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The *N*-Formamide as carbonyl precursor in the catalytic synthesis of Passerini adducts under aqua and mechanochemical conditions.

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Materials and Methods.

Mechanochemical experiments were carried out in an in-house modified Makita (Jigsaw) ball mill that was equipped with (reactor diameter: 2.0 cm; height: 2.0 cm; volume of reactor: 13.2 mL). All reactors are stainless steel and equipped with stainless steel balls (diameter: 6 mm; mass: 0.90 g;). A FT-IR-Eco ATR Bruker Alpha II Spectrometer was used for the FT-IR analysis. The IR spectra were obtained by the attenuated total reflection (ATR) method. For each experiment, 16 scans were performed in the frequency range from 650 to 4000 $cm^{-}1$. Melting points of all the compounds were determined using a Koffler hot-stage apparatus and are uncorrected. NMR spectra were recorded on a Bruker Advance III 400 spectrometer using $CDCl_3$ or DMSO-d_6 as a solvent with tetramethyl silane used as internal standard. LC-MS/MS data was recorded on a Bruker Compact quadrupole time of flight (QToF) mass spectrometer. Raw mass spectrometry data were processed using MZmine software (version 2.38). Solvents and chemicals used were of analytical grade, which were purchased from Sigma Aldrich and used without further purification. The purity determination of the starting materials and reaction monitoring was performed by thin-layer chromatography (TLC) on Merck silica gel G F254plates.

Preparation of Sulfuric Acid Adsorbed on Silica Gel (SiO_2-H_2SO_4)

This has been reported previously. [38] In short, to a suspension of silica gel (29.5 g, 230–400 mesh size) in EtOAc (60 mL), H_2SO_4 (1.5 g, 15.5 mmol, 0.8 mL of a 98% aq. solution of H_2SO_4) was added and the mixture was stirred magnetically for 30 min at room temperature. EtOAc was removed under reduced pressure (rotary evaporator) and the residue was heated at 100 °C for 72 h under vacuum to afford SiO_2-H_2SO_4 as a free-flowing powder.

General Experimental Procedures for the Aqua Synthesis of Passerini adducts (4a-s) in the presence of catalyst.

A mixture of benzoic acid (1a, 1 mmol) 1-naphthylisocyanides (2a, 1 mmol), and 4-formamido pyridine (3a, 1 mmol) was vigorously stirred in 2 mL water at room temperature for 10 minutes in the presence of 0.02g of SiO_2-H_2SO_4. Upon completion, the organic layer was separated, and the combined organic phases were concentrated under reduced pressure and the residue was purify by column chromatography using DCM/Hexane (3: 1) as eluent to afford the desired products. Typical yields range from 83 to 96%. All other products **(a-s)** were obtained by similar approach.

General Procedure for the Mechanochemical Synthesis of Passerini adducts (4a-b, 4f, 4j, 4n, 4p).

Experiment A. A mixture of benzoic acid (1a, 1 mmol) 1-naphthylisocyanides (2a, 1 mmol), and 4-formamido pyridine (3a, 1 mmol) and additive (SiO_2-H_2SO_4 0.03g) was milled in a 13.2 mL stainless

steel milling vessel contained two balls of the same material (diameter: 6 mm; mass: 0.90 g) at 25 Hz for 20 min. After the milling was complete, the content in the milling vessel was transferred into a beaker using a small amount of organic solvent (DCM). Then, purification was done by column chromatography to afford the corresponding Passerini adducts in high to excellent yield.

General Procedure for the Mechanochemical Synthesis of Passerini adducts (4c-e, 4g-i, 4k-m, 4o, 4s).

Experiment B. A mixture of benzoic acid (1a, 1 mmol) 1-naphthylisocyanides (2a, 1 mmol), and 2-formamidoanthracene-9,10-dione (3o, 1 mmol) and additive (water 75 μL) was milled in a 13.2 mL stainless steel milling vessel contained two balls of the same material (diameter: 6 mm; mass: 0.90 g) at 25 Hz for 30 min. After the milling was complete, the content in the milling vessel was transferred into a beaker using a small amount of organic solvent (DCM). Then, purification was done by column chromatography to afford the corresponding oxindole derivatives in high yield.

{[(naphthalen-1-yl)carbamoyl](pyridin-4-yl)methyl}amino benzoate white solid (Yield: Met A 95%, Met B, 97%); m.p. 128 ºC. IR (NaCl) ν(cm^{-1}) 3324 (NH), 1730 (CO) ester, and 1643 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (d, *J* = 9.9 Hz, 1H, NH-amide), 8.48 (d, *J* = 10.9 Hz, 1H, NH-ester), 8.00 (t, *J* = 9.6 Hz, 3H, Ar-H), 7.71 (d, *J* = 7.3 Hz, 1H, Ar-H), 7.63 (d, *J* = 8.2 Hz, 1H, Ar-H), 7.50 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.43 (td, *J* = 11.8, 3.8 Hz, 2H, Ar-H), 7.31 (t, *J* = 7.7 Hz, 2H, Ar-H), 7.26 (d, *J* = 7.9 Hz, 1H, Ar-H), 7.14 (d, *J* = 7.3 Hz, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.08 (CO-ester), 166.14 (CO-amide), 134.28, 133.76, 132.27, 129.90, 128.53, 128.08, 127.97, 127.29, 127.16, 126.91, 126.37, 125.52, 124.98, 122.92, 121.74, 120.81, 118.80. HR-MS (ESI): [M+H^+] calcd for $C_{24}H_{19}N_3O_3$: 398.1447, found: 398.1530.

{[(naphthalen-1-yl)carbamoyl](pyridin-2-yl)methyl}amino benzoate white solid (Yield: Met A 87%, Met B, 90%); m.p. 142 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (d, *J* = 7.4 Hz, 1H, NH-amide), 8.51 (d, *J* = 10.9 Hz, 1H, NH-ester), 8.06 (d, *J* = 8.4 Hz, 1H, Ar-H), 8.03 (t, *J* = 8.7 Hz, 2H, Ar-H), 7.76 (d, *J* = 8.3 Hz, 1H, Ar-H), 7.67 (d, *J* = 8.3 Hz, 1H, Ar-H), 7.55 (d, *J* = 7.1 Hz, 1H, Ar-H), 7.51 – 7.41 (m, 1H, Ar-H), 7.41 – 7.26 (m, 2H, Ar-H), 7.23 – 7.09 (m, 1H, Ar-H), 4.80 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.26 (CO-ester), 166.09 (CO-amide), 134.28, 133.78, 132.16, 130.24, 129.81, 129.54, 128.52, 128.08, 127.98, 127.73, 127.55, 127.17, 126.70, 126.19, 125.51, 124.98, 124.64, 122.94, 121.71, 118.78. HR-MS (ESI): [M+H^+] calcd for $C_{24}H_{19}N_3O_3$: 398.1450, found: 398.2406.

{[(naphthalen-1-yl)carbamoyl](5-sulfanyl-1H-1,2,3-triazol-4-yl)methyl}amino benzoate white solid (Yield: Met A 93%, Met B, 82%); m.p. 136 ºC. IR (NaCl) ν(cm^{-1}) 3330 (NH), 1660 (CO) ester, and 1628 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.32 (s, 1H, NH-amide), 10.42 (d, J = 4.4 Hz, 1H, NH-ester), 9.60 (d, J = 8.5 Hz, 1H, Ar-H), 9.51 (d, J = 8.4 Hz, 1H, Ar-H), 9.25 (d, J = 4.4 Hz, 1H, Ar-H), 9.19 (t, J = 7.6 Hz, 1H, Ar-H), 9.02 (t, J = 7.6 Hz, 1H, Ar-H), 8.13 (s, 1H, SH), 7.91 (d, J = 4.5 Hz, 1H, Ar-H), 7.56 (d, J = 4.5 Hz, 1H, Ar-H), 7.35 (d, J = 2.3 Hz, 1H, Ar-H), 4.87 (s, 5H, Het-H), 4.67

(d, J = 5.2 Hz, 1H, Het-H), 4.00 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 155.70, (CO-ester), 154.53, (CO-amide), 152.78, 146.47, 138.76, 134.48, 134.16, 131.39, 130.73, 129.36, 123.19, 122.85, 112.26, 111.23, 70.20, 53.88. HR-MS (ESI): [M+H$^+$] calcd for $C_{21}H_{17}N_5O_3S$: 419.1622, found: 419.1819.

{[(naphthalen-1-yl)carbamoyl](1H-1,2,3-triazol-4-yl)methyl}amino benzoate white solid (Yield: Met A 90%, Met B, 94%); 114 ºC. IR (NaCl) *v*(cm^{-1}) 3222 (NH), 1687 (CO) ester, and 1655 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H, NH-amide), 8.58 (d, J = 1.3 Hz, 1H, NH-ester), 8.49 (d, J = 10.9 Hz, 1H, Ar-H), 8.05 (s, 1H, Ar-H), 8.00 (d, J = 7.4 Hz, 9H, Ar-H), 7.73 (d, J = 8.2 Hz, 3H, Ar-H), 7.64 (d, J = 8.3 Hz, 1H, Ar-H), 7.49 – 7.39 (m, 12H, Ar-H), 7.32 (t, J = 7.8 Hz, 20H, Ar-H), 7.18 – 7.07 (m, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.24 (CO-ester), 166.22 (CO-amide), 161.18, 156.21, 149.07, 145.86, 134.29, 133.77, 132.26, 129.56, 128.52, 127.48, 127.32, 126.90, 125.51, 124.64, 122.94, 121.75, 120.72, 118.83, 114.08. HR-MS (ESI): [M+H$^+$] calcd for $C_{21}H_{17}N_5O_3$: 388.1363, found: 388.2044.

[(1,5-dimethyl-3-oxo-2-phenylpyrazol-4-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate brown solid (Yield: Met A 96%, Met B, 86%); m.p. 107 ºC. IR (NaCl) *v*(cm^{-1}) 3328 (NH), 1720 (CO) ester, and 1618 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (d, J = 10.2 Hz, 1H), 9.63 (s, 1H, NH-amide), 9.30 (s, 1H, NH-ester), 8.50 (d, J = 11.0 Hz, 1H, Ar-H), 8.05 (d, J = 8.4 Hz, 1H, Ar-H), 7.99 (d, J = 7.8 Hz, 2H, Ar-H), 7.86 (d, J = 7.5 Hz, 1H, Ar-H), 7.75 (d, J = 7.8 Hz, 1H, Ar-H), 7.65 (d, J = 8.3 Hz, 1H, Ar-H), 7.54 (d, J = 8.1 Hz, 1H, Ar-H), 7.45 (t, J = 7.3 Hz, 1H, Ar-H), 7.32 (t, J = 7.5 Hz, 2H, Ar-H), 7.23 (d, J = 7.4 Hz, 1H, Ar-H), 7.17 (t, J = 7.1 Hz, 1H, Ar-H), 2.98 (s, 1H, CH_3), 2.17 (s, 1H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.26 (CO-amide), 165.71 (CO-hetero), 161.06 (CO-ester), 148.68, 134.26, 133.49, 129.92, 129.54, 128.45, 127.74, 127.48, 127.19, 127.08, 126.85, 126.10, 125.70, 125.51, 124.64, 122.89, 121.76, 120.81, 118.84, 106.23, 35.43 (CH_3), 12.29 (CH_3). HR-MS (ESI): [M+H$^+$] calcd for $C_{30}H_{26}N_4O_4$: 507.2215, found: 507.2319.

{3-methyl-1-[(naphthalen-1-yl)carbamoyl]butyl}amino benzoate yellow solid (Yield: Met A 92%, Met B, 95%); m.p. 125 ºC. IR (NaCl) *v*(cm^{-1}) 3386 (NH), 1703 (CO) ester, and 1627 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (d, J = 9.3 Hz, 1H, NH-amide), 8.55 (d, J = 11.1 Hz, 1H, CO-ester), 8.05 (d, J = 7.6 Hz, 5H, Ar-H), 7.83 (d, J = 8.3 Hz, 1H, Ar-H), 7.73 (d, J = 8.3 Hz, 1H, Ar-H), 7.59 – 7.48 (m, 4H, Ar-H), 7.40 (t, J = 7.7 Hz, 6H, Ar-H), 7.25 (d, J = 7.2 Hz, 1H, Ar-H), 3.08 (t, J = 6.6 Hz, 1H, CH_2), 1.78 (dt, J = 13.4, 6.7 Hz, 1H, CH_3), 0.87 (d, J = 6.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.74 (CO-ester), 165.37 (CO-amide), 160.07, 134.24, 133.68, 132.16, 130.31, 129.58, 128.49, 127.78, 127.17, 126.89, 125.52, 121.59, 120.53, 118.97, 47.07 (CH_2), 28.42 (CH_2), 20.09 (CH_3). HR-MS (ESI): [M+H$^+$] calcd for $C_{23}H_{24}N_2O_3$: 377.1826, found: 377.3040.

{1H-1,3-benzodiazol-2-yl[(naphthalen-1-yl)carbamoyl]methyl}amino benzoate white solid (Yield: Met A 85%, Met B, 80%); m.p. 139 ºC. IR (NaCl) *v*(cm^{-1}) 3273 (NH), 1696 (CO) ester, and 1624 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 10.03 (d, J = 9.5 Hz, 1H), 8.59 (s, 1H, NH-amide), 8.54 (d, J = 11.0 Hz, 1H, NH-ester), 8.05 (d, J = 8.2 Hz, 3H, Ar-H), 7.81 (d, J = 8.2 Hz, 1H, Ar-H), 7.72 (d, J = 8.3 Hz, 1H, Ar-H), 7.53 (t, J = 7.4 Hz, 2H, Ar-H), 7.39 (t, J = 7.6 Hz, 3H, Ar-H), 7.24 (d, J = 7.3 Hz, 1H, Ar-H), 5.20 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.38 (CO-ester), 165.90 (CO-amide), 134.31, 133.83, 132.22, 130.12, 129.43, 128.42, 127.82, 127.29, 127.13, 126.90, 125.50, 121.65, 121.12, 120.33, 118.85, 112.47, 109.39, 102.62. HR-MS (ESI): [M+H^+] calcd for $C_{26}H_{20}N_4O_3$: 437.1502, found: 437.2008.

{1,3-benzothiazol-2-yl[(naphthalen-1-yl)carbamoyl]methyl}amino benzoate white solid (Yield: Met A 95%, Met B, 88%); m.p. 142 ºC. IR (NaCl) *v*(cm^{-1}) 3406 (NH), 1683 (CO) ester, and 1626 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 1H, NH-amide), 9.67 (d, J = 9.5 Hz, 1H, NH-ester), 8.64 (s, 1H), 8.53 (d, J = 10.8 Hz, 1H, Ar-H), 8.35 (d, J = 8.4 Hz, 1H, Ar-H), 8.21 (s, 1H, Ar-H), 8.09 (d, J = 8.4 Hz, 1H, Ar-H), 8.04 (d, J = 7.9 Hz, 2H, Ar-H), 7.99 (d, J = 8.1 Hz, 1H, Ar-H), 7.90 (d, J = 7.5 Hz, 1H, Ar-H), 7.80 (d, J = 8.1 Hz, 1H, Ar-H), 7.68 (dd, J = 18.8, 8.5 Hz, 1H, Ar-H), 7.57 (d, J = 8.0 Hz, 1H, Ar-H), 7.54 – 7.44 (m, 2H, Ar-H), 7.37 (t, J = 7.8 Hz, 3H, Ar-H), 7.22 (d, J = 7.2 Hz, 1H, Ar-H), 7.18 – 7.09 (m, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.77 (CO-amide), 165.52 (CO-ester), 160.07 (C-C Hetero), 154.11 (C-S, Hetero), 138.92, 134.28, 133.43, 132.21, 130.15, 129.85, 128.44, 128.20, 127.47, 127.14, 126.84, 126.16, 125.72, 124.98, 124.62, 122.97, 121.59, 120.14, 118.94, 116.54. HR-MS (ESI): [M+H^+] calcd for $C_{26}H_{19}N_3O_3S$: 454.1123, found: 454.2017.

[(5-methyl-1,2-oxazol-3-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate brown solid (Yield: Met A 83%, Met B, 83%); m.p. 115 ºC. IR (NaCl) *v*(cm^{-1}) 3258 (NH), 1690 (CO) ester, and 1625 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.04 (s, 1H, NH-amide), 10.12 (s, 1H, NH-ester), 8.53 (d, J = 10.9 Hz, 1H, Ar-H), 8.38 (s, 1H, Ar-H), 8.03 (d, J = 7.9 Hz, 2H, Ar-H), 7.79 (d, J = 8.0 Hz, 1H, Ar-H), 7.69 (d, J = 8.2 Hz, 1H, Ar-H), 7.50 (t, J = 7.4 Hz, 1H, Ar-H), 7.37 (t, J = 7.7 Hz, 2H, Ar-H), 7.22 (d, J = 7.3 Hz, 1H, Ar-H), 6.69 (s, 1H,), 2.31 (s, 3H (CH_3)). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.40 (CO-ester), 166.08 (CO-amide), 159.07 (C-C-Hetero), 148.23, 147.65, 144.31, 138.20, 135.74, 133.74, 132.21, 130.21, 129.57, 128.50, 127.74, 127.15, 126.86, 125.50, 121.70, 118.82, 97.18, 12.63 (CH_3). HR-MS (ESI): [M+H^+] calcd for $C_{23}H_{19}N_3O_4$; 402.1455, found: 402.0983.

