Supporting Information

Acceleration of Pd-catalyzed amide N-arylations using co-catalytic metal triflates: Substrate scope and mechanistic study

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I. Experimental procedures

1.1 General information: Air-free manipulations were performed under a dry N_2 atmosphere using a Vacuum Atmospheres inert atmosphere glovebox or using standard Schlenk technique. NMR spectra were collected on Bruker Avance III 500 MHz and DRX 500 MHz instruments. ^{1}H NMR chemical shifts (δ, ppm) are referenced to residual protiosolvent resonances, and ^{13}C NMR chemical shifts are referenced to the deuterated solvent peak. ^{31}P NMR and ^{19}F NMR chemical shifts are referenced to external standards. High resolution electrospray ionization mass spectra were recorded on an Agilent 6520 Accurate Mass Q-TOF LC/MS. Toluene was purified using a commercial solvent purification system. Bromobenzene and iodobenzene were degassed and purged with N_2 and dried over over activated 4 Å molecular sieves for 48 h before use. Tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) was purified via sublimation (100 mTorr, 90°C) prior to use. Other chemicals were used as received from commercial suppliers. Pd(xantphos)(Ph)(Br)[1] and Pd(xantphos)(Ph)(I)[2] were synthesized from literature procedures.

All experimental data reported in this study uses $Pd(dba)_2$ purchased from Strem Chemicals. It is known that matured samples of $Pd_2(dba)_3$ contain Pd nanoparticles, with high variability of purity depending on the supplier.[3] Kinetic measurements of catalysis were found to be irreproducible when $Pd(dba)_2$ purchased from other suppliers was used. We have assayed the quality of $Pd(dba)_2$ by measuring the rate of catalysis of the coupling of pyrrolidin-2-one and bromobenzene through the procedure described in Section S1.5. In our hands, the rate of this coupling reaction was found to be highly reproducible. Multiple bottles of $Pd(dba)_2$ (Strem) were used in this study, were stored indefinitely under a nitrogen atmosphere and were found to perform this coupling reaction at reproducible rate, independent of the duration of storage (within one year).

1.2 Procedures for catalytic reactions

Note: NMR yield is determined by adding a measured quantity of 1,3,5-trimethoxybenzene (0.05 to 0.25 mmol) to the crude reaction mixture after completion of the catalytic reaction. An aliquot of the crude reaction was removed for ^{1}H NMR. The NMR yield of the product is measured versus the internal standard.

General procedure A: In an oven-dried 8 mL vial, pyrrolidin-2-one (0.434 mmol, 37 mg) and bromobenzene (0.434 mmol, 68 mg) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), $Al(OTf)_3$ (0.022 mmol, 10.3 mg), K_3PO_4 (0.675 mmol, 143 mg) and 2 mL toluene under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110°C for 2 hrs. Then, the mixture was cooled to rt and the vial was opened to air. The solution was diluted with 3 mL CH_2Cl_2 and 5 mL H_2O. The organic layer was separated, dried over $MgSO_4$, then evaporated *in vacuo*.

General procedure B: The same as procedure A, except the reaction stirred at 110°C for 18 hrs.

General procedure C: The same as procedure B, except $Pd(dba)_2$ and xantphos were used at 5 mol % loading (0.025 mmol 12 mg), and Cs_2CO_3 (0.675 mmol, 220 mg) was used rather than K_3PO_4.

General procedure D: The same as procedure B, except Cs_2CO_3 (0.675 mmol, 220 mg) was used rather than K_3PO_4.

General procedure E: In an oven-dried 16 mL vial, α-fluorophenylacetamide (0.434 mmol, 66 mg) and methyl 4-bromobenzoate (1.085 mmol, 233 mg) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), $Al(OTf)_3$ (0.022 mmol, 10.3 mg), Cs_2CO_3 (1.302 mmol, 425 mg) and 5 mL toluene under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110°C for 18 hrs. Then, the mixture was cooled to rt and the vial was opened to air. The solution was diluted with 3 mL CH_2Cl_2 and 5 mL H_2O. The organic layer was separated, dried over $MgSO_4$, then evaporated *in vacuo*.

1.3 Characterization of cross coupling products

N-phenylpyrrolidin-2-one[4] **(2)**. Procedure A was followed. The resulting yellow residue was purified by flash chromatography on a plug of silica gel using CH_2Cl_2 as eluent to yield a white solid. NMR yield: 79%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.60 (2H, d), 7.36 (2H, t), 7.13 (1H, t), 3.81 (2H, t), 2.58 (2H, t), 2.11 (2H, m).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 174.2, 139.5, 128.8, 124.4, 119.8, 48.7, 32.8, 17.9.

HRMS (ESI) m/z calculated for $[C_{10}H_{11}NOH^+]$: 162.0919, found: 162.0910.

N-phenyloxazolidin-2-one[5] **(3)**. Procedure B was followed using oxazolidin-2-one (0.434 mmol, 38 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. Isolated yield: 70 mg (99%).

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.53 (2H, d), 7.37 (2H, t), 7.13 (1H, t), 4.47 (2H, m), 4.05 (2H, m).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 155.2, 138.2, 129.0, 124.0, 118.2, 61.2, 45.1.

HRMS (ESI) m/z calculated for $[C_9H_9NO_2H^+]$: 164.0712, found: 164.0706.

4-methyl-N-phenylbenzamide[6] **(4)**. Procedure B was followed using 4-methylbenzamide (0.434 mmol, 59 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. NMR yield: 64%. Isolated yield: 43 mg, 46%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.81 (1H, br s), 7.79 (2H, d), 7.66 (2H, d), 7.39

(2H, t), 7.31 (2H, d), 7.16 (2H, t), 2.44 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 165.8, 142.2, 138.0, 132.0, 129.3, 129.0, 127.0, 124.3, 120.2, 21.5.

HRMS (ESI) m/z calculated for [$C_{14}H_{13}NOH^+$]: 212.1075, found: 212.1065.

4-methyl-N-(pyridin-3-yl)benzamide[7,8] **(5)**. Procedure B was followed using 4-methylbenzamide (0.434 mmol, 59 mg) and 3-bromopyridine (0.434 mmol, 69 mg). The compound was purified on silica gel using 9:1 CH_2Cl_2:MeOH. NMR yield: 94%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 9.40 (1H, br s), 8.71 (1H, d), 8.22 (2H, m), 7.76 (2H, d), 7.19–7.17 (1H, m), 7.13 (2H, d), 2.33 (3H, d).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 166.8, 144.8, 142.5, 141.8, 125.5, 131.3, 129.2, 128.1, 127.4, 123.6, 21.4.

HRMS (ESI) m/z calculated for [$C_{13}H_{12}N_2OH^+$]: 213.1028, found: 213.1033.

N-(pyridin-3-yl)oxazolidin-2-one[5] **(7)**. Procedure B was followed using oxazolidin-2-one (0.434 mmol, 38 mg) and 3-bromopyridine (0.434 mmol, 69 mg). NMR yield: 18%. The product was not isolated.

^{1}H-NMR (500 MHz, C_6D_6, 295 K, ppm): δ 8.58 (1H, d), 8.33 (1H, d), 8.10 (1H, m), 4.46 (2H, t), 4.02 (2H, t). A fourth aromatic resonance was obscured by impurities.

HRMS (ESI) m/z calculated for [$C_8H_9N_2O_2H^+$]: 165.0664, found: 165.0657.

N-(pyridin-3-yl)pyrrolidin-2-one[9] **(7)**. Procedure B was followed using 3-bromopyridine (0.434 mmol, 69 mg). The compound was purified on silica gel using 9:1 CH_2Cl_2:MeOH. NMR yield: 79%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.65 (1H, d), 8.25 (1H, m), 8.05 (1H, m), 7.17 (1H, m), 3.74 (2H, t), 2.48 (2H, t), 2.07 (2H, m).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 174.6, 145.0, 140.4, 126.5, 123.2, 47.7, 32.1, 17.8.

HRMS (ESI) m/z calculated for [$C_9H_{10}N_2OH^+$]: 163.0871, found: 163.0873.

N,4-dimethyl-N-phenylbenzenesulfonamide[10] **(8)**. Procedure C was followed using *p*-toluenesulfonamide (0.434 mmol, 85 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. NMR Yield: 72%. Isolated yield: 65 mg, 57%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.44 (2H, d), 7.33-7.25 (5H, m), 7.12 (2H, d), 3.18

(3H, s), 2.43 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 143.6, 141.6, 133.4, 129.4, 128.8, 127.9, 127.3, 126.6, 38.1, 21.6.

HRMS (ESI) m/z calculated for [$C_{14}H_{15}NO_2SH^+$]: 262.0902, found: 262.1632.

N,4-dimethyl-N-(pyridin-3-yl)benzenesulfonamide[11] **(9)**. Procedure C was followed using *p*-toluenesulfonamide (0.434 mmol, 85 mg) and 3-bromopyridine (0.434 mmol, 69 mg). NMR Yield: 54%. The compound was not purified.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.48 (1H, dd), 8.31 (1H, d), 7.72 (1H, d), 7.51 (1H, dq), 7.25-7.23 (2H, m), 7.17-7.13 (2H, m), 3.18 (3H, s), 2.41 (3H, s).

HRMS (ESI) m/z calculated for [$C_{13}H_{14}N_2O_2SH^+$]: 263.0854, found: 263.1593.

2-(4-fluorophenyl)-N-phenylacetamide[12] **(10)**. Procedure C was followed using α-fluorophenylacetamide (0.434 mmol, 66 mg) and bromobenzene (0.434 mmol, 68 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. NMR yield: 61%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.44 (2H, d), 7.33 (m, 3H), 7.11 (m 2H), 3.73 (s, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 168.7, 162.3 (d), 137.5, 131.1 (d), 129.0, 124.6, 119.8, 116.1 (d), 43.9.

^{19}F-NMR (470 mHz, $CDCl_3$, 295 K, ppm): δ -114.57.

HRMS (ESI) m/z calculated for [$C_{14}H_{12}FNOH^+$]: 230.0981, found: 230.1666.

2-(4-fluorophenyl)-N-(pyridin-3-yl)acetamide (11). Procedure C was followed using α-fluorophenylacetamide (0.434 mmol, 66 mg) and 3-bromopyridine (0.434 mmol, 69 mg). The compound was purified on a plug of silica gel using 9:1 CH_2Cl_2:MeOH. NMR yield: 65%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 9.36 (1H, s), 8.60 (1H, d), 8.24 (1H, d), 8.03 (1H, dq), 7.23 (3H, t), 6.92 (2H, t), 3.59 (2H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 169.9, 162.3 (d), 145.0, 141.1, 130.9 (d), 129.9, 128.2, 123.9, 115.8 (d), 43.3.

^{19}F-NMR (470 mHz, $CDCl_3$, 295 K, ppm): δ -114.76.

HRMS (ESI) m/z calculated for [$C_{13}H_{11}FN_2OH^+$]: 231.0934, found: 231.1642.

2-(4-fluorophenyl)-N,2-di(pyridin-3-yl)acetamide (11b). HRMS (ESI) m/z calculated for

$[C_{18}H_{14}FN_3OH^+]$: 308.1199, found: 308.1995.

methyl 4-(2-(4-fluorophenyl)acetamido)benzoate (12). Procedure D was followed using α-fluorophenylacetamide (0.434 mmol, 66 mg) and methyl 4-bromobenzoate (0.434 mmol, 93 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. NMR yield: 72%. Isolated yield: 76 mg, 61%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.97 (2H, d), 7.55 (2H, d), 7.30 (2H, m), 7.08 (2H, t), 3.90 (3H, s), 3.73 (2H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 169.4, 166.8, 162.5 (d), 142.1, 131.3, 131.0, 129.0, 125.0, 119.1, 116.4 (d), 52.3, 44.1.

HRMS (ESI) m/z calculated for $[C_{16}H_{14}FNO_3H^+]$: 288.1036, found: 288.1805.

methyl 4-(1-(4-fluorophenyl)-2-((4-(methoxycarbonyl)phenyl)amino)-2-oxoethyl)benzoate (12b). HRMS (ESI) m/z calculated for $[C_{24}H_{20}FNO_5H^+]$: 422.1404, found: 422.2241.

(S)-2-(2-oxopyrrolidin-1-yl)-N-(pyridin-3-yl)butanamide (13). Procedure C was followed using Levetiracetam (0.434 mmol, 74 mg) and 3-bromopyridine (0.434 mmol, 69 mg). The resulting residue was purified by flash chromatography with a plug of silica gel using 9:1 CH_2Cl_2:MeOH to yield a colourless oil. Isolated yield: 71 mg, 66%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 9.62 (1H, s), 8.61 (1H, d), 8.24 (1H, dd), 8.08 (1H, ddd), 7.17 (1H, dt), 4.62 (1H, ddd), 3.56 (1H, ddt), 3.43 (1H, m), 2.40 (1H, ddd), 2.00 (2H, m), 1.71 (1H, m), 0.86 (3H, m).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 176.4, 169.1, 144.9, 141.4, 135.2, 127.1, 123.5, 75.4, 44.3, 31.2, 21.7, 18.2, 10.6.

HRMS (ESI) m/z calculated for $[C_{13}H_{17}N_3O_2H^+]$: 248.1399, found: 248.2118.

N-methyl-N-phenylacetamide[13] **(14).** Procedure C was followed using N-methylacetamide (0.434 mmol, 37 mg) and bromobenzene (0.434 mmol, 68 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent to yield a yellow oil. NMR yield: 48%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.44 (2H, m), 7.35 (1H, m), 7.21 (2H, d), 3.29 (3H, s), 1.89 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 170.6, 144.6, 129.7, 127.7, 127.1, 37.2, 22.5.

HRMS (ESI) m/z calculated for $[C_9H_{11}NOH^+]$: 150.0919, found: 150.1471.

methyl 4-(N-methylacetamido)benzoate[14] **(15)**. Procedure D was followed using N-

methylacetamide (0.434 mmol, 37 mg) and methyl 4-bromobenzoate (0.434 mmol, 93 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent to yield a red oil. NMR yield: 89%. Isolated yield: 56 mg, 62%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.01 (2H, d), 7.20 (2H, d), 3.86 (3H, d), 3.22 (3H, d), 1.85 (3H, br s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 170.1, 166.1, 148.5, 143.3, 131.1, 129.0, 128.4, 126.8, 42.5, 37.1 (br), 22.5.

HRMS (ESI) m/z calculated for $[C_{11}H_{13}NO_3H^+]$: 208.0974, found: 208.1630.

N-methyl-N-(pyridin-3-yl)acetamide (16). Procedure C was followed using N-methylacetamide (0.434 mmol, 37 mg) and 3-bromopyridine (0.434 mmol, 69 mg). The compound was not purified. NMR yield: 54%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.55 (1H, d), 8.48 (1H, d), 7.51 (1H, d), 7.36 (1H), 3.24 (3H, br s), 1.84 (br, s).

HRMS (ESI) m/z calculated for $[C_8H_{10}N_2OH^+]$: 151.0872, found: 151.1426.

methyl 4-(N-butylpropionamido)benzoate (17). Procedure D was followed using N-butylpropionamide (0.434 mmol, 56 mg) and methyl 4-bromobenzoate (0.434 mmol, 93 mg). The compound was not purified. NMR yield: 40%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.10 (2H, d), 7.24 (2H, d), 3.95 (3H, s), 3.72 (2H, t), 2.06 (2H, br m), 1.47 (2H, m), 1.30 (2H, m), 1.05 (3H, t), 0.89 (3H, m).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 173.2, 166.4, 146.9, 131.0, 128.1, 52.2, 49.1, 30.2, 28.0, 19.9, 13.9, 9.6.

HRMS (ESI) m/z calculated for $[C_{15}H_{21}NO_3H^+]$: 264.1600, found: 264.2344.

methyl 4-(N-phenylpropionamido)benzoate (18). Procedure D was followed using N-phenylpropionamide (0.434 mmol, 65 mg) and methyl 4-bromobenzoate (0.434 mmol, 93 mg). The compound was purified on a plug of silica gel using CH_2Cl_2 as eluent. NMR Yield: 89%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.09 (2H, d), 7.28 (2H, d), 3.93 (3H, s), 3.30 (3H, s), 1.93 (3H, br s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 173.9, 166.4, 147.0, 143.3, 142.2, 130.5, 130.4, 129.8, 129.0, 128.4, 127.9, 126.1, 52.2, 29.2, 9.6.

HRMS (ESI) m/z calculated for $[C_{17}H_{17}NO_3H^+]$: 284.1287, found: 284.2060.

N-(2-(6-methoxy-1-phenyl-1H-indol-3-yl)ethyl)acetamide[15] **(19)**. Procedure B was followed using melatonin (0.434 mmol, 101 mg) and bromobenzene (0.434 mmol, 69 mg). The resulting residue was purified by flash chromatography with a plug of silica gel using CH_2Cl_2 as eluent. NMR Yield: 60%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.37-7.31 (5H, m), 7.18-7.11 (2H, m), 6.98 (1H, d), 7.76 (1H, dd), 5.90 (1H, br t), 3.75 (3H, s), 3.48 (2H, q), 2.86 (2H, t), 1.81 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 169.0, 153.5, 138.7, 130.3, 128.6, 125.0, 122.7, 112.7, 11.9, 110.5, 99.7, 54.9, 28.7, 24.2, 22.4.

HRMS (ESI) m/z calculated for [$C_{19}H_{20}N_2O_2H^+$]: 309.1603, found: 309.2400.

methyl 4-(3-(2-acetamidoethyl)-5-methoxy-1H-indol-1-yl)benzoate (20). Procedure E was followed using melatonin (0.434 mmol, 101 mg) and methyl 4-bromobenzoate (1.085 mmol, 173 mg). The compound was purified by flash chromatography on silica gel (9:1 EtOAc:MeOH). NMR Yield: 67%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.18 (2H, d), 7.56 (1H, s), 7.55 (2H, dd), 7.23 (1H, s), 7.10 (1H, d), 6.94 (1H, dd), 5.64 (1H, br s), 3.97 (3H, s), 3.90 (3H, s), 3.65 (2H, q), 3.01 (2H, t), 1.98 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 170.1, 166.4, 154.9, 143.6, 131.3, 130.8, 130.1, 125.5, 122.5, 115.3, 113.0, 111.7, 101.2, 55.9, 52.3, 39.6, 25.3, 23.5.

HRMS (ESI) m/z calculated for [$C_{21}H_{22}N_2O_4^+$]: 366.1580, found: 367.2526.

methyl 4-(N-(2-(5-methoxy-1-(4-(methoxycarbonyl)phenyl)-1H-indol-3-yl)ethyl)acetamido)benzoate (21). Procedure E was followed using melatonin (0.434 mmol, 101 mg) and methyl 4-bromobenzoate (1.085 mmol, 173 mg). The compound was purified by flash chromatography on silica (2:1 EtOAc:petroleum ether). NMR Yield: 27%.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 8.16 (2H, d), 8.08 (2H, d), 7.52 (3H, m), 7.22 (2H, d), 7.18 (1H, s), 7.06 (1H, s), 6.90 (1H, dd), 4.10 (4H, t), 3.96 (6H, s), 3.87 (3H, s), 3.05 (2H, t), 1.93 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 169.9, 166.4, 166.1, 154.8, 143.7, 131.7, 131.3, 131.1, 130.6, 130.2, 129.5, 127.9, 127.0, 125.5, 122.4, 114.9, 113.0, 111.6, 101.8, 55.8, 52.4, 52.2, 49.5, 23.7, 22.9.

HRMS (ESI) m/z calculated for [$C_{29}H_{28}N_2O_6H^+$]: 501.2026, found: 501.3040.

1.4 Synthesis and characterization of amide starting materials

4-methylbenzamide.[16] A solution of aqueous NH_4OH (50 mL, 28% v/v) was cooled to -78°C (CO_2/acetone). Neat p-toluoyl chloride (7.7 g, 0.050 mol) was added dropwise to the vigorously stirring solution. Immediately, a white solid precipitated. The solution stirred for 10 minutes and then was diluted with 50 mL H_2O.The white solid was collected by filtration, rinsed extensively with H_2O and then hexane, and was dried further under vacuum. Yield: 6.5 g, 0.048 mol (96%).

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.73 (2H, d), 7.26 (2H, d), 6.07 (2H, br d), 2.42 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 169.5, 142.5, 130.5, 129.3, 127.4, 21.5.

N-phenylpropionamide.[17] A solution of aniline hydrochloride (7 g, 0.054 mol) and pyridine (13 mL, 12.8 g, 0.162 mol) in 50 mL CH_2Cl_2 was immersed in a cooling bath at 0°C. Neat propionyl chloride (4.7 mL, 5.0 g, 0.054 mol) was added dropwise to the solution with vigorous stirring. The reaction mixture stirred for 1 h and then was warmed to rt. The solution was washed with aqueous NH_4Cl and then $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated in vacuo to yield a grey solid. Yield: 6.2 g, 0.044 mol (81%).

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.90 (1H, br s), 7.55 (2H, d), 7.30 (2H, t), 7.10 (1H, t), 2.39 (2H, q), 1.24 (3H, t).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 172.5, 138.1, 128.8, 124.1, 120.0, 30.6, 9.7.

N-butylpropionamide.[18] A solution of n-butylamine (5 g, 0.064 mol) and pyridine (6 g, 0.076 mol) in 50 mL CH_2Cl_2 was immersed in a cooling bath at 0°C. An addition funnel was charged with a solution of propionyl chloride (5.6 g, 0.060 mol) in 20 mL CH_2Cl_2 which was then added dropwise to the solution. The reaction mixture stirred for 1 h and then was warmed to rt. The solution was washed with aqueous NH_4Cl and then $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated in vacuo to yield a yellow oil. The oil was purified using flash chromatography on silica gel (1:1 EtOAc:Petroleum ether). Yield: 3.5 g, 0.027 mol (45%).

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 5.52 (1H, br s), 3.26 (2H, q), 2.20 (2H, q), 1.52-1.46 (2H, m), 1.39-1.32 (2H, m), 1.16 (3H, t), 0.93 (3H, t).

^{13}C-NMR (126 MHz, $CDCl_3$, 295 K, ppm): δ 173.4, 39.2, 31.7, 29.8, 20.1, 13.8, 9.7.

2-(4-fluorophenyl)acetamide.[19] A 16 mL vial was charged with methyl 2-(4-fluorophenyl)acetate (2 g, 0.012 mol) and 5 mL of aqueous NH_4OH (50 mL, 28% v/v). The biphasic solution stirred for 18 h at rt. A white solid precipitated from solution. The solid was collected by filtration and rinsed thoroughly with H_2O and then hexane, and was dried further under vacuum.

^{1}H-NMR (500 MHz, $CDCl_3$, 295 K, ppm): δ 7.26 (2H, m), 7.07 (2H, t), 5.62 (2H, br d), 3.57

(2H, s), 1.78 (2H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 173.3, 162.1 (d), 130.9 (d), 130.5, 115.9 (d), 42.3.

N-(2-(5-methoxy-1H-indol-3-yl)ethyl)acetamide.[20] Commercial 5 mg melatonin tablets (x 240) were ground with a mortar and pestle to yield 72 g of a fine white powder. The powder was added added to a 500 mL Erlenmeyer flask and suspended in 250 mL CH_2Cl_2. The solution stirred for 1 h at room temperature, and was then filtered through celite. The filtrate was dried over $MgSO_4$ and evaporated to yield a white solid. Yield: 1.1 g, 5.2 mmol (92%).

^{1}H-NMR (500 mHz, $CDCl_3$, 295 K, ppm): δ 8.30 (1H, br s), 7.17 (1H, d), 6.95 (1H, d), 6.90 (1H, d), 6.78 (1H, dd), 5.63 (1H, br s), 3.77 (3H, s), 3.49 (2H, q), 2.85 (2H, t), 1.84 (3H, s).

^{13}C-NMR (125 MHz, $CDCl_3$, 295 K, ppm): δ 170.2, 153.9, 131.5, 127.7, 122.9, 112.3, 112.0, 100.4, 55.9, 39.8, 25.2, 23.4.

1.5 General procedure for kinetic measurements of catalysis

In a nitrogen atmosphere glovebox, an oven-dried test tube was charged with pyrrolidin-2-one (various concentrations), aryl halide (various concentrations), K_3PO_4 (1.2 eq, 300 mg, 1.412 mmol), $Pd(dba)_2$ (1.5 mol %, 10 mg, 0.0174 mmol), xantphos (1.6 mol %, 10 mg, 0.019 mmol), additive (various concentrations), trimethoxybenzene (internal NMR standard) and anhydrous toluene (5.00 g). The test tube was equipped with a stir bar, sealed with a rubber septum, and removed from the glovebox. The test tube was placed in a thermostated aluminum block preheated to 110°C. Aliquots of the reaction solution were removed by syringe at 15 minute intervals. For each interval, the reaction stirred at 110°C for 12 minutes, at which point the stirring was arrested to allow insoluble solids to settle for 3 minutes, subsequently a 100 µL aliquot was removed and then stirring was restored. The solvent volume of the aliquot was removed *in vacuo*. The formation of the N-arylamide product and conversion of the amide starting material was quantified by ^{1}H-NMR spectroscopy versus trimethoxybenzene. Each reaction condition was performed in triplicate. Initial rates of catalysis are determined from the slope of the plot of concentration versus time in the initial pseudo-zero order regime.

1.6 Screening of bases in preparation of N-phenylpyrrolidin-2-one

In an oven-dried 8 mL vial, pyrrolidin-2-one (0.434 mmol, 37 mg) and bromobenzene (0.434 mmol, 68 mg) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), 1 equiv base (0.434 mmol) and 2 mL toluene under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110^{o}C for 2 hrs. Then, the mixture was cooled to rt and the vial was opened to air. The reaction mixture was filtered through celite and evaporated *in vacuo*. The resulting residue was completely dissolved in 1 mL $CDCl_3$ along with 10 mg 1,3,5-trimethoxybenzene. The yield of 3-phenylpyrrolidin-2-one was measured versus the internal standard 1,3,5-trimethoxybenzene.

Table S1. Screen of bases

Entry	Aryl halide	Base	Yield
1	PhBr	K_3PO_4	46%
2	PhBr	K_2CO_3	42%
3	PhBr	Cs_2CO_3	60%
4	PhBr	KO^{t}Bu	<1%
5	PhBr	NaHMDS	<1%
6	PhI	K_3PO_4	36%
7	PhI	K_2CO_3	10%
8	PhI	Cs_2CO_3	56%
9	PhI	KO^{t}Bu	<1%
10	PhI	NaHMDS	<1%

1.7 Screening of additional Lewis acids in preparation of N-phenylpyrrolidin-2-one (2) and N-(pyridin-3-yl)pyrrolidin-2-one (4)

In an oven-dried 8 mL vial, pyrrolidin-2-one (0.434 mmol, 37 mg) and bromobenzene (0.434 mmol, 68 mg) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), Lewis acid (indicated quantity), K_3PO_4 (0.675 mmol, 143 mg) and 2 mL toluene under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110°C for 2-18 hrs. Then, the mixture was cooled to rt and the vial was opened to air. The reaction mixture was filtered through celite and evaporated *in vacuo*. The resulting residue was completely dissolved in 1 mL $CDCl_3$ along with 10 mg 1,3,5-trimethoxybenzene. The yield of **2** or **7** was measured versus the internal standard 1,3,5-trimethoxybenzene. Solution molarity is determined with respect to pyrrolidin-2-one. Entries 2-4 refer to conditions reported by Hartwig and Shen[7] and were not reproduced in our laboratory. PyBr refers to 3-bromopyridine. $PyBEt_2$ refers to 3-pyridyldiethylborane.

Table S2. Screen of additional Lewis acids.

Entry	Aryl halide	Product	Lewis Acid	Time (h)	Molarity	Yield
1	PyBr	**7**	N/A	18	0.2 M	42%
2	PyBr	**7**	N/A	24	1 M	17%
3	PyBr	**7**	BEt_3 (100 mol %)	24	1 M	84%
4	PyBr	**7**	BEt_3 (20 mol %)	1.5	1 M	83%
5	PyBr	**7**	$B(C_6F_5)_3$ (5 mol %)	2	0.2 M	<1%
6	PyBr	**7**	$B(C_6F_5)_3$ (5 mol %)	18	0.2 M	50%
7	PyBr	**7**	$B(C_6F_5)_3$ (100 mol %)	18	0.2 M	<1%
8	PyBr	**7**	$PyBEt_2$ (5 mol %)	2	0.2 M	26%
9	PyBr	**7**	$PyBEt_2$ (5 mol %)	18	0.2 M	58%
9	PyBr	**7**	$Zn(OAc)_2$ (5 mol %)	18	0.2 M	71%
10	PyBr	**7**	$Zn(CN)_2$ (5 mol %)	18	0.2 M	62%
11	PyBr	**7**	$Zr(acac)_4$ (5 mol %)	18	0.2 M	81%
12	PhBr	**2**	N/A	2	0.2 M	38%
13	PhBr	**2**	$Zn(CN)_2$ (5 mol %)	2	0.2 M	83%
14	PhBr	**2**	$Zr(acac)_4$ (5 mol %)	2	0.2 M	71%
15	PhI	**2**	N/A	2	0.2 M	36%
16	PhI	**2**	$Zn(CN)_2$ (5 mol %)	2	0.2 M	53%
17	PhI	**2**	$Zr(acac)_4$ (5 mol %)	2	0.2 M	89%

1.8 Synthesis and characterization of [(xantphos)Pd(Ph)][BAr^F_4]

In a nitrogen-atmosphere glovebox, (xantphos)Pd(Ph)(I) (200 mg, 0.225 mmol) was dissolved in 5 mL CH_2Cl_2. The Pd solution was added to an excess of $NaBAr^F_4$ (1.2 equiv, 239 mg, 270 mmol). The resulting reaction mixture stirred under inert atmosphere at rt for 1 hr. Then, the solution was removed from the glovebox and opened to air. The reaction mixture was filtered through celite. The filtrate was evaporated *in vacuo* to yield a foamy solid, which was triturated with hexane until 190 mg (52% yield) of an air-stable beige powder was obtained.

^{1}H-NMR (500 MHz, $CDCl_3$, 292 K, ppm): δ 7.76 (2H, dd), 7.32 (8H, br t), 7.54 (4H, m), 7.50 (4H, br s), 7.46-7.39 (12H), 7.34 (8H, m), 1.75 (6H, s)

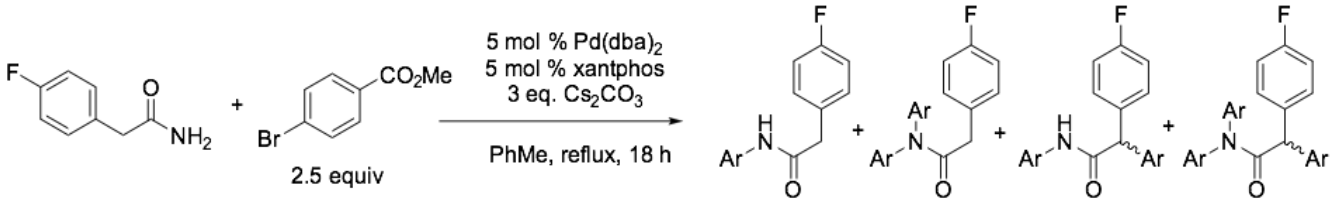
^{13}C-NMR (125 MHz, $CDCl_3$, 292 K, ppm): δ 161.7 (q), 152.7 (t), 140.7, 135.2, 134.8 (br), 133.3 (t), 132.9 (t), 132.4, 132.2, 131.9 (t), 129.5 (t), 128.9 (m), 127.7, 127.4 (t), 126.3 (t), 125.6, 124.8, 123.4, 121.3, 119.2 (t), 34.7, 33.3.

^{31}P-NMR (202 mHz, $CDCl_3$, 292 K, ppm): δ 13.4.

^{19}F-NMR (470 mHz, $CDCl_3$, 292 K, ppm): δ -62.40.

^{11}B-NMR (160 mHz, $CDCl_3$, 292 K, ppm): δ -6.60.

2.1 Identification of byproducts in the arylation of α-4-fluorophenylacetamide (in the absence of $Al(OTf)_3$)



In an oven-dried 8 mL vial, α-4-fluorophenylacetamide (0.434 mmol, 66 mg) and 2.5 equiv methyl 4-bromobenzoate (1.085 mmol, 233 mg) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), 3 equiv Cs_2CO_3 (1.300 mmol, 424 mg) and 3 mL toluene under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110°C for 18 hrs. Then, the mixture was cooled to rt and the vial was opened to air. The solution was diluted with 3 mL CH_2Cl_2 and 5 mL H_2O. The organic layer was separated, dried over $MgSO_4$, then evaporated *in vacuo*.

In the ^{1}H-NMR spectrum, two peaks corresponding to the expected benzylic protons were observed at 3.53 and 3.47 ppm (products were distinct from the amide starting material). Two unexpected products were also observed at 5.02 and 4.95 ppm. The ^{19}F-NMR spectrum confirms four major fluorine-containing products in an approximately 1:1:1:2 ratio. The COSY and HSQC provide further evidence for four distinct products: no $^1J_{HH}$ or $^2J_{HH}$ coupling is observed between any peaks in the ^{1}H-NMR spectrum, and each peak shows a $^1J_{HC}$ coupling to four different carbon atoms. The phasing of peaks in the HSQC indicates that the peaks at 3.53 and 3.47 in the ^{1}H-NMR spectrum correspond to methylene protons and the peaks at 5.02 and 4.95 ppm correspond to methine protons. The connectivity of these methylene and methine groups are indicated by HMBC. Each ^{1}H peak shows the expected $^2J_{HC}$ coupling to an amide CO (169-171 ppm). Each ^{1}H peak shows $^2J_{HC}$ coupling and $^3J_{HC}$ coupling to the ipso and ortho carbons of the 4-fluorophenyl ring (128-134 ppm). The methine peaks have an additional $^2J_{HC}$ coupling to a ^{13}C resonance at 143.8 or 144.2 ppm. HMBC further indicates the connectivity of this arene: the ^{13}C resonances at 143.8 and 144.2 ppm can be correlated to the ester moiety of the methyl benzoate arene. This combination of 2-dimensional NMR techniques provide strong evidence the addition of the arene to the α-position of α-4-fluorophenylacetamide.

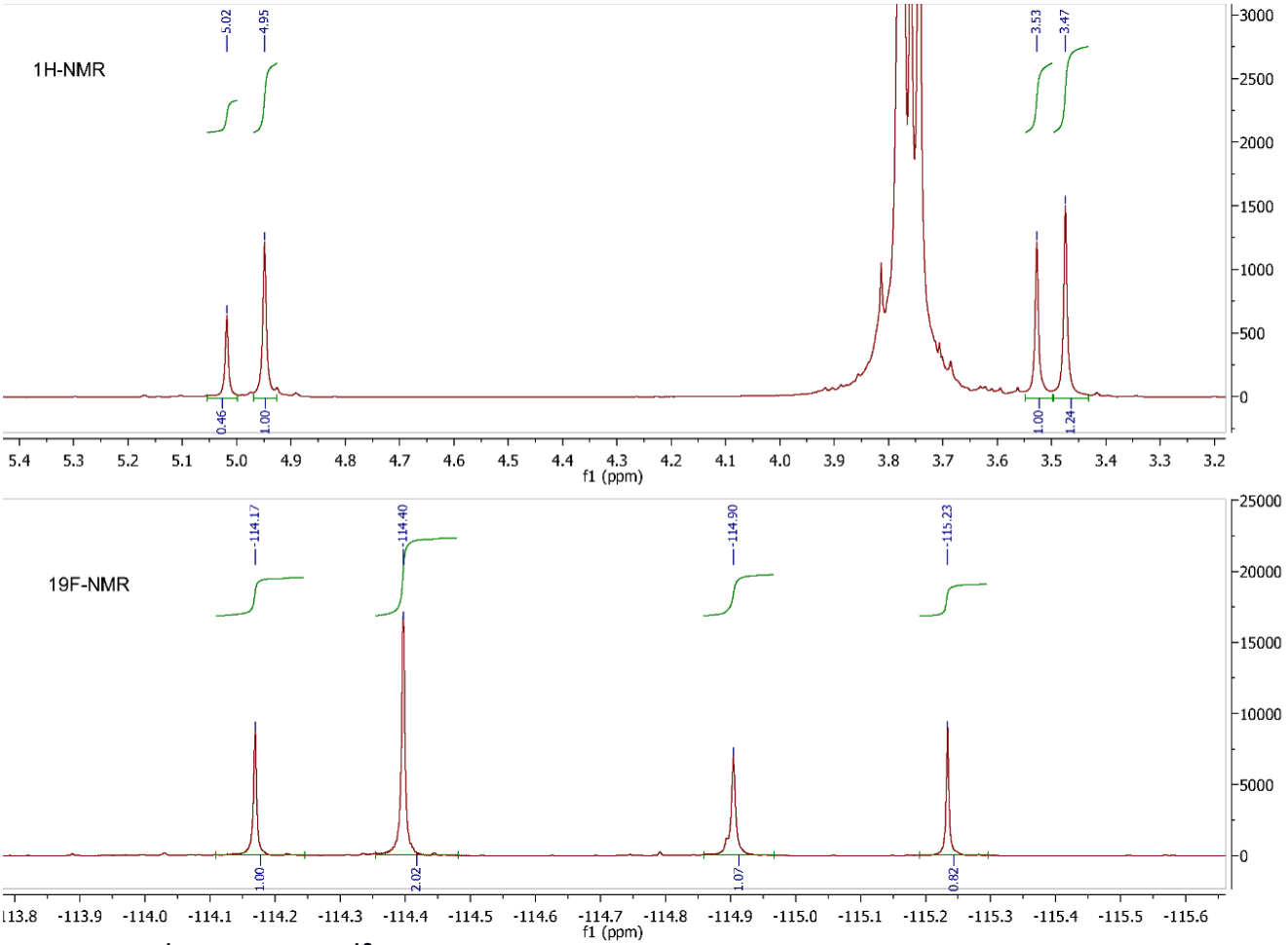


Figure S1. ^{1}H-NMR and ^{19}F-NMR spectra of the reaction of α-fluorophenylacetamide and methyl 4-bromobenzoate in the absence of Lewis acid

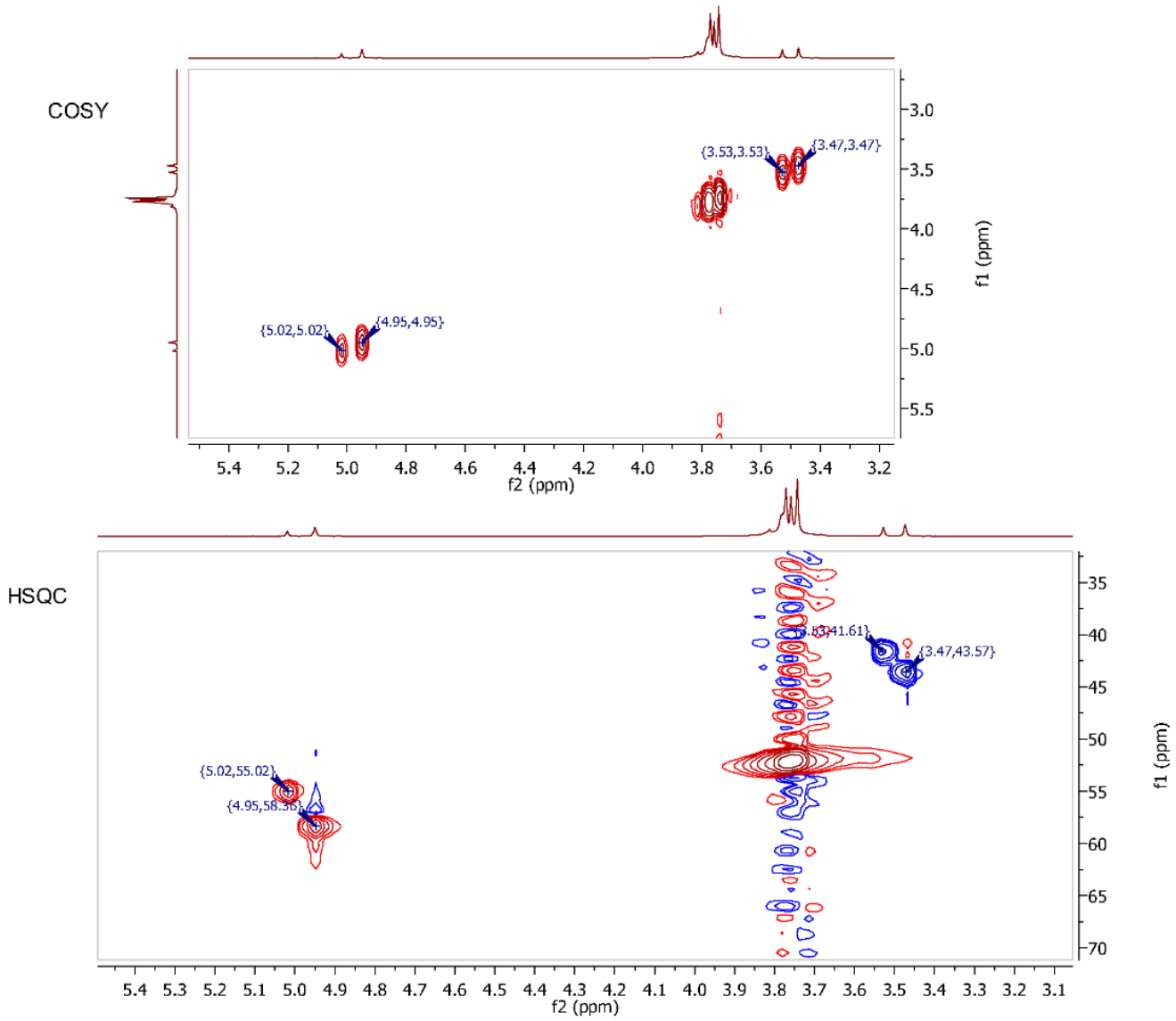


Figure S2. COSY and HSQC spectra of the reaction of α-fluorophenylacetamide and methyl 4-bromobenzoate in the absence of Lewis acid

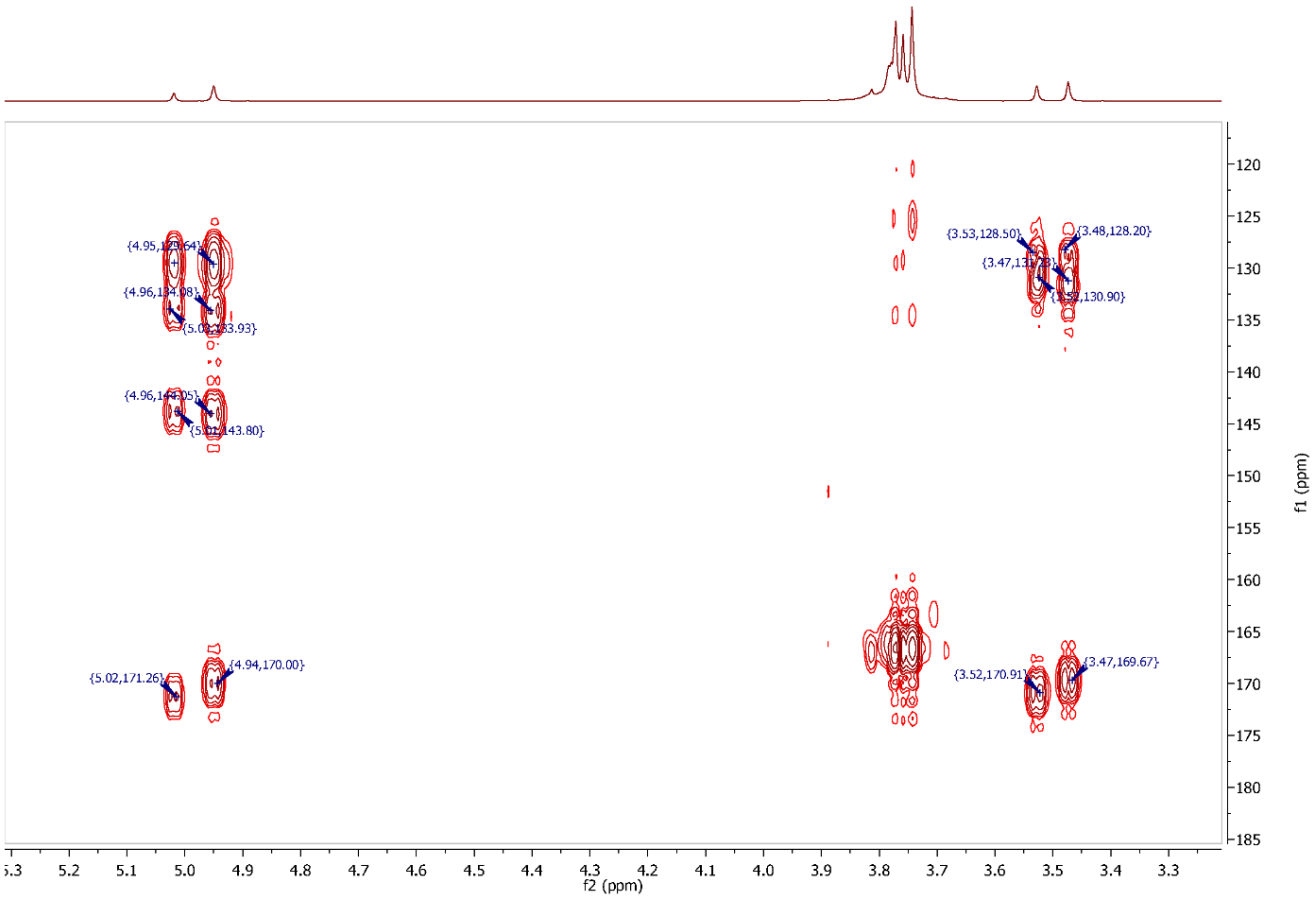


Figure S3. HMBC spectrum of the reaction of α-fluorophenylacetamide and methyl 4-bromobenzoate in the absence of Lewis acid

2.2 Variable temperature ^{31}P-NMR of (xant)Pd(Ph)(X) complexes

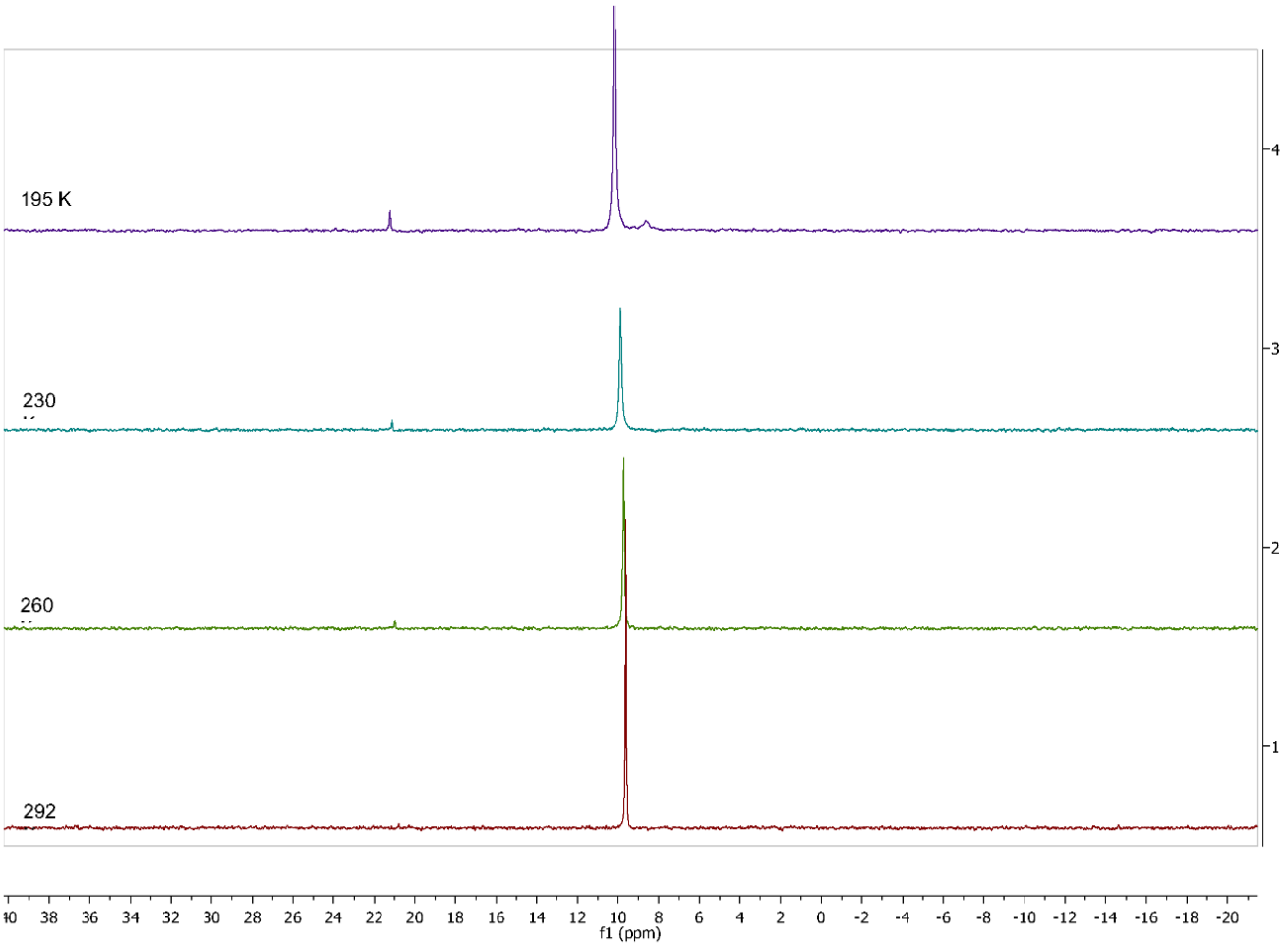


Figure S4. Variable temperature ^{31}P-NMR of Pd(xantphos)(Ph)(Br) (0.02M, CD_2Cl_2)

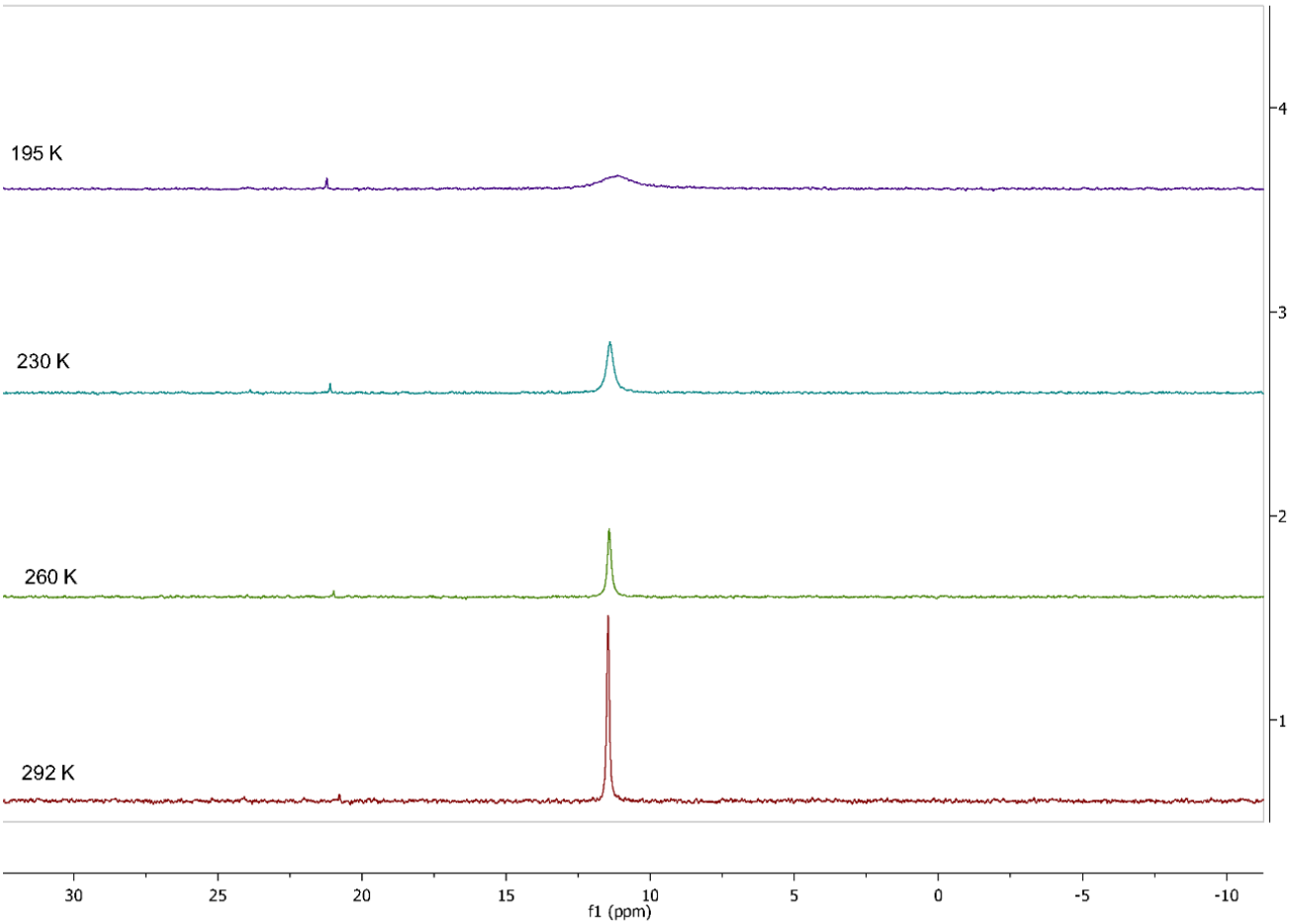


Figure S5. Variable temperature ^{31}P-NMR of Pd(xantphos)(Ph)(Br) and 1 equiv. $Yb(OTf)_3$ (0.02M, CD_2Cl_2)

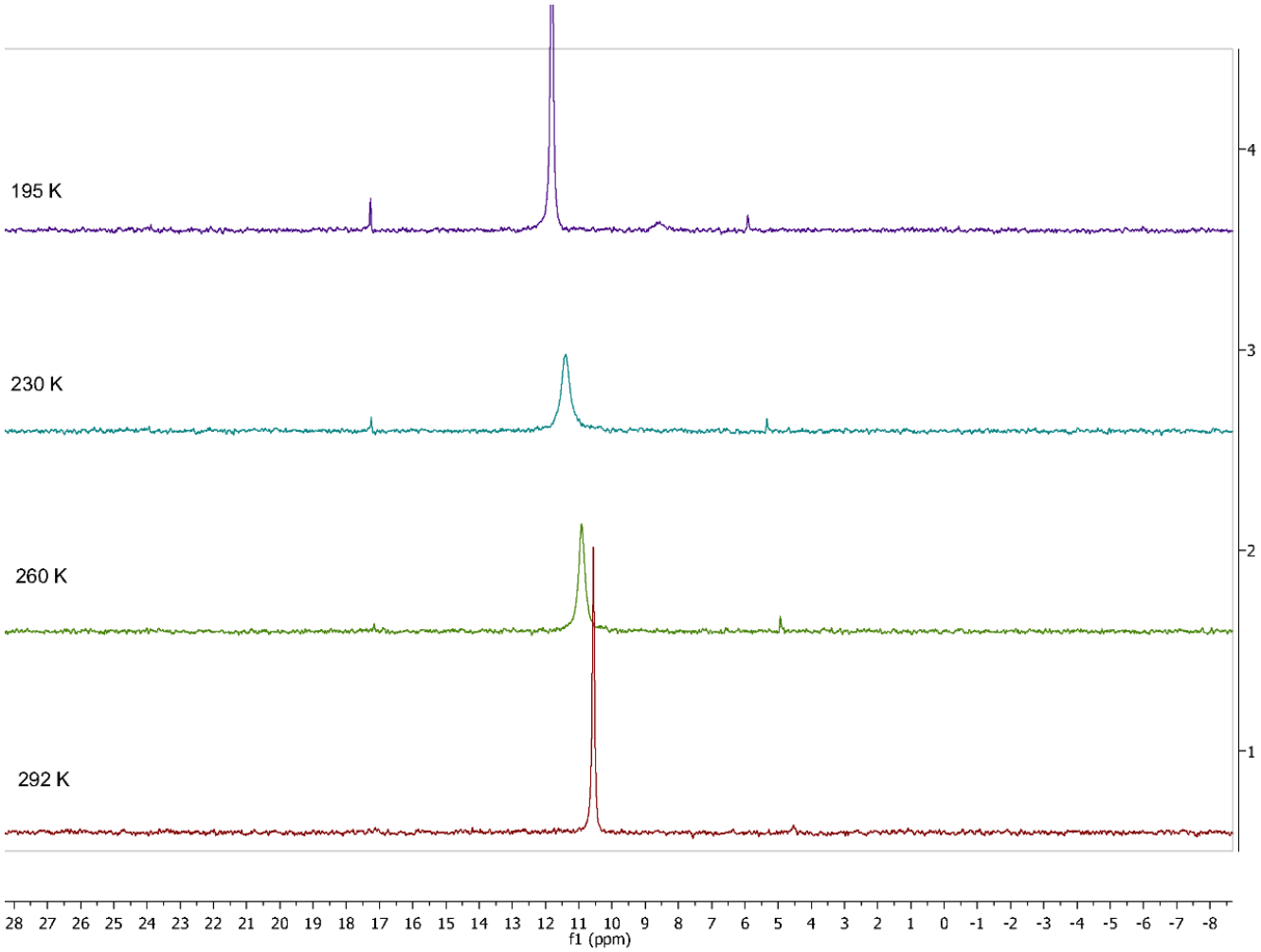


Figure S6. Variable temperature ^{31}P-NMR of Pd(xantphos)(Ph)(I) (0.02M, CD_2Cl_2)

The minor peaks at ~17 ppm and ~4.5-6 ppm correspond to the *cis*- and *trans*- isomers of Pd(xantphos)$(I)_2$, which form as a decomposition product of Pd(xantphos)(Ph)(I). These compounds were previously isolated by Grushin and characterized by VT-NMR. The temperature dependent cis/trans ratios of (xant)Pd$(I)_2$ observed in our experiment are identical to those observed by Grushin.

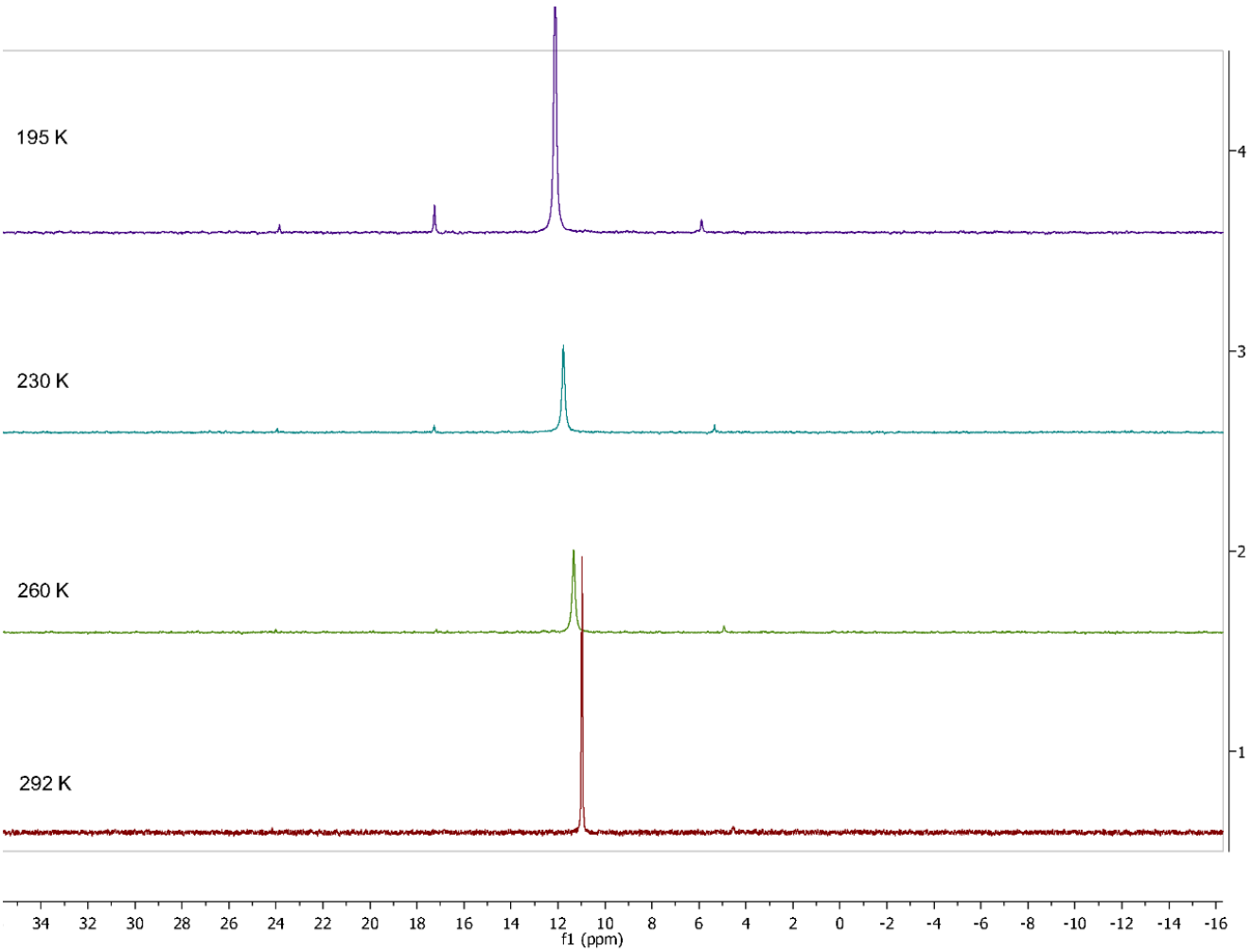


Figure S7. Variable temperature ^{31}P-NMR of Pd(xantphos)(Ph)(I) and 1 equiv. Yb(OTf)$_3$ (0.02M, CD_2Cl_2)

2.3 Determination of catalyst resting state

In an oven-dried 8 mL vial, pyrrolidin-2-one (0.434 mmol, 37 mg) and bromobenzene or iodobenzene (0.434 mmol) were combined with $Pd(dba)_2$ (0.010 mmol, 5 mg), xantphos (0.010 mmol, 5 mg), $Al(OTf)_3$ (0.022 mmol, 10.3 mg), K_3PO_4 (0.675 mmol, 143 mg) and 2 mL C_7D_8 under N_2 atmosphere. The mixture was heated in a capped vial in an aluminum heating block at 110°C for 30 mins. Then, the reaction mixture was allowed to cool, then opened to air and filtered through a pad of celite. ^{31}P NMR spectra of the filtrate was recorded.

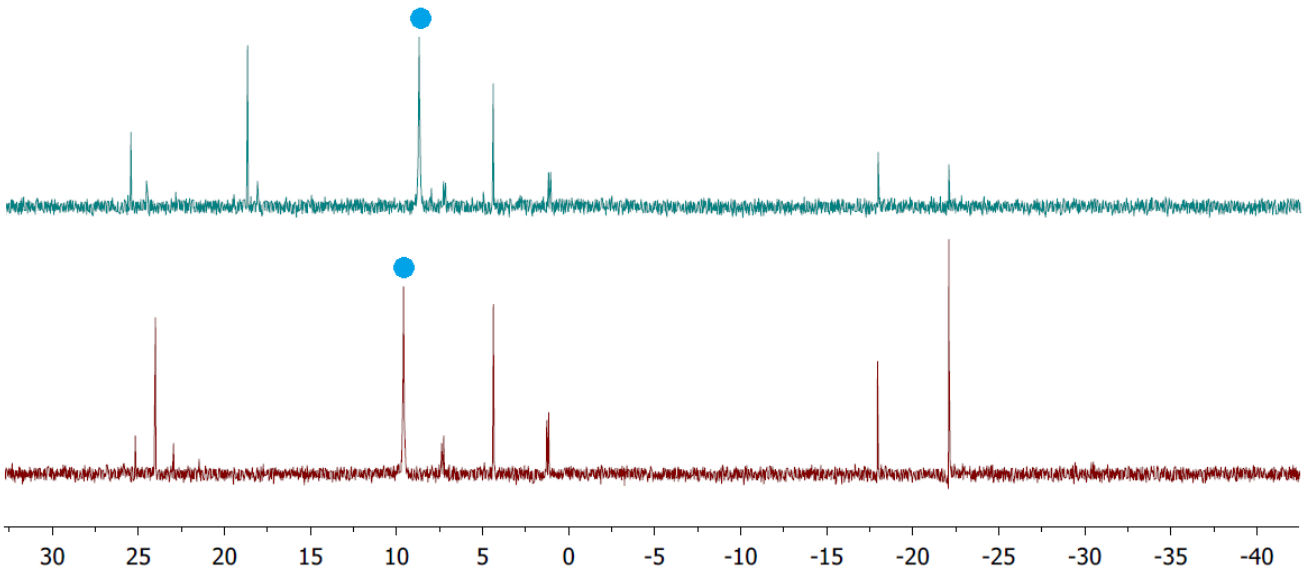


Figure S8. ^{31}P NMR spectra of (top) reaction mixture when bromobenzene was used, and (bottom) reaction mixture when iodobenzene was used. The blue marker indicates the peak corresponding to (xant)Pd(Ph)(Br) and (xant)Pd(Ph)(I), respectively.

2.4 ^{31}P NMR of (xant)Pd(Ph)(X)/[(xant)Pd(Ph)][BAr$^F_4$] mixtures

Stock solutions of (xant)Pd(Ph)(X) (**22** X = Br, **23** X = I) (6.16 mM, $CDCl_3$) and [(xant)Pd(Ph)][BAr$^F_4$] (**25**) (6.16 mM, $CDCl_3$) were prepared. NMR samples were prepared using different volumes of each stock solution in a manner such that the total [Pd] was constant. A total volume of 600 µL $CDCL_3$ was used for each sample. A range of mole fractions (X_{25} = 0.05 to X_{25} = 0.95) were observed.

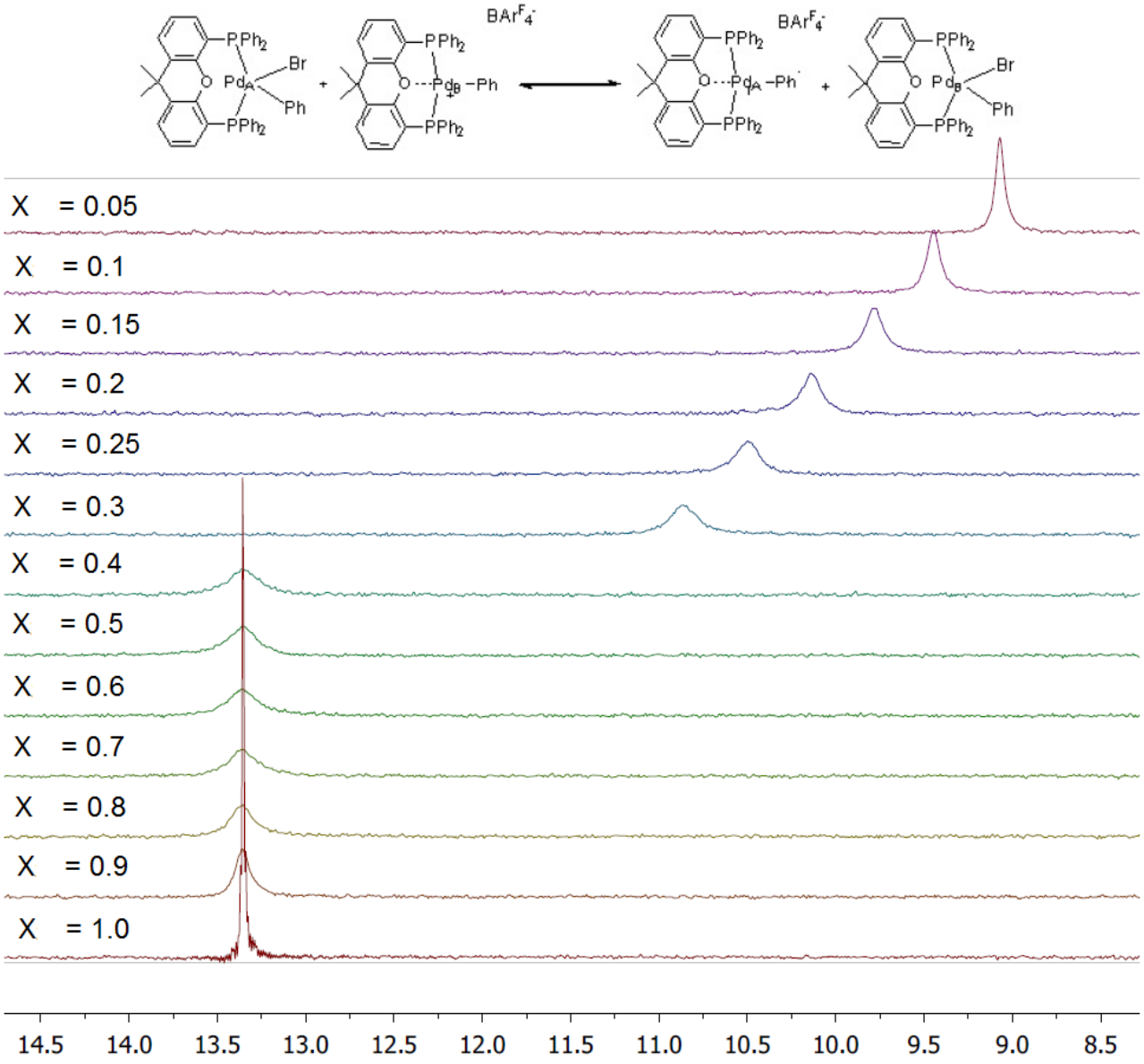


Figure S9. ^{31}P NMR spectra of (xant)Pd(Ph)(Br)/[(xant)Pd(Ph)][BAr$^F_4$] mixtures**.** X corresponds to the mole fraction of [(xant)Pd(Ph)][BAr$^F_4$].

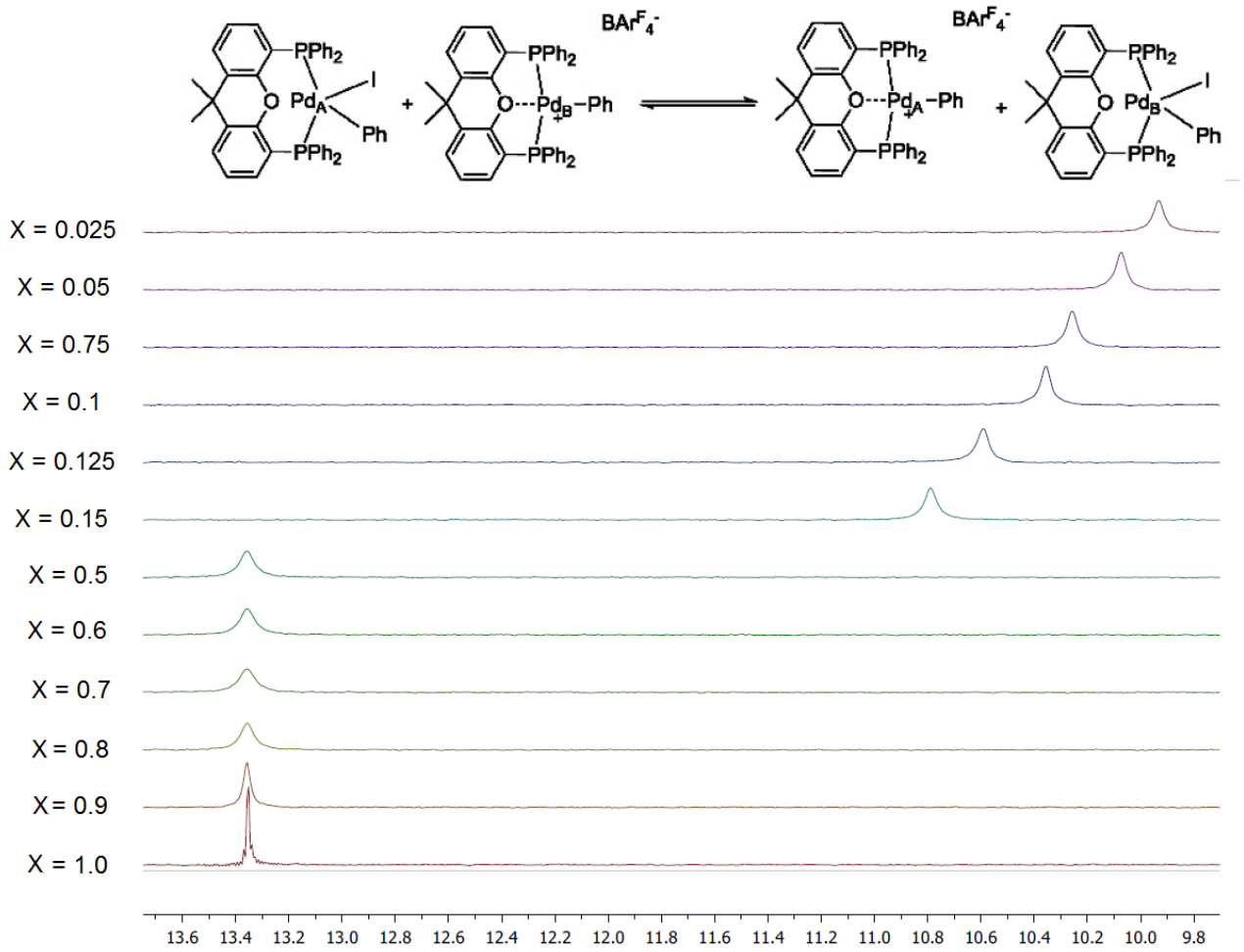


Figure S10. ^{31}P NMR spectra of (xant)Pd(Ph)(I)/[(xant)Pd(Ph)][BAr$^F_4$] mixtures**.** X corresponds to the mole fraction of [(xant)Pd(Ph)][BAr$^F_4$].

III. Kinetic Plots

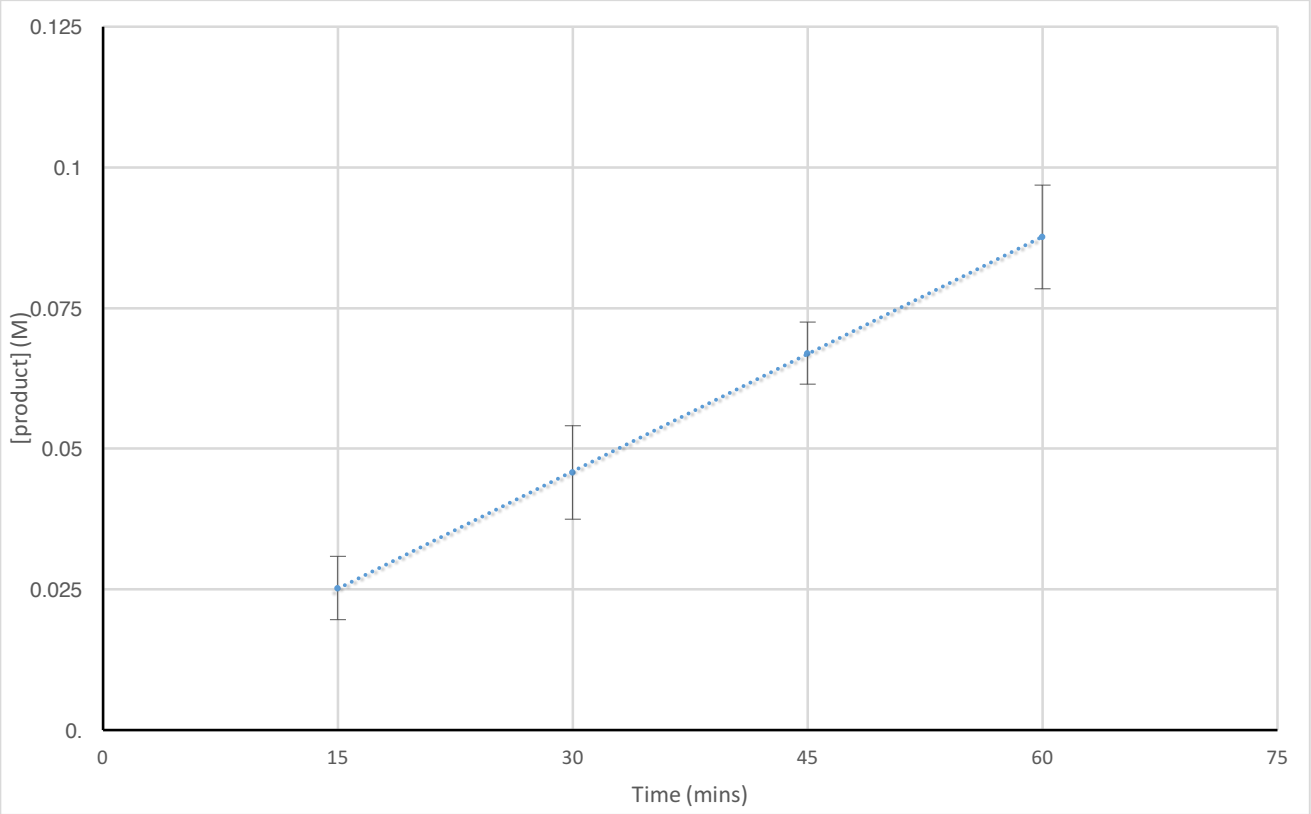


Figure S11. Aryl halide = PhBr ; No Lewis Acid

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 5.00 g anhydrous toluene.

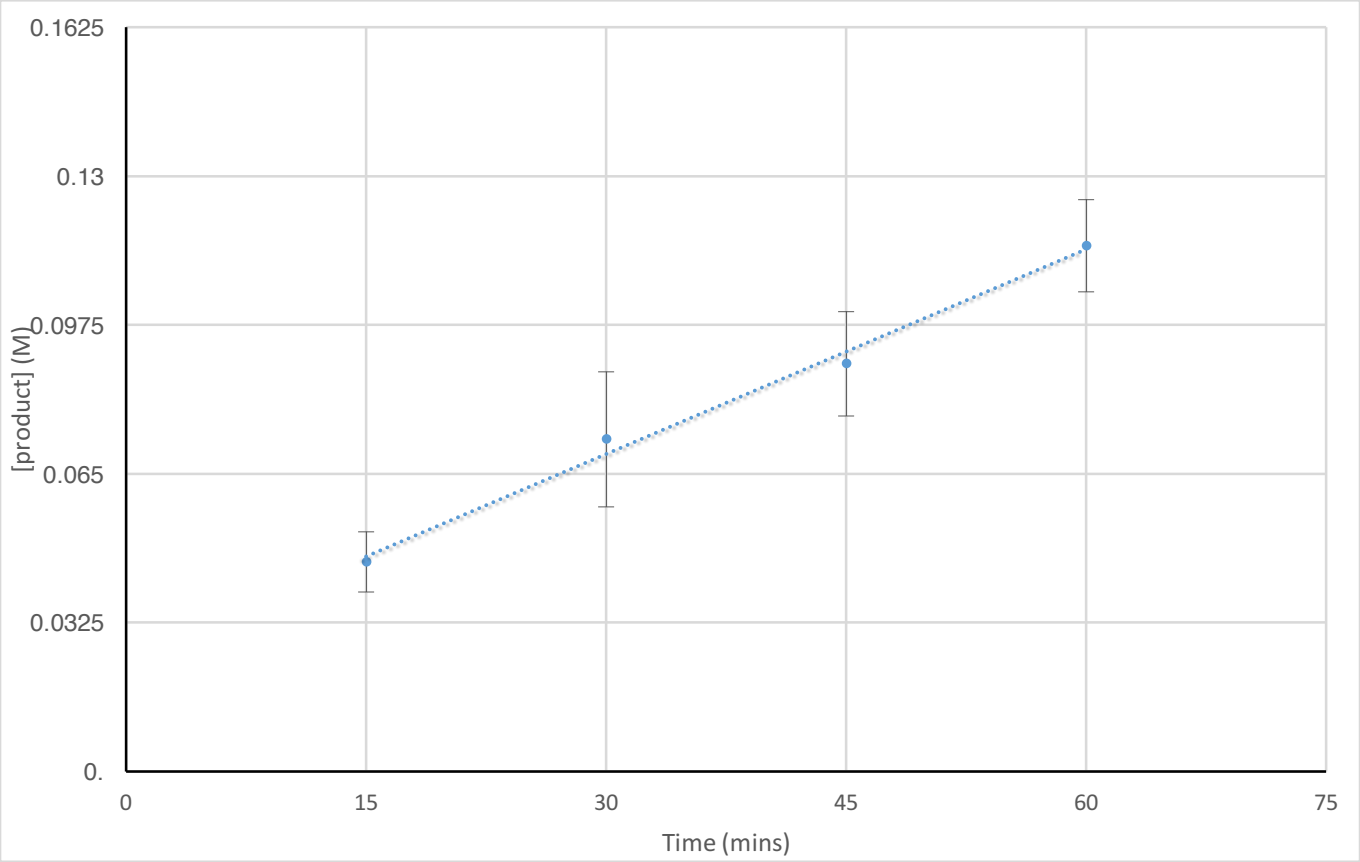


Figure S12. Aryl halide = PhBr ; Lewis acid = $In(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $In(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

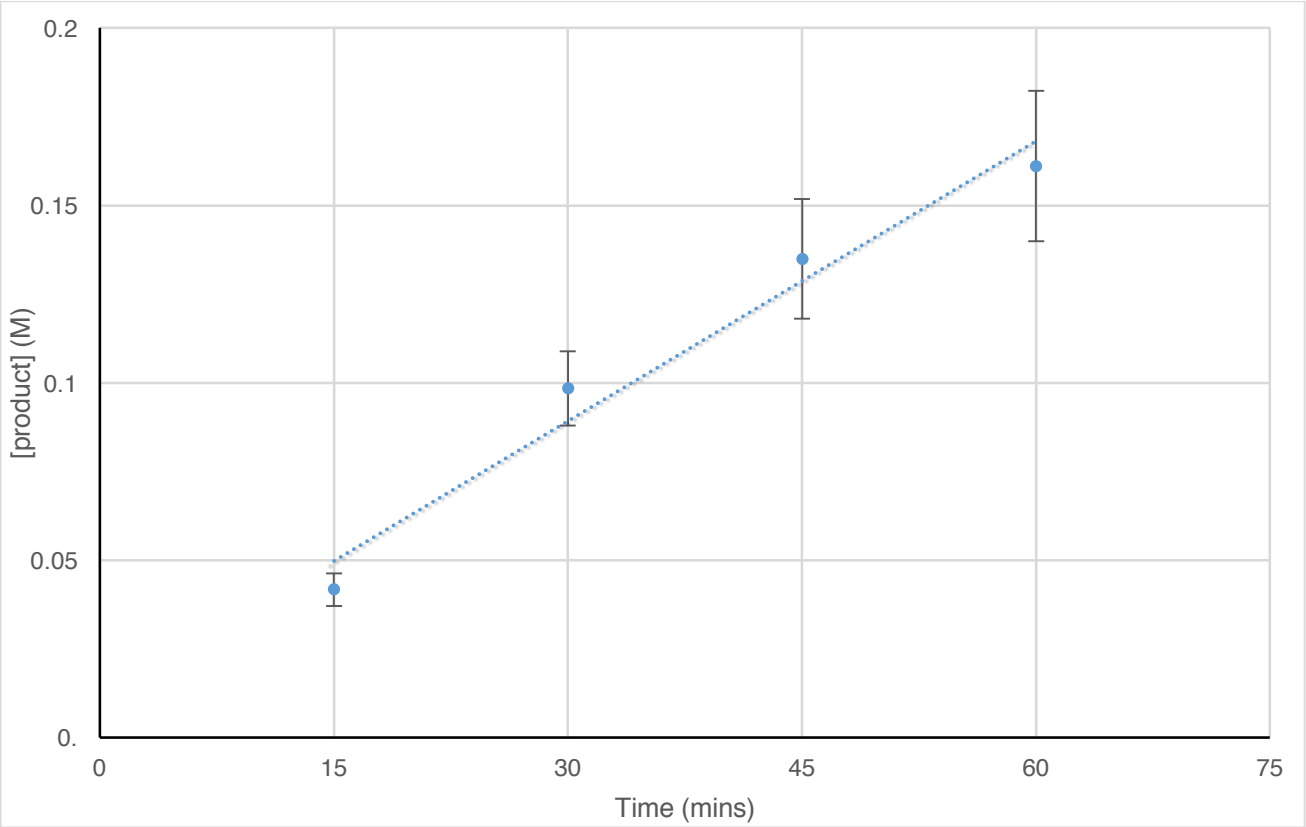


Figure S13. Aryl halide = PhBr ; Lewis acid = $Sc(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Sc(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

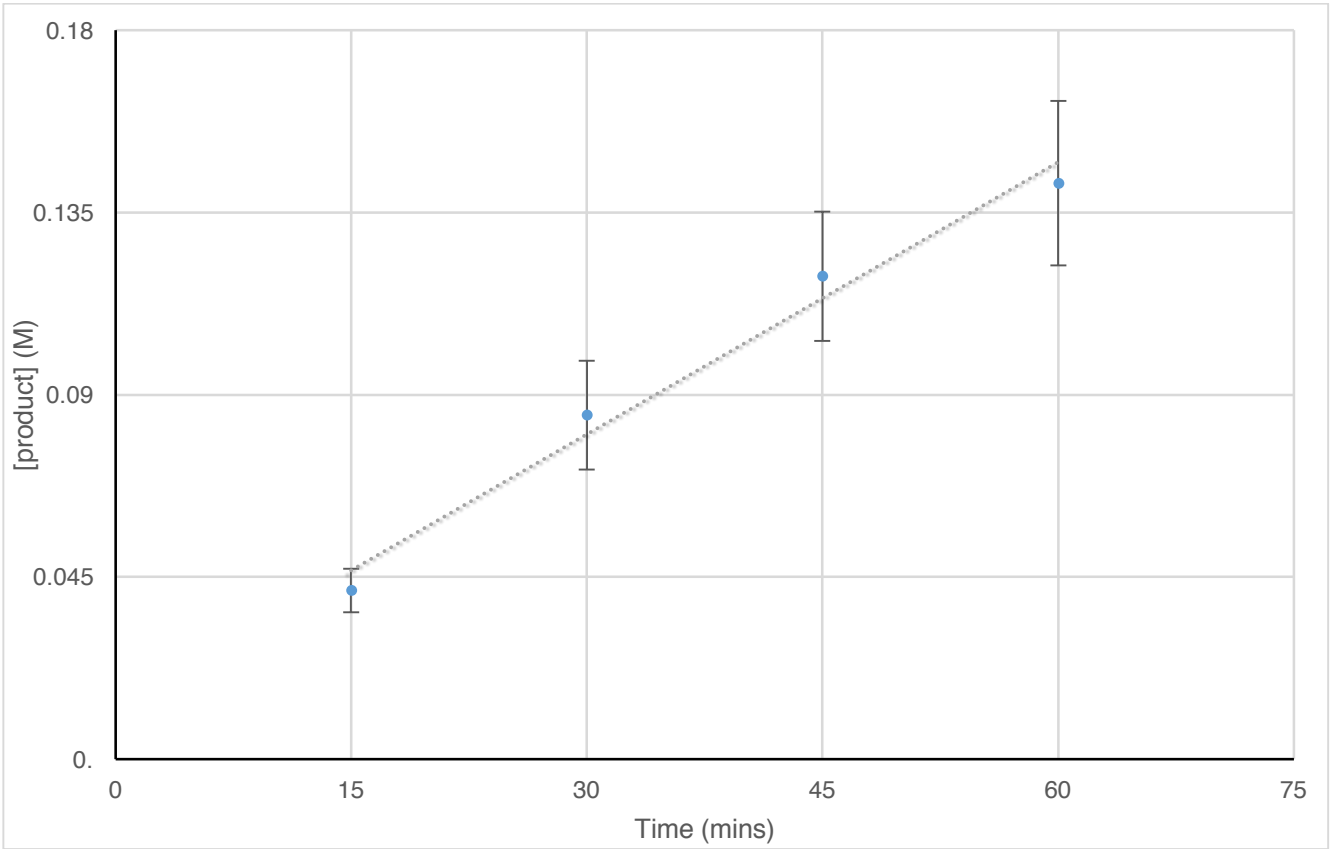


Figure S14. Aryl halide = PhBr ; Lewis acid = $Al(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Al(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

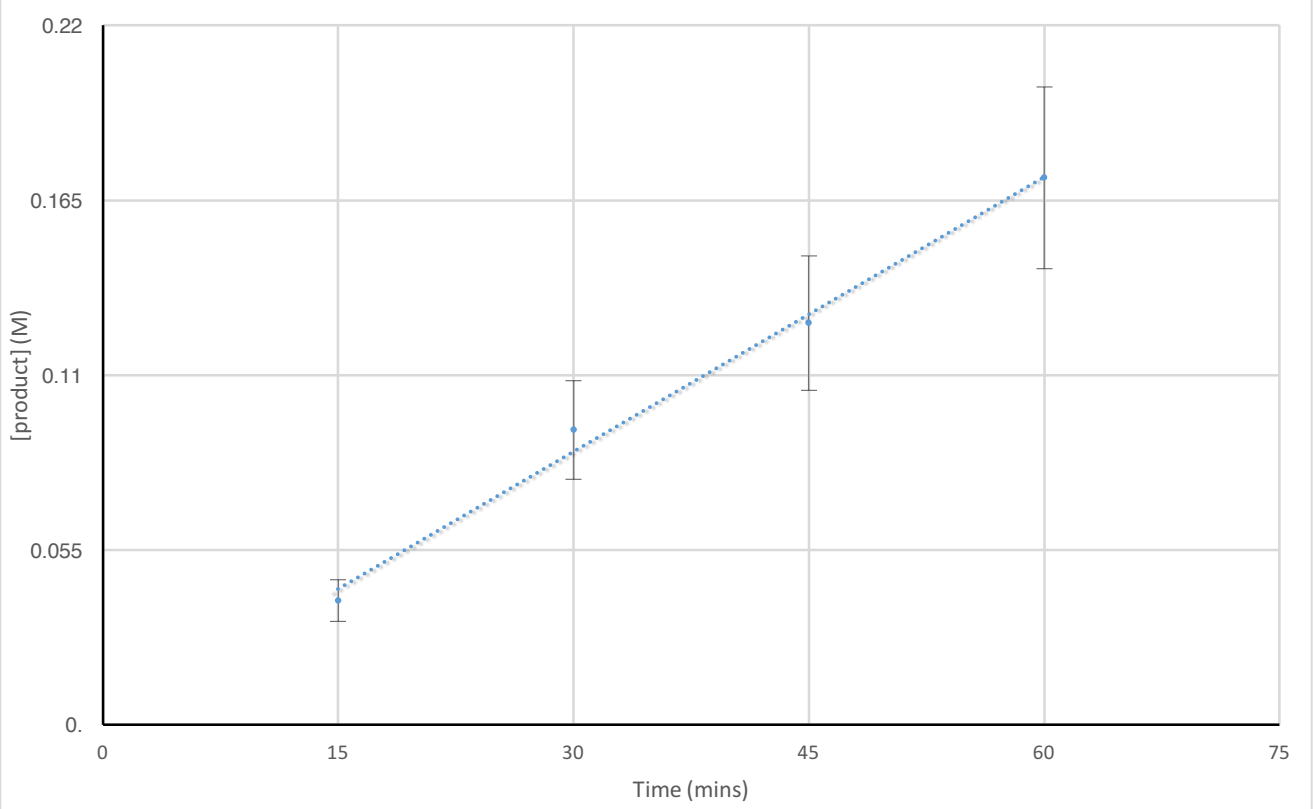


Figure S15. Aryl halide = PhBr ; Lewis acid = $Yb(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Yb(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

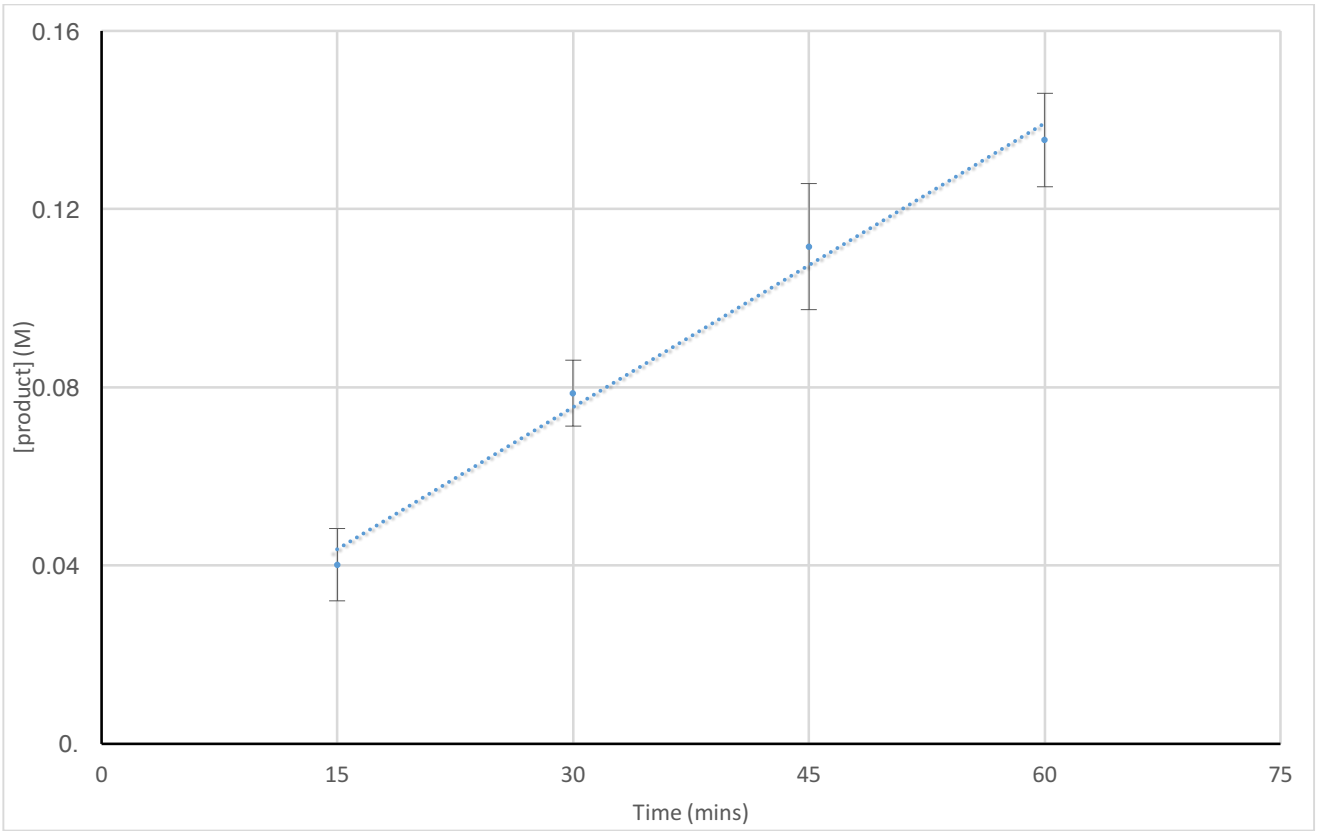


Figure S16. Aryl halide = PhBr ; Lewis acid = $Zn(OTf)_2$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol bromobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Zn(OTf)_2$ (1.5 mol %), 5.00 g anhydrous toluene.

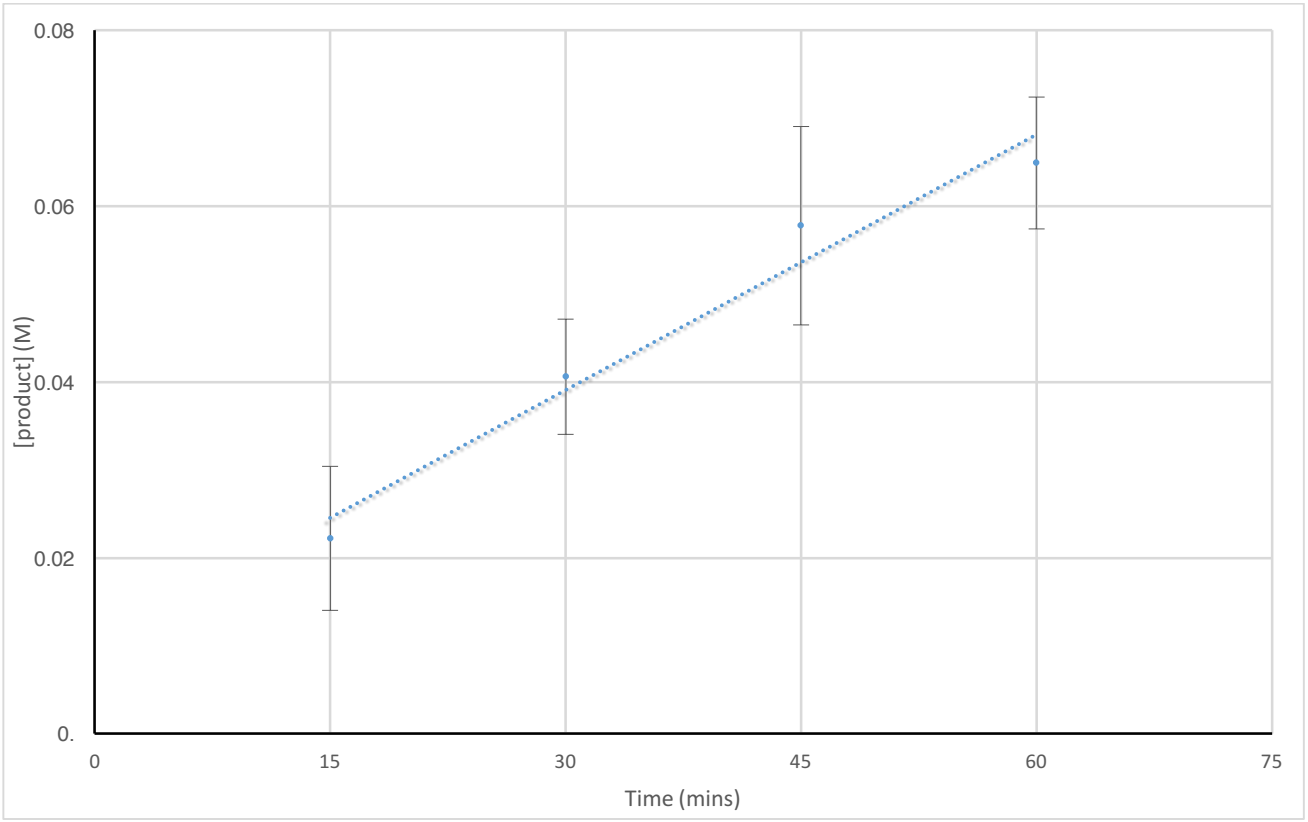


Figure S17. Aryl halide = PhI ; No Lewis Acid

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol iodoobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 5.00 g anhydrous toluene.

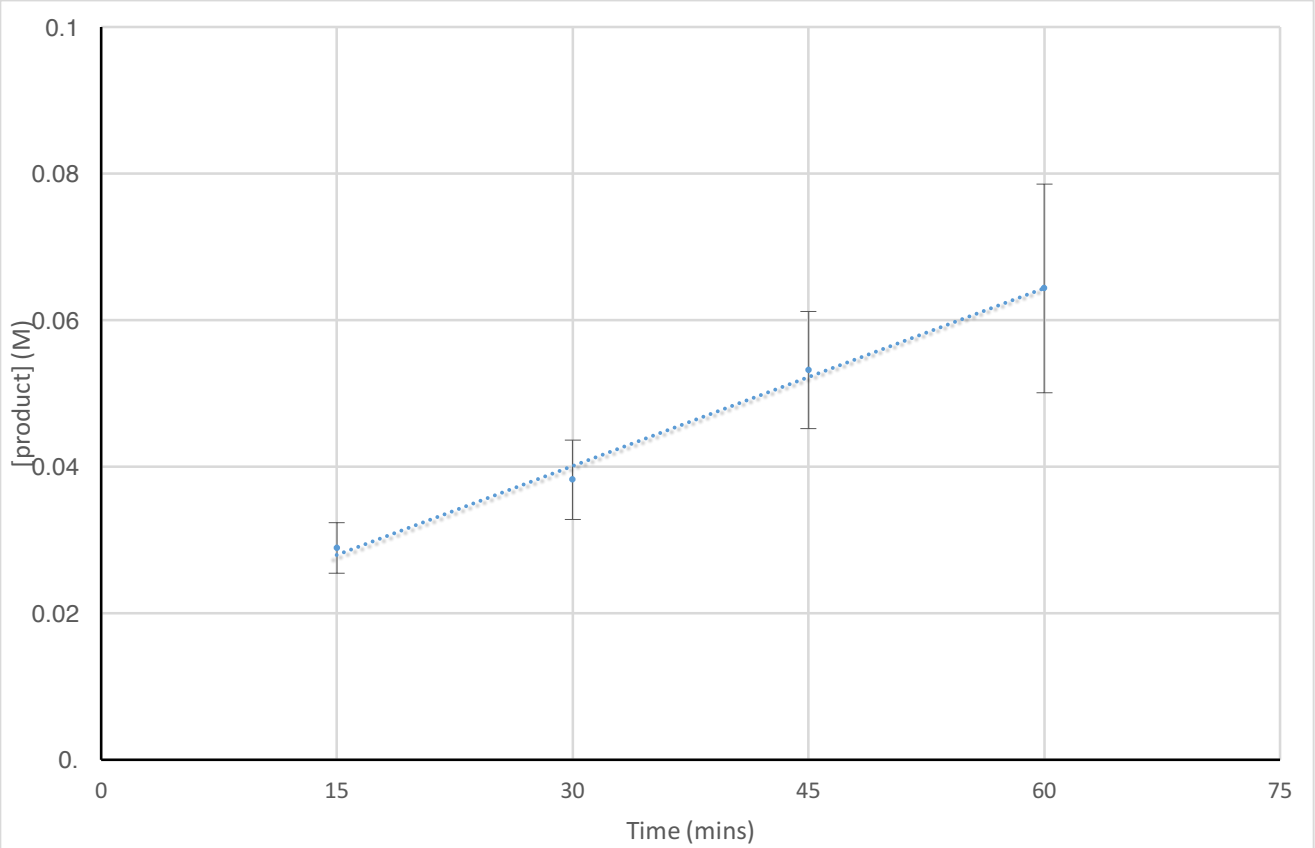


Figure S18. Aryl halide = PhI ; Lewis acid = $In(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol iodobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $In(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

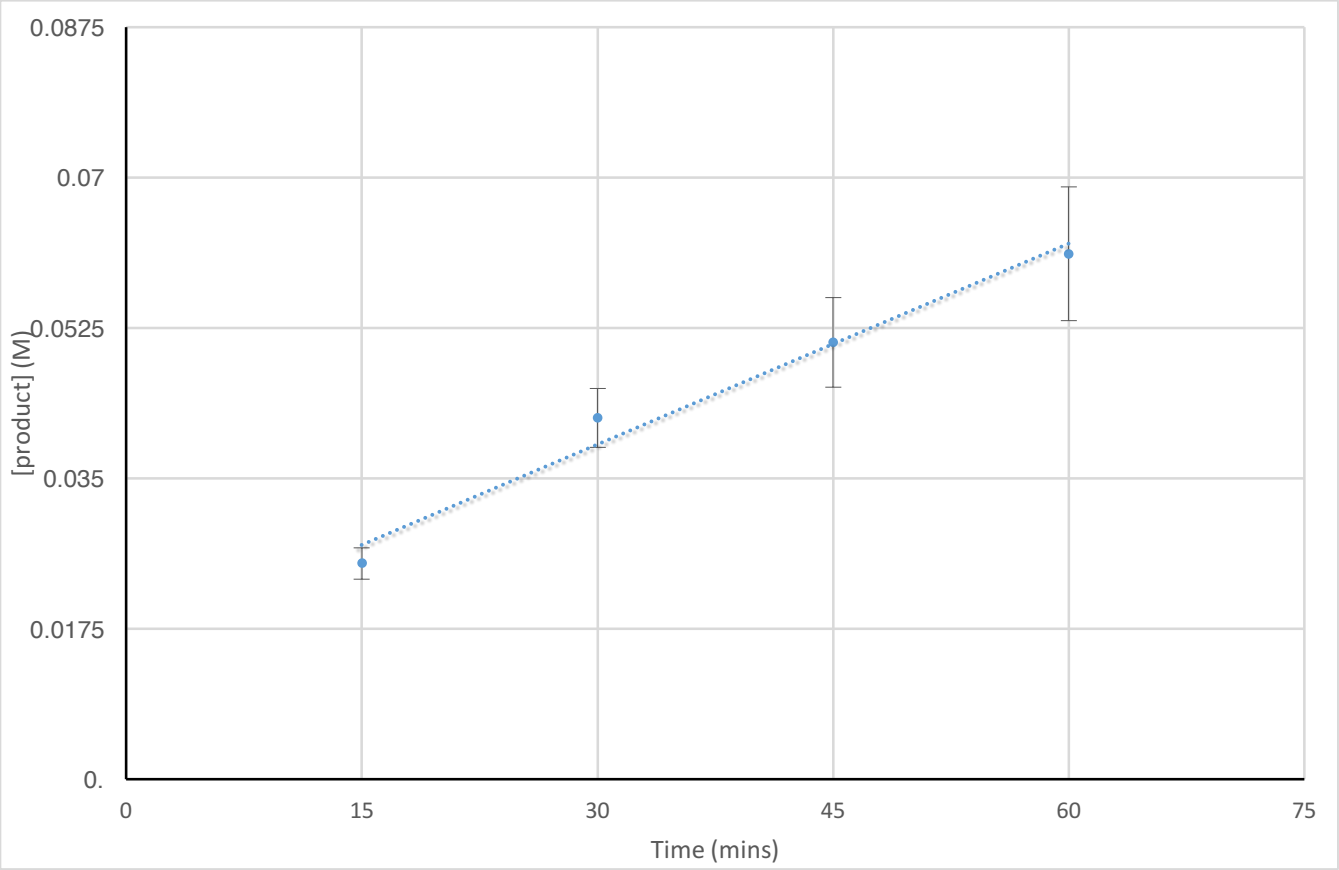


Figure S19. Aryl halide = PhI ; Lewis acid = $Zn(OTf)_2$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol iodobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Zn(OTf)_2$ (1.5 mol %), 5.00 g anhydrous toluene.

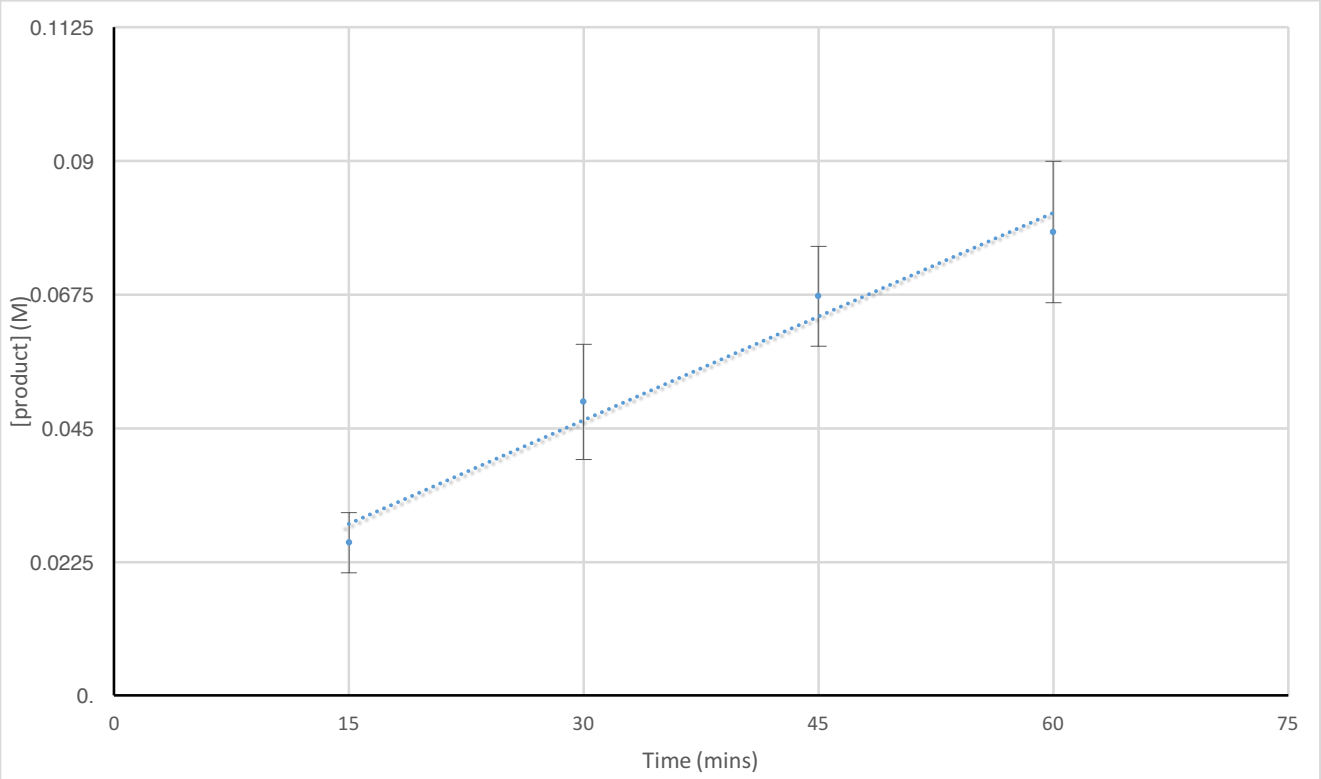


Figure S20. Aryl halide = PhI ; Lewis acid = $Yb(OTf)_3$

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.29 mmol iodobenzene (1.1 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 0.017 mmol $Yb(OTf)_3$ (1.5 mol %), 5.00 g anhydrous toluene.

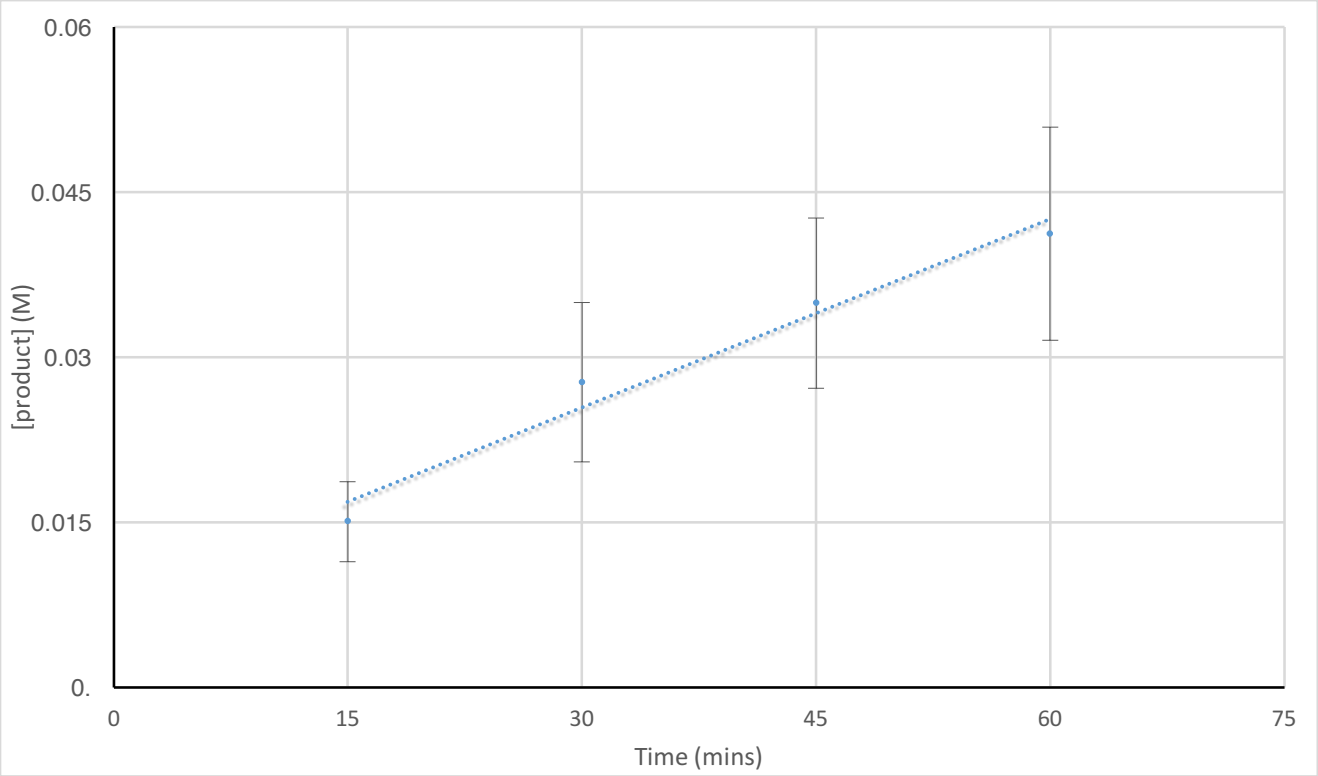


Figure S21. Aryl halide = PhOTf ; No Lewis Acid

Reaction conditions: 1.18 mmol pyrrolidin-2-one (1 eq), 1.18 mmol phenyl triflate (1.0 eq), 1.5 mmol K_3PO_4 (1.2 eq), 0.017 mmol $Pd(dba)_2$ (1.5 mol%), 0.019 mmol xantphos (1.6 mol %), 5.00 g anhydrous toluene.

IV. References

(1) Fujita, K.; Yamashita, M.; Puschmann, F.; Alvarez-Falcon, M. M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 9044-9045.
(2) Miloserdov, F. M.; McMullin, C. L.; Belmonte, M. M.; Benet-Buchholz, J.; Bakhmutov, V. I.; MacGregor, S. A.; Grushin, V. V.*Organometallics* **2014**, *33*, 736-752.
(3) Zalesskiy, S. S.; Ananikov, V. P. *Organometallics* **2012**, *31*, 2302-2309.
(4) Wu, Z.; Peng, S.; Zhang, L.; Yang, T.; Yao, H.; Lin, A. J. *J. Org. Chem.* **2016**, *81*, 2166-2173.
(5) Maity, P.; Kundu, D.; Ranu, B. C. *Adv. Synth. Catal.* **2015**, *357*, 3617-3626.
(6) Mahy, W.; Plucinski, P. K.; Frost, C. G. *Org. Lett.* **2014**, *16*, 5020-5023.
(7) Elemans, J. A. A. W.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Eur. J. Org. Chem.* **2007**, *5*, 751-757.
(8) Mocilac, P.; Tallon, M.; Lough, A. J.; Gallagher, J. F. *CrystEngComm* **2010**, *12*, 3080-3090.
(9) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.*, **2007**, *129*, 7734-7735.
(10) Laha, J. K.; Jethava, K. P.; Dayal, N. *J. Org. Chem*. **2014**, *79*, 8010-8019.
(11) Han, X. *Tetrahedron Lett*. **2010**, *51*, 360-362.
(12) Liu, H.; Laurenczy, G.; Yan, N.; Dyson, P. J. *Chem. Commun.* **2014**, *50*, 341-343.
(13) Li, Y.; Ma, L.; Jia, F.; Li, Z. *J. Org. Chem.* **2014**, 78, 5638-5646.
(14) Yin, J.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 1101-1104.
(15) Antilla, J. C.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 11684-11688.
(16) Kerr, W. J.; Reid, M.; Tuttle, T. *ACS Catal.* **2015**, *5*, 402-410.
(17) Karimi, B.; Behzadnia, H. *Synlett* **2010**, *13*, 2019-2023.
(18) Steffel, L. R.; Cashman, T. J.; Reutershan, M. H.; Linton, B. R. *J. Am. Chem. Soc*. **2007**, *129*, 12956-12957.
(19) Yoshimura, A.; Middleton, K. R.; Luedtke, M. W.; Zhu, C.; Zhdankin, V. V. *J. Org. Chem.* **2012**, *77*, 11399-11404.
(20) Bartolucci, S.; Mari, M.; Bedini, A.; Piersanti, G.; Spadoni, G. *J. Org. Chem*. **2015**, *80*, 3217-3222.

V. NMR spectra (^{1}H and ^{13}C) of cross coupling products and amide starting materials

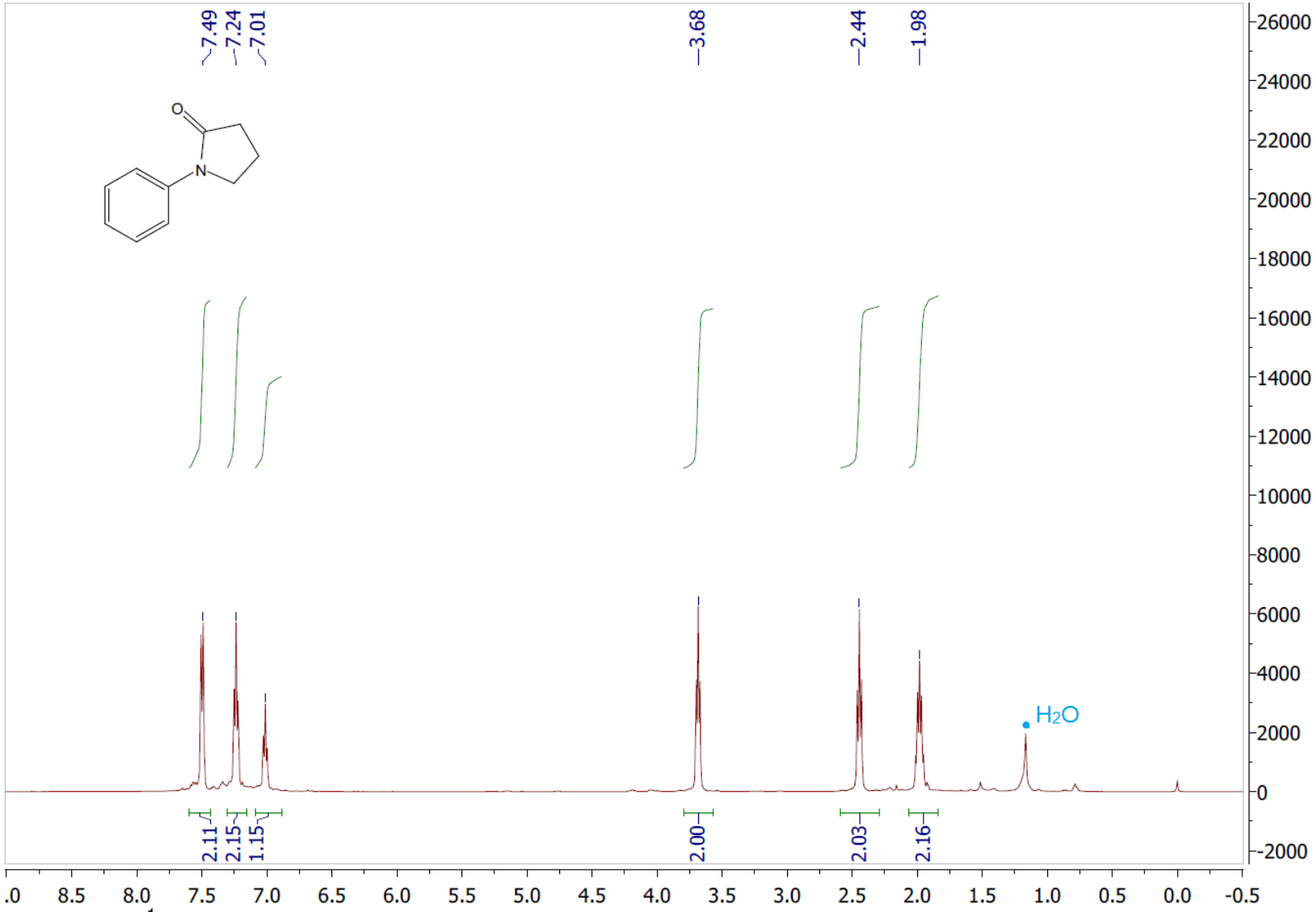


Figure S22. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-phenylpyrrolidin-2-one (**2**).

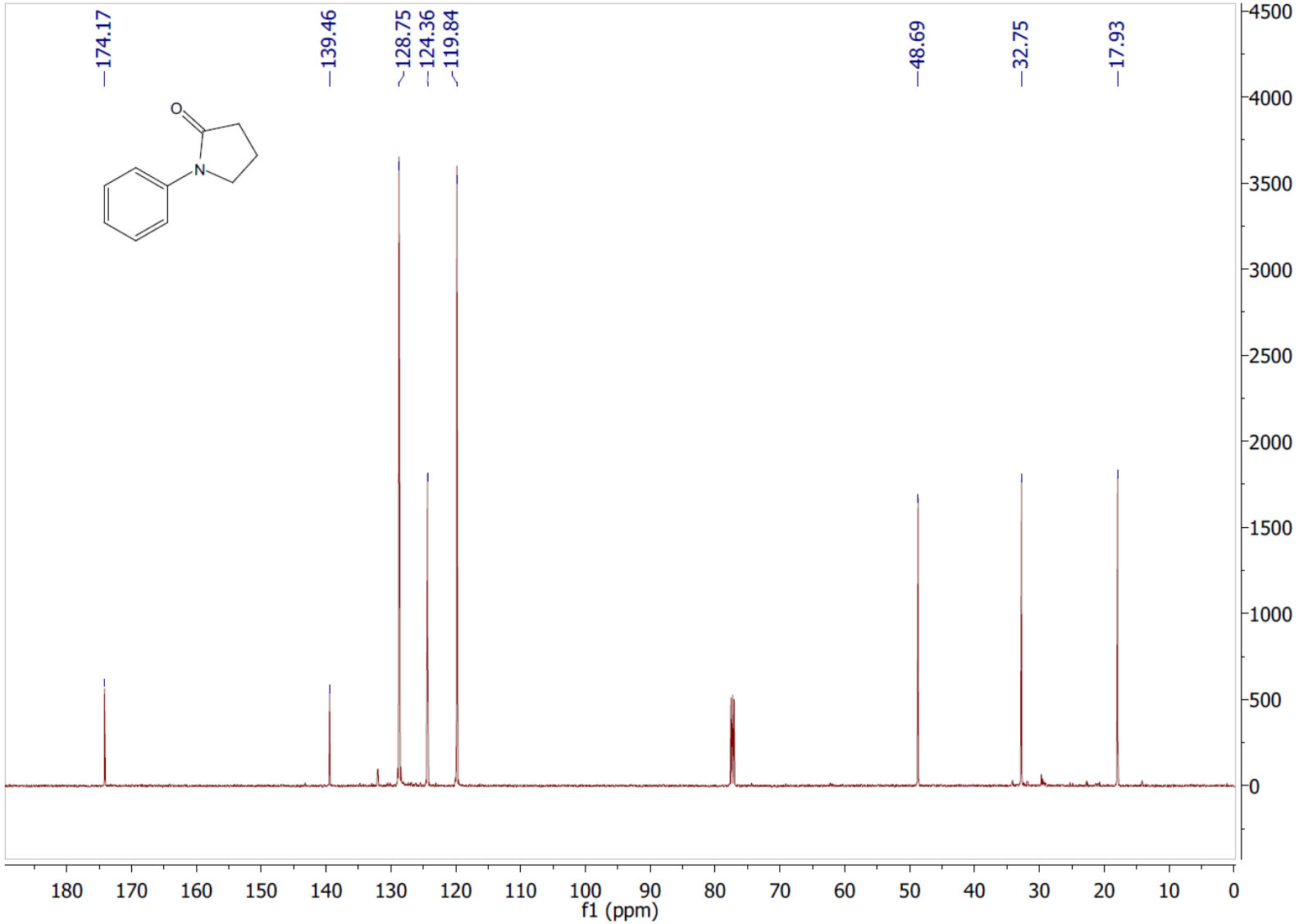


Figure S23. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-phenylpyrrolidin-2-one (**2**).

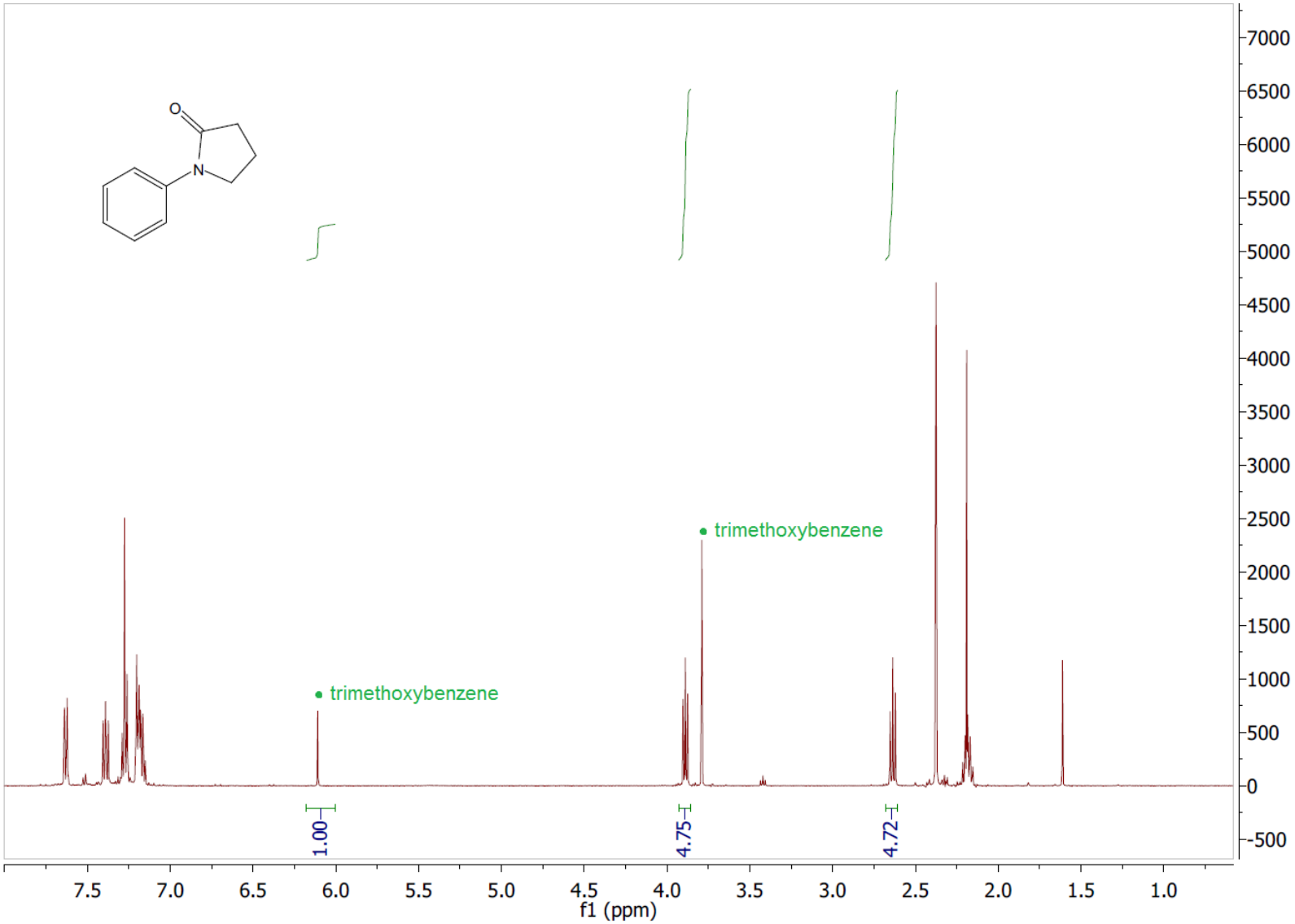


Figure S24. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-phenylpyrrolidin-2-one (**2**) and trimethoxybenzene.

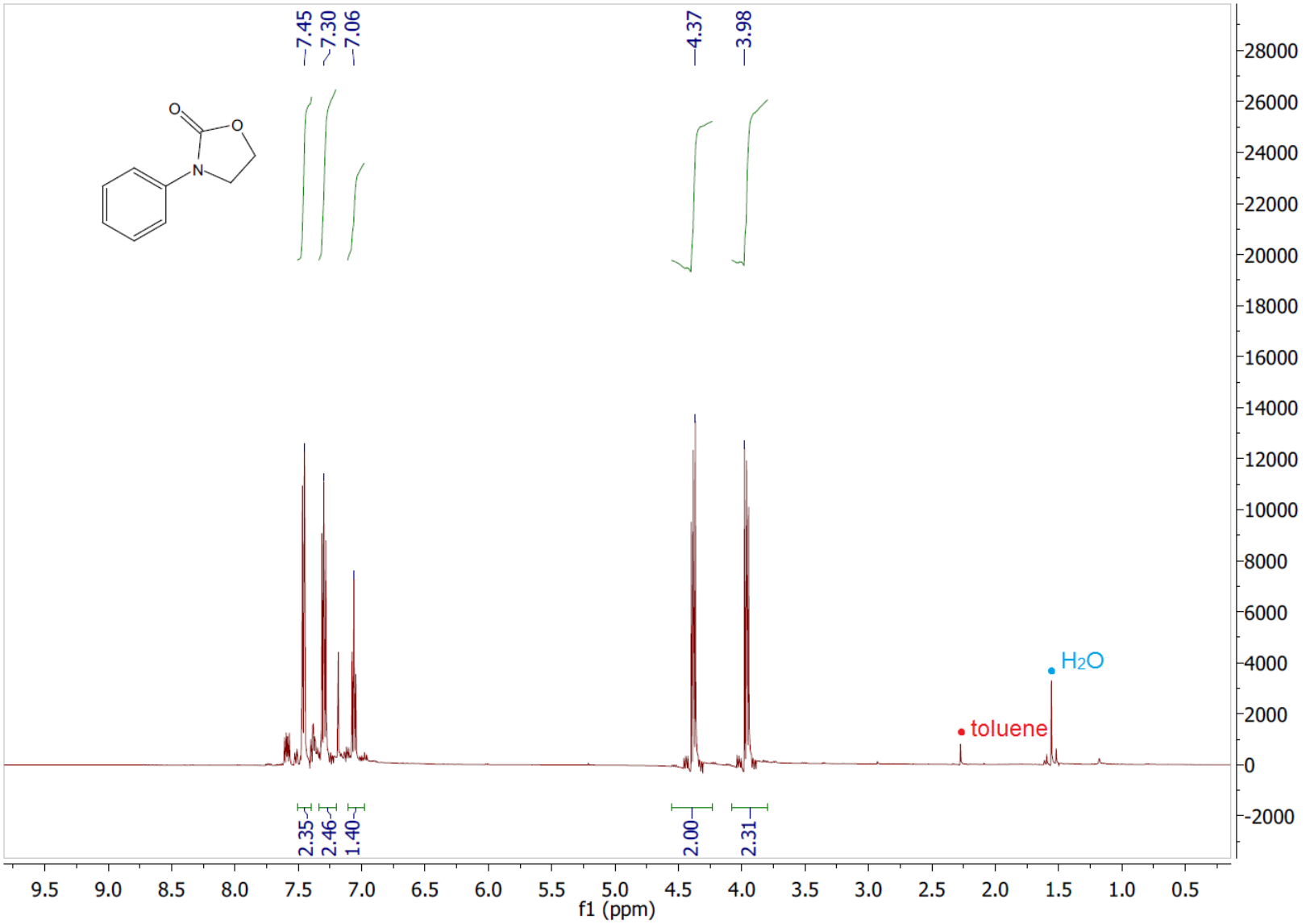


Figure S25. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-phenyloxazolidin-2-one (**3**).

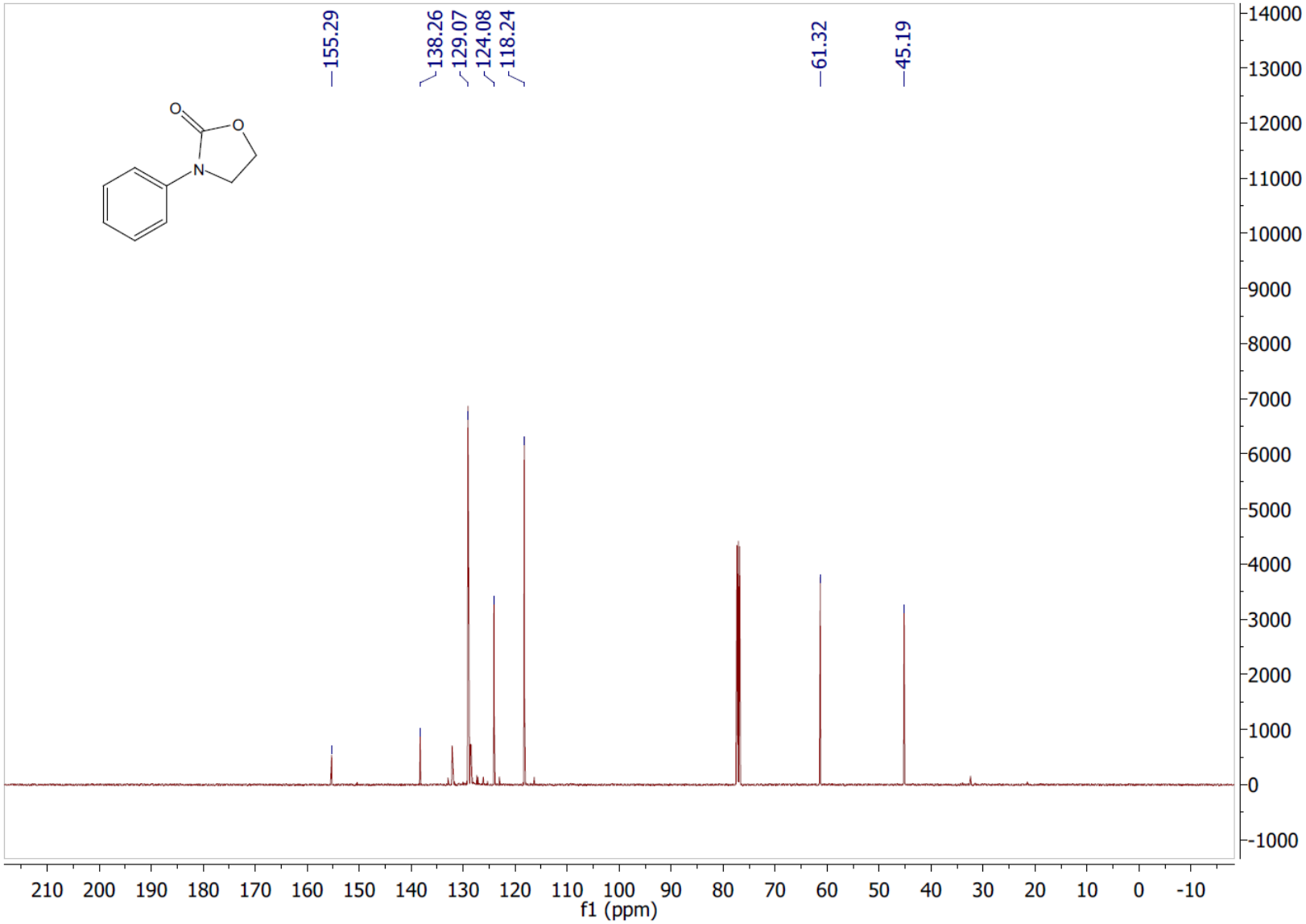


Figure S26. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-phenyloxazolidin-2-one (**3**).

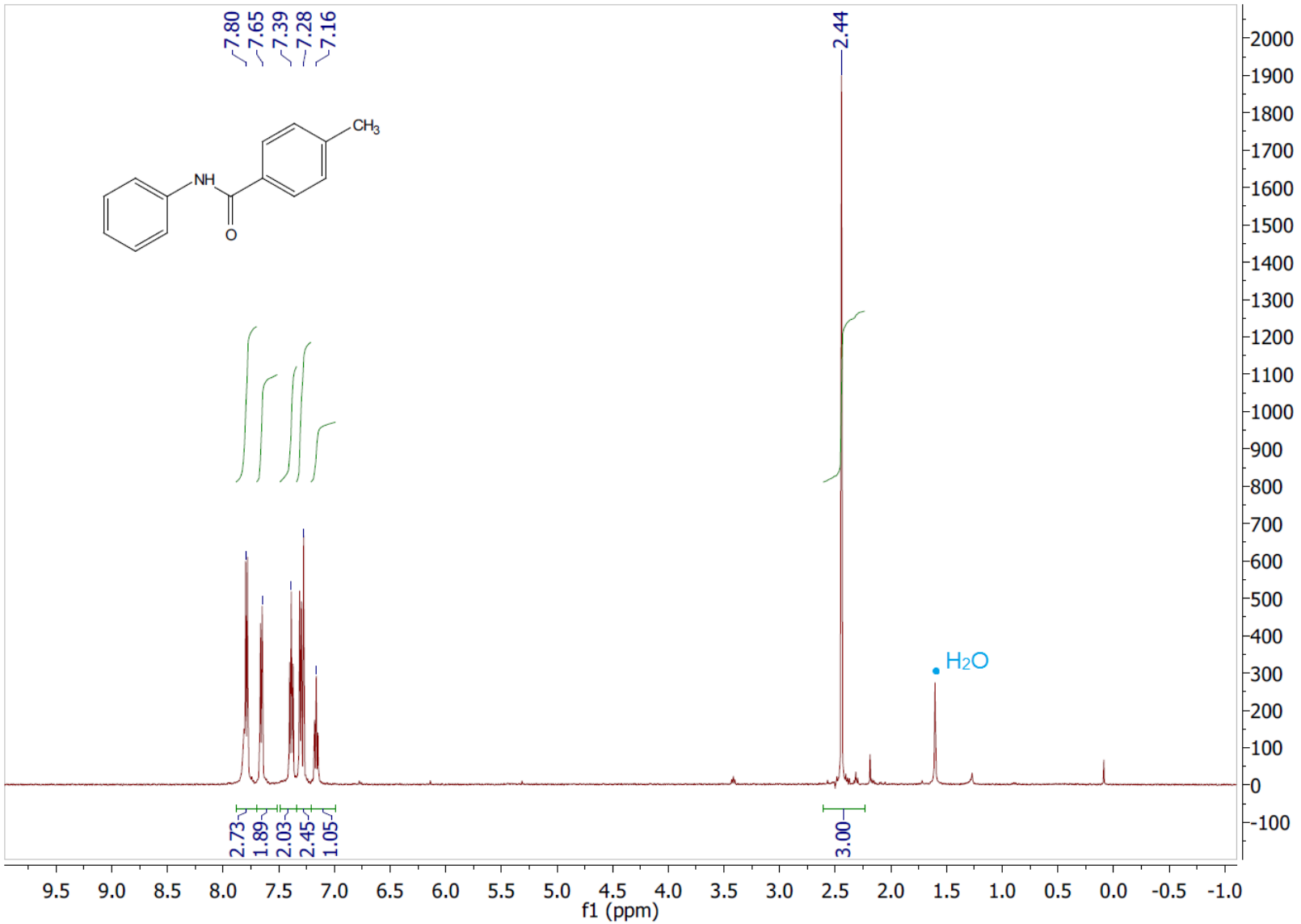


Figure S27. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of 4-methyl-N-phenylbenzamide (**4**).

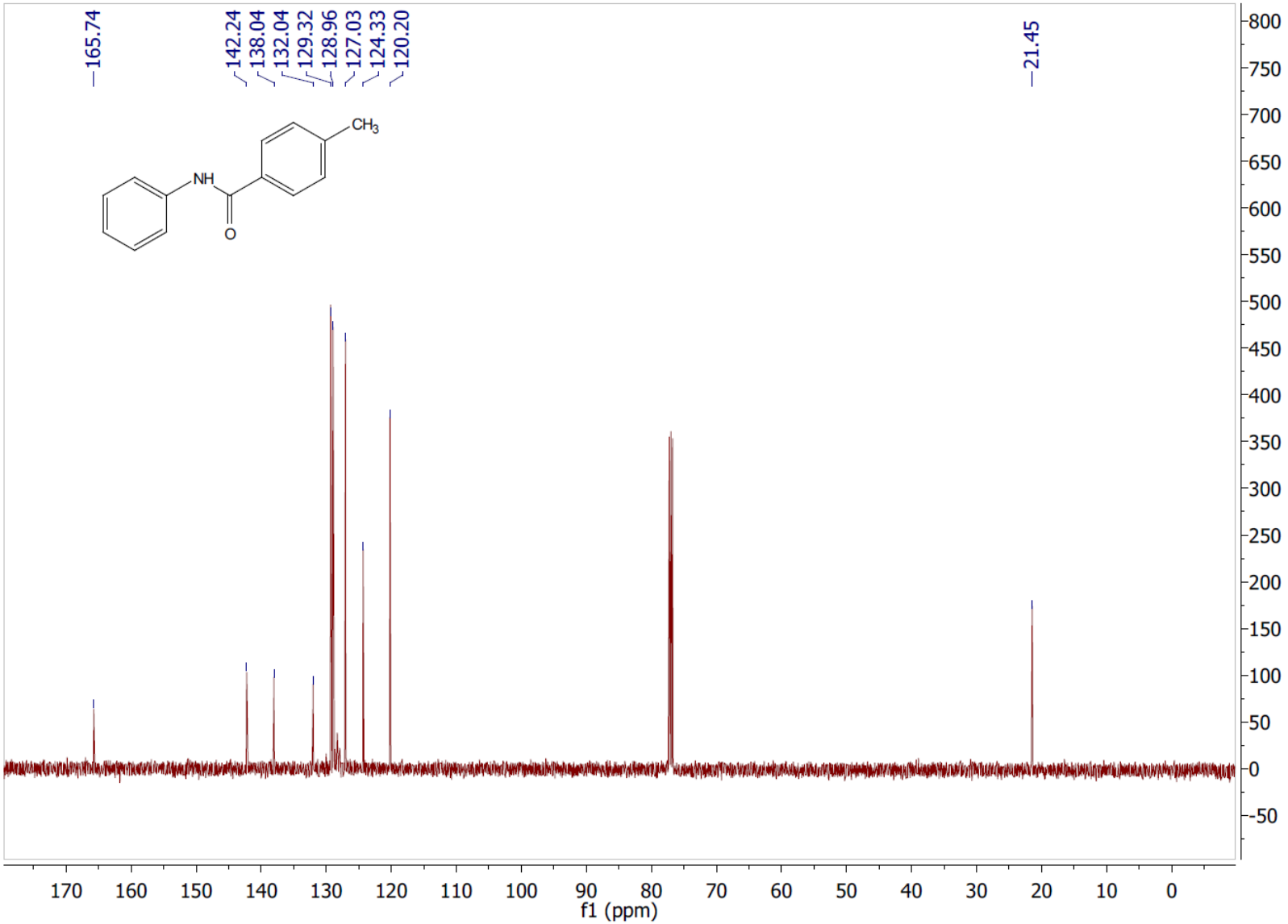


Figure S28. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of 4-methyl-N-phenylbenzamide (**4**).

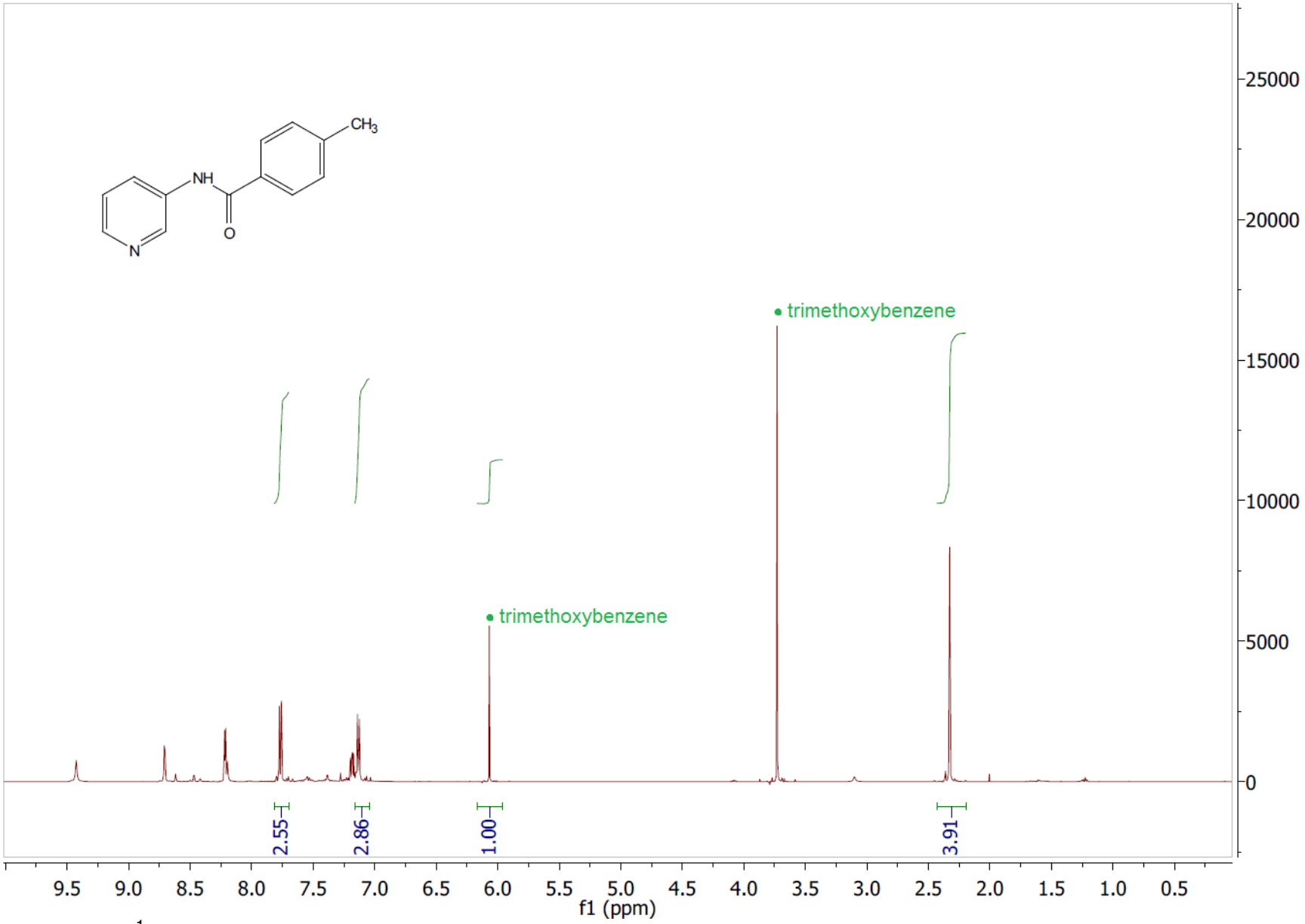


Figure S29. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-(pyridin-3-yl)pyrrolidin-2-one (**5**).

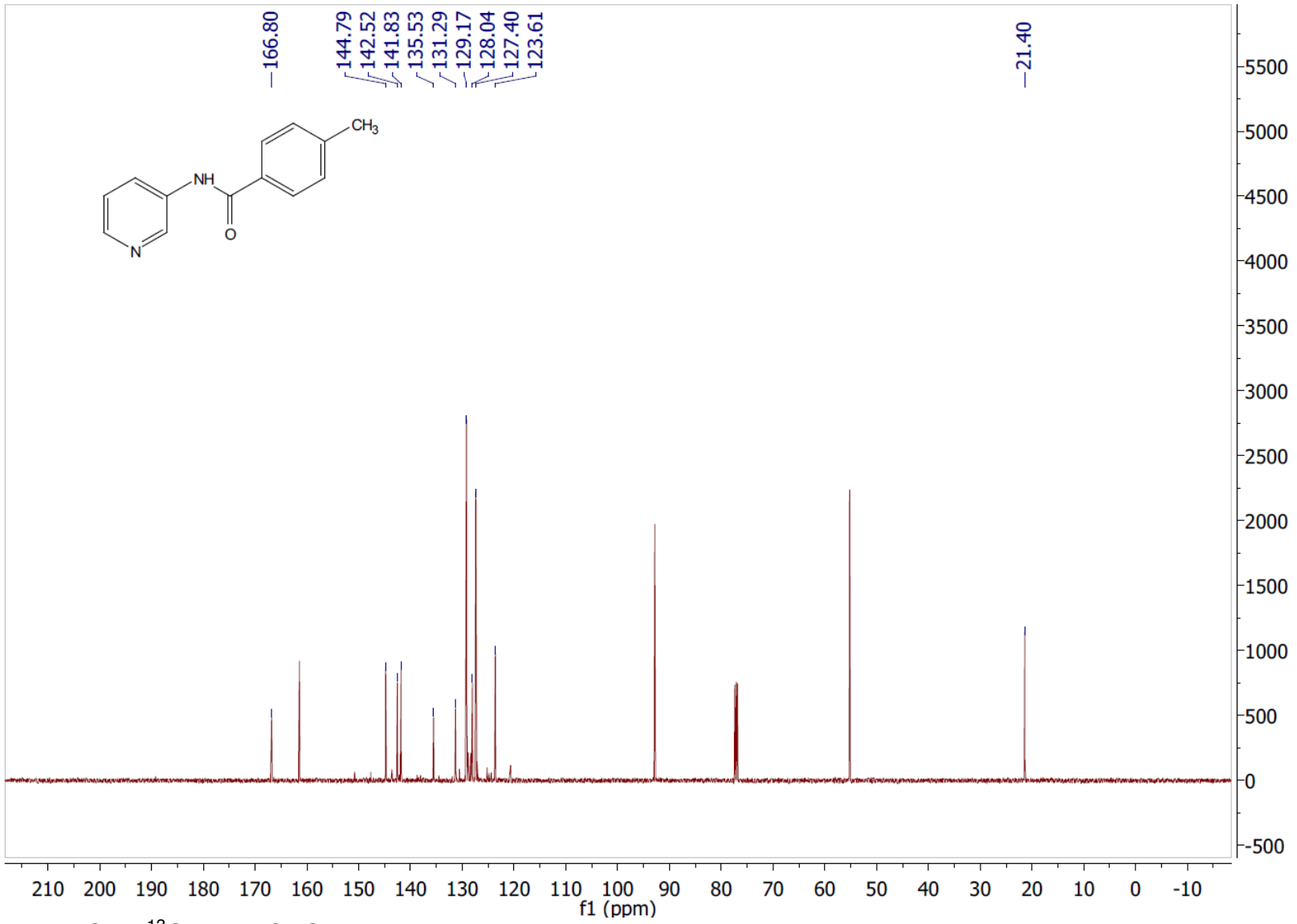


Figure S30. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-(pyridin-3-yl)pyrrolidin-2-one (**5**).

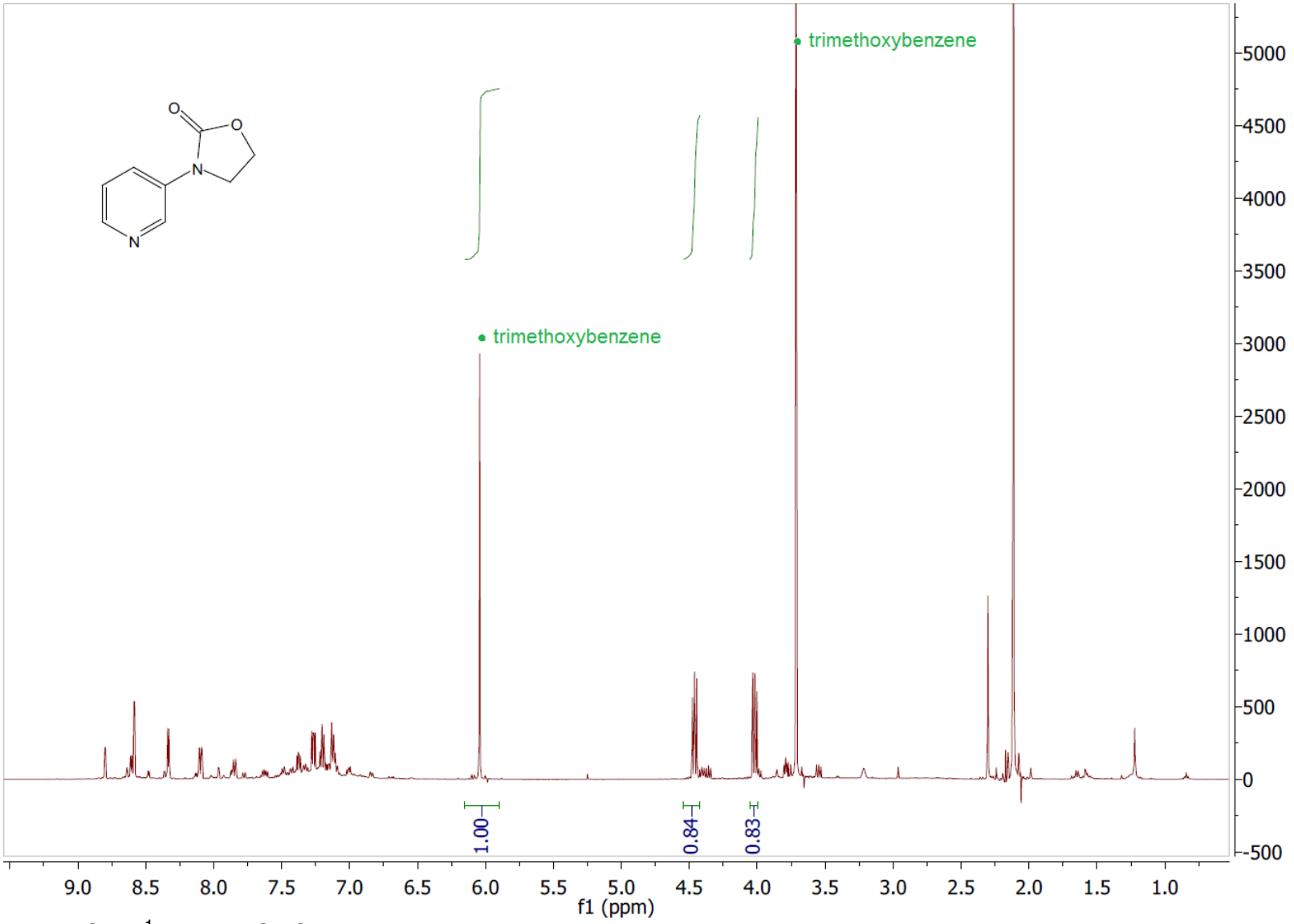


Figure S31. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-(pyridin-3-yl)oxazolidin-2-one (**6**) and trimethoxybenzene.

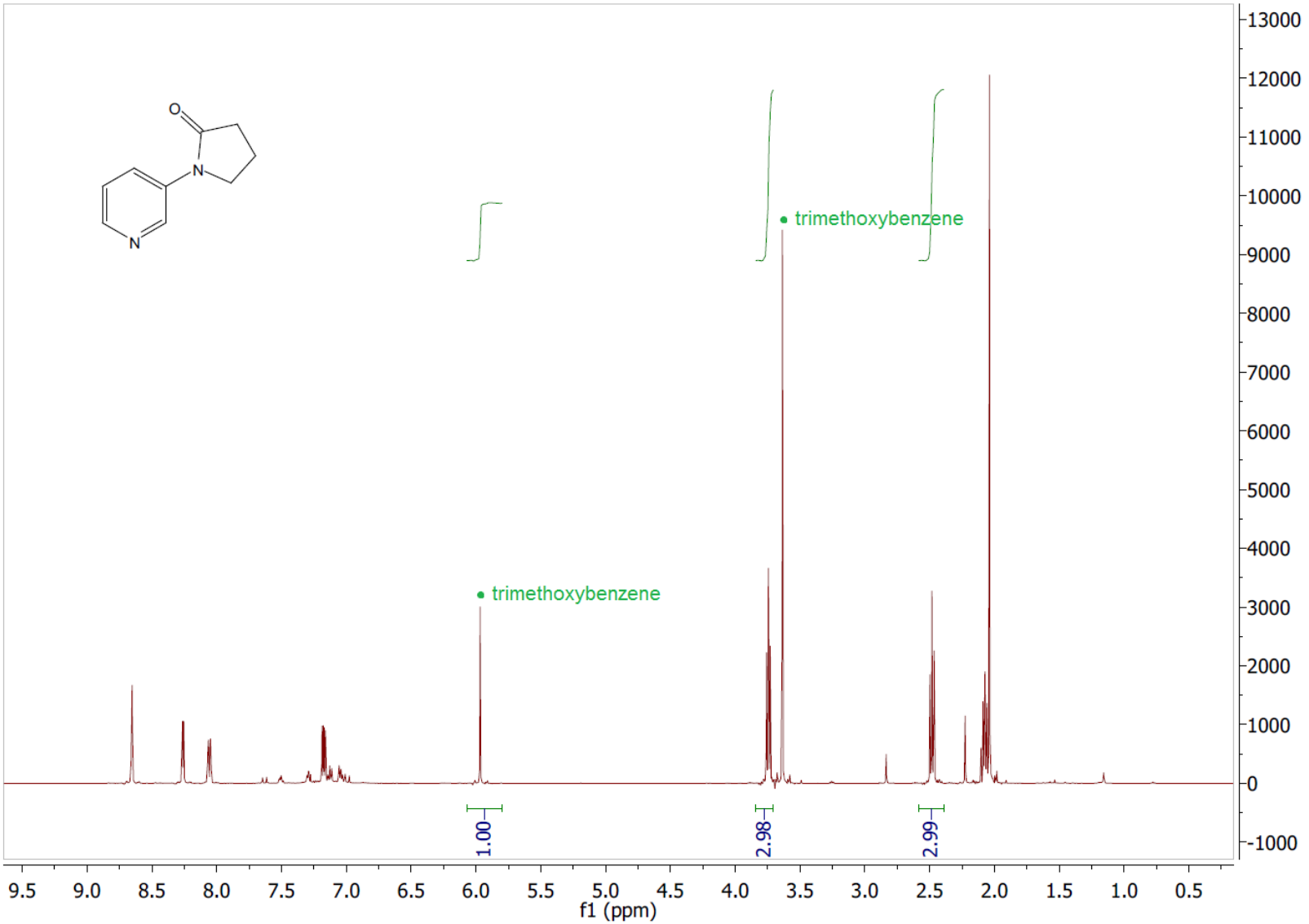


Figure S32. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-(pyridin-3-yl)pyrrolidin-2-one (**7**) and trimethoxybenzene.

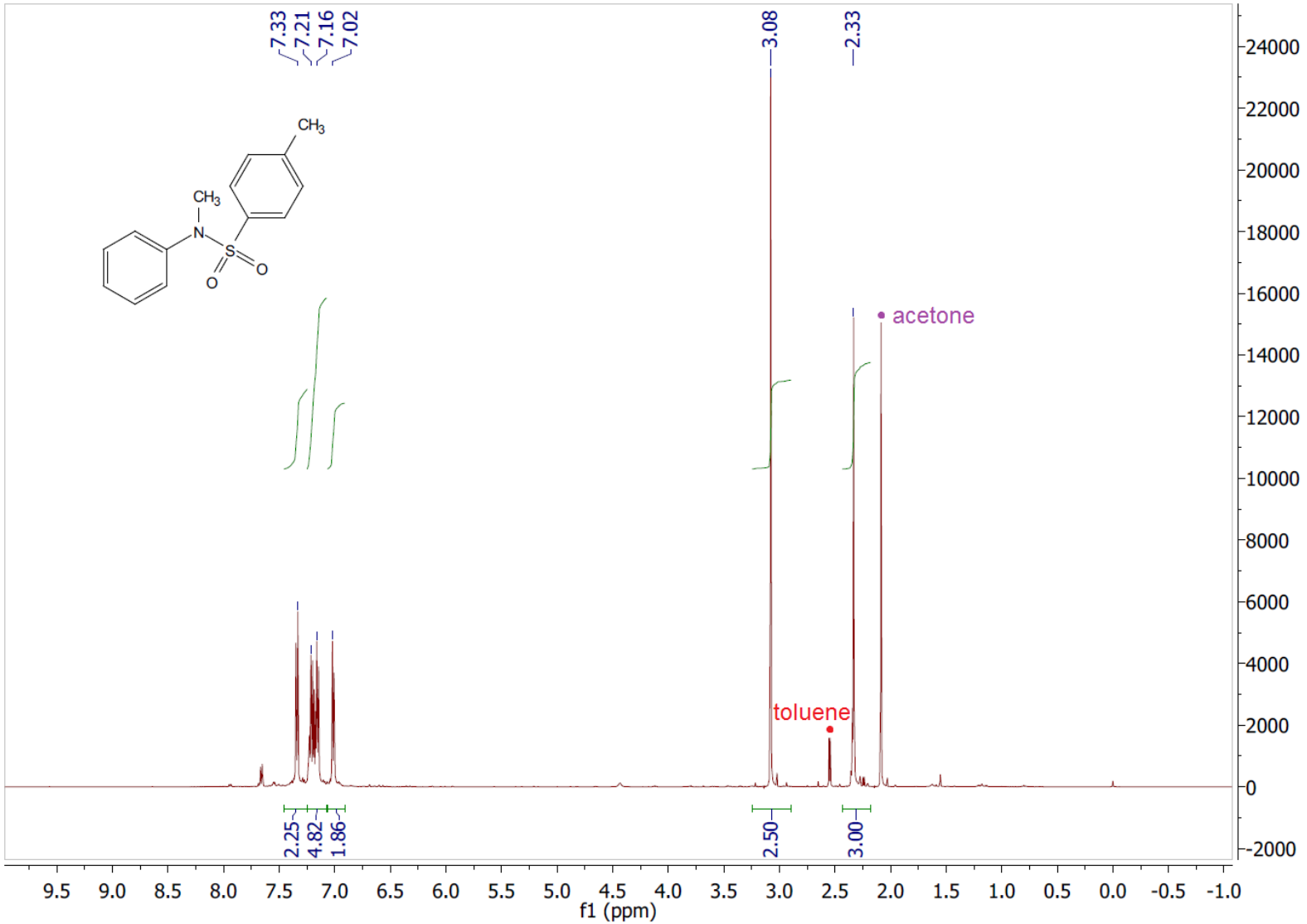


Figure S33. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N,4-dimethyl-N-phenylbenzenesulfonamide (**8**).

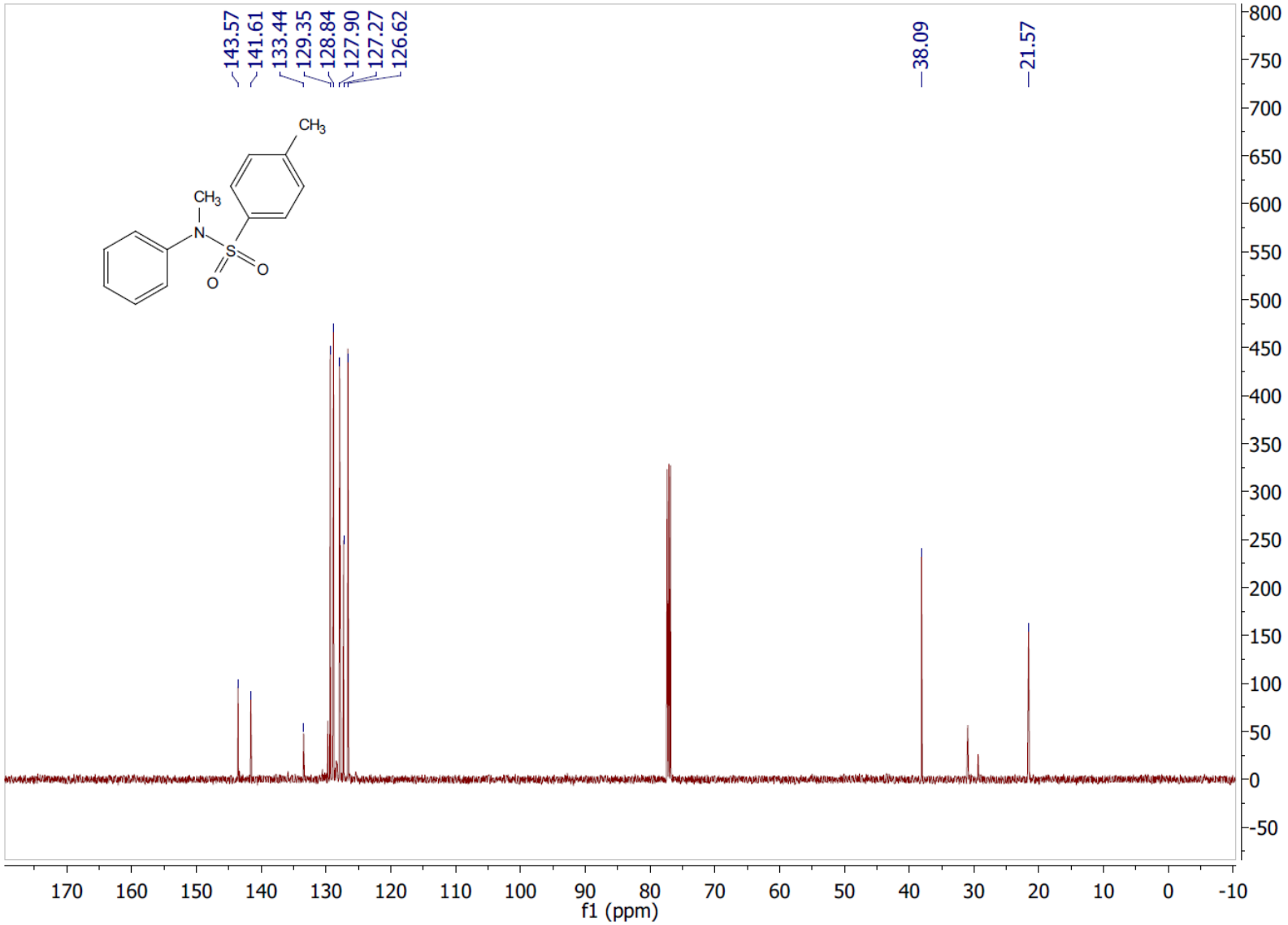


Figure S34. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N,4-dimethyl-N-phenylbenzenesulfonamide (**8**).

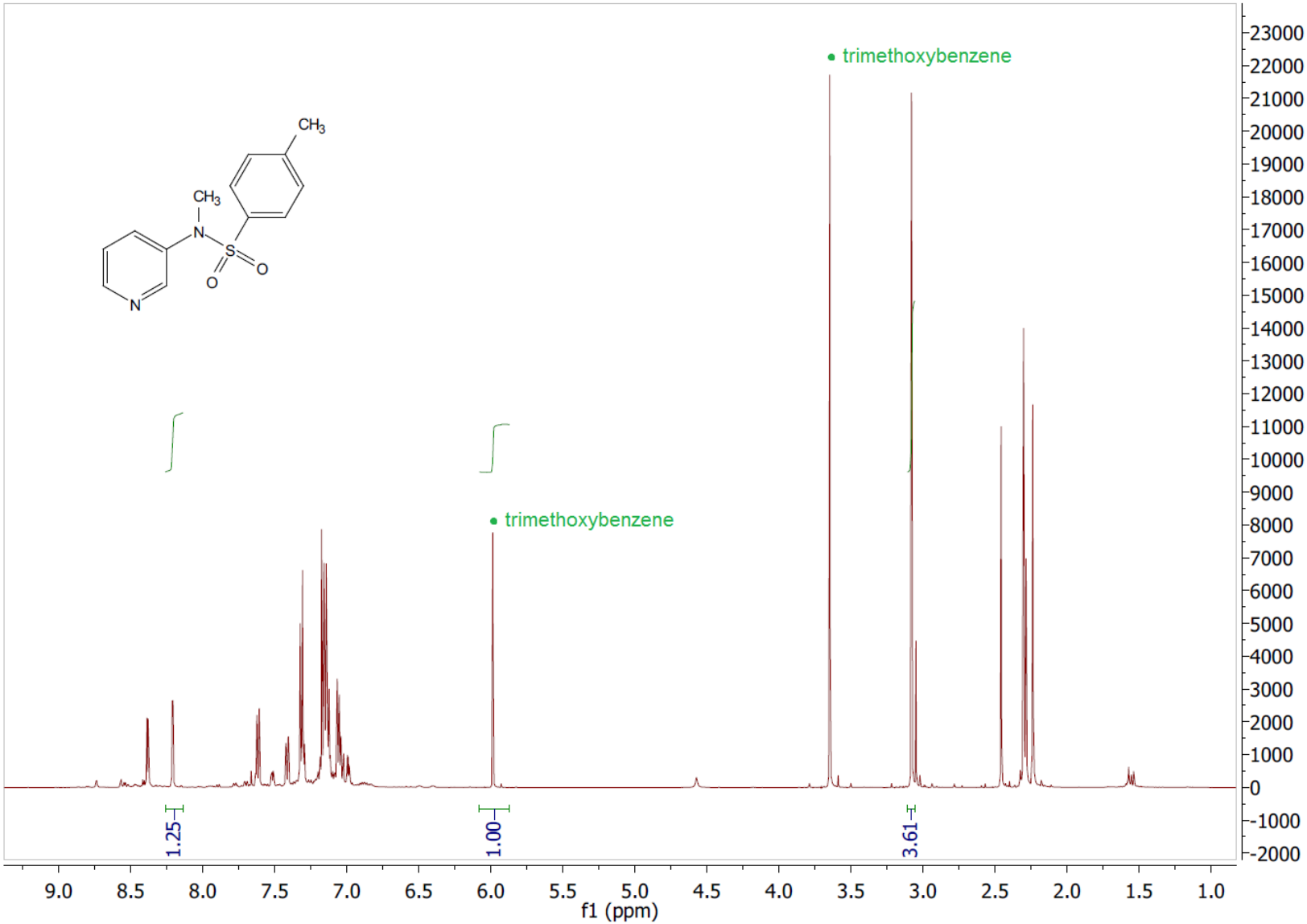


Figure S35. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N,4-dimethyl-N-(pyridin-3-yl)benzenesulfonamide (**9**) and trimethoxybenzene.

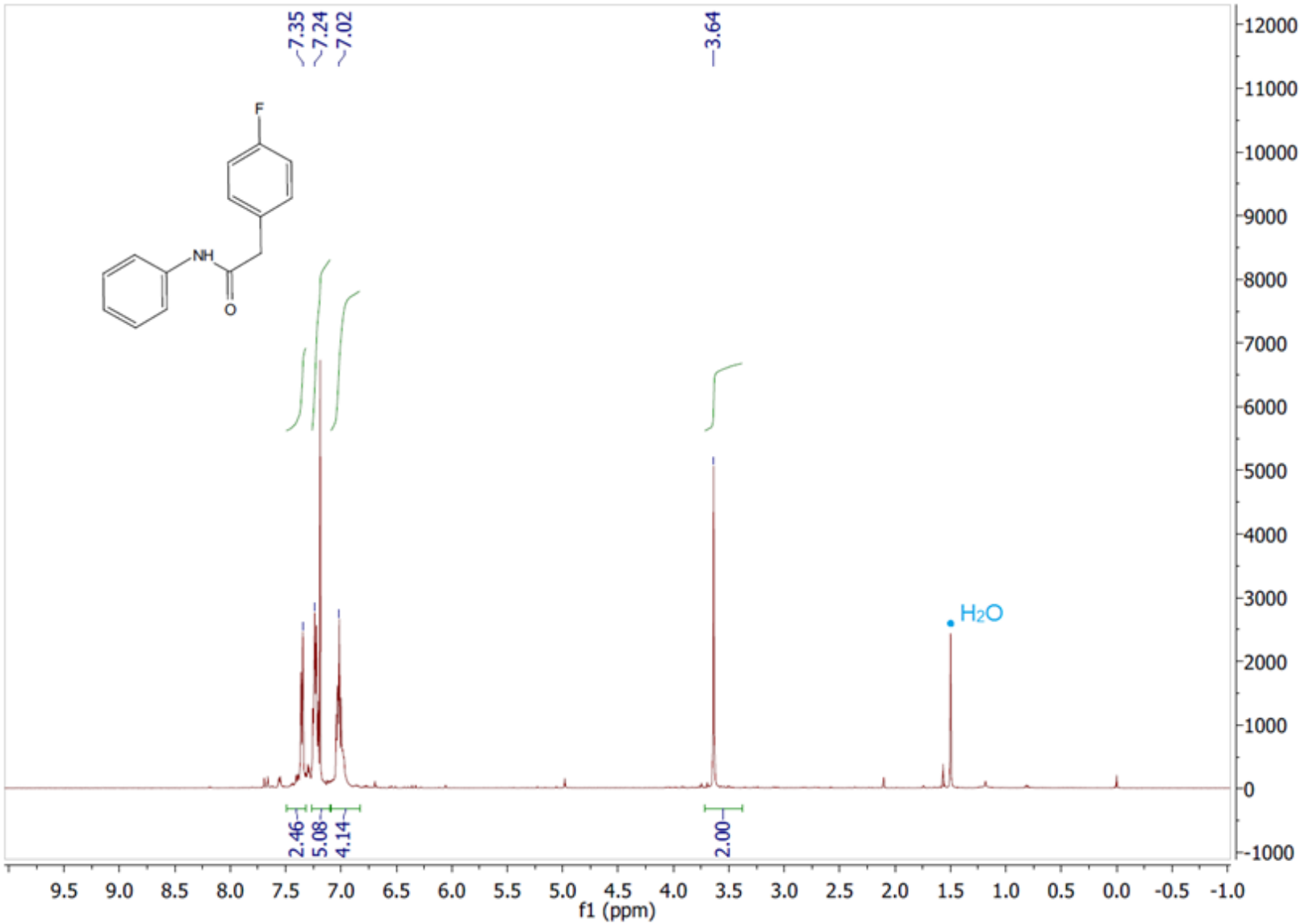


Figure S36. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)-N-phenylacetamide (**10**).

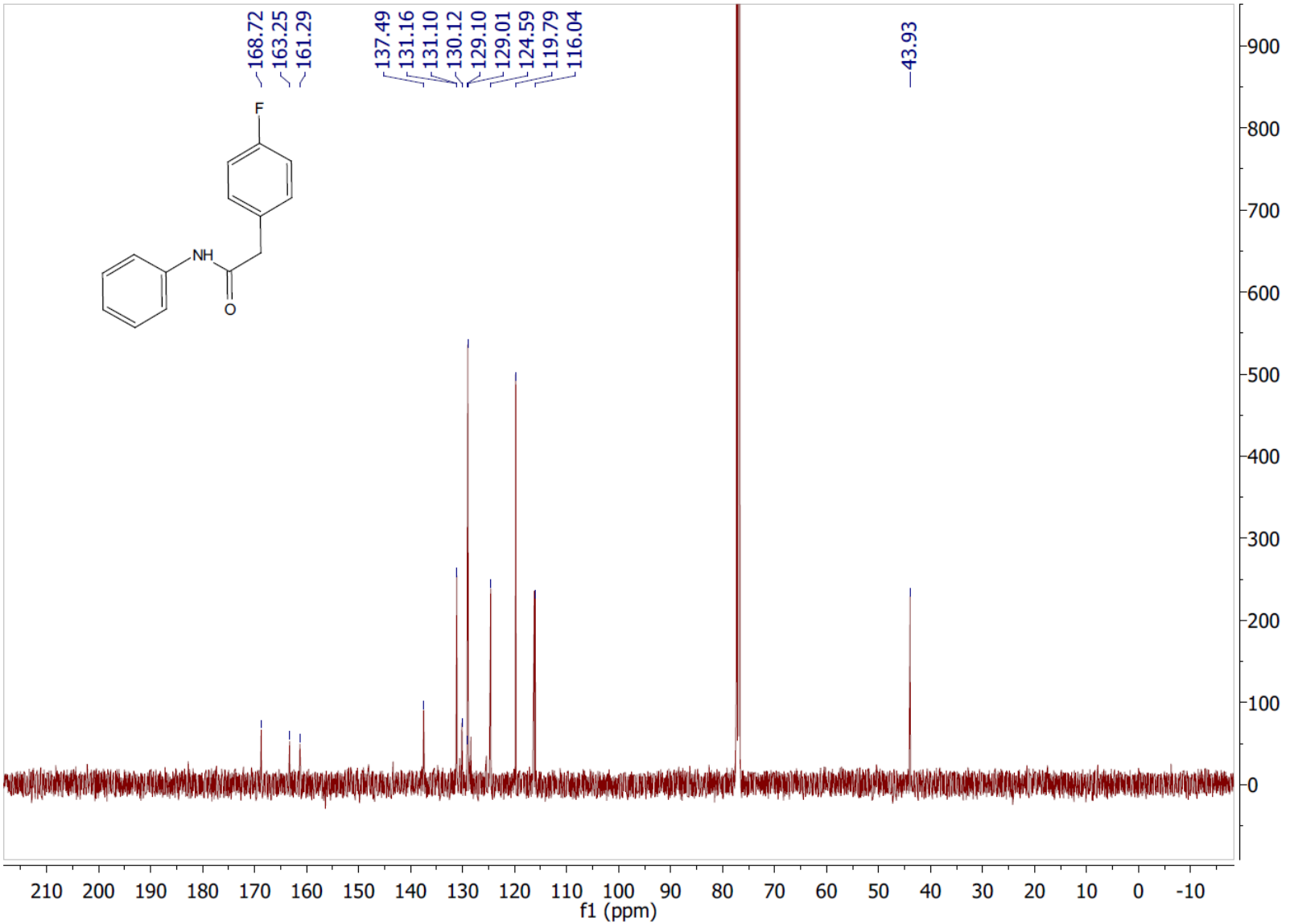


Figure S37. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)-N-phenylacetamide (**10**).

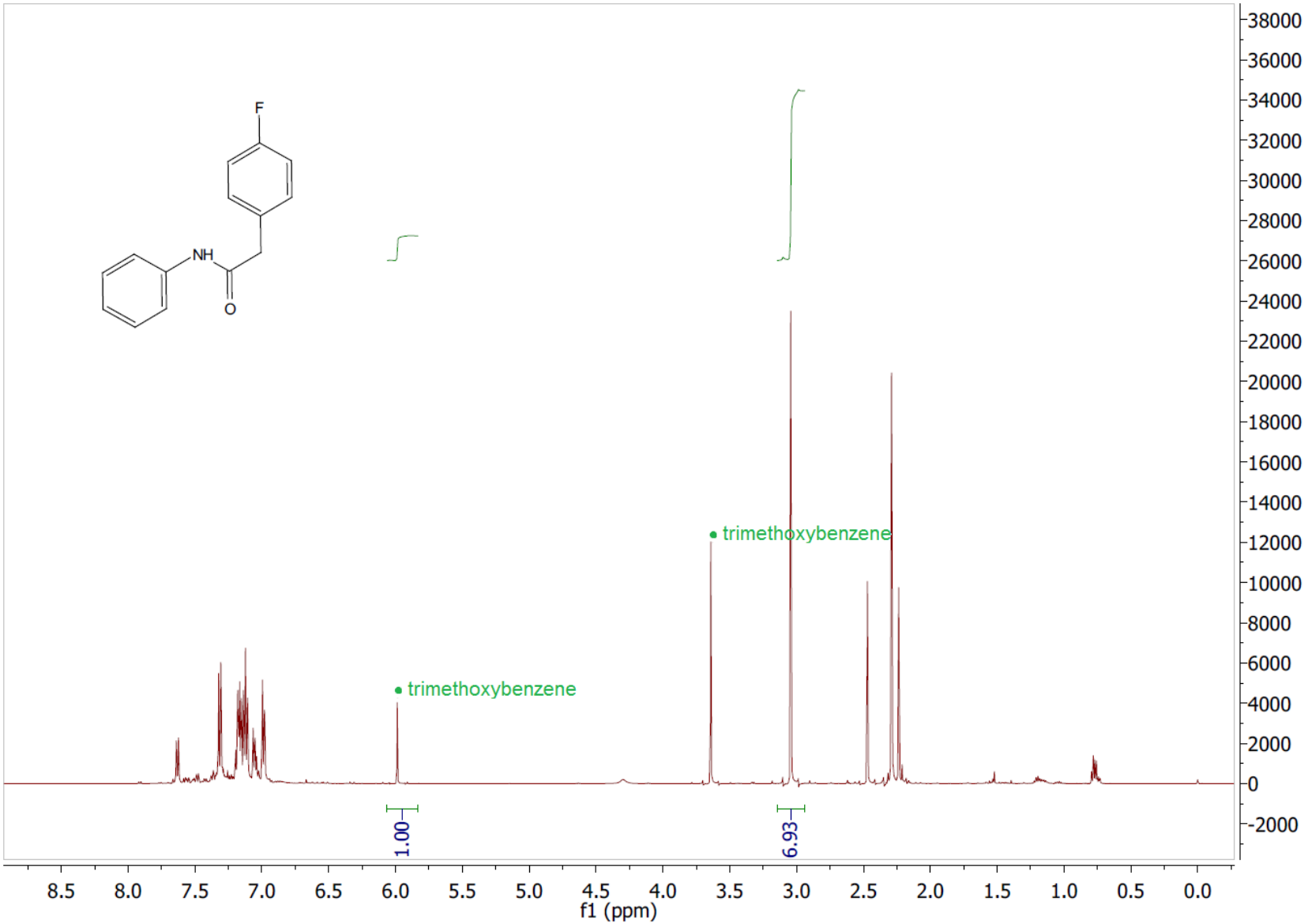


Figure S38. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including 2-(4-fluorophenyl)-N-phenylacetamide (**10**) and trimethoxybenzene.

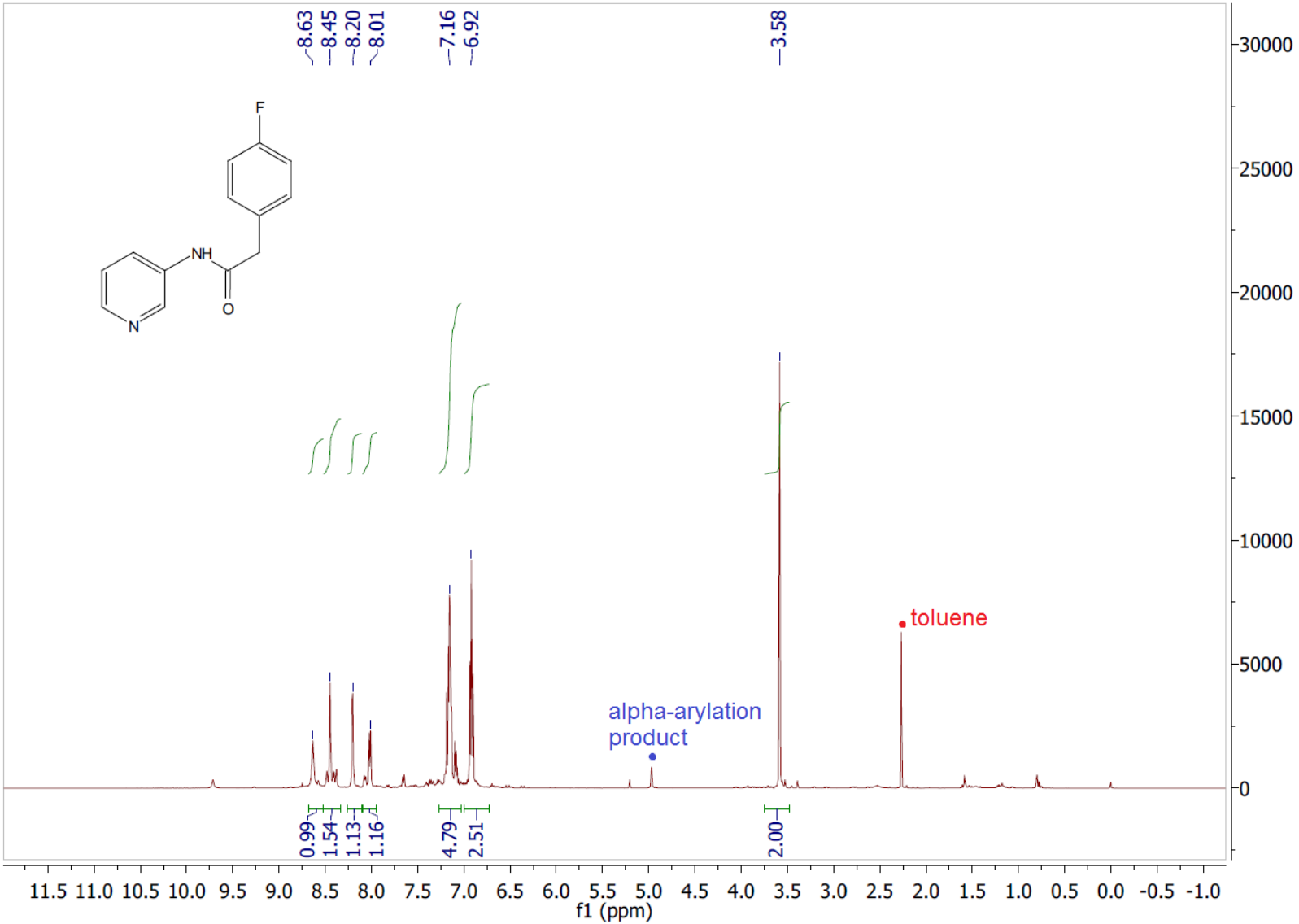


Figure S39. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)-N-(pyridin-3-yl)acetamide (**11**). Material was purified as best possible for analysis of crude spectra in NMR yield determination. Product could not be completely separated from α-arylation byproducts by column chromatography.

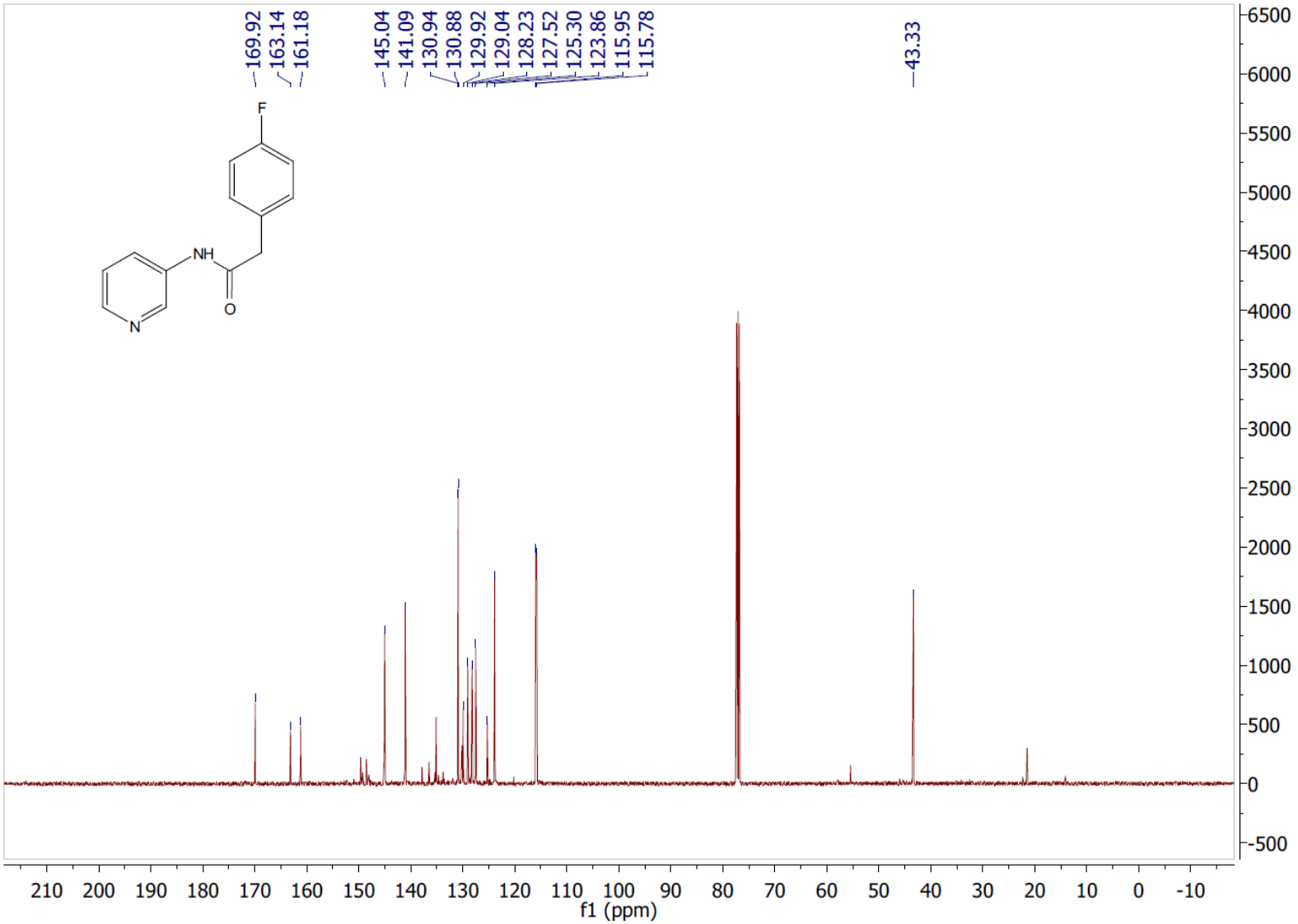


Figure S40. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)-N-(pyridin-3-yl)acetamide (**11**).

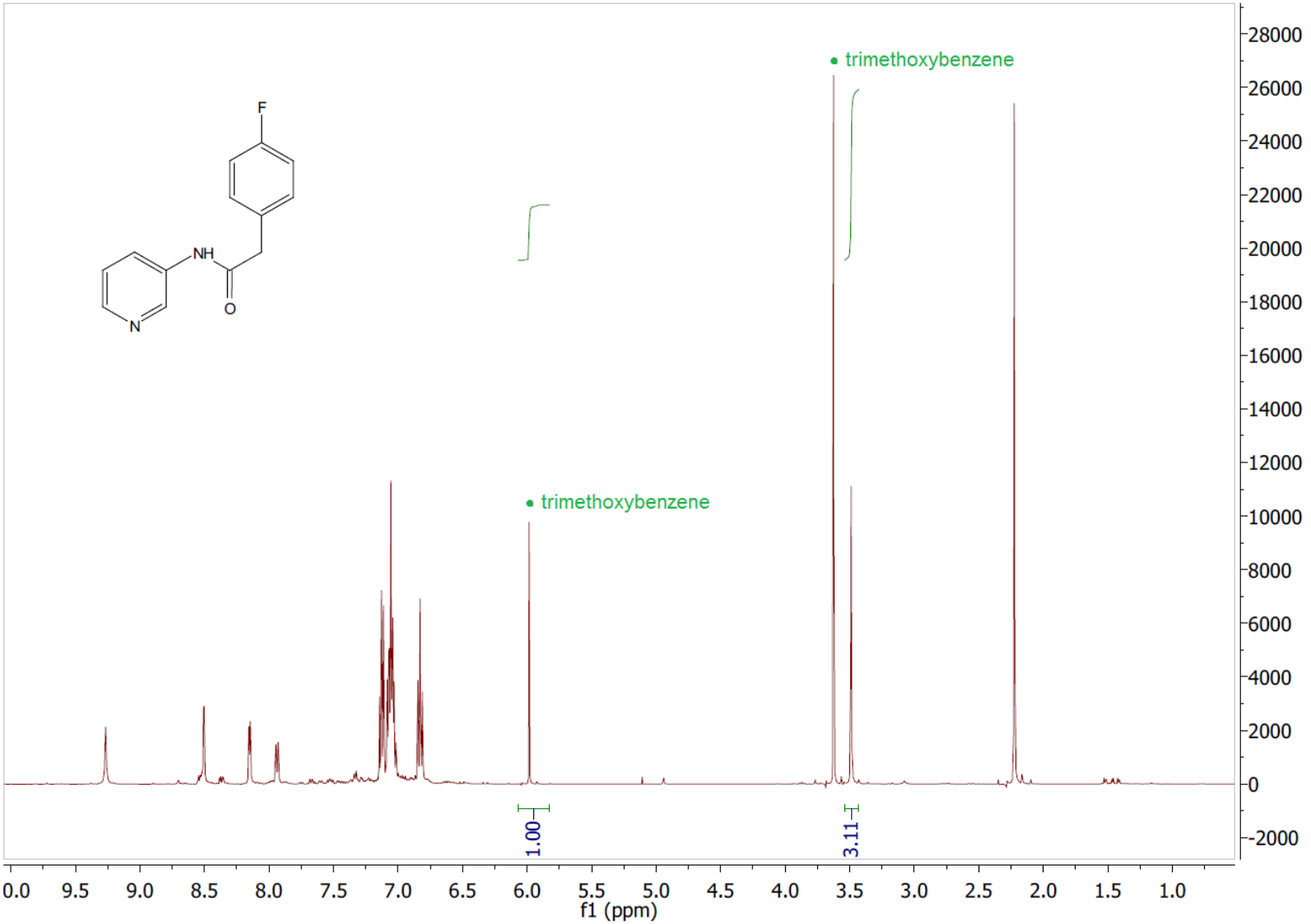


Figure S41. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including 2-(4-fluorophenyl)-N-(pyridin-3-yl)acetamide (**11**) and trimethoxybenzene.

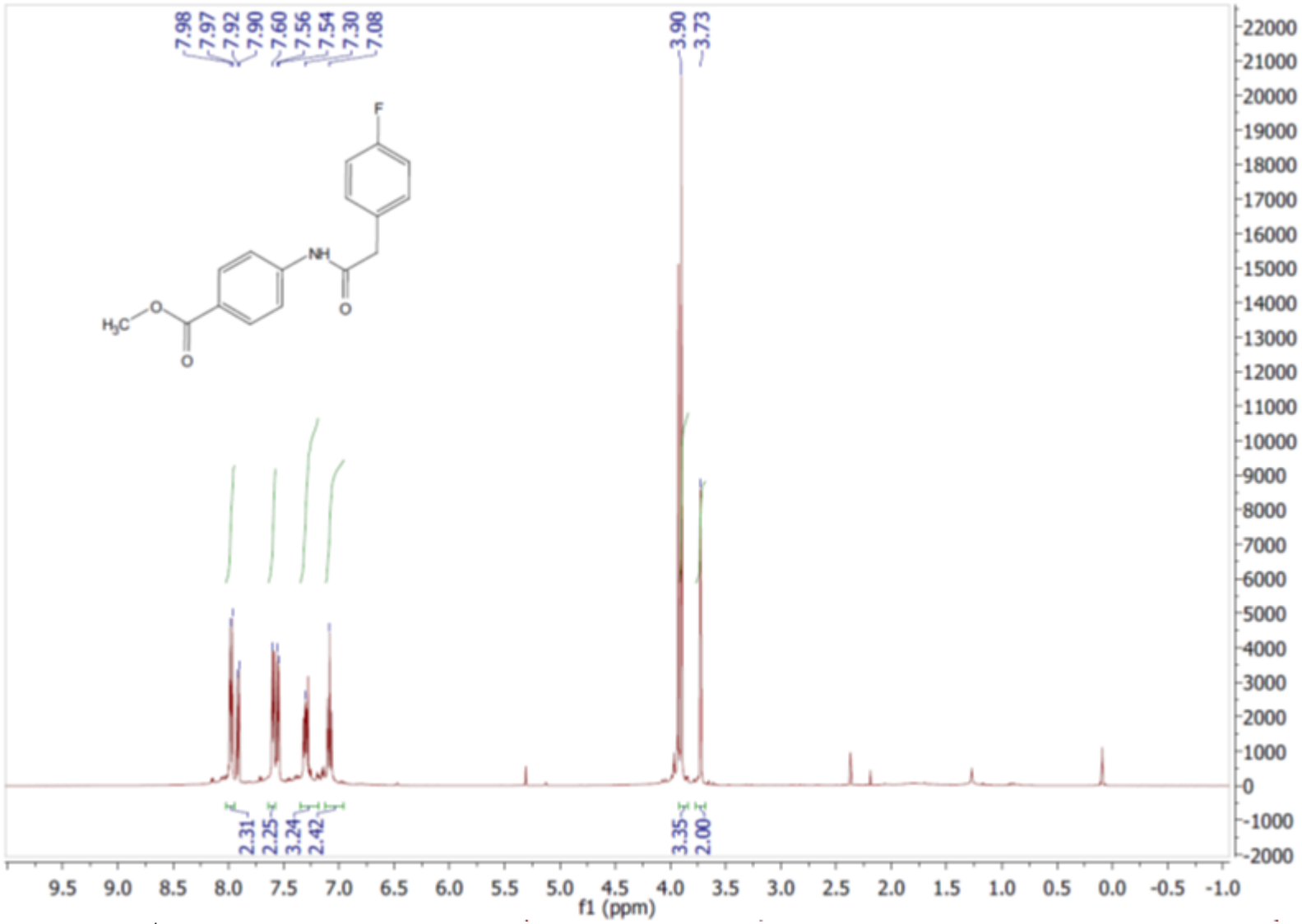


Figure S42. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(2-(4-fluorophenyl)acetamido)benzoate (**12**).

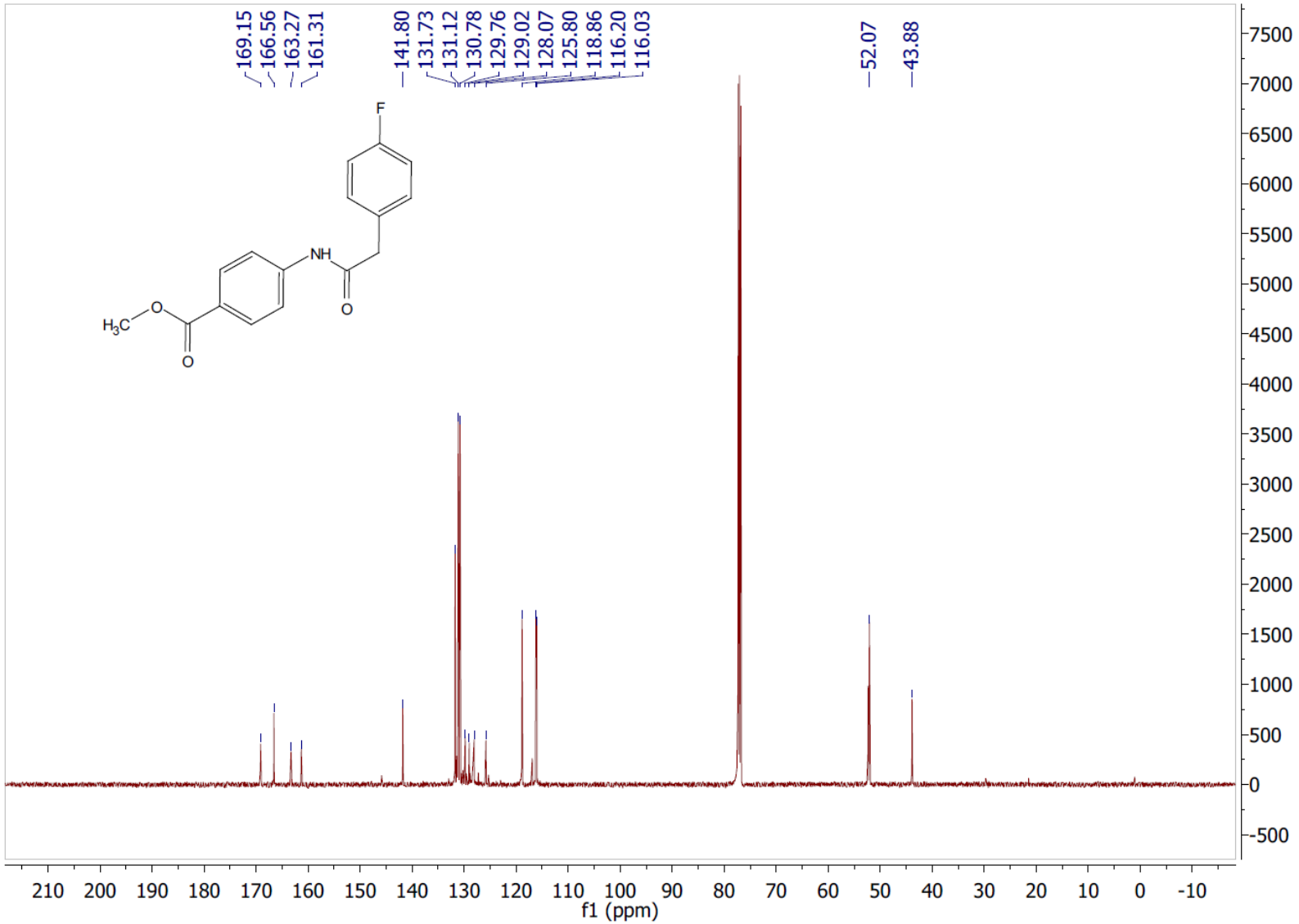


Figure S43. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(2-(4-fluorophenyl)acetamido)benzoate (**12**).

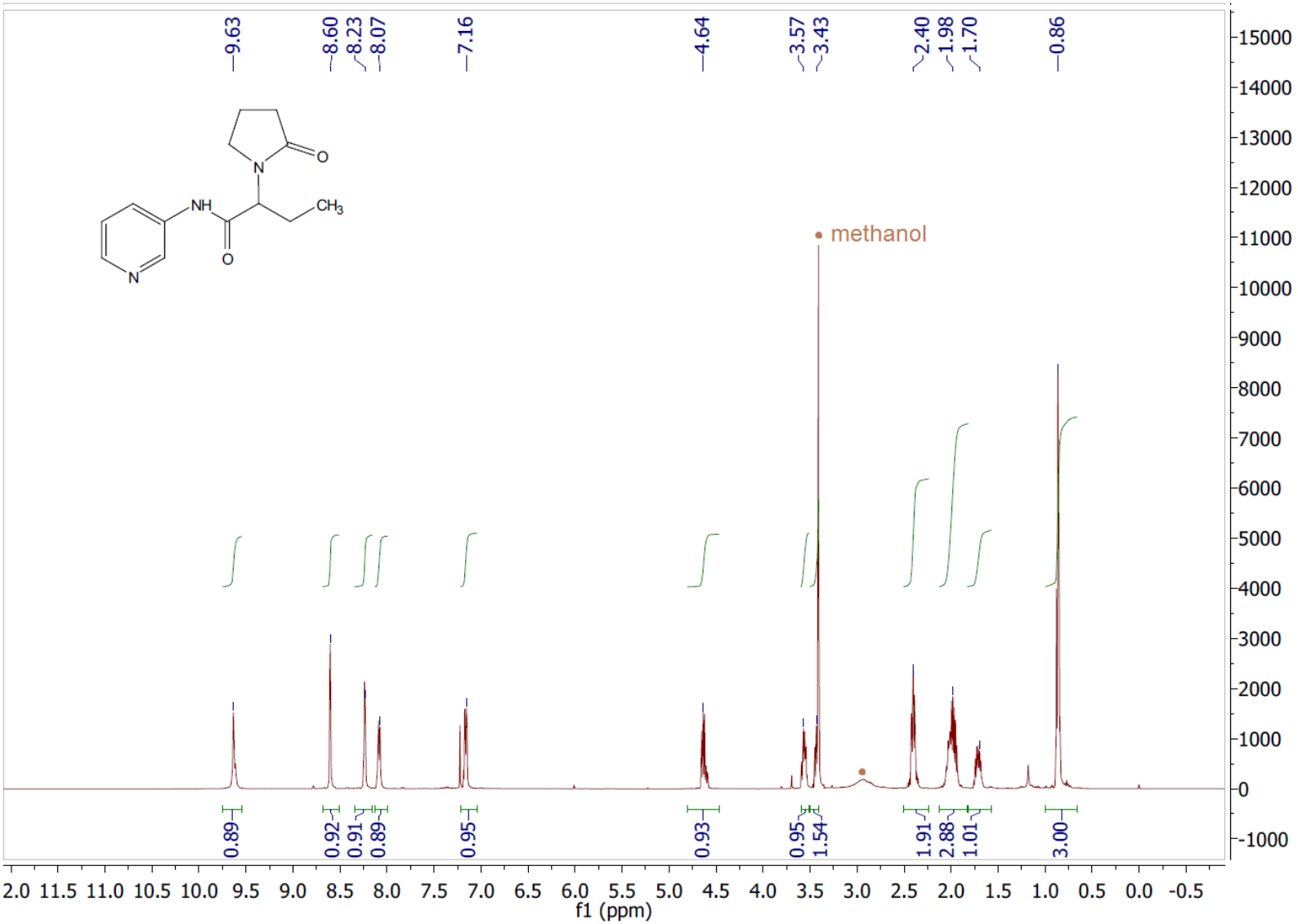


Figure S44. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of (S)-2-(2-oxopyrrolidin-1-yl)-N-(pyridin-3-yl) (**13**). Residual solvent could not be removed completely from oily product.

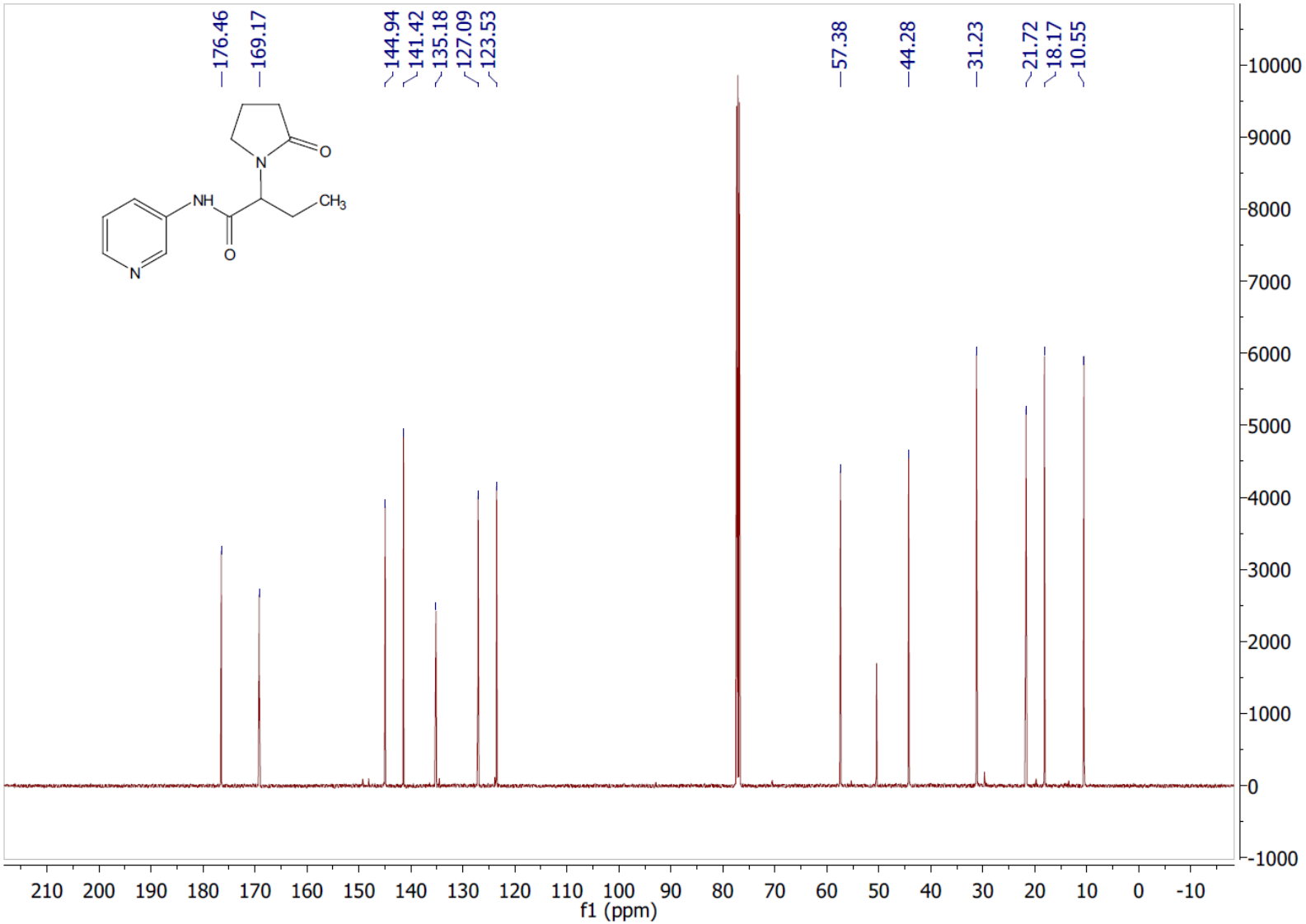


Figure S45. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of (S)-2-(2-oxopyrrolidin-1-yl)-N-(pyridin-3-yl) (**13**).

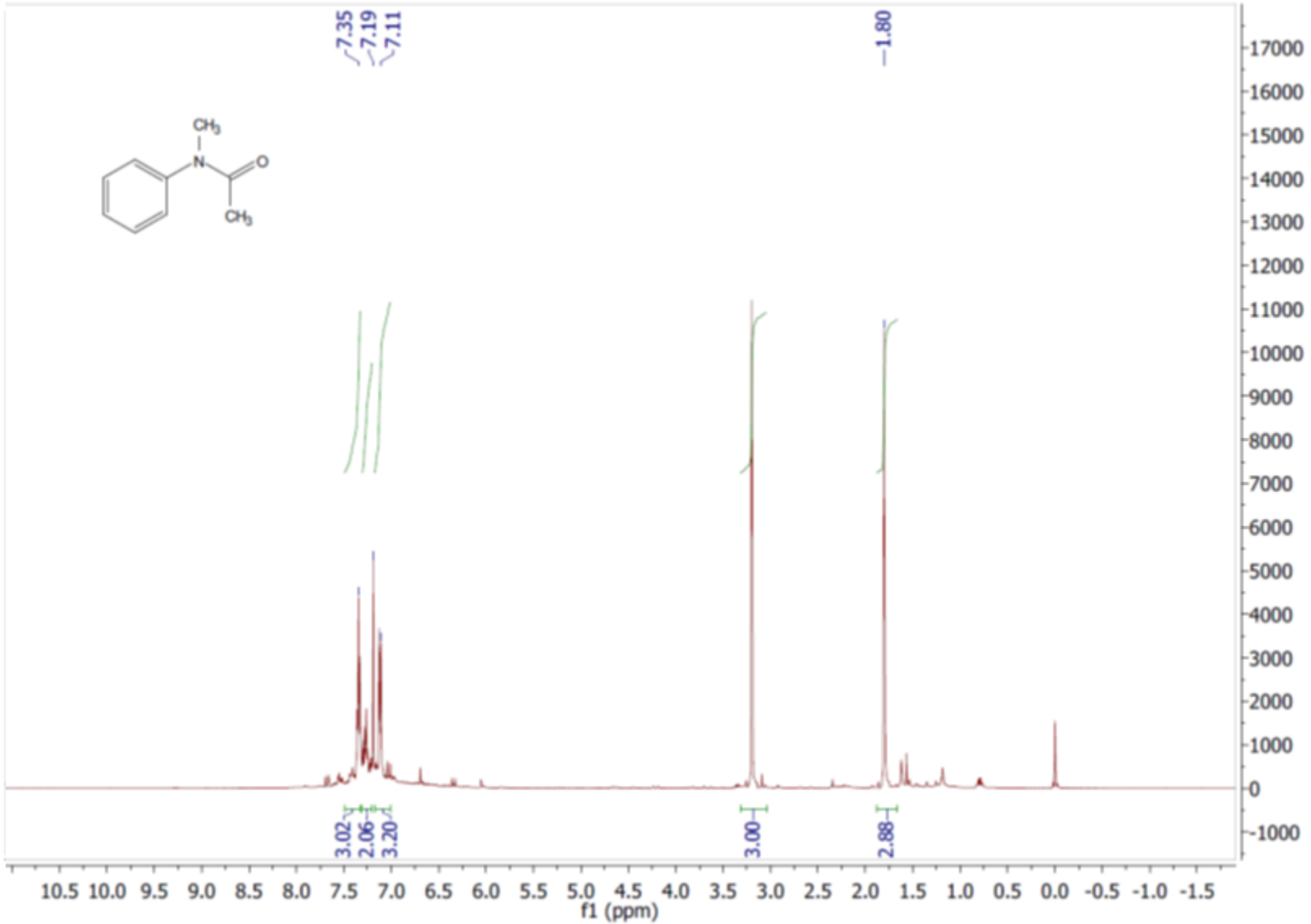


Figure S46. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-methyl-N-phenylacetamide (**14**). Unidentified impurities could not be completely separated by column chromatography.

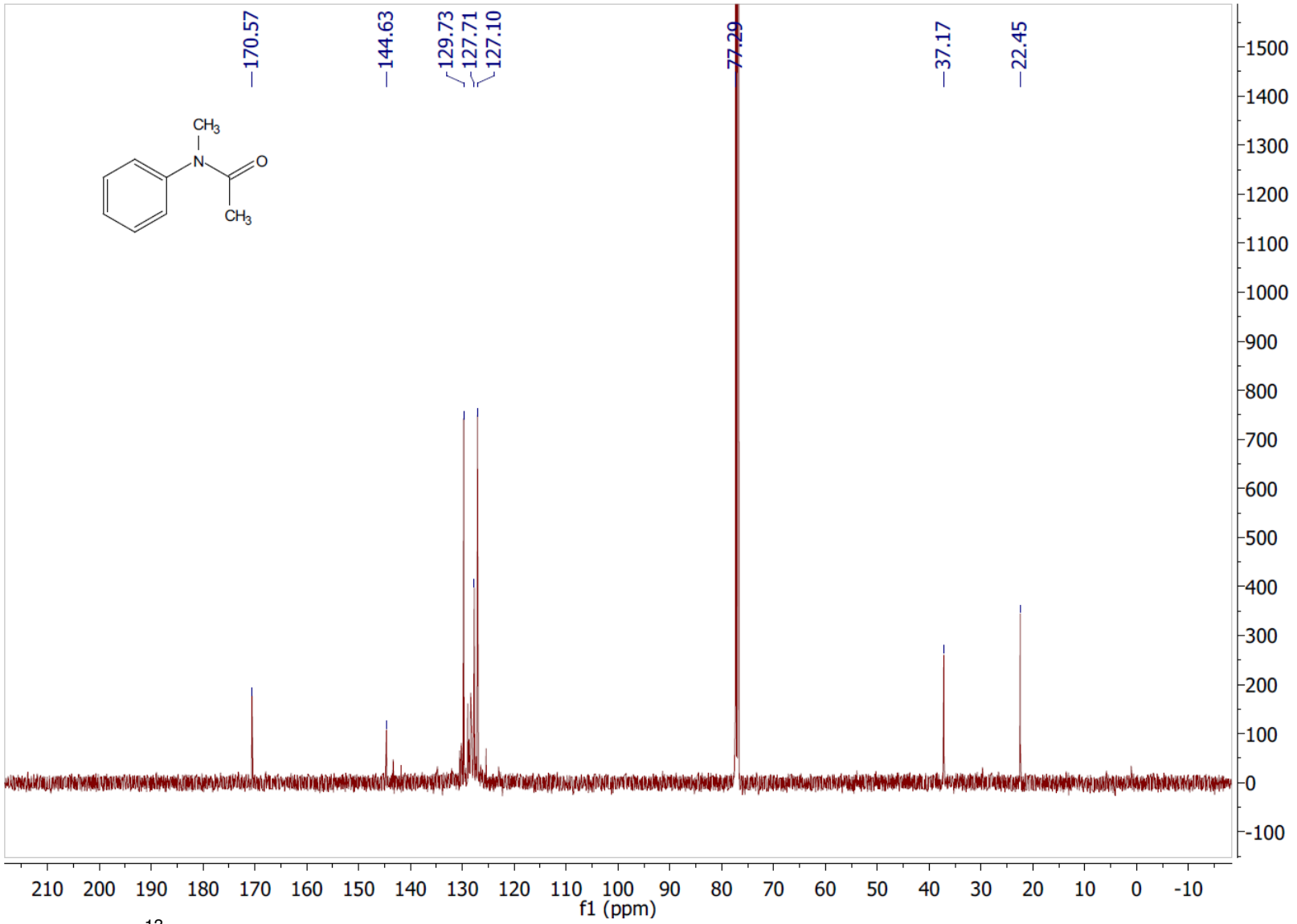


Figure S47. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-methyl-N-phenylacetamide (**14**).

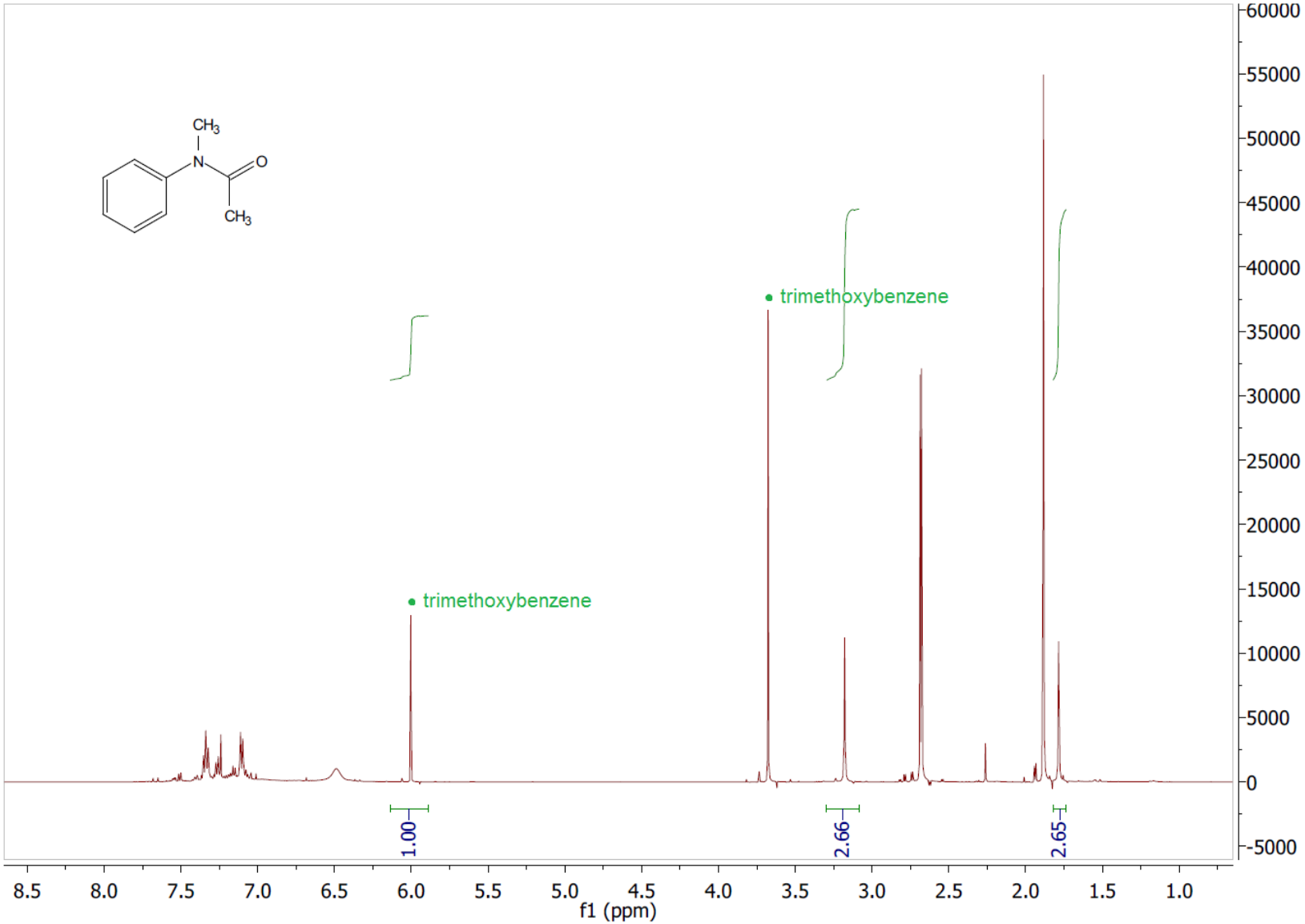


Figure S48. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-methyl-N-phenylacetamide (**14**) and trimethoxybenzene.

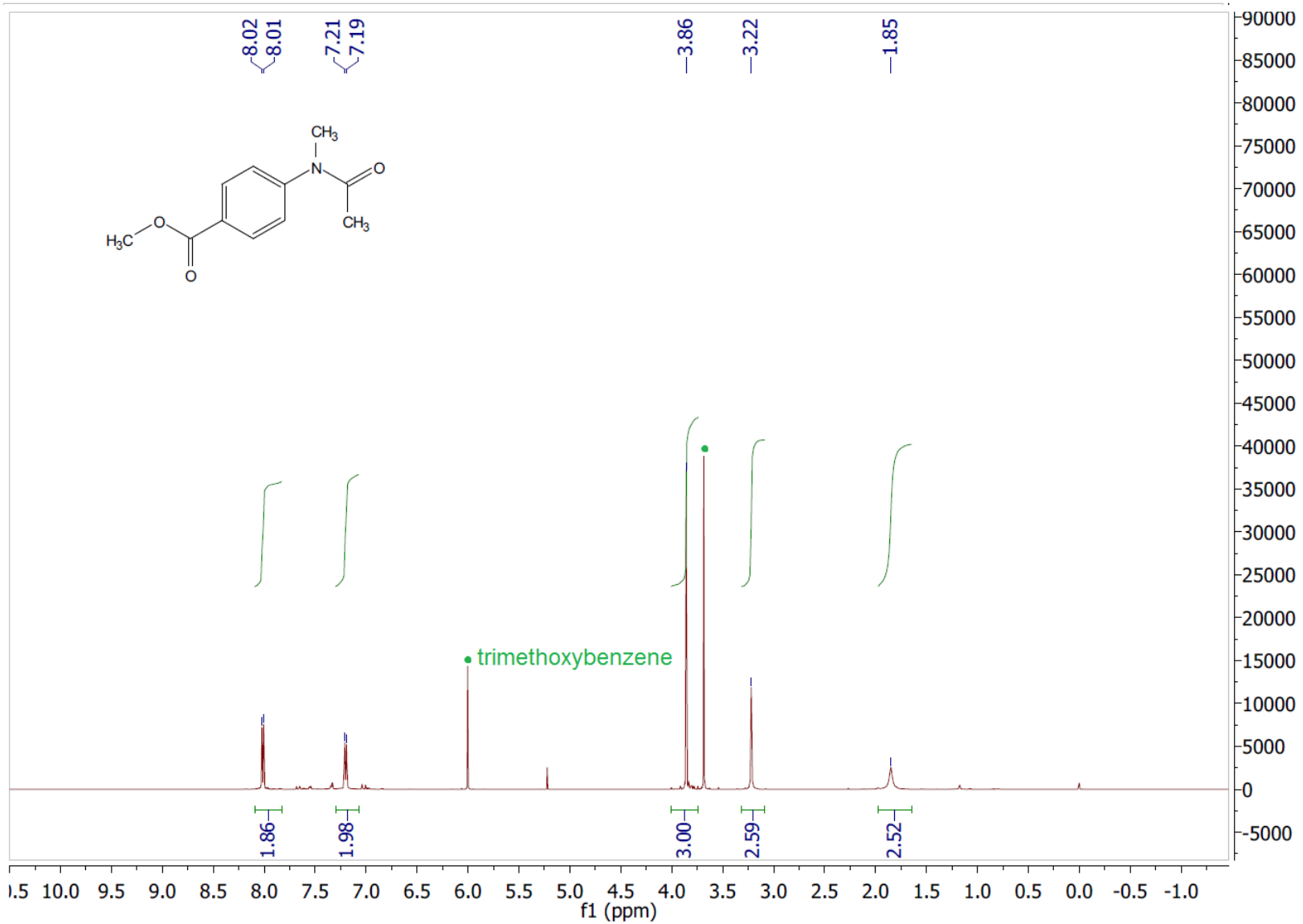


Figure S49. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-methylacetamido)benzoate (**15**).

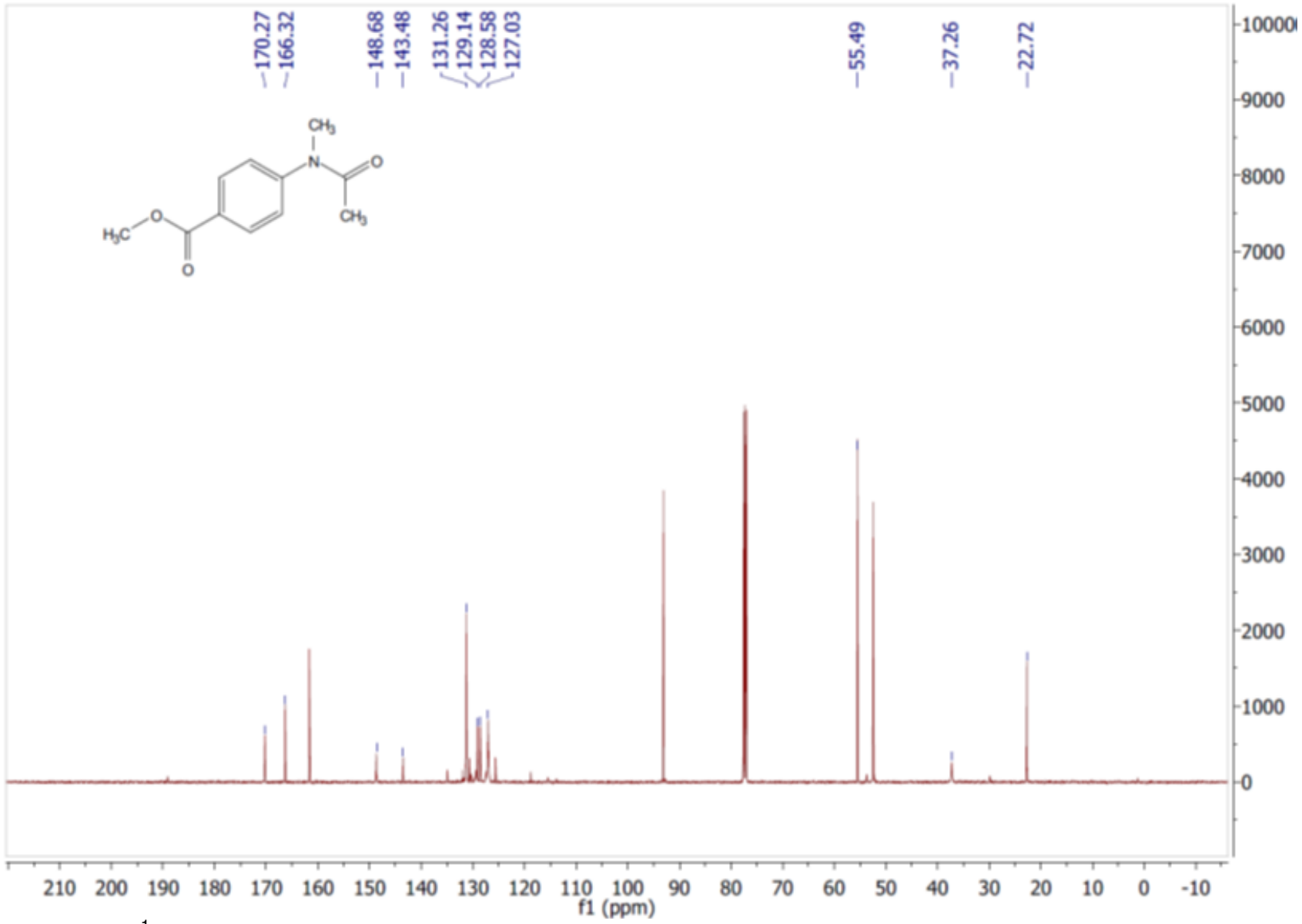


Figure S50. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-methylacetamido)benzoate (**15**).

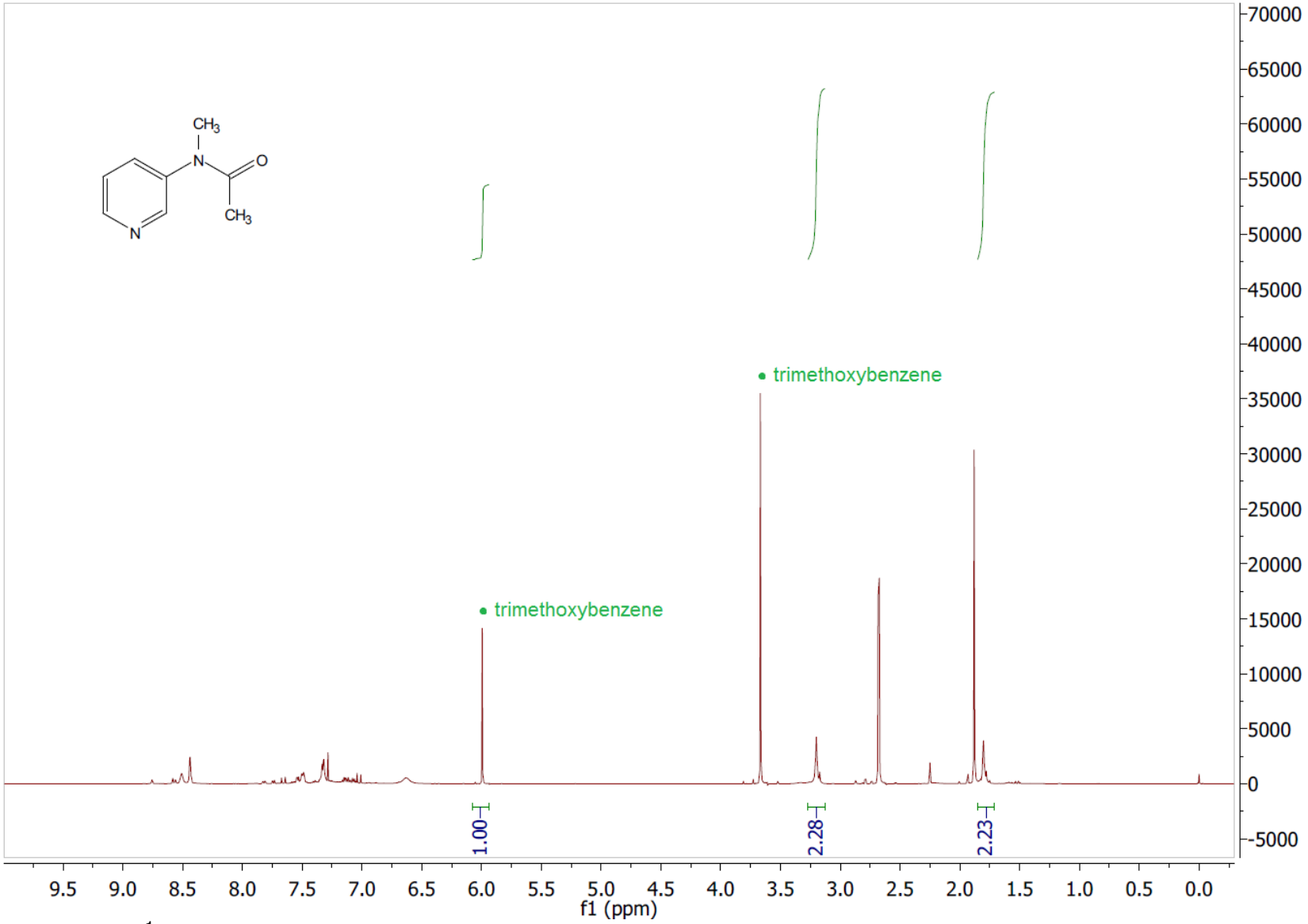


Figure S51. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-methyl-N-(pyridin-3-yl)acetamide (**16**) and trimethoxybenzene.

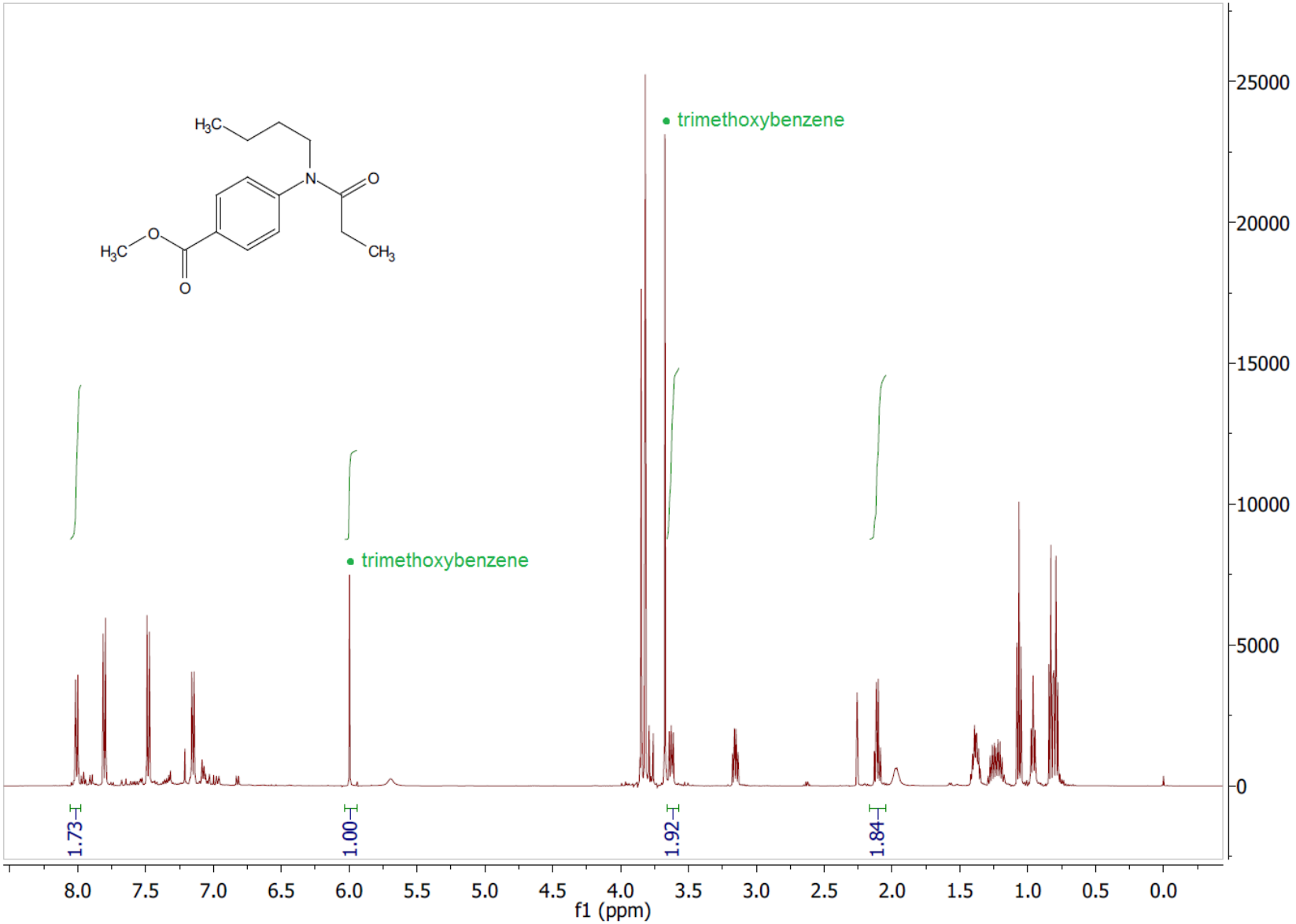


Figure S52. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including methyl 4-(N-butylpropionamido)benzoate (**17**) and trimethoxybenzene.

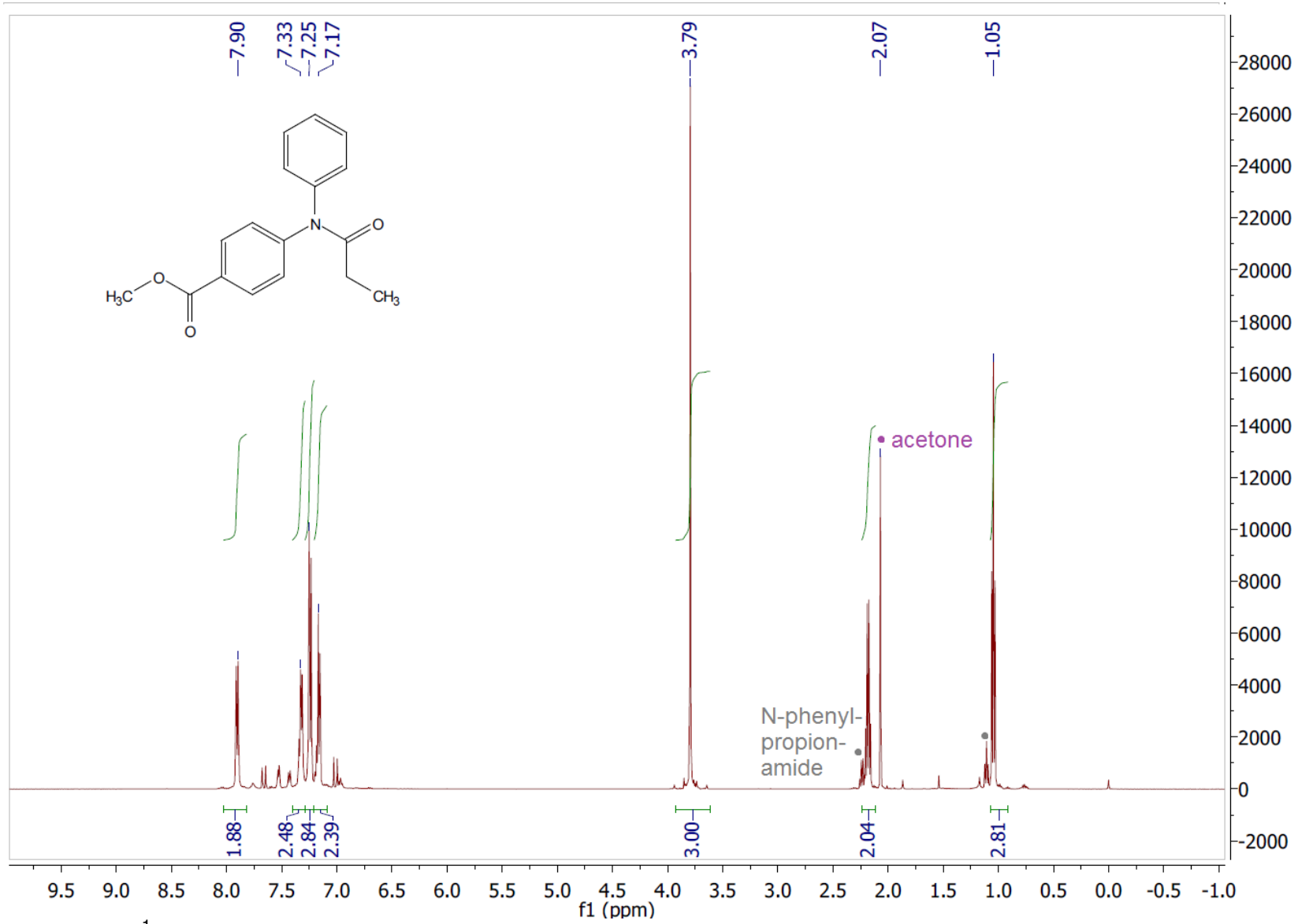


Figure S53. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-phenylpropionamido)benzoate (**18**).

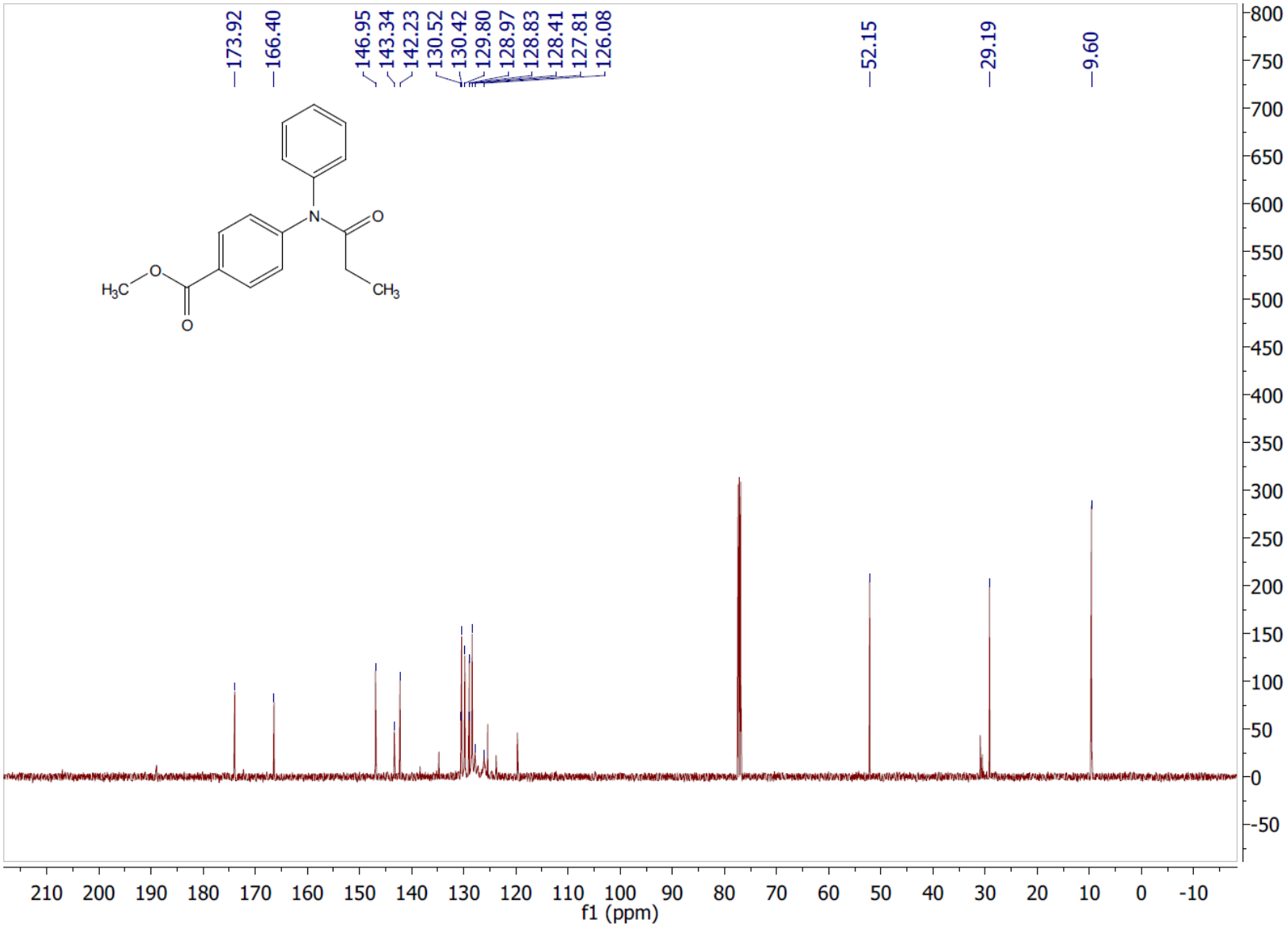


Figure S54. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-phenylpropionamido)benzoate (**18**).

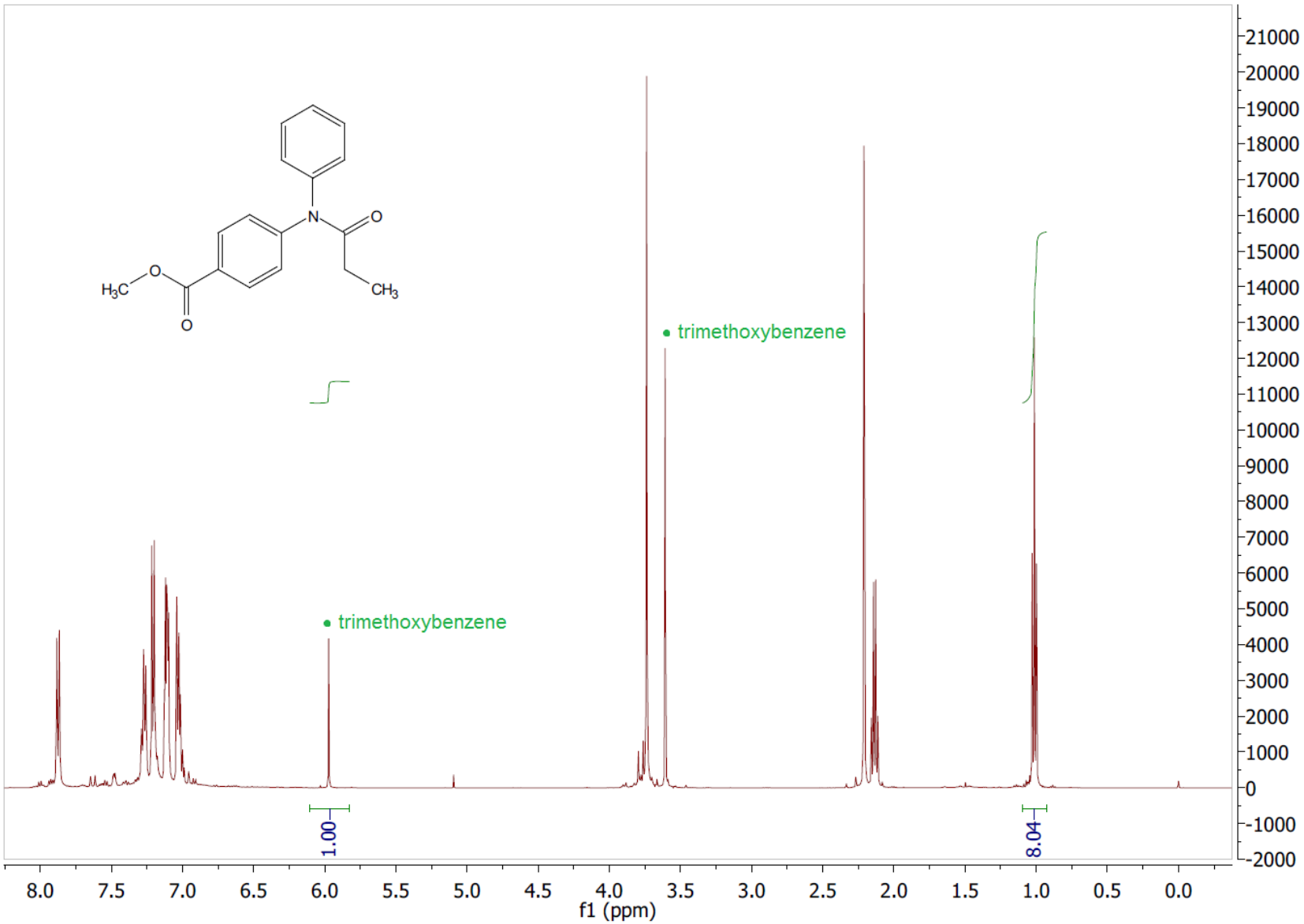


Figure S55. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including methyl 4-(N-phenylpropionamido)benzoate (**18**) and trimethoxybenzene.

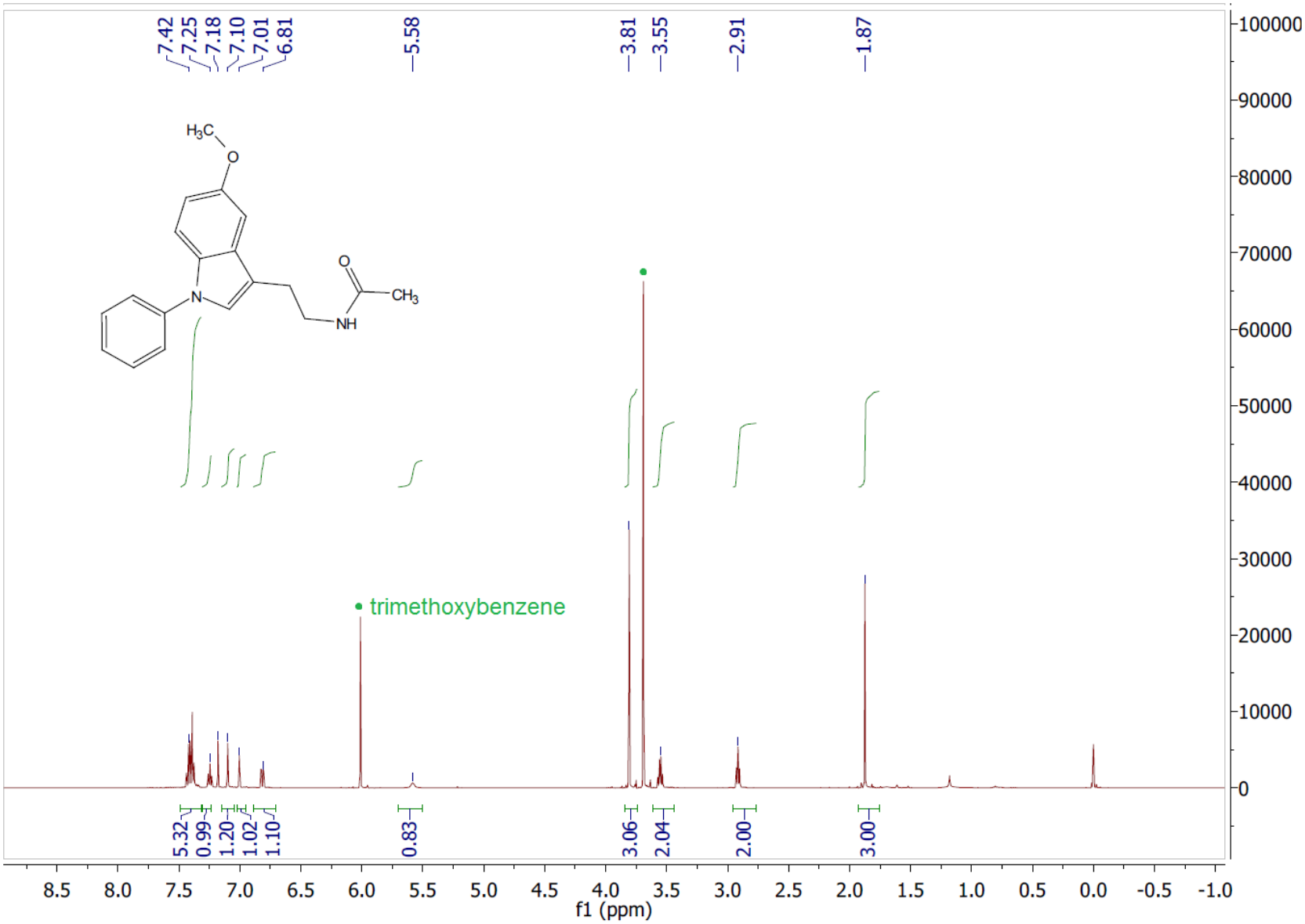


Figure S56. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-(2-(6-methoxy-1-phenyl-1H-indol-3-yl)ethyl)acetamide (**19**).

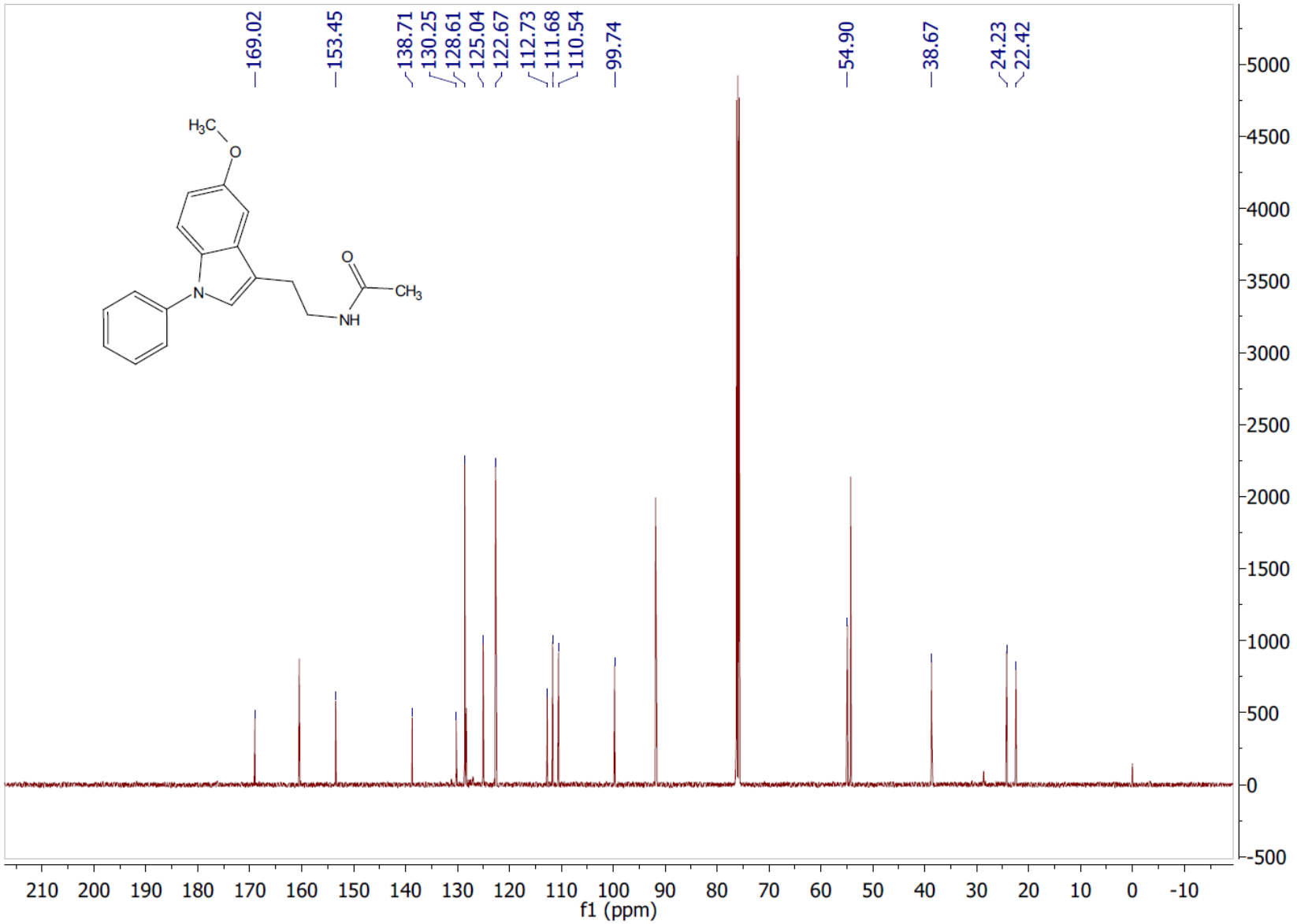


Figure S57. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-(2-(6-methoxy-1-phenyl-1H-indol-3-yl)ethyl)acetamide (**19**).

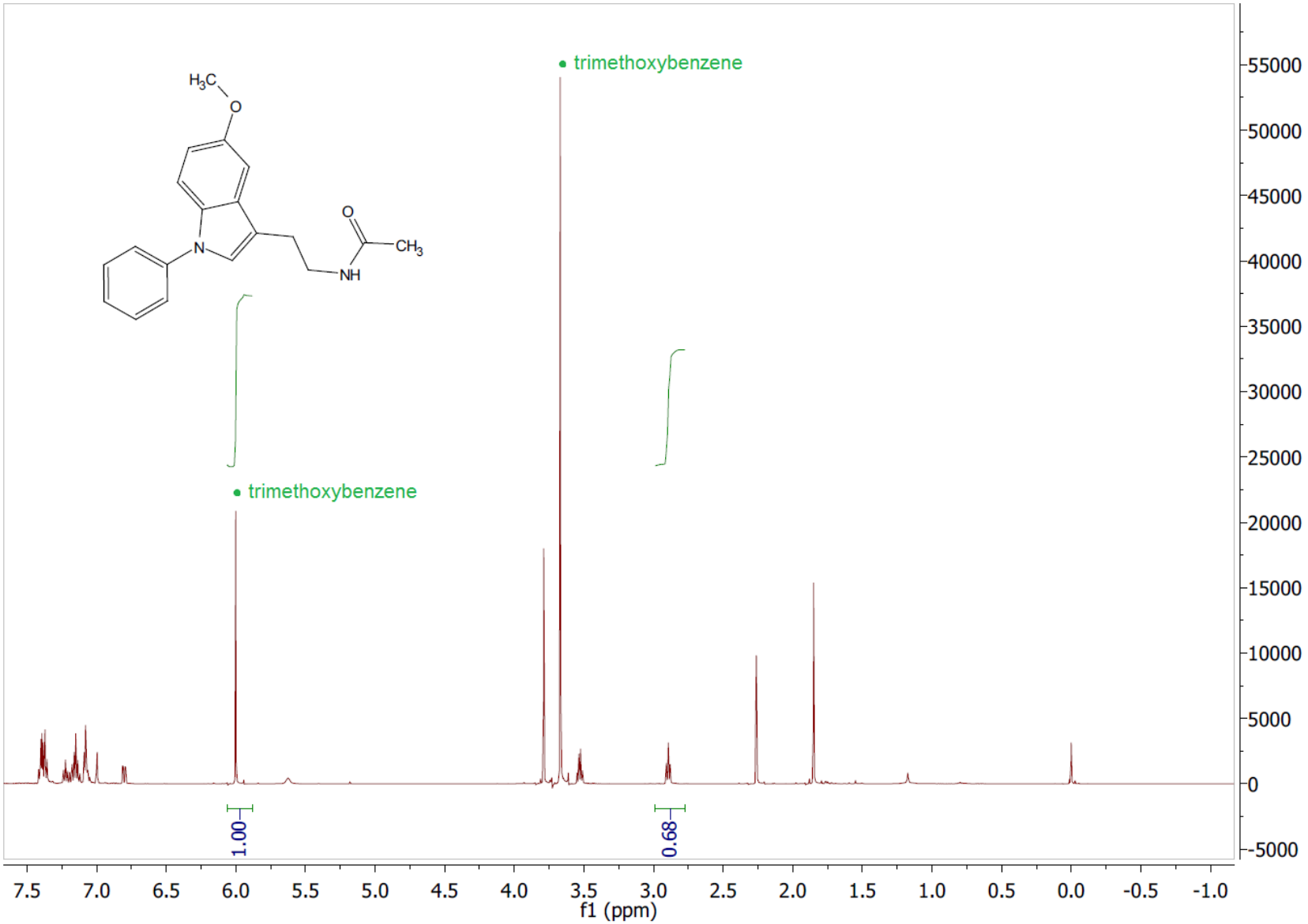


Figure S58. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture including N-(2-(6-methoxy-1-phenyl-1H-indol-3-yl)ethyl)acetamide (**19**) and trimethoxybenzene.

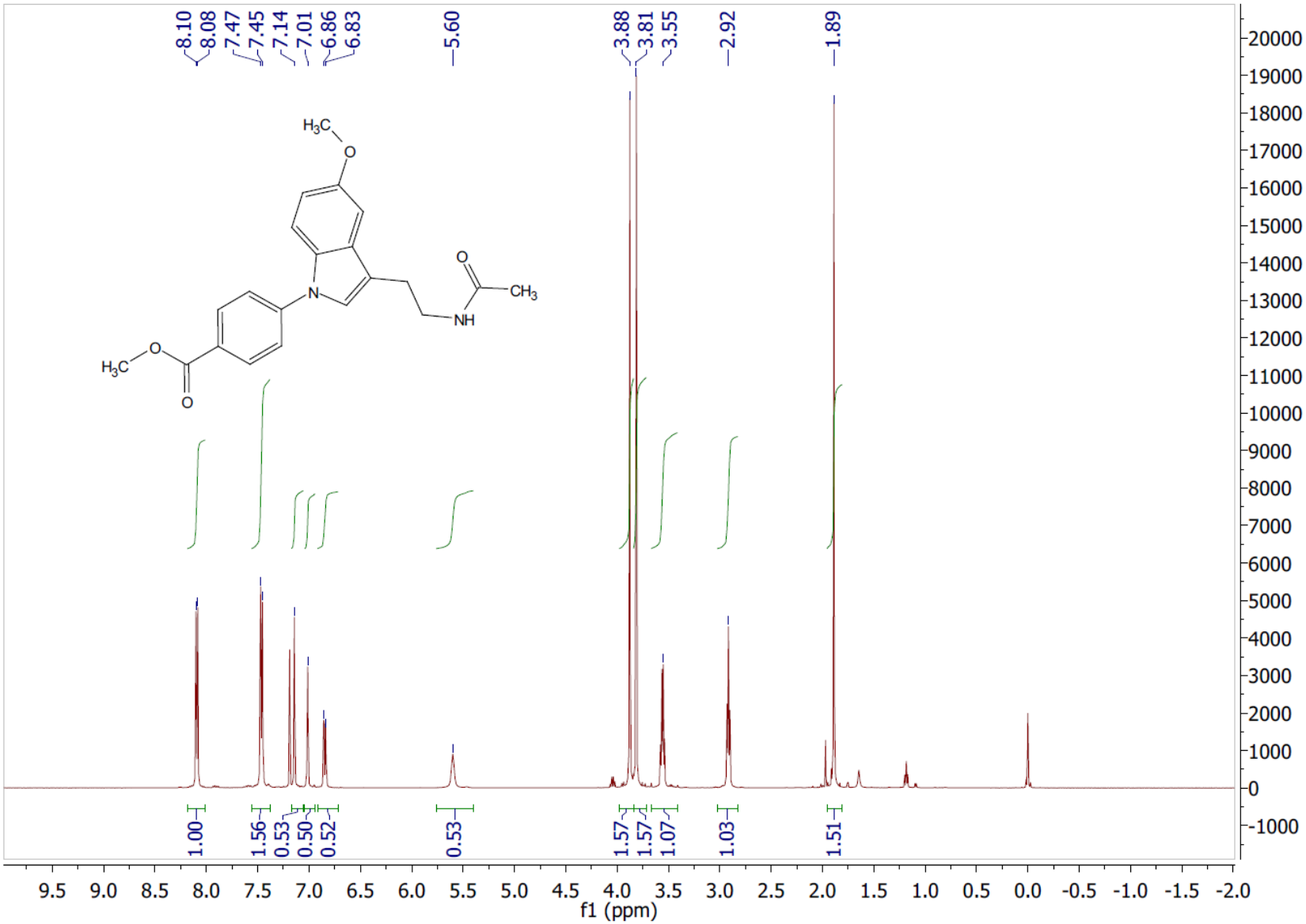


Figure S59. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(3-(2-acetamidoethyl)-5-methoxy-1H-indol-1-yl)benzoate (**20**).

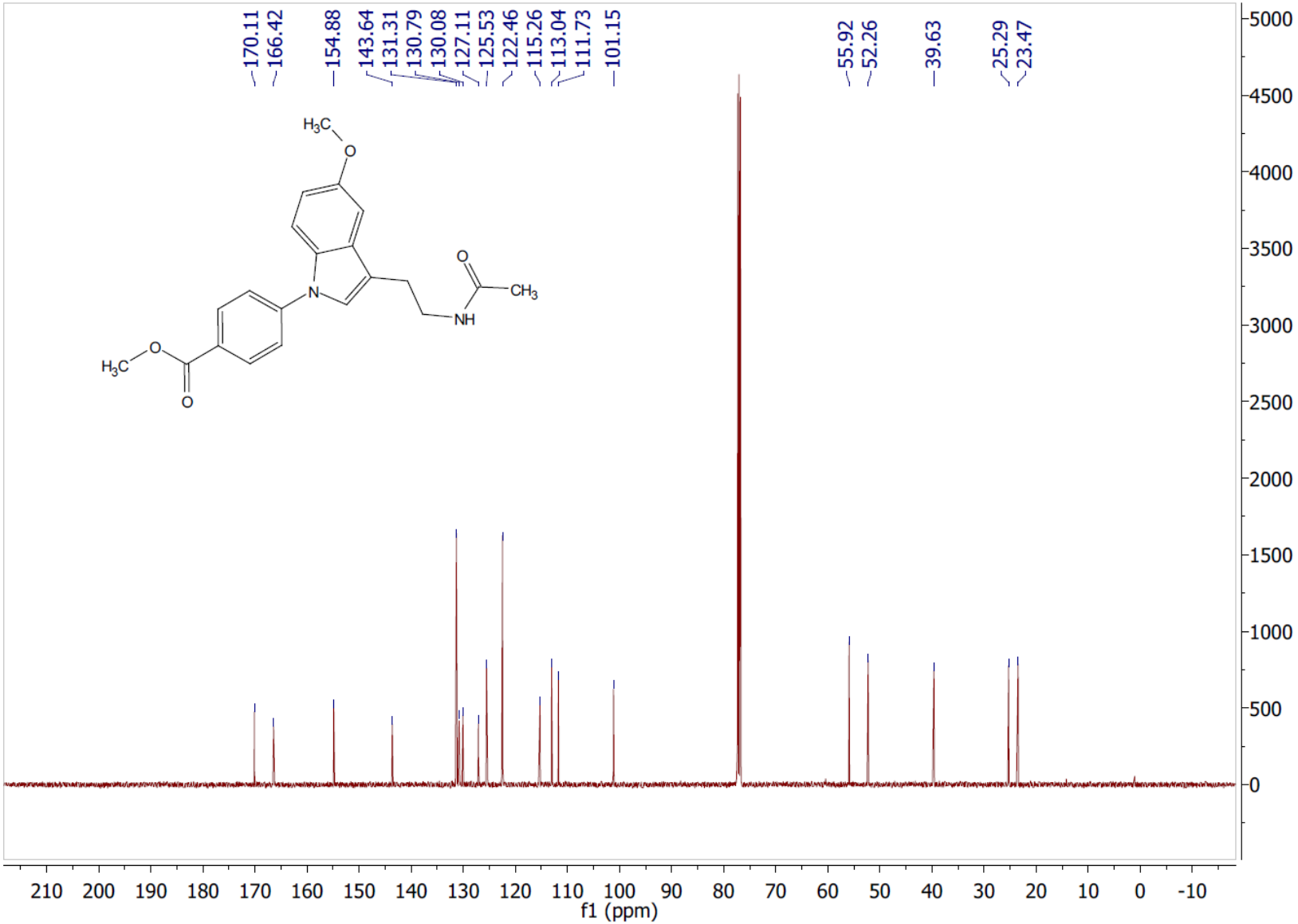


Figure S60. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(3-(2-acetamidoethyl)-5-methoxy-1H-indol-1-yl)benzoate (**20**).

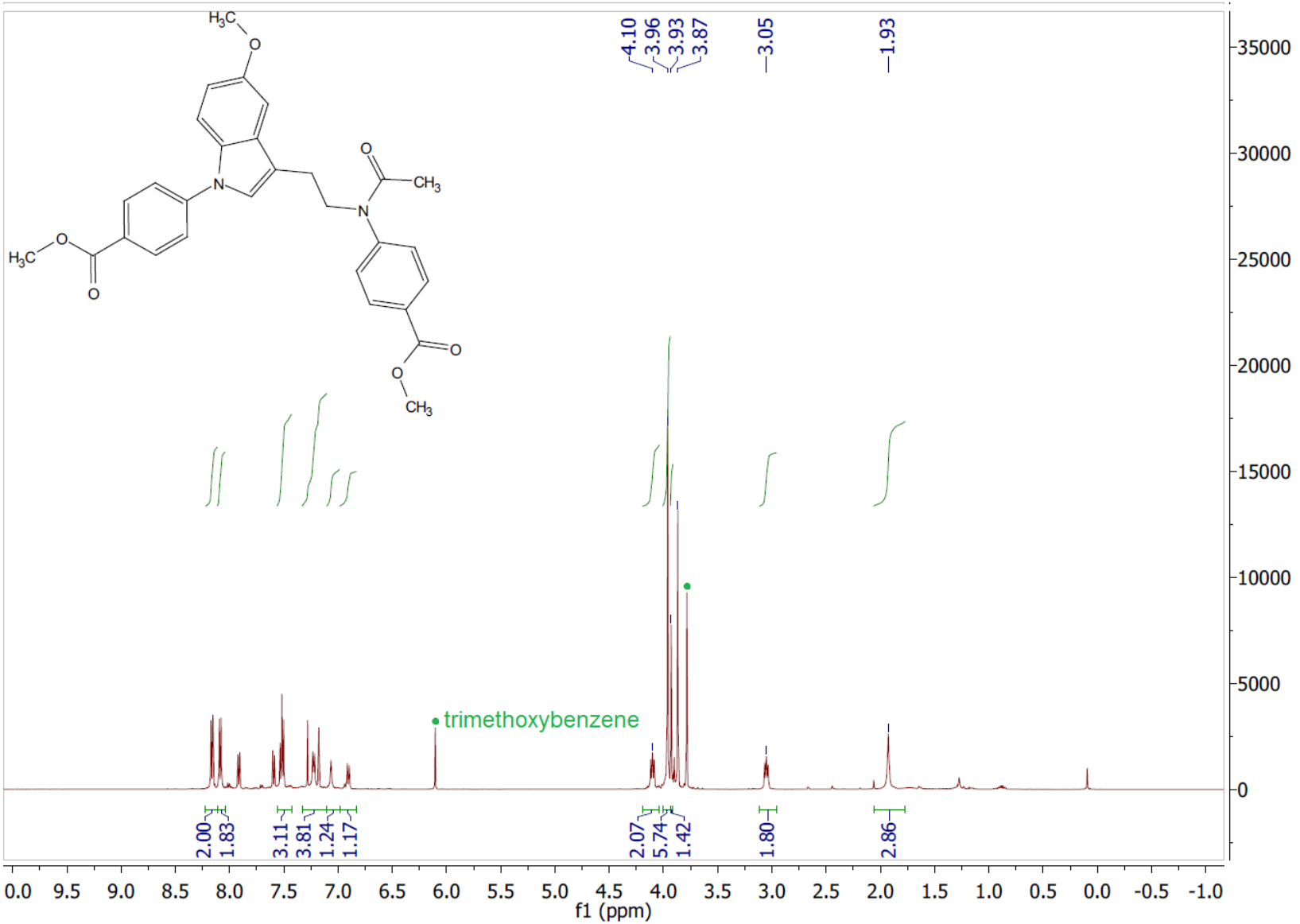


Figure S61. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-(2-(5-methoxy-1-(4-(methoxycarbonyl)phenyl)-1H-indol-3-yl)ethyl)acetamido)benzoate (**21**).

