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An Expeditious Synthetic Route To Proteomimetic Foldamers

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SUPPORTING INFORMATION

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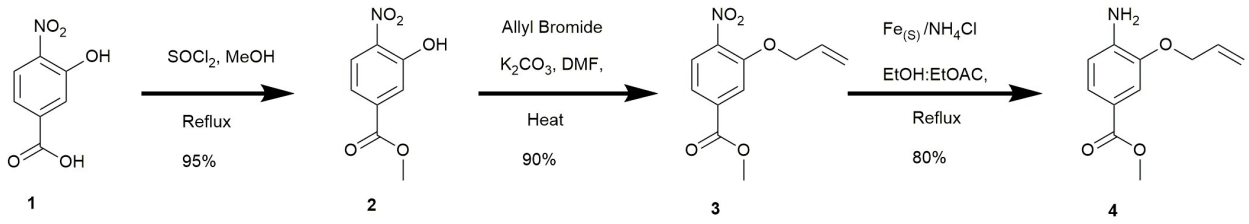
General experimental considerations

General methods: All commercially available compounds (Alfa-aesar, Sigma-Aldrich, TCI Chemicals, Merck, Spectrochem) were used without purification. All reactions were performed in oven-dried glassware and run under argon or nitrogen atmosphere wherever stated. Tetrahydrofuran was distilled from sodium and benzophenone; $CHCl_3$ and EtOAc were distilled from CaH_2. Analytical thin layer chromatography was performed on silica gel 60 F_{254} plates (Merck). Column chromatographic purifications were performed with flash silica gel (230-400 mesh) from Merck. Melting points were recorded on a digital melting point apparatus. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance III 500MHz NMR Spectrometer or Bruker Avance III 700MHz NMR Spectrometer. NMR spectra were recorded at 295 K in $CDCl_3$ or DMSO-d_6 and chemical shifts were calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^1H δ 7.26 ppm; ^{13}C δ 77.16 ppm), DMSO-d_6 (^1H δ 2.50 ppm; ^{13}C δ 39.52 ppm). All chemical shifts are reported in δ ppm downfield of TMS and peak multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), heptet (hept), doublet of doublet (dd) doublet of triplet (dt), doublet of doublet of doublet (ddd), broad (broad) and multiplet (m). LC-HRMS was recorded on Bruker Daltonics MicroTOF-Q-II in electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) mode.



Scheme S1: Synthesis of sub-monomers **2**-**4**.[1,2]

Synthetic procedures

Standard procedure A: Alkylation

The phenol substrate was dissolved in DMF. The solution was heated at 80^0C followed by addition of K_2CO_3 and the corresponding halide reagent. The reaction mixture was heated and monitored using TLC. After completion of reaction, the reaction mixture was concentrated *in vacuo* and diluted with either EtOAc or DCM. The solution was neutralized using a saturated solution of aq. NH_4Cl, and washed with water and brine. The organic phase was dried over Na_2SO_4 and purified using flash column chromatography to yield the desired compound.

Standard procedure B: Iron mediated nitro reduction

1 eq. of the nitro compound was added to a EtOH:EtOAc mixture (4:1) and refluxed at 80 ^{0}C. After obtaining a clear solution, 5 eq. of Fe solid was added followed by 2 eq. of aq. NH_4Cl solution. The reaction was monitored using TLC and filtered on a pad of celite. The solvent was evaporated *in vacuo.* The resulting solid was diluted with either EtOAc or DCM, followed by washing with water and brine. The organic layer was dried over Na_2SO_4 and the residue was purified by flash column chromatography to yield the desired compound.

Standard procedure C: Palladium-carbon mediated nitro reduction

Palladium on charcoal (10 mol %) was added under nitrogen atmosphere to a solution of the nitro compound (1 eq.) in anhydrous EtOAc:THF mixture (4:1). The nitrogen atmosphere was replaced with hydrogen, and the reaction was stirred vigorously until complete by TLC. The hydrogen atmosphere was vented and the reaction mixture filtered through a pad of celite with EtOAc or DCM, concentrated *in vacuo* and purified by flash column chromatography to yield the desired compound.

Standard procedure D: Cleavage of the prenyl ether

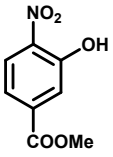
Prenyl ether functionalized molecules (1 eq.) were treated with $CeCl_3 \bullet 7H_2O$ (3 eq.) and NaI (3 eq.) in anhydrous MeCN (5 ml). The reaction mixture was refluxed under inert atmosphere and monitored using TLC. The reaction mixture was treated with 1N HCl and extracted using DCM.

The organic phase was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The residue was purified by column chromatography to yield the desired compound.

Standard procedure E: Cleavage of the allyl ether

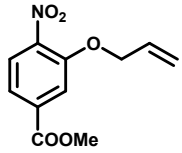
Allyl ether functionalized molecules (1 eq.) were treated with $Pd(PPh_3)_4$ (10 mol%) and sodium toluenesulfinate (1.2 eq.) in anhydrous $CHCl_3$ (5 ml). The reaction was performed under inert atmosphere at room temperature and monitored by TLC. After completion, the reaction mixture was treated with 1N HCl and extracted using $CHCl_3$. The organic phase was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The residue was purified by column chromatography.

Methyl 3-hydroxy-4-nitrobenzoate **(2)**



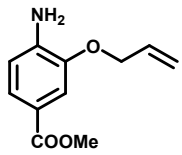
Compound **2** was synthesized as reported[1]. **MP**: 79-81 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.50 (s, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 1.8 Hz, 1H), 7.62 (dd, *J* = 8.8, 1.8 Hz, 1H), 3.96 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 164.97, 154.81, 138.13, 135.93, 125.41, 121.81, 120.74, 53.07. **HRMS (ESI)** for $C_8H_7NO_5$ $[M+H]^+$ m/z 198.0402 (calc), 198.0426 (found).

Methyl 3-(allyloxy)-4-nitrobenzoate **(3)**



Compound **3** was synthesized as reported[2]. **MP**: 59-61 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 1.5 Hz, 1H), 7.69 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.08 – 6.00 (m, 1H), 5.52 – 5.47 (m, 1H), 5.37 – 5.34 (m, 1H), 4.74 (dt, *J* = 5.0, 1.6 Hz, 2H), 3.96 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 165.33, 151.53, 142.85, 134.89, 131.37, 125.48, 121.70, 118.93, 116.05, 70.37, 52.98. **HRMS (APCI)** for: $C_{11}H_{11}NO_5$ $[M+H]^+$ m/z 238.0715 (calc), 238.0740(found).

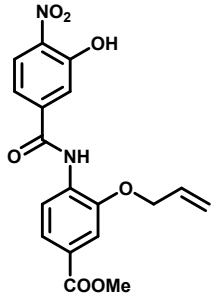
Methyl 3-(allyloxy)-4-aminobenzoate **(4)**



Compound **4** was synthesized according to the standard procedure B by refluxing **3** (500mg, 2.1 mmol, 1 eq.), with Fe solid (590 mg, 10.5 mmol, 5 eq.) and NH_4Cl (225 mg, 4.2 mmol, 2 eq.) in a EtOH:EtOAc mixture (18:2 ml) for 2 hrs. The residue was purified by flash column chromatography eluting with 20% EtOAc in hexane to give the title compound **4** as a brown semi-solid (350 mg, 80% yield). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.57 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.48 (d, *J* = 1.5 Hz, 1H), 6.70 (d, *J* = 8.2 Hz, 1H), 6.14 – 6.07 (m, 1H), 5.46 – 5.42 (m, 1H), 5.34 – 5.32 (m, 1H), 4.66 – 4.63 (m, 2H), 4.28 (s,

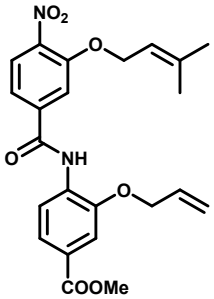
2H), 3.88 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 167.39, 145.12, 141.49, 133.14, 124.38, 119.56, 118.03, 113.44, 112.76, 69.40, 51.82. **HRMS (ESI)** for: $C_{11}H_{13}NO_3$ $[M+H]^+$ m/z 208.0973 (calc), 208.0989 (found).

Methyl 3-(allyloxy)-4-(3-hydroxy-4-nitrobenzamido)benzoate **(5)**



3-hydroxy 4-nitrobenzoic acid **(1)** (108mg, 0.5 mmol, 1.2 eq.) and PPh_3Cl_2 (321mg, 0.9 mmol, 2 eq.) were dissolved in anhydrous chloroform (5ml) under inert atmosphere. The reaction was stirred at room temperature to obtain a clear solution followed by addition of compound **4** (100mg, 0.5 mmol, 1 eq.). The reaction was completed within 30 min. The reaction mixture was diluted with $CHCl_3$ and partitioned between $CHCl_3$ and H_2O. The organic layer was separated and washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The resulting residue was purified by column chromatography eluting with 1% MeOH in CH_2Cl_2 to yield the title compound **5** as a yellow solid (0.168 mg, 86% yield). **MP**: 168-170 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.62 (s, 1H), 8.72 (s, 1H), 8.58 (d, *J* = 8.5 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 7.76 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.66 (d, *J* = 1.9 Hz, 1H), 7.62 (d, *J* = 1.7 Hz, 1H), 7.46 (dd, *J* = 8.8, 1.9 Hz, 1H), 6.14 – 6.07 (m, 1H), 5.48 – 5.44 (m, 1H), 5.41 – 5.38 (m, 1H), 4.74 (dt, *J* = 5.4, 1.4 Hz, 2H), 3.92 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.59, 162.78, 155.19, 146.77, 142.94, 135.30, 132.14, 131.52, 126.14, 126.11, 123.72, 119.18, 119.14, 118.52, 112.33, 70.01, 52.34. **HRMS (ESI)** for: $C_{18}H_{16}N_2O_7$ $[M+H]^+$ m/z 373.1036(calc), 373.1022 (found).

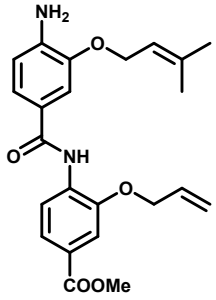
Methyl 3-(allyloxy)-4-(3-((3-methylbut-2-en-1-yl)oxy)-4-nitrobenzamido)benzoate **(6)**



Compound **6** was synthesized according to the standard procedure A by heating compound **5** (920mg, 2.4 mmol, 1 eq.), prenyl bromide (549mg, 3.7 mmol, 1.5 eq.), K_2CO_3 (511mg, 3.7 mmol, 1.5 eq.) in DMF (25ml) for 30 min. The residue was purified by flash column chromatography eluting with 1% MeOH in CH_2Cl_2 to yield the title compound **6** as an off-white solid (1.06mg, 97% yield). **MP**: 75-77 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.75 (s, 1H), 8.59 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.77 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.62 (d, *J* = 1.7 Hz, 1H), 7.38 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.14 – 6.06 (m, 1H), 5.51 – 5.44 (m, 2H), 5.42 – 5.40 (m, 1H), 4.76 (d, *J* = 6.7 Hz, 2H), 4.76 – 4.74 (m, 2H), 3.92 (s, 3H), 1.80 (d, *J* = 0.7 Hz, 3H), 1.78 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.64, 163.38, 152.57, 146.77, 142.23, 140.26, 139.68, 132.18, 131.71, 126.00, 125.98, 123.79, 119.18, 119.08, 118.02, 117.52, 114.87,

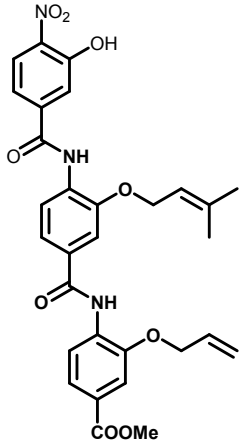
112.29, 69.99, 66.99, 52.35, 25.95, 18.53. **HRMS (ESI)** for: $C_{23}H_{24}N_2O_7$ $[M+Na]^+$ m/z 463.1482(calc), 463.1497 (found).

Methyl-3-(allyloxy)-4-(4-amino-3-((3-methylbut-2-en-1-yl)oxy)benzamido)benzoate **(7)**



Compound **7** was synthesized according to the standard procedure B by refluxing **6** (500mg, 2.1 mmol, 1 eq.), Fe solid (590 mg, 10.5 mmol, 5 eq.) and NH_4Cl (225 mg, 4.2 mmol, 2 eq.) in EtOH:EtOAc mixture (18:2 ml) for 2 hrs. The residue was purified by flash column chromatography eluting with 10% EtOAc in CH_2Cl_2 to yield the title compound **7** as a crystalline white solid (440mg, 94% yield). **MP**: 78-80 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.71 (s, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.58 (s, 1H), 7.46 (s, 1H), 7.28 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.72 (d, *J* = 8.1 Hz, 1H), 6.15 – 6.07 (m, 1H), 5.53 – 5.46 (m, 2H), 5.36 (d, *J* = 10.5 Hz, 1H), 4.71 – 4.70 (m, 2H), 4.63 (d, *J* = 6.7 Hz, 2H), 4.24 (s broad, 2H), 3.91 (s, 3H), 1.81 (s, 3H), 1.76 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.90, 165.31, 146.48, 146.13, 140.92, 138.46, 133.01, 132.48, 124.52, 123.99, 123.90, 120.15, 119.51, 118.61, 118.57, 113.34, 112.11, 111.11, 69.79, 65.44, 52.15, 25.91, 18.35. **HRMS (ESI)** for: $C_{23}H_{26}N_2O_5$ $[M+H]^+$ m/z 411.1920 (calc), 411.1916 (found).

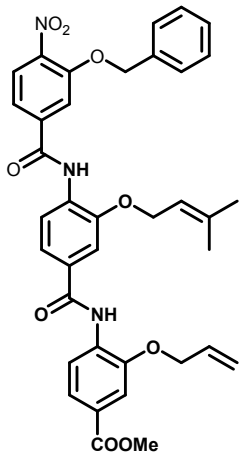
Methyl-3-(allyloxy)-4-(4-(3-hydroxy-4-nitrobenzamido)-3-((3-methylbut-2-en-1-yl) oxy)benzamido)benzoate **(8)**



3-Hydroxy 4-nitrobenzoic acid **(1)** (49mg, 0.2 mmol, 1.1 eq.) and PPh_3Cl_2 (161mg, 0.4 mmol, 2 eq.) were dissolved in anhydrous $CHCl_3$ (5ml) under inert atmosphere. The mixture was allowed to stir at room temperature to obtain clear solution followed by addition of compound **7** (100mg, 0.2 mmol, 1 eq.). The reaction was completed within 30 min. The reaction mixture was diluted with $CHCl_3$ and partitioned between $CHCl_3$ and H_2O. The organic layer was separated and washed with brine, dried over Na_2SO_4 and concentrated *in vacuo.* The resulting residue was purified by column chromatography eluting with 1% MeOH in CH_2Cl_2 to yield the title compound **8** as a yellow solid (120mg, 85% yield). **MP**: 148-150 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 10.62 (s, 1H), 8.83 (s, 1H), 8.73 (s, 1H), 8.63 (d, *J* = 8.4 Hz, 2H), 8.27 (d, *J* = 8.7 Hz, 1H), 7.76 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.66 (d, *J* = 1.7 Hz, 1H), 7.65 (d, *J* = 1.6 Hz, 1H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.47 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.44 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.17 – 6.09 (m, 1H),

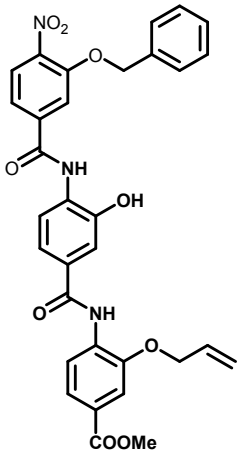
5.53 – 5.47 (m, 2H), 5.40 (dd, *J* = 10.5, 0.8 Hz, 1H), 4.75 – 4.72 (m, 4H), 3.92 (s, 3H), 1.83 (s, 3H), 1.80 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.76, 164.50, 162.82, 155.17, 147.85, 146.65, 142.90, 139.93, 135.30, 132.38, 132.32, 130.92, 130.70, 126.08, 125.23, 123.82, 119.26, 119.15, 119.12, 118.95, 118.76, 118.58, 118.53, 112.16, 111.30, 69.91, 66.31, 52.24, 25.97, 18.53. **HRMS (ESI)** for: $C_{30}H_{29}N_3O_9$ $[M+H]^+$ m/z 576.1982 (calc), 576.1992 (found).

Methyl 3-(allyloxy)-4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-((3-methylbut-2-en-1-yl) oxy)benzamido)benzoate **(9a)**



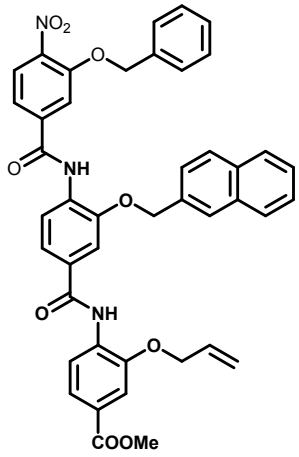
Compound **9a** was synthesized according to the standard procedure A by heating compound **8** (0.345mg, 0.6 mmol, 1 eq.), benzyl bromide (205mg, 1.2 mmol, 2 eq.) and K_2CO_3 (165mg, 1.2 mmol, 2 eq.) in DMF (15ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **9a** as an off-white solid (360mg, 90%). **MP**: 145-147 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.74 (s, 1H), 8.65 – 8.61 (m, 2H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.78 – 7.75 (m, 2H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.49 – 7.34 (m, 7H), 6.17 – 6.09 (m, 1H), 5.52– 5.47 (m, 2H), 5.40 (dd, *J* = 10.5, 1.2 Hz, 1H), 5.33 (s, 2H), 4.75 – 4.73 (m, 4H), 3.92 (s, 3H), 1.81 (s, 3H), 1.79 (s, 3H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.76, 164.53, 163.18, 152.22, 147.81, 146.65, 142.16, 139.86, 139.78, 135.03, 132.39, 132.34, 130.97, 130.59, 128.93, 128.62, 127.31, 126.08, 125.23, 123.82, 119.17, 119.14, 118.90, 118.76, 118.52, 118.14, 114.85, 112.17, 111.16, 71.52, 69.89, 66.23, 52.23, 25.99, 18.51. **HRMS (APCI)** for: $C_{37}H_{35}N_3O_9$ $[M+H]^+$ m/z 666.2451(calc), 666.2449(found).

Methyl 3-(allyloxy)-4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-hydroxybenzamido)benzoate **(9b)**



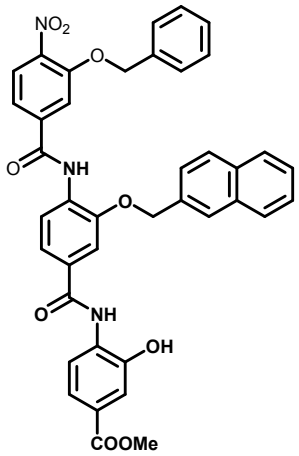
Compound **9b** was synthesized according to the standard procedure D by refluxing compound **9a** (170mg, 0.2 mmol, 1 eq.), $CeCl_3 \bullet 7H_2O$ (188, 0.7 mmol, 3 eq.) and NaI (114mg, 0.7 mmol, 3 eq.) in anhydrous MeCN (15 ml) for 7 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield the title compound **9b** as a yellow solid (140mg, 92% yield). **MP**: 200-202 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.37 (s, 1H), 9.87 (s, 1H), 9.44 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.99 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.70 – 7.37 (m, 10H), 6.16 – 6.09 (m, 1H), 5.48 – 5.44 (m, 3H), 5.31 (d, *J* = 10.5 Hz, 1H), 4.77 (d, *J* = 4.7 Hz, 2H), 3.86 (s, 3H). **^{13}C NMR (126 MHz, DMSO)** δ 165.85, 164.53, 163.76, 150.64, 149.45, 148.88, 141.43, 139.34, 135.79, 133.27, 132.10, 131.49, 128.94, 128.63, 128.24, 127.53, 125.70, 125.11, 123.96, 122.32, 122.02, 120.09, 118.11, 117.55, 114.91, 114.82, 112.78, 70.82, 69.23, 52.17. **HRMS (APCI)** for: $C_{32}H_{27}N_3O_9$ $[M+H]^+$ m/z 598.1825 (calc), 598.1798 (found).

Methyl 3-(allyloxy)-4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-(naphthalen-2-ylmethoxy) benzamido)benzoate **(9c)**



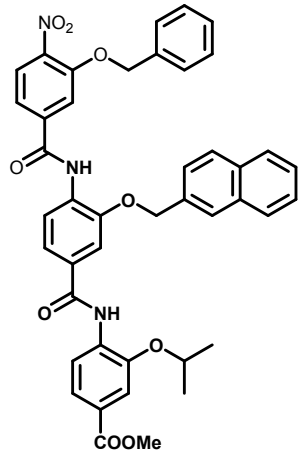
Compound **9c** was synthesized according to the standard procedure A by heating compound **9b** (95mg, 0.1 mmol, 1 eq.), 2-(bromomethyl)naphthalene (70mg, 0.3 mmol, 2 eq.) and K_2CO_3 (43mg, 0.3 mmol, 2 eq.) in DMF (10 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **9c** as an off-white solid (82mg, 70% yield). **MP**: 176-178 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.76 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.83 – 7.80 (m, 3H), 7.77 – 7.74 (m, 2H), 7.64 (d, *J* = 1.3 Hz, 1H), 7.60 (d, *J* = 1.5 Hz, 1H), 7.55 – 7.48 (m, 4H), 7.38 – 7.31 (m, 5H), 7.27 – 7.25 (m, 1H), 6.17 – 6.09 (m, 1H), 5.49 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.41 – 5.39 (m, 3H), 5.12 (s, 2H), 4.72 (d, *J* = 5.4 Hz, 2H), 3.91 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.80, 164.40, 163.08, 152.16, 147.96, 146.69, 142.17, 139.45, 134.91, 133.45, 133.37, 133.08, 132.36, 131.24, 130.80, 129.11, 128.90, 128.60, 128.02, 128.01, 127.35, 127.34, 127.33, 126.98, 126.93, 126.05, 125.33, 125.25, 123.87, 119.83, 119.36, 118.96, 118.83, 118.23, 114.44, 112.24, 111.88, 72.16, 71.41, 69.93, 52.29. **HRMS (ESI)** for: $C_{43}H_{35}N_3O_9$ $[M+Na]^+$ m/z 760.2271 (calc), 760.2251 (found).

Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-(naphthalen-2yl-methoxy)benzamido)-3-hydroxybenzoate **(9d)**



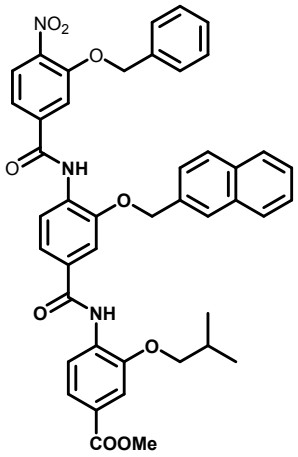
Compound **9d** was synthesized according to the standard procedure E by stirring compound **9c** (50mg, 0.06 mmol, 1 eq.), $Pd(PPh_3)_4$ (10 mol%), sodium toluenesulfinate (24mg, 0.1 mmol, 2 eq.) in anhydrous $CHCl_3$ (5 ml) for 5 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield the title compound **9d** as an off-white solid (32mg, 67% yield). **MP**: 190-192 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.43 (s, 1H), 10.06 (s, 1H), 9.56 (s, 1H), 8.06 – 8.04 (m, 2H), 8.00 – 7.96 (m, 3H), 7.91 – 7.80 (m, 4H), 7.72 – 7.67 (m, 3H), 7.54 (d, *J* = 1.8 Hz, 1H), 7.49 – 7.48 (m, 3H), 7.41 – 7.34 (m, 5H), 5.50 (s, 2H), 5.33 (s, 2H), 3.84 (s, 3H). **^{13}C NMR (176 MHz, DMSO)** δ 165.92, 164.53, 163.71, 150.67, 150.61, 148.44, 141.45, 139.30, 135.63, 134.41, 132.74, 132.55, 131.77, 130.68, 130.27, 128.58, 128.23, 128.08, 127.68, 127.63, 127.51, 126.38, 126.16, 125.97, 125.91, 125.39, 125.14, 124.29, 122.73, 120.51, 120.28, 120.05, 115.74, 114.66, 112.52, 70.82, 70.31, 52.05. **HRMS (ESI)** for: $C_{40}H_{31}N_3O_9$ $[M+Na]^+$ m/z 720.1958 (calc), 720.1945 (found).

Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-(naphthalen-2yl-methoxy)benzamido)-3-isopropoxybenzoate **(9e)**



Compound **9e** was synthesized according to the standard procedure A by heating compound **9d** (90mg, 0.1 mmol, 1 eq.), 2-iodopropane (65 mg, 0.3 mmol, 3 eq.) and K_2CO_3 (35mg, 0.2 mmol, 2 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **9e** as a yellow solid (60mg, 63% yield). **MP**: 173-175 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.76 (s, 1H), 8.67 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.91 – 7.72 (m, 7H), 7.65 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.55 – 7.47 (m, 4H), 7.37 – 7.34 (m, 5H), 7.28 – 7.27 (m, 1H), 5.42 (s, 2H), 5.13 (s, 2H), 4.80 (hept, *J* = 6.1 Hz, 1H), 3.92 (s, 3H), 1.45 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ 166.93, 165.80, 164.31, 163.12, 152.17, 147.99, 145.94, 142.17, 139.48, 134.90, 133.45, 133.36, 133.07, 133.00, 131.19, 130.95, 129.12, 128.92, 128.61, 128.03, 128.01, 127.35, 127.34, 126.99, 126.94, 126.08, 125.30, 125.25, 123.45, 119.63, 119.38, 118.79, 118.24, 114.44, 113.26, 111.94, 72.15, 72.01, 71.41, 52.28, 22.37. **HRMS (ESI)** for: $C_{43}H_{37}N_3O_9$ $[M+H]^+$ m/z 740.2608 (calc), 740.2590 (found).

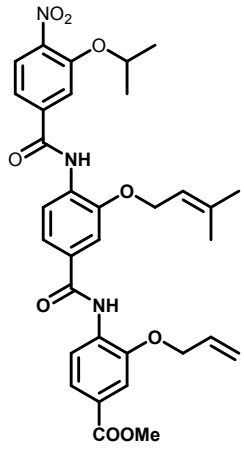
Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-(naphthalen-2ylmethoxy)benzamido)-3-isobutoxybenzoate **(9f)**



Compound **9f** was synthesized according to the standard procedure A by heating compound **9d** (36 mg, 0.05 mmol, 1 eq.), 1-bromo-2-methylpropane (35mg, 0.2 mmol, 5 eq.) and K_2CO_3 (10mg, 0.07 mmol, 1.5 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **9f** as an off-white solid (32mg, 84% yield). **MP**: 165-167 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.88 (s, 1H), 8.77 (s, 1H), 8.67 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 7.91 – 7.74 (m, 7H), 7.64 (d, *J* = 1.5 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.55 – 7.49 (m, 4H), 7.37 – 7.33 (m, 5H), 7.28-7.26 (m, 1H), 5.42 (s, 2H), 5.13 (s, 2H), 3.96 – 3.92 (m, 5H), 2.27 – 2.17 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.92, 164.30, 161.59, 152.18, 148.01, 147.18, 142.22, 139.46, 134.91, 133.48, 133.38, 133.06, 132.27, 131.26, 130.91, 129.14, 128.92, 128.62, 128.04, 128.02, 127.40, 127.34, 127.01, 126.96, 126.08, 125.35, 125.27, 123.56, 119.64, 119.37, 118.60, 118.23, 114.45, 111.89,

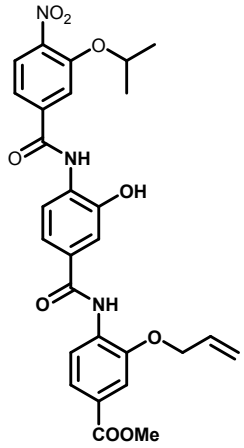
111.72, 75.30, 72.21, 71.43, 52.28, 28.50, 19.52. **HRMS (APCI)** for: $C_{44}H_{39}N_3O_9$ $[M+H]^+$ m/z 754.2764 (calc), 754.2742 (found).

Methyl 3-(allyloxy)-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-((3-methylbut-2-en-1-yl) oxy)benzamido)benzoate **(10a)**



Compound **10a** was synthesized according to the standard procedure A by heating compound **8** (350mg, 0.6 mmol, 1 eq.), 2-bromopropane (445mg, 3.6 mmol, 6 eq.) and K_2CO_3 (167mg, 1.2 mmol, 2 eq.) in DMF (20 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethylether in CH_2Cl_2 to yield the title compound **10a** as a yellow solid (343mg, 91% yield). **MP**: 167-169 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.75 (s, 1H), 8.64 - 8.62 (m, 2H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.76 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.67 (d, *J* = 1.4 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 1H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.45 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.39 (dd, *J* = 8.3, 1.6 Hz, 1H), 6.17 – 6.09 (m, 1H), 5.52 – 5.47 (m, 2H), 5.40 (dd, *J* = 10.5, 1.1 Hz, 1H), 4.83 (hept, *J* = 1.6 Hz, 1H), 4.74 – 4.73 (m, 4H), 3.92 (s, 3H), 1.82 (s, 3H), 1.79 (s, 3H), 1.45 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.80, 164.60, 163.48, 151.64, 147.82, 146.67, 143.04, 139.91, 139.53, 132.43, 132.34, 131.06, 130.58, 125.89, 125.26, 123.87, 119.18, 119.10, 118.93, 118.80, 118.49, 117.69, 115.46, 112.22, 111.14, 73.27, 69.92, 66.23, 52.26, 26.01, 21.95, 18.51 **HRMS (ESI)** for: $C_{33}H_{35}N_3O_9$ $[M+Na]^+$ m/z 640.2271 (calc), 640.2260 (found).

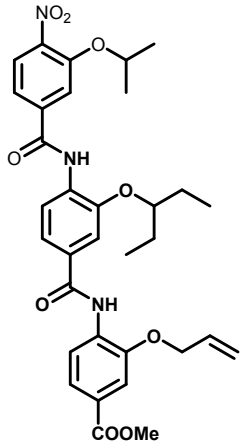
Methyl 3-(allyloxy)-4-(3-hydroxy-4-(3-isopropoxy-4-nitrobenzamido)benzamido)benzoate (**10b)**



Compound **10b** was synthesized according to the standard procedure D by refluxing compound **10a** (300mg, 0.5 mmol, 1 eq.), $CeCl_3 \bullet 7H_2O$ (358mg, 1.4 mmol, 3 eq.) and NaI (218mg, 1.4 mmol, 3 eq.) in anhydrous MeCN (20 ml) for 7 hrs. The residue was purified by column chromatography eluting with 5% THF in DCM to yield the title compound **10b** as a yellow solid (214mg, 80% yield). **MP**: 189-191 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 9.43 (s broad, 1H), 8.70 (s, 1H), 8.50 – 8.47 (m, 2H), 8.36 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 1.9 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.62 – 7.50 (m, 2H), 7.50 (d, *J* = 1.5 Hz, 1H), 7.25 – 7.19 (m, 2H), 6.26 – 6.19 (m, 1H), 5.59 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.49 (dd, *J* = 10.5, 1.1 Hz, 1H), 4.84 – 4.78 (m, 3H), 3.78 (s, 3H), 1.43 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ 166.34, 165.35, 163.42, 151.55, 147.08, 146.82, 143.02, 138.46, 132.39, 131.53, 130.36, 125.84, 125.64, 123.45,

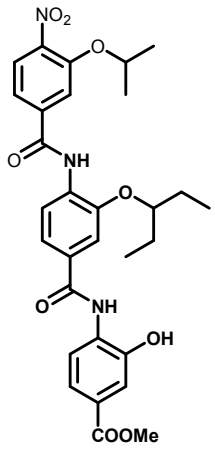
119.93, 119.01, 118.79, 118.21, 117.50, 115.72, 115.37, 112.23, 73.26, 69.88, 52.32, 51.05, 21.94. **HRMS (ESI)** for: $C_{28}H_{27}N_3O_9$ $[M+Na]^+$ m/z 572.1645 (calc), 572.1634 (found).

Methyl 3-(allyloxy)-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-(pentan-3-yloxy)benzamido) benzoate **(10c)**



Compound **10c** was synthesized according to the standard procedure A by heating compound **10b** (100mg, 0.1 mmol, 1 eq.), 2-bromopentane (137mg, 0.9 mmol, 5 eq.) and K_2CO_3 (50mg, 0.3 mmol, 2 eq.) in DMF (5 ml) for 18 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **10c** as an off white-solid (96mg, 86% yield). **MP**: 148-150 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 2H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.76 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.44 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.35 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.17 – 6.09 (m, 1H), 5.49 (ddd, *J* = 17.2, 2.8, 1.5 Hz, 1H), 5.40 (ddd, *J* = 10.5, 2.4, 1.2 Hz, 1H), 4.81 (hept, *J* = 6.1 Hz, 1H), 4.73 (dt, *J* = 5.4, 1.3 Hz, 2H), 4.46 (p, *J* = 5.8 Hz, 1H), 3.92 (s, 3H), 1.86 – 1.74 (m, 4H), 1.45 (d, *J* = 6.1 Hz, 6H), 1.01 (t, *J* = 7.5 Hz, 6H).**^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.78, 164.63, 163.33, 151.69, 147.28, 146.66, 143.03, 139.55, 132.41, 132.32, 131.62, 130.58, 125.95, 125.25, 123.84, 119.18, 118.97, 118.93, 118.76, 117.32, 115.48, 112.19, 112.11, 81.96, 73.27, 69.91, 52.25, 26.12, 21.95, 9.65. **HRMS (ESI)** for: $C_{33}H_{37}N_3O_9$ $[M+Na]^+$ m/z 642.2428 (calc), 642.2422 (found).

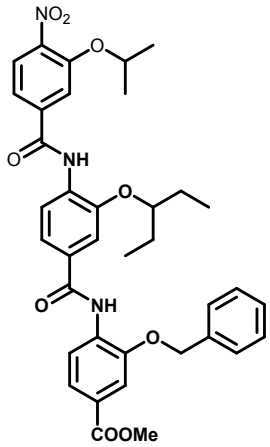
Methyl 3-hydroxy-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-(pentan-3-yloxy)benzamido) benzoate **(10d)**



Compound **10d** was synthesized according to the standard procedure E by stirring compound **10c** (100mg, 0.1 mmol, 1 eq.), $Pd(PPh_3)_4$ (10 mol%), sodium toluenesulfinate (57mg, 0.3 mmol, 2 eq.) in anhydrous $CHCl_3$ (10 ml) for 5 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield title compound **10d** as an off-white solid (80mg, 86% yield). **MP**: 218-220 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.41 (s broad, 1H), 9.73 (s, 1H), 9.53 (s, 1H), 8.03 – 7.98 (m, 3H), 7.80 (s, 1H), 7.65 (d, *J* = 1.2 Hz, 1H), 7.61 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.58 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.53 (d, *J* = 1.8 Hz, 1H), 7.49 (dd, *J* = 8.3, 1.8 Hz, 1H), 4.94 (hept, *J* = 6.0 Hz, 1H), 4.44 (p, *J* = 5.7 Hz, 1H), 3.83 (s, 3H), 1.72– 1.66 (m, 4H), 1.34 (d, *J* = 6.0 Hz, 6H), 0.93 (t, *J* =

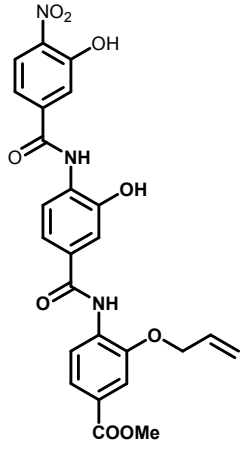
7.4 Hz, 6H).**^{13}C NMR (176 MHz, DMSO)** δ 165.92, 164.60, 163.79, 149.83, 149.76, 148.48, 142.34, 139.26, 131.44, 130.90, 130.72, 125.91, 125.03, 123.53, 122.75, 120.50, 119.78, 119.53, 115.72, 115.12, 112.98, 80.91, 72.50, 52.04, 25.32, 21.59, 9.28. **HRMS (ESI)** for: $C_{30}H_{33}N_3O_9$ $[M+Na]^+$ m/z 602.2115 (calc), 602.2092 (found).

Methyl3-(benzyloxy)-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-(pentan-3-yloxy)benzamido) benzoate **(10e)**



Compound **10e** was synthesized according to the standard procedure A by heating compound **10d** (50mg, 0.08 mmol, 1 eq.), benzyl bromide (18mg, 0.1 mmol, 1.5 eq.) and K_2CO_3 (29mg, 0.1 mmol, 2 eq.) in DMF (5ml) for 5 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **10e** as an off-white solid (50mg, 87% yield). **MP**: 181-183 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.82 (s, 1H), 8.81 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.57 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.73 (s, 1H), 7.68 (s, 1H), 7.56 (s, 1H), 7.48 – 7.41 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 5.23 (s, 2H), 4.81 (hept, *J* = 5.8 Hz, 1H), 4.40 – 4.36 (m, 1H), 3.93 (s, 3H), 1.80 – 1.71 (m, 4H), 1.45 (d, *J* = 5.9 Hz, 6H), 0.98 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.80, 164.54, 163.32, 151.73, 147.23, 147.00, 143.06, 139.56, 135.99, 132.59, 131.62, 130.41, 129.08, 128.93, 127.92, 125.98, 125.33, 124.09, 119.10, 119.02, 118.80, 117.28, 115.50, 112.52, 112.02, 81.91, 73.29, 71.63, 52.30, 26.12, 21.97, 9.64**. HRMS (APCI)** for: $C_{37}H_{39}N_3O_9$ $[M+H]^+$ m/z 670.2764 (calc), 670.2782 (found).

