Electronic Supporting Information

Endoplasmic reticulum targeting fluorescent probes to image mobile Zn^{2+}

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Contents

General experimental

Unless otherwise stated, reactions were carried out using commercially available reagents, used as supplied from Sigma Aldrich, Alfa Aesar, or Tokyo Chemical Industry (TCI), in combination with solvents from Honeywell Solvents. ER-tracker red, Mito-tracker red and Lyso-tracker red were purchased from Enzo Life Sciences. The HeLa and HepG2 cell lines used for fluorescence imaging were provided from ATCC, the MCF-7 cell line was sourced from American Type Culture Collection (ATCC Middlesex, UK), and the EC23 cell line was provided by Prof. Michael P. Philpott. Anhydrous DCM and DMF were obtained from an MBRAUN MB SPS-800 solvent purification system. "H_2O" refers to deionized water.

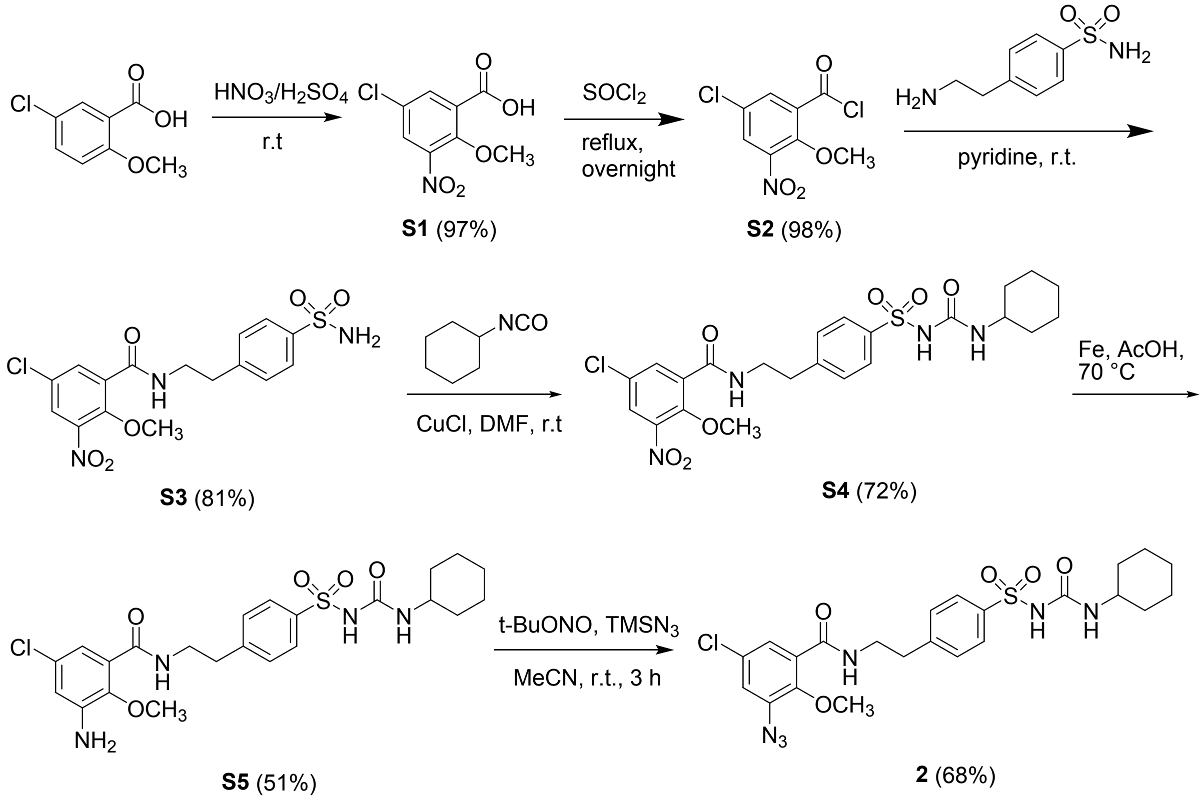
For syntheses requiring anhydrous conditions, reactions were carried out under a nitrogen atmosphere using oven-dried glassware. Solvents were removed *in vacuo* using a Heidolph Hei-VAP Value G1 rotary evaporator with a water and dry ice bath condenser. Analytical thin layer chromatography was carried out on Merck Kiesel gel 60 aluminium-backed silica plates, with visualization using short-wave ultraviolet light (254 nm) or staining with $KMnO_4$ or PMA stain. Column chromatography was carried out using BDH (40-60 μm) silica gel.

Infrared spectra were obtained on a Bruker Tensor 37 FTIR spectrometer with the range 4000-600 cm^{-1}. UV-Vis spectra were obtained on a PerkinElmer Lambda 35 UV/Vis spectrometer. Fluorescence spectra were measured on an Agilent Cary eclipse fluorescence spectrophotometer with a 1 cm pathlength cell. The fluorescence microscope images were obtained from a Logos CELENA S digital imaging system with 40× magnification. ^{1}H NMR spectra were recorded at 400 MHz on a Bruker Avance I or Bruker Avance III spectrometer. Chemical shifts are reported in δ (ppm) and quoted to the nearest 0.01 ppm, also referenced to the residual solvent peak used as the internal standard: $CHCl_3$ (7.26 ppm), MeOH (3.31 ppm), DMSO (2.50 ppm) and CH_3CN (1.94 ppm). Coupling constants (*J*) are measured in Hertz (Hz) and reported to 1 d.p. Peak multiplicities for resonances are noted as standard abbreviations: s, singlet; d, doublet; dd, double doublet; dt, doublet of triplets, t, triplet; q, quartet; m, unresolved multiplet; bs, broad singlet. ^{13}C NMR spectra were recorded at 101 MHz on a Bruker Avance III spectrometer. Chemical shifts (δ) are quoted to the nearest 0.1 ppm, with reference to the given solvent $CDCl_3$ (77.2 ppm), MeOD (49.0 ppm), DMSO (39.5 ppm) and CD_3CN (118.3 ppm) as the internal standard. Electrospray ionization mass spectrometry was carried out by the EPSRC National Mass Spectrometry Service, University of Wales, Swansea on a Thermofisher LTQ Orbitrap XL. Molecular ions are reported for ^{35}Cl and ^{79}Br isotope. Melting points were measured on a Stuart SMP3 melting point apparatus and are uncorrected.

Unless noted otherwise, the solution for photophysical tests is 0.01 mM HEPES buffer (pH 7.4) with 1% DMSO to dissolve probes, and $ZnCl_2$ was used as the Zn^{2+} source to simulate the chloride-rich biological environment. The medium used to incubate HeLa, MCF-7 and HepG2 cells was Dulbecco's Modified Eagle Medium (DMEM), supplemented with 10% heat-deactivated fetal bovine serum (FBS); the medium used for EC23 cells was DMEM/F12 1:1 supplemented with 10% heat-deactivated FBS and RM$^+$ (Rheinwald Media). AlamarBlue^{TM} was used to check cells'viability according to manufacturer's instructions. For co-localisation experiments, all cells were treated with probes **9** (20 μM) or **12** (20 μM) for 1 h and then ER-tracker red, Mito-tracker red and Lyso-tracker red were added in different groups respectively for another 0.5 h incubation. For the Zn^{2+} response experiment, all cells were treated with **9** (20 μM) or **12** (20 μM) for 1 h, and then zinc pyrithione (100 μM) and *N*,*N*,*N*',*N*'-tetrakis(2-pyridinylmethyl)-1,2-ethanediamine (TPEN, 100 μM) were added in different groups respectively for 15 minutes incubation. For ER stress experiments, the HepG2 cells were first treated with probe **9** (20 μM) for 1 hour, washed with PBS, then either tunicamycin (5 μg/mL) or thapsigargin (1 μM) was added to the medium to induce ER stress. The images were taken every 2 minutes to track the fluorescence intensity change. All the images of cells were processed by ImageJ software and the fluorescence intensity in cells was read directly from ImageJ before processing.

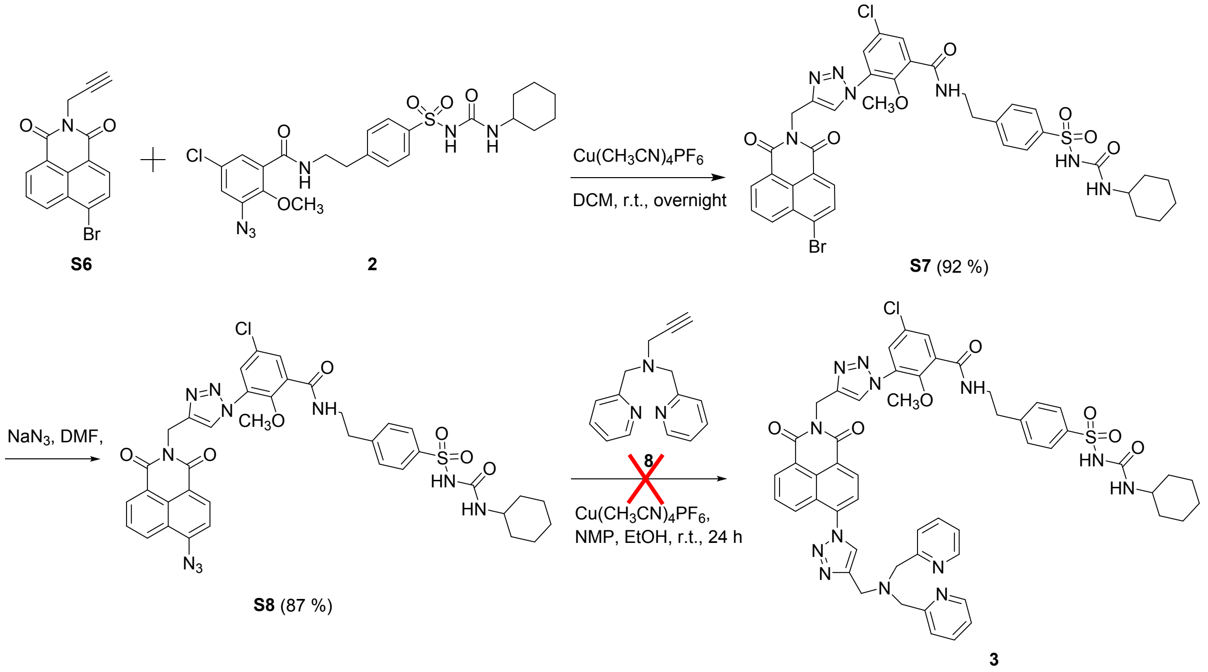
Experimental procedures

The synthetic route to glibenclamide azide **2**:



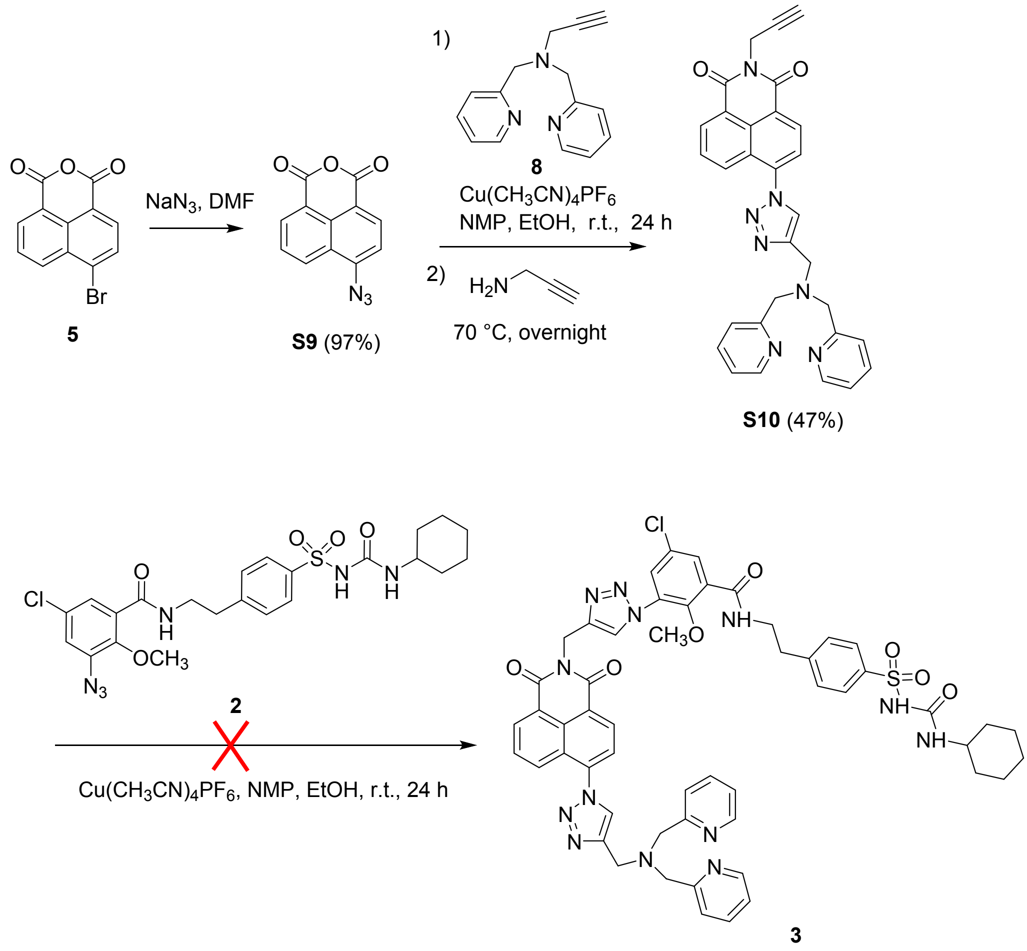
Scheme S1 The synthetic route towards glibenclamide azide **2**.

Compound **2** was then was then used in an attempt to generate the ER-targeting sensor, starting from alkyne **S6**[1] ('top to bottom click'), but the second click reaction with the Zn-binding domain failed:



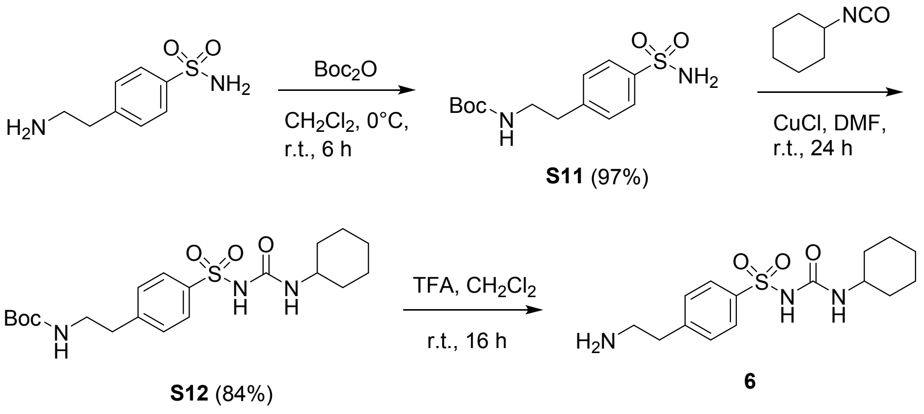
Scheme S2 The modular click reaction method from ‘top to bottom’ click.

Another route to the same sensor target was investigated, involving initial installation of the Zn-binding portion (i.e. ‘bottom to top click’), but the second click reaction again failed:



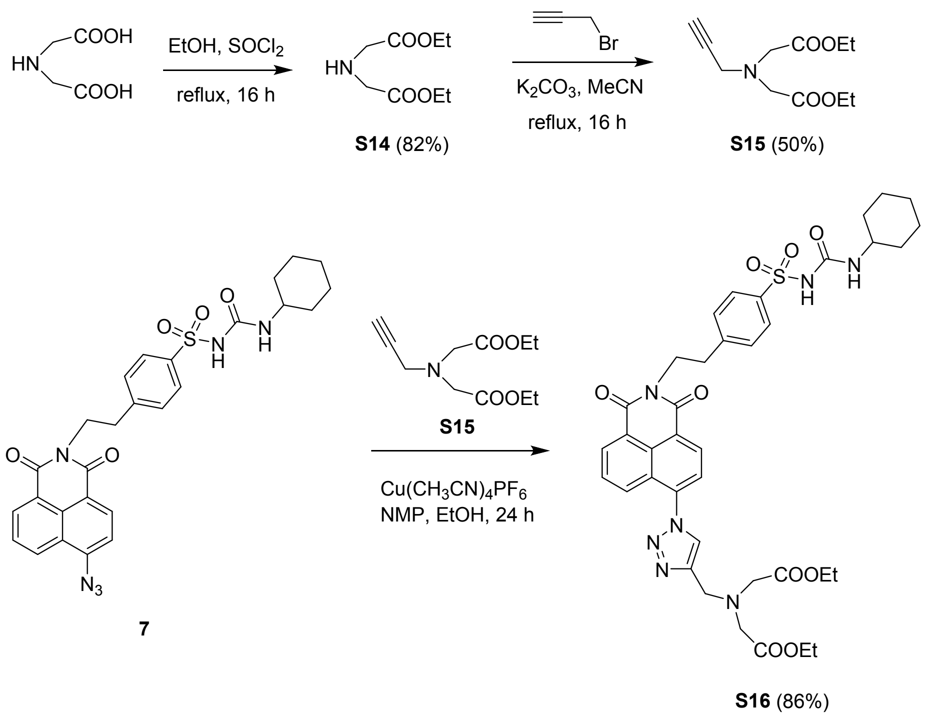
Scheme S3 The modular click reaction method from ‘bottom to top’ click.

Failure to prepare glibenclamide-containing sensor led to the design of cyclohexyl sulfonylurea target; the synthetic route towards sulfonylurea **6** is shown in Scheme S4.



Scheme S4 The synthetic route toward ER-targeting unit **6**.

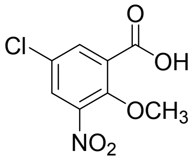
Another probe, **S16**, with the same ER-targeting unit but a different Zn^{2+} ligand was also prepared as shown in Scheme S5. The carboxyl ester should be hydrolysed by esterase enzymes in cells after which it has been reported to have Zn^{2+} binding ability.[2–4] However, it proved to be cytotoxic (shown in Fig. S20) and was not taken forward to studies *in cellulo*.



Scheme S5 The synthetic route toward **S16**.

Experimental procedures

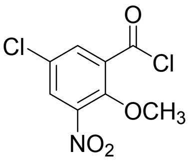
5-Chloro-2-methoxy-3-nitrobenzoic acid (**S1**)



S1

5-Chloro-2-methoxybenzoic acid (1.08 g, 5.80 mmol) and concentrated sulfuric acid (3.8 mL) were cooled to 0 ˚C in an ice-salt water bath. A mixture of concentrated sulfuric acid (0.9 mL) and nitric acid (0.4 mL) was added dropwise over 30 min while the temperature was kept below 5 °C. Then the cooling bath was removed and the reaction was stirred for another 5 h. When the starting material was completely consumed, the reaction was quenched by pouring into ice water. The precipitate that formed was collected by filtration and washed with water (100 mL). The product was dried *in vacuo* to obtain **S1** (1.30 g, 97%, M.p. 171-174 °C) as a pale yellow solid. ^{1}H NMR (400 MHz, DMSO) δ 8.55-8.47 (bs, 1H), 8.35-8.21 (bs, 1H), 8.09-8.76 (bs, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 164.4, 150.3, 145.6, 134.4, 129.7, 127.8, 127.3, 64.0. IR: (υ_{max}/cm^{-1}) 3080, 1709, 1533, 1361, 1293, 1248, 1167, 979, 900, 693. HR-NSI MS (*m/z*) [M+H]$^+$ calcd for $C_8H_6ClNO_5$ 229.9862, found 229.9863. This product is prepared following previously reported literature procedures.[5]

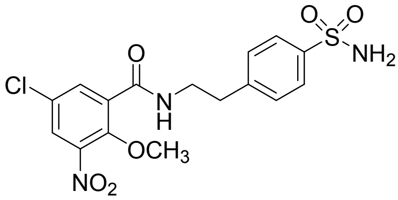
5-Chloro-2-methoxy-3-nitrobenzoyl chloride (**S2**)



S2

Compound **S1** (1.16 g, 5.0 mmol) was dissolved in thionyl chloride (2.0 mL), and the mixture was heated at reflux for 6 hours. When the starting material was consumed, as confirmed by TLC, the reaction mixture was cooled and evaporated under reduced pressure to obtain **S2** (1.23 g, 98 %) as a red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, 1H, *J* = 2.6), 8.01 (d, 1H, *J* = 2.6), 4.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 151.6, 145.5, 136.3, 131.9, 130.2, 129.5, 65.0. IR: (υ_{max}/cm^{-1}) 3081, 1785, 1753, 1534, 1342, 1219, 960, 887, 782. EI MS (*m/z*) $[M]^+$ calcd for $C_8H_5Cl_2NO_4$ 249.0, found 248.9.

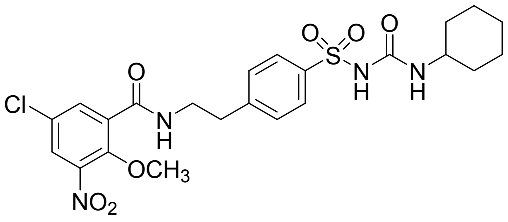
5-Chloro-2-methoxy-3-nitro-*N*-(4-sulfamoylphenethyl)benzamide (**S3**)



S3

The benzoyl chloride **S2** (720 mg, 2.88 mmol) was added slowly to a stirred solution of 4-(2-aminoethyl)benzenesulfonamide (576 mg, 2.88 mmol) in dry pyridine (15 mL). The resultant mixture was stirred at room temperature for 16 hours. Pyridine was removed *in vacuo* and absolute ethanol (10 mL) was added to the residue. The precipitate that formed was collected by filtration and dried *in vacuo* to obtain **S3** (963 mg, 81%, M.p. 208-212 °C) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 8.70-8.65 (m, 1H), 8.11 (d, 1H, *J* = 2.6), 7.75 (d, 2H, *J* = 8.1), 7.70 (d, 1H, *J* = 2.6), 7.45 (d, 2H, *J* = 8.1), 7.28 (s, 2H), 3.69 (s, 3H), 3.58-3.51 (m, 2H), 2.96-2.90 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 163.4, 148.4, 144.5, 143.4, 142.2, 134.0, 132.9, 129.2, 127.5, 125.7, 125.4, 63.2, 40.3, 34.4. IR: (υ_{max}/cm^{-1}) 3152, 1600, 1540, 1453, 1331, 1156, 968, 807, 693. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{16}H_{17}ClN_3O_6S$ 414.0521, found 414.0519. This product is prepared following previously reported literature procedures.[6]

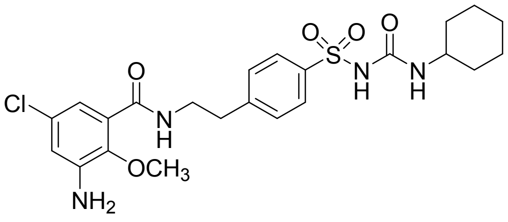
5-Chloro-*N*-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-2-methoxy-3-nitrobenzamide (**S4**)



S4

To a stirred solution of sulfonylamine **S3** (207 mg, 0.500 mmol) and CuCl (2.5 mg, 0.025 mmol) in DMF (2.0 mL) under N_2 atmosphere, cyclohexyl isocyanate (0.1 mL, 0.750 mmol) was added dropwise. The reaction was stirred for 24 hours at room temperature. The resulting mixture was filtered and the filtrate poured slowly into ice cold water (50 mL) and acidified with concentrated HCl (0.1 mL). The precipitate formed was collected by filtration, washed with H_2O (100 mL), dried *in vacuo* to obtain **S4** (194 mg, 72%, M.p. 221-225 °C) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, 1H, *J* = 2.8), 7.90 (d, 1H, *J* = 2.8), 7.85 (d, 2H, *J* = 8.3), 7.66-7.60 (bs, 1H), 7.44 (d, 2H, *J* = 8.3), 6.44 (d, 1H, *J* = 7.7), 3.84-3.76 (m, 2H), 3.76 (s, 3H), 3.63-3.54 (m, 1H), 3.07 (t, 2H, *J* = 7.1), 1.88-1.18 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 149.9, 149.1, 144.9, 144.6, 135.8, 130.9, 130.3, 129.7, 128.4, 127.9, 125.0, 64.2, 49.5, 41.1, 35.2, 33.9, 25.6, 24.7. IR: (υ_{max}/cm^{-1}) 3293, 2930, 2854, 1622, 1535, 1449, 1342, 1163, 904, 661. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{23}H_{28}ClN_4O_7S$ 539.1362, found 539.1357. This product is prepared following previously reported literature procedures.[7]

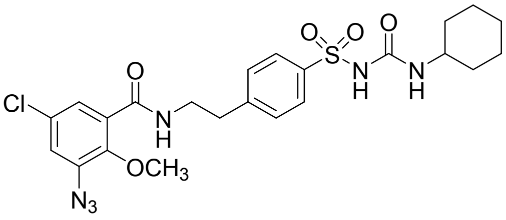
3-Amino-5-chloro-*N*-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-2-methoxybenzamide (**S5**)



S5

Compound **S4** (568 mg, 1.05 mmol) was dissolved in acetic acid (9 mL) and heated to 70 °C under a N_2 atmosphere. Fe powder (177 mg, 3.16 mmol) was added to this solution and the reaction mixture was stirred at 70 °C for 30 minutes. The mixture was then cooled to room temperature and concentrated under reduced pressure. The residue was dissolved in ethyl acetate (30 mL) and washed with saturated $NaHCO_3$ (30 mL × 3). The organic layer was dried over $MgSO_4$ and the solution was concentrated *in vacuo*. The product was purified by silica gel chromatography (2% methanol in dichloromethane) to give **S5** (260 mg, 51%, M.p. 101-104 °C) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, 2H, *J* = 8.4), 7.75-7.68 (m, 1H), 7.41 (d, 2H, *J* = 8.4), 7.29 (d, 1H, *J* = 2.6), 6.80 (d, 1H, *J* = 2.6), 6.42 (d, 1H, *J* = 7.9), 3.80-3.73 (m, 2H), 3.61-3.53 (m, 1H), 3.48 (s, 3H), 3.08-3.01 (m, 2H), 1.82-1.15 (m, 10H). ^{13}C NMR (101 MHz, MeOD) δ 166.5, 151.5, 145.5, 143.3, 143.0, 138.3, 129.5, 129.3, 128.4, 127.5, 117.0, 116.5, 59.6, 48.8, 40.1, 34.6, 32.4, 25.1, 24.4. IR: (υ_{max}/cm^{-1}) 3459, 3016, 2970, 1757, 1714, 1426, 1367, 1216, 1092, 900. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{23}H_{30}ClN_4O_5S$ 509.1620, found 509.1613. This product is prepared following previously reported literature procedures.[8]

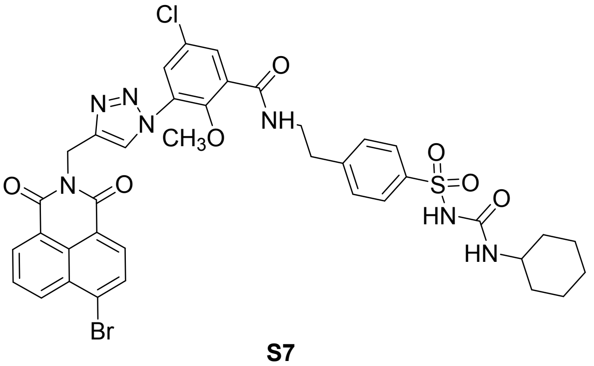
3-Azido-5-chloro-*N*-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-2-methoxybenzamide (**2**)



2

The compound **S5** (127 mg, 0.250 mmol) was dissolved in acetonitrile (3.0 mL) and cooled to 0 ˚C in an ice-water bath. To this solution was added dropwise *t*-BuONO (50 µL, 0.38 mmol) and $TMSN_3$ (38 µL, 0.30 mmol). After stirring for 30 min, the ice-water bath was removed and the stirring was continued for 6 hours at room temperature. Then the solvent was evaporated under reduced pressure and the residue was then washed with hexane (30 mL) and water (50 mL), dried *in vacuo* to obtain **2** (91 mg, 68%, M.p. 191-194 °C) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (bs, 1H), 7.85 (d, 2H, *J* = 8.3), 7.78 (d, 1H, *J* = 2.4), 7.41 (d, 2H, *J* = 8.3), 7.16 (d, 1H, *J* = 2.4), 6.42 (d, 1H, *J* = 7.7), 3.82-3.70 (m, 2H), 3.63 (s, 3H), 3.61-3.52 (m, 1H), 3.08-3.00 (m, 2H), 1.83-1.16 (m, 10H). ^{13}C NMR (101 MHz, MeOD) δ 166.0, 149.6, 146.3, 139.4, 136.1, 131.2, 130.8, 130.3, 128.6, 127.2, 126.8, 123.7, 62.9, 54.4, 41.4, 35.7, 33.6, 26.2, 25.4. IR: (υ_{max}/cm^{-1}) 2930, 2111, 1739, 1631, 1533, 1445, 1345, 1169, 983, 900, 691. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{23}H_{28}ClN_6O_5S$ 535.1525, found 535.1520. This product is prepared following previously reported literature procedures.[9]

3-(4-((6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)-5-chloro-*N*-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-2-methoxybenzamide (**S7**)

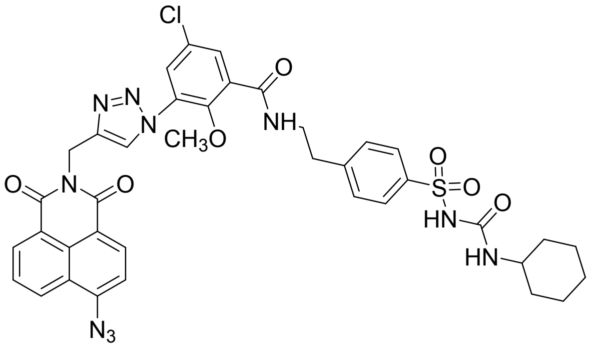


S7

Under a nitrogen atmosphere, the glibenclamide azide **2** (53.5 mg, 0.10 mmol) and alkyne **S6**[1] (31.4 mg, 0.10 mmol) were dissolved in anhydrous dichloromethane (5.0 mL), then *N*,*N*-Diisopropylethylamine (DIPEA, 20 µL, 0.18 mmol) and tetrakis(acetonitrile)copper(I) hexafluorophosphate (7.5 mg, 0.020 mmol) were added. The flask was covered with aluminium foil and stirred at room temperature for 48 h. After the reaction was complete, the reaction mixture was diluted with dichloromethane (20 mL) and washed with saturated EDTA in 17 % $NH_3{\cdot}H_2O$ (10 mL), water (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give **S7** (78.1 mg, 92%, M.p. 117-120 °C) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, 1H, *J* = 6.5), 8.62 (d, 1H, *J* = 8.5), 8.53 (d, 1H, *J* = 7.9), 8.20 (s, 1H), 8.11 (d, 1H, *J* = 2.7), 8.09 (d, 1H, *J* = 7.9), 7.95 (d, 2H, *J* = 8.3), 7.92-7.86 (m, 1H), 7.82 (d, 1H, *J* = 2.7,), 7.57-7.51 (m, 1H), 7.46 (d, 2H, *J* = 8.3), 6.48 (d, 1H, *J* = 8.0), 5.63 (s, 2H), 3.85-3.78 (m, 2H), 3.63-3.50 (m, 1H), 3.16 (s, 3H), 3.06 (t, 2H, *J* = 6.7), 1.81-1.17 (m, 10H).^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 167.5, 163.6, 148.7, 147.7, 145.1, 144.1, 142.1, 138.5, 135.3, 133.8, 132.6, 131.9, 131.8, 131.3, 131.0, 130.7, 129.8, 129.0, 128.8, 128.3, 127.5, 125.4, 124.0, 122.7, 121.8, 62.2, 60.4, 53.5, 35.2, 33.0, 25.3, 24.6, 21.1. IR: (υ_{max}/cm^{-1})

3142, 1600, 1534, 1483, 1344, 1242, 1169, 1025, 968, 807, 777, 688. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{38}H_{36}BrClN_7O_7S$ 848.1262, found 848.1263.

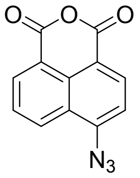
3-(4-((6-Azido-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)-5-chloro-*N*-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-2-methoxybenzamide **(S8)**



S8

Compound **S7** (67.9 mg, 0.08 mmol) was dissolved in DMF (2.0 mL), and sodium azide (6.5 mg, 0.1 mmol) was added to the reaction mixture and it was stirred at room temperature for 24 h. Then the reaction mixture was diluted with water (20 mL) and extracted with EtOAc (3×20 mL). The organic layers were combined and washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to obtain **S8** (56.5 mg, 87 %, M.p. 190-194 °C) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.80-8.72 (m, 2H), 8.51 (d, 1H, *J* = 8.6), 8.21 (s, 1H), 8.13 (d, 1H, *J* = 2.8), 7.98 (d, 2H, *J* = 8.3), 7.85 (d, 1H, *J* = 2.8), 7.83-7.78 (m, 1H), 7.58-7.52 (m, 2H), 7.48 (d, 2H, *J* = 8.3), 6.51-6.45 (bs, 1H), 5.65 (s, 2H), 3.87-3.82 (m, 2H), 3.60-3.55 (bs, 1H), 3.17 (s, 3H), 3.10-3.07 (m, 2H), 1.85-1.23 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 163.7, 163.1, 150.5, 148.8, 145.3, 144.5, 138.6, 133.0, 132.6, 132.0, 131.8, 131.1, 129.9, 129.8, 129.5, 129.1, 128.9, 127.6, 127.2, 125.5, 124.5, 123.1, 122.3, 118.5, 115.0, 62.3, 49.3, 40.6, 35.3 (overlapping signal), 33.1, 25.5, 24.7. IR: (υ_{max}/cm^{-1}) 2930, 2124, 1704, 1663, 1534, 1342, 1242, 1161, 1042, 904, 784, 659. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{38}H_{36}ClN_{10}O_7S$ 811.2172, found 811.2172.

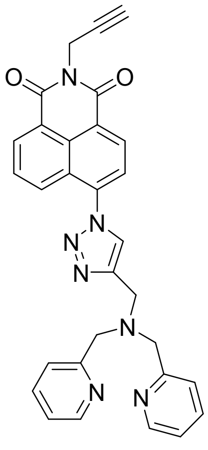
6-Azido-1*H*,3*H*-benzo[*de*]isochromene-1,3-dione (**S9**)



S9

To a solution of 4-bromo-1,8-naphthalic anhydride (500 mg, 1.80 mmol) in DMF (5.0 mL), NaN_3 (175 mg, 2.69 mmol) was added and the mixture stirred at room temperature for 12 h. After the reaction was complete, as judged by TLC, water (30 mL) was added and the precipitate that formed was collected by filtration, then washed with water (50 mL) and dried *in vacuo* to obtain **S9** (418 mg, 97 %) as a pale-yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, 1H, J = 7.3, 1.1), 8.62 (d, 1H, J = 8.0), 8.55 (dd, 1H, J = 8.5, 1.1), 7.82 (dd, 1H, J = 8.5, 7.3), 7.53 (d, 1H, J = 8.0). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 160.2, 145.4, 134.4, 134.1, 131.4, 130.5, 127.3, 124.5, 118.6, 115.2, 114.3. All other spectroscopic data were consistent with those previously reported.[10]

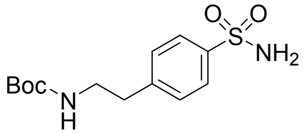
6-(4-((bis(Pyridin-2-ylmethyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-2-(prop-2-yn-1-yl)-1*H*-benzo[*de*]isoquinoline-1,3(2*H*)-dione (**S10**)



S10

Under a nitrogen atmosphere, the azide **S9** (23.9 mg, 0.100 mmol), alkyne **5** (23.7 mg, 0.100 mmol), and tetrakis(acetonitrile)copper(I) hexafluorophosphate (10.0 mg, 0.0300 mmol), were added to a mixture of NMP (1.0 mL) and EtOH (1.0 mL). The flask was covered with aluminium foil and stirred at room temperature for 24 h, after the starting material consumed, as judged by TLC, propargylamine (9.00 μL, 0.140 mmol) was added and the mixture was stirred at room temperature for 16 hours. After the reaction was complete, saturated EDTA in 10% $NH_3{\cdot}H_2O$ (5.0 mL) was added and the precipitate that formed collected by filtration. The crude product was purified by column chromatography on silica gel (eluent DCM: MeOH = 20:1) to give **S10** (24 mg, 47%, M.p. 182-185 °C) as a brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79-8.73 (m, 2H), 8.57 (d, 2H, *J* = 4.2), 8.32 (dd, 1H, J = 8.6, 0.9), 8.17 (s, 1H), 7.85 (dt, 2H, *J* = 7.4, 4.0), 7.69 (td, 2H, *J* = 7.6, 1.8), 7.60 (d, 2H. *J* = 7.7), 7.21 – 7.15 (m, 2H), 5.00 (d, 2H, *J* = 2.4), 4.09 (s, 2H), 3.97 (s, 4H), 2.23 (t, 1H, J = 2.4). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 162.5, 159.0, 149.3, 145.1, 138.8, 136.8, 135.8, 132.7, 131.2, 130.3, 129.3, 128.7, 126.6, 125.8, 123.6, 123.5, 122.7, 122.4, 78.3, 71.0, 59.9, 48.6, 29.8. IR: (υ_{max}/cm^{-1}) 1744, 1707, 1665, 1581, 1483, 1378, 1232, 1040, 845, 782, 754. HR-NSI MS (*m/z*) $[M+Na]^+$ calcd for $C_{30}H_{23}N_7O_2Na$ 536.1805, found 536.1796.

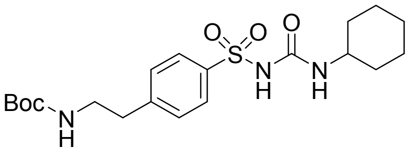
tert-Butyl (4-sulfamoylphenethyl) carbamate (**S11**)



S11

4-(2-Aminoethyl) benzenesulfonamide (0.40 g, 2.0 mmol) was dissolved in CH_2Cl_2 (5.0 mL) and cooled to 0 °C in an ice bath. Di-*tert*-butyl dicarbonate (0.44 g, 2.0 mmol) was dissolved in CH_2Cl_2 (5.0 mL) and then added slowly to the above solution. After completion of the addition, the ice bath was removed and the mixture was stirred at room temperature for 6 hours. The solvent was evaporated *in vacuo* and the residue was diluted with water (20 mL) and extracted with CH_2Cl_2 (20 mL × 2). The organic layers were combined and dried over $MgSO_4$, filtered and dried *in vacuo* to give **S11** as a white solid (0.58 g, 97%, M.p. 188-189 °C). ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, 2H, *J* = 8.3), 7.39 (d, 2H, *J* = 8.3), 7.30 (s, 2H), 6.92 (t, 1H, *J* = 5.2), 3.22-3.15 (m, 2H), 2.82-2.76 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 155.5, 143.7, 142.0, 129.1, 125.6, 77.6, 41.1, 35.1, 28.2. IR: (υ_{max}/cm^{-1}) 3384, 3333, 3235, 1660, 1524, 1338, 1307, 1280, 1154, 1094, 906, 683. HR-NSI MS (*m/z*) $[M+NH_4]^+$ calcd for $C_{13}H_{24}N_3O_4S$ 318.1482, found 318.1486.

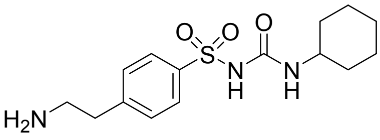
tert-Butyl (4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)carbamate **(S12)**



S12

Under a nitrogen atmosphere, **S11** (0.15 g, 0.50 mmol) and CuCl (5.0 mg, 0.050 mmol) were dissolved in DMF (2.0 mL), cyclohexyl isocyanate (0.10 mL, 0.75 mmol) was added dropwise and the mixture was stirred for 24 hours at room temperature. The resultant precipitate was removed by filtration and the filtrate poured slowly into ice cold water (50 mL). Concentrated HCl (0.1 ml) was added to acidify the resultant mixture and the precipitate that formed was isolated by suction filtration and washed with water (50 mL) to give **S12** as a white solid (0.18 g, 84%, M.p. 184-186 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.73 (bs, 2H), 7.42-7.32 (bs, 2H), 6.56-6.30 (bs, 1H), 4.66-4.52 (bs, 1H), 3.66-3.54 (bs, 1H), 3.43-3.32 (bs, 2H), 2.96-2.83 (bs, 2H), 1.96-1.59 (m, 6H), 1.43 (s, 9H), 1.32-1.10 (m, 4H) ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.4, 155.9, 145.3, 129.6, 127.5, 79.5, 49.3, 41.4, 36.1, 33.7, 28.4, 25.4, 24.6. IR: (υ_{max}/cm^{-1}) 3331, 3271, 2935, 2856, 1690, 1660, 1532, 1435, 1352, 1296, 1250, 1163, 1038, 967, 869, 683. HR-NSI MS (*m/z*) [M+H]$^+$ calcd for $C_{20}H_{32}N_3O_5S$ 426.2057, found 426.2057.

