Supporting Information

Scalable and Sustainable Reductive Amidation of Nitroarenes, Nitroalkenes, and Nitroalkyls with Acyl Saccharins in Aqueous Media

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Supporting Information:

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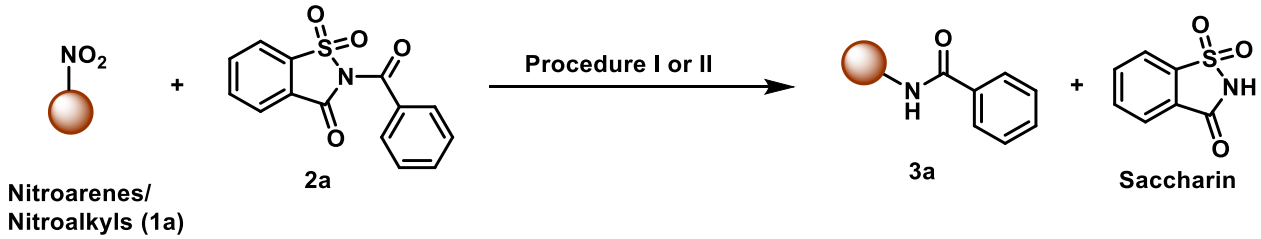
General Method:

All reactions, unless specified otherwise, were conducted in non-dry glassware within an air atmosphere. A magnetic stirrer was employed to ensure thorough and efficient mixing of the reaction mixture throughout the experiment. For the hydrogenation reaction, an autoclave was used under positive pressure of hydrogen with an agitator. When anhydrous conditions were needed, the reactions were conducted under a nitrogen or argon atmosphere using oven-dried glassware. All required starting materials, regents and solvents were procured from commercial suppliers and were utilized in their received form without undergoing any additional purification or treatment. Monitoring of the reactions was carried out via LCMS, HPLC and TLC (thin-layer chromatography) on 0.25 mm pre-coated silica gel plates (60 F254). The visualization of TLC spots was performed under a UV lamp or with the aid of staining solutions, including $KMnO_4$ solution, phosphomolybdic acid, para-anisaldehyde, or iodine which is adsorbed on silica gel, followed by a heating process using a heat gun for approximately 15 seconds. For NMR spectroscopic analyses, deuterated solvents were utilized without any modification. The acquisition of all ^{1}H (proton) NMR and ^{13}C (carbon) NMR spectra was performed with either a 300 MHz or a 500 MHz spectrometer. The coupling constants in these spectra were determined and reported in hertz. The reported chemical shifts were measured in parts per million (ppm), referenced to $CDCl_3$, and DMSO-d_6, using the residual solvent peak as the standard reference. The following abbreviations were adopted to express the multiplicities: s is assigned to singlet, d to doublet, t to triplet, q to quartet, p to pentet, dd to doublet of doublet, dt to doublet of triplet, m to multiplet, and bs to broad singlet. High-resolution mass spectra (HRMS) utilizing electrospray ionization (ESI) were obtained using mass analyzer (ORBITRAP), specifically the Thermo Scientific Q Exactive model. Infrared (IR) spectra were collected through the use of a Fourier transform infrared (FTIR) spectrometer, with the sample prepared as a thin film. The chemical names for the compounds were created using Chem Bio Draw Ultra version 14.0 software.

Experimental Section:

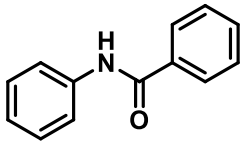
General Representative Experimental Procedures for Reductive Amidation of Nitroarenes and Nitroalkyls:



General procedure I for the amidation of nitro compounds and acyl saccharin using Fe-NH_4Cl: To a stirred solution of nitroarenes or nitroalkyls or nitroalkenes (1.0 mmol) and acyl saccharin (1.0 mmol) in propane-2-ol (iPrOH) and water (1:1, 10V) was added ammonium chloride (5.0 mmol), Fe powder (3.0 mmol) at room temperature and reaction mixture heated at 60 °C for 4 to 8 h in oil bath. Monitored the reaction with TLC and LCMS. The reaction mixture was cooled to rt and subjected to filtration by celite and the residue washed with iPrOH (4V). The filtrate was evaporated and resulting the residue was diluted with ethyl acetate and water. The organic layer was extracted and then washed with a sodium bicarbonate saturated solution ($NaHCO_3$), followed by 1M hydrochloric acid (HCl) and brine. It was then dried over Na_2SO_4, filtered, and concentrated under vacuum to produce the corresponding amides.

General procedure II for the amidation of nitro compounds and acyl saccharin using H_2-Pd/C: A solution of nitroarenes or nitroalkyls (1.0 mmol) and acyl saccharin (1.0 mmol) in propane-2-ol (iPrOH) and water (1:1) was added Pd/C (10 wt.% loading, 5 mole%) and reaction mixture heated in autoclave under H_2 atmosphere (~5 bar) at 40 °C for 4 h. The reaction mixture was filtered using celite and subsequently washed with isopropanol (2 volumes). The filtrate was then concentrated, and the resulting residue was diluted with a mixture of ethyl acetate and water. The organic layer was extracted and then washed with a sodium bicarbonate saturated solution ($NaHCO_3$), followed by 1M hydrochloric acid (HCl) and brine. It was then dried over Na_2SO_4, filtered, and concentrated under vacuum to produce the corresponding amides.

Synthesis of N- phenylbenzamide (3a):



Compound **3a** as off white solid (0.173 g, 88%) was prepared from nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.177 g, 90%) by general procedure **II.**

IR (film): 3343, 1654, 1598, 1524, 688 cm^{-1}.

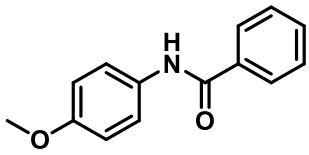
^{1}H NMR (500 MHz , $CDCl_3$) δ 7.90 (s, 1H), 7.87 (d, *J* = 6.9 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 9.5 Hz, 1H), 7.50 – 7.46 (m, 2H), 7.39 – 7.35 (m, 2H), 7.17 – 7.14 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 137.9, 135.0, 133.7, 131.9, 130.2, 129.1 (2C), 128.8, 128.4, 127.0, 124.6, 120.2.

HRMS (ESI): *m/z* calculated for $C_{13}H_{12}NO$ $[M + H]^+$ 198.0918, found 198.0920.

The spectroscopic data is identical with previously reported in the literature[1].

Synthesis of N- (- 4 - methoxyphenyl) benzamide (3b):



Compound **3b** as a white solid (0.193 g, 85%) was prepared from 4-nitro anisole (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.188 g, 83%) by general procedure **II.**

IR (film): 3334, 2838, 1646, 1512, 823, 649 cm^{-1}.

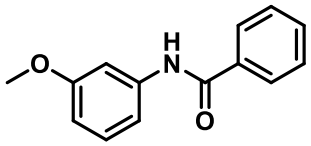
^{1}H NMR (300 MHz , DMSO d_6) δ 10.13 (s, 1H), 7.94 (d, *J* = 9.7 Hz, 2H), 7.71 – 7.65 (m, 2H), 7.60 – 7.49 (m, 3H), 6.96 – 6.91 (m, 2H), 3.75 (s, 3H).

^{13}C NMR (75 MHz, DMSO d_6) δ 165.1, 155.5, 135.1, 132.2, 131.4, 128.4 (2C), 127.5 (2C), 122.0 (2C), 113.7 (2C), 55.2.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1024, found 228.1022.

The spectroscopic data is identical with previously reported in the literature[2].

Synthesis of N- (- 3 - methoxyphenyl) benzamide (3c):



Compound **3c** as white solid (0.188 g, 83%) was prepared from nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.195 g, 86%) by general procedure **II.**

IR (film): 3330, 2963, 1646, 1512, 823, 649 cm^{-1}.

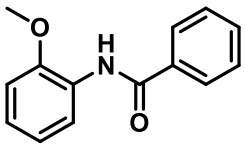
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.86 (d, *J* = 6.9 Hz, 3H), 7.58 – 7.44 (m, 4H), 7.29 (s, 1H), 7.10 (d, *J* = 10.1 Hz, 1H), 6.71 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.83 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 160.2, 139.2, 134.9, 131.9, 129.8, 128.8 (2C), 127.0 (2C), 112.3, 110.6, 105.8, 55.3.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1024, found 228.1022.

The spectroscopic data is identical with previously reported in the literature[3].

Synthesis of N- (- 2 - methoxyphenyl) benzamide (3d):



Compound **3d** as white solid (0.183 g, 81%) was prepared from 2-nitroanisole (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.227 g, 85%) by general procedure **II**.

IR (film): 3330, 2963, 1646, 1512, 823, 649 cm^{-1}.

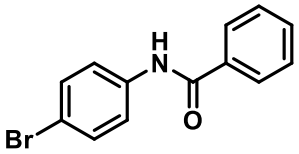
^{1}H NMR (300 MHz , DMSO *d*$_6$) δ 9.42 (s, 1H), 7.97 (d, *J* = 6.8 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.62 – 7.50 (m, 3H), 7.19 (t, *J* = 6.9 Hz, 1H), 7.09 (d, *J* = 6.9 Hz, 1H), 6.98 (d, *J* = 13.7 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (75 MHz, DMSO *d*$_6$) δ 165.4, 152.0, 135.0, 132.1, 129.0, 127.9 (2C), 127.3 (2C), 126.2, 124.8, 120.7, 111.8, 56.2.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1024, found 228.1022.

The spectroscopic data is identical with previously reported in the literature[4].

Synthesis of N- (- 4- bromophenyl) benzamide (3e):



Compound **3e** as light-yellow solid (0.220 g, 80%) was prepared from 4-bromonitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3335, 1646, 1515, 1489, 1392, 1311, 819, 716 cm^{-1}.

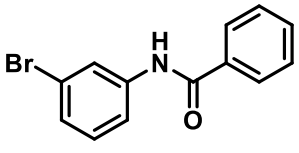
^{1}H NMR (500 MHz , CDCl$_3$) δ 7.87 (s, 1H), 7.81 (s, 1H), 7.56 – 7.54 (m, 3H), 7.51 (s, 1H), 7.49 (dd, *J* = 8.9, 2.1 Hz, 4H).

^{13}C NMR (125 MHz, CDCl$_3$) δ 165.7, 137.0, 134.6, 133.7, 132.1 (2C), 130.2, 128.9 (2C), 128.5, 127.0, 121.7, 117.2.

HRMS (ESI): *m/z* calculated for $C_{13}H_{11}BrNO$ $[M + H]^+$ 276.0023, found 276.0020.

The spectroscopic data closely match the ones previously reported in the literature[5].

Synthesis of N- (- 3- bromophenyl) benzamide (3f):



Compound **3f** as pale-yellow solid (0.214 g, 78%) was prepared from 4-bromonitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3296, 1736, 1374, 1229, 1032 cm^{-1}.

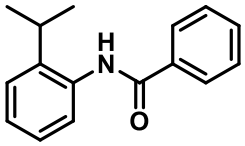
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.93 (s, 1H), 7.90 (s, 1H), 7.85 (s, 2H), 7.57 – 7.52 (m, 2H), 7.46 (s, 2H), 7.28 (t, *J* = 1.5 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 139.3, 134.6, 132.2, 130.5, 129.0 (2C), 127.7, 127.2 (2C), 123.3, 122.8, 118.8.

HRMS (ESI): *m/z* calculated for $C_{13}H_{11}BrNO$ $[M + H]^+$ 276.0023, found 276.0020.

The spectroscopic data closely match the ones previously reported in the literature[6].

Synthesis of N- (- 2- Isopropyl phenyl) benzamide (3g):



Compound **3g** as white solid (0.186 g, 78%) was prepared from 2-isopropyl phenyl nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.200 g, 84%) by general procedure **II**.

IR (film): 3215, 2656, 1635, 1530, 1311, 756, 695 cm^{-1}.

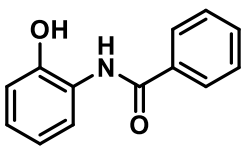
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.89 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.34 (dd, *J* = 7.2, 2.2 Hz, 1H), 7.23 (dd, *J* = 7.1, 1.9 Hz, 2H), 3.14 (sept, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 140.7, 135.0, 134.2, 131.8, 128.9 (2C), 127.1, 126.5, 126.2 (2C), 125.7, 124.8, 28.2, 23.1 (2C).

HRMS (ESI): *m/z* calculated for $C_{16}H_{18}NO$ $[M + H]^+$ 240.1383 found 240.1384.

The spectroscopic data closely match the ones previously reported in the literature[7].

Synthesis of N- (- 2- hydroxy phenyl) benzamide (3h):



Compound **3h** as white solid (0.155 g, 73%) was prepared from 2-hydroxy nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.169 g, 80%) by general procedure **II**.

IR (film): 3413, 3034, 1642, 1539, 1451, 746, 619 cm^{-1}.

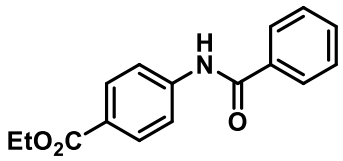
^{1}H NMR (500 MHz , $CDCl_3$) δ 8.62 (s, 1H), 8.16 (s, 1H), 7.91 (d, *J* = 7.0 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.55 – 7.48 (m, 2H), 7.24 (s, 1H), 7.17 (d, *J* = 5.6 Hz, 1H), 7.08 (s, 1H), 6.94 – 6.87 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 148.8, 133.2, 132.6, 129.0 (2C), 127.4, 127.3, 125.7, 122.4, 120.7, 119.8.

HRMS (ESI): *m/z* calculated for $C_{13}H_{12}NO_2$ $[M + H]^+$ 213.0789 found 213.0789.

The spectroscopic data closely match the ones previously reported in the literature[8].

Synthesis of ethyl 4-benzamidobenzoate (3i):



Compound **3i** as off white solid (0.209 g, 78%) was prepared from ethyl 4-nitrobenzoate (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.231 g, 86%) by general procedure **II**.

IR (film): 3329, 2990, 1704, 1660, 1599, 1279, 1104, 768 cm^{-1} .

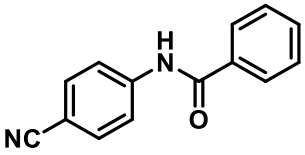
^{1}H NMR (500 MHz , $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 3H), 7.88 (d, *J* = 6.9 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 165.8, 142.1, 134.6, 132.2, 130.9 (2C), 128.9 (2C), 127.1 (2C), 126.2, 119.2 (2C), 60.9, 14.4.

HRMS (ESI): *m/z* calculated for $C_{16}H_{16}NO_3$ $[M + H]^+$ 270.1130 found 270.1136.

The spectroscopic data closely match the ones previously reported in the literature[9].

Synthesis of 4-nitrobenzonitrile (3j):



Compound **3j** as off white solid (0.155 g, 70%) was prepared from ethyl 4-nitrobenzonitrile (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3351, 2925, 2225, 1659, 1519 cm^{-1}.

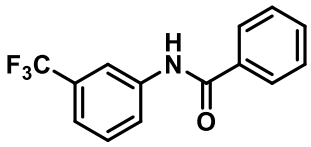
^{1}H NMR (300 MHz , DMSO *d_6*) δ 10.66 (s, 1H), 7.99 (dd, *J* = 12.1, 7.8 Hz, 4H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.66 – 7.54 (m, 3H).

^{13}C NMR (75 MHz, DMSO *d_6*) δ 166.7, 144.0, 134.9, 133.6 (2C), 132.5, 129.0 (2C), 128.3 (2C), 120.6 (2C), 119.5, 105.8.

HRMS (ESI): *m/z* calculated for $C_{14}H_{11}N_2O$ $[M + H]^+$ 223.0793 found 223.0793.

The spectroscopic data closely match the ones previously reported in the literature[10].

Synthesis N-[3-(trifluoromethyl) phenyl] benzamide (3k):



Compound **3k** as off white solid (0.200 g, 76%) was prepared from ethyl 1-nitro-3-(trifluoromethyl) benzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3320, 1651, 1607, 1547, 1439, 1171, 896, 696 cm^{-1}.

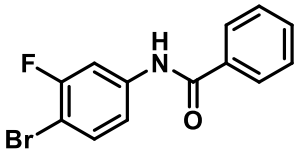
^{1}H NMR (300 MHz , DMSO *d_6*) δ 10.57 (s, 1H), 8.27 (s, 1H), 8.07 (d, *J* = 9.1 Hz, 1H), 8.02 – 7.97 (m, 2H), 7.59 (dt, *J* = 14.3, 6.9 Hz, 4H), 7.46 (d, *J* = 8.6 Hz, 1H).

^{13}C NMR (75 MHz, DMSO *d_6*) δ 166.4, 140.5, 134.9, 132.4, 130.3, 128.9 (2C), 128.2 (2C), 124.2, 120.4, 116.8.

HRMS (ESI): *m/z* calculated for $C_{14}H_{11}F_3NO$ $[M + H]^+$ 265.0714 found 265.0710.

The spectroscopic data closely match the ones previously reported in the literature[11].

Synthesis of N-(4-bromo-3-fluoro-phenyl) benzamide (3l):



Compound **3l** as pale-yellow solid (0.219 g, 75%) was prepared from ethyl 1-bromo-2-fluoro-4-nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mml) according to the general procedure **I**.

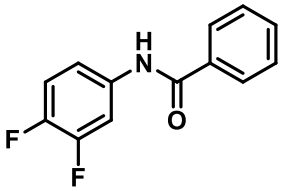
IR (film): 3346, 1656, 1599, 1417, 715 cm^{-1}.

^{1}H NMR (500 MHz , $CDCl_3$) δ 7.89 (s, 1H), 7.86 – 7.83 (m, 2H), 7.74 (dd, *J* = 10.5, 2.5 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.52 – 7.48 (m, 3H), 7.20 (dd, *J* = 8.7, 2.4 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 158.2, 138.7, 138.6, 134.3, 133.4, 132.3, 128.9, 127.0, 116.5, 116.5, 108.8, 108.5.

HRMS (ESI): *m/z* calculated for $C_{13}H_{10}BrFNO$ $[M + H]^+$ 293.9929 found 293.9928.

Synthesis of N-(3,4-difluorophenyl) benzamide (3m):



Compound **3m** as off white solid (0.179 g, 77%) was prepared from 1,2-difluoro-4-nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3364, 1660, 1512, 1208, 606 cm^{-1}.

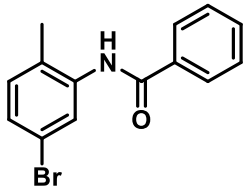
^{1}H NMR (300 MHz , DMSO d_6) δ 10.45 (s, 1H), 7.99 – 7.91 (m, 3H), 7.62 – 7.51 (m, 4H), 7.48 – 7.38 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 134.4, 132.2, 130.2, 128.9 (2C), 128.5 (2C), 127.0 (2C), 117.4, 115.8, 110.2.

HRMS (ESI): *m/z* calculated for $C_{13}H_{10}F_2NO$ $[M + H]^+$ 234.0730 found 234.0732.

The spectroscopic data closely match the ones previously reported in the literature[12].

Synthesis of N-(5-bromo-2-methyl-phenyl) benzamide (3n):



Compound **3n** as pale-yellow solid (0.213 g, 74%) was prepared from 3-bromo-2-methyl-1-nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

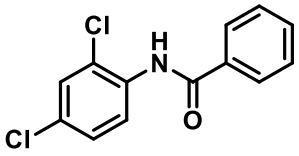
IR (film): 3197, 1635, 1520, 1312, 693 cm^{-1}.

^{1}H NMR (300 MHz , $CDCl_3$) δ 8.24 (s, 1H), 7.89 – 7.85 (m, 2H), 7.67 (s, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.23 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 137.0, 314.5, 132.2, 131.7, 129.0 (2C), 128.1, 127.5, 127.0 (2C), 125.5, 120.0, 17.5.

HRMS (ESI): *m/z* calculated for $C_{14}H_{13}BrNO$ $[M + H]^+$ 290.0180 found 290.0182.

Synthesis of N-(2,4-dichlorophenyl) benzamide (3o):



Compound **3o** as off white solid (0.191 g, 72%) was prepared from 2,4-dichloro-1-nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3289, 1647, 1519, 1301, 821, 712 cm^{-1}.

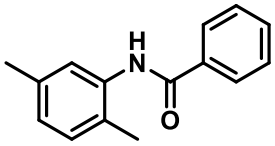
^{1}H NMR (500 MHz , $CDCl_3$) δ 8.55 (d, *J* = 9.0 Hz, 1H), 8.39 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.43 (s, 1H), 7.32 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2, 134.3, 133.5, 132.4, 129.2 (2C), 129.0, 128.8, 128.0, 127.1 (2C), 123.5, 122.2.

HRMS (ESI): *m/z* calculated for $C_{13}H_{10}Cl_2NO$ $[M + H]^+$ 266.0139 found 266.0139.

The spectroscopic data closely match the ones previously reported in the literature[13].

Synthesis of N-(2,5-dimethylphenyl) benzamide (3p):



Compound **3p** as off white solid (0.191 g, 85%) was prepared from 1,4-dimethyl-2-nitrobenzene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **II**.

IR (film): 3254, 1642, 1523, 1306, 709 cm^{-1}.

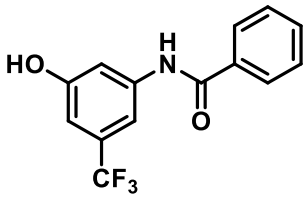
^{1}H NMR (500 MHz , $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.81 (s, 1H), 7.63 (s, 1H), 7.57 (t, *J* = 7.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 7.1 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 2.35 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 135.6, 135.1, 131.8, 130.5, 128.8, 127.0, 126.1, 123.6, 21.2, 17.4.

HRMS (ESI): *m/z* calculated for $C_{15}H_{16}NO$ $[M + H]^+$ 226.1226 found 226.1227.

The spectroscopic data closely match the ones previously reported in the literature[14].

Synthesis of N-[2-hydroxy-4-(trifluoromethyl) phenyl] benzamide (3q):



Compound **3q** as white solid (0.197 g, 70%) was prepared from 2-nitro-5-(trifluoromethyl) phenol (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I.**

IR (film): 3310, 3400-2800, 1655, 1615, 1557, 1451, 1254, 1175, 696 cm^{-1}.

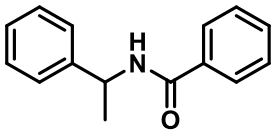
^{1}H NMR (500 MHz , $CDCl_3$) δ 8.22 (s, 1H), 7.97 (s, 1H), 7.86 (d, *J* = 8.5 Hz, 2H), 7.64 – 7.59 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 7.6 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 158.0, 139.0, 134.1, 132.7, 132.5, 129.2 (2C), 127.0 (2C), 122.5, 110.4, 109.3, 107.7.

HRMS (ESI): *m/z* calculated for $C_{14}H_{11}F_3NO_2$ $[M + H]^+$ 282.0663 found 282.0660.

The spectroscopic data closely match the ones previously reported in the literature[15].

Synthesis of N-(1-phenylethyl) benzamide (3r):



Compound **3r** as off white solid (0.186 g, 83%) was prepared from 1-nitroethylbenzene. (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **II.**
IR (film): 3356, 2928, 1632, 1516, 1321, 551 cm^{-1}.

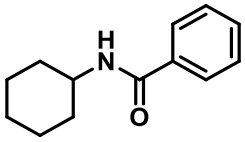
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.79 – 7.76 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.34 (m, 6H), 7.29 (d, *J* = 7.2 Hz, 1H), 6.34 (bs, 1H), 5.35 (p, *J* = 6.9 Hz, 1H), 1.61 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 143.1, 134.6, 131.5, 128.8 (2C), 128.6 (2C), 127.5, 126.9 (2C), 126.3 (2C), 49.2, 21.7.

HRMS (ESI): *m/z* calculated for $C_{15}H_{16}NO$ $[M + H]^+$ 226.1231 found 226.1230.

The spectroscopic data closely match the ones previously reported in the literature[16].

Synthesis of N-cyclohexyl benzamide (3s):



Compound **3s** as off white solid (0.136 g, 67%) was prepared from nitro cyclohexane (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.150 g, 74%) by general procedure **II**.
IR (film): 3318, 2926, 2852, 1626, 1533, 1329, 691 cm^{-1}.

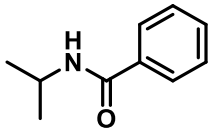
^{1}H NMR (500 MHz , $CDCl_3$) δ 7.77 – 7.73 (m, 2H), 7.48 (t, *J* = 6.6 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 2H), 5.95 (bs, 1H), 4.03 – 3.93 (m, 1H), 2.04 (dd, *J* = 12.5, 4.1 Hz, 2H), 1.76 (dd, *J* = 14.2, 4.0 Hz, 2H), 1.66 (d, *J* = 13.1 Hz, 1H), 1.48 – 1.41 (m, 2H), 1.30 – 1.26 (m, 1H), 1.23 – 1.20 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 135.1, 131.2, 128.5 (2C), 126.8 (2C), 48.7, 33.3 (2C), 25.6, 24.9 (2C).

HRMS (ESI): *m/z* calculated for $C_{13}H_{18}NO$ $[M + H]^+$ 204.1388 found 204.1388.

The spectroscopic data closely match the ones previously reported in the literature[17].

Synthesis of N-isopropyl benzamide (3t):



Compound **3t** as off white solid (0.105 g, 65%) was prepared from 2-nitropropane (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I** and as off white solid (0.114 g, 70%) by general procedure **II**.
IR (film): 3289, 2977, 1631, 1541, 696, cm^{-1}.

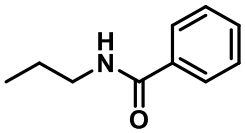
^{1}H NMR (500 MHz , $CDCl_3$) δ 7.75 (d, *J* = 9.5 Hz, 2H), 7.51 – 7.45 (m, 1H), 7.42 (t, *J* = 8.3 Hz, 2H), 5.91 (s, 1H), 4.29 (h, *J* = 6.7 Hz, 1H), 1.27 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 135.0, 131.3, 128.5 (2C), 126.8 (2C), 41.9, 22.9 (2C).

HRMS (ESI): *m/z* calculated for $C_{10}H_{14}NO$ $[M + H]^+$ 164.1075 found 164.1078.

The spectroscopic data closely match the ones previously reported in the literature[18].

Synthesis of N-propyl benzamide (3u):



Compound **3u** as off white solid (0.114 g, 70%) was prepared from 1-nitropropane (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

IR (film): 3301, 2928, 1632, 1547, 1315, 695 cm^{-1}.

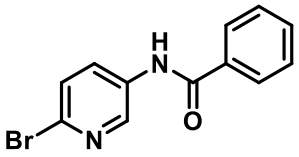
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.77 – 7.74 (m, 2H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.43 – 7.39 (m, 2H), 6.22 (bs, 1H), 3.45 – 3.37 (m, 2H), 1.64 (h, *J* = 7.3 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 134.9, 131.3, 128.5 (2C), 126.8 (2C), 41.8, 22.9, 11.4.

HRMS (ESI): *m/z* calculated for $C_{10}H_{14}NO$ $[M + H]^+$ 164.1075 found 164.1070.

The spectroscopic data closely match the ones previously reported in the literature[19].

Synthesis of N-(6-bromo-3-pyridyl) benzamide (3v):



Compound **3v** as light brown solid **(**0.179 g, 65%) was prepared from 2-methyl-5-nitro-pyridine (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.
IR (film): 3296, 2924, 1656, 1506, 1369, 709, 686 cm^{-1}.

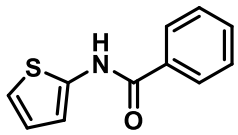
^{1}H NMR (300 MHz , $CDCl_3$) δ 8.49 (d, *J* = 2.9 Hz, 1H), 8.22 (dd, *J* = 8.7, 2.9 Hz, 1H), 8.10 (d, *J* = 7.9 Hz, 1H), 8.00 (s, 1H), 7.88 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.50 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 141.4, 136.1, 134.4, 133.8, 132.5, 130.3, 129.0 (2C), 128.2, 127.1(2C).

HRMS (ESI): *m/z* calculated for $C_{12}H_{10}BrN_2O$ $[M + H]^+$ 276.9976 found 276.9978.

The spectroscopic data closely match the ones previously reported in the literature[20].

Synthesis of N-(2-thienyl) benzamide (3w):



Compound **3w** as off white solid (0.138 g, 68%) was prepared from 2-nitrothiophene (0.10 g,) and benzoyl saccharin (0.222 g) according to the general procedure **I** and as off white solid (0.166 g, 82%) by general procedure **II**.

IR (film): 3231, 3030, 1643, 1565, 1495, 1366, 1301, 893, 817, 701 cm^{-1}.

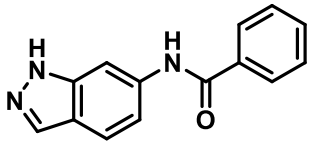
^{1}H NMR (300 MHz , DMSO d_6) δ 11.54 (s, 1H), 8.00 (d, *J* = 6.7 Hz, 2H), 7.59 (dd, *J* = 12.2, 7.0 Hz, 3H), 7.01 (dd, *J* = 5.2, 1.8 Hz, 1H), 6.95 – 6.90 (m, 2H)

^{13}C NMR (75 MHz, DMSO d_6) δ 163.7, 140.5, 133.6, 132.4, 129.0 (2C), 128.1 (2C), 124.5, 117.9, 112.6.

HRMS (ESI): *m/z* calculated for $C_{11}H_{10}NOS$ $[M + H]^+$ 204.0478 found 204.0476.

The spectroscopic data closely match the ones previously reported in the literature[21].

Synthesis of N-(1H-indazol-6-yl) benzamide (3x):



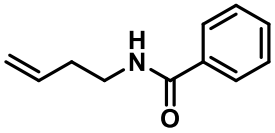
Compound **3x** as light brown solid (0.163 g, 69%) was prepared from 6-nitro-1H-indazole (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.
IR (film): 3356, 3169, 1644, 1517, 1269, 886 cm^{-1}.

^{1}H NMR (300 MHz , DMSO d_6) δ 12.94 (s, 1H), 10.36 (s, 1H), 8.27 (s, 1H), 7.97 (d, *J* = 7.9 Hz, 3H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.62 – 7.51 (m, 3H), 7.38 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (75 MHz, DMSO d_6) δ 165.8, 140.3, 137.4, 135.1, 133.3, 131.5, 128.4 (2C), 127.7 (2C), 120.4, 119.4, 115.1, 100.0.

HRMS (ESI): *m/z* calculated for $C_{14}H_{12}N_3O$ $[M + H]^+$ 238.0980 found 238.0985

Synthesis of N-but-3-enylbenzamide (3y):



Compound **3y** as colorless oil (0.126 g, 72%) was prepared from 4-nitrobut-1-ene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

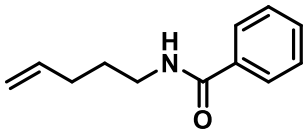
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.52 – 7.38 (m, 3H), 6.19 (s, 1H), 5.92 – 5.76 (m, 1H), 5.21 – 5.10 (m, 2H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.42 – 2.35 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 135.5, 134.9, 131.5, 128.7 (2C), 126.9 (2C), 117.6, 38.9, 33.9.

HRMS (ESI): *m/z* calculated for $C_{11}H_{14}NO$ $[M + H]^+$ 176.1075 found 176.1072.

The spectroscopic data closely match the ones previously reported in the literature[22].

Synthesis of N-pent-4-enylbenzamide (3z):



Compound **3z** as colorless oil (0.139 g, 74%) was prepared from 5-nitropent-1-ene (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

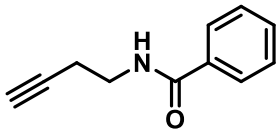
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 6.16 (s, 1H), 5.90 – 5.78 (m, 1H), 5.15 – 4.96 (m, 2H), 3.49 (q, *J* = 6.6 Hz, 2H), 2.17 (q, *J* = 7.2 Hz, 2H), 1.77 – 1.72 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6, 138.0, 134.9, 131.5, 128.7, 128.7, 126.9, 115.5, 39.8, 31.4, 29.8, 28.9.

HRMS (ESI): *m/z* calculated for $C_{12}H_{16}NO$ $[M + H]^+$ 190.1231 found 190.1235.

The spectroscopic data closely match the ones previously reported in the literature[23].

Synthesis of N-but-3-ynylbenzamide (3aa):



Compound **3aa** as brown oil (0.118 g, 68%) was prepared from 4-nitrobut-1-yne (1.0 mmol) and benzoyl saccharin (1.0 mmol) according to the general procedure **I**.

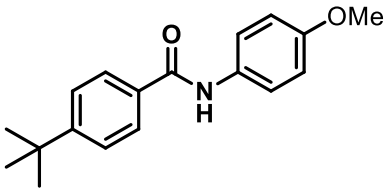
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.71 (m, 2H), 7.56 – 7.39 (m, 3H), 6.51 (s, 1H), 3.62 (d, *J* = 6.2 Hz, 2H), 2.55 – 2.49 (m, 2H), 2.05 (t, *J* = 2.7 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 133.4, 130.6, 127.6 (2C), 125.9 (2C), 80.5, 69.2, 37.4, 18.5

HRMS (ESI): *m/z* calculated for $C_{11}H_{12}NO$ $[M + H]^+$ 174.0918 found 174.0915.

The spectroscopic data closely match the ones previously reported in the literature[24].

Synthesis of 4-tert-butyl-N-(4-methoxyphenyl)benzamide (5a):



Compound **5a** as off white solid (0.246 g, 87%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(4-tert-butylbenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as white solid (0.251 g, 89%) by general procedure **II**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 – 7.76 (m, 3H), 7.57 – 7.46 (m, 4H), 6.92 – 6.86 (m, 2H), 3.81 (s, 3H), 1.35 (s, 9H).

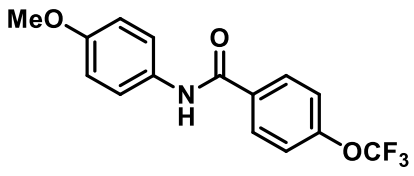
^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 156.7, 155.4, 132.3, 131.3, 127.0 (2C), 125.8 (2C), 122.2 (2C), 114.3 (2C), 55.6, 35.1, 31.3 (3C).

HRMS (ESI): *m/z* calculated for $C_{18}H_{22}NO_2$ $[M + H]^+$ 284.1650 found 284.1655.

HRMS (ESI): *m/z* calculated for $C_{11}H_{12}NO$ $[M + H]^+$ 174.0918 found 174.0915.

The spectroscopic data closely match the ones previously reported in the literature[25].

Synthesis of N-(4-methoxyphenyl)-4-(trifluoromethoxy) benzamide (5b):



Compound 5b as white solid (0.264 g, 85%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 1,1-dioxo-2-[4-(trifluoromethoxy) benzoyl]-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as off white solid (0.267 g, 86%) by procedure **II**.

IR (film): 3314, 2928, 1644, 1513, 1209, 1160, 1104, 1031, 825 cm^{-1}.

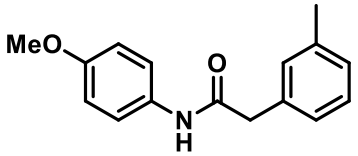
^{1}H NMR (500 MHz , DMSO d_6) δ 10.24 (s, 1H), 8.06 (d, *J* = 6.6 Hz, 2H), 7.66 (d, *J* = 6.6 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 6.94 (s, 2H), 3.74 (s, 3H).

^{13}C NMR (125 MHz, DMSO d_6) δ 163.9, 155.7, 150.4, 134.2, 132.0, 130.0 (2C), 122.0 (2C), 121.9, 120.7 (2C), 113.8 (2C), 55.2.

HRMS (ESI): *m/z* calculated for $C_{15}H_{13}F_3NO_3$ $[M + H]^+$ 312.0848 found 312.0846.

The spectroscopic data closely match the ones previously reported in the literature[26].

Synthesis of N-(4-methoxyphenyl)-4-(trifluoromethoxy) benzamide (5c):



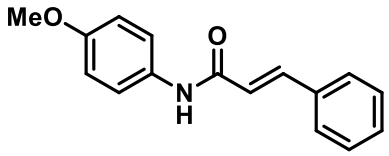
Compound **5c** as off white solid (0.198 g, 78%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-[2-(m-tolyl) acetyl]-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as off white solid (0.204 g, 80%) by general procedure **II**.
IR (film): 3289, 2921, 1651, 1540, 1505, 1408, 1238, 1035, 825, 765 cm^{-1}.

^{1}H NMR (300 MHz , $CDCl_3$) δ 7.24 (d, *J* = 9.0 Hz, 2H), 7.19 (d, *J* = 5.3 Hz, 1H), 7.08 – 7.03 (m, 3H), 6.75 (s, 1H), 6.72 (s, 1H), 3.69 (s, 3H), 3.60 (s, 2H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 156.5, 138.9, 134.5, 130.8, 130.3, 129.1, 128.4, 126.5, 121.8 (2C), 114.1 (2C), 55.5, 44.6, 21.4.

HRMS (ESI): *m/z* calculated for $C_{16}H_{18}NO_2$ $[M + H]^+$ 256.1332 found 256.1327.

Synthesis of (E)-N-(4-methoxyphenyl)-3-phenyl-prop-2-enamide (5d):



Compound **5d** as white solid (0.156 g, 62%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 1,1-dioxo-2-[(E)-3-phenylprop-2-enoyl]-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3310, 2921, 1659, 1507, 1226, 987, 826, 705, 545 cm^{-1}.

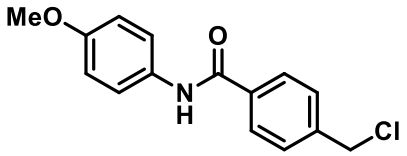
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.73 (d, *J* = 15.6 Hz, 1H), 7.59 – 7.38 (m, 4H), 7.40 – 7.30 (m, 4H), 6.88 (d, *J* = 9.2 Hz, 2H), 6.58 (d, *J* = 15.5 Hz, 1H), 3.78 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 156.5, 142.0, 134.7, 131.2, 129.9, 128.9, 127.9, 121.9, 121.0, 114.2, 55.5.

HRMS (ESI): *m/z* calculated for $C_{16}H_{16}NO_2$ $[M + H]^+$ 254.1176 found 254.1184.

The spectroscopic data closely match the ones previously reported in the literature[27].

Synthesis of 4-(chloromethyl)-N-(4-methoxyphenyl) benzamide (5e):



Compound **5e** as white solid (0.209 g, 76%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-[4-(chloromethyl) benzoyl]-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3335, 2921, 1649, 1510, 1228, 1034, 822, 748, 633 cm^{-1}.

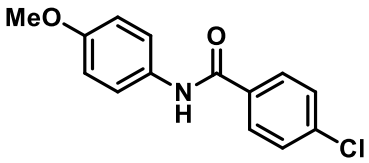
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.71 (s, 1H), 7.53 (d, *J* = 9.0 Hz, 2H), 7.29 (s, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H), 2.42 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 156.5, 142.2, 132.1, 131.1, 130.2, 129.4 (2C), 127.0 (2C), 122.0 (2C), 114.2 (2C), 55.5.

HRMS (ESI): *m/z* calculated for $C_{15}H_{15}ClNO_2$ $[M + H]^+$ 276.0786 found 276.0782.

The spectroscopic data closely match the ones previously reported in the literature[28].

Synthesis of 4-chloro-N-(4-methoxyphenyl) benzamide (5f):



Compound **5f** as off white solid (0.183 g, 70%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(4-chlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3349, 2924, 1647, 1528, 1512, 11229, 1028, 830, 821, 523 cm^{-1}.

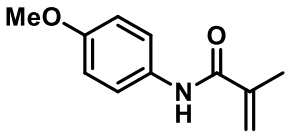
^{1}H NMR (300 MHz , $CDCl_3$) δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.82 (s, 1H), 7.68 (s, 1H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 164.0, 155.7, 136.2, 133.7, 132.0, 131.2, 129.5 (2C), 128.8, 128.4, 122.0, 113.8 (2C), 55.2.

HRMS (ESI): *m/z* calculated for $C_{14}H_{13}ClNO_2$ $[M + H]^+$ 262.0629 found 262.0628.

The spectroscopic data closely match the ones previously reported in the literature[29].

Synthesis of N-(4-methoxyphenyl)-2-methyl-prop-2-enamide (5g):



Compound **5g** as off white solid (0.139 g, 73%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(2-methylprop-2-enoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3318, 2921, 1656, 1509, 1409, 1234, 1033, 824, 526 cm^{-1}.

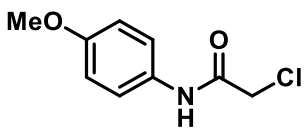
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.54 (s, 1H), 7.46 (d, *J* = 10.1 Hz, 2H), 6.85 (s, 2H), 5.77 (s, 1H), 5.42 (s, 1H), 3.79 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 156.5, 140.8, 130.9, 122.0 (2C), 119.7, 114.1 (2C), 55.5, 18.8.

HRMS (ESI): *m/z* calculated for $C_{11}H_{14}NO_2$ $[M + H]^+$ 192.1019 found 192.1019.

The spectroscopic data closely match the ones previously reported in the literature[30].

Synthesis of 2-chloro-N-(4-methoxyphenyl) acetamide (5h):



Compound **5h** as off white solid (0.155 g, 78%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and (2-chloroacetyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3293, 2960, 1662, 1543, 1509, 1245, 1029, 828, 788, 688, 518 cm^{-1}.

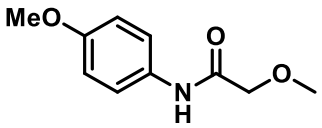
^{1}H NMR (300 MHz , $CDCl_3$) δ 8.15 (s, 1H), 7.44 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 6.7 Hz, 2H), 4.19 (s, 2H), 3.80 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7, 157.1, 129.7, 122.1 (2C), 114.3 (2C), 55.5, 42.9.

HRMS (ESI): *m/z* calculated for $C_9H_{11}ClNO_2$ $[M + H]^+$ 200.0473 found 200.0479.

The spectroscopic data closely match the ones previously reported in the literature[31].

Synthesis of 2-methoxy-N-(4-methoxyphenyl) acetamide (5i):



Compound **5i** as colorless oil (0.122 g, 63%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(2-methoxyacetyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as colorless oil (0.152 g, 78%) by general procedure **II**.

IR (film): 3392, 2935, 1668, 1528, 1509, 1234, 1109, 827, 520 cm^{-1}.

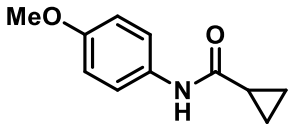
^{1}H NMR (300 MHz , $CDCl_3$) δ 8.15 (s, 1H), 7.49 – 7.45 (m, 2H), 6.89 – 6.85 (m, 2H), 4.01 (s, 2H), 3.79 (s, 3H), 3.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 156.6, 130.2, 121.6 (2C), 114.2 (2C), 72.1, 59.3, 55.5.

HRMS (ESI): *m/z* calculated for $C_{10}H_{13}NO_3$ $[M + H]^+$ 196.0973 found 196.0972.

The spectroscopic data closely match the ones previously reported in the literature[32].

Synthesis of N-(4-methoxyphenyl) cyclopropane carboxamide enamide (5j):



Compound **5j** as off white solid (0.129 g, 68%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(cyclopropane carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3307, 2921, 1647, 1511, 1143, 1240, 1175, 1028, 825, 691 cm^{-1}.

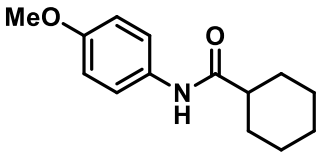
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.50 (s, 1H), 7.40 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 3.78 (s, 3H), 1.52 – 1.44 (m, 1H), 1.09 – 1.03 (m, 2H), 0.84 – 0.78 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 156.2, 131.3, 121.6 (2C), 114.1 (2C), 55.5, 15.5, 7.8 (2C).

HRMS (ESI): *m/z* calculated for $C_{11}H_{14}NO_2$ $[M + H]^+$ 192.1019 found 192.1017.

The spectroscopic data closely match the ones previously reported in the literature[33].

Synthesis of N-(4-methoxyphenyl) cyclohexane carboxamide (5k):



Compound **5k** as white solid (0.186 g, 80%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(cyclohexanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as off white solid (0.200 g, 86%) by general procedure **II**.
IR (film): 3295, 2922, 2853, 1528, 1514, 1384, 1247, 1031, 824, cm^{-1}.

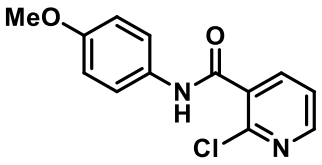
^{1}H NMR (300 MHz , $CDCl_3$) δ 7.48 – 7.37 (m, 2H), 7.11 (s, 1H), 6.89 – 6.80 (m, 2H), 3.78 (s, 3H), 2.27 – 2.16 (m, 1H), 1.95 – 1.90 (m, 2H), 1.83 –1.78 (m, 2H), 1.70 – 1.66 (m, 2H), 1.59 – 1.49 (m, 2H), 1.31– 1.21 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 156.4, 131.3, 121.8 (2C), 114.2 (2C), 55.6 (2C), 46.5, 29.8 (2C), 25.8 (2C).

HRMS (ESI): *m/z* calculated for $C_{14}H_{20}NO_2$ $[M + H]^+$ 234.3062 found 234.3068.

The spectroscopic data closely match the ones previously reported in the literature[34].

Synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide (5l):



Compound **5l** as white solid (0.196 g, 75%) was prepared from 1-methoxy-4-nitrobenzene (1.0 mmol) and 2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as off white solid (0.188 g, 72%) by procedure **II**.

IR (film): 3232, 2921, 1656, 1531, 1509, 1398, 1282, 1246, 1026, 821, 744, 706 cm^{-1}.

^{1}H NMR (300 MHz , $CDCl_3$) δ 8.50 (d, *J* = 4.8 Hz, 1H), 8.19 (dd, *J* = 7.7, 2.0 Hz, 1H), 8.11 (s, 1H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.39 (dd, *J* = 7.7, 4.8 Hz, 1H), 6.92 (d, *J* = 9.1 Hz, 2H), 3.82 (s, 3H).

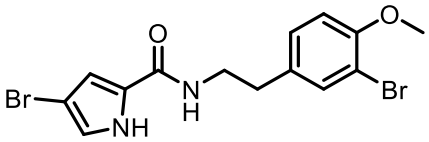
^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 157.1, 151.1, 147.0, 140.1, 131.5, 130.2, 123.0, 122.2 (2C), 114.4 (2C), 55.5.

HRMS (ESI): *m/z* calculated for $C_{13}H_{12}N_2ClO_2$ $[M + H]^+$ 263.0582 found 263.0579.

Synthesis of Biologically Active Compounds:

1) Formal Synthesis of Dispyrin (9):

Synthesis of 4-bromo-N-[2-(3-bromo-4-methoxy-phenyl) ethyl]-1H-pyrrole-2-carboxamide (8):



Compound **8** as off white solid (0.327 g, 82%) was prepared from 2-bromo-1-methoxy-4-(2-nitroethyl) benzene (1.0 mmol) and 2-(4-bromo-1H-pyrrole-2-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3224, 2941, 1631, 1565, 1521, 1465, 1455, 1383, 1055, 921, 744 cm^{-1}.

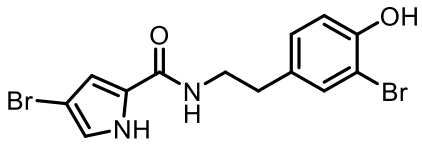
^{1}H NMR (300 MHz, DMSO d_6) δ 11.80 (s, 1H), 8.14 (t, *J* = 5.8 Hz, 1H), 7.45 (d, *J* = 2.2 Hz, 1H), 7.19 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 6.98 – 6.95 (m, 1H), 6.81 (s, 1H), 3.81 (s, 3H), 3.41 (t, *J* = 6.6 Hz, 2H), 2.74 (t, *J* = 7.2 Hz, 2H).

^{13}C NMR (75 MHz, DMSO d_6) δ 159.4, 153.7, 133.2, 132.9, 129.1, 126.8, 121.0, 112.4, 111.2, 110.3, 94.8, 56.0, 40.2, 33.8.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}Br_2N_2O_2$ $[M + H]^+$ 400.9517 found 400.9515.

The spectroscopic data closely match the ones previously reported in the literature[35].

Synthesis of 4-bromo-N-[2-(3-bromo-4-hydroxy-phenyl) ethyl]-1H-pyrrole-2-carboxamide (8a):



To a stirred solution of compound (8a) (0.20 g, 0.50 mmol) in dichloromethane at -78 °C was added BBr_3 (0.2 mL, 2.0 mmol, 1.0 M solution in dichloromethane) over 10 minutes under N_2 atmosphere and stirred the reaction mixture for at -78 °C for 30 minutes then allowed to warm to 25 °C over 1.5 h. The reaction was quenched with saturated solution of sodium bicarbonate solution until the P^H becomes slightly basic. Diluted the reaction mixture with water and extracted with dichloromethane 3 X (20 mL). Organic layer was separated dried and concentrated in *vacuo* to yield (0.17 g, 90%).

IR (film): 3409, 1608, 1564, 1508, 1425, 1384, 1327, 921, 600 cm^{-1}.

^{1}H NMR (300 MHz , DMSO- d_6) δ 11.78 (s, 1H), 10.00 (s, 1H), 8.11 (t, *J* = 5.2 Hz, 1H), 7.33 (d, *J* = 2.2 Hz, 1H), 7.01 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.95 (m, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.82 – 6.78 (m, 1H), 3.38 (t, *J* = 6.1 Hz, 2H), 2.68 (t, *J* = 7.4 Hz, 2H).

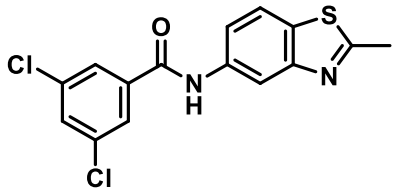
^{13}C NMR (75 MHz, DMSO- *d*$_6$) δ 160.0, 152.8, 133.2, 132.1, 129.4, 127.4, 121.5, 116.6, 111.7, 109.5, 95.3, 40.8, 34.4.

HRMS (ESI): *m/z* calculated for $C_{13}H_{12}Br_2N_2O_2$ $[M + H]^+$ 386.9359 found 386.9360.

The spectroscopic data closely match the ones previously reported in the literature[35].

2) Synthesis of API's:

Synthesis of 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide (10):



Compound **10** as white amorphous solid (0.252 g, 75%) was prepared from 2-methyl-5-nitro-1,3-benzothiazole (1.0 mmol) and 2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

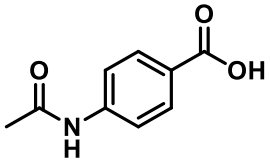
^{1}H NMR (300 MHz , $CDCl_3$) δ 8.15 (s, 1H), 7.97 (s, 1H), 7.82 – 7.75 (m, 3H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.54 (s, 1H), 2.84 (s, 3H).

^{13}C NMR (75 MHz, DMSO *d*$_6$) δ 168.6, 163.3, 153.8, 138.5, 137.5, 134.8 (2C), 131.5, 131.0, 127.0 (2C), 122.3, 118.7, 113.8, 20.3.

HRMS (ESI): *m/z* calculated for $C_{15}H_{11}Cl_2N_2OS$ $[M + H]^+$ 336.9969 found 336.9969.

The spectroscopic data closely match the ones previously reported in the literature[36].

Synthesis of 4-acetamidobenzoic acid (11):



Compound **11** as off white solid (0.170 g, 95%) was prepared from 4-nitrobenzoic acid (1.0 mmol) and 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **II**.

IR (film): 3305, 2924, 1671, 1522, 1426, 1314, 1296, 1264, 768, 701, 546 cm^{-1}.

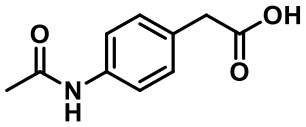
^{1}H NMR (300 MHz, DMSO d_6) δ 10.24 (s, 1H), 7.87 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.9 Hz, 2H), 2.08 (s, 3H).

^{13}C NMR (75 MHz, DMSO d_6) δ 169.3, 167.3, 143.8, 130.8 (2C), 125.3, 118.6 (2C), 24.6.

HRMS (ESI): *m/z* calculated for $C_9H_{10}NO_3$ $[M + H]^+$ 180.1727 found 180.1730.

The spectroscopic data closely match the ones previously reported in the literature[37].

Synthesis of 2-(4-acetamidophenyl) acetic acid (12):



Compound **12** as off white solid (0.179 g, 93%) was prepared from 2-(4-nitrophenyl) acetic acid (1.0 mmol) and 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **II**.

IR (film): 3348, 1709, 1638, 1601, 1542, 1538, 1221, 1195, 968, 806, 723 cm^{-1}.

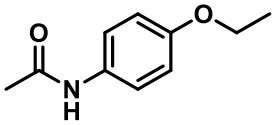
^{1}H NMR (300 MHz, DMSO d_6) δ 12.27 (s, 1H), 9.90 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 3.49 (s, 2H), 2.03 (s, 3H).

^{13}C NMR (76 MHz, DMSO d_6) δ 173.3, 168.6, 138.3, 130.0 (2C), 130.0, 129.4, 119.4, 119.3, 24.4.

HRMS (ESI): *m/z* calculated for $C_{10}H_{12}NO_3$ $[M + H]^+$ 194.1992 found 194.1995.

The spectroscopic data closely match the ones previously reported in the literature[38].

Synthesis of N-(4-ethoxyphenyl) acetamide (13):



Compound **13** as white solid (0.170 g, 95%) was prepared from 1-ethoxy-4-nitrobenzene (1.0 mmol) and 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **II**.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (bs, 1H), 7.38 – 7.35 (m, 2H), 6.85 – 6.78 (m, 2H), 4.00 (q, *J* = 7.0 Hz, 2H), 2.12 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H).

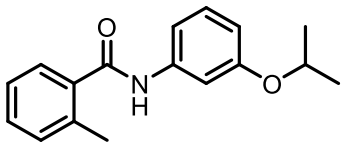
^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 154.8, 129.8, 121 (2C), 113.7 (2C), 62.7, 23.2, 13.8.

HRMS (ESI): *m/z* calculated for $C_{10}H_{14}NO_2$ $[M + H]^+$ 180.1033 found 180.1030.

The spectroscopic data closely match the ones previously reported in the literature[39].

3) Synthesis of Agrochemicals:

Synthesis of N**-(4-isopropoxyphenyl)-2-methyl-benzamide (14):**



Compound **14** as off white solid (0.214 g, 81%) was prepared from 1-isopropoxy-4-nitrobenzene (1.0 mmol) and 2-(2-methylbenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I** and as white solid (0.238 g, 90%) by general procedure **II**.

IR (film): 3293, 2981, 1652, 1597, 1488, 1435, 1265, 736, 688 cm^{-1}.

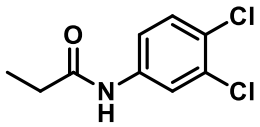
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.5 Hz, 1H), 7.42 (s, 1H), 7.39 – 7.33 (m, 2H), 7.28 (d, *J* = 2.6 Hz, 1H), 7.25 (s, 1H), 7.25 – 7.21 (m, 1H), 7.04 (d, *J* = 5.8 Hz, 1H), 6.69 (dd, *J* = 8.3, 3.3 Hz, 1H), 4.59 (p, *J* = 5.9 Hz, 1H), 2.51 (s, 3H), 1.35 (d, *J* = 6.1 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 158.6, 139.2, 136.4, 131.3, 130.3, 129.8, 126.6, 125.9, 112.2, 111.8, 107.5, 70.0, 22.1, 19.8.

HRMS (ESI): *m/z* calculated for $C_{17}H_{20}NO_2$ $[M + H]^+$ 270.1494 found 270.1490.

The spectroscopic data closely match the ones previously reported in the literature[40].

Synthesis of N-(3,4-dichlorophenyl) propanamide (15):



Compound **15** as white solid (0.178 g, 82%) was prepared from 1,2-dichloro-4-nitrobenzene (1.0 mmol) and 1,1-dioxo-2-propanoyl-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

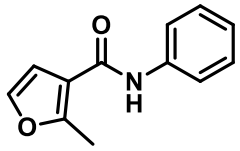
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.34 (s, 2H), 2.39 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 137.4, 132.8, 130.5, 127.3, 121.5, 119.0, 30.1, 9.5.

HRMS (ESI): *m/z* calculated for $C_9H_{10}Cl_2NO$ $[M + H]^+$ 219.0799 found 219.0795.

The spectroscopic data closely match the ones previously reported in the literature[41].

Synthesis of 2-methyl-N-phenyl-furan-3-carboxamide (16):



Compound as off white solid **16** (0.152 g, 76%) was prepared from nitrobenzene (1.0 mmol) and 2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

IR (film): 3317, 1738, 1641, 1597, 1098, 897, 741, 583 cm^{-1}.

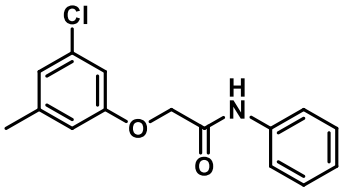
^{1}H NMR (300 MHz, DMSO d_6) δ 9.69 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.61 (s, 1H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.1 Hz, 2H), 2.56 (s, 3H).

^{13}C NMR (75 MHz, DMSO d_6) δ 162.2, 157.4, 141.2, 139.4, 129.0 (2C), 123.9, 120.8 (2C), 116.5, 109.9, 13.8.

HRMS (ESI): *m/z* calculated for $C_{12}H_{12}NO_2$ $[M + H]^+$ 202.0863 found 202.0862.

The spectroscopic data closely match the ones previously reported in the literature[42].

Synthesis of 2-(3-chloro-5-methyl-phenoxy)-N-phenyl-acetamide (17):



Compound **17** as off white solid (0.214 g, 78%) was prepared from nitrobenzene (1.0 mmol) and 2-[2-(3-chloro-5-methyl-phenoxy) acetyl]-1,1-dioxo-1,2-benzothiazol-3-one (1.0 mmol) according to the general procedure **I**.

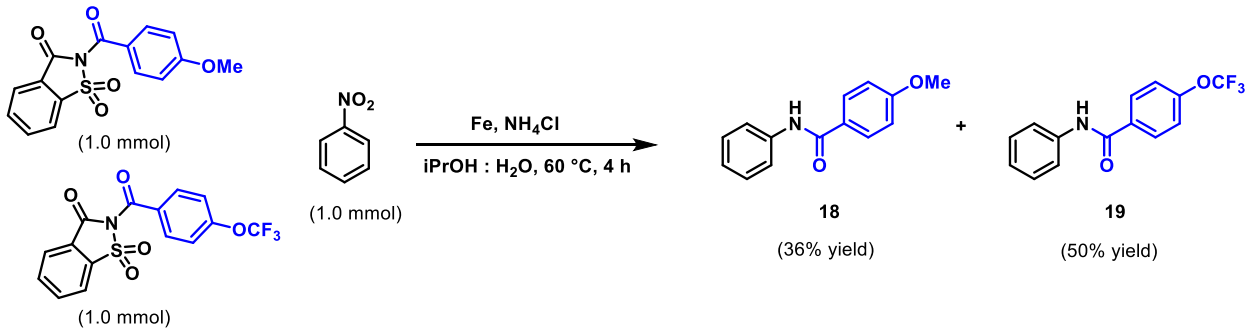
IR (film): 3276, 1739, 1667, 1541, 1032, 1233, 1138, 734 cm^{-1}.

^{1}H NMR (500 MHz , $CDCl_3$) δ 8.25 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.20 – 7.15 (m, 3H), 6.77 (d, *J* = 8.7 Hz, 1H), 4.58 (s, 2H), 2.34 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 153.8, 136.7, 131.0, 129.2 (2C), 128.4, 127.1, 127.0, 125.0, 120.0 (2C), 113.1, 68.0, 16.3.

HRMS (ESI): *m/z* calculated for $C_{15}H_{15}ClNO_2$ $[M + H]^+$ 276.0786 found 276.0795.

Competing experiment between EDGs and EWGs in acyl saccharin:



To a stirred solution of nitrobenzene (1.0 mmol), 2-(4-methoxybenzoyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide (1.0 mmol), 2-(4-(trifluoromethoxy)benzoyl)benzo[d]isothiazol-3(2H)-one 1,1-dioxide (1.0 mmol) in propane-2-ol and water (1:1, 7.0 mL) was added ammonium chloride (7.0 mmol), Fe powder (3.0 mmol) at rt and heated the reaction mixture at 65°C for 4 h in oil bath. Monitored the reaction by LCMS. Cool the reaction mixture at rt, filtered it through celite, washed with ethyl acetate (2V), filtrate was concentrated, crude was diluted with ethyl acetate and water.

Organic layer was washed with saturated solution of sodium bicarbonate followed by 1M HCl and brine wash. Organic layer was dried, filtered, and concentrated under *vacuo* to afford the corresponding amides which was purified by flash column chromatography to yield **18** as white solid (0.081 g, 36%) and **19** as a white solid (0.140 g, 50%).

4-Methoxy-N-phenyl-benzamide (18):

IR (film): 3285, 1725, 1369, 1229, 1027 cm^{-1}.

^{1}H NMR (300 MHz , $CDCl_3$) δ 7.33 (d, *J* = 8.9 Hz, 2H), 7.26 (s, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.85 (t, *J* = 7.7 Hz, 2H), 6.62 (t, *J* = 6.9 Hz, 1H), 6.45 (d, *J* = 8.9 Hz, 2H), 3.35 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 162.5, 138.2, 129.2 (2C), 129.0 (2C), 127.3, 124.5, 120.3 (2C), 114.1 (2C), 55.6.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1024 found 228.1020.

The spectroscopic data closely match the ones previously reported in the literature[43].

N-(4-Methoxyphenyl)-4-(trifluoromethoxy)benzamide (19):

IR (film): 3336, 1740, 1654, 1435, 1232, 1026, 750, 690 cm^{-1}.

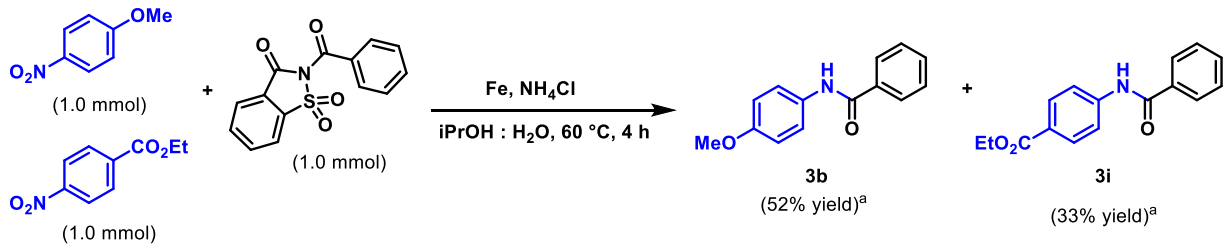
^{1}H NMR (500 MHz , $CDCl_3$) δ 7.92 (d, *J* = 8.9 Hz, 2H), 7.81 (s, 1H), 7.62 (d, *J* = 9.8 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.7 Hz, 2H), 7.20 – 7.15 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 151.7, 137.6, 133.4, 129.2 (2C), 129.0 (2C), 124.9 (2C), 120.9 (2C), 120.3 (2C).

HRMS (ESI): *m/z* calculated for $C_{14}H_{11}F_3NO_2$ $[M + H]^+$ 282.0741 found 282.0740.

The spectroscopic data closely match the ones previously reported in the literature[44].

Competing experiment between EDGs and EWGs in nitroarenes:



To a stirred solution of 2-benzoylbenzo[d]isothiazol-3(2H)-one 1,1-dioxide (1.0 mmol), 1-methoxy-4-nitrobenzene (1.0 mmol) and ethyl 4-nitrobenzoate (1.0 mmol) in propane-2-ol and water (1:1, 7.0 mL) was added ammonium chloride (7.0 mmol), Fe powder (3.0 mmol) at rt and heated the reaction mixture at 65°C for 4 h in oil bath. Monitored the reaction by LCMS. Cool the reaction mixture at rt, filtered it through celite, washed with ethyl acetate (2V), filtrate was concentrated, crude was diluted with ethyl acetate and water. Organic layer was washed with saturated solution of sodium bicarbonate followed by 1M HCl and brine wash. Organic layer was dried, filtered, and concentrated under *vacuo* to afford the corresponding amides which was purified by flash column chromatography to yield **5a** as white solid (0.118 g, 52%) and **21** as a white solid (0.088 g, 33%).

N-(4-methoxyphenyl) benzamide (3b):

IR (film): 3296, 1736, 1374, 1229, 1032 cm^{-1}.

^{1}H NMR (500 MHz , $CDCl_3$) δ 7.86 (d, *J* = 7.0 Hz, 2H), 7.82 (s, 1H), 7.52 (d, *J* = 6.6 Hz, 3H), 7.48 (s, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 156.7, 135.0, 133.6, 131.7, 131.0, 130.2, 129.4, 128.8, 128.5, 127.0, 122.2, 114.3, 55.5.

HRMS (ESI): *m/z* calculated for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1024 found 228.1020.

Ethyl 4-benzamidobenzoate (3i):

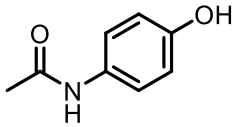
IR (film): 3298, 1742, 1370, 1229, 1029 cm^{-1}.

^{1}H NMR (500 MHz , $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 3H), 7.88 (d, *J* = 6.9 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 165.8, 142.1, 134.6, 132.2, 130.9 (2C), 128.9 (2C), 127.1 (2C), 126.2, 119.2 (2C), 60.9, 14.4.

HRMS (ESI): *m/z* calculated for $C_{16}H_{16}NO_3$ $[M + H]^+$ 270.1130 found 270.1136.

Gram Scale Synthesis of N-(4-hydroxyphenyl) acetamide (20)



A solution of 4-nitrophenol (10.0 g, 71.93 mmol) and acetyl saccharin (16.19 g, 71.93 mmol) in propane-2-ol and water (1:1) (200 mL) was added Pd/C (10 wt.% loading, 0.59 g, 5 mole%) and the reaction mixture heated in in autoclave under H_2 atmosphere (~5 bar) at 40 °C for 4 h. Monitored the reaction by HPLC, after the completion, the reaction mixture was cooled to rt and subjected to filtration through celite and filtrate was collected to afford propane-2-ol through distillation (67.5 g, 86%). The collected crude residue was dissolved in ethyl acetate (150mL). The ethyl acetate layer was subsequently washed with a saturated sodium bicarbonate solution (2 X 25 mL) followed by 20 mL of 1M hydrochloric acid and 20 mL of brine. The organic layer was subjected to drying using Na_2SO_4, followed by filtration and concentration under reduced pressure, resulting in the formation of the titled compound **20**, 9.88 g with 91% yield. The aqueous layer was adjusted to an acidic pH of approximately 4 by the addition of 1N HCl. The resulting precipitate was subsequently filtered and dried under vacuum, yielding saccharin 11.45 g with 87% yield. The recycled saccharin was converted to acetyl saccharin (13.59 g, 97%) according to the general procedure **IV**.

First cycle for synthesis of N-(4-hydroxyphenyl) acetamide (20): A solution of 4-nitrophenol (8.20 g, 58.94 mmol) and acetyl saccharin (13.2 g, 58.94 mmol) in propane-2-ol and water (1:1) (170 mL) was added Pd/C (10 wt.% loading, 0.49 g, 5 mole%) and reaction mixture heated in in autoclave under H_2 atmosphere (~5 bar) at 40 °C for 4 h. Monitored the reaction by HPLC, after the completion, reaction mixture was cooled to rt and subjected to filtration through celite and filtrate was collected to afford propane-2-ol through distillation (54.7 g, 82%). The collected crude residue was dissolved in ethyl acetate (120 mL). The ethyl acetate layer was subsequently washed with a saturated sodium bicarbonate solution (2 X 25 mL) followed by 20 mL of 1M hydrochloric acid and 20 mL of brine. The organic layer was subjected to drying using Na_2SO_4, followed by filtration and concentration under reduced pressure, resulting in the formation of the titled compound **20**, 8.0 g with 90% yield. The aqueous layer was adjusted to an acidic pH of approximately 4 by the addition of 1N HCl. The resulting precipitate was subsequently filtered

and dried under vacuum, yielding saccharin 9.10 g with 85% yield. The recycled saccharin was converted to acetyl saccharin (10.70 g, 95%) according to the general procedure **IV**.

Second cycle for synthesis of N-(4-hydroxyphenyl) acetamide (20): A solution of 4-nitrophenol (6.5 g, 46.72 mmol) and acetyl saccharin (10.5 g, 46.72 mmol) in propane-2-ol and water (1:1) (130 mL) was added Pd/C (10 wt.% loading, 0.39 g, 5 mole%) and reaction mixture heated in in autoclave under H_2 atmosphere (~5 bar) at 40 °C for 4 h. Monitored the reaction by HPLC, after the completion, reaction mixture was cooled to rt and subjected to filtration through celite and filtrate was collected to afford propane-2-ol through distillation (41.89 g, 86%). The collected crude residue was dissolved in ethyl acetate (90 mL). The ethyl acetate layer was subsequently washed with a saturated sodium bicarbonate solution (2 X 25 mL) followed by 20 mL of 1M hydrochloric acid and 20 mL of brine. The organic layer was subjected to drying using Na_2SO_4, followed by filtration and concentration under reduced pressure, resulting in the formation of the titled compound **20**, 6.21 g with 88% yield. The aqueous layer was adjusted to an acidic pH of approximately 4 by the addition of 1N HCl. The resulting precipitate was subsequently filtered and dried under vacuum, yielding saccharin 7.30 g with 86% yield. The recycled saccharin was converted to acetyl saccharin (8.60 g, 96%) according to the general procedure **IV**.

Third cycle for synthesis of N-(4-hydroxyphenyl) acetamide (20):: A solution of 4-nitrophenol (5.0 g, 35.94 mmol) and acetyl saccharin (8.1 g, 35.94 mmol) in propane-2-ol and water (1:1) (100 mL) was added Pd/C (10 wt.% loading, 0.29 g, 5 mole%) and reaction mixture heated in in autoclave under H_2 atmosphere (~5 bar) at 40 °C for 4 h. Monitored the reaction by HPLC, after the completion, reaction mixture was cooled to rt and subjected to filtration through celite and filtrate was collected to afford propane-2-ol through distillation (33.4 g, 85%). The collected crude residue was dissolved in ethyl acetate (75 mL). The ethyl acetate layer was subsequently washed with a saturated sodium bicarbonate solution (2 X 20 mL) followed by 20 mL of 1M hydrochloric acid and 20 mL of brine. The organic layer was subjected to drying using Na_2SO_4, followed by filtration and concentration under reduced pressure, resulting in the formation of the titled compound **20**, 4.90 g with 91% yield. The aqueous layer was adjusted to an acidic pH of approximately 4 by the addition of 1N HCl. The resulting precipitate was subsequently filtered and dried under vacuum, yielding saccharin 5.72 g with 87% yield. The recycled saccharin was converted to acetyl saccharin (6.72 g, 97%) according to the general procedure **IV**.

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IR (film): 3296, 1736, 1374, 1229, 1032 cm^{-1}.

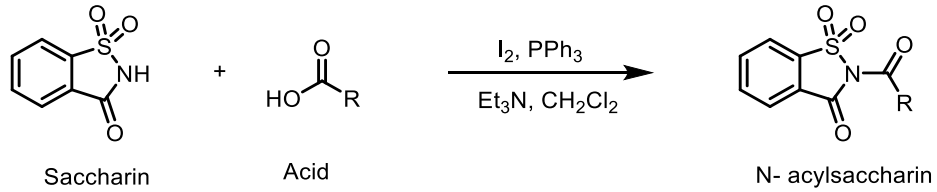
^{1}H NMR (500 MHz , DMSO *d*$_6$) δ 9.66 (s, 1H), 9.15 (s, 1H), 7.33 (d, *J* = 8.9 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 1.97 (s, 3H).

^{13}C NMR (125 MHz, DMSO *d*$_6$) δ 168.0, 153.6, 131.5, 121.2 (2C), 115.4 (2C), 24.22.

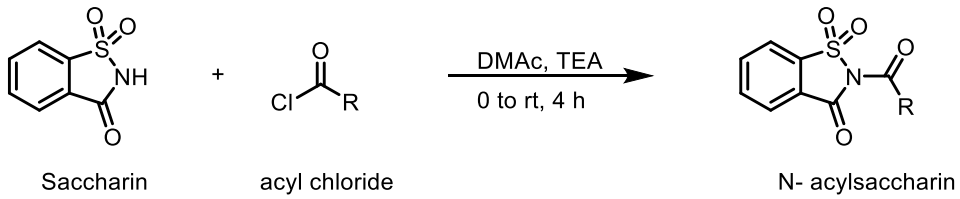
HRMS (ESI): *m/z* calculated for $C_8H_{10}NO_2$ $[M + H]^+$ 152.0712 found 152.0712.

The spectroscopic data closely match the ones previously reported in the literature[45].

General Procedure for N-Acylsaccharins Synthesis:

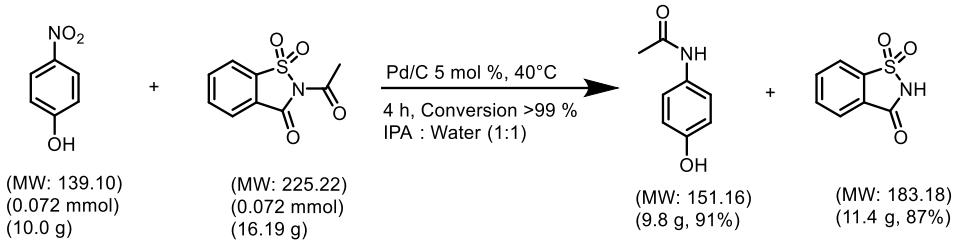


General procedure for synthesis of N-acylsaccharins from acid (III): To a stirred solution of iodine (1.50 mmol) in CH_2Cl_2 (10 mL) was added triphenylphosphine (1.50 mmol) in one portion at 0 °C. Carboxylic acid (1.00 mmol) was then added into the mixture, followed by addition of saccharin (2.00 mmol) and triethylamine (3.00 mmol) at 0 °C. The reaction mixture was allowed to warm up to room temperature and stirred until completion of the reaction. The crude mixture was concentrated under reduced pressure and then purified by column chromatography using ethyl acetate in hexane to give the desired N-acylsaccharin products.



General procedure for synthesis of N-acylsaccharins from acid chloride (IV): To a stirred solution of saccharin (1.0 eq) and NEt_3 (1.0 eq) in DMAc (10 V) was added acyl chloride (1.0 eq) at 0 °C. The mixture was stirred for 2 h and slowly poured in water (10 V) at 0 °C. The precipitate was filtered and washed with water (10 V) 0 to 5 °C and dried in vacuo to afford the acyl saccharin.

Calculation of Green Chemistry Matrix



$$\text{Atom Economy} = \frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{151.16 + 183.18}{139.10 + 225.22} \times 100 = \mathbf{91.77\ \%}$$

$$\text{Reaction Mass Efficiency} = \frac{\text{Actual Mass of desired product}}{\text{Mass of reactant}} \times 100 = \frac{151.16}{139.10 + 225.22} = \mathbf{41.49\ \%}$$

$$\text{Environmental Factor} = \frac{\text{Mass of Total Waste}}{\text{Mass of desired product}} = \frac{0}{151.16} = \mathbf{0}$$

The Eco Scale Score for the synthesis of Paracetamol

Reagents	MF	MW	G	mmol	Eq
4 nitrophenol	C6H5NO3	139.10	10.0	71.89	1.0
N-acetyl saccharin	C9H7NO4S	225.22	16.19	71.89	1.0
Product	MF	MW	G	mmol	Yield
Paracetamol	C8H9NO2	151.16	9.88	65.36	91 %

Eco Scale: 100-Penalty Points

Entry	Parameters	Penalty Points
1	Yield (91%)	-5
2	Price/availability	-10
3	safety	0
4	Technical set-up (Pressure equipment, >1 atm)	-3
5	Temperature/Time (heating;<1 h)	-2
6	Work up and purification (adding solvents)	0

The eco scale calculation source: https://ecoscale.cheminfo.org/calculator

Life Cycle Analysis Data

S Table 1a: List of Input Chemicals analysed with LCA as extended input for analysis with reference to API 1-AP9 Synthesis by NAR and AR routes

Sl. No	Names
1	Toluene
2	Chlorosulfonic acid
3	Ammonium hydroxide
4	2-methylbenzenesulfonamide
5	Periodic acid
6	Chromium trioxide
7	Acetonitrile
8	Isopropanol
9	Bromo Benzene
10	Sodium methoxide
11	Copper(I)Bromide
12	Methanol
13	Ethyl acetate
14	n-Heptane
15	Sodium thiosulfate
16	Tert-butyl hydroperoxide
17	Sulfuryl chloride
18	Anisole
19	Tetrahydrofuran
20	Saccharine
21	Benzoyl chloride
22	Triethylamine
23	N N dimethyl acetamide
24	1-methoxy-4-nitrobenzene
25	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one
26	Iron Powder
27	Potassium permanganate
28	Ammonium Chloride
29	HCl
30	$NaHCO_3$
31	Palladium (Pd/C)
32	Sodium chloride
33	nicotinic acid
34	Hydrogen peroxide
35	Phosphorous pentachloride
36	Phosphorous oxychloride
37	Acetic acid
38	2-chloropyridine-3-carboxylic acid
39	Thionyl chloride
40	2-chloropyridine-3-carbonyl chloride
41	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one
42	cyclopropanecarbonyl chloride

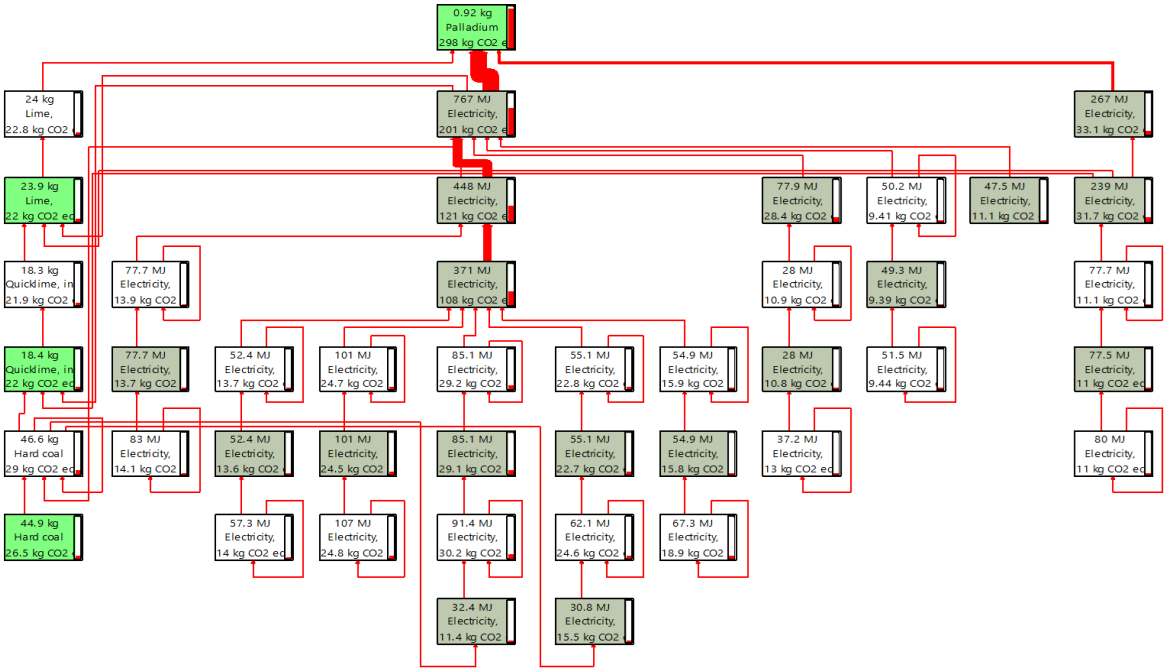
43	4-Methoxyaniline
44	Acetyl chloride
45	Dichloromethane
46	Ethyl 2-methylfuran-3-carboxylate
47	Aniline
48	Nitrobenzene
49	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one
50	2-methyl-5-nitro-1,3-benzothiazole
51	3,5-dichlorobenzamide
52	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one
53	4-nitrobenzoic acid
54	Platinum
55	2-(4-nitrophenyl) acetic acid
56	Nickel
57	Titania
58	Hydrogen gas
59	4-Nitrophenol
60	Activated Carbon
61	Potassium chloride
62	1-ethoxy-4 Nitro benzene
63	Isopropyl Alcohol
64	Ethyl 4-chlorobutanoate
65	Sodium Hydroxide
66	Dimethylacetamide
67	Pyridine
68	Acetaldehyde
69	Ethylene glycol monoethyl ether
70	2-methylfuran-3-carboxylic acid
71	N,N-dimethylformamide
72	Sodium hypochlorite
73	Chromium Oxide
74	2-Bromoaniline
75	Potassium Nitrate
76	Sulphuric acid
77	Ammonia
78	2-bromo-5-nitro-aniline
79	Acetic anhydride
80	N-(2-bromo-5-nitro-phenyl)acetamide
81	sodium sulphide
82	Sulphur
83	O-dichlorobenzene
84	Benzyl triphenyl phosphonium chloride
85	3,5-dichlorobenzoyl chloride
86	Magnetite
87	Sodium Nitrite
88	Nitric oxide
89	Sodium phenolate
90	Dimethyl sulfoxide

91	Zeolite powder
92	Phenol
93	Hexamethyldisilazane
94	Sodium fluoride

S Table 1b: List of API Chemicals

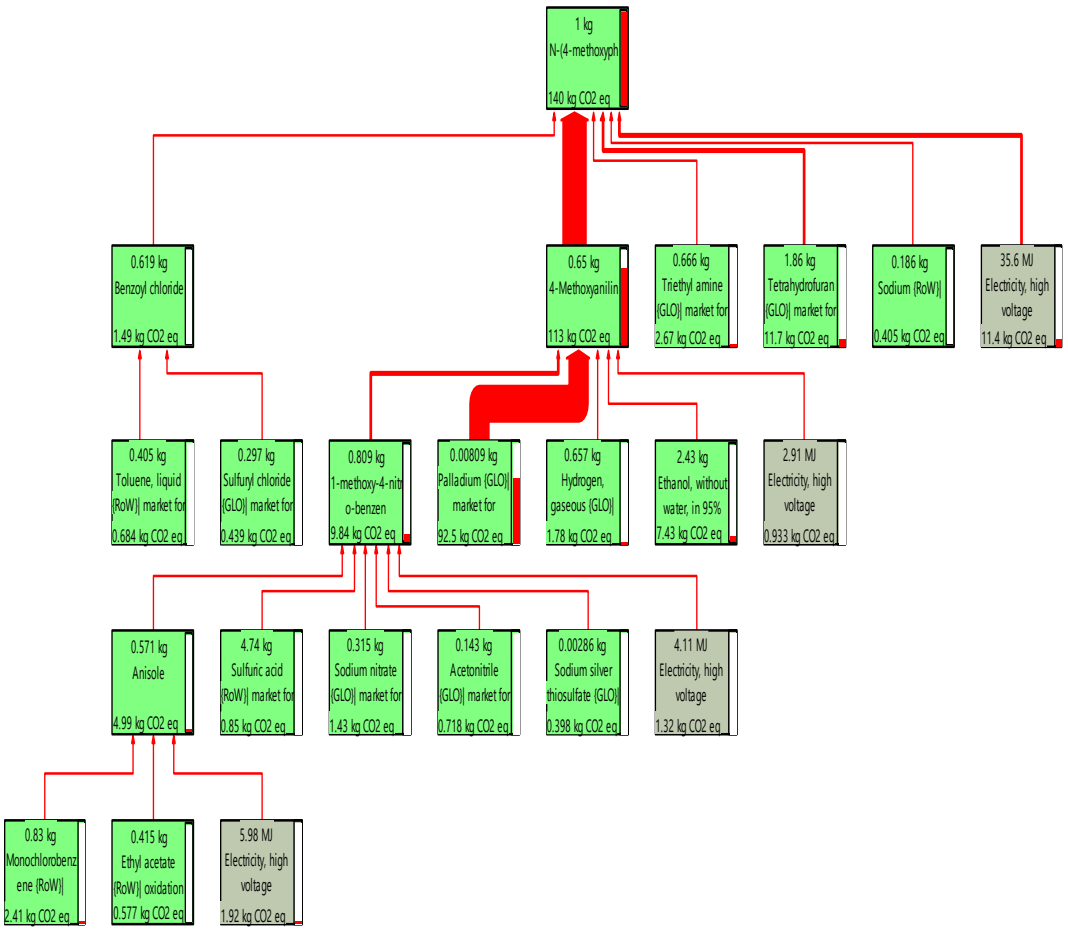
S. No	Names
API-1	N-(4-methoxyphenyl) benzamide
API-2	2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide
API-3	N-(4-methoxyphenyl) cyclopropane carboxamide
API-4	Fenfuram (2-methyl-N-phenyl-furan-3-carboxamide)
API-5	11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide)
API-6	Acedoben (4-acetamidobenzoic acid)
API-7	Actarit (*(2-(4-acetamidophenyl)acetic acid)*
API-8	Paracetamol (N-(4-hydroxyphenyl) acetamide)
API-9	Phenacetin (N-(4-ethoxy phenyl) acetamide)

Life Cycle Analysis Data (API 1-9)

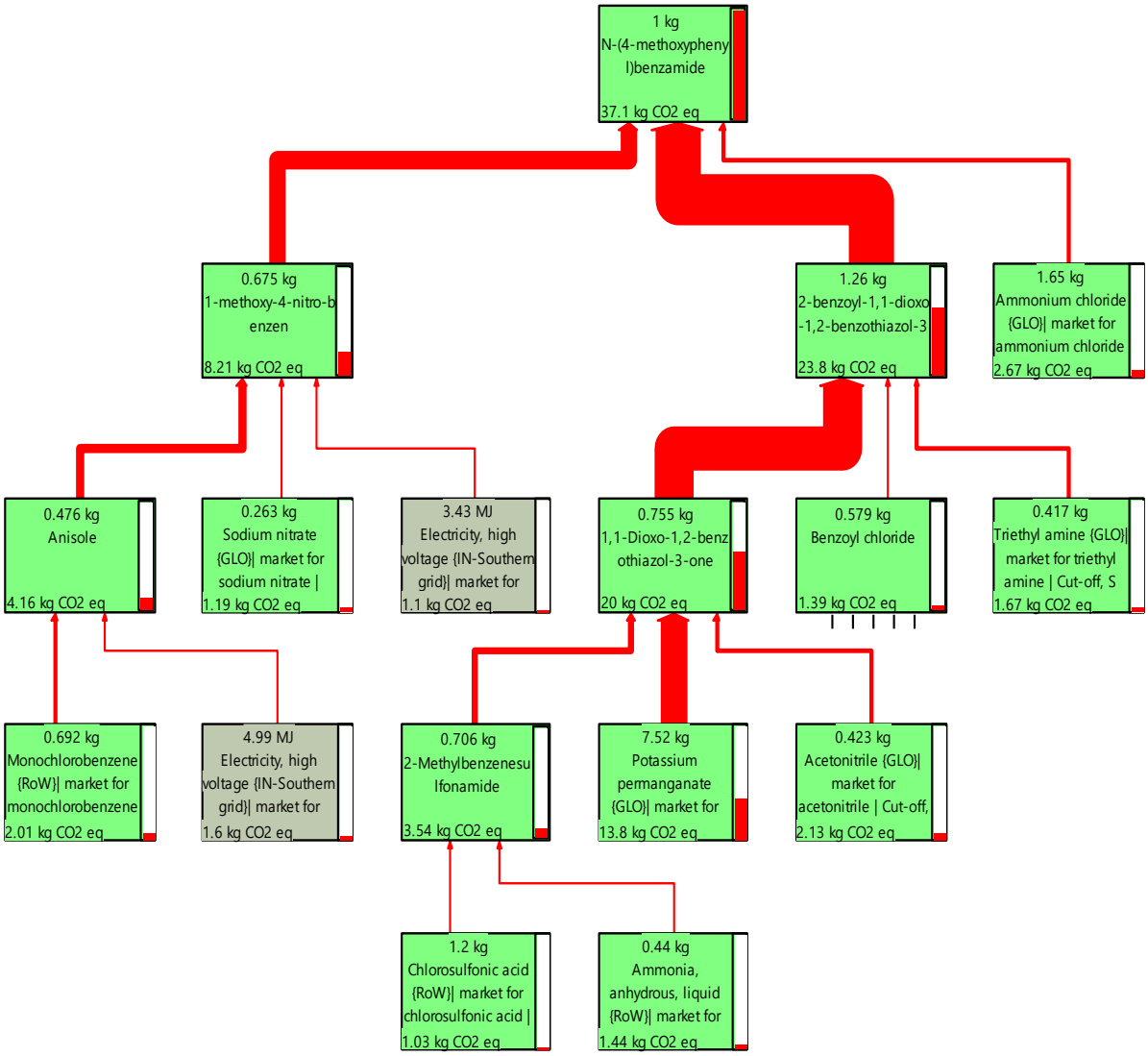


S Fig. 1a: Sankey diagram of the Palladium catalyst: The Sankey diagram illustrates the synthesis of a palladium catalyst (0.92 kg), essential for the preparation of paracetamol (N-(4-hydroxyphenyl) acetamide) within the NAR process. The entire synthesis process for the palladium catalyst results in emissions of 298 kg CO_2 eq. A significant portion of this global warming potential (GWP) stems from the energy consumption required during synthesis, which amounts to 767 MJ and contributes 201 kg CO2 eq. This substantial energy use highlights the critical environmental impact associated with the production of the palladium catalyst, underscoring its role as a major contributor to CO_2 emissions in the overall process. The Sankey diagram effectively envisions these impacts, providing clear insights into the areas where improvements can be made to enhance the sustainability of paracetamol production.

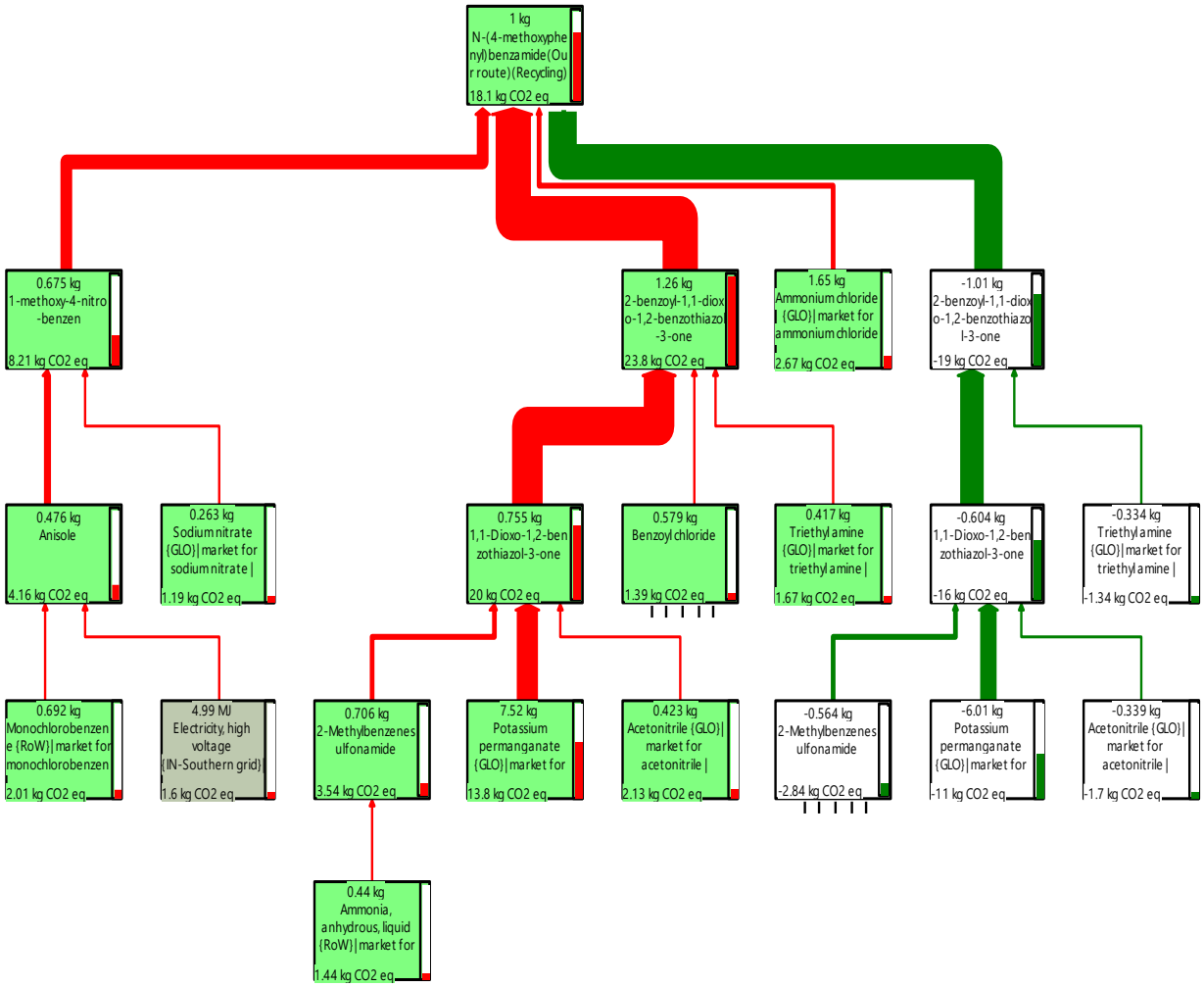
API-1: N-(4-methoxyphenyl) benzamide



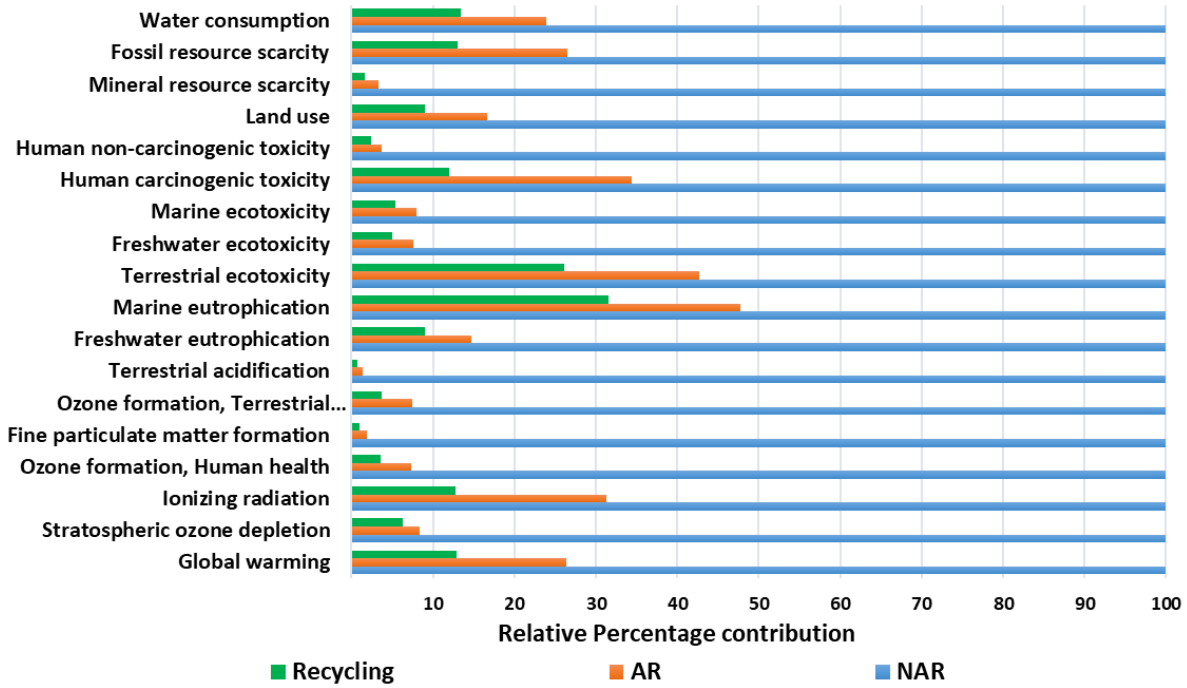
S Fig. 2a: Sankey diagram of NAR process of N-(4-methoxyphenyl) benzamide synthesis: The Sankey diagram represents the synthesis of N-(4-methoxyphenyl) benzamide in the NAR process, which results in the emission of 140 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 4-methoxyaniline (0.65 kg), used as a secondary starting material, which emits 113 kg CO_2 eq., making it a significant CO_2 contributor.



