5,677	0.05	500	0.56
4	"	DMSO	NaOH	497	23,700	575	78	2,729	0.69	**16,300**	6.91
5	**7**	DMSO	-	368	16,400	461	93	5,482	0.04	700	0.22
6	"	DMSO	NaOH	486	23,000	574	88	3,155	0.25	5,800	2.08
7	**8**	DMSO	-	359	16,000	-[c]	-	-	-	-	-
8	"	DMSO	NaOH	520	26,500	535	15	539	0.22	5,800	3.47
9	**9**	DMSO	-	365	17,100	-[c]	-	-	-	-	-
10	"	DMSO	NaOH	501	26,500	-[c]	-	-	-	-	-
11	**10**	DMSO	-	367	18,000	474	107	6,151	0.52	9,400	-
12	"	DMSO	NaOH	493	26,000	587	94	3,248	0.36	9,400	-
13	**11**	DMSO	-	365	15,000	466	101	5,938	0.07	1,100	-
14	"	DMSO	NaOH	493	23,800	575	82	2,893	0.67	15,500	9.46
15	**13**	DMSO	-	372	13,900	468	96	5,514	0.45	6,300	-
16	"	DMSO	NaOH	464	16,000	575	111	4,160	0.23	3,700	-
17	**18**	DMSO	-	375	16,000	465	90	5,161	0.68	10,900	4.57
18	"	DMSO	NaOH	498	20,900	589	91	3,102	0.38	7,900	5.30

Entry	Compound	Solvent	Additive	Absorption Properties		Emission Properties					
				λ_{abs} (nm)	ε_M (M^{-1} cm^{-1})	λ_{em} (nm)	Stokes shift (nm)	Stokes shift (cm^{-1})	Φ_F	Brightness[a] (M^{-1} cm^{-1})	Lifetime[b] (ns)
19	**23**	DMSO	-	355	30,200	463	108	6,571	0.13	3,900	0.68 (77%), 3.01 (33%)
20	"	PB[d]	-	347	7,800	470	123	7,542	0.65	5,100	5.58
21	"	CH_2Cl_2	-	353	12,100	440	87	5,601	0.91	11,000	5.42
22	**36**	DMSO	HCl	359	27,600	545	186	9,507	0.57	15,700	-
23	"	DMSO	NaOH	455	4,700	543	88	3,562	0.69	3,200	-
24	"	CH_2Cl_2	-	355	27,600	440	85	5,442	0.52	14,400	-

a) Brightness = $\varepsilon_M \times \Phi_F$; b) Fluorescence decay profiles satisfactorily fitted with a single exponential decay function apart from entry 19 which required a bi-exponential function. % contribution to initial decay amplitude of each lifetime component in parentheses; c) Non-fluorescent; d) PB = Sodium phosphate buffer (100 mM) at pH 7.4.

Photophysical materials and methods

Absorbance spectra were recorded on a Cary 60 UV-visible spectrophotometer (Agilent) in 1.0 cm quartz cuvettes. Steady-state fluorescence measurements were taken on a Cary Eclipse fluorescence spectrophotometer (Agilent) with emission intensity corrected for detector efficiency as a function of wavelength. Solvents were of highest purity available and used as received (CH_2Cl_2,, Aldrich; DMSO, EtOH, Merck). Fluorescence quantum yields were determined using the comparative method with Rhodamine 6G, (Φ_F = 0.95 in EtOH)[15] as the reference standard. Solutions were prepared in 1.0 cm quartz cuvettes, with absorbance maxima less than 0.10 in order to prevent inner filter effects. Samples were deoxygenated by bubbling with N_2 for 20 minutes immediately prior to measurement of fluorescence emission spectra.

Time-resolved fluorescence decays were measured on a previously described home built set-up.[16] Briefly, excitation was provided by a pulse-picked supercontinuum fiber laser (Fianium, SC 400-4-pp) with excitation wavelength selected using 10 nm band pass filters (Chroma). Emission was passed through a monochromator (CVI, dk480) and detected by a microchannel plate photomultiplier tube (Hamamatsu, R3809U-50). Emission times were recorded and histogrammed using a photon counting device (Picoquant, PicoHarp 300) with a trigger diode assembly (PicoQuant, TDA 200) to provide the start signal and the stop signal being from the microchannel plate. Decay histograms were fit by exponential decay components convolved with the instrument response function (typically ~90–100 ps, recorded using a scattering solution of dilute milk powder in water) using home written software based on the Marquardt algorithm. Goodness-of-fit of the data by the fitting function was determined by the χ^2 fitting parameter and the distribution of the residuals (data minus fit).

Single molecule samples of **6** were prepared by serial dilution into 1% solution of PVA (Aldrich) in water (MilliQ) that had excess base (2M NaOH, Aldrich) added to ensure **6** was deprotonated, until a final concentration of ~100 pM to 1 nM. Samples were spin-cast onto

thoroughly cleaned glass cover slips at 2000 rpm for 60 seconds yielding a film thickness of ~100–200 nm. Widefield imaging was achieved using a previously described set up,[17] with excitation from a 532 nm diode laser (Dragon lasers) directly coupled into an IX71 microscope frame (Olympus) and focussed onto the back focal plane (Köhler illumination) of a 100× 1.3 N.A. oil immersion objective (Olympus). Emission was passed through dichroic and longpass filters (Chroma) to reject scattered excitation light and imaged on an EMCCD camera (Andor, iXon Ultra-897).

