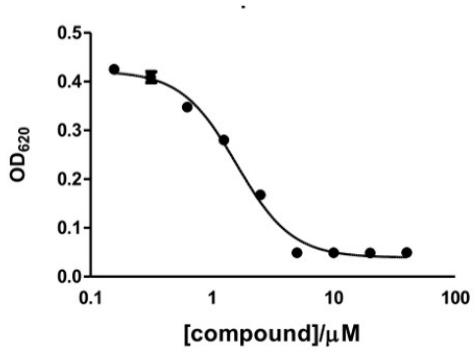
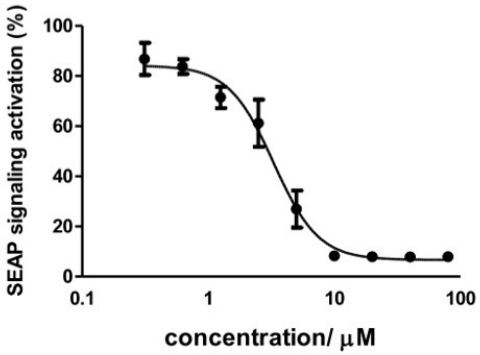
Supporting Information

Design and optimisation of a small-molecule TLR2/4 antagonist for anti-tumour therapy

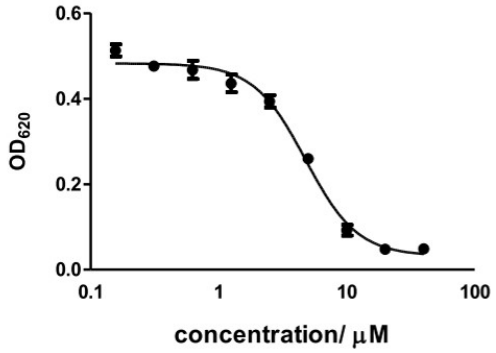
Qun Xu, Tian Li*, Hekai Chen, Jun Kong, Liwei Zhang, Hang Yin*

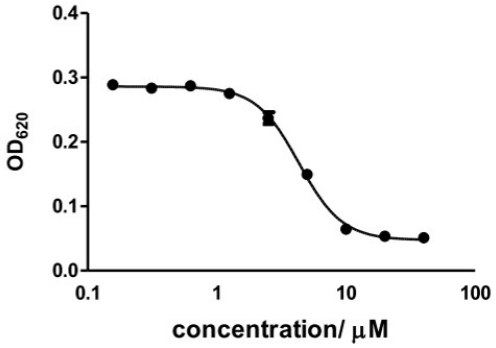
1. SEAP test result of all small molecule compounds on TLR2 inhibiting



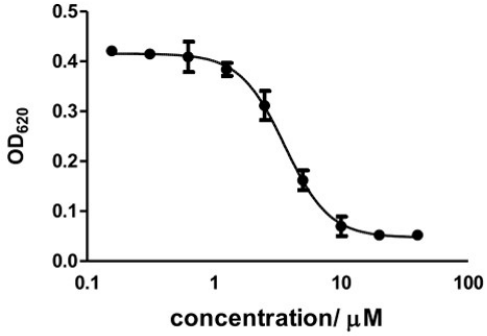


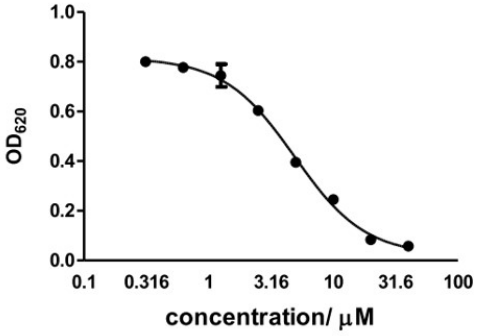
Compound TX-0 IC50=1.6±0.3 μM Compound TX-1 IC50=3.4±0.4 μM



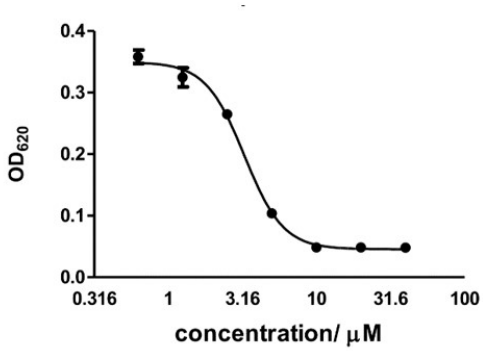


Compound TX-5 IC50=5.0±0.5 μM Compound TX-7 IC50=4.4±0.2 μM

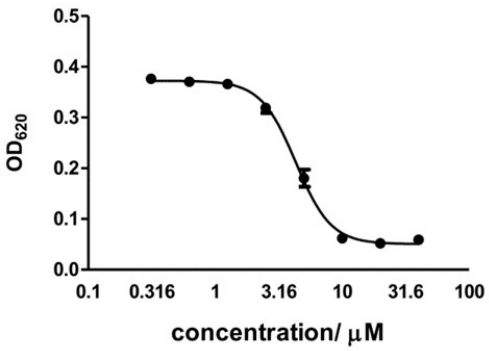




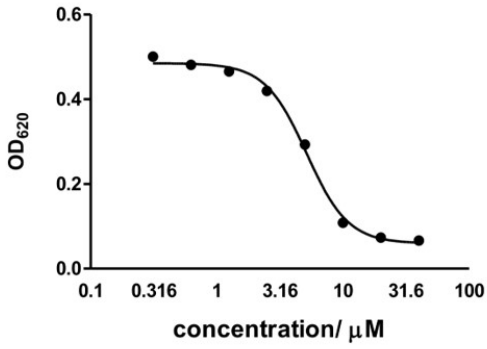
Compound TX-8 IC50=3.7±0.4 μM Compound TX-9 IC50=5.0±0.7 μM



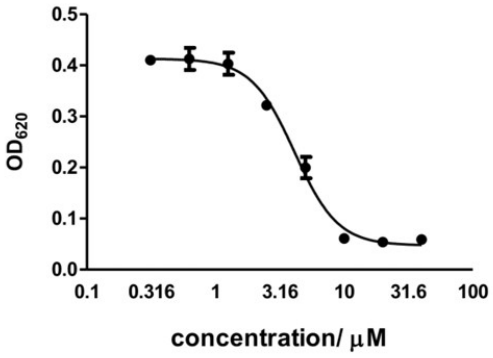
Compound TX-10 IC50=3.3±0.3 μM



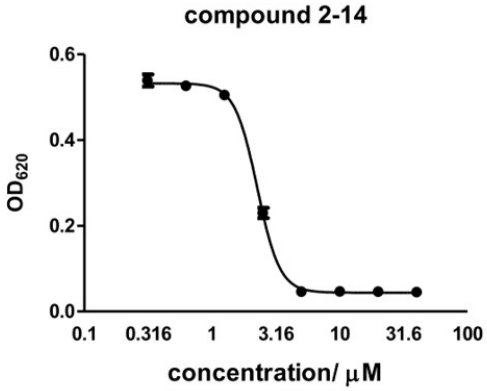
Compound TX-11 IC50=4.4±0.3 μM



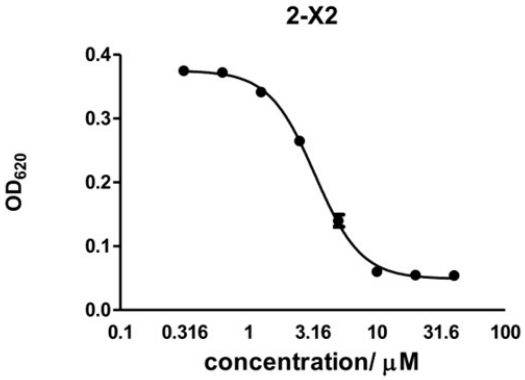
Compound TX-12 IC50=5.5±0.5 μM



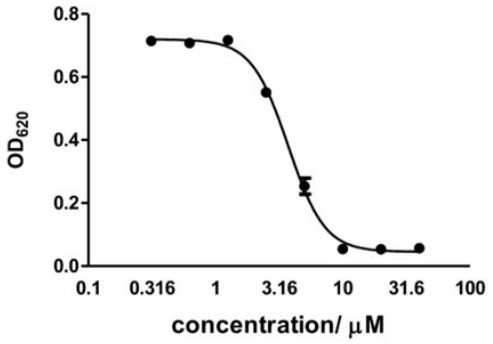
Compound TX-13 IC50=4.3±0.4 μM



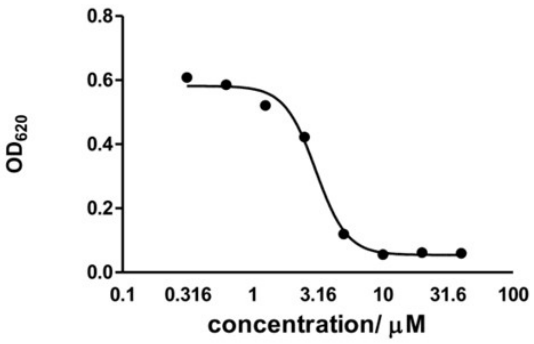
Compound TX-15 IC50=2.4±0.5 μM



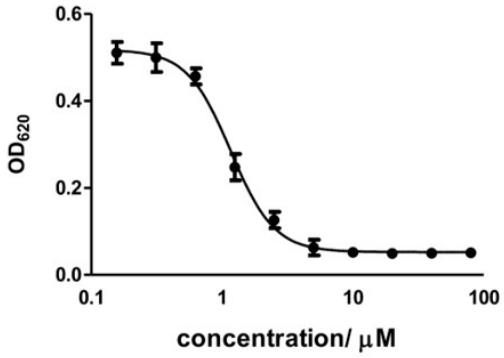
Compound TX-16 IC50=3.4±0.3 μM



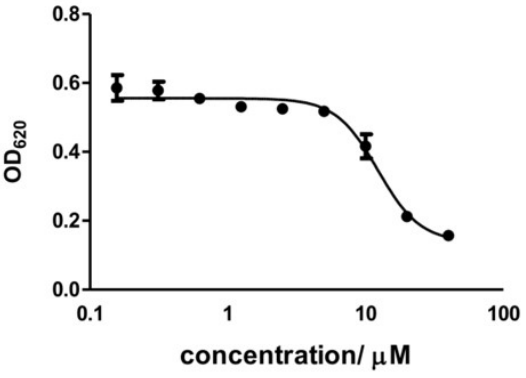
Compound TX-17 IC50=3.9±0.7 μM



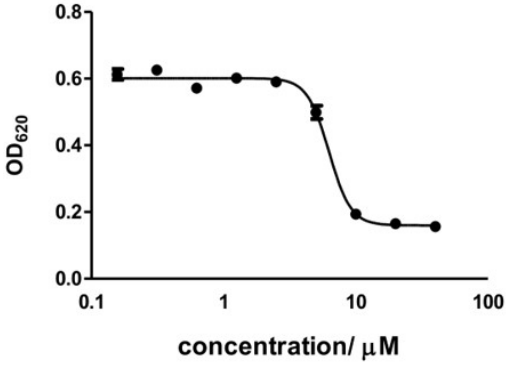
Compound TX-18 IC50=3.2±0.5 μM



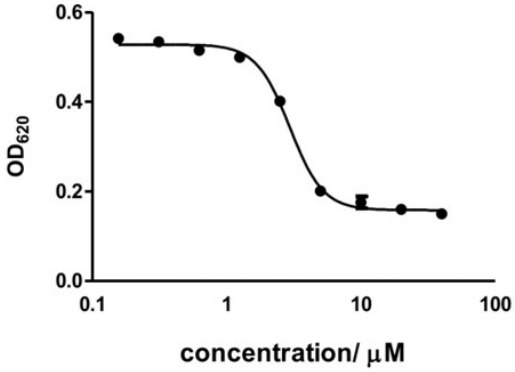
Compound TX-19 IC50=1.1±0.4 μM



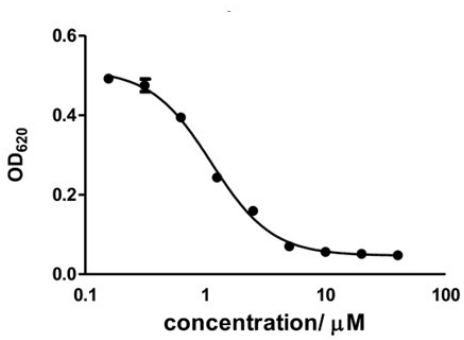
Compound TX-20 IC50=12.3±2.8 μM



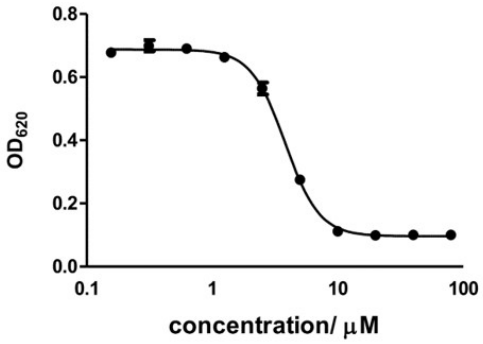
Compound TX-21 IC50=6.5±0.5 μM



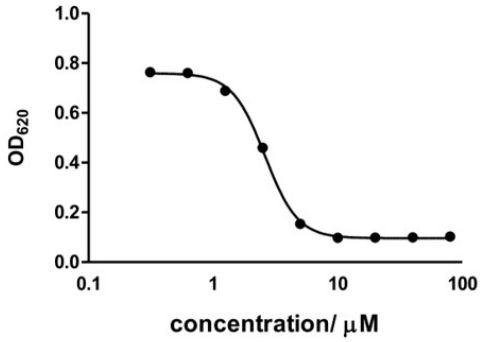
Compound TX-22 IC50=3.1±0.4 μM



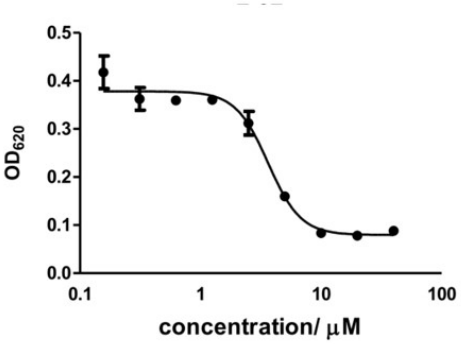
Compound TX-23 IC50=1.2±0.5 μM



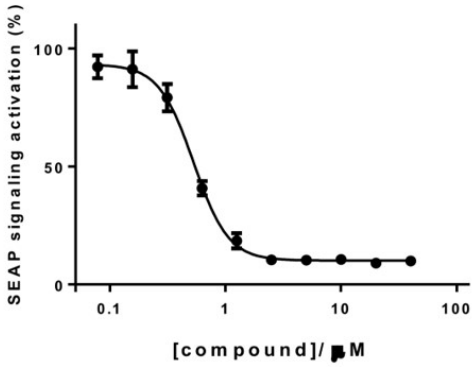
Compound TX-24 IC50=4.0±0.6 μM



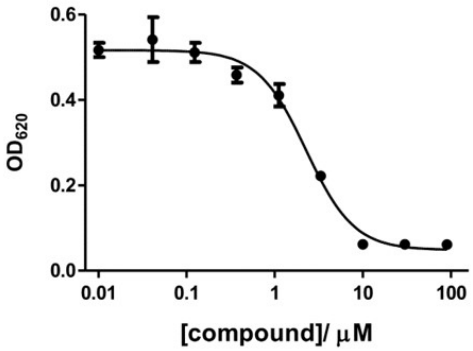
Compound TX-25 IC50=2.8±0.2 μM



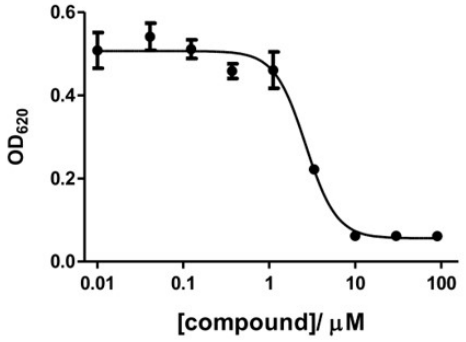
Compound TX-32 IC50=3.8±0.4 μM



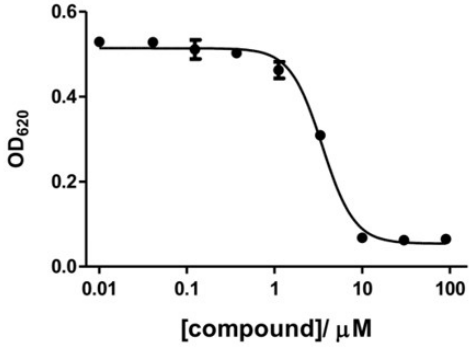
Compound TX-33 IC50=0.52±0.03 μM



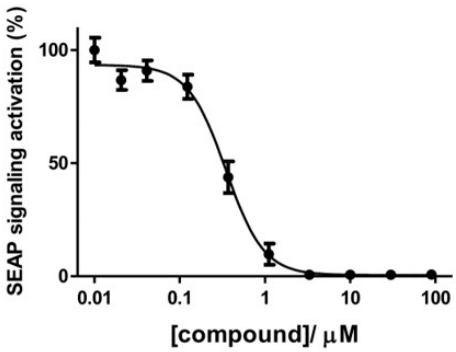
Compound TX-34 IC50=2.3±0.5 μM



Compound TX-35 IC50=2.6±0.4 μM

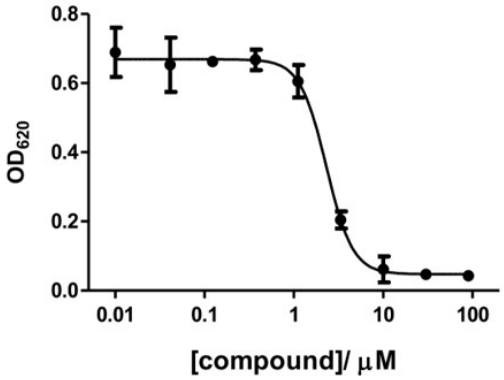


Compound TX-36 IC50=3.6±0.2 μM

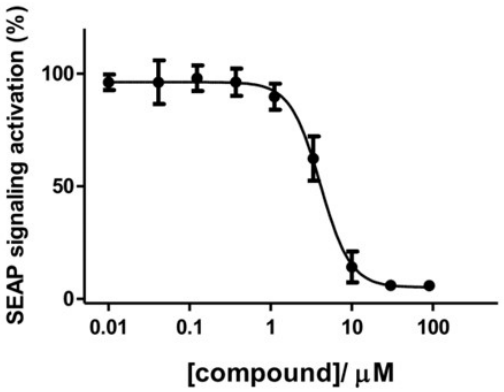


Compound TX-37 IC50=0.35±0.04 μM

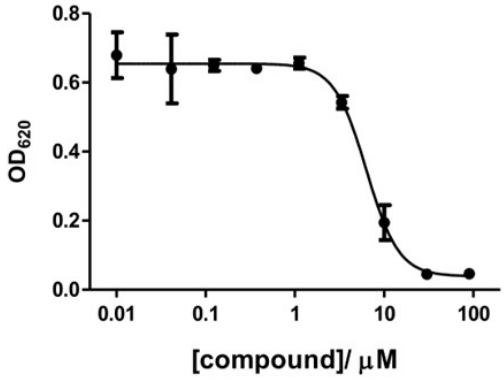
2. SEAP test result of all small molecule compounds on TLR4 inhibiting



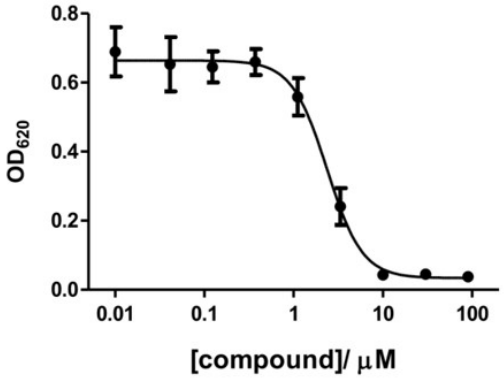
TX-0 IC50=2.3±0.5 μM



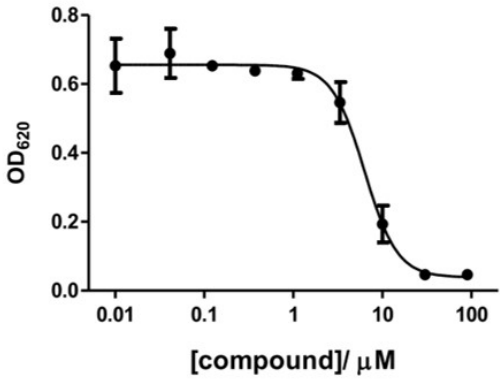
TX-1 IC50=4.3±0.5 μM



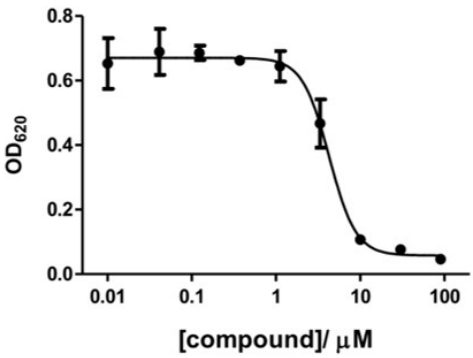
TX-5 IC50=6.3±0.6 μM



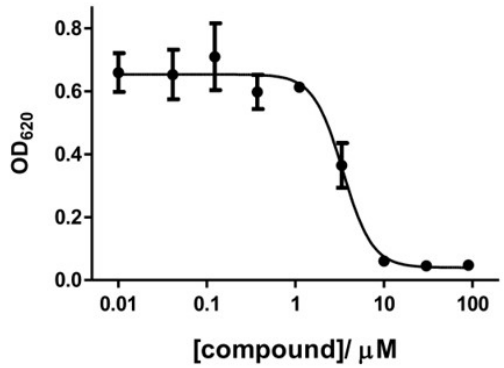
TX-7 IC50=2.5±0.6 μM



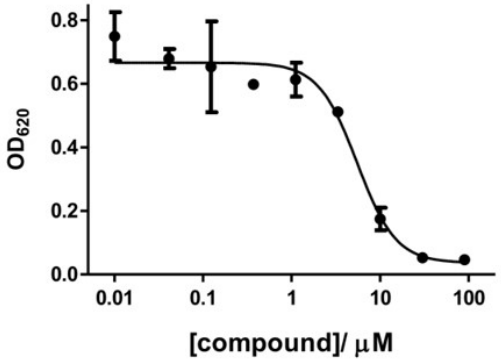
TX-8 IC50=6.5±0.6 μM



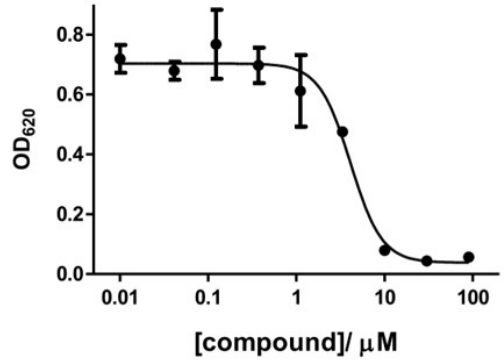
TX-9 IC50=4.4±0.65μM



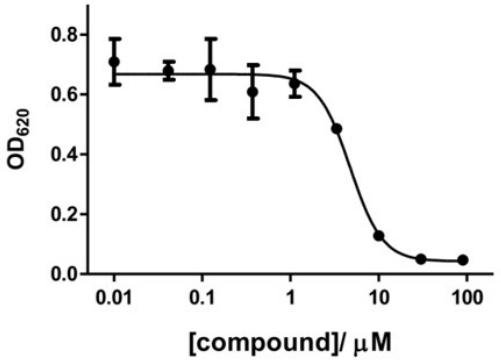
TX-10 IC50=3.5±0.6 μM



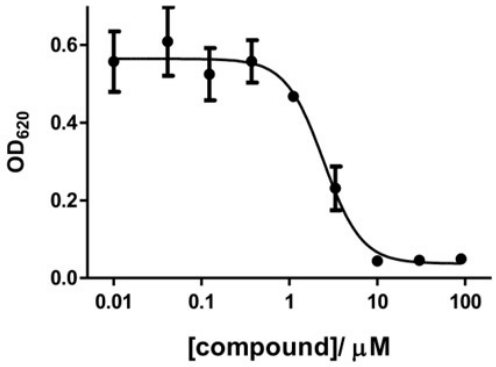
TX-11 IC50=5.6±0.9 μM



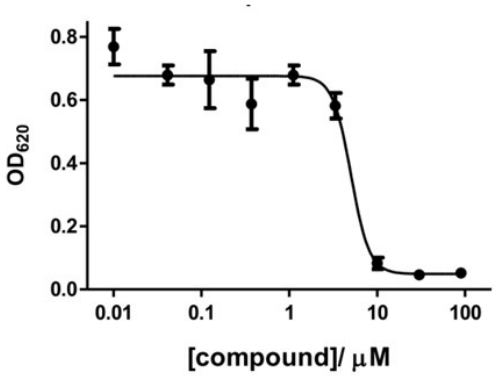
TX-12 IC50=4.2±0.7 μM



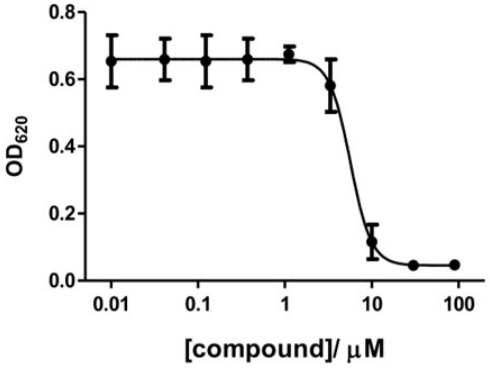
TX-13 IC50=4.8±0.7 μM



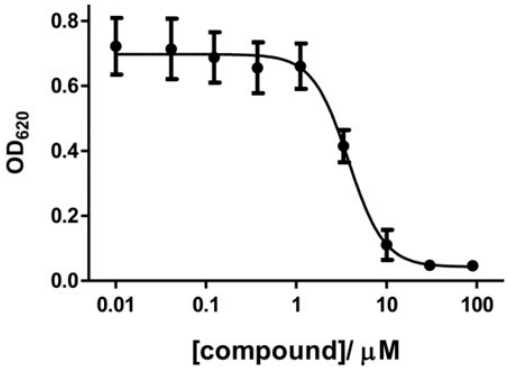
TX-15 IC50=2.5±0.8 μM



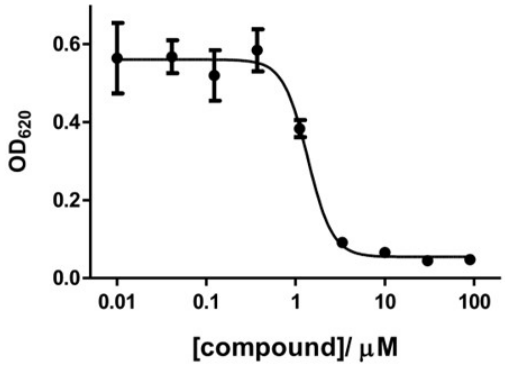
TX-16 IC50=5.2±0.9 μM



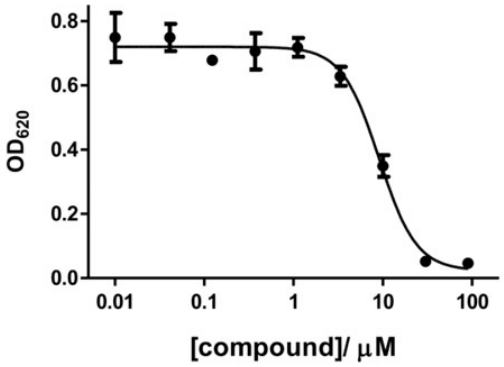
TX-17 IC50=5.8±0.7 μM



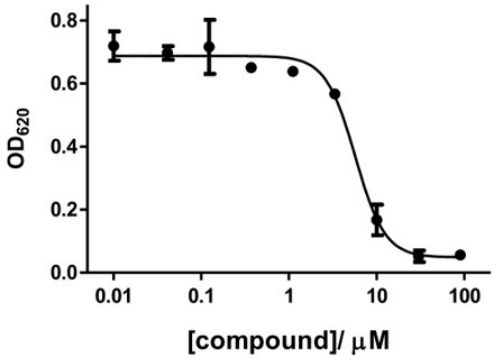
TX-18 IC50=3.9±0.7 μM



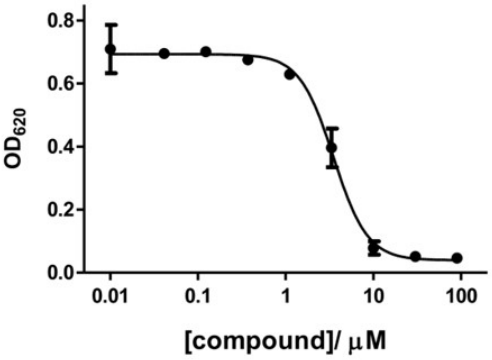
TX-19 IC50=1.4±0.3 μM



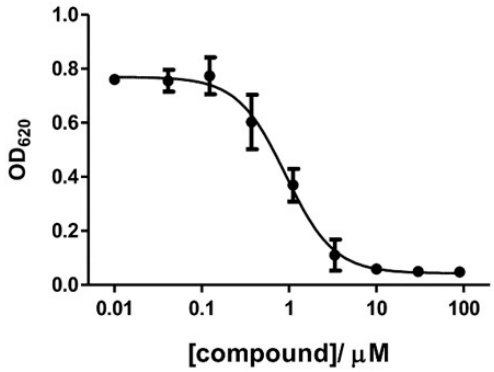
TX-20 IC50=9.2±0.5 μM



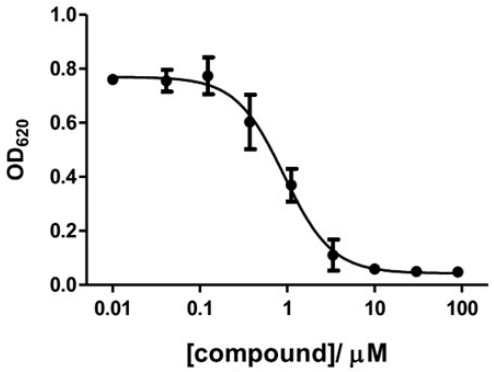
TX-21 IC50=5.9±0.5 μM



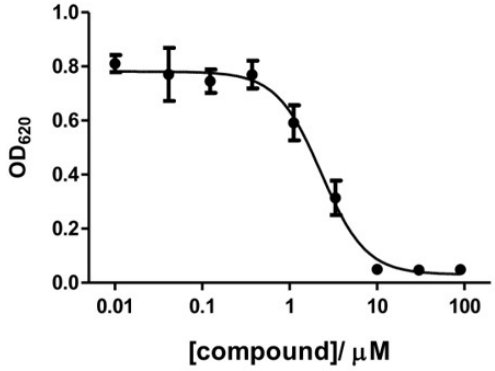
TX-22 IC50=3.7±0.4 μM



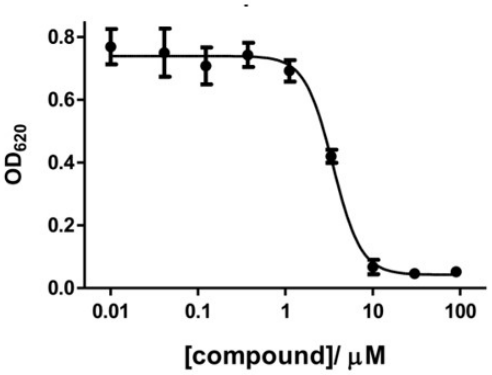
TX-23 IC50=1.0±0.3 μM



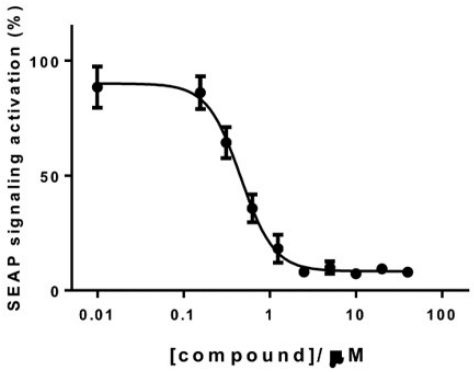
TX-24 IC50=6.2±0.6 μM



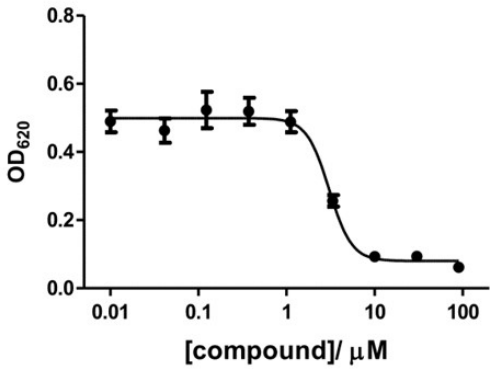
TX-25 IC50=2.4±0.7 μM



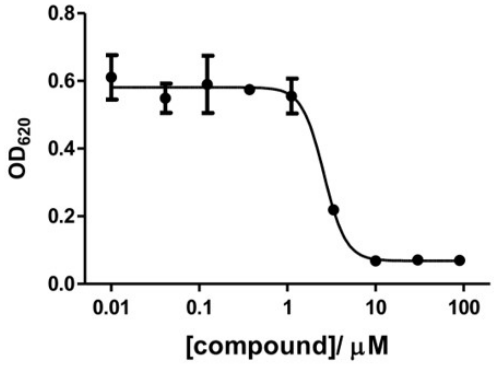
TX-32 IC50=3.6±0.4 μM



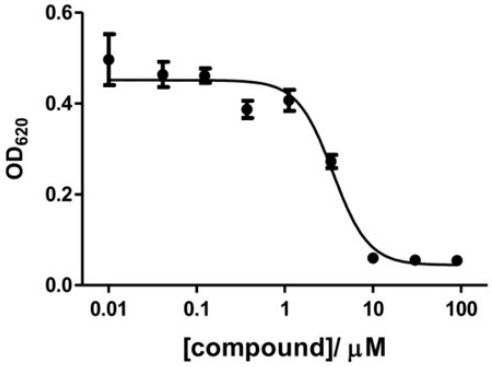
TX-33 IC50=0.46±0.04 μM



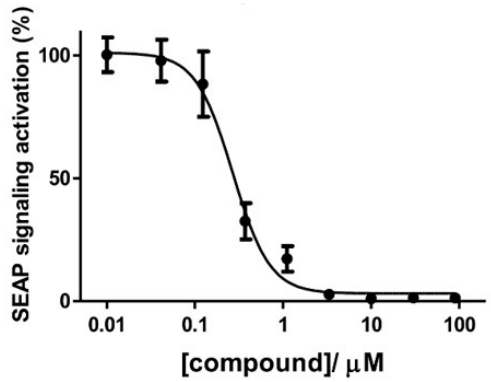
TX-34 IC50=3.1±0.4 μM



TX-35 IC50=2.8±0.6 μM

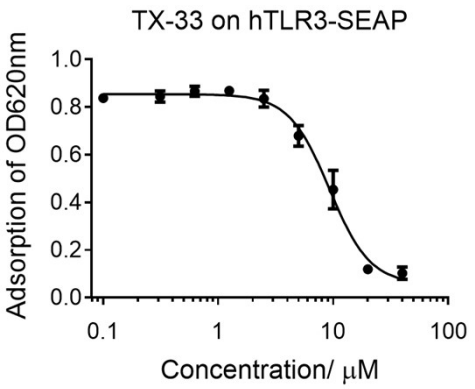


TX-36 IC50=3.7±0.6 μM

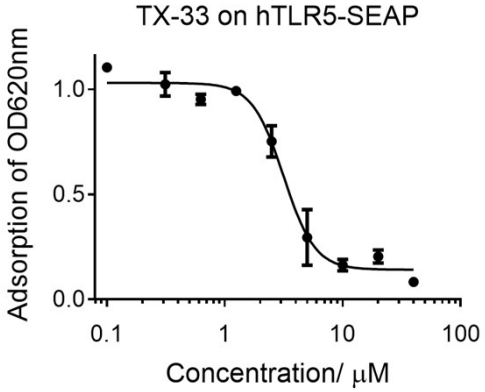


TX-37 IC50=0.28±0.06 μM

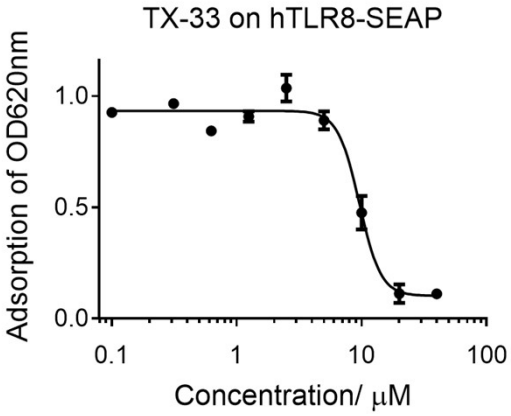
3. SEAP test result of the compounds TX-33 on TLR3/5/8/9 inhibiting.



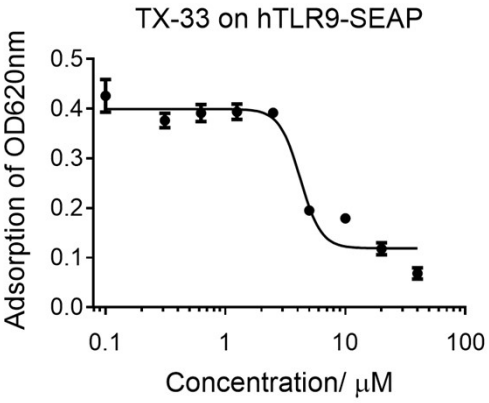
TLR3 IC50=9.28±0.04 μM



TLR5 IC50=3.15±0.04 μM



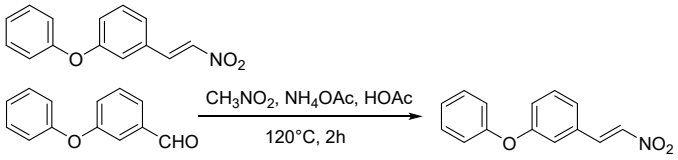
TLR8 IC50=9.59±0.02 μM



TLR9 IC50=4.21±0.04 μM

4. Chemical synthesis and the data of the compounds

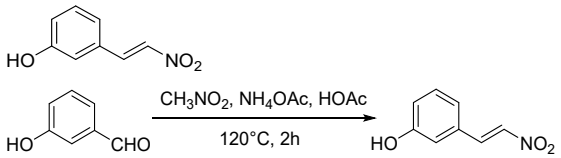
TX-1: (E)-1-(2-nitrovinyl)-3-phenoxybenzene



To an acetic acid (5 mL) solution of 3-phenoxybenzal-dehyde (495mg, 2.5mmol) were added nitromethane (4 ml) and ammonium acetate (385mg, 5mmol) at room temperature, stirred for 2 hours at 120℃. After that, water and ethyl acetate were added to the reaction mixture, and the organic layer was extracted with ethyl acetate, then washed with saturated sodium chloride aqueous and dried by anhydrous magnesium sulfate. Last, it was concentrated under a reduced pressure to obtain the crude product. The crude product is separated by column chromatography (PE: EA=20:1) to obtain the final product (376mg, light yellow compound). Product yield 63%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 13.7 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.43 – 7.36 (m, 3H), 7.27 (d, *J* = 6.0 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.16 – 7.09 (m, 2H), 7.04 (d, *J* = 7.7 Hz, 2H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.13 (d, *J* = 13.6 Hz, 1H), 8.07 – 8.00 (m, 1H), 7.31 – 7.26 (m, 2H), 7.19 (d, *J* = 1.4 Hz, 1H), 6.97 – 6.91 (m, 1H). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 242.08117, found: 242.0812

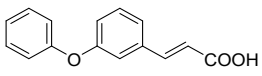
TX-0: (E)-3-(2-nitrovinyl)phenol

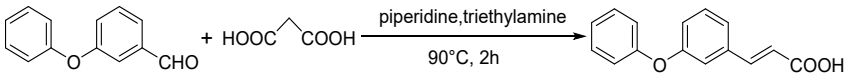


The synthesis method is basically the same as TX-1. To an acetic acid (5 mL) solution of 3-hydroxybenzaldehyde (244g, 2mmol) were added nitromethane (3 ml) and ammonium acetate (308mg, 4mmol) at room temperature, stirred for 2 hours at 120℃. After that, water and ethyl acetate were added to the reaction mixture, and the organic layer was extracted with ethyl acetate, then washed with saturated sodium chloride aqueous and dried by anhydrous magnesium sulfate. Last, it was concentrated under a reduced pressure to obtain the crude product (284mg) without column chromatography separation. Product yield 86%.

^{1}H NMR (400 MHz, d6-DMSO) δ 9.79 (s, 1H), 8.13 (d, *J* = 13.6 Hz, 1H), 8.07 – 8.00 (m, 1H), 7.31 – 7.26 (m, 2H), 7.19 (d, *J* = 1.4 Hz, 1H), 6.97 – 6.91 (m, 1H). ^{13}C NMR (101 MHz, d6-DMSO) δ 163.03 (s), 144.72 (s), 143.16 (s), 136.72 (s), 135.41 (s), 125.88 (s), 124.46 (s), 121.47 (s), 45.36 (s), 45.05 (d, *J* = 21.0 Hz), 44.74 (s), 44.42 (d, *J* = 21.0 Hz), 44.32 – 44.27 (m), 44.11 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 166.04987. Found: 116.0500

TX-2: (E)-3-(3-phenoxyphenyl)acrylic acid

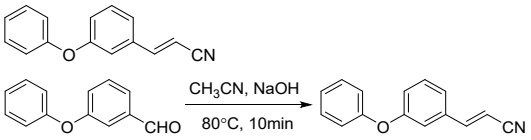




A 25 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 1.5 g, (7.6 mmol) of 3-Phenoxybenzaldehyde, 1.9 g (2.5 mmol) of malonic acid, 5ml triethylamine and 0.2 mL piperidine. The slurry was heated to 90°C overnight, at that temperature a clear yellow solution formed. After 12 hours, the reaction was completed, and the heating was resumed to room temperature. 25 ml of EA was added to the system, and the mixture was evaporated under reduced pressure to remove most of piperidine and triethylamine. After that, adding 50 ml water, the pH was adjusted to 1.5 by HCl, and the solid was collected by filtration under reduced pressure, last, recrystallized with methanol to got the final product (899mg). product yield: 49%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 13.7 Hz, 1H), 7.51 (d, *J* = 13.7 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.27 (d, *J* = 5.8 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.15 – 7.09 (m, 2H), 7.06 – 7.01 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.48 (s), 158.02 (s), 156.58 (s), 146.44 (s), 135.82 (s), 130.29 (s), 129.96 (s), 123.87 (s), 123.25 (s), 120.93 (s), 119.27 (s), 118.09 (s), 117.87 (s), 77.32 (d, *J* = 11.5 Hz), 77.06 (s), 76.75 (s), 1.08 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 241.08592, found: 241.0858

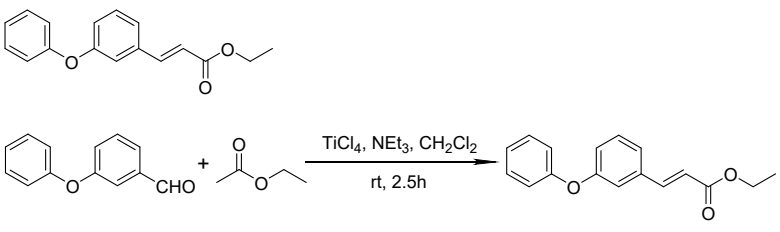
TX-3: (E)-3-(3-phenoxyphenyl)acrylonitrile



3-(3-Phenoxyphenyl)-2-acrylonitrile (III). Potassium hydroxide 99mg, and 1.5 ml of acetonitrile were placed in the round-bottom flask with a mechanic stirrer. The mixture was heated to boiling and kept under nitrogen until the complete dissolution of potassium hydroxide. After that a solution of 300mg of 3-phenoxybenzaldehyde in 1.5 ml of acetonitrile was added dropwise in the course of 1-2 min. After the addition was complete the reaction mixture was stirred for 10 min. After the reaction is completed, 4°C water is added to the system, followed by EA/H_2O extraction. The organic phase is collected and dried over by anhydrous sodium sulfate. The final product is then separated by column chromatography (EA: PE=1:20). Product yield 97mg, 29%.

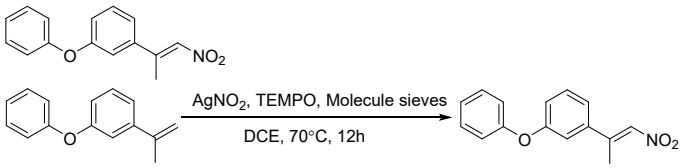
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 4H), 7.16 (t, *J* = 7.3 Hz, 2H), 7.08 – 7.05 (m, 2H), 7.02 (d, *J* = 7.7 Hz, 2H), 5.83 (d, *J* = 16.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.16 (s), 156.35 (s), 149.89 (s), 135.24 (s), 130.47 (s), 130.00 (s), 124.04 (s), 122.17 (s), 121.21 (s), 119.30 (s), 117.87 (s), 116.80 (s), 97.20 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated: 222.09134 found: 222.0914

TX-4: ethyl (E)-3-(3-phenoxyphenyl)acrylate



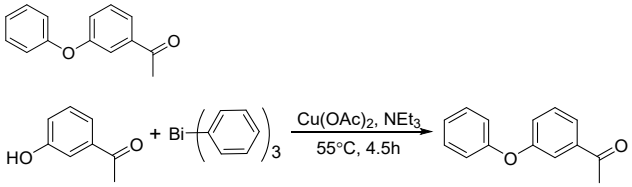
In anhydrous Schlenk bottle under Ar atmosphere, $TiCl_4$ (1.8mmol) was added dropwise to a mixture of benzaldehyde (1.5mmol), Et_3N (4.5mmol), and Ethyl acetate (2.25mmol) in anhydrous DCM (5ml). The mixture was then stirred for 2.5 h at room temperature, when the reaction is over, it was slowly quenched with water and then extracted with EA/water. After that, the organic phase was concentrated, and the final product was separated by column chromatography (EA: PE=1:50).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.43 – 7.32 (m, 3H), 7.26 (s, 1H), 7.21 – 7.11 (m, 2H), 7.12 – 6.89 (m, 3H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.48 (s), 158.02 (s), 156.58 (s), 146.44 (s), 135.82 (s), 130.29 (s), 129.96 (s), 123.87 (s), 123.25 (s), 120.93 (s), 119.27 (s), 118.09 (s), 117.87 (s), 77.32 (d, *J* = 11.5 Hz), 77.06 (s), 76.75 (s), 1.08 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated: 269.11722, found: 269.1173

TX-5: (E)-1-(1-nitroprop-1-en-2-yl)-3-phenoxybenzene



To an oven-dried Schlenk tube charged with a magnetic bar was added $AgNO_2$ (220mg, 1.43mmol), TEMPO (30mg, 1.9mmol), 1-phenoxy-3-(prop-1-en-2-yl) benzene (100mg, 0.47mmol) and oven-dried molecular sieves (200 mg), and solvent (DCE 3mL) were added by syringe. The tube was placed in a preheated oil bath at 70 ºC and the reaction mixture was stirred vigorously for 12h. Then the reaction mixture was cooled to room temperature. The reaction mixture was filtered through a celite bed filter with ethyl acetate as the washing solvent. Finally, organic extract was concentrated and product was purified by column chromatography (PE: EA=30:1). Product yield 85.5mg, 71%.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 3H), 7.27 (t, *J* = 2.1 Hz, 1H), 7.16 (dd, *J* = 10.5, 4.2 Hz, 2H), 7.11 – 7.00 (m, 4H), 2.60 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.93 (s), 156.41 (s), 149.16 (s), 140.08 (s), 136.57 (s), 130.39 (s), 130.01 (s), 124.01 (s), 121.46 (s), 120.33 (s), 119.24 (s), 116.94 (s), 18.58 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 256.09682, found 256.0967

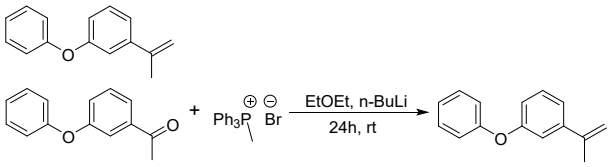
TX-5-S1: 1-(3-phenoxyphenyl)ethan-1-one



To a 25 ml schlenk bottle containing 1-(3-hydroxyphenyl)ethan-1-one (68 ml, 0.55 mmol) was added 3 ml of dichloromethane. Triphenylbismuth (330 mg, 0.75 mmol), copper acetate (91 mg, 0.5 mmol), and triethylamine (0.21 ml, 1.5 mmol) were then added sequentially under argon atmosphere. Heat to 55°C and react for 4.5 hours. After the end of the reaction, the final product was obtained by column chromatography (DCM:PE=2:5), product yield 75 mg, 78%.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.68 (m, 1H), 7.64 – 7.59 (m, 1H), 7.44 (t, *J* = 7.9 Hz, 1H),

7.41 – 7.34 (m, 2H), 7.23 (ddd, *J* = 8.1, 2.5, 0.8 Hz, 1H), 7.19 – 7.13 (m, 1H), 7.07 – 7.02 (m, 2H), 2.59 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.39 (s), 157.77 (s), 156.62 (s), 138.91 (s), 129.97 (s), 123.85 (s), 123.32 (s), 123.12 (s), 119.14 (s), 118.10 (s), 26.74 (s).

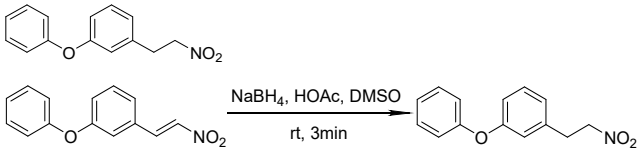
TX-5-S2: 1-phenoxy-3-(prop-1-en-2-yl)benzene



To a suspension of Methyltriphenylphosphonium bromide (367mg, 1mmol) in dry ethyl ether (5 mL) under nitrogen was added n-BuLi (2.5M in hexane, 1mmol, 0.4mL). After 60 min 1-arylalkanone (1mmol) was added and the mixture was stirred for 24h at room temperature. The solution was poured to water and extracted with diethyl ether. The organic layer was washed with brine and was dried over by anhydrous Na_2SO_4, then the solvent was evaporated under reduced pressure. The final product was obtained by column chromatography separation (EA: PE=1:30). Product yield: 123mg, 59%.

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.39 (s), 157.77 (s), 156.62 (s), 138.91 (s), 129.97 (s), 123.85 (s), 123.32 (s), 123.12 (s), 119.14 (s), 118.10 (s), 26.74 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.54 (s), 156.98 (s), 155.52 (s), 138.40 (s), 129.83 (s), 129.79 (s), 123.45 (s), 120.92 (s), 119.54 (s), 118.96 (s), 117.66 (s), 116.55 (s), 12.23 (s).

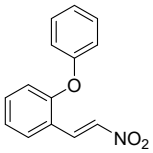
TX-6: 1-(2-nitroethyl)-3-phenoxybenzene



To a dimethyl sulfoxide (1 mL) solution of l-((E)-2- nitro-vinyl)-3-phenoxy-benzene (48mg, 0.2 mmol) and acetic acid (41μmL) was added sodium borohydride (20 mg, 0.5 mmol) at room temperature in Schlenk tube, which was stirred for 3 minutes. Water was then added dropwise at room temperature while cooling appropriately. The reaction mixture was extracted with ethyl acetate, and the organic layer was washed with water and dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under a reduce pressure, and the residue was purified by column chromatography (EA: PE=l:6) to obtain the final product 27.7mg. Product yield 57%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.13 (d, *J* = 13.6 Hz, 1H), 8.07 – 8.00 (m, 1H), 7.31 – 7.26 (m, 2H), 7.19 (d, *J* = 1.4 Hz, 1H), 6.97 – 6.91 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.85 (s), 156.79 (s), 137.58 (s), 130.28 (s), 129.86 (s), 123.60 (s), 123.23 (s), 119.12 (s), 118.79 (s), 117.62 (s), 76.00 (s), 33.22 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 244.09682, found 244.0969.

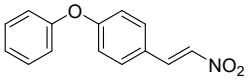
TX-7: (E)-1-(2-nitrovinyl)-2-phenoxybenzene



The reaction was performed by the same procedure as TX-1. 2-phenoxybenzaldehyde (300g, 1.52mmol) as the substrate, and final product was separated by column chromatography (PE: EA=40:1) to obtain the final product (276mg, light yellow compound). Product yield 76%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 13.7 Hz, 1H), 7.87 (d, *J* = 13.7 Hz, 1H), 7.56 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.39 (dt, *J* = 8.8, 4.8 Hz, 3H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.75 (s), 155.40 (s), 138.70 (s), 134.64 (s), 133.21 (s), 131.55 (s), 130.18 (s), 124.74 (s), 123.37 (s), 121.01 (s), 119.83 (s), 117.89 (s), 77.38 (s), 77.19 (d, *J* = 31.9 Hz), 76.71 (s), 0.01 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 242.08117, found 242.0814.

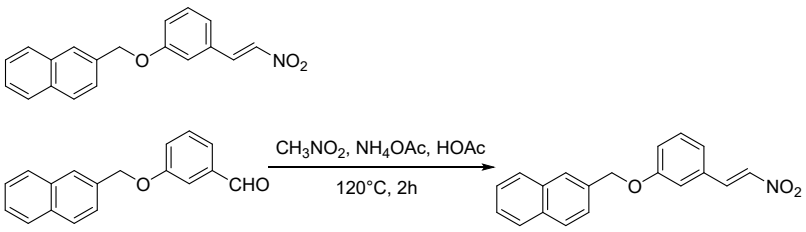
TX-8: (E)-1-(2-nitrovinyl)-4-phenoxybenzene



The reaction was performed by the same procedure as TX-1. 4-phenoxybenzaldehyde (450mg, 2.27mmol) as the substrate, and final product was separated by column chromatography (PE: EA=40:1) to obtain the final product (403mg, light yellow compound). Product yield 74%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 13.6 Hz, 1H), 7.56 – 7.47 (m, 3H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 7.02 (dd, *J* = 8.5, 1.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.47 (s), 155.32 (s), 138.57 (s), 135.83 (s), 131.12 (s), 130.13 (s), 124.79 (s), 124.34 (s), 120.18 (s), 118.38 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 242.08117, found 242.0815.

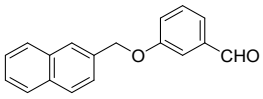
TX-9: (E)-2-((3-(2-nitrovinyl)phenoxy)methyl)naphthalene

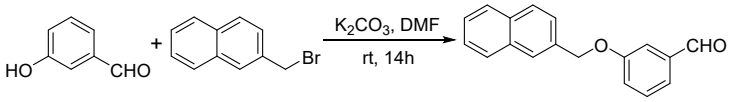


The reaction was performed by the same procedure as TX-1. 4-(naphthalen-2-ylmethoxy) benzaldehyde (450mg, 1.72mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product (283mg). Product yield 54%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 13.7 Hz, 1H), 7.86 (ddd, *J* = 6.0, 5.1, 3.5 Hz, 4H), 7.58 – 7.47 (m, 4H), 7.39 – 7.32 (m, 1H), 7.22 – 7.08 (m, 3H), 5.27 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.31 (s), 138.96 (s), 137.40 (s), 133.79 (s), 133.23 (d, *J* = 11.6 Hz), 131.42 (s), 130.51 (s), 128.62 (s), 127.87 (d, *J* = 15.9 Hz), 126.36 (d, *J* = 12.5 Hz), 125.08 (s), 122.02 (s), 118.79 (s), 115.20 (s), 70.40 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 306.11247, found 306.1126.

TX-9-S1: 3-(naphthalen-2-ylmethoxy)benzaldehyde

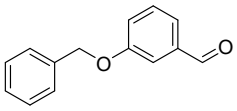




3-Hydroxybenzaldehyde (300mg, 2.46mmol) and potassium carbonate (1020mg, 7.38mmol) were suspended in N,N-dimethylformamide (8mL). 2-(bromomethyl)naphthalene (600mg, 2.71mmol) was added to this suspension, and stirred overnight at room temperature. This mixture was poured into ethyl acetate and water. The organic layer was separated, washed with brine, dried over by anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under a reduced pressure, and the residue was purified by silica gel column chromatography (EA: PE=1:12) to obtain the final compound (569g, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.94 – 7.87 (m, 4H), 7.59 – 7.49 (m, 6H), 7.33 (s, 1H), 5.32 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.03 (s), 159.35 (s), 137.88 (s), 133.78 (s), 133.23 (d, *J* = 13.0 Hz), 130.16 (s), 128.55 (s), 127.98 (s), 127.77 (s), 126.78 – 126.09 (m), 125.20 (s), 123.71 (s), 122.21 (s), 113.45 (s), 70.40 (s).