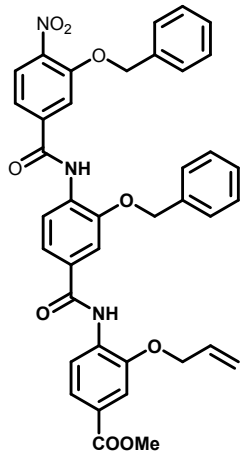
Methyl 3-(allyloxy)-4-(3-hydroxy-4-(3-hydroxy-4-nitrobenzamido)benzamido)benzoate **(11)**



Compound **11** was synthesized according to the standard procedure D by refluxing compound **8** (150mg, 0.2 mmol, 1 eq.), $CeCl_3$•$7H_2O$ (192mg, 0.7 mmol, 3 eq.) and NaI (117mg, 0.7 mmol, 3 eq.) in anhydrous MeCN (10 ml) for 12 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield the title compound **11** as a yellow solid (115mg, 86% yield). **MP**: 202-204 °C. **^{1}H NMR (500 MHz, DMSO)** δ 11.38 (s broad, 1H), 10.37 (s, 1H), 9.74 (s, 1H), 9.42 (s, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.59 (s, 1H), 7.55 – 7.47 (m, 3H), 6.17 – 6.07 (m, 1H), 5.48 – 5.45 (m, 1H), 5.31 (d, *J* = 10.5 Hz, 1H), 4.77 (d, *J* = 4.7 Hz, 2H), 3.86 (s, 3H). **^{13}C NMR (176 MHz,**

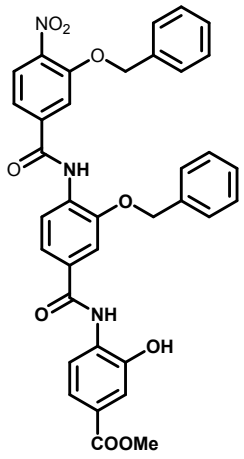
DMSO) δ 165.83, 164.50, 163.72, 151.53, 149.10, 148.84, 139.82, 138.96, 133.27, 132.10, 131.25, 129.09, 125.65, 125.44, 123.29, 122.31, 121.97, 118.37, 118.15, 118.03, 117.53, 114.78, 112.75, 69.21, 52.16. **HRMS (ESI)** for: $C_{25}H_{21}N_3O_9$ $[M+Na]^+$ m/z 530.1176 (calc), 530.1178 (found).

Methyl 3-(allyloxy)-4-(3-(benzyloxy)-4-(3-(benzyloxy)-4-nitrobenzamido)benzamido) benzoate **(11a)**



Compound **11a** was synthesized according to the standard procedure A by heating compound **11** (218mg, 0.4 mmol, 1 eq.), benzyl bromide (178mg, 1.2 mmol, 3 eq.) and K_2CO_3 (220mg, 1.2 mmol, 3 eq.) in DMF (20 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **11a** as an off-white solid (254mg, 86% yield). **MP**: 177-179 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.75 (s, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 8.66 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.78 – 7.76 (m, 2H), 7.68 (d, *J* = 1.3 Hz, 1H), 7.62 (d, *J* = 1.5 Hz, 1H), 7.50 – 7.31 (m, 12H), 6.17 – 6.09 (m, 1H), 5.51 – 5.47 (m, 1H), 5.41 – 5.39 (m, 1H), 5.26 (s, 2H), 5.21 (s, 2H), 4.74 (d, *J* = 5.4 Hz, 2H), 3.92 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.79, 164.39, 163.04, 152.21, 147.83, 146.68, 142.21, 139.51, 135.73, 134.96, 132.36, 131.11, 130.74, 129.15, 129.11, 128.93, 128.66, 128.00, 127.40, 126.07, 125.33, 123.86, 119.70, 119.29, 118.96, 118.83, 118.29, 114.51, 112.23, 111.56, 71.76, 71.51, 69.93, 52.28. **HRMS (ESI)** for: $C_{39}H_{33}N_3O_9$ $[M+Na]^+$ m/z 710.2115 (calc), 710.2103 (found).

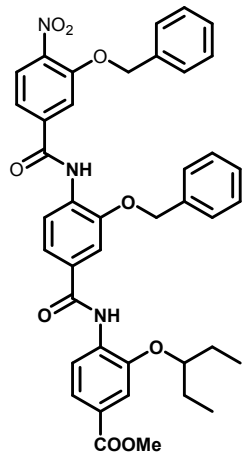
Methyl 4-(3-(benzyloxy)-4-(3-(benzyloxy)-4-nitrobenzamido)benzamido)-3-hydroxy benzoate **(11b)**



Compound **11b** was synthesized according to the standard procedure E by stirring compound **11a** (160 mg, 0.2 mmol, 1 eq.), $Pd(PPh3_3)_4$ (10 mol%), sodium toluenesulfinate (83mg, 0.4 mmol, 2 eq.) in anhydrous $CHCl_3$ (10 ml) for 12 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield the title compound **11b** as an off-white solid (80mg, 53% yield). **MP**: 220-222 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.44 (s, 1H), 9.99 (s, 1H), 9.52 (s, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 8.01 – 7.94 (m, 2H), 7.78 (d, *J* = 1.7 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.69 – 7.65 (m, 12H), 5.36 (s, 2H), 5.34 (s, 2H), 3.84 (s, 3H). **^{13}C NMR (176 MHz,**

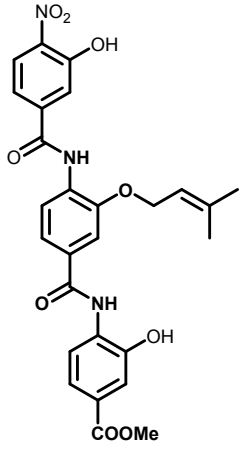
DMSO) δ 165.93, 164.54, 163.69, 150.67, 150.47, 148.41, 141.45, 139.35, 136.75, 135.68, 131.69, 130.70, 130.17, 128.63, 128.47, 128.28, 127.91, 127.56, 127.40, 125.91, 125.17, 124.19, 122.66, 120.53, 120.19, 120.03, 115.71, 114.66, 112.33, 70.84, 70.11, 52.06. **HRMS (ESI)** for: $C_{36}H_{29}N_3O_9$ $[M+Na]^+$ m/z 670.1802 (calc), 670.1771 (found).

Methyl4-(3-(benzyloxy)-4-(3-(benzyloxy)-4-nitrobenzamido)benzamido)-3-(pentan-3-yloxy) benzoate **(11c)**



Compound **11c** was synthesized according to the standard procedure A by heating compound **11b** (74mg, 0.1 mmol, 1 eq.), 2-bromopentane (51mg, 0.3 mmol, 3 eq.) and K_2CO_3 (31mg, 0.2 mmol, 2 eq.) in DMF (10 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **11c** as an off-white solid (47mg, 57% yield). **MP**: 145-147 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.92 (s, 1H), 8.75 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 1.7 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.67 (d, *J* = 1.4 Hz, 1H), 7.60 (d, *J* = 1.5 Hz, 1H), 7.46 – 7.31 (m, 12H), 5.26 (s, 2H), 5.21 (s, 2H), 4.42 (p, *J* = 5.7 Hz, 1H), 3.92 (s, 3H), 1.84 – 1.75 (m, 4H), 1.01 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.93, 164.29, 163.08, 152.21, 147.89, 146.46, 142.24, 139.51, 135.72, 134.96, 133.03, 131.06, 130.92, 129.15, 129.12, 128.94, 128.67, 128.00, 127.40, 126.08, 125.29, 123.35, 119.43, 119.33, 118.72, 118.30, 114.52, 113.26, 111.60, 81.78, 71.75, 71.51, 29.84, 26.12, 9.64. **HRMS (ESI)** for: $C_{41}H_{39}N_3O_9$ $[M+H]^+$ m/z 718.2764 (calc), 718.2797 (found).

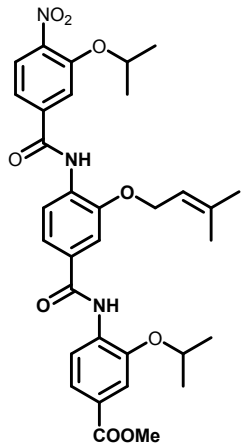
Methyl 3-hydroxy-4-(4-(3-hydroxy-4-nitrobenzamido)-3-((3-methylbut-2-en-1-yl)oxy) benzamido)benzoate **(12)**



Compound **12** was synthesized according to the standard procedure E by refluxing compound **8** (300mg, 0.5 mmol, 1 eq.), $Pd(PPh_3)_4$ (10 mol%), sodium toluenesulfinate (185mg, 1.0 mmol, 2 eq.) in anhydrous $CHCl_3$ (15 ml) for 3 hrs. The residue was purified by column chromatography eluting with 10% THF in CH_2Cl_2 to yield the title compound **12** as a yellow solid (226mg, 81% yield). **MP**: 230-232 °C. **^{1}H NMR (500 MHz, DMSO)** δ 11.37 (s broad, 1H), 10.43 (s, 1H), 9.72 (s, 1H), 9.48 (s, 1H), 8.07 – 7.99 (m, 3H), 7.67 – 7.61 (m, 3H), 7.53 – 7.38 (m, 3H), 5.47 (t, *J* = 5.8 Hz, 1H), 4.76 (d, *J* = 6.1 Hz, 2H), 3.83 (s, 3H), 1.75 (s, 6H). **^{13}C NMR (176 MHz, DMSO)** δ 165.92,

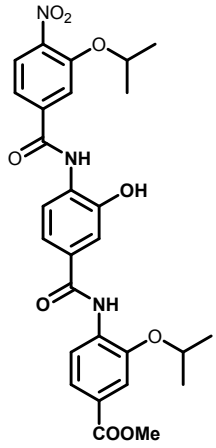
164.62, 163.79, 151.61, 149.95, 148.32, 139.91, 138.99, 137.27, 131.22, 130.74, 130.28, 125.83, 125.48, 123.26, 122.54, 120.54, 119.89, 119.73, 118.42, 117.87, 115.70, 112.02, 65.75, 52.04, 25.51, 18.21. **HRMS (ESI)** for: $C_{27}H_{25}N_3O_9$ $[M+Na]^+$ m/z 558.1489 (calc), 558.1483 (found).

Methyl 3-isopropoxy-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-((3-methylbut-2-en-1-yl)oxy)benzamido)benzoate **(12a)**



Compound **12a** was synthesized according to the standard procedure A by heating compound **12** (400mg, 0.7 mmol, 1 eq.), 2-bromopropane (638mg, 5.2 mmol, 7 eq.) and K_2CO_3 (309mg, 2.2 mmol, 3 eq.) in DMF (20 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **12a** as an off-white solid (350mg, 75% yield). **MP**: 150-152 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.75 (s, 1H), 8.65 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.67 (d, *J* = 1.1 Hz, 1H), 7.66 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 1.3 Hz, 1H), 7.43 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.39 (dd, *J* = 8.3, 1.4 Hz, 1H), 5.57 – 5.50 (m, 1H), 4.83 – 4.73 (m, 4H), 3.92 (s, 3H), 1.82 (s, 3H), 1.79 (s, 3H), 1.44 (m, 12H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.91, 164.48, 163.50, 151.64, 147.84, 145.93, 143.05, 139.89, 139.55, 133.08, 131.00, 130.71, 125.89, 125.23, 123.45, 119.13, 119.02, 118.75, 118.49, 117.71, 115.46, 113.27, 111.16, 73.27, 72.00, 66.22, 52.24, 26.01, 22.36, 21.95, 18.51. **HRMS (APCI)** for: $C_{33}H_{37}N_3O_9$ $[M+H]^+$ m/z 620.2608 (calc), 620.2623 (found).

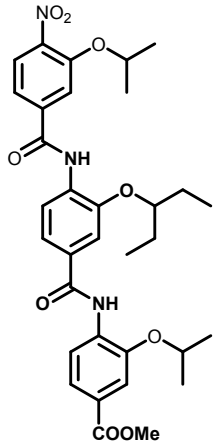
Methyl 4-(3-hydroxy-4-(3-isopropoxy-4-nitrobenzamido)benzamido)-3-isopropoxybenzoate **(12b)**



Compound **12b** was synthesized according to the standard procedure D by refluxing compound **12a** (250mg, 0.4 mmol, 1 eq.), $CeCl_3$•$7H_2O$ (298mg, 1.2 mmol, 3 eq.) and NaI (175mg, 1.2 mmol, 3 eq.) in anhydrous MeCN (15 ml) for 5 hrs. The residue was purified by column chromatography eluting with 5% THF in CH_2Cl_2 to yield the title compound **12b** as a yellow solid (157mg, 70% yield). **MP**: 250-252 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.37 (s, 1H), 9.87 (s, 1H), 9.24 (s, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 1.2 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.97 (hept, *J* = 6.0 Hz, 1H), 4.77 (hept, *J* = 6.0 Hz, 1H), 3.86 (s, 3H), 1.37 (d, *J*= 6.0 Hz, 6H), 1.34 (d *J*= 6.0Hz, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 165.85, 164.26, 163.88, 149.76,

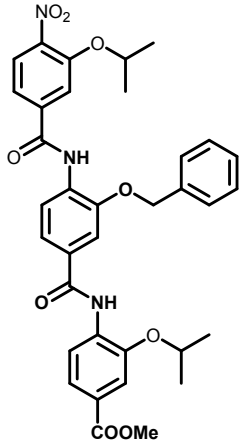
149.55, 147.39, 142.39, 139.15, 132.86, 131.44, 129.02, 125.34, 124.81, 124.21, 122.20, 120.96, 119.75, 117.92, 115.47, 114.66, 113.66, 72.55, 71.56, 52.12, 21.70, 21.61. **HRMS (ESI)** for: $C_{28}H_{29}N_3O_9$ $[M+H]^+$ m/z 552.1982 (calc), 552.1954 (found).

Methyl 3-isopropoxy-4-(4-(3-isopropoxy-4-nitrobenzamido)-3-(pentan-3yloxy)benzamido) benzoate **(12c)**



Compound **12c** was synthesized according to the standard procedure A by heating compound **12b** (50mg, 0.09 mmol, 1 eq.), 2-bromopentane (41mg, 0.2 mmol, 3 eq.) and K_2CO_3 (19mg, 0.1 mmol, 1.5 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **12c** as an off-white solid (43mg, 76% yield). **MP**: 135-137 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.86 (s, 1H), 8.82 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.69 (s, 1H), 7.62 (d, *J* = 1.0 Hz, 1H), 7.61 (s, 1H), 7.42 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.36 (dd, *J* = 8.3, 1.1 Hz, 1H), 4.87 – 4.73 (m, 2H), 4.46 (p, *J* = 5.7 Hz, 1H), 3.91 (s, 3H), 1.84 – 1.60 (m, 4H), 1.45-1.44 (m, 12H), 1.01 (t, *J* = 7.4 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.93, 164.57, 163.38, 151.73, 147.33, 145.92, 143.07, 139.60, 133.09, 131.59, 130.76, 125.98, 125.25, 123.47, 119.24, 118.87, 118.74, 117.35, 115.51, 113.27, 112.15, 82.00, 73.30, 71.98, 52.24, 26.16, 22.36, 21.97, 9.68. **HRMS (ESI)** for: $C_{33}H_{39}N_3O_9$ $[M+H]^+$ m/z 622.2764 (calc), 622.2731 (found).

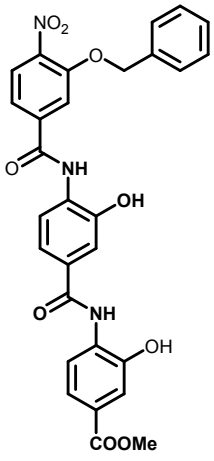
Methyl 4-(3-(benzyloxy)-4-(3-isopropoxy-4-nitrobenzamido)benzamido)-3isopropoxybenzoate **(12d)**



Compound **12d** was synthesized according to the standard procedure A by heating compound **12b** (50mg, 0.09 mmol, 1 eq.), benzyl bromide (20mg, 0.1 mmol, 1.3 eq.) and K_2CO_3 (16mg, 0.1 mmol, 1.3 eq.) in DMF (5 ml) for 5 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **12d** as an off-white solid (49mg, 84% yield). **MP**: 213-215 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.75 (s, 1H), 8.68 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.78 – 7.77 (m, 2H), 7.73 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.61 (d, *J* = 1.5 Hz, 1H), 7.58 (d, *J* = 1.3 Hz, 1H), 7.50 – 7.39 (m, 6H), 7.28 (dd, *J* = 8.3, 1.6 Hz, 1H), 5.26 (s, 2H), 4.78 (hept, *J* = 6.1 Hz, 1H), 4.67 (hept, *J* = 6.1 Hz, 1H), 3.92 (s, 3H), 1.46 (d, *J* = 6.0 Hz, 6H), 1.37 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR (126 MHz,**

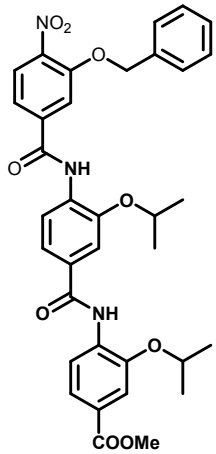
$CDCl_3$) δ 166.92, 164.33, 163.35, 151.60, 147.87, 145.95, 143.08, 139.23, 135.72, 133.03, 131.12, 130.84, 129.14, 129.07, 128.08, 125.84, 125.30, 123.47, 119.51, 119.28, 118.80, 117.74, 115.24, 113.29, 111.56, 73.21, 72.03, 71.73, 52.26, 22.38, 21.89. **HRMS (APCI)** for: $C_{35}H_{35}N_3O_9$ $[M+H]^+$ m/z 642.2451 (calc), 642.2441 (found).

Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-hydroxybenzamido)-3-hydroxybenzoate **(13a)**



Compound **13a** was synthesized according to the standard procedure E by stirring compound **9b** (150mg, 0.2 mmol, 1 eq.), $Pd(PPh_3)_4$ (10 mol%), and sodium toluenesulfinate (90mg, 0.5 mmol, 2 eq.) in anhydrous $CHCl_3$:THF (10:1 ml) for 12 hrs. The residue was purified by column chromatography eluting with 10% THF in CH_2Cl_2 to yield the title compound **13a** as an off-white solid (84mg, 60% yield). **MP**: 245-247 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.49 (s, 1H), 10.36 (s, 1H), 9.86 (s, 1H), 9.36 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.57 – 7.47 (m, 6H), 7.45 – 7.35 (m, 3H), 5.43 (s, 2H), 3.83 (s, 3H). **^{13}C NMR (176 MHz, DMSO)** δ 165.92, 164.51, 163.71, 150.62, 149.42, 147.80, 141.40, 139.34, 135.79, 131.39, 130.91, 128.89, 128.62, 128.23, 127.52, 125.51, 125.10, 123.98, 121.63, 120.68, 120.07, 118.19, 115.52, 114.81, 114.76, 70.79, 52.03. **HRMS (ESI)** for: $C_{29}H_{23}N_3O_9$ $[M+H]^+$ m/z 558.1512 (calc), 558.1504 (found).

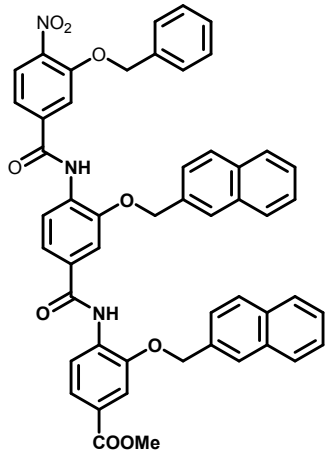
Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-isopropoxybenzamido)-3-isopropoxybenzoate **(13b)**



Compound **13b** was synthesized according to the standard procedure A by heating compound **13a** (40mg, 0.07 mmol, 1 eq.), 2-bromopropane (52mg, 0.4 mmol, 6 eq.) and K_2CO_3 (29mg, 0.2 mmol, 3 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **13b** as an off-white solid (31mg, 67% yield). **MP**: 167-169 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.86 (s, 1H), 8.77 (s, 1H), 8.64 - 8.61 (m, 2H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.80 (s, 1H), 7.73 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.63 (d, *J* = 1.2 Hz, 1H), 7.61 (d, *J* = 1.2 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.43 – 7.34 (m, 5H), 5.34 (s, 2H), 4.86 – 4.74 (m, 2H), 3.92 (s, 3H), 1.48 – 1.43 (m, 12H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.89, 164.45, 163.11, 152.32, 146.79, 145.90, 142.20, 139.88, 135.03, 133.06, 131.40, 130.77, 128.96, 128.64, 127.26, 126.16, 125.23, 123.44, 119.35, 118.87, 118.71, 117.87, 114.94, 113.24,

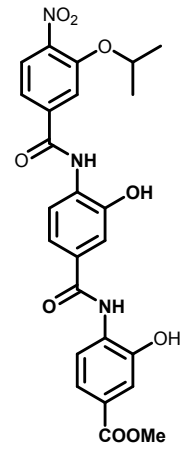
111.98, 72.08, 71.97, 71.55, 52.23, 22.35, 22.33. **HRMS (APCI)** for: $C_{35}H_{35}N_3O_9$ $[M+H]^+$ m/z 642.2451 (calc), 642.2444 (found).

Methyl 4-(4-(3-(benzyloxy)-4-nitrobenzamido)-3-(naphthalen-2-yl-methoxy)benzamido)-3-(naphthalen-2-ylmethoxy)benzoate **(13c)**



Compound **13c** was synthesized according to the standard procedure A by heating compound **13a** (44mg, 0.07 mmol, 1 eq.), 2-(bromomethyl)naphthalene (69mg, 0.3 mmol, 4 eq.) and K_2CO_3 (38mg, 0.2 mmol, 3.5 eq.) in DMF (5ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **13c** as a yellow solid (20mg, 30% yield). **MP**: 219-221 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.71 – 8.65 (m, 2H), 8.55 (d, *J* = 8.4 Hz, 1H), 7.94 (s, 1H), 7.91 – 7.72 (m, 10H), 7.66 (d, *J* = 1.7 Hz, 1H), 7.61 – 7.60 (m, 2H), 7.53 – 7.32 (m, 11H), 7.21 (dd, *J* = 8.3, 1.6 Hz, 1H), 5.39 (s, 2H), 5.19 (s, 2H), 5.11 (s, 2H), 3.93 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.81, 164.31, 162.99, 152.16, 147.79, 147.08, 142.16, 139.48, 134.91, 133.45, 133.41, 133.39, 133.34, 132.96, 132.57, 131.26, 130.56 , 129.05, 129.03, 128.91, 128.61, 128.08, 128.03, 128.00, 127.46, 127.34, 127.25, 126.97, 126.94, 126.86, 126.73, 126.04, 125.44, 125.30, 124.18, 120.37, 119.40, 118.92, 118.19, 114.42, 112.58, 111.32, 72.08, 71.84, 71.42, 52.34. **HRMS (APCI)** for: $C_{51}H_{39}N_3O_9$ $[M+H]^+$ m/z 838.2764 (calc), 838.2793 (found).

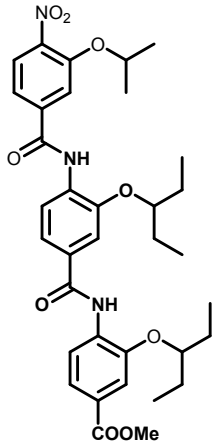
Methyl 3-hydroxy-4-(3-hydroxy-4-(3-isopropoxy-4-nitrobenzamido)benzamido)benzoate **(14a)**



Compound **14a** was synthesized according to the standard procedure E by stirring compound **10b** (130mg, 0.2 mmol, 1 eq.), $Pd(PPh_3)_4$ (10 mole%) and sodium toluenesulfinate (84mg, 0.4 mmol, 2 eq.) in anhydrous $CHCl_3$:THF (9:1 ml) for 12 hrs. The residue was purified by column chromatography eluting with 10% THF in CH_2Cl_2 to yield the title compound **14a** as an off-white solid (57mg, 48% yield). **MP**: 241-243 °C. **^{1}H NMR (500 MHz, DMSO)** δ 10.48 (s, 1H), 10.31 (s, 1H), 9.87 (s, 1H), 9.36 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.64 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.54 - 7.47 (m, 4H), 4.97 (hept, *J* = 6.0 Hz, 1H), 3.83 (s, 3H), 1.34 (d, *J* = 6.0 Hz, 6H). **^{13}C NMR (126 MHz, DMSO)** δ 165.89, 164.49, 163.85, 149.75, 149.45, 147.77, 142.39, 139.14, 131.38, 130.89, 128.92, 125.49, 124.79, 124.09, 121.58, 120.66, 119.74, 118.17,

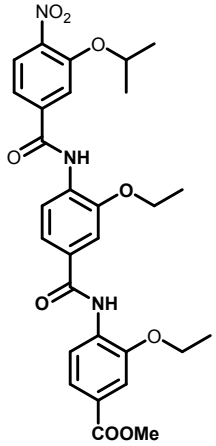
115.52, 115.47, 114.80, 72.54, 51.99, 21.61. **HRMS (APCI)** for: $C_{25}H_{23}N_3O_9$ $[M+H]^+$ m/z 510.1512 (calc), 510.1486 (found).

Methyl 4-(4-(3-isopropoxy-4-nitrobenzamido)-3-(pentan-3-yloxy)benzamido)-3-(pentan-3-yloxy)benzoate **(14b)**



Compound **14b** was synthesized according to the standard procedure A by heating compound **14a** (30mg, 0.05 mmol, 1 eq.), 2-bromopentane (53mg, 0.3 mmol, 6 eq.) and K_2CO_3 (24mg, 0.1 mmol, 3 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **14b** as an off-white solid (20mg, 52% yield). **MP**: 153-155 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.91 (s, 1H), 8.83 (s, 1H), 8.69 – 8.59 (m, 2H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.69 (d, *J* = 0.7 Hz, 1H), 7.63 (d, *J* = 1.0 Hz, 1H), 7.59 (d, *J* = 1.0 Hz, 1H), 7.40 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.36 (dd, *J* = 8.3, 1.3 Hz, 1H), 4.82 (hept, *J* = 6 Hz, 1H), 4.50 – 4.36 (m, 2H), 3.92 (s, 3H), 1.87 – 1.72 (m, 8H), 1.45 (d, *J* = 6.1 Hz, 6H), 1.03 – 0.99 (m, 12H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.95, 164.54, 163.39, 151.72, 147.33, 146.44, 143.06, 139.58, 133.09, 131.58, 130.77, 125.98, 125.22, 123.34, 119.24, 118.76, 118.67, 117.33, 115.49, 113.24, 112.14, 81.97, 81.74, 73.30, 52.25, 26.13, 26.11, 21.97, 9.65, 9.63. **HRMS (APCI)** for: $C_{35}H_{43}N_3O_9$ $[M+H]^+$ m/z 650.3077 (calc), 650.3078 (found).

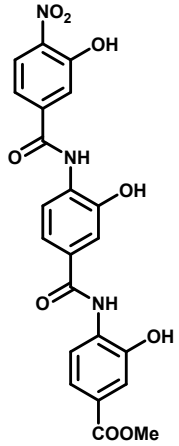
Methyl 3-ethoxy-4-(3-ethoxy-4-(3-isopropoxy-4-nitrobenzamido)benzamido)benzoate **(14c)**



Compound **14c** was synthesized according to the standard procedure A by heating compound **14a** (30mg, 0.05 mmol, 1 eq.), iodoethane (54mg, 0.3 mmol, 6 eq.) and K_2CO_3 (24mg, 0.1 mmol, 3 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **14c** as an off-white solid (18mg, 54% yield). **MP**: 205-207 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.74 (s, 1H), 8.64 (d, *J* = 8.4 Hz, 1H), 8.61 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.75 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.69 (d, *J* = 1.5 Hz, 1H), 7.62 (d, *J* = 1.8 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.44 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.38 (dd, *J* = 8.3, 1.7 Hz, 1H), 4.83 (hept, *J* = 6 Hz, 1H), 4.31 – 4.23 (m, 4H), 3.92 (s, 3H), 1.55 – 1.52 (m, 6H), 1.45 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.91, 164.55, 163.48, 151.70, 147.82, 147.03, 143.06, 139.54, 132.22, 130.79, 130.73, 125.92, 125.27, 123.55, 119.13, 119.09,

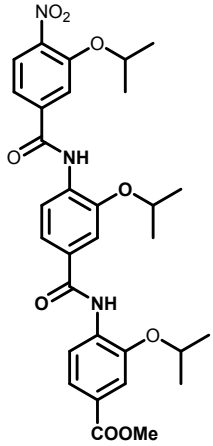
118.61, 117.46, 115.57, 111.70, 110.72, 73.29, 64.89, 64.81, 52.25, 21.96, 14.97, 14.95**. HRMS (ESI)** for: $C_{29}H_{31}N_3O_9$ $[M+H]^+$ m/z 566.2138 (calc), 566.2134(found).

Methyl 3-hydroxy-4-(3-hydroxy-4-(3-hydroxy-4-nitrobenzamido)benzamido)benzoate **(15)**



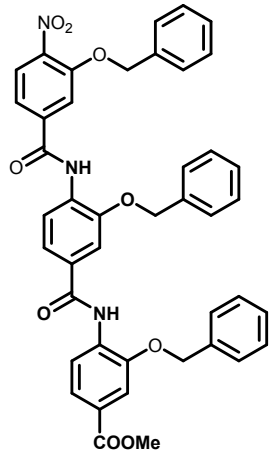
Compound **15** was synthesized according to the standard procedure D by refluxing compound **12** (100mg, 0.2 mmol, 1 eq.), $CeCl_3 \bullet 7H_2O$ (277mg, 1.1 mmol, 4 eq.) and NaI (126mg, 0.8 mmol, 3 eq.) in anhydrous MeCN (15 ml) for 5 hrs. The residue was purified by column chromatography eluting with 20% THF in CH_2Cl_2 to yield the title compound **15** as a yellow solid (57mg, 65% yield). **MP**: 269-271°C. **^{1}H NMR (500 MHz, DMSO)** δ 11.38 (s, 1H), 10.50 (s, 1H), 10.38 (s, 1H), 9.73 (s, 1H), 9.34 (s, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.65 (s, 1H), 7.53 – 7.48 (m, 5H), 3.83 (s, 3H). **^{13}C NMR (176 MHz, DMSO)** δ 165.93, 164.51, 163.73, 151.54, 149.05, 147.76, 139.83, 138.97, 131.16, 130.93, 129.07, 125.48, 125.45, 123.28, 121.56, 120.69, 118.37, 118.27, 118.03, 115.51, 114.63, 52.03. **HRMS (ESI)** for: $C_{22}H_{17}N_3O_9$ $[M+H]^+$ m/z 468.1043 (calc), 468.1052 (found).

Methyl 3-isopropoxy-4-(3-isopropoxy-4-(3-isopropoxy-4-nitrobenzamido)benzamido) benzoate (**15a)**



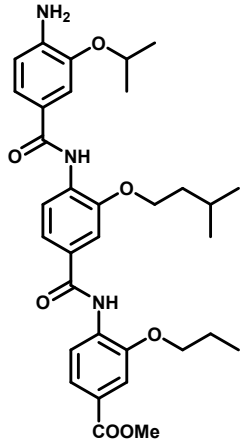
Compound **15a** was synthesized according to the standard procedure A by heating compound **15** (50mg, 0.1 mmol, 1 eq.), 2-bromopropane (130mg, 1.0 mmol, 10 eq. 59mg) and K_2CO_3 (59mg, 0.4 mmol, 4 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **15a** as a yellow solid (40mg, 63% yield). **MP**: 161-163 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.77 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.61 (d, *J* = 1.7 Hz, 1H), 7.42 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.7 Hz, 1H), 4.87 – 4.74 (m, 3H), 3.92 (s, 3H), 1.47 – 1.45 (m, 18H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.92, 164.50, 163.40, 151.71, 146.77, 145.92, 143.06, 139.59, 133.08, 131.50, 130.73, 125.94, 125.24, 123.46, 119.28, 118.90, 118.73, 117.40, 115.55, 113.26, 111.99, 73.28, 72.06, 71.99, 52.24, 22.36, 22.34, 21.97. **HRMS (ESI)** for: $C_{31}H_{35}N_3O_9$ $[M+H]^+$ m/z 594.2451 (calc), 594.2426 (found).

Methyl 3-(benzyloxy)-4-(3-(benzyloxy)-4-(3-(benzyloxy)-4-nitrobenzamido)benzamido)benzoate **(15b)**



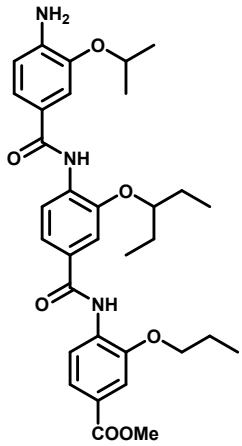
Compound **15b** was synthesized according to the standard procedure A by heating compound **15** (49mg, 0.1 mmol, 1 eq.), benzyl bromide (71mg, 0.4 mmol, 4 eq.) and K_2CO_3 (58mg, 0.4 mmol, 4 eq.) in DMF (5 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **15b** as an off-white solid (49mg, 64% yield). **MP**: 199-201 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.83 (s, 1H), 8.72 (s, 1H), 8.65 (d, *J* = 8.5 Hz, 1H), 8.57 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.79 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.68 (d, *J* = 1.8 Hz, 1H), 7.49 – 7.33 (m, 16H), 7.29 (dd, *J* = 8.3, 1.7 Hz, 1H), 5.23 (s, 2H), 5.19 (s, 2H), 5.14 (s, 2H), 3.93 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.79, 164.23, 162.99, 152.22, 147.73, 147.01, 142.22, 139.48, 136.01, 135.68, 134.96, 132.52, 131.10, 130.49, 129.14, 129.09, 128.98, 128.94, 128.67, 128.12, 128.00, 127.40, 126.07, 125.38, 124.09, 120.02, 119.64, 119.25, 118.81, 118.27, 114.48, 112.48, 111.17, 71.72, 71.65, 71.50, 52.31. **HRMS (APCI)** for: $C_{43}H_{35}N_3O_9$ $[M+H]^+$ m/z 738.2451 (calc), 738.2475 (found).

Methyl 4-(4-(4-amino-3-isopropoxybenzamido)-3-(isopentyloxy)benzamido)-3-propoxy benzoate **(16a)**



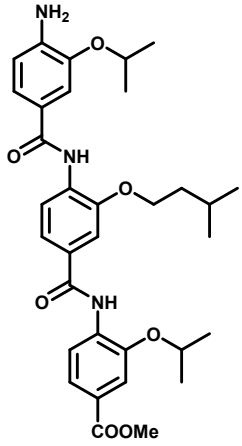
Compound **16a** was synthesized according to the standard procedure C by stirring compound **10a** (20mg, 0.03 mmol, 1 eq), Pd/C (10 mol%) in anhydrous EtOAc:THF mixture (4:1 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **16a** as a white solid (8mg, 63% yield). **MP**: 190-192 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.86 (s, 1H), 8.70 – 8.67 (m, 2H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.59 – 7.58 (m, 2H), 7.45 (d, *J* = 1.4 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.28 – 7.27 (m, 1H), 6.73 (d, *J* = 7.3 Hz, 1H), 4.69 (hept, *J* = 6.0 Hz, 1H), 4.22 – 4.20 (m, 4H), 4.13 (t, *J* = 6.4 Hz, 2H), 3.91 (s, 3H), 1.97 – 1.79 (m, 5H), 1.40 (d, *J* = 6.0 Hz, 6H), 1.12 (t, 3H), 1.02 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$)** δ 166.98, 165.37, 164.85, 147.73, 147.12, 145.00, 141.64, 132.51, 132.15, 129.28, 125.05, 124.14, 123.57, 120.12, 119.14, 118.58, 118.50, 113.74, 112.51, 111.69, 110.45, 71.04, 70.59, 67.58, 52.22, 38.12, 25.54, 22.78, 22.73, 22.35, 10.80. **HRMS (ESI)** for: $C_{33}H_{41}N_3O_7$ $[M+Na]^+$ m/z 614.2843 (calc), 614.2862 (found).

Methyl 4-(4-(4-amino-3-isopropoxybenzamido)-3-(pentan-3-yloxy)benzamido)
-3-propoxybenzoate **(16b)**



Compound **16b** was synthesized according to the standard procedure C by stirring compound **10c** (20mg, 0.03 mmol, 1 eq), Pd/C (10 mol %) in anhydrous EtOAc:THF mixture (4:1 ml) for 12 hrs. The residue was purified by flash column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **16b** as a white solid (14mg, 75% yield). **MP**: 168-170 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.85 (s, 1H), 8.78 (s, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.63 (d, *J* = 1.5 Hz, 1H), 7.61 (d, *J* = 1.3 Hz, 1H), 7.45 (d, *J* = 1.7 Hz, 1H), 7.39 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.28 – 7.26 (m, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.68 (hept, *J* = 6.0 Hz, 1H), 4.44 (p, *J* = 5.7 Hz, 1H), 4.22 (s, 2H), 4.13 (t, *J* = 6.5 Hz, 2H), 3.91 (s, 3H), 1.97 – 1.90 (m, 2H), 1.82 – 1.76 (m, 4H), 1.40 (d, *J* = 6.1 Hz, 6H), 1.13 (t, *J* = 7.4 Hz, 3H), 1.01 (t, *J* = 7.5 Hz, 6H).**^{13}C NMR (176 MHz, $CDCl_3$)** δ 166.99, 165.33, 164.91, 147.10, 147.04, 144.98, 141.57, 132.93, 132.50, 129.23, 125.03, 124.19, 123.55, 120.04, 118.93, 118.72, 118.46, 113.79, 112.39, 111.99, 111.67, 81.68, 70.99, 70.58,52.23, 26.15, 22.71, 22.35, 10.80, 9.67. **HRMS (ESI)** for: $C_{33}H_{41}N_3O_7$ $[M+Na]^+$ m/z 614.2843 (calc), 614.2866 (found).

Methyl 4-(4-(4-amino-3-isopropoxybenzamido)-3-(isopentyloxy)benzamido)-3-
isopropoxybenzoate **(16c)**



Compound **16c** was synthesized according to the standard procedure C by stirring compound **12a** (10mg, 0.01 mmol, 1 eq.), Pd/C (10 mol%) in anhydrous EtOAc:THF mixture (4:1 ml) for 12 hrs. The residue was purified by column chromatography eluting with 5% diethyl ether in CH_2Cl_2 to yield the title compound **16c** as a white solid (7mg, 74% yield). **MP**: 193-195 °C. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.87 (s, 1H), 8.69 – 8.67 (m, 2H), 8.62 (d, *J* = 8.5 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.61 – 7.60 (m, 2H), 7.45 (d, *J* = 1.7 Hz, 1H), 7.41 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.28 – 7.27 (m, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.79 – 4.65 (m, 2H), 4.22 (t, *J* = 6.6 Hz, 2H), 3.91 (s, 3H), 1.92 – 1.84 (m, 1H), 1.82 – 1.78 (m, 2H), 1.45 (d, *J* = 6.1 Hz, 6H), 1.41 (d, *J* = 6.0 Hz, 6H), 1.02 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR (176 MHz, $CDCl_3$)** δ 167.00, 165.38, 164.83, 147.72, 145.90, 144.99, 141.62, 133.29, 132.10, 129.32, 125.01, 124.15, 123.48, 120.13, 119.10, 118.68, 118.58, 113.74, 113.26, 112.49, 110.48, 71.99, 71.03, 67.56, 52.24, 38.09, 25.54, 22.78, 22.36, 22.35. **HRMS (ESI)** for: $C_{33}H_{41}N_3O_7$ $[M+Na]^+$ m/z 614.2843 (calc), 614.2828 (found).

