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Supporting Information

Use of Azido Naphthalimide Carboxylic Acids as Fluorescent Template with Built-in Photo-reactive Group and Flexible Linker Simplifies Protein Labeling Study: Applications in Selective Tagging of HCAII and Penicillin Binding Proteins

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Experimental Section

General

All the reactions under inert atmosphere were conducted with oven-dried glassware with anhydrous solvents dried using standard methods and purified by distillation prior to use. All common reagents were of commercial grade unless otherwise specified. Silica gel 60–120 mesh was used for column chromatography. Thin layer chromatography (TLC) was performed on aluminium-backed plates coated with Silica gel 60. Locally available Ultra violet light chamber was used as the TLC spot indicator. All new compounds were characterized using proton (^{1}H) nuclear magnetic resonance (NMR), ^{13}C NMR spectroscopy. The NMR spectra were recorded using Bruker 400 MHz and 600 MHz spectrometer. Proton and carbon spectra were referenced internally to solvent signals, using values of δ = 2.50 for proton and δ = 39.52 for carbon (middle peak) in DMSO-d_6 and of δ = 7.26 for proton and δ = 77.16 for carbon (middle peak) in chloroform-d and of δ = 2.05 for proton and δ = 206.26, 29.84 for carbon (middle peak) in acetone-d_6.The following abbreviations have been used for NMR peak assignments: s = singlet, bs = broad singlet, d = doublet, t = triplet, p = pentet, m = multiplet, dd = double of doublet.

Preparation of 4-azido-1,8-naphthalic anhydride

To a solution of 4-bromo-1,8-naphthalic anhydride (1.08 mmol) in DMF (7 mL) a solution of sodium azide (0.106 g, 1.624 mmol) in water (0.5 mL) was added at room temperature. The mixture was stirred vigorously for 12 h at room temperature and the solution was poured into ice water (80 mL). The yellow precipitate was filtered to get the compound **3** (0.232 g, 90 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.66 (d, *J* = 7.2 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.55 (d, *J* = 8.4 Hz, 1H), 7.81 (t, *J* = 7.9 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H).[1]

General method for the preparation of carboxylic acid derivatives of 4-azido-1,8-naphthalimide

To a solution of 4-azido-1,8-naphthalic anhydride (0.05 g, 0.2 mmol) in dry ethanol (7 mL) DMAP (0.002 g, 0.02 mmol) was added and stirred for 10 min. Corresponding amino acids (**6a-6i**) (0.272 mmol) were added to the reaction mixture and refluxed for 12 h. After cooling the precipitated yellow solids were separated from the solution, washed with cold ethanol and were

air dried to furnish the azidonaphthalimide carboxylic acids **4a-4i.** The compounds were reprecipitated from DCM-hexane mixture and washed with hexane to get carboxylic acid **4a-4i** as yellow solid.

Glycine naphthalimide (4a): Yellow solid (0.047 g, 80%); mp 130-132 ^{o}C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.59 (d, *J* = 7.3 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.88 (s, 2H); ^{13}C NMR (100 MHz, Acetone-d_6) δ 169.5, 164.0, 163.5, 144.6, 132.8, 132.7, 129.9, 129.7, 128.0, 125.1, 123.1, 119.2, 116.4, 41.6. HRMS: Calcd. for $C_{14}H_8N_4O_4Na$ $(M+Na)^+$ 319.0443, found 319.0443.

β-alanine naphthalimide (4b): Yellow solid (0.050 g, 81%); mp 164-165 ^{o}C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (d, *J* = 7.3 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 7.87 (t, *J* = 7.9 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 4.24 (t, *J* = 7.8 Hz, 2H), 2.58 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 163.0, 162.5, 142.7, 131.4, 131.3, 128.2, 128.1, 127.1, 123.3, 121.9, 117.9, 115.8, 35.8, 32.3. HRMS: Calcd. for $C_{15}H_{10}N_4O_4Na$ $(M+Na)^+$ 333.0600, found 333.0602.[1]

GABA naphthalimide (4c): Yellow solid (0.052 g, 80%); mp 145-147 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 8.54 (d, *J* = 7.3 Hz, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 4.08 (t, *J* = 6.8 Hz, 2H), 2.30 (t, *J* = 7.3 Hz, 2H), 1.88 (p, *J* = 6.9, 2H);^{13}C NMR (150 MHz, DMSO-d_6) δ 173.9, 163.2, 162.8, 142.6, 131.4, 131.3, 128.2, 128.1, 127.1, 123.4, 122.1, 118.1, 115.8, 31.3, 23.0. HRMS: Calcd. for $C_{16}H_{12}N_4O_4Na$ $(M+Na)^+$ 347.0756, found 347.0759.

Valeric naphthalimide (4d): Yellow solid (0.055 g, 82%); mp 150-151 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H), 8.55 (d, *J* = 7.2 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H) 8.42 (d, *J* = 8.3 Hz, 1H), 7.87 (t, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 4.03 (t, *J* = 6.8 Hz, 2H), 2.27 (t, *J* = 7.0 Hz, 2H), 1.69-1.51 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.3, 163.3, 162.8, 142.9, 131.6, 131.6, 128.4, 128.3, 127.3, 123.6, 122.2, 118.2, 116.0, 33.3, 27.1, 22.0. HRMS: Calcd. for $C_{17}H_{14}N_4O_4Na$ $(M+Na)^+$ 361.0913, found 361.0913.

Caproic naphthalimide (4e): Yellow solid (0.057 g, 82%); mp 128-129 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (s, 1H), 8.36 (d, *J* = 7.2 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 3.94 (t, *J* = 7.1 Hz, 2H), 2.22 (t, *J* = 7.2 Hz, 2H), 1.63 – 1.51 (m, 4H), 1.37 – 1.29 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ

174.4, 163.0, 162.5, 142.5, 131.4, 131.3, 128.1, 128.0, 127.1, 123.3, 121.9, 117.9, 115.7, 33.5, 27.2, 26.0, 24.2. HRMS: Calcd. for $C_{18}H_{16}N_4O_4Na$ $(M+Na)^+$ 375.1069, found 375.1069.

L-Leucine naphthalimide (4f): Yellow solid (0.058 g, 82%); mp 149-150 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 7.2 Hz, 1H), 8.57 (d, *J* = 7.9 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 5.81 (dd, *J* = 8.9, 5.0 Hz, 1H), 2.25-2.18 (m,1H), 2.11 – 2.04 (m, 1H), 1.62-1.52 (m, 1H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 163.8, 163.3, 144.0, 132.9, 132.4, 129.5, 129.3, 127.1, 124.5, 122.3, 118.5, 114.9, 51.9, 38.1, 25.5, 23.2, 22.2. HRMS: Calcd. for $C_{18}H_{16}N_4O_4Na$ $(M+Na)^+$ 375.1069, found 375.1069.

L-Valine naphthalimide (4g): Yellow solid (0.055 g, 82%); mp 112-114 ^oC (dec); ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 7.2 Hz, 1H), 8.59 (d, *J* = 8.0 Hz, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 5.40 (d, *J* = 9.2 Hz, 1H), 2.84 (m, 1H), 1.29 (d, *J* = 6.4 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 164.0, 163.5, 144.2, 133.0, 132.6, 129.5, 129.4, 127.1, 124.5, 122.1, 118.3, 114.9, 58.6, 27.6, 22.2, 19.2. HRMS: Calcd. for $C_{17}H_{14}N_4O_4Na$ $(M+Na)^+$ 361.0913, found 361.0913.

L-Serine naphthalimide (4h): Yellow solid (0.052 g, 80%); mp 124-125 ^oC; ^1H NMR (400 MHz, Acetone-d_6) δ 8.62-8.54 (complex m, 2H), 8.47 (d, *J* = 8.5 Hz, 1H), 7.88 (t, *J* = 7.8 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 5.90 (dd, *J* = 8.6, 5.4 Hz, 1H), 4.35 (dd, *J* = 11.6, 5.4 Hz, 1H), 4.26 (dd, *J* = 11.6, 8.6 Hz, 1H);^{13}C NMR (100 MHz, DMSO-d_6) δ 170.0, 163.2, 162.7, 143.1, 131.9, 131.8, 128.6, 128.5, 127.4, 123.5, 122.1, 118.1, 116.1, 58.6, 55.4. HRMS: Calcd. for $C_{15}H_{10}N_4O_5Na$ $(M+Na)^+$ 349.0549, found 349.0549.

L-Phenylalanine naphthalimide (4i): Yellow solid (0.061 g, 80%); mp 80-81 ^oC; ^1H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, *J* = 7.0 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.39 (d, *J* = 7.8 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.06 (dd, *J* = 9.6, 5.7 Hz, 1H), 3.68 (dd, *J* = 14.3, 5.7 Hz, 1H), 3.47 (dd, *J* = 14.3, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.9, 163.6, 163.1, 144.0, 137.3, 132.8, 132.3, 129.4, 129.3, 128.4, 127.0, 126.7, 124.5, 122.1, 118.3, 114.9, 54.3, 34.9. HRMS: Calcd. for $C_{21}H_{14}N_4O_4Na$ $(M+Na)^+$ 409.0913, found 409.0914.

Preparation of 2-bromo-N-(4-sulfamoyl-phenyl)-acetamide (7)

At 0 ºC, to a solution of sulfanilamide (0.35 g, 2.03 mmol) in dry THF (10 mL), K_2CO_3 (0.561g, 4.06 mmol) was added. Bromoacetyl chloride (0.2 mL, 2.44 mmol) was added dropwise to the reaction mixture and was stirred for 30 mins at 0ºC. Water was added and the mixture was extracted with EtOAc (50 mL × 2), washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to get the product as white crystalline solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.72 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H), 7.29 (s, 2H), 4.08 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 171.5, 141.5, 138.5, 126.5, 119.2, 61.9. HRMS: Calcd. for $C_8H_9N_2O_3SBrNa$ $(M+Na)^+$ 314.9415, found 314.9416.

General method for the preparation of the sulfonamides 1a-1i

To a solution of azidonaphthalimide carboxylic acids **4a-4i** (0.15 mmol) in dry DMF (5 mL) under N_2, anhydrous K_2CO_3 (0.025 g, 0.18 mmol) was added and stirred for 30 mins at room temperature. A solution of 2-bromo-N-(4-sulfamoyl-phenyl)-acetamide (0.053 g, 0.18 mmol) in dry DMF (2 mL) was added and stirring was continued for 10 h at room temperature. The reaction was quenched by adding water (30 mL) and the aqueous layer was extracted with EtOAc (30 mL x 2). The combined organic layers was washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. For compounds **1a-1g**, the yellowish brown gummy product was first precipitated from acetone-hexane mixture to get dark yellow solid which was washed with DCM to furnish the target materials as bright yellow solids. Further purification was done by washing with hexane. For compounds **1h-1i,** the yellowish brown gummy product was precipitated from acetone-hexane to get dark yellow solid. The final purification was done by column chromatography (DCM/MeOH=7:0.5) followed by washing of the yellow solid with hexane. The spectral and other details are mentioned below:

Glycine sulfonamide 1a: Yellow solid (0.062 g, 82%); mp 150-151 ^{o}C; R_f0.50 (DCM/MeOH) (7:0.5); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.45 (s, 1H), 8.58 (d, *J* = 7.3 Hz, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.49 (d, *J* = 7.5 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.80 – 7.73 (m, 7H), 7.26 (s, 2H), 4.98 (s, 2H), 4.83 (s, 2H). ^{13}C NMR (150 MHz, DMSO) δ 167.8, 165.4, 162.9, 162.4, 143.6, 141.2, 138.8, 132.1, 132.1, 129.1, 128.4, 127.5, 126.7, 123.7, 121.5, 118.9, 117.4, 116.2, 63.2,

40.9. IR (KBr, cm^{-1}) 3358, 2926, 2854, 2130, 1702, 1654, 1592, 1382, 1320, 1158, 838, 782. HRMS: Calcd for $C_{22}H_{16}N_6O_7SNa$ $(M+Na)^+$ 531.0699, found 531.0699.

β-alanine sulfonamide 1b: Yellow solid (0.064 g, 82%); mp 176-178 ^oC (dec); R_f 0.49 (DCM/MeOH) (7:0.5); ^1H NMR (600 MHz, DMSO-d_6) δ 10.40 (s, 1H), 8.54 (d, *J* = 6.4 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 7.87 (m, 1H), 7.75 (dd, *J* = 8.4, 3.7 Hz, 3H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.27 (s, 2H), 4.71 (s, 2H), 4.34 (t, *J* = 7.6 Hz, 2H), 2.84 (t, *J* = 7.6 Hz, 2H).^{13}C NMR (150 MHz, DMSO-d_6) δ 170.6, 165.8, 163.2, 162.8, 143.0, 141.2, 138.7, 131.6, 131.6, 128.5, 128.4, 127.3, 126.7, 126.7, 123.6, 122.2, 118.8, 118.2, 116.0, 62.8, 35.6, 31.8; IR (KBr, cm^{-1}) 3332, 2926, 2372, 2128, 1658, 1592, 1358, 1302, 1156, 836, 782. HRMS: Calcd for $C_{23}H_{19}N_6O_7S$ $(M+H)^+$ 523.1036, found 523.1032.

GABA sulfonamide 1c: Yellow solid (0.068 g, 84%); mp 150-152 ^oC ; R_f 0.49 (DCM/MeOH) (7:0.5); ^1H NMR (600 MHz, DMSO-d_6) δ 10.35 (s, 1H), 8.52 (d, *J* = 6.4 Hz, 1H), 8.46 (d, *J* = 7.9 Hz, 1H), 8.41 (d, *J* = 7.6 Hz, 1H), 7.87 – 7.84 (m, 1H), 7.77 (m, 4H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.25 (s, 2H), 4.65 (s, 2H), 4.11 (t, *J* = 6.9 Hz, 2H), 2.54 (t, *J* = 7.4 Hz, 2H), 2.00 – 1.95 (m, 2H).^{13}C NMR (150 MHz, DMSO-d_6) δ 172.1, 165.9, 163.4, 163.0, 142.8, 141.2, 138.7, 131.6, 131.5, 128.4, 128.3, 127.2, 126.8, 126.7, 123.5, 122.2, 118.8, 115.9, 62.4, 30.9, 22.9; IR (KBr, cm^{-1}) 3337, 2125, 1676, 1593, 1353, 1158, 1098, 840, 783. HRMS: Calcd for $C_{24}H_{20}N_6O_7SNa$ $(M+Na)^+$ 559.1012, found 559.1011.

Valeric sulfonamide 1d: Yellow solid (0.069 g, 84%); mp 160-163 ^oC; R_f 0.48 (DCM/MeOH) (7:0.5); ^1H NMR (400 MHz, DMSO-d_6) δ 10.43 (s, 1H), 8.51 (d, *J* = 7.2 Hz, 1H), 8.46 (d, *J* = 8.0 Hz, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 7.85 (t, *J* = 7.2 Hz, 1H), 7.76-7.68 (m, 5H), 7.28 (s, 2H), 4.68 (s, 2H), 4.05 (t, *J* = 6.8 Hz, 2H), 2.50-2.47 (m, 2H), 1.74-1.61 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 172.4, 166.0, 163.3, 162.8, 142.8, 141.3, 138.6, 131.6, 131.5, 128.4, 128.3, 127.3, 126.7, 123.5, 122.1, 118.8, 118.2, 116.0, 62.4, 32.8, 27.0, 21.9. IR (KBr, cm^{-1}) 3334, 3250, 2129, 1740, 1684, 1648, 1618, 1595, 1388, 1347, 1285, 1158, 842, 785. HRMS: Calcd for $C_{25}H_{22}N_6O_7SNa$ $(M+Na)^+$ 573.1168, found 573.1168.

Caproic sulfonamide 1e: Yellow solid (0.069 g, 82%); mp 146-148 ^oC; R_f 0.43(DCM/MeOH) (7:0.5); ^1H NMR (400 MHz, DMSO-d_6) δ 10.43 (s, 1H), 8.55 (d, *J* = 7.2 Hz, 1H), 8.50 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 8.3 Hz, 1H), 7.87 (t, *J* = 7.2 Hz 1H), 7.78 – 7.68 (m, 5H), 7.28 (s, 2H), 4.68

(s, 2H), 4.04 (t, *J* = 7.3 Hz, 2H), 2.44 (t, *J* = 7.3 Hz, 2H), 1.69 – 1.60 (m, 4H), 1.44 – 1.35 (m, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 172.5, 166.0, 163.2, 162.8, 142.8, 141.3, 138.6, 131.6, 131.5, 128.3, 127.3, 126.8, 126.7, 123.5, 122.2, 118.8, 118.2, 115.9, 62.3, 33.0, 27.1, 25.8, 24.1. IR (KBr, cm^{-1}) 3351, 2936, 2128, 1696, 1654, 1593, 1355, 1240, 1158, 784. HRMS: Calcd for $C_{26}H_{24}N_6O_7SNa$ $(M+Na)^+$ 587.1325, found 587.1325.

Leucine sulfonamide 1f: Yellow solid (0.068 g, 81%); mp 160-162 ^{o}C; R_f 0.43, (DCM/MeOH) (7:0.5); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.29 (s, 1H), 8.59 (d, *J* = 7.2 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 7.87 (t, *J* = 9 Hz, 1H), 7.77 (dd, *J* = 15.8, 8.4 Hz, 3H), 7.67 (d, *J* = 8.8 Hz, 2H), 7.25 (s, 2H), 5.81 (dd, *J* = 8.9, 5.0 Hz, 1H), 4.76, 4.70 (ABq, J_{AB}= 14.4Hz, 2H), 2.16 – 2.12 (m, 1H), 2.05-2.00 (m, 1H), 1.59 – 1.53 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.6, 165.6, 163.1, 162.6, 143.7, 141.1, 138.7, 132.4, 132.3, 129.1, 128.5, 127.5, 126.7, 123.6, 121.5, 118.8, 117.4, 116.2, 63.2, 51.1, 37.5, 24.7, 22.9, 21.9. IR (KBr, cm^{-1}) 3319, 2959, 2125, 1758, 1677, 1654, 1589, 1534, 1380, 1342, 1163, 786. HRMS: Calcd for $C_{26}H_{25}N_6O_7S$ $(M+H)^+$ 565.1505, found 565.1504.

Valine sulfonamide 1g: Yellow solid (0.069 g, 84%); mp 127-128 ^{o}C; R_f 0.47 (DCM/MeOH) (7:0.5); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.60 (d, *J* = 7.2 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 7.92 (t, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.7 Hz, 2H), 7.25 (s, 2H), 5.40 (d, *J* = 9.1 Hz, 1H), 4.74, 4.66 (ABq, J_{AB}= 14.7,2H), 2.75-2.69 (m, 1H), 1.24 (d, *J* = 6.5 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.8, 165.6, 163.2, 162.8, 143.8, 141.1, 138.7, 132.6, 132.5, 129.2, 128.5, 127.6, 126.7, 123.6, 121.2, 118.7, 117.1, 116.3, 63.1, 57.6, 27.1, 21.7, 18.7. IR (KBr, cm^{-1}) 3344, 2126, 1654, 1589, 1380, 1289, 1246, 1161, 840, 784. HRMS: Calcd for $C_{25}H_{22}N_6O_7SNa$ $(M+Na)^+$ 573.1168, found 573.1167.

Serine sulfonamide 1h: Yellow solid (0.057 g, 71%); mp 130-131 ^{o}C; R_f 0.32 (DCM/MeOH) (7:0.5); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.59 (d, *J* = 7.3 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.92 (t, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.25 (s, 2H), 5.91 (dd, *J* = 9.0, 5.1 Hz, 1H), 5.02 (t, *J* = 6.5 Hz, 1H), 4.76, 4.72 (ABq, J_{AB}= 15 Hz, 2H), 4.19 – 4.15 (m, 1H), 4.12 – 4.07 (m, 1H). ^{13}C

NMR (100 MHz, DMSO-d_6) δ 168.0, 165.6, 163.3, 162.8, 143.6, 141.2, 138.8, 132.2, 132.2, 129.0, 128.6, 127.5, 126.8, 123.6, 121.8, 118.8, 117.7, 116.2, 63.1, 58.1, 54.7. IR (KBr, cm^{-1}) 3349, 2127, 1696, 1586, 1380, 1281, 1257, 1157, 835, 782. HRMS: Calcd for $C_{23}H_{18}N_6O_8SNa$ $(M+Na)^+$ 561.0805, found 561.0806.

Phenylalanine sulfonamide 1i: Yellow solid (0.065 g, 72%); mp 101-103 ^oC; R_f 0.22 (DCM/MeOH) (7:0.5); ^1H NMR (600 MHz, DMSO-d_6) δ 10.42 (s, 1H), 8.52 (d, *J* = 7.2 Hz, 1H), 8.47 (t, *J* = 9.2 Hz, 2H) 7.90 – 7.85 (m, 3H), 7.81 – 7.74 (m, 4H), 7.27 (s, 2H), 7.16 (d, *J* = 7.3 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 6.10 (dd, *J* = 9.6, 5.7 Hz, 1H), 4.81, 4.74 (ABq, J_{AB}= 14.7,2H), 3.63 (dd, *J* =14.1, 5.7 Hz, 1H), 3.39 (dd, *J* =14.0, 9.6 Hz, 1H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.0, 168.1, 165.7, 162.8, 143.8, 141.3, 138.8, 137.1, 132.2, 129.1, 129.0, 128.5, 128.2, 128.1, 127.5, 126.8, 126.4, 123.6, 121.2, 119.1, 118.8, 117.0, 116.3, 63.4, 55.8, 34.1. IR (KBr, cm^{-1}) 3251, 2127, 1690, 1590, 1539, 1333, 1157, 839, 777. MS: Calcd for $C_{29}H_{22}N_4O_5H$ $(M-SO_2-N_2)^+$ 507.1, found 507.0.

Preparation of the NHS ester (5)

To a solution of NHS (0.016 mg, 0.05 mmol) in dry EtOAc (4 mL) compound **4c** (0.007 mg, 0.06 mmol) was added under inert atmosphere. To this solution EDC.HCl (0.012 mg, 0.06 mmol) was added and was stirred for 12 h at room temperature. The reaction was quenched by adding water (30 mL) and the organic layer was extracted with EtOAc (30 mL×2). The organic layer was dried over Na_2SO_4 and was concentrated *in vacuo* to get the compound **5**.

NHS ester 5: Yellow solid (0.020g, 80%) ^1H NMR (600 MHz, Chloroform-*d*) δ 8.64 (dd, *J* = 7.2, 1.2 Hz, 1H), 8.59 (d, *J* = 8.0 Hz, 1H), 8.45 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.75 (dd, *J* = 8.5, 7.3 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 4.30 (t, *J* = 7.1 Hz, 2H), 2.81 (bs, 4H), 2.77 (t, *J* = 7.7 Hz, 2H), 2.21 (p, *J* = 7.4 Hz, 2H);^{13}C NMR (150 MHz, $CDCl_3$) δ 169.2, 168.2, 164.2, 163.8, 143.9, 132.7, 132.2, 129.5, 129.2, 127.1, 124.6, 122.7, 118.9, 114.9, 39.4, 29.1, 25.8, 23.4. HRMS: Calcd. for $C_{20}H_{15}N_5O_6Na$ $(M+Na)^+$ 444.0918, found 444.0919.

Preparation of the compound 1j

To a solution of ampicillin (0.024 g, 0.07 mmol) in dry DMF (4 mL) DIEA (1 drop) was added at 0 ºC under stirring condition. The NHS ester **5** (0.019 g, 0.04 mmol) in DMF (1 mL) was

added dropwise to the reaction mixture and stirred for 12 h at room temperature. The reaction was quenched by adding 10% citric acid aq. and the mixture was extracted with EtOAc. The organic layer was washed with 10% citric acid aq. And water, then was dried over Na_2SO_4 and was concentrated *in vacuo.* The crude product was purified by precipitating from EtOAc-hexane layer. Isolated as a yellow solid (0.034 g, 75%); mp 200-202 ^oC (dec); R_f 0.3 (DCM/MeOH) (7:0.5); ^1H NMR (600 MHz, DMSO-d_6) δ 9.01 (d, *J* = 8.0 Hz, 1H), 8.54 (d, *J*= 7.2 Hz, 1H), 8.51 – 8.49 (m, 2H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.88 (t, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.27 (d, *J* = 7.2 Hz, 1H), 5.68 (d, *J* = 8.1 Hz, 1H), 5.47 (dd, *J* = 7.9, 4.0 Hz, 1H), 5.36 (d, *J* = 4.1 Hz, 1H), 4.13 (s, 1H), 4.07 (t, *J* = 7.1 Hz, 2H), 2.31 (t, *J* = 7.8 Hz, 2H), 1.91-1.86 (m, 2H), 1.51 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 172.9, 171.2, 169.9, 168.8, 163.1, 162.7, 142.7, 137.9, 131.5, 131.4, 128.3, 128.2, 127.9, 127.3, 127.1, 126.9, 123.4, 122.1, 118.1, 115.8, 66.9, 63.7, 57.8, 55.3, 32.6, 30.5, 26.6, 23.8. IR (KBr, cm^{-1}) 3422, 2366, 2124, 1649, 1356.Calcd for $C_{32}H_{29}N_7O_7SNa$ $(M+Na)^+$ 678.1741, found 678.1746.

Determination of IC_{50} Values

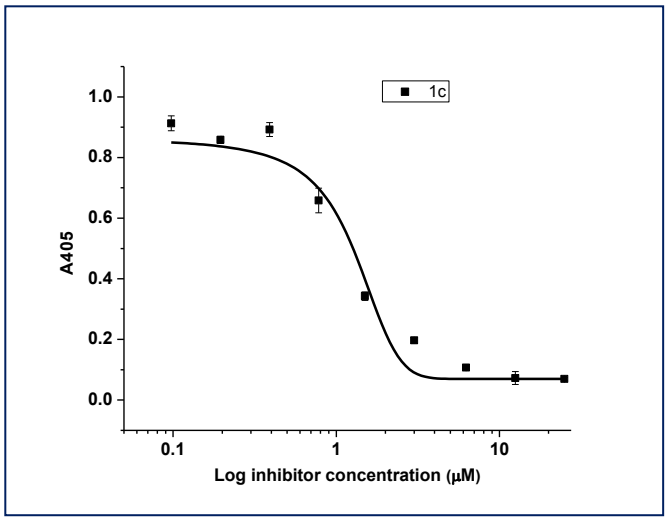


Figure S1: Representative picture of Inhibition profile: IC_{50} determination of compound 1c by using 2 mM PNPA (p-nitrophenyl acetate) as the substrate and 14 μM HCA II (working concentration). Absorbance was measured at 405 nm on a microplate spectrophotometer. 50 mM HEPES (pH 7.2) was used for the measurements.

Entry	Name of Inhibitory Compounds	IC_{50} (μM)
1	**1a** Gly	1.6
2	**1b** β-Ala	1.5
3	**1c** GABA	1.3
4	**1d** Valeric	1.2
5	**1e** Caproic	1.3
6	**1g** Valine	2.0
7	**1i** Phe	9.2

Table S1: IC_{50} values of the sulfonamides (The α-amino acids used had L-configuration)

SDS-PAGE Gel Experiments

- **HCA II Cross-linking experiment with α-amino acid based capture compounds (1a, 1f-1i)**

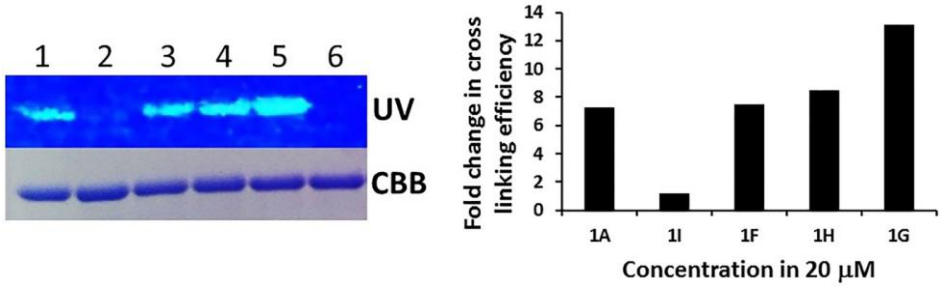
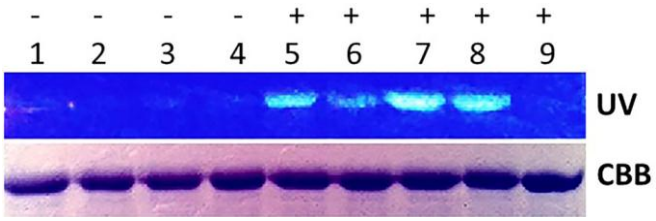


Figure S2: Gel pictures and relative cross-linking efficiencies of α-amino acid based sulfonamides: (**a**) Lanes 1–5: Irradiation of a 50 µL mixture with HCA II (20 µM) with compounds **1A**, **1I**, **1F**, **1H**, **1G** respectively (all at 20 µM) and lane 6: irradiation of a 50 µL mixture of HCA II (20 µM) in DMSO (2%) as the control. (b) Image analysis of **Figure 4a**.

- **Demonstration of requirement of UV for cross-linking**



(-) = No UV irradiation, (+) = UV irradiation

Figure S3: Gel pictures of cross-linking efficiencies of amino acid based sulfonamides with or without UV irradiation: (**a**) Lanes 1–4: No UV irradiation was applied to a 50 µL mixture with HCA II (20 µM) with compound **1a** and **1d** respectively (lanes 1, 3: 20 µM and lanes 2, 4: 10 µM) and lanes 5-9: UV irradiation was applied to a 50 µL mixture of HCA II with compound **1a** and **1d** respectively (lanes 5, 7: 20 µM and lanes 6, 8: 10 µM) and lane 9: UV irradiated mixture of HCA II in DMSO (2%) as the control.