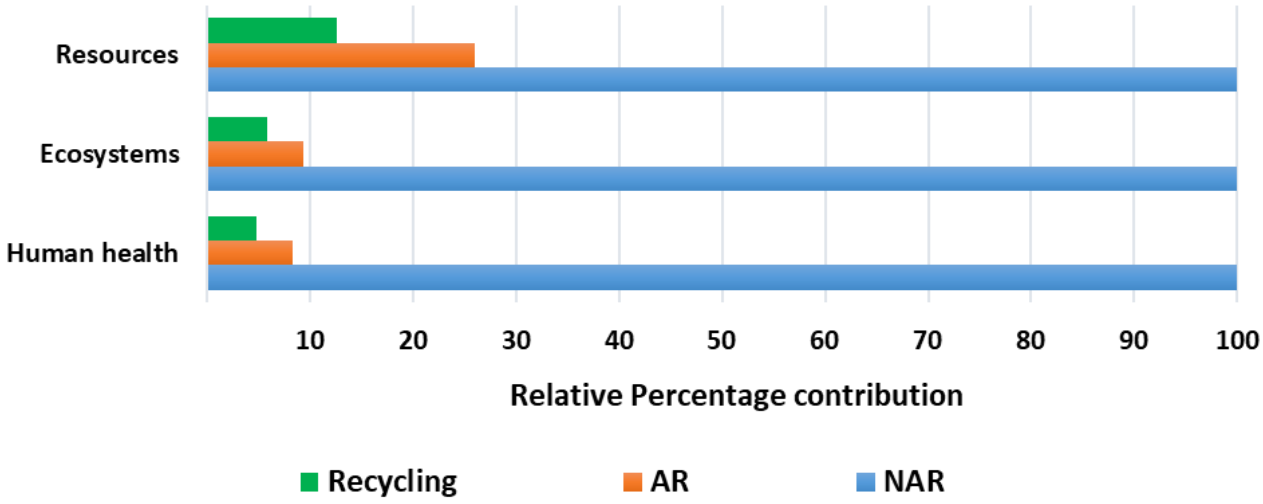
S Fig. 2b: Sankey diagram of AR process of N-(4-methoxyphenyl) benzamide synthesis: The Sankey diagram represents the synthesis of N-(4-methoxyphenyl) benzamide in the AR process, which emits 37.1 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-benzoyl-1,1-dioxo-1,2-benzothiazole-3-one (1.26 kg), used as a secondary starting material, which emits 23.8 kg CO_2 eq., making it a significant CO_2 contributor.



S Fig. 2c: Sankey diagram of the recycling process of N-(4-methoxyphenyl) benzamide synthesis: The Sankey diagram represents the synthesis of N-(4-methoxyphenyl) benzamide in the recycling process, which emits 18.1 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-benzoyl-1,1-dioxo-1,2-benzothiazole-3-one (1.26 kg), used as a secondary starting material, which emits 4.8 kg CO_2 eq. after recycling. This is followed by the starting material 1-methoxy-4-nitrobenzene.

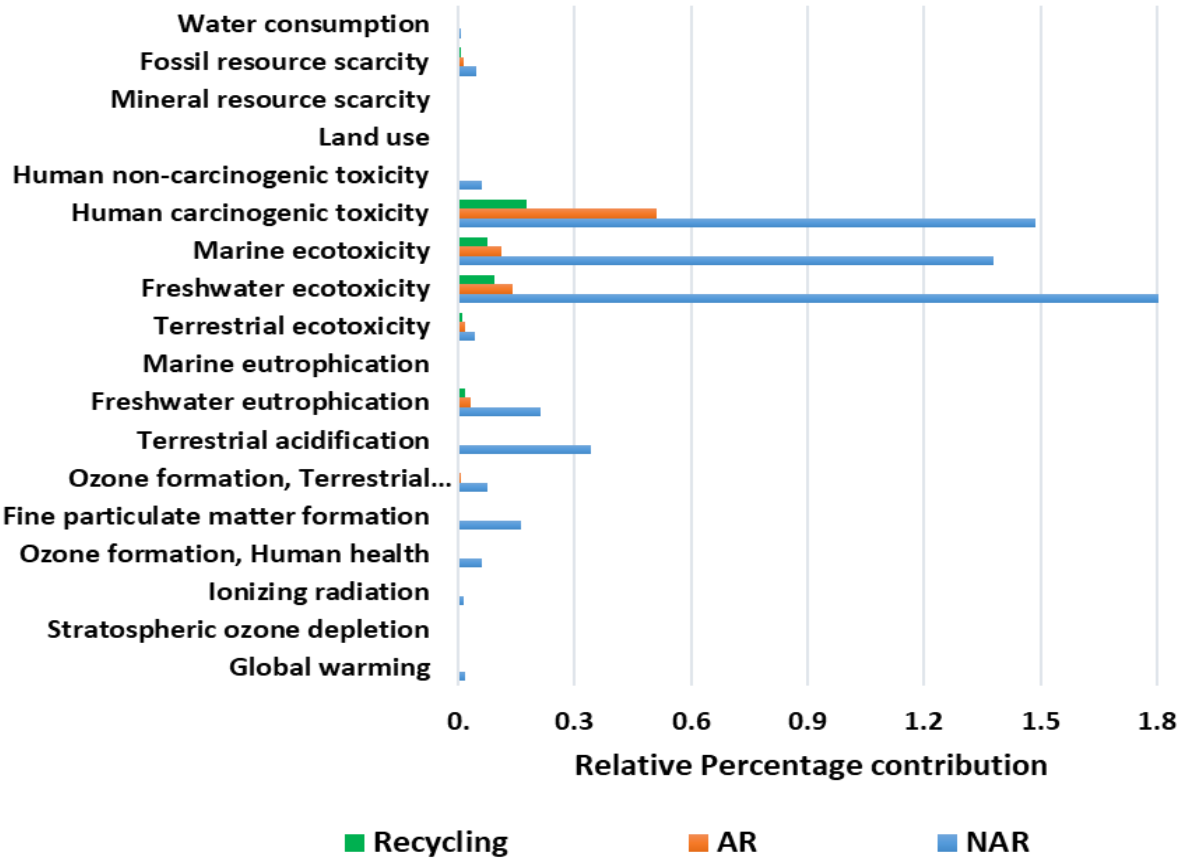


S Fig. 2d: Comparison of Midpoint category for NAR, AR, and Recycling for N-(4-methoxyphenyl) benzamide synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis of N-(4-methoxyphenyl) benzamide. Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing N-(4-methoxyphenyl) benzamide.



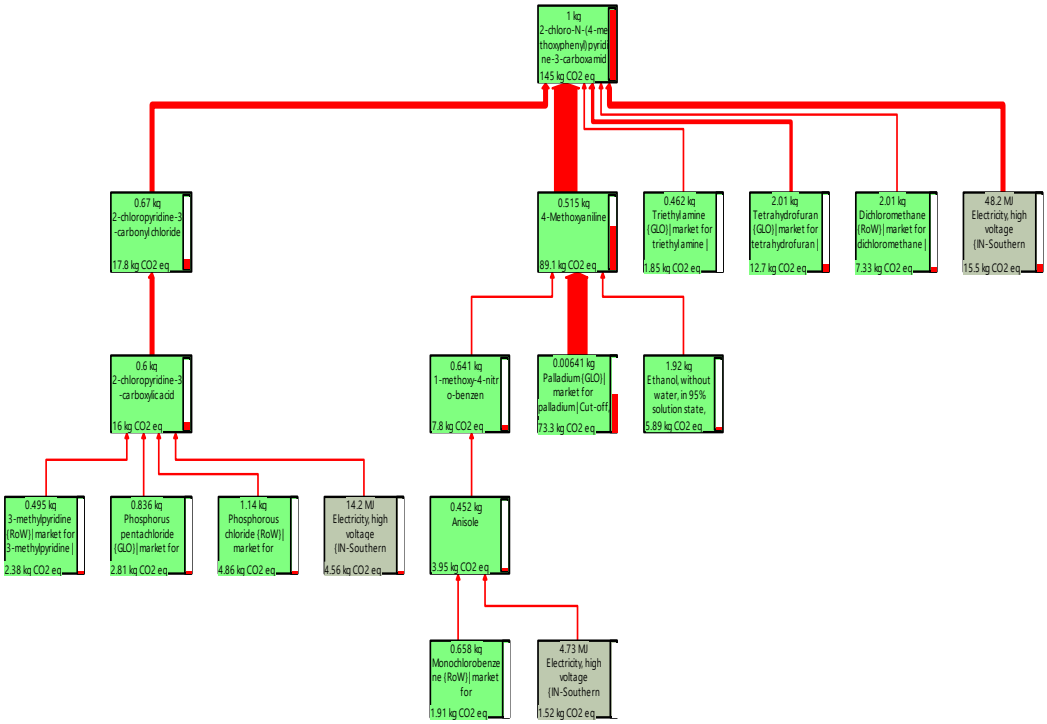
S Fig. 2e: Comparison of Endpoint category for NAR, AR, and Recycling for N-(4-methoxyphenyl) benzamide synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of N-(4-methoxyphenyl) benzamide. Each endpoint

category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing N-(4-methoxyphenyl) benzamide.

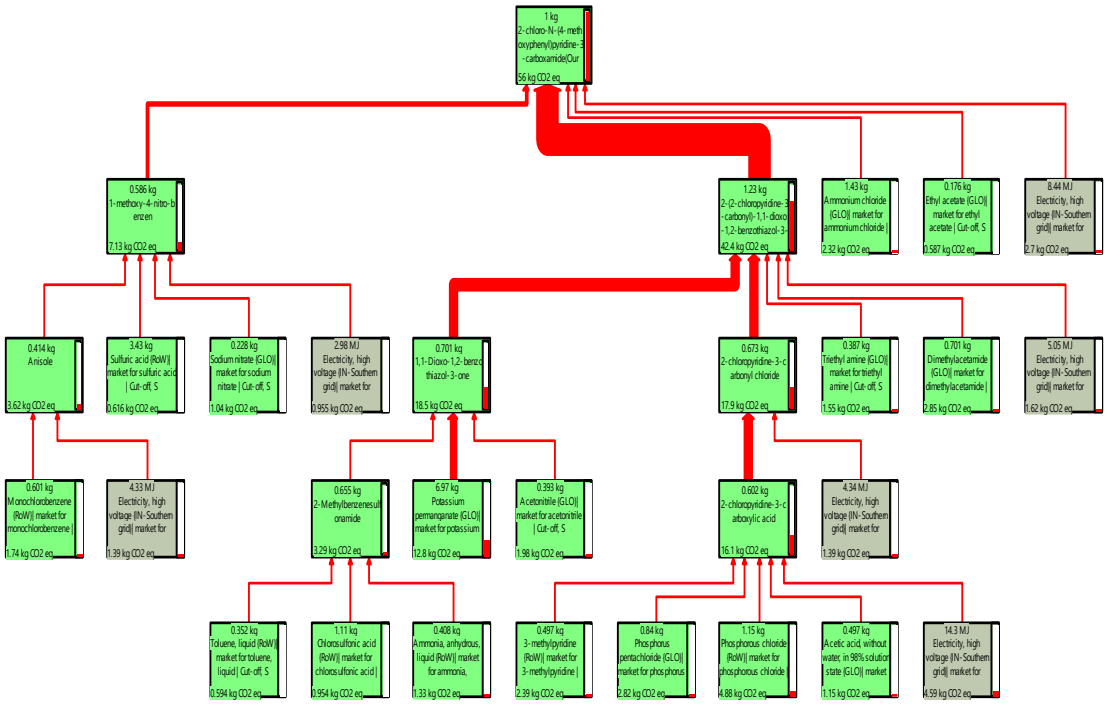


S Fig. 2f: Comparison of Normalization category for NAR, AR, and Recycling for N-(4-methoxyphenyl) benzamide synthesis: The diagram illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of N-(4-methoxyphenyl) benzamide. Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing N-(4-methoxyphenyl) benzamide.

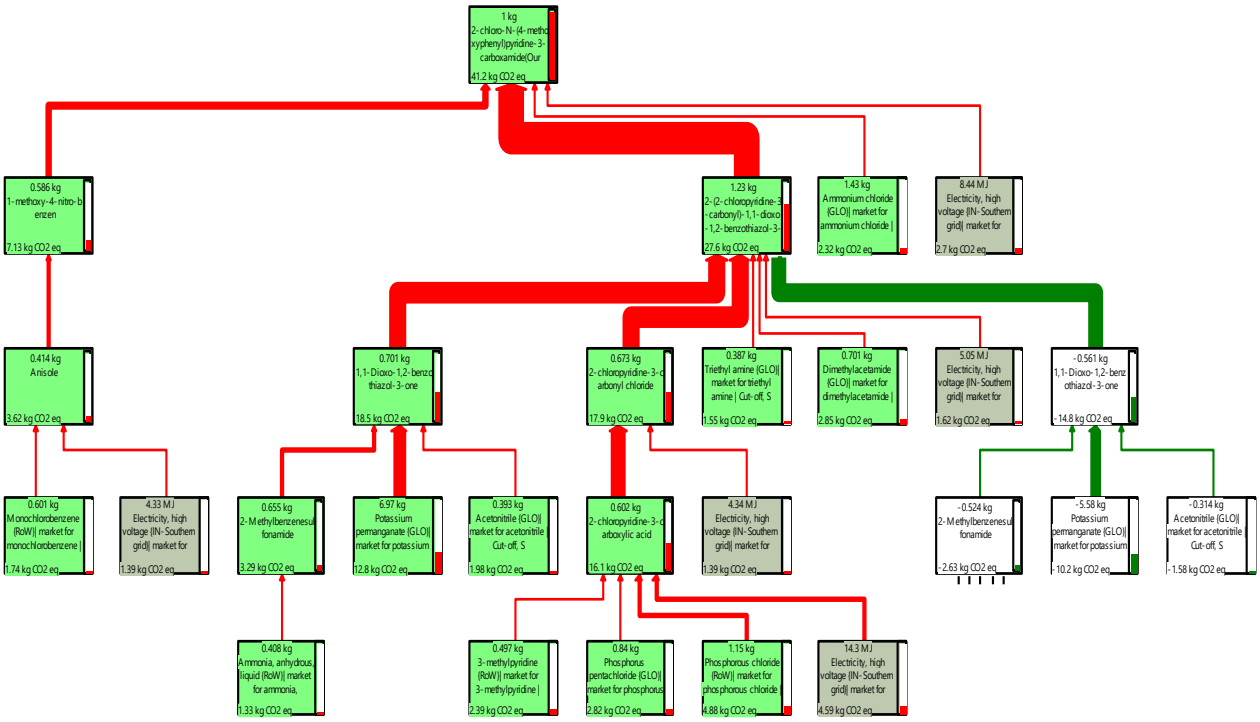
API-2: 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide



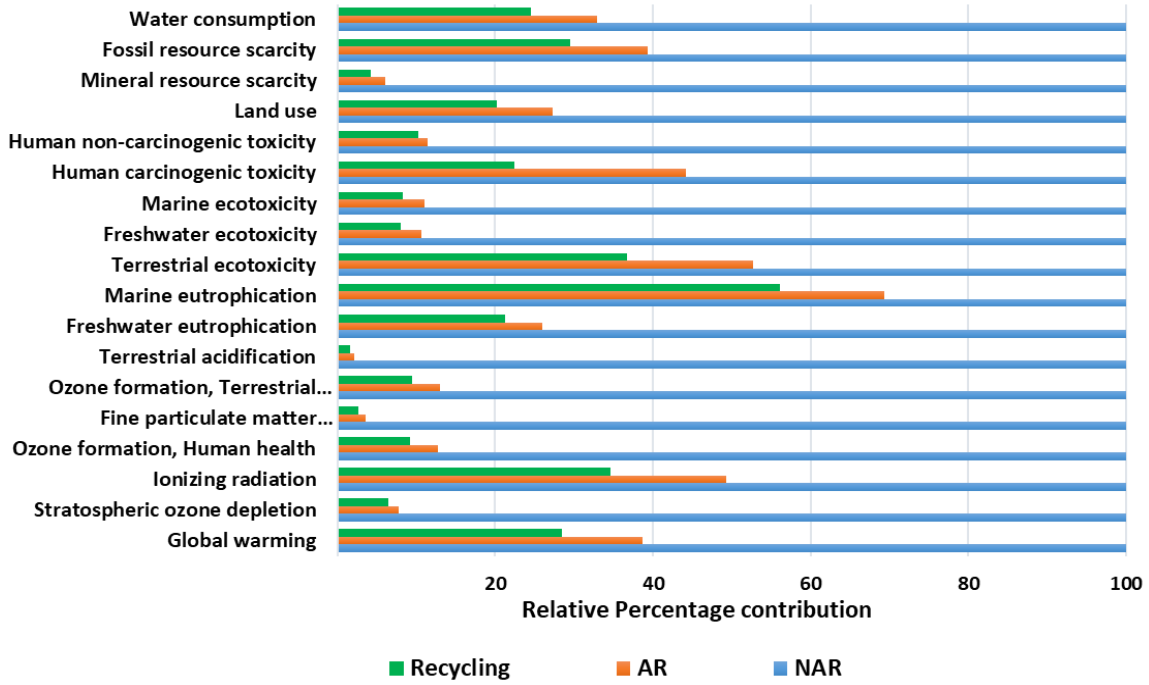
S Fig. 3a: Sankey diagram of NAR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The Sankey diagram represents the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide in the NAR process, which results in the emission of 145 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 4-methoxyaniline (0.515 kg), used as a secondary starting material, which emits 89.1 kg CO_2 eq., making it a significant CO_2 contributor.



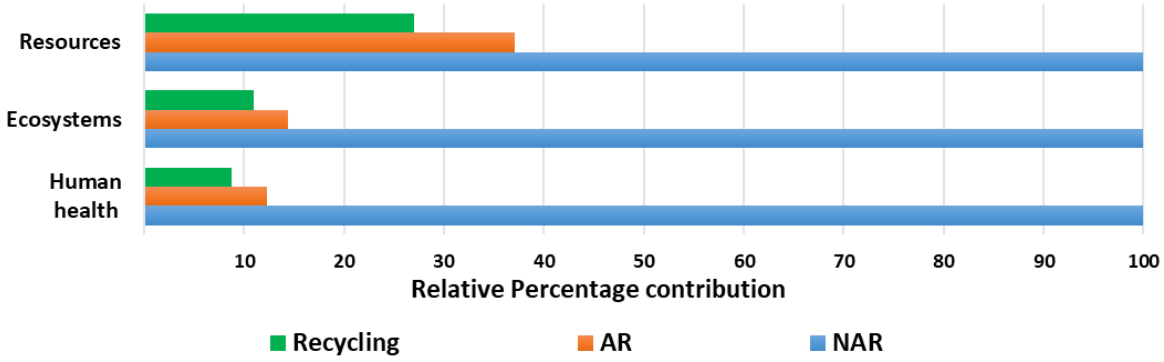
S Fig. 3b: Sankey diagram of AR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The Sankey diagram represents the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide in the AR process, which emits 56 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.23 kg), used as a secondary starting material, which emits 42.4 kg CO_2 eq., making it a significant CO_2 contributor.



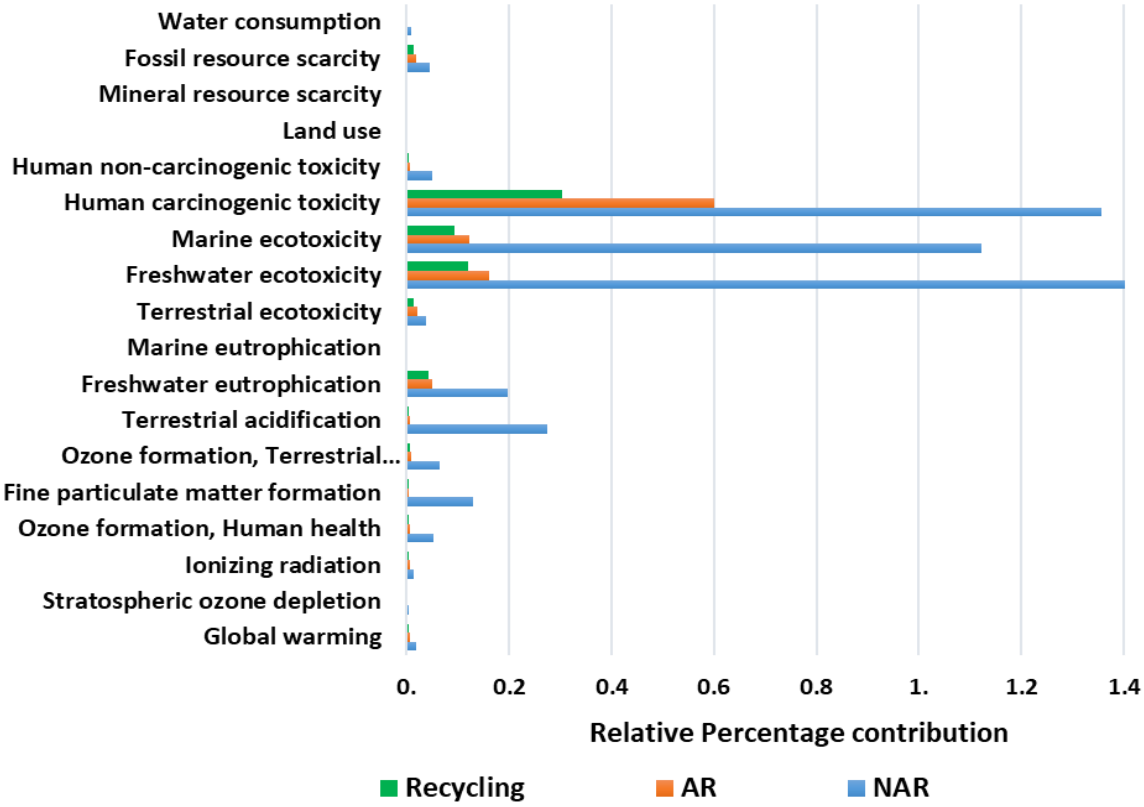
S Fig. 3c: Sankey diagram of AR process after recycling for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The Sankey diagram represents the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide in the recycling process, which emits 18.1 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (0.547 kg), used as a secondary starting material, which emits 27.6 kg CO_2 eq. after recycling. This is followed by the starting material 1-methoxy-4-nitrobenzene.



S Fig. 3d: Comparison of Midpoint category for NAR, AR, and Recycling for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide. Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide.

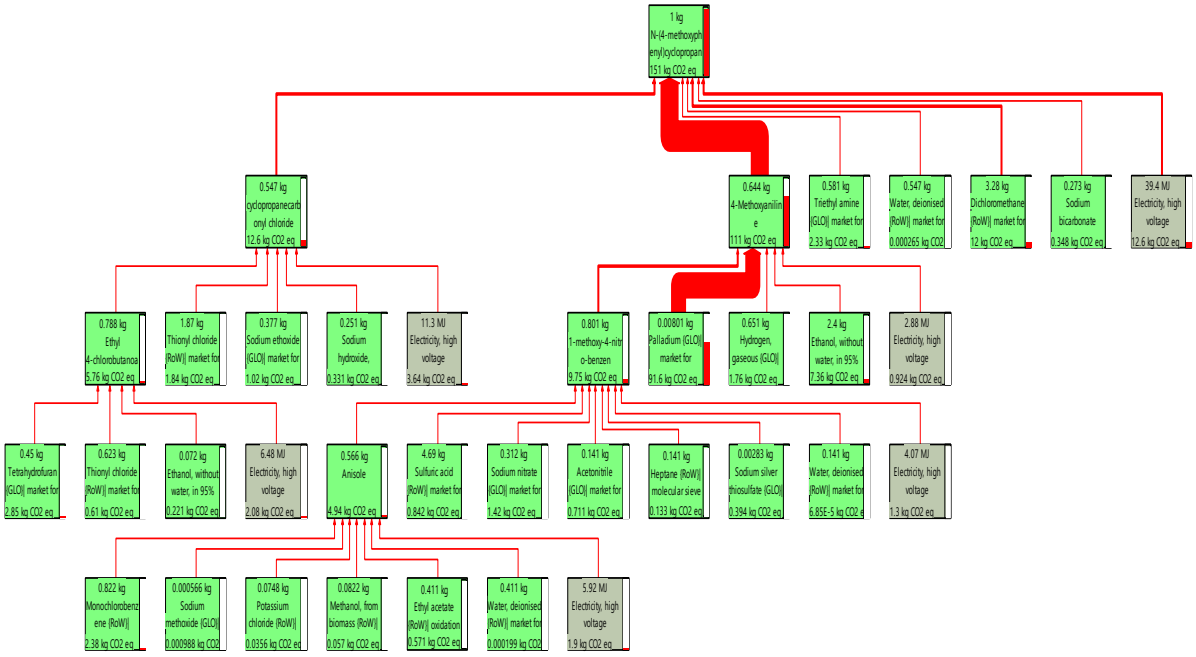


S Fig. 3e: Comparison of Endpoint category for NAR, AR, and Recycling for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide. Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide.

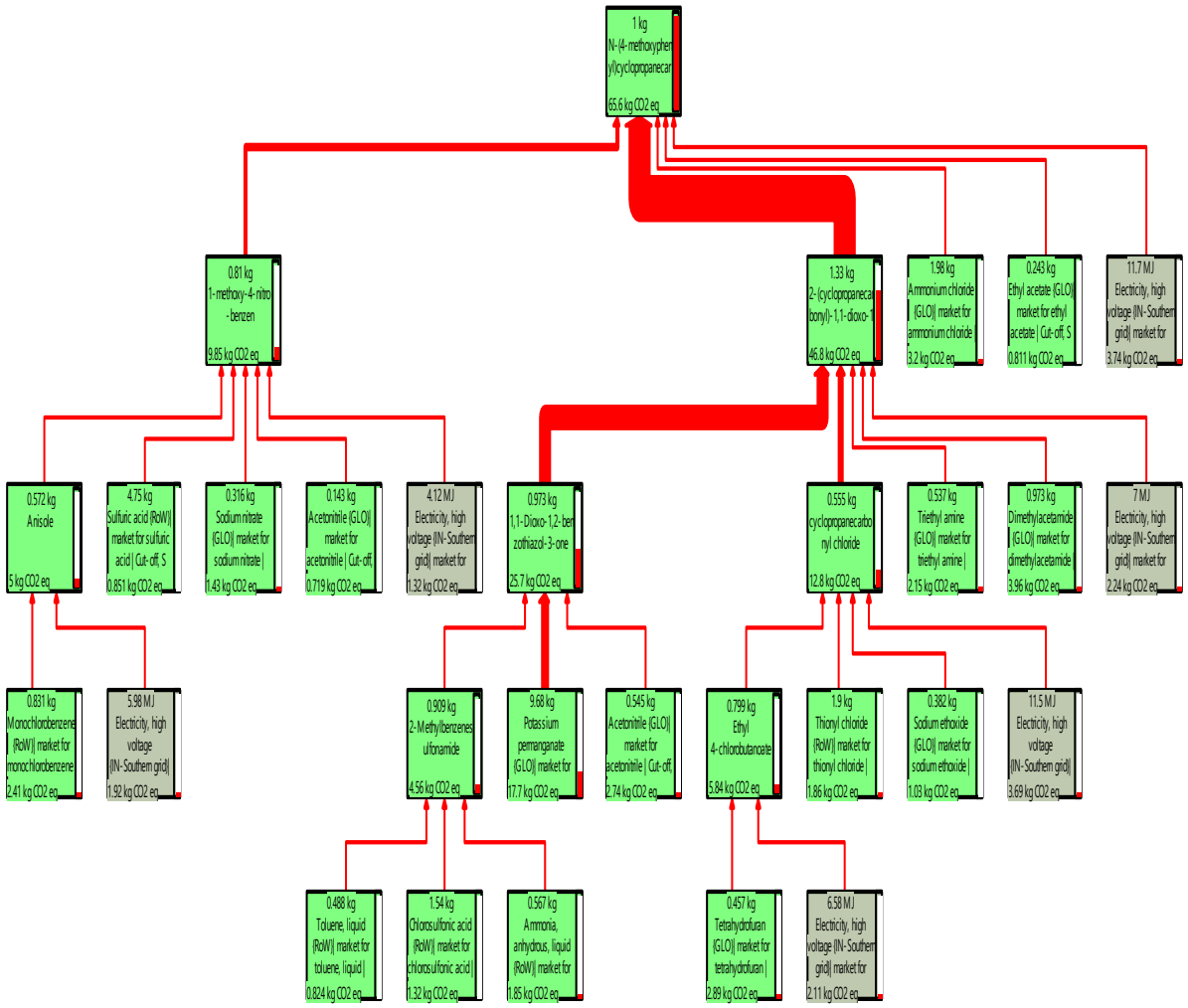


S Fig. 3f: Comparison of Normalization category for NAR, AR, and Recycling for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis: The diagram illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide. Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide.

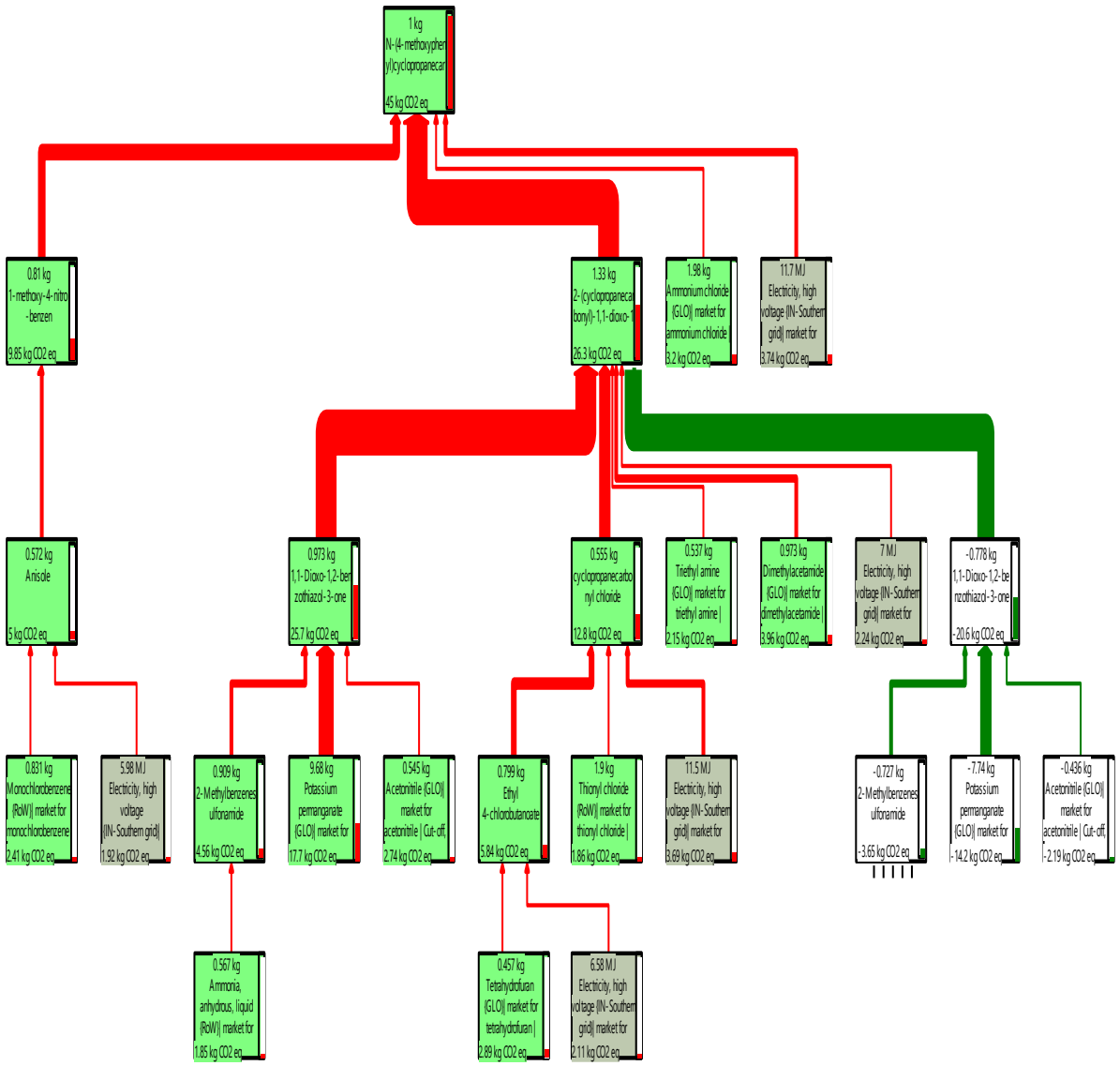
S API-3: N-(4-methoxyphenyl) cyclopropane carboxamide synthesis



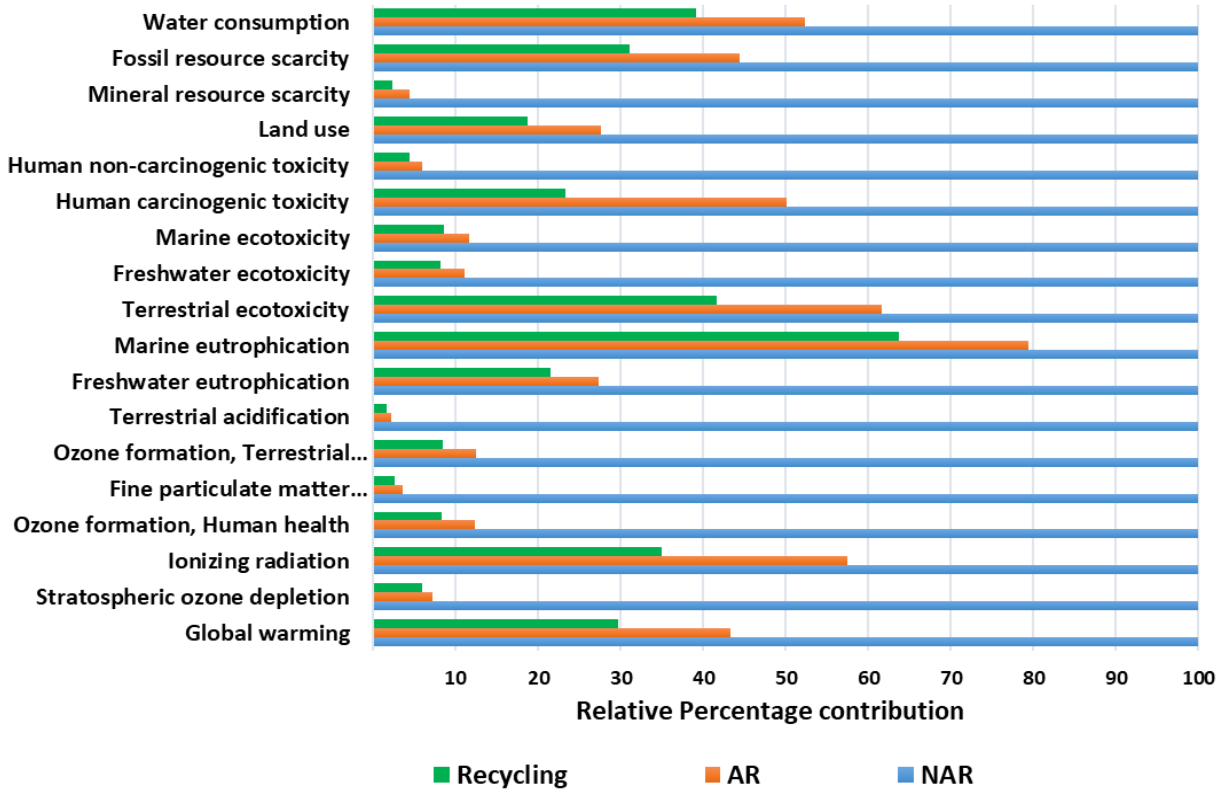
S Fig. 4a: Sankey diagram of NAR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The Sankey diagram represents the synthesis of N-(4-methoxyphenyl) cyclopropane carboxamide in the NAR process, which results in the emission of 151 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 4-methoxyaniline (0.644 kg), used as a secondary starting material, which emits 111 kg CO_2 eq., making it a significant CO_2 contributor.



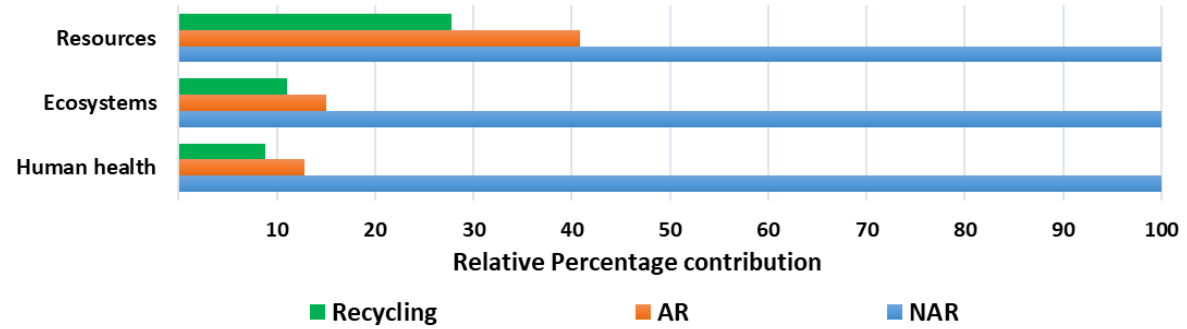
S Fig. 4b: Sankey diagram of AR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The Sankey diagram represents the synthesis of N-(4-methoxyphenyl) cyclopropane carboxamide in the AR process, which emits 65.6 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.33 kg), used as a secondary starting material, which emits 46.4 kg CO_2 eq., making it a significant CO_2 contributor.



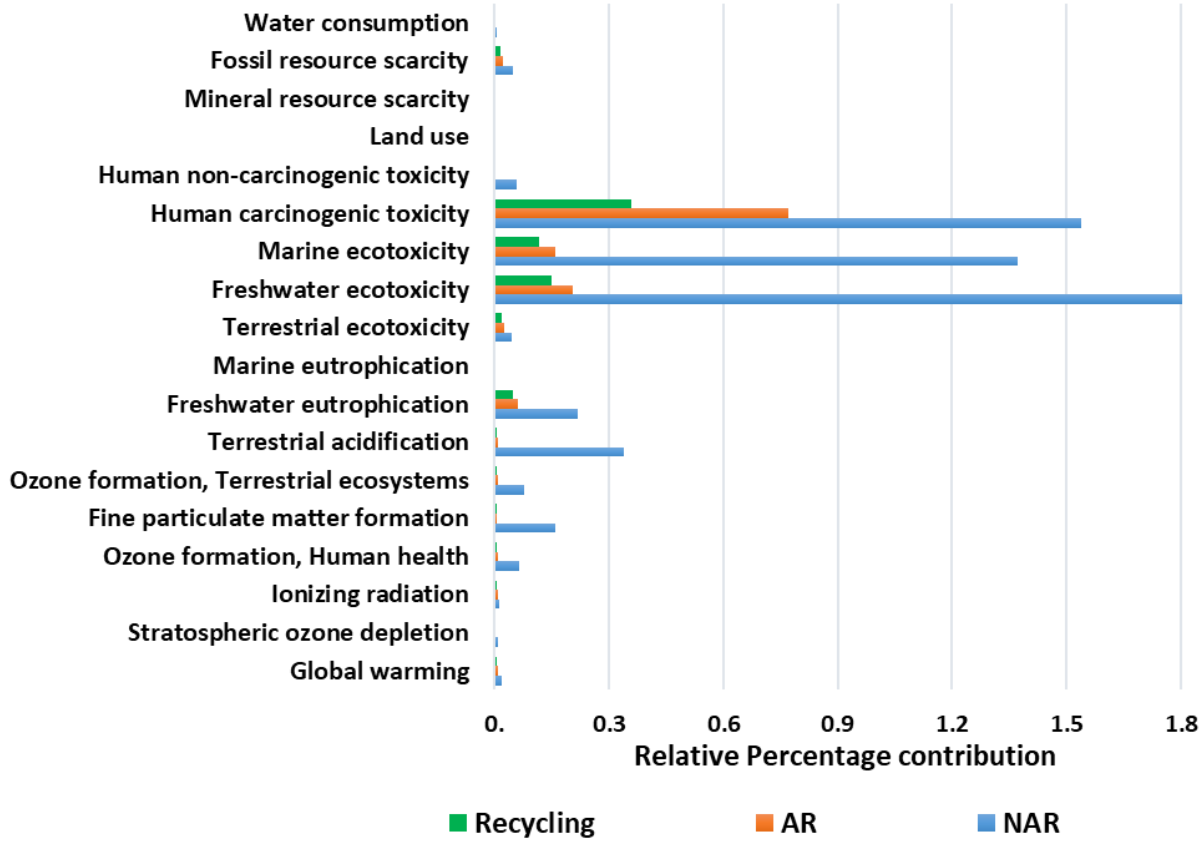
S Fig. 4c: Sankey diagram of AR process after recycling for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The Sankey diagram represents the synthesis of 2 N-(4-methoxyphenyl) cyclopropane carboxamide in the recycling process, which emits 45 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one, used as a secondary starting material, which emits 26.3 kg CO_2 eq. after recycling. This is followed by the starting material 1-methoxy-4-nitrobenzene.



S Fig. 4d: Comparison of Midpoint category for NAR, AR, and Recycling for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The figure illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis N-(4-methoxyphenyl) cyclopropane carboxamide. Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing 2 N-(4-methoxyphenyl) cyclopropane carboxamide

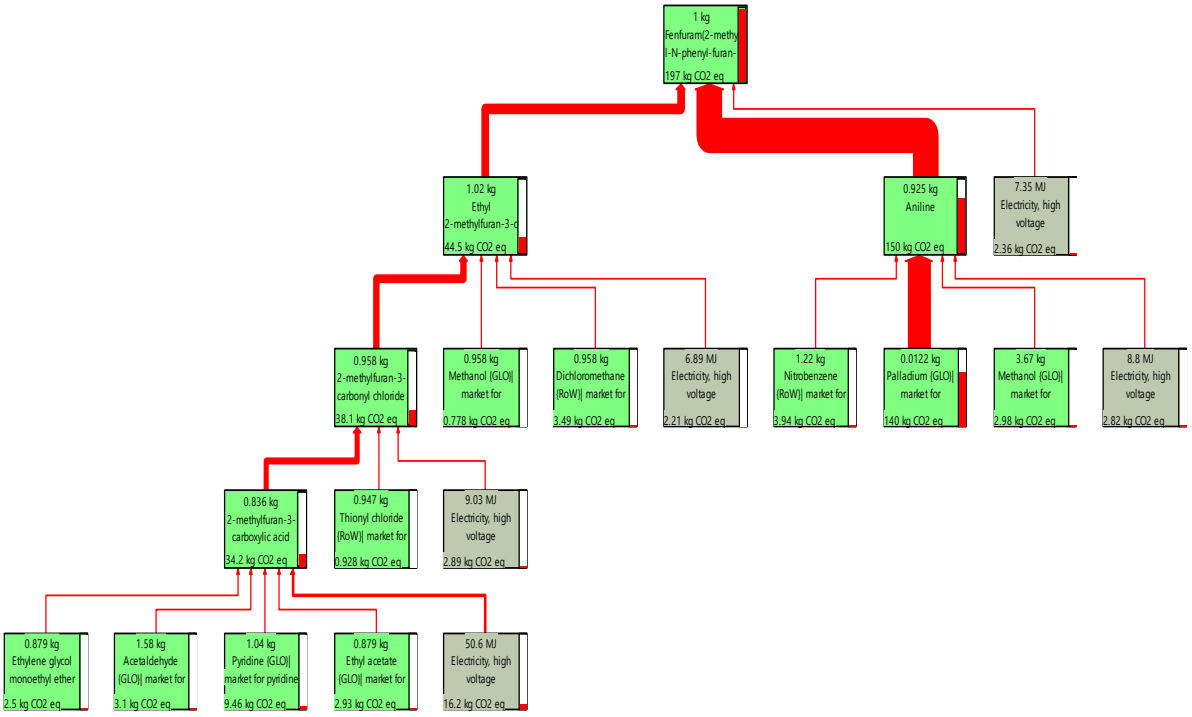


S Fig. 4e: Comparison of Endpoint category for NAR, AR, and Recycling for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The figure illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of N-(4-methoxyphenyl) cyclopropane carboxamide. Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing N-(4-methoxyphenyl) cyclopropane carboxamide

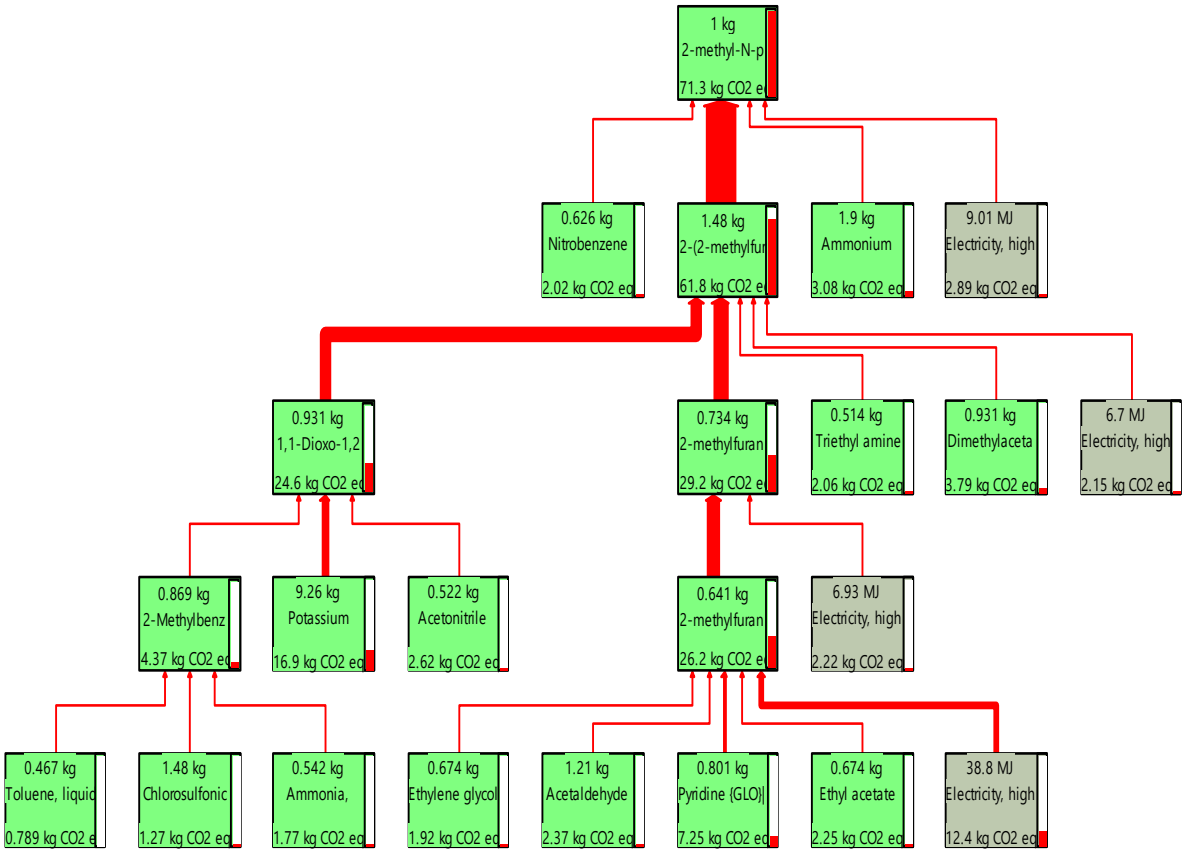


S Fig. 4f: Comparison of Normalization category for NAR, AR, and Recycling for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis: The figure illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of N-(4-methoxyphenyl) cyclopropane carboxamide. Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing N-(4-methoxyphenyl) cyclopropane carboxamide.

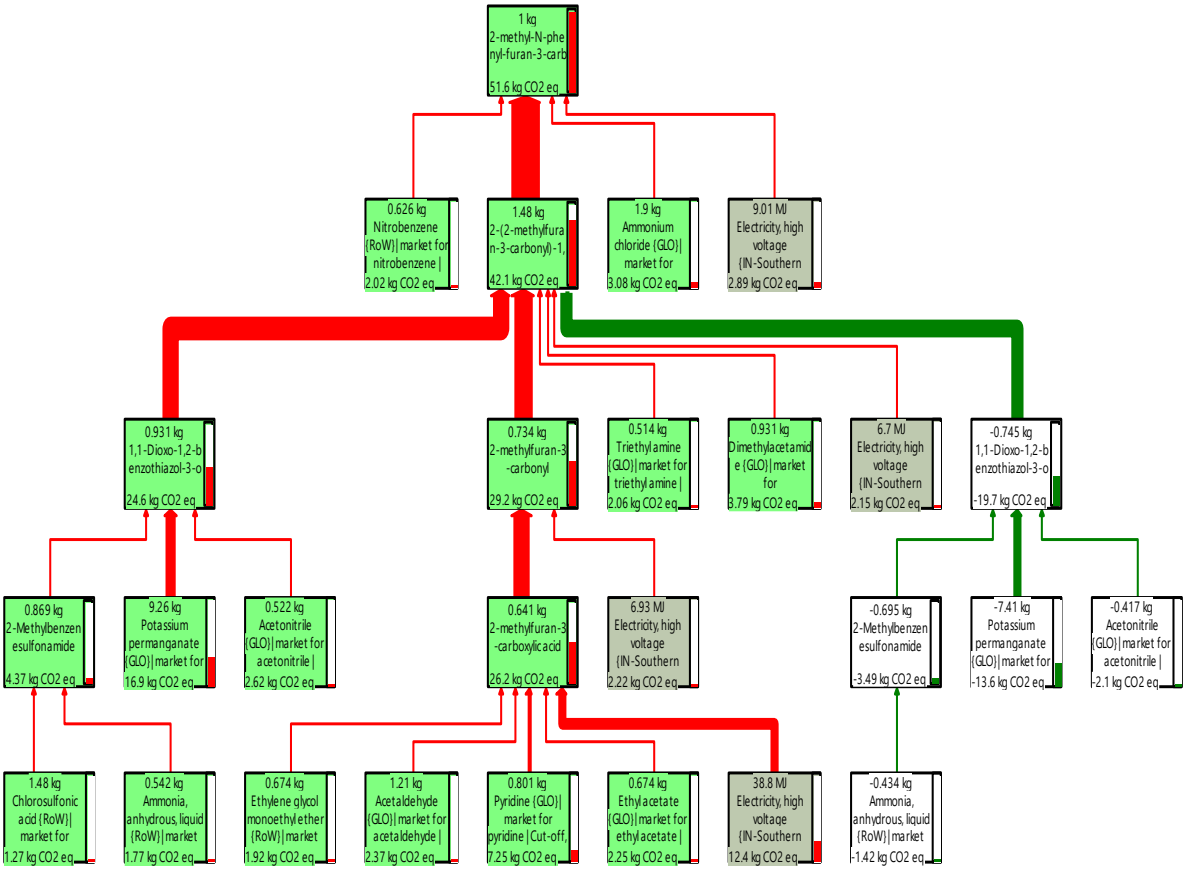
API-4: Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide) synthesis



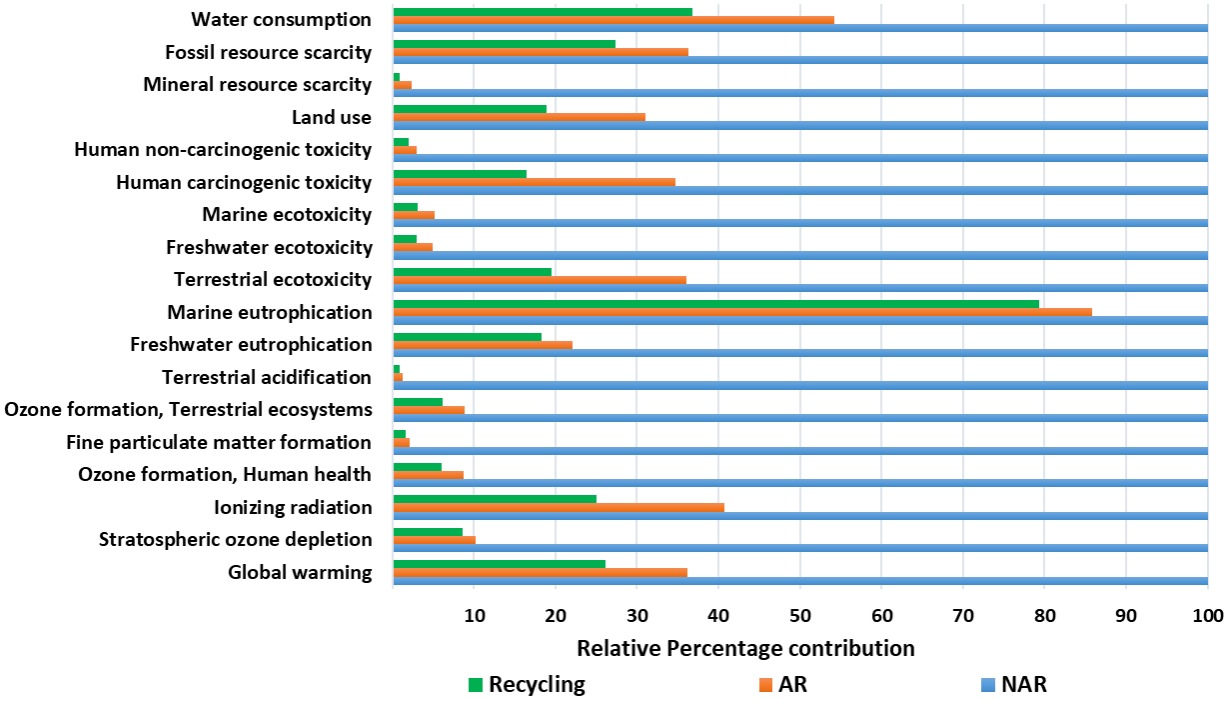
S Fig. 5a: Sankey diagram of NAR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The Sankey diagram represents the synthesis of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide) in the NAR process, which results in the emission of 197 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is Aniline (0.925 kg), used as a secondary starting material, which emits 150 kg CO_2 eq., making it a significant CO_2 contributor.



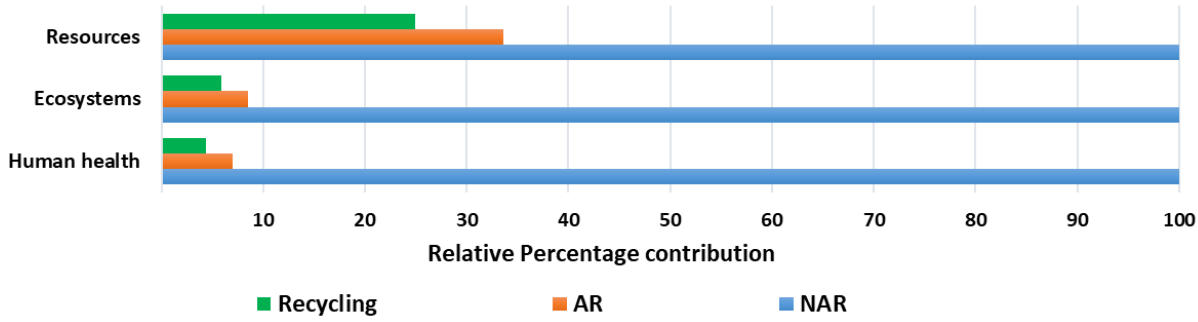
S Fig. 5b: Sankey diagram of AR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The Sankey diagram represents the synthesis of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide) in the AR process, which emits 71.3 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.48 kg), used as a secondary starting material, which emits 61.8 kg CO_2 eq., making it a significant CO_2 contributor.



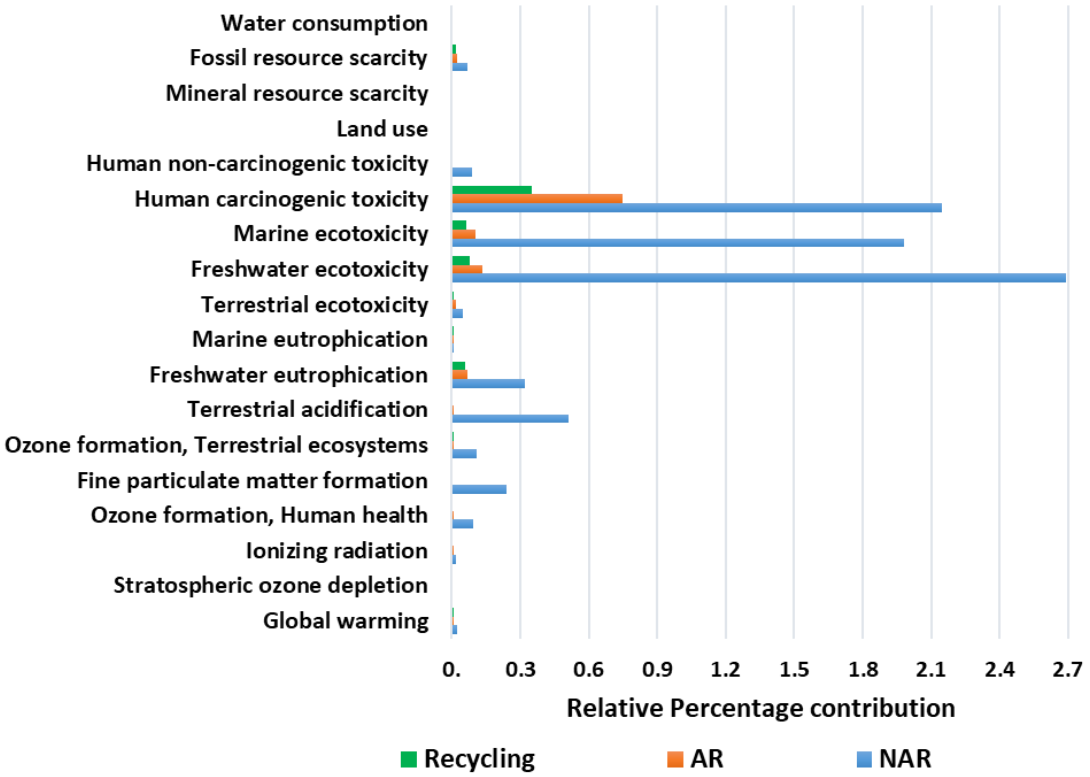
S Fig. 5c: Sankey diagram of the recycling for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The Sankey diagram represents the synthesis of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide) in the recycling process, which emits 51.6 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one, used as a secondary starting material, which emits 42.1 kg CO_2 eq. after recycling. This is followed by the starting material nitrobenzene.



S Fig. 5d: Comparison of Midpoint category for NAR, AR, and Recycling for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide). Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide).

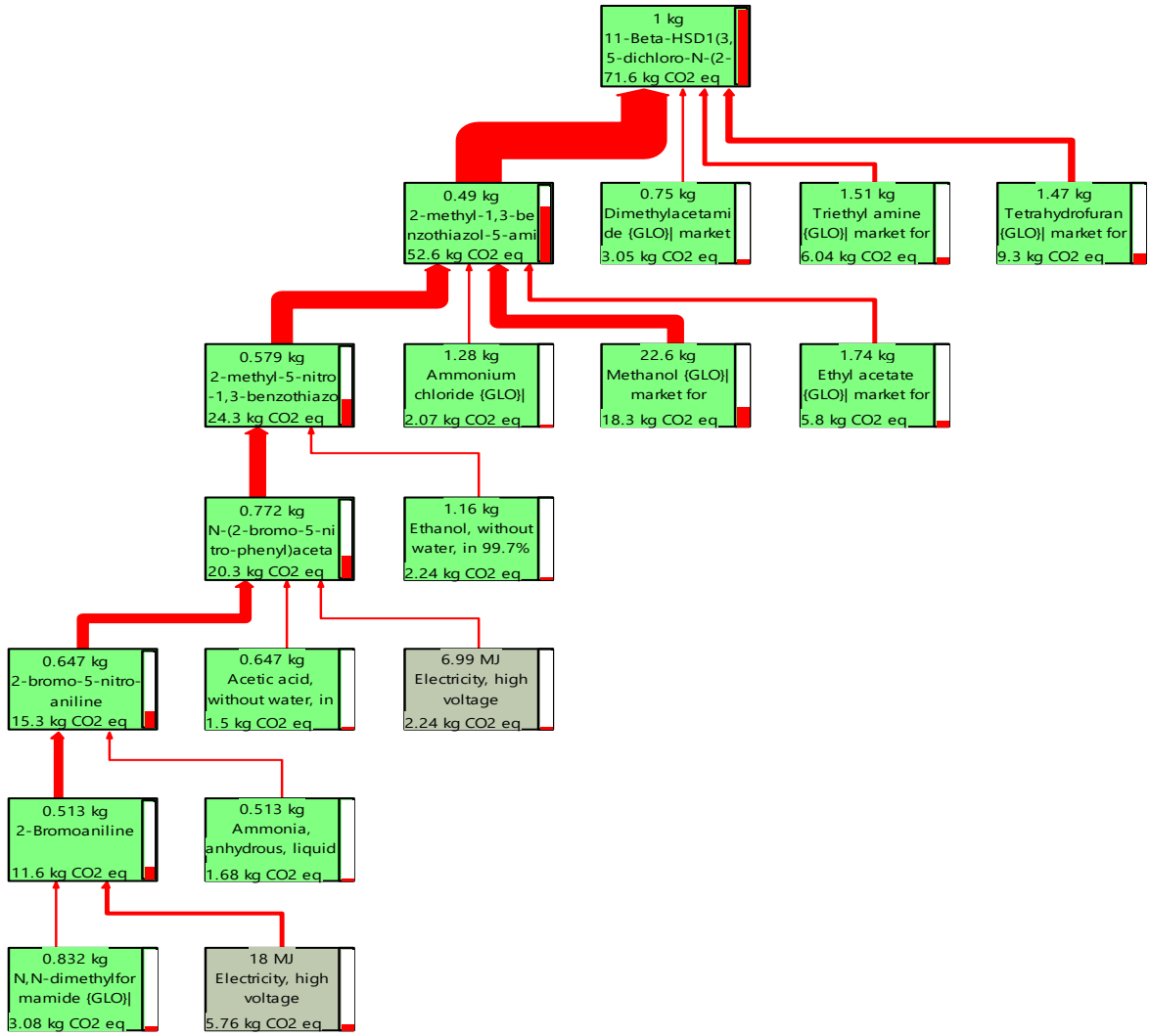


S Fig. 5e: Comparison of Endpoint category for NAR, AR, and Recycling for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide). Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide).

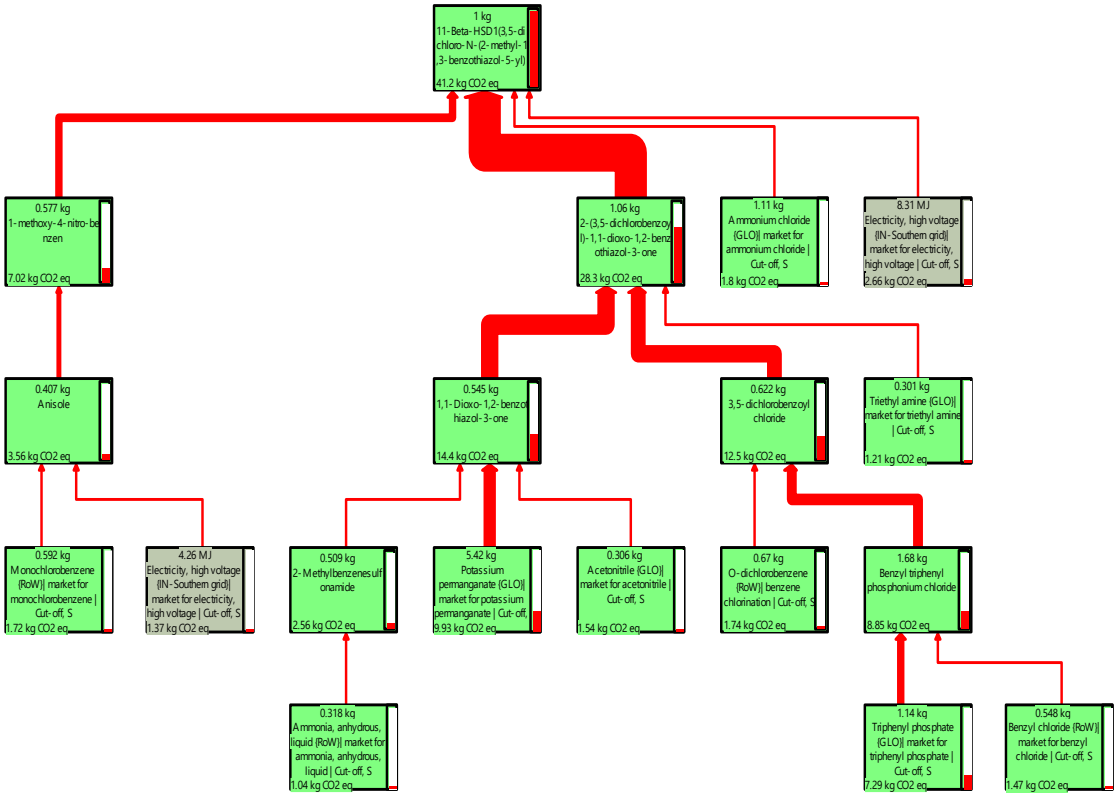


S Fig. 5f: Comparison of Normalization category for NAR, AR, and Recycling for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis: The figure illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide). Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide).

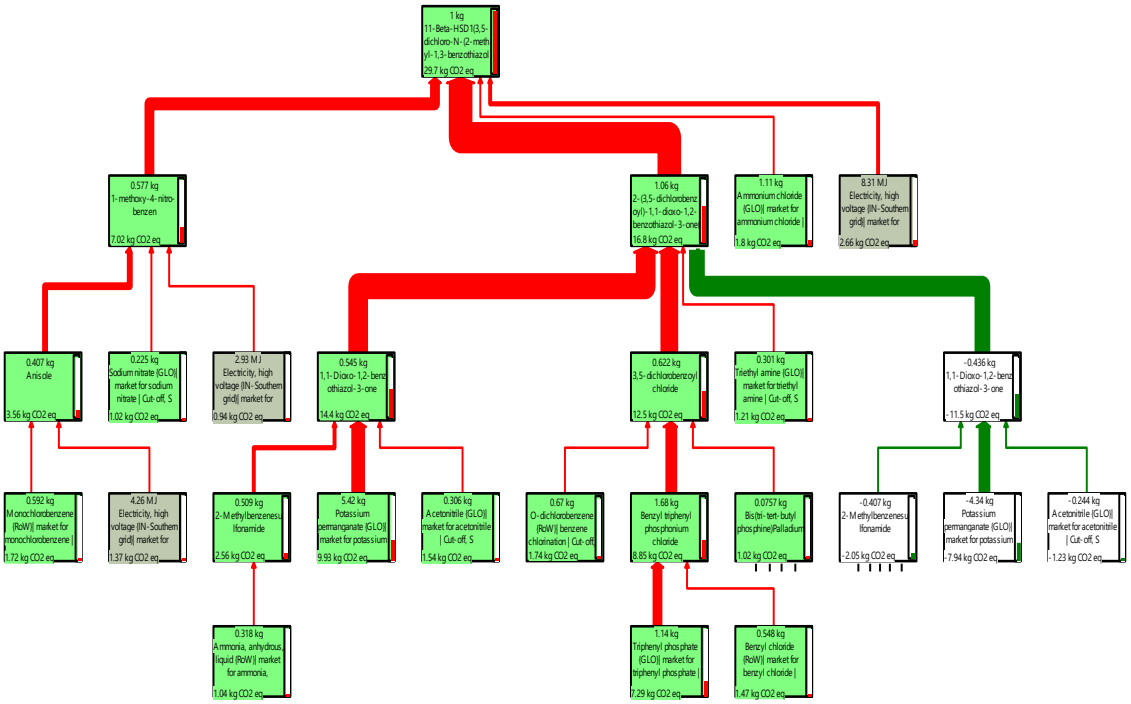
API-5: 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide) synthesis



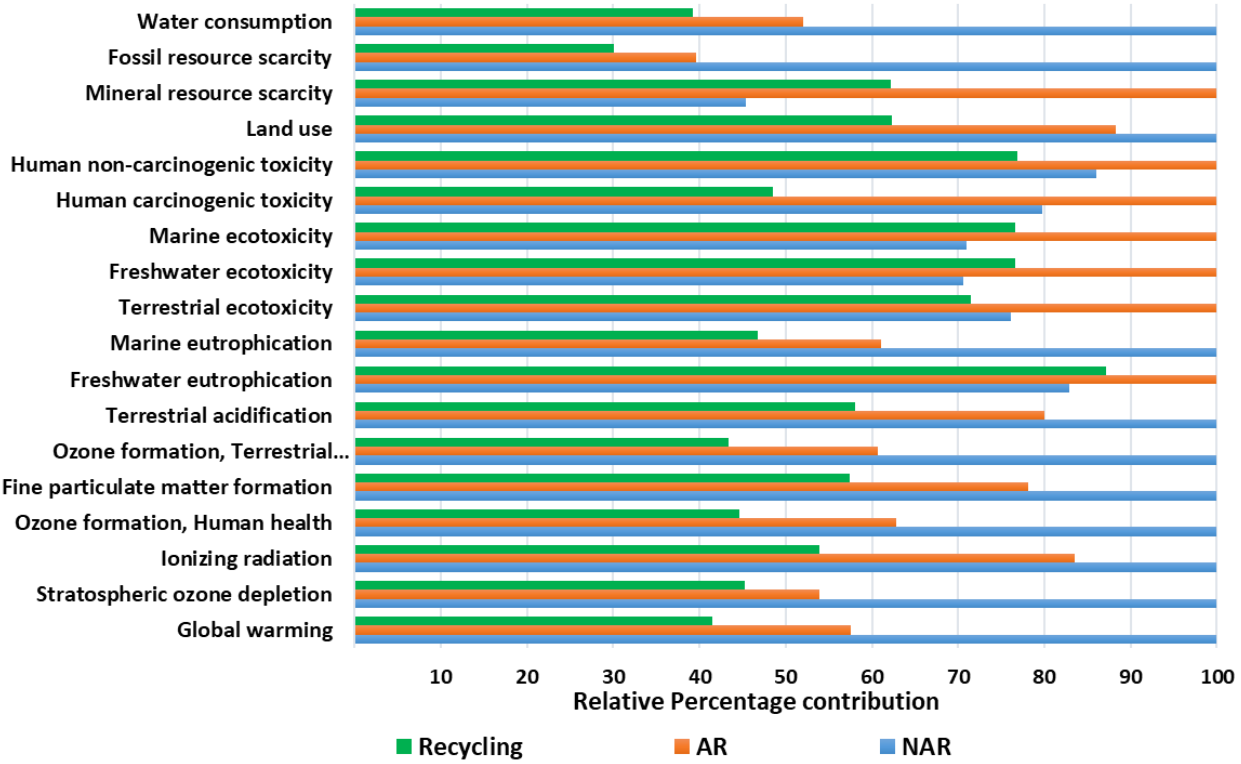
S Fig. 6a: Sankey diagram of NAR process for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The Sankey diagram represents the synthesis of 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide) in the NAR process, which results in the emission of 71.6 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-methyl-5-nitro-1,3-benzothiazole (0.49 kg), used as a starting material, which emits 52.6 kg CO_2 eq., making it a significant CO_2 contributor.



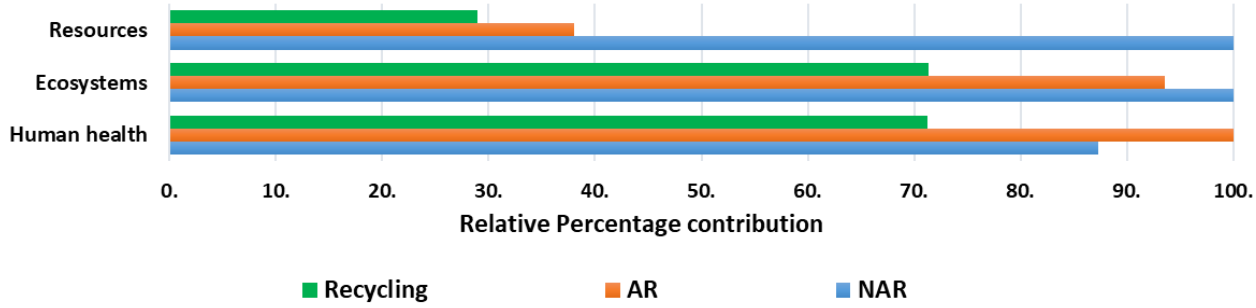
S Fig. 6b: Sankey diagram of AR process for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The Sankey diagram represents the synthesis of 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide) in the AR process, which emits 41.2 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one (1.06 kg), used as a secondary starting material, which emits 28.3 kg CO_2 eq., making it a significant CO_2 contributor.



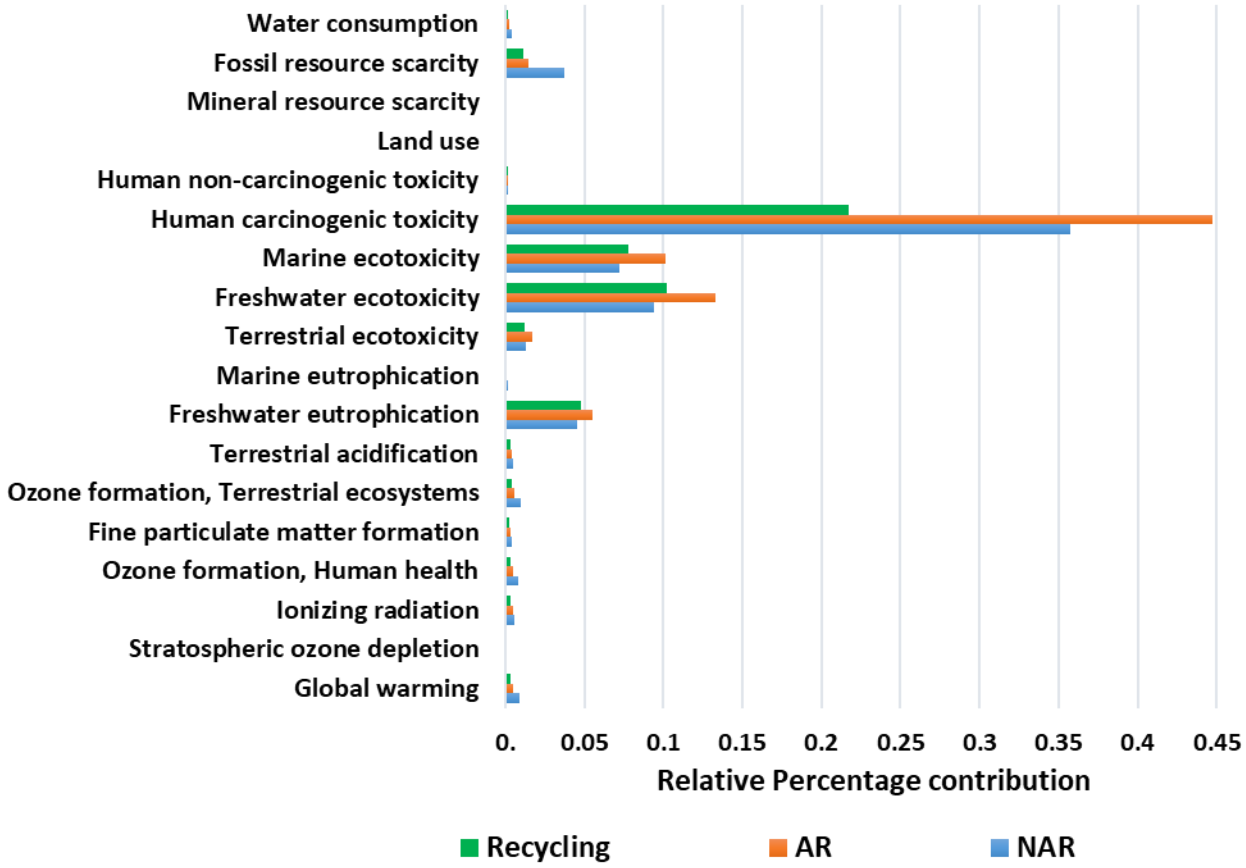
S Fig. 6c: Sankey diagram of the recycling for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The Sankey diagram represents the synthesis of 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide) in the recycling process, which emits 29.7 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one, used as a secondary starting material, which emits 16.8 kg CO_2 eq. after recycling. This is followed by the starting material nitrobenzene.



S Fig. 6d: Comparison of Midpoint category for NAR, AR, and Recycling for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide). Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide).

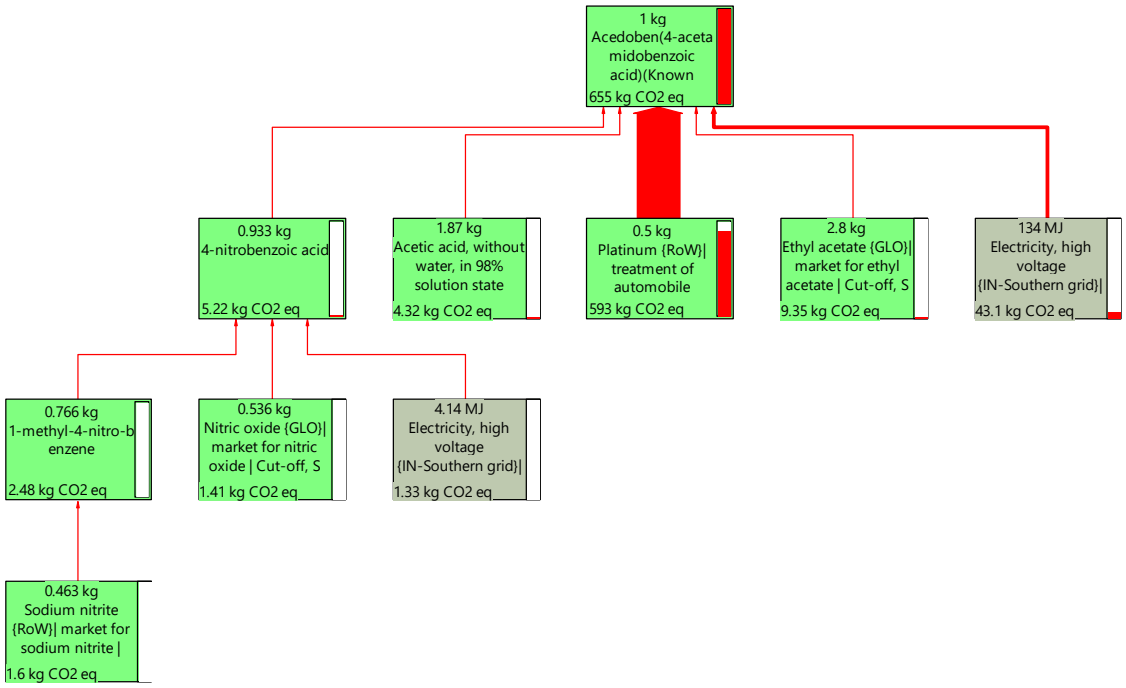


S Fig. 6e Comparison of Endpoint category for NAR, AR, and Recycling for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide). Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide).

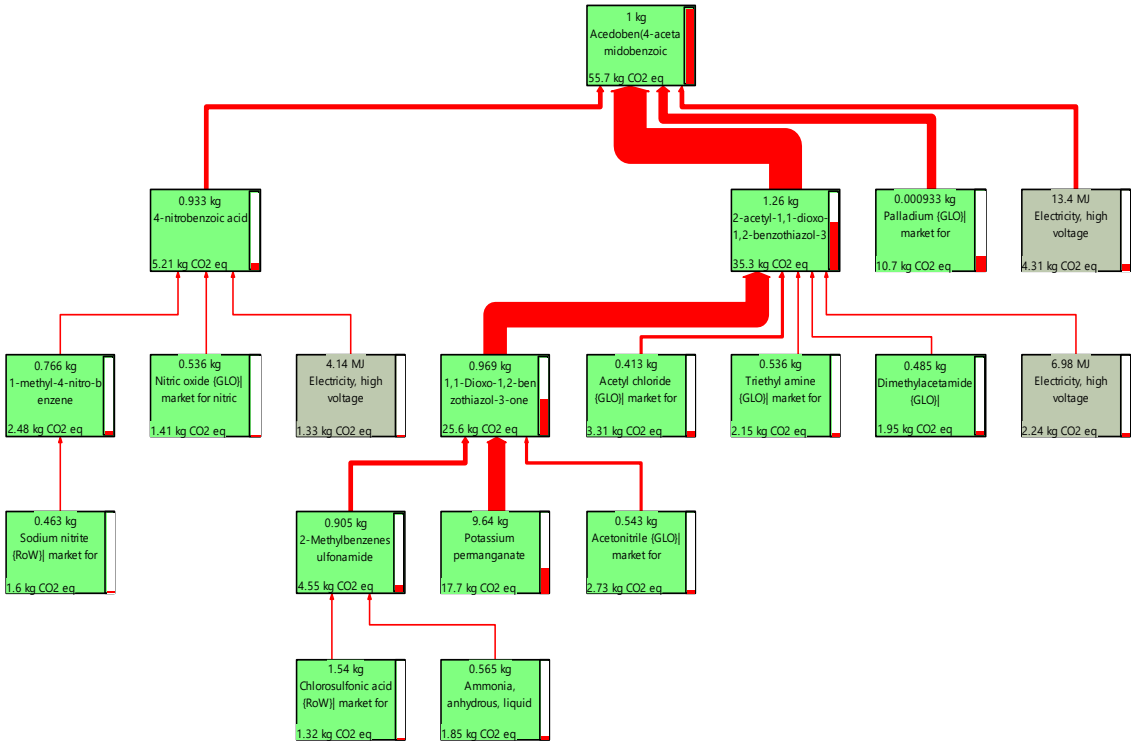


S Fig. 6f: Comparison of Normalization category for NAR, AR, and Recycling for 3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide synthesis: The diagram illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide). Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing 11-beta-HSD1 (3, 5-dichloro-N-(2-methyl-1, 3-benzothiazol-5-yl) benzamide).

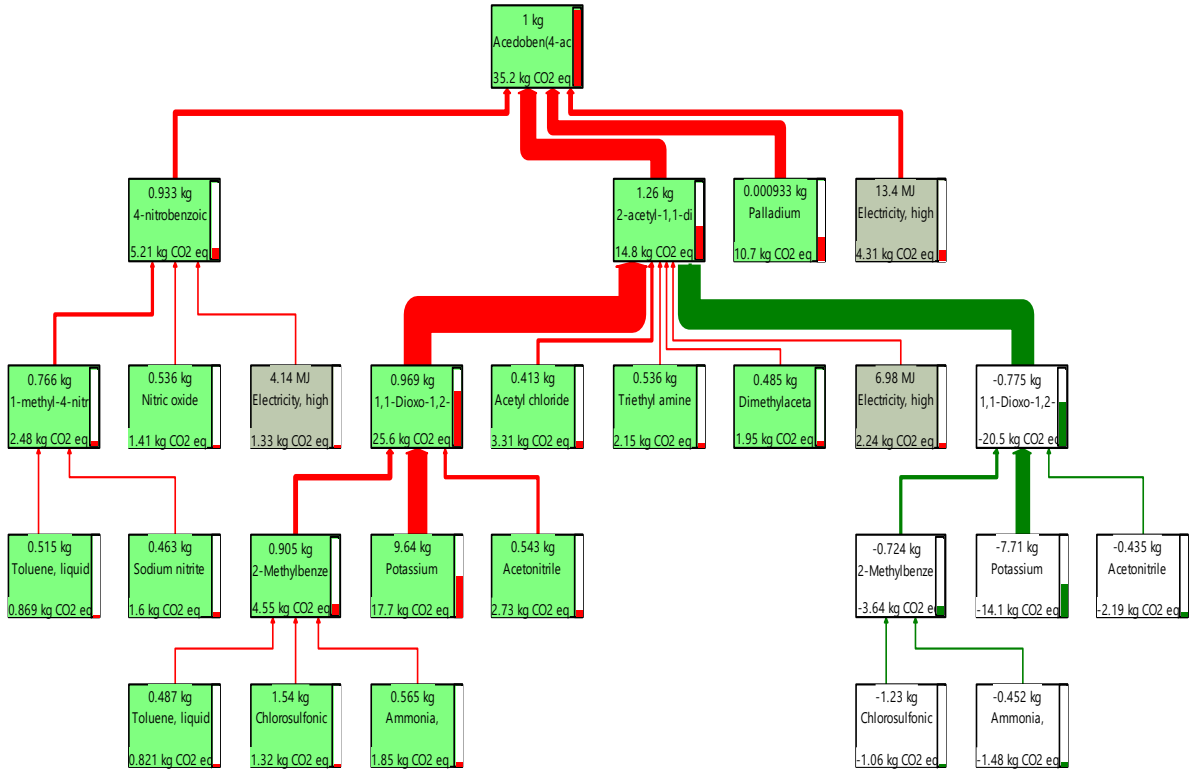
API-6: Acedoben (4-acetamidobenzoic acid) synthesis



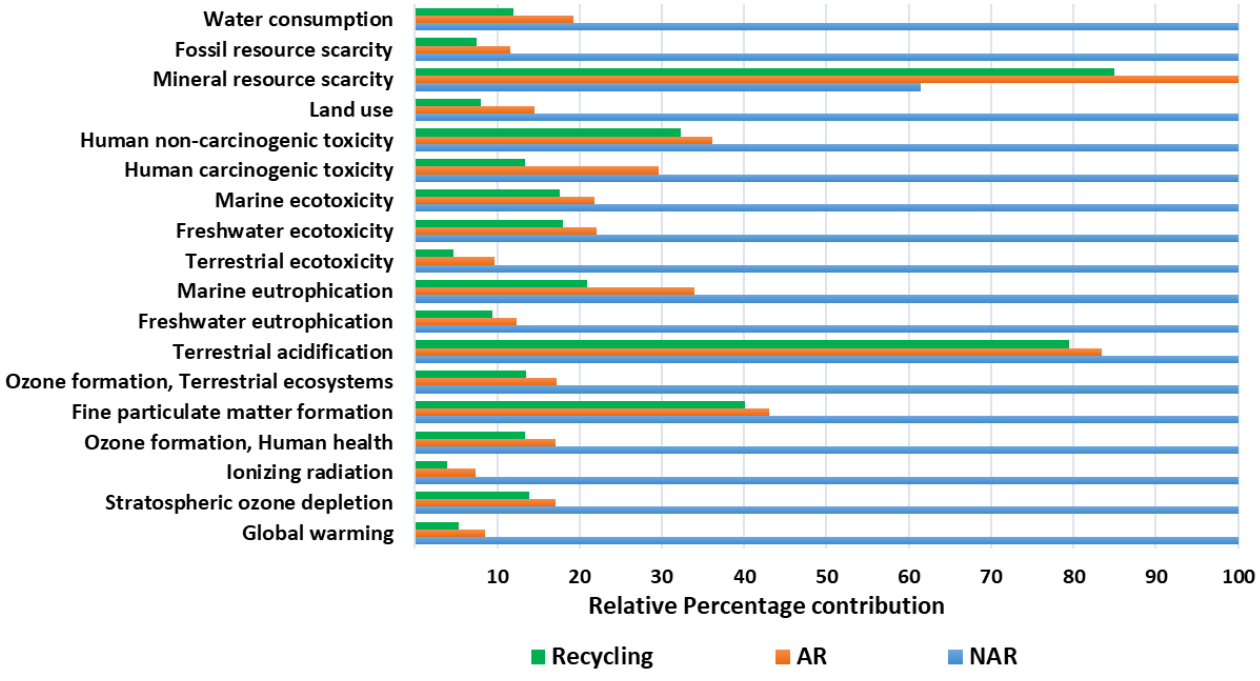
S Fig. 7a: Sankey diagram of NAR process for 4-acetamidobenzoic acid synthesis: The Sankey diagram represents the synthesis of Acedoben (4-acetamidobenzoic acid) in the NAR process, which results in the emission of 655 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is platinum (0.55 kg), used as a catalyst, which emits 593 kg CO_2 eq., making it a significant CO_2 contributor.



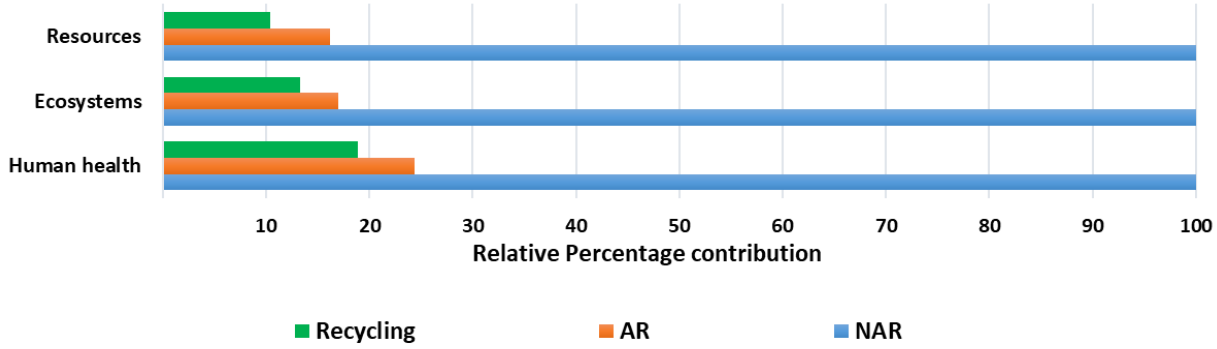
S Fig. 7b: Sankey diagram of AR process for 4-acetamidobenzoic acid synthesis: The Sankey diagram represents the synthesis of Acedoben (4-acetamidobenzoic acid) in the AR process, which emits 41.2 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one (1.26 kg), used as a secondary starting material, which emits 35.3 kg CO_2 eq., making it a significant CO_2 contributor.



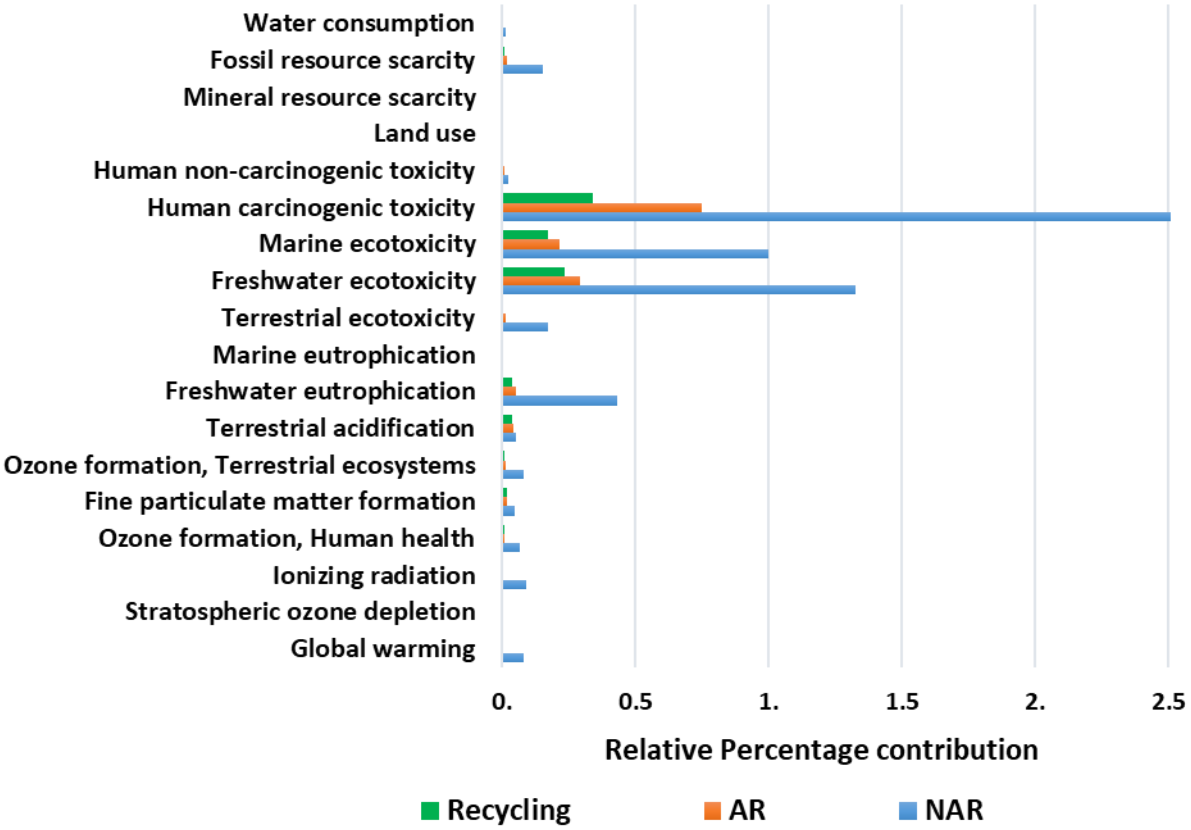
S Fig. 7c: Sankey diagram of the recycling for 4-acetamidobenzoic acid synthesis: The Sankey diagram represents the synthesis of Acedoben (4-acetamidobenzoic acid) in the recycling process, which emits 35.2 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one, used as a secondary starting material, which emits 14.8 kg CO_2 eq. after recycling. This is followed by the starting material 4-nitrobenzoic acid.



S Fig. 7d: Comparison of Midpoint category for NAR, AR, and Recycling for 4-acetamidobenzoic acid synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis Acedoben (4-acetamidobenzoic acid). Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing Acedoben (4-acetamidobenzoic acid).