NMR Data

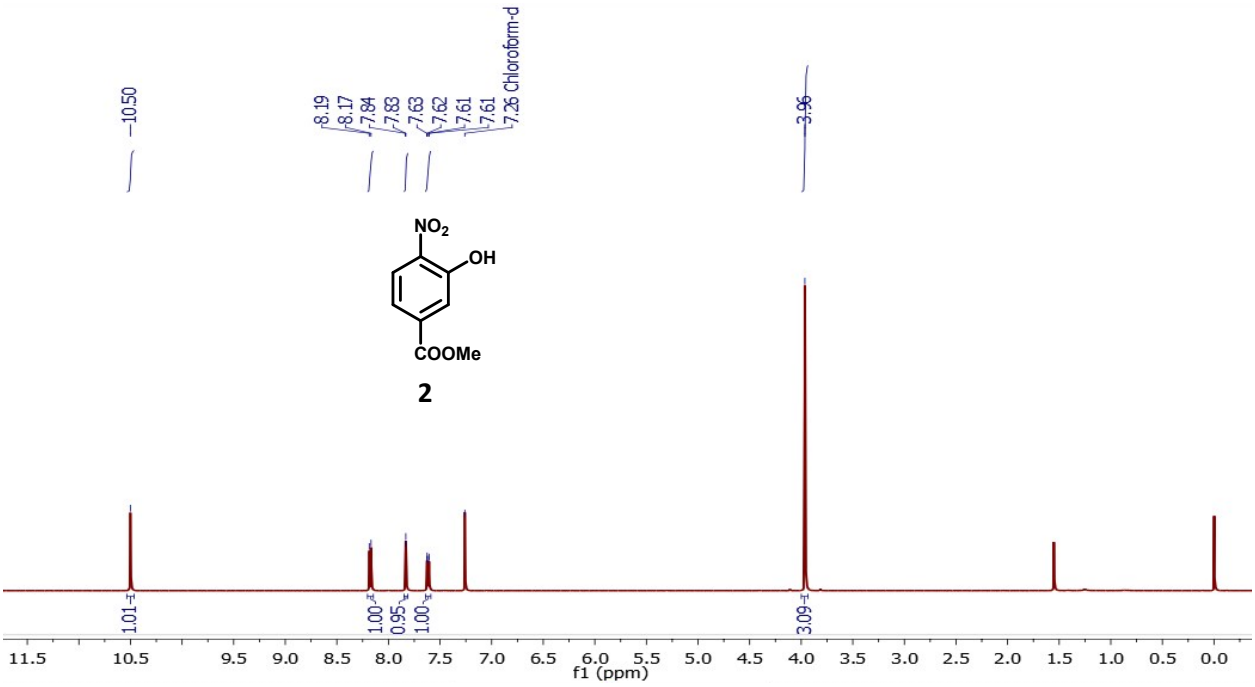


Figure S1. ^{1}H NMR spectrum (500 MHz) of compound **2** in $CDCl_3$ at 298 K

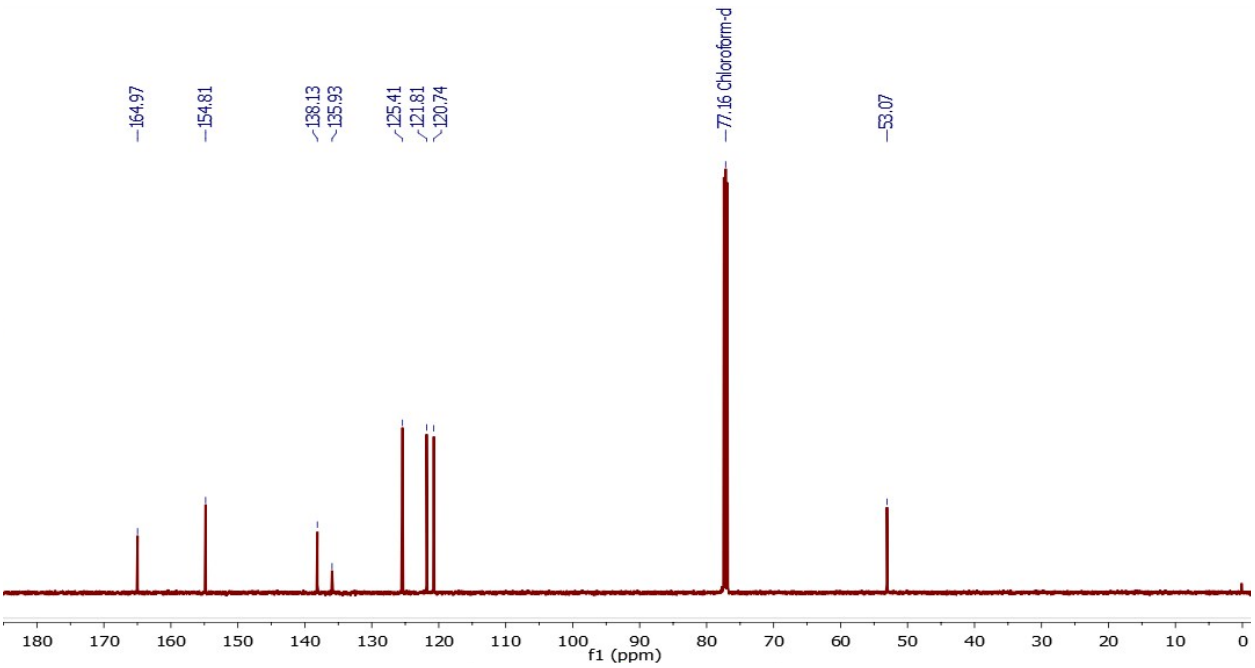


Figure S2. ^{13}C NMR spectrum (126 MHz) of compound **2** in $CDCl_3$ at 298 K

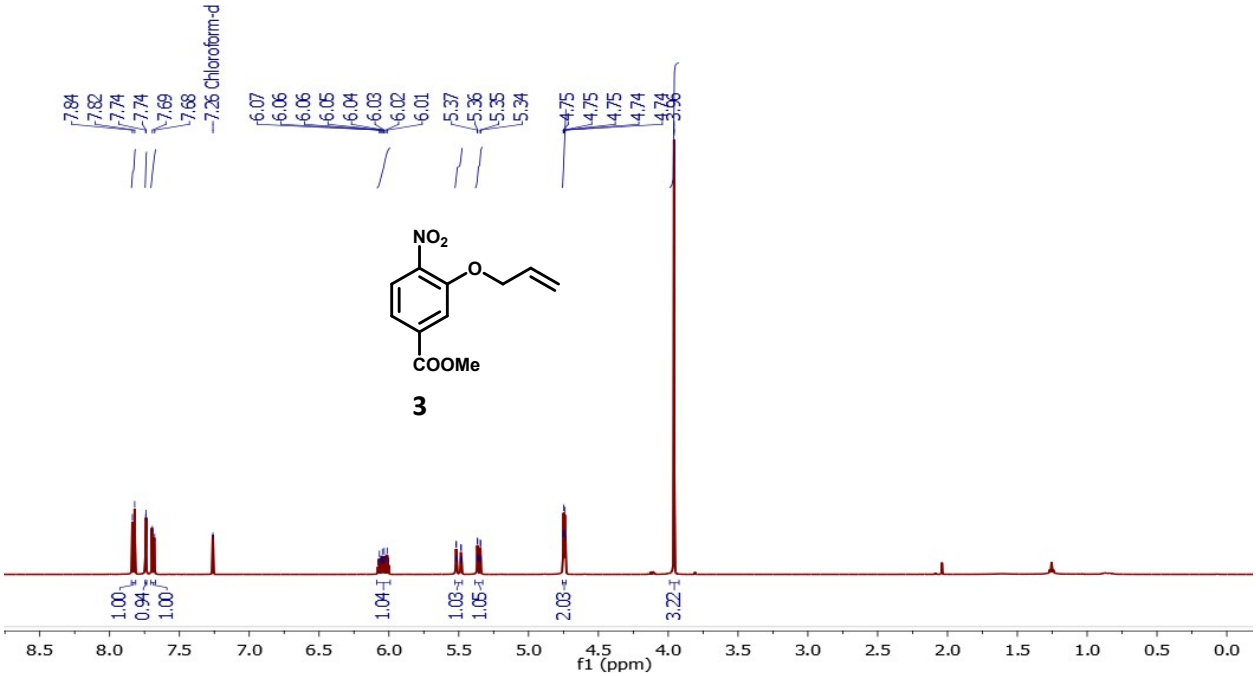


Figure S3. ^{1}H NMR spectrum (500 MHz) of compound **3** in $CDCl_3$ at 298 K

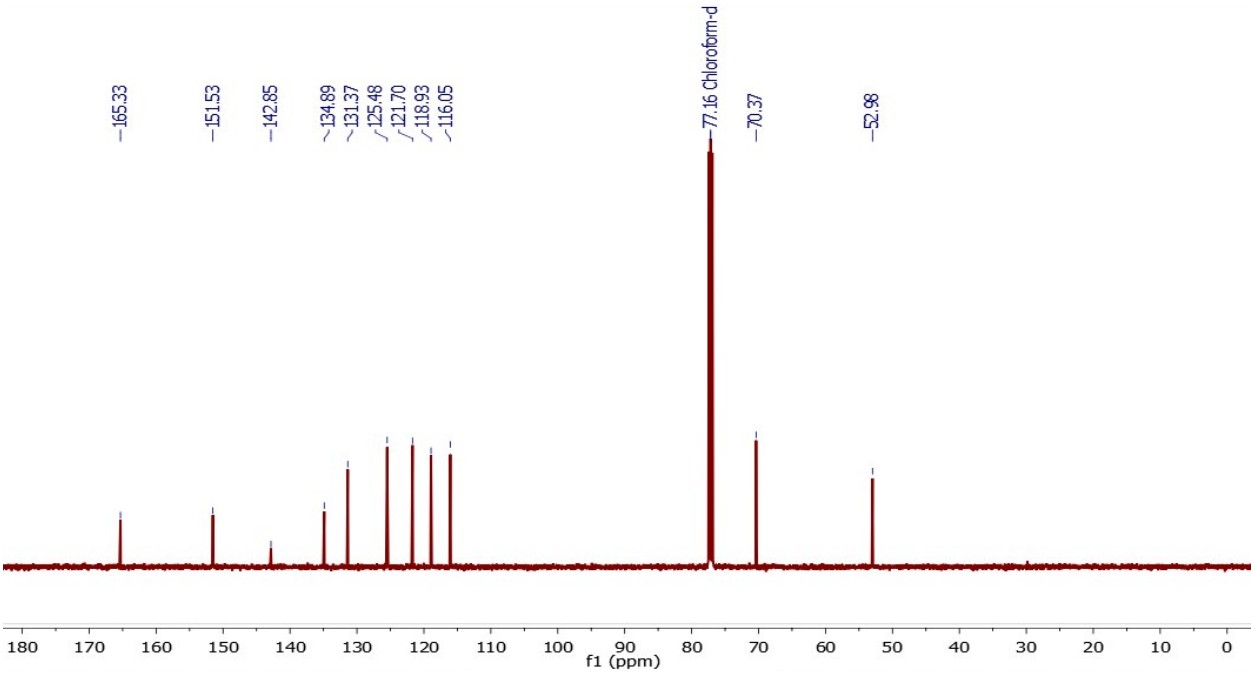


Figure S4. ^{13}C NMR spectrum (126 MHz) of compound **3** in $CDCl_3$ at 298 K

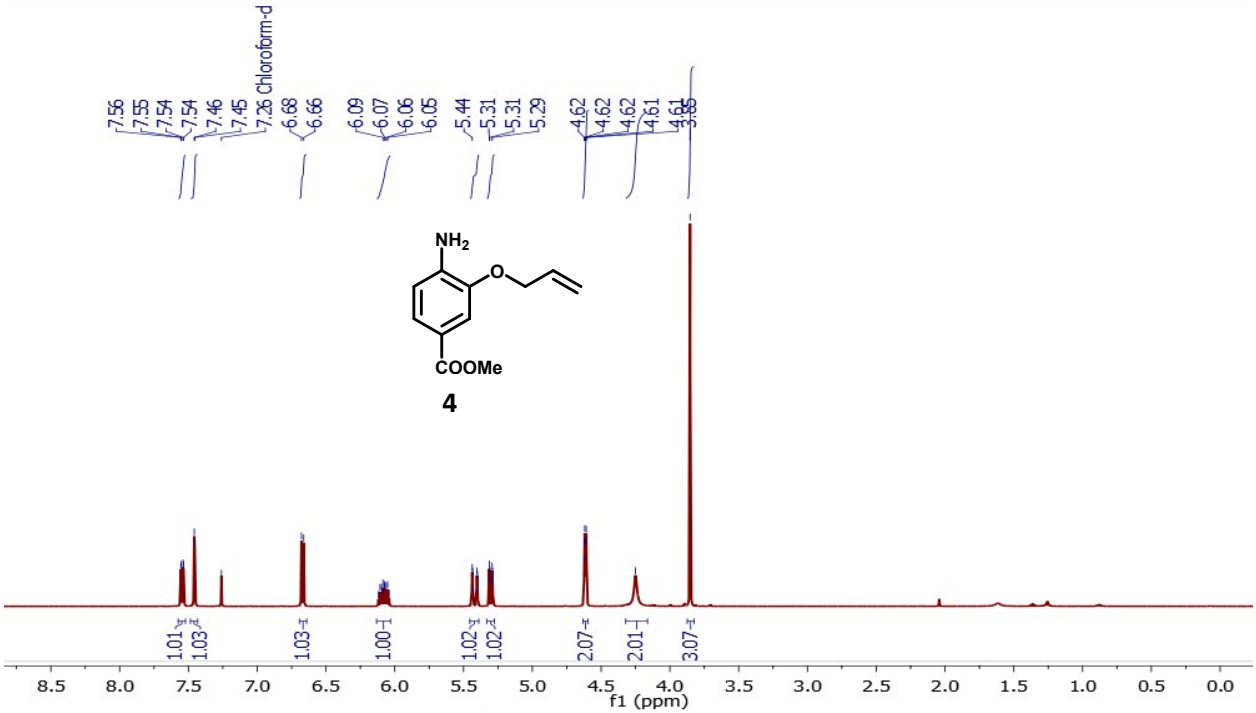


Figure S5. ^{1}H NMR spectrum (500 MHz) of compound **4** in $CDCl_3$ at 298 K

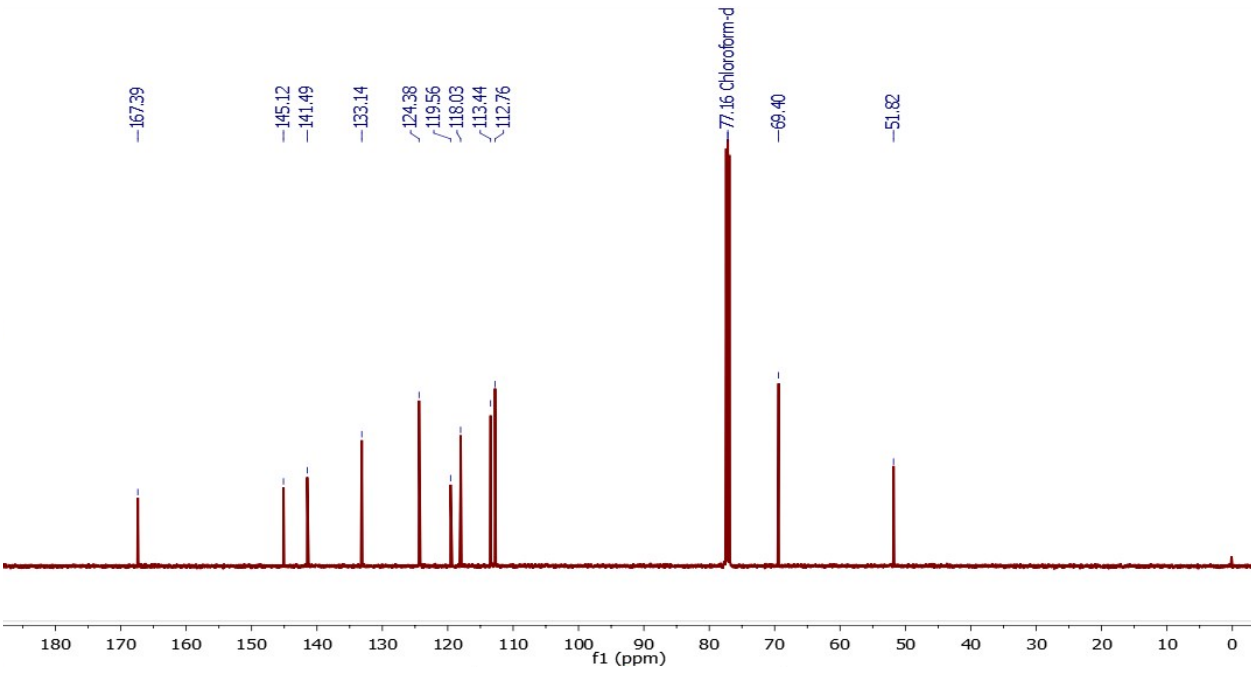


Figure S6. ^{13}C NMR spectrum (126 MHz) of compound **4** in $CDCl_3$ at 298 K

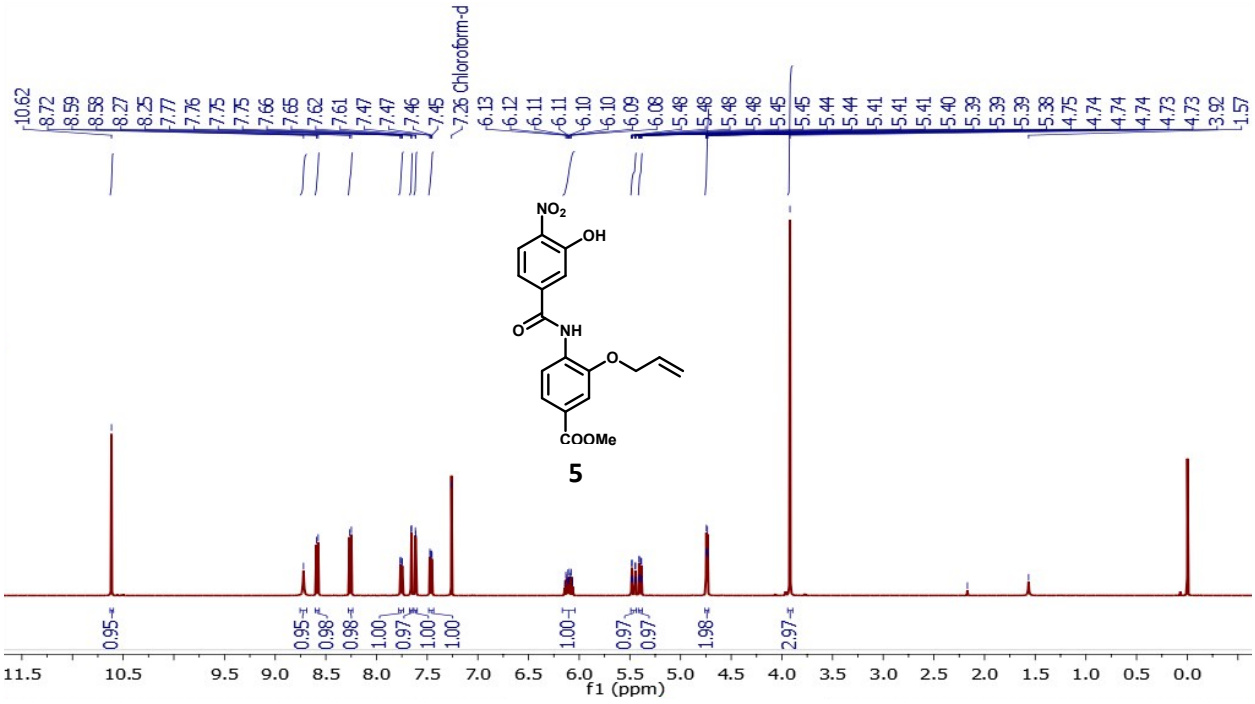


Figure S7. ^{1}H NMR spectrum (500 MHz) of compound **5** in $CDCl_3$ at 298 K

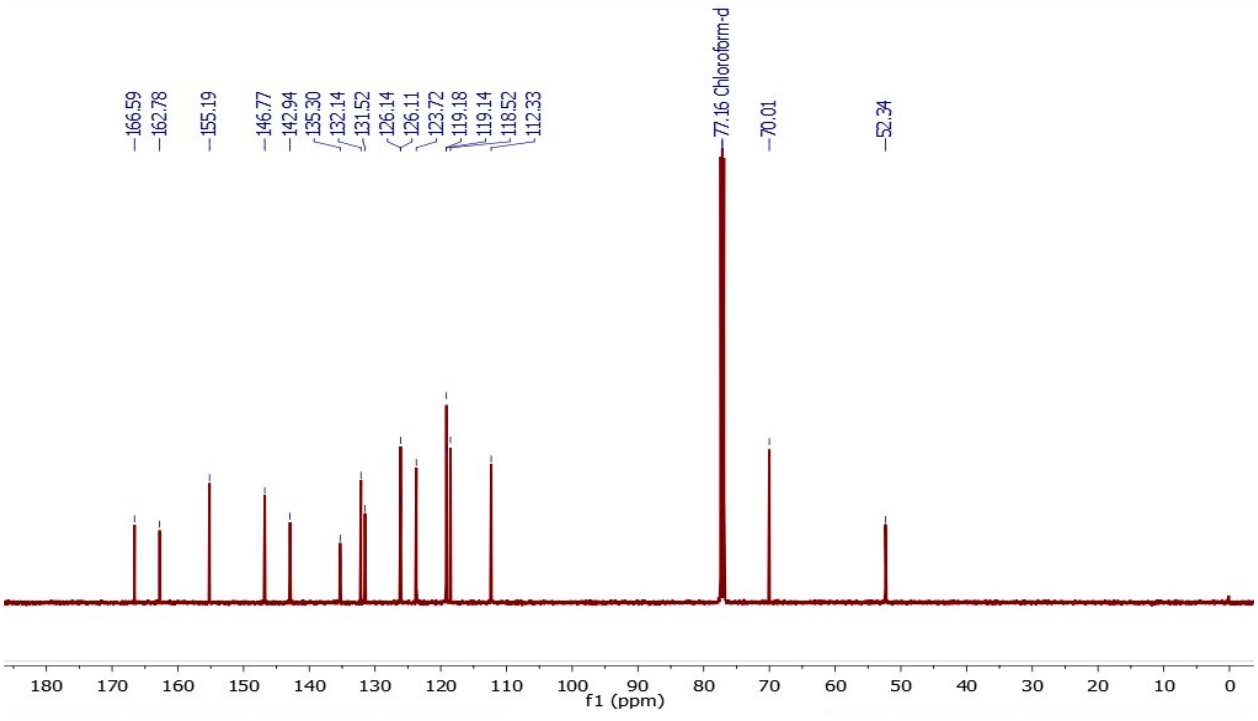


Figure S8. ^{13}C NMR spectrum (126 MHz) of compound **5** in $CDCl_3$ at 298 K

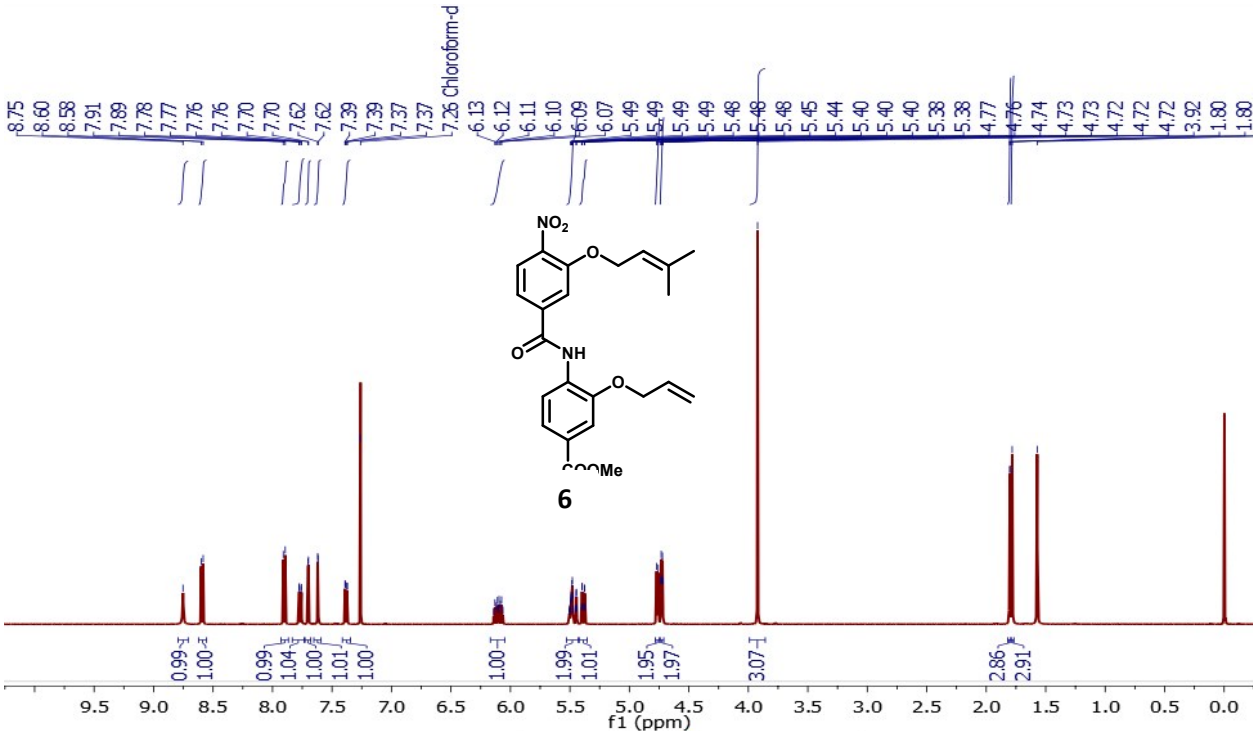


Figure S9. ^{1}H NMR spectrum (500 MHz) of compound **6** in $CDCl_3$ at 298 K

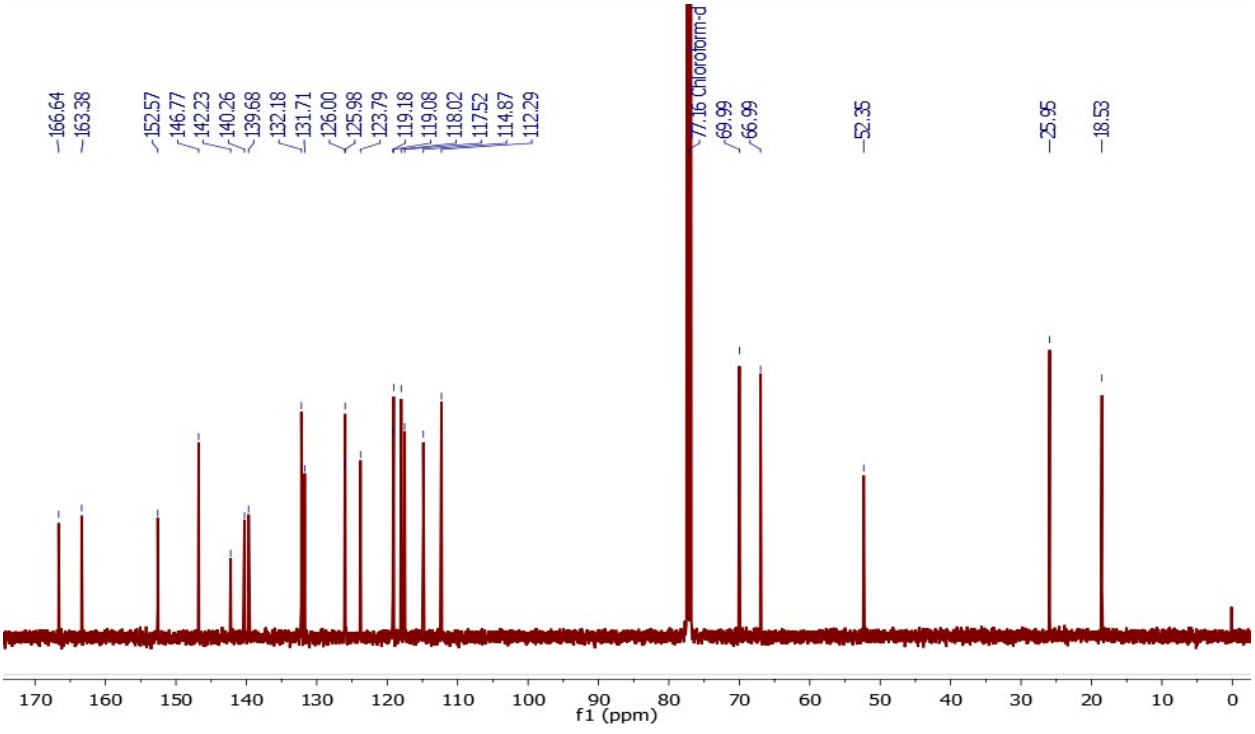


Figure S10. ^{13}C NMR spectrum (126 MHz) of compound **6** in $CDCl_3$ at 298 K

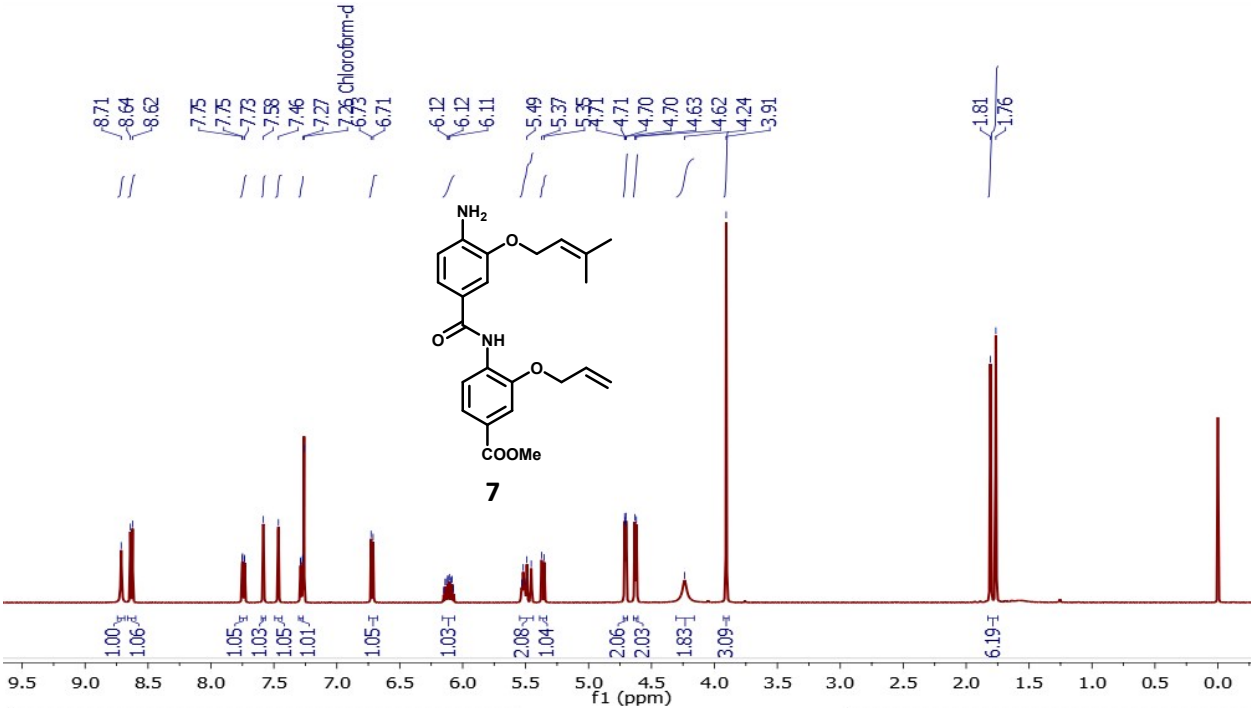


Figure S11. ^{1}H NMR spectrum (500 MHz) of compound **7** in $CDCl_3$ at 298 K

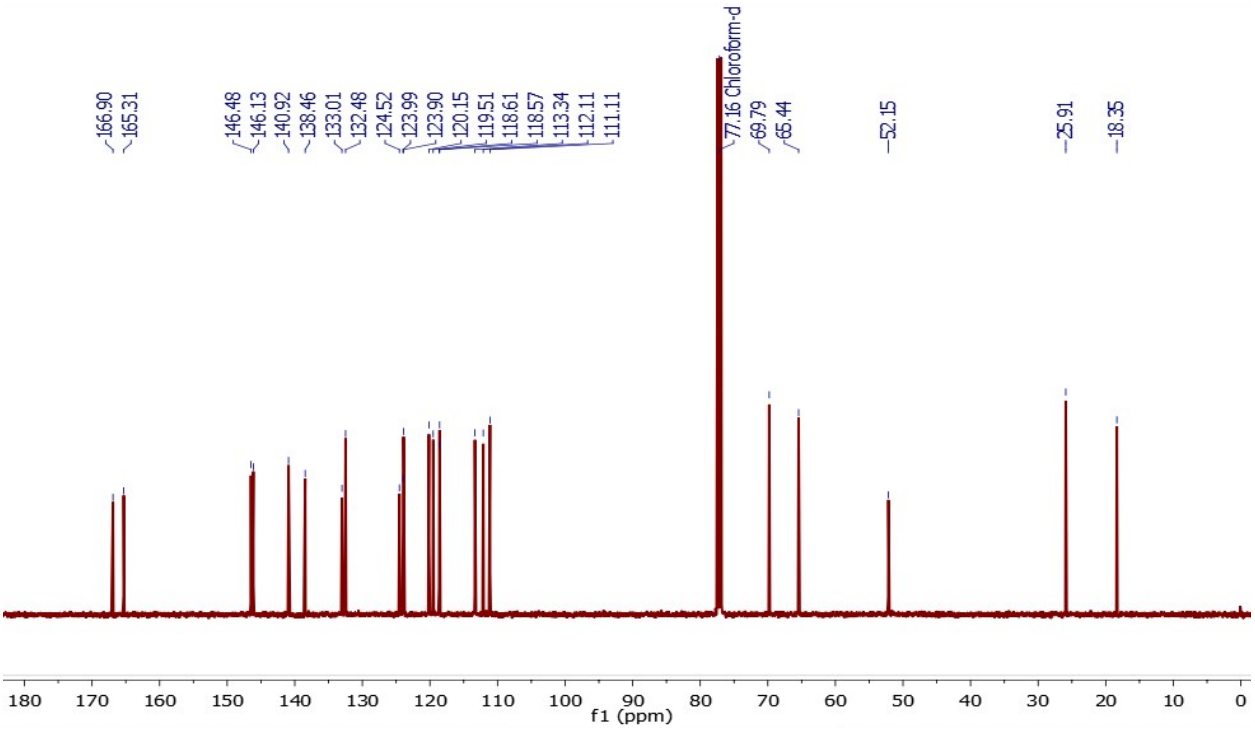


Figure S12. ^{13}C NMR spectrum (126 MHz) of compound **7** in $CDCl_3$ at 298 K

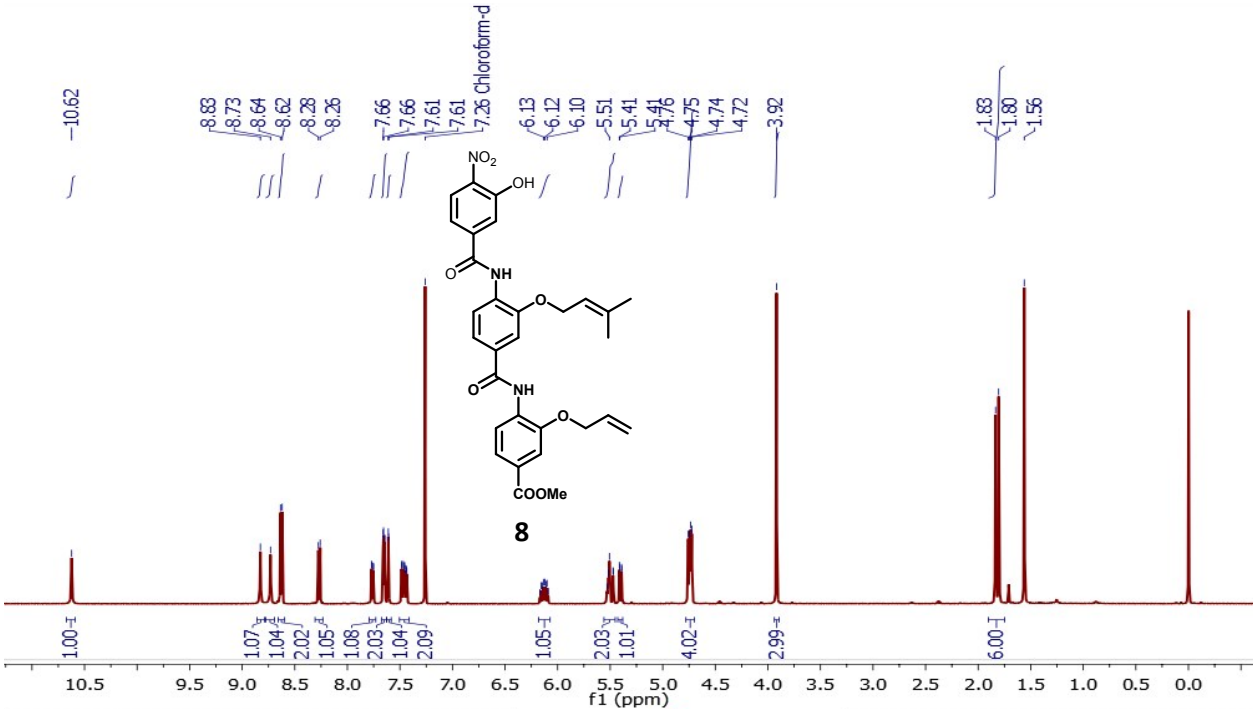


Figure S13. ^{1}H NMR spectrum (500 MHz) of compound **8** in $CDCl_3$ at 298 K