- **Efficiency of Gaba-sulfonamide (1c) at different protein concentration**

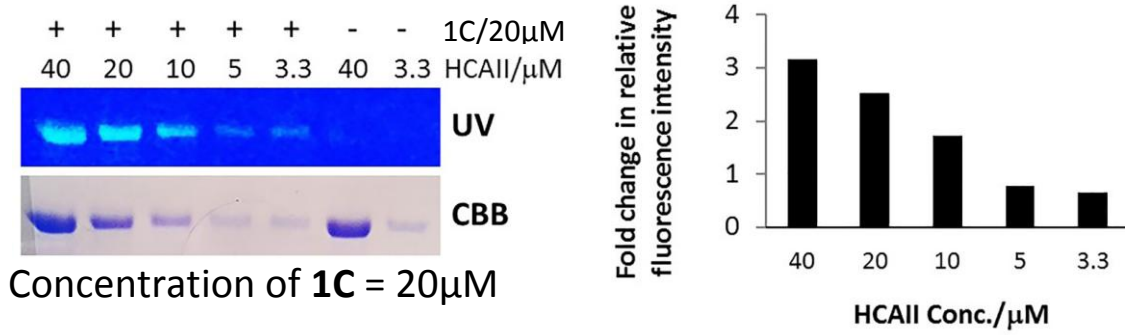


Figure S4: Results of Gel electrophoresis analysis of 1C (20 µM) at different protein concentrations

- **Efficiency of Gaba-sulfonamide (1c) at different compound concentration**

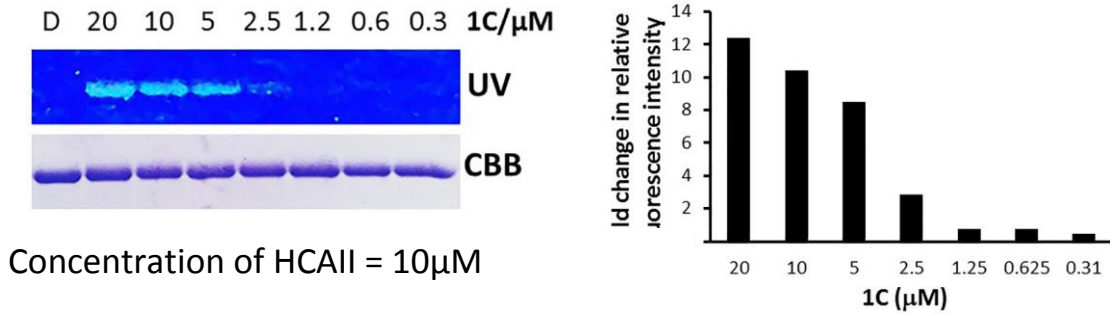


Figure S5: Results of Gel electrophoresis analysis of 1C at different concentrations with constant HCAII concentration 10 µM

- **Crosslinking of compound 1I with PBP5 and comparison with commercially available Bocillin FL**

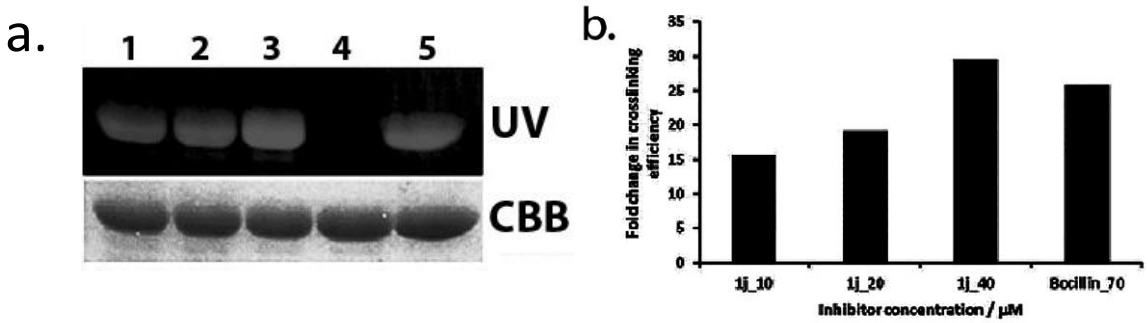


Figure S6: Gel pictures and relative cross-linking efficiencies with penicillin binding protein (EC sPBP5). (**a**) Lanes 1–3: Irradiation of a 25 µL mixture with EC sPBP5 (20 µM) with compound **1j** (10, 20, 40 µM respectively) and irradiation of a 25 µL mixture of EC sPBP5 (20 µM) either in DMSO (2%) (lane 4) or Bocillin (70 µM) (lane 5) as the controls. (**b**) Image analysis of **Figure 10a**. The reaction was done in 10 mM Tris-HCl at pH 7.8.

- **Cross-linking of membrane protein lysate from E. coli (uninduced)**

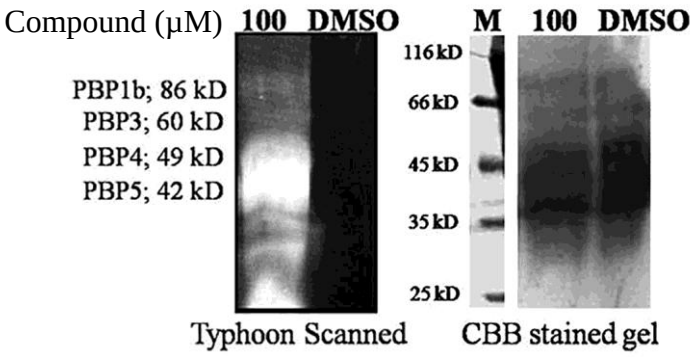


Figure S7: Results of Gel electrophoresis analysis of uninduced membrane lysate of *E. Coli* (**A**) Typhoon scanned **(B)** Coomassie stained.

- **Cross-linking of membrane protein lysate from E. coli (induced)**

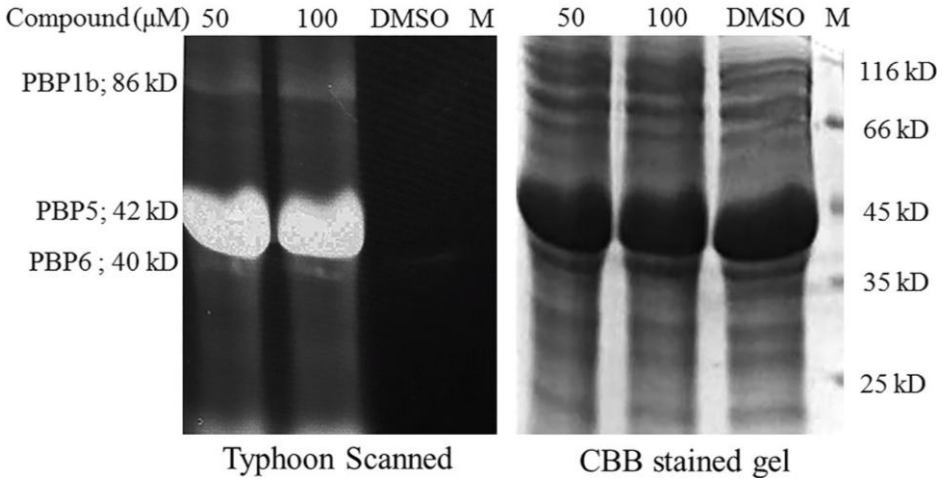


Figure S8: Results of Gel electrophoresis analysis of PBP5 over expressed membrane lysate of *E. Coli* (**A**) Typhoon scanned **(B)** Coomassie stained.

Capture experiment protocol

The HCA II concentration was kept at 40 μM for initial experiment with **1b** and the total volume was made up to 50 μL with buffer (50 mM HEPES; pH 7.2). HCA II and capture compound (**1b**: 40, 20, 10 μM) in DMSO were mixed by vortexing followed by centrifugation. For all comparison experiments of **1a-1c** (10 μM), **1c-1e** (20, 10 mM respectively) and **1a, 1f-1i** (10 μM) the HCA II was kept constant at 20 μM concentration. The compounds were incubated with proteins for 15 min at room temperature, and then photo-irradiated (UV λ ≥254 nm, 15 watts each x 5 bulbs, 15 pulses, using auto cross-linking mode and has a duration of 120 s) in a 96 well plate followed by SDS-PAGE and trypsin digestion for mass spectrometric analysis.

The experiment was repeated with cell lysates of *E. coli* where the selective capturing of HCA II was clearly apparent by PAGE. For cell lysate preparation, 10 mL of induced, lag phase BL21(DE3) pLysS cells carrying plasmid pACA/HCA II were resuspended in 1 mL of buffer (50 mM Tris; pH 8.0, 50 mM NaCl, 10 mM EDTA, 1 mM dithiothreitol, 1 mM phenyl methane sulfonyl fluoride, 0.2 mM $ZnSO_4$), sonicated and centrifuged at 10 000 rpm for 10 minutes. 10 μL the supernatant (cell lysate) thus obtained was mixed with each of the 100, 50 and 25 □M capture compounds and the total volume was made up to 50 μL with buffer (50 mM HEPES; pH 7.2).

SDS-polyacrylamide gel electrophoresis

For SDS-polyacrylamide gel analysis, the samples were mixed with 6× Laemmli buffer (1× buffer composition was 63 mMTris-HCl (pH 6.8), 2% SDS, 10% glycerol, 0.1% 2-mercaptoethanol and 0.01% bromophenol blue) (U. K. Laemmli, Cleavage of structural proteins during the assembly of the head of bacteriophage T4, *Nature*, 1970, 227, 680–685) and kept at 95 °C for 5 min. A 20 μL sample from each mixture was loaded in each well of 12% discontinuous SDS-PAGE (Mini-PROTEAN 3, Multi casting chamber, BioRad Instruments). The electrophoresis was performed under denaturing conditions. The stacking and resolving gels were composed of 5% (w/v) and 12% (w/v) acrylamide with Tris (pH 6.8 and pH 8.8)

respectively, and 0.1% SDS. The composition of the electrophoresis buffer was 0.025 M Tris, 0.2 M glycine, pH 8.3 and 0.1% SDS. An electric potential of 160 volts was applied to run the gel until the bromophenol blue dye reached the end of the resolving gel. The gel was visualized under UV light in a UVP gel documentation system. The position of the fluorescent bands was confirmed by staining the gels with 0.1% (w/v) Coomassie Brilliant Blue R-250 in 50% (v/v) methanol and 10% (v/v) acetic acid and destained with methanol/acetic acid.

Expression, purification and compound 1j binding analysis of soluble penicillin-binding protein 5 (sPBP5)

The sPBP5 from *Escherichia coli* was expressed and purified by essentially following the method as described earlier.[2] Briefly, the gene for the soluble PBP5 (devoid of signal peptide and partially the membrane anchor) was cloned in pET28a (+) vector (Addgene, Cambridge, MA, USA). Hexa-histidine tagged sPBP5 was expressed in *E. coli* BL21 Star under the control of T7 promoter by inducing with 0.05 mM isopropyl β-D-1-thiogalacto pyranoside (IPTG) and subsequently incubating at 30 °C for 8 h. The protein was purified through Ni-NTA affinity chromatography (QIAGEN GmbH, Hilden, Germany) in presence of 60 and 150 mM imidazole in the following buffer conditions: 10 mMTris-HCl, 300 mM NaCl, pH 7.8. The protein concentration was estimated by Bradford assay before performing the binding reaction.

The binding assays were performed with purified protein (20 µM) and the test compound **1j** (10, 20 and 40 µM) in total reaction volume of 25 µl. After incubating for 15 min at room temperature (25 ºC), the reaction mixtures were subjected to crosslink under Ultra Violet Crosslinker for 30 min. For each set of experiment, Bocillin-FL (Thermo Fischer Scientific, Waltham, MA, USA) was used as positive control while the protein in DMSO was used as negative control. The cross-linked proteins in the reaction mixtures were denatured and subjected to 12% Sodium Dodecyl Sulphate Poly Acrylamide Gel Electrophoresis (SDS-PAGE) to study the nature of binding. The sPBP5 bound with **1j** was assessed by scanning the gel using Typhoon FLA 7000 scanner at an excitation wavelength of 488 nm and an emission wavelength of 526 nm[25] and the protein bands in the gel were visualized by staining with Coomassie brilliant blue.

Membrane isolation from *E. coli* cells

The membrane proteins were isolated from *E. coli* BL21 (DE3) cells. The cells were grown in 200 ml of LB broth at 37 °C and 180 rpm agitation. The cells were harvested at OD_{600} ~ 1.0 and pellets were washed twice with 10 mM Tris-buffer pH 7.8 before sonication. The bulk debris of sonicated cells were removed by spinning at 10,000 rpm for 2 min at 4 °C in the Oakridge tube. The supernatant was further centrifuged at 20,000 rpm for 1 h at 4 °C and pellet (membrane proteins) was dissolved in 100 µl of above buffer. The compound, 1j was allowed to bind with 300 µg of membrane protein in 30 µl of reaction volume. After 30 min of UV crossliniking the reaction mix was treated with 1% sarcosyl and incubated at 37 °C and 200 rpm shaking. The reaction mixture was centrifuged for 20,000 rpm for 1 h at 4 °C. The clear supernatant was collected and mixed with the protein loading dye (denaturing buffer) before resolving in 15% SDS PAGE. Post run, the gel was scanned in Typhoon, stained with coomassie brilliant blue, destained with destaining solution (methanol:glacial acetic acid: water:: 2:1:7) and documented using Gel-doc.

MALDI Mass Spectra

Trypsin digestion and matrix assisted laser desorption ionization spectrometry (MALDI analysis): This was carried out following the protocol as described by Basak *et al.*[3]

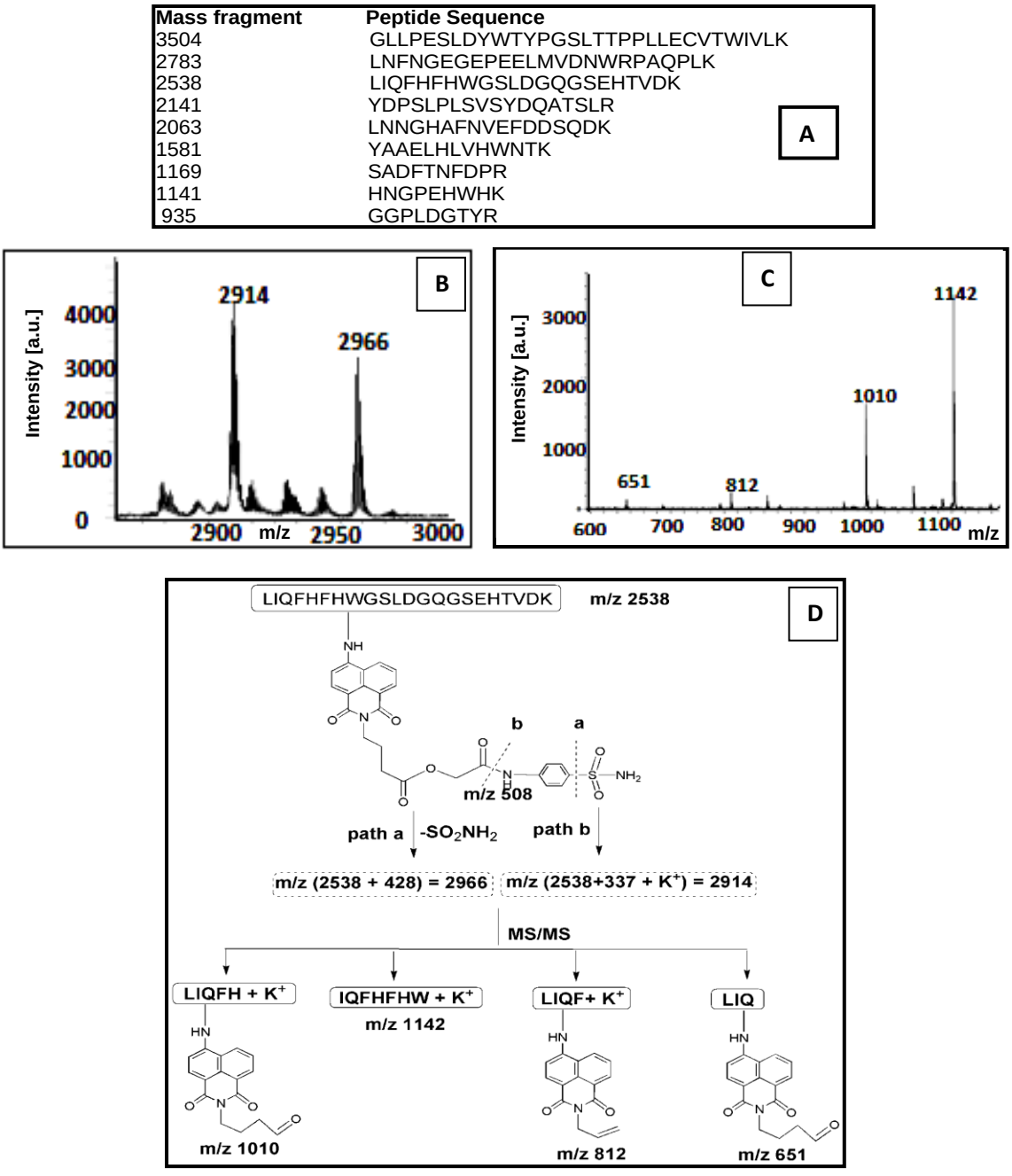


Figure S9: A) Reported[4] fragments from tryptic digest of HCA II; B) MALDI-MS spectra of tryptic digestion HCA II + Capture compound **1c**; C) MS/MS on fragment at m/z 2966; D) MALDI TOF analysis of tryptic digested fragments

Docking Information

The number of distinct conformational clusters from the docking analyses was found to be 5-8 out of 10 runs with rmsd-tolerance of 2.0 Å. The docking poses of each capturing inhibitors, **GABA sulfonamide 1c**, **Valine sulfonamide 1g**, **Glycine sulfonamide 1a** and **Phenylalanine sulfonamide 1i** with HCA II as shown in **Figure 6** in the manuscript revealed binding energies of -7.30, -8.56, -7.63 and -6.42 kcal/mol, respectively.

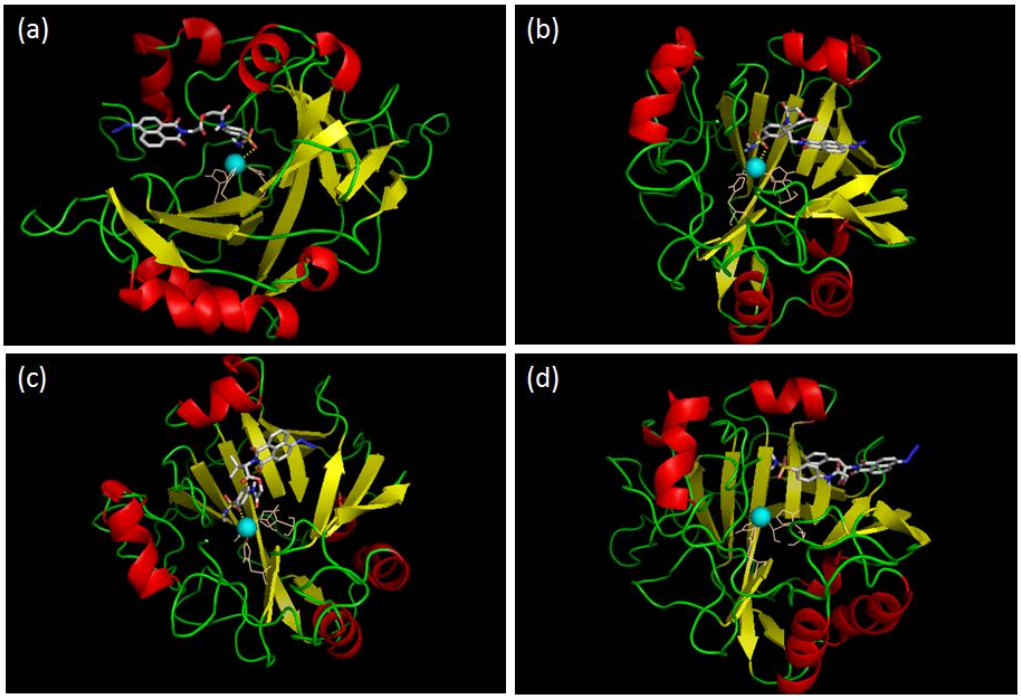


Figure S10. Docking pose of various sulfonamides with HCA II: (**a**) Glycine sulfonamide **1a**, (**b**) Gaba sulfonamide **1c**, (**c**) Valine sulfonamide **1g**, (**d**) Phenyl alanine sulfonamide **1i**

Capture Compound	Distances
GABA sulfonamide 1c	6.58 Å
Valine sulfonamide 1g	6.72 Å
Glycine sulfonamide 1a	12.87 Å
Phenylalanine sulfonamide 1i	13.19 Å

Table S2: Distances between amido-N of Q (92 A) in protein and azido-N (directly attached to the aromatic ring) of capture compounds

The capturing inhibitors involved in various types of interactions with HCA II protein as is shown in **Figure 2a-d** below. For the case of capturing inhibitor **GABA sulfonamide 1c**, the residues Leu (60A), Gln (92A), Val (121A) and Leu (198A) of HCA II protein hydrophobically interacted with the ligand. The ligand's carbonyls and amine functionalities are involved in H-bonding interactions with protein's side chain residues, Asn (62A), Hi s(64A), Glu (69A), Ile (91A), Gln (92A) and Thr (199A) (**Figure 2a)**.

The side chain amino acids Gln (92A) involved both in hydrophobic and in H-bonding interactions with the capturing inhibitor **Valine sulfonamide 1g**. The Ile (91A), Val (121A/135A), Phe (131A), and Leu (198A) are also involved in hydrophobic interaction. The tetrahedral Zn complexation with three His (64A/96A/119A) and sulphonamido-N unit of the ligand was observed in the complex. The compound **1g** is also surrounded by other side chain residues such as, Asn (62A), His (64A), Phe (70A), Thr (199A) *via* H-bonding interactions. Histidine (94A) is involved in π-cationic interactions with naphthalimido aromatic unit of **Valine sulfonamide 1g**. The carboxylate group of the ligand is involved in salt bridge interaction with His (64A) of the protein (**Figure 2b)**.

In case of **Glycine sulfonamide 1a**-HCA II complex, both the His residues of HCAII are engaged in "T"-shaped π-stacking interaction. The stabilization of the complex is also assisted by the hydrophobic interaction among the aromatic moieties of **1a** and the side chain amino acids. The ligand's carbonyls and amine functionalities are involved in H-bonding interactions with protein's side chain residues, Trp (5A), Asn (62A), Val (121A), and Leu (198A) of the HCA II. Further, involvement of H-bonding interactions with Asn (62A), His (64A), Gln (92A), Glu (106A), Lys (170A), Thr (199A/200A) makes the compound **1a** to interact moderately with the protein HCA II (**Figure 2c**).

Among the four capturing inhibitors, the weakest interaction is observed for the case of **Phenylalanine sulfonamide 1i** which might be because of sterically bulky benzyl side chain. In this case, both the hydrophobic and H-bonding interactions with Glu (69A), hydrophobic interactions with Leu (57A), Ile (91), Gln (92A), Phe (131A) and H-bonding interactions with Asn (62A/67A), Thr (200A) played a role for possible interaction (**Figure 2d**).

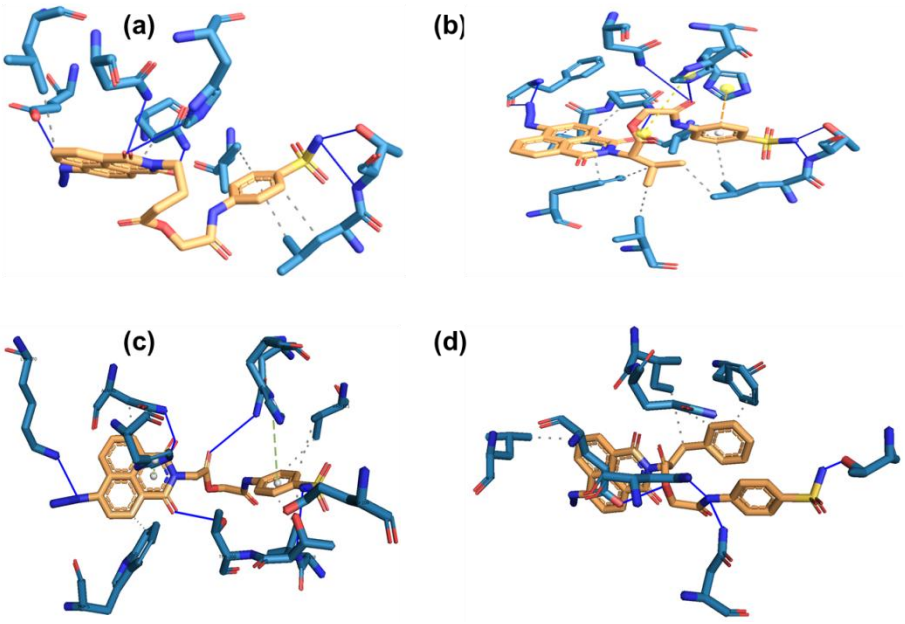


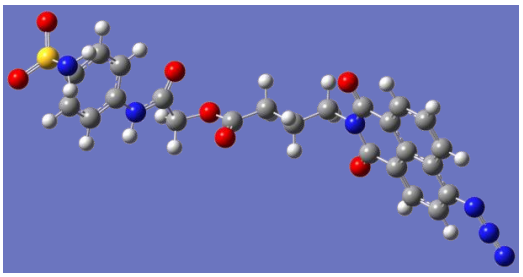
Figure S11. Various interactions exhibited by the capturing inhibitors-(**a**) **Gaba sulfonamide 1c**, (**b**) **Valine sulfonamide 1g**, (**c**) **Glycine sulfonamide 1a**, (**d**) **Phenylalanine sulfonamide 1i** with HCA II.

More interestingly, as the capture efficiency rely possibly on the covalent bond formation between nitrene generated from azido functionality from the ligand and the amino acids Q (92/103), S (99/105) and T (108) of the fragment 90-111 from HCA II, we analysed the docked conformations to find out the closeness of these amino acids. Our analysis revealed that none of the ligands are in close proximity or involved in interactions with S or T. However, in all the cases we observed that only Q (92A) side chain residue is involved in interactions and maintain a closeness with the azido functionality allowing us to measure the distance for a comparison. The proximal distance between azido-N directly attached to the aromatic ring and the amido-N of Q (92A) could be a probe for predicting the capturing efficiency of the ligands. Thus, we observed that the distance increases as we move from **GABA sulfonamide 1c** (6.58 Å) to **Phenylalanine sulfonamide 1i** (13.19 Å) through **Valine sulfonamide 1g** (6.72 Å) and **Glycine sulfonamide 1a** (12.87 Å). Thus, the capturing efficiency follows the descending order as **GABA sulfonamide 1c**>**Valine sulfonamide1g**>**Glycine sulfonamide 1a**>**Phenylalanine sulfonamide 1i** corroborating our experimental result of cross linking efficiency.

1. DFT Optimized Geometries, Energy and Cartesian Coordinates of the Synthesized Compounds

The ground state structures of the synthesized inhibitors fluorophores were optimized using density functional theory (DFT) with B3LYP functional and 6-31G (d) basis set with Gaussian 09 program package.[5] There were no imaginary frequencies observed in frequency analysis for all the calculated structures; therefore, each calculated structure was a local energy minimum.

