Supporting information

for

A new and straightforward route to synthesize novel pyrazolo[3,4-*b*]pyridine-5-carboxylate scaffolds from 1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitriles using sulfonated amorphous carbon

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Section S1. The mechanism proposed for the synthesis of (1b) was detected by HRMS-ESI

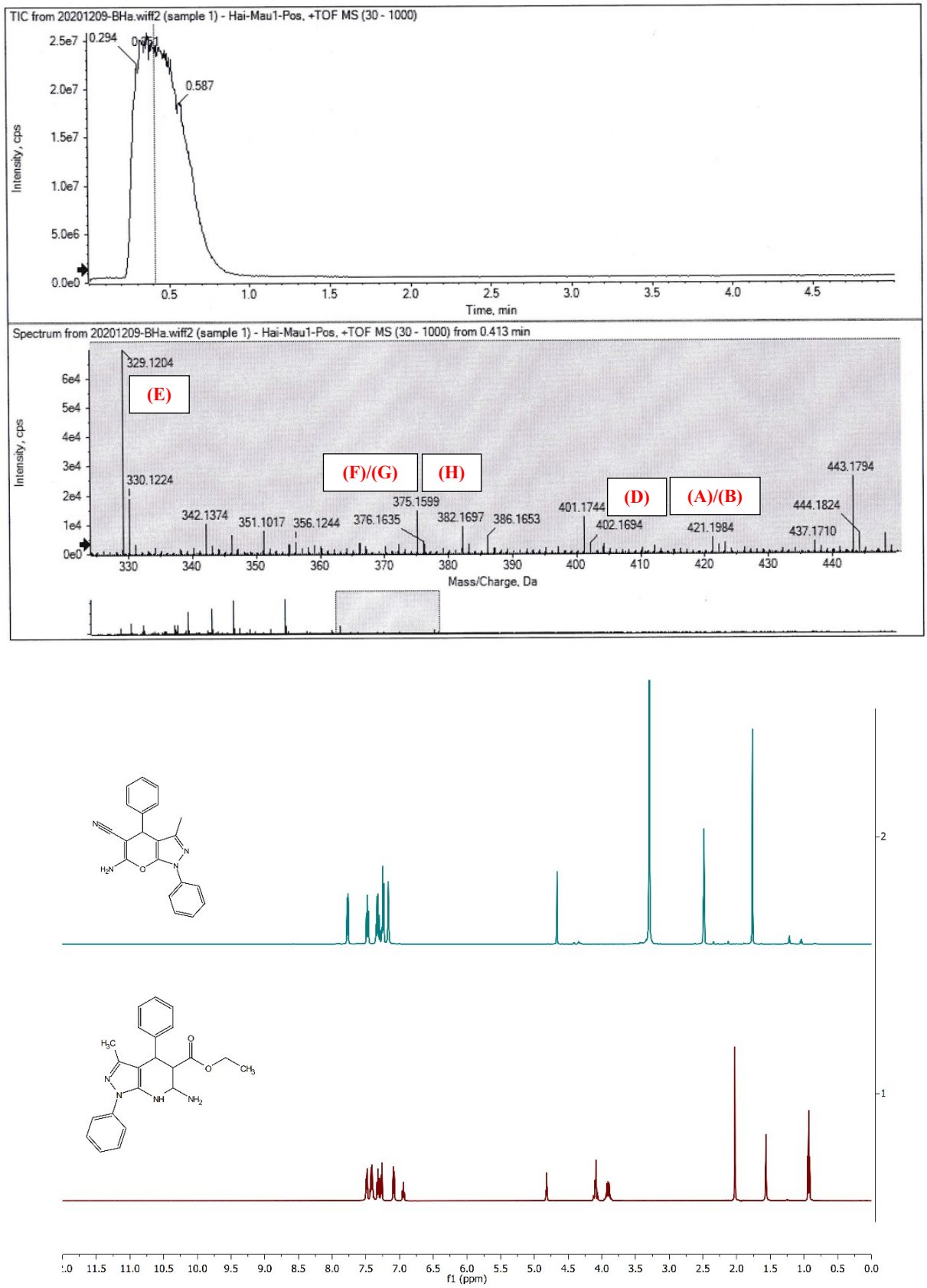
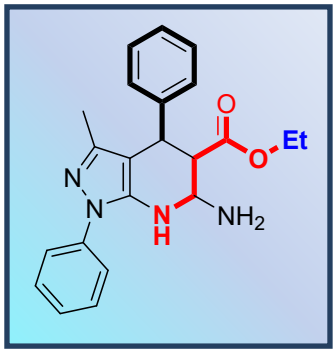


Figure S1. ^{1}H NMR spectrum of 6-amino-3-methyl-1,4-diphenyl-1,4-dihydro-pyrano[2,3-*c*]pyrazole-5-carbonitrile and ethyl 3-methyl-1,4-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate.

Section S2. Spectral data

Ethyl 6-amino-3-methyl-1,4-diphenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (Compound 1b, Scheme 2)



Following the general procedure: 6-Amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**1**, 0.25 mmol, 82.0 mg), and aniline (0.25 mmol, 23.5 mg) in ethanol (2.0 mL). The white solids were obtained with 84.5 mg (**1b**, 97%). R_f = 0.39 (*n*-hexane/ethyl acetate = 8:2).

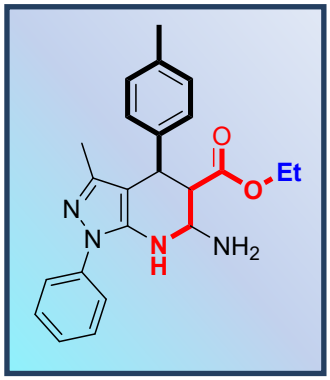
M.p. = 167-169 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.50-7.48 (m, 2H), 7.40-7.38 (m, 3H), 7.32 (t, J = 8.5 Hz, 2H), 7.27 (s, 1H), 7.09 (d, J = 8.0 Hz, 2H), 6.95 (t, J = 7.5 Hz, 1H), 4.82 (d, J = 4.5 Hz, 1H), 4.13-4.06 (m, 2H), 3.96-3.86 (m, 2H), 2.03 (s, 3H), 0.94 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.7, 144.4, 137.1, 134.8, 129.5, 129.3, 129.1, 128.7, 121.1, 113.1, 111.7, 111.5, 62.0, 56.2, 44.7, 27.4, 14.1, 13.7.

HRMS (ESI+) *m/z* calculated for $C_{22}H_{24}N_4O_2^+$ $[M]^+$ 376.1899, found 376.1840.

Ethyl 6-amino-3-methyl-1-phenyl-4-(p-tolyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (Compound 2b, Scheme 2)



Following the general procedure: 6-Amino-3-methyl-1-phenyl-4-(*p*-tolyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**2**, 0.25 mmol, 85.0 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The yellow solids were obtained with 64.4 mg (**2b**, 69%). R_f = 0.46 (*n*-hexane/ethyl acetate = 8:2).

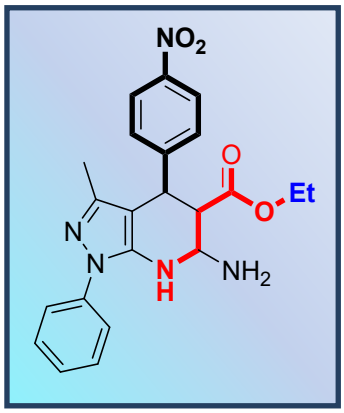
M.p. = 159-161 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.37 (d, J = 7.5 Hz, 2H), 7.32 (t, J = 8.0 Hz, 2H), 7.26 (s, 1H), 7.22 (d, J = 7.5 Hz, 2H), 7.08 (d, J = 7.5 Hz, 2H), 6.94 (t, J = 7.5 Hz, 1H), 4.78 (d, J = 1.5 Hz, 1H), 4.06 (s, 2H), 3.97 – 3.87 (m, 2H), 2.36 (s, 3H), 2.02 (s, 3H), 0.96 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.8, 144.4, 139.2, 137.3, 131.7, 129.7, 129.5, 128.5, 121.1, 113.1, 111.8, 111.6, 61.5, 56.3, 44.4, 27.6, 21.1, 14.0, 13.7.

HRMS (ESI+) *m/z* calculated for $C_{23}H_{26}N_4O_2^+$ $[M]^+$ 390.2056, found 390.1989.

Ethyl 6-amino-3-methyl-4-(4-nitrophenyl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 3b, Scheme 2)



Following the general procedure: 6-Amino-3-methyl-4-(4-nitrophenyl)-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**3**, 0.25 mmol, 93.2 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The yellow solids were obtained with 71.1 mg (**3b**, 79%). R_f = 0.51 (*n*-hexane/ethyl acetate = 8:2).

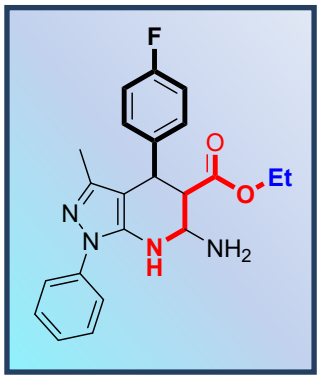
M.p. = 163-164 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.31 (d, J = 8.5 Hz, 2H), 7.71 (d, J = 9.0 Hz, 2H), 7.35 – 7.31 (m, 3H), 7.08 (d, J = 7.5 Hz, 2H), 6.97 (t, J = 7.0 Hz, 1H), 4.90 (d, J = 5.0 Hz, 1H), 4.29 (dd, J = 5.0 Hz, 4.5 Hz, 1H), 4.07 (d, J = 11.5 Hz, 1H), 3.99 – 3.90 (m, 2H), 2.06 (s, 3H), 1.00 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.2, 148.5, 144.1, 141.9, 136.1, 129.9, 129.6, 124.2, 121.4, 113.1, 111.2, 111.0, 62.0, 55.7, 44.3, 26.9, 14.3, 13.8.

HRMS (ESI+) *m/z* calculated for $C_{22}H_{23}N_5O_4^+$ $[M]^+$ 421.1750, found 421.1683.

Ethyl 6-amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 4b, Scheme 2)



Following the general procedure: 6-Amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**4**, 0.25 mmol, 86.5 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The white solids were obtained with 71.9 mg (**4b**, 76%). R_f = 0.48 (*n*-hexane/ethyl acetate = 8:2).

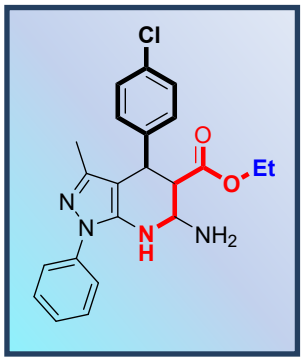
M.p. = 166-168 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.50 – 7.47 (m, 2H), 7.33 (t, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.13 (t, J = 8.5 Hz, 2H), 7.08 (d, J = 7.5 Hz, 2H), 6.95 (t, J = 7.0 Hz, 1H), 4.84 (d, J = 4.5 Hz, 1H), 4.13 (dd, J = 4.5 Hz, 1H), 4.02 (d, J = 11.5 Hz, 1H), 3.97 – 3.89 (m, 2H), 2.02 (s, 3H), 0.98 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.6, 164.2, 144.3, 136.8, 130.5 (d, J = 8.3 Hz), 129.6, 121.2, 116.3, 116.1, 113.1, 111.5 (d, J = 25.5 Hz), 61.7, 56.2, 44.0, 27.4, 14.1, 13.8

HRMS (ESI-) *m/z* calculated for $C_{22}H_{23}N_4O_2F^-$ $[M-3H]^-$ 391.1571, found 391.1581

Ethyl 6-amino-4-(4-chlorophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 5b, Scheme 2)



Following the general procedure: 6-Amino-4-(4-chlorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**5**, 0.25 mmol, 90.5 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The white solids were obtained with 66.2 mg (**5b**, 67%). R_f = 0.49 (*n*-hexane/ethyl acetate = 8:2).