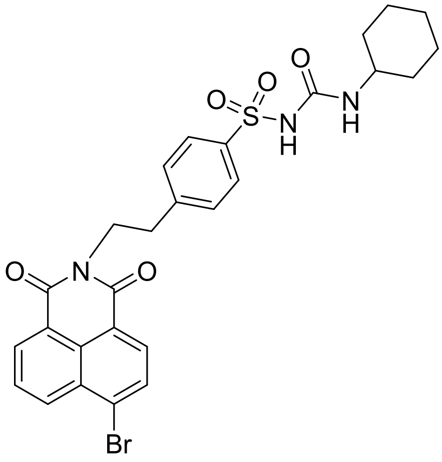
4-(2-Aminoethyl)-*N*-(cyclohexylcarbamoyl)benzenesulfonamide (**6**)



6

Boc-protected **S12** (132 mg, 0.310 mmol) was dissolved in CH_2Cl_2 (4.0 mL) and trifluoracetic acid (0.4 mL) was added dropwise. The reaction was stirred at room temperature for 16 hours. The solvent was evaporated under reduced pressure and the product **6** (colourless oil) was used without purification in the next step. ^{1}H NMR (400 MHz, CD_3CN) δ 10.48-9.62 (bs, 1H), 7.87 (d, 2H, J = 8.1), 7.42 (d, 2H, J = 8.1), 7.29-7.13 (bs, 2H), 6.83 (m, 1H), 3.40-3.33 (m, 1H), 3.25-3.18 (m, 2H), 3.08-3.00 (m, 2H), 1.75-1.10 (m, 10H). ^{13}C NMR (101 MHz, CD_3CN) δ 152.6, 144.1, 140.6, 131.0, 129.1, 50.3, 42.0, 34.0, 33.9, 26.5, 25.8. IR: (υ_{max}/cm^{-1}) 3064, 2934, 2857, 1671, 1544, 1452, 1338, 1202, 1162, 1035, 906, 723. HR-ESI MS (*m/z*) $[M+H]^+$ calcd for $C_{15}H_{24}N_3O_3S$ 326.1538, found 326.1578.

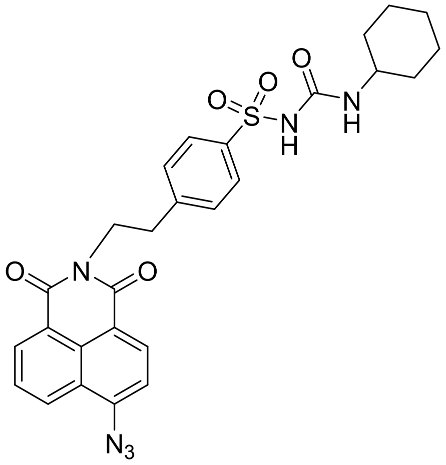
4-(2-(6-Bromo-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)ethyl)-*N*-(cyclohexylcarbamoyl)benzenesulfonamide (**S13**)



S13

After de-protection, the product **6** was dissolved in ethanol (2.0 mL), then Na_2CO_3 (65.7 mg, 0.620 mmol) was added to the above solution. 4-Bromo-1,8-naphthalic anhydride (85.9 mg, 0.310 mmol) was added and the mixture was refluxed for 6 hours. After the reaction was completed, as judged by TLC, the solvent was evaporated *in vacuo.* Then water (30 mL) was poured in to the residue and the precipitate formed was collected by filtration and dried *in vacuo* to obtain **S13** (149 mg, 82%, M.p. 264-268 °C) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 8.61-8.53 (m, 2H), 8.35 (d, 1H, *J* = 7.9), 8.23 (d, 1H, *J* = 7.9), 8.05-7.97 (m, 1H), 7.65 (d, 2H, *J* = 7.9), 7.25 (d, 2H, *J* = 7.9), 5.70-5.58 (bs, 1H), 4.29-4.18 (m, 2H), 3.27-3.14 (bs, 1H), 2.99-2.88 (m, 2H), 1.72-1.47 (m, 6H), 1.20-0.99 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 162.6 (overlapping signals), 142.0, 132.6, 131.5, 131.3, 130.9, 129.6, 129.2, 128.7, 128.5, 128.1, 127.8, 127.1, 127.0, 122.5, 121.7, 48.6, 40.9, 33.2, 32.8, 25.2, 24.6. IR: (υ_{max}/cm^{-1}) 3378, 2929, 2854, 1700, 1653, 1590, 1344, 1254, 1231, 1122, 1086, 1007, 880, 779, 655. HR-NSI MS (*m/z*) [M+H]$^+$ calcd for $C_{27}H_{26}BrN_3O_5S$ 584.0849, found 584.0846.

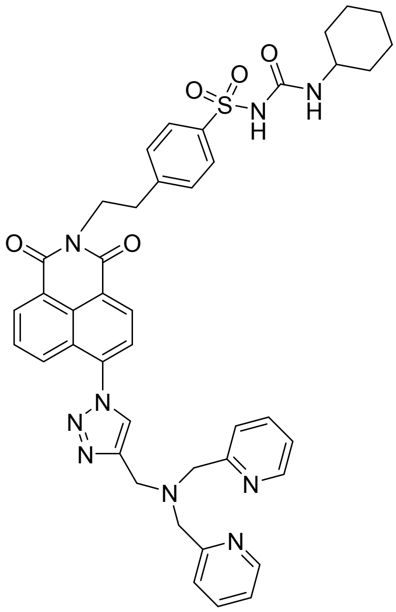
4-(2-(6-Azido-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)ethyl)-*N*-(cyclohexylcarbamoyl)benzenesulfonamide (**7**)



7

The compound **S13** (148 mg, 0.253 mmol) was dissolved in DMF (2.0 mL) and NaN_3 (25 mg, 0.385 mol) was added to the solution. The mixture was stirred for 24 hours at room temperature. The reaction mixture was poured into water (20 mL) and the precipitate was collected by filtration and dried *in vacuo* to obtain **7** (94.0 mg, 68%, M.p. 200-204 °C) as a yellow solid. ^1H NMR (400 MHz, DMSO) δ 8.51 (d, 1H, *J* = 7.3), 8.46 (d, 1H, *J* = 7.9), 8.42 (d, 1H, *J* = 8.5), 7.90- 7.83 (m, 1H), 7.80 (d, 2H, *J* = 7.9), 7.74 (d, 1H, *J* = 7.9), 7.48 (d, 2H, *J* = 7.9), 6.34-6.26 (bs, 1H), 4.31-4.21 (m, 2H), 3.06-2.95 (m, 2H), 1.68-1.46 (m, 6H), 1.21-1.06 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 163.0, 162.6, 156.6, 150.8, 144.3, 142.8, 138.7, 131.6, 129.2, 128.4, 128.2, 127.5, 127.2, 123.4, 121.9, 117.9, 115.9, 48.1, 40.5, 33.4, 32.3, 25.0, 24.2. IR: (υ_{max}/cm^{-1}) 3299, 2930, 2854, 2123, 1738, 1651, 1591, 1533, 1437, 1353, 1229, 1129, 1087, 843, 780, 690. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{27}H_{26}N_6O_5S$ 547.1758, found 547.1753.

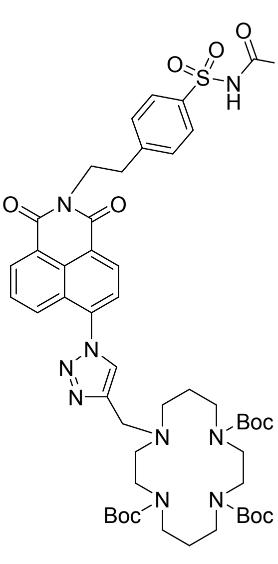
4-(2-(6-(4-((bis(Pyridin-2-ylmethyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)-1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)ethyl)-*N*-(cyclohexylcarbamoyl)benzenesulfonamide (**9**)



9

Under an atmosphere of nitrogen, **7** (76.0 mg, 0.150 mmol) and **8** (35.6 mg, 0.150 mmol) were dissolved in NMP (1.0 mL) and EtOH (1.0 mL), then tetrakis(acetonitrile)copper(I) hexafluorophosphate (11.2 mg, 0.030 mmol) was added. The flask was covered with aluminum foil and the mixture was stirred at room temperature for 24 hours. After the reaction finished, as judged by TLC, saturated EDTA in 17% NH_3:H_2O (20 mL) was poured into the mixture and the precipitate that formed was collected by filtration, and washed with water (30 mL). This crude product was purified by flash chromatography (eluent: DCM/MeOH 20:1), and then dissolved in the minimum amount of DCM and poured into *n*-hexane (30 mL) to give **9** as a brown solid (96 mg, 82%, M.p. 148-151 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72-8.66 (m, 2H), 8.56 (d, 2H, $J = 4.3$), 8.31 (d, 1H, $J = 8.3$), 8.19 (s, 1H), 7.98-7.80 (m, 4H), 7.72-7.66 (m, 2H), 7.61 (d, 2H, $J = 7.8$), 7.54 (d, 2H, $J = 8.5$), 7.21-7.15 (m, 2H), 6.47 (s, 1H), 4.48-4.41 (m, 2H), 4.09 (s, 2H), 3.97 (s, 4H), 3.64-3.55 (bs, 1H), 3.19-3.12 (m, 2H), 1.87-1.55 (m, 6H), 1.32-1.18 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 163.1, 159.0, 149.2, 145.0, 142.0, 138.6, 136.8, 135.2, 133.8, 132.4, 131.0, 130.2, 130.0, 129.8, 129.2, 128.7, 127.4, 126.5, 125.9, 123.6, 123.5, 122.7, 122.4, 59.9, 49.2, 48.6, 41.4, 34.2, 33.0, 25.5, 24.7. IR: (υ_{max}/cm^{-1}) 3288, 2926, 2853, 1699, 1654, 1590, 1534, 1433, 1342, 1230, 1157, 1036, 998, 882, 783, 754, 691. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{42}H_{42}N_9O_5S$ 784.3024, found 784.3017.

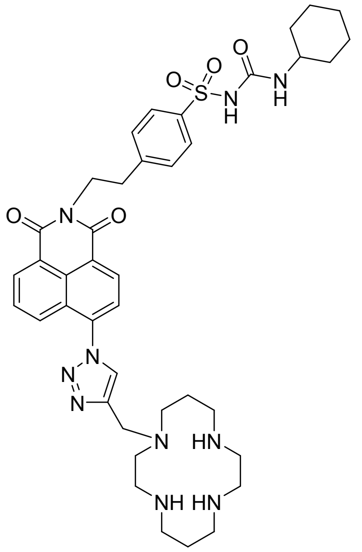
tri-*tert*-Butyl 11-((1-(2-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-1,4,8,11-tetraazacyclotetradecane-1,4,8-tricarboxylate (**11**)



11

Under an atmosphere of nitrogen, **7** (109 mg, 0.200 mmol) and **10** (108 mg, 0.200 mmol) were dissolved in NMP (1.0 mL) and EtOH (1.0 mL), then tetrakis(acetonitrile)copper(I) hexafluorophosphate (14.9 mg, 0.0400 mmol) was added. The flask was covered with aluminum foil and the mixture was stirred at room temperature for 24 hours. After the reaction had finished as judged by TLC, saturated EDTA in 17% NH_3:H_2O (20 mL) was poured into the mixture and the precipitate formed was collected by filtration, and washed with water (30 mL). This crude product was purified by flash chromatography (eluent: DCM/MeOH 20:1) to give **11** as a brown solid (193 mg, 89%, M.p. 126-129 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 8.64-8.52 (m, 2H), 8.28-8.17 (bs, 1H), 8.09-7.96 (bs, 1H), 7.90-7.72 (m, 4H), 7.48-7.33 (m, 2H), 5.78 (bs, 1H), 4.42-4.25 (bs, 2H), 4.03-3.81 (bs, 2H), 3.63-3.48 (bs, 1H), 3.42-3.25 (bs, 12H), 3.09-2.99 (m, 2H), 2.74-2.65 (bs, 2H), 2.59-2.49 (bs, 2H), 1.89-1.49 (m, 8H), 1.39-1.06 (m, 33H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 163.0, 155.9, 155.6, 143.4, 141.0, 138.4, 132.3, 130.9, 130.0, 129.6, 129.5, 129.0, 128.6, 127.6, 126.6, 126.4, 123.6, 123.4, 122.6, 79.7, 53.5, 53.2, 49.1, 48.9, 47.3, 45.6, 41.4, 34.0, 33.9, 33.8, 32.9, 29.5, 28.5 (overlapping signals), 25.6, 25.4, 24.9, 24.6. IR: (υ_{max}/cm^{-1}) 2972, 2930, 1740, 1663, 1589, 1411, 1365, 1230, 1157, 1034, 782, 728. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{55}H_{77}N_{10}O_{11}S$ 1085.5489, found 1085.5474.

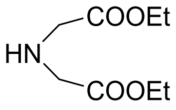
4-(2-(6-(4-((1,4,8,11-Tetraazacyclotetradecan-1-yl)methyl)-1*H*-1,2,3-triazol-1-yl)-1,3-dioxo-1*H*-benzo[de]isoquinolin-2(3*H*)-yl)ethyl)-*N*-(cyclohexylcarbamoyl)benzenesulfonamide (**12**)



12

The tri-Boc-protected compound **11** (109 mg, 0.100 mmol) was dissolved in a solution of 20% TFA in DCM (2.0 mL) and stirred for 10 h at room temperature. Then the solvent was removed *in vacuo* and the residue was dissolved in chloroform (10 mL) and washed with 1 M aqueous NaOH solution (2 mL). The aqueous layer was extracted with chloroform (3 × 10 mL) and the organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give **12** as a brown solid (42 mg, 54 %, M.p. 202-205 °C). ^{1}H NMR (400 MHz, MeOD) δ 8.62-8.54 (m, 3H), 8.26 (d, 1H, *J* = 8.4), 7.99 (d, 1H, *J* = 7.8), 7.89-7.82 (m, 3H), 7.47 (d, 2H, *J* = 8.3), 4.35-4.28 (m, 2H), 4.03 (bs, 2H), 3.46-3.37 (m, 4H), 3.34-3.32 (m, 1H), 3.30-3.18 (m, 4H), 3.13-2.90 (m, 10H), 2.19 (bs, 2H), 1.93 (bs, 2H), 1.79-1.52 (m, 5H), 1.35-1.13 (m, 5H). ^{13}C NMR (101 MHz, MeOD) δ 164.7, 164.2, 163.1, 153.1, 146.4, 139.8, 139.3, 133.1, 131.8, 130.6, 130.0, 129.8, 128.8, 127.4, 125.3, 124.9, 123.9, 119.6, 116.7, 55.5, 54.2, 50.7, 50.4, 50.1, 49.8, 48.2 (overlapping signals), 46.6, 45.9, 42.2, 34.8, 33.8, 26.4(overlapping signals), 25.8, 24.1. IR: (υ_{max}/cm^{-1}) 2929, 2853, 1661, 1587, 1516, 1433, 1347, 1231, 1200, 1121, 864, 782, 719. HR-NSI MS (*m/z*) $[M+H]^+$ calcd for $C_{40}H_{53}N_{10}O_5S$ 785.3916, found 785.3905.

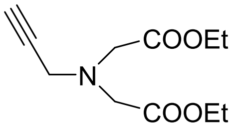
Diethyl 2,2'-azanediyldiacetate (**S14**)



S14

Thionyl chloride (7.26 mL, 100 mmol) was added slowly to stirred absolute ethanol (30 mL) in an ice-water bath and the mixture stirred for about 30 mins at room temperature. After the addition of iminodiacetic acid (3.33 g, 25.0 mmol), the reaction mixture was heated at reflux overnight and then the solution was evaporated *in vacuo*. Saturated $NaHCO_3$ solution (20 mL) was added and extracted with CH_2Cl_2 (3 × 30 mL), the organic layers combined, dried over $MgSO_4$, filtered and dried *in vacuo* to give **S14** (3.89 g, 82 %) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (q, 4H, *J* = 7.2), 3.35 (s, 4H), 1.98 (s, 1H), 1.17 (t, 6H, *J* = 7.2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 60.6, 50.0, 14.0. All other spectroscopic data were consistent with those previously reported.[11]

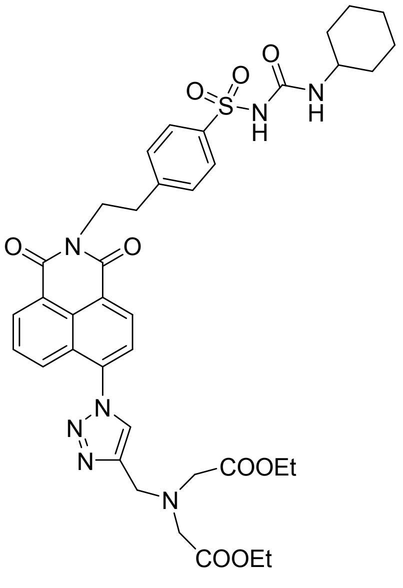
Diethyl 2,2'-(prop-2-yn-1-ylazanediyl)diacetate **(S15)**



S15

Diethyl iminodiacetate **S14** (2.68 g, 14.2 mmol) was dissolved in MeCN (30 mL), then K_2CO_3 (3.92 g, 28.4 mmol) and propargyl bromide (2.52 mL, 17.0 mmol) were added slowly and the mixture heated at reflux for 16 h. After cooling to room temperature, the suspension was filtered and the filtrate evaporated *in vacuo*. The resultant oil was purified by column chromatography (petrol/EtOAc = 20:1 to petrol/EtOAc = 5:1) to obtain **S15** as a red oil (1.61 g, 50 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.04 (q, 4H, *J* = 7.1), 3.53 (d, 2H, *J* = 2.4), 3.40 (s, 4H), 2.18 (t, 1H, *J* = 2.4), 1.13 (t, 6H, *J* = 7.1).^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 78.1, 73.6, 60.4, 54.0, 43.0, 13.9. All other spectroscopic data were consistent with those previously reported.[12]

Diethyl 2,2'-(((1-(2-(4-(*N*-(cyclohexylcarbamoyl)sulfamoyl)phenethyl)-1,3-dioxo-2,3-dihydro-1*H*-benzo[*de*]isoquinolin-6-yl)-1*H*-1,2,3-triazol-4-yl)methyl)azanediyl)diacetate (**S16**)



S16

Under an atmosphere of nitrogen, **7** (109 mg, 0.200 mmol) and **S15** (45.4 mg, 0.200 mmol) were dissolved in NMP (1.0 mL) and EtOH (1.0 mL), then tetrakis(acetonitrile)copper(I) hexafluorophosphate (14.9 mg, 0.0400 mmol) was added. The flask was covered with aluminium foil and the mixture was stirred at room temperature for 24 hours. After the reaction had finished saturated EDTA in 17% NH_3:H_2O (20 mL) was poured into the mixture and the precipitate formed was collected by filtration, and washed with water (30 mL). This crude product was purified by flash chromatography (eluent: DCM/MeOH 20:1) to give **S16** as a brown solid (133 mg, 86%, M.p. 164-168 °C). ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (m, 2H), 8.30 (d, 1H, *J* = 8.6), 8.16 (s, 1H), 7.86-7.80 (m, 4H), 7.52 (d, 2H, *J* = 8.3), 6.48 (m, 1H), 4.47-4.40 (m, 2H), 4.24 (s, 2H), 4.18 (q, 4H, *J* = 7.1), 3.69 (s, 4H), 3.66-3.55 (m, 1H), 3.18-3.10 (m, 2H), 1.85-1.56 (m, 6H), 1.35-1.17 (m, 10H).^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 163.7, 163.1, 150.7, 146.5, 145.2, 139.3, 138.6, 138.0, 135.6, 132.5, 131.0, 130.0, 129.2, 128.8, 127.4, 126.6, 125.8, 123.7, 123.6, 122.8, 60.9, 55.1, 49.3, 49.2, 41.4, 34.2, 33.0, 25.5, 24.6, 14.4. IR:

(υ_{max}/cm^{-1}) 3287, 2930, 2853, 1697, 1656, 1589, 1535, 1433, 1344, 1229, 1157, 1037, 783, 605. HR-NSI MS (*m/z*) [M+H]$^+$ calcd for $C_{38}H_{44}N_7O_9S$ 774.2916, found 774.2907.

Photophysical properties

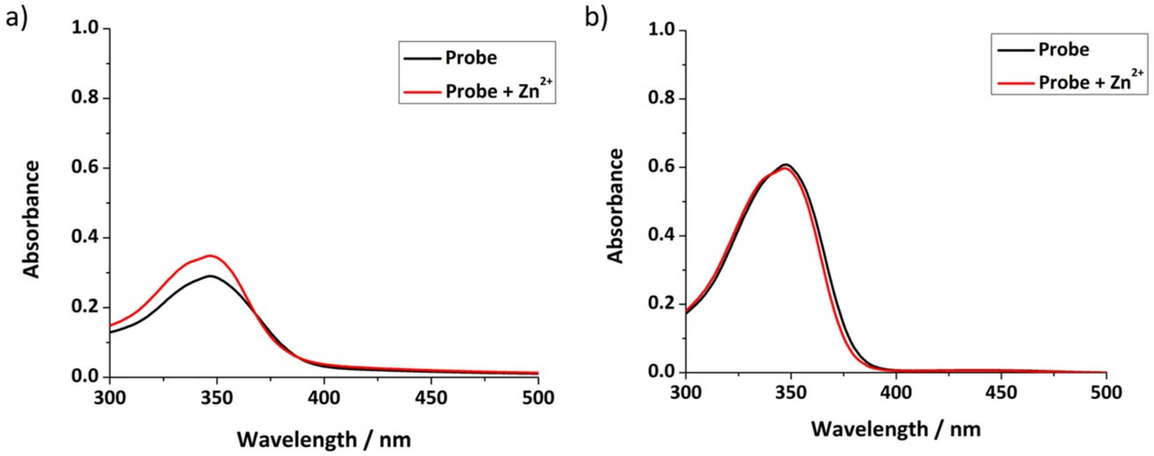


Fig. S1 The UV-Vis spectra of a) **9** (50 μM) and b) **12** (50 μM), and their complex with 1 equivalent of Zn^{2+}.

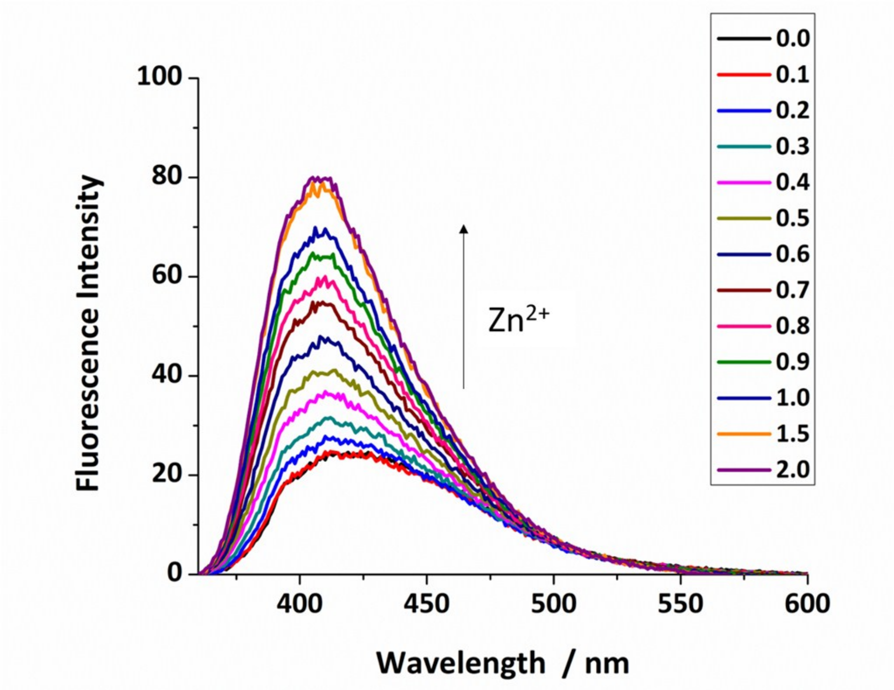


Fig. S2 The fluorescence response of **12** (10 μM) to different equivalents of Zn^{2+}. (λ_{ex} = 346 nm, slit width: 5/5 nm)

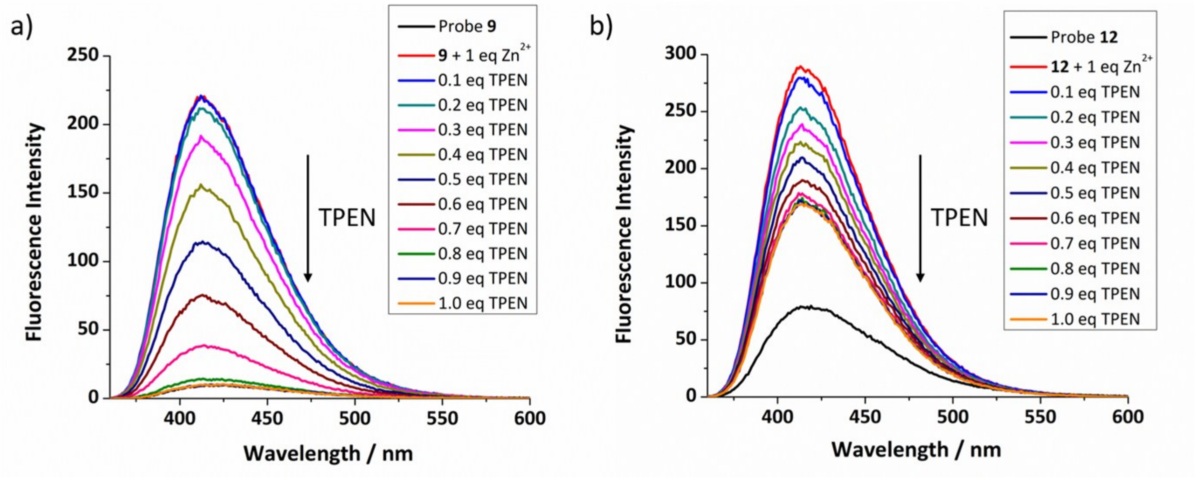


Fig. S3 The fluorescence response of a) **9** (50 µM) and b) **12** (50 µM) with 1 equivalent Zn^{2+} to different equivalents TPEN. (λ_{ex} = 346 nm).

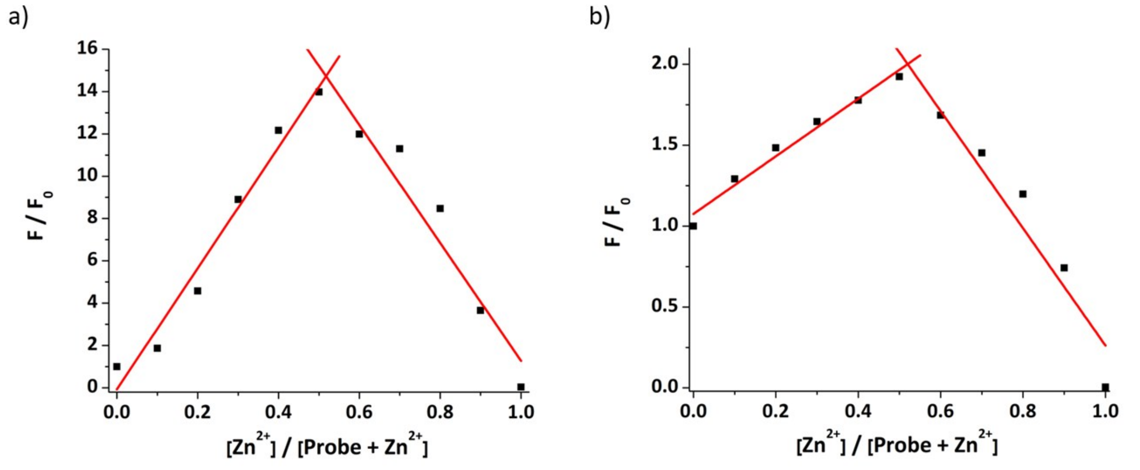


Fig. S4 The Job's plot to determine the stoichiometry of the complex formed between a) **9** and Zn^{2+}, b) **12** and Zn^{2+}. The total amount of [Probe + Zn^{2+}] is 50 µM, (λ_{ex} = 346 nm, λ_{em} = 414 nm).

Fluorescence titration to determine dissociation constant K_d (free Zn^{2+} method)

[Probe] Probe **9** Probe **12**

50 µM

10 µM

1 µM

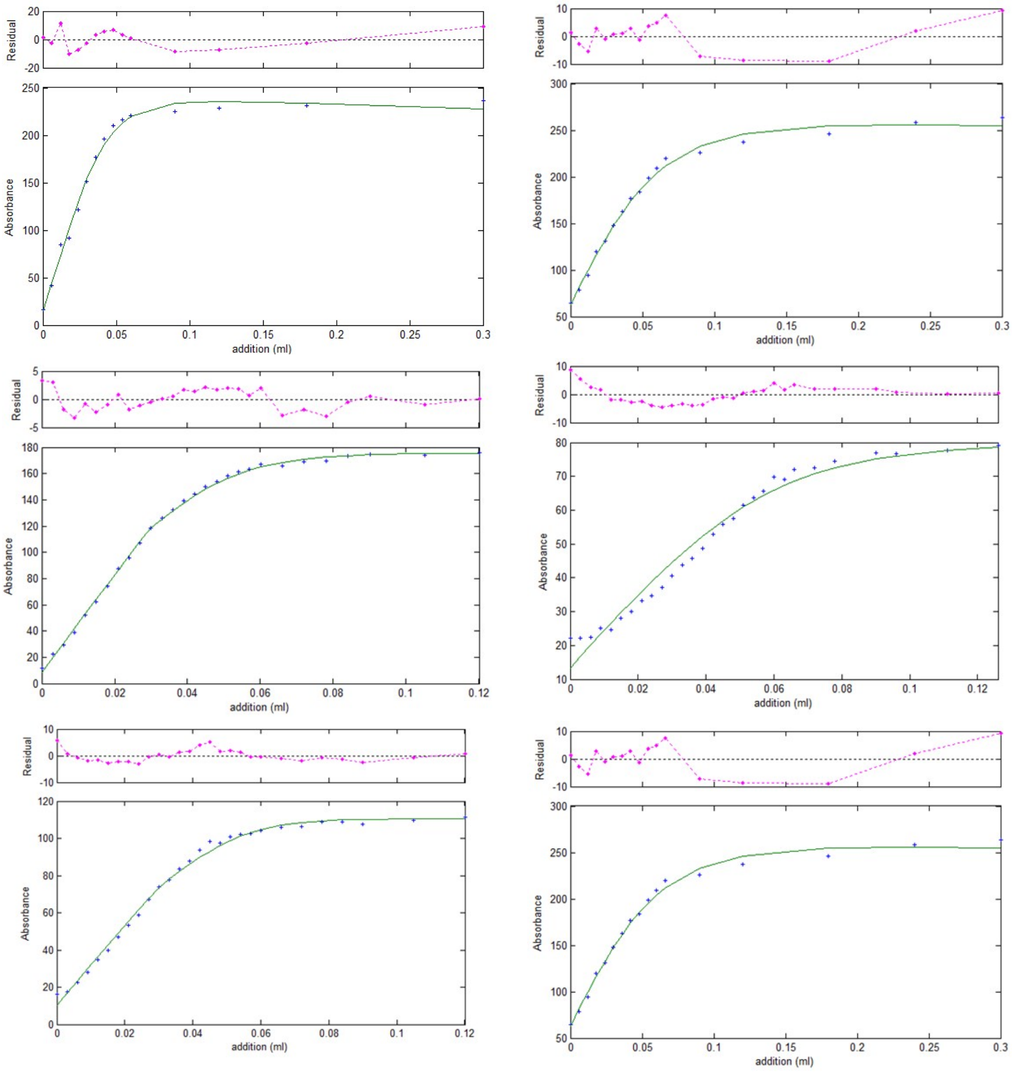


Fig. S5 The non-linear curve fitting of the fluorescence intensity as a function of [Zn^{2+}] of **9** and **12** at different concentrations to determine K_d (Blue = measured data, Green = fit). Residuals at each datapoint are shown in pink. For all complexes, 0.06 mL addition of Zn^{2+} solutions represents a 1:1 ratio of probe and Zn^{2+}. (λ_{ex} = 346 nm, λ_{em} = 414 nm (probe **9**), λ_{em} = 406 nm (probe **12**)). Fits for probe **9** incorporate fitting of an ML_2 species at low abundance (see Table S1). Non-linear regression was carried out using Reactlab Equilibria software.[13]

Table S1 Summary of apparent K_d calculated for probes **9** and **12** using the free Zn^{2+} method as a function of concentration

Probe	[Probe] = 50 µM	[Probe] = 10 µM	[Probe] = 1 µM
	K_d	K_d	K_d
9[i]	1.0×10^{-7} M	3.0×10^{-10} M	2.8×10^{-10} M
12	1.0×10^{-5} M	1.1×10^{-6} M	4.5×10^{-8} M

[i] The best fit for probe **9** by this method was obtained by also allowing for the presence of a second species of the form ML_2. In all cases, the second stepwise association constant K_2 was 1-2 orders of magnitude smaller than K_1 indicative of strongly negative cooperativity, and this species was only observed in the presence of a large excess of probe in the early parts of the titration. No improvement in fitting was observed by including any other stoichiometries in the fitting for probe **12**.

A series of HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) buffer solutions (50 mM, pH 7.2, 0.1 M KCl) containing various amounts of $ZnCl_2$ (0 ~ 9.0 mM) and 10 mM of EGTA (ethylene glycol-bis(2-aminoethylether)-*N*,*N*,*N′*,*N′*-tetraacetic acid) were prepared. The $[Zn^{2+}]_{free}$ was calculated following the reported method.[14–16]

The calculated $[Zn^{2+}]_{free}$ concentration of each solution was:

$[Zn^{2+}]_{total}$ (mM)	0.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5
$[Zn^{2+}]_{free}$ (nM)	0.00	0.14	0.29	0.46	0.66	0.87	1.11	1.39
$[Zn^{2+}]_{total}$ (mM)	4.0	4.5	5.0	6.0	7.0	8.0	9.0	
$[Zn^{2+}]_{free}$ (nM)	1.73	2.12	2.59	3.88	6.04	10.36	23.31	

To determine the apparent dissociation constants, the fluorescence titration curves at concentrations of 1 µM, 0.1 µM and 0.01 µM of the probe were obtained and fitted to Equation S1[16,17] (shown in Fig. S6).

$$\frac{F}{F_0} = 1 + \left(\frac{F_{max}}{F_0} - 1\right)\frac{[Zn^{2+}]_{free}}{K_d + [Zn^{2+}]_{free}}$$

Equation S1 Equation used to determine K_d for all probes. F is the observed fluorescence intensity, F_0 is the observed fluorescence of the probe alone. Non-linear curve fitting analysis was used to determine F_{max}/F_0 and K_d.

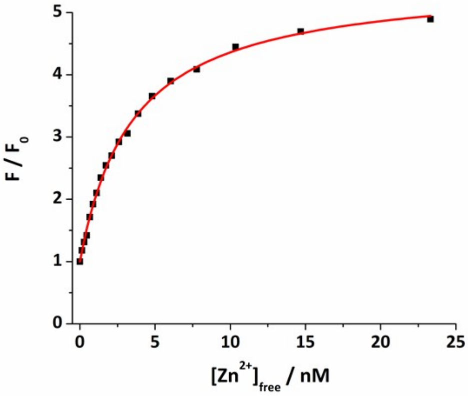
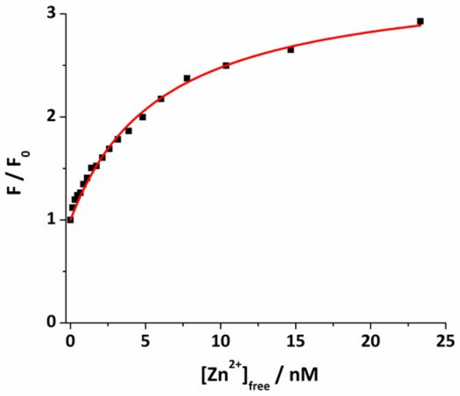
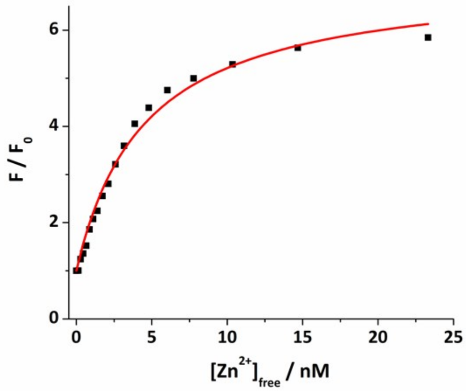
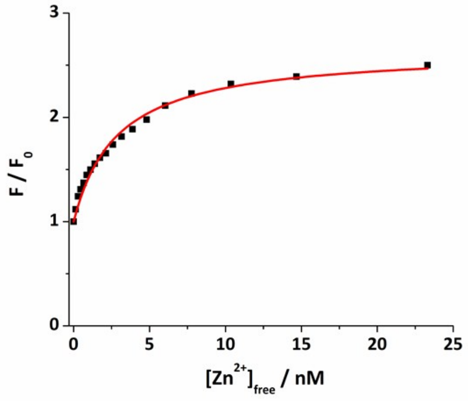
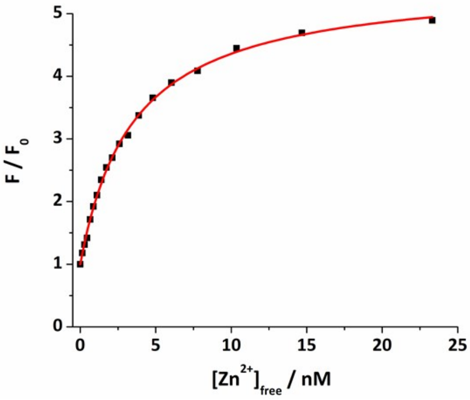
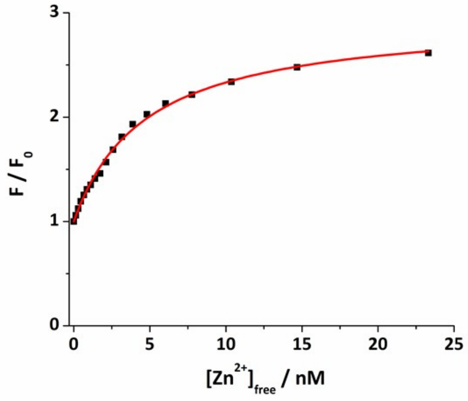
[Probe]	Probe **9**	Probe **12**
1 μM		
0.1 μM		
0.01 μM		

Fig. S6 The non-linear curve fitting of the fluorescence intensity of **9** and **12** at different concentrations against different equivalents of Zn^{2+} to determine K_d applying Equation S1. (λ_{ex} = 346 nm, λ_{em} = 414 nm)

Table S2 Summary of K_d values for probes **9** and **12**.

	[Probe] = 1 μM		[Probe] = 0.1 μM		[Probe] = 0.01 μM	
	K_d	R^2	K_d	R^2	K_d	R^2
9	4.70 ± 0.49 nM	0.9825	4.54 ± 0.38 nM	0.9883	3.50 ± 0.10 nM	0.9985
12	6.11 ± 0.41 nM	0.9926	2.87 ± 0.22 nM	0.9871	4.73 ± 0.20 nM	0.9968

Detection limit (LOD) calculation

To determine detection limit, fluorescence spectrum of probe only was measured 20 times and the standard deviation of this blank measurement was obtained as σ. The slope K was obtained from linear fitting of the fluorescence Zn^{2+} titration data (see Fig. S7). Then the detection limit was then calculated through Equation S2[18,19]:

$$LOD = \frac{3\sigma}{K} \qquad \text{(Equation S2)}$$

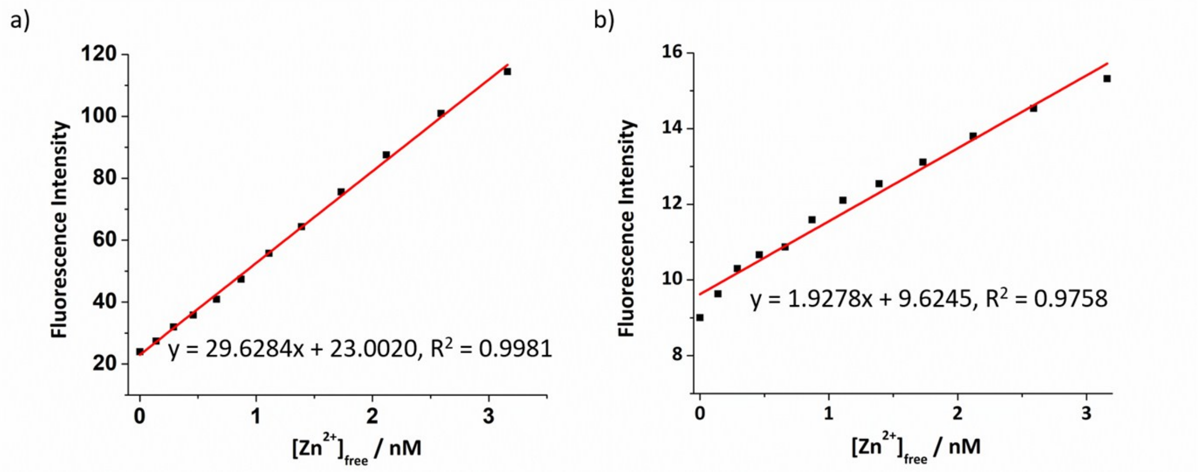


Fig. S7 Fluorescence response of a) **9** (1 μM) and b) **12** (1 μM) against $[Zn^{2+}]_{free}$. (λ_{ex} = 346 nm, λ_{em} = 414 nm)

Quantum yield

$$\Phi_X = \Phi_{ST}(\frac{Grad_X}{Grad_{ST}})(\frac{\eta_X}{\eta_{ST}})^2$$

Equation S3 Equation used to calculate fluorescence quantum yield.[7] Where the subscripts *ST* and *X* denote standard and test respectively, *Φ* is the fluorescence quantum yield, *Grad* the gradient from the plot of integrated fluorescence intensity *vs* absorbance, and *η* the refractive index of the solvent.