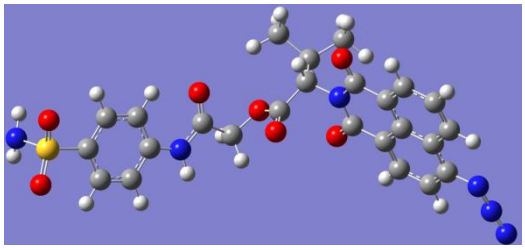
1.1. GABA sulfonamide 1c



E(RB3LYP)= -2179.82251043 a.u.; Imaginary Freq = 0;
Dipole Moment = 8.9036 Debye
Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	6.071648	-3.279199	1.498396
2	6	0	7.051656	-2.861947	0.619692
3	6	0	6.997406	-1.568965	0.041430
4	6	0	5.914774	-0.704407	0.383625
5	6	0	4.921828	-1.157786	1.288893
6	6	0	5.001395	-2.426717	1.834792
7	6	0	7.981131	-1.082219	-0.875860
8	6	0	7.877404	0.193617	-1.413616
9	6	0	6.802328	1.025634	-1.064093
10	6	0	5.829784	0.594509	-0.178227
11	6	0	-5.855978	0.930403	-0.584685
12	6	0	3.785210	-0.277111	1.658776
13	6	0	-6.703513	0.653617	-1.671208
14	6	0	4.708943	1.496241	0.170020
15	6	0	-7.728488	-0.275895	-1.550774
16	6	0	-7.913292	-0.938318	-0.334950
17	6	0	2.653815	1.897641	1.458153
18	6	0	1.460677	1.751756	0.507805
19	6	0	0.323714	2.697921	0.897987
20	6	0	-0.885313	2.559023	0.002118
21	6	0	-7.085552	-0.660178	0.755025
22	6	0	-3.866074	2.303672	0.094021
23	6	0	-6.054084	0.267246	0.638625
24	6	0	-3.003227	3.444264	-0.473412

1.2. Valine sulfonamide 1g



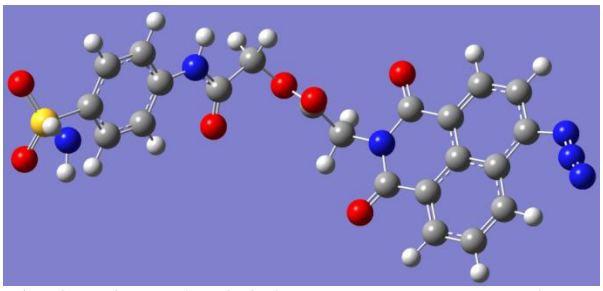
E(RB3LYP)= -2219.12869571 a.u.; Imaginary Freq = 0;
Dipole Moment = 8.9410 Debye
Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	5.645963	-1.404127	3.180297
2	6	0	6.316590	-1.860885	2.062886
3	6	0	5.928993	-1.437595	0.767033
4	6	0	4.833479	-0.532947	0.634968
5	6	0	4.161921	-0.079016	1.798716
6	6	0	4.565935	-0.509053	3.050665
7	6	0	6.586842	-1.874832	-0.425755
8	6	0	6.166155	-1.427213	-1.671197
9	6	0	5.086556	-0.537130	-1.777088
10	6	0	4.422058	-0.090261	-0.647527
11	6	0	3.020946	0.863549	1.690396
12	6	0	3.284206	0.841270	-0.787583
13	6	0	1.463887	2.128676	0.258090
14	1	0	5.951533	-1.735627	4.168026
15	1	0	7.148734	-2.549493	2.161539
16	1	0	4.032560	-0.142873	3.921513
17	1	0	6.671543	-1.764909	-2.571312
18	1	0	4.755145	-0.186485	-2.748853
19	1	0	1.073883	2.171711	1.281289
20	7	0	7.662497	-2.768426	-0.234528
21	7	0	2.653489	1.259471	0.391605
22	7	0	8.270419	-3.184388	-1.231793
23	7	0	8.913718	-3.643316	-2.052078
24	8	0	2.887936	1.252617	-1.871561

25	1	0	-5.406732	0.486582	1.475606
26	1	0	-8.196987	-3.729413	-1.486695
27	1	0	-7.824123	-3.936875	0.148619
28	1	0	-3.519146	4.397157	-0.322157
29	1	0	-2.810276	3.299705	-1.541846
30	1	0	-6.562311	1.177401	-2.614239
31	1	0	6.123406	-4.272155	1.934701
32	1	0	7.875790	-3.517361	0.359571
33	1	0	4.224661	-2.744149	2.522614
34	1	0	8.629254	0.554926	-2.109246
35	1	0	6.717877	2.022496	-1.483847
36	1	0	2.365969	1.640276	2.478669
37	1	0	3.042724	2.917040	1.433937
38	1	0	1.784408	1.966200	-0.516205
39	1	0	1.099909	0.718762	0.526676
40	1	0	-0.018508	2.504667	1.924446
41	1	0	0.645119	3.746973	0.883215
42	1	0	-4.808694	2.282069	-1.714668
43	1	0	-8.396520	-0.473728	-2.382349
44	1	0	-7.261203	-1.155157	1.704844
45	7	0	9.029758	-1.979100	-1.175285
46	7	0	3.769296	1.007749	1.092552
47	7	0	-8.533175	-3.667388	-0.528886
48	7	0	-4.844976	1.888119	-0.783070
49	7	0	9.909757	-1.616611	-1.969628
50	7	0	10.780525	-1.417902	-2.676500
51	8	0	4.589566	2.617977	-0.307321
52	8	0	2.897898	-0.633963	2.422325
53	8	0	-1.781678	3.557954	0.241617
54	8	0	-3.704031	1.871636	1.219958
55	8	0	-1.073119	1.695591	-0.824991
56	8	0	-10.174129	-1.915024	-1.258966
57	8	0	-9.596958	-2.227079	1.227815
58	16	0	-9.216278	-2.163940	-0.182165

25	8	0	2.430149	1.291029	2.671888
26	6	0	0.422554	1.331427	-0.534880
27	8	0	-0.320657	2.106939	-1.360997
28	8	0	0.253506	0.138512	-0.423011
29	6	0	-1.382511	1.431198	-2.018211
30	6	0	-2.552173	1.196625	-1.047216
31	1	0	-1.027118	0.489070	-2.447161
32	1	0	-1.703232	2.103195	-2.819803
33	7	0	-3.455710	0.267184	-1.515056
34	8	0	-2.662188	1.818760	-0.006866
35	6	0	-4.676879	-0.139229	-0.946755
36	1	0	-3.199714	-0.216712	-2.366546
37	6	0	-5.150482	0.349306	0.283049
38	6	0	-5.435891	-1.083930	-1.658722
39	6	0	-6.372043	-0.102903	0.774346
40	1	0	-4.556935	1.060079	0.840111
41	6	0	-6.654717	-1.530595	-1.164413
42	1	0	-5.063234	-1.476714	-2.602445
43	6	0	-7.125802	-1.029969	0.051500
44	1	0	-6.729008	0.247476	1.737624
45	1	0	-7.230253	-2.277104	-1.701460
46	16	0	-8.714513	-1.581778	0.680271
47	7	0	-9.874547	-0.476583	0.150601
48	8	0	-8.683781	-1.443075	2.134952
49	8	0	-9.036794	-2.836489	0.001845
50	1	0	-9.736100	0.451130	0.543622
51	1	0	-9.961773	-0.460108	-0.862487
52	6	0	1.759678	3.580682	-0.205728
53	1	0	1.863730	3.568580	-1.294570
54	6	0	0.596726	4.513933	0.186295
55	1	0	0.766393	5.515125	-0.225361
56	1	0	-0.370158	4.158262	-0.174967
57	1	0	0.531723	4.615981	1.276468
58	6	0	3.068636	4.101106	0.408716
59	1	0	3.043575	4.030585	1.503264
60	1	0	3.947779	3.559433	0.051170
61	1	0	3.204931	5.155399	0.143452

1.3. Glycine-sulfonamide 1a

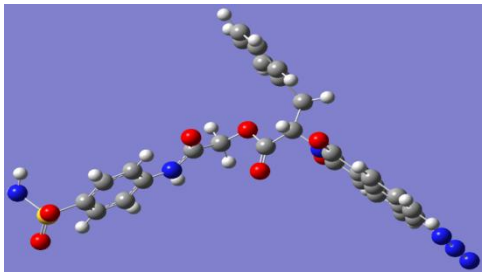


E(RB3LYP) = -2101.18591055 a.u.; Imaginary Freq = 0; Dipole Moment = 6.4226 Debye

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1.4. Phe-sulfonamide 1i



E(RB3LYP) = -2371.55081759 a.u.; Imaginary Freq = 0; Dipole Moment = 8.2719 Debye

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	6	0	5.181307	-0.250264	-0.320900
2	6	0	4.318683	-0.833209	-1.286010
3	6	0	4.618894	-2.061427	-1.845979
4	6	0	5.794857	-2.738305	-1.472179
5	6	0	6.648427	-2.198315	-0.530492
6	6	0	6.360503	-0.953596	0.089674
7	6	0	7.190377	-0.332362	1.082775
8	6	0	6.891105	0.934664	1.560604
9	6	0	5.739382	1.611306	1.132685
10	6	0	4.882790	1.028198	0.216254
11	7	0	8.385211	-0.899383	1.598168
12	7	0	8.489211	-2.115935	1.802715
13	7	0	8.757725	-3.194597	2.059633
14	6	0	3.659242	1.753689	-0.194011
15	7	0	2.848651	1.132052	-1.155549
16	6	0	3.081940	-0.132103	-1.721578
17	6	0	1.621689	1.829532	-1.513026
18	6	0	0.600018	1.752943	-0.389619
19	8	0	-0.343875	2.713326	-0.567030
20	6	0	-1.436819	2.663597	0.335182
21	6	0	-2.507173	1.689565	-0.187003
22	7	0	-3.649278	1.701194	0.585428
23	1	0	-3.641860	2.319998	1.386986
24	8	0	2.308977	-0.606748	-2.539797
25	8	0	3.345706	2.847678	0.256547
26	1	0	1.203171	1.340838	-2.395005
27	1	0	1.838651	2.874798	-1.737979
28	8	0	0.609948	0.965139	0.523318
29	1	0	-1.096212	2.348117	1.327154
30	1	0	-1.835070	3.681818	0.391012
31	8	0	-2.333136	0.999709	-1.173493
32	6	0	-4.820345	0.932405	0.443706
33	6	0	-5.823856	1.104491	1.413354
34	6	0	-7.007903	0.383676	1.341395
35	6	0	-7.194134	-0.518932	0.292447
36	6	0	-6.211686	-0.689035	-0.683000
37	6	0	-5.020878	0.030101	-0.613864
38	16	0	-8.715941	-1.451159	0.199208
39	8	0	-8.875726	-1.899771	-1.187956
40	8	0	-9.755618	-0.692669	0.902412
41	7	0	-8.409255	-2.818396	1.164644
42	1	0	3.938662	-2.478450	-2.581018
43	1	0	6.036596	-3.690883	-1.933621
44	1	0	7.554183	-2.737929	-0.281895
45	1	0	7.553445	1.380908	2.294526
46	1	0	5.494659	2.592526	1.525237
47	1	0	-5.675706	1.812567	2.226023
48	1	0	-7.789202	0.529122	2.079587
49	1	0	-6.384113	-1.372865	-1.507258
50	1	0	-4.253706	-0.093983	-1.364764
51	1	0	-9.186591	-2.935492	1.812079
52	1	0	-8.306451	-3.640128	0.571857

Number	Number	Type	X	Y	Z
1	6	0	5.647358	-1.605700	3.240234
2	6	0	6.265821	-2.220129	2.169298
3	6	0	5.855192	-1.939914	0.842053
4	6	0	4.790974	-1.013547	0.629376
5	6	0	4.174251	-0.395202	1.746627
6	6	0	4.598876	-0.688736	3.030928
7	6	0	6.458824	-2.545154	-0.305092
8	6	0	6.016307	-2.235199	-1.584458
9	6	0	4.967051	-1.322339	-1.769763
10	6	0	4.355695	-0.714278	-0.686320
11	6	0	3.070123	0.575369	1.553110
12	6	0	3.249248	0.237268	-0.912179
13	6	0	1.544517	1.740886	0.014507
14	1	0	5.969840	-1.829117	4.252605
15	1	0	7.073759	-2.925845	2.329344
16	1	0	4.106329	-0.199514	3.864631
17	1	0	6.480270	-2.699829	-2.449588
18	1	0	4.617057	-1.080855	-2.767855
19	1	0	1.145640	1.914655	1.017925
20	7	0	7.505584	-3.451792	-0.034263
21	7	0	2.675237	0.822950	0.225661
22	7	0	8.065799	-4.010706	-0.988955
23	7	0	8.665334	-4.592064	-1.763252
24	8	0	2.833343	0.525635	-2.028470
25	8	0	2.528288	1.149399	2.488303
26	6	0	0.443345	0.989312	-0.732054
27	8	0	-0.287177	1.810606	-1.520553
28	8	0	0.201523	-0.187349	-0.591810
29	6	0	-1.396023	1.184883	-2.153633
30	6	0	-2.495717	0.840806	-1.134650
31	1	0	-1.064533	0.296167	-2.700537
32	1	0	-1.778866	1.927497	-2.859558
33	7	0	-3.355760	-0.137134	-1.588835
34	8	0	-2.601110	1.428667	-0.075268
35	6	0	-4.515724	-0.642603	-0.975240
36	1	0	-3.100949	-0.589733	-2.457381
37	6	0	-4.959731	-0.221301	0.290250
38	6	0	-5.242957	-1.619262	-1.677492
39	6	0	-6.121303	-0.770554	0.825739
40	1	0	-4.388177	0.513579	0.838922
41	6	0	-6.402021	-2.163083	-1.138942
42	1	0	-4.891744	-1.959693	-2.649334
43	6	0	-6.845150	-1.728696	0.112500
44	1	0	-6.452901	-0.471040	1.814915
45	1	0	-6.951424	-2.933058	-1.670212
46	16	0	-8.361499	-2.402243	0.797641
47	7	0	-9.613163	-1.355886	0.364788
48	8	0	-8.267839	-2.309532	2.253407
49	8	0	-8.639033	-3.652469	0.091586
50	1	0	-9.512629	-0.436330	0.787599
51	1	0	-9.747324	-1.306526	-0.642068
52	6	0	1.982899	3.101663	-0.583562
53	1	0	2.048344	3.025245	-1.670138
54	1	0	3.000878	3.282175	-0.215534
55	6	0	1.098274	4.264647	-0.177100
56	6	0	0.378912	4.992849	-1.130854
57	6	0	1.007099	4.649903	1.168458
58	6	0	-0.410823	6.080701	-0.754799
59	1	0	0.437411	4.701327	-2.176535
60	6	0	0.214954	5.732778	1.548707

	61 1 0 1.559784 4.095231 1.924426 62 6 0 -0.496102 6.453651 0.586860 63 1 0 -0.960918 6.635336 -1.510843 64 1 0 0.155752 6.015671 2.596449 65 1 0 -1.111826 7.299198 0.881898 ---

2. Molecular Docking Study

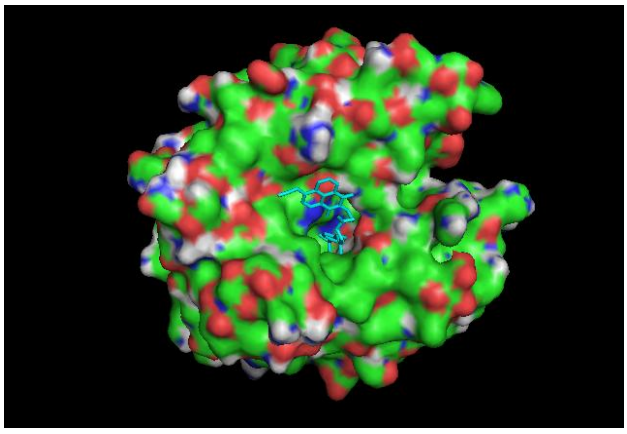
Molecular Docking study was carried out using **AutoDock4** (Bikadi, Hazai, 2009). The amino acid sequence of HCA II protein was observed from the website, http://www.rcsb.org/pdb/explore.do?structureId=1CA2. Following is the HCAII sequence which was used to generate the 3D model. >1CA2:A|PDBID|CHAIN|SEQUENCE Human Carbonic Anhydrase II:

SHHWGYGKHNGPEHWHKDFPIAKGERQSPVDIDTHTAKYDPSLKPLSVSYDQATSL
RILNNGHAFNVEFDDSQDKAVLKGGPLDGTYRLIQFHFHWGSLDGQGSEHTVDKKKYA
AELHLVHWNTKYGDFGKAVQQPDGLAVLGIFLKVGSAKPGLQKVVDVLDSIKTKGKS
ADFTNFDPRGLLPESLDYWTYPGSLTTPPLLECVTWIVLKEPISVSSEQVLKFRKLNFNGE
GEPEELMVDNWRPAQPLKNRQIKASFK

The Binding interaction was studied from protein-ligand interaction profiler https://projects.biotec.tu-dresden.de/plip-web/plip/index.

2.1. Results for Docking/Interaction of GABA sulfonamide (1c) with HCA II

2.1.1. DOCKED CONFORMATION and the Energy

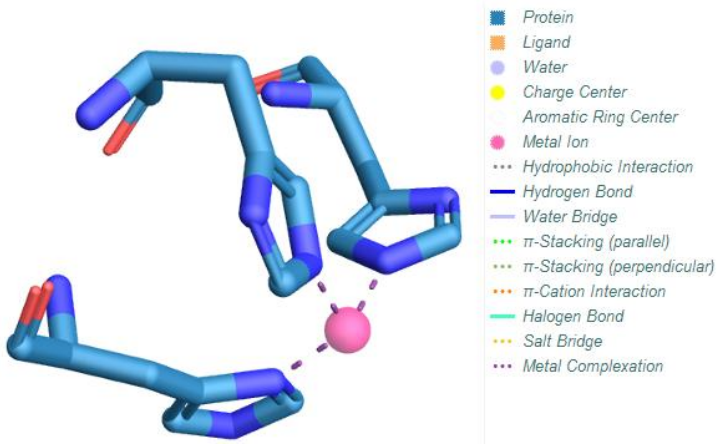


Estimated Free Energy of Binding = -7.30 kcal/mol

2.1.2. Interaction Study:

We have detected 2 binding site(s) in GABA sulfonamide –HCA II complex.

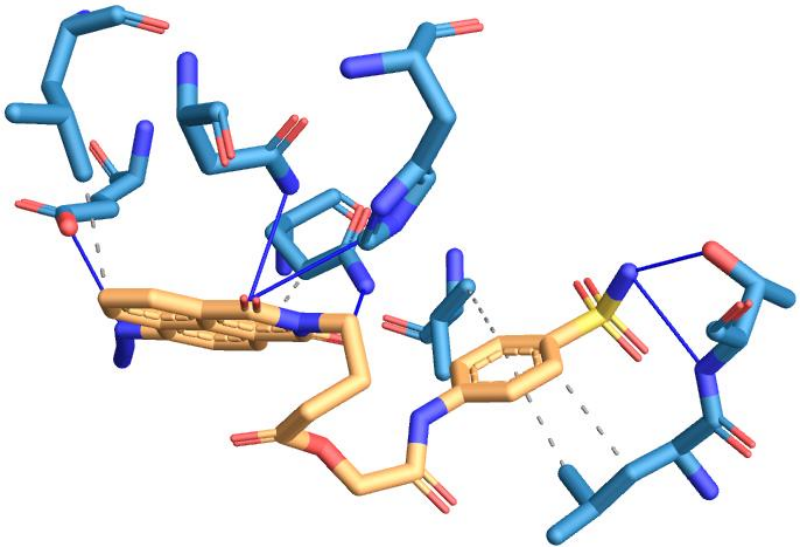
ION-ZN (zinc ion); ZN-A-262; Interacting chains A-Metal Complexation



Metal Complexes

Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Zn, trigonal.pyramidal (3)						
1	94A	HIS	2491	900	1.99	protein.sidechain
2	96A	HIS	2491	924	2.10	protein.sidechain
3	119A	HIS	2491	1143	1.91	protein.sidechain

SMALL MOLECULE-FRA Interacting chains: A



Hydrophobic Interactions

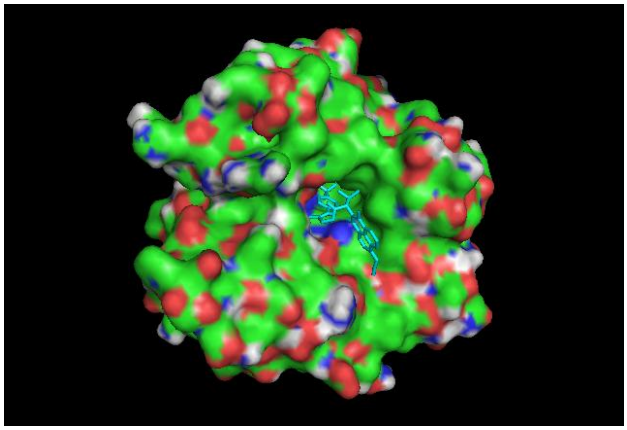
Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	60A	LEU	3.28	2499	572
2	92A	GLN	3.28	2508	873
3	121A	VAL	3.88	2525	1164
4	198A	LEU	3.79	2525	1880
5	198A	LEU	3.33	2523	1877

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	62A	ASN	2.32	2.98	121.32	√	√	592 [Nam]	2504 [O2]
2	64A	HIS	3.71	4.09	104.53	√	√	611 [Npl]	2504 [O2]
3	69A	GLU	2.96	3.28	101.72	√	√	659 [O3]	2492 [N2]
4	91A	ILE	3.11	3.96	144.57	X	X	2494 [N2]	862 [O2]
5	92A	GLN	2.22	2.68	107.01	√	√	876 [Nam]	2507 [O2]
6	199A	THR	2.44	3.36	149.43	√	X	1881 [Nam]	2530 [N3]
7	199A	THR	2.06	2.52	105.12	X	√	2530 [N3]	1887 [O3]

2.2. Results for Docking/Interaction of Valine sulfonamide (1g) with HCA II

2.2.1. DOCKED CONFORMATION and Energy

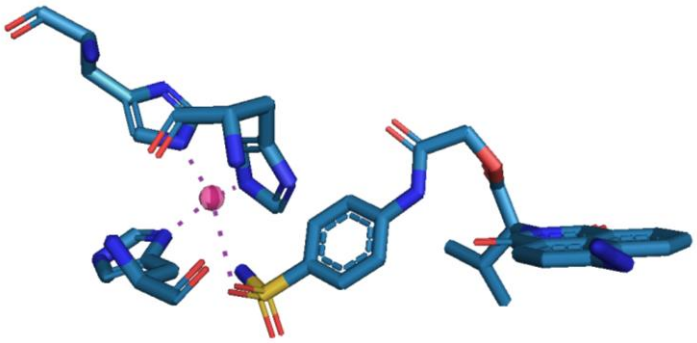


Estimated Free Energy of Binding = -8.56 kcal/mol

2.2.2. Interaction Study

We have detected 2 binding site(s) in valine sulfonamide(1g) –HCA II complex

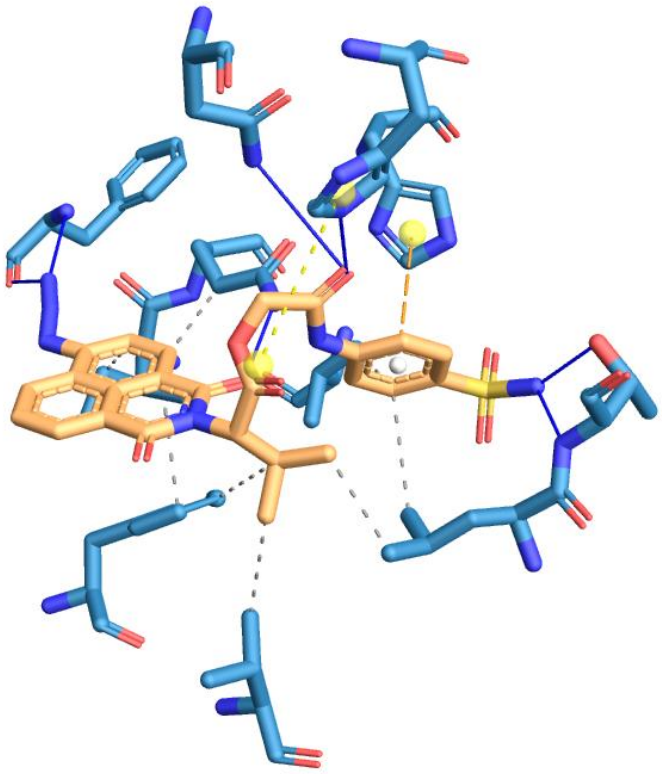
Metal Complexes



Metal Complexes

Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Zn, tetrahedral (4)						
1	0Z	LIG	2491	2526	2.94	protein.mainchain
2	94A	HIS	2491	900	1.99	protein.sidechain
3	96A	HIS	2491	924	2.10	protein.sidechain
4	119A	HIS	2491	1143	1.91	protein.sidechain

SMALLMOLECULE-Interacting chains: A



Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	91A	ILE	3.26	2509	864
2	92A	GLN	3.32	2508	873
3	121A	VAL	3.60	2521	1164
4	131A	PHE	3.81	2506	1266
5	131A	PHE	3.86	2531	1268
6	135A	VAL	3.72	2533	1299
7	198A	LEU	3.78	2521	1880
8	198A	LEU	3.24	2532	1879

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	62A	ASN	3.31	4.03	128.77	√	√	592 [Nam]	2518 [O2]
2	64A	HIS	1.80	2.71	147.20	√	√	√	2518 [O2]
3	70A	PHE	3.26	4.01	131.87	√	X	660 [Nam]	2494 [N2]
4	92A	GLN	2.38	3.18	137.02	√	√	√	2507 [O2]
5	199A	THR	1.92	2.78	140.20	√	X	1881 [Nam]	2528 [N3]
6	199A	THR	2.21	2.62	102.73	X	√	2528 [N3]	1887 [O3]

π-Cation Interactions

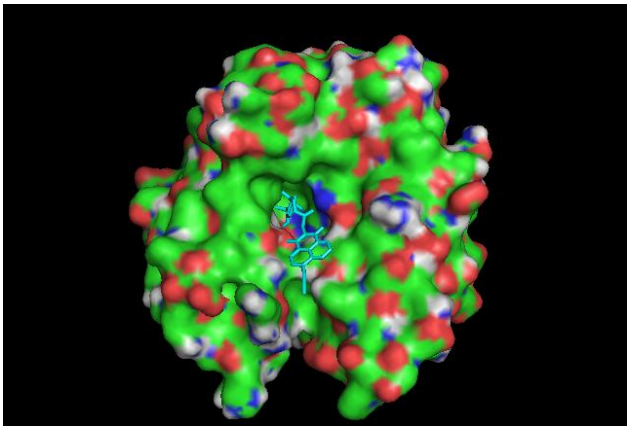
Index	Residue	AA	Distance	Offset	Protein charged?	Ligand Group	Ligand Atoms
1	94A	HIS	4.25	0.65	√	Aromatic	2519, 2520, 2521, 2522, 2523, 2524

Salt Bridges

Index	Residue	AA	Distance	Protein positive?	Ligand Group	Ligand Atoms
1	64A	HIS	5.49	√	Carboxylate	2513, 2512

2.3 Results for Docking/Interaction of Glycine sulfonamide (1a) with HCA II

2.3.1. DOCKED CONFORMATION and Energy

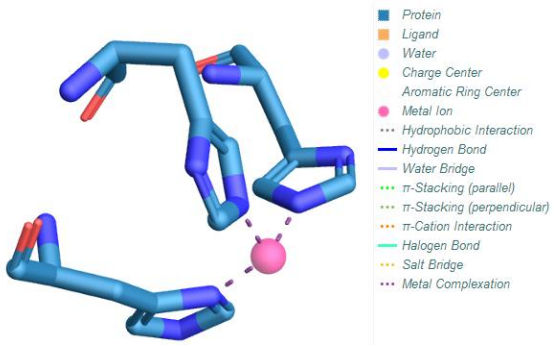


Estimated Free Energy of Binding = -7.63 kcal/mol

2.3.2. Interaction Study:

We have detected 2 binding site(s) in Glycine sulfonamide(1a) –HCA II complex.

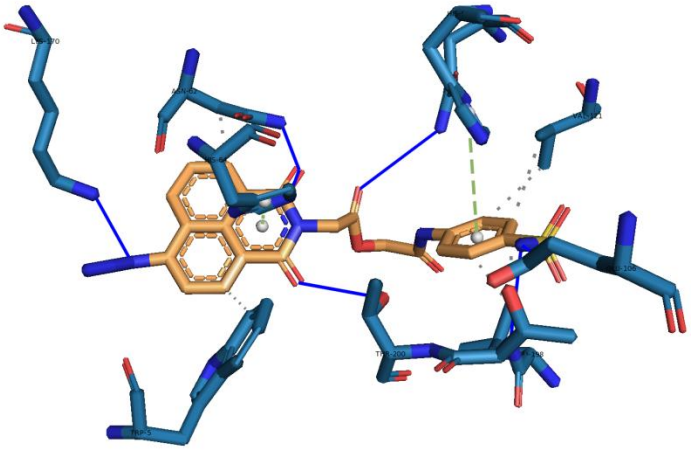
Metal Complexes



Metal Complexes

Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Zn, trigonal.pyramidal (3)						
1	94A	HIS	2491	900	1.99	protein.sidechain
2	96A	HIS	2491	924	2.10	protein.sidechain
3	119A	HIS	2491	1143	1.91	protein.sidechain

SMALLMOLECULE-Interacting chains: A



Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	5A	TRP	3.67	2508	29
2	62A	ASN	3.13	2501	589
3	121A	VAL	3.60	2523	1164
4	121A	VAL	3.77	2524	1163
5	198A	LEU	3.33	2523	1880
6	198A	LEU	3.81	2521	1880

Hydrogen Bonds

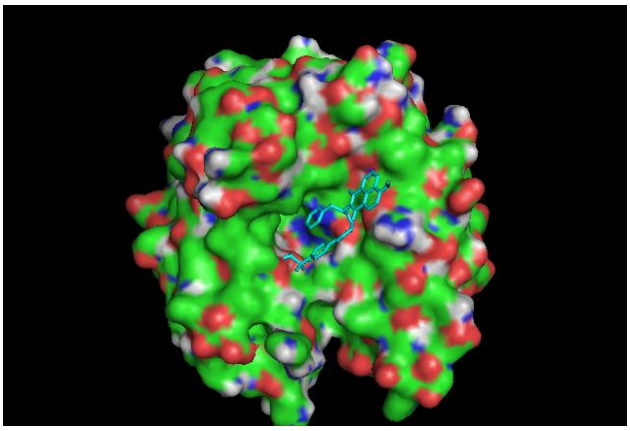
Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	62A	ASN	2.38	3.10	126.95	√	√	592 [Nam]	2505 [O2]
2	64A	HIS	3.46	4.07	120.43	√	√	611 [Npl]	2505 [O2]
3	92A	GLN	3.52	4.05	116.19	√	√	876 [Nam]	2512 [O2]
4	106A	GLU	3.20	3.99	135.77	X	√	2528 [N3]	1010 [O3]
5	170A	LYS	2.83	3.85	176.23	√	√	1611 [N3+]	2492 [N2]
6	199A	THR	2.57	3.47	147.01	√	X	1881 [Nam]	2528 [N3]
7	200A	THR	3.62	3.96	103.88	√	√	1896 [O3]	2507 [O2]

π-Stacking

Index	Residue	AA	Distance	Angle	Offset	Type	Ligand Atoms
1	64A	HIS	4.00	78.77	0.55	T	2497, 2499, 2500, 2502, 2504, 2506
2	94A	HIS	5.36	72.00	1.61	T	2519, 2520, 2521, 2522, 2523, 2524

2.4. Results for Docking/Interaction of Phenylalanine sulfonamide (1i) with HCA II

2.4.1. DOCKED CONFORMATION and Energy

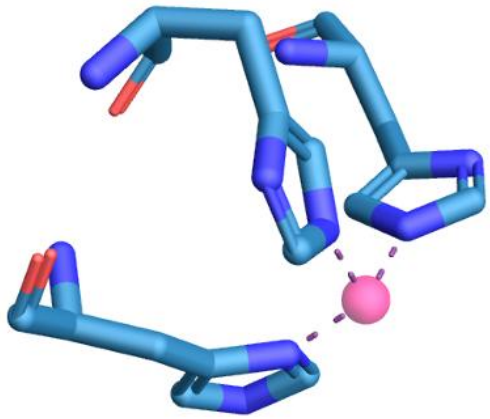


Estimated Free Energy of Binding = -6.42 kcal/mol

2.4.2. Interaction Study:

We have detected 2 binding site(s) in Phenylalanine sulfonamide(1i) –HCA II complex.