Figure S38 – Normalised absorption and emission spectra of **4** in DMSO

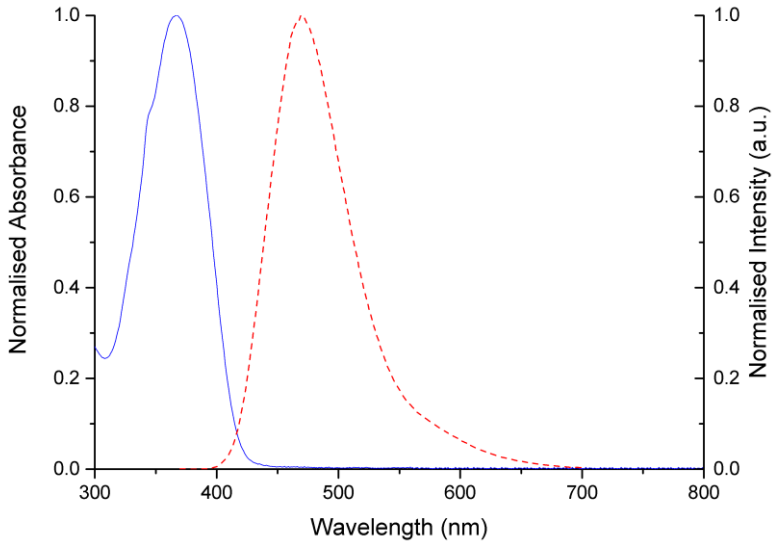


Figure S39 – Normalised absorption and emission spectra of **4** in DMSO with NaOH

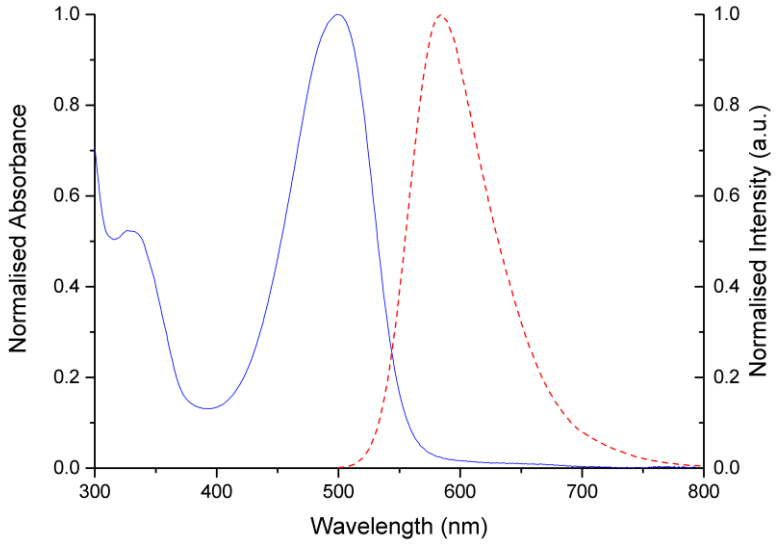


Figure S40 – Normalised absorption and emission spectra of **6** in DMSO

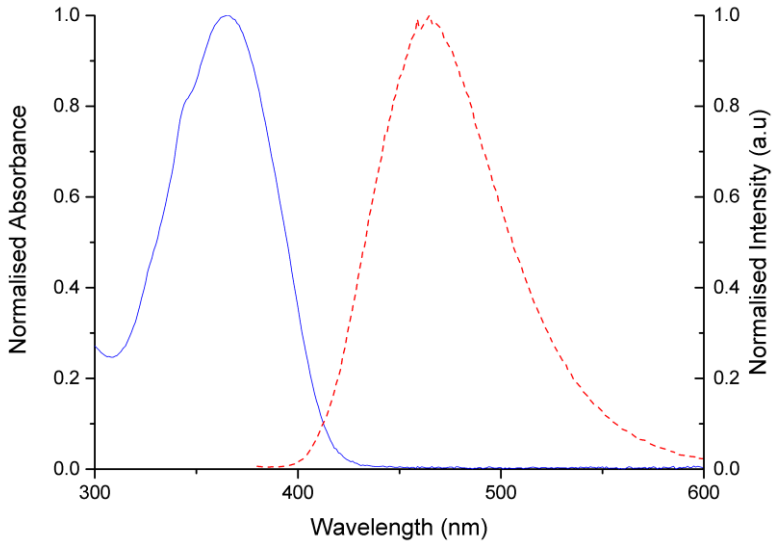


Figure S41 – Normalised absorption and emission spectra of **6** in DMSO with NaOH