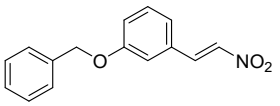
TX-10-S1: 3-(benzyloxy)benzaldehyde



The reaction was performed by the same procedure as TX-11-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and (bromomethyl)benzene (320μl, 2.71mmol) as the substrate, and final product was separated by column chromatography (PE: EA=12:1) to obtain the final product (466mg). Product yield 89%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.53 – 7.46 (m, 5H), 7.43 (s, 2H), 7.38 (s, 1H), 7.28 (s, 1H), 5.16 (s, 2H).

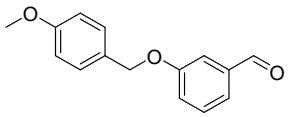
TX-10: (E)-1-(benzyloxy)-3-(2-nitrovinyl)benzene



The reaction was performed by the same procedure as TX-1. 3-(benzyloxy)benzaldehyde (400mg, 1.89mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product (323mg). Product yield 67%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.57 (s, 1H), 7.49 – 7.35 (m, 6H), 7.17 (d, *J* = 15.6 Hz, 3H), 5.13 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.97 (s), 137.38 (s), 136.17 (s), 131.33 (s), 130.48 (s), 128.74 (s), 128.27 (s), 127.45 (s), 121.99 (s), 118.78 (s), 115.07 (s), 70.27 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 256.09682, found 256.0969.

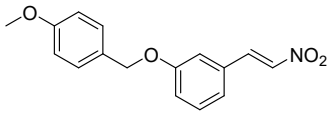
TX-11-S1: 3-((4-methoxybenzyl)oxy)benzaldehyde



The reaction shared the same procedure with TX-9-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and 1-(bromomethyl)-4-methoxybenzene (544mg, 358μl, 2.7mmol) as the substrate, and final product was separated by column chromatography (PE: EA=12:1) to obtain the final product 494mg, 83%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.46 (s, 3H), 7.37 (s, 2H), 7.23 (s, 1H), 6.93 (s, 2H), 5.04 (s, 2H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.89 (s), 159.63 (s), 159.37 (s), 137.80 (s), 130.09 (s), 129.35 (s), 128.31 (s), 123.62 (s), 122.28 (s), 114.04 (s), 113.24 (s), 70.06 (s), 55.33 (s).

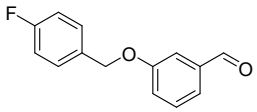
TX-11: (E)-1-((4-methoxybenzyl)oxy)-3-(2-nitrovinyl)benzene



The reaction shared the same procedure with TX-1. 3-((4-methoxybenzyl)oxy)benzaldehyde (189mg, 0.78mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product. Product yield 120mg, 54%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.59 (s, 1H), 7.37 (s, 3H), 7.15 (d, J = 9.7 Hz, 3H), 6.97 (s, 2H), 5.05 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.67 (s), 159.35 (s), 139.02 (s), 137.29 (s), 131.34 (s), 130.44 (s), 129.23 (s), 128.24 (s), 121.90 (s), 118.82 (s), 115.04 – 114.85 (m), 114.01 (s), 70.07 (s), 55.33 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 286.10738, found 286.1075.

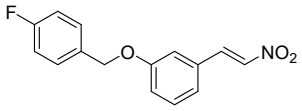
TX-12-S1: 3-((4-fluorobenzyl)oxy)benzaldehyde



The reaction shared the same procedure with TX-9-S1. 3-hydroxybenzaldehyde (260mg, 2.13mmol) and 1-(bromomethyl)-4-chlorobenzene (356mg, 211μl, 1.77mmol) as the substrate, and final product was separated by column chromatography (PE: EA=15:1) to obtain the final product 397mg, 81%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.69 – 7.31 (m, 5H), 7.25 (s, 1H), 7.08 (s, 2H), 5.08 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.98 (s), 163.85 (s), 159.16 (s), 137.87 (s), 130.17 (s), 129.46 (s), 123.91 (s), 122.20 (s), 115.73 (s), 115.51 (s), 113.10 (s), 69.57 (s).

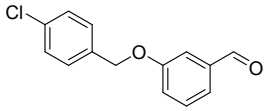
TX-12: (E)-1-((4-fluorobenzyl)oxy)-3-(2-nitrovinyl)benzene



The reaction was performed by the same procedure as TX-1. 3-((4-fluorobenzyl)oxy)benzaldehyde (200mg, 0.97mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product. Product yield 131mg, 49.5%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.59 (s, 1H), 7.41 (d, *J* = 14.5 Hz, 3H), 7.20 (s, 1H), 7.12 (s, 4H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.13 (s), 138.87 (s), 137.39 – 137.19 (m), 131.78 (d, *J* = 49.0 Hz), 131.44 (s), 130.52 (s), 129.30 (s), 122.00 (s), 118.68 (s), 115.79 (s), 115.57 (s), 115.04 (s), 69.51 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 274.08740, found 274.0875.

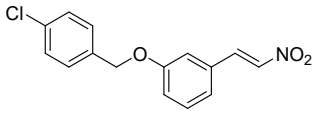
TX-13-S1: 3-((4-chlorobenzyl)oxy)benzaldehyde



The reaction shared the same procedure with TX-9-S1. 3-hydroxybenzaldehyde (260mg, 2.13mmol) and 1-(bromomethyl)-4-chlorobenzene (370mg, 1.77mmol) as the substrate, and final product was separated by column chromatography (PE: EA=15:1) to obtain the final product 432.5mg, 82.5%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.47 (d, *J* = 7.5 Hz, 3H), 7.37 (s, 4H), 7.24 (d, *J* = 7.6 Hz, 1H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.94 (s), 159.08 (s), 137.88 (s), 134.82 (s), 134.05 (s), 130.19 (s), 128.85 (d, *J* = 5.3 Hz), 123.98 (s), 122.18 (s), 113.09 (s), 69.45 (s).

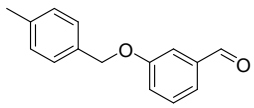
TX-13: (E)-1-((4-chlorobenzyl)oxy)-3-(2-nitrovinyl)benzene



The reaction was performed by the same procedure as TX-1. 3-((4-chlorobenzyl)oxy)benzaldehyde (200mg, 0.81mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product. Product yield 153mg, 65.5%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.57 (s, 1H), 7.37 (s, 5H), 7.17 (s, 1H), 7.08 (d, *J* = 10.1 Hz, 2H), 5.07 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.07 (s), 138.84 (s), 137.45 (s), 134.62 (s), 133.92 (s), 131.58 (s), 130.43 (s), 128.83 (d, *J* = 18.6 Hz), 122.13 (s), 118.65 (s), 69.38 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 290.05785, found 290.0589.

TX-14-S1: 3-((4-methylbenzyl)oxy)benzaldehyde

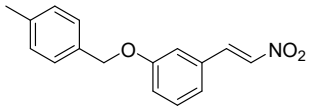


The reaction shared the same procedure with TX-9-S1. 3-hydroxybenzaldehyde (300mg,

2.46mmol) and 1-(bromomethyl)-4-methylbenzene (364mg, 1.97mmol) as the substrate, and final product was separated by column chromatography (PE: EA=12:1) to obtain the final product 415mg, 93%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.45 (t, *J* = 6.1 Hz, 3H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 8.1 Hz, 3H), 5.08 (s, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.07 (s), 159.39 (s), 138.05 (s), 137.83 (s), 133.27 (s), 130.09 (s), 129.37 (s), 127.70 (s), 123.56 (s), 122.22 (s), 113.34 (s), 70.20 (s), 21.00 (s).

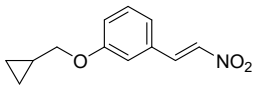
TX-14: (E)-1-((4-methylbenzyl)oxy)-3-(2-nitrovinyl)benzene



The reaction shared the same procedure with TX-1. 3-((4-methylbenzyl)oxy)benzaldehyde (200mg, 0.89mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product. Product yield 112mg, 47%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 13.6 Hz, 1H), 7.53 (dd, *J* = 13.6, 1.8 Hz, 1H), 7.36 – 7.29 (m, 3H), 7.21 (d, *J* = 7.7 Hz, 2H), 7.11 (dd, *J* = 14.2, 7.0 Hz, 3H), 5.04 (d, *J* = 7.3 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.36 (s), 139.03 (s), 138.12 (s), 137.34 (s), 133.30 (s), 131.34 (s), 130.45 (s), 129.42 (s), 127.60 (s), 121.91 (s), 118.83 (s), 115.06 (s), 69.91 (s), 21.23 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 270.11247, found 270.1125

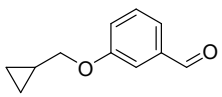
TX-15: (E)-1-(cyclopropylmethoxy)-3-(2-nitrovinyl)benzene



The reaction was performed by the same procedure as TX-1. 3-(cyclopropylmethoxy)benzaldehyde (200mg, 1.14mmol) as the substrate, and final product was separated by column chromatography (PE: EA=30:1) to obtain the final product (180mg). Product yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 13.7 Hz, 1H), 7.55 (d, *J* = 13.7 Hz, 1H), 7.34 (ddd, *J* = 11.3, 7.1, 3.2 Hz, 1H), 7.17 – 7.09 (m, 1H), 7.07 – 6.99 (m, 2H), 3.84 (d, *J* = 6.9 Hz, 2H), 1.35 – 1.21 (m, 1H), 0.72 – 0.62 (m, 2H), 0.42 – 0.33 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.57 (s), 139.07 (s), 137.29 (s), 131.30 (s), 130.40 (s), 121.73 (s), 118.57 (s), 114.64 (s), 73.03 (s), 10.16 (s), 3.24 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 220.09682, found 220.0969.

TX-15-S1: 3-(cyclopropylmethoxy)benzaldehyde

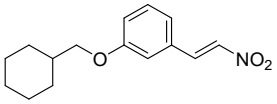


The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (400mg, 3.68mmol) and (bromomethyl)cyclopropane (400μl, 4.6mmol) as the substrate, and final product was separated by column chromatography (PE: EA=12:1) to obtain the final product (646mg).

Product yield 99%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.46 (s, 2H), 7.39 (s, 1H), 7.21 (s, 1H), 3.88 (s, 2H), 1.32 (s, 1H), 0.70 (s, 2H), 0.39 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.16 (s), 159.58 (s), 137.65 (s), 130.02 (s), 123.43 (s), 122.13 (s), 112.76 (s), 73.06 (s), 10.14 (s), 3.23 (s).

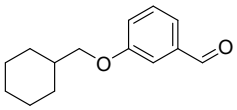
TX-16: (E)-1-(cyclohexylmethoxy)-3-(2-nitrovinyl)benzene



The reaction was performed by the same procedure as TX-1. 3-(cyclohexylmethoxy)benzaldehyde (170mg, 0.78mmol) as the substrate, and final product was separated by column chromatography (PE: EA=30:1) to obtain the final product (116mg). Product yield 57%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 13.7 Hz, 1H), 7.55 (t, *J* = 13.0 Hz, 1H), 7.38 – 7.30 (m, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.02 (dd, *J* = 7.7, 1.7 Hz, 2H), 3.76 (dd, *J* = 14.2, 6.3 Hz, 2H), 1.91 – 1.68 (m, 6H), 1.35 – 1.21 (m, 3H), 1.07 (ddd, *J* = 15.1, 12.3, 3.3 Hz, 2H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 13.7 Hz, 1H), 7.55 (t, *J* = 13.0 Hz, 1H), 7.38 – 7.30 (m, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.02 (dd, *J* = 7.7, 1.7 Hz, 2H), 3.76 (dd, *J* = 14.2, 6.3 Hz, 2H), 1.91 – 1.68 (m, 6H), 1.35 – 1.21 (m, 3H), 1.07 (ddd, *J* = 15.1, 12.3, 3.3 Hz, 2H). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 262.14377, found 262.1439.

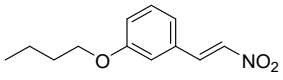
TX-16-S1: 3-(cyclohexylmethoxy)benzaldehyde



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and cyclohexylmethyl bromide (342μl, 2.7mmol) as the substrate, and final product was separated by column chromatography (PE: EA=25:1) to obtain the final product (469mg). Product yield 88%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.43 (s, 2H), 7.40 (s, 1H), 7.15 (s, 1H), 3.80 (s, 2H), 1.81 (d, *J* = 35.4 Hz, 6H), 1.29 (s, 3H), 1.05 (s, 2H).

TX-17: (E)-1-butoxy-3-(2-nitrovinyl)benzene

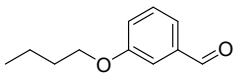


The reaction was performed by the same procedure as TX-1. 3-butoxybenzaldehyde (317mg, 1.77mmol) as the substrate, and final product was separated by column chromatography (PE: EA=20:1) to obtain the final product (239mg). Product yield 61%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 13.7 Hz, 1H), 7.86 (ddd, *J* = 6.0, 5.1, 3.5 Hz, 4H), 7.58 – 7.47 (m, 4H), 7.39 – 7.32 (m, 1H), 7.22 – 7.08 (m, 3H), 5.27 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.45 (s), 139.15 (s), 137.25 (s), 131.27 (s), 130.32 (s), 121.75 (s), 118.50 (s), 114.52 (s), 67.89 (s), 31.21 (s), 19.22 (s), 13.83 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 222.11247,

found 222.1123.

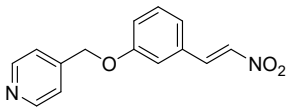
TX-17-S1: 3-butoxybenzaldehyde



The reaction was performed by the same procedure as TX-11-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and 1-bromobutane (310μl, 3.0mmol) as the substrate, and final product was separated by column chromatography (PE: EA=12:1) to obtain the final product (418mg, oil liquid). Product yield 95%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.46 (s, 2H), 7.40 (s, 1H), 7.19 (s, 1H), 4.03 (s, 2H), 1.81 (s, 2H), 1.52 (s, 2H), 1.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.19 (s), 159.74 (s), 137.79 (s), 129.98 (s), 123.26 (s), 121.94 (s), 112.81 (s), 68.00 (s), 31.18 (s), 19.21 (s), 13.81 (s), 1.03 (s).

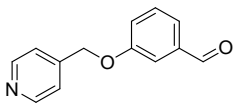
TX-18: (E)-4-((3-(2-nitrovinyl)phenoxy)methyl)pyridine



The reaction was performed by the same procedure as TX-1. 3-(pyridin-4-ylmethoxy)benzaldehyde (150mg, 0.7mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product (66mg). Product yield 37%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 – 8.54 (m, 2H), 7.96 (d, J = 13.7 Hz, 1H), 7.56 (d, J = 13.7 Hz, 1H), 7.38 (dd, J = 15.3, 7.0 Hz, 3H), 7.19 (d, J = 7.7 Hz, 1H), 7.09 (dd, J = 12.0, 3.8 Hz, 2H), 5.14 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.71 – 158.51 (m), 150.13 (s), 145.35 (s), 138.59 (s), 137.58 (s), 131.60 (s), 130.65 (s), 122.38 (s), 121.39 (s), 118.46 (s), 115.15 (s), 68.17 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 257.09207, found 257.0923.

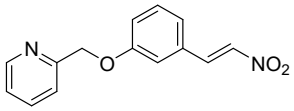
TX-18-S1: 3-(pyridin-4-ylmethoxy)benzaldehyde



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and 4-(Bromomethyl)pyridine hydrobromide (495mg, 1.97mmol, 0.8equiv) as the substrate, and final product was separated by column chromatography (PE: EA=3:2) to obtain the final product (271mg). Product yield 65%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.65 (s, 2H), 7.51 (s, 2H), 7.46 (s, 1H), 7.37 (s, 2H), 7.27 (s, 1H), 5.16 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.80 (s), 158.74 (s), 150.13 (s), 145.42 (s), 137.93 (s), 130.32 (s), 124.35 (s), 122.07 (s), 121.34 (s), 112.87 (s), 68.32 (s).

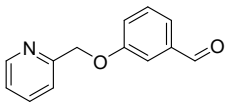
TX-19: (E)-2-((3-(2-nitrovinyl)phenoxy)methyl)pyridine



The reaction was performed by the same procedure as TX-1. 3-(pyridin-2-ylmethoxy)benzaldehyde (150mg, 0.7mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product (46mg). Product yield 26%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 4.1 Hz, 1H), 7.95 (d, *J* = 13.7 Hz, 1H), 7.74 (td, *J* = 7.7, 1.6 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.37 (t, *J* = 8.1 Hz, 1H), 7.26 (t, *J* = 6.2 Hz, 1H), 7.20 – 7.09 (m, 3H), 5.24 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.49 (s), 149.43 (s), 138.85 (s), 137.45 (s), 136.93 (s), 131.45 (s), 130.53 (s), 122.92 (s), 122.16 (s), 121.42 (s), 118.63 (s), 115.15 (s), 70.93 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 257.09207, found 257.0922.

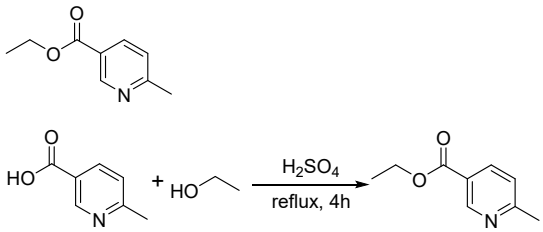
TX-19-S1: 3-(pyridin-2-ylmethoxy)benzaldehyde



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (300mg, 2.46mmol) and 2-(Bromomethyl)pyridine hydrobromide (680mg, 2.7mmol, 1.1equiv) as the substrate, and final product was separated by column chromatography (PE: EA=6:1) to obtain the final product (487mg). Product yield 93%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.63 (s, 1H), 7.73 (s, 1H), 7.49 (d, *J* = 5.8 Hz, 3H), 7.46 (s, 1H), 7.26 (d, *J* = 12.1 Hz, 2H), 5.26 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.89 (s), 159.01 (s), 156.50 (s), 149.41 (s), 137.97 (s), 136.88 (s), 130.19 (s), 123.49 (s), 122.85 (s), 121.71 (s), 121.40 (s), 114.05 (s), 70.91 (s).

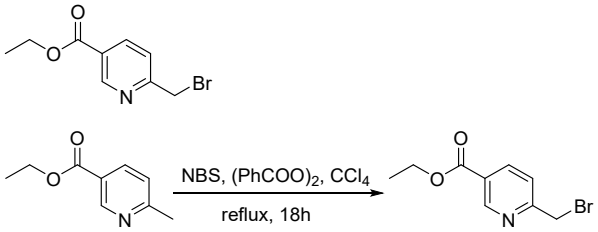
TX-20-S1: ethyl 6-methylnicotinate



6-methylnicotinic acid (1000mg; 7.3mmol) and molecular sieves (5 g) were suspended in absolute ethanol (4ml). Concentrated H_2SO_4 (1.3ml) was added and the mixture was heated to reflux for approximately 4 hours. It was then filtered, evaporated to a small volume under reduced pressure. The residue was diluted with sodium hydroxide and extracted with ether. Meanwhile, neutralized by anhydrous potassium carbonate, and evaporated under reduced pressure, giving product without further purification. Yield: 723mg, 60.0%

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.20 (s, 1H), 7.23 (s, 1H), 4.40 (s, 2H), 2.64 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.39 (s), 163.01 (s), 150.48 (s), 137.24 (s), 123.61 (s), 122.83 (s), 61.21 (s), 24.76 (s), 14.29 (s).

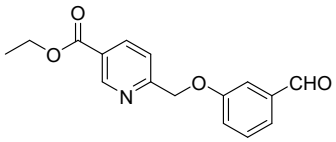
TX-20-S2: ethyl 6-(bromomethyl)nicotinate



To a round-bottom flask containing ethyl 6-methylnicotinate (723mg, 4.4mmol) were added NBS (858mg, 4.8mmol), benzoyl peroxide (10.7mg, 0.044mmol) and CCl_4 (25ml) solvent and the reaction was heat to 90℃ for 18 hours. When the reaction was complete, the solution was diluted with CH_2Cl_2, and washed twice with saturated sodium bicarbonate solution. The organic layer was then dried over Na_2SO_4 and concentrated under reduced pressure to get final product without further purification. Yield 187mg, 17.5%

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.34 (s, 1H), 7.58 (s, 1H), 4.62 (s, 2H), 4.44 (s, 2H), 1.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.44 (s), 138.53 (s), 125.77 (s), 123.21 (s), 61.65 (s), 32.56 (s), 14.28 (s).

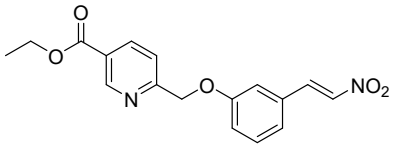
TX-20-S3: ethyl 6-((3-formylphenoxy)methyl)nicotinate



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (117mg, 0.96mmol) and ethyl 6-(bromomethyl)nicotinate (187mg, 0.76mmol) as the substrate, and final product was separated by column chromatography (PE: EA=7:1) to obtain the final product 123mg, 56.4%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 9.23 (s, 1H), 8.34 (s, 1H), 7.64 (s, 1H), 7.51 (d, J = 11.0 Hz, 3H), 7.28 (s, 1H), 5.34 (s, 2H), 4.43 (s, 2H), 1.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.80 (s), 165.05 (s), 160.83 (s), 158.71 (s), 150.57 (s), 137.96 (d, J = 4.4 Hz), 130.30 (s), 125.52 (s), 123.84 (s), 121.66 (s), 120.59 (s), 113.83 (s), 70.52 (s), 61.49 (s), 14.29 (s).

TX-20: ethyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate

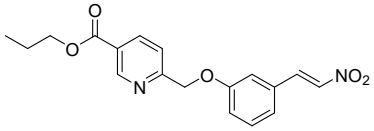


The reaction was performed by the same procedure as TX-33. ethyl 6-((3-formylphenoxy)methyl)nicotinate (123mg, 043mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product. Product yield

108mg, 76.6%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (t, *J* = 10.5 Hz, 1H), 8.41 – 8.28 (m, 1H), 7.96 (d, *J* = 13.7 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.53 (dd, *J* = 20.8, 15.8 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.14 (ddd, *J* = 11.5, 10.7, 5.1 Hz, 3H), 5.31 (d, *J* = 9.3 Hz, 2H), 4.43 (dt, *J* = 7.1, 5.2 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.04 (s), 160.80 (s), 158.69 (s), 150.60 (s), 138.72 (s), 138.05 (s), 137.57 (s), 131.58 (s), 130.65 (s), 125.62 (s), 122.36 (s), 120.65 (s), 118.48 (s), 115.16 (s), 70.53 (s), 61.54 (s), 14.29 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 329.11320, found 329.1135.

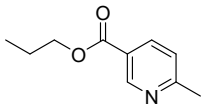
TX-21: propyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate



The reaction was performed by the same procedure as TX-33. propyl 6-((3-formylphenoxy)methyl)nicotinate (155mg, 0.52mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product. Product yield 115mg, 65.9%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, *J* = 1.6 Hz, 1H), 8.34 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.96 (d, *J* = 13.7 Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 13.7 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.14 (ddd, *J* = 11.4, 10.3, 4.9 Hz, 3H), 5.30 (s, 2H), 4.33 (t, *J* = 6.7 Hz, 2H), 1.87 – 1.76 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07 (s), 160.79 (s), 158.67 (s), 150.57 (s), 138.70 (s), 138.03 (s), 137.55 (s), 131.57 (s), 130.63 (s), 125.62 (s), 122.35 (s), 120.65 (s), 118.47 (s), 115.15 (s), 70.52 (s), 67.06 (s), 22.06 (s), 10.46 (s), -0.00 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 343.12885, found 343.1290.

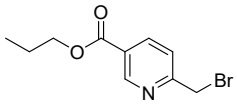
TX-21-S1: propyl 6-methylnicotinate



The reaction shared the same procedure with TX-20-S1. 6-methylnicotinic acid (1000mg, 7.3mmol) and propan-1-ol (4ml) as the substrate. Product yield 995.7mg, 76.2%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.17 (s, 1H), 7.22 (s, 1H), 4.30 (s, 2H), 2.63 (s, 3H), 1.79 (s, 2H), 1.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.56 (s), 163.02 (s), 150.49 (s), 137.24 (s), 123.64 (s), 122.85 (s), 66.76 (s), 24.77 (s), 22.07 (s), 10.47 (s).

TX-21-S2: propyl 6-(bromomethyl)nicotinate

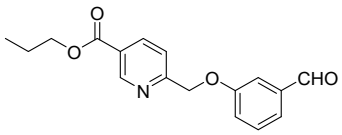


The reaction shared the same procedure with TX-20-S2. propyl 6-methylnicotinate (995mg,

5.5mmol), NBS (1086mg, 6.1mmol), benzoyl peroxide (13.6mg, 0.056mmol) as the substrate. Yield 168mg, 11.8%

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.32 (s, 1H), 7.54 (s, 1H), 4.61 (s, 2H), 4.35 (s, 2H), 1.82 (s, 2H), 1.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.87 (s), 160.78 (s), 150.76 (s), 138.21 (s), 125.58 (s), 123.04 (s), 67.10 (s), 32.91 (s), 22.05 (s), 10.45 (s).

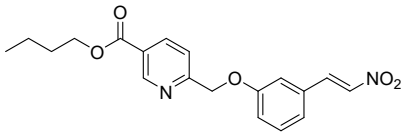
TX-21-S3: propyl 6-((3-formylphenoxy)methyl)nicotinate



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (96mg, 0.79mmol) and propyl 6-(bromomethyl)nicotinate (170mg, 0.66mmol) as the substrate, and final product was separated by column chromatography (PE: EA=7:1) to obtain the final product 155mg, 79.9%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 9.22 (s, 1H), 8.37 (s, 1H), 7.65 (s, 1H), 7.55 – 7.44 (m, 3H), 7.33 (s, 1H), 5.33 (s, 2H), 4.33 (s, 2H), 1.81 (s, 2H), 1.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.88 (s), 165.06 (s), 160.77 (s), 158.66 (s), 150.44 (s), 138.12 (s), 137.90 (s), 130.31 (s), 125.62 (s), 123.88 (s), 121.69 (s), 120.75 (s), 113.81 (s), 70.38 (s), 67.07 (s), 22.03 (s), 10.45 (s).

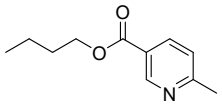
TX-22: butyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate



The reaction was performed by the same procedure as TX-33. butyl 6-((3-formylphenoxy)methyl)nicotinate (164mg, 0.52mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product. Product yield 129mg, 69.7%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (d, J = 1.5 Hz, 1H), 8.34 (dd, J = 8.2, 2.1 Hz, 1H), 7.96 (d, J = 13.7 Hz, 1H), 7.60 (t, J = 8.3 Hz, 1H), 7.55 (d, J = 13.7 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.14 (ddd, J = 11.4, 10.6, 5.1 Hz, 3H), 5.30 (s, 2H), 4.37 (t, J = 6.6 Hz, 2H), 1.78 (dt, J = 14.5, 6.7 Hz, 2H), 1.58 – 1.39 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07 (s), 160.78 (s), 158.67 (s), 150.57 (s), 138.70 (s), 138.02 (s), 137.55 (s), 131.57 (s), 130.63 (s), 125.63 (s), 122.34 (s), 120.65 (s), 118.47 (s), 115.15 (s), 70.52 (s), 65.38 (s), 30.68 (s), 19.23 (s), 13.73 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 357.14450, found 357.1448.

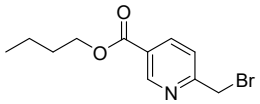
TX-22-S1: butyl 6-methylnicotinate



The reaction shared the same procedure with TX-20-S1. 6-methylnicotinic acid (1000mg, 7.3mmol) and butan-1-ol (4.5ml) as the substrate. Product yield 737mg, 52.3%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.15 (s, 1H), 7.25 (s, 1H), 4.37 (s, 2H), 2.64 (s, 3H), 1.77 (s, 2H), 1.48 (s, 2H), 0.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.56 (s), 163.00 (s), 150.48 (s), 137.23 (s), 123.64 (s), 122.84 (s), 65.07 (s), 30.70 (s), 24.76 (s), 19.23 (s), 13.73 (s).

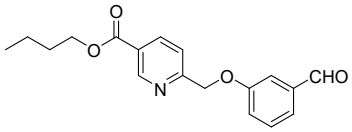
TX-22-S2: butyl 6-(bromomethyl)nicotinate



The reaction shared the same procedure with TX-20-S2. butyl 6-methylnicotinate (736mg, 3.8mmol), NBS (745mg, 4.2mmol), benzoyl peroxide (9.3mg, 0.038mmol) as the substrate. Yield 260mg, 25.1%

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.33 (s, 1H), 7.57 (s, 1H), 4.61 (s, 2H), 4.39 (s, 1H), 1.79 (s, 1H), 1.51 (s, 1H), 1.01 (dd, J = 9.6, 5.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.89 – 162.53 (m), 150.73 (s), 138.23 (s), 123.05 (s), 115.03 (s), 103.01 (s), 65.43 (s), 32.88 (s), 30.67 (s), 13.73 (s).

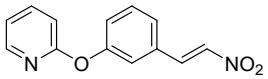
TX-22-S3: butyl 6-((3-formylphenoxy)methyl)nicotinate



The reaction was performed by the same procedure as TX-9-S1. 3-hydroxybenzaldehyde (145mg, 1.2mmol) and butyl 6-(bromomethyl)nicotinate (260mg, 0.96mmol) as the substrate, and final product was separated by column chromatography (PE: EA=7:1) to obtain the final product 164mg, 56.7%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 9.22 (s, 1H), 8.33 (s, 1H), 7.64 (s, 1H), 7.51 (t, J = 8.1 Hz, 3H), 7.29 (s, 1H), 5.33 (s, 2H), 4.38 (s, 2H), 1.78 (s, 2H), 1.50 (s, 2H), 1.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.79 (s), 165.09 (s), 160.82 (s), 158.70 (s), 150.55 (s), 137.96 (d, J = 4.9 Hz), 130.30 (s), 125.55 (s), 123.84 (s), 121.66 (s), 120.62 (s), 113.81 (s), 70.50 (s), 65.34 (s), 30.68 (s), 19.22 (s), 13.73 (s).

TX-23: (E)-2-(3-(2-nitrovinyl)phenoxy)pyridine

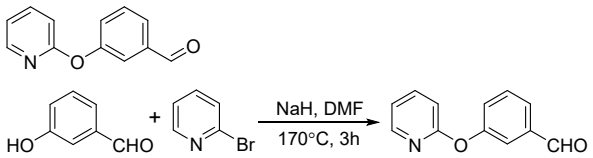


The reaction was performed by the same procedure as TX-1. 3-(pyridin-2-yloxy)benzaldehyde (150mg, 0.75mmol) as the substrate, and final product was separated by column chromatography (PE: EA=30:1) to obtain the final product (95mg). Product yield 52.5%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.16 (m, 1H), 7.99 (d, J = 13.7 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.56 (d, J = 13.7 Hz, 1H), 7.48 (t, J = 7.9 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.31 – 7.27 (m, 1H), 7.05

(dd, J = 7.0, 5.2 Hz, 1H), 6.99 (d, J = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.00 (s), 154.84 (s), 147.65 (s), 139.81 (s), 138.46 (s), 137.65 (s), 131.63 (s), 130.61 (s), 125.45 (s), 124.98 (s), 121.35 (s), 119.15 (s), 112.05 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 243.07642, found 243.0765.

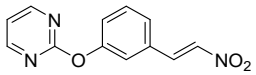
TX-23-S1: 3-(pyridin-2-yloxy)benzaldehyde



3-Hydroxybenzaldehyde (200mg, 1.64mmol) and NaH 60% in oil (66mg, 1.65mmol) were suspended in anhydrous N,N-dimethylformamide (3mL) in Schlenk tube under Ar atmosphere. 2-Bromopyridine (260mg, 1.64mmol) was added to this suspension, then stirred 3h at 170℃. This mixture was poured into ethyl acetate and water for extraction and the organic layer was separated, washed with brine, dried over by anhydrous magnesium sulfate. The filtrate was concentrated under a reduced pressure, and the residue was purified by silica gel column chromatography (EA: PE=1:4) to obtain the final compound (241mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.22 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.68 (s, 1H), 7.59 (s, 1H), 7.44 (s, 1H), 7.07 (s, 1H), 7.02 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.52 (s), 163.05 (s), 154.90 (s), 147.82 (s), 139.75 (s), 137.98 (s), 130.41 (s), 127.36 (s), 126.14 (s), 121.51 (s), 119.18 (s), 112.06 (s).

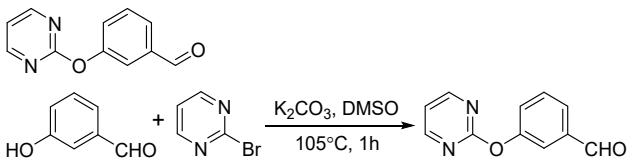
TX-24: (E)-2-(3-(2-nitrovinyl)phenoxy)pyrimidine



The reaction was performed by the same procedure as TX-1. 3-(pyrimidin-2-yloxy)benzaldehyde (120mg, 0.6mmol) as the substrate, and final product was separated by column chromatography (PE: EA=2:1) to obtain the final product (91mg). Product yield 62.3%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 4.8 Hz, 2H), 8.03 (d, J = 13.7 Hz, 1H), 7.59 (d, J = 13.7 Hz, 1H), 7.55 (t, J = 6.5 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.12 (t, J = 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.93 (s), 159.86 (s), 153.50 (s), 138.17 (s), 137.82 (s), 131.73 (s), 130.67 (s), 126.29 (s), 125.46 (s), 122.03 (s), 116.74 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 244.07167, found 244.0719.

TX-24-S1: 3-(pyrimidin-2-yloxy)benzaldehyde

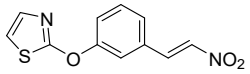


3-Hydroxybenzaldehyde (244mg, 2mmol), 2-bromopyrimidine (315mg, 2.0mmol) and K_2CO_3 (330mg, 2.4mmol) were suspended in anhydrous dimethyl sulfoxide (4mL) in Schlenk tube under Ar atmosphere. Then stirred 1h at 105℃. This mixture was poured into ethyl acetate and water for

extraction and the organic layer was separated, washed with brine, dried over by anhydrous magnesium sulfate. The filtrate was concentrated under a reduced pressure, and the residue was purified by silica gel column chromatography (EA: PE=1:3) to obtain the final compound (275mg, 68.8%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.60 (s, 2H), 7.79 (s, 1H), 7.76 (s, 1H), 7.63 (s, 1H), 7.50 (s, 1H), 7.11 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.22 (s), 164.96 (s), 159.81 (s), 153.55 (s), 138.00 (s), 130.35 (s), 127.82 (s), 126.99 (s), 122.22 (s), 116.67 (s).

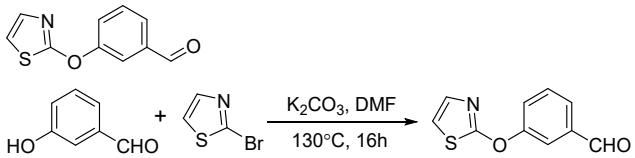
TX-25: (E)-2-(3-(2-nitrovinyl)phenoxy)thiazole



The reaction was performed by the same procedure as TX-1. 3-(thiazol-2-yloxy)benzaldehyde (100mg, 0.49mmol) as the substrate, and final product was separated by column chromatography (PE: EA=4:1) to obtain the final product. Product yield 99mg, 81%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 13.7 Hz, 1H), 7.57 (d, J = 13.7 Hz, 1H), 7.51 (t, J = 7.9 Hz, 2H), 7.43 (dd, J = 6.2, 4.5 Hz, 2H), 7.26 (s, 1H), 6.90 (d, J = 3.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.62 (s), 155.80 (s), 137.96 (d, J = 10.7 Hz), 137.57 (s), 131.92 (s), 130.88 (s), 126.27 (s), 123.52 (s), 120.02 (s), 113.71 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 249.03284, found 249.0330.

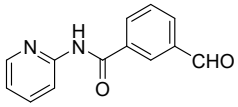
TX-25-S1: 3-(thiazol-2-yloxy)benzaldehyde

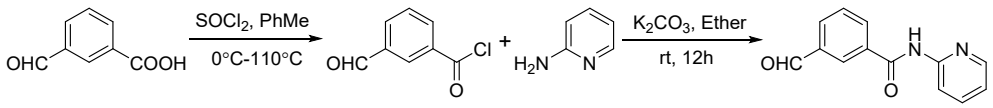


3-Hydroxybenzaldehyde (200mg, 1.64mmol), 2-bromothiazole (350mg, 192μl, 2.13mmol) and K_2CO_3 (295mg, 2.13mmol) were suspended in anhydrous N,N-Dimethylformamide (4mL) in Schlenk tube under Ar atmosphere. Then stirred 16h at 130℃. This mixture was poured into ethyl acetate and water for extraction and the organic layer was separated, washed with brine, dried over by anhydrous magnesium sulfate. The filtrate was concentrated under a reduced pressure, and the residue was purified by silica gel column chromatography (EA: PE=1:10) to obtain the final compound (211mg, 62.8%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.59 (d, J = 7.2 Hz, 2H), 7.25 (s, 1H), 6.89 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.05 (s), 155.85 (s), 138.11 (s), 137.63 (s), 130.61 (s), 126.95 (d, J = 13.4 Hz), 126.00 (s), 120.26 (s), 113.68 (s).

TX-32-S1: 3-formyl-N-(pyridin-2-yl)benzamide

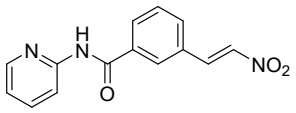




To an anhydrous 25ml Schlenk flask with 3-formylbenzoic acid (300mg, 2mmol), 3ml anhydrous toluene and a magnetic bar was added redistilled thionyl chloride (220μl, 3mmol) drop by drop at 0℃in an Ar atmosphere. Then heat to 110℃ for one hour. After the reaction competed, dried the solution in the schlenk bottle with a vacuum pump and a gas absorption trap to get the crude intermediate product 3-formylbenzoyl chloride. We next added dichloromethane (5ml), pyridin-2-amine (230mg, 2.4mmol) and K_2CO_3 (410mg, 3mmol) to the Schlenk flask at Ar atmosphere. Reacted at room temperature for three hours. After the reaction competed, the system was extracted with ether, washed with brine, dried over $MgSO_4$, evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (PE: EA=3:1) to get final product (273.5mg, 60.5%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 9.94 (s, 1H), 8.61 (s, 1H), 8.54 (s, 1H), 8.34 (s, 2H), 8.19 – 8.13 (m, 1H), 7.88 (s, 1H), 7.74 (s, 1H), 7.19 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.26 (s), 164.88 (s), 151.47 (s), 146.78 (s), 139.44 (s), 136.72 (s), 135.53 (s), 133.50 (s), 132.80 (s), 129.63 (s), 128.94 (s), 120.25 (s), 115.14 (s).

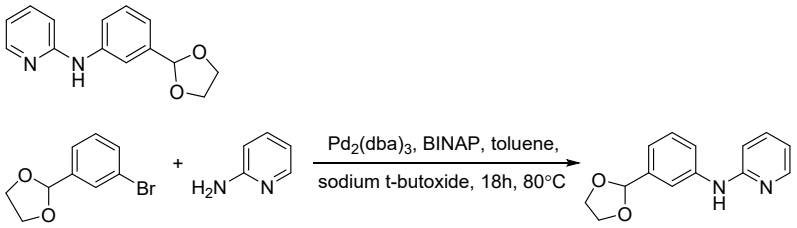
TX-32: (E)-3-(2-nitrovinyl)-N-(pyridin-2-yl)benzamide



The reaction was performed by the same procedure as TX-33. 3-formyl-N-(pyridin-2-yl)benzamide (72mg, 0.32mmol) as the substrate, and final product was separated by column chromatography (PE: EA=3:1) to obtain the final product. Product yield 56mg, 65%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.31 (dd, J = 4.9, 1.0 Hz, 1H), 8.15 (s, 1H), 8.05 (d, J = 13.7 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 13.7 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.12 (ddd, J = 7.3, 4.9, 0.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.35 (s), 151.17 (s), 147.99 (s), 138.68 (s), 138.33 (s), 137.62 (s), 135.61 (s), 132.39 (s), 131.72 (s), 131.01 (s), 129.96 (s), 128.03 (s), 120.39 (s), 114.28 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 270.08732, found 270.0877.

TX-33-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-2-amine

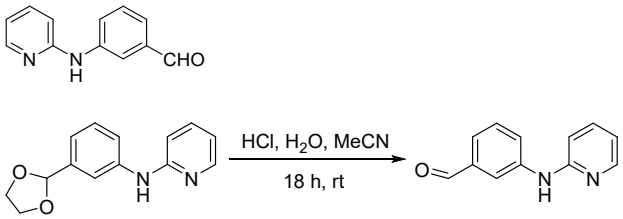


BINAP (20mg, 0.03mol), $Pd_2(dba)_3$ (10.0mg, 0.01mmol) were first pretreated in 3 ml toluene at 110°C for 3 minutes. Then to a Schlenk tube loaded with sodium t-butoxide (600mg, 6.0mmol) and pyridin-2-amine (492mg, 4.7mmol) was added the already mixed palladium catalyst and its ligand,

after the mixture of the above reagent, 2-(3-bromophenyl)-1,3-dioxolane (653μl, 4.3mmol) and 3 ml of toluene were injected into the reaction system. Heat to 90°C and react for 18 hours. All procedure was executed at Ar atmosphere. After the reaction completed, cool to room temperature, diluted the system with ether, filtered, and concentrated under reduced pressure to give a residue. and the residue was purified by silica gel column chromatography (EA: PE= 1:5 to 1:2) to obtain the final compound (780mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.51 (s, 1H), 7.44 (s, 1H), 7.38 (s, 2H), 7.18 (s, 1H), 6.89 (s, 1H), 6.78 (d, *J* = 16.2 Hz, 2H), 5.84 (s, 1H), 4.11 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.71 (s), 148.44 (s), 140.67 (s), 139.26 (s), 137.71 (s), 129.37 (s), 120.83 (d, *J* = 12.1 Hz), 118.09 (s), 115.17 (s), 108.30 (s), 103.50 (s), 65.31 (s).

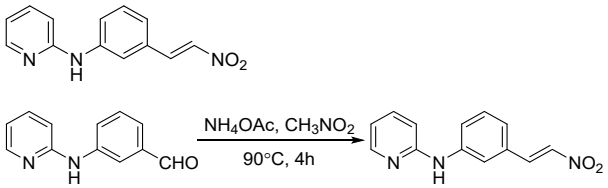
TX-33-S2: 3-(pyridin-2-ylamino)benzaldehyde



To N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-2-amine (400mg, 1.65mmol) and acetonitrile (10ml) was add a solution of hydrochloric acid (1N, 2.7ml). Stirred at room temperature for 18 hours. After the reaction completed, concentrated in vacuum to remove most of the acetonitrile, dilute with water and extract with ether. Combine the organic extracts and wash with saturated sodium bicarbonate, then with brine. Dry (Na_2SO_4) the organics, filter, and purified by a short silica gel column chromatography to get final product (309mg, 94.6%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.29 (s, 1H), 7.97 (s, 1H), 7.69 (s, 1H), 7.57 (s, 1H), 7.53 (s, 1H), 7.49 (s, 1H), 6.94 (s, 1H), 6.89 (s, 1H), 6.83 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.32 (s), 155.13 (s), 148.29 (s), 141.67 (s), 137.88 (s), 137.35 (s), 129.86 (s), 125.17 (s), 123.86 (s), 119.14 (s), 115.88 (s), 109.41 (s).

TX-33: (E)-N-(3-(2-nitrovinyl)phenyl)pyridin-2-amine

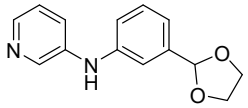


- 3-(pyridin-2-ylamino)benzaldehyde (1mmol, 200mg) was added to a stirred solution of ammonium acetate (20mg, 0.25mmol) in dry nitromethane (9 mL) at 90°C. The mixture was heated for 4 h, poured into water and extracted with diethyl ether. The extract was washed with brine, dried over by $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (PE: EA=4:1) to get final product (137mg, 57%). The method described at compound 2-1 did not work here.

  ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.31 (dd, *J* = 4.9, 1.0 Hz, 1H),

8.15 (s, 1H), 8.05 (d, J = 13.7 Hz, 1H), 8.01 (d, J = 7.8 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 13.7 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.12 (ddd, J = 7.3, 4.9, 0.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.00 (s), 148.29 (s), 141.73 (s), 139.23 (s), 137.87 (s), 137.31 (s), 131.05 (s), 130.12 (s), 122.78 (d, J = 2.2 Hz), 119.17 (s), 115.96 (s), 109.56 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 242.09240, found 242.0928.

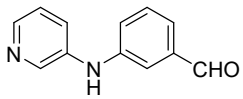
TX-34-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-3-amine



The reaction shared the same procedure with TX-33-S1. 2-(3-bromophenyl)-1,3-dioxolane (300mg, 200μl, 1.3mmol) and pyridin-3-amine (182mg, 1.9mmol) as the substrate. BINAP (40mg, 0.06mol), $Pd_2(dba)_3$ (20.0mg, 0.02mmol) and sodium t-butoxide (400mg, 3.9mmol) as the catalyst. Toluene (5ml) as the solvent. Purification by silica gel column chromatography (DCM: MeOH= 20:1) to obtain the product (260mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.17 (s, 1H), 7.39 (s, 1H), 7.30 (s, 1H), 7.18 (d, J = 12.8 Hz, 1H), 7.10 (d, J = 7.8 Hz, 1H), 5.82 (s, 1H), 5.77 (s, 1H), 4.07 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.30 (d, J = 13.1 Hz), 142.30 (d, J = 13.1 Hz), 140.46 (s), 139.64 (s), 139.60 (s), 129.60 (s), 123.76 (s), 123.69 (s), 120.09 (s), 118.81 (s), 116.05 (s), 103.44 (s), 65.31 (s).

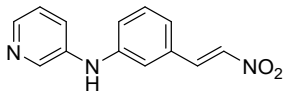
TX-34-S2: 3-(pyridin-3-ylamino)benzaldehyde



This reaction shared the same procedure with TX-33-S2. N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-3-amine (250mg, 1mmol) as the substrate. purification by a short silica gel column chromatography (DCM: MeOH=20:1) to get final product (170mg, 86%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 8.44 (s, 1H), 8.27 (s, 1H), 7.55 (s, 1H), 7.47 (d, J = 11.7 Hz, 3H), 7.30 (s, 1H), 7.24 (s, 1H), 5.94 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.92 (s), 143.43 (s), 143.30 (s), 141.27 (s), 138.63 (s), 137.82 (s), 130.23 (s), 124.94 (s), 123.84 (s), 123.61 (s), 123.12 (s), 116.74 (s).

TX-34: (E)-N-(3-(2-nitrovinyl)phenyl)pyridin-3-amine

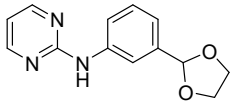


The reaction shared the same procedure with TX-33. 3-(pyridin-3-ylamino)benzaldehyde (110mg, 0.56mmol) as the substrate, and final product was separated by column chromatography (PE: EA=15:1) to obtain the final product. Product yield 99mg, 73%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 2.7 Hz, 1H), 8.26 (dt, J = 8.8, 4.4 Hz, 1H), 7.94 (d, J = 13.7 Hz, 1H), 7.53 (d, J = 13.7 Hz, 1H), 7.45 (ddd, J = 8.2, 2.7, 1.4 Hz, 1H), 7.36 (t, J = 7.8 Hz,

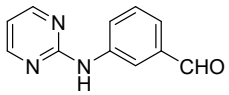
2H), 7.25 – 7.22 (m, 1H), 7.16 (dd, *J* = 10.8, 8.6 Hz, 3H), 5.93 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.56 (s), 143.27 (s), 141.29 (s), 138.75 (s), 138.62 (s), 137.45 (s), 131.48 (s), 130.58 (s), 125.12 (s), 123.89 (s), 122.14 (s), 120.94 (s), 117.25 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 242.09240, found 242.0926.

TX-35-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyrimidin-2-amine



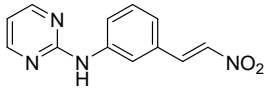
The reaction shared the same procedure with TX-33-S1. 2-(3-bromophenyl)-1,3-dioxolane (1000mg, 670μl, 4.4mmol) and pyrimidin-2-amine (456mg, 4.8mmol) as the substrate. Xantphos (27mg, 0.045mol), $Pd_2(dba)_3$ (14mg, 0.015mmol) and sodium t-butoxide (630mg, 6.5mmol) as the catalyst. Toluene (20ml) as the solvent. Purification by silica gel column chromatography (DCM: MeOH= 20:1) to obtain the product (535mg, 50.0%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.73 (s, 1H), 7.38 (s, 1H), 7.20 (s, 1H), 6.73 (s, 1H), 5.87 (s, 1H), 4.10 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.20 (s), 157.96 (s), 139.46 (s), 138.92 (s), 128.97 (s), 120.55 (s), 120.04 (s), 117.41 (s), 112.47 (s), 103.80 (s), 65.25 (s).

TX-35-S2: 3-(pyrimidin-2-ylamino)benzaldehyde



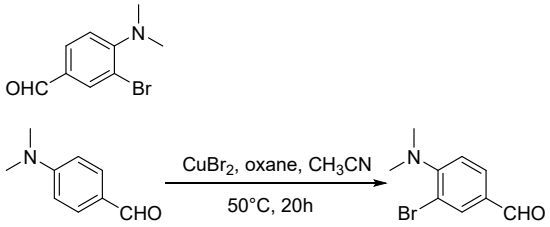
This reaction shared the same procedure with 2-33-S2. N-(3-(1,3-dioxolan-2-yl)phenyl)pyrimidin-2-amine (500mg, 2.05mmol) as the substrate. purification by a short silica gel column chromatography (DCM: MeOH=15:1) to get product (370mg, 90.7%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.49 (s, 2H), 8.27 (s, 1H), 7.88 (s, 1H), 7.57 (s, 1H), 7.52 (s, 1H), 7.45 (s, 1H), 6.82 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.26 (s), 159.86 (s), 158.05 (s), 140.35 (s), 137.26 (s), 129.55 (s), 124.90 (s), 123.97 (s), 119.63 (s), 113.26 (s).

TX-35: (E)-N-(3-(2-nitrovinyl)phenyl)pyrimidin-2-amine



The reaction shared the same procedure with TX-33. 3-(pyrimidin-2-ylamino)benzaldehyde (120mg, 0.6mmol) as the substrate, and final product was separated by column chromatography (PE: EA=15:1) to obtain the final product. Product yield 99.5mg, 68.5%.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 2H), 8.13 (s, 1H), 8.05 (s, 1H), 7.65 (s, 1H), 7.58 (s, 1H), 7.40 (s, 1H), 7.34 (s, 1H), 7.23 (s, 1H), 6.81 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.76 (s), 158.00 (s), 140.50 (s), 139.37 (s), 137.35 (s), 130.89 (s), 129.86 (s), 123.09 (s), 122.58 (s), 118.96 (s), 113.34 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 243.08765, found 243.0878.

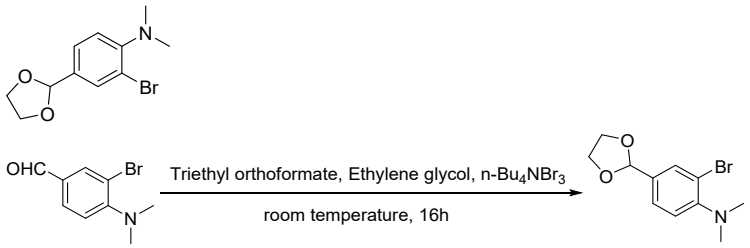
TX-36-S1: 3-bromo-4-(dimethylamino)benzaldehyde



A three necked flask was charged with 4-(dimethylamino) benzaldehyde (149mg, 1mmol), cupric bromide (112mg, 0.5mmol), and oxone1 (738mg, 1.2mmol). After CH_3CN (8 mL) was added, the mixture was stirred for 16 h at room temperature. When the reaction was complete (monitored by TLC). Saturated sodium carbonate was added and then 10mL of water added. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by column chromatography (PE: EA=15:1). Yield 103.5mg, 45.5%.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.07 (s, 1H), 7.75 (s, 1H), 7.09 (s, 1H), 2.98 (s, 6H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.07 (s, 1H), 7.75 (s, 1H), 7.09 (s, 1H), 2.98 (s, 6H).

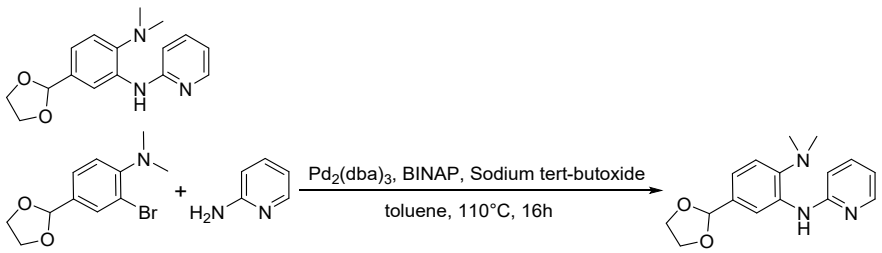
TX-36-S2: 2-bromo-4-(1,3-dioxolan-2-yl)-N,N-dimethylaniline



To the mixture of 3-bromo-4-(dimethylamino)benzaldehyde (664mg, 3mmol), tri-ethyl ortho-formate (1.2ml, 7.5mmol), and 1,2-ethanediol (15mmol) was added tetra-butyl-ammonium tri-bromide (30mg, 0.06mmol). The reaction was left at room temperature, and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was poured into saturated $NaHCO_3$ solution, and the product extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Further purification was achieved by Silica gel column chromatography separation (PE: EA=10:1). Yield 667.5mg, 82.1%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.37 (s, 1H), 7.08 (s, 1H), 5.76 (s, 1H), 4.08 (s, 4H), 2.83 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.65 (s), 133.49 (s), 132.02 (s), 126.36 (s), 120.13 (s), 118.83 (s), 102.81 (s), 65.32 (s), 44.16 (s).

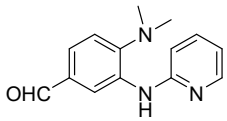
TX-36-S3: 4-(1,3-dioxolan-2-yl)-N1,N1-dimethyl-N2-(pyridin-2-yl)benzene-1,2-diamine



$Pd_2(dba)_3$ (9 mg, 0.01 mmol) and BINAP (19mg, 0.03 mmol) were first pretreated in 3 ml toluene at 110°C for 3 minutes. Then to a Schlenk tube loaded with sodium tert-butoxide (67 mg, 0.7 mmol) and 2-amino Pyridine (56 mg, 0.6 mmol) was added the already mixed palladium catalyst and its ligand, after the mixture of the above reagent, 2-bromo-4-(1,3-dioxolan-2-yl)-N,N-dimethylaniline (136 mg, 0.5 mmol) and 3 ml of toluene were injected into the reaction system. Heat to 110°C and react for 16 hours. All procedure was executed at Ar atmosphere. After completion of the reaction, the mixture was extracted with ether and water, the organic phase was washed with saturated saline, dried over anhydrous sodium sulfate, concentrated under reduced pressure, and separated by silica gel column chromatography (PE: EA=5:1 to 2:1) to give the product. Yield 91mg, 64%

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.13 (s, 1H), 7.51 (d, J = 8.6 Hz, 2H), 7.14 (s, 1H), 7.10 (s, 1H), 6.93 (s, 1H), 6.75 (s, 1H), 5.83 (s, 1H), 4.10 (s, 4H), 2.68 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.46 (s), 148.37 (s), 144.03 (s), 137.53 (s), 135.38 (s), 133.60 (s), 119.59 (s), 119.35 (s), 115.65 (s), 114.91 (s), 109.37 (s), 103.86 (s), 65.28 (s), 44.17 (s).