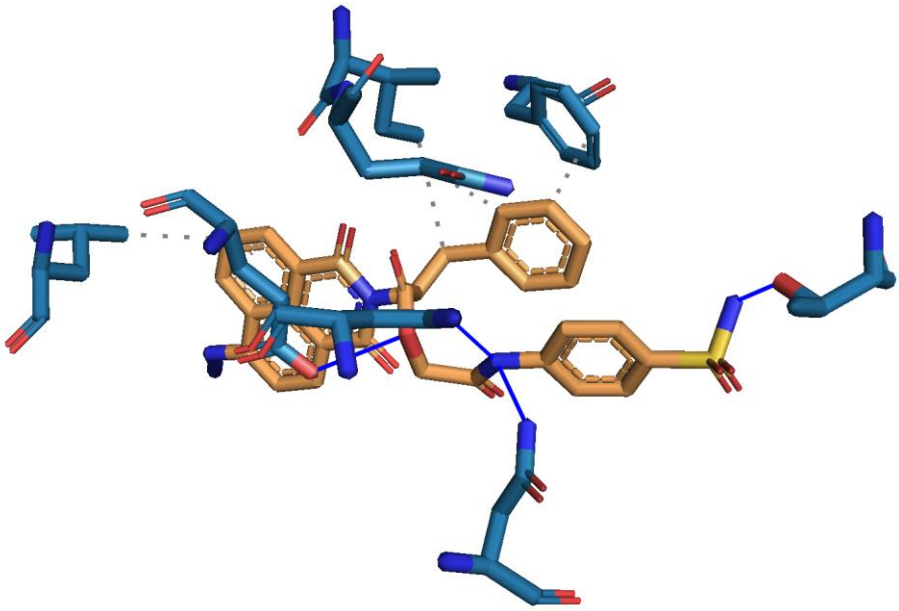
Metal Complexes



Metal Complexes

Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Zn, trigonal.pyramidal (3)						
1	94A	HIS	2491	900	1.99	protein.sidechain
2	96A	HIS	2491	924	2.10	protein.sidechain
3	119A	HIS	2491	1143	1.91	protein.sidechain

SMALLMOLECULE-Interacting chains: A



Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	57A	LEU	3.21	2499	536
2	69A	GLU	3.30	2500	655
3	91A	ILE	3.95	2531	866
4	92A	GLN	3.70	2537	873
5	131A	PHE	3.36	2536	1268

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	62A	ASN	2.76	3.75	164.51	√	√	592 [Nam]	2516 [Nam]
2	67A	ASN	1.87	2.83	158.77	X	√	2516 [Nam]	638 [O2]
3	69A	GLU	2.13	3.06	170.67	√	√	659 [O3]	2513 [O3]
4	200A	THR	2.26	2.75	111.39	√	√	1896 [O3]	2528 [N3]
5	200A	THR	1.87	2.75	142.71	X	√	2528 [N3]	1896 [O3]