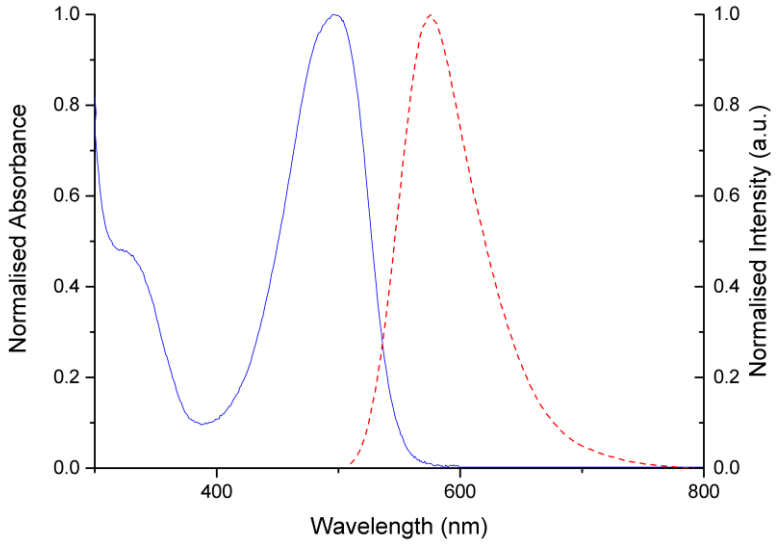


Figure S42 – Normalised absorption and emission spectra of **7** in DMSO

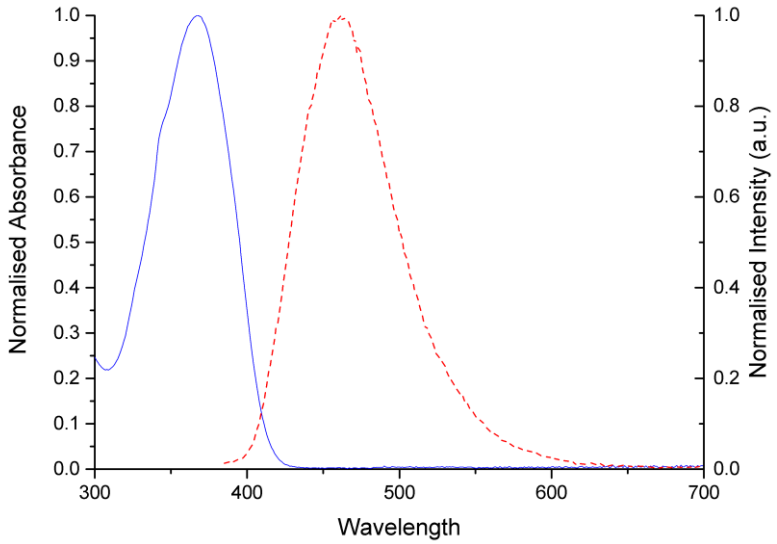


Figure S43 – Normalised absorption and emission spectra of **7** in DMSO with NaOH

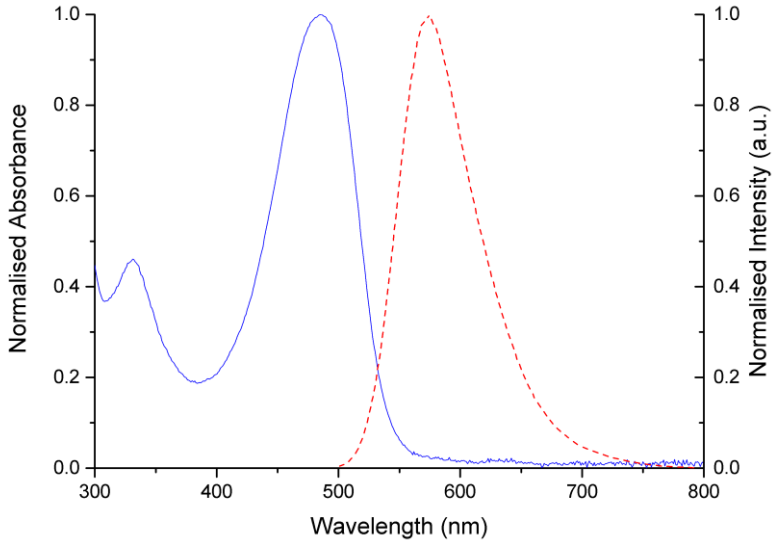


Figure S44 – Normalised absorption spectra of **8** in DMSO

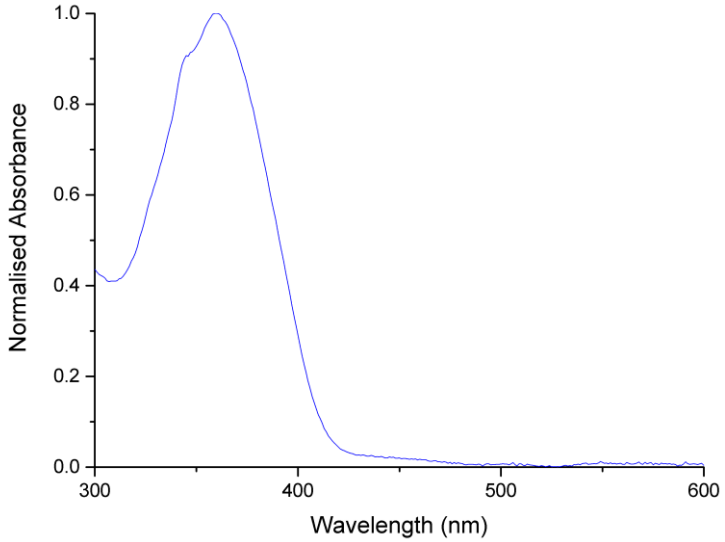


Figure S45 – Normalised absorption and emission spectra of **8** in DMSO with NaOH