M.p. = 167-168 °C.

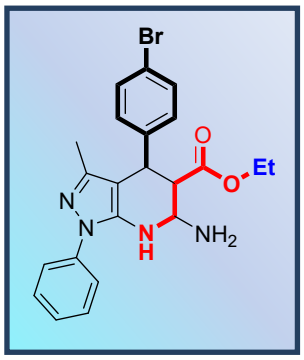
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.64 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.37 (d, J = 8.5 Hz, 1H), 7.31 (t, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.13 (d, J = 8.5 Hz, 1H),

7.06 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 7.5 Hz, 1H), 4.82 (d, J = 4.5 Hz, 1H), 4.09 (dd, J = 4.5 Hz, 1H), 4.01 (d, J = 11.5 Hz, 1H), 3.98 – 3.90 (m, 2H), 2.02 (s, 3H), 0.98 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.5, 144.3, 136.7, 133.8, 132.4, 132.0, 130.3, 129.6, 129.6, 129.3, 126.9, 123.6, 121.3, 121.2, 113.1, 111.3, 61.8, 55.9, 44.1, 37.0, 27.2, 14.2, 13.8.

HRMS (ESI-) *m/z* calculated for $C_{22}H_{21}ClN_4O_2^-$ $[M-2H]^-$ 408.1354, found 408.1244

Ethyl 6-amino-4-(4-bromophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 6b, Scheme 2)



Following the general procedure: 6-Amino-4-(4-bromophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**6,** 0.25 mmol, 101.5 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The white solids were obtained with 55.8 mg (**6b**, 56%). R_f = 0.50 (*n*-hexane/ethyl acetate = 8:2).

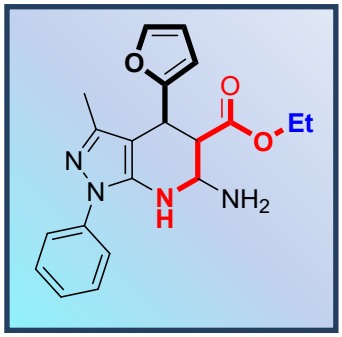
M.p. = 166-167 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.5 Hz, 2H), 7.48 (t, J = 8.5 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 7.32 (t, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.14 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 4.83 (d, J = 4.5 Hz, 1H), 4.11 (dd, J = 4.5 Hz, 1H), 4.03 (d, J = 11.5 Hz, 1H), 3.98 – 3.90 (m, 2H), 2.03 (s, 3H), 1.00 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.5, 144.3, 136.7, 133.8, 132.4, 132.0, 130.3, 129.6, 129.6, 129.3, 126.9, 123.6, 121.3, 121.2, 113.1, 111.3, 61.8, 55.9, 44.1, 37.0, 27.2, 14.2, 13.8, 12.9.

HRMS (ESI+) *m/z* calculated for $C_{22}H_{24}N_4O_2Br^+$ $[M+H]^+$ 455.1082, found 455.0896.

Ethyl 6-amino-4-(furan-2-yl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 7b, Scheme 2)



Following the general procedure: 6-Amino-4-(furan-2-yl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**7**, 0.25 mmol, 79.5 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The white solids were obtained with 52.3 mg (**7b**, 71%). R_f = 0.58 (*n*-hexane/ethyl acetate = 8:2).

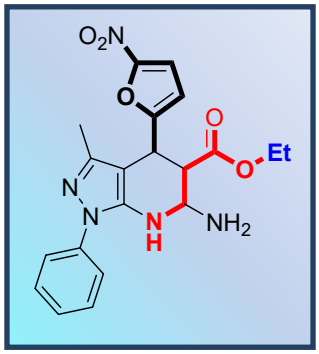
M.p. = 173-174 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (s, 1H), 7.31 (t, J = 8.0 Hz, 2H), 7.25 (s, 1H), 7.06 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 7.5 Hz, 1H), 6.50 (d, J = 3.0 Hz, 1H), 6.41 – 6.40 (m, 1H), 4.78 (d, J = 5.0 Hz, 1H), 4.33 (dd, J = 5.0 Hz, 1H), 4.12 – 4.02 (m, 2H), 2.00 (s, 3H), 1.12 (t, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.7, 148.4, 144.3, 143.5, 136.7, 129.5, 129.2, 121.1, 120.1, 113.1, 111.5, 111.1, 110.8, 110.1, 61.8, 55.0, 39.3, 26.0, 14.3, 13.9.

HRMS (ESI+) *m/z* calculated for $C_{20}H_{22}N_4O_3^+$ $[M]^+$ 366.1692, found 366.1629.

Ethyl 6-amino-3-methyl-4-(5-nitrofuran-2-yl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 8b, Scheme 2)



Following the general procedure: 6-Amino-4-(5-nitrofuran-2-yl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**9**, 0.25 mmol, 90.7 mg), and aniline (0.25 mmol, 23.5 mg) in Ethanol (2.0 mL). The white solids were obtained with 67.3 mg (**9b**, 68%). R_f = 0.56 (*n*-hexane/ethyl acetate = 8:2).

M.p. = 179-180 °C.

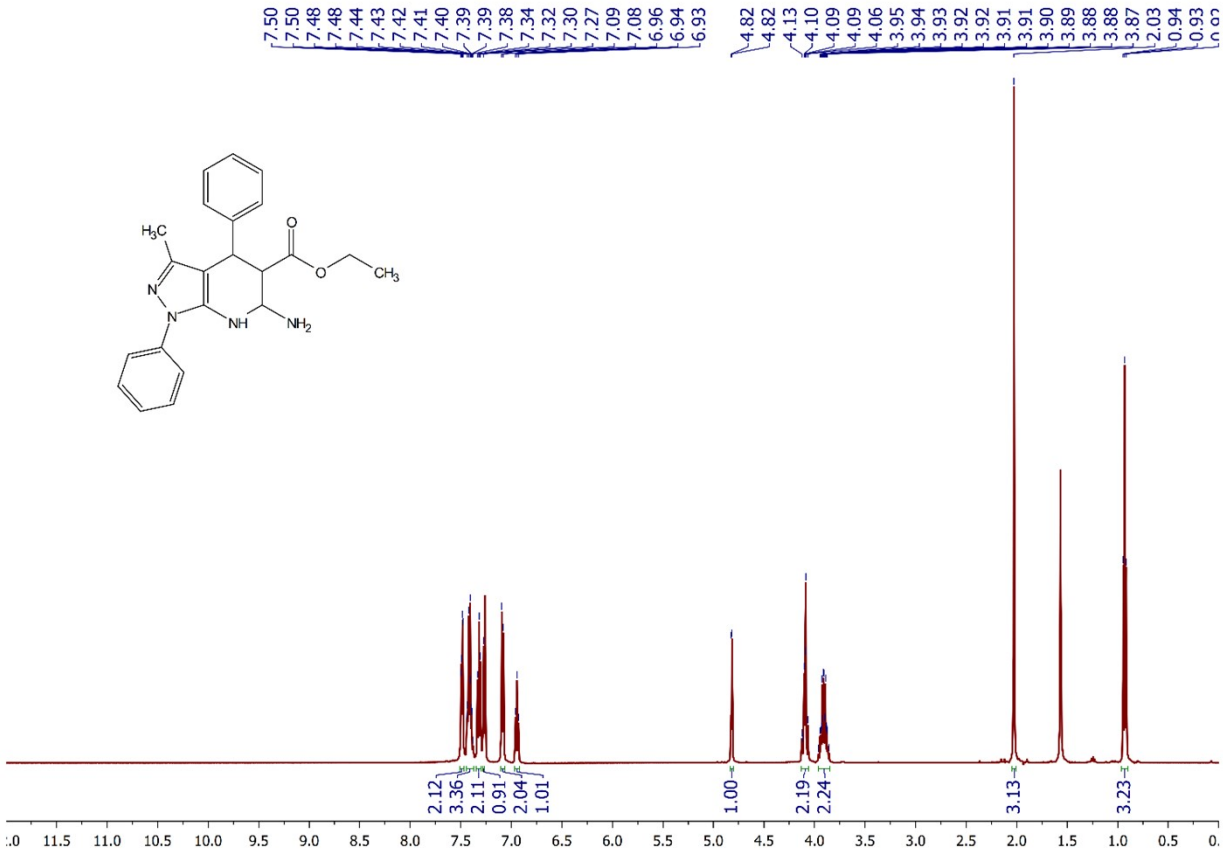
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.50 (s, 1H), 7.32 (t, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.08 – 7.06 (d, J = 8.0 Hz, 2H), 6.95 (t, J = 7.5 Hz, 1H), 6.51 (d, J = 3.0 Hz, 1H), 6.42 (m, 1H), 4.79 (d, J = 5.0 Hz, 1H), 4.12 – 4.03 (m, 2H), 2.01 (s, 3H), 1.14 (t, J = 7.0 Hz, 3H).

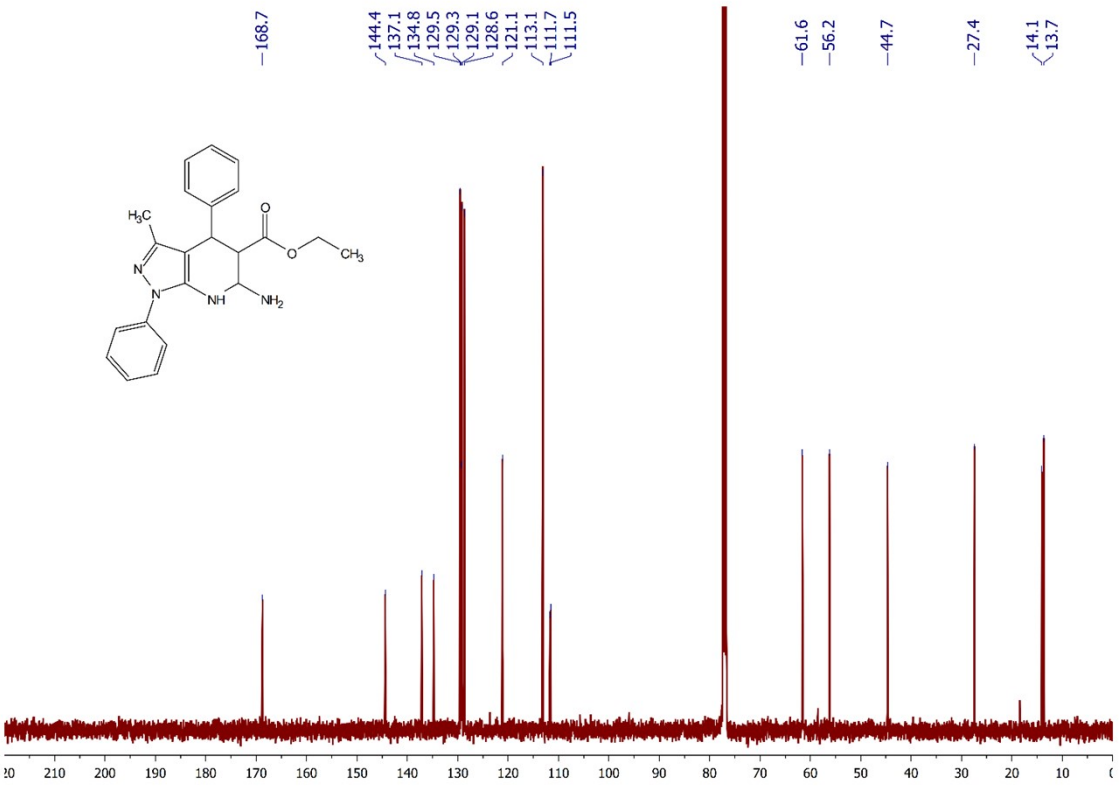
^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.9, 148.6, 144.5, 143.7, 136.9, 129.7, 129.3, 121.3, 120.2, 113.3, 111.6, 111.3, 111.0, 110.3, 62.0, 55.2, 39.5, 26.2, 14.5, 14.1.