NMR Spectra

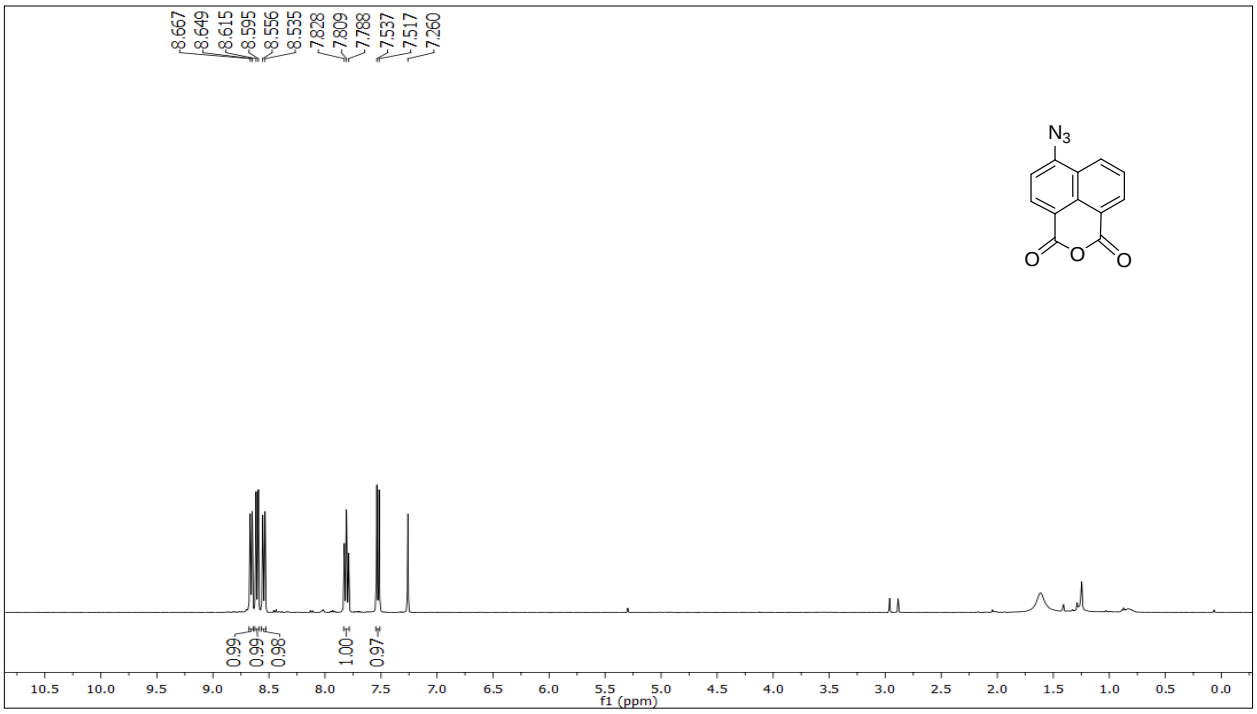


Figure S12. The ^{1}H NMR (400 MHz, Acetone-d_6) spectrum of compound **3**

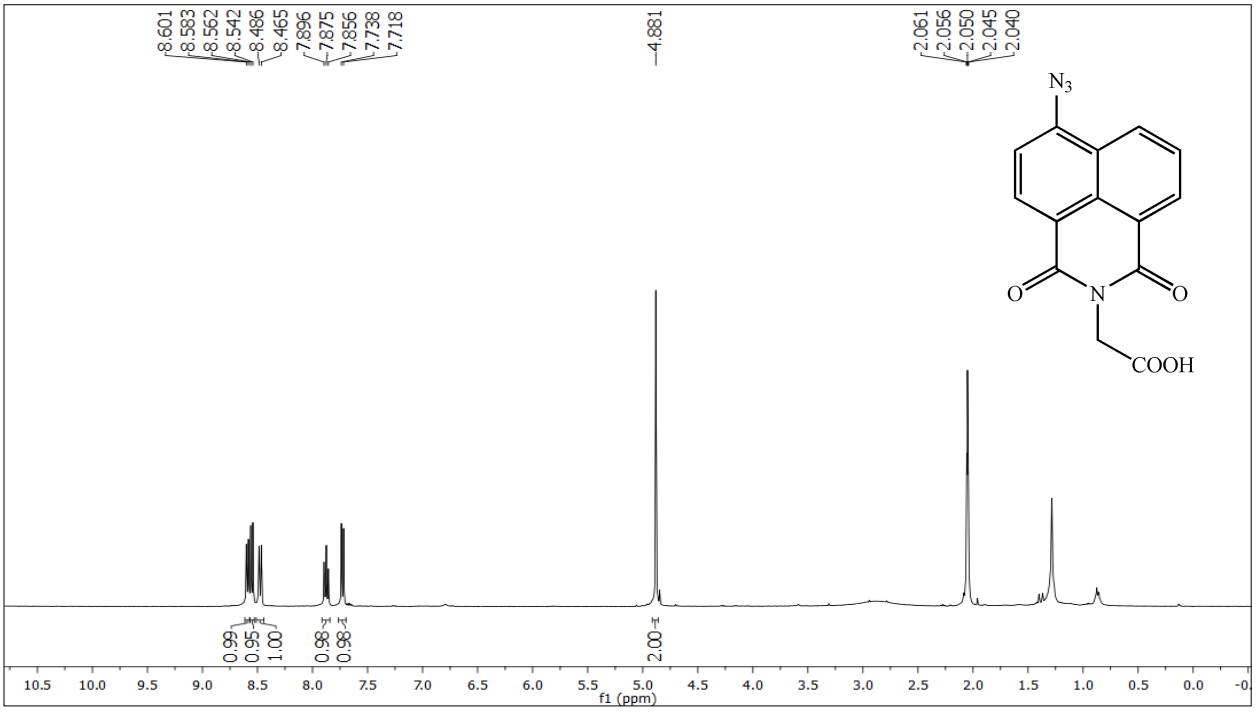


Figure S13. The ^{1}H NMR (400 MHz, Acetone-d_6) spectrum of compound **4a**

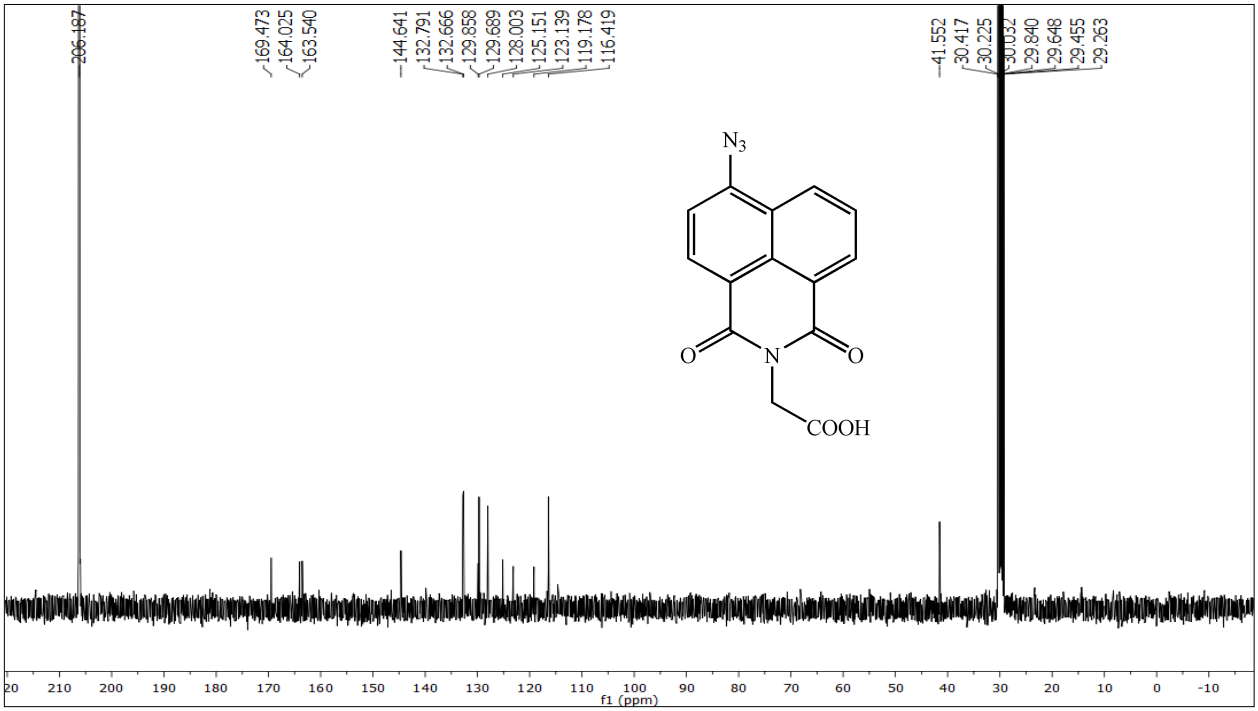


Figure S14. The ^{13}C NMR (100 MHz, Acetone-d_6) spectrum of compound **4a**

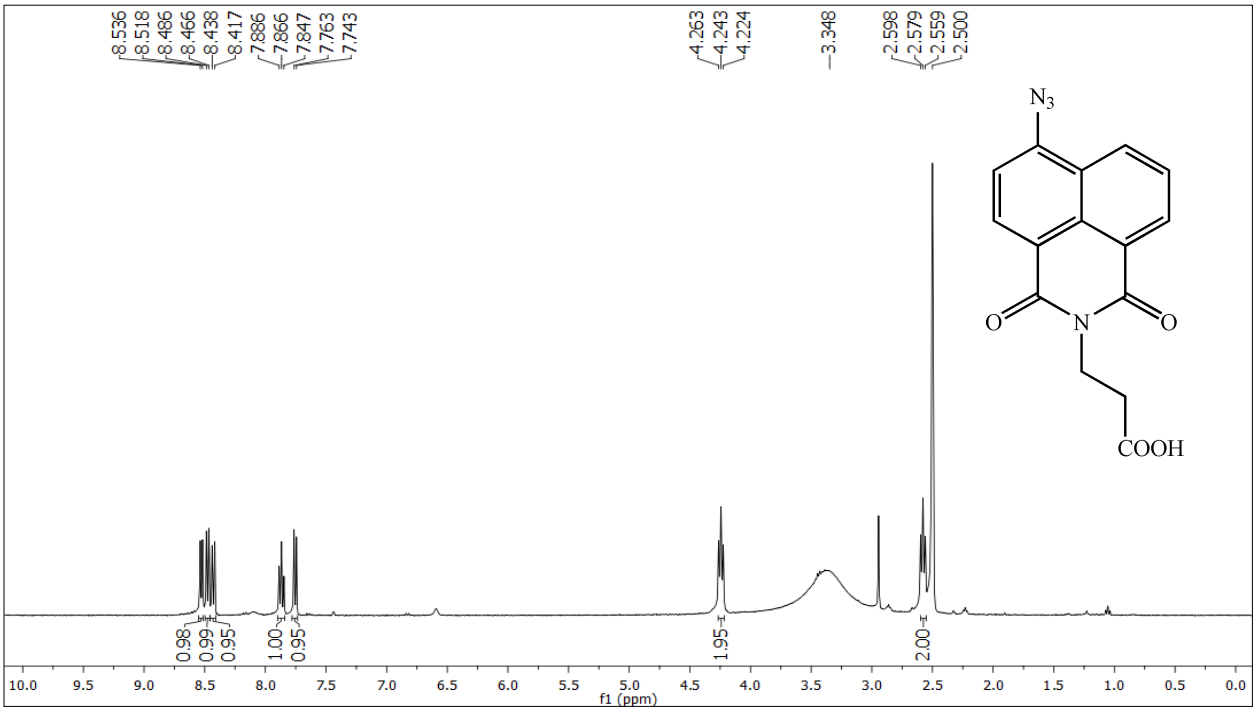


Figure S15. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **4b**

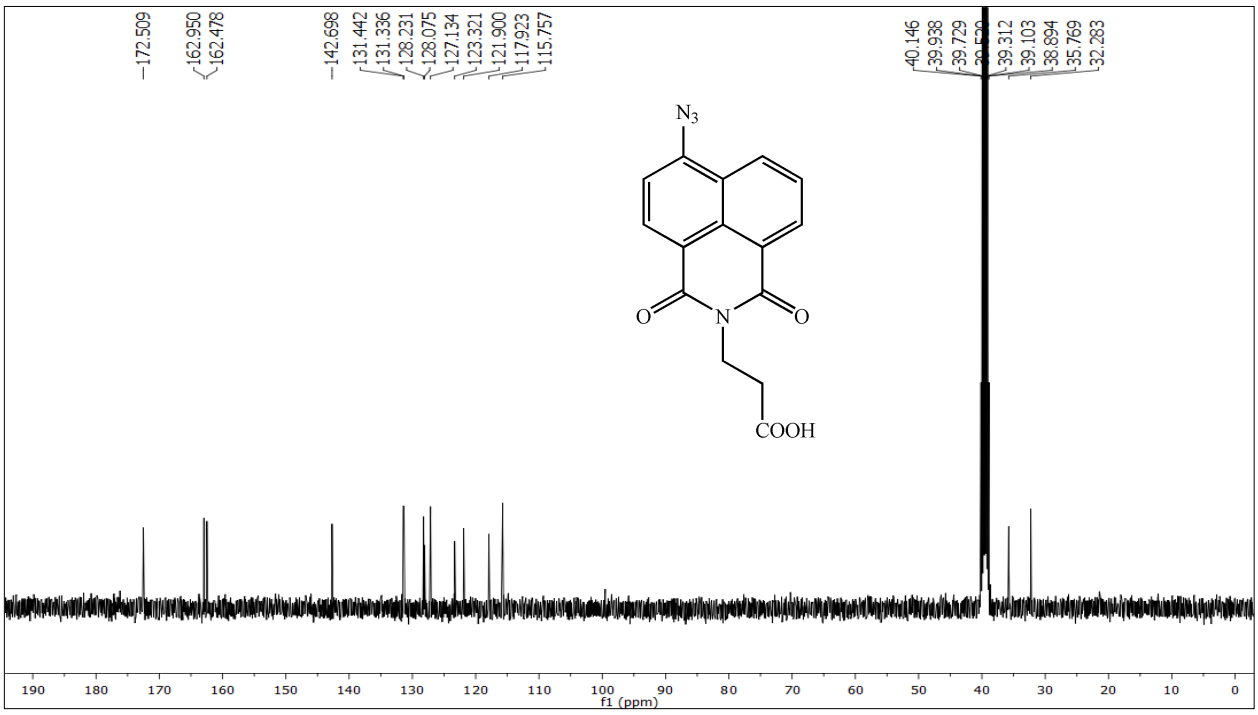


Figure S16. The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **4b**

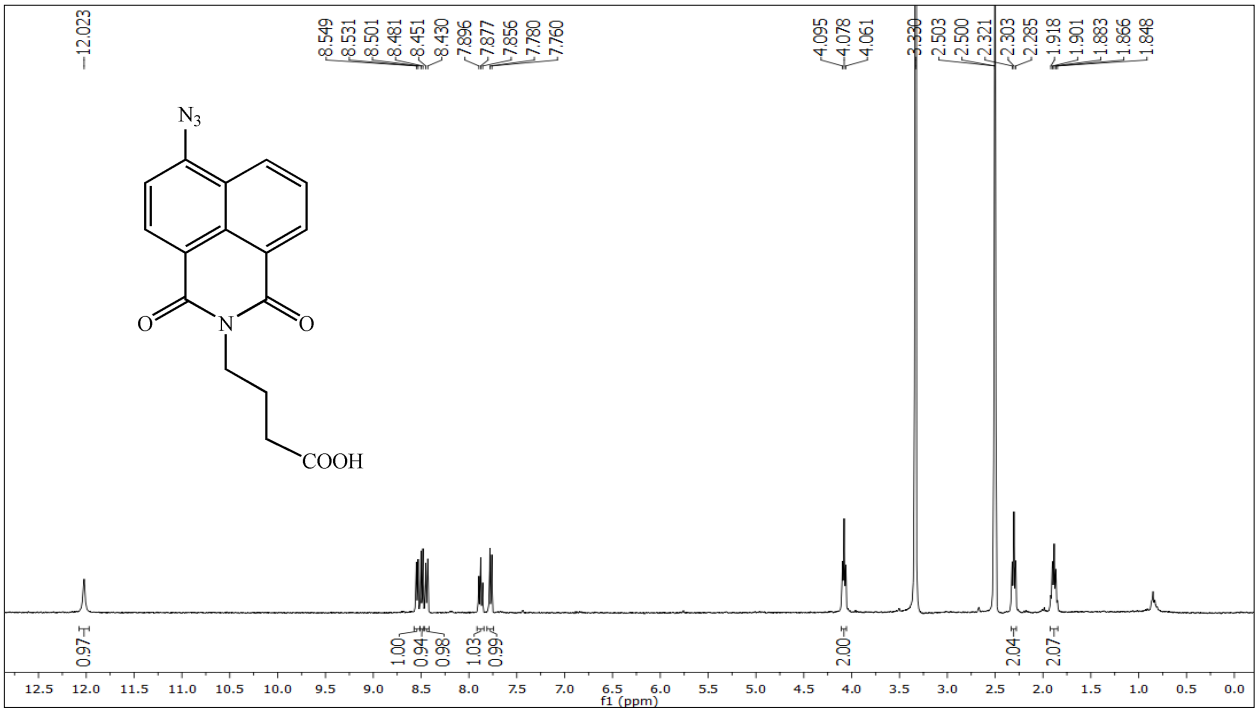


Figure S17. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **4c**

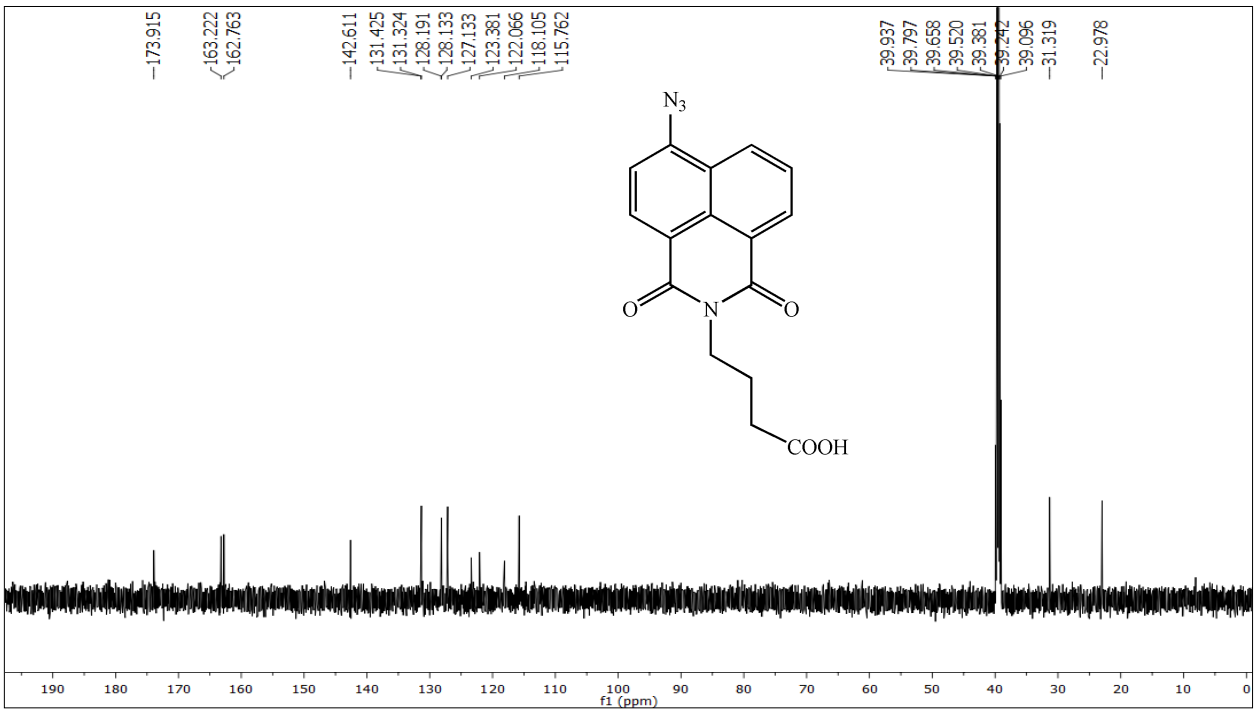


Figure S18. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **4c**

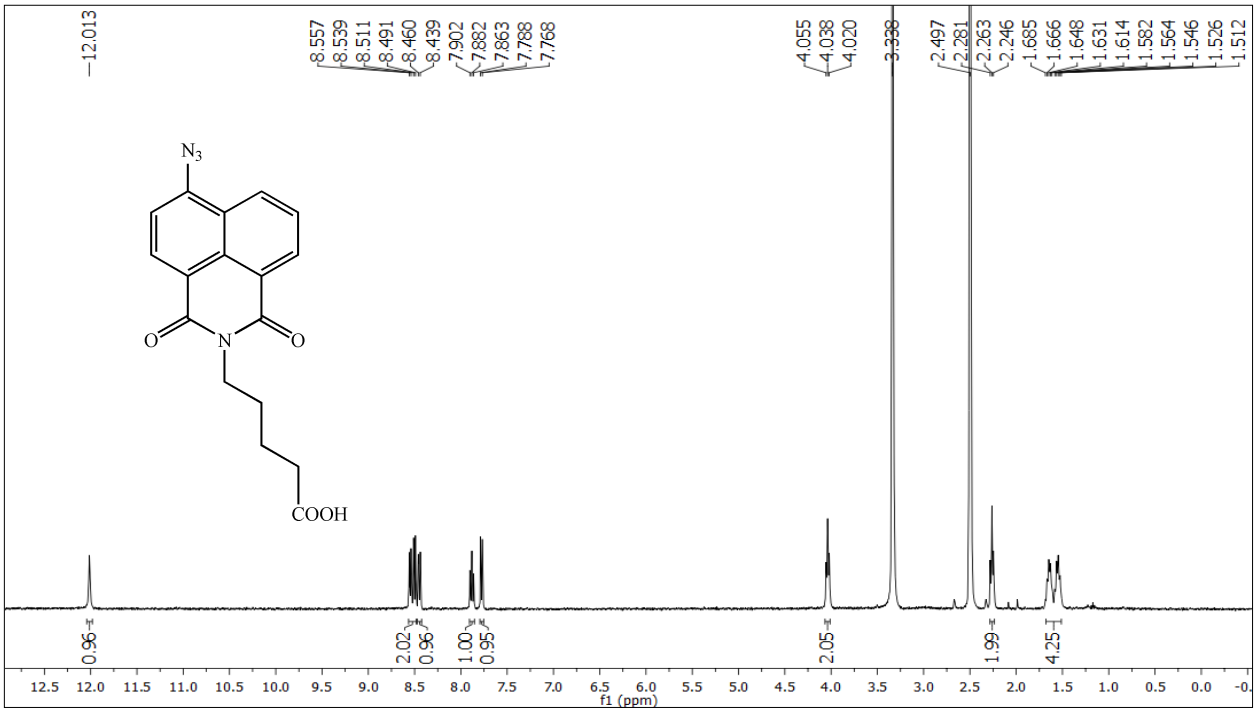


Figure S19. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **4d**

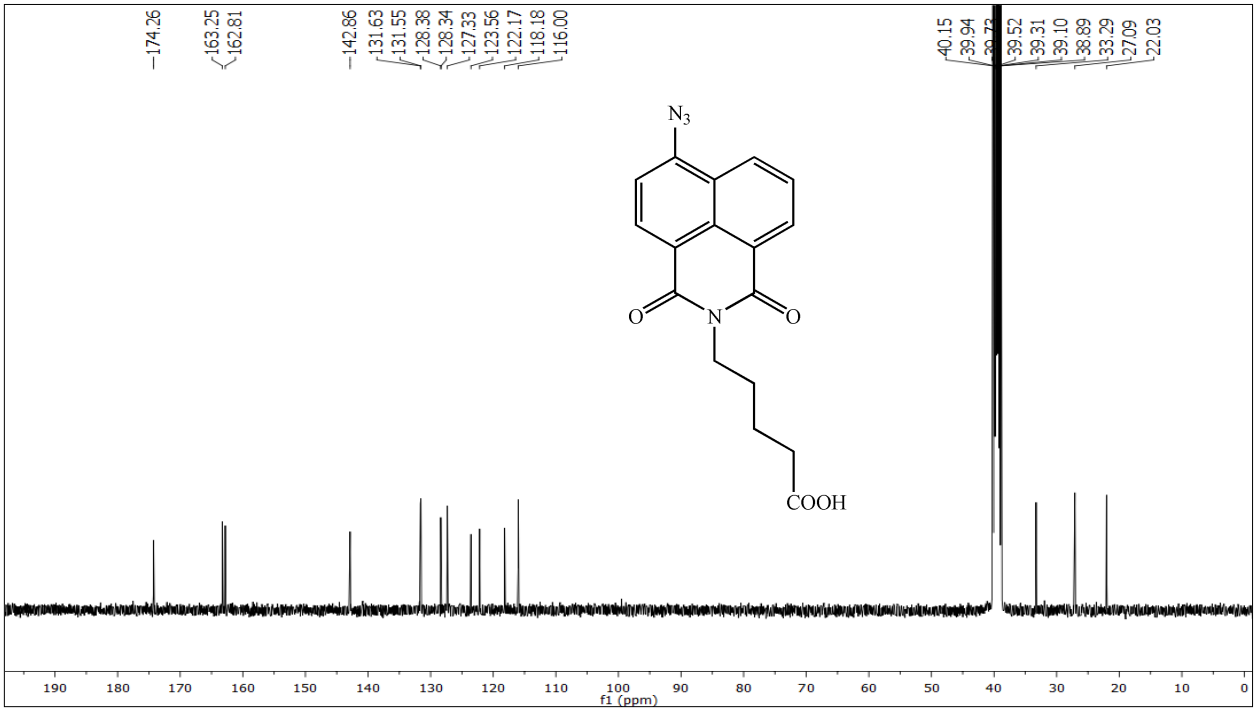


Figure S20. The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **4d**

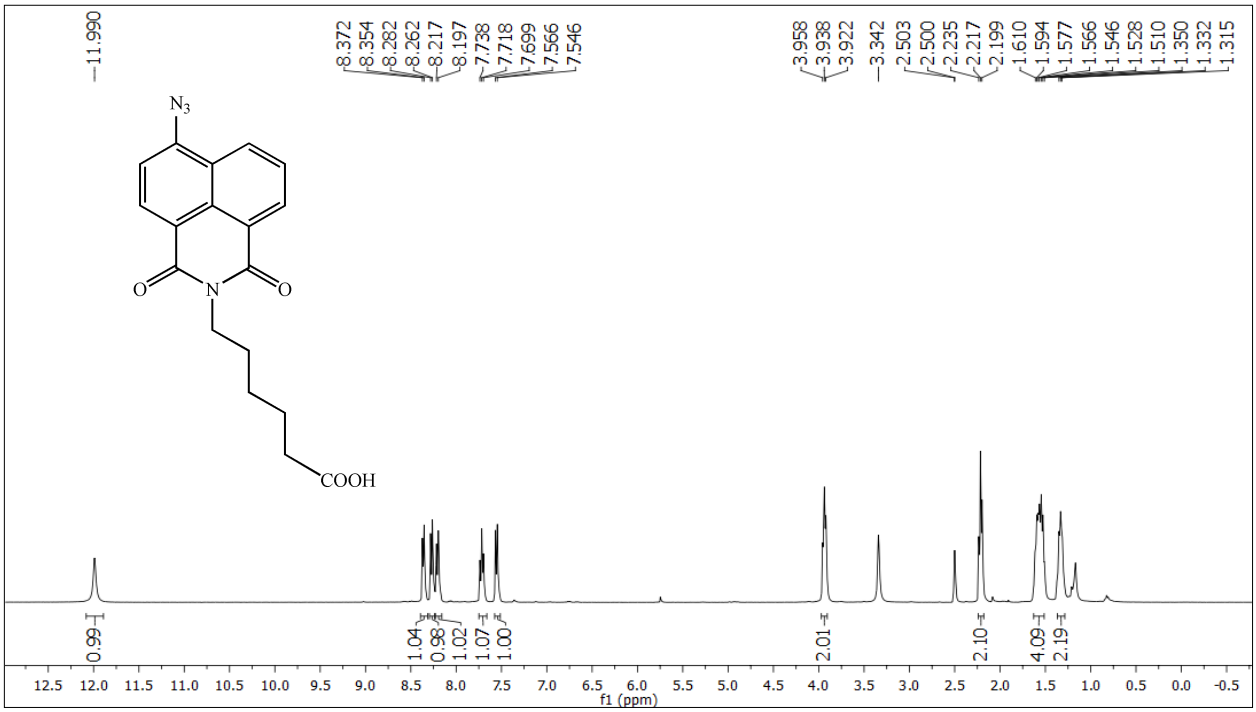


Figure S21. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **4e**

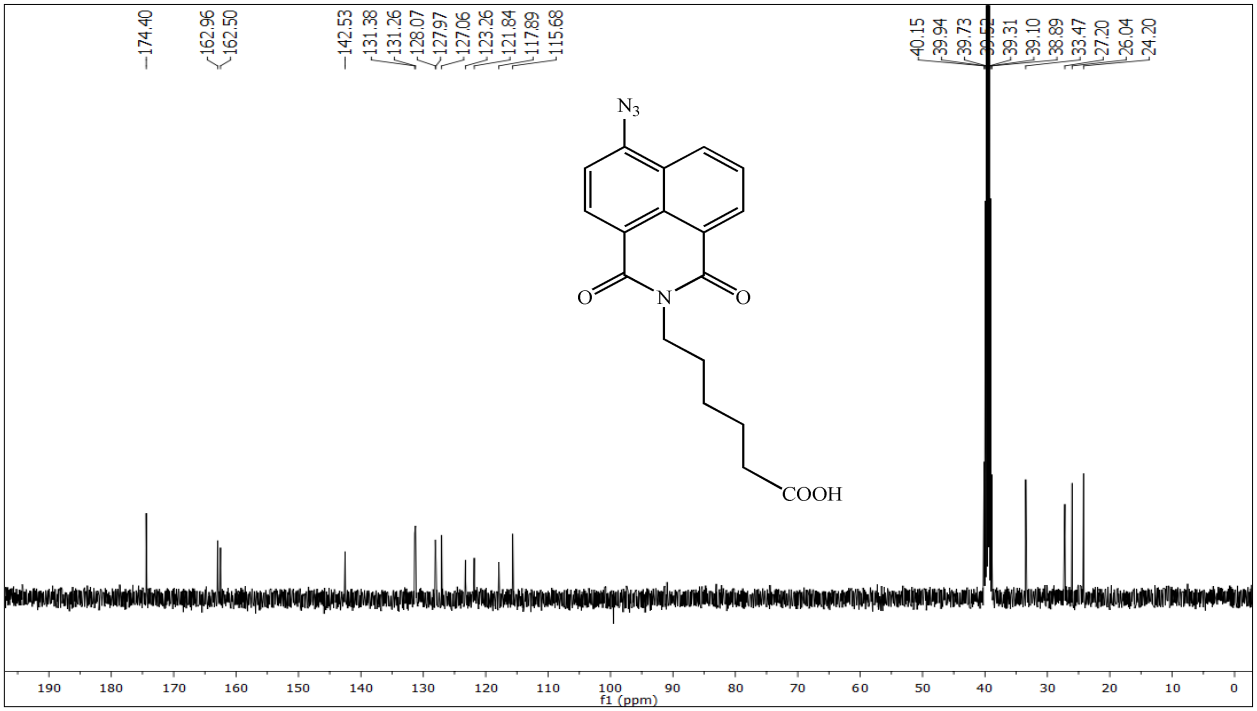


Figure S22. The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **4e**

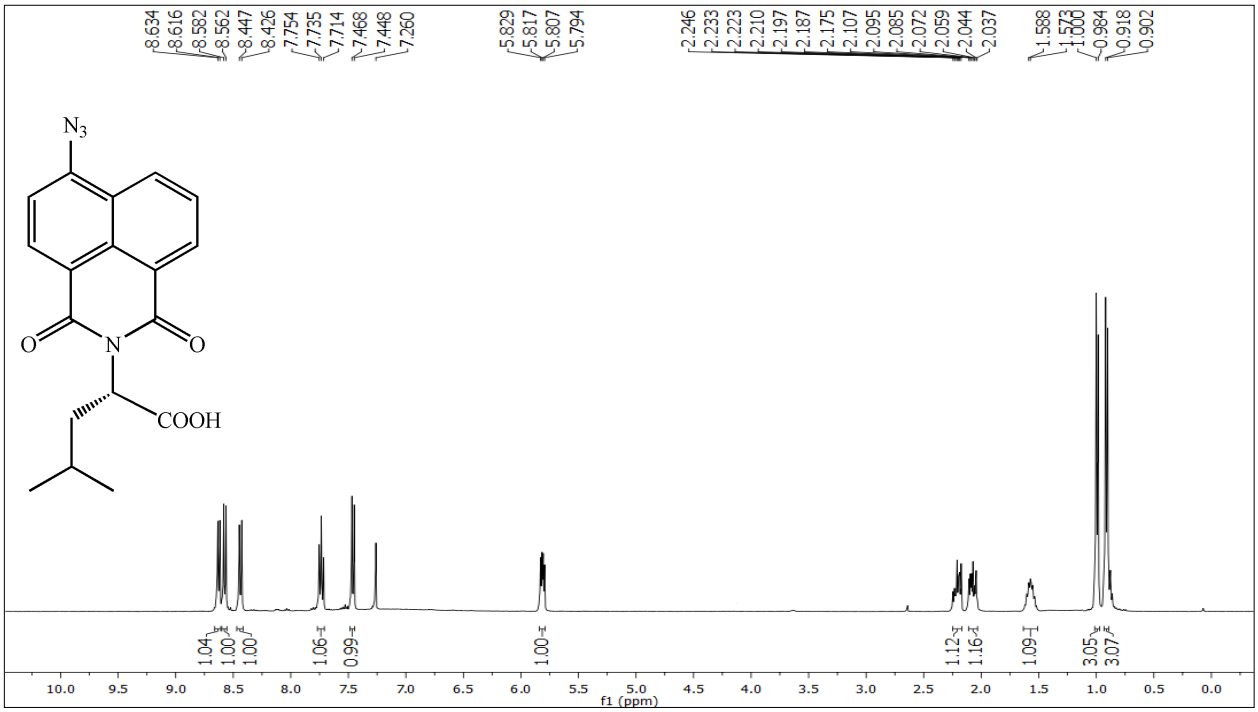


Figure S23. The ^{1}H NMR (400 MHz, Chloroform-d) spectrum of compound **4f**

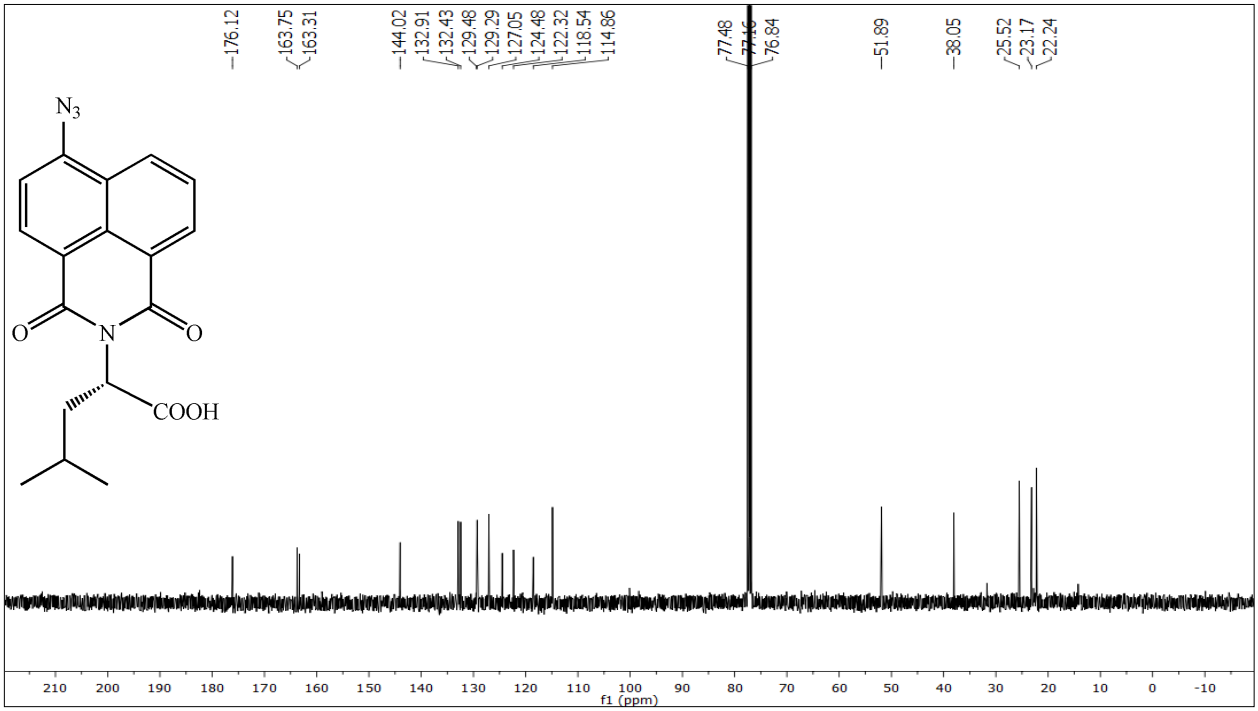


Figure S24. The ^{13}C NMR (100 MHz, Chloroform-d) spectrum of compound **4f**