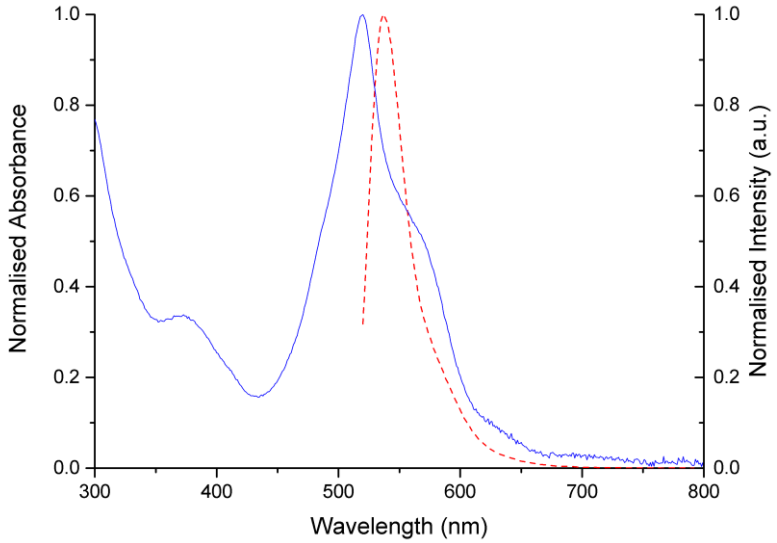


Figure S46 – Normalised absorption spectra of **9** in DMSO

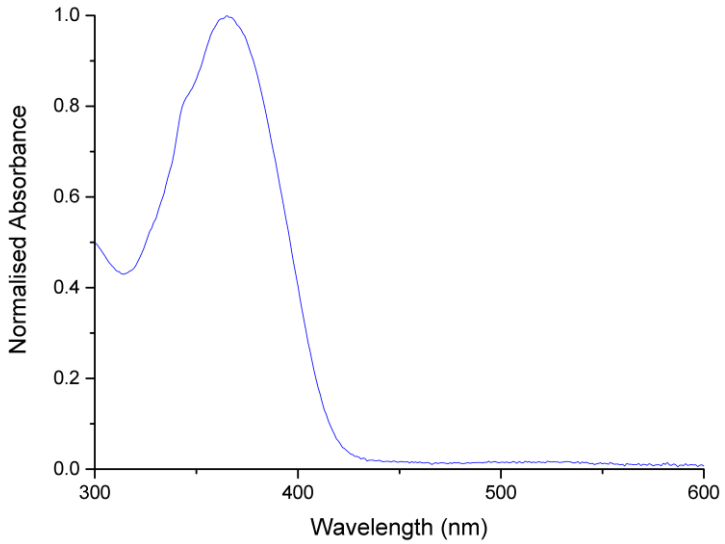


Figure S47 – Normalised absorption spectra of **9** in DMSO with NaOH

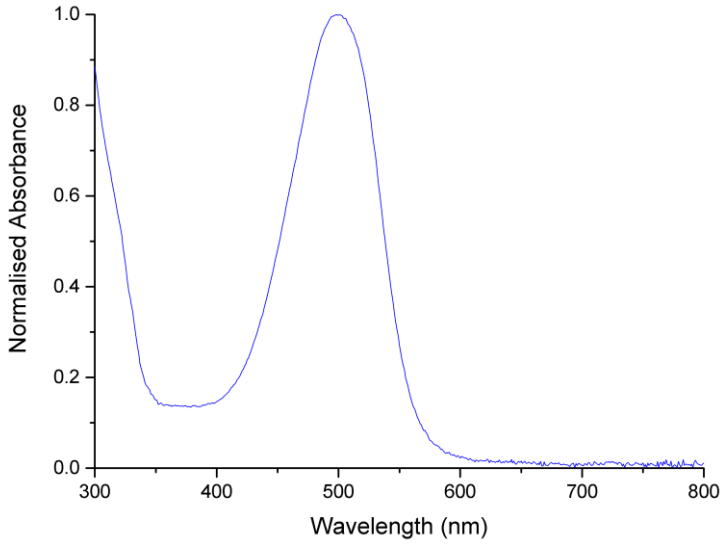


Figure S48 – Normalised absorption and emission spectra of **10** in DMSO

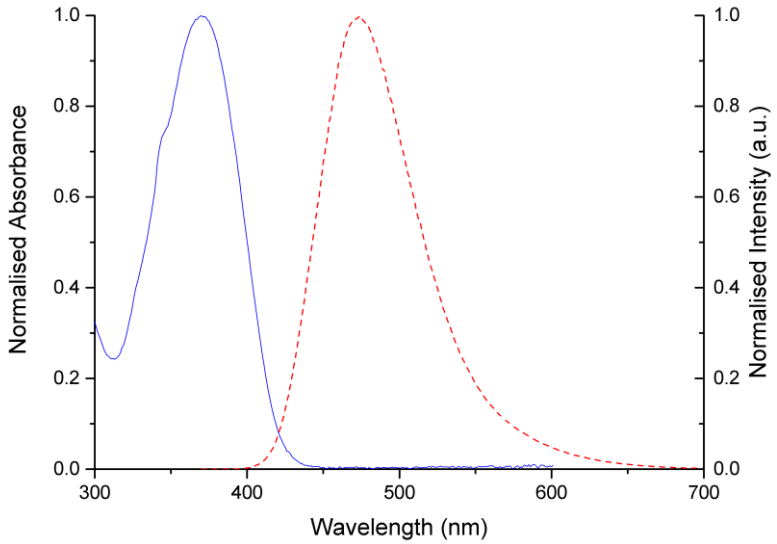


Figure S49 – Normalised absorption and emission spectra of **10** in DMSO with NaOH