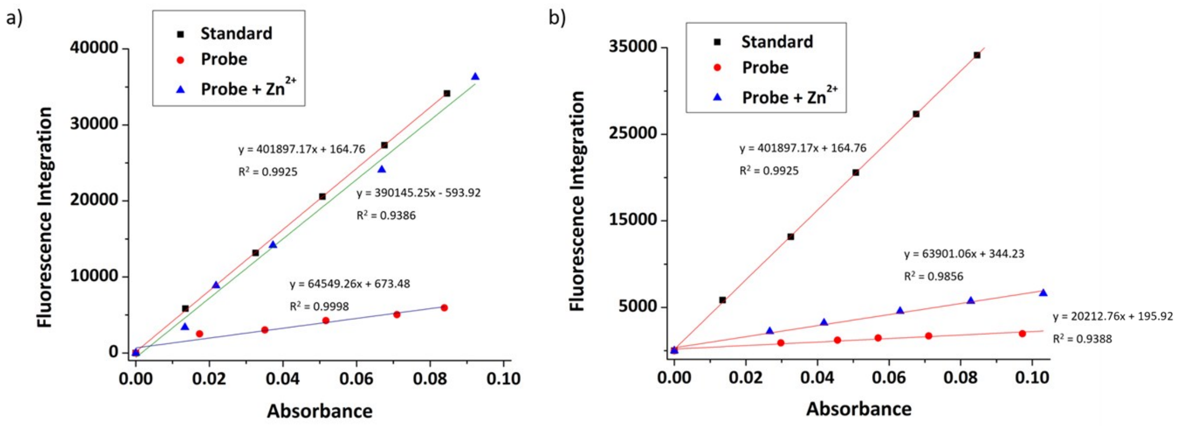


Fig. S8 Linear plots for a) standard sample, **9**, and **9** + Zn^{2+}, b) standard sample, **12**, and **12** + Zn^{2+} to obtain quantum yields. (λ_{ex} = 346 nm)

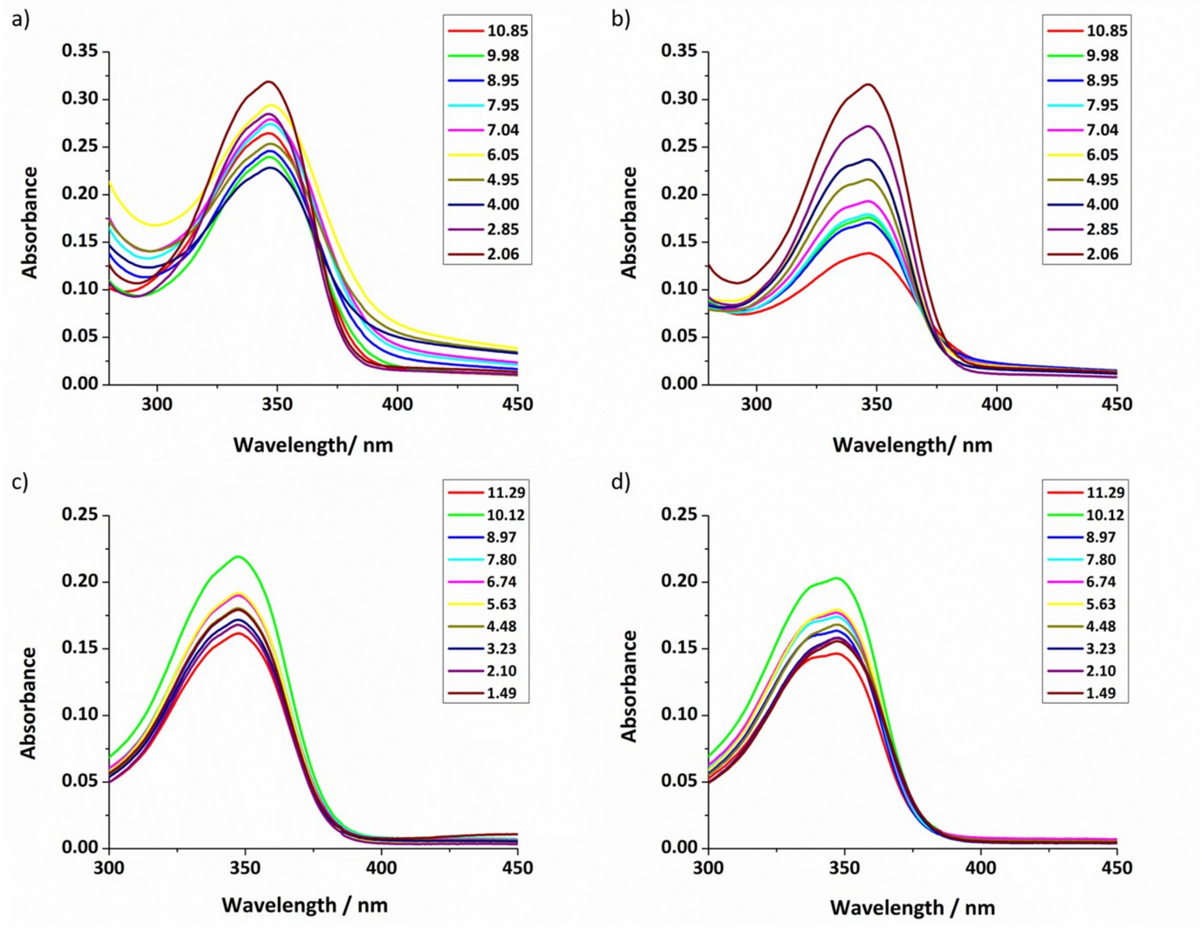


Fig. S9 The UV-Vis spectra of sensor a) **9** (50 μM), b) **9** + Zn^{2+} (50 μM), c) **12** (50 μM), d) **12** + Zn^{2+} (50 μM), at different pH.

pH profile to establish pK_a values of **9**

$$\frac{F - F_0}{F_{max} - F_0} = \frac{\Delta F_{1max}}{(1 + 10^{(pH - pK_{a1})})} + \frac{\Delta F_{2max}}{(1 + 10^{(pH - pK_{a2})})} + \frac{\Delta F_{3max}}{(1 + 10^{(pH - pK_{a3})})} +$$

Equation S4 The equation used to calculate pK_a values. F_{max} is the maximum normalized emission integration ($F_{max} = 1$), F_0 is the minimum normalized emission integration obtained at pH = 12.82, and ΔF_{1max}, ΔF_{2max}, ΔF_{3max} and ΔF_{4max} are the maximum fluorescence integration changes associated with the corresponding pK_a values.

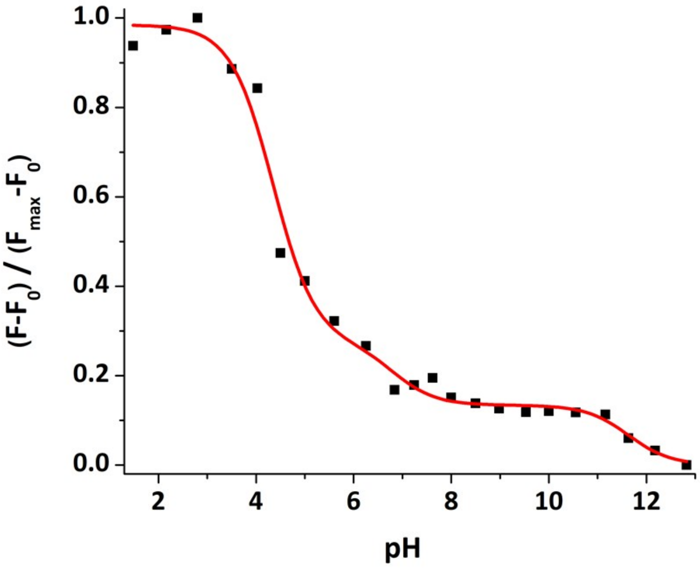


Fig. S10 Normalized integrated fluorescence emission of **9** (50 µM) *vs* pH, the nonlinear curve fitting used to determine the apparent pK_a values applying Equation S3. The determined pK_a values are: pK_{a1} = 0.81 ± 0.19, pK_{a2} = 4.34 ± 0.11, pK_{a3} = 6.83 ± 0.53, pK_{a4} = 11.63 ± 0.41, $R^2 = 0.98$.

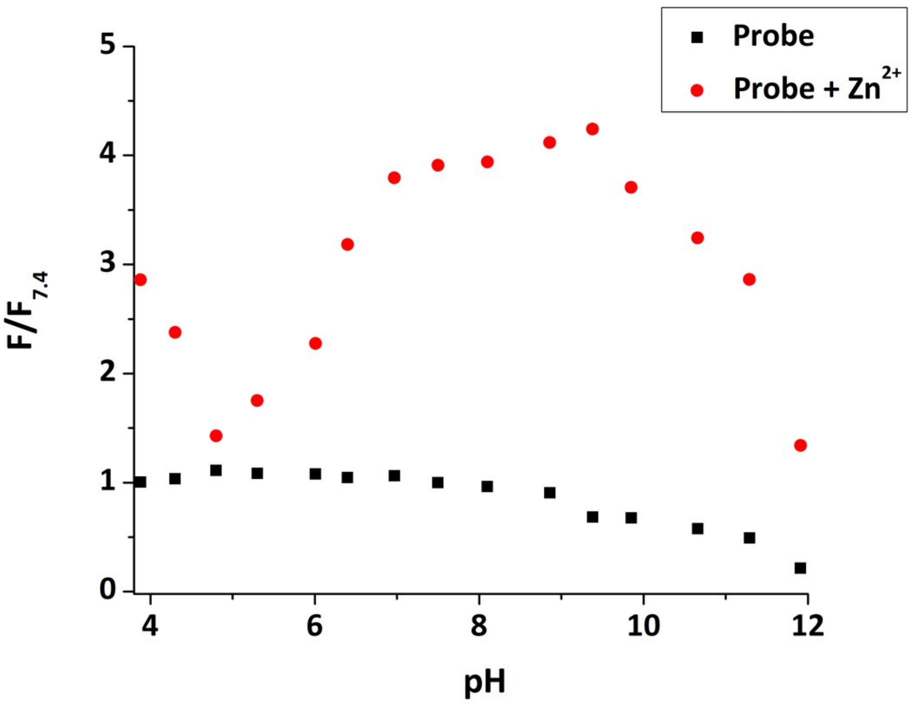


Fig. S11 The pH profile of **12** (50 μM, black dots) and complex with 1 equivalent of Zn^{2+} (red dots).

pH profile to establish pK_a values of **12**

$$\frac{F - F_0}{F_{max} - F_0} = \frac{\Delta F_{1max}}{(1 + 10^{(pH - pK_{a1})})} + \frac{\Delta F_{2max}}{(1 + 10^{(pH - pK_{a2})})} + \frac{\Delta F_{3max}}{(1 + 10^{(pH - pK_{a3})})}$$

Equation S5 The equation used to calculate pK_a values. F_{max} is the maximum normalized emission integration ($F_{max} = 1$), F_0 is the minimum normalized emission integration obtained at pH = 12.43, and ΔF_{1max}, ΔF_{2max} and ΔF_{3max} are the maximum fluorescence integration changes associated with the corresponding pK_a values.

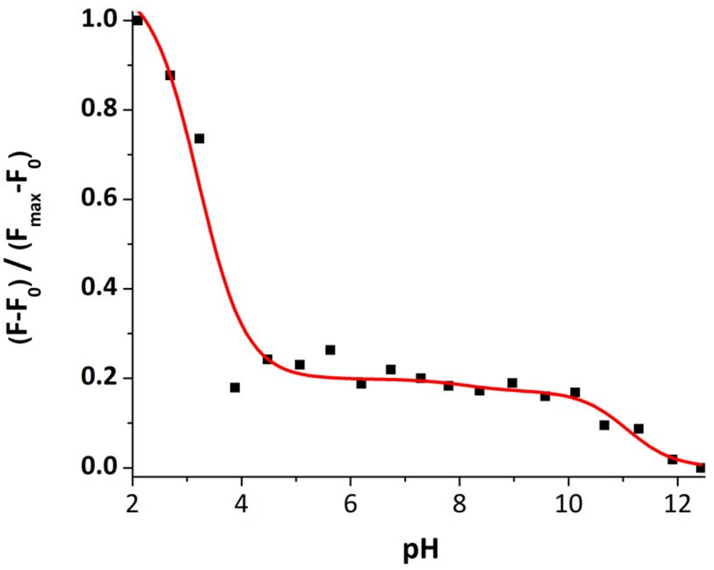


Fig. S12 Normalized integrated fluorescence emission of **12** (50 μM) *vs* pH, the nonlinear curve fitting used to determine the apparent pK_a values applying Equation S4. The determined pK_a values are: pK_{a1} = 3.20 ± 0.14, pK_{a2} = 8.07 ± 0.11, pK_{a3} = 11.07 ± 0.58, R^2 = 0.95.

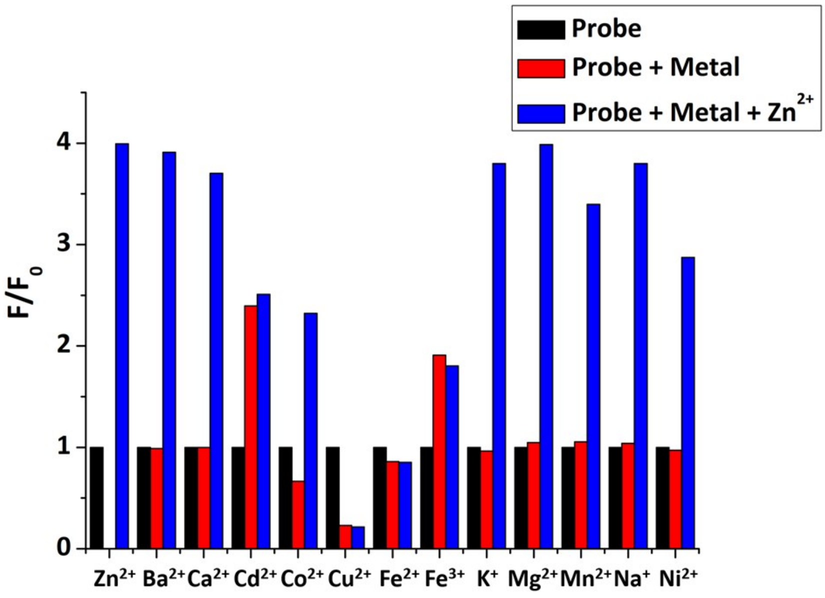
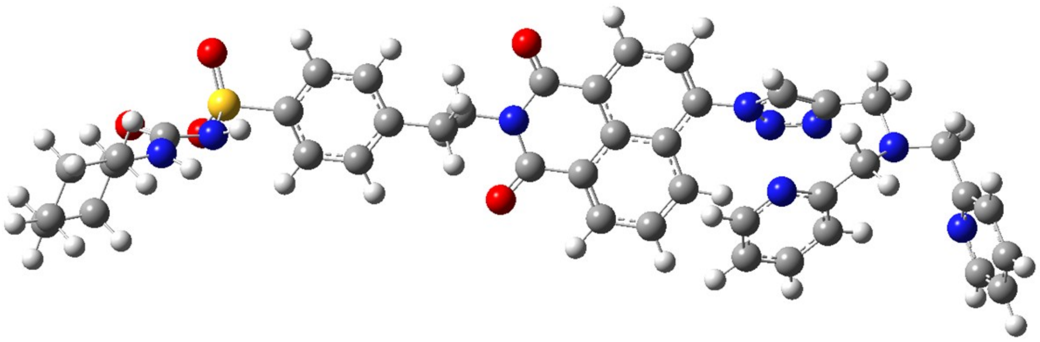


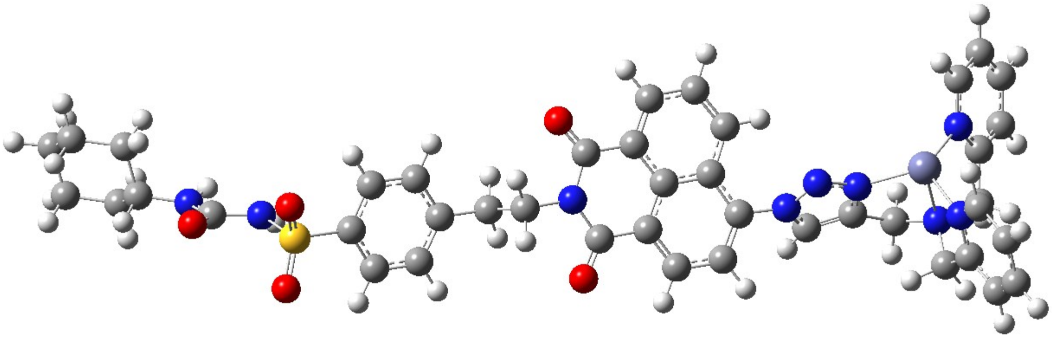
Fig. S13 Metal ion selectivity of **12**. Average normalized fluorescence intensities for **12** (50 μM) (black bars), after addition of 5 equivalents of various cations (red bars), followed by addition of 1 equivalent of $ZnCl_2$ (blue bars).

Theoretical calculations

To understand the binding behaviour of the two probes with Zn^{2+} and its fundamental electronic structure, DFT and TDDFT studies were performed. The structure of **9**, **12** and their complexes with Zn^{2+} were first optimized using B3LYP functional including dispersion corrections (G3) and 6-31G* basic set in Gaussian 09. Then the calculation of excited states and structures of the S_1 minima were obtained at CAMB3LYP/6-31G* level of theory. All calculations considered H_2O as solvent using a continuum model (PCM). The vertical excitations and emission energies are shown in Table S3 and Table S4.

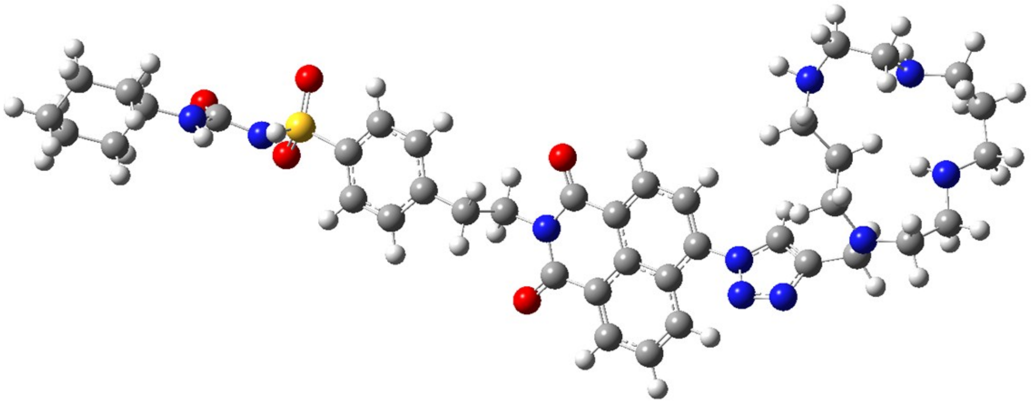


Probe **9**

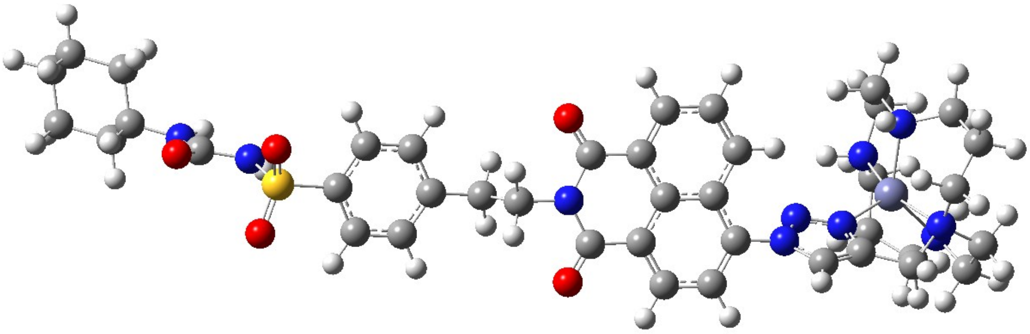


Complex with Zn^{2+}

Fig. S14 The optimized structures of **9** and its complex with Zn^{2+}.



Probe **12**



Complex with Zn^{2+}

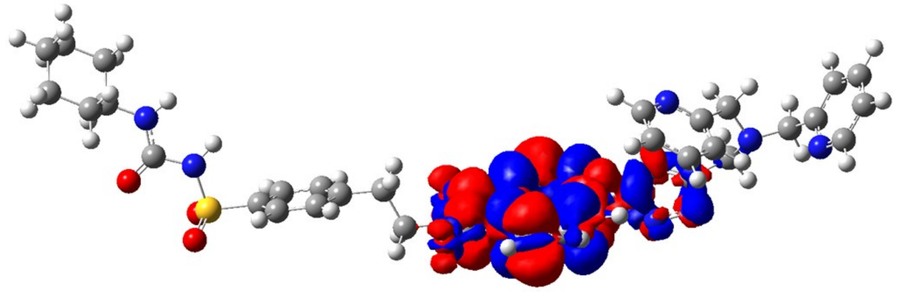
Fig. S15 The optimized structures of **12** and its complex with Zn^{2+}.

Table S3. Comparison of the experimental data with the calculated result of vertical electronic excitation energies (eV) and the emission from S_1 to ground state of **9** and its Zn^{2+} complex.

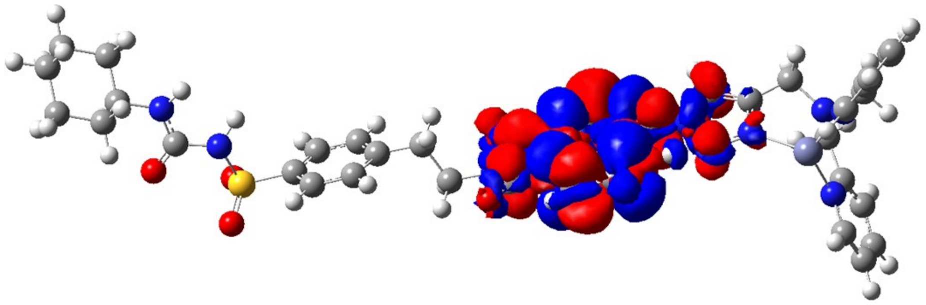
	Electronic transition	Energy (eV)	Wavelength (nm)	Oscillator strengths (f)	Experimental data
9					
Absorption	$S_0 \rightarrow S_1$	3.84	322	0.5747	3.58 eV/346 nm
	$S_0 \rightarrow S_2$	4.27	290	0.0384	
	$S_0 \rightarrow S_3$	4.39	282	0.0002	
	$S_0 \rightarrow S_4$	4.71	263	0.0041	
	$S_0 \rightarrow S_5$	4.72	262	0.0043	
	$S_0 \rightarrow S_6$	4.90	253	0.0043	
Emission	$S_1 \rightarrow S_0$	3.19	388	0.7145	3.01 eV/412 nm
Complex of **9** with Zn^{2+}					
Absorption	$S_0 \rightarrow S_1$	3.95	314	0.5437	3.58 eV/346 nm
	$S_0 \rightarrow S_2$	4.26	291	0.0501	
	$S_0 \rightarrow S_3$	4.33	286	0.0006	
	$S_0 \rightarrow S_4$	4.68	265	0.0082	
	$S_0 \rightarrow S_5$	4.93	252	0.0328	
	$S_0 \rightarrow S_6$	5.33	233	0.0138	
Emission	$S_1 \rightarrow S_0$	3.18	390	0.7059	3.01 eV/412 nm

Table S4. Comparison of the experimental data with the calculated result of vertical electronic excitation energies (eV) and the emission from S_1 to ground state of **12** and its Zn^{2+} complex.

	Electronic transition	Energy (eV)	Wavelength (nm)	Oscillator strengths (f)	Experimental data
12					
Absorption	$S_0 \rightarrow S_1$	3.87	320	0.5642	3.58 eV/346 nm
	$S_0 \rightarrow S_2$	4.06	305	0.0021	
	$S_0 \rightarrow S_3$	4.27	290	0.0424	
	$S_0 \rightarrow S_4$	4.39	283	0.0010	
	$S_0 \rightarrow S_5$	4.68	265	0.0000	
	$S_0 \rightarrow S_6$	4.73	262	0.0064	
Emission	$S_1 \rightarrow S_0$	3.18	390	0.7329	3.01 eV/412 nm
Complex of **12** with Zn^{2+}					
Absorption	$S_0 \rightarrow S_1$	3.97	312	0.5188	3.58 eV/346 nm
	$S_0 \rightarrow S_2$	4.27	290	0.0534	
	$S_0 \rightarrow S_3$	4.33	286	0.0008	
	$S_0 \rightarrow S_4$	4.69	264	0.0045	
	$S_0 \rightarrow S_5$	4.93	251	0.0310	
	$S_0 \rightarrow S_6$	5.41	229	0.0126	
Emission	$S_1 \rightarrow S_0$	3.20	387	0.6879	3.01 eV/412 nm

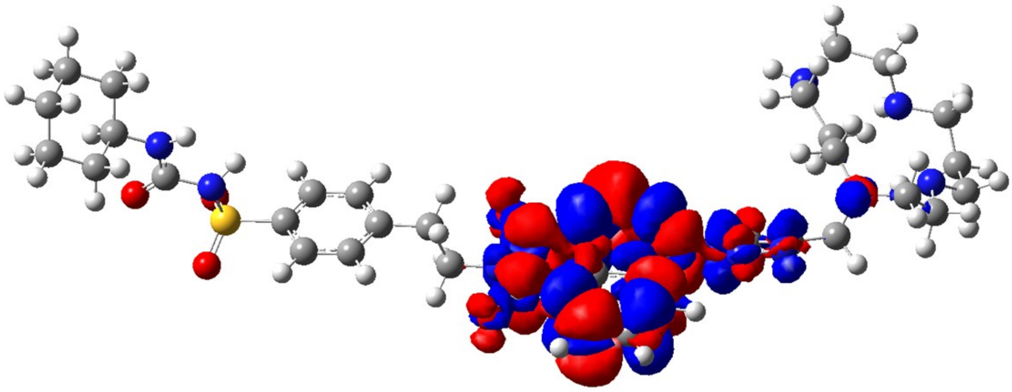


Probe **9**

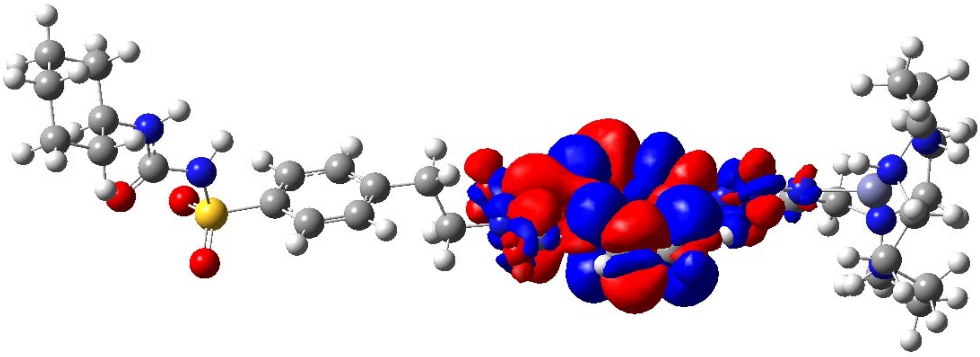


Complex with Zn^{2+}

Fig. S16. S_1-S_0 electron density map for probe **9** and its complex with Zn^{2+} (S_1 minima). Red represents positive densities and blue negative values.



Probe **12**



Complex with Zn^{2+}

Fig. S17. S_1-S_0 electron density map for probe **12** and its complex with Zn^{2+} (S_1 minima). Red represents positive densities and blue negative values.

Biological applications

Toxicity test of probes **9** and **12** to cells

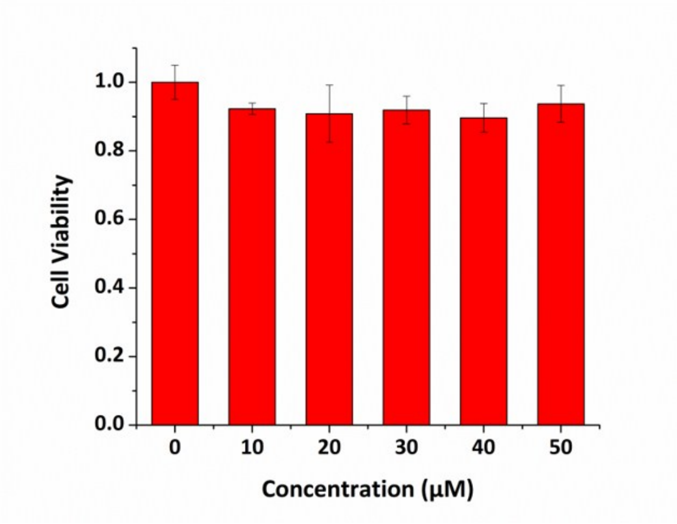


Fig. S18. The HeLa cell viability against probe **9** at different concentrations.

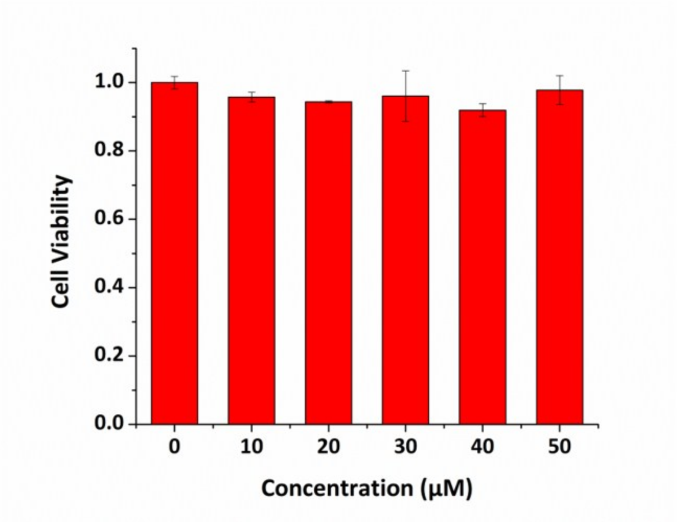


Fig. S19. The HeLa cell viability against probe **12** at different concentrations.

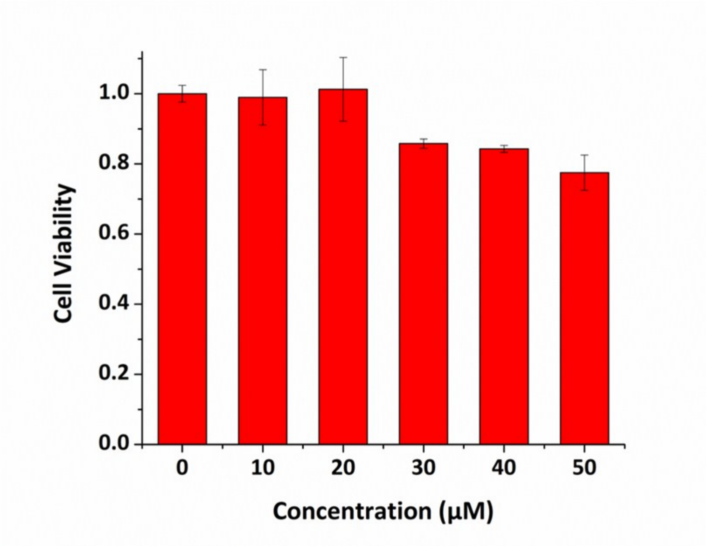


Fig. S20. The HeLa cell viability of **S16** at different concentrations showing its toxicity.

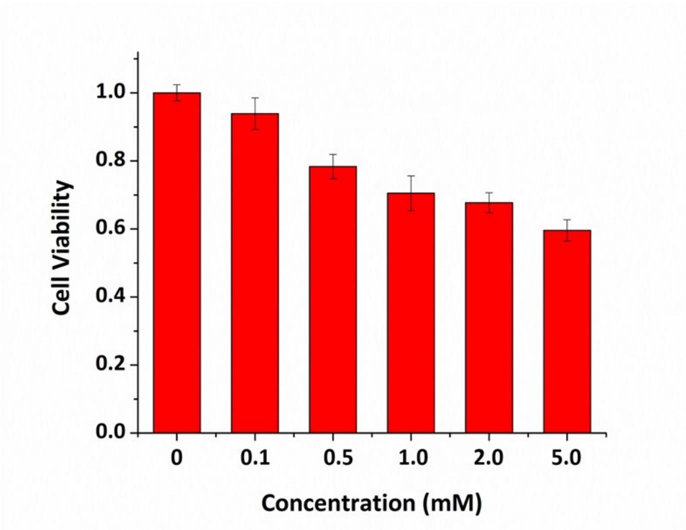


Fig. S21. The HeLa cell viability against sodium azide at different concentrations, as a control experiment.

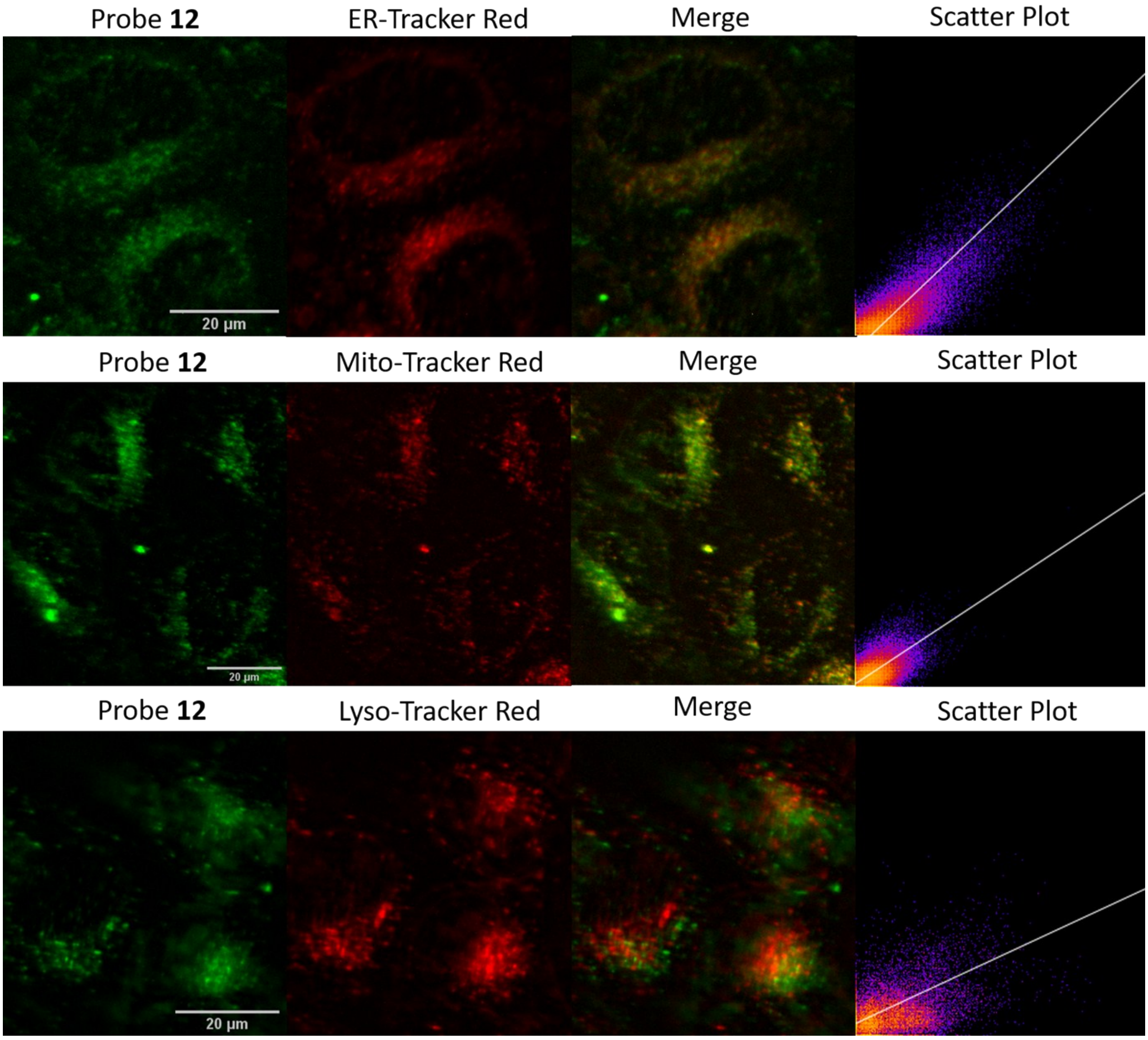


Fig. S22 The colocalization images of HeLa cells incubated with probe **12** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm).