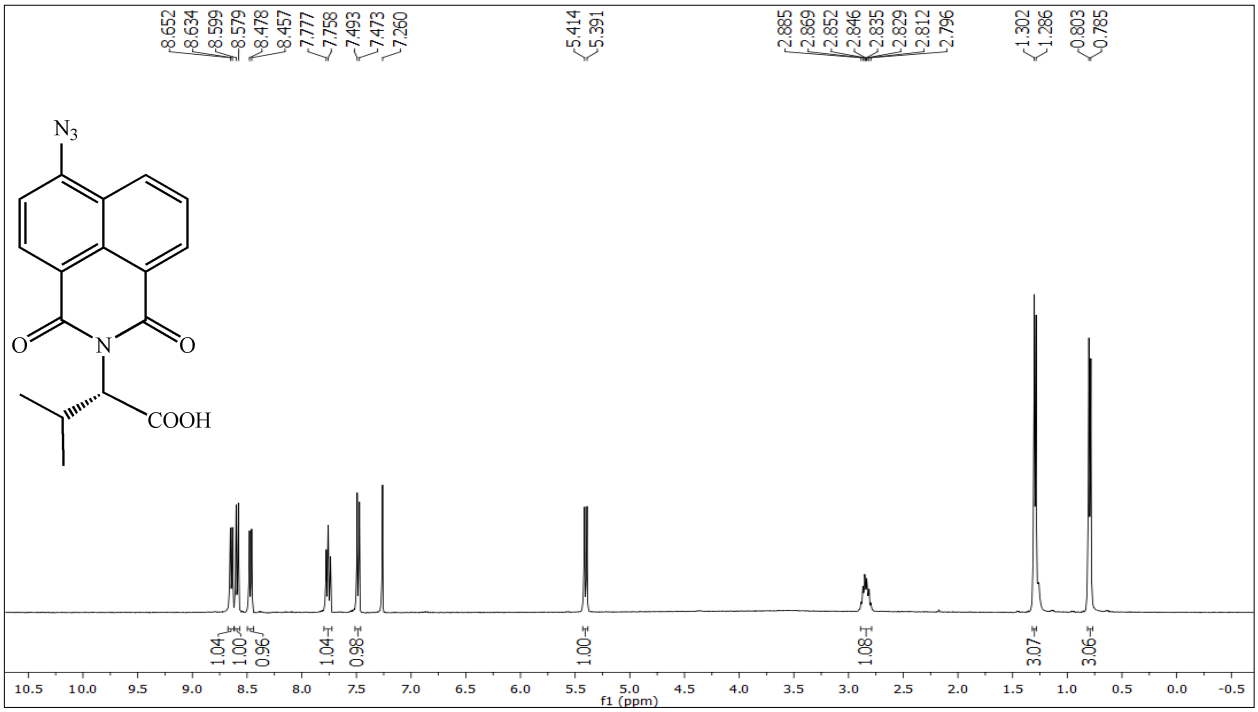


Figure S25. The ^{1}H NMR (400 MHz, Chloroform-d) spectrum of compound **4g**

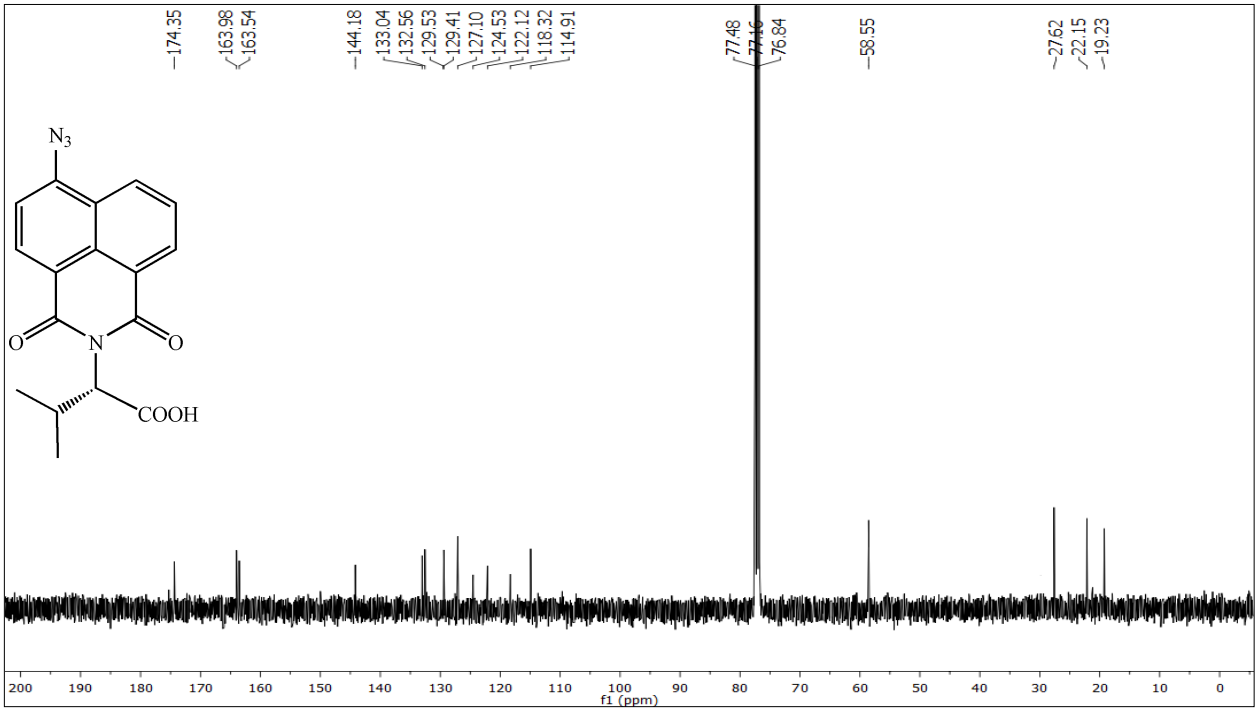


Figure S26. The ^{13}C NMR (100 MHz, Chloroform-d) spectrum of compound **4g**

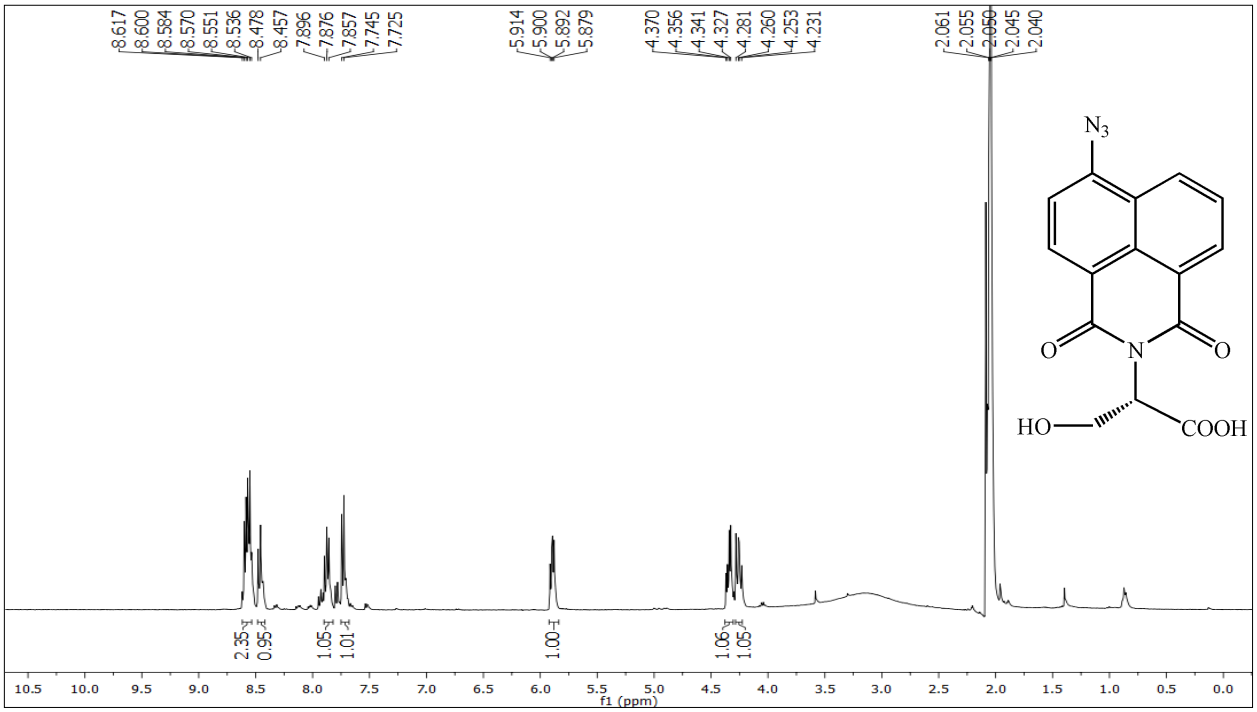


Figure S27. The ^{1}H NMR (400 MHz, Acetone-d_6) spectrum of compound **4h**

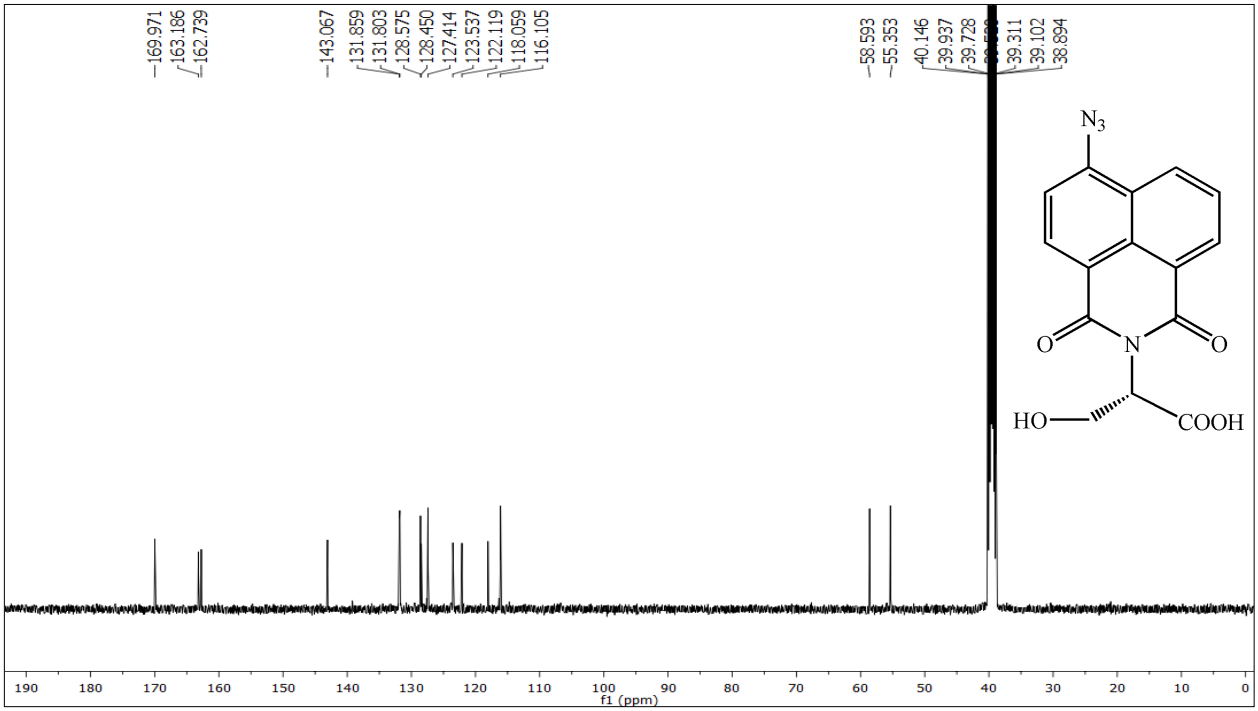


Figure S28. The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **4h**

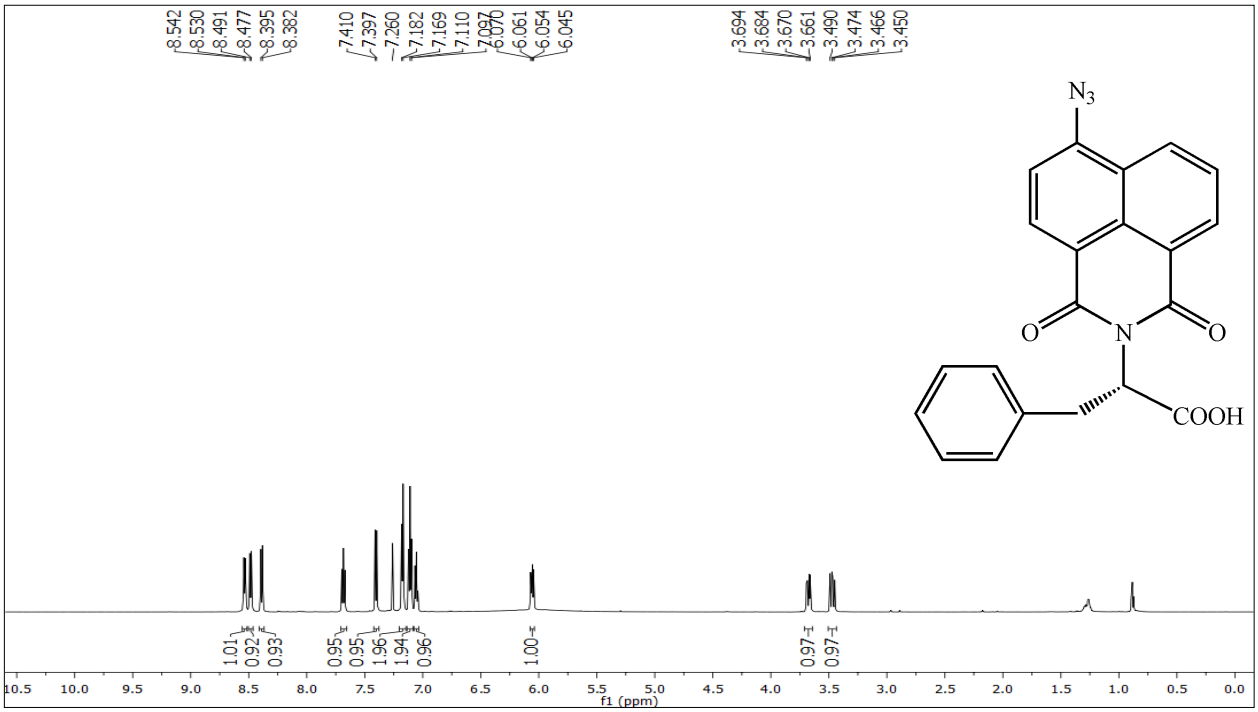


Figure S29. The ^{1}H NMR (400 MHz, Chloroform-d) spectrum of compound **4i**

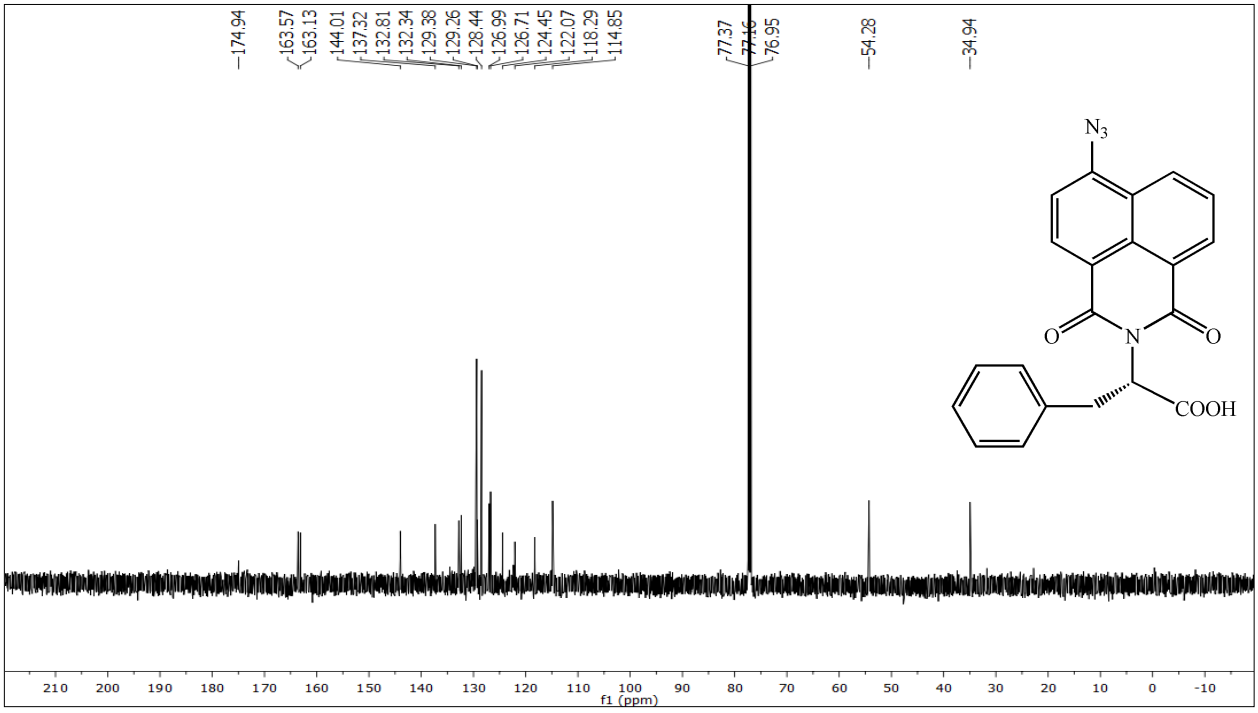


Figure S30. The ^{13}C NMR (100 MHz, Chloroform-d) spectrum of compound **4i**

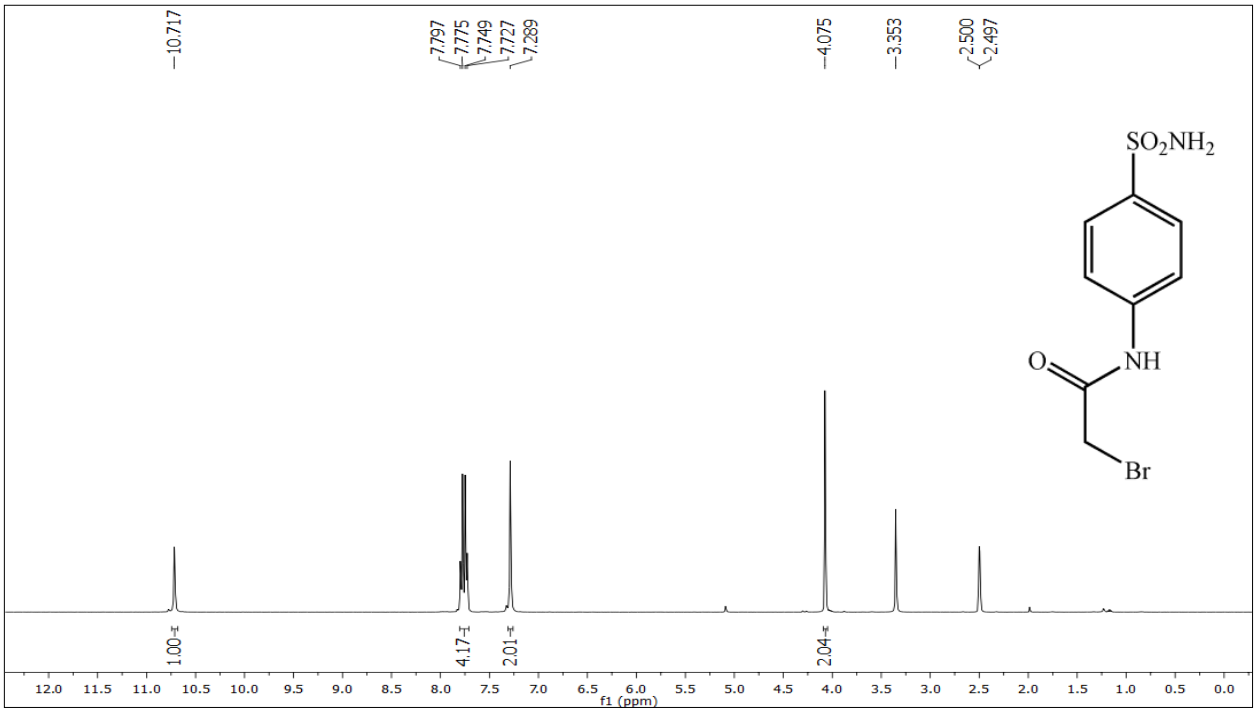


Figure S31. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **7**

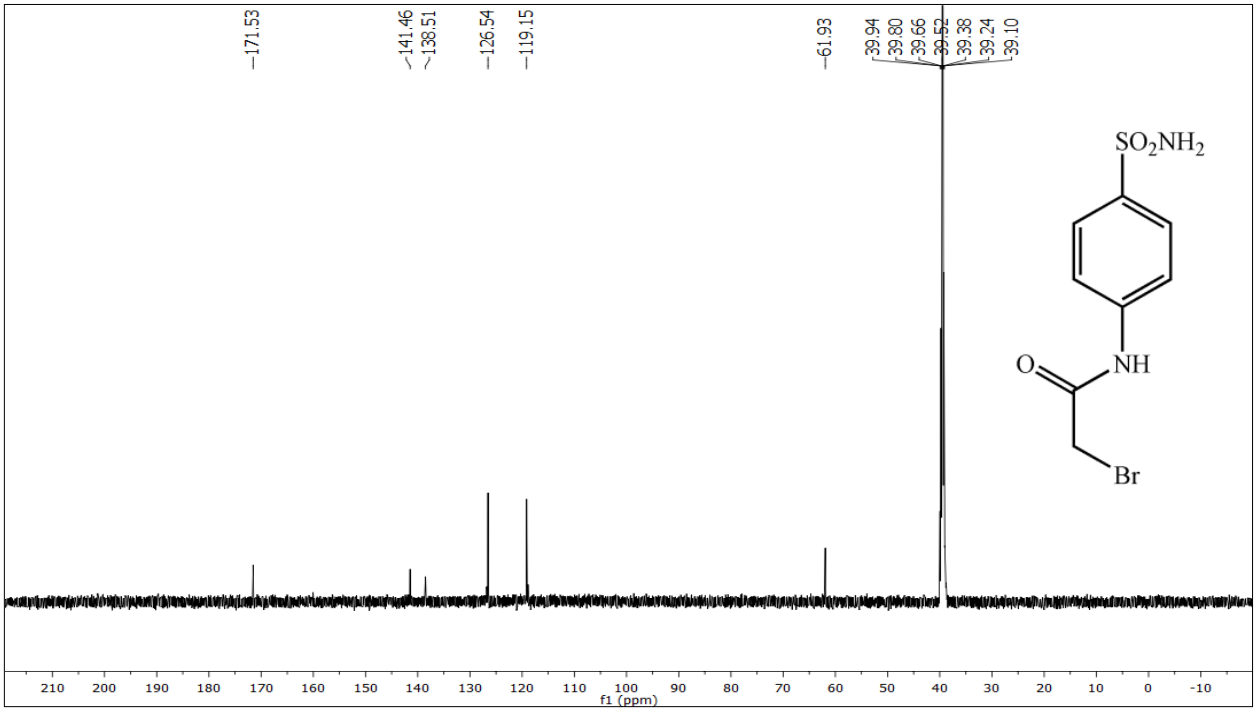


Figure S32. The ^{13}C NMR (400 MHz, DMSO-d_6) spectrum of **7**

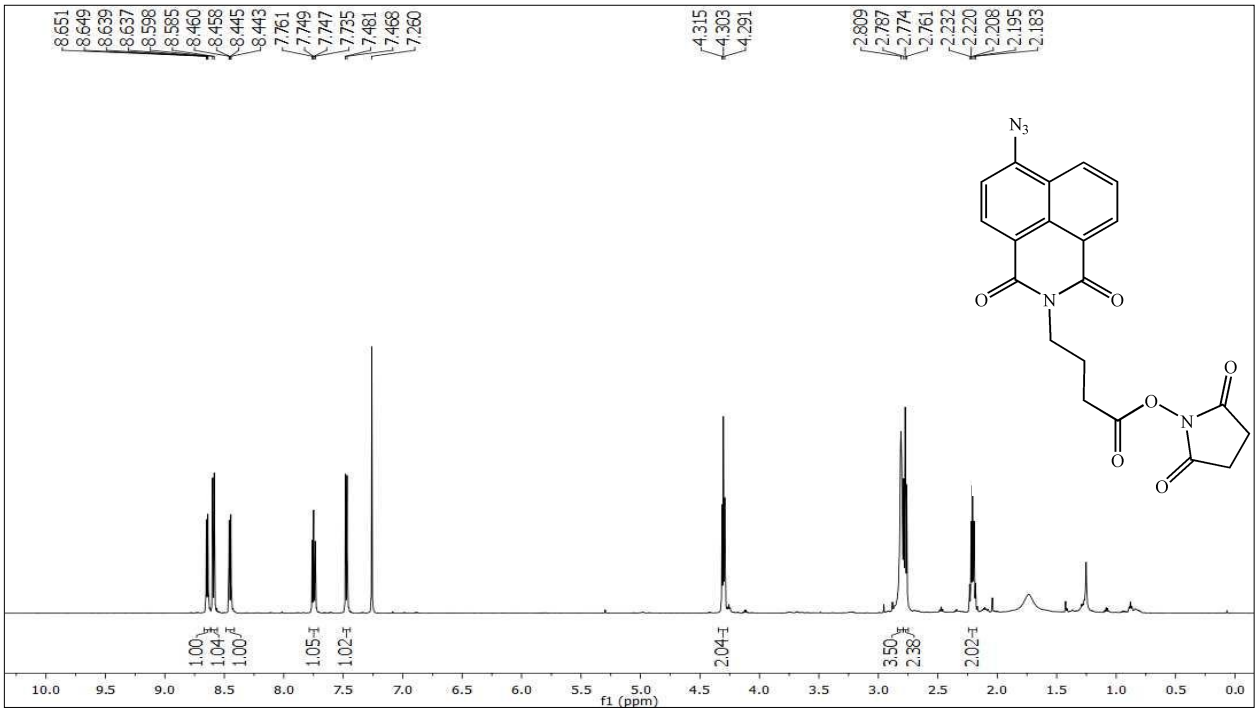


Figure S33. The ^{1}H NMR (600 MHz, Chloroform-d) spectrum of compound **5**

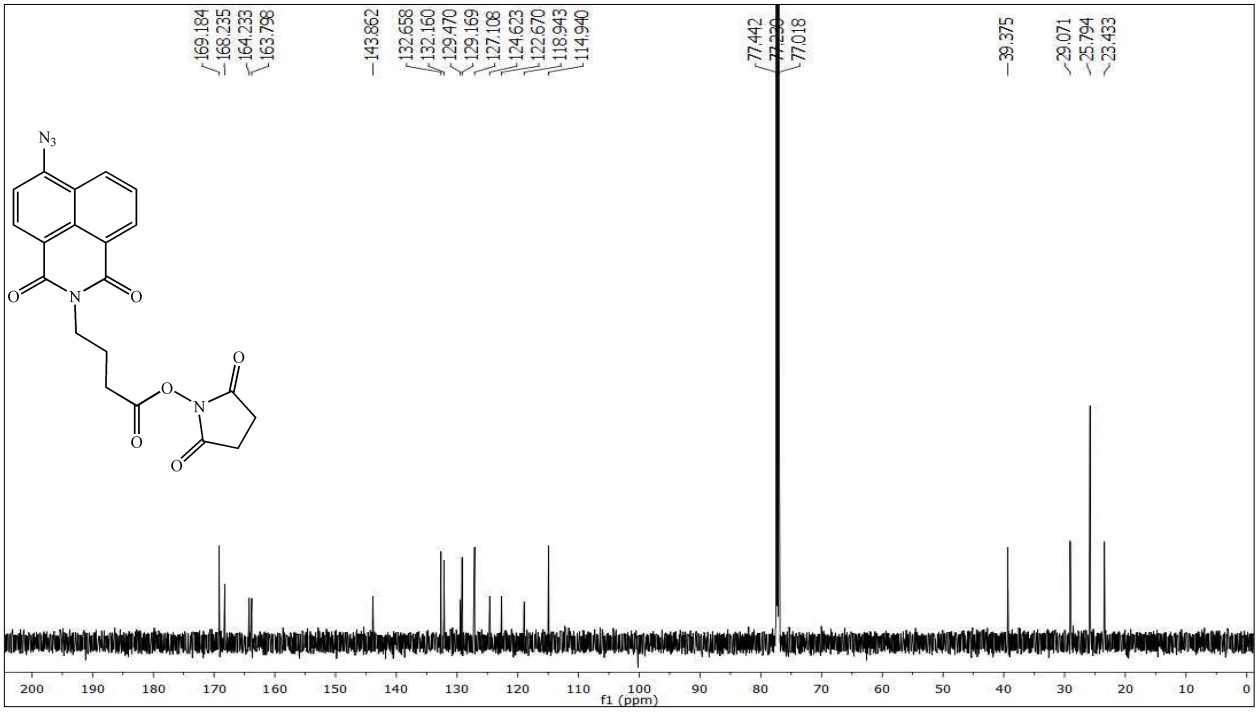


Figure S34. The ^{13}C NMR (150 MHz, Chloroform-d) spectrum of compound **5**

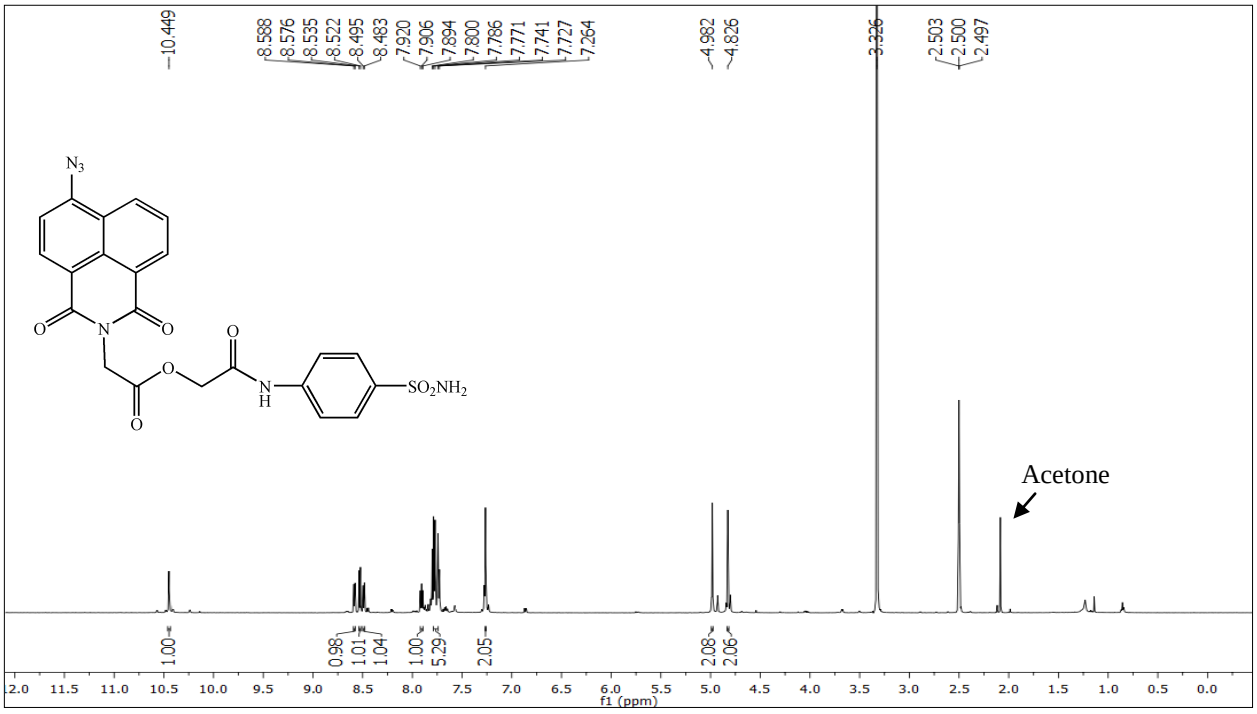


Figure S35. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1a**

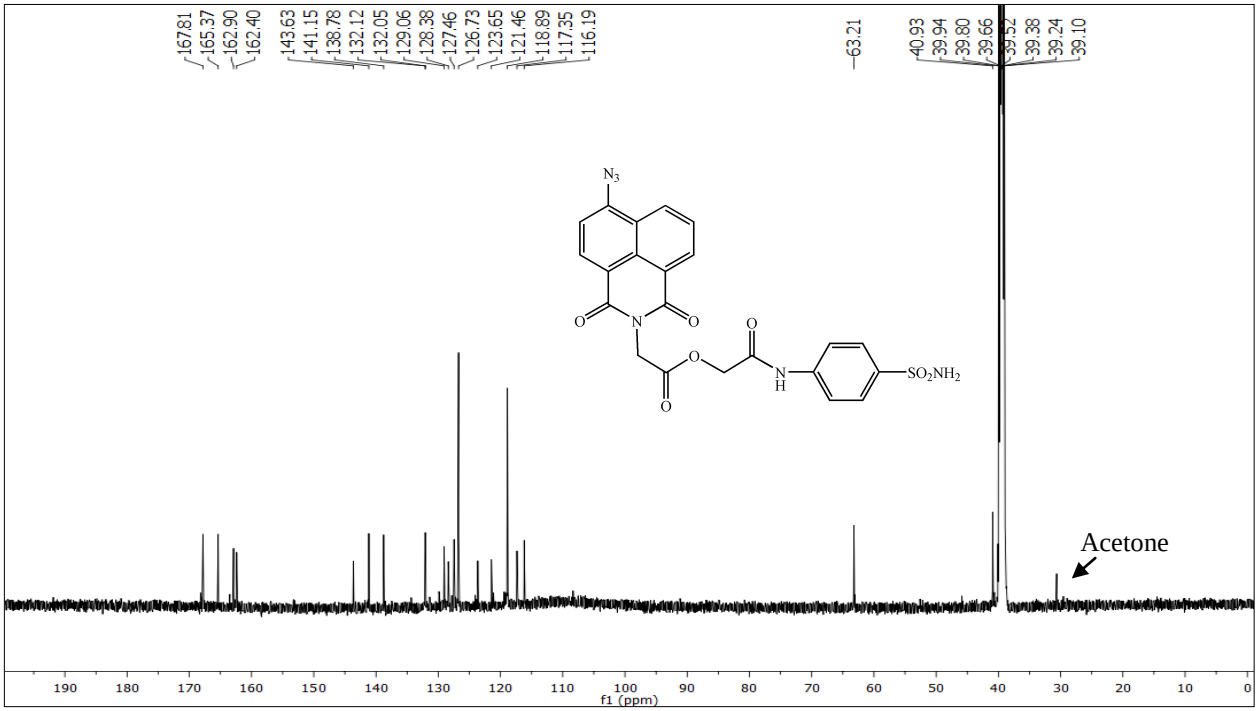


Figure S36. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1a**

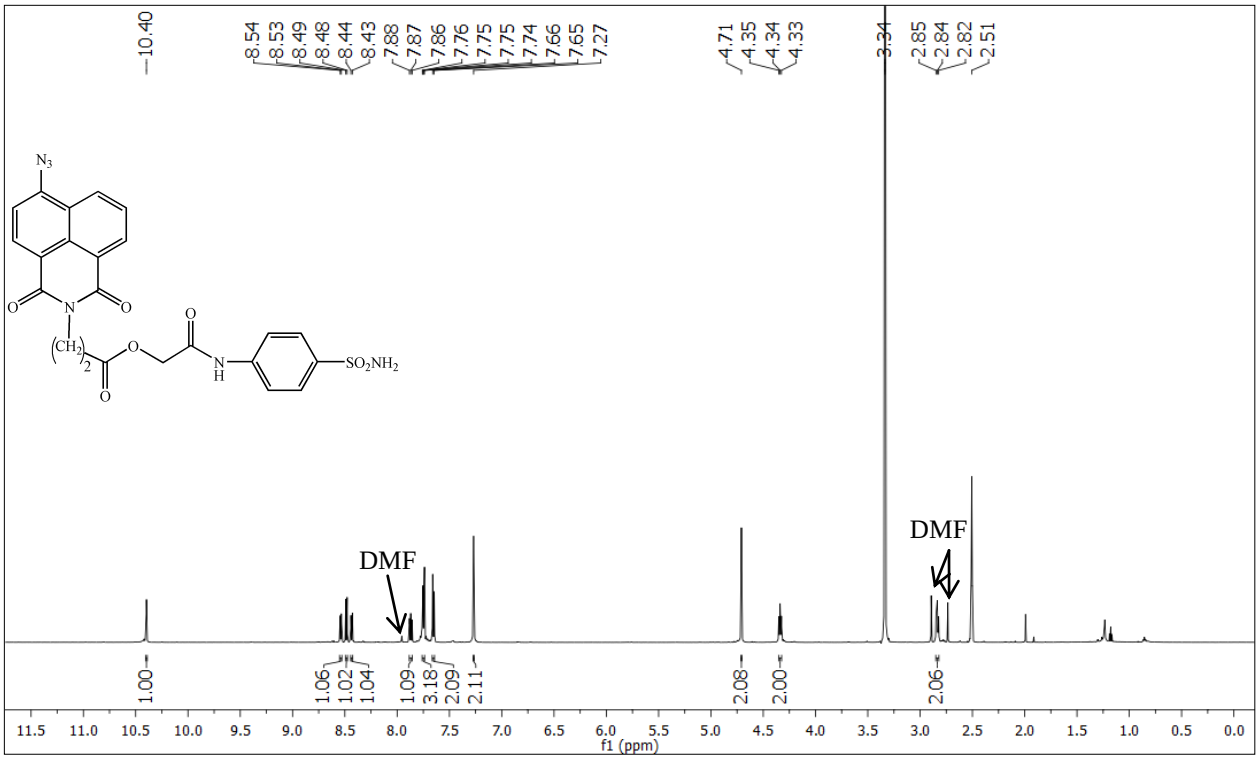


Figure S37. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1b**

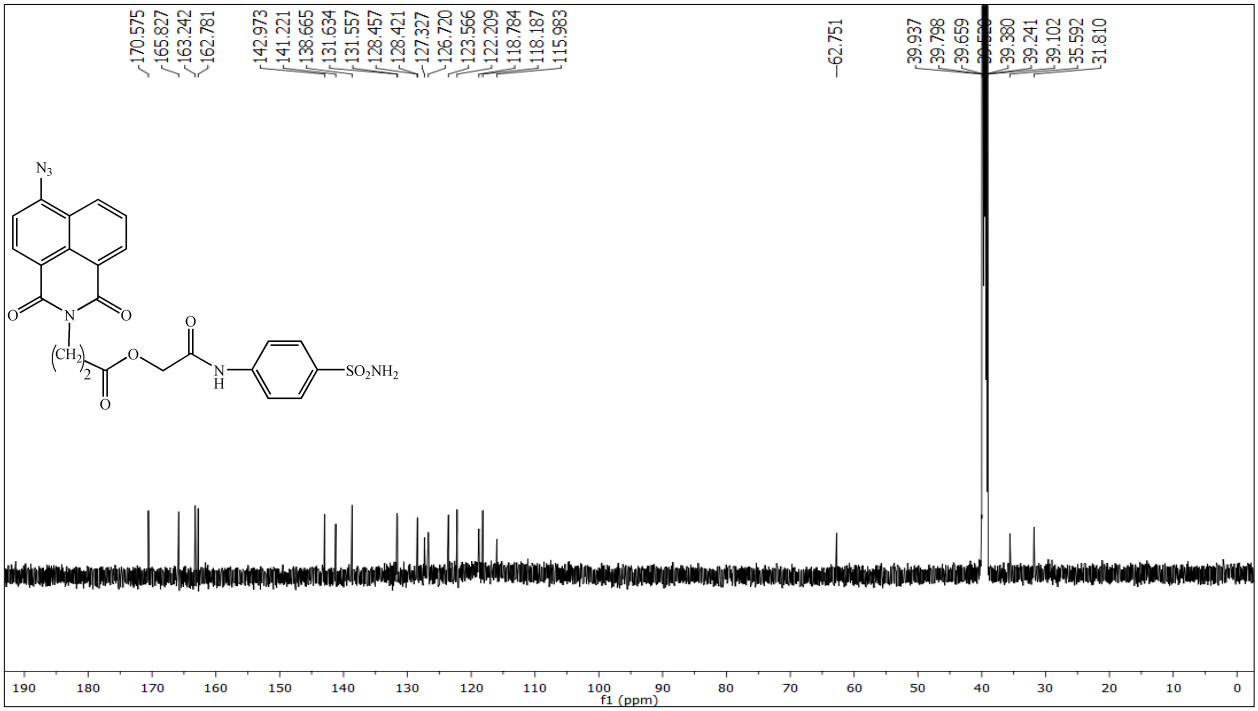


Figure S38. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1b**

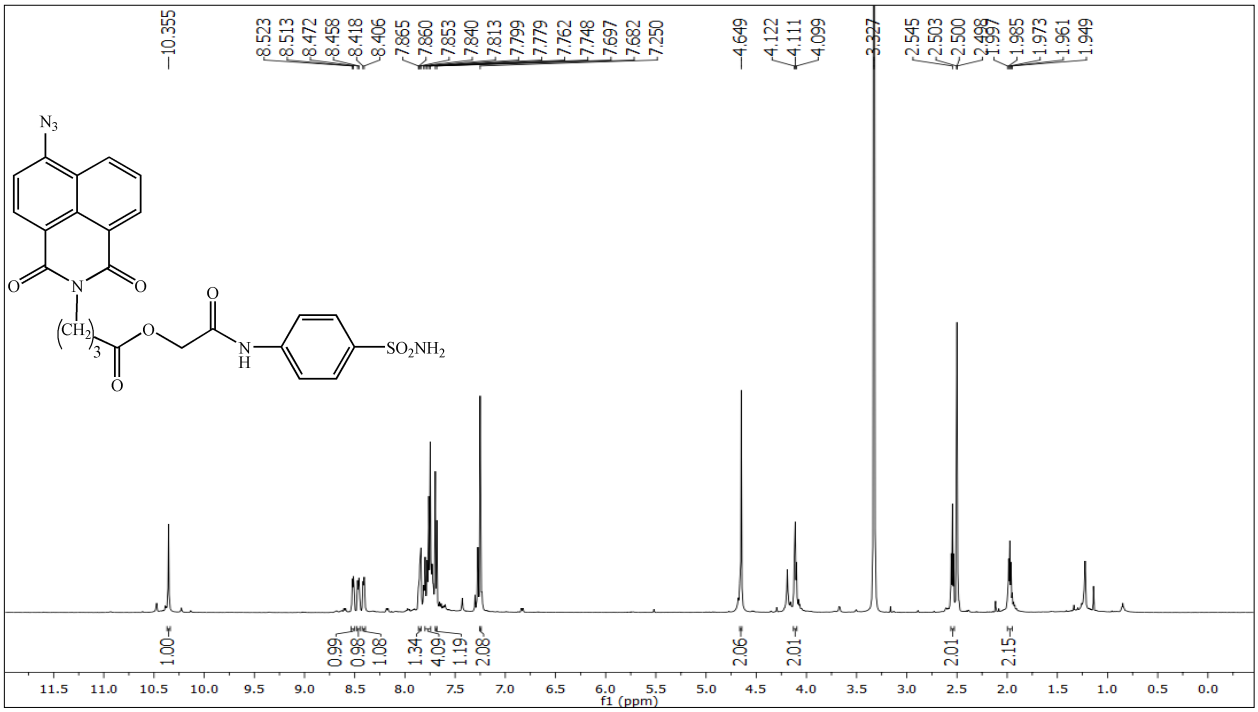


Figure S39. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1c**

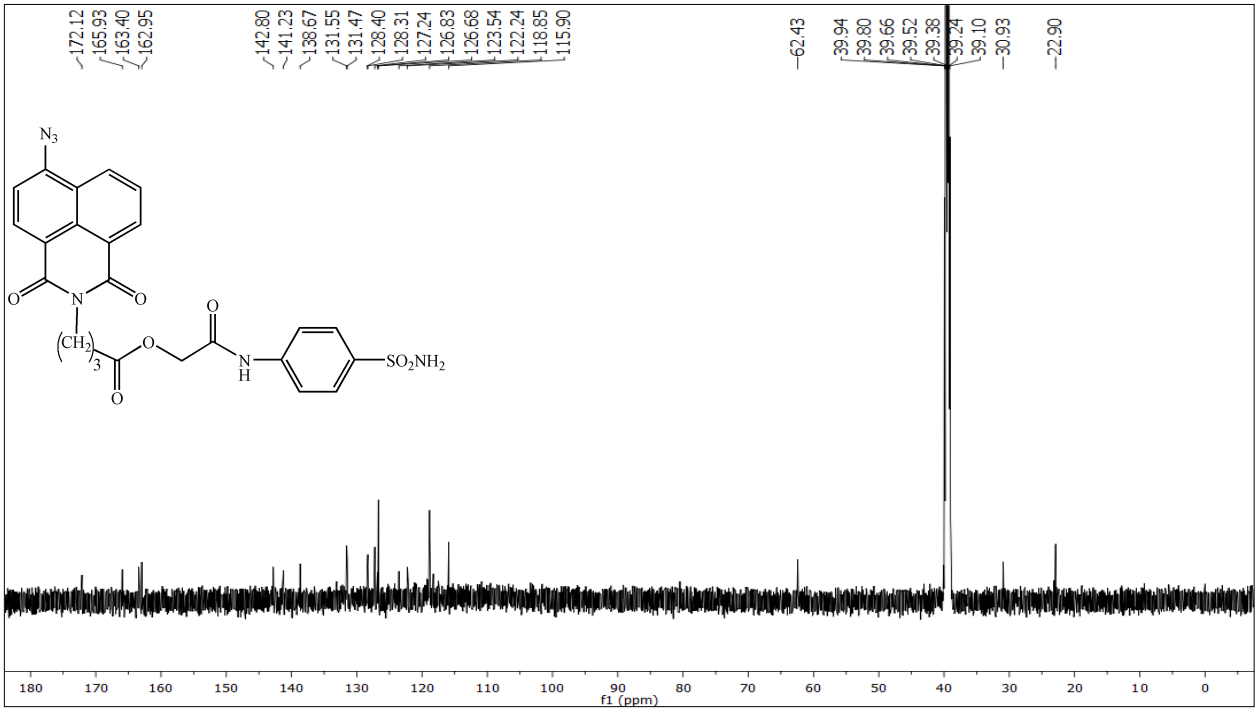


Figure S40. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1c**

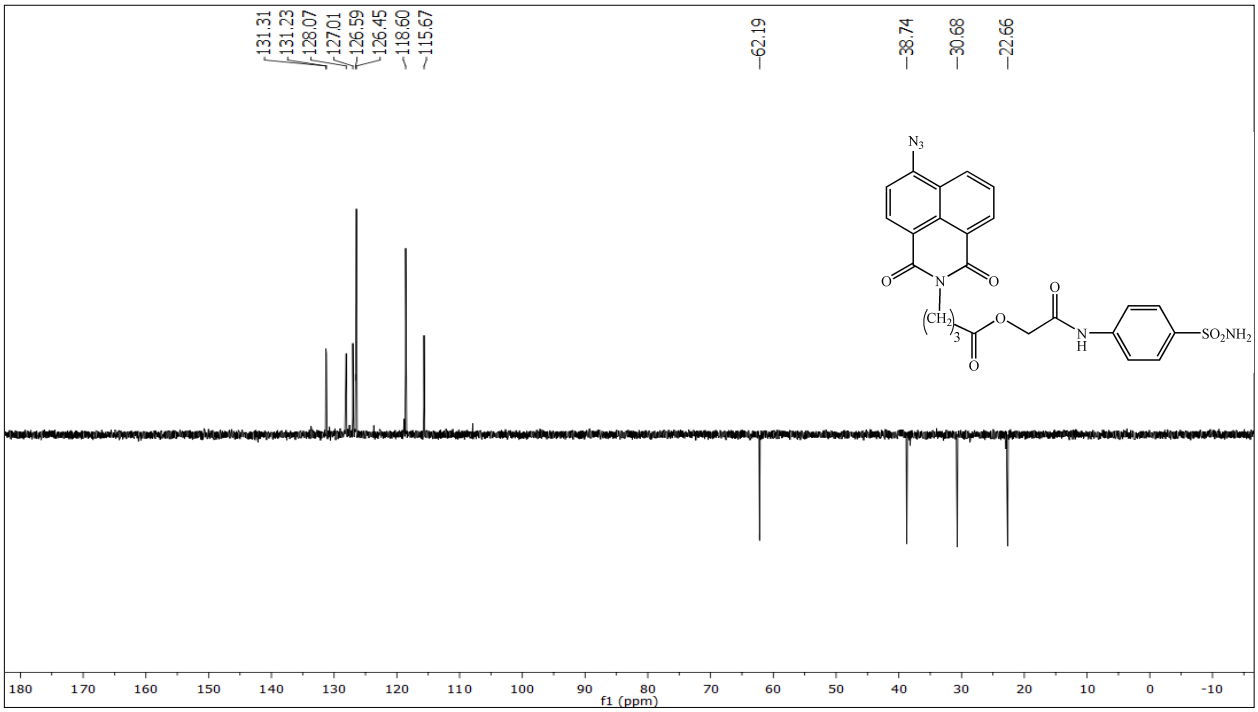


Figure S41. The DEPT 135 NMR (150 MHz, DMSO-d_6) spectrum of compound **1c**

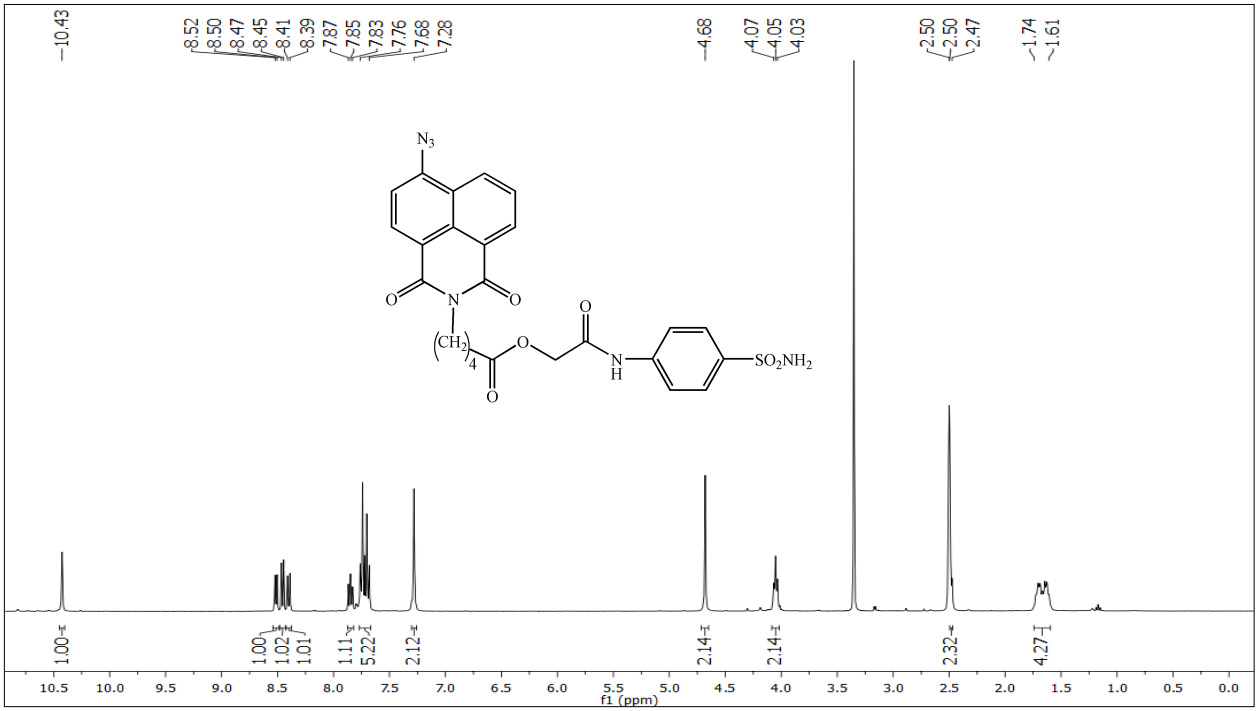


Figure S42. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **1d**

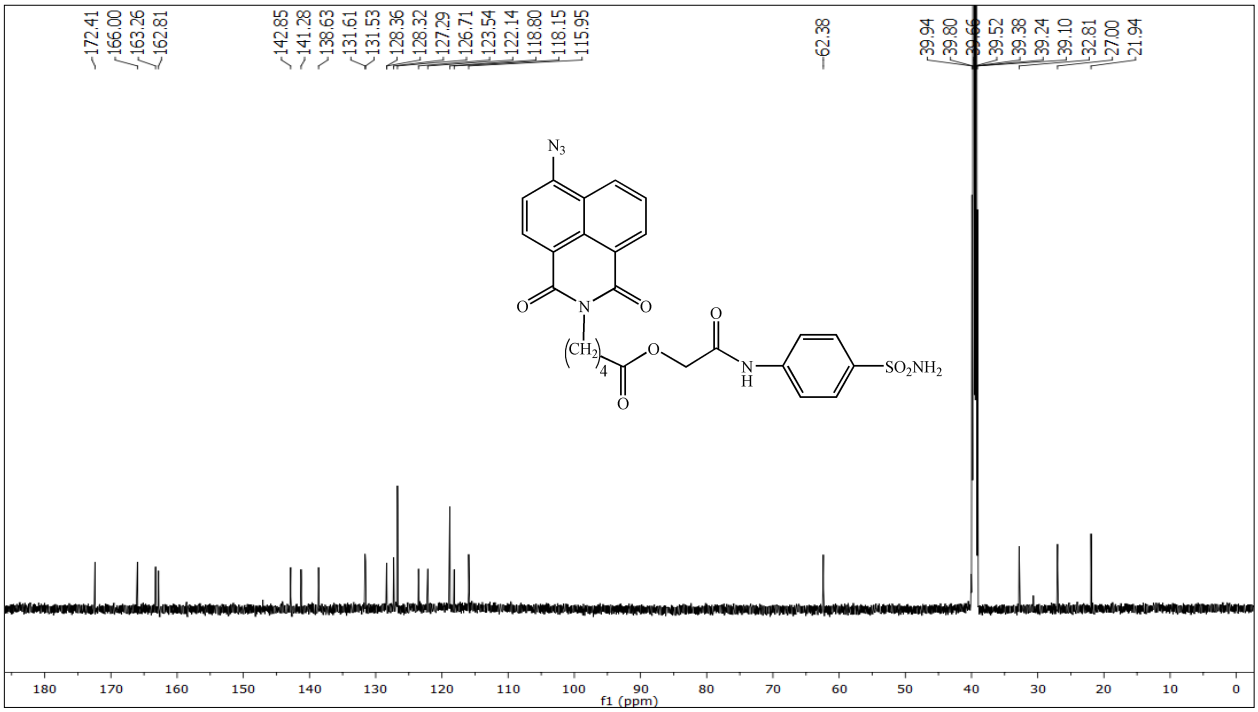


Figure S43. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1d**

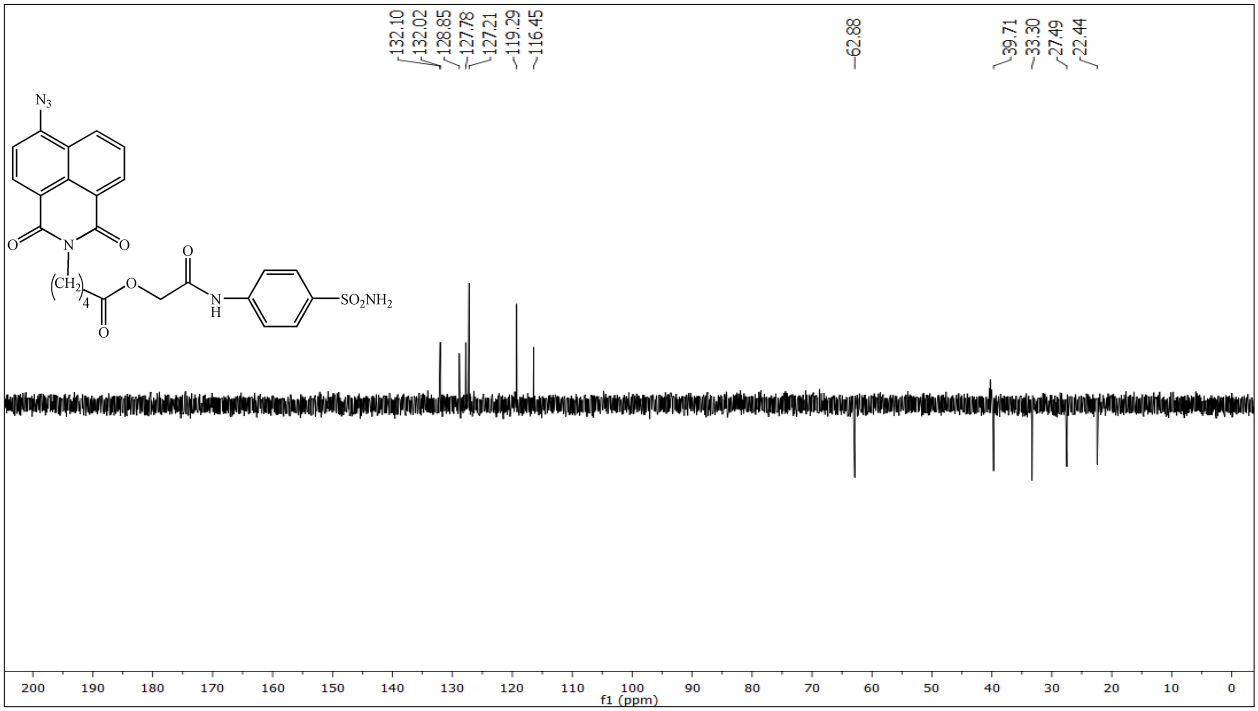


Figure S44. The DEPT 135 NMR (150 MHz, DMSO-d_6) spectrum of compound **1d**

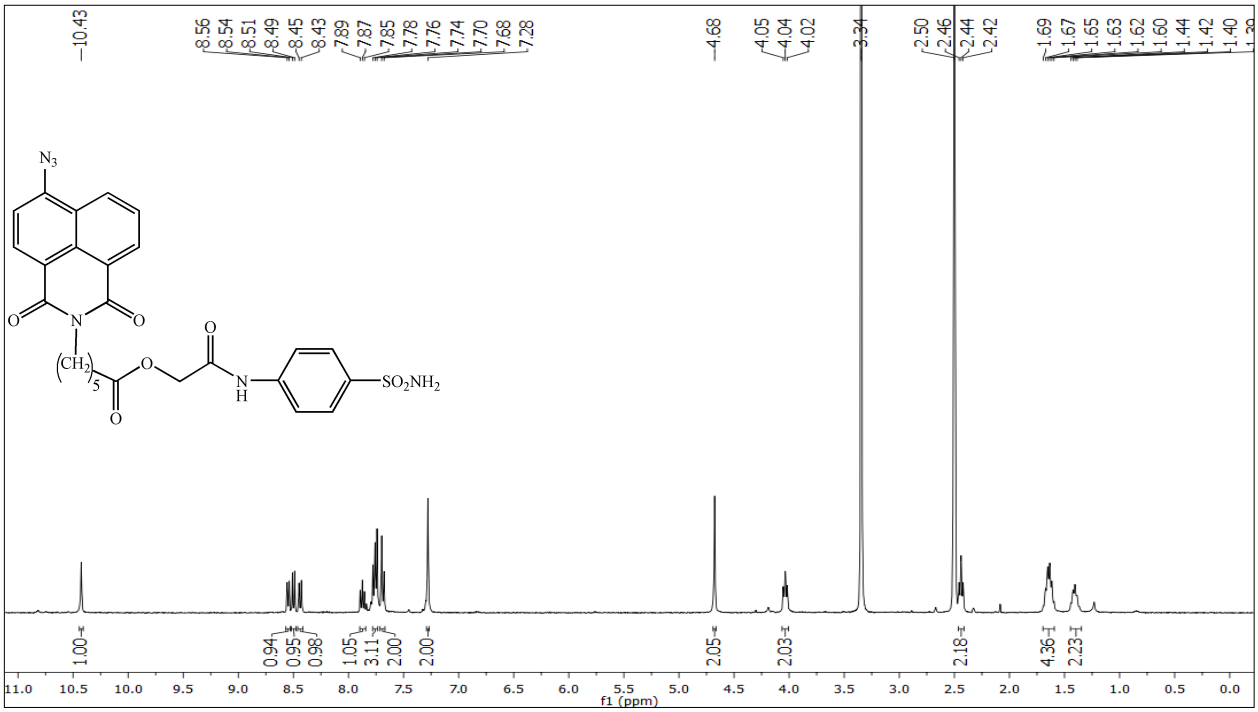


Figure S45. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **1e**

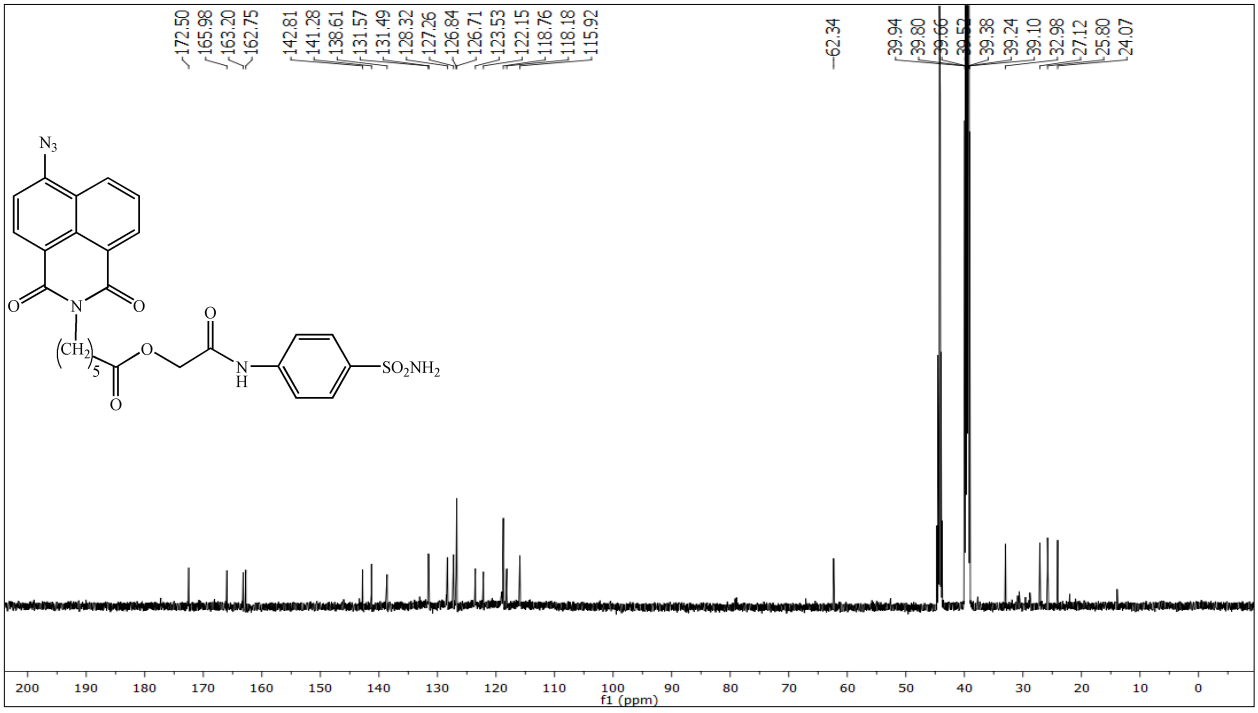


Figure S46. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1e**

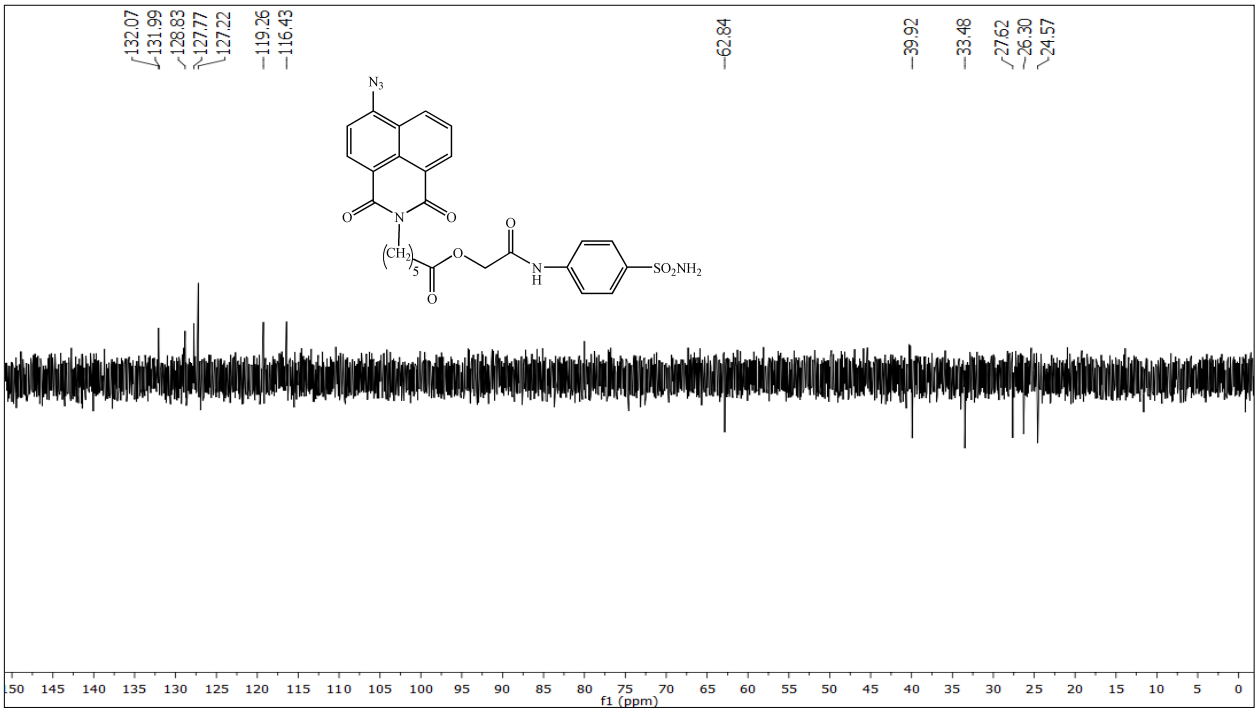


Figure S47. The DEPT 135 NMR (150 MHz, DMSO-d_6) spectrum of compound **1e**

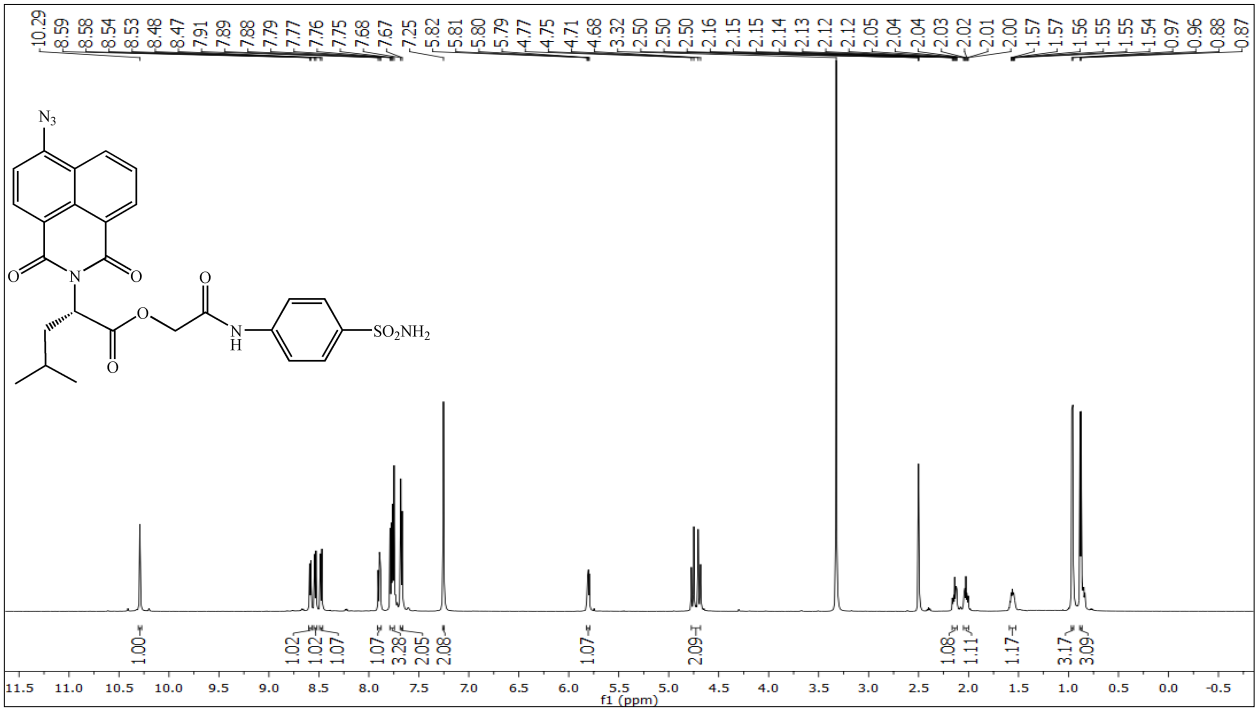


Figure S48. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1f**

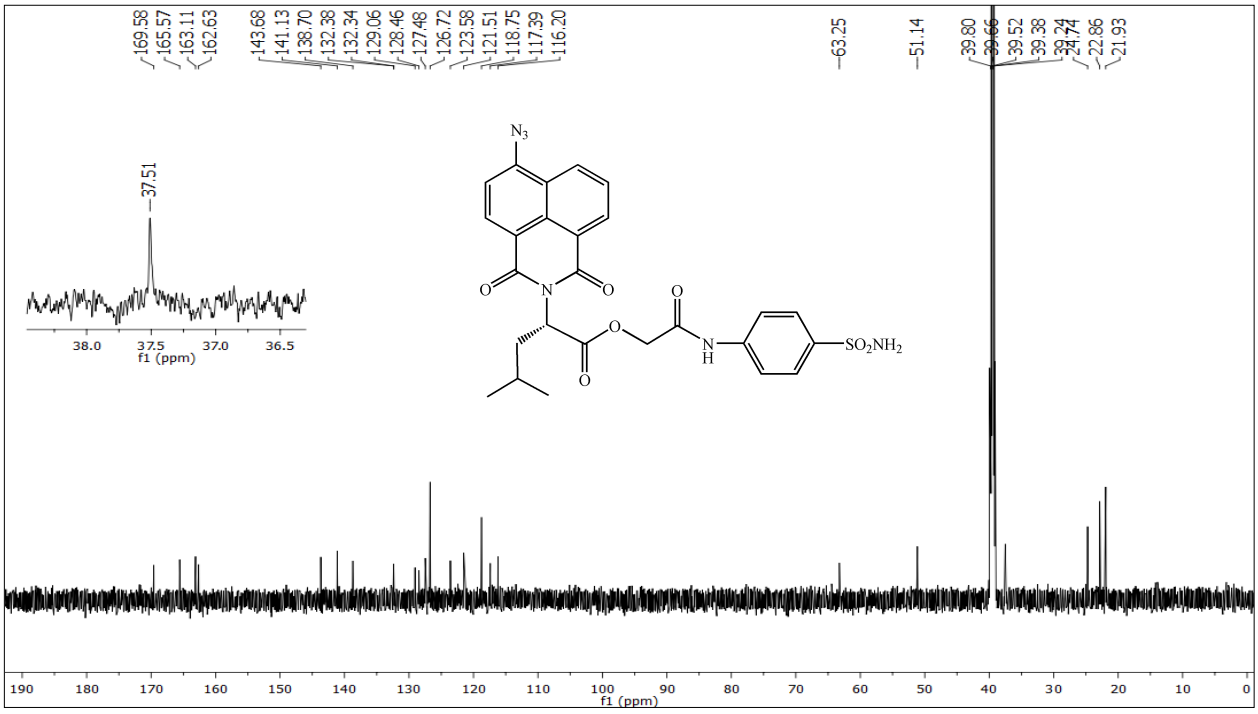


Figure S49. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1f**

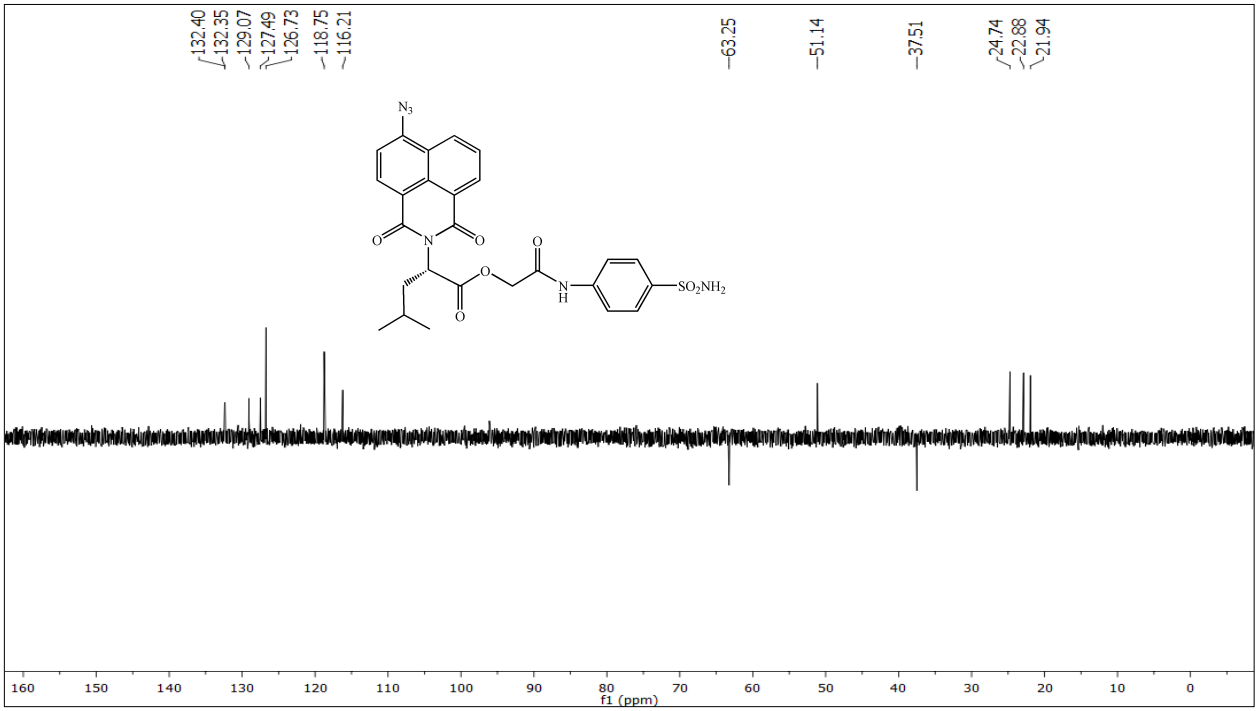


Figure S50. The DEPT 135 NMR (150 MHz, DMSO-d_6) spectrum of compound **1f**