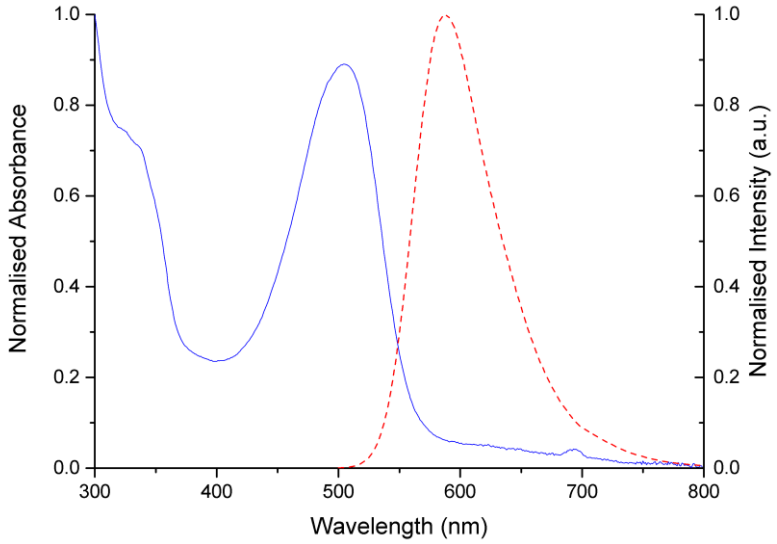


Figure S50 – Normalised absorption and emission spectra of **11** in DMSO

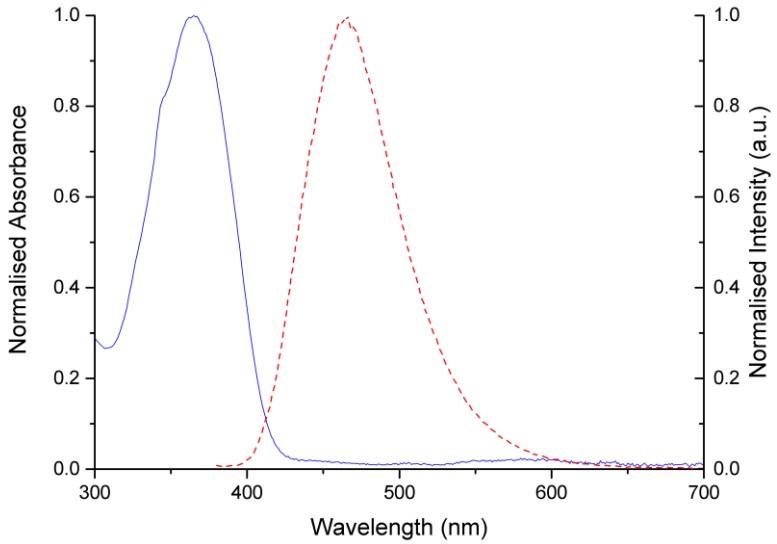


Figure S51 – Normalised absorption and emission spectra of **11** in DMSO with NaOH