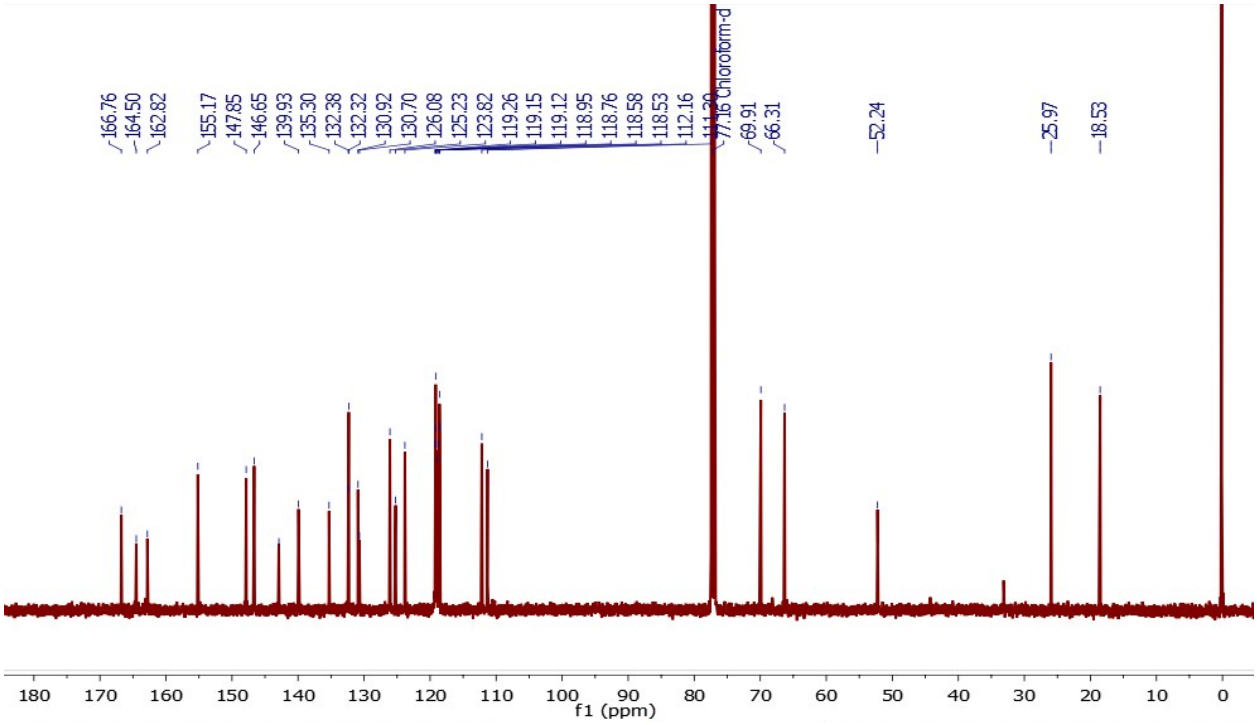


Figure S14. ^{13}C NMR spectrum (126 MHz) of compound **8** in $CDCl_3$ at 298 K

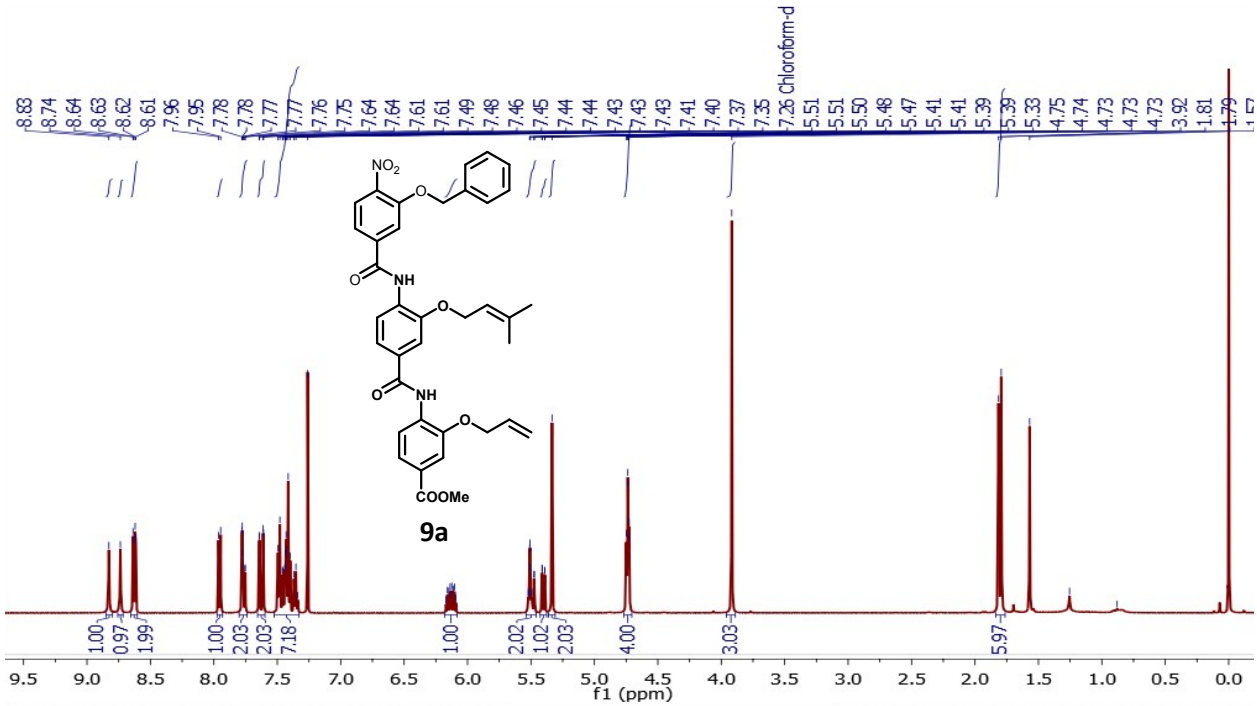


Figure S15. ^{1}H NMR spectrum (500 MHz) of compound **9a** in $CDCl_3$ at 298 K

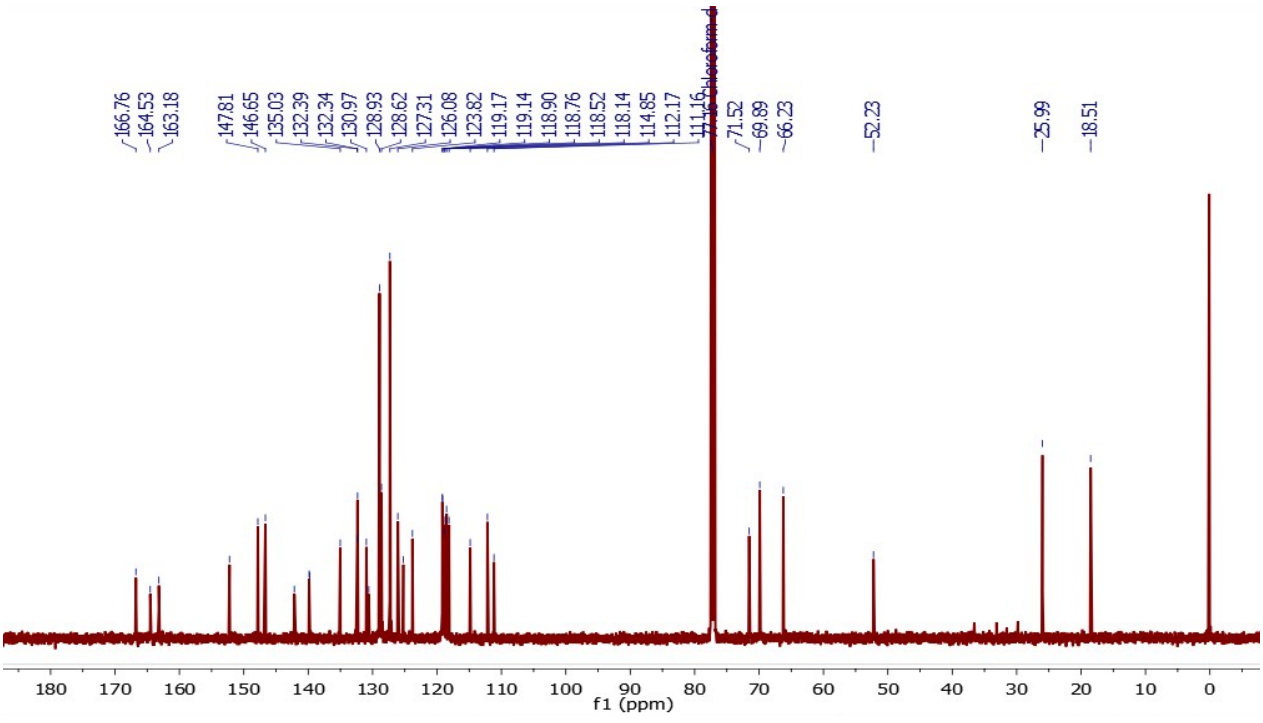


Figure S16. ^{13}C NMR spectrum (126 MHz) of compound **9a** in $CDCl_3$ at 298 K

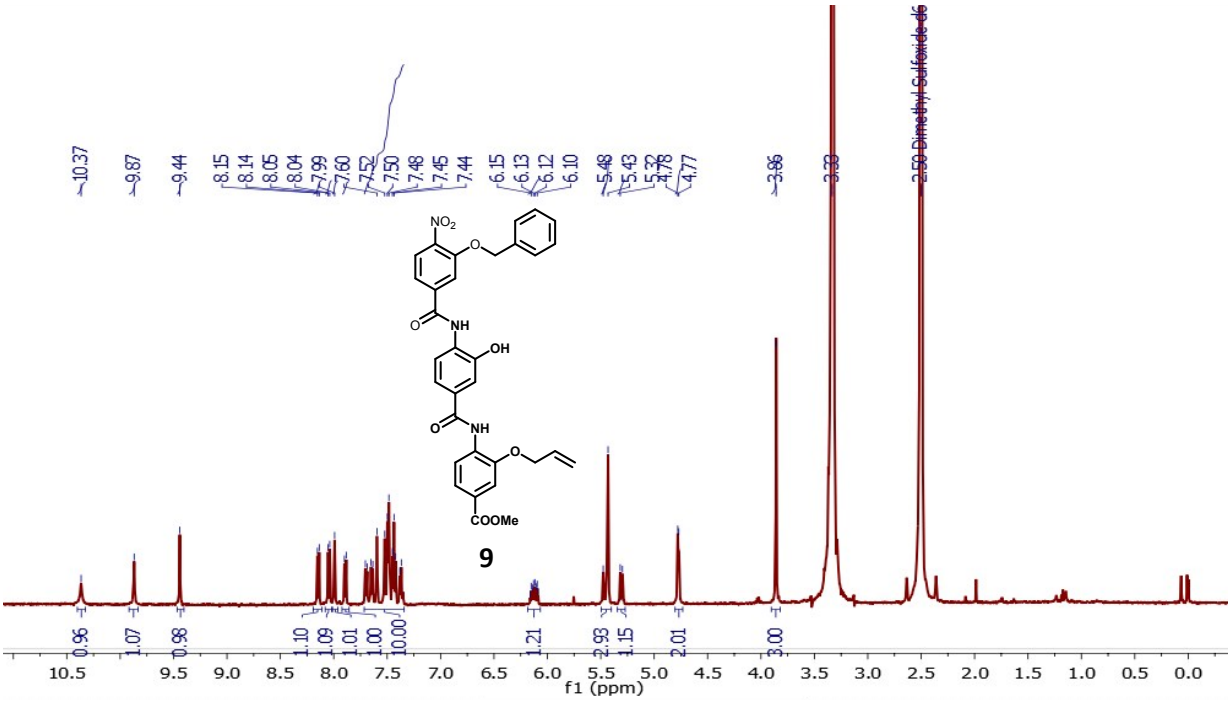


Figure S17. ^{1}H NMR spectrum (500 MHz) of compound **9b** in DMSO-*d6* at 298 K

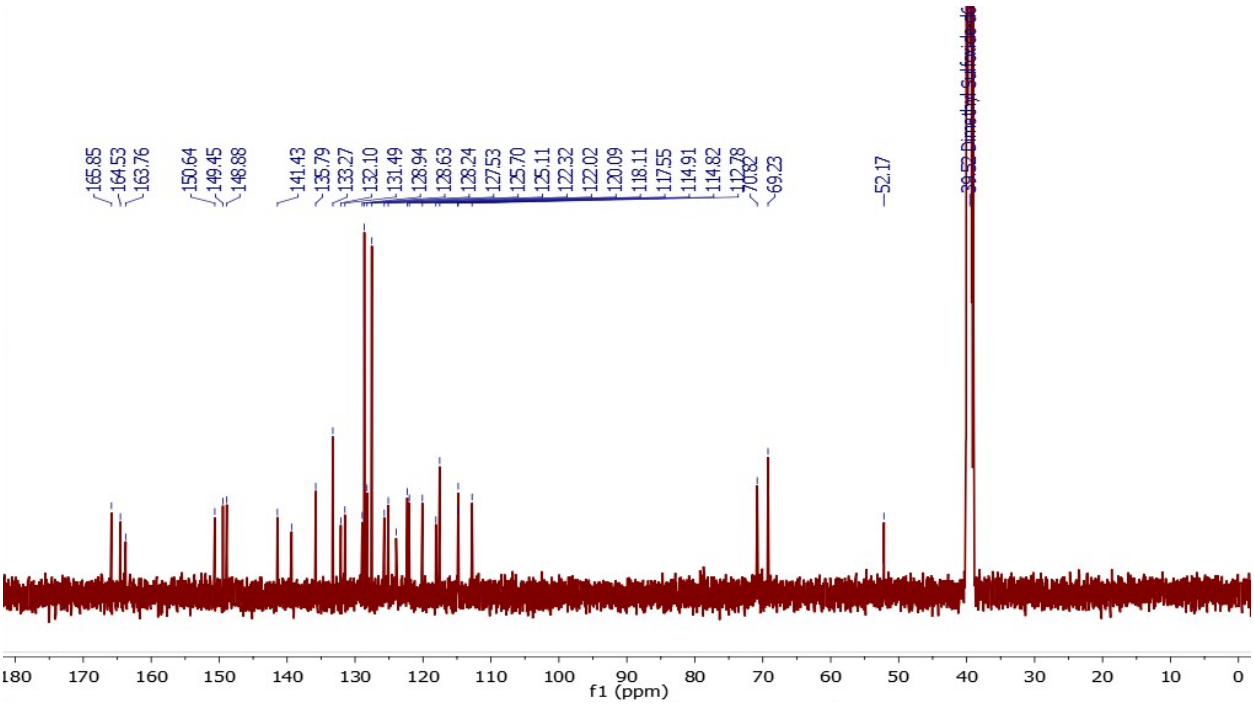


Figure S18. ^{13}C NMR spectrum (126 MHz) of compound **9b** in DMSO-*d6* at 298 K

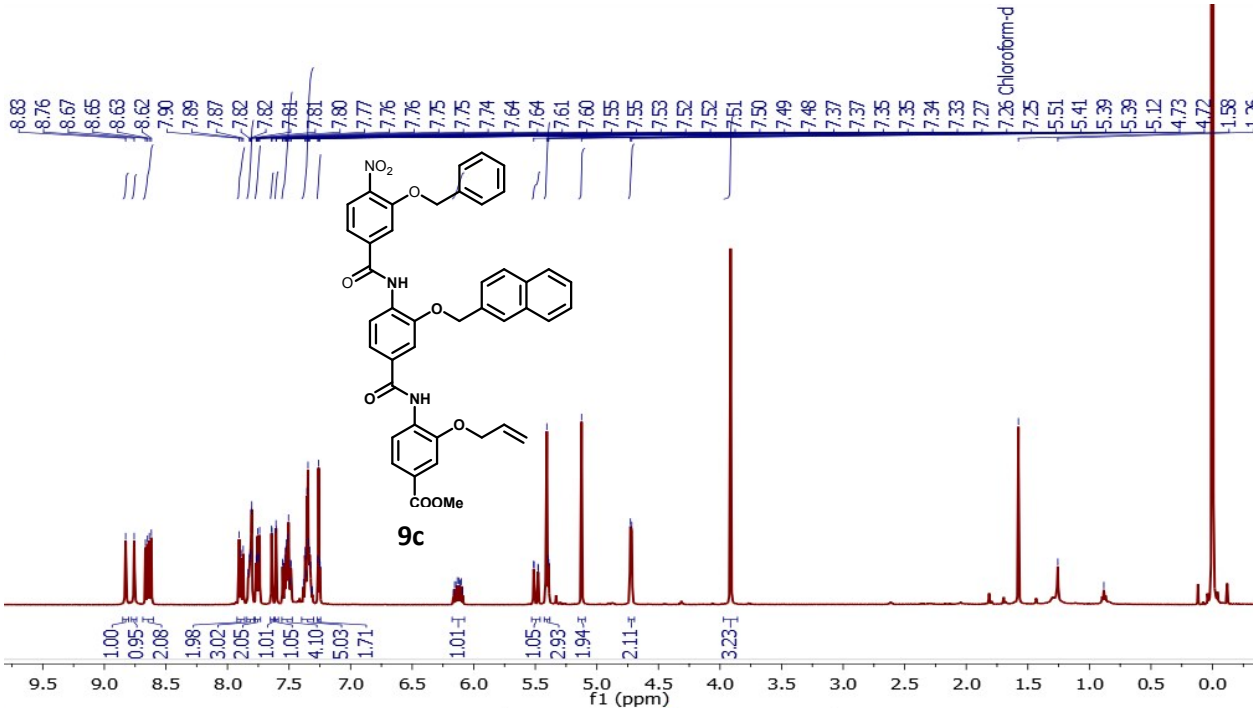


Figure S19. ^{1}H NMR spectrum (500 MHz) of compound **9c** in $CDCl_3$ at 298 K

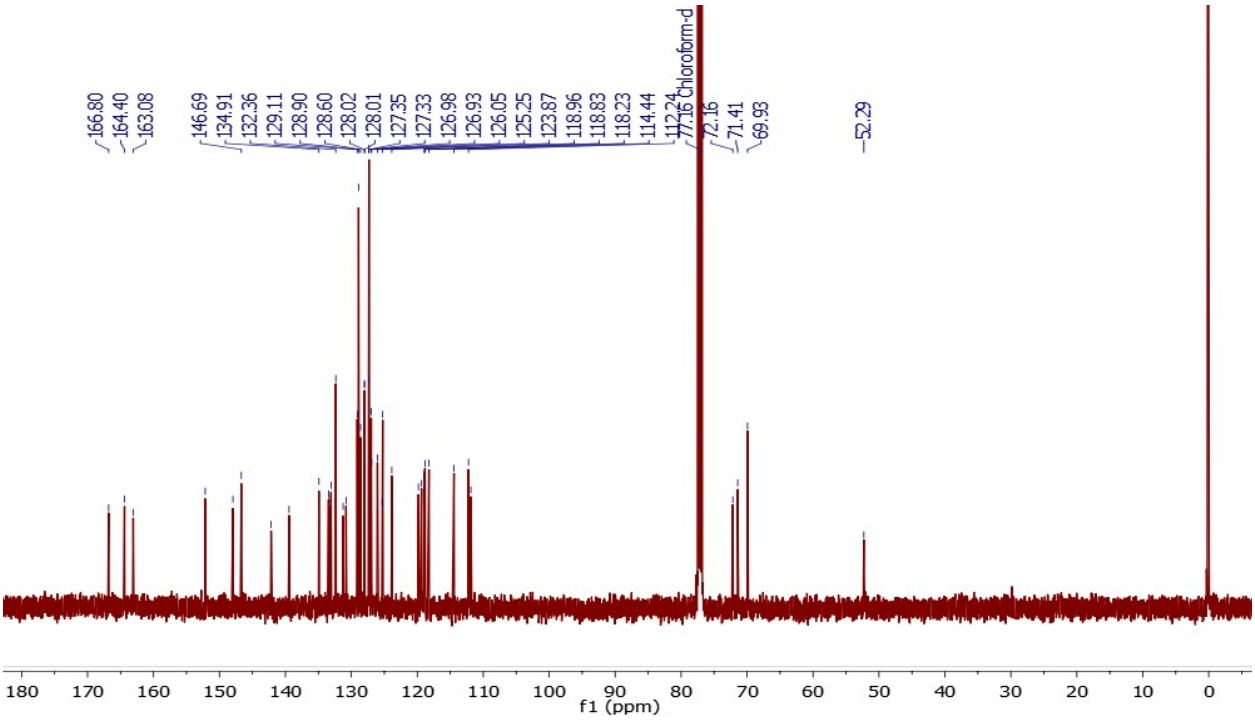


Figure S20. ^{13}C NMR spectrum (126 MHz) of compound **9c** in $CDCl_3$ at 298 K

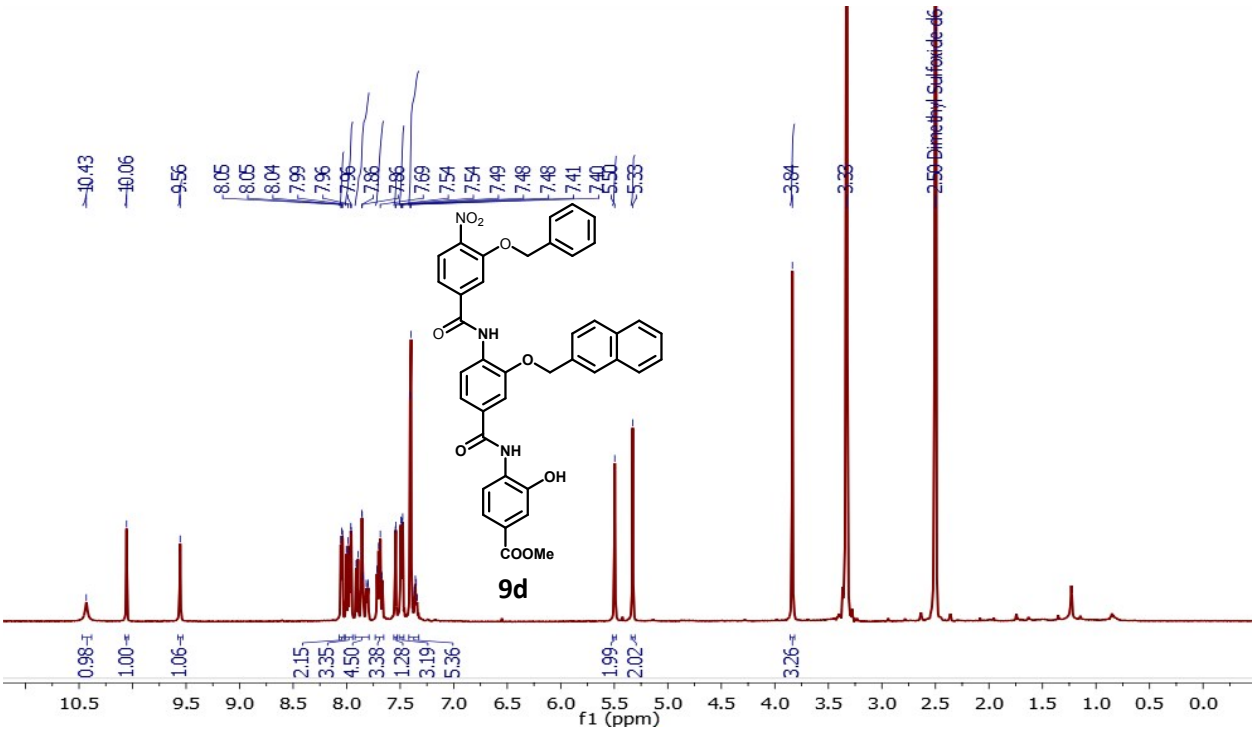


Figure S21. ^{1}H NMR spectrum (500 MHz) of compound **9d** in DMSO-*d6* at 298 K

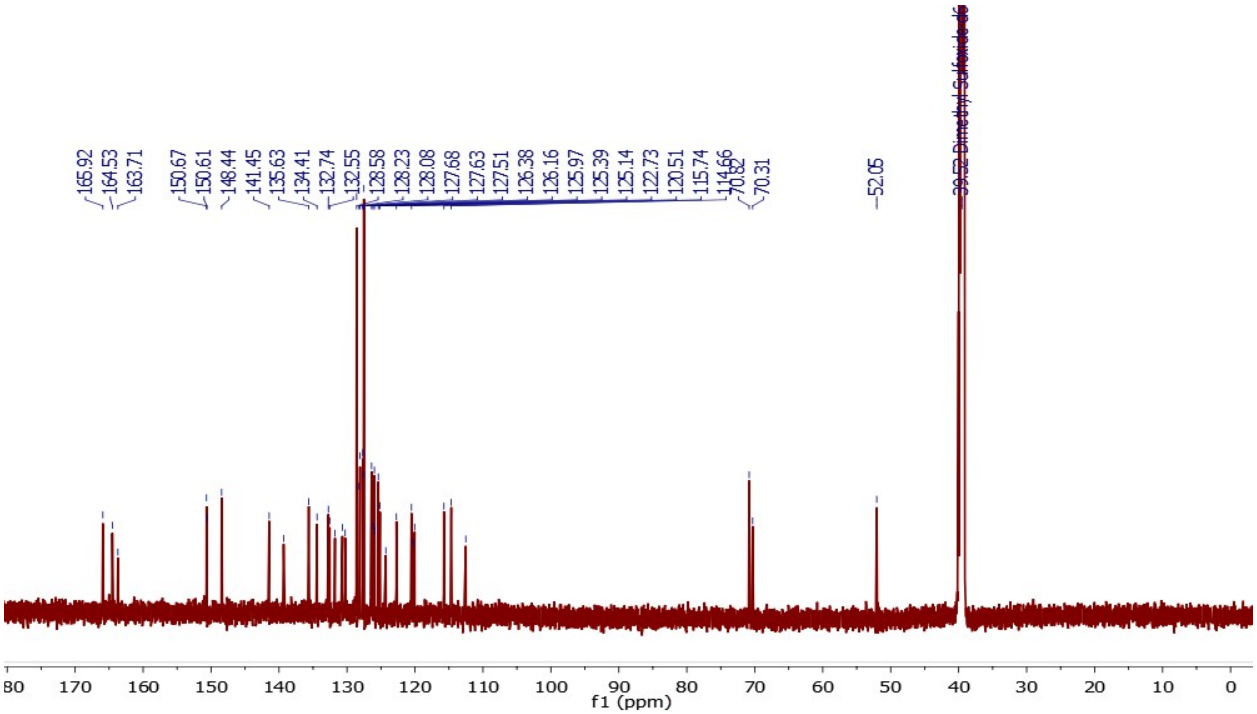


Figure S22. ^{13}C NMR spectrum (176 MHz) of compound **9d** in DMSO-*d6* at 298 K

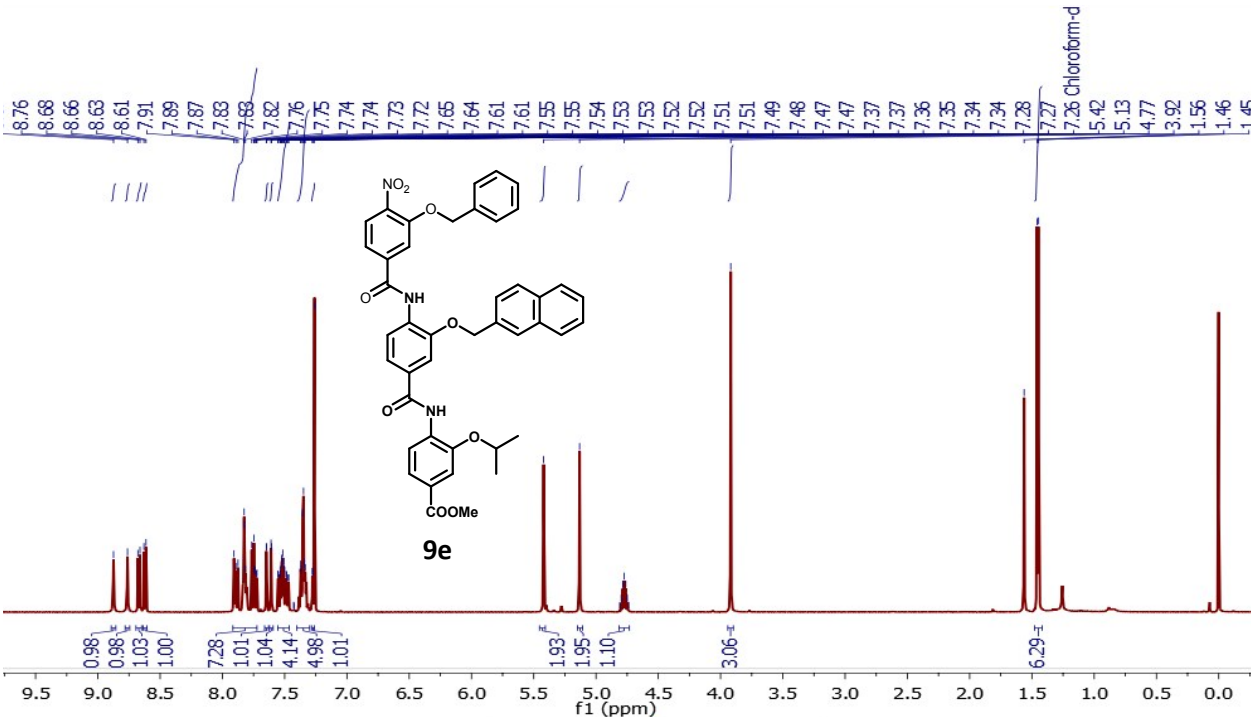


Figure S23. ^{1}H NMR spectrum (500 MHz) of compound **9e** in $CDCl_3$ at 298 K

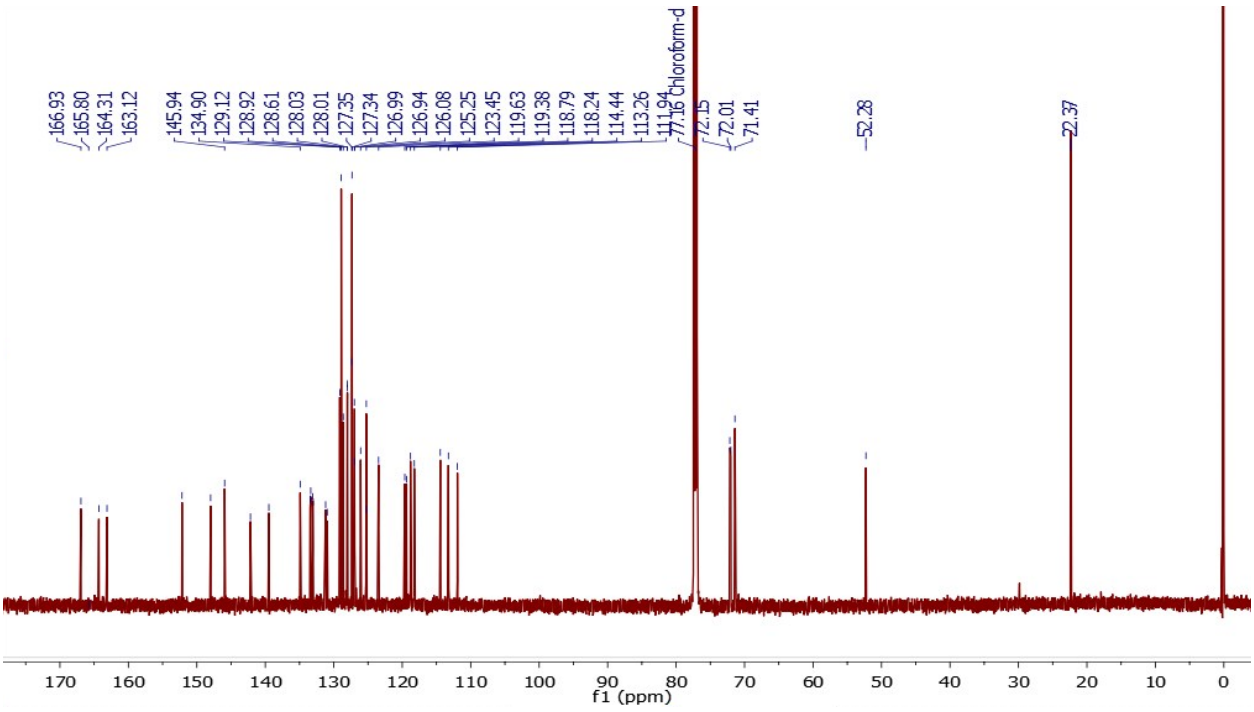


Figure S24. ^{13}C NMR spectrum (176 MHz) of compound **9e** in $CDCl_3$ at 298 K

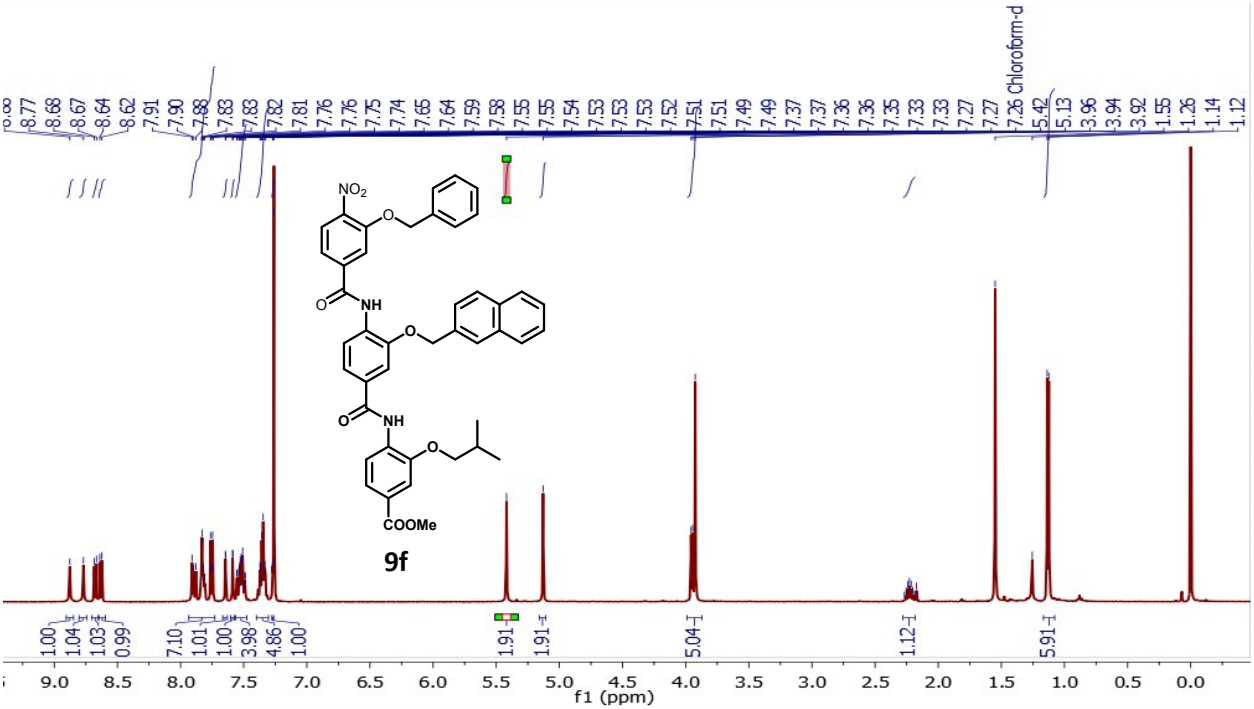


Figure S25. ^{1}H NMR spectrum (500 MHz) of compound **9f** in $CDCl_3$ at 298 K

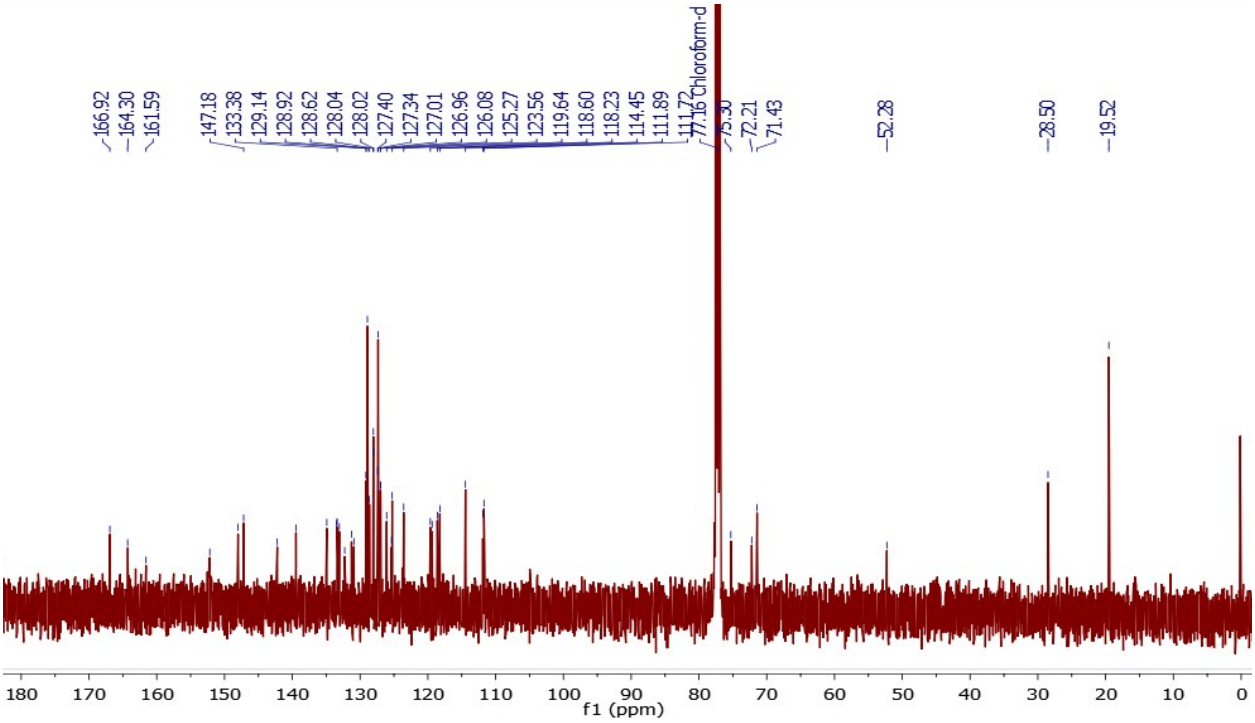


Figure S26. ^{13}C NMR spectrum (126 MHz) of compound **9f** in $CDCl_3$ at 298 K

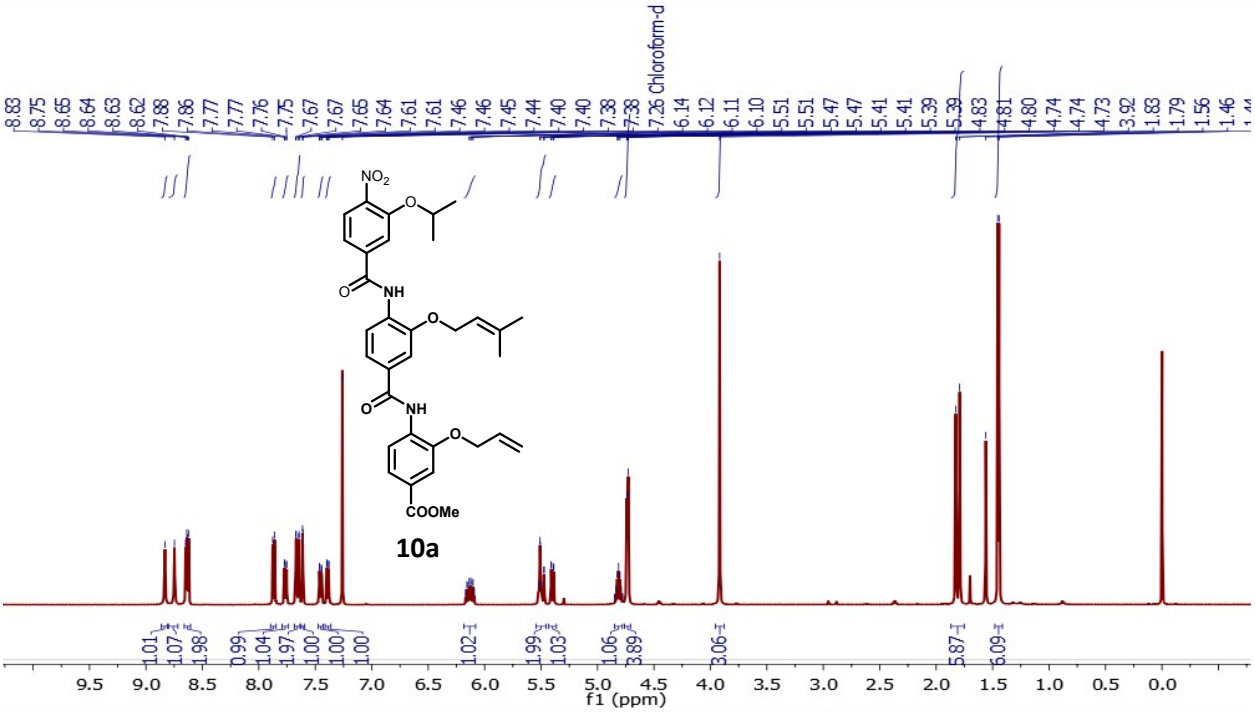


Figure S27. ^{1}H NMR spectrum (500 MHz) of compound **10a** in $CDCl_3$ at 298 K

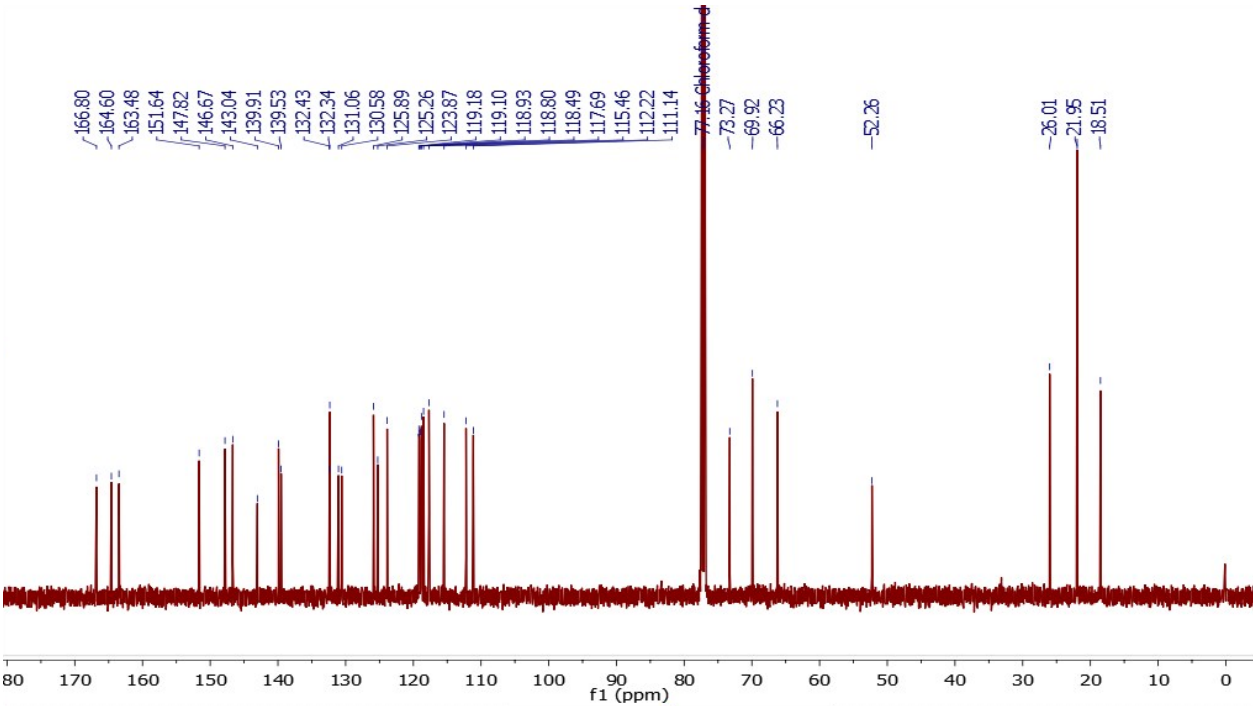


Figure S28. ^{13}C NMR spectrum (126 MHz) of compound **10a** in $CDCl_3$ at 298 K

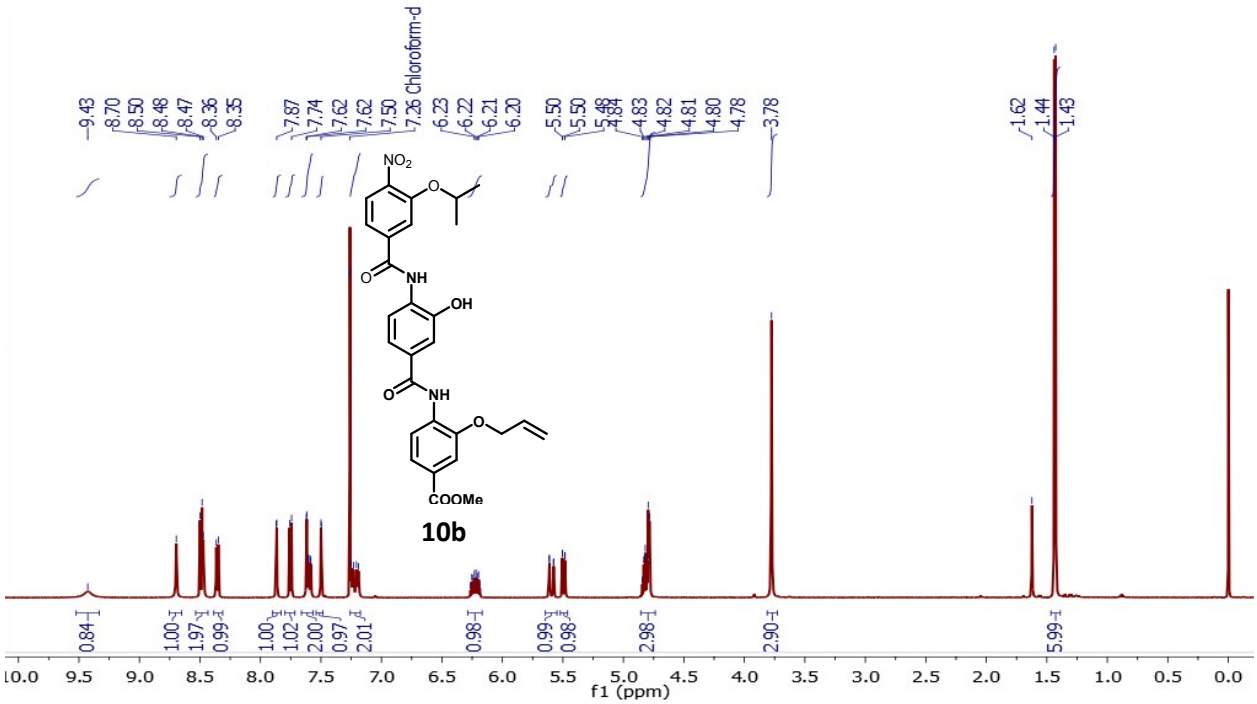


Figure S29. ^{1}H NMR spectrum (500 MHz) of compound **10b** in $CDCl_3$ at 298 K

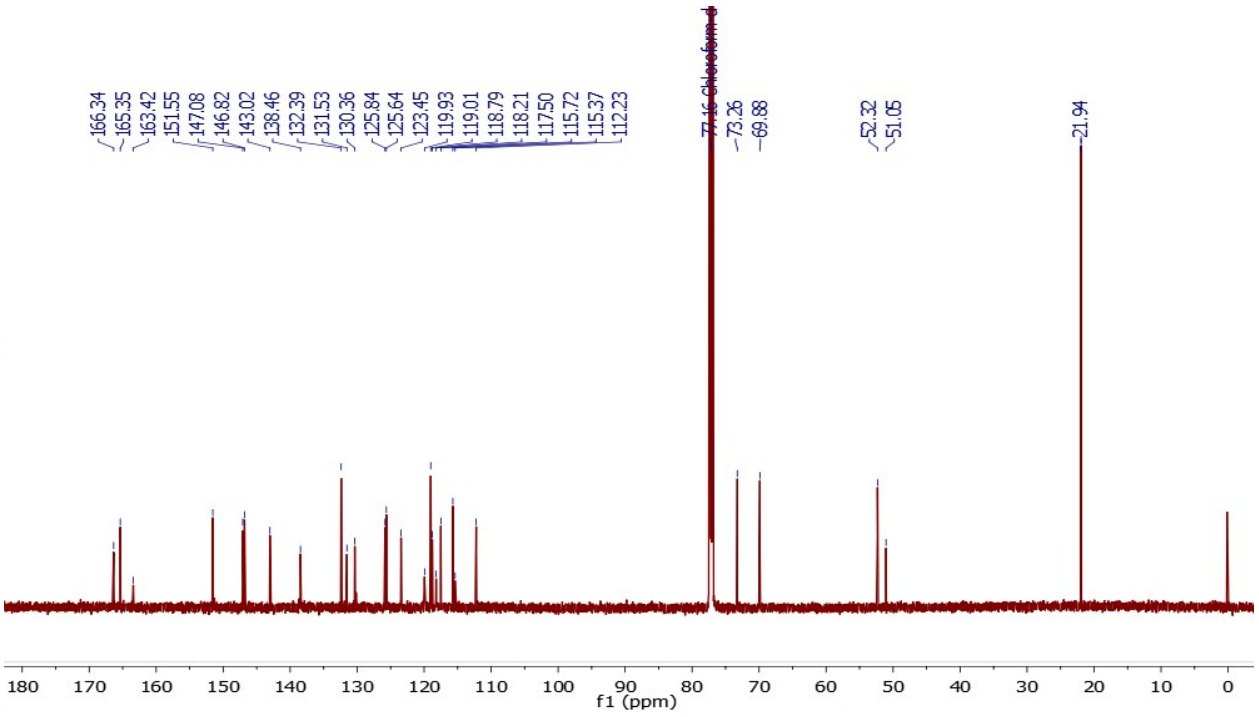


Figure S30. ^{13}C NMR spectrum (176 MHz) of compound **10b** in $CDCl_3$ at 298 K

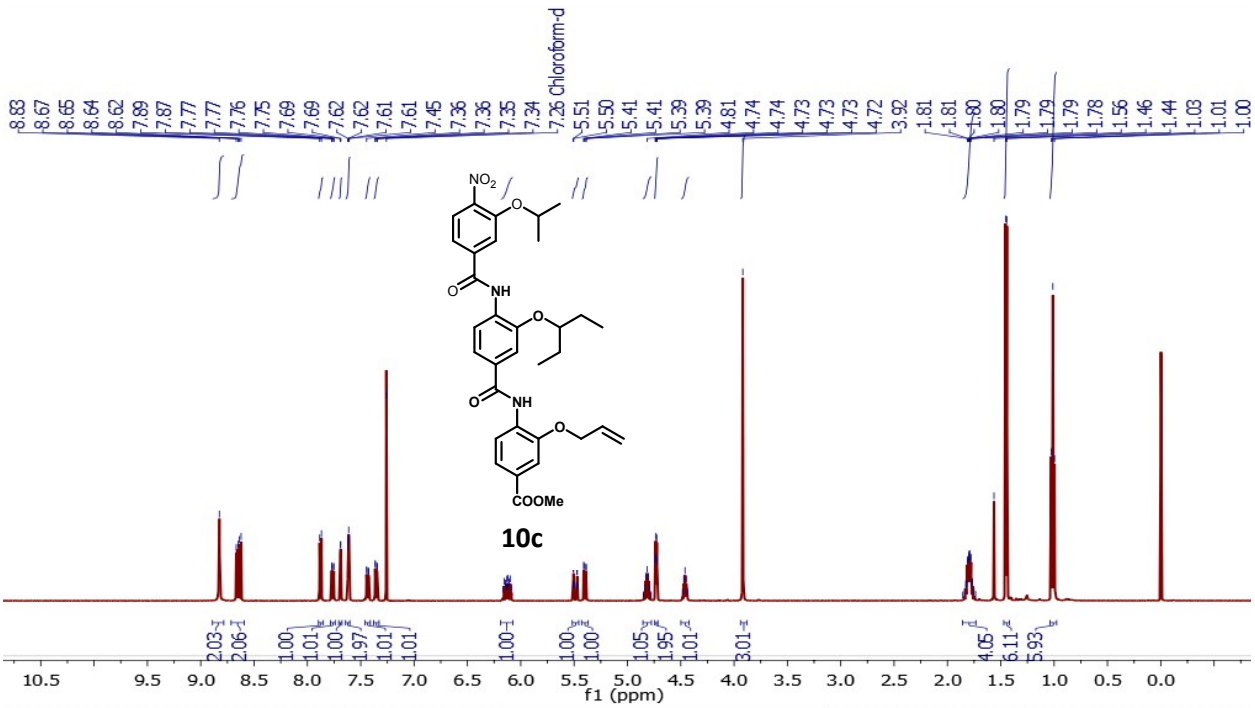


Figure S31. ^{1}H NMR spectrum (500 MHz) of compound **10c** in $CDCl_3$ at 298 K

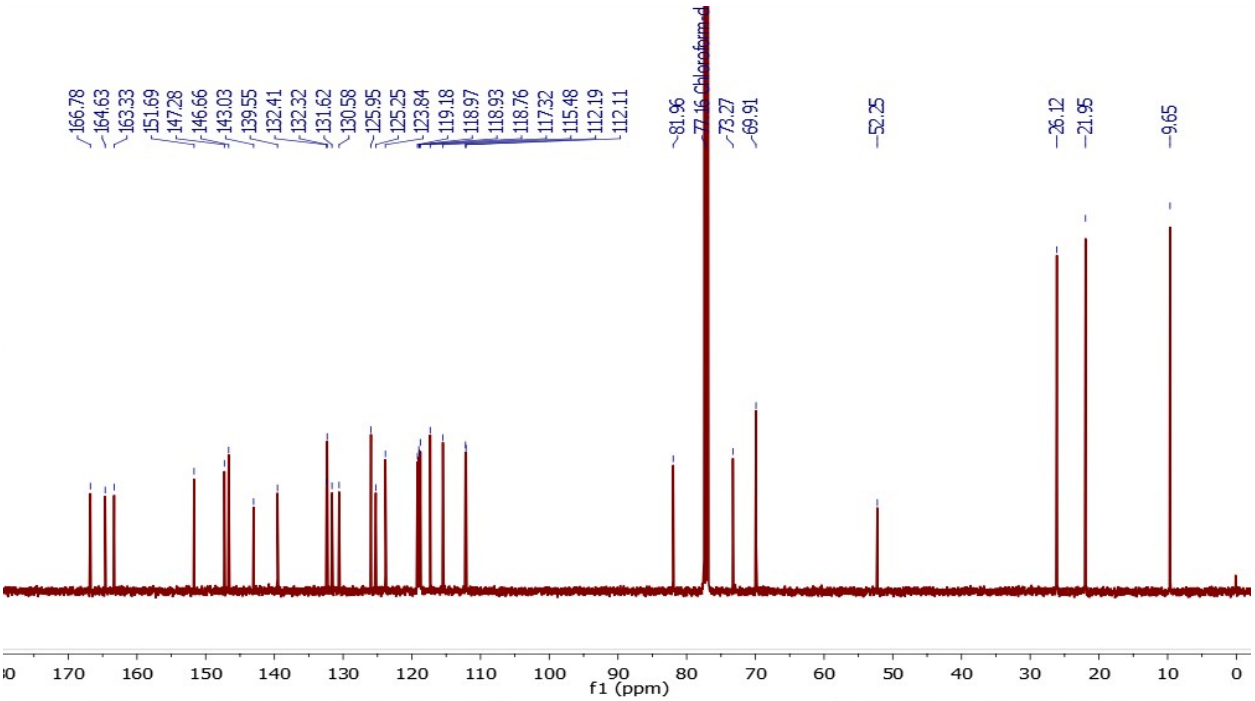


Figure S32. ^{13}C NMR spectrum (126 MHz) of compound **10c** in $CDCl_3$ at 298 K

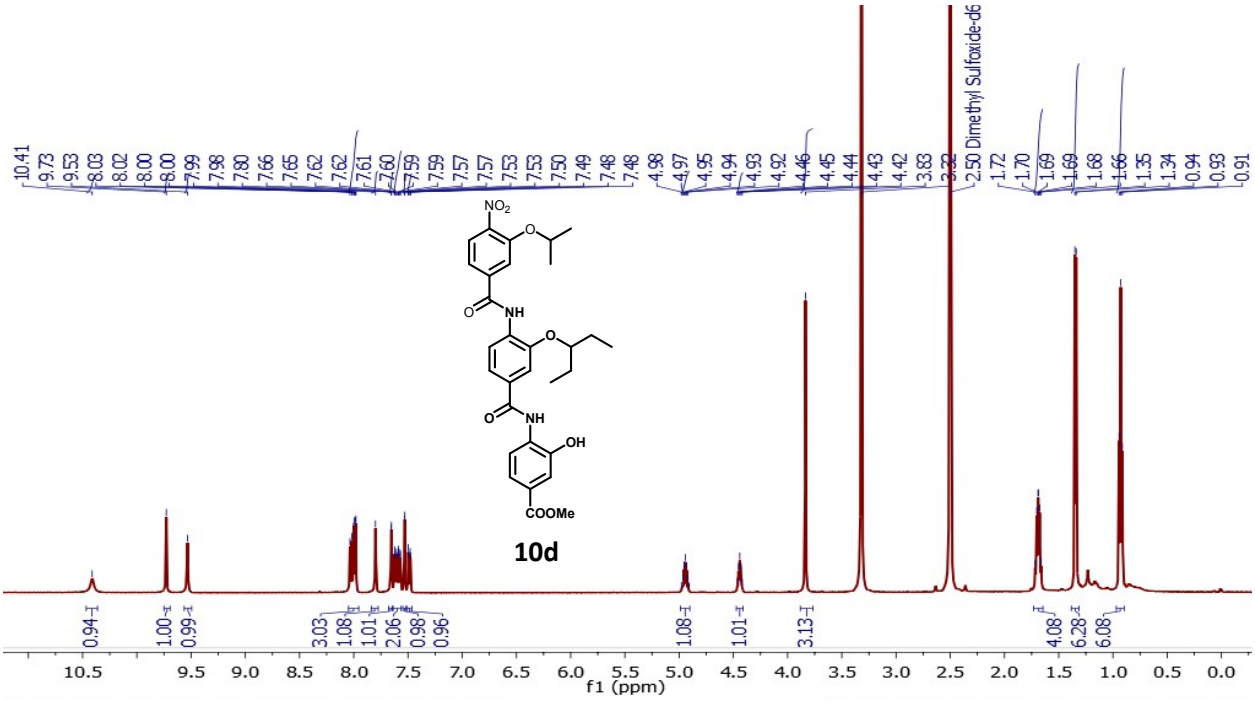


Figure S33. ^{1}H NMR spectrum (500 MHz) of compound **10d** in DMSO-*d6* at 298 K

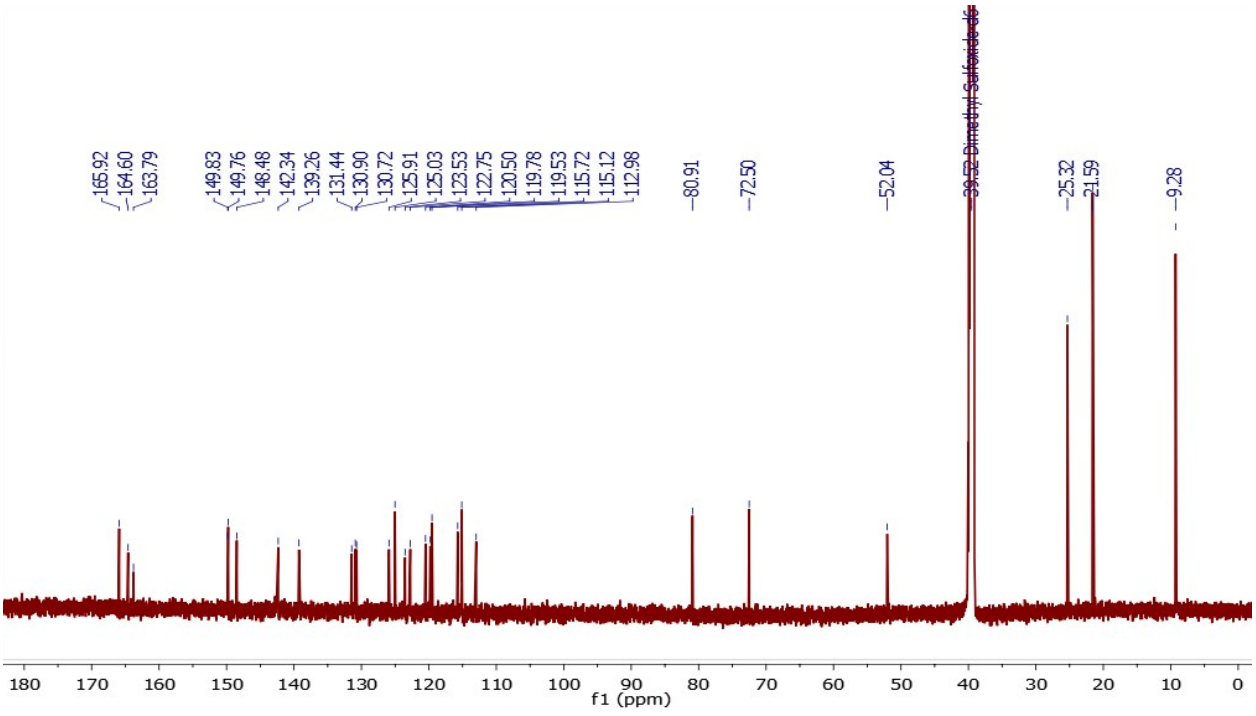


Figure S34. ^{13}C NMR spectrum (176 MHz) of compound **10d** in DMSO-*d6* at 298 K

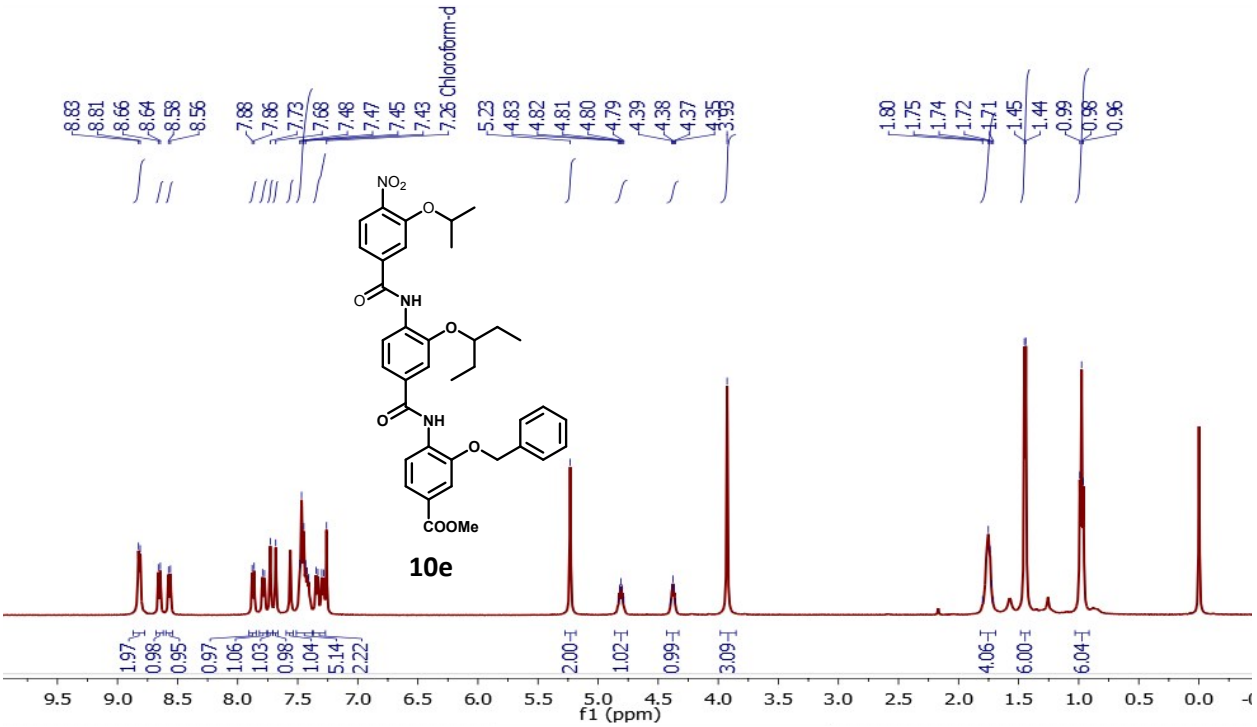


Figure S35. ^{1}H NMR spectrum (500 MHz) of compound **10e** in $CDCl_3$ at 298 K

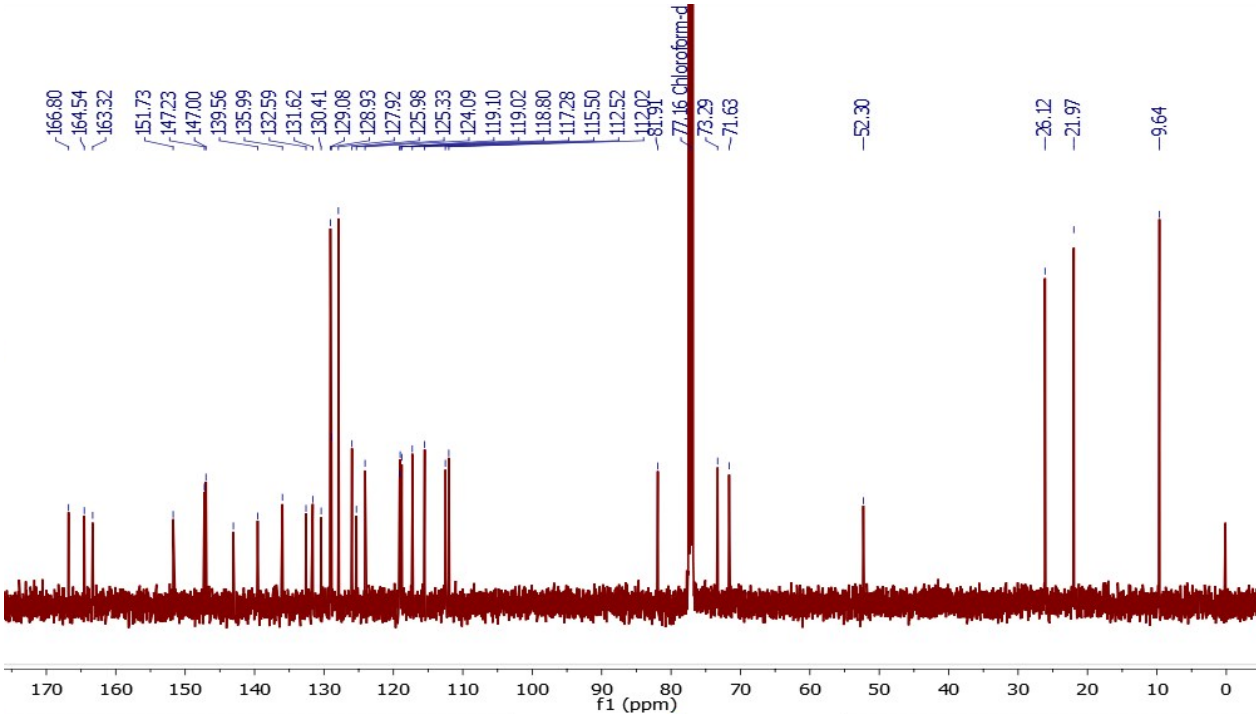


Figure S36. ^{13}C NMR spectrum (126 MHz) of compound **10e** in $CDCl_3$ at 298 K

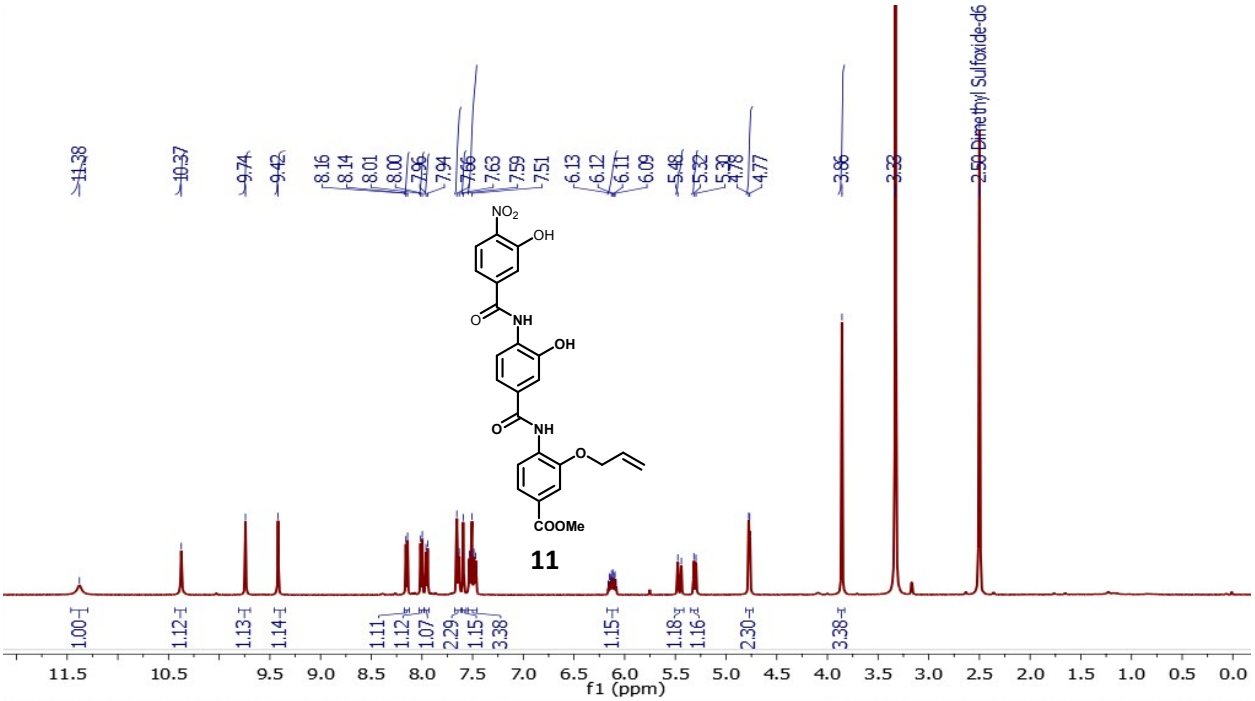


Figure S37. ^{1}H NMR spectrum (500 MHz) of compound **11** in DMSO-*d6* at 298 K

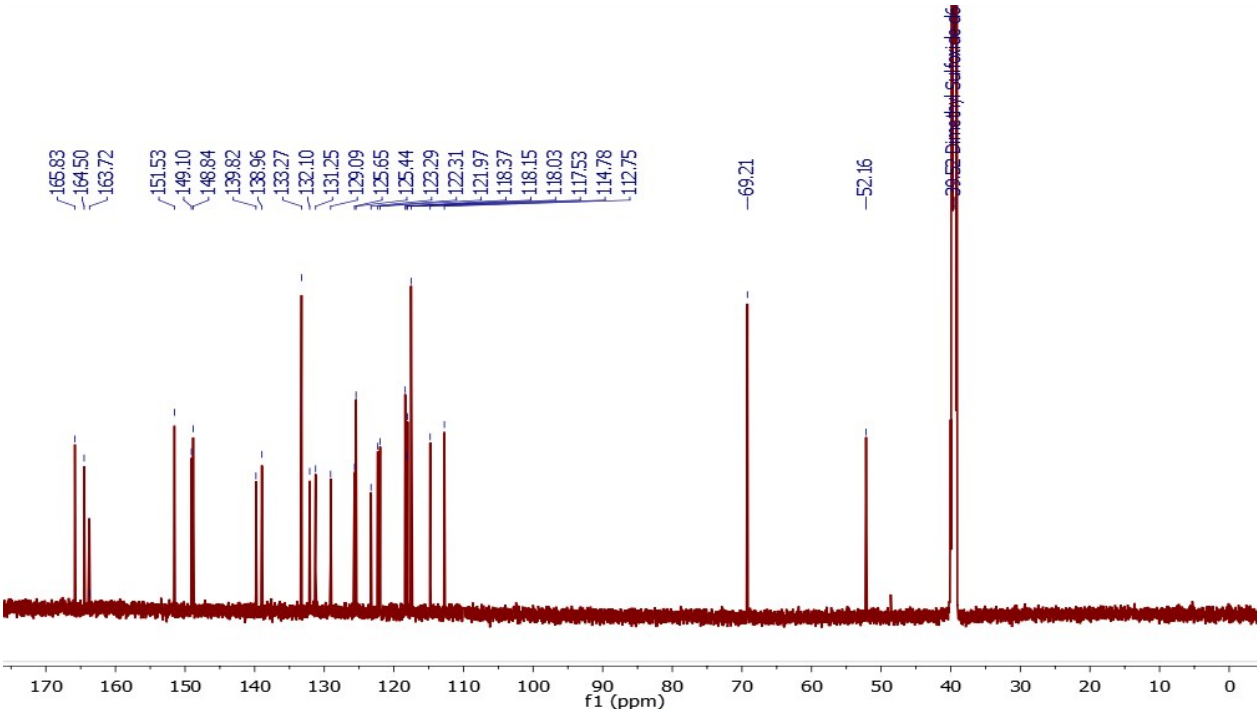


Figure S38. ^{13}C NMR spectrum (176 MHz) of compound **11** in DMSO-*d6* at 298 K

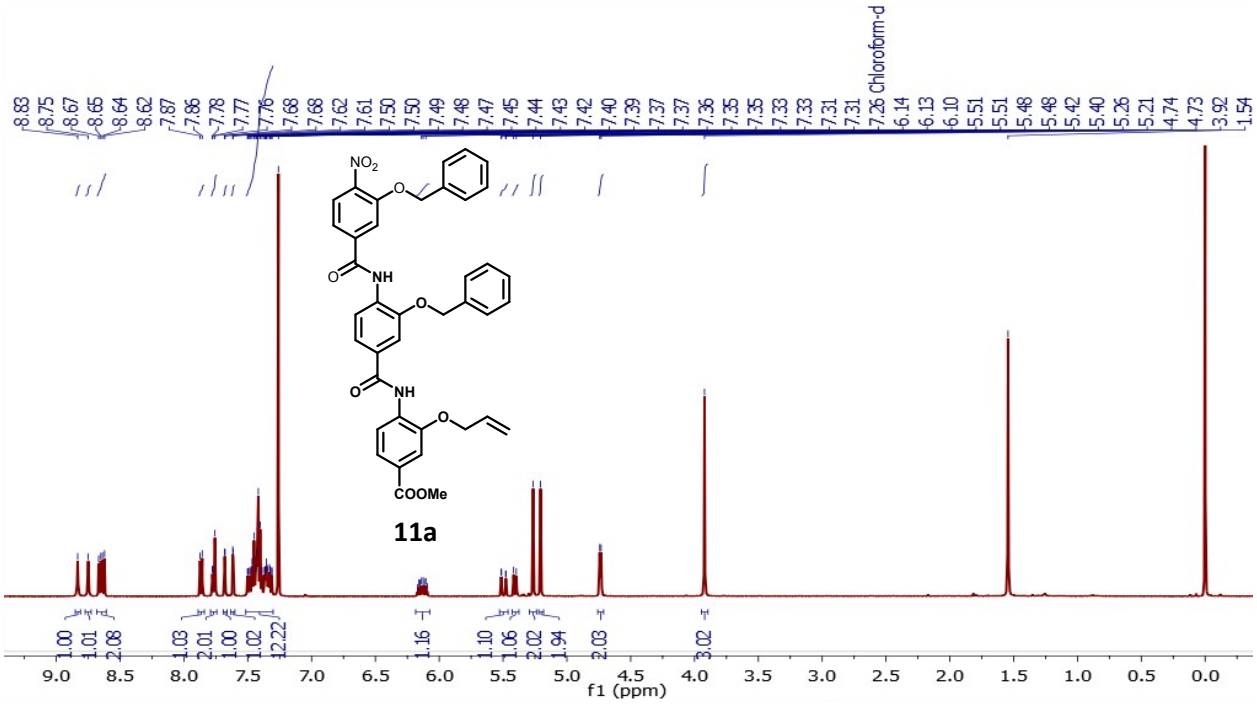


Figure S39. ^{1}H NMR spectrum (500 MHz) of compound **11a** in $CDCl_3$ at 298 K

