Supporting Information

A convenient approach for the preparation of imidazo[1,2-*a*]-fused bicyclic frameworks via IBX/NIS promoted oxidative annulation

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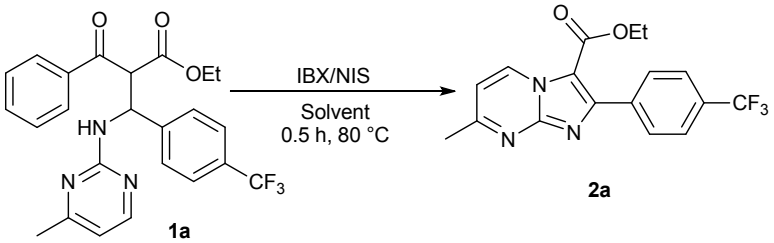
1. Supplementary information for control experiments

Table 1. Control experiments.



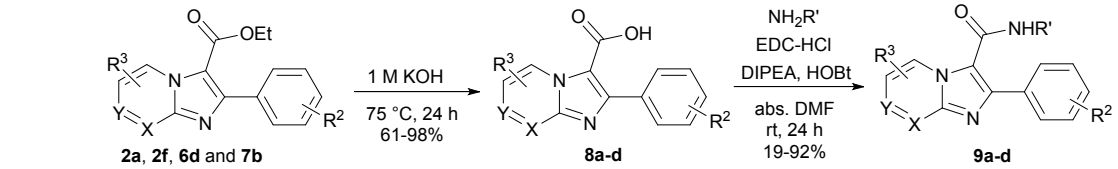
1a **2a**

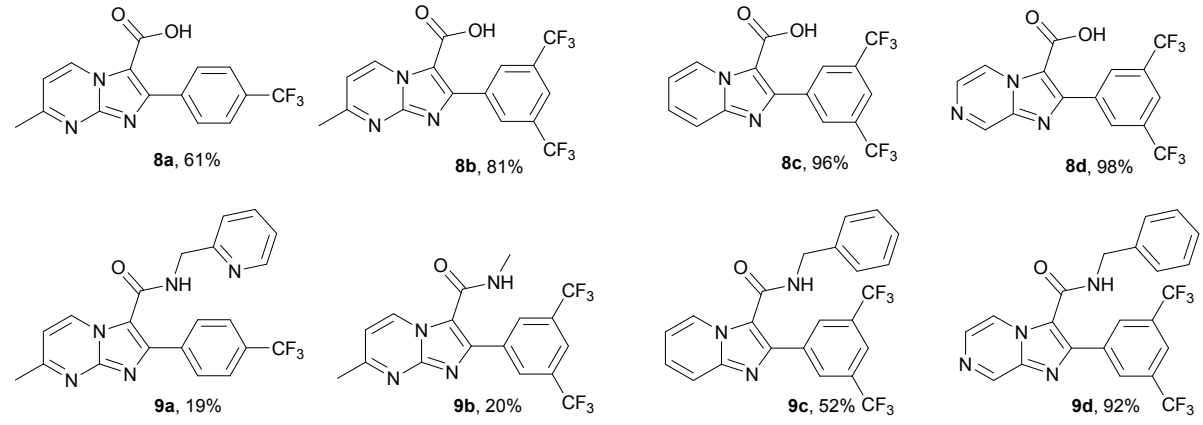
Entries	Solvent	Yield [%][a)]
1	DMF	62[b)]
2	Abs. DMF	65[c)]
3	DMF	20[d)]
4	Abs. DMF	24[d)]
5	DMA	trace[e)]
6	DMA	n.d.p.[f)]
7	DMA	73[g), h)]
8	DMA	77[i)]

Reaction conditions: 0.1 mmol **1a**, 1.1 equiv. IBX, 1.5 equiv. NIS, 2 mL solvent, 0.5 h, 80°C;
[a)]Yields were calculated on HPLC analysis by full conversion (based on HPLC);
[b)]Standard conditions;
[c)]Standard conditions and 100 mg 3Å molecular sieve;
[d)]Reaction conditions: 1.5 equiv. NIS, 80 °C, overnight, 60% conversion;
[e)]Reaction conditions: 3 equiv. I_2, 1.5 equiv. NIS, 80 °C, 0.5 h;
[f)]Reaction conditions: 5 equiv. I_2, 80 °C, 0.5 h;
[g)]Reaction conditions: 1.1 eq. IBX, 1.5 eq. NIS and 1 equiv. TEMPO, 80 °C, overnight, full conversion;
[h)]Isolated yield;
[i)]Reaction conditions: 1.1 eq. IBX, 1.5 eq. NIS, 0.5 h, dark.

2. Representative examples for further transformations of bicyclic products

Table 2. Preparation of carboxylic acids and carboxamides from **2a**, **2f**, **6d** and **7b**.





Reaction conditions (**8a–d**): 0.5 mmol starting material, 13 ml 1 M KOH, 75 °C, overnight.
Reaction conditions (**9a–d**): 0.2 mmol carboxylic acid, 1.16 equiv. EDC.HCl, 1.16 equiv. DIPEA, 1.0 equiv. amine, 1.38 equiv. HOBt, rt, abs. DMF, overnight.

3. General information

^{1}H-NMR spectra were recorded at 298 K on a Bruker Avance 500 or Bruker Ascend 500 with 5 mm BBO Prodigy Probe. Chemical shifts (δ) are given in ppm, and coupling constants (J) are given in Hz. Chemical

shifts were referenced to tetramethylsilane (TMS) (δ = 0 ppm) as an internal standard. ^{13}C-NMR spectra were obtained by using the same NMR spectrometer and were calibrated with $CDCl_3$-d_1 (δ = 76.6 ppm). Melting points were recorded with an Electrothermal IA9100 Digital Melting Point Apparatus. High-resolution mass spectra (HRMS) were measured on a Thermo Scientific Q Exactive hybrid quadrupole-Orbitrap mass spectrometer using HESI ion source. Samples (5 µL from 1 µg/ml solution) were injected to the MS using flow injection method (200 µL/min, acetonitrile/water = 50:50 with 0.1% TFA). HPLC analyses were recorded on Agilent 1100/1200 Series instrument (Kinetex column, 100 Å, 5 µm, 250 x 4.6 mm; Eluent: acetonitrile/water = 50:50). Visualization was accomplished under UV (254 and 366 nm). TLC was performed on aluminum sheets coated with silica gel 60 F_{254}. (Merck, 1.05554). Column chromatography was performed with Kieselgel 60 (Merck, 0.063-0.200 mm; elution mixtures: isomeric hexane mixture/ethyl acetate, isomeric hexane mixture/2-propanol, toluene/acetonitrile or ethyl acetate/methanol). All chemicals and solvents

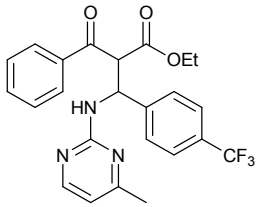
were of commercial grade and used without further purification. Mannich substrates were synthesized either following a literature method [20] (index 1) or using a slightly modified procedure (index 2, *see* Supplementary information). *N*-Iodophtalimide was prepared according to the literature.[25]

4. Modified procedure for preparation of Mannich precursors

To a solution of corresponding amine (8 mmol) and aldehyde (12 mmol) in acetonitrile (16 mL), β-keto ester (8 mmol) and phosphotungstic acid hydrate (PTA, 2.5 mol%) were added at room temperature. Then, the mixture was stirred for 24-72 hours at 60 °C. Afterwards, saturated bicarbonate solution was poured into the reaction mixture and extracted with EtOAc (3x25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed by vacuo, and the residue was purified on column chromatography (hexane/15% ethyl acetate mixture) and recrystallized from cyclohexane or *n*-pentane.

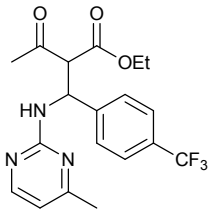
5. Characterization of Mannich precursors

Ethyl 2-benzoyl-3-(4-methylpyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1a)



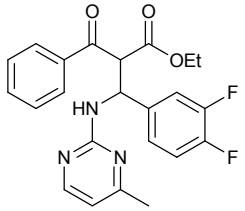
White solid, 60% yield[2]; Silica gel TLC R*f* = 0.25; 0.13 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 56:44. ^{1}H NMR (500 MHz, DMSO-*d6*) major diastereoisomer δ 8.10 (d, *J* = 4.3 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 2H), 7.82 (d, *J* = 7.9 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 3H), 7.69 – 7.65 (m, 4H), 7.63 (d, *J* = 11.3 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 6.45 (d, *J* = 5.0 Hz, 1H), 5.91 (t, *J* = 9.7 Hz, 1H), 5.32 (s, 1H), 3.76 (q, *J* = 7.0 Hz, 2H), 2.20 (s, 3H), 0.73 (t, *J* = 7.0 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-*d6*) minor diastereoisomer δ 8.10 (d, *J* = 4.3 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 2H), 7.82 (d, *J* = 7.9 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 3H), 7.69 – 7.65 (m, 4H), 7.63 (d, *J* = 11.3 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 6.47 (d, *J* = 4.9 Hz, 1H), 5.98 (t, *J* = 9.7 Hz, 1H), 5.46 (s, 1H), 4.11 – 3.93 (m, 1H), 2.15 (s, 1H), 0.96 (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-*d6*) major diastereoisomer δ 192.99, 191.98, 167.06, 166.45, 161.15, 145.79, 145.68, 135.98, 135.61, 134.11, 128.99, 128.72, 128.61, 128.31, 128.48 – 127.27 (m), 124.99 (dq, *J* = 8.6, 4.7, 4.1 Hz), 125.81 – 120.46 (m), 110.47, 61.22, 61.13, 58.61, 58.43, 53.60, 13.74, 13.33; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{23}F_3N_3O_3^+$ 458.16860; Found 458.16962.

Ethyl 2-(((4-methylpyrimidin-2-yl)amino)(4-(trifluoromethyl)phenyl)methyl)-3-oxobutanoate (1b)



White solid, 56% yield[2]; Silica gel TLC R*f* = 0.58 (toluene/acetonitrile 3:1); The ration of two diastereoisomers: 65:25. ^{1}H NMR (500 MHz, DMSO-d_6) major diastereoisomer δ 8.11 – 8.06 (m, 1H), 7.79 (d, *J* = 14.5 Hz, 1H), 7.68 – 7.60 (m, 6H), 6.46 (d, *J* = 5.4 Hz, 1H), 5.69 (dd, *J* = 11.4, 9.1 Hz, 1H), 4.30 (d, *J* = 11.1 Hz, 1H), 3.85 (tt, *J* = 7.3, 3.7 Hz, 2H), 2.26 (s, 3H), 2.19 (s, 3H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-d_6) minor diastereoisomer δ 8.10 (d, *J* = 6.3 Hz, 1H), 7.69 – 7.59 (m, 6H), 7.53 (d, *J* = 9.5 Hz, 1H), 6.48 (d, *J* = 4.9 Hz, 1H), 5.84 (t, *J* = 9.7 Hz, 1H), 4.45 (d, *J* = 9.6 Hz, 1H), 4.12 – 3.97 (m, 2H), 2.20 (s, 3H), 2.05 (s, 3H), 1.04 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) mixture of diastereoisomers δ 200.97, 200.55, 167.23, 166.28, 161.11, 161.06, 145.70, 145.57, 128.49, 128.31, 128.23 – 127.28 (m), 128.02 – 127.51 (m), 127.54 – 120.89 (m). 125.19 – 125.01 (m), 125.07 – 124.89 (m), 110.59, 109.47, 64.12, 63.87, 61.11, 61.05, 53.40, 52.63, 29.83, 29.63, 13.77, 13.44. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}F_3N_3O_3^+$ 396.15295; Found 396.15393.

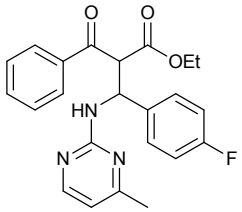
Ethyl 2-benzoyl-3-(3,4-difluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1c)



White solid, 26% yield[2]; Silica gel TLC R*f* = 0.19; 0.13 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 56:44. ^{1}H NMR (500 MHz, DMSO-d_6) δ major diastereoisomer 8.10 (d, *J* = 4.5 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.58 (ddt, *J* = 23.9, 16.4, 7.4 Hz, 4H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.39 – 7.29 (m, 1H), 7.28 – 7.17 (m, 2H), 6.47 (d, *J* = 5.1 Hz, 1H), 5.89 (t, *J* = 10.1 Hz, 1H), 5.39 (d, *J* = 10.5 Hz, 1H), 3.80 (q, *J* = 7.0 Hz, 2H), 2.20 (s, 3H), 0.96 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-d_6) minor diastereoisomer δ 8.10 (d, *J* = 4.5 Hz, 1H), 8.03 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.58 (ddt, *J* = 23.9, 16.4, 7.4 Hz, 4H), 7.50 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.39 – 7.29 (m, 1H), 7.28 – 7.17 (m, 2H), 6.45 (d, *J* = 5.0 Hz, 1H), 5.84 (t, *J* = 10.0 Hz, 1H), 5.39 (d, *J* = 10.5 Hz, 1H), 4.09 – 3.93 (m, 2H), 2.18 (s, 3H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) mixture of diastereoisomers δ 193.00, 192.01, 166.99, 166.40, 161.13, 161.12, 150.25 – 147.17 (m), 139.05 – 138.79 (m), 138.78 (q, *J* = 3.1 Hz), 135.99, 135.66, 134.12, 128.99, 128.73, 128.31, 124.84, 124.81, 117.03 (dd, *J* = 16.6, 9.9 Hz),

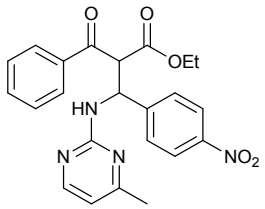
116.61 (d, *J* = 17.1 Hz), 110.55, 110.49, 61.19, 61.15, 58.75, 58.59, 53.20, 53.16, 13.74, 13.50. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{22}F_2N_3O_3^+$ 426.16237; Found 426.16371.

Ethyl 2-benzoyl-3-(4-fluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1d)



White solid, 51% yield[1]; Silica gel TLC R*f* = 0.17; 0.11 (hexane/etyl acetate 3:1); The ration of two diastereoisomer: 55:45. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.01 (d, *J* = 5.0 Hz, 1H), 7.91 – 7.85 (m, 2H), 7.52 (d, *J* = 7.0 Hz, 1H), 7.45 – 7.38 (m, 7H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.34 (d, *J* = 5.0 Hz, 1H), 6.15 (d, *J* = 6.0 Hz, 1H), 4.93 (d, *J* = 6.5 Hz, 1H), 4.18 – 4.03 (m, 2H), 2.20 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.09 (d, *J* = 5.0 Hz, 1H), 7.89 – 7.83 (m, 2H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.46 – 7.38 (m, 7H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.44 (d, *J* = 9.3 Hz, 1H), 6.38 (d, *J* = 5.0 Hz, 1H), 6.16 – 6.09 (m, 1H), 4.96 (d, *J* = 5.8 Hz, 1H), 4.02 (qd, *J* = 7.1, 2.0 Hz, 2H), 2.28 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.22, 192.74, 167.96, 167.89, 167.80, 167.53, 162.99 (d, *J* = 2.5 Hz), 161.54, 161.38, 161.03 (d, *J* = 2.7 Hz), 157.44, 157.34, 137.05, 136.64 (d, *J* = 3.2 Hz), 136.29, 133.50, 133.39, 128.78, 128.71 (d, *J* = 1.7 Hz), 128.65 (d, *J* = 1.6 Hz), 128.36, 128.33, 115.18 (dd, *J* = 21.5, 11.2 Hz), 110.95, 110.90, 61.67, 61.60, 60.05, 58.35, 53.95, 53.26, 23.97, 23.88, 13.82, 13.70. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}FN_3O_3^+$ 408.17179; Found 408.17257.

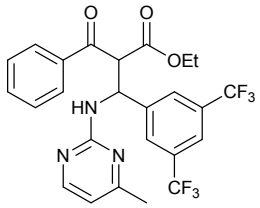
Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)-3-(4-nitrophenyl)propanoate (1e)



White solid, 33% yield[2]; Silica gel TLC R*f* = 0.15; 0.11 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 68:32. ^{1}H NMR (500 MHz, DMSO-d_6) mixture of diastereoisomers δ 8.19 (d, *J* = 8.5 Hz, 2H), 8.12 (d, *J* = 25.8 Hz, 1H), 8.04 (d, *J* = 6.1 Hz, 3H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.77 (d, *J* = 7.5 Hz, 2H), 7.70 (t, *J* = 9.0 Hz, 3H), 7.63 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.0 Hz, 1H), 7.49 (t, *J* = 7.0 Hz, 1H), 6.48 (d, *J* = 3.4 Hz, 1H), 6.46 (d, *J* = 3.3 Hz, 1H), 6.00 (t, *J* = 9.7 Hz, 1H), 5.93 (t, *J* = 9.8 Hz, 1H), 5.48 (s, 1H), 5.34 (s, 1H), 4.04 (ddt, *J* = 23.4, 16.2, 8.1 Hz, 2H), 3.77 (ttd, *J* = 7.1, 5.0, 2.5 Hz, 2H), 2.21 (s, 3H), 2.18 (s, 3H), 1.01 – 0.93 (m, 3H), 0.78 (dp, *J* = 7.1, 2.8, 2.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) mixture

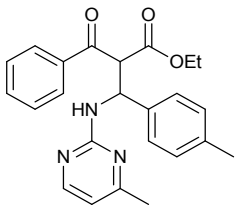
of diastereoisomers δ 193.26, 192.31, 167.35, 166.78, 161.53, 161.49, 149.26, 149.12, 147.25, 146.99, 136.33, 135.92, 134.71, 134.64, 129.66, 129.61, 129.50, 129.46, 129.22, 128.81, 123.80, 123.71, 111.16, 111.06, 61.78, 61.73, 58.78, 53.94, 14.20, 13.91. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}N_4O_5^+$ 435.16629; Found 435.16704.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1f)



White solid, 52% yield[2]; Silica gel TLC R*f* = 0.32; 0.25 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 65:35. ^{1}H NMR (500 MHz, DMSO-d_6) major diastereoisomer δ 8.22 (s, 2H), 8.14 (d, *J* = 9.1 Hz, 2H), 8.09 (d, *J* = 7.6 Hz, 2H), 8.03 (s, 1H), 7.84 (d, *J* = 6.5 Hz, 1H), 7.81 (s, 1H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 6.52 (d, *J* = 5.1 Hz, 1H), 5.97 (d, *J* = 12.4 Hz, 1H), 5.45 (s, 1H), 3.79 (q, *J* = 7.1 Hz, 2H), 2.24 (s, 3H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-d_6) minor diastereoisomer δ 8.22 (s, 2H), 8.14 (d, *J* = 9.1 Hz, 2H), 8.09 (d, *J* = 7.6 Hz, 2H), 8.03 (s, 1H), 7.84 (d, *J* = 6.5 Hz, 1H), 7.81 (s, 1H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 1H), 6.54 (d, *J* = 5.0 Hz, 1H), 6.02 (d, *J* = 10.2 Hz, 1H), 5.53 (s, 1H), 4.14 – 4.00 (m, 2H), 2.21 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) mixture of diastereoisomers δ 193.67, 192.15, 167.32, 166.74, 161.36, 161.32, 144.59, 136.26, 135.95, 134.74, 134.71, 130.95 – 130.10 (m), 129.51, 129.44, 129.29, 128.71, 127.02, 126.87, 127.54 – 120.05 (m). 122.01 – 121.79 (m), 121.57, 111.36, 61.83, 61.74, 54.04, 14.19, 13.70. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_6N_3O_3^+$ 526.15599; Found 526.15620.

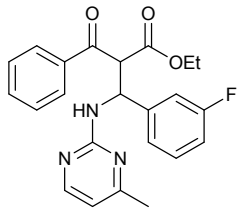
Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)-3-(p-tolyl)propanoate (1g)



White solid, 20% yield[2]; Silica gel TLC R*f* = 0.23; 0.17 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.10 (d, *J* = 5.0 Hz, 1H), 8.00 (d, *J* = 5.0 Hz, 1H), 7.93 – 7.90 (m, 2H), 7.90 – 7.86 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.44 (t, *J* = 6.7 Hz, 2H), 7.41 (t, *J* = 6.9 Hz, 2H), 7.35 (d, *J* = 1.6 Hz, 2H), 7.33 (s, 2H),

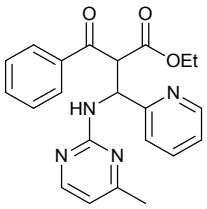
7.08 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.9 Hz, 2H), 6.48 (d, *J* = 9.6 Hz, 1H), 6.37 (d, *J* = 5.0 Hz, 1H), 6.33 (d, *J* = 5.0 Hz, 1H), 6.21 (d, *J* = 9.9 Hz, 1H), 6.17 (d, *J* = 5.5 Hz, 1H), 6.18 – 6.12 (m, 1H), 4.99 (d, *J* = 6.0 Hz, 1H), 4.97 (d, *J* = 6.7 Hz, 1H), 4.18 – 4.06 (m, 2H), 4.02 (th, *J* = 10.8, 3.6 Hz, 2H), 2.28 (s, 3H), 2.27 (s, 3H), 2.25 (s, 3H), 2.19 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.41, 193.01, 168.24, 167.88, 167.79, 167.77, 161.60, 161.42, 157.52, 157.38, 137.76, 137.36, 137.00, 136.90, 136.13, 133.50, 133.43, 129.19, 129.09, 128.73, 128.66, 128.47, 128.40, 126.84, 126.75, 110.81, 110.78, 61.69, 61.58, 60.05, 58.31, 54.13, 53.37, 24.11, 24.00, 21.06, 21.04, 13.90, 13.78. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}N_3O_3^+$ 404.19687; Found 404.19766.

Ethyl 2-benzoyl-3-(3-fluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1h)



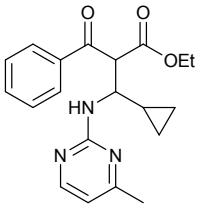
White solid, 26% yield[1]; Silica gel TLC R*f* = 0.24; 0.16 (hexane/etyl acetate 3:1)The ration of two diastereoisomers: 50:50. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.11 (d, *J* = 5.0 Hz, 1H), 8.01 (d, *J* = 5.0 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.89 – 7.83 (m, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.48 – 7.44 (m, 2H), 7.46 – 7.39 (m, 2H), 7.23 (ddd, *J* = 10.1, 5.1, 3.3 Hz, 4H), 7.18 (dt, *J* = 9.7, 1.7 Hz, 2H), 6.88 (dtt, *J* = 16.1, 6.7, 2.4 Hz, 2H), 6.54 (d, *J* = 9.4 Hz, 1H), 6.41 (d, *J* = 5.0 Hz, 1H), 6.36 (d, *J* = 5.0 Hz, 1H), 6.24 (d, *J* = 9.5 Hz, 1H), 6.17 (ddd, *J* = 15.1, 9.4, 6.1 Hz, 2H), 4.99 (d, *J* = 5.6 Hz, 1H), 4.96 (d, *J* = 6.6 Hz, 1H), 4.19 – 4.08 (m, 2H), 4.04 (ddp, *J* = 10.6, 7.1, 3.5 Hz, 2H), 2.30 (s, 3H), 2.21 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.20, 192.74, 168.03, 168.01, 167.92, 167.55, 162.84 (d, *J* = 246.1 Hz), 162.81 (d, *J* = 246.2 Hz), 161.36 (d, *J* = 25.3 Hz), 157.52, 157.40, 143.37 (d, *J* = 33.2 Hz), 143.32 (d, *J* = 33.6 Hz), 136.80, 135.93, 133.71, 133.61, 129.99 (d, *J* = 12.7 Hz), 129.93 (d, *J* = 12.8 Hz), 128.82, 128.75, 128.44, 128.37, 122.51 (d, *J* = 2.7 Hz), 122.46 (d, *J* = 2.7 Hz), 114.36 (d, *J* = 20.7 Hz), 114.30 (d, *J* = 9.1 Hz), 114.16 (d, *J* = 18.2 Hz), 114.11 (d, *J* = 15.1 Hz), 111.13, 111.09, 61.88, 61.76, 59.70, 57.88, 53.97, 53.24, 24.11, 24.00, 13.89, 13.77. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}FN_3O_3^+$ 408.17179; Found 408.17267.

Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)-3-(pyridin-2-yl)propanoate (1i)



Orange solid, 5% yield[1]; Silica gel TLC R*f* = 0.54 (toluene/acetonitrile 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.47 (d, *J* = 4.8 Hz, 1H), 8.42 (d, *J* = 4.8 Hz, 1H), 8.15 (d, *J* = 5.2 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 2H), 7.96 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 7.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.37 (m, 5H), 7.13 – 7.06 (m, 2H), 6.65 (d, *J* = 9.9 Hz, 1H), 6.50 (d, *J* = 5.0 Hz, 2H), 6.42 (d, *J* = 5.0 Hz, 1H), 6.37 (d, *J* = 5.1 Hz, 1H), 6.34 (d, *J* = 5.5 Hz, 1H), 6.32 (d, *J* = 5.5 Hz, 1H), 6.28 (d, *J* = 10.0 Hz, 1H), 5.63 (d, *J* = 5.5 Hz, 1H), 5.60 (d, *J* = 6.5 Hz, 1H), 4.18 – 4.04 (m, 2H), 4.00 (ddq, *J* = 10.4, 7.2, 3.5 Hz, 2H), 2.19 (s, 3H), 1.98 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 195.65, 194.11, 168.87, 168.52, 168.36, 168.06, 161.86, 161.64, 159.67, 159.65, 157.86, 157.58, 148.86, 148.69, 137.15, 136.60, 136.59, 136.06, 133.36, 133.32, 128.67, 128.65, 128.58, 128.54, 122.36, 122.24, 122.12, 121.85, 111.28, 110.97, 61.48, 61.41, 58.17, 56.02, 55.45, 54.79, 24.01, 23.97, 13.90, 13.78. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}N_4O_3^+$ 391.17647; Found 391.17732.

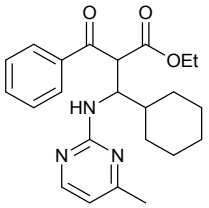
Ethyl 2-benzoyl-3-cyclopropyl-3-((4-methylpyrimidin-2-yl)amino)propanoate (1j)



White solid, 22% yield[2]; Silica gel TLC R*f* = 0.30; 0.24 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 68:32. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.15 (d, *J* = 5.1 Hz, 2H), 7.93 – 7.87 (m, 1H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 6.43 (d, *J* = 5.0 Hz, 1H), 5.92 (d, *J* = 8.6 Hz, 1H), 5.06 (d, *J* = 4.6 Hz, 1H), 4.17 – 4.07 (m, 2H), 4.06 – 3.96 (m, 1H), 2.36 (s, 3H), 2.19 (s, 1H), 1.80 (s, 1H), 1.61 (s, 1H), 1.46 – 1.35 (m, 1H), 1.14 (t, *J* = 7.1 Hz, 3H), 0.55 – 0.33 (m, 4H), 0.29 (q, *J* = 5.8, 5.4 Hz, 1H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.18 (d, *J* = 7.9 Hz, 2H), 8.00 (d, *J* = 5.0 Hz, 1H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 6.50 (d, *J* = 5.0 Hz, 1H), 6.33 (d, *J* = 5.0 Hz, 1H), 5.82 (d, *J* = 9.4 Hz, 1H), 5.03 – 4.95 (m, 1H), 4.94 (d, *J* = 5.5 Hz, 1H), 4.29 – 4.15 (m, 2H), 4.06 – 3.96 (m, 1H), 2.35 (s, 3H), 2.19 (s, 1H), 1.80 (s, 1H), 1.61 (s, 1H), 1.46 – 1.35 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.55 – 0.33 (m, 4H), 0.29 (q, *J* = 5.8, 5.4 Hz, 1H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.86, 194.25, 168.98, 168.91, 167.91, 167.74, 161.71,

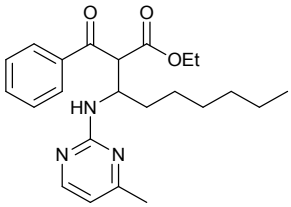
161.58, 157.91, 157.30, 136.83, 136.53, 133.59, 133.24, 128.80, 128.69, 128.65, 128.38, 110.43, 110.39, 61.37, 61.20, 57.73, 57.07, 56.20, 55.08, 24.18, 24.00, 14.92, 14.00, 13.94, 13.37, 5.14, 4.77, 3.53, 3.52. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}N_3O_3^+$ 354.18122; Found 354.18197.

Ethyl 2-benzoyl-3-cyclohexyl-3-((4-methylpyrimidin-2-yl)amino)propanoate (1k)



Colourless solid, 20% yield[2]; Silica gel TLC R*f* = 0.43; 0.37 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 53:47. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.95 (d, *J* = 7.3 Hz, 2H), 7.83 (d, *J* = 7.7 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.51 – 7.40 (m, 4H), 6.33 (d, *J* = 5.0 Hz, 1H), 6.27 – 6.21 (m, 1H), 6.17 (d, *J* = 10.4 Hz, 1H), 5.90 (d, *J* = 10.6 Hz, 1H), 4.77 (d, *J* = 5.2 Hz, 1H), 4.72 (d, *J* = 4.5 Hz, 1H), 4.25 – 4.07 (m, 2H), 3.96 (q, *J* = 7.1 Hz, 2H), 2.29 (s, 3H), 2.05 (s, 3H), 1.96 (d, *J* = 12.9 Hz, 2H), 1.85 (d, *J* = 12.0 Hz, 3H), 1.79 – 1.46 (m, 11H), 1.29 – 1.23 (m, 2H), 1.21 – 1.12 (m, 5H), 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 195.05, 194.58, 169.04, 167.75, 157.26, 157.25, 136.93, 136.34, 133.51, 133.17, 128.78, 128.66, 128.37, 128.23, 111.21, 109.94, 61.54, 61.31, 55.97, 55.77, 54.64, 53.90, 41.78, 41.30, 30.62, 30.60, 29.78, 26.21, 26.17, 26.09, 25.99, 14.01, 13.73. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{30}N_3O_3^+$ 396.22817; Found 396.22878.

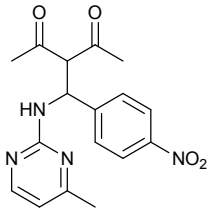
Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)decanoate (1l)



Colourless solid, 10% yield[1]; Silica gel TLC R*f* = 0.45; 0.39 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 60:40. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.89 (t, *J* = 7.8 Hz, 3H), 7.62 – 7.52 (m, 3H), 7.53 – 7.38 (m, 7H), 7.18 (t, *J* = 7.9 Hz, 1H), 6.42 (d, *J* = 5.0 Hz, 1H), 6.33 (d, *J* = 5.0 Hz, 1H), 5.66 (d, *J* = 9.1 Hz, 1H), 5.55 (d, *J* = 9.6 Hz, 1H), 4.77 (d, *J* = 5.6 Hz, 1H), 4.74 (d, *J* = 10.4 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.09 (q, *J* = 6.8 Hz, 2H), 2.59 (q, *J* = 7.7 Hz, 2H), 2.34 (s, 3H), 2.11 (q, *J* = 7.7 Hz, 2H), 1.48 – 1.36 (m, 4H), 1.32 – 1.08 (m, 15H), 0.92 – 0.78 (m, 10H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 195.18, 194.44, 168.92, 164.62, 161.91, 161.88, 152.01, 148.67, 137.45, 136.85, 136.69, 136.46, 133.64, 133.59, 129.08, 128.73, 128.68, 128.45,

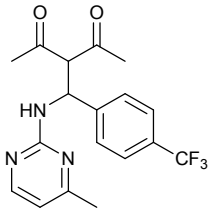
110.40, 110.30, 61.31, 61.11, 57.63, 56.71, 51.20, 50.78, 33.80, 31.77, 31.73, 31.63, 29.59, 29.16, 28.91, 28.38, 26.68, 26.43, 24.16, 22.61, 22.58, 14.09, 14.08, 13.99, 13.93. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{34}N_3O_3^+$ 412.25947; Found 412.26035.

3-(((4-methylpyrimidin-2-yl)amino)(4-nitrophenyl)methyl)pentane-2,4-dione (1m)



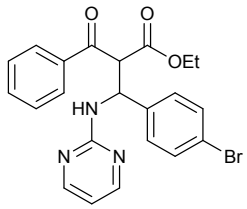
Colourless solid, 45% yield[2]; Silica gel TLC R*f* = 0.49 (toluene/acetonitrile 3:1); The ration of two diastereoisomers: 86:14. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.16 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 5.0 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 2H), 6.47 (d, *J* = 5.1 Hz, 1H), 6.30 (d, *J* = 9.7 Hz, 1H), 6.11 (dd, *J* = 9.7, 7.9 Hz, 1H), 4.30 (d, *J* = 7.9 Hz, 1H), 2.30 (s, 3H), 2.18 (s, 3H), 2.17 (s, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.25 (d, *J* = 8.8 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.13 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.56 (d, *J* = 5.1 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 5.70 (d, *J* = 8.0 Hz, 1H), 2.12 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 203.30, 201.63, 168.41, 160.87, 157.84, 157.55, 147.99, 147.27, 127.97, 127.02, 123.96, 123.88, 111.87, 111.77, 72.20, 53.51, 52.06, 31.45, 30.19. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_4O_4^+$ 343.14008; Found 343.14095.

3-(((4-methylpyrimidin-2-yl)amino)(4-(trifluoromethyl)phenyl)methyl)pentane-2,4-dione (1n)



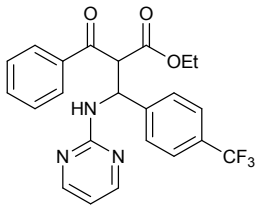
White solid, 54% yield[2]; Silica gel TLC R*f* = 0.54 (toluene/acetonitrile 3:1); The ration of two diastereoisomers: 98:2. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (d, *J* = 5.0 Hz, 1H), 7.75 (d, *J* = 6.4 Hz, 1H), 7.66 (s, 4H), 6.50 (d, *J* = 5.0 Hz, 1H), 5.78 (dd, *J* = 11.0, 9.5 Hz, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 2.27 (s, 3H), 2.22 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 202.26, 201.83, 161.56, 146.42, 128.90, 128.23 (q, *J* = 31.8 Hz), 125.58 (q, *J* = 4.0 Hz), 125.82 – 121.31 (m), 71.87, 53.87, 31.14, 31.02. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}F_3N_3O_2^+$ 366.14239; Found 366.14307.

Ethyl 2-benzoyl-3-(4-bromophenyl)-3-(pyrimidin-2-ylamino)propanoate (1o)



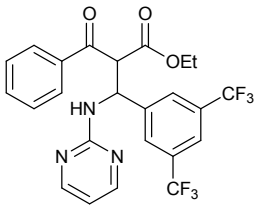
White solid, 16% yield[1]; Silica gel TLC R*f* = 0.26; 0.20 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 50:50. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.26 (d, *J* = 4.8 Hz, 2H), 8.17 (d, *J* = 4.8 Hz, 2H), 7.91 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.85 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.31 (m, 12H), 6.72 (d, *J* = 9.4 Hz, 1H), 6.53 (t, *J* = 4.8 Hz, 1H), 6.49 (t, *J* = 4.8 Hz, 1H), 6.35 (d, *J* = 9.4 Hz, 1H), 6.11 (dd, *J* = 9.5, 5.4 Hz, 1H), 6.05 (dd, *J* = 9.5, 6.9 Hz, 1H), 4.96 (d, *J* = 5.5 Hz, 1H), 4.92 (d, *J* = 6.8 Hz, 1H), 4.20 – 4.05 (m, 2H), 4.04 (ddt, *J* = 10.8, 7.0, 3.7 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.36, 192.55, 167.96, 167.52, 161.57, 161.37, 158.08, 157.95, 139.71, 139.39, 136.74, 135.80, 133.81, 133.73, 131.64, 131.56, 128.88, 128.79, 128.74, 128.71, 128.45, 128.36, 121.43, 121.32, 111.51, 111.43, 61.96, 61.86, 59.72, 57.74, 54.04, 53.37, 13.90, 13.80. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}BrN_3O_3^+$ 454.07608, 456.07403, 455.07943, 457.07739; Found 454.07692, 455.08048, 456.07482, 457.07825.

Ethyl 2-benzoyl-3-(pyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1p)



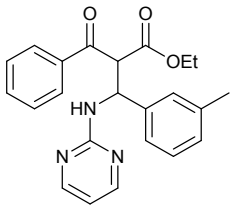
White solid, 76% yield[2]; Silica gel TLC R*f* = 0.17; 0.11 (hexane / etyl acetate 3:1); The ration of two diastereoisomers: 50:50. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.26 (d, *J* = 4.7 Hz, 2H), 8.18 (d, *J* = 4.7 Hz, 2H), 7.92 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.62 – 7.51 (m, 8H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 9.3 Hz, 1H), 6.54 (t, *J* = 4.8 Hz, 1H), 6.50 (t, *J* = 4.8 Hz, 1H), 6.46 (d, *J* = 9.3 Hz, 1H), 6.22 (dd, *J* = 9.2, 5.4 Hz, 1H), 6.18 – 6.12 (m, 1H), 5.01 (d, *J* = 5.4 Hz, 1H), 4.98 (d, *J* = 6.9 Hz, 1H), 4.19 – 4.09 (m, 2H), 4.11 – 3.98 (m, 2H), 1.08 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ mixture of diastereoisomers δ 193.66, 192.15, 167.64, 167.14, 161.27, 161.10, 158.14, 158.03, 143.50, 143.16, 136.33, 135.61, 134.10, 133.97, 131.68 (q, *J* = 33.5 Hz), 131.62 (q, *J* = 33.5 Hz), 128.96, 128.89, 128.41, 127.63 – 127.49 (m), 123.20 (q, *J* = 271.8 Hz), 121.60 (dq, *J* = 7.5, 3.7 Hz), 62.21, 62.18, 59.38, 57.78, 54.02, 53.45, 13.81, 13.71. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_3N_3O_3^+$ 444.15295; Found 444.15357.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyrimidin-2-ylamino)propanoate (1q)



White solid, 10% yield[1]; Silica gel TLC R*f* = 0.38; 0.30 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 56:44. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.20 (d, *J* = 4.8 Hz, 2H), 7.94 (s, 3H), 7.92 – 7.88 (m, 2H), 7.73 (s, 1H), 7.52 – 7.39 (m, 3H), 6.55 (t, *J* = 4.8 Hz, 1H), 6.40 (d, *J* = 8.8 Hz, 1H), 6.15 (dd, *J* = 8.8, 6.8 Hz, 1H), 4.94 (d, *J* = 6.8 Hz, 1H), 4.14 (tdd, *J* = 10.8, 7.9, 3.8 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.28 (d, *J* = 4.8 Hz, 2H), 7.94 (s, 3H), 7.88 – 7.84 (m, 2H), 7.70 (s, 1H), 7.63 – 7.54 (m, 2H), 6.67 (d, *J* = 8.9 Hz, 1H), 6.59 (t, *J* = 4.8 Hz, 1H), 6.23 (dd, *J* = 9.0, 5.6 Hz, 1H), 4.99 (d, *J* = 5.6 Hz, 1H), 4.08 – 4.00 (m, 2H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 193.66, 192.15, 167.64, 167.14, 161.27, 161.10, 158.14, 158.03, 143.50, 143.16, 136.33, 135.61, 134.10, 133.97, 131.68 (q, *J* = 33.5 Hz), 131.62 (q, *J* = 33.5 Hz), 128.96, 128.89, 128.41, 127.67 – 127.48 (m), 123.20 (q, *J* = 271.8 Hz), 121.60 (dp, *J* = 11.3, 3.7 Hz), 111.96, 111.02, 77.28, 62.21, 62.18, 59.38, 57.78, 54.02, 53.45, 13.81, 13.71. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}F_6N_3O_3^+$ 512.14034; Found 512.14042.

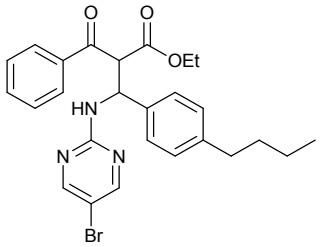
Ethyl 2-benzoyl-3-(pyrimidin-2-ylamino)-3-(m-tolyl)propanoate (1r)



White solid, 12% yield[1]; Silica gel TLC R*f* = 0.28; 0.24 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 92:8. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.16 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 6.8 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 10.4 Hz, 1H), 6.46 (t, *J* = 4.8 Hz, 1H), 6.39 (d, *J* = 9.7 Hz, 1H), 6.10 (dd, *J* = 9.7, 6.6 Hz, 1H), 4.96 (d, *J* = 6.6 Hz, 1H), 4.15 – 4.00 (m, 2H), 2.30 (s, 3H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.25 (d, *J* = 4.8 Hz, 2H), 7.84 (s, 2H), 7.56 – 7.50 (m, 1H), 7.44 – 7.37 (m, 2H), 7.17 – 7.11 (m, 1H), 6.98 (d, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 10.4 Hz, 1H), 6.50 (t, *J* = 4.8 Hz, 1H), 6.15 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.98 (d, *J* = 6.2 Hz, 1H), 4.18 – 4.14 (m, 2H), 2.28 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 192.97, 168.22, 161.55, 158.05, 157.92, 140.44, 138.19, 136.01, 133.55, 133.50, 128.78, 128.66, 128.45, 128.36, 128.31, 128.19, 127.52, 123.85, 123.80, 111.19, 111.12, 61.78, 61.64,

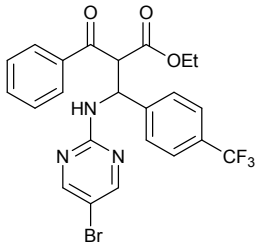
60.02, 58.13, 54.38, 53.64, 21.52, 13.89. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{24}N_3O_3^+$ 390.18122; Found 390.18194.

Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-(4-butylphenyl)propanoate (1s)



White solid, 10% yield[2]; Silica gel TLC R*f* = 0.60; 0.54 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: > 95. ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.16 (s, 2H), 7.91 (d, *J* = 7.1 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.50 (d, *J* = 9.7 Hz, 1H), 6.00 (dd, *J* = 9.6, 6.4 Hz, 1H), 4.94 (d, *J* = 6.5 Hz, 1H), 4.19 – 4.03 (m, 2H), 2.54 (t, *J* = 7.8 Hz, 2H), 1.58 – 1.45 (m, 2H), 1.29 (tt, *J* = 11.2, 5.6 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H).^{13}C NMR (126 MHz, chloroform-*d*) δ 192.41, 167.76, 159.45, 157.68, 141.89, 136.78, 135.46, 133.13, 128.36, 128.21, 127.99, 126.11, 106.60, 61.24, 59.27, 53.47, 34.77, 33.01, 21.88, 13.47. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{29}BrN_3O_3^+$ 510.13868, 512.13663, 511.14203, 513.13999; Found 510.13860, 512.13631, 513.13994.

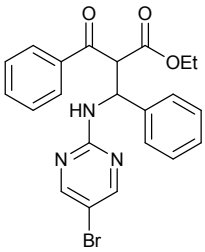
Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-(4-(trifluoromethyl)phenyl)propanoate (1t)



White solid, 28% yield[2]; Silica gel TLC R*f* = 0.42; 0.34 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 53:47. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.27 (s, 2H), 7.92 (dt, *J* = 7.3, 1.3 Hz, 2H), 7.56 (s, 4H), 7.58 – 7.49 (m, 4H), 7.48 (t, *J* = 7.8 Hz, 2H), 6.55 (d, *J* = 9.3 Hz, 1H), 6.03 (dd, *J* = 9.3, 6.5 Hz, 1H), 4.94 (d, *J* = 6.5 Hz, 1H), 4.08 (qd, *J* = 7.1, 6.1, 1.6 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.18 (s, 2H), 7.85 – 7.80 (m, 2H), 7.63 – 7.57 (m, 2H), 7.56 (s, 4H), 7.58 – 7.49 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 9.3 Hz, 1H), 6.12 (dd, *J* = 9.3, 5.1 Hz, 1H), 4.98 (d, *J* = 5.1 Hz, 1H), 4.19 – 4.12 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.35, 192.34 , 167.90 , 167.35 , 159.86 , 159.65 , 158.38, 158.26, 144.24, 143.98, 136.54, 135.54, 134.02, 133.95, 130.10 – 129.62 (m), 128.98, 128.85, 128.45, 128.35, 127.33, 127.25, 125.62 (q, *J* = 3.5 Hz), 125.64 – 125.42 (m)., 127.18 – 119.82 (m), 107.65, 107.53, 62.16, 62.03, 59.31, 57.36, 54.60, 53.88, 13.88, 13.82; HRMS

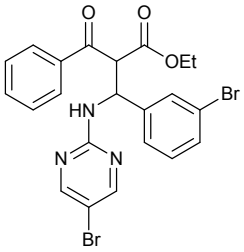
(ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}BrF_3N_3O_3^+$ 522.06346, 524.06142, 523.06682, 525.06477; Found 522.06329, 523.06651, 524.06102, 525.06430.

Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-phenylpropanoate (1u)



White solid, 10% yield[2]; Silica gel TLC R*f* = 0.49; 0.45 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 50:50. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.30 (s, 1H), 8.25 (s, 2H), 8.16 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 2H), 7.82 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.38 (m, 6H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 15.4 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 6.86 (d, *J* = 9.5 Hz, 1H), 6.55 (d, *J* = 9.6 Hz, 1H), 6.09 (dd, *J* = 9.5, 5.4 Hz, 1H), 6.02 (dd, *J* = 9.6, 6.3 Hz, 1H), 4.98 (d, *J* = 5.5 Hz, 1H), 4.96 (d, *J* = 6.4 Hz, 1H), 4.18 – 4.09 (m, 2H), 4.09 – 4.00 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.27, 194.12, 167.70, 167.09, 159.60, 159.42, 157.82, 157.69, 139.64, 139.35, 136.46, 135.38, 133.24, 133.21, 128.40, 128.26, 128.19, 128.10, 127.99, 127.89, 127.21, 127.10, 126.29, 106.72, 106.62, 61.46, 61.31, 59.20, 57.28, 54.43, 53.70, 13.45, 13.38. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}BrN_3O_3^+$ 454.07608, 456.07403, 455.07943, 457.07739; Found 454.07689, 456.07475.

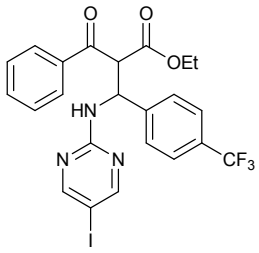
Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-bromopyrimidin-2-yl)amino)propanoate (1v)



White solid, 10% yield[1]; Silica gel TLC R*f* = 0.54; 0.46 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.27 (s, 1H), 8.18 (s, 1H), 7.95 – 7.88 (m, 1H), 7.88 – 7.82 (m, 1H), 7.62 – 7.53 (m, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.33 – 7.29 (m, 0H), 7.17 (t, *J* = 7.8 Hz, 0H), 7.13 (t, *J* = 7.9 Hz, 0H), 6.82 (d, *J* = 9.3 Hz, 0H), 6.53 (d, *J* = 9.3 Hz, 0H), 6.03 (dd, *J* = 9.4, 5.3 Hz, 0H), 5.95 (dd, *J* = 9.3, 6.2 Hz, 0H), 4.93 (d, *J* = 5.3 Hz, 0H), 4.90 (d, *J* = 6.2 Hz, 0H), 4.20 – 4.07 (m, 1H), 4.07 (q, *J* = 6.9, 6.1 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 1H), 1.05 (t, *J* = 7.1 Hz, 1H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of

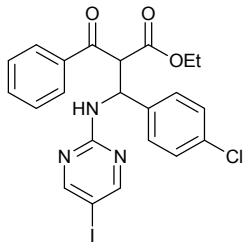
diastereoisomers δ 194.36, 192.47, 167.97, 167.31, 159.84, 159.65, 158.35, 158.22, 142.55, 142.27, 136.65, 135.61, 133.93, 133.85, 130.86, 130.73, 130.20, 130.11, 130.02, 129.93, 128.95, 128.82, 128.45, 128.39, 125.56, 125.49, 122.73, 122.68, 107.53, 107.44, 62.09, 61.96, 59.40, 57.54, 54.41, 53.67, 13.92, 13.85. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}Br_2N_3O_3^+$ 533.98455, 531.98659, 535.98250, 536.98585; Found 531.98660, 533.98448, 535.98229, 536.98567.

Ethyl 2-benzoyl-3-(5-iodopyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1w)



White solid, 32% yield[2]; Silica gel TLC R*f* = 0.42; 0.34 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 95:5. ^{1}H NMR (500 MHz, chloroform-*d*) δ 8.28 (s, 2H), 7.92 (d, *J* = 7.4 Hz, 2H), δ 7.63 – 7.58 (m, 1H), 7.56 (s, 4H), 7.48 (t, *J* = 7.7 Hz, 2H), 6.53 (d, *J* = 9.3 Hz, 1H), 6.02 (dd, *J* = 9.2, 6.5 Hz, 1H), 4.94 (d, *J* = 6.5 Hz, 1H), 4.21 – 4.03 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 192.32, 167.89, 162.82, 159.60, 144.22, 135.53, 133.95, 129.91 (q, *J* = 32.4 Hz), 128.98, 128.45, 127.33, 126.62, 125.62 (q, *J* = 3.6 Hz), 129.86 – 116.62 (m), 62.03, 59.28, 53.73, 13.88. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}F_3IN_3O_3^+$ 570.04959; Found 570.04981.

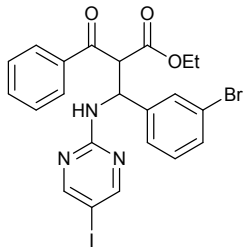
Ethyl 2-benzoyl-3-(4-chlorophenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1x)



White solid, 21% yield[1]; Silica gel TLC R*f* = 0.52; 0.47 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 57:43. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.36 (s, 2H), 7.83 (dt, *J* = 6.9, 1.2 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.35 (d, *J* = 7.1 Hz, 2H), 7.26 – 7.20 (m, 2H), 6.84 (d, *J* = 9.3 Hz, 1H), 6.03 (dd, *J* = 9.3, 5.3 Hz, 1H), 4.94 (d, *J* = 5.4 Hz, 1H), 4.07 (qd, *J* = 7.0, 1.2 Hz, 2H), 1.05 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.28 (s, 2H), 7.93 – 7.89 (m, 2H), 7.63 – 7.56 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.37 (d, *J* = 7.7 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 6.48 (d, *J* = 9.3 Hz, 1H), 5.95 (dd, *J* = 9.3, 6.6 Hz, 1H), 4.90 (d, *J* = 6.5 Hz, 1H), 4.20 – 4.08 (m, 2H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ mixture of diastereoisomers 194.49, 192.46, 167.97, 167.37, 162.90, 162.77, 159.82, 159.64, 138.68, 138.37, 136.66, 135.64,

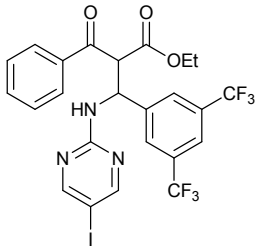
133.93, 133.86, 133.48, 133.36, 128.94, 128.83, 128.79, 128.71, 128.45, 128.36, 128.30, 128.26, 62.08, 61.95, 59.45, 57.48, 54.24, 53.53, 13.92, 13.85. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}ClIN_3O_3^+$ 536.02324, 538.02029; Found 536.02330, 538.01978.

Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1y)



White solid, 15% yield[1]; Silica gel TLC R*f* = 0.44; 0.36 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 53:47. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.37 (s, 2H), 8.28 (s, 2H), 7.91 (dt, *J* = 7.3, 1.3 Hz, 2H), 7.87 – 7.81 (m, 2H), 7.63 – 7.53 (m, 1H), 7.57 (s, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.33 (m, 3H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 9.3 Hz, 1H), 6.51 (d, *J* = 9.3 Hz, 1H), 6.03 (dd, *J* = 9.3, 5.3 Hz, 1H), 5.94 (dd, *J* = 9.3, 6.2 Hz, 1H), 4.93 (d, *J* = 5.3 Hz, 1H), 4.90 (d, *J* = 6.2 Hz, 1H), 4.20 – 4.10 (m, 2H), 4.07 (qd, *J* = 7.1, 1.3 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.35, 192.46, 167.96, 167.30, 162.92, 162.80, 159.78, 159.60, 142.52, 142.24, 136.64, 135.60, 133.93, 133.86, 130.86, 130.74, 130.20, 130.12, 130.02, 129.93, 128.95, 128.82, 128.45, 128.39, 125.56, 125.48, 122.74, 122.69, 62.10, 61.97, 59.37, 57.52, 54.25, 53.52, 13.92, 13.85. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}BrIN_3O_3^+$ 579.97272, 581.97068, 580.97608, 582.97403, 583.97739; Found 536.02330, 538.01978; Found 579.97325, 580.97620, 581.97090, 582.97407, 583.97683.

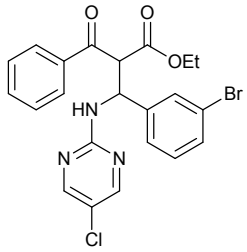
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1z)



White solid, 72% yield[1]; Silica gel TLC R*f* = 0.60; 0.54 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 68:32. ^{1}H NMR (500 MHz, DMSO-d_6) major diastereoisomer δ 8.49 (s, 2H), 8.19 (s, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 8.11 (s, 1H), 8.07 (s, 1H), 8.06 (d, *J* = 8.1 Hz, 2H), 7.87 (s, 1H), 7.83 – 7.77 (m, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 5.95 (d, *J* = 9.9 Hz, 1H), 5.40 (d, *J* = 10.9 Hz, 1H), 3.79 (q, *J* = 7.1 Hz, 2H), 0.76 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-d_6)

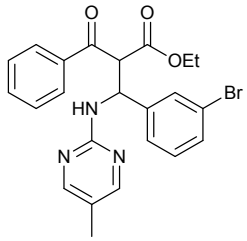
minor diastereoisomer δ 8.49 (s, 2H), 8.19 (s, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 8.11 (s, 1H), 8.07 (s, 1H), 8.06 (d, *J* = 8.1 Hz, 2H), 7.87 (s, 1H), 7.83 – 7.77 (m, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 5.99 (d, *J* = 10.1 Hz, 1H), 5.49 (d, *J* = 10.5 Hz, 1H), 4.13 – 4.01 (m, 2H), 1.00 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) mixture of diastereoisomers δ 193.52, 191.93, 167.19, 166.63, 159.80, 159.74, 144.26, 144.01, 136.10, 135.85, 134.81, 134.76, 131.18 – 130.27 (m), 129.55, 129.44, 129.26, 129.12, 128.73, 127.20 – 120.19 (m), 122.50 – 122.09 (m), 121.93 – 121.79 (m). 120.27, 78.58, 61.93, 61.85, 58.90, 58.66, 54.07, 53.92, 14.20, 13.71. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}F_6IN_3O_3^+$ 638.03698; Found 638.03823.

Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-chloropyrimidin-2-yl)amino)propanoate (1aa)



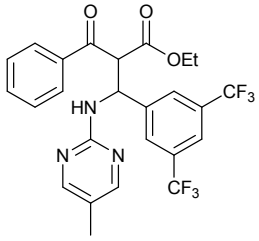
White solid, 20% yield[1]; Silica gel TLC R*f* = 0.49; 0.43 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 63:27. ^{1}H NMR (500 MHz, DMSO-d_6) major diastereoisomer δ 8.38 (s, 2H), 8.27 (s, 1H), 8.15 – 8.08 (m, 2H), 8.07 – 8.01 (m, 2H), 7.87 – 7.81 (m, 1H), 7.73 (d, *J* = 7.3 Hz, 1H), 7.70 (s, 1H), 7.67 – 7.62 (m, 1H), 7.60 (t, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.90 (s, 1H), 5.78 (dd, *J* = 10.8, 8.9 Hz, 1H), 5.28 (d, *J* = 10.9 Hz, 1H), 3.81 (q, *J* = 7.1 Hz, 2H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, DMSO-d_6) minor diastereoisomer δ 8.38 (s, 2H), 8.27 (s, 1H), 8.15 – 8.08 (m, 2H), 8.07 – 8.01 (m, 2H), 7.87 – 7.81 (m, 1H), 7.73 (d, *J* = 7.3 Hz, 1H), 7.70 (s, 1H), 7.67 – 7.62 (m, 1H), 7.60 (t, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.90 (s, 1H), 5.88 – 5.80 (m, 1H), 5.42 (d, *J* = 10.8 Hz, 1H), 4.14 – 3.96 (m, 2H), 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) mixture of diastereoisomers δ 193.27, 192.13, 167.32, 166.71, 162.50, 160.02, 156.56, 143.58, 143.44, 136.21, 136.00, 134.67, 130.96, 130.89, 130.82, 130.78, 130.72, 129.50, 129.48, 129.17, 128.77, 127.52, 127.45, 121.97, 121.88, 118.82, 118.78, 61.75, 61.70, 59.42, 58.75, 54.38, 54.21, 14.23, 13.93. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}BrClN_3O_3^+$ 488.03711, 490.03506, 491.03842, 493.03546; Found 488.03835, 490.03595, 491.03938, 493.03652.

Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-methylpyrimidin-2-yl)amino)propanoate (1bb)



White solid, 35% yield[1]; Silica gel TLC R*f* = 0.31; 0.25 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.10 (s, 2H), 8.02 (s, 2H), 7.94 – 7.89 (m, 2H), 7.89 – 7.83 (m, 2H), 7.60 (s, 2H), 7.59 – 7.53 (m, 2H), 7.46 (d, *J* = 7.9 Hz, 3H), 7.46 – 7.39 (m, 2H), 7.41 – 7.36 (m, 1H), 7.33 (dt, *J* = 8.0, 1.3 Hz, 3H), 7.31 – 7.28 (m, 2H), 7.16 (d, *J* = 7.9 Hz, 1H), 7.12 (t, *J* = 7.7 Hz, 1H), 6.49 (d, *J* = 9.4 Hz, 1H), 6.22 (d, *J* = 9.5 Hz, 1H), 6.10 (dd, *J* = 9.5, 5.7 Hz, 1H), 6.03 (dd, *J* = 9.5, 6.8 Hz, 1H), 4.95 (d, *J* = 5.7 Hz, 1H), 4.91 (d, *J* = 6.7 Hz, 1H), 4.18 – 4.08 (m, 2H), 4.04 (qd, *J* = 7.2, 2.3 Hz, 2H), 2.09 (s, 3H), 2.06 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.16, 192.60, 167.96, 167.48, 160.10, 159.91, 158.08, 157.95, 143.25, 136.79, 135.84, 133.74, 133.67, 130.60, 130.50, 130.14, 130.06, 129.99, 128.85, 128.76, 128.45, 128.39, 125.69, 125.62, 122.61, 122.57, 119.93, 119.86, 61.92, 61.82, 59.81, 57.99, 54.20, 53.51, 14.67, 14.64, 13.92, 13.82. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}BrN_3O_3^+$ 468.09173, 470.08968, 469.09508, 471.09304, 472.09639; Found 468.09284, 470.09071, 472.09704.

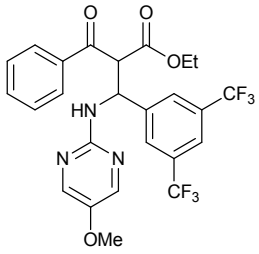
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-methylpyrimidin-2-yl)amino) propanoate (1cc)



White solid, 10% yield[1]; Silica gel TLC R*f* = 0.47; 0.37 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.11 (s, 2H), 8.04 (s, 2H), 7.93 (s, 4H), 7.92 – 7.88 (m, 2H), 7.88 – 7.85 (m, 2H), 7.70 (d, *J* = 12.2 Hz, 2H), 7.58 (q, *J* = 7.7 Hz, 2H), 7.45 (dt, *J* = 12.9, 7.6 Hz, 4H), 6.48 (d, *J* = 9.0 Hz, 1H), 6.24 (d, *J* = 8.8 Hz, 1H), 6.19 (dd, *J* = 8.9, 5.8 Hz, 1H), 6.11 (dd, *J* = 8.8, 7.0 Hz, 1H), 4.99 (d, *J* = 5.8 Hz, 1H), 4.94 (d, *J* = 7.0 Hz, 1H), 4.13 (dd, *J* = 11.1, 7.1 Hz, 2H), 4.04 (qd, *J* = 7.2, 5.5 Hz, 2H), 2.10 (s, 3H), 2.08 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 193.59, 192.17, 167.63, 167.17, 159.78, 159.61, 158.12, 158.02, 143.74, 143.39, 136.38, 135.66, 134.04, 133.93, 132.08 – 131.08 (m), 131.98 – 131.19 (m), 128.94, 128.87 128.41, 127.59 (q, *J* = 3.4

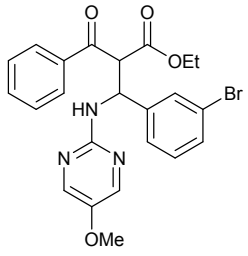
Hz), 129.40 – 121.96 (m), 121.71 – 121.44 (m), 121.57 – 121.35 (m), 120.51, 120.43, 62.16, 62.14, 59.45, 57.88, 54.19, 53.64, 14.67, 14.65, 13.83, 13.73. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_6N_3O_3^+$ 526.15599; Found 526.15636.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-methoxypyrimidin-2-yl)amino) propanoate (1dd)



White solid, 40% yield[1]; Silica gel TLC R*f* = 0.43; 0.33 (hexane/etyl acetate = 3/1); The ration of two diastereoisomers: 65:35. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.02 (s, 2H), 7.96 (s, 1H), 7.93 (s, 3H), 7.88 – 7.84 (m, 2H), 7.69 (s, 1H), 7.50 – 7.40 (m, 3H), 6.37 (d, *J* = 8.9 Hz, 1H), 6.12 (dd, *J* = 8.9, 6.0 Hz, 1H), 4.98 (d, *J* = 5.9 Hz, 1H), 4.10 – 3.99 (m, 2H), 3.77 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 7.93 (s, 3H), 7.91 – 7.88 (m, 2H), 7.72 (s, 1H), 7.62 – 7.53 (m, 3H), 6.15 (d, *J* = 8.9 Hz, 1H), 6.04 (dd, *J* = 8.7, 7.0 Hz, 1H), 4.92 (d, *J* = 7.0 Hz, 1H), 4.13 (dddd, *J* = 18.0, 10.9, 7.1, 3.8 Hz, 2H), 3.75 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 193.57, 192.18, 167.64, 167.18, 156.55, 156.36, 147.59, 147.56, 145.07, 144.94, 143.86, 143.51, 136.39, 135.66, 134.04, 133.94, 131.60 (q, *J* = 33.4 Hz), 131.55 (q, *J* = 33.5 Hz), 128.94, 128.87, 128.42, 127.60 (q, *J* = 3.8 Hz), 123.23 (q, *J* = 273.0 Hz), 121.75 – 121.31 (m). 62.15, 62.13, 59.53, 57.98, 56.71, 56.66, 54.70, 54.15, 13.84, 13.74. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_6N_3O_4^+$ 542.15090; Found 542.15137.

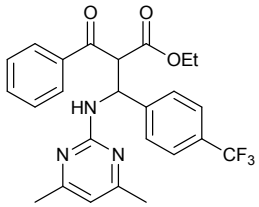
Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-methoxypyrimidin-2-yl)amino)propanoate (1ee)



White solid, 15% yield[1]; Silica gel TLC R*f* = 0.29; 0.23 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 60:40. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.02 (s, 2H), 7.94 (s, 1H), 7.93 – 7.88 (m, 1H), 7.86 (d, *J* = 6.9 Hz, 2H), 7.60 (s, 2H), 7.59 – 7.53 (m, 2H), 7.49 – 7.42 (m, 1H), 7.42 (d, *J* = 7.7 Hz, 2H), 7.39 (d, *J* = 7.1 Hz, 2H), 7.34 – 7.31 (m, 1H), 7.31 – 7.28 (m, 1H), 7.17 – 7.13 (m, 1H), 7.12 (t, *J* = 6.6 Hz, 1H), 6.39 (d, *J* = 9.4 Hz, 1H), 6.16 (d, *J* = 9.5 Hz, 1H), 6.03 (dd, *J*

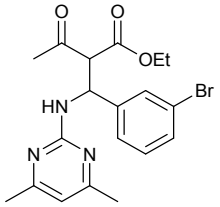
= 9.4, 5.9 Hz, 1H), 5.96 (dd, *J* = 9.5, 6.8 Hz, 1H), 4.94 (d, *J* = 5.9 Hz, 1H), 4.91 (d, *J* = 6.8 Hz, 1H), 4.19 – 4.05 (m, 1H), 4.04 (qd, *J* = 7.1, 2.5 Hz, 2H), 3.76 (s, 3H), 3.74 (s, 2H), 1.11 (t, *J* = 7.2 Hz, 2H), 1.04 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.14, 192.61, 167.97, 167.49, 156.96, 156.76, 147.25, 145.13, 144.98, 143.35, 143.05, 136.80, 135.84, 133.75, 133.68, 130.60, 130.51, 130.17, 130.06, 129.99, 128.85, 128.76, 128.45, 128.40, 125.71, 125.66, 122.61, 122.57, 61.92, 61.82, 59.91, 58.11, 56.79, 56.73, 54.73, 54.04, 13.93, 13.83. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{23}BrN_3O_4^+$ 484.08664, 486.08460, 485.09000, 488.09131; Found 484.08809, 486.08578, 488.09202.

Ethyl 2-benzoyl-3-((4,6-dimethylpyrimidin-2-yl)amino)-3-(4-(trifluoromethyl)phenyl)propanoate (1ff)



White solid, 58% yield[2]; Silica gel TLC R*f* = 0.30; 0.19 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 53:47. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.94 – 7.92 (m, 1H), 7.91 (dt, *J* = 7.9, 1.4 Hz, 3H), 7.62 – 7.41 (m, 18H), 6.44 (d, *J* = 9.4 Hz, 1H), 6.31 (s, 1H), 6.25 (s, 1H), 6.17 (d, *J* = 9.7 Hz, 1H), 5.03 (d, *J* = 6.0 Hz, 1H), 5.00 (d, *J* = 7.1 Hz, 1H), 4.19 – 4.05 (m, 2H), 4.01 (qd, *J* = 7.1, 3.3 Hz, 2H), 2.30 (s, 3H), 2.24 (s, 10H), 2.15 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of distereoisomers δ 193.81, 192.65, 167.94, 167.86, 167.46, 167.36, 145.11, 144.77, 136.64, 135.97, 133.77, 133.63, 129.93 – 129.19 (m), 129.11, 128.99, 128.79, 128.77, 127.61, 127.51, 125.36 (q, *J* = 3.6 Hz), 125.24 (q, *J* = 3.6 Hz), 110.69, 110.65, 61.85, 61.81, 59.67, 58.07, 54.02, 53.27, 23.84, 23.73, 13.87, 13.72. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{25}F_3N_3O_3^+$ 472.18425; Found 472.18517.

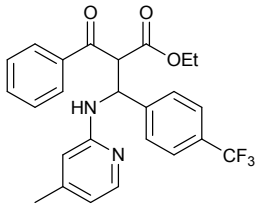
Ethyl 2-((3-bromophenyl)((4,6-dimethylpyrimidin-2-yl)amino)methyl)-3-oxobutanoate (1gg)



White solid, 30% yield[2]; Silica gel TLC R*f* = 0.22 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 58:42. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.56 (t, *J* = 1.9 Hz, 1H), 7.54 (t, *J* = 1.7 Hz, 1H), 7.35 (d, *J* = 6.6 Hz, 2H), 7.32 (d, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.9 Hz,

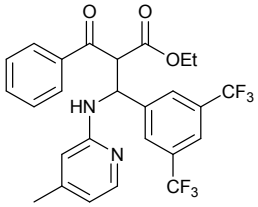
1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.38 – 6.33 (m, 1H), 6.32 (s, 2H), 6.13 (dd, *J* = 9.9, 5.4 Hz, 1H), 6.00 (dd, *J* = 9.7, 7.8 Hz, 1H), 5.86 (d, *J* = 9.7 Hz, 1H), 4.18 – 4.07 (m, 2H), 4.06 – 3.99 (m, 2H), 2.28 (s, 3H), 2.25 (s, 10H), 2.23 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 202.22, 201.02, 168.44, 167.56, 167.50, 167.30, 161.13, 161.04, 142.98, 142.89, 130.60, 130.47, 130.28, 130.04, 130.01, 129.82, 125.69, 125.37, 122.60, 122.51, 110.87, 110.85, 64.56, 64.43, 61.74, 61.57, 53.53, 52.45, 29.92, 29.13, 23.89, 23.87, 13.98, 13.84. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{23}BrN_3O_3^+$ 420.09173, 422.08968; Found 420.09254, 422.09035.

Ethyl 2-benzoyl-3-((4-methylpyridin-2-yl)amino)-3-(4-(trifluoromethyl)phenyl)propanoate (4a)



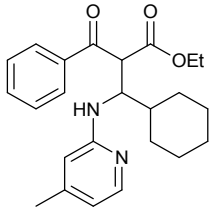
White solid, 31% yield[2]; Silica gel TLC R*f* = 0.26; 0.22 (hexane/etyl acetate 3:1); The ration of two diastereoisomer: 52:48. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.94 – 7.87 (m, 2H), 7.89 (d, *J* = 5.3 Hz, 1H), 7.87 – 7.81 (m, 2H), 7.75 (d, *J* = 5.2 Hz, 1H), 7.61 – 7.53 (m, 7H), 7.51 (t, *J* = 7.8 Hz, 3H), 7.44 (dt, *J* = 13.9, 7.8 Hz, 4H), 6.40 (d, *J* = 5.2 Hz, 1H), 6.36 (d, *J* = 5.2 Hz, 1H), 6.33 (s, 1H), 6.28 (s, 1H), 6.08 (dd, *J* = 9.3, 5.1 Hz, 1H), 6.03 (d, *J* = 9.4 Hz, 1H), 5.97 (dd, *J* = 9.2, 6.7 Hz, 1H), 5.74 (d, *J* = 9.2 Hz, 1H), 5.01 (d, *J* = 5.1 Hz, 1H), 4.94 (d, *J* = 6.6 Hz, 1H), 4.19 – 4.08 (m, 2H), 4.05 (ddt, *J* = 9.5, 7.1, 3.1 Hz, 2H), 2.20 (s, 3H), 2.17 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.67, 192.85, 168.22, 167.65, 157.51, 157.25, 148.44, 148.39, 147.58, 147.47, 145.12, 144.86, 136.67, 135.71, 133.90, 133.80, 129.61 (q, *J* = 32.3 Hz), 129.48 (q, *J* = 33.2, 32.7 Hz), 128.90, 128.82, 128.46, 128.34, 127.35, 127.30, 125.66 – 125.44 (m), 125.44 (q, *J* = 3.8 Hz), 126.89 – 120.16 (m), 115.44, 115.37, 108.63, 108.53, 61.99, 61.89, 59.98, 57.92, 54.57, 53.98, 21.10, 13.87, 13.78. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{24}F_3N_2O_3^+$ 457.17335; Found 457.17409.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((4-methylpyridin-2-yl)amino)propanoate (4b)



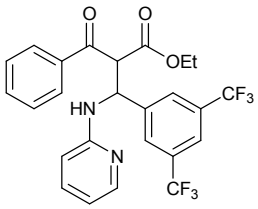
White solid, 64% yield[1]; Silica gel TLC R*f* = 0.44 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 54:46. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 7.93 (s, 2H), 7.91 (s, 2H), 7.89 (s, 1H), 7.91 – 7.85 (m, 2H), 7.86 – 7.83 (m, 2H), 7.73 (s, 1H), 7.72 (s, 1H), 7.67 (s, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.50 – 7.40 (m, 4H), 6.43 (d, *J* = 5.2 Hz, 1H), 6.38 (d, *J* = 5.5 Hz, 1H), 6.36 (s, 1H), 6.31 (s, 1H), 6.19 (dd, *J* = 8.8, 5.2 Hz, 1H), 6.08 (dd, *J* = 8.6, 6.2 Hz, 1H), 5.97 (d, *J* = 8.8 Hz, 1H), 5.76 (d, *J* = 8.7 Hz, 1H), 5.01 (d, *J* = 5.2 Hz, 1H), 4.94 (d, *J* = 6.1 Hz, 1H), 4.17 – 4.08 (m, 2H), 4.04 (qd, *J* = 7.1, 5.1 Hz, 2H), 2.21 (s, 3H), 2.19 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.44, 192.76, 168.13, 167.43, 157.08, 156.84, 148.51, 148.45 , 147.47, 147.34, 144.14, 143.79, 136.40, 135.59, 134.09, 133.92, 131.64 (q, *J* = 33.6 Hz), 131.54 (q, *J* = 33.1 Hz), 128.96, 128.88, 128.40, 128.36, 127.52 – 127.40 (m), 126.19 – 119.91 (m), 121.60 – 121.42 (m), 121.43 – 121.31 (m), 115.76, 115.72, 109.11, 108.97, 62.14, 62.05, 59.48, 57.78, 54.09, 53.51, 21.05, 21.03, 13.81, 13.73. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}F_6N_2O_3^+$ 525.16074; Found 525.16092.