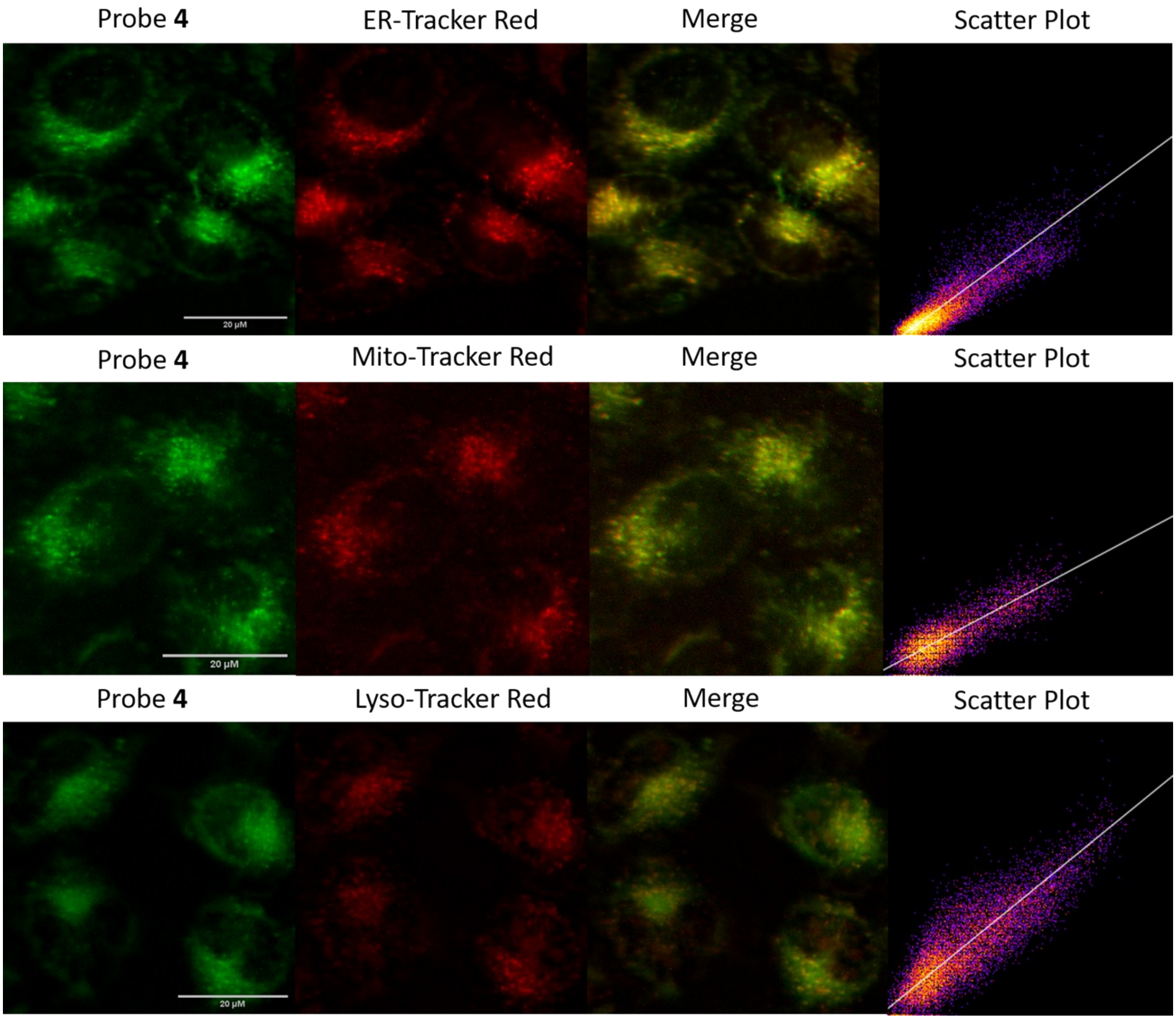


Fig. S23 The colocalization images of HeLa cells incubated with non-targeted probe **4** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.85, 0.78 and 0.81 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

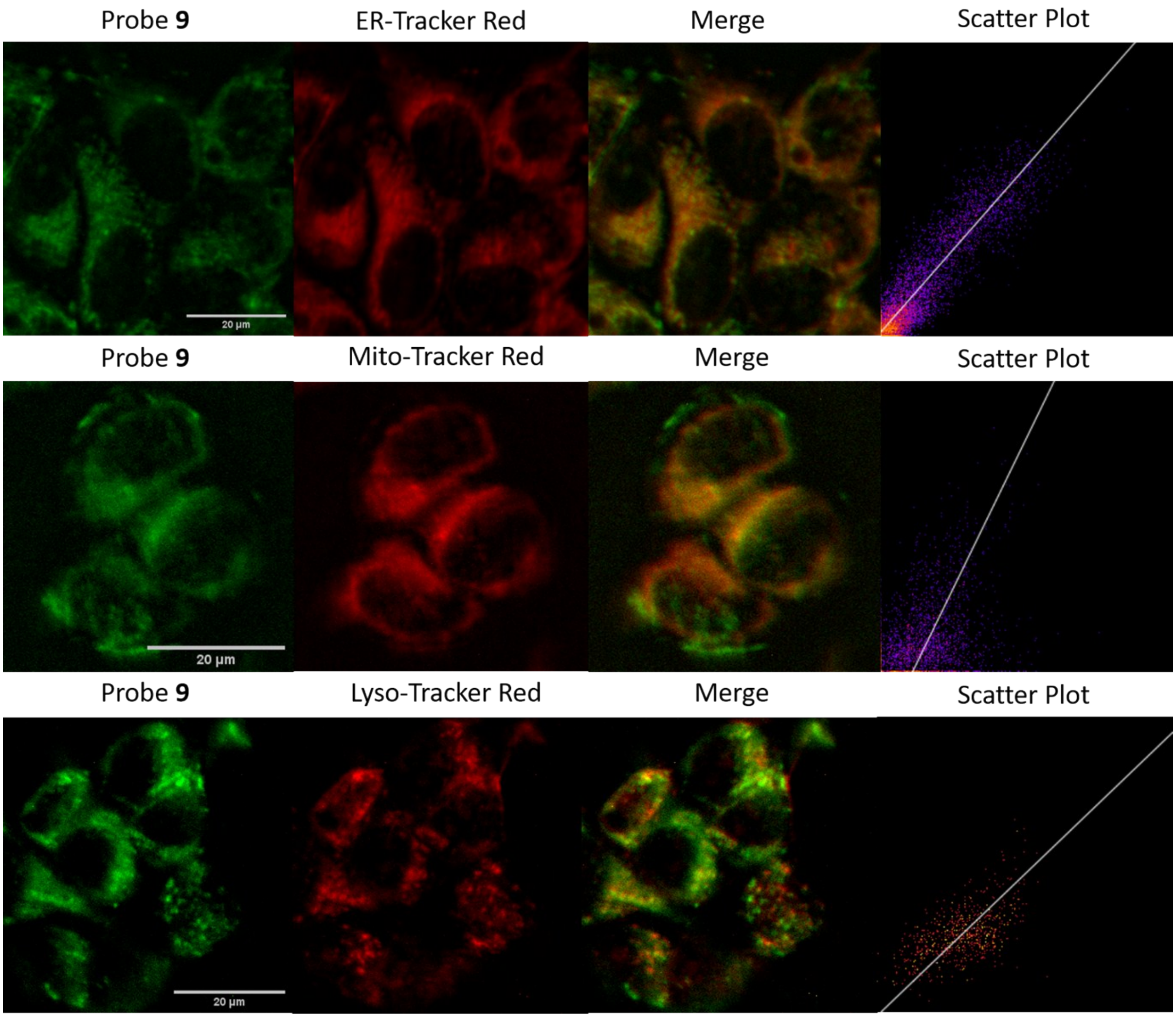


Fig. S24 The colocalization images of MCF-7 cells incubated with probe **9** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.87, 0.43 and 0.49 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

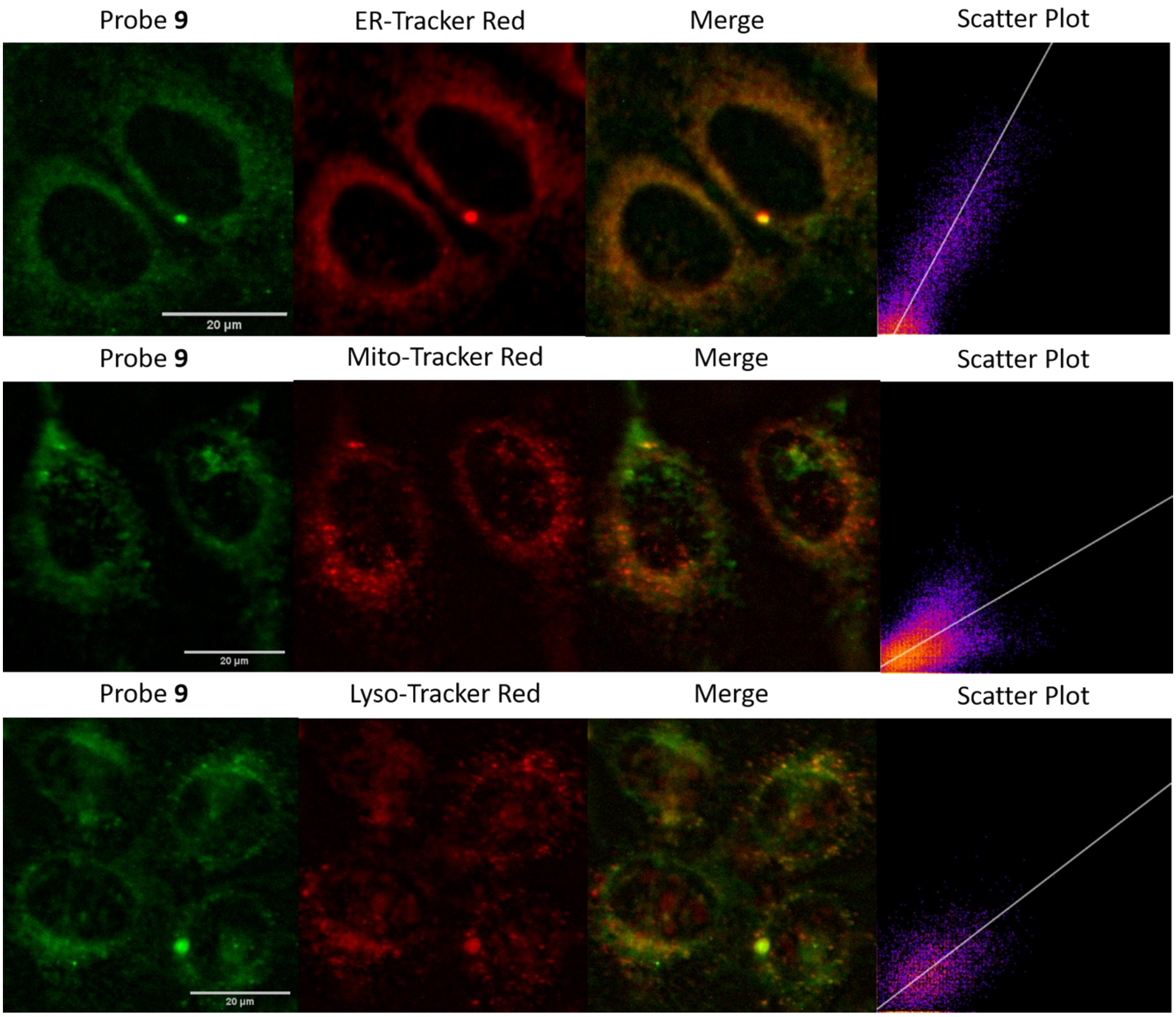


Fig. S25 The colocalization images of EC23 cells incubated with probe **9** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.84, 0.48 and 0.44 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

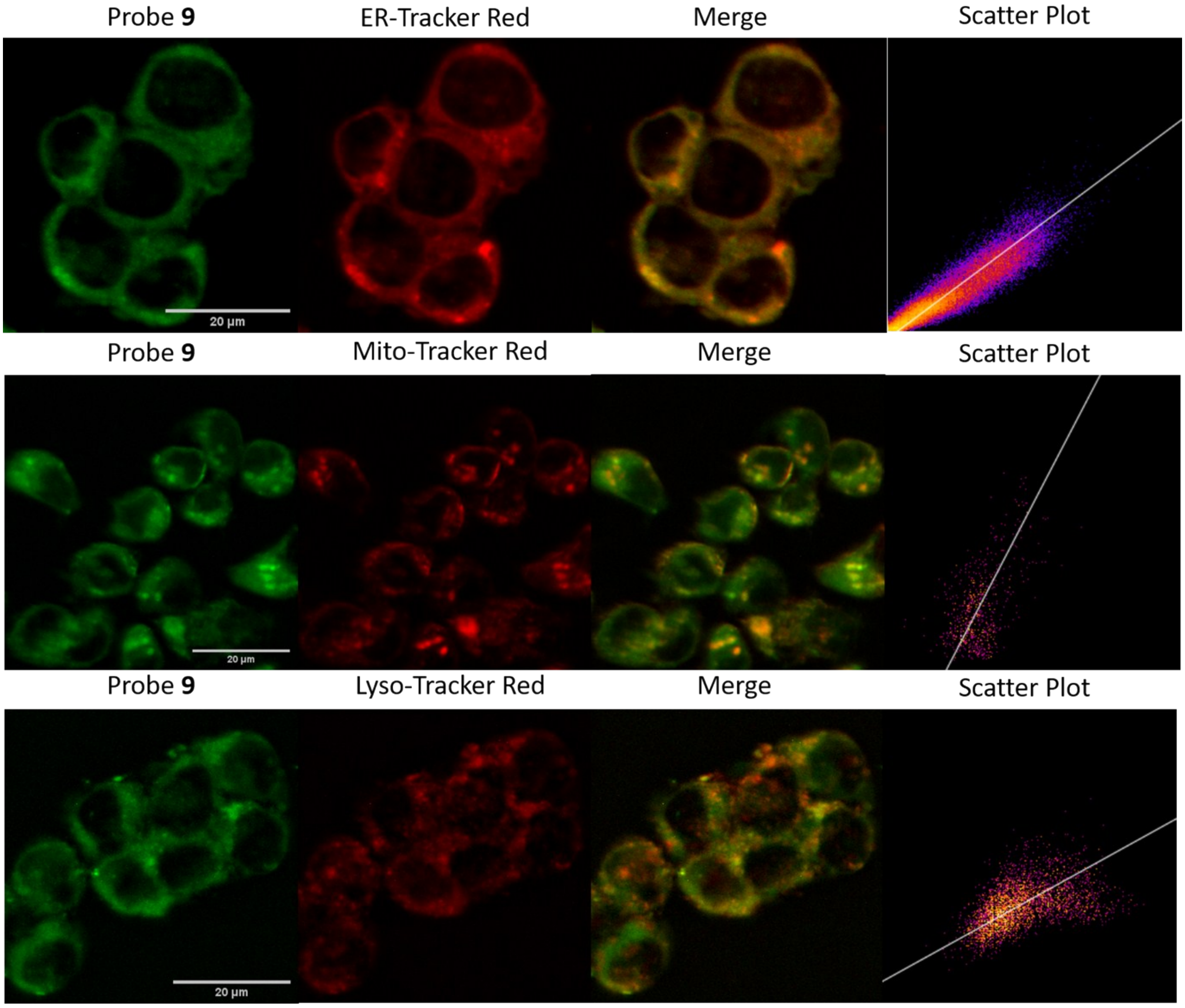


Fig. S26 The colocalization images of HepG2 cells incubated with probe **9** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.91, 0.64 and 0.46 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

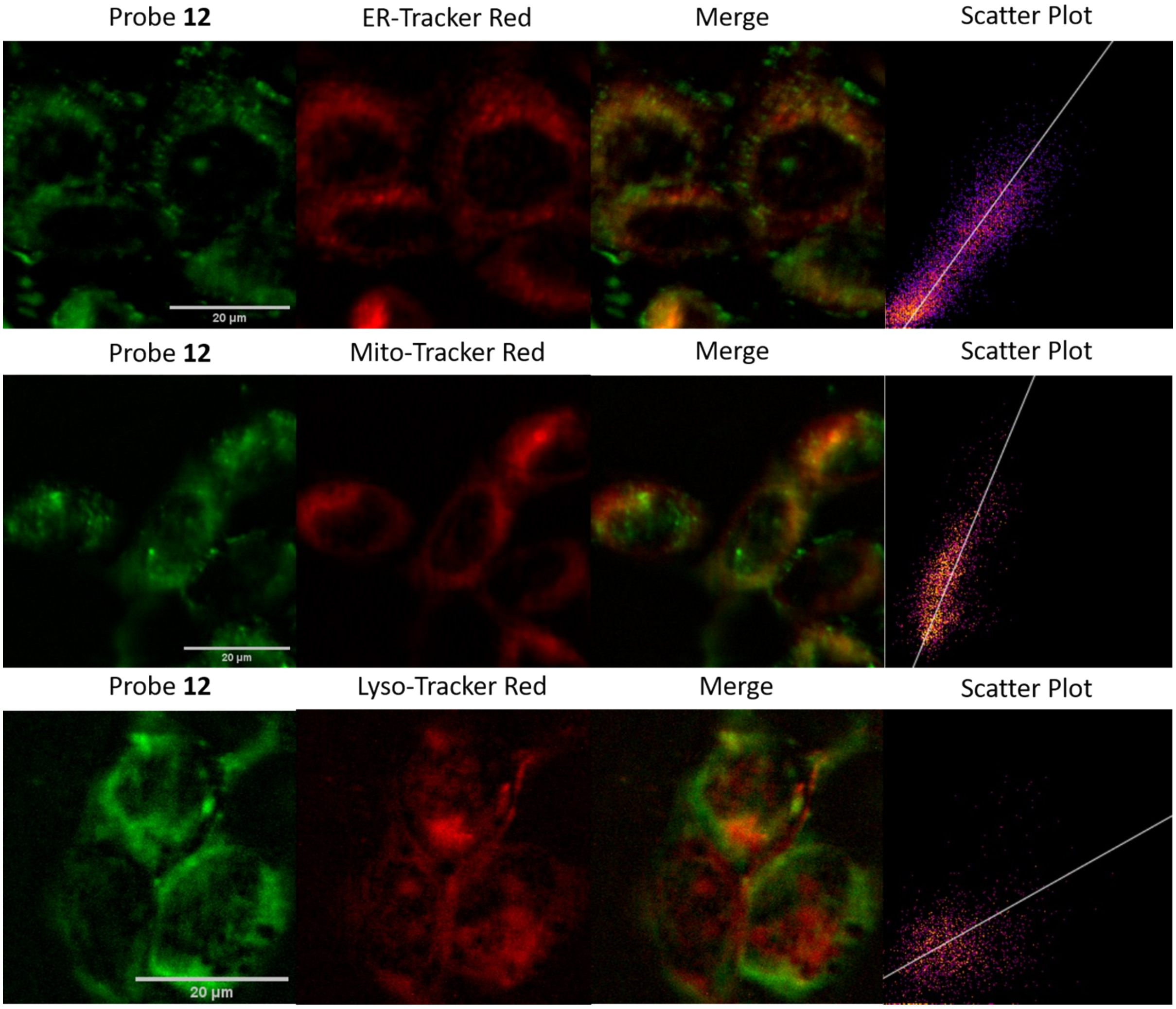


Fig. S27 The colocalization images of MCF-7 cells incubated with probe **12** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.82, 0.54 and 0.38 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

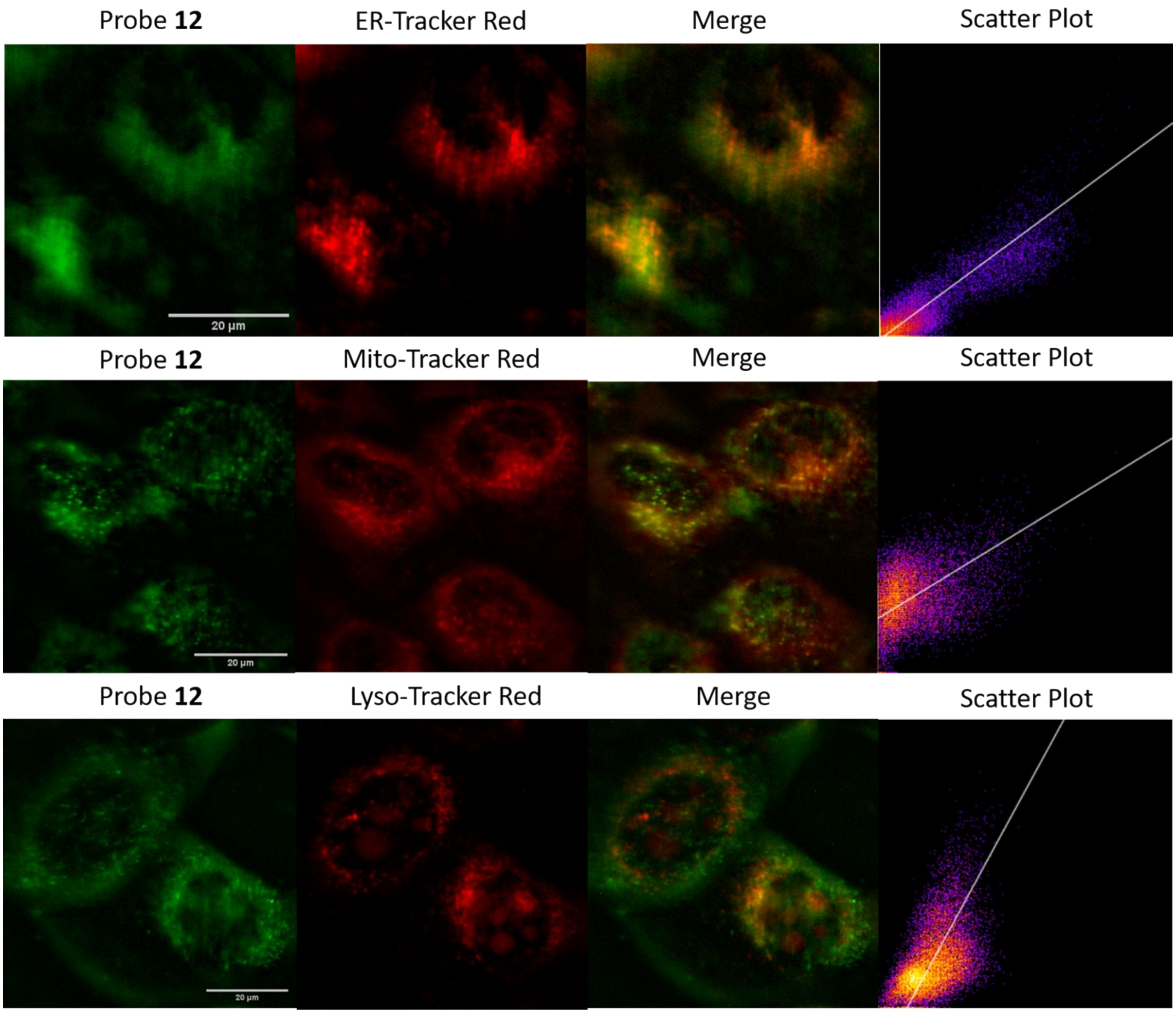


Fig. S28 The colocalization images of EC23 cells incubated with probe **12** (20 µM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 µm). Pearson's correlation coefficients were 0.87, 0.48 and 0.53 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

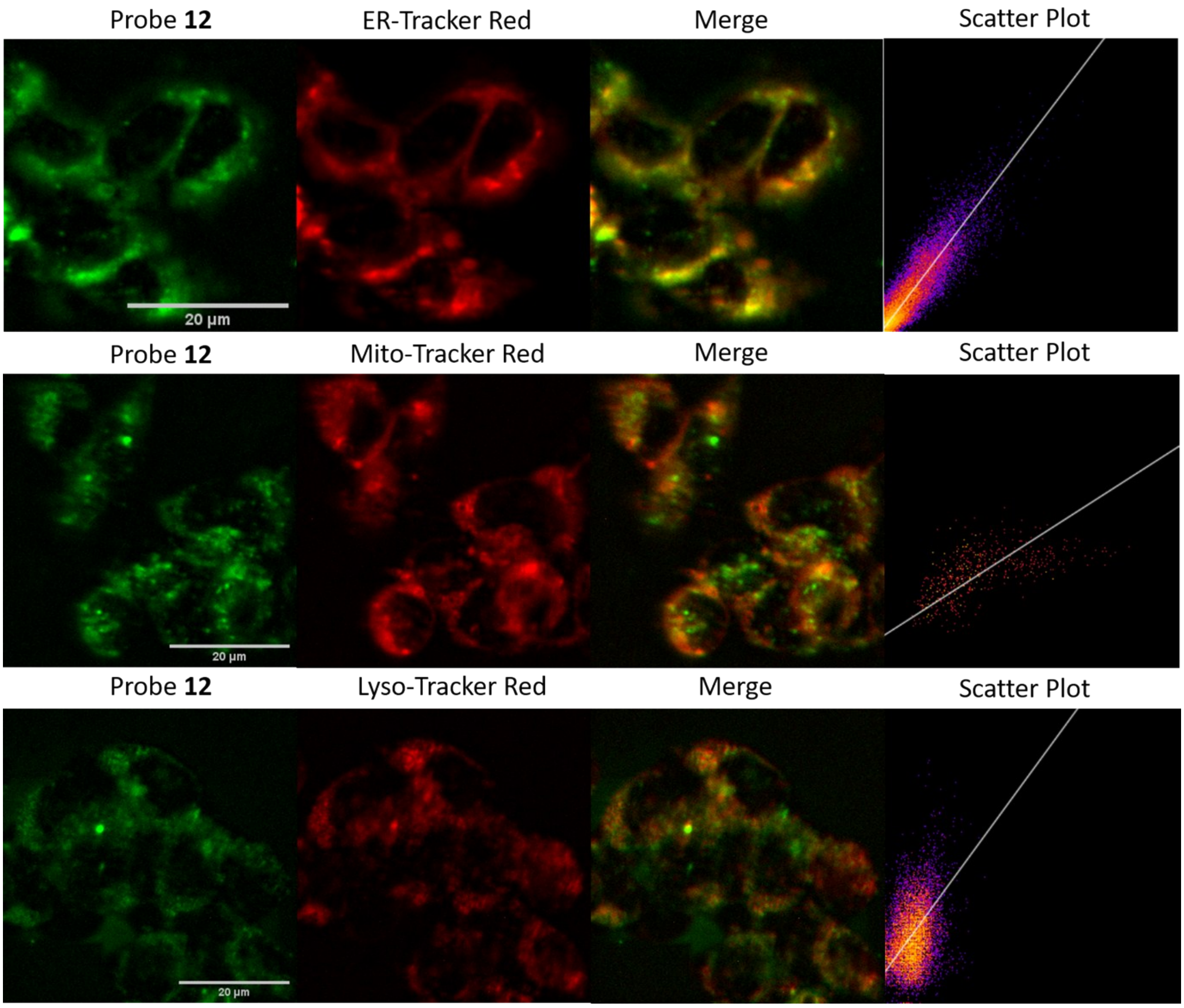


Fig. S29 The colocalization images of HepG2 cells incubated with probe **12** (20 μM, GFP filter: λ_{ex} = 470/30 nm, λ_{em} = 530/50 nm) and organelle tracker red dyes (RFP filter: λ_{ex} = 530/40 nm, λ_{em} = 605/55 nm). (Scale bars = 20 μm). Pearson's correlation coefficients were 0.88, 0.51 and 0.36 compared to ER-tracker red, Mito-tracker red and Lyso-tracker red, respectively.

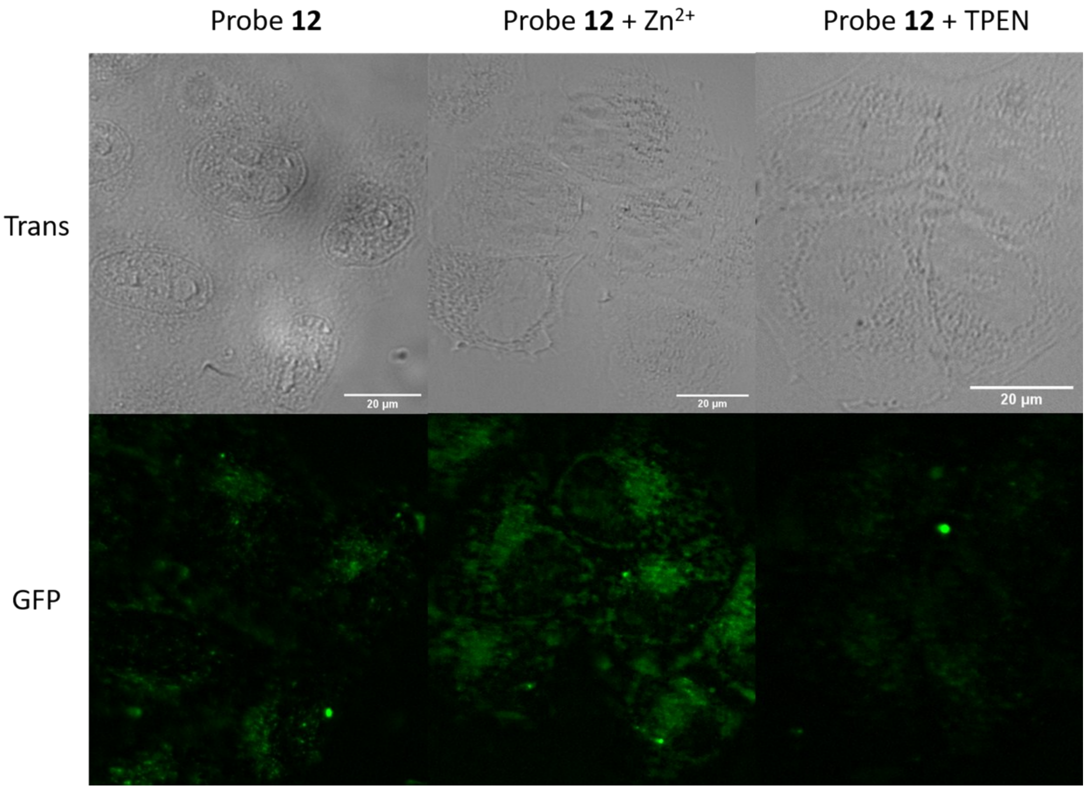


Fig. S30 Fluorescence microscopy images of HeLa cells treated with **12** (20 µM), **12** (20 µM) with zinc pyrithione (100 µM), and **12** (20 µM) with TPEN (100 µM) (Scale bars = 20 µm).

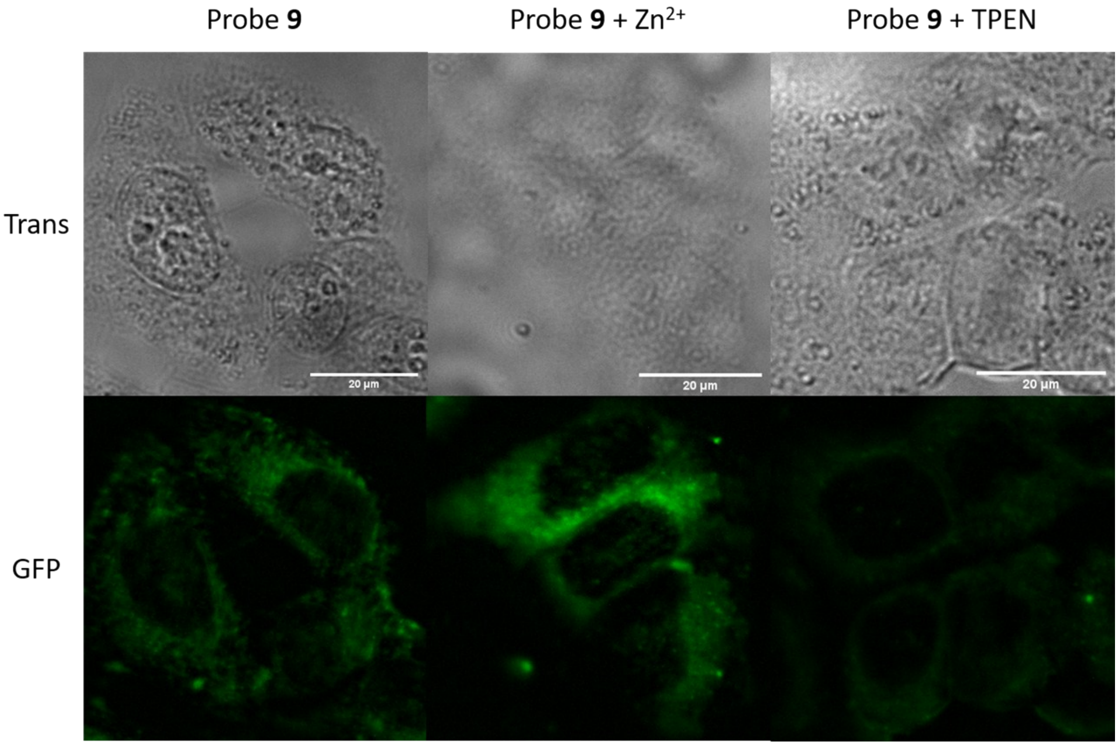


Fig. S31 Fluorescence microscopy images of MCF-7 cells treated with **9** (20 µM), **9** (20 µM) with zinc pyrithione (100 µM), and **9** (20 µM) with TPEN (100 µM) (Scale bars = 20 µm).

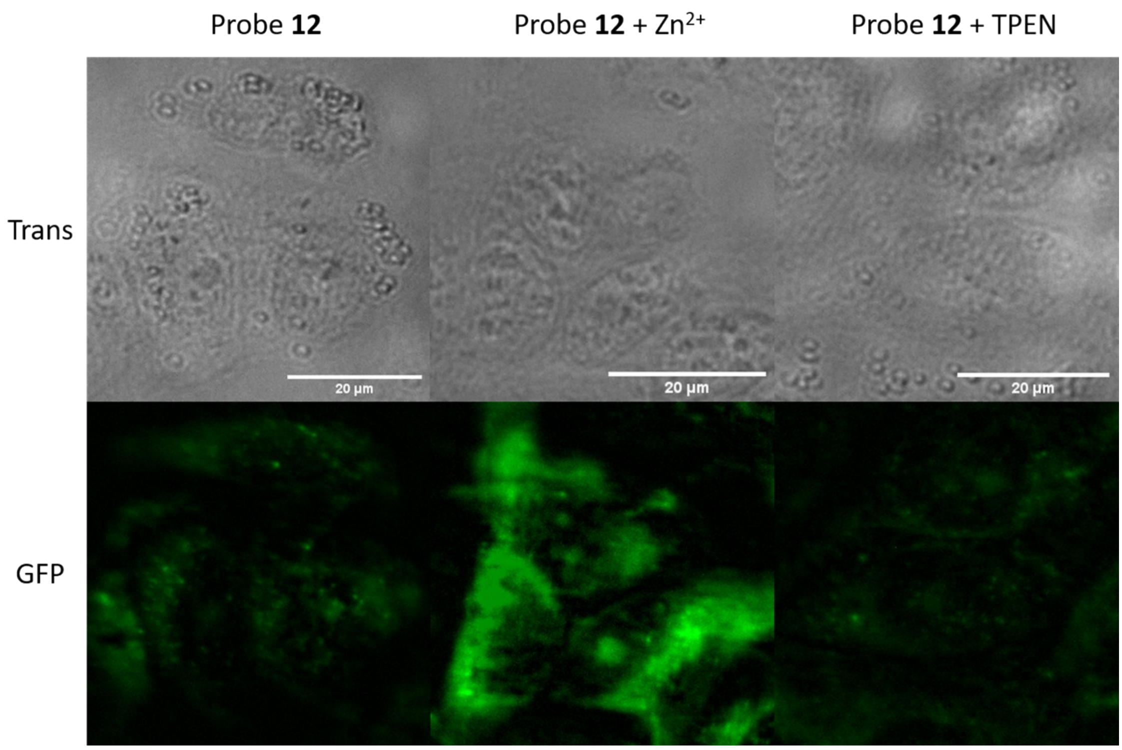


Fig. S32 Fluorescence microscopy images of MCF-7 cells treated with **12** (20 µM), **12** (20 µM) with zinc pyrithione (100 µM), and **12** (20 µM) with TPEN (100 µM) (Scale bars = 20 µm).

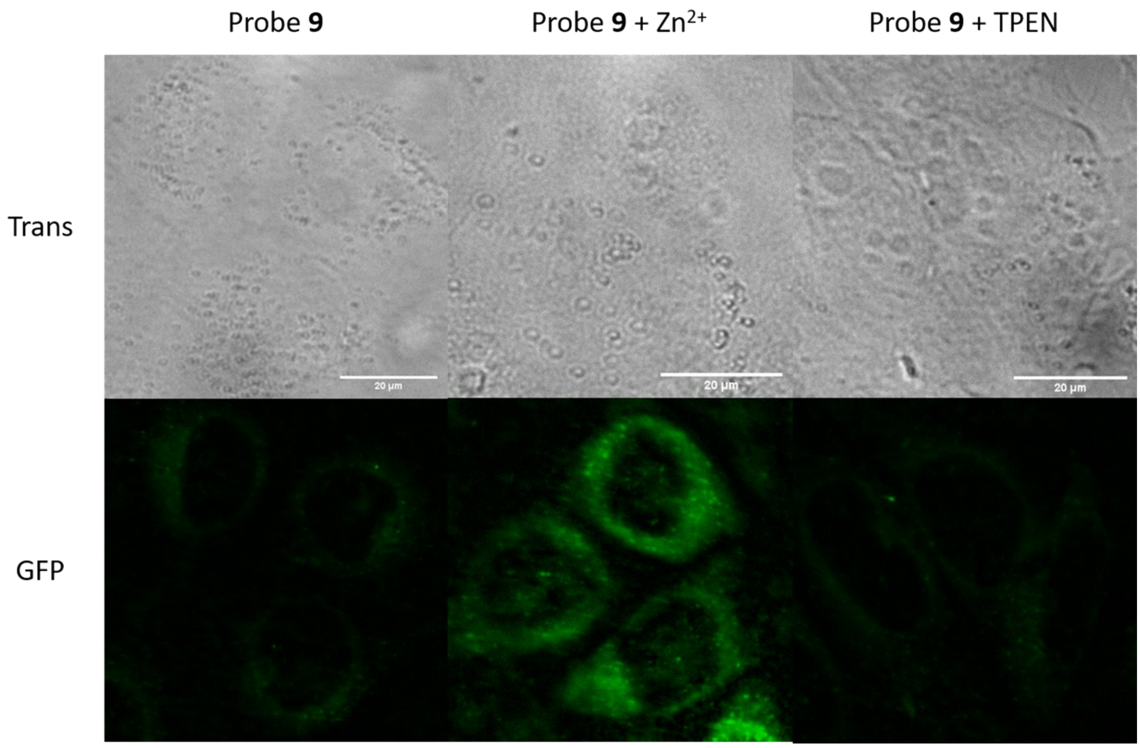


Fig. S33 Fluorescence microscopy images of EC23 cells treated with **9** (20 µM), **9** (20 µM) with zinc pyrithione (100 µM), and **9** (20 µM) with TPEN (100 µM) (Scale bars = 20 µm).

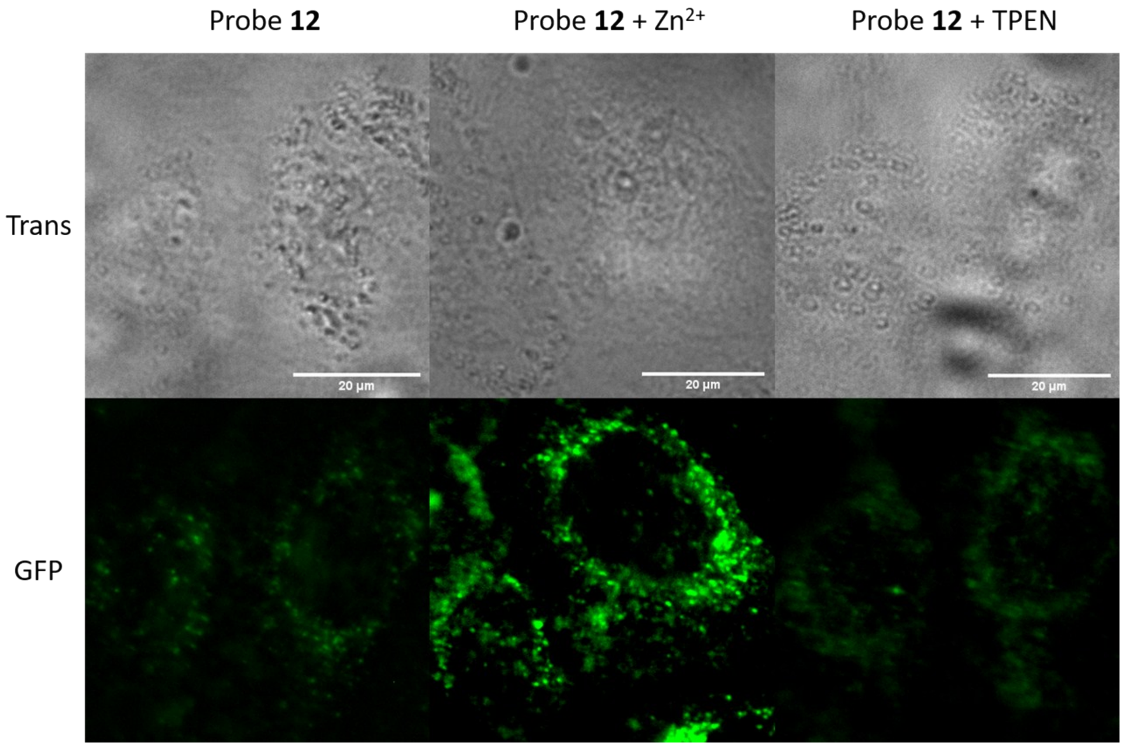


Fig. S34 Fluorescence microscopy images of EC23 cells treated with **12** (20 μM), **12** (20 μM) with zinc pyrithione (100 μM), and **12** (20 μM) with TPEN (100 μM) (Scale bars = 20 μm).

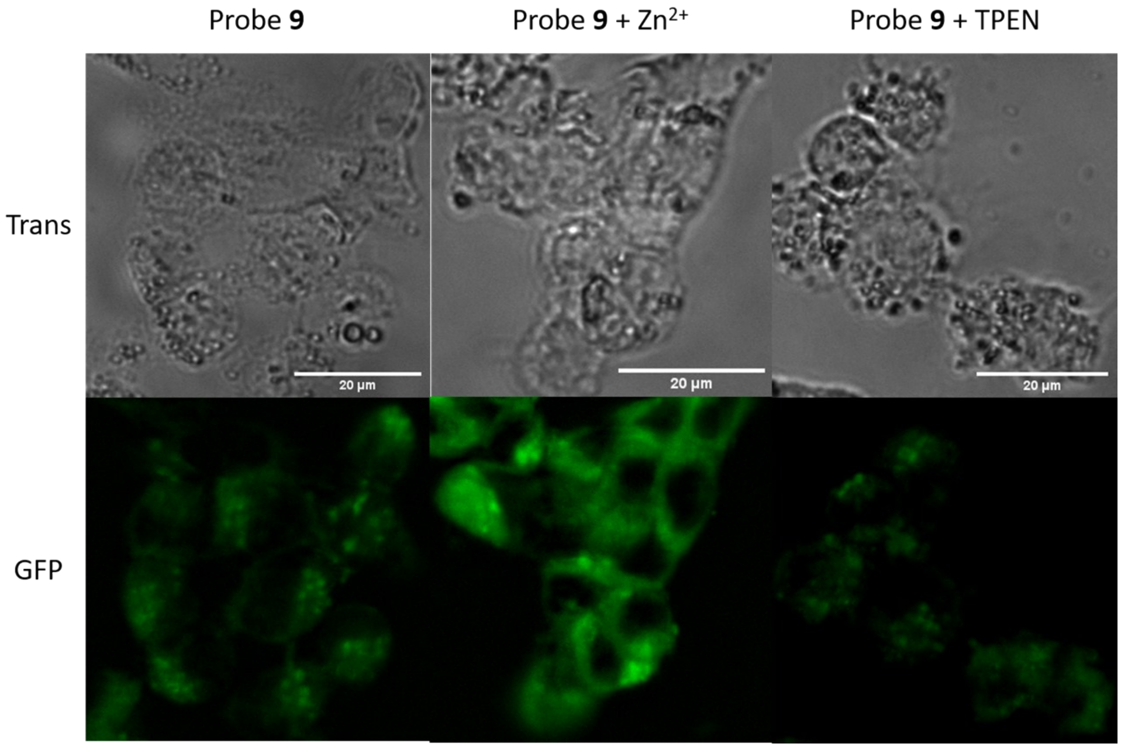


Fig. S35 Fluorescence microscopy images of HepG2 cells treated with **9** (20 μM), **9** (20 μM) with zinc pyrithione (100 μM), and **9** (20 μM) with TPEN (100 μM) (Scale bars = 20 μm).