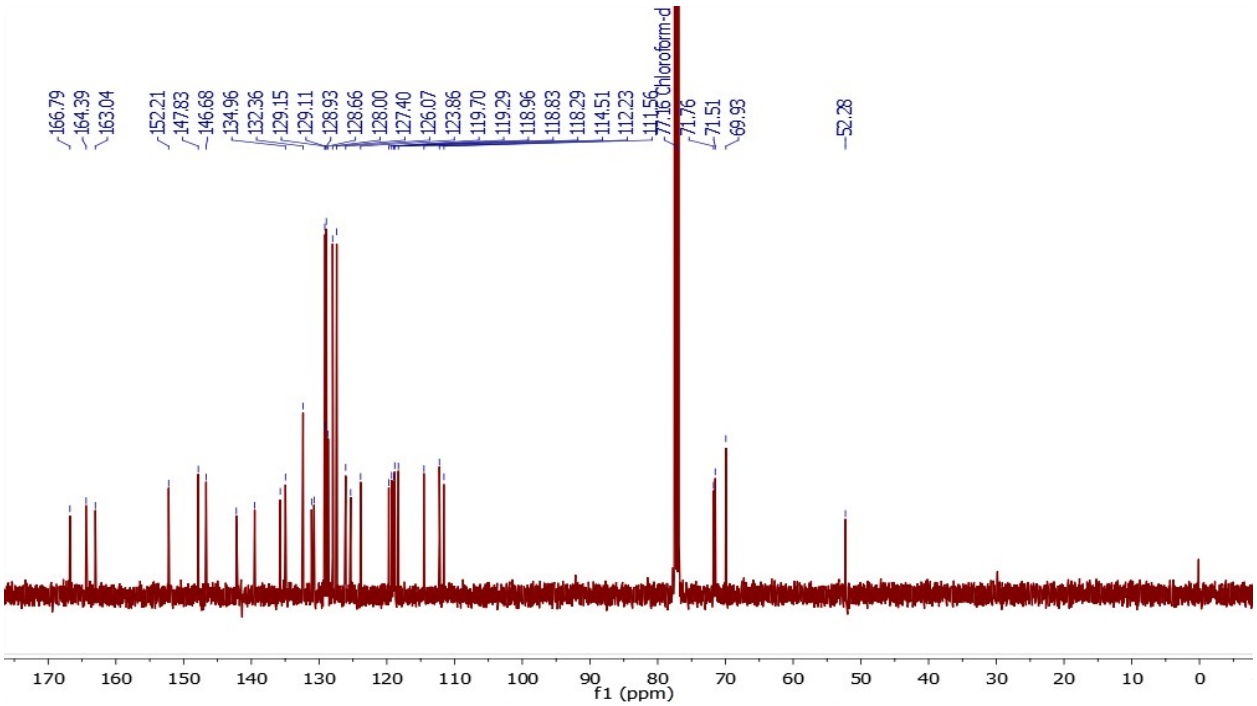


Figure S40. ^{13}C NMR spectrum (126 MHz) of compound **11a** in $CDCl_3$ at 298 K

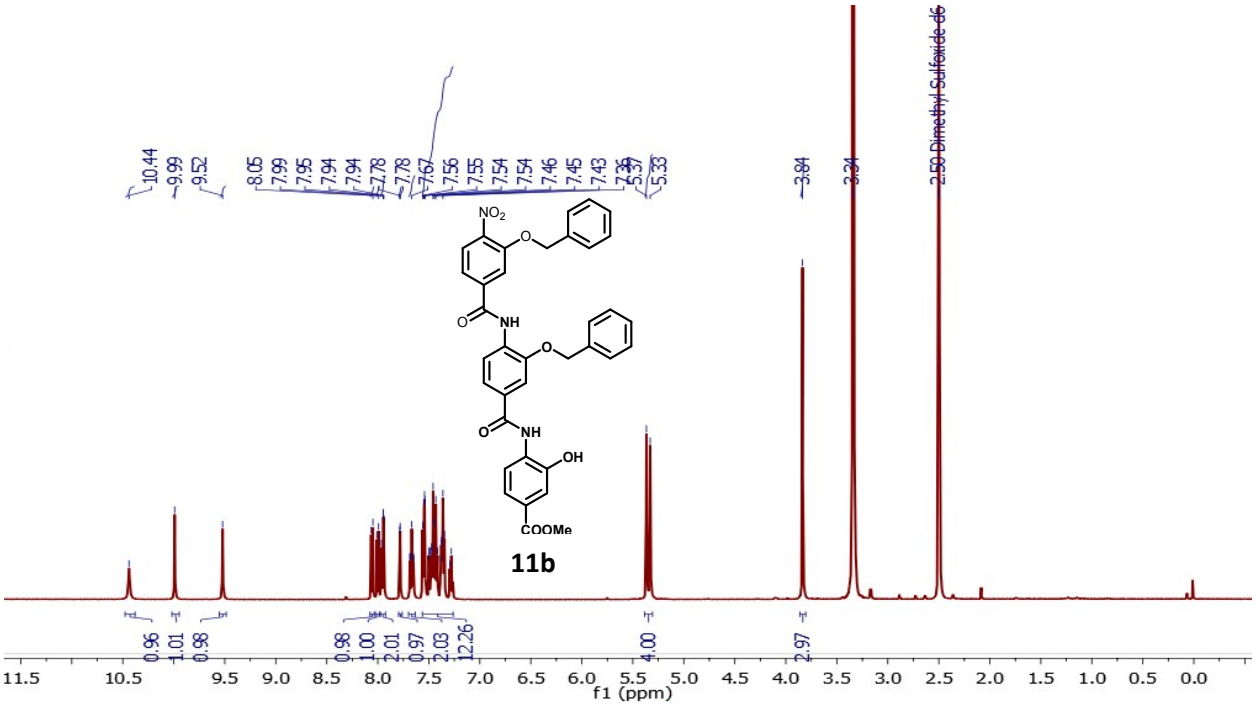


Figure S41. [1]H NMR spectrum (500 MHz) of compound **11b** in DMSO-*d6* at 298 K

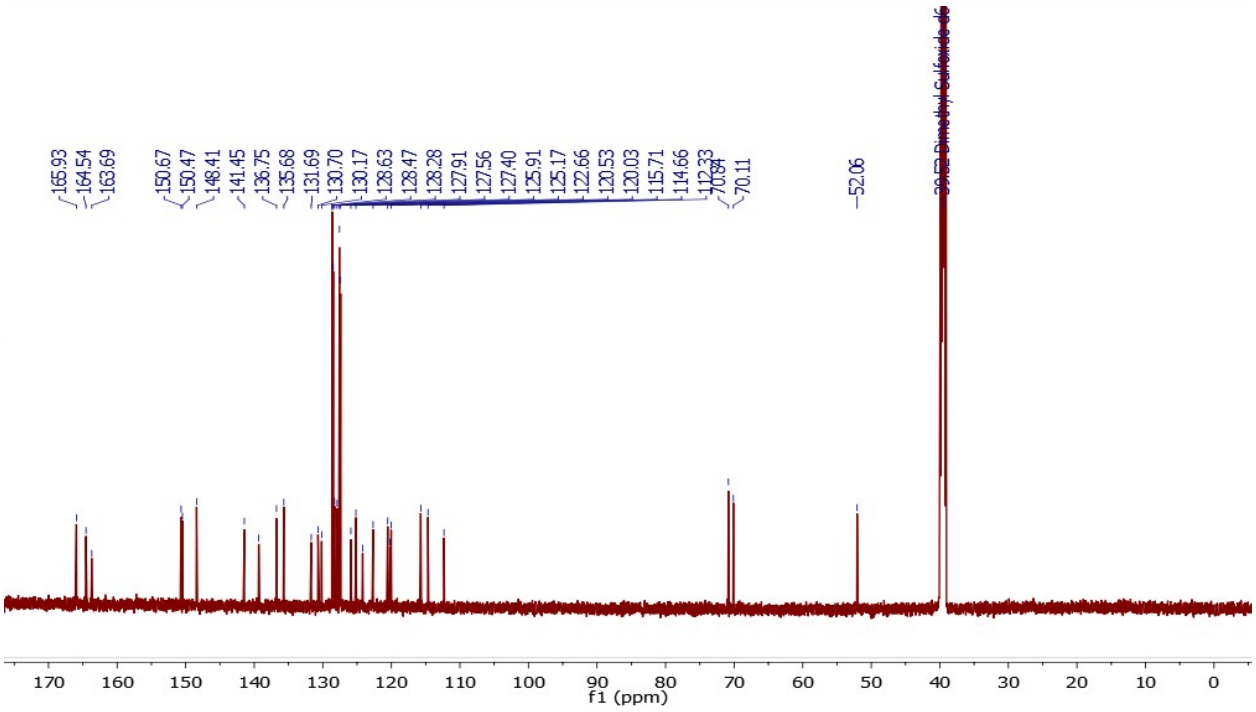


Figure S42. [13]C NMR spectrum (176 MHz) of compound **11b** in DMSO-*d6* at 298 K

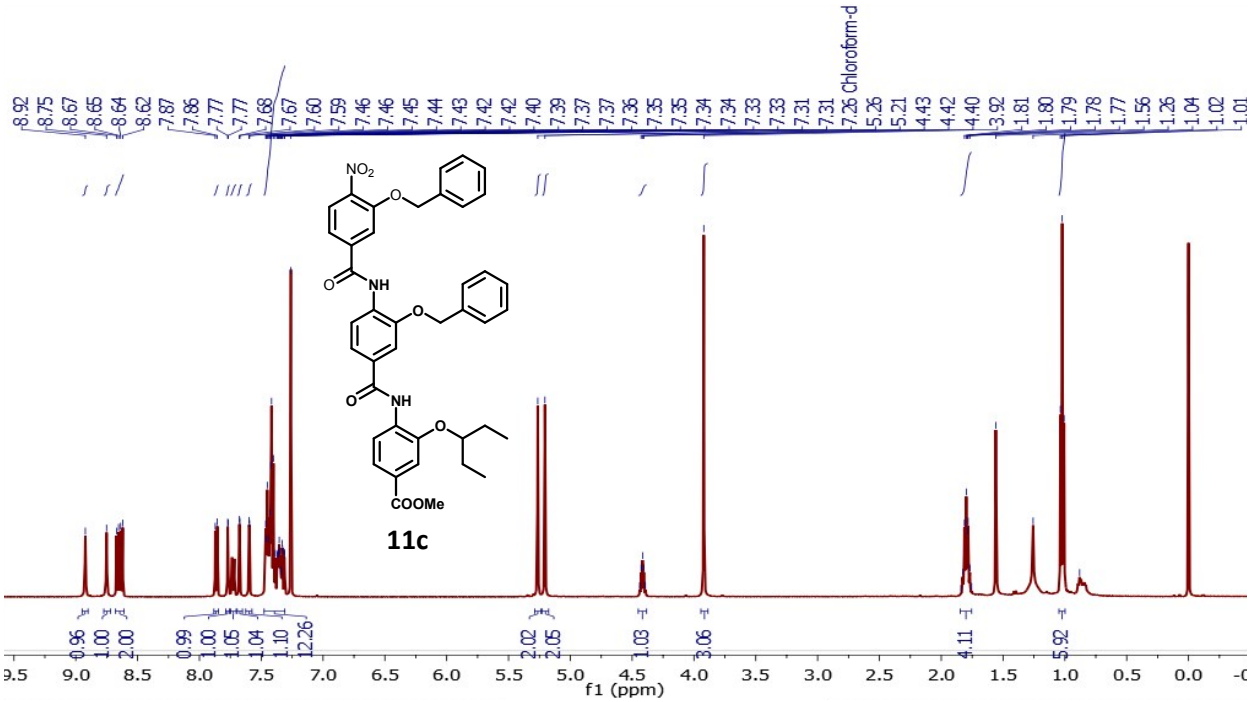


Figure S43. ^{1}H NMR spectrum (500 MHz) of compound **11c** in $CDCl_3$ at 298 K

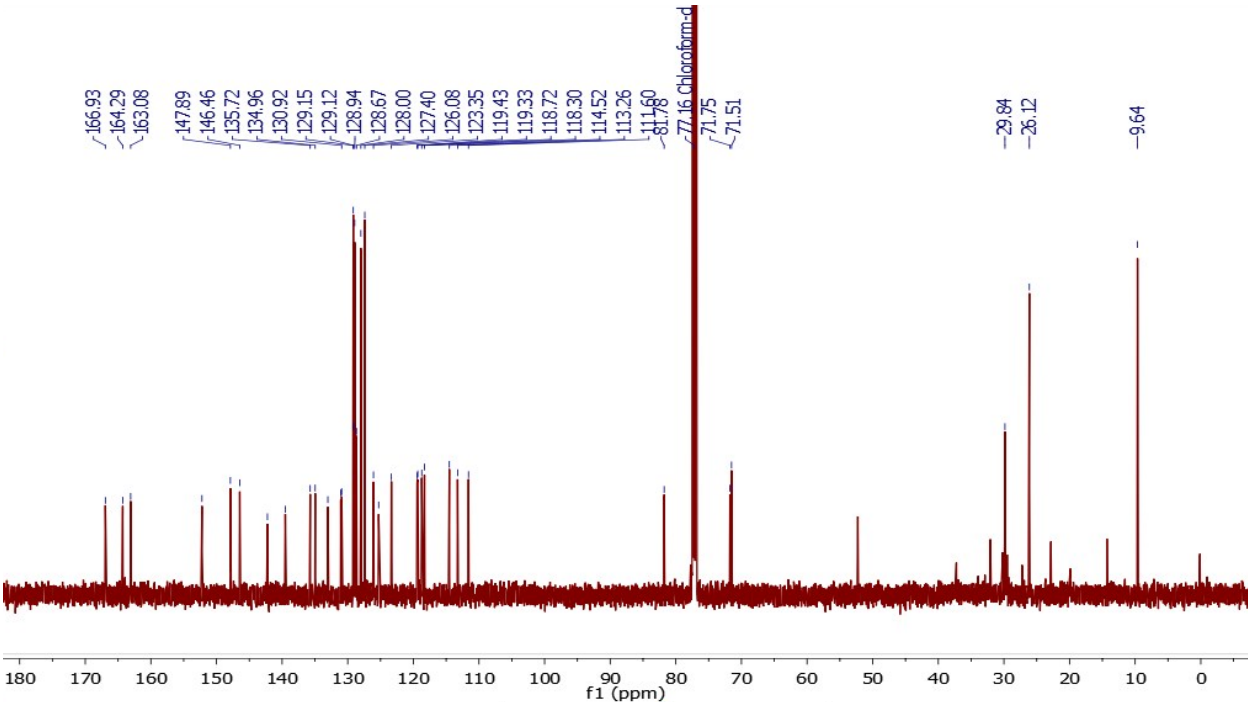


Figure S44. ^{13}C NMR spectrum (126 MHz) of compound **11c** in $CDCl_3$ at 298 K

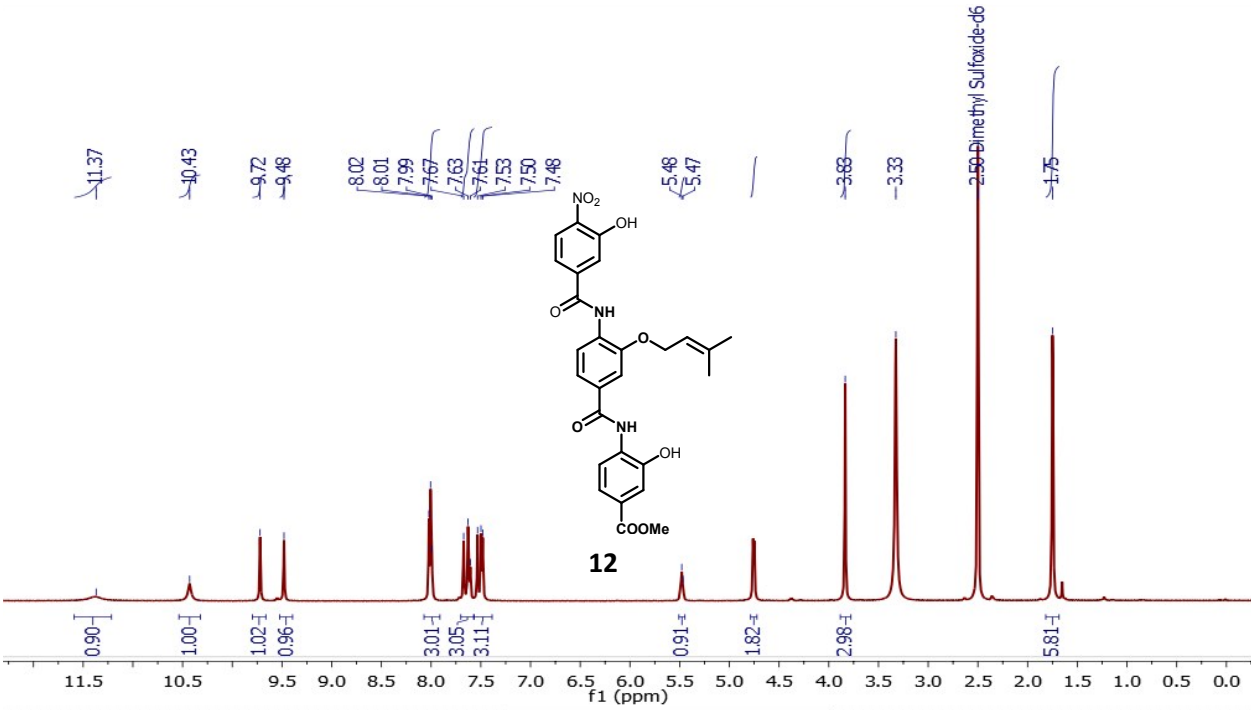


Figure S45. ^{1}H NMR spectrum (500 MHz) of compound **12** in DMSO-*d6* at 298 K

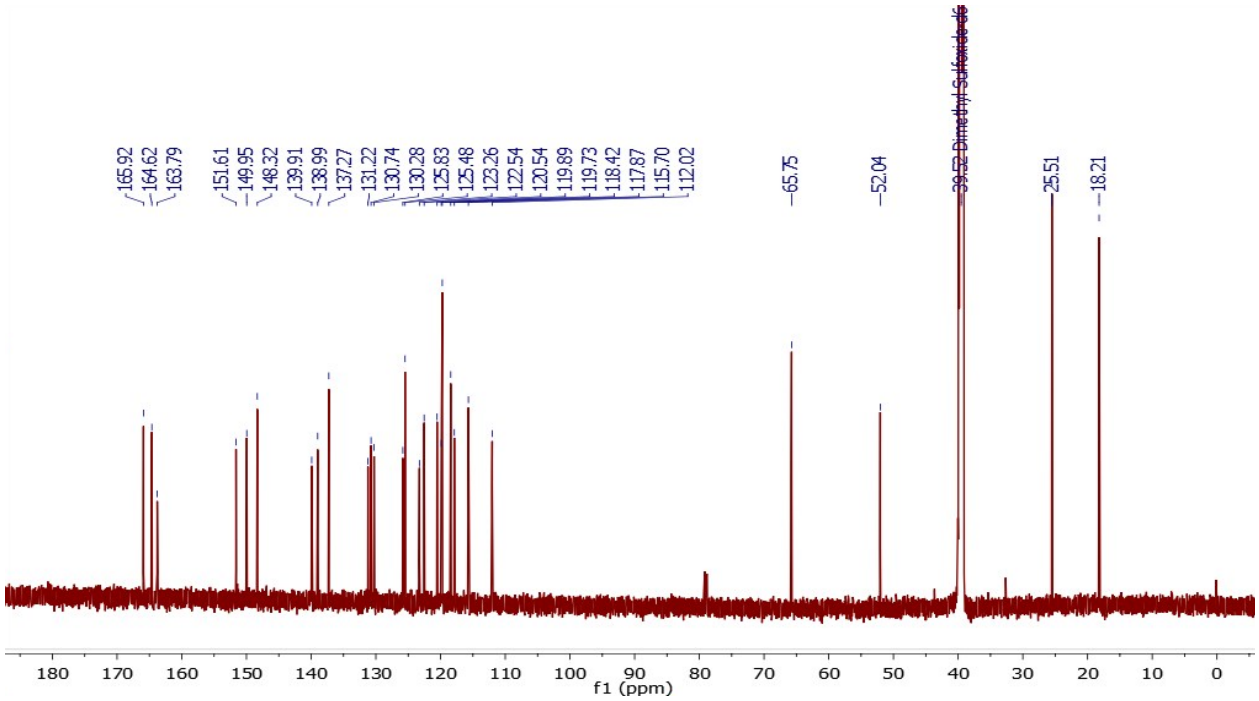


Figure S46. ^{13}C NMR spectrum (176 MHz) of compound **12** in DMSO-*d6* at 298 K

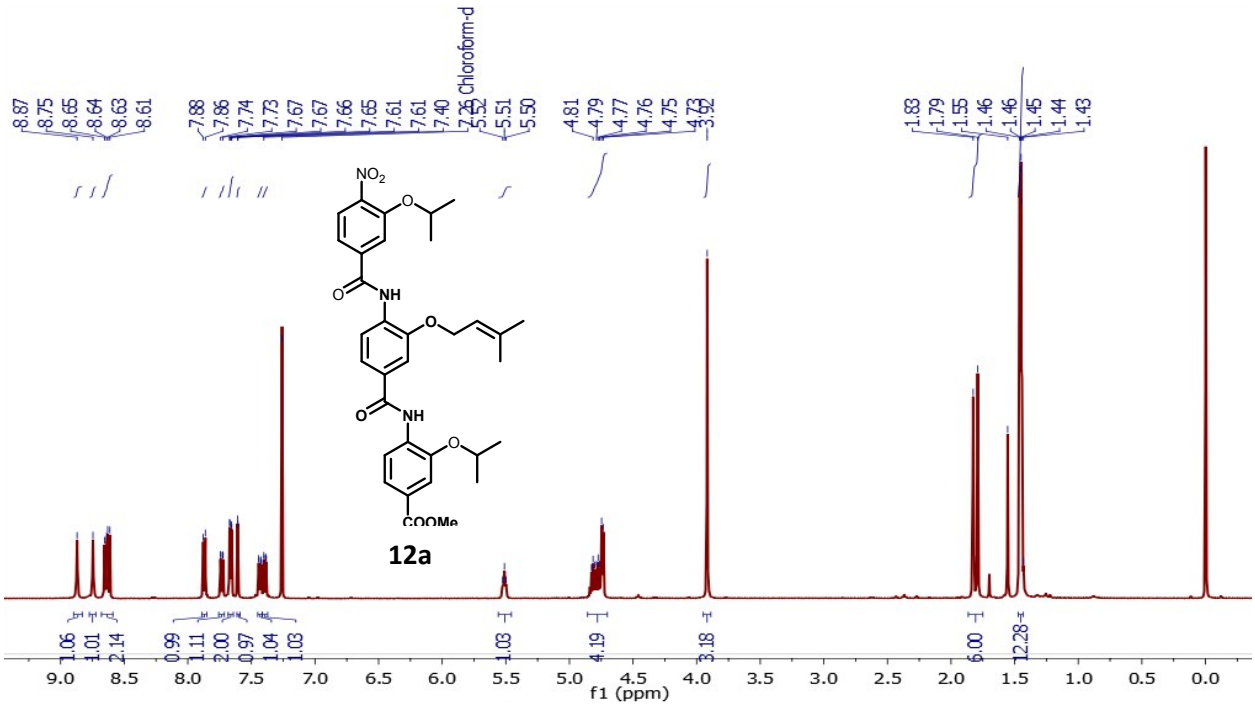


Figure S47. ^{1}H NMR spectrum (500 MHz) of compound **12a** in $CDCl_3$ at 298 K

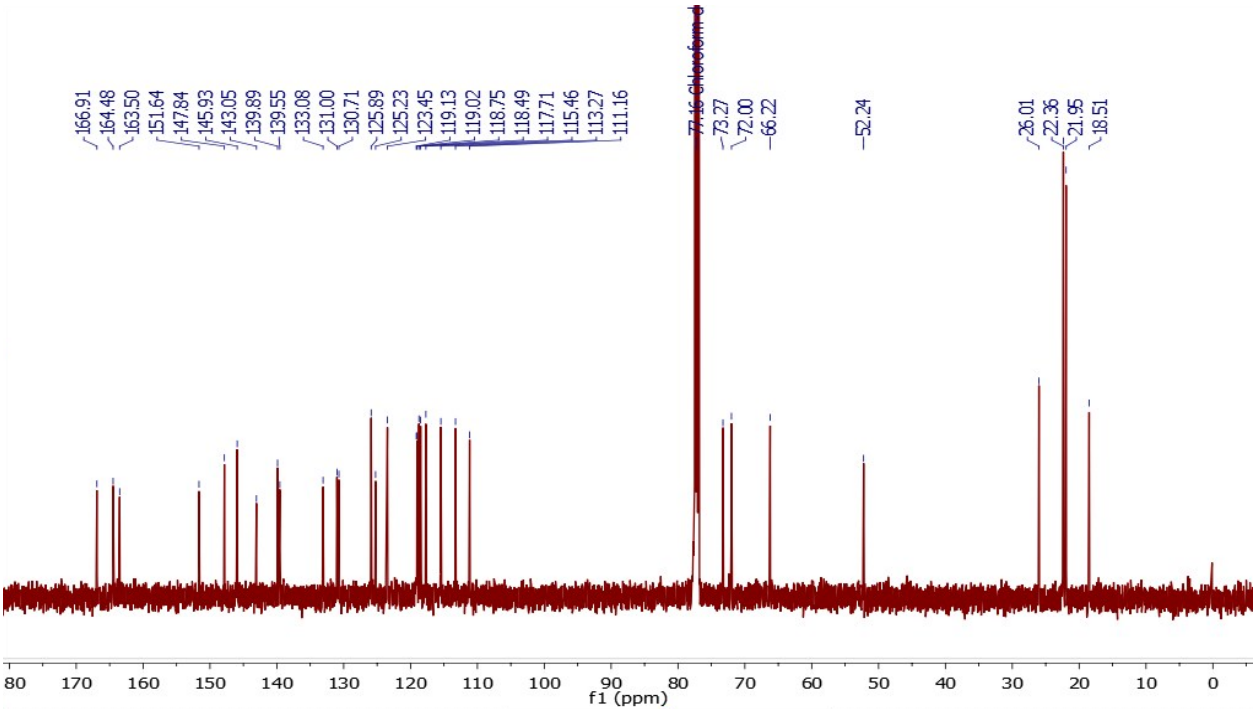


Figure S48. ^{13}C NMR spectrum (126 MHz) of compound **12a** in $CDCl_3$ at 298 K

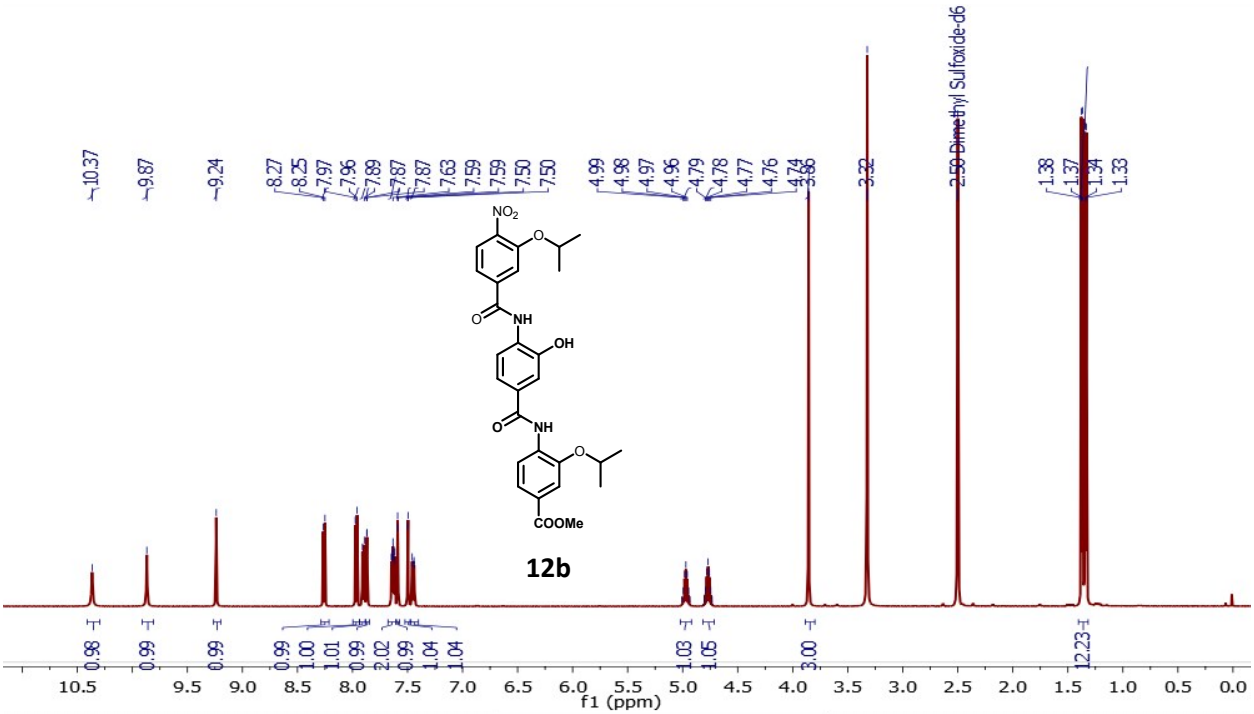


Figure S49. [1]H NMR spectrum (500 MHz) of compound **12b** in DMSO-*d6* at 298 K

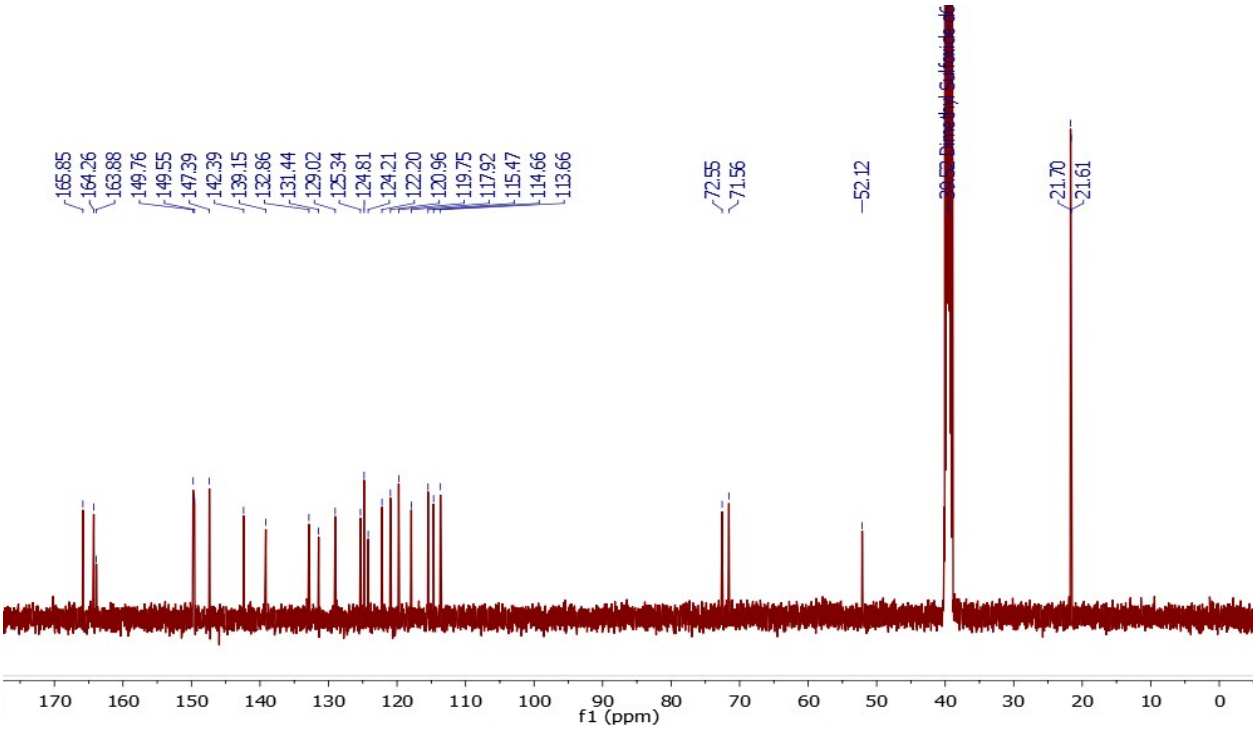


Figure S50. [13]C NMR spectrum (126 MHz) of compound **12b** in DMSO-*d6* at 298 K

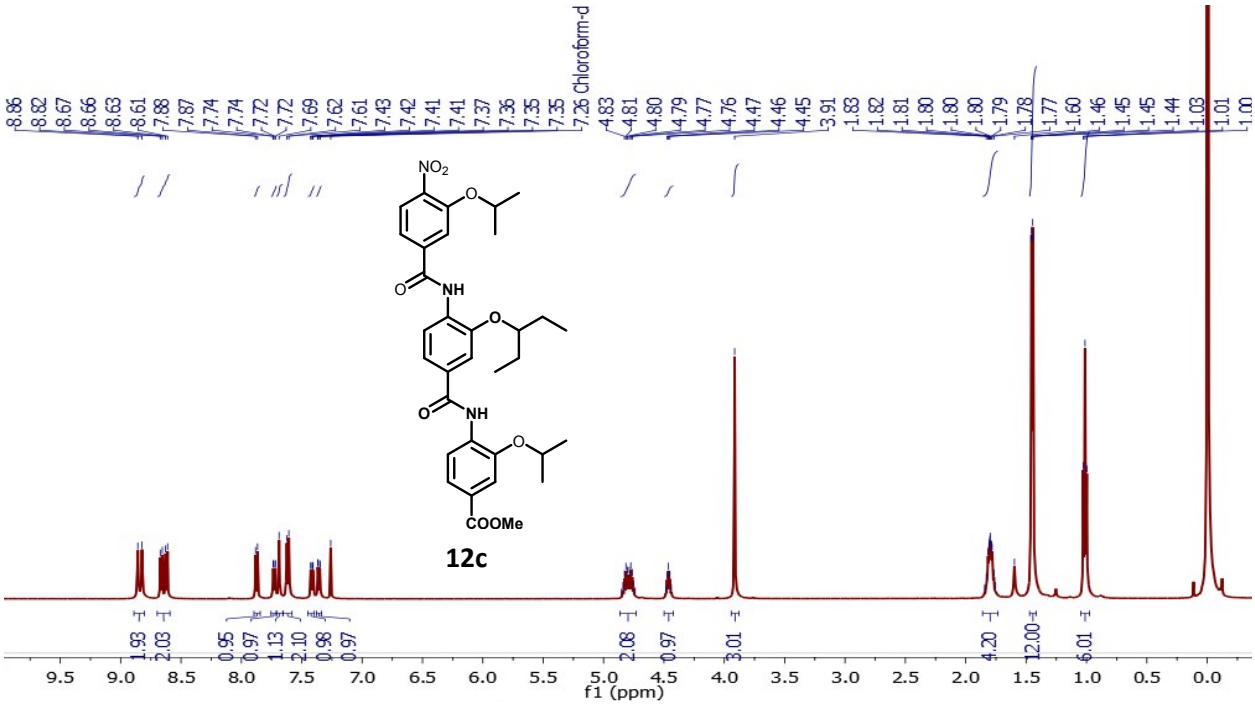


Figure S51. ^{1}H NMR spectrum (500 MHz) of compound **12c** in $CDCl_3$ at 298 K

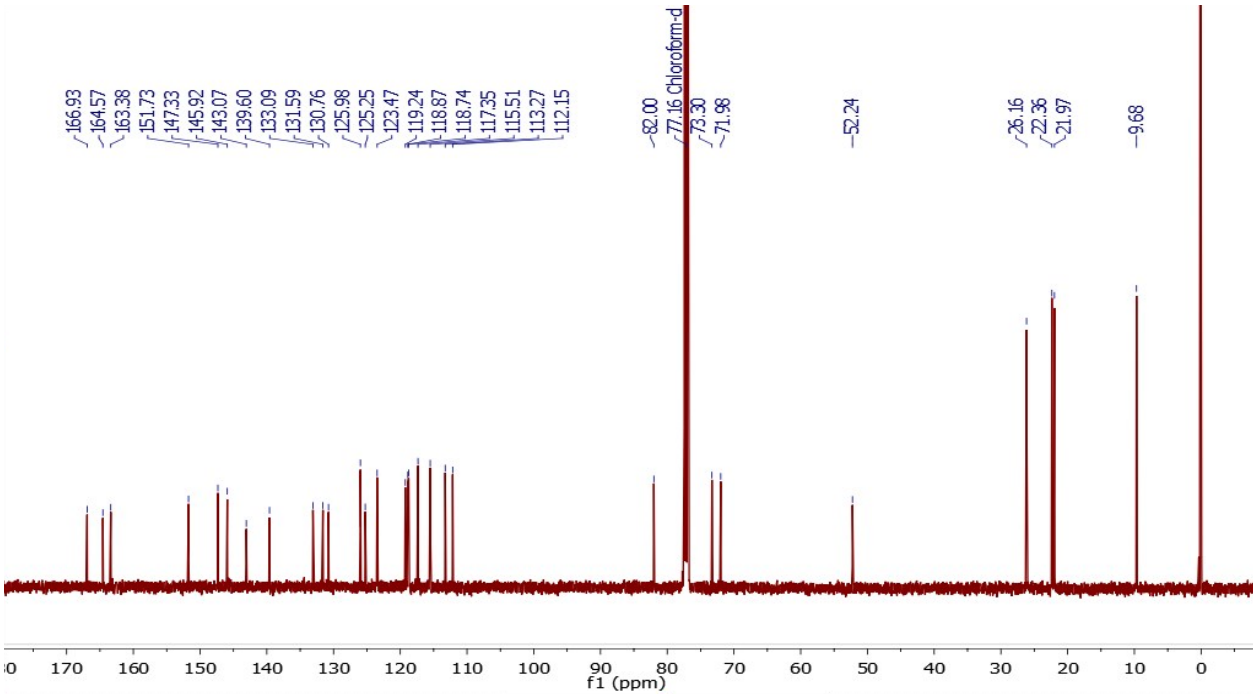


Figure S52. ^{13}C NMR spectrum (126 MHz) of compound **12c** in $CDCl_3$ at 298 K

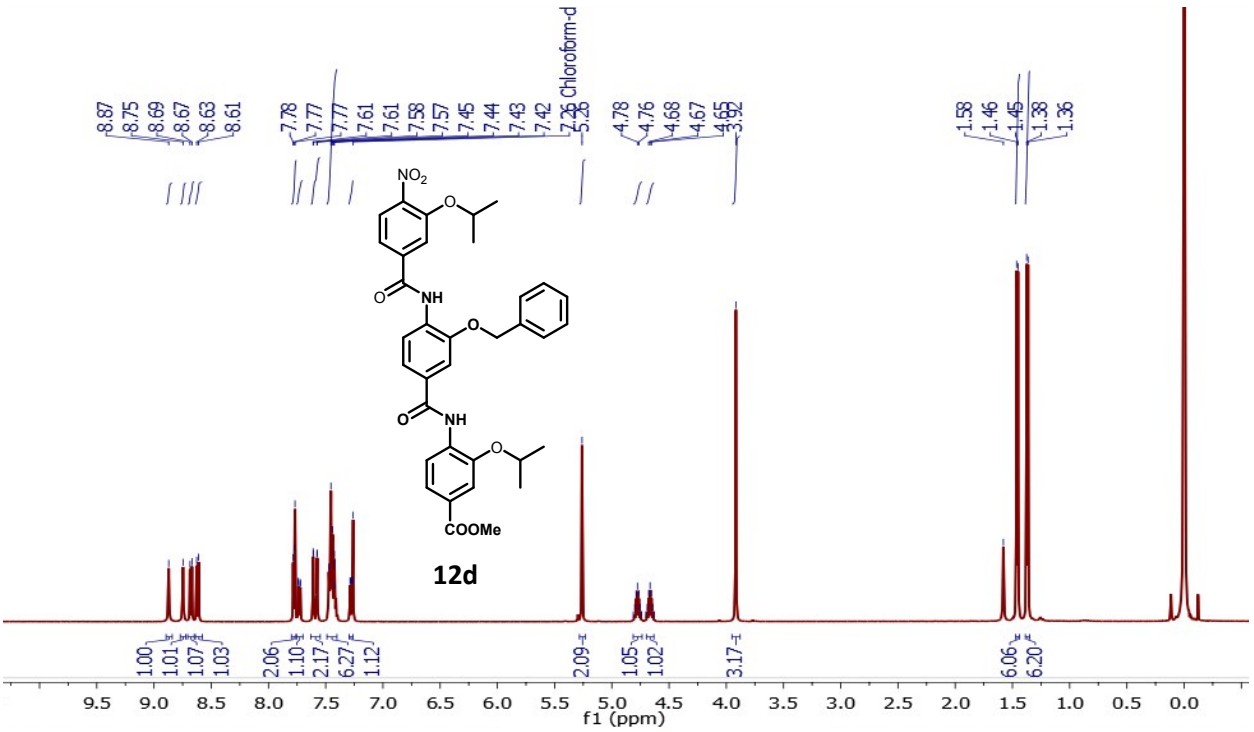


Figure S53. ^{1}H NMR spectrum (500 MHz) of compound **12d** in $CDCl_3$ at 298 K

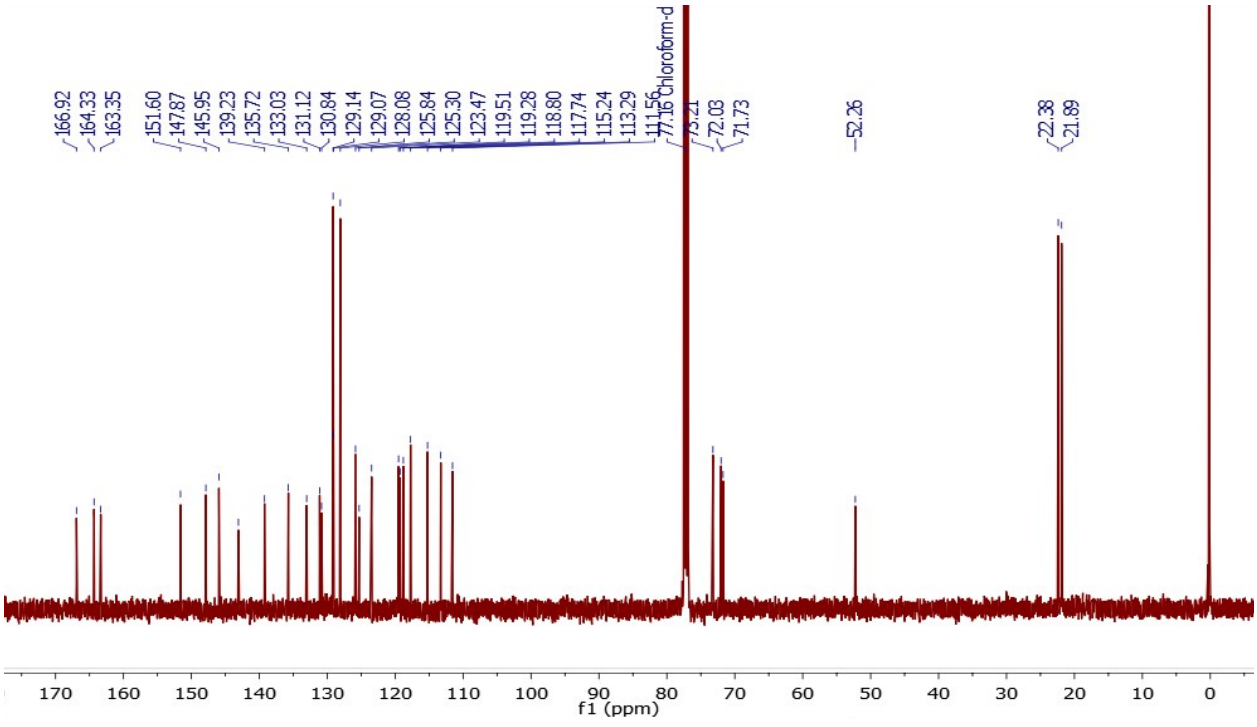


Figure S54. ^{13}C NMR spectrum (126 MHz) of compound **12d** in $CDCl_3$ at 298 K

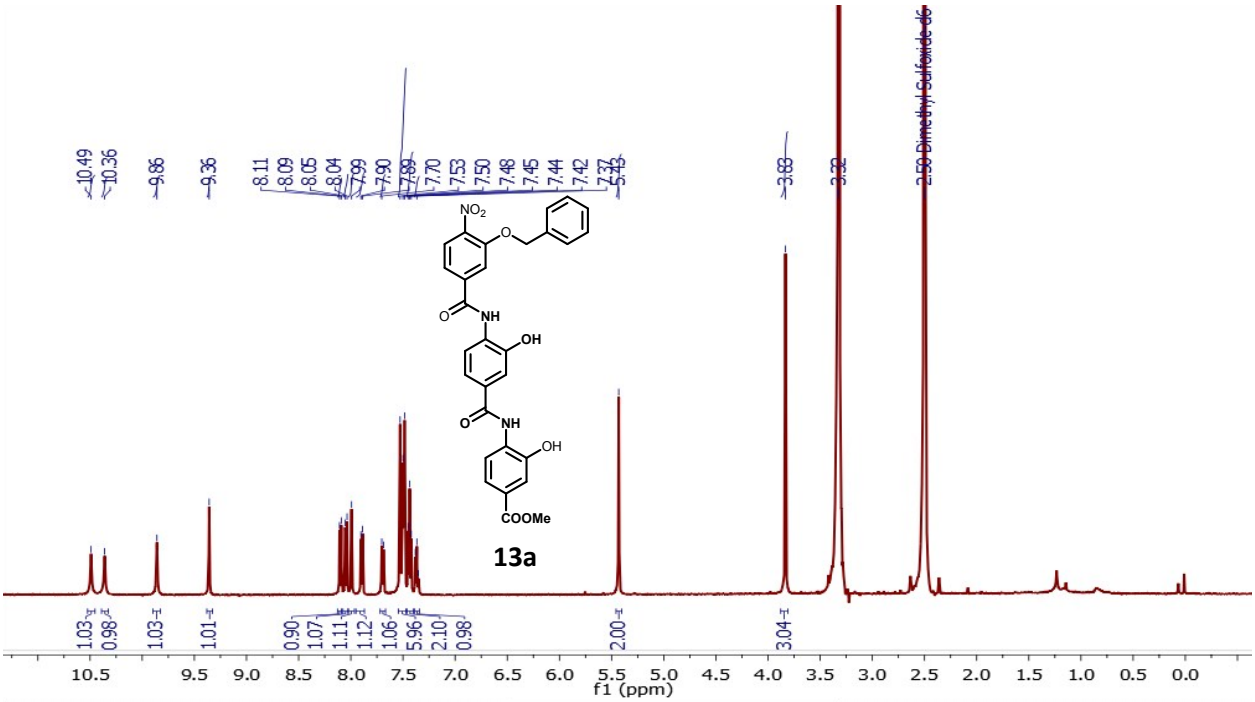


Figure S55. [1]H NMR spectrum (500 MHz) of compound **13a** in DMSO-*d6* at 298 K

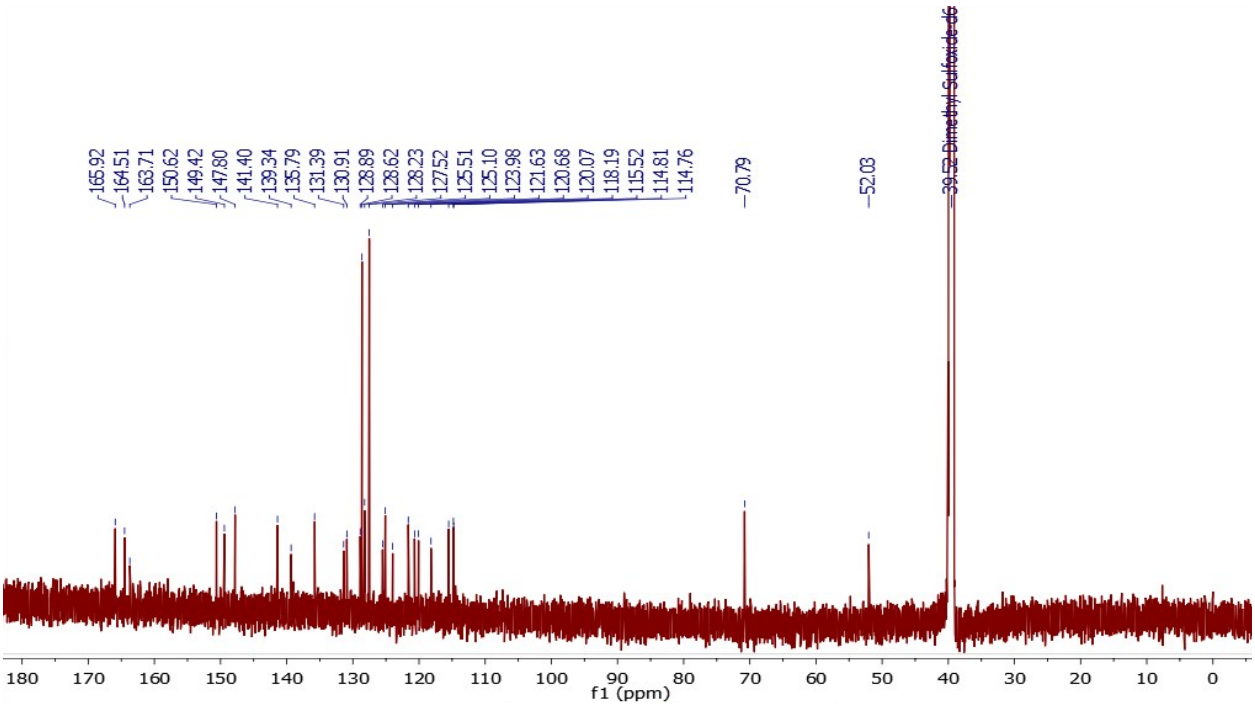


Figure S56. [13]C NMR spectrum (176 MHz) of compound **13a** in DMSO-*d6* at 298 K

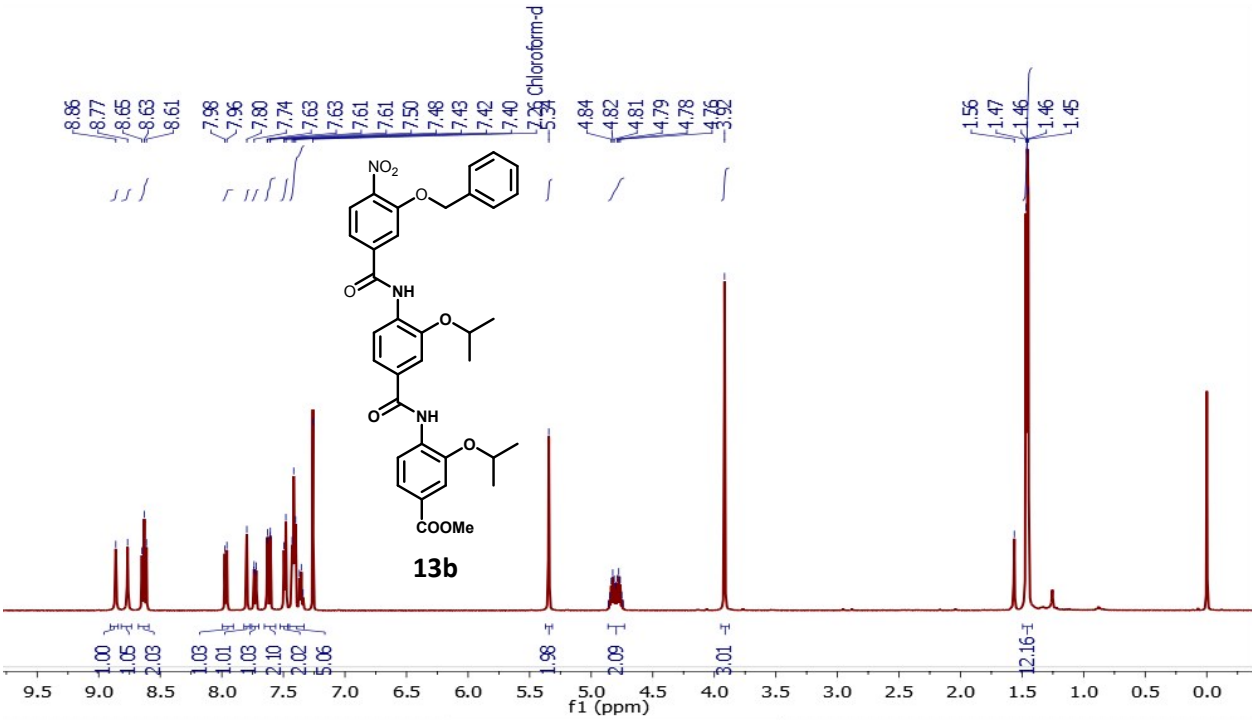


Figure S57. ^{1}H NMR spectrum (500 MHz) of compound **13b** in $CDCl_3$ at 298 K

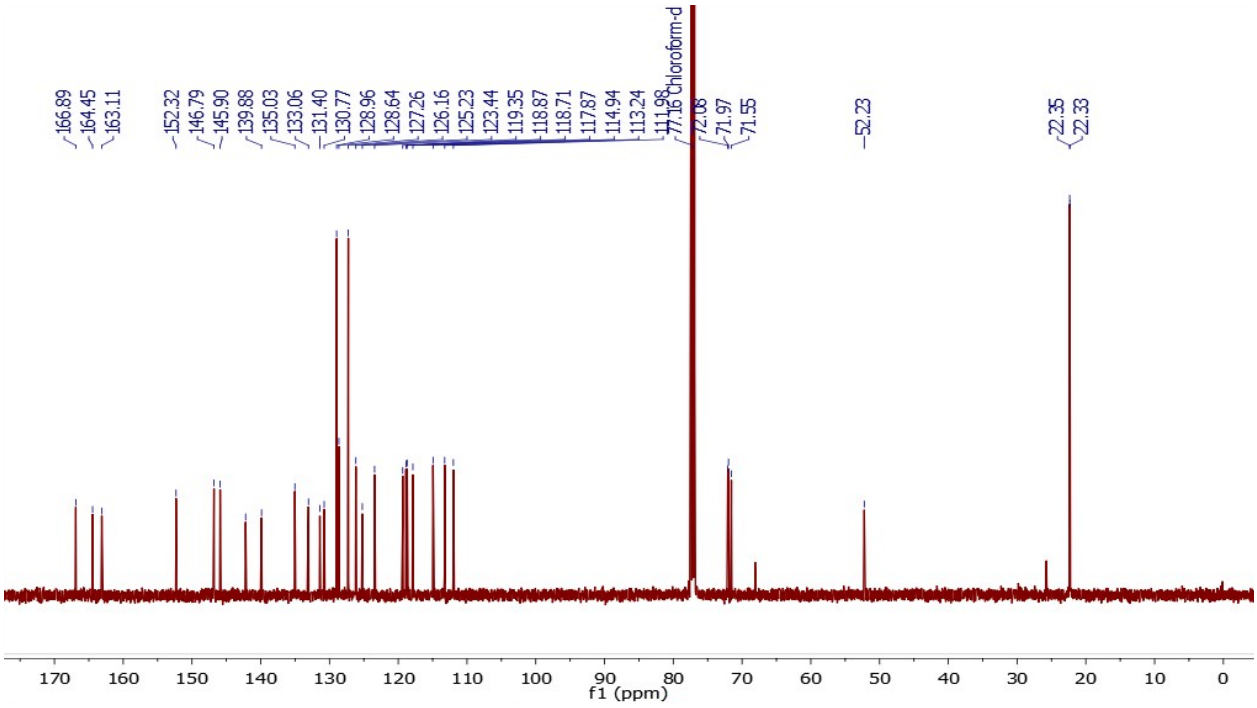


Figure S58. ^{13}C NMR spectrum (126 MHz) of compound **13b** in $CDCl_3$ at 298 K

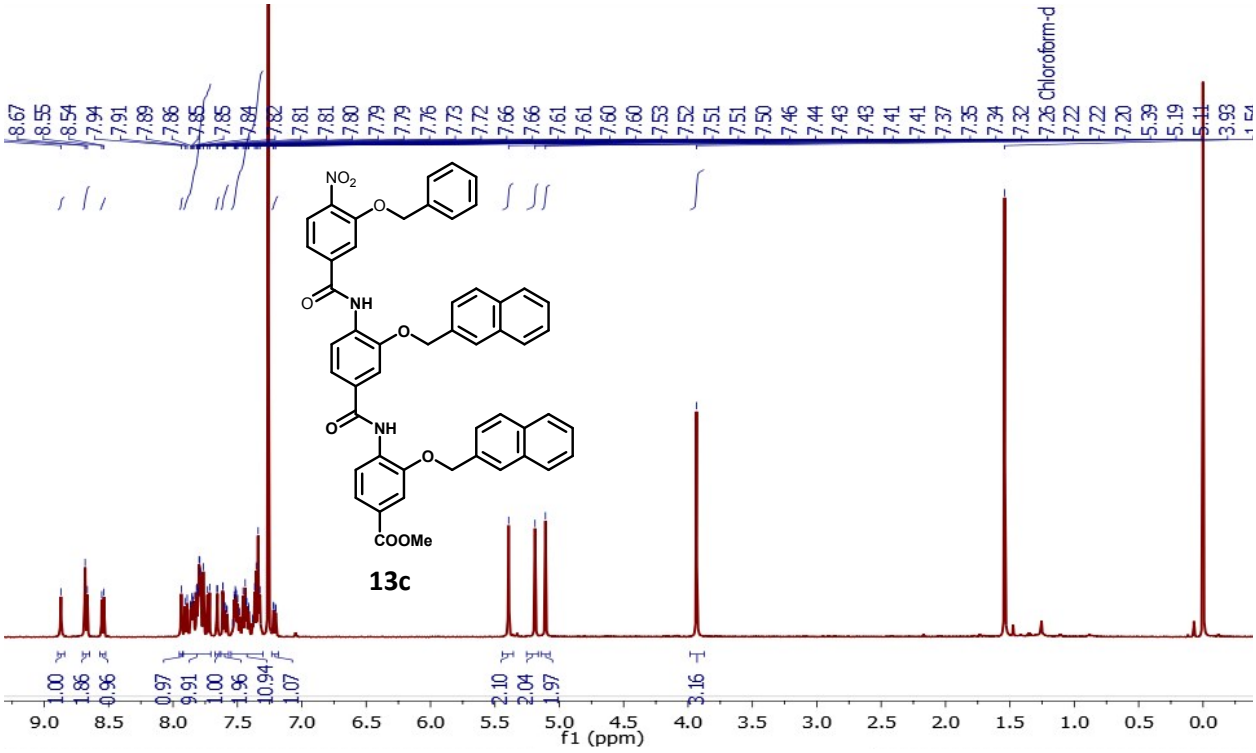


Figure S59. ^{1}H NMR spectrum (500 MHz) of compound **13c** in $CDCl_3$ at 298 K

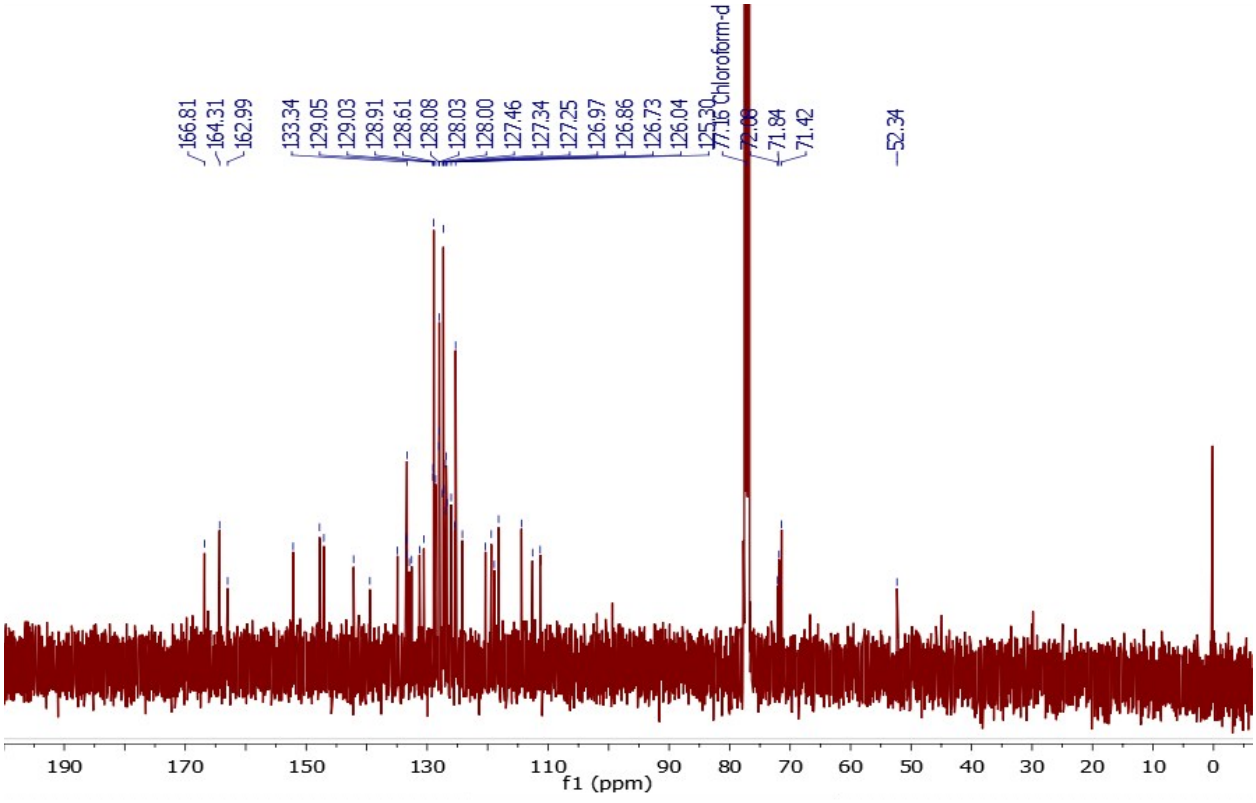


Figure S60. ^{13}C NMR spectrum (126 MHz) of compound **13c** in $CDCl_3$ at 298 K

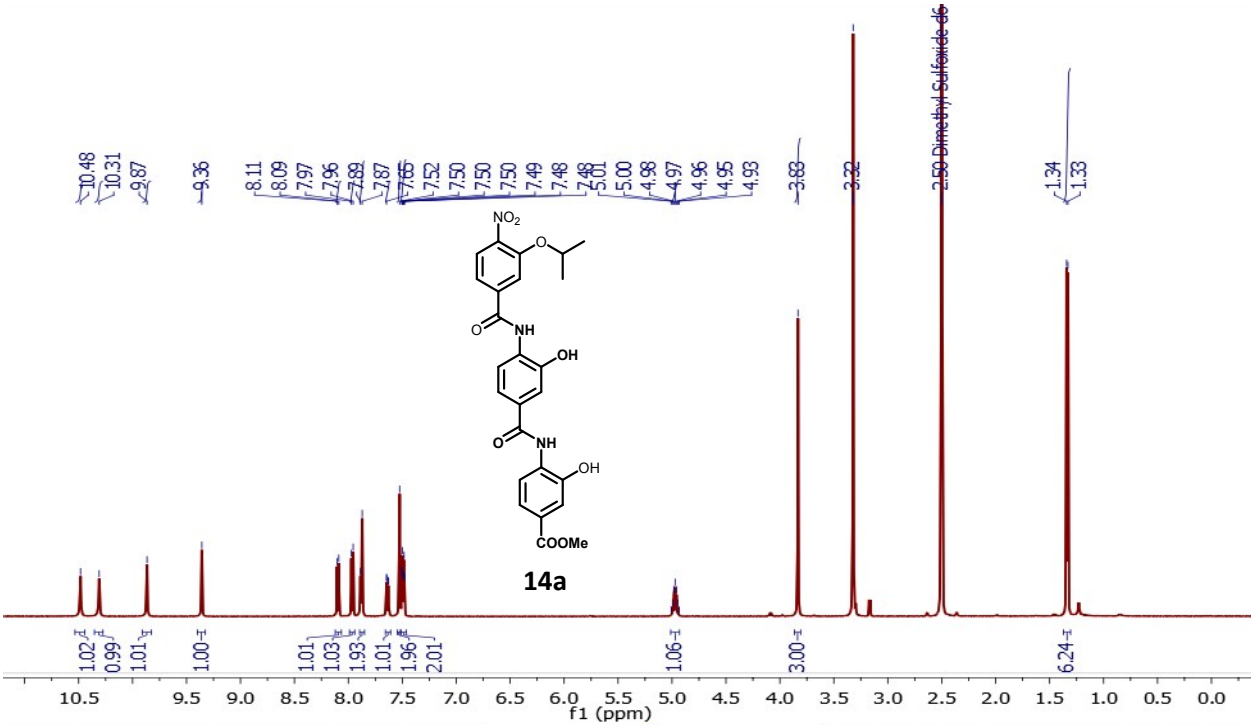


Figure S61. ^{1}H NMR spectrum (500 MHz) of compound **14a** in DMSO-*d6* at 298 K

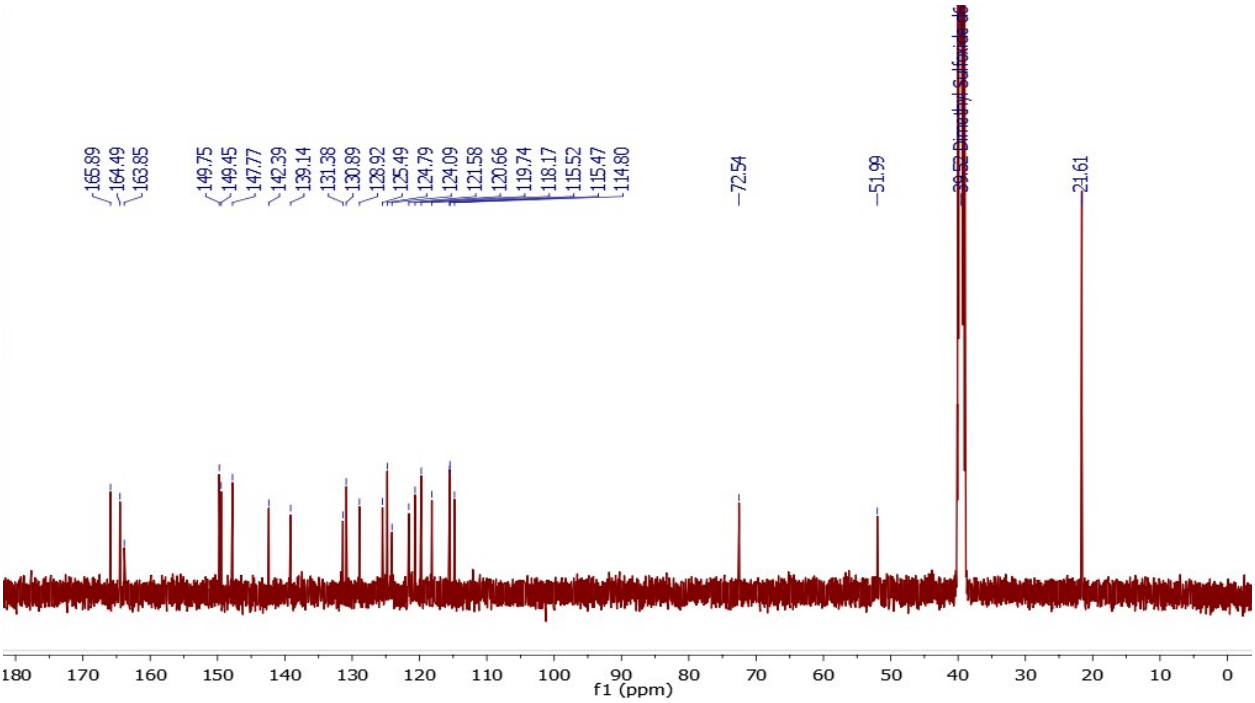


Figure S62. ^{13}C NMR spectrum (126 MHz) of compound **14a** in DMSO-*d6* at 298 K

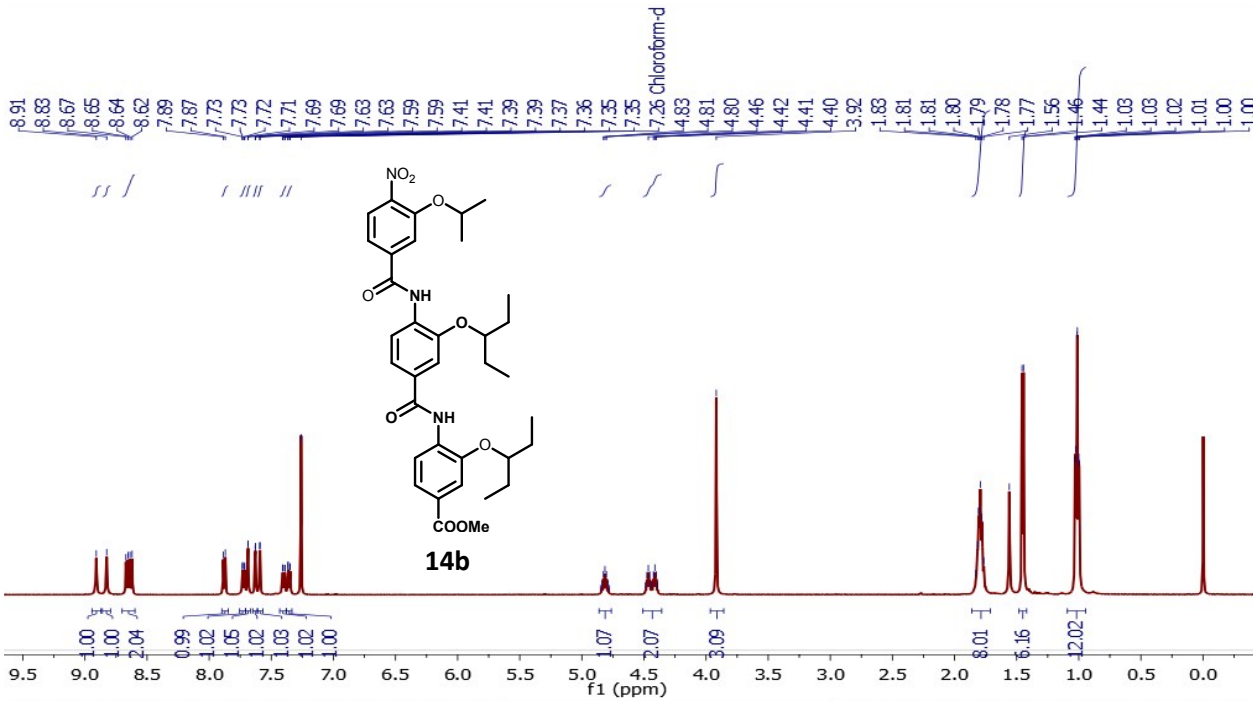


Figure S63 ^{1}H NMR spectrum (500 MHz) of compound **14b** in $CDCl_3$ at 298 K

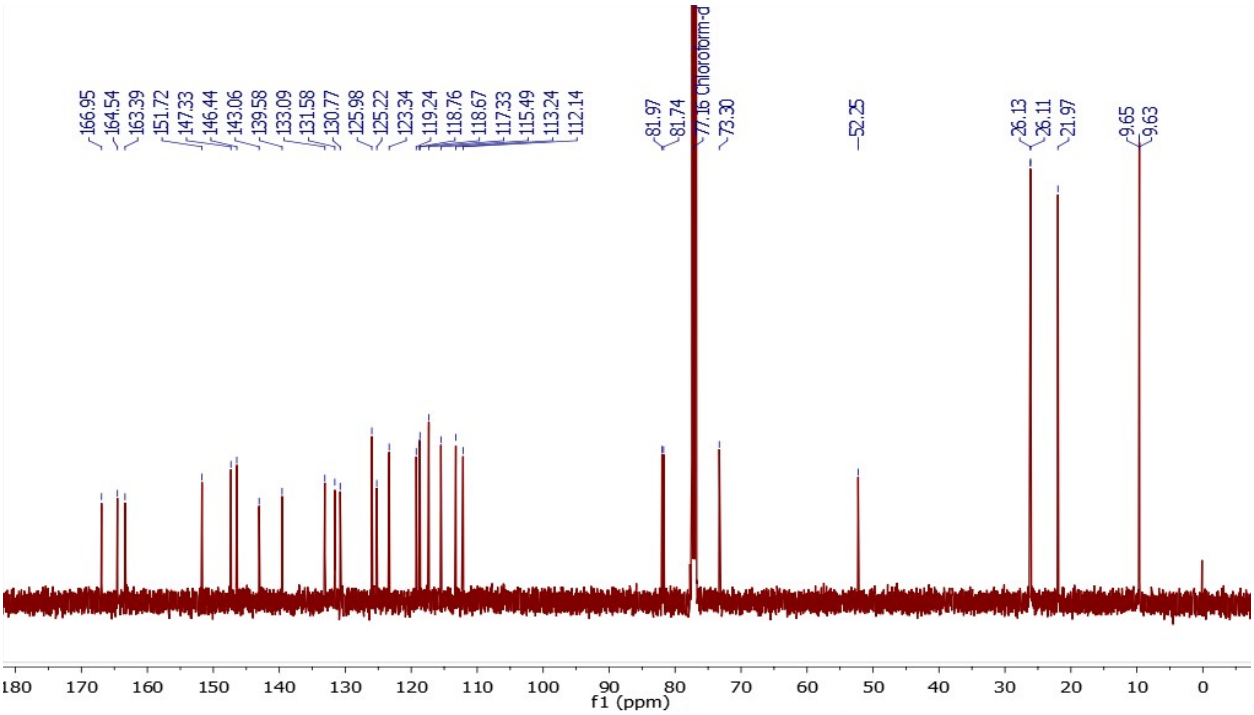


Figure S64. ^{13}C NMR spectrum (126 MHz) of compound **14b** in $CDCl_3$ at 298 K

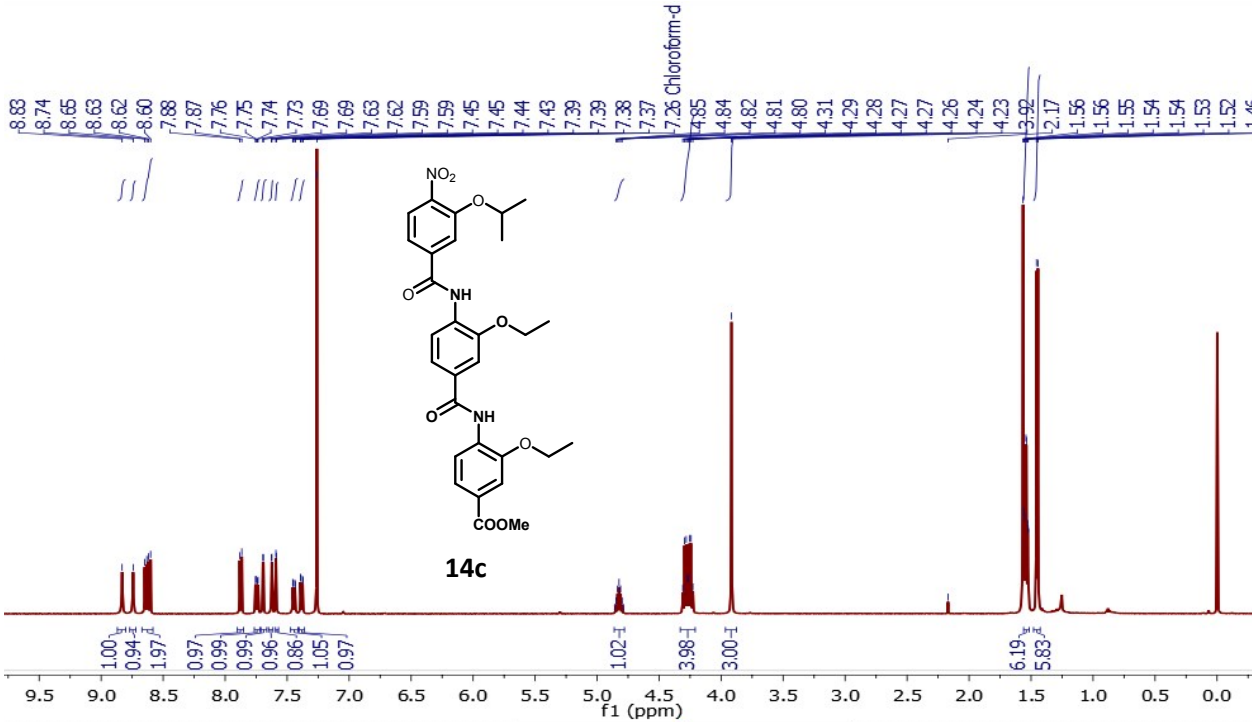


Figure S65. ^{1}H NMR spectrum (500 MHz) of compound **14c** in $CDCl_3$ at 298 K