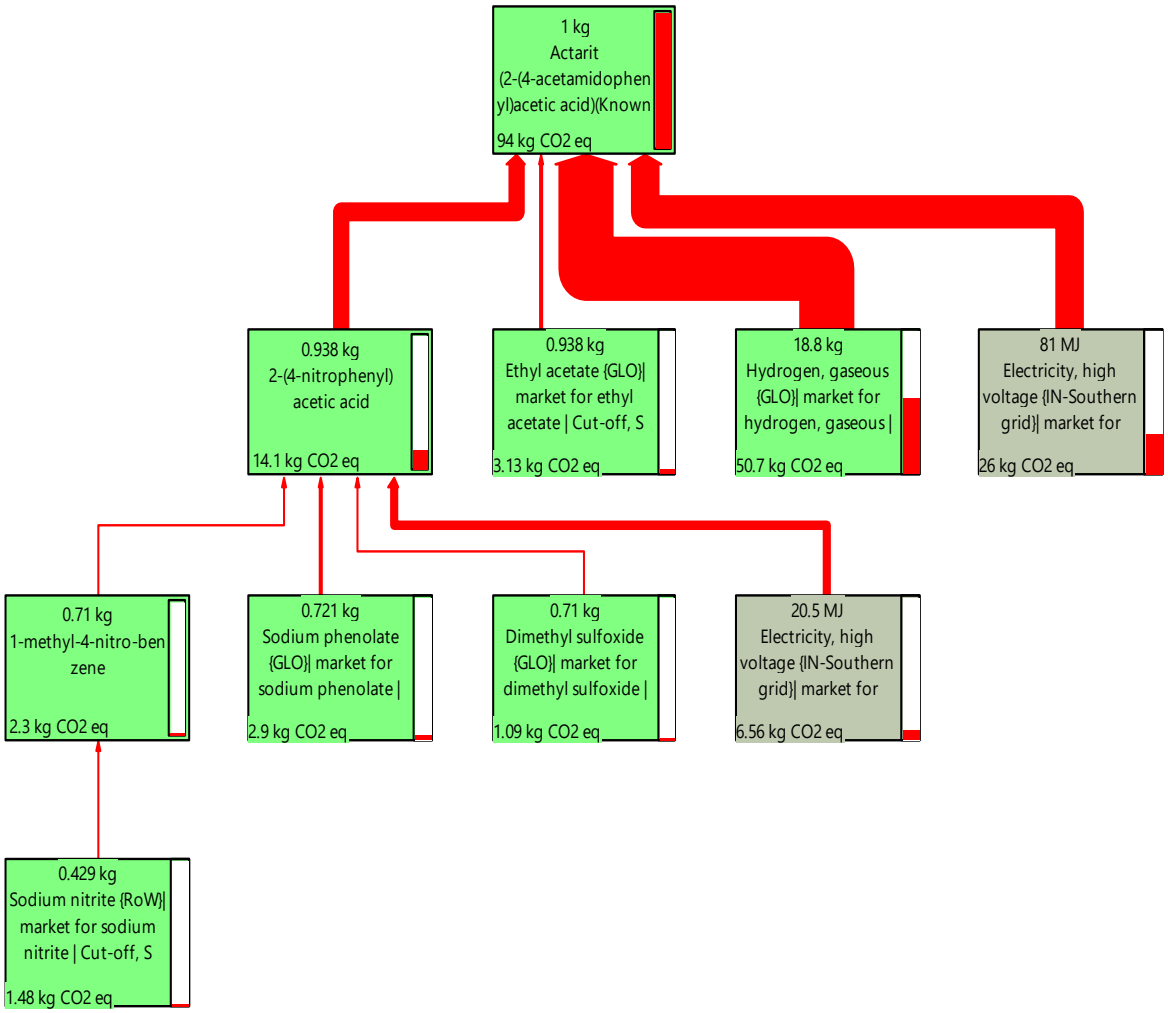


S Fig. 7e: Comparison of Endpoint category for NAR, AR, and Recycling for 4-acetamidobenzoic acid synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Acedoben (4-acetamidobenzoic acid). Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing Acedoben (4-acetamidobenzoic acid).

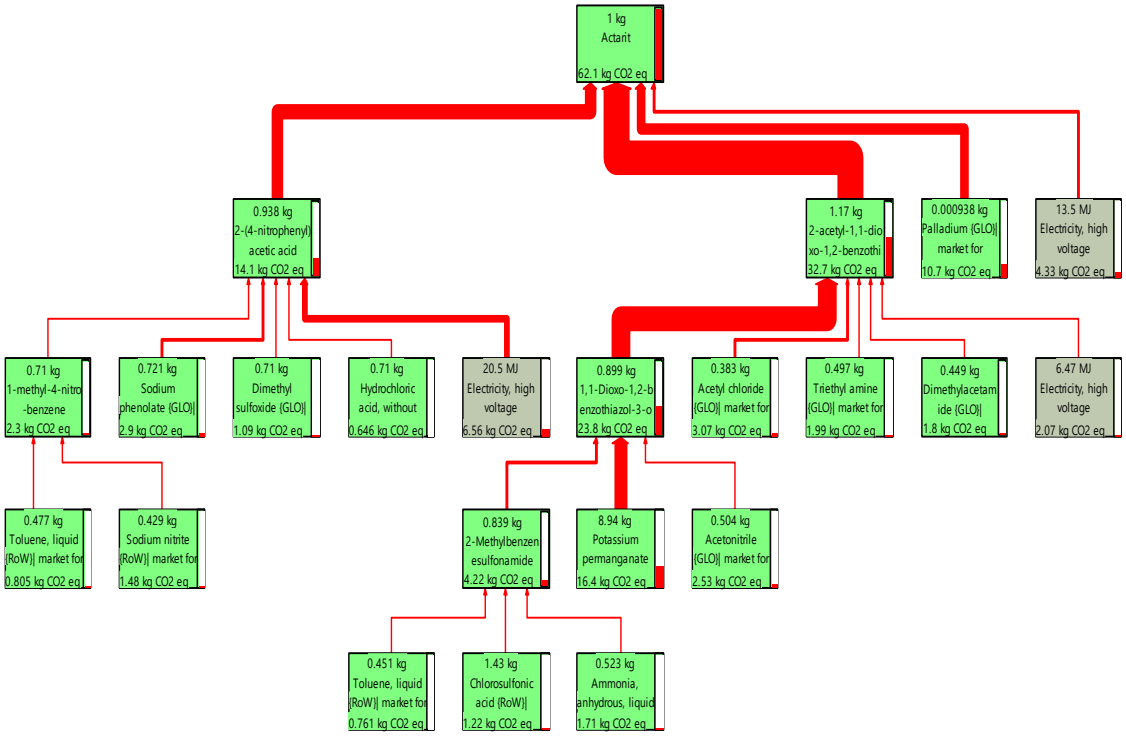


S Fig. 7f: Comparison of Normalization category for NAR, AR, and Recycling for 4-acetamidobenzoic acid synthesis: The figure illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Acedoben (4-acetamidobenzoic acid). Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing Acedoben (4-acetamidobenzoic acid).

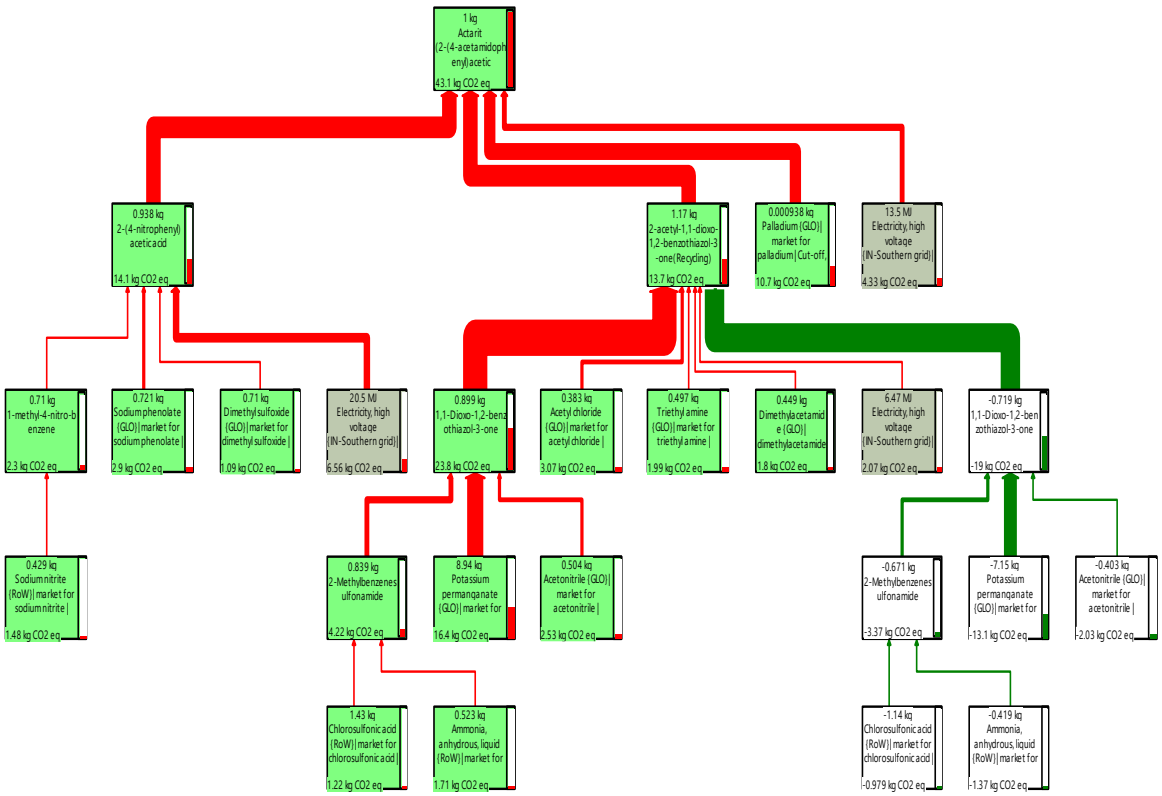
API-7: Actarit (2-(4-acetamidophenyl) acetic acid) synthesis



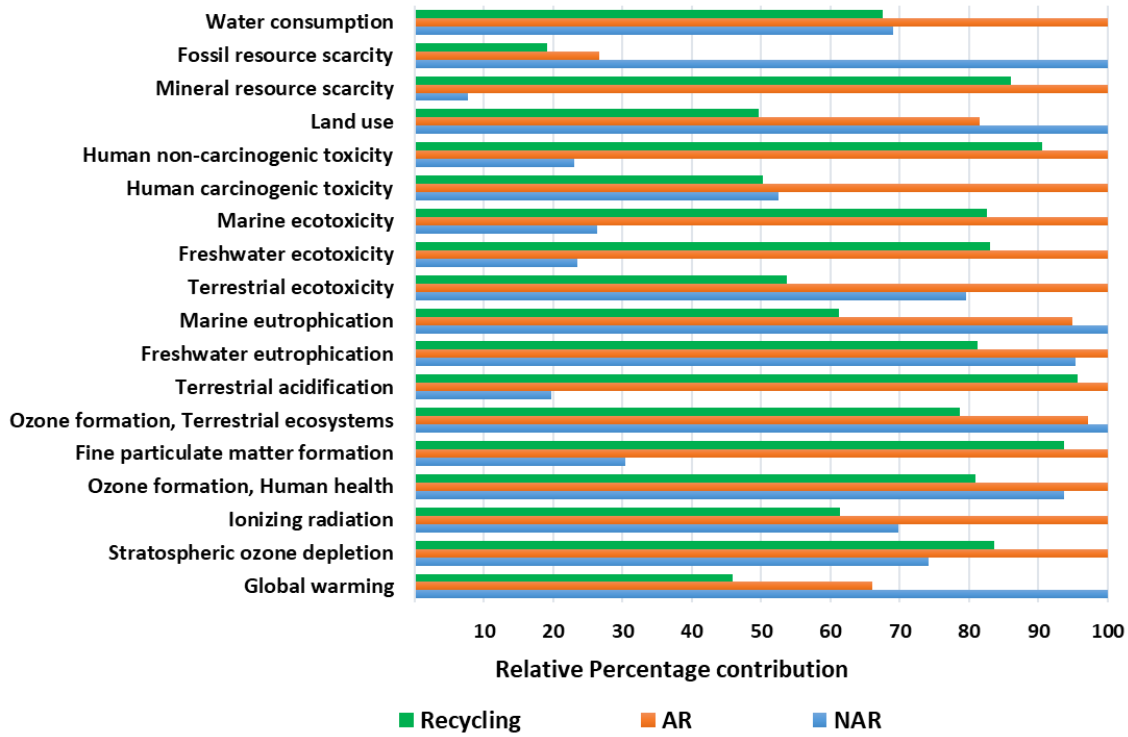
S Fig. 8a: Sankey diagram of NAR process for 2-(4-acetamidophenyl) acetic acid synthesis: The Sankey diagram represents the synthesis of Actarit (2-(4-acetamidophenyl) acetic acid) in the NAR process, which results in the emission of 94 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is hydrogen gas, which emits 50.7 kg CO_2 eq., making it a significant CO_2 contributor.



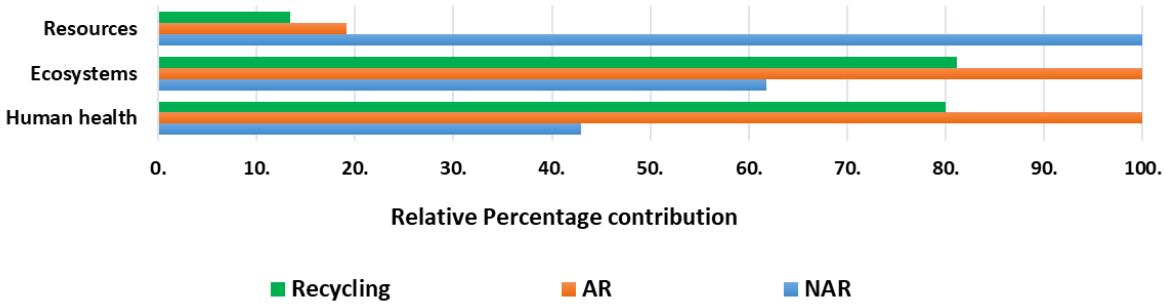
S Fig. 8b: Sankey diagram of AR process for 2-(4-acetamidophenyl) acetic acid synthesis: The Sankey diagram represents the synthesis of Actarit (2-(4-acetamidophenyl) acetic acid) in the AR process, which emits 62.1 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one (1.17 kg), used as a secondary starting material, which emits 32.7 kg CO_2 eq., making it a significant CO_2 contributor.



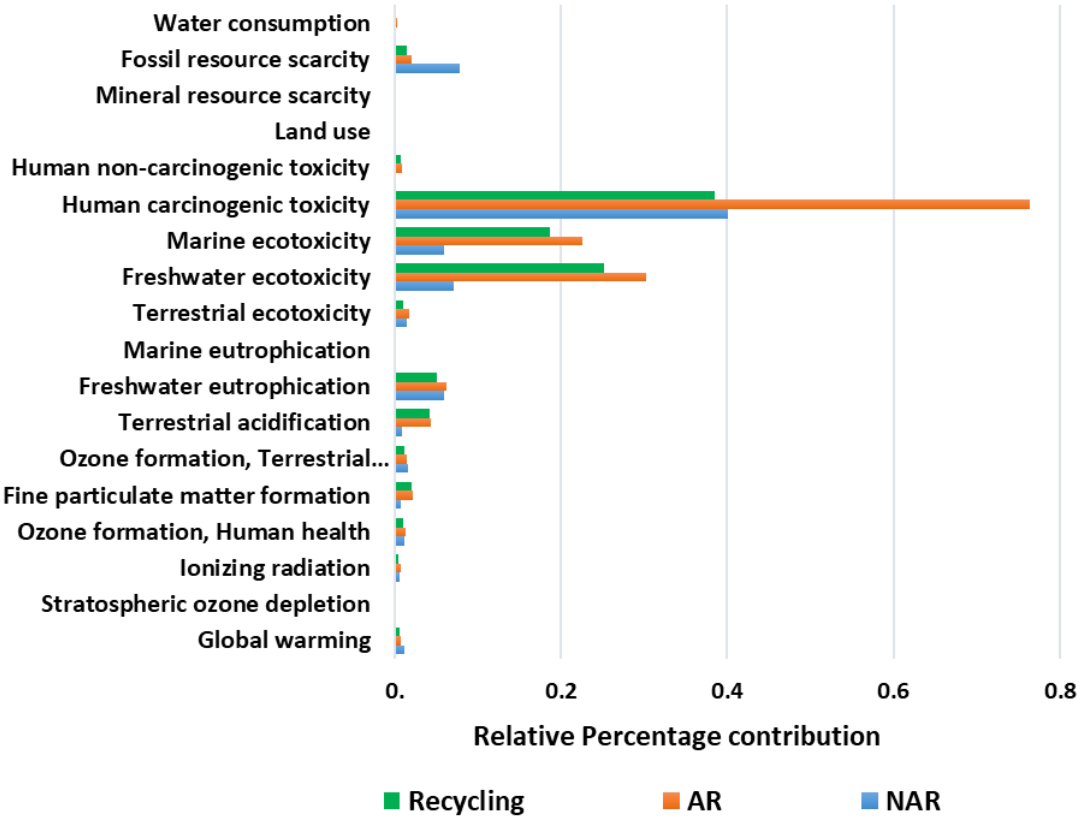
S Fig. 8c: Sankey diagram of the recycling for 2-(4-acetamidophenyl) acetic acid synthesis: The Sankey diagram represents the synthesis of Actarit (2-(4-acetamidophenyl) acetic acid) in the recycling process, which emits 43.1 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one, used as a secondary starting material, which emits 13.7 kg CO_2 eq. after recycling. This is followed by the starting material 2-(4-nitrophenyl) acetic acid.



S Fig. 8d: Comparison of Midpoint category for NAR, AR, and Recycling for 2-(4-acetamidophenyl) acetic acid synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis Actarit (2-(4-acetamidophenyl) acetic acid). Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing Actarit (2-(4-acetamidophenyl) acetic acid).

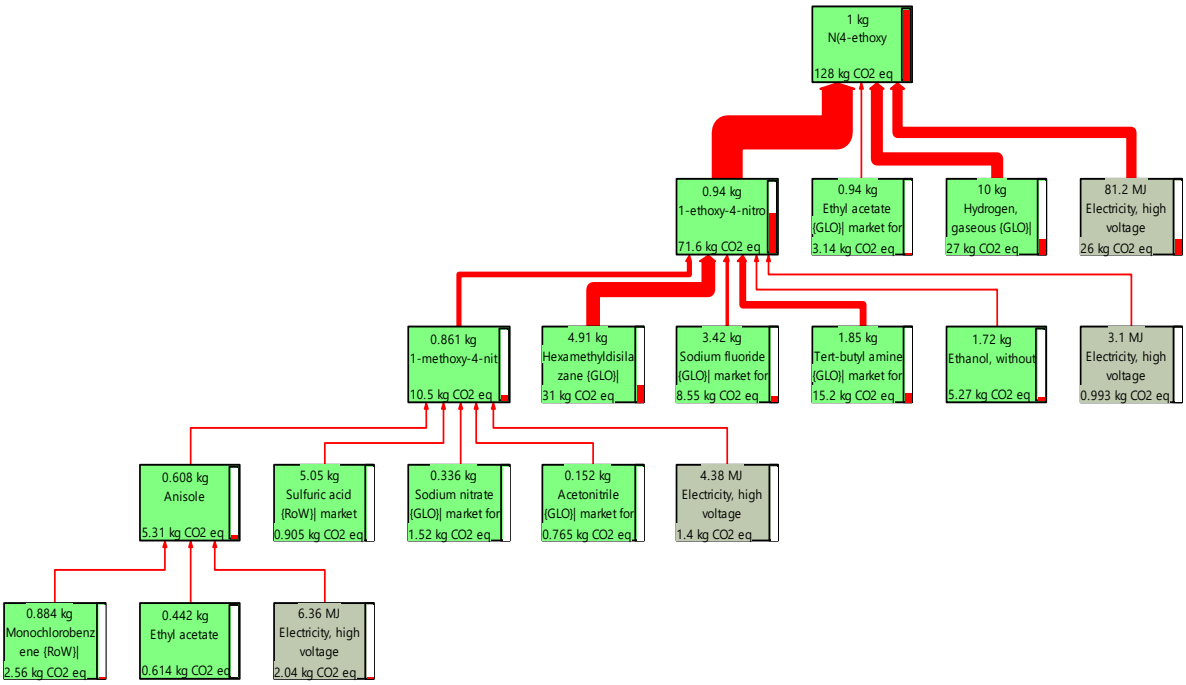


S Fig. 8e: Comparison of Endpoint category for NAR, AR, and Recycling for 2-(4-acetamidophenyl) acetic acid synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Actarit (2-(4-acetamidophenyl) acetic acid). Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing Actarit (2-(4-acetamidophenyl) acetic acid).

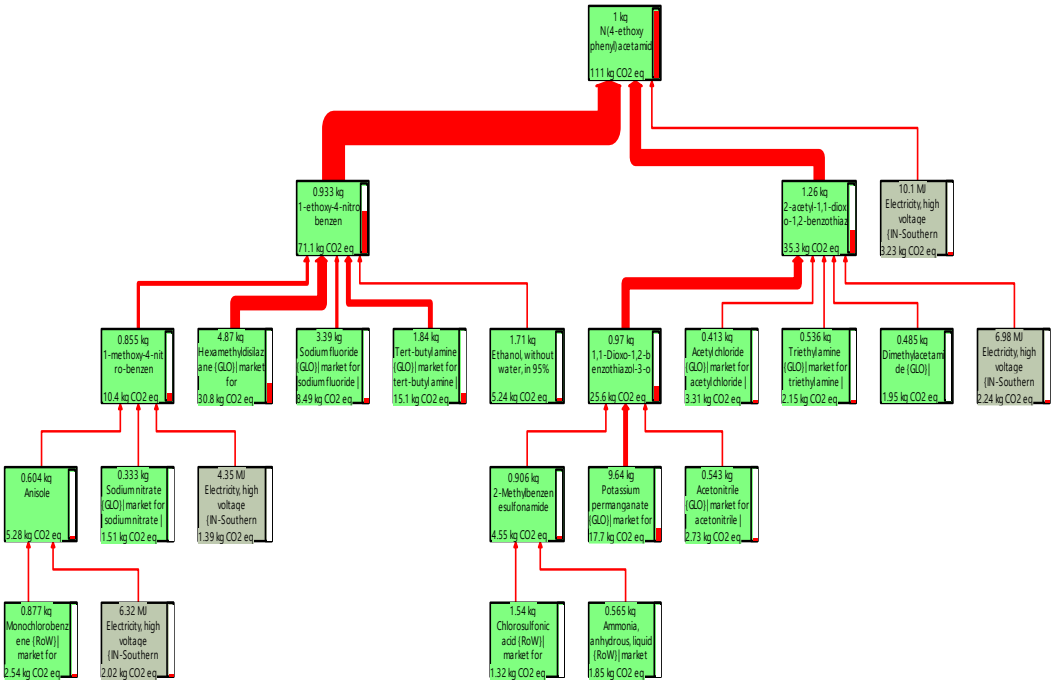


S Fig. 8f: Comparison of Normalization category for NAR, AR, and Recycling for 2-(4-acetamidophenyl) acetic acid synthesis: The diagram illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Actarit (2-(4-acetamidophenyl) acetic acid). Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing Actarit (2-(4-acetamidophenyl) acetic acid).

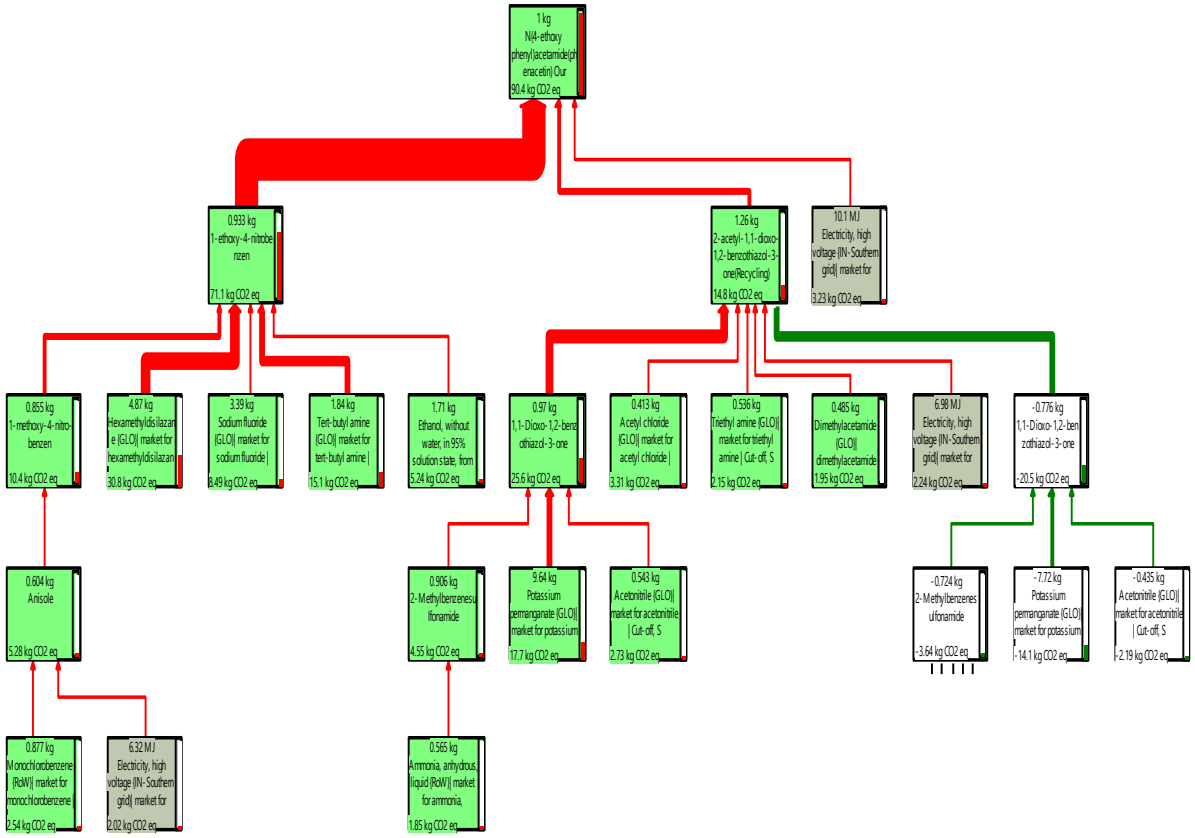
API-9: Phenacetin (N-(4-ethoxy phenyl) acetamide) synthesis



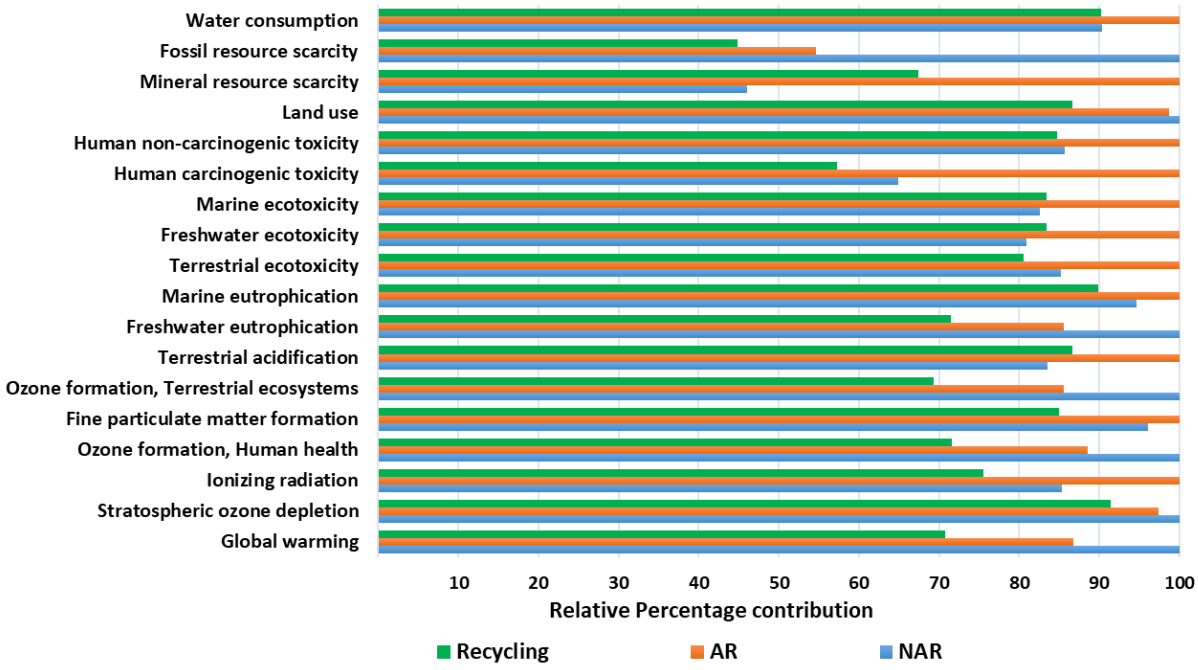
S Fig. 9a: Sankey diagram of NAR process for N-(4-ethoxy phenyl) acetamide synthesis: The Sankey diagram represents the synthesis of Phenacetin (N-(4-ethoxy phenyl) acetamide) in the NAR process, which results in the emission of 128 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 1-ethoxy-4 Nitro benzene (0.94 kg), used as a starting material, which emits 71.6 kg CO_2 eq., making it a significant CO_2 contributor.



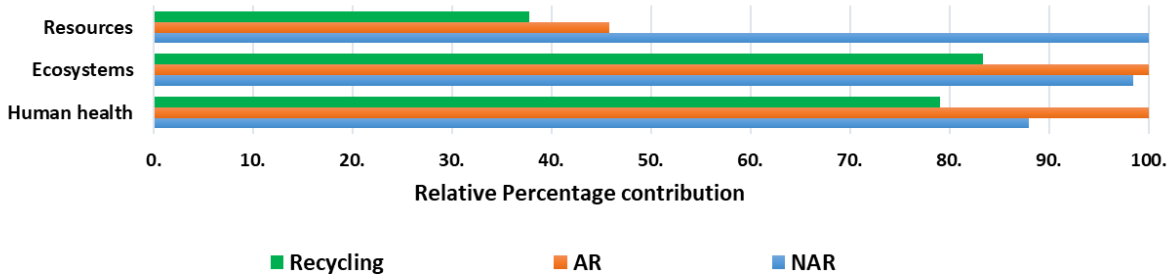
S Fig. 9b: Sankey diagram of AR process for N-(4-ethoxy phenyl) acetamide synthesis: The Sankey diagram represents the synthesis of Phenacetin (N-(4-ethoxy phenyl) acetamide) in the AR process, which emits 111 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 1-ethoxy-4 Nitro benzene (0.93 kg), used as a starting material, which emits 71.1 kg CO_2 eq., making it a significant CO_2 contributor.



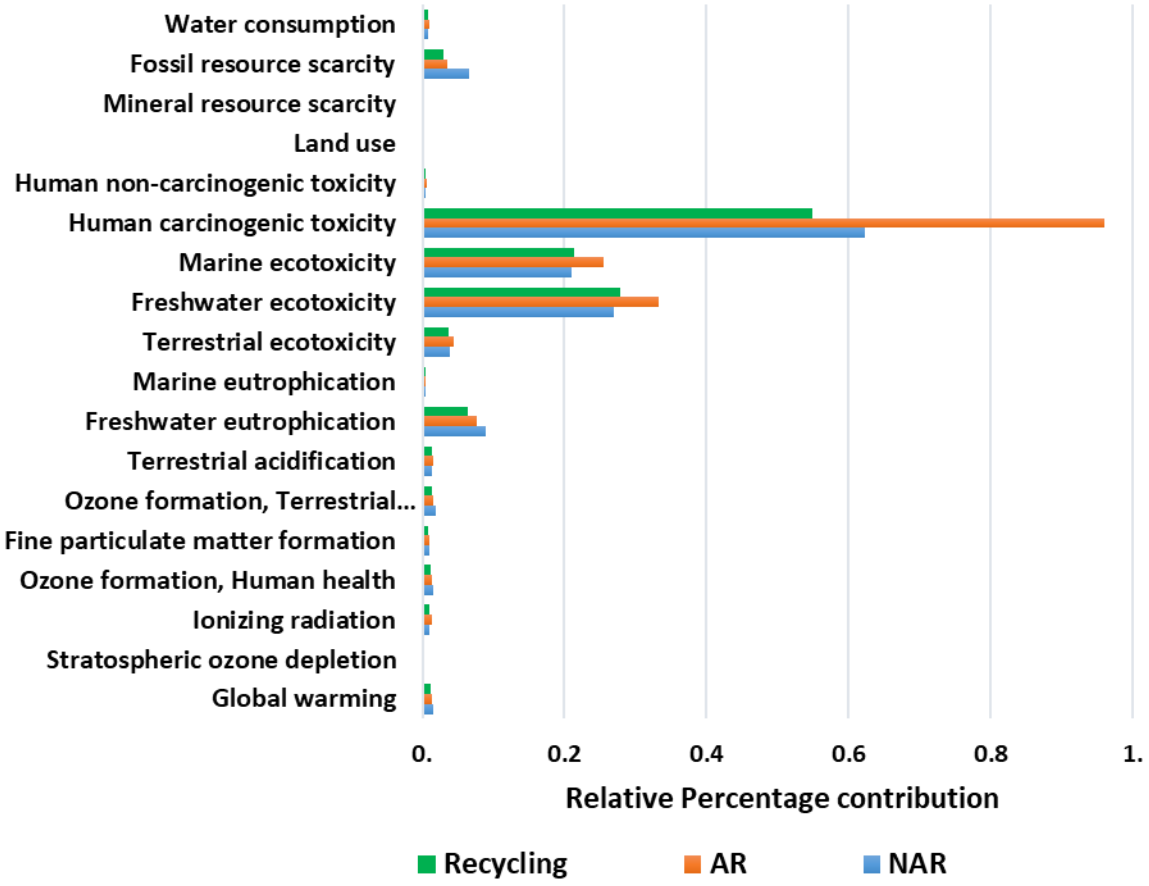
S Fig. 9c: Sankey diagram of the recycling for N-(4-ethoxy phenyl) acetamide synthesis: The Sankey diagram represents the synthesis of Phenacetin (N-(4-ethoxy phenyl) acetamide) in the recycling process, which emits 90.4 kg CO_2 eq. The major contributor to the global warming potential (GWP) in this process is 1-ethoxy-4 Nitro benzene (0.93 kg), used as a starting material, which emits 71.1 kg CO_2 eq., and followed by secondary starting material 2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one, which emits 14.8 kg CO_2 eq. after recycling.



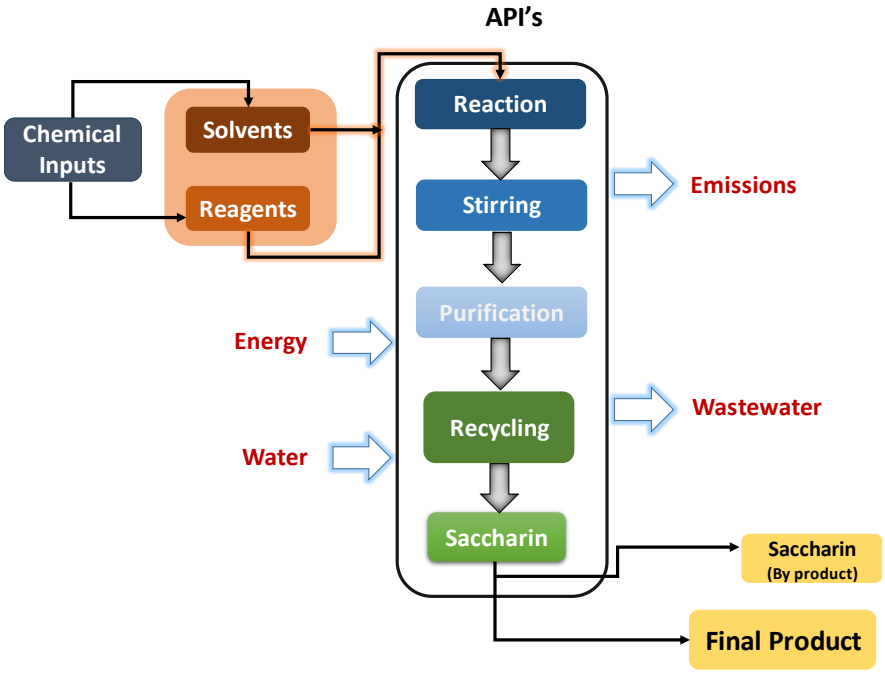
S Fig. 9d: Comparison of Midpoint category for NAR, AR, and Recycling for N-(4-ethoxy phenyl) acetamide synthesis: The diagram illustrates a comparison of 18 midpoint impact categories in three different processes: NAR, AR, and Recycling. These processes are analyzed for their efficiency and environmental impact in the synthesis Phenacetin (N-(4-ethoxy phenyl) acetamide). Each midpoint category, which represents different environmental impact factors such as global warming potential, ozone depletion, and water use, is compared across the three processes to evaluate their relative contributions and identify the most sustainable method for producing Phenacetin (N-(4-ethoxy phenyl) acetamide).



S Fig. 9e: Comparison of Endpoint category for NAR, AR, and Recycling for N-(4-ethoxy phenyl) acetamide synthesis: The diagram illustrates a comparison of three endpoint impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Phenacetin (N-(4-ethoxy phenyl) acetamide). Each endpoint category, representing areas such as human health, ecosystem quality, and resource depletion, is compared across the three processes to determine their overall environmental footprint and identify the most sustainable method for producing Phenacetin (N-(4-ethoxy phenyl) acetamide).



S Fig. 9f: Comparison of Normalization category for NAR, AR, and Recycling for N-(4-ethoxy phenyl) acetamide synthesis: The diagram illustrates a comparison of three normalization impact categories across three different processes: NAR, AR, and Recycling. These processes are evaluated for their environmental and sustainability impacts in the synthesis of Phenacetin (N-(4-ethoxy phenyl) acetamide). Each normalization category, representing metrics such as overall impact potential relative to a reference value or baseline, is compared across the three processes to assess their relative environmental footprint and identify the most sustainable method for producing Phenacetin (N-(4-ethoxy phenyl) acetamide).



S Fig. 10: System boundary of API's: This diagram illustrates the system boundary for APIs, detailing the environmental impacts of production with a focus on key chemical inputs like solvents and reagents. It tracks the types and quantities of these inputs, highlighting their roles in resource use and potential environmental effects. A key feature is the recycling of saccharin. The diagram shows how saccharin is recycled, showcasing the technologies involved and the benefits, such as reduced waste and lower demand for new raw materials. This approach demonstrates how recycling saccharin can enhance the sustainability of API production by minimizing its environmental footprint and conserving resources.

S Table 1c: Impact categories of NAR process for N-(4-hydroxyphenyl) acetamide synthesis

Impact category	Unit	Total	4-nitrophenol	Palladium	Acetic acid	Water	Ethyl acetate	Activated carbon	Electricity
Global warming	kg CO2 eq.	3.13E+02	4.44E+00	2.98E+02	1.60E+00	6.69E-04	2.30E+00	0.025028	6.369896
Stratospheric ozone depletion	kg CFC11 eq.	9.02E-05	4.57E-06	8.30E-05	4.17E-07	6.05E-10	5.51E-07	4.72E-09	1.61E-06
Ionizing radiation	kBq Co-60 eq.	21.30067	0.106531	2.07E+01	0.121145	4.43E-05	0.096427	0.000897	0.299068
Ozone formation, Human health	kg NOx eq.	0.689832	0.013603	6.52E-01	0.003952	1.58E-06	0.005906	5.91E-05	0.013934
Fine particulate matter formation	kg PM2.5 eq.	0.601797	0.010568	5.70E-01	0.002409	1.73E-06	0.00325	4.48E-05	0.015757
Ozone formation, Terrestrial ecosystems	kg NOx eq.	7.05E-01	1.43E-02	6.66E-01	4.35E-03	1.63E-06	0.006485	6.02E-05	0.014062
Terrestrial acidification	kg SO2 eq.	1.05E+00	5.01E-02	9.65E-01	4.68E-03	4.32E-06	7.72E-03	0.000118	0.019678
Freshwater eutrophication	kg P eq.	1.26E-01	1.43E-03	1.17E-01	5.13E-04	3.00E-07	9.72E-04	1.01E-05	0.006377
Marine eutrophication	kg N eq.	0.008061	8.01E-05	7.47E-03	5.12E-05	2.33E-08	6.03E-05	6.63E-07	0.0004
Terrestrial ecotoxicity	kg 1,4-DCB	1306.118	9.82	1280.00	4.89	0.00099	7.63	0.025	4.38
Freshwater ecotoxicity	kg 1,4-DCB	16.31611	0.121538	15.87103	0.056738	9.74E-05	0.086371	0.000404	0.179929
Marine ecotoxicity	kg 1,4-DCB	21.24245	0.16007	20.64445	0.075099	0.000127	0.113576	0.000558	0.24857
Human carcinogenic toxicity	kg 1,4-DCB	12.09392	0.204832	11.28	0.081	7.46E-05	0.12	0.000902	0.404261
Human non-carcinogenic toxicity	kg 1,4-DCB	341.255	2.805474	327.3319	1.241016	0.001929	1.892691	0.01756	7.964483
Land use	m2a crop eq.	4.402336	0.051938	4.172933	0.033094	1.66E-05	0.053187	0.00031	0.090858
Mineral resource scarcity	kg Cu eq.	0.690044	0.01043	0.66626	0.004304	8.02E-06	0.006853	1.23E-05	0.002176
Fossil resource scarcity	kg oil eq.	72.45825	1.786351	67.19845	0.769351	0.000158	1.105586	0.00629	1.592062
Water consumption	m3	1.66448	0.056426	1.501406	0.039296	0.001332	0.032424	5.62E-05	0.033541

S Table 1d: Impact categories of AR process for N-(4-hydroxyphenyl) acetamide synthesis

Impact category	Unit	Total	4-nitrophenol	2-acetyl-1,1-dioxo-1,2-benzothiazole-3-one	Palladium	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Global warming	kg CO2 eq.	5.29E+01	4.44	41.84	0.231888	0.22384	8.92E-05	0.922273	0.418997	0.585596	4.250589
Stratospheric ozone depletion	kg CFC11 eq.	1.81E-05	4.57E-06	1.13E-05	4.13E-07	2.68E-08	8.08E-11	2.21E-07	3.20E-07	1.50E-07	1.08E-06
Ionizing radiation	kBq Co-60 eq.	3.12E+00	1.07E-01	2.70E+00	1.16E-02	0.002822	5.91E-06	3.86E-02	0.03017	0.02315	0.199566
Ozone formation, Human health	kg NOx eq.	1.34E-01	1.36E-02	1.02E-01	2.92E-03	4.82E-04	2.10E-07	2.36E-03	1.08E-03	0.001683	0.009298
Fine particulate matter formation	kg PM2.5 eq.	1.09E-01	1.06E-02	7.34E-02	1.00E-02	2.57E-04	2.31E-07	1.30E-03	0.001085	0.001552	0.010514
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.39E-01	1.43E-02	1.07E-01	2.99E-03	0.000542	2.17E-07	2.60E-03	0.001094	0.00172	0.009383
Terrestrial acidification	kg SO2 eq.	2.68E-01	5.01E-02	1.59E-01	3.45E-02	7.05E-04	5.77E-07	3.09E-03	0.002191	0.005194	0.013131
Freshwater eutrophication	kg P eq.	2.58E-02	1.44E-03	1.88E-02	2.71E-04	5.57E-05	4.00E-08	3.89E-04	0.000208	0.000299	0.004255
Marine eutrophication	kg N eq.	6.39E-03	8.01E-05	5.96E-03	1.10E-05	2.79E-06	3.11E-09	2.41E-05	1.85E-05	2.03E-05	0.000267
Terrestrial ecotoxicity	kg 1,4-DCB	2.53E+02	9.83E+00	2.25E+02	1.08E+00	0.956491	0.001321	3.056606	4.373232	5.64977	2.92739
Freshwater ecotoxicity	kg 1,4-DCB	2.96E+00	1.22E-01	2.46E+00	1.09E-01	8.22E-03	1.30E-05	3.46E-02	4.71E-02	0.064949	0.120065
Marine ecotoxicity	kg 1,4-DCB	3.90E+00	1.60E-01	3.23E+00	1.39E-01	0.010884	1.70E-05	0.045473	0.061623	0.08503	0.165869
Human carcinogenic toxicity	kg 1,4-DCB	7.48E+00	2.05E-01	6.83E+00	3.16E-02	0.007771	9.96E-06	0.047761	0.033952	0.060088	0.26976
Human non-carcinogenic toxicity	kg 1,4-DCB	6.64E+01	2.808111	50.61915	4.51E+00	0.171027	0.000257	0.757788	0.93537	1.247269	5.314645
Land use	m2a crop eq.	1.278996	0.051987	1.08E+00	6.57E-03	0.001947	2.22E-06	0.021295	0.012882	0.042116	0.060629
Mineral resource scarcity	kg Cu eq.	5.92E-01	0.01044	5.30E-01	3.90E-02	6.03E-04	1.07E-06	2.74E-03	0.003171	0.005061	0.001452
Fossil resource scarcity	kg oil eq.	1.71E+01	1.79E+00	1.34E+01	7.42E-02	1.28E-01	2.10E-05	4.43E-01	1.12E-01	0.122763	1.062372
Water consumption	m3	7.21E-01	5.65E-02	5.96E-01	1.61E-03	1.41E-03	1.78E-04	1.30E-02	9.24E-03	0.021495	0.022382

S Table 1e: Impact categories of the Recycling process for N-(4-hydroxyphenyl) acetamide synthesis

Impact category	Unit	Total	4-nitrophenol	2-acetyl-1,1-dioxo-1,2-benzothiazole-3-one	Palladium	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Global warming	kg CO2 eq.	2.86E+01	4.44E+00	1.75E+01	2.32E-01	2.24E-01	8.92E-05	9.22E-01	0.418997	0.585596	4.250589
Stratospheric ozone depletion	kg CFC11 eq.	1.11E-05	4.57E-06	4.33E-06	4.13E-07	2.68E-08	8.08E-11	2.21E-07	3.20E-07	1.50E-07	1.08E-06
Ionizing radiation	kBq Co-60 eq.	1.36E+00	1.07E-01	9.46E-01	1.16E-02	2.82E-03	5.91E-06	3.86E-02	0.03017	0.02315	0.199566
Ozone formation, Human health	kg NOx eq.	7.12E-02	1.36E-02	3.98E-02	2.92E-03	4.82E-04	2.10E-07	2.36E-03	0.00108	0.001683	0.009298
Fine particulate matter formation	kg PM2.5 eq.	6.36E-02	0.010578	2.83E-02	1.00E-02	2.57E-04	2.31E-07	0.001301	0.001085	0.001552	0.010514
Ozone formation	kg NOx eq.	7.47E-02	1.43E-02	4.21E-02	2.99E-03	5.42E-04	2.17E-07	0.002596	0.001094	0.00172	0.009383
Terrestrial acidification	kg SO2 eq.	1.67E-01	5.01E-02	5.78E-02	3.45E-02	7.05E-04	5.77E-07	3.09E-03	2.19E-03	0.005194	0.013131
Freshwater eutrophication	kg P eq.	1.60E-02	1.44E-03	9.05E-03	2.71E-04	5.57E-05	4.00E-08	0.000389	0.000208	0.000299	0.004255
Marine eutrophication	kg N eq.	0.003554	8.01E-05	0.00313	1.10E-05	2.79E-06	3.11E-09	2.41E-05	1.85E-05	2.03E-05	0.000267
Terrestrial ecotoxicity	kg 1,4-DCB	9.59E+01	9.829681	6.80E+01	1.08E+00	0.956491	0.001321	3.056606	4.373232	5.64977	2.92739
Freshwater ecotoxicity	kg 1,4-DCB	1.31E+00	1.22E-01	8.05E-01	1.09E-01	0.008218	1.30E-05	0.034581	0.047143	0.064949	0.120065
Marine ecotoxicity	kg 1,4-DCB	1.72E+00	1.60E-01	1.05E+00	1.39E-01	1.09E-02	1.70E-05	4.55E-02	0.061623	0.08503	0.165869
Human carcinogenic	kg 1,4-DCB	2.48E+00	2.05E-01	1.82E+00	3.16E-02	7.77E-03	9.96E-06	4.78E-02	3.40E-02	0.060088	0.26976
Human non-carcinogenic toxicity	kg 1,4-DCB	3.36E+01	2.81E+00	1.79E+01	4.51E+00	1.71E-01	2.57E-04	7.58E-01	9.35E-01	1.247269	5.314645
Land use	m2a crop eq.	5.64E-01	5.20E-02	3.67E-01	6.57E-03	1.95E-03	2.22E-06	0.021295	0.012882	0.042116	0.060629
Mineral resource	kg Cu eq.	0.188528	1.04E-02	1.26E-01	3.90E-02	6.03E-04	1.07E-06	2.74E-03	3.17E-03	0.005061	0.001452
Fossil resource scarcity	kg oil eq.	9.76E+00	1.79E+00	6.03E+00	0.074213	0.128337	2.10E-05	0.44265	0.111951	0.122763	1.062372
Water consumption	m3	0.415326	0.056479	0.289552	0.001607	0.001409	0.000178	0.012982	0.009243	0.021495	0.022382

Table 1f: Comparison of Midpoint categories of N-(4-hydroxyphenyl) acetamide synthesis

		NAR	AR	Recycling
Impact category	**Unit**	**Total**	**Total**	**Total**
Global warming	**kg CO2 eq.**	313.00	52.90	28.60
Stratospheric ozone depletion	**kg CFC11 eq.**	0.0000902	0.0000181	0.0000111
Ionizing radiation	**kBq Co-60 eq.**	21.30	3.12	1.36
Ozone formation, Human health	**kg NOx eq.**	0.69	0.13	0.07
Fine particulate matter formation	**kg PM2.5 eq.**	0.60	0.11	0.06
Ozone formation, Terrestrial ecosystems	**kg NOx eq.**	0.71	0.14	0.07
Terrestrial acidification	**kg SO2 eq.**	1.05	0.27	0.17
Freshwater eutrophication	**kg P eq.**	0.13	0.03	0.02
Marine eutrophication	**kg N eq.**	0.008061	0.00639	0.003554
Terrestrial ecotoxicity	**kg 1,4-DCB**	1306.12	253.00	95.90
Freshwater ecotoxicity	**kg 1,4-DCB**	16.32	2.96	1.31
Marine ecotoxicity	**kg 1,4-DCB**	21.24	3.90	1.72
Human carcinogenic toxicity	**kg 1,4-DCB**	12.09	7.48	2.48
Human non-carcinogenic toxicity	**kg 1,4-DCB**	341.26	66.40	33.60
Land use	**m2a crop eq.**	4.40	1.28	0.56
Mineral resource scarcity	**kg Cu eq.**	0.69	0.59	0.19
Fossil resource scarcity	**kg oil eq.**	72.46	17.10	9.76
Water consumption	**m3**	1.66	0.72	0.42

Table 1g: Comparison of Endpoint categories of N-(4-hydroxyphenyl) acetamide synthesis

Damage category	**Unit**	**NAR**	**AR**	**Recycling**
Human health	DALY	0.021874	0.005456	0.002433
Ecosystems	Species.yr	1.57E-05	2.93E-06	1.49E-06
Resources	USD2013	15.67658	5.079073	2.839712

Table 1h: Comparison of Normalization categories of N-(4-hydroxyphenyl) acetamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.039152	0.006616	0.003575
Stratospheric ozone depletion	0.001506	0.000302	0.000186
Ionizing radiation	0.044305	0.006483	0.002826
Ozone formation, Human health	0.033526	0.006503	0.003462
Fine particulate matter formation	0.02353	0.00425	0.002488
Ozone formation, Terrestrial ecosystems	0.039703	0.007847	0.004207
Terrestrial acidification	0.02555	0.006541	0.00407
Freshwater eutrophication	0.194012	0.039658	0.024582
Marine eutrophication	0.001749	0.001386	0.000771
Terrestrial ecotoxicity	0.085943	0.016622	0.006311
Freshwater ecotoxicity	0.647749	0.11771	0.052053
Marine ecotoxicity	0.488576	0.089685	0.039524
Human carcinogenic toxicity	1.174319	0.726627	0.240387
Human non-carcinogenic toxicity	0.01092	0.002123	0.001076
Land use	0.000713	0.000207	9.14E-05
Mineral resource scarcity	5.75E-06	4.93E-06	1.57E-06
Fossil resource scarcity	0.073907	0.017476	0.009955
Water consumption	0.006242	0.002705	0.001557

S Table2a: Inventory data of N-(4-methoxyphenyl) benzamide for 1 kg of functional unit (API-1)

NAR - Inputs		**AR - Inputs**	
Benzoyl chloride	0.619 Kg	1-methoxy-4-nitro-benzene	0.675 Kg
4-Methoxyaniline	0.65 kg	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one	1.26 kg
Triethylamine	0.666 kg	Iron Powder	0.737 kg
Tetrahydrofuran	1.86 kg	Ammonium Chloride	1.65 kg
Sodium Bicarbonate solution	0.186 kg	Isopropanol	0.0675 kg
Water	0.309 kg	Water	2 kg
Sodium chloride	0.186 kg	Ethyl acetate	0.202 kg
Energy	35.6 MJ	1M HCl	0.337 kg
-	-	$NaHCO_3$ (aq.)	0.337 kg
-	-	Energy	2.43 MJ
AR - Output			
N-(4-methoxyphenyl) benzamide	1 kg	N-(4-methoxyphenyl) benzamide	1 kg
Byproducts			
-		1,1-dioxo-1,2-benzothiazol-3-one	0.031 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 2b: Comparison of the Midpoint category of the NAR process for N-(4-methoxyphenyl) benzamide synthesis

Impact category	Unit	Total	Benzoyl chloride	4-Methoxy aniline	Triethyl amine	Tetrahydrofuran	Sodium bicarbonate	Water	sodium chloride	Energy
Global warming	kg CO2 eq.	1.40E+02	1.49E+00	1.13E+02	2.67E+00	1.17E+01	2.36E-01	1.50E-04	0.404861	11.42077
Stratospheric ozone depletion	kg CFC11 eq.	2.41E-04	3.60E-07	0.000234	4.75E-07	3.09E-06	6.05E-08	1.36E-10	1.04E-07	2.89E-06
Ionizing radiation	kBq Co-60 eq.	6.82E+00	6.88E-02	5.23E+00	5.47E-02	8.94E-01	9.33E-03	9.92E-06	0.024826	0.536208
Ozone formation, Human health	kg NOx eq.	1.284026	0.003139	1.220784	6.14E-03	2.74E-02	6.78E-04	3.53E-07	0.000948	0.024983
Fine particulate matter formation	kg PM2.5 eq.	4.103679	0.00673	4.046639	2.89E-03	1.78E-02	6.26E-04	3.88E-07	0.000722	0.028251
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.319445	0.003286	1.253374	6.81E-03	2.91E-02	6.93E-04	3.65E-07	0.000977	0.025212
Terrestrial acidification	kg SO2 eq.	14.01152	0.020189	13.9057	0.008216	3.86E-02	0.002093	9.69E-07	0.001418	0.035281
Freshwater eutrophication	kg P eq.	1.38E-01	0.000493	1.21E-01	1.35E-03	3.81E-03	1.20E-04	6.72E-08	0.000159	0.011433
Marine eutrophication	kg N eq.	0.014946	3.47E-05	1.32E-02	0.0007	2.62E-04	8.16E-06	5.22E-09	1.77E-05	0.000716
Terrestrial ecotoxicity	kg 1,4-DCB	671.3611	4.370248	605.8488	7.346448	4.11E+01	2.277029	0.002219	2.504398	7.865513
Freshwater ecotoxicity	kg 1,4-DCB	46.98768	0.056535	46.06373	0.086094	4.07E-01	0.026176	2.18E-05	0.02559	0.3226
Marine ecotoxicity	kg 1,4-DCB	59.94842	0.07584	58.70459	0.114032	5.40E-01	0.03427	2.86E-05	0.033653	0.445669
Human carcinogenic toxicity	kg 1,4-DCB	1.53E+01	6.96E-02	13.78058	1.24E-01	5.72E-01	2.42E-02	1.67E-05	0.028107	0.724811
Human non-carcinogenic toxicity	kg 1,4-DCB	1.87E+03	1.53E+00	1.85E+03	1.96E+00	9.21E+00	5.03E-01	4.32E-04	0.508617	14.27975
Land use	m2a crop eq.	6.79E+00	1.96E-02	6.23E+00	3.70E-02	3.12E-01	1.70E-02	3.72E-06	0.009344	0.162901
Mineral resource scarcity	kg Cu eq.	15.81166	0.004145	15.76111	7.34E-03	3.12E-02	0.00204	1.80E-06	0.001868	0.003902
Fossil resource scarcity	kg oil eq.	46.371	7.71E-01	37.24938	1.29E+00	4.05E+00	4.95E-02	3.53E-05	0.101025	2.854455
Water consumption	m3	2.279656	0.030887	1.547348	0.018342	0.611058	0.008663	0.000299	0.002921	0.060137

S Table 2c: Comparison of the Midpoint category of the AR process for N-(4-methoxyphenyl) benzamide synthesis

Impact category	Unit	Total	Benzoyl chloride	4-Methoxy aniline	Triethyl amine	Tetrahydrofuran	Sodium bicarbonate	Water	sodium chloride	Energy
Global warming	kg CO2 eq.	1.40E+02	1.49E+00	1.13E+02	2.67E+00	1.17E+01	2.36E-01	1.50E-04	0.404861	11.42077
Stratospheric ozone depletion	kg CFC11 eq.	2.41E-04	3.60E-07	0.000234	4.75E-07	3.09E-06	6.05E-08	1.36E-10	1.04E-07	2.89E-06
Ionizing radiation	kBq Co-60 eq.	6.82E+00	6.88E-02	5.23E+00	5.47E-02	8.94E-01	9.33E-03	9.92E-06	0.024826	0.536208
Ozone formation, Human health	kg NOx eq.	1.284026	0.003139	1.220784	6.14E-03	2.74E-02	6.78E-04	3.53E-07	0.000948	0.024983
Fine particulate matter formation	kg PM2.5 eq.	4.103679	0.00673	4.046639	2.89E-03	1.78E-02	6.26E-04	3.88E-07	0.000722	0.028251
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.319445	0.003286	1.253374	6.81E-03	2.91E-02	6.93E-04	3.65E-07	0.000977	0.025212
Terrestrial acidification	kg SO2 eq.	14.01152	0.020189	13.9057	0.008216	3.86E-02	0.002093	9.69E-07	0.001418	0.035281
Freshwater eutrophication	kg P eq.	1.38E-01	0.000493	1.21E-01	1.35E-03	3.81E-03	1.20E-04	6.72E-08	0.000159	0.011433
Marine eutrophication	kg N eq.	0.014946	3.47E-05	1.32E-02	0.0007	2.62E-04	8.16E-06	5.22E-09	1.77E-05	0.000716
Terrestrial ecotoxicity	kg 1,4-DCB	671.3611	4.370248	605.8488	7.346448	4.11E+01	2.277029	0.002219	2.504398	7.865513
Freshwater ecotoxicity	kg 1,4-DCB	46.98768	0.056535	46.06373	0.086094	4.07E-01	0.026176	2.18E-05	0.02559	0.3226
Marine ecotoxicity	kg 1,4-DCB	59.94842	0.07584	58.70459	0.114032	5.40E-01	0.03427	2.86E-05	0.033653	0.445669
Human carcinogenic toxicity	kg 1,4-DCB	1.53E+01	6.96E-02	13.78058	1.24E-01	5.72E-01	2.42E-02	1.67E-05	0.028107	0.724811
Human non-carcinogenic toxicity	kg 1,4-DCB	1.87E+03	1.53E+00	1.85E+03	1.96E+00	9.21E+00	5.03E-01	4.32E-04	0.508617	14.27975
Land use	m2a crop eq.	6.79E+00	1.96E-02	6.23E+00	3.70E-02	3.12E-01	1.70E-02	3.72E-06	0.009344	0.162901
Mineral resource scarcity	kg Cu eq.	15.81166	0.004145	15.76111	7.34E-03	3.12E-02	0.00204	1.80E-06	0.001868	0.003902
Fossil resource scarcity	kg oil eq.	46.371	7.71E-01	37.24938	1.29E+00	4.05E+00	4.95E-02	3.53E-05	0.101025	2.854455
Water consumption	m3	2.279656	0.030887	1.547348	0.018342	0.611058	0.008663	0.000299	0.002921	0.060137

S Table 2d: Comparison of the Midpoint category of the Recycling process for N-(4-methoxyphenyl) benzamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzen	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one	Iron pellet	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid,	Sodium bicarbonate	Energy	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one
Global warming	kg CO2 eq.	18.06402	8.21E+00	2.38E+01	7.47E-02	2.67E+00	1.64E-01	6.53E-05	6.75E-01	3.07E-01	4.29E-01	0.778311	-19.0251
Stratospheric ozone depletion	kg CFC11 eq.	1.50E-05	1.23E-05	6.54E-06	3.65E-08	6.09E-07	1.96E-08	5.91E-11	1.62E-07	2.35E-07	1.10E-07	1.97E-07	-5.23E-06
Ionizing radiation	kBq Co-60 eq.	0.869693	3.27E-01	1.58E+00	4.16E-03	1.17E-01	2.07E-03	4.33E-06	2.83E-02	2.21E-02	0.016956	0.036542	-1.26286
Ozone formation, Human health	kg NOx eq.	0.046348	2.29E-02	5.98E-02	5.25E-04	5.16E-03	3.53E-04	1.54E-07	1.73E-03	7.91E-04	0.001233	0.001703	-0.04782
Fine particulate matter formation	kg PM2.5 eq.	0.042661	2.43E-02	4.66E-02	4.27E-04	3.60E-03	0.000188	1.69E-07	9.53E-04	7.94E-04	0.001137	0.001925	-0.03726
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.04875	2.43E-02	0.062121	5.33E-04	5.39E-03	3.97E-04	1.59E-07	1.90E-03	8.01E-04	0.00126	0.001718	-0.0497
Terrestrial acidification	kg SO2 eq.	1.01E-01	5.98E-02	1.09E-01	5.01E-04	8.55E-03	0.000516	4.23E-07	0.002265	0.001605	0.003804	0.002404	-0.0875
Freshwater eutrophication	kg P eq.	0.012528	8.23E-03	9.88E-03	3.02E-05	8.11E-04	4.08E-05	2.93E-08	2.85E-04	1.53E-04	0.000219	0.000779	-0.00791
Marine eutrophication	kg N eq.	0.004725	1.83E-03	0.003022	2.15E-06	2.19E-03	2.05E-06	2.28E-09	1.77E-05	1.36E-05	1.48E-05	4.88E-05	-0.00242
Terrestrial ecotoxicity	kg 1,4-DCB	175.4336	121.8767	1.39E+02	2.73E-01	1.47E+01	0.700559	0.000968	2.238739	3.20307	4.13804	0.536024	-110.981
Freshwater ecotoxicity	kg 1,4-DCB	2.38E+00	1.79E+00	1.49E+00	3.27E-03	1.48E-01	6.02E-03	9.52E-06	0.025328	0.034529	0.04757	0.021985	-1.19063
Marine ecotoxicity	kg 1,4-DCB	3.22E+00	2.45E+00	1.96E+00	4.34E-03	1.94E-01	0.007972	1.25E-05	0.033306	0.045134	0.062278	0.030372	-1.57168
Human carcinogenic toxicity	kg 1,4-DCB	1.83E+00	6.47E-01	4.30E+00	3.83E-03	1.59E-01	5.69E-03	7.30E-06	3.50E-02	2.49E-02	0.04401	0.049395	-3.43815
Human non-carcinogenic toxicity	kg 1,4-DCB	4.61E+01	3.39E+01	3.03E+01	8.25E-02	2.82E+00	1.25E-01	1.89E-04	5.55E-01	6.85E-01	9.14E-01	0.973147	-24.241

Land use	m2a crop eq.	6.16E-01	3.62E-01	6.40E-01	1.57E-03	5.56E-02	1.43E-03	1.62E-06	1.56E-02	9.44E-03	3.08E-02	0.011102	-0.51205
Mineral resource scarcity	kg Cu eq.	0.254403	1.28E-01	3.41E-01	3.73E-02	1.18E-02	0.000442	7.84E-07	2.01E-03	0.002322	0.003707	0.000266	-0.27294
Fossil resource scarcity	kg oil eq.	6.039035	3.01E+00	7.831944	2.07E-02	6.55E-01	9.40E-02	1.54E-05	3.24E-01	8.20E-02	0.089915	0.194527	-6.26556
Water consumption	m3	0.307313	0.165583	0.299012	0.000679	0.043966	0.001032	0.00013	0.009508	0.00677	0.015743	0.004098	-0.23921

S Table 2e: Comparison of End Point category in NAR for N-(4-methoxyphenyl) benzamide synthesis

Damage category	Unit	Total	Benzoyl chloride	4-Methoxyaniline	Triethyl amine	Tetrahydrofuran	Sodium bicarbonate	Water	sodium chloride	Energy
Human health	DALY	0.064158	0.000114	0.062144	1.51E-04	0.000694	3.27E-05	2.57E-08	3.50E-05	0.000988
Ecosystems	species.yr	3.09E-05	7.89E-08	2.95E-05	1.12E-07	5.12E-07	1.94E-08	1.81E-11	2.27E-08	6.38E-07
Resources	USD2013	1.46E+01	0.278076	1.23E+01	4.51E-01	1.18E+00	1.07E-02	9.83E-06	0.026233	0.360248

S Table 2f: Comparison of End Point category in AR for N-(4-methoxyphenyl) benzamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzen	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one	Iron pellet	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Human health	DALY	5.32E-03	2.16E-03	0.002738	5.82E-06	2.01E-04	8.96E-06	1.12E-08	4.15E-05	4.06E-05	5.94E-05	6.74E-05
Ecosystems	species.yr	2.89E-06	1.25E-06	1.36E-06	3.92E-09	1.35E-07	6.85E-09	7.88E-12	2.94E-08	2.44E-08	3.53E-08	4.35E-08
Resources	USD2013	3.79E+00	9.42E-01	2.44E+00	1.35E-02	1.78E-01	0.036134	4.29E-06	1.12E-01	1.98E-02	0.019469	0.02455

S Table 2g: Comparison of End Point category after Recycling for N-(4-methoxyphenyl) benzamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzen	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one	Iron pellet	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one
Human health	DALY	0.003133	2.16E-03	2.74E-03	5.82E-06	2.01E-04	8.96E-06	1.12E-08	4.15E-05	4.06E-05	5.94E-05	6.74E-05	-0.00219
Ecosystems	species.yr	1.81E-06	1.25E-06	1.36E-06	3.92E-09	1.35E-07	6.85E-09	7.88E-12	2.94E-08	2.44E-08	3.53E-08	4.35E-08	-1.09E-06
Resources	USD2013	1.834074	0.942202	2.44E+00	1.35E-02	1.78E-01	3.61E-02	4.29E-06	1.12E-01	0.019776	0.019469	0.02455	-1.95286

S Table 2h: Comparison of Normalization category in NAR for N-(4-methoxyphenyl) benzamide synthesis

Impact category	Total	Benzoyl chloride	4-Methoxyaniline	Triethyl amine	Tetrahydrofuran	Sodium bicarbonate	Water,	sodium chloride	Energy
Global warming	0.017562	0.000186	1.41E-02	0.000334	0.001468	2.95E-05	1.87E-08	5.06E-05	0.001428
Stratospheric ozone depletion	0.004017	6.02E-06	0.003901	7.92E-06	5.16E-05	1.01E-06	2.26E-09	1.74E-06	4.83E-05
Ionizing radiation	0.01418	1.43E-04	1.09E-02	1.14E-04	0.00186	1.94E-05	2.06E-08	5.16E-05	0.001115
Ozone formation, Human health	6.24E-02	1.53E-04	5.93E-02	2.98E-04	1.33E-03	3.30E-05	1.72E-08	4.61E-05	0.001214
Fine particulate matter formation	0.160454	0.000263	0.158224	0.000113	0.000697	2.45E-05	1.52E-08	2.82E-05	0.001105
Ozone formation, Terrestrial ecosystems	0.074285	0.000185	0.070565	0.000383	0.001638	3.90E-05	2.05E-08	5.50E-05	0.001419
Terrestrial acidification	0.341881	0.000493	0.339299	0.0002	0.000942	5.11E-05	2.36E-08	3.46E-05	0.000861
Freshwater eutrophication	0.213202	0.000759	1.86E-01	0.002085	0.005865	0.000185	1.04E-07	0.000245	0.017606
Marine eutrophication	0.003243	7.52E-06	2.87E-03	0.000152	5.69E-05	1.77E-06	1.13E-09	3.83E-06	0.000155
Terrestrial ecotoxicity	0.044176	0.000288	0.039865	0.000483	2.71E-03	0.00015	1.46E-07	0.000165	0.000518
Freshwater ecotoxicity	1.865411	0.002244	1.82873	0.003418	0.016155	0.001039	8.66E-07	0.001016	0.012807
Marine ecotoxicity	1.378814	0.001744	1.350206	0.002623	0.012428	0.000788	6.57E-07	0.000774	0.01025

Human carcinogenic toxicity	1.487923	0.006759	1.34E+00	0.012036	0.055572	0.002351	1.62E-06	0.002729	0.070379
Human non-carcinogenic toxicity	0.05995	4.89E-05	5.91E-02	6.26E-05	0.000295	1.61E-05	1.38E-08	1.63E-05	0.000457
Land use	1.10E-03	3.17E-06	1.01E-03	5.99E-06	5.06E-05	2.75E-06	6.03E-10	1.51E-06	2.64E-05
Mineral resource scarcity	0.000132	3.45E-08	0.000131	6.12E-08	2.60E-07	1.70E-08	1.50E-11	1.56E-08	3.25E-08
Fossil resource scarcity	0.047298	0.000787	3.80E-02	0.001317	0.004135	5.05E-05	3.60E-08	0.000103	0.002912
Water consumption	0.008549	0.000116	0.005803	6.88E-05	0.002291	3.25E-05	1.12E-06	1.10E-05	0.000226

S Table 2i: Comparison of Normalization Category in AR for N-(4-methoxyphenyl) benzamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzen	2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one	Iron pellet	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	4.64E-03	1.03E-03	2.97E-03	9.33E-06	0.000334	2.05E-05	8.17E-09	8.44E-05	3.84E-05	5.36E-05	9.73E-05
Stratospheric ozone depletion	3.38E-04	2.06E-04	1.09E-04	6.09E-07	1.02E-05	3.27E-07	9.88E-10	2.70E-06	3.92E-06	1.84E-06	3.29E-06
Ionizing radiation	4.44E-03	6.79E-04	3.28E-03	8.65E-06	2.44E-04	4.30E-06	9.00E-09	5.88E-05	4.60E-05	3.53E-05	7.60E-05
Ozone formation, Human health	4.58E-03	1.11E-03	2.91E-03	2.55E-05	0.000251	1.72E-05	7.49E-09	8.42E-05	3.84E-05	5.99E-05	8.27E-05
Fine particulate matter formation	3.12E-03	9.51E-04	1.82E-03	1.67E-05	1.41E-04	7.35E-06	6.61E-09	3.73E-05	3.11E-05	4.44E-05	7.53E-05
Ozone formation, Terrestrial ecosystems	5.54E-03	1.37E-03	3.50E-03	3.00E-05	3.04E-04	2.24E-05	8.95E-09	0.000107	4.51E-05	7.09E-05	9.67E-05
Terrestrial acidification	0.004607	1.46E-03	2.67E-03	1.22E-05	0.000209	1.26E-05	1.03E-08	5.53E-05	3.92E-05	9.28E-05	5.87E-05
Freshwater eutrophication	3.15E-02	1.27E-02	0.015219	4.66E-05	0.001249	6.28E-05	4.52E-08	0.000439	0.000235	0.000337	0.0012
Marine eutrophication	1.55E-03	3.97E-04	6.56E-04	4.66E-07	4.76E-04	4.44E-07	4.94E-10	3.84E-06	2.94E-06	3.22E-06	1.06E-05
Terrestrial ecotoxicity	1.88E-02	8.02E-03	9.13E-03	1.80E-05	9.69E-04	4.61E-05	6.37E-08	1.47E-04	2.11E-04	2.72E-04	3.53E-05
Freshwater ecotoxicity	0.141613	7.11E-02	0.059085	0.00013	0.005879	0.000239	3.78E-07	0.001006	0.001371	0.001889	0.000873
Marine ecotoxicity	0.11026	5.64E-02	0.045186	9.98E-05	0.004455	1.83E-04	2.86E-07	0.000766	0.001038	0.001432	0.000699

Human carcinogenic toxicity	5.11E-01	6.28E-02	0.417306	3.71E-04	0.015487	5.53E-04	7.08E-07	0.003397	0.002415	0.004273	0.004796
Human non-carcinogenic toxicity	2.25E-03	1.09E-03	9.70E-04	2.64E-06	9.02E-05	4.01E-06	6.03E-09	1.78E-05	2.19E-05	2.92E-05	3.11E-05
Land use	1.83E-04	5.87E-05	1.04E-04	2.54E-07	9.01E-06	2.31E-07	2.63E-10	2.53E-06	1.53E-06	5.00E-06	1.80E-06
Mineral resource scarcity	4.39E-06	1.07E-06	2.84E-06	3.11E-07	9.86E-08	3.68E-09	6.53E-12	1.67E-08	1.93E-08	3.09E-08	2.21E-09
Fossil resource scarcity	1.26E-02	3.07E-03	7.99E-03	2.11E-05	0.000668	9.59E-05	1.57E-08	0.000331	8.36E-05	9.17E-05	0.000198
Water consumption	2.05E-03	6.21E-04	1.12E-03	2.55E-06	0.000165	3.87E-06	4.88E-07	3.57E-05	2.54E-05	5.90E-05	1.54E-05

S Table 2j: Comparison of Normalization category after Recycling for N-(4-methoxyphenyl) benzamide synthesis

Impact category	**Total**	**1-methoxy-4-nitro-benzen**	**2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one**	**Iron pellet**	**Ammonium chloride**	**Isopropanol**	**Water, deionised**	**Ethyl acetate**	**Hydrochloric acid**	**Sodium bicarbonate**	**Energy**	**2-benzoyl-1,1-dioxo-1,2-benzothiazol-3-one**
Global warming	2.26E-03	1.03E-03	2.97E-03	9.33E-06	3.34E-04	2.05E-05	8.17E-09	8.44E-05	3.84E-05	5.36E-05	9.73E-05	-0.00238
Stratospheric ozone depletion	2.51E-04	0.000206	1.09E-04	6.09E-07	1.02E-05	3.27E-07	9.88E-10	2.70E-06	3.92E-06	1.84E-06	3.29E-06	-8.73E-05
Ionizing radiation	1.81E-03	6.79E-04	3.28E-03	8.65E-06	2.44E-04	4.30E-06	9.00E-09	5.88E-05	4.60E-05	3.53E-05	7.60E-05	-0.00263
Ozone formation, Human health	0.002252	0.001113	2.91E-03	2.55E-05	2.51E-04	1.72E-05	7.49E-09	8.42E-05	3.84E-05	5.99E-05	8.27E-05	-0.00232
Fine particulate matter formation	0.001668	0.000951	1.82E-03	1.67E-05	1.41E-04	7.35E-06	6.61E-09	3.73E-05	3.11E-05	4.44E-05	7.53E-05	-0.00146
Ozone formation, Terrestrial ecosystems	0.002745	0.001369	3.50E-03	3.00E-05	3.04E-04	2.24E-05	8.95E-09	0.000107	4.51E-05	7.09E-05	9.67E-05	-0.0028
Terrestrial acidification	0.002472	0.001459	0.002669	1.22E-05	0.000209	1.26E-05	1.03E-08	5.53E-05	3.92E-05	9.28E-05	5.87E-05	-0.00213
Freshwater eutrophication	1.93E-02	1.27E-02	1.52E-02	4.66E-05	1.25E-03	6.28E-05	4.52E-08	0.000439	0.000235	0.000337	0.0012	-0.01218
Marine eutrophication	0.001025	0.000397	6.56E-04	4.66E-07	4.76E-04	4.44E-07	4.94E-10	3.84E-06	2.94E-06	3.22E-06	1.06E-05	-0.00052
Terrestrial ecotoxicity	0.011544	0.008019	9.13E-03	1.80E-05	0.000969	4.61E-05	6.37E-08	0.000147	0.000211	0.000272	3.53E-05	-0.0073

Freshwater ecotoxicity	0.094344	0.071141	5.91E-02	0.00013	5.88E-03	2.39E-04	3.78E-07	0.001006	0.001371	0.001889	0.000873	-0.04727
Marine ecotoxicity	7.41E-02	5.64E-02	4.52E-02	9.98E-05	4.46E-03	1.83E-04	2.86E-07	7.66E-04	0.001038	0.001432	0.000699	-0.03615
Human carcinogenic toxicity	1.78E-01	6.28E-02	4.17E-01	3.71E-04	1.55E-02	5.53E-04	7.08E-07	0.003397	0.002415	0.004273	0.004796	-0.33384
Human non-carcinogenic toxicity	1.48E-03	1.09E-03	9.70E-04	2.64E-06	9.02E-05	4.01E-06	6.03E-09	1.78E-05	2.19E-05	2.92E-05	3.11E-05	-0.00078
Land use	9.98E-05	5.87E-05	1.04E-04	2.54E-07	9.01E-06	2.31E-07	2.63E-10	2.53E-06	1.53E-06	5.00E-06	1.80E-06	-8.30E-05
Mineral resource scarcity	2.12E-06	1.07E-06	2.84E-06	3.11E-07	9.86E-08	3.68E-09	6.53E-12	1.67E-08	1.93E-08	3.09E-08	2.21E-09	-2.27E-06
Fossil resource scarcity	0.00616	0.003072	7.99E-03	2.11E-05	6.68E-04	9.59E-05	1.57E-08	0.000331	8.36E-05	9.17E-05	0.000198	-0.00639
Water consumption	0.001152	0.000621	0.001121	2.55E-06	0.000165	3.87E-06	4.88E-07	3.57E-05	2.54E-05	5.90E-05	1.54E-05	-0.0009

S Table2k: Comparison of Endpoint category for N-(4-methoxyphenyl) benzamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.064158	0.005324	0.003133
Ecosystems	species.yr	3.09E-05	2.89E-06	1.81E-06
Resources	USD2013	14.56299	3.786937	1.834074

S Table 3a: Inventory Data of 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide for 1 kg functional unit (API-2)

NAR - Inputs		**AR - Inputs**	
2-chloropyridine-3-carboxylic acid	0.67 Kg	1-methoxy 4-nitrobenzene	0.586 Kg
4-methoxy aniline	0.515 kg	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	1.23 Kg
Triethylamine	0.462 kg	Iron Powder	0.64 kg
Tetrahydrofuran	2.01 kg	Ammonium Chloride	1.43 kg
Dichloromethane	2.01 kg	Isopropanol	0.0586 kg
Saturated Sodium bicarbonate	0.335 kg	Water	0.117 kg
Water	0.67 kg	Ethyl acetate	0.176 kg
Energy	48.2 MJ	Hcl	0.293 kg
-	-	$NaHCO_3$	0.293 kg
-	-	Energy	8.44 MJ
NAR – Output		**AR - Output**	
2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide	1 kg	2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide	1 kg
Byproducts		**Byproducts**	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.05305 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 3b: Comparison of the Midpoint category of the NAR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Unit	Total	2-chloropyridine-3-carbonyl chloride	4-Methoxyaniline	Triethyl amine	Tetrahydrofuran	Dichloromethane	Sodium bicarbonate	Water	Energy
Global warming	kg CO2 eq.	1.45E+02	1.78E+01	8.91E+01	1.851023	1.27E+01	7.33E+00	4.26E-01	0.000324	15.45582
Stratospheric ozone depletion	kg CFC11 eq.	3.27E-04	6.11E-06	0.000185	3.29E-07	3.34E-06	1.29E-04	1.09E-07	2.94E-10	3.91E-06
Ionizing radiation	kBq Co-60 eq.	7.32E+00	1.425468	4.142021	0.03789	9.68E-01	6.88E-04	0.016836	2.15E-05	0.725654
Ozone formation, Human health	kg NOx eq.	1.11E+00	4.52E-02	0.96705	0.004249	2.96E-02	2.89E-02	0.001224	7.65E-07	0.03381
Fine particulate matter formation	kg PM2.5 eq.	3.32E+00	3.90E-02	3.205564	0.001998	1.93E-02	1.32E-02	0.001129	8.39E-07	0.038232
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.14E+00	0.047854	0.992866	0.004714	3.15E-02	2.93E-02	0.001251	7.89E-07	0.034119
Terrestrial acidification	kg SO2 eq.	11.22493	0.074037	11.01546	0.005691	0.041815	3.64E-02	0.003777	2.10E-06	0.047746
Freshwater eutrophication	kg P eq.	1.28E-01	0.011189	9.59E-02	9.38E-04	4.12E-03	2.19E-04	0.000217	1.46E-07	0.015472
Marine eutrophication	kg N eq.	1.31E-02	8.80E-04	0.010461	0.000485	0.000284	5.71E-06	1.47E-05	1.13E-08	0.00097
Terrestrial ecotoxicity	kg 1,4-DCB	595.6099	49.45515	479.926	5.088237	44.54698	1.84E+00	4.108692	0.004805	10.64446
Freshwater ecotoxicity	kg 1,4-DCB	38.23871	0.73444	36.4896	0.05963	0.440562	3.06E-02	0.047233	4.73E-05	0.436577
Marine ecotoxicity	kg 1,4-DCB	4.88E+01	0.902097	46.50312	0.07898	0.584995	4.26E-02	0.061836	6.18E-05	0.603127
Human carcinogenic toxicity	kg 1,4-DCB	1.40E+01	1.07E+00	10.91635	8.59E-02	6.20E-01	2.47E-01	0.043698	3.62E-05	0.980892
Human non-carcinogenic toxicity	kg 1,4-DCB	1.61E+03	1.17E+02	1.46E+03	1.36E+00	9.97E+00	1.10E+00	9.07E-01	0.000936	19.3249
Land use	m2a crop eq.	6.13E+00	5.75E-01	4.93E+00	2.56E-02	3.38E-01	1.89E-03	3.06E-02	8.06E-06	0.220455
Mineral resource scarcity	kg Cu eq.	1.28E+01	0.29933	12.48524	0.005087	3.38E-02	1.07E-03	0.00368	3.89E-06	0.00528
Fossil resource scarcity	kg oil eq.	4.55E+01	5.42E+00	29.50727	8.94E-01	4.39E+00	1.36E+00	0.089277	7.65E-05	3.862955
Water consumption	m3	2.225379	0.206537	1.225739	0.012704	0.66156	0.021177	0.015632	0.000646	0.081383

S Table 3c: Comparison of the Midpoint category of the AR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	5.60E+01	7.13E+00	4.24E+01	6.48E-02	2.32E+00	1.42E-01	5.68E-05	5.87E-01	0.266549	0.372533	2.704057
Stratospheric ozone depletion	kg CFC11 eq.	2.52E-05	1.07E-05	1.28E-05	3.17E-08	5.29E-07	1.70E-08	5.14E-11	1.40E-07	2.04E-07	9.56E-08	6.84E-07
Ionizing radiation	kBq Co-60 eq.	3.60E+00	2.84E-01	3.03E+00	3.61E-03	1.02E-01	1.80E-03	3.76E-06	2.46E-02	0.019193	0.014727	0.126956
Ozone formation, Human health	kg NOx eq.	1.41E-01	1.99E-02	0.106382	4.56E-04	4.48E-03	3.07E-04	1.34E-07	1.50E-03	0.000687	0.001071	0.005915
Fine particulate matter formation	kg PM2.5 eq.	1.17E-01	2.11E-02	0.082713	3.71E-04	3.12E-03	0.000163	1.47E-07	0.000828	0.00069	0.000987	0.006689
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.48E-01	2.11E-02	1.12E-01	4.63E-04	4.68E-03	3.45E-04	1.38E-07	1.65E-03	6.96E-04	0.001094	0.005969
Terrestrial acidification	kg SO2 eq.	2.44E-01	5.19E-02	1.69E-01	4.35E-04	7.43E-03	0.000448	3.67E-07	0.001967	0.001394	0.003304	0.008353
Freshwater eutrophication	kg P eq.	3.32E-02	7.15E-03	2.20E-02	2.63E-05	7.04E-04	3.54E-05	2.55E-08	0.000248	0.000133	0.00019	0.002707
Marine eutrophication	kg N eq.	9.08E-03	1.59E-03	0.005377	1.87E-06	1.90E-03	1.78E-06	1.98E-09	1.54E-05	1.18E-05	1.29E-05	0.00017
Terrestrial ecotoxicity	kg 1,4-DCB	3.14E+02	1.06E+02	1.84E+02	0.237325	1.28E+01	0.608482	0.000841	1.944493	2.782079	3.594162	1.862291
Freshwater ecotoxicity	kg 1,4-DCB	4.06E+00	1.56E+00	2.20E+00	2.84E-03	1.29E-01	5.23E-03	8.27E-06	2.20E-02	0.02999	0.041318	0.076381
Marine ecotoxicity	kg 1,4-DCB	5.37E+00	2.13E+00	2.83E+00	3.77E-03	1.68E-01	6.92E-03	1.08E-05	2.89E-02	3.92E-02	0.054093	0.10552
Human carcinogenic toxicity	kg 1,4-DCB	6.18E+00	5.62E-01	5.21E+00	3.32E-03	1.39E-01	4.94E-03	6.34E-06	3.04E-02	2.16E-02	0.038225	0.171611
Human non-carcinogenic toxicity	kg 1,4-DCB	1.85E+02	2.95E+01	1.48E+02	7.16E-02	2.45E+00	0.108801	1.64E-04	4.82E-01	0.595046	0.793464	3.380969
Land use	m2a crop eq.	1.67E+00	3.15E-01	1.22E+00	1.36E-03	4.83E-02	1.24E-03	1.41E-06	1.35E-02	8.20E-03	0.026792	0.03857
Mineral resource scarcity	kg Cu eq.	7.84E-01	1.11E-01	6.22E-01	3.24E-02	1.03E-02	0.000384	6.81E-07	0.001745	0.002017	0.00322	0.000924
Fossil resource scarcity	kg oil eq.	17.89688	2.616213	1.35E+01	0.017998	0.569049	0.081643	1.34E-05	0.281597	0.071219	0.078097	0.67584
Water consumption	m3	0.73157	1.44E-01	0.505912	5.90E-04	3.82E-02	0.000897	0.000113	0.008258	0.00588	0.013674	0.014238

S Table 3d: Comparison of the Midpoint category of the Recycling process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	4.12E+01	7.13E+00	2.76E+01	6.48E-02	2.32E+00	0.142398	5.68E-05	0.586714	0.266549	0.372533	2.704057
Stratospheric ozone depletion	kg CFC11 eq.	2.10E-05	1.07E-05	8.52E-06	3.17E-08	5.29E-07	1.70E-08	5.14E-11	1.40E-07	2.04E-07	9.56E-08	6.84E-07
Ionizing radiation	kBq Co-60 eq.	2.53E+00	2.84E-01	1.96E+00	3.61E-03	1.02E-01	1.80E-03	3.76E-06	2.46E-02	1.92E-02	0.014727	0.126956
Ozone formation, Human health	kg NOx eq.	1.03E-01	1.99E-02	6.83E-02	4.56E-04	4.48E-03	3.07E-04	1.34E-07	1.50E-03	0.000687	0.001071	0.005915
Fine particulate matter formation	kg PM2.5 eq.	8.92E-02	2.11E-02	5.52E-02	3.71E-04	3.12E-03	1.63E-04	1.47E-07	8.28E-04	0.00069	0.000987	0.006689
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.08E-01	2.11E-02	7.23E-02	4.63E-04	4.68E-03	3.45E-04	1.38E-07	1.65E-03	0.000696	0.001094	0.005969
Terrestrial acidification	kg SO2 eq.	1.83E-01	5.19E-02	1.07E-01	4.35E-04	7.43E-03	4.48E-04	3.67E-07	1.97E-03	0.001394	0.003304	0.008353
Freshwater eutrophication	kg P eq.	0.027246	7.15E-03	1.61E-02	2.63E-05	7.04E-04	3.54E-05	2.55E-08	2.48E-04	0.000133	0.00019	0.002707
Marine eutrophication	kg N eq.	0.007355	1.59E-03	0.003649	1.87E-06	1.90E-03	1.78E-06	1.98E-09	1.54E-05	1.18E-05	1.29E-05	0.00017
Terrestrial ecotoxicity	kg 1,4-DCB	218.3791	1.06E+02	8.87E+01	2.37E-01	1.28E+01	6.08E-01	8.41E-04	1.94E+00	2.78E+00	3.594162	1.862291
Freshwater ecotoxicity	kg 1,4-DCB	3.05E+00	1.56E+00	1.19E+00	2.84E-03	1.29E-01	0.005228	8.27E-06	0.021999	0.02999	0.041318	0.076381
Marine ecotoxicity	kg 1,4-DCB	4.04E+00	2.13E+00	1.50E+00	0.00377	1.68E-01	0.006924	1.08E-05	0.028928	0.039202	0.054093	0.10552
Human carcinogenic toxicity	kg 1,4-DCB	3.13E+00	5.62E-01	2.16E+00	0.003323	1.39E-01	0.004943	6.34E-06	0.030384	0.021599	0.038225	0.171611
Human non-carcinogenic toxicity	kg 1,4-DCB	1.65E+02	2.95E+01	1.28E+02	0.071615	2.45E+00	0.108801	0.000164	0.482075	0.595046	0.793464	3.380969
Land use	m2a crop eq.	1.24E+00	3.15E-01	7.83E-01	1.36E-03	4.83E-02	1.24E-03	1.41E-06	1.35E-02	0.008195	0.026792	0.03857
Mineral resource scarcity	kg Cu eq.	5.38E-01	1.11E-01	3.76E-01	3.24E-02	1.03E-02	3.84E-04	6.81E-07	1.75E-03	2.02E-03	0.00322	0.000924
Fossil resource scarcity	kg oil eq.	1.34E+01	2.62E+00	9.01E+00	1.80E-02	5.69E-01	8.16E-02	1.34E-05	2.82E-01	7.12E-02	0.078097	0.67584
Water consumption	m3	0.54498	1.44E-01	0.319322	5.90E-04	3.82E-02	0.000897	1.13E-04	8.26E-03	0.00588	0.013674	0.014238

S Table 3e: Comparison of the Endpoint category of the NAR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Damage category	Unit	Total	2-chloropyridine-3-carbonyl chloride	4-Methoxyaniline	Triethyl amine	Tetrahydrofuran	Dichloromethane,	Sodium bicarbonate	Water	Energy
Human health	DALY	5.30E-02	1.39E-03	0.049228	1.04E-04	7.51E-04	1.68E-04	5.89E-05	5.57E-08	0.001338
Ecosystems	species.yr	2.60E-05	9.13E-07	2.34E-05	7.77E-08	5.55E-07	1.65E-07	3.50E-08	3.91E-11	8.63E-07
Resources	USD2013	1.36E+01	1.350196	9.706392	3.12E-01	1.28E+00	0.436727	1.93E-02	2.13E-05	0.487527

S Table 3f: Comparison of the Endpoint category of the AR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine -3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water,	Ethyl acetate	Hydrochloric	Sodium bicarbonate	Energy
Human health	DALY	6.51E-03	0.001877	4.09E-03	5.06E-06	1.74E-04	7.78E-06	9.74E-09	3.61E-05	3.53E-05	5.16E-05	0.000234
Ecosystems	species.yr	3.73E-06	1.09E-06	2.28E-06	3.40E-09	1.17E-07	5.95E-09	6.85E-12	2.55E-08	2.12E-08	3.06E-08	1.51E-07
Resources	USD2013	5.04E+00	8.18E-01	3.80E+00	1.17E-02	1.55E-01	3.14E-02	3.72E-06	9.72E-02	0.017177	0.01691	0.085295

S Table 3g: Comparison of the Endpoint category of the Recycling process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Human health	DALY	4.67E-03	1.88E-03	2.25E-03	5.06E-06	0.000174	7.78E-06	9.74E-09	3.61E-05	3.53E-05	5.16E-05	0.000234
Ecosystems	species.yr	2.85E-06	1.09E-06	1.41E-06	3.40E-09	1.17E-07	5.95E-09	6.85E-12	2.55E-08	2.12E-08	3.06E-08	1.51E-07
Resources	USD2013	3.67E+00	8.18E-01	2.44E+00	1.17E-02	1.55E-01	3.14E-02	3.72E-06	9.72E-02	0.017177	0.01691	0.085295

S Table 3h: Comparison of Normalization category of the NAR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Total	2-chloropyridine-3-carbonyl chloride	4-Methoxyaniline	Triethyl amine	Tetrahydrofuran	Dichloromethane	Sodium bicarbonate	Water	Energy
Global warming	1.81E-02	2.23E-03	0.011142	0.000231	0.00159	0.000917	5.32E-05	4.06E-08	0.001932
Stratospheric ozone depletion	5.47E-03	1.02E-04	3.09E-03	5.49E-06	5.58E-05	0.002149	1.82E-06	4.90E-09	6.53E-05
Ionizing radiation	1.52E-02	2.96E-03	8.62E-03	7.88E-05	0.002014	1.43E-06	3.50E-05	4.47E-08	0.001509
Ozone formation, Human health	5.39E-02	2.19E-03	4.70E-02	0.000207	0.001439	0.001406	5.95E-05	3.72E-08	0.001643
Fine particulate matter formation	1.30E-01	1.52E-03	1.25E-01	7.81E-05	0.000755	0.000518	4.41E-05	3.28E-08	0.001495
Ozone formation, Terrestrial ecosystems	6.43E-02	2.69E-03	5.59E-02	2.65E-04	0.001774	0.001649	7.04E-05	4.44E-08	0.001921
Terrestrial acidification	2.74E-01	1.81E-03	0.268777	0.000139	0.00102	0.000888	9.22E-05	5.12E-08	0.001165
Freshwater eutrophication	1.97E-01	0.017232	1.48E-01	0.001444	0.00635	0.000338	0.000335	2.24E-07	0.023827
Marine eutrophication	2.84E-03	1.91E-04	2.27E-03	0.000105	6.17E-05	1.24E-06	3.20E-06	2.45E-09	0.00021
Terrestrial ecotoxicity	3.92E-02	3.25E-03	3.16E-02	3.35E-04	0.002931	0.000121	0.00027	3.16E-07	0.0007
Freshwater ecotoxicity	1.518077	0.029157	1.45E+00	0.002367	0.01749	0.001215	0.001875	1.88E-06	0.017332
Marine ecotoxicity	1.12E+00	0.020748	1.07E+00	0.001817	0.013455	0.000981	0.001422	1.42E-06	0.013872
Human carcinogenic toxicity	1.36E+00	1.04E-01	1.06E+00	0.008336	0.060165	0.024012	0.004243	3.52E-06	0.095245
Human non-carcinogenic toxicity	5.16E-02	3.74E-03	0.04678	4.34E-05	0.000319	3.53E-05	2.90E-05	2.99E-08	0.000618
Land use	9.92E-04	9.31E-05	7.99E-04	4.15E-06	5.47E-05	3.07E-07	4.96E-06	1.31E-09	3.57E-05
Mineral resource scarcity	1.07E-04	2.49E-06	1.04E-04	4.24E-08	2.82E-07	8.91E-09	3.07E-08	3.24E-11	4.40E-08
Fossil resource scarcity	4.64E-02	5.53E-03	3.01E-02	0.000912	0.004477	0.001385	9.11E-05	7.80E-08	0.00394
Water consumption	8.35E-03	7.75E-04	4.60E-03	4.76E-05	0.002481	7.94E-05	5.86E-05	2.42E-06	0.000305