[3-(3,4-dihydroxyphenyl)-3-hydroxy-1-[(naphthalen-1-yl)carbamoyl]propyl](methyl)amino benzoate brown solid (Yield: Met A 89%, Met B, 92%); m.p. 133 ºC IR (NaCl) *v*(cm^{-1}) 3469 (OH), 3246 (NH), 1703 (CO) ester, and 1620 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (d, J = 10.1 Hz, 1H, NH-amide), 9.39 (s, 1H, -OH), 8.46 (d, J = 10.8 Hz, 1H, -OH), 7.96 (d, J = 7.7 Hz, 2H, Ar-H), 7.68 (d, J = 7.9 Hz, 1H, Ar-H), 7.59 (d, J = 8.3 Hz, 1H, Ar-H), 7.42 (ddd, J = 22.5, 15.5, 7.0 Hz, 2H,

Ar-H), 7.29 (d, J = 7.6 Hz, 2H, Ar-H), 7.22 (t, J = 7.8 Hz, 1H, Ar-H), 7.11 (d, J = 7.3 Hz, 1H, Ar-H), 4.79 (s, 1H, -CH (chiral)), 3.97 (q, J = 7.1 Hz, 1H, CH_2), 1.89 (s, 1H, CH_3), 1.09 (t, J = 7.2 Hz, 1H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.54 (CO-ester), 167.02 (CO-amide), 166.10 (C-OH), 161.34 (C-OH), 134.25, 133.61, 132.28, 130.15, 129.84, 129.64, 128.46, 128.35, 128.02, 127.42, 127.05, 126.82, 125.48, 124.92, 124.57, 122.82, 121.73, 118.73, 60.60, 21.04, 14.09. HR-MS (ESI): [M+H^+] calcd for $C_{28}H_{26}N_2O_6$; 487.1733, found: 487.2906.

[(2-hydroxyphenyl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate brown solid (Yield: Met A 95%, Met B, 78%); m.p. 112 ºC. IR (NaCl) *v*(cm^{-1}) 3451 (OH), 3234 (NH), 1679 (CO) ester, and 1628 (CO) amide. ^1H NMR (400 MHz, $CDCl_3$) δ 9.34 (d, J = 11.3 Hz, 1H, NH-amide), δ 8.59 (s, 1H, OH), 8.55 (d, J = 11.0 Hz, 1H, NH-ester), 8.06 (d, J = 7.9 Hz, 4H, Ar-H), 8.00 (d, J = 8.2 Hz, 1H, Ar-H), 7.84 (d, J = 7.9 Hz, 1H, Ar-H), 7.74 (d, J = 8.3 Hz, 1H, Ar-H), 7.58 – 7.49 (m, 4H, Ar-H), 7.41 (t, J = 7.6 Hz, 5H, Ar-H), 7.26 (d, J = 7.3 Hz, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.67 (CO-ester), 164.91 (CO-amide), 159.59 (C-OH), 134.28, 133.73, 132.10, 130.22, 129.49, 128.50, 127.76, 127.23, 127.13, 126.89, 126.32, 125.52, 121.47, 120.29, 118.99. HR-MS (ESI): [M+H^+] calcd for $C_{25}H_{20}N_2O_4$; 413.0014, found: 413.0030.

[(4-hydroxyphenyl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate brown solid (Yield: Met A 91%, Met B, 86%); m.p. 108 ºC. IR (NaCl) *v*(cm^{-1}) 3417 (OH), 3330 (NH), 1655 (CO) ester, and 1624 (CO) amide. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 10.5 Hz, 1H, NH-amide), 8.31 (s, 1H, NH-ester), 7.96 (s, 1H, C-OH), 7.92 (d, J = 9.0 Hz, 1H, Ar-H), 7.82 (dd, J = 15.3, 8.0 Hz, 1H, Ar-H), 7.73 (d, J = 8.3 Hz, 1H, Ar-H), 7.66 (d, J = 8.3 Hz, 1H, Ar-H), 7.57 – 7.49 (m, 2H, Ar-H), 7.48 – 7.43 (m, 1H, Ar-H), 7.40 (t, J = 6.7 Hz, 1H, Ar-H), 7.26 (d, J = 7.3 Hz, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.02 (CO-ester), 159.68 (CO-amide), 134.27, 131.97, 128.90, 128.62, 127.75, 127.14, 127.10, 126.87, 126.58, 126.29, 126.19, 125.74, 125.56, 121.23, 120.93, 120.36, 119.20. HR-MS (ESI): [M+H^+] calcd for $C_{25}H_{20}N_2O_4$; 413.1454, found: 413.2126.

ethyl 2-{[(benzoyloxy)amino][(naphthalen-1-yl)carbamoyl]methyl}benzoate white solid (Yield: Met A 87%, Met B, 93%); m.p. 146 ºC IR (NaCl) *v*(cm^{-1}) 3277 (NH), 1687 (CO) ester, and 1608 (CO) amide. ^1H NMR (400 MHz, $CDCl_3$) δ 11.11 (s, 1H, NH-amide), 10.60 (s, 1H, NH-ester), 8.98 (d, J = 11.1 Hz, 1H, Ar-H), 8.73 (d, J = 8.4 Hz, 1H, Ar-H), 8.55 (s, 1H, Ar-H), 8.19 (d, J = 8.4 Hz, 1H, Ar-H), 8.14 (d, J = 7.5 Hz, 2H, Ar-H), 8.07 (d, J = 7.6 Hz, 1H, Ar-H), 7.91 (d, J = 8.2 Hz, 1H, Ar-H), 7.68 (t, J = 7.5 Hz, 1H, Ar-H), 7.60 (dt, J = 7.0, 5.6 Hz, 2H, Ar-H), 7.55 (d, J = 7.7 Hz, 1H, Ar-H), 7.52 – 7.40 (m, 3H, Ar-H), 7.38 (d, J = 8.3 Hz, 1H, Ar-H), 7.14 (t, J = 7.6 Hz, 1H, Ar-H), 4.39 (q, J = 7.1 Hz, 2H, CH_2), 1.43 (t, J = 7.1 Hz, 4H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.74 (CO-ester), 168.11 (CO-benzoate), 159.90 (CO-amide), 140.36, 134.62, 133.65, 130.91, 130.17, 129.85, 129.62, 128.47,

128.36, 128.05, 127.45, 124.96, 124.60, 123.22, 122.92, 121.21, 115.89, 115.51, 61.60 (CH_2), 14.19 (CH_3). HR-MS (ESI): [M+H$^+$] calcd for $C_{28}H_{24}N_2O_5$; 469.1713, found: 469.2601.

{3-methoxy-1-[(naphthalen-1-yl)carbamoyl]propyl}amino benzoate white solid (Yield: Met A 84%, Met B, 86%); m.p. 125 ºC IR (NaCl) *v*(cm^{-1}) 3344 (NH), 1660 (CO) ester, and 1604 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.27 (s, 1H, NH-amide), 10.07 (d, J = 9.9 Hz, 1H, NH-ester), 8.50 (d, J = 10.1 Hz, 1H, Ar-H), 8.11 – 7.92 (m, 4H, Ar-H), 7.92 – 7.85 (m, 1H, Ar-H), 7.75 (d, J = 8.1 Hz, 3H, Ar-H), 7.66 (d, J = 8.3 Hz, 1H, Ar-H), 7.52 (dd, J = 14.4, 6.4 Hz, 2H, Ar-H), 7.43 (d, J = 6.3 Hz, 1H, Ar-H), 7.30 (dd, J = 14.1, 6.2 Hz, 2H, Ar-H), 7.17 (d, J = 7.3 Hz, 1H, Ar-H), 1.87 (s, 1H,), 1.14 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.99 (CO-ester), 165.88 (CO-amide), 134.27, 133.73, 132.28, 130.22, 129.88, 129.61, 128.52, 128.07, 127.48, 127.16, 126.90, 125.52, 124.98, 124.63, 122.93, 121.69, 118.77, 82.57, 24.91. HR-MS (ESI): [M+H$^+$] calcd for $C_{22}H_{22}N_2O_4$; 379.1630, found: 379.1625.

[(9,10-dioxo-9,10-dihydroanthracen-2-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate brown solid (Yield: Met A 90%, Met B, 92%); m.p. 143 ºC. IR (NaCl) *v*(cm^{-1}) 3328 (NH), 1714 (CO) ester, and 1633 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (d, J = 10.2 Hz, 1H, NH-amide), 10.07 (s, 1H, NH-ester), 8.49 (d, J = 10.9 Hz, 1H, Ar-H), 8.01 (t, J = 10.6 Hz, 3H, Ar-H), 7.72 (d, J = 8.1 Hz, 1H, Ar-H), 7.63 (d, J = 8.3 Hz, 1H, Ar-H), 7.55 – 7.36 (m, 3H, Ar-H), 7.38 – 7.21 (m, 3H, Ar-H), 7.25 – 7.11 (m, 1H, Ar-H), 4.76 (s, 1H, CH), 1.12 (t, J = 7.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.07 (CO-anthraquinone), 166.06 (CO-ester), 161.18 (CO-amide), 134.28, 133.76, 132.26, 130.23, 129.89, 129.56, 128.52, 128.38, 128.07, 127.47, 127.29, 127.15, 126.89, 125.51, 124.97, 124.63, 122.92, 121.73, 118.82, 60.66, 13.82. HR-MS (ESI): [M+H$^+$] calcd for $C_{33}H_{22}N_2O_5$; 527.1545, found: 527.1718.

[2-(furan-2-yl)-1-[(naphthalen-1-yl)carbamoyl]ethyl]amino benzoate yellow solid (Yield: Met A 88%, Met B, 93%); m.p. 121 ºC. IR (NaCl) *v*(cm^{-1}) 3226 (NH), 1660 (CO) ester, and 1600 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H, NH-amide), 10.18 (d, J = 9.9 Hz, 1H, NH-ester), 8.47 (d, J = 10.9 Hz, 1H, Ar-H), 7.99 (t, J = 10.0 Hz, 3H, Ar-H), 7.71 (d, J = 7.0 Hz, 1H, Ar-H), 7.62 (d, J = 8.2 Hz, 1H, Ar-H), 7.50 (d, J = 7.1 Hz, 1H, Ar-H), 7.44 (t, J = 7.7 Hz, 3H, Ar-H), 7.28 (dt, J = 23.2, 7.7 Hz, 3H, Ar-H), 7.13 (d, J = 7.3 Hz, 1H, Ar-H), 4.33 (d, J = 5.7 Hz, 1H), 1.88 (d, J = 21.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.02 (CO-ester), 166.11 (CO-amide), 161.16 (C-hetero), 134.29, 133.73, 132.27, 130.23, 129.89, 129.62, 128.51, 128.07, 127.47, 127.15, 126.89, 125.51, 124.97, 124.63, 122.91, 121.74, 118.80, 35.27. HR-MS (ESI): [M+H$^+$] calcd for $C_{33}H_{22}N_2O_5$; 527.1502, found: 527.1709.

ethyl 2-{2-[(benzoyloxy)amino]-2-(pyridin-4-yl)acetamido}benzoate white solid (Yield: Met A 94%, Met B, 92%); m.p. 138 ºC IR (NaCl) *v*(cm^{-1}) 3236 (NH), 1688 (CO) ester, and 1612 (CO) amide.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.95 (s, 1H, NH-amide), 10.48 (d, J = 9.5 Hz, 1H, NH-ester), 8.83 (d, J = 11.1 Hz, 1H, Ar-H), 8.76 – 8.57 (m, 1H, Ar-H), 8.57 (d, J = 8.5 Hz, 1H, Ar-H), 8.40 (s, 1H, Ar-H), 7.97 (d, J = 8.0 Hz, 2H, Ar-H), 7.89 (d, J = 8.0 Hz, 1H, Ar-H), 7.48 – 7.33 (m, 2H, Ar-H), 7.30 (t, J = 7.5 Hz, 2H, Ar-H), 7.22 (d, J = 8.1 Hz, 1H, Ar-H), 7.04 – 6.88 (m, 1H, Ar-H), 4.21 (q, J = 7.1 Hz, 3H, CH_2), 1.25 (t, J = 7.1 Hz, 4H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.90 (CO-ester), 167.97 (CO-amide), 160.14 (CO-ester), 140.24, 134.48, 133.44, 131.79, 130.85, 130.06, 129.70, 128.37, 123.18, 121.16, 115.40, 61.54, 60.26, 14.09. HR-MS (ESI): [M+H$^+$] calcd for $C_{23}H_{21}N_3O_5$; 420.1425, found: 420.1090.

{[(3-bromophenyl)carbamoyl](pyridin-4-yl)methyl}amino benzoate yellow solid (Yield: Met A 91%, Met B, 84%); m.p. 109 ºC. IR (NaCl) *v*(cm^{-1}) 3351 (NH), 1683 (CO) ester, and 1604(CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.61 (d, J = 10.9 Hz, 1H), 8.32 (s, 1H), 8.05 (d, J = 7.8 Hz, 6H), 7.73 (s, 1H), 7.54 (t, J = 7.3 Hz, 3H), 7.40 (dd, J = 13.9, 6.5 Hz, 7H), 7.31 – 7.21 (m, 2H), 7.15 (dt, J = 16.9, 8.7 Hz, 3H), 7.00 (d, J = 7.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.43 (CO-ester), 159.20 (CO-amide), 137.96, 133.74, 131.11, 130.45, 130.20, 129.50, 128.50, 127.93, 123.39, 122.92, 122.73, 121.80, 118.41, 117.31. HR-MS (ESI): [M+H$^+$] calcd for $C_{20}H_{16}BrN_3O_3$; 426.0314, found: 426.0618.

{[(naphthalen-1-yl)carbamoyl](1,3-thiazol-2-yl)methyl}amino benzoate brown solid (Yield: Met A 90%, Met B, 95%); m.p. 135 ºC. IR (NaCl) *v*(cm^{-1}) 3241 (NH), 1695 (CO) ester, and 1638 (CO) amide. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H, NH-amide), 10.00 (d, J = 10.1 Hz, 1H, NH-ester), 8.65 – 8.39 (m, 1H, Ar-H), 8.02 (t, J = 10.0 Hz, 2H, Ar-H), 7.90 (d, J = 7.5 Hz, 1H, Ar-H), 7.80 (d, J = 7.6 Hz, 1H, Ar-H), 7.69 (d, J = 8.2 Hz, 1H, Ar-H), 7.50 (t, J = 7.2 Hz, 1H, Ar-H), 7.45 – 7.29 (m, 3H, Ar-H), 7.21 (d, J = 7.5 Hz, 1H, Ar-H), 6.91 (d, J = 3.6 Hz, 1H, Ar-H), 6.70 (d, J = 7.0 Hz, 1H, Ar-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.78 (CO-ester0, 165.67 (CO-amide), 158.74 (C-thiazole), 135.62, 134.28, 133.50, 132.35, 130.09, 128.49, 127.74, 127.16, 127.09, 126.88, 126.36, 125.91, 124.97, 121.66, 118.87, 113.96, 109.97. HR-MS (ESI): [M+H$^+$] calcd for $C_{22}H_{17}N_3O_3S$; 404.1012, found: 404.1815.

2. Spectral data of synthesized compounds

4a. {[(naphthalen-1-yl)carbamoyl](pyridin-4-yl)methyl}amino benzoate.