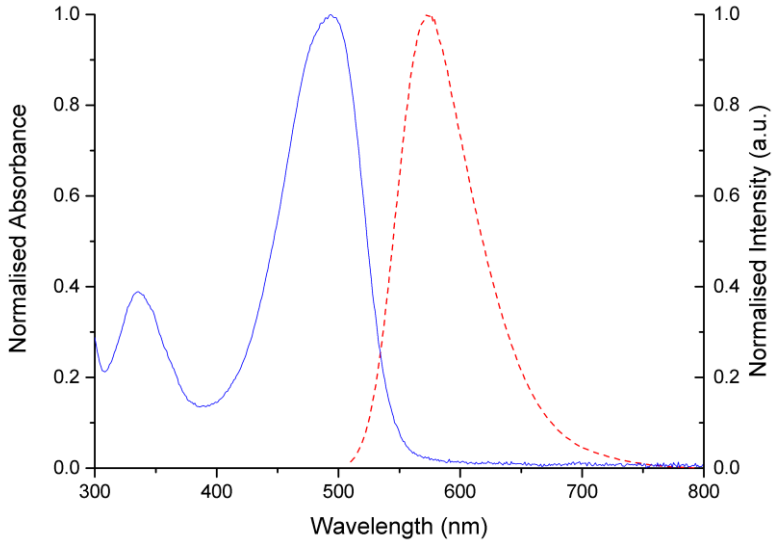


Figure S52 – Normalised absorption and emission spectra of **13** in DMSO

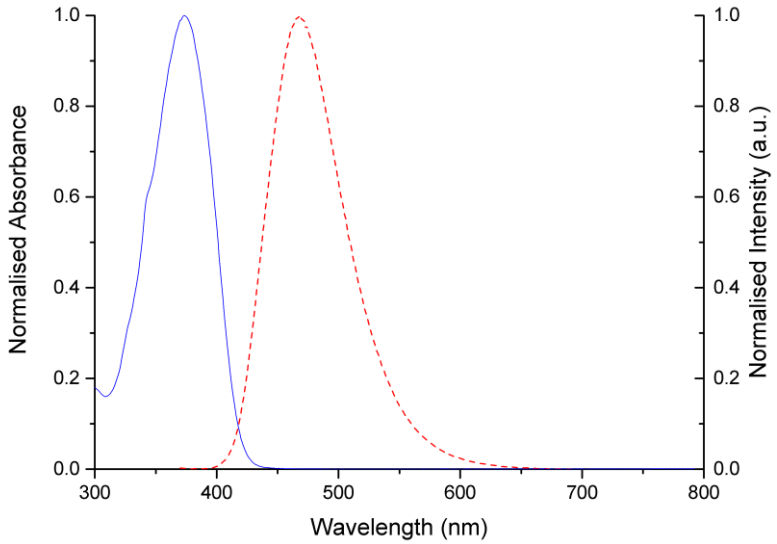


Figure S53 – Normalised absorption and emission spectra of **13** in DMSO with NaOH

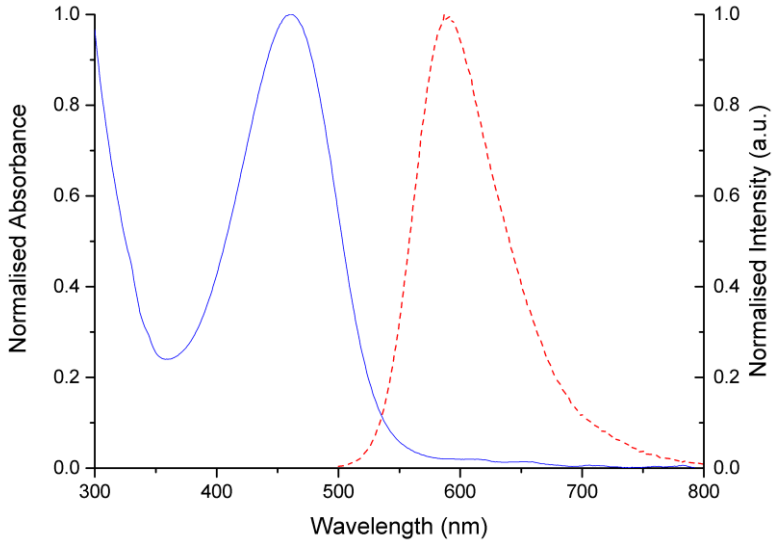


Figure S54 – Normalised absorption and emission spectra of **18** in DMSO

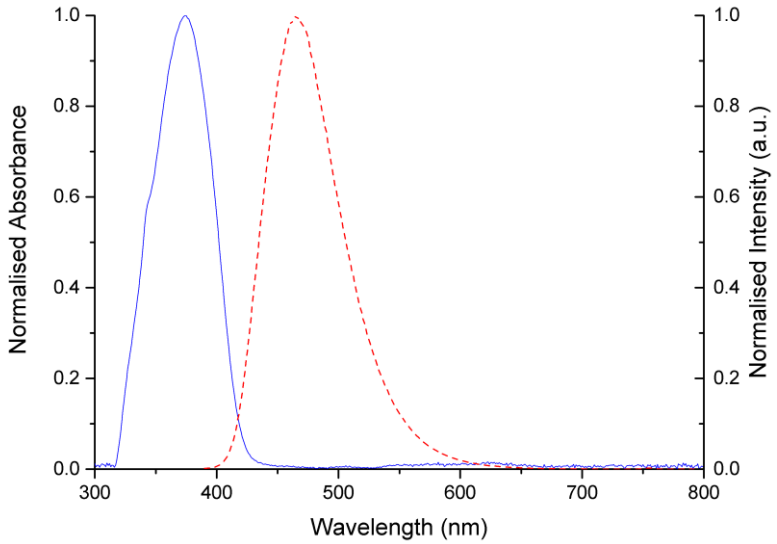


Figure S55 – Normalised absorption and emission spectra of **18** in DMSO with NaOH