Ethyl 2-benzoyl-3-cyclohexyl-3-((4-methylpyridin-2-yl)amino)propanoate (4c)



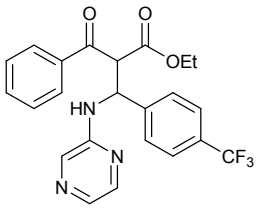
Dark yellow solid, 25% yield[1]; Silica gel TLC R*f* = 0.38; 0.34 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 55:45. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereomers δ 7.93 (t, *J* = 6.9 Hz, 2H), 7.91 – 7.88 (m, 2H), 7.85 (t, *J* = 6.4 Hz, 2H), 7.65 – 7.51 (m, 3H), 7.51 – 7.41 (m, 5H), 6.99 (d, *J* = 10.7 Hz, 1H), 6.49 (d, *J* = 5.3 Hz, 1H), 6.33 (s, 1H), 6.32 (d, *J* = 5.6 Hz, 1H), 6.26 (d, *J* = 4.8 Hz, 1H), 6.21 (s, 1H), 4.30 – 4.06 (m, 4H), 2.23 (s, 3H), 2.15 (s, 3H), 1.20 – 1.06 (m, 16H), 1.01 (t, *J* = 7.2 Hz, 1H), 0.88 (t, *J* = 6.7 Hz, 1H). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{31}N_2O_3^+$ 395.23292; Found 395.23347.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyridin-2-ylamino)propanoate (4d)



White solid, 64% yield[1]; Silica gel TLC R*f* = 0.54 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 55:45. ^{1}H NMR (500 MHz, chloroform-*d*) mixture of diastereoisomers δ 8.03 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.93 (d, *J* = 6.2 Hz, 4H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.85 (d, *J* = 7.1 Hz, 2H), 7.73 (s, 1H), 7.68 (s, 1H), 7.61 – 7.58 (m, 1H), 7.58 – 7.55 (m, 1H), 7.49 – 7.34 (m, 6H), 6.59 (dd, *J* = 7.1, 5.1 Hz, 1H), 6.54 (t, *J* = 7.1 Hz, 2H), 6.48 (d, *J* = 8.4 Hz, 1H), 6.20 (dd, *J* = 8.7, 5.2 Hz, 1H), 6.13 – 6.04 (m, 2H), 5.85 (d, *J* = 8.6 Hz, 1H), 5.02 (d, *J* = 5.1 Hz, 1H), 4.95 (d, *J* = 6.1 Hz, 1H), 4.18 – 4.08 (m, 2H), 4.08 – 3.98 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.46, 192.72, 168.14, 167.40, 156.86, 156.63, 147.87, 147.75, 144.01, 143.67, 137.48, 137.42, 136.37, 135.56,134.13 , 133.95, 131.68 (q, *J* = 33.2 Hz), 131.58 (q, *J* = 33.3 Hz), 128.98, 128.90, 128.39, 128.37, 127.59 – 127.35 (m), 127.32 – 119.58 (m), 121.49-121.61 (m), 121.54 – 121.29 (m). 114.11, 114.05, 108.87, 108.72, 62.17, 62.09, 59.47, 57.74, 54.11, 53.54, 13.81, 13.73. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{21}F_6N_2O_3^+$ 511.14509; Found 511.14544.

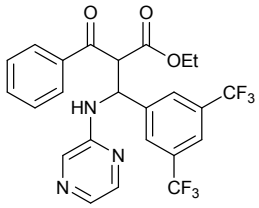
Ethyl 2-benzoyl-3-(pyrazin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (5a)



White solid, 26% yield[2]; Silica gel TLC R*f* = 0.16; 0.12 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 68:32. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 7.97 (s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.80 – 7.73 (m, 2H), 7.58 (s, 4H), 7.49 (t, *J* = 7.7 Hz, 2H), 6.21 (d, *J* = 8.8 Hz, 1H), 6.00 (dd, *J* = 8.8, 5.7 Hz, 1H), 4.96 (d, *J* = 5.6 Hz, 1H), 4.14 – 4.04 (m, 2H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.03 (s, 1H), 7.84 – 7.79 (m, 2H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.58 (s, 4H), 7.53 (d, *J* = 5.2 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 6.55 (d, *J* = 8.9 Hz, 1H), 6.13 (dd, *J* = 9.1, 4.6 Hz, 1H), 5.02 (d, *J* = 4.6 Hz, 1H), 4.16 (qd, *J* = 9.8, 8.7, 4.4 Hz, 2H), 1.05 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 195.23, 192.72, 168.42, 167.47, 153.47, 153.19, 144.27, 144.03, 141.75, 141.57, 136.50, 135.35, 134.17, 134.03, 133.71, 133.62, 133.21, 133.08, 129.98 (q, *J* = 32.7 Hz), 129.04, 128.90, 128.45, 128.34, 127.23, 127.17, 125.71 (q, *J* =

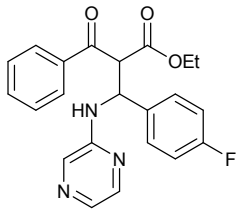
3.7 Hz), 125.71 – 125.49 (m), 125.12 – 120.61 (m), 62.22, 62.06, 59.28, 57.16, 54.00, 53.28, 13.86, 13.83. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_3N_3O_3^+$ 444.15295; Found 444.15438.

Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyrazin-2-ylamino)propanoate (5b)



White solid, 23% yield[1]; Silica gel TLC R*f* = 0.27; 0.19 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 93:7. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 8.06 (d, *J* = 1.5 Hz, 1H), 7.94 (s, 1H), 7.89 (s, 2H), 7.86 – 7.80 (m, 3H), 7.70 (s, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 6.48 (d, *J* = 8.4 Hz, 1H), 6.18 (dd, *J* = 8.5, 4.8 Hz, 1H), 5.00 (d, *J* = 4.7 Hz, 1H), 4.08 (qd, *J* = 7.2, 5.4 Hz, 2H), 1.06 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) δ minor diastereoisomer 8.01 (s, 1H), 7.91 (s, 1H), 7.78 (dt, *J* = 8.5, 3.2 Hz, 3H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 6.20 (d, *J* = 6.4 Hz, 1H), 6.04 (dd, *J* = 8.1, 5.6 Hz, 1H), 4.94 (d, *J* = 5.5 Hz, 1H), 4.15 (ddd, *J* = 16.4, 7.2, 3.2 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 194.77, 167.17, 153.10, 142.93, 141.61, 141.45, 136.21, 134.38, 134.18, 134.08, 134.01, 133.45, 133.34, 131.80 (q, *J* = 33.5 Hz), 129.10, 128.97, 128.39, 127.33 (q, *J* = 4.2 Hz), 123.12 (q, *J* = 272.9 Hz), 121.87 – 121.53 (m), 62.39, 62.30, 58.94, 57.18, 53.73, 53.06, 13.79. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}F_6N_3O_3^+$ 512.14034; Found 512.14065.

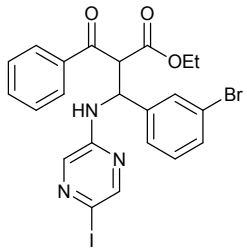
Ethyl 2-benzoyl-3-(4-fluorophenyl)-3-(pyrazin-2-ylamino)propanoate (5c)



White solid, 10% yield[1]; Silica gel TLC R*f* = 0.16; 0.10 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 65:35. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 7.94 (s, 1H), 7.93 – 7.89 (m, 2H), 7.79 (t, *J* = 2.0 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.42 (d, *J* = 7.3 Hz, 2H), 7.00 (t, *J* = 8.6 Hz, 2H), 6.14 (d, *J* = 8.9 Hz, 1H), 5.91 (dd, *J* = 8.9, 5.9 Hz, 1H), 4.93 (d, *J* = 5.8 Hz, 1H), 4.12 – 4.02 (m, 2H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 7.99 (s, 1H), 7.84 – 7.80 (m, 2H), 7.74 (d, *J* = 2.7 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.45 (d, *J* = 6.2 Hz, 2H), 7.41 (d, *J* = 5.5 Hz, 2H), 7.39 – 7.36 (m, 2H), 6.94 (t, *J* = 8.6 Hz, 1H), 6.47 (d, *J* = 8.9 Hz, 1H), 6.03 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.97 (d, *J* = 4.9 Hz, 1H), 4.20 – 4.12 (m, 2H), 1.05 (t, *J* = 7.1

Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastreoisomers δ 195.45, 192.89, 168.50, 167.53, 162.16 (d, *J* = 246.3 Hz), 162.06 (d, *J* = 246.3 Hz), 153.58, 153.33, 141.81, 141.64, 136.70, 135.82 (d, *J* = 3.0 Hz), 135.51 (d, *J* = 3.5 Hz), 134.03, 133.90, 133.55, 133.44, 133.09, 132.95, 128.99, 128.86, 128.50, 128.49 – 128.40 (m), 128.35, 115.64 (d, *J* = 21.4 Hz), 115.54 (d, *J* = 21.7 Hz), 62.08, 61.94, 59.72, 57.55, 53.87, 53.15, 13.90, 13.86. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}FN_3O_3^+$ 394.15614; Found 394.15696.

Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-iodopyrazin-2-yl)amino)propanoate (5d)



Beige solid, 53% yield[1]; Silica gel TLC R*f* = 0.41; 0.37 (hexane/etyl acetate 3:1); The ration of two diastereoisomers: 76:24. ^{1}H NMR (500 MHz, chloroform-*d*) major diastereoisomer δ 7.99 (d, *J* = 1.5 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.81 – 7.80 (m, 1H), 7.65 – 7.60 (m, 1H), 7.54 (s, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.39 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.36 – 7.33 (m, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.30 (d, *J* = 8.7 Hz, 1H), 5.79 (dd, *J* = 8.7, 5.2 Hz, 1H), 4.89 (d, *J* = 5.2 Hz, 1H), 4.15 (dqd, *J* = 10.1, 7.0, 3.5 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H). ^{1}H NMR (500 MHz, chloroform-*d*) minor diastereoisomer δ 8.16 (d, *J* = 1.5 Hz, 1H), 7.86 (d, *J* = 1.5 Hz, 2H), 7.84 – 7.78 (m, 1H), 7.60 – 7.56 (m, 1H), 7.52 (s, 1H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.9 Hz, 1H), 6.57 (d, *J* = 8.7 Hz, 1H), 5.92 (dd, *J* = 8.8, 4.6 Hz, 1H), 4.94 (d, *J* = 4.6 Hz, 1H), 4.09 (td, *J* = 7.1, 2.2 Hz, 2H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) mixture of diastereoisomers δ 195.35, 192.69, 168.49, 167.29, 152.66, 152.43, 149.33, 149.13, 142.10, 141.82, 136.53, 135.23, 134.20, 134.09, 133.98, 133.92, 131.10, 130.94, 130.37, 130.26, 129.87, 129.75, 129.09, 128.90, 128.46, 128.40, 125.40, 125.31, 122.92, 122.85, 99.84, 99.71, 62.27, 62.11, 59.07, 57.04, 54.13, 53.31, 13.91. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}BrIN_3O_3^+$ 579.97272, 581.97068, 580.97608, 582.97403; Found 579.97358, 580.97699, 581.97148, 582.97493.

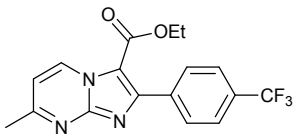
6. General procedure for the preparation of imidazo[1,2-*a*]-pyridines, -pyrimidines and –pyrazines

To a solution of Mannich precursor (0.25 mmol) in DMA (5 mL), IBX (0.28 mmol, 1.1 equiv. (175 mg) stabilized IBX, 45 wt%) and NIS (0.38 mmol, 1.5 equiv. (85.5 mg)) were added. The reaction mixture was stirred for 30 minutes at 80 ºC. Afterwards, the mixture was quenched with $Na_2S_2O_3.5H_2O$

solution (3.52 g in 10 mL water) and extracted with ethyl acetate (10 mL). The organic layer was washed with saturated sodium bicarbonate solution (10 mL) then with ethyl acetate (2×10mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed by vacuo. The crude material was subjected to column chromatographic separation (eluent: hexane/2-propanol or toluene/acetonitrile 9:1) and recrystallized with diethyl ether or diisopropyl ether to obtain the pure product.

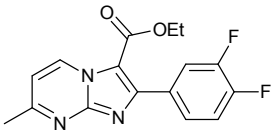
7. Characterization of new imidazo[1,2-*a*]-pyridine, -pyrimidine and –pyrazine products

Ethyl 7-methyl-2-(4-(trifluoromethyl)phenyl) imidazo[1,2-*a*]pyrimidine-3-carboxylate (2a)



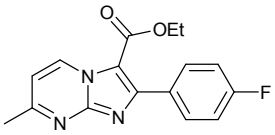
White solid, 78% isolated yield (68 mg) and 72% isolated yield (2012 mg; from 8 mmol **1a**) m.p.: 129.1–131.6 °C; R*f* = 0.20 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.51 (d, *J* = 7.1 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 7.1 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.72 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.68, 160.52, 152.74, 149.85, 137.32, 135.41, 130.89 (q, *J* = 32.6, 30.6 Hz), 130.83, 124.50 (q, *J* = 3.6 Hz), 124.19 (q, *J* = 275.5, 272.3 Hz), 111.51, 110.52, 61.03, 25.11, 14.05. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}F_3N_3O_2^+$ 350.11109; Found 350.11000.

Ethyl 2-(3,4-difluorophenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2c)



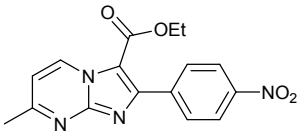
Pale yellow solid, 77% yield (61 mg), m.p.: 137.6–138.2 °C; R*f* = 0.22 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.43 (d, *J* = 7.1 Hz, 1H), 7.90 (ddd, *J* = 11.9, 8.0, 1.9 Hz, 1H), 7.70 (ddd, *J* = 8.3, 4.0, 2.1 Hz, 1H), 7.55 (dt, *J* = 9.8, 8.5 Hz, 1H). 7.28 (d, *J* = 7.1 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.62 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.08, 160.08, 150.68, 150.32 (dd, *J* = 248.0, 12.6 Hz), 149.41 , 149.12 (dd, *J* = 244.3, 12.8 Hz), 136.25, 131.52 (dd, *J* = 6.8, 3.8 Hz), 127.67 (dd, *J* = 6.7, 3.2 Hz), 119.73 (d, *J* = 18.5 Hz), 117.34 (d, *J* = 17.3 Hz), 112.41, 110.43, 61.12, 25.02, 14.17. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{14}F_2N_3O_2^+$ 318.10486; Found 318.10481.

Ethyl 2-(4-fluorophenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2d)



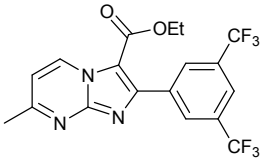
Pale yellow solid, 75% yield (56 mg), m.p.: 124.5–124.8 °C; R*f* = 0.19 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.50 (d, *J* = 7.0 Hz, 1H), 7.89 (dd, *J* = 8.6, 5.7 Hz, 2H), 7.13 (ddd, *J* = 8.7, 7.0, 1.8 Hz, 2H), 6.97 (d, *J* = 7.1 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.70 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.44 (d, *J* = 248.4 Hz), 163.38, 160.75, 153.48, 149.81, 135.40, 132.45 (d, *J* = 8.3 Hz), 129.76 (d, *J* = 3.4 Hz), 114.61 (d, *J* = 21.9 Hz), 111.22, 109.97, 60.87, 25.07, 14.08. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}FN_3O_2^+$ 300.11428; Found 300.11427.

Ethyl 2-(4-nitrophenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3 carboxylate (2e)



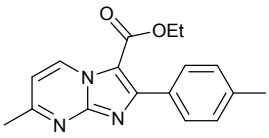
Pale yellow solid, 67% yield (55 mg), m.p.: 140.6–143.2 °C; R*f* = 0.08 (hexane/2-propanol 9:1), ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.45 (d, *J* = 7.1 Hz, 1H), 8.34 (d, *J* = 8.7 Hz, 2H), 8.10 (d, *J* = 8.7 Hz, 2H), 7.32 (d, *J* = 7.1 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.36, 159.99, 150.50, 149.60, 147.99, 140.67, 136.34, 131.88, 123.27, 112.65, 111.14, 61.30, 25.09, 14.24. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_4O_4^+$ 327.10878; Found 327.10886.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3 carboxylate (2f):



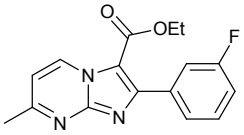
Pale yellow solid, 61% yield (64 mg), m.p.: 167.7–169.2 °C; R*f* = 0.35 (hexane/2-propanol 9:1). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.50 (d, *J* = 6.7 Hz, 1H), 8.51 (s, 2H), 8.26 (s, 1H), 7.34 (d, *J* = 6.8 Hz, 1H), 4.30 (q, *J* = 6.7 Hz, 2H), 2.66 (s, 3H), 1.19 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.56, 159.91, 149.23, 136.69, 136.35, 131.12, 130.32 (q, *J* = 32.8 Hz), 123.79 (q, *J* = 275.0, 272.8 Hz), 123.03 (q, *J* = 3.9 Hz), 112.82, 111.21, 61.32, 25.11, 13.93. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}F_6N_3O_2^+$ 418.09847; Found 418.09844.

Ethyl 7-methyl-2-(*p*-tolyl) imidazo[1,2-*a*]pyrimidine-3-carboxylate (2g)



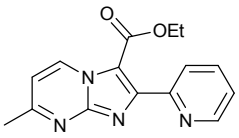
White solid, 49% yield (36 mg), m.p.: 112.6–114.6 °C; R*f* = 0.25 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.49 (d, *J* = 7.0 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 7.1 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.69 (s, 3H), 2.42 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.04, 160.99, 154.60, 149.85, 139.14, 135.35, 130.75, 130.43, 128.31, 110.98, 109.85, 60.75, 25.04, 21.47, 14.12. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{17}H_{18}N_3O_2^{+}$ 296.13935; Found 296.13936.

Ethyl 2-(3-fluorophenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2h)



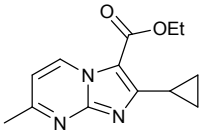
Pale orange solid, 48% yield (36 mg), m.p.: 105.6–107.7 °C; R*f* = 0.19 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.51 (d, *J* = 7.1 Hz, 1H), 7.69 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.62 (ddd, *J* = 10.1, 2.8, 1.5 Hz, 1H), 7.41 (td, *J* = 7.9, 6.3 Hz, 1H), 7.14 (tdd, *J* = 8.5, 2.7, 1.1 Hz, 1H), 6.98 (d, *J* = 7.1 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.71 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.51 , 162.10 (d, *J* = 244.4 Hz), 160.66 , 152.91 (d, *J* = 2.1 Hz), 149.78 , 135.76 (d, *J* = 8.7 Hz), 135.39, 129.08 (d, *J* = 8.2 Hz), 126.23 (d, *J* = 3.1 Hz), 117.56 (d, *J* = 23.1 Hz), 115.94 (d, *J* = 21.1 Hz), 111.37, 110.25, 60.96, 25.09, 13.96. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{16}H_{15}FN_3O_2^{+}$ 300.11428; Found 300.11460.

Ethyl 7-methyl-2-(pyridin-2-yl) imidazo[1,2-*a*]pyrimidine-3-carboxylate (2i)



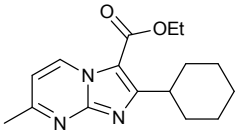
Brown solid, 48% yield (35 mg), m.p.: 83.4–85.6 °C; R*f* = 0.10 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.47 (d, *J* = 7.1 Hz, 1H), 8.73 (d, *J* = 4.4 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.5, 1.4 Hz, 1H), 7.35 (t, *J* = 5.4 Hz, 1H), 6.99 (d, *J* = 7.1 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.71 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.40, 160.70, 153.04, 152.67, 149.55, 148.82, 136.00, 135.07, 125.08, 123.46, 111.53, 111.29, 60.84, 25.16, 13.89. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{15}H_{15}N_4O_2^{+}$ 283.11895; Found 283.11904.

Ethyl 2-cyclopropyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2j)



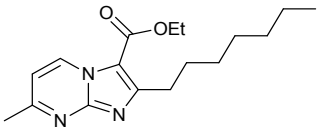
Pale yellow solid, 83% yield (51 mg), m.p.: 148.6–152 °C; R*f* = 0.27 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.35 (d, *J* = 7.0 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 2.80 (ddd, *J* = 13.0, 8.2, 4.8 Hz, 1H), 2.62 (s, 3H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.32 (dt, *J* = 6.3, 3.2 Hz, 2H), 1.09 (dq, *J* = 6.7, 3.7 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 167.54, 162.46, 161.64, 160.08, 150.13, 134.71, 110.19, 60.51, 24.86, 14.52, 10.58, 10.12. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}N_3O_2^+$ 246.12370; Found 246.12369.

Ethyl 2-cyclohexyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2k)



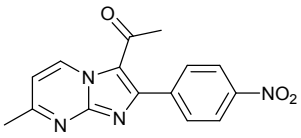
Pale yellow solid, 59% yield (42 mg), m.p.: 78.8–79.9 °C; R*f* = 0.32 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.38 (d, *J* = 7.0 Hz, 1H), 6.88 (d, *J* = 7.0 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.44 (tt, *J* = 11.6, 3.4 Hz, 1H), 1.96 – 1.85 (m, 4H), 1.85 – 1.71 (m, 4H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.43 – 1.36 (m, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 162.87, 162.23, 161.32, 149.97, 134.91, 109.49, 60.47, 38.32, 32.08, 26.68, 26.09, 24.89, 14.36. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}N_3O_2^+$ 288.17065; Found 288.17089.

Ethyl 2-heptyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2l)



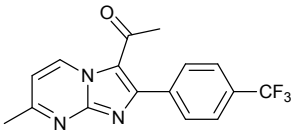
White solid, 57% yield (43 mg), m.p.: 58.4–59.8 °C; R*f* = 0.26 (hexane/2-propanol 9:1) ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.39 (d, *J* = 7.0 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.11 (t, *J* = 7.7 Hz, 2H), 2.65 (s, 3H), 1.80 (p, *J* = 7.6 Hz, 2H), 1.44 (t, *J* = 7.2 Hz, 3H), 1.42 – 1.22 (m, 8H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 162.41, 161.30, 158.77, 149.89, 134.83, 110.58, 110.36, 60.49, 31.82, 30.09, 29.60, 29.21, 29.17, 24.96, 22.69, 14.43, 14.12. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{26}N_3O_2^+$ 304.20195; Found 304.20191.

1-(7-Methyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyrimidin-3-yl)ethanone (2m)



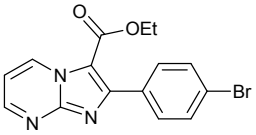
Pale yellow solid, 95% yield (70 mg), m.p.: 186.8–188.1 °C; R*f* = 0.06 (hexane/2-propanol 9:1); $C_{15}H_{12}N_4O_3$, ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.82 (d, *J* = 7.1 Hz, 1H), 8.39 (d, *J* = 8.7 Hz, 2H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.07 (d, *J* = 7.1 Hz, 1H), 2.74 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 188.71, 165.23, 153.21, 149.69, 148.52, 141.08, 136.08, 131.21, 123.64, 119.83, 29.84, 25.27. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_4O_3^+$ 297.09822; Found 297.09847.

1-(7-Methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidin-3-yl)ethanone (2n)



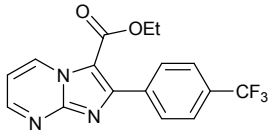
Pale yellow solid, 69% yield (55 mg), m.p.: 126.1–128.2 °C; R*f* = 0.10 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.83 (d, *J* = 7.1 Hz, 1H), 7.78 (s, 4H), 7.05 (d, *J* = 7.1 Hz, 1H), 2.73 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 189.03, 164.92, 154.43, 149.67, 138.27, 136.08, 131.56 (q, *J* = 32.8 Hz), 130.52, 125.41 (q, *J* = 3.7 Hz), 124.10 (q, *J* = 275.5 Hz, *J* = 272.3 Hz), 112.21, 29.79, 25.23. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}F_3N_3O^+$ 320.10052; Found 320.10055.

Ethyl 2-(4-bromophenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2o)



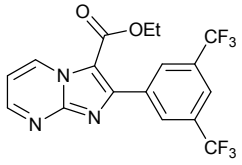
White solid, 64% yield (56 mg), m.p.: 136.6–137 °C; R*f* = 0.18 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.69 (dd, *J* = 6.9, 2.0 Hz, 1H), 8.75 (dd, *J* = 4.2, 2.1 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.13 (dd, *J* = 6.9, 4.2 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.61, 153.60, 152.79, 149.74, 136.24, 132.48, 132.13, 132.13, 130.86, 123.80, 110.45, 61.11, 14.11. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}BrN_3O_2^+$ 346.01857, 348.01652; Found 346.01895, 348.01669.

Ethyl 2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2p)



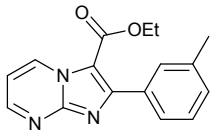
White solid, 58% yield (49 mg), m.p.: 131.8–133.2 °C; R*f* = 0.18 (hexane/2-propanol 9:1) ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.70 (dd, *J* = 6.9, 2.1 Hz, 1H), 8.78 (dd, *J* = 4.2, 2.1 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.16 (dd, *J* = 7.0, 4.2 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.46, 153.15, 152.96, 149.76, 137.17, 136.28, 131.31 (q, *J* = 32.4 Hz), 130.86, 124.56 (q, *J* = 3.6 Hz), 124.14 (q, J = 275.5 Hz, 272.3 Hz), 110.64, 61.19, 14.02. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}F_3N_3O_2^+$ 336.09544; Found 336.09565.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2q)



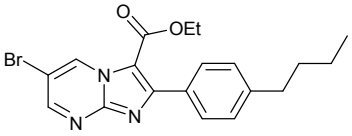
White solid, 56% yield (57 mg), m.p.: 140.7–142.7 °C; R*f* = 0.26 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.76 (dd, *J* = 7.0, 2.1 Hz, 1H), 8.81 (dd, *J* = 4.2, 2.1 Hz, 1H), 8.41 (s, 2H), 7.97 (s, 1H), 7.20 (dd, *J* = 7.0, 4.2 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.18, 157.79, 153.42, 151.02, 149.82, 136.44, 135.61, 131.13 (q, *J* = 33.6 Hz), 130.85 (q, *J* = 3.4 Hz), 123.33 (q, *J* = 275.0, 272.8 Hz), 123.02 – 122.65 (m, J = 3.8 Hz), 110.99, 61.56, 13.79. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{12}F_6N_3O_2^+$ 404.08282; Found 404.08219.

Ethyl 2-(*m*-tolyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2r)



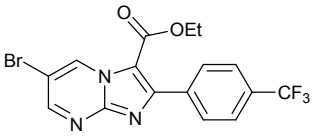
Pale orange solid, 48% yield (34 mg), m.p.: 74.6–75.5 °C, R*f* = 0.20 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.70 (dd, *J* = 6.9, 1.9 Hz, 1H), 8.74 (dd, *J* = 4.1, 2.0 Hz, 1H), 7.70 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 7.0 Hz, 1H), 7.11 (dd, *J* = 6.9, 4.2 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.94, 155.02, 152.53, 149.74, 137.19, 136.16, 133.37, 131.09, 130.00, 127.68, 127.49, 110.23, 60.88, 21.44, 13.99. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}N_3O_2^+$ 282.12370; Found 282.12385.

Ethyl 6-bromo-2-(4-butylphenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2s)



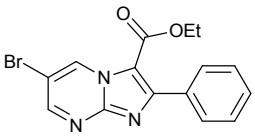
Pale yellow solid, 58% yield (58 mg), m.p.: 169.1–173.9 °C; R*f* = 0.55 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.84 (s, 1H), 8.70 (s, 1H), 7.78 (d, *J* = 7.7 Hz, 2H), 7.27 (s, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.68 (t, *J* = 7.8 Hz, 2H), 1.65 (p, *J* = 7.7 Hz, 2H), 1.38 (h, *J* = 7.4 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.45, 153.13, 144.63, 135.78, 130.39, 130.32, 127.82, 106.41, 61.21, 35.57, 33.49, 22.32, 13.96, 13.98. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}BrN_3O_2^+$ 402.08117, 404.07912; Found 402.08138, 404.07913.

Ethyl 6-bromo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2t)



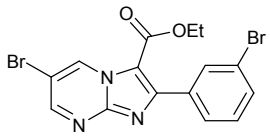
Pale yellow solid, 50% yield (52 mg), m.p.: 139.7–141 °C; R*f* = 0.50 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, DMSO-*d6*) δ 9.64 (d, *J* = 2.4 Hz, 1H), 8.90 (d, *J* = 2.4 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.2 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 159.49 , 153.97 , 151.47 , 147.39 , 137.19 , 136.09 , 130.94 , 129.40 (q, *J* = 31.8 Hz), 124.64 (q, *J* = 3.4 Hz), 124.23 (q, *J* = 273.5, 272.8 Hz), 111.00, 106.48, 61.12, 13.70. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}BrF_3N_3O_2^+$ 414.00595, 416.00390; Found 414.00598, 416.00373.

Ethyl 6-bromo-2-phenylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2u)



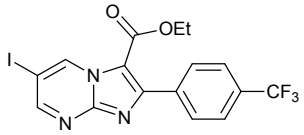
Pale yellow solid, 40% yield (35 mg), m.p.: 118.1–120.2 °C; R*f* = 0.48 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.85 (s, 1H), 8.71 (s, 1H), 7.84 (s, 2H), 7.45 (s, 3H), 4.35 (q, *J* = 6.7 Hz, 2H), 1.27 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.19, 154.79, 152.81, 147.46, 135.33, 132.65, 130.00, 129.02, 127.24, 110.08, 106.12, 60.79, 13.50. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}BrF_3N_3O_2^+$ 346.01857, 348.01652; Found 346.01894, 348.01668.

Ethyl 6-bromo-2-(3-bromophenyl) imidazo[1,2-*a*]pyrimidine-3-carboxylate (2v)



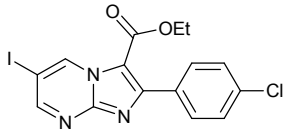
White solid, 38% yield (40 mg), m.p.: 122.8–125.9 °C; R*f* = 0.44 (toluene/MeCN 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.87 (d, *J* = 2.5 Hz, 1H), 8.74 (d, *J* = 2.4 Hz, 1H), 8.02 (t, *J* = 1.8 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.38, 153.65, 153.27, 135.02, 133.47, 132.38, 129.36, 129.07, 121.56, 106.91, 61.49, 13.98. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}Br_2N_3O_2^+$ 425.92703, 423.92908, 427.92498; Found 423.93015, 425.92813, 427.92597.

Ethyl 6-iodo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2w)



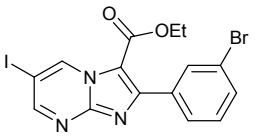
Pale yellow solid, 68% yield (78 mg), m.p.: 151.6–154 °C, R*f* = 0.50 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, DMSO-*d6*) δ 9.68 (s, 1H), 8.90 (s, 1H), 8.00 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 7.9 Hz, 2H), 4.27 (q, *J* = 6.8 Hz, 2H), 1.17 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 159.52, 157.96, 150.97, 147.35, 140.40, 137.22, 130.95, 129.34 (q, *J* = 32.4, 31.7 Hz), 129.02, 127.12, 124.59 (q, *J* = 3.8 Hz), 124.23 (q, *J* = 272.2 Hz), 110.50, 61.05, 13.68. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}F_3IN_3O_2^+$ 461.99208; Found 461.99221.

Ethyl 2-(4-chlorophenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2x)



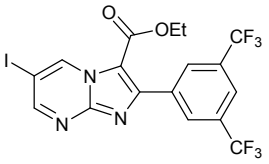
Pale orange solid, 54% yield (57 mg), m.p.: 184.3–185.6 °C; R*f* = 0.45 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.93 (d, *J* = 2.3 Hz, 1H), 8.80 (d, *J* = 2.3 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.44, 157.48, 153.49, 147.84, 140.45, 135.68, 131.85, 131.51, 127.98, 110.24, 75.84, 61.38, 14.05. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}ClIN_3O_2^+$ 427.96572, 429.96277; Found 427.96603, 429.96267.

Ethyl 2-(3-bromophenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2y)



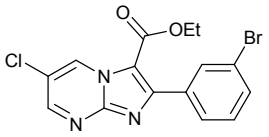
Pale yellow solid, 39% yield (46 mg), m.p.: 135.8–137.5 °C; R*f* = 0.42 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.96 (d, *J* = 2.3 Hz, 1H), 8.82 (d, *J* = 2.3 Hz, 1H), 8.02 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.40, 157.59, 152.86, 147.82, 142.05, 140.44, 134.99, 133.48, 132.36, 129.35, 129.09, 121.54, 61.45, 13.98. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{15}H_{12}BrIN_3O_2^{+}$ 471.91521, 473.91316; Found 471.91552, 473.91332.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2z)



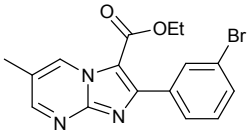
White solid, 61% yield (80 mg), m.p.: 157.2–158.0 °C; R*f* = 0.51 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 10.00 (d, *J* = 2.3 Hz, 1H), 8.87 (d, *J* = 2.4 Hz, 1H), 8.39 (s, 2H), 7.97 (s, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 159.98, 158.22, 150.86, 147.94, 140.61, 135.12, 131.23 (q, *J* = 33.3 Hz), 130.81 (q, *J* = 3.8 Hz), 123.28 (q, *J* = 272.8 Hz), 123.04 (dq, *J* = 7.3 and 3.7 Hz), 110.76, 61.86, 13.75. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{17}H_{11}F_6IN_3O_2^{+}$ 529.97947; Found 529.97917.

Ethyl 2-(3-bromophenyl)-6-chloroimidazo[1,2-*a*]pyrimidine-3-carboxylate (2aa)



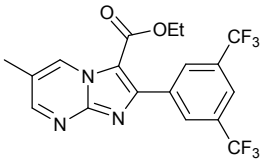
White solid, 50% yield (48 mg), m.p.: 124.7–125.9 °C; R*f* = 0.48 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.78 (d, *J* = 2.5 Hz, 1H), 8.69 (d, *J* = 2.7 Hz, 1H), 8.02 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.38, 153.47, 152.08, 147.86, 135.04, 133.71, 133.46, 132.38, 129.36, 129.05, 121.56, 120.09, 110.82, 61.49, 13.98. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{15}H_{12}BrClN_3O_2^{+}$ 379.97959, 381.97755, 381.97664, 383.97460; Found 379.97992, 381.97753, 383.97436.

Ethyl 2-(3-bromophenyl)-6-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2bb)



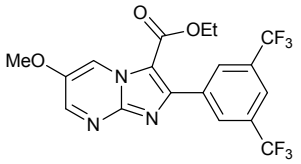
White solid, 79% yield (71 mg), m.p.: 124.6–126.2 °C; R*f* = 0.26 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.51 (s, 1H), 8.62 (d, *J* = 2.1 Hz, 1H), 8.02 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 2.47 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.73, 155.15, 152.70, 149.07, 135.72, 134.01, 133.47, 131.98, 129.24, 129.04, 121.43, 120.35, 110.13, 61.05, 15.68, 14.00. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}BrN_3O_2^+$ 360.03422, 362.03217; Found 360.03460, 362.03235.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2cc)



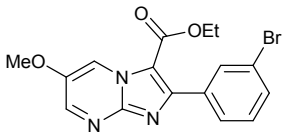
White solid, 65% yield (68 mg), m.p.: 150.0–150.2 °C; R*f* = 0.36 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.55 (s, 1H), 8.67 (d, *J* = 2.4 Hz, 1H), 8.39 (s, 2H), 7.95 (s, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.50 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.31, 155.72, 150.76, 149.18 , 135.83, 134.12, 131.06 (q, *J* = 33.3 Hz), 130.79 (q, *J* = 4.2 Hz), 123.31 (q, *J* = 272.4 Hz), 122.65 (dq, *J* = 7.6, 4.2 Hz), 120.91, 110.55, 61.43, 15.73, 13.78. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}F_6N_3O_2^+$ 418.09847; Found 418.09844.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-methoxyimidazo[1,2-*a*]pyrimidine-3-carboxylate (2dd)



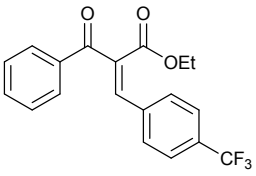
White solid, 75% yield (81 mg), m.p.: 161.4–162.2 °C; R*f* = 0.42 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.32 (d, *J* = 3.0 Hz, 1H), 8.64 (d, *J* = 3.0 Hz, 1H), 8.37 (s, 1H), 7.95 (s, 1H), 4.36 (q, *J* = 7.2 Hz, 1H), 3.98 (s, 1H), 1.27 (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.49, 150.42, 148.24, 147.08, 146.97, 135.91, 131.18 (q, *J* = 33.6 Hz), 130.69 (q, *J* = 5.1, 4.4 Hz), 123.36 (q, *J* = 272.7 Hz), 122.55 (dq, *J* = 7.4, 3.6 Hz), 116.94, 111.33, 61.44, 56.63, 13.76. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}F_6N_3O_3^+$ 434.09339; Found 434.09357.

Ethyl 2-(3-bromophenyl)-6-methoxyimidazo[1,2-*a*]pyrimidine-3-carboxylate (2ee)



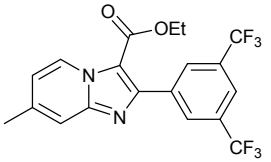
Pale yellow solid, 40% yield (38 mg), m.p.: 159.6–160.1 °C; R*f* = 0.35 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.29 (d, *J* = 3.0 Hz, 1H), 8.60 (d, *J* = 3.0 Hz, 1H), 8.00 (s, 1H), 7.79 (d, *J* = 7.8, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 3.96 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.91, 152.42, 147.59, 146.81, 135.81, 133.41, 131.88, 129.24, 128.95, 121.42, 116.98, 110.94, 61.06, 56.59, 13.99. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{16}H_{15}BrN_3O_3^{+}$ 376.02913, 378.02708; Found 376.02917, 378.02696.

Ethyl 2-benzoyl-3-(4-(trifluoromethyl)phenyl)acrylate (3)



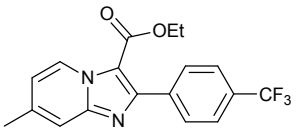
White solid, 35, 43 and 50% yield; R*f* = 0.50 (hexane /2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.96 (s, 1H), 7.93 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.48 – 7.41 (m, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 194.40, 164.08, 140.11, 135.84, 135.45, 133.76, 133.50, 131.24 (q, *J* = 32.9 Hz), 129.68, 128.64, 128.52, 125.27 (q, *J* = 3.5 Hz), 123.15 (q, *J* = 272.0 Hz), 61.42, 13.54.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-7-methylimidazo[1,2-*a*]pyridine-3-carboxylate (6a)



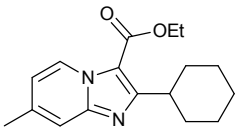
White solid, 93% yield (97 mg), m.p.: 110.9–112.7 °C; R*f* = 0.60 (hexane/2-propanol 9:1); $C_{19}H_{14}F_6N_2O_2$, ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.33 (d, *J* = 7.1 Hz, 1H), 8.28 (s, 2H), 7.93 (s, 1H), 7.53 (s, 1H), 6.95 (dd, *J* = 7.1, 1.8 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.51 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.51, 149.99, 147.77, 140.24, 136.73, 131.07 (q, *J* = 33.4 Hz), 130.59 (q, *J* = 3.8 Hz), 127.62 , 124.50 (q, *J* = 272.6 Hz), 122.24 (dq, *J* = 7.3, 3.7 Hz), 117.39, 116.28, 112.04, 60.86, 21.50, 13.80. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{19}H_{15}F_6N_2O_2^{+}$ 417.10322; Found 417.10361.

Ethyl 7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylate (6b)



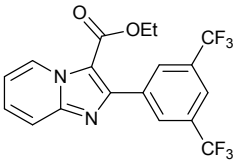
Pale brown solid, 65% yield (57 mg), m.p.: 139.1–140.1 °C; R*f* = 0.50 (hexane/2-propanol 9:1); $C_{18}H_{15}F_3N_2O_2$, ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.20 (d, *J* = 6.8 Hz, 1H), 7.99 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.63 (s, 1H), 7.14 (d, *J* = 6.5 Hz, 1H), 4.26 (q, *J* = 6.5 Hz, 2H), 2.46 (s, 3H), 1.17 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.44, 151.13, 147.40, 140.36, 138.91, 131.32, 129.25 (q, *J* = 31.2 Hz), 127.73, 124.83 (q, *J* = 3.6 Hz), 117.86, 116.27, 60.81, 21.25, 14.20. HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{18}H_{16}F_3N_2O_2^+$ 349.11584; Found 349.11600.

Ethyl 2-cyclohexyl-7-methylimidazo[1,2-*a*]pyridine-3-carboxylate (6c)



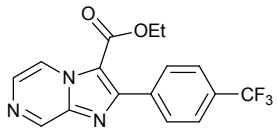
Orange solid, 35% yield (25 mg), m.p.: 111.8–113.8 °C; R*f* = 0.58 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.19 (d, *J* = 7.1 Hz, 1H), 7.46 (s, 1H), 6.81 (d, *J* = 5.3 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.46 (tt, *J* = 11.8, 3.0 Hz, 1H), 2.43 (s, 3H), 1.94 (d, *J* = 12.4 Hz, 2H), 1.88 (d, *J* = 12.6 Hz, 2H), 1.80 – 1.71 (m, 4H), 1.45 (t, *J* = 7.1 Hz, 3H), 1.43 – 1.33 (m, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 161.51, 147.39, 138.99, 127.28, 116.19, 115.68, 110.93, 77.29, 60.18, 38.11, 32.30, 26.79, 26.10, 21.41, 14.40. HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{17}H_{23}N_2O_2^+$ 287.17540; Found 287.17560.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylate (6d)



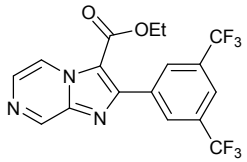
White solid, 75% yield (75 mg), m.p.: 134.7–136.0 °C; R*f* = 0.51 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.48 (d, *J* = 7.0 Hz, 1H), 8.30 (s, 2H), 7.94 (s, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 6.9 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.48, 149.95, 147.33, 131.48 – 130.44 (m), 130.61 (q, *J* = 3.8, 3.1 Hz), 128.71, 128.53, 125.34 – 122.66 (m), 122.33 (dq, *J* = 7.6, 3.9 Hz), 117.74, 114.86, 61.01, 13.79. HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{18}H_{13}F_6N_2O_2^+$ 403.08757; Found 403.08701.

Ethyl 2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7a)



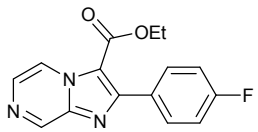
Pale yellow solid, 77% yield (64 mg), m.p.: 142–143.9 °C; R*f* =0.25 (hexane/2-propanol 9:1); $C_{16}H_{12}F_3N_3O_2$, ^{1}H NMR (500 MHz, DMSO-*d6*) δ 9.34 (d, *J* = 1.3 Hz, 1H), 9.18 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.26 (d, *J* = 4.7 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 159.99, 151.12, 144.08, 141.33, 137.85, 132.42, 131.40, 129.73 (q, *J* = 32.0 Hz), 124.69, 127.94, 125,78, 123,61, 121,45 (q, *J* = 272.1 Hz), 125.07 (q, *J* = 3.6 Hz), 121.29, 113.78, 61.58, 14.13. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{13}F_3N_3O_2^+$ 336.09544; Found 336.09588.

Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7b)



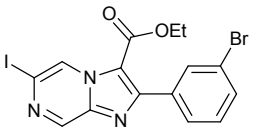
Yellow solid, 74% yield (75 mg), m.p.: 135.4–137.2 °C; R*f* = 0.53 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.31 (dd, *J* = 4.7, 1.4 Hz, 1H), 9.29 (d, *J* = 1.2 Hz, 1H), 8.34 (s, 2H), 8.22 (d, *J* = 4.6 Hz, 1H), 7.99 (s, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 159.89, 150.18, 144.09, 141.49, 135.49, 132.31, 131.30 (q, *J* = 33.4 Hz), 130.62 (q, *J* = 3.8 Hz), 126.74 – 119.72 (m), 122.89 (dq, *J* = 7.0, 3.5 Hz), 120.70, 113.61, 61.79, 13.77. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{12}F_6N_3O_2^+$ 404.08282; Found 404.08162.

Ethyl 2-(4-fluorophenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7c)



White solid, 63% yield (45 mg), m.p.: 97.2–97.6 °C; R*f* = 0.42 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.24 (d, *J* = 4.7 Hz, 1H), 9.23 (s, 1H), 8.16 (d, *J* = 4.6 Hz, 1H), 7.80 (ddd, *J* = 8.4, 5.2, 2.5 Hz, 2H), 7.21 – 7.12 (m, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 163.51 (d, *J* = 249.1 Hz), 160.39, 152.94, 143.71, 141.35, 132.21 (d, *J* = 8.5 Hz), 131.78, 129.44 (d, *J* = 3.2 Hz), 120.66, 114.89 (d, *J* = 21.9 Hz), 113.02, 61.30, 14.04. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}FN_3O_2^+$ 286.09863; Found 286.09884.

Ethyl 2-(3-bromophenyl)-6-iodoimidazo[1,2-*a*]pyrazine-3-carboxylate (7d)



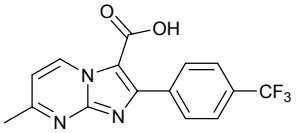
Pale brown solid, 55% yield (65 mg), m.p.: 142.1–143.5 °C; R*f* = 0.53 (hexane/2-propanol 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.62 (d, *J* = 1.4 Hz, 1H), 9.02 (d, *J* = 1.5 Hz, 1H), 7.95 (s, 1H), 7.73 (d, *J* = 7.7, 1H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.07, 152.33, 143.32, 140.52, 134.80, 133.30, 132.46, 129.48, 128.85, 126.52, 112.99, 96.50, 61.70, 13.94. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{15}H_{12}BrIN_3O_2^{+}$ 471.91521, 473.91316; Found 471.91511, 473.91307.

8. General procedure for the preparation of carboxylic acids **8a-d**

The hydrolysis of the corresponding esters **2a**, **2f**, **6d** and **7b** (0.5 mmol) were accomplished in 1 M KOH (13 mL), stirring for 12 hours at 75 °C. Afterwards, the reaction was neutralized by the addition of 1 M HCl and extracted with EtOAc (20 mL). Organic layer was dried over Na_2SO_4 and the solvent was removed to obtain the desired product **8a**-**d**.

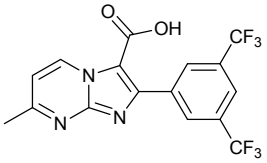
9. Characterization of carboxylic acids **8a-d**

7-Methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylic acid (8a)



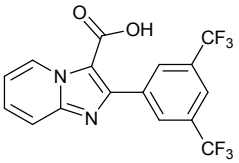
Pale orange solid, 61% yield (98 mg), R*f* = 0.57 (toluene/MeOH 7:3). ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.38 (s, 1H), 9.52 (d, J = 7.1 Hz, 1H), 8.05 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 7.1 Hz, 1H), 2.63 (s, 3H).^{13}C NMR (126 MHz, DMSO-d_6) δ 163.75, 161.72, 151.07, 149.45, 138.52, 136.52, 131.36, 129.35 (q, *J* = 32.0 Hz), δ 124.76 (q, *J* = 272.1 Hz), 124.99 (q, *J* = 3.5 Hz), 123.68, 121.69, 112.23, 111.51, 25.03. HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{15}H_{11}F_3N_3O_2^{+}$ 322.07979; Found 322.08009.

2-(3,5-Bis(trifluoromethyl)phenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylic acid (8b)



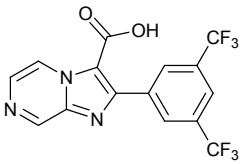
Pale yellow solid, 81% yield (158 mg), m.p.: 108.1–111.8 °C; R*f* = 0.62 (toluene/MeOH 7:3) ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.70 (s, 1H), 9.55 (d, *J* = 7.1 Hz, 1H), 8.60 (s, 2H), 8.21 (s, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.04, 161.55, 149.30, 136.78, 136.64, δ 131.13 (q, *J* = 4.6 Hz), 130.21 (q, *J* = 32.7 Hz), 124.92, 122.70, 112.43, 25.07. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{10}F_6N_3O_2^+$ 390.06717; Found 390.06756.

2-(3,5-Bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylic acid (8c)



Pale yellow solid, 96% yield (180 mg), m.p.: 148.3–151.0 °C; R*f* = 0.20 (toluene/MeOH 9:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.41 (d, *J* = 7.0 Hz, 1H), 8.52 (s, 2H), 8.20 (s, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.67 – 7.60 (m, 1H), 7.28 (t, *J* = 7.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.08, 161.78, 148.75, 146.87, 137.24, 131.20 (q, *J* = 4.2 Hz), 130.60 – 129.61 (m), 129.34, 129.04, 128.93, 123.84 (q, *J* = 272.9 Hz), 122.52 (dq, *J* = 7.3, 4.5, 3.7 Hz), 117.84, 115.54, 113.48. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_9F_6N_2O_2^+$ 375.05627; Found 375.05684.

2-(3,5-Bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylic acid (8d)



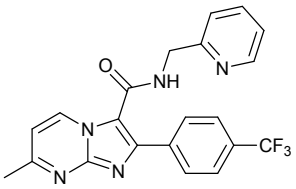
White solid, 98% yield (184 mg), m.p.: 223.7–224.5 °C; R*f* = 0.10 (toluene/MeOH 9:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.36 (s, 1H), 9.29 – 9.23 (m, 1H), 8.58 (s, 2H), 8.25 (d, *J* = 4.9 Hz, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.98, 161.40, 148.83, 144.19, 141.16, 136.37, 132.34, 131.24 (q, *J* = 4.4 Hz), 130.30 (q, *J* = 33.0 Hz), 123.78 (q, *J* = 273.0 Hz), 122.99 (dq, *J* = 7.6, 4.2 Hz), 121.52, 115.16. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_8F_6N_3O_2^+$ 376.05152; Found 376.05149.

10. General procedure for the preparation of carboxamides **9a-d**

To solution of carboxylic acid in DMF (6.5 mL), *N*-Ethyl-*N*'-(3-dimethylaminopropyl)carbodiimide hydrochloride (0.23 mmol, 1.16 equiv.), *N,N*-diisopropylethylamine (0.23 mmol, 1.16 equiv.), corresponding amine (0.2 mmol, 1 equiv.) and 1-Hydroxybenzotriazole (0.28 mmol, 1.38 equiv.) were added. The reaction was stirred at room temperature for 24 h, then saturated sodium bicarbonate solution (10 ml) was added to the reaction mixture and extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed by vacuo. The obtained crude product was purified on column chromatography (mixture of ethyl acetate/methanol) to isolate the pure carboxamides **9a**-**d**.

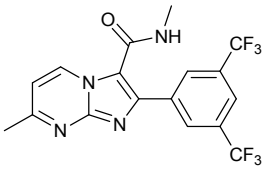
11. Characterization of carboxamides **9a-d**

7-Methyl-*N*-(pyridin-2-ylmethyl)-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxamide (9a)



Pale yellow solid, 19% yield (16 mg), m.p.: 181.2–182.4 °C; R*f* = 0.75 (EtOAc/MeOH 9:1) $C_{21}H_{16}F_3N_5O$, ^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.67 (d, *J* = 7.1 Hz, 1H), 8.23 (d, *J* = 4.8 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.65 (td, *J* = 7.7, 1.7 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.20 – 7.14 (m, 1H), 4.65 (d, *J* = 4.5 Hz, 2H), 2.69 (s, 3H). ^{13}C-NMR (126 MHz, chloroform-*d*) δ 163.03, 160.31, 154.84, 149.23, 148.77, 147.83, 136.98, 136.76, 135.48, 131.15 (q, *J* = 32.5 Hz), 130.43, 125.81 (q, *J* = 3.6 Hz), 124.07 (q, *J* = 272.3 Hz), 121.86, 122.52, 113.23, 111.08, 44.22, 25.11. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{17}F_3N_5O^+$ 412.13797; Found 412.13836.

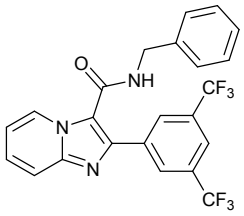
2-(3,5-Bis(trifluoromethyl)phenyl)-*N*,7-dimethylimidazo[1,2-*a*]pyrimidine-3-carboxamide (9b)



Pale yellow solid, 20% yield (16 mg), m.p.: 195.7–196.8 °C; R*f* = 0.90 (EtOAc/MeOH 9:1); ^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.54 (d, *J* = 7.1 Hz, 1H), 8.43 (s, 2H), 7.95 (s, 1H), 7.05 (d, *J* = 7.1 Hz, 1H), 3.89 (s, 3H), 2.74 (s, 3H). ^{13}C-NMR (126 MHz, chloroform-*d*) δ 164.34, 160.49, 150.76, 149.97, 135.54, 135.48, 131.08 (q, *J* = 33.5 Hz), 130.93 – 130.71 (m), 123.37 (q, *J* = 272.6 Hz), 122.62 (dq, *J* = 7.4, 4.0, 3.5 Hz),

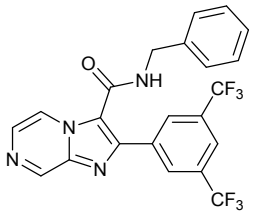
111.96, 110.52, 51.68, 25.17. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{14}F_6N_4O^{2+}$ 404.10608; Not found.

_N_-Benzyl-2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxamide (9c)



Orange solid, 52% yield (48 mg), m.p.: 209.4–210.4 °C; R*f* = 0.65 (toluene/MeOH 9:1); ^{1}H NMR (500 MHz, chloroform-*d*) δ 9.36 (d, *J* = 7.0 Hz, 1H), 8.23 (s, 2H), 7.90 (s, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.49 – 7.40 (m, 1H), 7.31 – 7.23 (m, 3H), 7.18 (d, *J* = 6.4 Hz, 2H), 7.04 (t, *J* = 6.9 Hz, 1H), 5.83 (t, *J* = 5.1 Hz, 1H), 4.54 (d, *J* = 5.6 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 160.45, 146.56, 144.37, 136.99, 136.01, 132.31 (q, *J* = 33.9 Hz), 129.77 (q, *J* = 4.0 Hz), 128.87, 128.14, 128.07, 127.86, 127.71, 123.00 (q, *J* = 273.1 Hz), 122.82 (dq, *J* = 7.2, 3.4 Hz), 117.50, 115.47, 114.31, 43.85. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{16}F_6N_3O^+$ 464.11921; Found 464.11908.

_N_-Benzyl-2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxamide (9d)



Orange solid, 92% yield (85 mg), m.p.: 158.1–159 °C; R*f* = 0.38 (toluene/MeOH 9:1). ^{1}H-NMR (500 MHz, chloroform-*d*) δ 9.23 (d, *J* = 5.3 Hz, 2H), 8.25 (s, 2H), 8.14 (d, *J* = 4.5 Hz, 1H), 7.96 (s, 1H), 7.31-7.23 (m, 3H), 7.19 (d, *J* = 6.4 Hz, 2H), 5.90 (t, *J* = 5.0 Hz, 1H), 4.56 (d, *J* = 5.6 Hz, 2H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 159.51, 145.08, 144.05, 141.00, 136.53, 135.03, 132.63 (q, *J* = 34.1 Hz), 131.62, 129.98 – 129.60 (m), 128.97, 128.08 ,127.78, 122.08 (q, *J* = 291.6 Hz), 123.57 – 123.28 (m), 120.47, 44.00. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}F_6N_4O^+$ 465.11446; Found 465.11460.

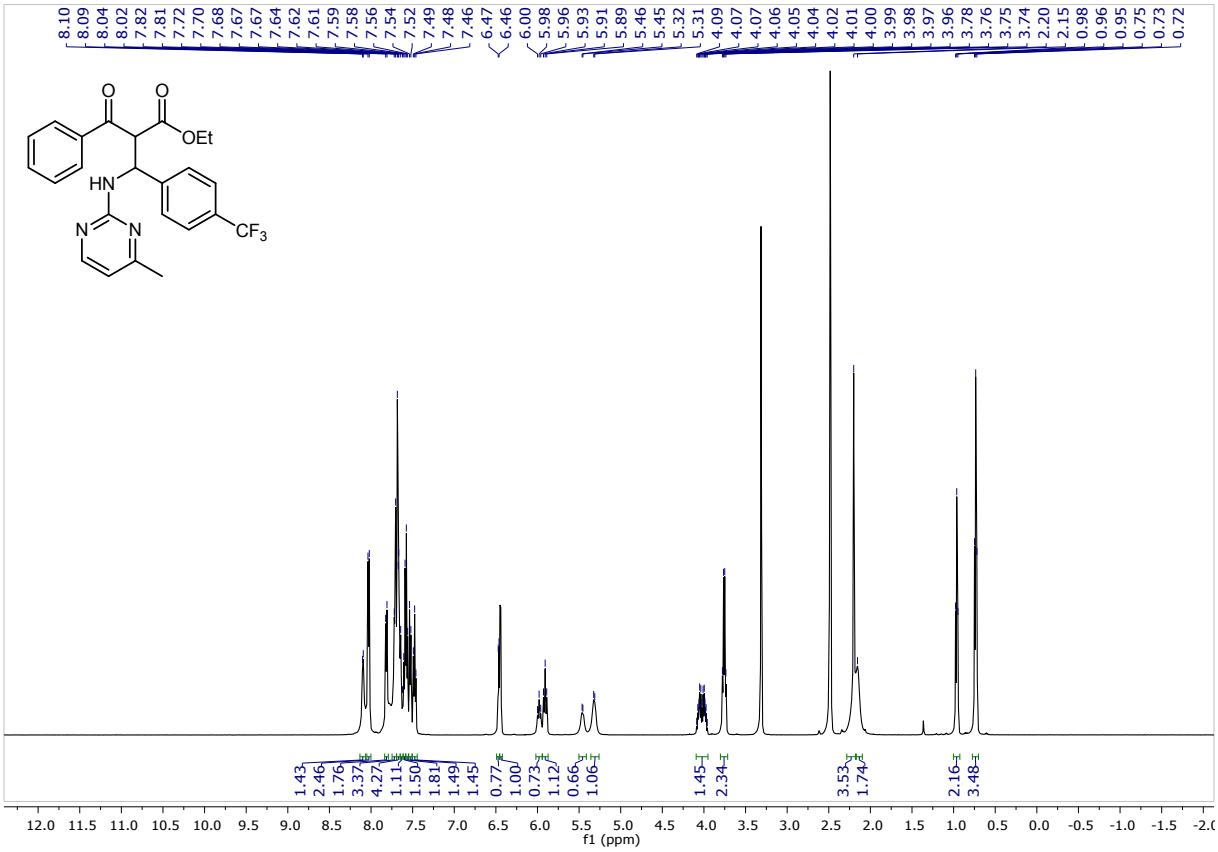
12. Procedure for the sequential one-pot synthesis

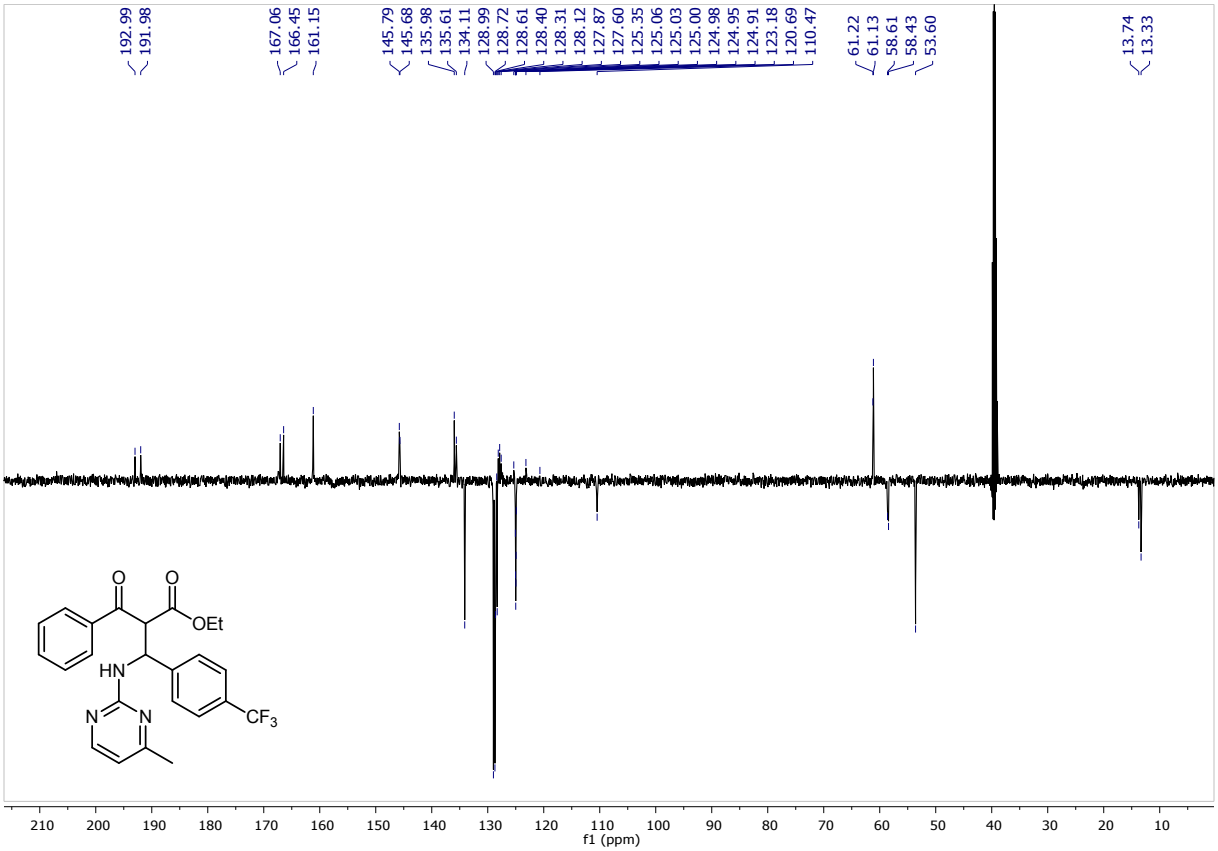
To a stirring solution of 2-amino-4-methylpyridine (1 mmol) or 2-amino-4-methylpyrimidine (1 mmol) or 2-aminopyrazine (1 mmol) and 4-(trifluoromethyl)benzaldehyde (1.5 mmol) in DMA (2 mL) were added ethyl benzoylacetate (1 mmol) and PTA (0.025 mmol). The mixture was stirred at 80 °C for 48 hours. At this time TLC was show that conversion did not change and arrive 65%. To a reaction

mixtures were added stabilized IBX (1.1 mmol IBX, 700 mg), NIS (1.5 mmol, 337.5 mg) and DMA (8 mL). The reaction mixtures were stirred at 80 ºC for 30 minutes at which time TLC showed that the reactions were completed. Mixtures were diluted with $Na_2S_2O_3.5H_2O$ (14 g in 40 mL water) solution and extracted with EtOAc (40 mL). Organic layers were washed with saturated sodium bicarbonate solution (40 mL) and two times extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Crude materials were subjected to column chromatographic separation (Eluent: toluene/acetonitrile 9:1) and products were recrystallized with diisopropyl ether.