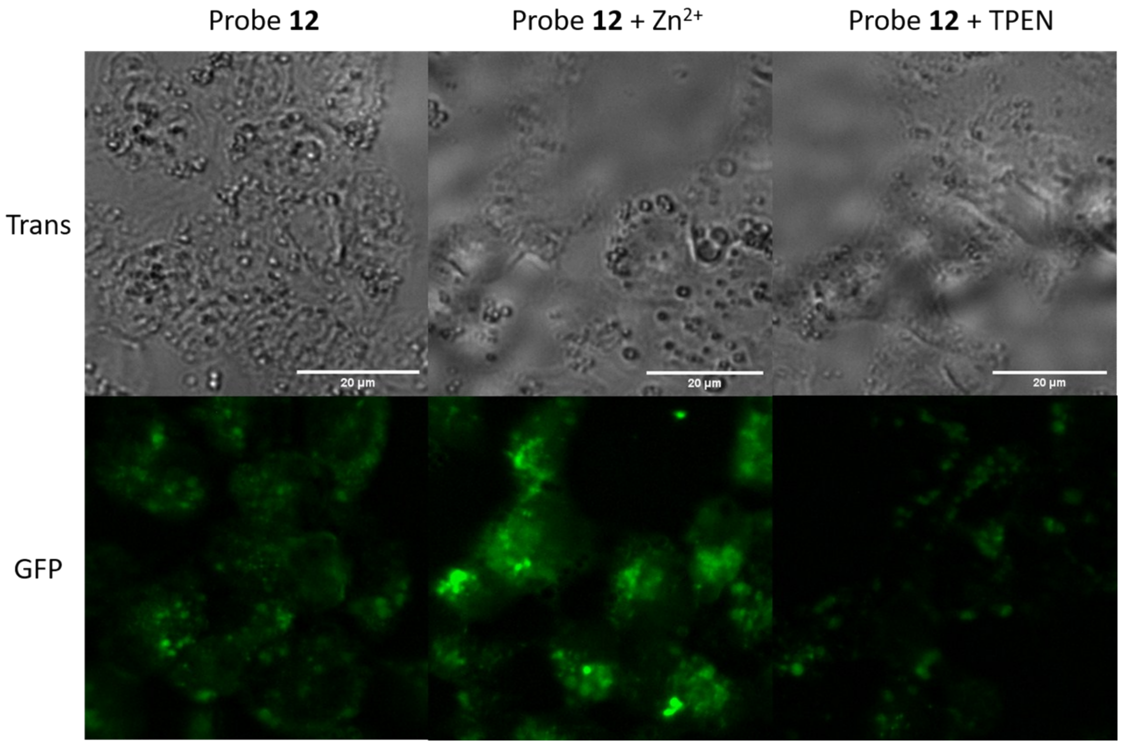


Fig. S36 Fluorescence microscopy images of HepG2 cells treated with **12** (20 µM), **12** (20 µM) with zinc pyrithione (100 µM), and **12** (20 µM) with TPEN (100 µM) (Scale bars = 20 µm).

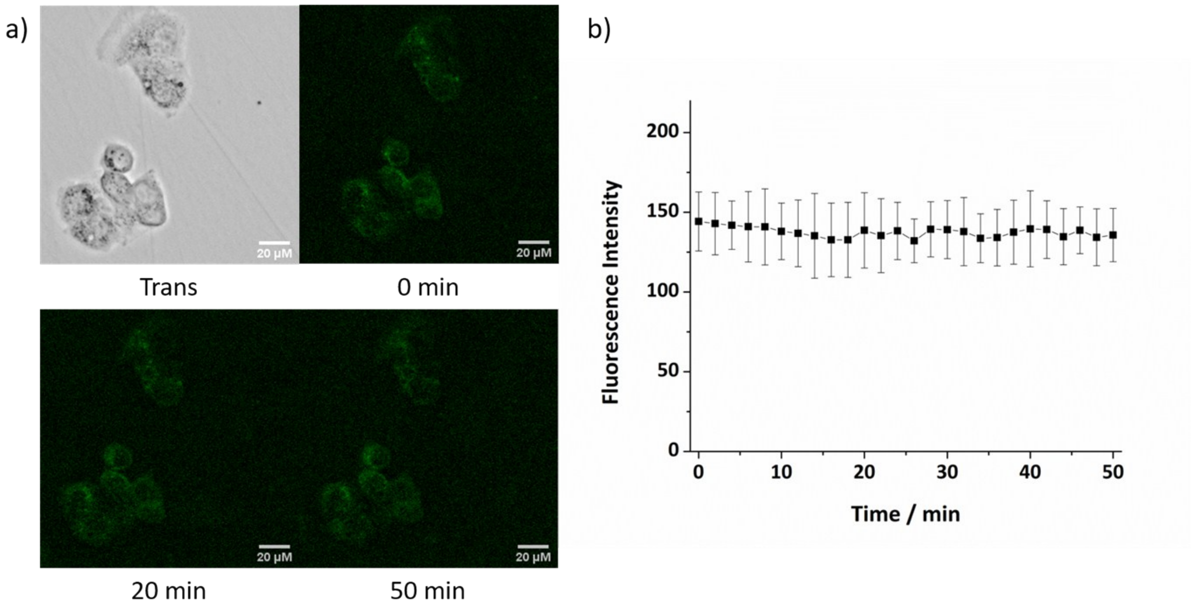


Fig. S37 a) Fluorescence microscopy images and b) fluorescence intensity changes of probe **9** (20 µM) in HepG2 cells against time. (Scale bars = 20 µM)

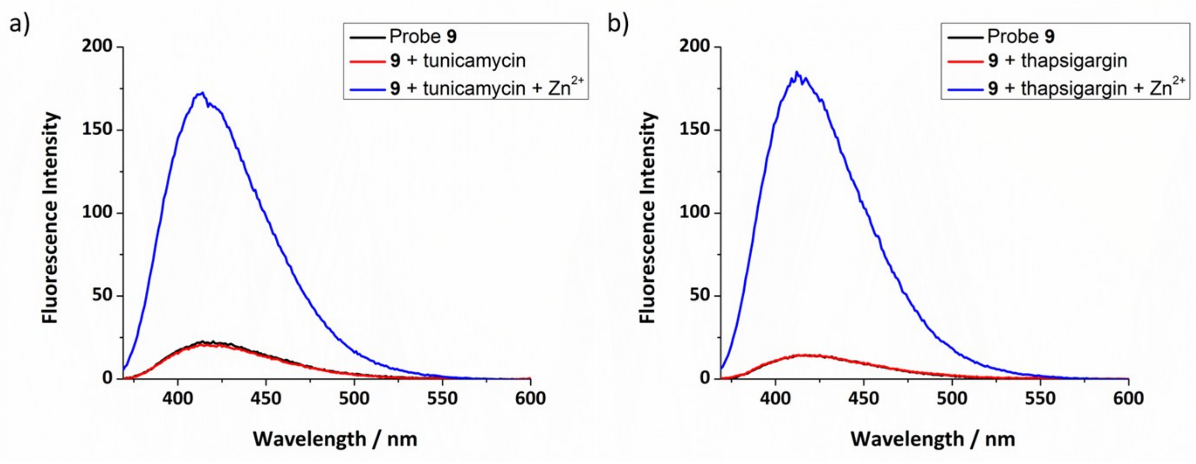


Fig. 38 Fluorescence spectra of probe **9** (20 μM) and after addition of ER stress inducers (1 equivalent), subsequent addition of $ZnCl_2$ (1 equivalent), to show ER stress inducers do not affect fluorescence of probe **9** and its response to Zn^{2+}.

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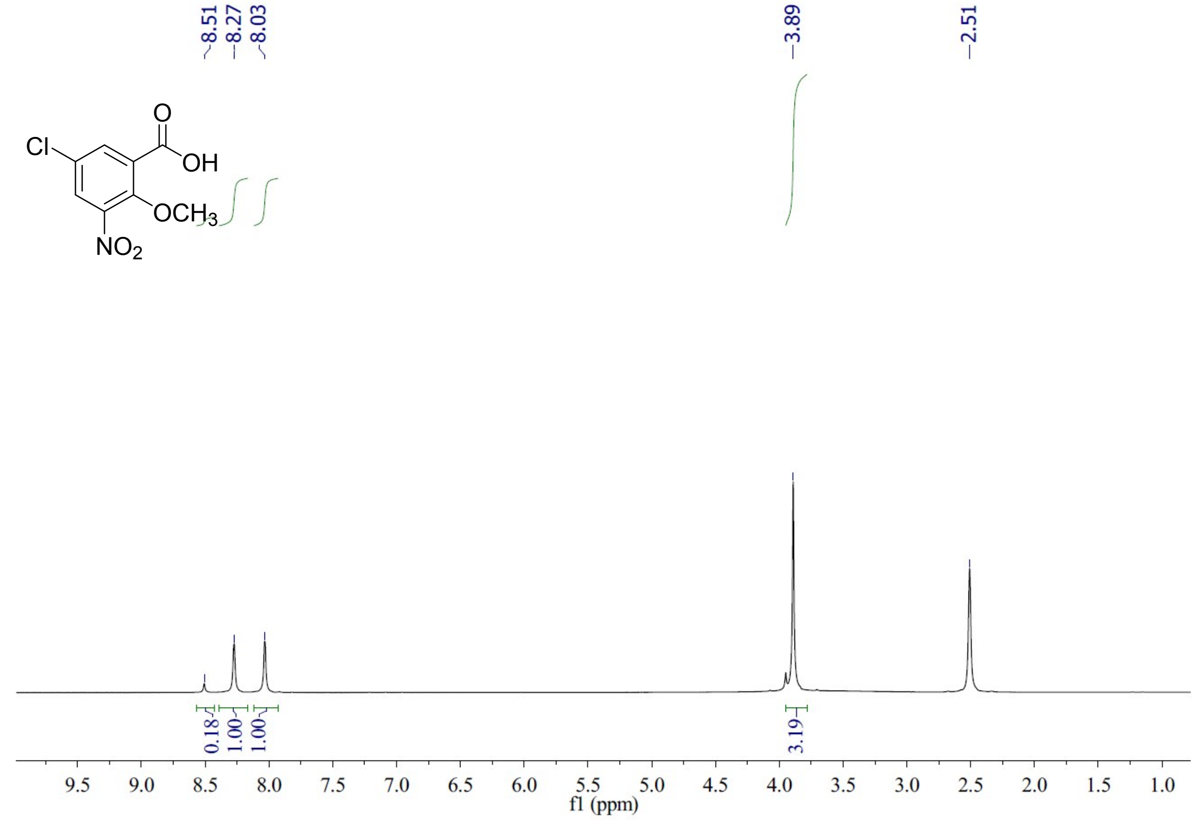
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8.27
8.03
3.89
2.51
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O
OH
OCH3
NO2
0.18
1.00
1.00
3.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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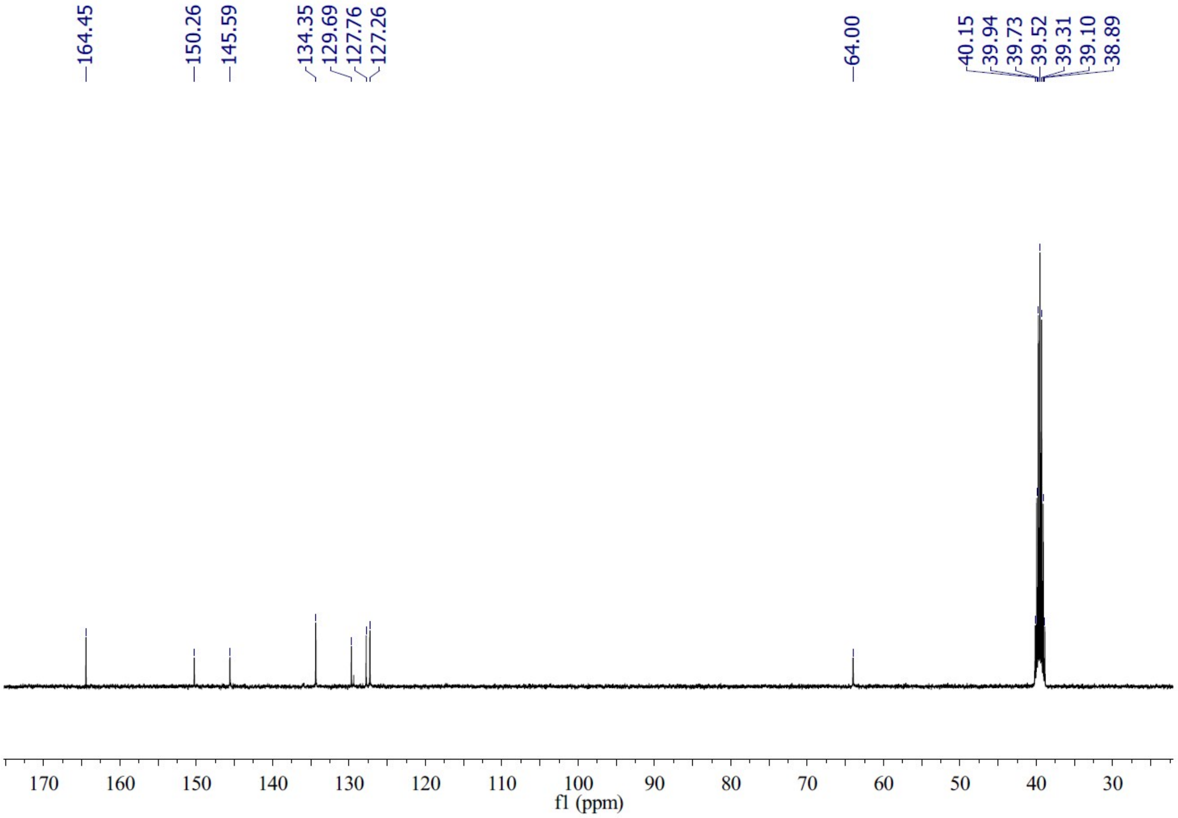
1.5
1.0
f1 (ppm)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150.26
145.59
134.35
129.69
127.76
127.26
64.00
40.15
39.94
39.73
39.52
39.31
39.10
38.89
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

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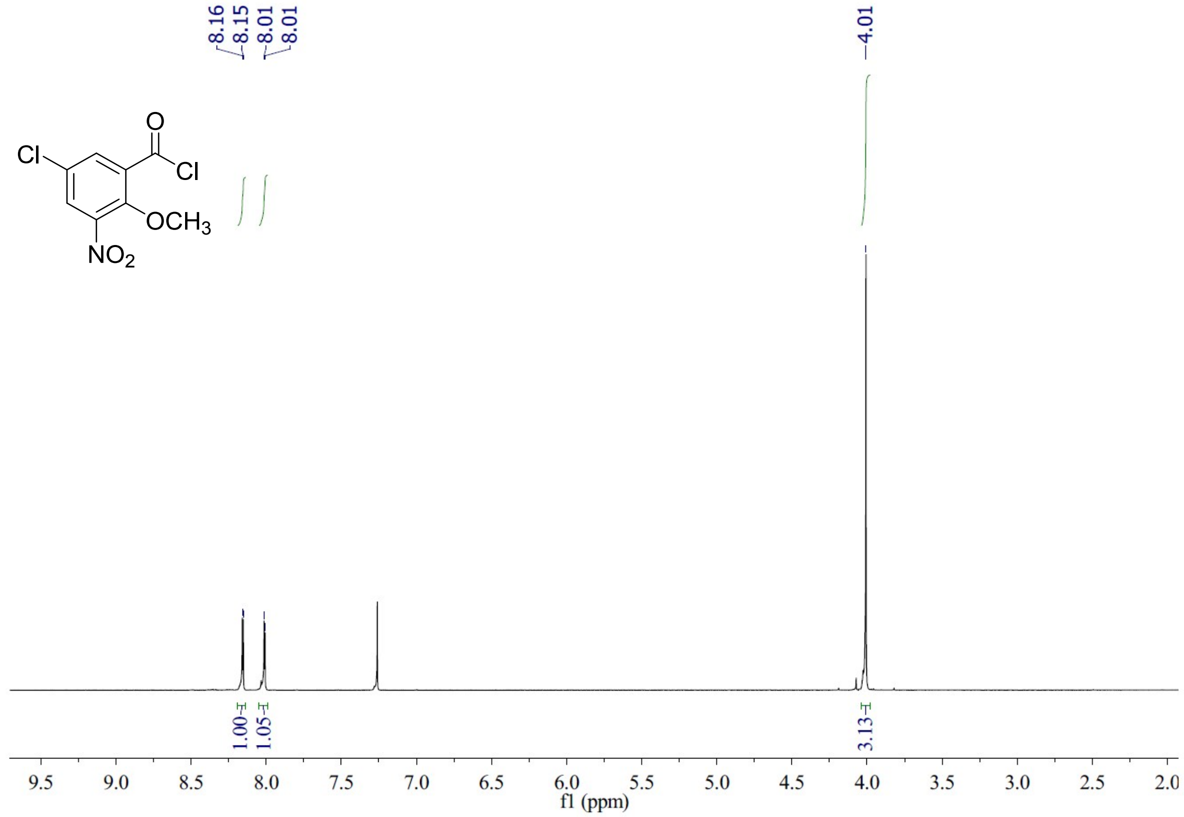
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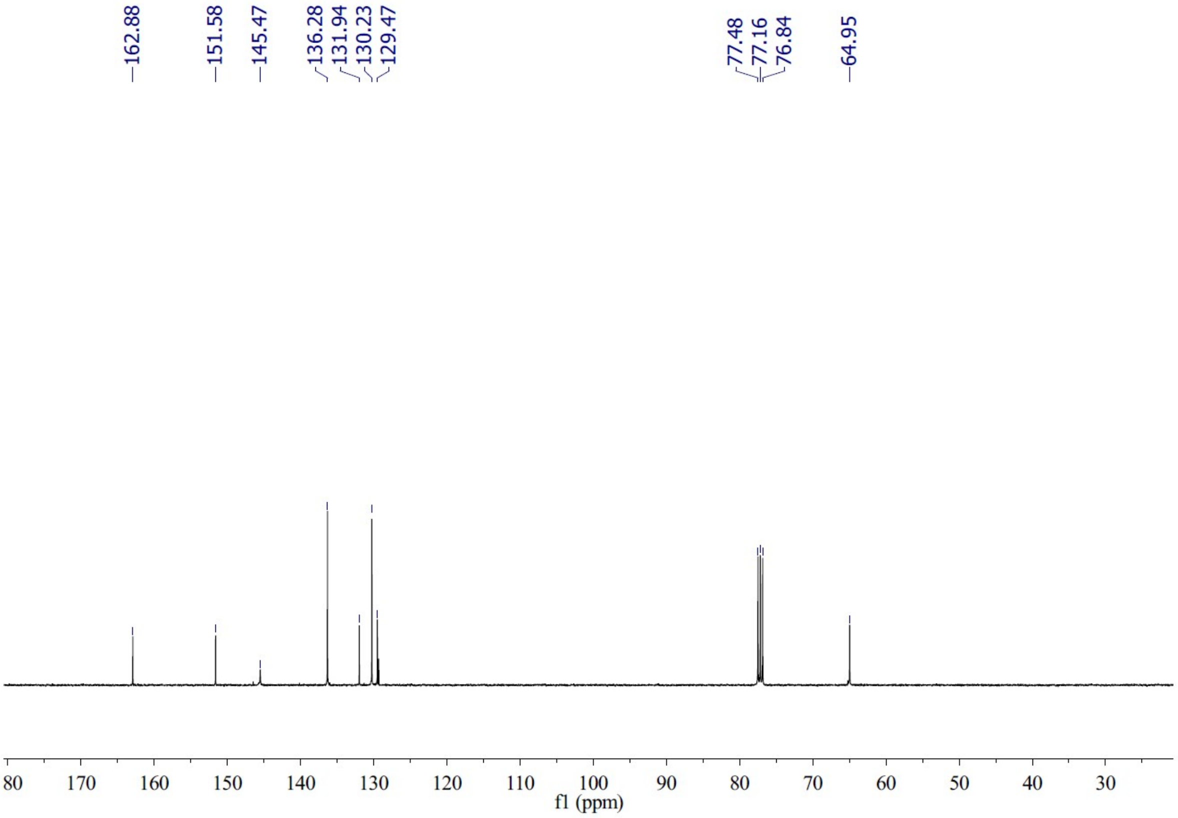
8.01
4.01
Cl
O
Cl
OCH3
NO2
1.00
1.05
3.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)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145.47
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130.23
129.47
77.48
77.16
76.84
64.95
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

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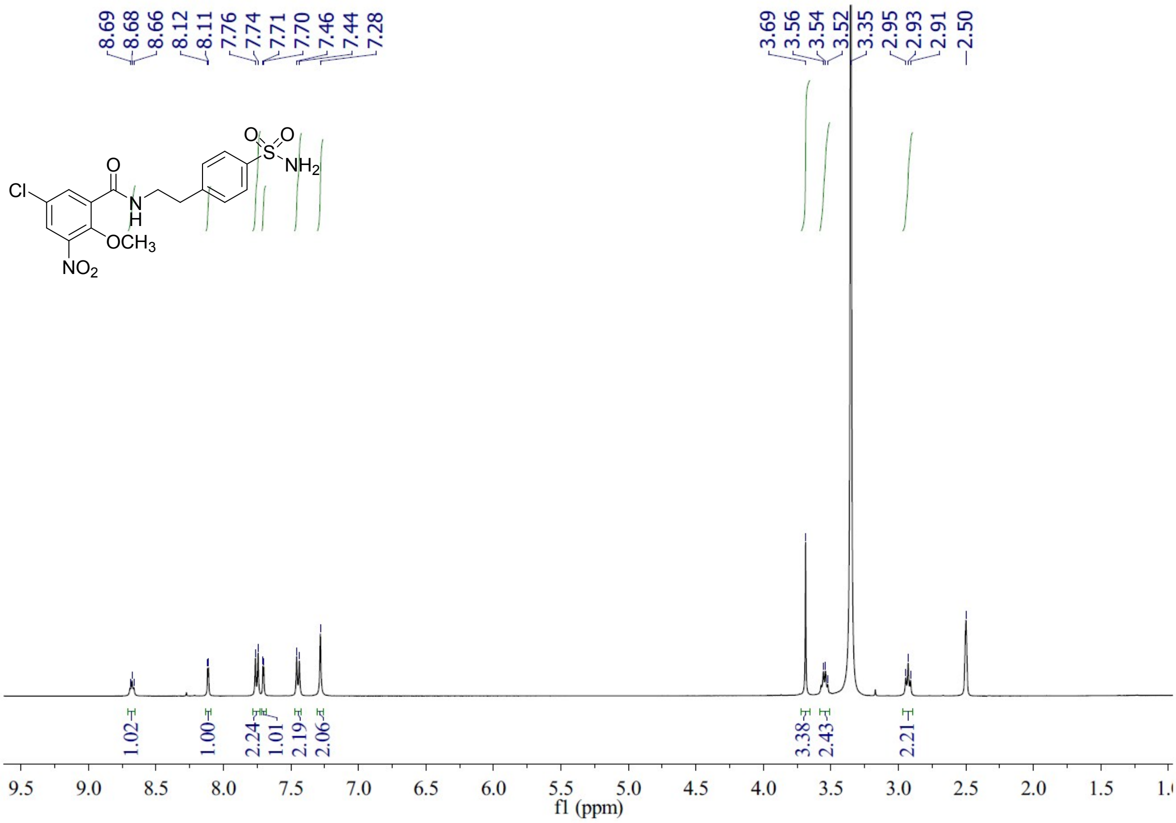
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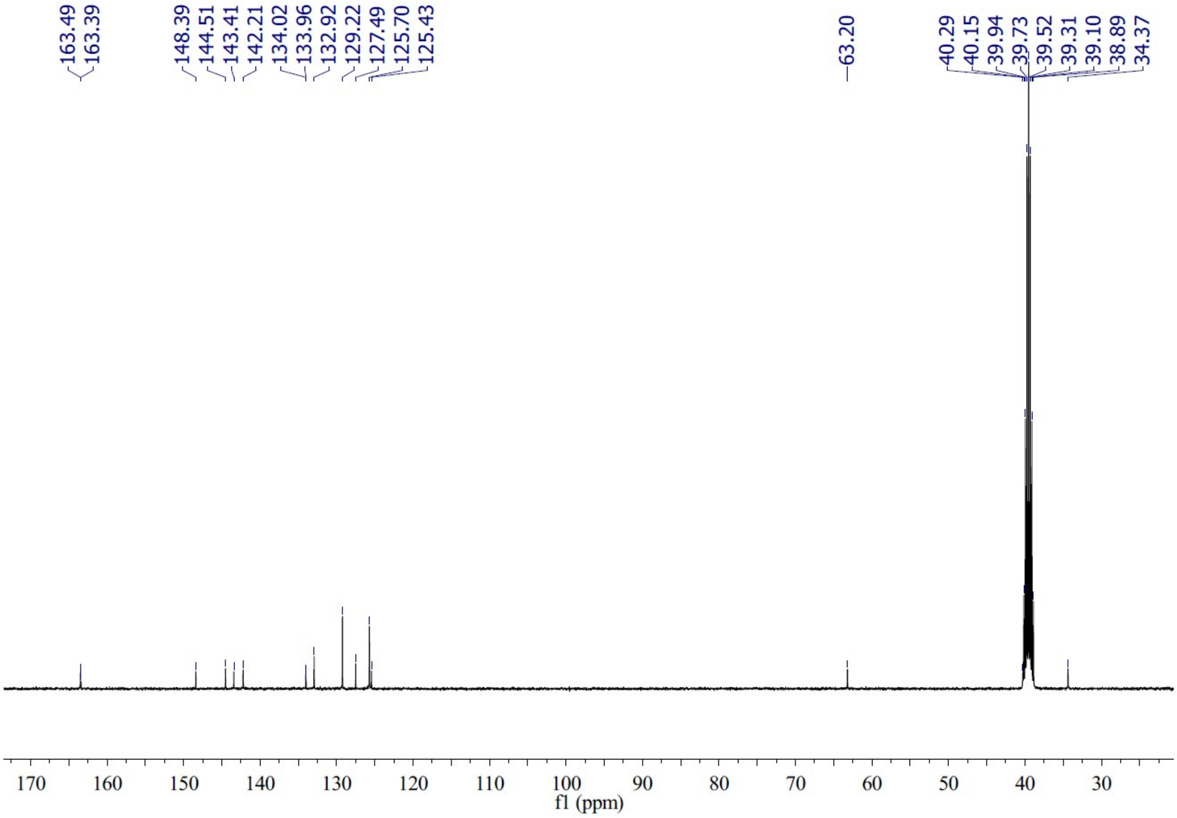
8.68
8.66
8.12
8.11
7.76
7.74
7.71
7.70
7.46
7.44
7.28
3.69
3.56
3.54
3.52
3.35
2.95
2.93
2.91
2.50
Cl
O
N
H
OCH3
NO2
O
S
O
NH2
1.02
1.00
2.24
1.01
2.19
2.06
3.38
2.43
2.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)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143.41
142.21
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133.96
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129.22
127.49
125.70
125.43
63.20
40.29
40.15
39.94
39.73
39.52
39.31
39.10
38.89
34.37
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

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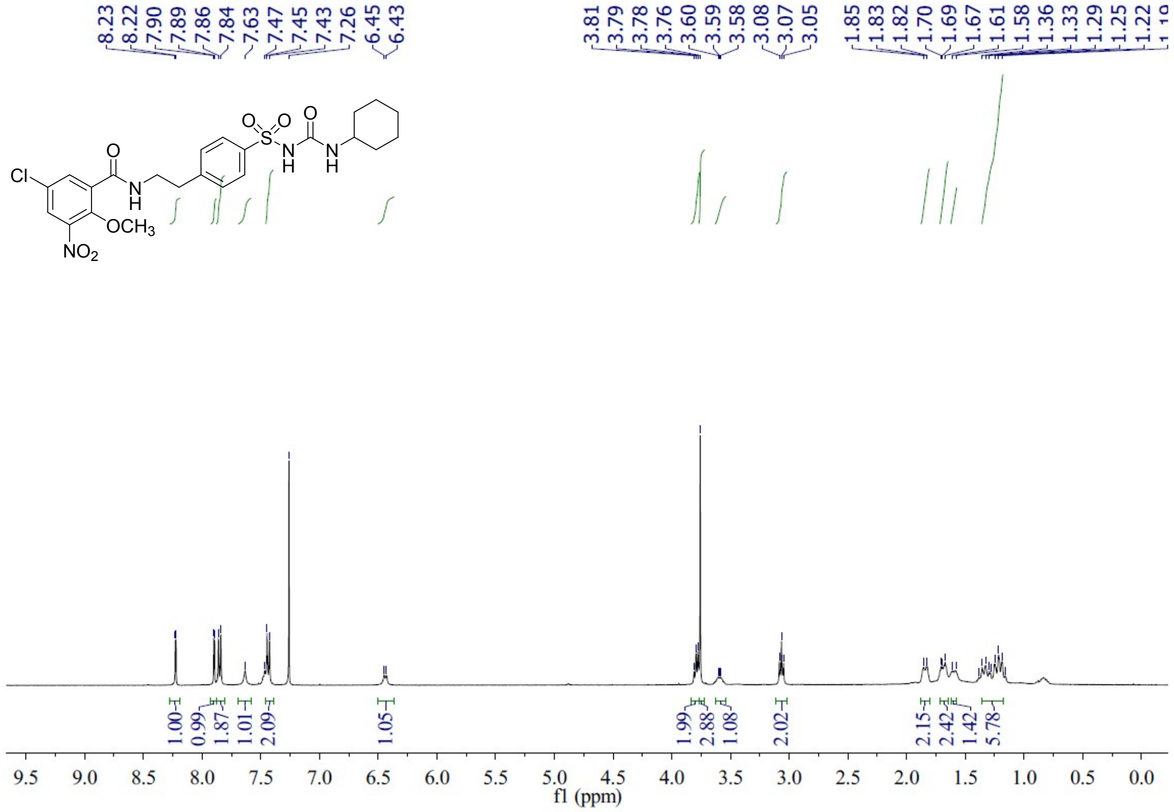

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8.22
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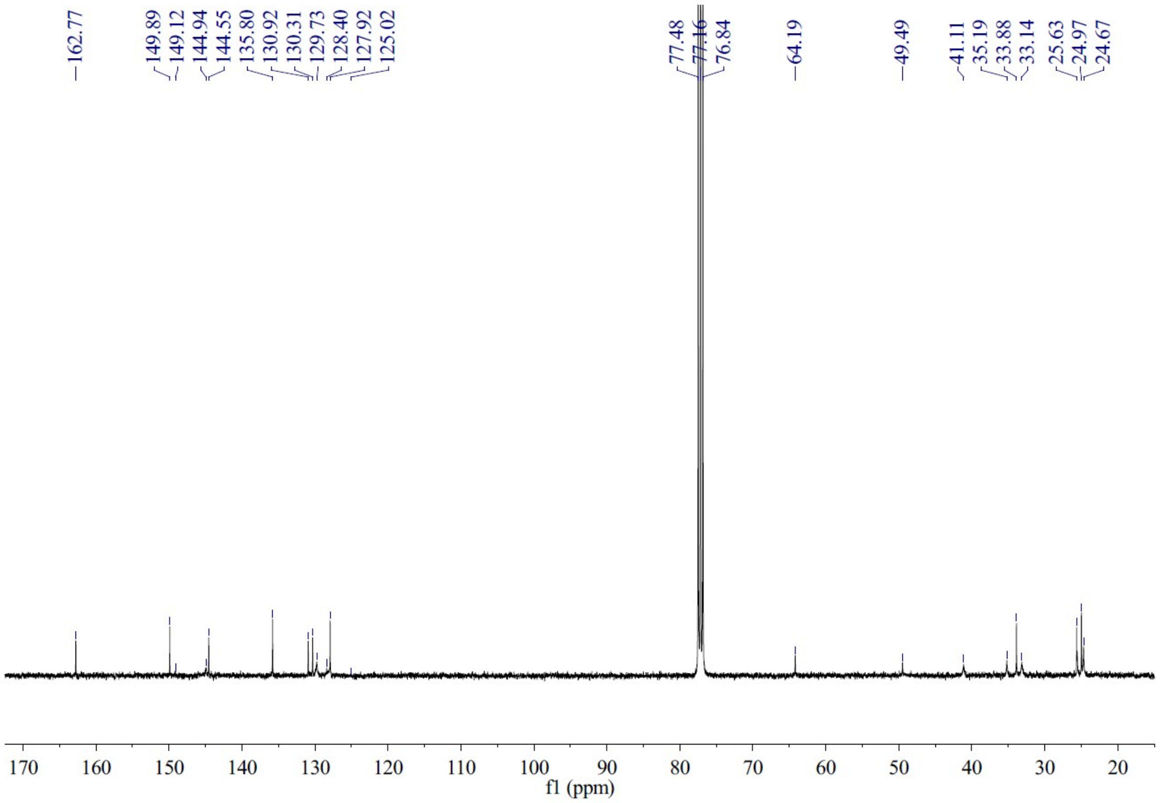
7.43
7.26
6.45
6.43
3.81
3.79
3.78
3.76
3.60
3.59
3.58
3.08
3.07
3.05
1.85
1.83
1.82
1.70
1.69
1.67
1.61
1.58
1.36
1.33
1.29
1.25
1.22
Cl
O
N
H
OCH3
NO2
O
S
O
N
H
O
N
H
1.00
0.99
1.87
1.01
2.09
1.05
1.99
2.88
1.08
2.02
2.15
2.42
1.42
5.78
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



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149.89
149.12
144.94
144.55
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130.92
130.31
129.73
128.40
127.92
125.02
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77.16
76.84
64.19
49.49
41.11
35.19
33.88
33.14
25.63
24.97
24.67
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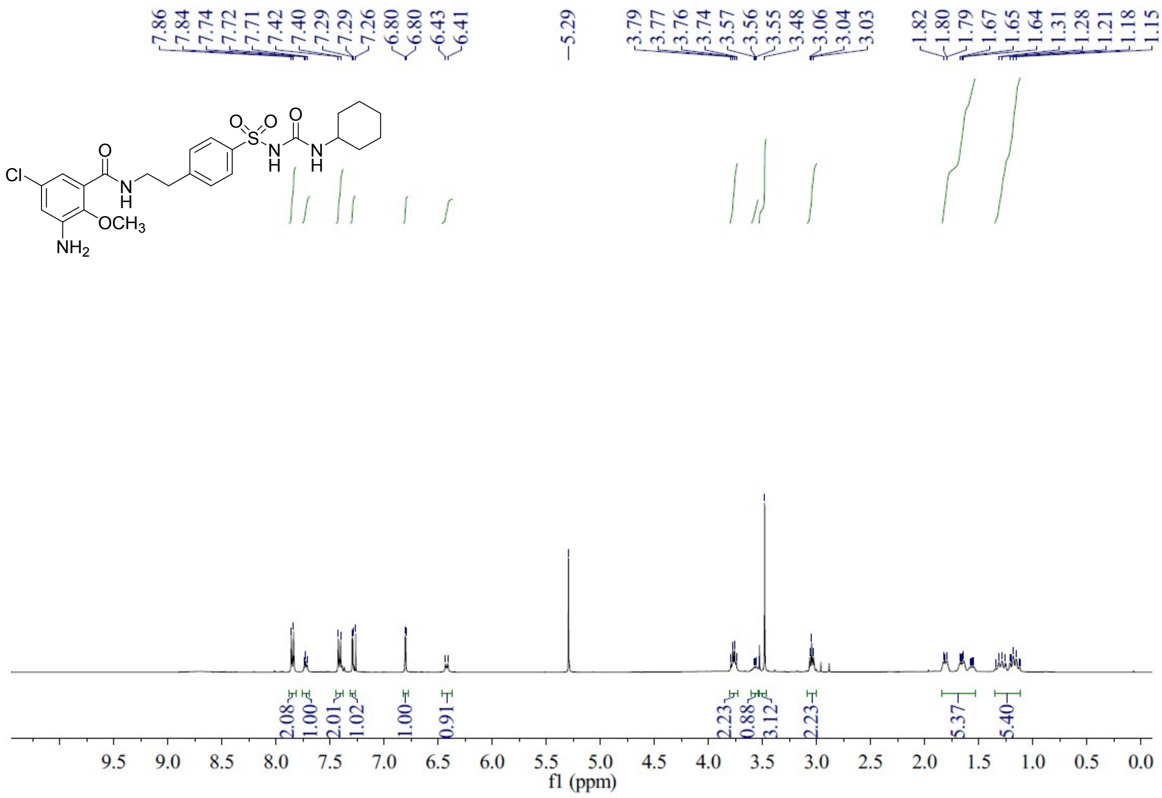
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