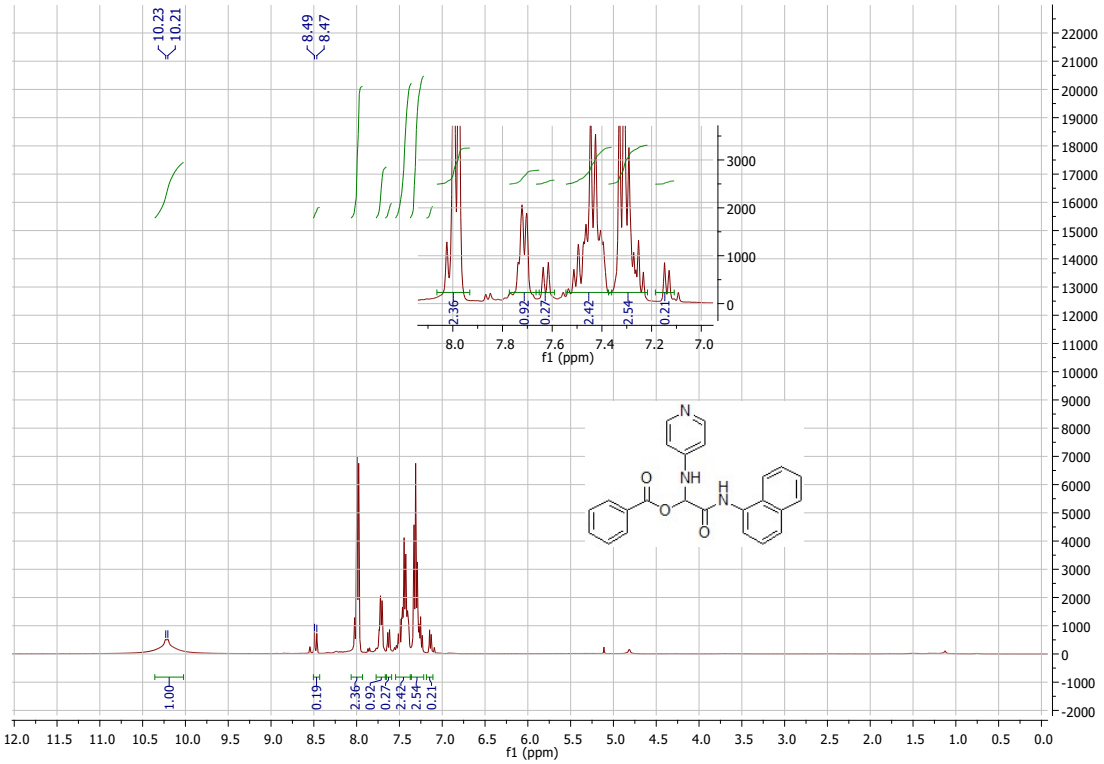

Figure S1.1 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

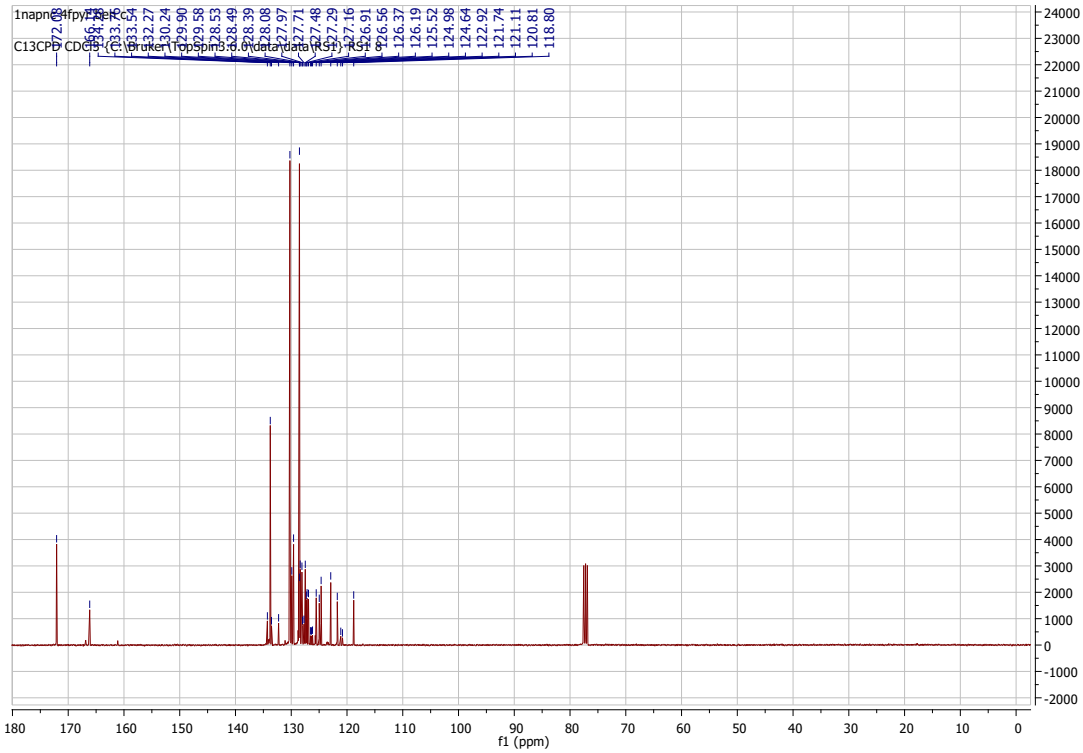

Figure S1.2. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4b. {[(naphthalen-1-yl)carbamoyl](pyridin-2-yl)methyl}amino benzoate

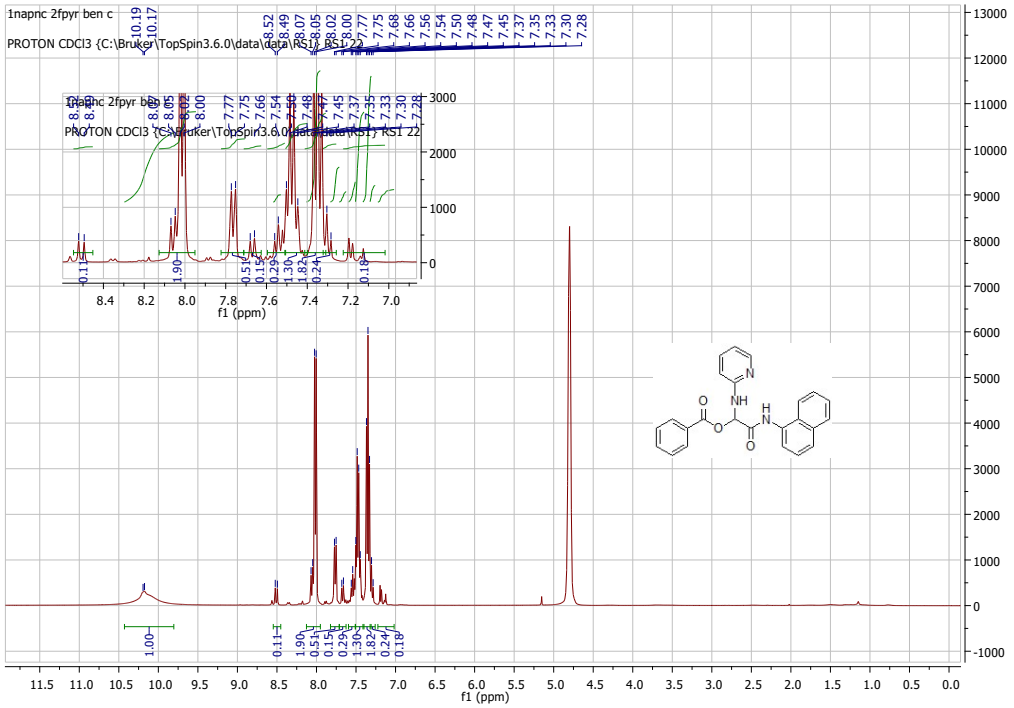

Figure S1.3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

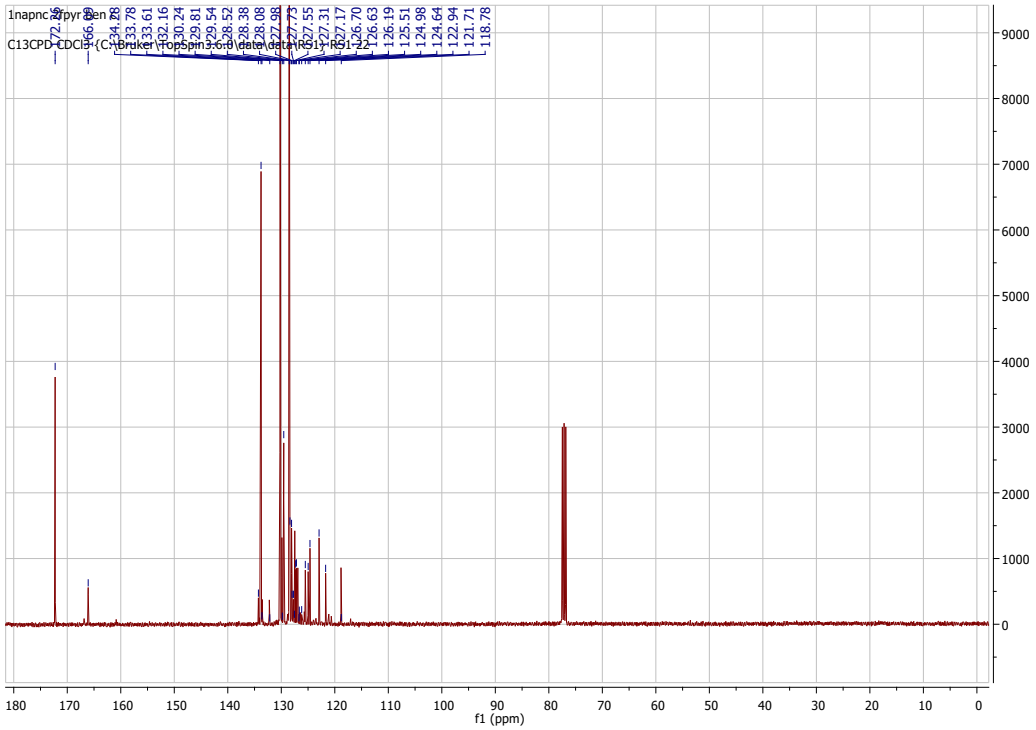

Figure S1.4. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4c. {[(naphthalen-1-yl)carbamoyl](5-sulfanyl-1H-1,2,3-triazol-4-yl)methyl}amino benzoate

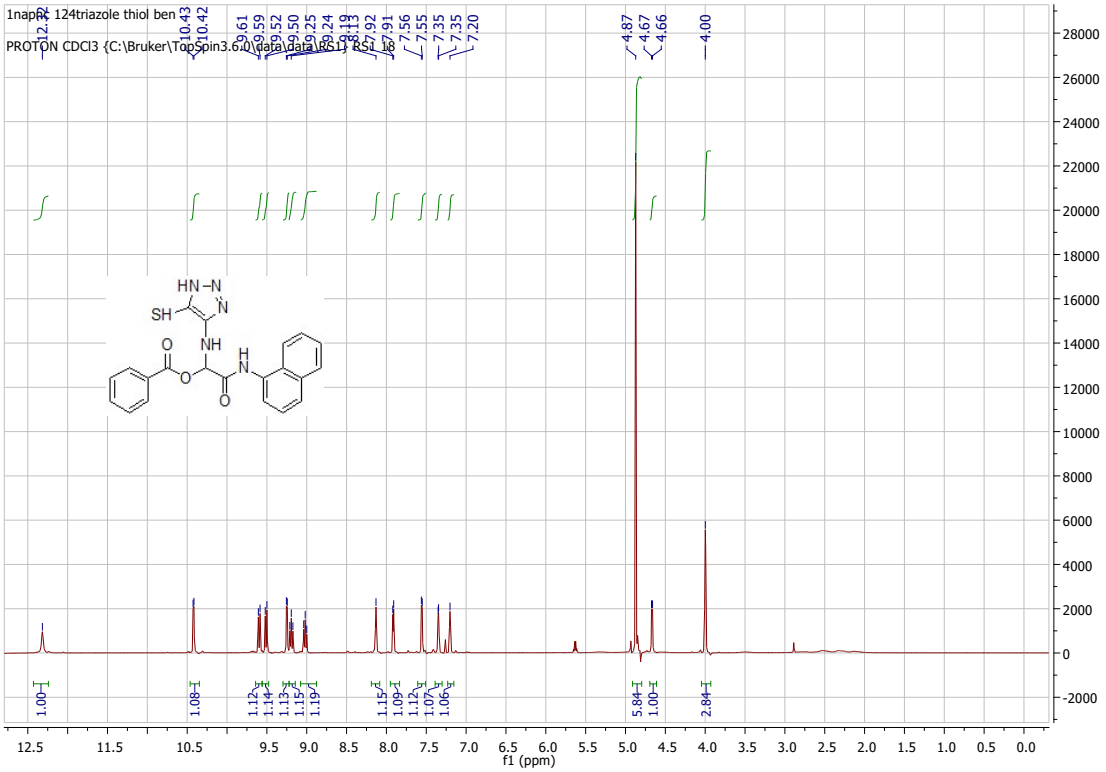

Figure S1.5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

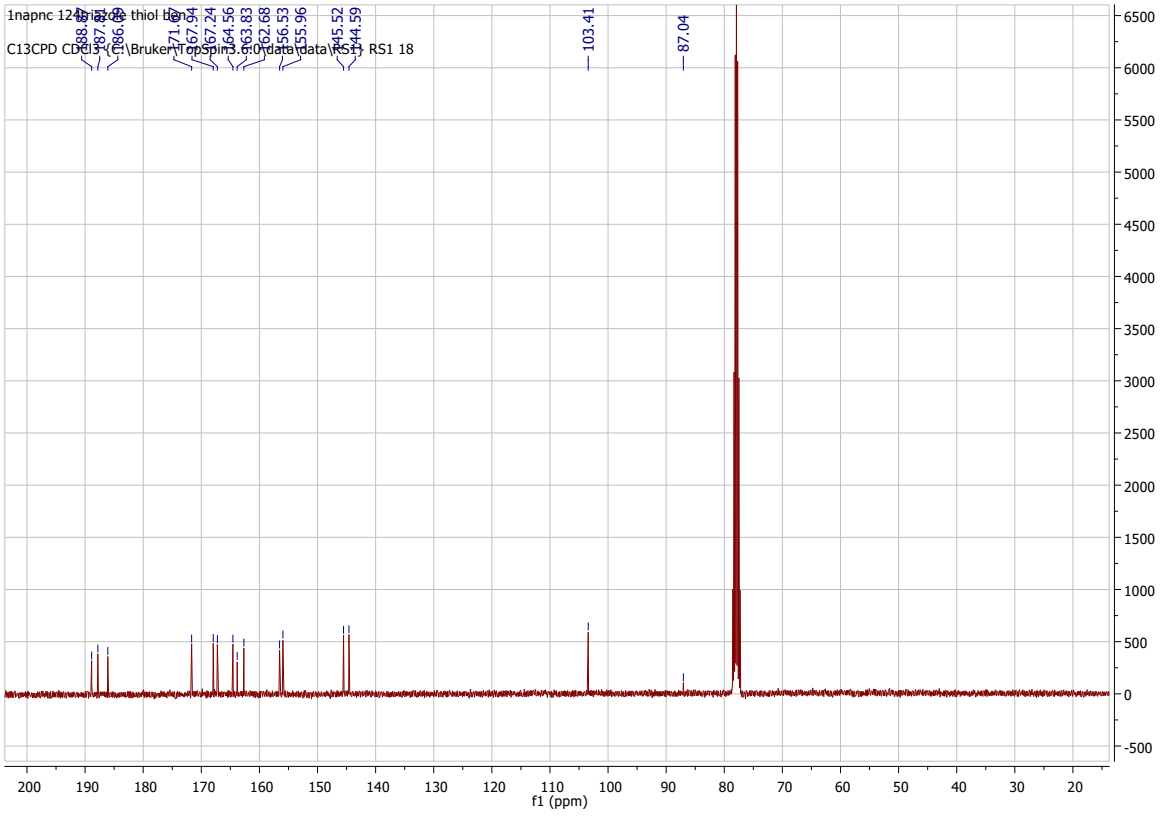

Figure S1.6. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4d. {[(naphthalen-1-yl)carbamoyl](1H-1,2,3-triazol-4-yl)methyl}amino benzoate