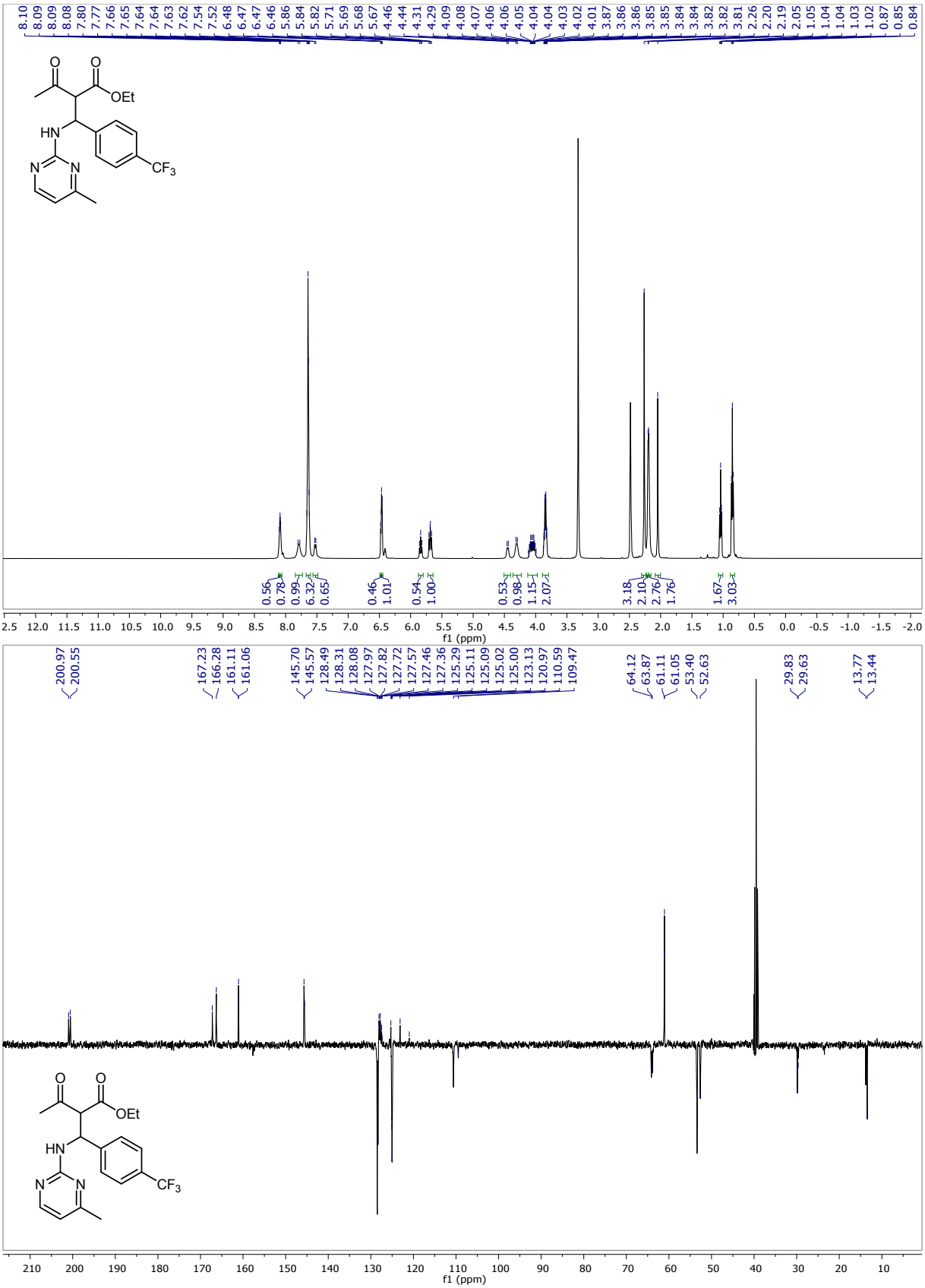
13. ^{1}H and ^{13}C NMR data of Mannich precursors

Ethyl 2-benzoyl-3-(4-methylpyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1a)

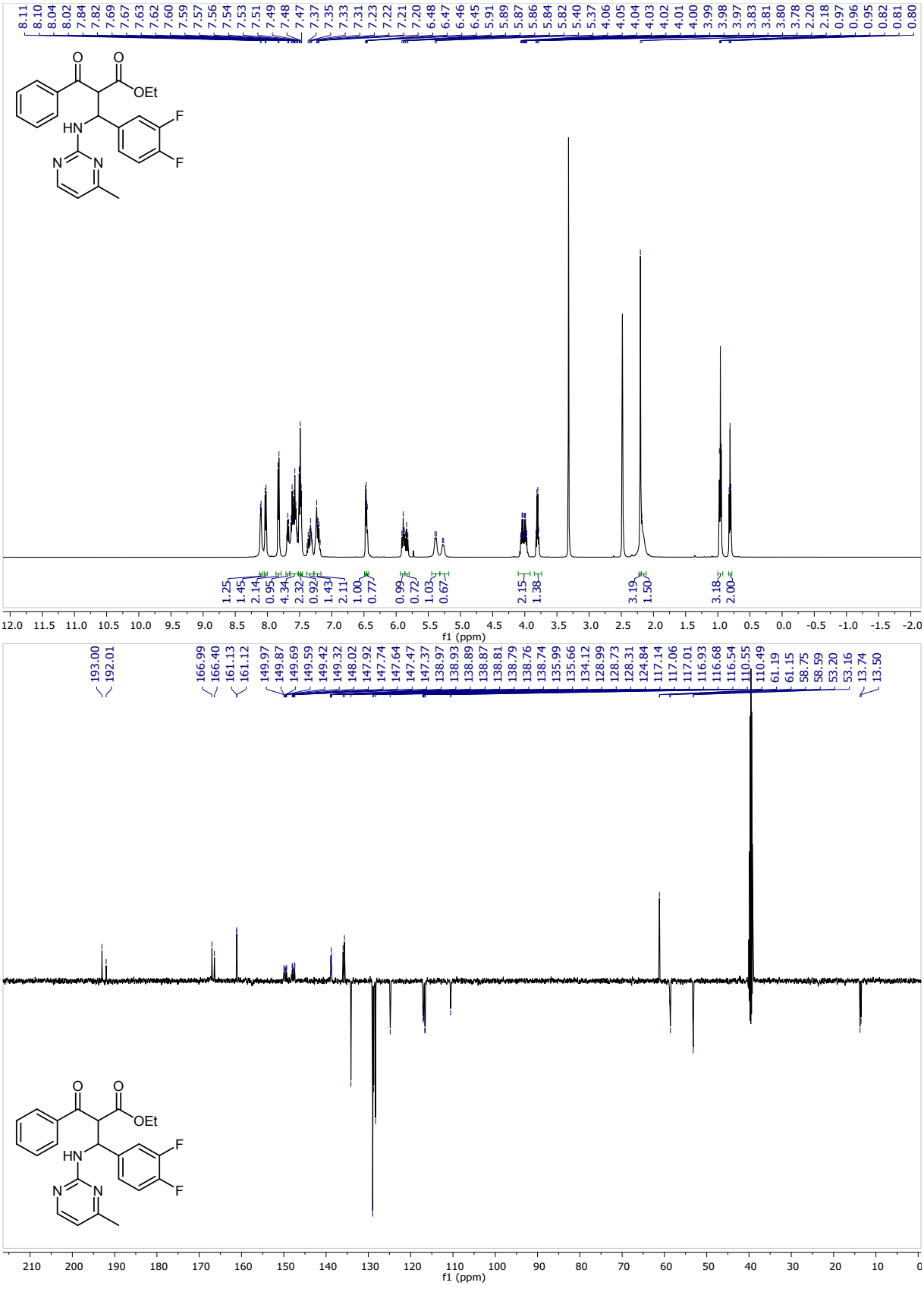




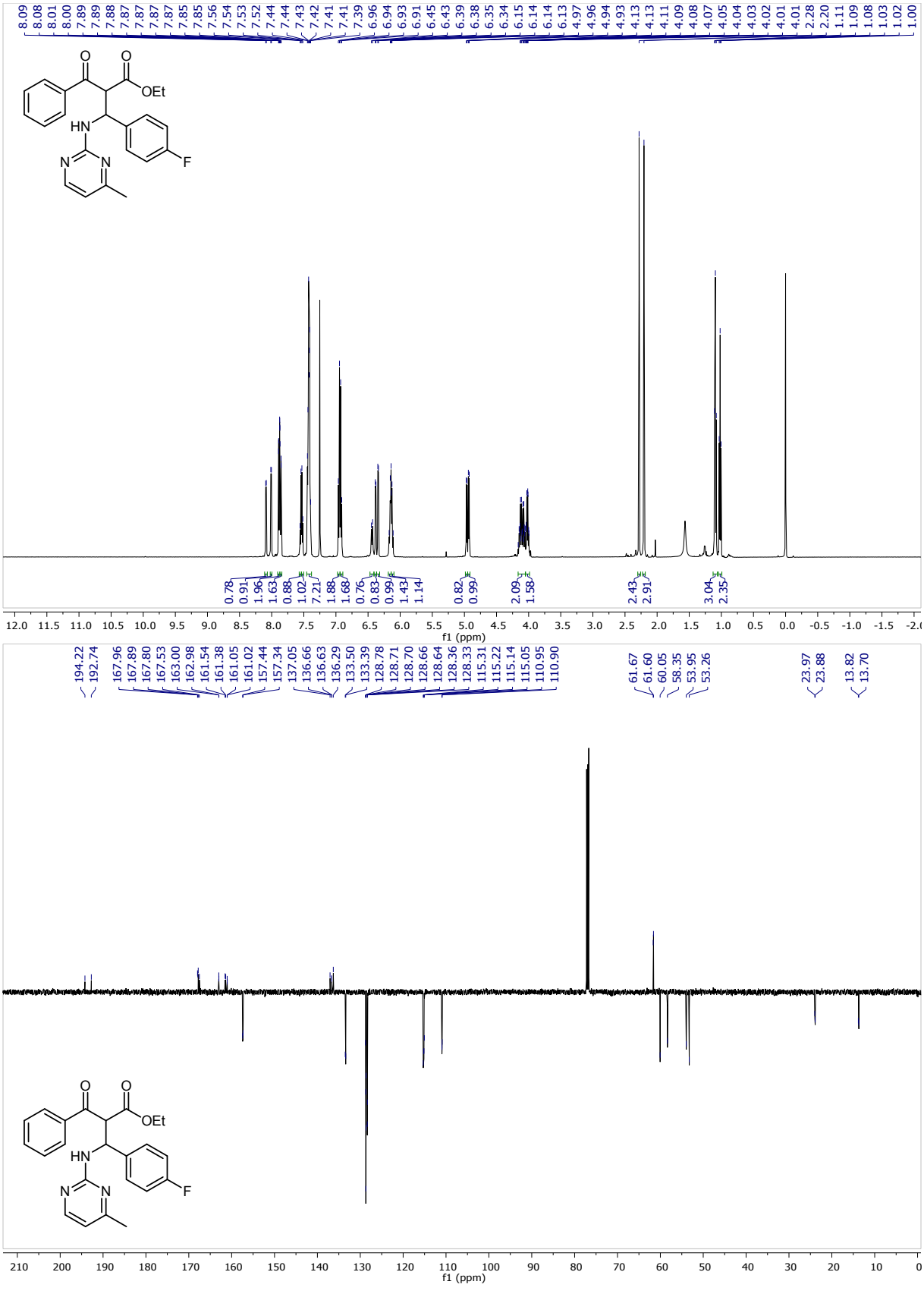
Ethyl 2-(((4-methylpyrimidin-2-ylamino)(4-(trifluoromethyl)phenyl)methyl)-3-oxobutanoate (1b)



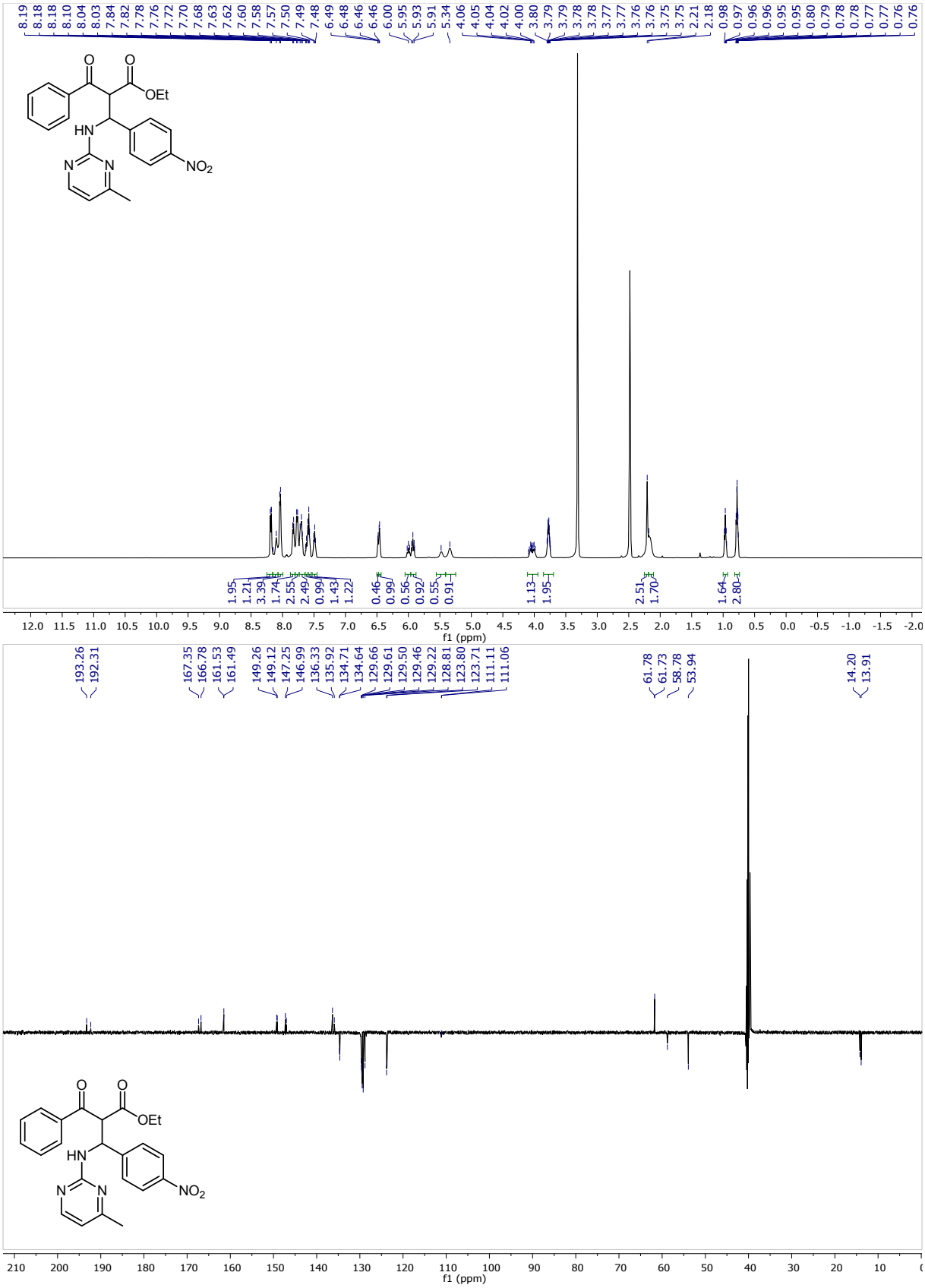
Ethyl 2-benzoyl-3-(3,4-difluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1c)



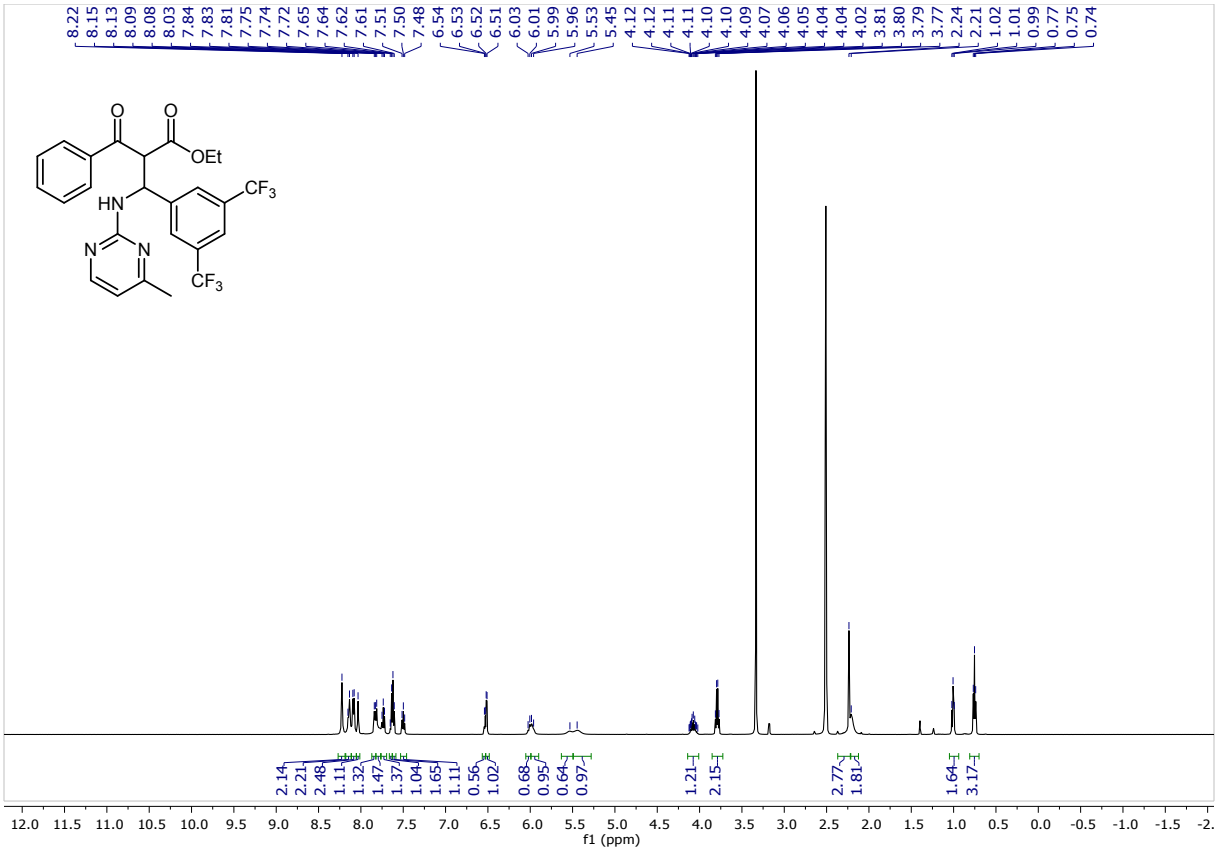
Ethyl 2-benzoyl-3-(4-fluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1d)

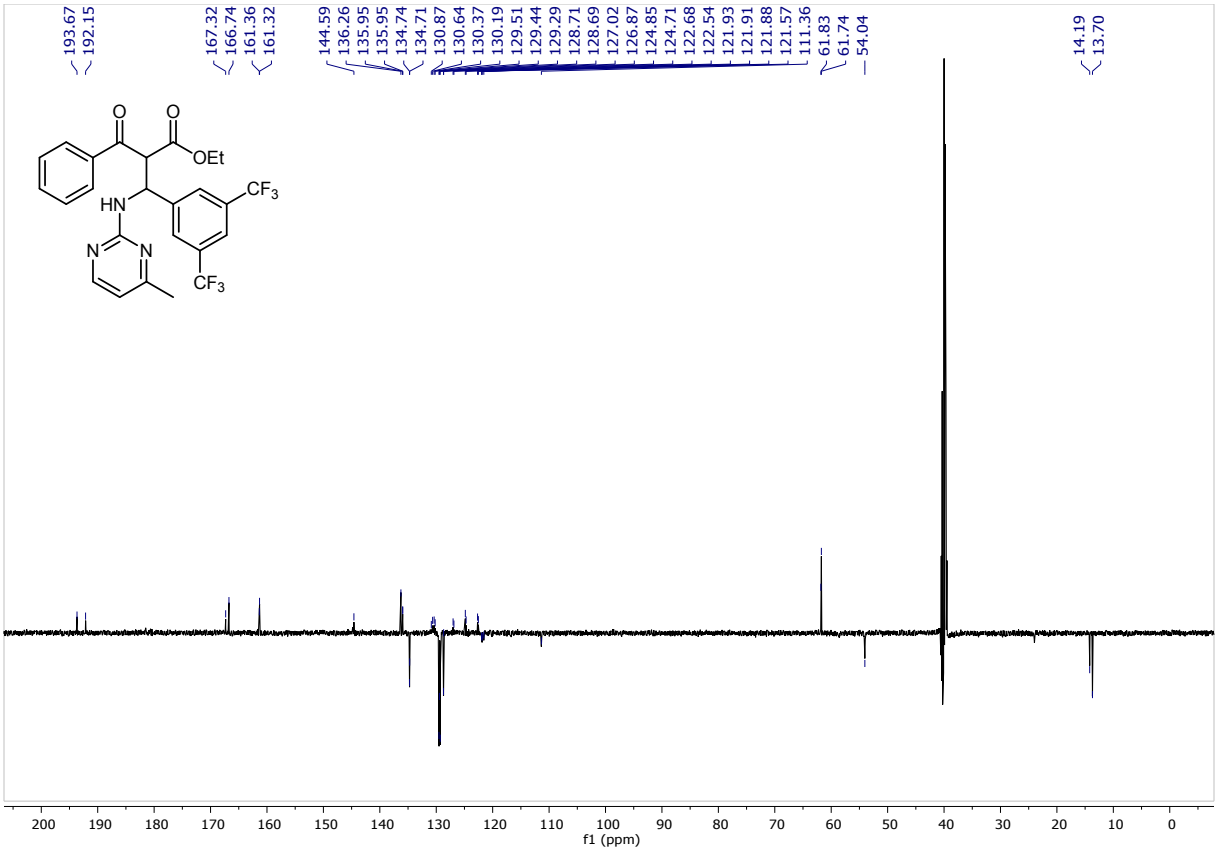


Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)-3-(4-nitrophenyl)propanoate (1e)

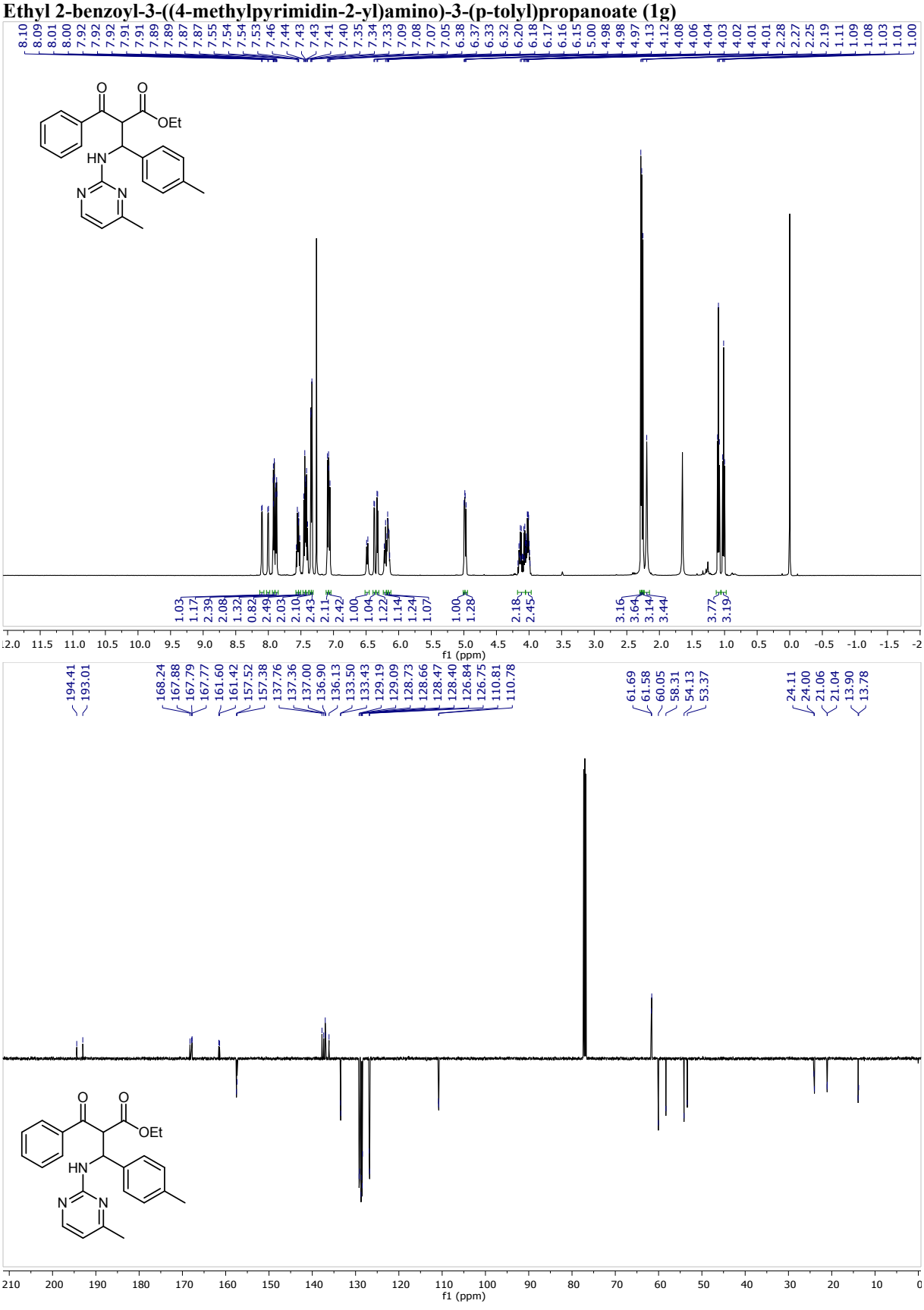


Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1f)

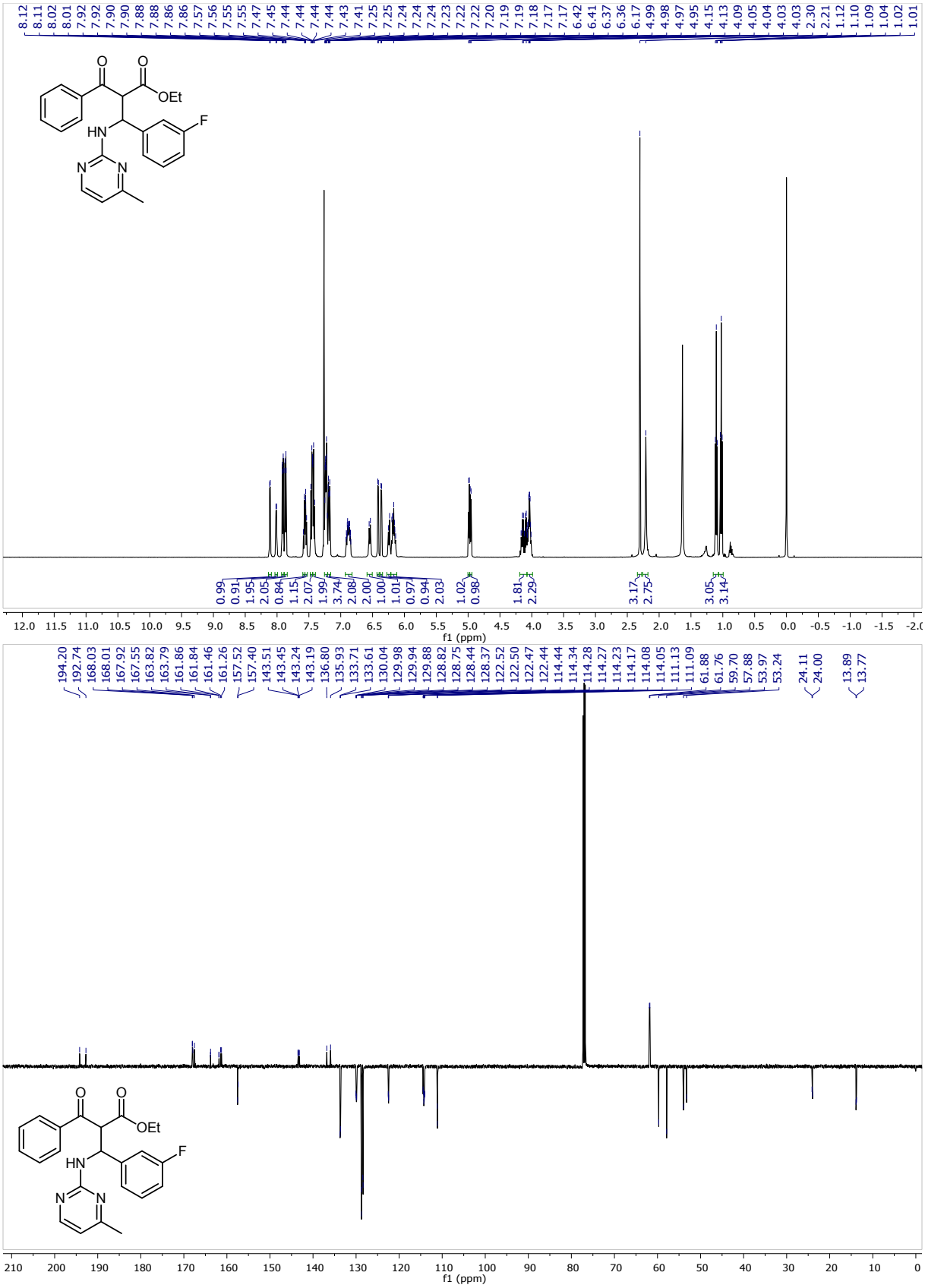




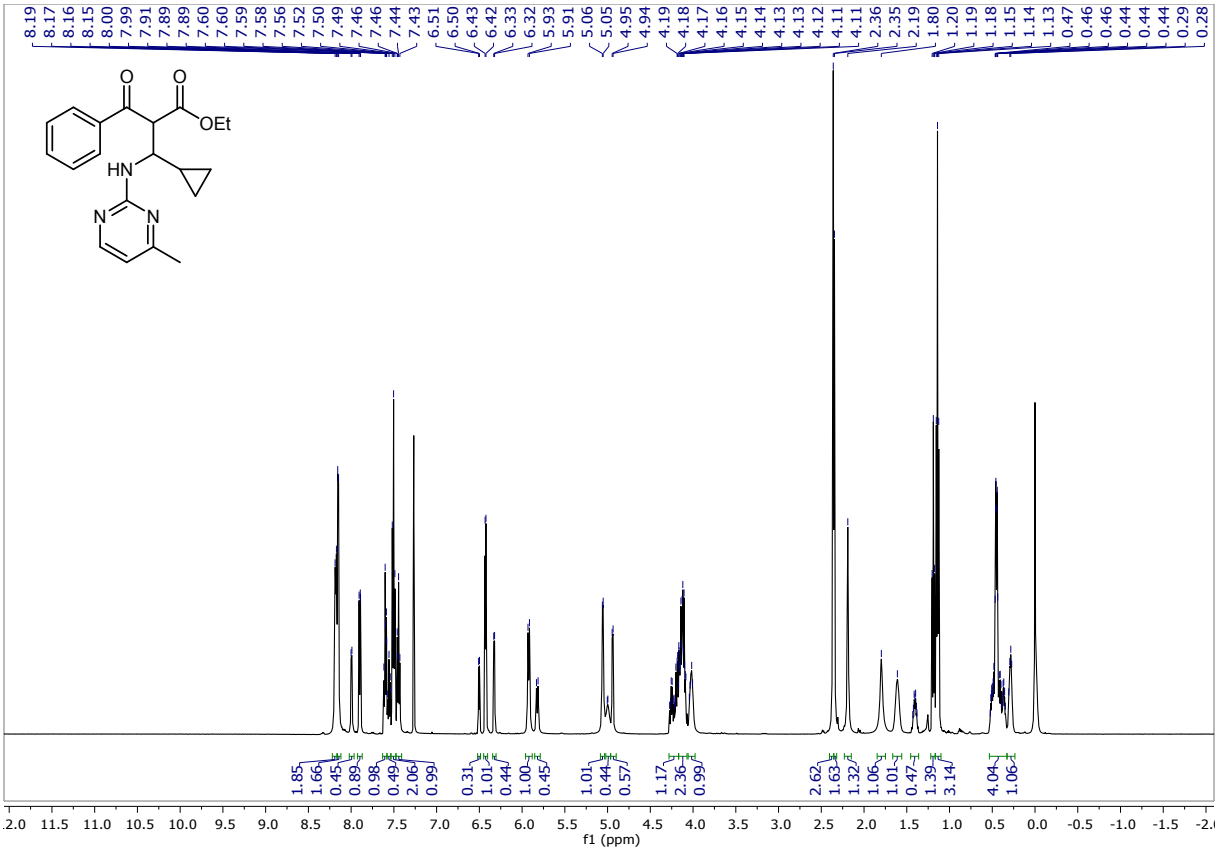
Ethyl 2-benzoyl-3-((4-methylpyrimidin-2-yl)amino)-3-(p-tolyl)propanoate (1g)

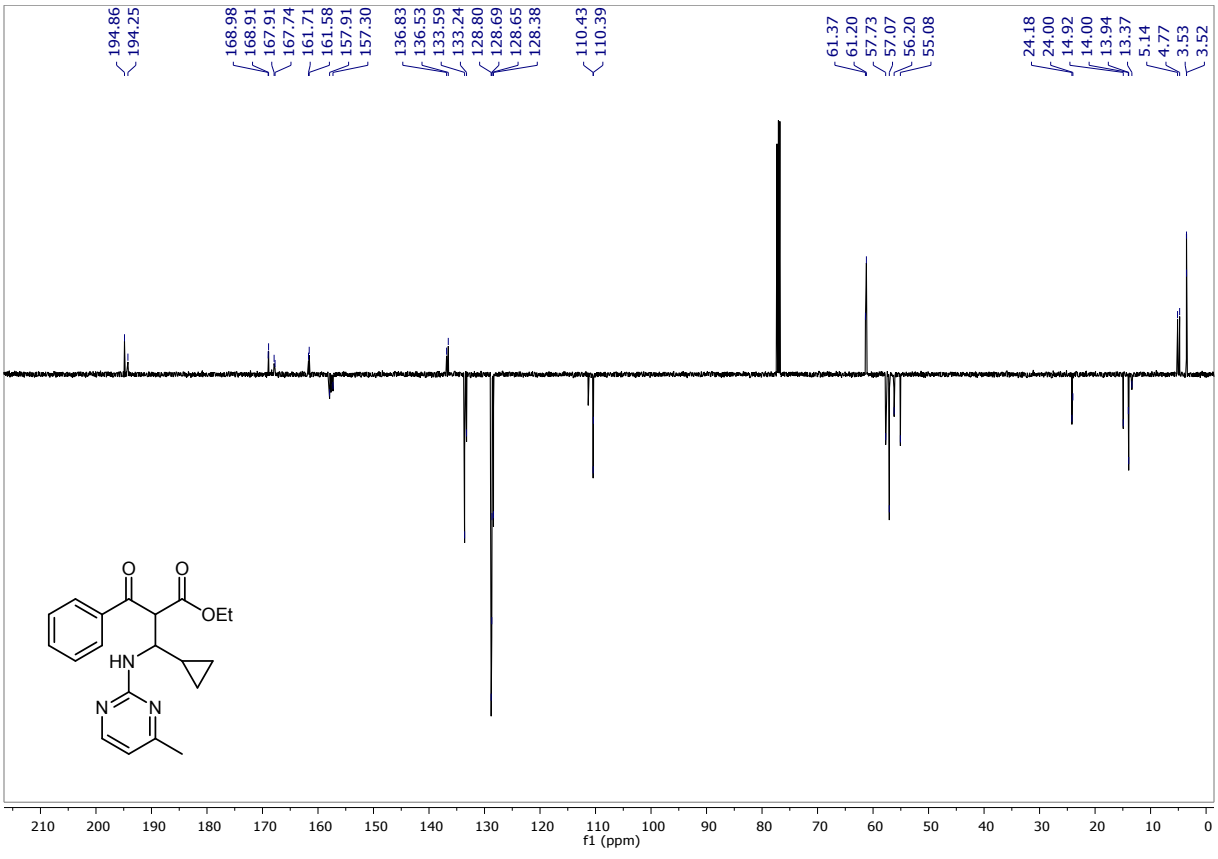


Ethyl 2-benzoyl-3-(3-fluorophenyl)-3-((4-methylpyrimidin-2-yl)amino)propanoate (1h)

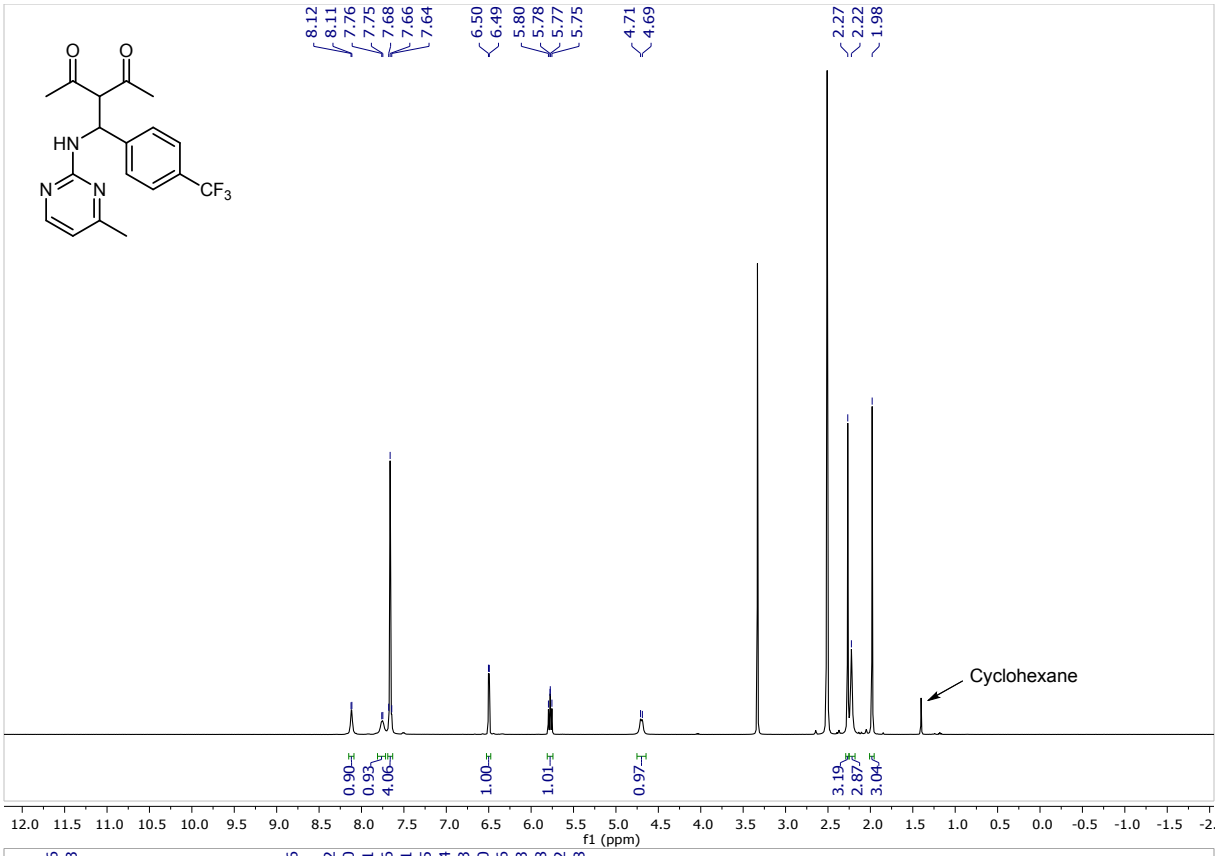


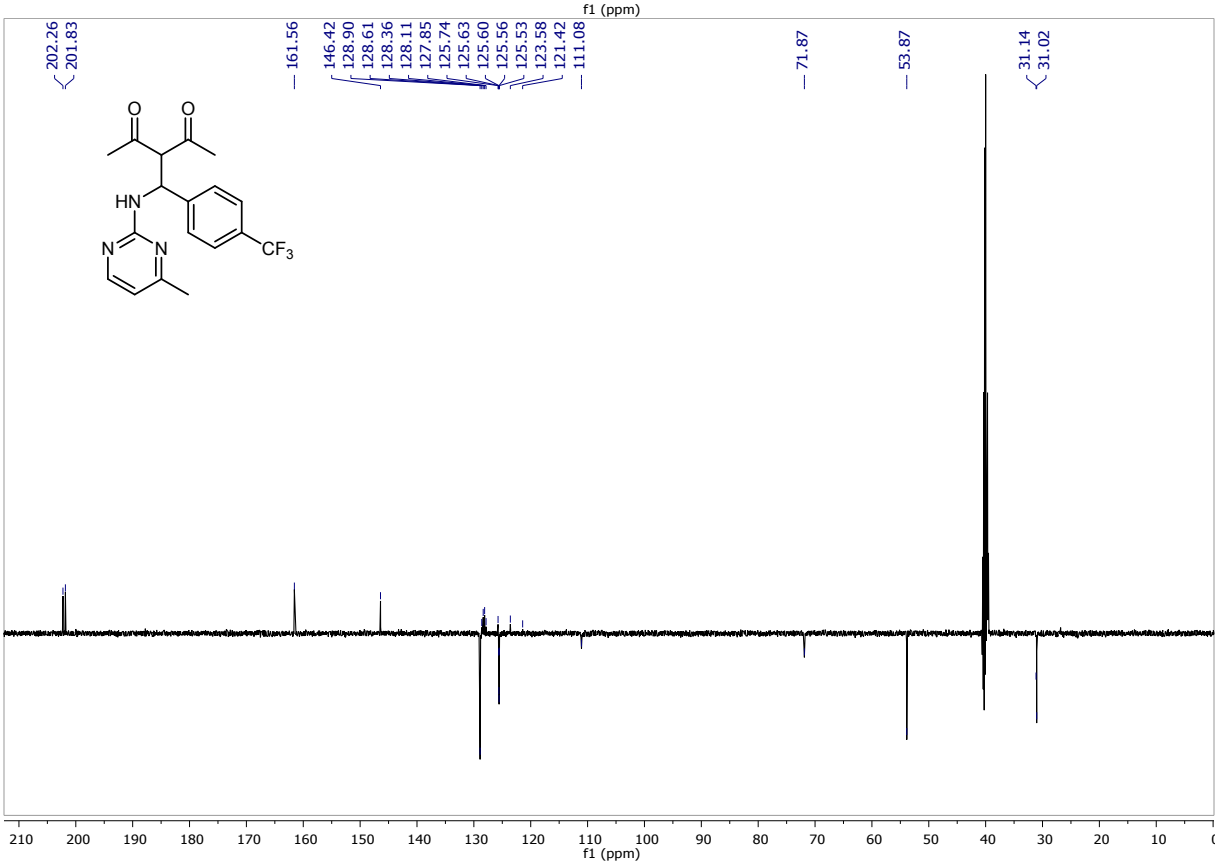
Ethyl 2-benzoyl-3-cyclopropyl-3-((4-methylpyrimidin-2-yl)amino)propanoate (1j)



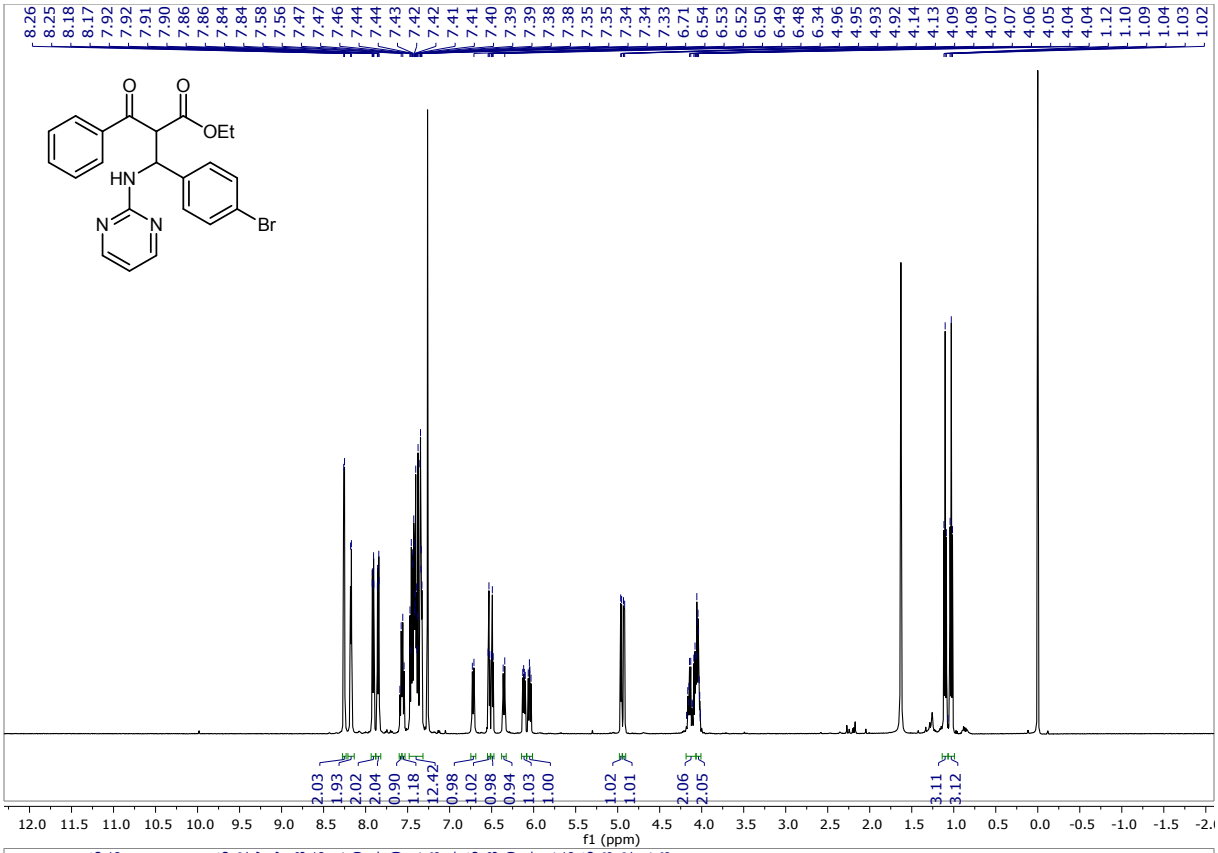


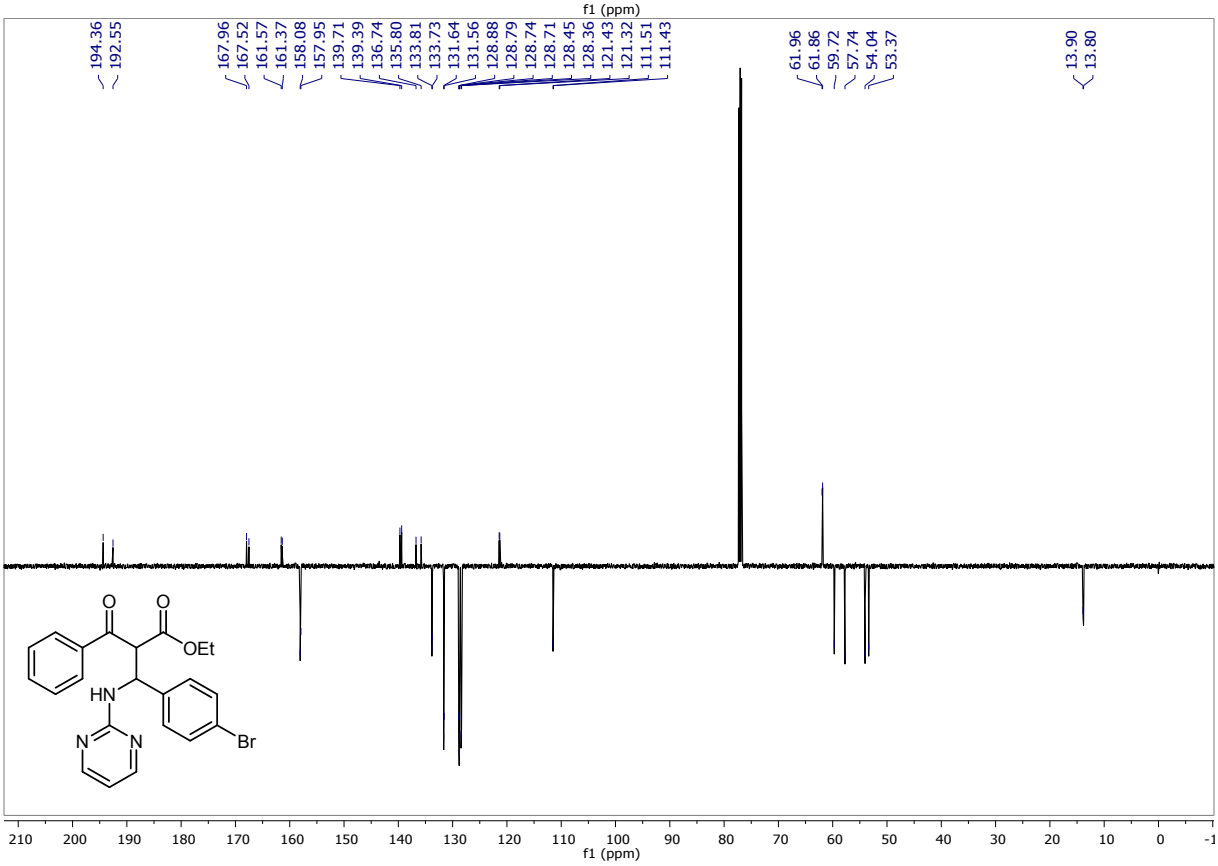
3-(((4-methylpyrimidin-2-yl)amino)(4-(trifluoromethyl)phenyl)methyl)pentane-2,4-dione (1n)



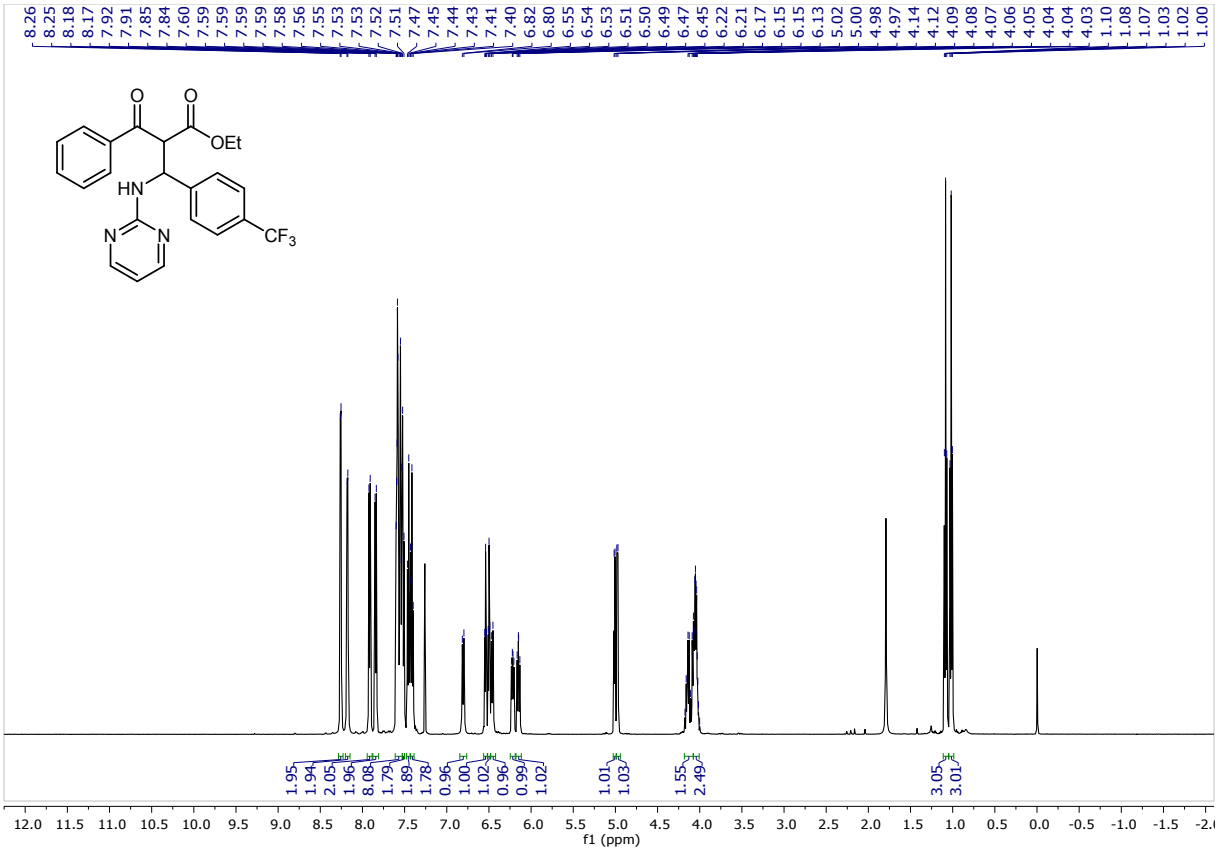


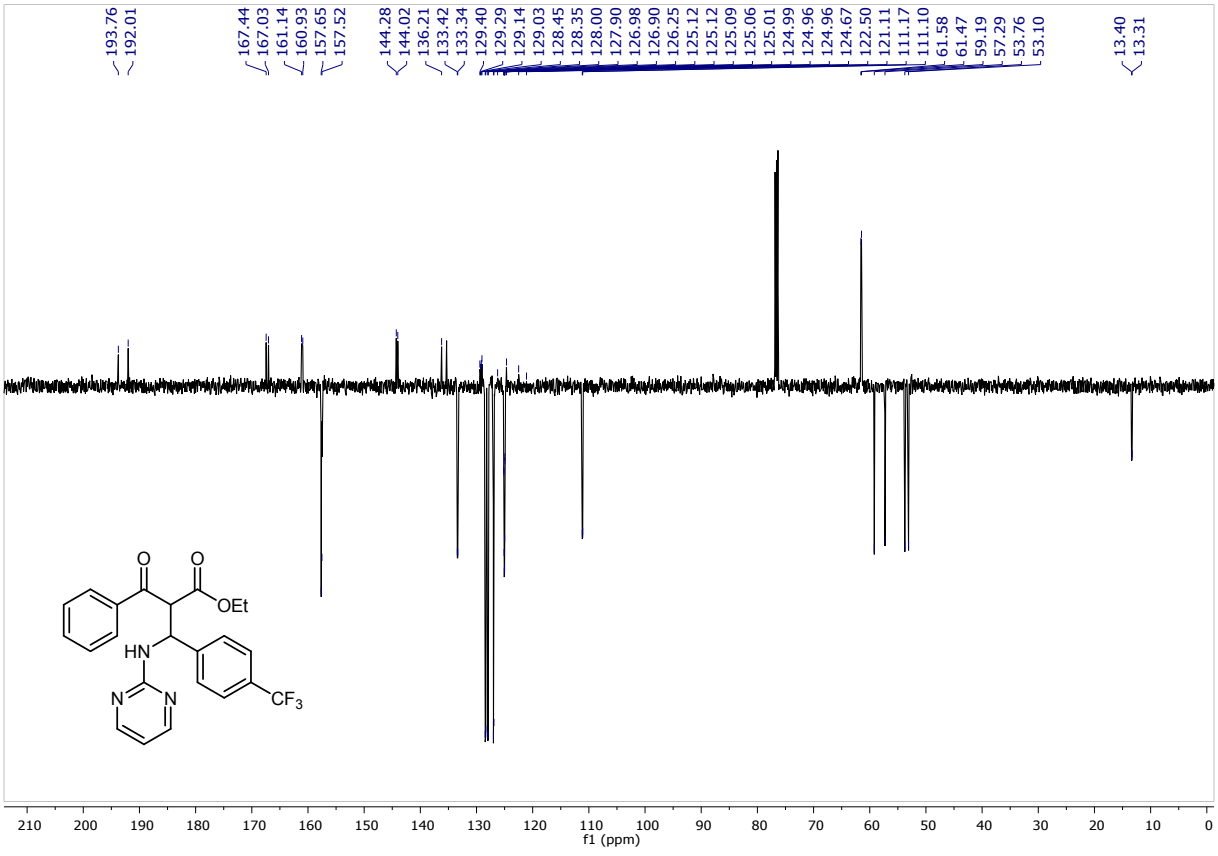
Ethyl 2-benzoyl-3-(4-bromophenyl)-3-(pyrimidin-2-ylamino)propanoate (1o)



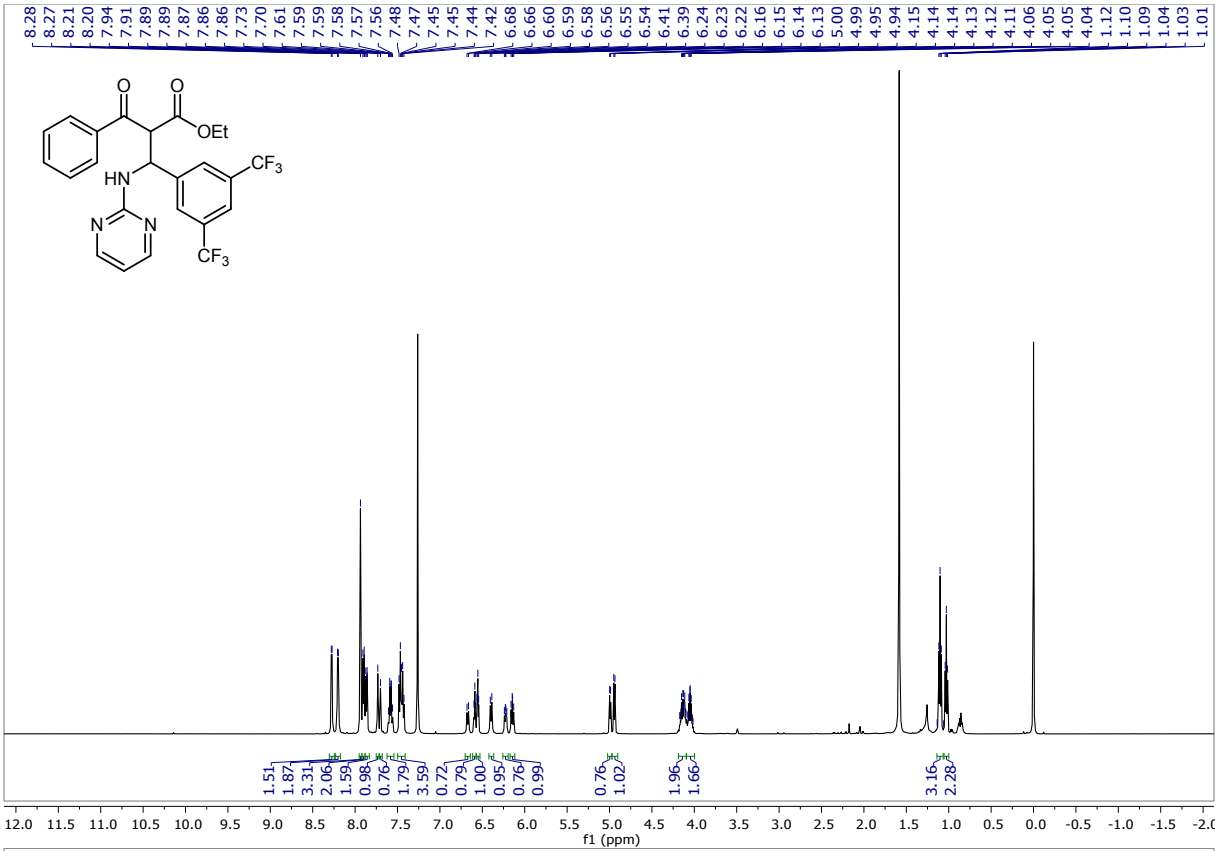


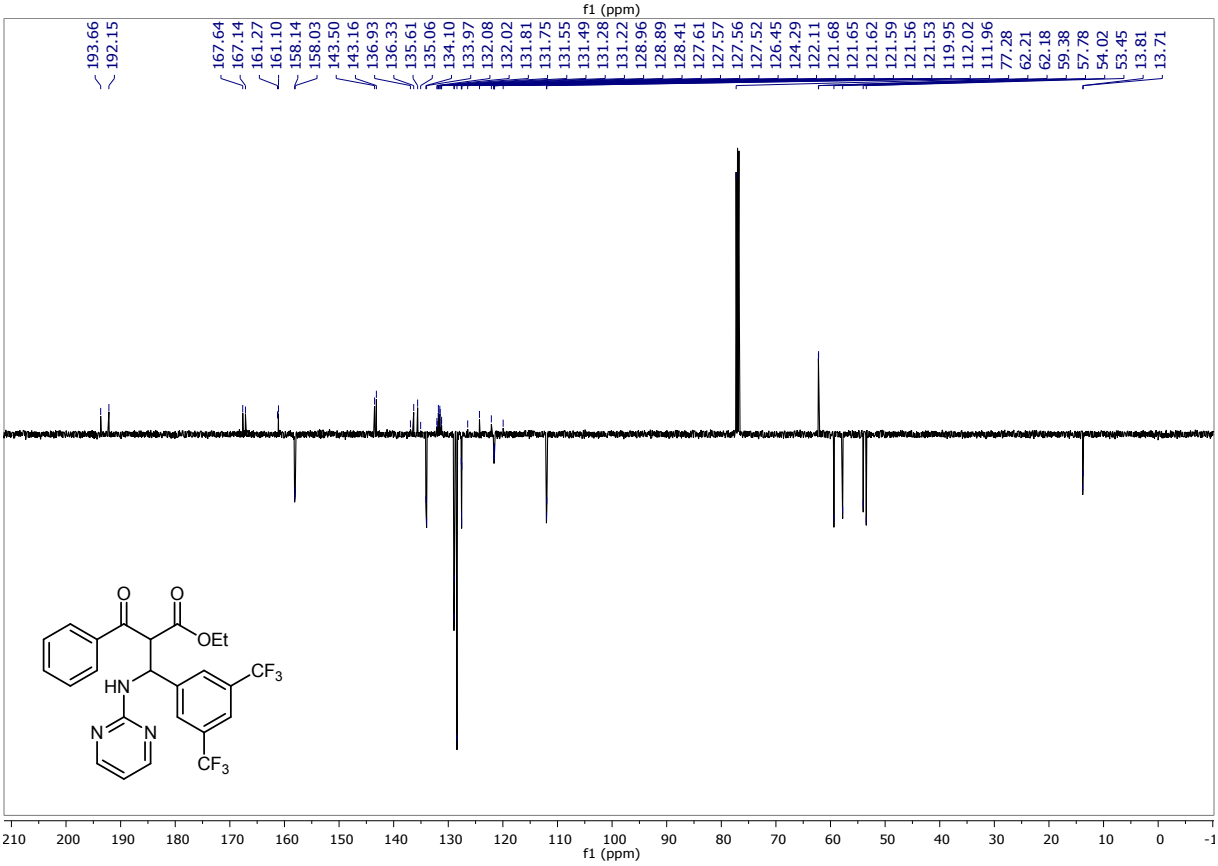
Ethyl 2-benzoyl-3-(pyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1p)



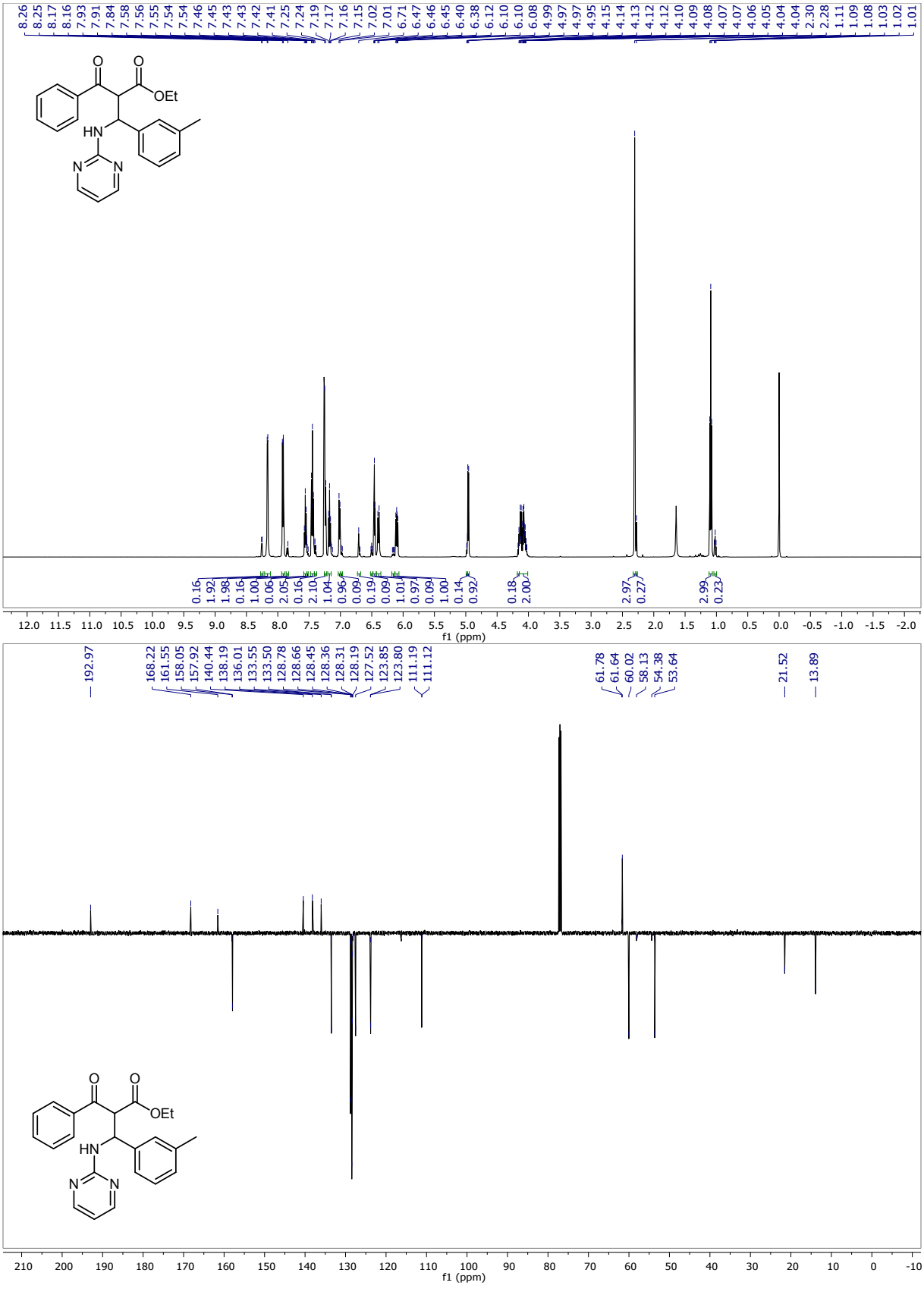


Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyrimidin-2-ylamino)propanoate (1q)

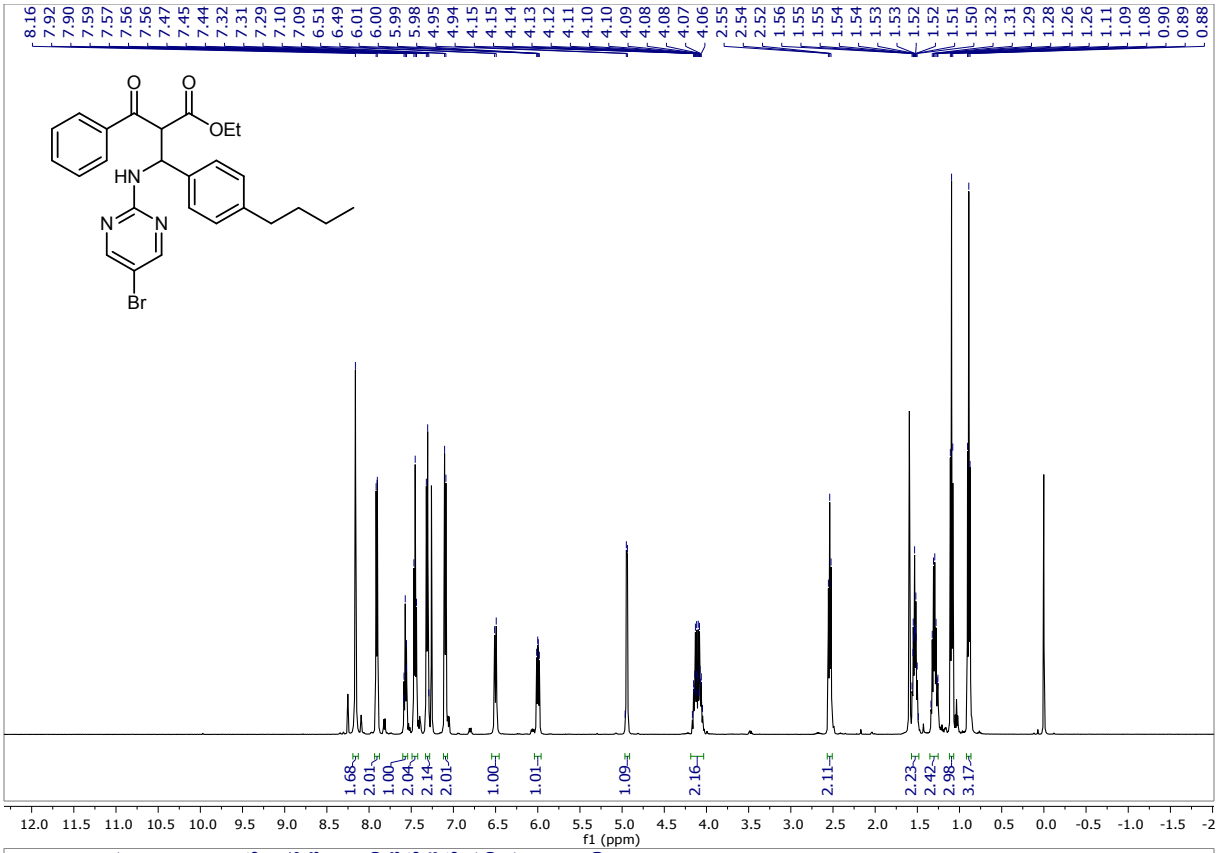


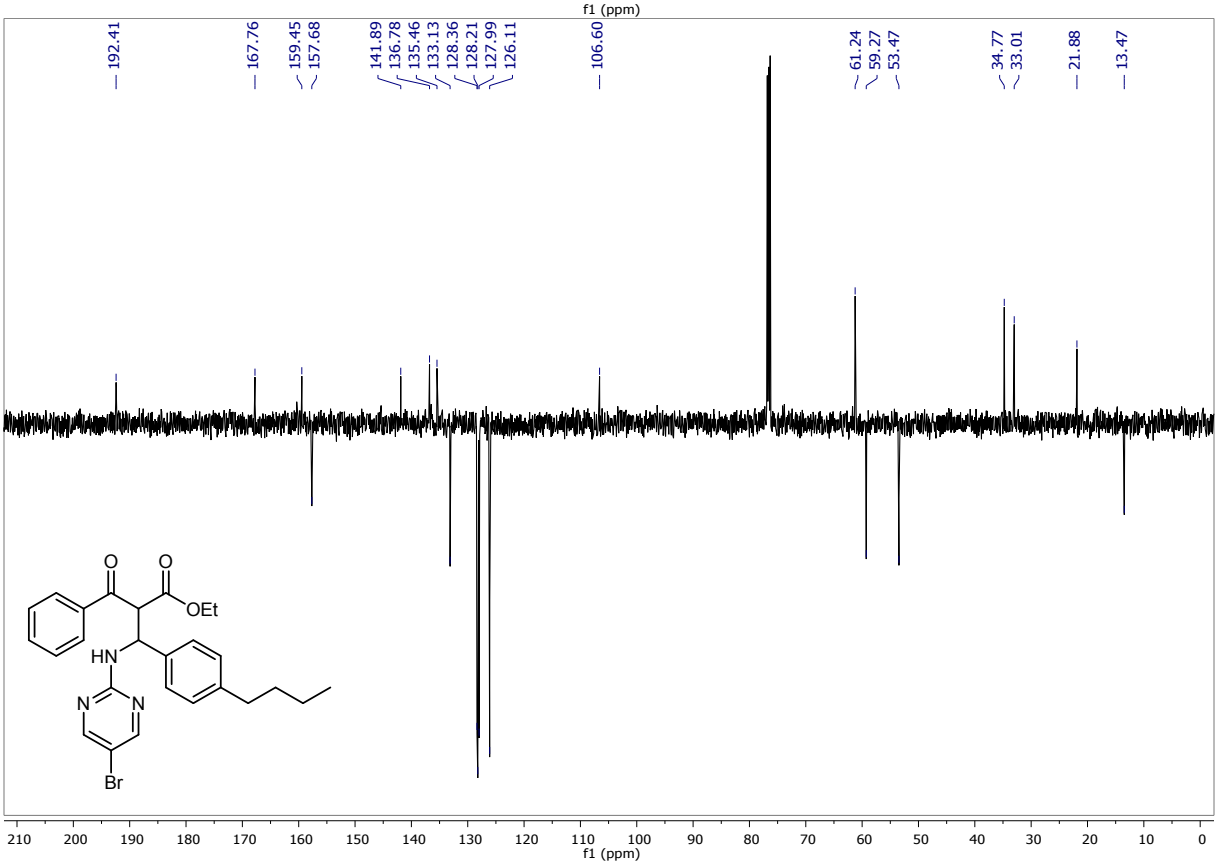


Ethyl 2-benzoyl-3-(pyrimidin-2-ylamino)-3-(m-tolyl)propanoate (1r)

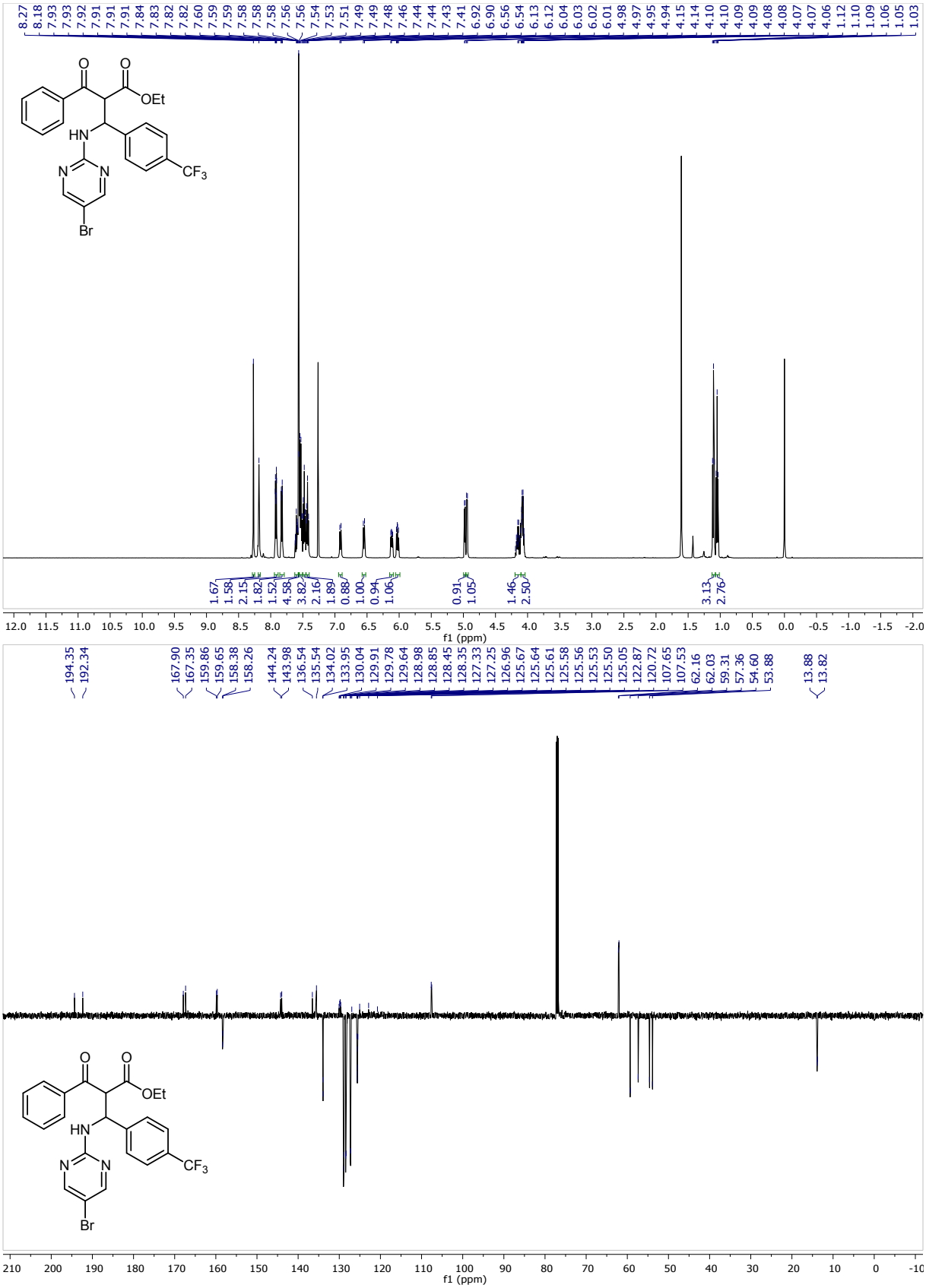


Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-(4-butylphenyl)propanoate (1s)

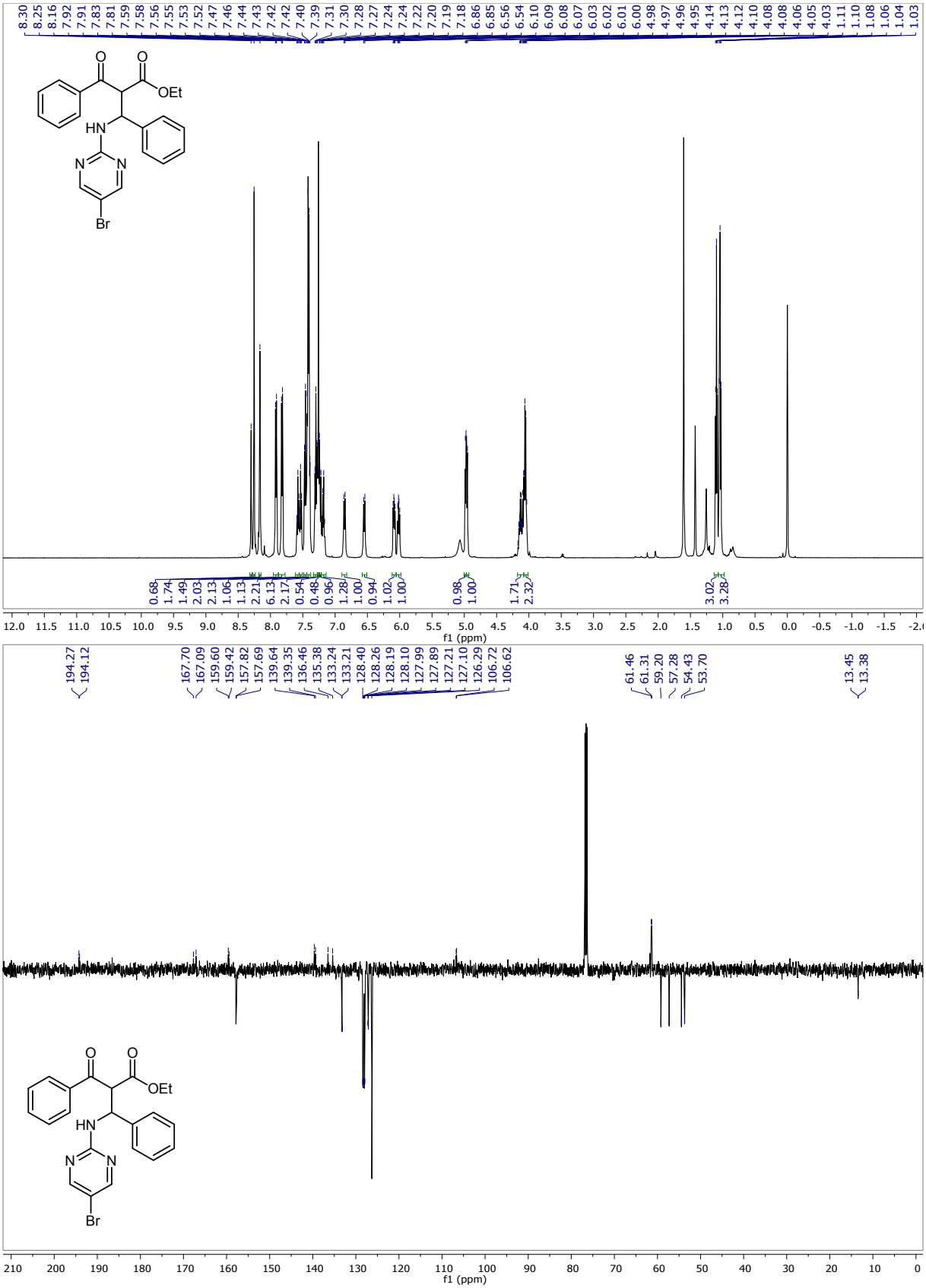




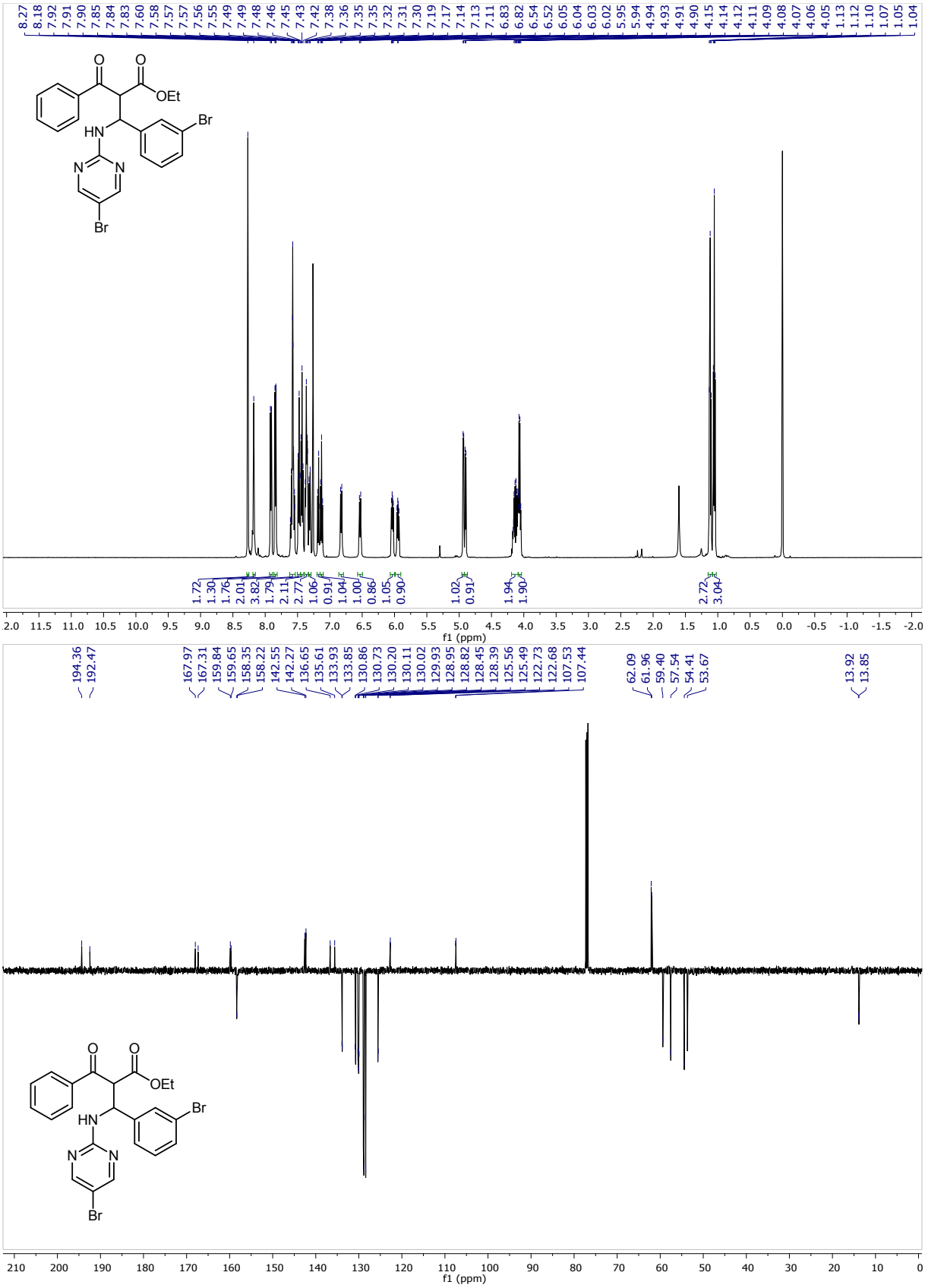
Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-(4-(trifluoromethyl)phenyl)propanoate (1t)



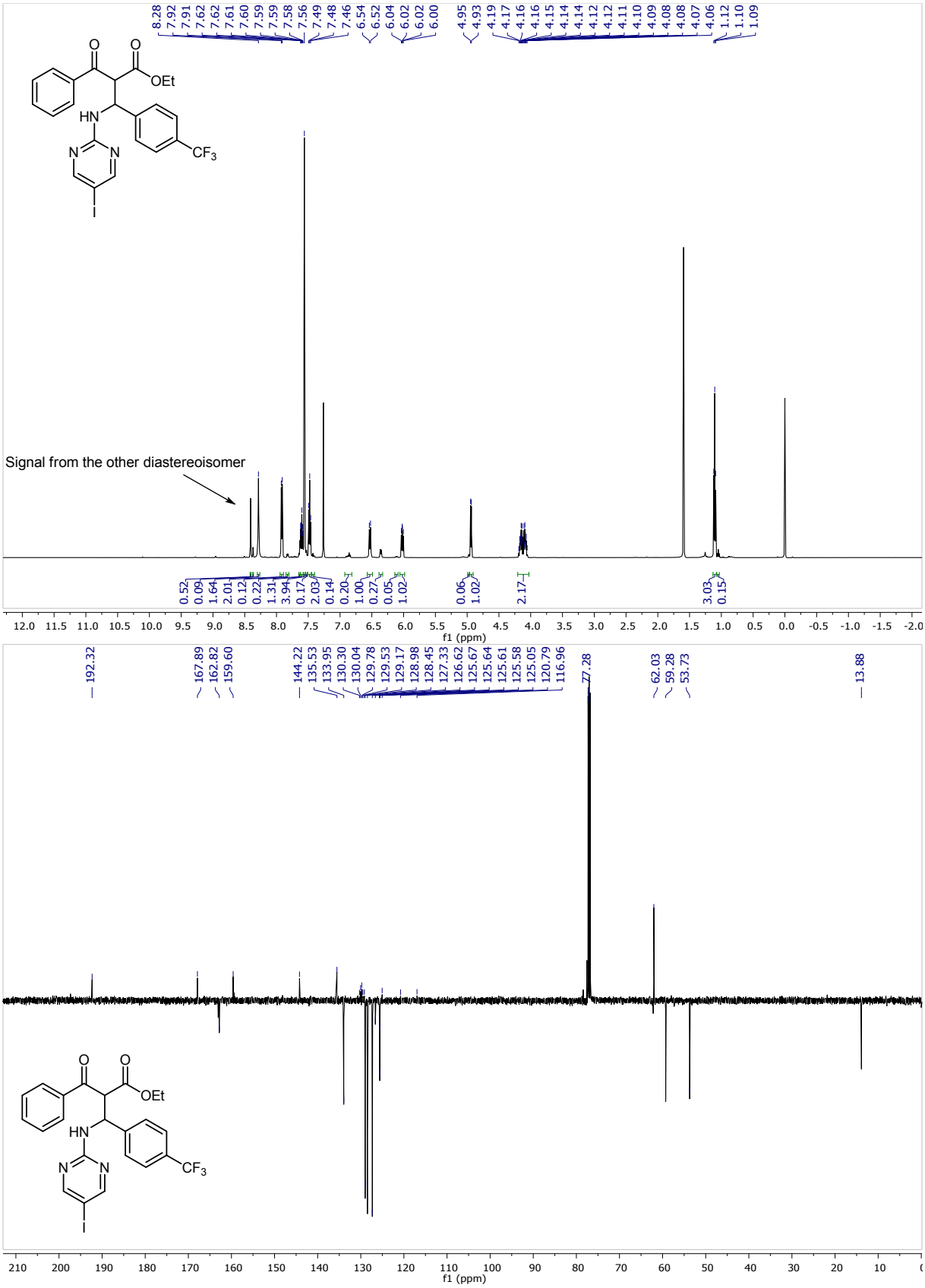
Ethyl 2-benzoyl-3-((5-bromopyrimidin-2-yl)amino)-3-phenylpropanoate (1u)



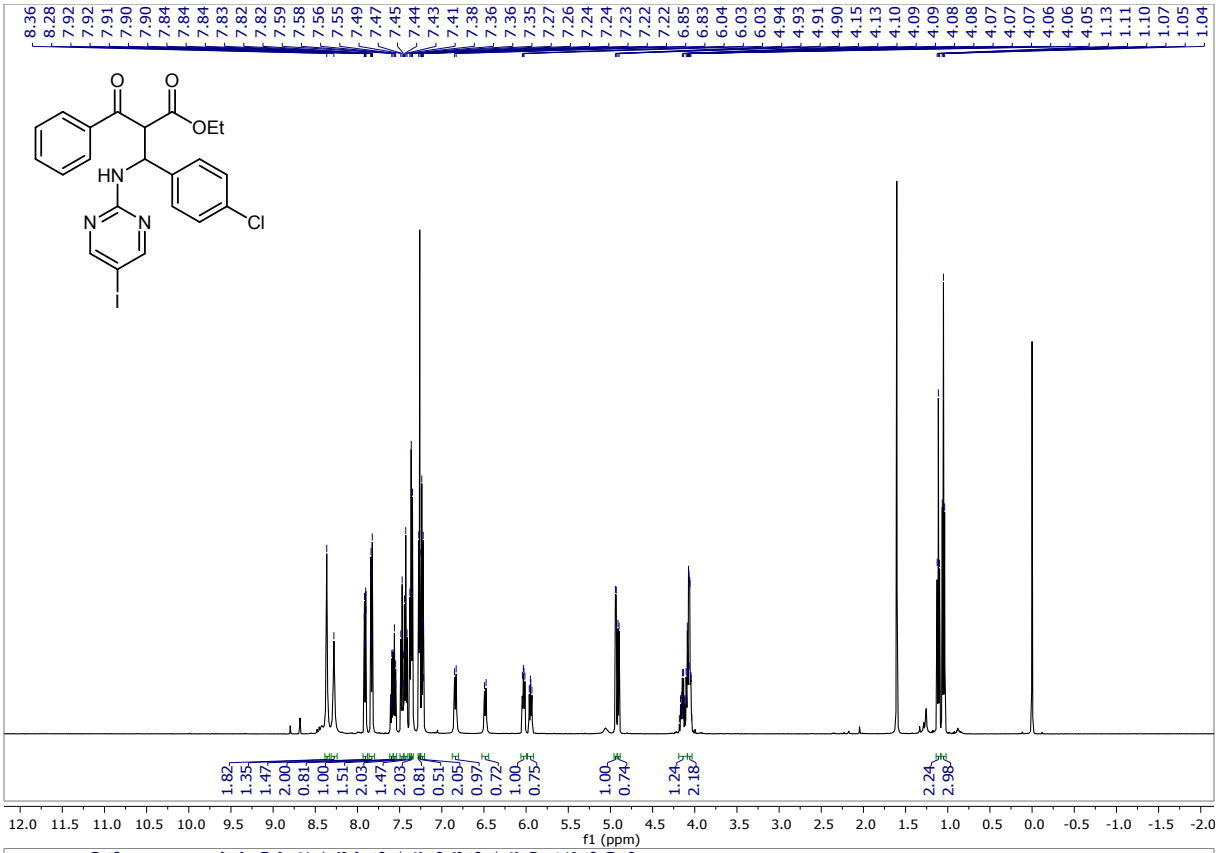
Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-bromopyrimidin-2-yl)amino)propanoate (1v)

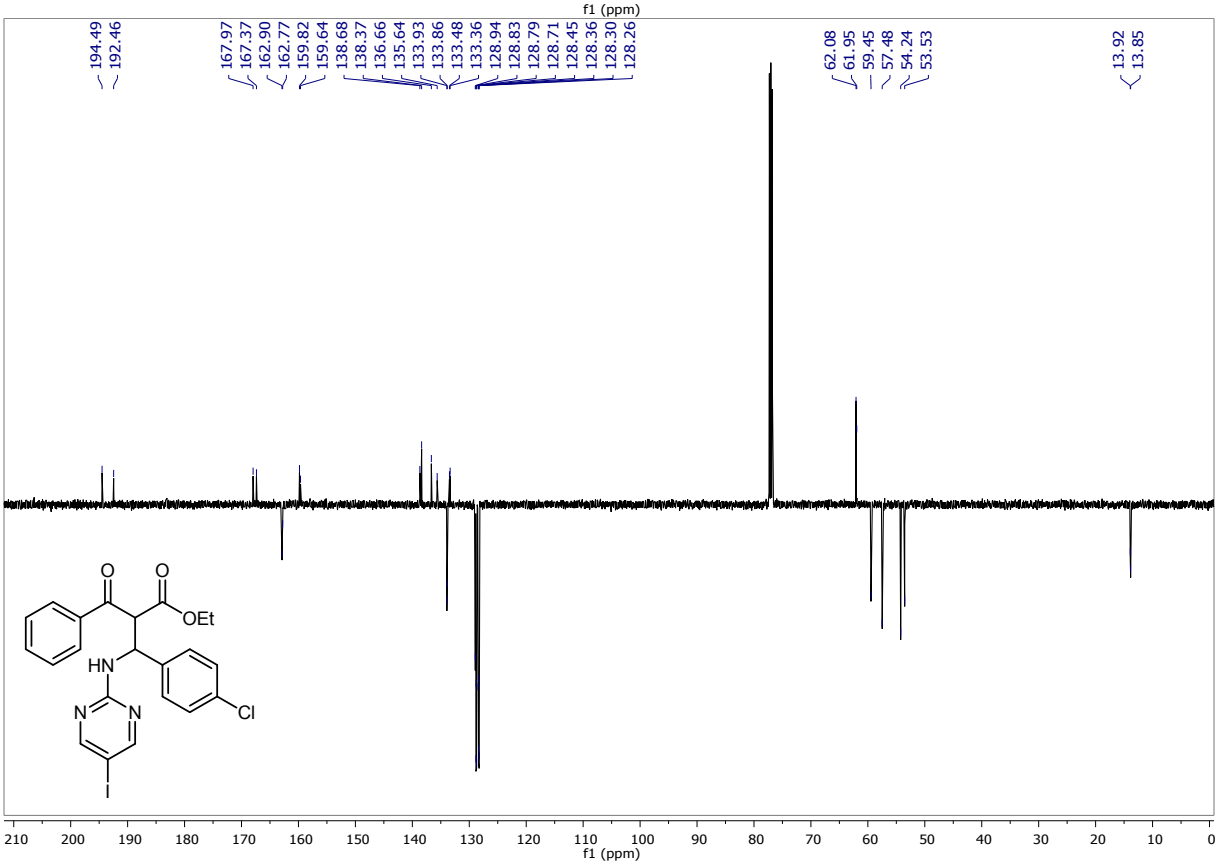


Ethyl 2-benzoyl-3-(5-iodopyrimidin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (1w)

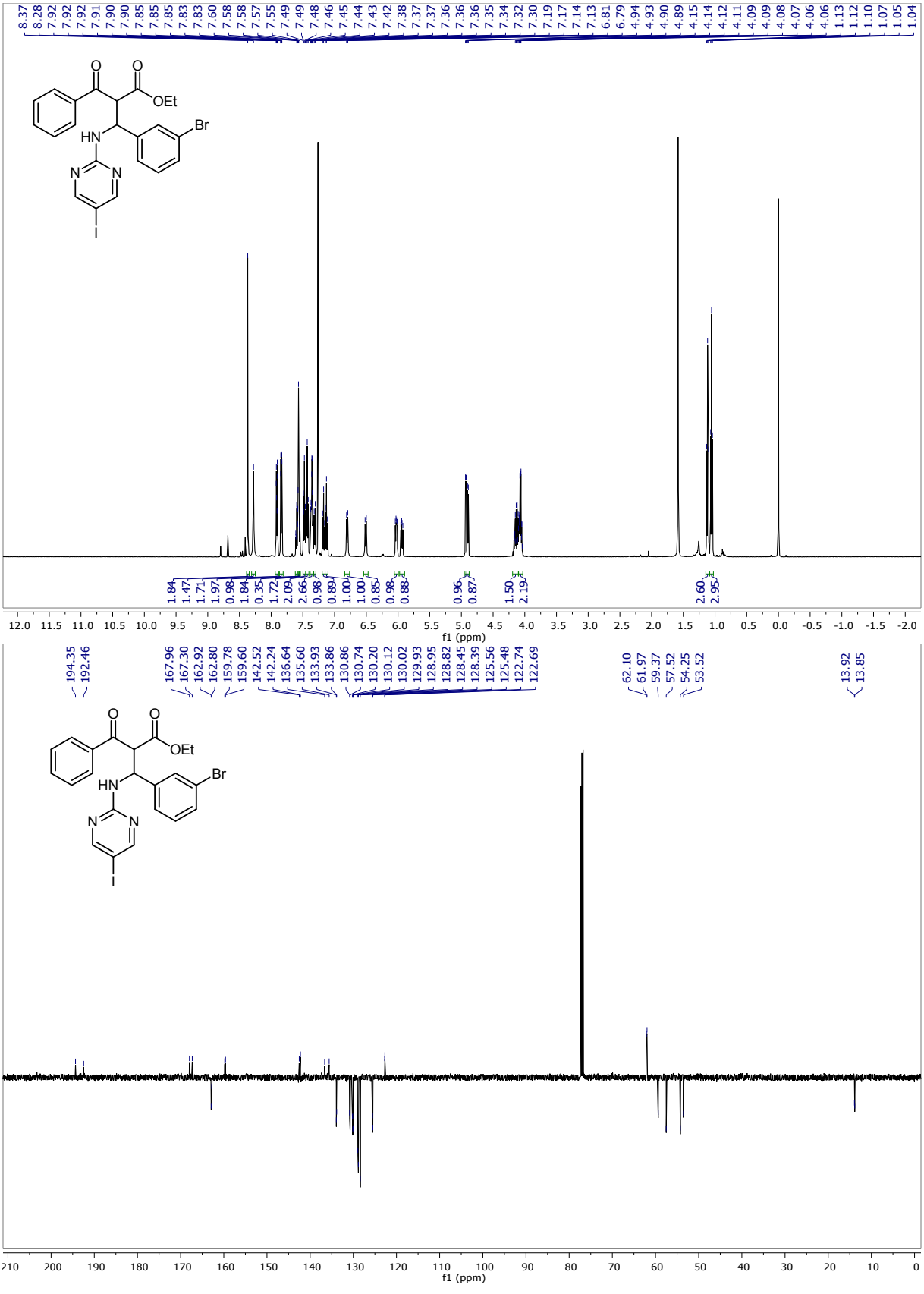


Ethyl 2-benzoyl-3-(4-chlorophenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1x)

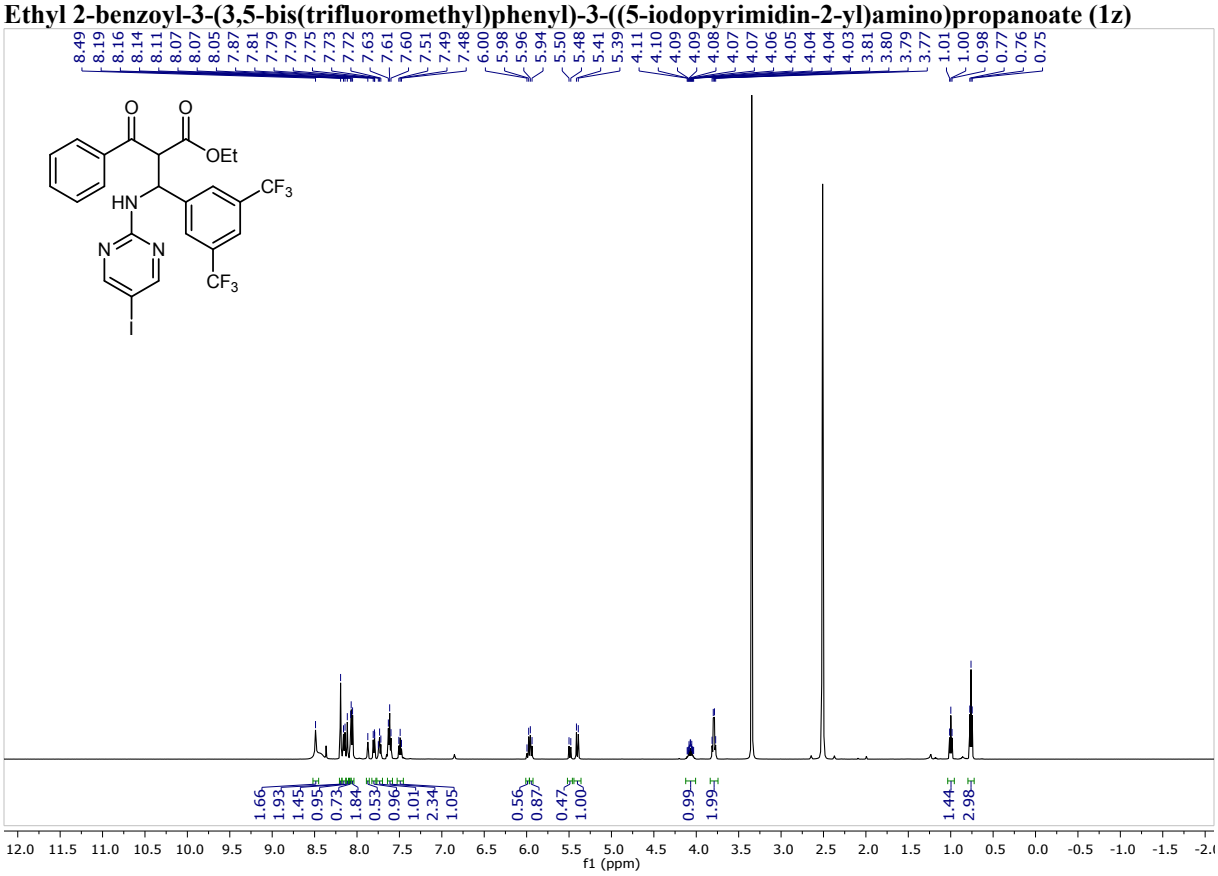


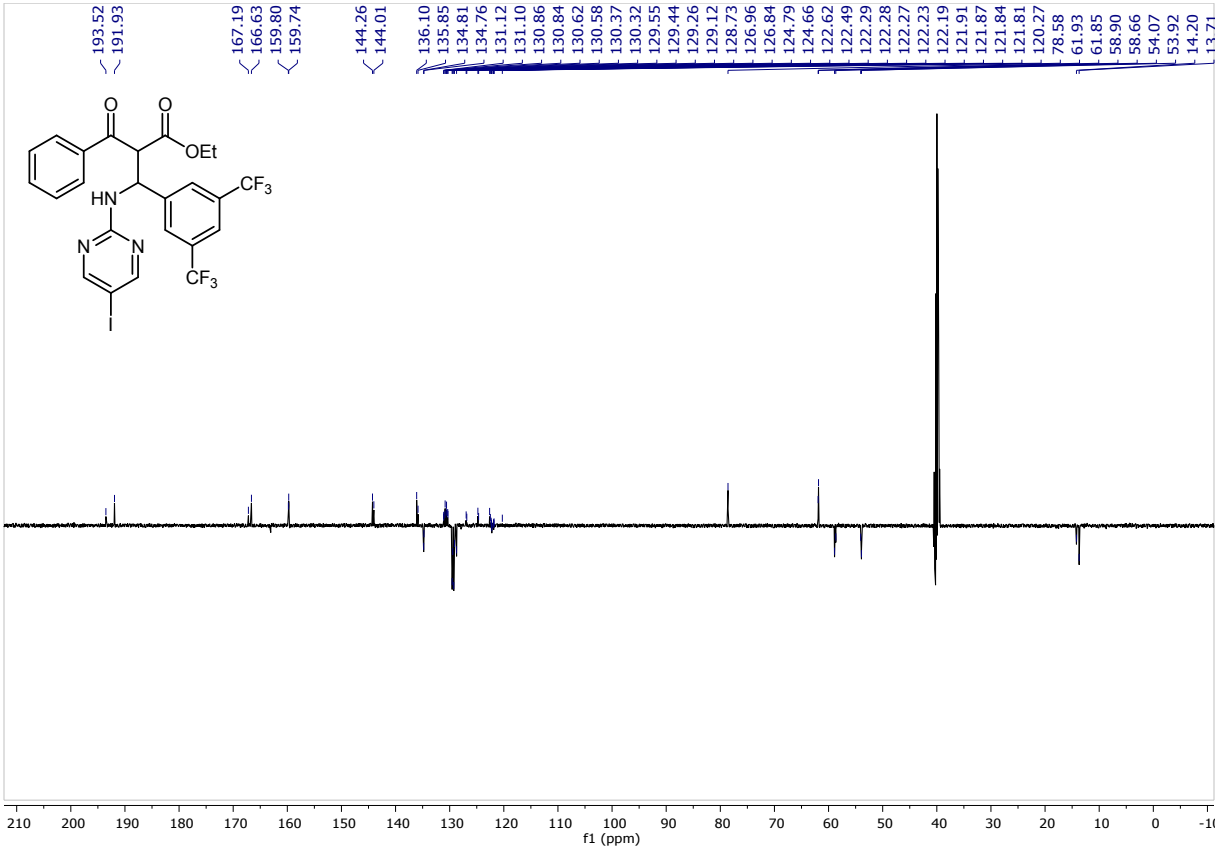


Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1y)

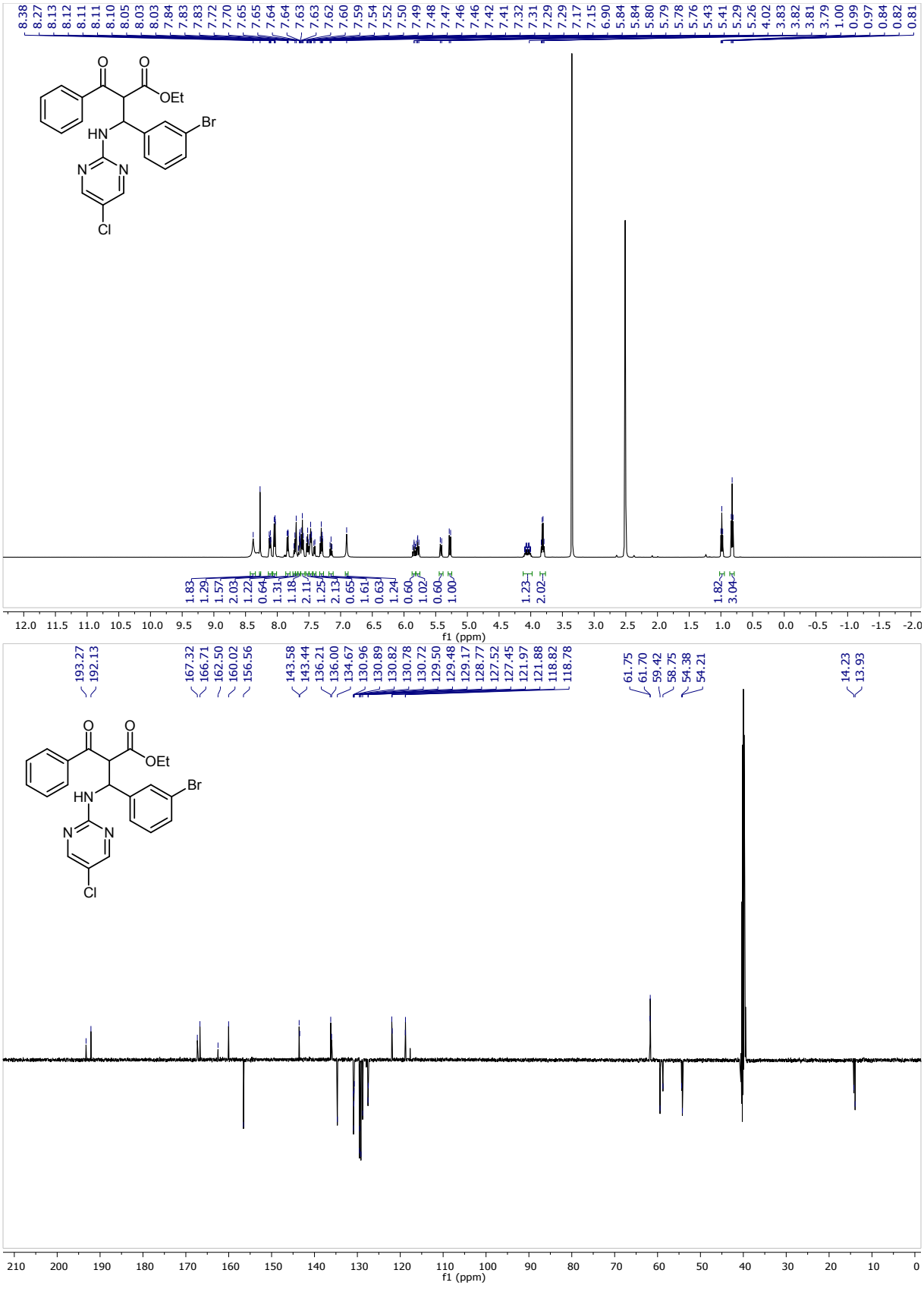


Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-iodopyrimidin-2-yl)amino)propanoate (1z)

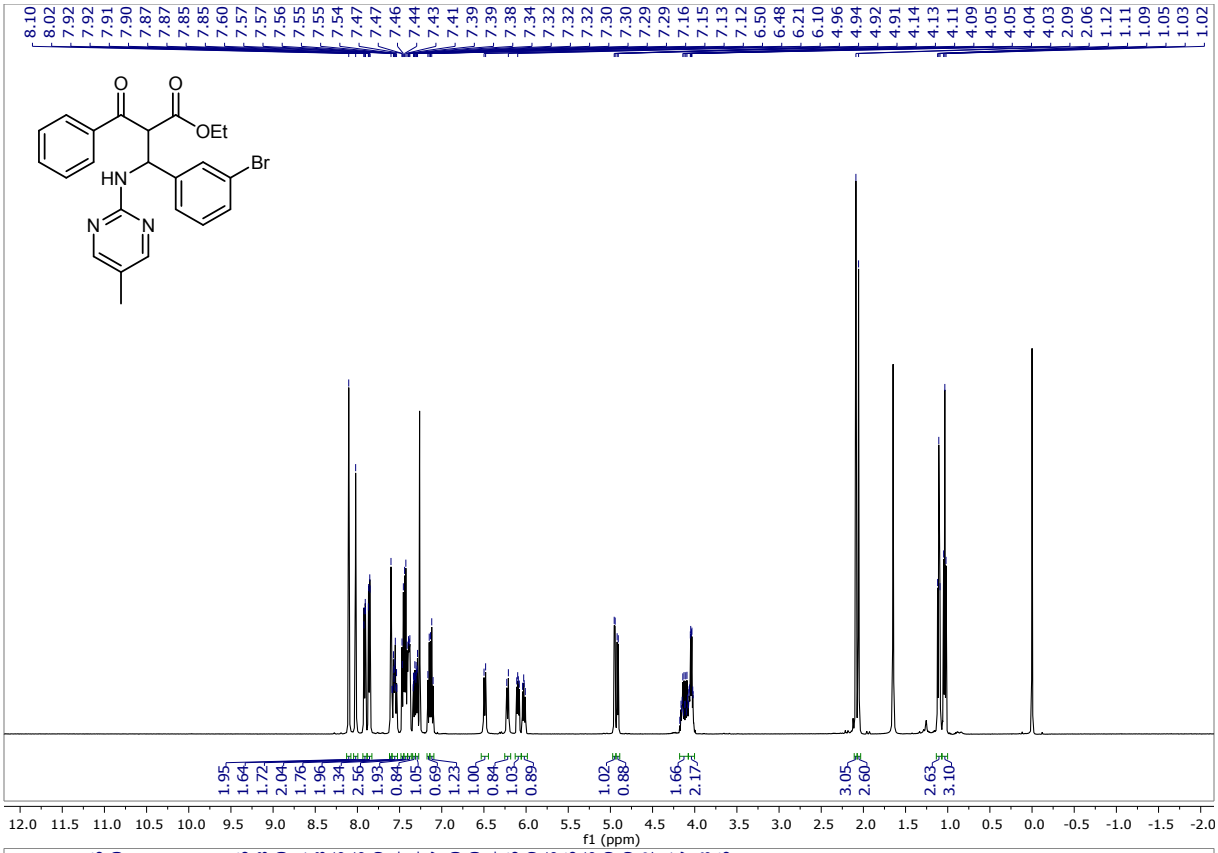


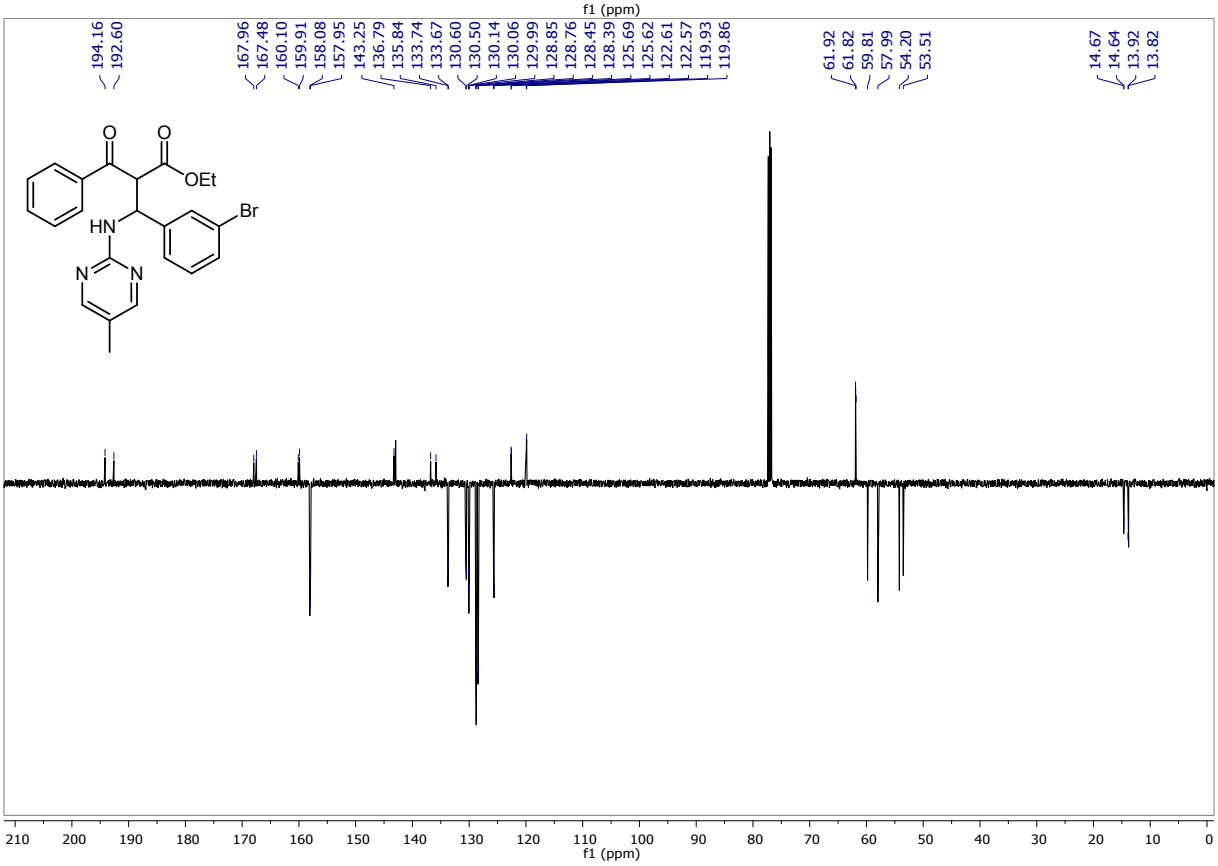


Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-chloropyrimidin-2-yl)amino)propanoate (1aa)

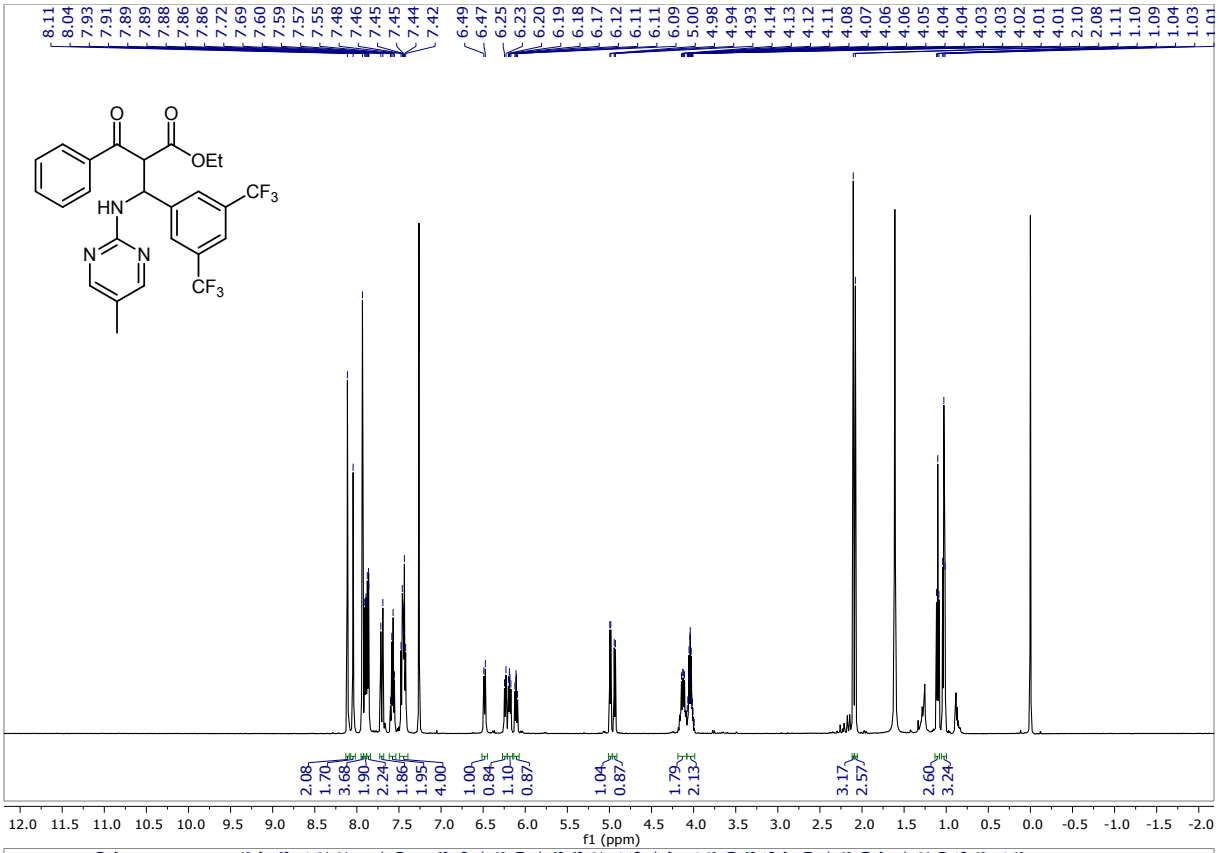


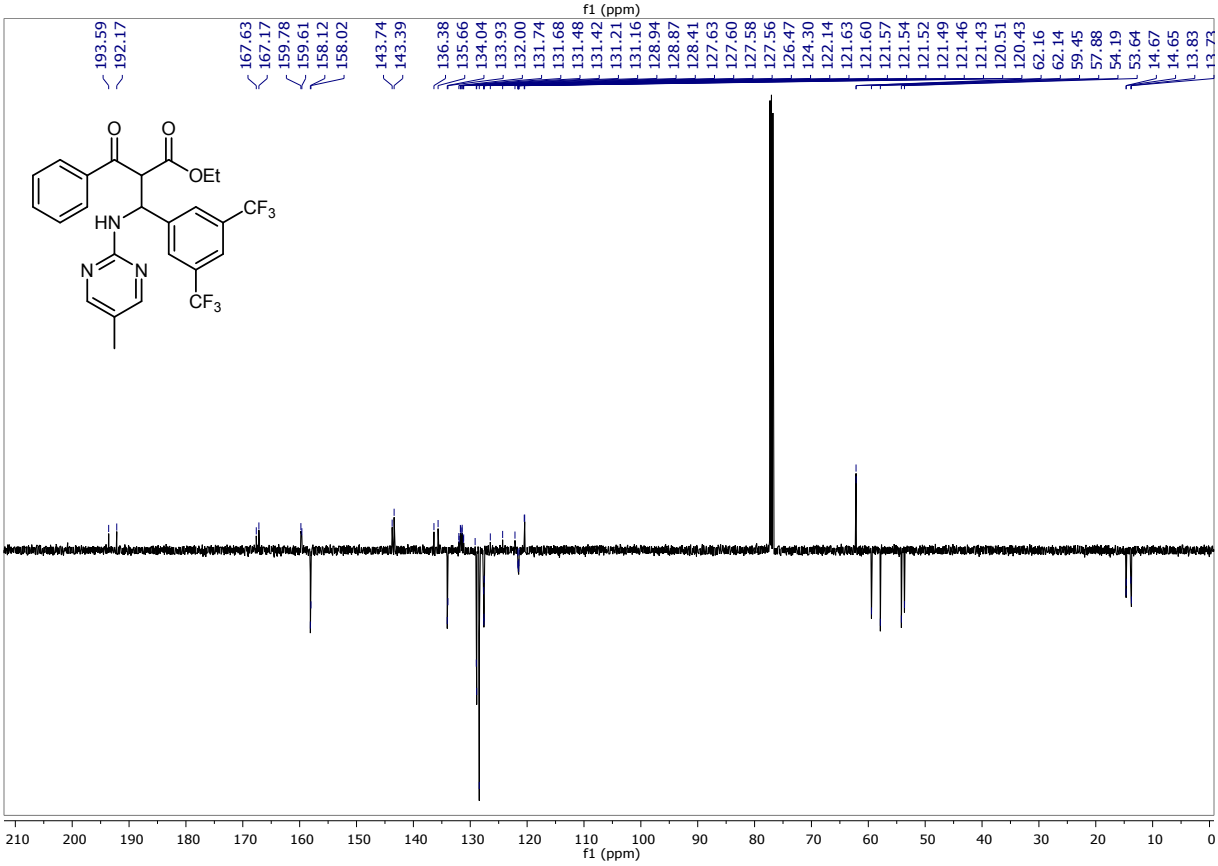
Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-methylpyrimidin-2-yl)amino)propanoate (1bb)



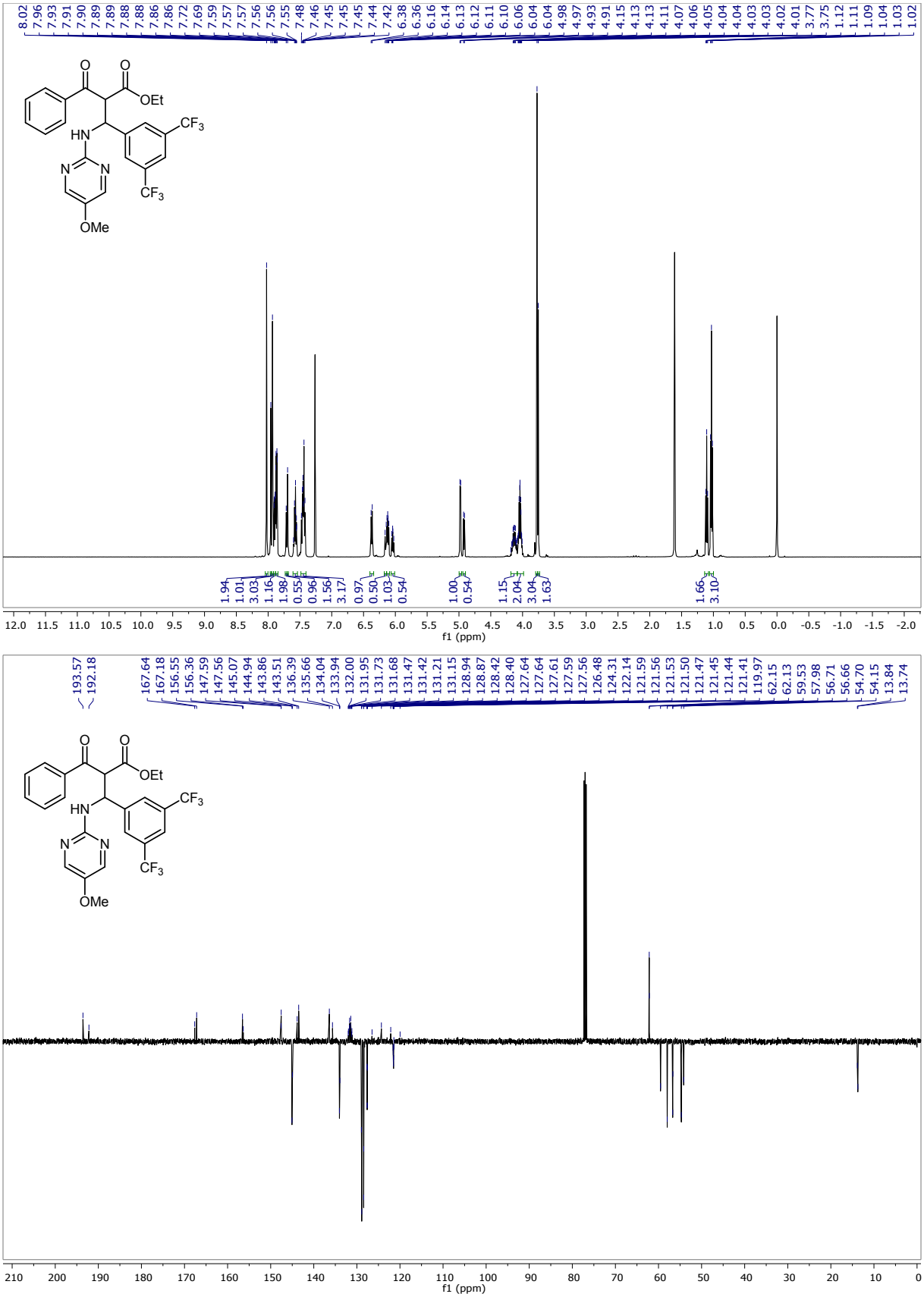


Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-methylpyrimidin-2-yl)amino)propanoate (1cc)

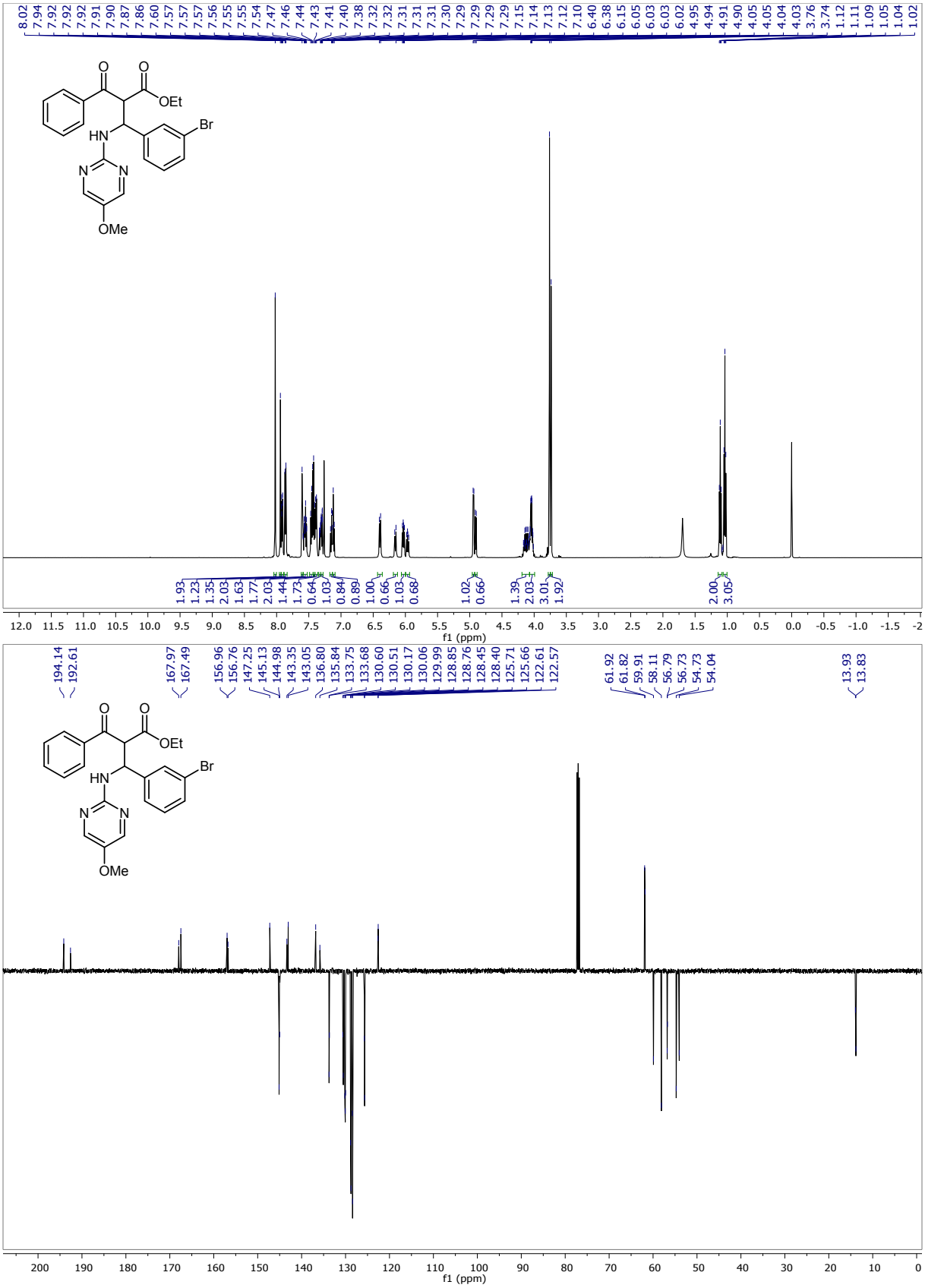




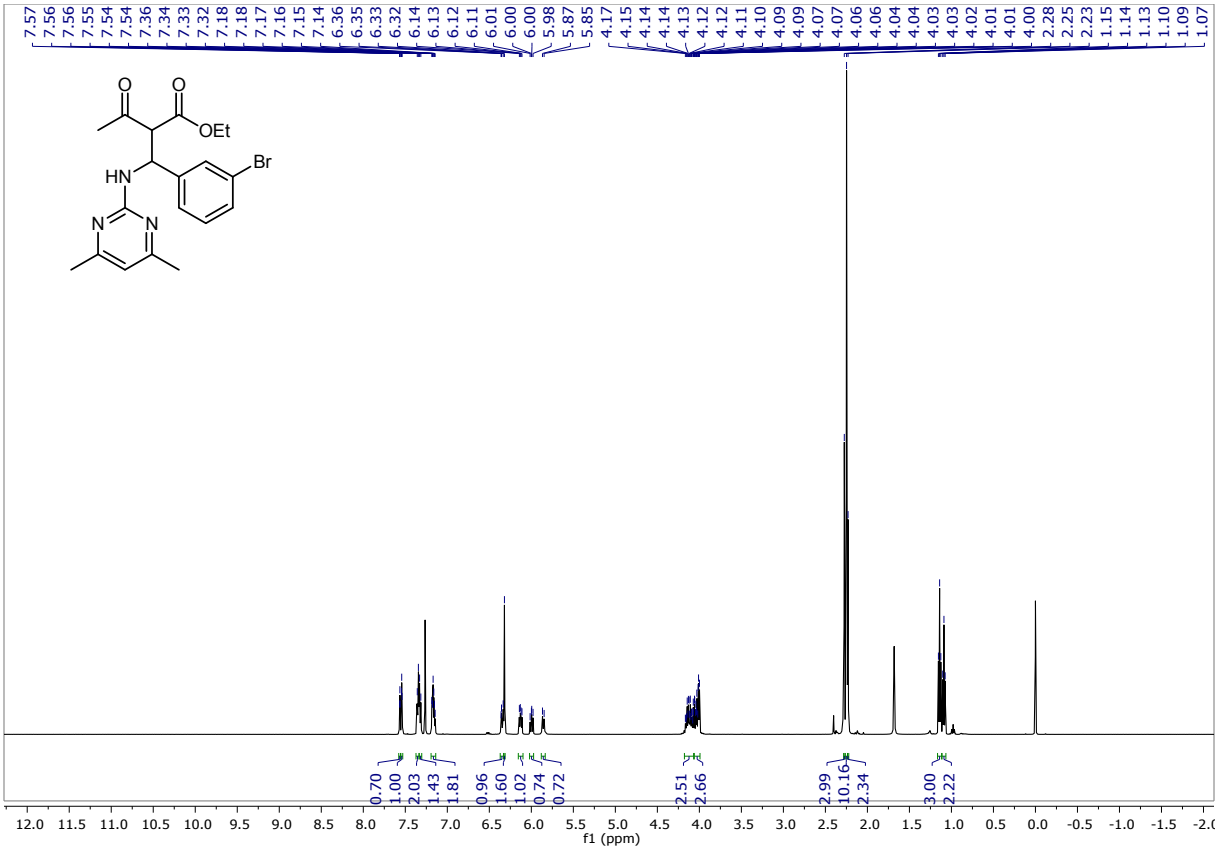
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((5-methoxypyrimidin-2-yl)amino)propanoate (1dd)

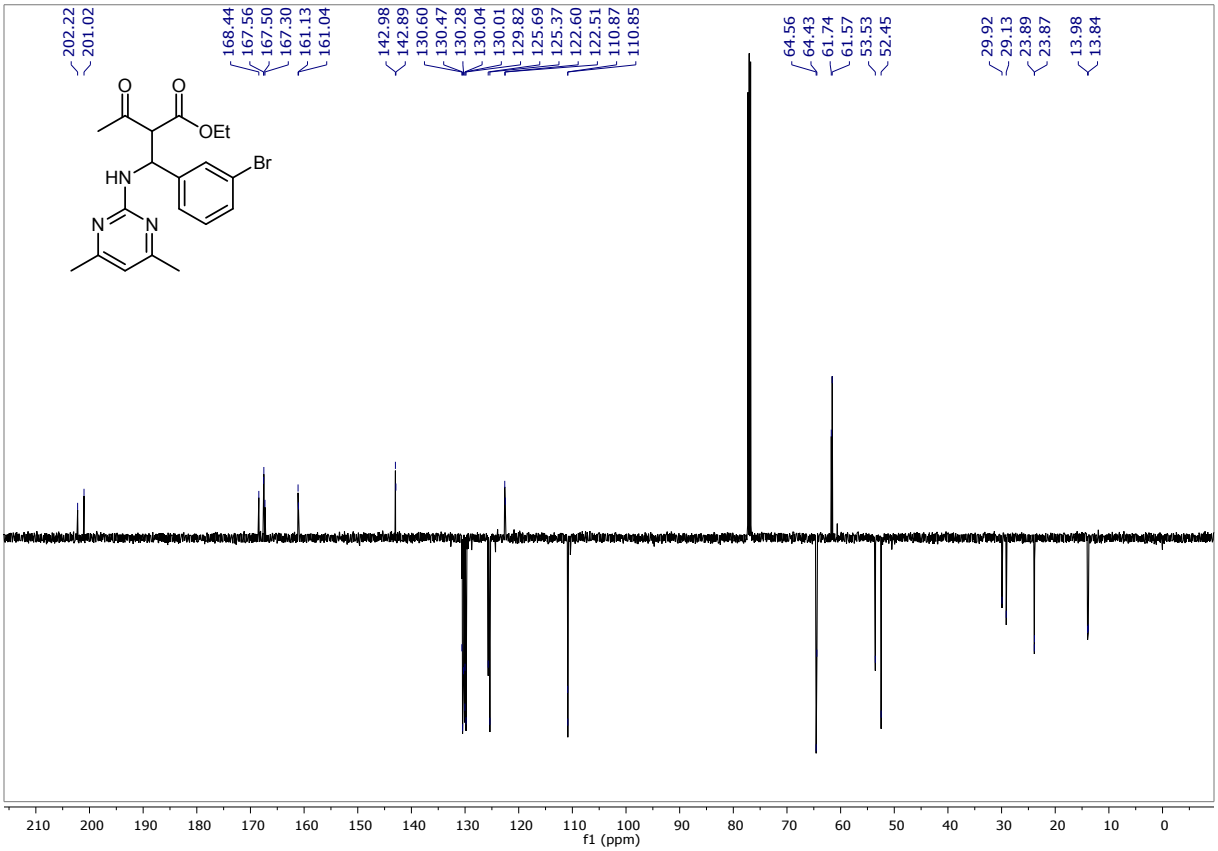


Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-methoxypyrimidin-2-yl)amino)propanoate (1ee)

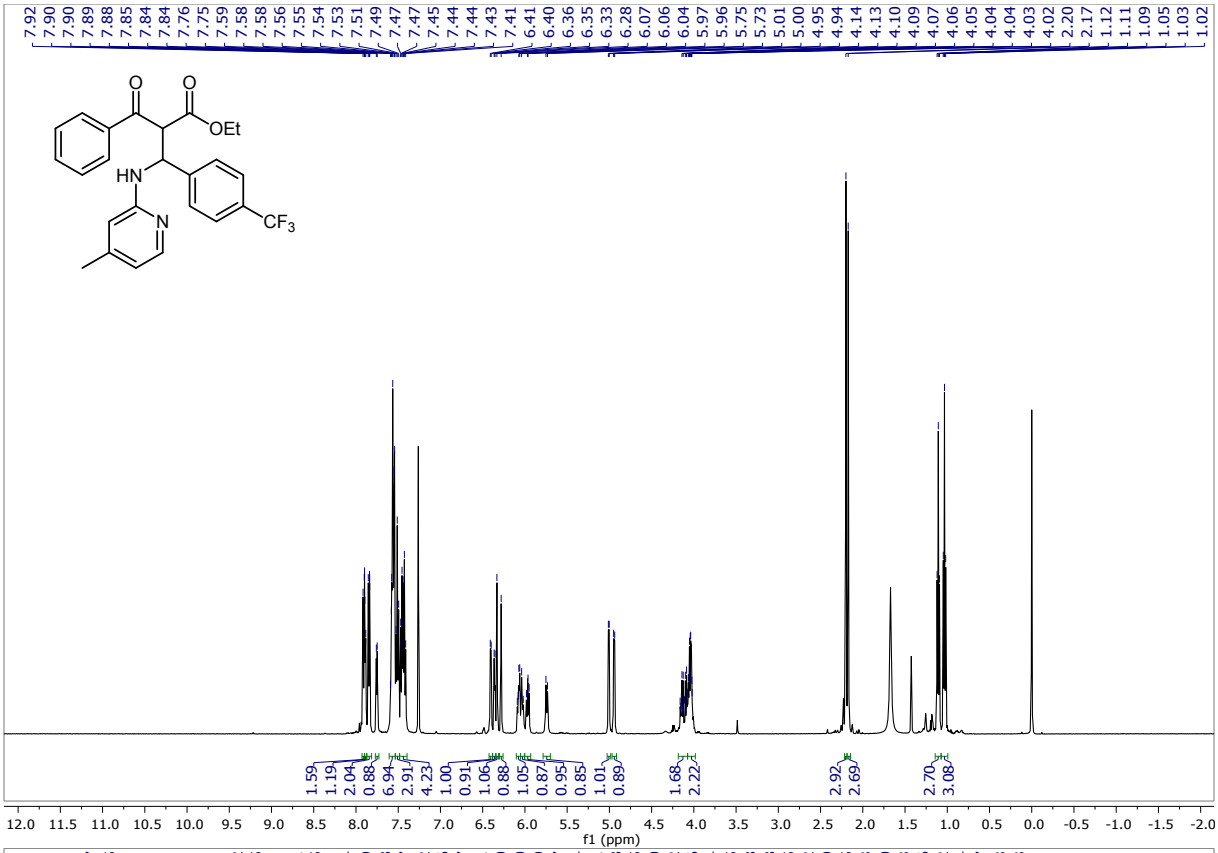


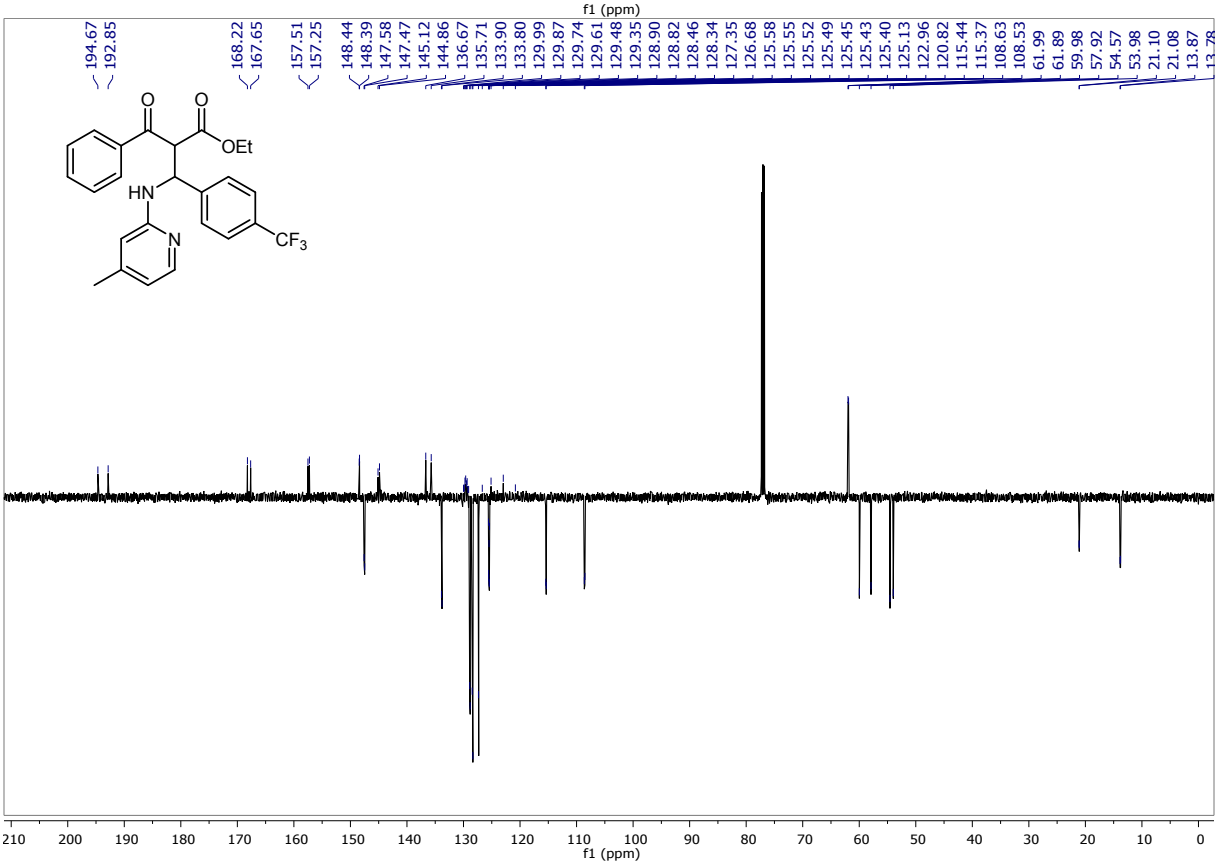
Ethyl 2-((3-bromophenyl)((4,6-dimethylpyrimidin-2-yl)amino)methyl)-3-oxobutanoate (1gg)



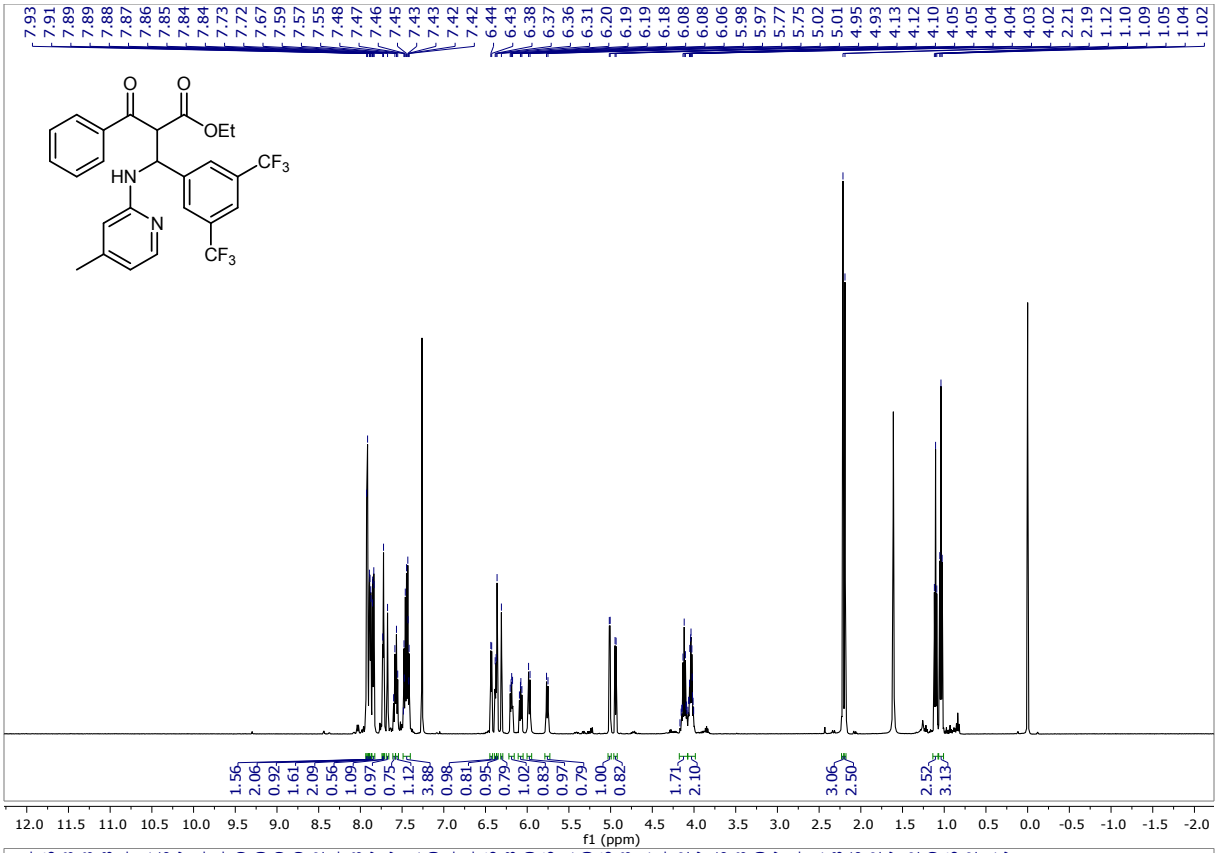


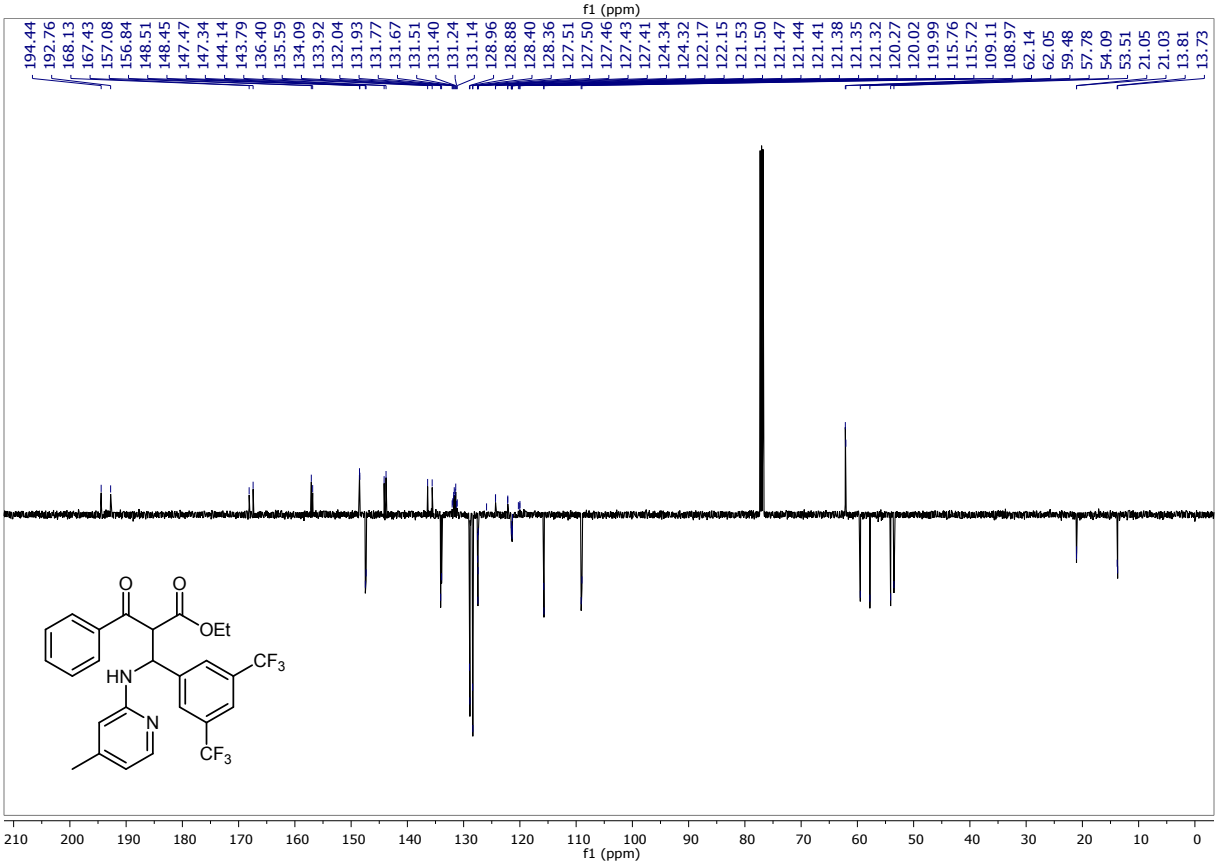
Ethyl 2-benzoyl-3-((4-methylpyridin-2-yl)amino)-3-(4-(trifluoromethyl)phenyl)propanoate (4a)



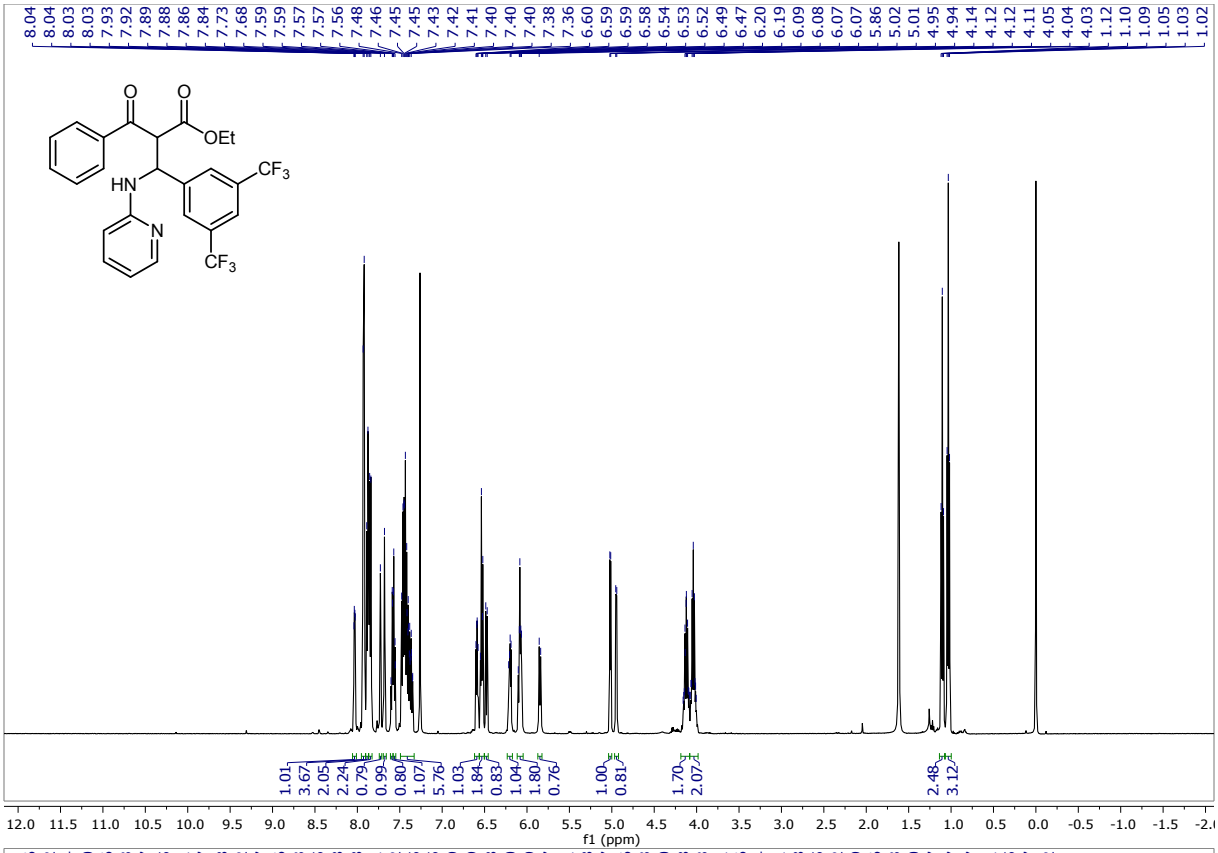


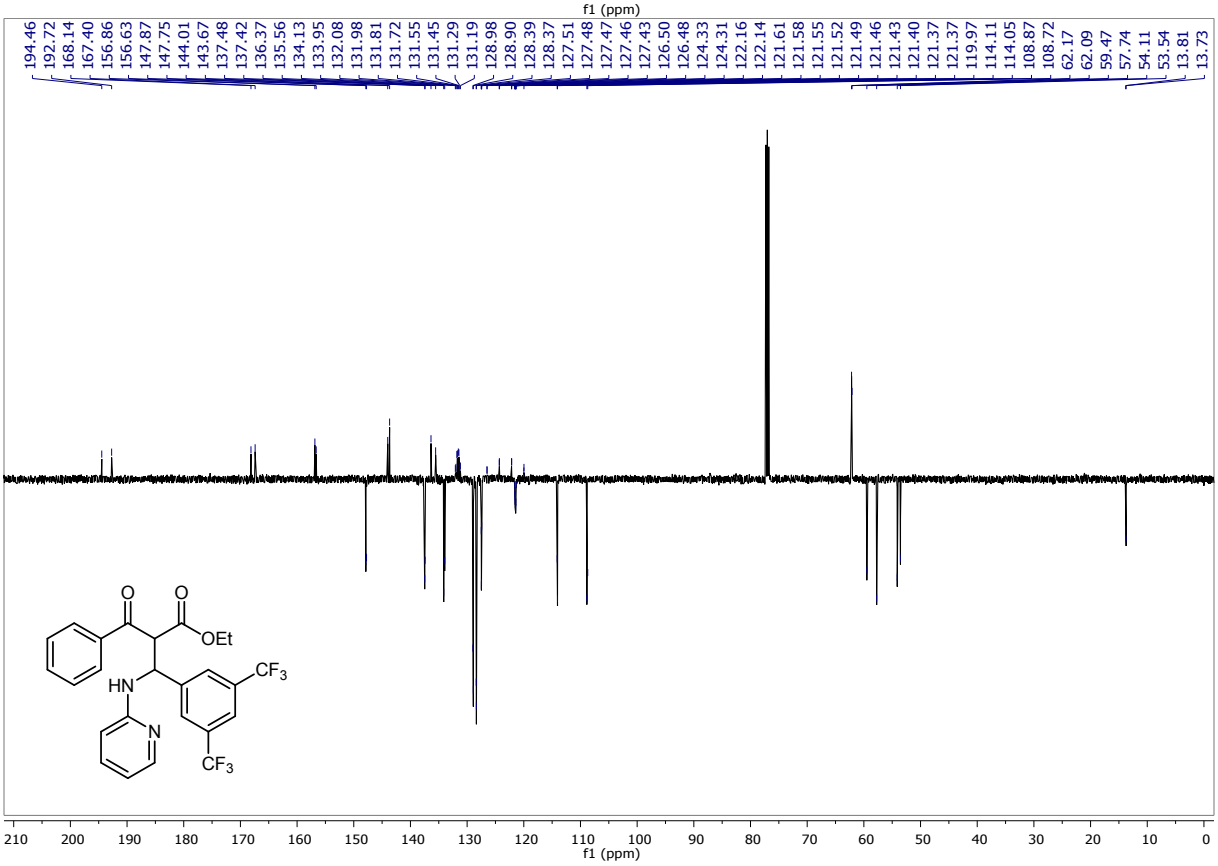
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-((4-methylpyridin-2-yl)amino)propanoate (4b)



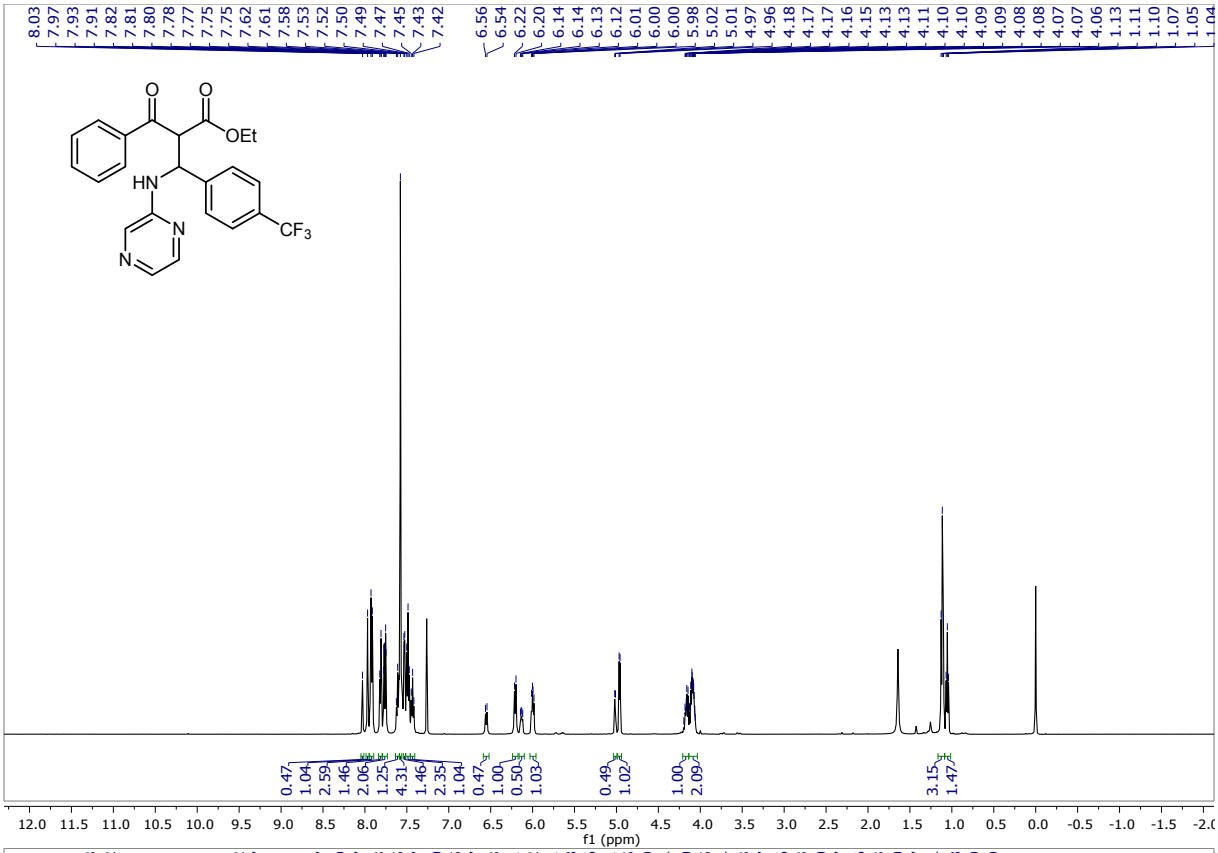


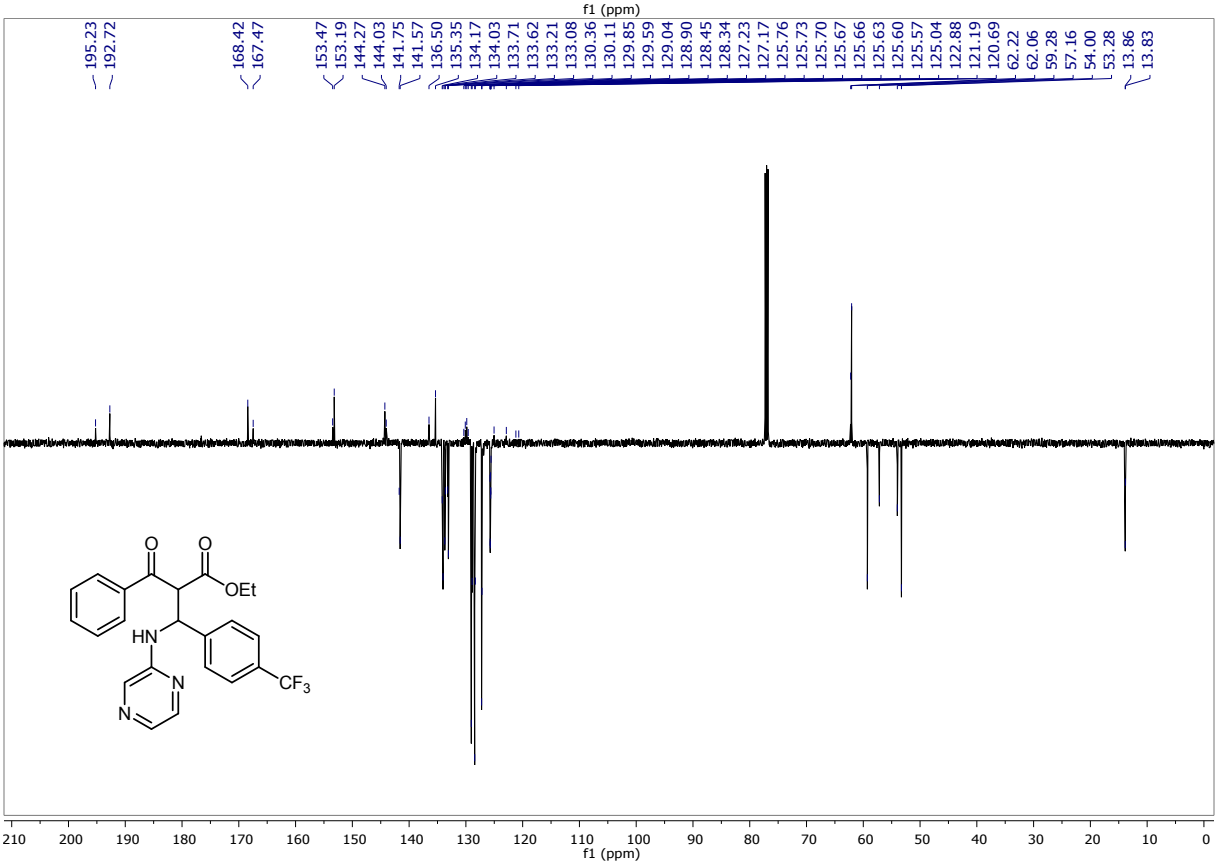
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyridin-2-ylamino)propanoate (4d)



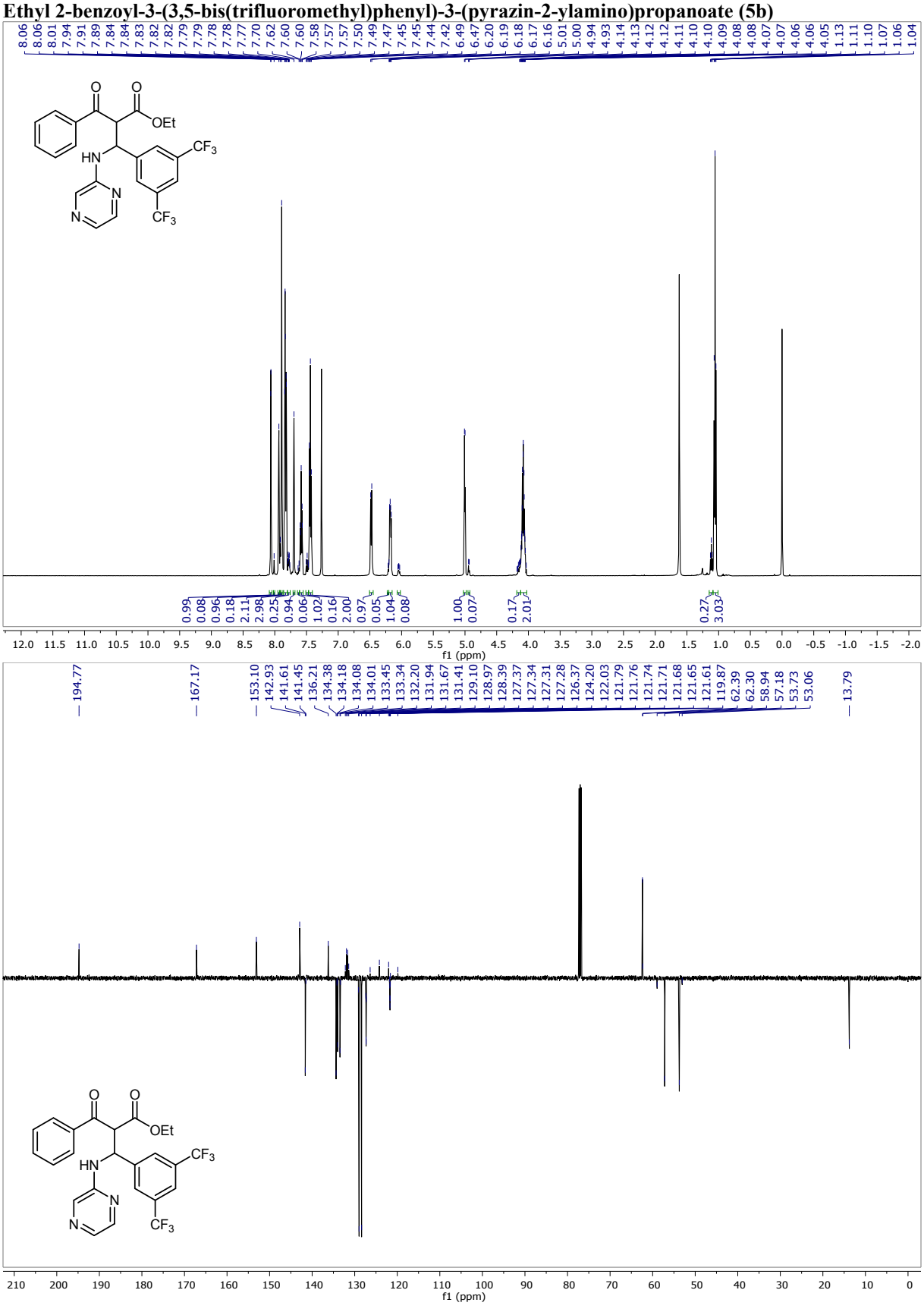


Ethyl 2-benzoyl-3-(pyrazin-2-ylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (5a)

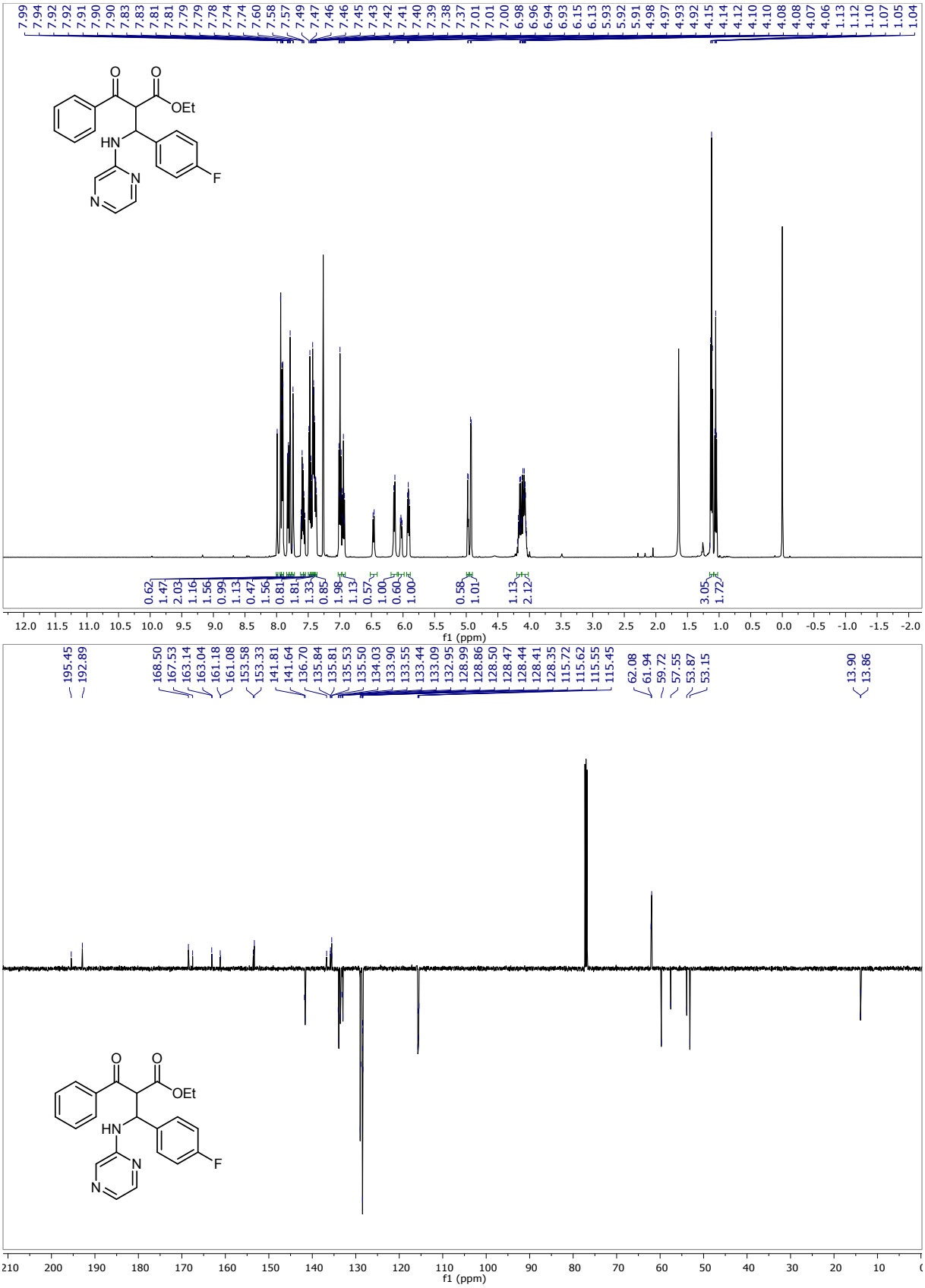




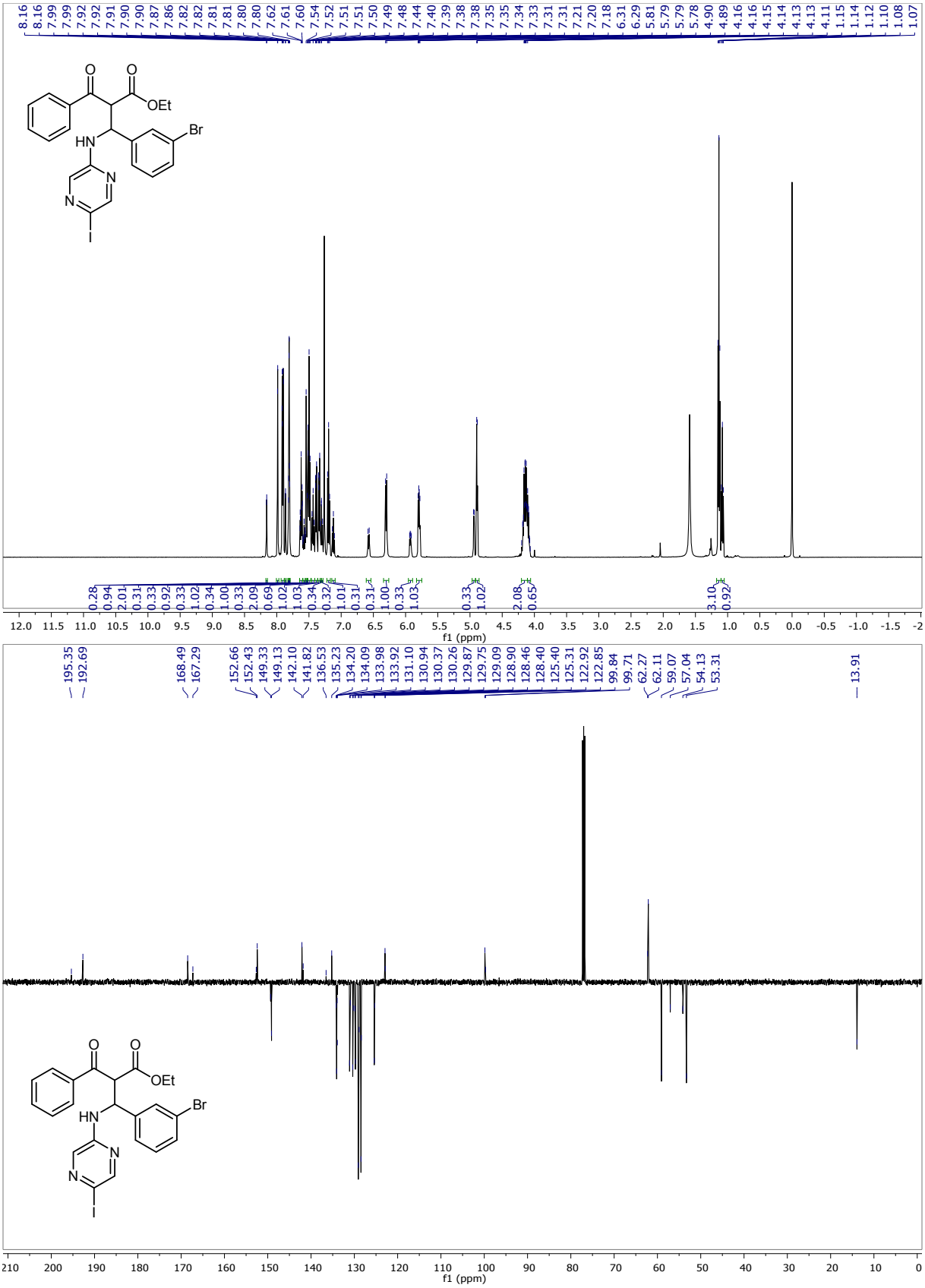
Ethyl 2-benzoyl-3-(3,5-bis(trifluoromethyl)phenyl)-3-(pyrazin-2-ylamino)propanoate (5b)



Ethyl 2-benzoyl-3-(4-fluorophenyl)-3-(pyrazin-2-ylamino)propanoate (5c)

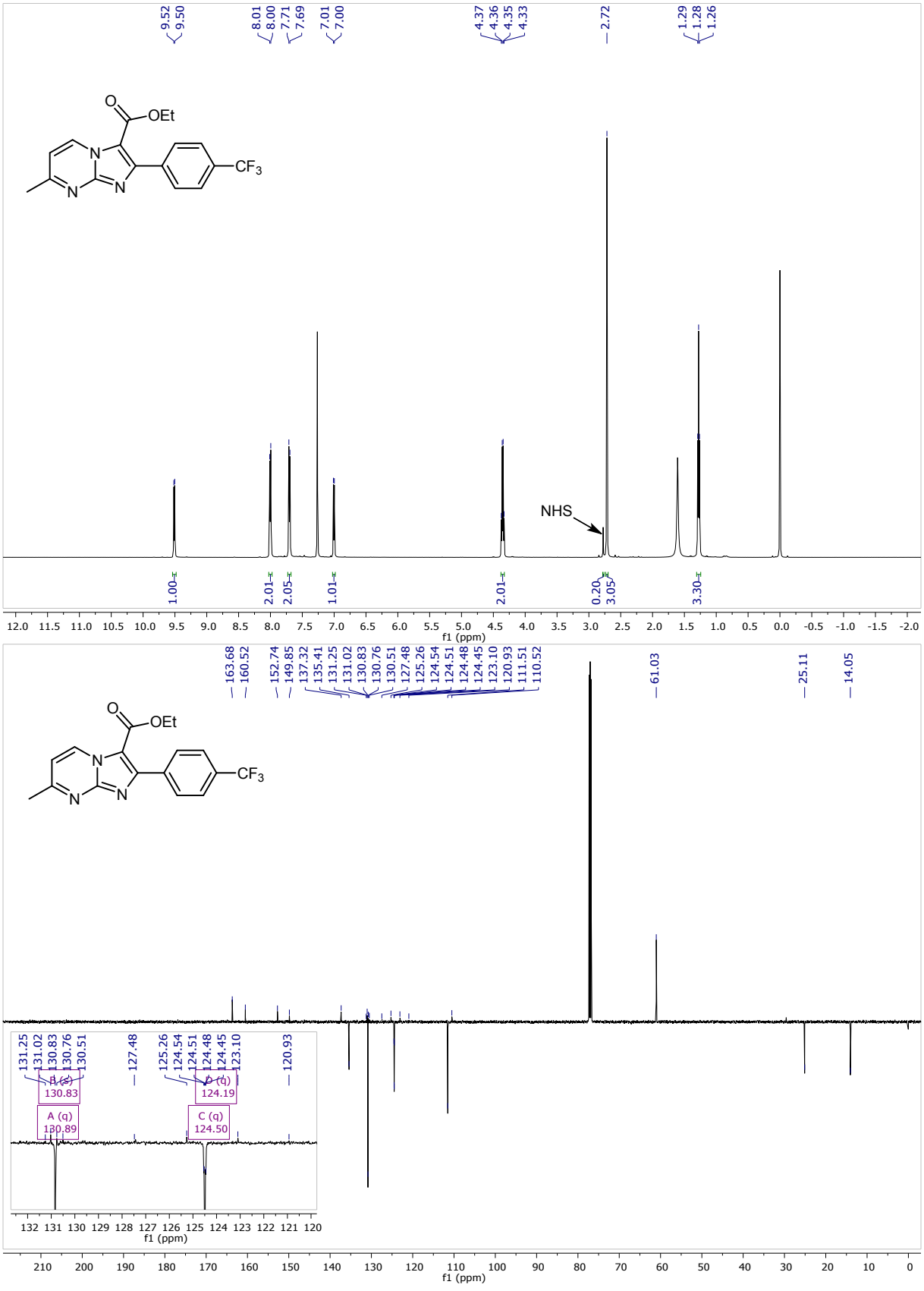


Ethyl 2-benzoyl-3-(3-bromophenyl)-3-((5-iodopyrazin-2-yl)amino)propanoate (5d)

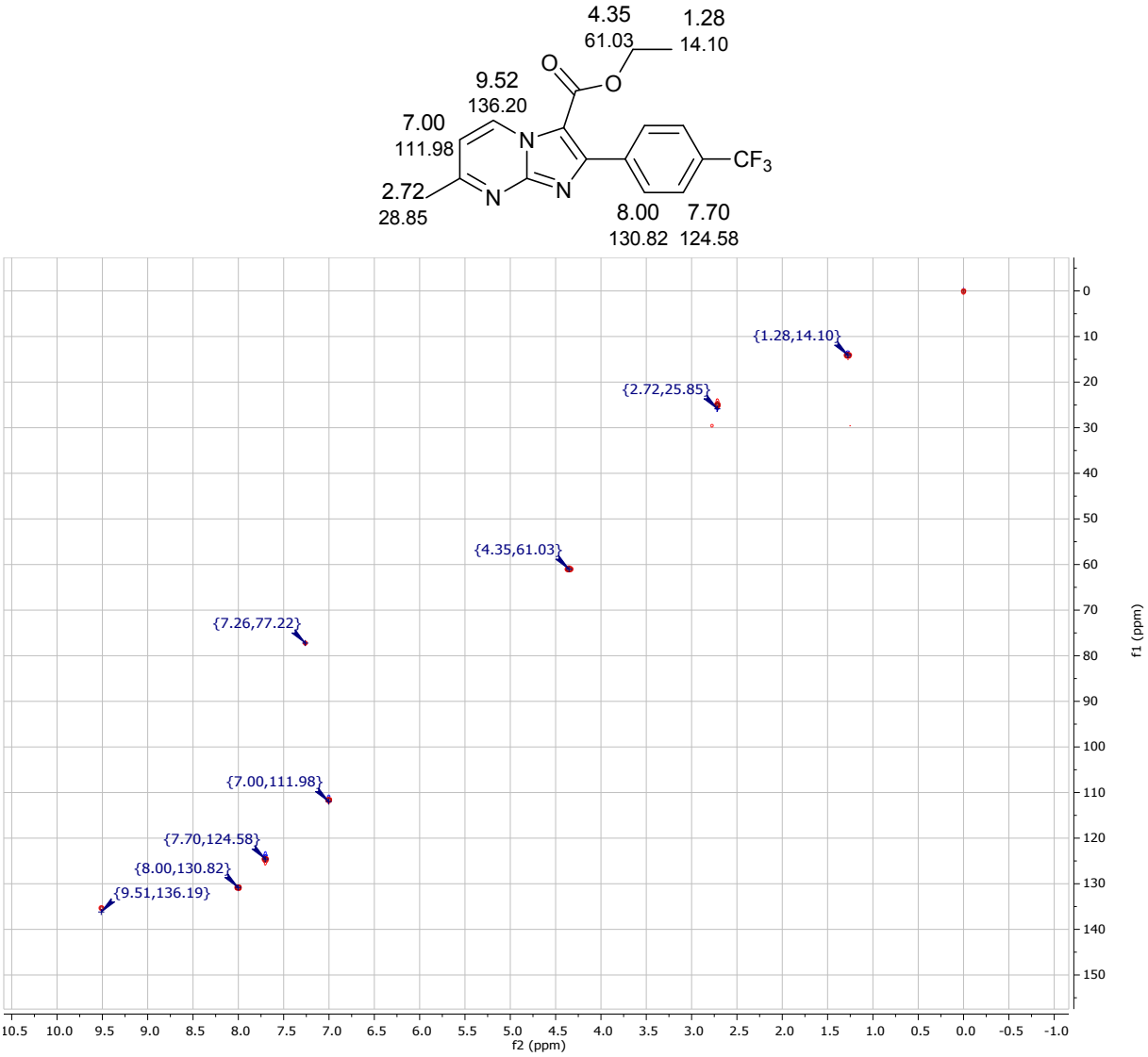


14. ^{1}H, ^{13}C and 2D NMR data of imidazo -pyridine, -pyrimidine and –pyrazine products

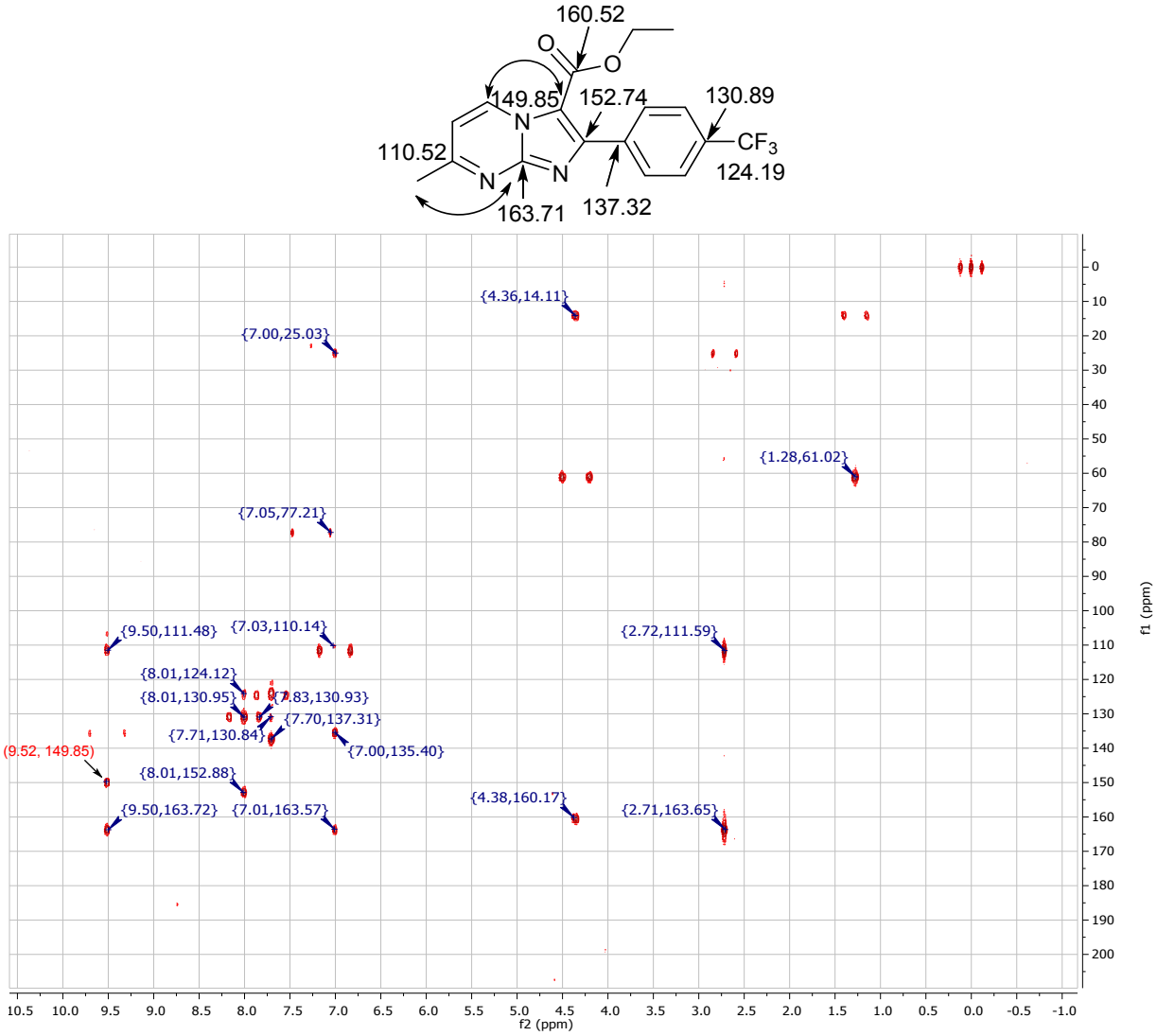
Ethyl 7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2a)



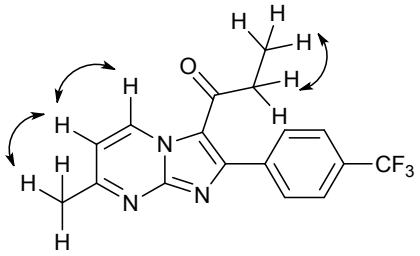
HSQC spectrum of the compound **2a** in $CDCl_3$

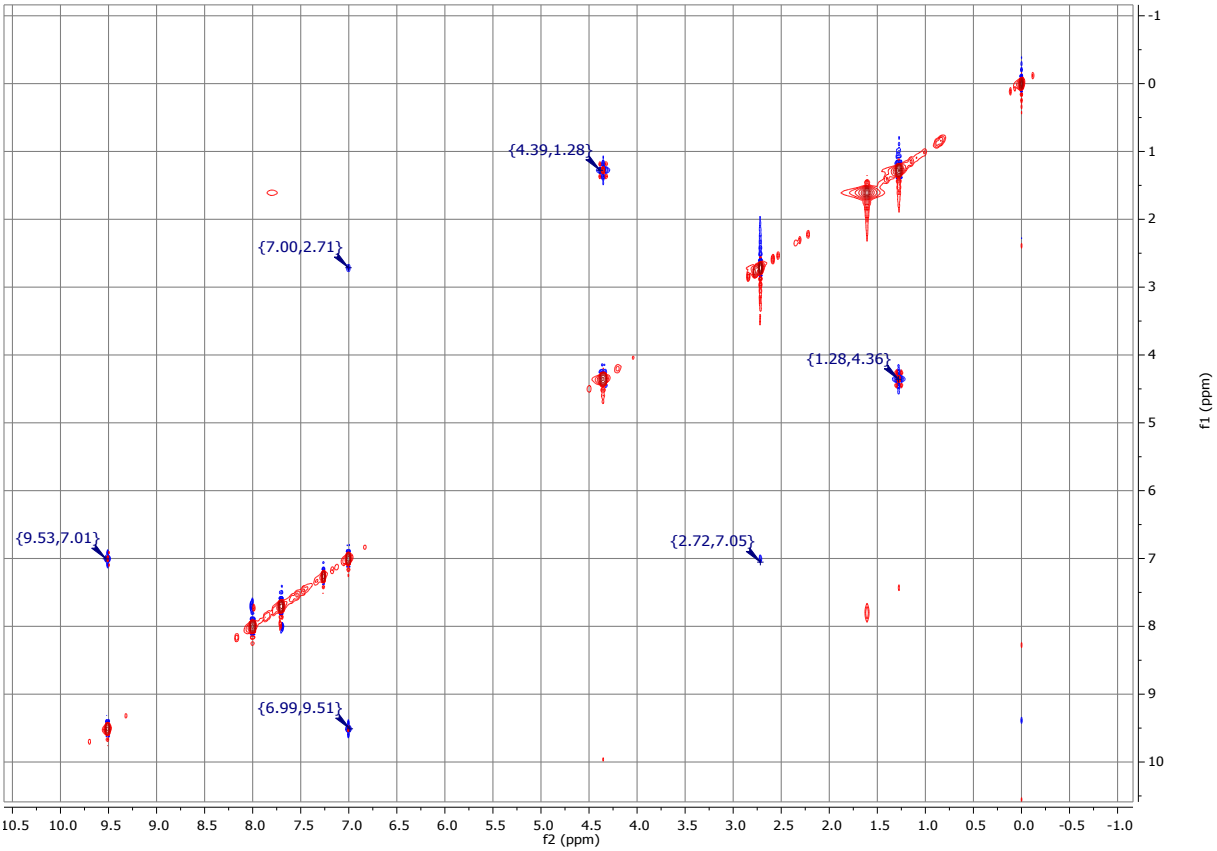


HMBC spectrum of the comound **2a** in $CDCl_3$

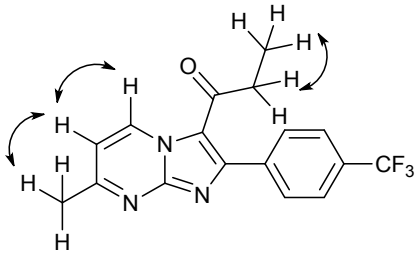


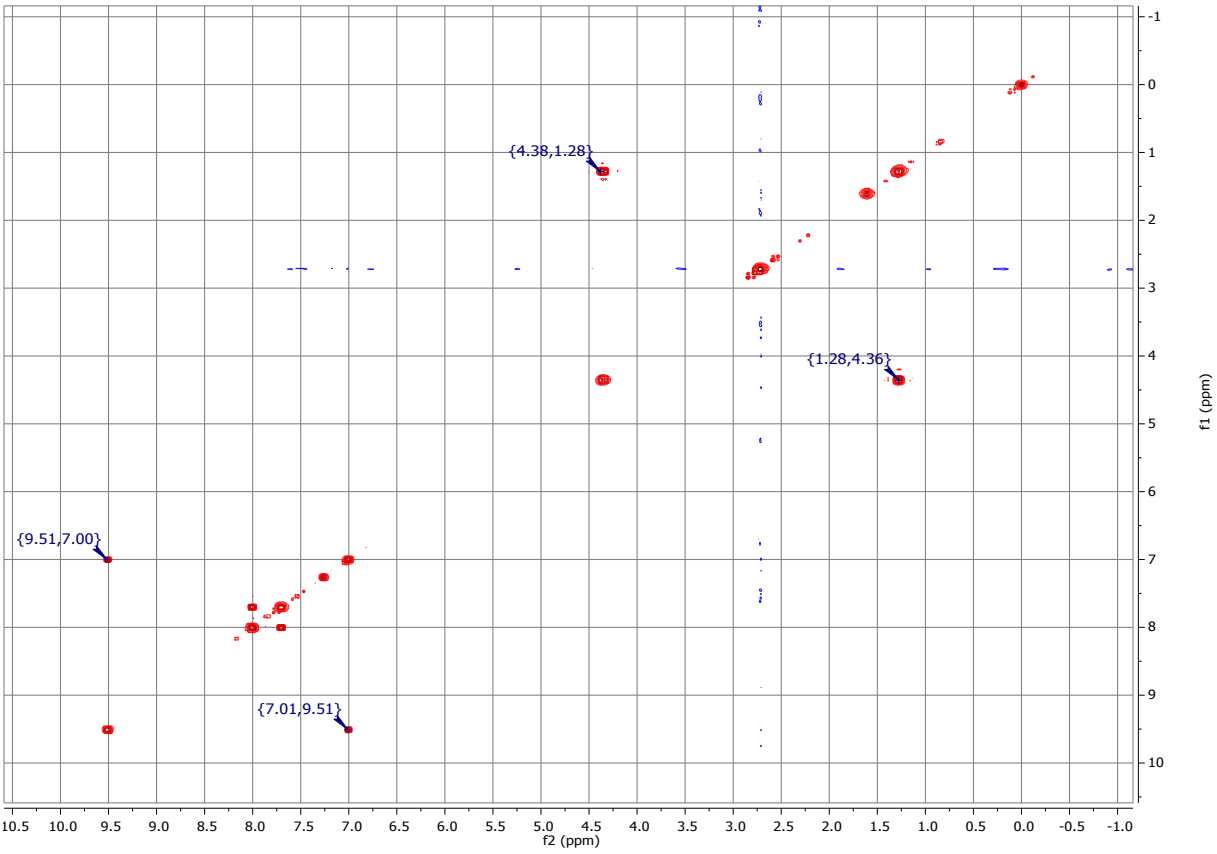
NOESY spectrum of the compound **2a** in $CDCl_3$



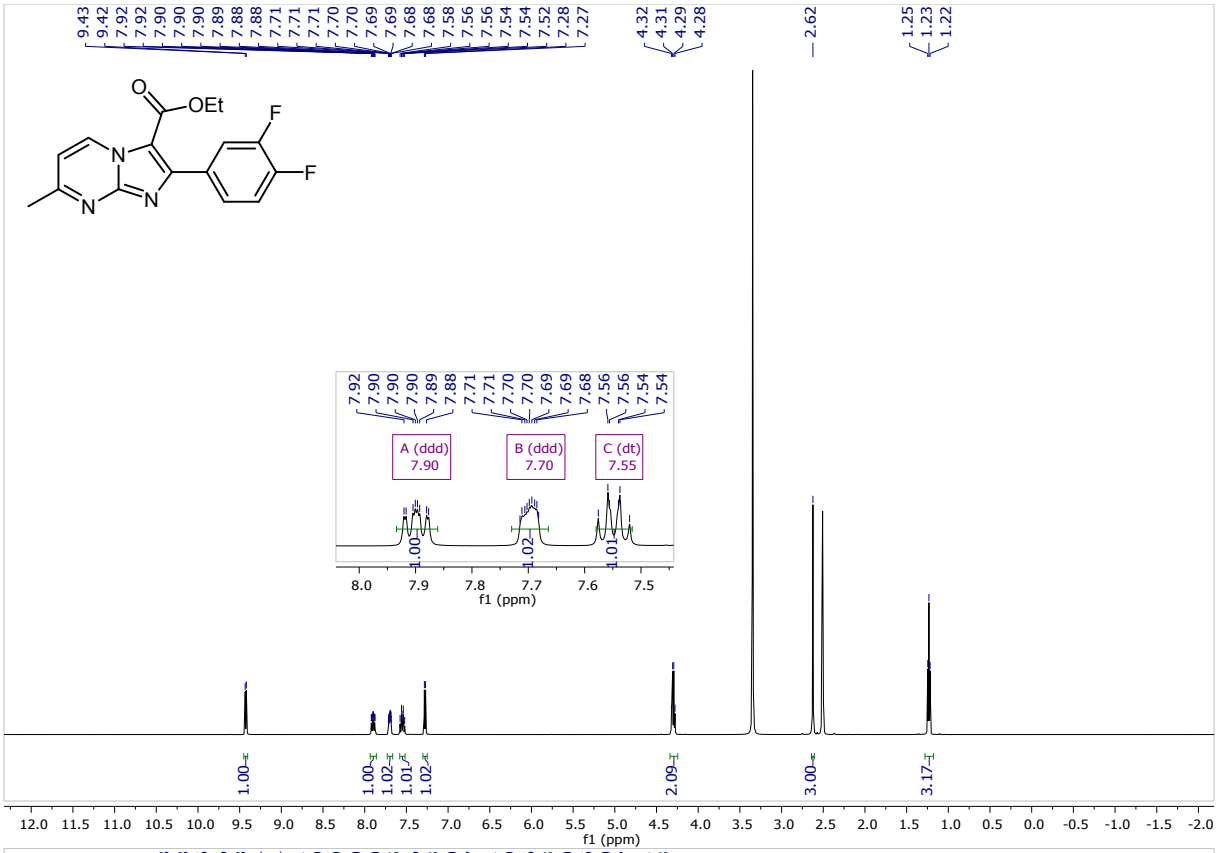


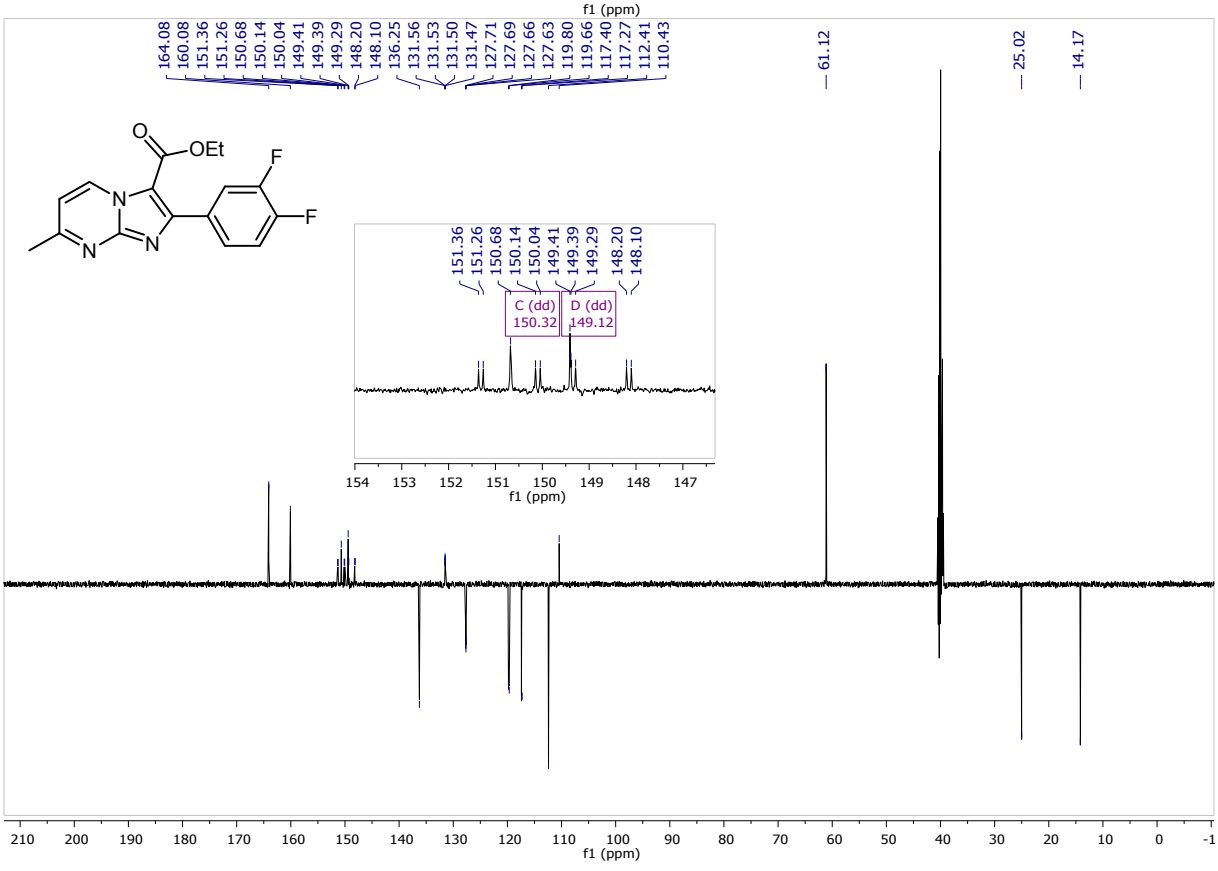
COSY spectrum of the compound **2a** in $CDCl_3$



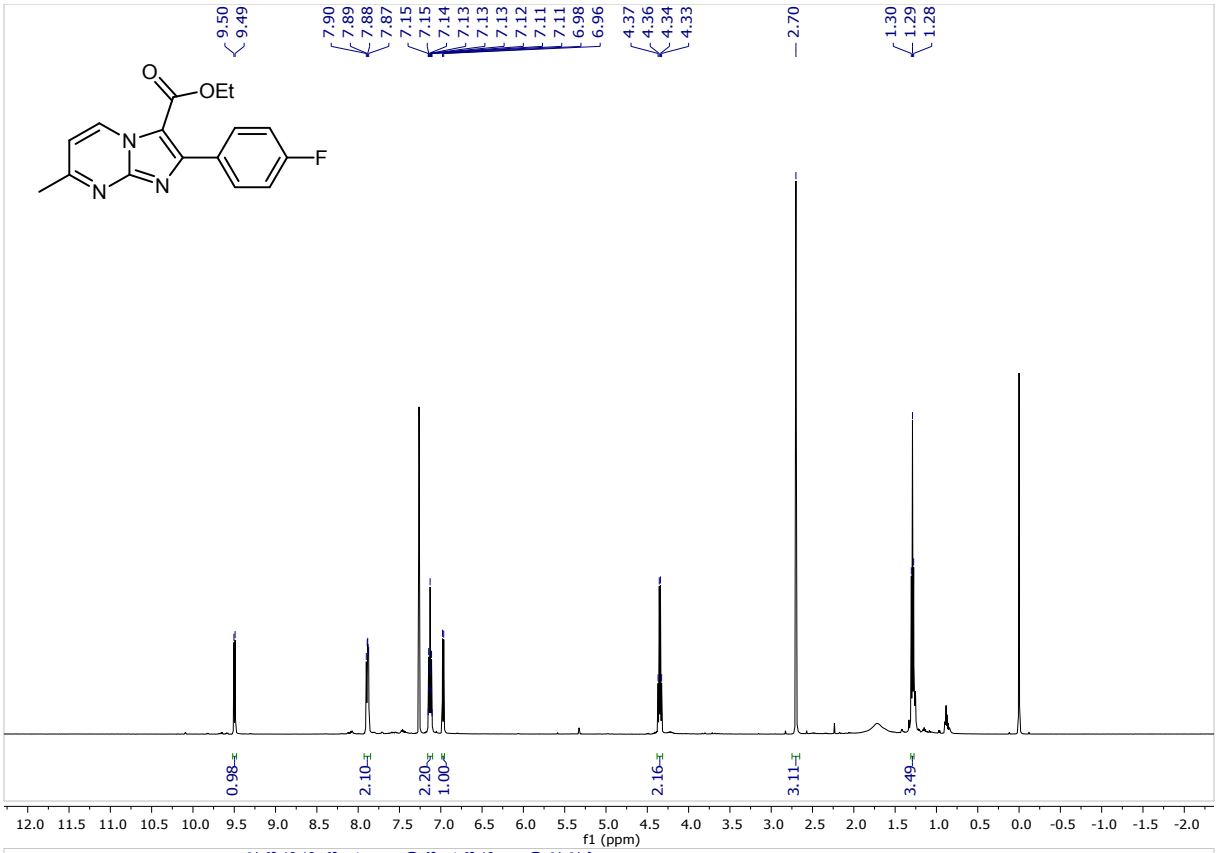


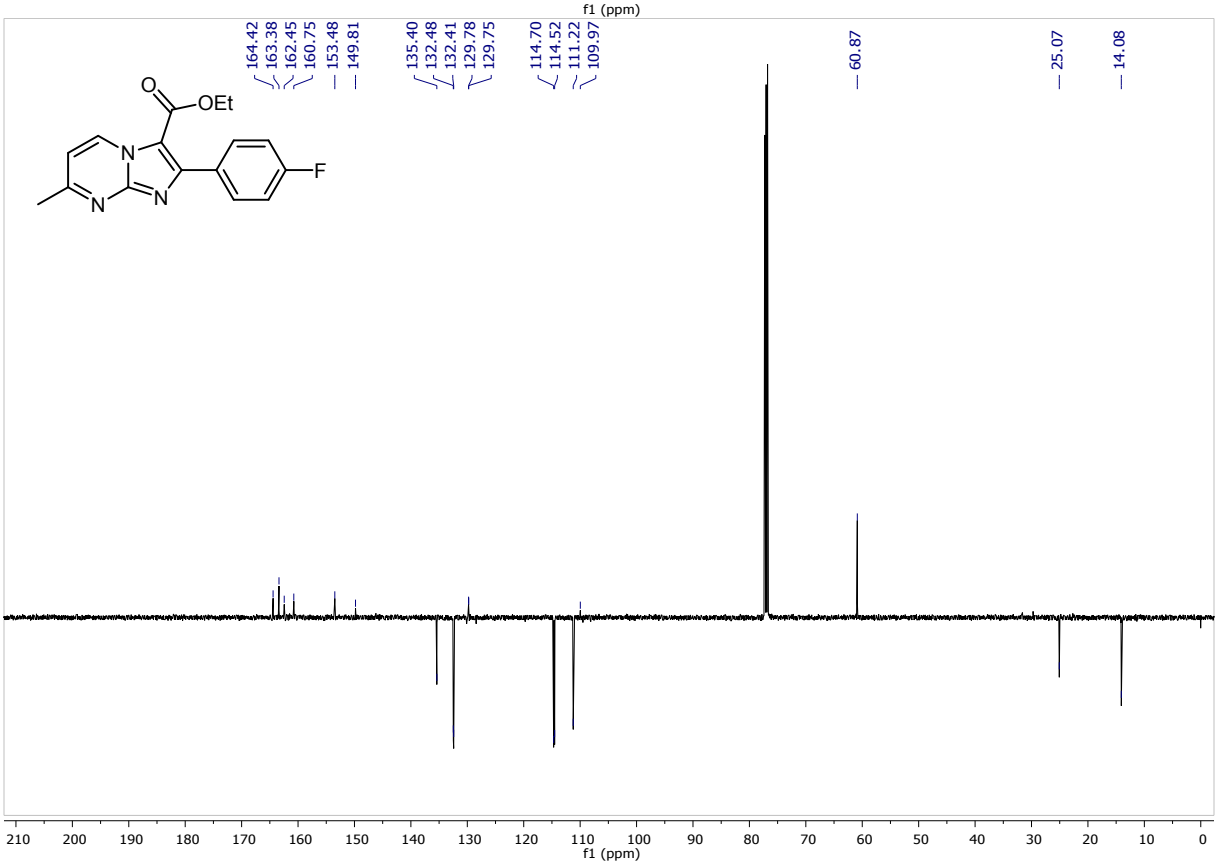
Ethyl 2-(3,4-difluorophenyl)-7-methylimidazo[1,2-a]pyrimidine-3-carboxylate (2c)



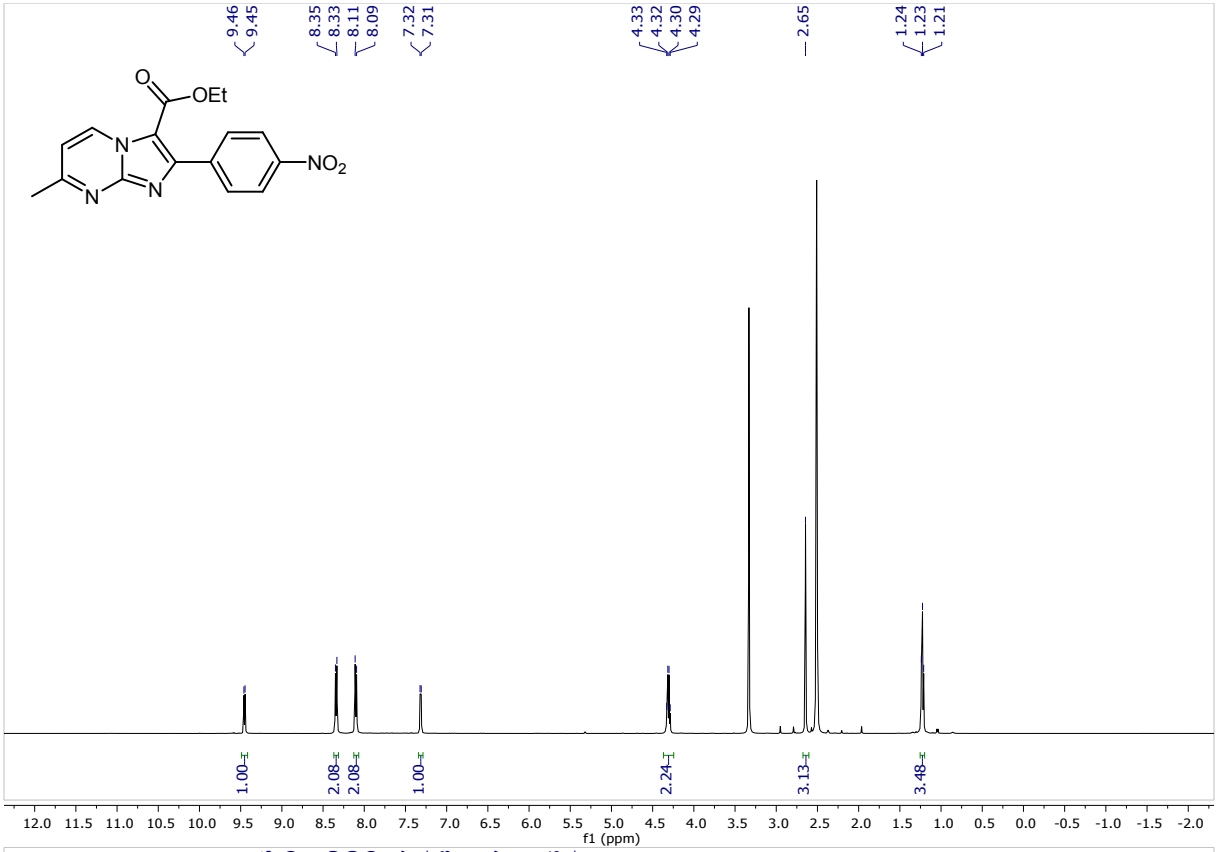


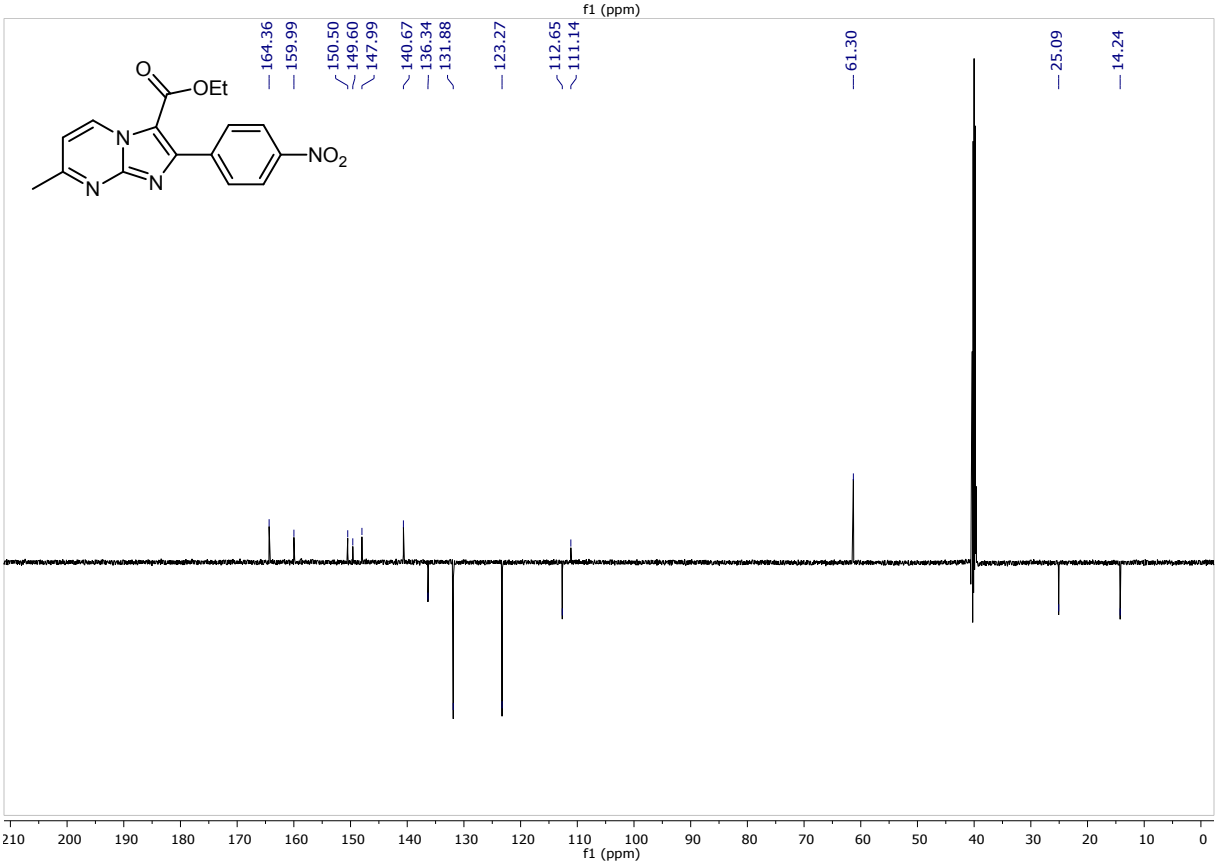
Ethyl 2-(4-fluorophenyl)-5-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2d)



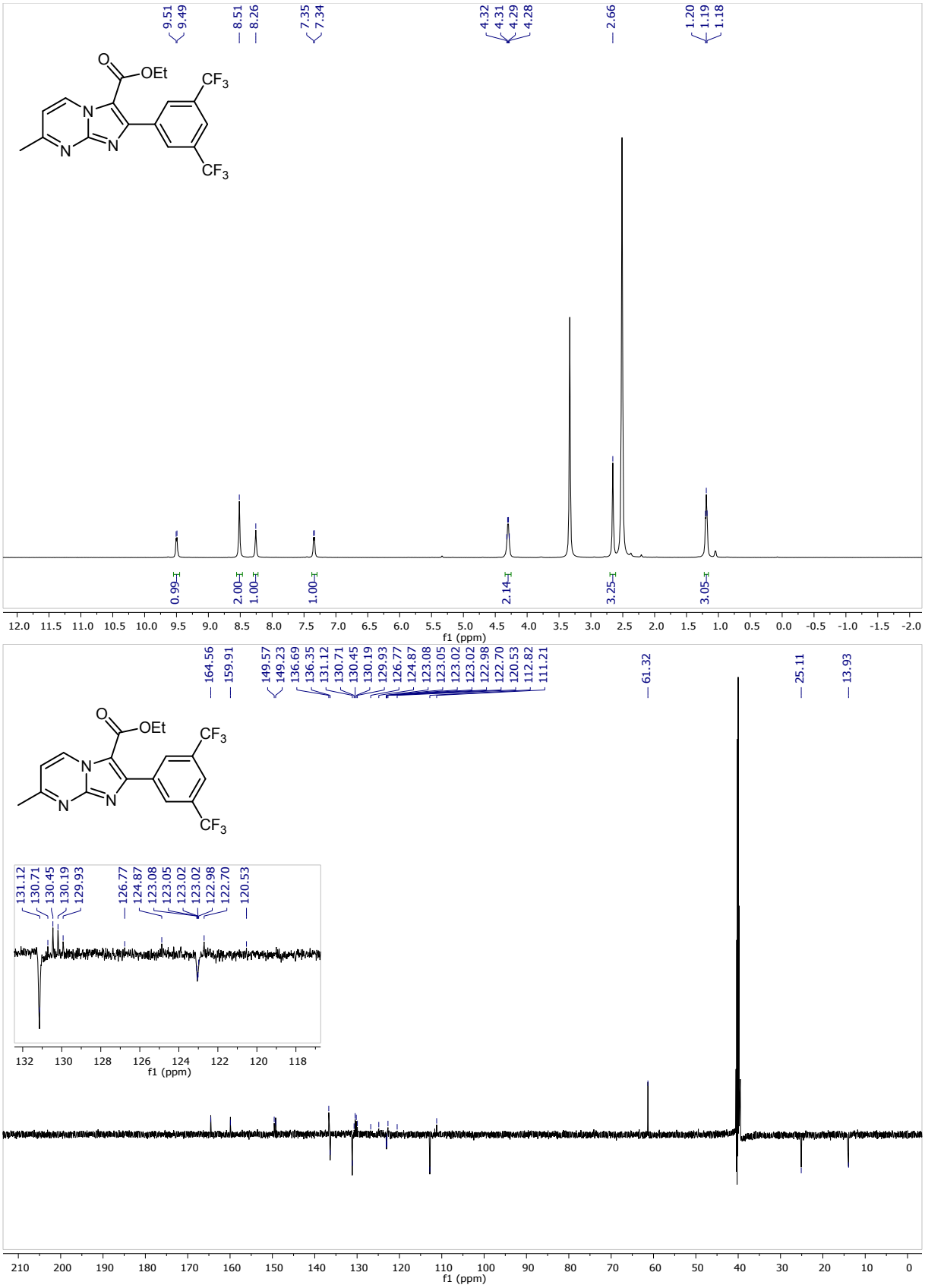


Ethyl 2-(4-nitrophenyl)-5-methylimidazo[1,2-*a*]pyrimidine-3 carboxylate (2e)

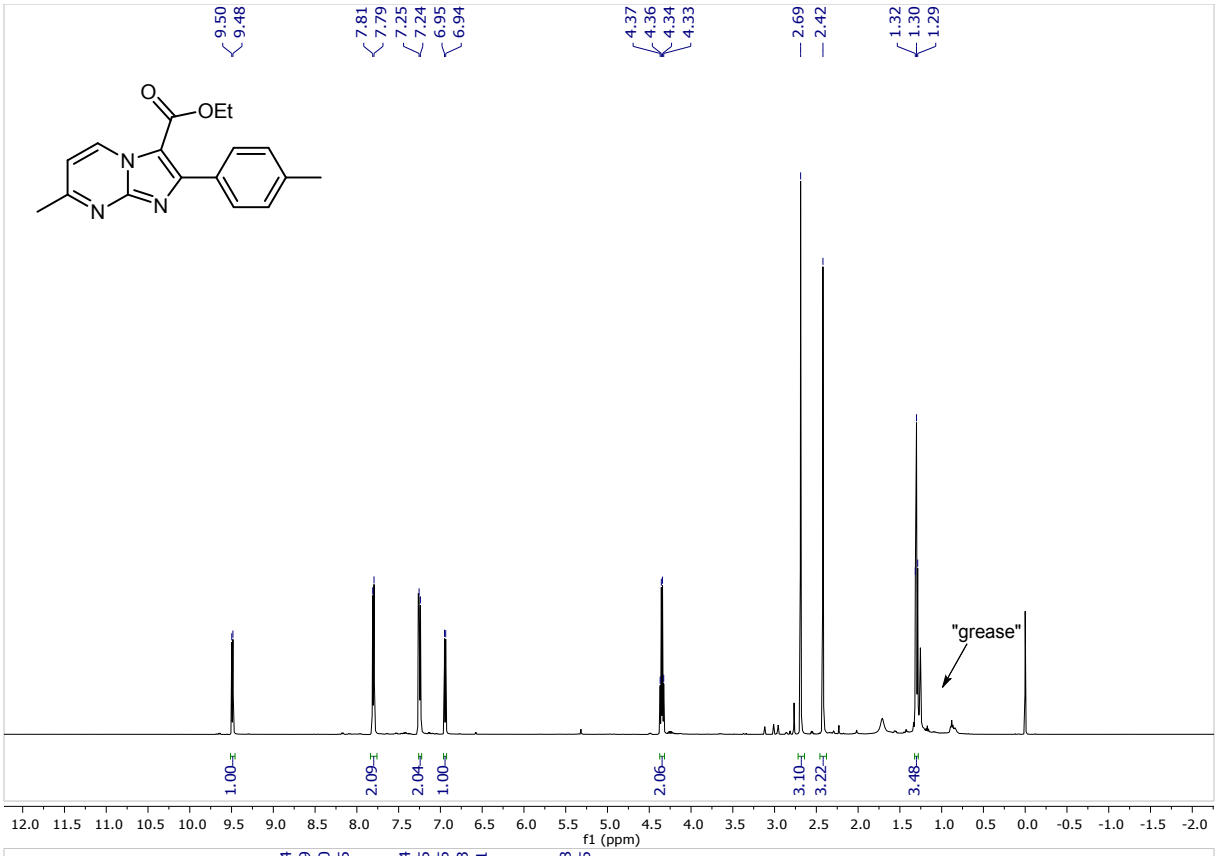


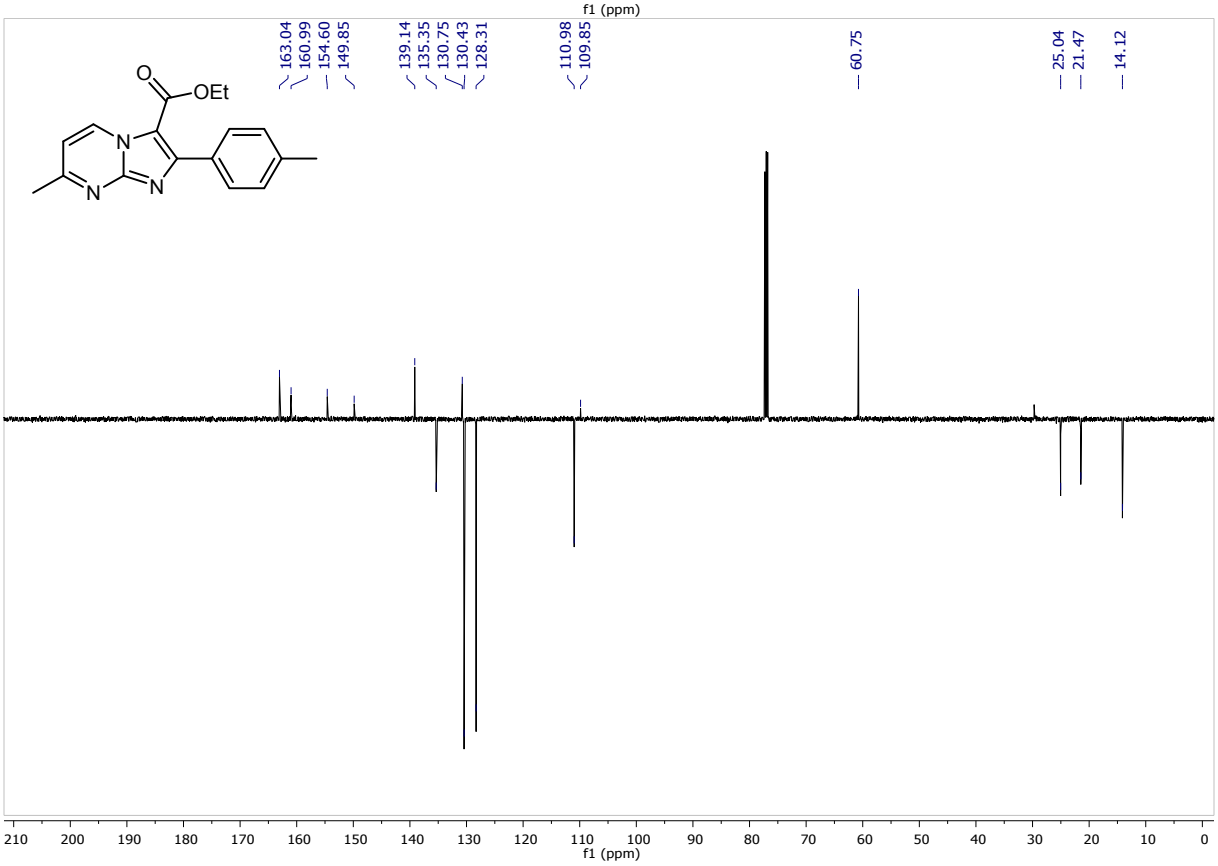


Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-5-methylimidazo[1,2-*a*]pyrimidine-3 carboxylate (2f)

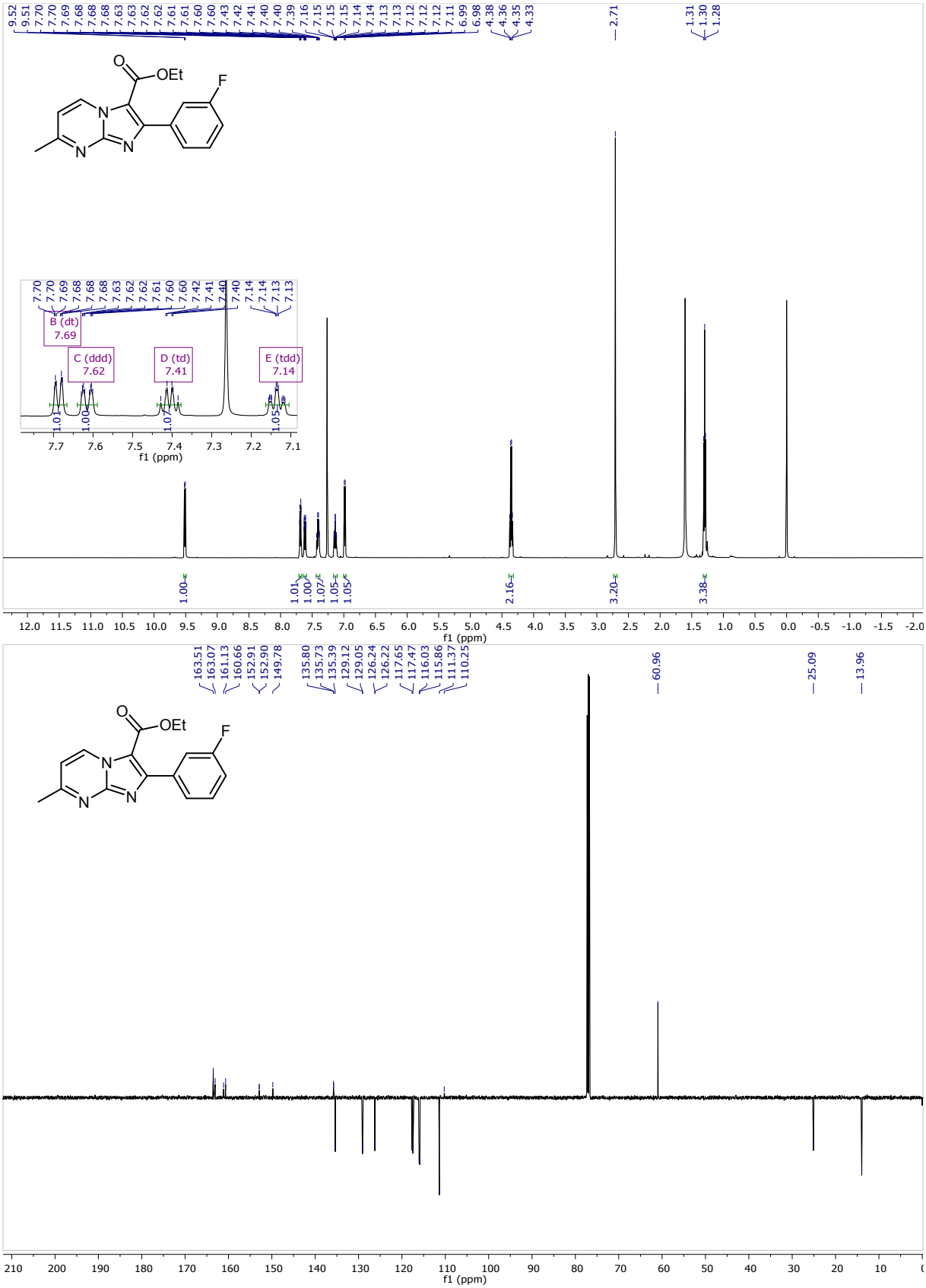


Ethyl 7-methyl-2-(p-tolyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2g)

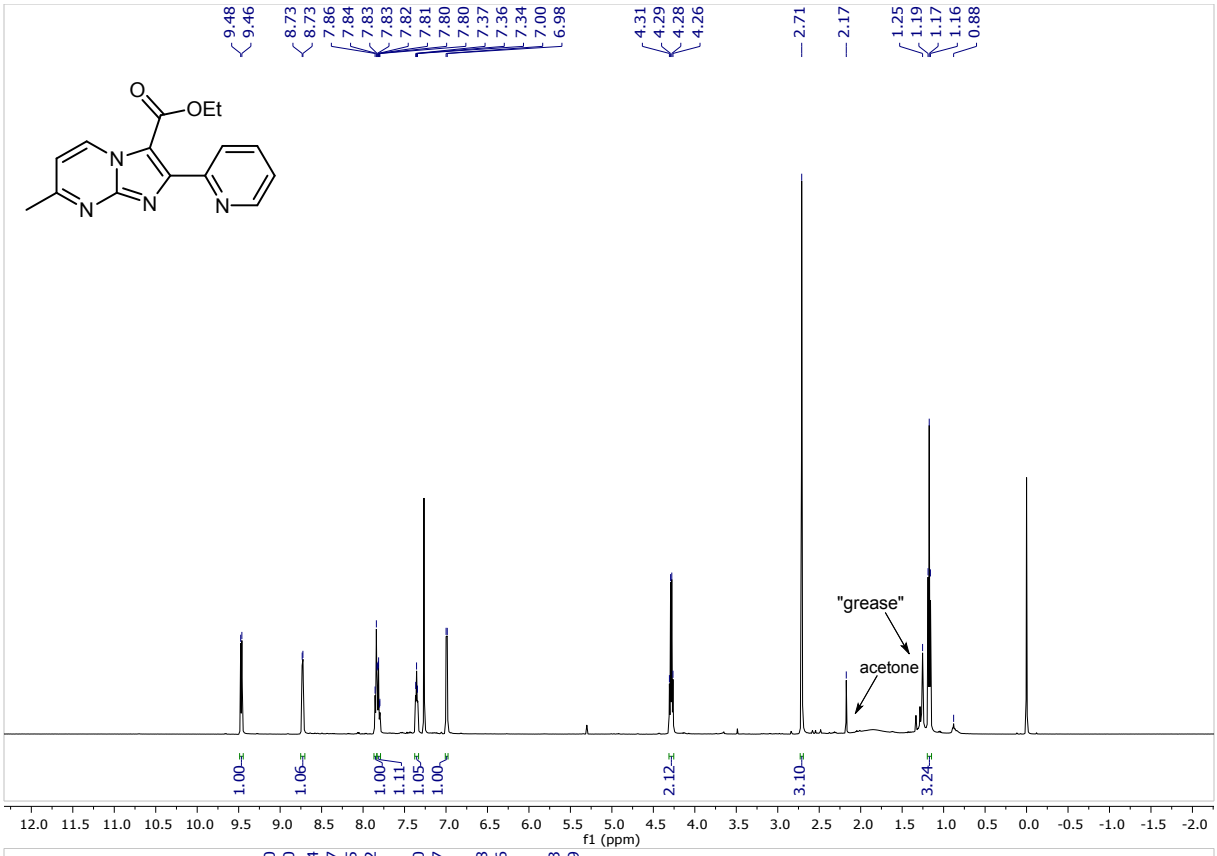


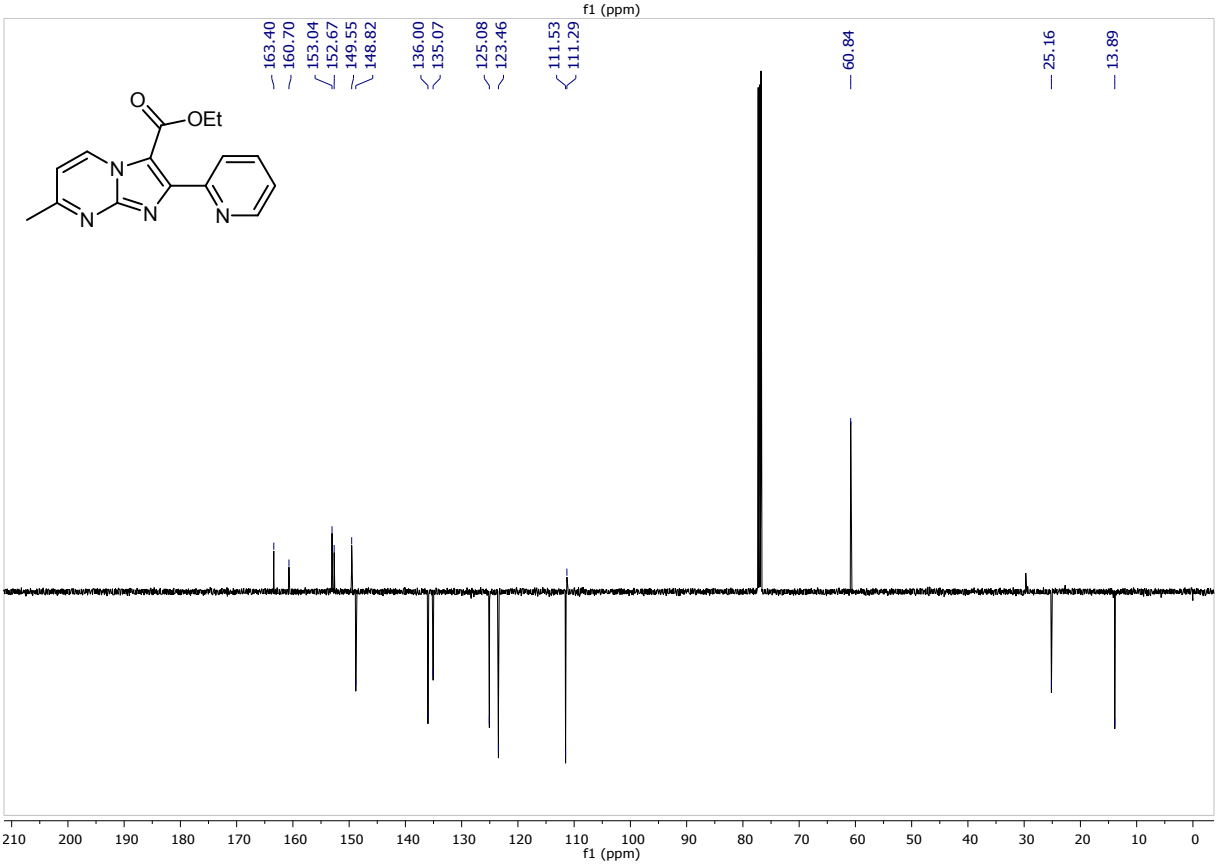


Ethyl 2-(3-fluorophenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2h)

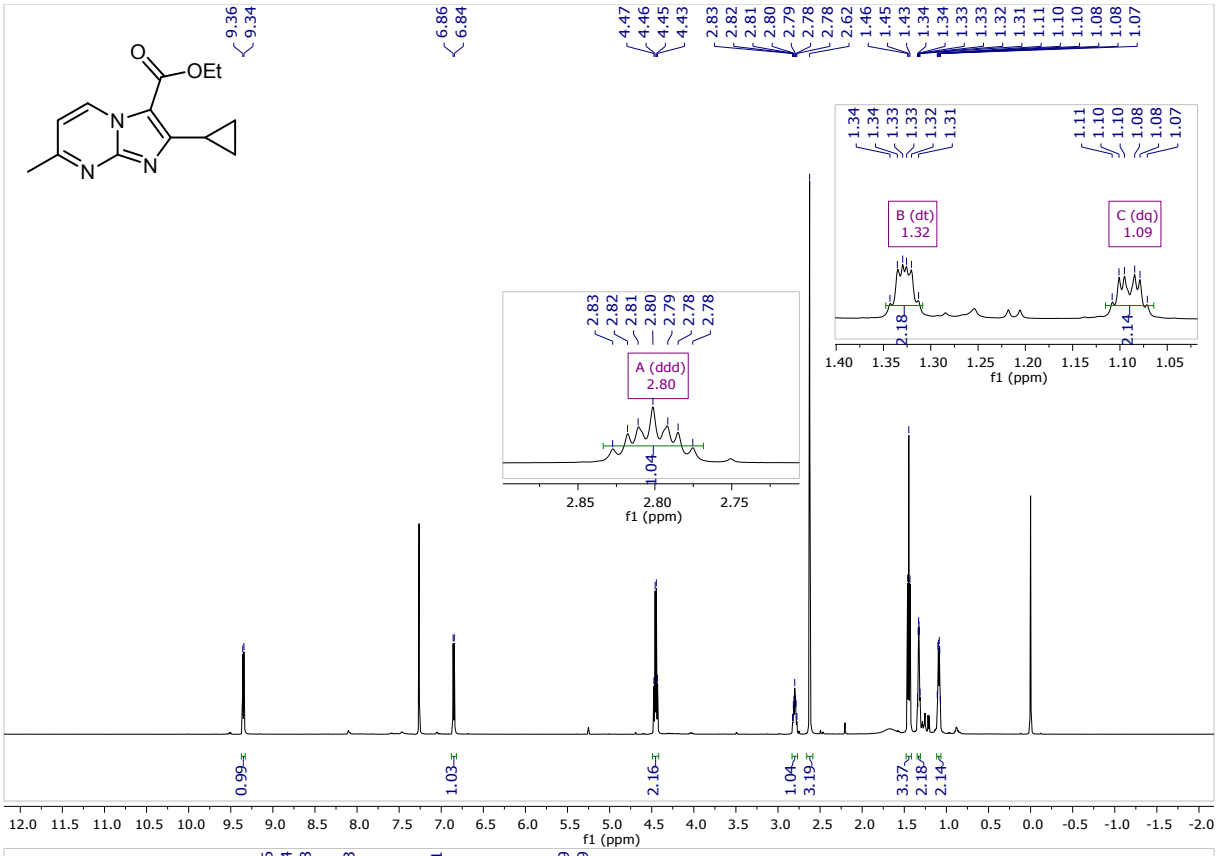


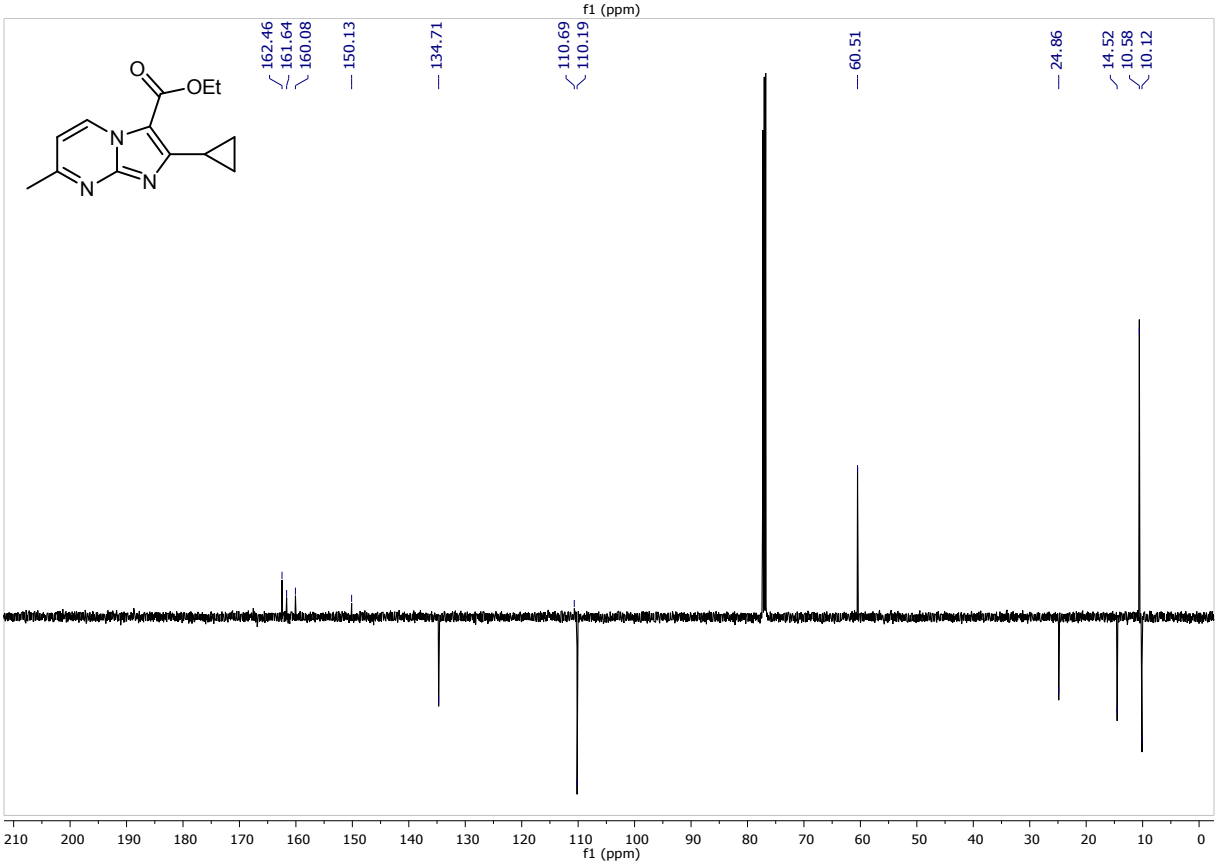
Ethyl 7-methyl-2-(pyridin-2-yl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2i)



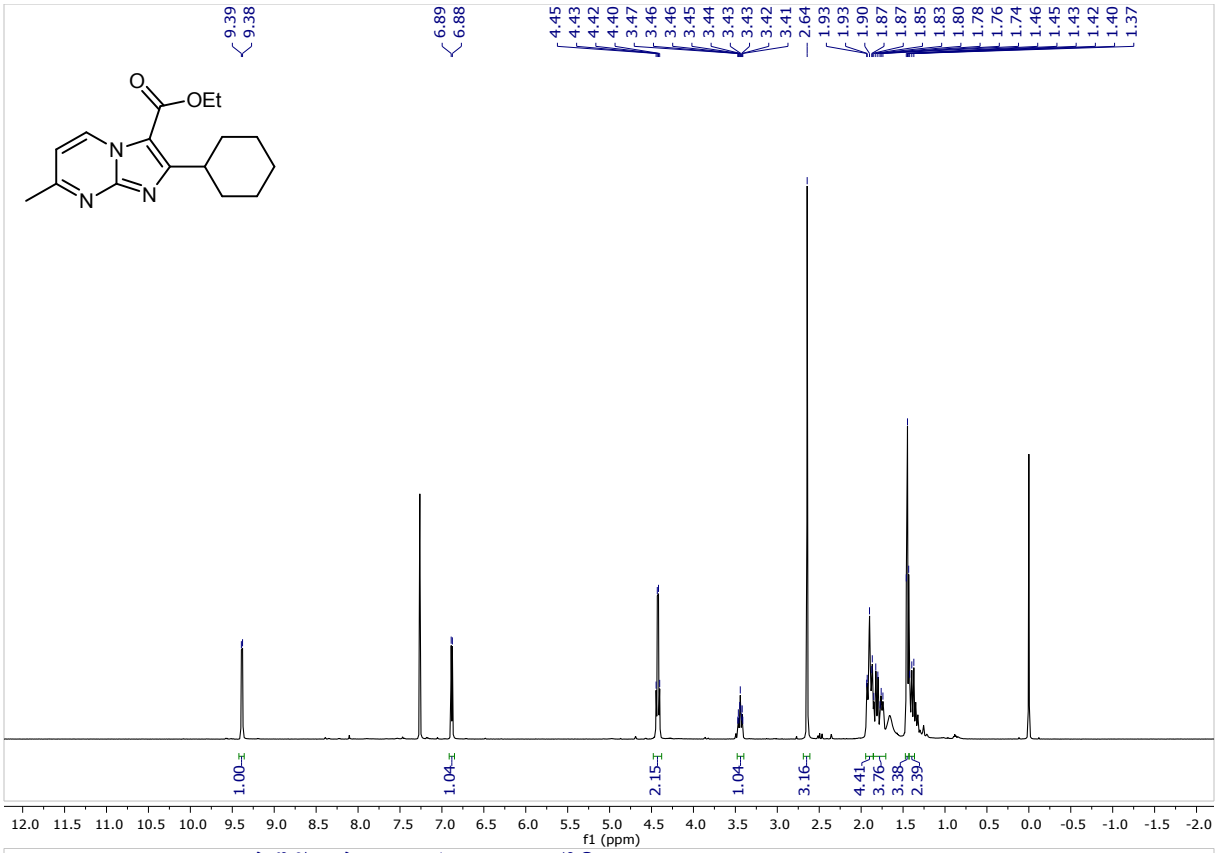


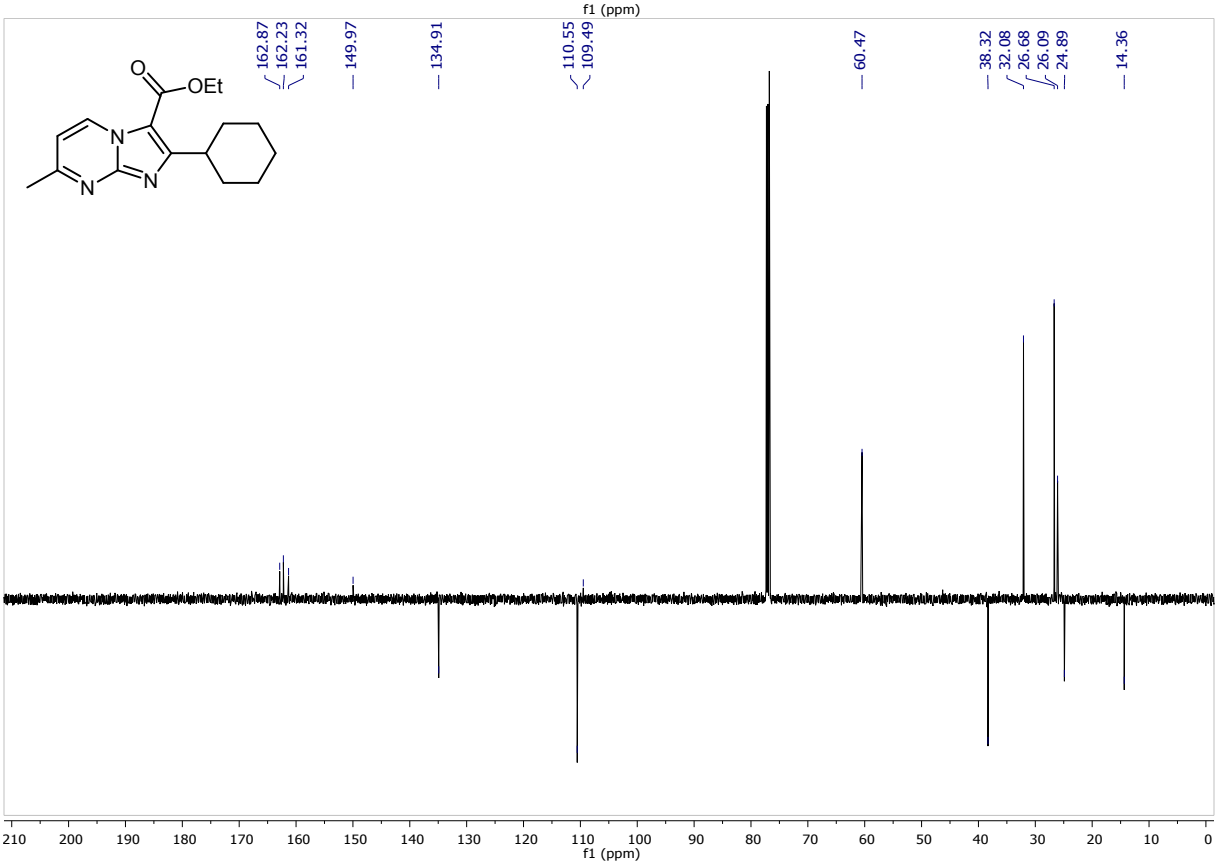
Ethyl 2-cyclopropyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2j)



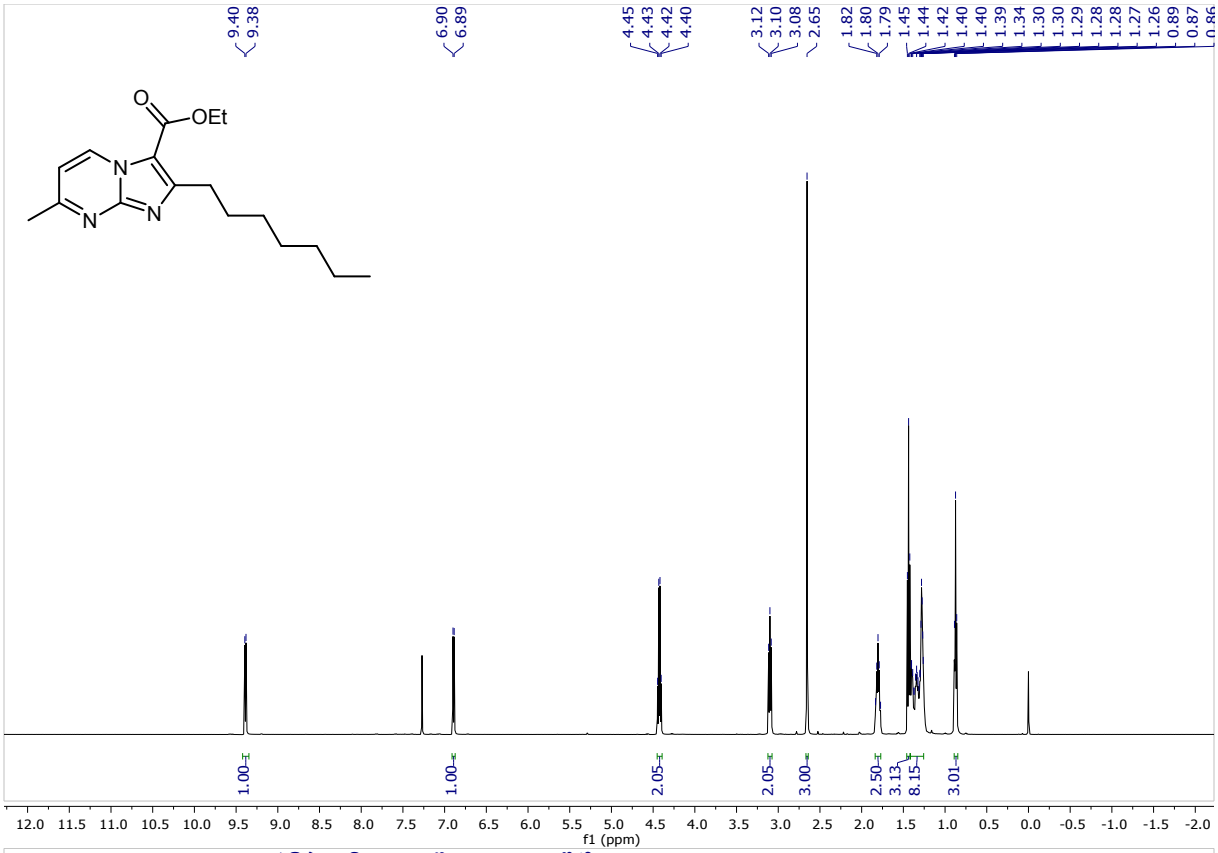


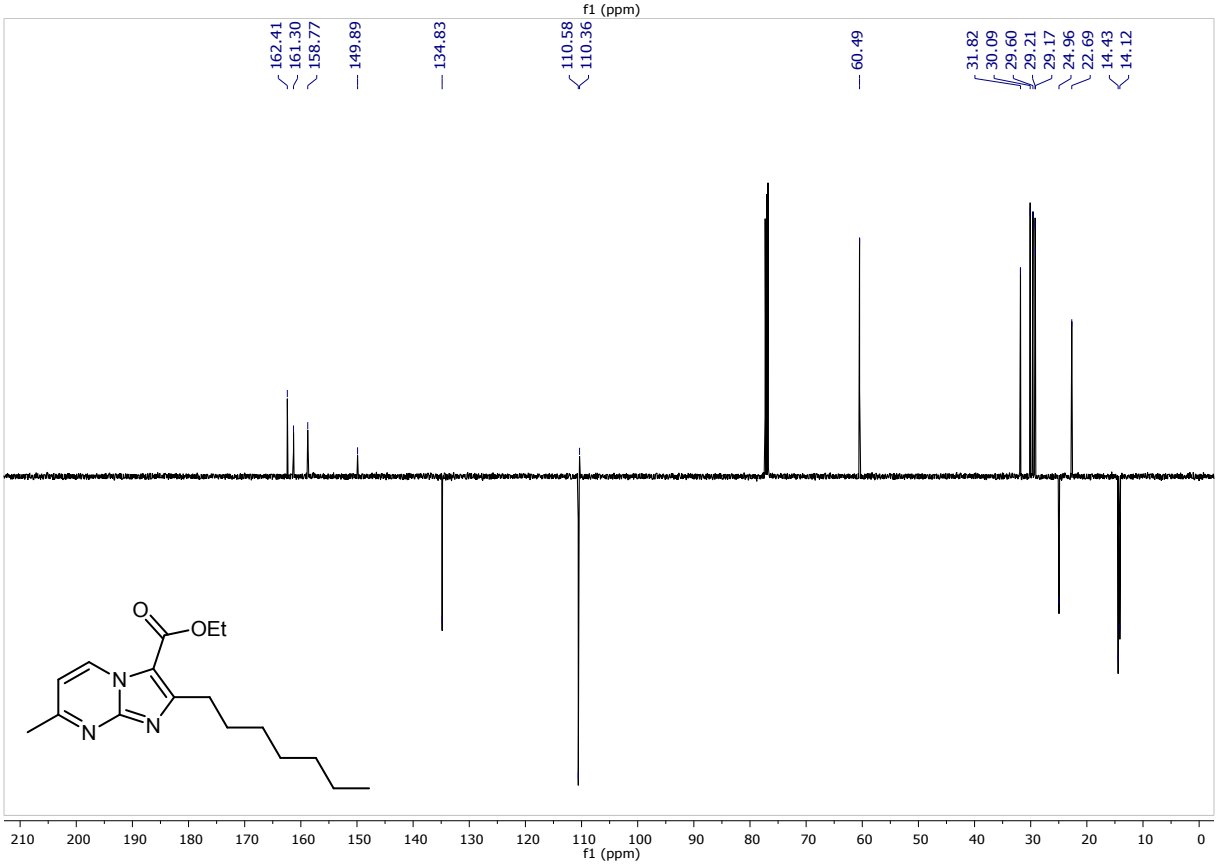
Ethyl 2-cyclohexyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2k)



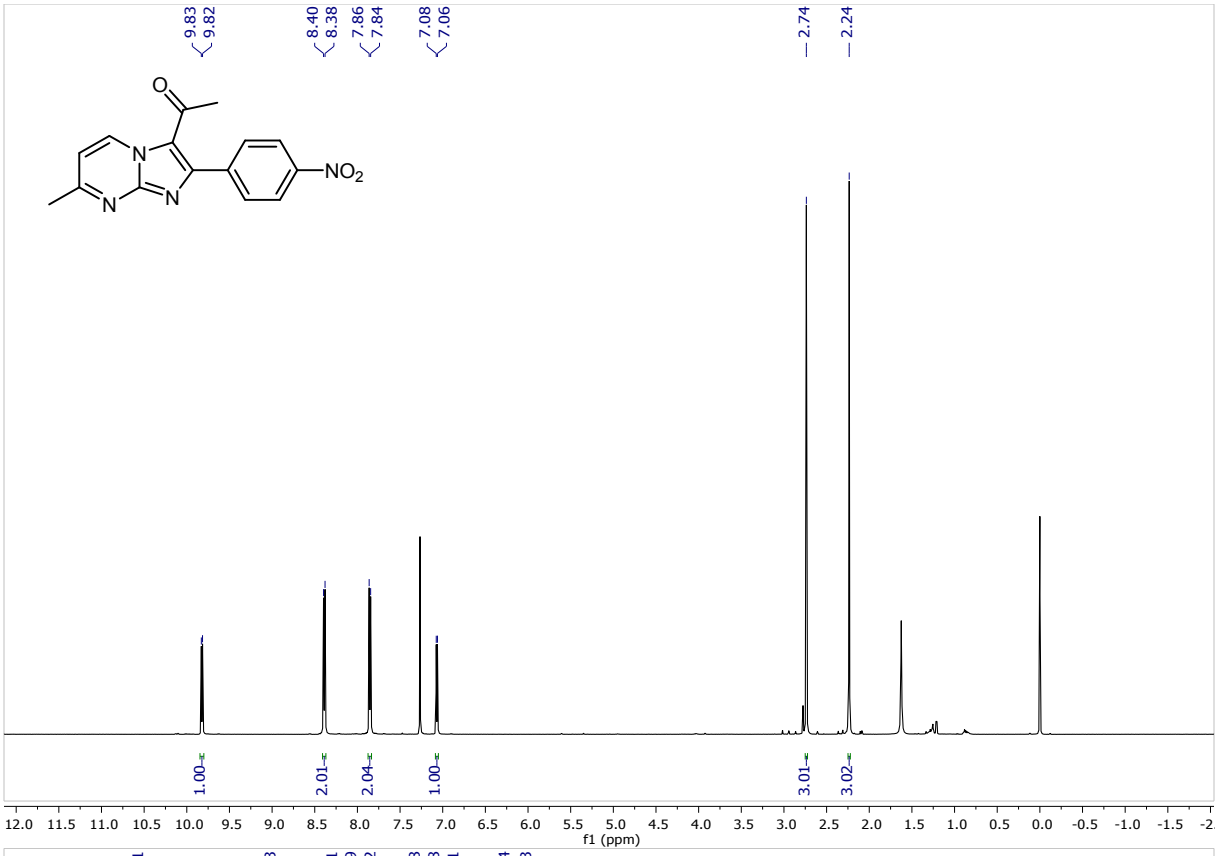


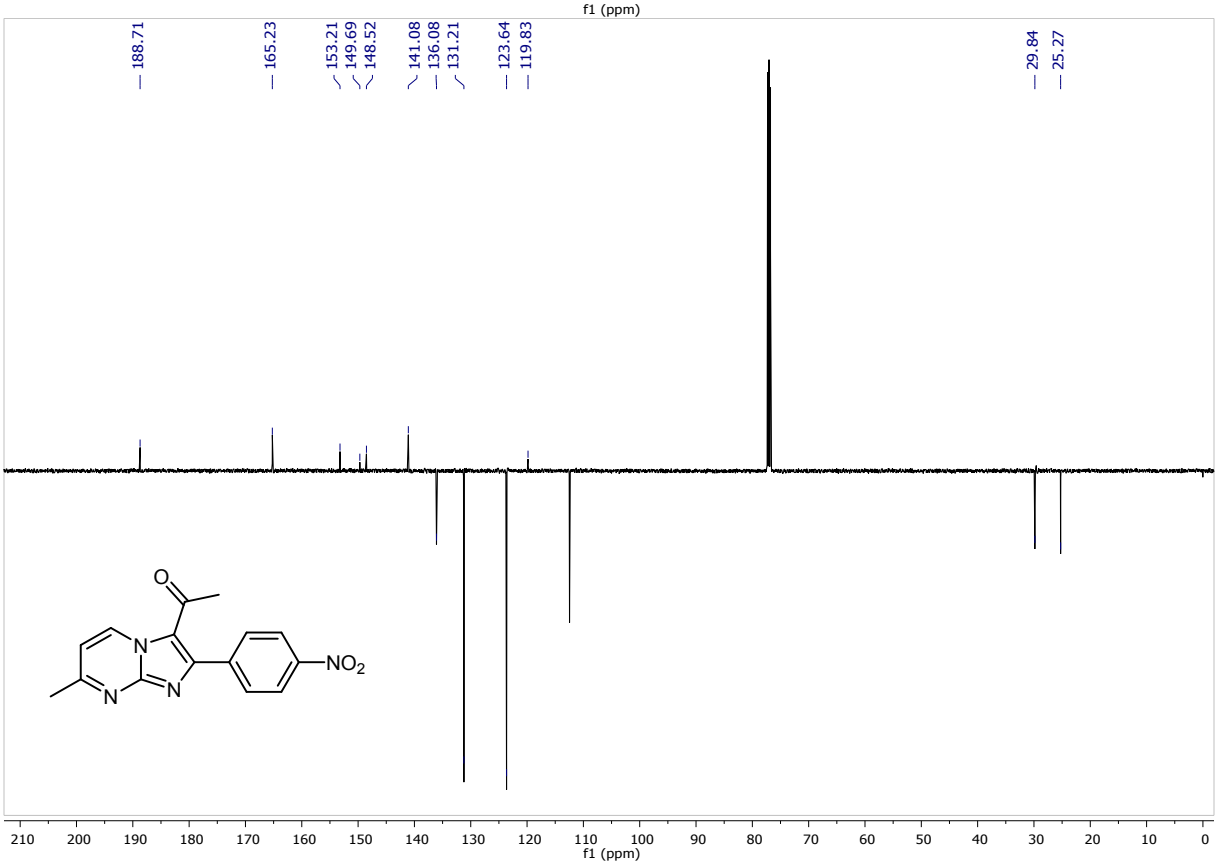
Ethyl 2-heptyl-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2l)



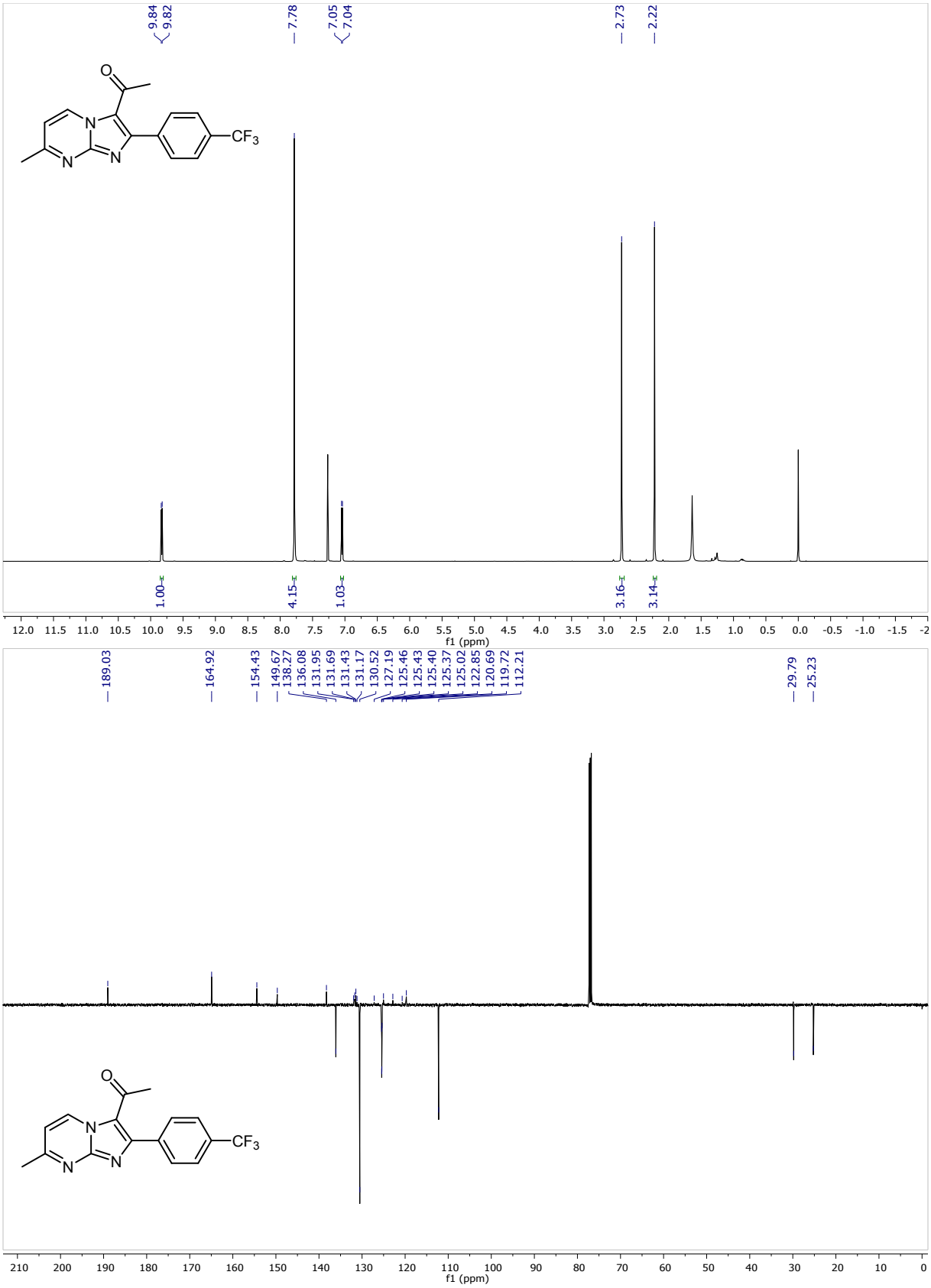


1-(7-methyl-2-(4-nitrophenyl)imidazo[1,2-*a*]pyrimidin-3-yl)ethanone (2m)

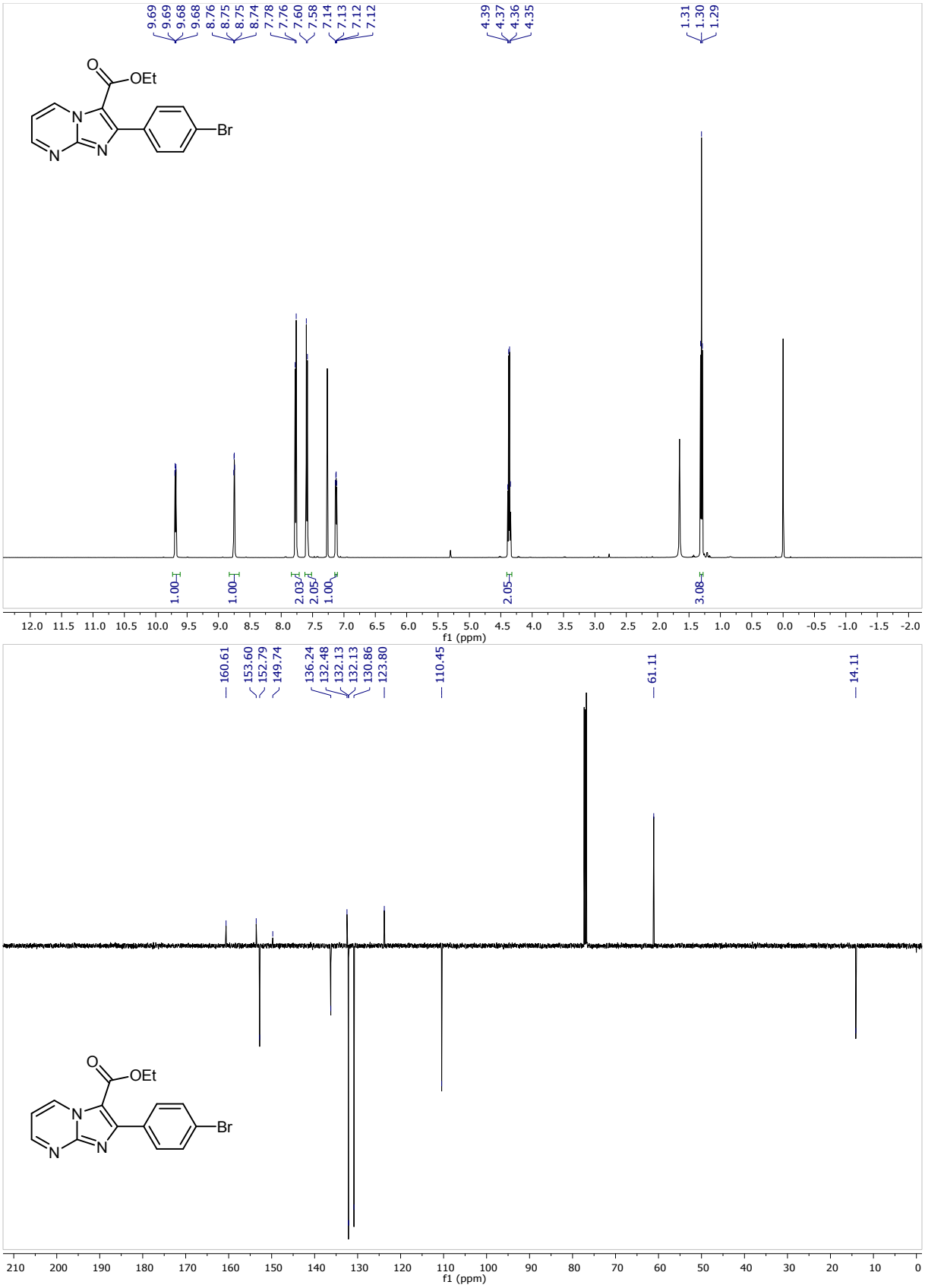




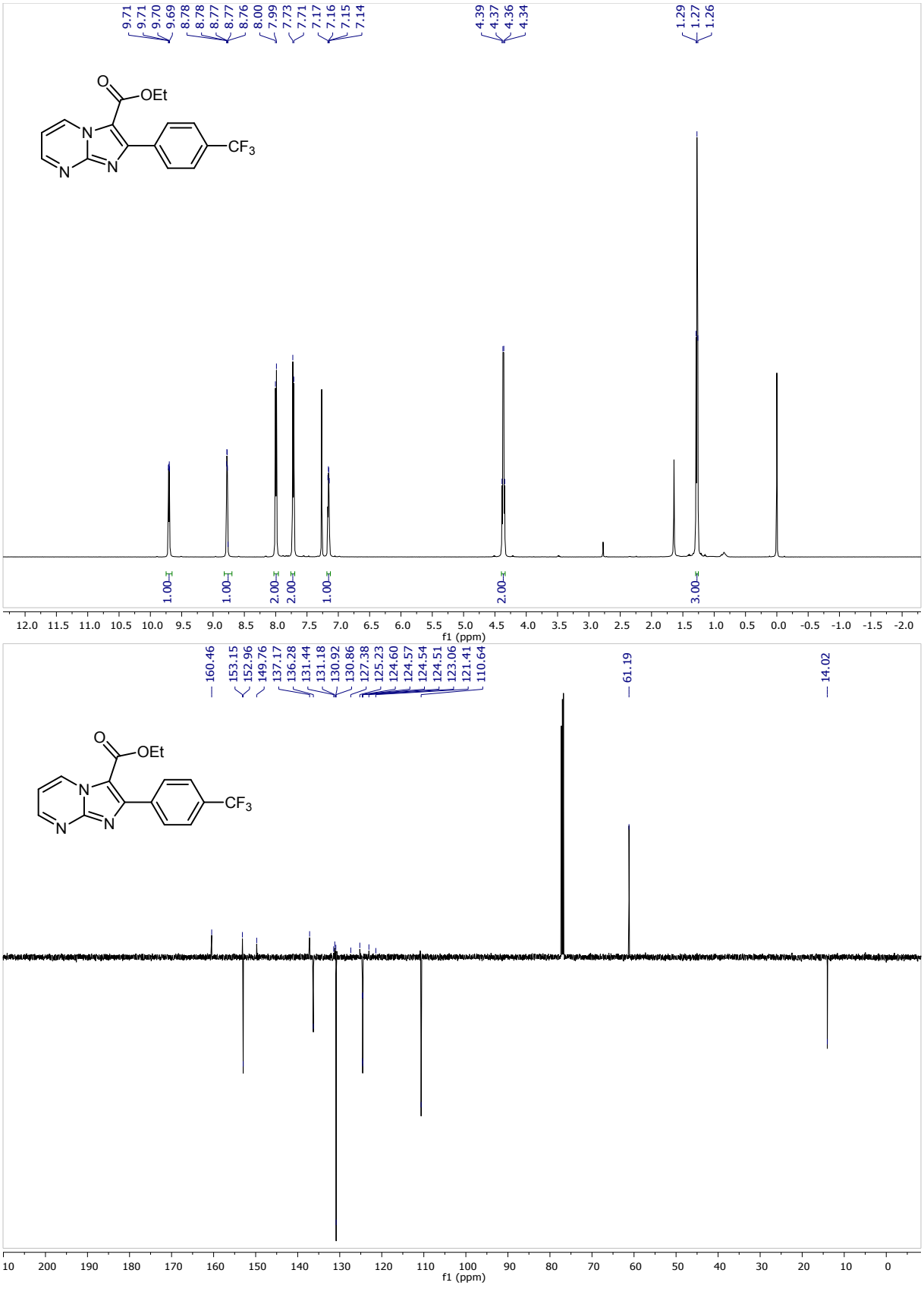
1-(7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyrimidin-3-yl)ethanone (2n)



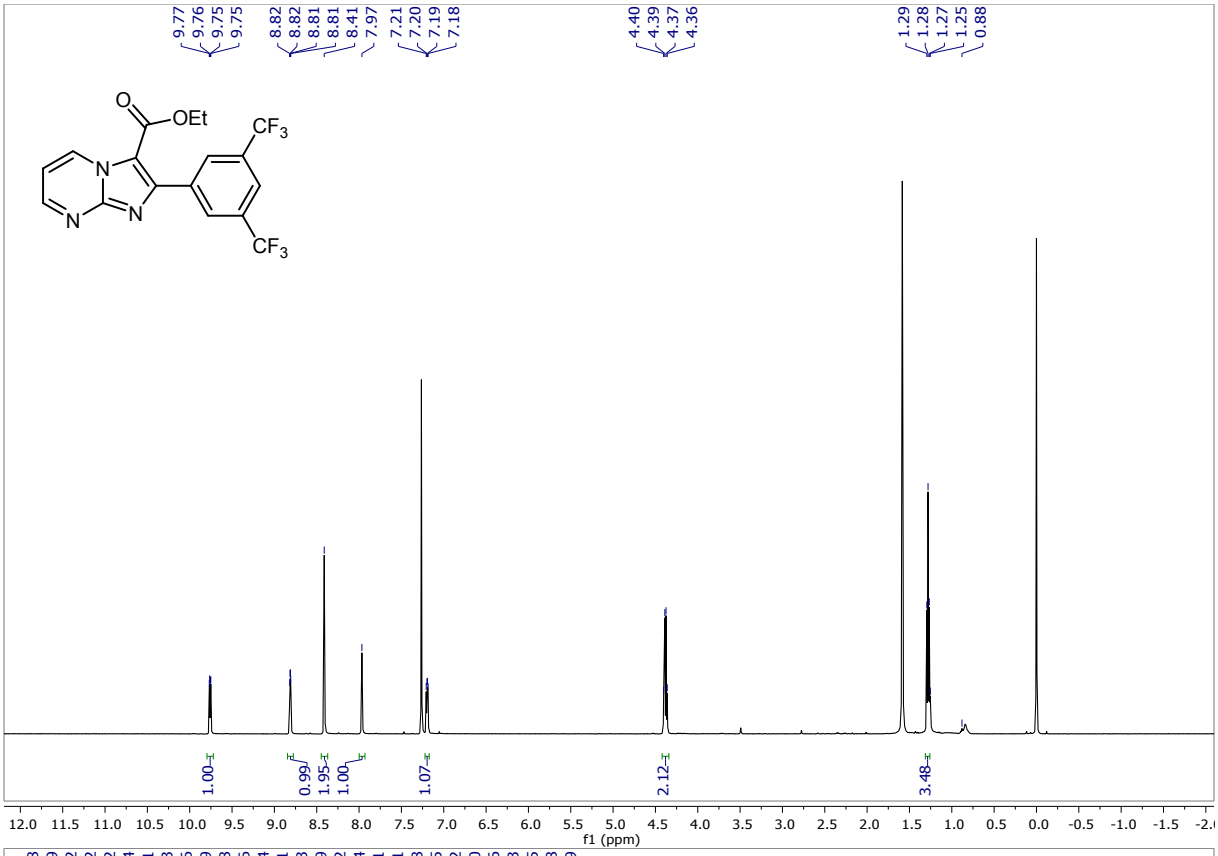
Ethyl 2-(4-bromophenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2o)

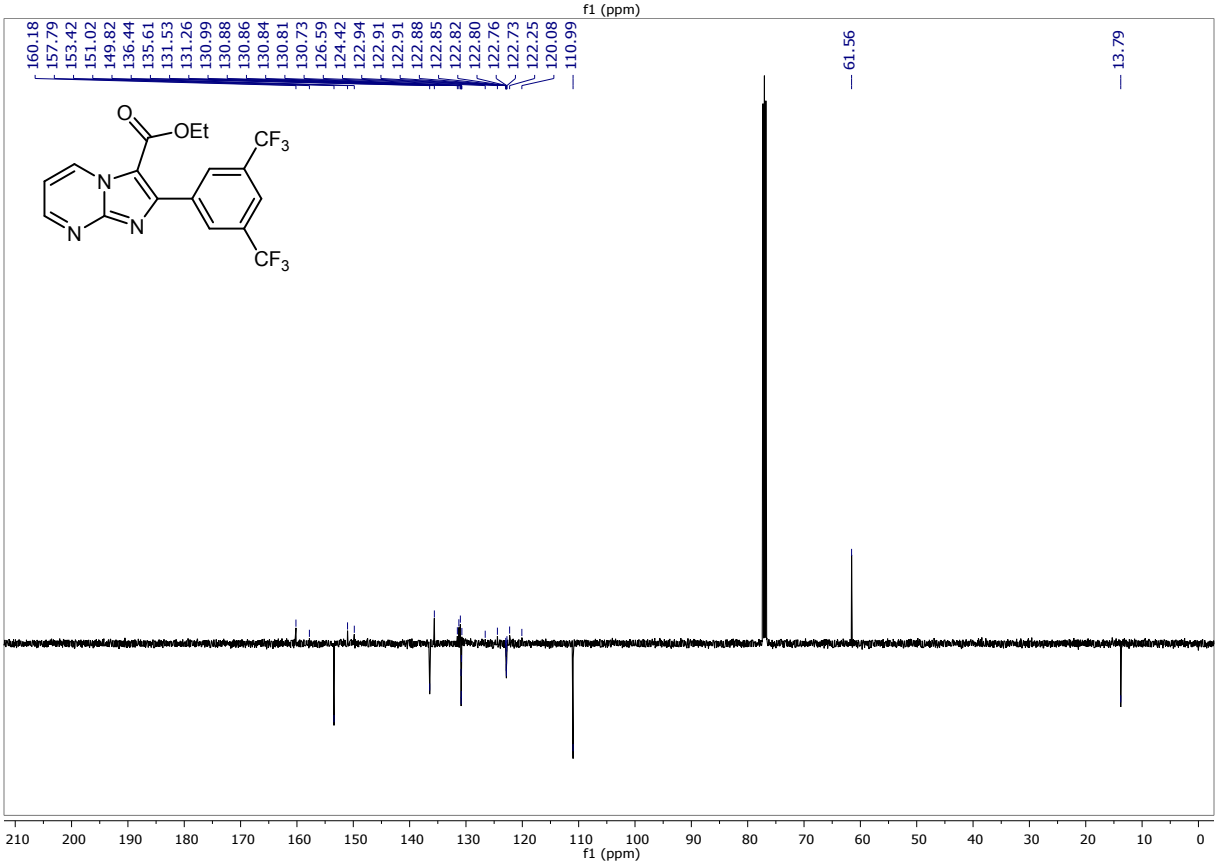


Ethyl 2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2p)

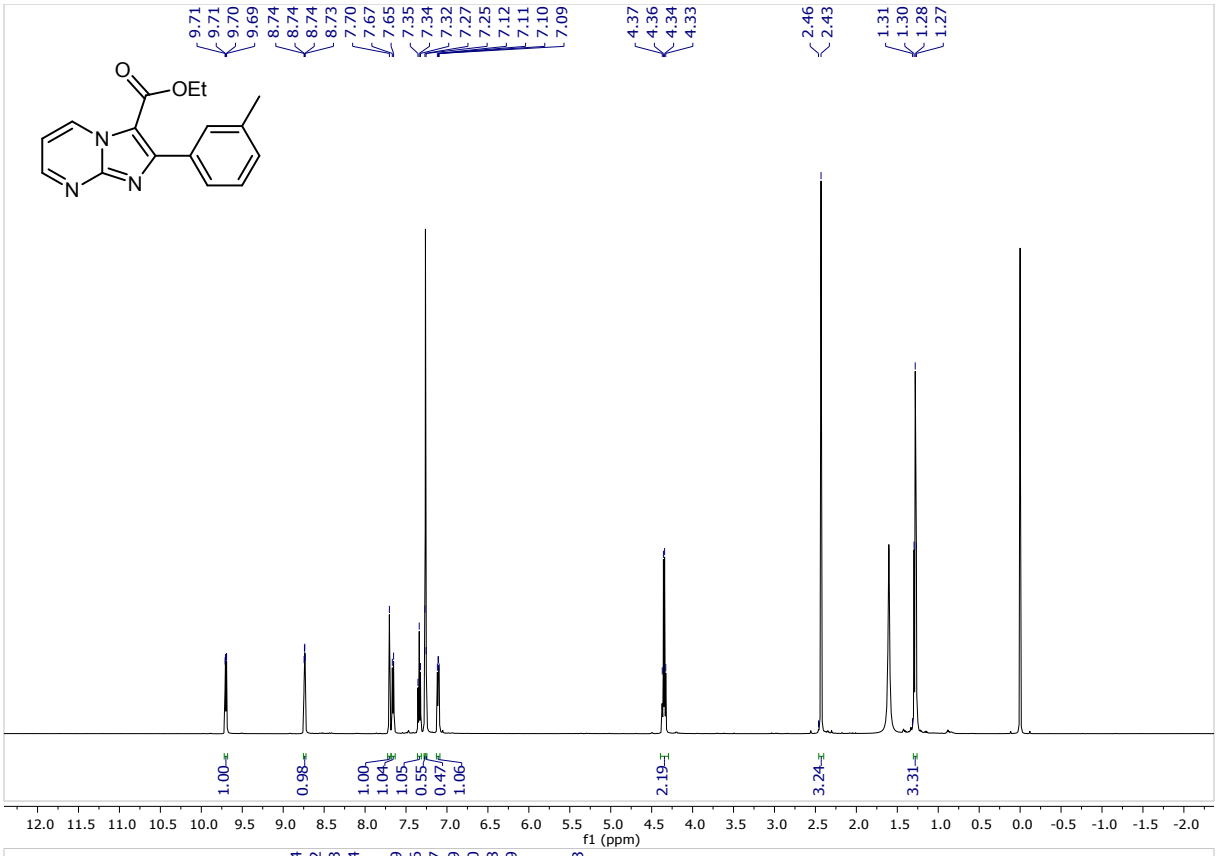


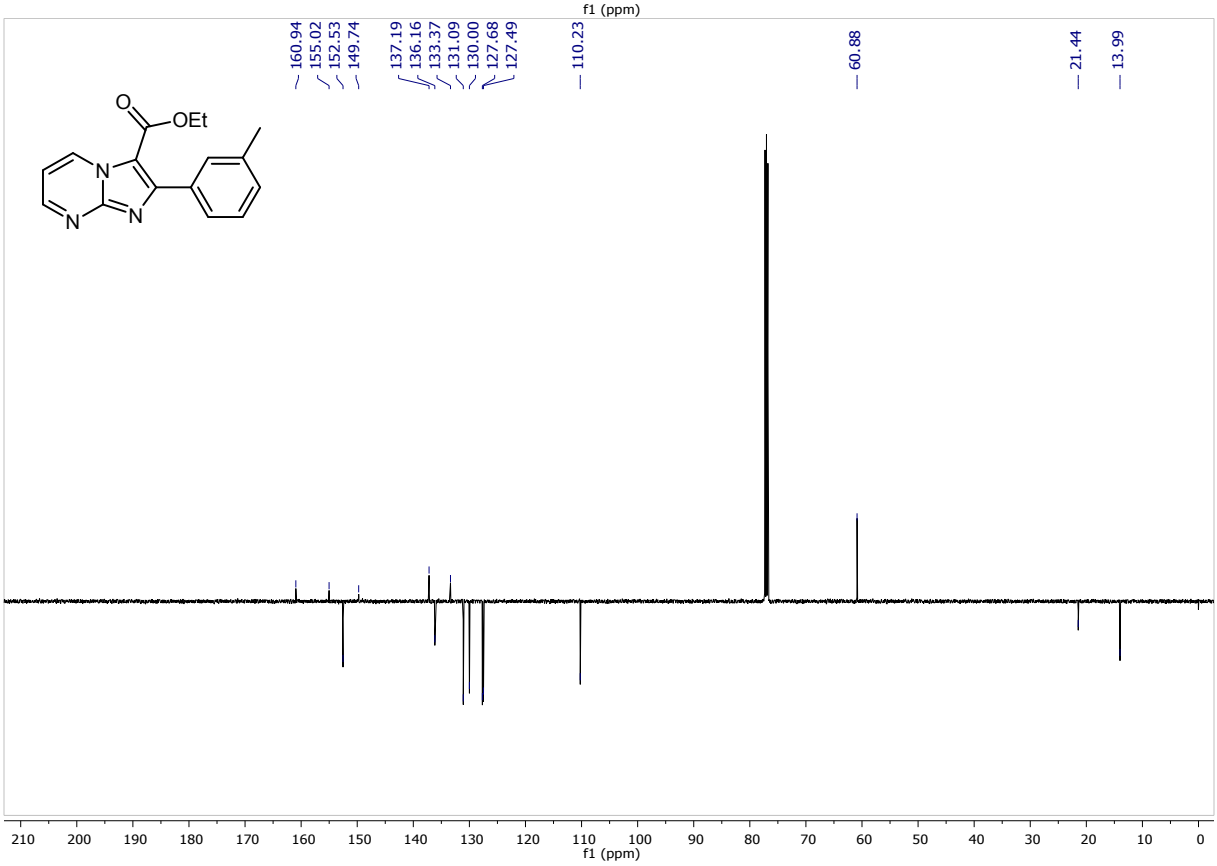
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2q)