Compound **S5**: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7.29
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6.80
6.43
6.41
5.29
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3.77
3.76
3.74
3.57
3.56
3.55
3.48
3.06
3.04
3.03
1.82
1.80
1.79
1.67
1.65
1.64
1.31
1.28
1.21
1.18
1.15
Cl
O
N
H
OCH3
NH2
O
S
O
N
H
O
N
H
2.08
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2.01
1.02
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3.12
2.23
5.37
5.40
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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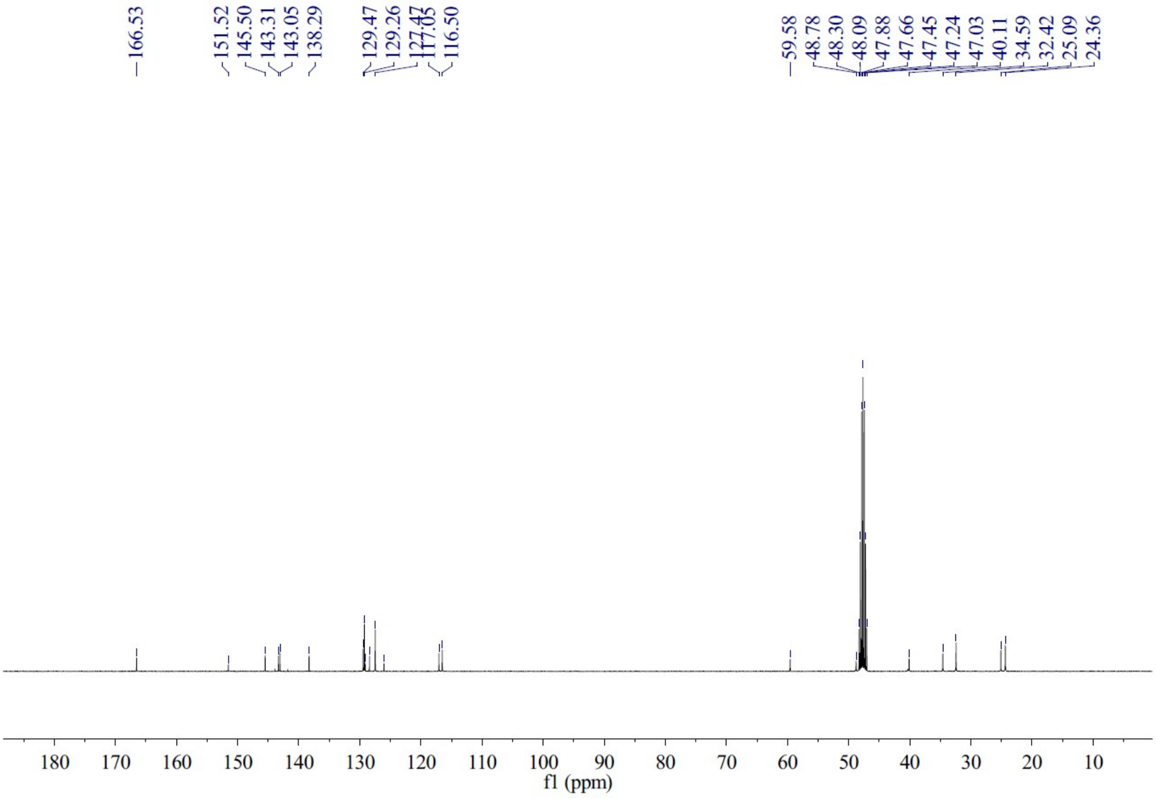
f1 (ppm)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48.30
48.09
47.88
47.66
47.45
47.24
47.03
40.11
34.59
32.42
25.09
24.36
180
170
160
150
140
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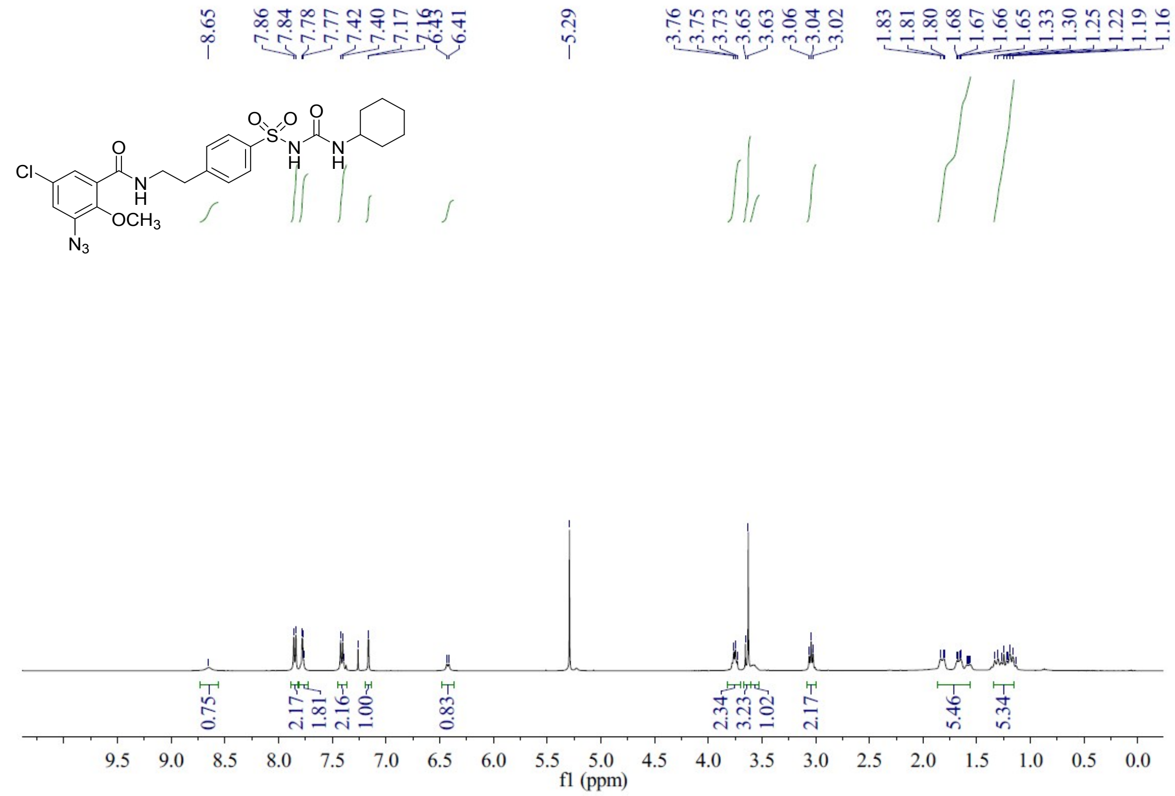
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Compound **2**: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7.78
7.77
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7.17
7.16
6.43
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3.76
3.75
3.73
3.65
3.63
3.06
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1.83
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1.80
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1.65
1.33
1.30
1.25
1.22
1.19
1.16
Cl
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N
H
OCH3
N3
O
O
S
N
H
O
N
H
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2.17
5.46
5.34
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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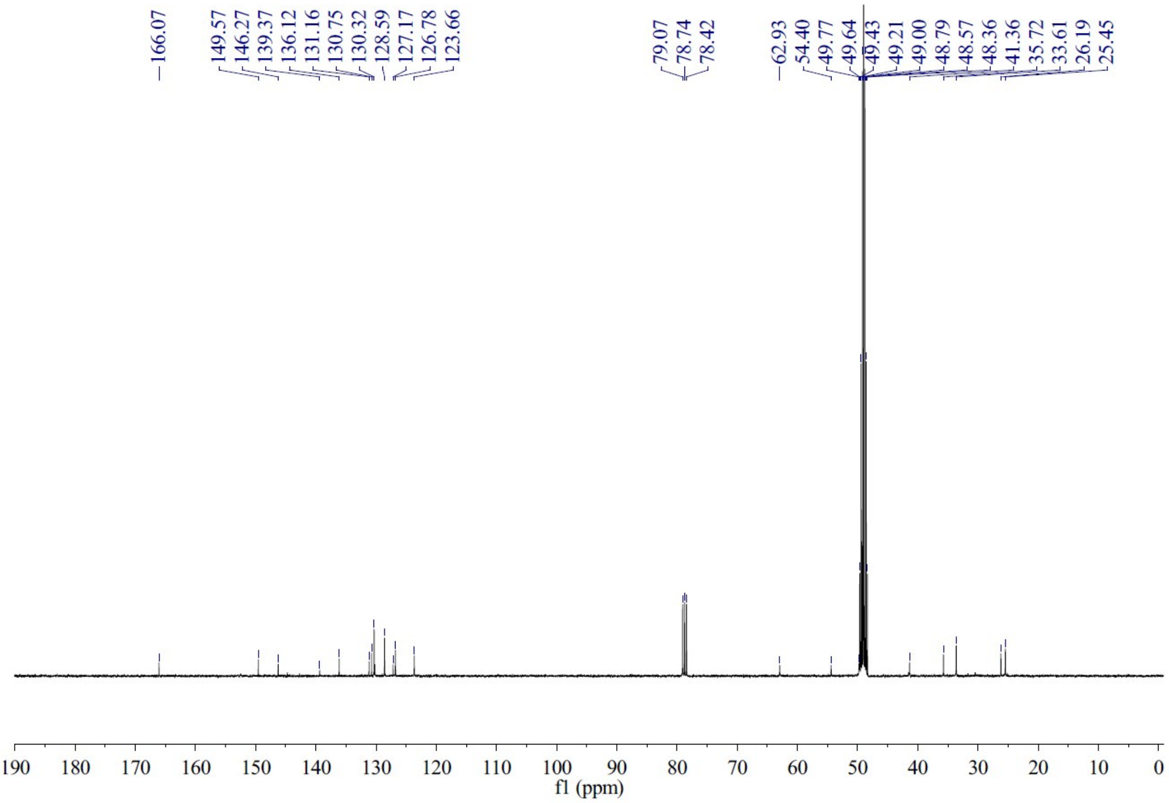
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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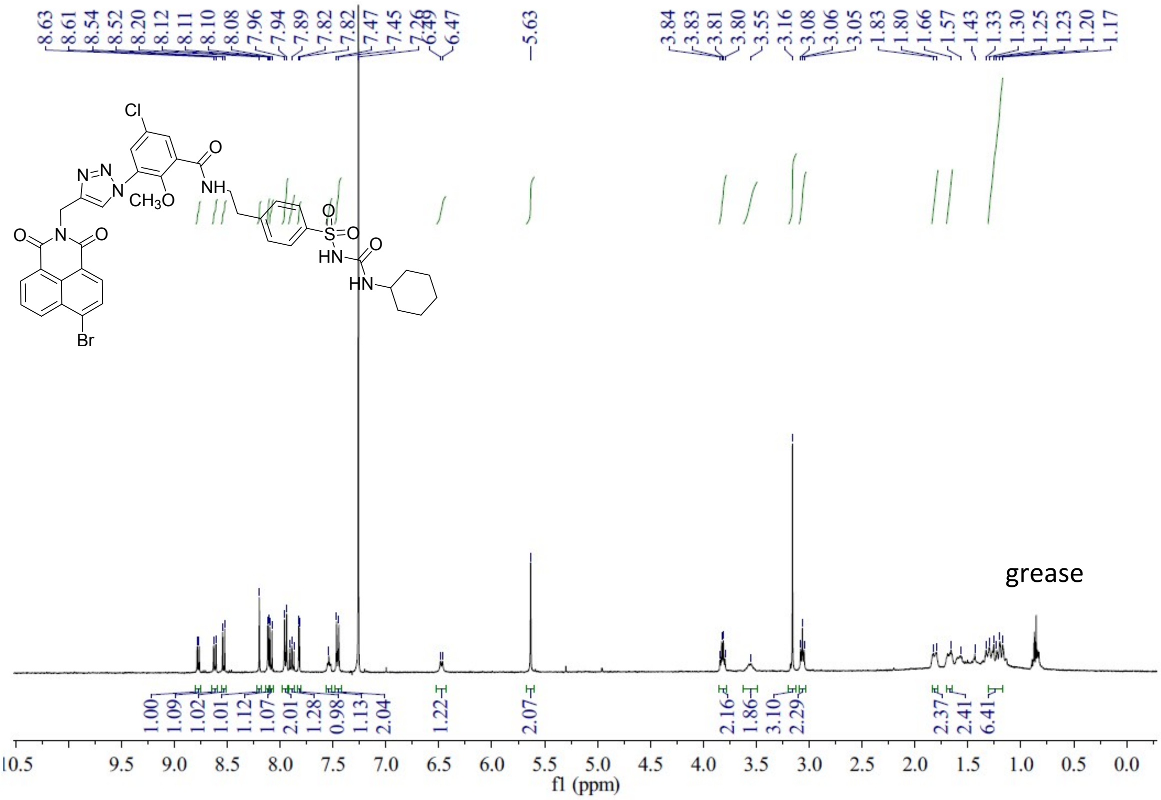
35.72
33.61
26.19
25.45
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Compound **S7**: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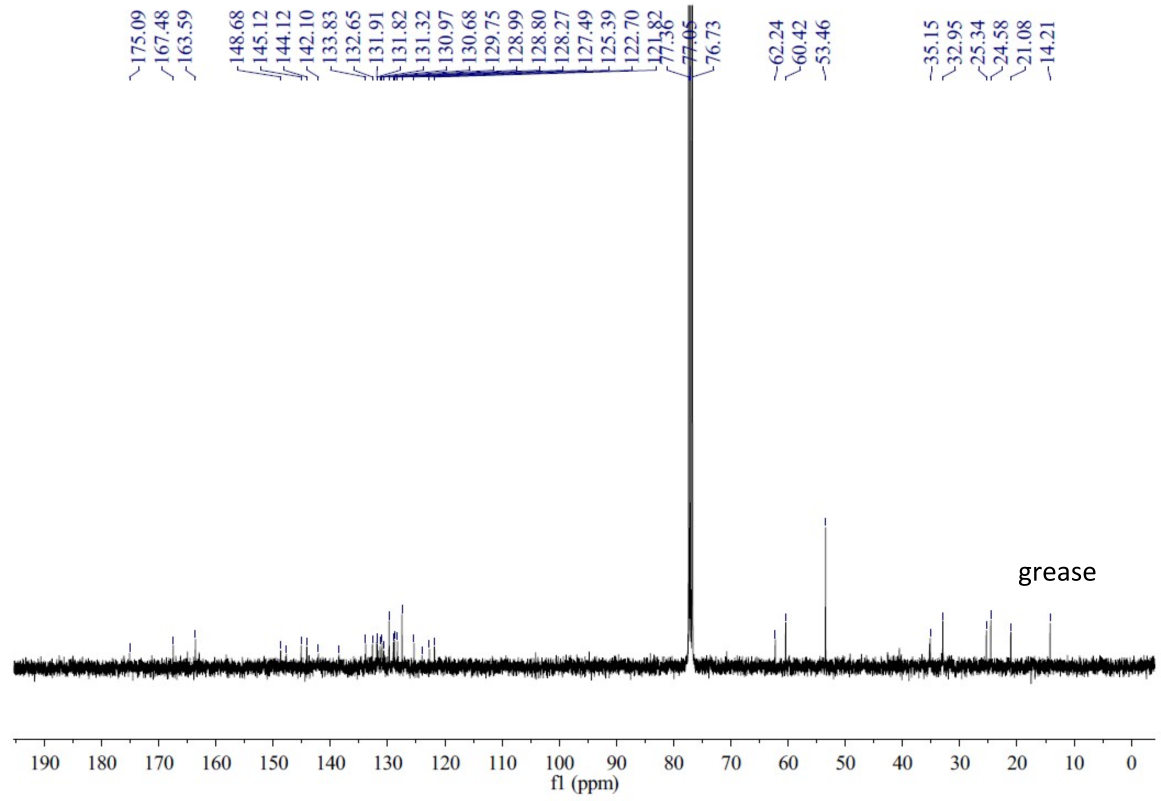
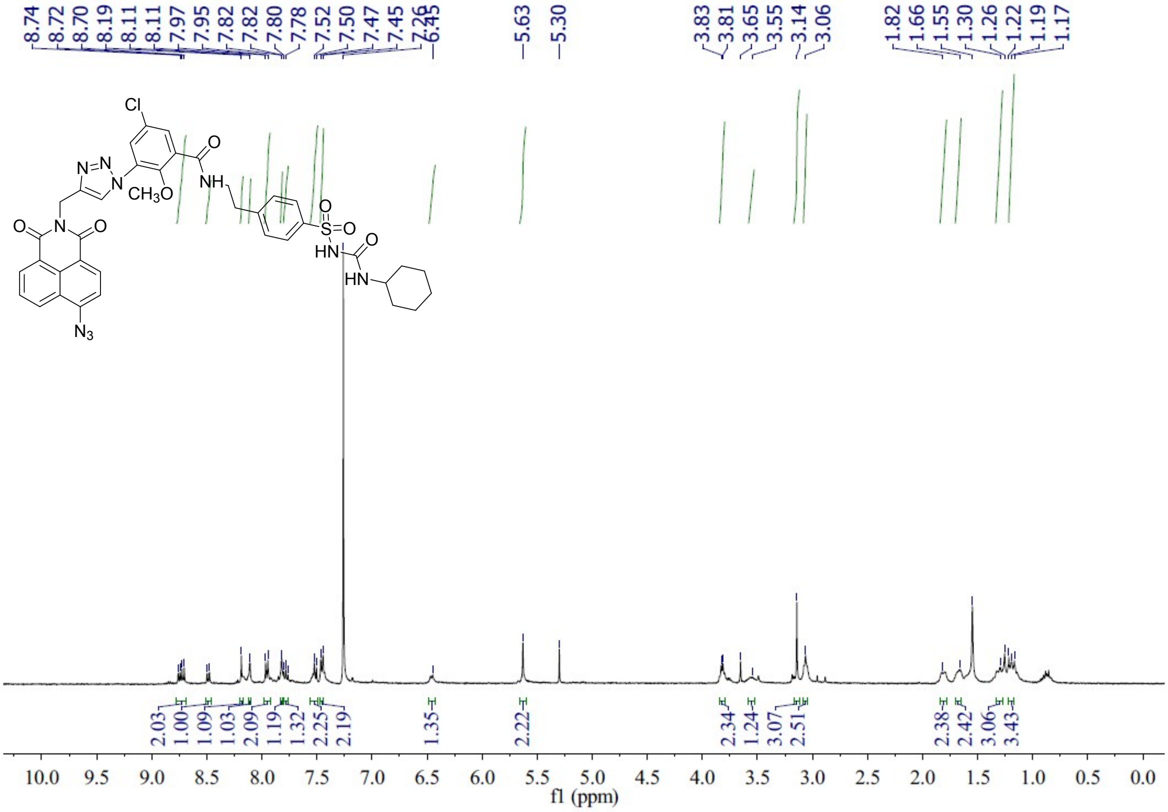
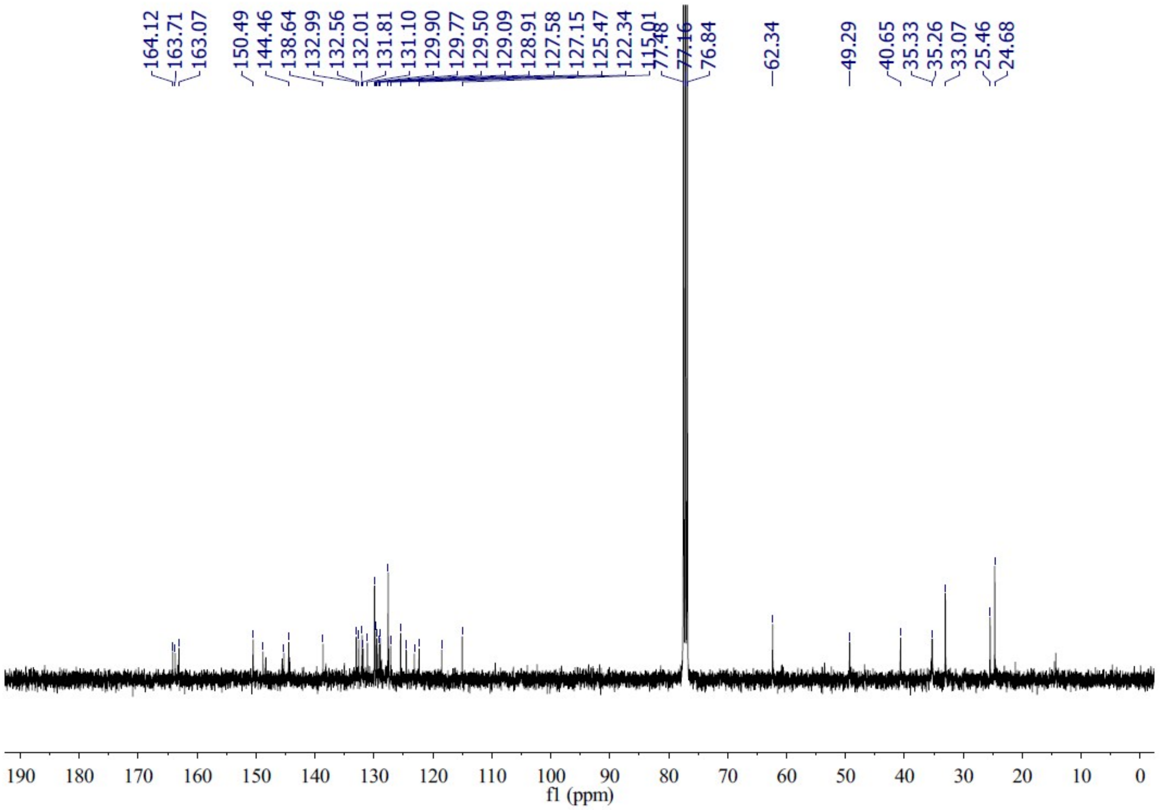
7.89
7.82
7.82
7.47
7.45
7.26
6.49
6.47
5.63
3.84
3.83
3.81
3.80
3.55
3.16
3.08
3.06
3.05
1.83
1.80
1.66
1.57
1.43
1.33
1.30
1.25
1.23
1.20
1.17
Cl
O
N=N
N
NH
CH3O
O
N
O
Br
O
S=O
HN
O
HN
grease
1.00
1.09
1.02
1.01
1.12
1.07
2.01
1.28
0.98
1.13
2.04
1.22
2.07
2.16
1.86
3.10
2.29
2.37
2.41
6.41
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

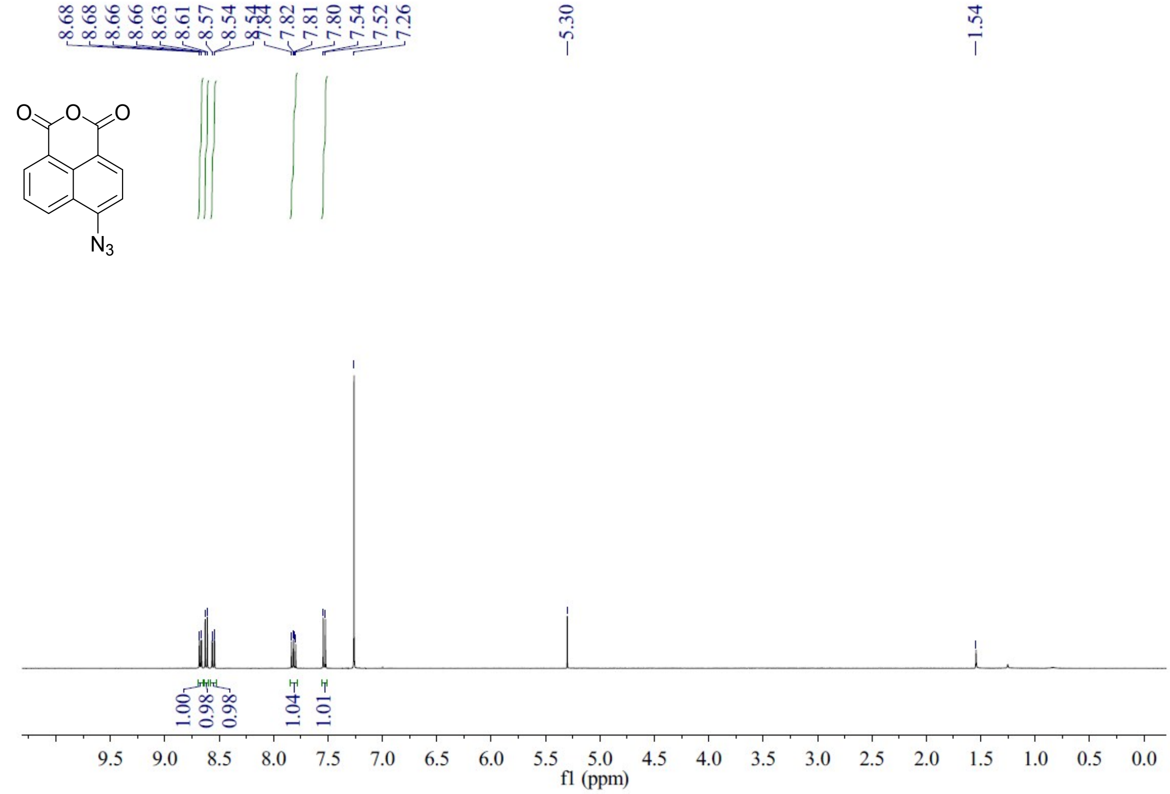

175.09
167.48
163.59
148.68
145.12
144.12
142.10
133.83
132.65
131.91
131.82
131.32
130.97
130.68
129.75
128.99
128.80
128.27
127.49
125.39
122.70
121.82
77.36
77.05
76.73
62.24
60.42
53.46
35.15
32.95
25.34
24.58
21.08
14.21
grease
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

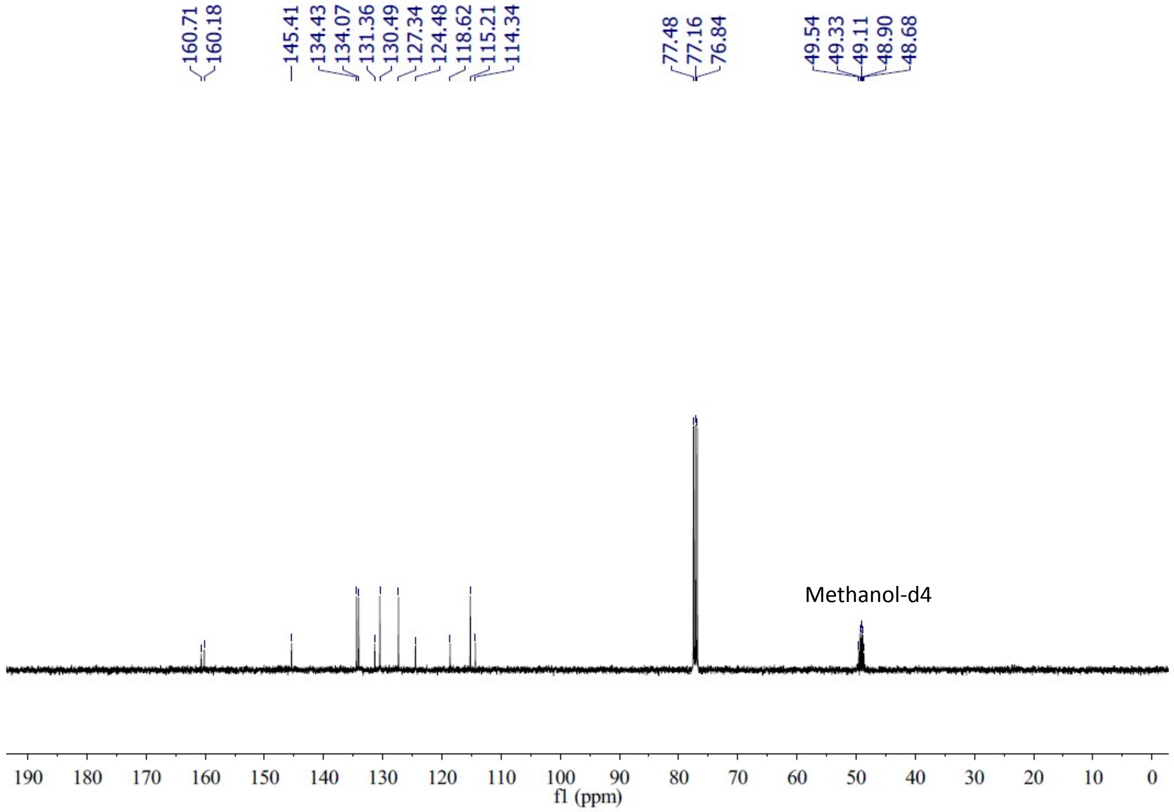
Compound **S8**:


8.74
8.72
8.70
8.19
8.11
8.11
7.97
7.95
7.82
7.80
7.78
7.52
7.50
7.47
7.45
7.26
6.45
5.63
5.30
3.83
3.81
3.65
3.55
3.14
3.06
1.82
1.66
1.55
1.30
1.26
1.22
1.19
1.17
Cl
N
N
N
CH3O
O
NH
O
O
N
O
S
O
O
HN
O
HN
N3
2.03
1.00
1.09
1.03
2.09
1.19
1.32
2.25
2.19
1.35
2.22
2.34
1.24
3.07
2.51
2.38
2.42
3.06
3.43
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

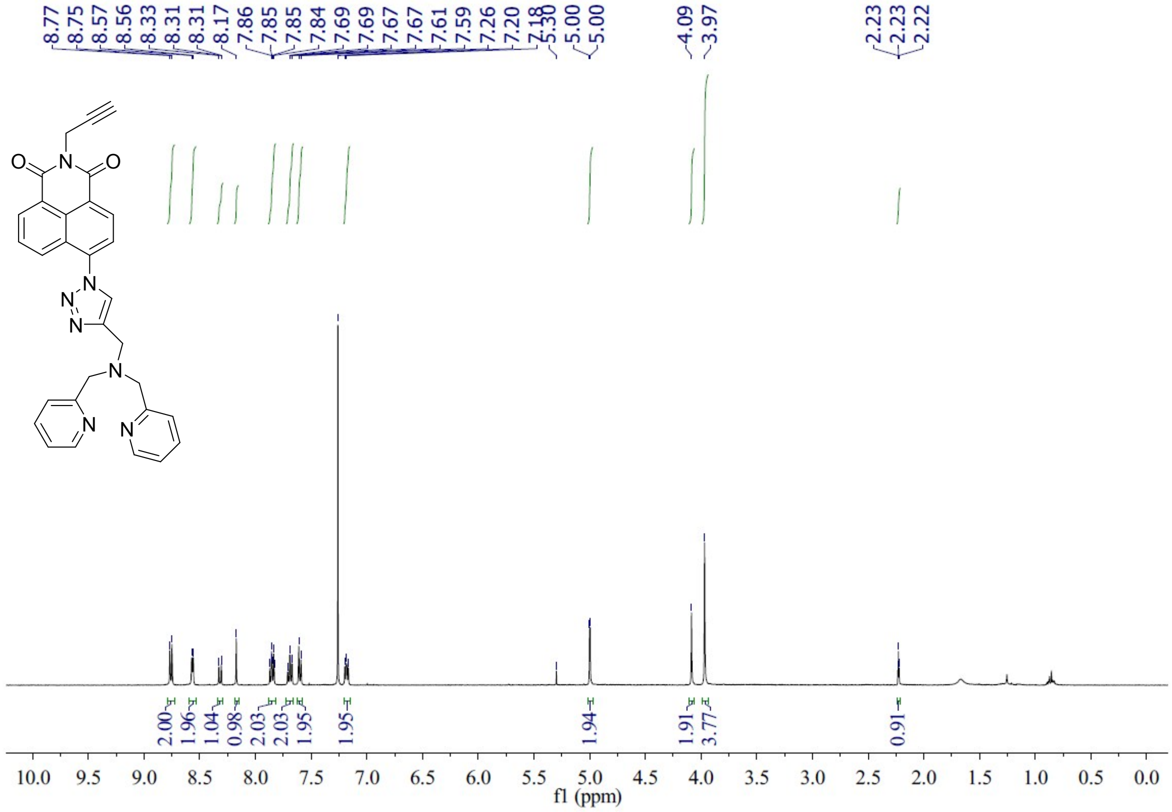

164.12
163.71
163.07
150.49
144.46
138.64
132.99
132.56
132.01
131.81
131.10
129.90
129.77
129.50
129.09
128.91
127.58
127.15
125.47
122.34
115.01
77.48
77.16
76.84
62.34
49.29
40.65
35.33
35.26
33.07
25.46
24.68
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

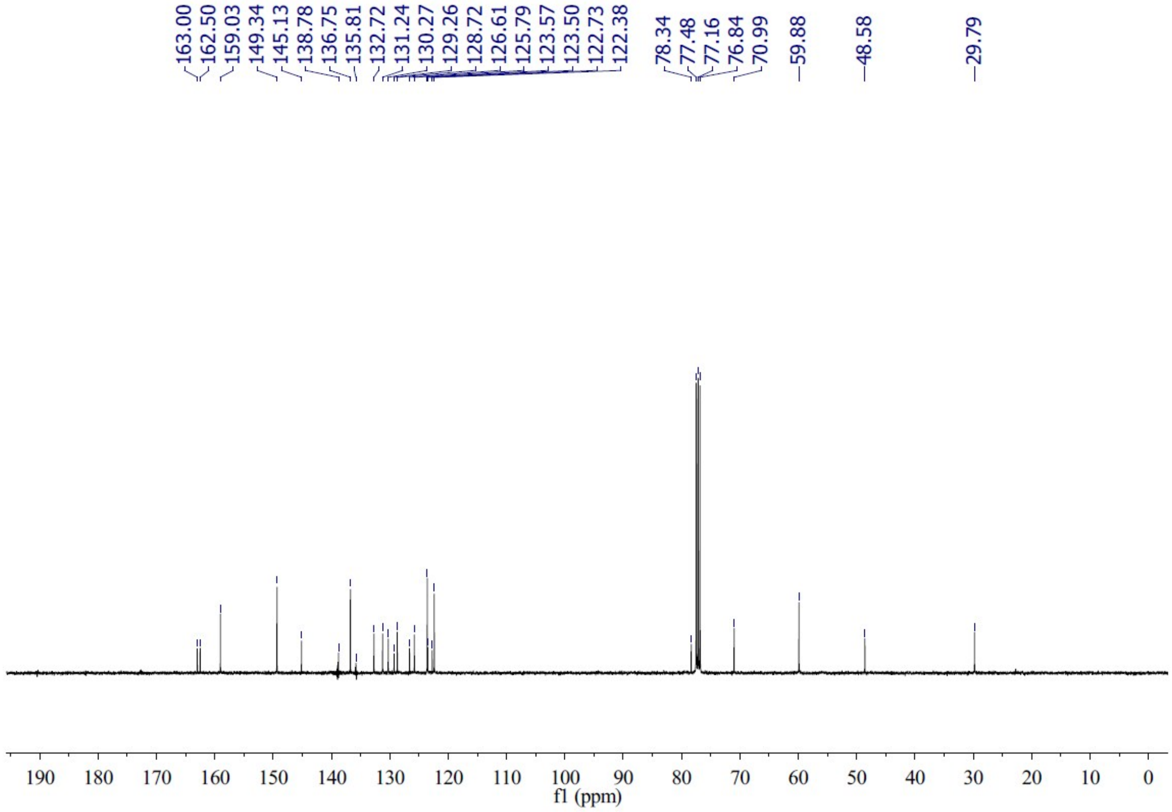
Compound **S9**:


8.68
8.68
8.66
8.66
8.63
8.61
8.57
8.54
8.54
7.84
7.82
7.81
7.80
7.54
7.52
7.26
5.30
1.54
O
O
O
N3
1.00
0.98
0.98
1.04
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

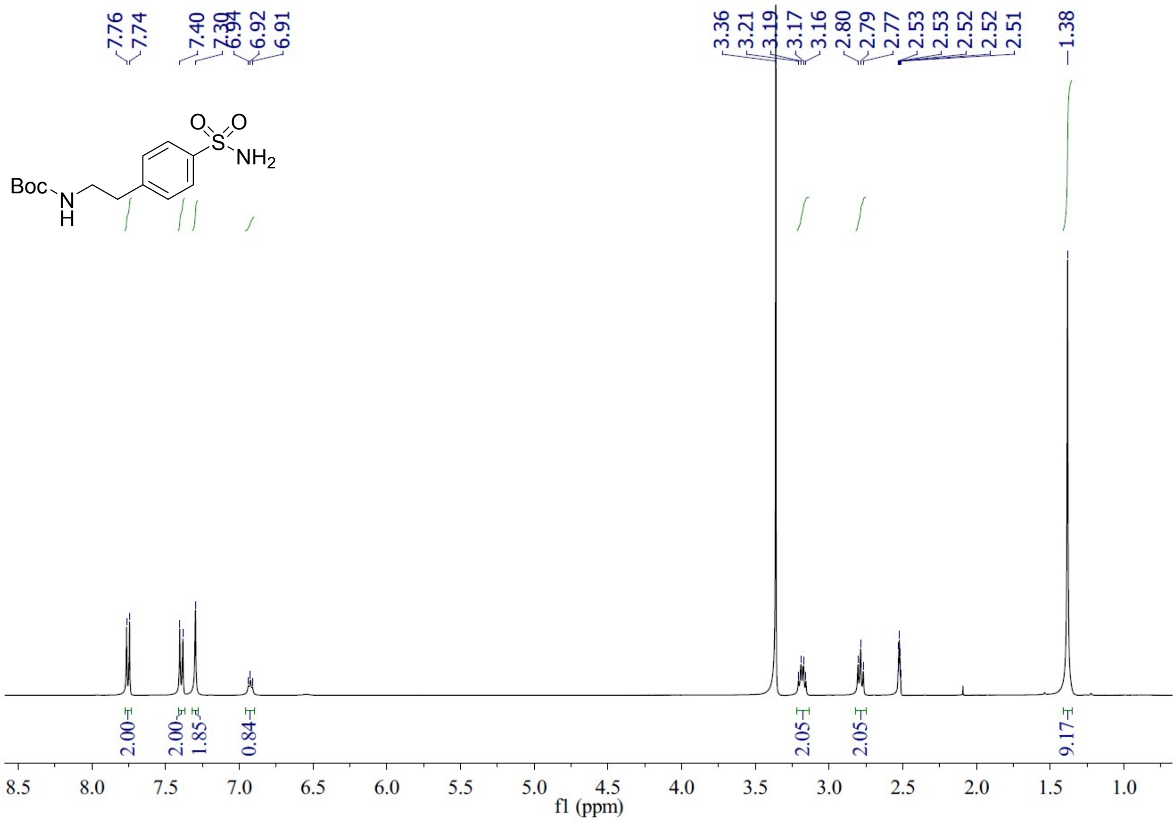

160.71
160.18
145.41
134.43
134.07
131.36
130.49
127.34
124.48
118.62
115.21
114.34
77.48
77.16
76.84
49.54
49.33
49.11
48.90
48.68
Methanol-d4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

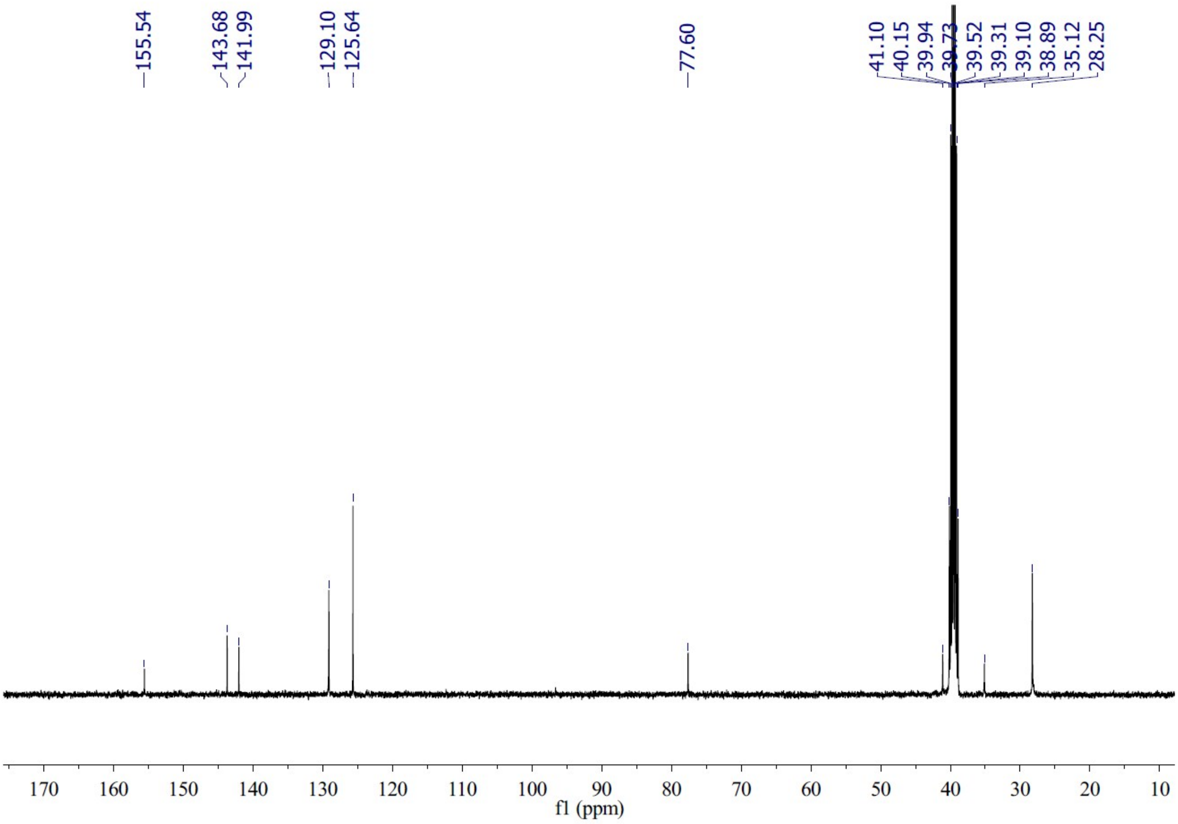
Compound **S10**:



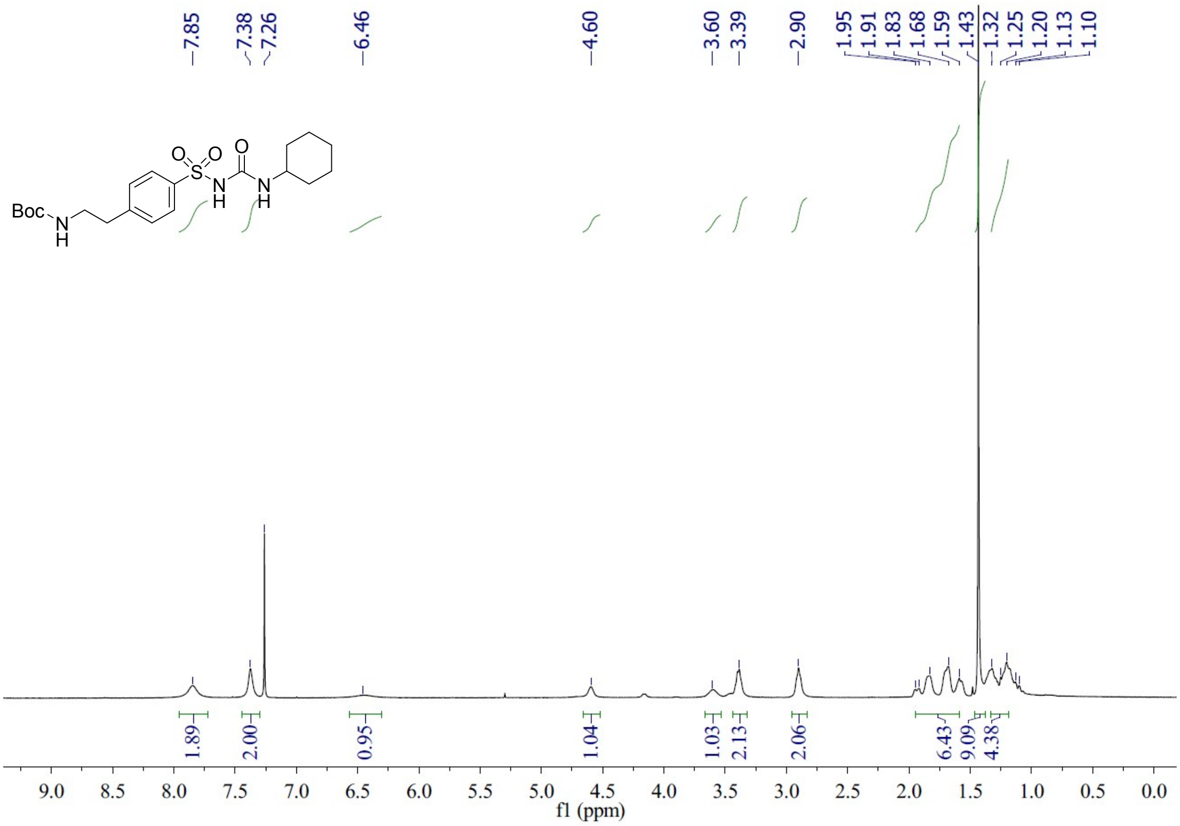


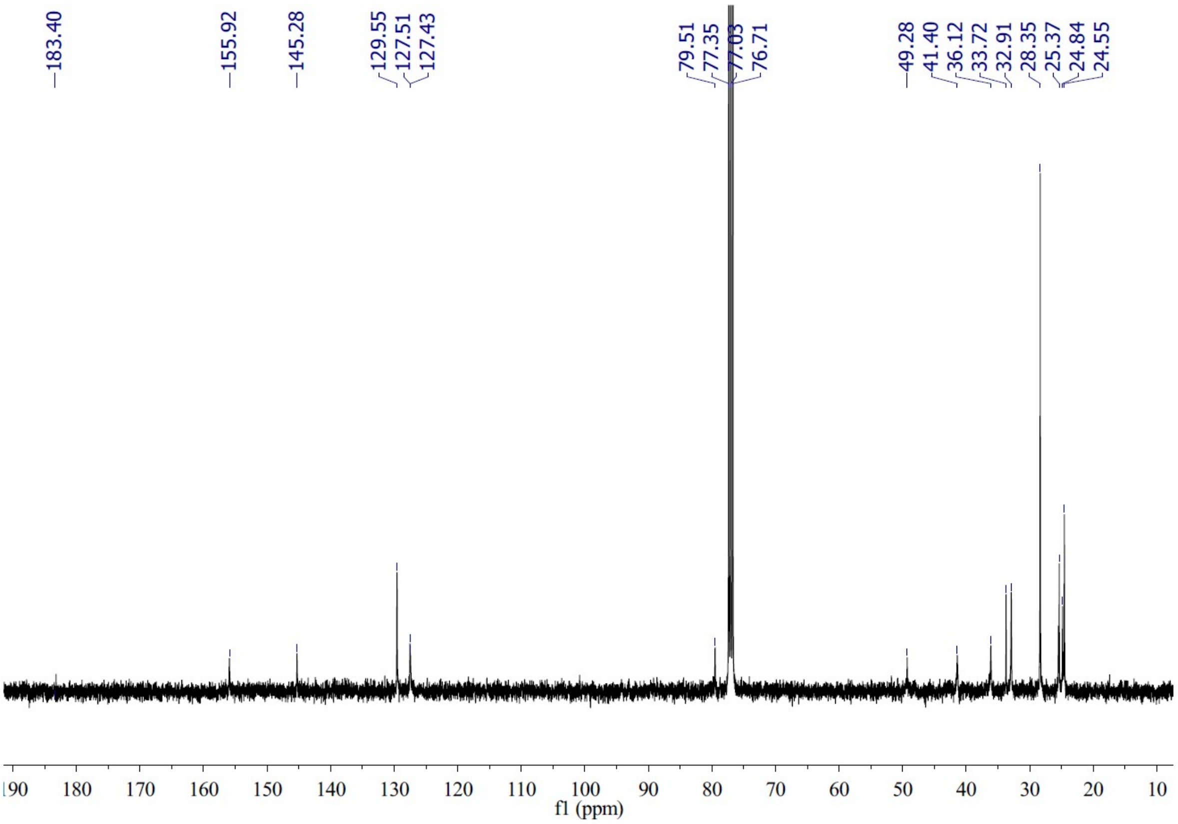
Compound **S11**:



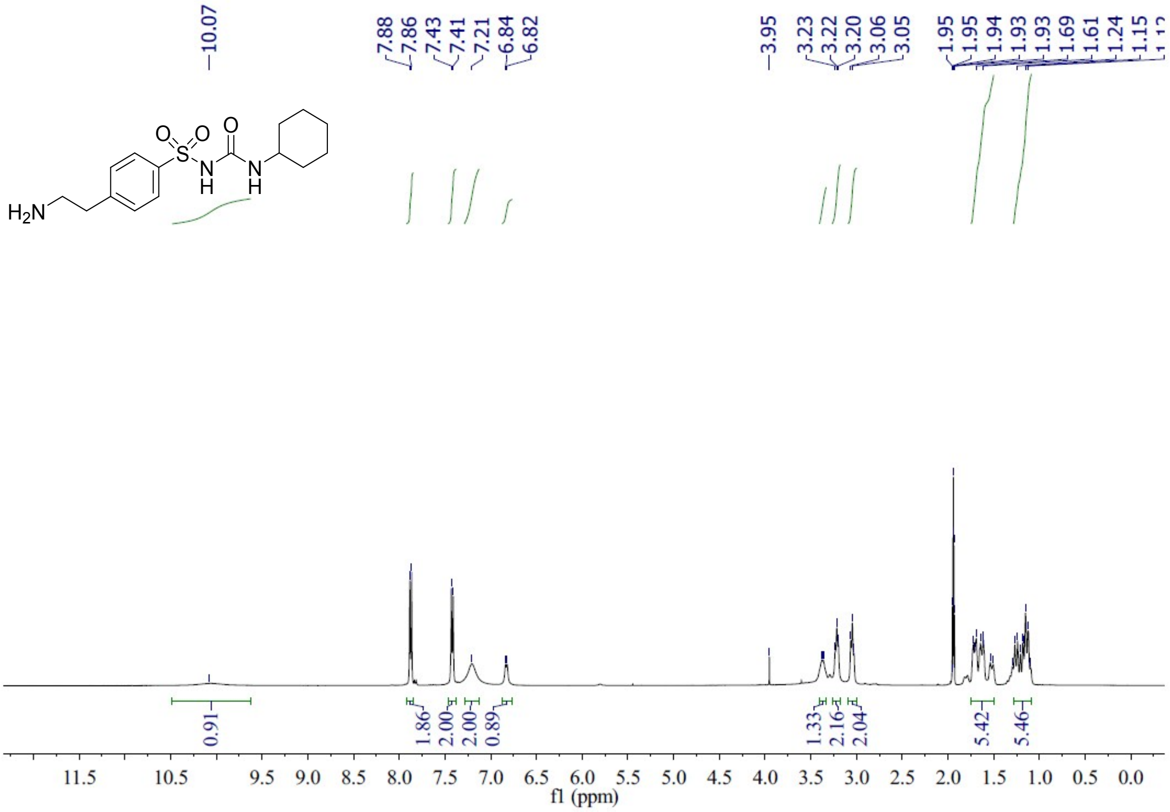


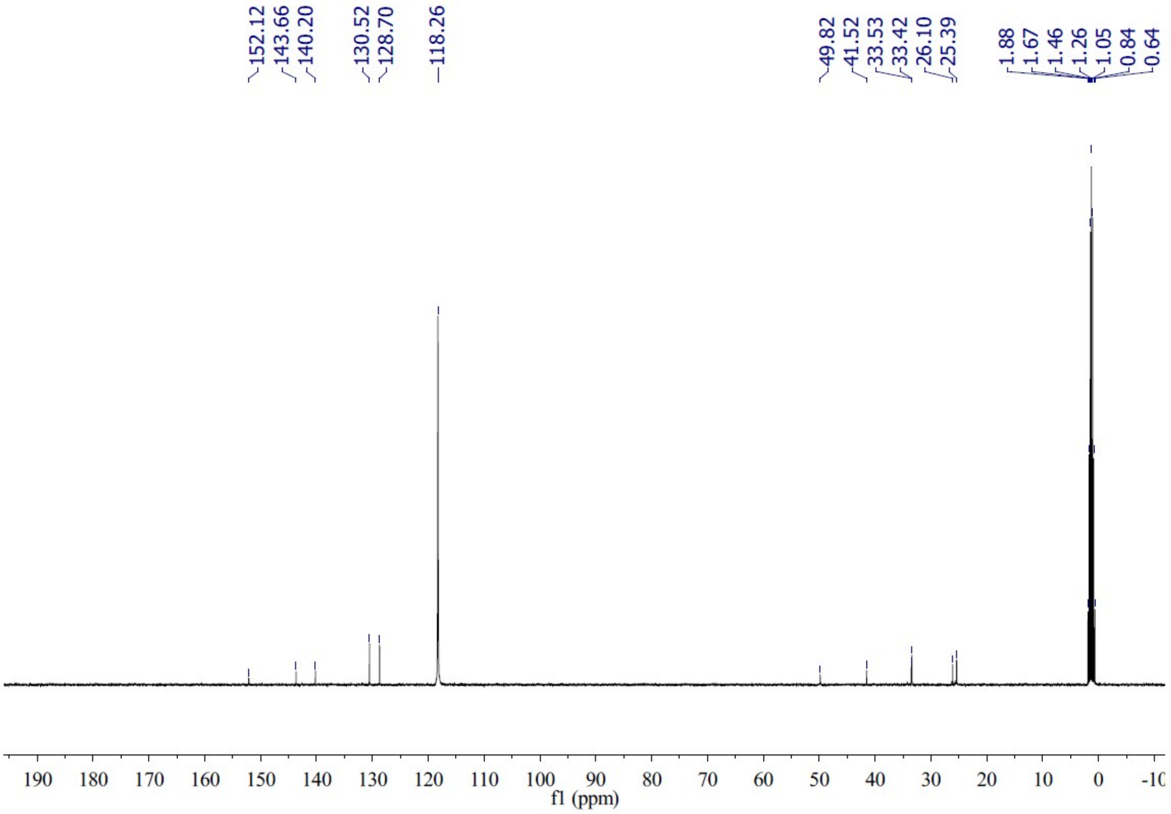
Compound **S12**:



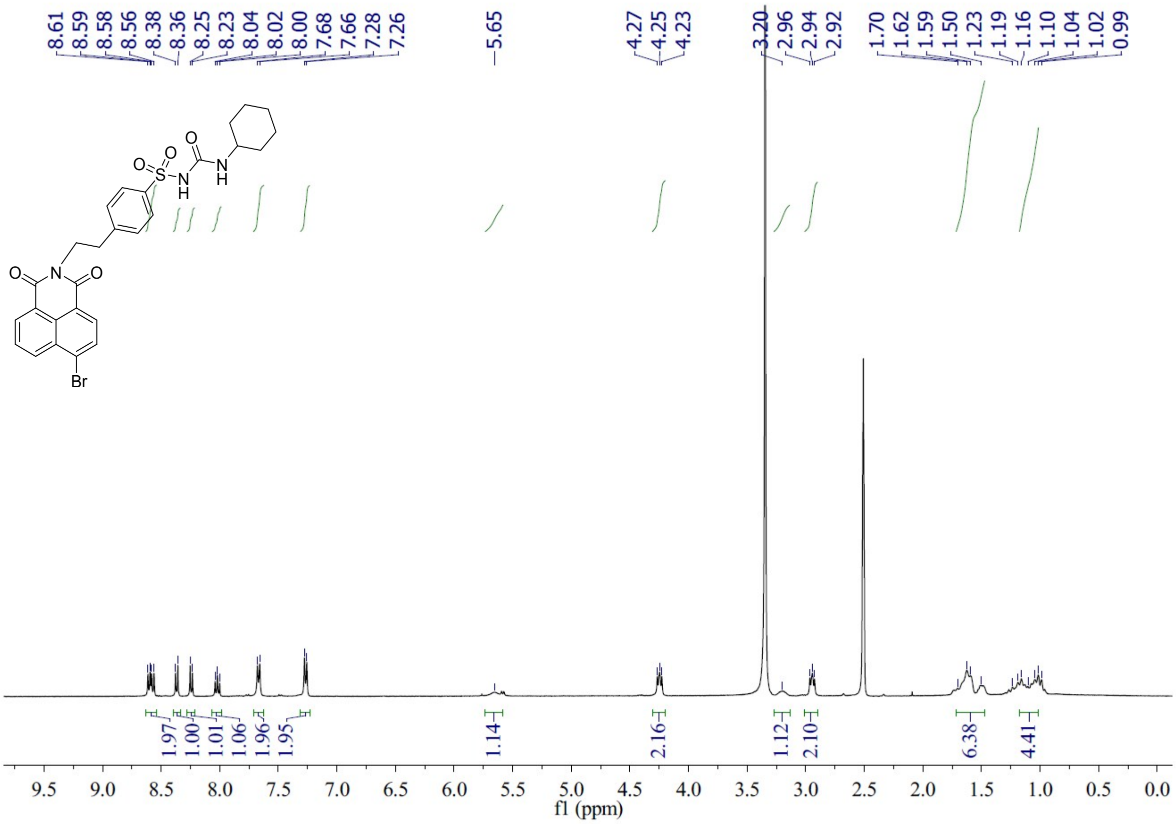


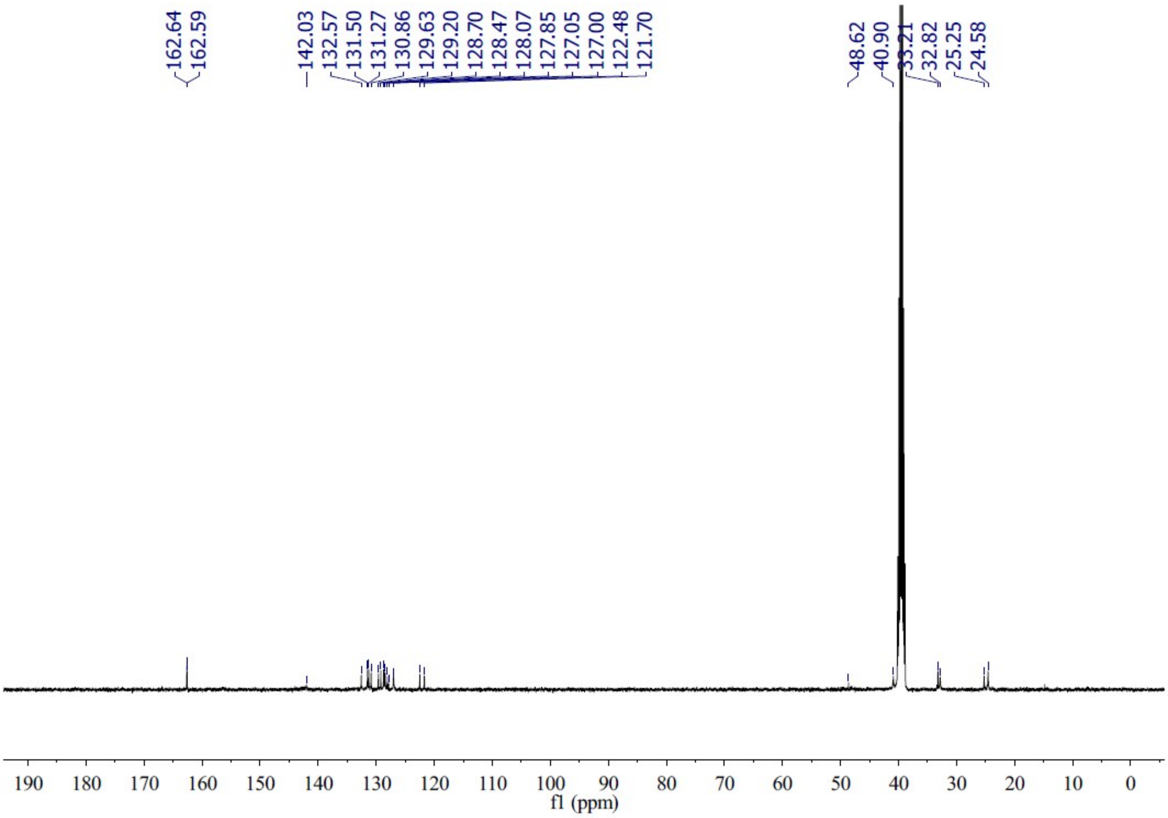
Compound **6**:


H2N
O
S
O
N
H
O
N
H
10.07
7.88
7.86
7.43
7.41
7.21
6.84
6.82
3.95
3.23
3.22
3.20
3.06
3.05
1.95
1.95
1.94
1.93
1.93
1.69
1.61
1.24
1.15
0.91
1.86
2.00
2.00
0.89
1.33
2.16
2.04
5.42
5.46
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

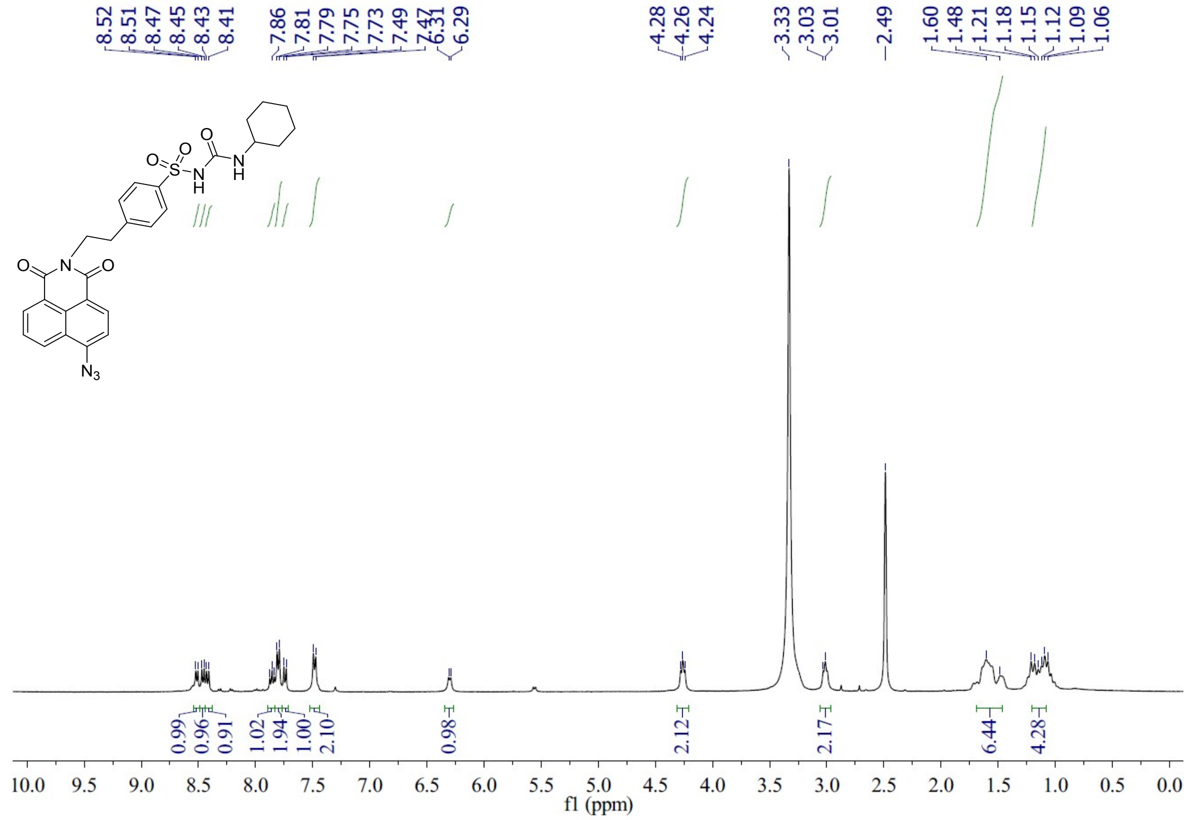

152.12
143.66
140.20
130.52
128.70
118.26
49.82
41.52
33.53
33.42
26.10
25.39
1.88
1.67
1.46
1.26
1.05
0.84
0.64
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

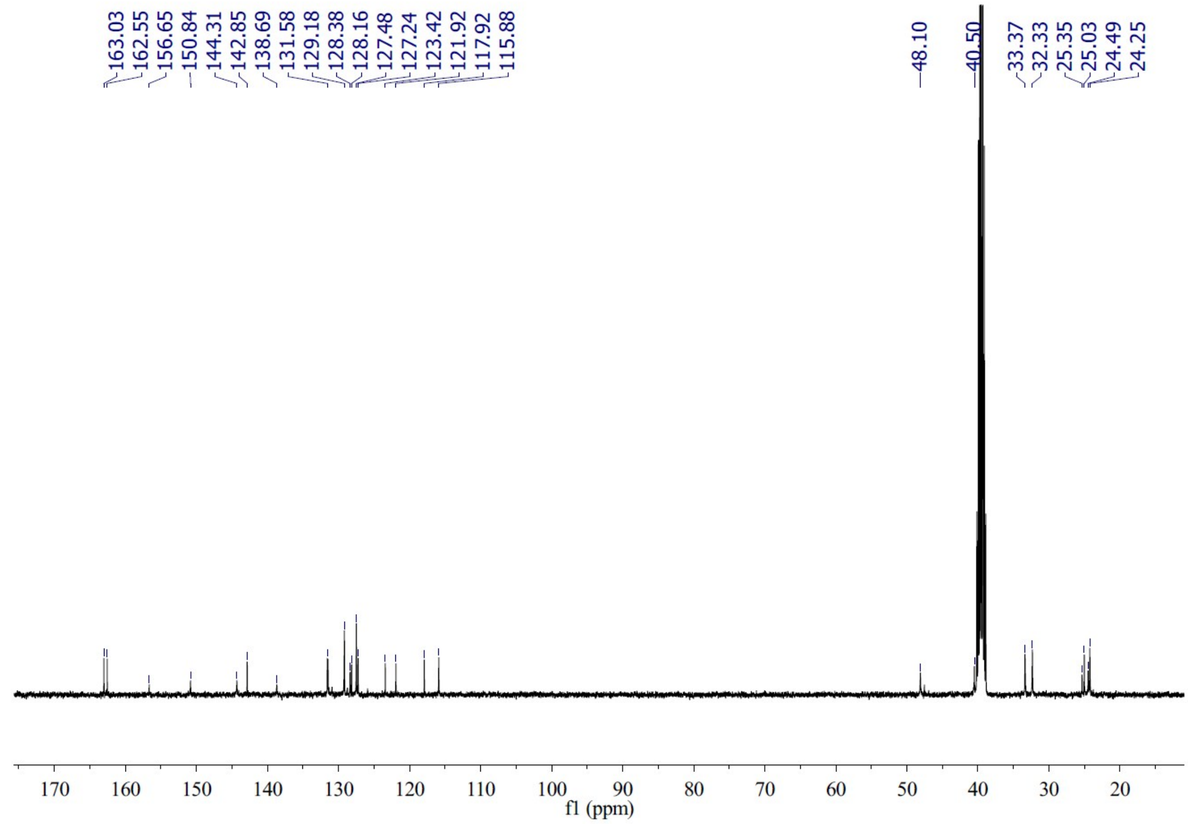
Compound **S13**:



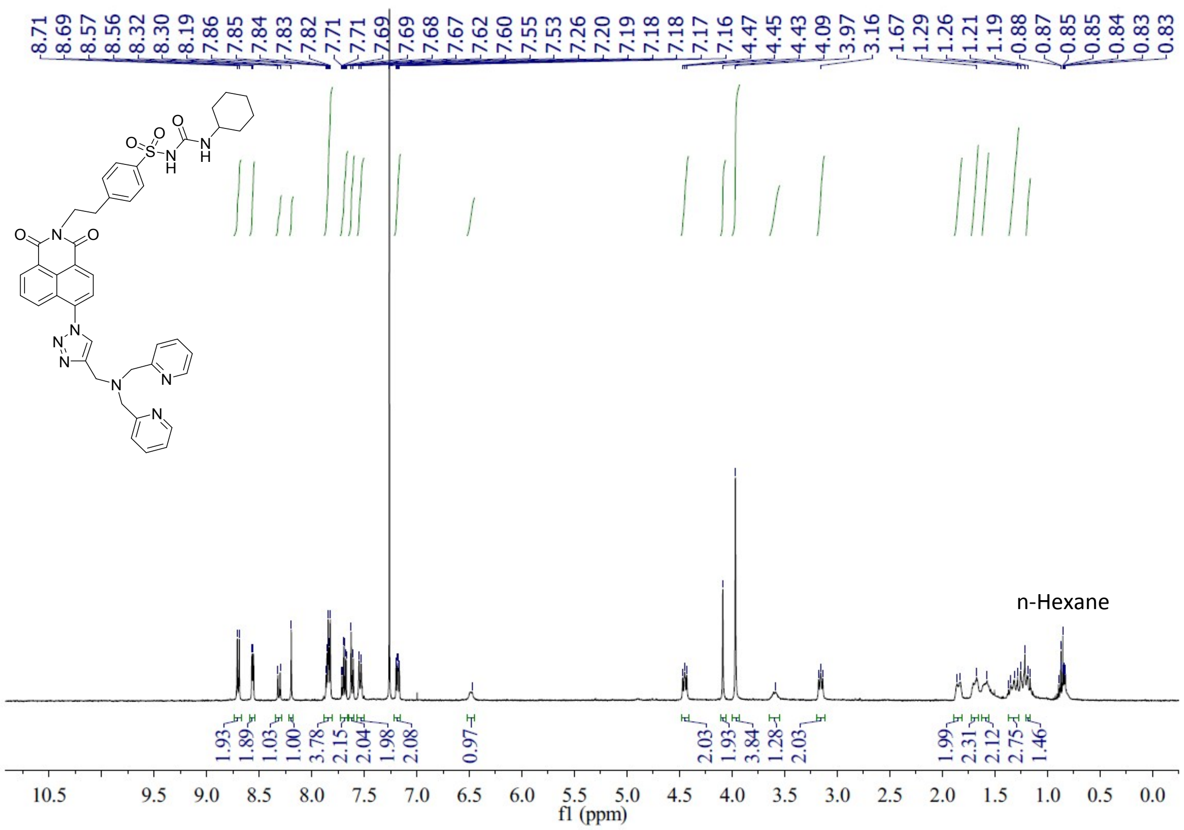


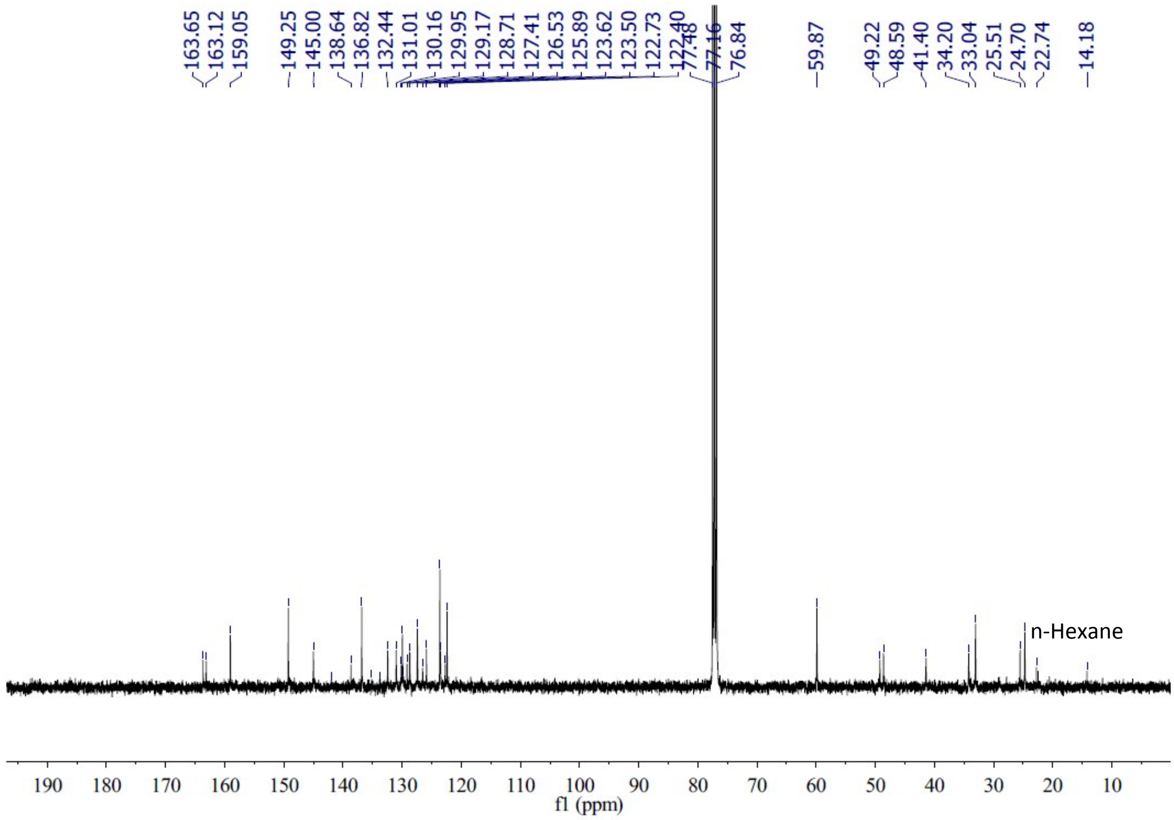
Compound **7**:


8.52
8.51
8.47
8.45
8.43
8.41
7.86
7.81
7.79
7.75
7.73
7.49
7.47
6.31
6.29
4.28
4.26
4.24
3.33
3.03
3.01
2.49
1.60
1.48
1.21
1.18
1.15
1.12
1.09
1.06
O
O
S
N
H
O
N
H
O
N
O
N_3
0.99
0.96
0.91
1.02
1.94
1.00
2.10
0.98
2.12
2.17
6.44
4.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

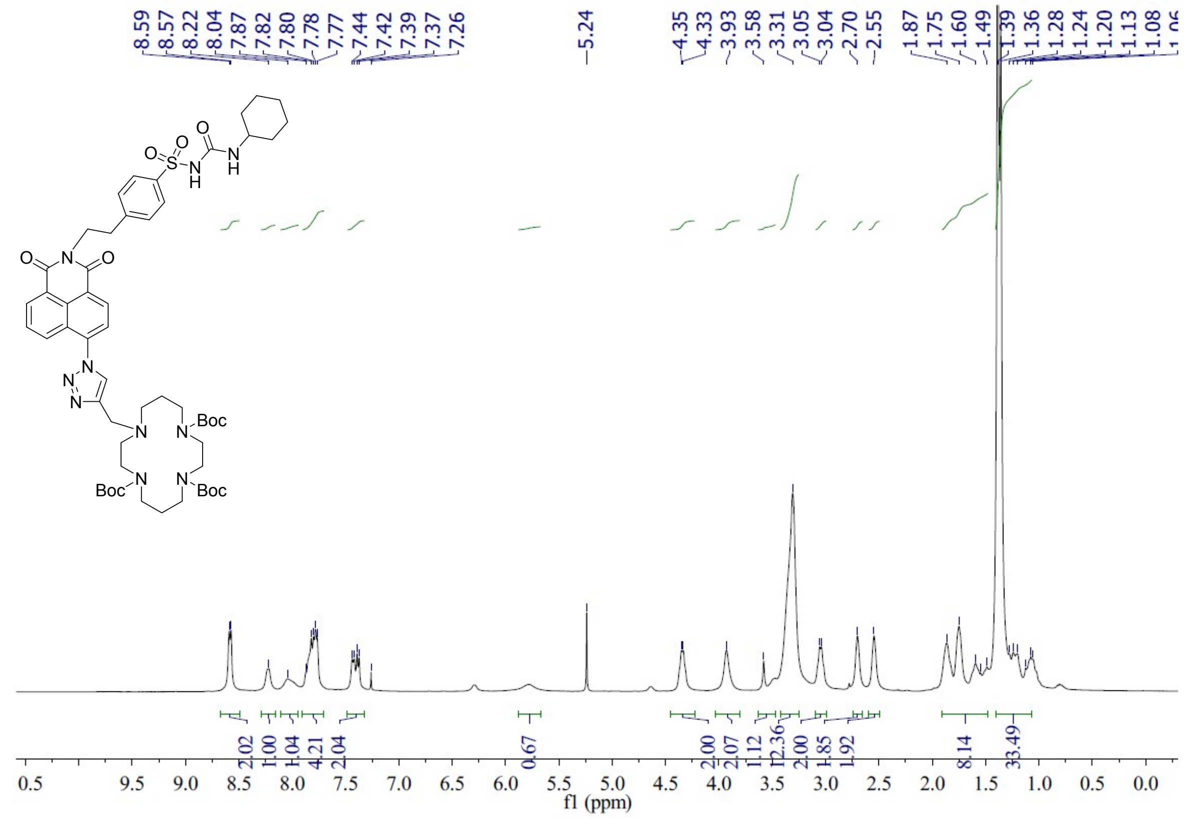

163.03
162.55
156.65
150.84
144.31
142.85
138.69
131.58
129.18
128.38
128.16
127.48
127.24
123.42
121.92
117.92
115.88
48.10
40.50
33.37
32.33
25.35
25.03
24.49
24.25
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

Compound **9**:

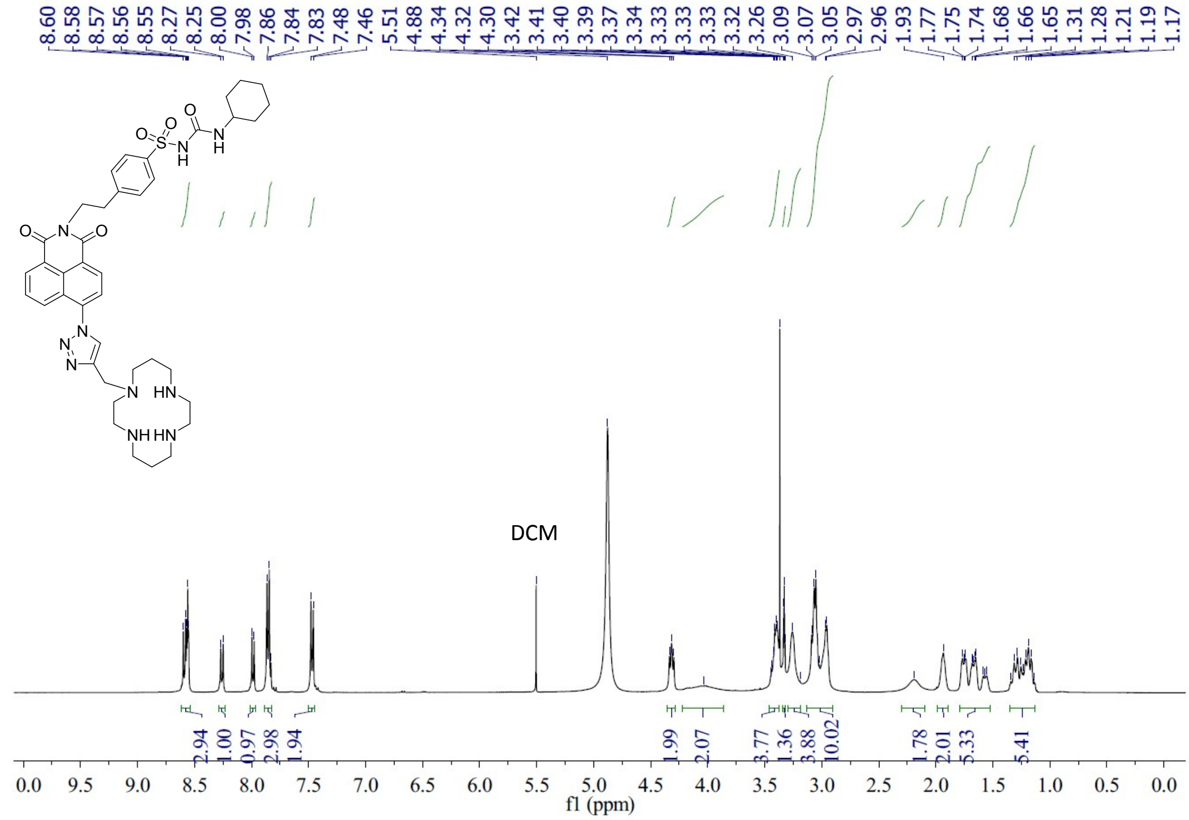

8.71
8.69
8.57
8.56
8.32
8.30
8.19
7.86
7.85
7.84
7.83
7.82
7.71
7.71
7.69
7.69
7.68
7.67
7.62
7.60
7.55
7.53
7.26
7.20
7.19
7.18
7.18
7.17
7.16
4.47
4.45
4.43
4.09
3.97
3.16
1.67
1.29
1.26
1.21
1.19
0.88
0.87
0.85
0.85
0.84
0.83
0.83
O
O
S
O
N
H
N
H
O
N
O
N
N
N
N
N
N
n-Hexane
1.93
1.89
1.03
1.00
3.78
2.15
2.04
1.98
2.08
0.97
2.03
1.93
3.84
1.28
2.03
1.99
2.31
2.12
2.75
1.46
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

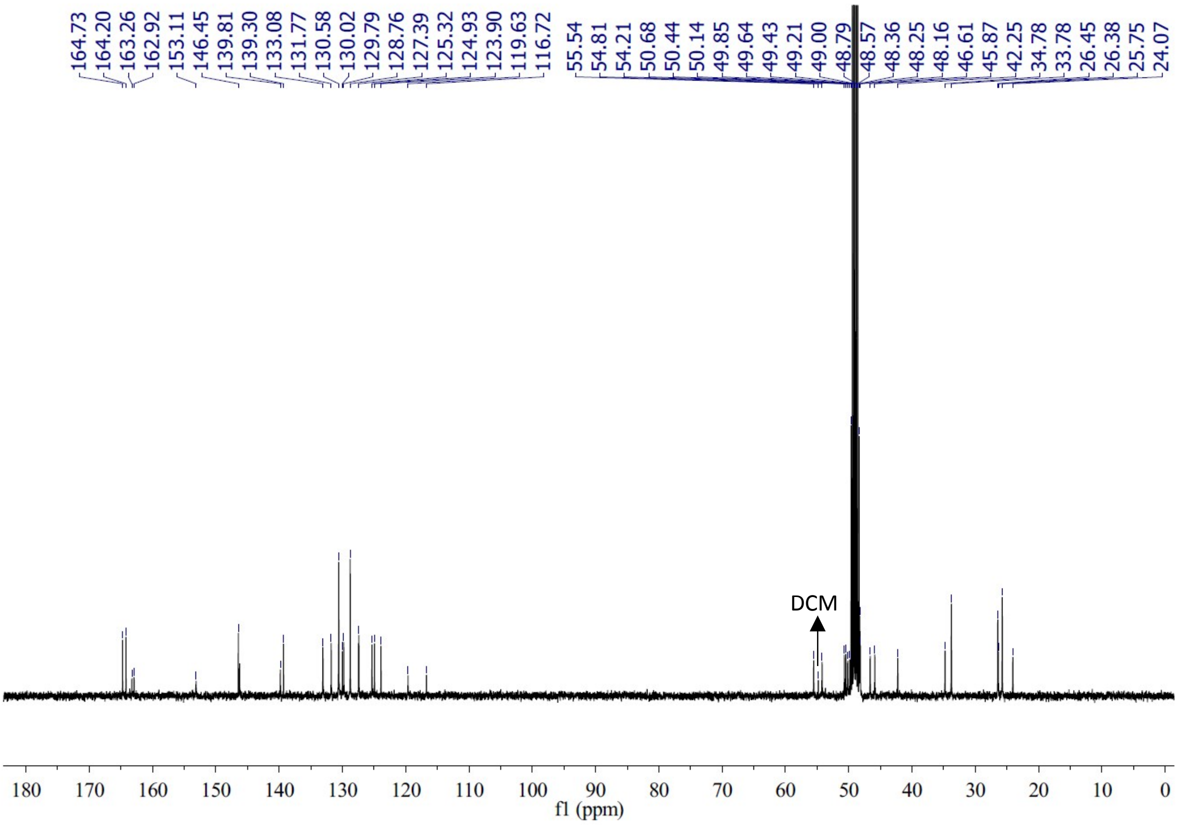

163.65
163.12
159.05
149.25
145.00
138.64
136.82
132.44
131.01
130.16
129.95
129.17
128.71
127.41
126.53
125.89
123.62
123.50
122.73
122.40
77.48
77.16
76.84
59.87
49.22
48.59
41.40
34.20
33.04
25.51
24.70
22.74
14.18
n-Hexane
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Compound **11**:

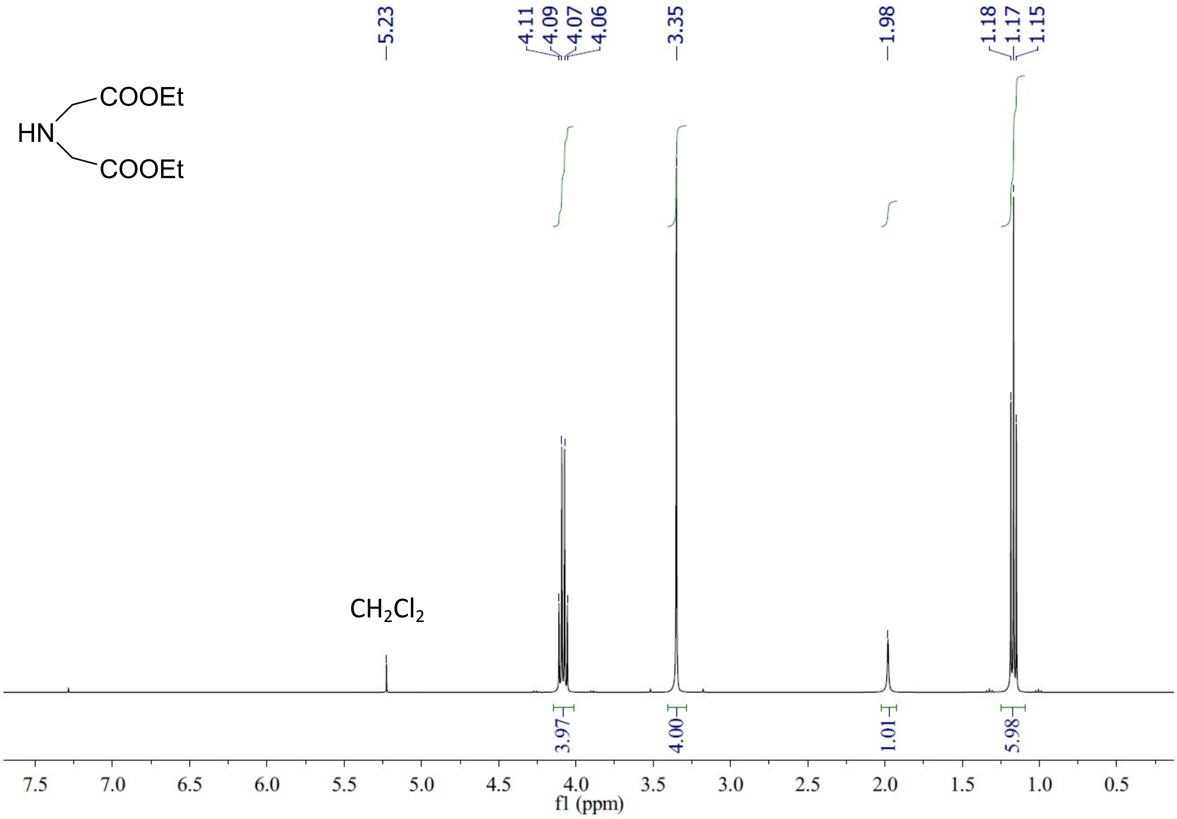

8.59
8.57
8.22
8.04
7.87
7.82
7.80
7.78
7.77
7.44
7.42
7.39
7.37
7.26
5.24
4.35
4.33
3.93
3.58
3.31
3.05
3.04
2.70
2.55
1.87
1.75
1.60
1.49
1.39
1.36
1.28
1.24
1.20
1.13
1.08
O
O
S
N
H
O
N
H
O
N
O
N
N
N
N
Boc
N
N
N
Boc
Boc
2.02
1.00
1.04
4.21
2.04
0.67
2.00
2.07
1.12
12.36
2.00
1.85
1.92
8.14
33.49
0.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

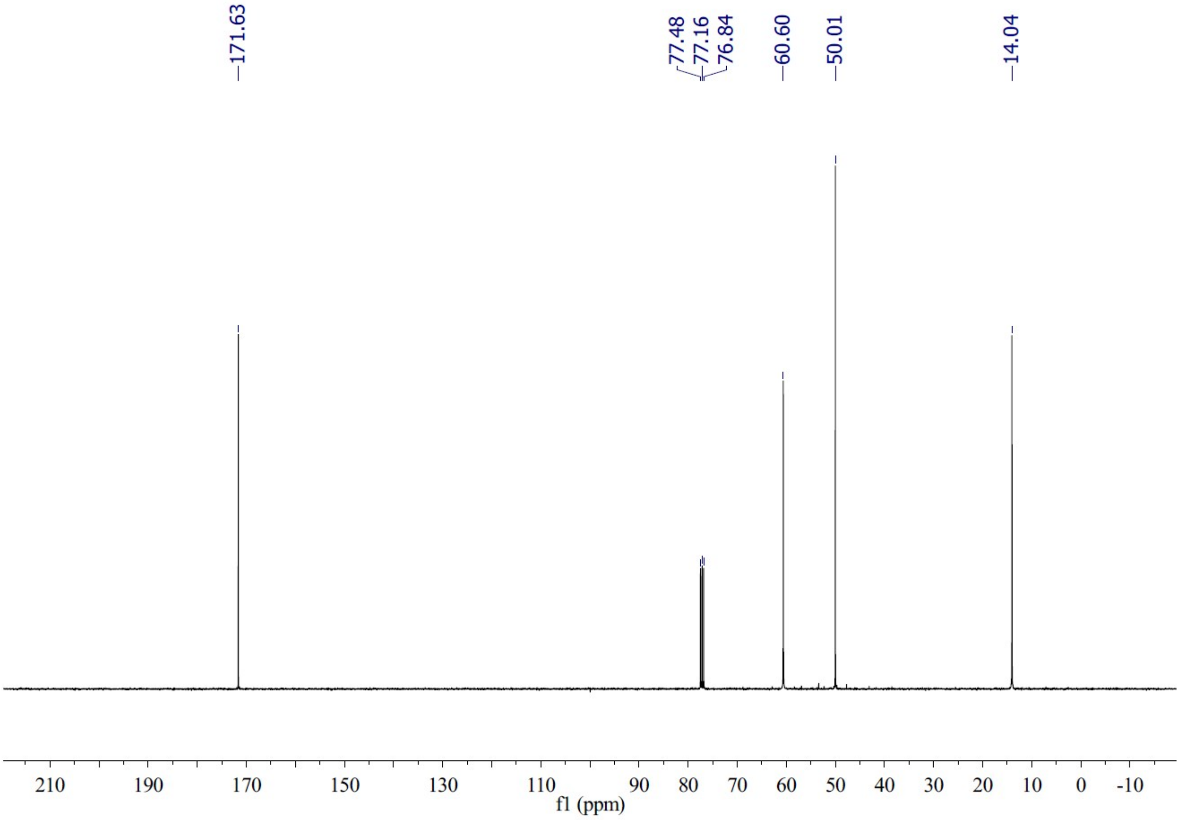
Compound **12**:


8.60 8.58 8.57 8.56 8.55 8.27 8.25 8.00 7.98 7.86 7.84 7.83 7.48 7.46 5.51 4.88 4.34 4.32 4.30 3.42 3.41 3.40 3.39 3.37 3.34 3.33 3.33 3.33 3.32 3.26 3.09 3.07 3.05 2.97 2.96 1.93 1.77 1.75 1.74 1.68 1.66 1.65 1.31 1.28 1.21 1.19 1.17
DCM
2.94 1.00 0.97 2.98 1.94 1.99 2.07 3.77 1.36 3.88 10.02 1.78 2.01 5.33 5.41
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

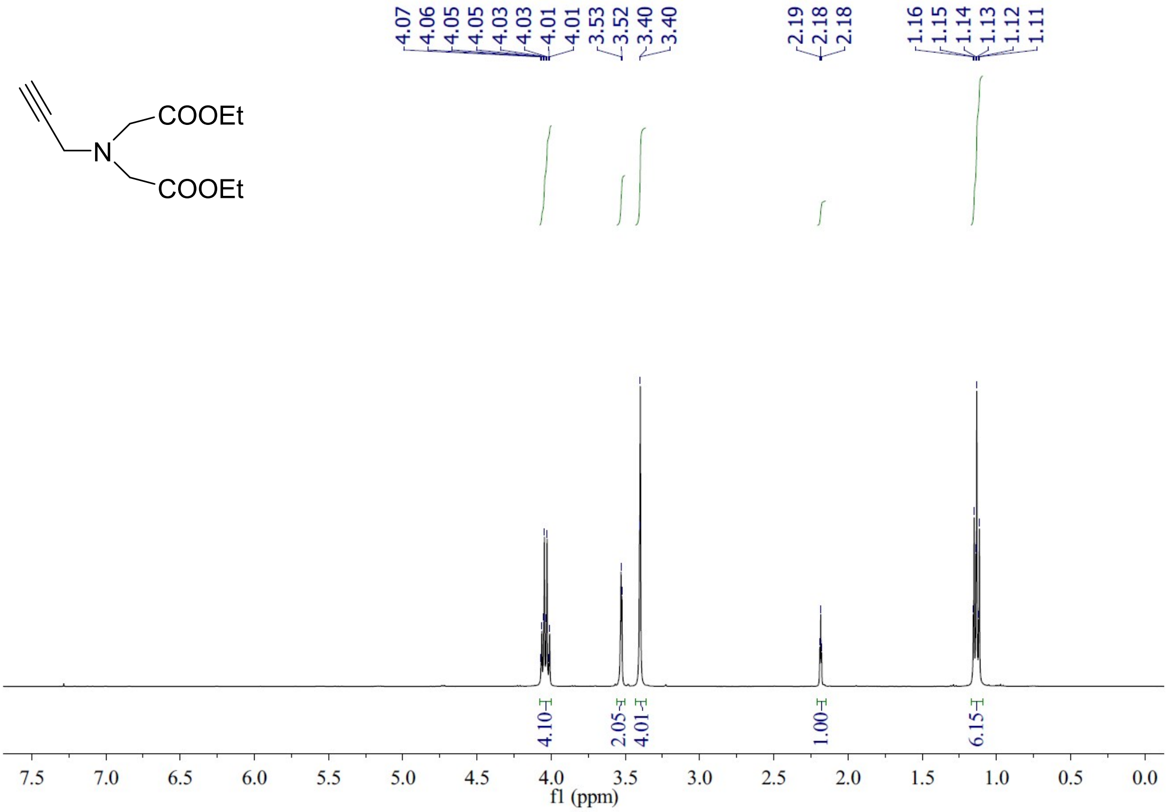

164.73 164.20 163.26 162.92 153.11 146.45 139.81 139.30 133.08 131.77 130.58 130.02 129.79 128.76 127.39 125.32 124.93 123.90 119.63 116.72 55.54 54.81 54.21 50.68 50.44 50.14 49.85 49.64 49.43 49.21 49.00 48.79 48.57 48.36 48.25 48.16 46.61 45.87 42.25 34.78 33.78 26.45 26.38 25.75 24.07
DCM
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

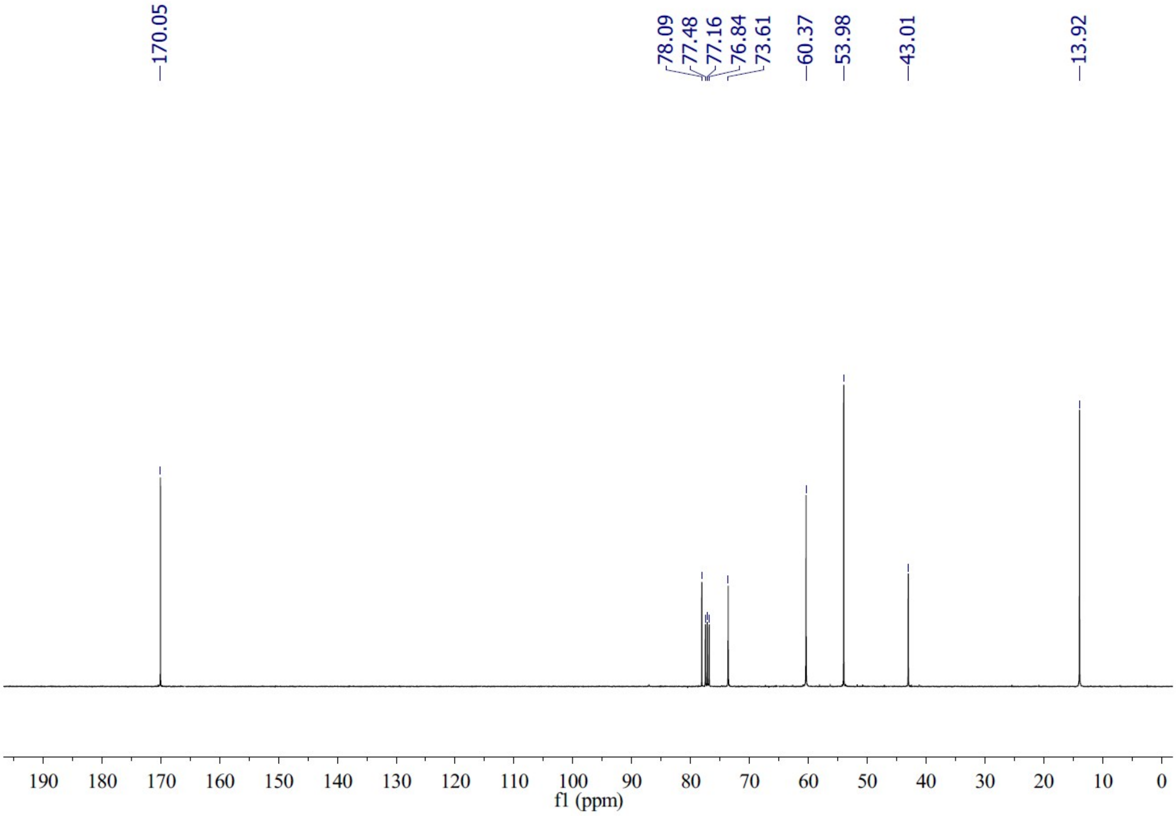
Compound **S14**:



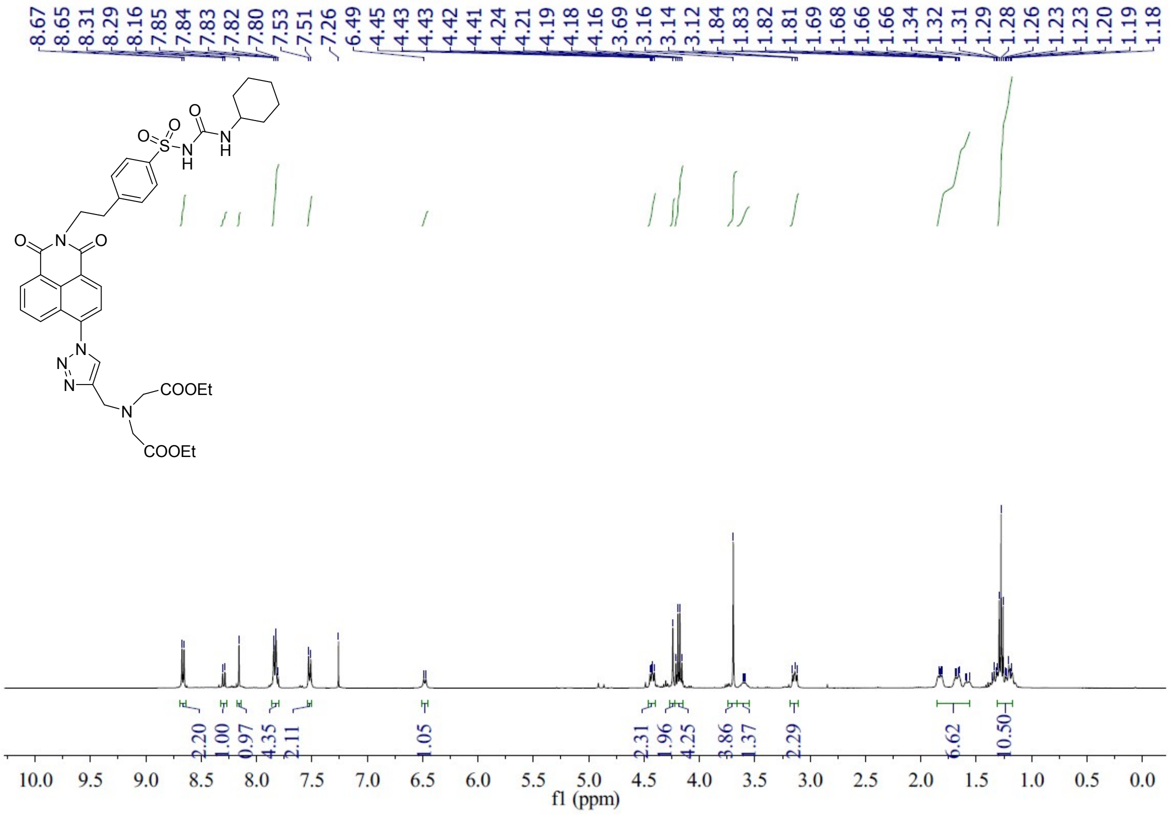


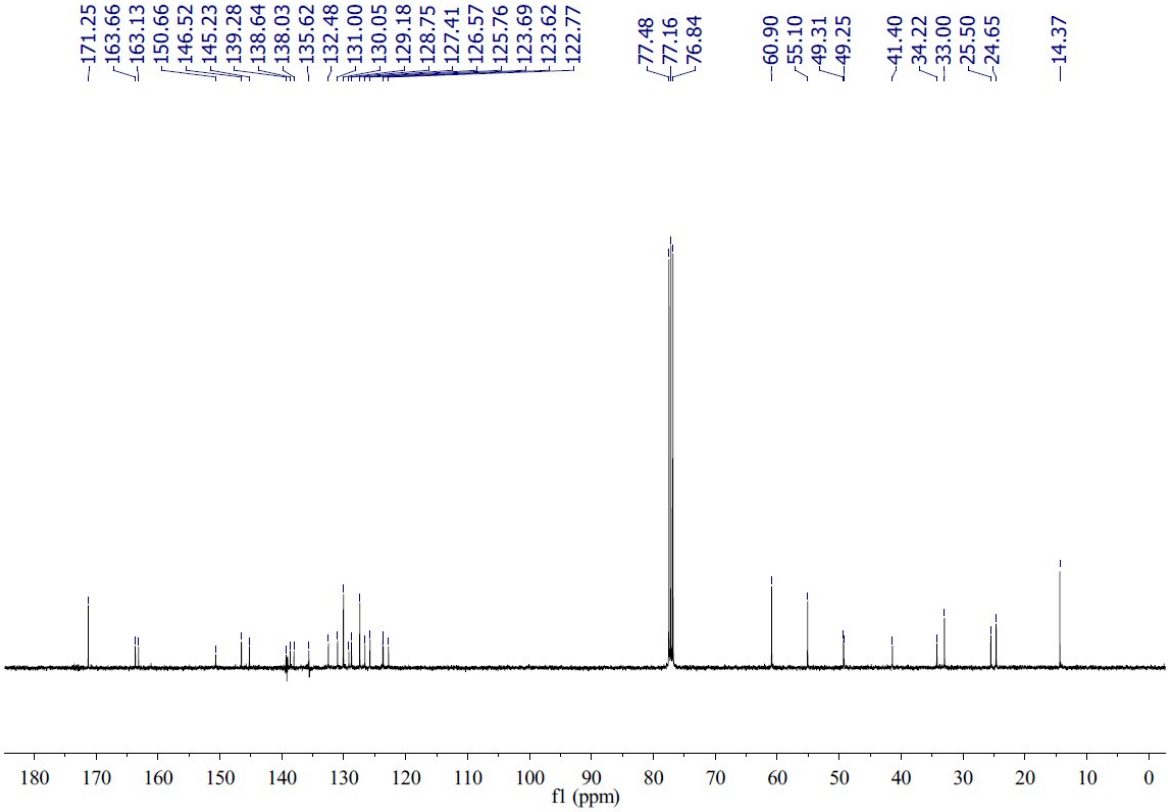
Compound **S15**:





Compound **S16**:





Cartesian coordinates of probe **9**:

0 1

N	5.81630800	-1.80179000	-0.60490900
N	6.60725800	-2.30194300	0.39159900
N	7.84135400	-2.05683900	0.05984000
C	7.87871900	-1.41233700	-1.14766100
C	6.58374800	-1.25455200	-1.58477300
C	9.16000300	-0.93670000	-1.75965000
N	9.61800100	0.33046800	-1.17466200
C	2.07015800	-0.75807200	2.77637300
C	3.46737700	-0.59151400	2.81478800
C	4.25065100	-0.96508100	1.74134700
C	3.66313500	-1.52735000	0.57741500
C	2.24160500	-1.67700800	0.53173700
C	1.46210300	-1.29049700	1.65243100
C	4.40083300	-1.92788500	-0.57801900
C	3.76696800	-2.41782400	-1.70515700
C	2.36774100	-2.53919000	-1.73485800
C	1.61121600	-2.18560600	-0.63217500
C	0.13869700	-2.33604600	-0.68583300
N	-0.57342300	-2.00695000	0.47458200
C	-0.01017500	-1.43837100	1.62686400
O	-0.72967800	-1.08954500	2.55831500
O	-0.45014700	-2.73268300	-1.68707900
C	10.99509900	0.64239800	-1.56866600
C	8.68194100	1.43396000	-1.41875200
C	11.59312200	1.73673200	-0.70503400
C	7.63816900	1.59913500	-0.32782200
C	7.98082300	1.42509500	1.01925700
C	7.01263700	1.65541100	1.99291600
C	5.73202600	2.04420800	1.59169400
C	5.48510600	2.18191200	0.22661000
N	6.40920700	1.96987400	-0.72325500
N	11.67207100	1.48371900	0.61513800
C	12.19144700	2.43237100	1.40333700
C	12.65685200	3.66456100	0.93596100
C	12.57575300	3.92082700	-0.43083300
C	12.03361600	2.94058000	-1.26410200
C	-2.03572200	-2.15636800	0.44188000
C	-2.72121900	-0.87332800	-0.06620000
C	-4.22274300	-1.02132800	-0.03293200
C	-4.92951200	-0.76665800	1.15327900
C	-6.30796300	-0.94563700	1.21727800
C	-6.98045100	-1.38554100	0.07367500
C	-6.30539200	-1.65380400	-1.11831700
C	-4.92457700	-1.46903600	-1.16079600
S	-8.74800200	-1.61398100	0.14735700
N	-9.22600800	0.01688300	-0.08075500
O	-9.16778600	-2.44692300	-0.98898800
O	-9.13733300	-2.00515600	1.50640500
C	-10.61161900	0.31810800	-0.15482700
N	-10.86570300	1.57646800	-0.59581000
C	-12.22764400	2.12118900	-0.60282500
C	-12.34033800	3.21785400	-1.66983700

C	-13.75678800	3.81322800	-1.69940500
C	-14.17790600	4.33406300	-0.31683200
C	-14.06160400	3.23372900	0.74863200
C	-12.64442900	2.64138200	0.78351700
O	-11.46776100	-0.50287200	0.15995700
H	6.15937500	-0.77471400	-2.45189400
H	9.93245700	-1.69044000	-1.57495400
H	9.02963800	-0.85979400	-2.85462500
H	1.45253000	-0.46561200	3.61856100
H	3.93252600	-0.15773700	3.69404100
H	5.32236600	-0.82600800	1.78106100
H	4.35676600	-2.72491000	-2.56189000
H	1.87015700	-2.92528000	-2.61725400
H	11.59006700	-0.26774400	-1.42987300
H	11.07806000	0.92282000	-2.63427400
H	8.16934900	1.34337000	-2.39002000
H	9.25664300	2.36663500	-1.46333500
H	8.98977300	1.11601900	1.27033100
H	7.24852500	1.53145300	3.04642300
H	4.94143800	2.22264900	2.31318200
H	4.49571200	2.46992800	-0.12514900
H	12.24176600	2.19658500	2.46514400
H	13.06768300	4.39384700	1.62694200
H	12.92211700	4.86447200	-0.84253500
H	11.94812100	3.10508400	-2.33407300
H	-2.36511800	-2.38685200	1.45487500
H	-2.26760600	-2.99718000	-0.21126500
H	-2.37574100	-0.67096100	-1.08494000
H	-2.40796100	-0.03909000	0.56992600
H	-4.39171300	-0.42602600	2.03387700
H	-6.85360900	-0.75314300	2.13473700
H	-6.85065400	-2.00272600	-1.98837000
H	-4.38558600	-1.67597400	-2.08106300
H	-8.60232400	0.51444100	-0.71332300
H	-10.10606100	2.24536000	-0.63136300
H	-12.88583800	1.28936600	-0.87634400
H	-11.61692300	4.01524800	-1.44129800
H	-12.06872900	2.80795400	-2.64983000
H	-13.80433200	4.61721300	-2.44369400
H	-14.46543400	3.03832400	-2.02566000
H	-13.53052800	5.17785000	-0.03621100
H	-15.20388800	4.72061700	-0.35464100
H	-14.32699600	3.62616400	1.73778800
H	-14.78171300	2.43349900	0.52310200
H	-11.92754200	3.41337400	1.09844000
H	-12.57933300	1.82175700	1.50835000

Cartesian coordinates of the Zn^{2+} complex of **9**:

2 1

N	-4.80516200	0.05953400	0.79704400
N	-5.61332400	0.06280800	-0.27340300
N	-6.81378600	0.28737800	0.19360500
C	-6.80369000	0.41678100	1.55323800

C	-5.49861900	0.26556200	1.95311000
C	-8.09526200	0.68512000	2.27052800
N	-9.19644800	0.05479600	1.50143000
C	-0.84466300	1.98235700	-1.88777100
C	-2.19703600	2.36210400	-1.77432600
C	-3.05931800	1.66179400	-0.95608200
C	-2.59701900	0.54494100	-0.21029000
C	-1.21972300	0.17380500	-0.30934300
C	-0.35971800	0.90582600	-1.16715800
C	-3.40982600	-0.23464200	0.66209800
C	-2.90169800	-1.27788700	1.40860200
C	-1.53884300	-1.60991000	1.31083900
C	-0.71141500	-0.90564400	0.45683000
C	0.71844800	-1.29242200	0.35597900
N	1.50019800	-0.58833400	-0.56622400
C	1.06744100	0.52887700	-1.29583800
O	1.85437800	1.14605000	-2.00582300
O	1.20547000	-2.18991200	1.03481200
C	-9.30826600	-1.39836100	1.73767100
C	-10.48087400	0.77170300	1.62208000
C	-9.82754600	-2.12624400	0.51091000
C	-10.51418500	1.98770400	0.71483700
C	-9.85026300	2.91806100	-1.32184000
C	-10.58998500	4.07017900	-1.08916800
C	-11.30764700	4.17097500	0.10343600
N	-9.53100100	-1.59114400	-0.69382200
C	-9.90215200	-2.22745700	-1.82110700
C	-10.58603900	-3.43553800	-1.79323600
C	-10.90495900	-3.99138000	-0.55345000
C	-10.52477100	-3.32662300	0.61171200
C	2.91257700	-0.97641800	-0.70044100
C	3.81119700	-0.19006900	0.27287500
C	5.25946000	-0.57136800	0.08463500
C	5.99104300	-0.03641300	-0.98849500
C	7.31112600	-0.41325200	-1.21225800
C	7.90230400	-1.33458000	-0.34223100
C	7.20123600	-1.88540700	0.73110600
C	5.87720100	-1.49846600	0.93446900
S	9.59328800	-1.82600500	-0.62860800
N	10.37158400	-0.43327000	-0.00413800
O	9.88969700	-3.00992200	0.19084400
O	9.85691200	-1.86845700	-2.07097000
C	11.79069800	-0.38078000	-0.00305700
N	12.28682000	0.66429800	0.70782500
C	13.72097500	0.97414000	0.69611500
C	14.09468300	1.75213300	1.96459100
C	15.59332500	2.09346100	1.97750500
C	16.00814200	2.85885500	0.71143100
C	15.62911100	2.07779300	-0.55595800
C	14.13016100	1.74144400	-0.57302400
O	12.46949800	-1.21154100	-0.59844300
H	-5.01969600	0.29914600	2.91836600
H	-8.06129400	0.33447300	3.30777700
H	-8.27889400	1.76387200	2.29295000
H	-0.16797200	2.52953600	-2.53485200

H	-2.56184900	3.21550300	-2.33629700
H	-4.09604900	1.96642200	-0.88108800
H	-3.55810600	-1.85207100	2.05303500
H	-1.13163000	-2.42999100	1.89067700
H	-8.30229800	-1.77735800	1.94935200
H	-9.92813800	-1.62262600	2.61320400
H	-10.69846000	1.05169200	2.65901200
H	-11.27202000	0.08594600	1.29928800
H	-9.26237400	2.78350800	-2.22248500
H	-10.59414900	4.86804700	-1.82270100
H	-11.88888700	5.06068200	0.32293400
H	-9.63797800	-1.73799100	-2.75138500
H	-10.86723300	-3.91993300	-2.72107100
H	-11.44833800	-4.92877900	-0.49328100
H	-10.76164100	-3.73091700	1.58986600
H	3.20860100	-0.78291300	-1.73143500
H	2.97990300	-2.04577200	-0.50303300
H	3.48736800	-0.39647700	1.29781000
H	3.67290900	0.87949800	0.08285700
H	5.51736500	0.68019100	-1.65405200
H	7.87319100	-0.00531400	-2.04551400
H	7.68216900	-2.60283400	1.38671500
H	5.31799000	-1.92255900	1.76365100
H	9.88869700	-0.05351600	0.80750700
H	11.65927200	1.41440100	0.97232900
H	14.24016300	0.00964900	0.70381500
H	13.51028000	2.68404400	1.99765800
H	13.81960200	1.16761600	2.85052500
H	15.83181100	2.67695800	2.87485900
H	16.17325700	1.16160100	2.04278600
H	15.50284100	3.83559600	0.69803000
H	17.08652800	3.05963500	0.72713800
H	15.89477200	2.64848200	-1.45407900
H	16.20890000	1.14392100	-0.59230500
H	13.54248500	2.66928100	-0.62566900
H	13.87237000	1.14138700	-1.45316800
N	-9.81620000	1.90272800	-0.43854800
C	-11.26600600	3.11864800	1.01788200
H	-11.80909500	3.16918200	1.95527100
Zn	-8.67736800	0.23890400	-0.62638100

Cartesian coordinates of probe **12**:

0 1

N	-5.37293200	1.88039800	0.64447500
N	-5.74494000	2.56928100	1.76409300
N	-7.04315500	2.50373400	1.84216900
C	-7.53525400	1.77443000	0.79220800
C	-6.46962900	1.36637500	0.02380800
C	-8.99284600	1.46611700	0.62488500
C	-1.16040900	4.80827700	0.08923600
C	-2.49861800	5.11022100	0.40793000
C	-3.44681200	4.11011800	0.48486600
C	-3.09106200	2.75541100	0.24806200

C	-1.73705900	2.45415100	-0.10103700
C	-0.78303600	3.50221300	-0.16943200
C	-4.00863600	1.66302900	0.30901600
C	-3.61038200	0.36859900	0.02705400
C	-2.27865800	0.09763700	-0.32713100
C	-1.34969600	1.12051700	-0.38713900
C	0.05023100	0.80566800	-0.75300700
N	0.93768400	1.88457700	-0.85163700
C	0.62539400	3.21210500	-0.52377300
O	1.49607800	4.07652700	-0.54554300
O	0.43674800	-0.33915500	-0.96973700
C	2.32607600	1.58125300	-1.22795500
C	3.18051000	1.21675000	0.00154900
C	4.57466500	0.82360900	-0.42197700
C	5.60581100	1.77377500	-0.47233500
C	6.87813200	1.42532900	-0.91834900
C	7.11154500	0.10641600	-1.31605800
C	6.10461600	-0.86063900	-1.28234700
C	4.83909600	-0.49118300	-0.83346700
S	8.73541900	-0.34821800	-1.89870100
N	9.50648800	-0.55828800	-0.38180900
O	8.63884900	-1.62547700	-2.61994100
O	9.36233100	0.80257800	-2.55812000
C	10.85078300	-1.01420100	-0.36076300
N	11.27936500	-1.37577300	0.87552500
C	12.68264600	-1.73112800	1.11539700
C	12.78806700	-2.61266200	2.36643600
C	14.24913600	-3.00169300	2.64235000
C	15.15149900	-1.76326300	2.75432300
C	15.03816900	-0.88057900	1.50220700
C	13.57860400	-0.48618600	1.23019900
O	11.53140000	-1.06058100	-1.38100000
N	-9.49012400	0.58974200	1.67938900
C	-8.70432800	-0.61912500	1.94829100
C	-8.54142700	-1.61739400	0.79644600
C	-7.56338900	-2.75549800	1.09894600
N	-7.45993800	-3.68917500	-0.03593700
C	-10.95001300	0.51302600	1.75347100
C	-11.77316900	0.30888300	0.46336100
N	-11.55375400	-0.97417000	-0.19409400
C	-8.31124400	-4.88148600	0.04784400
C	-9.82109900	-4.61686200	0.05372700
N	-10.27089300	-3.75126800	-1.03084300
C	-12.55578200	-1.29015400	-1.21244400
C	-12.18069800	-2.52891800	-2.03917700
C	-11.72811200	-3.73515700	-1.19498700
H	-6.40325800	0.78974700	-0.88505100
H	-9.56708900	2.40062900	0.67241500
H	-9.13909900	1.06451900	-0.39391300
H	-0.41280000	5.59199100	0.03237500
H	-2.78600600	6.14036900	0.59179700
H	-4.47118100	4.35346500	0.73680400
H	-4.32809100	-0.44152900	0.09931700
H	-1.96511400	-0.91721500	-0.54407700
H	2.73278700	2.45996300	-1.72757700

H	2.30022000	0.74823500	-1.93038700
H	2.69613000	0.38720900	0.52677300
H	3.20824700	2.07658500	0.67824000
H	5.40886800	2.79598700	-0.16153400
H	7.67362200	2.16141000	-0.96382800
H	6.31042900	-1.87508700	-1.60555200
H	4.04387200	-1.23108300	-0.80480800
H	8.87326300	-0.92390100	0.32642200
H	10.73143100	-1.10260800	1.68240700
H	13.00254400	-2.31186800	0.24317300
H	12.39121900	-2.05729100	3.22975600
H	12.16364200	-3.50544500	2.24270500
H	14.30494200	-3.60212600	3.55828700
H	14.61097700	-3.64008100	1.82340200
H	14.85397900	-1.17785000	3.63668700
H	16.19342500	-2.06790800	2.91272000
H	15.65529100	0.01974900	1.60922500
H	15.43068400	-1.43103000	0.63462400
H	13.20396100	0.14052900	2.05239000
H	13.49584500	0.10061500	0.30847800
H	-7.71063900	-0.29532900	2.28811200
H	-9.16915800	-1.12074800	2.80626200
H	-8.17587700	-1.10001200	-0.10101500
H	-9.51002600	-2.03954300	0.53722000
H	-6.56678400	-2.33349400	1.28554900
H	-7.86100600	-3.27291000	2.03032000
H	-6.49912400	-4.01666000	-0.09900300
H	-11.31379800	1.45626000	2.19327800
H	-11.20253200	-0.28807100	2.45636100
H	-11.62228700	1.16811000	-0.21735900
H	-12.82896200	0.35153100	0.76476900
H	-10.63342400	-0.99621100	-0.62470000
H	-8.06705900	-5.50828600	-0.82071200
H	-8.09822900	-5.48976600	0.94840300
H	-10.31356900	-5.60906300	0.04542900
H	-10.11265100	-4.14317700	1.00153700
H	-9.83979000	-4.05239300	-1.90410800
H	-12.74462300	-0.44497500	-1.90271700
H	-13.50607800	-1.47907500	-0.69155500
H	-13.05137400	-2.79836400	-2.65010100
H	-11.37631200	-2.27376300	-2.74304200
H	-12.10404900	-4.67635100	-1.63628600
H	-12.17168700	-3.66342000	-0.19471900

Cartesian coordinates of the Zn^{2+} complex of **12**:

2 1

N	4.98892200	-1.31817800	-0.68676300
N	5.49057700	-0.07896800	-0.57221000
N	6.79122500	-0.21750600	-0.60856800
C	7.14623800	-1.52514400	-0.74171600
C	5.97811900	-2.25006700	-0.79487100
C	8.60220000	-1.88231100	-0.81990200
C	1.14779700	-0.51397800	2.64492000
C	2.54003600	-0.31017300	2.71808800

C	3.35474500	-0.62869800	1.65133700
C	2.80444600	-1.16999000	0.45903500
C	1.39423000	-1.39485000	0.39357100
C	0.58065400	-1.05201900	1.50358100
C	3.56953600	-1.53063300	-0.68836100
C	2.99422000	-2.09326400	-1.80853300
C	1.60446900	-2.31272000	-1.84664500
C	0.81322300	-1.96404800	-0.76812800
C	-0.65319600	-2.19019200	-0.84201900
N	-1.40484000	-1.85501800	0.29022300
C	-0.88394800	-1.26928500	1.45398700
O	-1.62890900	-0.96225700	2.37847200
O	-1.19593000	-2.65078500	-1.84017700
C	-2.85845700	-2.08590800	0.24322800
C	-3.62263800	-0.84871400	-0.27195800
C	-5.11867500	-1.06012300	-0.21643500
C	-5.81957200	-0.83391200	0.97960900
C	-7.19242800	-1.04719100	1.05807300
C	-7.87131300	-1.48871600	-0.08179100
C	-7.20146900	-1.72961500	-1.28246000
C	-5.82514400	-1.51316200	-1.33913600
S	-9.63259600	-1.76978300	0.01014500
N	-10.16143000	-0.14256900	-0.07813200
O	-10.05348300	-2.52815900	-1.17656400
O	-9.98208800	-2.27800300	1.34102100
C	-11.55457500	0.13488600	-0.08566600
N	-11.84008800	1.42470600	-0.39671200
C	-13.20553000	1.95901100	-0.33816100
C	-13.38626700	3.03925200	-1.41501100
C	-14.80075000	3.63938800	-1.37195000
C	-15.14748200	4.17711400	0.02462200
C	-14.96800700	3.09384000	1.09845800
C	-13.55212700	2.49668400	1.06242200
O	-12.38407200	-0.73055400	0.17560900
N	9.40823900	-0.90870800	-0.02845500
C	9.47713900	-1.38960400	1.37995100
C	10.12190200	-0.46367800	2.42385000
C	9.61594100	0.99345700	2.54699700
N	8.26275200	1.20111000	1.96301400
C	10.73771600	-0.68217400	-0.64638800
C	10.62554100	0.22062900	-1.87900300
N	9.89656500	1.46956000	-1.54171200
C	7.66448400	2.52425000	2.29025900
C	8.12190800	3.59459700	1.29962500
N	7.82720400	3.14530200	-0.08355300
C	9.56877700	2.30706400	-2.73628000
C	8.39969600	3.27375500	-2.49736500
C	8.42462700	4.00270000	-1.14809900
H	5.77365100	-3.30543200	-0.87966300
H	8.77381200	-2.91011800	-0.47849100
H	8.92063100	-1.83982300	-1.86476500
H	0.50617800	-0.25940600	3.48126900
H	2.97407200	0.10053100	3.62377300
H	4.42340700	-0.46589500	1.72445600
H	3.60956600	-2.34755000	-2.66464800

H	1.14346400	-2.74596500	-2.72670100
H	-3.17711300	-2.33483200	1.25529100
H	-3.02978000	-2.94120200	-0.40962400
H	-3.30710400	-0.63916700	-1.29902200
H	-3.34739800	0.01269100	0.34537600
H	-5.28335300	-0.48433100	1.85768800
H	-7.72734800	-0.87418700	1.98574100
H	-7.74705900	-2.07966900	-2.15167100
H	-5.29577400	-1.69543700	-2.27019800
H	-9.56587400	0.42606900	-0.67606000
H	-11.08472000	2.09853400	-0.42924900
H	-13.86566900	1.11505500	-0.56338000
H	-12.64781700	3.83823800	-1.24826600
H	-13.17623900	2.61184000	-2.40272000
H	-14.88538500	4.43610900	-2.12101400
H	-15.52949900	2.86567400	-1.65390900
H	-14.49338500	5.03013600	0.25764800
H	-16.17657900	4.55731800	0.03753400
H	-15.17269800	3.50360600	2.09514600
H	-15.70321400	2.29292900	0.93234400
H	-12.81855400	3.26905200	1.33592100
H	-13.45389200	1.68659300	1.79486800
H	11.37433700	-0.19892300	0.09917600
H	11.22190200	-1.62877100	-0.92227200
H	10.07154700	-0.27410500	-2.68135300
H	11.62939500	0.43696000	-2.26249200
H	10.52839400	2.02466100	-0.96091700
H	6.57708400	2.41210000	2.23497100
H	7.91716600	2.82975700	3.31256900
H	7.62943700	4.54686900	1.52805200
H	9.20174400	3.75350100	1.37472900
H	6.81321500	3.18423900	-0.20930500
H	9.31025100	1.63030700	-3.55478600
H	10.46621400	2.85924900	-3.03931000
H	8.40951500	4.01074000	-3.30731100
H	7.44839200	2.73216000	-2.58481200
H	7.87651200	4.94966400	-1.20865300
H	9.44991200	4.24671100	-0.85013900
Zn	8.32559500	1.08659200	-0.17503300
H	9.61201700	1.28608200	3.60410600
H	10.29969000	1.67575300	2.03423500
H	11.20772300	-0.43495300	2.28878700
H	9.96027600	-0.97726700	3.37837100
H	10.01245000	-2.34999800	1.41132600
H	8.44486800	-1.60537400	1.67397300
H	7.64089900	0.48923400	2.34482500