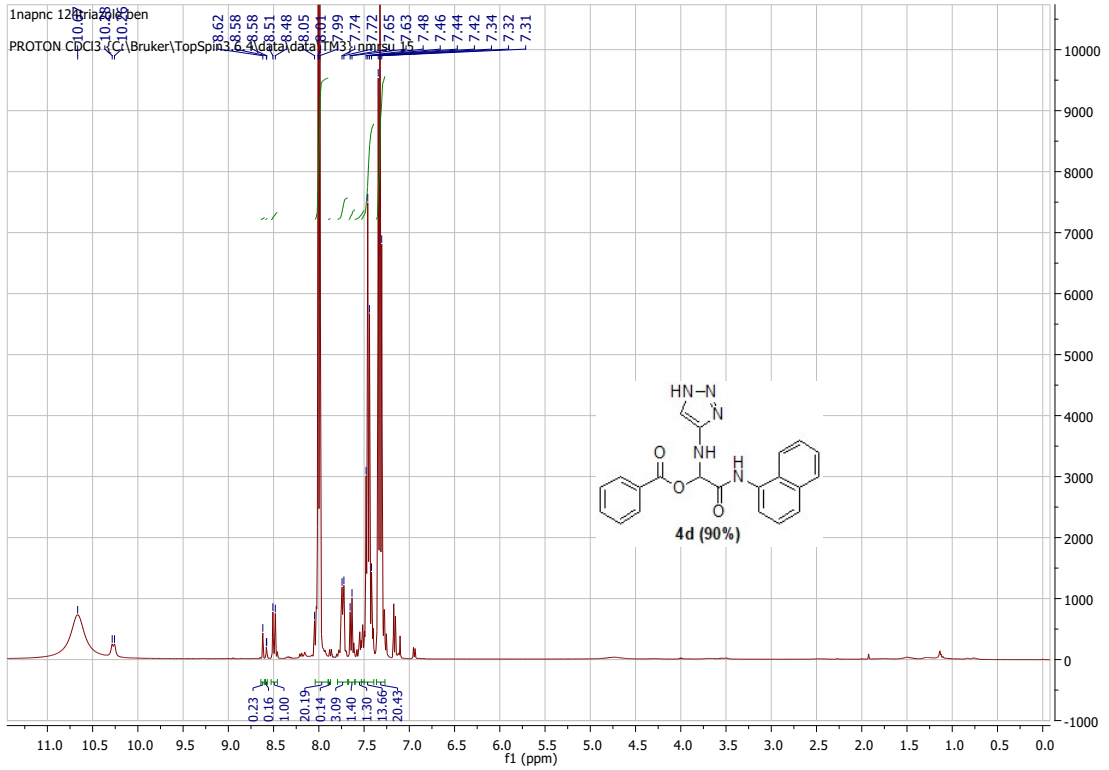

Figure S1.7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

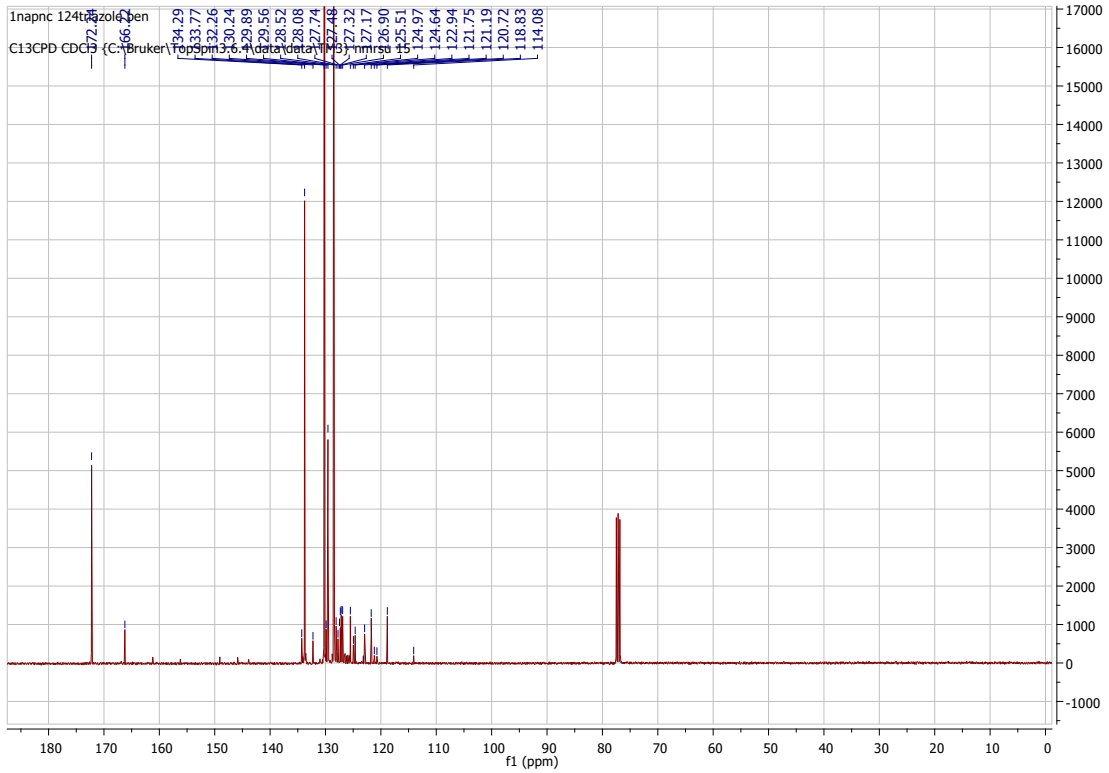

Figure S1.8. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4e. **[(1,5-dimethyl-3-oxo-2-phenylpyrazol-4-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate.**

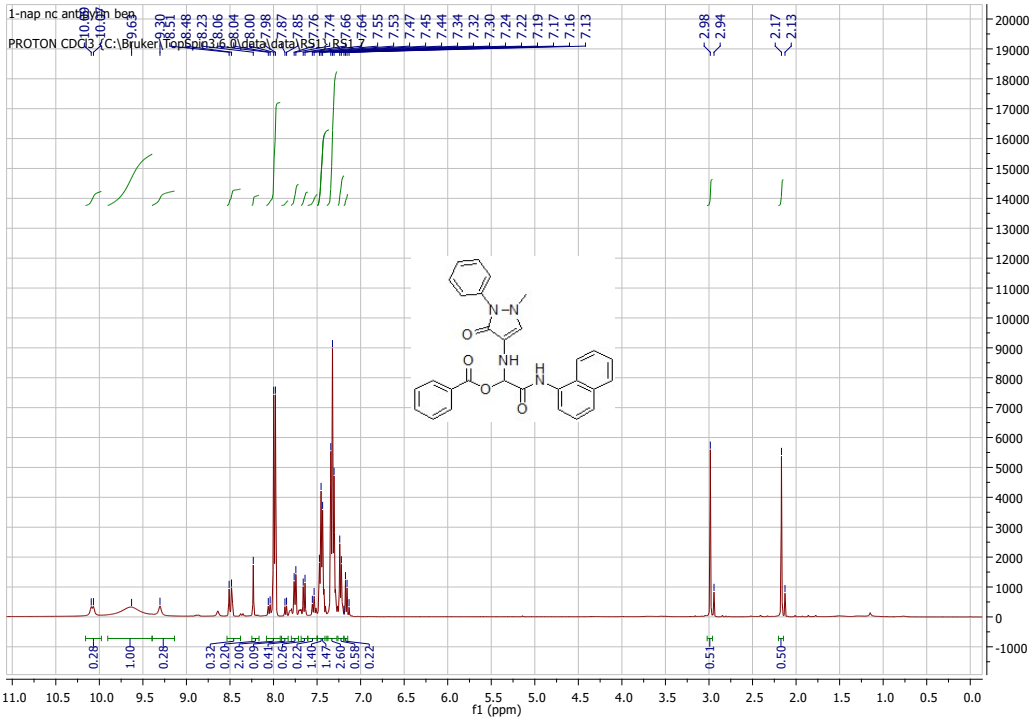

Figure S1.9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

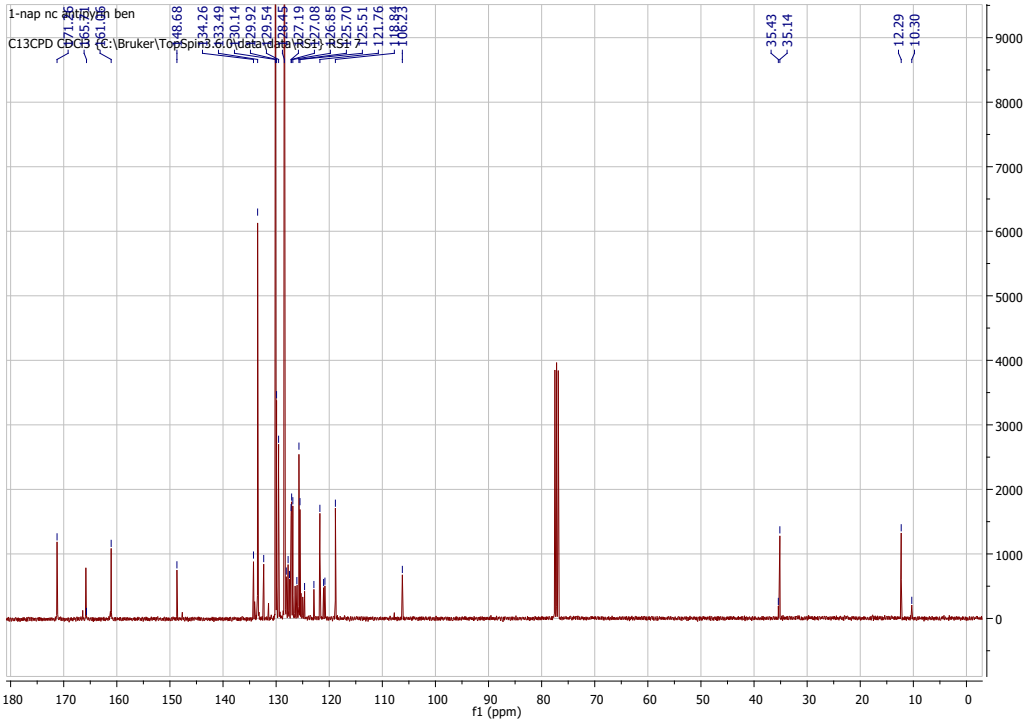

Figure S1.10. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4f. {3-methyl-1-[(naphthalen-1-yl)carbamoyl]butyl}amino benzoate

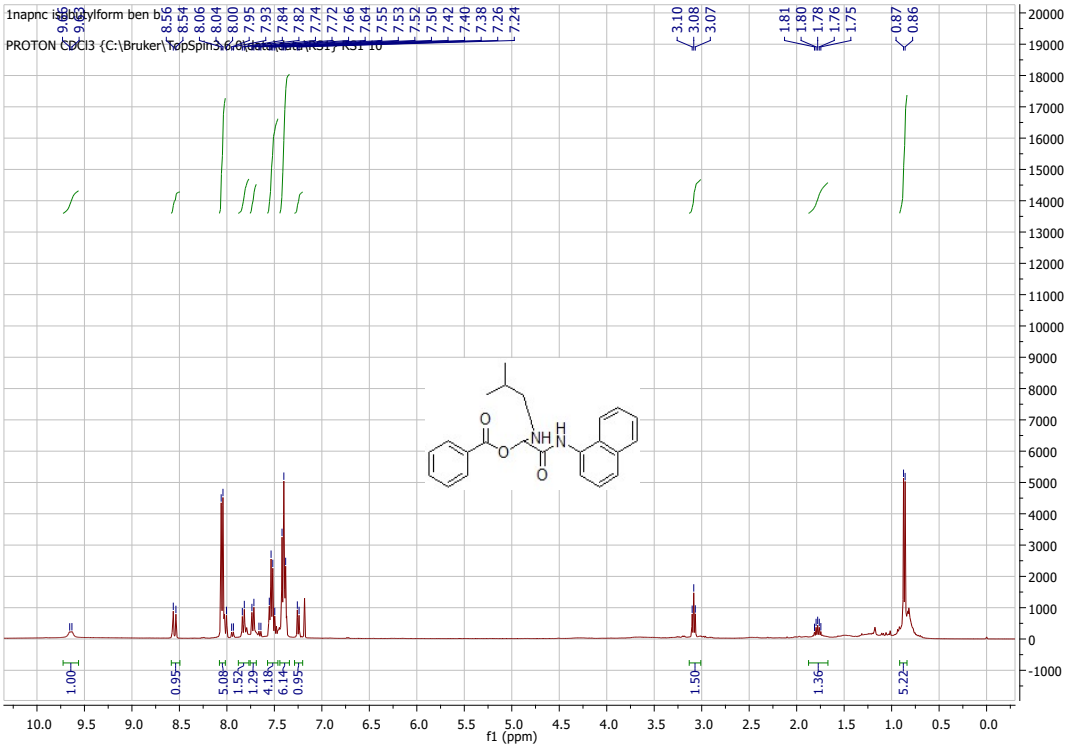

Figure S1.11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

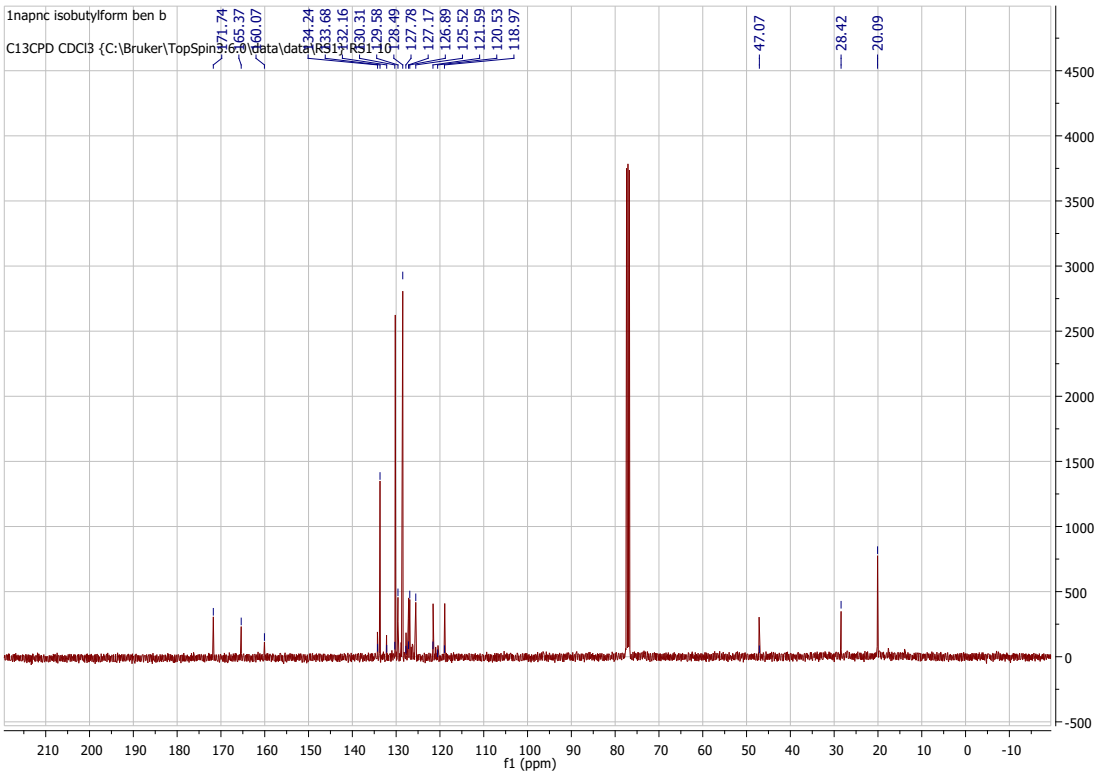

Figure S1.12. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4g. {1H-1,3-benzodiazol-2-yl[(naphthalen-1-yl)carbamoyl]methyl}amino benzoate