S Table 3i: Comparison of Normalization category of the AR process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	7.00E-03	8.91E-04	0.005305	8.11E-06	0.00029	1.78E-05	7.09E-09	7.33E-05	3.33E-05	4.66E-05	0.000338
Stratospheric ozone depletion	4.21E-04	1.79E-04	2.13E-04	5.29E-07	8.83E-06	2.84E-07	8.58E-10	2.35E-06	3.40E-06	1.60E-06	1.14E-05
Ionizing radiation	0.007495	5.90E-04	6.30E-03	7.51E-06	0.000212	3.73E-06	7.82E-09	5.11E-05	3.99E-05	3.06E-05	0.000264
Ozone formation, Human health	6.84E-03	9.66E-04	5.17E-03	2.22E-05	2.18E-04	1.49E-05	6.50E-09	7.31E-05	3.34E-05	5.20E-05	0.000287
Fine particulate matter formation	4.56E-03	8.26E-04	3.23E-03	1.45E-05	1.22E-04	6.38E-06	5.74E-09	3.24E-05	2.70E-05	3.86E-05	0.000262
Ozone formation, Terrestrial ecosystems	0.008318	1.19E-03	0.00629	2.61E-05	2.64E-04	1.94E-05	7.78E-09	9.30E-05	3.92E-05	6.16E-05	0.000336
Terrestrial acidification	0.00596	1.27E-03	4.12E-03	1.06E-05	0.000181	1.09E-05	8.96E-09	4.80E-05	3.40E-05	8.06E-05	0.000204
Freshwater eutrophication	0.051149	1.10E-02	3.39E-02	4.04E-05	0.001085	5.46E-05	3.92E-08	0.000381	0.000204	0.000293	0.004169
Marine eutrophication	0.001971	3.45E-04	1.17E-03	4.05E-07	4.13E-04	3.86E-07	4.29E-10	3.33E-06	2.55E-06	2.80E-06	3.68E-05
Terrestrial ecotoxicity	2.07E-02	6.97E-03	1.21E-02	1.56E-05	8.41E-04	4.00E-05	5.53E-08	0.000128	0.000183	0.000236	0.000123
Freshwater ecotoxicity	0.161175	6.18E-02	8.72E-02	1.13E-04	5.11E-03	2.08E-04	3.28E-07	0.000873	0.001191	0.00164	0.003032
Marine ecotoxicity	0.123445	4.90E-02	6.51E-02	8.67E-05	0.00387	0.000159	2.49E-07	0.000665	0.000902	0.001244	0.002427
Human carcinogenic toxicity	0.59993	5.46E-02	5.06E-01	3.23E-04	1.35E-02	0.00048	6.15E-07	0.00295	0.002097	0.003712	0.016663
Human non-carcinogenic toxicity	0.005922	9.43E-04	4.73E-03	2.29E-06	7.83E-05	3.48E-06	5.24E-09	1.54E-05	1.90E-05	2.54E-05	0.000108
Land use	0.000271	5.10E-05	1.97E-04	2.21E-07	7.82E-06	2.01E-07	2.28E-10	2.19E-06	1.33E-06	4.34E-06	6.25E-06
Mineral resource scarcity	6.53E-06	9.28E-07	5.18E-06	2.70E-07	8.57E-08	3.20E-09	5.67E-12	1.45E-08	1.68E-08	2.68E-08	7.70E-09
Fossil resource scarcity	1.83E-02	2.67E-03	1.38E-02	1.84E-05	5.80E-04	8.33E-05	1.36E-08	0.000287	7.26E-05	7.97E-05	0.000689
Water consumption	2.74E-03	5.39E-04	1.90E-03	2.21E-06	1.43E-04	3.36E-06	4.24E-07	3.10E-05	2.20E-05	5.13E-05	5.34E-05

S Table 3j: Comparison of Normalization category of the Recycling process for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzen	2-(2-chloropyridine-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	5.15E-03	8.91E-04	3.45E-03	8.11E-06	2.90E-04	1.78E-05	7.09E-09	7.33E-05	3.33E-05	4.66E-05	0.000338
Stratospheric ozone depletion	3.50E-04	1.79E-04	1.42E-04	5.29E-07	8.83E-06	2.84E-07	8.58E-10	2.35E-06	3.40E-06	1.60E-06	1.14E-05
Ionizing radiation	5.27E-03	5.90E-04	4.07E-03	7.51E-06	2.12E-04	3.73E-06	7.82E-09	5.11E-05	3.99E-05	3.06E-05	0.000264
Ozone formation, Human health	4.98E-03	9.66E-04	3.32E-03	2.22E-05	2.18E-04	1.49E-05	6.50E-09	7.31E-05	3.34E-05	5.20E-05	0.000287
Fine particulate matter formation	3.49E-03	8.26E-04	2.16E-03	1.45E-05	1.22E-04	6.38E-06	5.74E-09	3.24E-05	2.70E-05	3.86E-05	0.000262
Ozone formation, Terrestrial ecosystems	6.10E-03	1.19E-03	4.07E-03	2.61E-05	2.64E-04	1.94E-05	7.78E-09	9.30E-05	3.92E-05	6.16E-05	0.000336
Terrestrial acidification	4.45E-03	0.001267	2.62E-03	1.06E-05	1.81E-04	1.09E-05	8.96E-09	4.80E-05	3.40E-05	8.06E-05	0.000204
Freshwater eutrophication	4.20E-02	0.011013	2.47E-02	4.04E-05	0.001085	5.46E-05	3.92E-08	0.000381	0.000204	0.000293	0.004169
Marine eutrophication	1.60E-03	0.000345	7.92E-04	4.05E-07	4.13E-04	3.86E-07	4.29E-10	3.33E-06	2.55E-06	2.80E-06	3.68E-05
Terrestrial ecotoxicity	1.44E-02	6.97E-03	5.84E-03	1.56E-05	8.41E-04	4.00E-05	5.53E-08	0.000128	0.000183	0.000236	0.000123
Freshwater ecotoxicity	1.21E-01	6.18E-02	4.72E-02	1.13E-04	5.11E-03	0.000208	3.28E-07	0.000873	0.001191	0.00164	0.003032
Marine ecotoxicity	9.29E-02	4.90E-02	3.45E-02	8.67E-05	3.87E-03	0.000159	2.49E-07	0.000665	0.000902	0.001244	0.002427
Human carcinogenic toxicity	3.04E-01	5.46E-02	2.09E-01	3.23E-04	1.35E-02	0.00048	6.15E-07	0.00295	0.002097	0.003712	0.016663
Human non-carcinogenic toxicity	5.28E-03	9.43E-04	4.09E-03	2.29E-06	7.83E-05	3.48E-06	5.24E-09	1.54E-05	1.90E-05	2.54E-05	0.000108
Land use	0.0002	5.10E-05	1.27E-04	2.21E-07	7.82E-06	2.01E-07	2.28E-10	2.19E-06	1.33E-06	4.34E-06	6.25E-06
Mineral resource scarcity	4.48E-06	9.28E-07	3.13E-06	2.70E-07	8.57E-08	3.20E-09	5.67E-12	1.45E-08	1.68E-08	2.68E-08	7.70E-09
Fossil resource scarcity	0.013671	0.002669	0.009192	1.84E-05	0.00058	8.33E-05	1.36E-08	0.000287	7.26E-05	7.97E-05	0.000689
Water consumption	0.002044	0.000539	0.001197	2.21E-06	0.000143	3.36E-06	4.24E-07	3.10E-05	2.20E-05	5.13E-05	5.34E-05

S Table 3k: Comparison of the Midpoint category for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	144.7276	56.02819	41.20263
Stratospheric ozone depletion	kg CFC11 eq.	0.000327	2.52E-05	2.10E-05
Ionizing radiation	kBq Co-60 eq.	7.316951	3.603171	2.53168
Ozone formation, Human health	kg NOx eq.	1.110049	0.14069	0.10256
Fine particulate matter formation	kg PM2.5 eq.	3.318424	0.116692	0.089221
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.141592	0.147742	0.10834
Terrestrial acidification	kg SO2 eq.	11.22493	0.244242	0.182508
Freshwater eutrophication	kg P eq.	0.12807	0.033213	0.027246
Marine eutrophication	kg N eq.	0.013101	0.009083	0.007355
Terrestrial ecotoxicity	kg 1,4-DCB	595.6099	313.8966	218.3791
Freshwater ecotoxicity	kg 1,4-DCB	38.23871	4.05982	3.051808
Marine ecotoxicity	kg 1,4-DCB	48.77685	5.367162	4.037879
Human carcinogenic toxicity	kg 1,4-DCB	13.96531	6.178474	3.126309
Human non-carcinogenic toxicity	kg 1,4-DCB	1.61E+03	1.85E+02	165.1037
Land use	m2a crop eq.	6.125706	1.671089	1.235517
Mineral resource scarcity	kg Cu eq.	12.83352	0.784128	0.537979
Fossil resource scarcity	kg oil eq.	45.52158	17.89688	13.40298
Water consumption	m3	2.225379	0.73157	0.54498

S Table 3l: Comparison of the Endpoint category for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.053036	0.006509	0.004667
Ecosystems	species.yr	2.60E-05	3.73E-06	2.85E-06
Resources	USD2013	13.59391	5.035662	3.67076

S Table 3m: Comparison of the Normalization category for 2-chloro-N-(4-methoxyphenyl) pyridine-3-carboxamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.018091	0.007004	0.00515
Stratospheric ozone depletion	0.005469	4.21E-04	3.50E-04
Ionizing radiation	0.015219	0.007495	0.005266
Ozone formation, Human health	0.053948	0.006838	0.004984
Fine particulate matter formation	1.30E-01	4.56E-03	3.49E-03
Ozone formation, Terrestrial ecosystems	0.064272	0.008318	0.0061
Terrestrial acidification	0.273888	0.00596	0.004453
Freshwater eutrophication	0.197227	0.051149	0.041959
Marine eutrophication	0.002843	0.001971	0.001596
Terrestrial ecotoxicity	0.039191	0.020654	0.014369
Freshwater ecotoxicity	1.518077	0.161175	0.121157
Marine ecotoxicity	1.121868	1.23E-01	0.092871
Human carcinogenic toxicity	1.36E+00	6.00E-01	0.303565
Human non-carcinogenic toxicity	0.05157	0.005922	0.005283
Land use	0.000992	0.000271	0.0002
Mineral resource scarcity	0.000107	6.53E-06	4.48E-06
Fossil resource scarcity	0.046432	0.018255	0.013671
Water consumption	0.008345	0.002743	0.002044

S Table 4a: Inventory Data of N-(4-methoxyphenyl) cyclopropane carboxamide for 1 kg functional unit (API-3)

NAR - Inputs		**AR - Inputs**	
cyclopropanecarbonyl chloride	0.546 Kg	1-methoxy-4-nitro-benzen	0.81 Kg
4-Methoxyaniline	0.644 kg	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one (Recycling)	1.33 kg
Triethylamine	0.581 kg	Iron Powder	0.885 kg
Dichlromethane	3.28 kg	Ammonium Chloride	1.98 kg
Water	0.547 kg	Isopropanol	0.081 kg
Sodium bicarbonate	0.273 kg	Ethyl acetate	0.243 kg
Energy	39.4 MJ	Hcl	0.405 kg
-	-	$NaHCO_3$	0.405 kg
-	-	Water	0.162 kg
-	-	Energy	11.7 MJ
Outputs		**Outputs**	
N-(4-methoxyphenyl) cyclopropane carboxamide	1 kg	N-(4-methoxyphenyl) cyclopropane carboxamide	1kg
Byproducts		Byproducts	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.174 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 4b: Comparison of the Midpoint category of the NAR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Unit	Total	cyclopropanecarbonyl chloride	4-Methoxyaniline	Triethyl amine	Water	Dichloromethane	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	1.51E+02	1.26E+01	111.4338	2.330543	0.000265	11.96954	0.347538	12.61314
Stratospheric ozone depletion	kg CFC11 eq.	0.000451	6.42E-06	0.000231	4.14E-07	2.40E-10	0.00021	8.91E-08	3.19E-06
Ionizing radiation	kBq Co-60 eq.	6.606142	0.773361	5.178006	0.047706	1.75E-05	0.001122	0.013739	0.592189
Ozone formation, Human health	kg NOx eq.	1.32E+00	3.01E-02	1.21E+00	5.35E-03	6.24E-07	0.047224	0.000999	0.027592
Fine particulate matter formation	kg PM2.5 eq.	4.101785	3.82E-02	4.007326	0.002516	6.85E-07	0.021624	0.000921	0.0312
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.35E+00	0.031072	1.241198	5.94E-03	6.44E-07	0.0478	0.001021	0.027844
Terrestrial acidification	kg SO2 eq.	1.40E+01	8.41E-02	1.38E+01	7.16E-03	1.71E-06	0.059406	0.003082	0.038964
Freshwater eutrophication	kg P eq.	0.142761	0.00852	0.1199	0.001181	1.19E-07	0.000358	0.000177	0.012626
Marine eutrophication	kg N eq.	0.015247	0.000745	0.013078	0.000611	9.22E-09	9.33E-06	1.20E-05	0.000791
Terrestrial ecotoxicity	kg 1,4-DCB	663.2486	4.18E+01	599.963	6.406378	0.003921	2.995883	3.35301	8.686697
Freshwater ecotoxicity	kg 1,4-DCB	4.67E+01	0.596783	4.56E+01	7.51E-02	3.86E-05	0.049971	0.038546	0.356281
Marine ecotoxicity	kg 1,4-DCB	5.96E+01	7.97E-01	5.81E+01	0.09944	5.05E-05	0.069586	0.050463	0.492198
Human carcinogenic toxicity	kg 1,4-DCB	1.58E+01	0.837822	13.6467	0.108091	2.96E-05	0.40361	0.035661	0.800483
Human non-carcinogenic toxicity	kg 1,4-DCB	1.86E+03	16.67414	1827.524	1.707048	0.000764	1.801897	0.740226	15.77061
Land use	m2a crop eq.	6.76E+00	0.350668	6.168393	0.032235	6.58E-06	0.003091	0.024995	0.179909
Mineral resource scarcity	kg Cu eq.	15.65963	0.036178	15.60799	0.006405	3.18E-06	0.001746	0.003004	0.004309
Fossil resource scarcity	kg oil eq.	47.01987	3.56E+00	36.8875	1.126185	6.24E-05	2.21636	0.072857	3.152469
Water consumption	m3	1.96E+00	2.96E-01	1.53E+00	0.015995	0.000527	0.034565	0.012757	0.066415

S Table 4c: Comparison of the Midpoint category of the AR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzene	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	6.56E+01	9.85E+00	4.68E+01	8.96E-02	3.20E+00	1.97E-01	7.84E-05	8.11E-01	3.68E-01	0.514687	3.735891
Stratospheric ozone depletion	kg CFC11 eq.	3.29E-05	1.48E-05	1.57E-05	4.38E-08	7.30E-07	2.35E-08	7.10E-11	1.94E-07	2.82E-07	1.32E-07	9.45E-07
Ionizing radiation	kBq Co-60 eq.	3.79E+00	3.92E-01	3.00E+00	4.99E-03	1.41E-01	0.00248	5.19E-06	3.39E-02	0.026517	0.020347	0.175401
Ozone formation, Human health	kg NOx eq.	1.63E-01	2.75E-02	1.15E-01	6.30E-04	6.19E-03	4.24E-04	1.85E-07	2.08E-03	0.000949	0.001479	0.008172
Fine particulate matter formation	kg PM2.5 eq.	1.46E-01	2.92E-02	9.92E-02	5.13E-04	4.32E-03	0.000225	2.03E-07	1.14E-03	0.000953	0.001364	0.009241
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.70E-01	2.92E-02	0.119855	6.40E-04	6.47E-03	4.77E-04	1.91E-07	0.002282	0.000961	0.001512	0.008247
Terrestrial acidification	kg SO2 eq.	3.21E-01	7.18E-02	0.21664	6.01E-04	1.03E-02	0.000619	5.07E-07	0.002718	0.001926	0.004565	0.011541
Freshwater eutrophication	kg P eq.	3.91E-02	9.88E-03	0.023603	3.63E-05	9.73E-04	4.89E-05	3.52E-08	3.42E-04	1.83E-04	0.000263	0.00374
Marine eutrophication	kg N eq.	0.012112	2.20E-03	6.99E-03	2.58E-06	2.63E-03	2.46E-06	2.73E-09	2.12E-05	1.63E-05	1.78E-05	0.000234
Terrestrial ecotoxicity	kg 1,4-DCB	408.3396	1.46E+02	2.29E+02	0.327886	1.77E+01	0.840671	0.001161	2.686487	3.843684	4.965648	2.572917
Freshwater ecotoxicity	kg 1,4-DCB	5.204388	2.150367	2.63E+00	0.003923	1.78E-01	0.007223	1.14E-05	0.030393	0.041434	0.057085	0.105527
Marine ecotoxicity	kg 1,4-DCB	6.983558	2.942611	3.479059	0.005208	2.32E-01	0.009566	1.49E-05	0.039967	0.054161	0.074734	0.145784
Human carcinogenic toxicity	kg 1,4-DCB	7.92515	7.77E-01	6.58E+00	4.59E-03	1.91E-01	6.83E-03	8.76E-06	4.20E-02	0.029841	0.052812	0.237096
Human non-carcinogenic toxicity	kg 1,4-DCB	1.10E+02	4.07E+01	5.88E+01	9.89E-02	3.38E+00	1.50E-01	2.26E-04	6.66E-01	8.22E-01	1.096239	4.671103
Land use	m2a crop eq.	1.87E+00	4.35E-01	1.24E+00	1.88E-03	6.67E-02	1.71E-03	1.95E-06	1.87E-02	1.13E-02	0.037016	0.053287
Mineral resource scarcity	kg Cu eq.	0.706657	1.54E-01	0.482297	0.044733	1.42E-02	0.00053	9.41E-07	0.002411	0.002787	0.004448	0.001276
Fossil resource scarcity	kg oil eq.	20.87016	3.61E+00	14.80268	2.49E-02	7.86E-01	1.13E-01	1.85E-05	3.89E-01	9.84E-02	0.107898	0.933731
Water consumption	m3	1.026252	0.1987	0.714486	0.000815	0.05276	0.001239	0.000156	0.01141	0.008124	0.018892	0.019672

S Table 4d: Comparison of the Midpoint category of the Recycling process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzene	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	45.03789	9.85E+00	2.63E+01	8.96E-02	3.20E+00	1.97E-01	7.84E-05	8.11E-01	3.68E-01	0.514687	3.735891
Stratospheric ozone depletion	kg CFC11 eq.	2.70E-05	1.48E-05	9.82E-06	4.38E-08	7.30E-07	2.35E-08	7.10E-11	1.94E-07	2.82E-07	1.32E-07	9.45E-07
Ionizing radiation	kBq Co-60 eq.	2.31E+00	3.92E-01	1.510907	4.99E-03	1.41E-01	0.00248	5.19E-06	3.39E-02	0.026517	0.020347	0.175401
Ozone formation, Human health	kg NOx eq.	1.10E-01	2.75E-02	6.23E-02	6.30E-04	6.19E-03	4.24E-04	1.85E-07	2.08E-03	0.000949	0.001479	0.008172
Fine particulate matter formation	kg PM2.5 eq.	1.08E-01	2.92E-02	6.11E-02	5.13E-04	4.32E-03	0.000225	2.03E-07	1.14E-03	0.000953	0.001364	0.009241
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.15E-01	2.92E-02	6.52E-02	6.40E-04	6.47E-03	4.77E-04	1.91E-07	0.002282	0.000961	0.001512	0.008247
Terrestrial acidification	kg SO2 eq.	2.35E-01	7.18E-02	1.31E-01	6.01E-04	1.03E-02	0.000619	5.07E-07	0.002718	0.001926	0.004565	0.011541
Freshwater eutrophication	kg P eq.	0.030787	9.88E-03	1.53E-02	3.63E-05	9.73E-04	4.89E-05	3.52E-08	3.42E-04	1.83E-04	0.000263	0.00374
Marine eutrophication	kg N eq.	9.71E-03	2.20E-03	4.59E-03	2.58E-06	2.63E-03	2.46E-06	2.73E-09	2.12E-05	1.63E-05	1.78E-05	0.000234
Terrestrial ecotoxicity	kg 1,4-DCB	2.76E+02	146.252	9.66E+01	0.327886	1.77E+01	0.840671	0.001161	2.686487	3.843684	4.965648	2.572917
Freshwater ecotoxicity	kg 1,4-DCB	3.81E+00	2.15E+00	1.23E+00	0.003923	1.78E-01	0.007223	1.14E-05	0.030393	0.041434	0.057085	0.105527
Marine ecotoxicity	kg 1,4-DCB	5.14E+00	2.94E+00	1.63E+00	0.005208	2.32E-01	0.009566	1.49E-05	0.039967	0.054161	0.074734	0.145784
Human carcinogenic toxicity	kg 1,4-DCB	3.69E+00	7.77E-01	2.35E+00	4.59E-03	1.91E-01	6.83E-03	8.76E-06	4.20E-02	0.029841	0.052812	0.237096
Human non-carcinogenic toxicity	kg 1,4-DCB	8.27E+01	4.07E+01	3.11E+01	9.89E-02	3.38E+00	1.50E-01	2.26E-04	6.66E-01	8.22E-01	1.096239	4.671103
Land use	m2a crop eq.	1.27E+00	4.35E-01	6.40E-01	1.88E-03	6.67E-02	1.71E-03	1.95E-06	1.87E-02	1.13E-02	0.037016	0.053287
Mineral resource scarcity	kg Cu eq.	3.65E-01	1.54E-01	0.140651	0.044733	1.42E-02	0.00053	9.41E-07	0.002411	0.002787	0.004448	0.001276
Fossil resource scarcity	kg oil eq.	1.46E+01	3.61E+00	8.57E+00	2.49E-02	7.86E-01	1.13E-01	1.85E-05	3.89E-01	9.84E-02	0.107898	0.933731
Water consumption	m3	0.767272	0.1987	0.455505	0.000815	5.28E-02	0.001239	0.000156	0.01141	0.008124	0.018892	0.019672

S Table 4e: Comparison of the Endpoint category of the NAR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Damage category	Unit	Total	Cyclopropane carbonyl chloride	4-Methoxyaniline	Triethyl amine	Water	Dichloromethane	Sodium bicarbonate	Energy
Human health	DALY	6.42E-02	1.16E-03	6.15E-02	1.31E-04	4.54E-08	0.000274	4.81E-05	0.001092
Ecosystems	species.yr	3.10E-05	7.46E-07	2.92E-05	9.78E-08	3.19E-11	2.69E-07	2.86E-08	7.05E-07
Resources	USD2013	14.4399	7.86E-01	1.21E+01	0.393345	1.74E-05	0.712806	0.015775	0.397859

S Table 4f: Comparison of the Endpoint category of the AR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzene	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Human health	DALY	8.26E-03	0.002593	4.91E-03	6.99E-06	0.000241	1.07E-05	1.35E-08	4.99E-05	4.87E-05	7.12E-05	0.000323
Ecosystems	species.yr	4.65E-06	1.51E-06	2.65E-06	4.70E-09	1.62E-07	8.22E-09	9.46E-12	3.52E-08	2.93E-08	4.23E-08	2.09E-07
Resources	USD2013	5.896241	1.13E+00	4.19E+00	1.62E-02	2.14E-01	4.34E-02	5.14E-06	1.34E-01	2.37E-02	0.023363	0.117842

S Table 4g: Comparison of the Endpoint category of the Recycling process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzene	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Human health	DALY	5.70E-03	0.002593	2.35E-03	6.99E-06	0.000241	1.07E-05	1.35E-08	4.99E-05	4.87E-05	7.12E-05	0.000323
Ecosystems	species.yr	3.43E-06	1.51E-06	1.44E-06	4.70E-09	1.62E-07	8.22E-09	9.46E-12	3.52E-08	2.93E-08	4.23E-08	2.09E-07
Resources	USD2013	4.00E+00	1.13E+00	2.30E+00	1.62E-02	0.213903	4.34E-02	5.14E-06	0.134354	0.023731	0.023363	0.117842

S Table 4h: Comparison of Normalization category the NAR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Total	cyclopropanecarbonyl chloride	4-Methoxyaniline	Triethyl amine	Water	Dichloromethane	Sodium	Energy
Global warming	0.018909	0.001573	1.39E-02	2.91E-04	3.31E-08	1.50E-03	4.34E-05	0.001577
Stratospheric ozone depletion	0.007538	0.000107	0.003863	6.91E-06	4.00E-09	0.003507	1.49E-06	5.33E-05
Ionizing radiation	1.37E-02	1.61E-03	1.08E-02	9.92E-05	3.65E-08	2.33E-06	2.86E-05	0.001232
Ozone formation, Human health	0.064162	0.001464	0.058754	2.60E-04	3.03E-08	0.002295	4.85E-05	0.001341
Fine particulate matter formation	1.60E-01	0.001494	1.57E-01	9.84E-05	2.68E-08	0.000846	3.60E-05	0.00122
Ozone formation, Terrestrial ecosystems	7.63E-02	1.75E-03	6.99E-02	3.34E-04	3.63E-08	0.002691	5.75E-05	0.001568
Terrestrial acidification	0.340706	0.002053	0.336003	1.75E-04	4.18E-08	0.00145	7.52E-05	0.000951
Freshwater eutrophication	0.219853	0.01312	0.184645	1.82E-03	1.83E-07	5.51E-04	0.000273	0.019444
Marine eutrophication	0.003309	0.000162	0.002838	0.000132	2.00E-09	2.02E-06	2.61E-06	0.000172
Terrestrial ecotoxicity	4.36E-02	2.75E-03	3.95E-02	4.22E-04	2.58E-07	0.000197	0.000221	0.000572
Freshwater ecotoxicity	1.86E+00	2.37E-02	1.810964	2.98E-03	1.53E-06	0.001984	0.00153	0.014144
Marine ecotoxicity	1.37E+00	0.018321	1.337088	2.29E-03	1.16E-06	0.0016	0.001161	0.011321
Human carcinogenic toxicity	1.54E+00	0.081353	1.325094	0.010496	2.87E-06	0.039191	0.003463	0.077727
Human non-carcinogenic toxicity	5.97E-02	0.000534	0.058481	5.46E-05	2.44E-08	5.77E-05	2.37E-05	0.000505
Land use	0.001095	5.68E-05	0.000999	5.22E-06	1.07E-09	5.01E-07	4.05E-06	2.91E-05
Mineral resource scarcity	0.00013	3.01E-07	0.00013	5.33E-08	2.65E-11	1.45E-08	2.50E-08	3.59E-08
Fossil resource scarcity	4.80E-02	3.64E-03	0.037625	0.001149	6.37E-08	0.002261	7.43E-05	0.003216
Water consumption	7.34E-03	1.11E-03	0.005746	6.00E-05	1.98E-06	0.00013	4.78E-05	0.000249

S Table 4i: Comparison of Normalization category of the AR process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzene	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	8.20E-03	1.23E-03	5.86E-03	1.12E-05	4.00E-04	2.46E-05	9.80E-09	0.000101	4.60E-05	6.43E-05	0.000467
Stratospheric ozone depletion	0.000549	2.47E-04	2.62E-04	7.31E-07	1.22E-05	3.93E-07	1.19E-09	3.24E-06	4.70E-06	2.20E-06	1.58E-05
Ionizing radiation	0.007892	8.15E-04	6.24E-03	1.04E-05	0.000293	5.16E-06	1.08E-08	7.06E-05	5.52E-05	4.23E-05	0.000365
Ozone formation, Human health	7.90E-03	1.34E-03	5.60E-03	3.06E-05	3.01E-04	2.06E-05	8.99E-09	0.000101	4.61E-05	7.19E-05	0.000397
Fine particulate matter formation	5.72E-03	1.14E-03	3.88E-03	2.01E-05	1.69E-04	8.82E-06	7.93E-09	4.47E-05	3.73E-05	5.33E-05	0.000361
Ozone formation, Terrestrial ecosystems	0.00955	1.64E-03	0.006748	3.60E-05	3.64E-04	2.68E-05	1.07E-08	0.000128	5.41E-05	8.51E-05	0.000464
Terrestrial acidification	0.007824	1.75E-03	5.29E-03	1.47E-05	0.00025	1.51E-05	1.24E-08	6.63E-05	4.70E-05	0.000111	0.000282
Freshwater eutrophication	6.02E-02	1.52E-02	3.63E-02	5.59E-05	0.001499	7.54E-05	5.42E-08	0.000527	0.000282	0.000404	0.005759
Marine eutrophication	2.63E-03	4.76E-04	1.52E-03	5.60E-07	0.000571	5.33E-07	5.93E-10	4.61E-06	3.53E-06	3.86E-06	5.09E-05
Terrestrial ecotoxicity	0.026869	0.009623	1.51E-02	2.16E-05	1.16E-03	5.53E-05	7.64E-08	0.000177	0.000253	0.000327	0.000169
Freshwater ecotoxicity	0.206614	0.08537	1.04E-01	1.56E-04	7.06E-03	0.000287	4.53E-07	0.001207	0.001645	0.002266	0.004189
Marine ecotoxicity	0.160622	0.06768	0.080018	0.00012	5.35E-03	0.00022	3.44E-07	0.000919	0.001246	0.001719	0.003353
Human carcinogenic toxicity	0.769532	0.075406	0.639309	0.000446	0.018584	0.000663	8.50E-07	0.004076	0.002898	0.005128	0.023022
Human non-carcinogenic toxicity	0.003532	0.001303	0.001881	3.17E-06	1.08E-04	4.81E-06	7.24E-09	2.13E-05	2.63E-05	3.51E-05	0.000149
Land use	0.000303	7.05E-05	0.000202	3.05E-07	1.08E-05	2.77E-07	3.16E-10	3.03E-06	1.83E-06	6.00E-06	8.63E-06
Mineral resource scarcity	5.89E-06	1.28E-06	4.02E-06	3.73E-07	1.18E-07	4.42E-09	7.84E-12	2.01E-08	2.32E-08	3.71E-08	1.06E-08
Fossil resource scarcity	0.021288	0.003687	0.015099	2.54E-05	0.000802	0.000115	1.89E-08	0.000397	0.0001	0.00011	0.000952
Water consumption	0.003848	0.000745	0.002679	3.06E-06	0.000198	4.65E-06	5.86E-07	4.28E-05	3.05E-05	7.08E-05	7.38E-05

S Table 4j: Comparison of Normalization category of the Recycling process for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzen	2-(cyclopropanecarbonyl)-1,1-dioxo-1,2-benzothiazol-3-one(Recycling)	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	5.63E-03	1.23E-03	3.28E-03	1.12E-05	4.00E-04	2.46E-05	9.80E-09	0.000101	4.60E-05	6.43E-05	0.000467
Stratospheric ozone depletion	4.51E-04	0.000247	1.64E-04	7.31E-07	1.22E-05	3.93E-07	1.19E-09	3.24E-06	4.70E-06	2.20E-06	1.58E-05
Ionizing radiation	4.80E-03	8.15E-04	3.14E-03	1.04E-05	0.000293	5.16E-06	1.08E-08	7.06E-05	5.52E-05	4.23E-05	0.000365
Ozone formation, Human health	5.33E-03	1.34E-03	3.03E-03	3.06E-05	0.000301	2.06E-05	8.99E-09	0.000101	4.61E-05	7.19E-05	0.000397
Fine particulate matter formation	4.22E-03	1.14E-03	2.39E-03	2.01E-05	1.69E-04	8.82E-06	7.93E-09	4.47E-05	3.73E-05	5.33E-05	0.000361
Ozone formation, Terrestrial ecosystems	0.006471	1.64E-03	3.67E-03	3.60E-05	3.64E-04	2.68E-05	1.07E-08	0.000128	5.41E-05	8.51E-05	0.000464
Terrestrial acidification	5.73E-03	1.75E-03	3.20E-03	1.47E-05	2.50E-04	1.51E-05	1.24E-08	6.63E-05	4.70E-05	0.000111	0.000282
Freshwater eutrophication	0.047412	1.52E-02	2.36E-02	5.59E-05	1.50E-03	7.54E-05	5.42E-08	0.000527	0.000282	0.000404	0.005759
Marine eutrophication	2.11E-03	0.000476	9.97E-04	5.60E-07	5.71E-04	5.33E-07	5.93E-10	4.61E-06	3.53E-06	3.86E-06	5.09E-05
Terrestrial ecotoxicity	0.018145	9.62E-03	6.36E-03	2.16E-05	1.16E-03	5.53E-05	7.64E-08	0.000177	0.000253	0.000327	0.000169
Freshwater ecotoxicity	0.151071	8.54E-02	4.89E-02	0.000156	7.06E-03	0.000287	4.53E-07	0.001207	0.001645	0.002266	0.004189
Marine ecotoxicity	0.118187	6.77E-02	3.76E-02	1.20E-04	5.35E-03	0.00022	3.44E-07	0.000919	0.001246	0.001719	0.003353
Human carcinogenic toxicity	3.58E-01	7.54E-02	2.28E-01	4.46E-04	1.86E-02	0.000663	8.50E-07	0.004076	0.002898	0.005128	0.023022
Human non-carcinogenic toxicity	2.65E-03	1.30E-03	9.95E-04	3.17E-06	1.08E-04	4.81E-06	7.24E-09	2.13E-05	2.63E-05	3.51E-05	0.000149
Land use	2.05E-04	7.05E-05	1.04E-04	3.05E-07	1.08E-05	2.77E-07	3.16E-10	3.03E-06	1.83E-06	6.00E-06	8.63E-06
Mineral resource scarcity	3.04E-06	1.28E-06	1.17E-06	3.73E-07	1.18E-07	4.42E-09	7.84E-12	2.01E-08	2.32E-08	3.71E-08	1.06E-08
Fossil resource scarcity	0.014925	3.69E-03	8.74E-03	2.54E-05	0.000802	0.000115	1.89E-08	0.000397	0.0001	0.00011	0.000952
Water consumption	2.88E-03	7.45E-04	0.001708	3.06E-06	1.98E-04	4.65E-06	5.86E-07	4.28E-05	3.05E-05	7.08E-05	7.38E-05

S Table 4k: Comparison of the Midpoint category for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	151.2758	65.61525	45.03789
Stratospheric ozone depletion	kg CFC11 eq.	0.000451	3.29E-05	2.70E-05
Ionizing radiation	kBq Co-60 eq.	6.606142	3.794423	2.307231
Ozone formation, Human health	kg NOx eq.	1.32E+00	0.162645	0.109722
Fine particulate matter formation	kg PM2.5 eq.	4.101785	0.146185	0.108056
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.354871	0.169631	0.114942
Terrestrial acidification	kg SO2 eq.	1.40E+01	3.21E-01	0.234958
Freshwater eutrophication	kg P eq.	0.142761	0.039069	0.030787
Marine eutrophication	kg N eq.	0.015247	0.012112	0.009714
Terrestrial ecotoxicity	kg 1,4-DCB	663.2486	408.3396	275.7648
Freshwater ecotoxicity	kg 1,4-DCB	46.73292	5.204388	3.805303
Marine ecotoxicity	kg 1,4-DCB	59.64259	6.983558	5.138559
Human carcinogenic toxicity	kg 1,4-DCB	15.8324	7.92515	3.688853
Human non-carcinogenic toxicity	kg 1,4-DCB	1864.219	110.3767	82.68703
Land use	m2a crop eq.	6.759297	1.870586	1.266028
Mineral resource scarcity	kg Cu eq.	15.65963	0.706657	0.365011
Fossil resource scarcity	kg oil eq.	47.01987	20.87016	14.63278
Water consumption	m3	1.958572	1.026252	0.767272

S Table 4l: Comparison of the Endpoint category for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	6.42E-02	0.008255	0.005698
Ecosystems	species.yr	3.10E-05	4.65E-06	3.43E-06
Resources	USD2013	14.4399	5.896241	4.001806

S Table 4m: Comparison of Normalization category for N-(4-methoxyphenyl) cyclopropane carboxamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.018909	8.20E-03	5.63E-03
Stratospheric ozone depletion	0.007538	0.000549	0.000451
Ionizing radiation	1.37E-02	7.89E-03	4.80E-03
Ozone formation, Human health	0.064162	0.007905	0.005332
Fine particulate matter formation	0.16038	0.005716	0.004225
Ozone formation, Terrestrial ecosystems	0.076279	0.00955	0.006471
Terrestrial acidification	0.340706	0.007824	0.005733
Freshwater eutrophication	0.219853	0.060166	0.047412
Marine eutrophication	0.003309	0.002628	0.002108
Terrestrial ecotoxicity	0.043642	0.026869	0.018145
Freshwater ecotoxicity	1.855297	0.206614	0.151071
Marine ecotoxicity	1.37178	0.160622	0.118187
Human carcinogenic toxicity	1.54E+00	7.70E-01	0.358188
Human non-carcinogenic toxicity	0.059655	0.003532	0.002646
Land use	0.001095	0.000303	0.000205
Mineral resource scarcity	0.00013	5.89E-06	3.04E-06
Fossil resource scarcity	0.04796	0.021288	0.014925
Water consumption	0.007345	0.003848	0.002877

S Table 5a: Inventory Data of Fenfuram (2-Methyl-N-phenyl-furan-3-carboxamide) for 1 kg functional unit (API-4)

NAR – Inputs		**AR – Inputs**	
Ethyl 2-methylfuran-3-carboxylate	1.02 Kg	Nitrobenzene	0.626 Kg
Aniline	0.925 kg	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	1.48 kg
Sodium tert-butoxide	0.636 kg	Iron Powder	0.851 kg
Energy	7.35 MJ	Ammonium Chloride	1.9 kg
-	-	Isopropanol	0.626 kg
-	-	Water	0.125 kg
-	-	Ethyl acetate	0.188 kg
-	-	1M HCl	0.313 kg
-	-	$NaHCO_3$ (aq)	0.313 kg
-	-	Energy	9.01 MJ
NAR – Output		**AR – Output**	
Fenfuram(2-methyl-N-phenyl-furan-3-carboxamide)	1 kg	Fenfuram(2-methyl-N-phenyl-furan-3-carboxamide)	1 kg
Byproducts		Byproducts	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.380 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 5b: Comparison of the Midpoint category of the NAR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Unit	Total	Ethyl 2-methylfuran-3-carboxylate	Aniline	Sodium tert-butoxide	Energy
Global warming	kg CO2 eq.	1.97E+02	4.45E+01	1.50E+02	0.470281	2.356959
Stratospheric ozone depletion	kg CFC11 eq.	3.60E-04	7.06E-05	0.000288	1.23E-07	5.96E-07
Ionizing radiation	kBq Co-60 eq.	9.022154	1.67E+00	7.229381	0.013069	0.11066
Ozone formation, Human health	kg NOx eq.	1.893452	1.05E-01	1.78251	0.001139	0.005156
Fine particulate matter formation	kg PM2.5 eq.	6.16E+00	8.74E-02	6.064571	0.000551	0.00583
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.943419	1.09E-01	1.828117	0.001234	0.005203
Terrestrial acidification	kg SO2 eq.	2.10E+01	0.155484	20.87003	0.00134	0.007281
Freshwater eutrophication	kg P eq.	2.07E-01	3.68E-02	1.68E-01	7.63E-05	0.002359
Marine eutrophication	kg N eq.	0.035272	0.028225	0.006892	6.62E-06	0.000148
Terrestrial ecotoxicity	kg 1,4-DCB	765.7515	71.34817	691.2196	1.560427	1.623243
Freshwater ecotoxicity	kg 1,4-DCB	6.78E+01	1.297746	66.40189	0.017028	0.066577
Marine ecotoxicity	kg 1,4-DCB	8.62E+01	1.734936	84.37516	0.02231	0.091975
Human carcinogenic toxicity	kg 1,4-DCB	2.21E+01	2.44E+00	1.95E+01	0.020941	0.149583
Human non-carcinogenic toxicity	kg 1,4-DCB	2.77E+03	4.17E+01	2.73E+03	0.308283	2.94698
Land use	m2a crop eq.	4.75E+00	6.18E-01	4.09E+00	0.006134	0.033619
Mineral resource scarcity	kg Cu eq.	23.64321	0.059864	23.58112	0.001416	0.000805
Fossil resource scarcity	kg oil eq.	6.66E+01	1.58E+01	4.98E+01	0.414106	0.589087
Water consumption	m3	1.430326	0.359521	1.053373	0.005022	0.012411

S Table 5c: Comparison of the Midpoint category of the AR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Unit	Total	Nitrobenzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	71.32144	2.016573	61.79171	0.086212	3.0787	0.152047	6.06E-05	0.62647	0.284611	0.397776	2.887286
Stratospheric ozone depletion	kg CFC11 eq.	3.67E-05	1.94E-05	1.54E-05	4.21E-08	7.02E-07	1.82E-08	5.49E-11	1.50E-07	2.18E-07	1.02E-07	7.31E-07
Ionizing radiation	kBq Co-60 eq.	3.68E+00	2.81E-02	3.31E+00	4.80E-03	1.35E-01	1.92E-03	4.01E-06	2.62E-02	2.05E-02	0.015725	0.135559
Ozone formation, Human health	kg NOx eq.	1.66E-01	3.74E-03	1.46E-01	6.06E-04	5.95E-03	3.27E-04	1.43E-07	1.61E-03	0.000734	0.001143	0.006316
Fine particulate matter formation	kg PM2.5 eq.	1.34E-01	3.44E-03	0.115468	4.94E-04	4.15E-03	1.74E-04	1.57E-07	8.84E-04	0.000737	0.001054	0.007142
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.73E-01	4.04E-03	1.52E-01	6.16E-04	6.22E-03	3.68E-04	1.47E-07	1.76E-03	0.000743	0.001168	0.006374
Terrestrial acidification	kg SO2 eq.	2.62E-01	1.01E-02	2.25E-01	5.78E-04	9.87E-03	4.79E-04	3.92E-07	2.10E-03	0.001488	0.003528	0.008919
Freshwater eutrophication	kg P eq.	4.57E-02	4.68E-04	4.07E-02	3.49E-05	9.35E-04	3.78E-05	2.72E-08	2.64E-04	0.000142	0.000203	0.00289
Marine eutrophication	kg N eq.	0.030282	2.61E-05	2.75E-02	2.48E-06	2.53E-03	1.90E-06	2.11E-09	1.64E-05	1.26E-05	1.38E-05	0.000181
Terrestrial ecotoxicity	kg 1,4-DCB	2.77E+02	1.69E+01	2.31E+02	3.16E-01	1.70E+01	6.50E-01	8.98E-04	2.08E+00	2.97E+00	3.837705	1.988481
Freshwater ecotoxicity	kg 1,4-DCB	3.384897	1.58E-01	2.865478	3.78E-03	1.71E-01	0.005583	8.83E-06	0.02349	0.032022	0.044118	0.081557
Marine ecotoxicity	kg 1,4-DCB	4.48E+00	0.206974	3.79E+00	0.005012	2.23E-01	0.007393	1.15E-05	0.030888	0.041859	0.057758	0.11267
Human carcinogenic toxicity	kg 1,4-DCB	7.69E+00	8.39E-02	7.13E+00	0.004418	1.84E-01	0.005278	6.77E-06	0.032442	0.023063	0.040816	0.183239
Human non-carcinogenic toxicity	kg 1,4-DCB	8.15E+01	3.07E+00	6.93E+01	0.095217	3.25E+00	0.116173	0.000175	0.514741	0.635367	0.847229	3.610065
Land use	m2a crop eq.	1.48E+00	2.45E-02	1.292418	1.81E-03	6.41E-02	1.32E-03	1.51E-06	1.45E-02	0.00875	0.028608	0.041183
Mineral resource scarcity	kg Cu eq.	5.46E-01	1.08E-02	4.70E-01	4.30E-02	1.37E-02	4.10E-04	7.27E-07	1.86E-03	2.15E-03	0.003438	0.000986
Fossil resource scarcity	kg oil eq.	2.42E+01	7.94E-01	2.14E+01	2.39E-02	7.56E-01	8.72E-02	1.43E-05	3.01E-01	7.60E-02	0.083389	0.721635
Water consumption	m3	7.75E-01	2.60E-02	6.52E-01	7.84E-04	5.07E-02	0.000957	1.21E-04	8.82E-03	0.006278	0.014601	0.015203

S Table 5d: Comparison of the Midpoint category of the Recycling process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Unit	Total	Nitrobenzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	5.16E+01	2.02E+00	4.21E+01	8.62E-02	3.08E+00	1.52E-01	6.06E-05	6.26E-01	0.284611	0.397776	2.887286
Stratospheric ozone depletion	kg CFC11 eq.	3.10E-05	1.94E-05	9.71E-06	4.21E-08	7.02E-07	1.82E-08	5.49E-11	1.50E-07	2.18E-07	1.02E-07	7.31E-07
Ionizing radiation	kBq Co-60 eq.	2.25E+00	2.81E-02	1.89E+00	4.80E-03	1.35E-01	1.92E-03	4.01E-06	2.62E-02	0.020493	0.015725	0.135559
Ozone formation, Human health	kg NOx eq.	1.15E-01	3.74E-03	9.50E-02	6.06E-04	5.95E-03	3.27E-04	1.43E-07	1.61E-03	0.000734	0.001143	0.006316
Fine particulate matter formation	kg PM2.5 eq.	9.71E-02	3.44E-03	7.90E-02	4.94E-04	4.15E-03	1.74E-04	1.57E-07	8.84E-04	0.000737	0.001054	0.007142
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.21E-01	4.04E-03	9.97E-02	6.16E-04	6.22E-03	3.68E-04	1.47E-07	1.76E-03	0.000743	0.001168	0.006374
Terrestrial acidification	kg SO2 eq.	1.80E-01	1.01E-02	1.43E-01	5.78E-04	9.87E-03	4.79E-04	3.92E-07	2.10E-03	0.001488	0.003528	0.008919
Freshwater eutrophication	kg P eq.	3.78E-02	4.68E-04	3.28E-02	3.49E-05	9.35E-04	3.78E-05	2.72E-08	0.000264	0.000142	0.000203	0.00289
Marine eutrophication	kg N eq.	2.80E-02	2.61E-05	2.52E-02	2.48E-06	2.53E-03	1.90E-06	2.11E-09	1.64E-05	1.26E-05	1.38E-05	0.000181
Terrestrial ecotoxicity	kg 1,4-DCB	149.6672	1.69E+01	103.9148	3.16E-01	1.70E+01	0.649713	0.000898	2.076253	2.970594	3.837705	1.988481
Freshwater ecotoxicity	kg 1,4-DCB	2.05E+00	1.58E-01	1.526836	3.78E-03	1.71E-01	0.005583	8.83E-06	0.02349	0.032022	0.044118	0.081557
Marine ecotoxicity	kg 1,4-DCB	2.71E+00	2.07E-01	2.027688	5.01E-03	2.23E-01	0.007393	1.15E-05	0.030888	0.041859	0.057758	0.11267
Human carcinogenic toxicity	kg 1,4-DCB	3.63E+00	8.39E-02	3.077033	0.004418	1.84E-01	0.005278	6.77E-06	0.032442	0.023063	0.040816	0.183239
Human non-carcinogenic toxicity	kg 1,4-DCB	5.50E+01	3.07E+00	4.28E+01	9.52E-02	3.25E+00	1.16E-01	1.75E-04	5.15E-01	0.635367	0.847229	3.610065
Land use	m2a crop eq.	8.99E-01	2.45E-02	7.14E-01	1.81E-03	6.41E-02	1.32E-03	1.51E-06	1.45E-02	8.75E-03	0.028608	0.041183
Mineral resource scarcity	kg Cu eq.	2.19E-01	1.08E-02	1.43E-01	4.30E-02	1.37E-02	4.10E-04	7.27E-07	1.86E-03	2.15E-03	0.003438	0.000986
Fossil resource scarcity	kg oil eq.	1.82E+01	7.94E-01	15.38681	2.39E-02	7.56E-01	0.087175	1.43E-05	3.01E-01	0.076044	0.083389	0.721635
Water consumption	m3	5.27E-01	2.60E-02	4.04E-01	7.84E-04	5.07E-02	9.57E-04	1.21E-04	8.82E-03	6.28E-03	0.014601	0.015203

S Table 5e: Comparison of the Endpoint category of the NAR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Damage category	Unit	Total	Ethyl 2-methylfuran-3-carboxylate	Aniline	Sodium tert-butoxide	Energy
Human health	DALY	9.33E-02	0.003052	0.089987	2.48E-05	0.000204
Ecosystems	species.yr	4.44E-05	2.11E-06	4.21E-05	1.87E-08	1.32E-07
Resources	USD2013	2.08E+01	4.390843	16.11883	0.168095	0.074346

S Table 5f: Comparison of the Endpoint category of the AR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Damage category	Unit	Total	Nitro benzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Human health	DALY	6.50E-03	1.80E-04	5.69E-03	6.72E-06	2.31E-04	8.31E-06	1.04E-08	3.85E-05	3.77E-05	5.51E-05	0.00025
Ecosystems	species.yr	3.79E-06	1.15E-07	3.26E-06	4.52E-09	1.56E-07	6.36E-09	7.31E-12	2.72E-08	2.27E-08	3.27E-08	1.61E-07
Resources	USD2013	6.98E+00	2.83E-01	6.21E+00	1.56E-02	2.06E-01	3.35E-02	3.98E-06	0.103835	0.01834	0.018056	0.091074

S Table 5g: Comparison of the End Point category of the Recycling process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Damage category	Unit	Total	Nitro benzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Human health	DALY	4.05E-03	1.80E-04	3.24E-03	6.72E-06	2.31E-04	8.31E-06	1.04E-08	3.85E-05	3.77E-05	5.51E-05	0.00025
Ecosystems	species.yr	2.62E-06	1.15E-07	2.10E-06	4.52E-09	1.56E-07	6.36E-09	7.31E-12	2.72E-08	2.27E-08	3.27E-08	1.61E-07
Resources	USD2013	5.17E+00	2.83E-01	4.40E+00	1.56E-02	2.06E-01	3.35E-02	3.98E-06	0.103835	0.01834	0.018056	0.091074

S Table 5h: Comparison of Normalization category of the NAR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Total	Ethyl 2-methylfuran-3-carboxylate	Aniline	Sodium tert-butoxide	Energy
Global warming	0.024629	0.005567	0.018709	5.88E-05	0.000295
Stratospheric ozone depletion	6.01E-03	1.18E-03	4.82E-03	2.05E-06	9.96E-06
Ionizing radiation	1.88E-02	3.47E-03	0.015037	2.72E-05	0.00023
Ozone formation, Human health	9.20E-02	0.005086	0.08663	5.54E-05	0.000251
Fine particulate matter formation	2.41E-01	0.003417	0.237125	2.15E-05	0.000228
Ozone formation, Terrestrial ecosystems	1.09E-01	6.13E-03	1.03E-01	6.95E-05	0.000293
Terrestrial acidification	5.13E-01	0.003794	0.509229	3.27E-05	0.000178
Freshwater eutrophication	3.19E-01	5.67E-02	2.58E-01	0.000117	0.003633
Marine eutrophication	7.65E-03	6.12E-03	1.50E-03	1.44E-06	3.21E-05
Terrestrial ecotoxicity	5.04E-02	0.004695	0.045482	0.000103	0.000107
Freshwater ecotoxicity	2.690995	0.051521	2.636155	0.000676	0.002643
Marine ecotoxicity	1.98E+00	3.99E-02	1.940629	0.000513	0.002115
Human carcinogenic toxicity	2.15E+00	2.36E-01	1.90E+00	0.002033	0.014524
Human non-carcinogenic toxicity	8.88E-02	1.33E-03	0.087336	9.87E-06	9.43E-05
Land use	7.70E-04	1.00E-04	0.000663	9.94E-07	5.45E-06
Mineral resource scarcity	1.97E-04	4.99E-07	0.000196	1.18E-08	6.71E-09
Fossil resource scarcity	6.79E-02	0.016123	0.050789	0.000422	0.000601
Water consumption	5.36E-03	1.35E-03	0.00395	1.88E-05	4.65E-05

S Table 5i: Comparison of Normalization category of the AR process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Total	Nitro benzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	8.92E-03	0.000252	7.72E-03	1.08E-05	3.85E-04	1.90E-05	7.58E-09	7.83E-05	3.56E-05	4.97E-05	0.000361
Stratospheric ozone depletion	6.13E-04	3.23E-04	2.56E-04	7.04E-07	1.17E-05	3.04E-07	9.16E-10	2.50E-06	3.63E-06	1.70E-06	1.22E-05
Ionizing radiation	7.65E-03	5.85E-05	0.006884	9.99E-06	2.81E-04	3.99E-06	8.35E-09	5.45E-05	4.26E-05	3.27E-05	0.000282
Ozone formation, Human health	8.07E-03	1.82E-04	0.007078	2.95E-05	0.000289	1.59E-05	6.95E-09	7.81E-05	3.57E-05	5.56E-05	0.000307
Fine particulate matter formation	5.22E-03	1.35E-04	4.51E-03	1.93E-05	1.62E-04	6.81E-06	6.13E-09	3.46E-05	2.88E-05	4.12E-05	0.000279
Ozone formation, Terrestrial ecosystems	9.76E-03	2.27E-04	8.56E-03	3.47E-05	3.50E-04	2.07E-05	8.30E-09	9.93E-05	4.18E-05	6.58E-05	0.000359
Terrestrial acidification	6.40E-03	2.45E-04	5.50E-03	1.41E-05	2.41E-04	1.17E-05	9.57E-09	5.12E-05	3.63E-05	8.61E-05	0.000218
Freshwater eutrophication	7.04E-02	0.000721	6.27E-02	5.38E-05	1.44E-03	5.83E-05	4.19E-08	0.000407	0.000218	0.000313	0.004451
Marine eutrophication	0.006571	5.66E-06	5.97E-03	5.38E-07	5.49E-04	4.12E-07	4.58E-10	3.56E-06	2.73E-06	2.99E-06	3.93E-05
Terrestrial ecotoxicity	0.018195	0.001114	1.52E-02	2.08E-05	0.001117	4.28E-05	5.91E-08	0.000137	0.000195	0.000253	0.000131
Freshwater ecotoxicity	0.13438	6.27E-03	1.14E-01	0.00015	6.78E-03	0.000222	3.50E-07	0.000933	0.001271	0.001751	0.003238
Marine ecotoxicity	0.103017	4.76E-03	8.72E-02	1.15E-04	5.14E-03	0.00017	2.66E-07	0.00071	0.000963	0.001328	0.002591
Human carcinogenic toxicity	0.746456	8.15E-03	6.92E-01	4.29E-04	1.79E-02	0.000513	6.57E-07	0.00315	0.002239	0.003963	0.017793
Human non-carcinogenic toxicity	2.61E-03	9.83E-05	2.22E-03	3.05E-06	0.000104	3.72E-06	5.59E-09	1.65E-05	2.03E-05	2.71E-05	0.000116
Land use	2.39E-04	3.97E-06	2.09E-04	2.93E-07	1.04E-05	2.14E-07	2.44E-10	2.34E-06	1.42E-06	4.63E-06	6.67E-06
Mineral resource scarcity	4.55E-06	9.02E-08	3.91E-06	3.59E-07	1.14E-07	3.41E-09	6.06E-12	1.55E-08	1.79E-08	2.86E-08	8.22E-09
Fossil resource scarcity	0.024681	8.10E-04	2.18E-02	2.44E-05	7.71E-04	8.89E-05	1.46E-08	0.000307	7.76E-05	8.51E-05	0.000736
Water consumption	2.91E-03	9.74E-05	2.44E-03	2.94E-06	1.90E-04	3.59E-06	4.53E-07	3.31E-05	2.35E-05	5.48E-05	5.70E-05

S Table 5j: Comparison of Normalization category of the Recycling process for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Total	Nitro benzene	2-(2-methylfuran-3-carbonyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	6.45E-03	2.52E-04	5.26E-03	1.08E-05	3.85E-04	1.90E-05	7.58E-09	7.83E-05	3.56E-05	4.97E-05	0.000361
Stratospheric ozone depletion	5.18E-04	3.23E-04	1.62E-04	7.04E-07	1.17E-05	3.04E-07	9.16E-10	2.50E-06	3.63E-06	1.70E-06	1.22E-05
Ionizing radiation	4.69E-03	5.85E-05	3.92E-03	9.99E-06	2.81E-04	3.99E-06	8.35E-09	5.45E-05	4.26E-05	3.27E-05	0.000282
Ozone formation, Human health	5.61E-03	1.82E-04	4.62E-03	2.95E-05	2.89E-04	1.59E-05	6.95E-09	7.81E-05	3.57E-05	5.56E-05	0.000307
Fine particulate matter formation	3.80E-03	1.35E-04	3.09E-03	1.93E-05	1.62E-04	6.81E-06	6.13E-09	3.46E-05	2.88E-05	4.12E-05	0.000279
Ozone formation, Terrestrial ecosystems	6.81E-03	2.27E-04	5.61E-03	3.47E-05	3.50E-04	2.07E-05	8.30E-09	9.93E-05	4.18E-05	6.58E-05	0.000359
Terrestrial acidification	4.40E-03	2.45E-04	3.50E-03	1.41E-05	2.41E-04	1.17E-05	9.57E-09	5.12E-05	3.63E-05	8.61E-05	0.000218
Freshwater eutrophication	0.058168	7.21E-04	5.05E-02	5.38E-05	1.44E-03	5.83E-05	4.19E-08	4.07E-04	0.000218	0.000313	0.004451
Marine eutrophication	6.07E-03	5.66E-06	5.47E-03	5.38E-07	5.49E-04	4.12E-07	4.58E-10	3.56E-06	2.73E-06	2.99E-06	3.93E-05
Terrestrial ecotoxicity	0.009848	0.001114	6.84E-03	2.08E-05	0.001117	4.28E-05	5.91E-08	0.000137	0.000195	0.000253	0.000131
Freshwater ecotoxicity	8.12E-02	6.27E-03	0.060615	1.50E-04	0.006782	2.22E-04	3.50E-07	0.000933	0.001271	0.001751	0.003238
Marine ecotoxicity	6.24E-02	4.76E-03	0.046637	1.15E-04	0.005139	1.70E-04	2.66E-07	0.00071	0.000963	0.001328	0.002591
Human carcinogenic toxicity	3.53E-01	8.15E-03	0.29878	4.29E-04	0.017864	0.000513	6.57E-07	0.00315	0.002239	0.003963	0.017793
Human non-carcinogenic toxicity	1.76E-03	9.83E-05	1.37E-03	3.05E-06	1.04E-04	3.72E-06	5.59E-09	1.65E-05	2.03E-05	2.71E-05	0.000116
Land use	1.46E-04	3.97E-06	1.16E-04	2.93E-07	1.04E-05	2.14E-07	2.44E-10	2.34E-06	1.42E-06	4.63E-06	6.67E-06
Mineral resource scarcity	1.83E-06	9.02E-08	1.19E-06	3.59E-07	1.14E-07	3.41E-09	6.06E-12	1.55E-08	1.79E-08	2.86E-08	8.22E-09
Fossil resource scarcity	1.86E-02	8.10E-04	1.57E-02	2.44E-05	0.000771	8.89E-05	1.46E-08	0.000307	7.76E-05	8.51E-05	0.000736
Water consumption	1.98E-03	9.74E-05	1.51E-03	2.94E-06	1.90E-04	3.59E-06	4.53E-07	3.31E-05	2.35E-05	5.48E-05	5.70E-05

S Table 5k: Comparison of the Midpoint category for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	197.0328	71.32144	51.63306
Stratospheric ozone depletion	kg CFC11 eq.	3.60E-04	3.67E-05	3.10E-05
Ionizing radiation	kBq Co-60 eq.	9.022154	3.677573	2.25463
Ozone formation, Human health	kg NOx eq.	1.893452	0.166075	0.115438
Fine particulate matter formation	kg PM2.5 eq.	6.158333	0.133544	0.097062
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.943419	0.173282	0.120955
Terrestrial acidification	kg SO2 eq.	21.03413	0.262427	0.180445
Freshwater eutrophication	kg P eq.	0.206858	0.045696	0.037771
Marine eutrophication	kg N eq.	0.035272	0.030282	0.027988
Terrestrial ecotoxicity	kg 1,4-DCB	765.7515	276.5145	149.6672
Freshwater ecotoxicity	kg 1,4-DCB	67.78324	3.384897	2.046255
Marine ecotoxicity	kg 1,4-DCB	86.22438	4.478987	2.713697
Human carcinogenic toxicity	kg 1,4-DCB	2.21E+01	7.69E+00	3.634214
Human non-carcinogenic toxicity	kg 1,4-DCB	2774.193	81.48154	54.98808
Land use	m2a crop eq.	4.751985	1.477184	0.898743
Mineral resource scarcity	kg Cu eq.	23.64321	0.546257	0.219371
Fossil resource scarcity	kg oil eq.	66.60287	24.19741	18.2295
Water consumption	m3	1.430326	0.775153	0.527361

S Table 5l: Comparison of the Endpoint category for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.093268	0.006497	0.00405
Ecosystems	species.yr	4.44E-05	3.79E-06	2.62E-06
Resources	USD2013	20.75211	6.977796	5.165203

S Table 5m: Comparison of the Normalization category for 2-Methyl-N-phenyl-furan-3-carboxamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.024629	0.008915	0.006454
Stratospheric ozone depletion	6.01E-03	0.000613	0.000518
Ionizing radiation	1.88E-02	7.65E-03	4.69E-03
Ozone formation, Human health	0.092022	0.008071	0.00561
Fine particulate matter formation	2.41E-01	5.22E-03	0.003795
Ozone formation, Terrestrial ecosystems	0.109414	0.009756	0.00681
Terrestrial acidification	0.513233	0.006403	0.004403
Freshwater eutrophication	0.318561	0.070371	0.058168
Marine eutrophication	0.007654	0.006571	0.006073
Terrestrial ecotoxicity	0.050386	0.018195	0.009848
Freshwater ecotoxicity	2.690995	0.13438	0.081236
Marine ecotoxicity	1.983161	0.103017	0.062415
Human carcinogenic toxicity	2.148958	0.746456	0.352882
Human non-carcinogenic toxicity	0.088774	0.002607	0.00176
Land use	0.00077	0.000239	0.000146
Mineral resource scarcity	0.000197	4.55E-06	1.83E-06
Fossil resource scarcity	0.067935	0.024681	0.018594
Water consumption	0.005364	0.002907	0.001978

S Table 6a: Inventory Data of 11-Beta-HSD1 (3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide) for 1 kg functional unit (API-5)

NAR - Inputs		AR – Inputs	
2-methyl-5-nitro-1,3-benzothiazole	0.49 Kg	1-methoxy-4-nitro-benzen	0.577 Kg
3,5-dichlorobenzamide	0.75 kg	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	1.06 kg
Triethylamine	1.51 kg	Iron Powder	0.497 kg
Tetrahydrofuran	1.47 kg	Ammonium Chloride	1.11 kg
Energy	1.76 MJ	Isopropanol	0.0577 kg
-	-	Water	0.115 kg
-	-	Ethyl acetate	0.173 kg
-	-	1M HCl	0.288 kg
-	-	$NaHCO_3$ (aq.)	0.288 kg
-	-	Energy	8.31 MJ
NAR – Output		AR - Output	
11-Beta-HSD1 (3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide)	1 kg	11-Beta-HSD1 (3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl)benzamide)	1 kg
Byproducts		Byproducts	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.325 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 6b: Comparison of the Midpoint category of the NAR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Unit	Total	2-methyl-1,3-benzothiazol-5-amine	Dimethylacetamide	Triethyl amine	Tetrahydrofuran	Energy
Global warming	kg CO2 eq.	7.16E+01	5.26E+01	3.05E+00	6.04E+00	9.30E+00	5.65E-01
Stratospheric ozone depletion	kg CFC11 eq.	3.78E-05	3.35E-05	6.78E-07	1.07E-06	2.45E-06	1.43E-07
Ionizing radiation	kBq Co-60 eq.	2.82E+00	1.80E+00	0.158049	1.24E-01	0.708431	0.026543
Ozone formation, Human health	kg NOx eq.	1.63E-01	1.19E-01	6.68E-03	1.39E-02	0.021668	0.001237
Fine particulate matter formation	kg PM2.5 eq.	1.04E-01	7.78E-02	3.82E-03	6.52E-03	1.41E-02	1.40E-03
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.77E-01	1.30E-01	7.35E-03	1.54E-02	0.023045	0.001248
Terrestrial acidification	kg SO2 eq.	2.19E-01	0.159464	8.19E-03	1.86E-02	0.03059	0.001746
Freshwater eutrophication	kg P eq.	2.98E-02	0.022199	9.78E-04	0.003061	3.02E-03	0.000566
Marine eutrophication	kg N eq.	0.009419	0.00564	1.95E-03	1.58E-03	0.000208	3.55E-05
Terrestrial ecotoxicity	kg 1,4-DCB	198.0356	138.0027	1.04E+01	1.66E+01	32.58916	0.389357
Freshwater ecotoxicity	kg 1,4-DCB	2.37E+00	1.72E+00	1.11E-01	1.95E-01	0.322301	0.015969
Marine ecotoxicity	kg 1,4-DCB	3.14E+00	2.284599	1.43E-01	0.257868	0.427964	0.022061
Human carcinogenic toxicity	kg 1,4-DCB	3.678104	2.75732	0.151311	0.280301	0.453292	0.035879
Human non-carcinogenic toxicity	kg 1,4-DCB	57.69544	43.05558	2.21E+00	4.43E+00	7.292072	0.706874
Land use	m2a crop eq.	1.304728	9.11E-01	5.53E-02	8.36E-02	0.24719	0.008064
Mineral resource scarcity	kg Cu eq.	2.29E-01	1.79E-01	9.13E-03	1.66E-02	0.024748	0.000193
Fossil resource scarcity	kg oil eq.	3.65E+01	2.89E+01	1.38E+00	2.92E+00	3.210787	0.141301
Water consumption	m3	1.13E+00	5.55E-01	4.85E-02	4.15E-02	0.483976	0.002977

S Table 6c: Comparison of the Midpoint category of the AR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzen	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	4.12E+01	7.02E+00	2.83E+01	5.04E-02	1.80E+00	0.140207	5.59E-05	0.577687	0.262449	0.366802	2.662457
Stratospheric ozone depletion	kg CFC11 eq.	2.04E-05	1.06E-05	8.29E-06	2.46E-08	4.10E-07	1.68E-08	5.06E-11	1.38E-07	2.01E-07	9.41E-08	6.74E-07
Ionizing radiation	kBq Co-60 eq.	2.35E+00	2.79E-01	1.806915	2.80E-03	7.91E-02	1.77E-03	3.70E-06	2.42E-02	0.018898	0.014501	0.125003
Ozone formation, Human health	kg NOx eq.	1.02E-01	1.96E-02	6.94E-02	3.54E-04	3.48E-03	3.02E-04	1.32E-07	1.48E-03	6.76E-04	0.001054	0.005824
Fine particulate matter formation	kg PM2.5 eq.	8.09E-02	2.08E-02	4.82E-02	2.88E-04	2.43E-03	1.61E-04	1.45E-07	8.15E-04	0.000679	0.000972	0.006586
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.07E-01	2.08E-02	7.29E-02	3.60E-04	3.64E-03	3.40E-04	1.36E-07	1.63E-03	0.000685	0.001077	0.005877
Terrestrial acidification	kg SO2 eq.	1.75E-01	5.11E-02	1.02E-01	3.38E-04	5.77E-03	4.41E-04	3.61E-07	1.94E-03	0.001372	0.003253	0.008225
Freshwater eutrophication	kg P eq.	3.60E-02	7.04E-03	2.51E-02	2.04E-05	5.47E-04	3.49E-05	2.51E-08	2.44E-04	0.000131	0.000187	0.002665
Marine eutrophication	kg N eq.	5.75E-03	1.56E-03	2.49E-03	1.45E-06	1.48E-03	1.75E-06	1.95E-09	1.51E-05	1.16E-05	1.27E-05	0.000167
Terrestrial ecotoxicity	kg 1,4-DCB	2.60E+02	1.04E+02	1.35E+02	1.84E-01	9.93E+00	0.599121	0.000828	1.914578	2.739277	3.538867	1.83364
Freshwater ecotoxicity	kg 1,4-DCB	3.3517	1.53E+00	1.54E+00	2.20E-03	9.99E-02	5.15E-03	8.14E-06	2.17E-02	2.95E-02	0.040682	0.075206
Marine ecotoxicity	kg 1,4-DCB	4.42E+00	2.10E+00	1.958682	2.93E-03	1.31E-01	0.006818	1.07E-05	0.028483	0.038599	0.05326	0.103896
Human carcinogenic toxicity	kg 1,4-DCB	4.61E+00	5.53E-01	3.68E+00	2.58E-03	1.08E-01	0.004867	6.24E-06	0.029916	0.021267	0.037637	0.168971
Human non-carcinogenic toxicity	kg 1,4-DCB	6.71E+01	2.90E+01	3.08E+01	5.56E-02	1.90E+00	0.107127	0.000161	0.474658	0.585891	0.781256	3.328954
Land use	m2a crop eq.	1.15E+00	3.10E-01	7.17E-01	1.06E-03	3.75E-02	0.00122	1.39E-06	0.013338	0.008069	0.02638	0.037976
Mineral resource scarcity	kg Cu eq.	5.06E-01	1.10E-01	3.55E-01	2.51E-02	7.99E-03	3.78E-04	6.70E-07	1.72E-03	0.001986	0.00317	0.00091
Fossil resource scarcity	kg oil eq.	1.45E+01	2.58E+00	1.03E+01	1.40E-02	4.42E-01	8.04E-02	1.32E-05	2.77E-01	7.01E-02	0.076896	0.665442
Water consumption	m3	5.89E-01	1.42E-01	3.75E-01	4.58E-04	2.96E-02	8.83E-04	1.11E-04	8.13E-03	5.79E-03	0.013464	0.014019

S Table 6d: Comparison of the Midpoint category of the Recycling process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Unit	Total	1-methoxy-4-nitro-benzene	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	kg CO2 eq.	29.69248	7.021619	16.81094	0.050351	1.799909	0.140207	5.59E-05	0.577687	0.262449	0.366802	2.662457
Stratospheric ozone depletion	kg CFC11 eq.	1.71E-05	1.06E-05	4.98E-06	2.46E-08	4.10E-07	1.68E-08	5.06E-11	1.38E-07	2.01E-07	9.41E-08	6.74E-07
Ionizing radiation	kBq Co-60 eq.	1.518872	0.279313	0.973314	0.002804	0.079085	0.001768	3.70E-06	0.024182	0.018898	0.014501	0.125003
Ozone formation, Human health	kg NOx eq.	0.072473	0.01958	0.03972	0.000354	0.003481	0.000302	1.32E-07	0.001481	0.000676	0.001054	0.005824
Fine particulate matter formation	kg PM2.5 eq.	0.059567	0.020802	0.026837	0.000288	0.002425	0.000161	1.45E-07	0.000815	0.000679	0.000972	0.006586
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.07669	0.020801	0.042288	0.00036	0.003636	0.00034	1.36E-07	0.001626	0.000685	0.001077	0.005877
Terrestrial acidification	kg SO2 eq.	0.126875	0.051146	0.054393	0.000338	0.005769	0.000441	3.61E-07	0.001937	0.001372	0.003253	0.008225
Freshwater eutrophication	kg P eq.	0.031329	0.007041	0.020459	2.04E-05	0.000547	3.49E-05	2.51E-08	0.000244	0.000131	0.000187	0.002665
Marine eutrophication	kg N eq.	0.004402	0.001565	0.00115	1.45E-06	0.001478	1.75E-06	1.95E-09	1.51E-05	1.16E-05	1.27E-05	0.000167
Terrestrial ecotoxicity	kg 1,4-DCB	185.8333	104.2294	60.86583	0.184288	9.927461	0.599121	0.000828	1.914578	2.739277	3.538867	1.83364
Freshwater ecotoxicity	kg 1,4-DCB	2.567485	1.532501	0.760677	0.002205	0.099868	0.005148	8.14E-06	0.02166	0.029529	0.040682	0.075206
Marine ecotoxicity	kg 1,4-DCB	3.38626	2.09711	0.924524	0.002927	0.130633	0.006818	1.07E-05	0.028483	0.038599	0.05326	0.103896
Human carcinogenic toxicity	kg 1,4-DCB	2.234943	0.553443	1.308698	0.00258	0.107557	0.004867	6.24E-06	0.029916	0.021267	0.037637	0.168971
Human non-carcinogenic toxicity	kg 1,4-DCB	51.53606	29.00914	15.29305	0.05561	1.900215	0.107127	0.000161	0.474658	0.585891	0.781256	3.328954
Land use	m2a crop eq.	0.813317	0.309985	0.377798	0.001057	0.037492	0.00122	1.39E-06	0.013338	0.008069	0.02638	0.037976
Mineral resource scarcity	kg Cu eq.	0.314119	0.109725	0.163104	0.025142	0.007986	0.000378	6.70E-07	0.001719	0.001986	0.00317	0.00091
Fossil resource scarcity	kg oil eq.	10.97882	2.575964	6.776938	0.013976	0.441819	0.080387	1.32E-05	0.277264	0.070123	0.076896	0.665442
Water consumption	m3	0.444006	0.141607	0.229894	0.000458	0.02965	0.000883	0.000111	0.008131	0.005789	0.013464	0.014019

S Table 6e: Comparison of the Endpoint category of the NAR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Damage category	Unit	Total	2-methyl-1,3-benzothiazol-5-amine	Dimethylacetamide	Triethyl amine	Tetrahydrofuran	Energy
Human health	DALY	4.36E-03	0.003243	1.74E-04	0.000341	0.000549	4.89E-05
Ecosystems	species.yr	3.07E-06	2.25E-06	1.25E-07	2.54E-07	4.06E-07	3.16E-08
Resources	USD2013	1.17E+01	9.31E+00	4.57E-01	1.02E+00	9.37E-01	0.017833

S Table 6f: Comparison of the Endpoint category of the AR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzen	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Human health	DALY	4.99E-03	1.85E-03	2.64E-03	3.93E-06	1.35E-04	7.66E-06	9.59E-09	3.55E-05	3.47E-05	5.08E-05	0.00023
Ecosystems	species.yr	2.87E-06	1.07E-06	1.47E-06	2.64E-09	9.10E-08	5.86E-09	6.74E-12	2.51E-08	2.09E-08	3.02E-08	1.49E-07
Resources	USD2013	4.46E+00	8.06E-01	3.28E+00	9.11E-03	0.120208	0.030902	3.67E-06	0.09575	0.016912	0.01665	0.083983

S Table 6g: Comparison of the Endpoint category of the Recycling process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Damage category	Unit	Total	1-methoxy-4-nitro-benzene	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Electricity
Human health	DALY	0.003556	0.001848	0.001209	3.93E-06	0.000135	7.66E-06	9.59E-09	3.55E-05	3.47E-05	5.08E-05	0.00023
Ecosystems	species.yr	2.19E-06	1.07E-06	7.90E-07	2.64E-09	9.10E-08	5.86E-09	6.74E-12	2.51E-08	2.09E-08	3.02E-08	1.49E-07
Resources	USD2013	3.402316	0.805774	2.223021	0.009112	0.120208	0.030902	3.67E-06	0.09575	0.016912	0.01665	0.083983

S Table 6h: Comparison of Normalization category of the NAR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Total	2-methyl-1,3-benzothiazol-5-amine	Dimethylacetamide	Triethyl amine	Tetrahydrofuran	Energy
Global warming	8.95E-03	6.58E-03	3.82E-04	7.55E-04	1.16E-03	7.07E-05
Stratospheric ozone depletion	6.32E-04	0.00056	1.13E-05	1.79E-05	4.08E-05	2.39E-06
Ionizing radiation	5.86E-03	3.74E-03	0.000329	2.57E-04	0.001474	5.52E-05
Ozone formation, Human health	0.007898	5.79E-03	3.25E-04	6.74E-04	1.05E-03	6.01E-05
Fine particulate matter formation	4.05E-03	3.04E-03	1.49E-04	2.55E-04	5.52E-04	5.47E-05
Ozone formation, Terrestrial ecosystems	9.96E-03	7.31E-03	0.000414	8.67E-04	1.30E-03	7.03E-05
Terrestrial acidification	0.005333	3.89E-03	2.00E-04	0.000453	7.46E-04	4.26E-05
Freshwater eutrophication	0.045924	3.42E-02	1.51E-03	0.004715	4.65E-03	0.000872
Marine eutrophication	2.04E-03	0.001224	4.24E-04	0.000344	4.51E-05	7.70E-06
Terrestrial ecotoxicity	0.013031	0.009081	6.87E-04	0.001093	2.14E-03	2.56E-05
Freshwater ecotoxicity	0.09393	6.84E-02	4.39E-03	7.73E-03	1.28E-02	6.34E-04
Marine ecotoxicity	7.21E-02	5.25E-02	3.28E-03	0.005931	9.84E-03	0.000507
Human carcinogenic toxicity	0.357144	0.267736	1.47E-02	0.027217	0.044015	0.003484
Human non-carcinogenic toxicity	0.001846	0.001378	7.09E-05	0.000142	2.33E-04	2.26E-05
Land use	2.11E-04	0.000148	8.95E-06	1.35E-05	4.00E-05	1.31E-06
Mineral resource scarcity	1.91E-06	1.49E-06	7.61E-08	1.38E-07	2.06E-07	1.61E-09
Fossil resource scarcity	0.037239	2.94E-02	1.41E-03	2.98E-03	3.28E-03	1.44E-04
Water consumption	4.25E-03	2.08E-03	1.82E-04	1.56E-04	1.81E-03	1.12E-05

S Table 6i: Comparison of Normalization category of the AR process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzene	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	5.15E-03	8.78E-04	3.54E-03	6.29E-06	0.000225	1.75E-05	6.99E-09	7.22E-05	3.28E-05	4.59E-05	0.000333
Stratospheric ozone depletion	3.41E-04	1.76E-04	1.38E-04	4.11E-07	6.85E-06	2.80E-07	8.45E-10	2.31E-06	3.35E-06	1.57E-06	1.13E-05
Ionizing radiation	4.89E-03	5.81E-04	3.76E-03	5.83E-06	1.64E-04	3.68E-06	7.70E-09	5.03E-05	3.93E-05	3.02E-05	0.00026
Ozone formation, Human health	4.96E-03	9.52E-04	3.37E-03	1.72E-05	1.69E-04	1.47E-05	6.40E-09	7.20E-05	3.29E-05	5.12E-05	0.000283
Fine particulate matter formation	3.16E-03	8.13E-04	1.88E-03	1.13E-05	9.48E-05	6.28E-06	5.65E-09	3.19E-05	2.66E-05	3.80E-05	0.000258
Ozone formation, Terrestrial ecosystems	6.04E-03	1.17E-03	4.11E-03	2.03E-05	2.05E-04	1.91E-05	7.66E-09	9.16E-05	3.86E-05	6.07E-05	0.000331
Terrestrial acidification	4.27E-03	1.25E-03	2.50E-03	8.24E-06	1.41E-04	1.08E-05	8.82E-09	4.73E-05	3.35E-05	7.94E-05	0.000201
Freshwater eutrophication	5.54E-02	1.08E-02	3.87E-02	3.14E-05	8.42E-04	5.37E-05	3.86E-08	0.000375	0.000201	0.000288	0.004104
Marine eutrophication	0.001247	0.00034	5.41E-04	3.14E-07	3.21E-04	3.80E-07	4.22E-10	3.28E-06	2.52E-06	2.75E-06	3.62E-05
Terrestrial ecotoxicity	1.71E-02	6.86E-03	8.89E-03	1.21E-05	0.000653	3.94E-05	5.45E-08	0.000126	0.00018	0.000233	0.000121
Freshwater ecotoxicity	1.33E-01	6.08E-02	6.13E-02	8.75E-05	3.96E-03	2.04E-04	3.23E-07	0.00086	0.001172	0.001615	0.002986
Marine ecotoxicity	1.02E-01	4.82E-02	4.50E-02	6.73E-05	3.00E-03	1.57E-04	2.45E-07	0.000655	0.000888	0.001225	0.00239
Human carcinogenic toxicity	4.48E-01	5.37E-02	3.58E-01	2.51E-04	1.04E-02	4.73E-04	6.06E-07	0.002905	0.002065	0.003655	0.016407
Human non-carcinogenic toxicity	2.15E-03	9.28E-04	9.86E-04	1.78E-06	6.08E-05	3.43E-06	5.16E-09	1.52E-05	1.87E-05	2.50E-05	0.000107
Land use	0.000187	5.02E-05	1.16E-04	1.71E-07	6.07E-06	1.98E-07	2.25E-10	2.16E-06	1.31E-06	4.27E-06	6.15E-06
Mineral resource scarcity	4.21E-06	9.14E-07	2.95E-06	2.09E-07	6.65E-08	3.15E-09	5.58E-12	1.43E-08	1.65E-08	2.64E-08	7.58E-09
Fossil resource scarcity	0.014764	0.002627	0.010479	1.43E-05	4.51E-04	8.20E-05	1.34E-08	0.000283	7.15E-05	7.84E-05	0.000679
Water consumption	0.002209	0.000531	0.001406	1.72E-06	0.000111	3.31E-06	4.18E-07	3.05E-05	2.17E-05	5.05E-05	5.26E-05

S Table 6j: Comparison of Normalization category of the Recycling process for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Total	1-methoxy-4-nitro-benzene	2-(3,5-dichlorobenzoyl)-1,1-dioxo-1,2-benzothiazol-3-one	Iron Powder	Ammonium chloride	Isopropanol	Water	Ethyl acetate	Hydrochloric acid	Sodium bicarbonate	Energy
Global warming	3.71E-03	8.78E-04	2.10E-03	6.29E-06	2.25E-04	1.75E-05	6.99E-09	7.22E-05	3.28E-05	4.59E-05	0.000333
Stratospheric ozone depletion	2.86E-04	1.76E-04	8.32E-05	4.11E-07	6.85E-06	2.80E-07	8.45E-10	2.31E-06	3.35E-06	1.57E-06	1.13E-05
Ionizing radiation	3.16E-03	5.81E-04	2.02E-03	5.83E-06	1.64E-04	3.68E-06	7.70E-09	5.03E-05	3.93E-05	3.02E-05	0.00026
Ozone formation, Human health	3.52E-03	9.52E-04	1.93E-03	1.72E-05	1.69E-04	1.47E-05	6.40E-09	7.20E-05	3.29E-05	5.12E-05	0.000283
Fine particulate matter formation	2.33E-03	8.13E-04	1.05E-03	1.13E-05	9.48E-05	6.28E-06	5.65E-09	3.19E-05	2.66E-05	3.80E-05	0.000258
Ozone formation, Terrestrial ecosystems	4.32E-03	1.17E-03	2.38E-03	2.03E-05	2.05E-04	1.91E-05	7.66E-09	9.16E-05	3.86E-05	6.07E-05	0.000331
Terrestrial acidification	3.10E-03	0.001248	1.33E-03	8.24E-06	1.41E-04	1.08E-05	8.82E-09	4.73E-05	3.35E-05	7.94E-05	0.000201
Freshwater eutrophication	4.82E-02	1.08E-02	3.15E-02	3.14E-05	8.42E-04	5.37E-05	3.86E-08	0.000375	0.000201	0.000288	0.004104
Marine eutrophication	0.000955	3.40E-04	2.49E-04	3.14E-07	3.21E-04	3.80E-07	4.22E-10	3.28E-06	2.52E-06	2.75E-06	3.62E-05
Terrestrial ecotoxicity	1.22E-02	0.006858	4.00E-03	1.21E-05	0.000653	3.94E-05	5.45E-08	0.000126	0.00018	0.000233	0.000121
Freshwater ecotoxicity	1.02E-01	0.06084	3.02E-02	8.75E-05	3.96E-03	2.04E-04	3.23E-07	0.00086	0.001172	0.001615	0.002986
Marine ecotoxicity	7.79E-02	0.048234	2.13E-02	6.73E-05	3.00E-03	1.57E-04	2.45E-07	0.000655	0.000888	0.001225	0.00239
Human carcinogenic toxicity	2.17E-01	5.37E-02	1.27E-01	2.51E-04	1.04E-02	4.73E-04	6.06E-07	0.002905	0.002065	0.003655	0.016407
Human non-carcinogenic toxicity	1.65E-03	9.28E-04	4.89E-04	1.78E-06	6.08E-05	3.43E-06	5.16E-09	1.52E-05	1.87E-05	2.50E-05	0.000107
Land use	1.32E-04	5.02E-05	6.12E-05	1.71E-07	6.07E-06	1.98E-07	2.25E-10	2.16E-06	1.31E-06	4.27E-06	6.15E-06
Mineral resource scarcity	2.62E-06	9.14E-07	1.36E-06	2.09E-07	6.65E-08	3.15E-09	5.58E-12	1.43E-08	1.65E-08	2.64E-08	7.58E-09
Fossil resource scarcity	1.12E-02	2.63E-03	6.91E-03	1.43E-05	4.51E-04	8.20E-05	1.34E-08	0.000283	7.15E-05	7.84E-05	0.000679
Water consumption	0.001665	0.000531	0.000862	1.72E-06	0.000111	3.31E-06	4.18E-07	3.05E-05	2.17E-05	5.05E-05	5.26E-05

S Table 6k: Comparison of the Midpoint category for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	71.58865	41.2265	29.69248
Stratospheric ozone depletion	kg CFC11 eq.	3.78E-05	2.04E-05	1.71E-05
Ionizing radiation	kBq Co-60 eq.	2.82E+00	2.35E+00	1.52E+00
Ozone formation, Human health	kg NOx eq.	0.162501	0.102137	0.072473
Fine particulate matter formation	kg PM2.5 eq.	0.103689	0.080939	0.059567
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.176932	0.107345	0.07669
Terrestrial acidification	kg SO2 eq.	0.218569	0.174902	0.126875
Freshwater eutrophication	kg P eq.	0.029821	0.035971	0.031329
Marine eutrophication	kg N eq.	0.009419	0.005746	0.004402
Terrestrial ecotoxicity	kg 1,4-DCB	198.0356	260.1441	185.8333
Freshwater ecotoxicity	kg 1,4-DCB	2.37E+00	3.35E+00	2.567485
Marine ecotoxicity	kg 1,4-DCB	3.135183	4.420419	3.38626
Human carcinogenic toxicity	kg 1,4-DCB	3.678104	4.609472	2.234943
Human non-carcinogenic toxicity	kg 1,4-DCB	57.69544	67.05669	51.53606
Land use	m2a crop eq.	1.304728	1.152184	0.813317
Mineral resource scarcity	kg Cu eq.	0.229222	0.505619	0.314119
Fossil resource scarcity	kg oil eq.	36.50842	14.47499	10.97882
Water consumption	m3	1.132367	0.58917	0.444006

S Table 6l: Comparison of Endpoint category for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.004356	0.004989	0.003556
Ecosystems	species.yr	3.07E-06	2.87E-06	2.19E-06
Resources	USD2013	11.74284	4.464185	3.402316

S Table 6m: Comparison of Normalization category for 3,5-dichloro-N-(2-methyl-1,3-benzothiazol-5-yl) benzamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.008949	0.005153	0.003712
Stratospheric ozone depletion	0.000632	0.000341	0.000286
Ionizing radiation	0.005856	0.004893	0.003159
Ozone formation, Human health	0.007898	0.004964	0.003522
Fine particulate matter formation	0.004054	0.003165	0.002329
Ozone formation, Terrestrial ecosystems	0.009961	0.006044	0.004318
Terrestrial acidification	0.005333	0.004268	0.003096
Freshwater eutrophication	0.045924	0.055396	0.048247
Marine eutrophication	0.002044	0.001247	0.000955
Terrestrial ecotoxicity	0.013031	0.017117	0.012228
Freshwater ecotoxicity	0.09393	0.133062	0.101929
Marine ecotoxicity	0.072109	0.10167	0.077884
Human carcinogenic toxicity	0.357144	0.44758	0.217013
Human non-carcinogenic toxicity	0.001846	0.002146	0.001649
Land use	0.000211	0.000187	0.000132
Mineral resource scarcity	1.91E-06	4.21E-06	2.62E-06
Fossil resource scarcity	0.037239	0.014764	0.011198
Water consumption	0.004246	0.002209	0.001665

S Table 7a: Inventory Data of Acedoben (4-acetamidobenzoic acid) for 1 kg functional unit (API-6)

NAR - Inputs		**AR - Inputs**	
4-nitrobenzoic acid	0.933 Kg	4-nitrobenzoic acid	0.933 Kg
Acetic acid	1.87 kg	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	1.26 kg
Platinum	0.5 kg	Pd/c	0.00093 kg
Ethyl acetate	2.8 kg	IPA	0.0933 kg
Water	2.8 kg	Water	0.0933 kg
Energy	134 MJ	Energy	13.4 MJ
NAR - Output		**AR - Output**	
Acedoben(4-acetamidobenzoic acid)	1 kg	Acedoben(4-acetamidobenzoic acid)	1 kg
Byproducts		**Byproducts**	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.0509 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 7b: Comparison of the Midpoint category of the NAR process for 4-acetamidobenzoic acid synthesis

Impact category	Unit	Total	4-nitrobenzoic acid	Acetic acid	Platinum	Ethyl acetate	Water	Energy
Global warming	kg CO2 eq.	654.6435	5.22E+00	4.323726	5.93E+02	9.345696	0.001356	43.07263
Stratospheric ozone depletion	kg CFC11 eq.	1.80E-04	1.17E-06	1.13E-06	1.65E-04	2.24E-06	1.23E-09	1.09E-05
Ionizing radiation	kBq Co-60 eq.	44.00991	2.11E-01	0.327669	4.11E+01	0.391218	8.98E-05	2.022269
Ozone formation, Human health	kg NOx eq.	1.44E+00	1.46E-02	0.010689	1.30E+00	0.023962	3.20E-06	0.094223
Fine particulate matter formation	kg PM2.5 eq.	1.27E+00	1.20E-02	0.006515	1.13E+00	0.013186	3.51E-06	0.106545
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.47E+00	1.50E-02	0.01176	1.32E+00	0.026309	3.30E-06	0.095084
Terrestrial acidification	kg SO2 eq.	2.14E+00	4.73E-02	0.012662	1.92E+00	0.031334	8.77E-06	0.133059
Freshwater eutrophication	kg P eq.	2.82E-01	2.20E-03	0.001387	2.32E-01	0.003943	6.09E-07	0.043117
Marine eutrophication	kg N eq.	1.83E-02	4.03E-04	1.39E-04	1.48E-02	0.000245	4.72E-08	0.002702
Terrestrial ecotoxicity	kg 1,4-DCB	2.63E+03	1.14E+01	13.23803	2.54E+03	30.97361	0.020085	29.66422
Freshwater ecotoxicity	kg 1,4-DCB	3.34E+01	1.47E-01	0.153463	3.15E+01	0.350418	0.000198	1.216664
Marine ecotoxicity	kg 1,4-DCB	4.35E+01	1.97E-01	0.203124	4.10E+01	0.460792	0.000258	1.680808
Human carcinogenic toxicity	kg 1,4-DCB	26.07423	2.31E-01	2.21E-01	2.24E+01	0.483977	0.000151	2.733572
Human non-carcinogenic toxicity	kg 1,4-DCB	7.19E+02	4.00E+00	3.356652	6.50E+02	7.678918	0.003912	53.85507
Land use	m2a crop eq.	9.28E+00	7.05E-02	8.95E-02	8.29E+00	2.16E-01	3.37E-05	0.61437
Mineral resource scarcity	kg Cu eq.	1.39E+00	9.13E-03	1.16E-02	1.32E+00	2.78E-02	1.63E-05	0.014715
Fossil resource scarcity	kg oil eq.	152.5821	1.81E+00	2.080911	1.33E+02	4.485522	0.00032	10.76537
Water consumption	m3	3.53E+00	8.09E-02	0.106286	2.98E+00	0.131547	0.002702	0.226801

S Table 7c: Comparison of the Midpoint category of the AR process for 4-acetamidobenzoic acid synthesis

Impact category	Unit	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Energy
Global warming	kg CO2 eq.	5.57E+01	5.214676	3.53E+01	1.07E+01	4.52E-05	0.226792	4.306659
Stratospheric ozone depletion	kg CFC11 eq.	3.08E-05	1.17E-06	9.53E-06	1.90E-05	4.09E-11	2.71E-08	1.09E-06
Ionizing radiation	kBq Co-60 eq.	3.230029	0.211236	2.28E+00	5.34E-01	2.99E-06	0.002859	0.202199
Ozone formation, Human health	kg NOx eq.	2.45E-01	0.014615	8.63E-02	1.34E-01	1.07E-07	0.000488	0.009421
Fine particulate matter formation	kg PM2.5 eq.	5.46E-01	0.012007	6.19E-02	4.62E-01	1.17E-07	0.00026	0.010653
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.252898	0.015011	9.00E-02	1.38E-01	1.10E-07	0.000549	0.009507
Terrestrial acidification	kg SO2 eq.	1.785649	0.047244	1.34E-01	1.59E+00	2.92E-07	0.000714	0.013304
Freshwater eutrophication	kg P eq.	0.034924	0.002197	1.59E-02	1.25E-02	2.03E-08	5.64E-05	0.004311
Marine eutrophication	kg N eq.	6.21E-03	0.000403	5.03E-03	5.07E-04	1.57E-09	2.83E-06	0.00027
Terrestrial ecotoxicity	kg 1,4-DCB	2.55E+02	11.39519	1.89E+02	4.98E+01	0.000669	0.969108	2.966006
Freshwater ecotoxicity	kg 1,4-DCB	7.38E+00	1.47E-01	2.07E+00	5.034848	6.58E-06	0.008327	0.121649
Marine ecotoxicity	kg 1,4-DCB	9.495686	0.196807	2.72E+00	6.395835	8.61E-06	0.011028	0.168057
Human carcinogenic toxicity	kg 1,4-DCB	7.721677	0.23115	5.76E+00	1.454086	5.05E-06	0.007873	0.273319
Human non-carcinogenic toxicity	kg 1,4-DCB	259.7321	3.998323	4.27E+01	2.08E+02	0.00013	0.173283	5.384752
Land use	m2a crop eq.	1.35E+00	7.05E-02	9.12E-01	3.03E-01	1.12E-06	0.001973	0.061428
Mineral resource scarcity	kg Cu eq.	2.26E+00	9.13E-03	4.47E-01	1.80E+00	5.42E-07	0.000611	0.001471
Fossil resource scarcity	kg oil eq.	1.77E+01	1.813941	1.13E+01	3.417836	1.07E-05	0.13003	1.076386
Water consumption	m3	0.681226	0.080899	5.02E-01	7.40E-02	9.00E-05	0.001428	0.022677

S Table 7d: Comparison of the Midpoint category of the Recycling process for 4-acetamidobenzoic acid synthesis

Impact category	Unit	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Energy
Global warming	kg CO2 eq.	3.52E+01	5.21E+00	1.48E+01	1.07E+01	4.52E-05	0.226792	4.306659
Stratospheric ozone depletion	kg CFC11 eq.	2.50E-05	1.17E-06	3.65E-06	1.90E-05	4.09E-11	2.71E-08	1.09E-06
Ionizing radiation	kBq Co-60 eq.	1.75E+00	2.11E-01	7.98E-01	5.34E-01	2.99E-06	0.002859	0.202199
Ozone formation, Human health	kg NOx eq.	1.93E-01	1.46E-02	3.35E-02	1.34E-01	1.07E-07	0.000488	0.009421
Fine particulate matter formation	kg PM2.5 eq.	5.08E-01	1.20E-02	2.39E-02	4.62E-01	1.17E-07	0.00026	0.010653
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.98E-01	1.50E-02	3.55E-02	1.38E-01	1.10E-07	0.000549	0.009507
Terrestrial acidification	kg SO2 eq.	1.70E+00	4.72E-02	4.87E-02	1.59E+00	2.92E-07	0.000714	0.013304
Freshwater eutrophication	kg P eq.	2.67E-02	2.20E-03	7.63E-03	1.25E-02	2.03E-08	5.64E-05	0.004311
Marine eutrophication	kg N eq.	3.82E-03	0.000403	2.64E-03	5.07E-04	1.57E-09	2.83E-06	0.00027
Terrestrial ecotoxicity	kg 1,4-DCB	1.22E+02	1.14E+01	5.73E+01	4.98E+01	0.000669	0.969108	2.966006
Freshwater ecotoxicity	kg 1,4-DCB	5.99E+00	1.47E-01	6.79E-01	5.034848	6.58E-06	0.008327	0.121649
Marine ecotoxicity	kg 1,4-DCB	7.66E+00	1.97E-01	8.85E-01	6.395835	8.61E-06	0.011028	0.168057
Human carcinogenic toxicity	kg 1,4-DCB	3.50E+00	0.23115	1.53E+00	1.454086	5.05E-06	0.007873	0.273319
Human non-carcinogenic toxicity	kg 1,4-DCB	2.32E+02	4.00E+00	1.51E+01	2.08E+02	0.00013	0.173283	5.384752
Land use	m2a crop eq.	7.46E-01	7.05E-02	3.09E-01	3.03E-01	1.12E-06	0.001973	0.061428
Mineral resource scarcity	kg Cu eq.	1.91E+00	9.13E-03	1.06E-01	1.80E+00	5.42E-07	0.000611	0.001471
Fossil resource scarcity	kg oil eq.	1.15E+01	1.81E+00	5.08E+00	3.417836	1.07E-05	0.13003	1.076386
Water consumption	m3	4.23E-01	0.080899	2.44E-01	7.40E-02	9.00E-05	0.001428	0.022677

S Table 7e: Comparison of the Endpoint category of the NAR process for 4-acetamidobenzoic acid synthesis

Damage category	Unit	Total	4-nitrobenzoic acid	Acetic acid	Platinum	Ethyl acetate	Water	Energy
Human health	DALY	0.046271	0.000307	2.56E-04	0.041405	5.75E-04	2.33E-07	0.003728
Ecosystems	species.yr	3.30E-05	2.32E-07	1.79E-07	2.98E-05	4.06E-07	1.64E-10	2.41E-06
Resources	USD2013	3.24E+01	0.539297	7.17E-01	28.26256	1.55E+00	8.90E-05	1.358651

S Table 7f: Comparison of the Endpoint category of the AR process for 4-acetamidobenzoic acid synthesis

Damage category	Unit	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Energy
Human health	DALY	1.13E-02	3.07E-04	3.79E-03	6.81E-03	7.76E-09	1.24E-05	0.000373
Ecosystems	species.yr	5.61E-06	2.32E-07	1.95E-06	3.18E-06	5.45E-12	9.48E-09	2.41E-07
Resources	USD2013	5.26E+00	5.39E-01	3.43E+00	1.11E+00	2.97E-06	0.049985	0.135846

S Table 7g: Comparison of the Endpoint category of the Recycling process for 4-acetamidobenzoic acid synthesis

Damage category	Unit	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Electricity
Human health	DALY	8.75E-03	3.07E-04	1.25E-03	6.81E-03	7.76E-09	1.24E-05	0.000373
Ecosystems	species.yr	4.40E-06	2.32E-07	7.37E-07	3.18E-06	5.45E-12	9.48E-09	2.41E-07
Resources	USD2013	3.38E+00	5.39E-01	1.54E+00	1.11E+00	2.97E-06	5.00E-02	1.36E-01

S Table 7h: Comparison of Normalization category of the NAR process for 4-acetamidobenzoic acid synthesis

Impact category	Total	4-nitrobenzoic acid	Acetic acid	Platinum	Ethyl acetate	Water	Electricity
Global warming	8.18E-02	0.000652	0.00054	7.41E-02	0.001168	1.70E-07	0.005384
Stratospheric ozone depletion	3.01E-03	1.95E-05	1.88E-05	2.75E-03	3.74E-05	2.05E-08	0.000182
Ionizing radiation	0.091541	0.000439	0.000682	8.54E-02	0.000814	1.87E-07	0.004206
Ozone formation, Human health	6.99E-02	7.10E-04	5.19E-04	6.30E-02	0.001165	1.55E-07	0.004579
Fine particulate matter formation	4.96E-02	4.70E-04	2.55E-04	4.42E-02	0.000516	1.37E-07	0.004166
Ozone formation, Terrestrial ecosystems	8.28E-02	8.45E-04	6.62E-04	7.45E-02	0.001481	1.86E-07	0.005353
Terrestrial acidification	5.22E-02	1.15E-03	3.09E-04	4.67E-02	0.000765	2.14E-07	0.003247
Freshwater eutrophication	4.35E-01	3.38E-03	2.14E-03	3.57E-01	0.006072	9.37E-07	0.066401
Marine eutrophication	3.98E-03	8.75E-05	3.01E-05	3.22E-03	5.31E-05	1.03E-08	0.000586
Terrestrial ecotoxicity	1.73E-01	7.50E-04	8.71E-04	1.67E-01	0.002038	1.32E-06	0.001952
Freshwater ecotoxicity	1.33E+00	5.84E-03	6.09E-03	1.25E+00	0.013912	7.84E-06	0.048302
Marine ecotoxicity	1.00E+00	4.53E-03	4.67E-03	9.43E-01	0.010598	5.94E-06	0.038659
Human carcinogenic toxicity	2.53E+00	0.022448	2.15E-02	2.18E+00	4.70E-02	1.47E-05	0.26543
Human non-carcinogenic toxicity	2.30E-02	1.28E-04	1.07E-04	2.08E-02	0.000246	1.25E-07	0.001723
Land use	1.50E-03	1.14E-05	1.45E-05	1.34E-03	3.50E-05	5.46E-09	9.95E-05
Mineral resource scarcity	1.15E-05	7.61E-08	9.70E-08	1.10E-05	2.32E-07	1.36E-10	1.23E-07
Fossil resource scarcity	1.56E-01	0.00185	2.12E-03	1.36E-01	0.004575	3.26E-07	0.010981
Water consumption	1.32E-02	3.03E-04	3.99E-04	1.12E-02	0.000493	1.01E-05	0.000851

S Table 7i: Comparison of Normalization category of the AR process for 4-acetamidobenzoic acid synthesis

Impact category	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Energy
Global warming	6.96E-03	6.52E-04	4.41E-03	0.001335	5.65E-09	2.83E-05	0.000538
Stratospheric ozone depletion	5.15E-04	1.95E-05	1.59E-04	3.18E-04	6.83E-10	4.53E-07	1.82E-05
Ionizing radiation	6.72E-03	0.000439	4.74E-03	0.001111	6.23E-09	5.95E-06	0.000421
Ozone formation, Human health	1.19E-02	7.10E-04	4.19E-03	0.006536	5.18E-09	2.37E-05	0.000458
Fine particulate matter formation	2.14E-02	4.69E-04	0.002419	0.018051	4.57E-09	1.02E-05	0.000417
Ozone formation, Terrestrial ecosystems	1.42E-02	0.000845	5.07E-03	0.007761	6.19E-09	3.09E-05	0.000535
Terrestrial acidification	4.36E-02	0.001153	3.27E-03	0.038803	7.13E-09	1.74E-05	0.000325
Freshwater eutrophication	5.38E-02	0.003384	2.45E-02	0.019218	3.12E-08	8.69E-05	0.006639
Marine eutrophication	1.35E-03	8.75E-05	1.09E-03	0.00011	3.42E-10	6.14E-07	5.86E-05
Terrestrial ecotoxicity	1.68E-02	7.50E-04	1.25E-02	0.003275	4.40E-08	6.38E-05	0.000195
Freshwater ecotoxicity	2.93E-01	5.84E-03	8.23E-02	2.00E-01	2.61E-07	0.000331	0.004829
Marine ecotoxicity	2.18E-01	0.004527	0.062651	0.147104	1.98E-07	0.000254	0.003865
Human carcinogenic toxicity	7.50E-01	0.022445	5.59E-01	0.141192	4.90E-07	0.000764	0.026539
Human non-carcinogenic toxicity	8.31E-03	0.000128	1.37E-03	0.00664	4.17E-09	5.55E-06	0.000172
Land use	2.18E-04	1.14E-05	1.48E-04	4.91E-05	1.82E-10	3.20E-07	9.95E-06
Mineral resource scarcity	1.88E-05	7.61E-08	3.72E-06	1.50E-05	4.52E-12	5.09E-09	1.23E-08
Fossil resource scarcity	1.81E-02	1.85E-03	1.15E-02	0.003486	1.09E-08	0.000133	0.001098
Water consumption	0.002555	0.000303	1.88E-03	0.000277	3.38E-07	5.36E-06	8.50E-05

S Table 7j: Comparison of Normalization category of the Recycling process for 4-acetamidobenzoic acid synthesis

Impact category	Total	4-nitrobenzoic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Water	Isopropanol	Energy
Global warming	4.40E-03	6.52E-04	1.85E-03	1.33E-03	5.65E-09	2.83E-05	0.000538
Stratospheric ozone depletion	4.17E-04	1.95E-05	6.09E-05	3.18E-04	6.83E-10	4.53E-07	1.82E-05
Ionizing radiation	3.64E-03	4.39E-04	1.66E-03	1.11E-03	6.23E-09	5.95E-06	0.000421
Ozone formation, Human health	9.36E-03	7.10E-04	1.63E-03	6.54E-03	5.18E-09	2.37E-05	0.000458
Fine particulate matter formation	0.01988	4.69E-04	9.34E-04	1.81E-02	4.57E-09	1.02E-05	0.000417
Ozone formation, Terrestrial ecosystems	0.01117	8.45E-04	2.00E-03	7.76E-03	6.19E-09	3.09E-05	0.000535
Terrestrial acidification	0.041487	1.15E-03	1.19E-03	3.88E-02	7.13E-09	1.74E-05	0.000325
Freshwater eutrophication	4.11E-02	3.38E-03	1.17E-02	1.92E-02	3.12E-08	8.69E-05	0.006639
Marine eutrophication	8.29E-04	8.75E-05	5.73E-04	0.00011	3.42E-10	6.14E-07	5.86E-05
Terrestrial ecotoxicity	8.06E-03	7.50E-04	0.003774	3.28E-03	4.40E-08	6.38E-05	0.000195
Freshwater ecotoxicity	0.237828	5.84E-03	0.026947	2.00E-01	2.61E-07	0.000331	0.004829
Marine ecotoxicity	0.176116	4.53E-03	0.020366	1.47E-01	1.98E-07	0.000254	0.003865
Human carcinogenic toxicity	0.33989	2.24E-02	1.49E-01	0.141192	4.90E-07	0.000764	0.026539
Human non-carcinogenic toxicity	7.43E-03	1.28E-04	4.83E-04	6.64E-03	4.17E-09	5.55E-06	0.000172
Land use	1.21E-04	1.14E-05	5.01E-05	4.91E-05	1.82E-10	3.20E-07	9.95E-06
Mineral resource scarcity	1.60E-05	7.61E-08	8.85E-07	1.50E-05	4.52E-12	5.09E-09	1.23E-08
Fossil resource scarcity	0.011752	1.85E-03	5.18E-03	3.49E-03	1.09E-08	0.000133	0.001098
Water consumption	0.001587	3.03E-04	9.15E-04	0.000277	3.38E-07	5.36E-06	8.50E-05

S Table 7k: Comparison of the Midpoint category for 4-acetamidobenzoic acid synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	654.6435	55.70521	35.20086
Stratospheric ozone depletion	kg CFC11 eq.	0.00018	3.08E-05	2.50E-05
Ionizing radiation	kBq Co-60 eq.	44.00991	3.230029	1.748113
Ozone formation, Human health	kg NOx eq.	1.438918	0.245303	0.192568
Fine particulate matter formation	kg PM2.5 eq.	1.269643	0.54644	0.508446
Ozone formation, Terrestrial ecosystems	kg NOx eq.	1.470585	0.252898	0.198403
Terrestrial acidification	kg SO2 eq.	2.140145	1.785649	1.700269
Freshwater eutrophication	kg P eq.	0.282329	0.034924	0.026672
Marine eutrophication	kg N eq.	0.01832	0.006211	0.003822
Terrestrial ecotoxicity	kg 1,4-DCB	2625.688	254.5625	122.458
Freshwater ecotoxicity	kg 1,4-DCB	33.38288	7.384761	5.99064
Marine ecotoxicity	kg 1,4-DCB	43.53547	9.495686	7.657234
Human carcinogenic toxicity	kg 1,4-DCB	26.07423	7.721677	3.50041
Human non-carcinogenic toxicity	kg 1,4-DCB	718.8759	259.7321	232.1406
Land use	m2a crop eq.	9.276405	1.348418	0.746004
Mineral resource scarcity	kg Cu eq.	1.386301	2.255359	1.914925
Fossil resource scarcity	kg oil eq.	152.5821	17.73642	11.52118
Water consumption	m3	3.529683	0.681226	0.423164

S Table 7l: Comparison of the Endpoint category for 4-acetamidobenzoic acid synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.046271	0.011301	0.008753
Ecosystems	species.yr	3.30E-05	5.61E-06	4.40E-06
Resources	USD2013	32.42707	5.262938	3.375223

S Table 7m: Comparison of Normalization category for 4-acetamidobenzoic acid synthesis

Impact category	NAR	AR	Recycling
Global warming	0.08183	0.006963	0.0044
Stratospheric ozone depletion	0.00301	0.000515	0.000417
Ionizing radiation	0.091541	0.006718	0.003636
Ozone formation, Human health	0.069931	0.011922	0.009359
Fine particulate matter formation	4.96E-02	2.14E-02	0.01988
Ozone formation, Terrestrial ecosystems	0.082794	0.014238	0.01117
Terrestrial acidification	5.22E-02	4.36E-02	0.041487
Freshwater eutrophication	0.434786	0.053784	0.041074
Marine eutrophication	0.003975	0.001348	0.000829
Terrestrial ecotoxicity	0.17277	1.68E-02	8.06E-03
Freshwater ecotoxicity	1.3253	0.293175	0.237828
Marine ecotoxicity	1.001316	0.218401	0.176116
Human carcinogenic toxicity	2.531808	0.749775	0.33989
Human non-carcinogenic toxicity	0.023004	0.008311	0.007428
Land use	1.50E-03	2.18E-04	0.000121
Mineral resource scarcity	1.15E-05	1.88E-05	1.60E-05
Fossil resource scarcity	0.155634	0.018091	0.011752
Water consumption	1.32E-02	2.55E-03	0.001587

S Table 8a: Inventory Data of Actarit (2-(4-acetamidophenyl) aceticacid) for 1 kg functional unit (API-7)

NAR - Inputs		**AR - Inputs**	
2-(4-nitrophenyl) acetic acid	0.938 Kg	2-(4-nitrophenyl) acetic acid	0.938 Kg
Ethyl acetate	0.938 kg	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	1.17 kg
Nickel	0.000937 kg	Pd/C	0.000938 kg
Titania	0.000937 kg	IPA	0.0938 kg
Hydrogen gas	18.8 kg	Water	0.0938 kg
Energy	81 MJ	Energy	13.5 MJ
NAR - Output		**AR - Output**	
Actarit (2-(4-acetamidophenyl) acetic acid)	1 kg	2-(4-acetamidophenyl)acetic acid	1 kg
Byproducts		**Byproducts**	
-		1,1-dioxo-1,2-benzothiazol-3-one	0.06944 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 8b: Comparison of the Midpoint category of the NAR process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Unit	Total	2-(4-nitrophenyl) acetic acid	Ethyl acetate	Titania	Nickel	Hydrogen gas	Energy
Global warming	kg CO2 eq.	94.02642	1.41E+01	3.13E+00	0.021542	0.168489	50.67014	25.95895
Stratospheric ozone depletion	kg CFC11 eq.	2.46E-05	4.07E-06	7.49E-07	4.42E-09	1.30E-07	1.30E-05	6.57E-06
Ionizing radiation	kBq Co-60 eq.	2.483203	7.00E-01	1.31E-01	0.00056	0.024472	0.408577	1.218778
Ozone formation, Human health	kg NOx eq.	0.240469	3.16E-02	0.008023	6.56E-05	0.00075	0.143246	0.056786
Fine particulate matter formation	kg PM2.5 eq.	0.17011	2.87E-02	0.004415	3.66E-05	0.004191	0.06857	0.064212
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.272688	3.28E-02	8.81E-03	6.68E-05	0.000774	0.172885	0.057305
Terrestrial acidification	kg SO2 eq.	0.352222	4.98E-02	0.010491	9.04E-05	0.014185	0.197476	0.080192
Freshwater eutrophication	kg P eq.	0.038723	8.99E-03	0.00132	4.32E-06	0.000157	0.002267	0.025986
Marine eutrophication	kg N eq.	0.006588	8.08E-04	8.19E-05	3.82E-07	1.17E-05	0.004058	0.001628
Terrestrial ecotoxicity	kg 1,4-DCB	210.3621	3.48E+01	10.37063	0.02295	25.37108	121.9468	17.87799
Freshwater ecotoxicity	kg 1,4-DCB	1.781257	5.06E-01	1.17E-01	0.000273	0.090865	0.3332	0.733257
Marine ecotoxicity	kg 1,4-DCB	2.59E+00	6.74E-01	1.54E-01	0.000374	1.25E-01	0.620394	1.012987
Human carcinogenic toxicity	kg 1,4-DCB	4.13E+00	7.93E-01	1.62E-01	6.75E-04	2.57E-02	1.503849	1.647465
Human non-carcinogenic toxicity	kg 1,4-DCB	61.87377	1.46E+01	2.57E+00	0.009759	1.56065	10.65322	32.4573
Land use	m2a crop eq.	1.75188	2.15E-01	7.23E-02	0.000876	0.005917	1.087306	0.370268
Mineral resource scarcity	kg Cu eq.	0.173149	0.0261	0.009309	0.008319	0.050771	0.069783	0.008868
Fossil resource scarcity	kg oil eq.	75.86613	5.118534	1.501849	0.005349	0.047113	62.70522	6.48806
Water consumption	m3	0.509749	0.173611	0.044045	3.94E-05	0.013899	0.141467	0.136688

S Table 8c: Comparison of the Midpoint category of the AR process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Unit	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	kg CO2 eq.	6.21E+01	14.07816	32.70381	10.72859	0.227837	4.54E-05	4.326492
Stratospheric ozone depletion	kg CFC11 eq.	3.31E-05	4.07E-06	8.83E-06	1.91E-05	2.72E-08	4.11E-11	1.09E-06
Ionizing radiation	kBq Co-60 eq.	3.56E+00	7.00E-01	2.11E+00	5.37E-01	2.87E-03	3.01E-06	0.20313
Ozone formation, Human health	kg NOx eq.	2.57E-01	3.16E-02	8.00E-02	1.35E-01	4.90E-04	1.07E-07	0.009464
Fine particulate matter formation	kg PM2.5 eq.	5.61E-01	2.87E-02	5.74E-02	4.64E-01	2.61E-04	1.17E-07	1.07E-02
Ozone formation, Terrestrial ecosystems	kg NOx eq.	2.65E-01	3.28E-02	8.34E-02	0.138479	5.52E-04	1.10E-07	0.009551
Terrestrial acidification	kg SO2 eq.	1.79E+00	0.049788	1.24E-01	1.597603	7.17E-04	2.94E-07	0.013365
Freshwater eutrophication	kg P eq.	4.06E-02	8.99E-03	1.47E-02	0.012536	5.67E-05	2.04E-08	0.004331
Marine eutrophication	kg N eq.	6.25E-03	8.08E-04	0.004661	5.09E-04	2.84E-06	1.58E-09	0.000271
Terrestrial ecotoxicity	kg 1,4-DCB	2.64E+02	3.48E+01	1.76E+02	5.00E+01	9.74E-01	6.72E-04	2.979665
Freshwater ecotoxicity	kg 1,4-DCB	7.616612	0.506335	1.921661	5.06E+00	0.008365	6.61E-06	0.12221
Marine ecotoxicity	kg 1,4-DCB	9.804127	0.673705	2.525214	6.43E+00	0.011078	8.65E-06	0.168831
Human carcinogenic toxicity	kg 1,4-DCB	7.87E+00	0.793265	5.335348	1.46E+00	0.007909	5.07E-06	0.274578
Human non-carcinogenic toxicity	kg 1,4-DCB	268.2236	14.62177	39.55724	2.08E+02	0.174081	1.31E-04	5.40955
Land use	m2a crop eq.	1.43E+00	2.15E-01	8.45E-01	3.04E-01	0.001982	1.13E-06	0.061711
Mineral resource scarcity	kg Cu eq.	2.25E+00	2.61E-02	4.14E-01	1.81E+00	6.14E-04	5.45E-07	0.001478
Fossil resource scarcity	kg oil eq.	2.02E+01	5.12E+00	1.05E+01	3.43E+00	1.31E-01	1.07E-05	1.081343
Water consumption	m3	0.737754	0.173611	0.465509	7.43E-02	0.001435	9.05E-05	0.022781

S Table 8d: Comparison of the Midpoint category of the Recycling process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Unit	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	kg CO2 eq.	4.31E+01	14.07816	1.37E+01	1.07E+01	0.227837	4.54E-05	4.326492
Stratospheric ozone depletion	kg CFC11 eq.	2.77E-05	4.07E-06	3.38E-06	1.91E-05	2.72E-08	4.11E-11	1.09E-06
Ionizing radiation	kBq Co-60 eq.	2.18E+00	7.00E-01	7.39E-01	5.37E-01	0.002873	3.01E-06	0.20313
Ozone formation, Human health	kg NOx eq.	2.08E-01	3.16E-02	3.11E-02	1.35E-01	0.00049	1.07E-07	0.009464
Fine particulate matter formation	kg PM2.5 eq.	5.26E-01	2.87E-02	2.21E-02	4.64E-01	0.000261	1.17E-07	0.010702
Ozone formation, Terrestrial ecosystems	kg NOx eq.	2.14E-01	3.28E-02	3.29E-02	1.38E-01	0.000552	1.10E-07	0.009551
Terrestrial acidification	kg SO2 eq.	1.706646	4.98E-02	4.52E-02	1.60E+00	7.17E-04	2.94E-07	0.013365
Freshwater eutrophication	kg P eq.	0.032984	8.99E-03	7.07E-03	1.25E-02	5.67E-05	2.04E-08	0.004331
Marine eutrophication	kg N eq.	0.004037	8.08E-04	0.002446	5.09E-04	2.84E-06	1.58E-09	0.000271
Terrestrial ecotoxicity	kg 1,4-DCB	141.8988	3.48E+01	53.16462	5.00E+01	0.973571	0.000672	2.979665
Freshwater ecotoxicity	kg 1,4-DCB	6.324204	5.06E-01	0.629253	5.06E+00	0.008365	6.61E-06	0.12221
Marine ecotoxicity	kg 1,4-DCB	8.10E+00	6.74E-01	8.21E-01	6.43E+00	0.011078	8.65E-06	0.168831
Human carcinogenic toxicity	kg 1,4-DCB	3.96E+00	7.93E-01	1.42E+00	1.46E+00	7.91E-03	5.07E-06	0.274578
Human non-carcinogenic toxicity	kg 1,4-DCB	2.43E+02	1.46E+01	1.40E+01	2.08E+02	1.74E-01	0.000131	5.40955
Land use	m2a crop eq.	0.869878	2.15E-01	2.87E-01	3.04E-01	0.001982	1.13E-06	0.061711
Mineral resource scarcity	kg Cu eq.	1.93E+00	2.61E-02	9.85E-02	1.81E+00	6.14E-04	5.45E-07	0.001478
Fossil resource scarcity	kg oil eq.	1.45E+01	5.12E+00	4.71E+00	3.433576	0.130629	1.07E-05	1.081343
Water consumption	m3	0.49852	0.173611	0.226276	0.074327	1.43E-03	9.05E-05	2.28E-02

S Table 8e: Comparison of the End Point category of the NAR process for 2-(4-acetamidophenyl) aceticacid synthesis

Damage category	Unit	Total	2-(4-nitrophenyl) acetic acid	Ethyl acetate	Titanium	Nickel	Hydrogen gas	Energy
Human health	DALY	0.005062	1.04E-03	0.000192	8.06E-07	8.25E-05	0.001497	0.002247
Ecosystems	species.yr	3.68E-06	7.04E-07	1.36E-07	7.09E-10	4.80E-08	1.34E-06	1.45E-06
Resources	USD2013	30.86051	1.410064	5.19E-01	0.003058	0.025015	28.0849	0.81883

S Table 8f: Comparison of the End Point category of the AR process for 2-(4-acetamidophenyl) aceticacid synthesis

Damage category	Unit	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Human health	DALY	0.011793	0.001043	3.52E-03	0.006846	1.24E-05	7.79E-09	0.000374
Ecosystems	species.yr	5.96E-06	7.04E-07	1.81E-06	3.20E-06	9.52E-09	5.48E-12	2.42E-07
Resources	USD2013	5.89E+00	1.41E+00	3.18E+00	1.11E+00	5.02E-02	2.98E-06	0.136472

S Table 8g: Comparison of the Endpoint category of the Recycling process for 2-(4-acetamidophenyl) aceticacid synthesis

Damage category	Unit	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Human health	DALY	9.43E-03	1.04E-03	1.15E-03	0.006846	1.24E-05	7.79E-09	0.000374
Ecosystems	species.yr	4.83E-06	7.04E-07	6.84E-07	3.20E-06	9.52E-09	5.48E-12	2.42E-07
Resources	USD2013	4.14E+00	1.41E+00	1.43E+00	1.111947	5.02E-02	2.98E-06	0.136472

S Table 8h: Comparison of Normalization category of the NAR process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Total	2-(4-nitrophenyl) acetic acid	Ethyl acetate	Titania	Nickel	Hydrogen gas	Energy
Global warming	0.011753	0.00176	0.000391	2.69E-06	2.11E-05	0.006334	0.003245
Stratospheric ozone depletion	0.00041	6.79E-05	1.25E-05	7.39E-08	2.18E-06	0.000218	0.00011
Ionizing radiation	0.005165	0.001456	0.000272	1.16E-06	5.09E-05	0.00085	0.002535
Ozone formation, Human health	0.011687	0.001536	0.00039	3.19E-06	3.64E-05	0.006962	0.00276
Fine particulate matter formation	0.006651	0.001122	0.000173	1.43E-06	0.000164	0.002681	0.002511
Ozone formation, Terrestrial ecosystems	0.015352	0.001849	0.000496	3.76E-06	4.36E-05	0.009733	0.003226
Terrestrial acidification	0.008594	0.001215	0.000256	2.21E-06	0.000346	0.004818	0.001957
Freshwater eutrophication	0.059633	0.013842	0.002033	6.65E-06	0.000243	0.003491	0.040018
Marine eutrophication	0.00143	0.000175	1.78E-05	8.28E-08	2.53E-06	0.000881	0.000353
Terrestrial ecotoxicity	0.013842	0.002288	0.000682	1.51E-06	0.001669	0.008024	0.001176
Freshwater ecotoxicity	0.070716	0.020102	0.004658	1.08E-05	0.003607	0.013228	0.02911
Marine ecotoxicity	0.059501	0.015495	0.003549	8.60E-06	0.002881	0.014269	0.023299
Human carcinogenic toxicity	0.401316	0.077026	0.015735	6.55E-05	0.002497	0.146024	0.159969
Human non-carcinogenic toxicity	0.00198	0.000468	8.23E-05	3.12E-07	4.99E-05	0.000341	0.001039
Land use	0.000284	3.49E-05	1.17E-05	1.42E-07	9.59E-07	0.000176	6.00E-05
Mineral resource scarcity	1.44E-06	2.17E-07	7.75E-08	6.93E-08	4.23E-07	5.81E-07	7.39E-08
Fossil resource scarcity	0.077383	0.005221	0.001532	5.46E-06	4.81E-05	0.063959	0.006618
Water consumption	0.001912	0.000651	0.000165	1.48E-07	5.21E-05	0.000531	0.000513

S Table 8i: Comparison of Normalization category of the AR process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	7.76E-03	1.76E-03	4.09E-03	1.34E-03	2.85E-05	5.68E-09	0.000541
Stratospheric ozone depletion	5.53E-04	6.79E-05	1.47E-04	3.19E-04	4.55E-07	6.86E-10	1.83E-05
Ionizing radiation	7.40E-03	1.46E-03	4.40E-03	1.12E-03	5.98E-06	6.26E-09	0.000423
Ozone formation, Human health	1.25E-02	1.54E-03	3.89E-03	6.57E-03	2.38E-05	5.20E-09	0.00046
Fine particulate matter formation	2.19E-02	1.12E-03	0.002243	1.81E-02	1.02E-05	4.59E-09	0.000418
Ozone formation, Terrestrial ecosystems	1.49E-02	1.85E-03	0.004697	7.80E-03	3.11E-05	6.22E-09	0.000538
Terrestrial acidification	4.36E-02	1.21E-03	0.003033	3.90E-02	1.75E-05	7.17E-09	0.000326
Freshwater eutrophication	6.26E-02	0.013842	2.27E-02	1.93E-02	8.73E-05	3.14E-08	0.00667
Marine eutrophication	1.36E-03	1.75E-04	1.01E-03	1.10E-04	6.17E-07	3.43E-10	5.89E-05
Terrestrial ecotoxicity	0.017395	0.002288	1.16E-02	0.00329	6.41E-05	4.42E-08	0.000196
Freshwater ecotoxicity	0.302379	0.020102	7.63E-02	0.200804	3.32E-04	2.63E-07	0.004852
Marine ecotoxicity	2.25E-01	0.015495	5.81E-02	0.147782	2.55E-04	1.99E-07	0.003883
Human carcinogenic toxicity	0.76436	0.077026	5.18E-01	0.141842	7.68E-04	4.92E-07	0.026661
Human non-carcinogenic toxicity	8.58E-03	4.68E-04	1.27E-03	0.006671	5.57E-06	4.19E-09	0.000173
Land use	2.31E-04	3.49E-05	1.37E-04	4.93E-05	3.21E-07	1.83E-10	1.00E-05
Mineral resource scarcity	1.87E-05	2.17E-07	3.45E-06	1.50E-05	5.11E-09	4.54E-12	1.23E-08
Fossil resource scarcity	0.020643	0.005221	1.07E-02	0.003502	1.33E-04	1.09E-08	0.001103
Water consumption	2.77E-03	6.51E-04	1.75E-03	0.000279	5.38E-06	3.39E-07	8.54E-05

S Table 8j: Comparison of Normalization category of the Recycling process for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Total	2-(4-nitrophenyl) acetic acid	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	5.38E-03	1.76E-03	1.71E-03	1.34E-03	2.85E-05	5.68E-09	0.000541
Stratospheric ozone depletion	4.62E-04	6.79E-05	5.65E-05	0.000319	4.55E-07	6.86E-10	1.83E-05
Ionizing radiation	4.54E-03	1.46E-03	1.54E-03	0.001116	5.98E-06	6.26E-09	0.000423
Ozone formation, Human health	1.01E-02	1.54E-03	1.51E-03	6.57E-03	2.38E-05	5.20E-09	0.00046
Fine particulate matter formation	2.05E-02	1.12E-03	8.65E-04	1.81E-02	1.02E-05	4.59E-09	0.000418
Ozone formation, Terrestrial ecosystems	1.21E-02	1.85E-03	1.85E-03	7.80E-03	3.11E-05	6.22E-09	0.000538
Terrestrial acidification	0.041642	1.21E-03	1.10E-03	3.90E-02	1.75E-05	7.17E-09	0.000326
Freshwater eutrophication	5.08E-02	1.38E-02	1.09E-02	1.93E-02	8.73E-05	3.14E-08	0.00667
Marine eutrophication	0.000876	0.000175	5.31E-04	1.10E-04	6.17E-07	3.43E-10	5.89E-05
Terrestrial ecotoxicity	0.009337	0.002288	3.50E-03	3.29E-03	6.41E-05	4.42E-08	0.000196
Freshwater ecotoxicity	0.251071	0.020102	2.50E-02	2.01E-01	0.000332	2.63E-07	0.004852
Marine ecotoxicity	0.186296	0.015495	1.89E-02	1.48E-01	0.000255	1.99E-07	0.003883
Human carcinogenic toxicity	3.84E-01	0.077026	1.38E-01	1.42E-01	0.000768	4.92E-07	0.026661
Human non-carcinogenic toxicity	7.76E-03	4.68E-04	4.47E-04	6.67E-03	5.57E-06	4.19E-09	0.000173
Land use	1.41E-04	3.49E-05	4.65E-05	4.93E-05	3.21E-07	1.83E-10	1.00E-05
Mineral resource scarcity	1.61E-05	2.17E-07	8.20E-07	1.50E-05	5.11E-09	4.54E-12	1.23E-08
Fossil resource scarcity	1.48E-02	0.005221	4.81E-03	3.50E-03	1.33E-04	1.09E-08	0.001103
Water consumption	1.87E-03	6.51E-04	8.49E-04	2.79E-04	5.38E-06	3.39E-07	8.54E-05

S Table 8k: Comparison of the Midpoint category for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	94.02642	62.06494	43.05656
Stratospheric ozone depletion	kg CFC11 eq.	2.46E-05	3.31E-05	2.77E-05
Ionizing radiation	kBq Co-60 eq.	2.483203	3.555708	2.181911
Ozone formation, Human health	kg NOx eq.	0.240469	0.256655	0.207767
Fine particulate matter formation	kg PM2.5 eq.	0.17011	0.560781	0.525559
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.272688	0.264852	0.214333
Terrestrial acidification	kg SO2 eq.	3.52E-01	1.785797	1.706646
Freshwater eutrophication	kg P eq.	0.038723	0.040635	0.032984
Marine eutrophication	kg N eq.	6.59E-03	0.006252	0.004037
Terrestrial ecotoxicity	kg 1,4-DCB	210.3621	264.3651	141.8988
Freshwater ecotoxicity	kg 1,4-DCB	1.781257	7.616612	6.324204
Marine ecotoxicity	kg 1,4-DCB	2.59E+00	9.80E+00	8.099806
Human carcinogenic toxicity	kg 1,4-DCB	4.13302	7.871887	3.958599
Human non-carcinogenic toxicity	kg 1,4-DCB	61.87377	268.2236	242.6451
Land use	m2a crop eq.	1.75188	1.42834	0.869878
Mineral resource scarcity	kg Cu eq.	0.173149	2.248025	1.932428
Fossil resource scarcity	kg oil eq.	7.59E+01	20.23801	14.47622
Water consumption	m3	5.10E-01	7.38E-01	0.49852

S Table 8l: Comparison of the Endpoint category for 2-(4-acetamidophenyl) aceticacid synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	0.005062	0.011793	0.009431
Ecosystems	species.yr	3.68E-06	5.96E-06	4.83E-06
Resources	USD2013	30.86051	5.889409	4.13942

S Table 8m: Comparison of Normalization category for 2-(4-acetamidophenyl) aceticacid synthesis

Impact category	NAR	AR	Recycling
Global warming	0.011753	0.007758	0.005382
Stratospheric ozone depletion	0.00041	0.000553	0.000462
Ionizing radiation	0.005165	0.007396	0.004538
Ozone formation, Human health	0.011687	0.012473	0.010097
Fine particulate matter formation	0.006651	0.021927	0.020549
Ozone formation, Terrestrial ecosystems	0.015352	1.49E-02	1.21E-02
Terrestrial acidification	0.008594	0.043573	0.041642
Freshwater eutrophication	0.059633	0.062577	0.050795
Marine eutrophication	0.00143	0.001357	0.000876
Terrestrial ecotoxicity	0.013842	0.017395	0.009337
Freshwater ecotoxicity	0.070716	0.302379	0.251071
Marine ecotoxicity	0.059501	0.225495	0.186296
Human carcinogenic toxicity	0.401316	0.76436	0.38438
Human non-carcinogenic toxicity	0.00198	0.008583	0.007765
Land use	0.000284	0.000231	0.000141
Mineral resource scarcity	1.44E-06	1.87E-05	1.61E-05
Fossil resource scarcity	0.077383	0.020643	0.014766
Water consumption	0.001912	0.002767	0.001869

S Table 9a: Inventory Data of Phenacetin (N-(4-ethoxy phenyl) acetamide for 1 kg functional unit (API-9)

NAR - Inputs		**AR - Inputs**	
1-ethoxy-4 Nitro benzene	0.94 kg	1-ethoxy-4 Nitro benzene	0.933 kg
Ethyl acetate	0.94 kg	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	1.26 kg
Nickel	0.00094 kg	Pd(Catalyst)	0.00009 kg
Titania	0.00094 kg	Isopropyl Alcohol	0.0933 kg
Hydrogen	10 kg	water	0.0933 kg
Energy	82.1 MJ	Energy	10.1 MJ
NAR - Output		**AR - Output**	
Phenacetin(N-(4-ethoxy phenyl) acetamide	1 kg	Phenacetin(N-(4-ethoxy phenyl)acetamide	1 kg
Byproducts		**Byproducts**	
Byproducts	0.06042 kg	Byproducts(1,1dioxo-1,2 benthiazol-3-one	0.125 kg

NAR - Non Amidation Route; AR – Amidation Route

S Table 9b: Comparison of the Midpoint category of the NAR process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Unit	Total	1-ethoxy-4-nitrobenzene	Ethyl acetate	Nickel	Titanium	Hydrogen gas	Energy
Global warming	kg CO2 eq.	127.7717	7.16E+01	3.14E+00	0.0054	0.00216	27.0284	26.02818
Stratospheric ozone depletion	kg CFC11 eq.	9.91E-05	8.48E-05	7.51E-07	6.38E-09	4.44E-10	6.95E-06	6.59E-06
Ionizing radiation	kBq Co-60 eq.	5.172624	3.60E+00	1.31E-01	0.000383	5.61E-05	0.217942	1.222028
Ozone formation, Human health	kg NOx eq.	0.31033	1.69E-01	8.04E-03	2.66E-05	6.58E-06	0.07641	0.056938
Fine particulate matter formation	kg PM2.5 eq.	0.24237	1.37E-01	4.43E-03	1.00E-05	3.67E-06	0.036576	0.064384
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.33497	1.76E-01	8.83E-03	2.73E-05	6.70E-06	0.09222	0.057458
Terrestrial acidification	kg SO2 eq.	0.536232	3.40E-01	1.05E-02	2.17E-05	9.06E-06	0.105337	0.080406
Freshwater eutrophication	kg P eq.	0.058258	2.97E-02	1.32E-03	1.08E-05	4.33E-07	0.001209	0.026055
Marine eutrophication	kg N eq.	0.022321	1.84E-02	8.21E-05	4.10E-07	3.83E-08	0.002165	0.001633
Terrestrial ecotoxicity	kg 1,4-DCB	579.3488	4.86E+02	1.04E+01	0.053359	0.002301	65.04869	17.92566
Freshwater ecotoxicity	kg 1,4-DCB	6.798654	5.759605	1.18E-01	0.008433	2.74E-05	0.177735	0.735212
Marine ecotoxicity	kg 1,4-DCB	9.169044	7.657068	1.55E-01	0.010626	3.75E-05	0.33093	1.015689
Human carcinogenic toxicity	kg 1,4-DCB	6.417509	3.799741	1.62E-01	0.001183	6.77E-05	0.802181	1.651858
Human non-carcinogenic toxicity	kg 1,4-DCB	155.169	1.14E+02	2.58E+00	0.097773	0.000978	5.682629	32.54385
Land use	m2a crop eq.	4.985821	3.96E+00	7.24E-02	3.96E-04	8.78E-05	0.579989	0.371255
Mineral resource scarcity	kg Cu eq.	4.83E-01	4.22E-01	9.33E-03	4.35E-03	8.34E-04	0.037223	0.008892
Fossil resource scarcity	kg oil eq.	63.9743	2.25E+01	1.51E+00	0.001336	0.000536	33.44814	6.505361
Water consumption	m3	2.393678	2.14E+00	4.42E-02	0.000181	3.95E-06	0.075461	0.137053

S Table 9c: Comparison of the Midpoint category of the AR process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Unit	Total	1-ethoxy-4-nitrobenzene	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	kg CO2 eq.	1.11E+02	7.11E+01	3.53E+01	1.07E+00	2.27E-01	4.52E-05	3.230447
Stratospheric ozone depletion	kg CFC11 eq.	9.64E-05	8.42E-05	9.53E-06	1.90E-06	2.71E-08	4.09E-11	8.17E-07
Ionizing radiation	kBq Co-60 eq.	6.06322	3.58E+00	2.279928	0.05342	0.00286	2.99E-06	0.15167
Ozone formation, Human health	kg NOx eq.	0.275009	1.68E-01	0.086295	0.013451	0.000488	1.07E-07	0.007067
Fine particulate matter formation	kg PM2.5 eq.	0.252299	0.135998	6.19E-02	0.046172	0.00026	1.17E-07	0.007991
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.286641	1.75E-01	9.00E-02	1.38E-02	0.000549	1.10E-07	0.007131
Terrestrial acidification	kg SO2 eq.	0.641399	0.337528	0.134127	0.15905	0.000714	2.92E-07	0.009979
Freshwater eutrophication	kg P eq.	0.04987	2.94E-02	0.015883	0.001248	5.64E-05	2.03E-08	0.003234
Marine eutrophication	kg N eq.	2.36E-02	1.83E-02	0.005028	5.07E-05	2.83E-06	1.57E-09	0.000203
Terrestrial ecotoxicity	kg 1,4-DCB	6.80E+02	4.82E+02	1.89E+02	4.98E+00	0.969244	0.000669	2.224816
Freshwater ecotoxicity	kg 1,4-DCB	8.395085	5.72E+00	2.073188	0.503555	0.008328	6.58E-06	0.09125
Marine ecotoxicity	kg 1,4-DCB	11.10387	7.60E+00	2.724333	0.639673	0.011029	8.61E-06	0.126061
Human carcinogenic toxicity	kg 1,4-DCB	9.887171	3.772793	5.756052	0.145429	0.007874	5.05E-06	0.205018
Human non-carcinogenic toxicity	kg 1,4-DCB	181.0979	113.4554	42.67642	20.75343	0.173308	0.00013	4.039131
Land use	m2a crop eq.	4.923741	3.933553	9.12E-01	0.030282	0.001973	1.12E-06	0.046078
Mineral resource scarcity	kg Cu eq.	1.047229	0.419008	0.446734	0.179772	0.000611	5.42E-07	0.001104
Fossil resource scarcity	kg oil eq.	34.93251	22.35341	11.29981	0.341832	0.130048	1.07E-05	0.807403
Water consumption	m3	2.649806	2.121662	0.502216	0.0074	0.001428	9.01E-05	0.01701

S Table 9d: Comparison of the Midpoint category of the Recycling process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Unit	Total	1-ethoxy-4-nitrobenzene	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	kg CO2 eq.	9.04E+01	71.06254	1.48E+01	1.07E+00	0.226824	4.52E-05	3.230447
Stratospheric ozone depletion	kg CFC11 eq.	9.06E-05	8.42E-05	3.65E-06	1.90E-06	2.71E-08	4.09E-11	8.17E-07
Ionizing radiation	kBq Co-60 eq.	4.581096	3.58E+00	7.98E-01	5.34E-02	0.00286	2.99E-06	0.15167
Ozone formation, Human health	kg NOx eq.	0.222266	1.68E-01	3.36E-02	1.35E-02	0.000488	1.07E-07	0.007067
Fine particulate matter formation	kg PM2.5 eq.	2.14E-01	1.36E-01	2.39E-02	4.62E-02	0.00026	1.17E-07	0.007991
Ozone formation, Terrestrial ecosystems	kg NOx eq.	2.32E-01	1.75E-01	3.55E-02	1.38E-02	0.000549	1.10E-07	0.007131
Terrestrial acidification	kg SO2 eq.	0.556006	3.38E-01	4.87E-02	1.59E-01	0.000714	2.92E-07	0.009979
Freshwater eutrophication	kg P eq.	0.041616	2.94E-02	7.63E-03	1.25E-03	5.64E-05	2.03E-08	0.003234
Marine eutrophication	kg N eq.	0.021205	1.83E-02	2.64E-03	5.07E-05	2.83E-06	1.57E-09	0.000203
Terrestrial ecotoxicity	kg 1,4-DCB	548.0043	4.82E+02	5.74E+01	4.98E+00	0.969244	0.000669	2.224816
Freshwater ecotoxicity	kg 1,4-DCB	7.000768	5.72E+00	0.678871	5.04E-01	0.008328	6.58E-06	0.09125
Marine ecotoxicity	kg 1,4-DCB	9.27E+00	7.60E+00	8.86E-01	6.40E-01	0.011029	8.61E-06	0.126061
Human carcinogenic toxicity	kg 1,4-DCB	5.67E+00	3.77E+00	1.53E+00	1.45E-01	0.007874	5.05E-06	0.205018
Human non-carcinogenic toxicity	kg 1,4-DCB	153.5025	1.13E+02	1.51E+01	2.08E+01	0.173308	0.00013	4.039131
Land use	m2a crop eq.	4.32E+00	3.93E+00	3.09E-01	3.03E-02	1.97E-03	1.12E-06	0.046078
Mineral resource scarcity	kg Cu eq.	7.07E-01	4.19E-01	1.06E-01	1.80E-01	6.11E-04	5.42E-07	0.001104
Fossil resource scarcity	kg oil eq.	28.7164	22.35341	5.08369	3.42E-01	0.130048	1.07E-05	0.807403
Water consumption	m3	2.391708	2.12E+00	2.44E-01	7.40E-03	1.43E-03	9.01E-05	0.01701

S Table 9e: Comparison of the Endpoint category of the NAR process for N-(4-ethoxy phenyl) acetamide synthesis

Damage category	Unit	Total	1-ethoxy-4-nitrobenzene	Ethyl acetate	Nickel	Titanium	Hydrogen gas	Energy
Human health	DALY	0.010723	7.47E-03	1.93E-04	6.51E-06	8.08E-08	0.000799	0.002253
Ecosystems	species.yr	7.17E-06	4.86E-06	1.36E-07	3.77E-09	7.11E-11	7.16E-07	1.45E-06
Resources	USD2013	23.40131	7.08E+00	5.20E-01	1.47E-03	0.000307	14.98101	0.821013

S Table 9f: Comparison of the Endpoint category of the AR process for N-(4-ethoxy phenyl) acetamide synthesis

Damage category	Unit	Total	1-ethoxy-4-nitrobenzene	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Human health	DALY	1.22E-02	7.42E-03	3.79E-03	6.82E-04	1.24E-05	7.76E-09	0.00028
Ecosystems	species.yr	7.28E-06	4.82E-06	1.95E-06	3.18E-07	9.48E-09	5.45E-12	1.80E-07
Resources	USD2013	10.7214	7.027292	3.43E+00	1.11E-01	0.049992	2.97E-06	0.101899

S Table 9g: Comparison of the End Point category of the Recycling process for N-(4-ethoxy phenyl) acetamide synthesis

Damage category	Unit	Total	1-ethoxy-4-nitrobenzen	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Human health	DALY	0.009639	7.42E-03	1.25E-03	0.000682	1.24E-05	7.76E-09	0.00028
Ecosystems	species.yr	6.07E-06	4.82E-06	7.37E-07	3.18E-07	9.48E-09	5.45E-12	1.80E-07
Resources	USD2013	8.83E+00	7.03E+00	1.54E+00	0.110701	5.00E-02	2.97E-06	0.101899

S Table 9h: Comparison of Normalization category of the NAR process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Total	1-ethoxy-4-nitrobenzene	Ethyl acetate	Nickel	Titanium	Hydrogen gas	Energy
Global warming	0.015971	0.008946	0.000392	6.75E-07	2.70E-07	0.003379	0.003254
Stratospheric ozone depletion	0.001654	0.001415	1.25E-05	1.07E-07	7.41E-09	0.000116	0.00011
Ionizing radiation	0.010759	0.00749	0.000273	7.96E-07	1.17E-07	0.000453	0.002542
Ozone formation, Human health	0.015082	0.008209	0.000391	1.29E-06	3.20E-07	0.003714	0.002767
Fine particulate matter formation	0.009477	0.005356	0.000173	3.91E-07	1.44E-07	0.00143	0.002517
Ozone formation, Terrestrial ecosystems	0.018859	0.009933	0.000497	1.54E-06	3.77E-07	0.005192	0.003235
Terrestrial acidification	0.013084	0.008295	0.000257	5.28E-07	2.21E-07	0.00257	0.001962
Freshwater eutrophication	0.089717	0.045674	0.002038	1.66E-05	6.67E-07	0.001862	0.040125
Marine eutrophication	0.004844	0.004002	1.78E-05	8.89E-08	8.31E-09	0.00047	0.000354
Terrestrial ecotoxicity	0.038121	0.031974	0.000684	3.51E-06	1.51E-07	0.00428	0.00118
Freshwater ecotoxicity	0.269907	0.228656	0.00467	0.000335	1.09E-06	0.007056	0.029188
Marine ecotoxicity	0.210888	0.176113	0.003558	0.000244	8.62E-07	0.007611	0.023361
Human carcinogenic toxicity	0.62314	0.368955	0.015777	0.000115	6.57E-06	0.077892	0.160395
Human non-carcinogenic toxicity	0.004965	0.003657	8.25E-05	3.13E-06	3.13E-08	0.000182	0.001041
Land use	0.000808	0.000642	1.17E-05	6.41E-08	1.42E-08	9.40E-05	6.01E-05
Mineral resource scarcity	4.02E-06	3.52E-06	7.77E-08	3.62E-08	6.95E-09	3.10E-07	7.41E-08
Fossil resource scarcity	0.065254	0.022963	0.001536	1.36E-06	5.47E-07	0.034117	0.006635
Water consumption	0.008976	0.008013	0.000166	6.81E-07	1.48E-08	0.000283	0.000514

S Table 9i: Comparison of Normalization category of the AR process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Total	1-ethoxy-4-nitrobenzene	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	1.39E-02	8.88E-03	4.41E-03	1.34E-04	2.84E-05	5.65E-09	0.000404
Stratospheric ozone depletion	1.61E-03	1.41E-03	1.59E-04	3.18E-05	4.53E-07	6.83E-10	1.37E-05
Ionizing radiation	0.012611	0.007437	0.004742	0.000111	5.95E-06	6.23E-09	0.000315
Ozone formation, Human health	0.013365	0.008151	0.004194	0.000654	2.37E-05	5.18E-09	0.000343
Fine particulate matter formation	0.009865	5.32E-03	0.002419	0.001805	1.02E-05	4.57E-09	0.000312
Ozone formation, Terrestrial ecosystems	0.016138	9.86E-03	5.07E-03	0.000776	3.09E-05	6.19E-09	0.000401
Terrestrial acidification	0.01565	0.008236	0.003273	0.003881	1.74E-05	7.13E-09	0.000243
Freshwater eutrophication	0.076799	0.04535	0.02446	1.92E-03	8.69E-05	3.12E-08	0.00498
Marine eutrophication	5.12E-03	0.003973	1.09E-03	1.10E-05	6.14E-07	3.42E-10	4.40E-05
Terrestrial ecotoxicity	4.48E-02	3.17E-02	1.25E-02	0.000328	6.38E-05	4.41E-08	0.000146
Freshwater ecotoxicity	0.333285	0.227035	0.082306	0.019991	3.31E-04	2.61E-07	0.003623
Marine ecotoxicity	0.255389	0.174864	0.06266	0.014712	2.54E-04	1.98E-07	0.002899
Human carcinogenic toxicity	0.960044	0.366338	0.558913	0.014121	7.65E-04	4.90E-07	0.019907
Human non-carcinogenic toxicity	0.005795	0.003631	0.001366	0.000664	5.55E-06	4.17E-09	0.000129
Land use	0.000798	6.37E-04	0.000148	4.91E-06	3.20E-07	1.82E-10	7.46E-06
Mineral resource scarcity	8.72E-06	3.49E-06	3.72E-06	1.50E-06	5.09E-09	4.52E-12	9.19E-09
Fossil resource scarcity	0.035631	0.0228	0.011526	0.000349	1.33E-04	1.09E-08	0.000824
Water consumption	0.009937	0.007956	0.001883	2.77E-05	5.36E-06	3.38E-07	6.38E-05

S Table 9j: Comparison of Normalization category of the Recycling process for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Total	1-ethoxy-4-nitrobenzene	2-acetyl-1,1-dioxo-1,2-benzothiazol-3-one	Palladium	Isopropanol	Water	Energy
Global warming	0.011295	8.88E-03	1.85E-03	0.000134	2.84E-05	5.65E-09	0.000404
Stratospheric ozone depletion	1.51E-03	1.41E-03	6.10E-05	3.18E-05	4.53E-07	6.83E-10	1.37E-05
Ionizing radiation	9.53E-03	0.007437	1.66E-03	1.11E-04	5.95E-06	6.23E-09	0.000315
Ozone formation, Human health	0.010802	0.008151	1.63E-03	6.54E-04	2.37E-05	5.18E-09	0.000343
Fine particulate matter formation	0.008379	5.32E-03	9.34E-04	1.81E-03	1.02E-05	4.57E-09	0.000312
Ozone formation, Terrestrial ecosystems	0.013069	9.86E-03	2.00E-03	7.76E-04	3.09E-05	6.19E-09	0.000401
Terrestrial acidification	1.36E-02	0.008236	1.19E-03	3.88E-03	1.74E-05	7.13E-09	0.000243
Freshwater eutrophication	0.064088	0.04535	1.17E-02	1.92E-03	8.69E-05	3.12E-08	0.00498
Marine eutrophication	0.004602	0.003973	5.73E-04	1.10E-05	6.14E-07	3.42E-10	4.40E-05
Terrestrial ecotoxicity	0.036059	0.031747	3.77E-03	3.28E-04	6.38E-05	4.41E-08	0.000146
Freshwater ecotoxicity	0.27793	0.227035	2.70E-02	2.00E-02	0.000331	2.61E-07	0.003623
Marine ecotoxicity	2.13E-01	1.75E-01	2.04E-02	1.47E-02	2.54E-04	1.98E-07	0.002899
Human carcinogenic toxicity	5.50E-01	3.66E-01	1.49E-01	1.41E-02	7.65E-04	4.90E-07	0.019907
Human non-carcinogenic toxicity	0.004912	0.003631	4.83E-04	6.64E-04	5.55E-06	4.17E-09	0.000129
Land use	0.0007	6.37E-04	5.01E-05	4.91E-06	3.20E-07	1.82E-10	7.46E-06
Mineral resource scarcity	5.89E-06	3.49E-06	8.85E-07	1.50E-06	5.09E-09	4.52E-12	9.19E-09
Fossil resource scarcity	0.029291	0.0228	0.005185	0.000349	0.000133	1.09E-08	0.000824
Water consumption	0.008969	0.007956	0.000915	2.77E-05	5.36E-06	3.38E-07	6.38E-05

S Table 9k: Comparison of the Midpoint category for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	NAR	AR	Recycling
Global warming	0.015971	0.013859	0.011295
Stratospheric ozone depletion	0.001654	0.00161	0.001512
Ionizing radiation	1.08E-02	1.26E-02	9.53E-03
Ozone formation, Human health	0.015082	0.013365	0.010802
Fine particulate matter formation	0.009477	0.009865	0.008379
Ozone formation, Terrestrial ecosystems	0.018859	0.016138	0.013069
Terrestrial acidification	0.013084	0.01565	0.013567
Freshwater eutrophication	8.97E-02	0.076799	0.064088
Marine eutrophication	0.004844	0.00512	0.004602
Terrestrial ecotoxicity	3.81E-02	0.044752	0.036059
Freshwater ecotoxicity	0.269907	0.333285	0.27793
Marine ecotoxicity	0.210888	0.255389	0.213099
Human carcinogenic toxicity	6.23E-01	9.60E-01	0.550102
Human non-carcinogenic toxicity	0.004965	0.005795	0.004912
Land use	0.000808	0.000798	0.0007
Mineral resource scarcity	4.02E-06	8.72E-06	5.89E-06
Fossil resource scarcity	0.065254	0.035631	0.029291
Water consumption	8.98E-03	0.009937	0.008969

S Table 9l: Comparison of the Endpoint category for N-(4-ethoxy phenyl) acetamide synthesis

Damage category	Unit	NAR	AR	Recycling
Human health	DALY	1.07E-02	1.22E-02	0.009639
Ecosystems	species.yr	7.17E-06	7.28E-06	6.07E-06
Resources	USD2013	2.34E+01	1.07E+01	8.83E+00

S Table 9m: Comparison of Normalization category for N-(4-ethoxy phenyl) acetamide synthesis

Impact category	Unit	NAR	AR	Recycling
Global warming	kg CO2 eq.	127.7717	110.8705	90.36329
Stratospheric ozone depletion	kg CFC11 eq.	9.91E-05	9.64E-05	9.06E-05
Ionizing radiation	kBq Co-60 eq.	5.172624	6.06322	4.581096
Ozone formation, Human health	kg NOx eq.	0.31033	0.275009	0.222266
Fine particulate matter formation	kg PM2.5 eq.	0.24237	0.252299	0.2143
Ozone formation, Terrestrial ecosystems	kg NOx eq.	0.33497	0.286641	0.232138
Terrestrial acidification	kg SO2 eq.	0.536232	0.641399	0.556006
Freshwater eutrophication	kg P eq.	5.83E-02	4.99E-02	0.041616
Marine eutrophication	kg N eq.	0.022321	0.023595	0.021205
Terrestrial ecotoxicity	kg 1,4-DCB	579.3488	680.1273	548.0043
Freshwater ecotoxicity	kg 1,4-DCB	6.798654	8.395085	7.000768
Marine ecotoxicity	kg 1,4-DCB	9.169044	11.10387	9.265157
Human carcinogenic toxicity	kg 1,4-DCB	6.417509	9.887171	5.665312
Human non-carcinogenic toxicity	kg 1,4-DCB	155.169	181.0979	153.5025
Land use	m2a crop eq.	4.985821	4.923741	4.321242
Mineral resource scarcity	kg Cu eq.	0.482634	1.047229	0.706747
Fossil resource scarcity	kg oil eq.	63.9743	34.93251	28.7164
Water consumption	m3	2.39E+00	2.65E+00	2.391708

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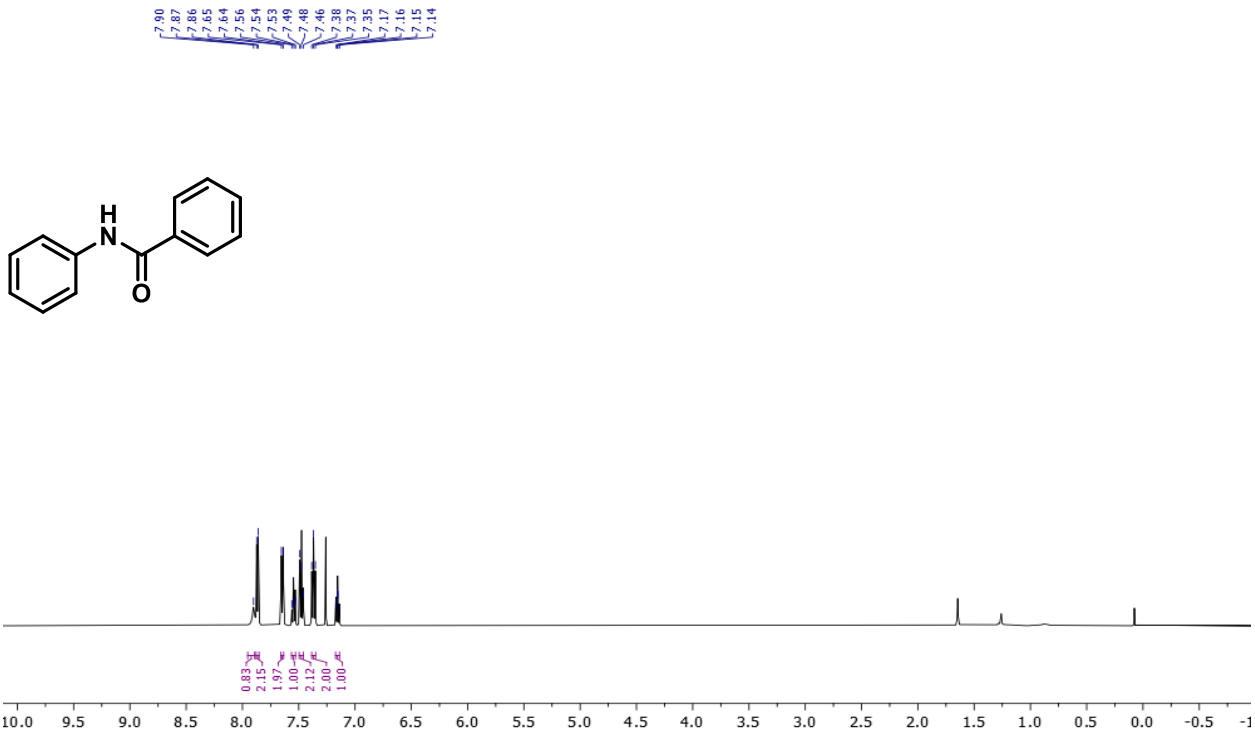
Spectral Data

(^{1}H-NMR and ^{13}C-NMR)

^{1}H NMR of Compound 3a ($CDCl_3$; 500 MHz)



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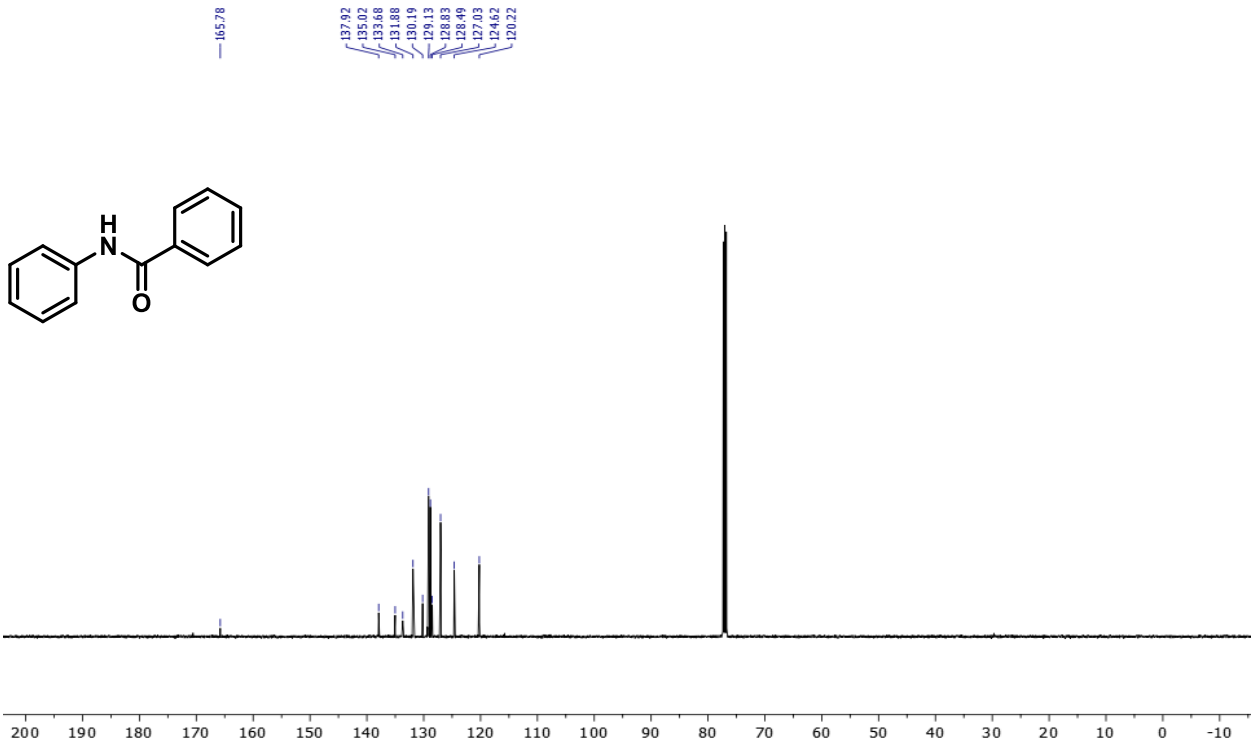

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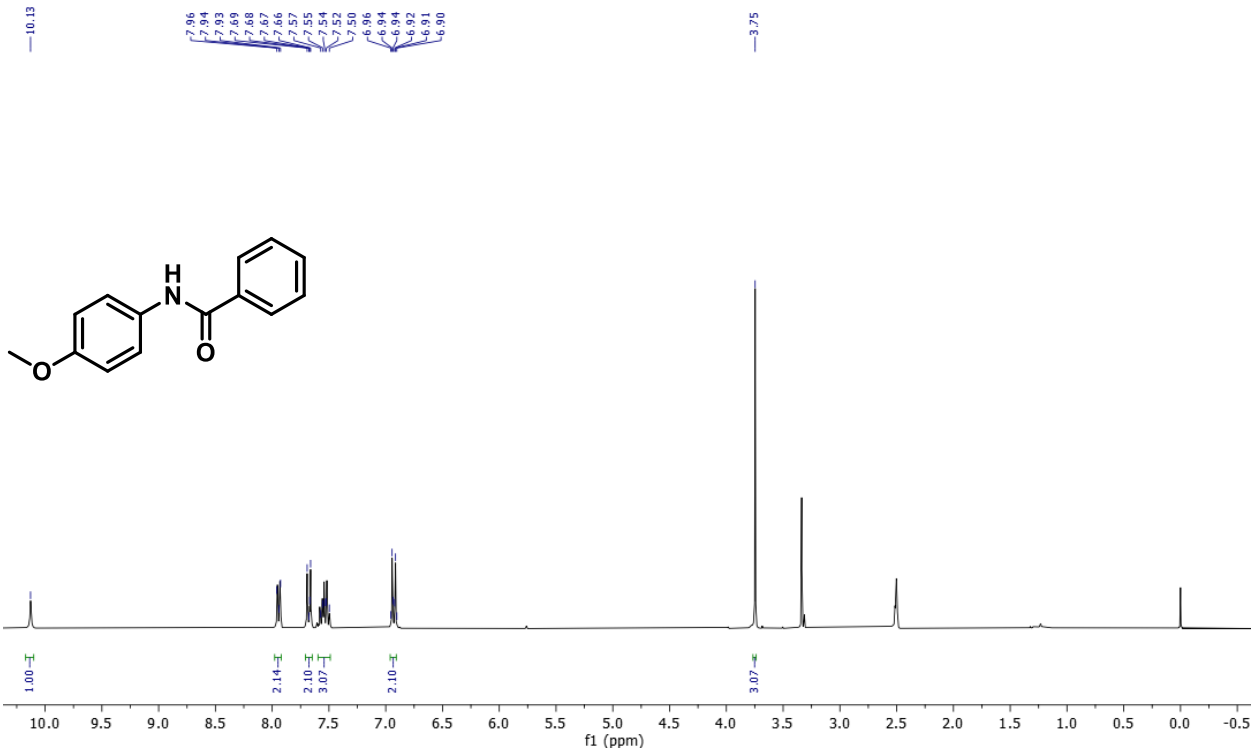

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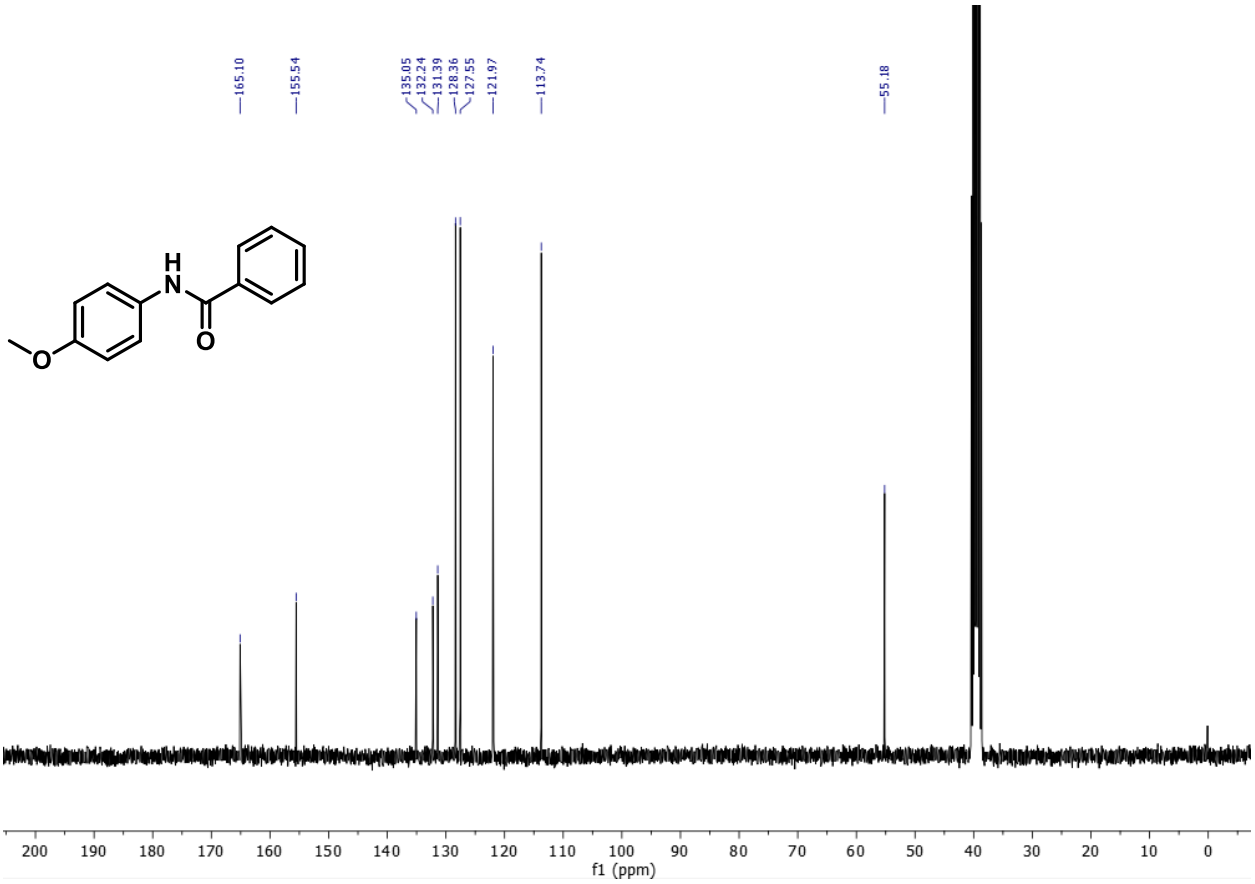

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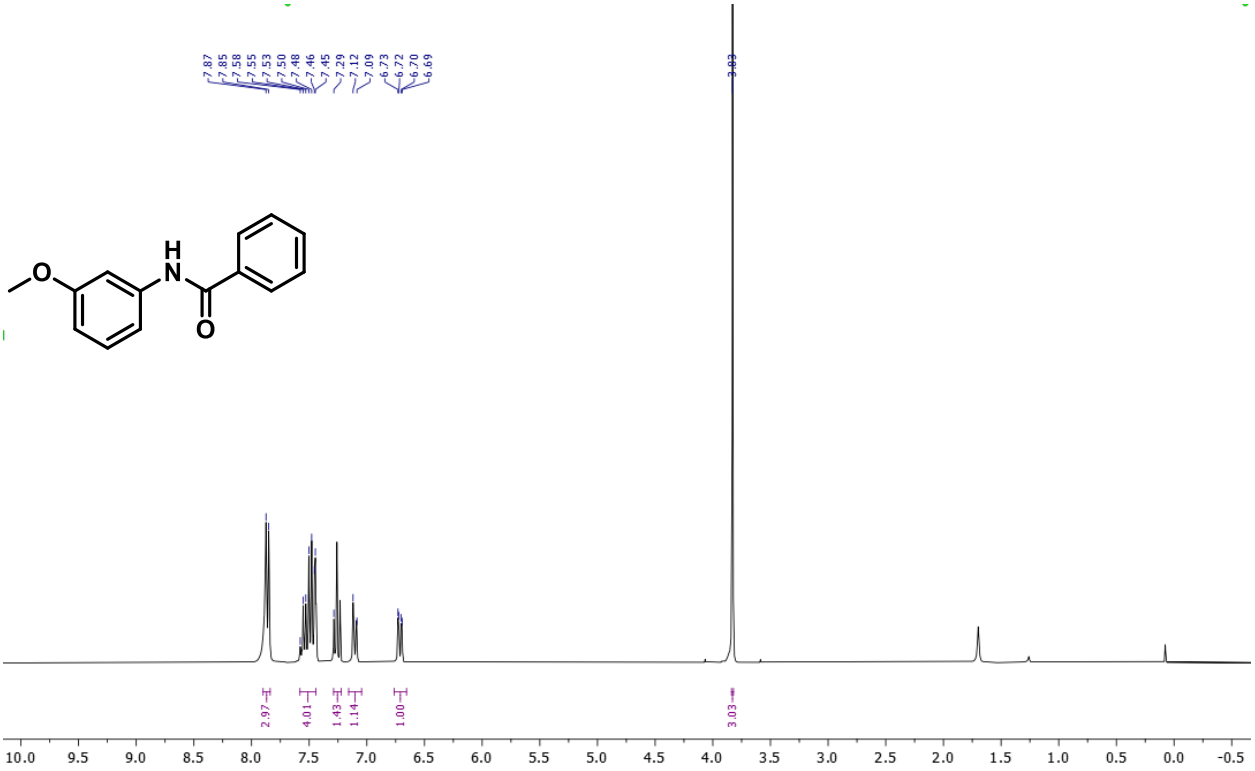

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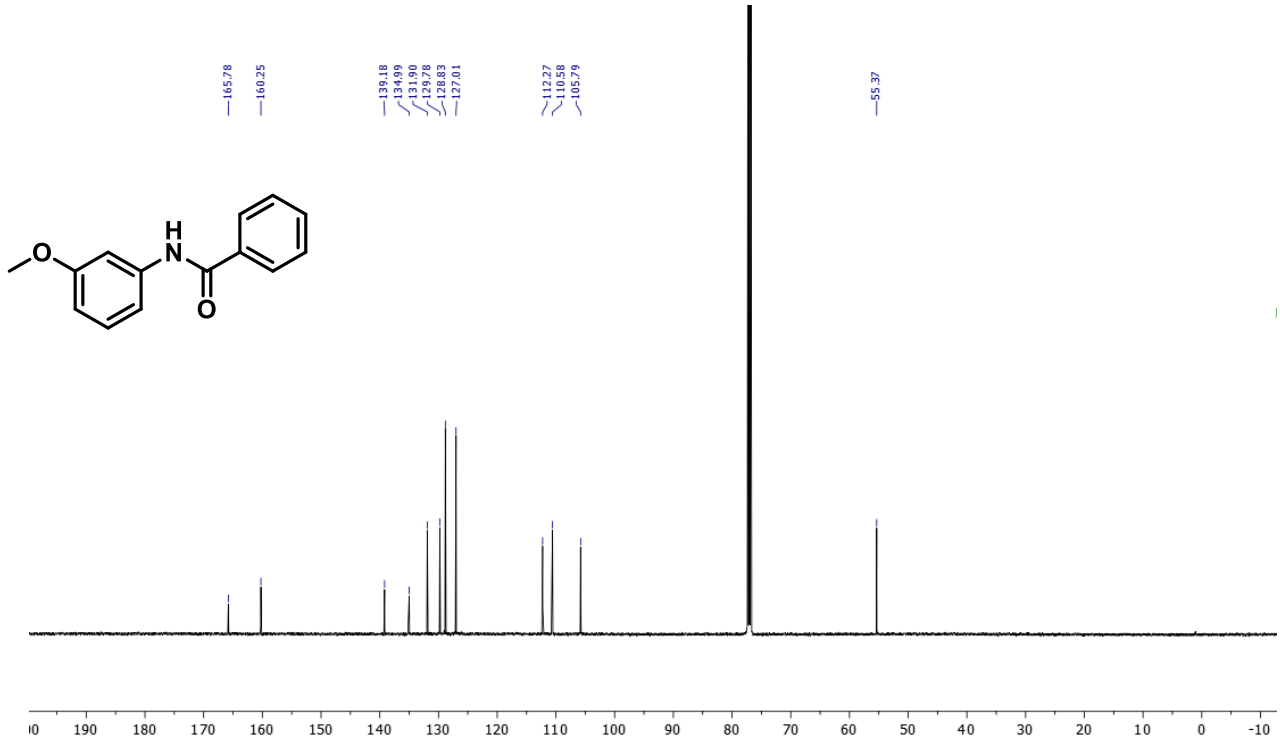
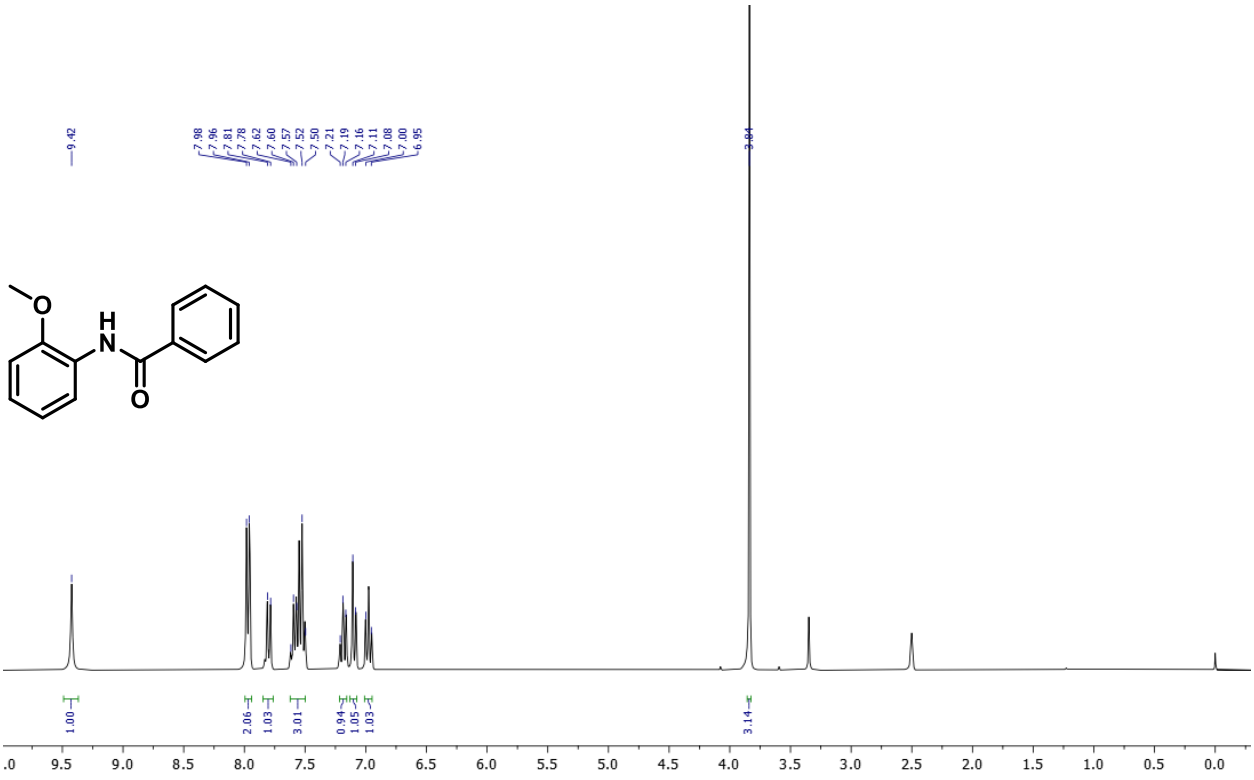


^{1}H NMR of Compound 3d (DMSO d_6; 300 MHz)



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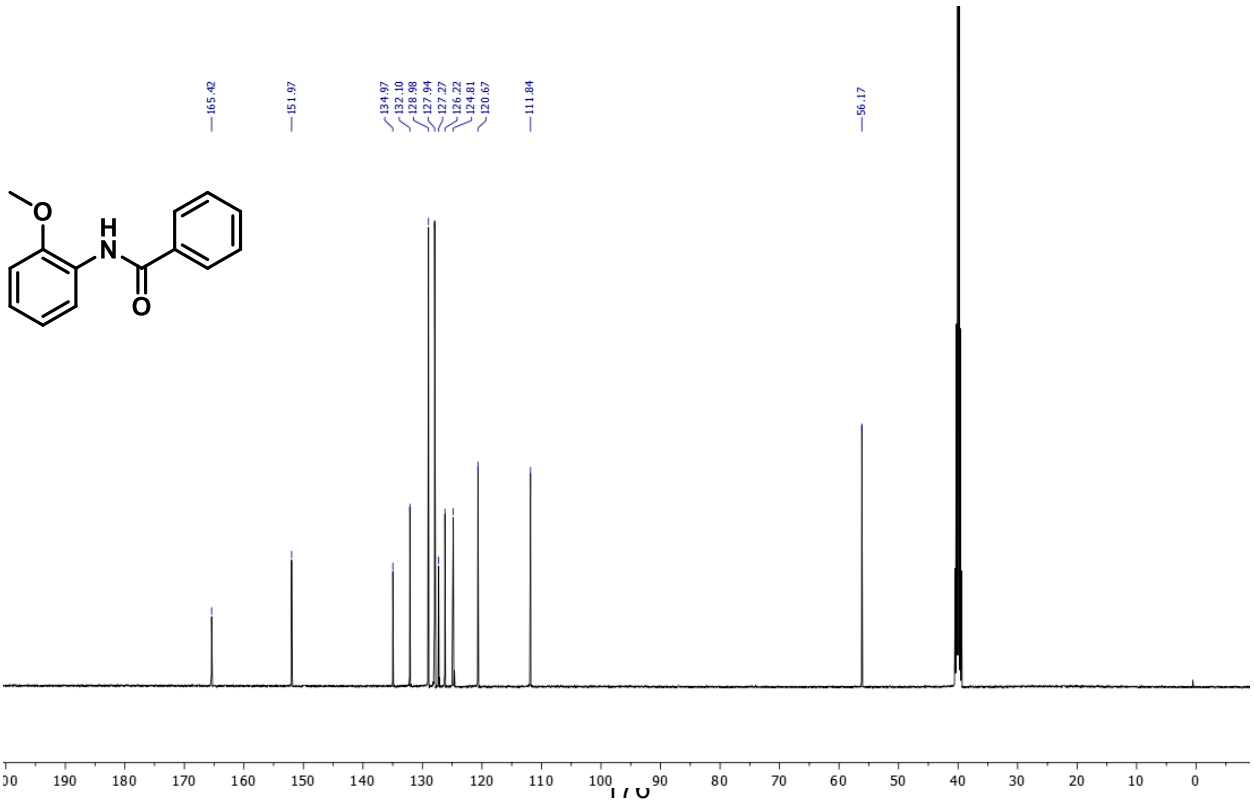
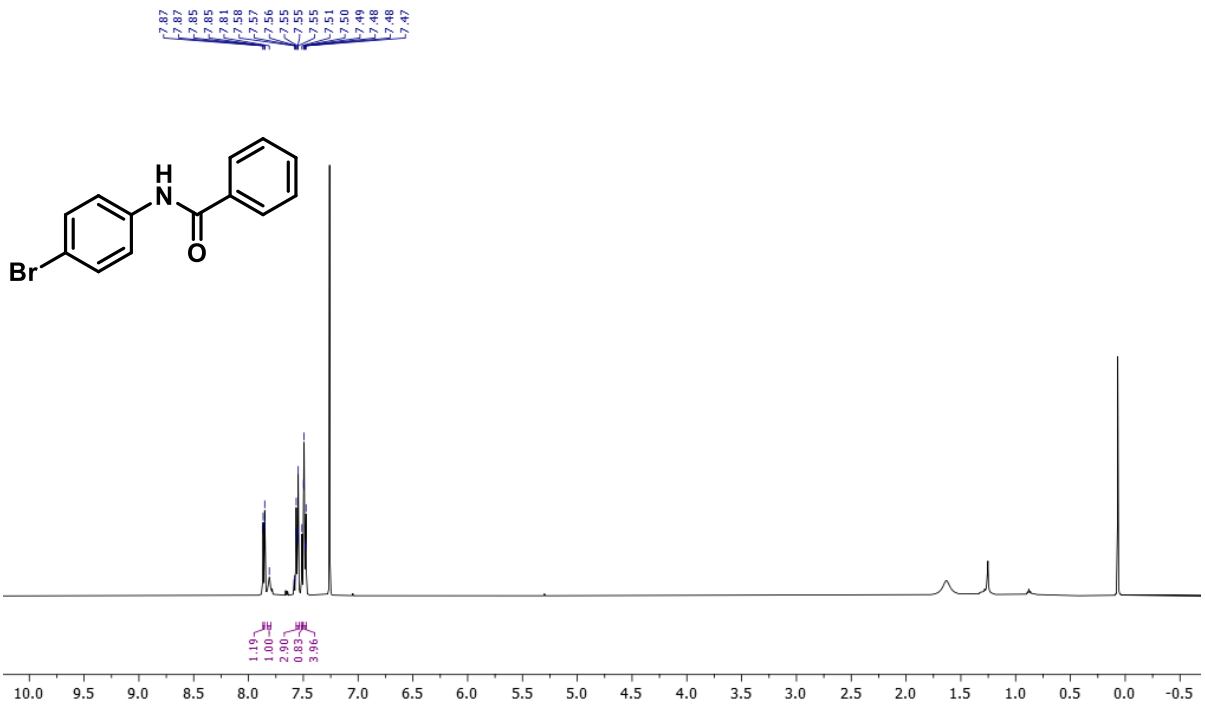
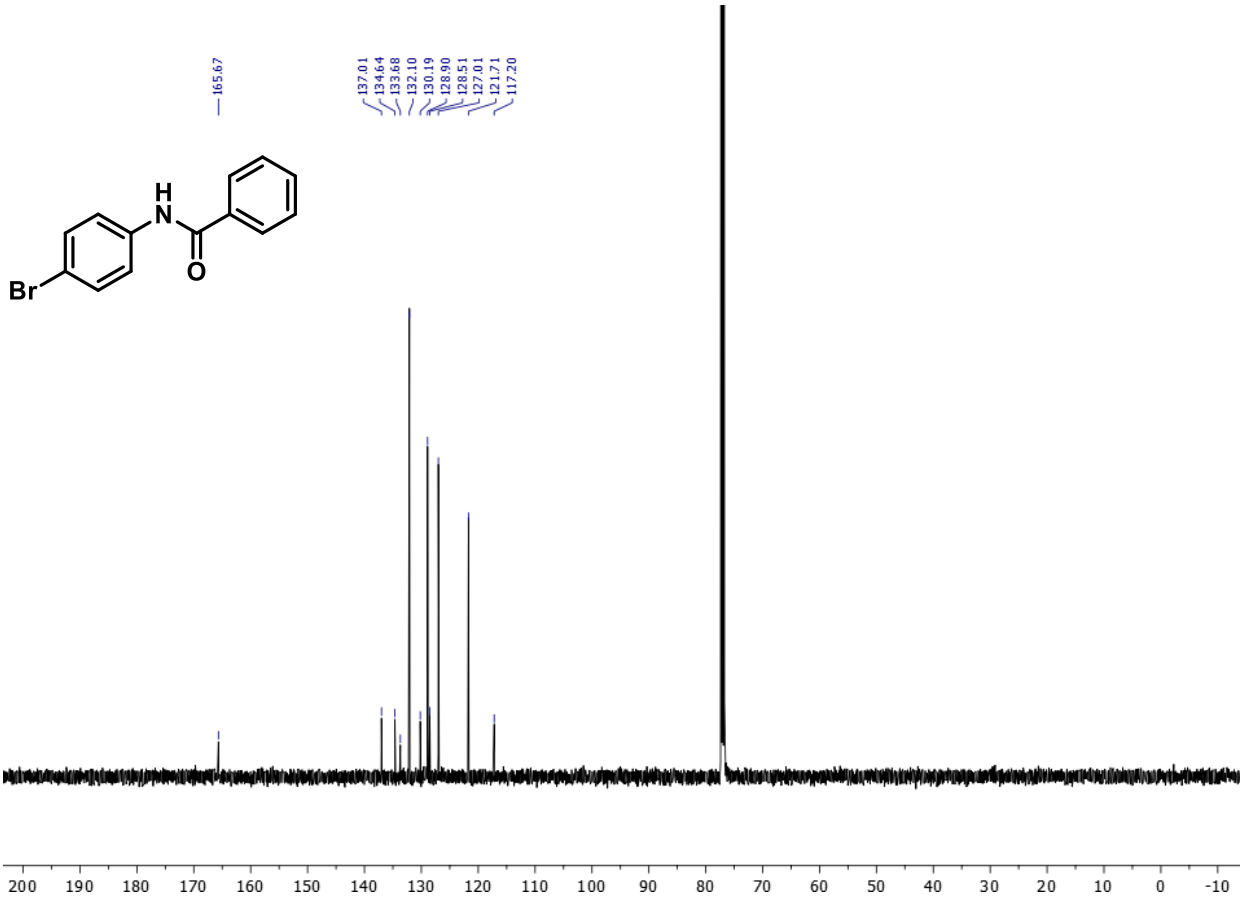


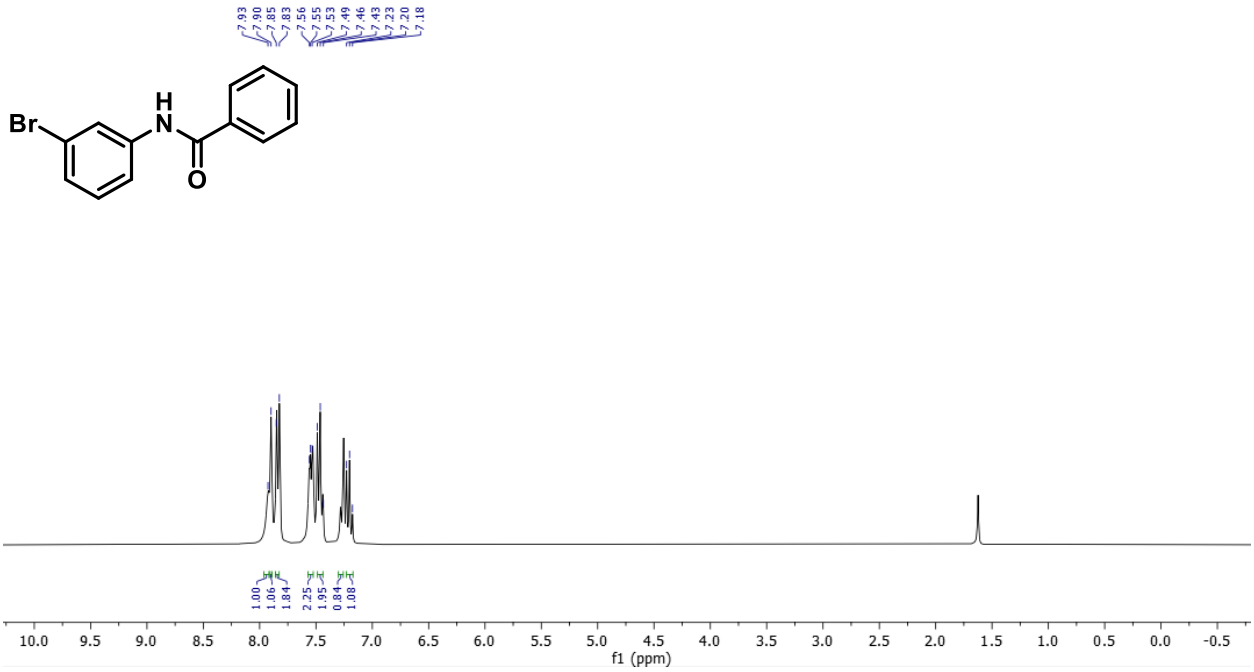
^{1}H NMR of Compound 3e ($CDCl_3$; 500 MHz)



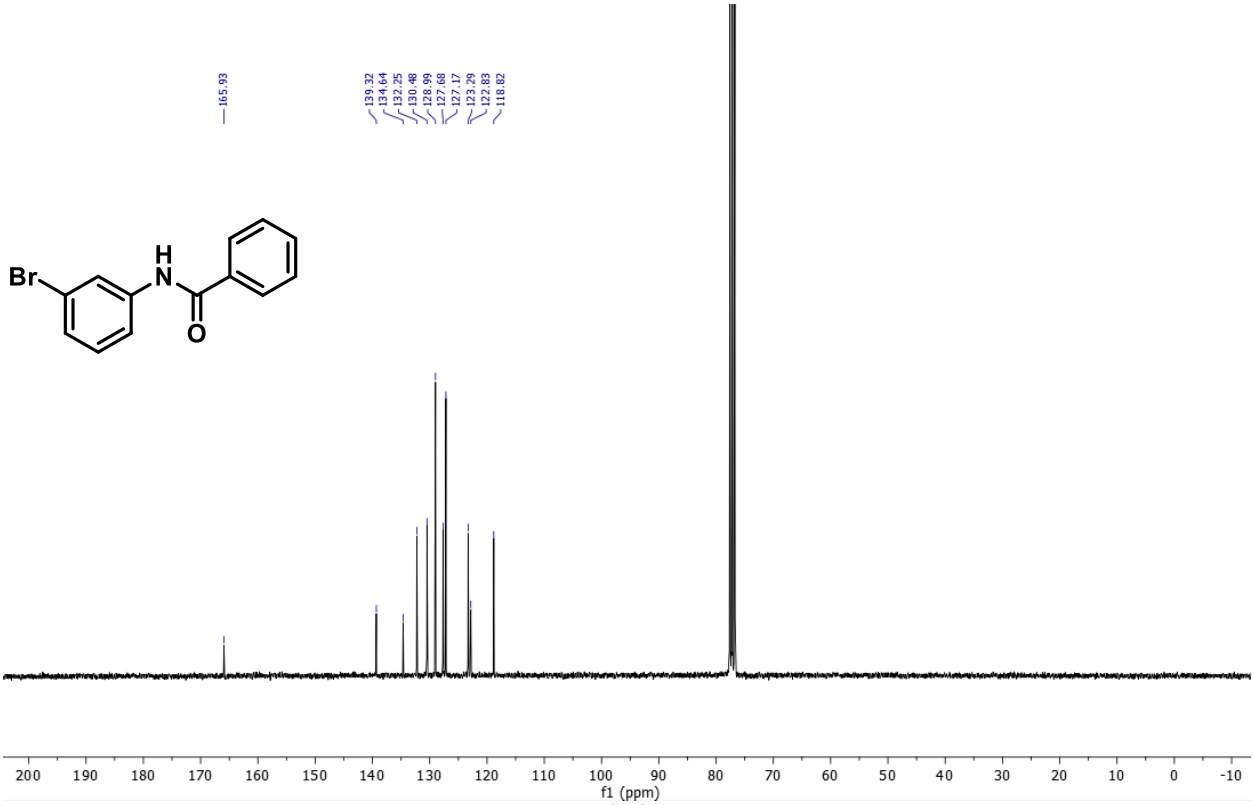
^{13}C NMR of Compound 3e ($CDCl_3$; 125 MHz)



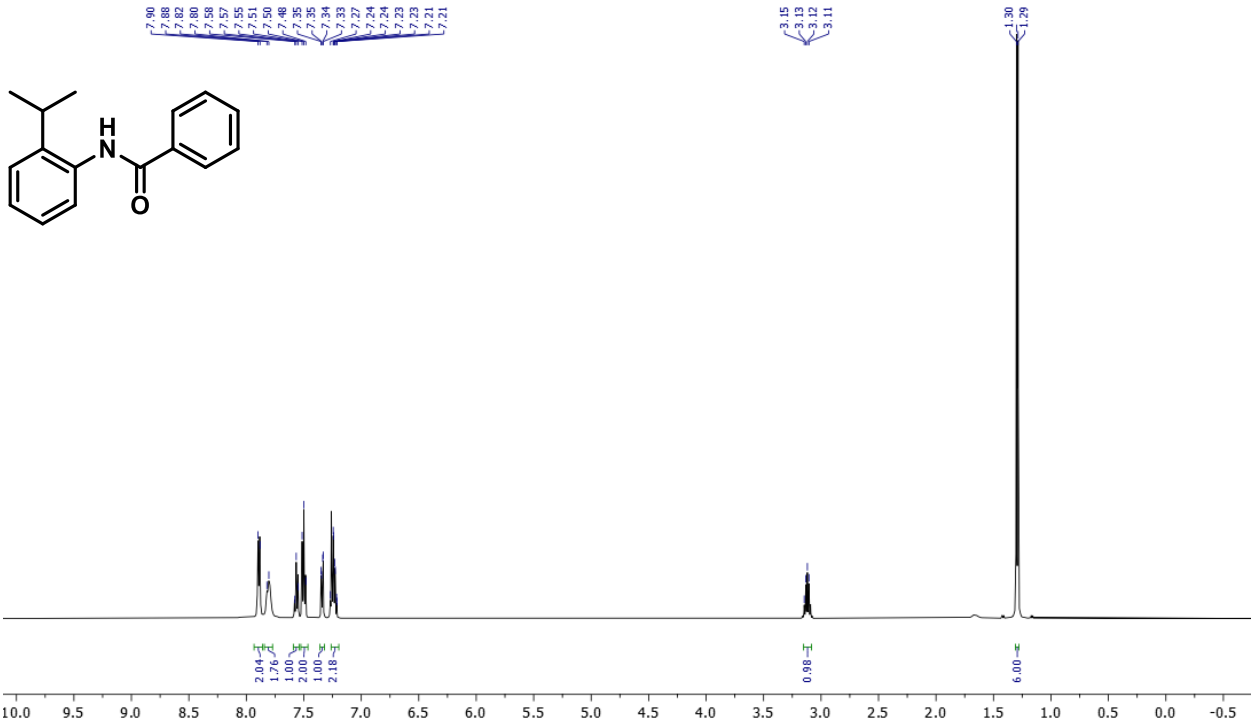
NMR of Compound 3f ($CDCl_3$; 300 MHz)



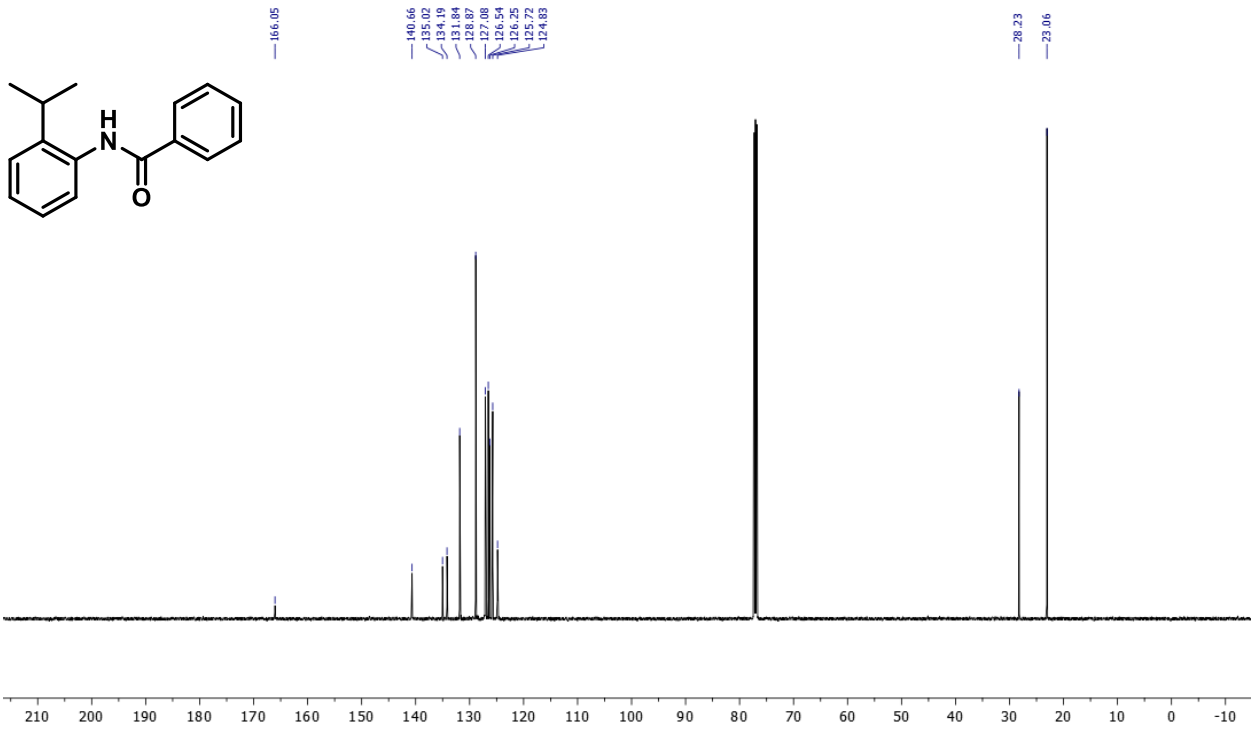
^{13}C NMR of Compound 3f ($CDCl_3$; 75 MHz)



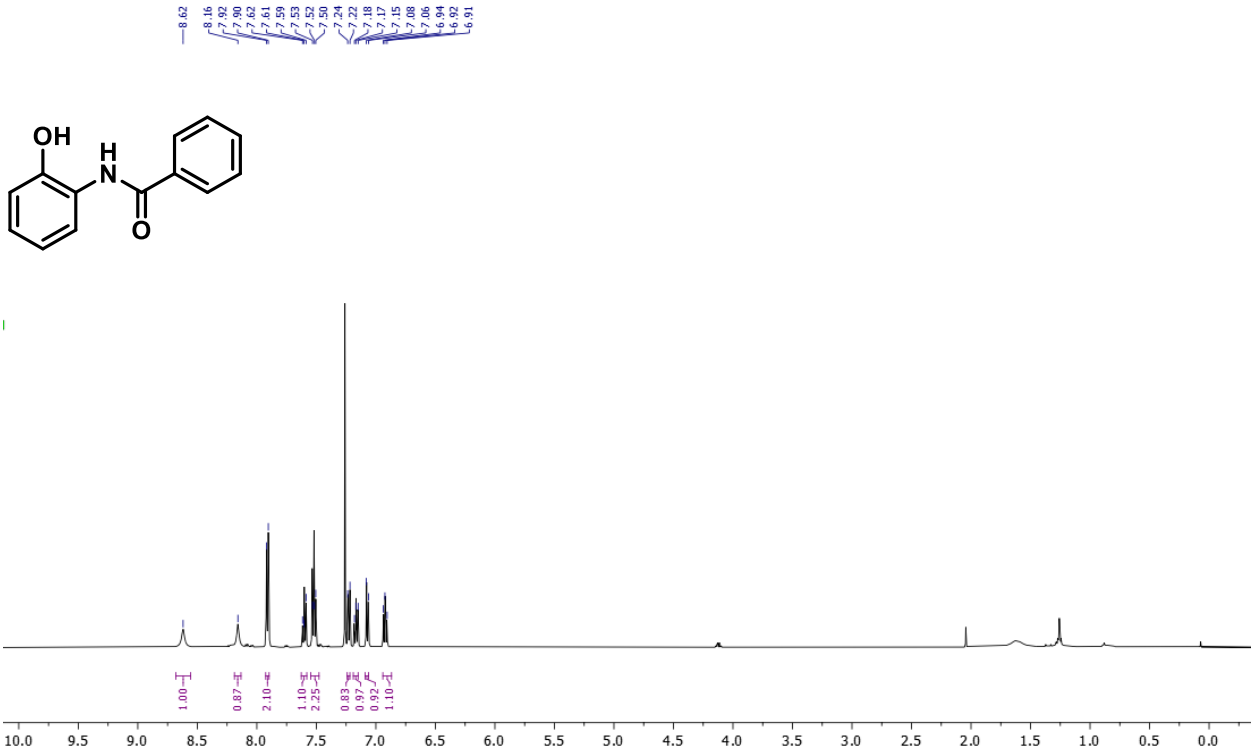
^{1}H NMR of Compound 3g ($CDCl_3$; 300 MHz)



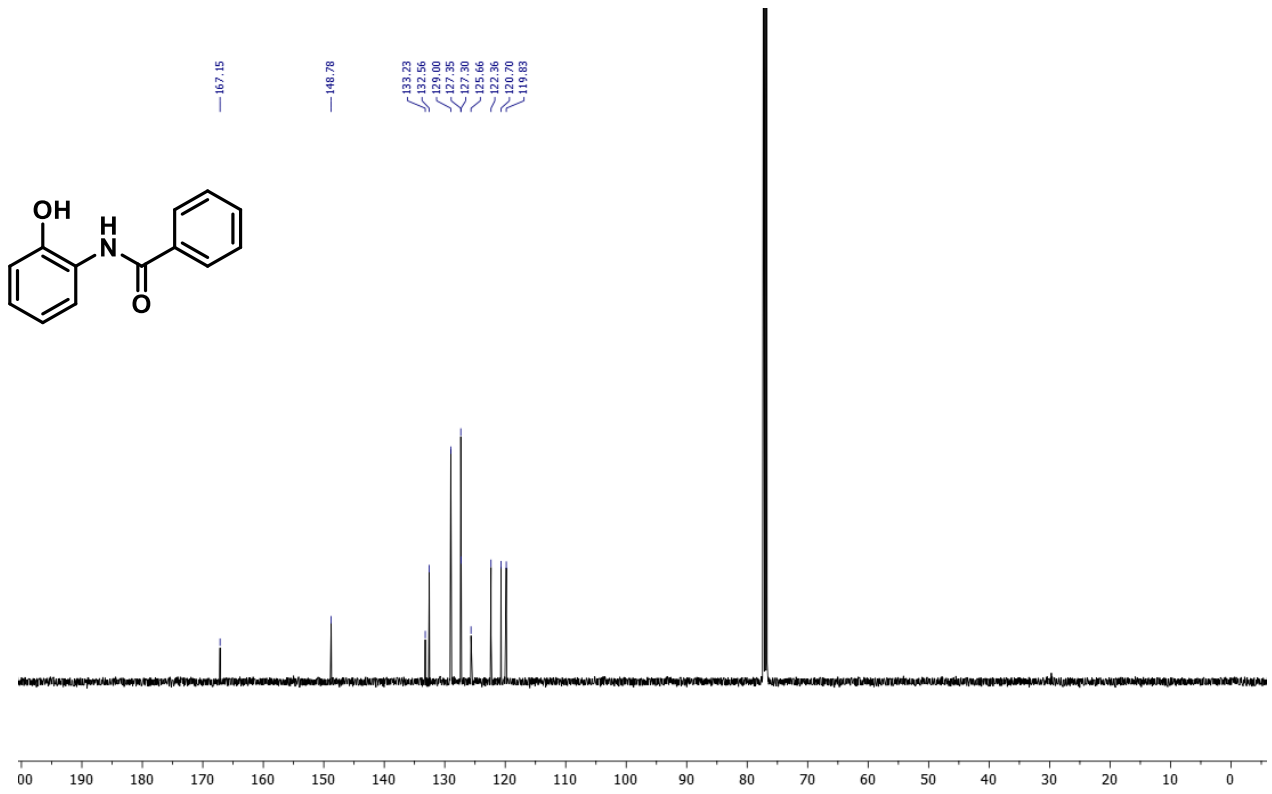
^{13}C NMR of Compound 3g ($CDCl_3$; 75 MHz)



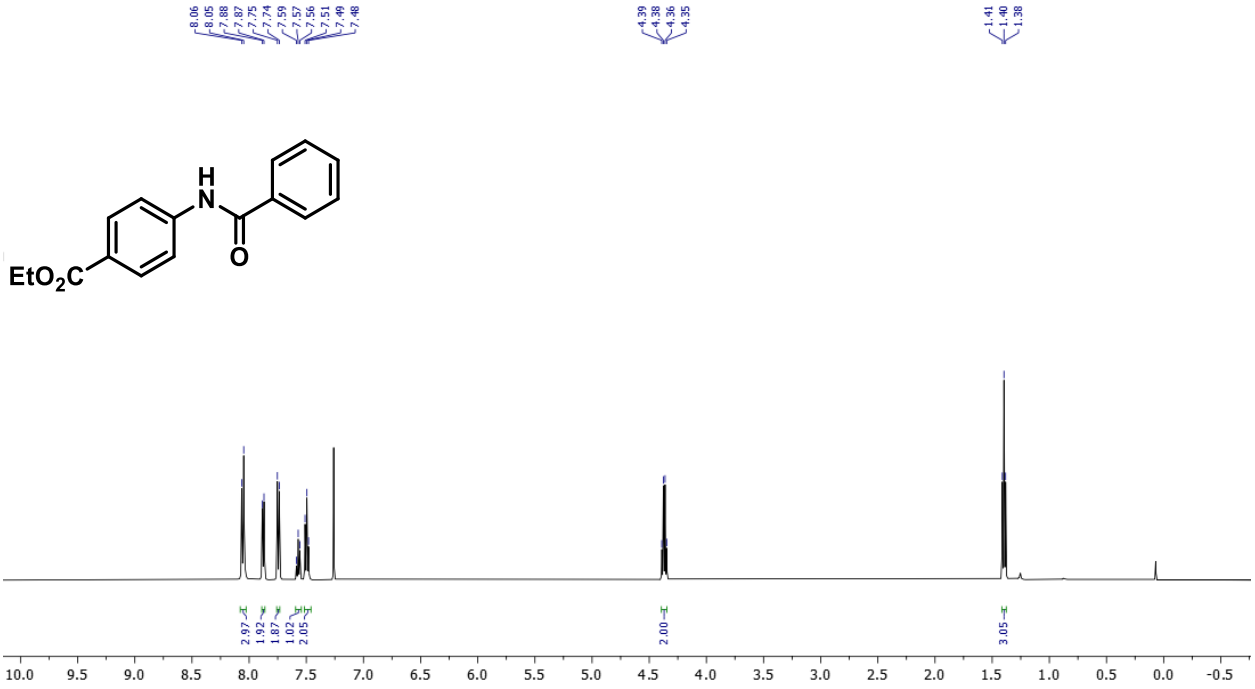
^{1}H NMR of Compound 3h ($CDCl_3$; 500 MHz)



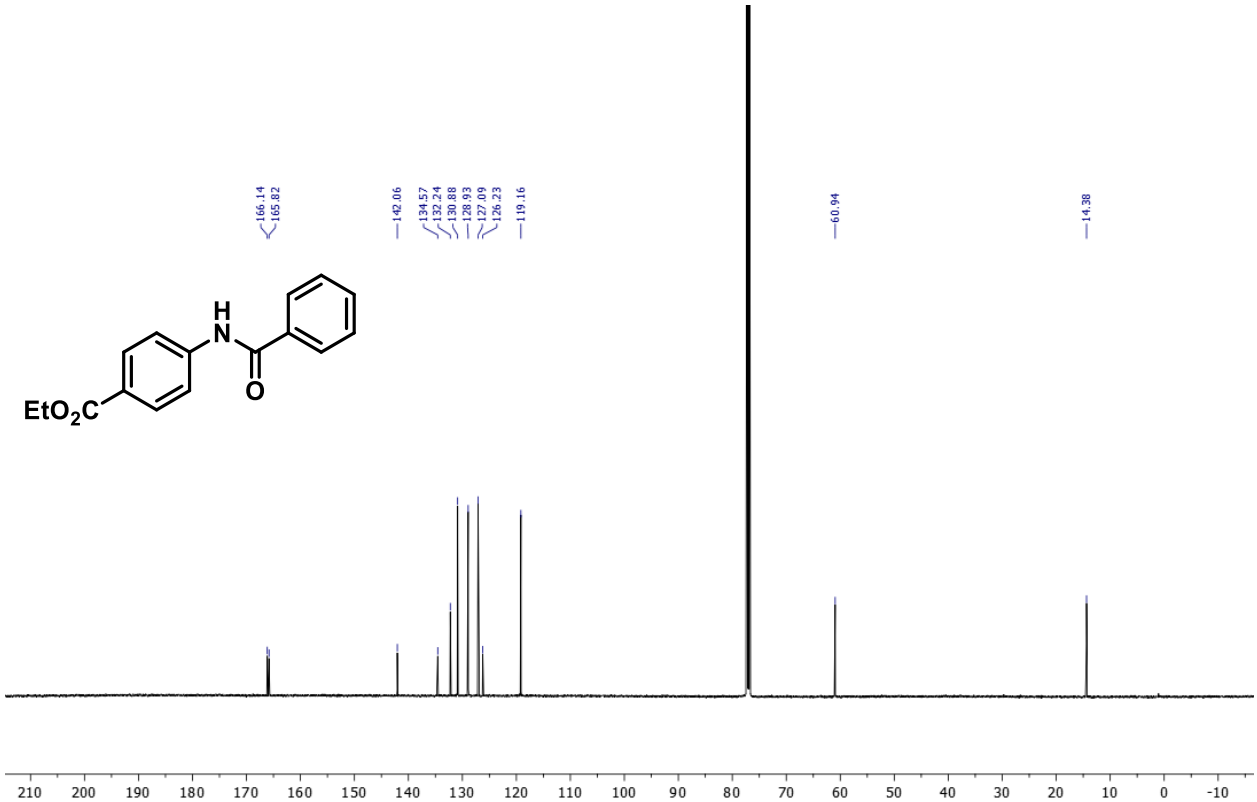
^{13}C NMR of Compound 3h ($CDCl_3$; 125 MHz)



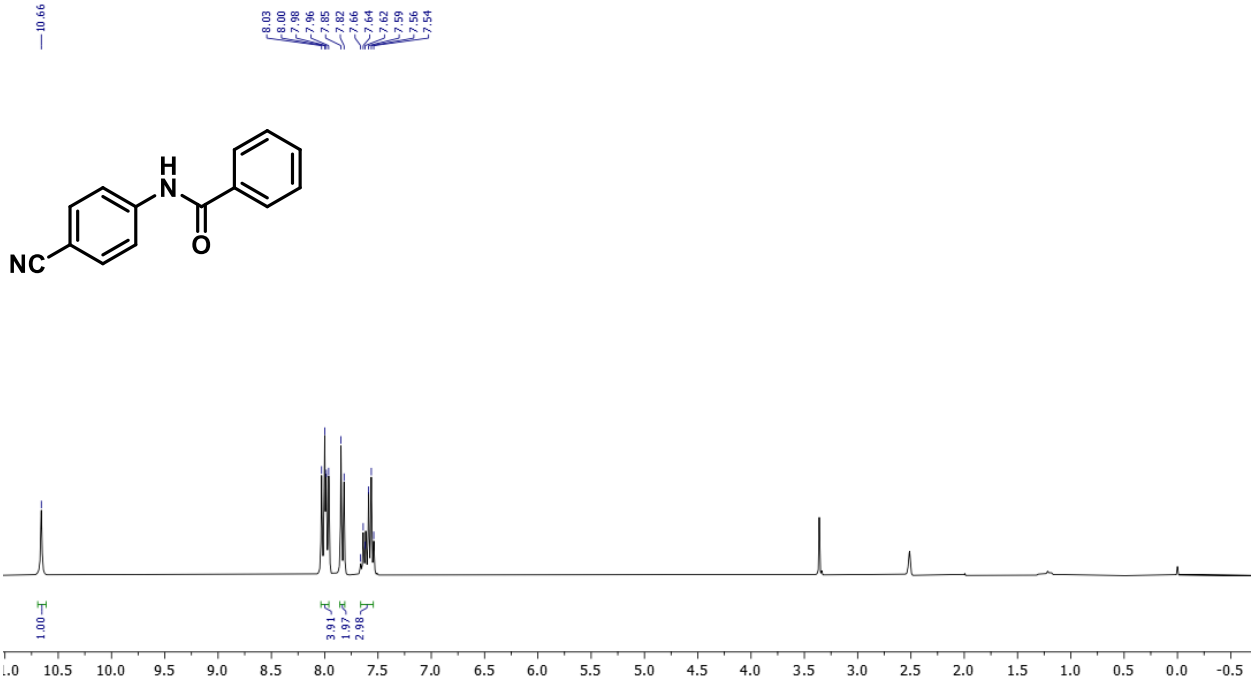
^{1}H NMR of Compound 3i ($CDCl_3$; 500 MHz)



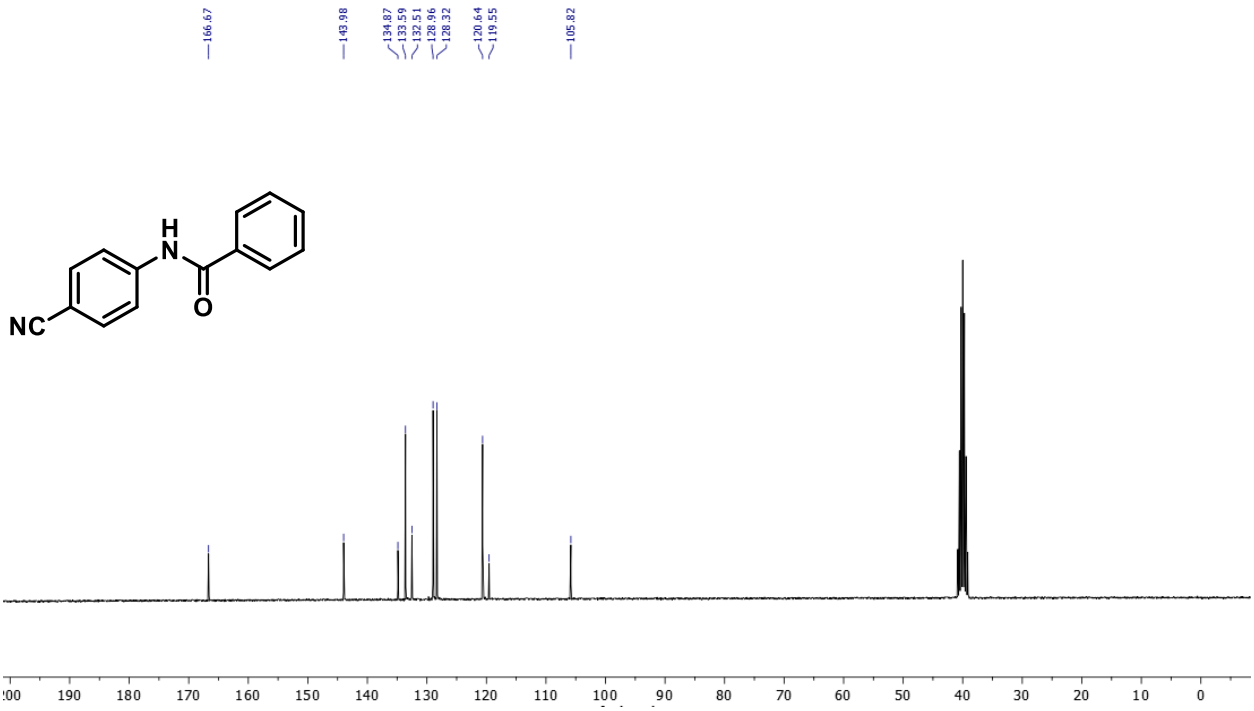
^{13}C NMR of Compound 3i ($CDCl_3$; 75 MHz)



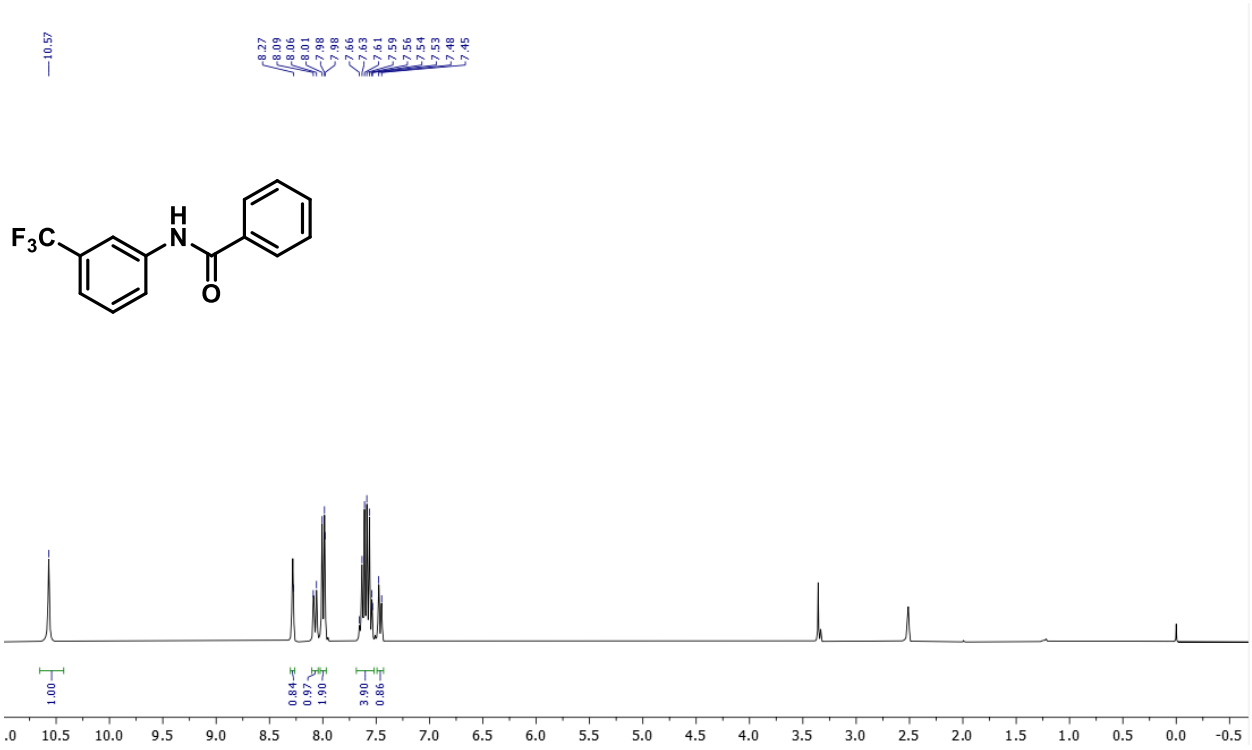
^{1}H NMR of Compound 3j (DMSO d_6; 300 MHz)



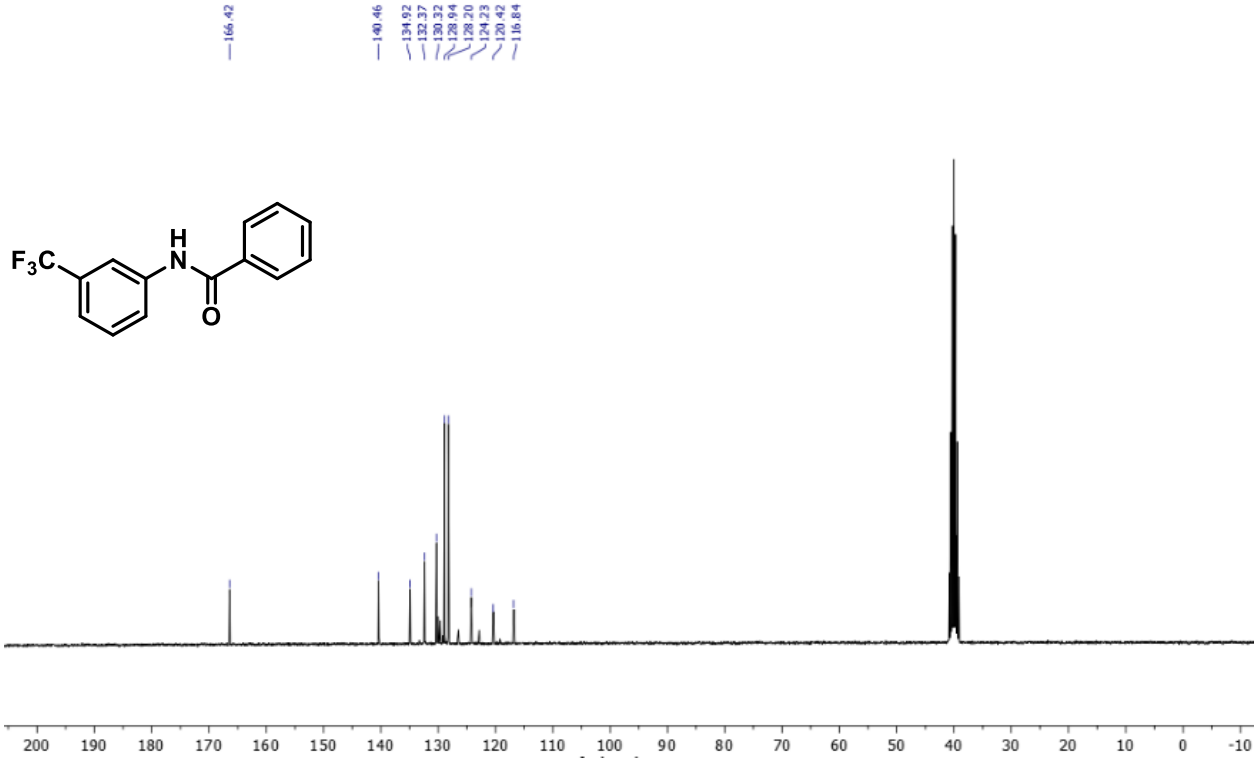
^{13}C NMR of Compound 3j (DMSO d_6; 75 MHz)



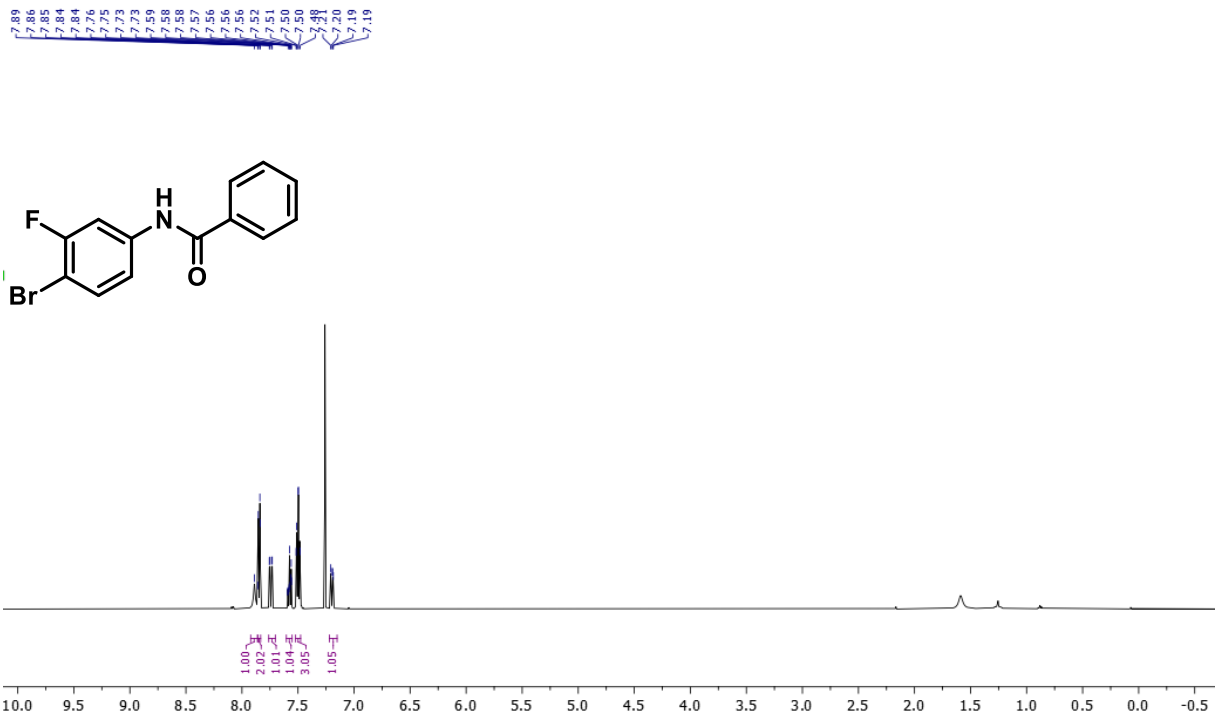
^{1}H NMR of Compound 3k (DMSO d_6; 300 MHz)



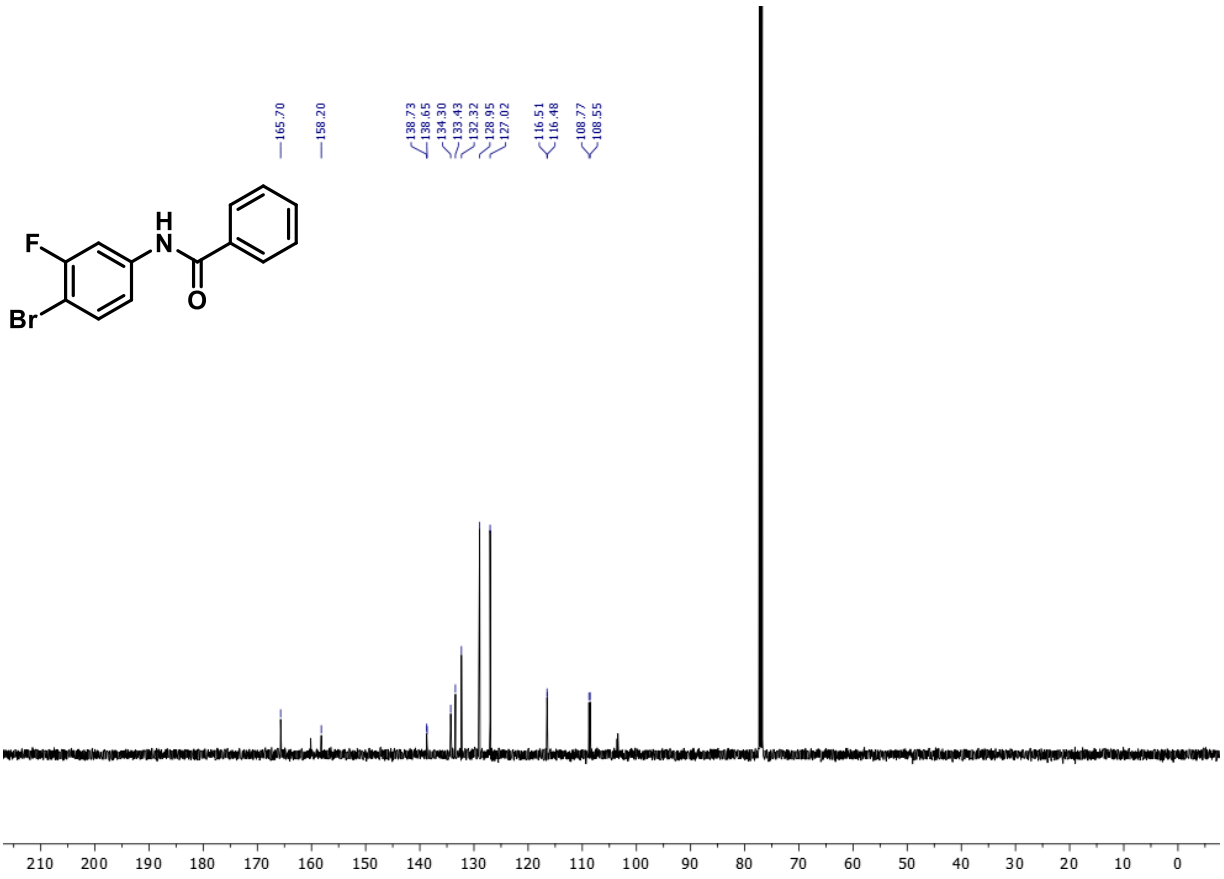
^{13}C NMR of Compound 3k (DMSO d_6; 75 MHz)



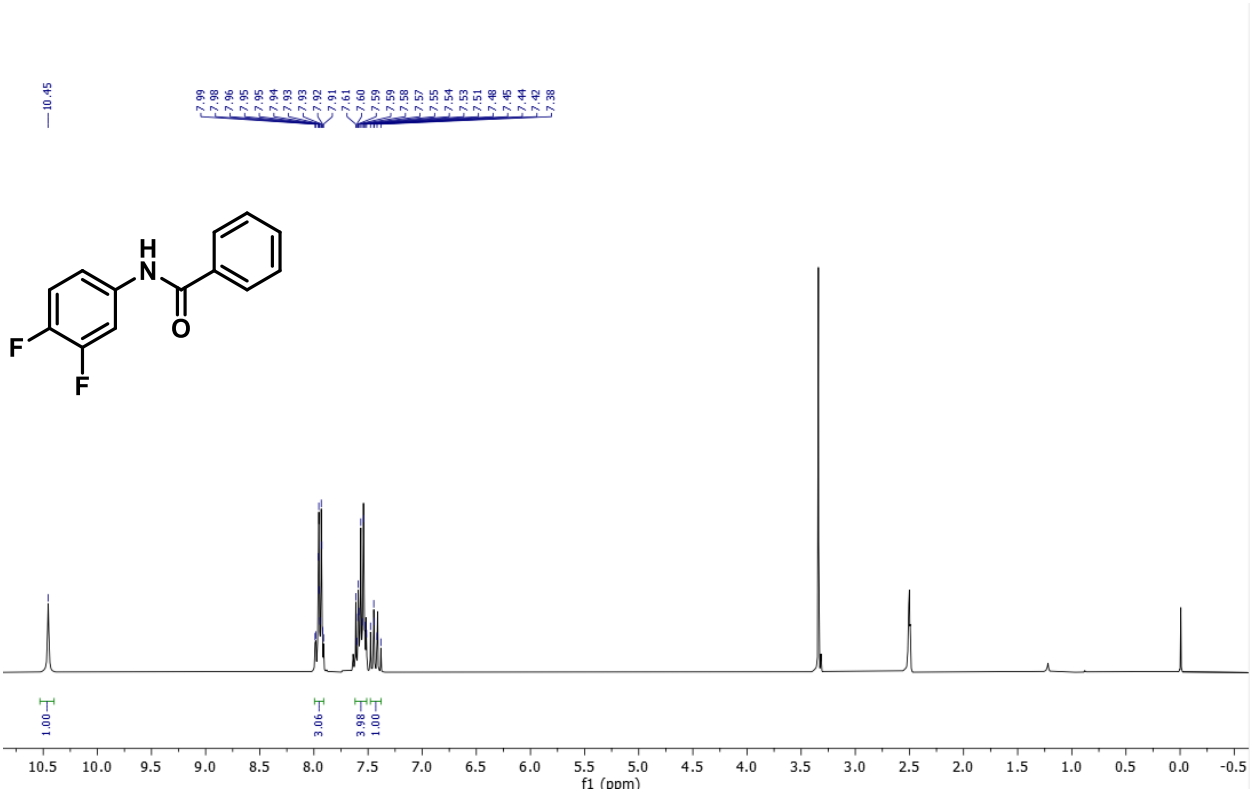
^{1}H NMR of Compound 3l ($CDCl_3$; 500 MHz)



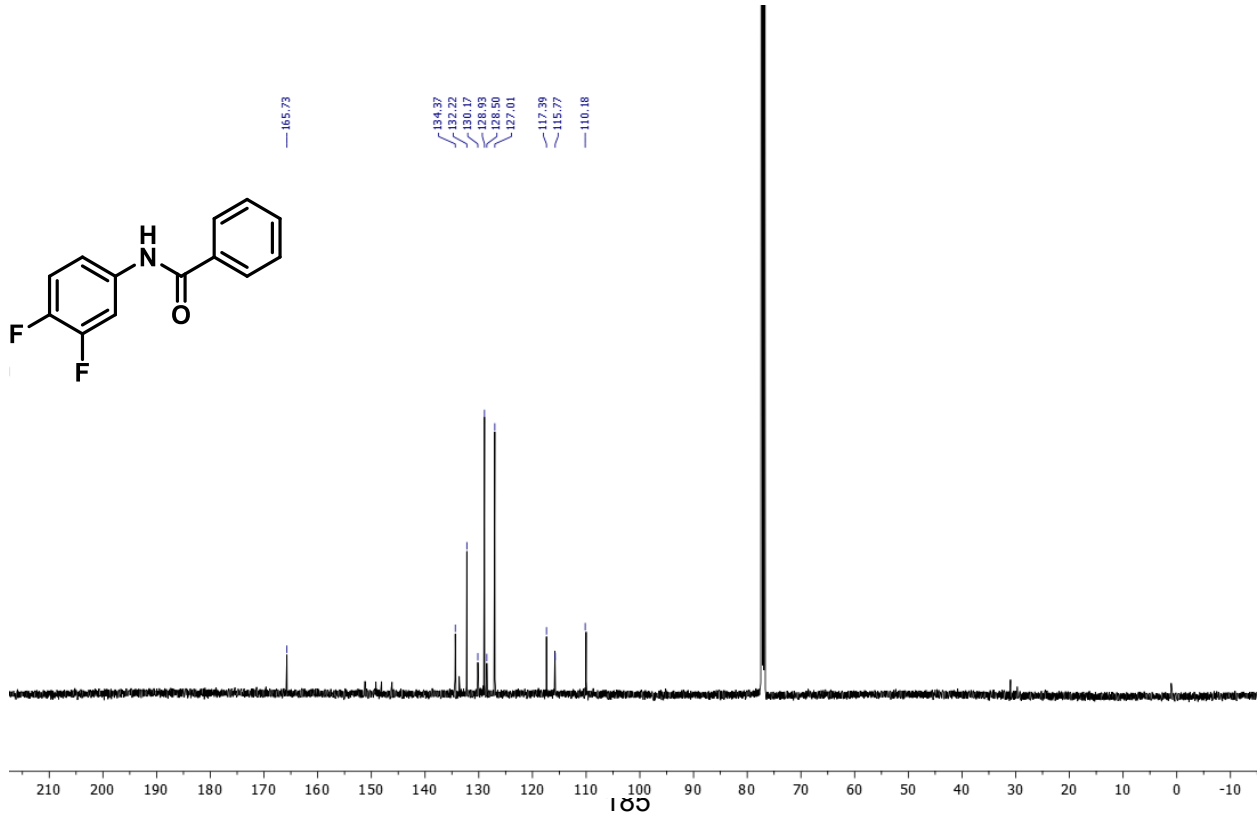
^{13}C NMR of Compound 3l ($CDCl_3$; 125 MHz)



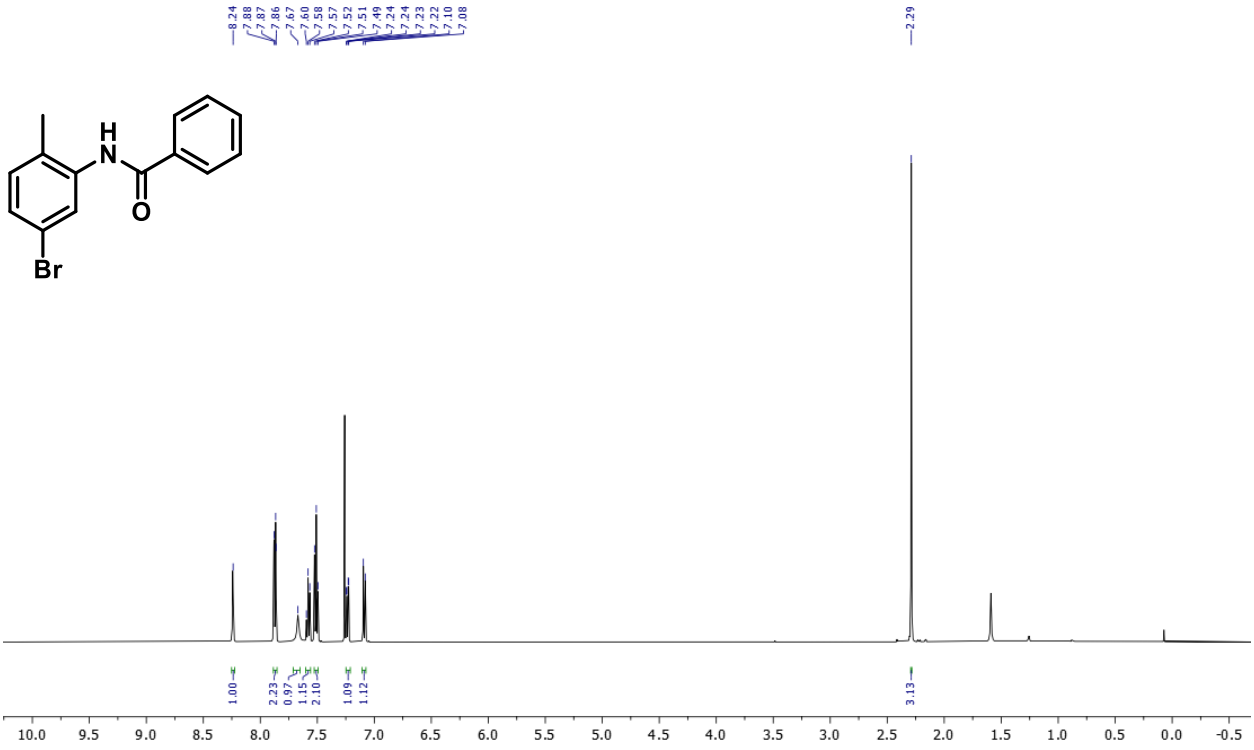
^{1}H NMR of Compound 3m (DMSO d_6; 300 MHz)



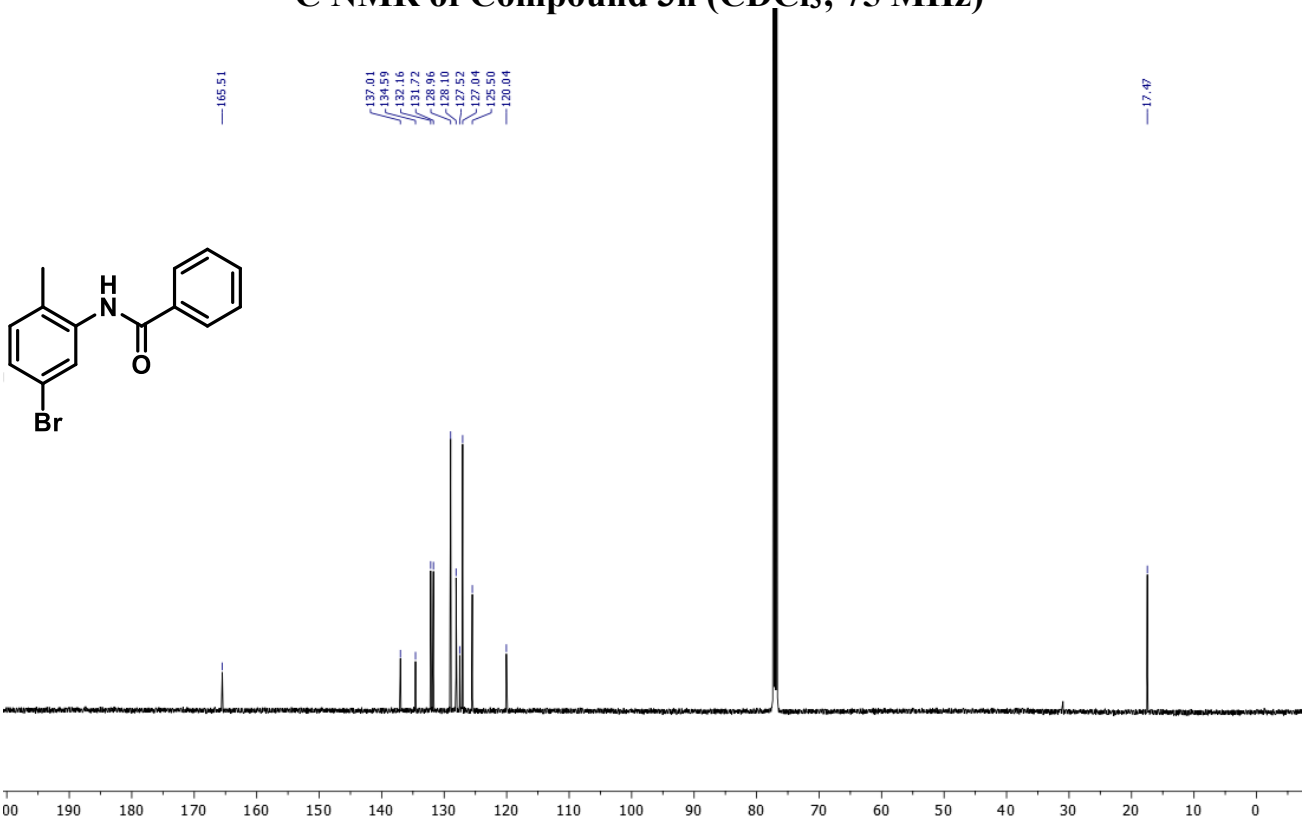
^{13}C NMR of Compound 3m ($CDCl_3$; 75 MHz)



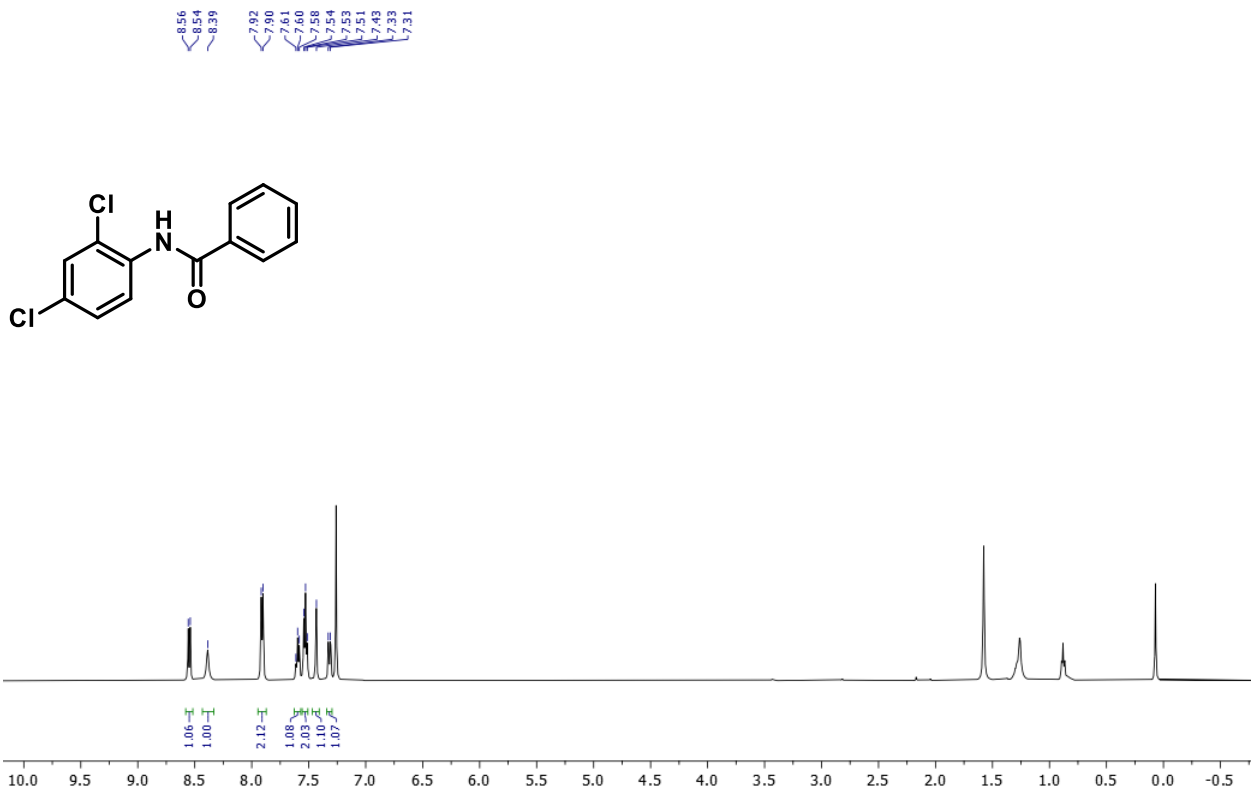
^{1}H NMR of Compound 3n ($CDCl_3$; 300 MHz)



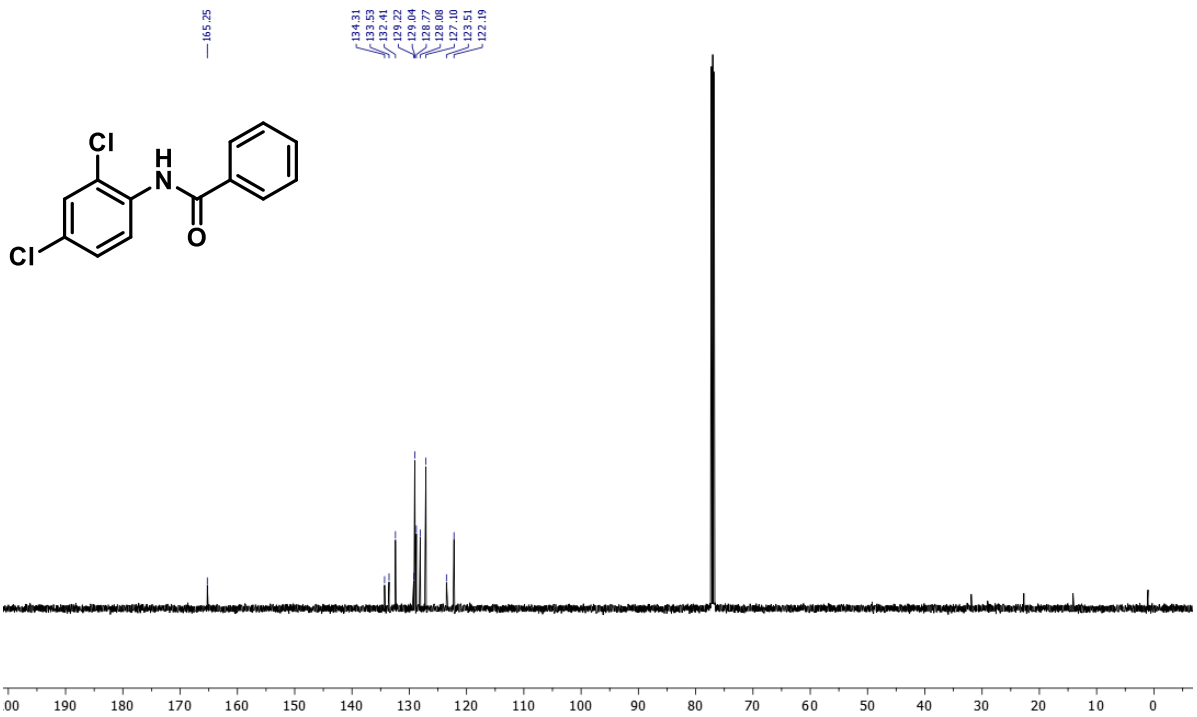
^{13}C NMR of Compound 3n ($CDCl_3$; 75 MHz)



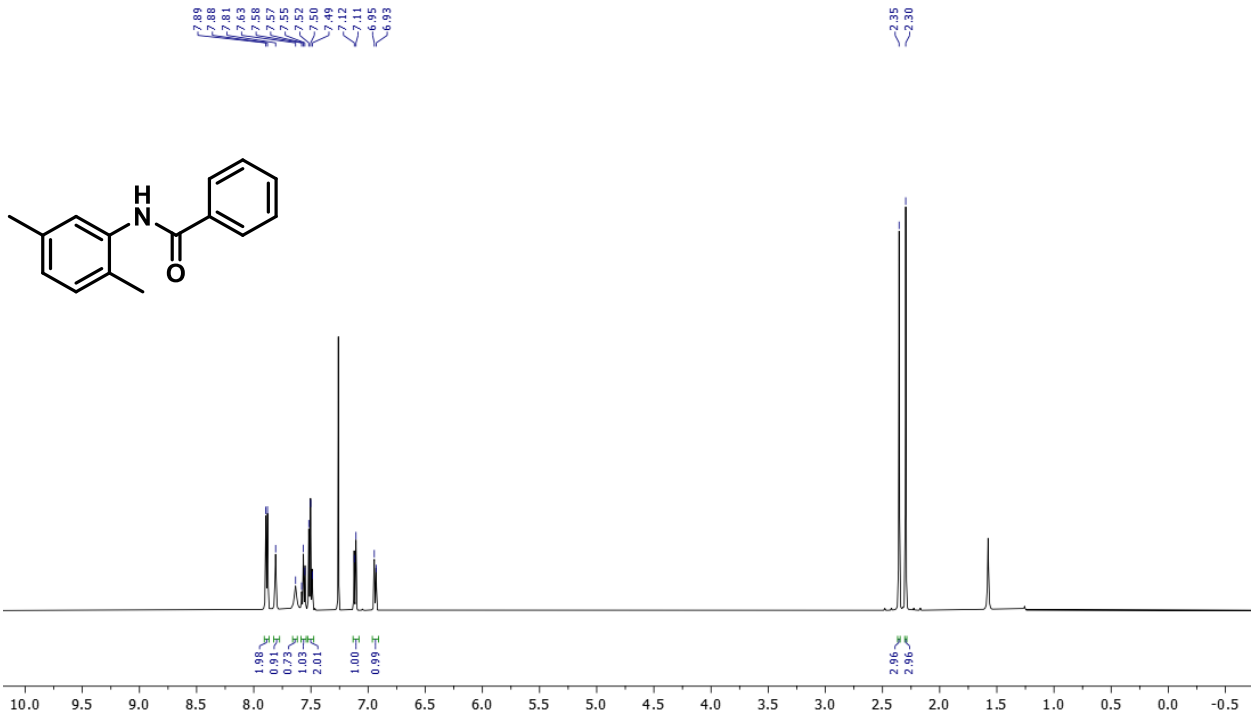
^{1}H NMR of Compound 3o ($CDCl_3$; 500 MHz)



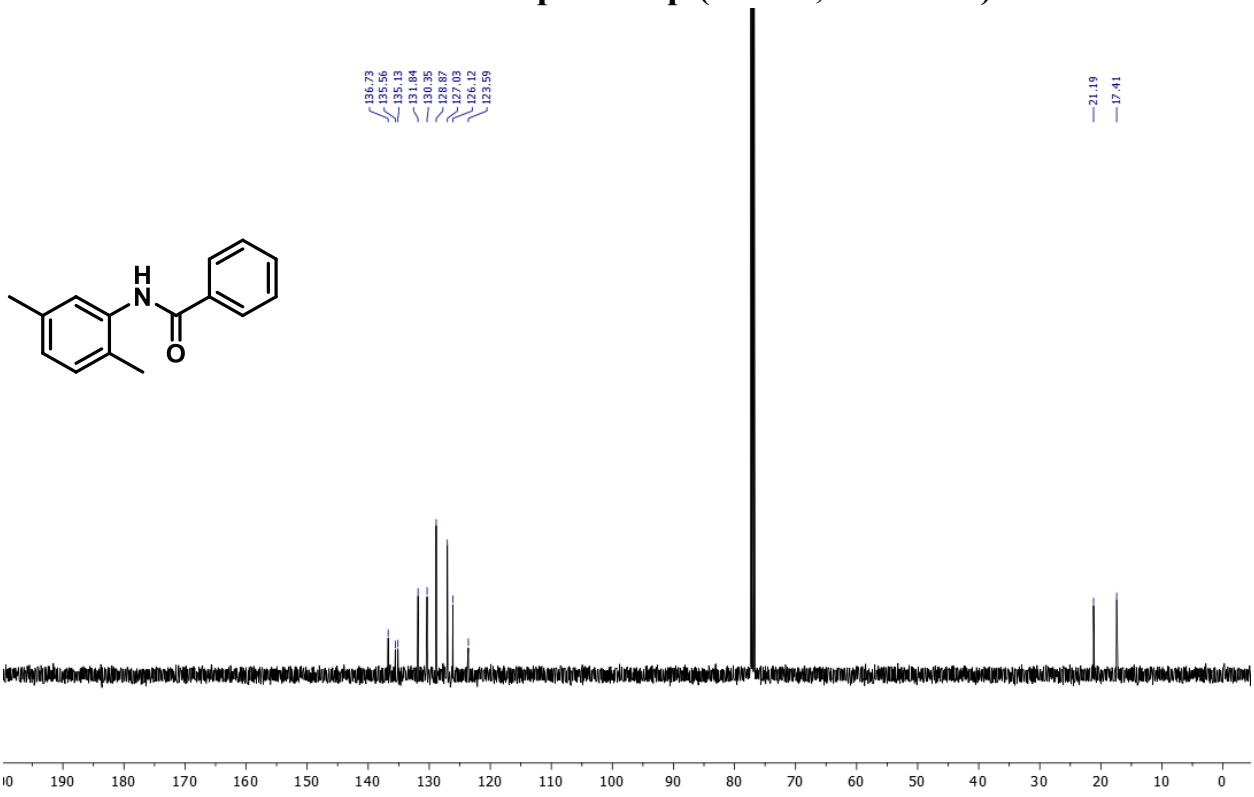
^{13}C NMR of Compound 3o ($CDCl_3$; 75 MHz)



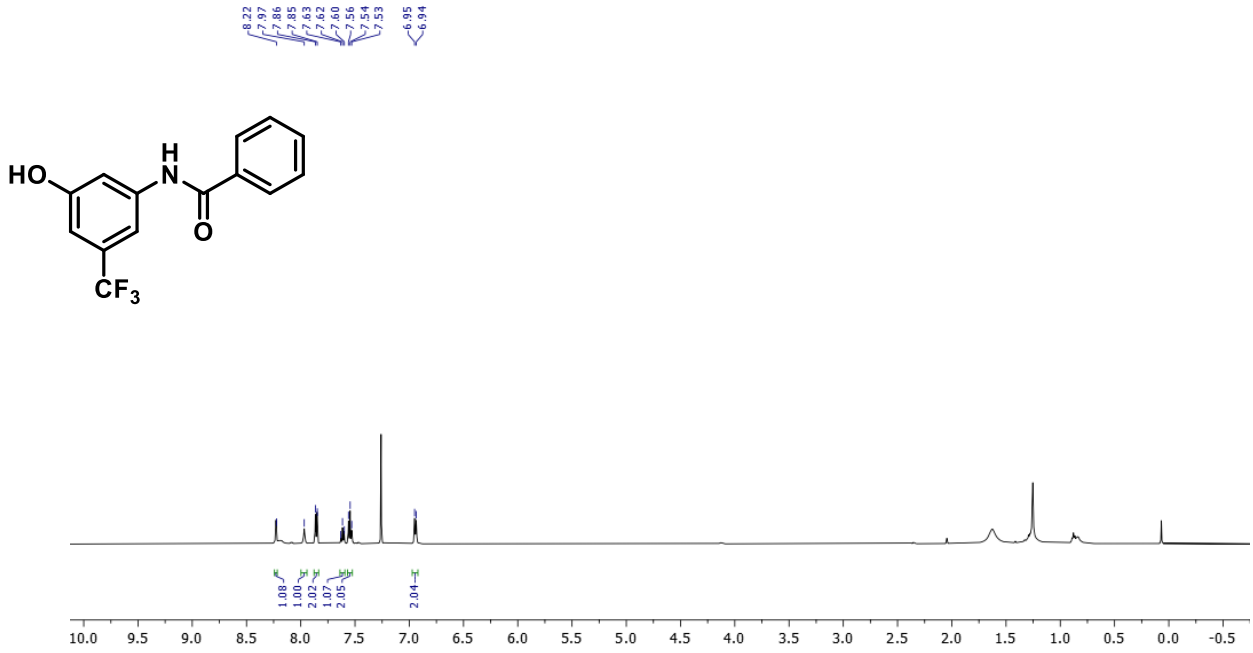
^{1}H NMR of Compound 3p ($CDCl_3$; 500 MHz)



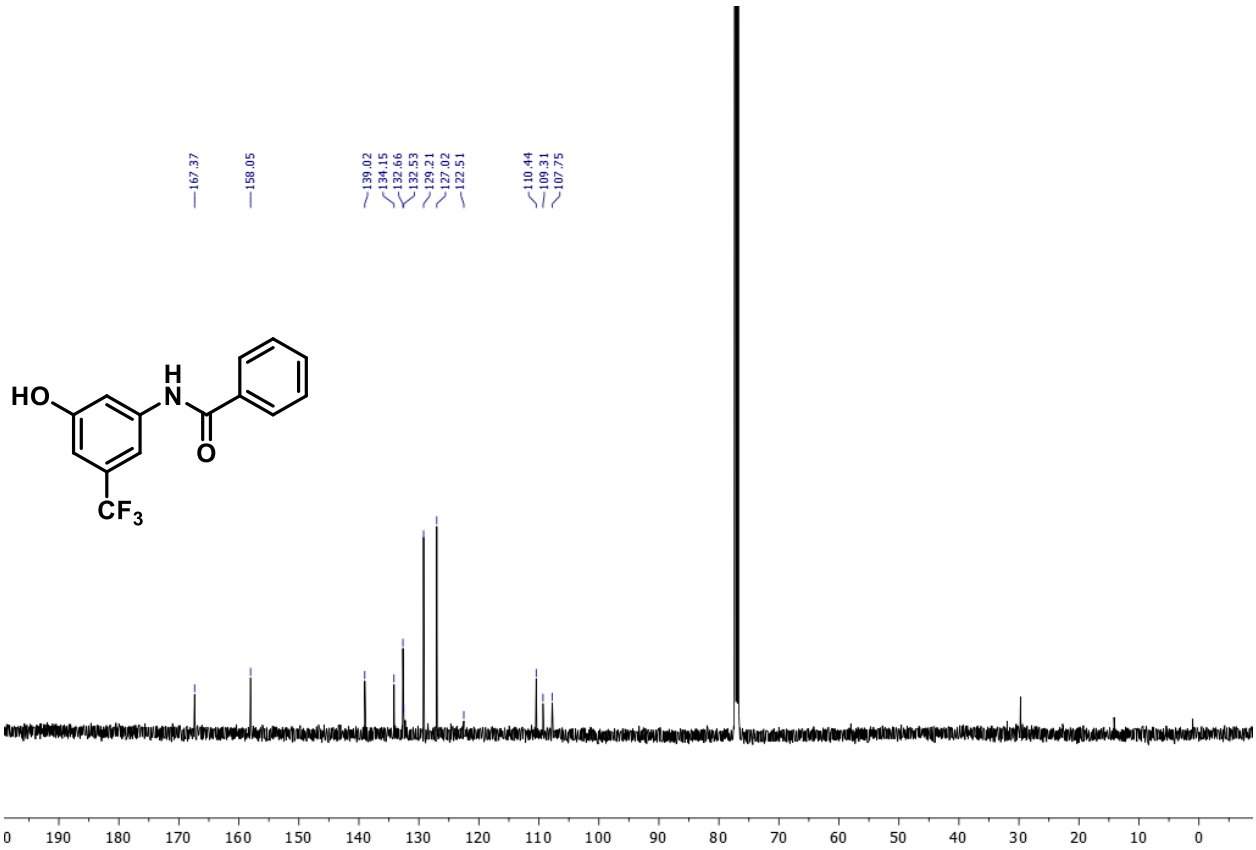
^{13}C NMR of Compound 3p ($CDCl_3$; 125 MHz)



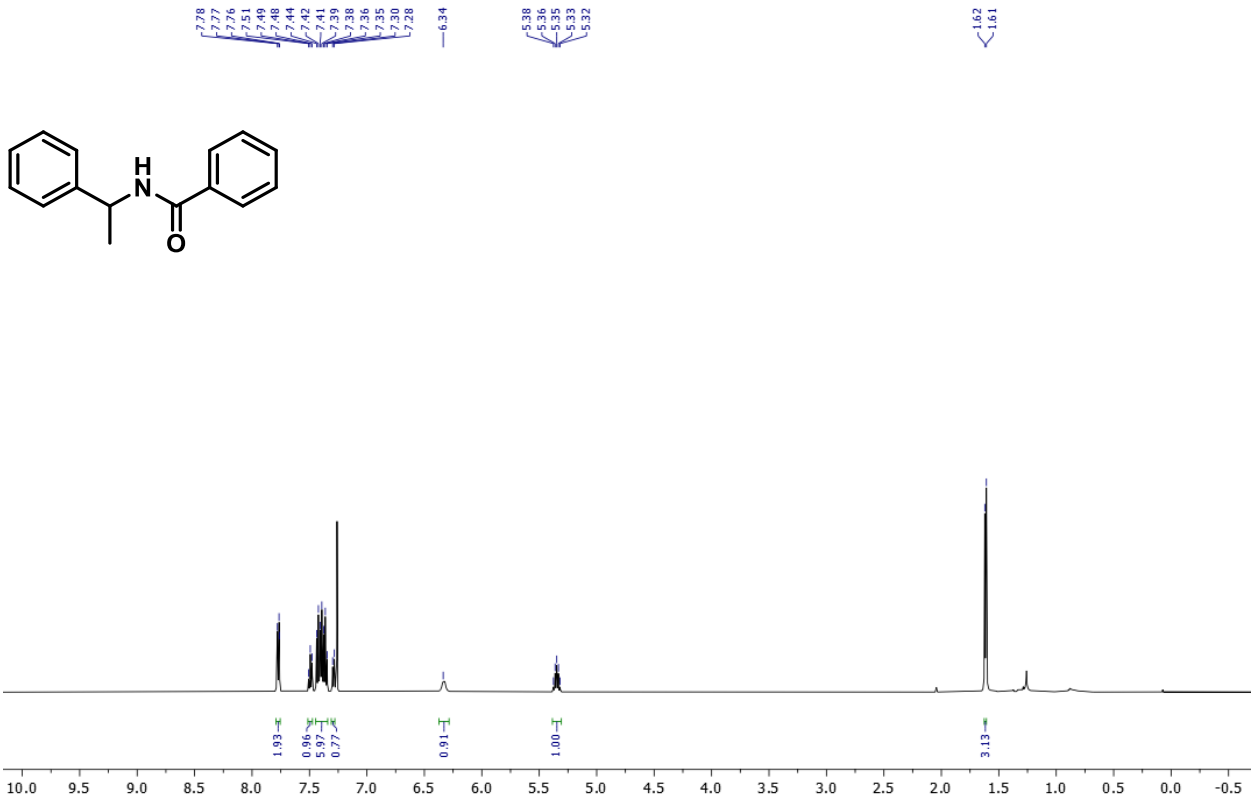
^{1}H NMR of Compound 3q ($CDCl_3$; 500 MHz)



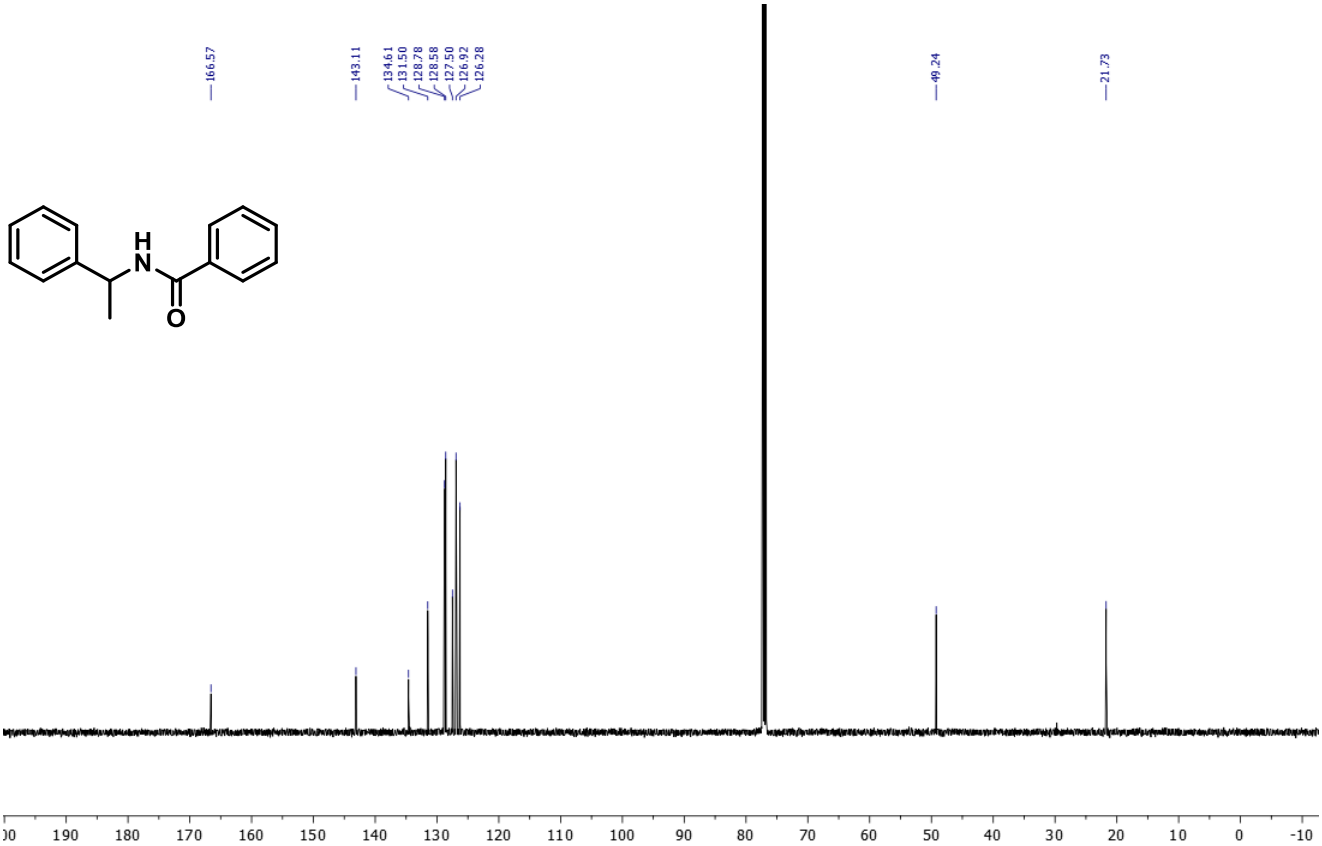
^{13}C NMR of Compound 3q ($CDCl_3$; 75 MHz)



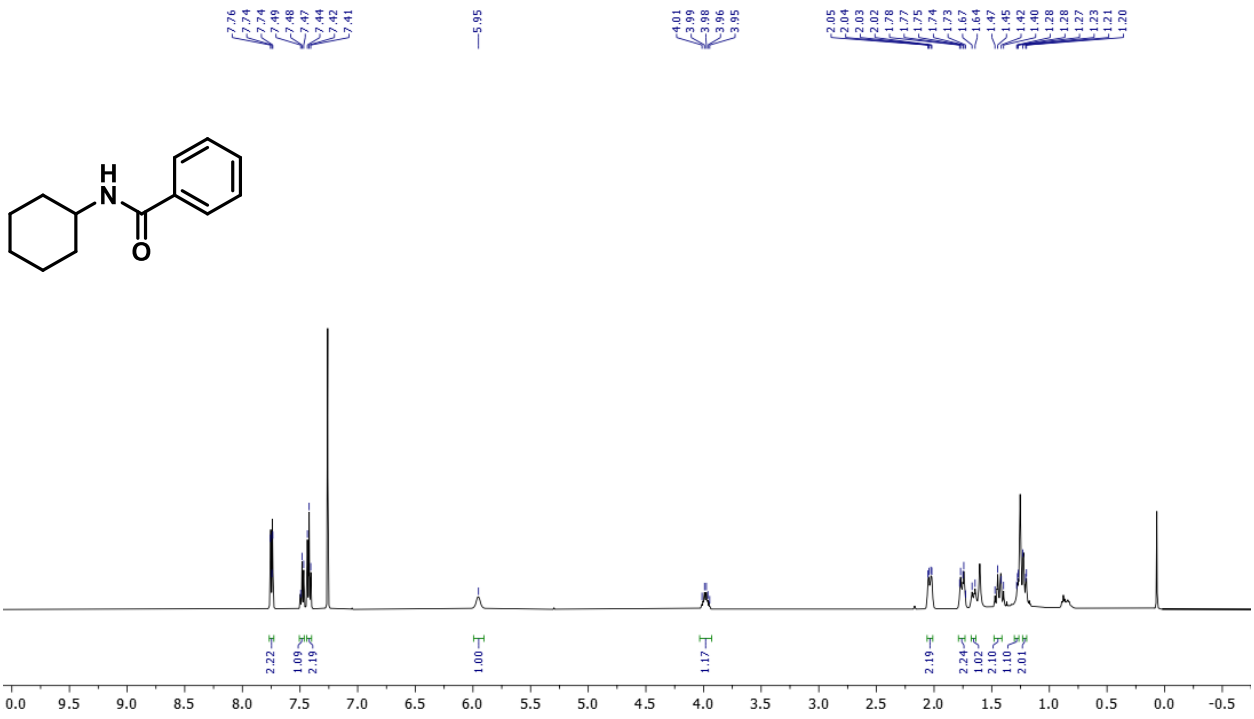
^{1}H NMR of Compound 3r ($CDCl_3$; 500 MHz)



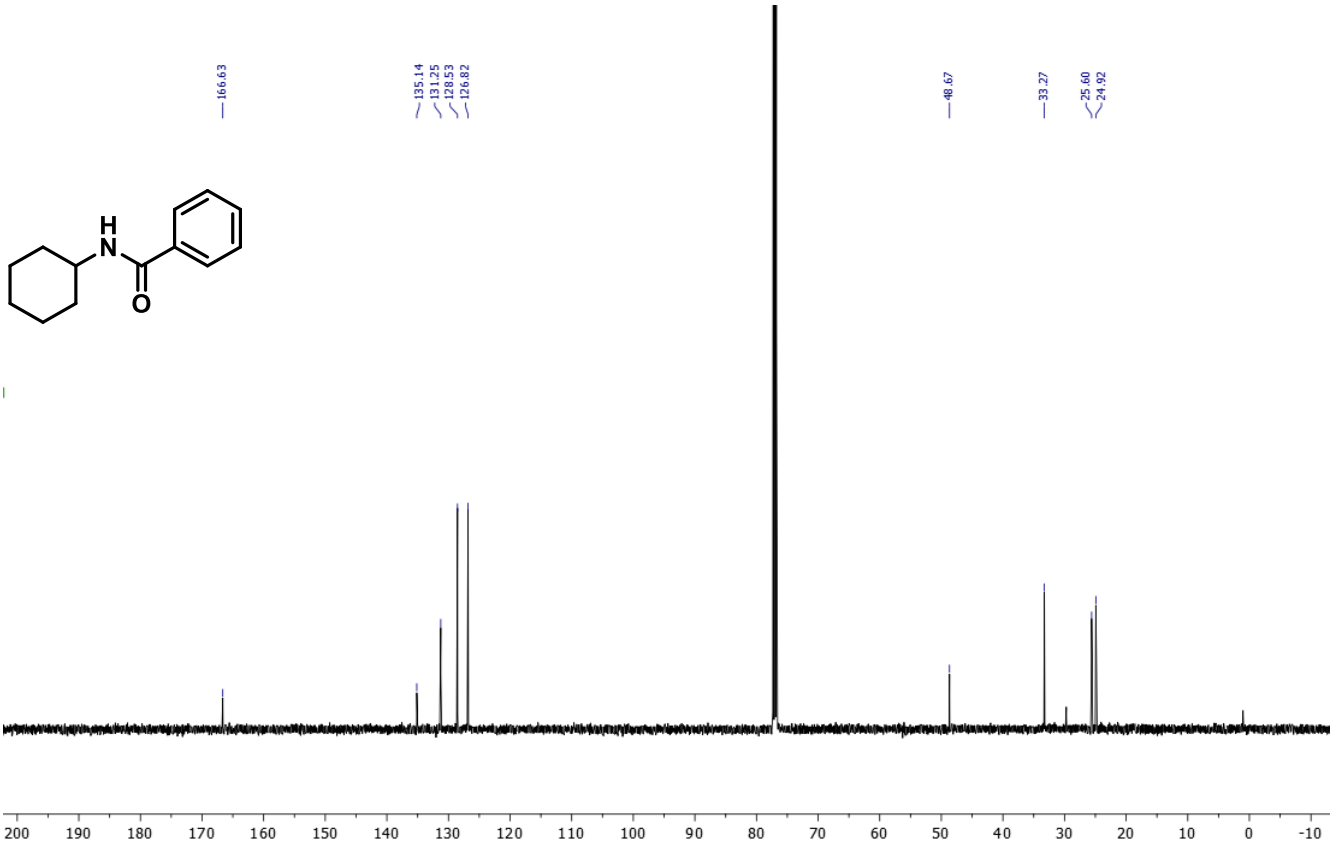
^{13}C NMR of Compound 3r ($CDCl_3$; 125 MHz)



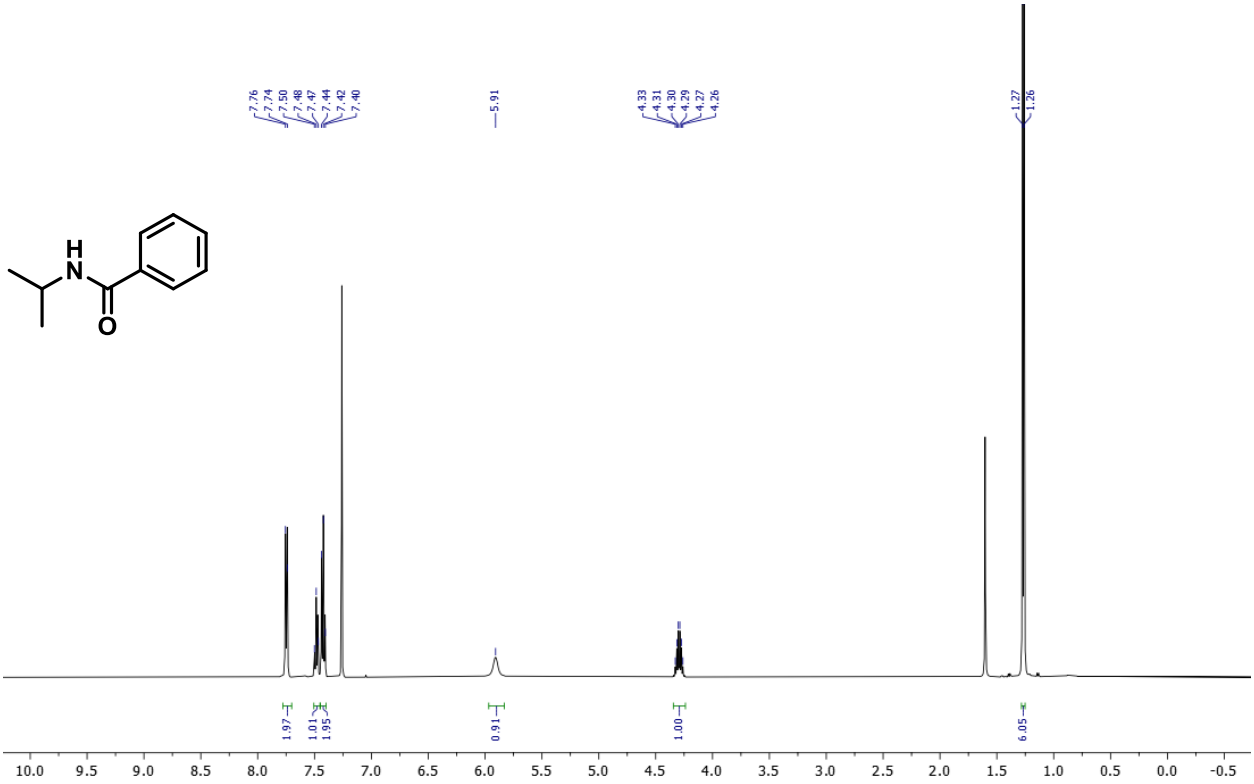
^{1}H NMR of Compound 3s ($CDCl_3$; 500 MHz)



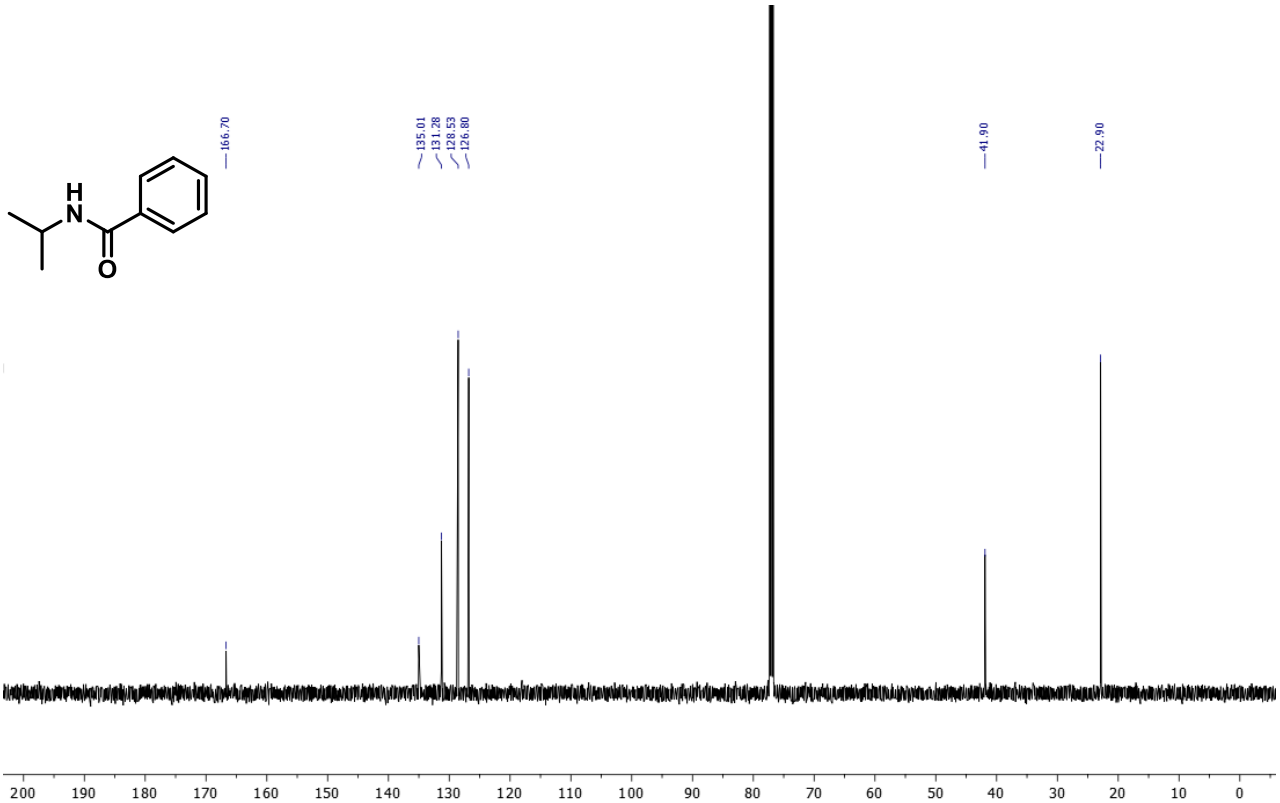
^{13}C NMR of Compound 3s ($CDCl_3$; 125 MHz)



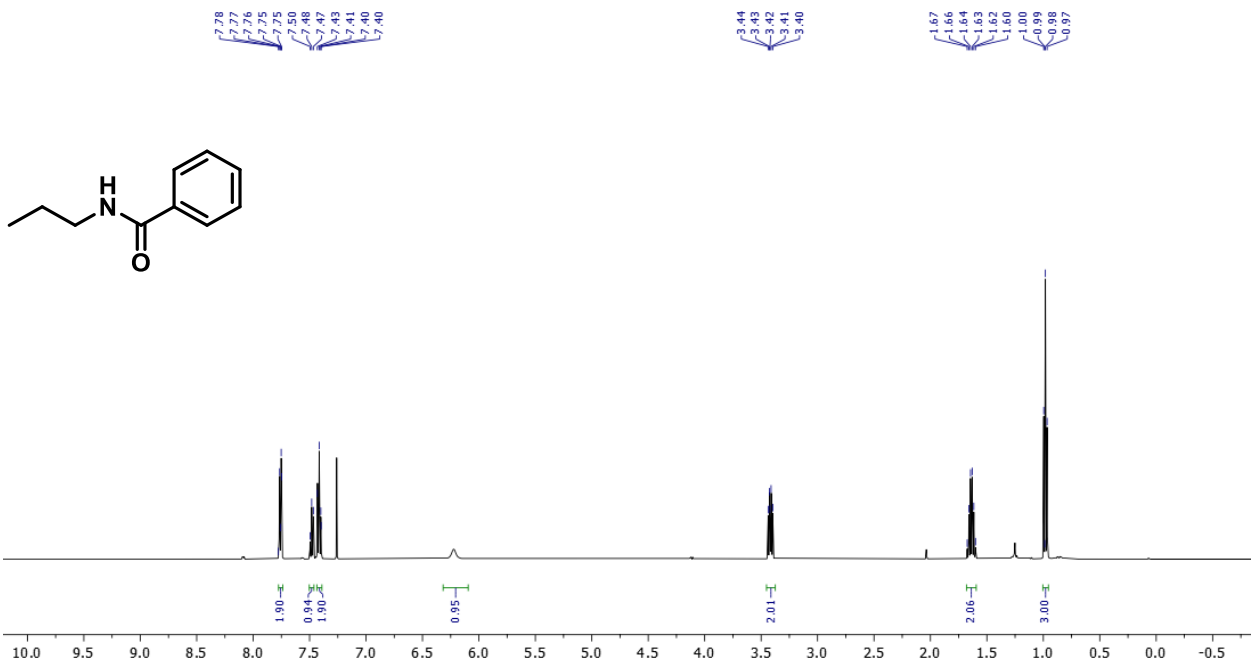
^{1}H NMR of Compound 3t ($CDCl_3$; 500 MHz)



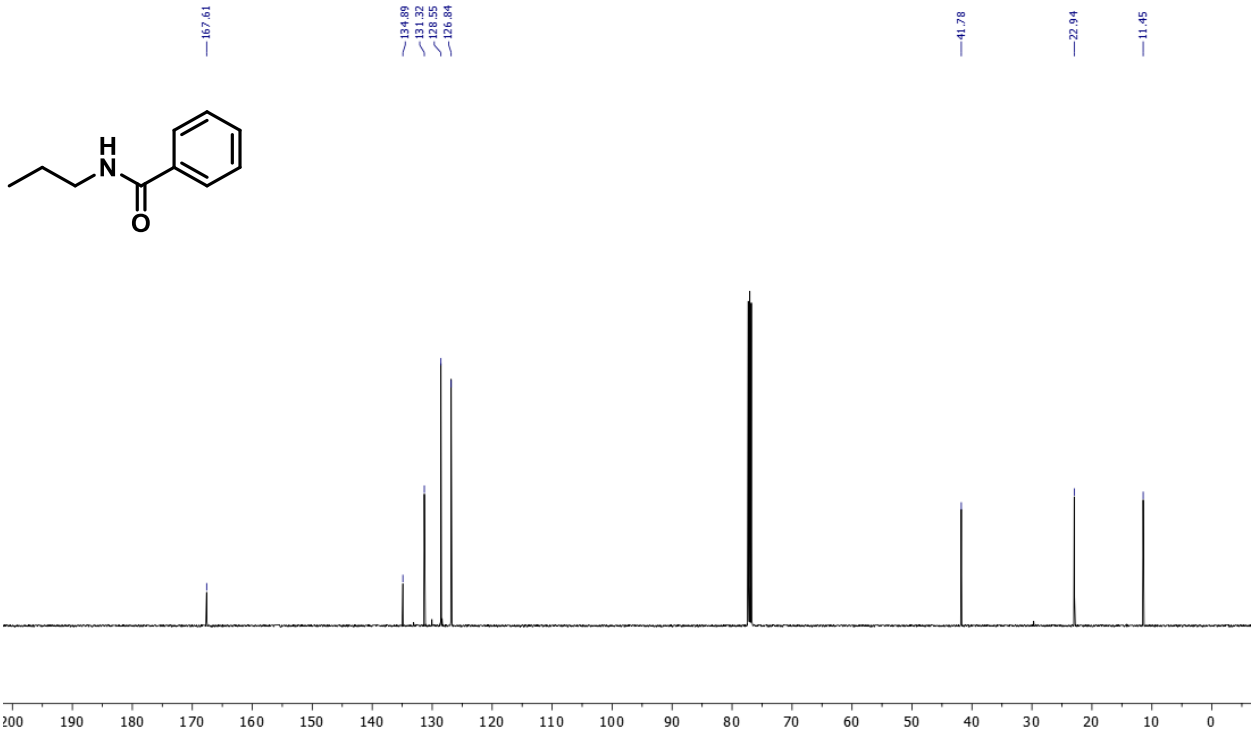
^{13}C NMR of Compound 3t ($CDCl_3$; 125 MHz)



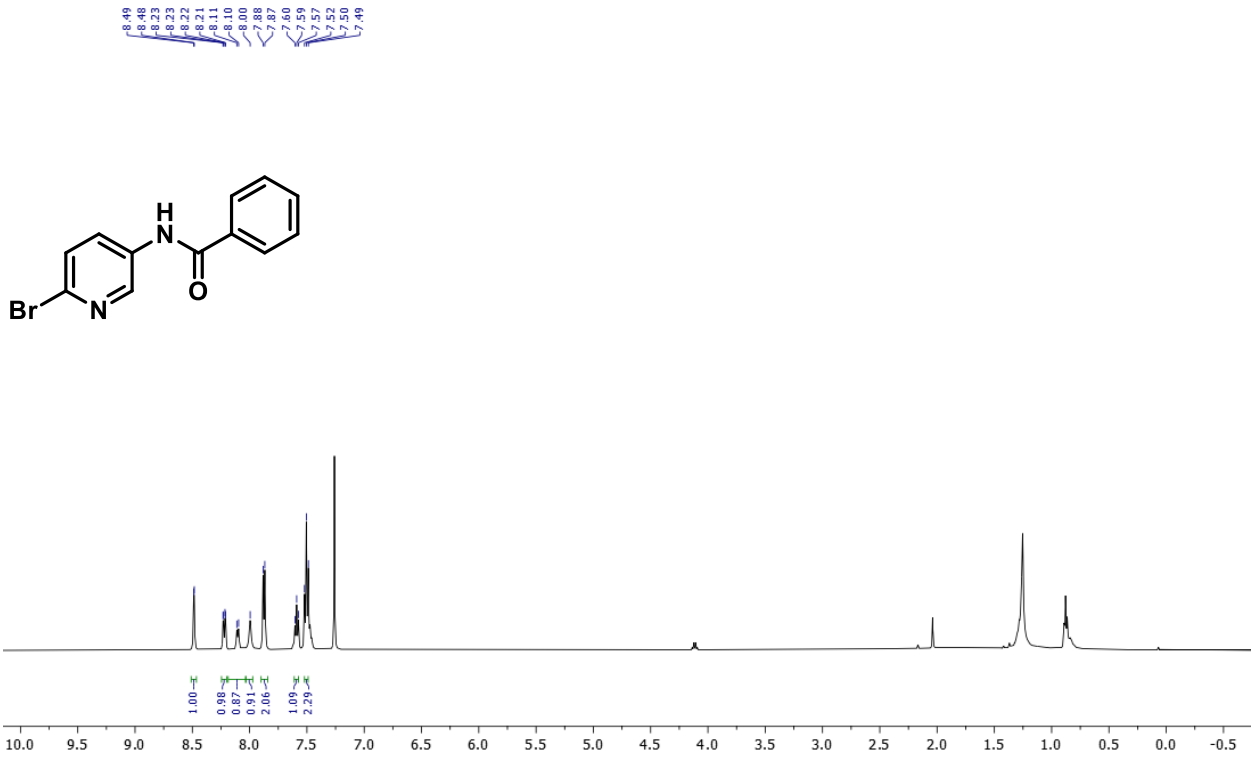
^{1}H NMR of Compound 3u ($CDCl_3$; 300 MHz)



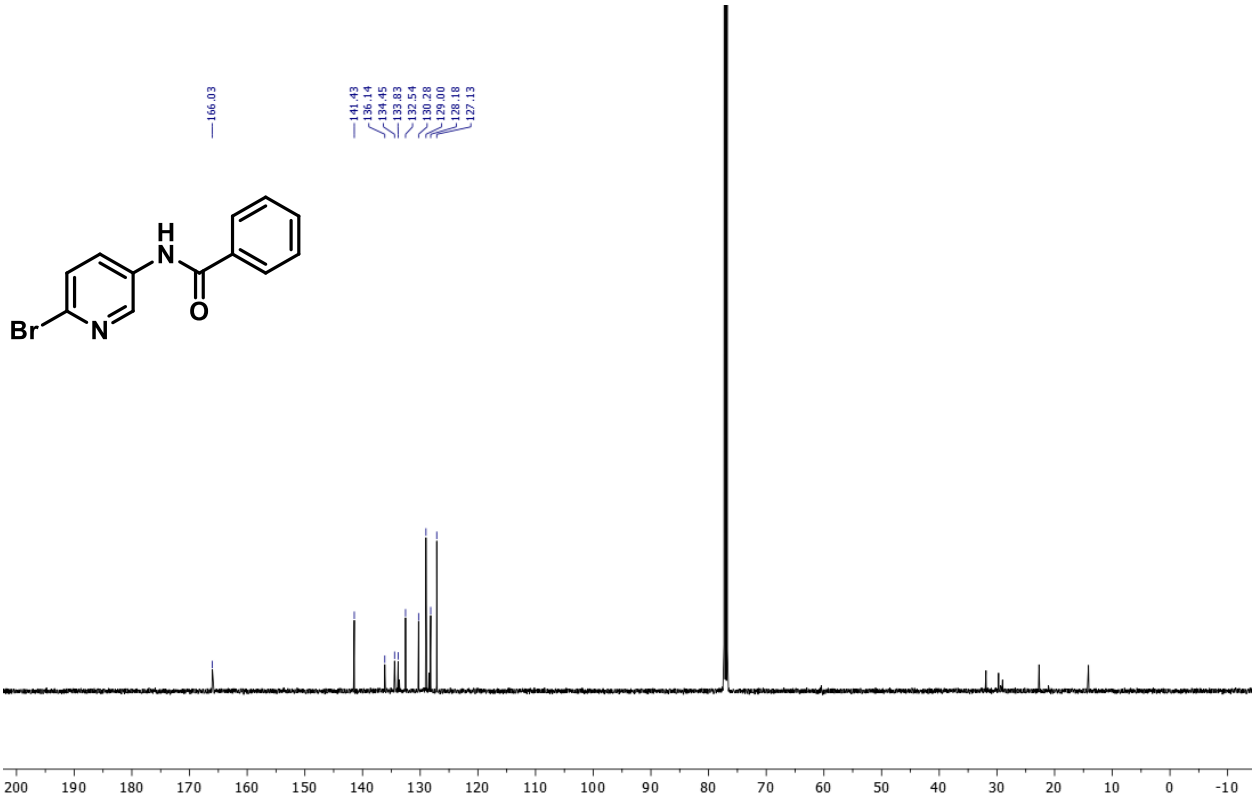
^{13}C NMR of Compound 3u ($CDCl_3$; 75 MHz)



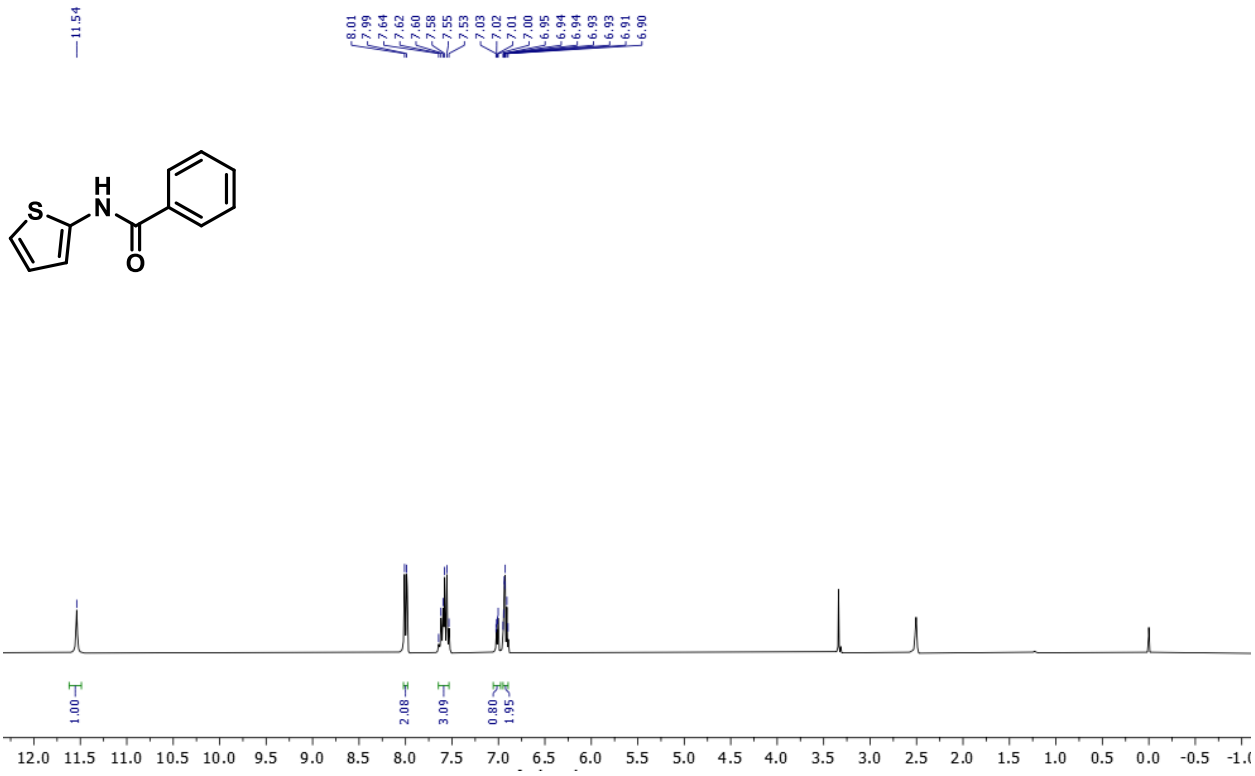
^{1}H NMR of Compound 3v ($CDCl_3$; 300 MHz)



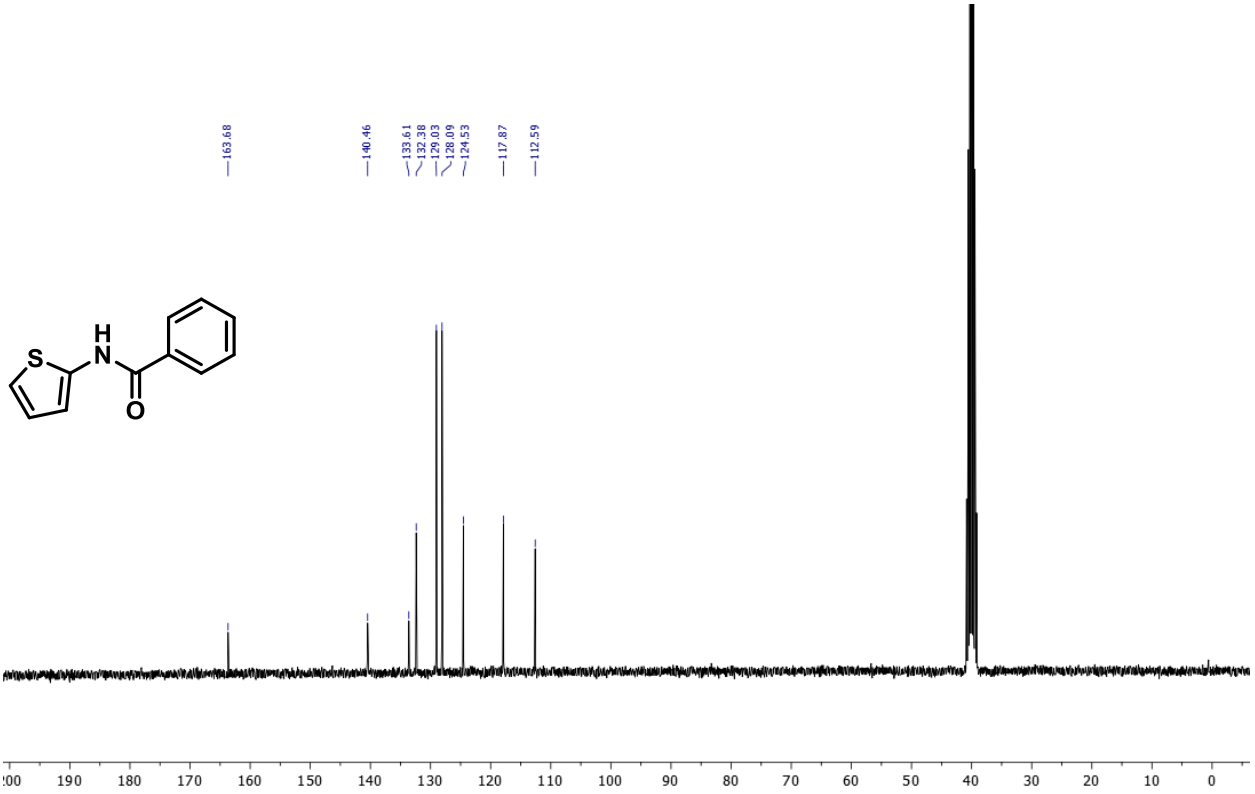
^{13}C NMR of Compound 3v ($CDCl_3$; 75 MHz)



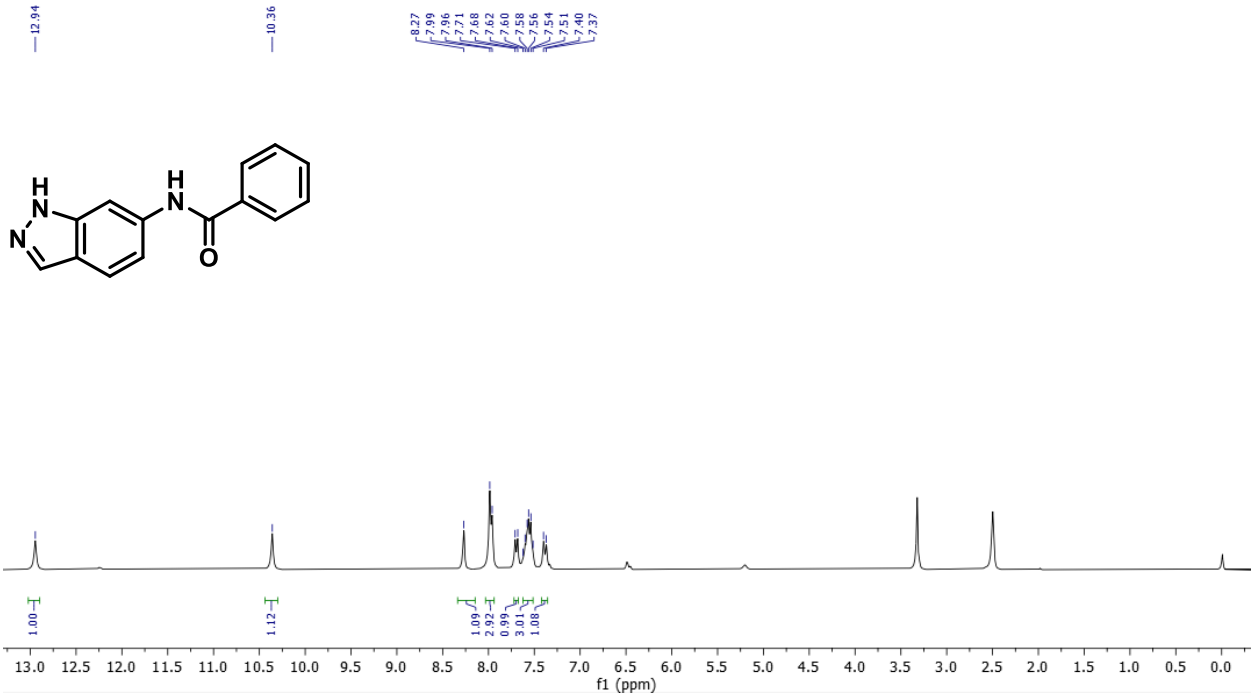
^{1}H NMR of Compound 3w (DMSO d_6; 300 MHz)



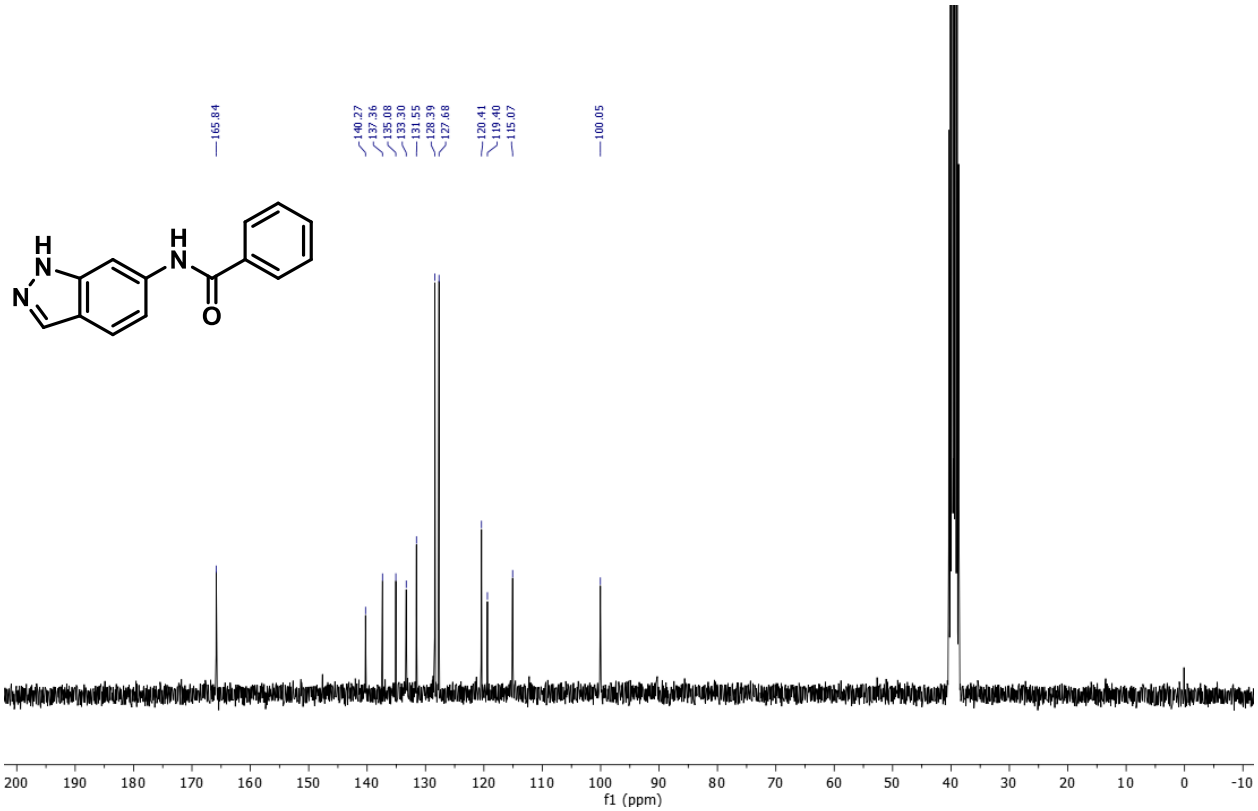
^{13}C NMR of Compound 3w (DMSO d_6; 75 MHz)



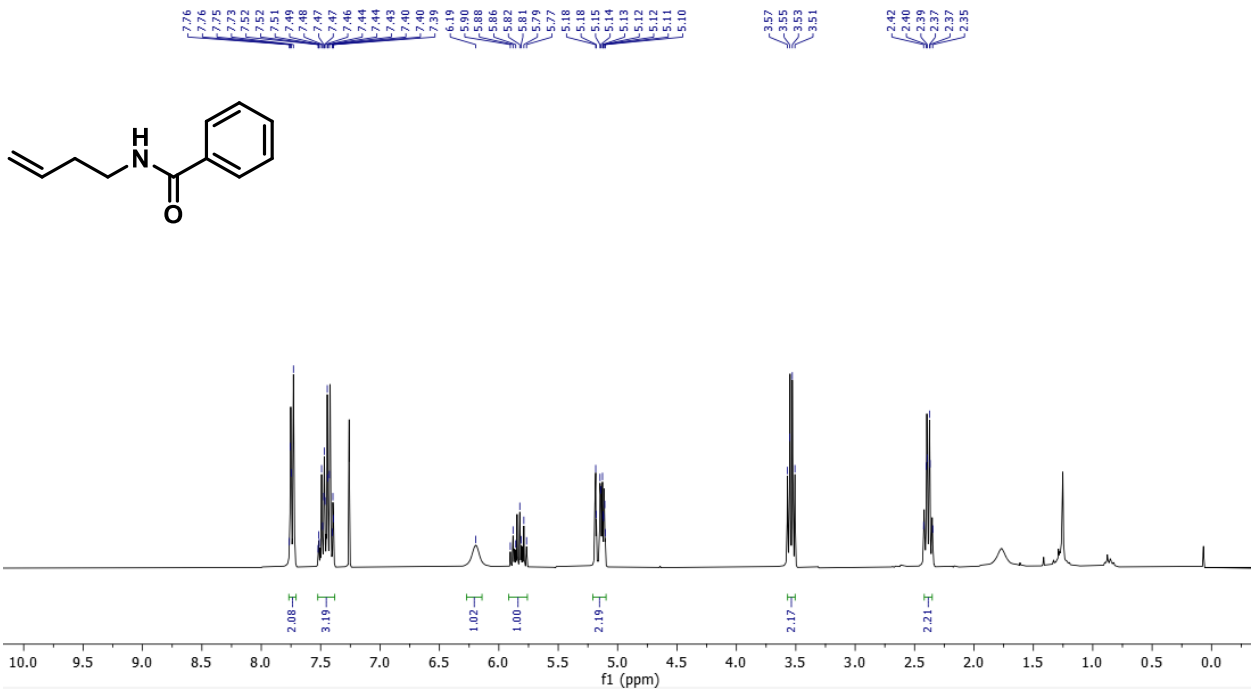
^{1}H NMR of Compound 3x (DMSO d_6; 300 MHz)



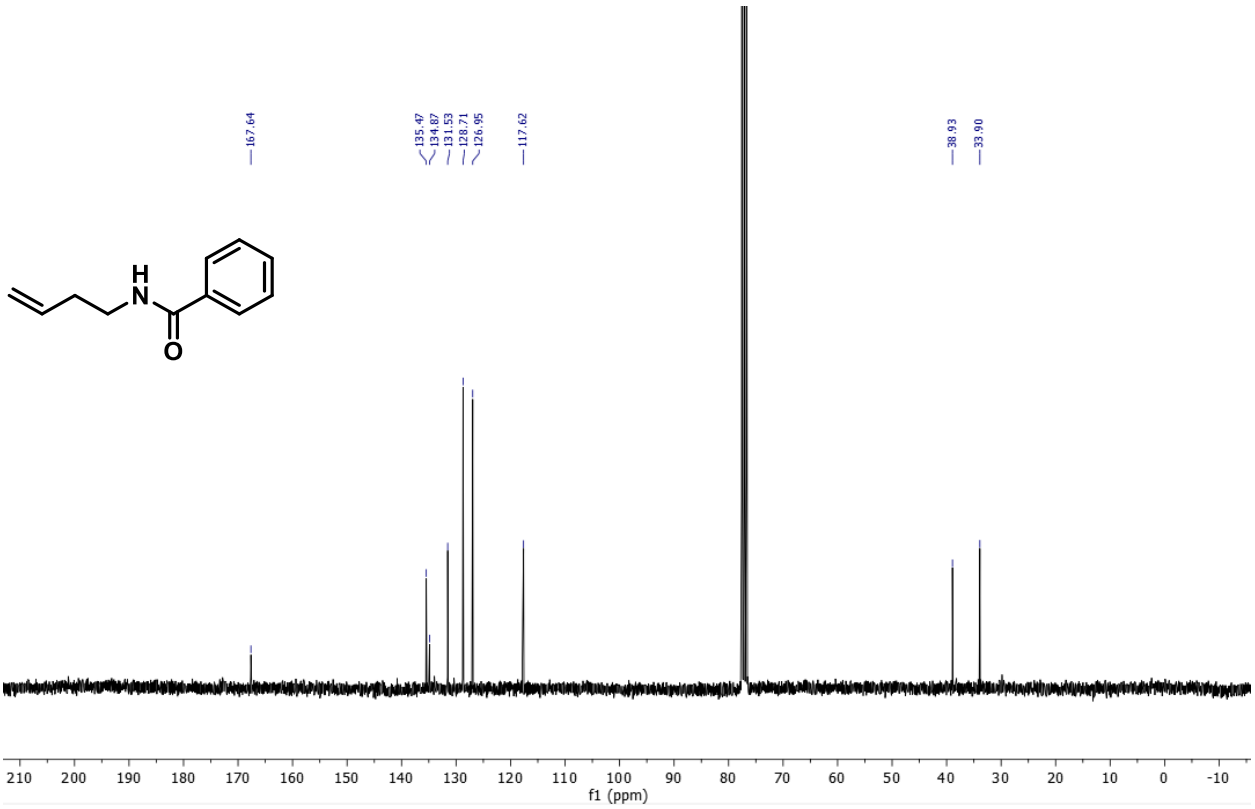
^{13}C NMR of Compound (DMSO d_6; 75 MHz)



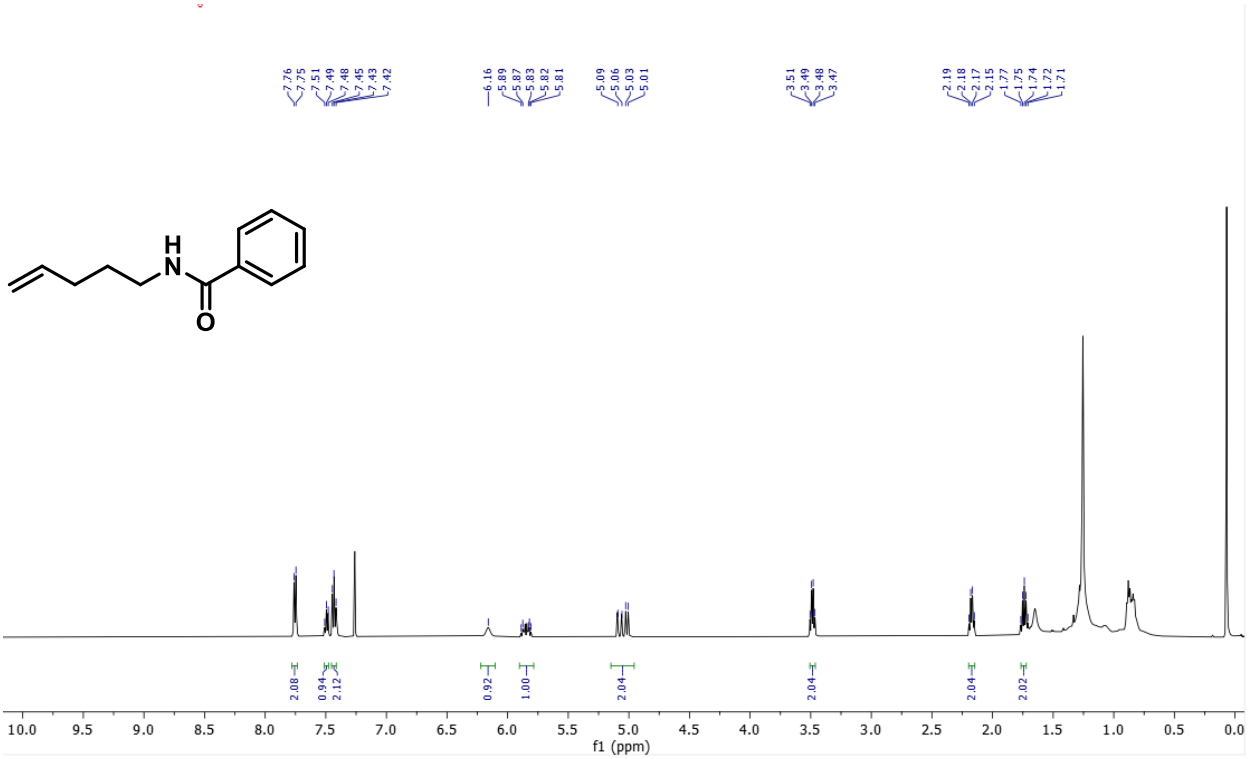
^{1}H NMR of Compound 3y ($CDCl_3$; 300 MHz)



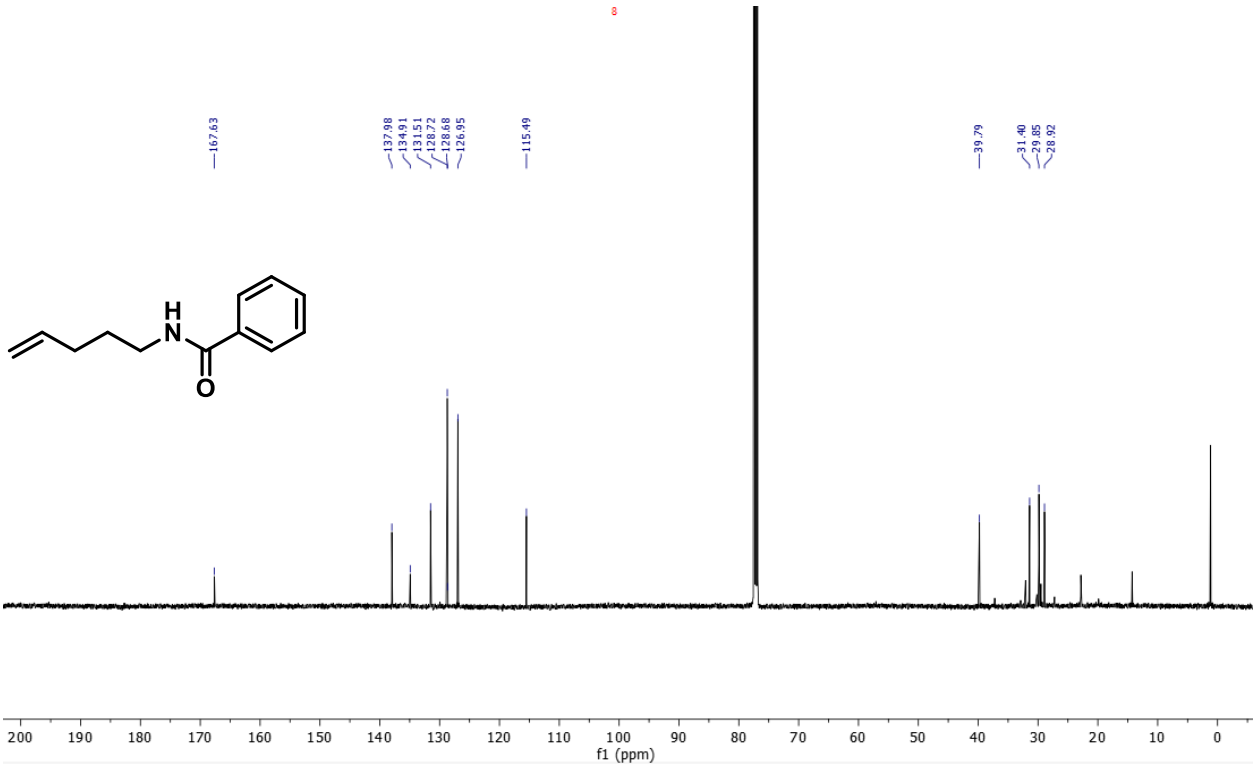
^{13}C NMR of Compound 3y ($CDCl_3$; 75 MHz)



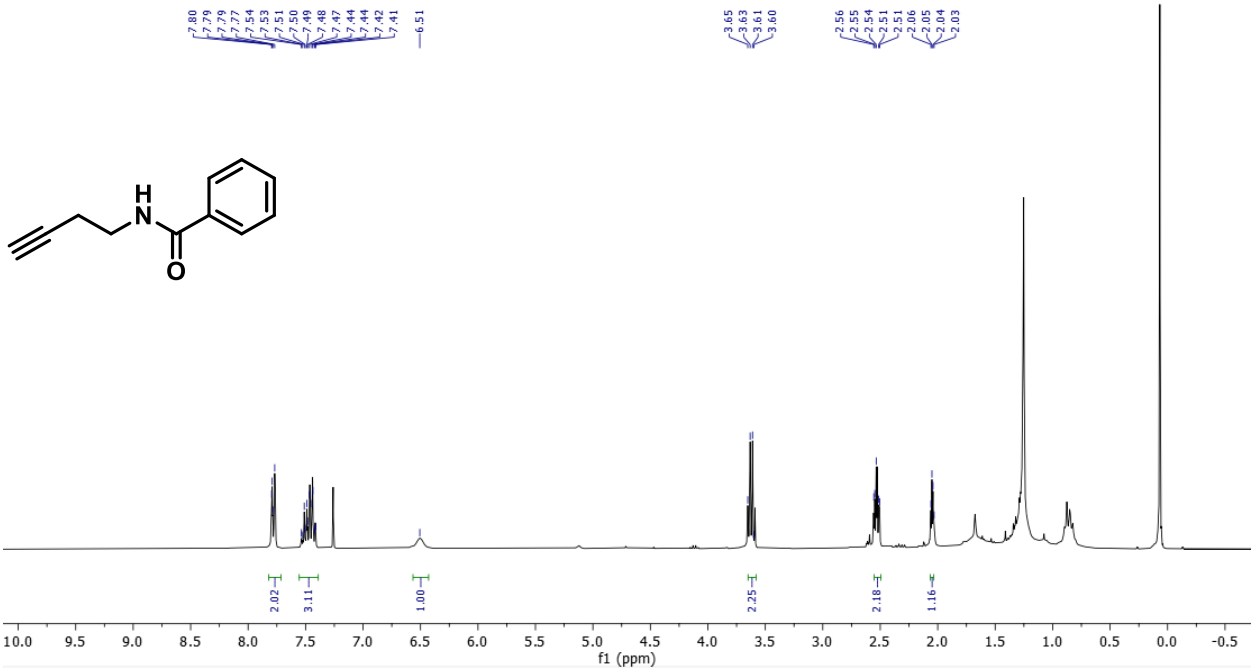
^{1}H NMR of Compound 3z ($CDCl_3$; 500 MHz)



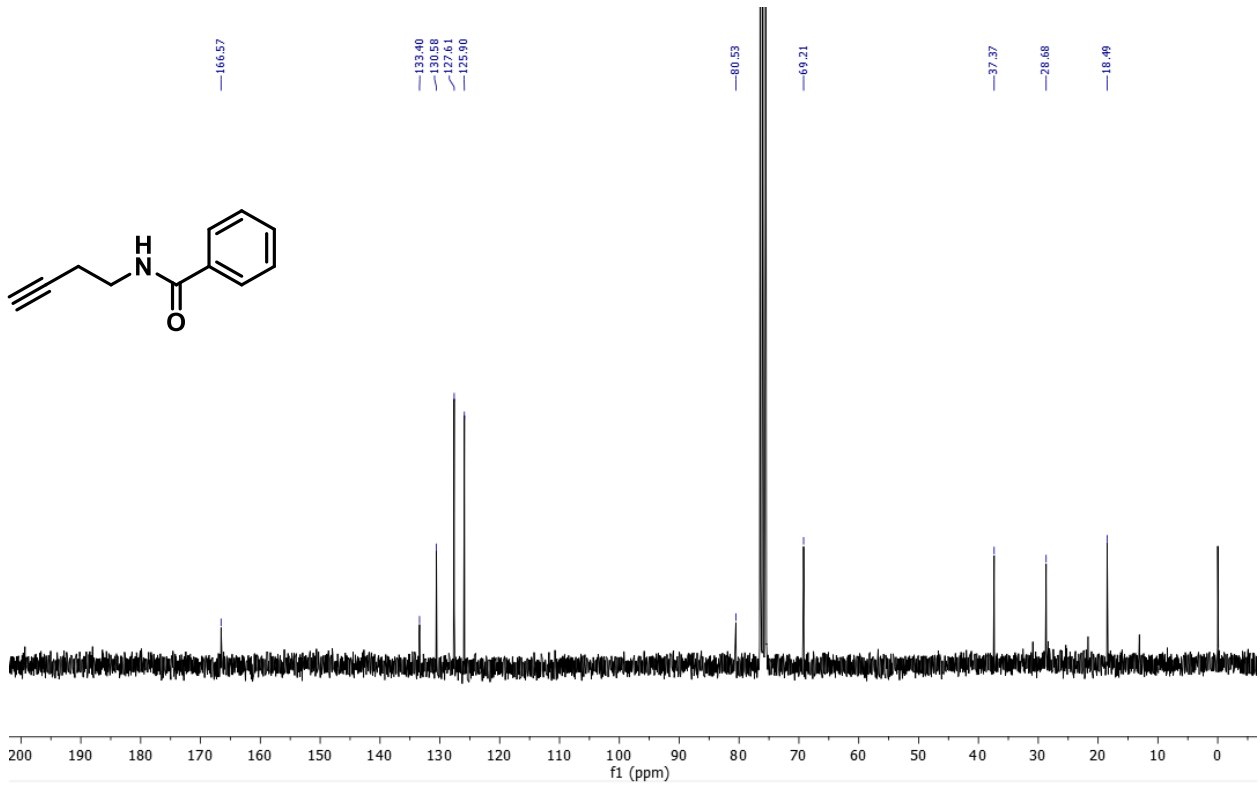
^{13}C NMR of Compound 3z ($CDCl_3$; 125 MHz)



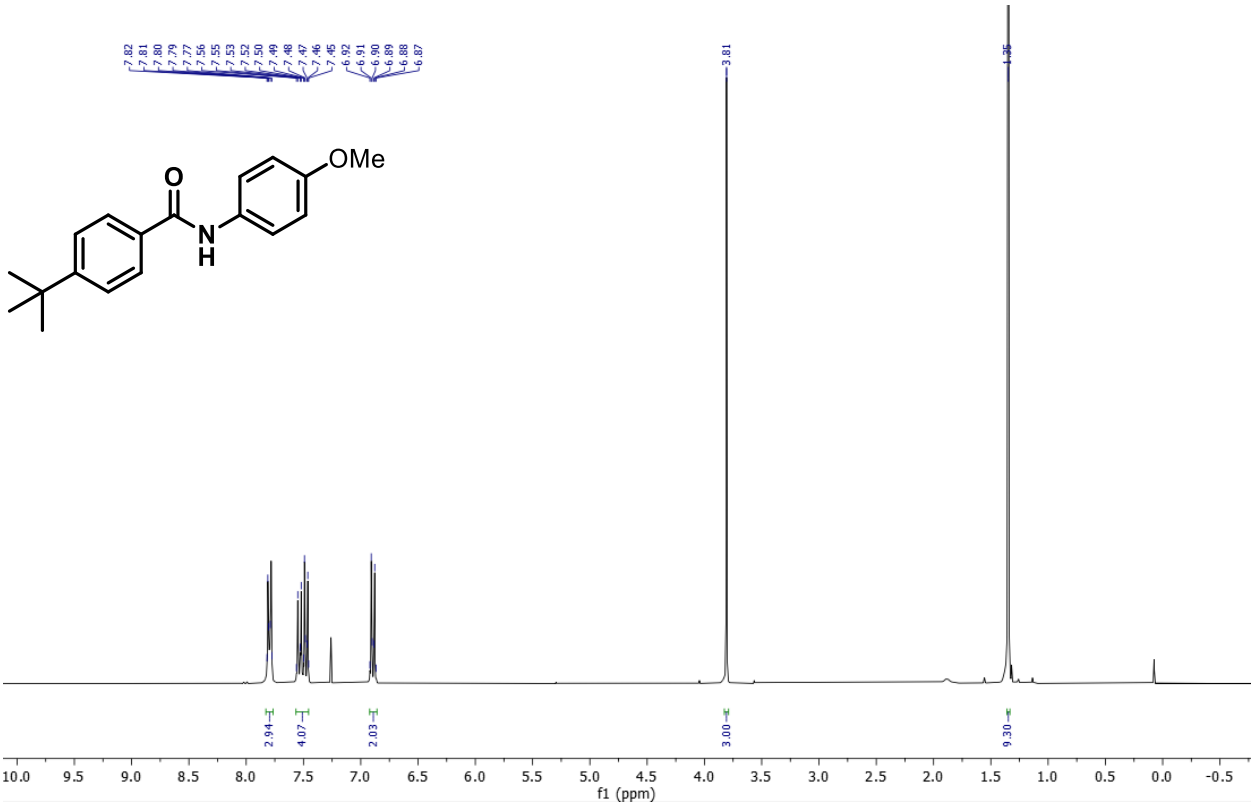
^{1}H NMR of Compound 3aa ($CDCl_3$; 300 MHz)



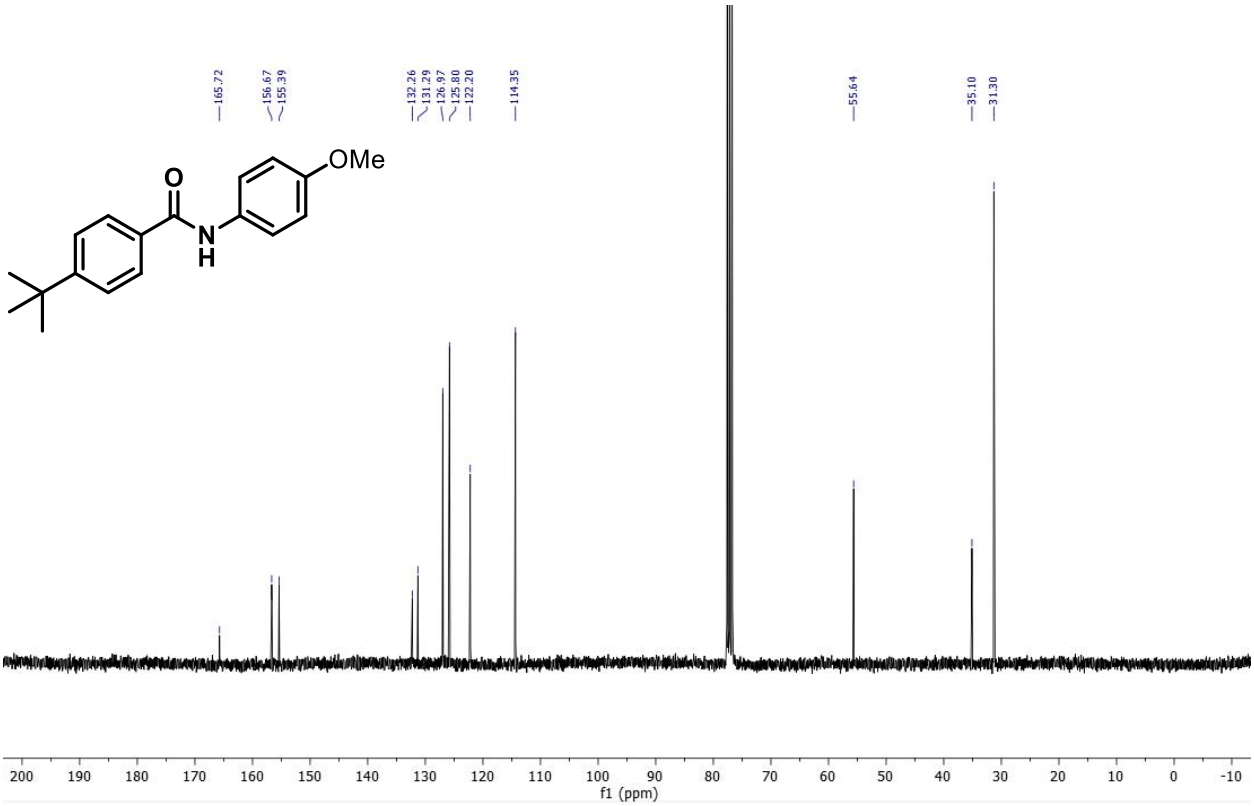
^{13}C NMR of Compound 3aa ($CDCl_3$; 75 MHz)



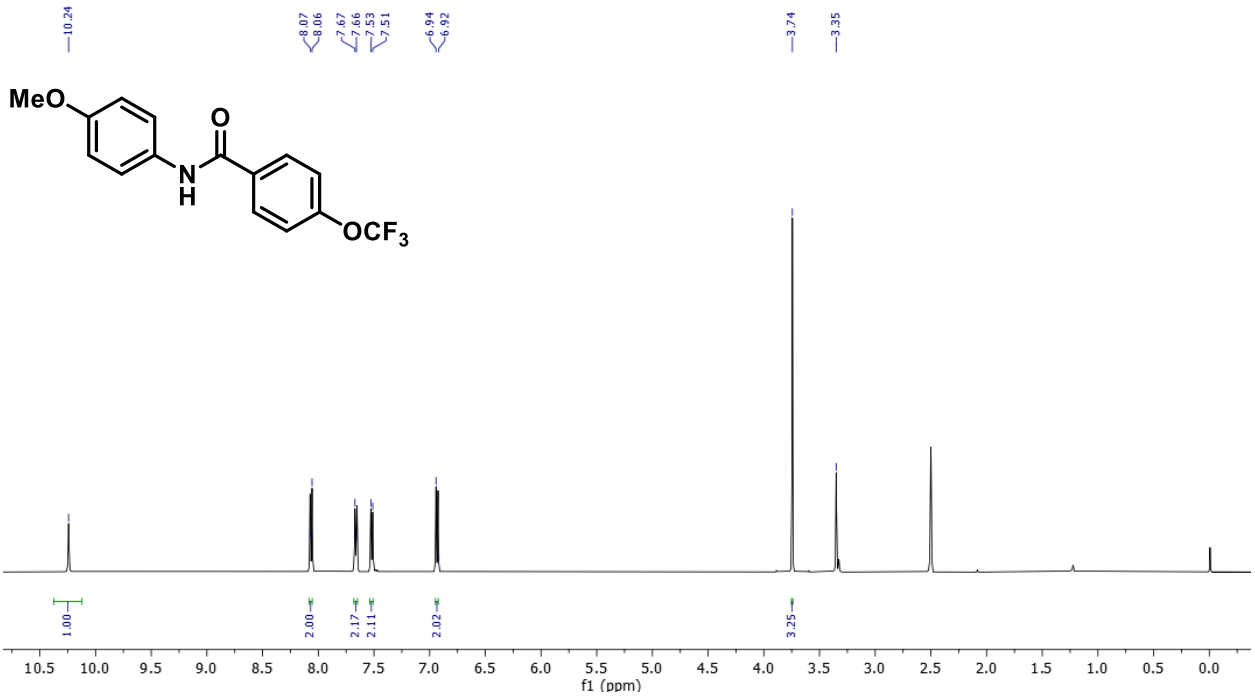
^{1}H NMR of Compound 5a ($CDCl_3$; 300 MHz)



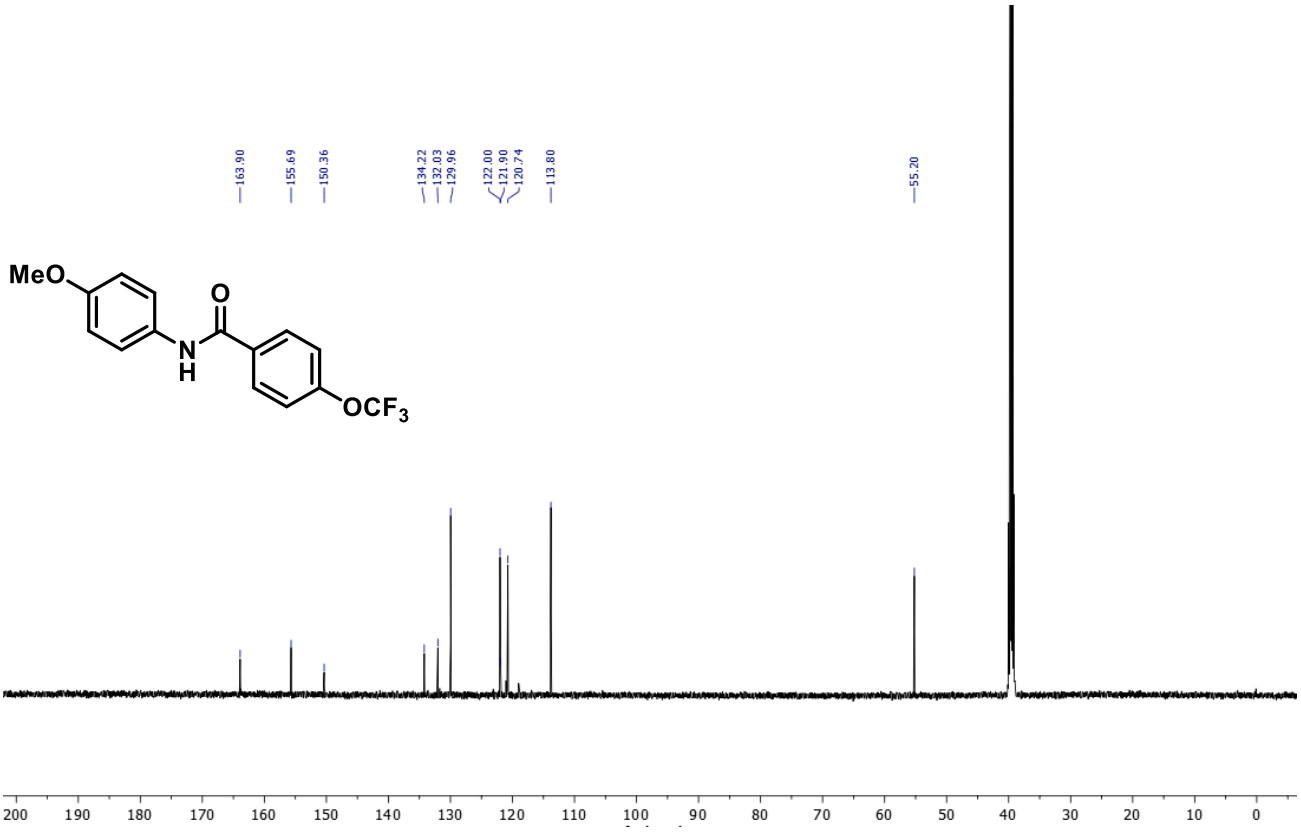
^{13}C NMR of Compound 5a ($CDCl_3$; 75 MHz)



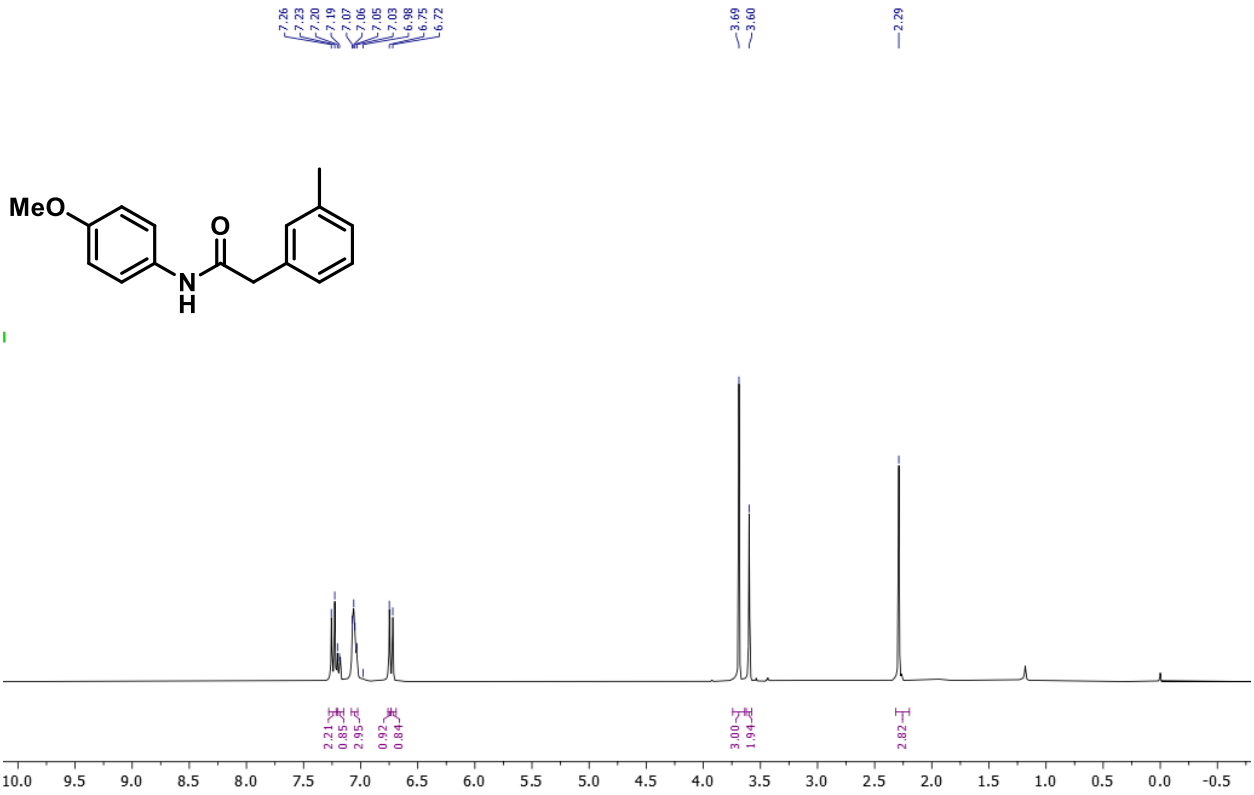
^{1}H NMR of Compound 5b (DMSO d_6; 500 MHz)



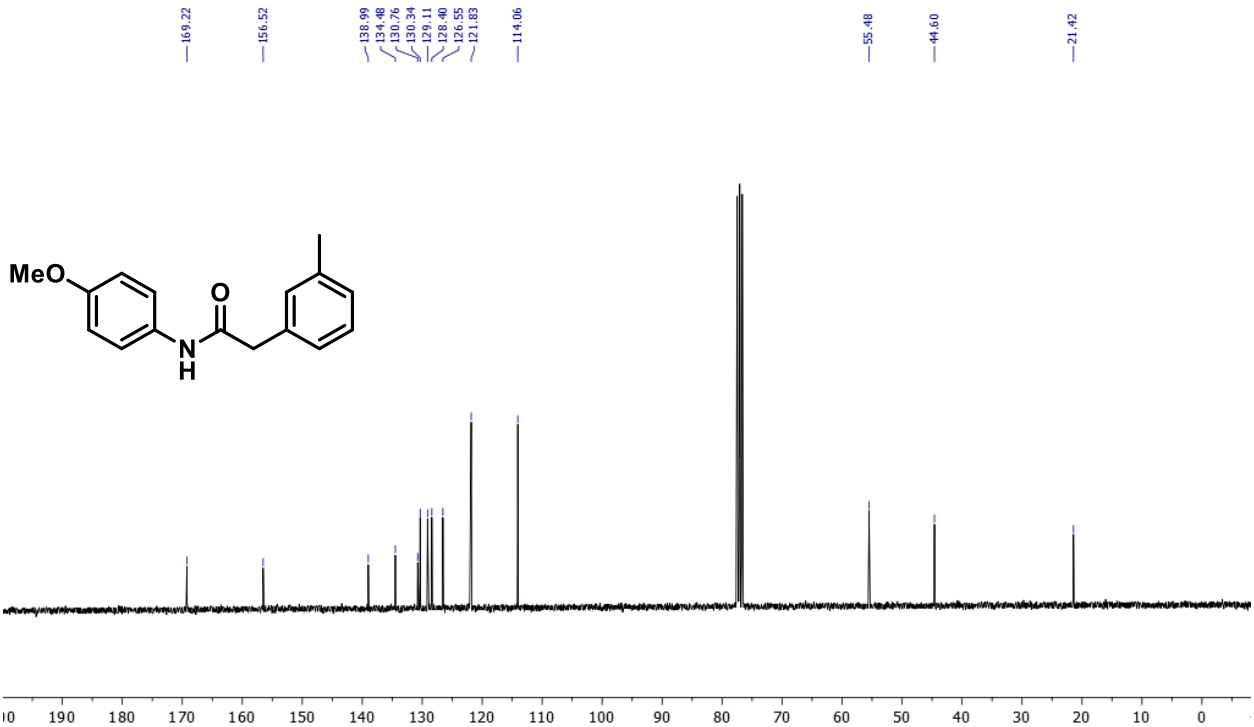
^{13}C NMR of Compound 5b (DMSO d_6; 125 MHz)



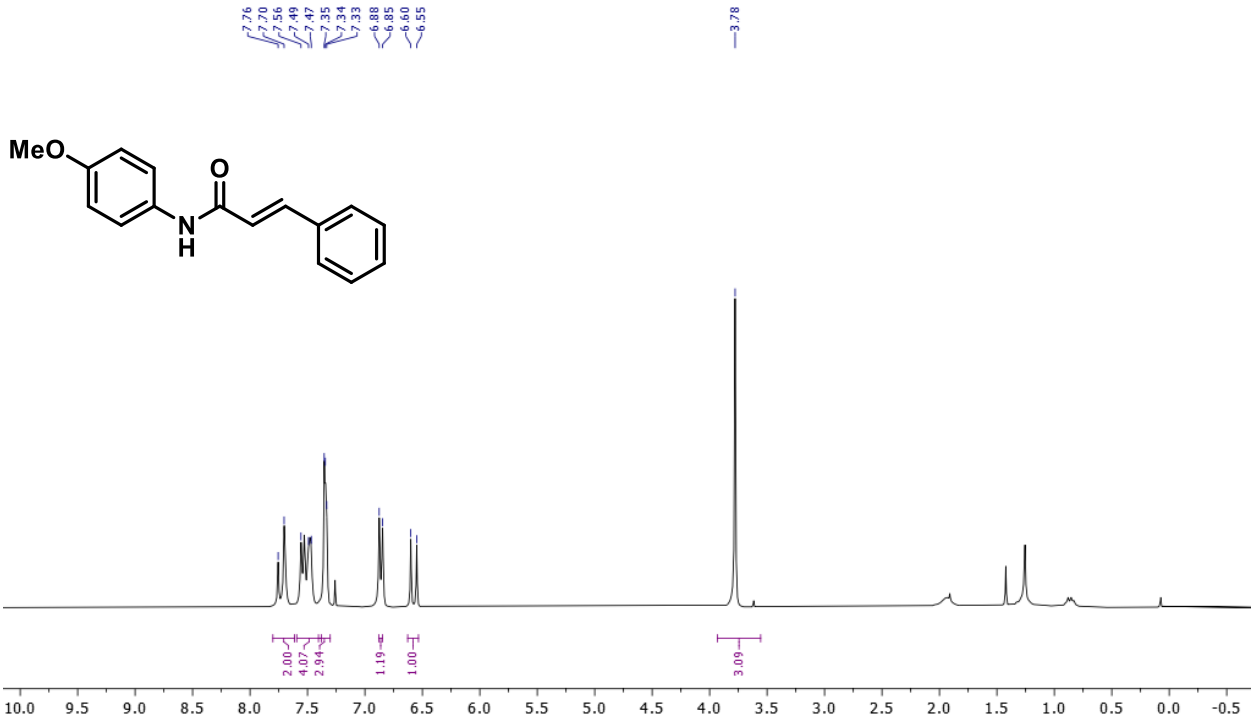
^{1}H NMR of Compound 5c ($CDCl_3$; 300 MHz)



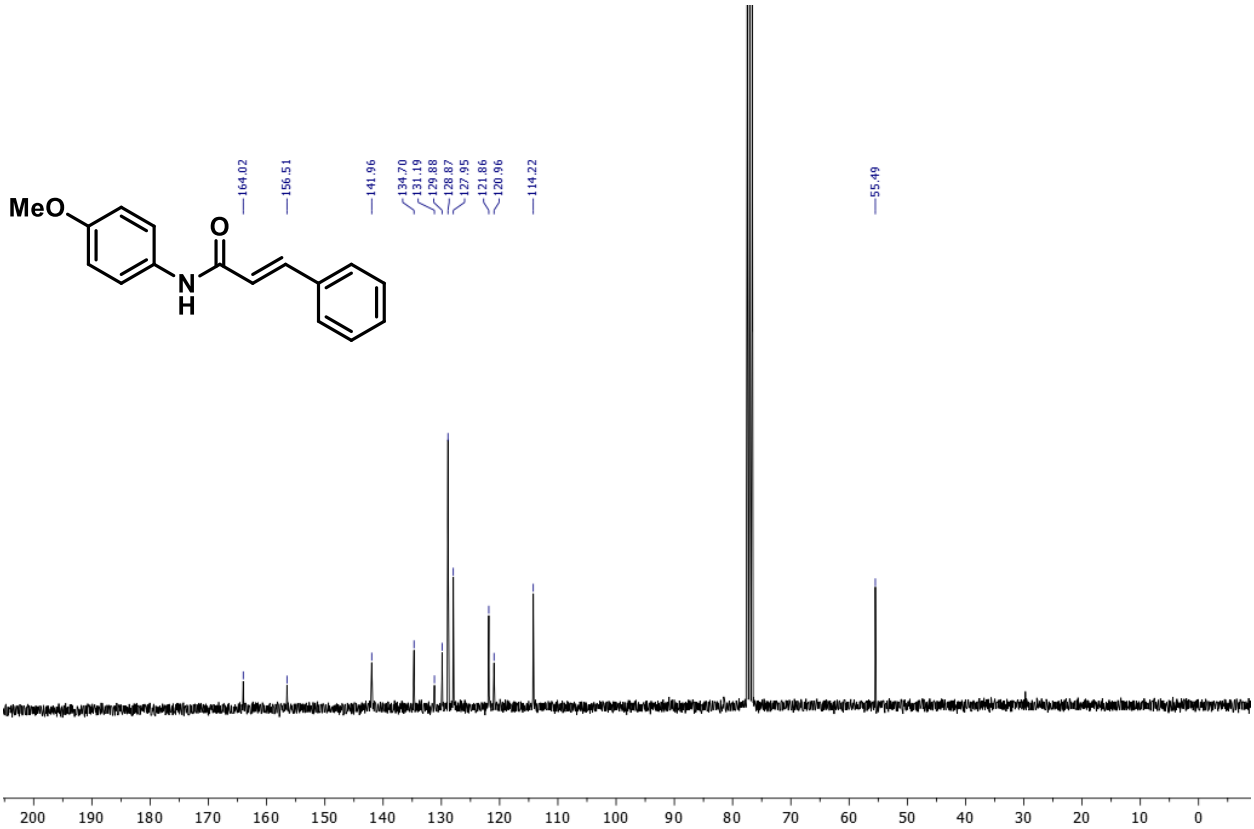
^{13}C NMR of Compound 5c ($CDCl_3$; 75 MHz)



^{1}H NMR of Compound 5d ($CDCl_3$; 300 MHz)

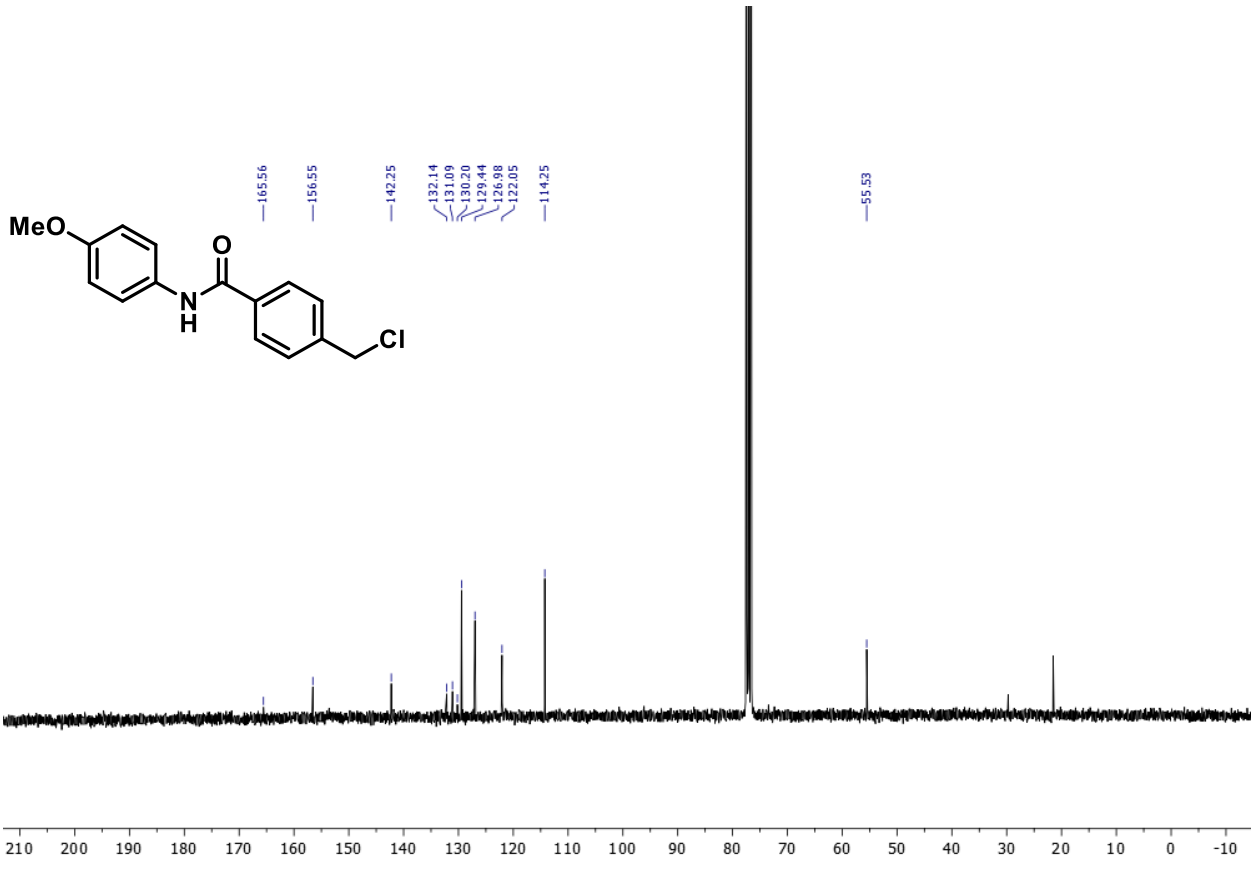


^{13}C NMR of Compound 5d ($CDCl_3$; 75 MHz)

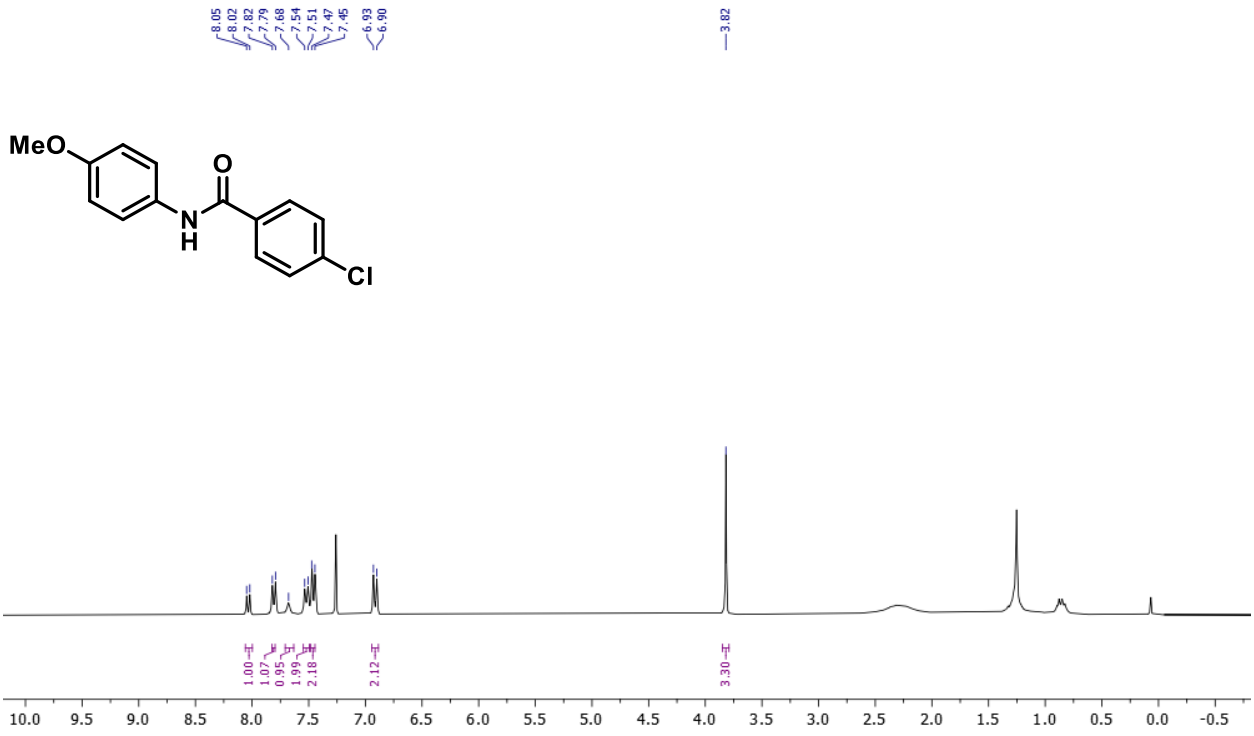


^{1}H NMR of Compound 5e ($CDCl_3$; 300 MHz)

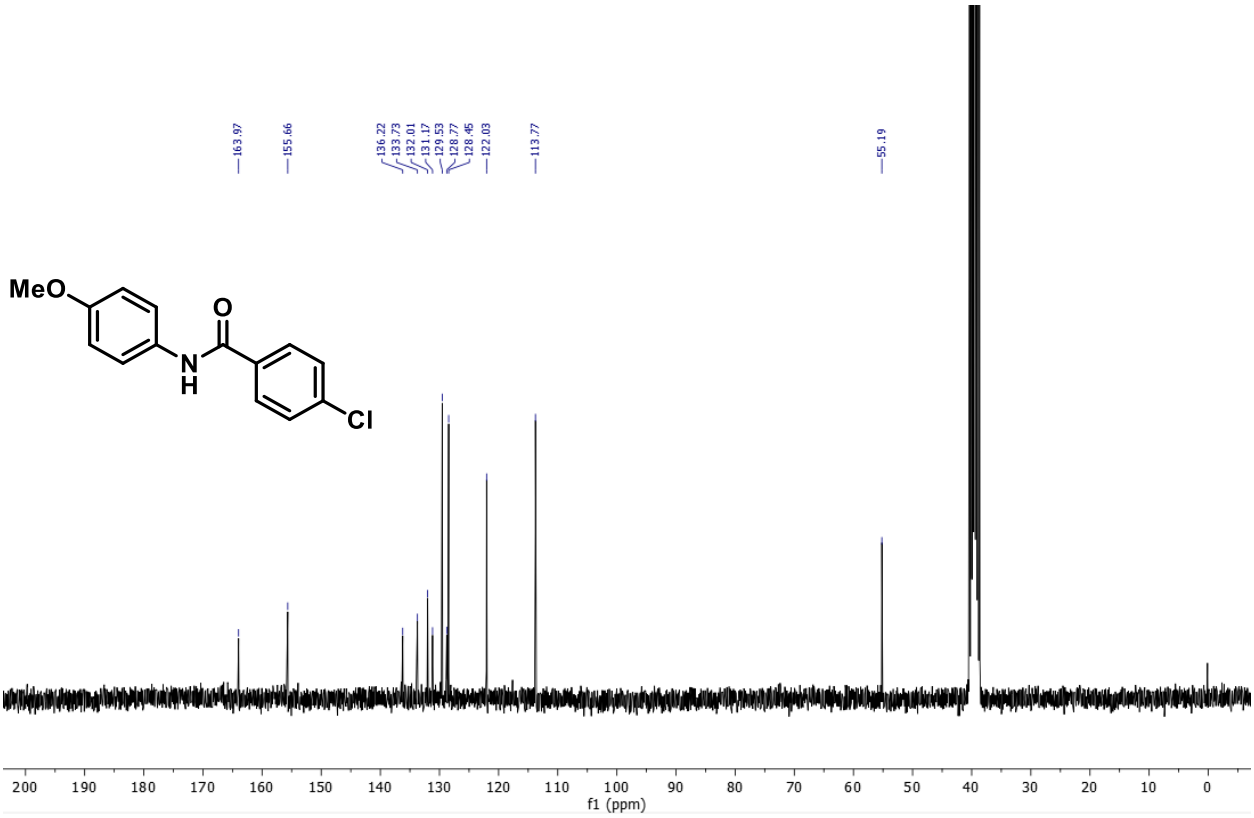
^{13}C NMR of Compound 5e ($CDCl_3$; 75 MHz)



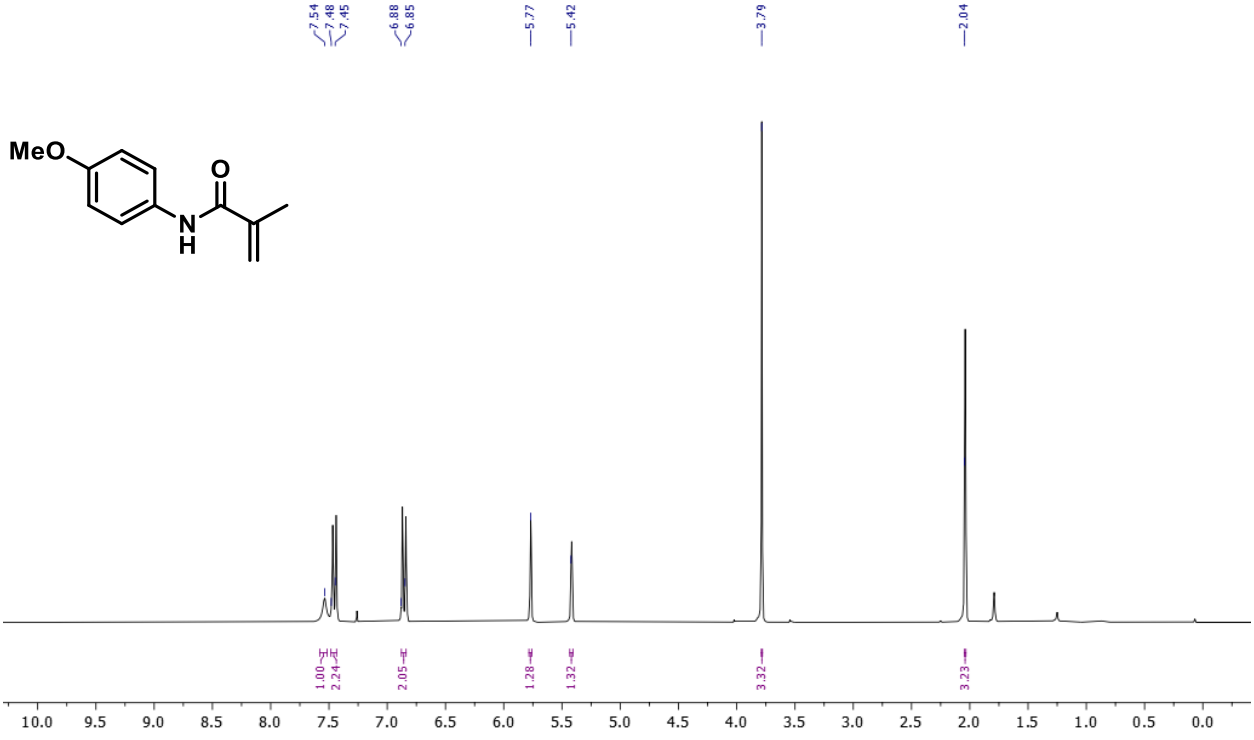
^{1}H NMR of Compound 5f ($CDCl_3$; 300 MHz)



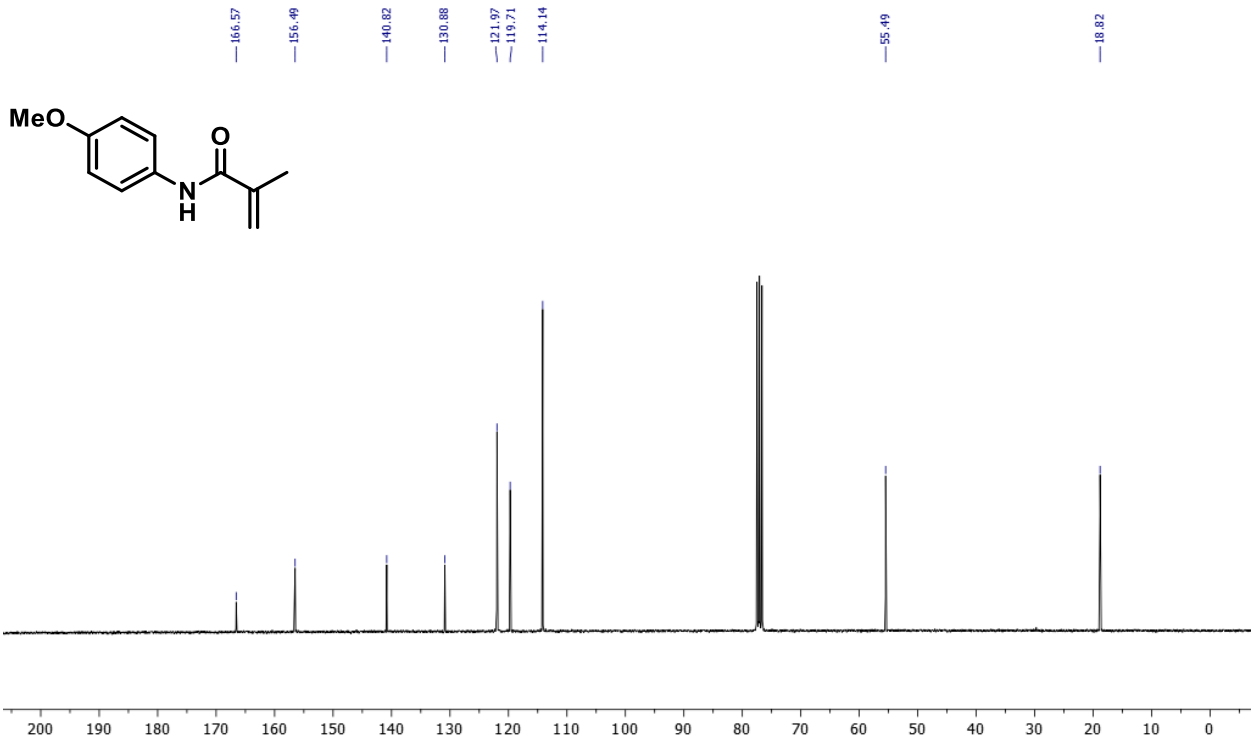
^{13}C NMR of Compound 5f (DMSO d_6; 75 MHz)



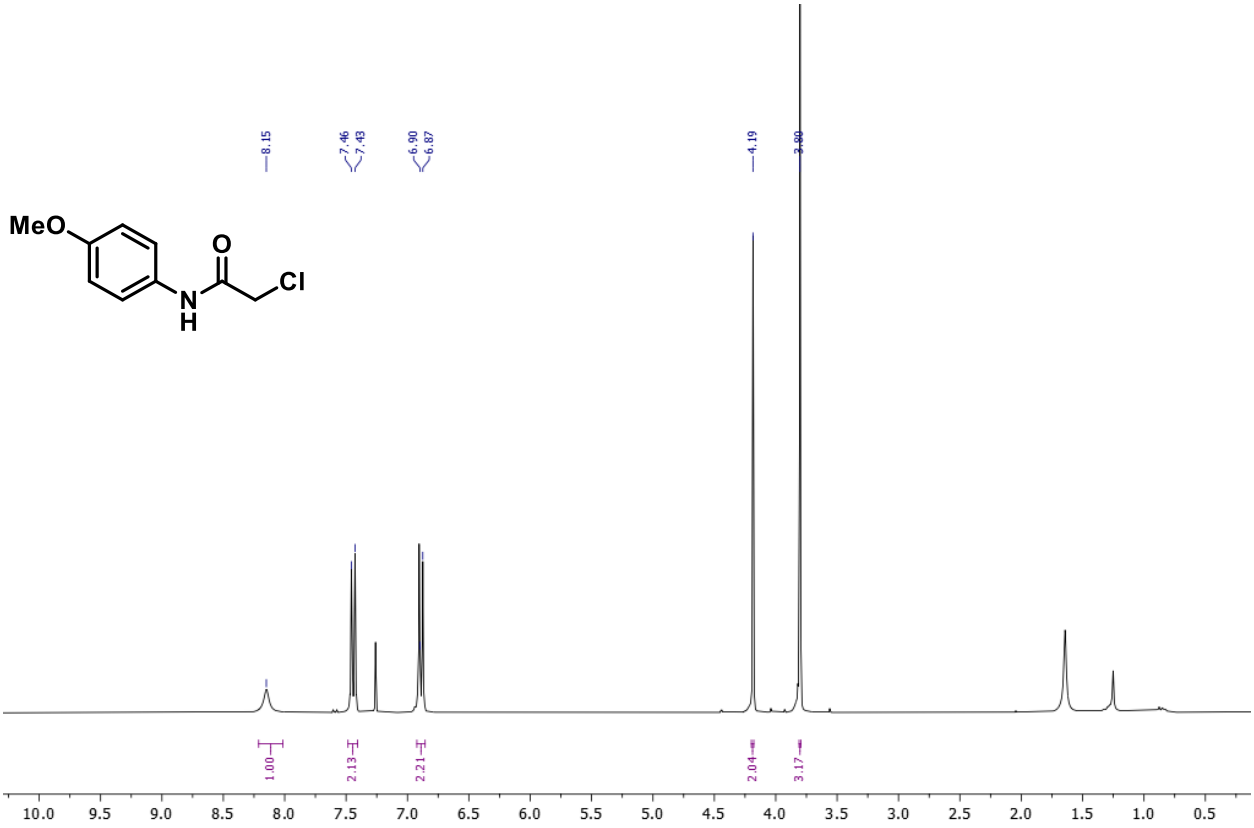
^{1}H NMR of Compound 5g ($CDCl_3$; 300 MHz)



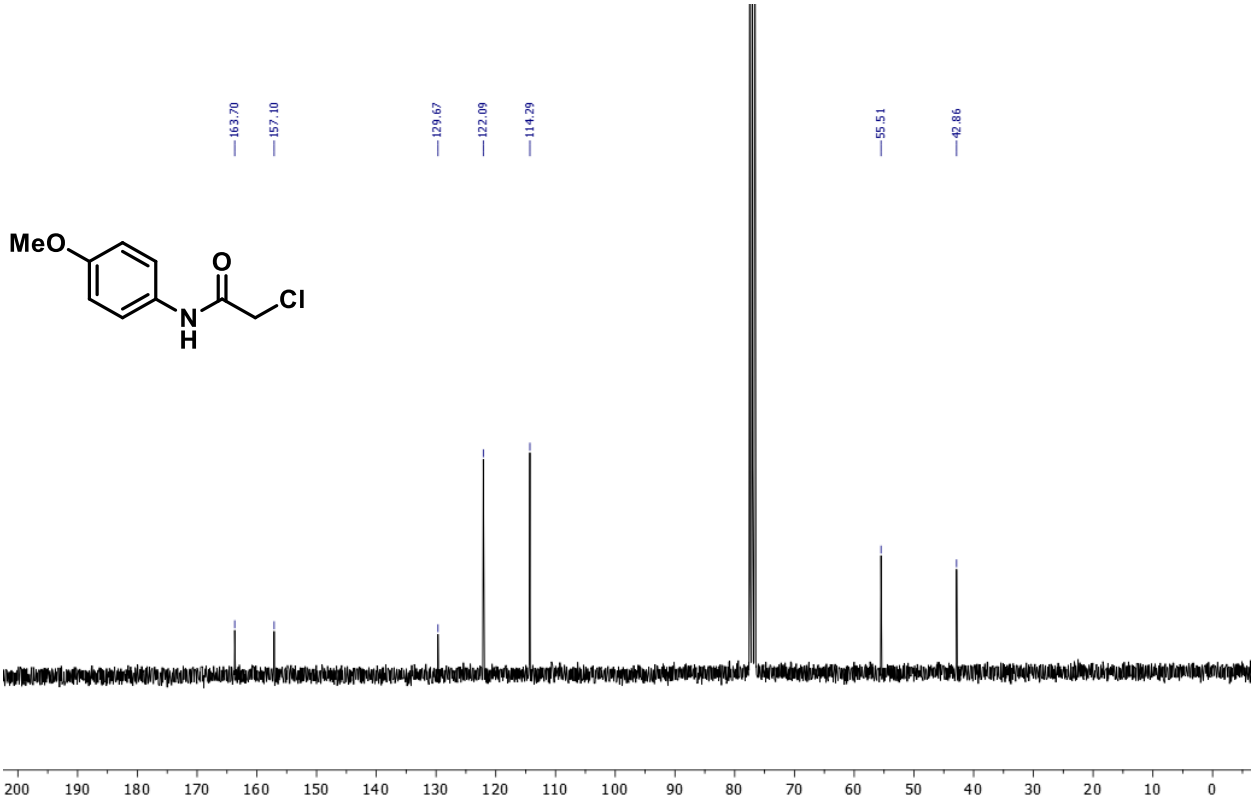
^{13}C NMR of Compound 5g ($CDCl_3$; 75 MHz)



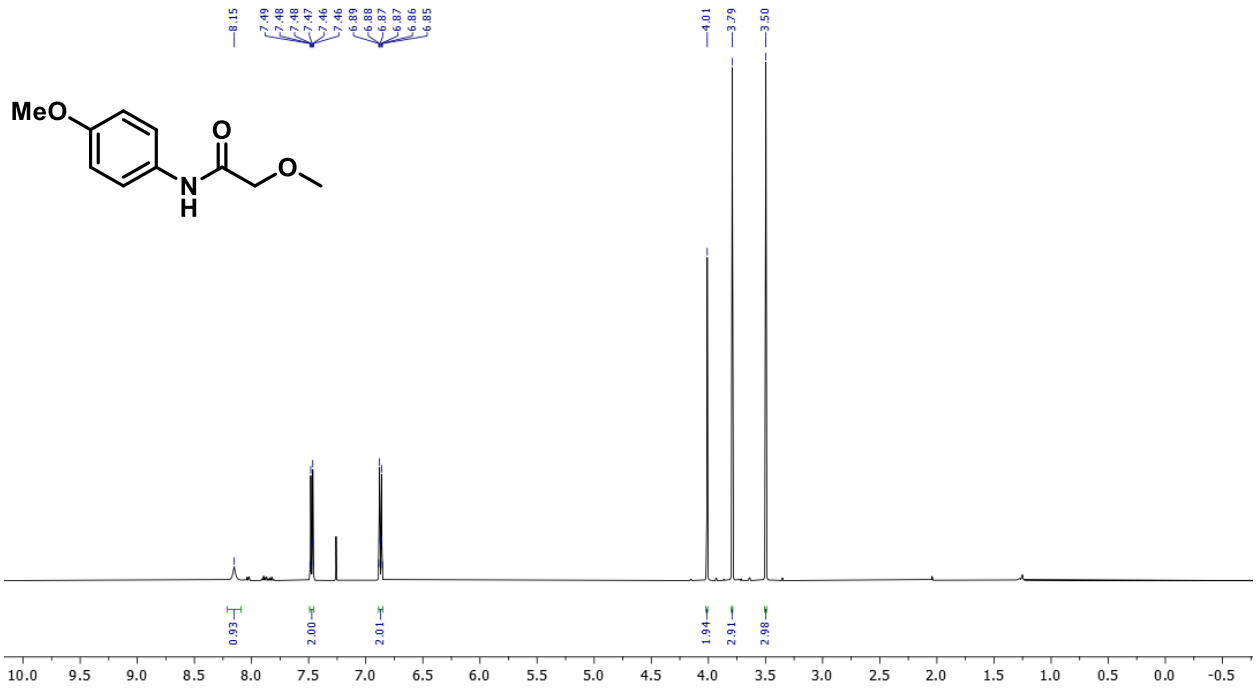
^{1}H NMR of Compound 5h ($CDCl_3$; 300 MHz)



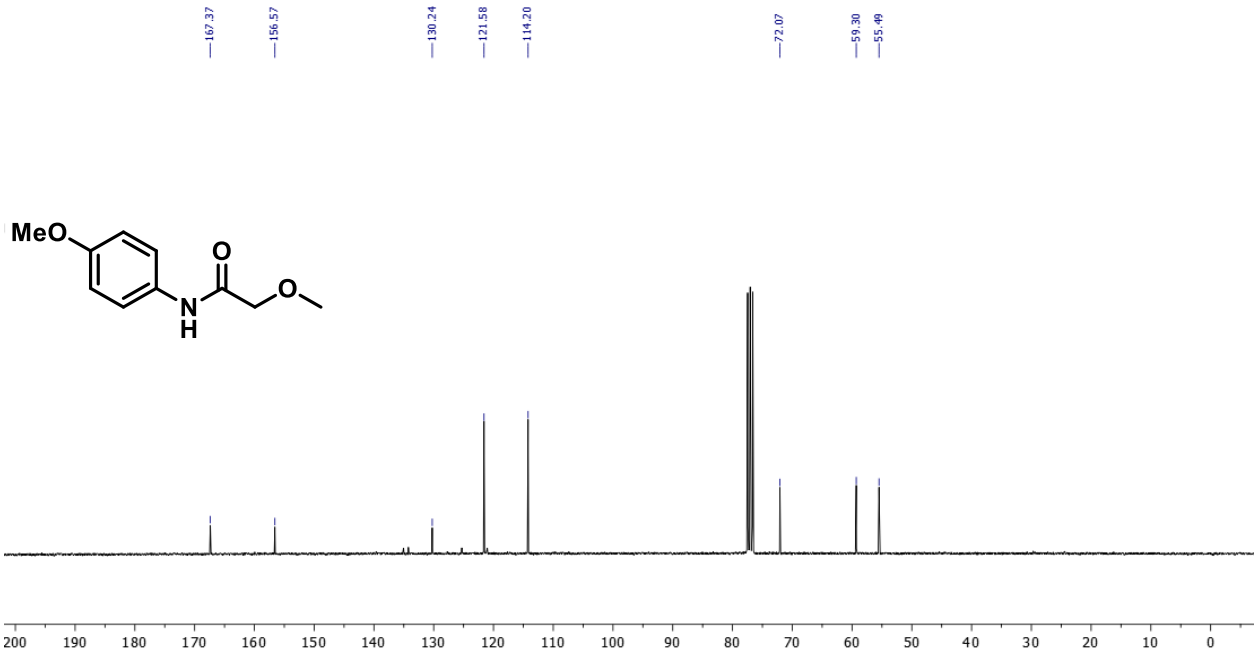
^{13}C NMR of Compound 5h ($CDCl_3$; 75 MHz)



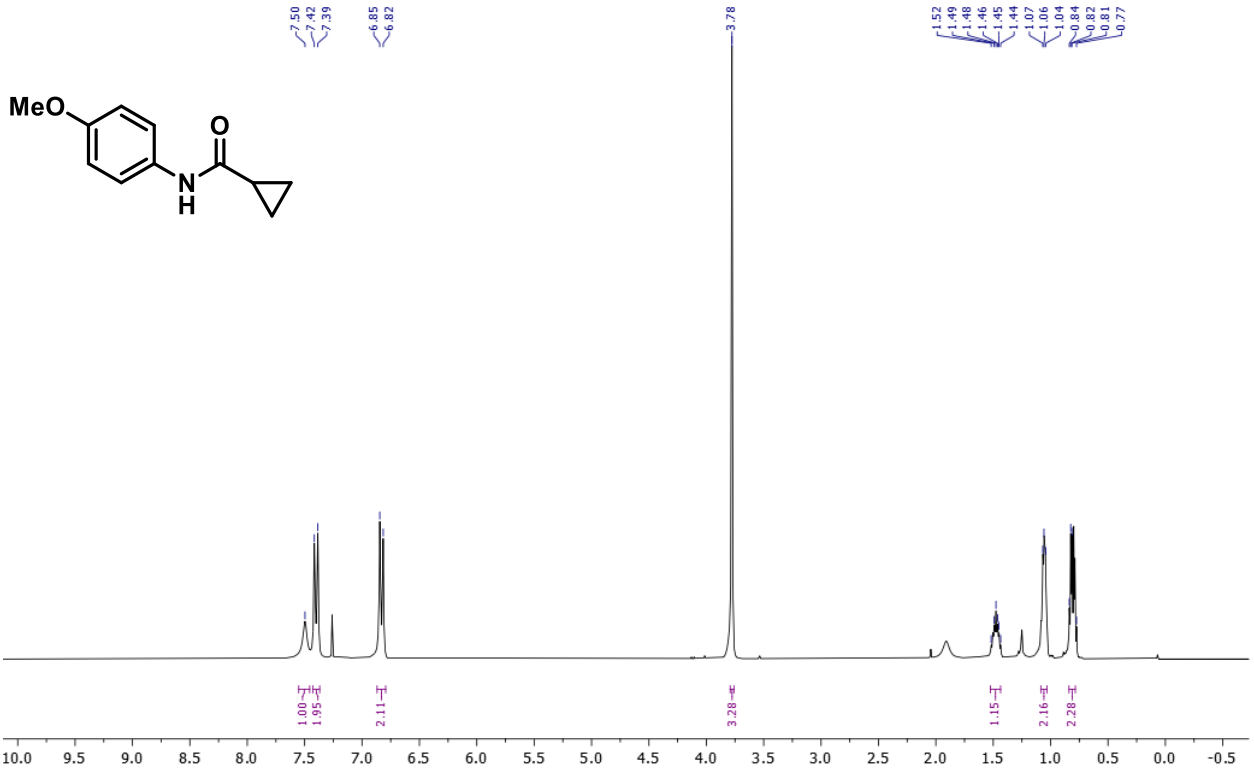
^{1}H NMR of Compound 5l ($CDCl_3$; 300 MHz)



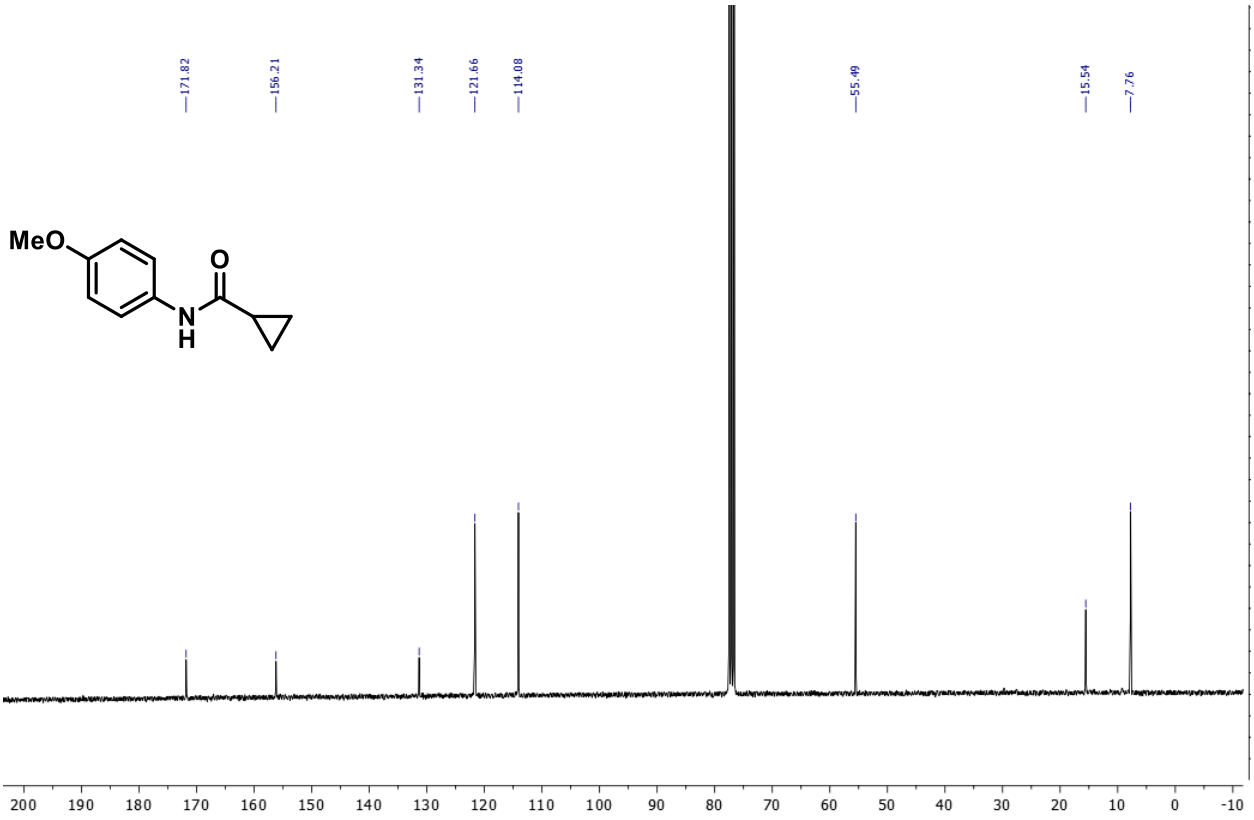
^{13}C NMR of Compound 5l ($CDCl_3$; 75 MHz)



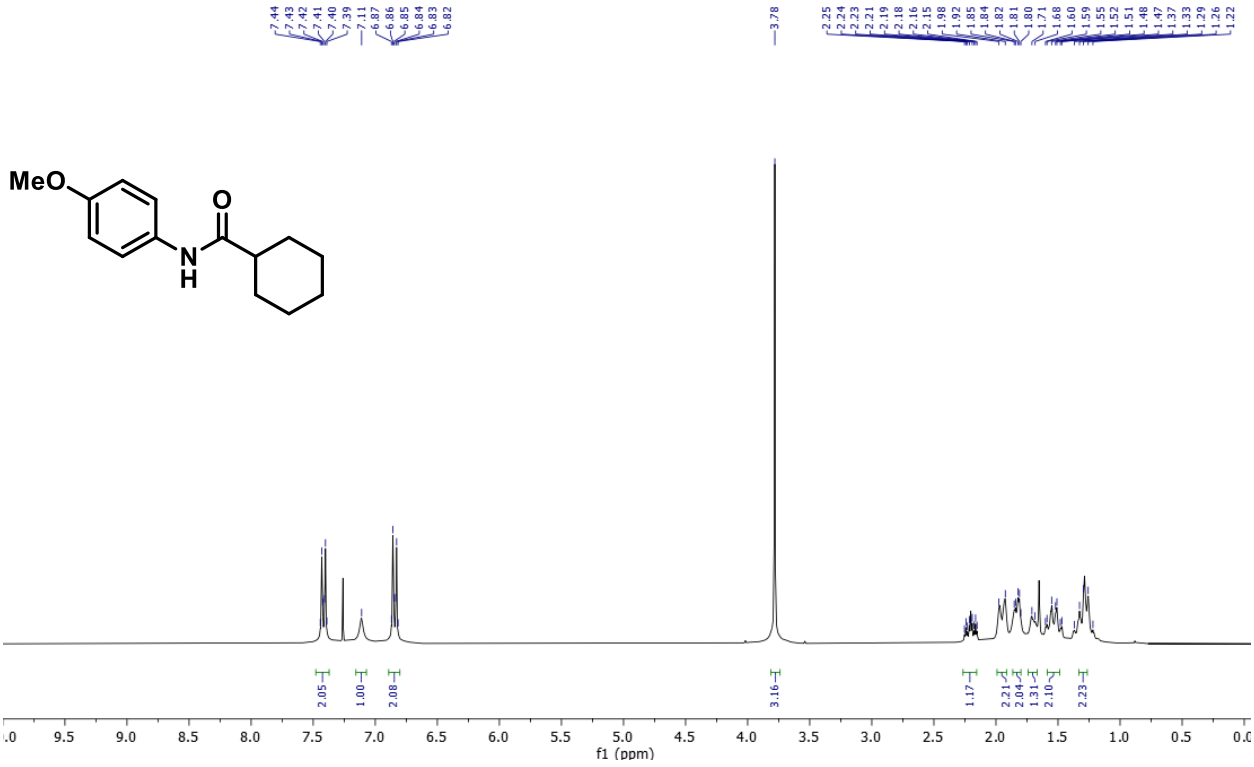
^{1}H NMR of Compound 5j ($CDCl_3$; 300 MHz)



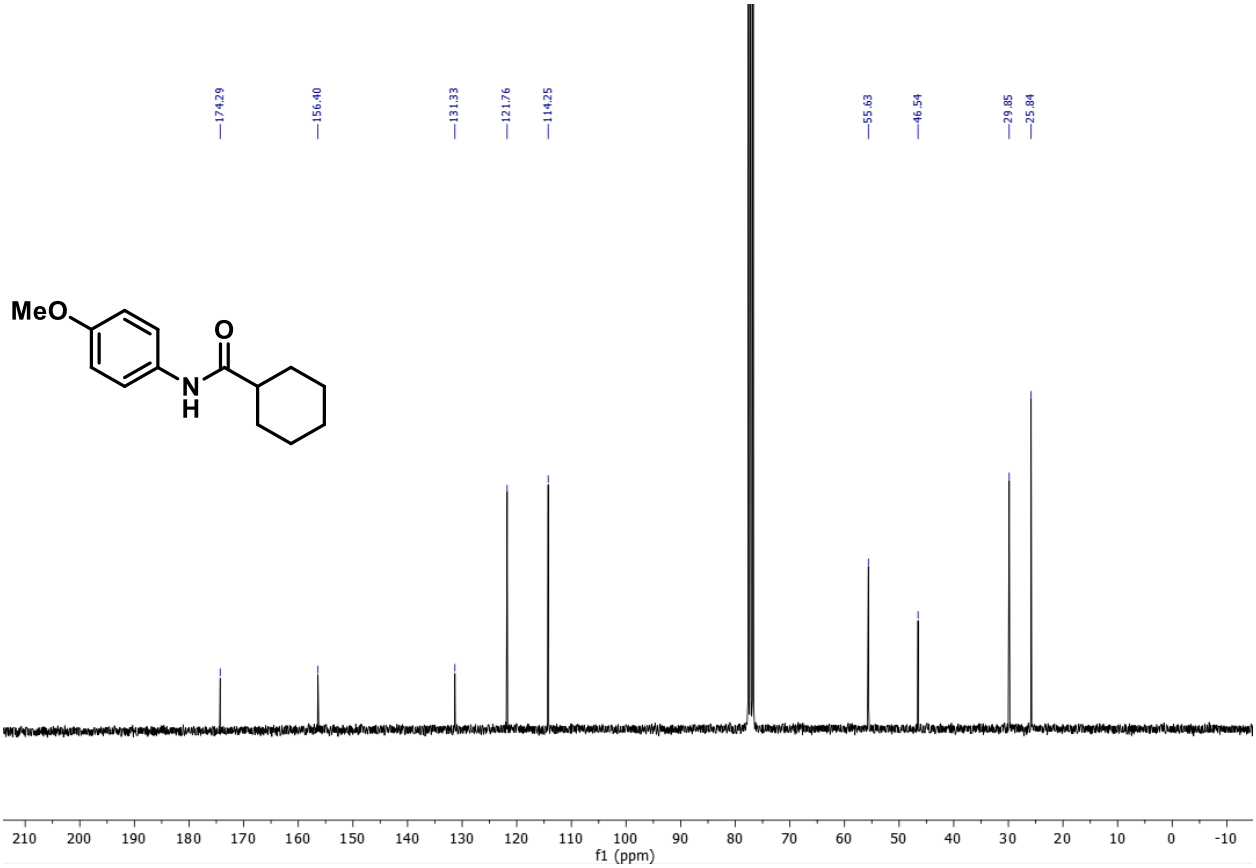
^{13}C NMR of Compound 5j ($CDCl_3$; 75 MHz)



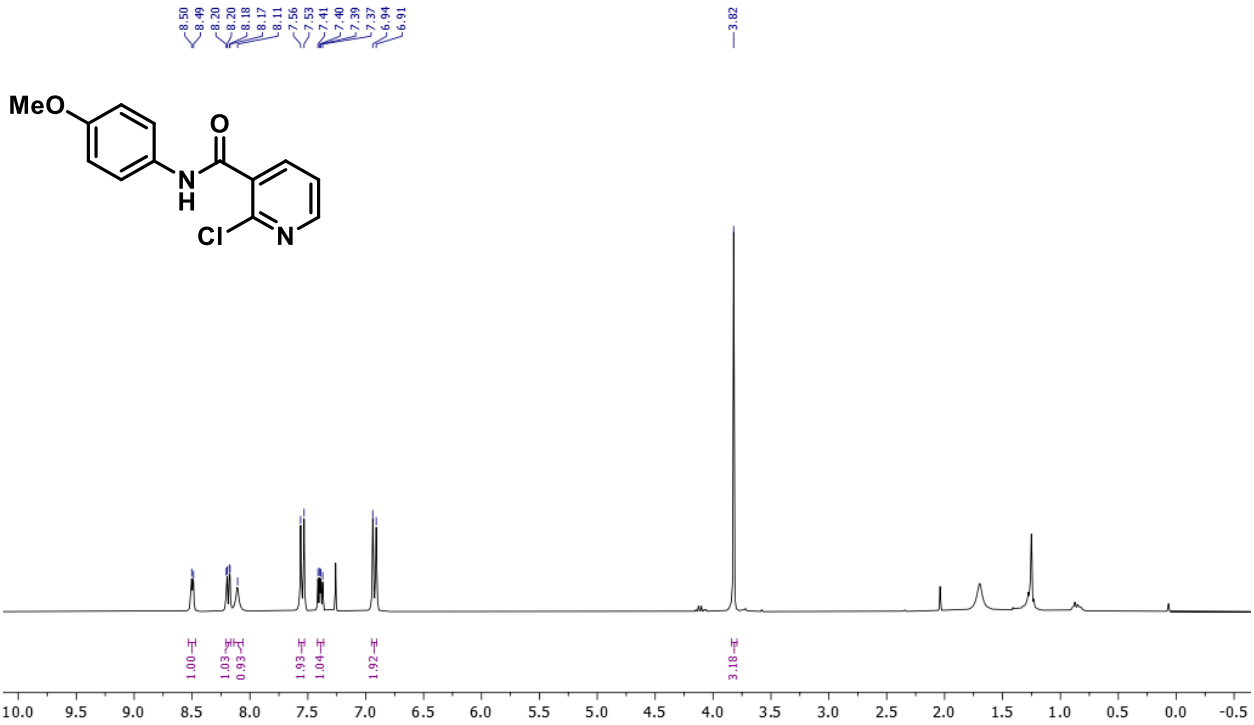
^{1}H NMR of Compound 5k ($CDCl_3$; 300 MHz)



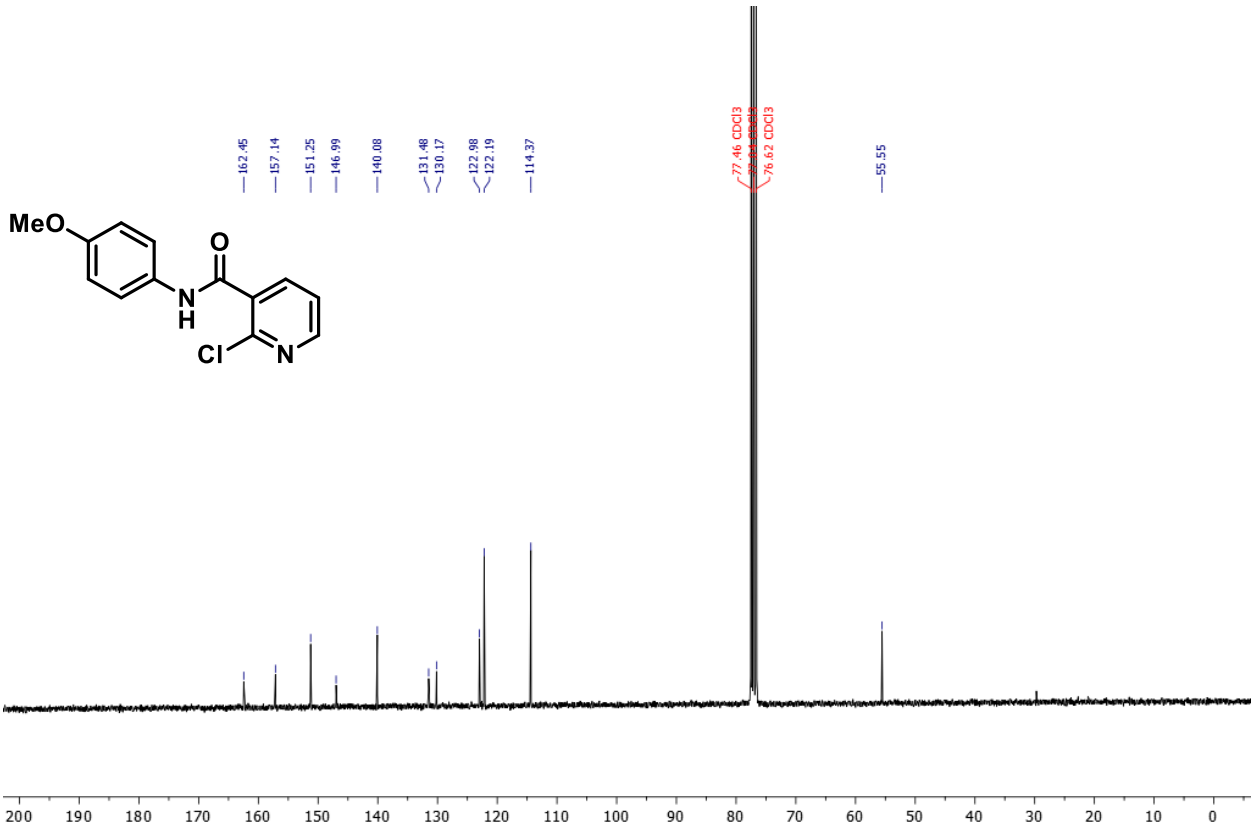
^{13}C NMR of Compound 5k ($CDCl_3$; 75 MHz)



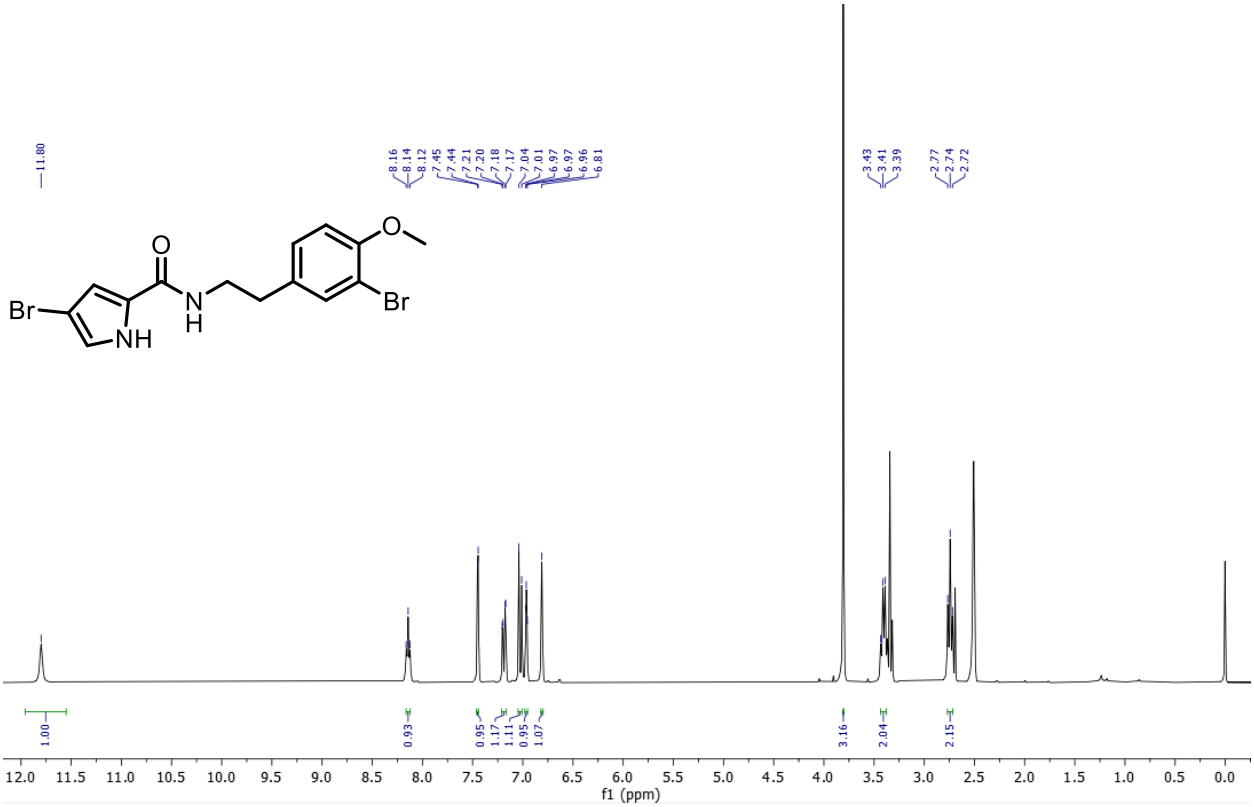
^{1}H NMR of Compound 5l ($CDCl_3$; 300 MHz)



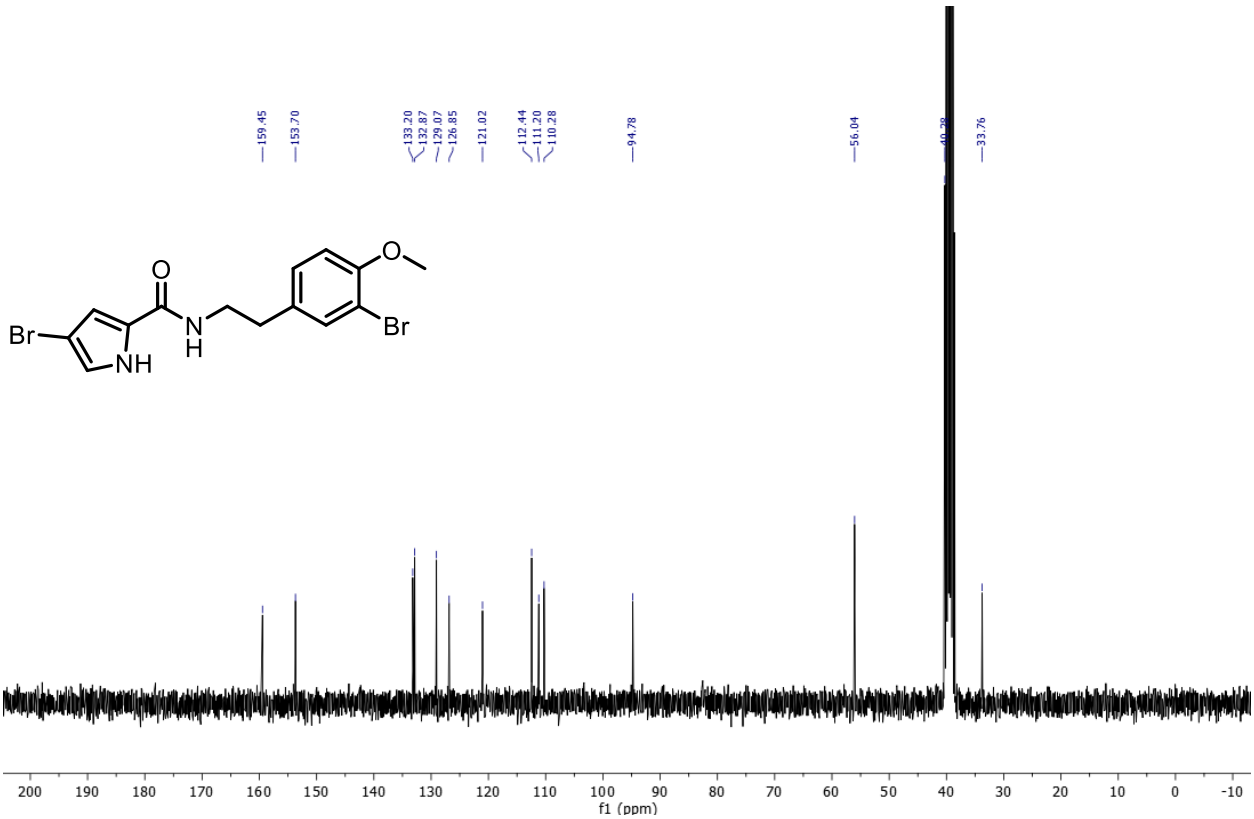
^{13}C NMR of Compound 5l ($CDCl_3$; 75 MHz)



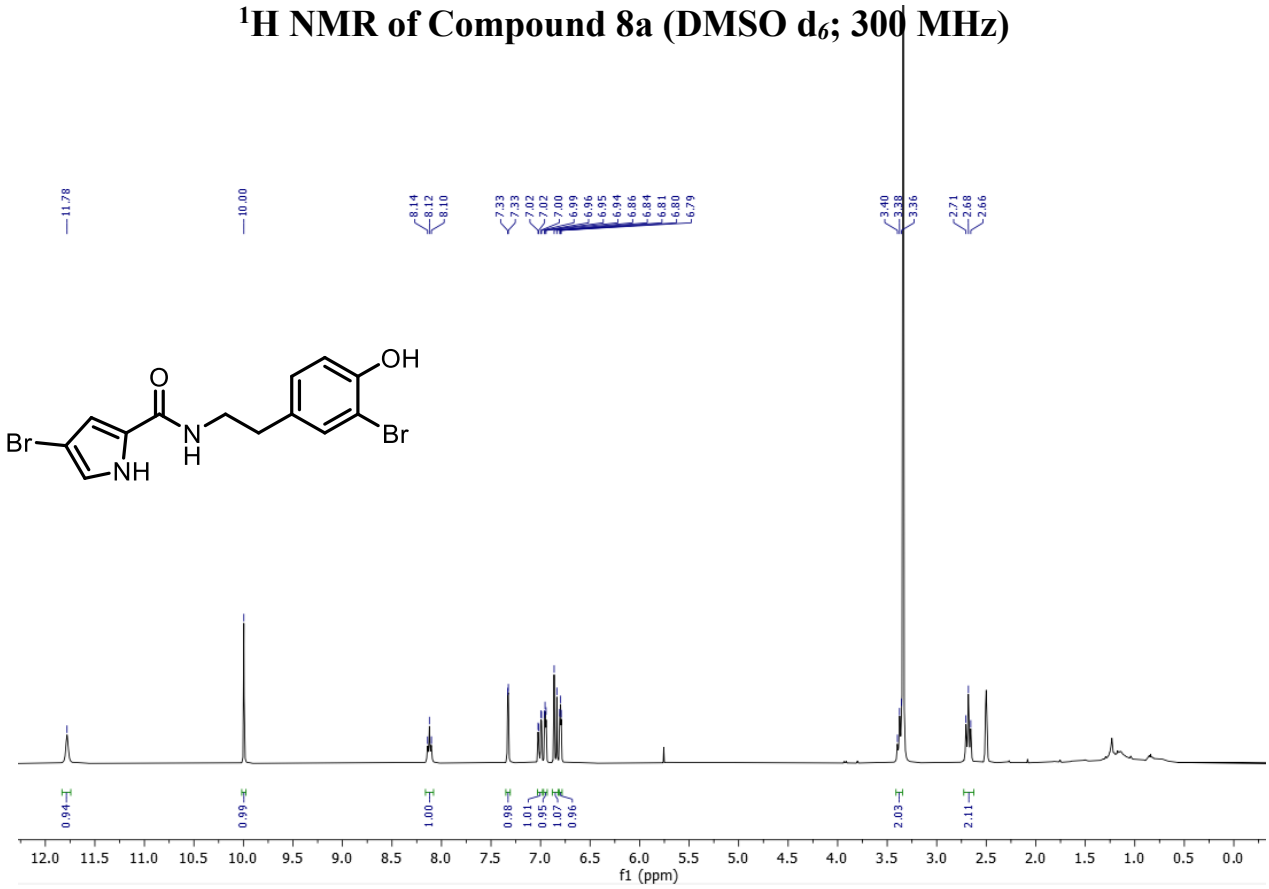
^{1}H NMR of Compound 8 (DMSO d_6; 300 MHz)



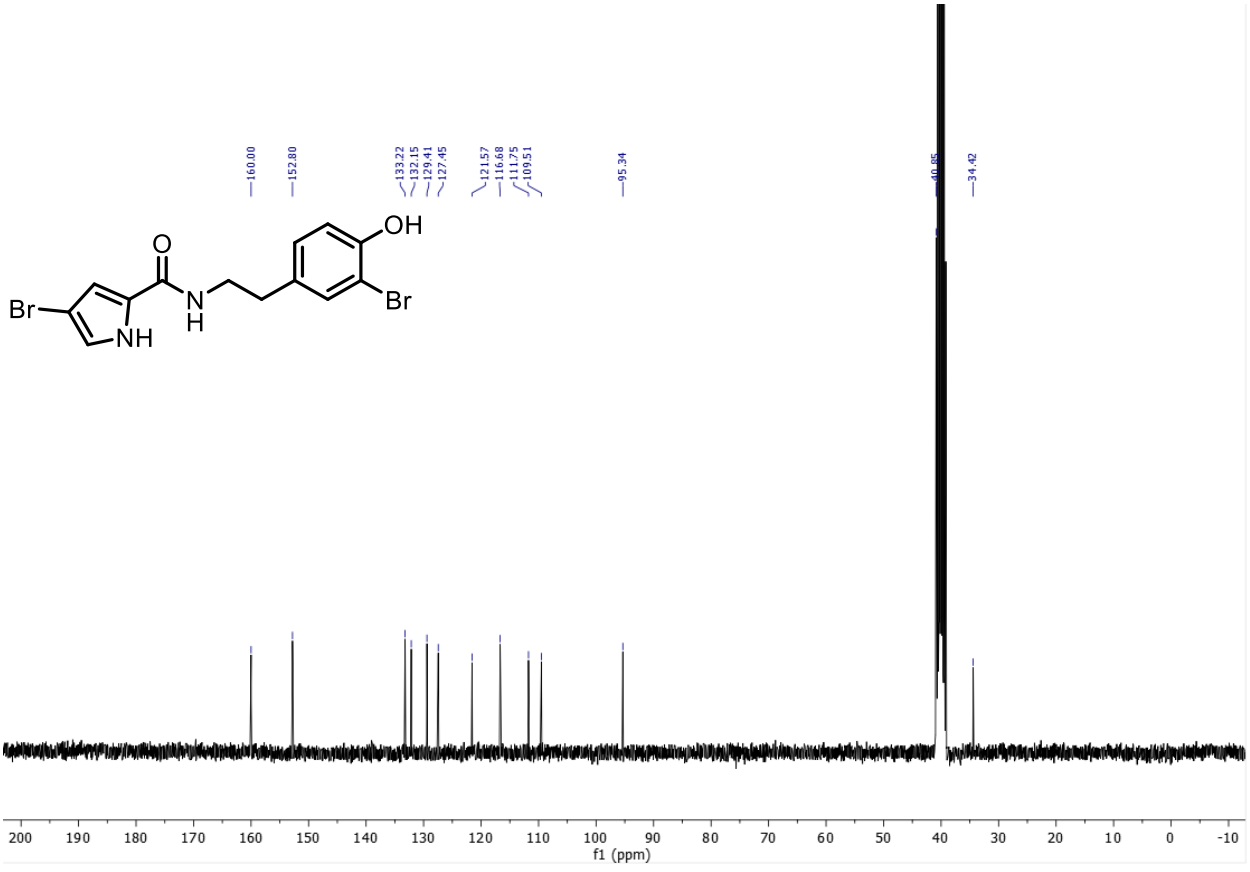
^{13}C NMR of Compound 8 (DMSO d_6; 75 MHz)



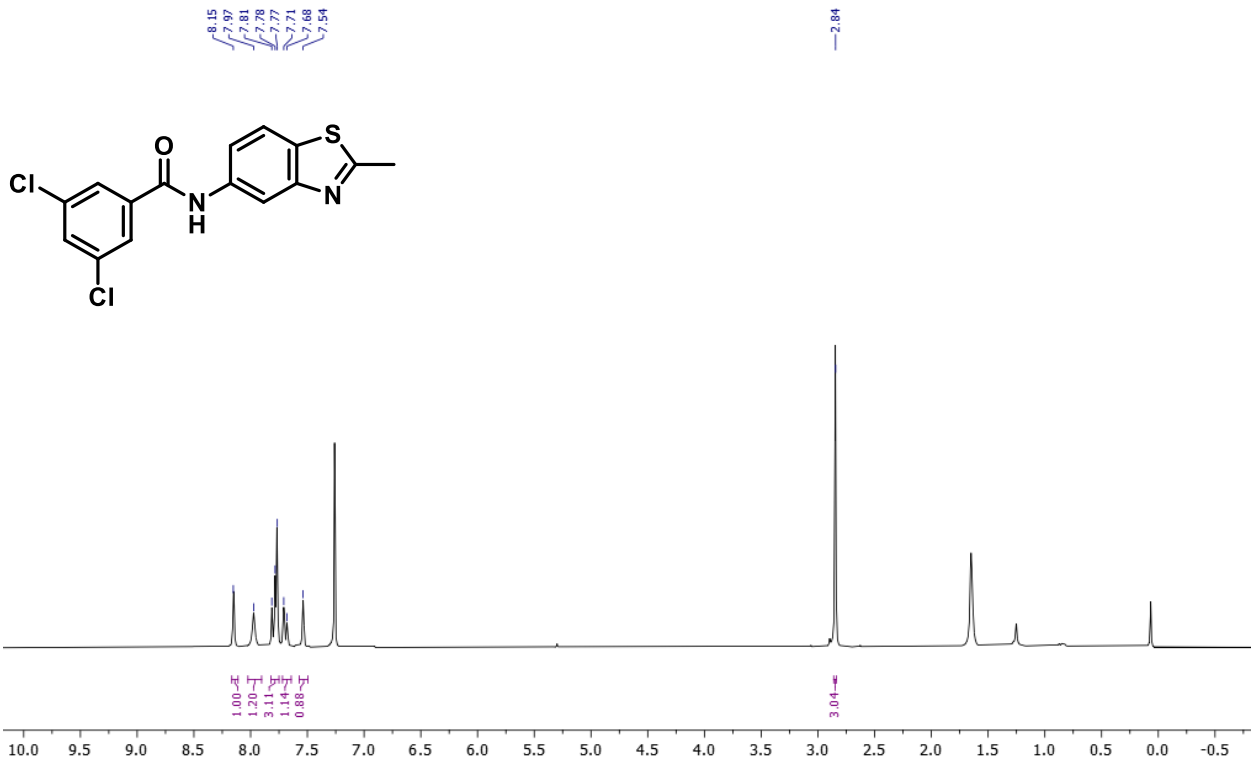
^{1}H NMR of Compound 8a (DMSO d_6; 300 MHz)



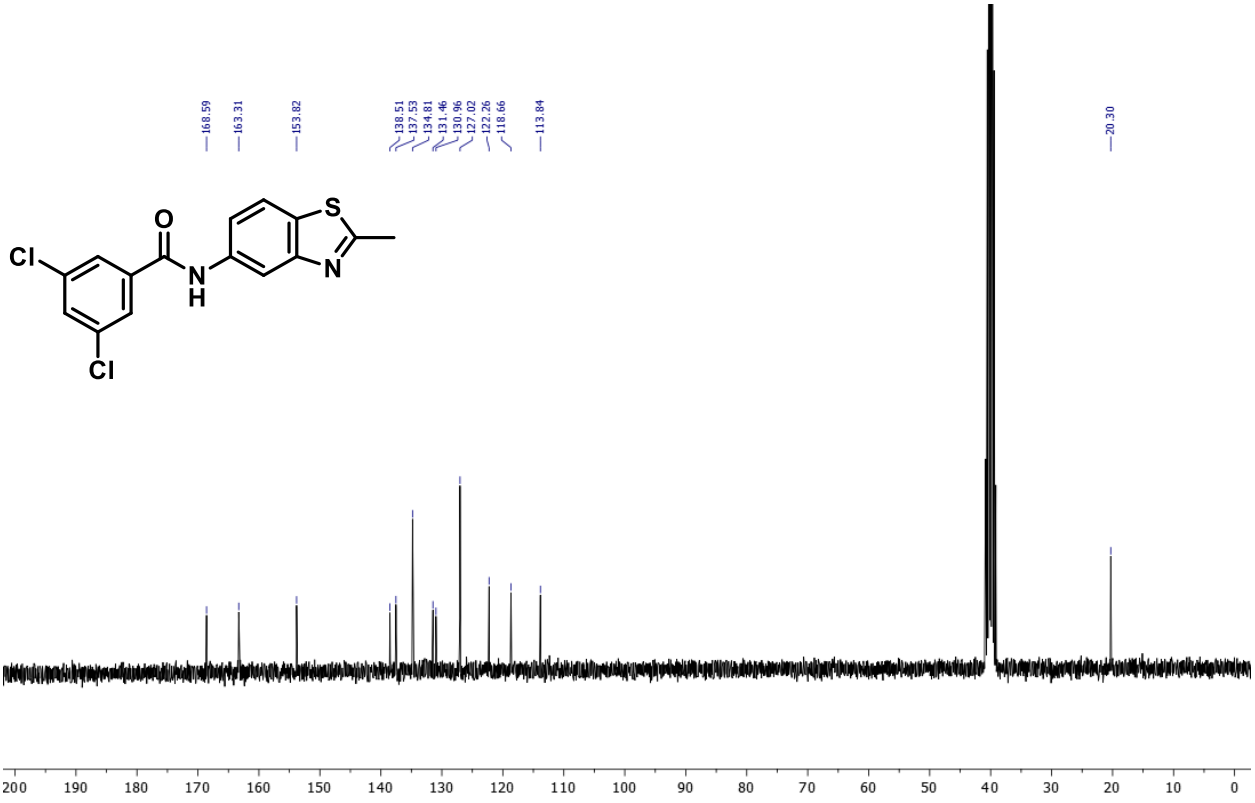
^{13}C NMR of Compound 8a (DMSO d_6; 75 MHz)



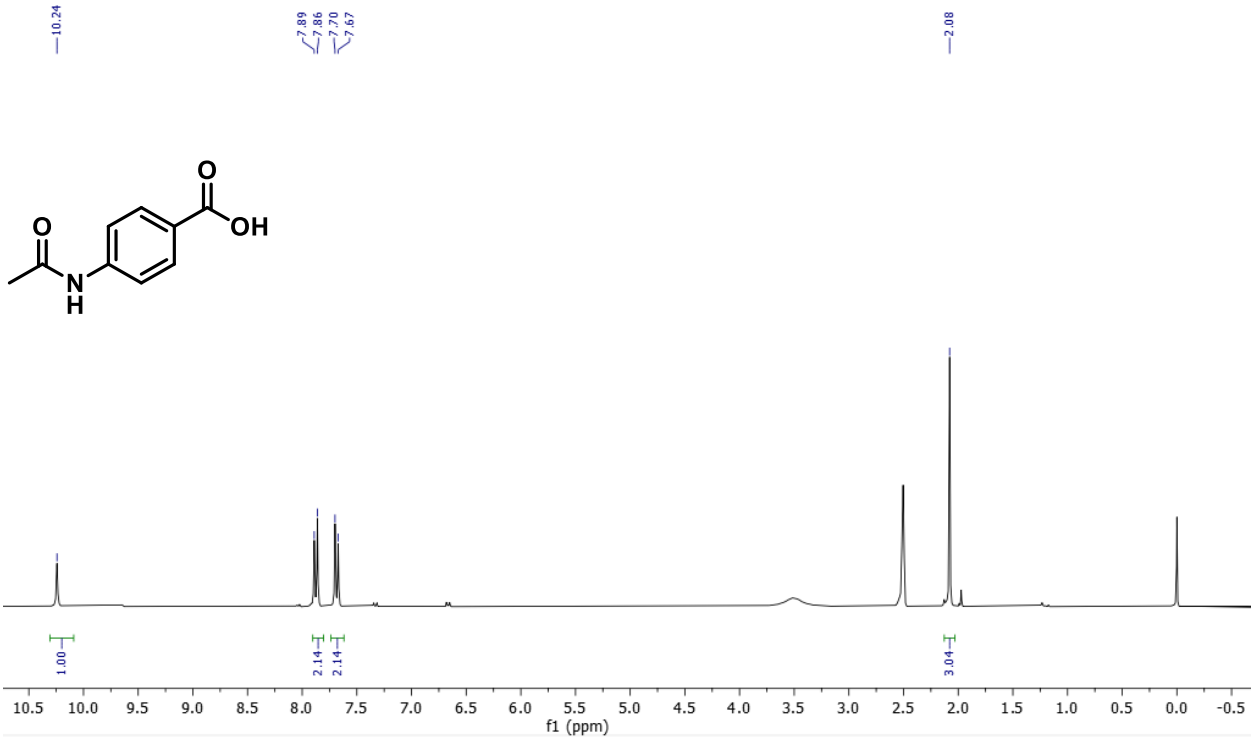
^{1}H NMR of Compound 10 ($CDCl_3$; 300 MHz)



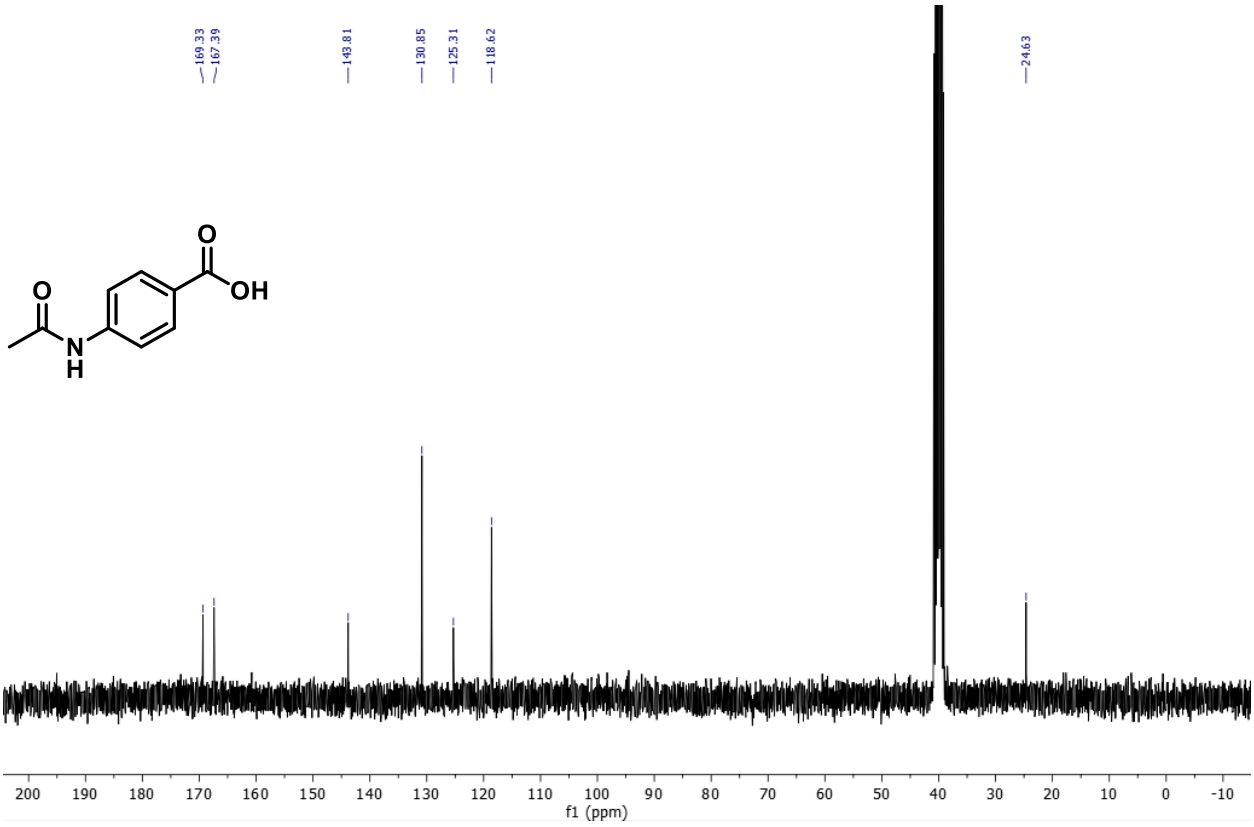
^{13}C NMR of Compound 10 (DMSO d_6; 75 MHz)



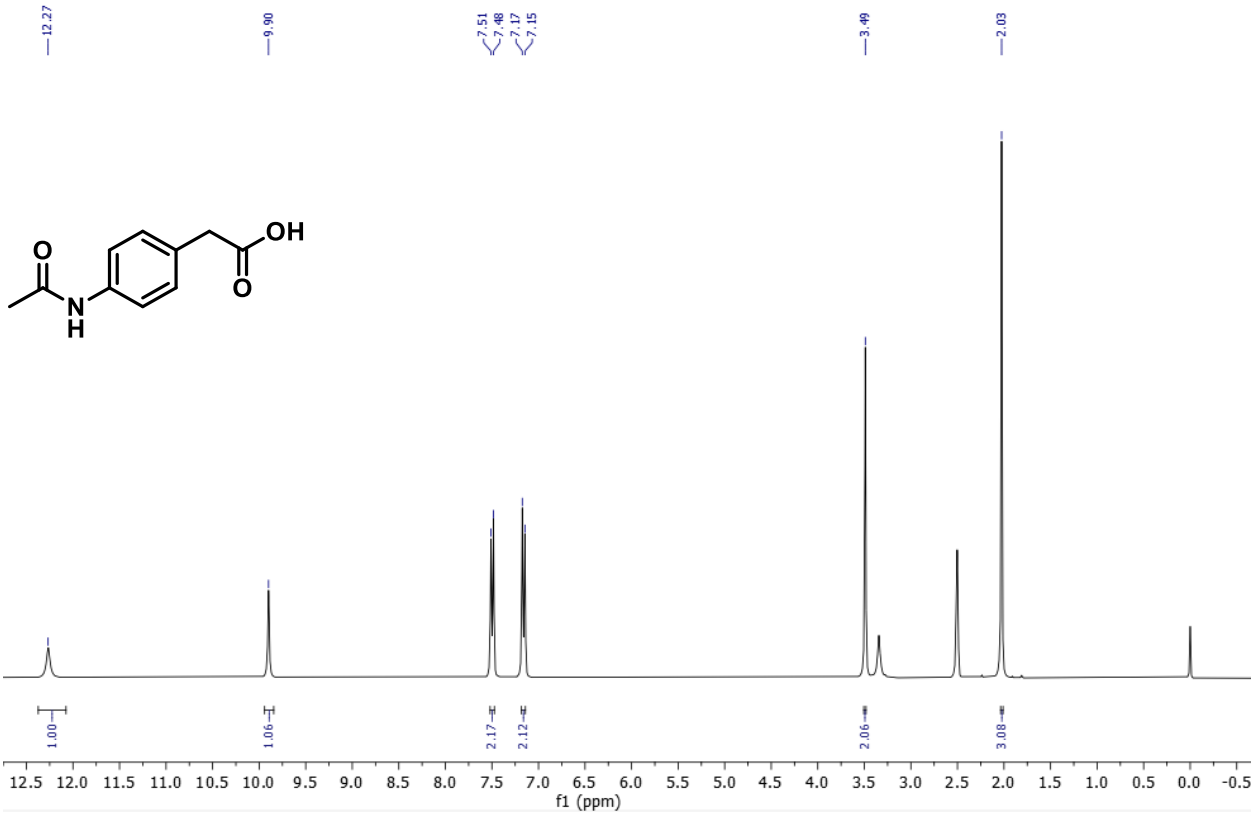
^{1}H NMR of Compound 11 (DMSO d_6; 300 MHz)



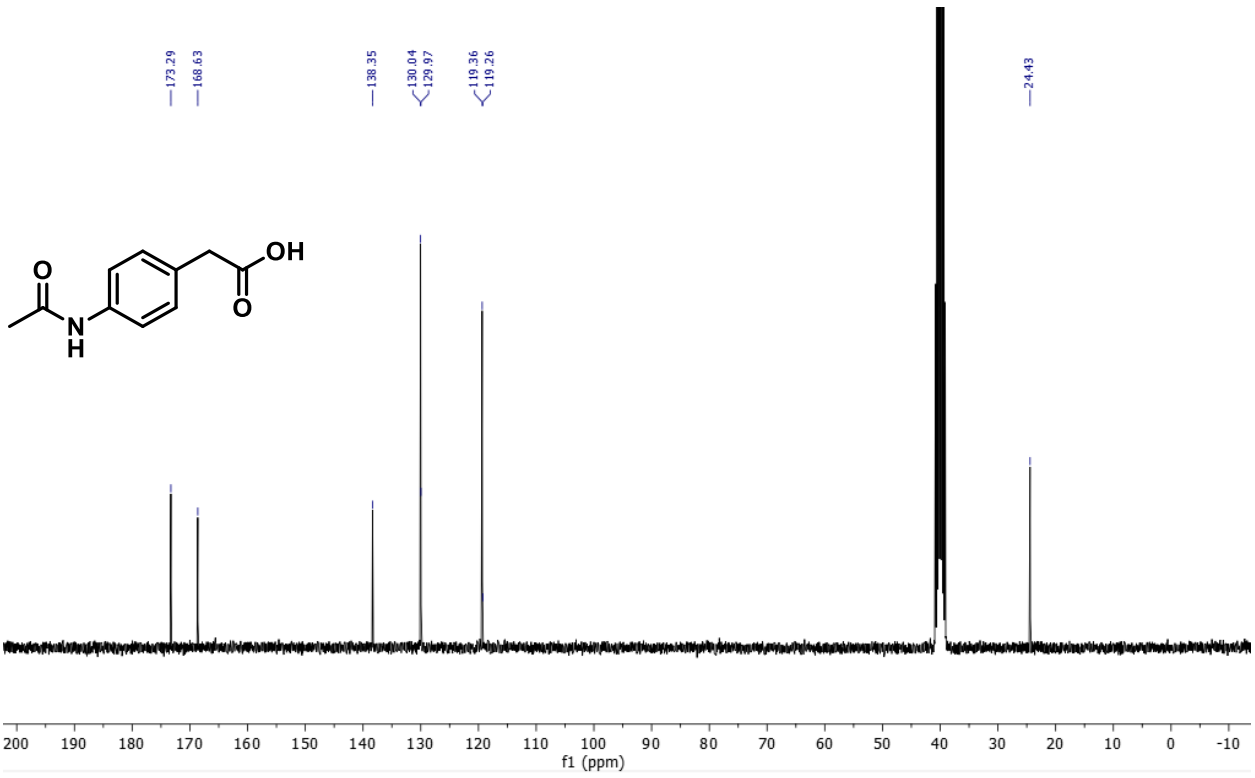
^{13}C NMR of Compound 11 (DMSO d_6; 76 MHz)



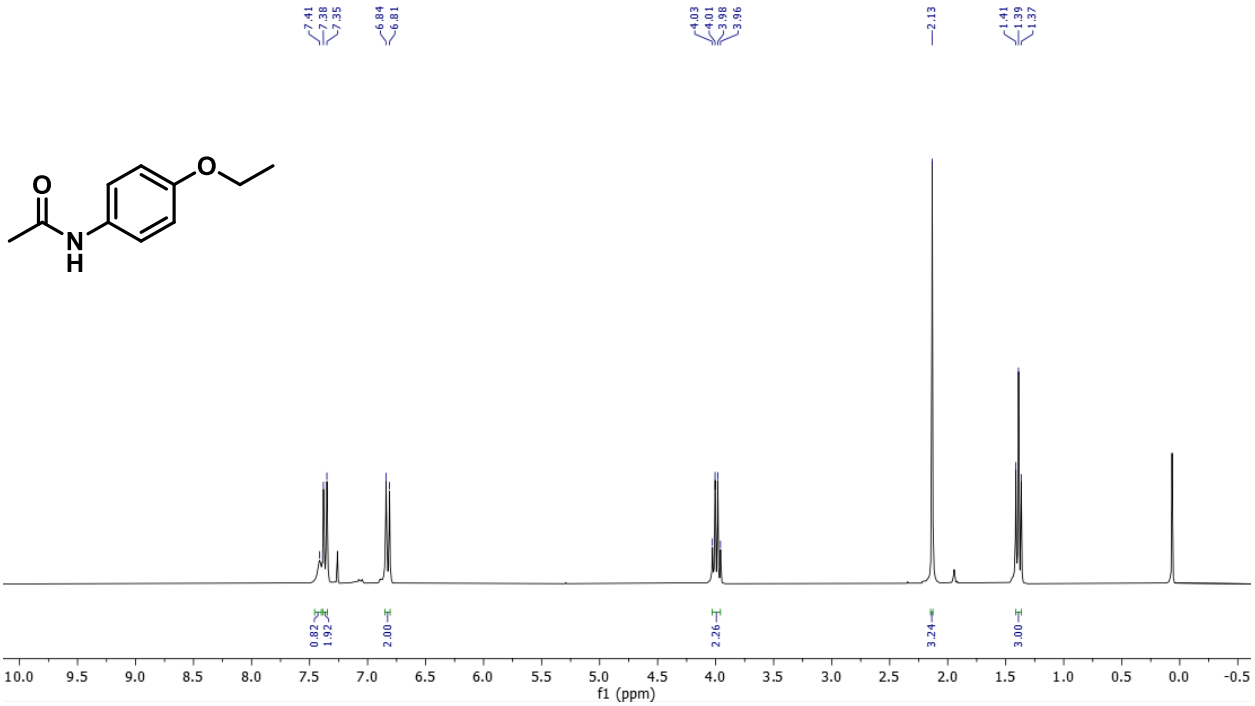
^{1}H NMR of Compound 12 (DMSO d_6; 300 MHz)



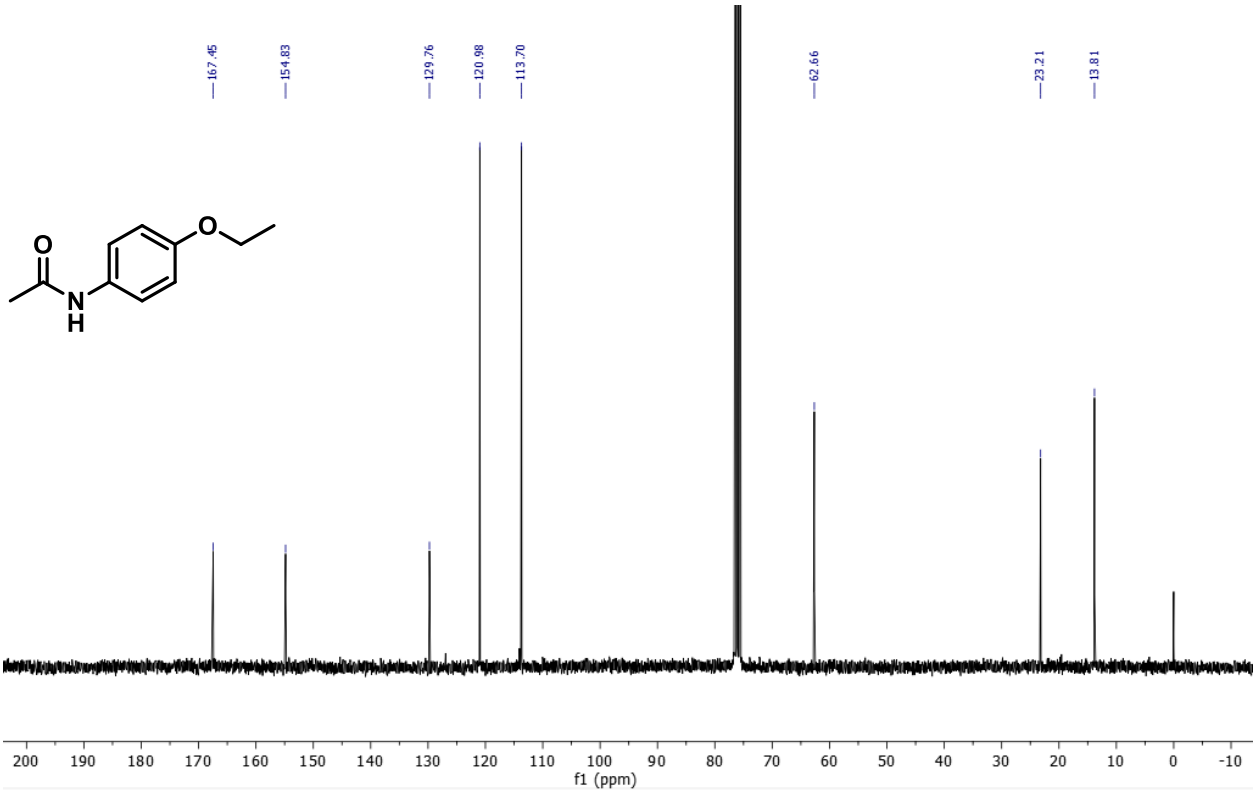
^{13}C NMR of Compound 12 (DMSO d_6; 75 MHz)



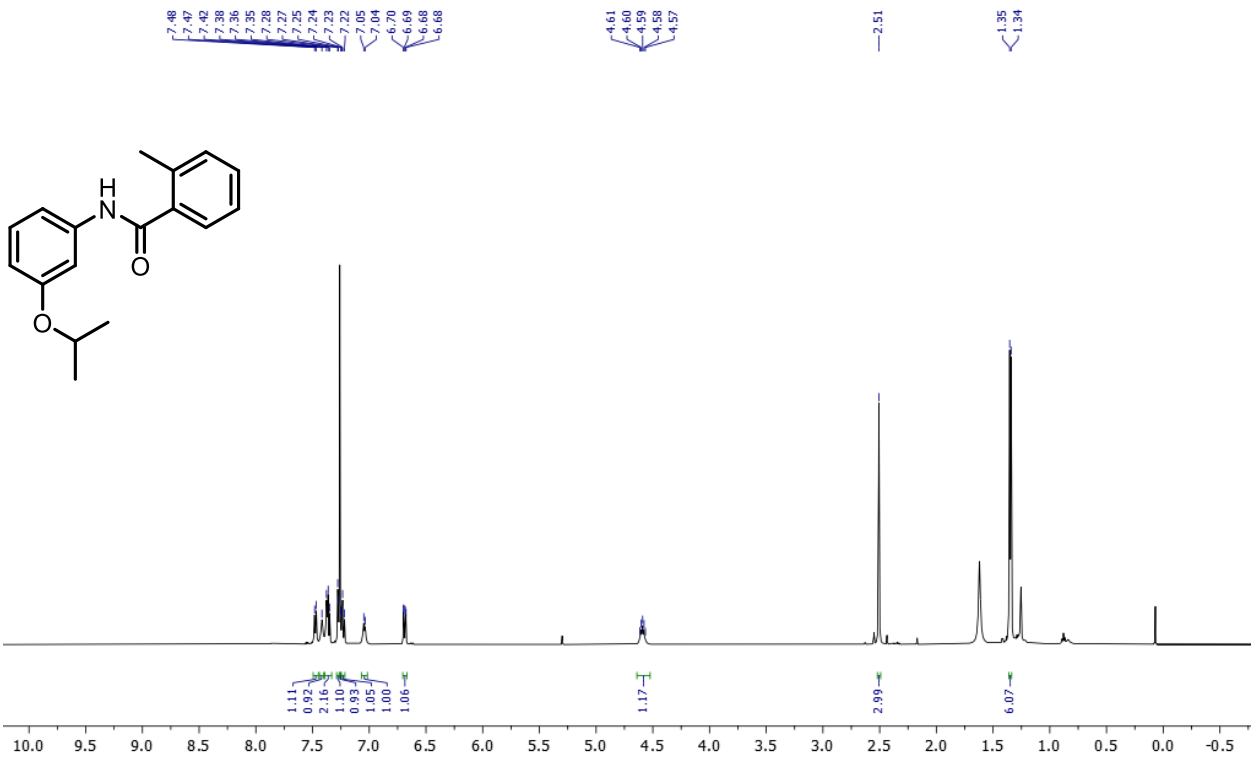
^{1}H NMR of Compound 13 ($CDCl_3$; 300 MHz)



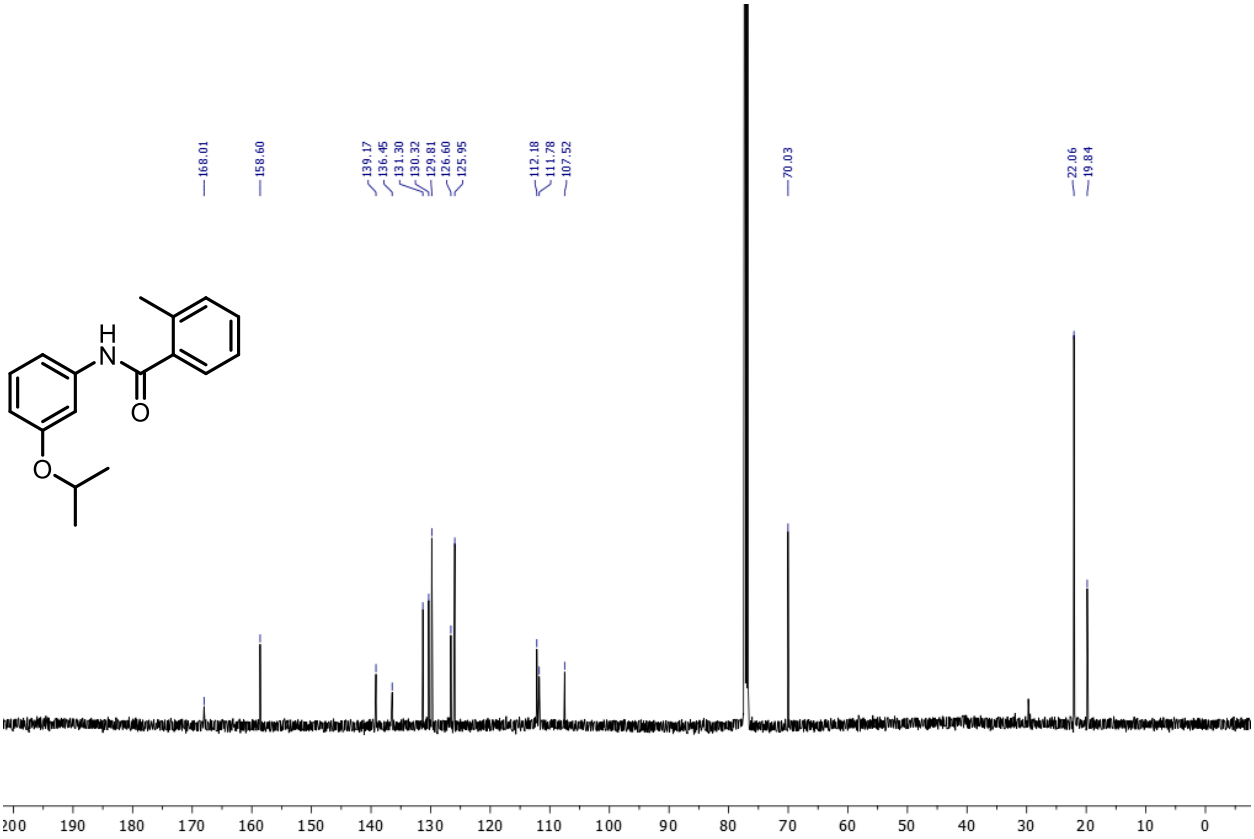
^{13}C NMR of Compound 13 ($CDCl_3$; 75 MHz)



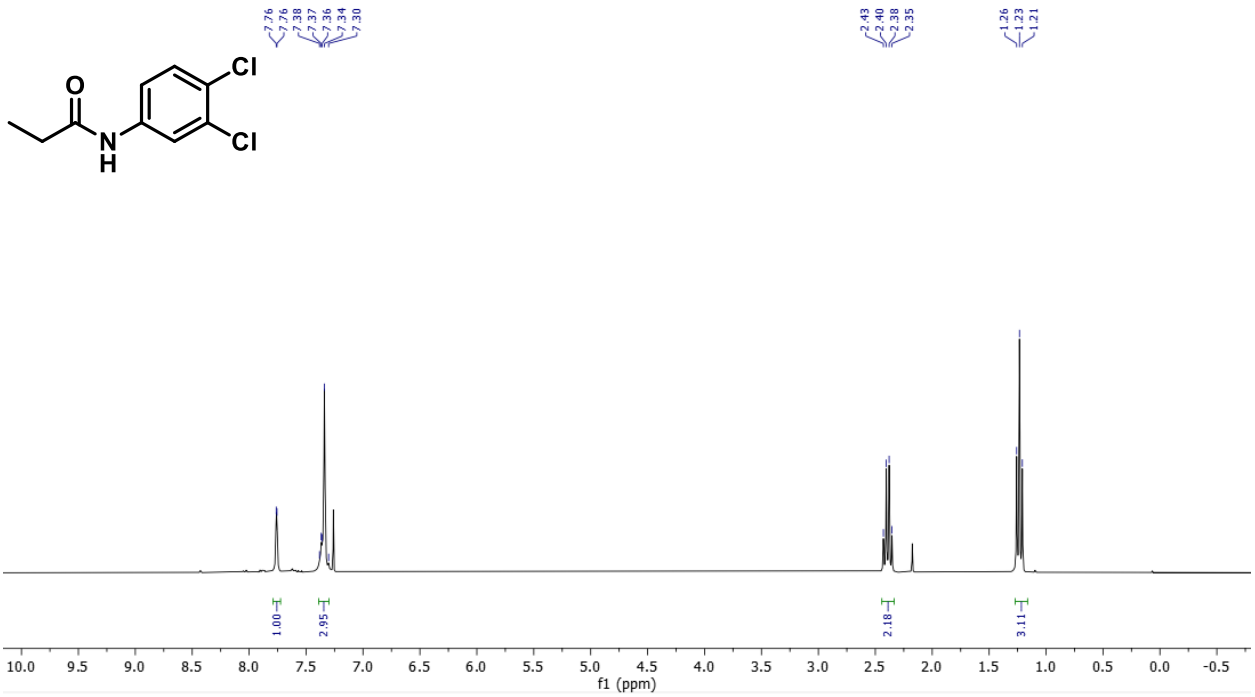
^{1}H NMR of Compound 14 ($CDCl_3$; 300 MHz)



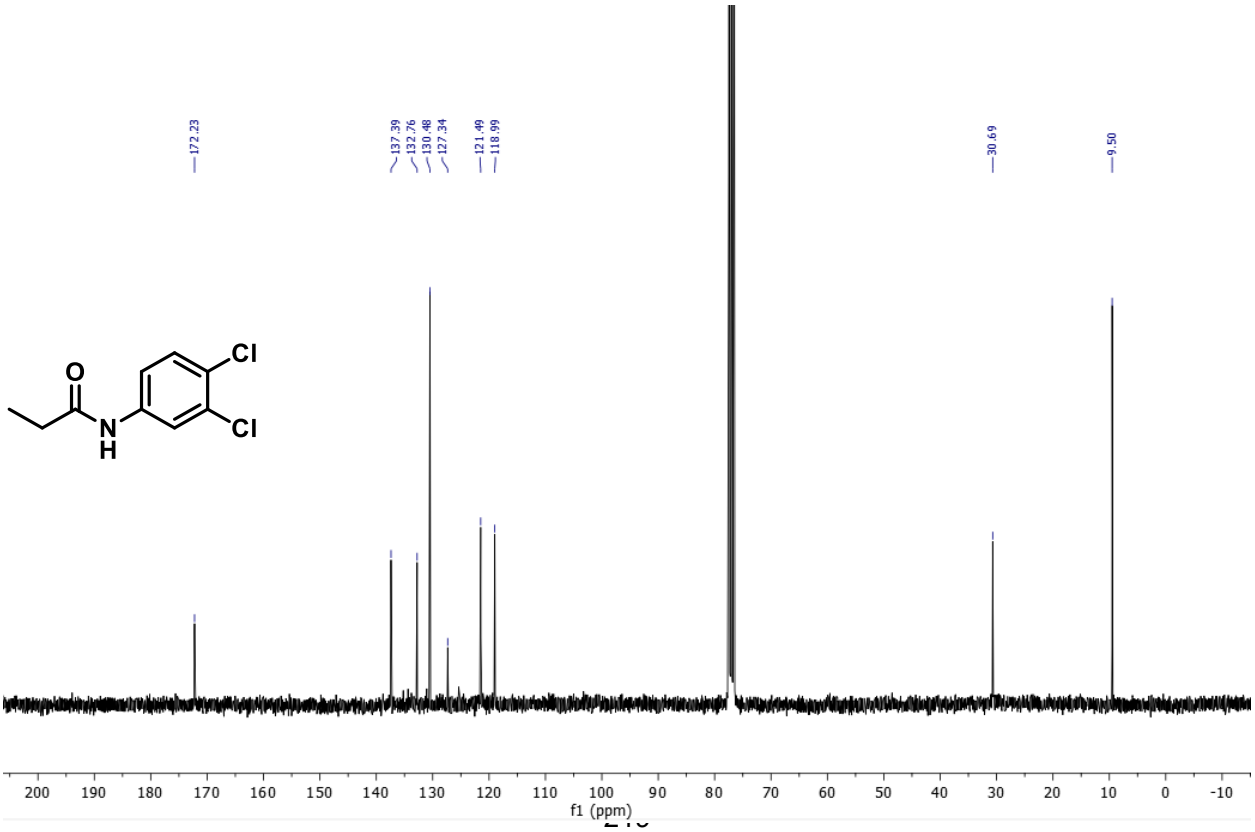
^{13}C NMR of Compound 14 ($CDCl_3$; 75 MHz)



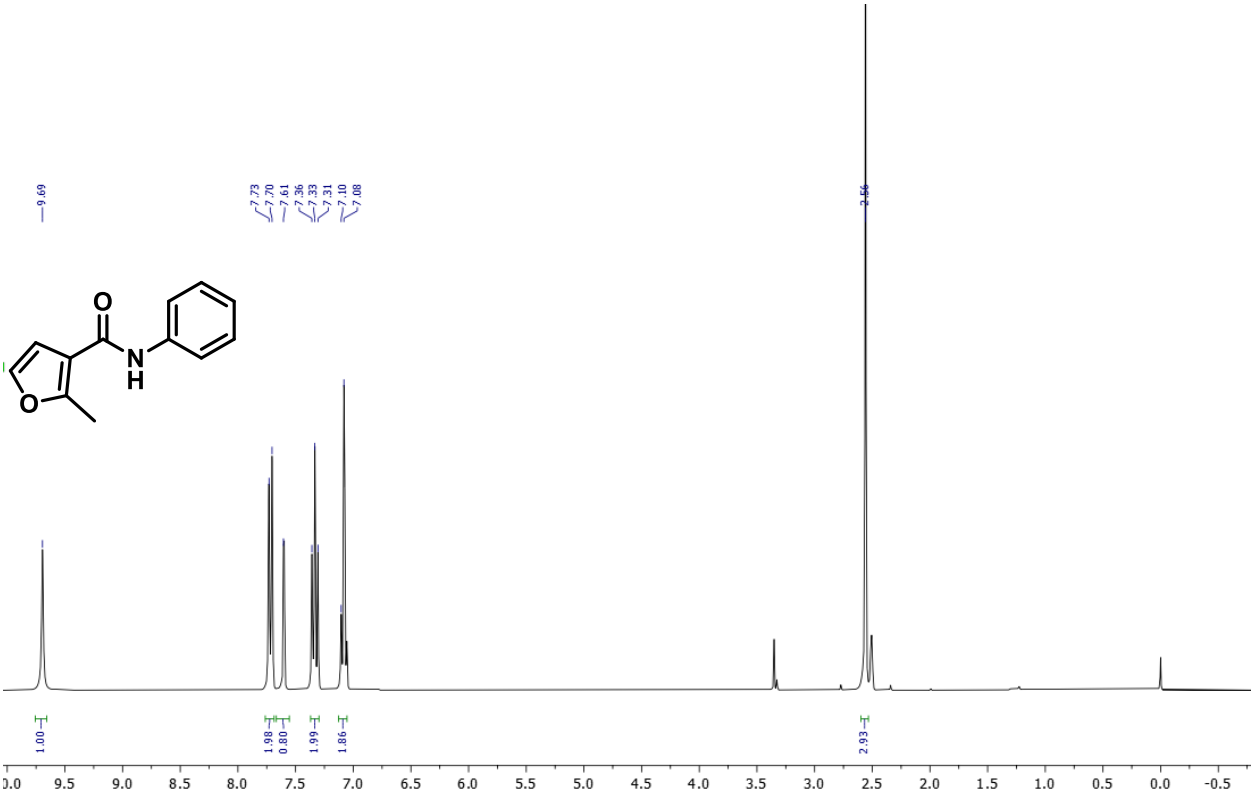
^{1}H NMR of Compound 15 ($CDCl_3$; 300 MHz)



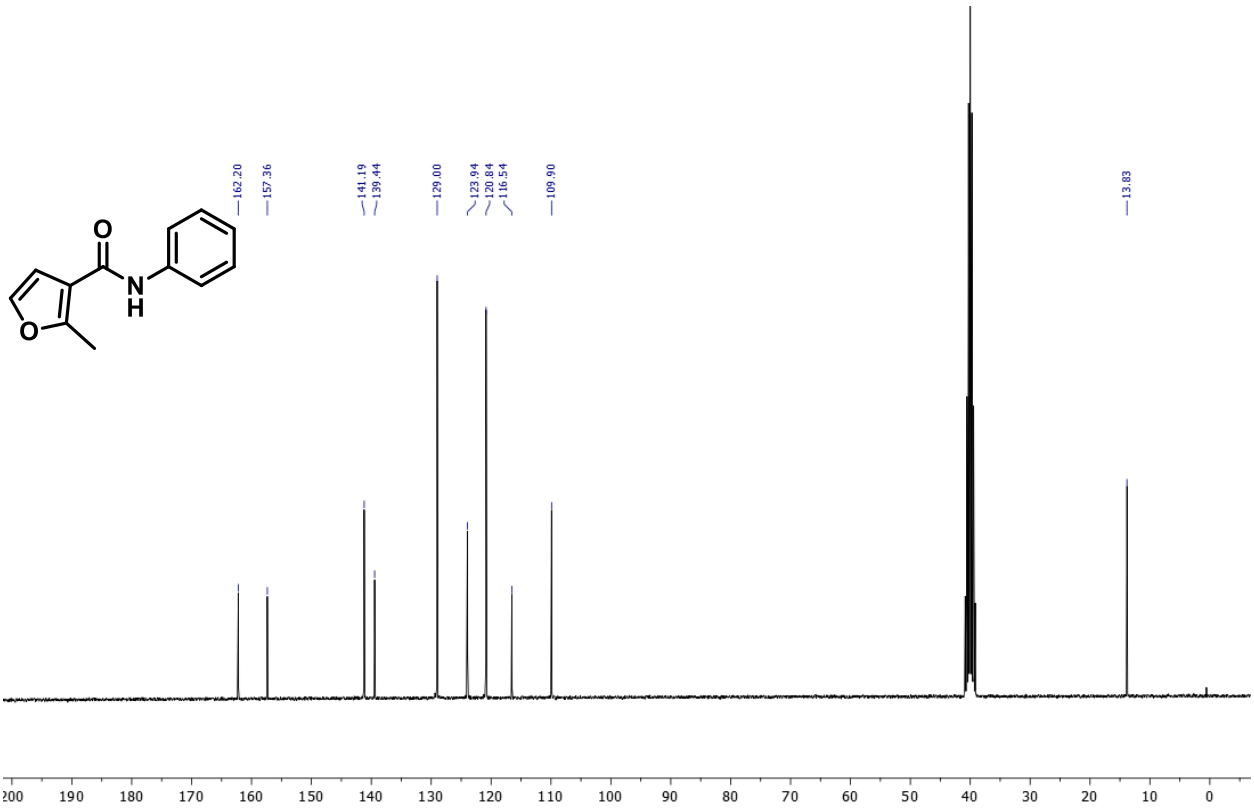
^{13}C NMR of Compound 15 ($CDCl_3$; 75 MHz)



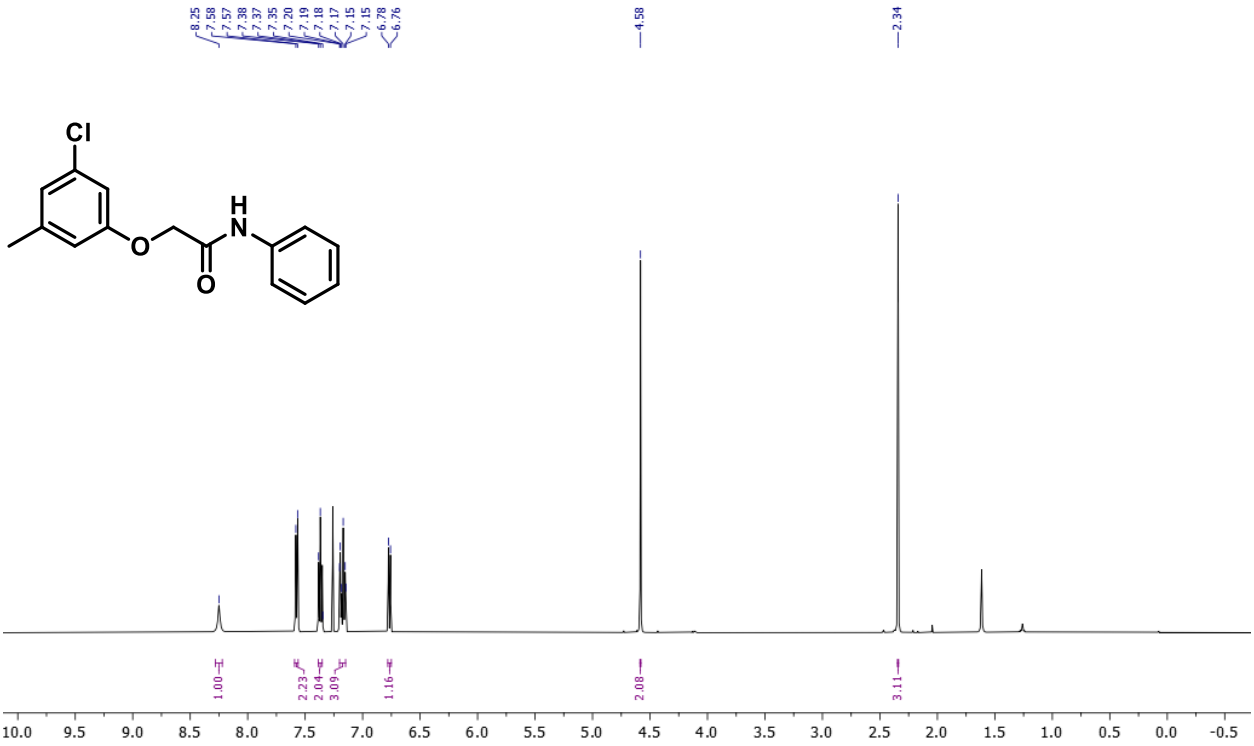
^{1}H NMR of Compound 16 (DMSO d_6; 300 MHz)



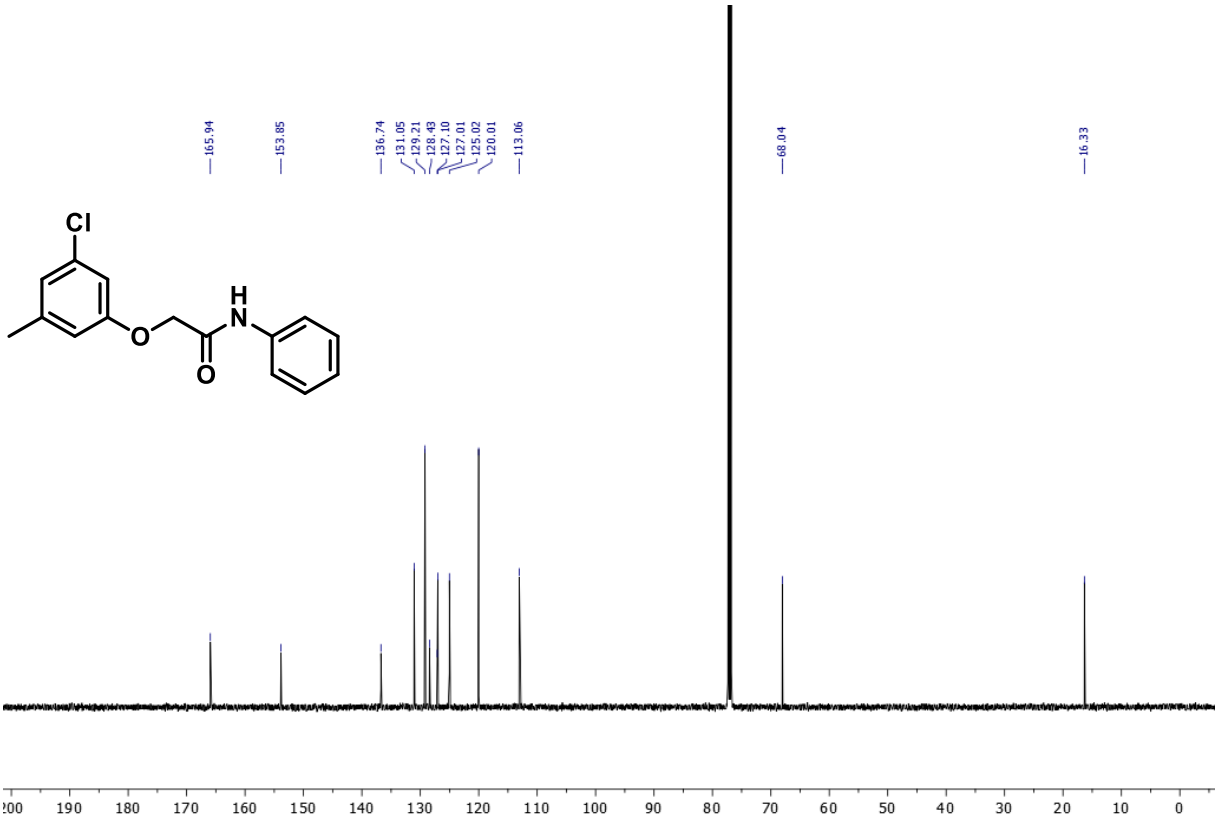
^{13}C NMR of Compound 16 (DMSO d_6; 75 MHz)



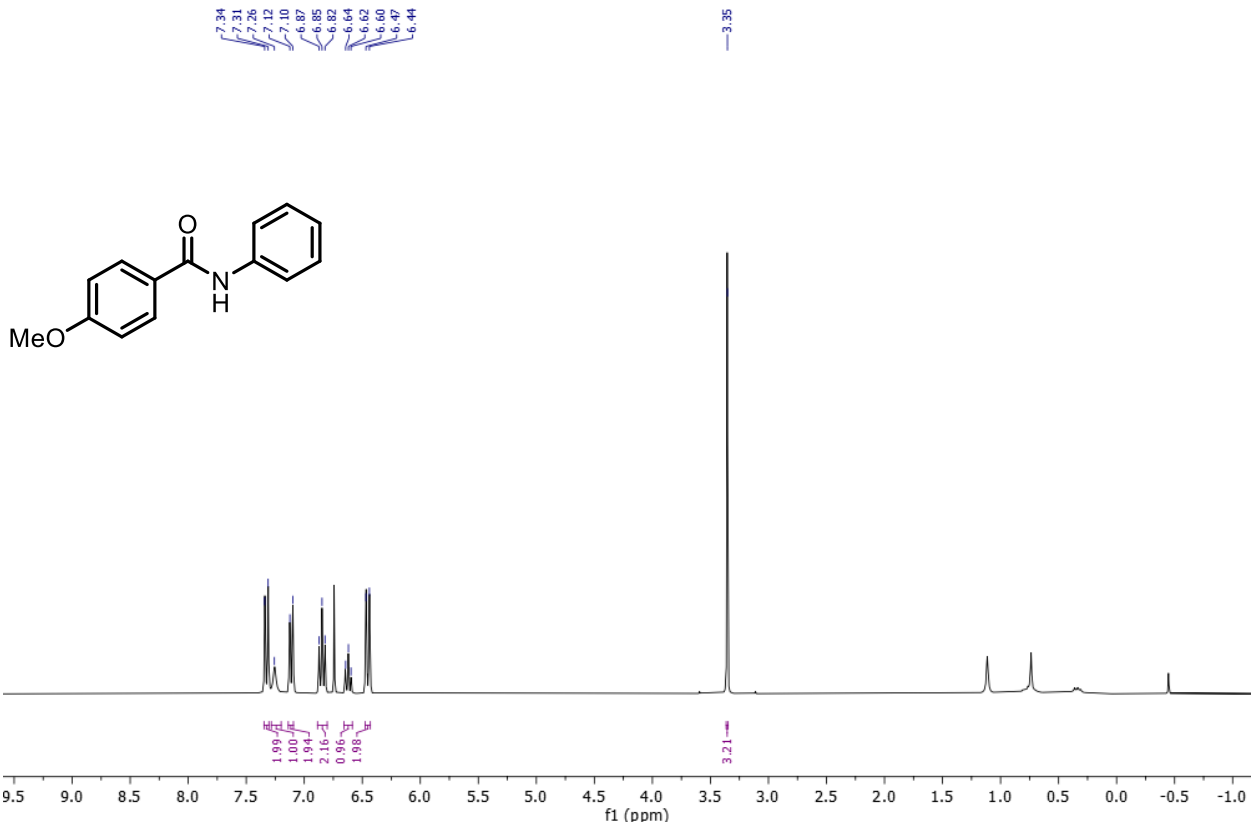
^{1}H NMR of Compound 17 ($CDCl_3$; 500 MHz)



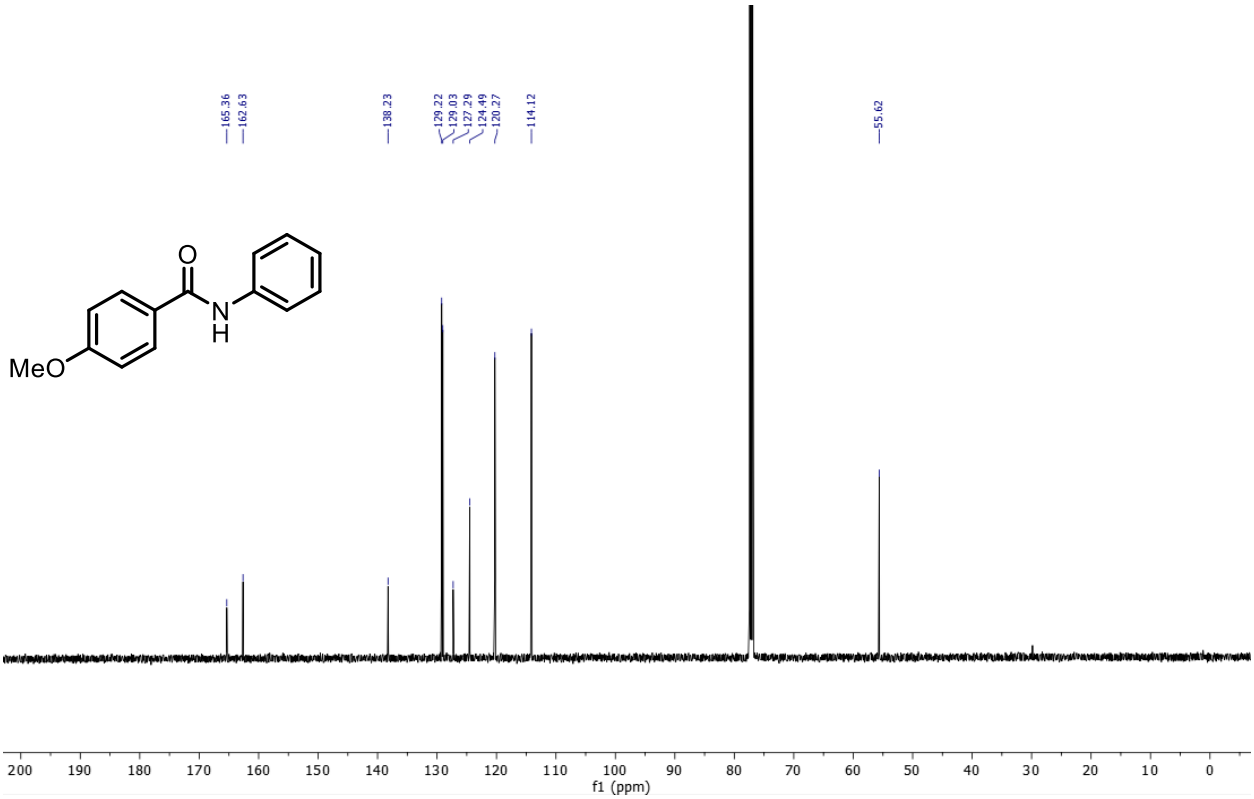
^{13}C NMR of Compound 17 ($CDCl_3$; 75 MHz)



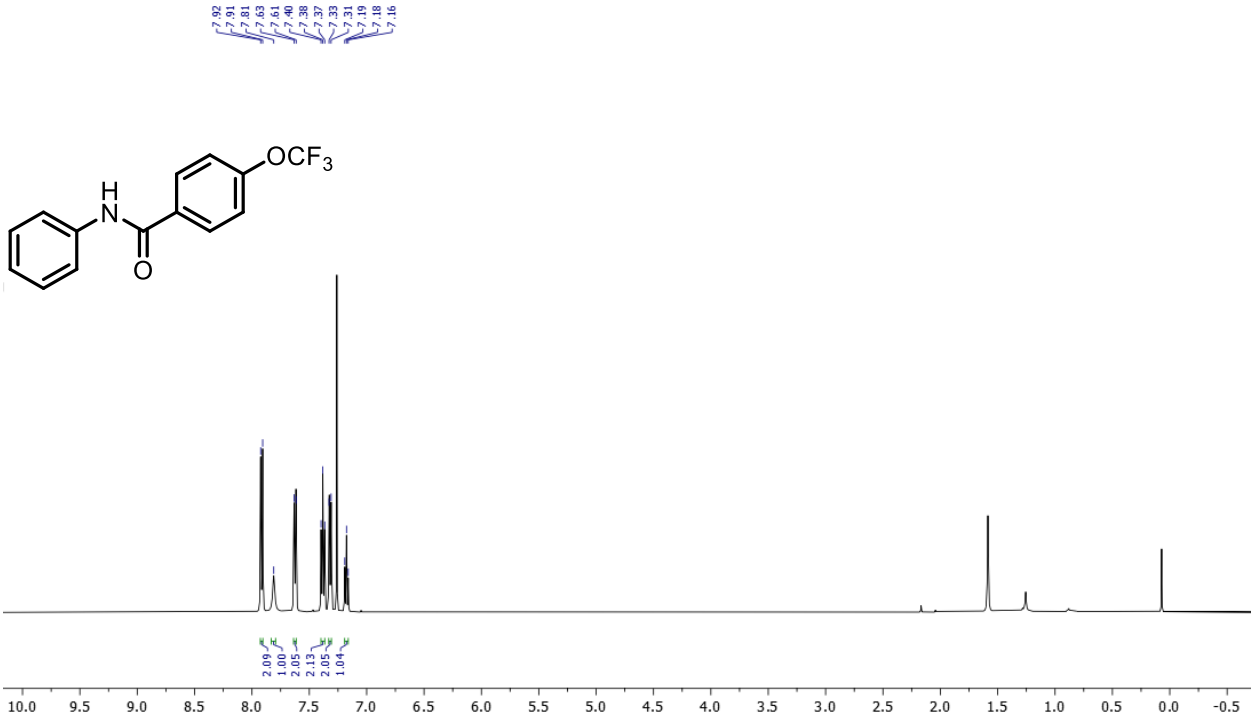
^{1}H NMR of Compound 18 ($CDCl_3$; 300 MHz)



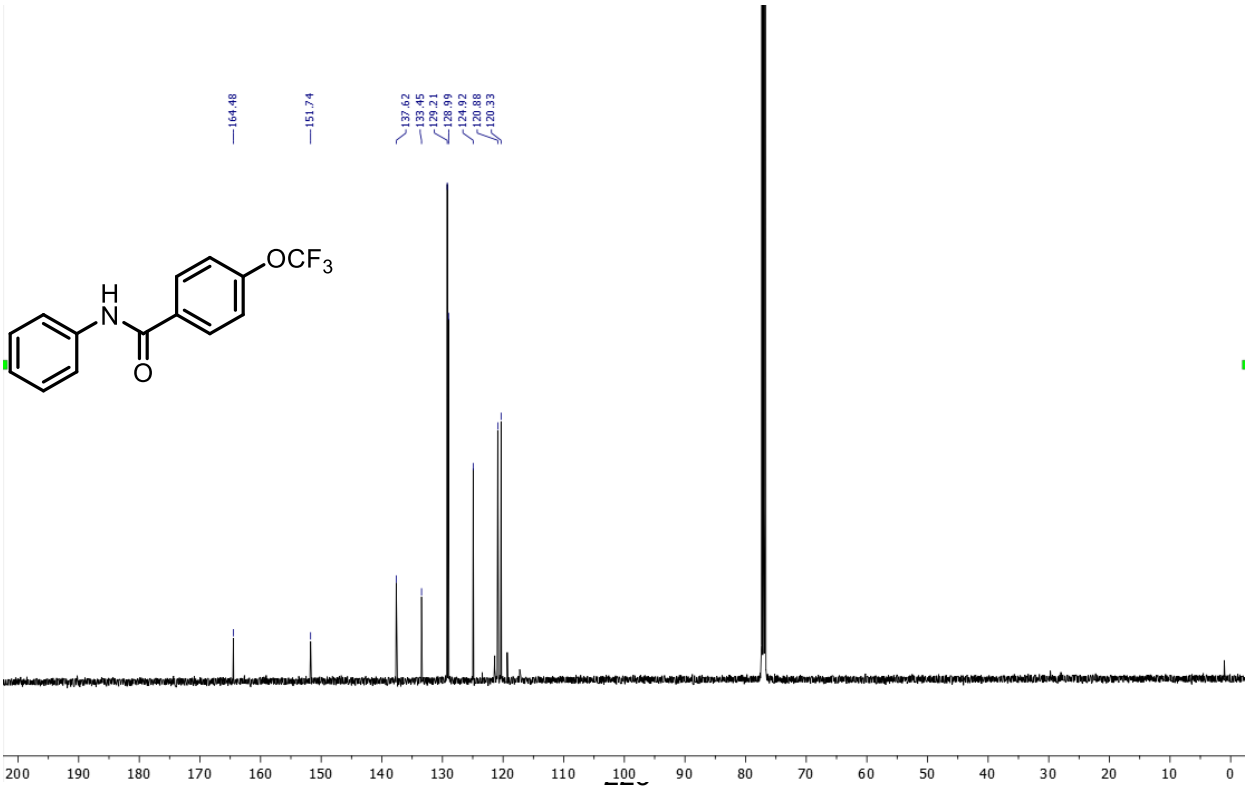
^{13}C NMR of Compound 18 ($CDCl_3$; 75 MHz)



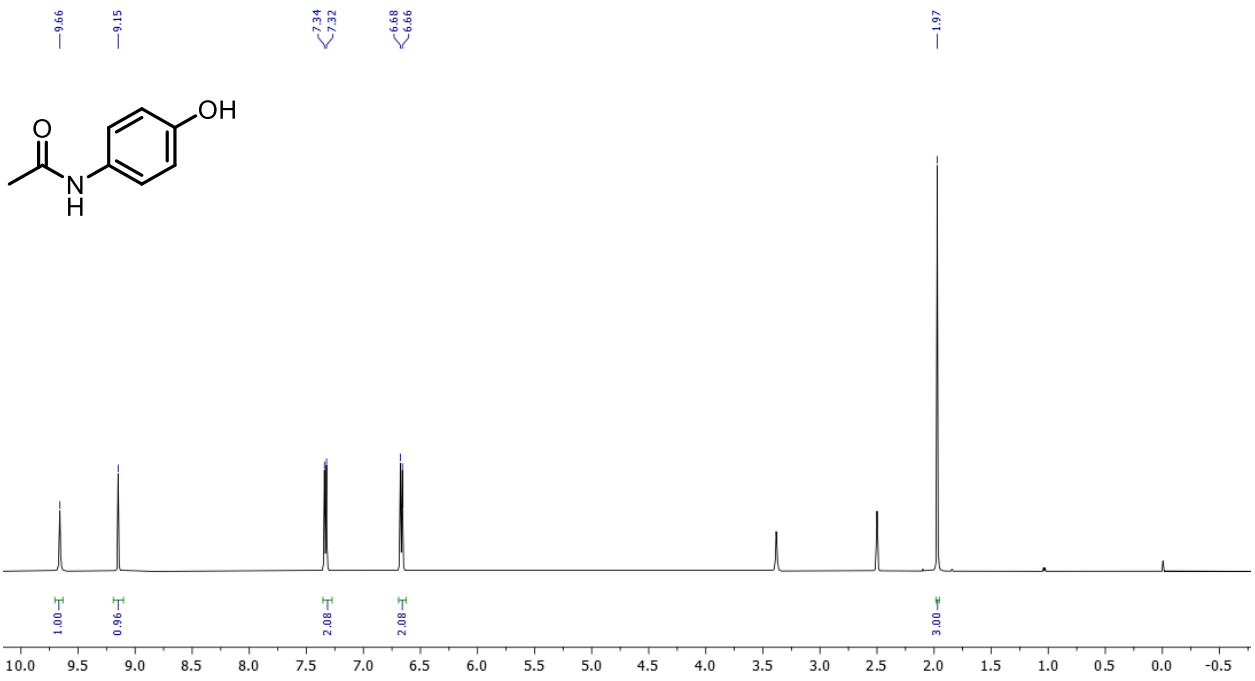
^{1}H NMR of Compound 19 ($CDCl_3$; 500 MHz)



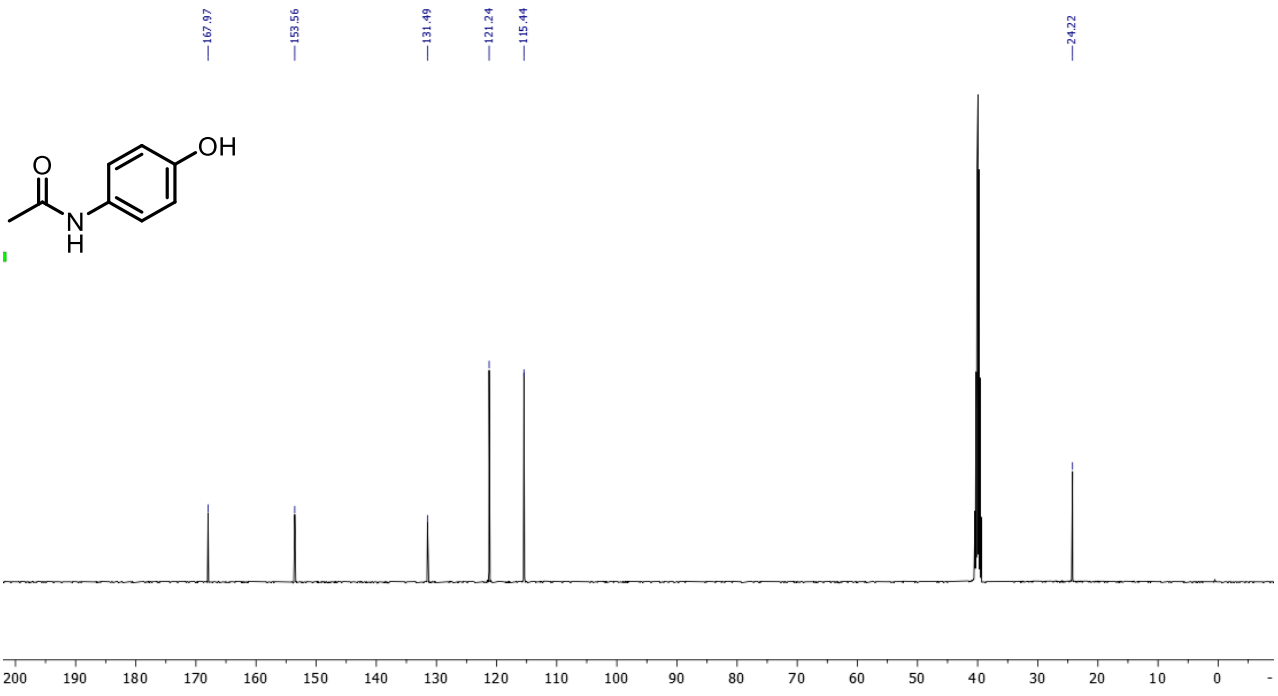
^{13}C NMR of Compound 19 ($CDCl_3$; 125 MHz)



^{1}H NMR of Compound 20 (DMSO d_6; 500 MHz)



^{13}C NMR of Compound 20 (DMSO d_6; 125 MHz)



Q NMR of saccharin ($CDCl_3$; 500 MHz)