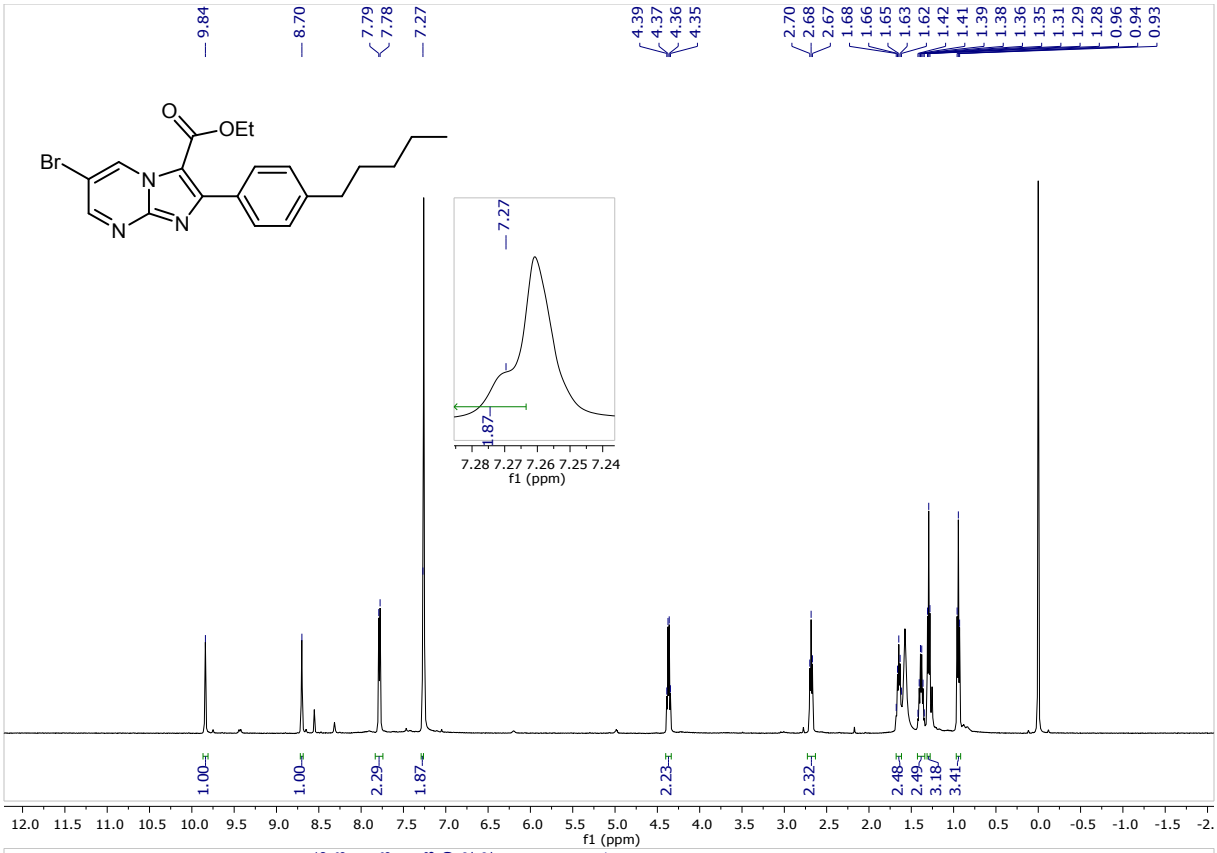


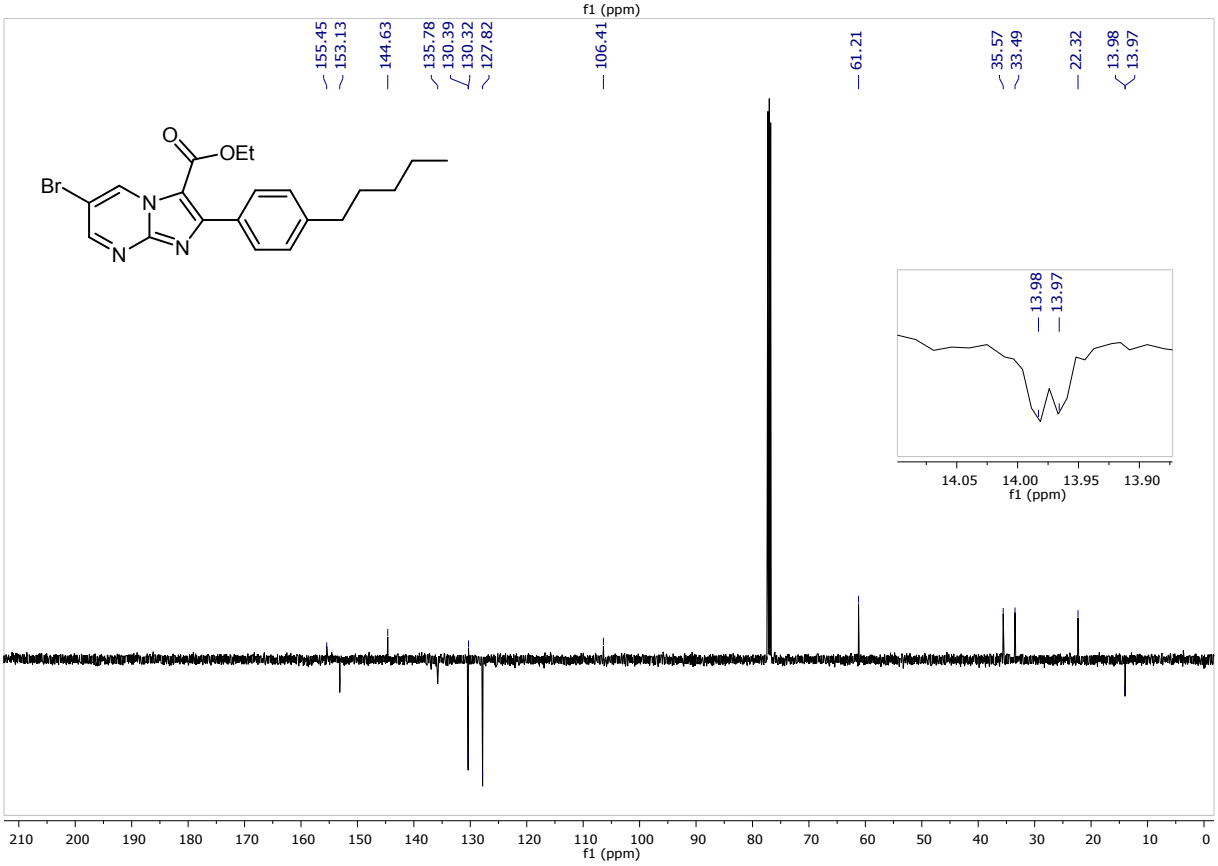
Ethyl 2-(m-tolyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2r)



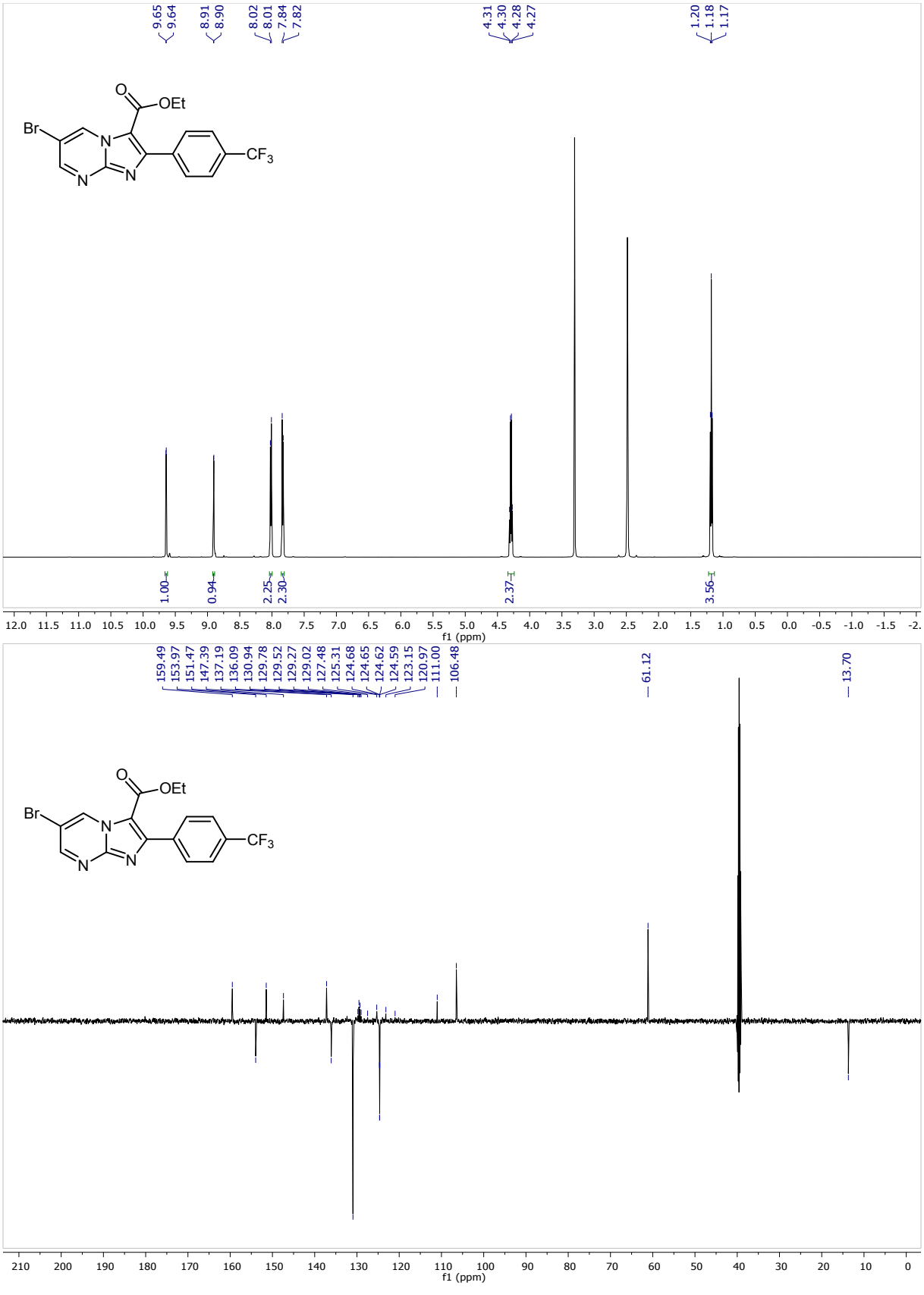


Ethyl 6-bromo-2-(4-butylphenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2s)

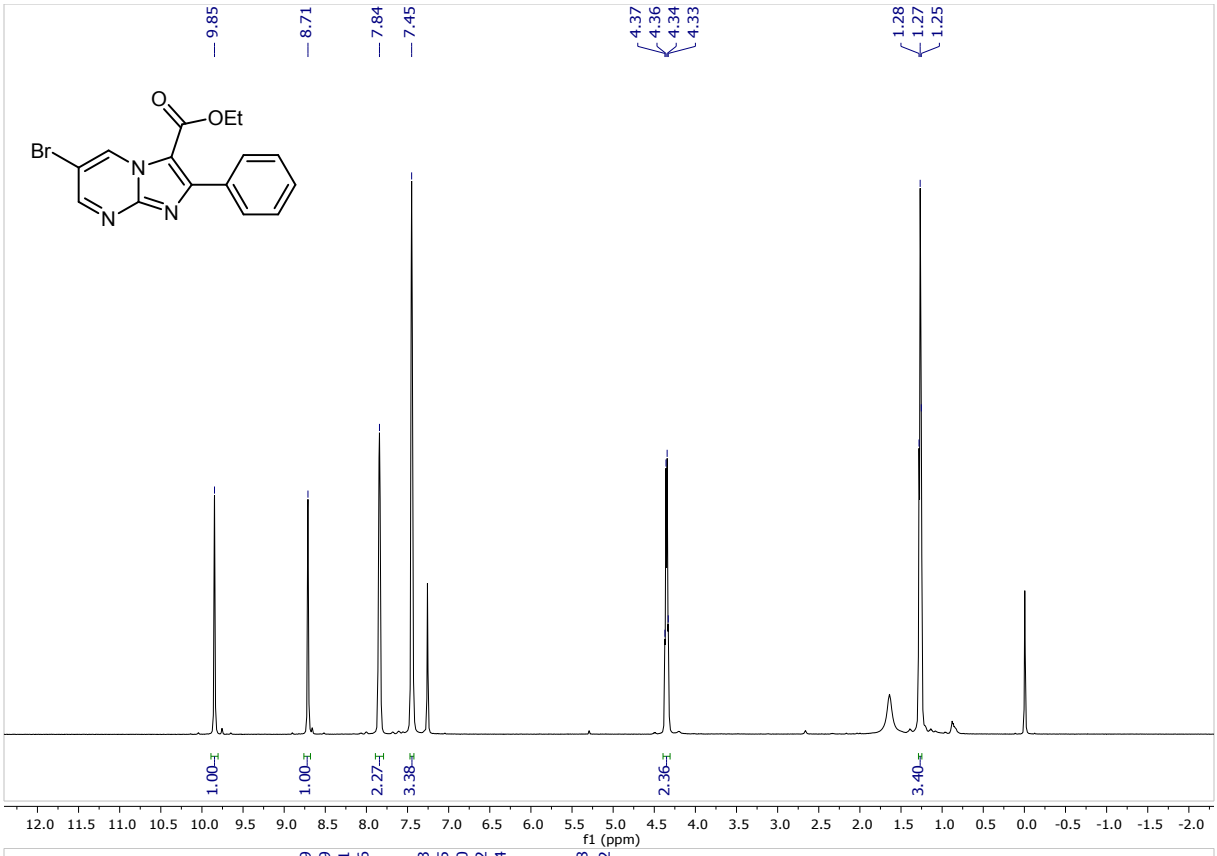


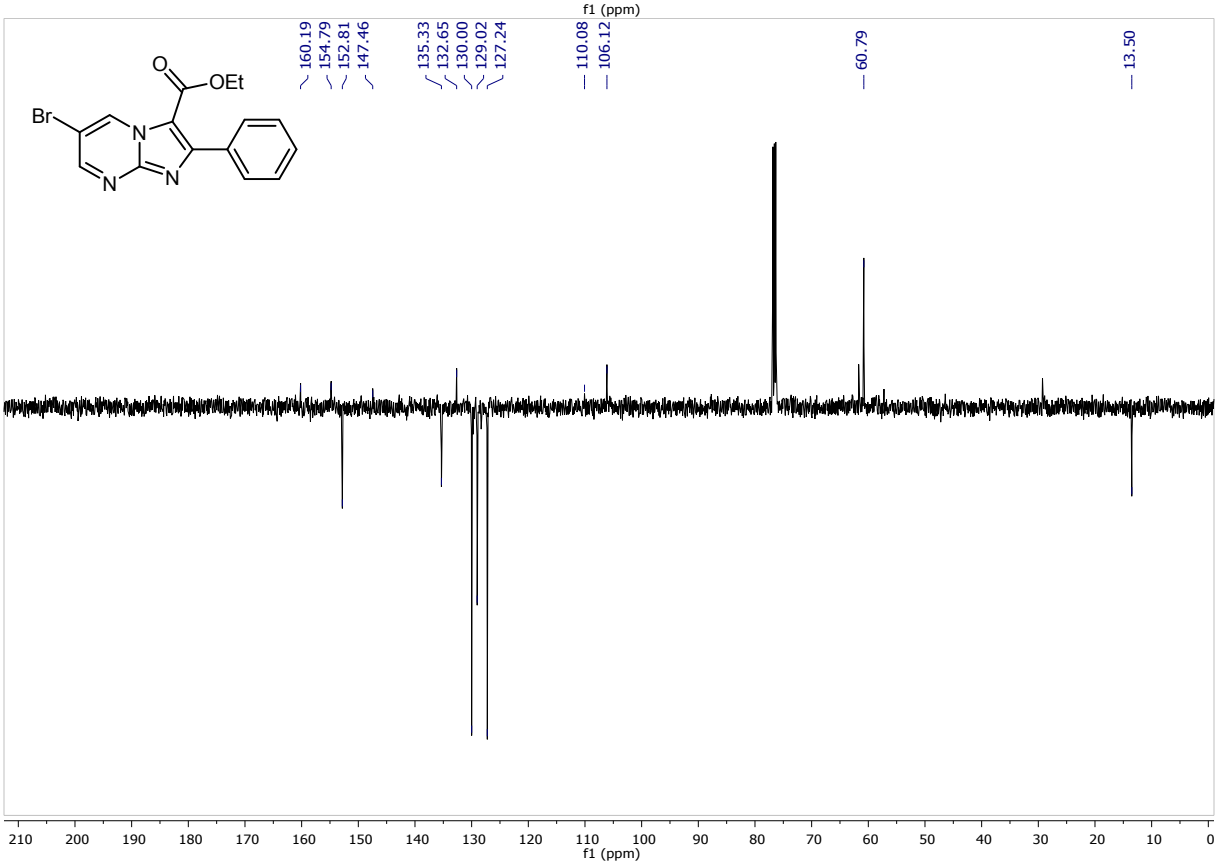


Ethyl 6-bromo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2t)

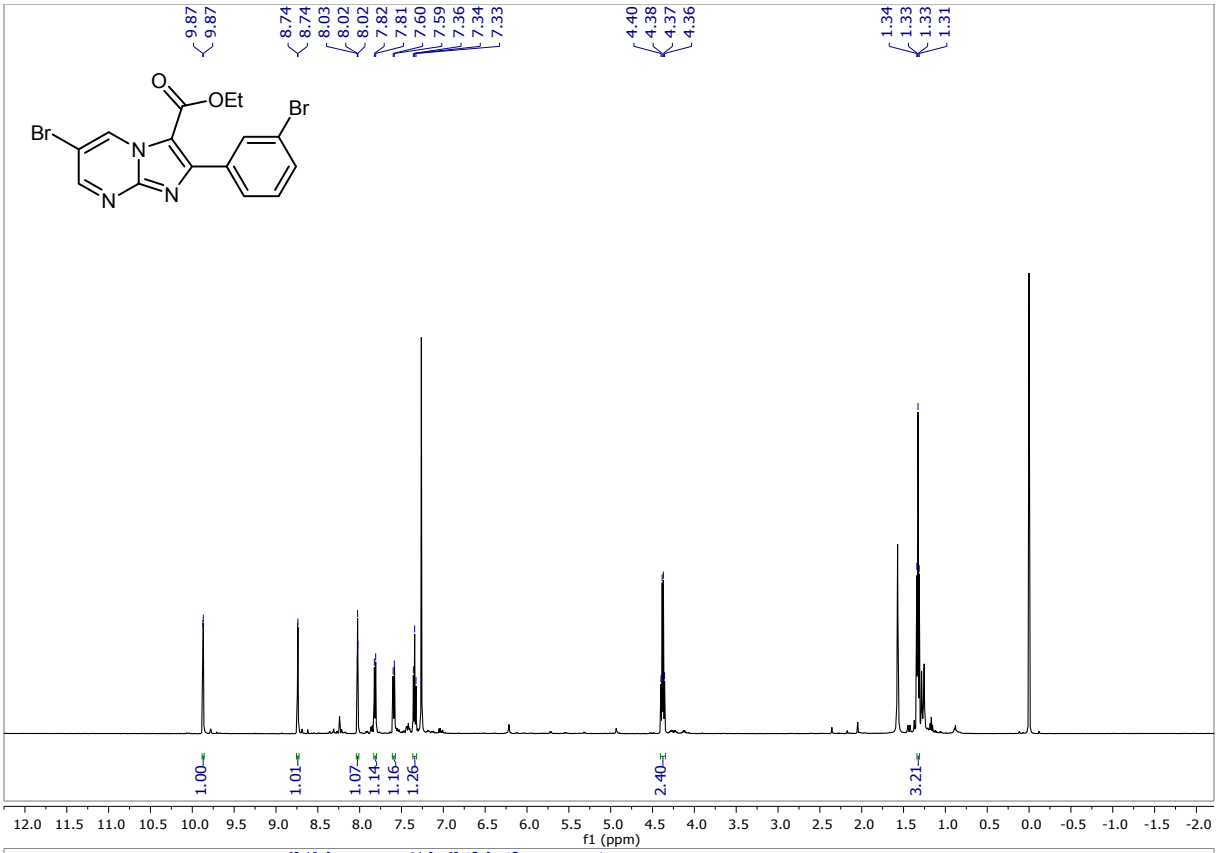


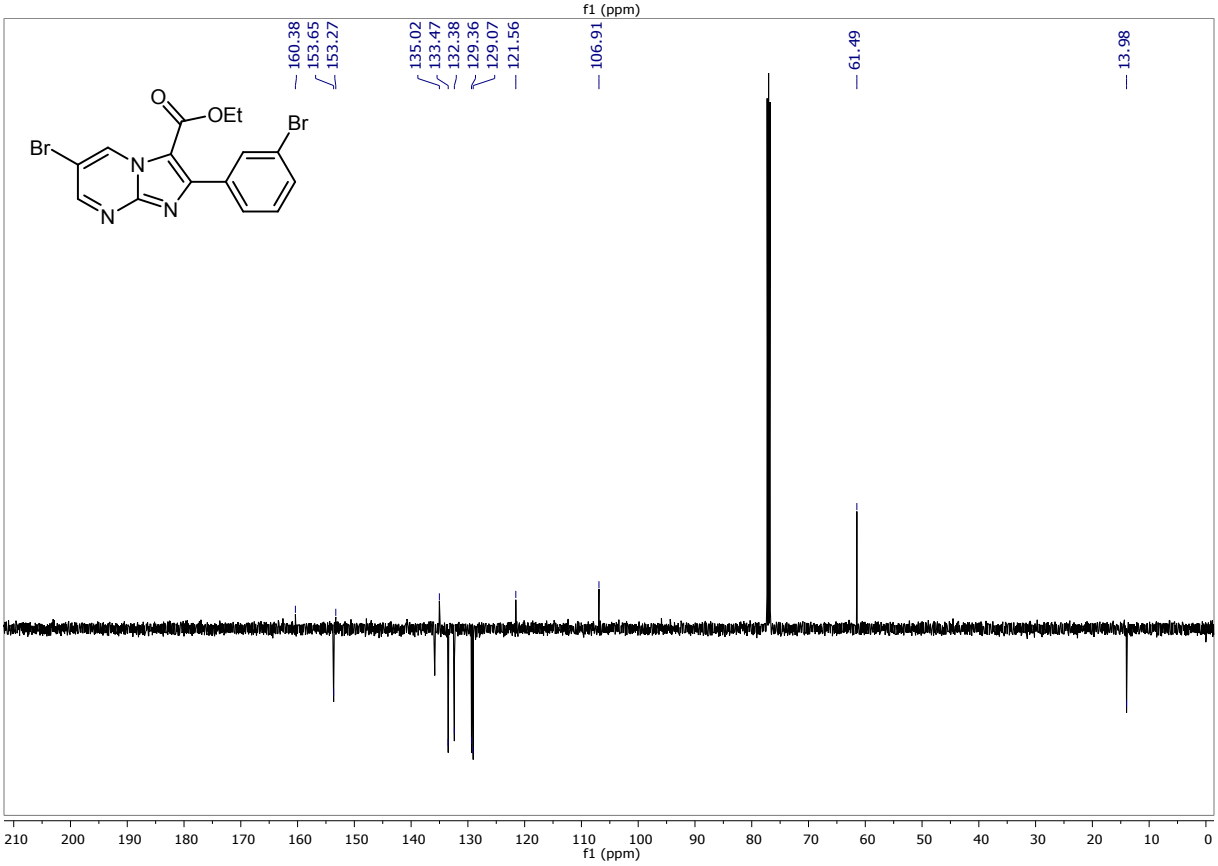
Ethyl 6-bromo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2u)



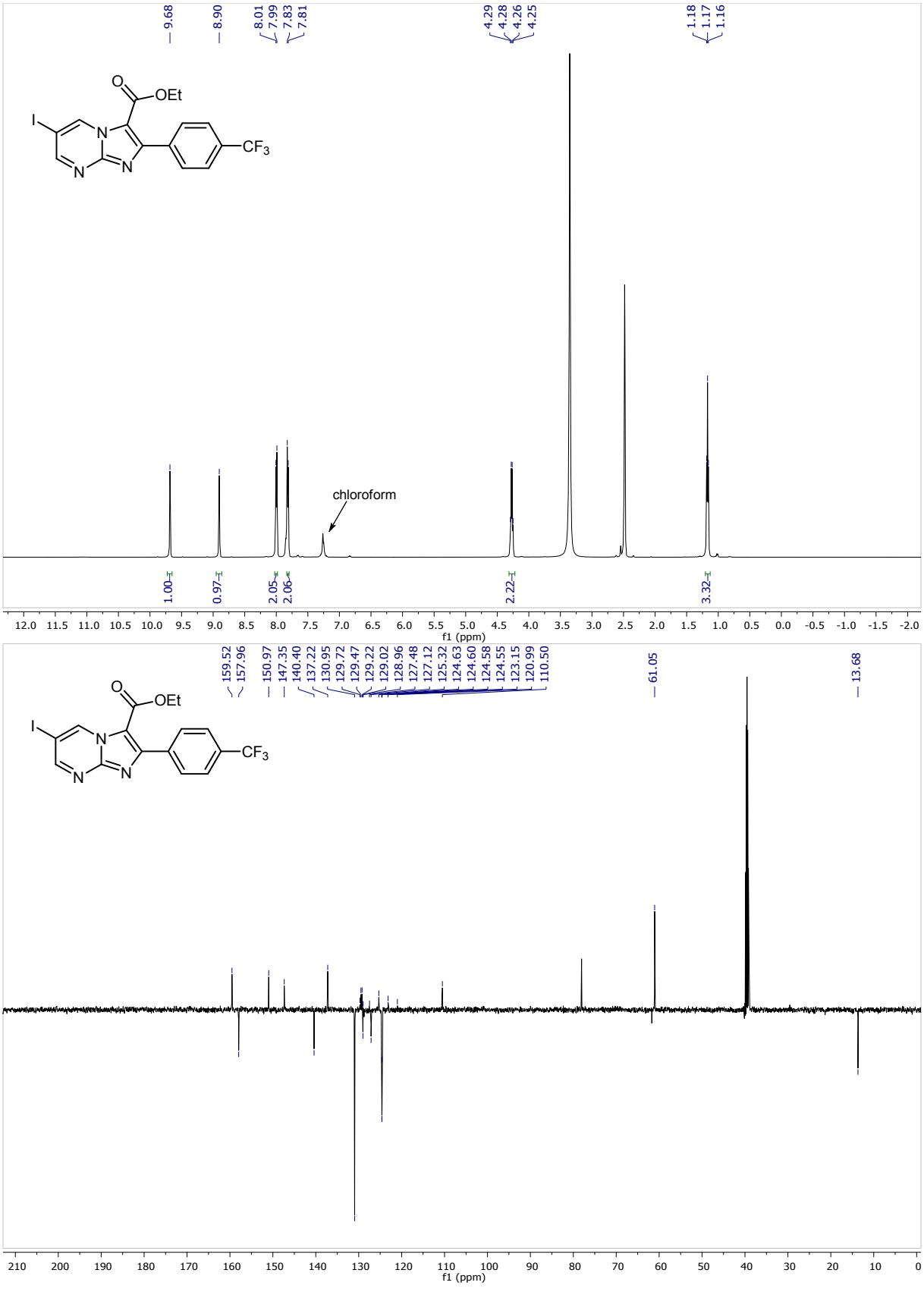


Ethyl 6-bromo-2-(3-bromophenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2v)

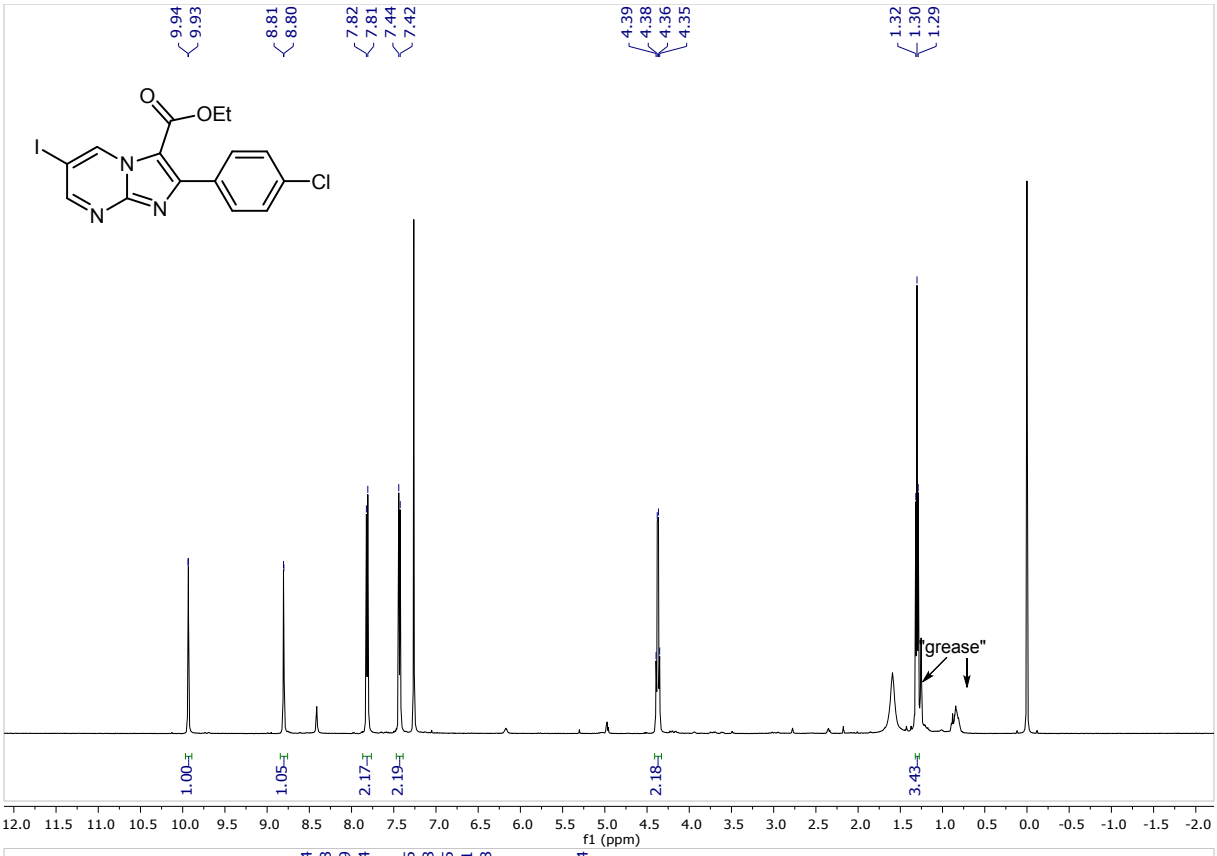


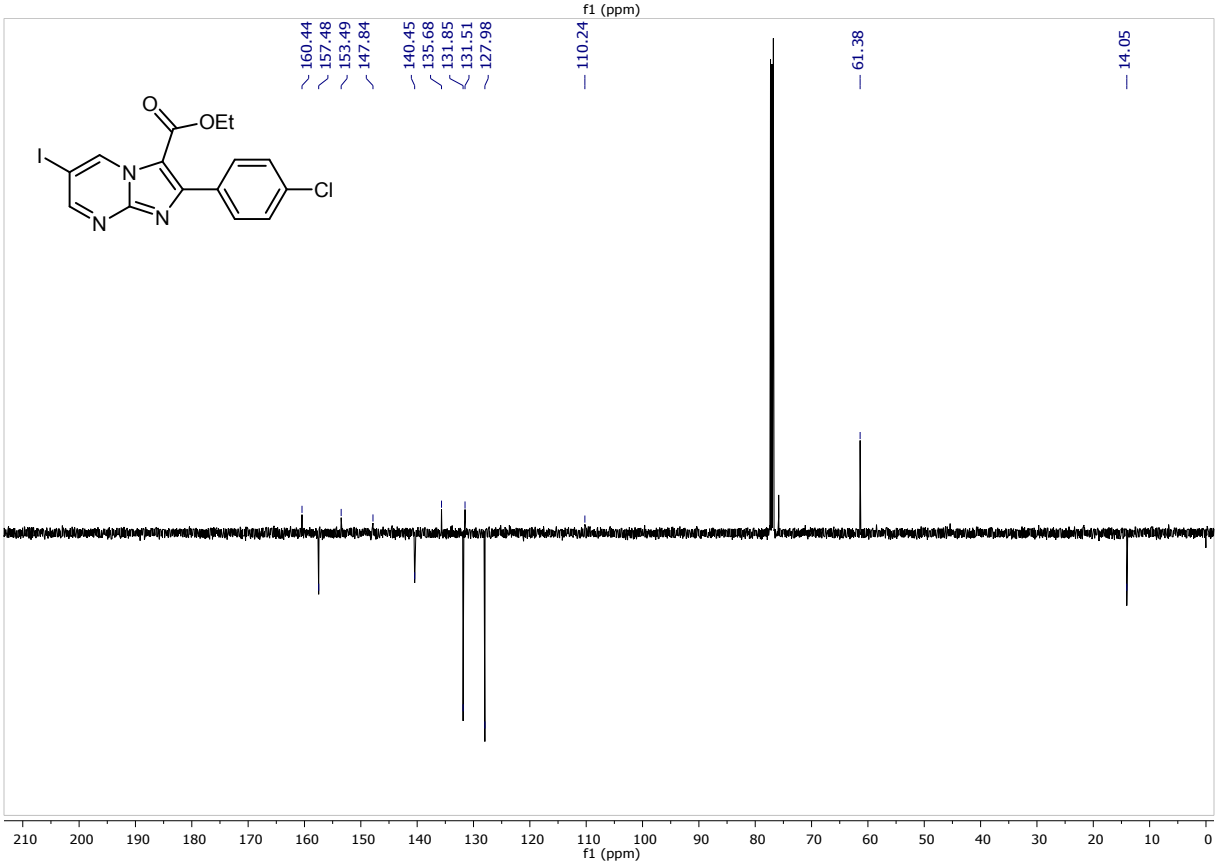


Ethyl 6-iodo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylate (2w)

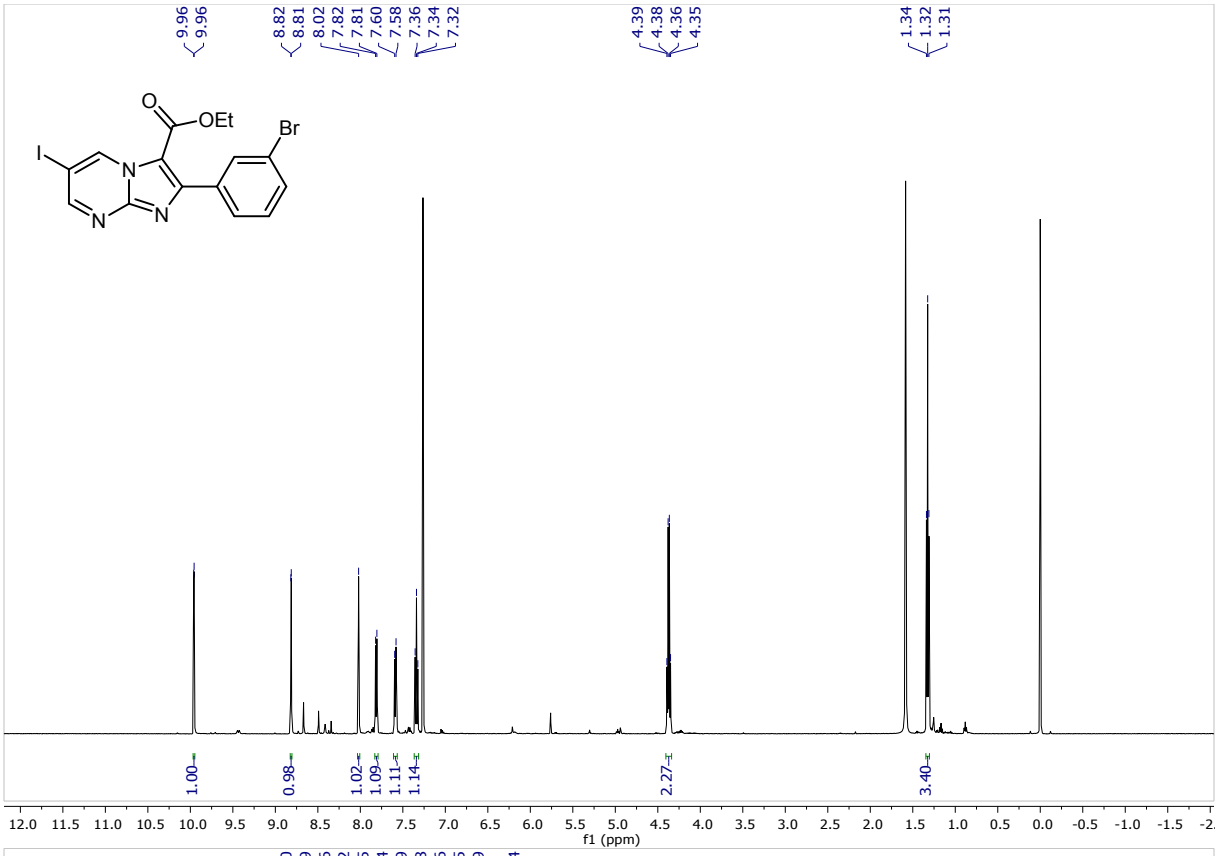


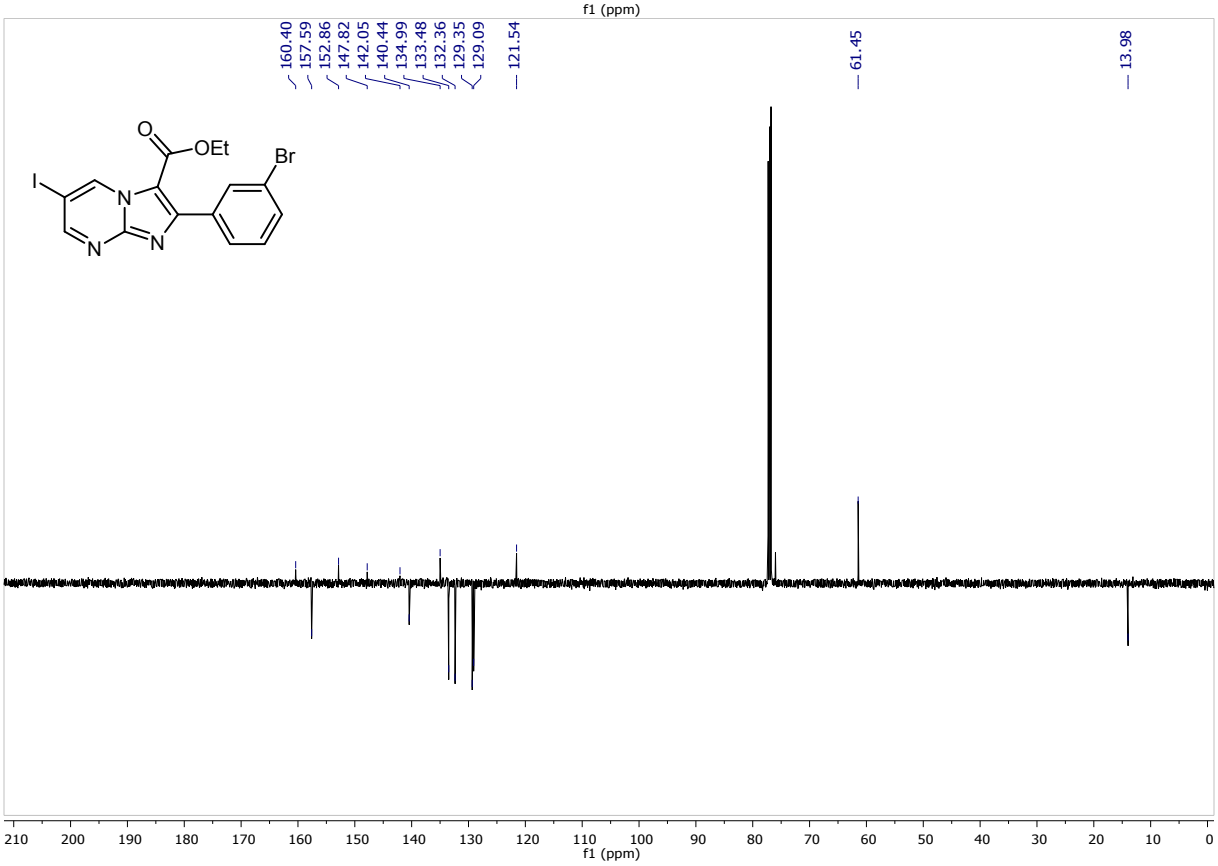
Ethyl 2-(4-chlorophenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2x)



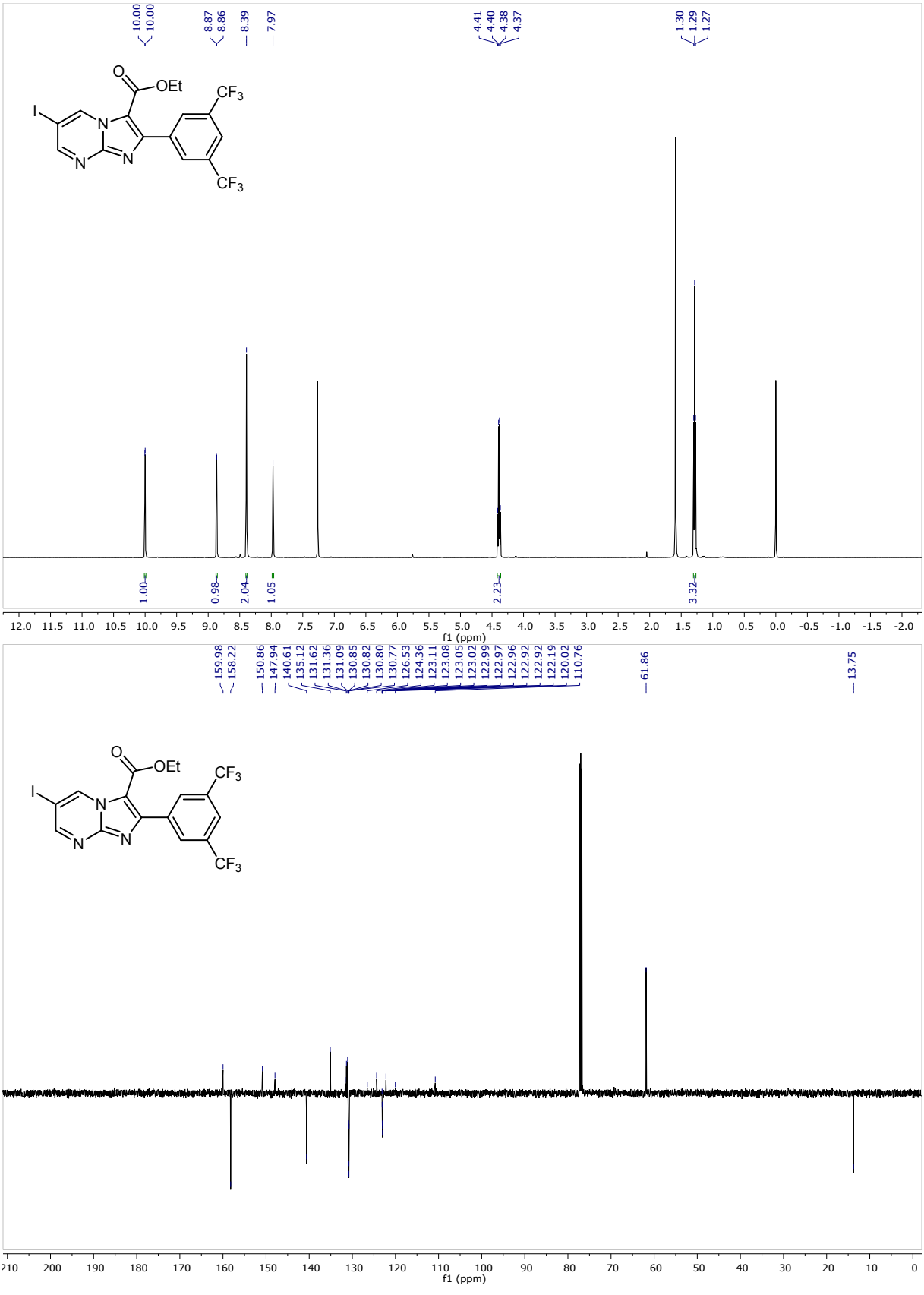


Ethyl 2-(3-bromophenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2y)

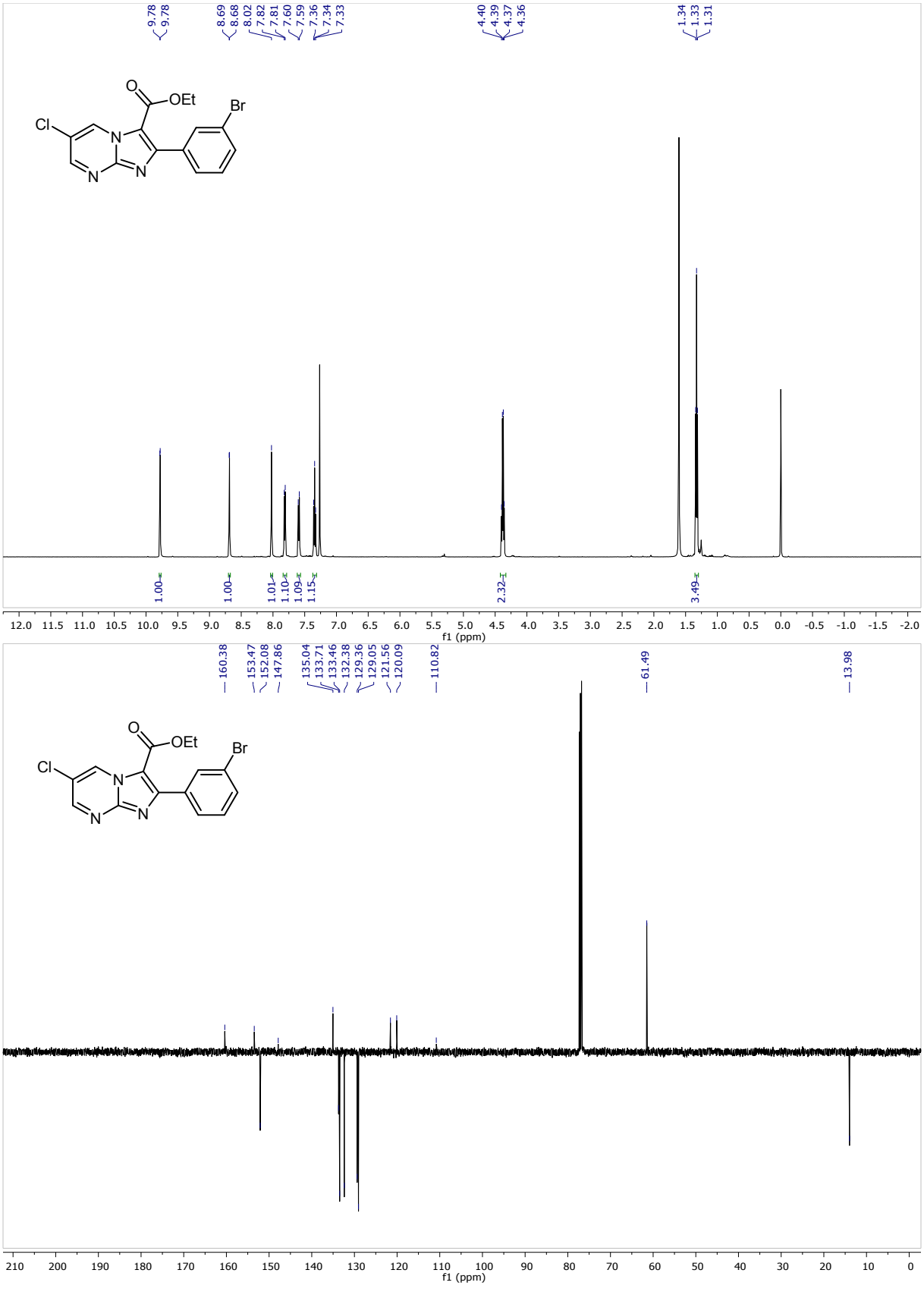




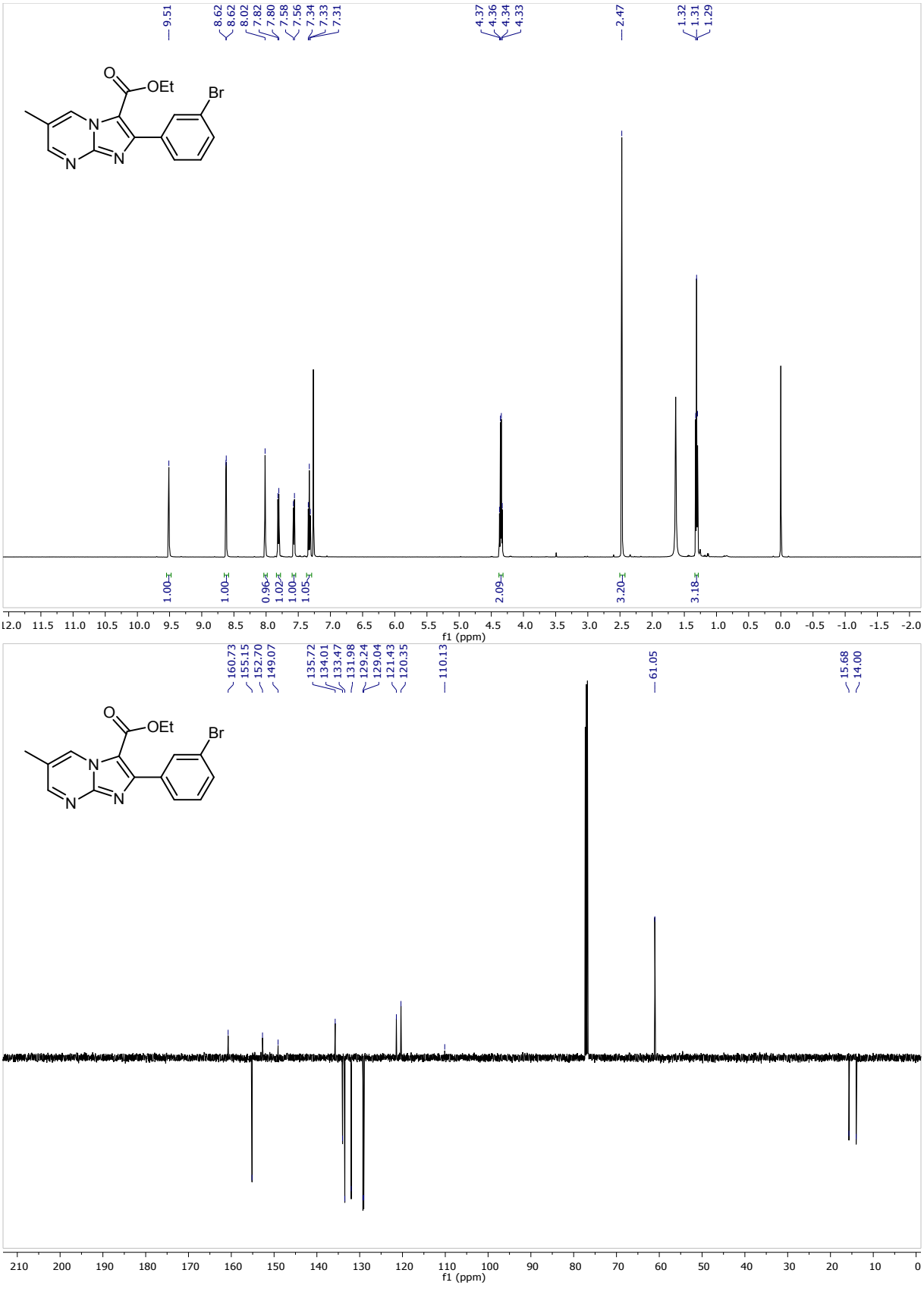
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-iodoimidazo[1,2-*a*]pyrimidine-3-carboxylate (2z)



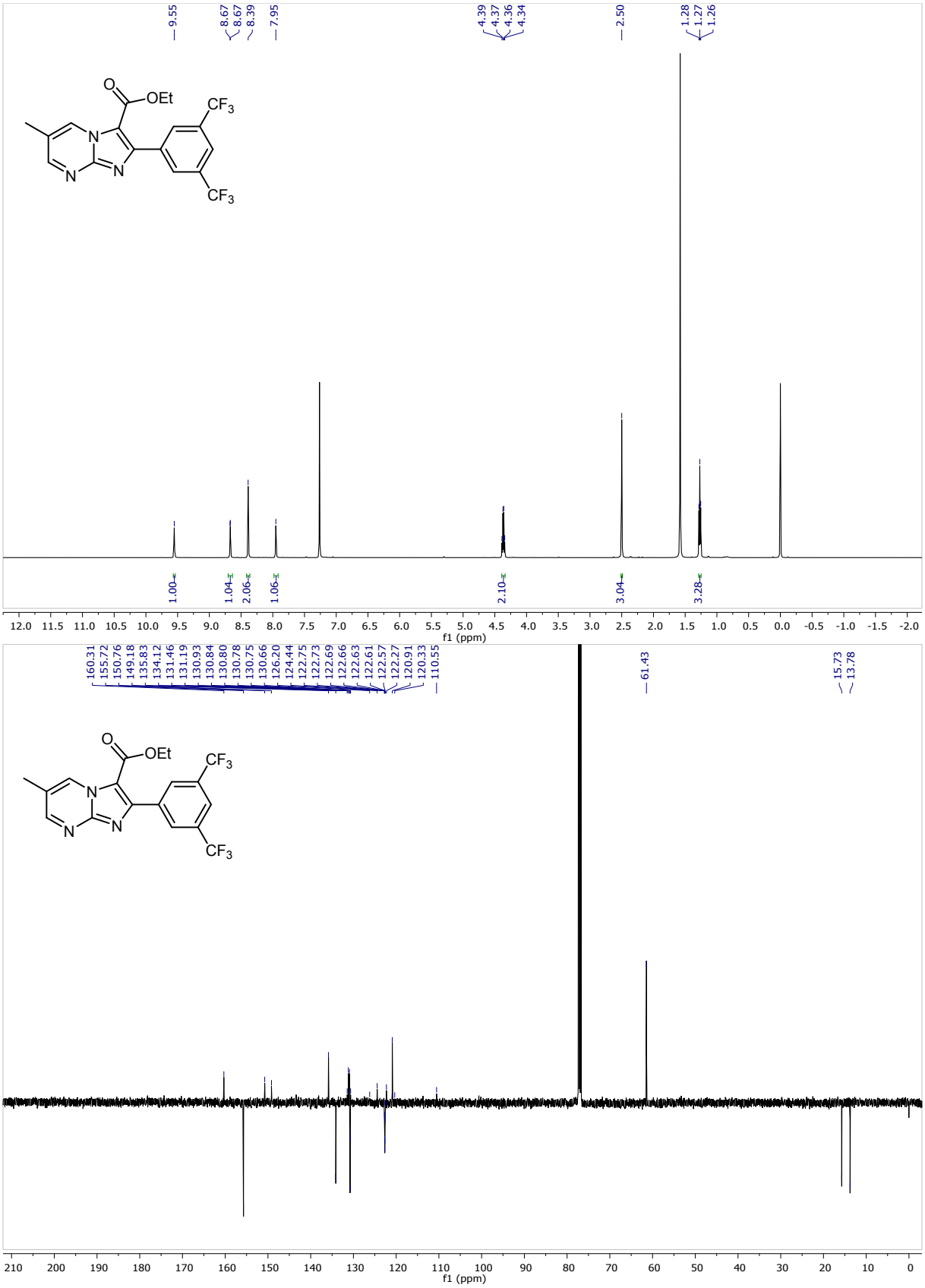
Ethyl 2-(3-bromophenyl)-6-chloroimidazo[1,2-*a*]pyrimidine-3-carboxylate (2aa)



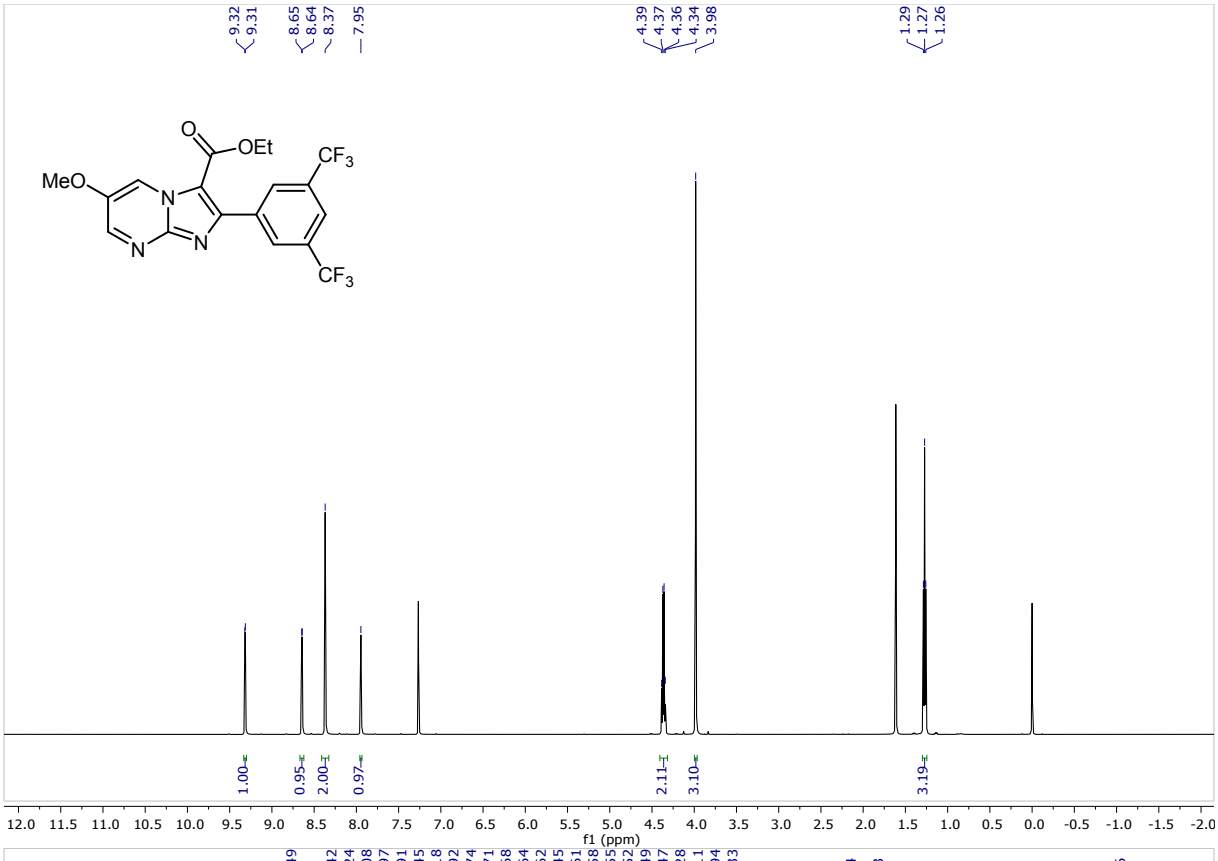
Ethyl 2-(3-bromophenyl)-6-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2bb)

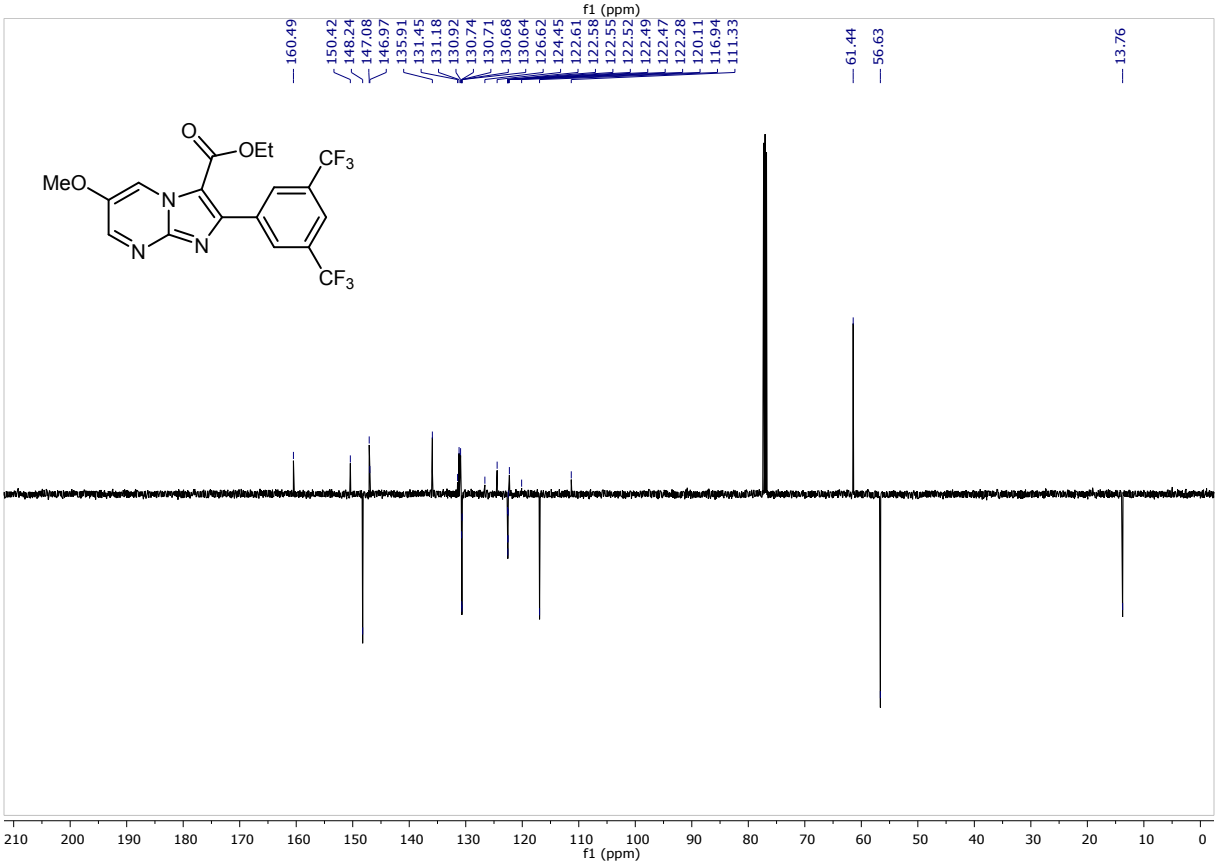


Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-methylimidazo[1,2-*a*]pyrimidine-3-carboxylate (2cc)

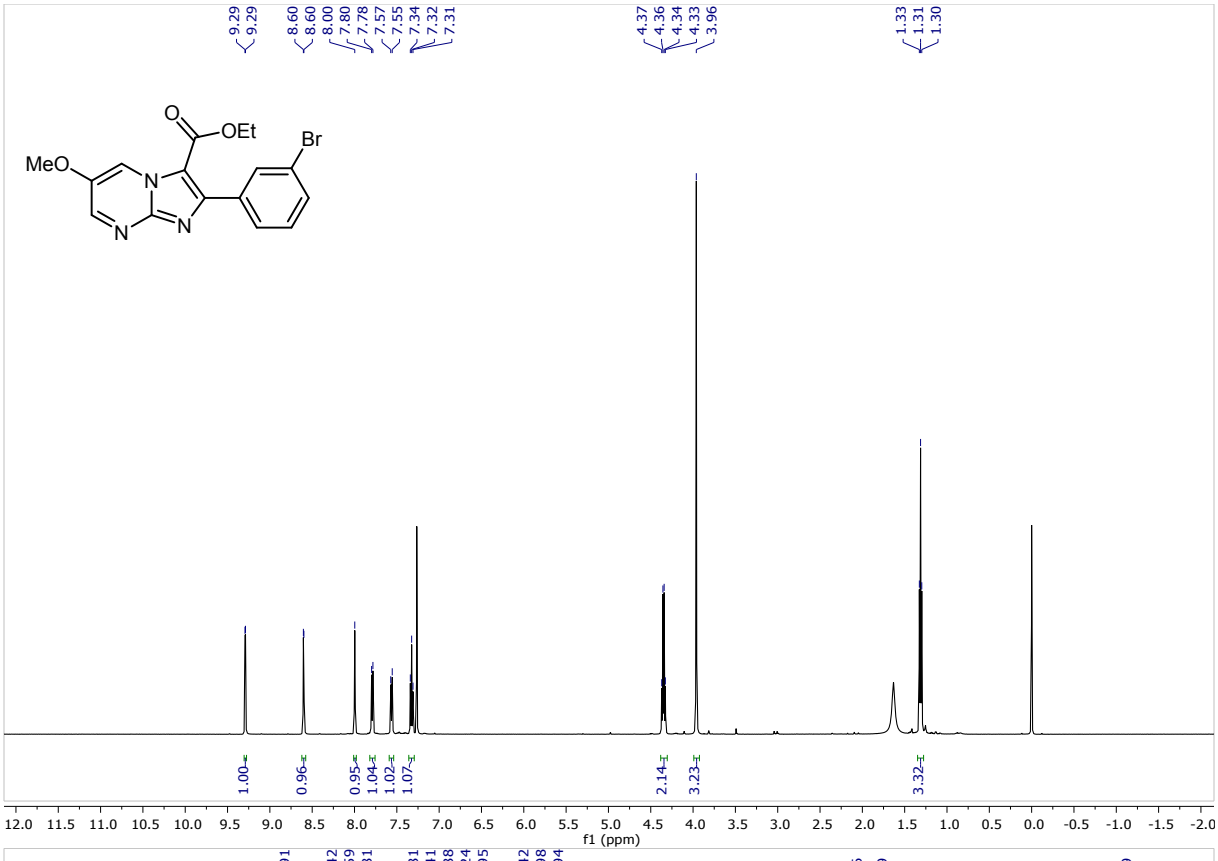


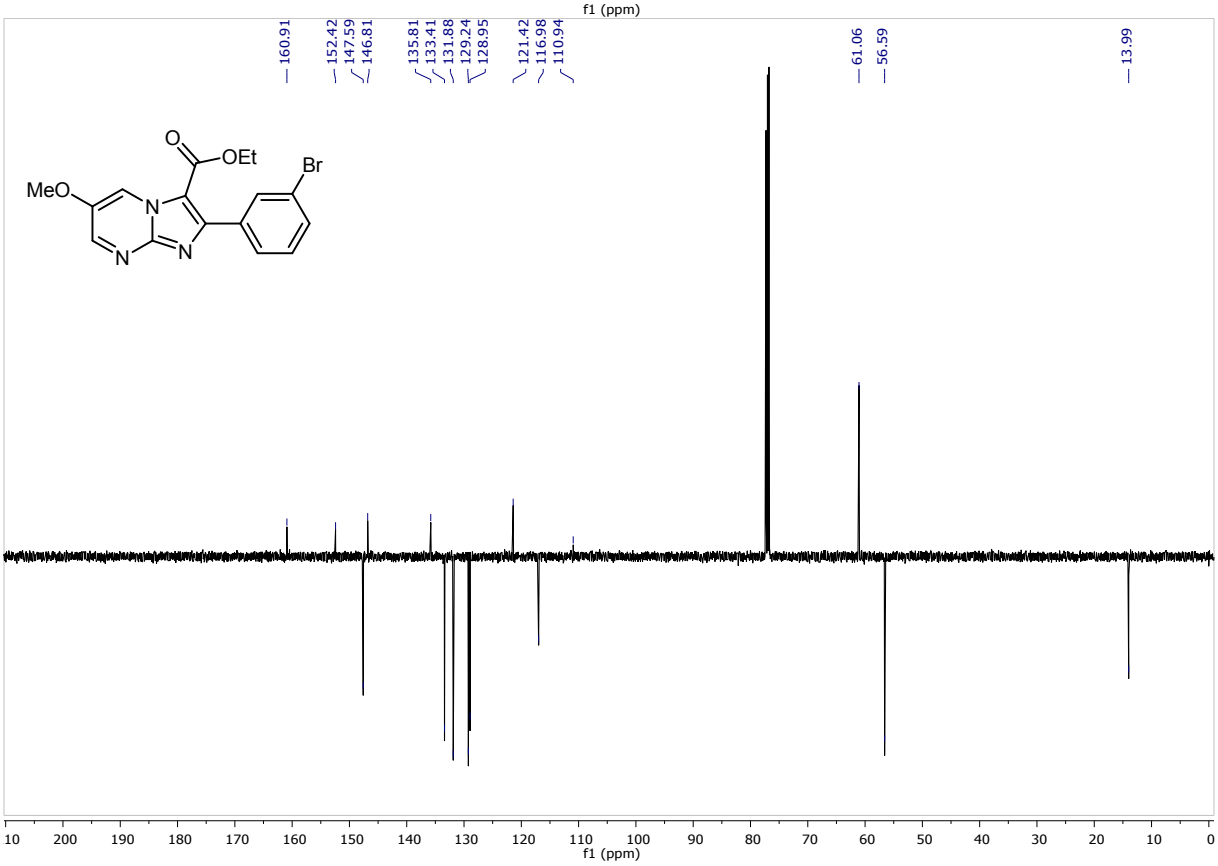
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-6-methoxyimidazo[1,2-*a*]pyrimidine-3-carboxylate (2dd)



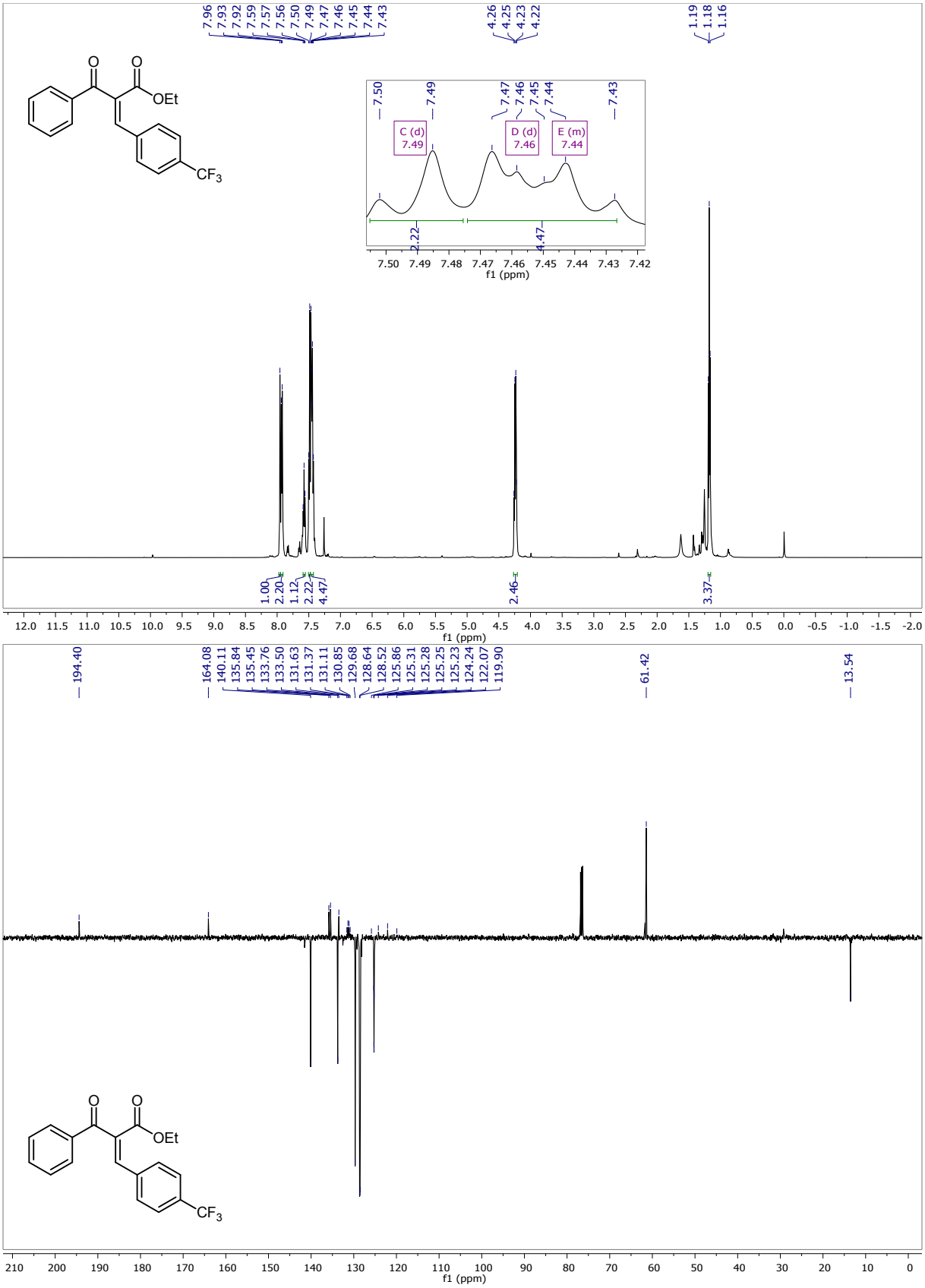


Ethyl 2-(3-bromophenyl)-6-methoxyimidazo[1,2-*a*]pyrimidine-3-carboxylate (2ee)