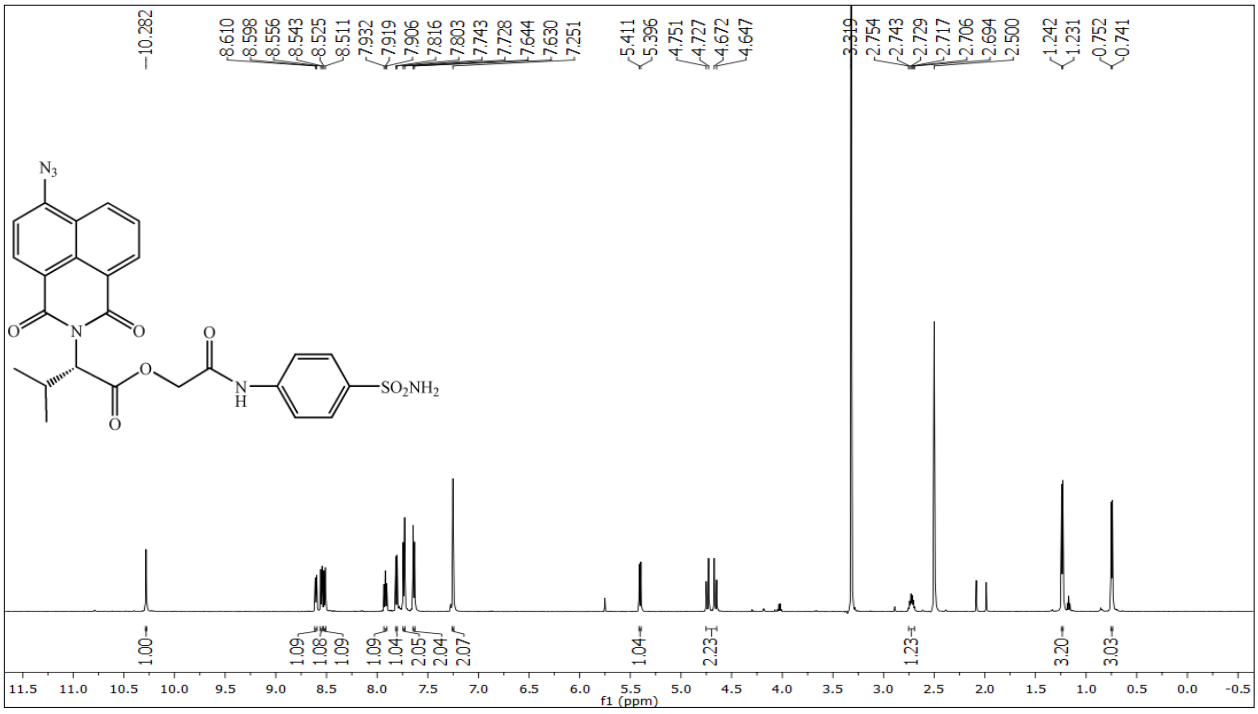


Figure S51. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1g**

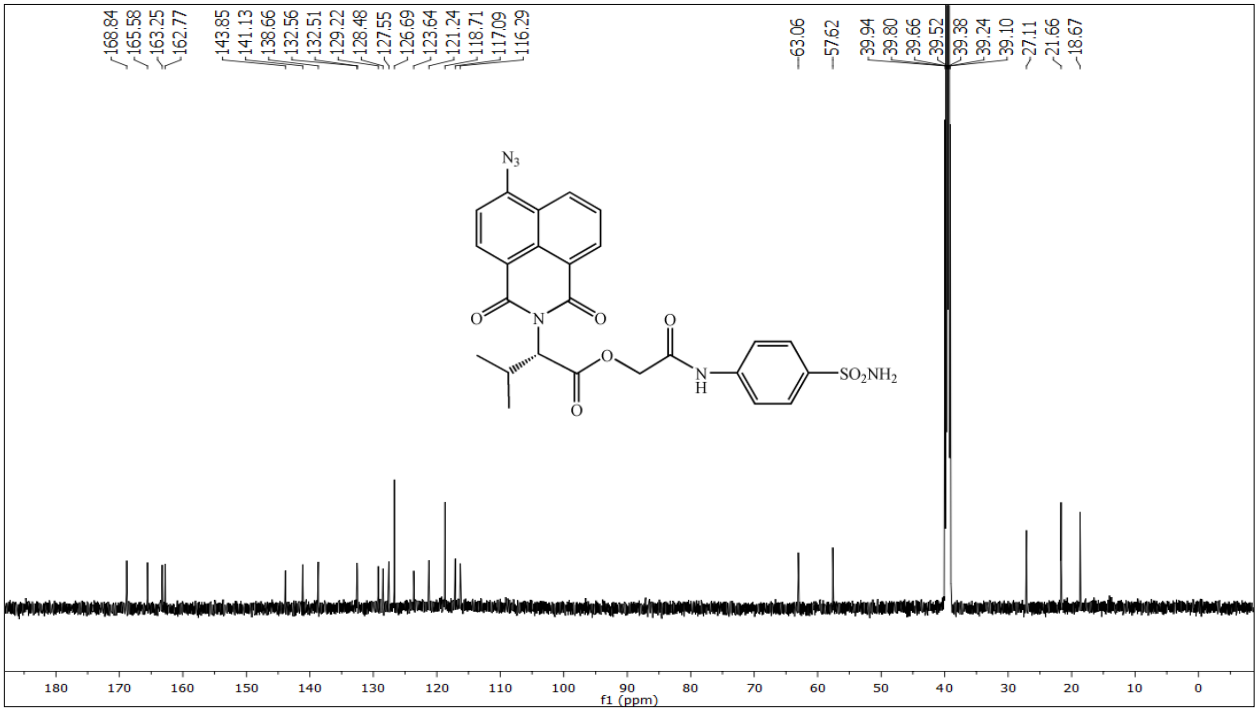


Figure S52. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1g**

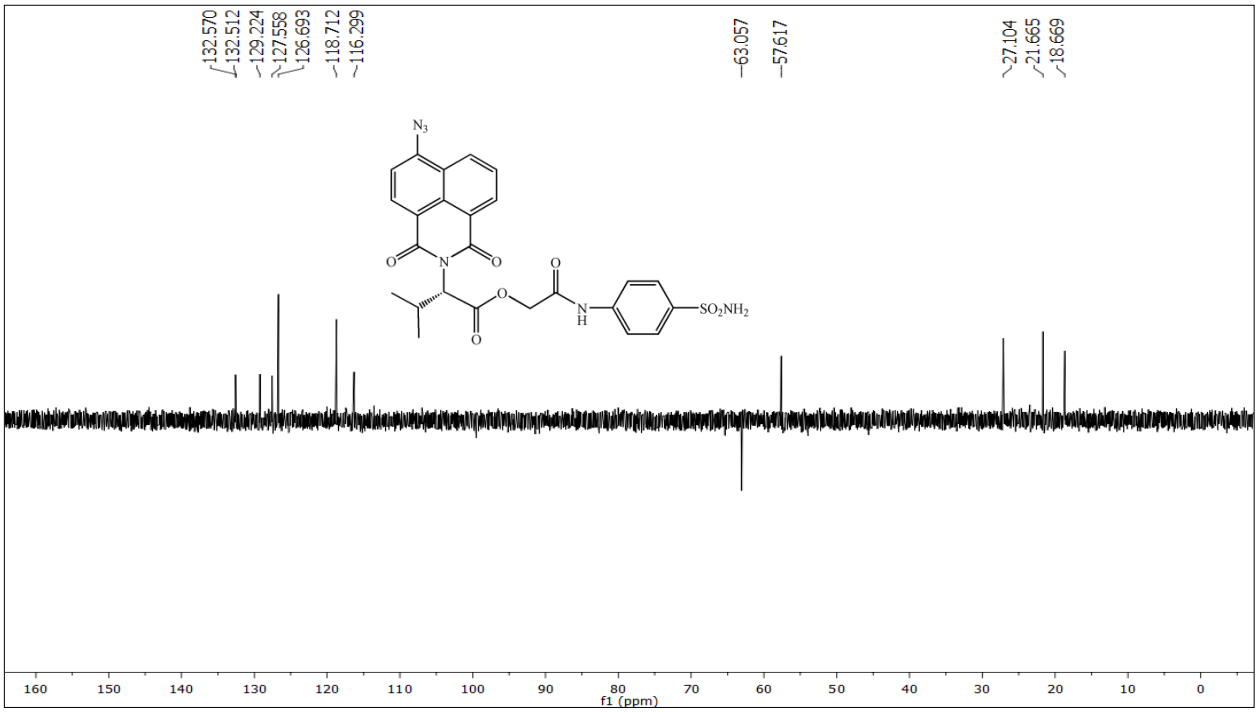


Figure S53. The DEPT 135 NMR (150 MHz, DMSO-d_6) spectrum of compound **1g**

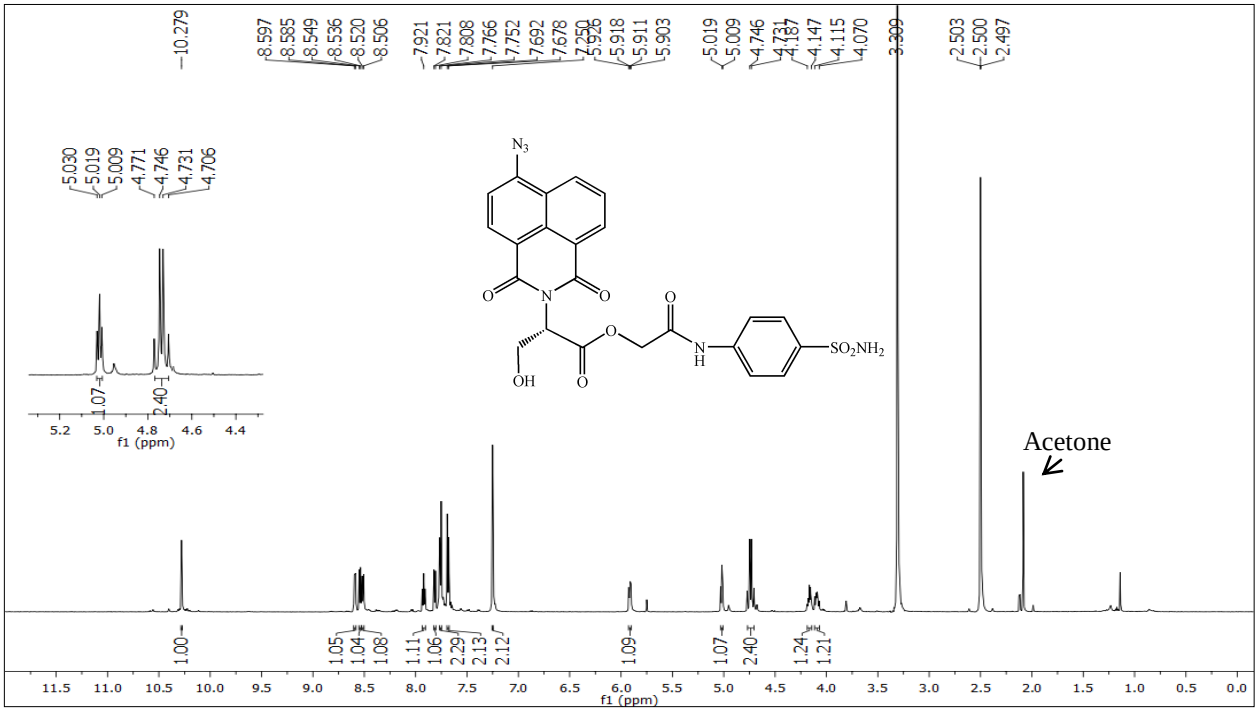


Figure S54. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1h**

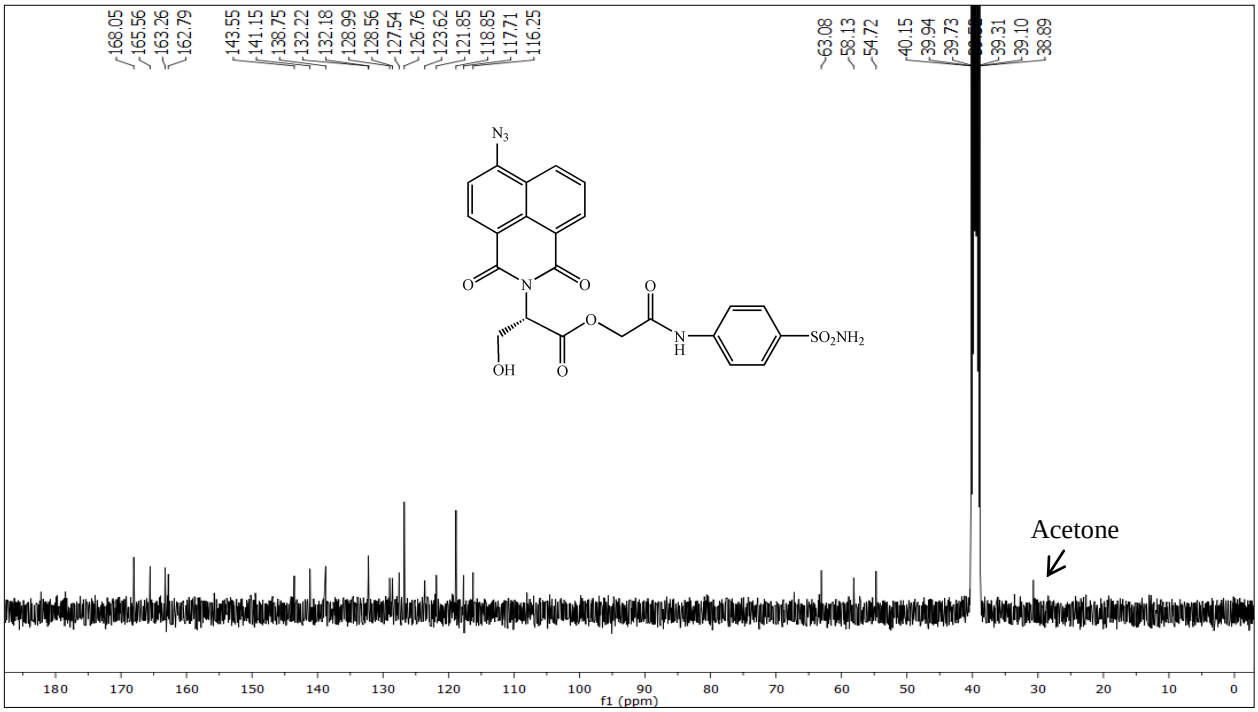


Figure S55. The ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **1h**

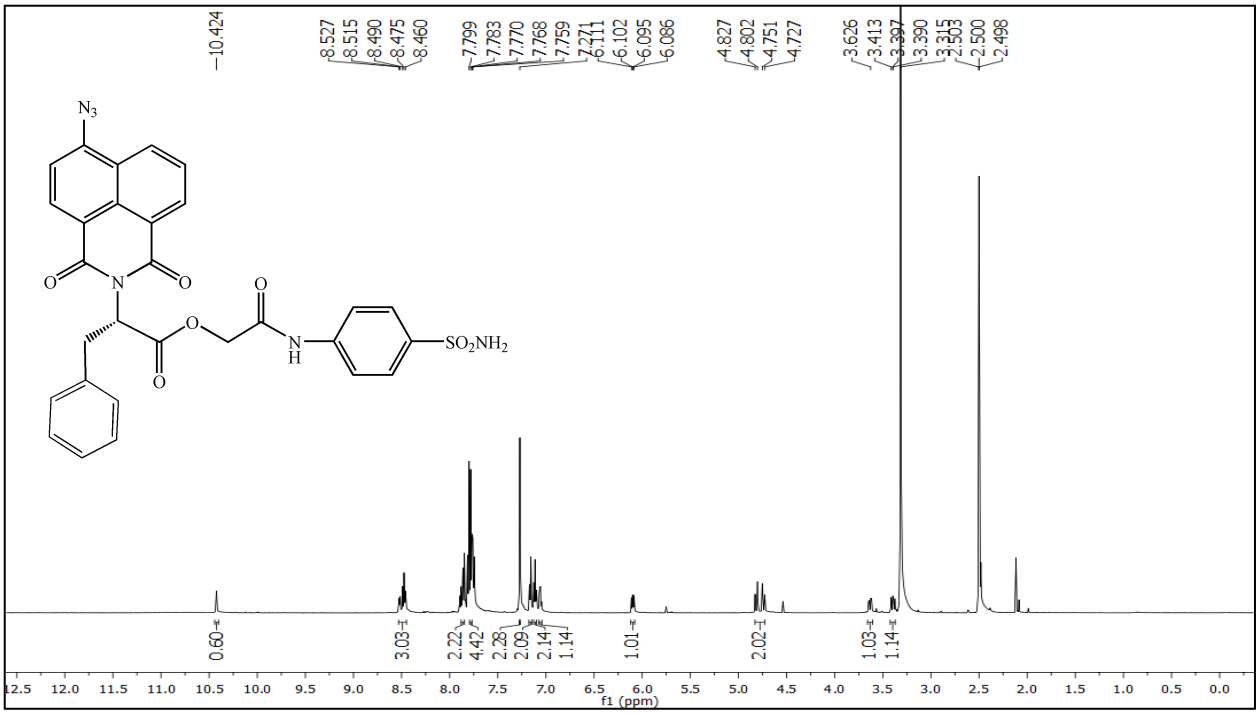


Figure S56. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1i**

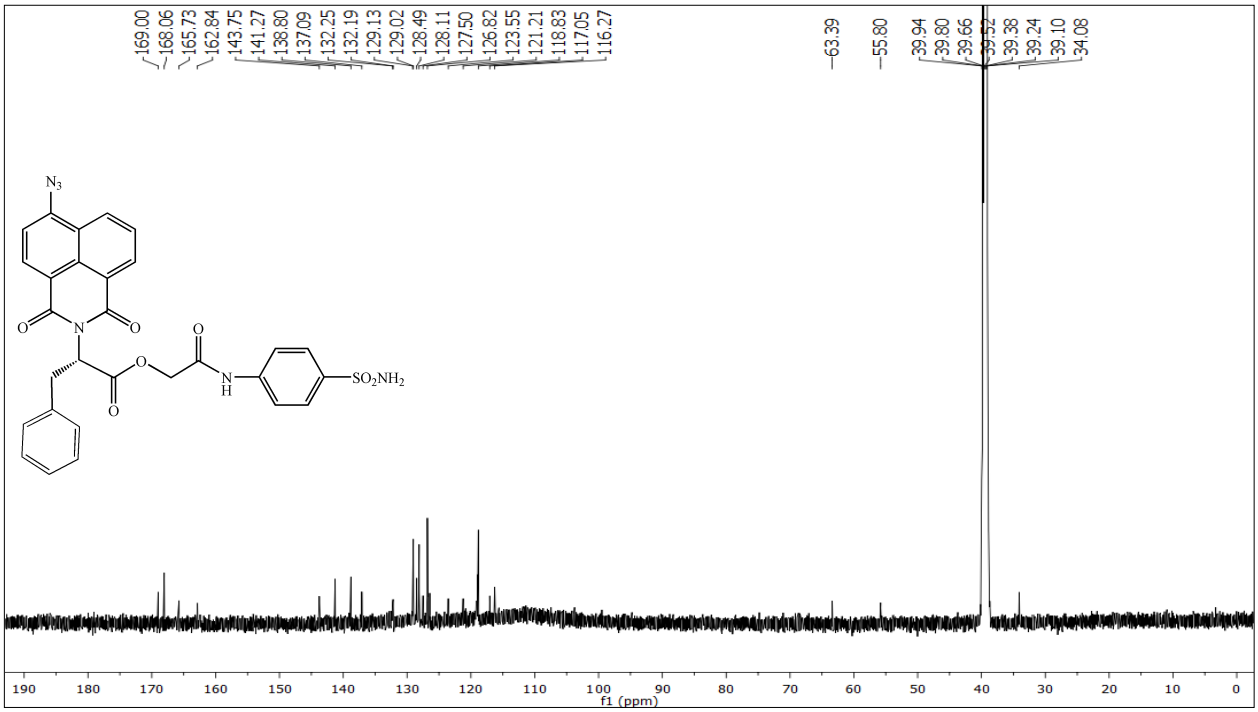


Figure S57. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1i**

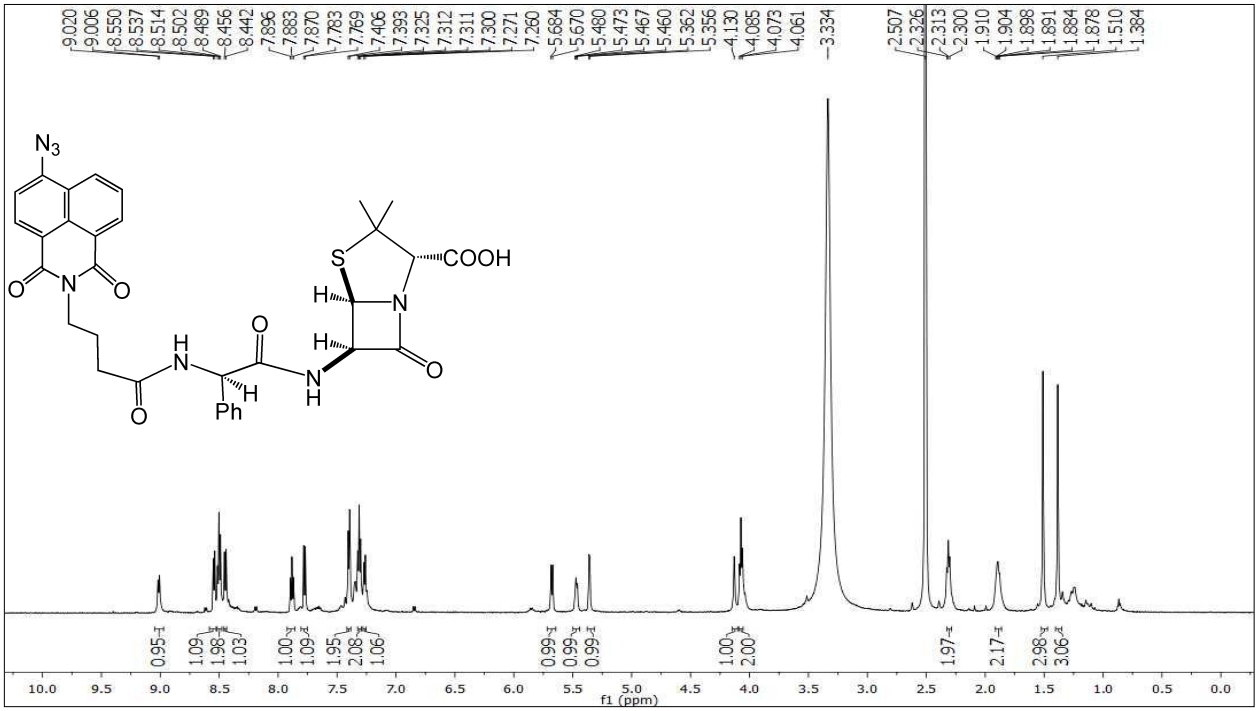


Figure S58. The ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **1j**

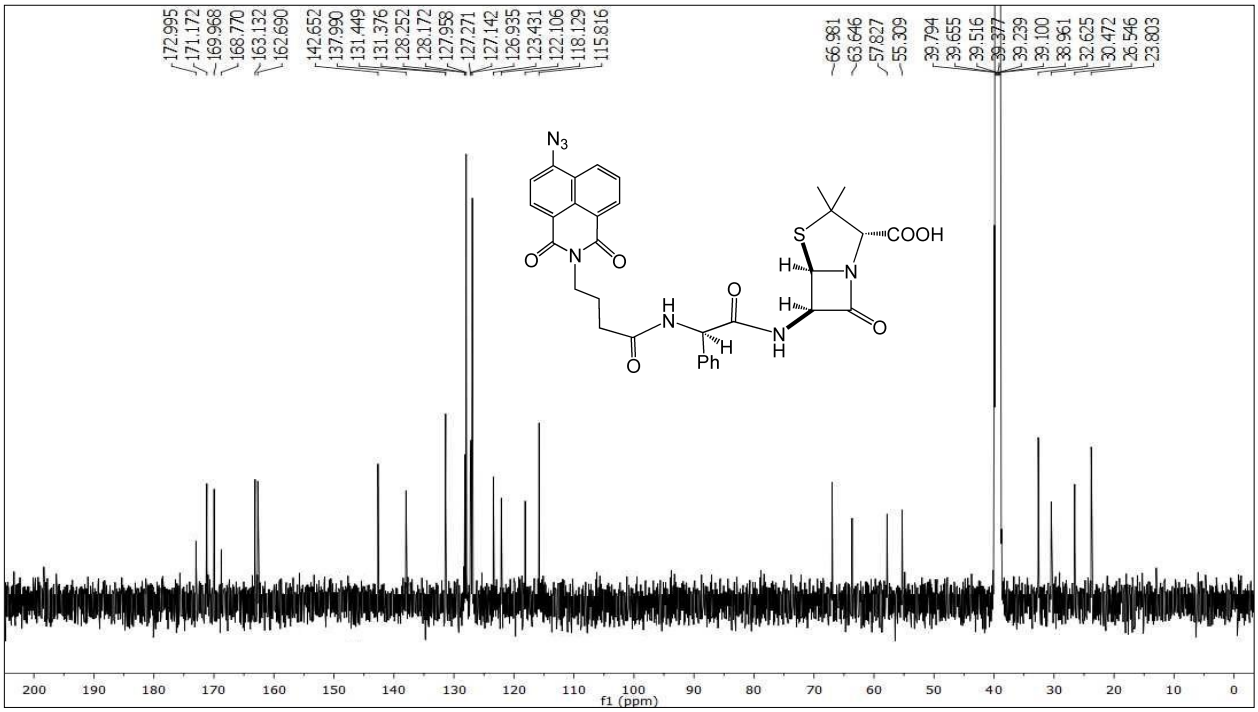
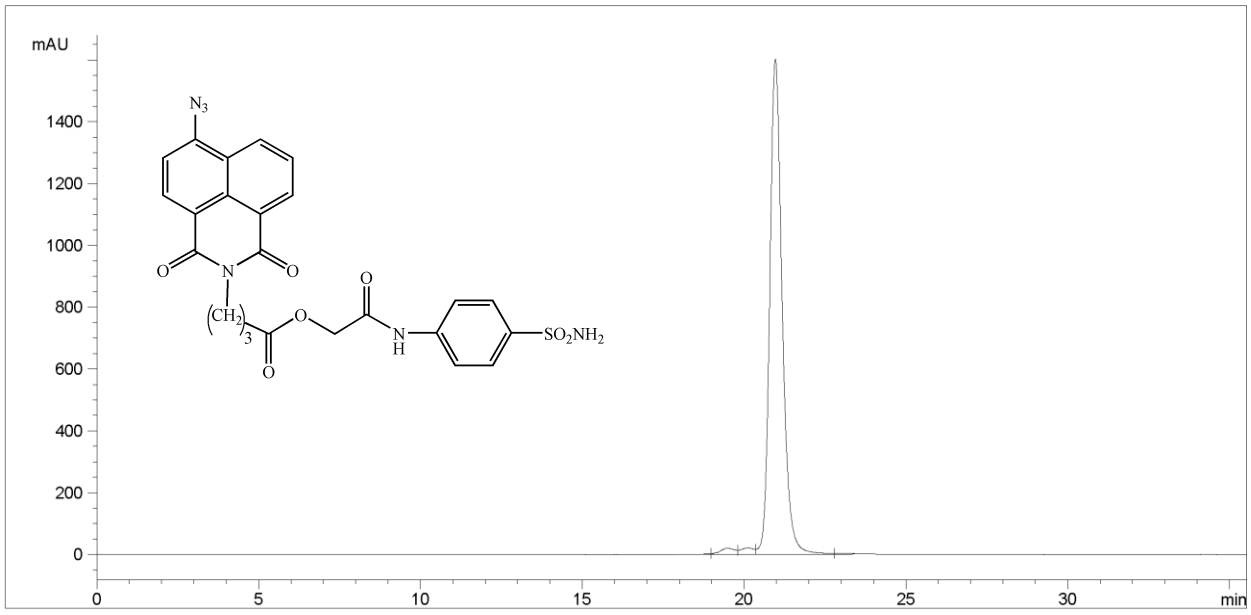
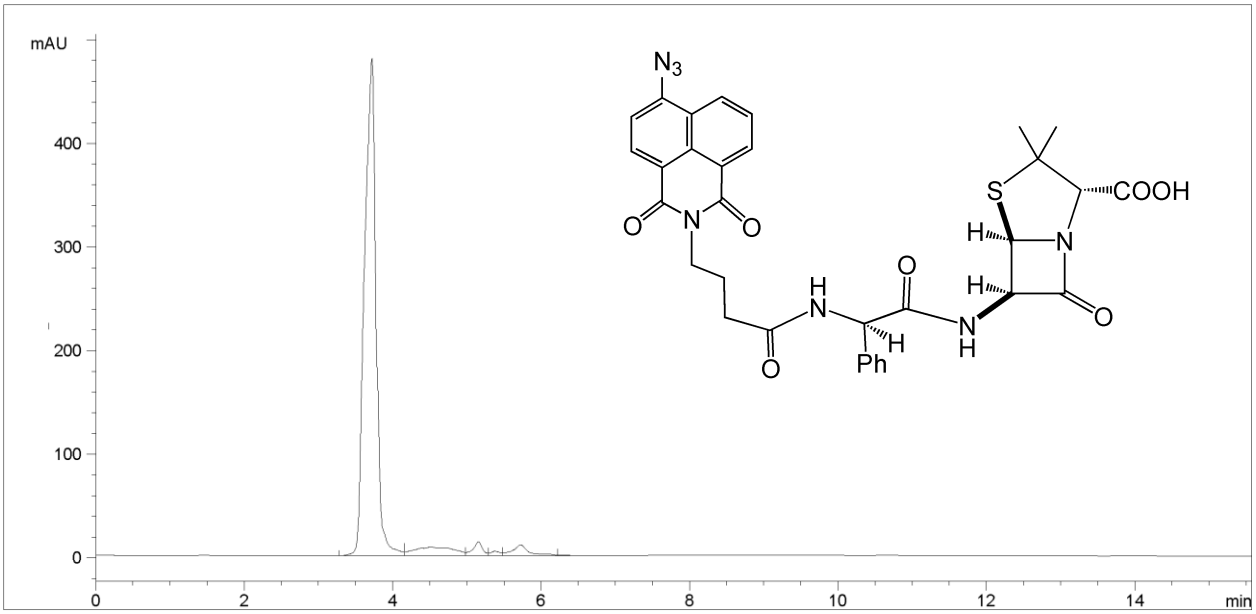


Figure S59. The ^{13}C NMR (150 MHz, DMSO-d_6) spectrum of compound **1j**

HPLC Data



Peak	Retention Time [min.]	Area	Area %
1	19.489	663.29934	1.4834
2	20.109	584.95901	1.3082
3	20.968	43466.54164	97.2084



Peak	Retention Time [min.]	Area	Area %
1	3.722	8241.26666	95.1431
2	4.515	179.25080	2.0694
3	5.157	95.50688	1.1026
4	5.379	32.94147	0.3803
5	5.843	113.00406	1.3046

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