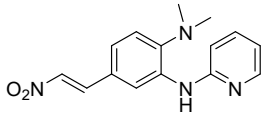
TX-36-S4: 4-(dimethylamino)-3-(pyridin-2-ylamino)benzaldehyde



This reaction shared the same procedure with TX-33-S2. 4-(1,3-dioxolan-2-yl)-N1,N1-dimethyl-N2-(pyridin-2-yl)benzene-1,2-diamine (295mg, 1mmol) as the substrate. purification by a short silica gel column chromatography (DCM: MeOH=50:1) to get final product (230mg, 92%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.52 (s, 1H), 8.32 (s, 1H), 7.56 (s, 1H), 7.50 (s, 1H), 7.20 (s, 1H), 7.15 (s, 1H), 6.91 (s, 1H), 6.83 (s, 1H), 2.79 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.74 (s), 155.05 (s), 149.18 (s), 148.43 (s), 137.78 (s), 135.15 (s), 132.04 (s), 124.23 (s), 119.25 (s), 118.78 (s), 115.54 (s), 109.82 (s), 43.44 (s).

TX-36: (E)-N1,N1-dimethyl-4-(2-nitrovinyl)-N2-(pyridin-2-yl)benzene-1,2-diamine

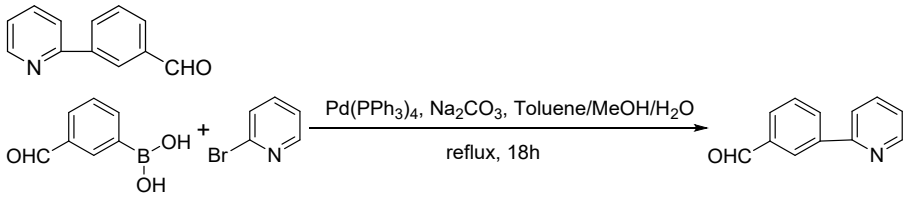


This reaction shared the same procedure with TX-33. 4-(dimethylamino)-3-(pyridin-2-ylamino)benzaldehyde (120mg, 0.5mmol) as the substrate. purification by a short silica gel column chromatography (DCM: MeOH=40:1) to get final product (96mg, 67.5%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.30 (s, 1H), 8.01 (s, 1H), 7.57 (d, J = 18.7 Hz, 2H), 7.26 (s, 1H), 7.13 (d, J = 2.4 Hz, 2H), 6.82 (d, J = 9.7 Hz, 2H), 2.74 (s, 6H). ^{13}C NMR (101 MHz,

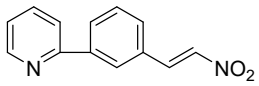
$CDCl_3$) δ 155.04 (s), 148.22 (s), 146.97 (s), 139.92 (s), 137.72 (s), 135.75 (s), 135.65 (s), 125.45 (s), 123.53 (s), 119.83 (s), 117.62 (s), 115.56 (s), 110.42 (s), 43.69 (s).
HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated 285.13460, found 285.1346.

TX-37-S1: 3-(pyridin-2-yl)benzaldehyde



To a Schlenk tube containing $Pd(PPh_3)_4$ (35 mg, 0.03 mmol), 2-bromopyridine (158 mg, 1 mmol) and anhydrous toluene (3 ml) was added (3-formylphenyl)boronic acid (180 mg, 1.2 mmol)/MeOH. (1.5ml), and 2M Na_2CO_3 aqueous one by one. Heat to 105°C for 18h, all operations were performed in an anhydrous and oxygen-free environment. After completion of the reaction, the mixture was extracted with DCM and water, the organic phase was washed with saturated saline, dried over anhydrous sodium sulfate, concentrated under reduced pressure, and separated by silica gel column chromatography (PE: EA=4:1) to give the product. Yield 168.4mg, 92%
^{1}H NMR (400 MHz, DMSO) δ 10.11 (s, 1H), 8.70 (s, 1H), 8.62 (s, 1H), 8.38 (s, 1H), 8.03 (s, 1H), 7.94 (s, 1H), 7.91 (s, 1H), 7.70 (s, 1H), 7.40 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 193.58 (s), 150.15 (s), 139.94 (s), 137.89 (s), 137.03 (s), 132.53 (s), 130.10 (s), 129.97 (s), 128.28 (s), 123.65 (s), 120.92 (s).

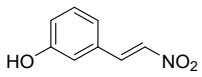
TX-37: (E)-2-(3-(2-nitrovinyl)phenyl)pyridine

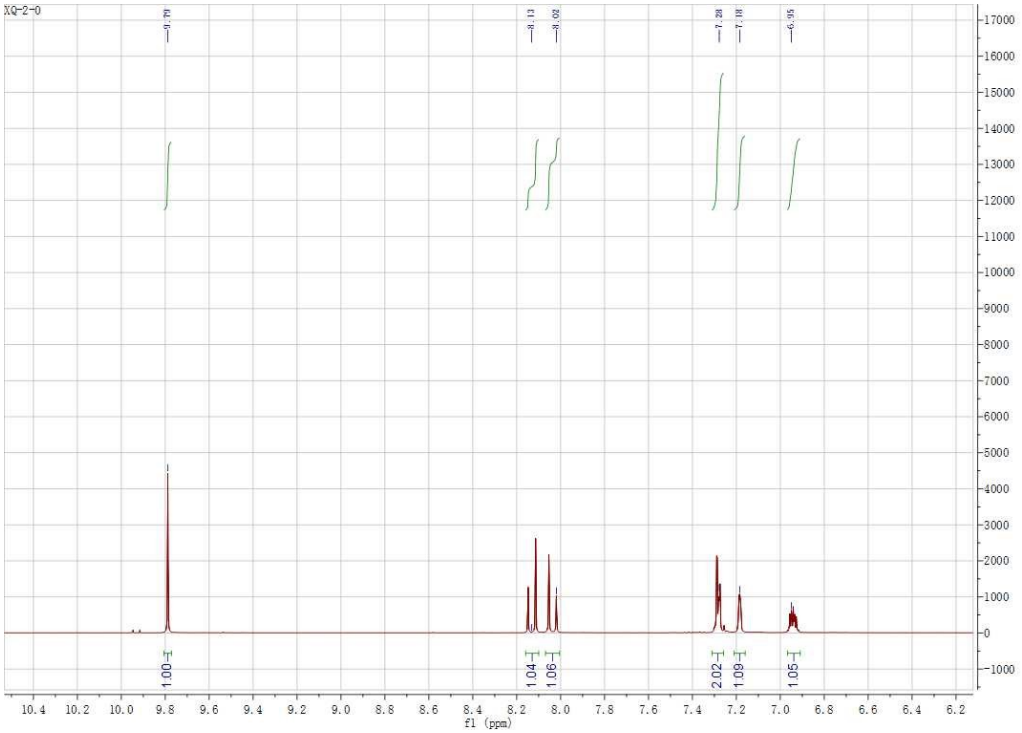


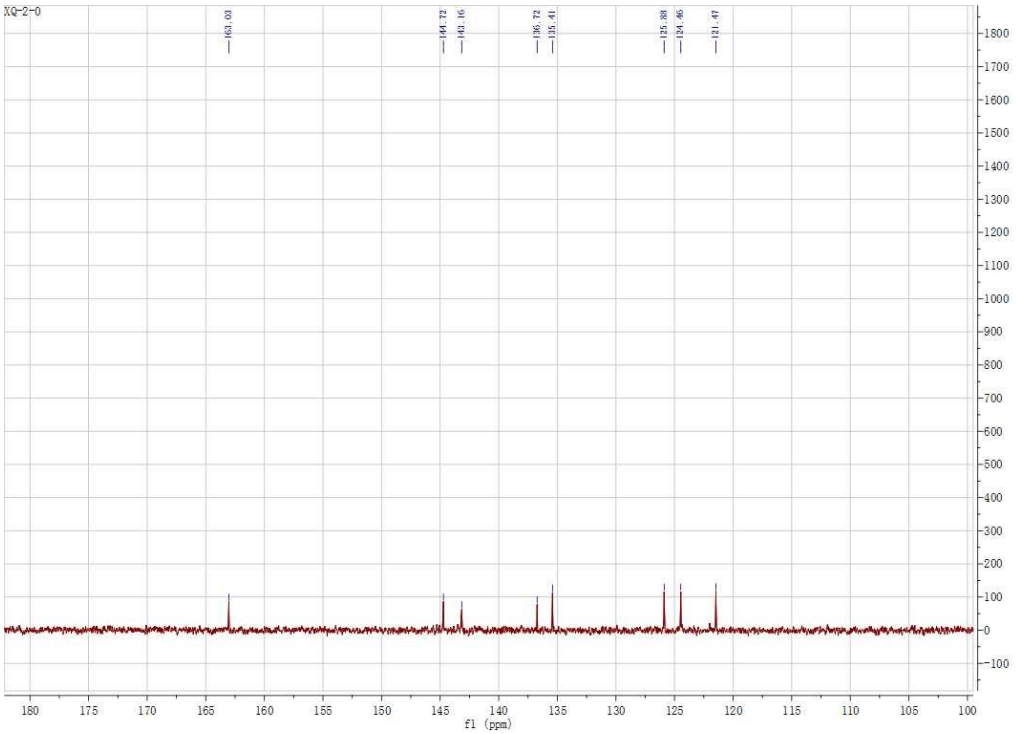
The reaction shared the same procedure with TX-33. 3-(pyridin-2-yl)benzaldehyde (100mg, 0.55mmol) as the substrate, and final product was separated by column chromatography (PE: EA=5:1) to obtain the final product. Product yield 90mg, 72.5%.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 4.3 Hz, 1H), 8.24 (s, 1H), 8.12 – 8.06 (m, 2H), 7.80 (tt, J = 5.4, 2.7 Hz, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.69 (d, J = 13.7 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.30 (ddd, J = 7.1, 4.8, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.84 (s), 149.91 (s), 140.61 (s), 138.89 (s), 137.54 (s), 137.05 (s), 130.67 (s), 130.34 (s), 129.78 (s), 129.42 (s), 127.64 (s), 122.88 (s), 120.56 (s). HRMS: $C_{13}H_{12}N_3O_2$ for +, calculated,227.08150, found 227.0816.

5. NMR of all compounds

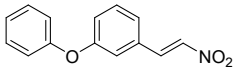
TX-0: (E)-3-(2-nitrovinyl)phenol

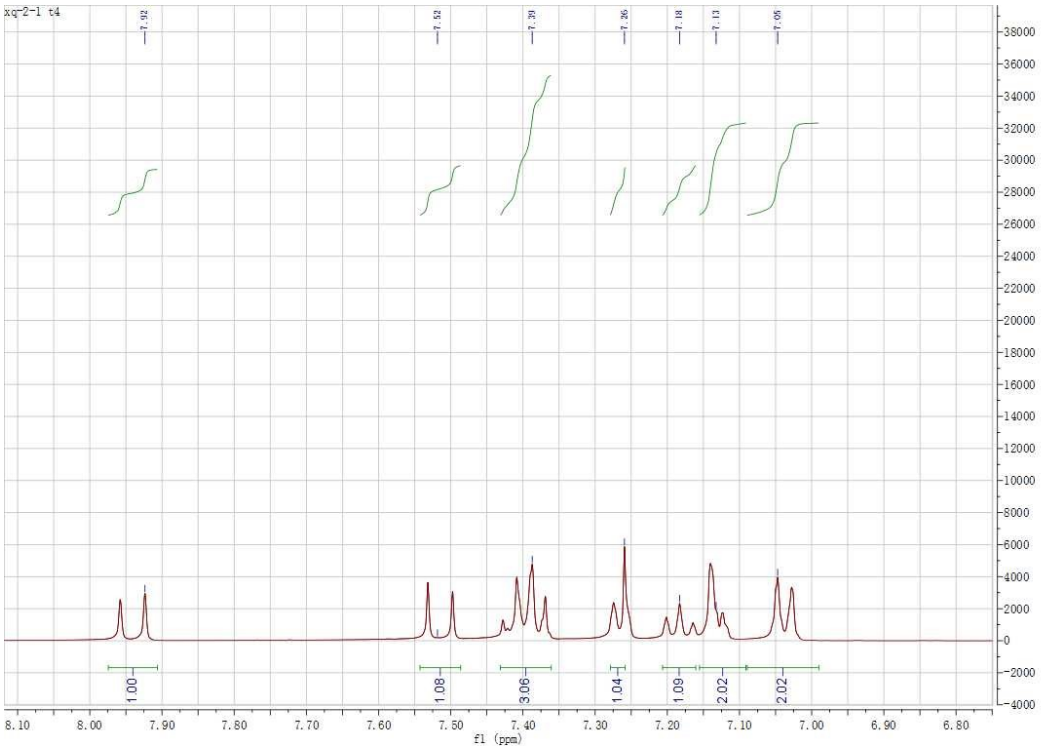


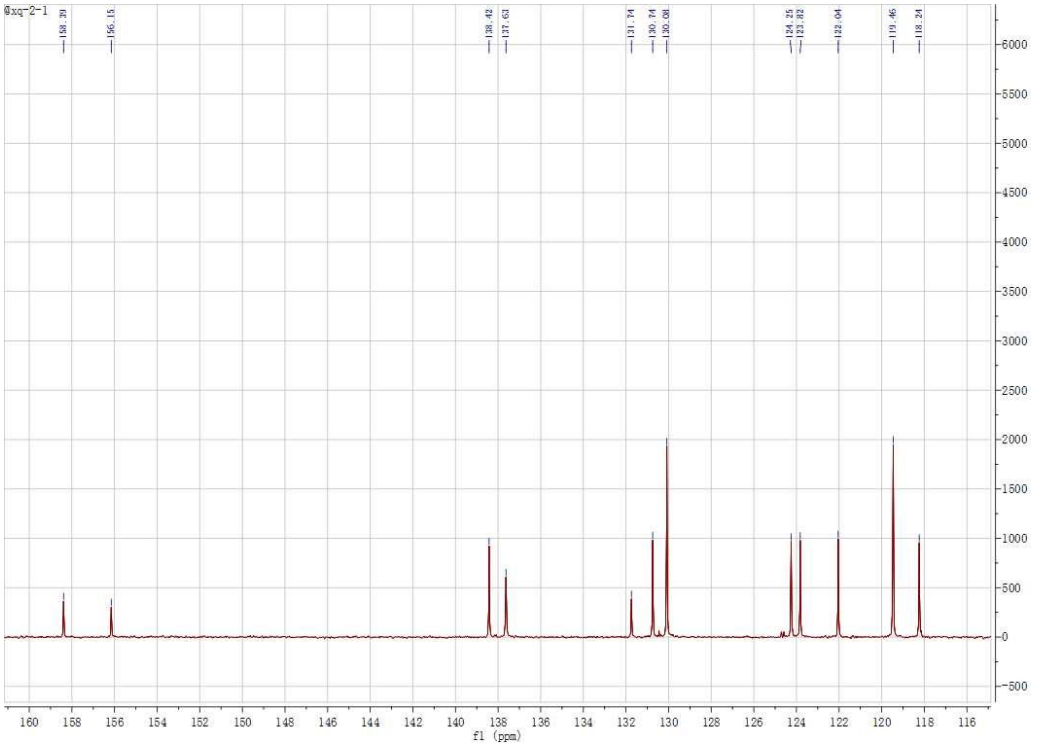




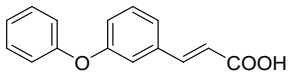
TX-1: (E)-1-(2-nitrovinyl)-3-phenoxybenzene

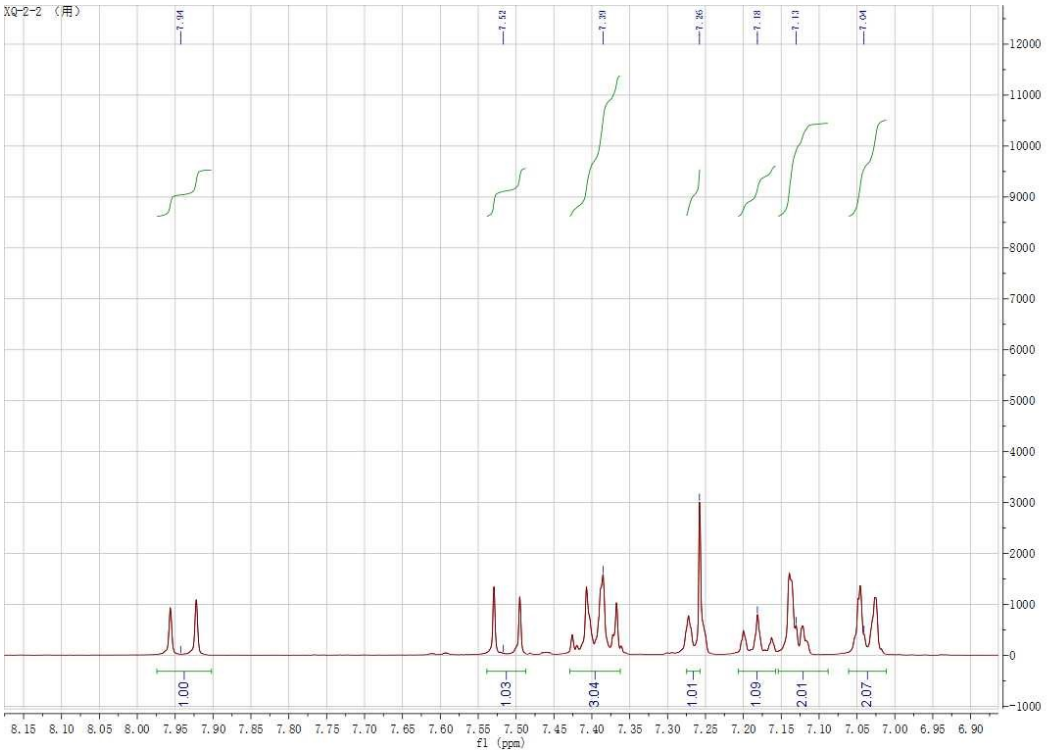


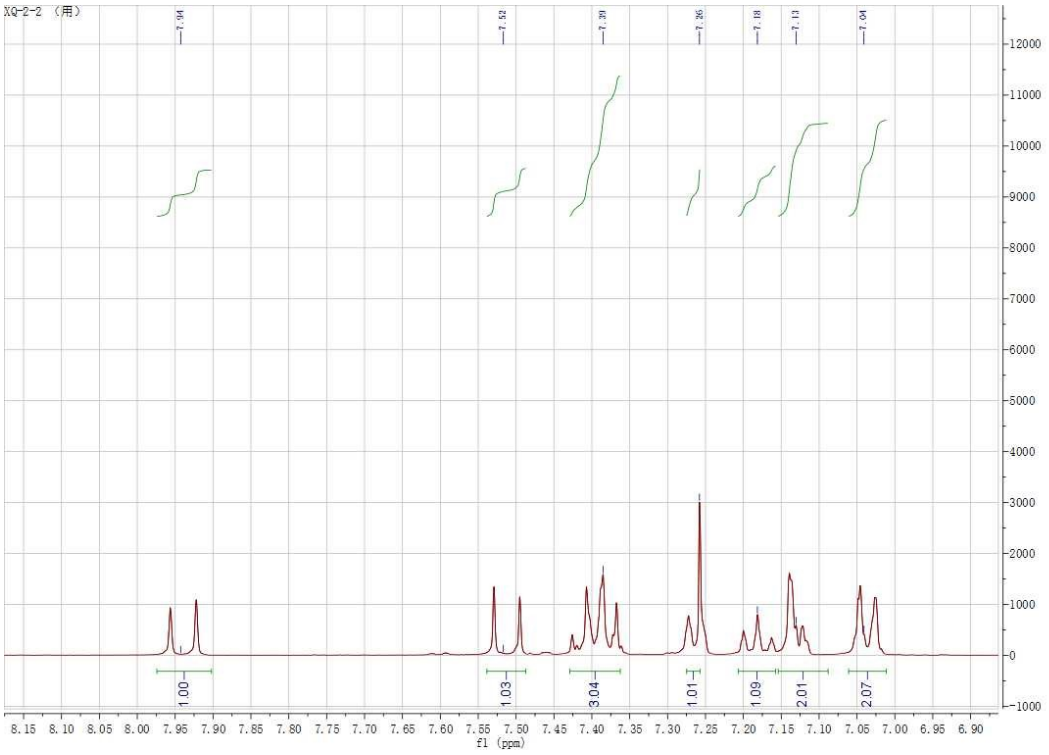




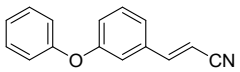
TX-2: (E)-3-(3-phenoxyphenyl)acrylic acid

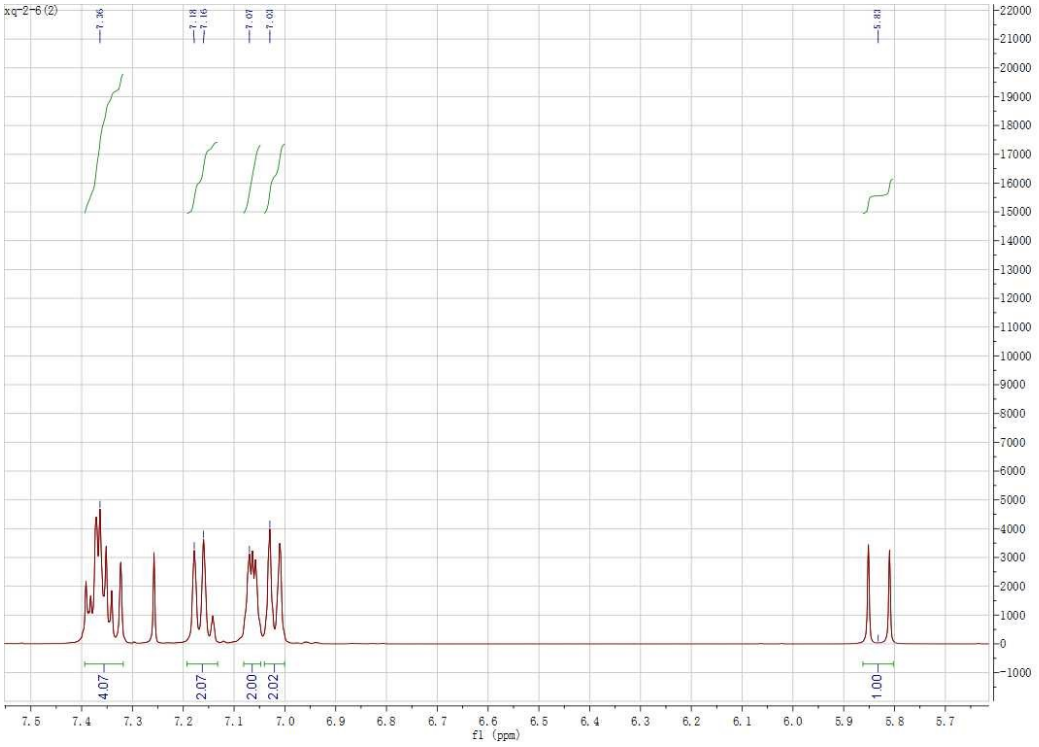


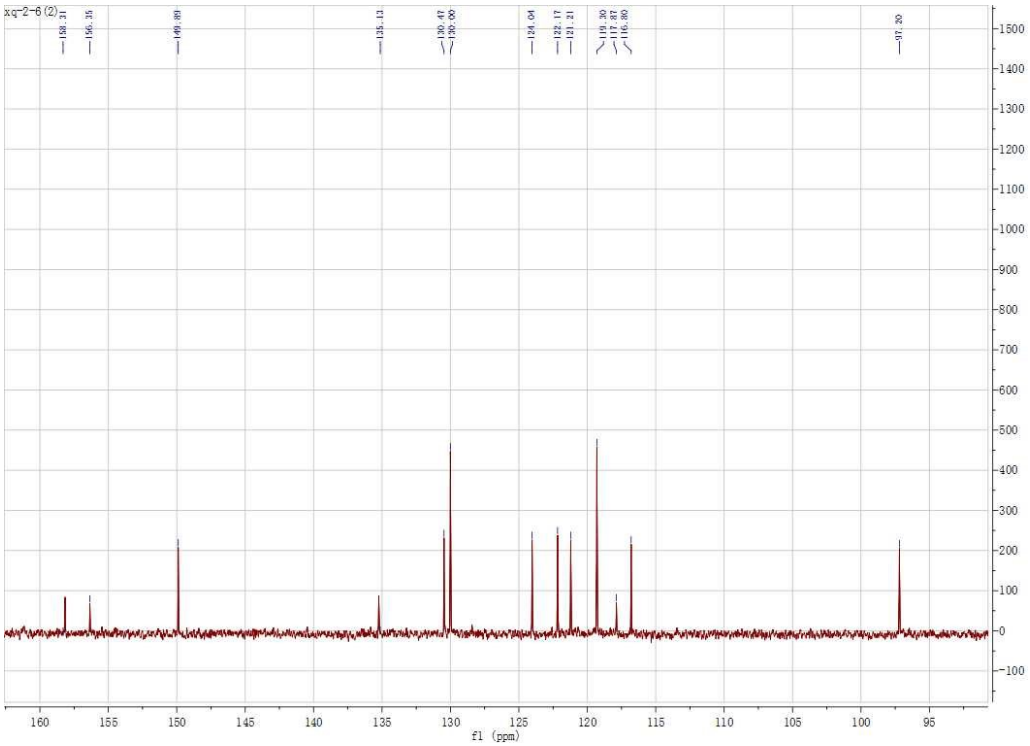




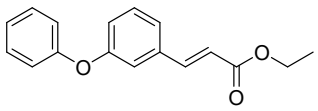
TX-3: (E)-3-(3-phenoxyphenyl)acrylonitrile

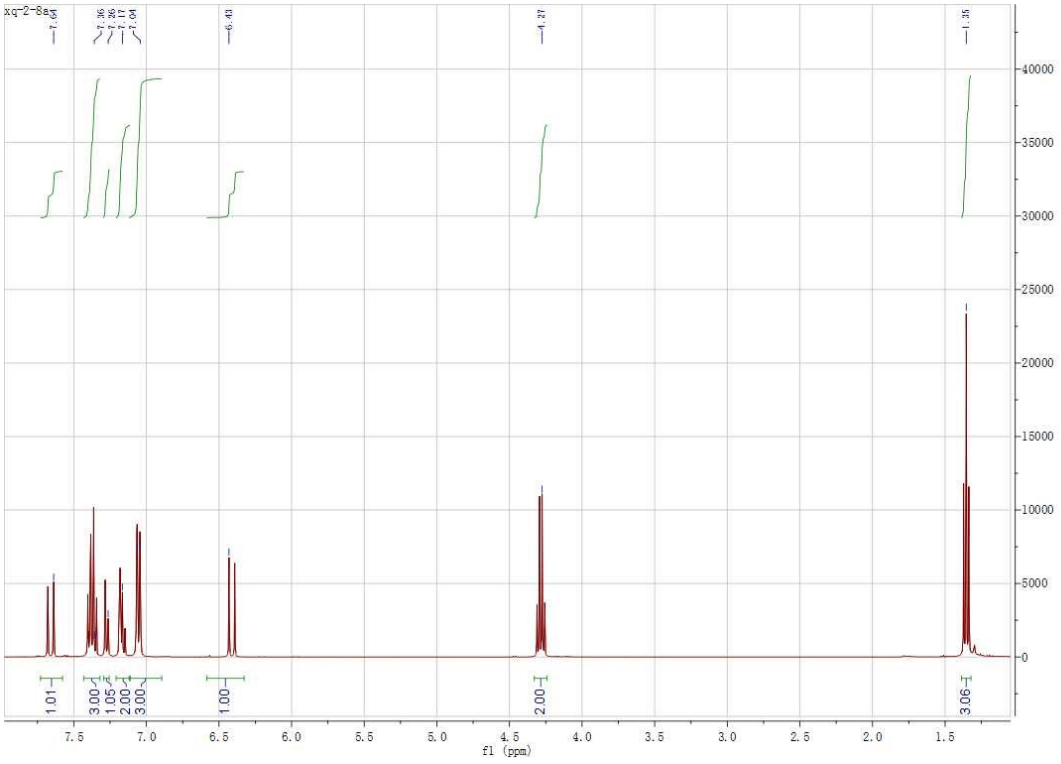


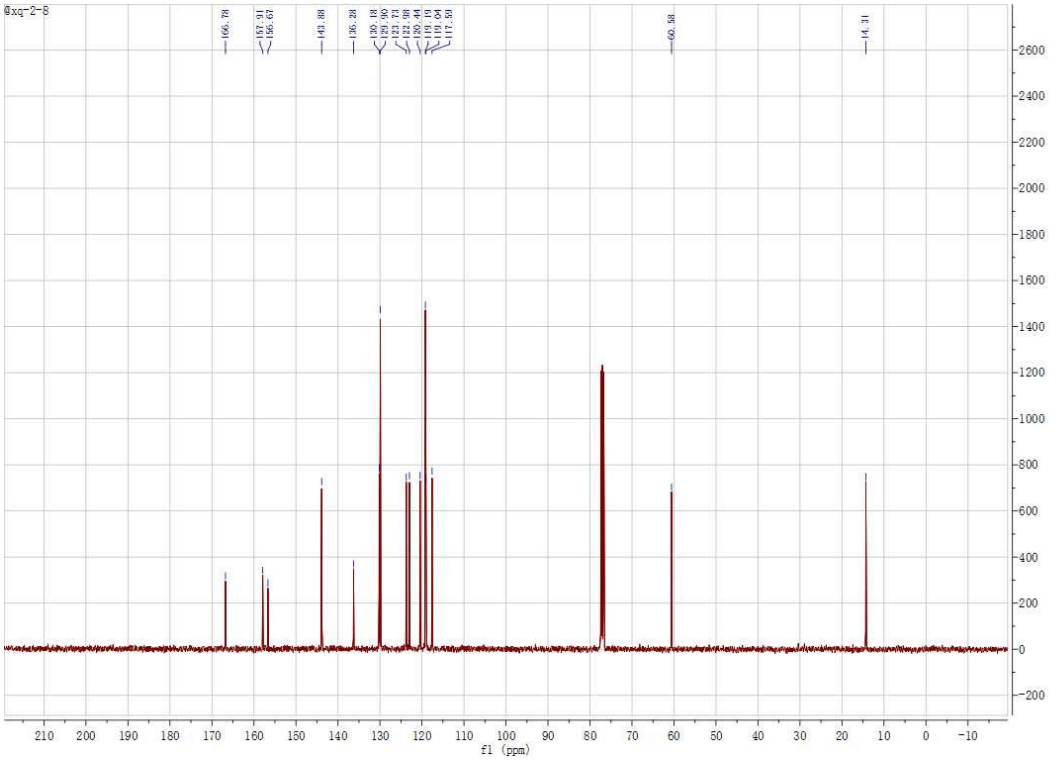




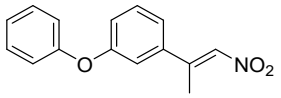
TX-4: ethyl (E)-3-(3-phenoxyphenyl)acrylate

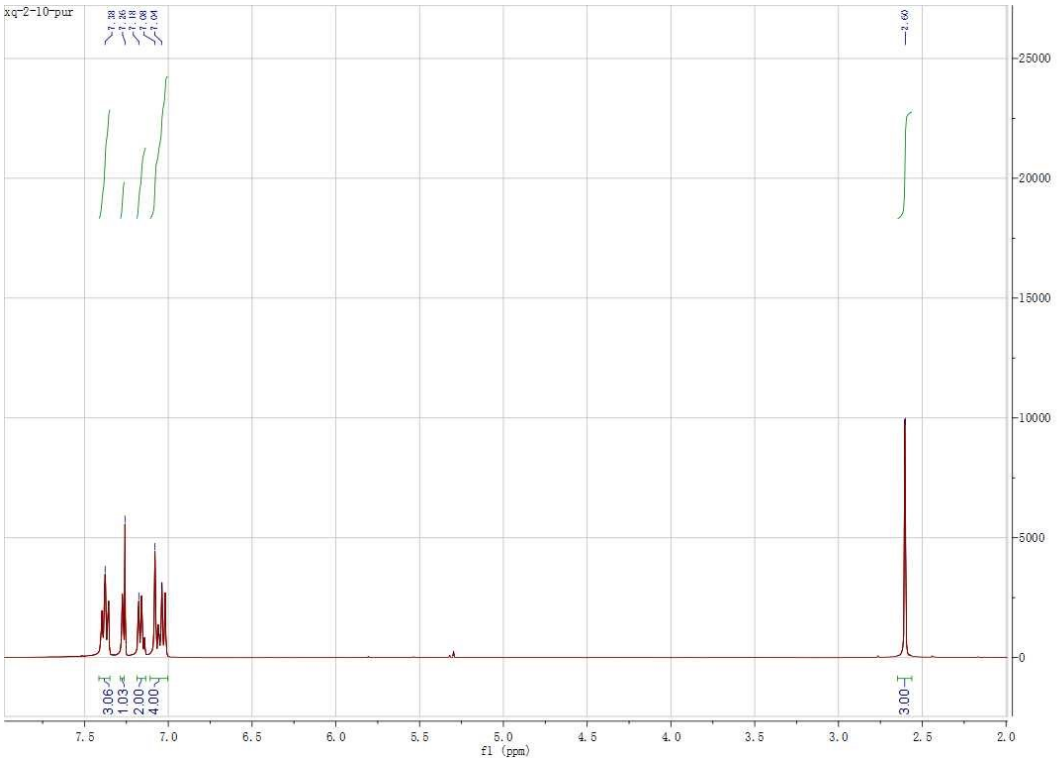


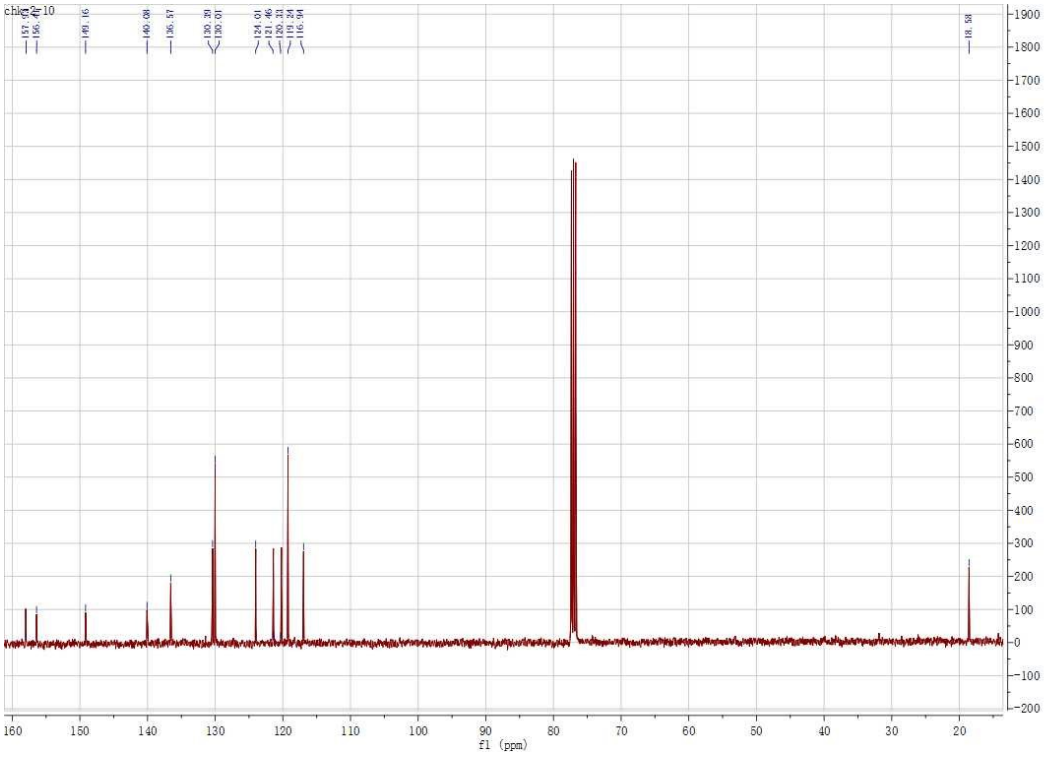




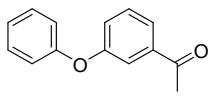
TX-5: (E)-1-(1-nitroprop-1-en-2-yl)-3-phenoxybenzene

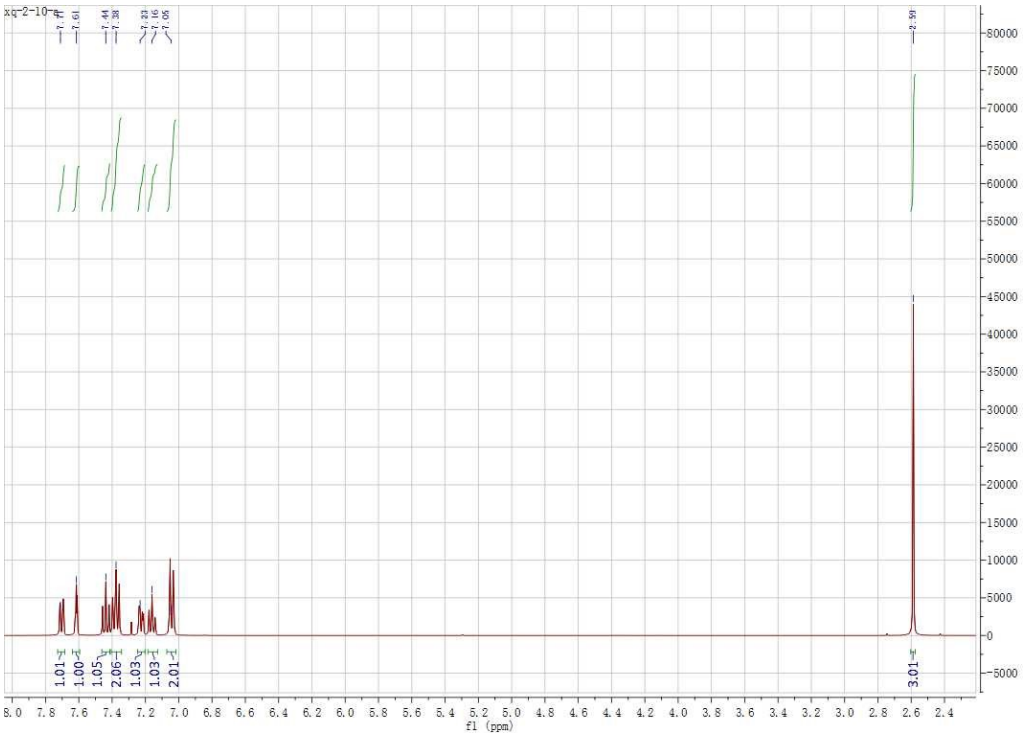


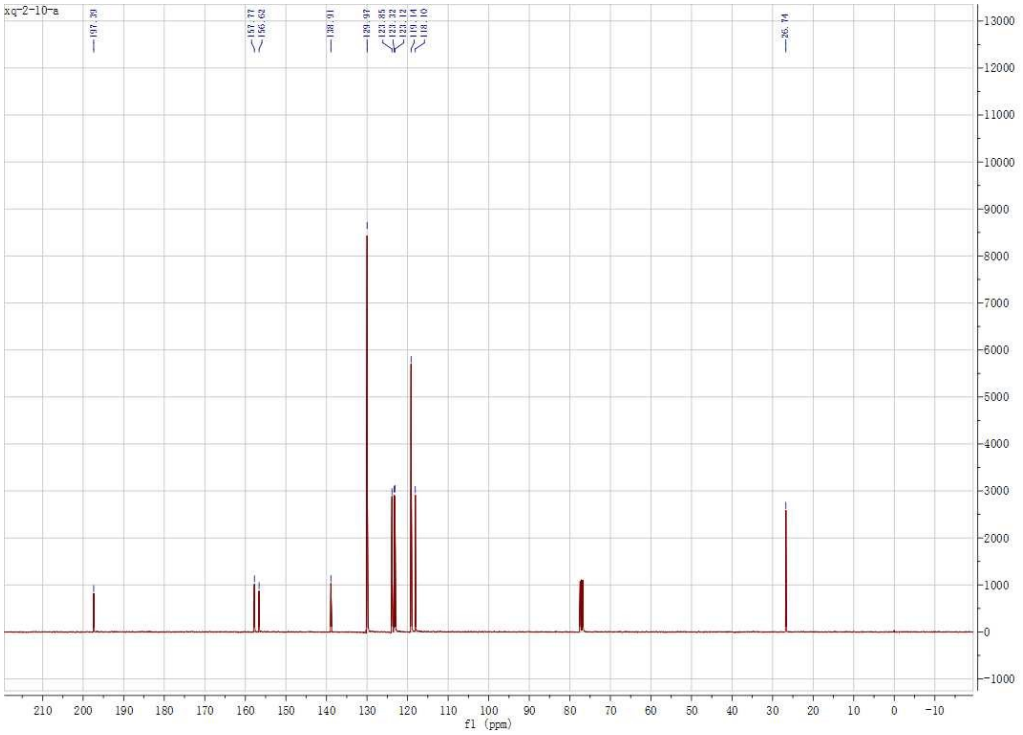




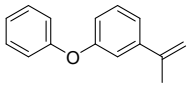
TX-5-S1: 1-(3-phenoxyphenyl)ethan-1-one

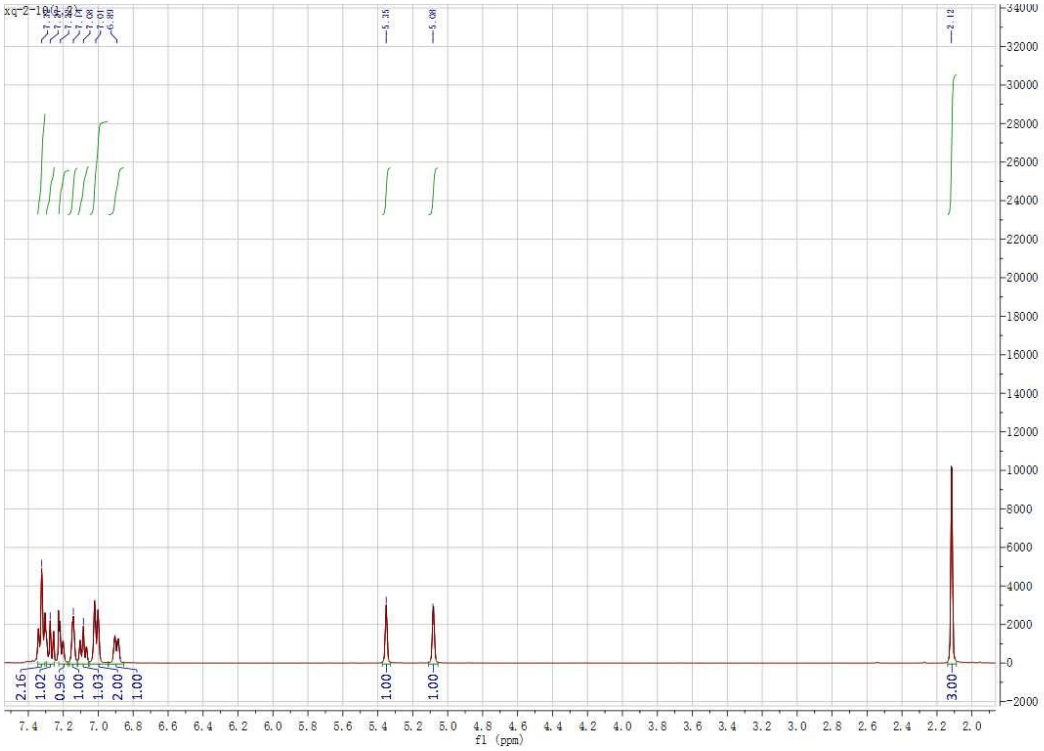


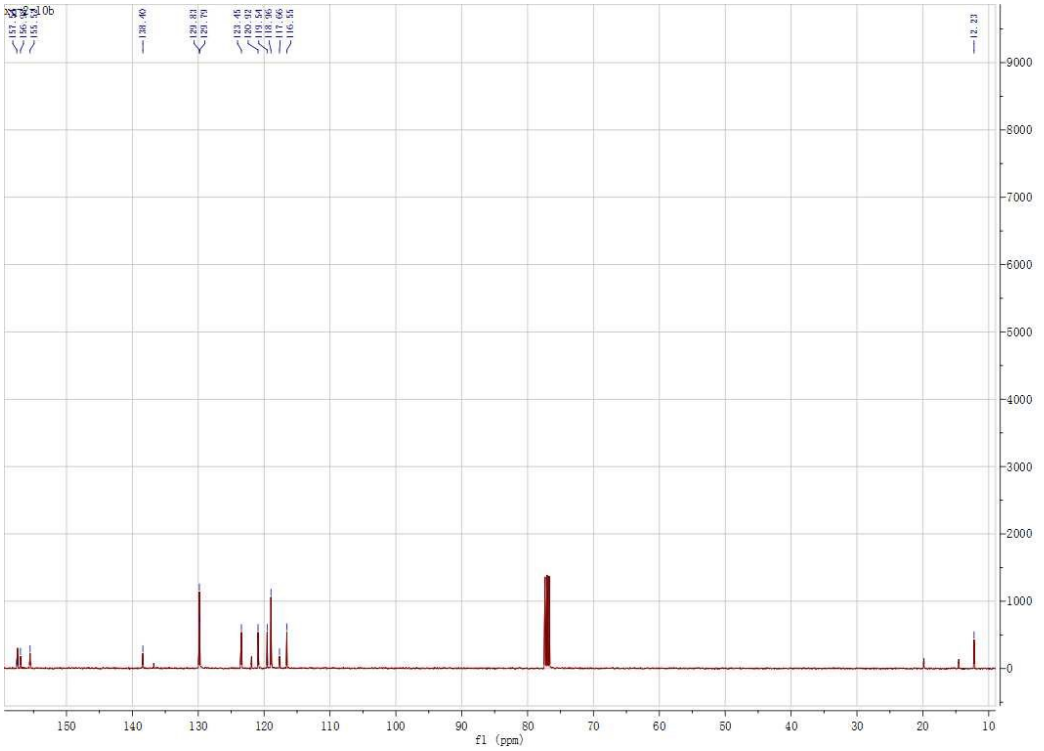




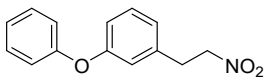
TX-5-S2: 1-phenoxy-3-(prop-1-en-2-yl)benzene

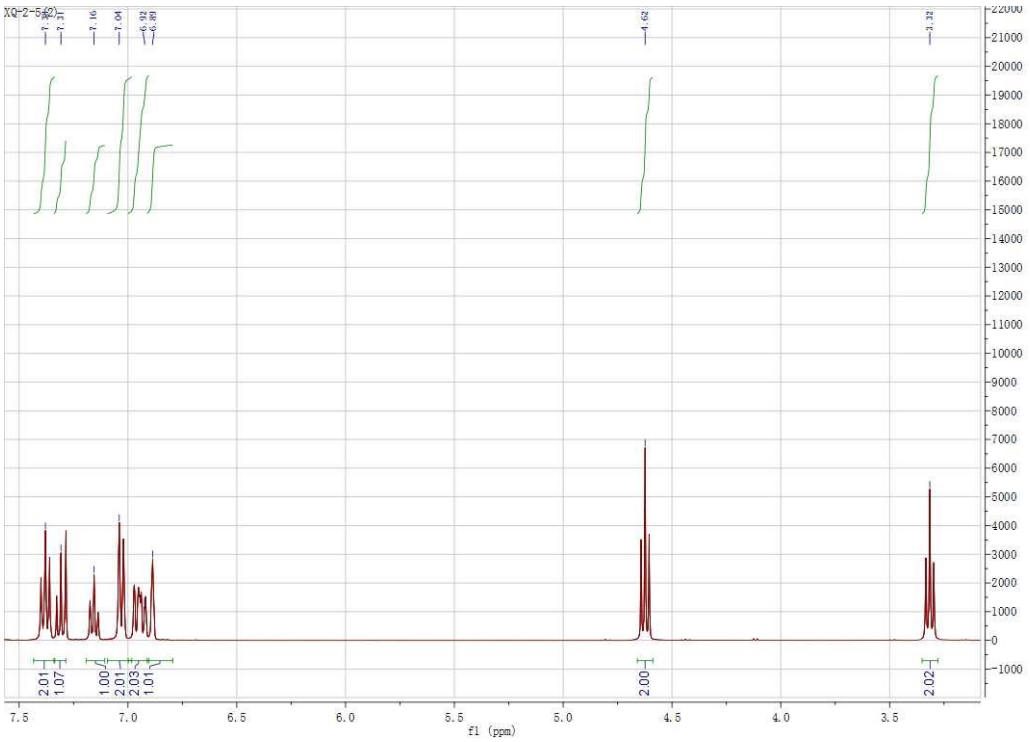


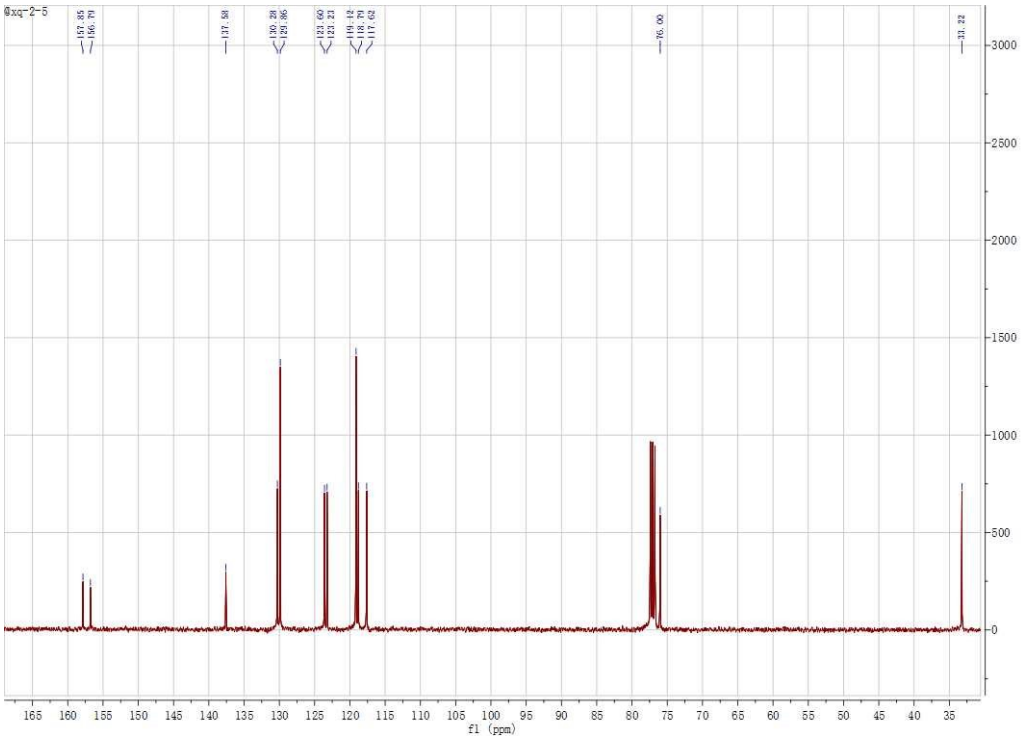




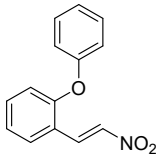
TX-6: 1-(2-nitroethyl)-3-phenoxybenzene

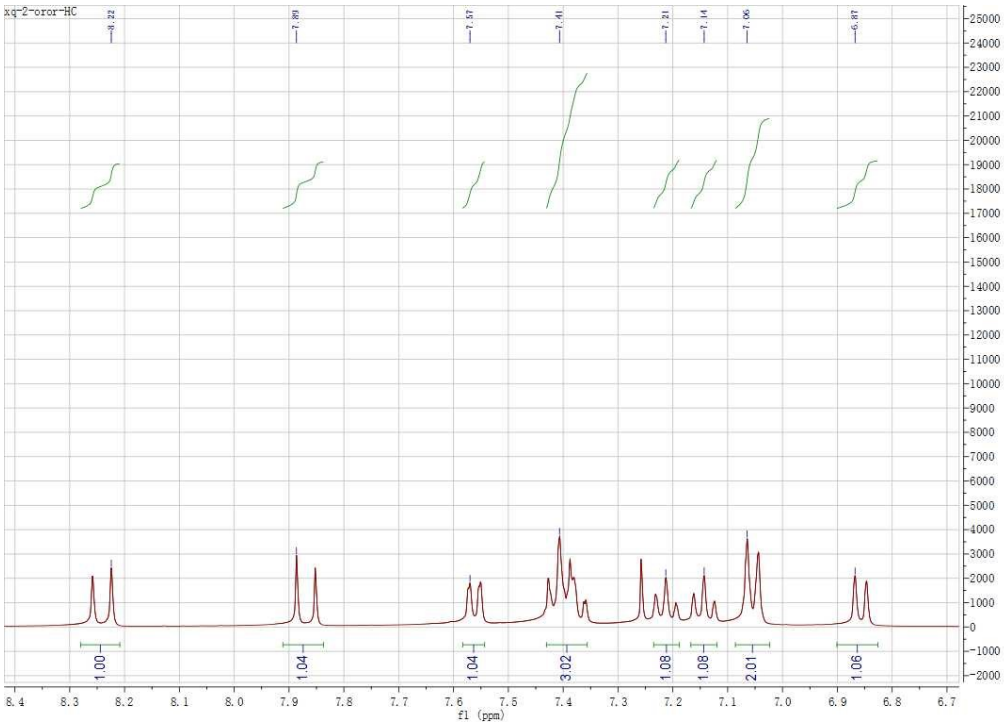


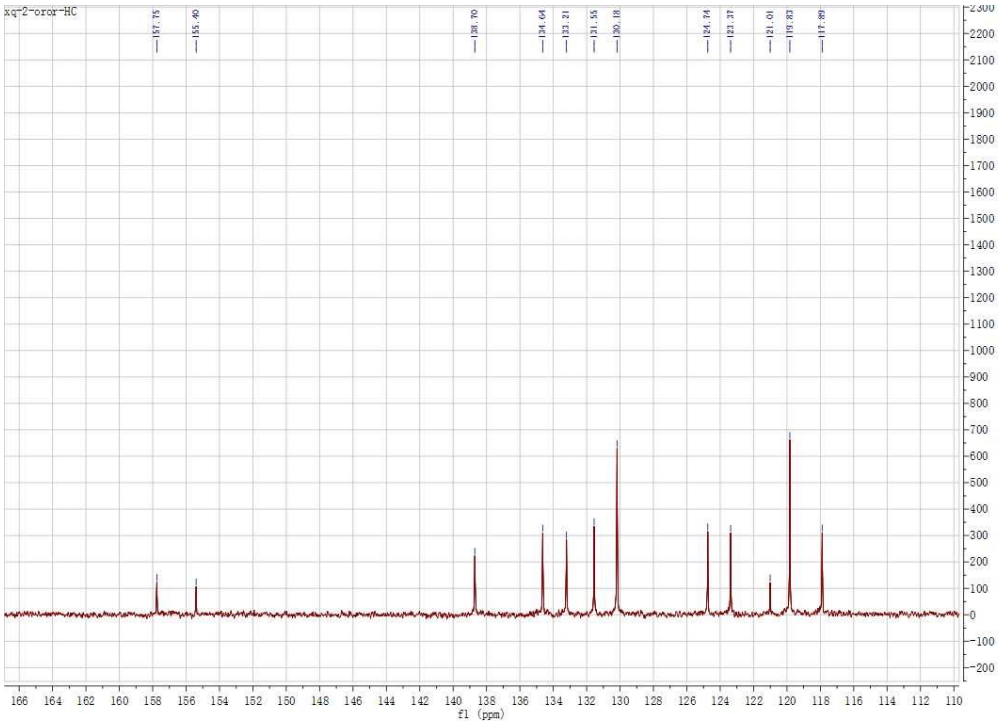




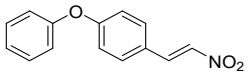
TX-7: (E)-1-(2-nitrovinyl)-2-phenoxybenzene