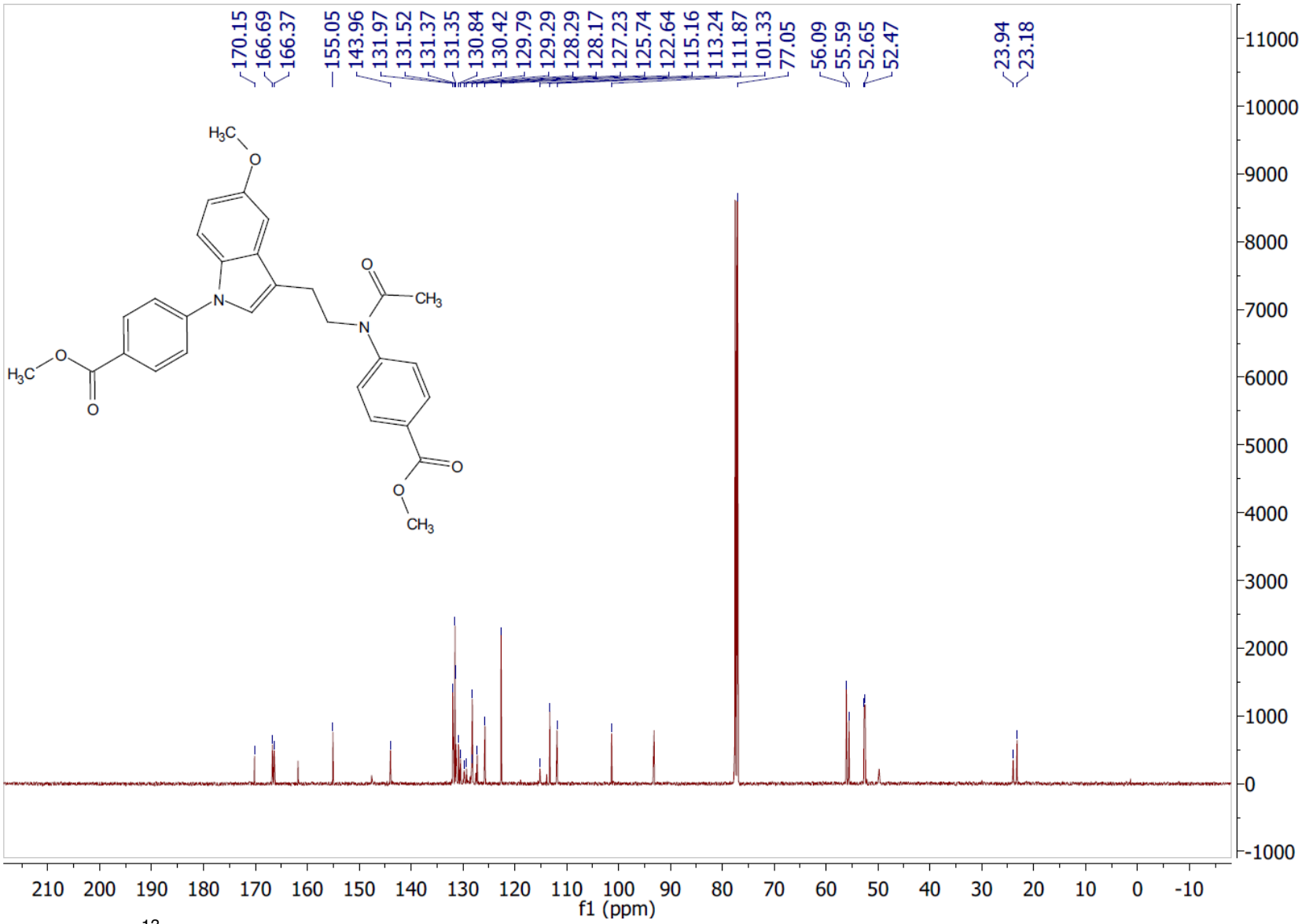


Figure S62. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of methyl 4-(N-(2-(5-methoxy-1-(4-(methoxycarbonyl)phenyl)-1H-indol-3-yl)ethyl)acetamido)benzoate (**21**).

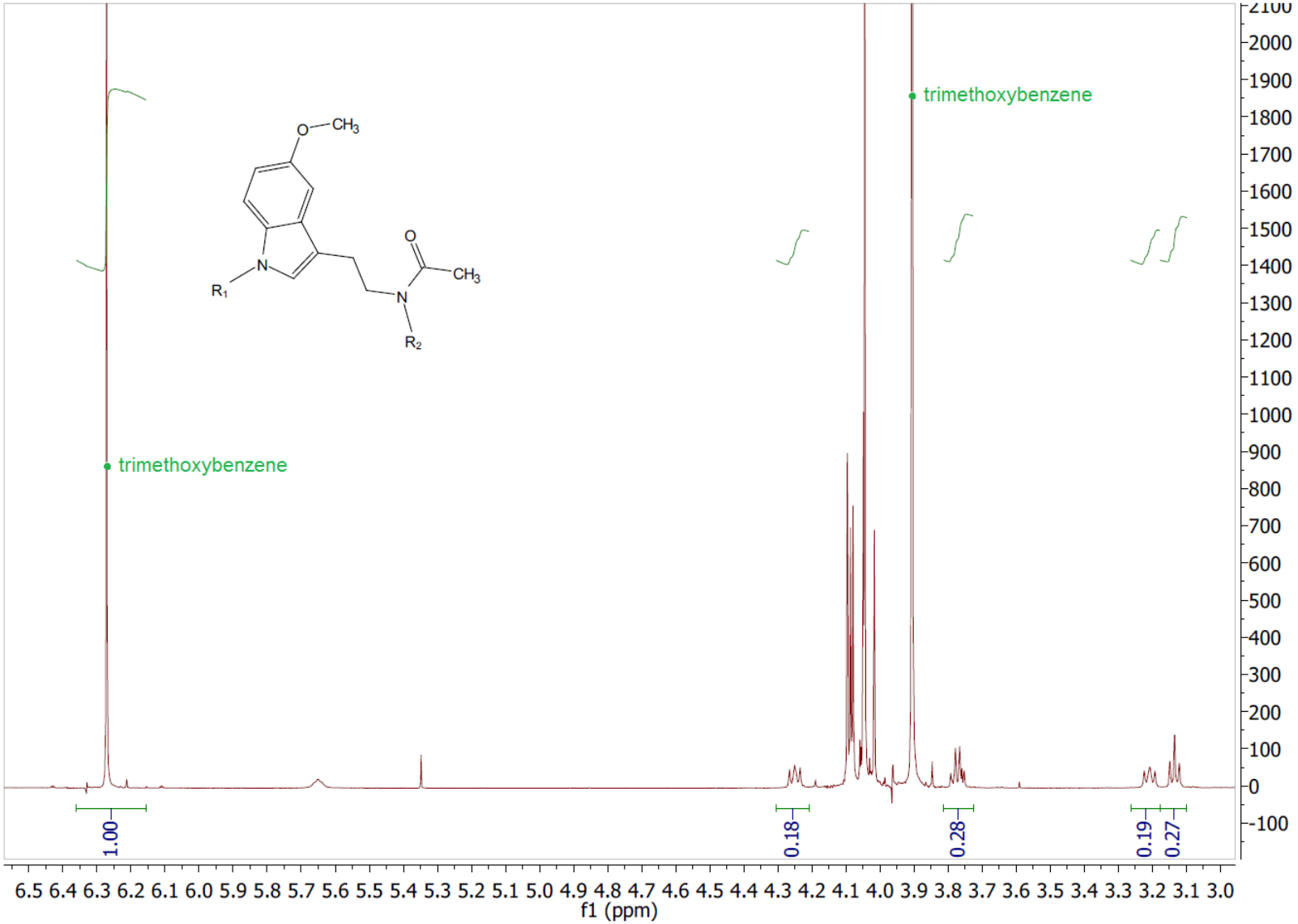


Figure S63. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of crude reaction mixture methyl 4-(3-(2-acetamidoethyl)-5-methoxy-1H-indol-1-yl)benzoate (**20**), methyl 4-(N-(2-(5-methoxy-1-(4-(methoxycarbonyl)phenyl)-1H-indol-3-yl)ethyl)acetamido)benzoate (**21**) and trimethoxybenzene.

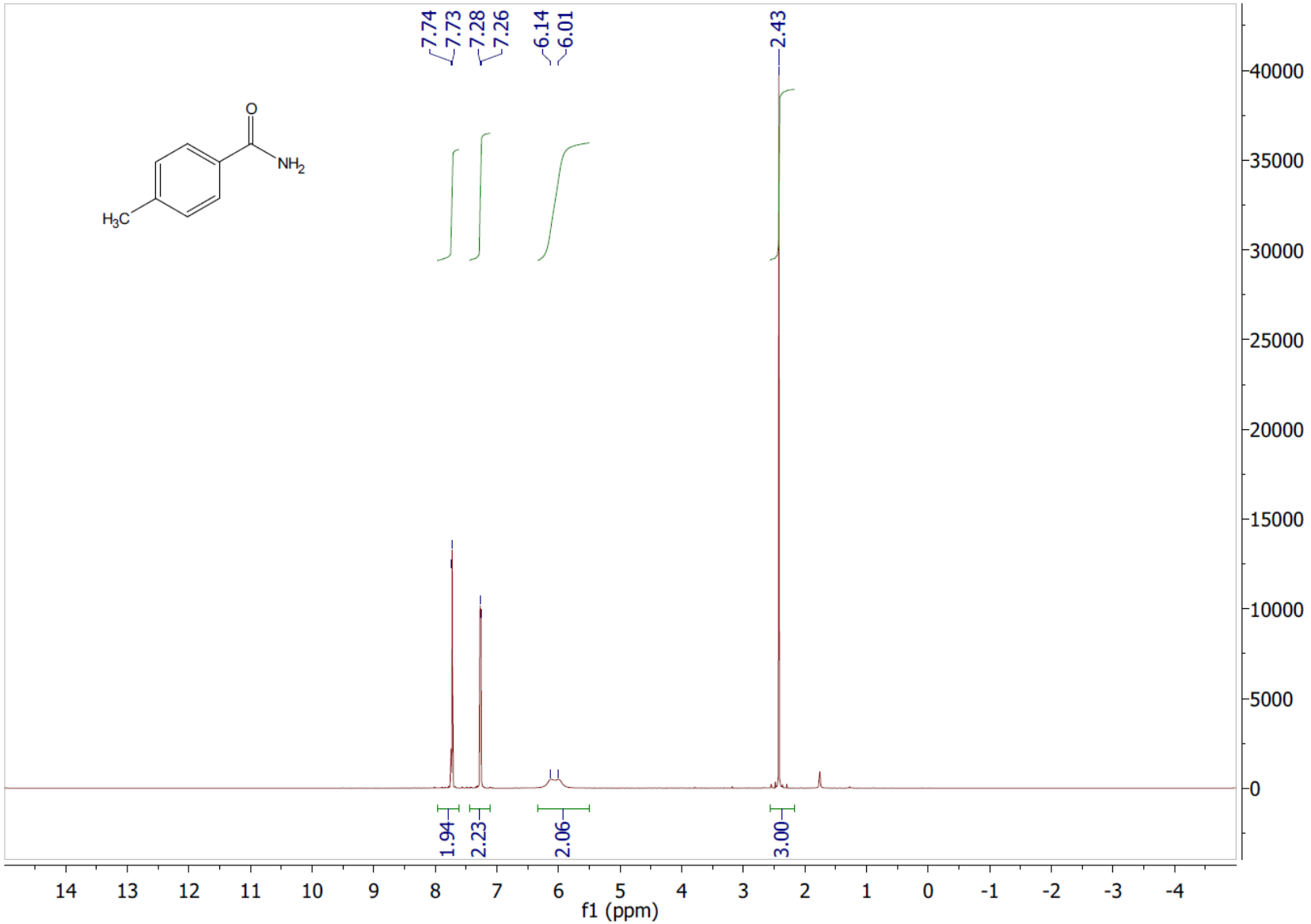


Figure S64. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of 4-methylbenzamide.

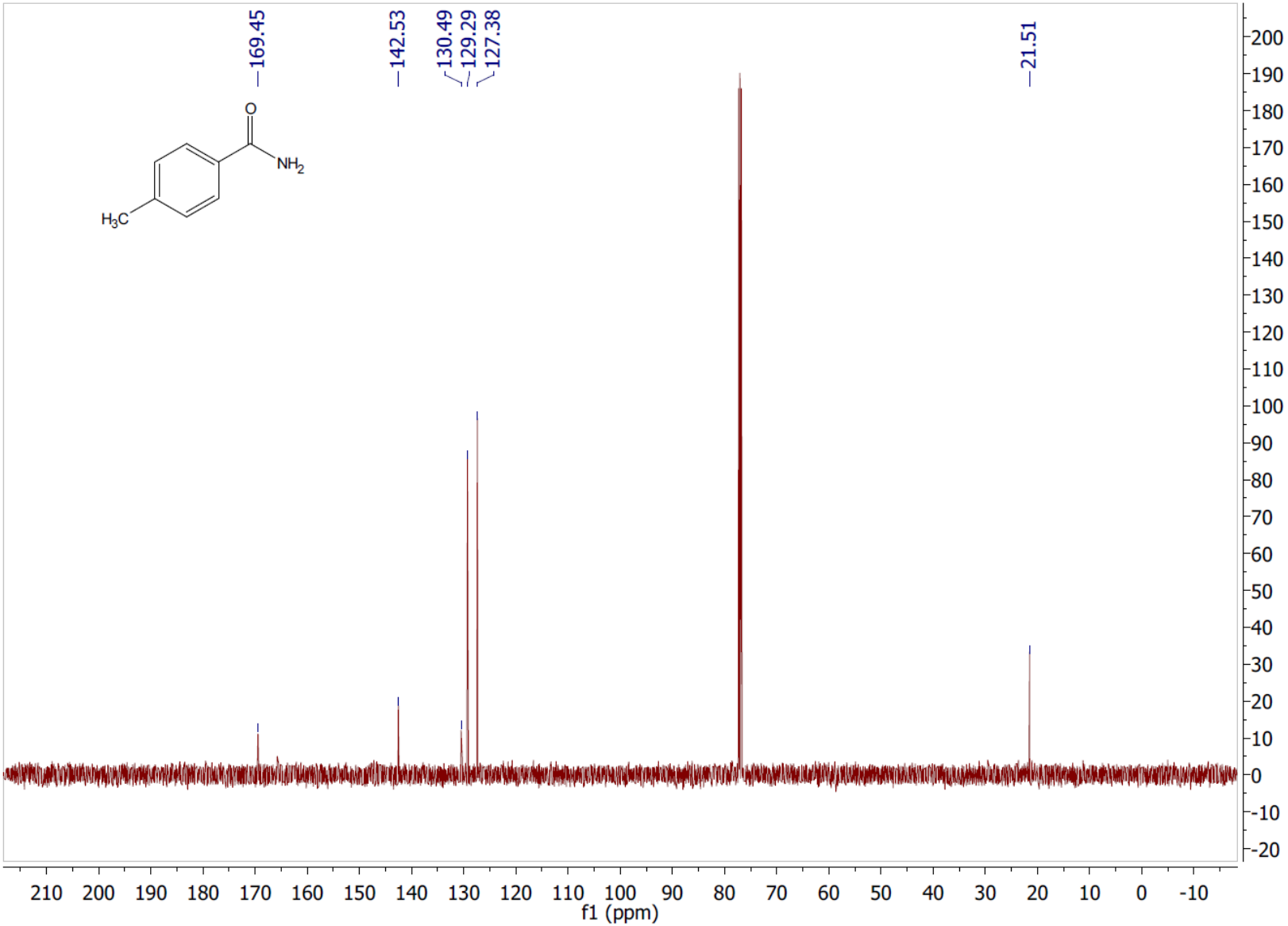


Figure S65. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of 4-methylbenzamide.

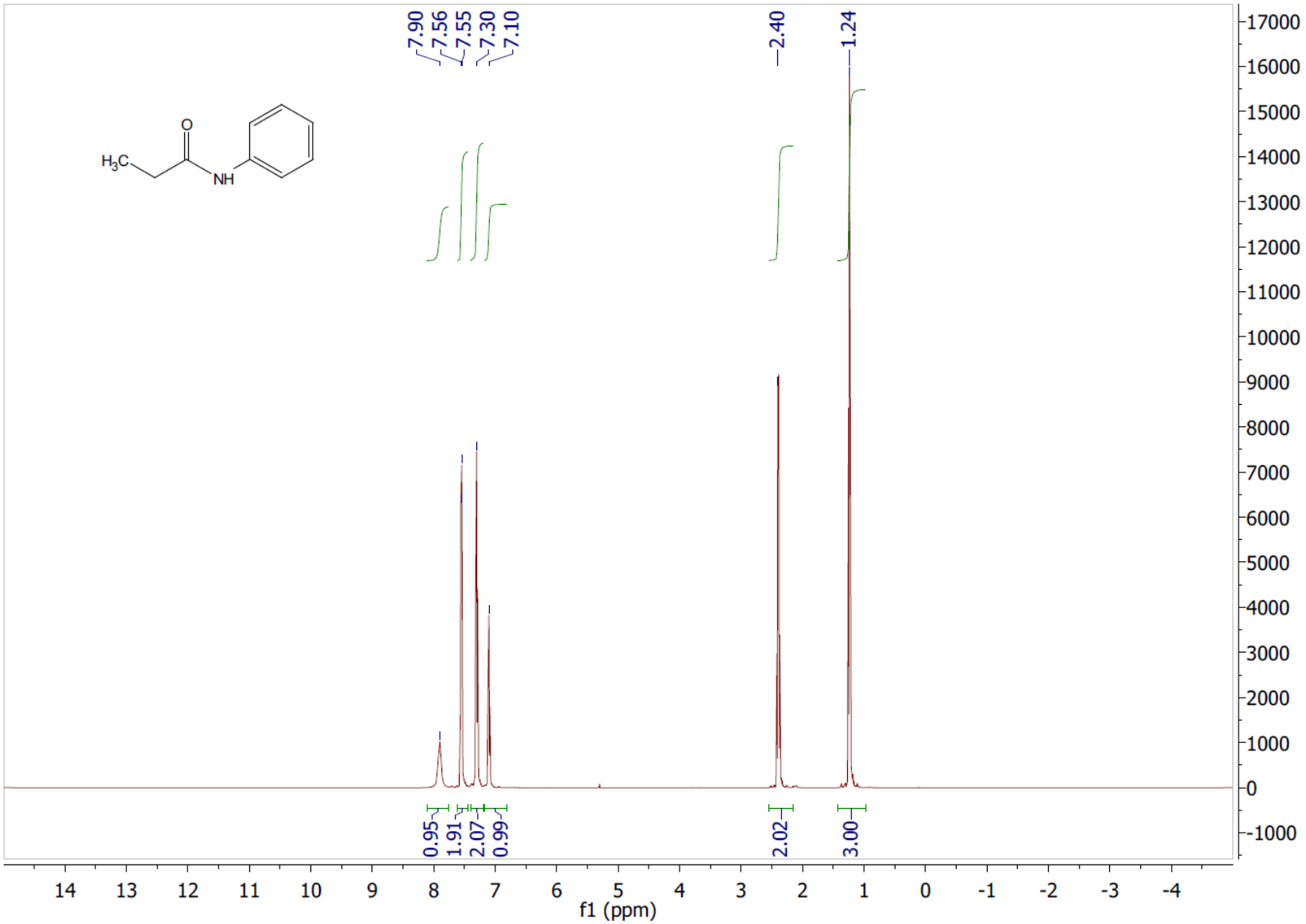


Figure S66. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-phenylpropionamide.

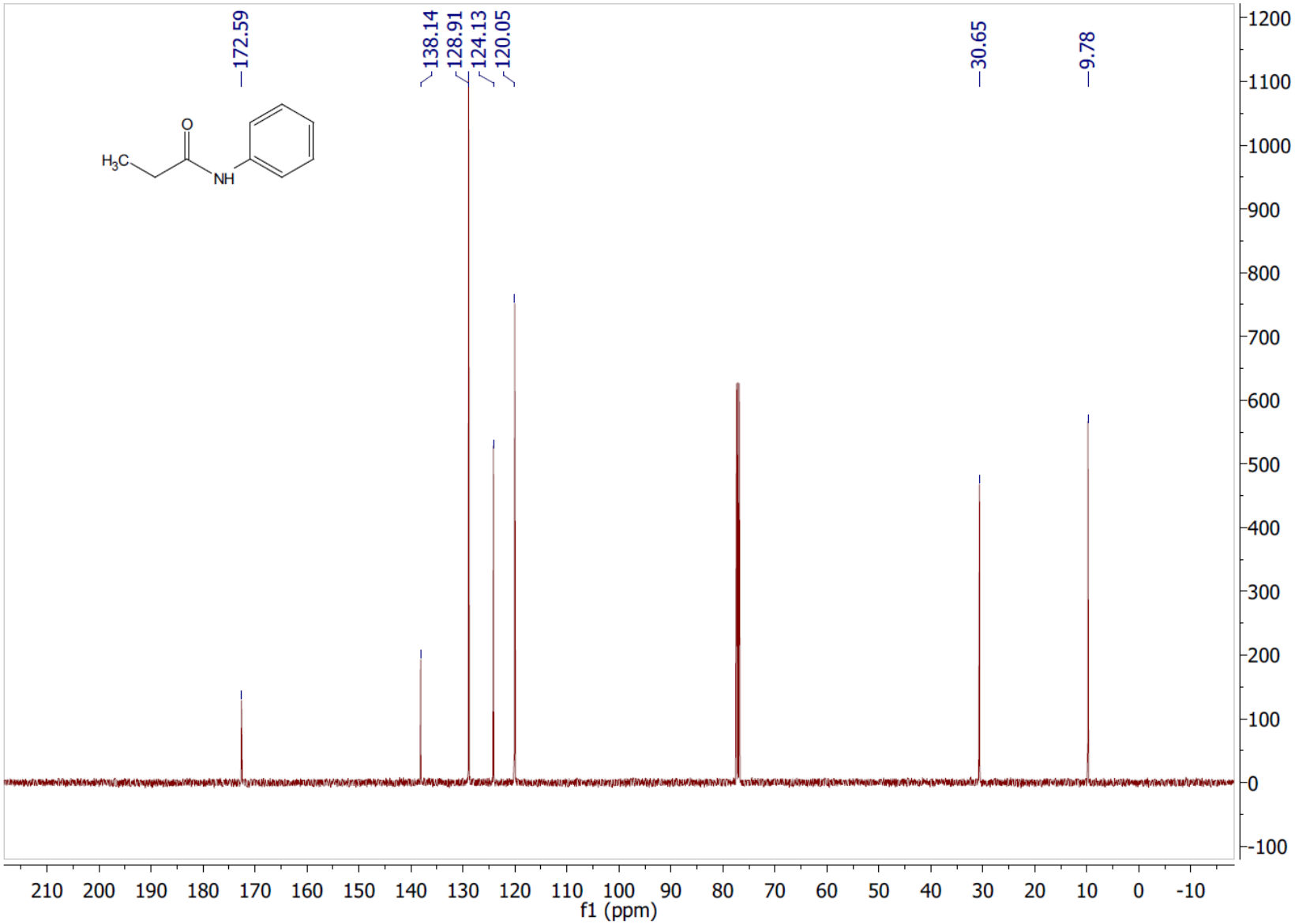


Figure S67. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-phenylpropionamide.

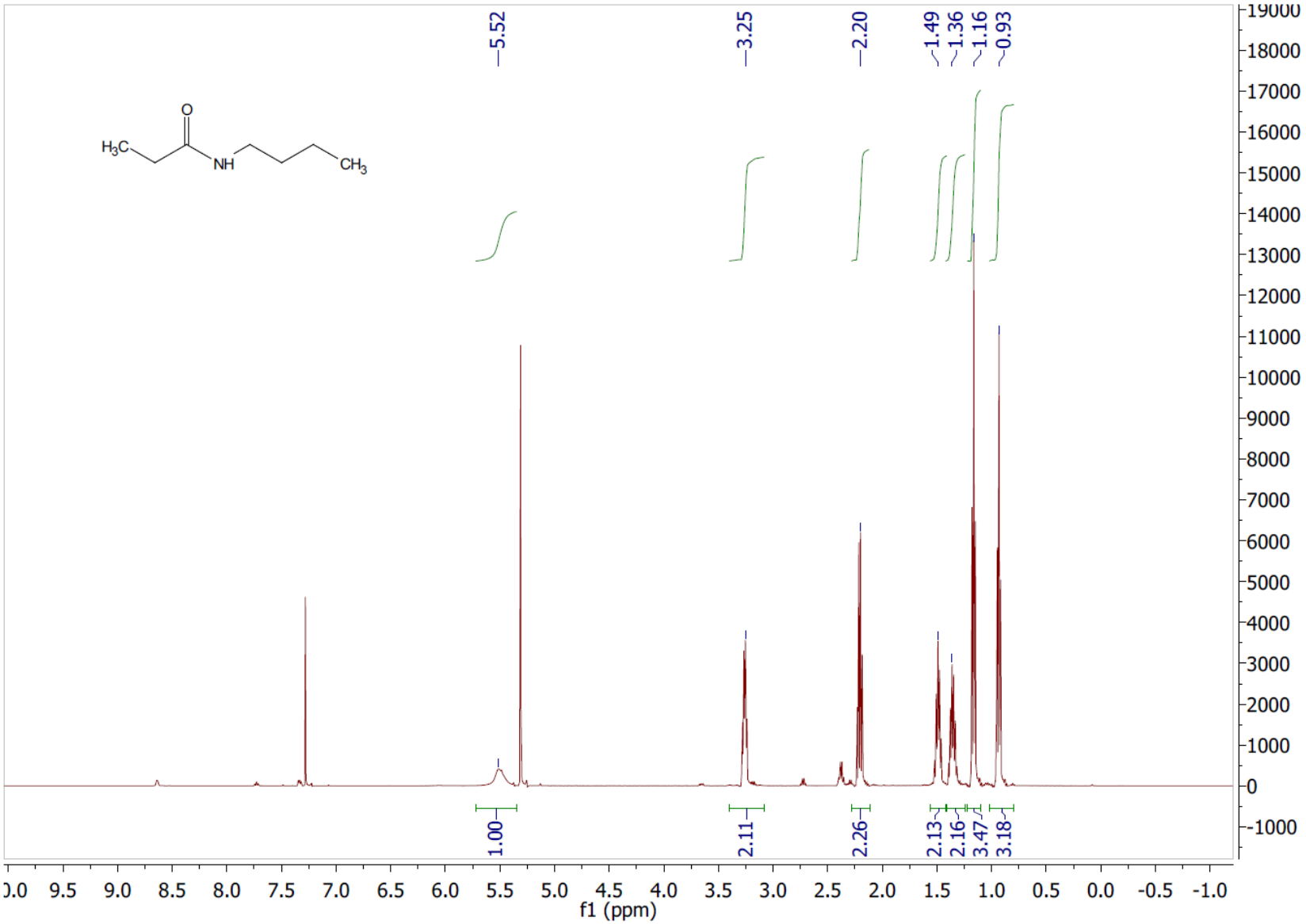


Figure S68. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of N-butylpropionamide.

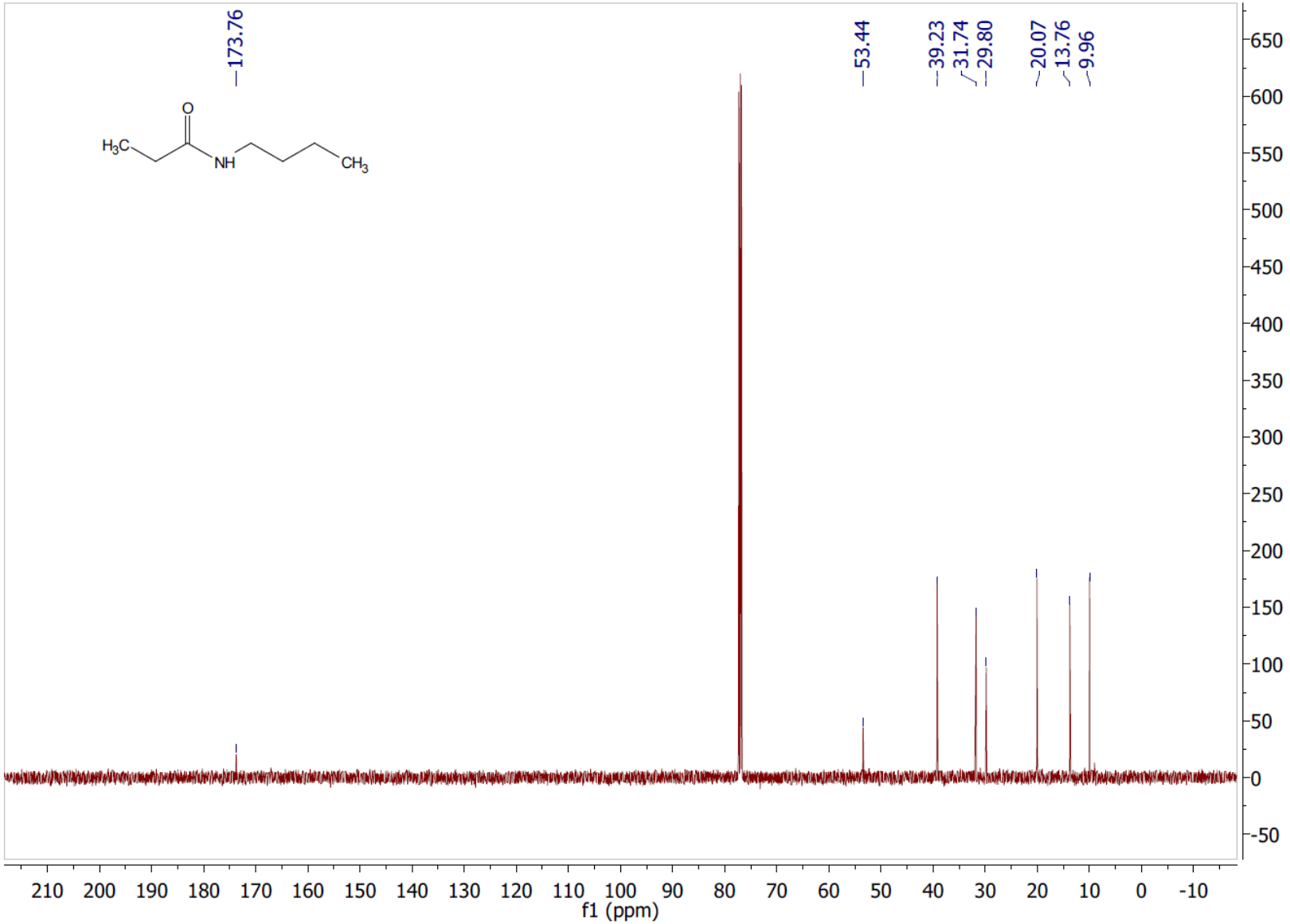


Figure S69. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of N-butylpropionamide.

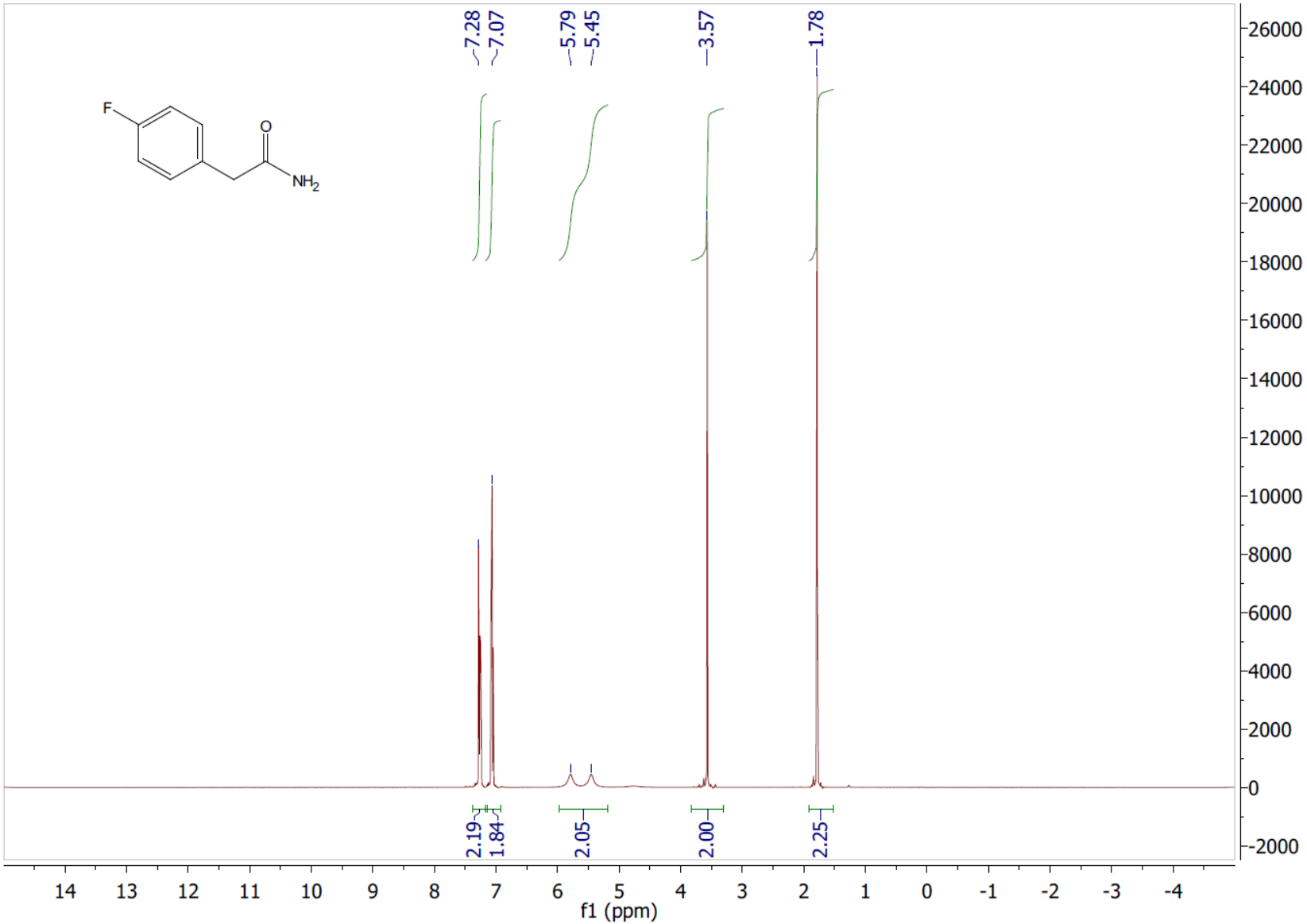


Figure S70. ^{1}H NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)acetamide.

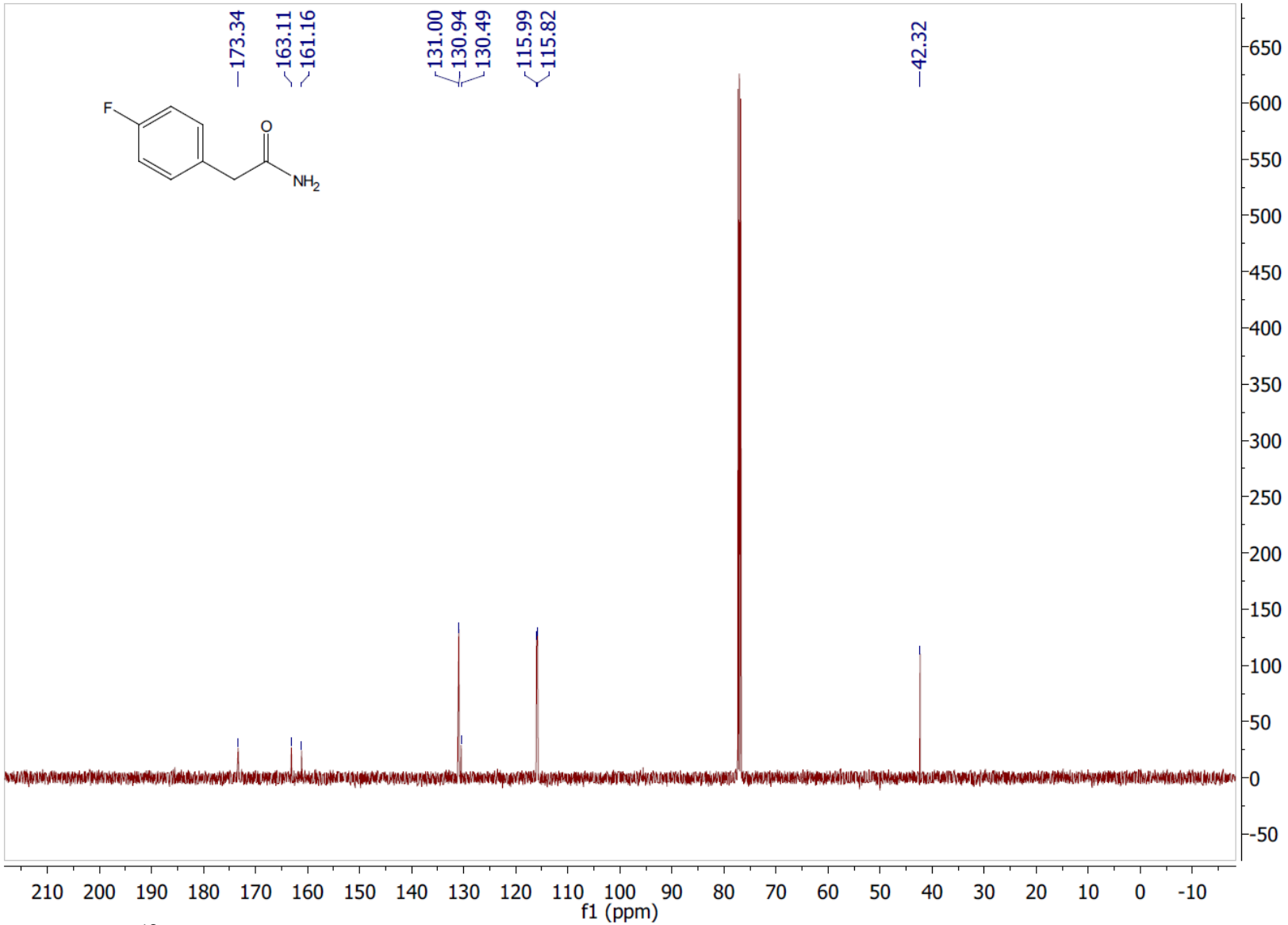


Figure S71. ^{13}C NMR ($CDCl_3$, 292 K) spectrum of 2-(4-fluorophenyl)acetamide.