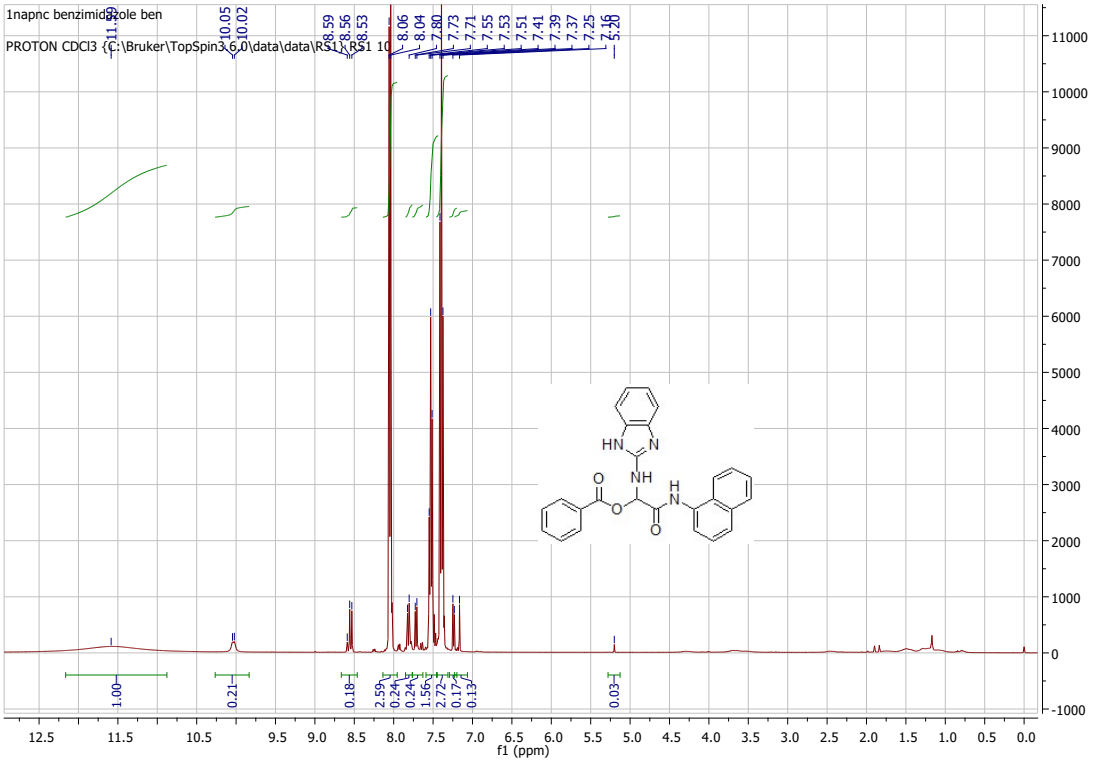

Figure S1.13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

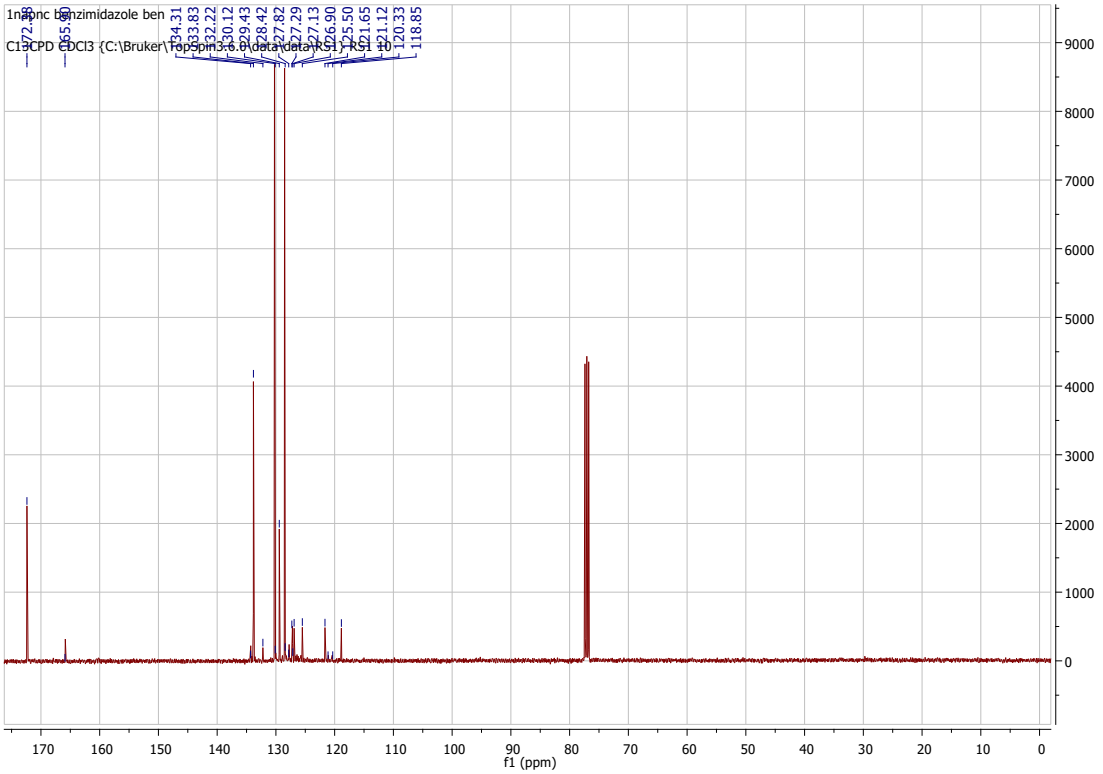

Figure S1.14. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4h. {1,3-benzothiazol-2-yl[(naphthalen-1-yl)carbamoyl]methyl}amino benzoate

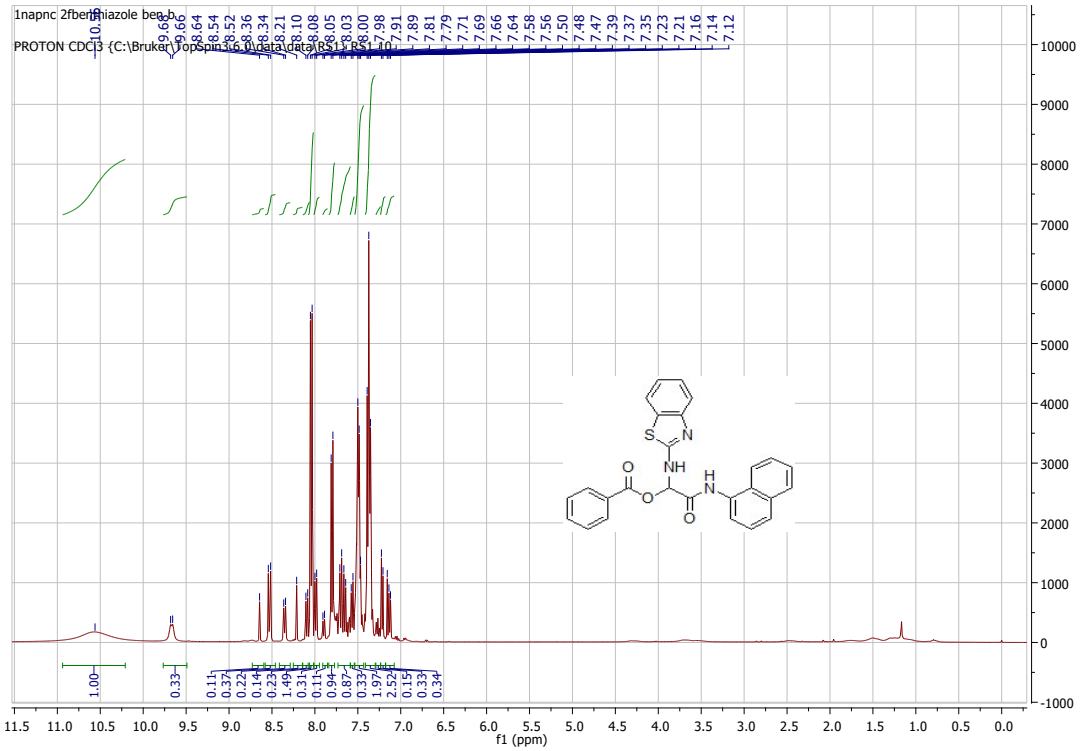

Figure S1.15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

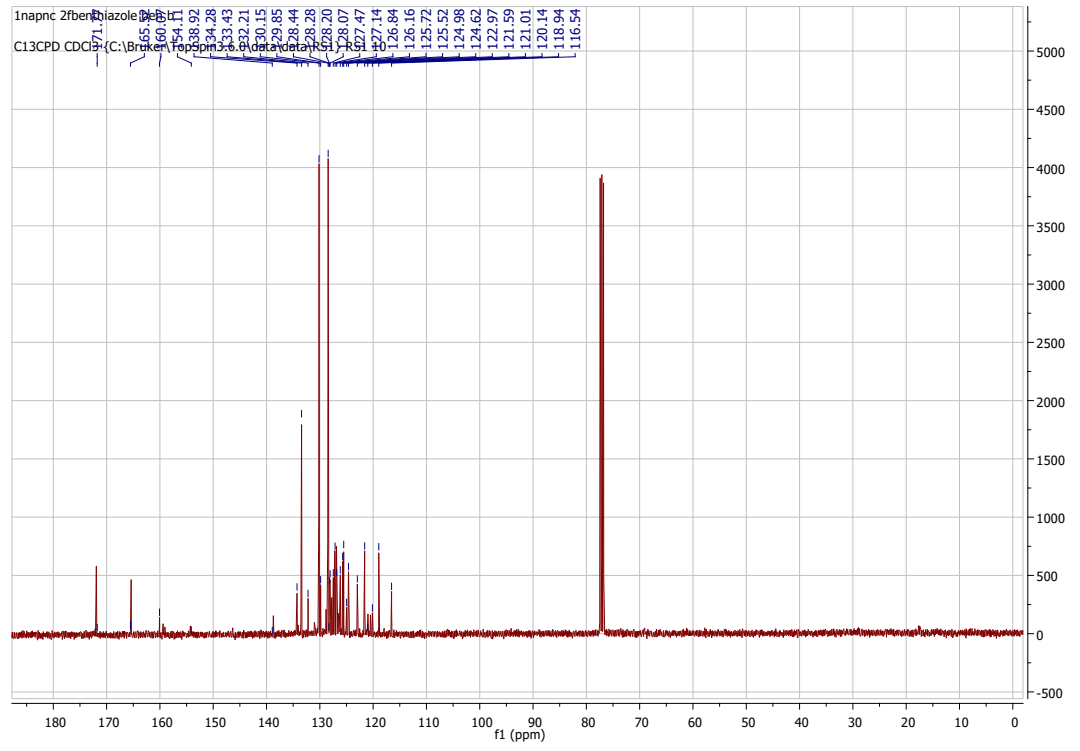

Figure S1.16. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4i. [(5-methyl-1,2-oxazol-3-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate

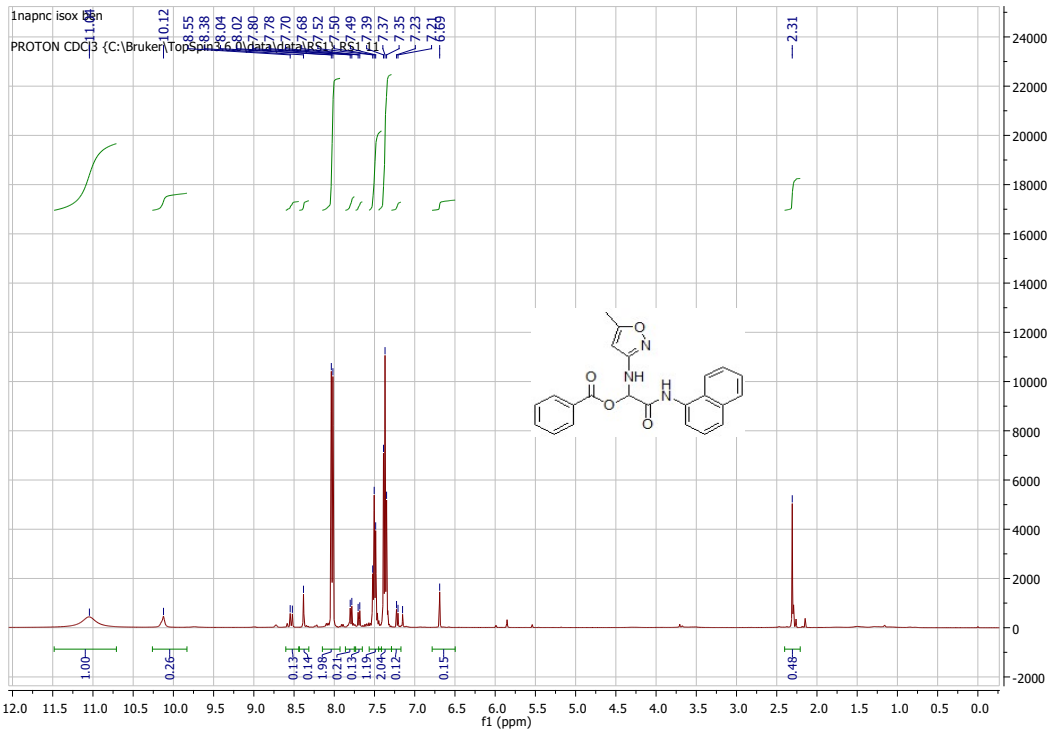

Figure S1.17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

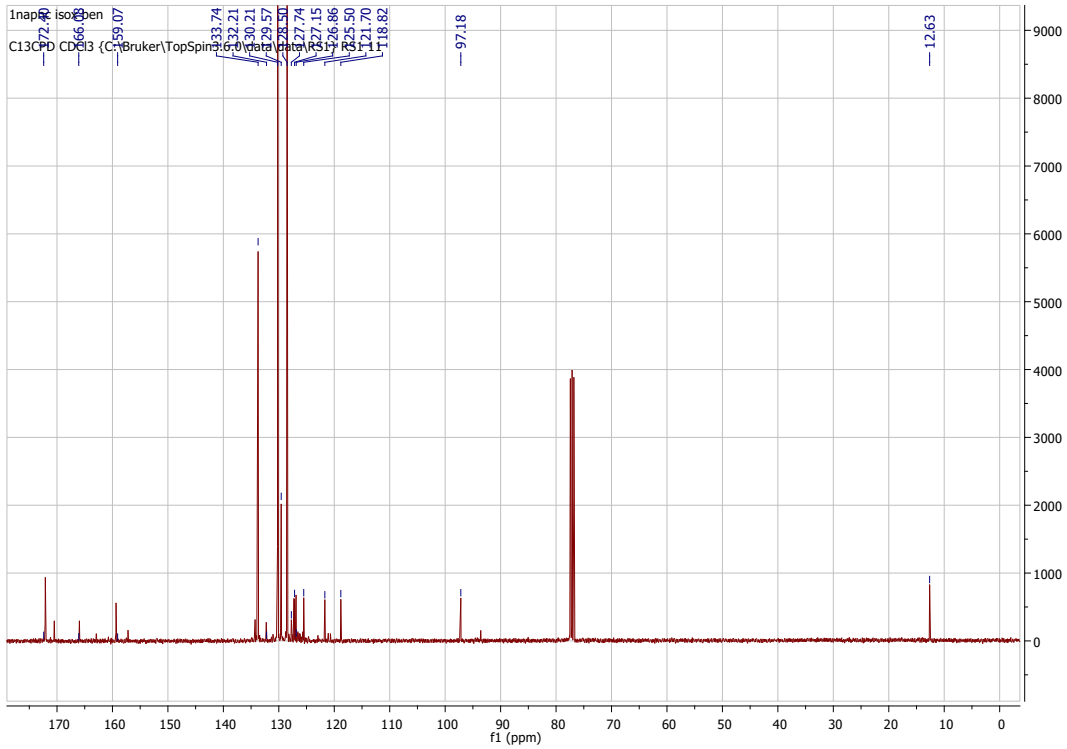

Figure S1.18. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4j. [3-(3,4-dihydroxyphenyl)-3-hydroxy-1-[(naphthalen-1-yl)carbamoyl]propyl](methyl)amino benzoate.

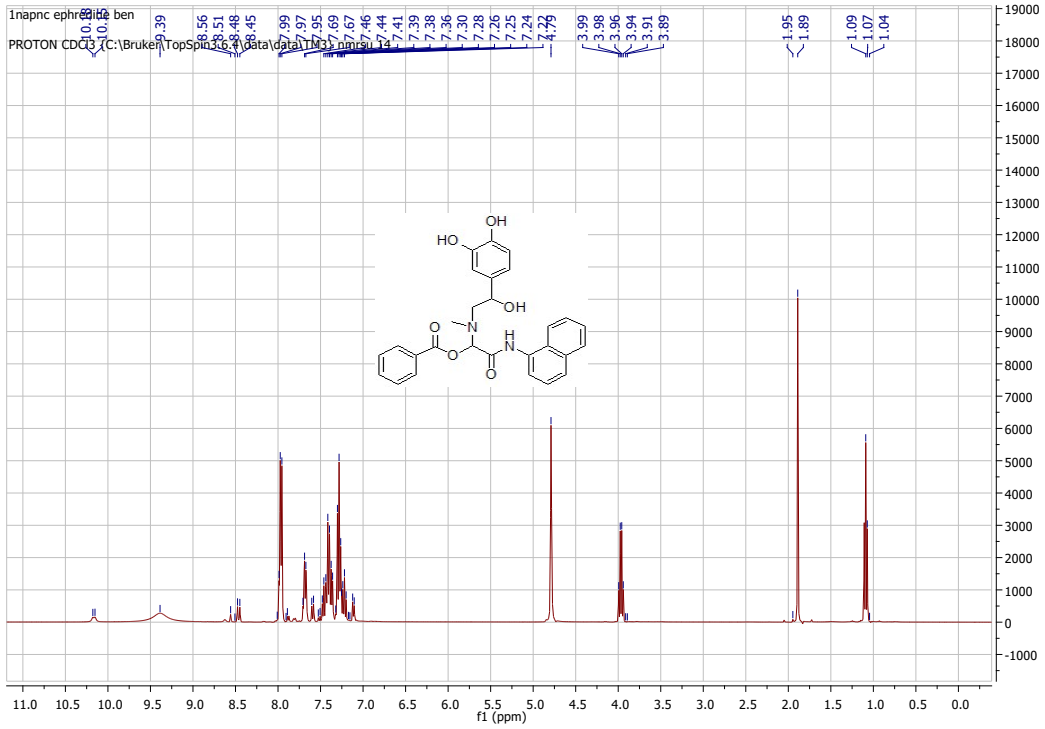

Figure S1.19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

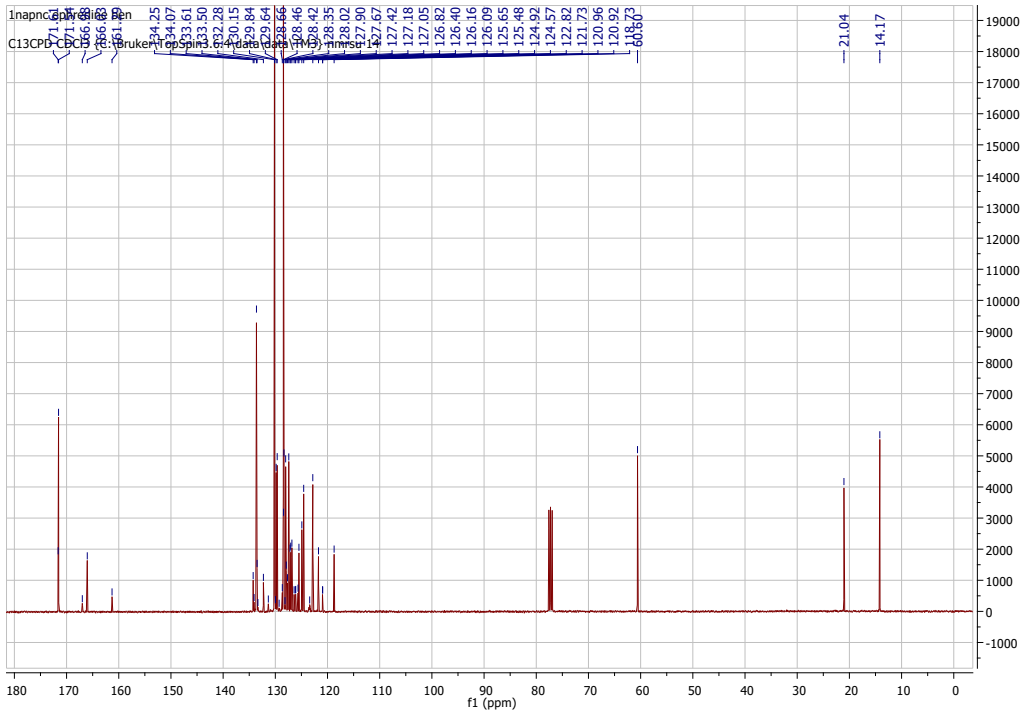

Figure S1.20. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4k. [(2-hydroxyphenyl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate

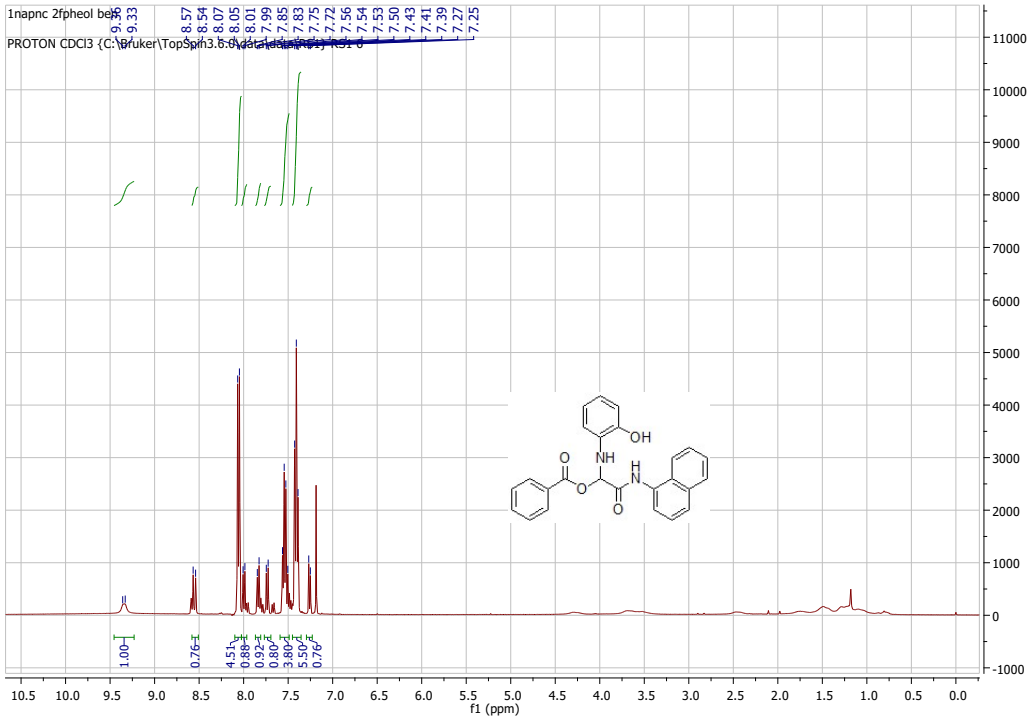

Figure S1.21. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

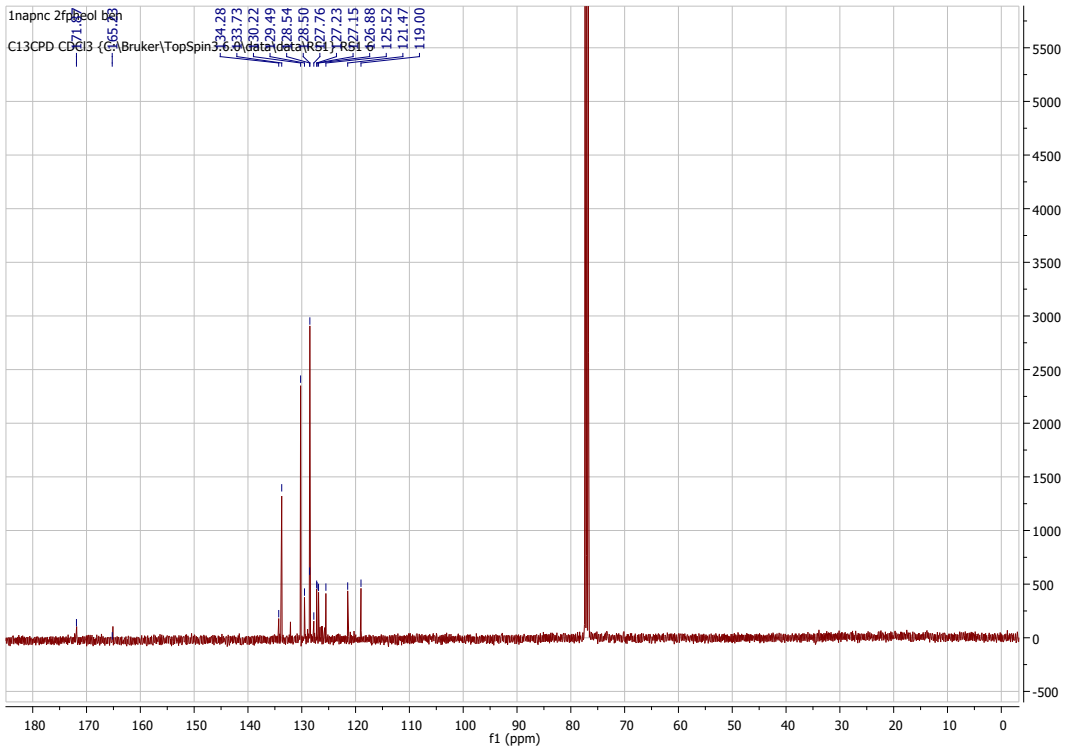

Figure S1.22. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4l. [(4-hydroxyphenyl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate

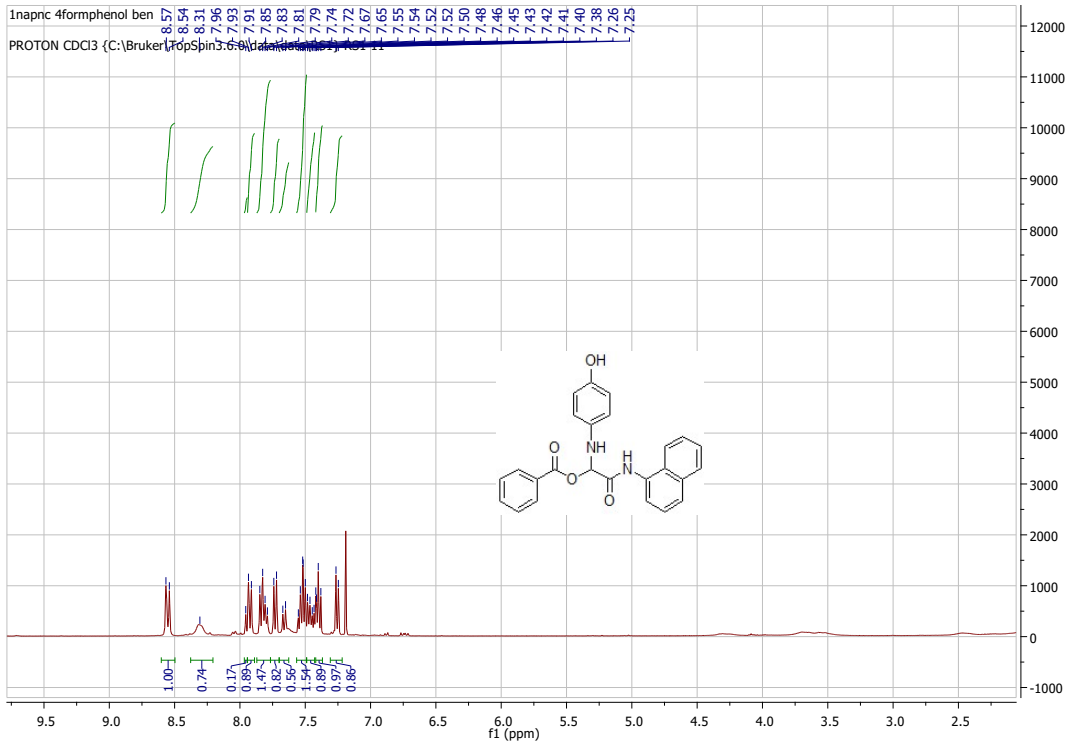

Figure S1.23. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

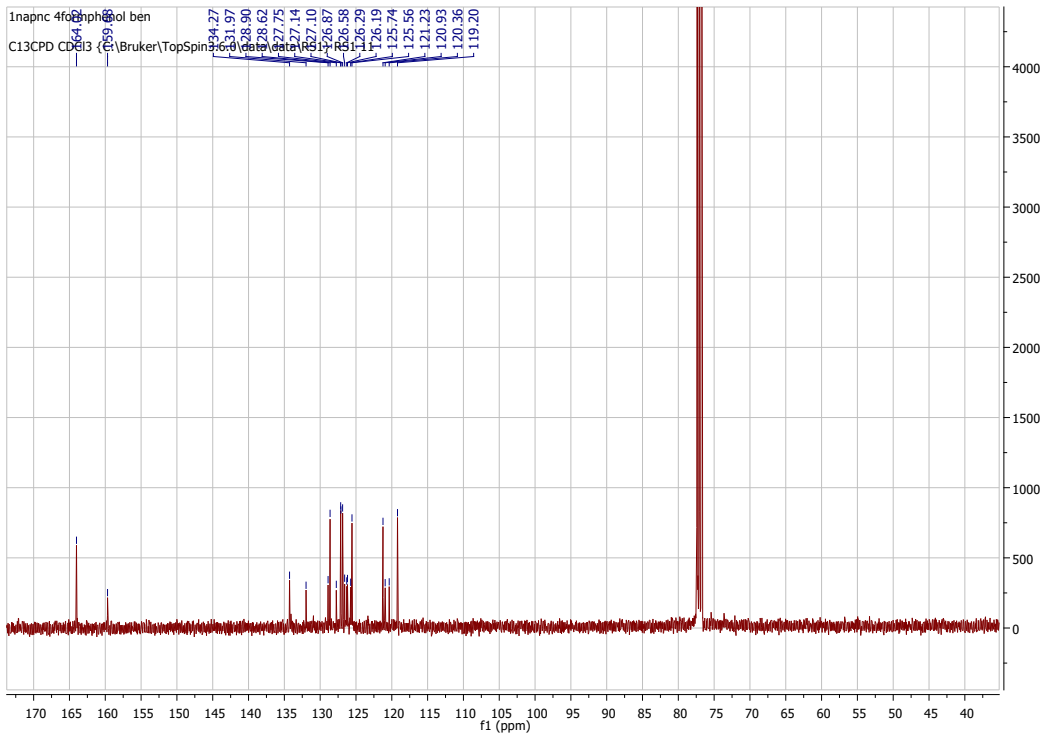

Figure S1.24. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4m. ethyl 2-{[(benzoyloxy)amino][(naphthalen-1-yl)carbamoyl]methyl}benzoate

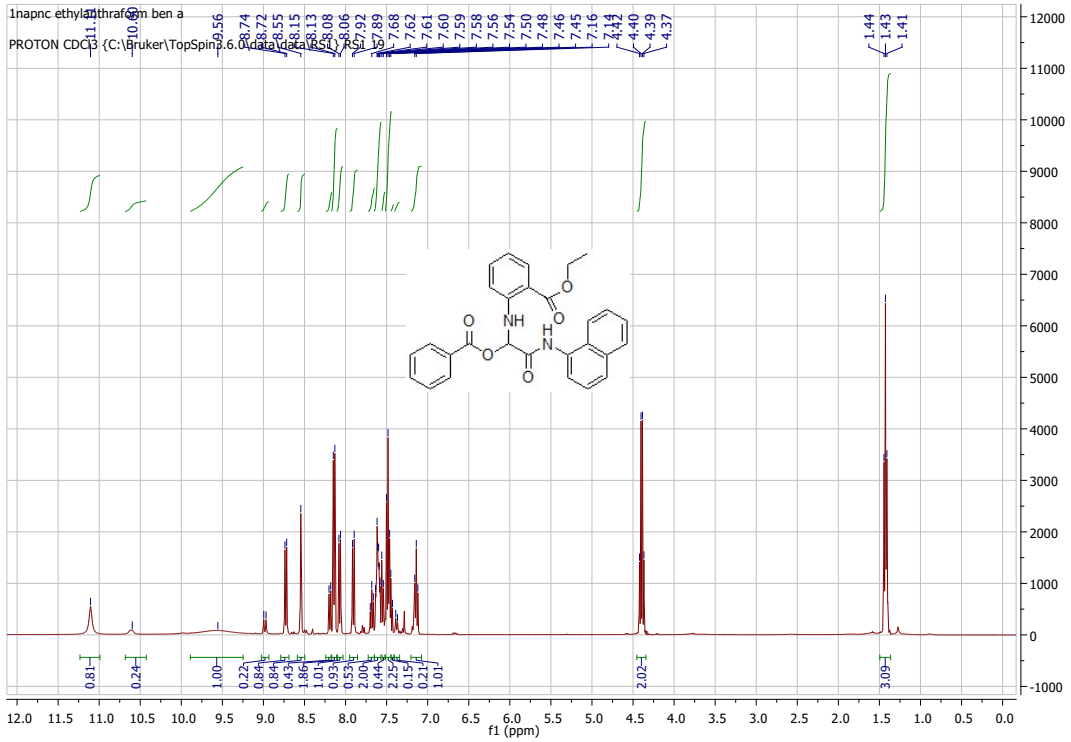

Figure S1.25. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

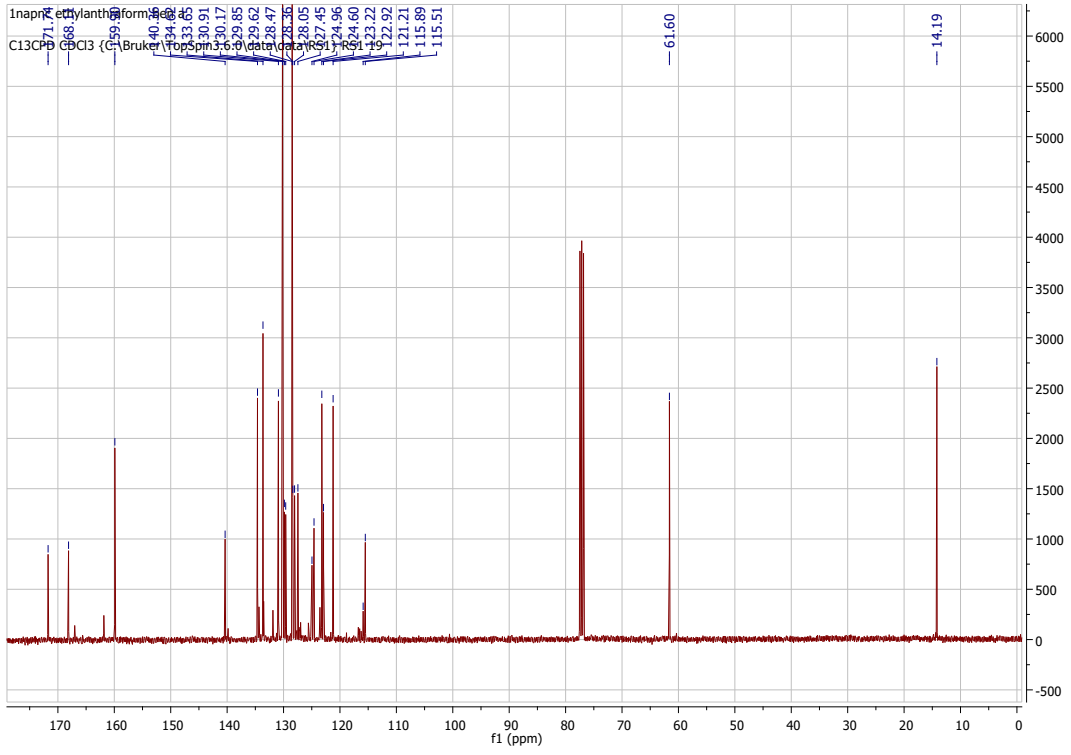

Figure S1.26. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4n. {3-methoxy-1-[(naphthalen-1-yl)carbamoyl]propyl}amino benzoate