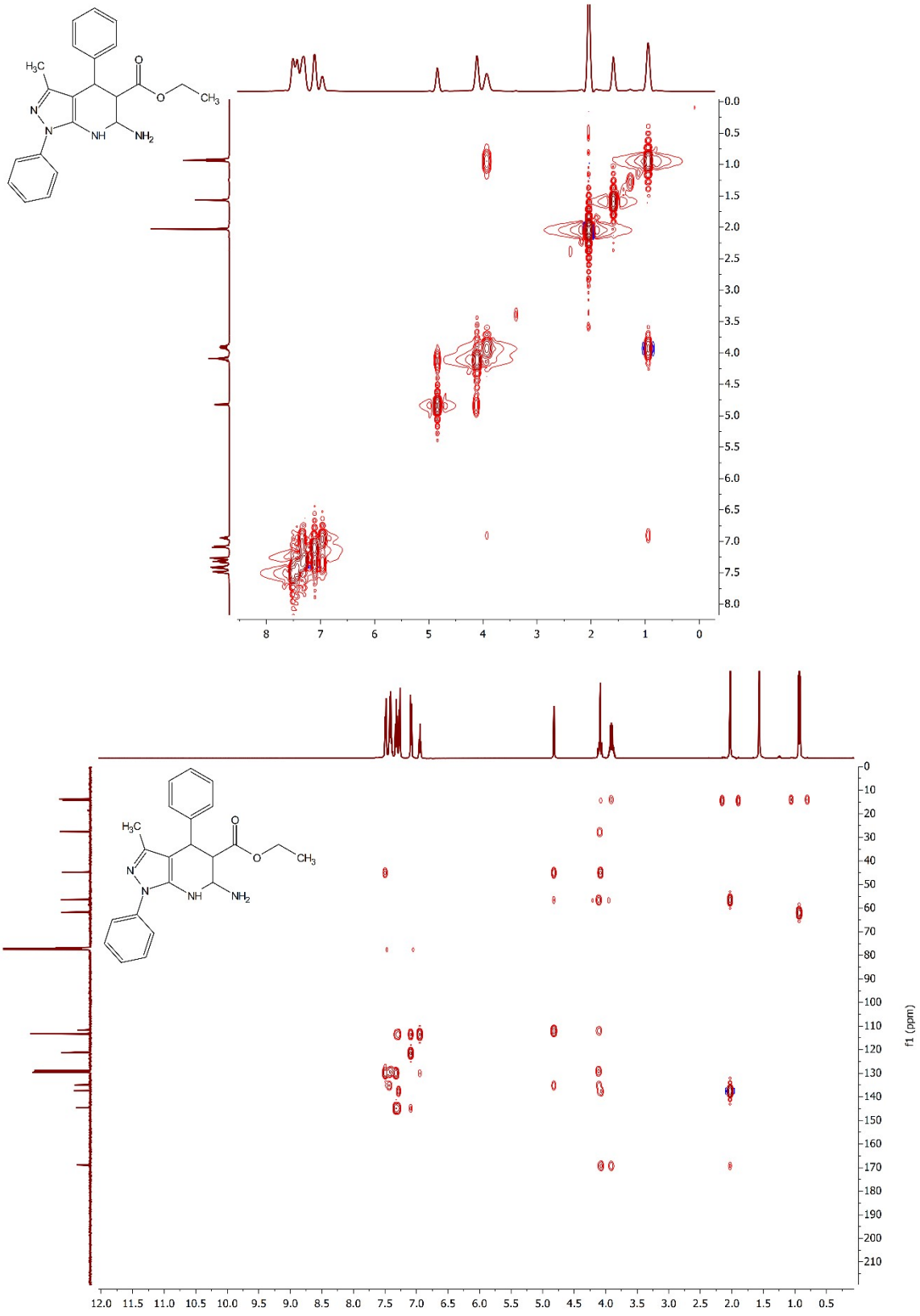
HRMS (ESI+) *m/z* calculated for $C_{20}H_{21}N_5O_5^+$ $[M]^+$ 411.1543, found 411.1787.

Section S3. ^{1}H, ^{13}C NMR, and HRMS spectroscopy

^{1}H, ^{13}C, COSY, HMMBC, HSQC NMR, and HRMS spectroscopy of ethyl 6-amino-3-methyl-1,4-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 1b)



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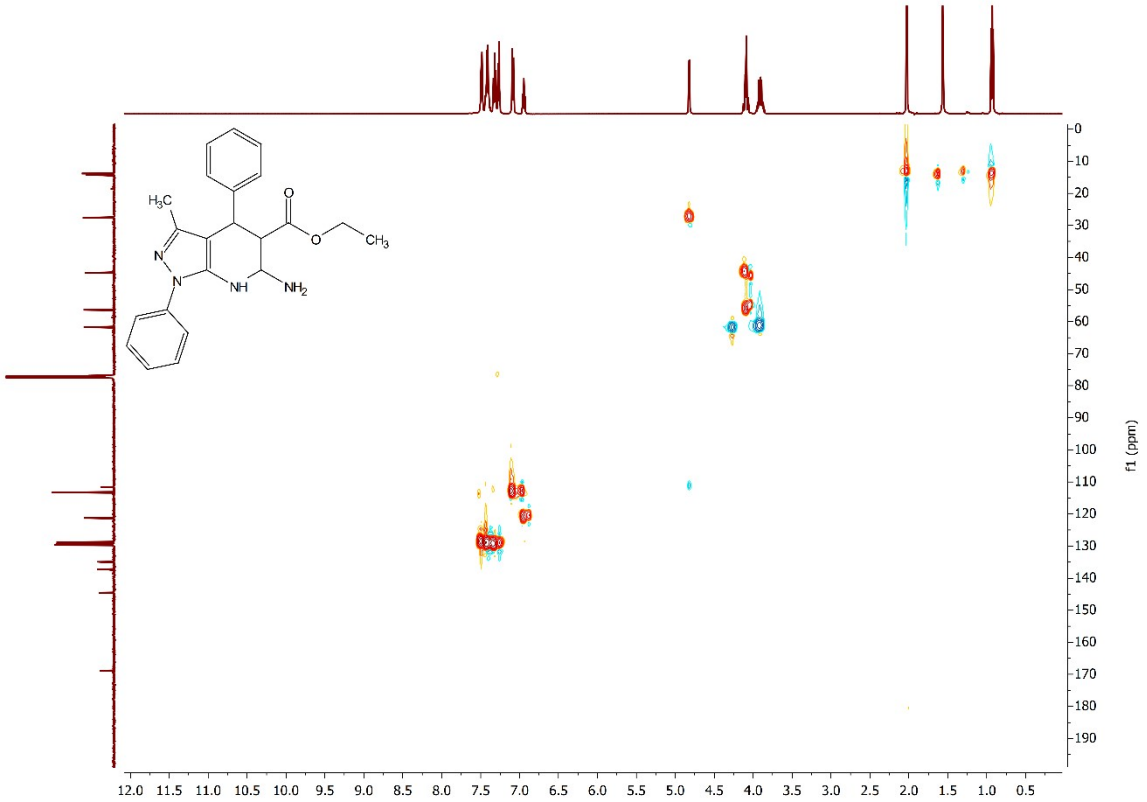
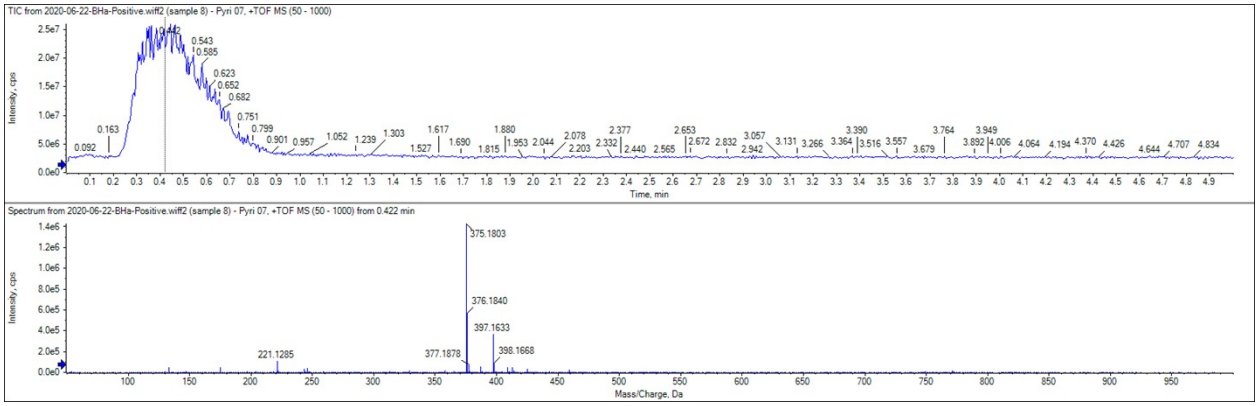
O
O
CH3
N
N
NH
NH2
f1 (ppm)


f1 (ppm)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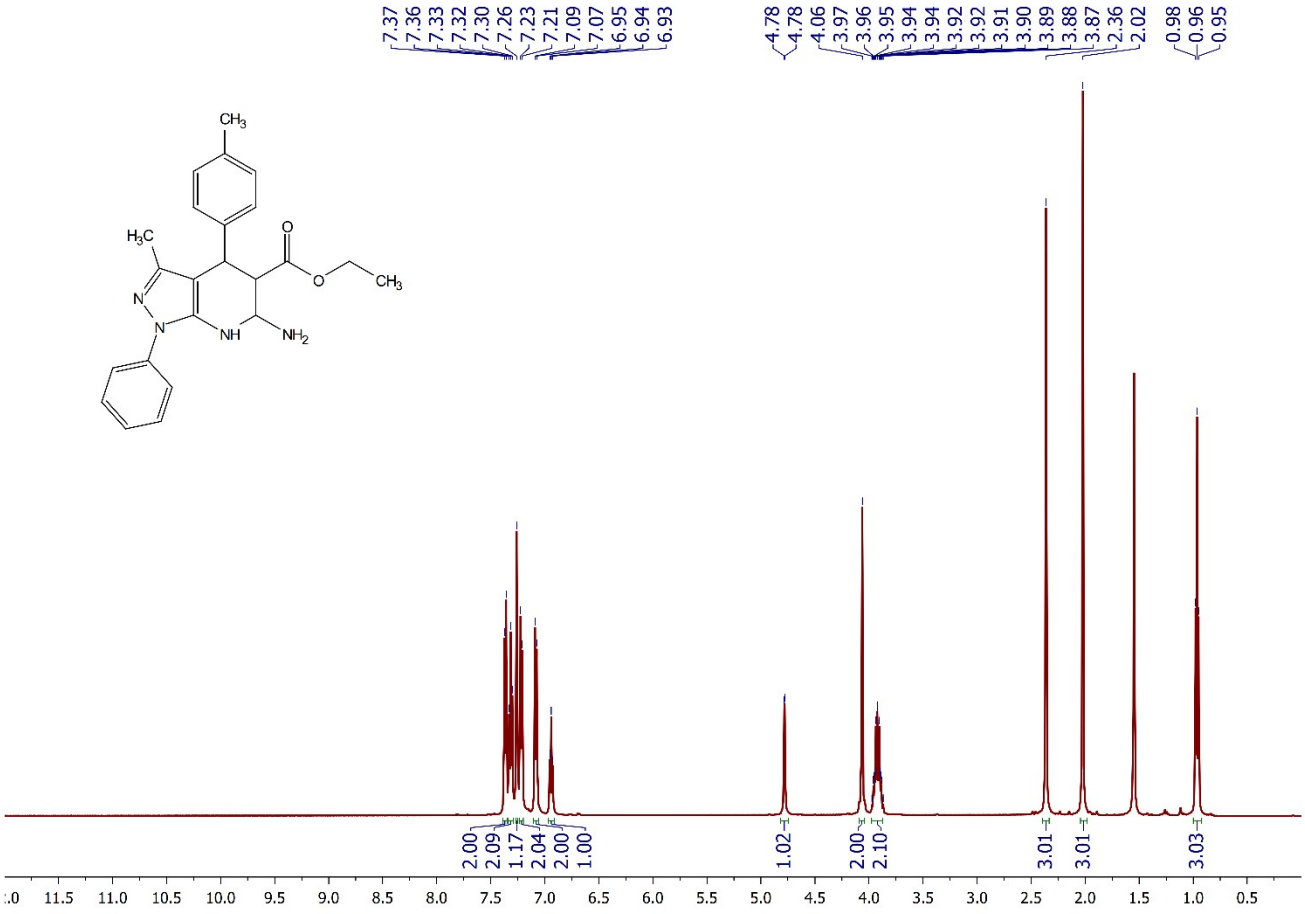
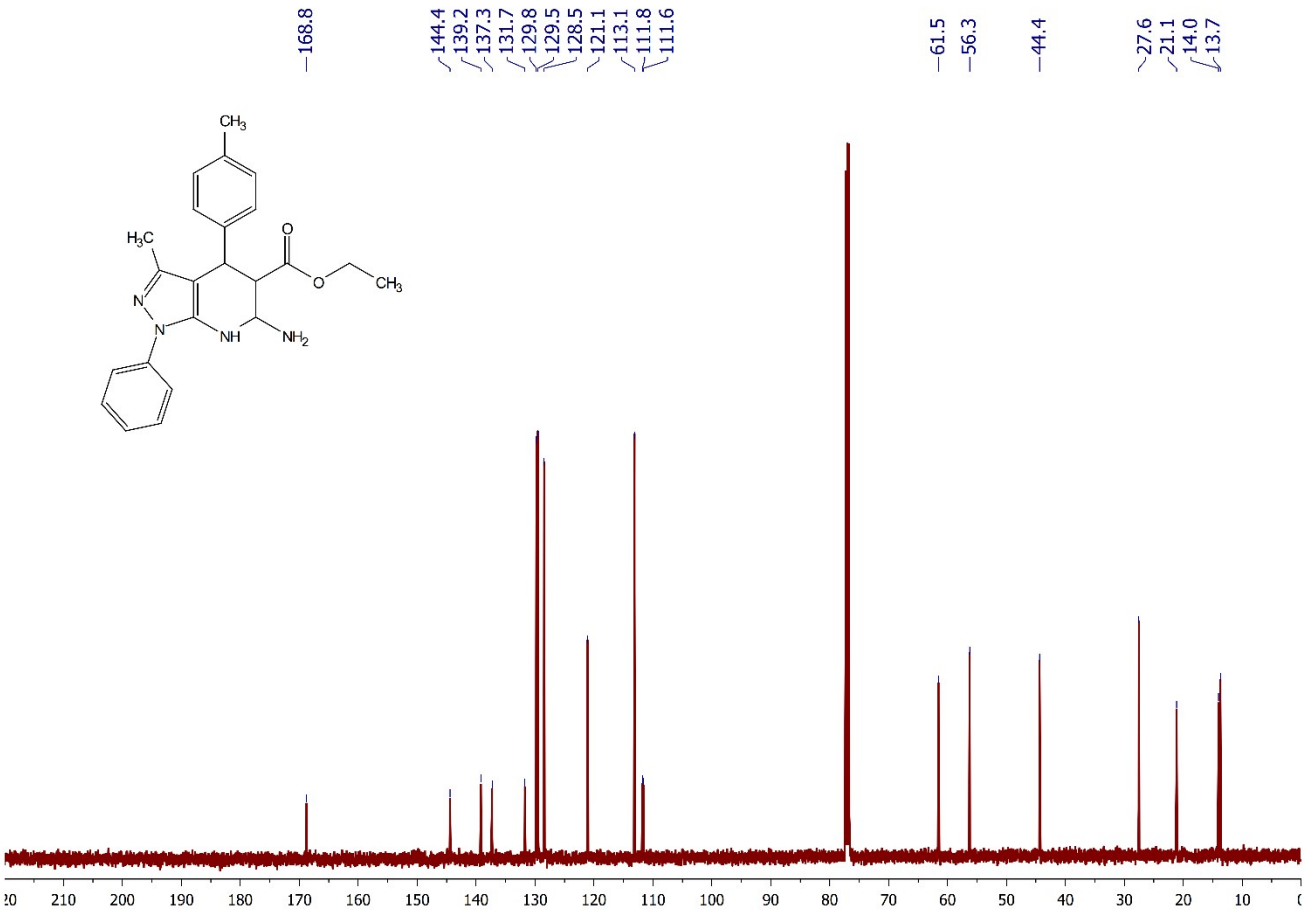
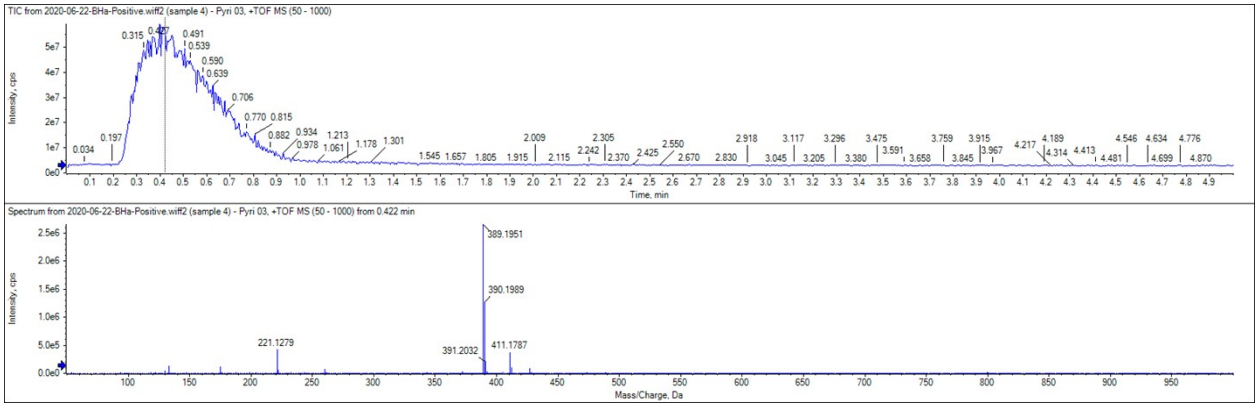
Intensity, cps
Time, min
Spectrum from 2020-06-22-BHa-Positive.wiff2 (sample 8) - Pyri 07, +TOF MS (50 - 1000) from 0.422 min
375.1803
376.1840
397.1633
398.1668
377.1878
221.1285
Mass/Charge, Da

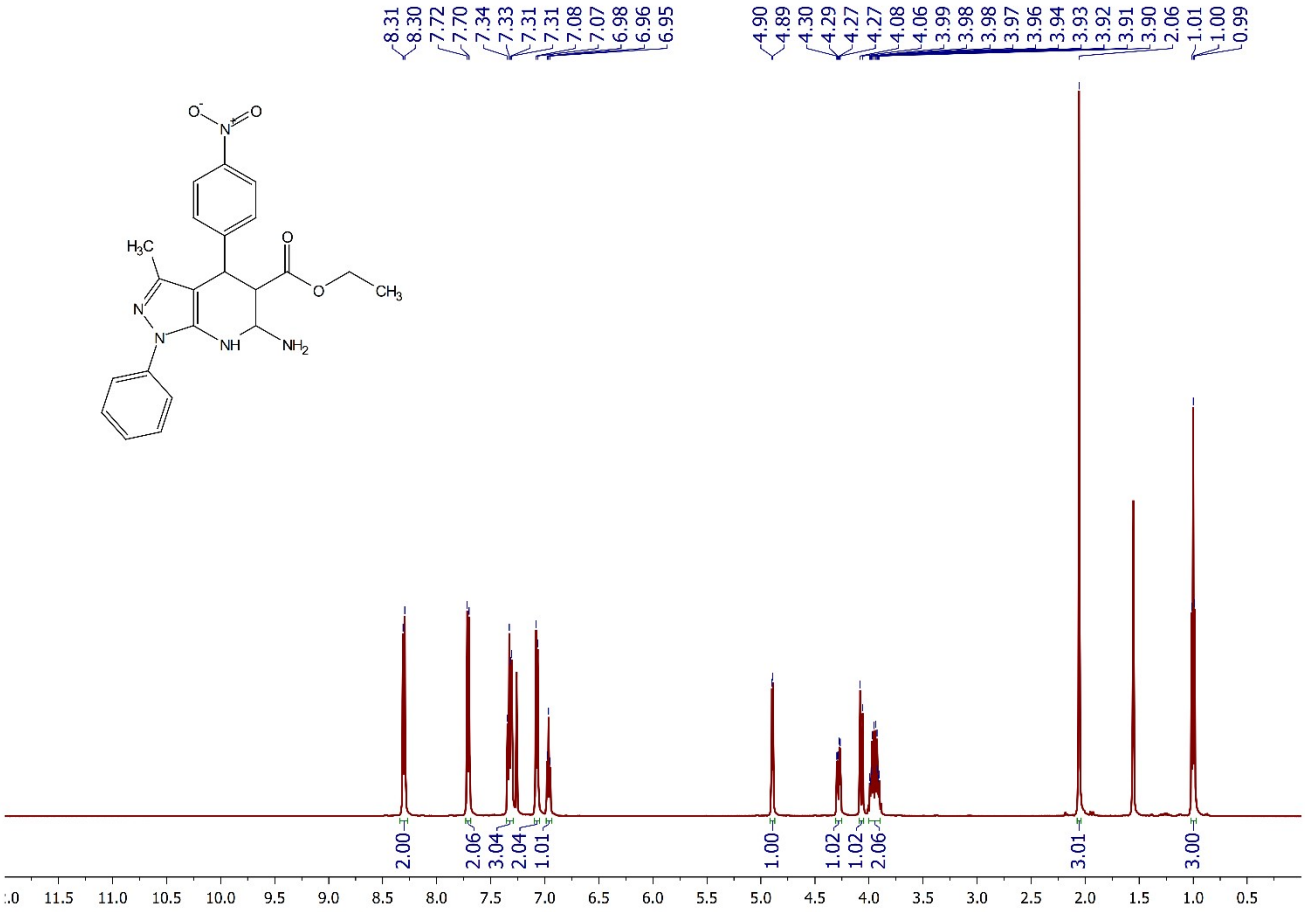
^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-3-methyl-1-phenyl-4-(*p*-tolyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 2b)

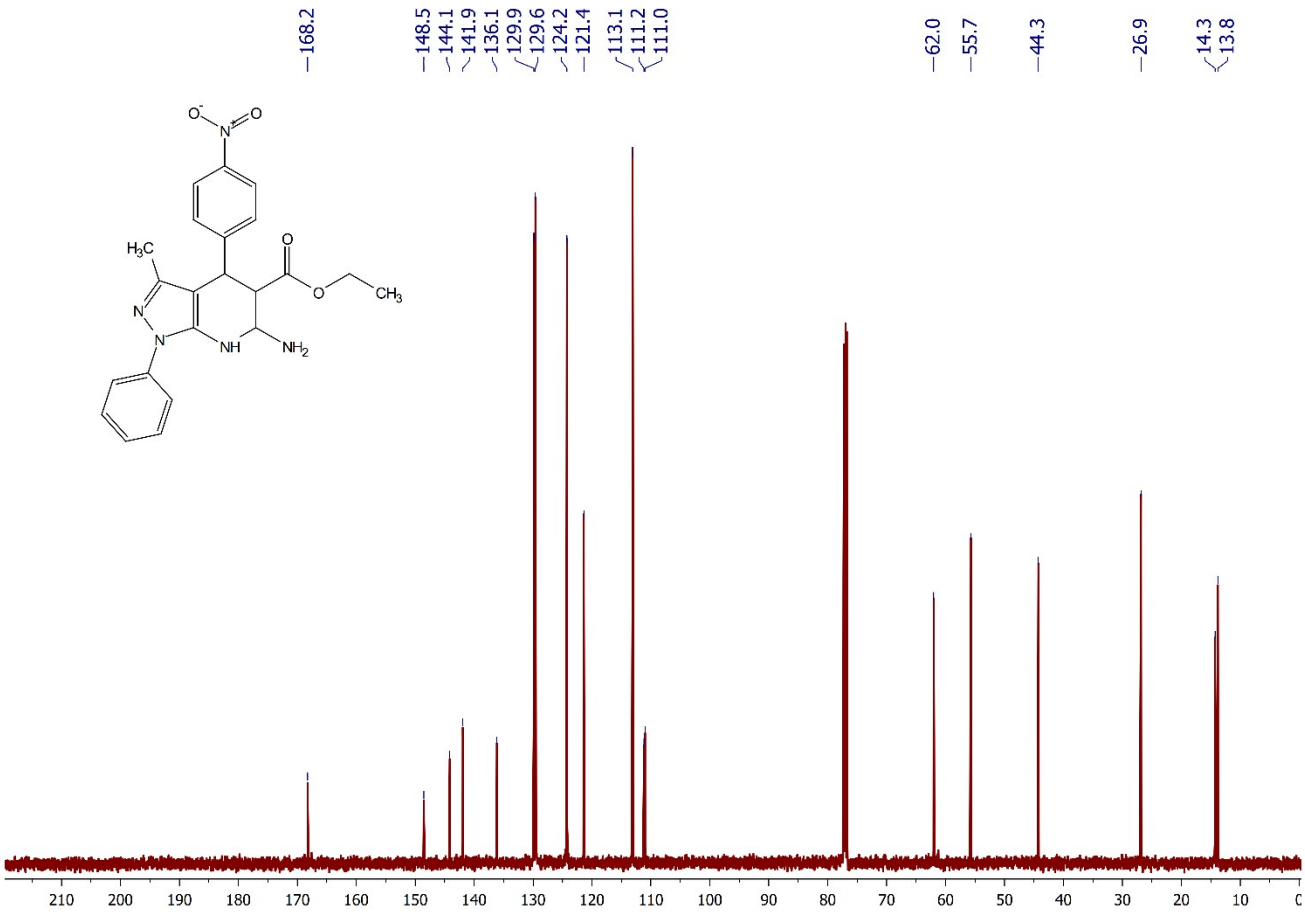


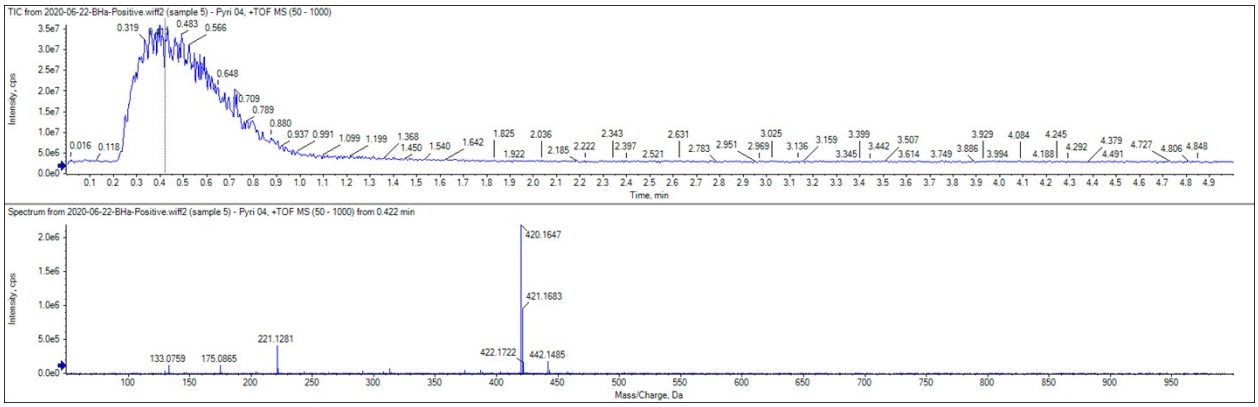



TIC from 2020-06-22-BHa-Positive.wiff2 (sample 4) - Pyri 03, +TOF MS (50 - 1000)
Intensity, cps
Time, min
Spectrum from 2020-06-22-BHa-Positive.wiff2 (sample 4) - Pyri 03, +TOF MS (50 - 1000) from 0.422 min
Intensity, cps
Mass/Charge, Da
389.1951
390.1989
221.1279
391.2032
411.1787

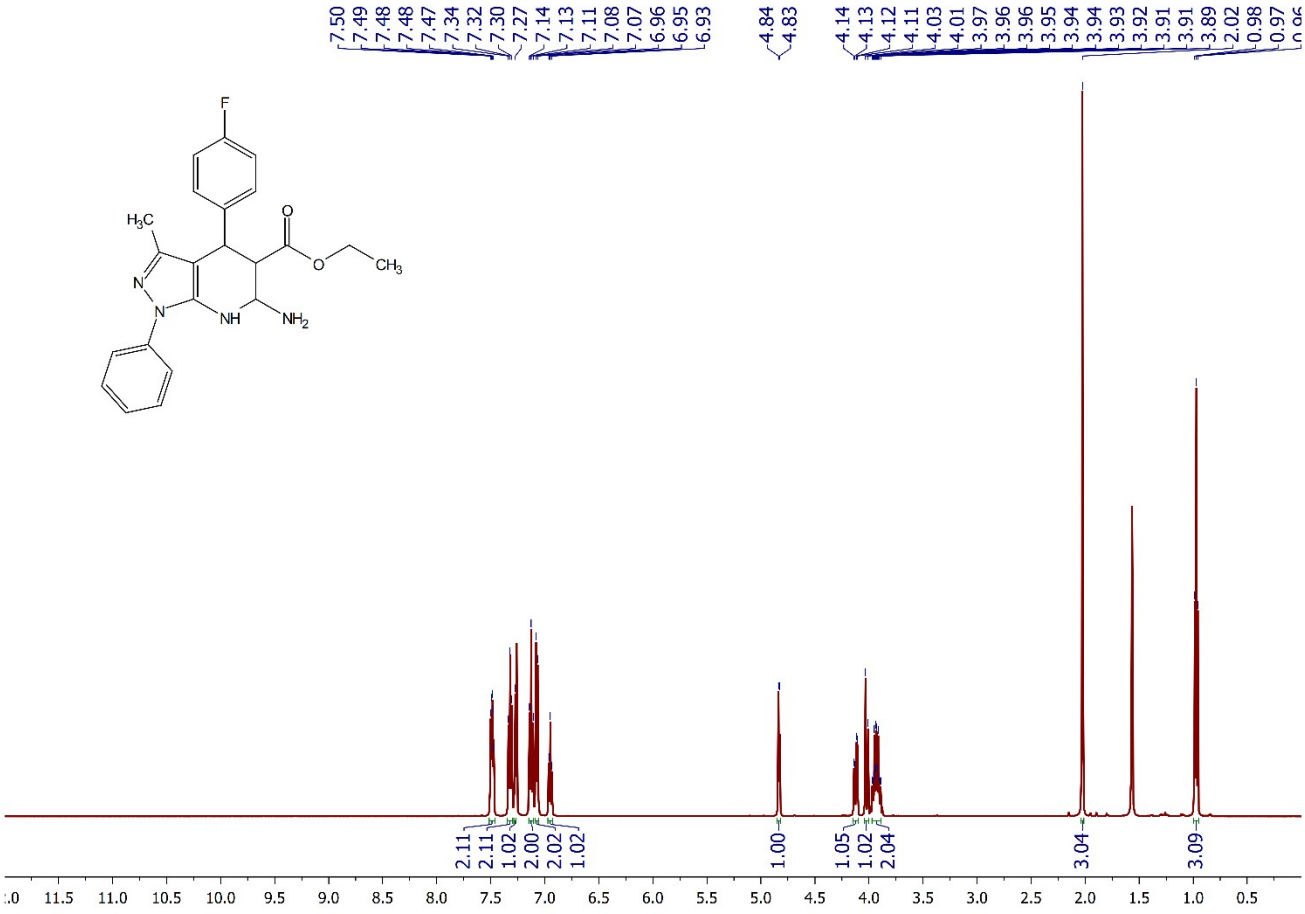
^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-3-methyl-4-(4-nitrophenyl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 4b)

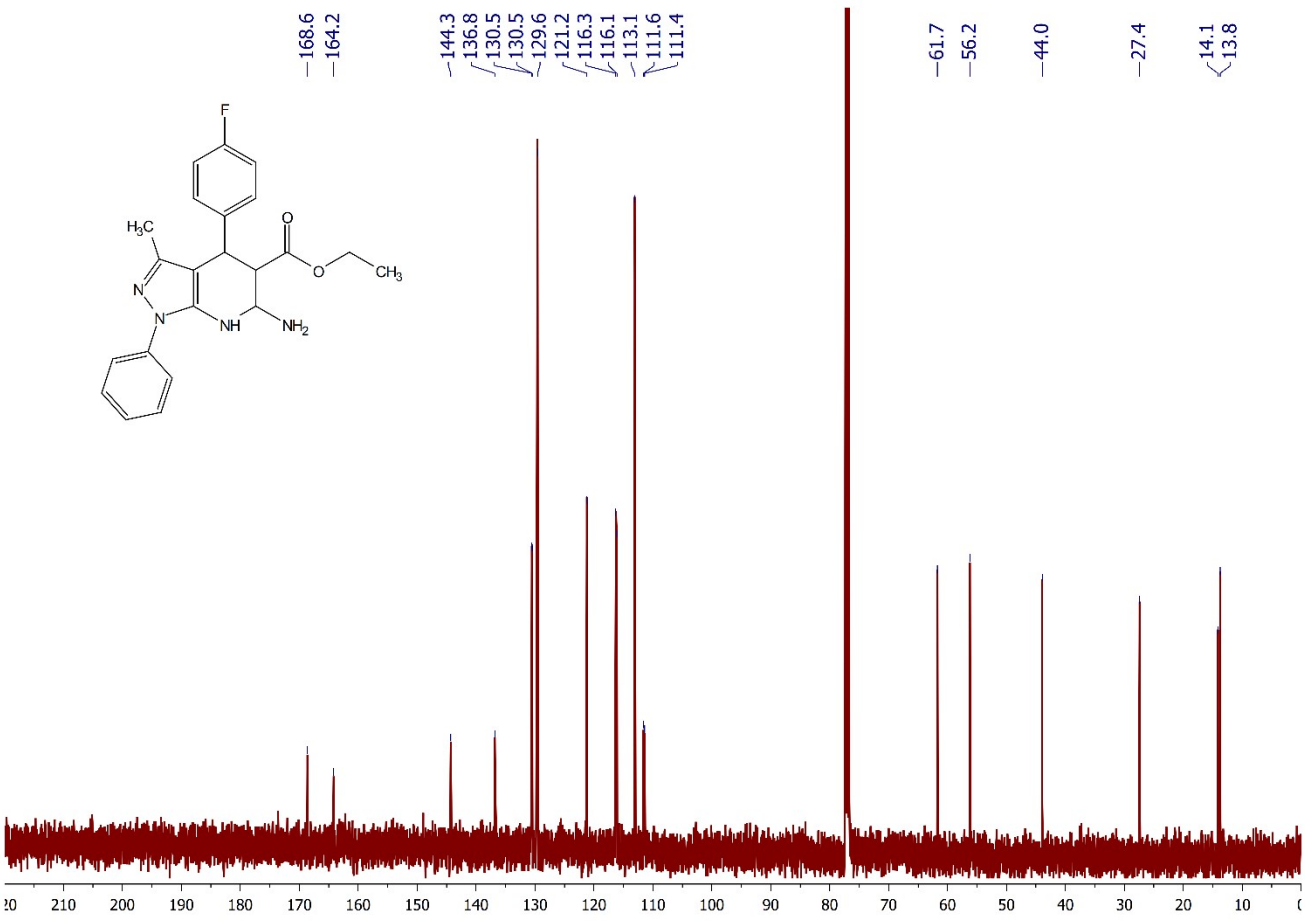


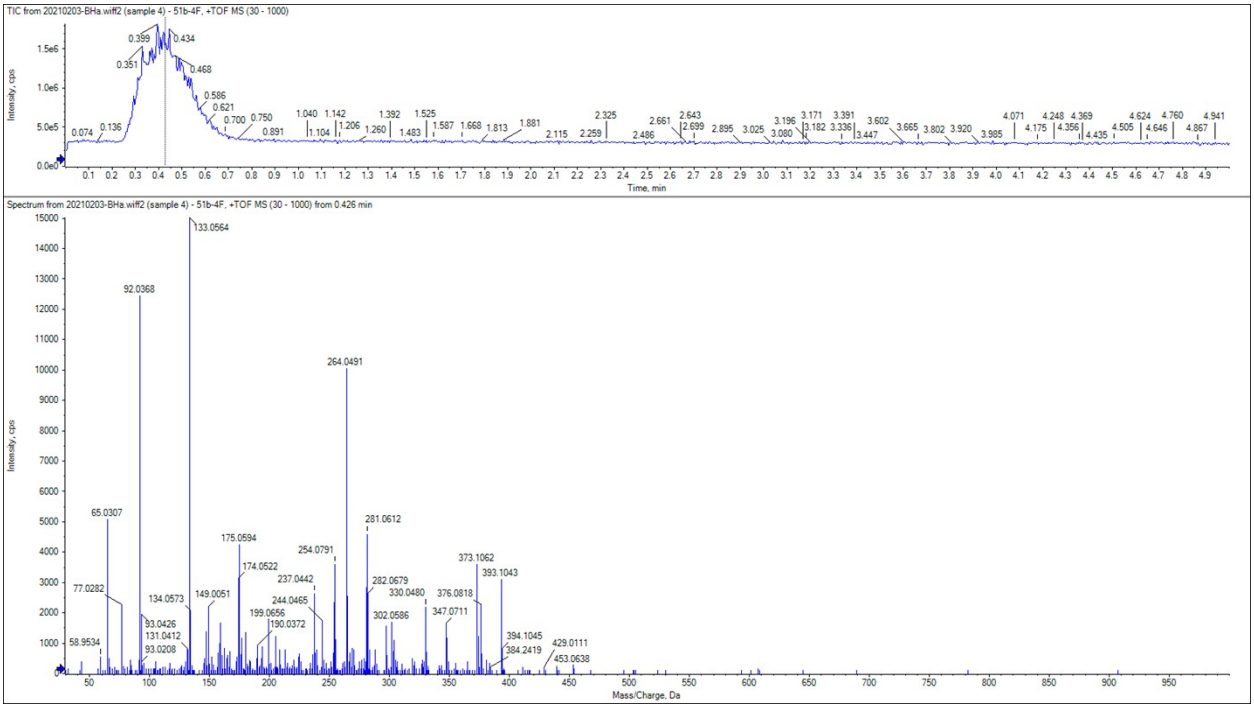



TIC from 2020-06-22-BHa-Positive.wiff2 (sample 5) - Pyri 04, +TOF MS (50 - 1000)
Intensity, cps
Time, min
Spectrum from 2020-06-22-BHa-Positive.wiff2 (sample 5) - Pyri 04, +TOF MS (50 - 1000) from 0.422 min
Intensity, cps
Mass/Charge, Da
420.1647
421.1683
221.1281
133.0759
175.0865
422.1722
442.1485

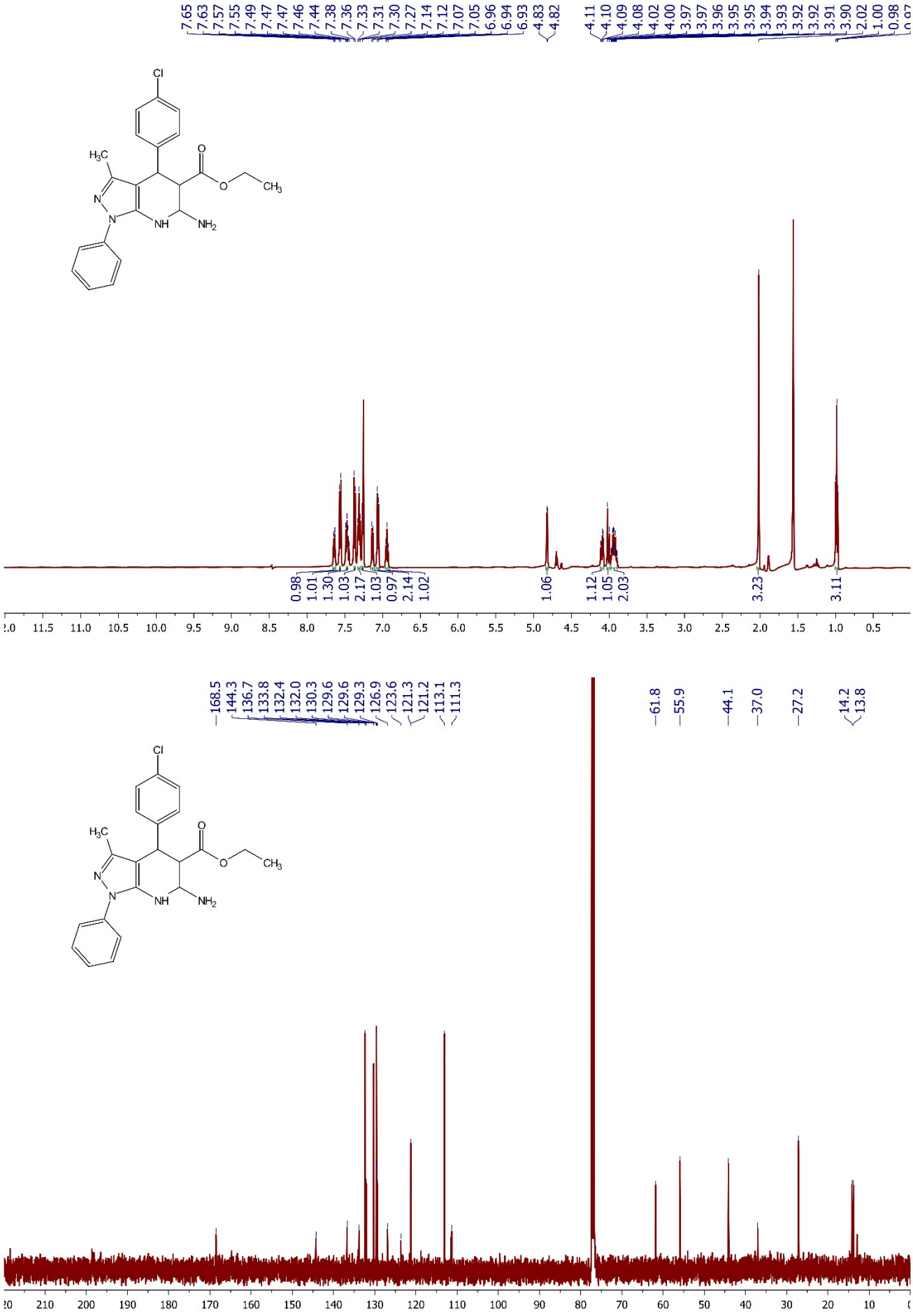
^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 5b)

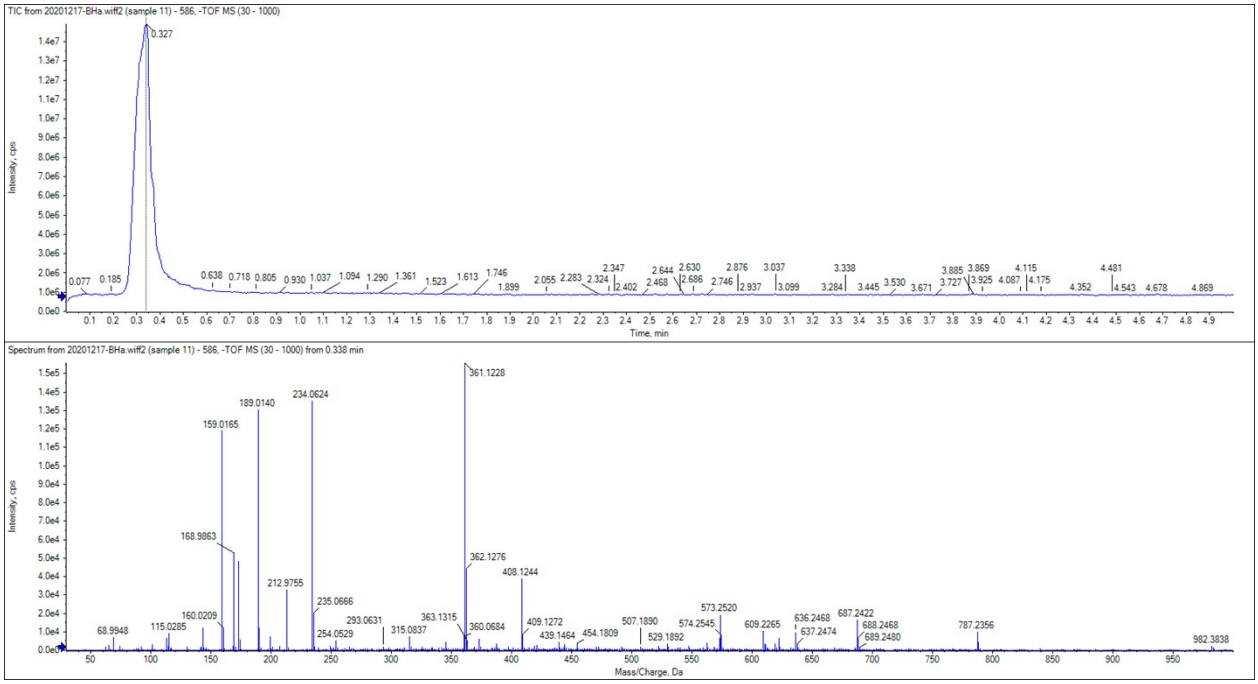




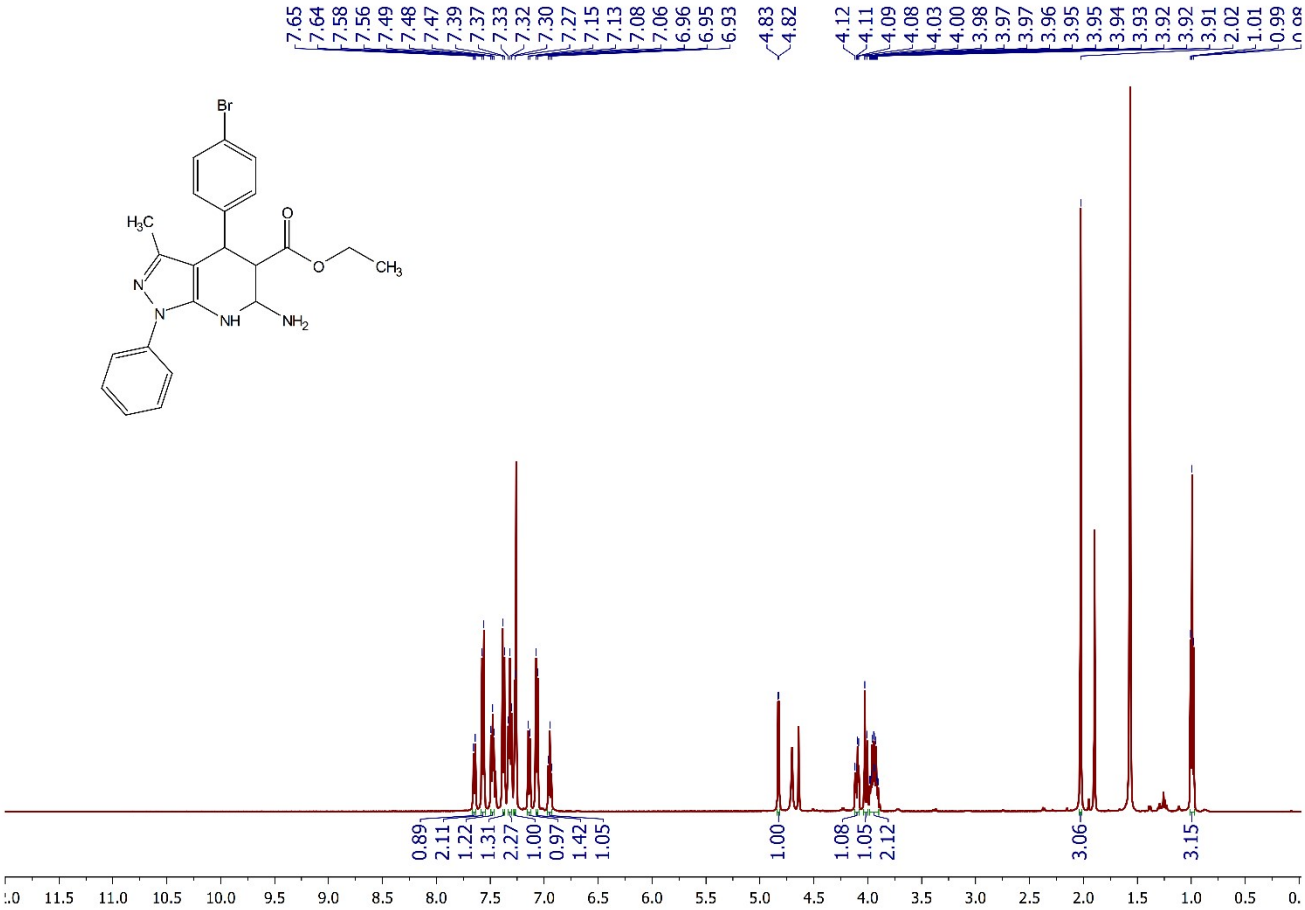

TIC from 20210203-BHa.wiff2 (sample 4) - 51b-4F, +TOF MS (30 - 1000)
Intensity, cps
Time, min
Spectrum from 20210203-BHa.wiff2 (sample 4) - 51b-4F, +TOF MS (30 - 1000) from 0.426 min
Intensity, cps
Mass/Charge, Da
133.0564
92.0368
264.0491
65.0307
281.0612
175.0594
254.0791
373.1062
174.0522
237.0442
393.1043
77.0282
282.0679
330.0480
134.0573
149.0051
376.0818
244.0465
302.0586
347.0711
199.0656
190.0372
394.1045
93.0426
131.0412
384.2419
429.0111
58.9534
93.0208
453.0638

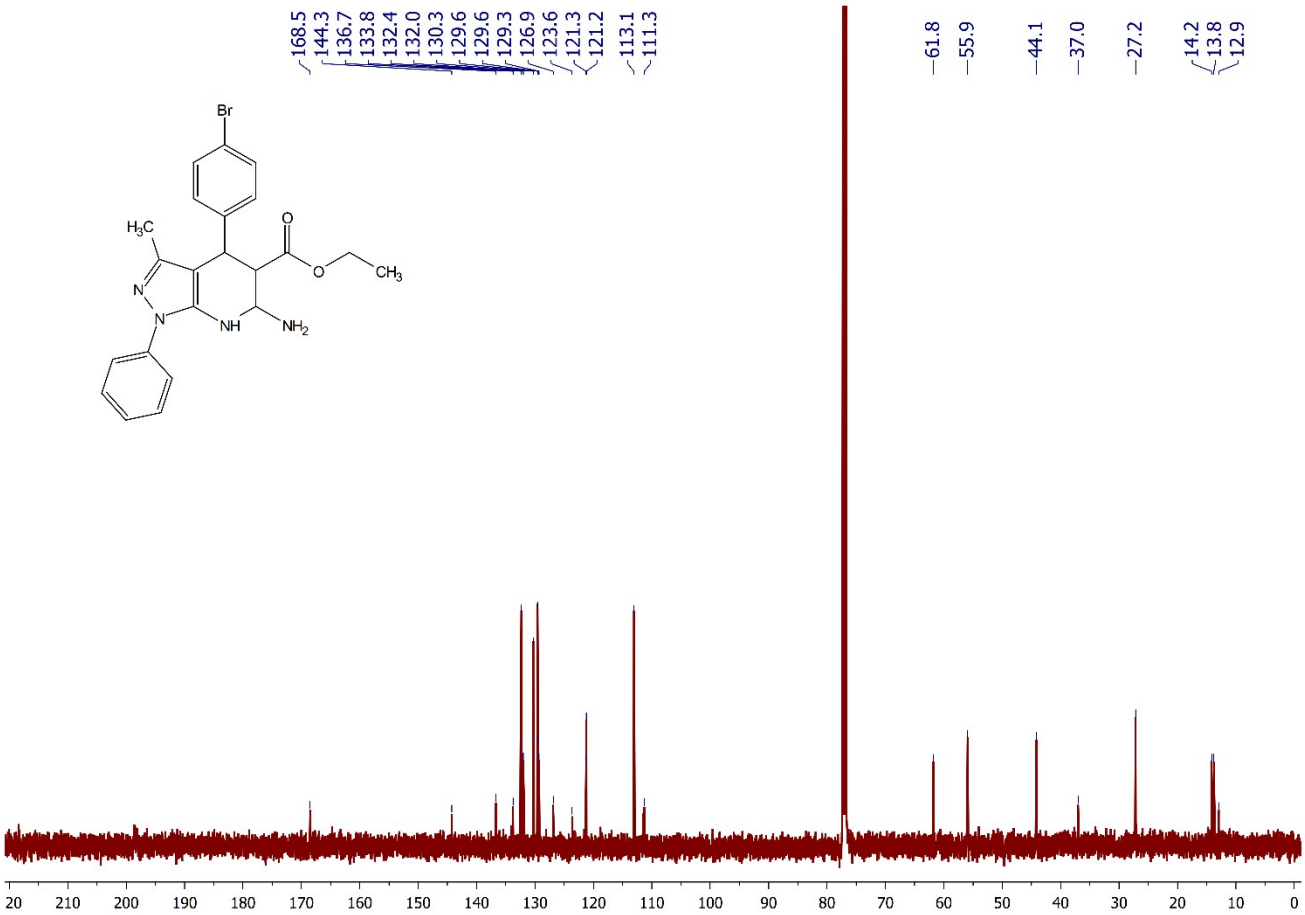
^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-4-(4-chlorophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 6b)

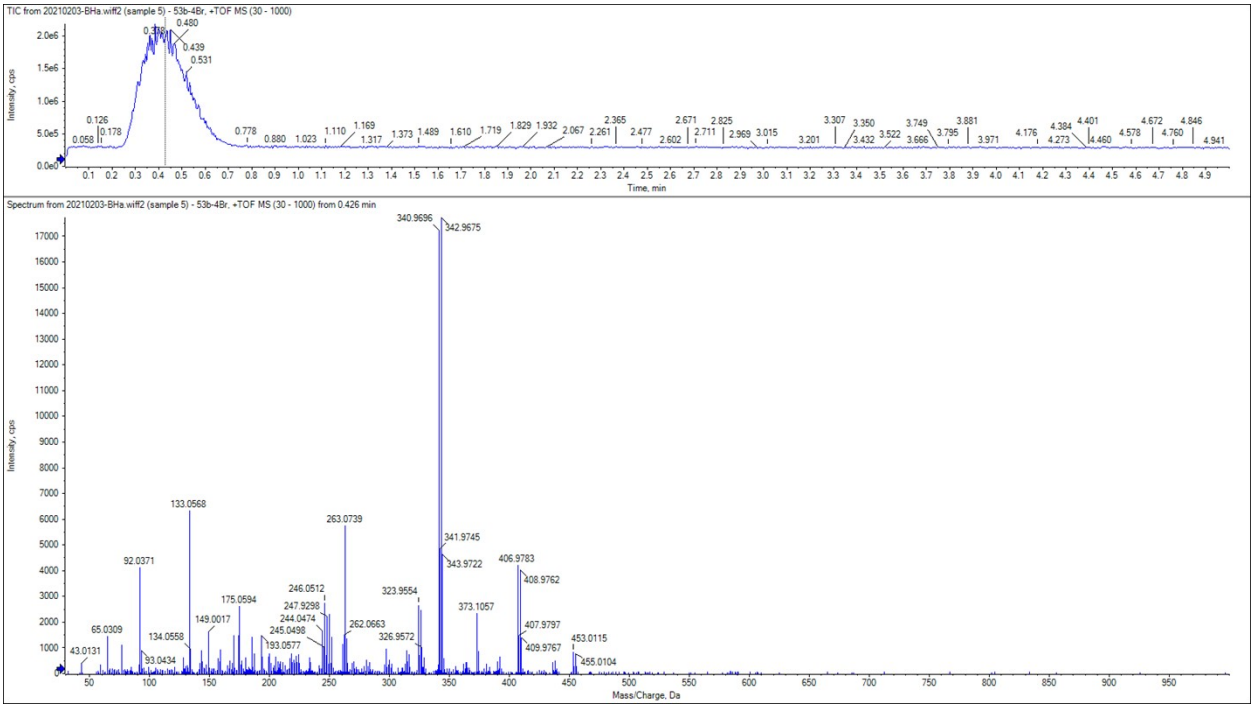



TIC from 20201217-BHa.wiff2 (sample 11) - 586, -TOF MS (30 - 1000)
Intensity, cps
Time, min
Spectrum from 20201217-BHa.wiff2 (sample 11) - 586, -TOF MS (30 - 1000) from 0.338 min
Intensity, cps
Mass/Charge, Da

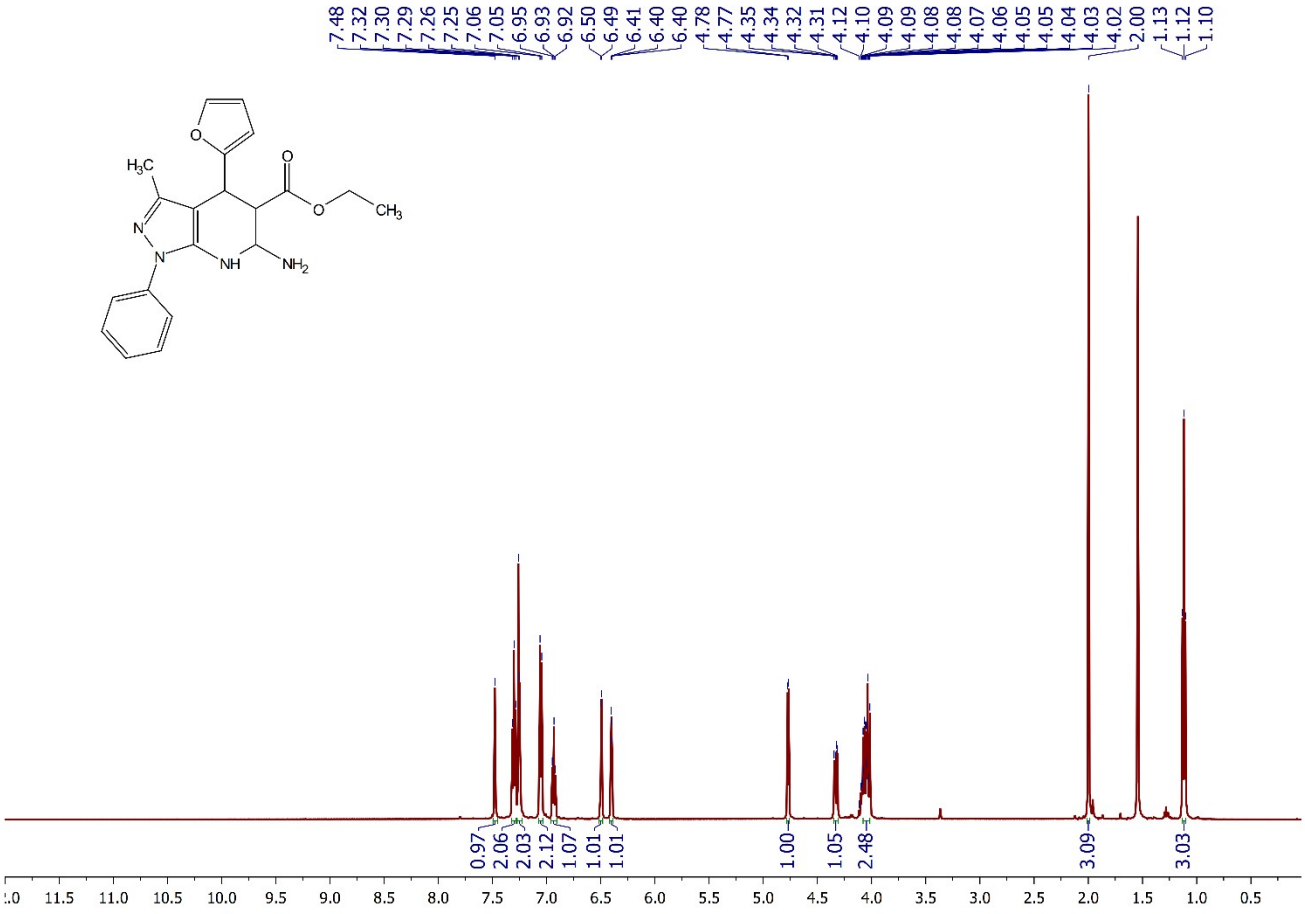
^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-4-(4-bromophenyl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 7b)

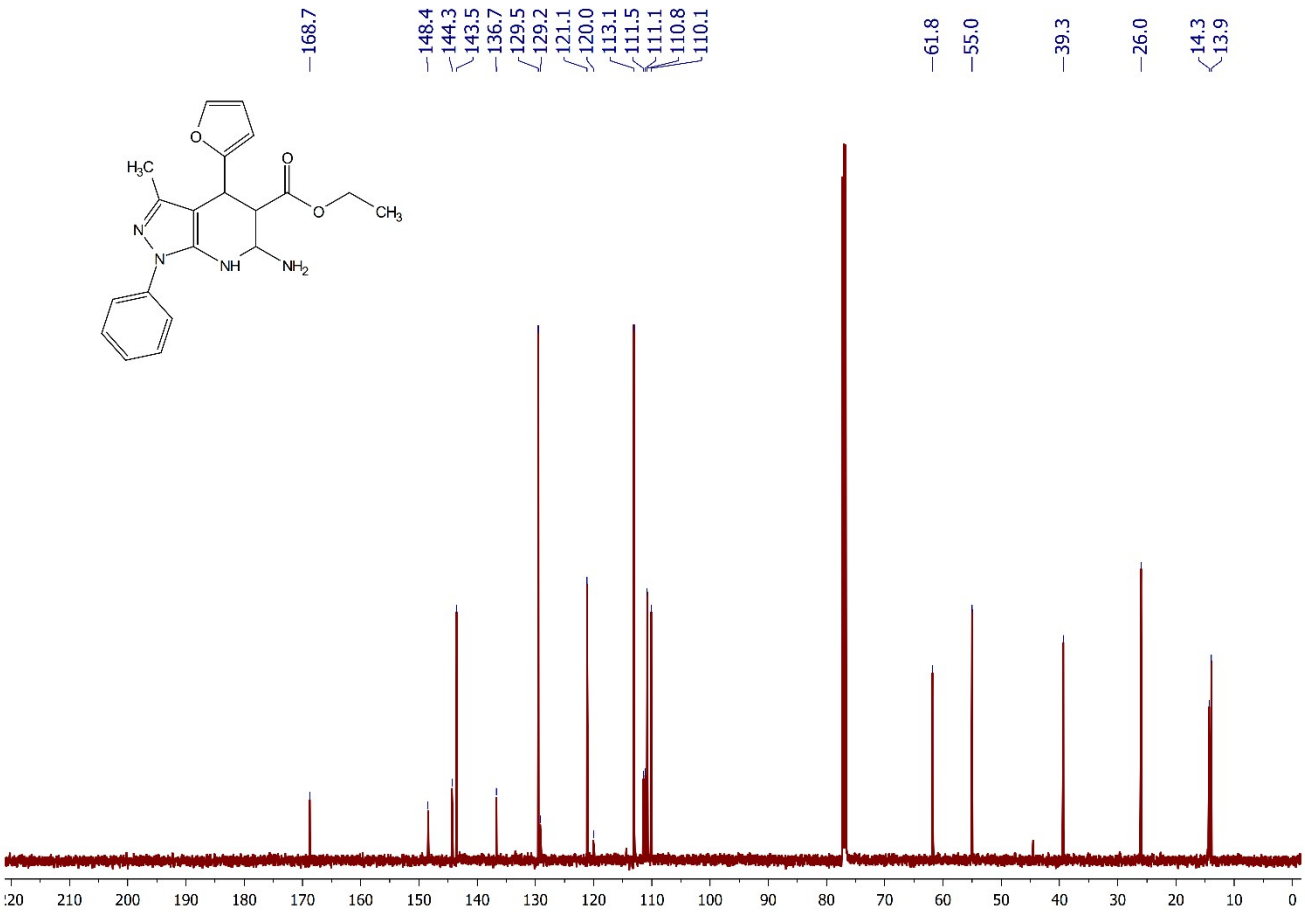


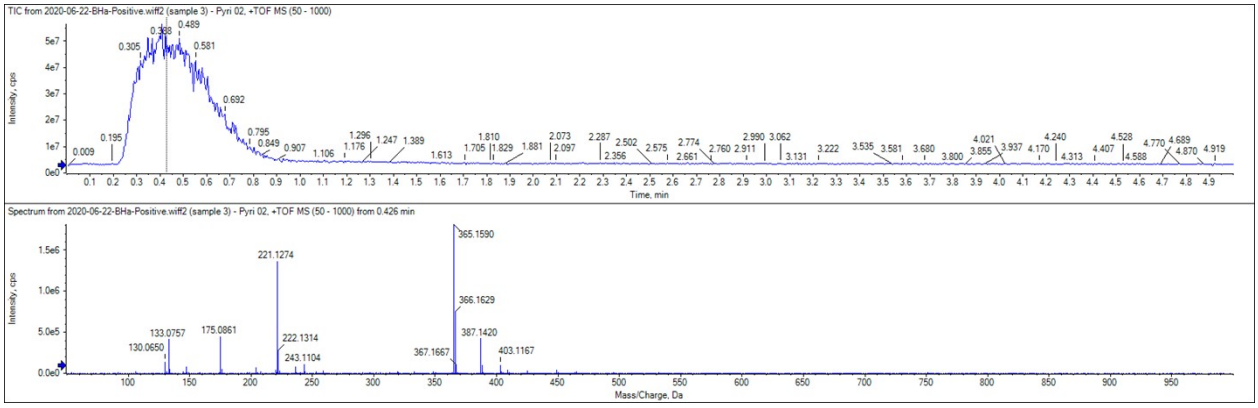



TIC from 20210203-BHa.wiff2 (sample 5) - 53b-4Br, +TOF MS (30 - 1000)
Intensity, cps
Time, min
Spectrum from 20210203-BHa.wiff2 (sample 5) - 53b-4Br, +TOF MS (30 - 1000) from 0.426 min
Intensity, cps
Mass/Charge, Da
340.9696
342.9675
133.0568
263.0739
341.9745
343.9722
92.0371
406.9783
408.9762
175.0594
246.0512
323.9554
247.9298
373.1057
149.0017
244.0474
262.0663
407.9797
65.0309
245.0498
326.9572
409.9767
134.0558
193.0577
453.0115
43.0131
93.0434
455.0104

^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-4-(furan-2-yl)-3-methyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 8b)






TIC from 2020-06-22-BHa-Positive.wiff2 (sample 3) - Pyri 02, +TOF MS (50 - 1000)
Intensity, cps
Time, min
Spectrum from 2020-06-22-BHa-Positive.wiff2 (sample 3) - Pyri 02, +TOF MS (50 - 1000) from 0.426 min
Intensity, cps
Mass/Charge, Da
365.1590
221.1274
366.1629
133.0757
175.0861
387.1420
130.0650
222.1314
243.1104
367.1667
403.1167

^{1}H, ^{13}C NMR, and HRMS spectroscopy of Ethyl 6-amino-3-methyl-4-(5-nitrofuran-2-yl)-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-carboxylate (Compound 9b)