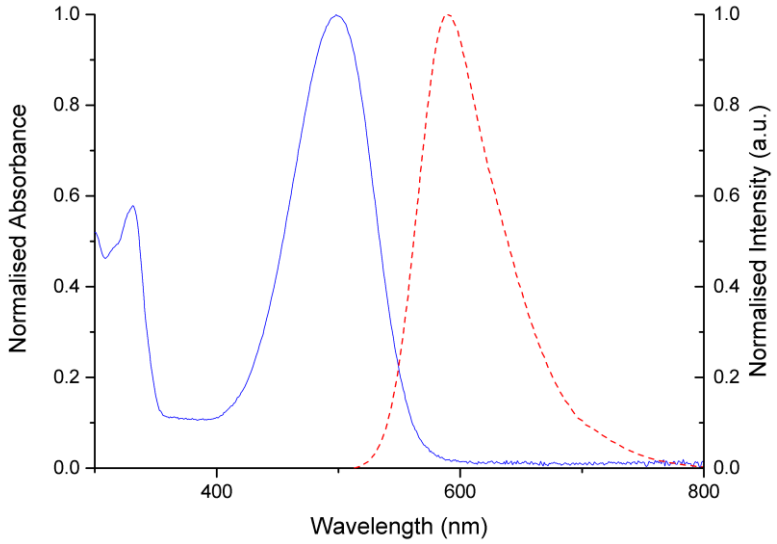


Figure S56 – Normalised absorption and emission spectra of **23** in DMSO

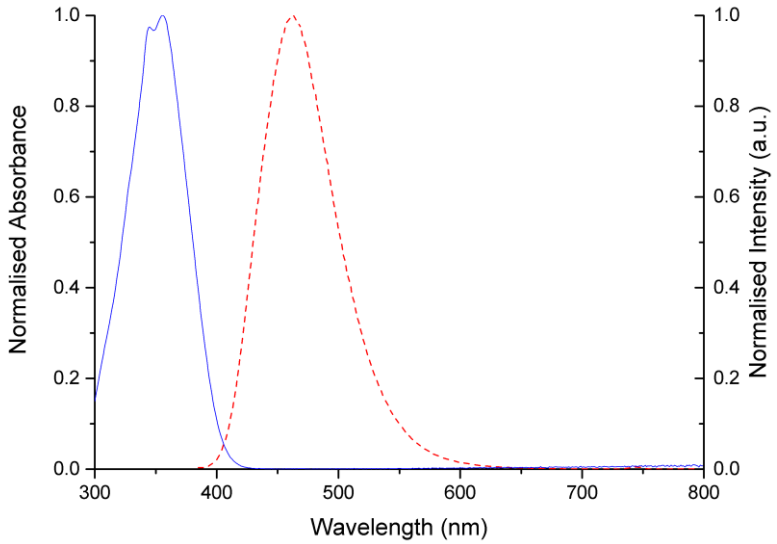


Figure S57 – Normalised absorption and emission spectra of **23** in phosphate buffer

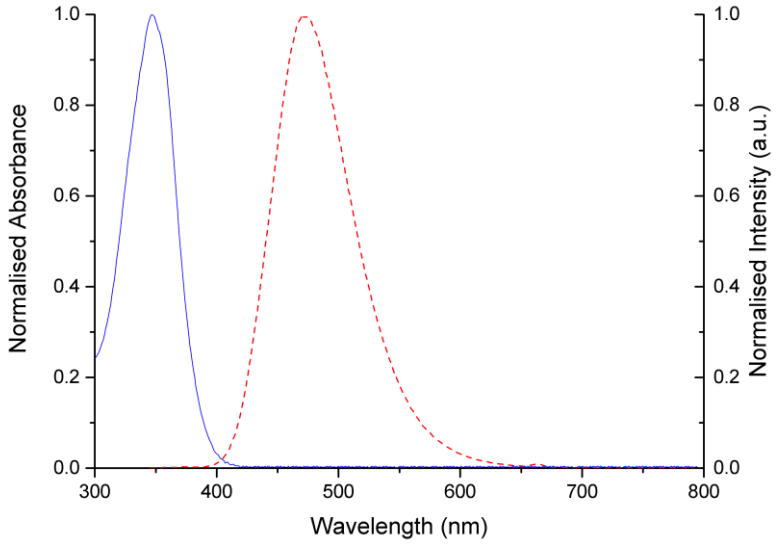


Figure S58 – Normalised absorption and emission spectra of **23** in CH_2Cl_2

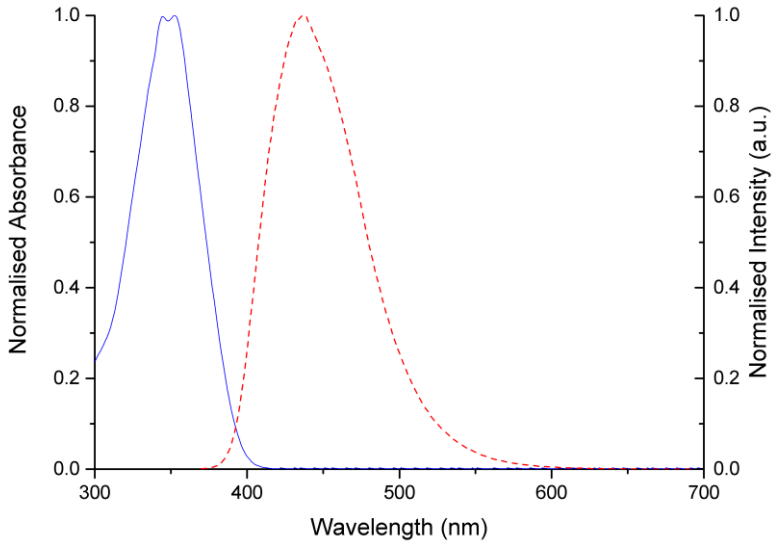


Figure S59 – Normalised absorption and emission spectra of **36** in DMSO with HCl

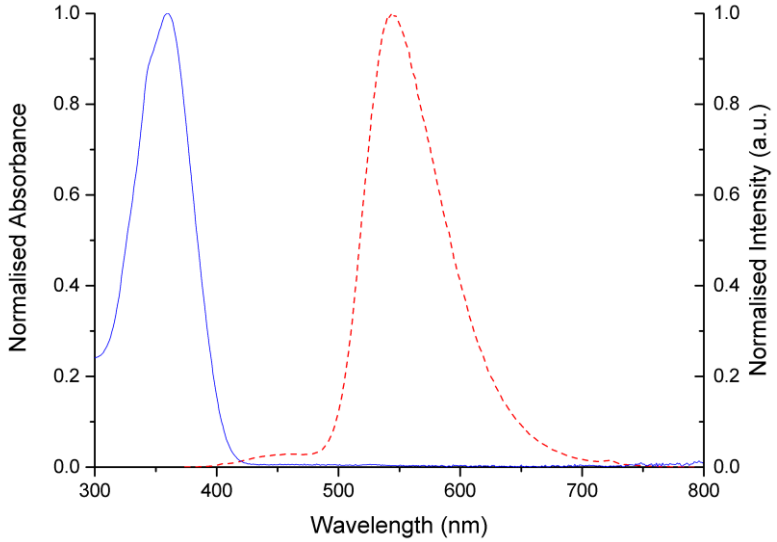


Figure S60 – Normalised absorption and emission spectra of **36** in DMSO with NaOH

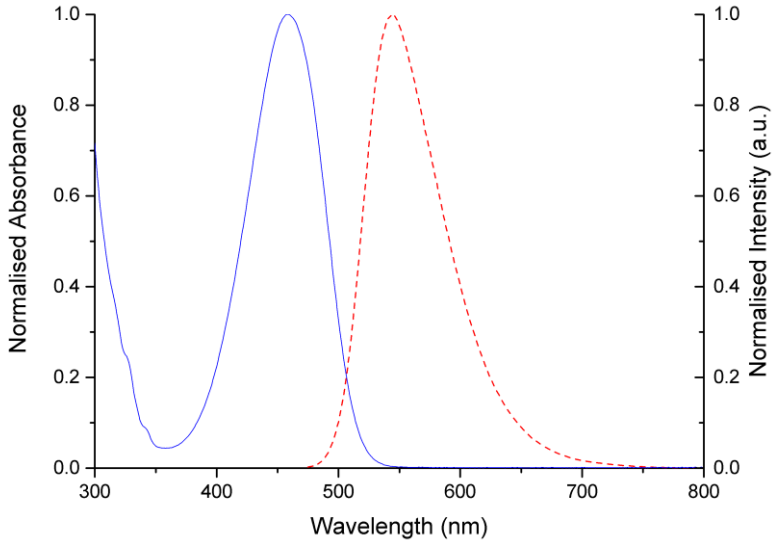


Figure S61 – Normalised absorption and emission spectra of **36** in CH_2Cl_2

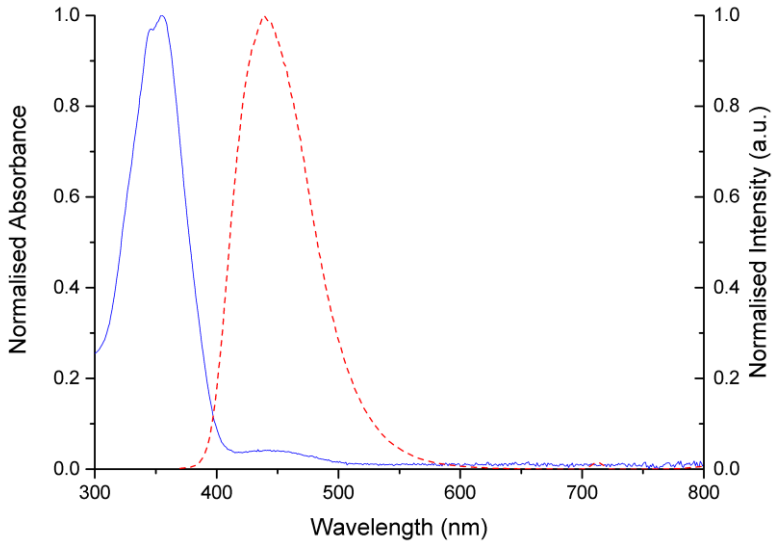
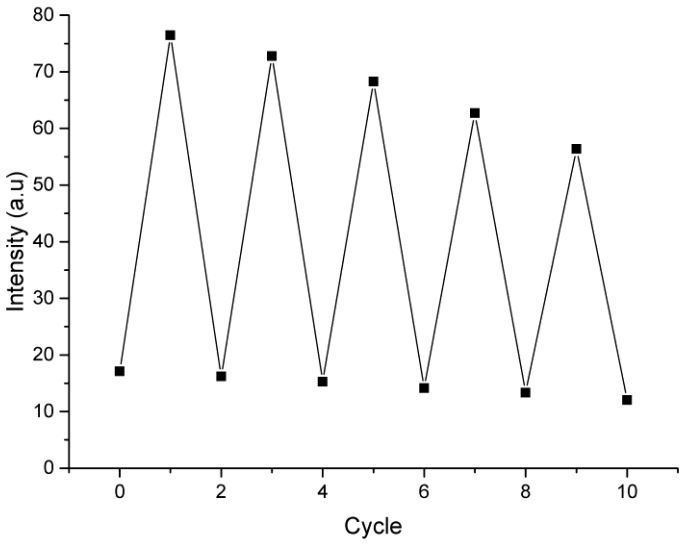


Figure S62 – Effect on emission at 582 nm due to the presence of excess HCl or NaOH



A solution containing compound **6** in DMSO/H_2O (1:1) was treated successively with 1 M KOH and 1 M HCl (*ca.* 50 or 100 μL over 5 cycles each) and the absorption and emission spectra were recorded after each addition and the fluorescence intensity at 582 nm (λ_{ex} = 430 nm) was plotted against cycle number. Decrease in emission intensity is a consequence of dilution after each addition.

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