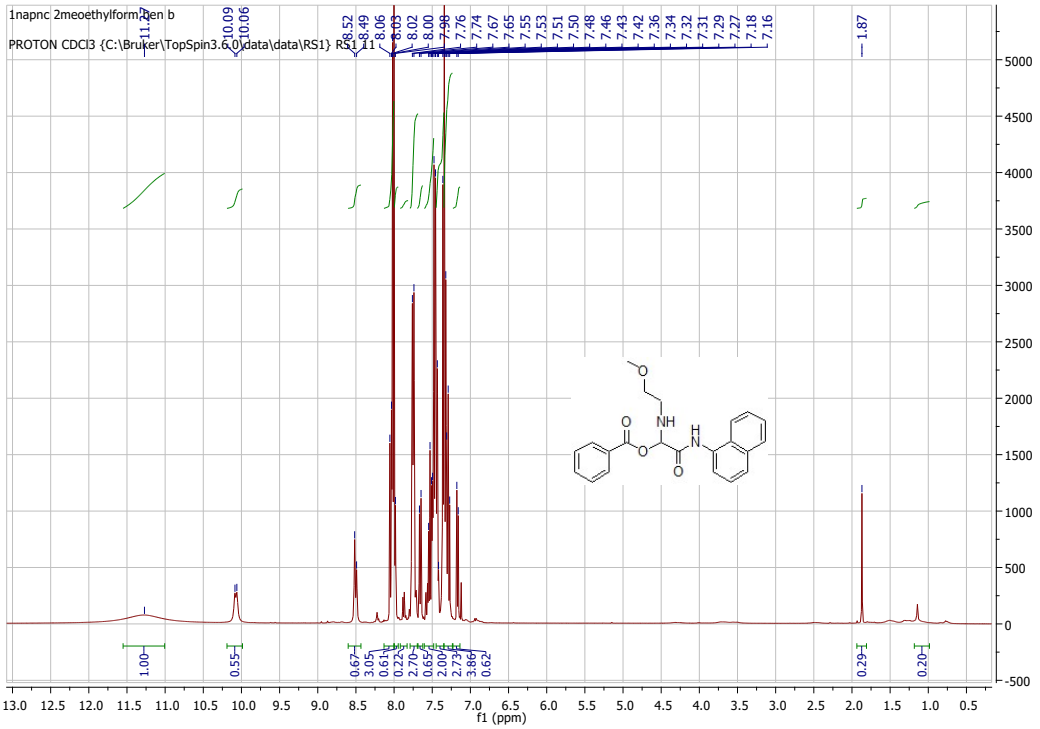

Figure S1.27. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

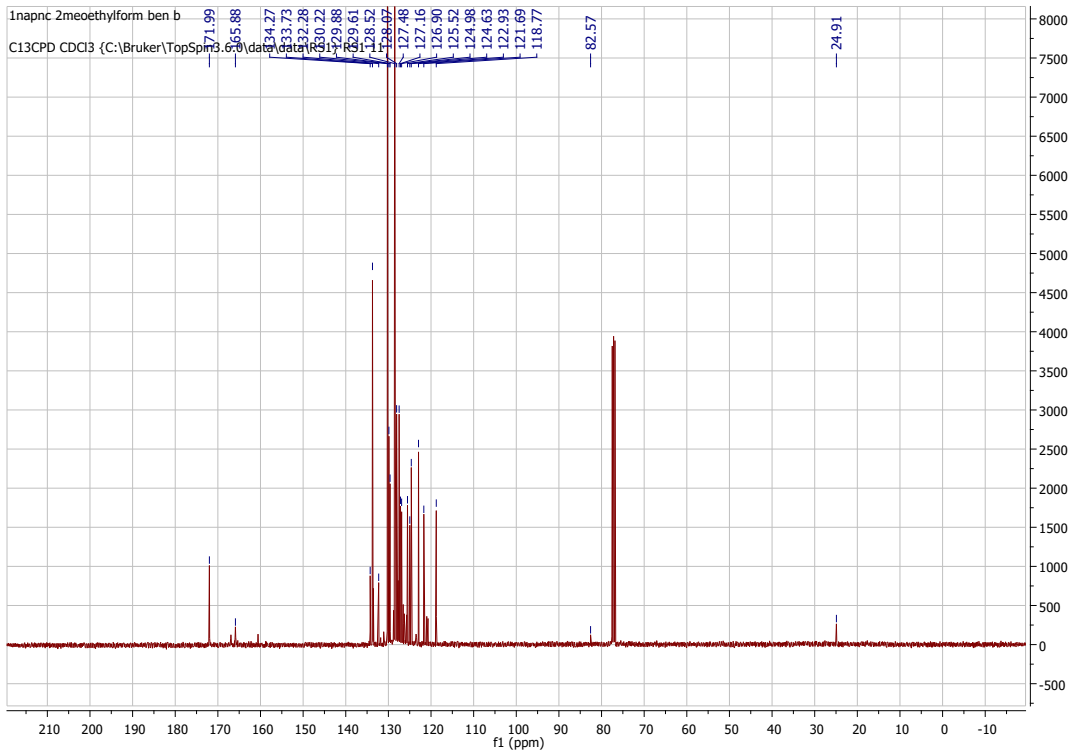

Figure S1.28. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4o. [(9,10-dioxo-9,10-dihydroanthracen-2-yl)[(naphthalen-1-yl)carbamoyl]methyl]amino benzoate.

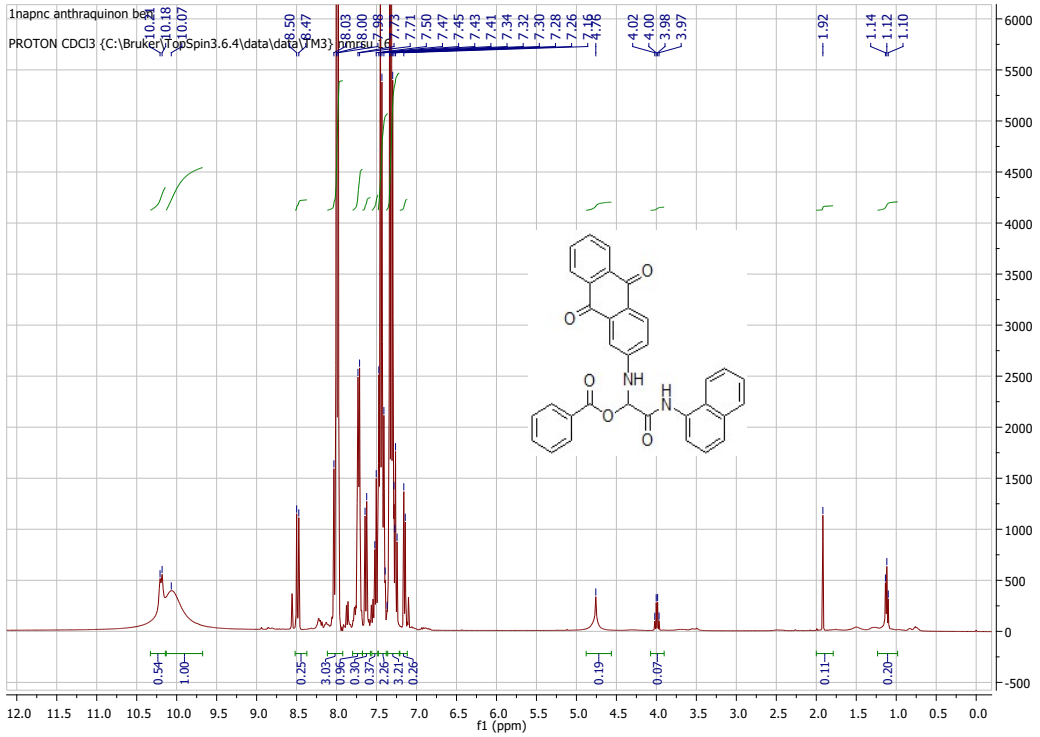

Figure S1.29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

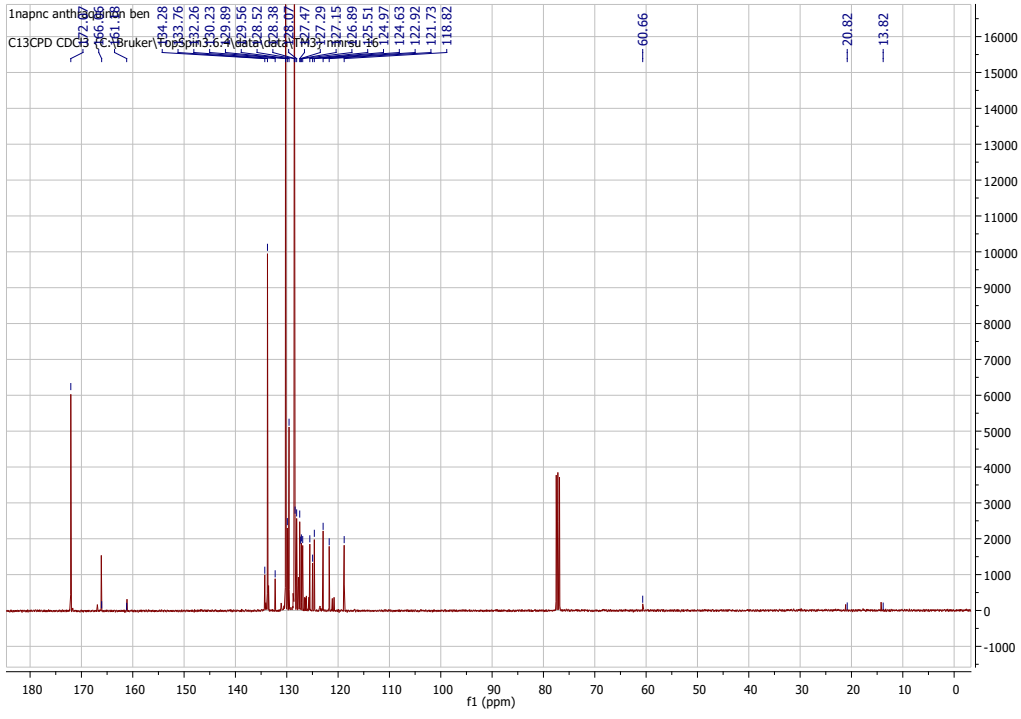

Figure S1.30. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4p. [2-(furan-2-yl)-1-[(naphthalen-1-yl)carbamoyl]ethyl]amino benzoate.

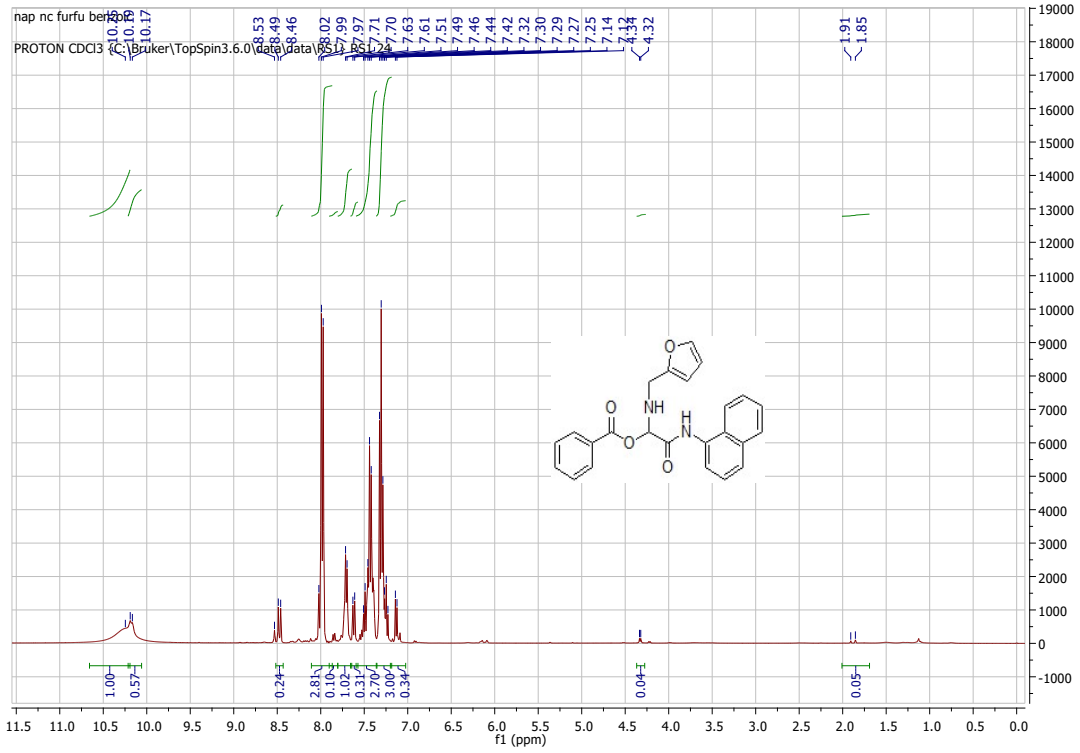

Figure S1.31. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

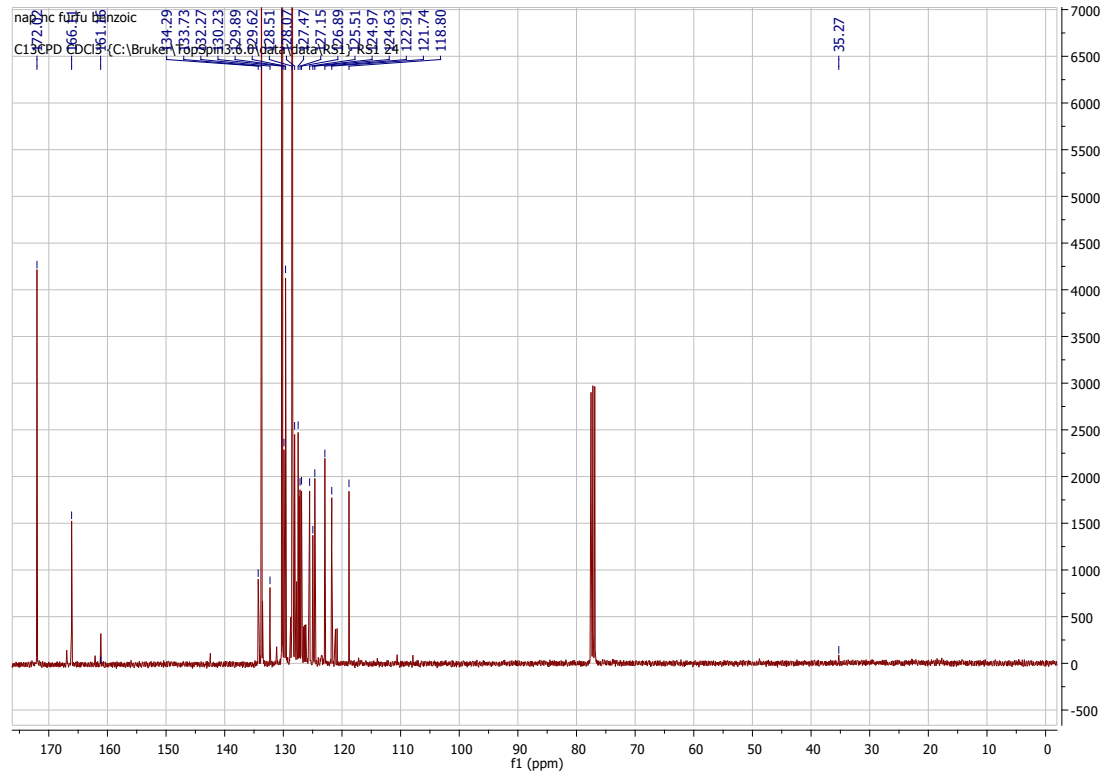

Figure S1.32. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4q. ethyl 2-{2-[(benzoyloxy)amino]-2-(pyridin-4-yl)acetamido}benzoate