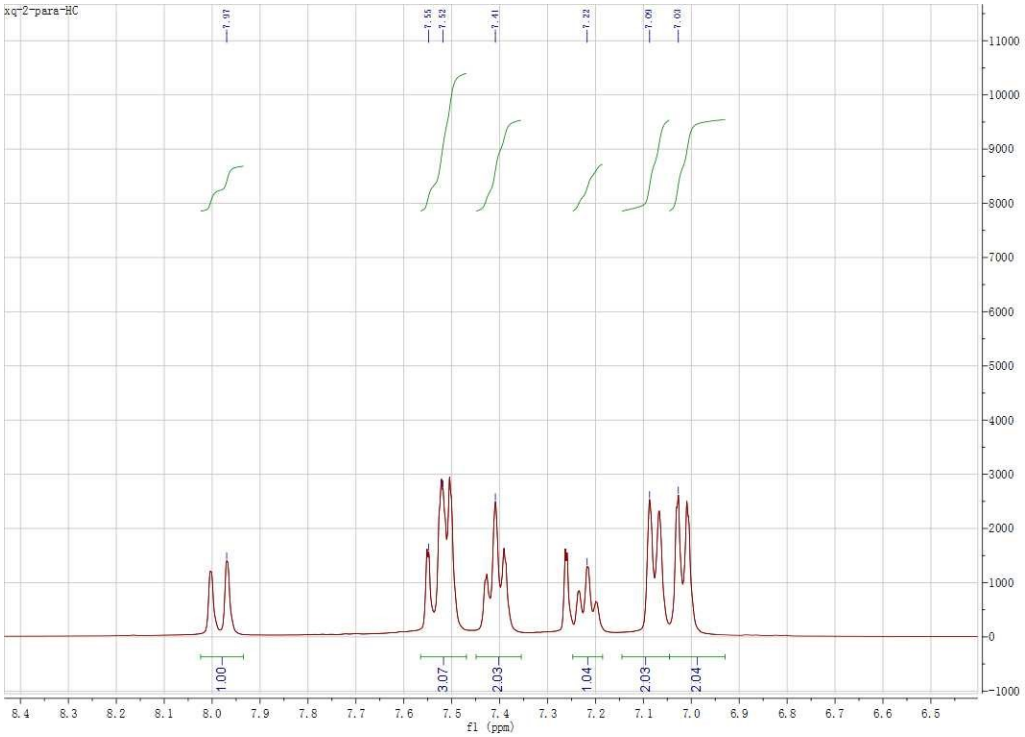


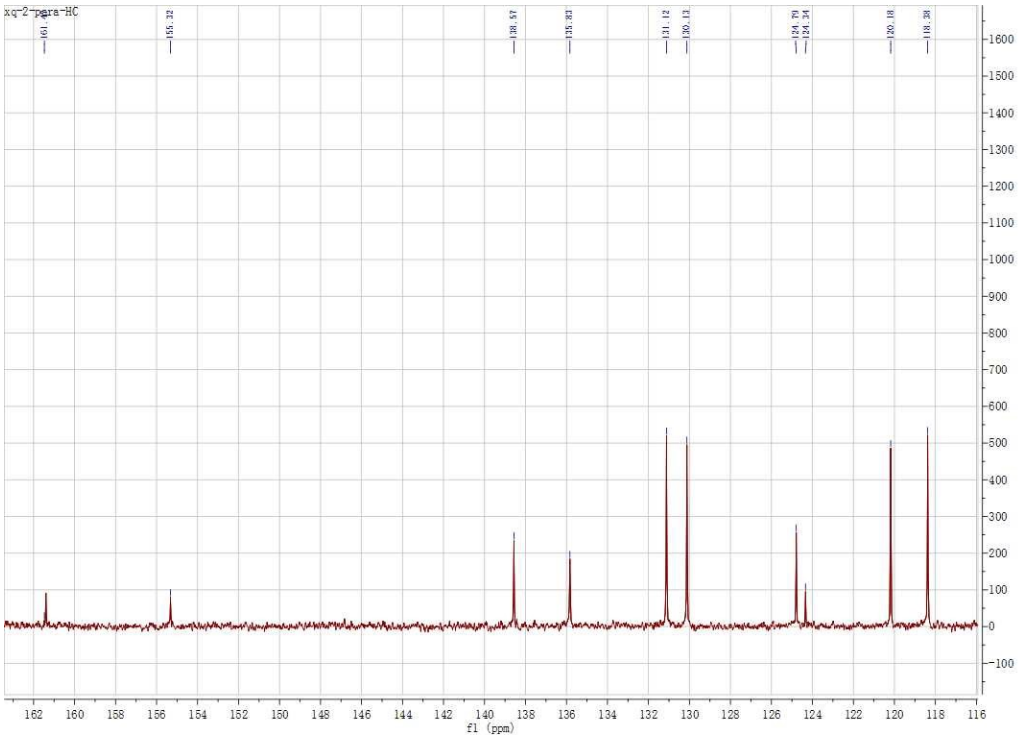




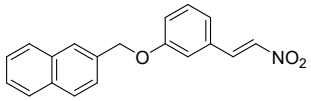
TX-8: (E)-1-(2-nitrovinyl)-4-phenoxybenzene

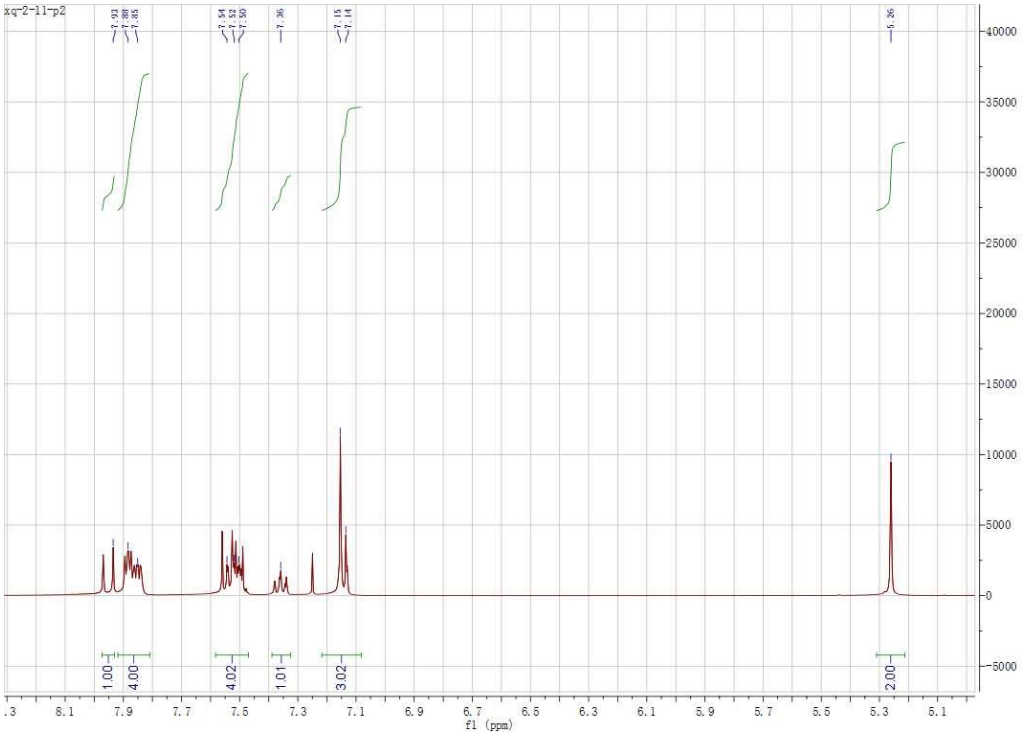


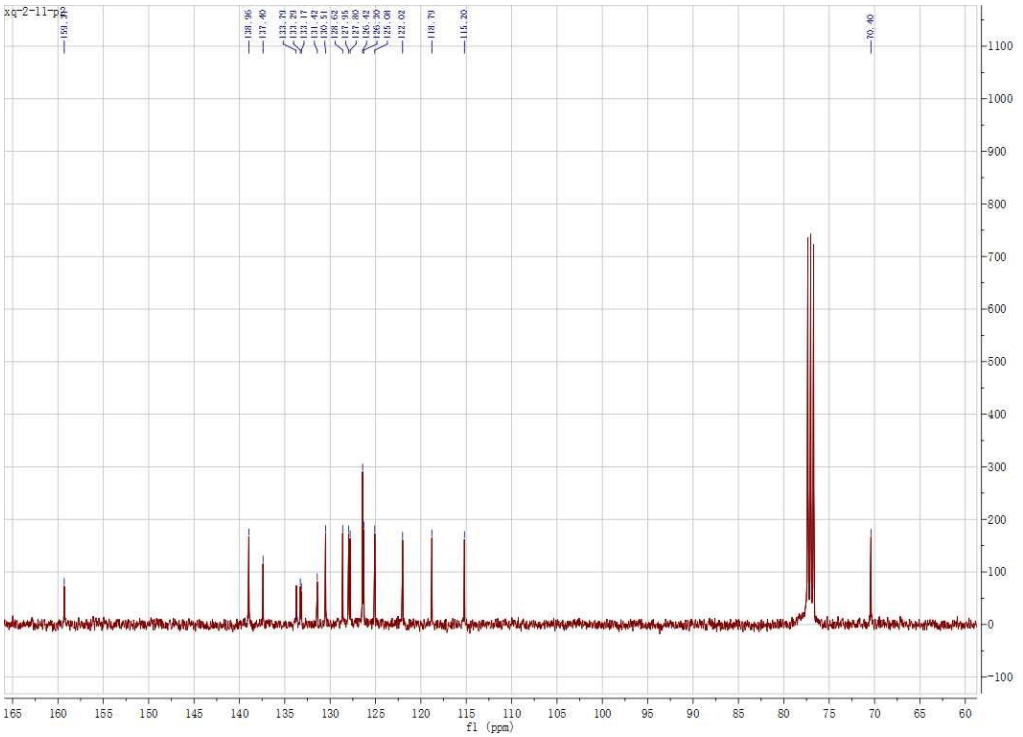




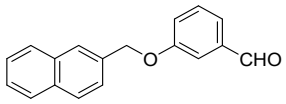
TX-9: (E)-2-((3-(2-nitrovinyl)phenoxy)methyl)naphthalene

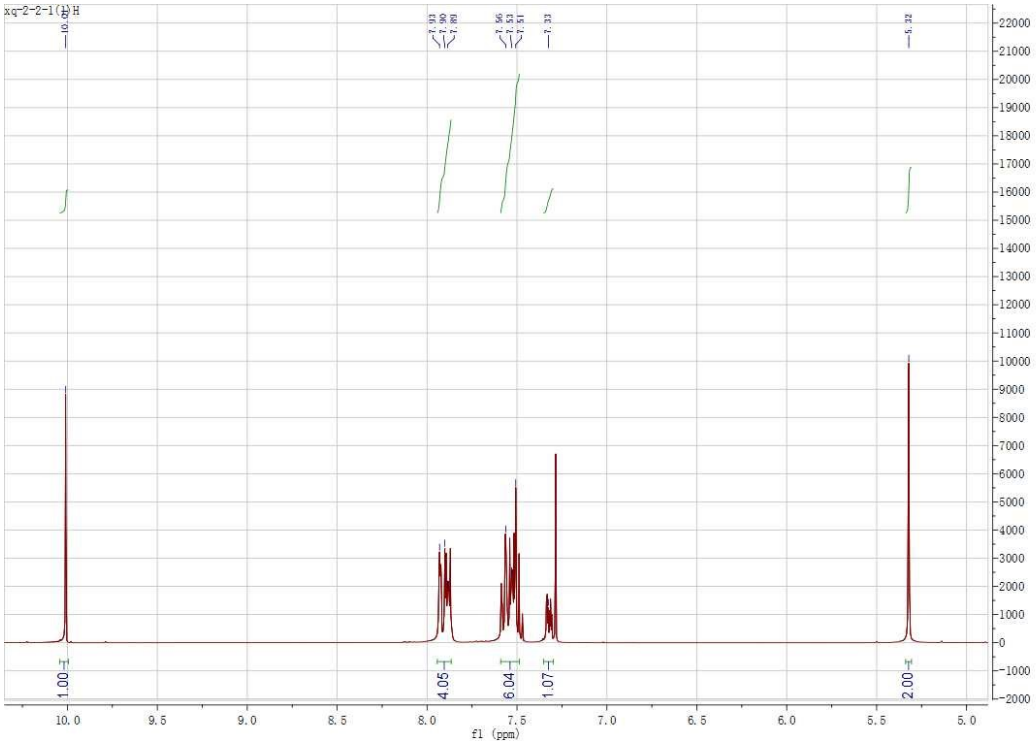


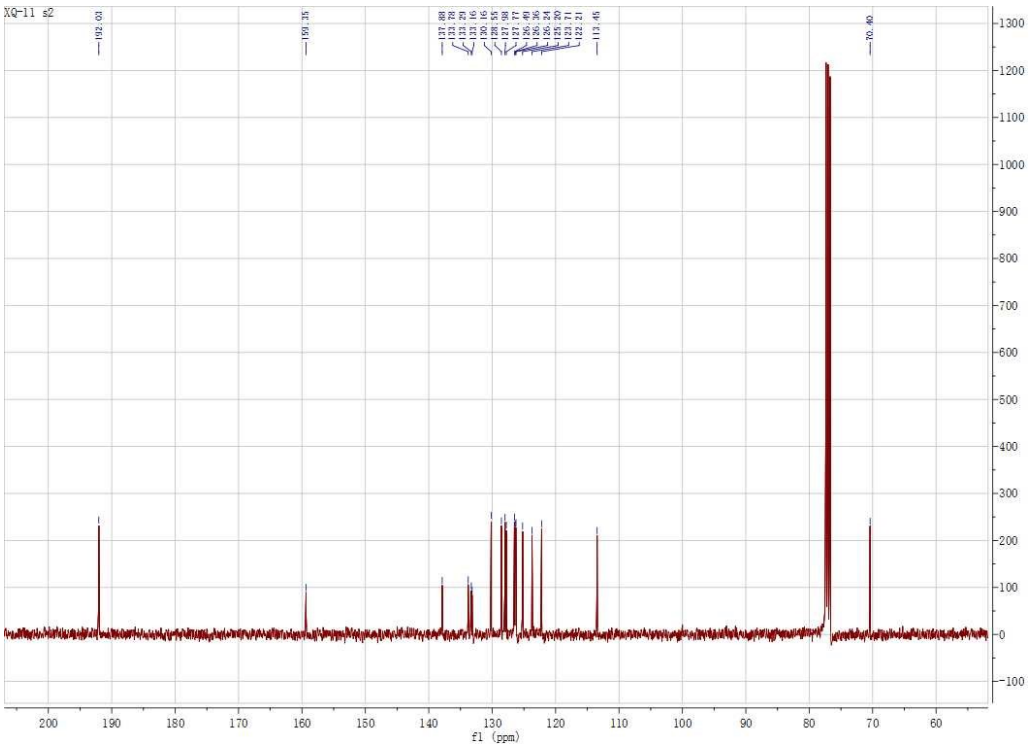




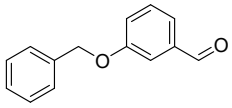
TX-9-S1: 3-(naphthalen-2-ylmethoxy)benzaldehyde

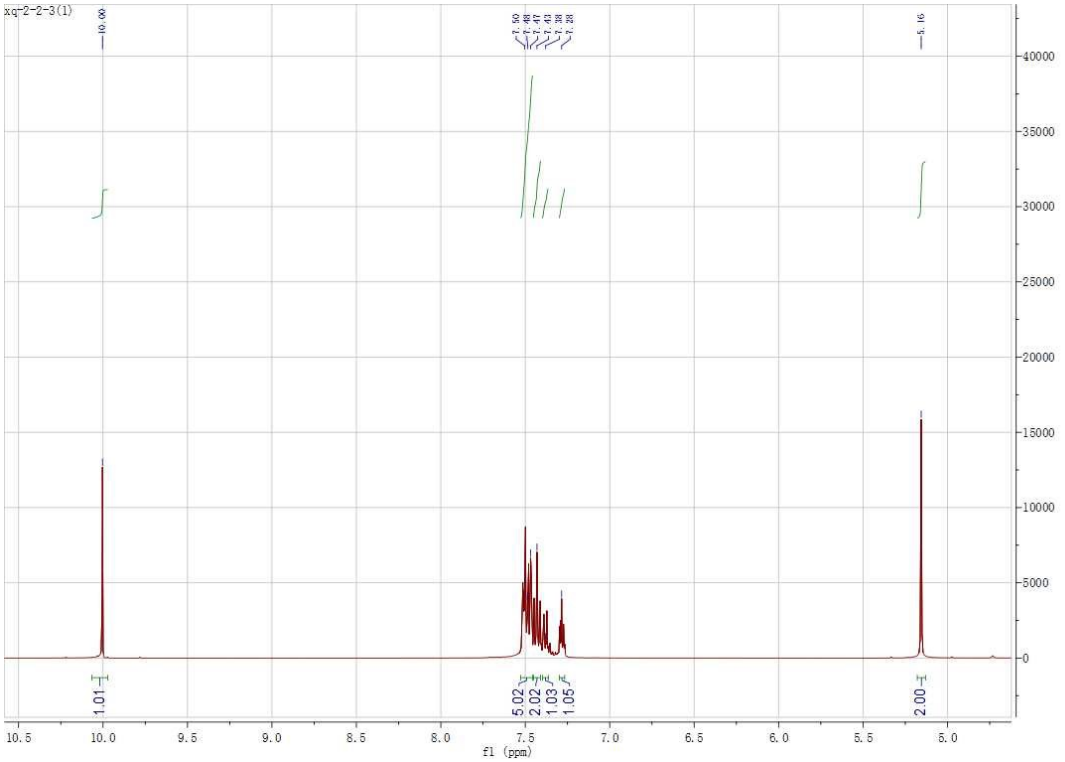




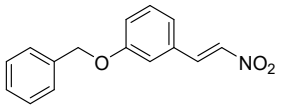


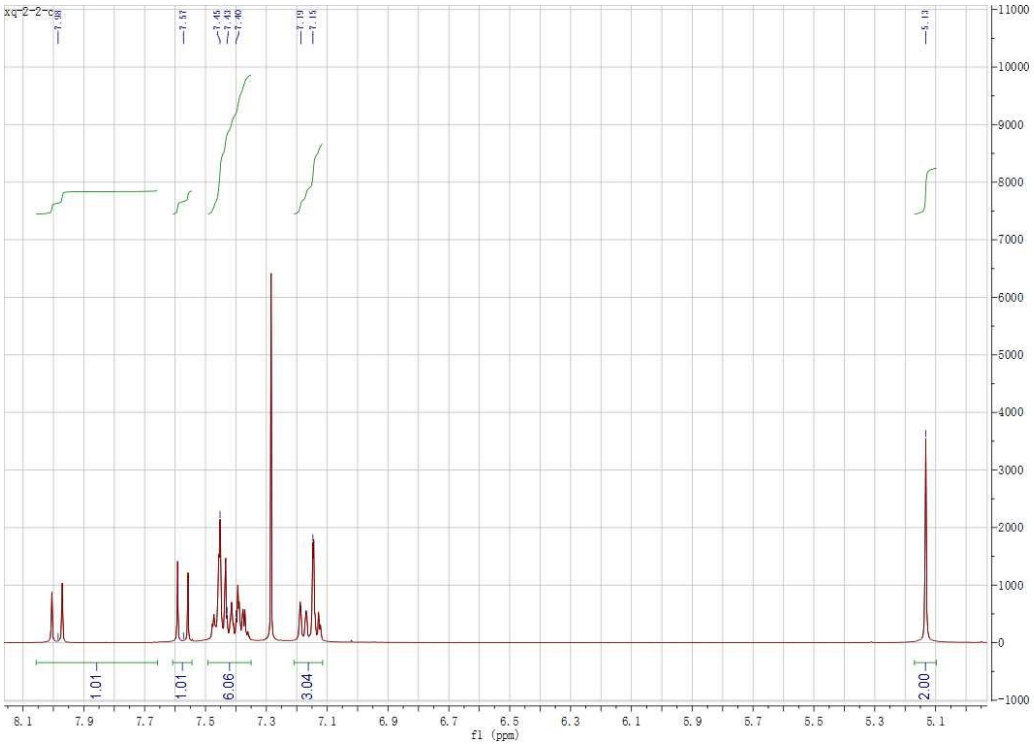
TX-10-S1: 3-(benzyloxy)benzaldehyde

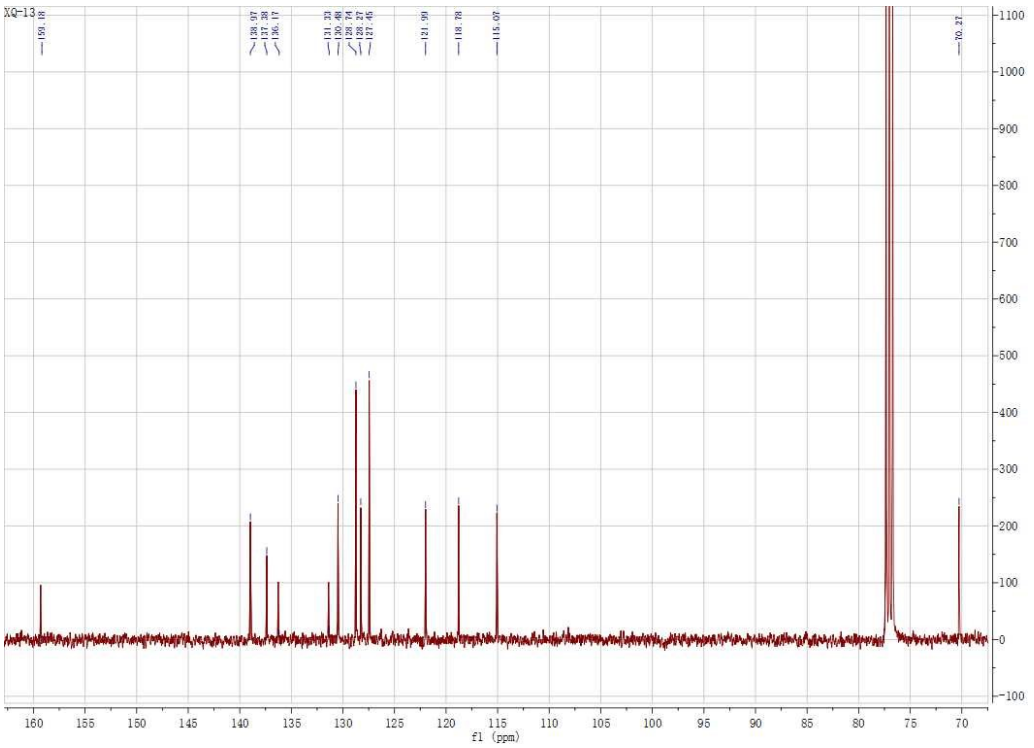




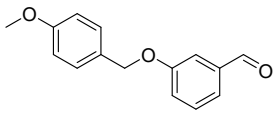
TX-10: (E)-1-(benzyloxy)-3-(2-nitrovinyl)benzene

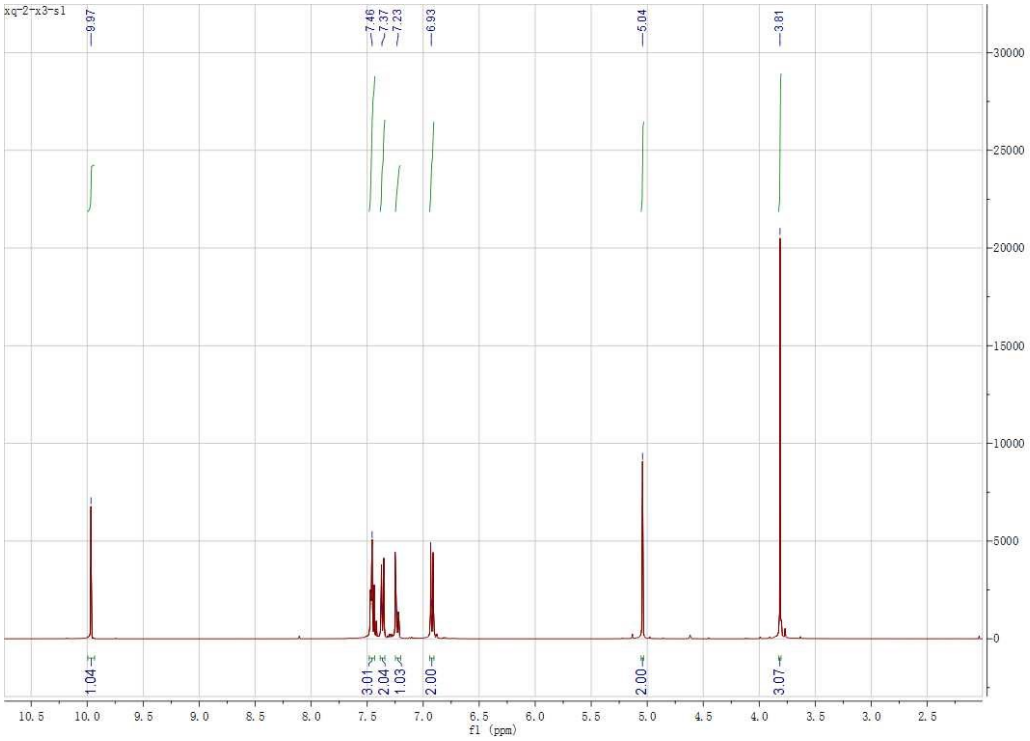


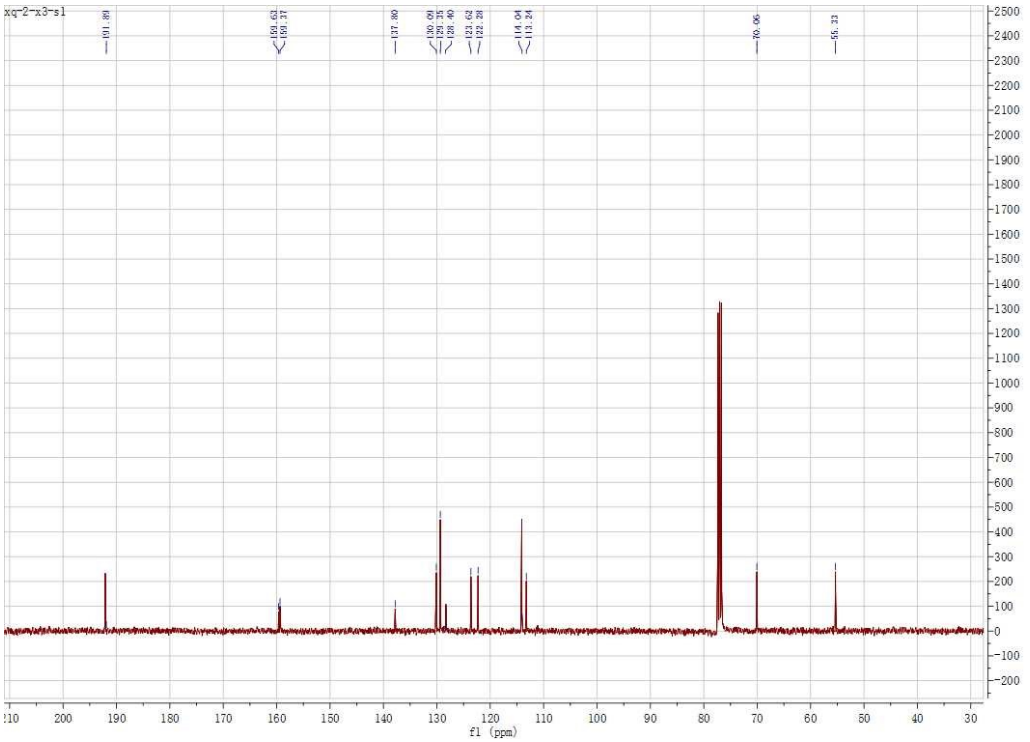




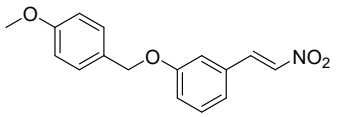
TX-11-S1: 3-((4-methoxybenzyl)oxy)benzaldehyde

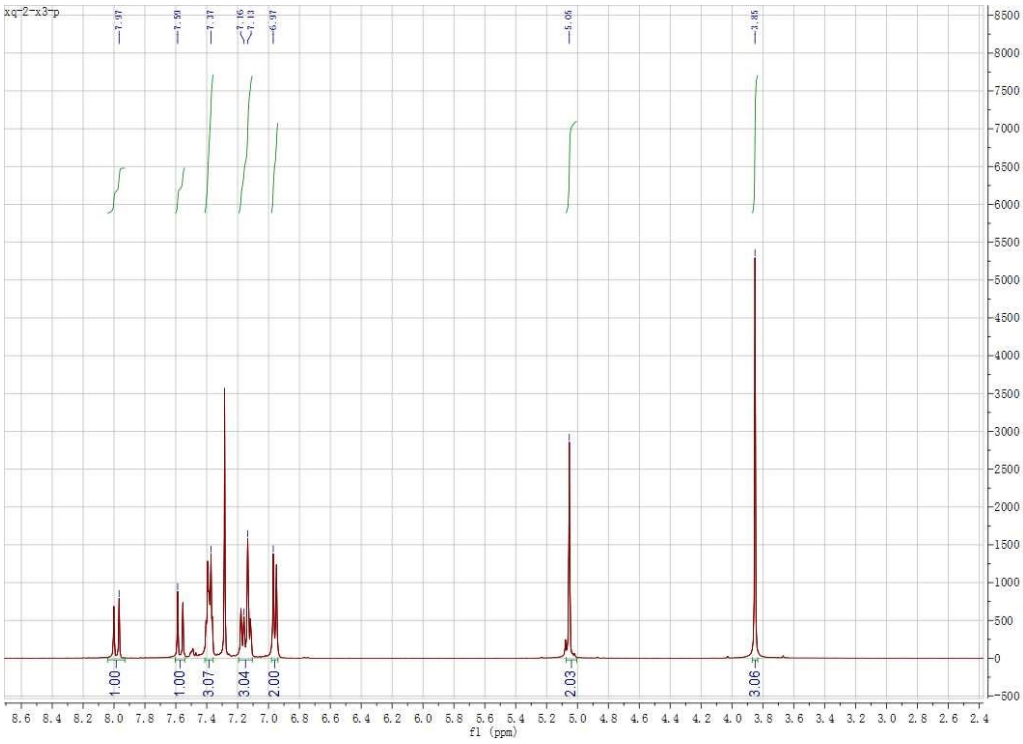


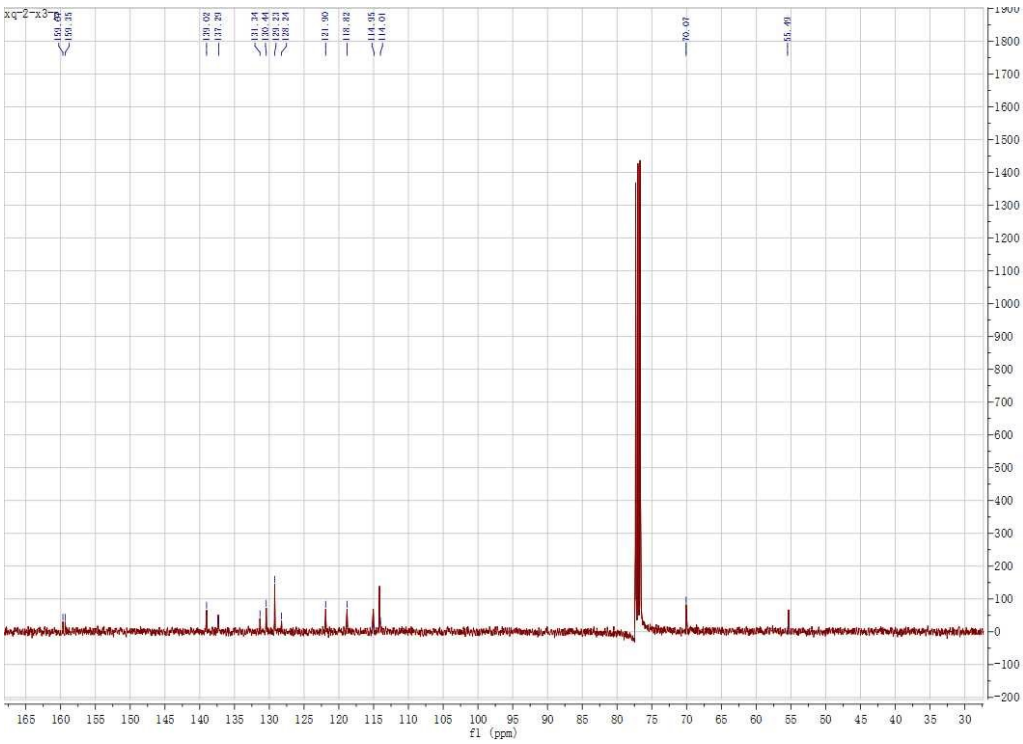




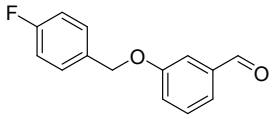
TX-11: (E)-1-((4-methoxybenzyl)oxy)-3-(2-nitrovinyl)benzene

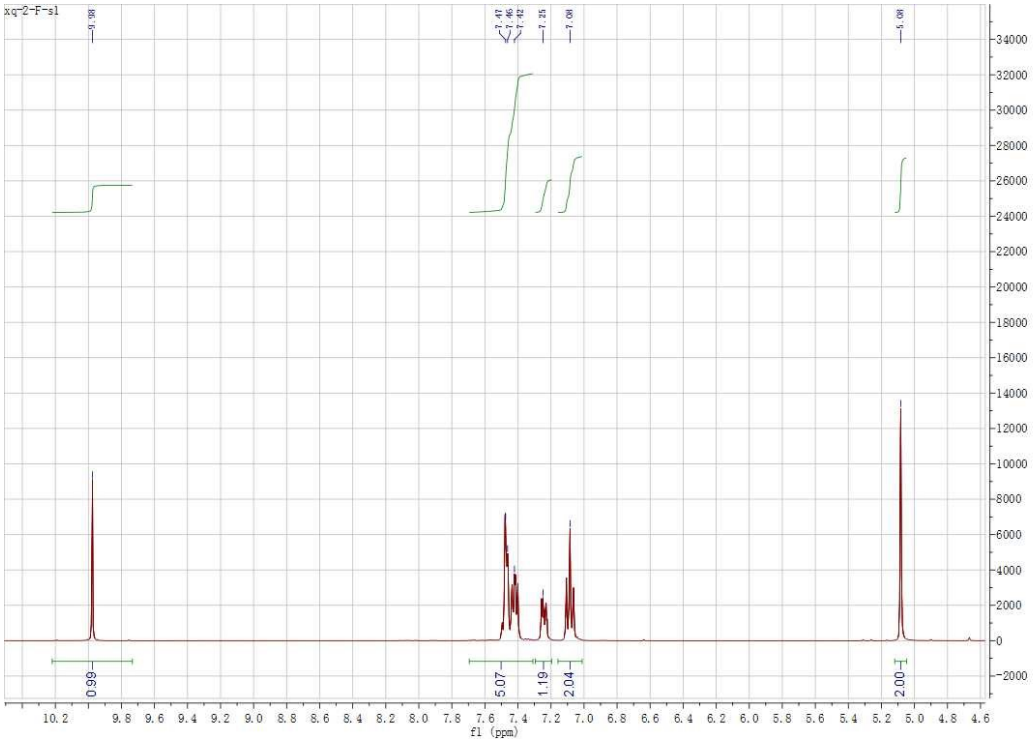


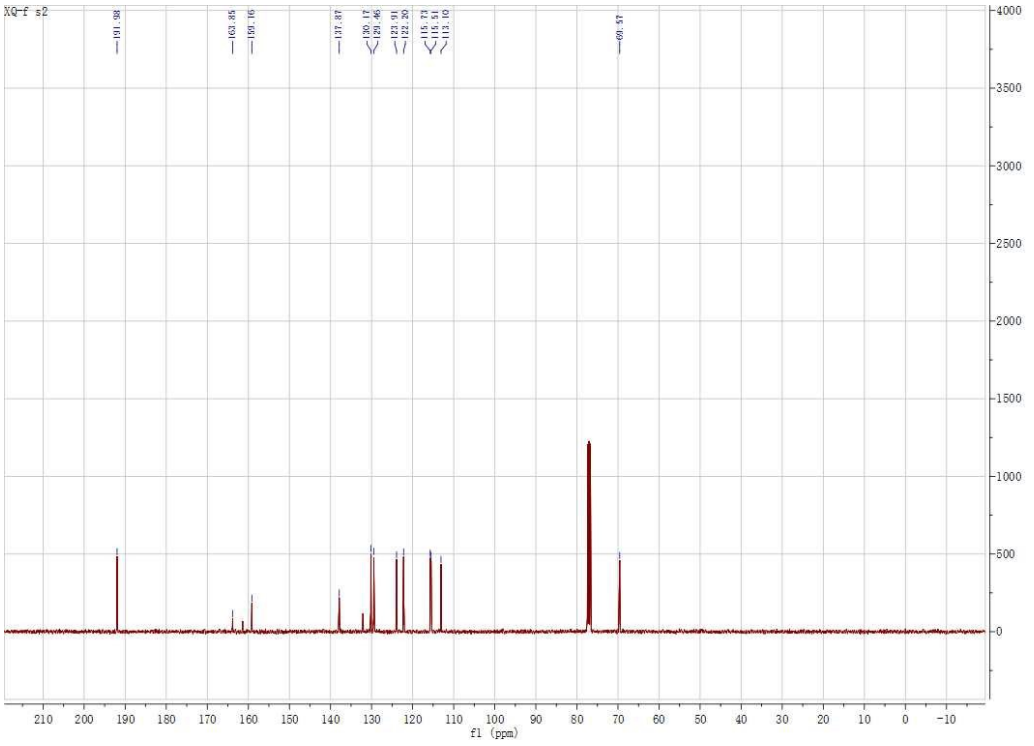




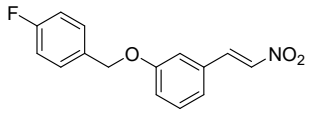
TX-12-S1: 3-((4-fluorobenzyl)oxy)benzaldehyde

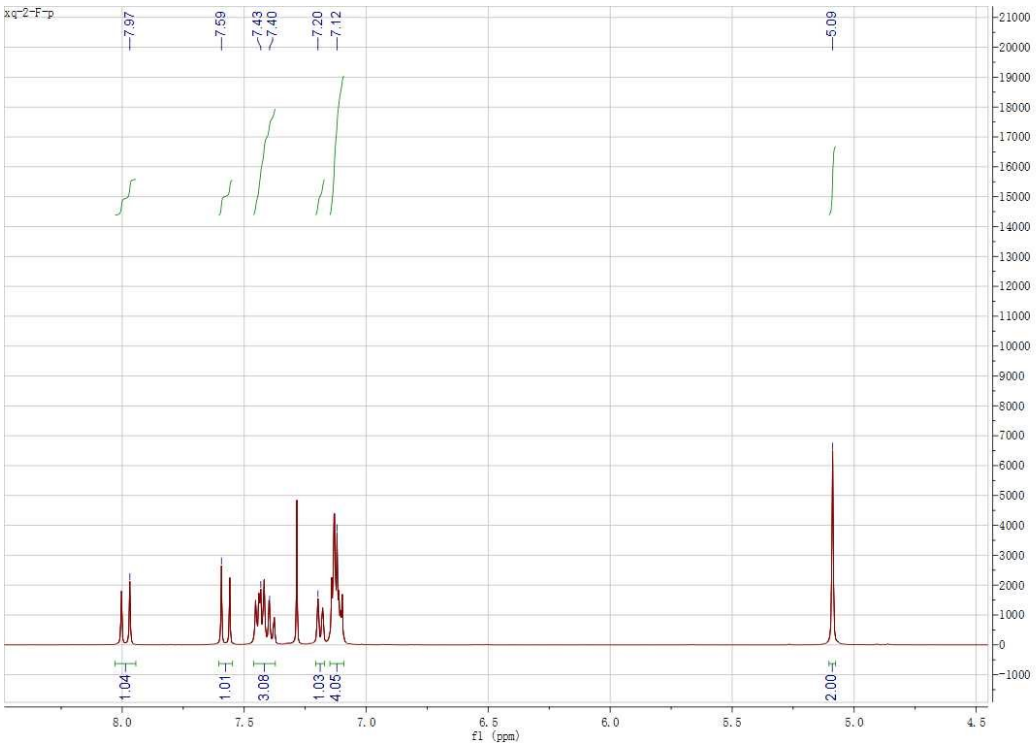


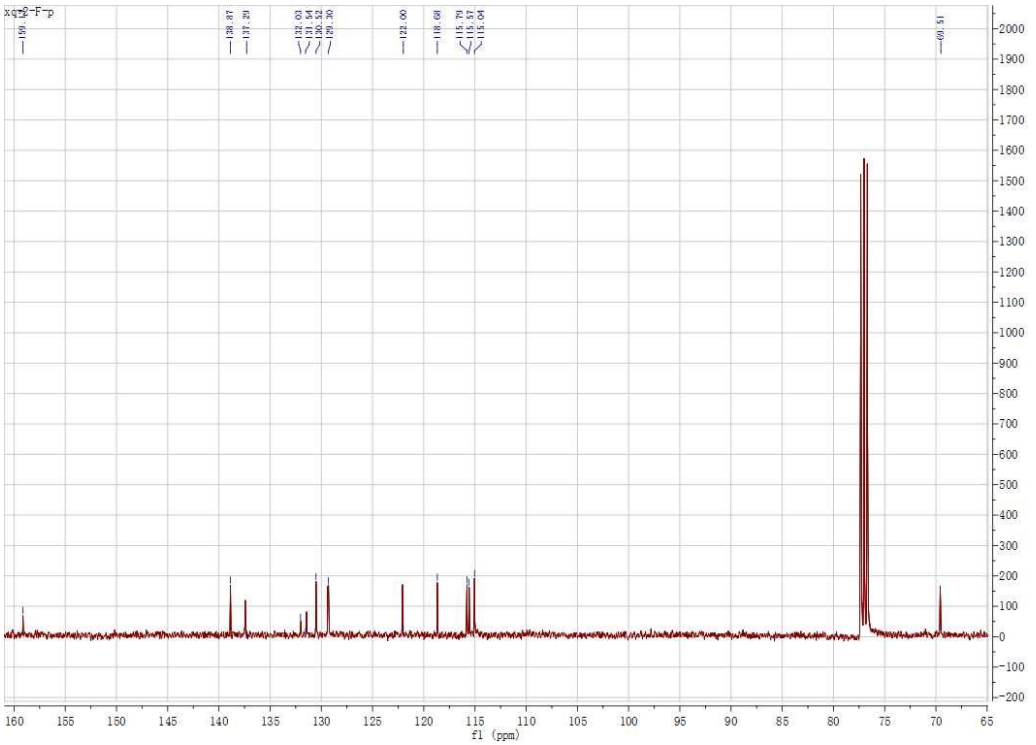




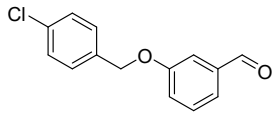
TX-12: (E)-1-((4-fluorobenzyl)oxy)-3-(2-nitrovinyl)benzene

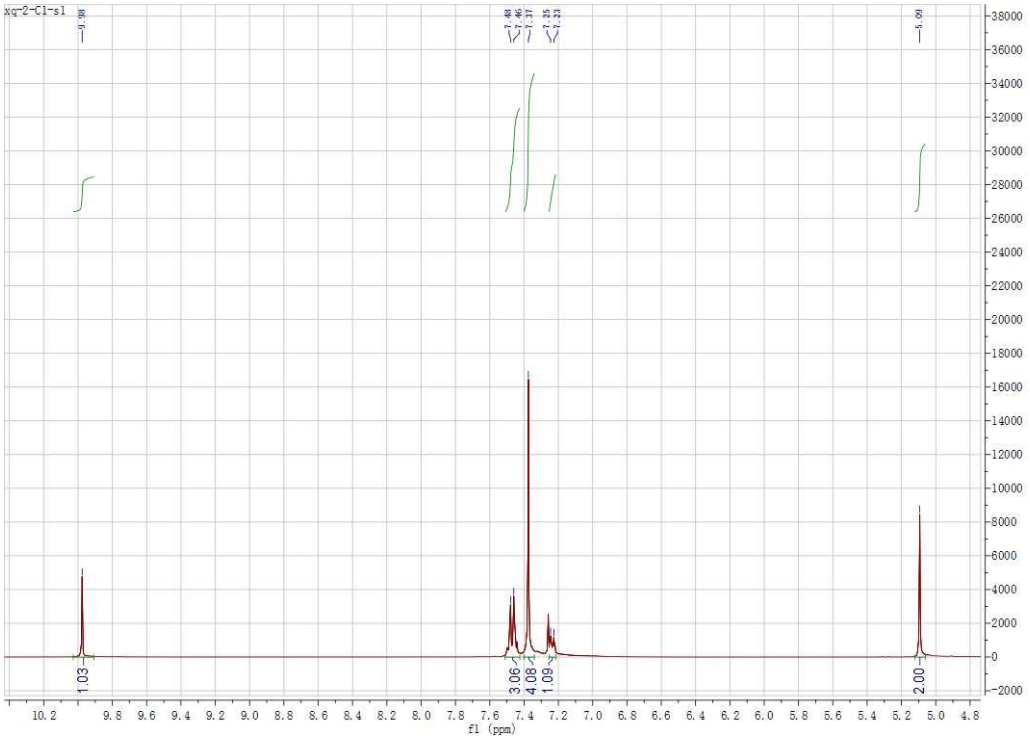


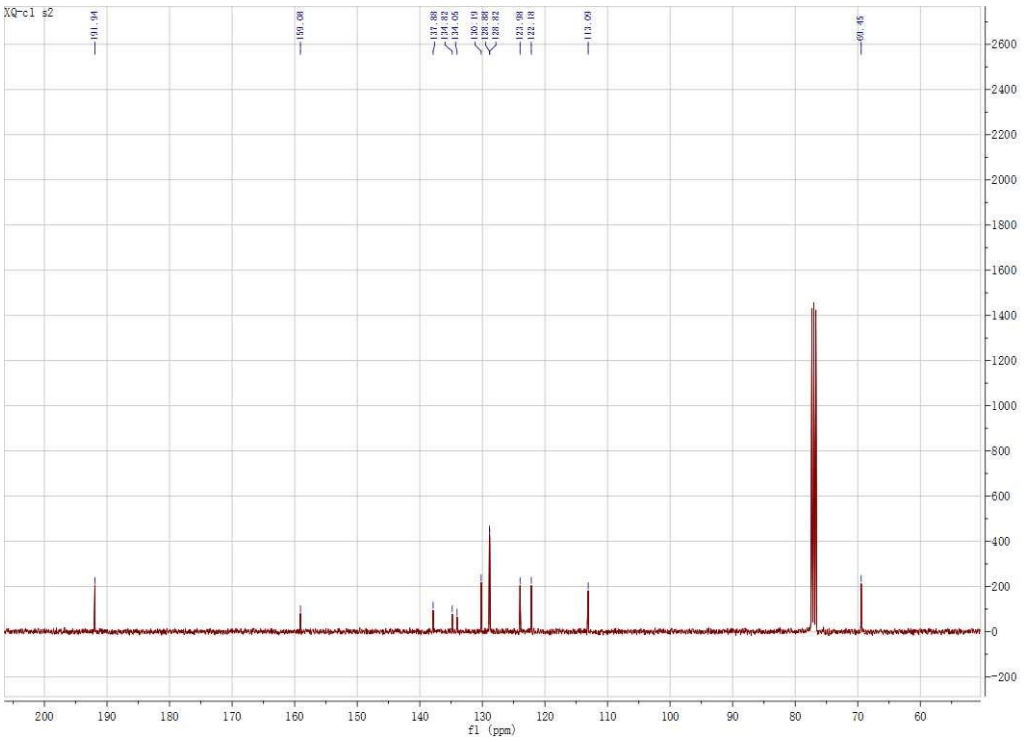




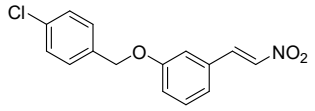
TX-13-S1: 3-((4-chlorobenzyl)oxy)benzaldehyde

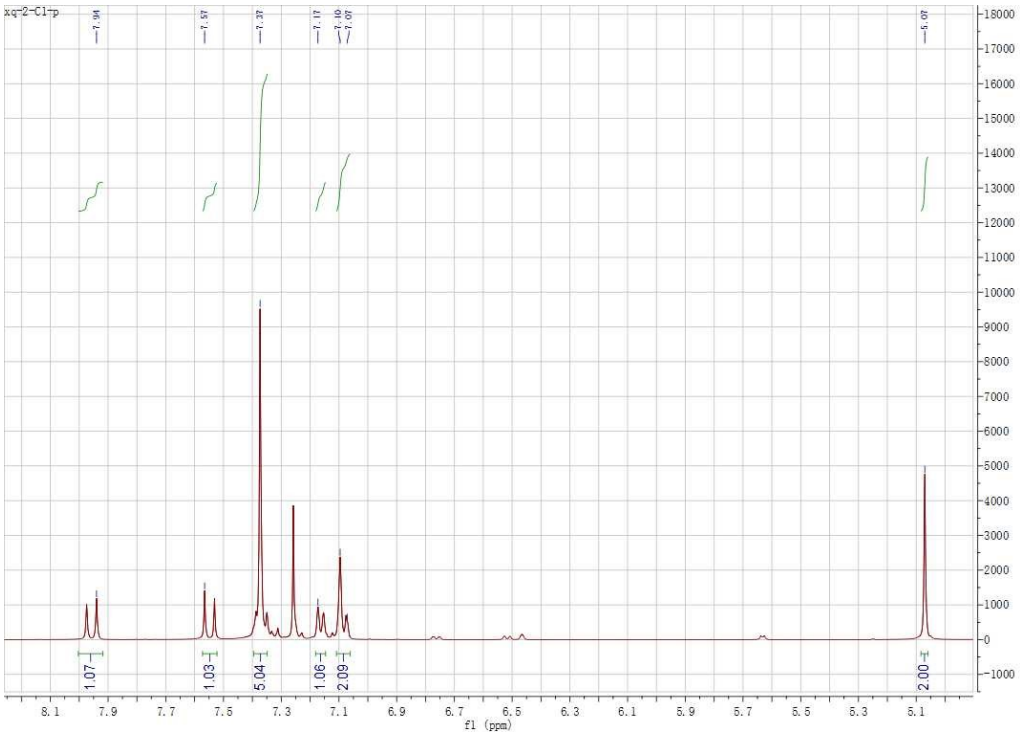


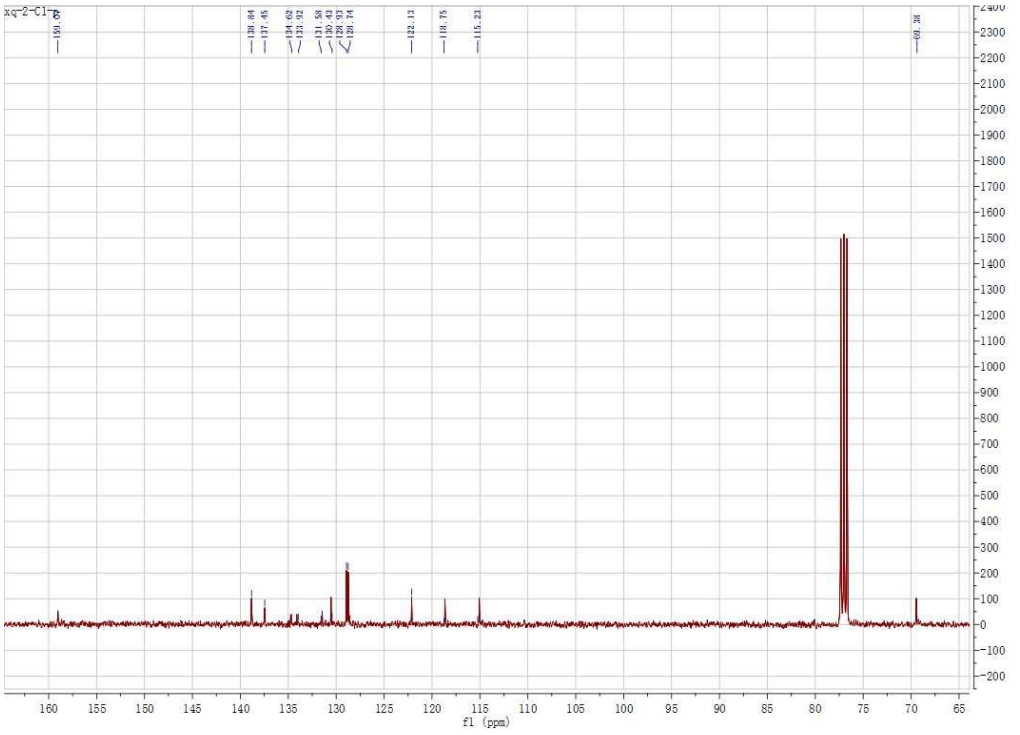




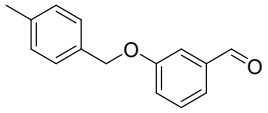
TX-13: (E)-1-((4-chlorobenzyl)oxy)-3-(2-nitrovinyl)benzene

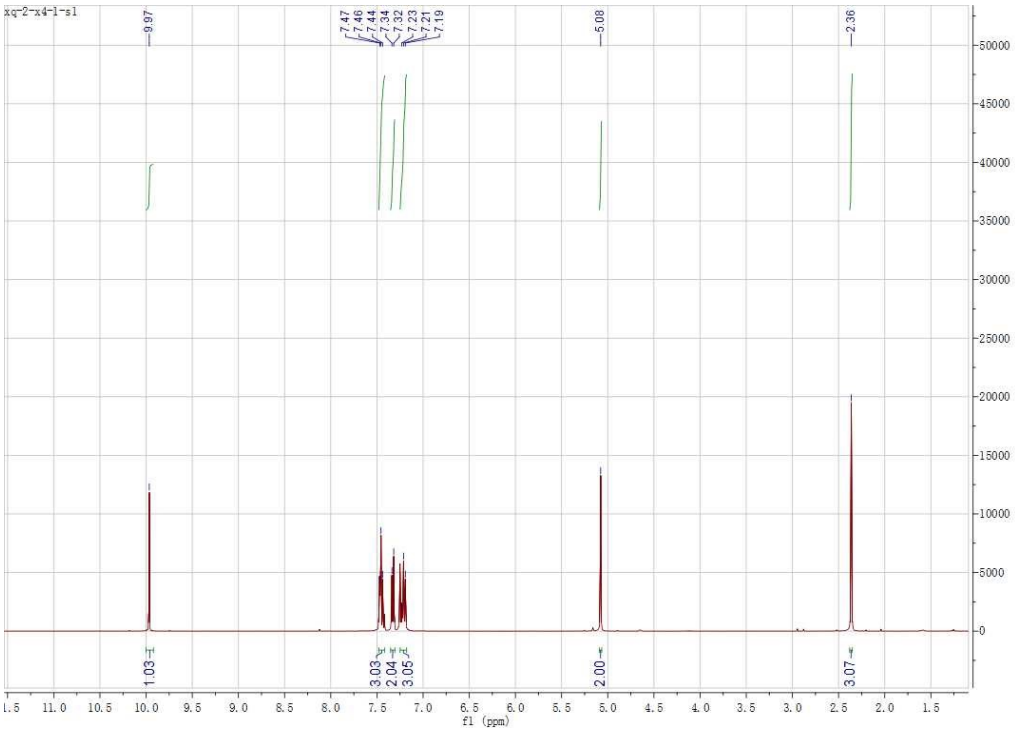


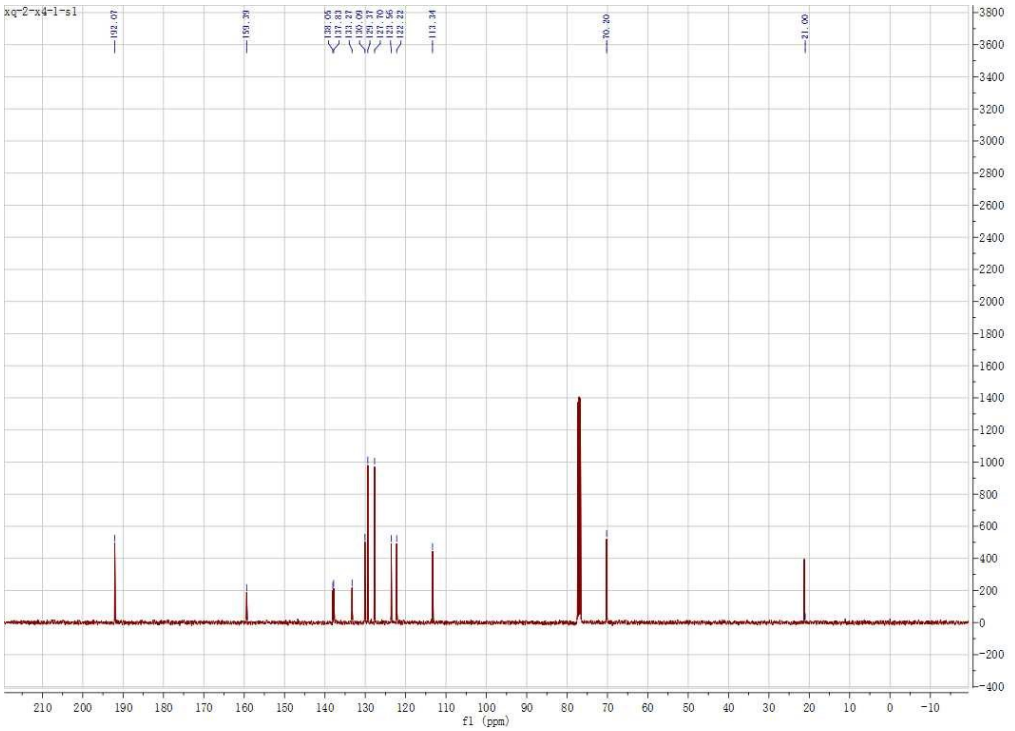




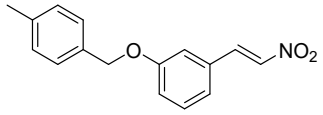
TX-14-S1: 3-((4-methylbenzyl)oxy)benzaldehyde