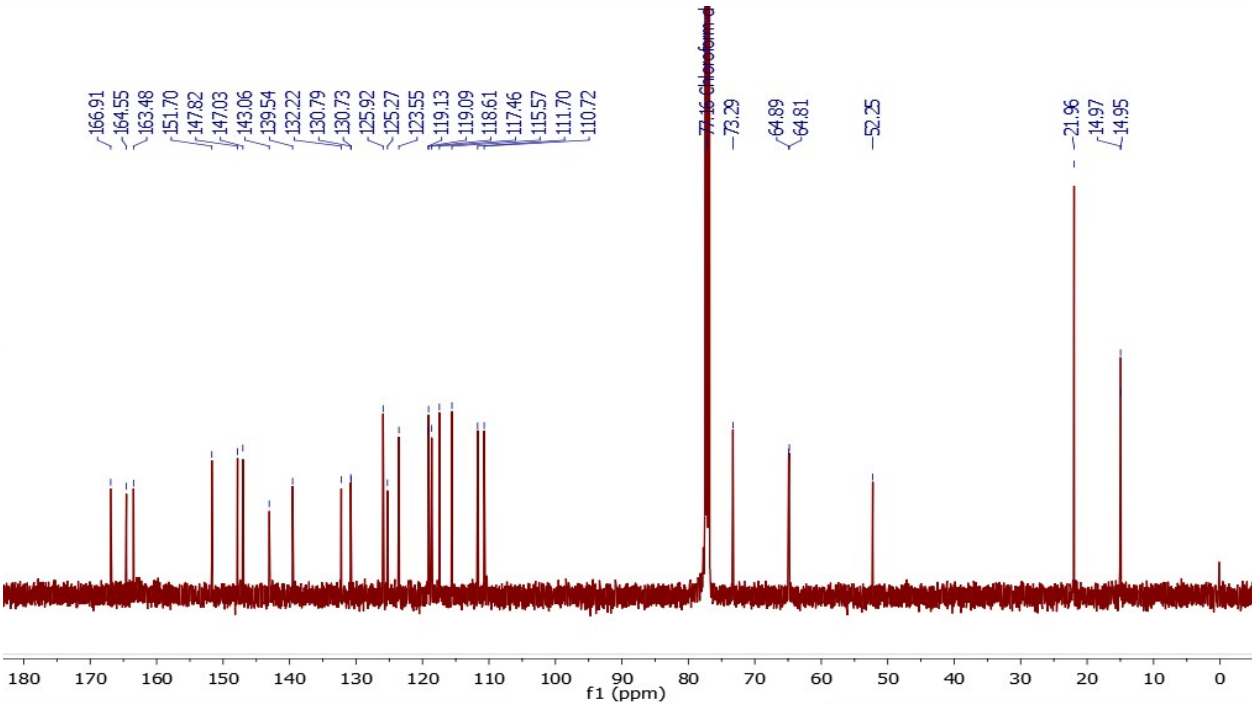


Figure S66. ^{13}C NMR spectrum (126 MHz) of compound **14c** in $CDCl_3$ at 298 K

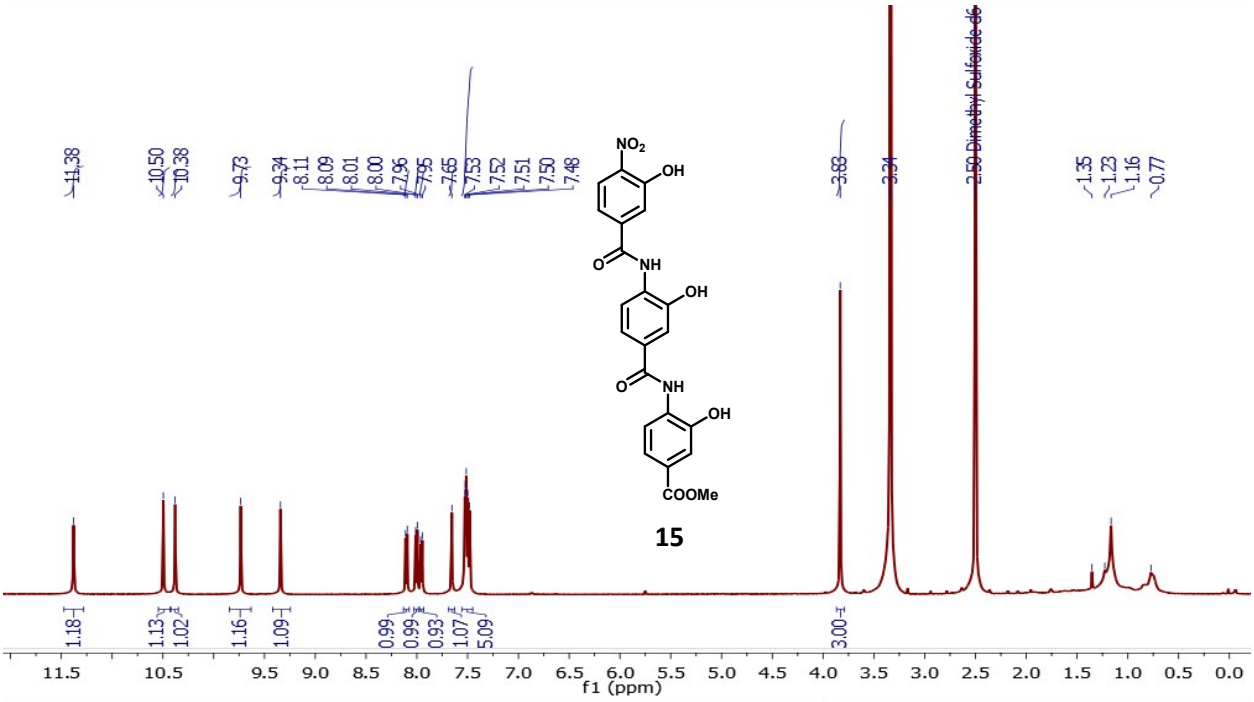


Figure S67. ^{1}H NMR spectrum (500 MHz) of compound **15** in DMSO-*d6* at 298 K

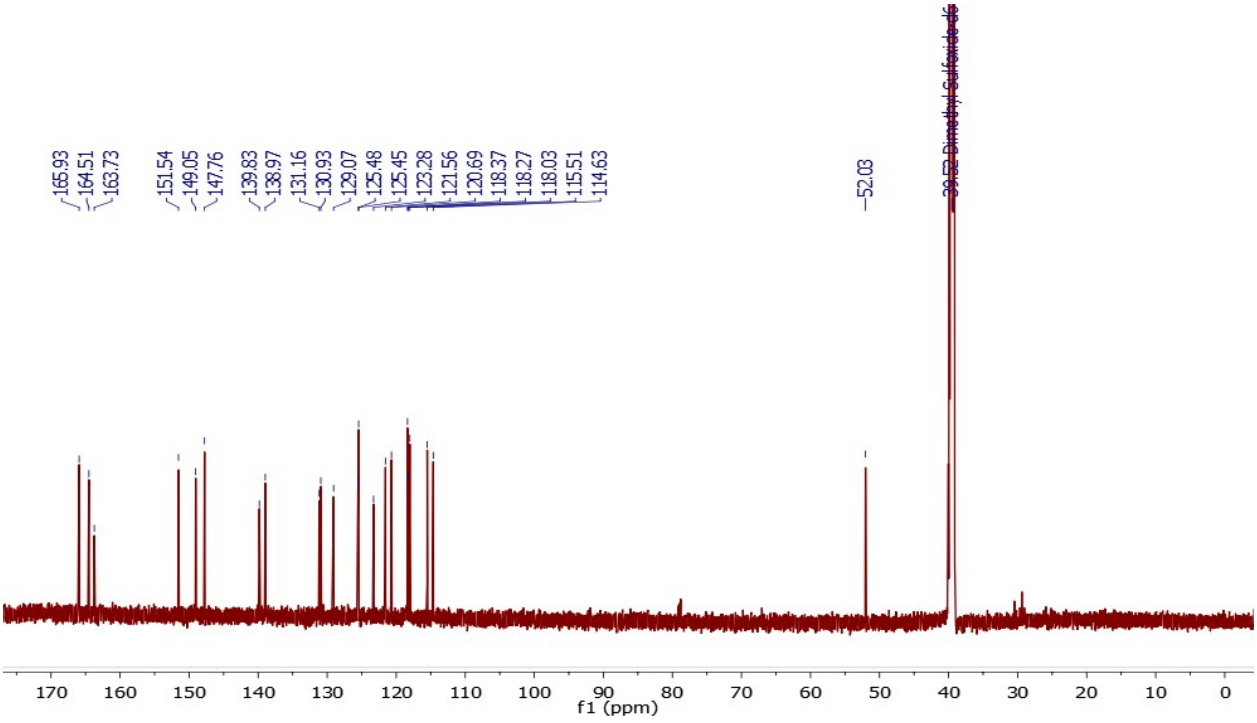


Figure S68. ^{13}C NMR spectrum (176 MHz) of compound **15** in DMSO-*d6* at 298 K

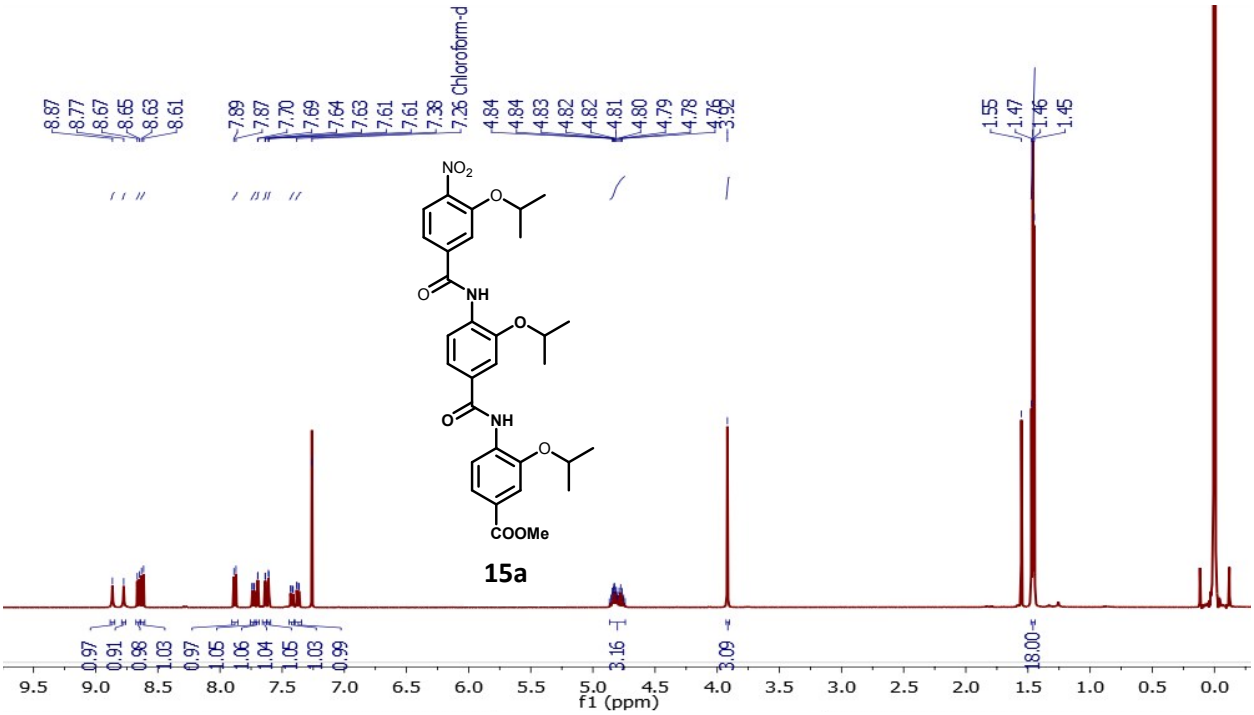


Figure S69. ^{1}H NMR spectrum (500 MHz) of compound **15a** in $CDCl_3$ at 298 K

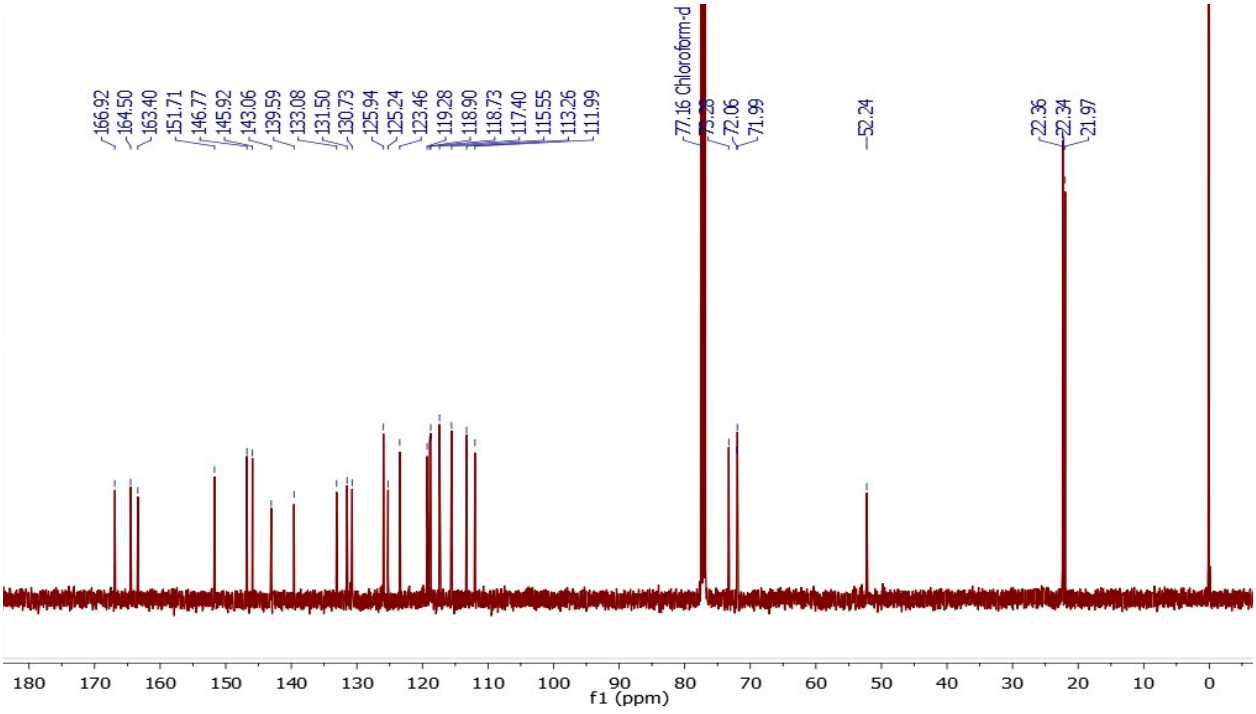


Figure S70. ^{13}C NMR spectrum (126 MHz) of compound **15a** in $CDCl_3$ at 298 K

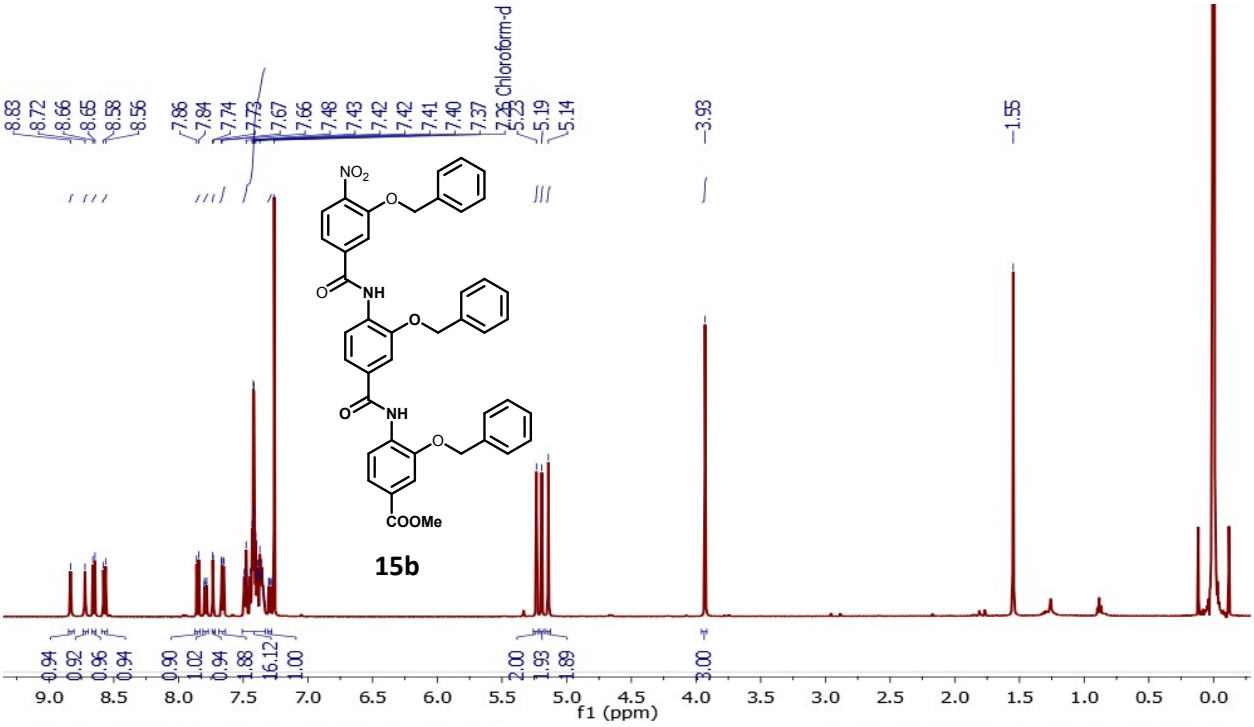


Figure S71. ^{1}H NMR spectrum (500 MHz) of compound **15b** in $CDCl_3$ at 298 K

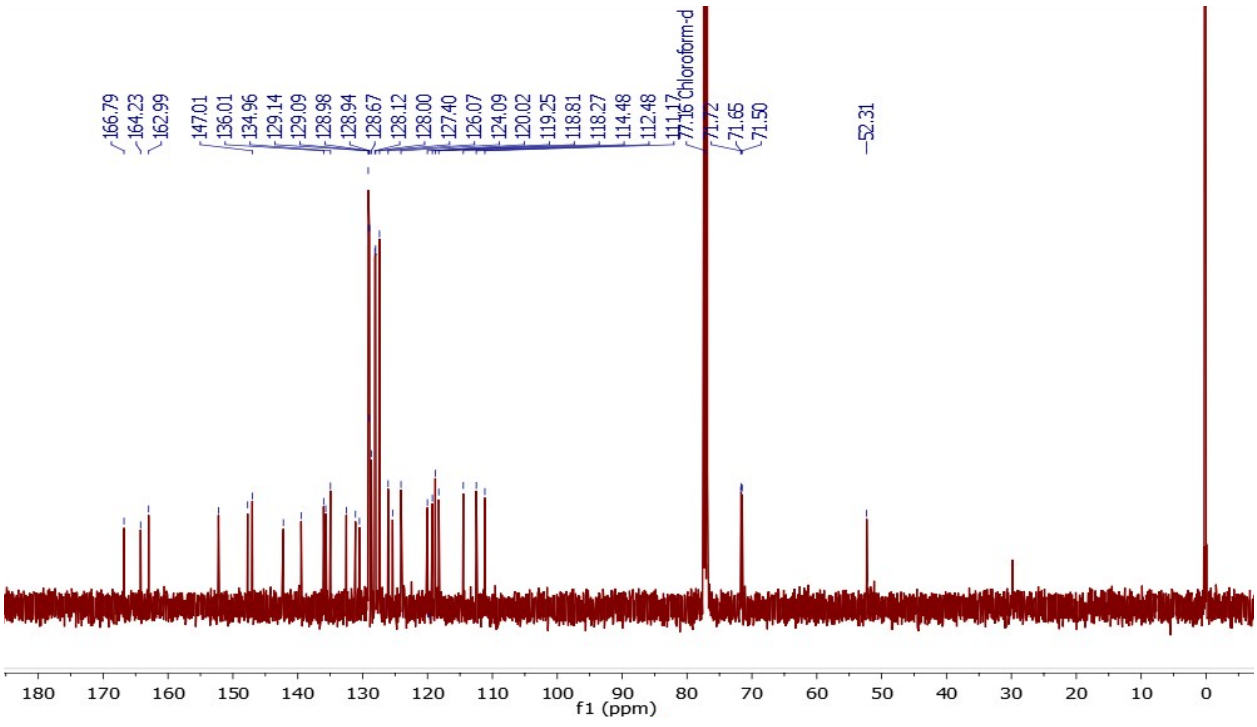


Figure S72. ^{13}C NMR spectrum (126 MHz) of compound **15b** in $CDCl_3$ at 298 K

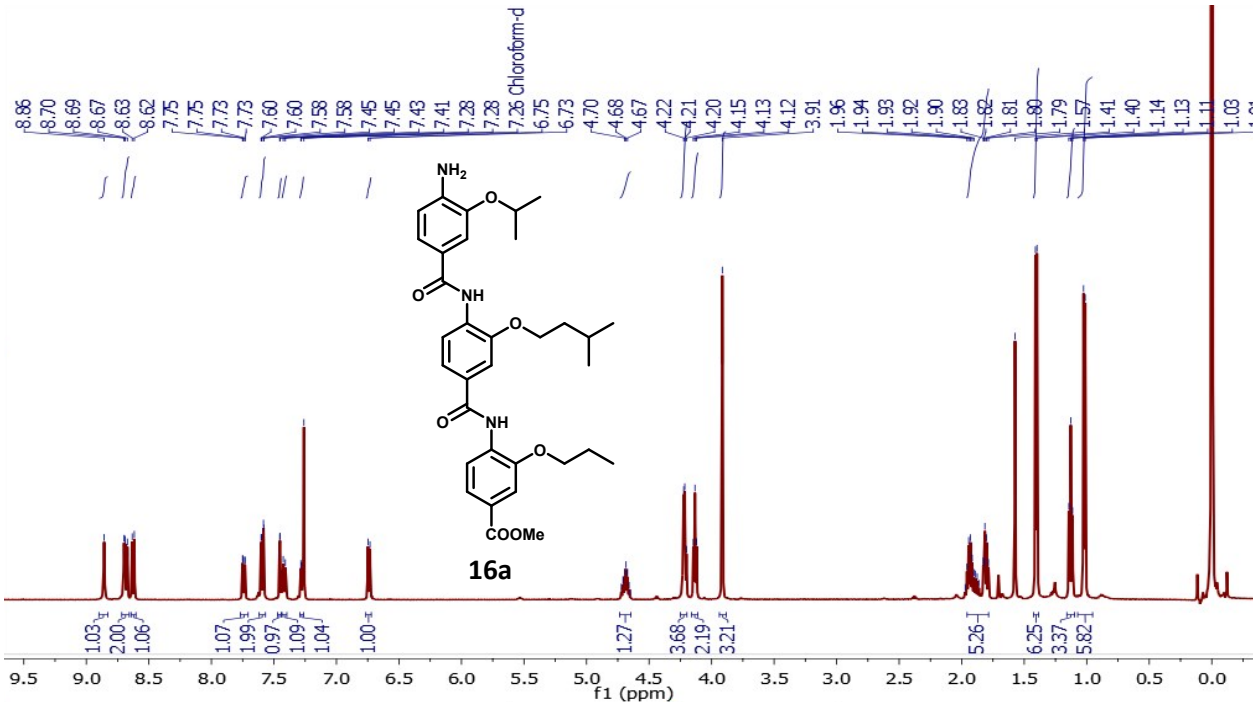


Figure S73. ^{1}H NMR spectrum (500 MHz) of compound **16a** in $CDCl_3$ at 298 K

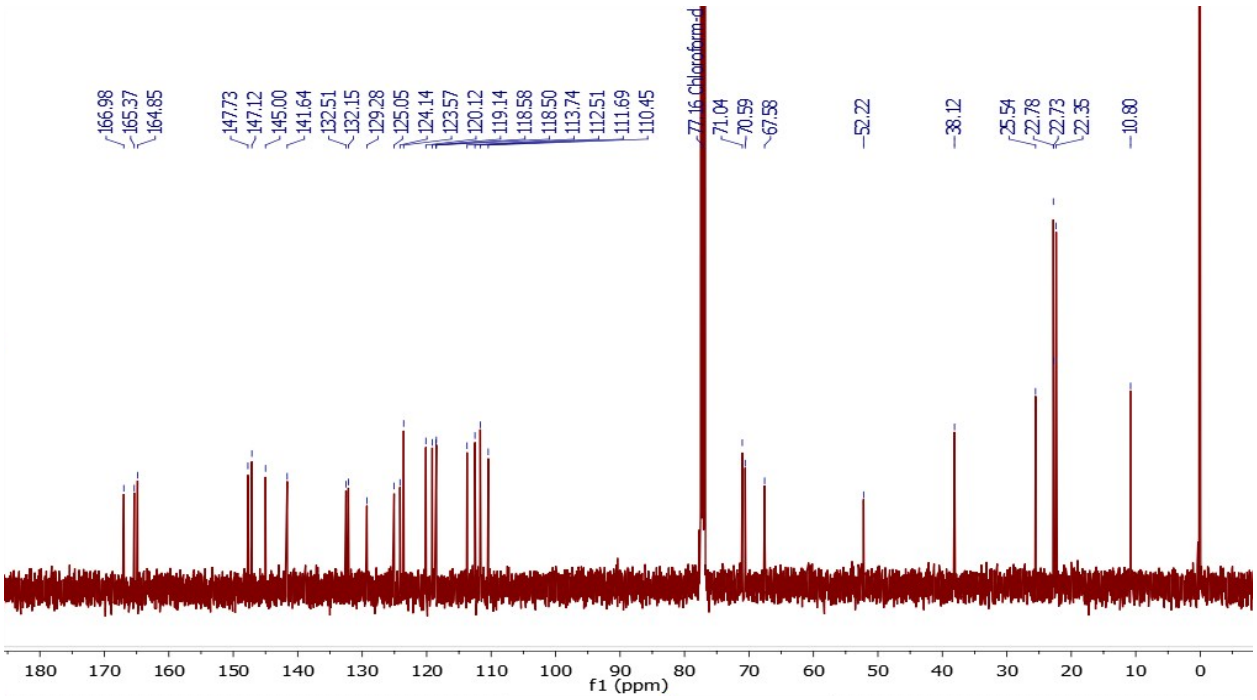


Figure S74. ^{13}C NMR spectrum (126 MHz) of compound **16a** in $CDCl_3$ at 298 K

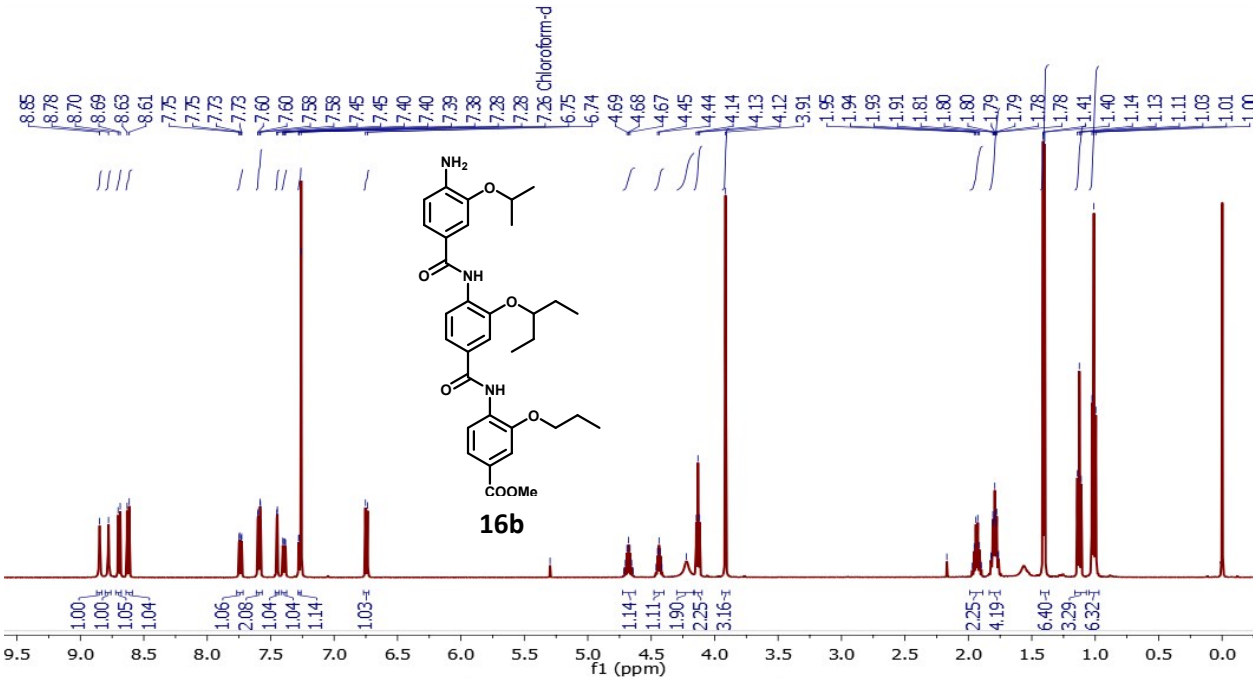


Figure S75. ^{1}H NMR spectrum (500 MHz) of compound **16b** in $CDCl_3$ at 298 K

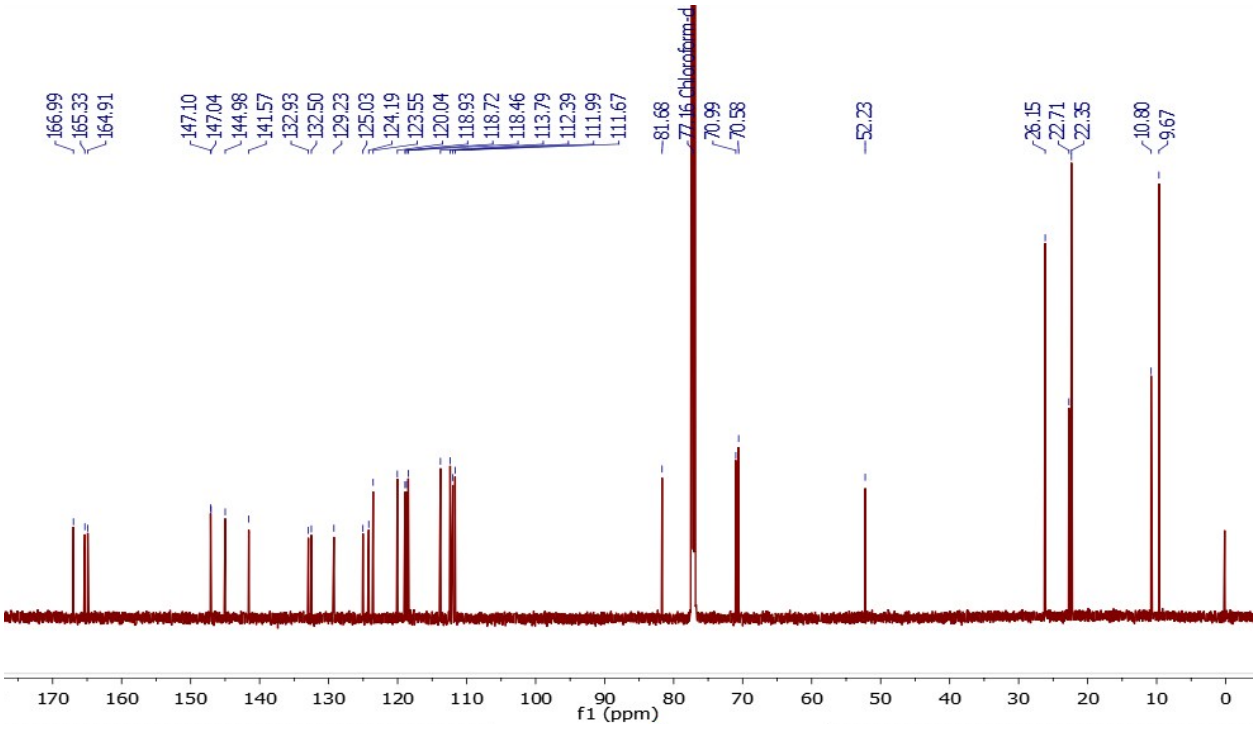


Figure S76. ^{13}C NMR spectrum (176 MHz) of compound **16b** in $CDCl_3$ at 298 K

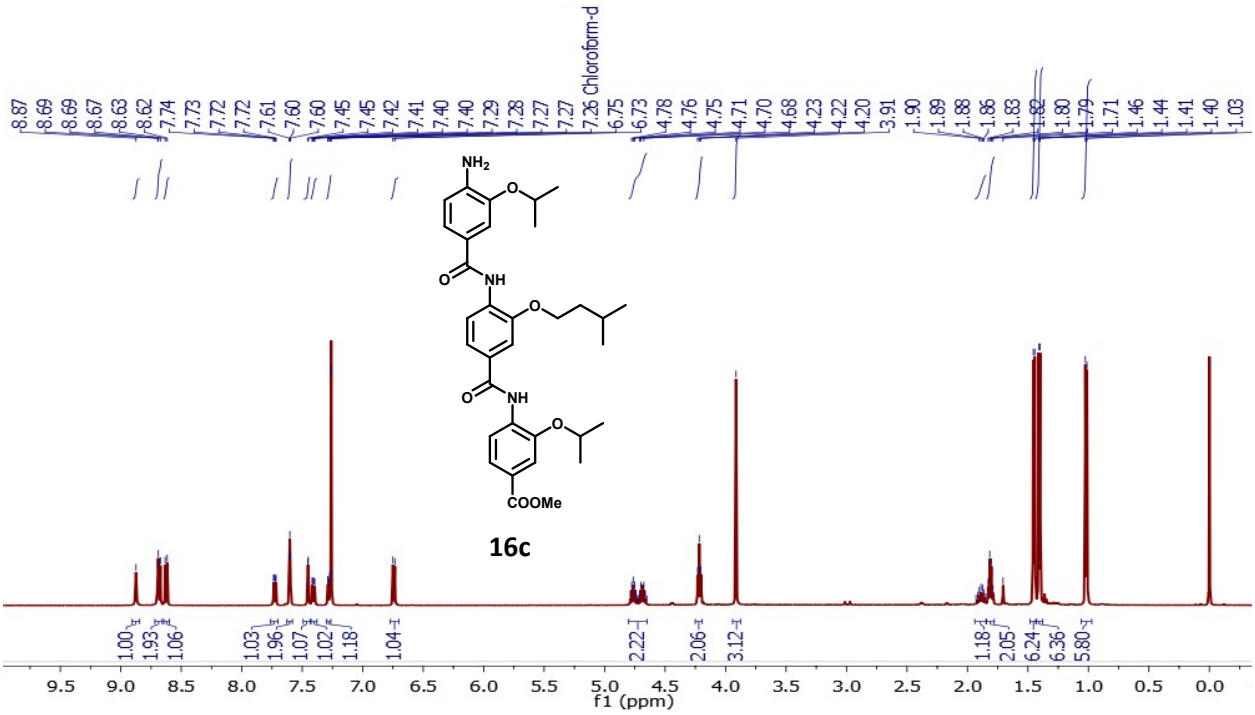


Figure S77. ^{1}H NMR spectrum (500 MHz) of compound **16c** in $CDCl_3$ at 298 K

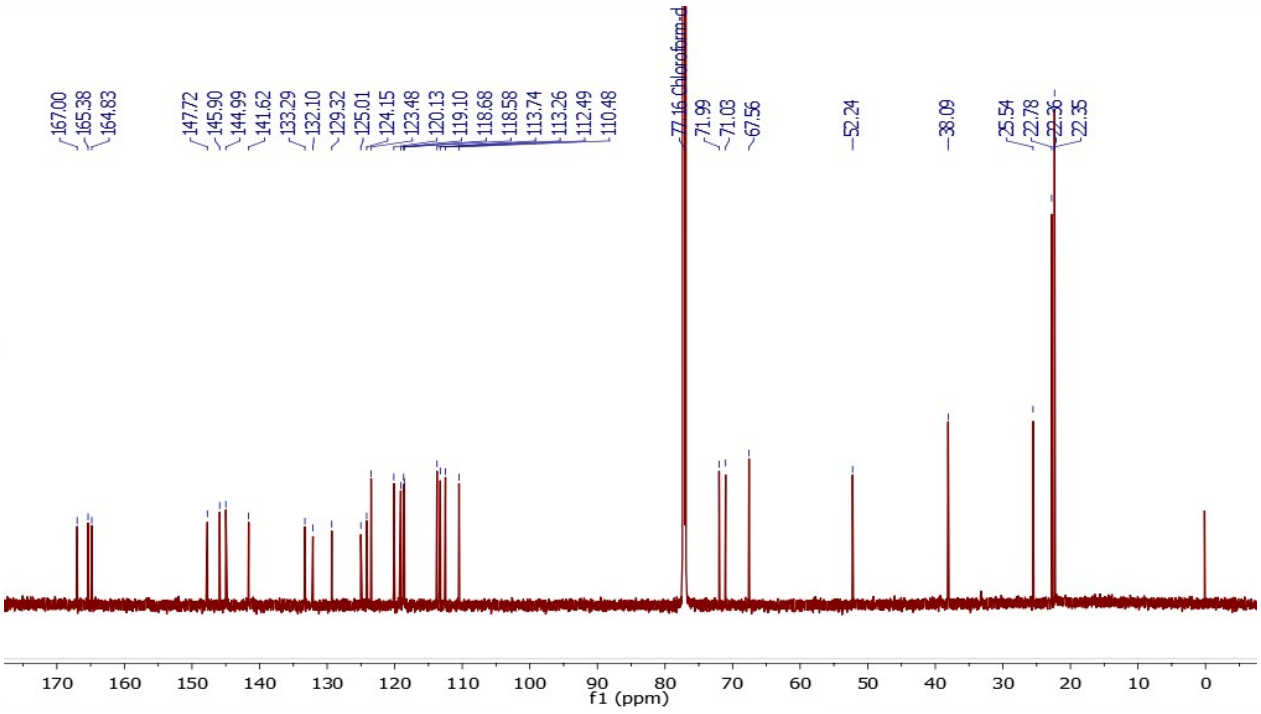


Figure 78. ^{13}C NMR spectrum (176 MHz) of compound **16c** in $CDCl_3$ at 298 K

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