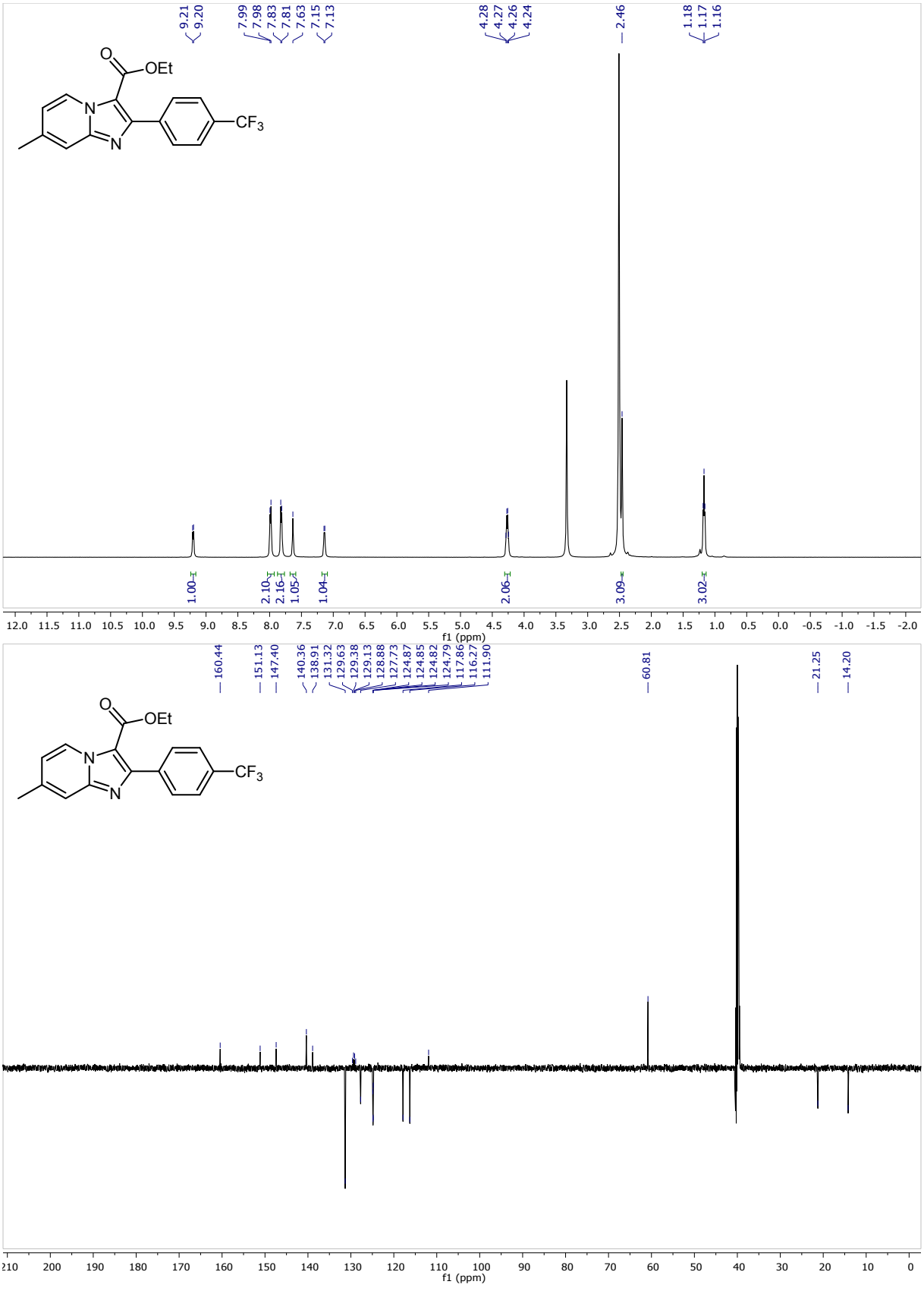




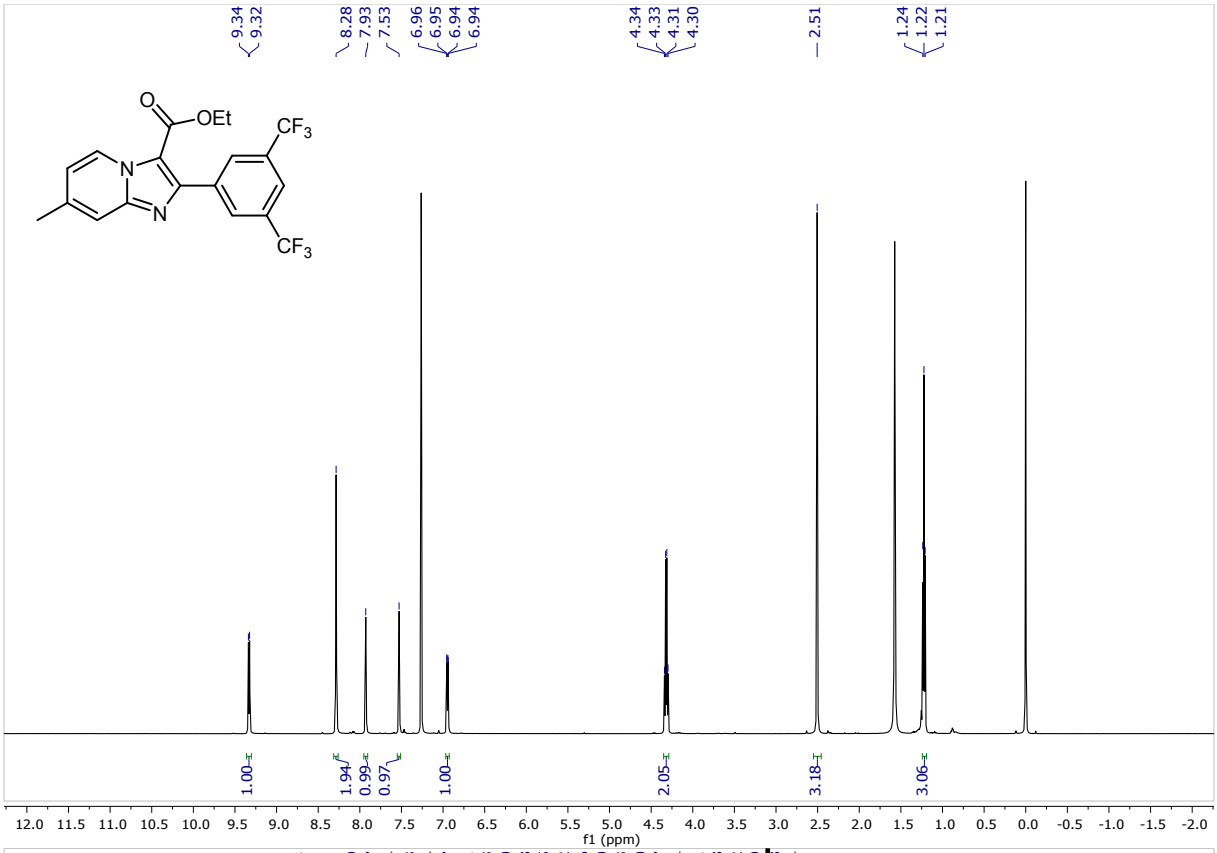
Ethyl 2-benzoyl-3-(4-(trifluoromethyl)phenyl)acrylate (3)

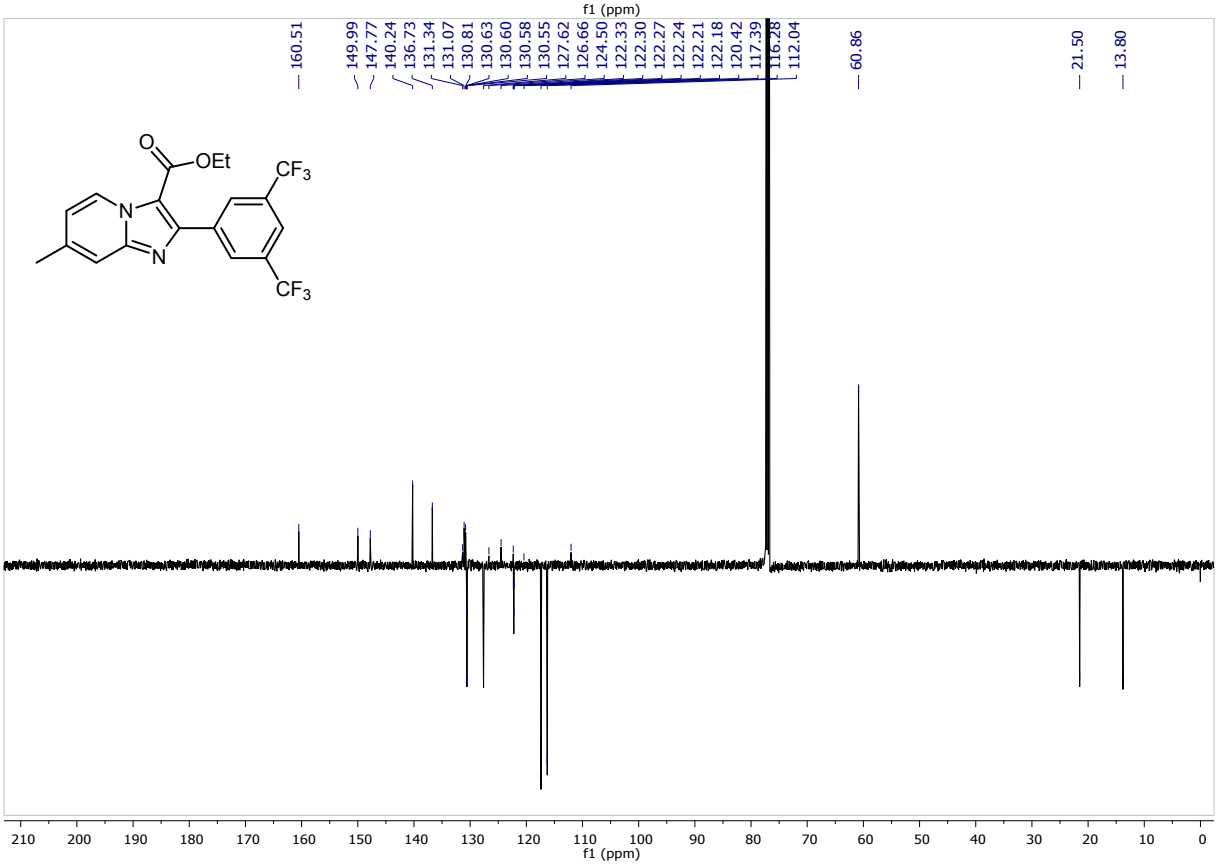


Ethyl 7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylate (6a)

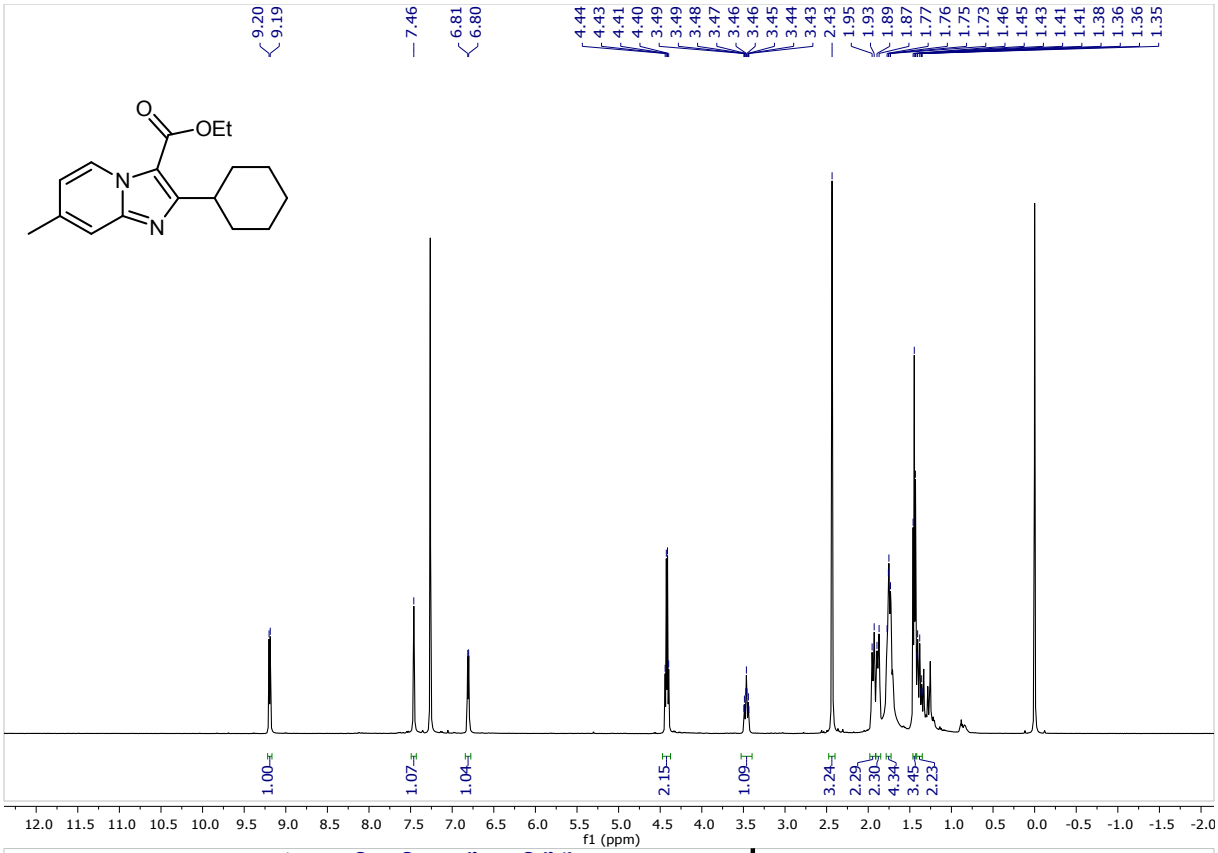


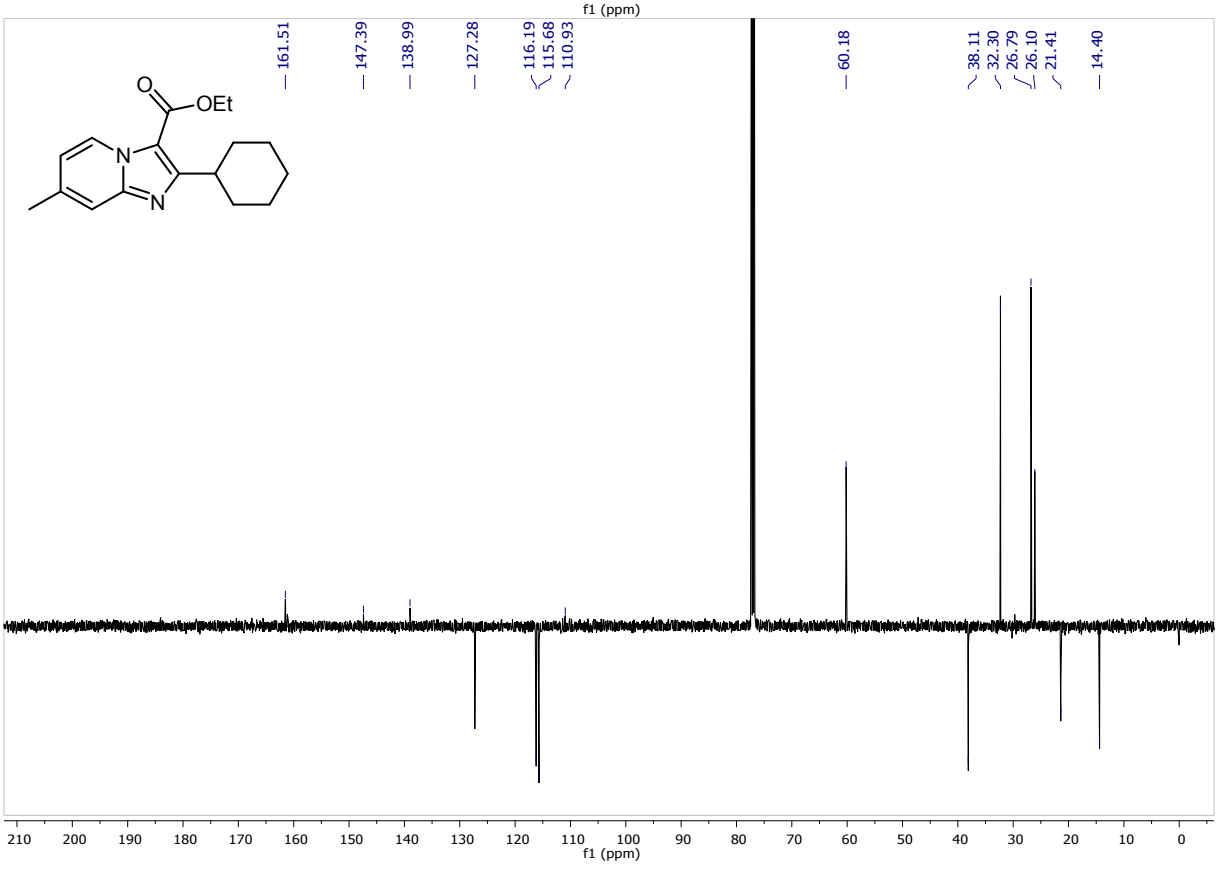
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)-7-methylimidazo[1,2-*a*]pyridine-3-carboxylate (6b)



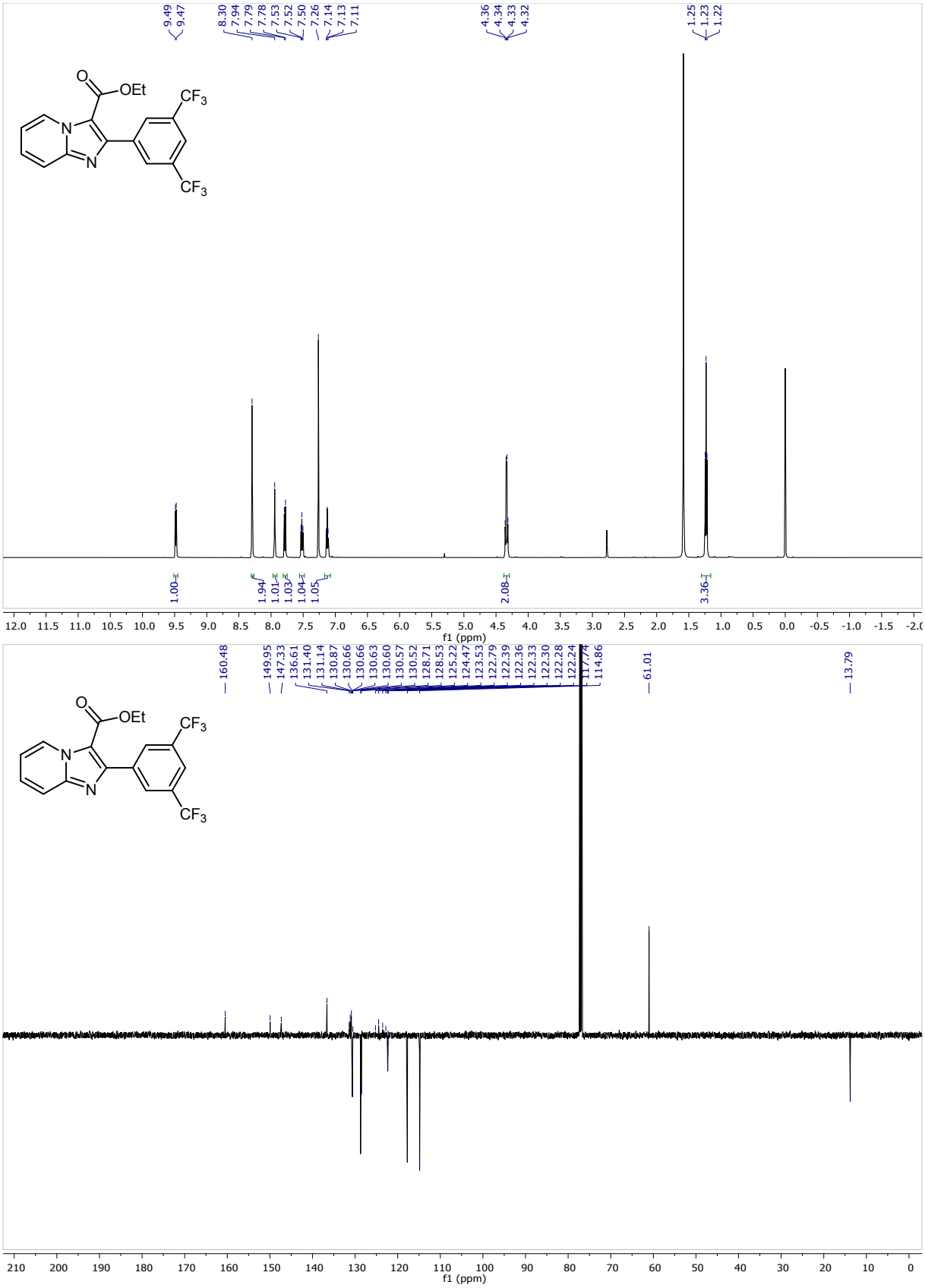


Ethyl 2-cyclohexyl-7-methylimidazo[1,2-*a*]pyridine-3-carboxylate (6c)

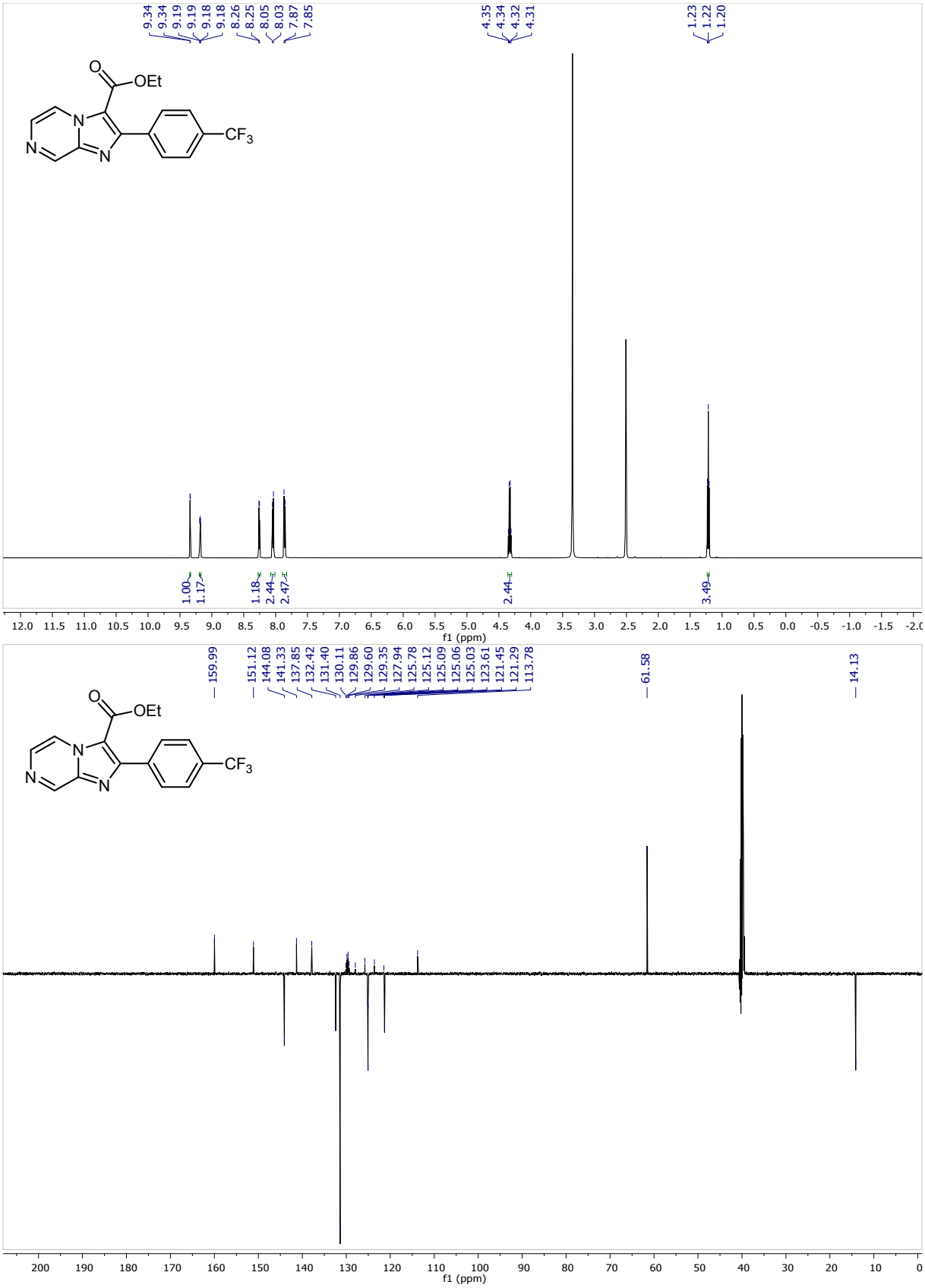




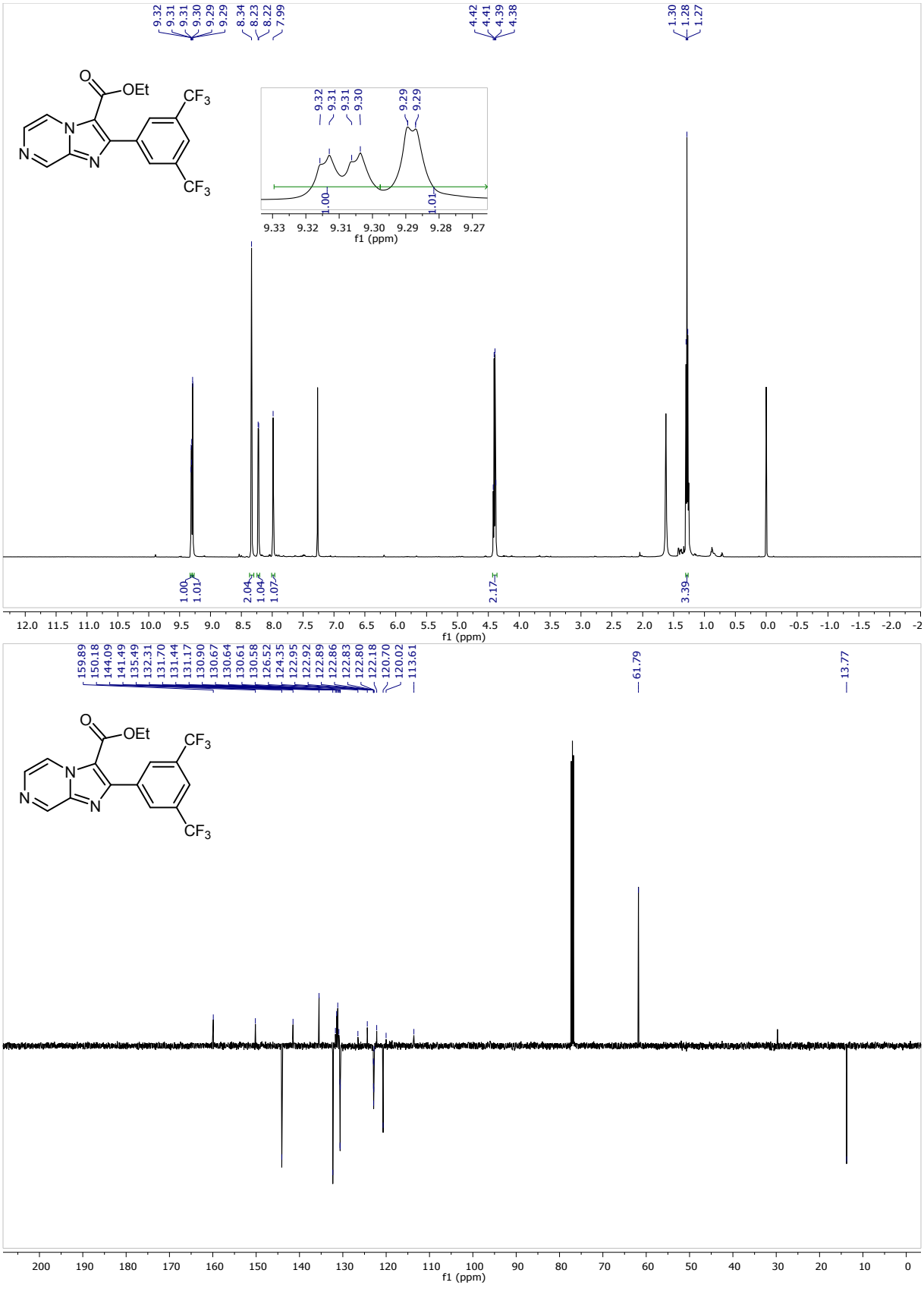
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylate (6d)



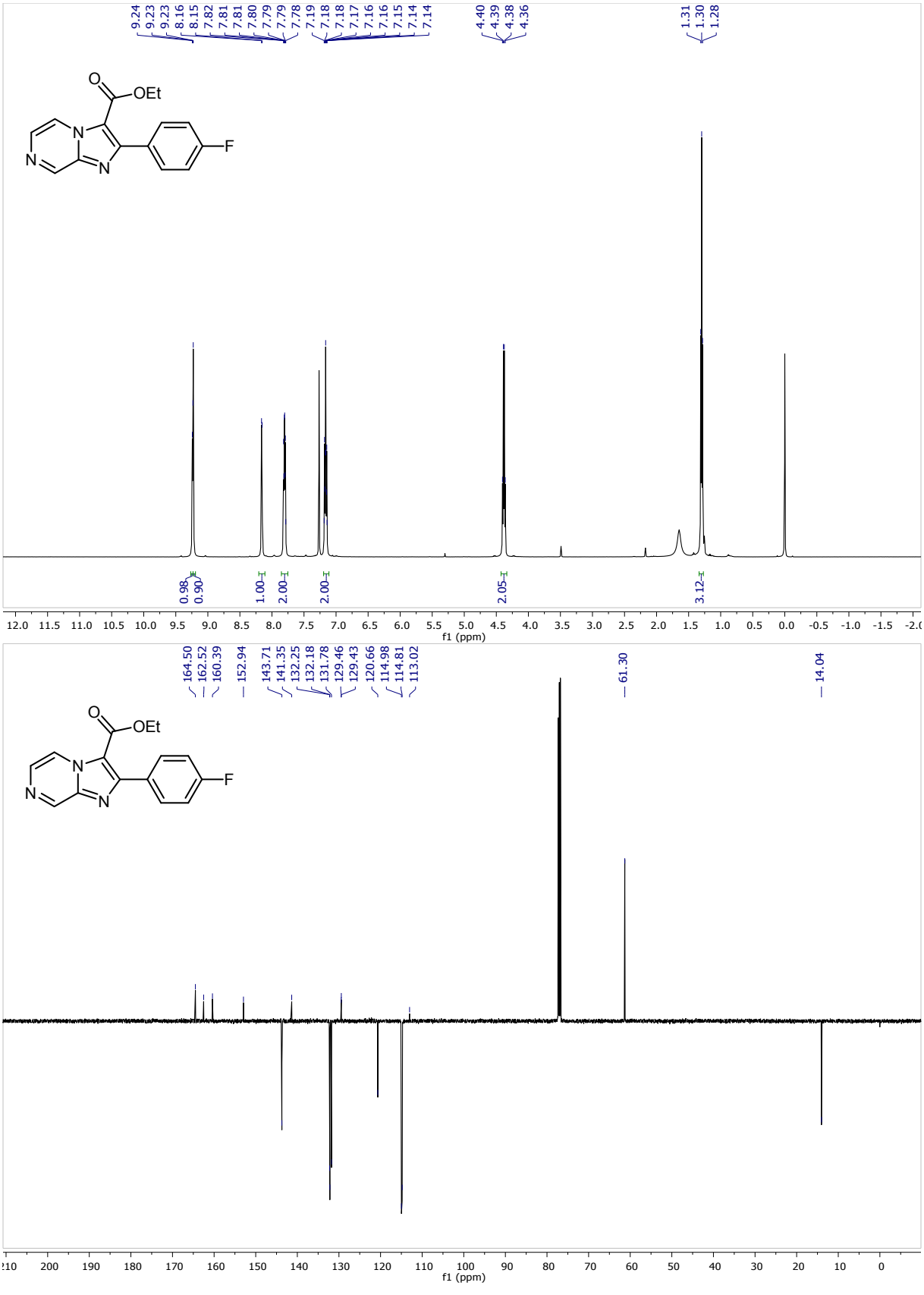
Ethyl 2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7a)



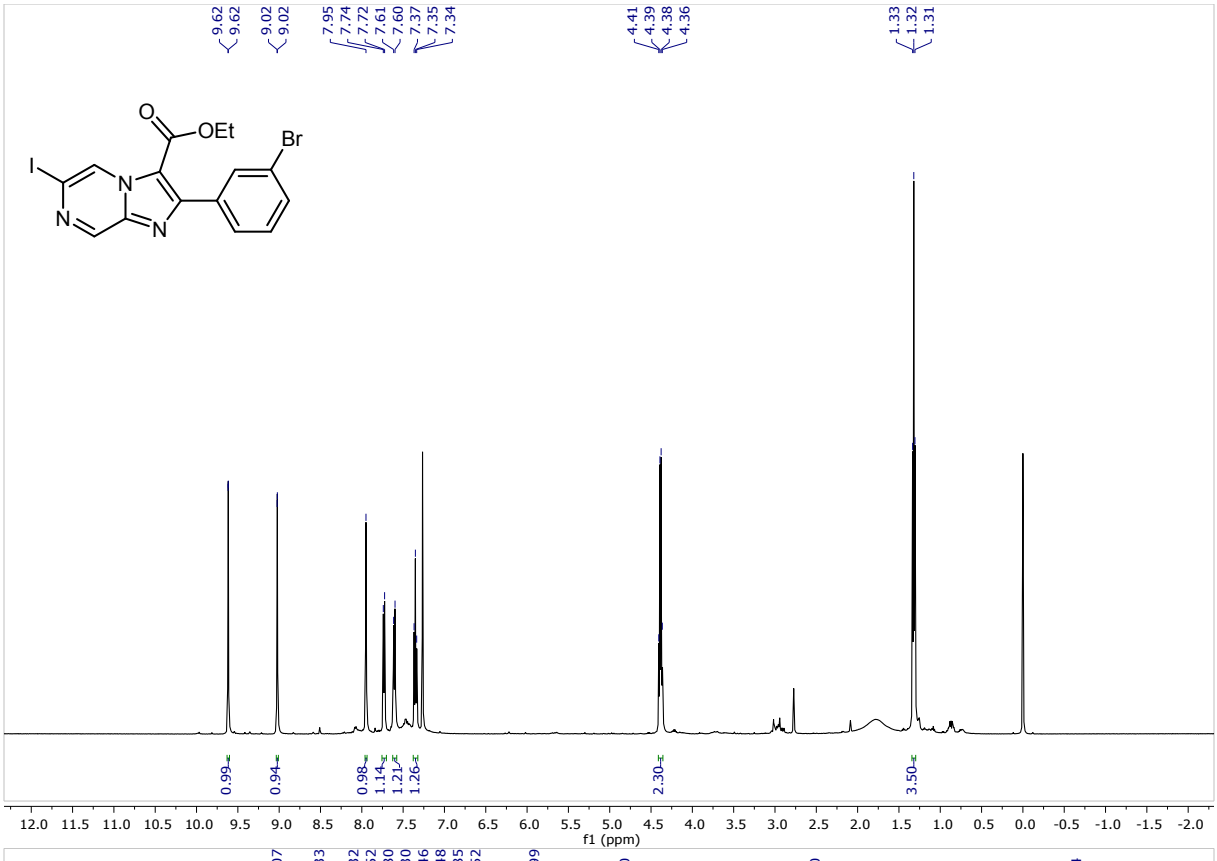
Ethyl 2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7b)

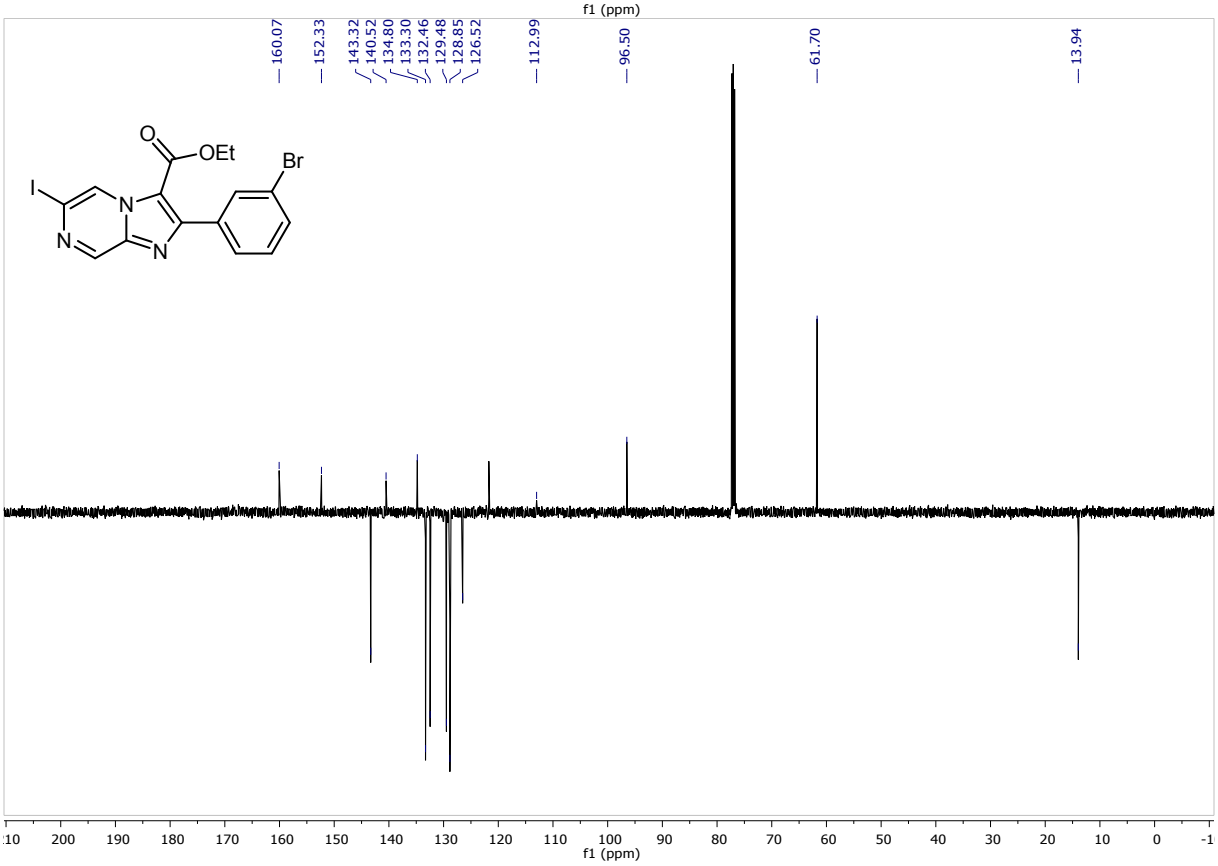


Ethyl 2-(4-fluorophenyl)imidazo[1,2-*a*]pyrazine-3-carboxylate (7c)

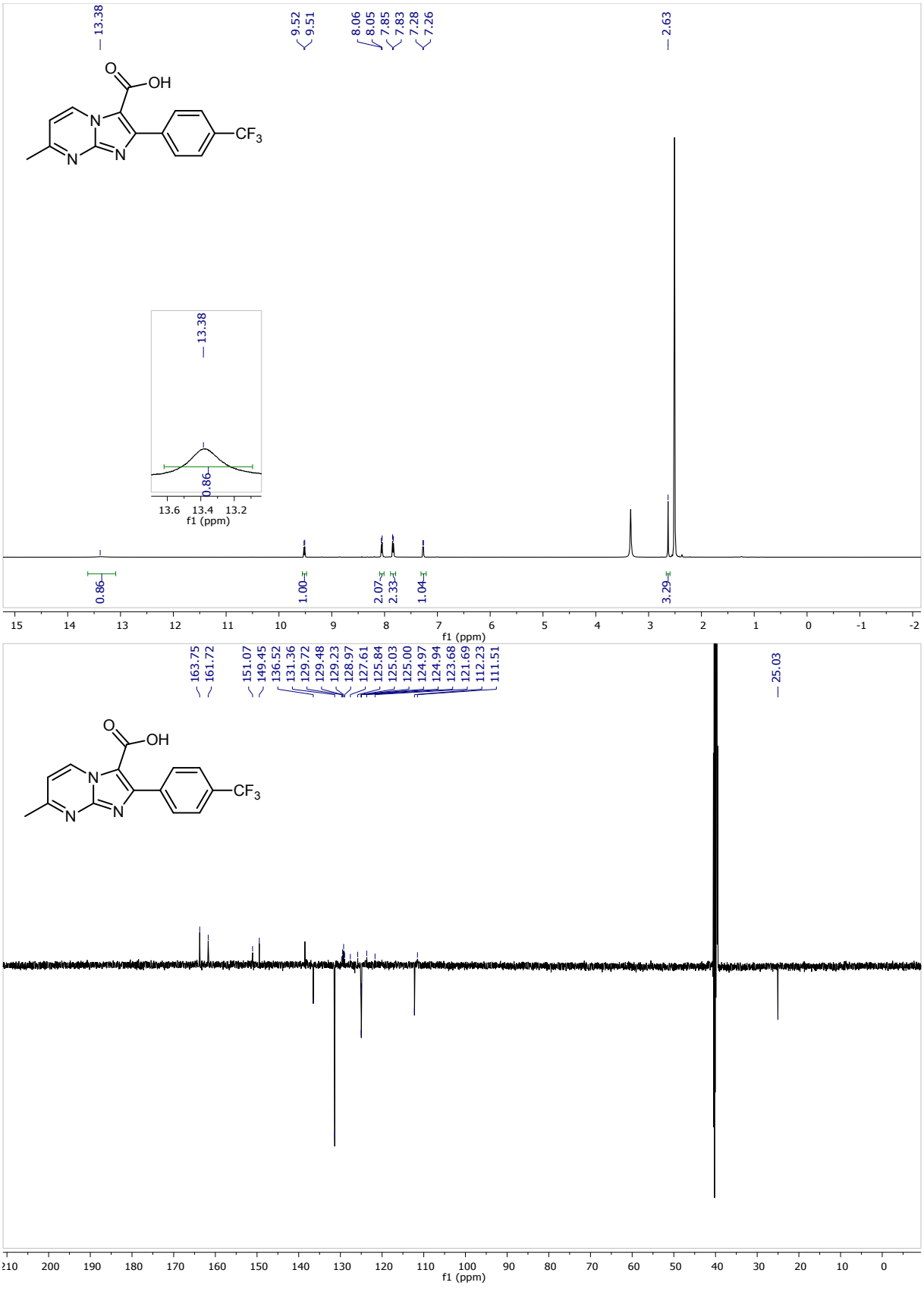


Ethyl 2-(3-bromophenyl)-6-iodoimidazo[1,2-*a*]pyrazine-3-carboxylate (7d)

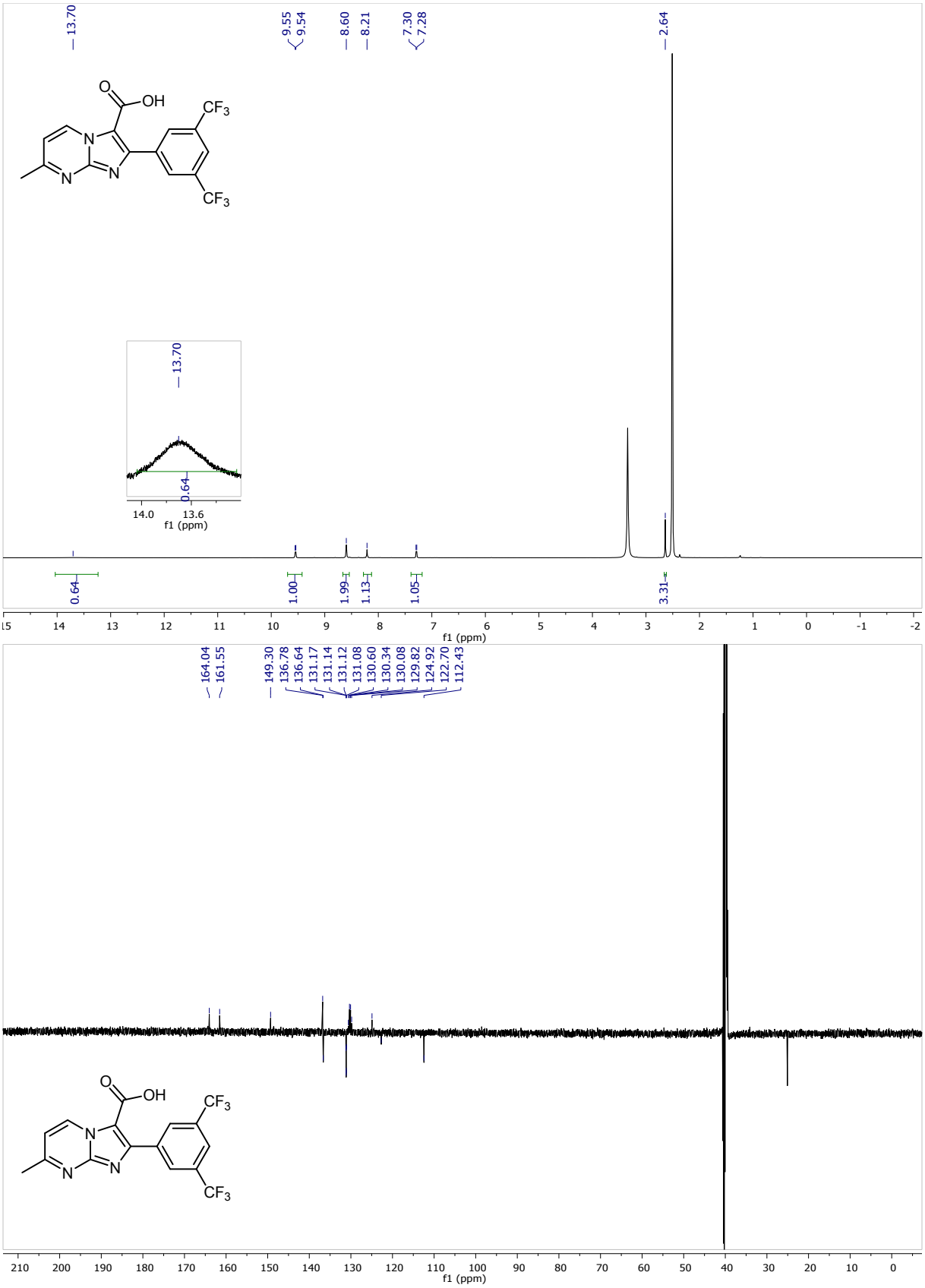




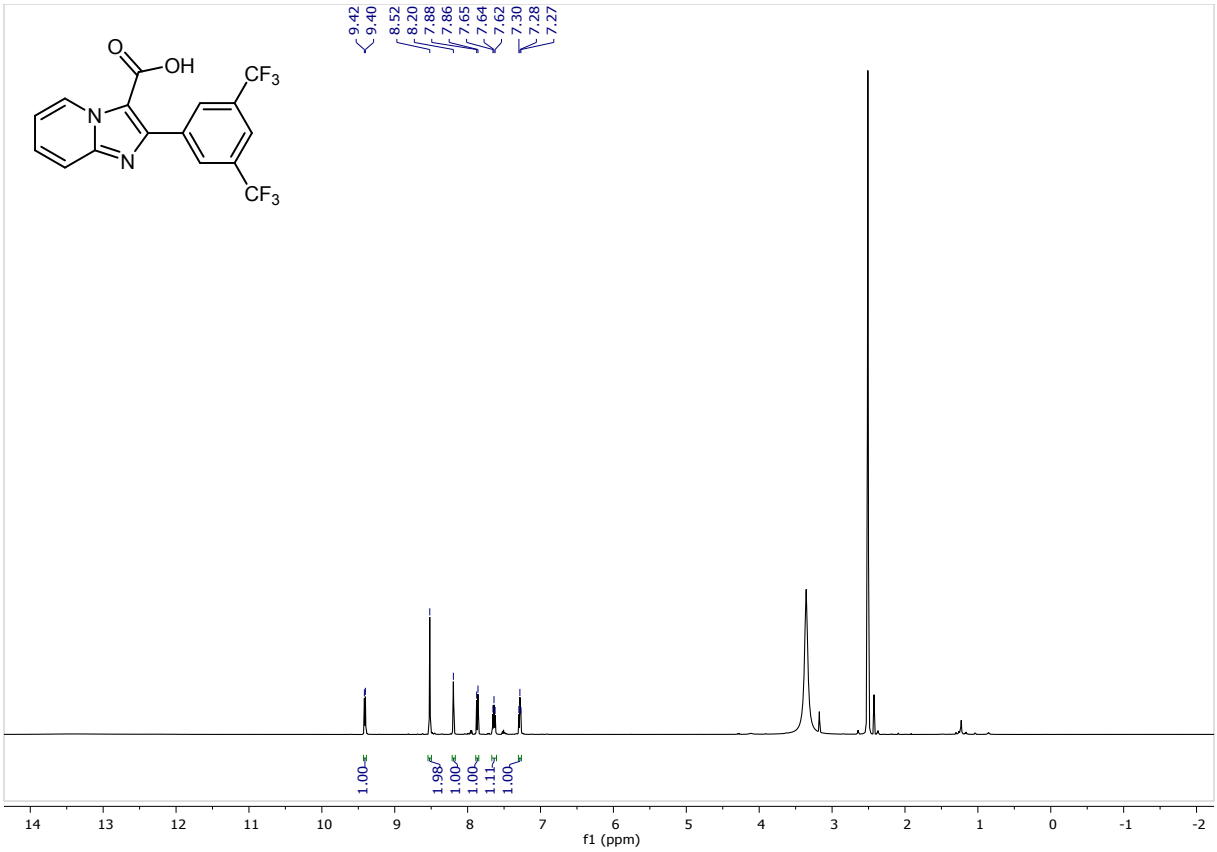
7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxylic acid (8a)

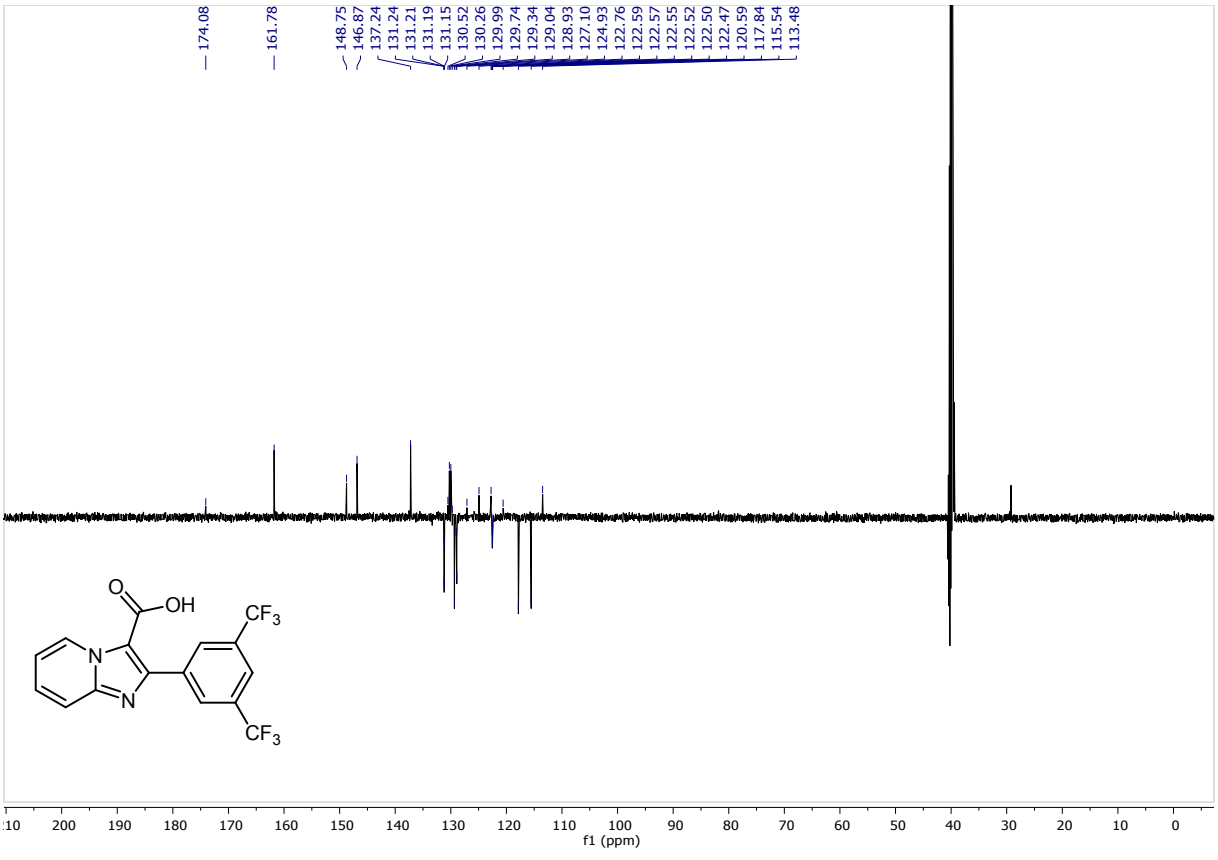


2-(3,5-bis(trifluoromethyl)phenyl)-7-methylimidazo[1,2-*a*]pyrimidine-3-carboxylic acid (8b)

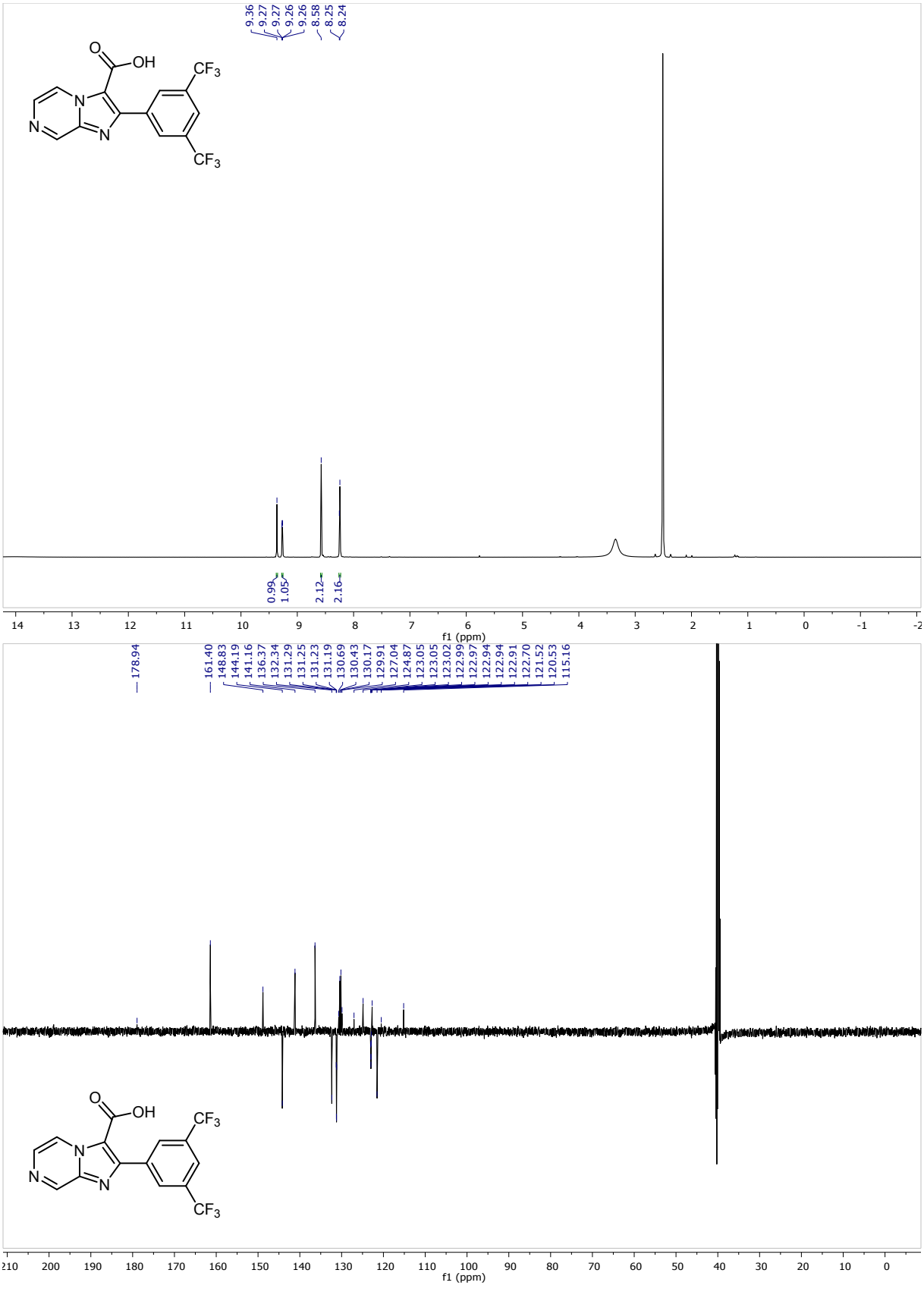


2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxylic acid (8c)

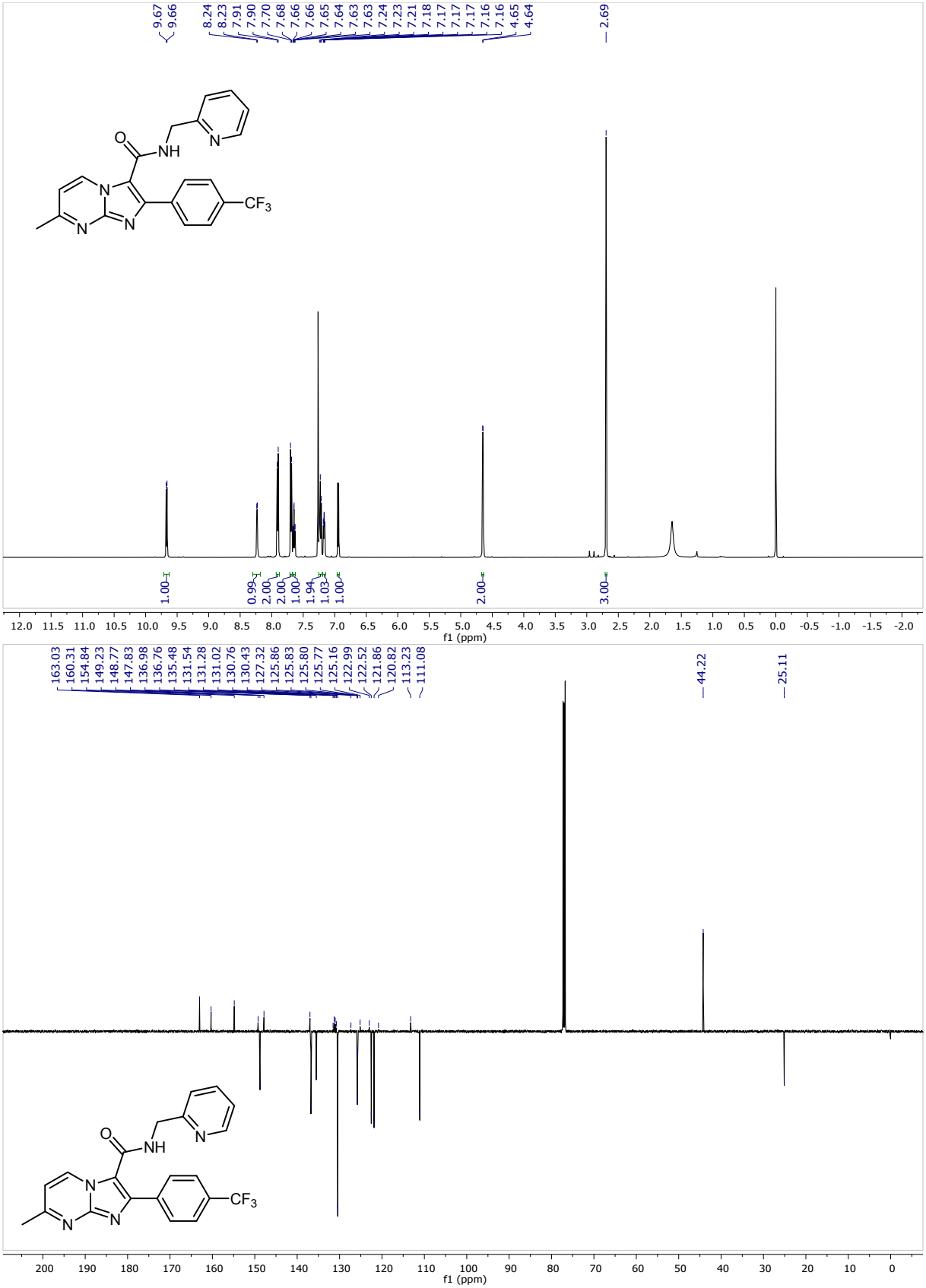




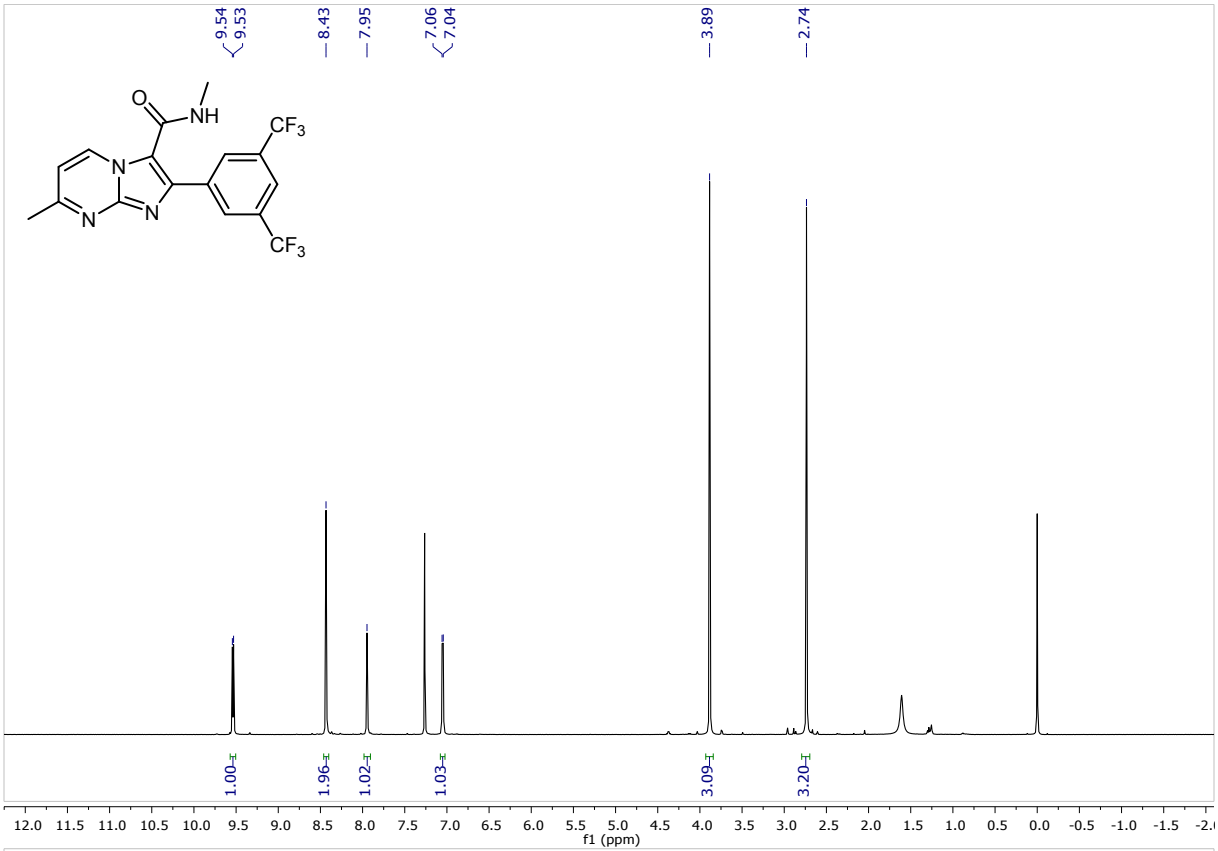
2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxylic acid (8d)

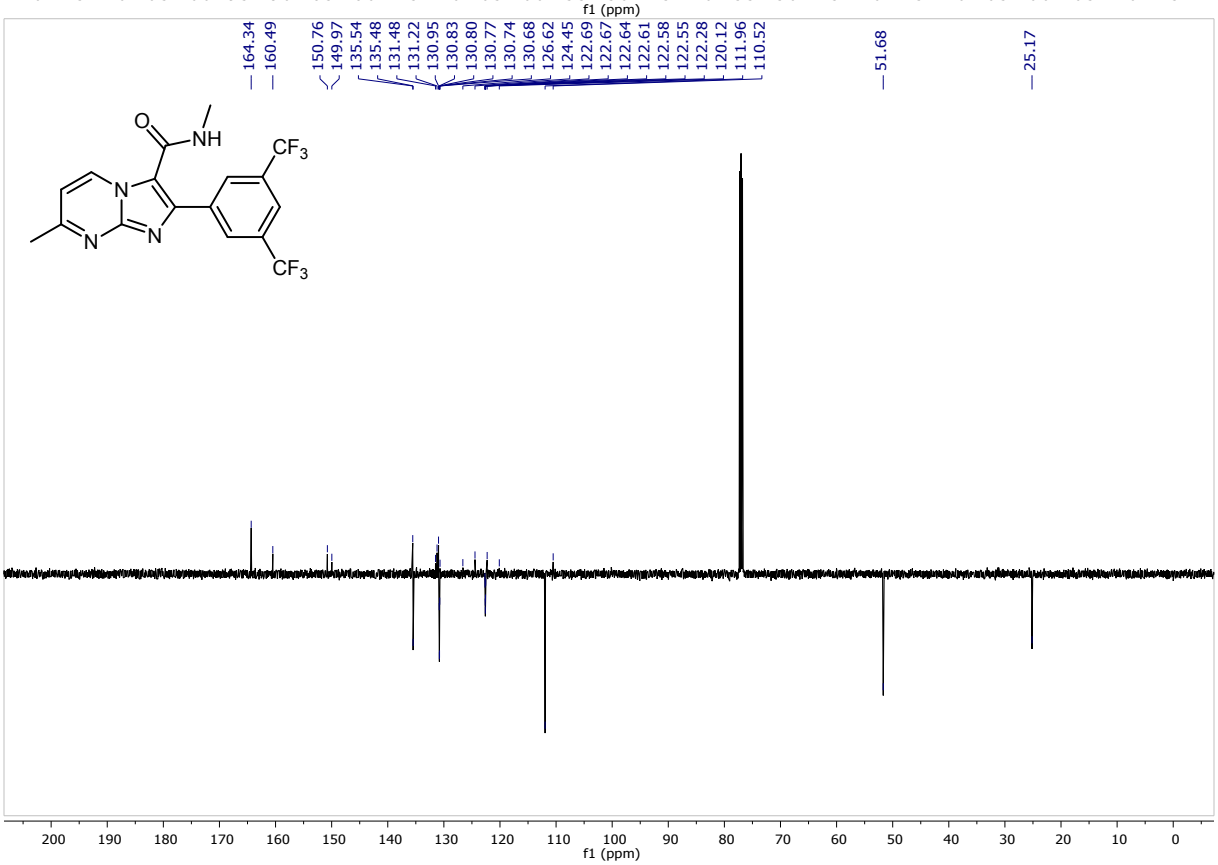


7-methyl-N-(pyridin-2-ylmethyl)-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrimidine-3-carboxamide (9a)

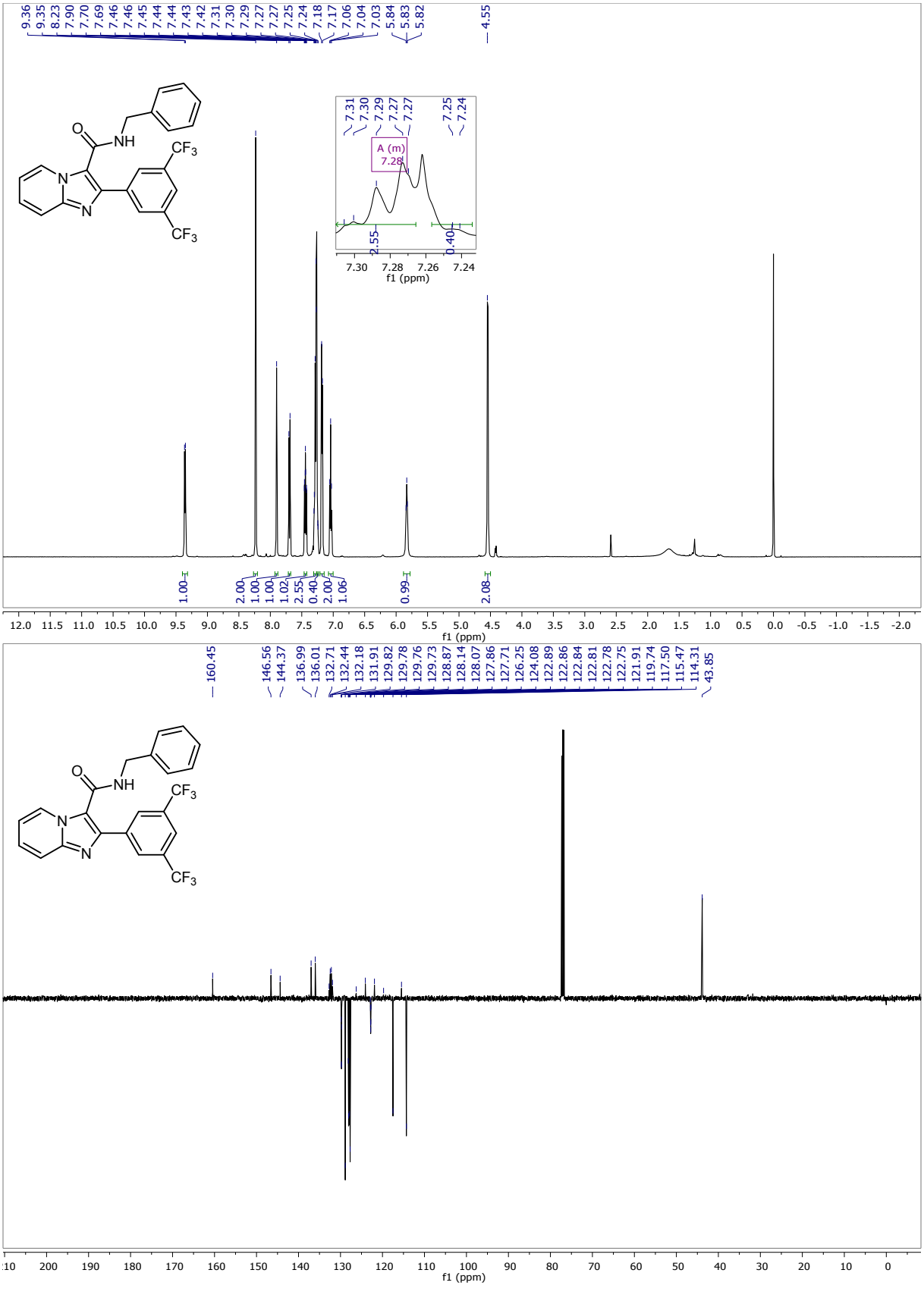


2-(3,5-bis(trifluoromethyl)phenyl)-N,7-dimethylimidazo[1,2-*a*]pyrimidine-3-carboxamide (9b)





N-benzyl-2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine-3-carboxamide (9c)



N-benzyl-2-(3,5-bis(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyrazine-3-carboxamide (9d)