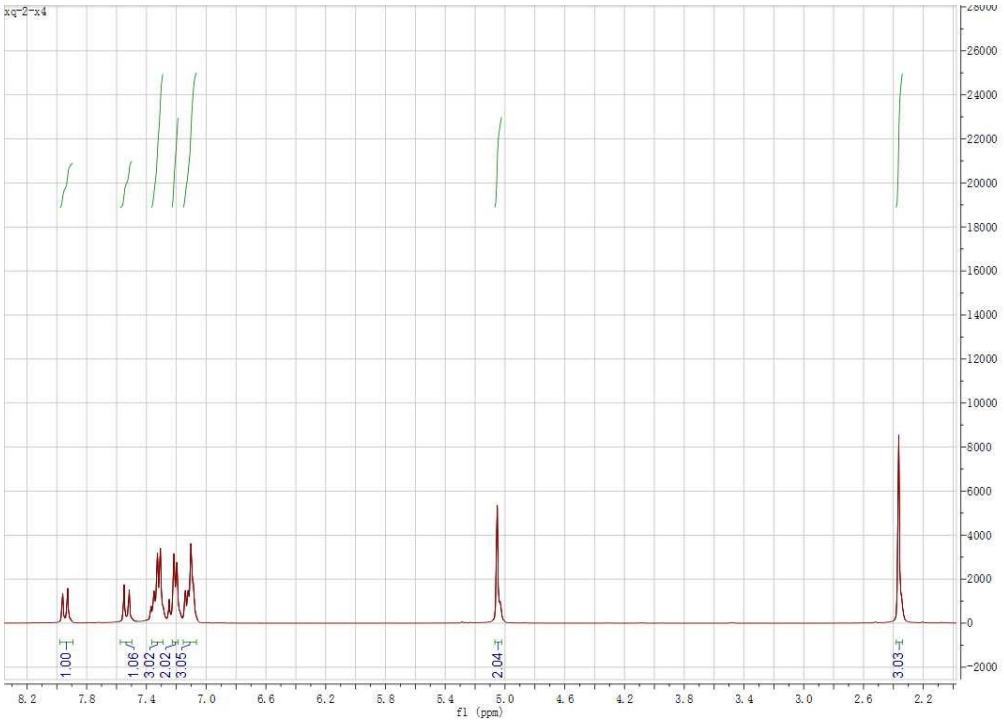


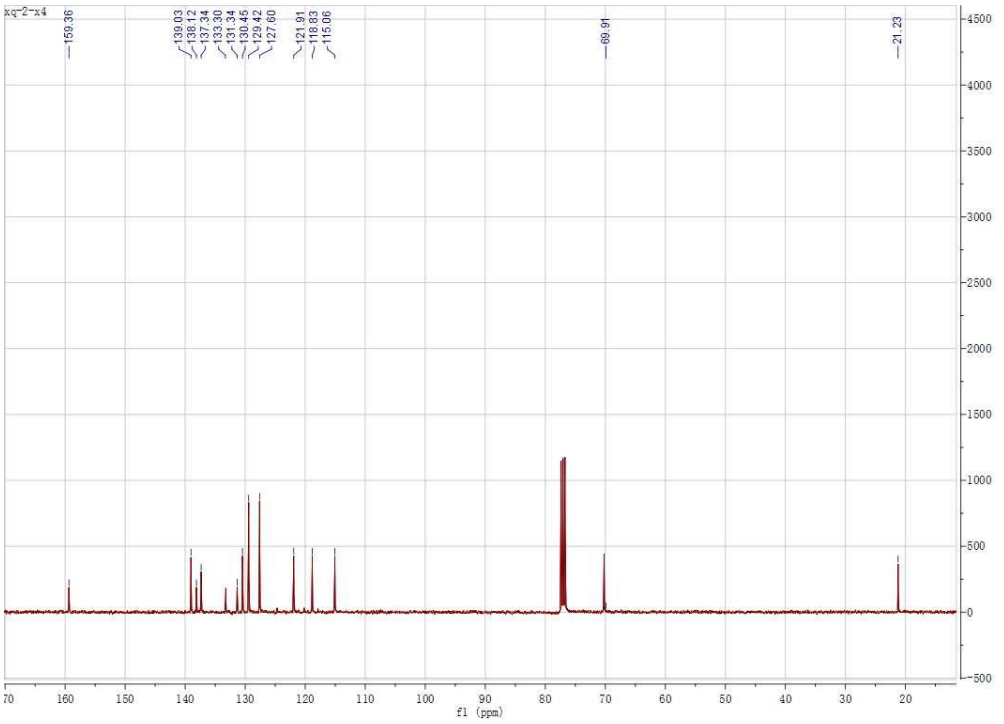




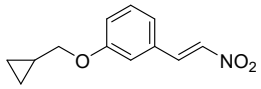
TX-14: (E)-1-((4-methylbenzyl)oxy)-3-(2-nitrovinyl)benzene

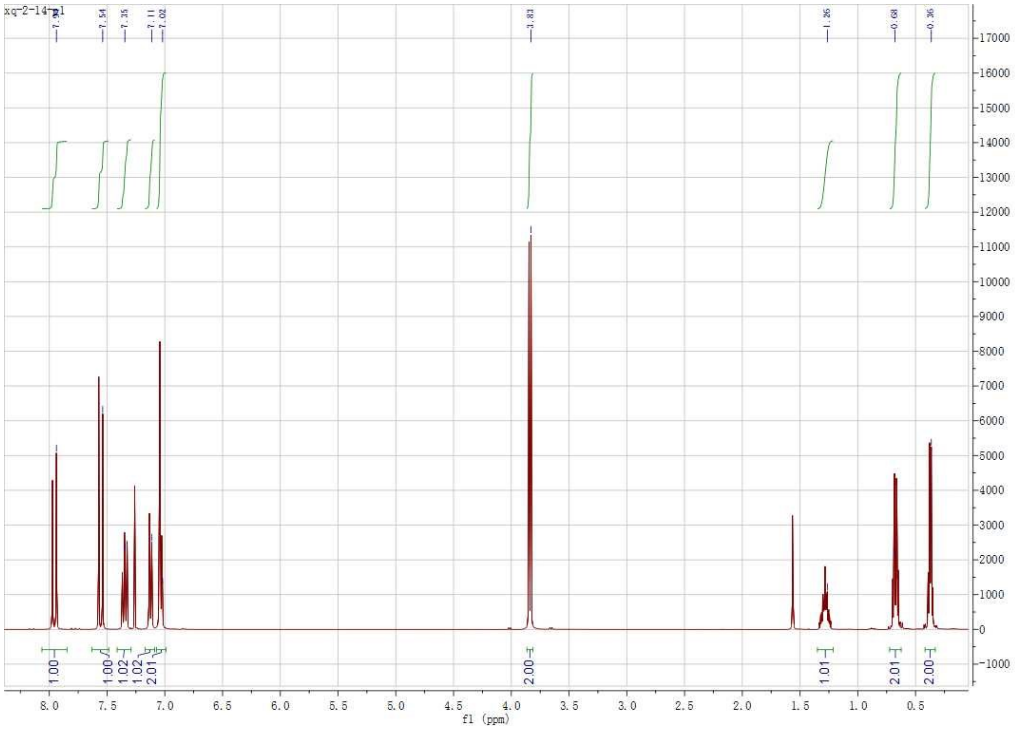


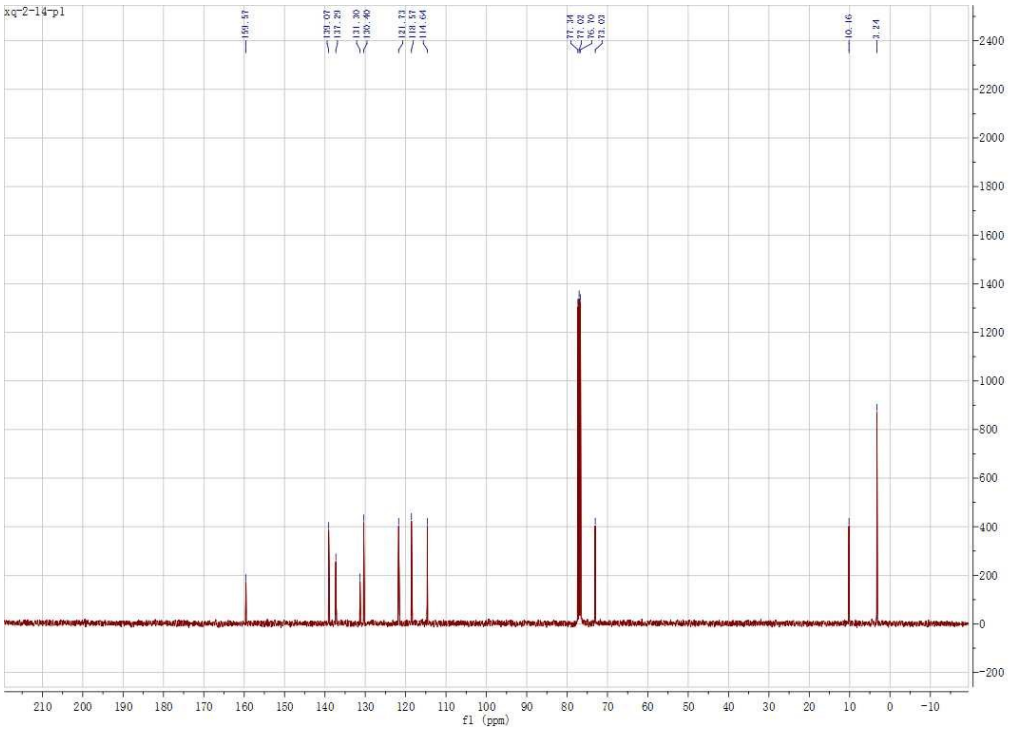




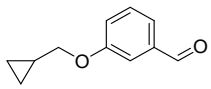
TX-15: (E)-1-(cyclopropylmethoxy)-3-(2-nitrovinyl)benzene

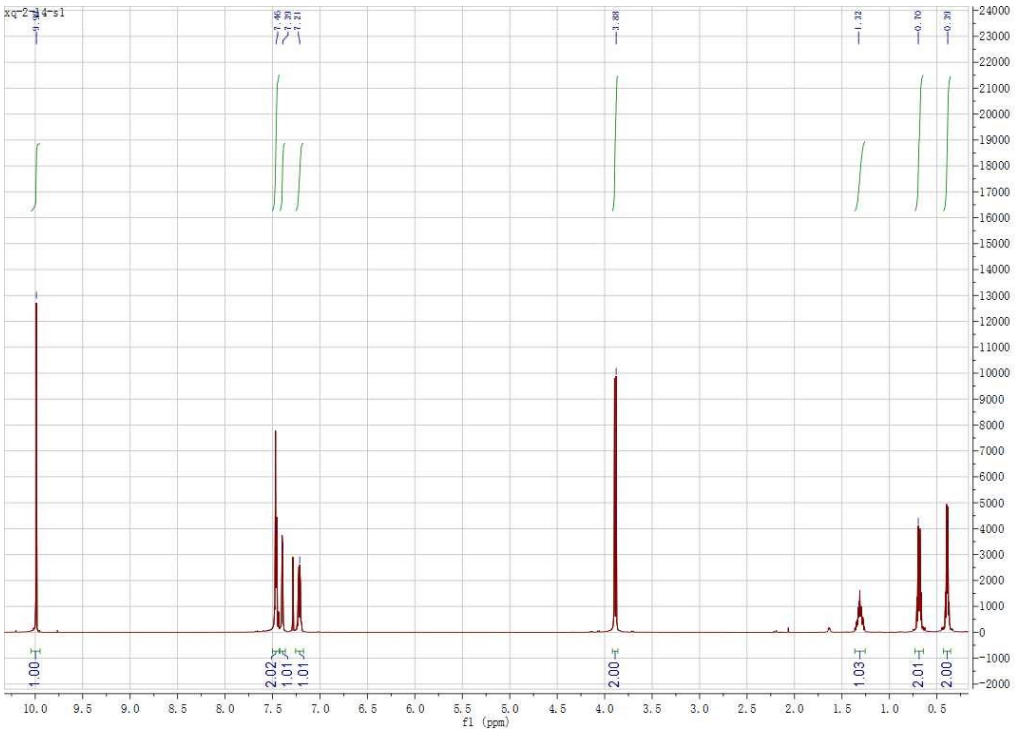


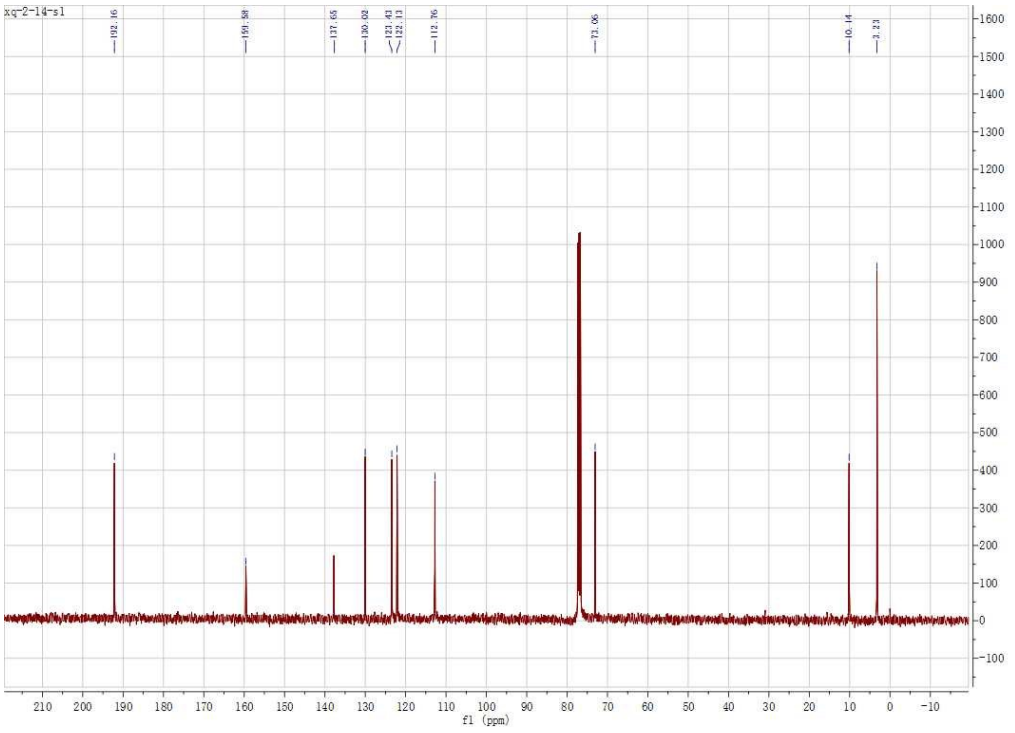




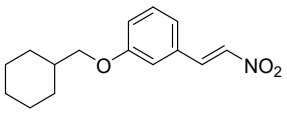
TX-15-S1: 3-(cyclopropylmethoxy)benzaldehyde

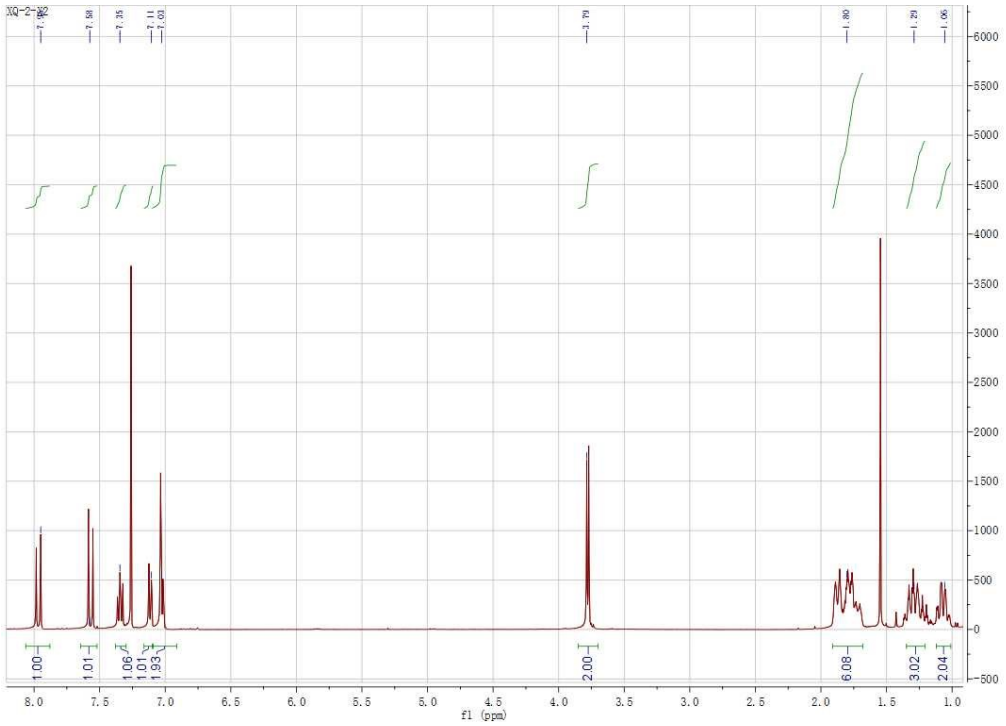


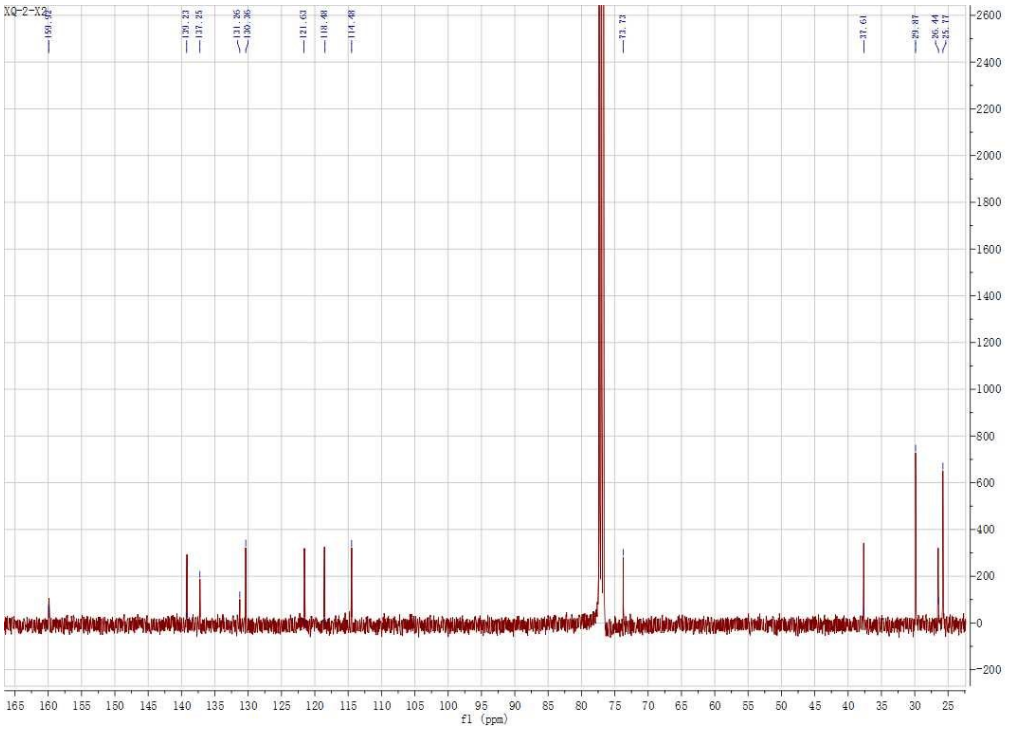




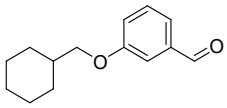
TX-16: (E)-1-(cyclohexylmethoxy)-3-(2-nitrovinyl)benzene

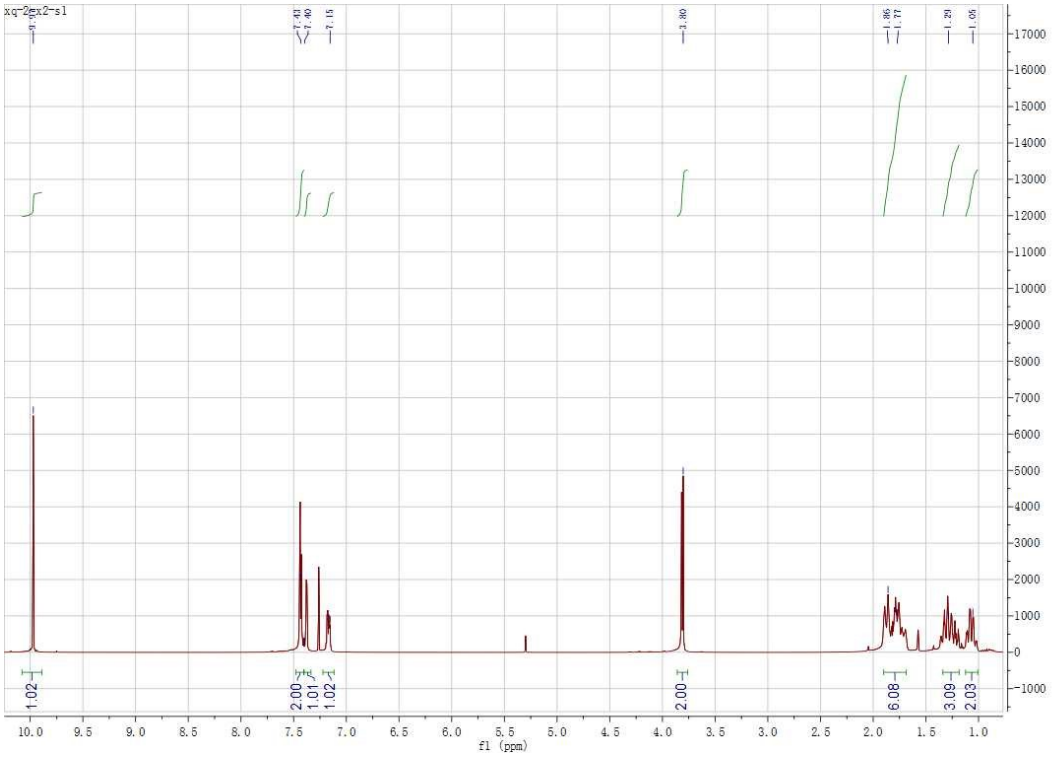




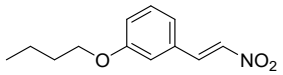


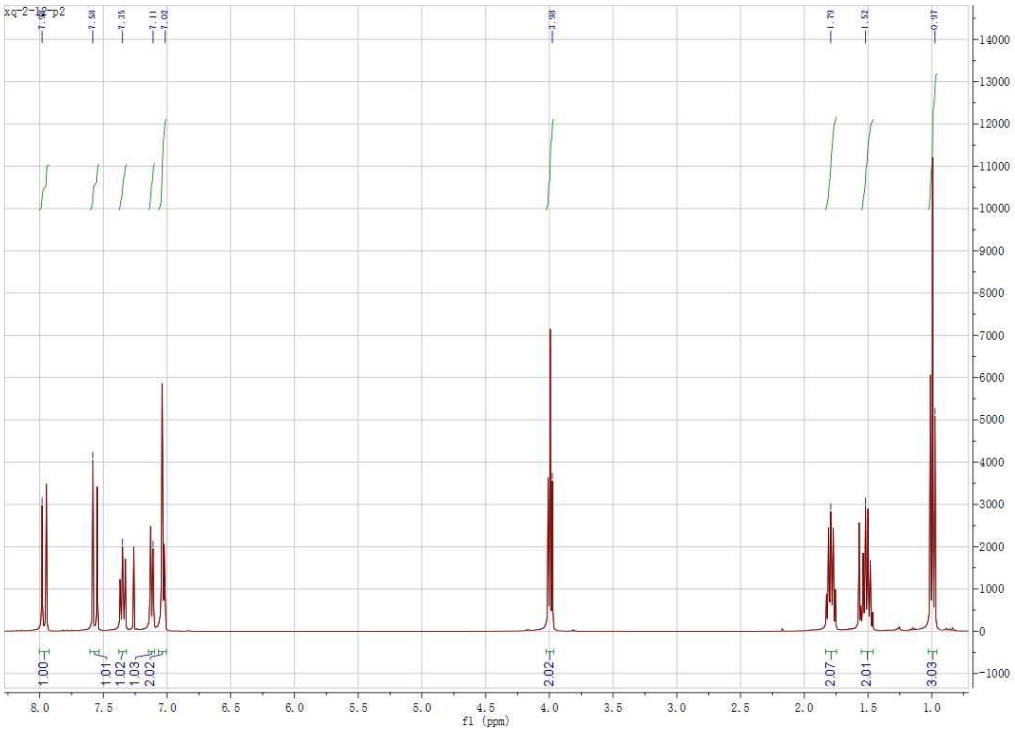
TX-16-S1: 3-(cyclohexylmethoxy)benzaldehyde

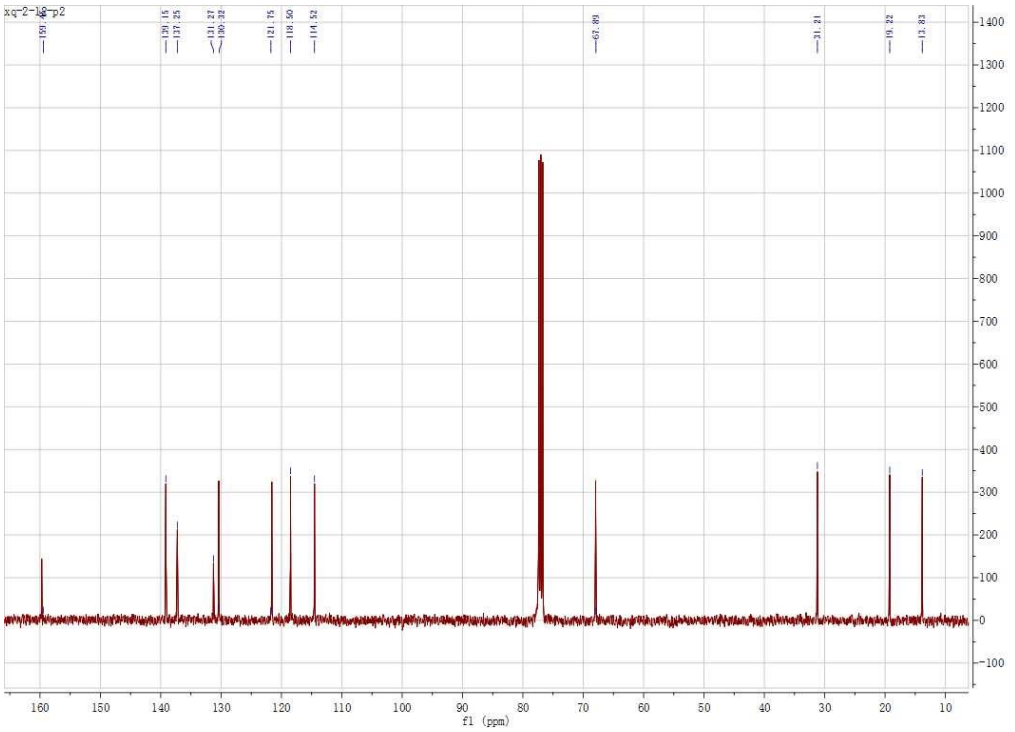




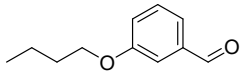
TX-17: (E)-1-butoxy-3-(2-nitrovinyl)benzene

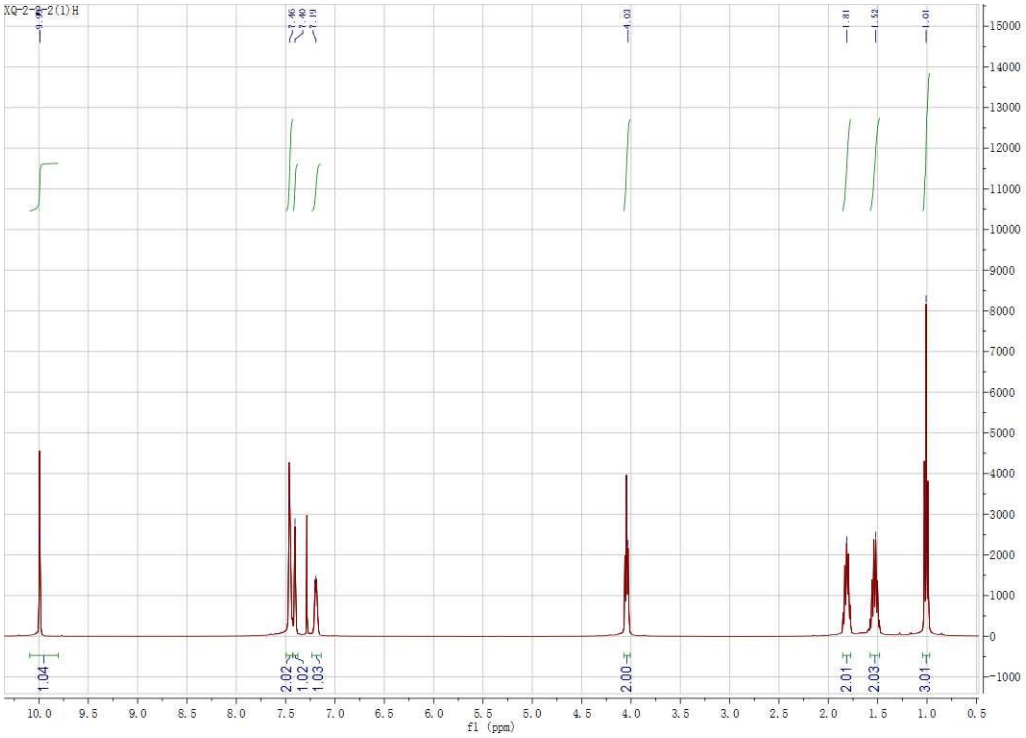


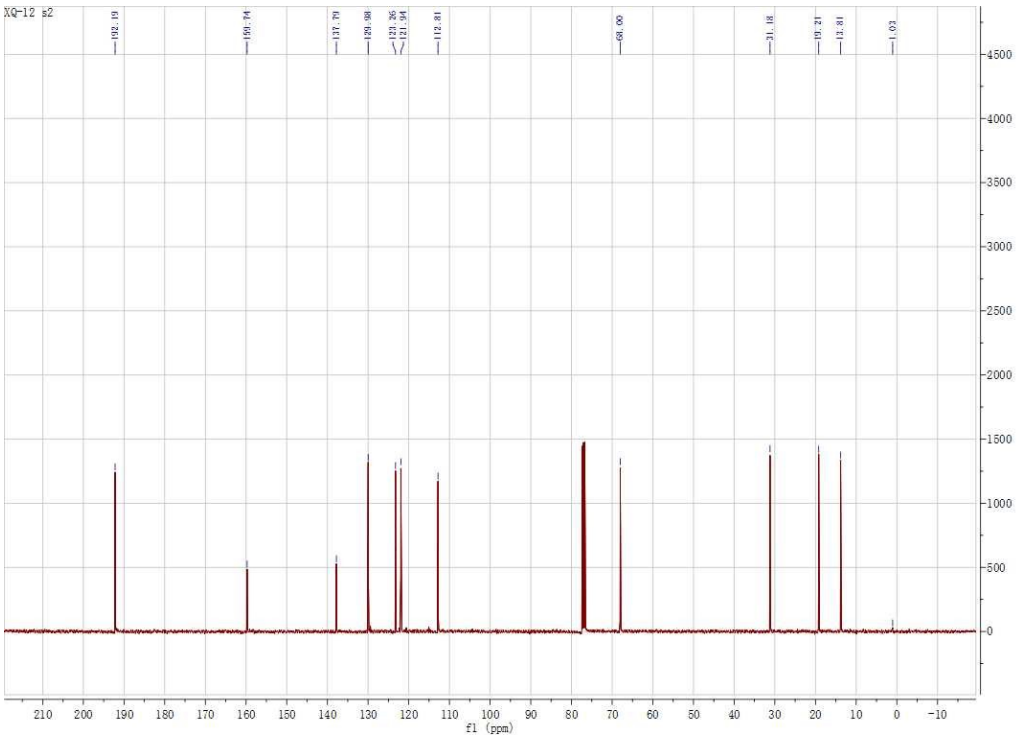




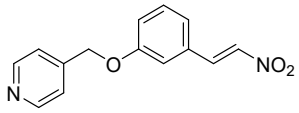
TX-17-S1: 3-butoxybenzaldehyde

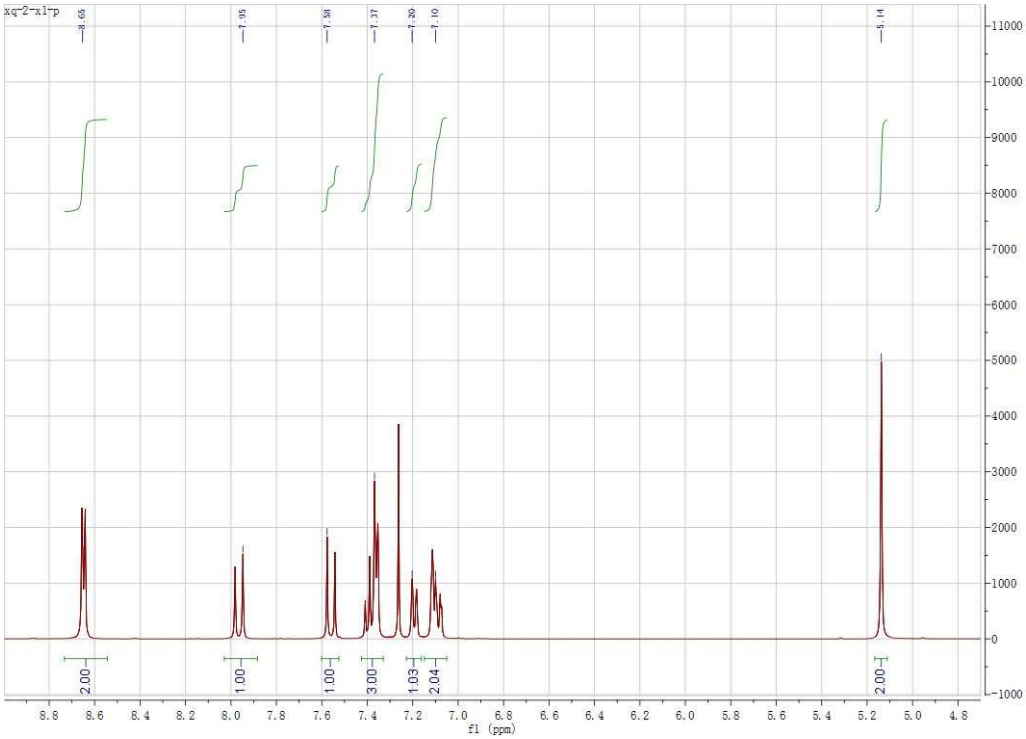


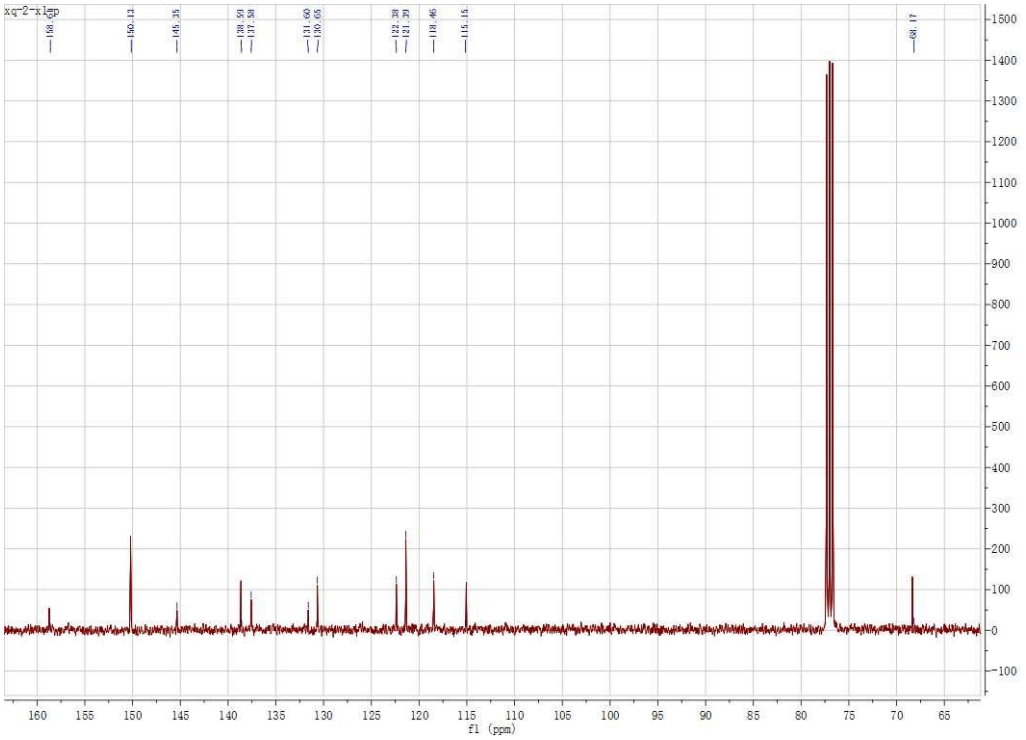




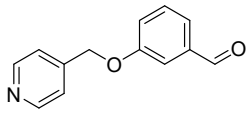
TX-18: (E)-4-((3-(2-nitrovinyl)phenoxy)methyl)pyridine

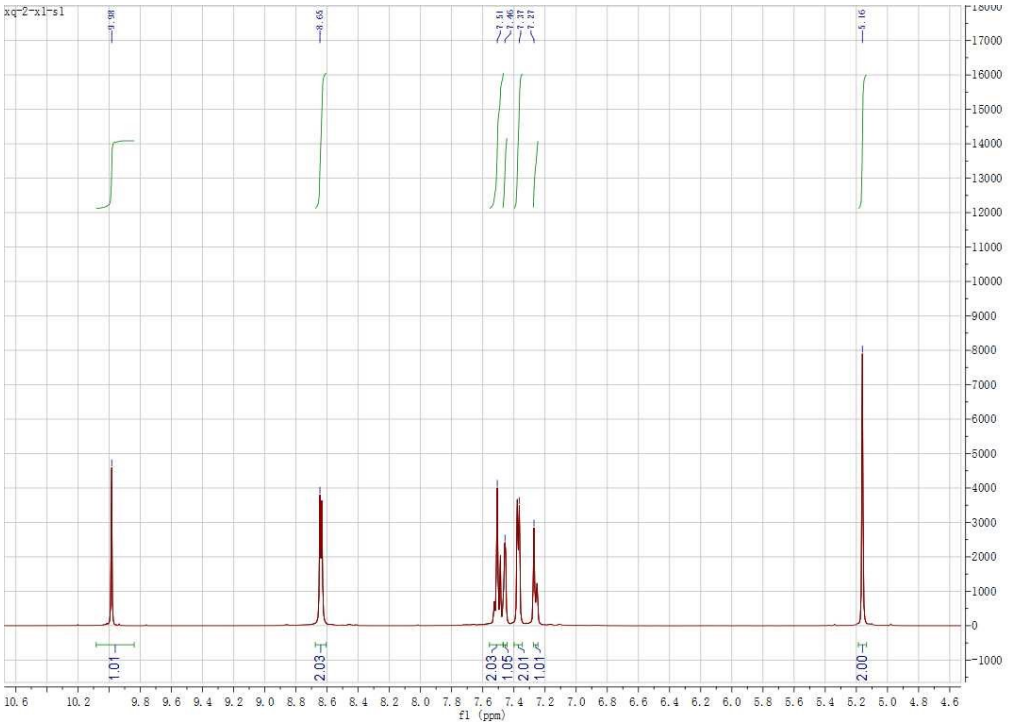


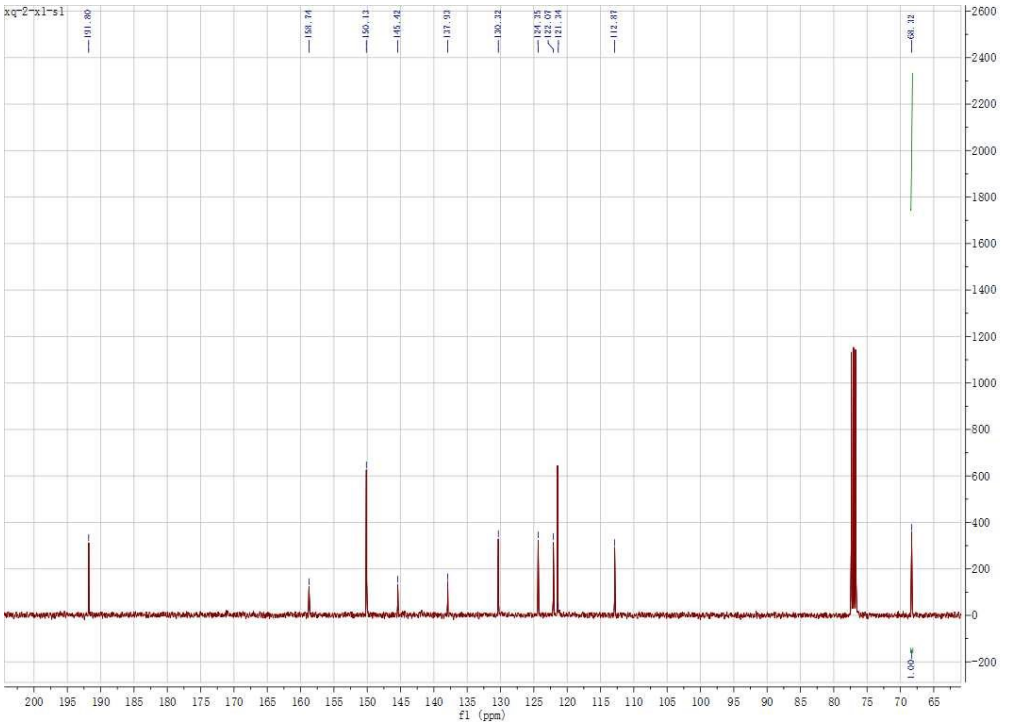




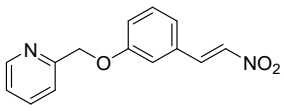
TX-18-S1: 3-(pyridin-4-ylmethoxy)benzaldehyde

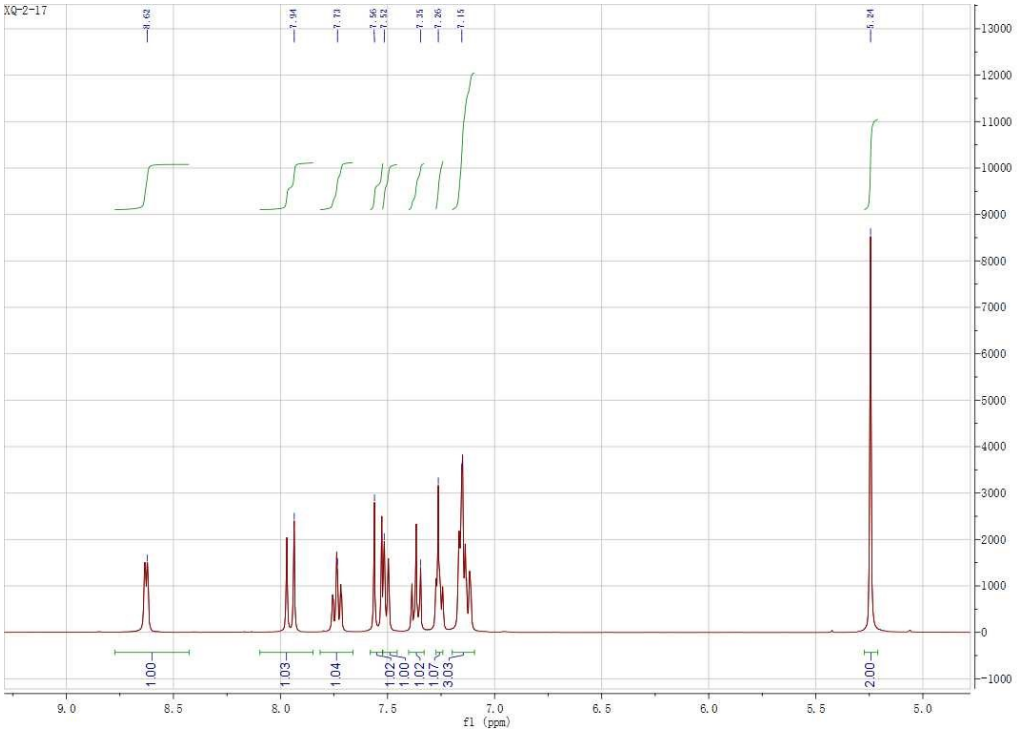


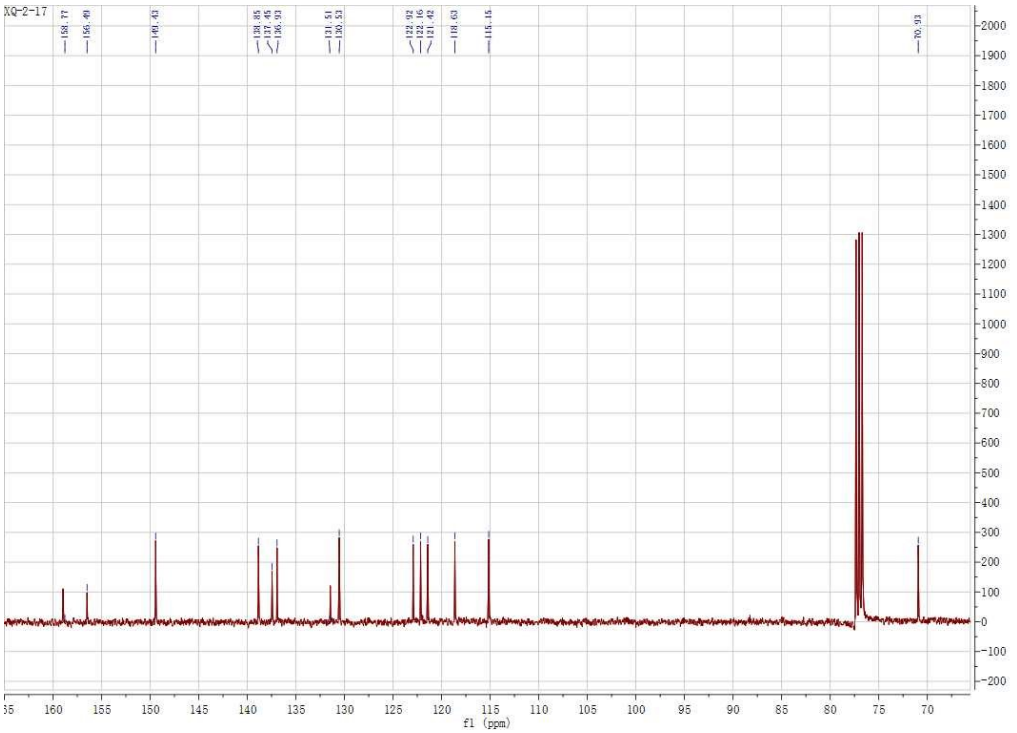




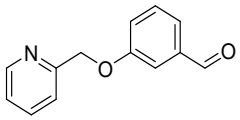
TX-19: (E)-2-((3-(2-nitrovinyl)phenoxy)methyl)pyridine

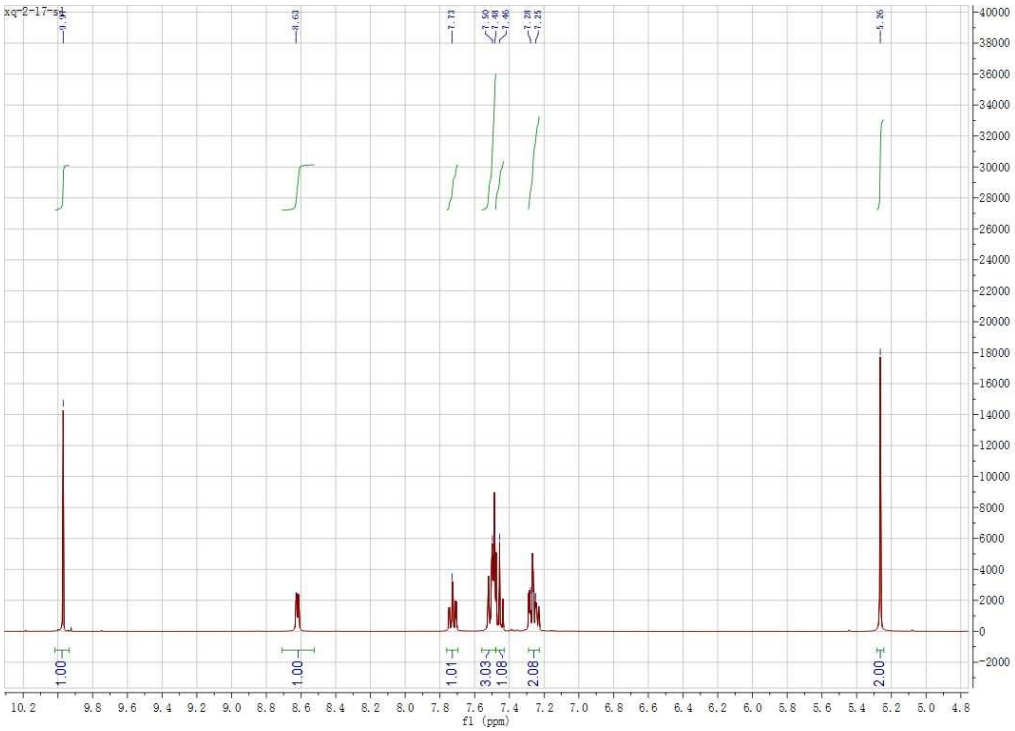


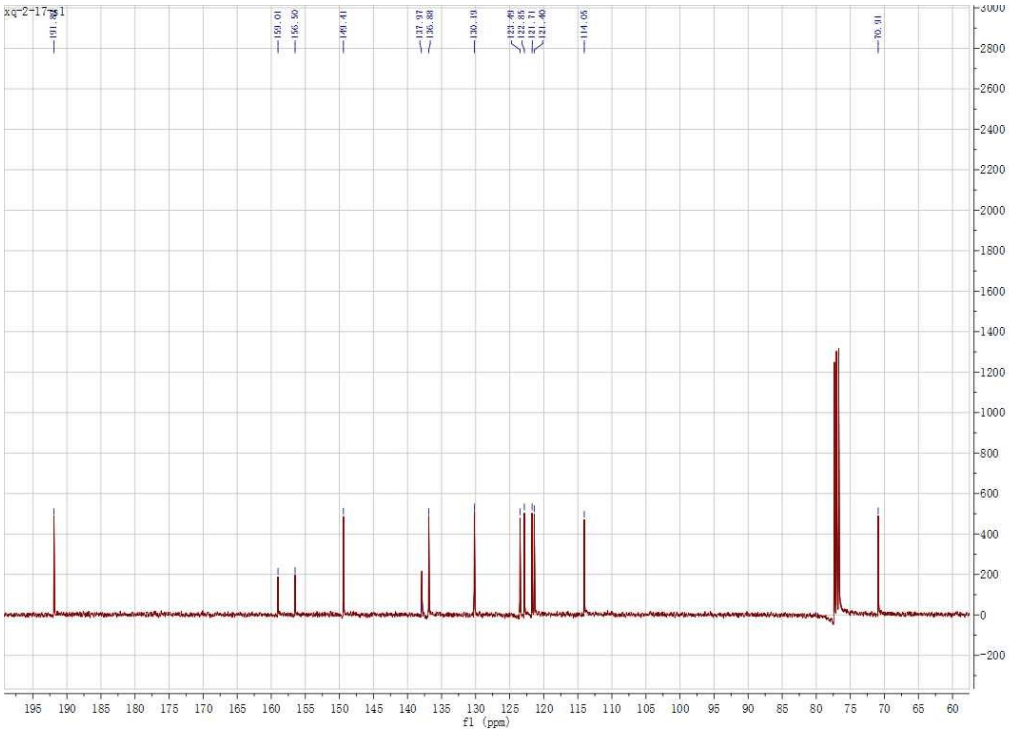




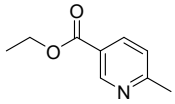
TX-19-S1: 3-(pyridin-2-ylmethoxy)benzaldehyde

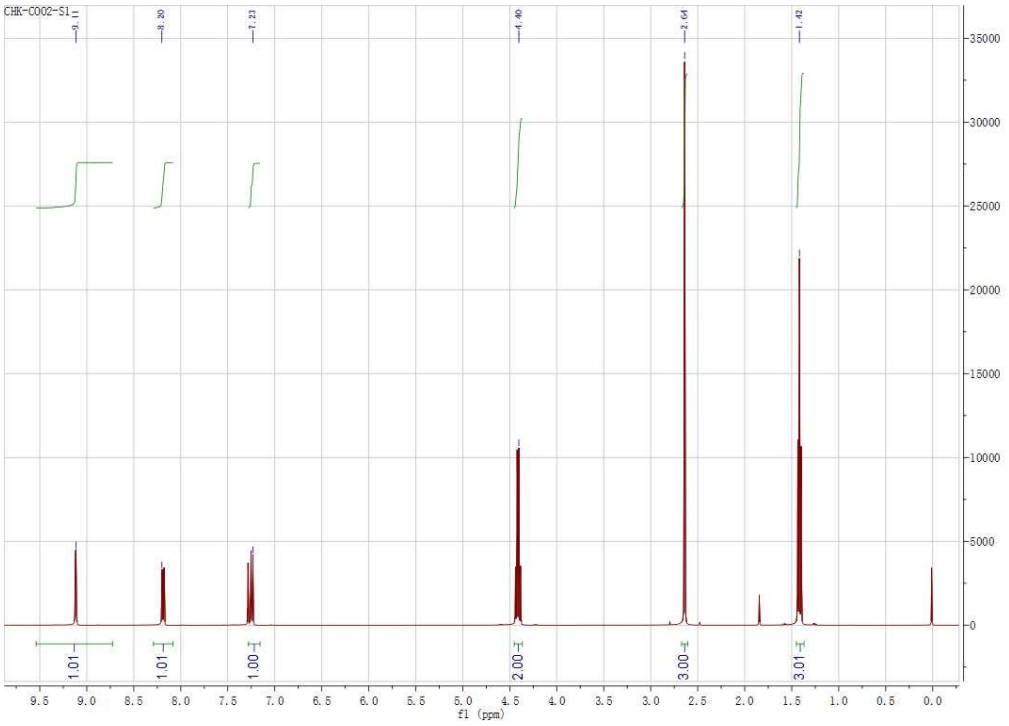


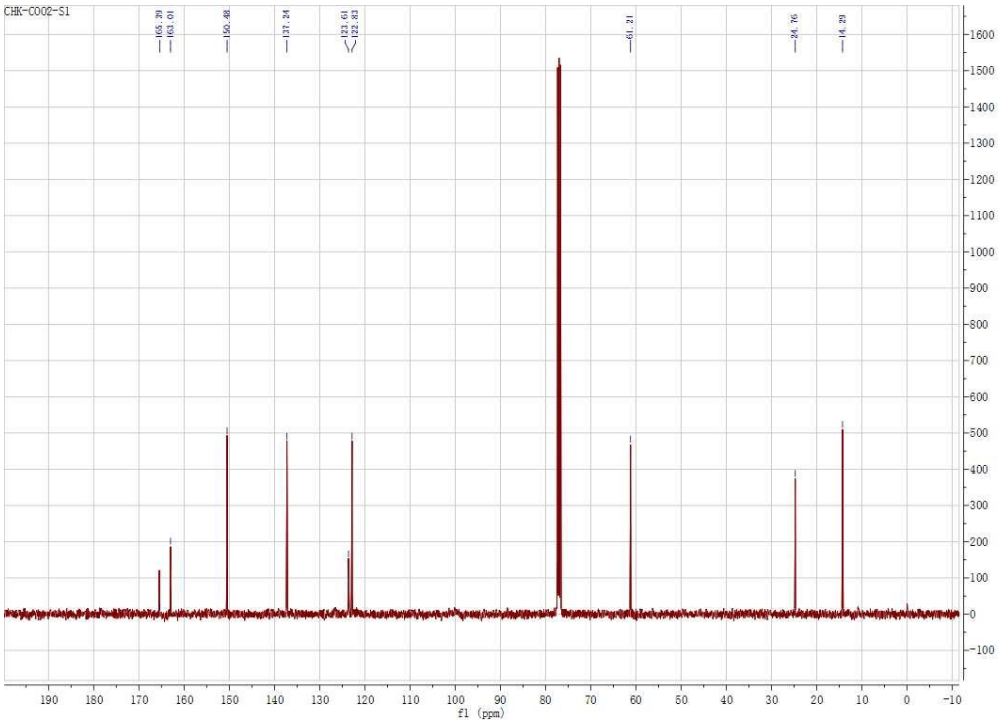




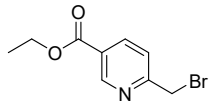
TX-20-S1: ethyl 6-methylnicotinate

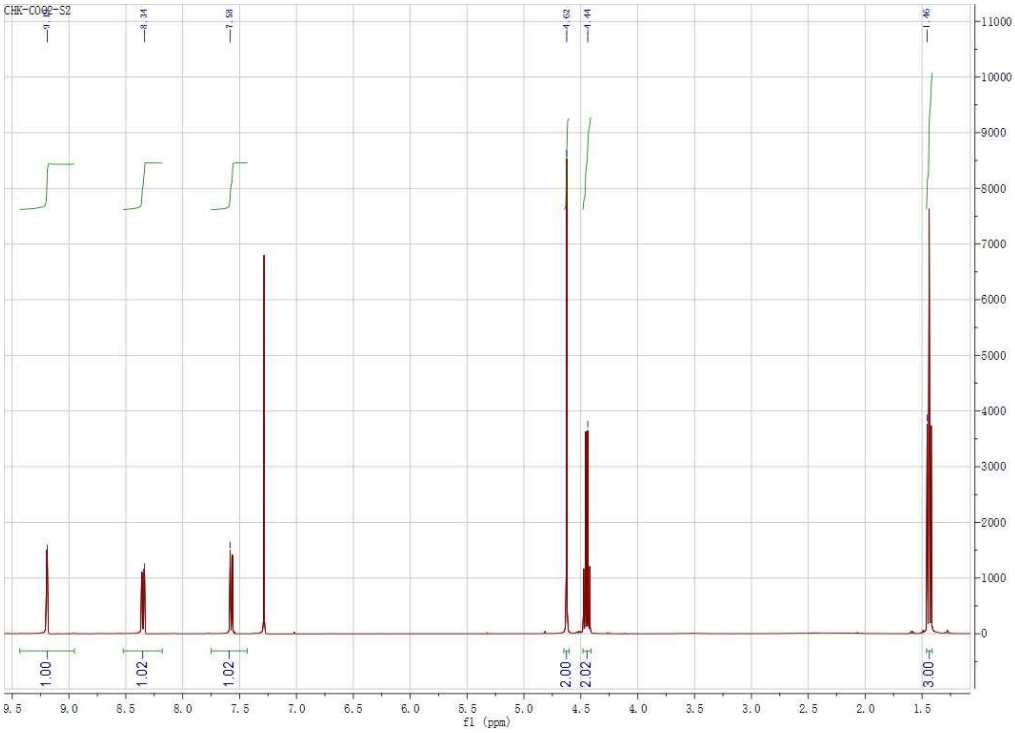


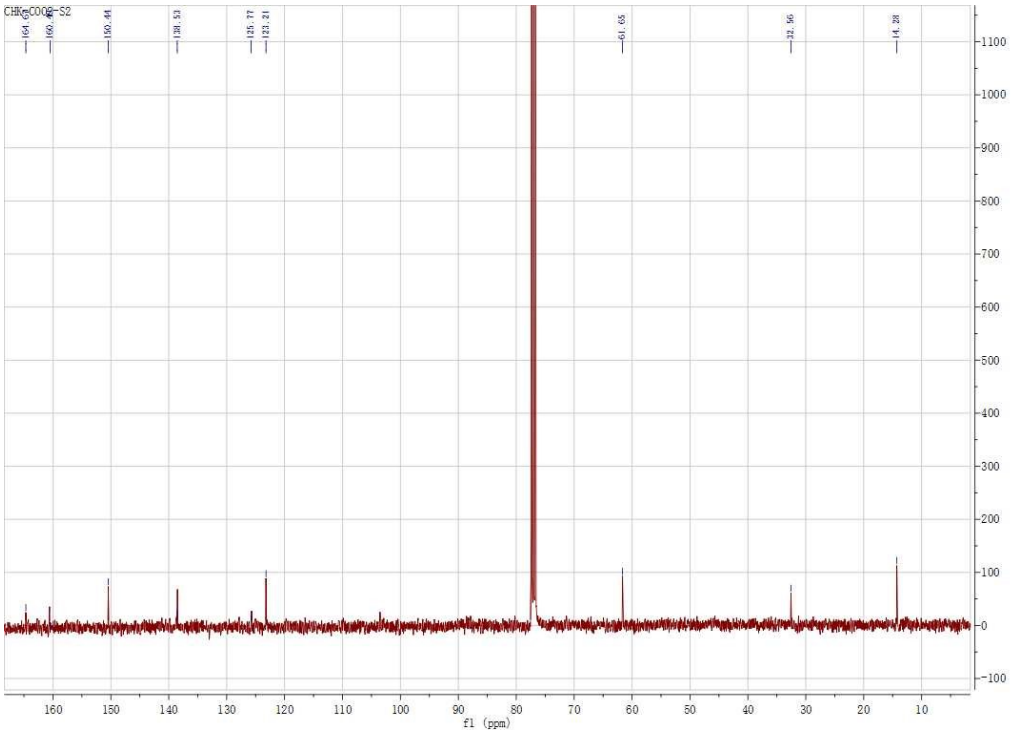




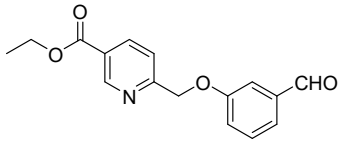
TX-20-S2: ethyl 6-(bromomethyl)nicotinate

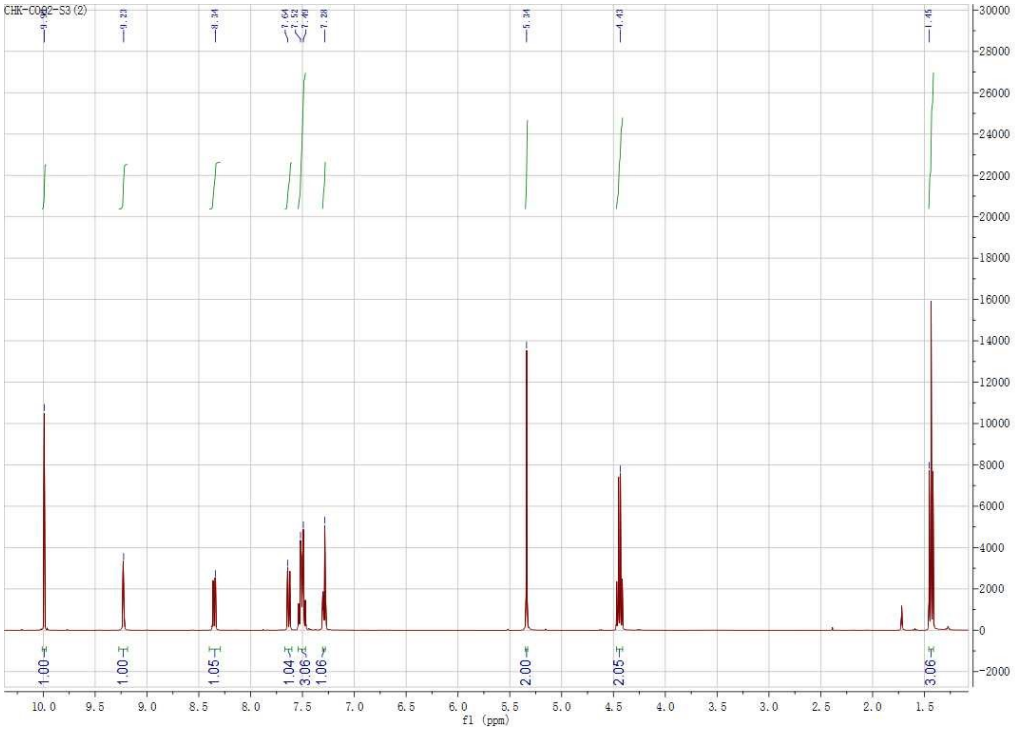


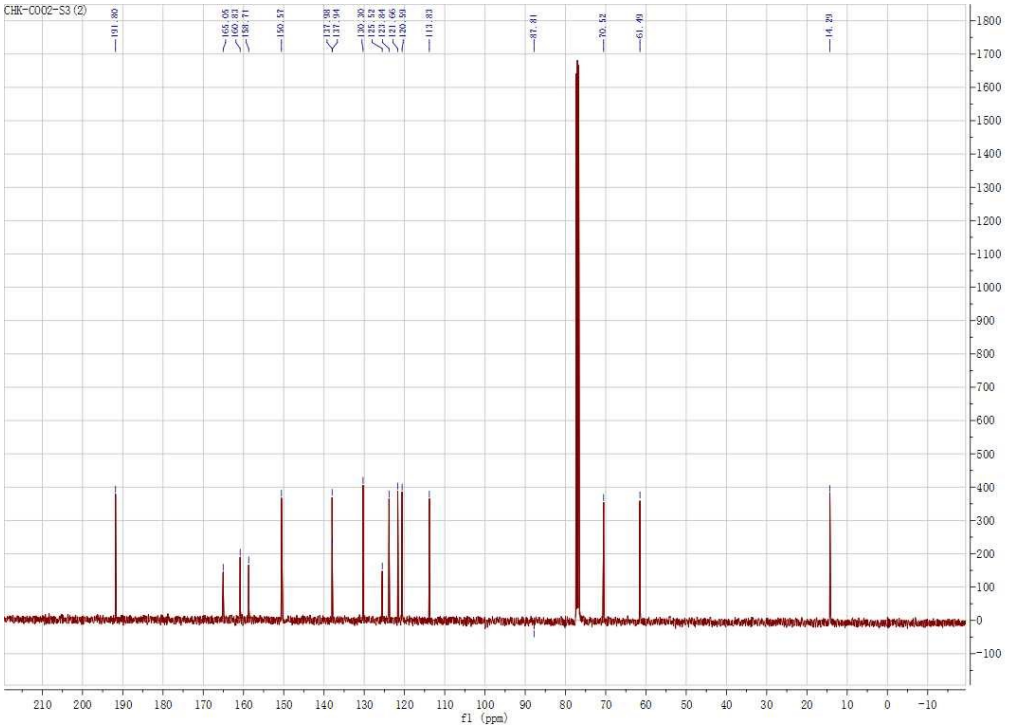




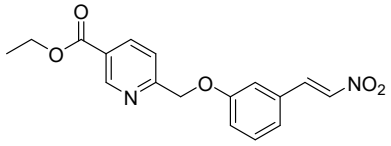
TX-20-S3: ethyl 6-((3-formylphenoxy)methyl)nicotinate

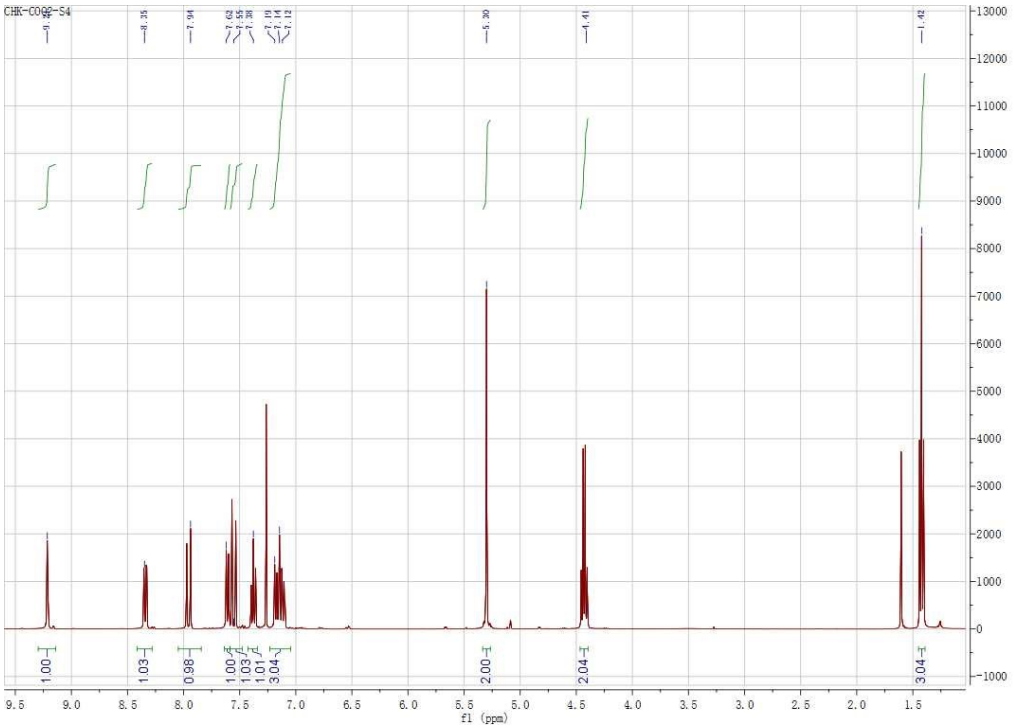


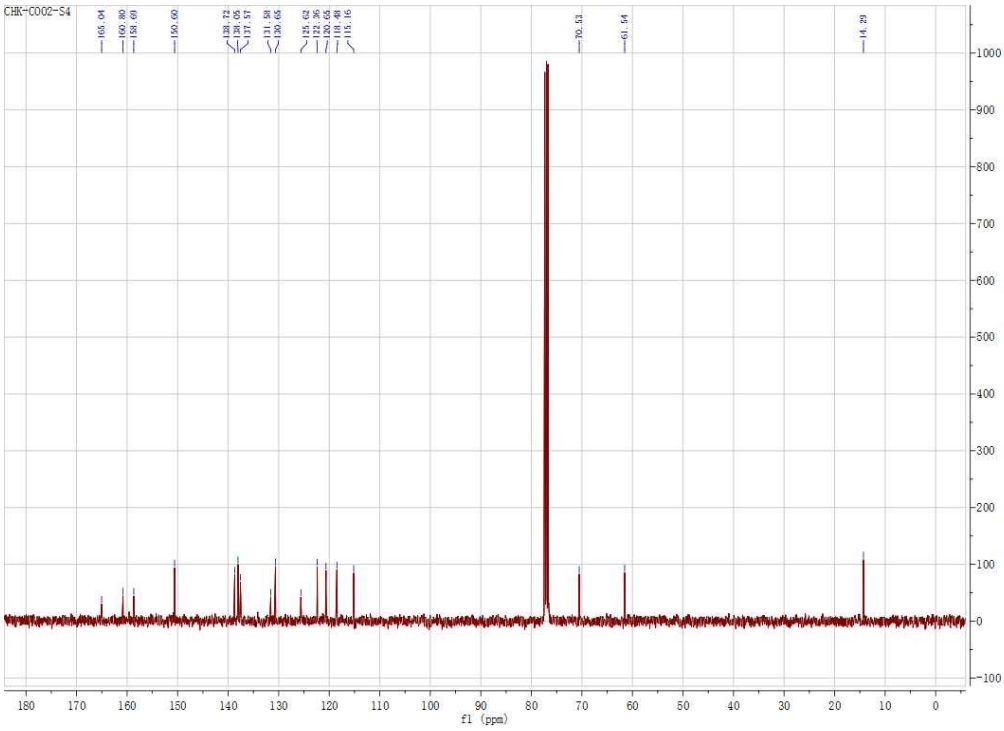




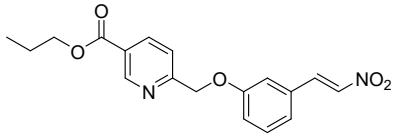
TX-20: ethyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate

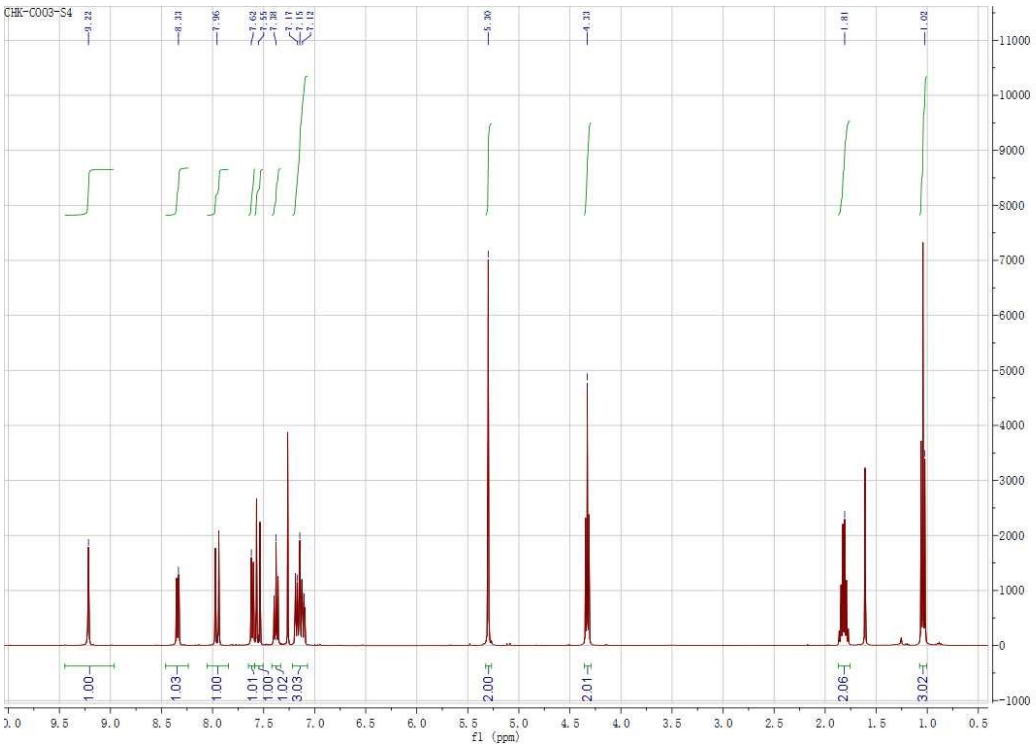


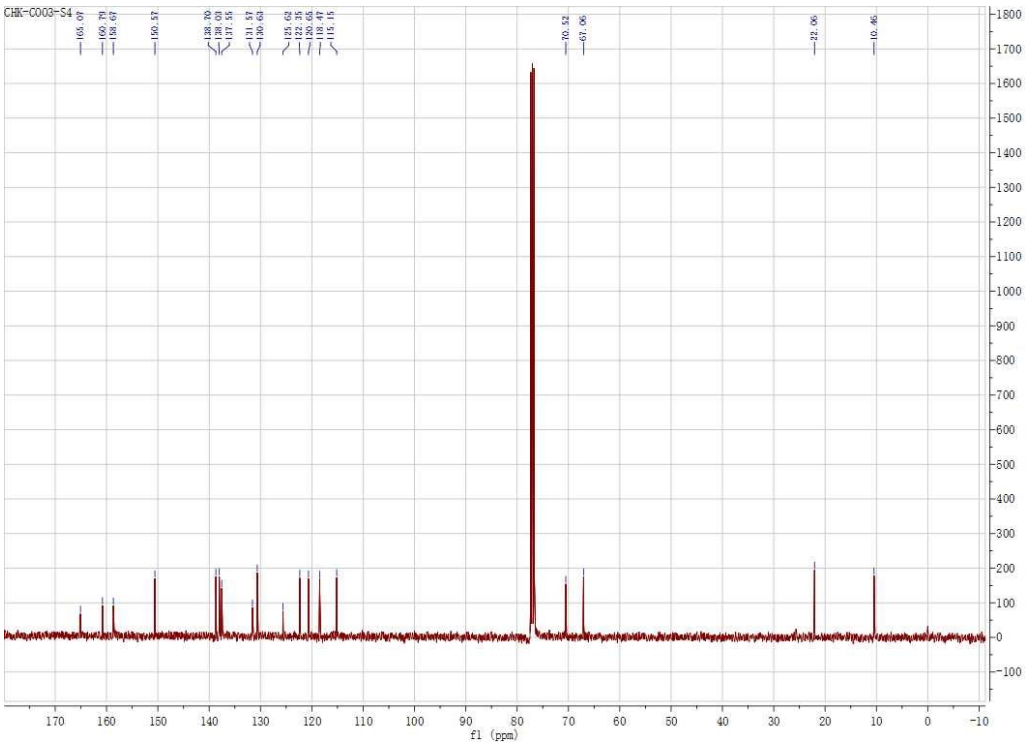




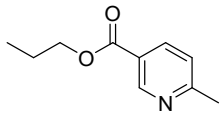
TX-21: propyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate

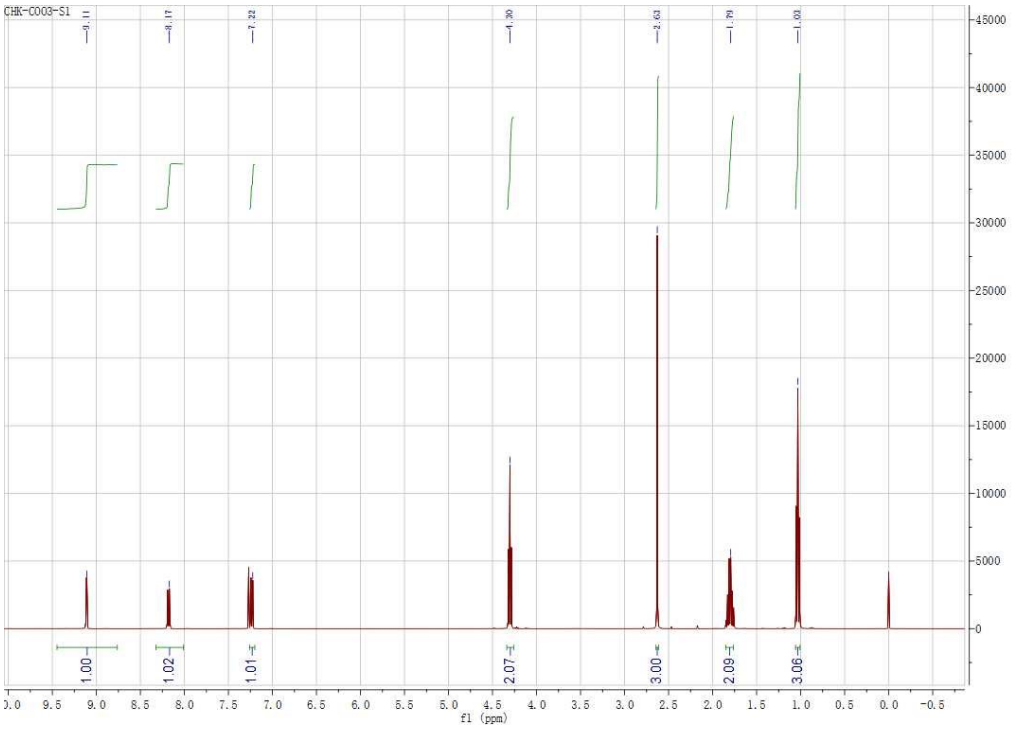


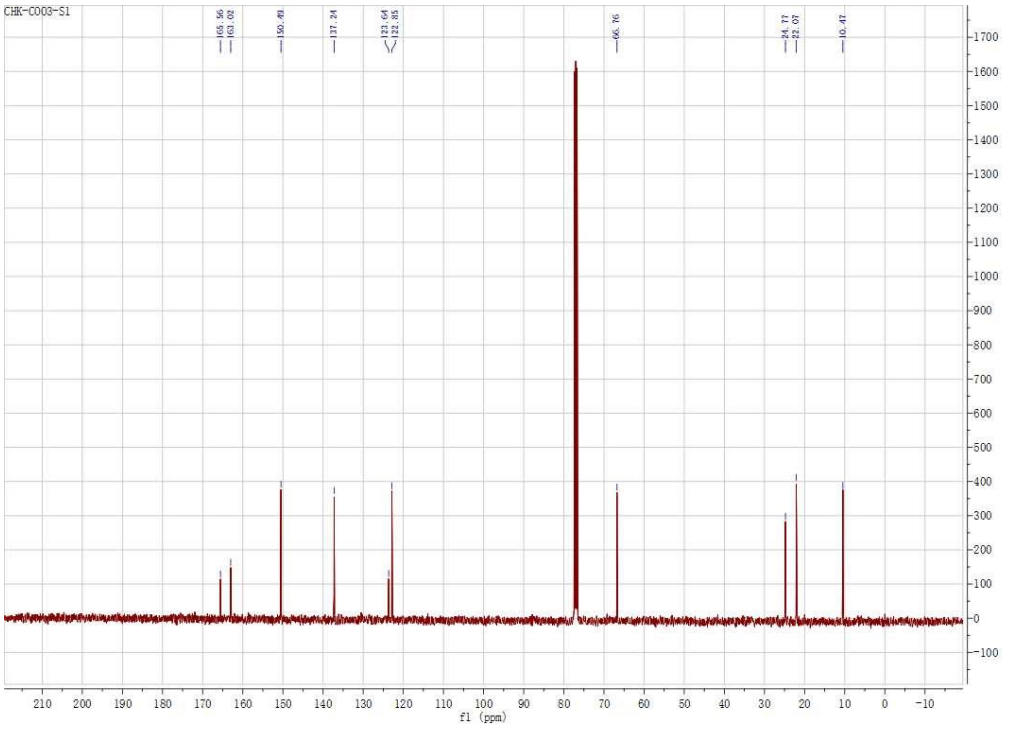




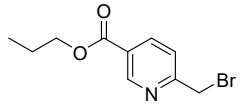
TX-21-S1: propyl 6-methylnicotinate

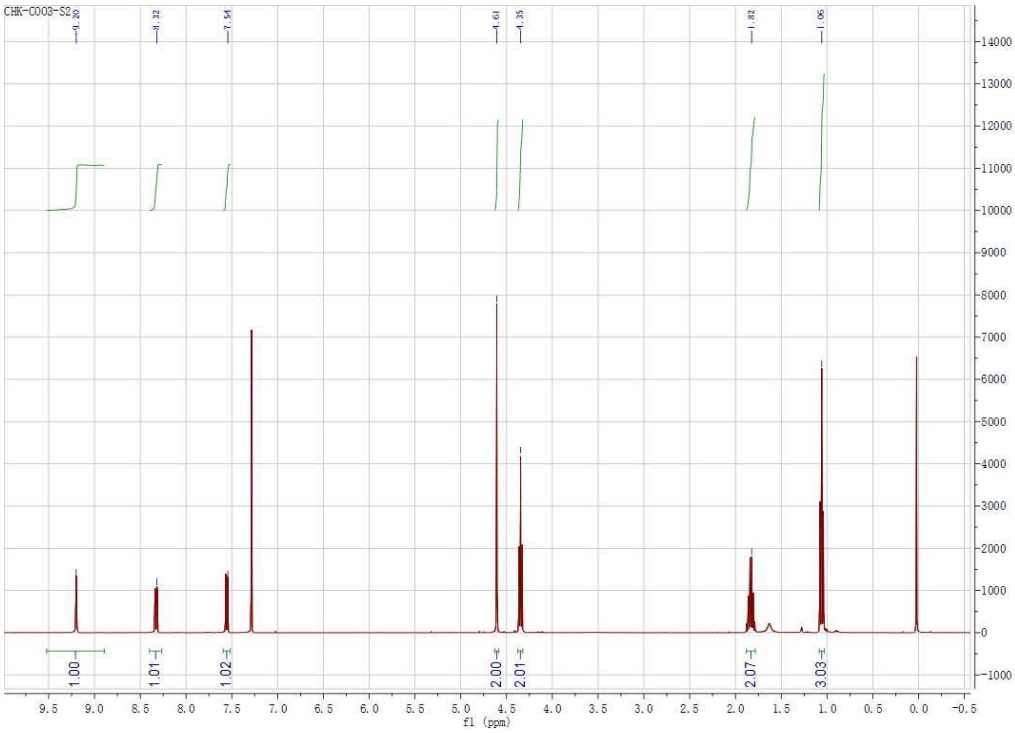


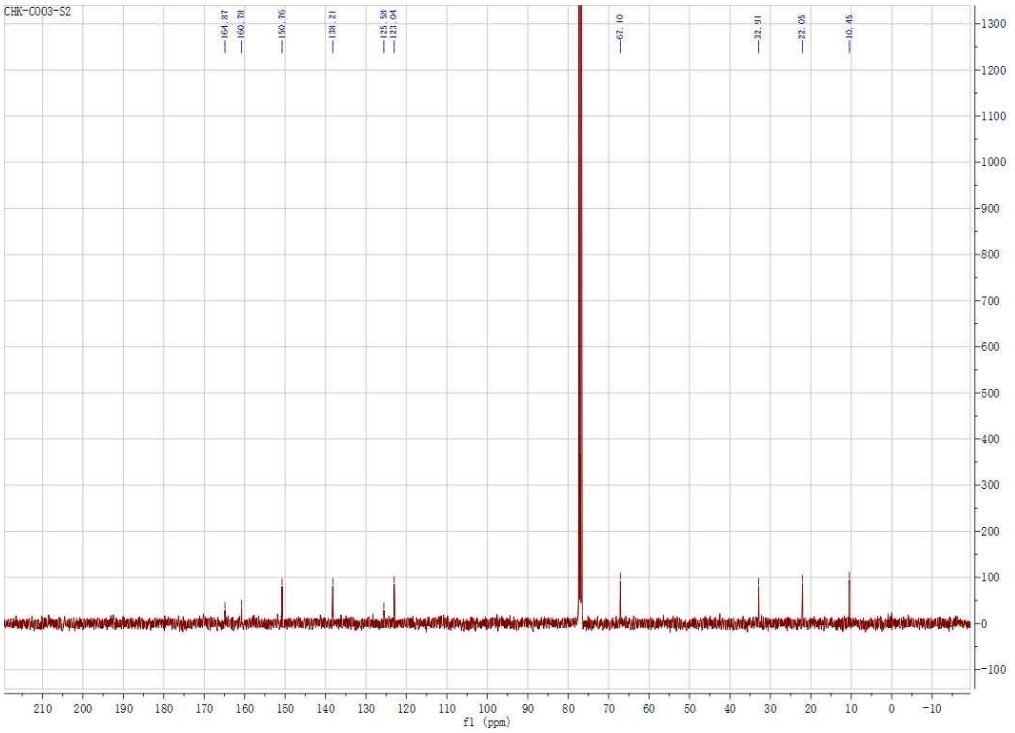




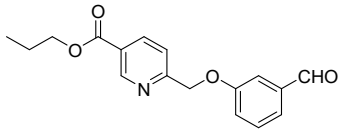
TX-21-S2: propyl 6-(bromomethyl)nicotinate

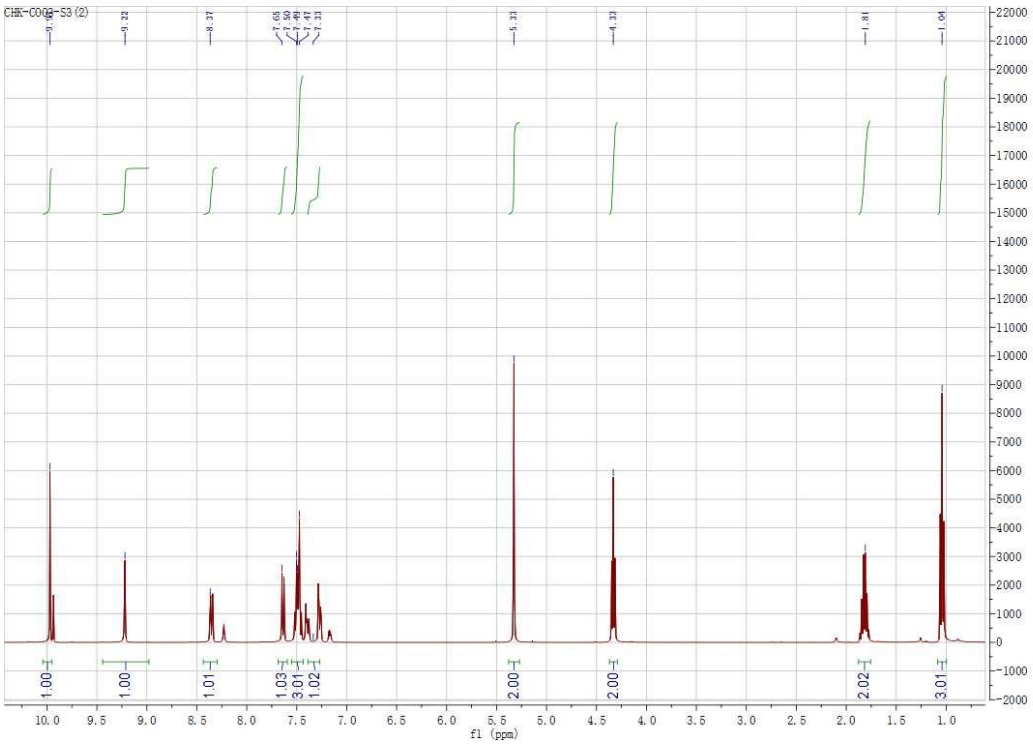


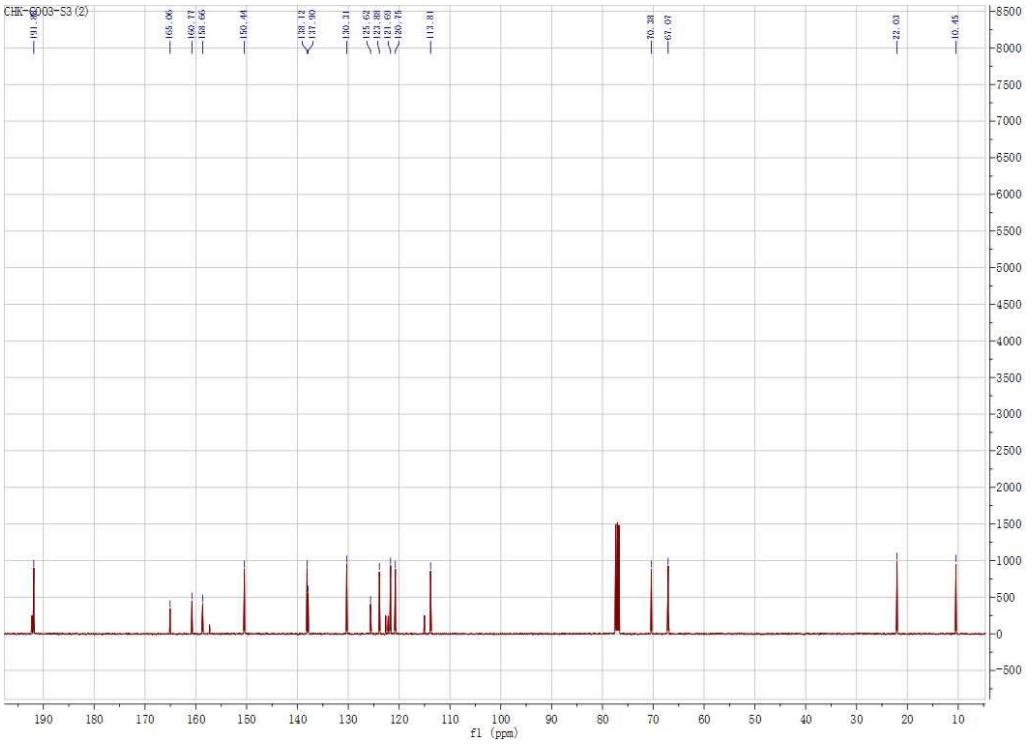




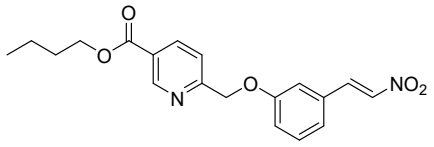
TX-21-S3: propyl 6-((3-formylphenoxy)methyl)nicotinate

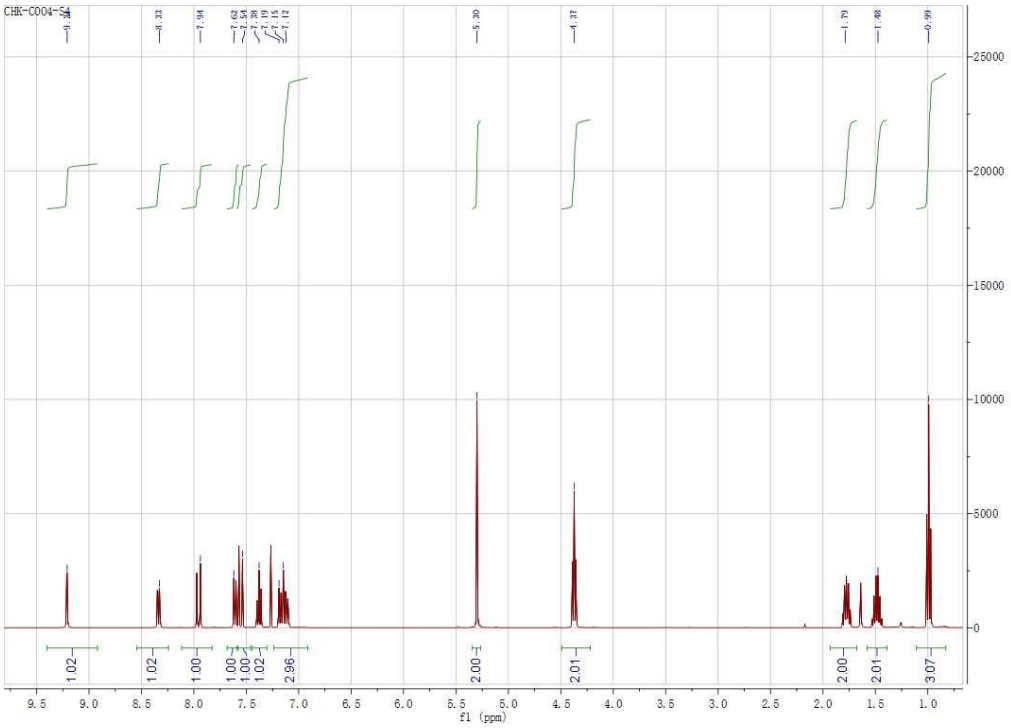


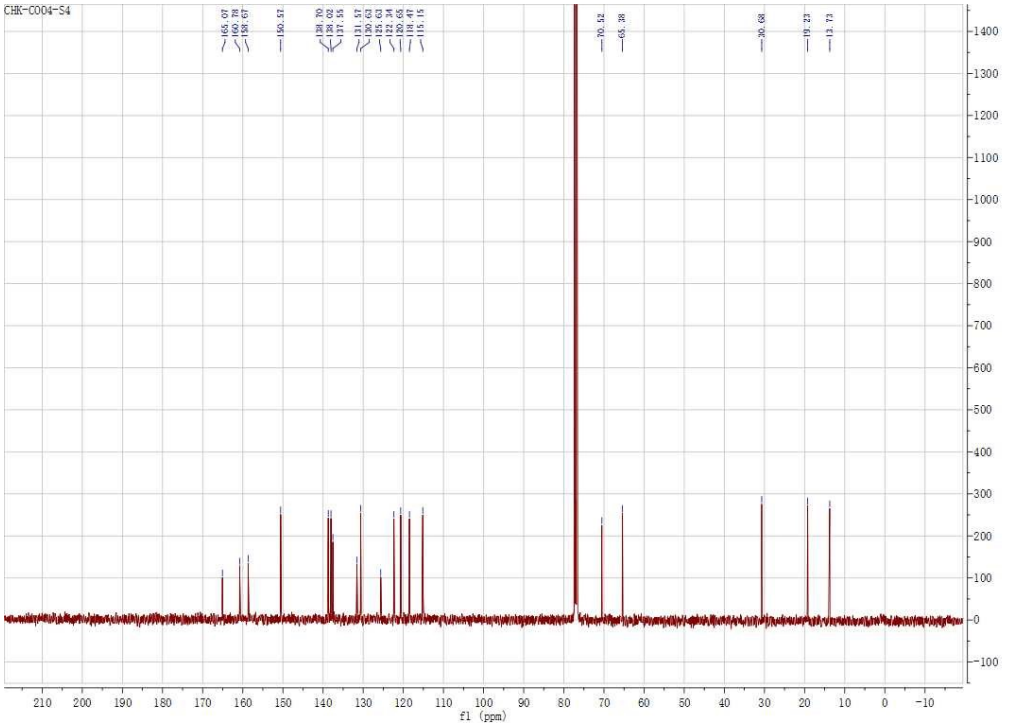




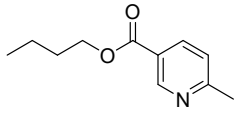
TX-22: butyl (E)-6-((3-(2-nitrovinyl)phenoxy)methyl)nicotinate

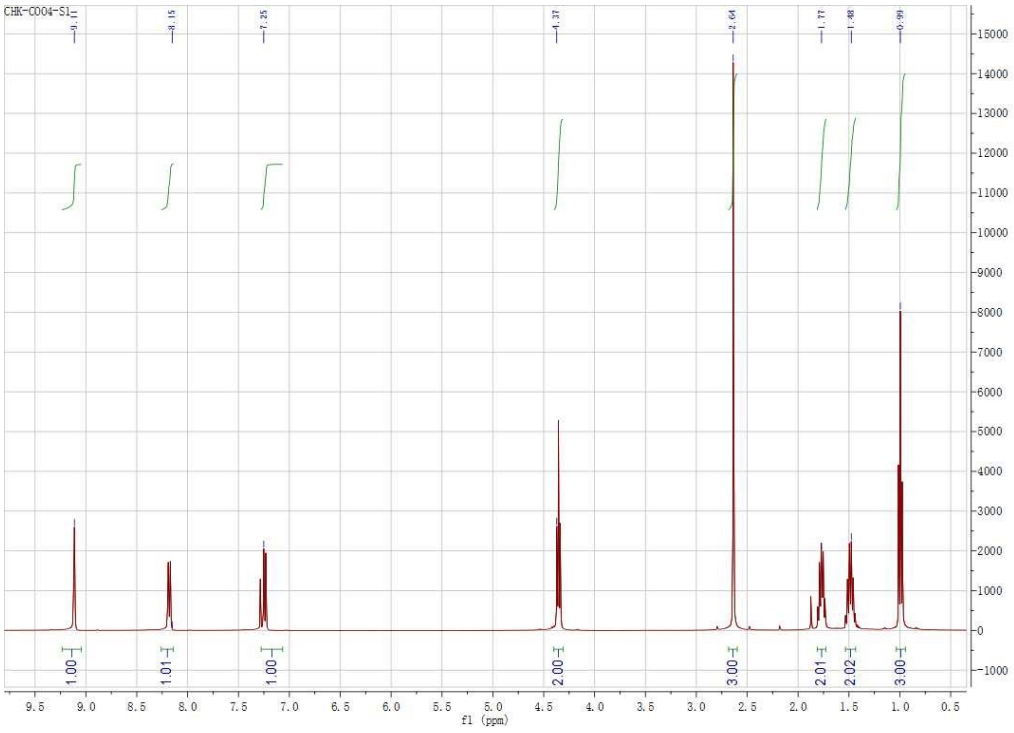


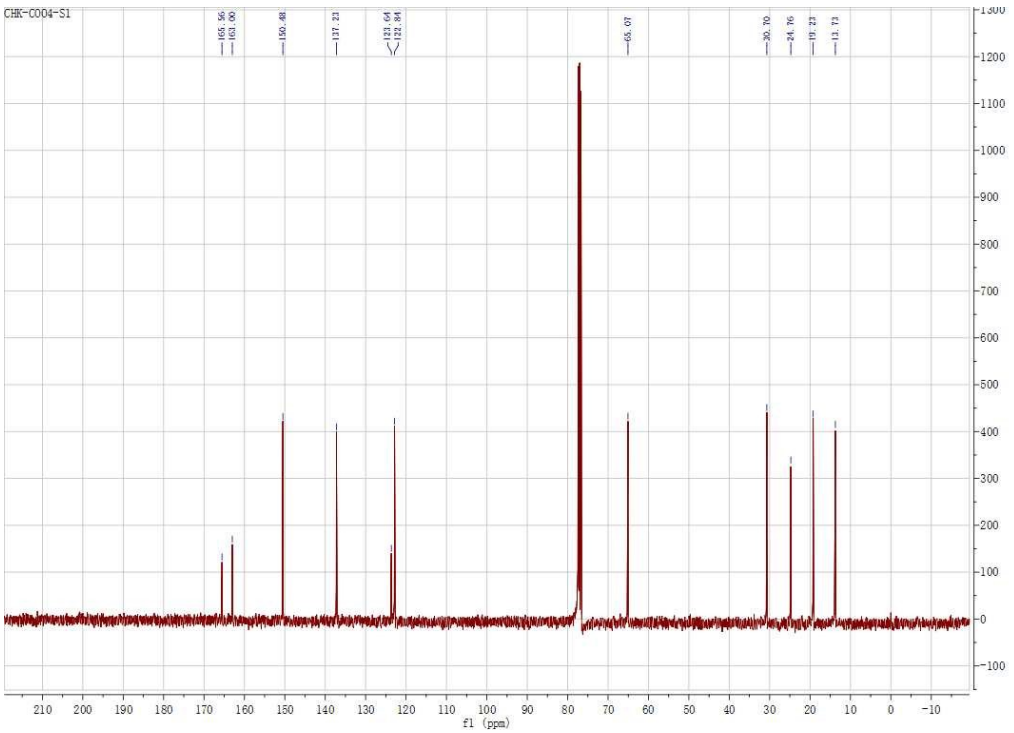




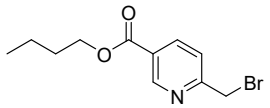
TX-22-S1: butyl 6-methylnicotinate

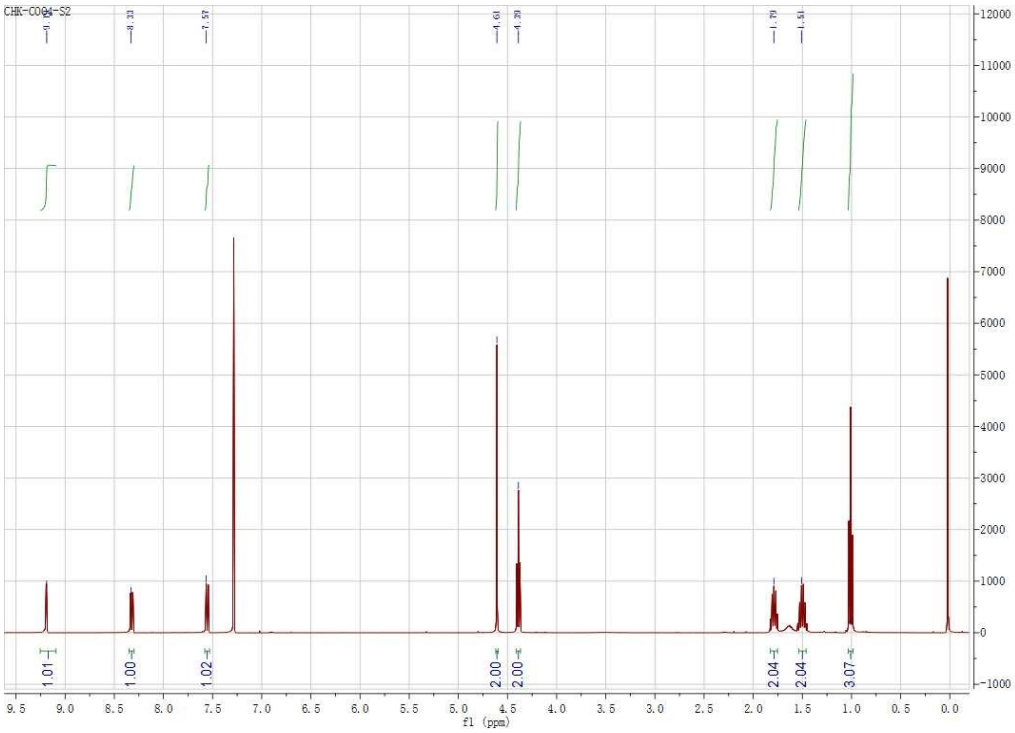


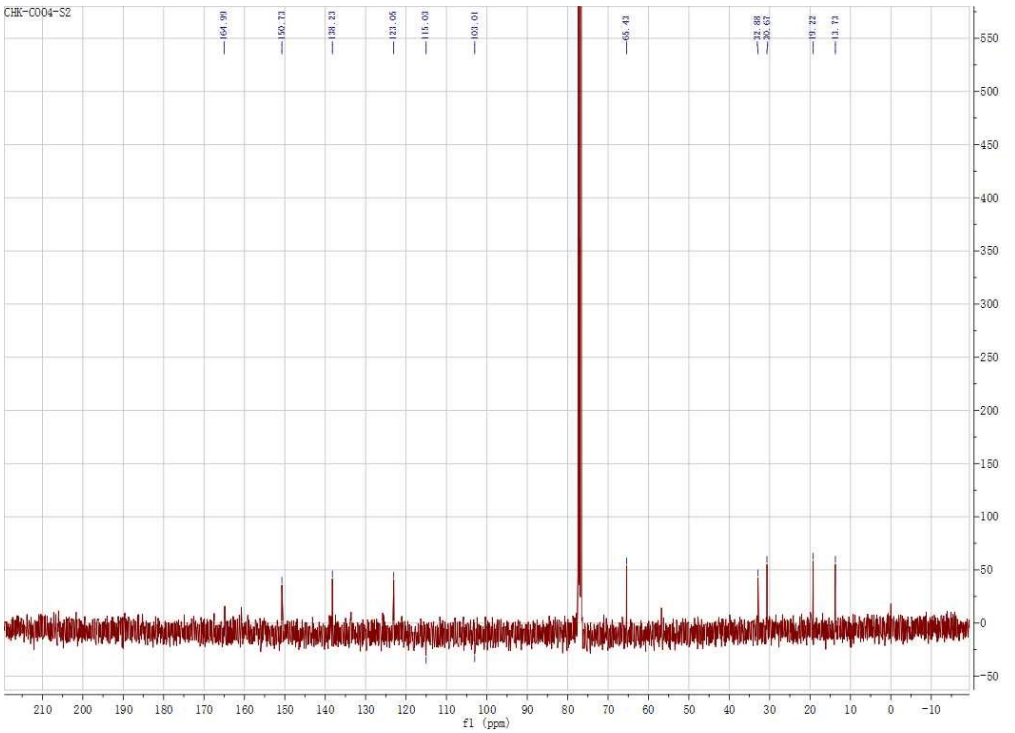




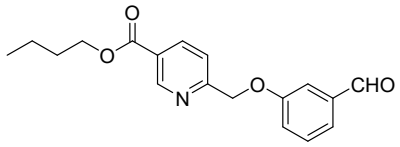
TX-22-S2: butyl 6-(bromomethyl)nicotinate

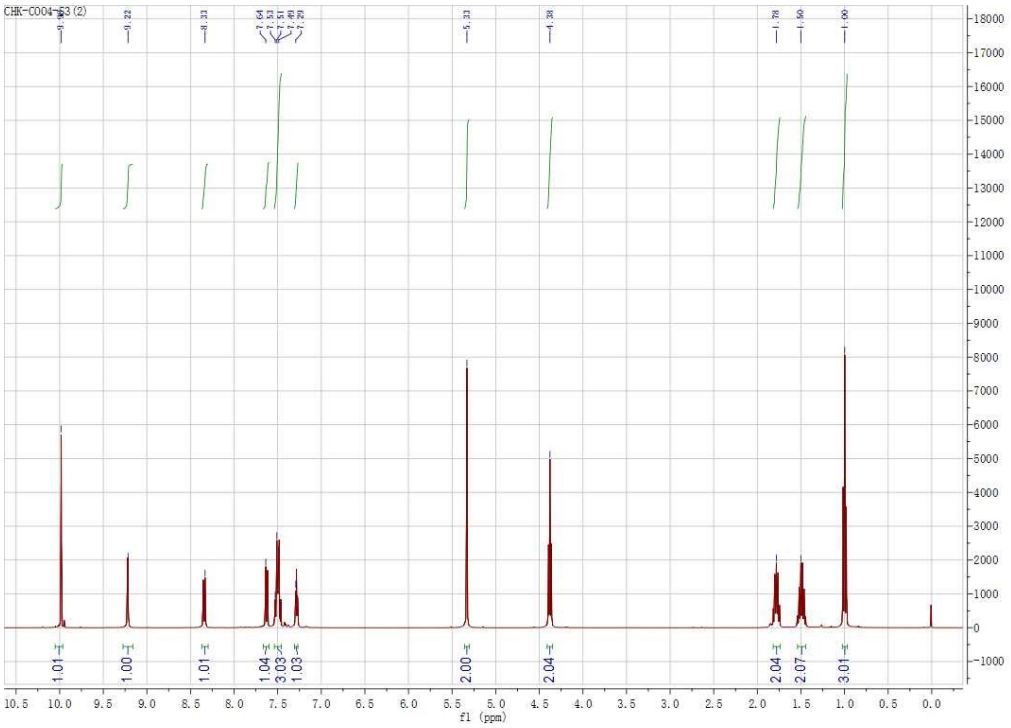


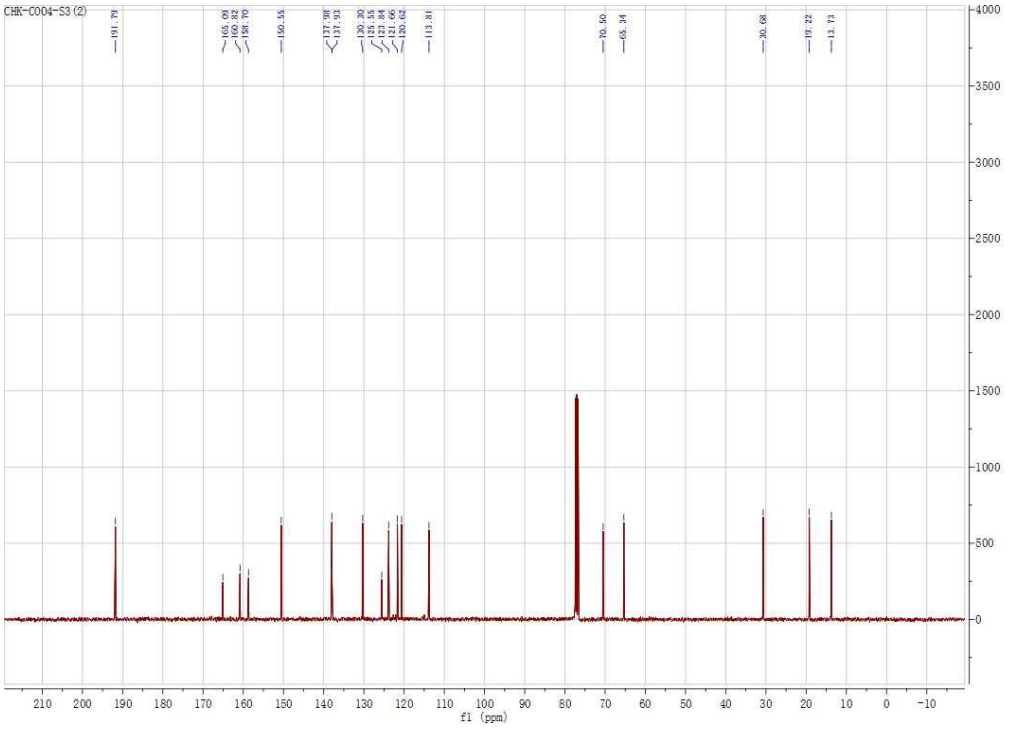




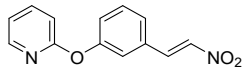
TX-22-S3: butyl 6-((3-formylphenoxy)methyl)nicotinate

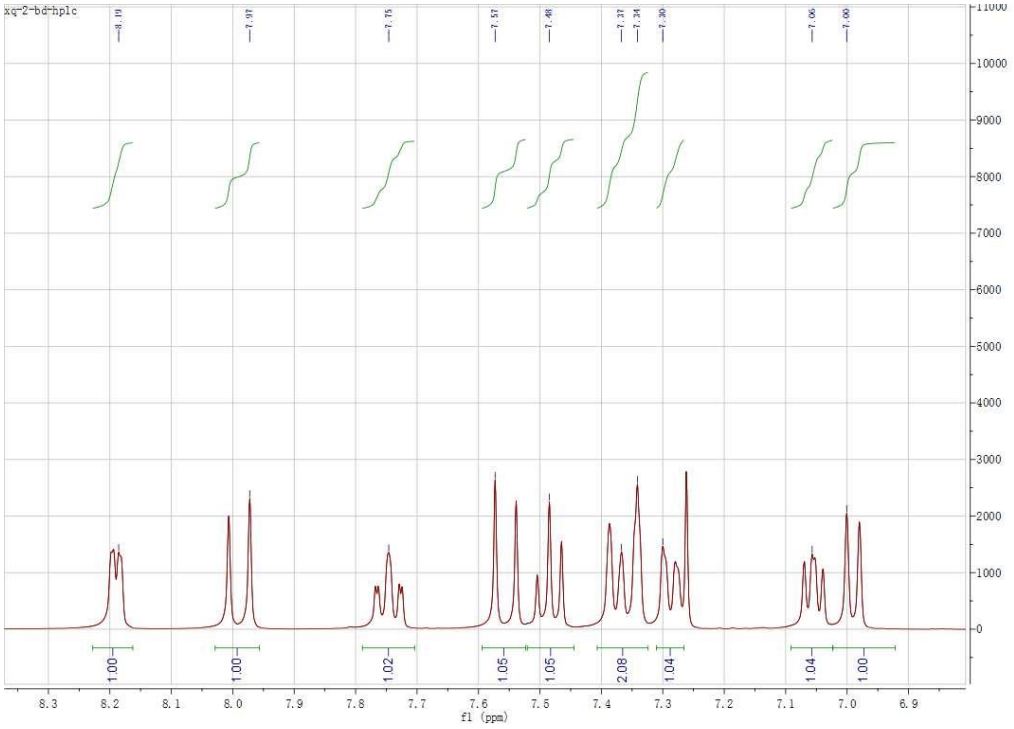


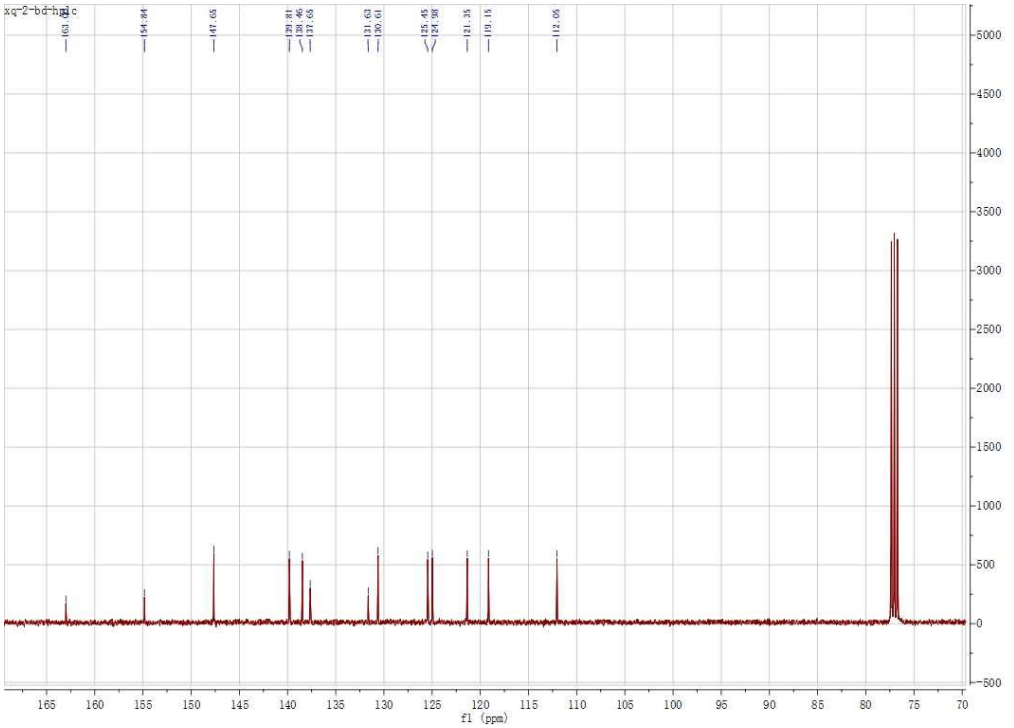




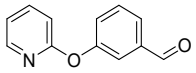
TX-23: (E)-2-(3-(2-nitrovinyl)phenoxy)pyridine

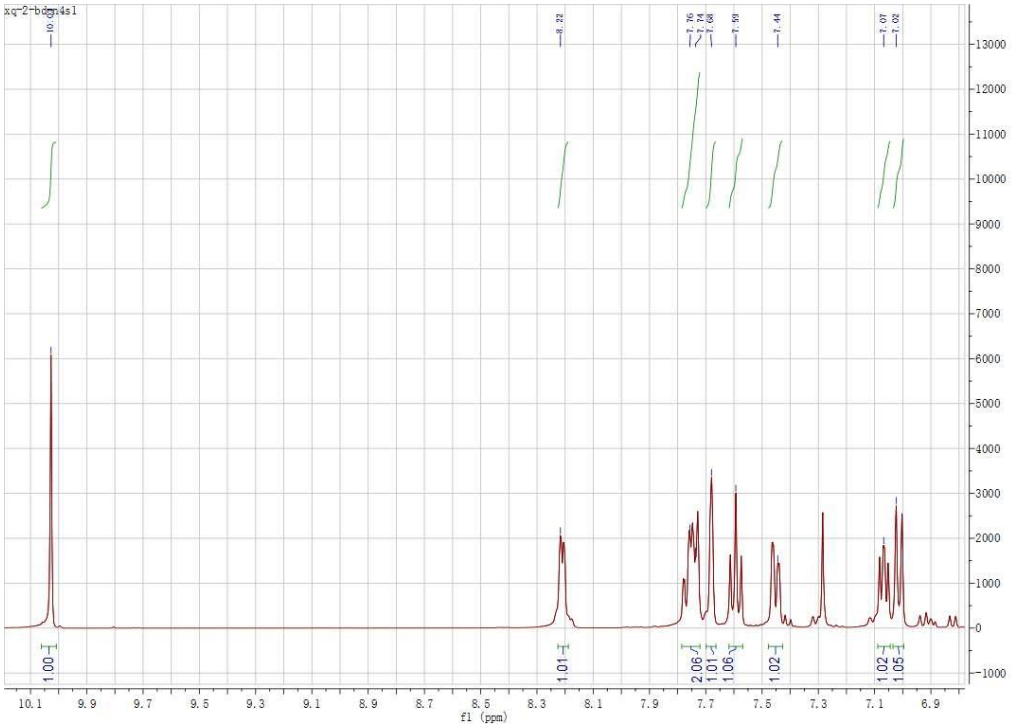


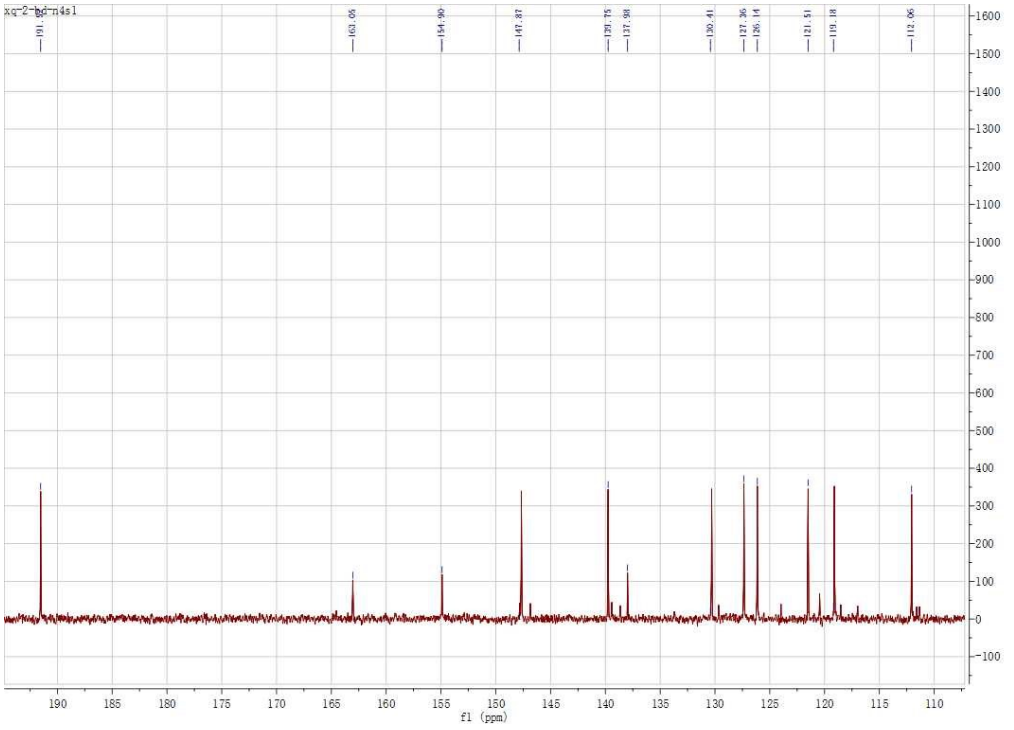




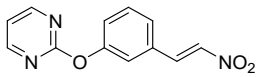
TX-23-S1: 3-(pyridin-2-yloxy)benzaldehyde

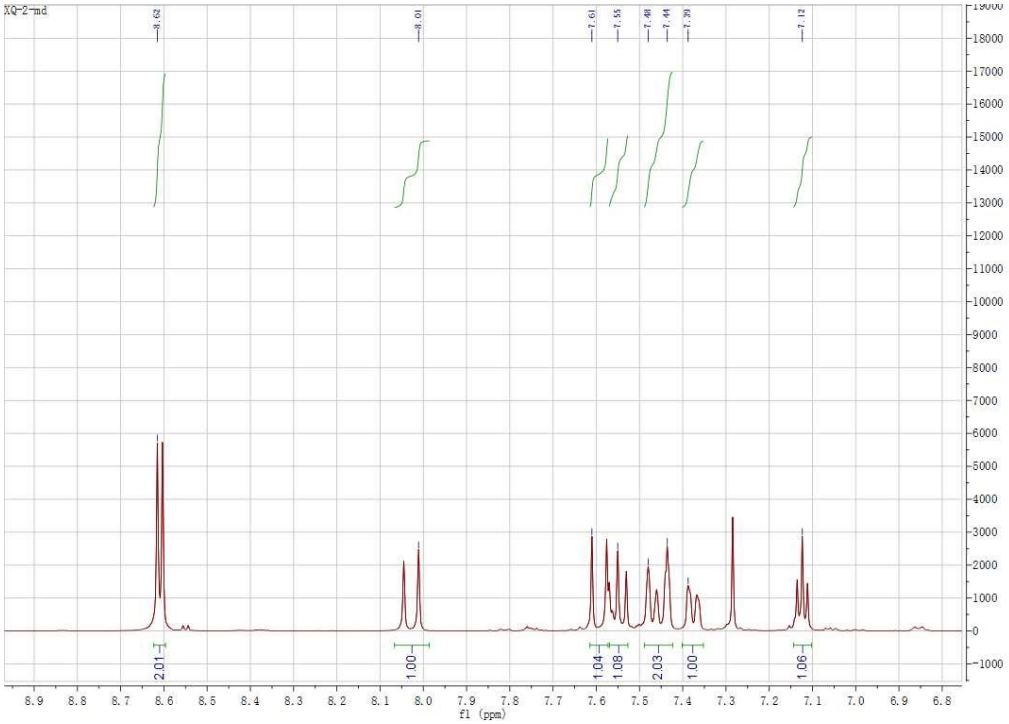


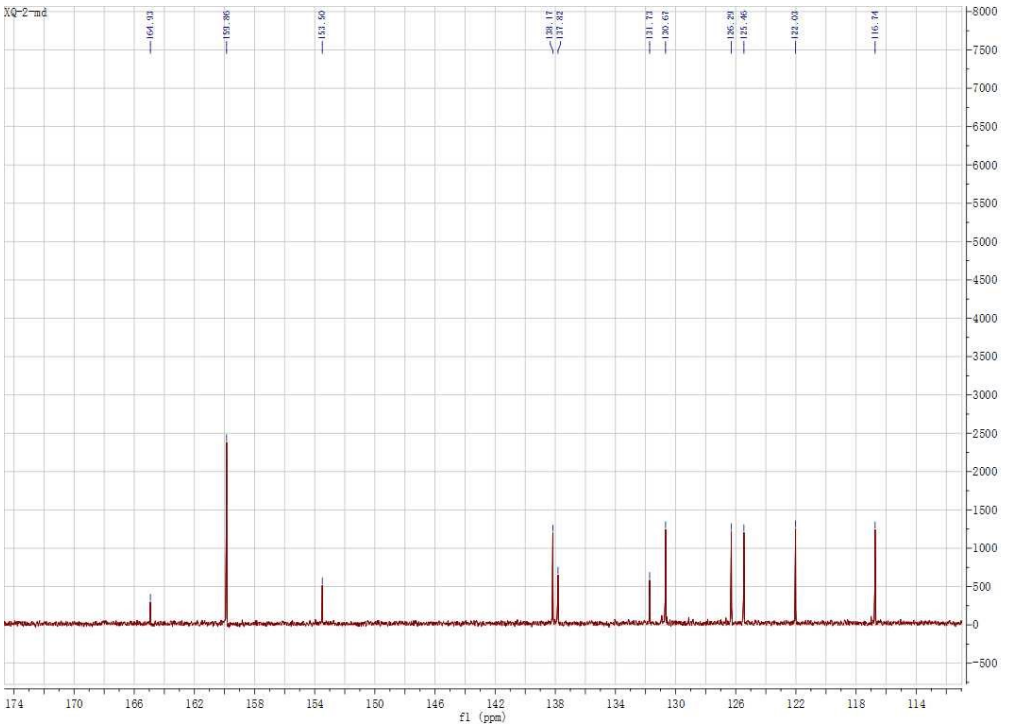




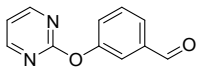
TX-24: (E)-2-(3-(2-nitrovinyl)phenoxy)pyrimidine

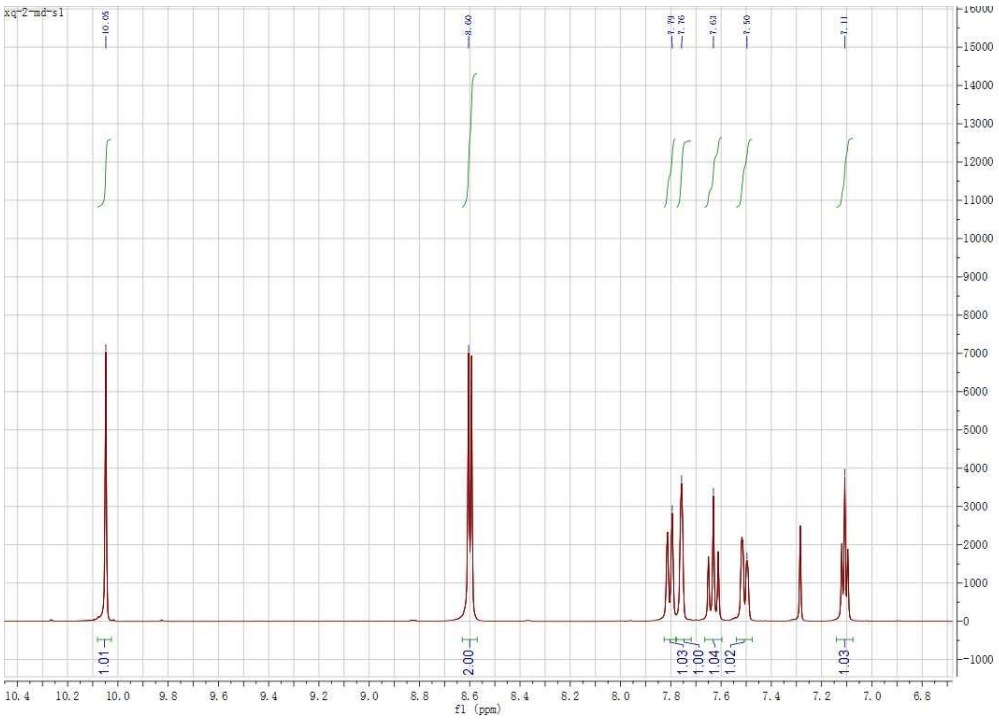


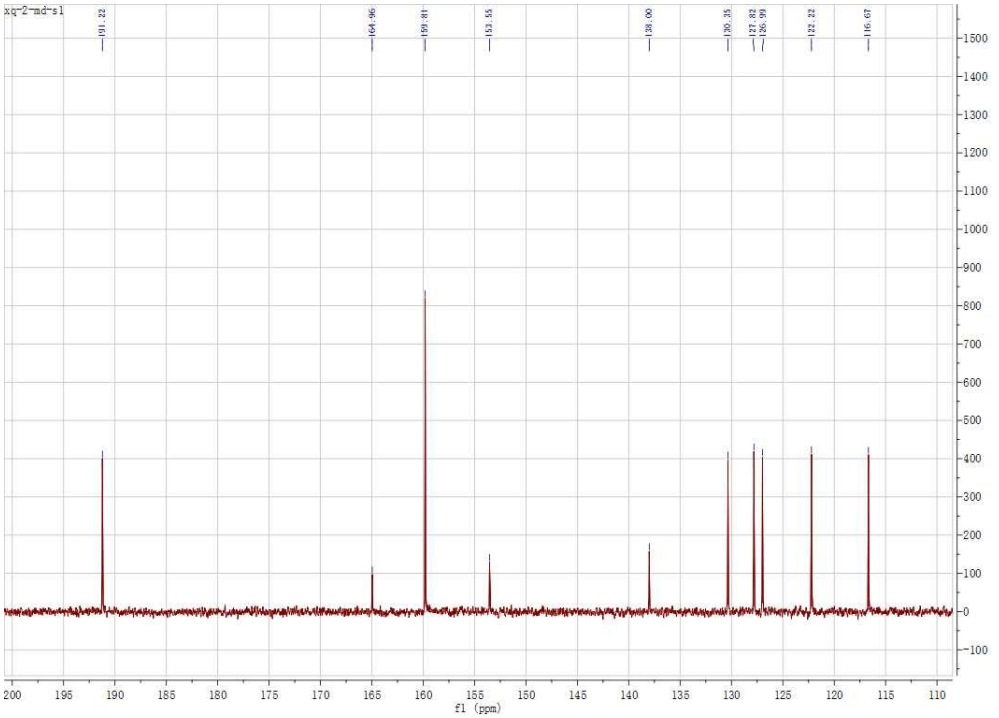




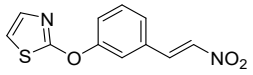
TX-24-S1: 3-(pyrimidin-2-yloxy)benzaldehyde

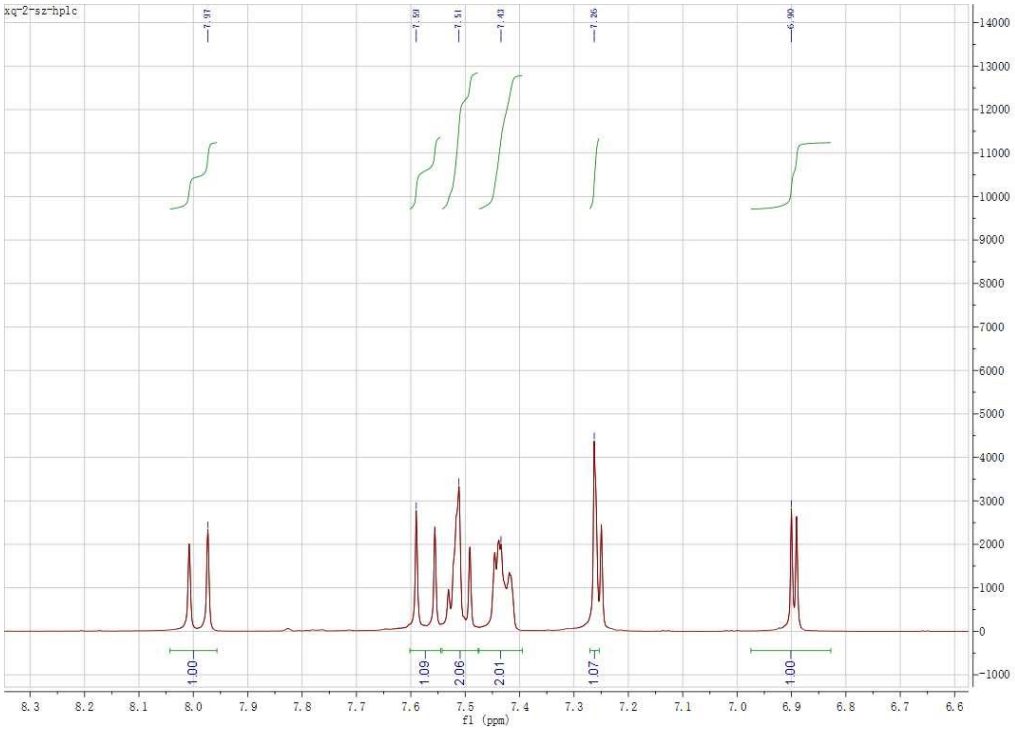


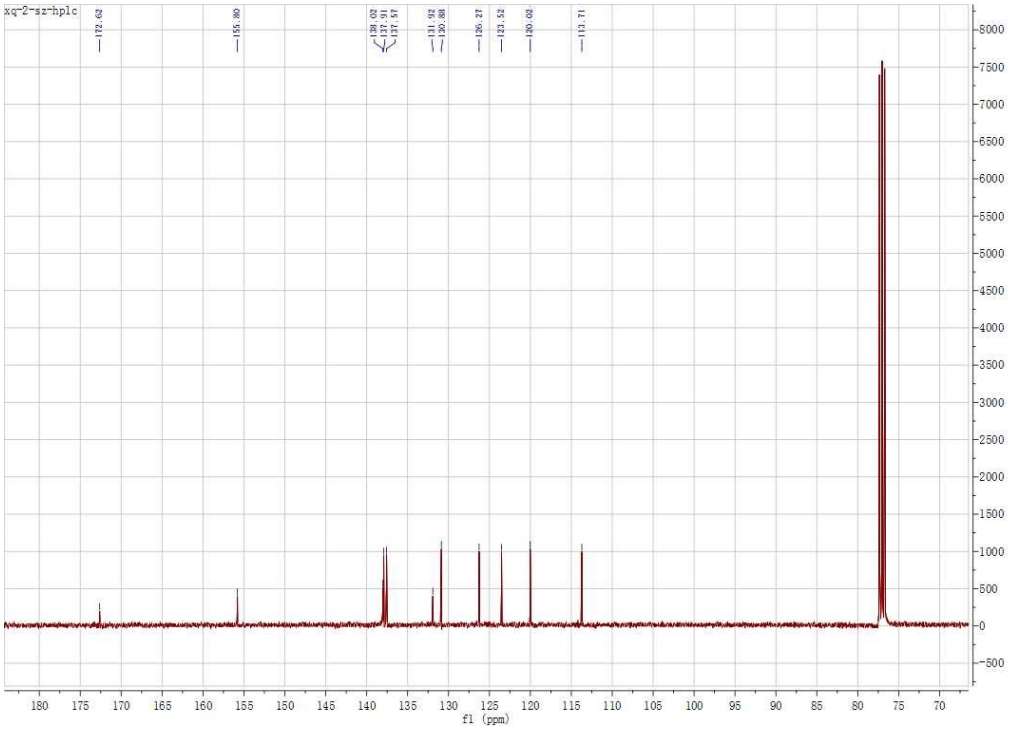




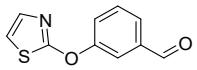
TX-25: (E)-2-(3-(2-nitrovinyl)phenoxy)thiazole

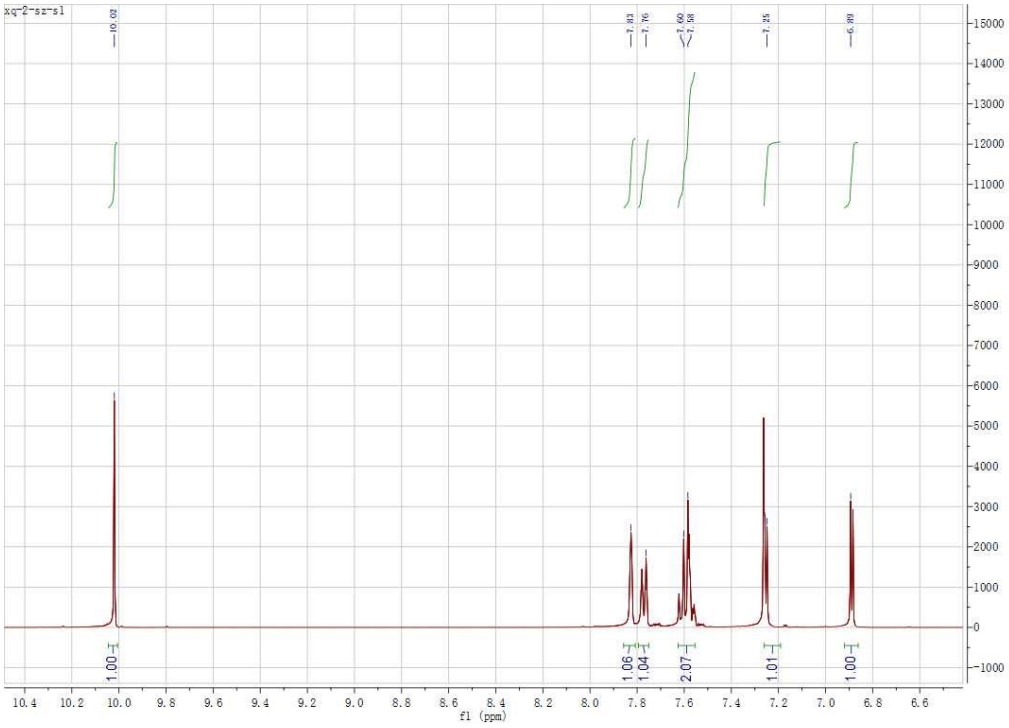


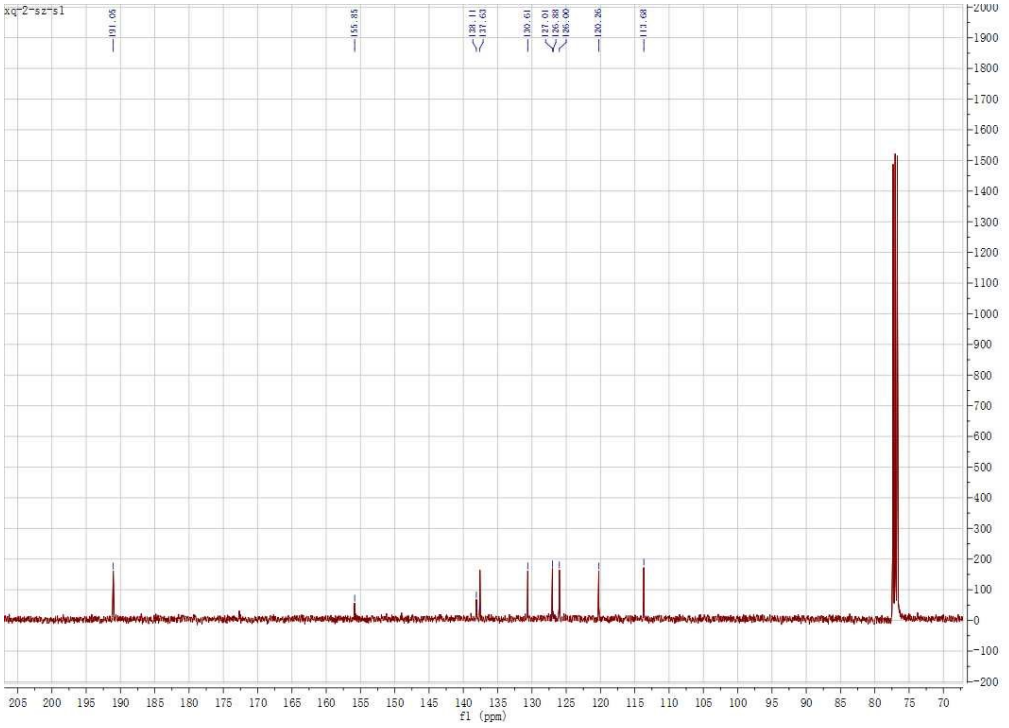




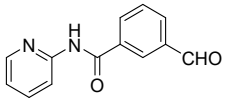
TX-25-S1: 3-(thiazol-2-yloxy)benzaldehyde

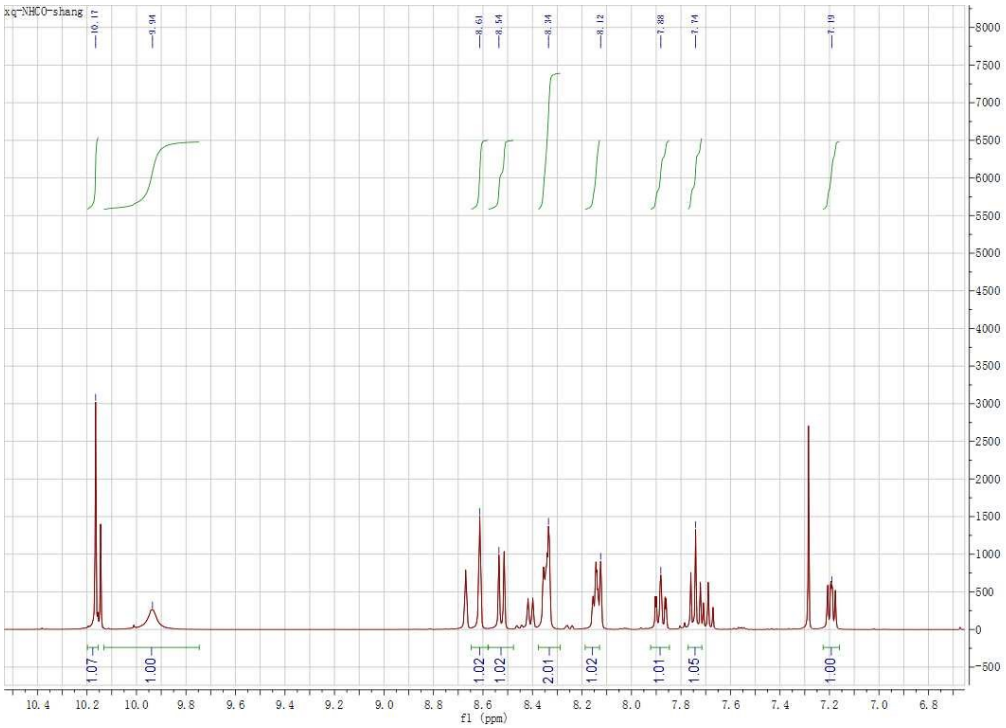


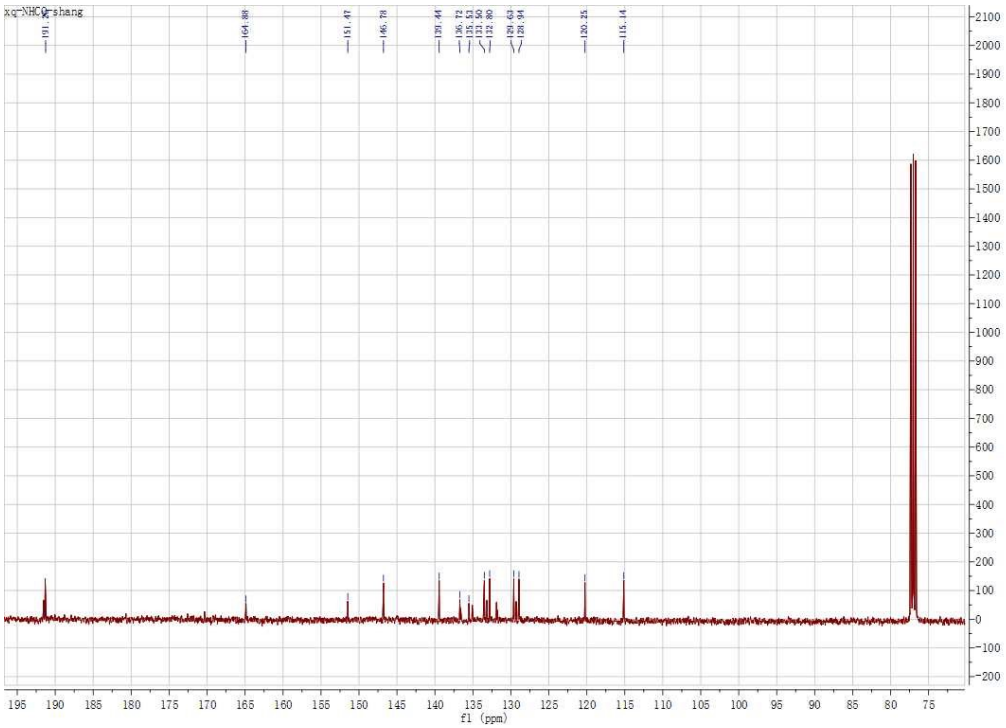




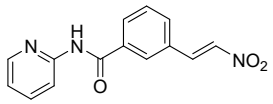
TX-32-S1: 3-formyl-N-(pyridin-2-yl)benzamide

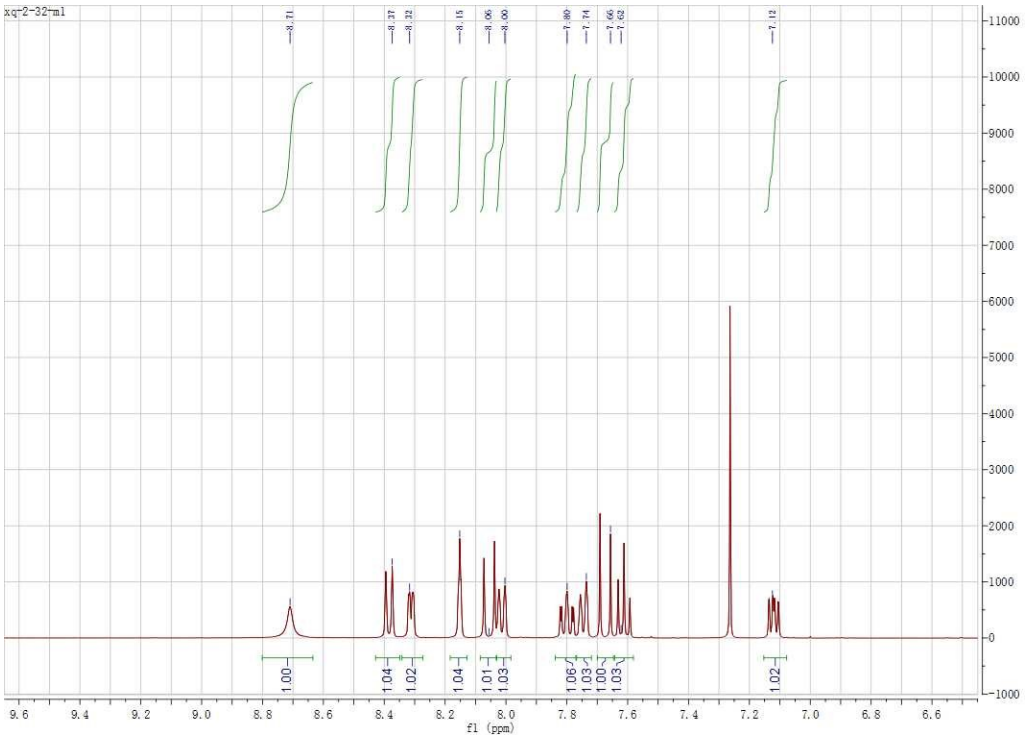


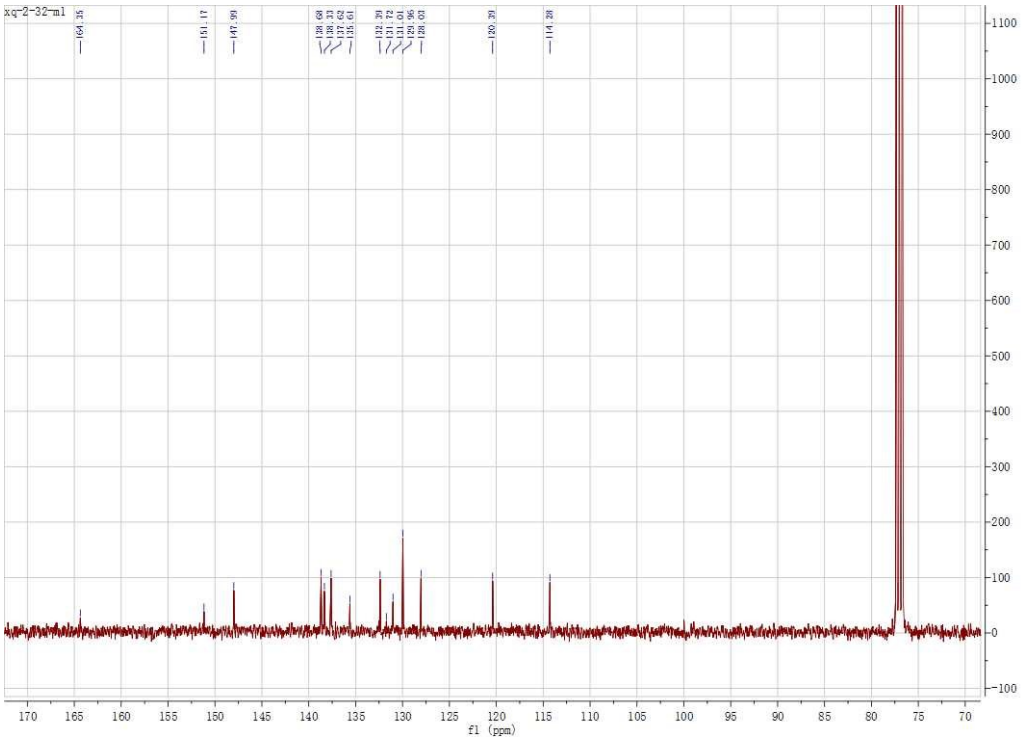




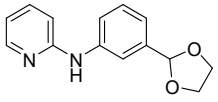
TX-32: (E)-3-(2-nitrovinyl)-N-(pyridin-2-yl)benzamide

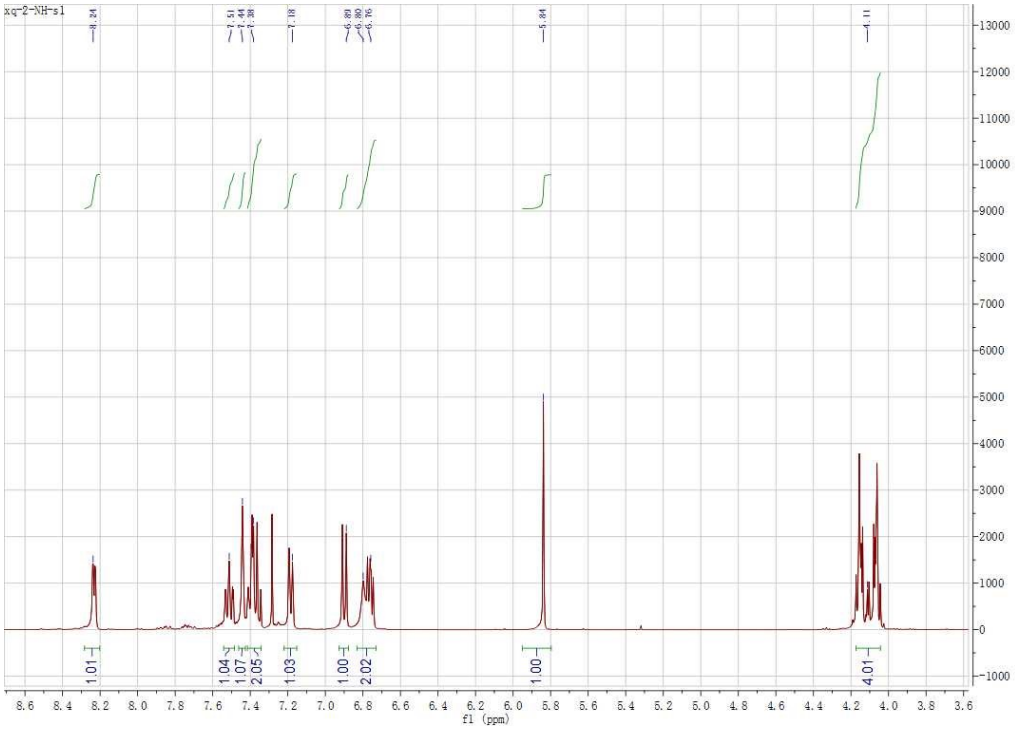


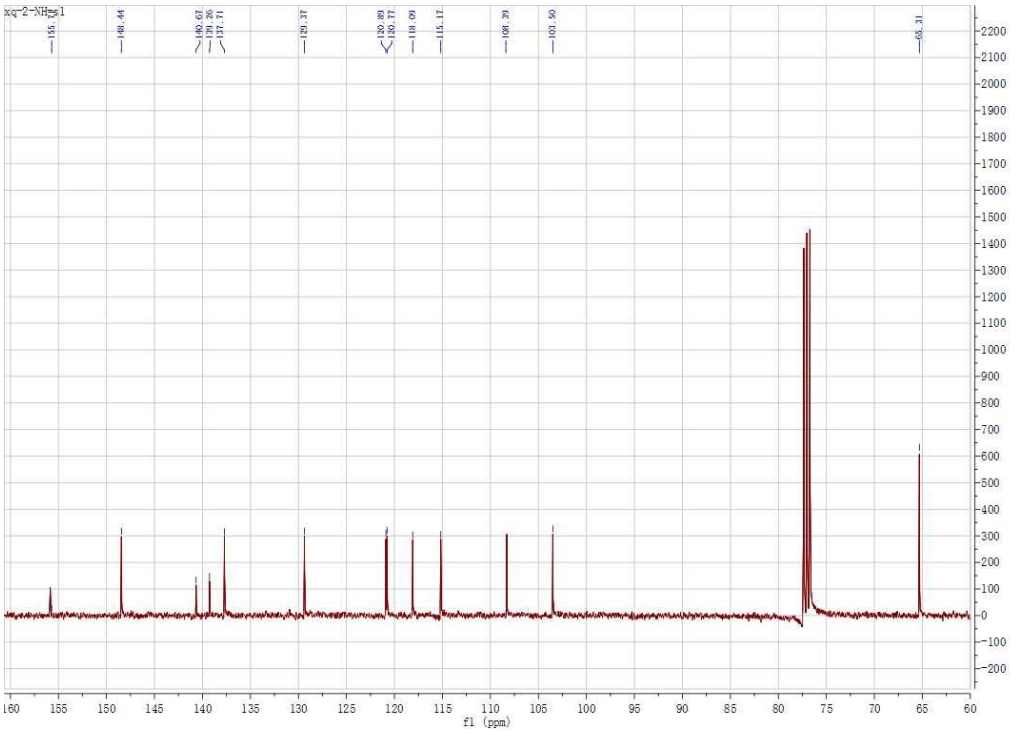




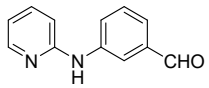
TX-33-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-2-amine

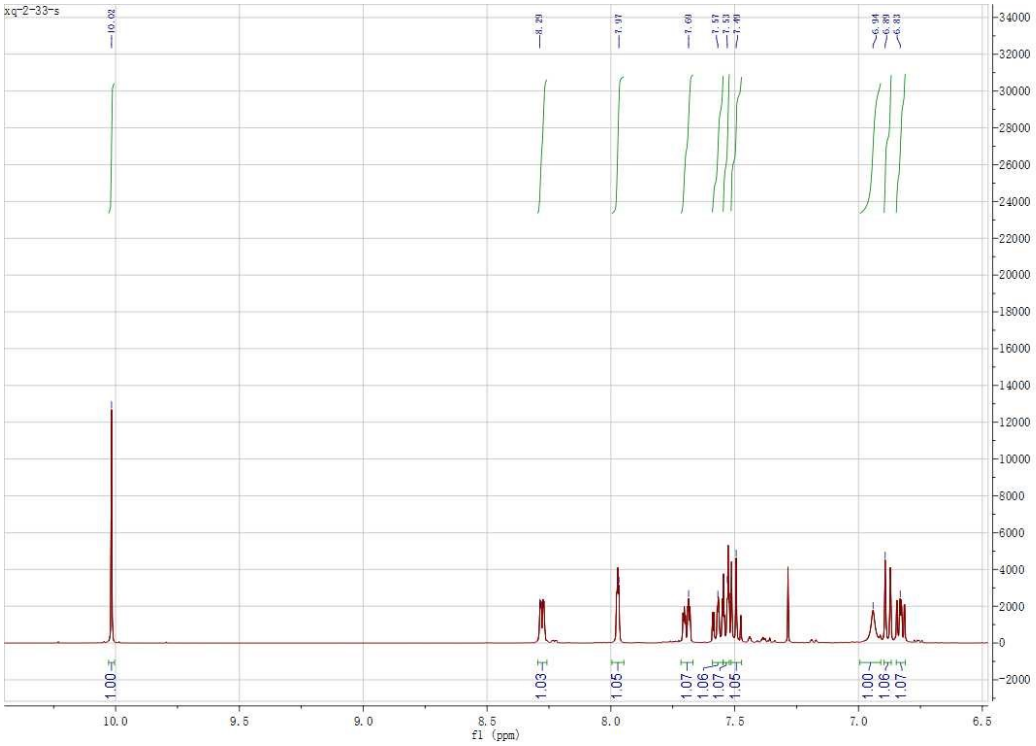


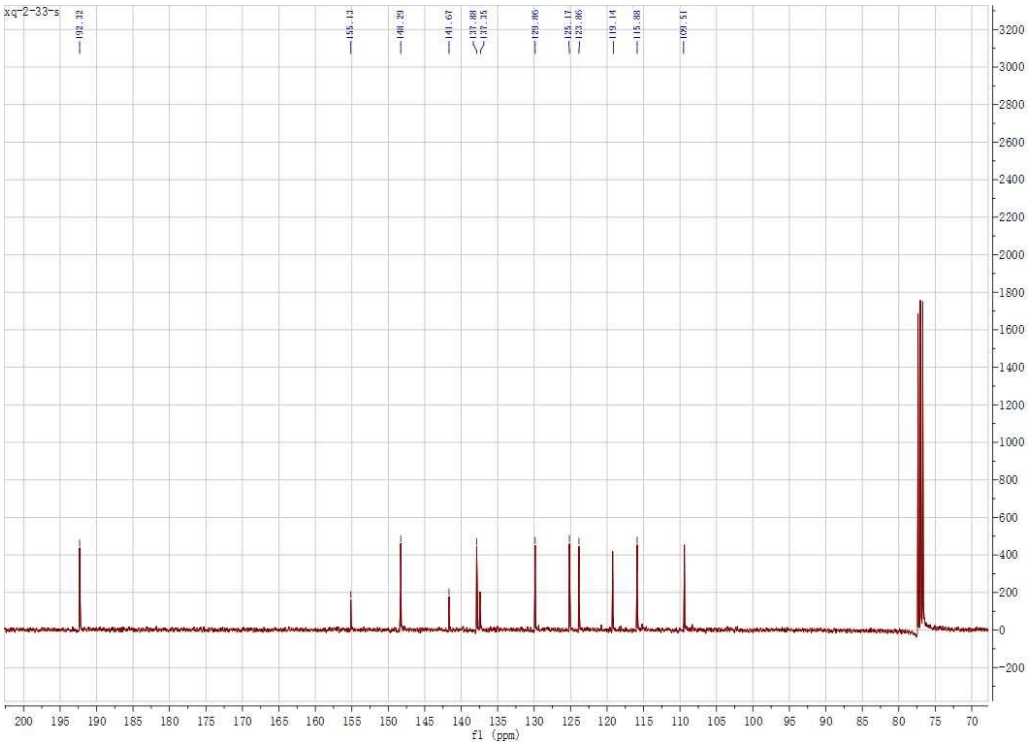




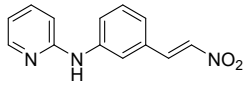
TX-33-S2: 3-(pyridin-2-ylamino)benzaldehyde

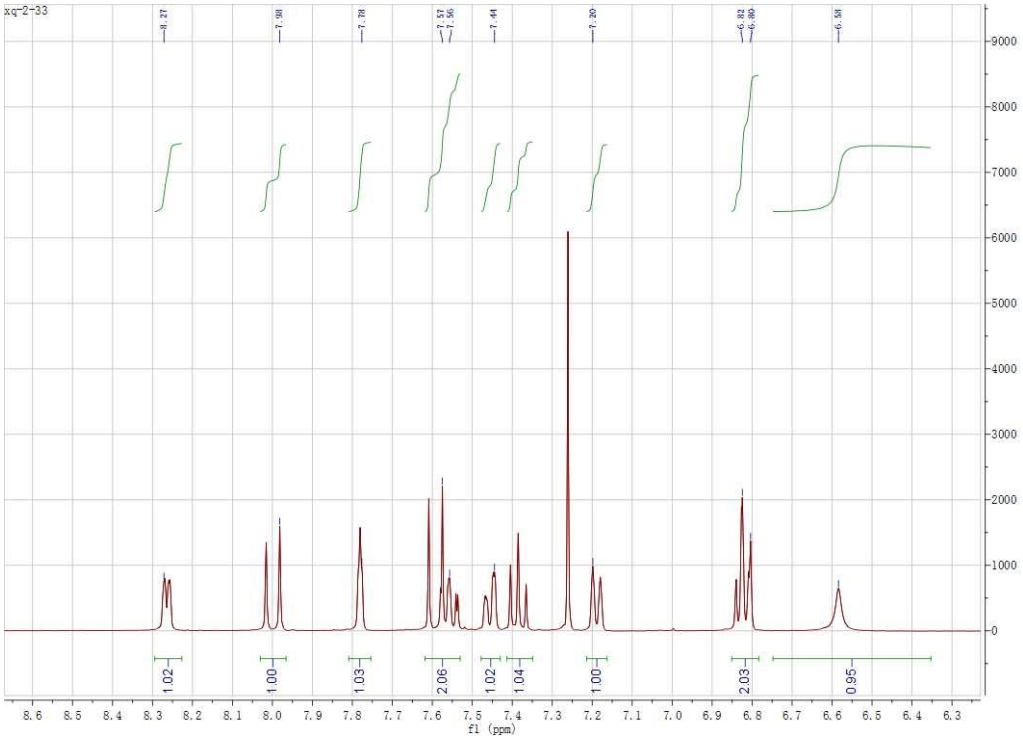


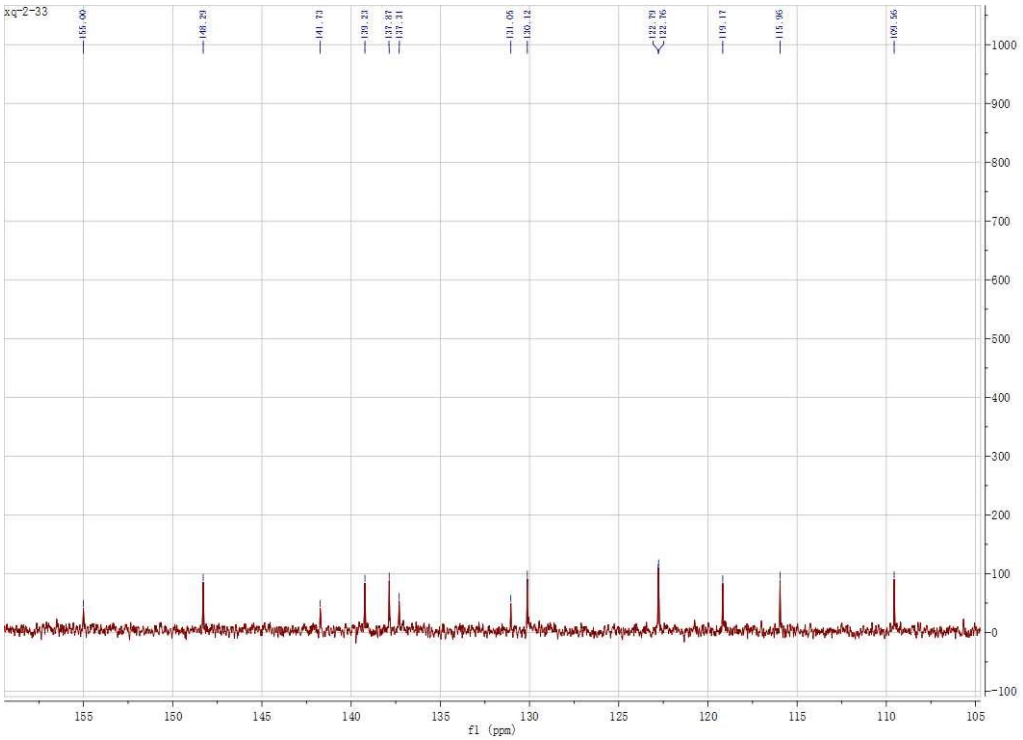




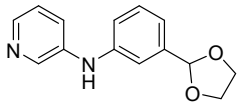
TX-33: (E)-N-(3-(2-nitrovinyl)phenyl)pyridin-2-amine

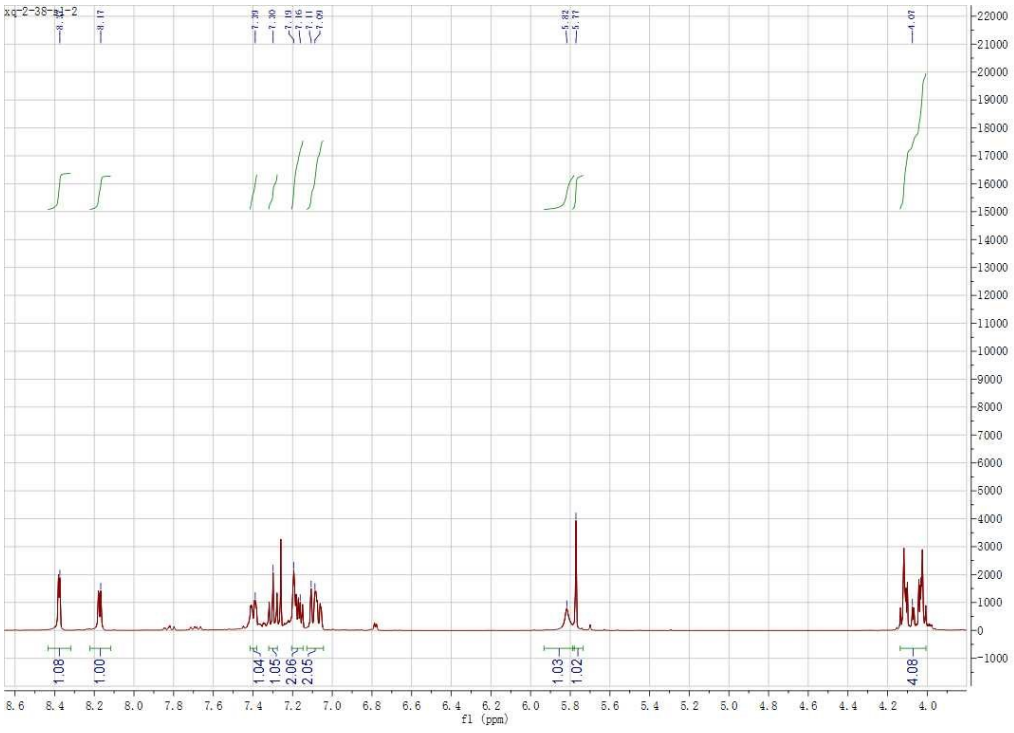


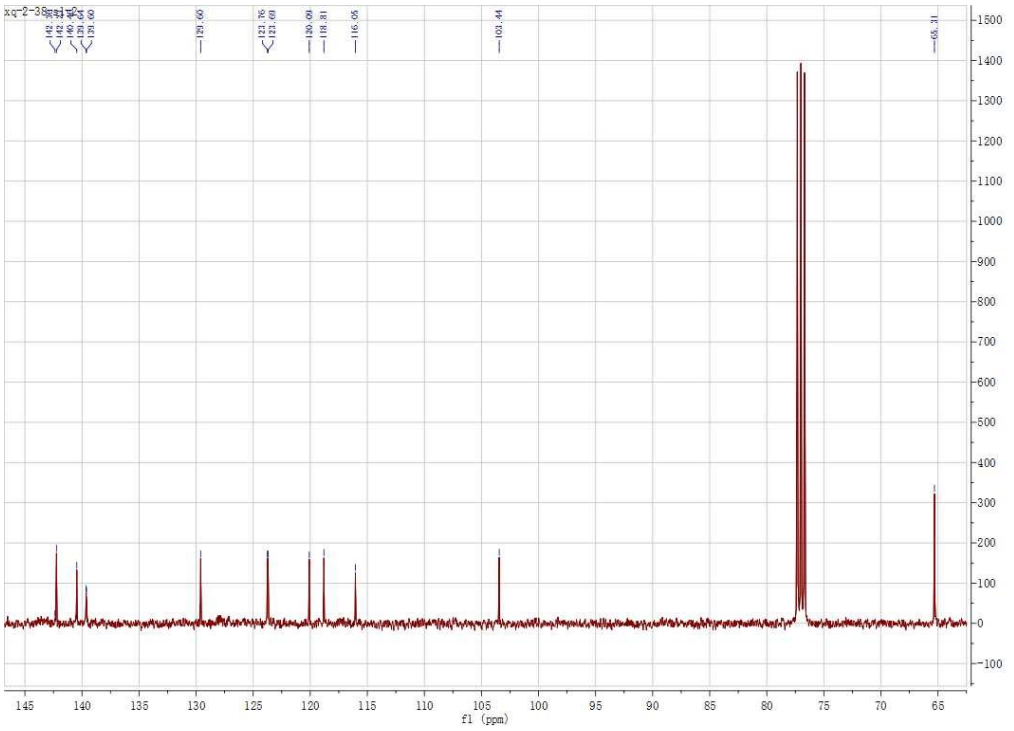




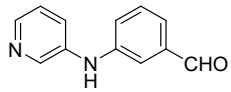
TX-34-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyridin-3-amine

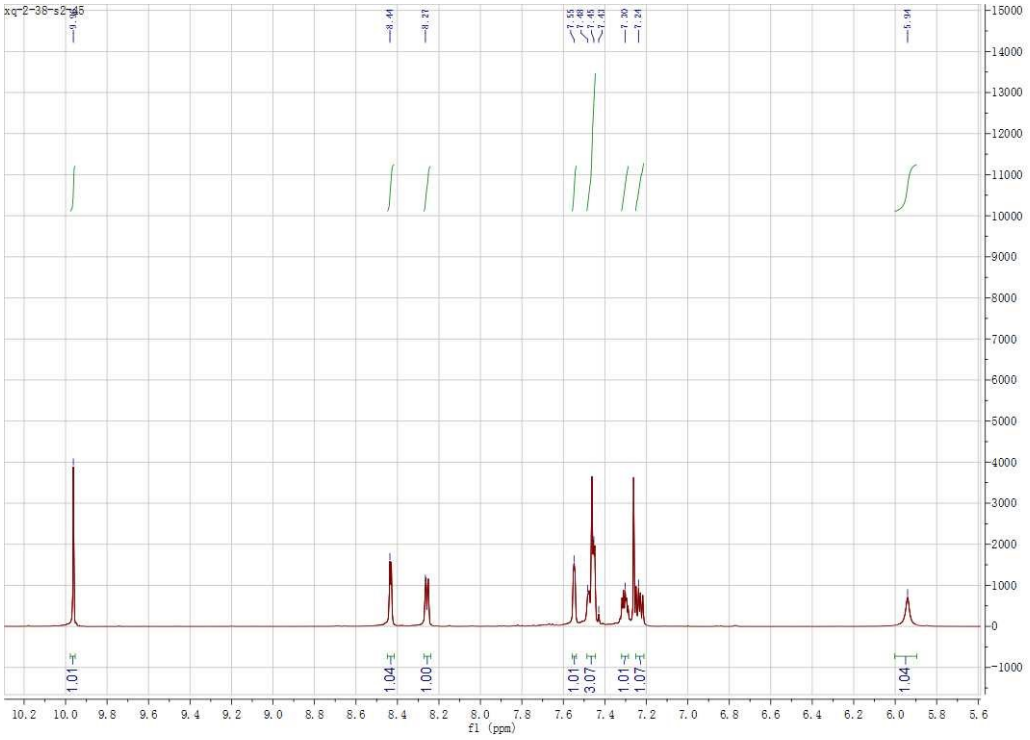


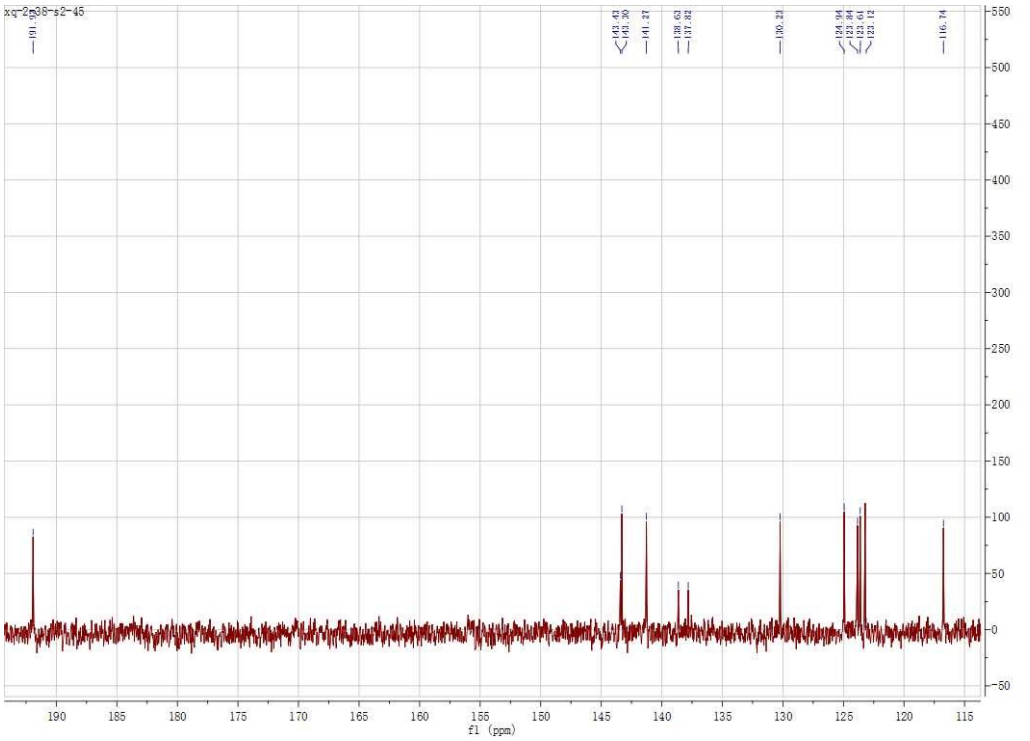




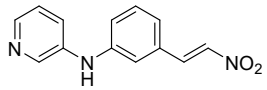
TX-34-S2: 3-(pyridin-3-ylamino)benzaldehyde

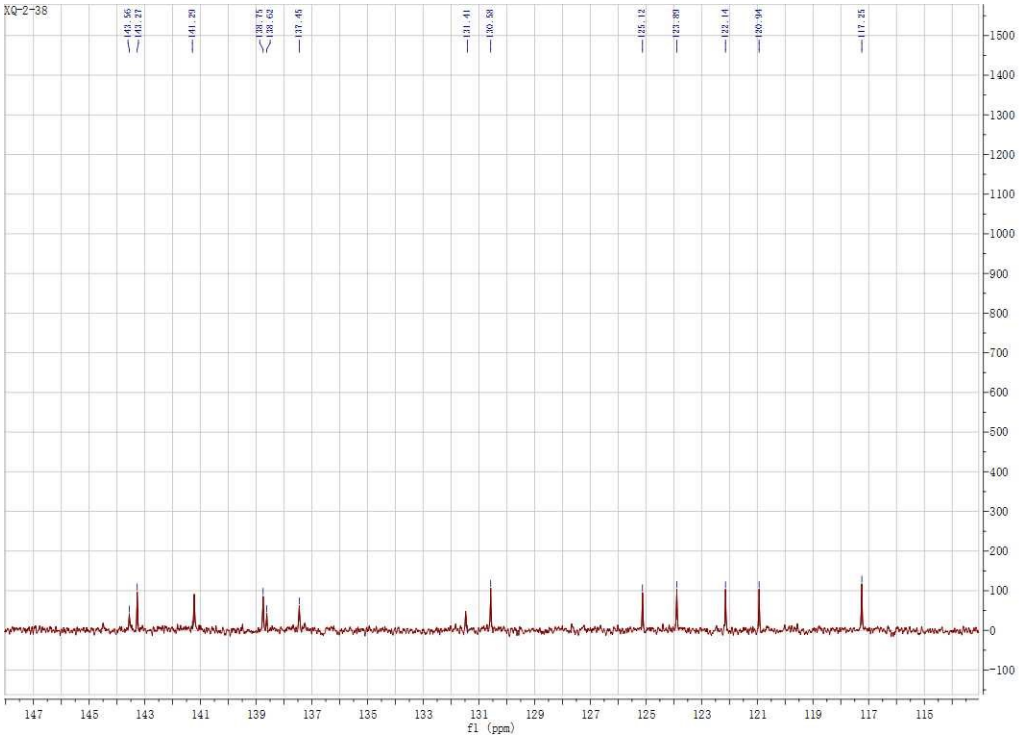


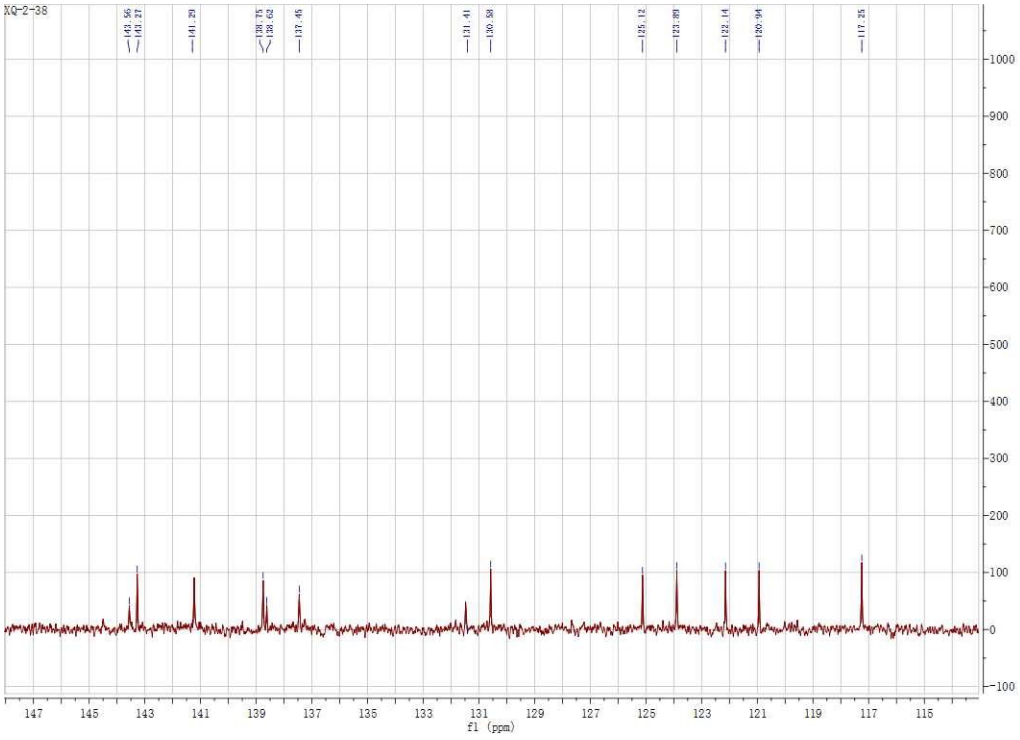




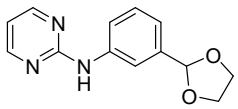
TX-34: (E)-N-(3-(2-nitrovinyl)phenyl)pyridin-3-amine

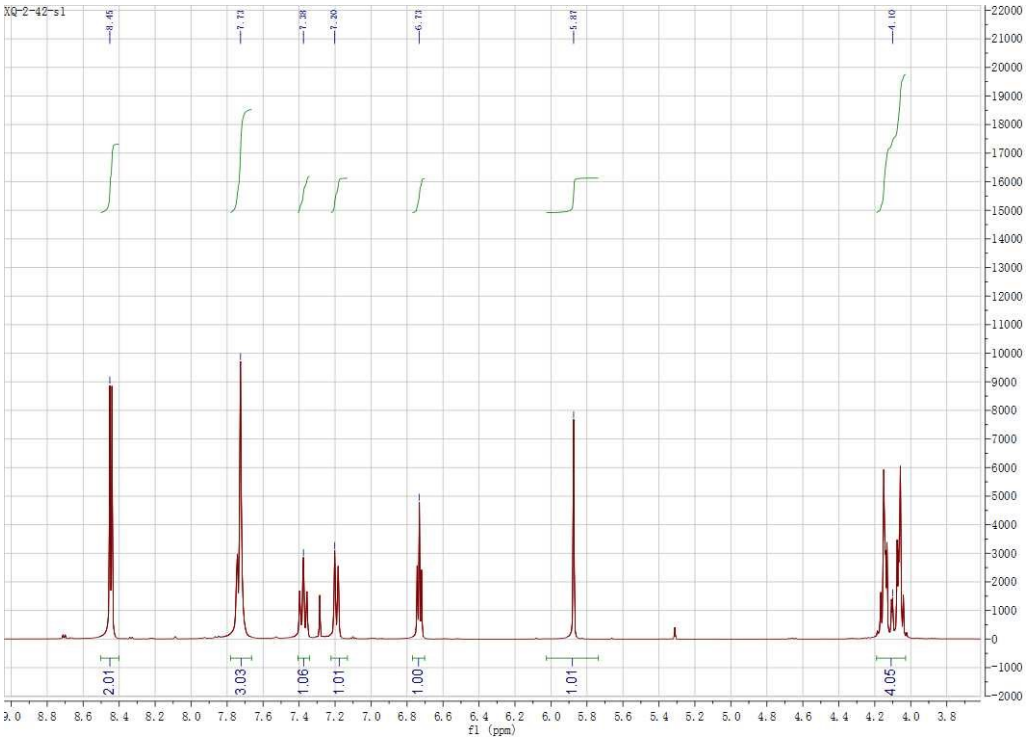


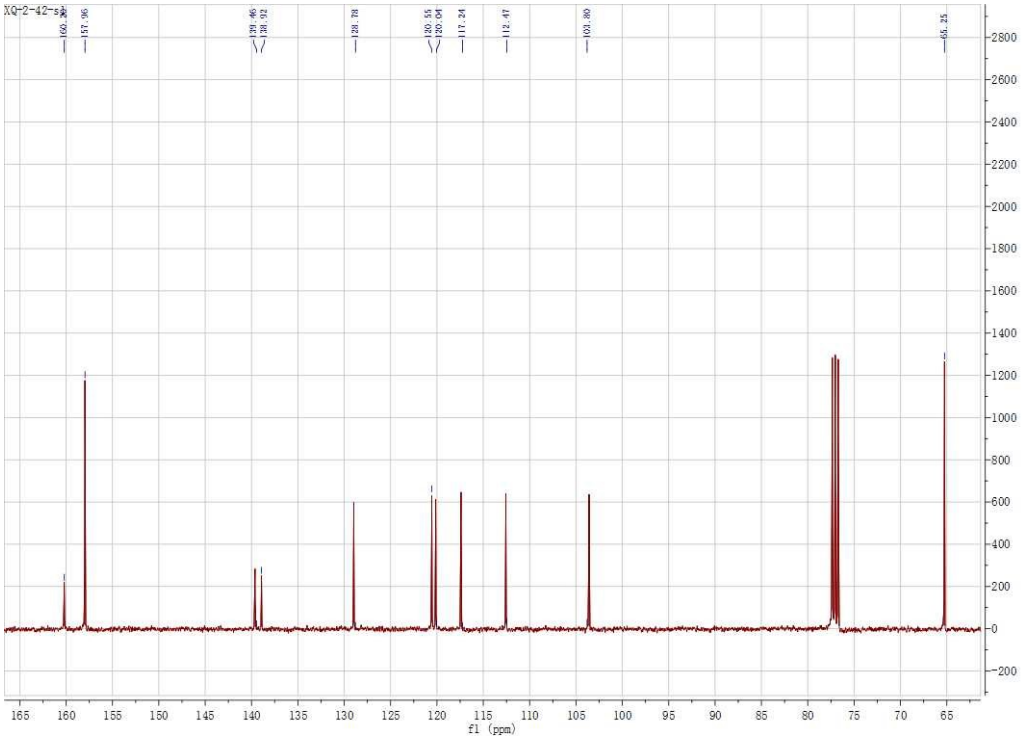




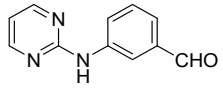
TX-35-S1: N-(3-(1,3-dioxolan-2-yl)phenyl)pyrimidin-2-amine

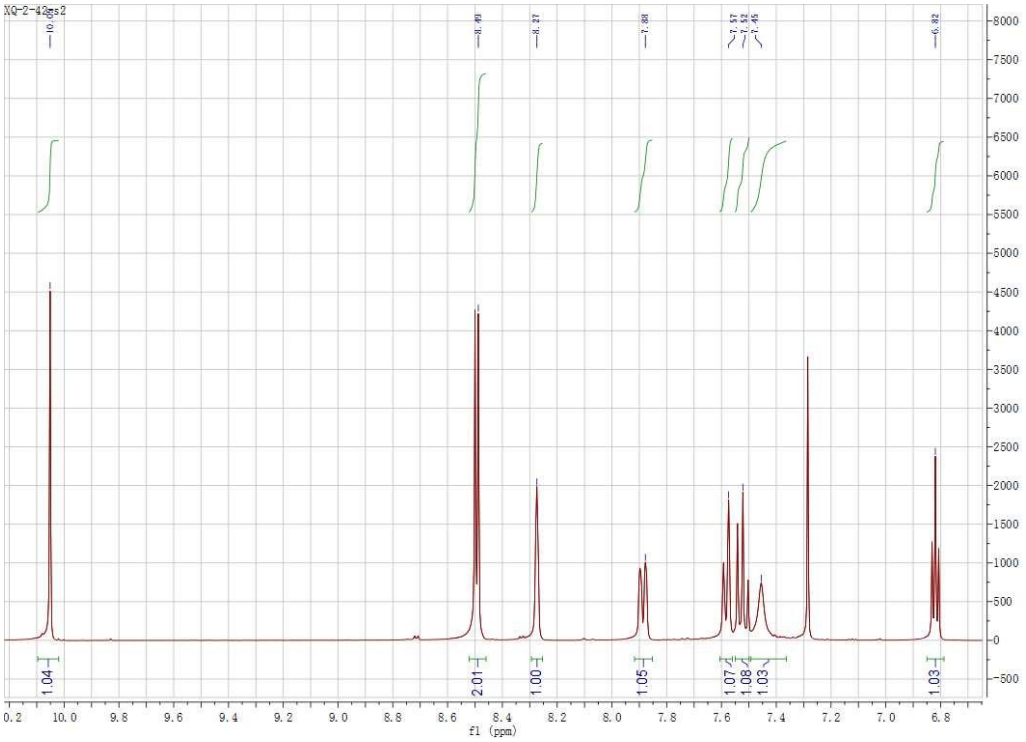


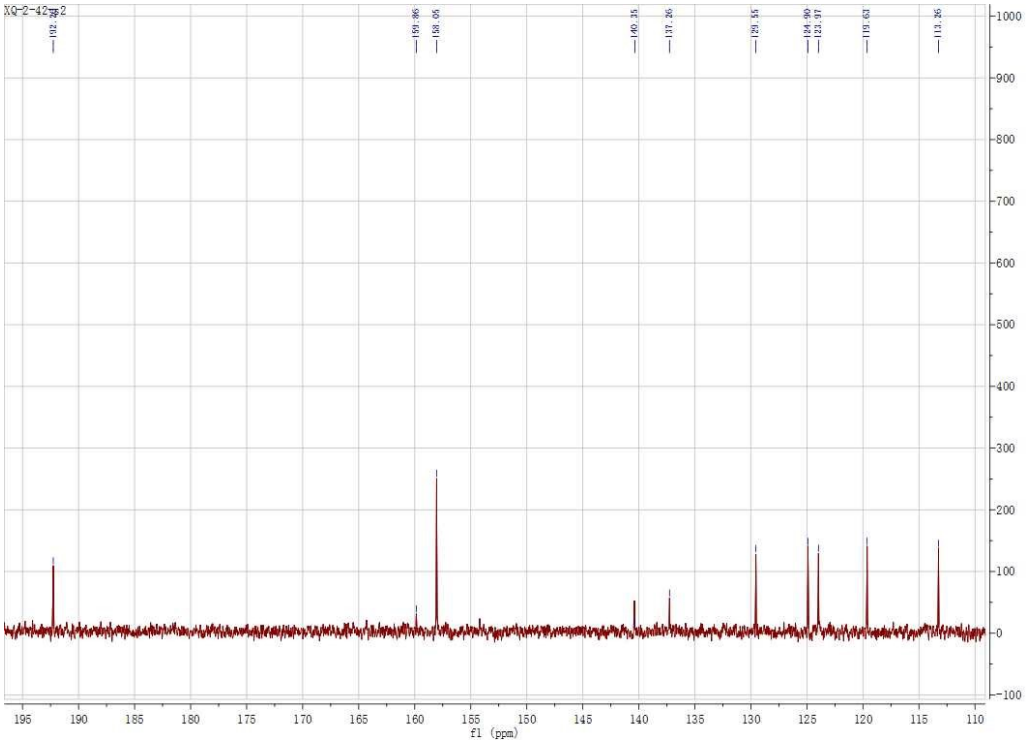




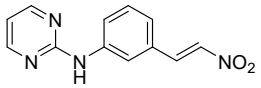
TX-35-S2: 3-(pyrimidin-2-ylamino)benzaldehyde

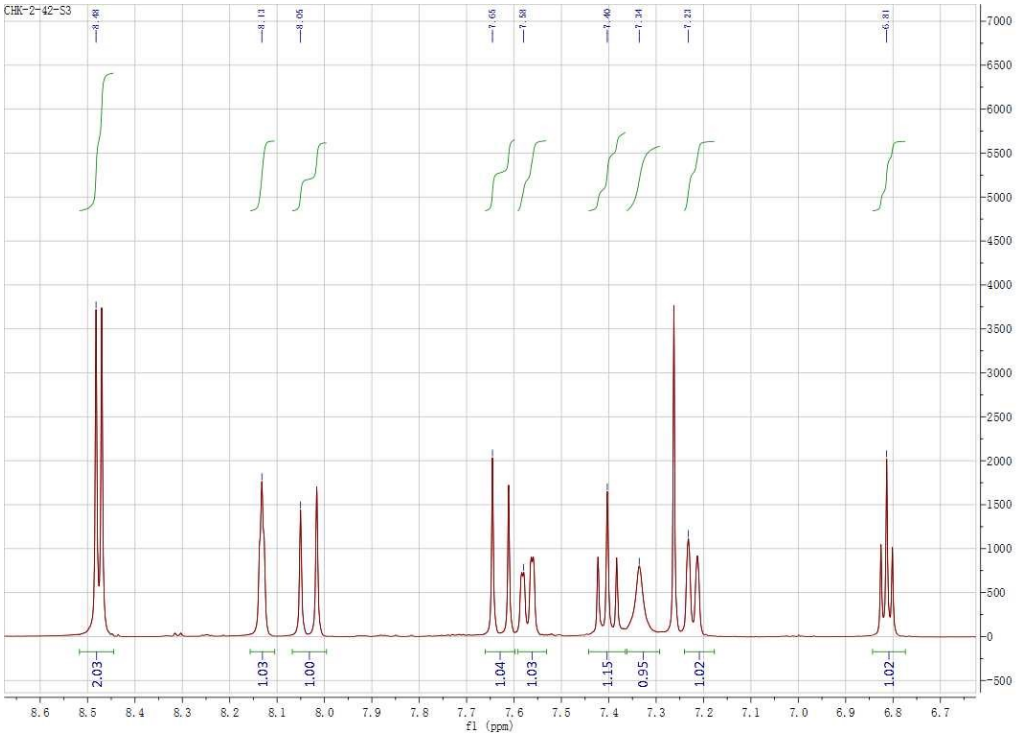


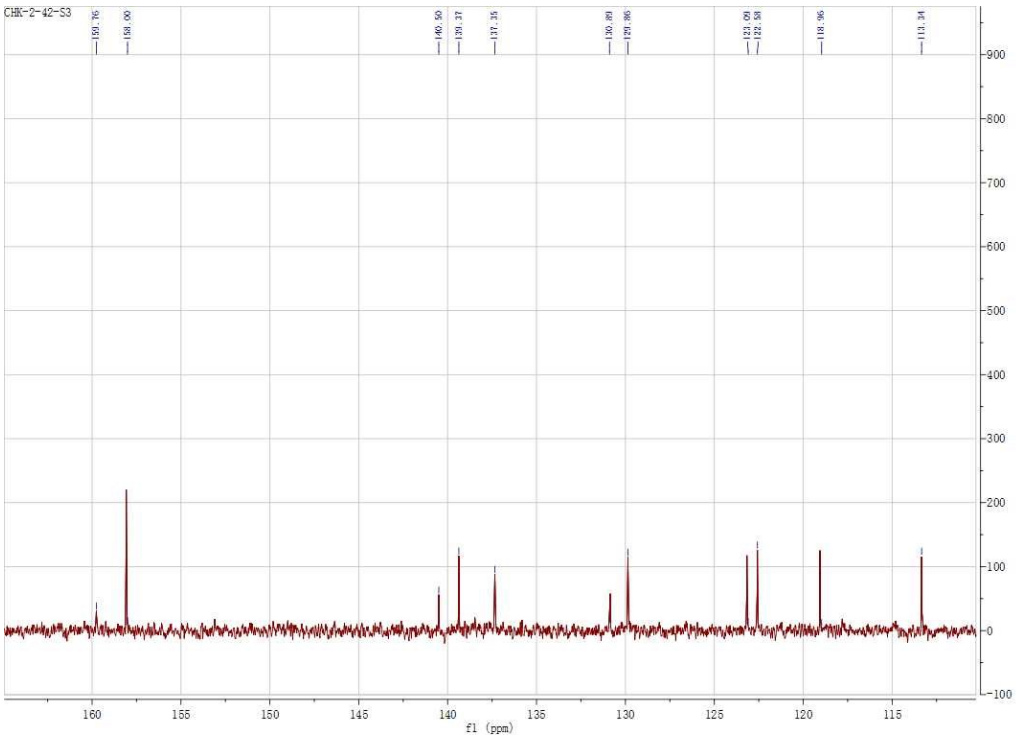




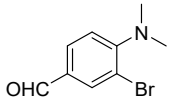
TX-35: (E)-N-(3-(2-nitrovinyl)phenyl)pyrimidin-2-amine

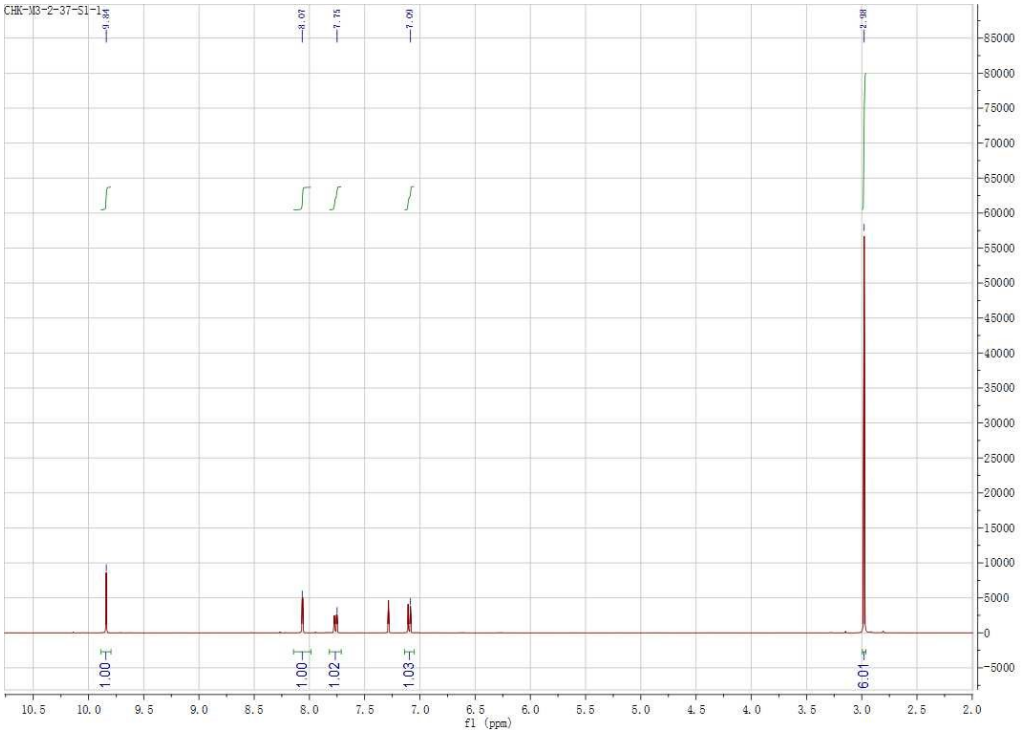


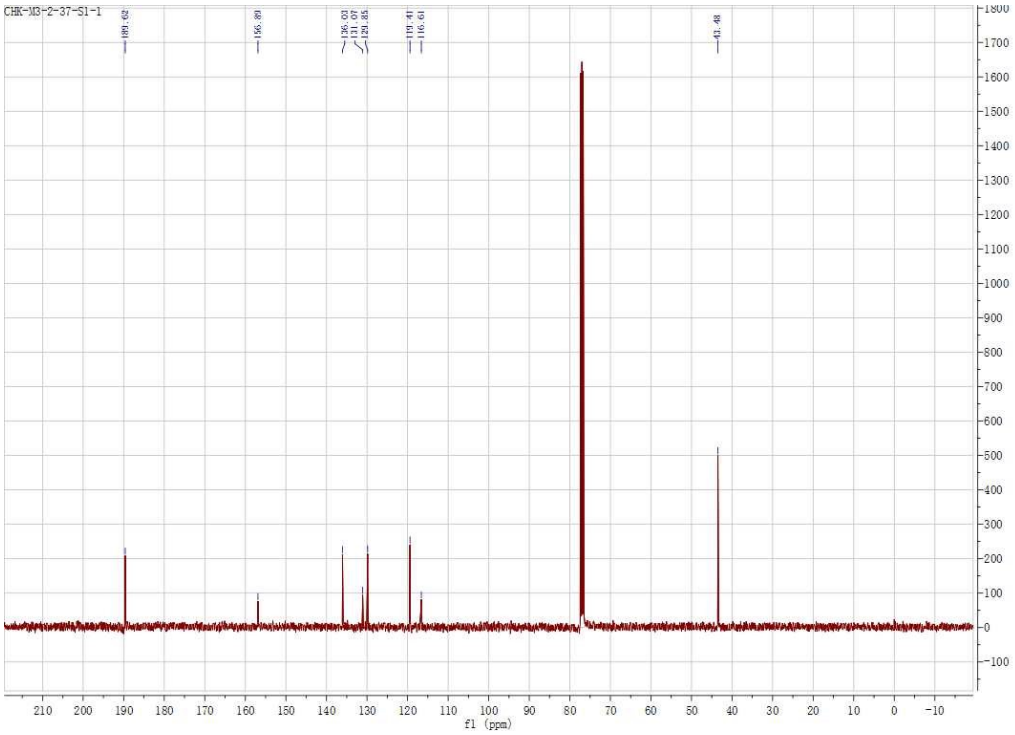




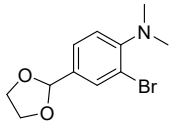
TX-36-S1: 3-bromo-4-(dimethylamino)benzaldehyde

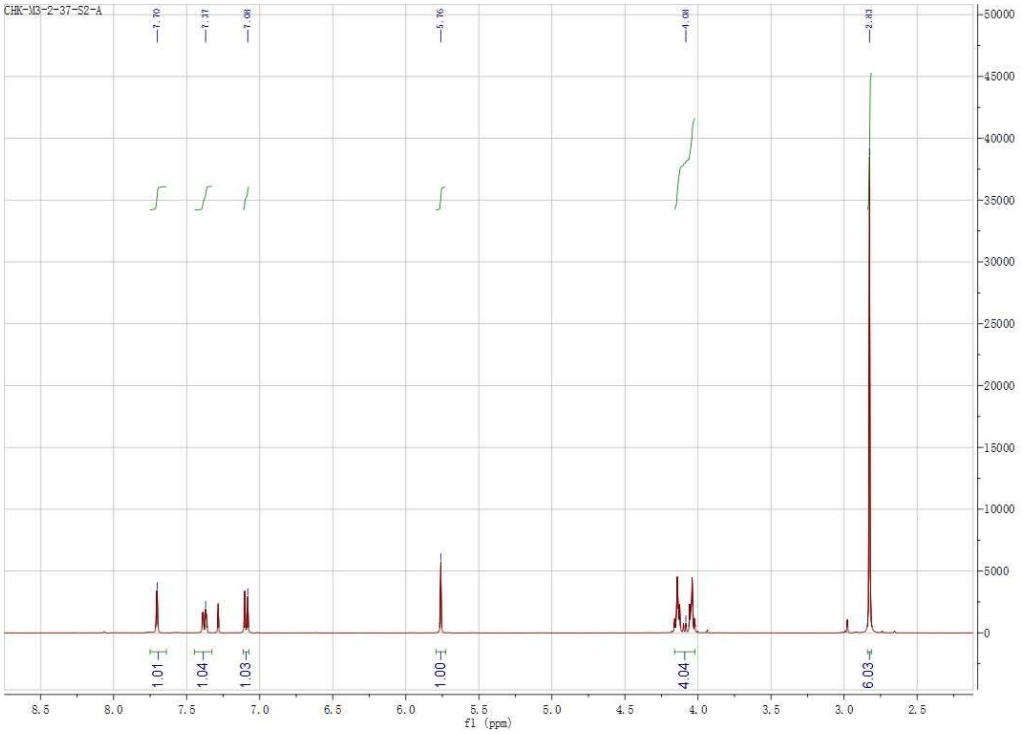


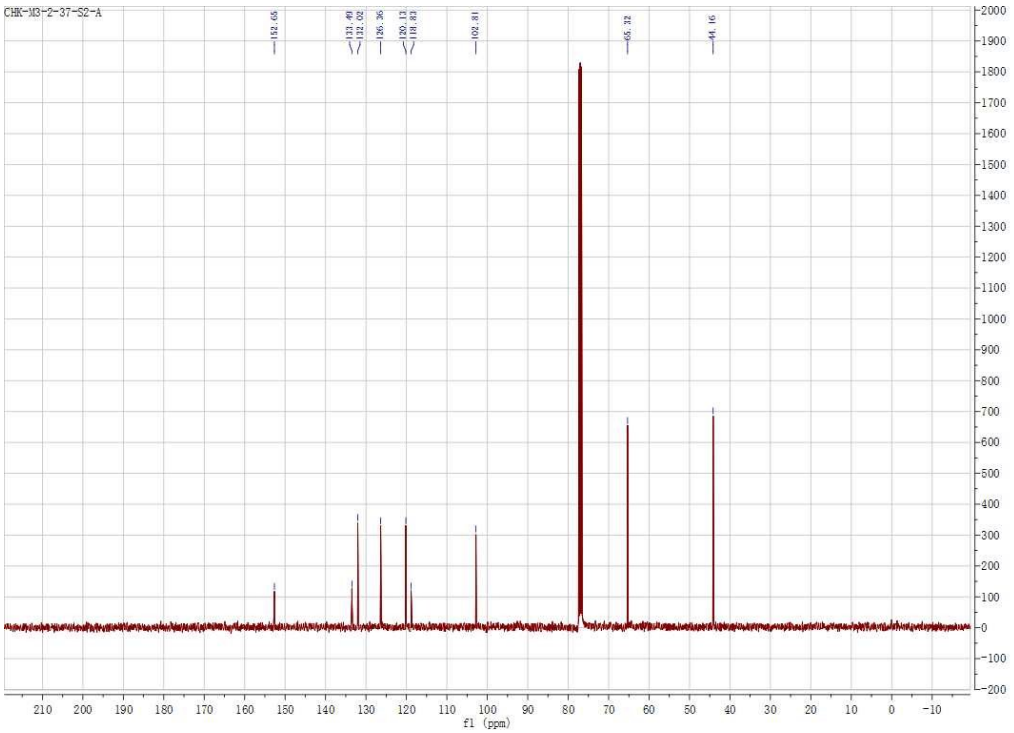




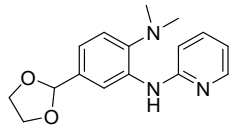
TX-36-S2: 2-bromo-4-(1,3-dioxolan-2-yl)-N,N-dimethylaniline

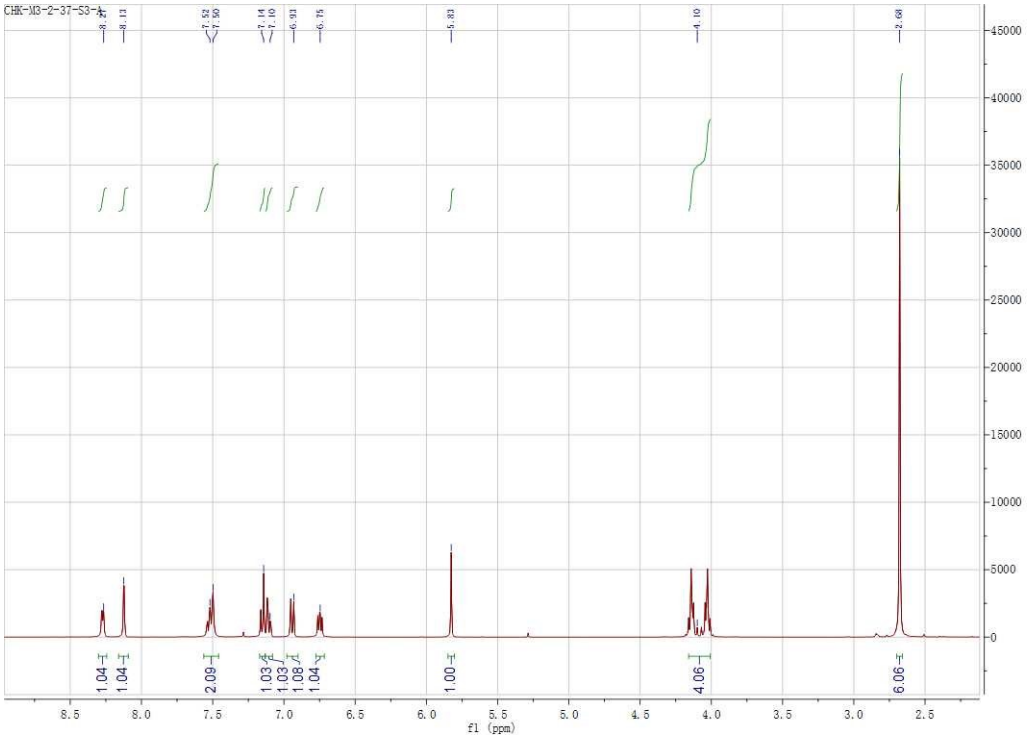


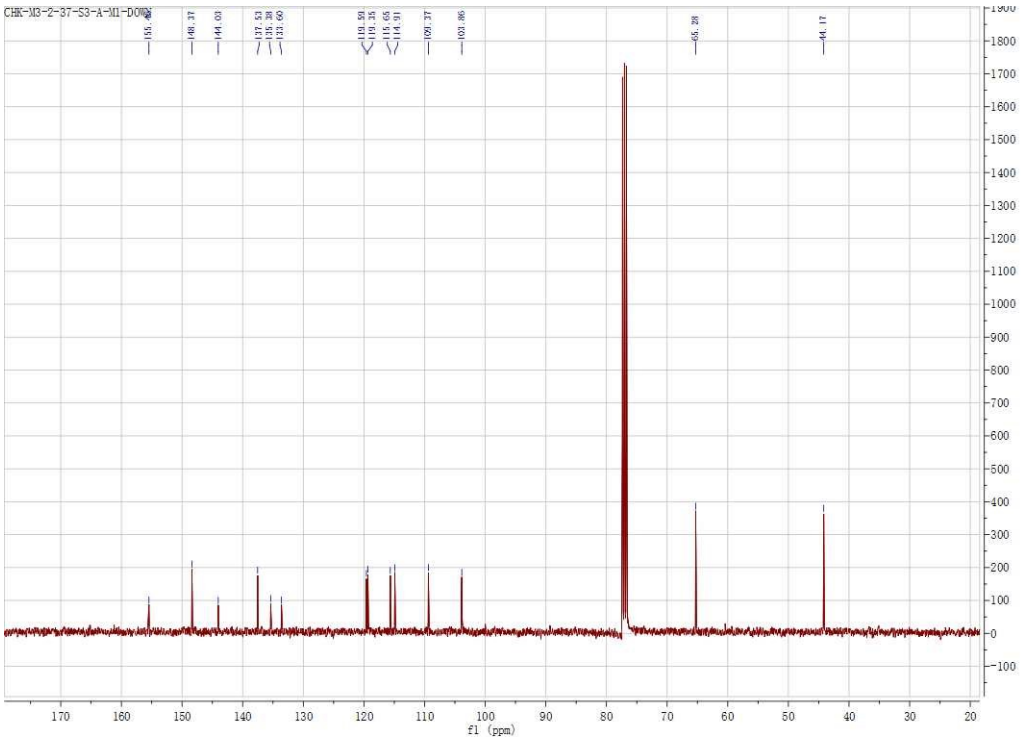




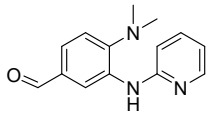
TX-36-S4: 4-(dimethylamino)-3-(pyridin-2-ylamino)benzaldehyde

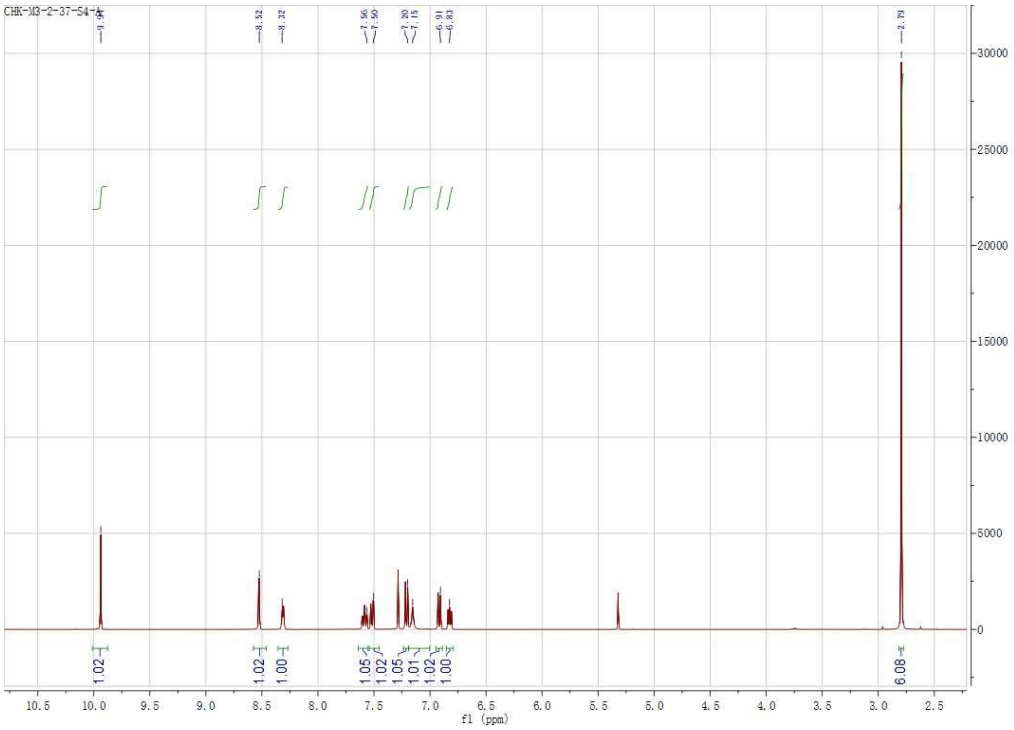


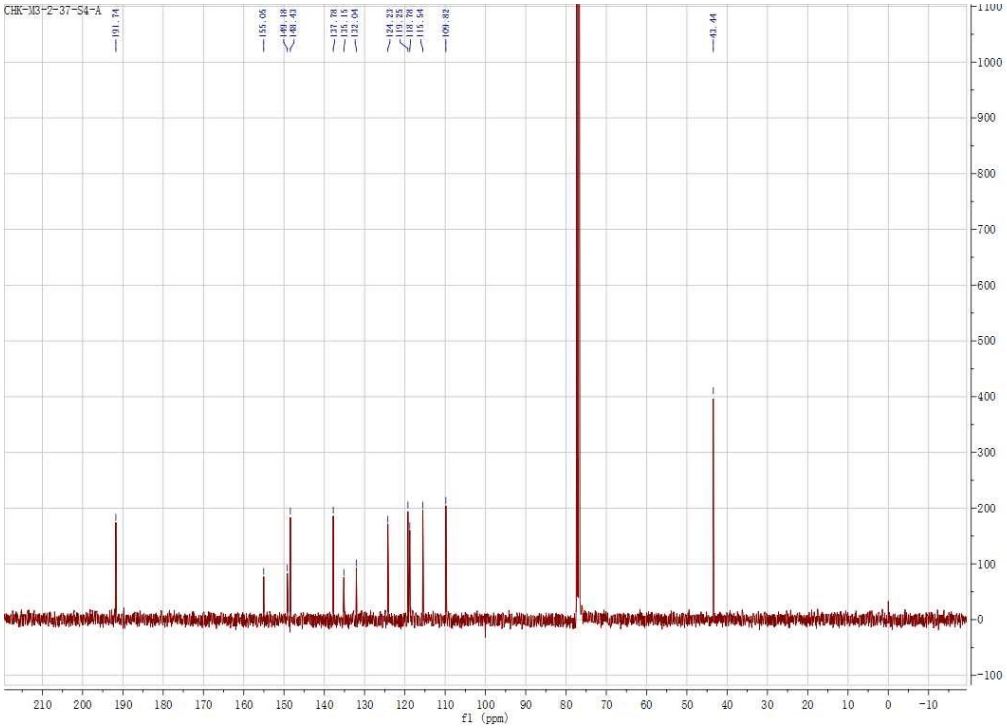




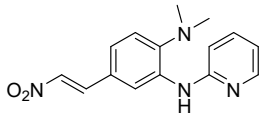
TX-36-S3: 4-(1,3-dioxolan-2-yl)-N1,N1-dimethyl-N2-(pyridin-2-yl)benzene-1,2-diamine

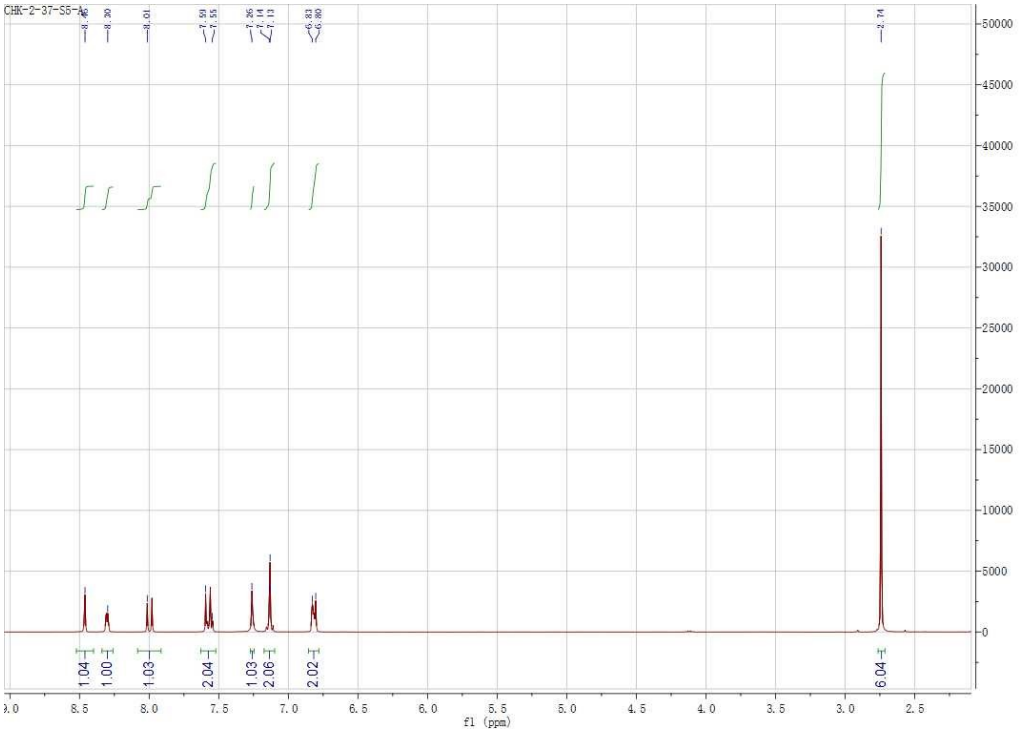


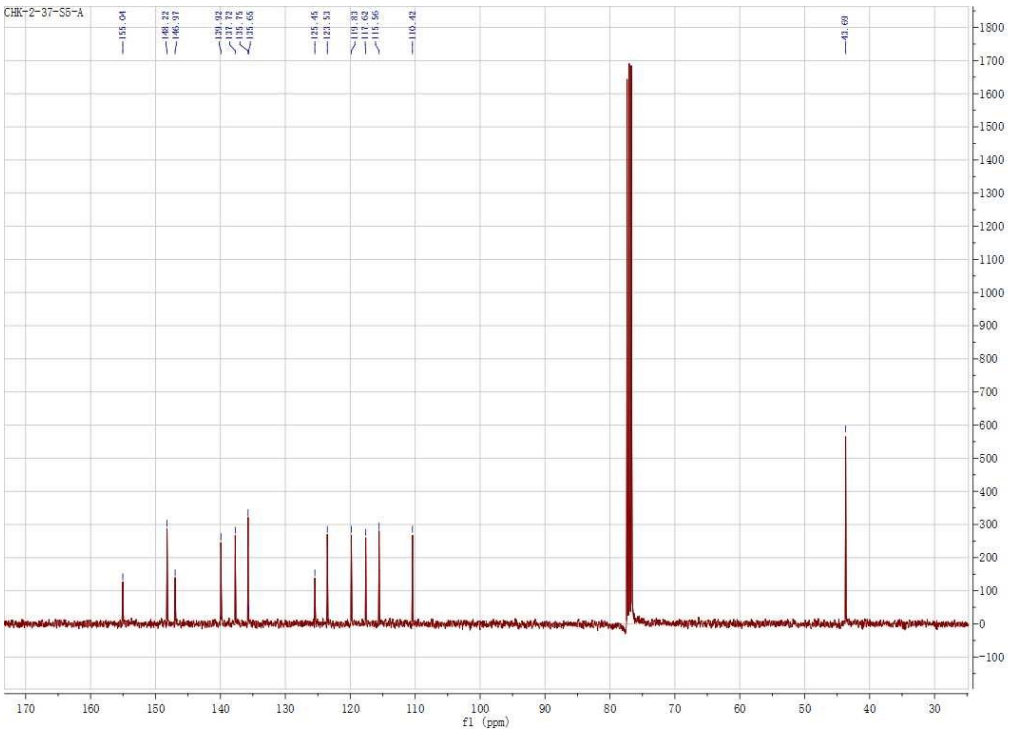




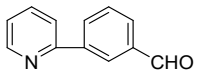
TX-36: (E)-N1,N1-dimethyl-4-(2-nitrovinyl)-N2-(pyridin-2-yl)benzene-1,2-diamine

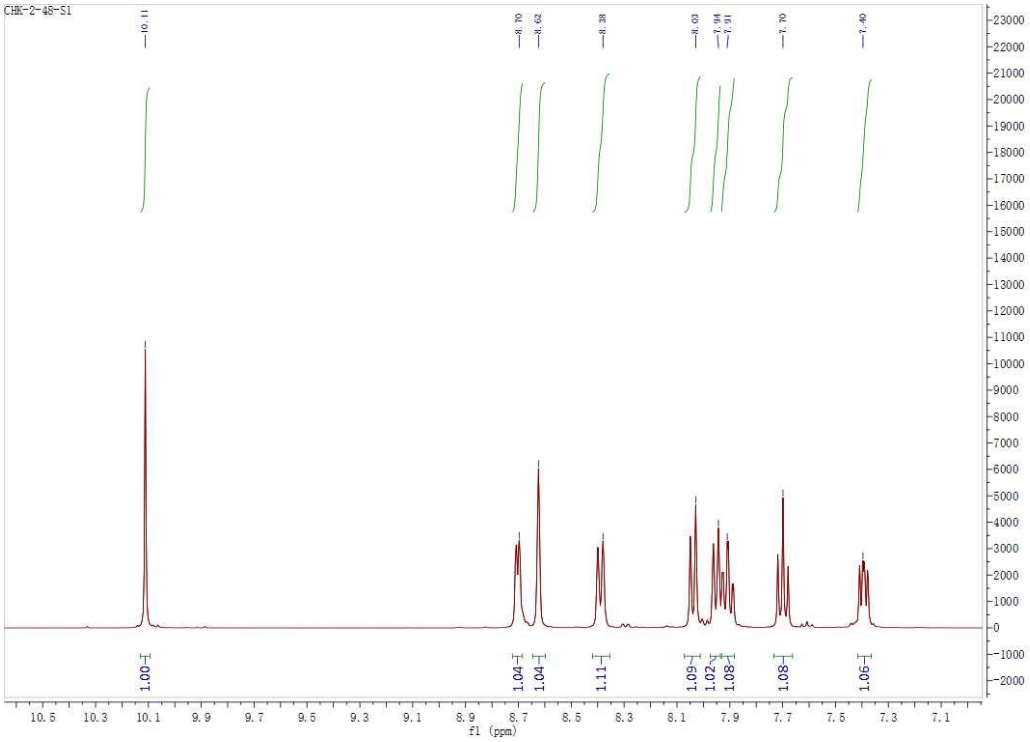


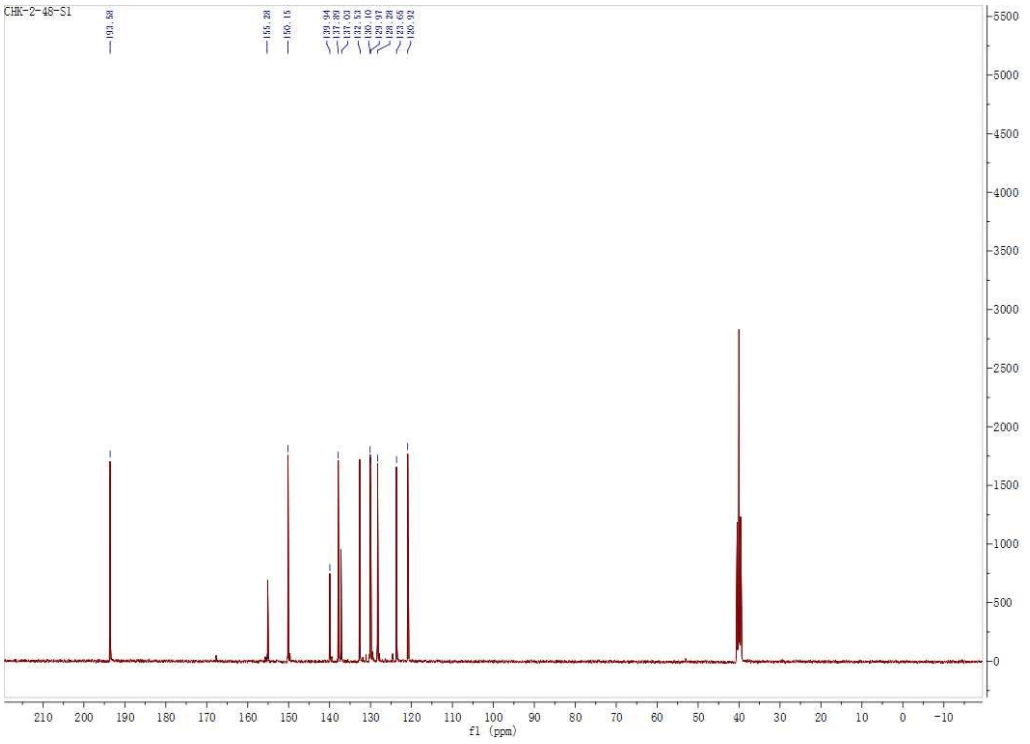




TX-37-S1: 3-(pyridin-2-yl)benzaldehyde







TX-37: (E)-2-(3-(2-nitrovinyl)phenyl)pyridine