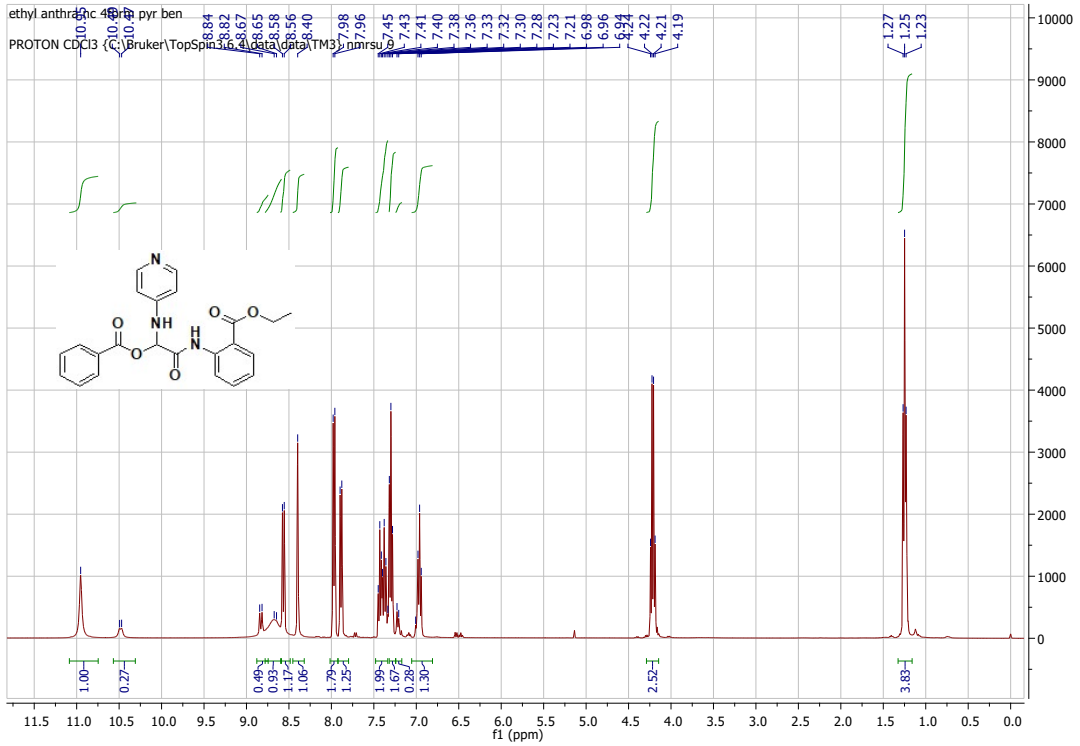

Figure S1.33. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

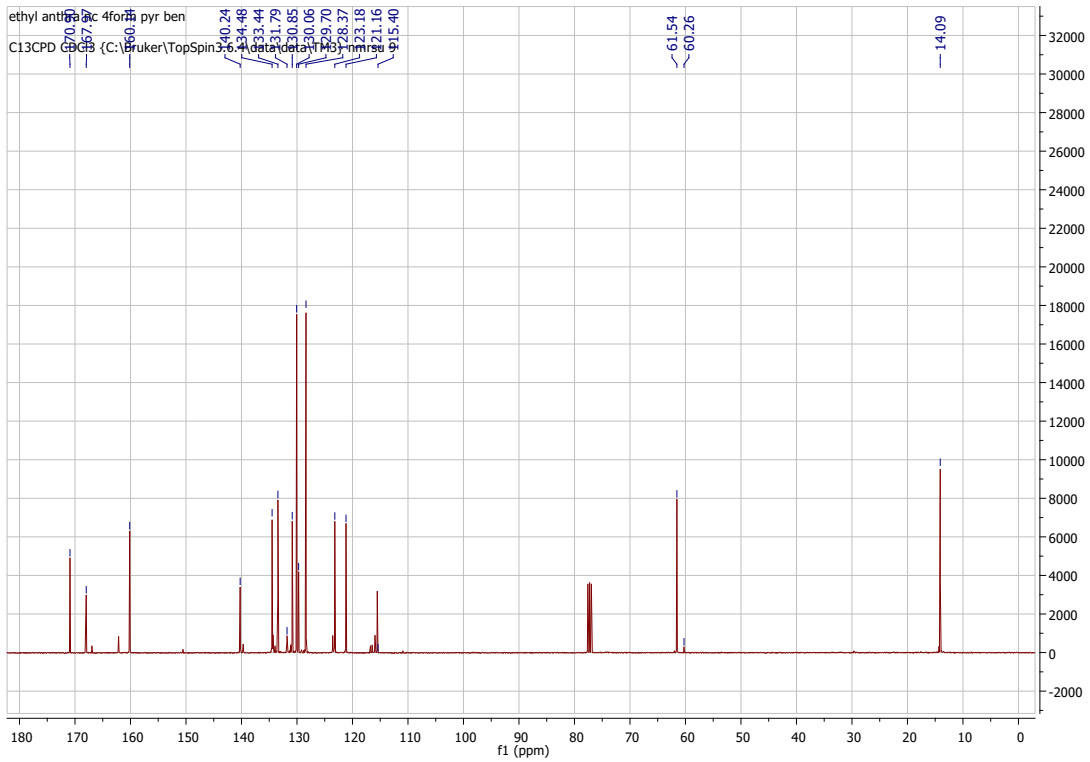

Figure S1.34. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4r. {[(3-bromophenyl)carbamoyl](pyridin-4-yl)methyl}amino benzoate.

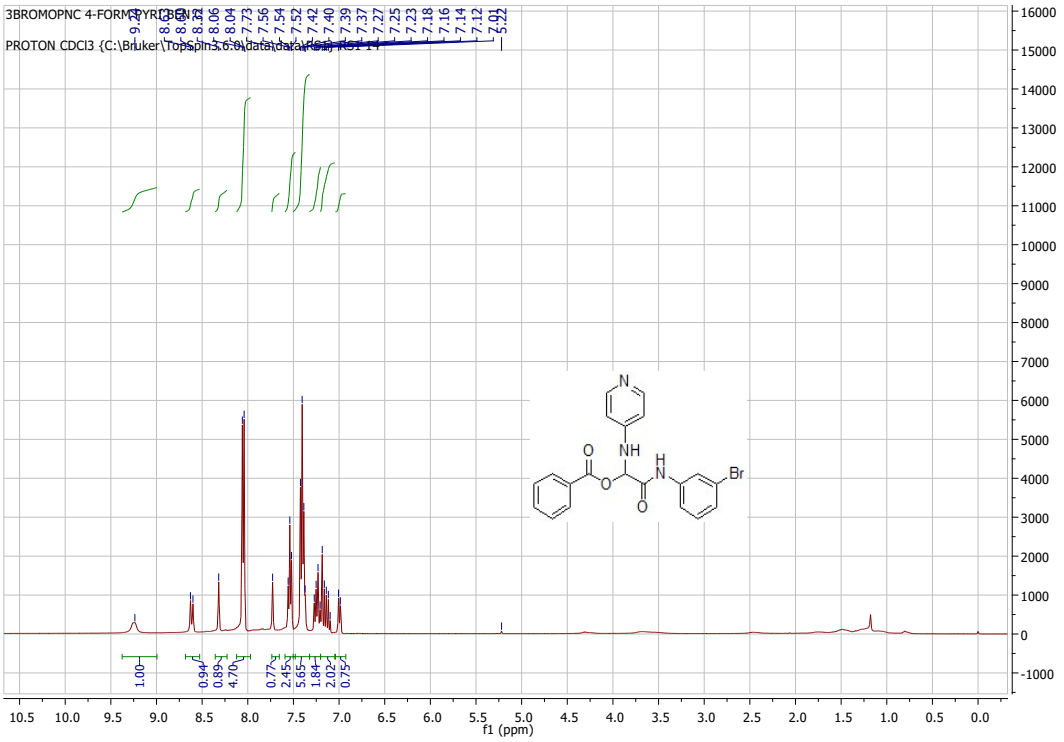

Figure S1.35. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

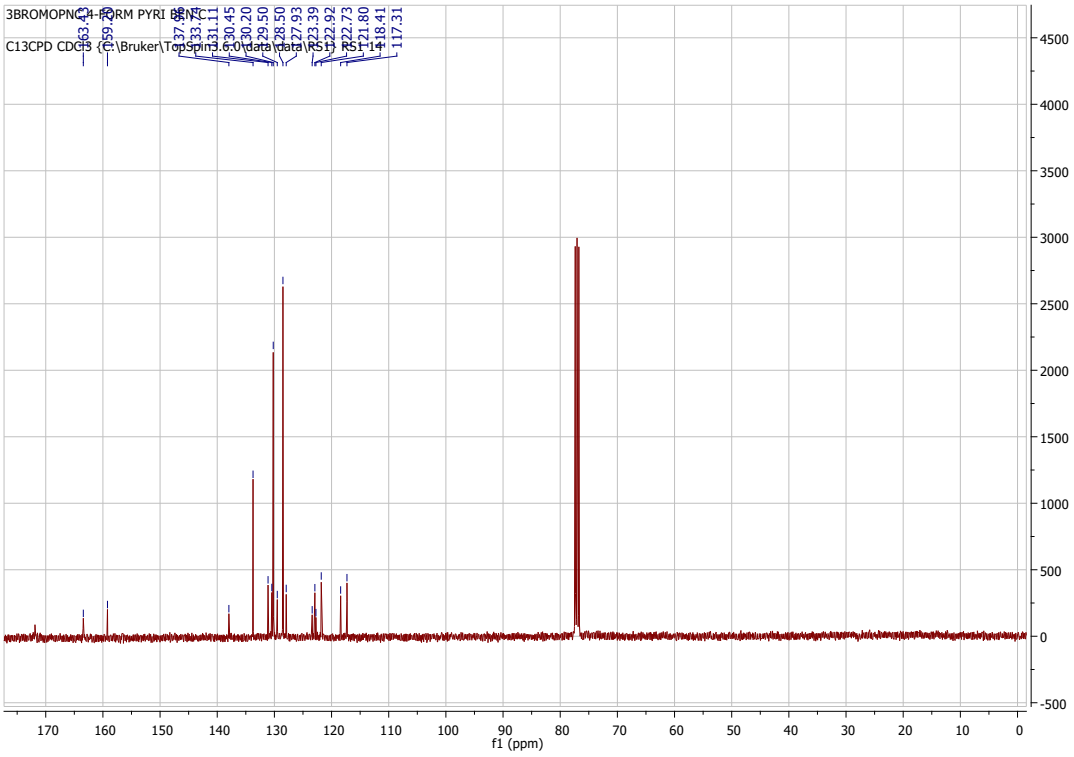

Figure S1.36. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum

4s. [(naphthalen-1-yl)carbamoyl](1,3-thiazol-2-ylamino)methyl benzoate.

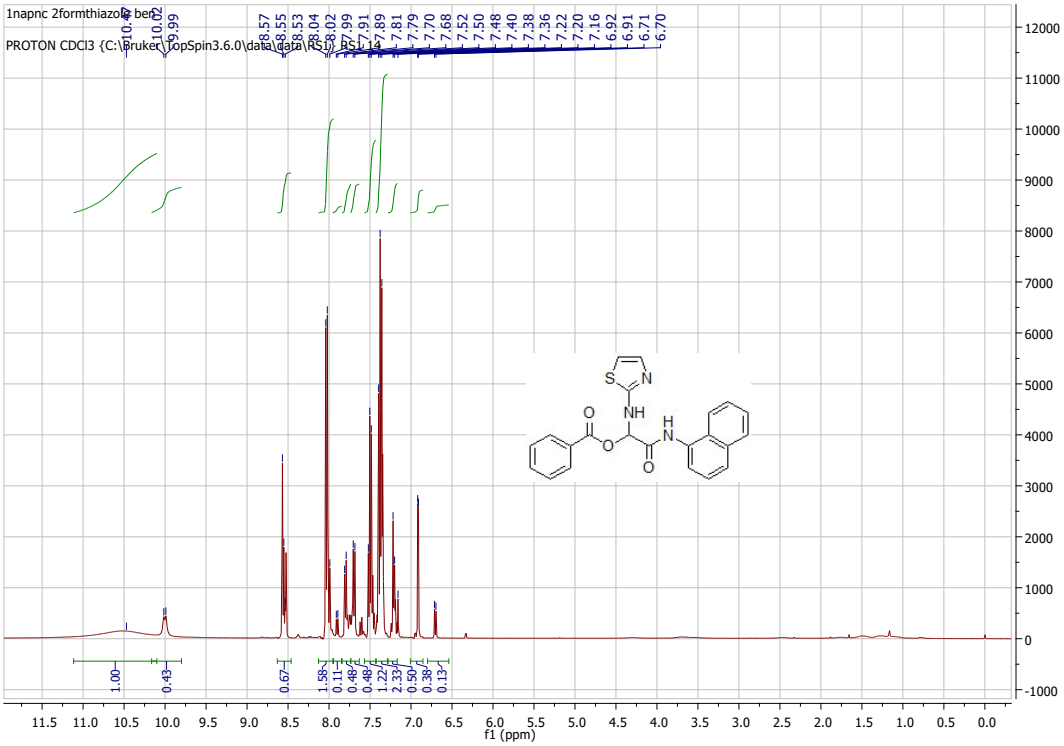

Figure S1.37. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum

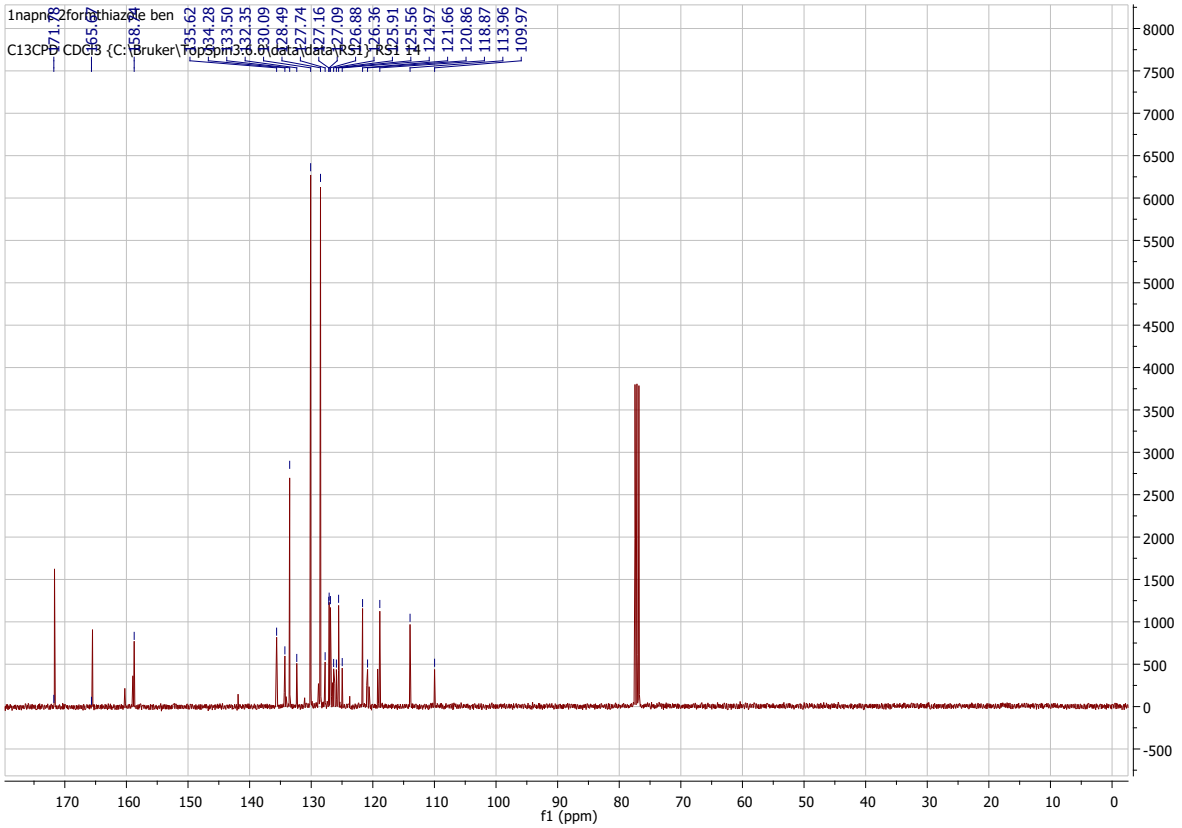

Figure S1.38. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum.