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Supplementary Material

A New Synthesis of 4,5,6,7-Tetrahydropyrazolo[1,5-*c*]pyrimidines by a Retro-Mannich Cascade Rearrangement

Raffaele Colombo,[A] *Kyu Ok Jeon,*[A] *Donna M. Huryn,*[A] *Matthew G. LaPorte,*[A] *and Peter Wipf*[A,B]

[A] Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, USA.
[B] Corresponding author. Email: pwipf@pitt.edu

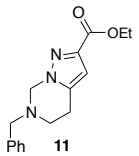
General Procedure 1

Sodium triacetoxyborohydride (167 mg, 0.788 mmol), the selected amine (0.439 mmol) and acetic acid (23.0 μL, 0.402 mmol) were added to a solution of aldehyde **44** (100 mg, 0.394 mmol) in DCE (15.0 mL). The reaction mixture was stirred at rt for 3 h, quenched with saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 (3x). The organic phases were combined, washed with brine, dried ($MgSO_4$), and concentrated. The crude residue was purified by chromatography on SiO_2 or basic alumina (*vide infra*) to afford the desired product.

General Procedure 2

To a solution of carboxylate salt **52** (90.0 mg, 0.342 mmol) in DMF (3.0 mL) was added HATU (260 mg, 0.684 mmol), *N*,*N*-diisopropylethylamine (240 μL, 1.38 mmol) and the selected amine (0.418 mmol). The reaction mixture was stirred at rt for 24 h, diluted with EtOAc (20 mL) and washed with water and brine. The organic phase was dried (Na_2SO_4) and concentrated. The crude was purified by chromatography to afford the desired product.

1-Benzyl-3-methylpiperidin-4-one **28**,[1] 9-benzyl-9-azabicyclo[3.3.1]nonan-3-one **30**,[2] 1-benzyl-2,3-dihydroquinolin-4(1*H*)-one **32**,[3] and 1-benzylazepan-4-one **39**,[4] and were prepared according to literature procedures.



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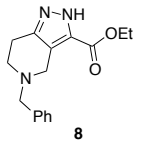

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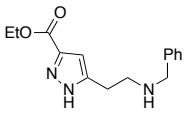

16

*Ethyl 6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxylate **11**, ethyl 5-benzyl-4,5,6,7-tetrahydro-2H-pyrazolo[4,3-c]pyridine-3-carboxylate **8**, ethyl 5-(2-(benzylamino)ethyl)-1H-pyrazole-3-carboxylate **16***

Sodium (0.11 g, 4.7 mmol) was added to ice-cooled EtOH (15 mL) under a nitrogen atmosphere. After 2 h, the solution was cooled to -10 °C and diethyl oxalate (0.59 mL, 4.3 mmol) was added dropwise. *N*-Benzyl-piperidinone (0.80 mL, 4.3 mmol) was added dropwise within an hour. The mixture was warmed to rt and stirred for 10 h. The hydrazine monohydrate (0.23 mL, 4.7 mmol) was added and the mixture was stirred for 5 min. Then, pyridinium *p*-toluenesulfonate (PPTS) (2.2 g, 8.6 mmol, 2 equiv) was added and the mixture was stirred for 5-6 h at rt. The reaction was monitored by LC-MS (gradient of 92% water/0.1% formic acid, 3% acetonitrile/0.1% formic acid/5% MeOH to 2% water/0.1% formic acid, 93% acetonitrile/0.1% formic acid, 5% MeOH). The reaction mixture was diluted with sat. $NaHCO_3$ (100 mL) and extracted with EtOAc (3x). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. The crude residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 1:1, then EtOAc, and finally EtOAc:MeOH, 4:1) to give ethyl 6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-*c*]pyrimidine-2-carboxylate **11** (0.77 g, 2.7 mmol, 62%), ethyl 5-benzyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **8** (0.17 g, 0.60 mmol, 14%) and ethyl 5-(2-(benzylamino)ethyl)-1*H*-pyrazole-3-carboxylate **16** (0.12 g, 0.44 mmol, 10%) as viscous oils.

11: IR 2982, 2924, 1711, 1452, 1221, 1191, 1094, 1023, 775, 734 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.27 (m, 5 H), 6.60 (s, 1 H), 4.92 (s, 2 H), 4.38 (q, J = 7.1 Hz, 2 H), 3.79 (s, 2 H), 3.10 (t, J = 6.1 Hz, 2 H), 2.92 (t, J = 6.1 Hz, 2 H), 1.38 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz; $CDCl_3$) δ 162.6, 142.9, 138.0, 136.9, 128.7, 128.5, 127.6, 106.1, 68.7, 60.8, 56.3, 46.3, 19.7, 14.3; HRMS (ESI) *m/z* calcd for $C_{16}H_{20}O_2N_3$ $(M+H)^+$ 286.1550, found 286.1540.

8: IR 3147, 2983, 2931, 1712, 1451, 1245, 1324, 1245, 1145, 1044, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.29 (m, 5 H), 4.35 (q, J = 7.1 Hz, 2 H), 3.77 (s, 4 H), 2.81-2.80 (m, 4 H), 1.34 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 143.9, 138.2, 134.1, 129.1, 128.5, 127.2, 118.2, 61.9, 60.8, 49.7, 49.4, 22.7, 14.3; HRMS (ESI) *m/z* calcd for $C_{16}H_{20}O_2N_3$ $(M+H)^+$ 286.1550, found 286.1543.

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[1] D. Burdi, K. L. Spear, L. W. Hardy, *WO2010/114971,* **2010**

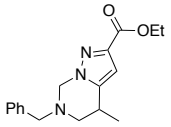
[2] R. H. Mach, R. R. Luedtke, C. D. Unsworth, V. A. Boundy, P. A. Nowak, J. G. Scripko, S. T. Elder, J. R. Jackson, P. L. Hoffman, P. H. Evora, A. V. Rae, P. B. Molinoff, S. R. Childers, R. L. Ehrenkaufert, *J. Med. Chem.* **1993**, *36*, 3707-3720. doi:10.1021/jm00075a028

[3] (a) H. B. Josien, J. W. Clader, W. J. Greenlee, M. J. Mayer, R. J. Herr, J. L. Davis, K. Deng, M. M Hsia, S. Wan, *WO2010/085525,* **2010**; (b) E. K. Bayburt, J. F. Daanen, A. R. Gomtsyan, S. P. Latshaw, C. H. Lee, R. G. Schmidt, *US patent 2008153871* **2008**

[4] Adapted from Y. S. Huang, W. Q. Zhang; P. F. Zhang, X. G. Liu, *Ind. Eng. Chem. Res.,* **2010**, *49*, 12164-12167. doi:10.1021/ie101807g

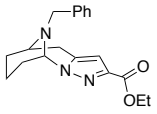
16: IR 3203, 3083, 2975, 2844, 1715, 1450, 1420, 1301, 1226, 1159, 1107 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34-7.25 (m, 5H), 6.58 (s, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 2H), 2.99 (t, *J* = 6.3 Hz, 2H), 2.88 (t, *J* = 6.3 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.0, 145.3, 141.9, 138.9, 128.5, 128.2, 127.2, 106.3, 60.7, 53.4, 47.8, 25.7, 14.2; HRMS (ESI) *m/z* calcd for $C_{15}H_{20}O_2N_3$ $(M+H)^+$ 274.1550, found 274.1548.

Reaction Optimization:
Sodium (0.109 g, 4.74 mmol) was added to ice-cooled EtOH (15 mL) under a nitrogen atmosphere. After 2 h, the solution was further cooled to -10 °C and diethyl oxalate (0.591 mL, 4.32 mmol) was added dropwise. *N*-benzyl-piperidinone **10** (0.8 mL, 4.32 mmol) was added dropwise within an hour. The mixture was warmed to rt and stirred for 10 h. The hydrazine monohydrate (0.234 mL, 4.75 mmol) was added and the mixture was stirred for 5 min. Then, the selected acid (see Table 1) was added and the mixture was stirred for 5-6 h at rt. The reaction was monitored by HPLC-MS. The reaction mixture was diluted with sat. $NaHCO_3$ (100 mL) and extracted with EtOAc (3x). The organic phases were combined, washed with brine, dried (Na_2SO_4), concentrated. The crude residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 1:1, then EtOAc, and finally EtOAc:MeOH, 4:1) to give ethyl 6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-*c*]pyrimidine-2-carboxylate **11**, ethyl 5-benzyl-4,5,6,7-tetrahydro-2*H*-pyrazolo[4,3-*c*]pyridine-3-carboxylate **8** and ethyl 5-(2-(benzylamino)ethyl)-1*H*-pyrazole-3-carboxylate **16** as viscous oils. See Table 1 in the manuscript for the isolated yields.



29

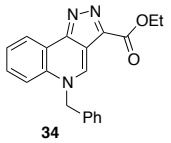
*Ethyl 6-benzyl-4-methyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxylate **29***
Sodium (0.045 g, 1.9 mmol) was added to ice-cooled EtOH (10 mL) under a nitrogen atmosphere. After 2 h, the solution was cooled to -10 °C and diethyl oxalate (0.24 mL, 1.8 mmol) was added dropwise. A solution of 1-benzyl-3-methylpiperidin-4-one **28** (0.36 g, 1.8 mmol) in EtOH (1 mL) was added dropwise within an hour. The mixture was warmed to rt and stirred for 10 h. Hydrazine monohydrate (0.10 mL, 2.0 mmol) and after 5 min acetic acid (0.13 mL, 2.2 mmol) were added. The reaction mixture was stirred for 3 h at rt, diluted with sat. $NaHCO_3$ (20 mL) and extracted EtOAc (3x). The organic phases were combined, washed with brine, dried (Na_2SO_4), and concentrated. The crude residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 7:3) to afford the desired product **29** as a clear colorless oil (0.20 g, 37%): IR (film) 2975, 2805, 1711, 1452, 1379, 1363, 1327, 1217, 1193, 1107, 775, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.33-7.26 (m, 5 H), 6.65 (s, 1 H), 4.86 (q, J_{AB} = 11.4 Hz, 2 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 3.79 (s, 2 H), 3.26-3.17 (m, 1 H), 3.12 (dd, *J* = 12.8, 5.8 Hz, 1 H), 2.59 (dd, *J* = 12.5, 10.3 Hz, 1 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 1.24 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.6, 144.1, 143.0, 136.9, 128.7, 128.5, 127.6, 105.3, 68.7, 60.8, 57.1, 54.7, 26.1, 17.7, 14.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_2N_3$ $(M+H)^+$ 300.1707, found 300.1695.



31

*Ethyl 11-benzyl-4,5,6,7,8,9-hexahydro-5,9-epiminopyrazolo[1,5-a]azocine-2-carboxylate **31***
Sodium (0.055 g, 2.4 mmol) was added to ice-cooled EtOH (12 mL) under a nitrogen atmosphere. After 2 h, the solution was cooled to -10 °C and diethyl oxalate (0.30 mL, 2.2 mmol) was added dropwise. 9-Benzyl-9-azabicyclo[3.3.1]nonan-3-one **30** (0.5 g, 2.2 mmol) was added as solid in one portion. The mixture was warmed to rt and stirred for 10 h. The hydrazine monohydrate (0.12 mL, 2.4 mmol) and after 5 min acetic acid (0.15, 2.6 mmol) were added. The reaction mixture was stirred for 3 h at rt, diluted with sat. $NaHCO_3$ (40 mL) and extracted EtOAc (3x). The organic phases were combined, washed with brine, dried (Na_2SO_4), and concentrated. The crude residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 4:1, to 100% EtOAc) to afford **31** as a colorless oil (0.22 g, 31%): IR (film) 2946, 2883, 2845, 1715, 1432, 1242, 1193, 1108, 1025, 910, 723, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28-7.23 (m, 5 H), 6.58 (s, 1 H), 5.18 (s, 1 H), 4.39-4.38 (m, 2 H), 3.64 (q, J_{AB}, 2 H), 3.28-3.25 (m, 2 H), 2.58 (d, *J* = 15.9 Hz, 1 H), 1.96-1.89 (m, 3 H), 1.62 (d, *J* = 13.0 Hz, 1 H), 1.50 (d, *J* = 13.8 Hz, 1 H), 1.38 (s, 3 H), 1.06 (q, *J* = 13.3 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7,

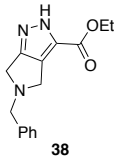
142.6, 138.8, 137.4, 128.4, 128.3, 127.2, 105.0, 73.0, 60.6, 56.9, 48.6, 32.1, 30.7, 22.5, 15.3, 14.2; HRMS (ESI) *m/z* calcd for $C_{19}H_{24}O_2N_3$ $(M+H)^+$ 326.1863, found 326.1854.



34

*Ethyl 5-benzyl-5H-pyrazolo[4,3-c]quinoline-3-carboxylate **34***

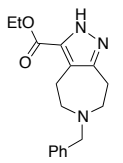
Sodium (0.053 g, 2.3 mmol) was added to ice-cooled EtOH (15 mL) under a nitrogen atmosphere. After 1 h, the solution was cooled to -10 °C and diethyl oxalate (0.29 mL, 2.1 mmol) was added dropwise, then **32** (0.50 g, 2.1 mmol) was added as solid in one portion (it dissolved in 2-3 h). The mixture was warmed to rt and stirred for 10 h. The hydrazine monohydrate (0.11 mL, 2.3 mmol) and after 5 min acetic acid (0.15 mL, 2.5 mmol) were added. The mixture was stirred for 3 h at rt, then diluted with sat. $NaHCO_3$ and extracted with EtOAc (3x). The organic phases were combined, washed with brine, dried (Na_2SO_4), concentrated and the crude residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 1:4 to 1:1) to afford **33** as a yellow-orange solid, which was not air stable and spontaneously converted into a orange solid **34** (0.28 g, 40%): Mp 180-182 °C; IR (film) 3379, 3065, 2983, 2927, 1689, 1615, 1473, 1451, 1413, 1383, 1369, 1204, 1193, 1025, 999, 757, 693 cm^{-1}; ^1H NMR (400 MHz, DMSO) δ 9.81 (s, 1 H), 8.81 (d, *J* = 7.2 Hz, 1 H), 8.19 (d, *J* = 8.1 Hz, 1 H), 7.85-7.81 (m, 2 H), 7.40-7.28 (m, 5 H), 6.27 (s, 2 H), 4.44 (q, *J* = 7.0 Hz, 2 H), 1.41 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (101 MHz, DMSO) δ 162.7, 149.8, 146.0, 142.7, 135.8, 133.4, 130.0, 129.5, 128.7, 127.2, 123.9, 121.1, 119.8, 116.3, 60.6, 58.8, 14.9; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}O_2N_3$ $(M+H)^+$ 332.1394, found 332.1389.



38

*Ethyl 5-benzyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole-3-carboxylate **38***

Sodium (0.328 mg, 14.3 mmol) was added to ice-cooled ethanol (30 mL) under a nitrogen atmosphere. After 2 h, the solution was cooled to -10 °C and diethyl oxalate (0.183 g, 12.6 mmol) was added dropwise. 1-Benzyl-3-pyrrolidinone **35** (2 g, 11.4 mmol) was added dropwise within an hour. The mixture was warmed to rt and stirred for 10 h. The hydrazine monohydrate (1.23 mL, 12.6 mmol) and after 5 min acetic acid (2.0 mL, 34 mmol) were added. The reaction mixture was stirred for 10 h at rt, then 12 h at reflux. The HPLC-MS showed the formation of hydrazone **37**. The solvents were evaporated and the crude residue was redissolved in acetic acid (10 mL) and heated at reflux for 3h. The reaction mixture was diluted with sat. $NaHCO_3$ (100 mL) and extracted EtOAc (3x). The organic phase were combined, washed with brine, dried (Na_2SO_4) and concentrated. The crude black residue was purified by chromatography on SiO_2 (solid load, EtOAc:hexanes, 4:6 to 7:3) to afford **38** as a brown oil (1.4 g, 50%): IR 3139, 3068, 2901, 2785, 1723, 1439, 1309, 1212, 1134, 1040, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.25 (m, 5 H), 4.31 (q, *J* = 7.1 Hz, 2 H), 3.99 (s, 2 H), 3.93 (t, *J* = 1.4 Hz, 2 H), 3.88 (t, *J* = 1.4 Hz, 2 H), 1.31 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 157.7, 138.5, 128.5, 128.3, 127.5, 127.1, 125.1, 61.0, 60.2, 51.5, 51.4, 14.1; HRMS (ESI) *m/z* calcd for $C_{15}H_{18}O_2N_3$ $(M+H)^+$ 272.1394, found 272.1389.



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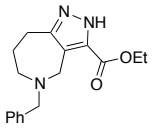

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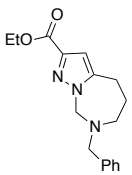


43

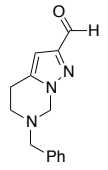
*Ethyl 6-benzyl-2,4,5,6,7,8-hexahydropyrazolo[3,4-d]azepine-3-carboxylate **41**, ethyl 5-benzyl-2,4,5,6,7,8-hexahydropyrazolo[4,3-c]azepine-3-carboxylate **42**, and ethyl 7-benzyl-5,6,7,8-tetrahydro-4H-pyrazolo[1,5-c][1,3]diazepine-2-carboxylate **43***

Sodium (127 mg, 5.53 mmol) was added to ice-cooled ethanol (10 mL) under a nitrogen atmosphere. After 2 h, the solution was cooled to -10 °C and diethyl oxalate (0.661 mL, 4.87 mmol) was added dropwise. 1-Benzylazepan-4-one 15 (0.9 g, 4.43 mmol) was added dropwise within an hour. The mixture was warmed to room temperature and stirred for 10 h. The hydrazine monohydrate (0.239 mL, 4.87 mmol) and after 5 min acetic acid (0.768 mL, 13.3 mmol) were added. The reaction mixture was stirred for 3 h at rt. The reaction mixture was diluted with sat. $NaHCO_3$ (40 mL) and extracted with EtOAc (3x). The organic phase were combined, washed with brine, dried (Na_2SO_4) and concentrated. The crude residue was purified by chromatography on SiO_2 (solid load, EtOAc/hexanes, 4:6, to 7:3) to afford the product **43** as a oil (0.10 g, 8%), and a mixture of **41** and **42** as a oil. The mixture of **41** and **42** was further purified by chromatography on SiO_2 (liquid load, toluene:MeOH, 100:6) to afford **41** (0.40 g, 30%) and **42** (0.54 g, 41%), both as colorless oils.

41: IR (film) 3128, 2938, 2908, 2819, 1711, 1450, 1312, 1256, 1160, 1130, 731, 679; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.29 (m, 5 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 3.82 (s, 2 H), 3.10-3.07 (m, 2 H), 2.97-2.95 (m, 2 H), 2.85-2.82 (m, 4 H), 1.38 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 151.3, 139.0, 133.6, 128.9, 128.3, 127.1, 123.5, 61.7, 60.9, 55.4, 54.0, 28.1, 23.8, 14.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_2N_3$ $(M+H)^+$ 300.1707, found 300.1700.

42: IR (film) 3285, 3151, 3106, 2920, 1708, 1447, 1309, 1253, 1171, 1052, 1022, 735, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.25 (m, 5 H), 4.20 (q, *J* = 6.9 Hz, 2 H), 4.07 (s, 2 H), 3.64 (s, 2 H), 3.15 (br t, *J* = 2.5 Hz, 2 H), 2.93 (br t, *J* = 2.5 Hz, 2 H), 1.81 (s, 2 H), 1.19 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.9, 152.6, 139.0, 133.6, 128.9, 128.2, 126.9, 121.6, 60.9, 58.3, 58.2, 48.4, 27.9, 24.1, 14.0; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_2N_3$ $(M+H)^+$ 300.1707, found 300.1697.

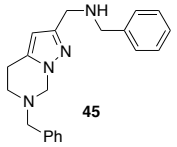
43: IR (film) 2938, 2849, 1715, 1450, 1432, 1204, 1186, 1115, 1096, 1044, 749, 735; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 5 H), 6.63 (s, 1 H), 5.27 (s, 2 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 3.53 (s, 2 H), 3.14 (t, *J* = 4.5 Hz, 2 H), 2.86 (t, *J* = 4.5 Hz, 2 H), 1.70 (br s, 2 H), 1.39 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (101 MHz, CDCl3) δ 162.4, 144.6, 141.4, 137.4, 128.5, 128.2, 127.0, 107.9, 71.9, 60.5, 54.3, 52.2, 25.4, 21.8, 14.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}O_2N_3$ $(M+H)^+$ 300.1707, found 300.1707.



44

*6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carbaldehyde **44***

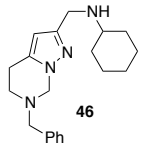
At -78 ºC, DIBAL-H (0.90 mL, 0.90 mmol, 1 M solution in toluene, pre cooled to -78 ºC under inert atmosphere) was slowly added to a solution of **11** (0.10 mg, 0.35 mmol) in CH_2Cl_2 (2.0 mL). The reaction mixture was stirred at - 78 ºC for 1 h, quenched with methanol (1.0 mL) at -78 ºC and warmed to rt. The solution was diluted with aqueous 1 M HCl and extracted with CH_2Cl_2 (3x). The organic phases were combined, washed with brine, dried (Na_2SO_4), and concentrated to afford **44** as colorless oil (78 mg, 83%): IR (thin film, CH_2Cl_2) 2937, 2805, 1691, 1452, 1115, 788 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1 H), 7.37-7.32 (m, 5 H), 6.60 (s, 1 H), 4.94 (s, 2 H), 3.83 (s, 2 H), 3.14 (t, *J* = 6.4 Hz, 2 H), 2.96 (t, *J* = 6.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.8, 150.7, 138.9, 136.8, 128.8, 128.7, 127.8, 103.2, 68.8, 56.5, 46.5, 19.9; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}N_3O$ $(M+H)^+$ 242.1288, found 242.1289.



45

*N-Benzyl-1-(6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)methanamine **45***

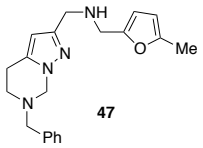
Prepared according to the General Procedure 1, using benzylamine (48.0 μL, 0.439 mmol). The crude residue was purified by chromatography on SiO_2 (MeOH:CH_2Cl_2, 1:20, with 0.1% Et_3N) to afford the desired product **45** (86.0 mg, 66%) as a colorless oil: IR (thin film, CH_2Cl_2) 3359, 3019, 2919, 1541, 1493, 1450, 1025 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.23 (m, 10 H), 6.01 (s, 1 H), 4.81 (s, 2 H), 3.86 (s, 2 H), 3.81 (s, 2 H), 3.05 (t, *J* = 6.4 Hz, 2 H), 2.88 (t, *J* = 6.4 Hz, 2 H), 1.95 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 140.2, 137.4, 137.3, 128.9, 128.5, 128.31, 128.25, 127.6, 126.9, 101.9, 68.0, 56.7, 53.4, 46.9, 46.7, 20.1; HRMS (ESI) *m/z* calcd for $C_{21}H_{25}N_4$ $(M+H)^+$ 333.2074, found 333.2078.



46

N-((6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)methyl)cyclohexanamine ***46***

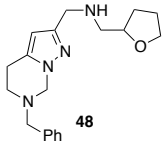
Prepared according to the General Procedure 1, using cyclohexylamine (50.0 μL, 0.436 mmol). The residue was purified by chromatography on basic Al_2O_3 ($MeOH:CH_2Cl_2$, 1:25) to afford the desired **46** (73.0 mg, 57%) as a colorless oil: IR (film, CH_2Cl_2) 3334, 2924, 2850, 1448, 1109 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 5 H), 5.98 (s, 1 H), 4.79 (s, 2 H), 3.79 (s, 4 H), 3.03 (t, *J* = 6.0 Hz, 2 H), 2.86 (t, *J* = 6.0 Hz, 2 H), 2.55 (tt, *J* = 10.4, 4.0 Hz, 1 H), 1.92 (d, *J* = 12.4 Hz, 2 H), 1.84 (br s, 1 H), 1.73 (dt, *J* = 12.8, 3.6 Hz, 2 H), 1.61 (d, *J* = 11.6 Hz, 1 H), 1.31-1.08 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 137.33, 137.30, 128.8, 128.5, 127.5, 101.8, 68.0, 56.6, 56.4, 46.8, 44.3, 33.3, 26.1, 25.0, 20.0; HRMS (ESI) *m/z* calcd for $C_{20}H_{29}N_4$ $(M+H)^+$ 325.2387, found 325.2386.



47

1-(6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)-N-((5-methylfuran-2-yl)methyl)methanamine ***47***

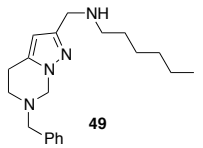
Prepared according to the General Procedure 1, using 5-methylfurfurylamine (50.0 uL, 0.435 mmol). The crude residue was purified by chromatography on basic Al_2O_3 ($MeOH:CH_2Cl_2$, 1:25) to afford the desired **47** (93.0 mg, 70%) as a colorless oil: IR (film, CH_2Cl_2) 3334, 2924, 1493, 1450, 1342 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5 H), 6.06 (d, *J* = 2.8 Hz, 1 H), 6.00 (s, 1H), 5.87 (dd, *J* = 2.8, 0.8 Hz, 1 H), 4.81 (s, 2 H), 3.81 (s, 2 H), 3.79 (s, 2 H), 3.77 (s, 2 H), 3.05 (t, *J* = 6.0 Hz, 2 H), 2.88 (t, *J* = 6.0 Hz, 2 H), 2.27 (s, 3 H), 1.85 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 151.3, 150.7, 137.40, 137.35, 128.9, 128.5, 127.6, 107.8, 105.9, 102.0, 68.0, 56.7, 46.9, 46.3, 45.8, 20.0, 13.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{25}N_4O$ $(M+H)^+$ 337.2023, found 337.2021.



48

1-(6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)-N-((tetrahydrofuran-2-yl)methyl)methanamine ***48***

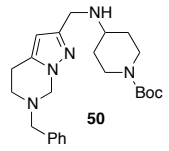
Prepared according to the General Procedure 1, using tetrahydrofurylmethylamine (46.0 μL, 0.433 mmol). The crude residue was purified by chromatography on basic Al_2O_3 ($MeOH:CH_2Cl_2$, 1:25) to afford the desired **48** (90.0 mg, 70%) as a colorless oil: IR (film, CH_2Cl_2) 3359, 2937, 1541, 1451, 1062 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5 H), 6.00 (s, 1 H), 4.79 (s, 2 H), 4.04 (ddd, *J* = 14.0, 7.0, 4.0 Hz, 1 H), 3.86-3.79 (m, 5 H), 3.73 (q, *J* = 7.0 Hz, 1 H), 3.04 (t, *J* = 6.0 Hz, 2 H), 2.87 (t, *J* = 6.0 Hz, 2 H), 2.73 (ddd, *J* = 14.0, 7.5, 4.0 Hz, 2 H), 2.10 (br s, 1 H), 2.00-1.94 (m, 1 H), 1.90-1.83 (m, 2 H), 1.60-1.53 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 137.4, 128.9, 128.5, 127.5, 101.8, 78.3, 68.0, 67.8, 56.7, 53.8, 47.4, 46.9, 29.3, 25.7, 20.1; HRMS (ESI) *m/z* calcd for $C_{19}H_{27}N_4O$ $(M+H)^+$ 327.2179, found 327.2174.



49

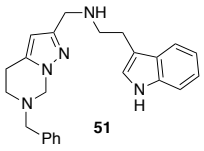
N-((6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)methyl)hexan-1-amine ***49***

Prepared according to the General Procedure 1, using hexylamine (57.0 μL, 0.432 mmol). The crude residue was purified by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 1:25, with 0.05% Et_3N) to afford the desired **49** (74.6 mg, 58%) as a yellow oil: IR (film, CH_2Cl_2) 3346, 2924, 1716, 1493, 1364 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5 H), 6.04 (s, 1 H), 4.80 (s, 2 H), 3.83 (s, 2 H), 3.80 (s, 2 H), 3.70 (br s, 1 H), 3.04 (t, *J* = 6.5 Hz, 2 H), 2.87 (t, *J* = 6.5 Hz, 2 H), 2.70 (t, *J* = 7.5 Hz, 2 H), 1.55 (p, *J* = 8.5 Hz, 2 H), 1.34-1.26 (m, 6 H), 0.88 (t, *J* = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 137.6, 137.3, 128.8, 128.5, 127.6, 102.2, 68.0, 56.7, 49.0, 46.8, 46.6, 31.6, 29.2, 26.9, 22.5, 20.1, 14.0; HRMS (ESI) *m/z* calcd for $C_{20}H_{31}N_4$ $(M+H)^+$ 327.2543, found 327.2542.



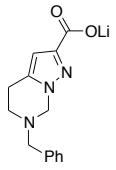
50

*tert-Butyl 4-(((6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)methyl)amino)piperidine-1-carboxylate **50***
Prepared according to the General Procedure 1, using 4-amino-1-Boc-piperidine (90.0 mg, 0.436 mmol). The crude residue was purified by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 1:20, with 0.05% Et_3N) to afford the desired **50** (118 mg, 70%) as a colorless oil: IR (film, CH_2Cl_2) 3327, 2932, 1684, 1420, 1167, 1141 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5 H), 5.98 (s, 1 H), 4.80 (s, 2 H), 4.04 (br s, 2 H), 3.81 (s, 4 H), 3.05 (t, *J* = 6.4 Hz, 2 H), 2.88 (t, *J* = 6.0 Hz, 2 H), 2.80 (t, *J* = 11.2 Hz, 2 H), 2.71 (tt, *J* = 10.4, 3.6 Hz, 1 H), 1.88 (d, *J* = 11.2 Hz, 2 H), 1.46 (s, 9 H), 1.36-1.26 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 150.7, 137.5, 137.3, 128.8, 128.5, 127.6, 101.8, 79.3, 68.0, 56.7, 54.4, 46.9, 44.2, 32.3, 28.4, 20.1; HRMS (ESI) *m/z* calcd for $C_{24}H_{36}N_2O_2$ $(M+H)^+$ 426.2864, found 426.2864.



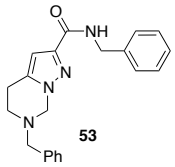
51

*N-((6-Benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidin-2-yl)methyl)-2-(1H-indol-3-yl)ethanamine **51***
Prepared according to the General Procedure 1, using tryptamine (69.0 mg 0.430 mmol). The crude residue was purified by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 1:25, with 0.02% Et_3N) to afford the desired **51** (0.91 g, 60%) as a yellow oil: IR (film, CH_2Cl_2) 3195, 2924, 1453, 1342, 1105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 15.5 Hz, 1 H), 7.62 (d, *J* = 8.0 Hz, 1 H), 7.36-7.28 (m, 5 H), 7.19 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.11 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.05 (s, 1 H), 5.95 (s, 1 H), 4.78 (s, 2 H), 3.82 (s, 2 H), 3.79 (s, 2 H), 3.04-3.02 (m, 6 H), 2.85 (t, *J* = 6.0 Hz, 2 H), 1.83 (br s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 137.4, 136.4, 128.9, 128.5, 127.6, 127.5, 121.9, 119.2, 118.9, 114.0, 111.1, 101.9, 68.0, 56.7, 49.5, 47.2, 46.9, 25.7, 20.0; HRMS (ESI) *m/z* calcd for $C_{24}H_{28}N_5$ $(M+H)^+$ 386.2339, found 386.2339.



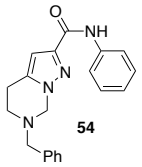
52

*Lithium 6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxylate **52***
A solution of LiOH (5.8 mL, 5.80 mmol, 1 M in H_2O) was added to a solution of **11** (550 mg, 1.93 mmol) in THF (18 mL). The reaction mixture was stirred at rt for 15 h. Another portion of LiOH (500 μL, 0.500 mmol, 1 M solution in H_2O) was added and the reaction mixture was stirred at rt for 6 h, concentrated, and water was azeotropically removed with toluene to afford the desired **52** (498 mg, 98%) as a white solid: Mp 230 ºC; ^1H NMR (400 MHz, MeOH-d_4) δ 7.38-7.28 (m, 5 H), 6.44 (s, 1 H), 4.80 (s, 2 H), 3.82 (s, 2 H), 3.10 (t, *J* = 6.0 Hz, 2 H), 2.93 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, MeOH-d_4) δ 170.7, 150.5, 139.3, 138.7, 130.2, 129.6, 128.7, 105.6, 68.9, 57.4, 47.9, 20.8; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}N_3O_2$ $(M-Li+2H)^+$ 258.1237, found 258.1236.



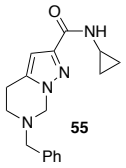
*N,6-Dibenzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **53***

Prepared according to General Procedure 2, using benzylamine (46 μL, 0.42 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:1) to afford the desired **53** (56 mg, 50%) as a white solid: Mp 92-93 ºC; IR (film, CH_2Cl_2) 3327, 2924, 1655, 1528, 1451 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.30 (m, 10 H), 7.11 (br s, 1 H), 6.62 (s, 1 H), 4.81 (s, 2 H), 4.61 (d, *J* = 7.6 Hz, 2 H), 3.81 (s, 2 H), 3.11 (t, *J* = 6.0 Hz, 2 H), 2.94 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 145.9, 138.5, 137.1, 128.8, 128.6, 127.9, 127.7, 127.5, 127.34, 127.26, 104.1, 68.4, 56.5, 46.7, 43.1, 19.9; HRMS (ESI) *m/z* calcd for $C_{21}H_{23}N_4O$ $(M+H)^+$ 347.1866, found 347.1862.



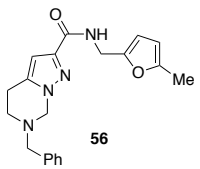
*6-Benzyl-N-phenyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **54***

Prepared according to General Procedure 2, using aniline (95 μL, 1.0 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:1) to afford the desired **54** (95 mg, 84%) as a white solid: Mp 94-95 ºC; IR (film, CH_2Cl_2) 3364, 2931, 1676, 1593, 1526, 1427, 1308 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (br s, 1 H), 7.69 (d, *J* = 8.0 Hz, 2 H), 7.70-7.34 (m, 7 H), 7.11 (t, *J* = 7.2 Hz, 1 H), 6.69 (s, 1 H), 4.89 (s, 2 H), 3.84 (s, 2 H), 3.15 (t, *J* = 6.0 Hz, 2 H), 2.97 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 146.1, 138.9, 138.1, 129.0, 128.8, 128.6, 127.8, 123.8, 119.6, 104.3, 68.4, 56.5, 46.7, 20.0; HRMS (ESI) *m/z* calcd for $C_{20}H_{21}N_4O$ $(M+H)^+$ 333.1710, found 333.1712.



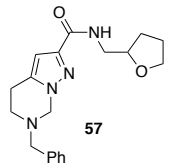
*6-Benzyl-N-cyclopropyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **55***

Prepared according to General Procedure 2, using cyclopropylamine (50 μL, 0.71 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:4) to afford the desired **55** (53.5 mg, 53%) as a yellow solid: Mp 87-88 ºC; IR (film, CH_2Cl_2) 3390, 2924, 1653, 1524 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5 H), 6.85 (br s, 1 H), 6.59 (s, 1 H), 4.81 (s, 2 H), 3.80 (s, 2 H), 3.12 (t, *J* = 6.0 Hz, 2 H), 2.93 (t, *J* = 6.5 Hz, 2 H), 2.86 (app oct, *J* = 4.0 Hz, 1 H), 0.82 (m, 2 H), 0.60 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 146.0, 138.4, 137.0, 128.8, 128.6, 127.7, 104.0, 68.3, 56.5, 46.7, 22.2, 19.9, 6.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{21}N_4O$ $(M+H)^+$ 297.1710, found 297.1707.



*6-Benzyl-N-((5-methylfuran-2-yl)methyl)-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **56***

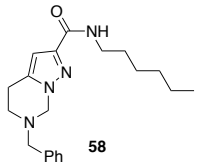
Prepared according to General Procedure 2, using 5-methylfurfurylamine (80 μL, 0.71 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:3) to afford the desired **56** (80 mg, 67%) as a yellow oil: IR (thin film, CH_2Cl_2) 3334, 2924, 1659, 1527, 1196 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5 H), 7.03 (br s, 1 H), 6.61 (s, 1 H), 6.14 (d, *J* = 3.5 Hz, 1 H), 5.88 (dd, *J* = 3.5, 1.0 Hz, 1 H), 4.83 (s, 2 H), 4.54 (d, *J* = 5.5 Hz, 2 H), 3.81 (s, 2 H), 3.11 (t, *J* = 6.0 Hz, 2 H), 2.94 (t, *J* = 6.0 Hz, 2 H), 2.65 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 151.8, 149.6, 145.8, 138.4, 137.1, 128.8, 128.6, 127.7, 108.3, 106.2, 104.1, 68.4, 56.5, 46.7, 36.2, 19.9, 13.5; HRMS (ESI) *m/z* calcd for $C_{20}H_{23}N_4O_2$ $(M+H)^+$ 351.1816, found 351.1818.



57

*6-Benzyl-N-((tetrahydrofuran-2-yl)methyl)-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **57***

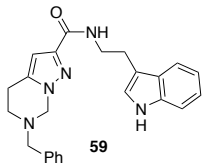
Prepared according to General Procedure 2, using tetrahydrofurfurylamine (110 μL, 1.06 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:3) to afford the desired **57** (64 mg, 55%) as a yellow solid: Mp 76-77 ºC; IR (film, CH_2Cl_2) 3409, 2919, 1655, 1545, 1232 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (m, 5 H), 7.11 (br s, 1 H), 6.58 (s, 1 H), 4.84 (s, 2 H), 4.06-4.04 (m, 1 H), 3.89 (q, *J* = 7.6 Hz, 1 H), 3.81 (s, 2 H), 3.77 (q, *J* = 8.0 Hz, 1 H), 3.70-3.67 (m, 1 H), 3.36 (p, *J* = 6.0 Hz, 1 H), 3.10 (t, *J* = 6.0 Hz, 2 H), 2.93 (t, *J* = 5.6 Hz, 2 H), 2.04-1.96 (m, 1 H), 1.91-1.86 (m, 2 H), 1.65-1.58 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 145.9, 138.3, 137.1, 128.8, 128.6, 127.7, 103.9, 77.9, 68.4, 68.2, 56.5, 46.6, 42.7, 28.7, 25.9, 19.9; HRMS (ESI) *m/z* calcd for $C_{19}H_{25}N_4O_2$ $(M+H)^+$ 341.1972, found 341.1972.



58

*6-Benzyl-N-hexyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **58***

Prepared according to General Procedure 2, using hexylamine (137 μL, 1.03 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:3) to afford the desired **58** (85 mg, 73%) as a yellow solid: Mp 83-84 ºC; IR (thin film, CH_2Cl_2) 3346, 2919, 1655, 1547, 1235 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 5 H), 6.79 (t, *J* = 5.2 Hz, 1 H), 6.59 (s, 1 H), 4.83 (s, 2 H), 3.81 (s, 2 H), 3.40 (q, *J* = 6.8 Hz, 2 H), 3.11 (t, *J* = 6.4 Hz, 2 H), 2.93 (t, *J* = 6.0 Hz, 2 H), 1.58 (p, *J* = 6.8 Hz, 2 H), 1.41-1.26 (m, 6 H), 0.89 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 146.2, 138.4, 137.1, 128.8, 128.6, 127.7, 104.0, 68.3, 56.5, 46.7, 39.1, 31.5, 29.7, 26.6, 22.5, 19.9, 14.0; HRMS (ESI) *m/z* calcd for $C_{20}H_{29}N_4O$ $(M+H)^+$ 341.2336, found 341.2334.

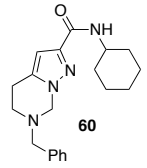


59

*N-(2-(1H-Indol-3-yl)ethyl)-6-benzyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide **59***

Prepared according to General Procedure 2, using tryptamine (166 mg, 1.03 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:4) to afford the desired **59** (94 mg, 69%) as a white solid: Mp 154-155 ºC; IR (film, CH_2Cl_2) 3284, 2919, 1647, 1551, 1530, 1455 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1 H), 7.66 (dd, *J* = 2.6, 0.4 Hz, 1 H), 7.38-7.31 (m, 5 H), 7.20 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.12 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.08 (d, *J* = 2.0 Hz, 1 H), 6.95 (t, *J* = 5.6 Hz, 1 H), 6.59 (s, 1 H), 4.80 (s, 2 H), 3.80 (s, 2 H), 3.77 (q, *J* = 6.8 Hz, 2 H), 3.10 (t, *J* = 6.4 Hz, 2 H), 3.07 (t, *J* = 6.8 Hz, 2 H), 2.93 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 146.1, 138.3, 137.1, 136.4, 128.8,

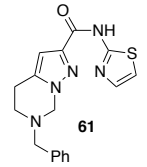
128.6, 127.7, 127.4, 122.1, 121.9, 119.4, 118.9, 113.3, 111.1, 103.9, 68.3, 56.5, 46.7, 39.3, 25.6, 19.9; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}N_5O$ $(M+H)^+$ 400.2118, found 400.2122.



60

6-Benzyl-N-cyclohexyl-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide ***60***

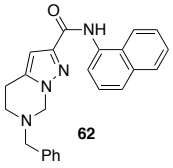
Prepared according to General Procedure 2, using cyclohexylamine (120 μL, 1.04 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:3) to afford the desired product **60** (53 mg, 45%) as a yellow solid: Mp 104-105 ºC; IR (thin film, CH_2Cl_2) 3403, 2924, 1659, 1527, 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.30 (m, 5 H), 6.68 (d, *J* = 8.4 Hz, 1 H), 6.59 (s, 1 H), 4.84 (s, 2 H), 3.99-3.89 (m, 1 H), 3.82 (s, 2 H), 3.10 (t, *J* = 6.4 Hz, 2 H), 2.93 (t, *J* = 6.0 Hz, 2 H), 2.00 (dd, *J* = 12.4, 3.6 Hz, 2 H), 1.74 (dt, *J* = 14.0, 3.6 Hz, 2 H), 1.41 (qt, *J* = 15.2, 3.2 Hz, 2 H), 1.29-1.15 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 146.4, 138.4, 137.1, 128.8, 128.6, 127.7, 104.0, 68.4, 56.5, 47.7, 46.7, 33.2, 25.6, 24.9, 19.9; HRMS (ESI) *m/z* calcd for $C_{20}H_{27}N_4O$ $(M+H)^+$ 339.2179, found 339.2179.



61

6-Benzyl-N-(thiazol-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide ***61***

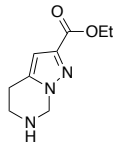
Prepared according to General Procedure 2, using 2-aminothiazole (104 mg, 1.03 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:3) to afford the desired **61** (69 mg, 59%) as a white solid: Mp 138-139 ºC; IR (film, CH_2Cl_2) 3120, 2924, 1672, 1528, 1315, 1187 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.09 (br s, 1H), 7.48 (d, *J* = 3.6 Hz, 1 H), 7.41-7.32 (m, 5 H), 6.98 (d, *J* = 3.6 Hz, 1 H), 6.72 (s, 1 H), 4.90 (s, 2 H), 3.83 (s, 2 H), 3.15 (t, *J* = 6.4 Hz, 2 H), 2.98 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 157.8, 143.8, 139.2, 137.8, 136.9, 128.9, 128.7, 127.8, 113.4, 104.8, 68.6, 56.4, 46.4, 19.9; HRMS (ESI) *m/z* calcd for $C_{17}H_{18}N_5OS$ $(M+H)^+$ 340.1227, found 340.1225.



62

6-Benzyl-N-(naphthalen-1-yl)-4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxamide ***62***

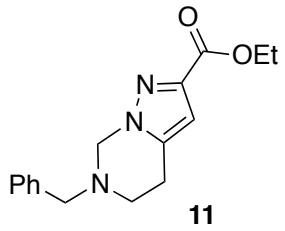
Prepared according to General Procedure 2, using 1-aminonaphthalene (124 mg, 0.855 mmol). The crude residue was purified by chromatography on SiO_2 (hexanes:EtOAc, 1:1) to afford the desired **62** (104 mg, 80%) as a purple solid: Mp 117-118 ºC; IR (film, CH_2Cl_2) 3384, 2931, 1687, 1530, 1502, 1342, 1193 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.27 (br s, 1H), 8.28 (d, *J* = 7.6 Hz, 1 H), 8.01 (d, *J* = 8.0 Hz, 1 H), 7.88 (d, *J* = 7.6 Hz, 1 H), 7.69 (d, *J* = 8.0 Hz, 1 H), 7.57-7.51 (m, 3 H), 7.40-7.34 (m, 5 H), 6.75 (s, 1 H), 4.96 (s, 2 H), 3.88 (s, 2 H), 3.17 (t, *J* = 6.0 Hz, 2 H), 3.00 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 146.2, 139.0, 137.1, 134.1, 132.5, 128.9, 128.73, 128.66, 127.8, 126.5, 126.1, 125.95, 125.85, 124.8, 120.5, 119.1, 104.4, 68.6, 56.5, 46.7, 20.0; HRMS (ESI) *m/z* calcd for $C_{24}H_{23}N_4O$ $(M+H)^+$ 383.1866, found 383.1867.



63

*Ethyl 4,5,6,7-tetrahydropyrazolo[1,5-c]pyrimidine-2-carboxylate **63***

To a solution of **11** (1.3 g, 4.6 mmol) in *i*-PrOH (60 mL) was added 30% Pd/C (0.32 g, 0.91 mmol) and the flask was purged three times with vacuum/H_2. The mixture was stirred at 40 °C for 4 d under a H_2 atmosphere (balloon), then filtered through a pad of Celite, concentrated, and the crude residue was purified by chromatography on a small pad of SiO_2 (EtOAc, 100%) to afford the desired **63** as a colorless oil (0.42 g, 47%): IR (film) 3308, 2975, 2932, 2868, 1712, 1465, 1441, 1230, 1191, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.49 (s, 1 H), 5.01 (s, 2 H), 4.31 (q, J = 7.1 Hz, 2 H), 3.14 (t, J = 6.1 Hz, 2 H), 2.79 (t, J = 6.0 Hz, 2 H), 1.32 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6, 142.4, 138.5, 106.2, 63.8, 60.6, 40.9, 24.0, 14.2; HRMS (ESI) m/z calcd for $C_9H_{14}O_2N_3$ $(M+H)^+$ 196.1081, found 196.1082.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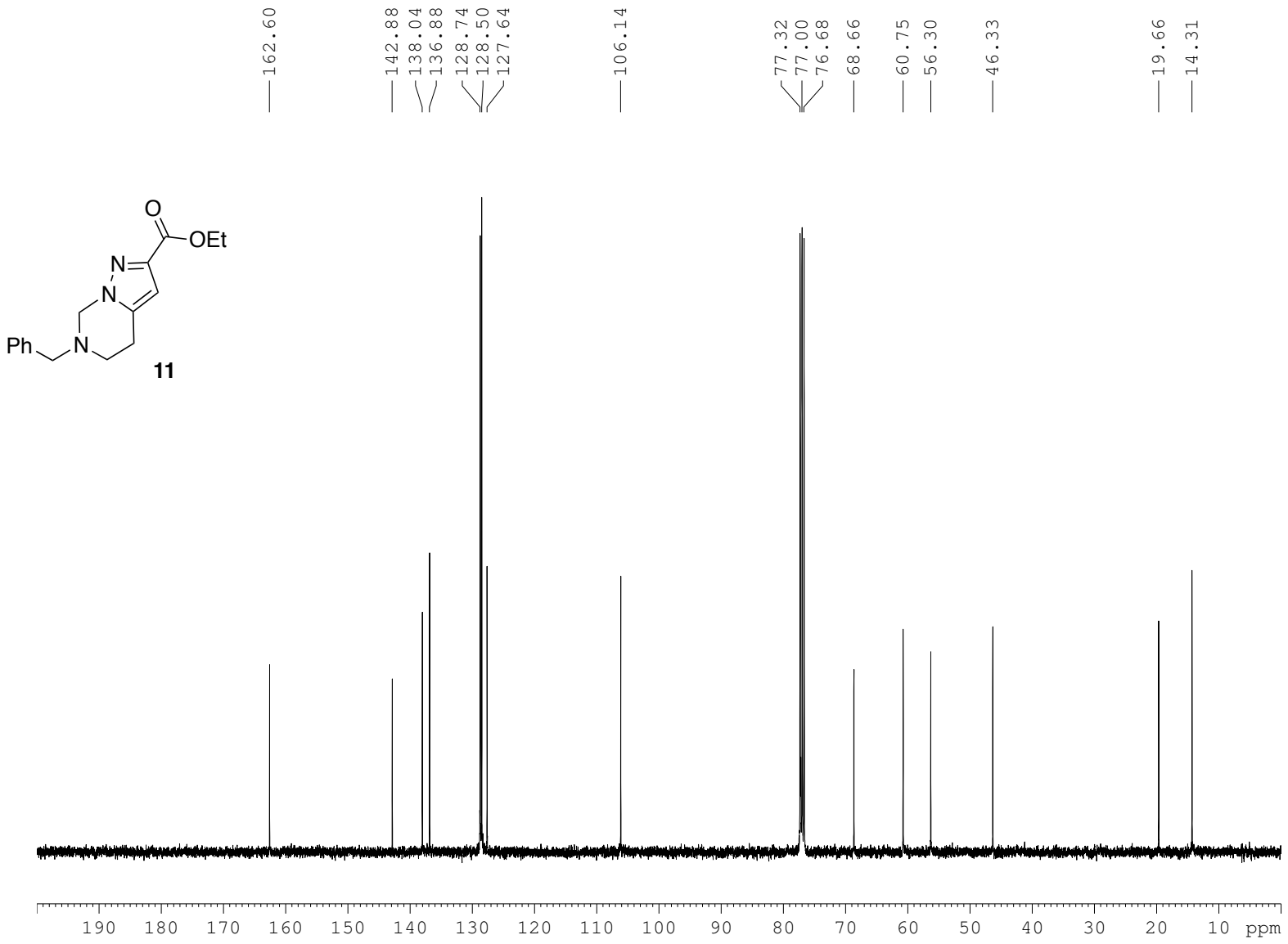
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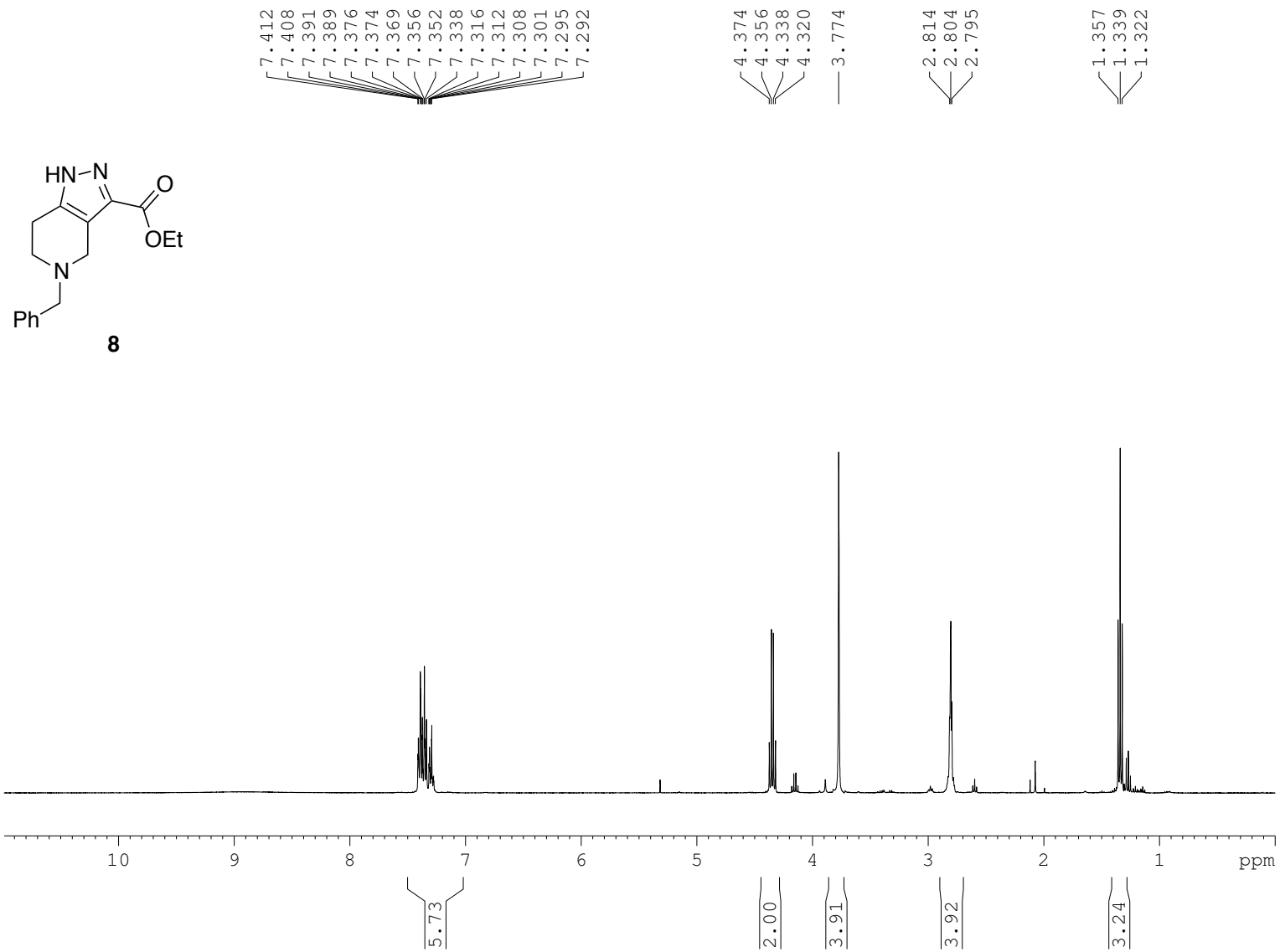
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4.356
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2.804
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Ph
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3.24

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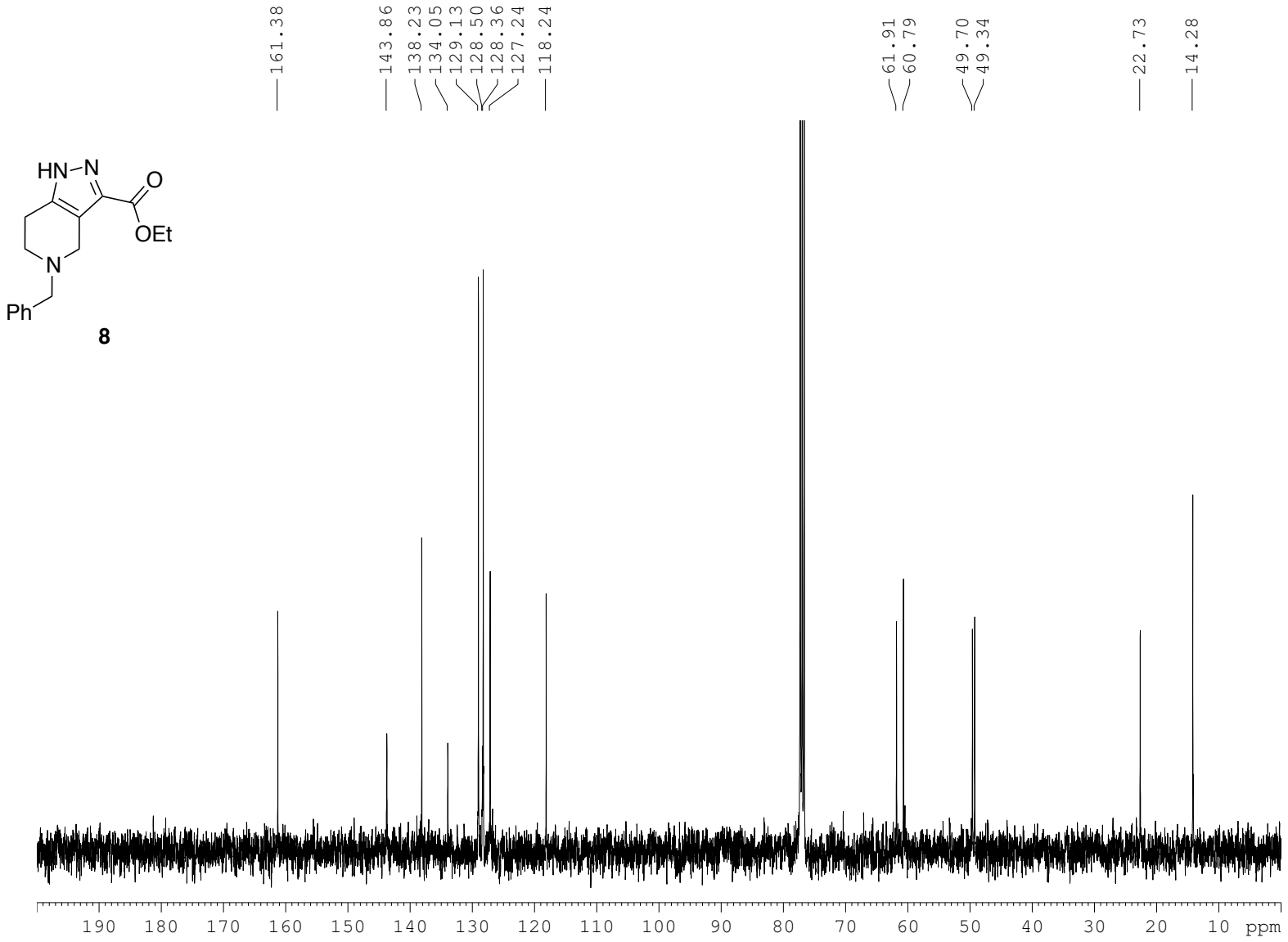
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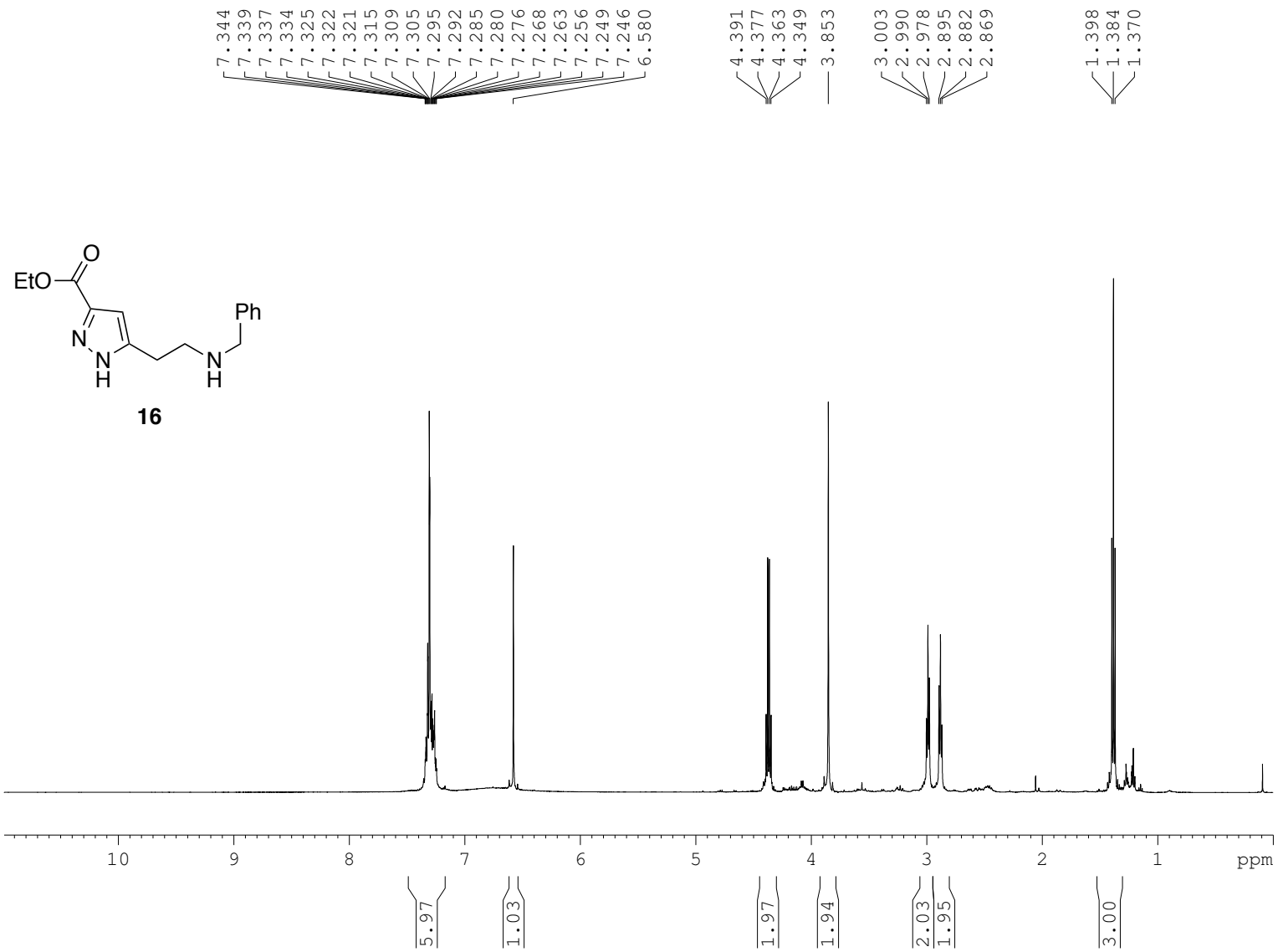
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4.349
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3.003
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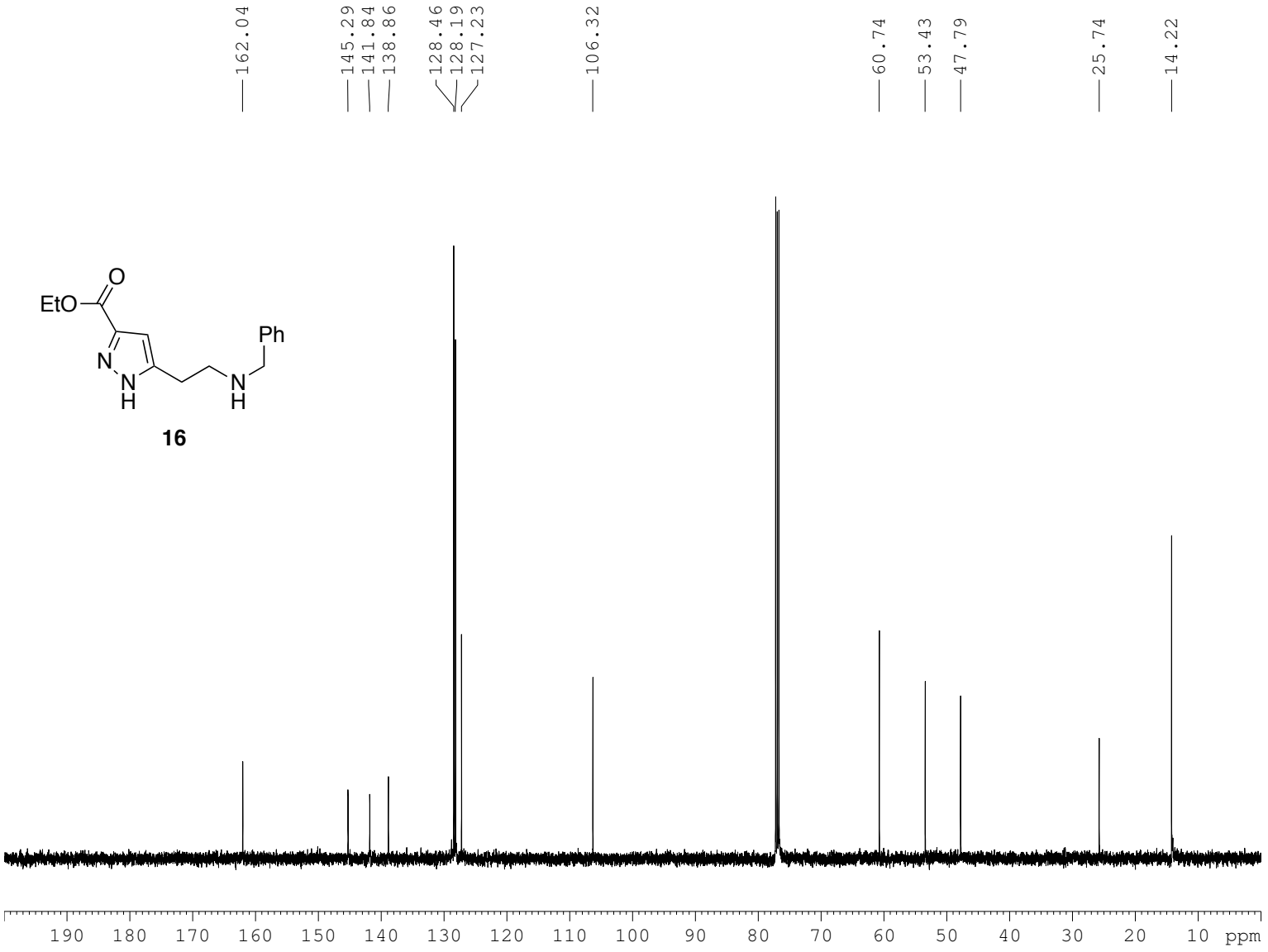
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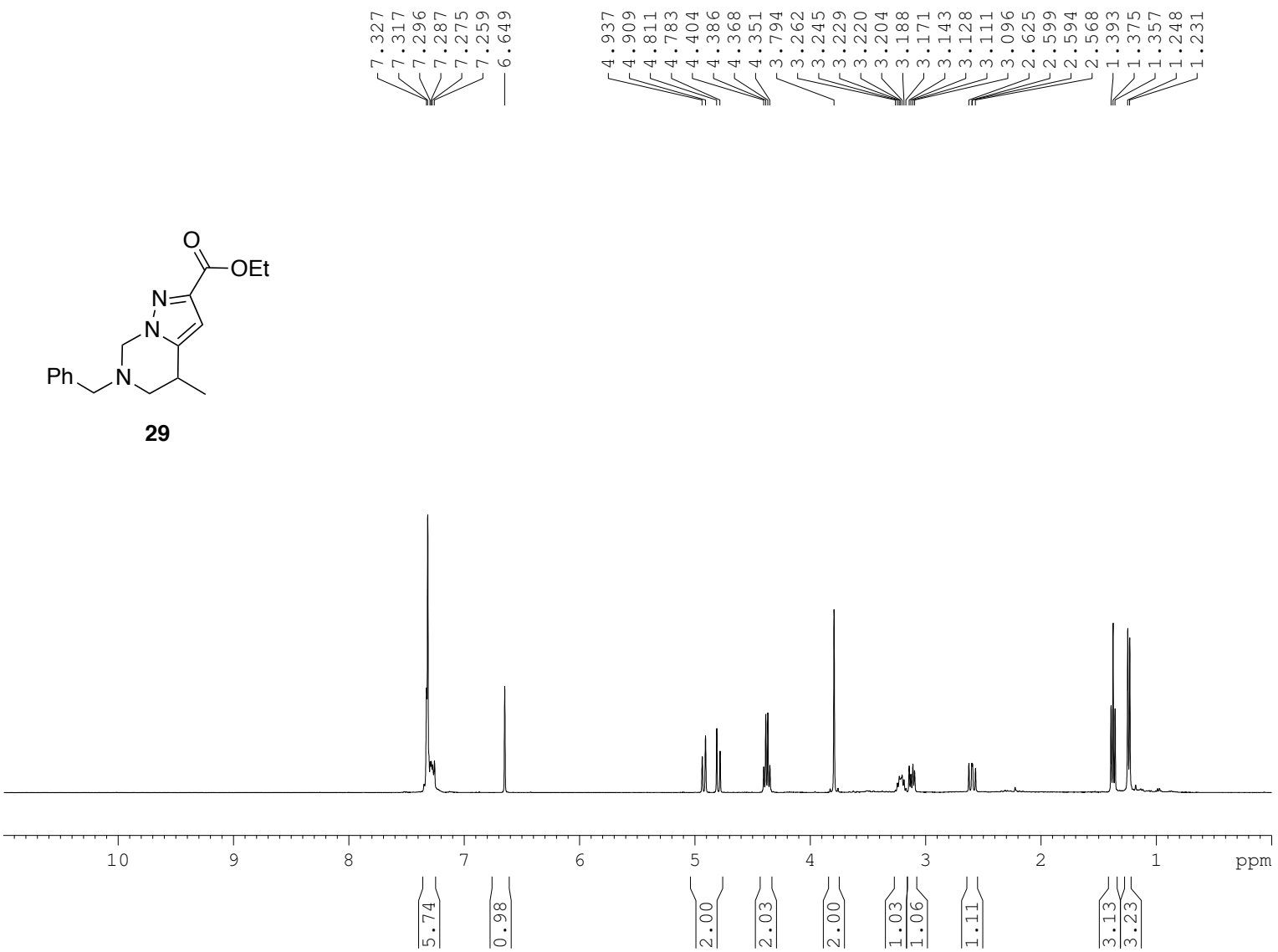
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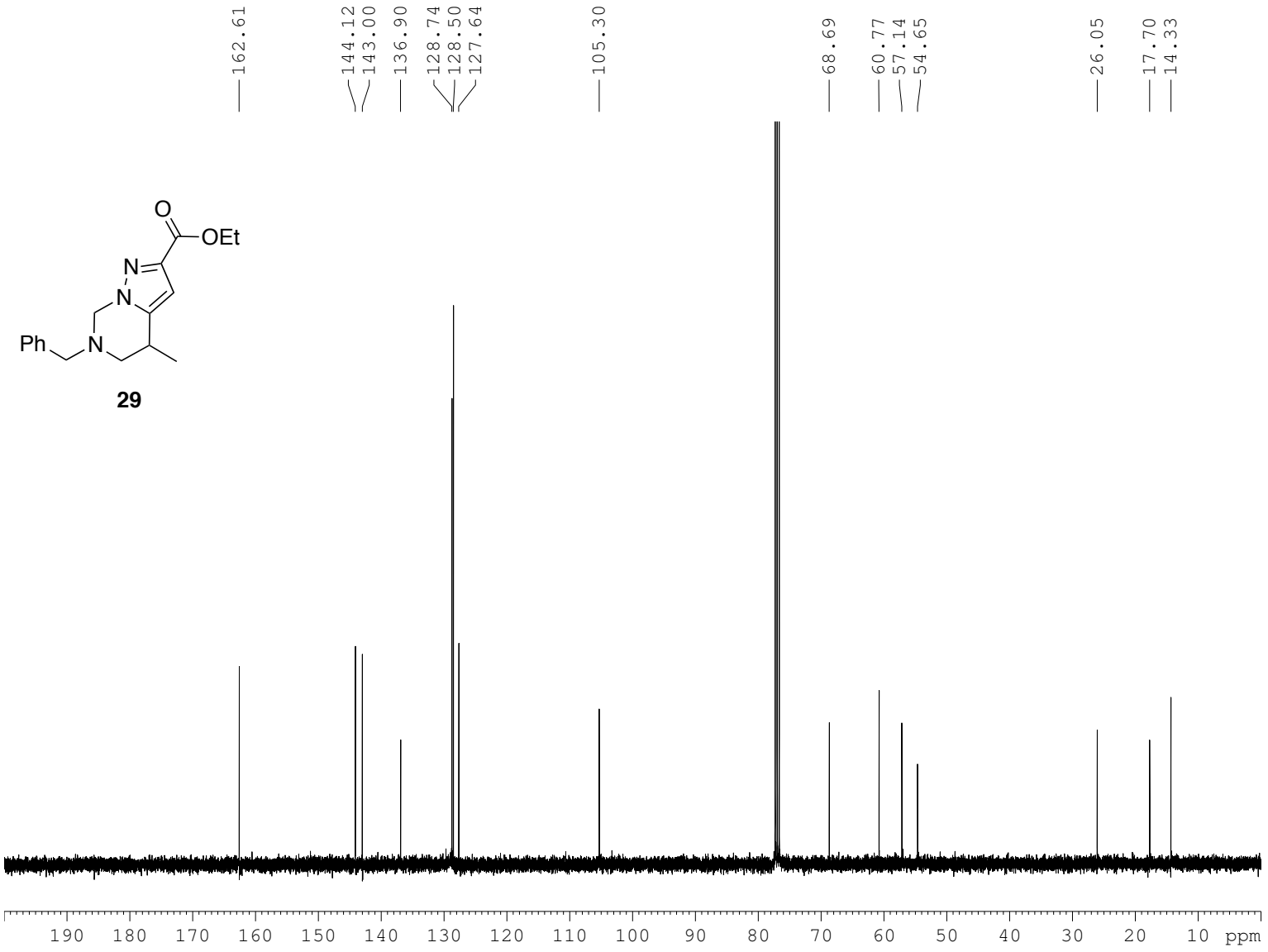
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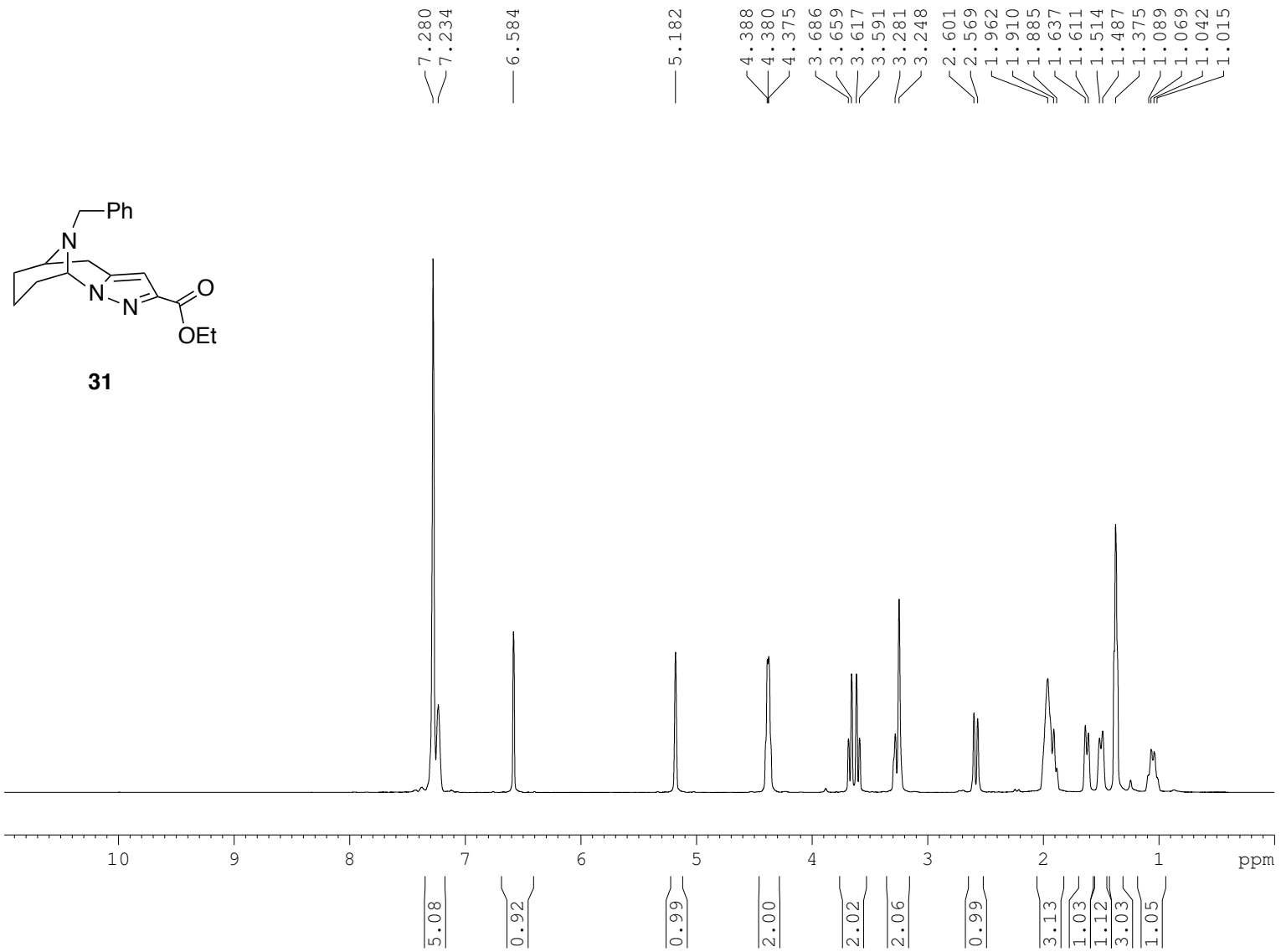
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1.05

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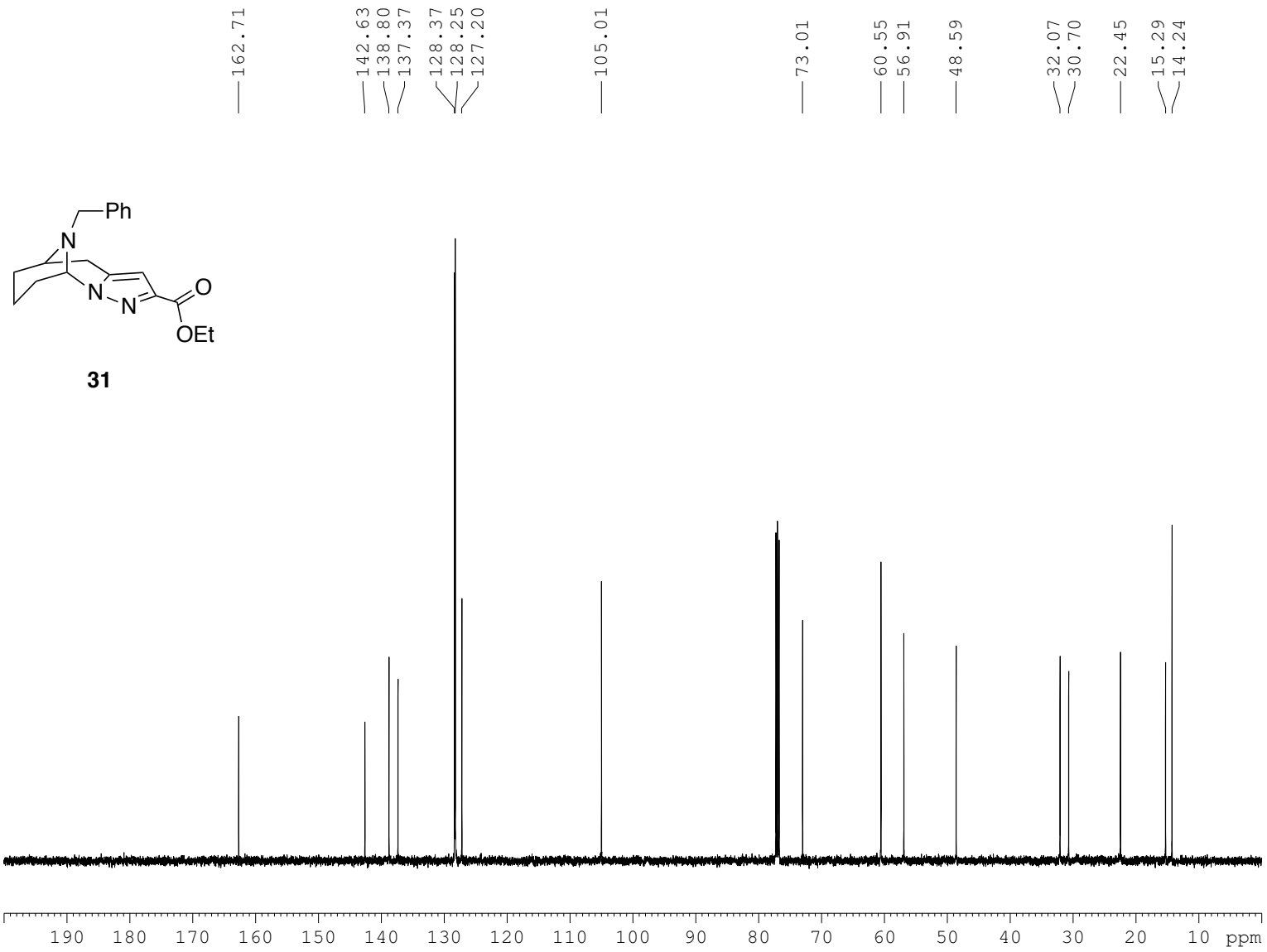
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OEt
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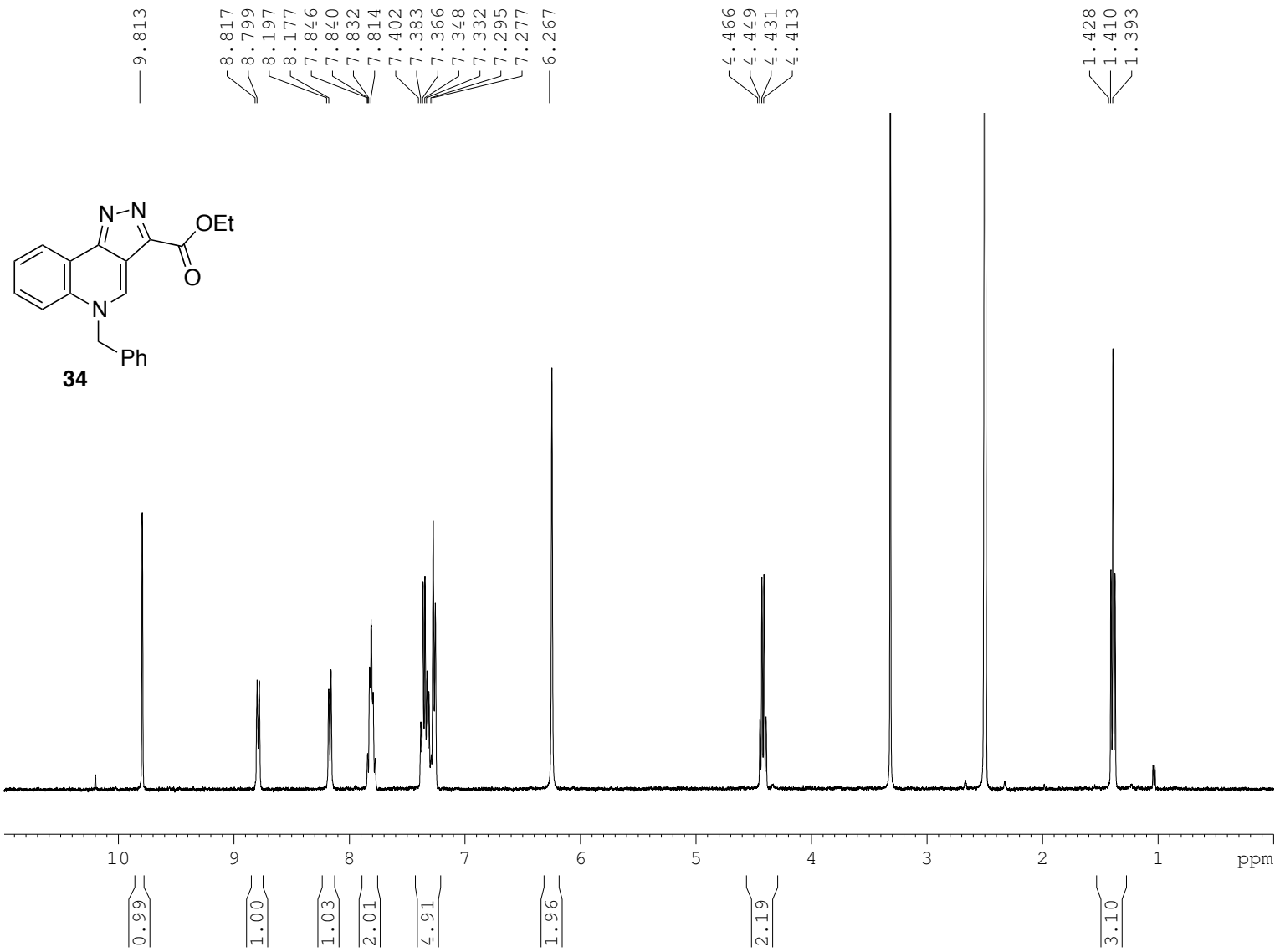
31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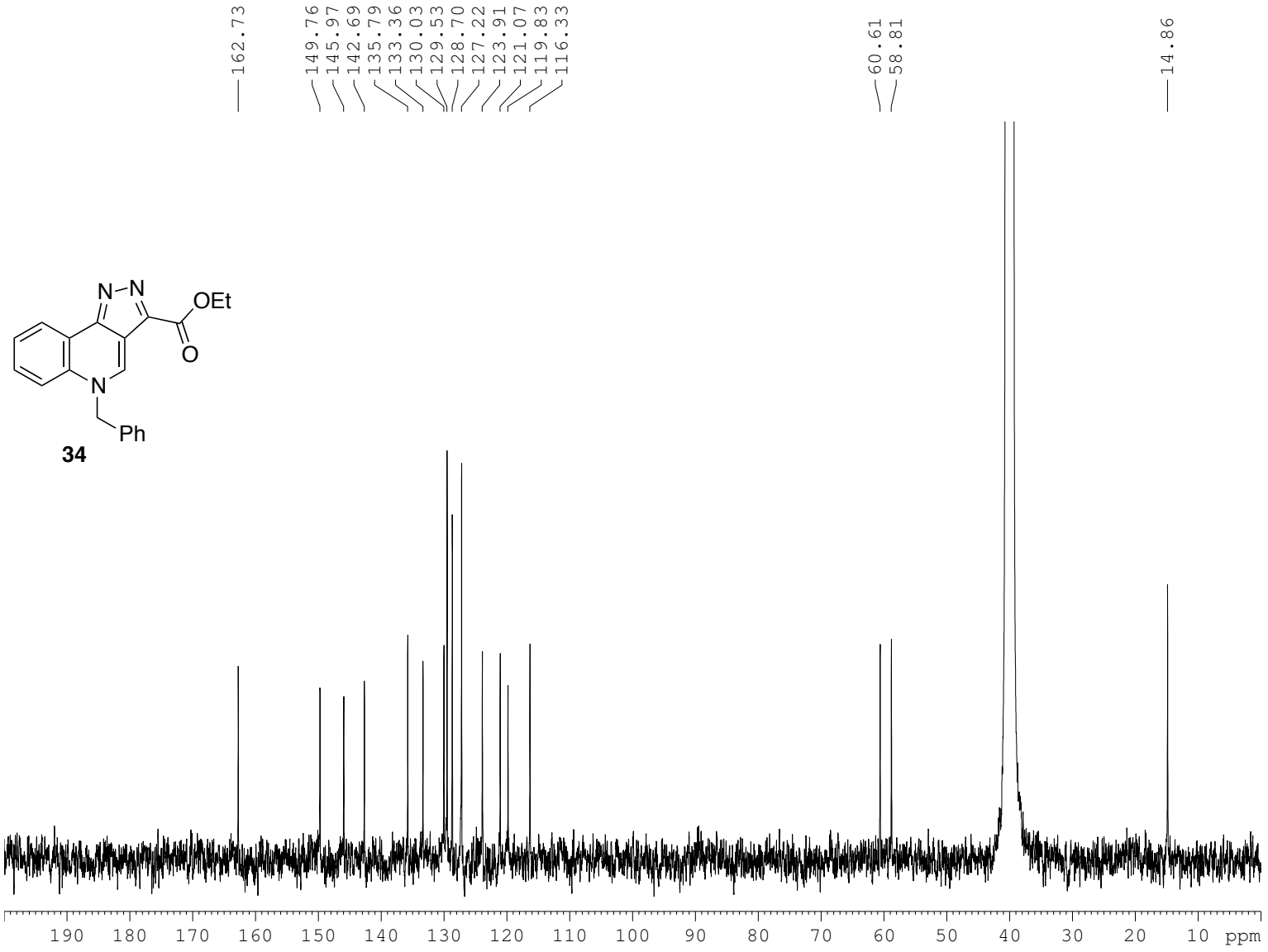
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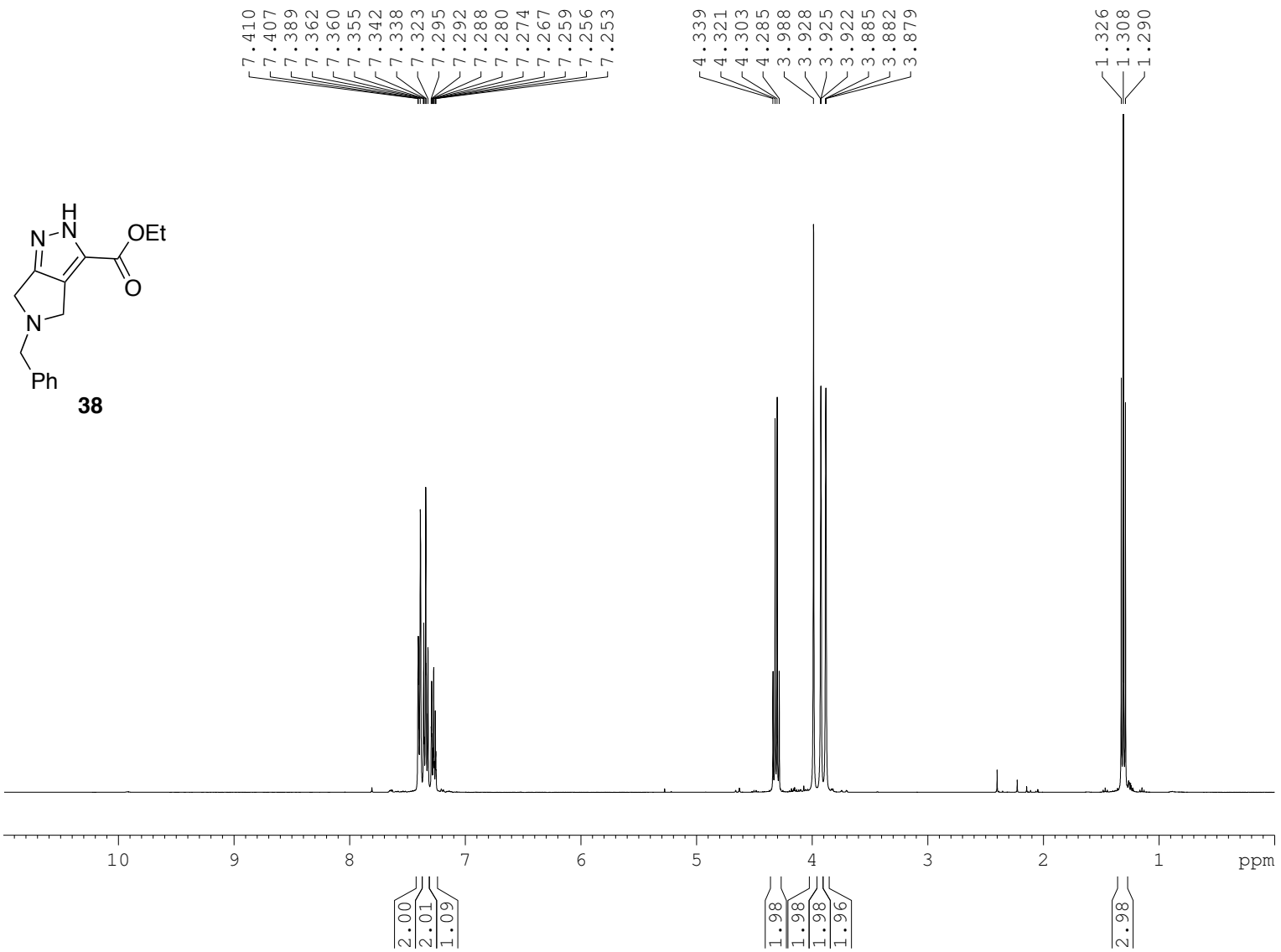
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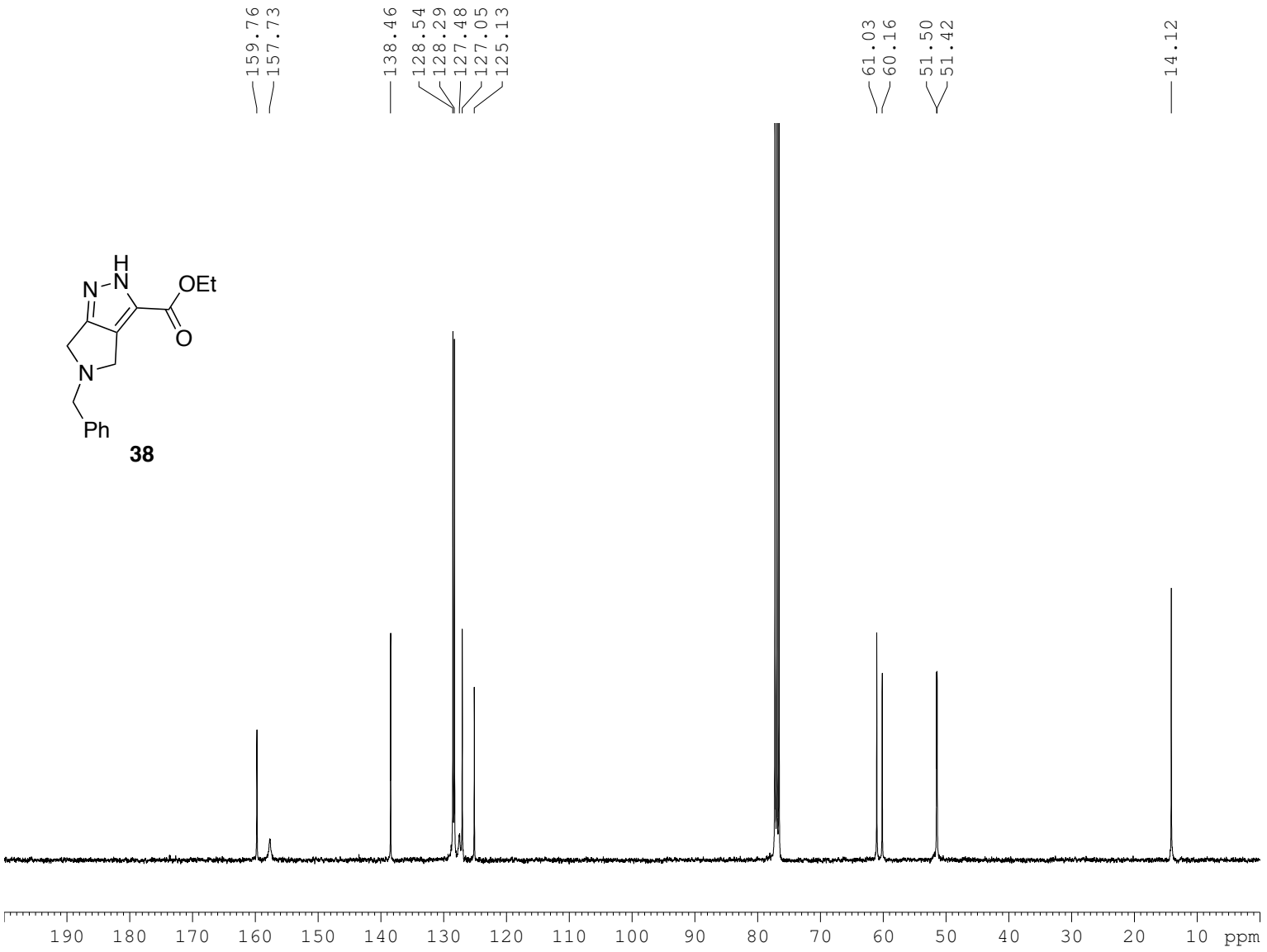
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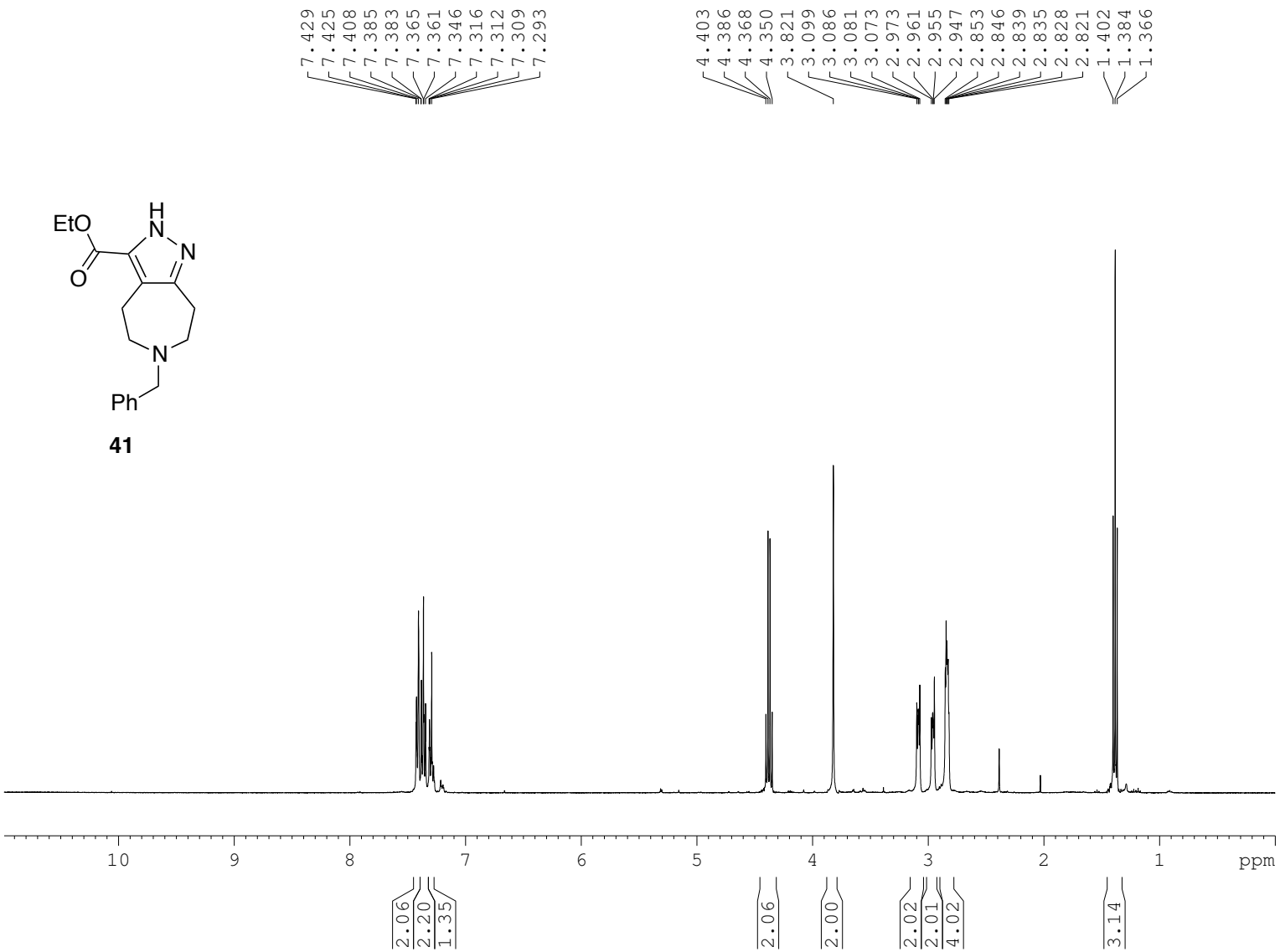
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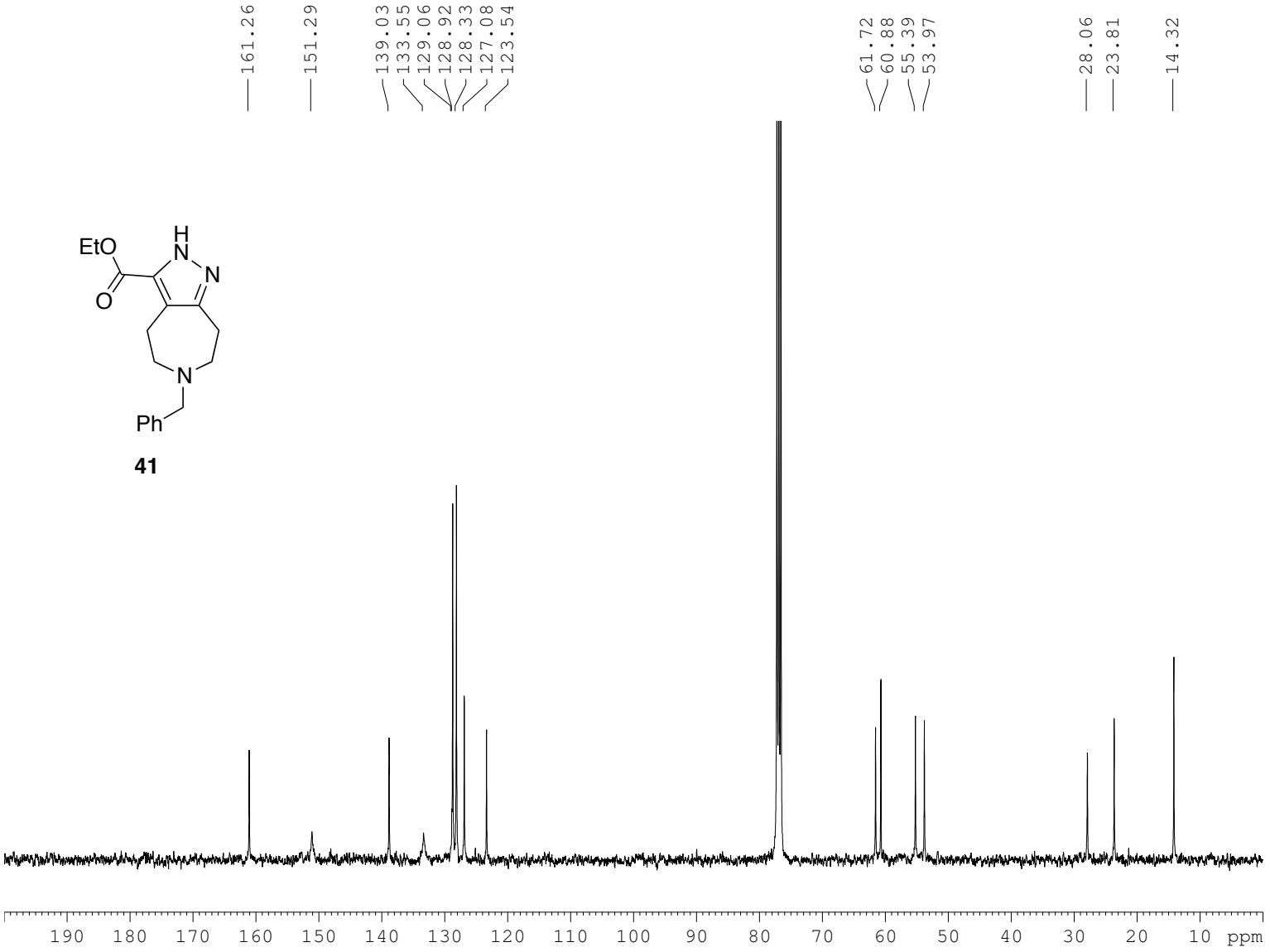
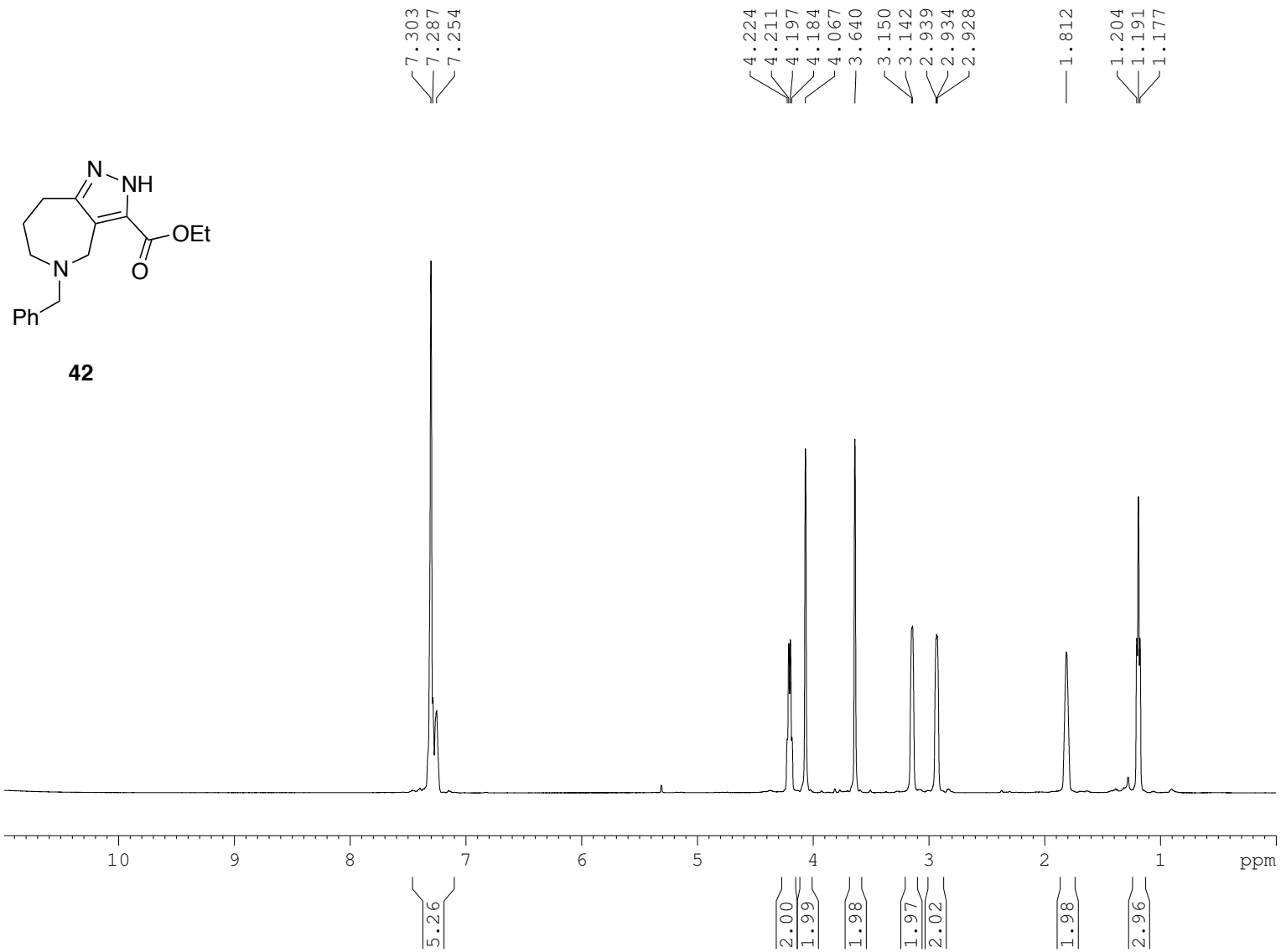
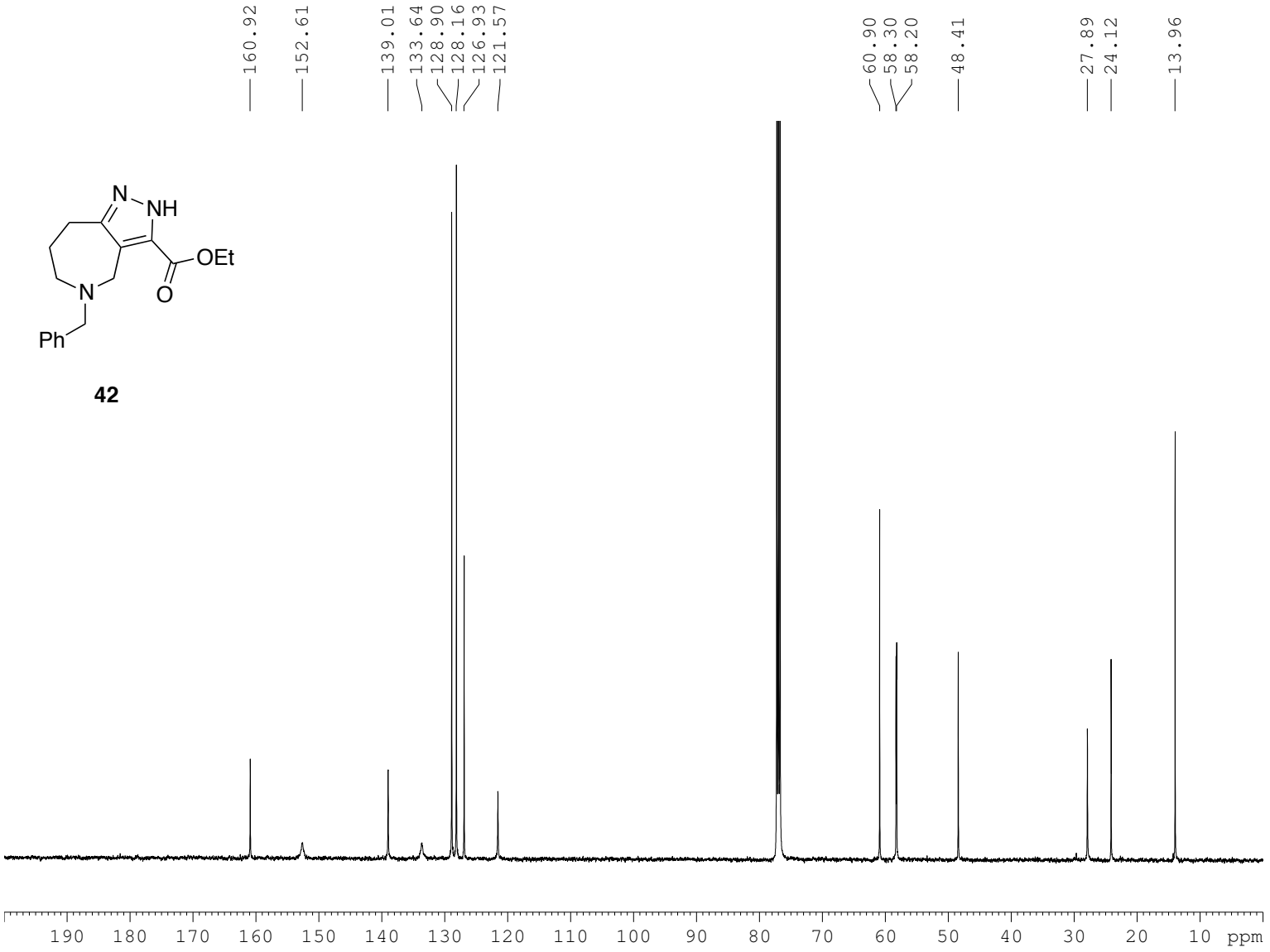
4.350
3.821
3.099
3.086
3.081
3.073
2.973
2.961
2.955
2.947
2.853
2.846
2.839
2.835
2.828
2.821
1.402
1.384
1.366
EtO
O
H
N
N
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm
2.06
2.20
1.35
2.06
2.00
2.02
2.01
4.02
3.14

41

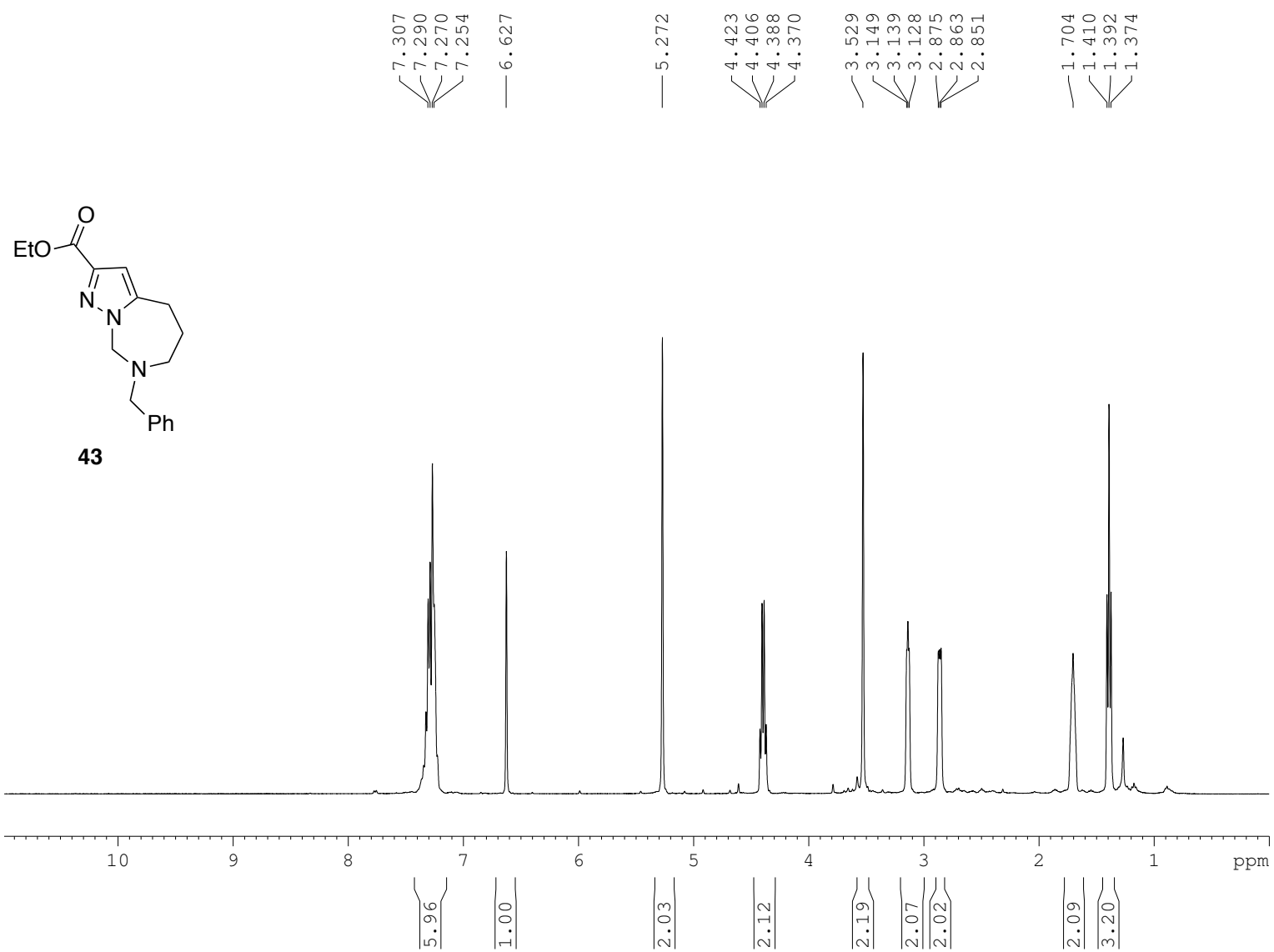

161.26
151.29
139.03
133.55
129.06
128.92
128.33
127.08
123.54
61.72
60.88
55.39
53.97
28.06
23.81
14.32
EtO
O
H
N
N
N
Ph
41
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.303
7.287
7.254
4.224
4.211
4.197
4.184
4.067
3.640
3.150
3.142
2.939
2.934
2.928
1.812
1.204
1.191
1.177
N
NH
OEt
O
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm
5.26
2.00
1.99
1.98
1.97
2.02
1.98
2.96

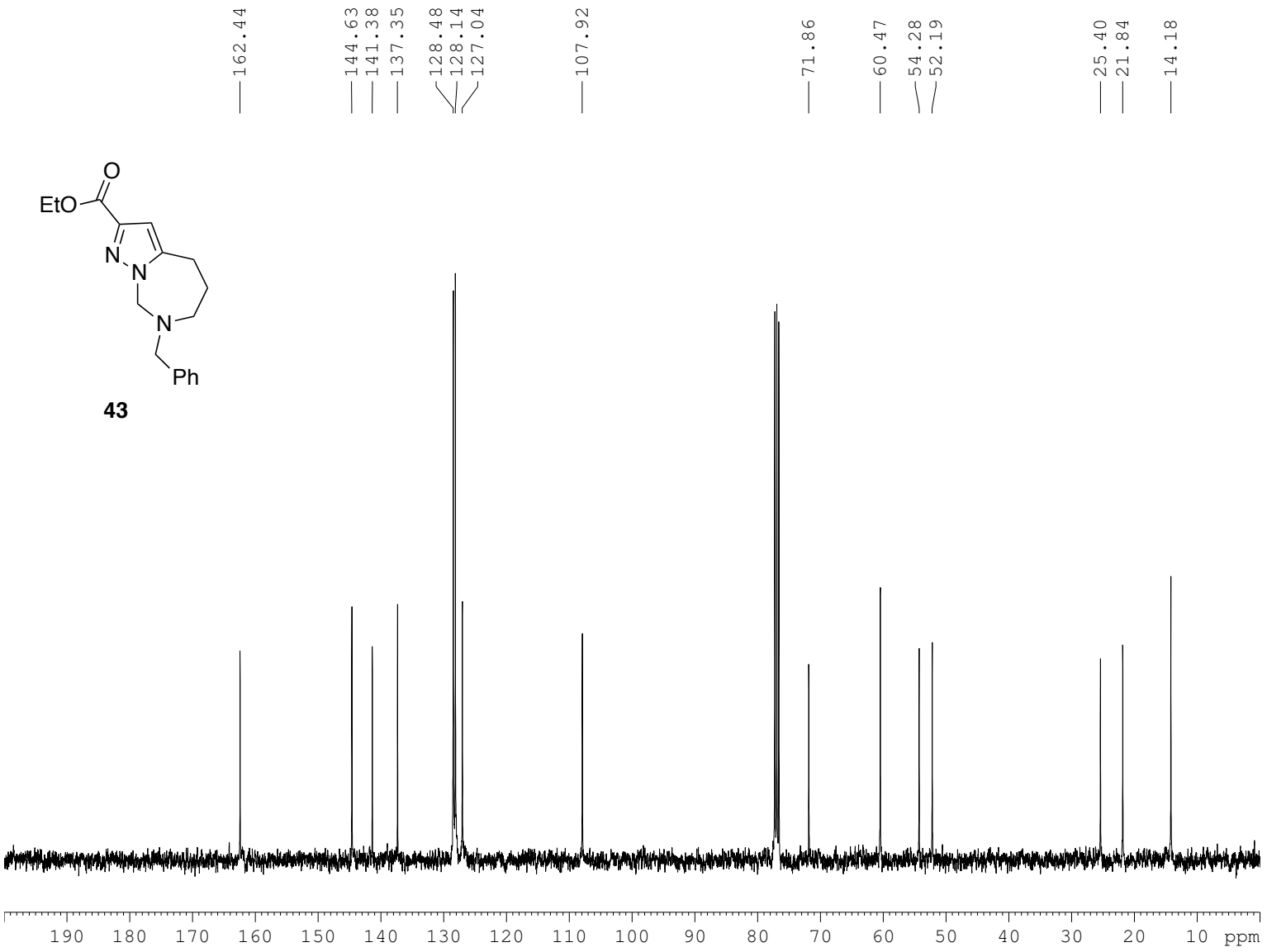
42

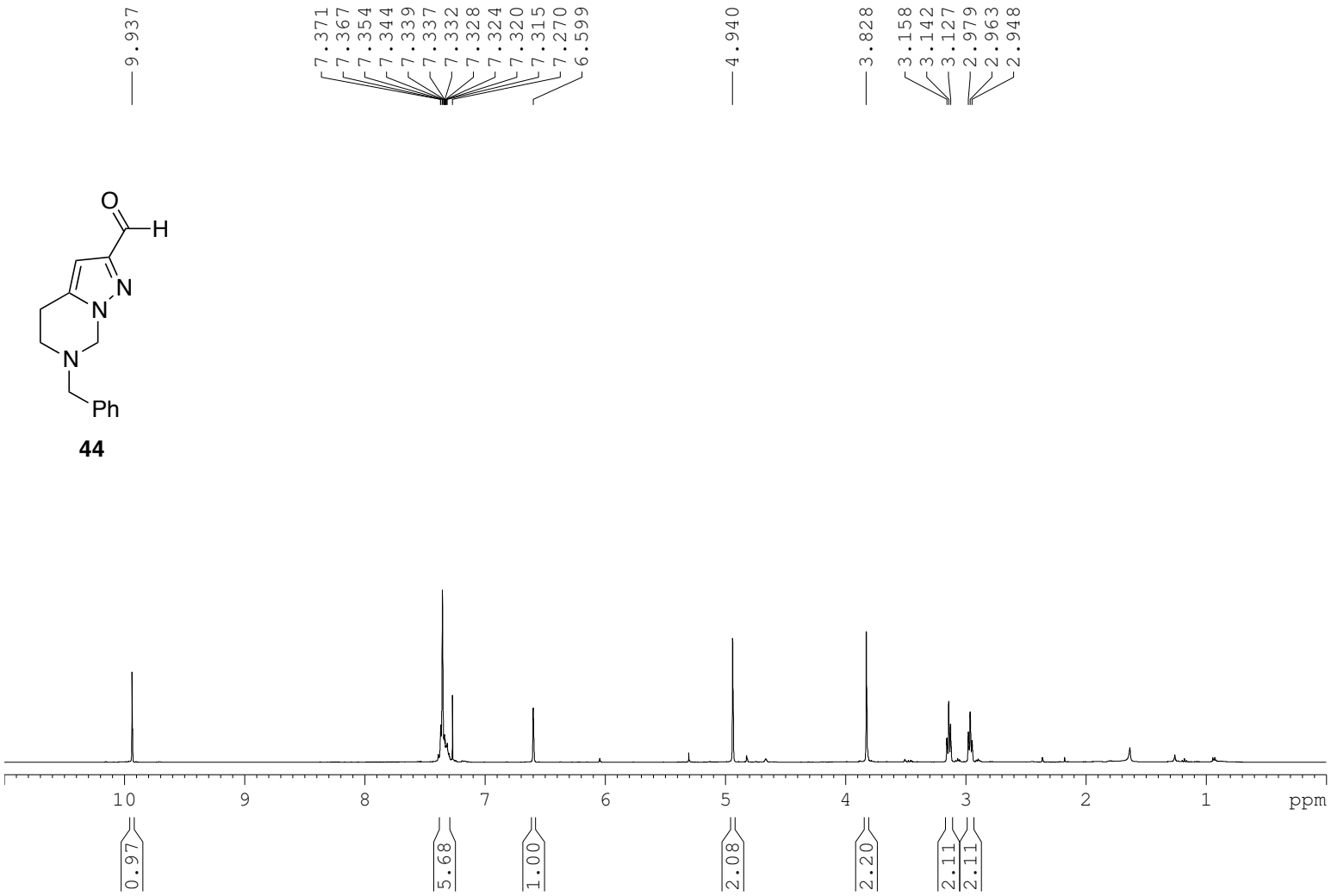

160.92
152.61
139.01
133.64
128.90
128.16
126.93
121.57
60.90
58.30
58.20
48.41
27.89
24.12
13.96
N
NH
OEt
O
N
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

42

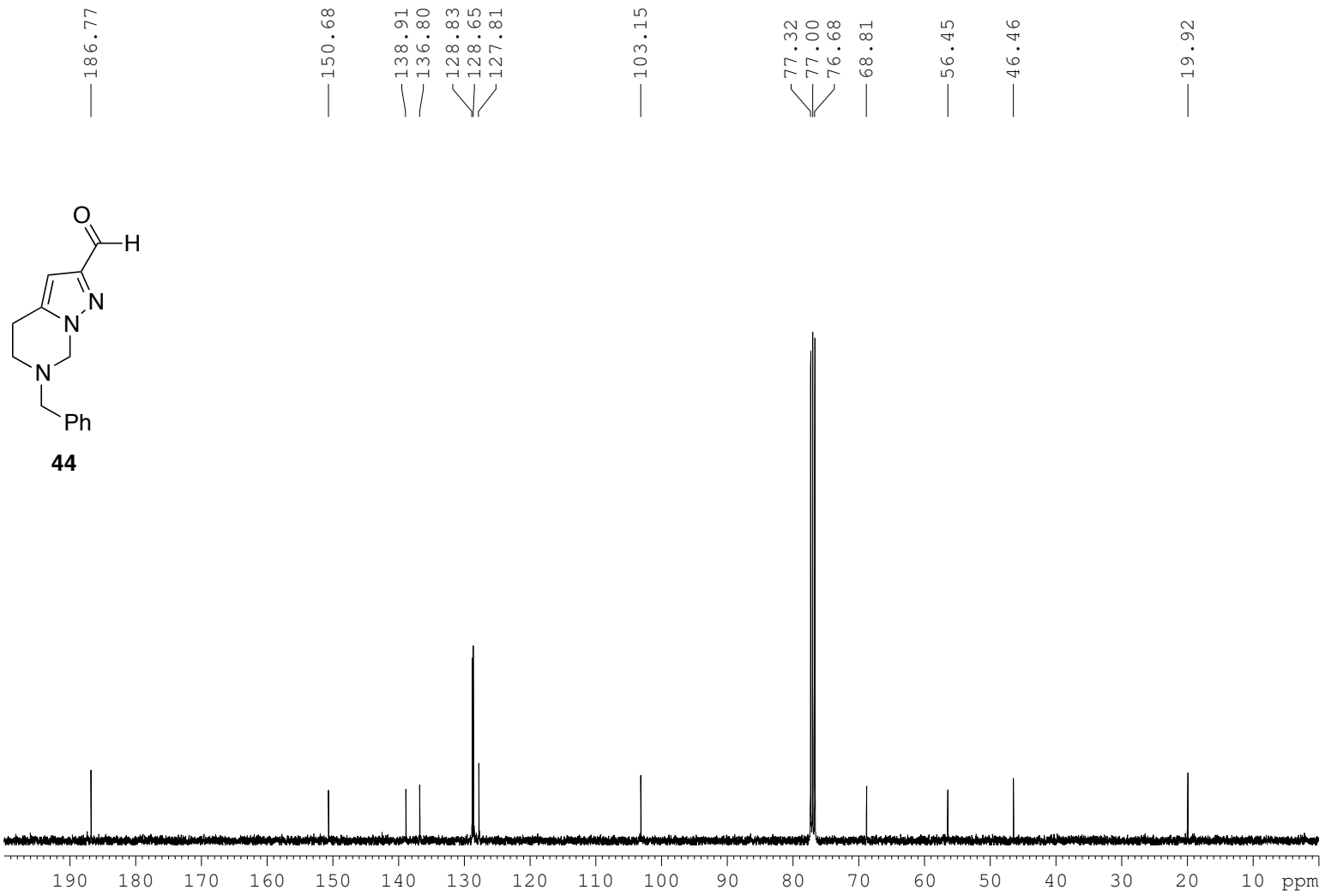

7.307
7.290
7.270
7.254
6.627
5.272
4.423
4.406
4.388
4.370
3.529
3.149
3.139
3.128
2.875
2.863
2.851
1.704
1.410
1.392
1.374
O
EtO
N
N
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm
5.96
1.00
2.03
2.12
2.19
2.07
2.02
2.09
3.20

43

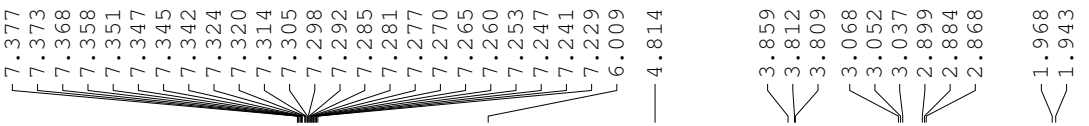

162.44
144.63
141.38
137.35
128.48
128.14
127.04
107.92
71.86
60.47
54.28
52.19
25.40
21.84
14.18
O
EtO
N
N
N
Ph
43
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

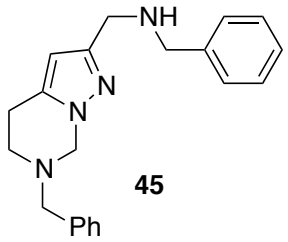

9.937
7.371
7.367
7.354
7.344
7.339
7.337
7.332
7.328
7.324
7.320
7.315
7.270
6.599
4.940
3.828
3.158
3.142
3.127
2.979
2.963
2.948
O
H
N
N
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm
0.97
5.68
1.00
2.08
2.20
2.11
2.11

44

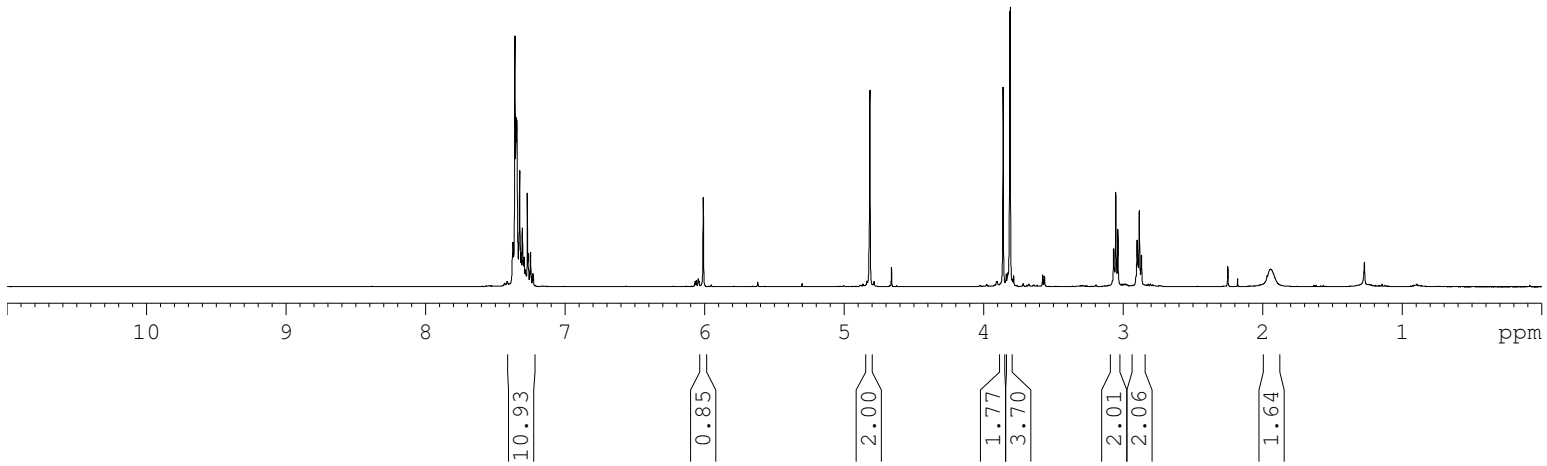

186.77
150.68
138.91
136.80
128.83
128.65
127.81
103.15
77.32
77.00
76.68
68.81
56.45
46.46
19.92
O
H
N
N
N
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

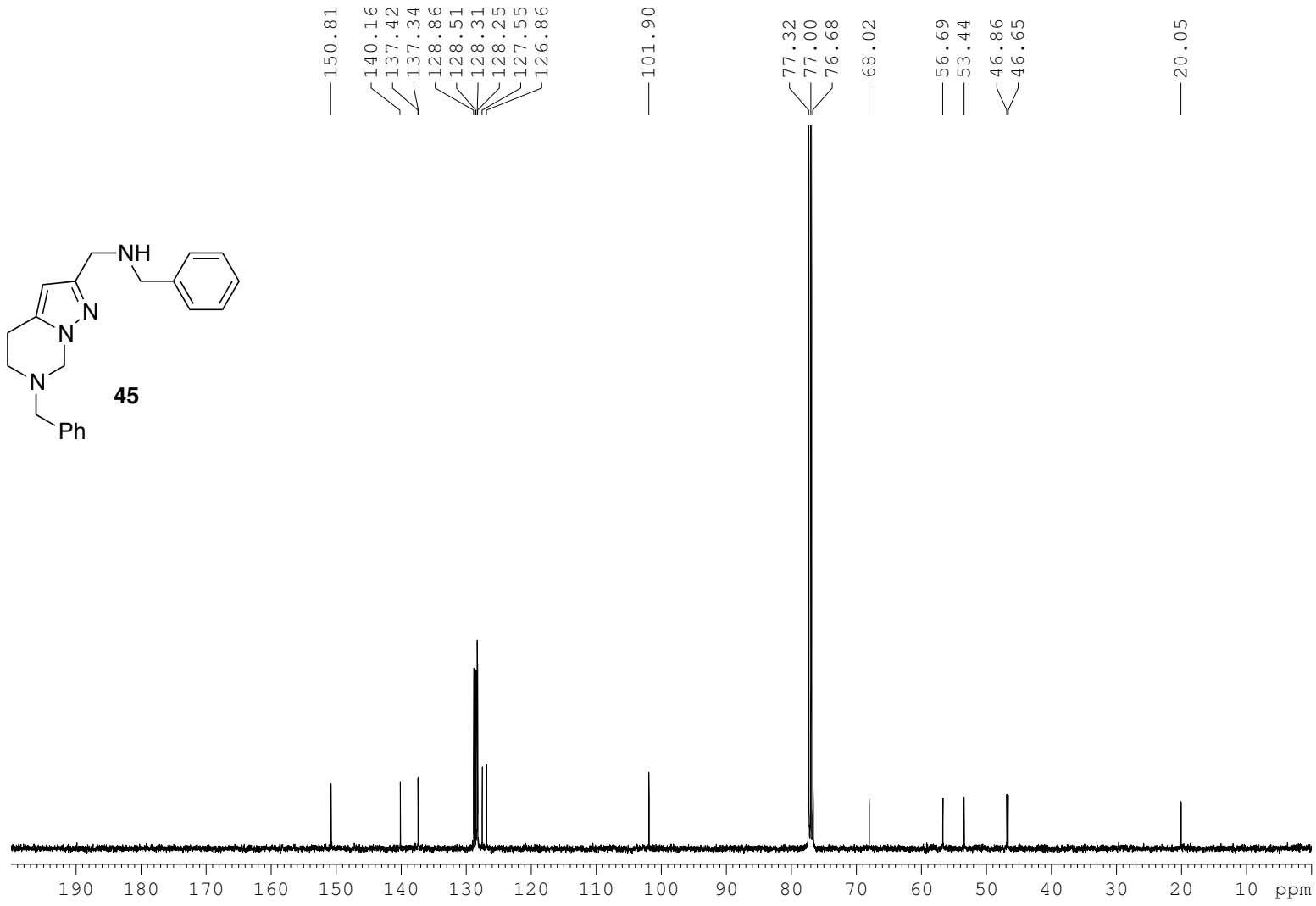
44

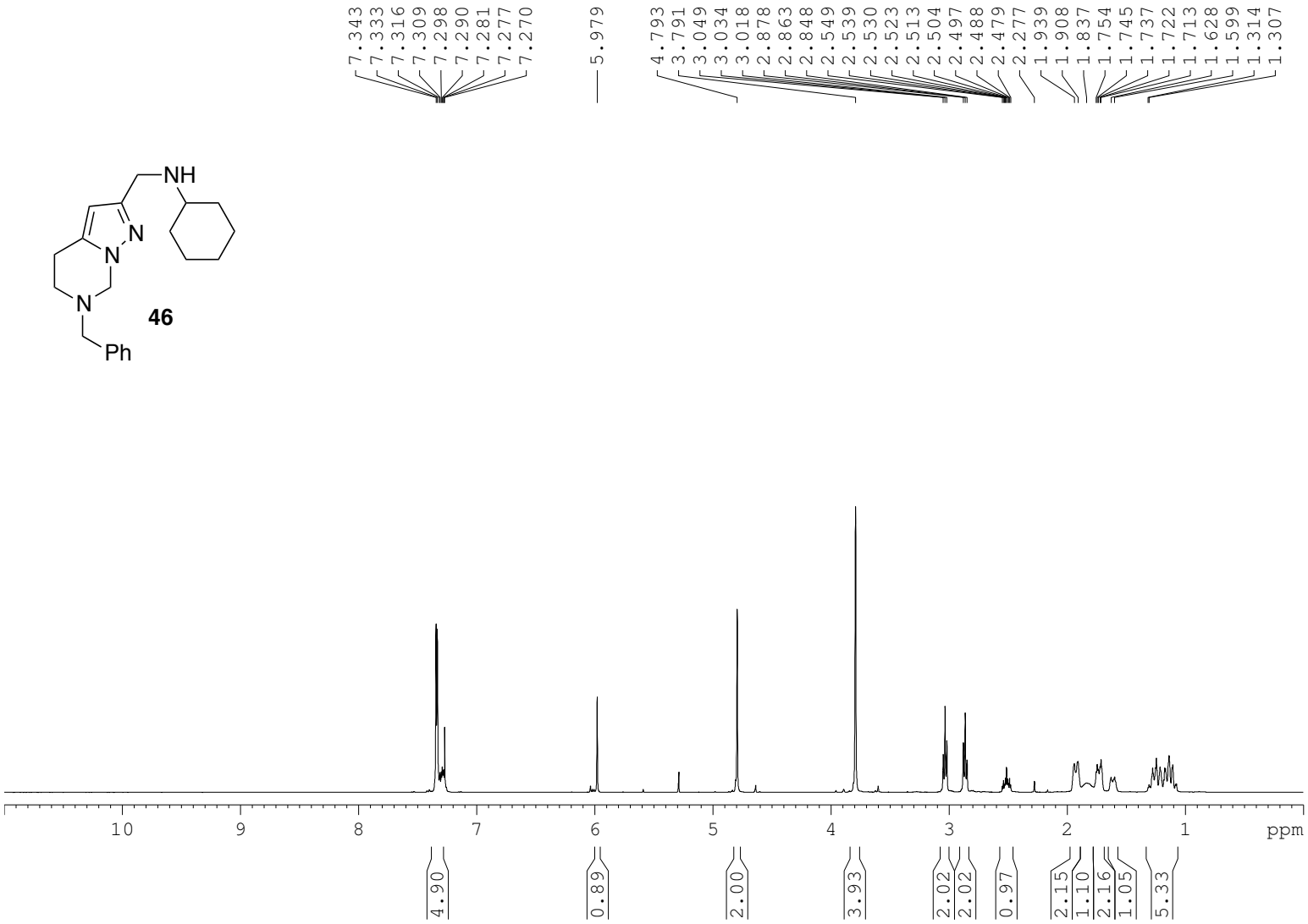

7.377
7.373
7.368
7.358
7.351
7.347
7.345
7.342
7.324
7.320
7.314
7.305
7.298
7.292
7.285
7.281
7.277
7.270
7.265
7.260
7.253
7.247
7.241
7.229
6.009
4.814
3.859
3.812
3.809
3.068
3.052
3.037
2.899
2.884
2.868
1.968
1.943

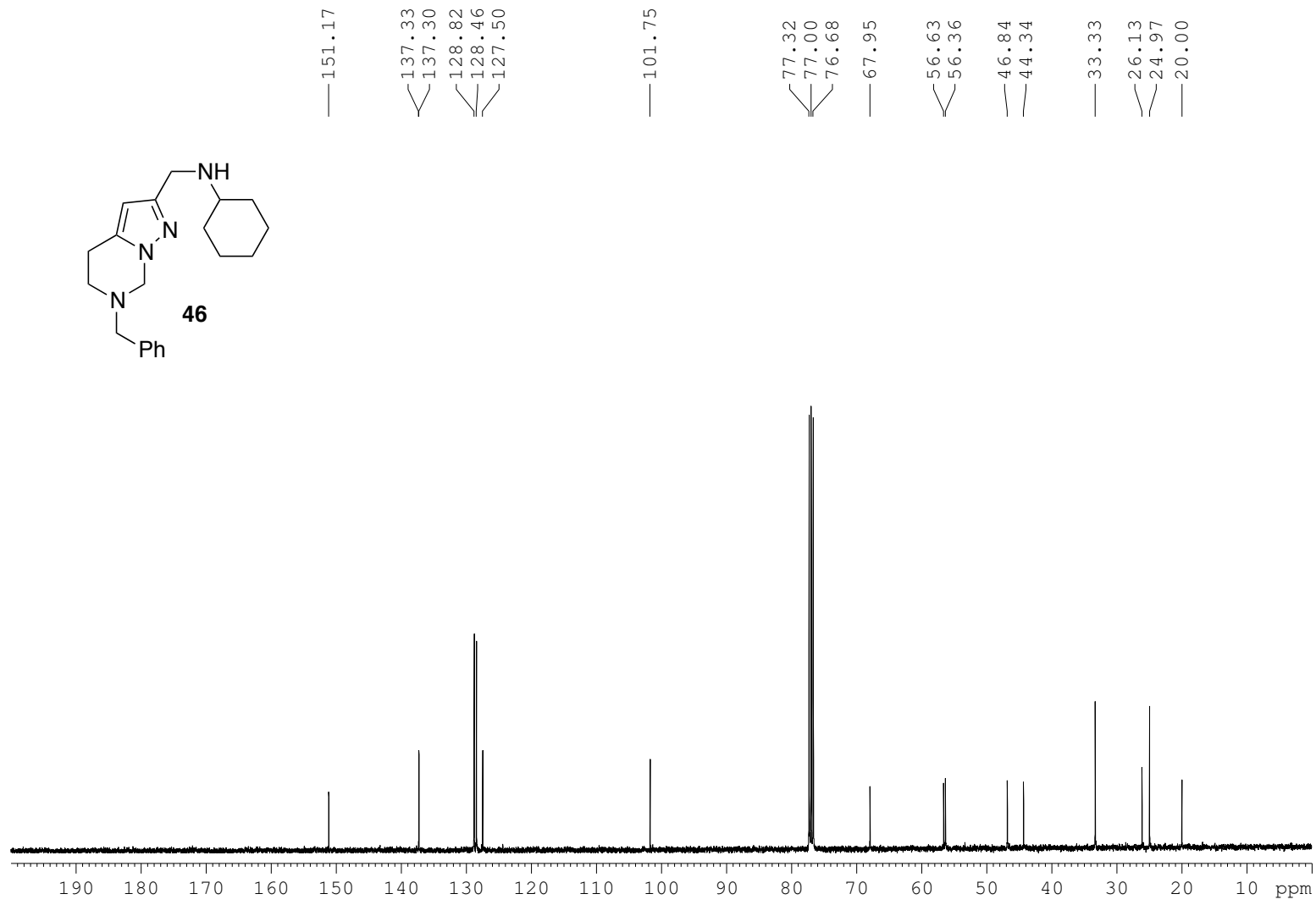

NH
N
N
N
Ph

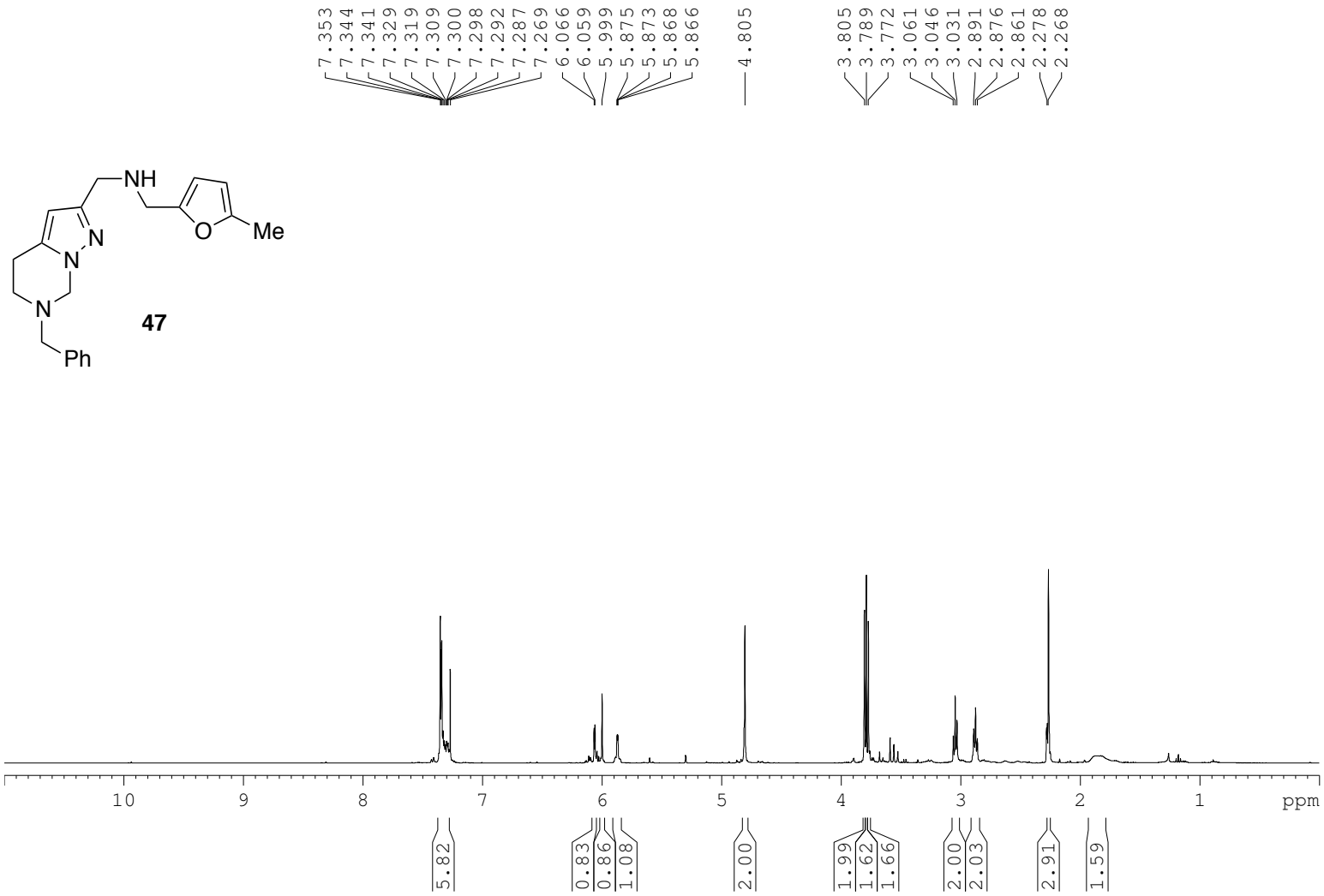
45

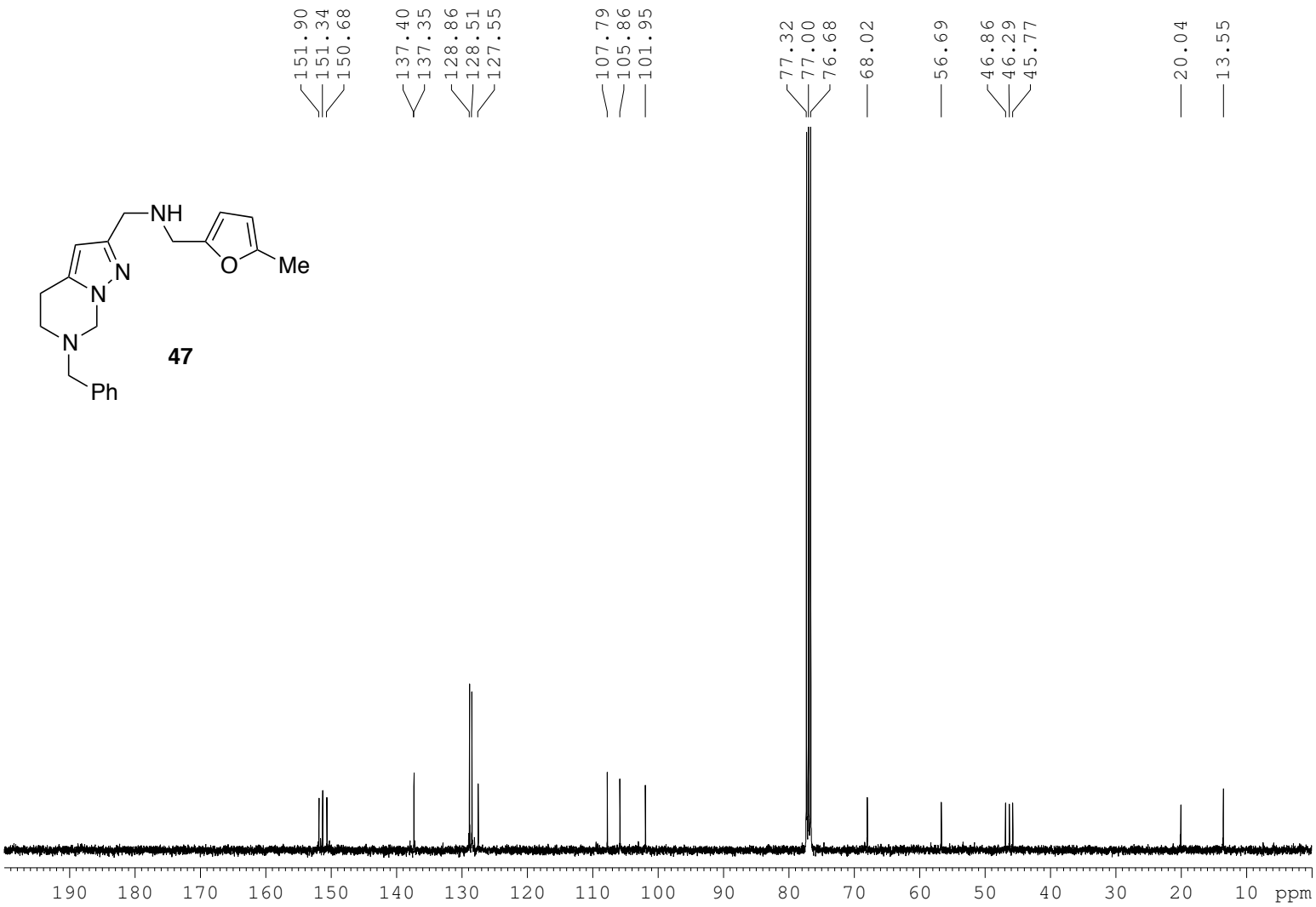

10
9
8
7
6
5
4
3
2
1
ppm
10.93
0.85
2.00
1.77
3.70
2.01
2.06
1.64

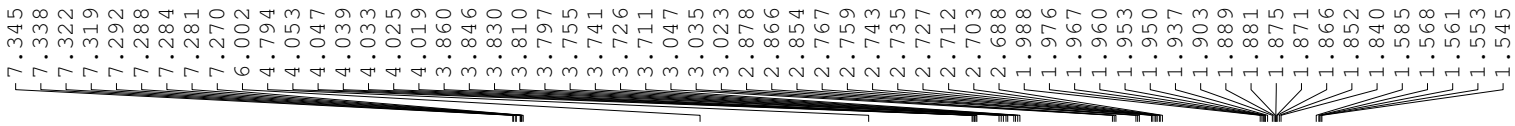

150.81
140.16
137.42
137.34
128.86
128.51
128.31
128.25
127.55
126.86
101.90
77.32
77.00
76.68
68.02
56.69
53.44
46.86
46.65
20.05
NH
N
N
N
Ph
45
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

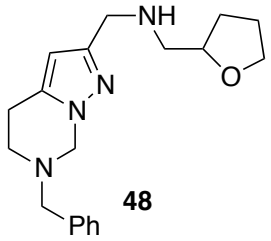

7.343
7.333
7.316
7.309
7.298
7.290
7.281
7.277
7.270
5.979
4.793
3.791
3.049
3.034
3.018
2.878
2.863
2.848
2.549
2.539
2.530
2.523
2.513
2.504
2.497
2.488
2.479
2.277
1.939
1.908
1.837
1.754
1.745
1.737
1.722
1.713
1.628
1.599
1.314
1.307
NH
N
N
N
Ph
46
10
9
8
7
6
5
4
3
2
1
ppm
4.90
0.89
2.00
3.93
2.02
2.02
0.97
2.15
1.10
2.16
1.05
5.33


151.17
137.33
137.30
128.82
128.46
127.50
101.75
77.32
77.00
76.68
67.95
56.63
56.36
46.84
44.34
33.33
26.13
24.97
20.00
NH
N
N
N
Ph
46
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

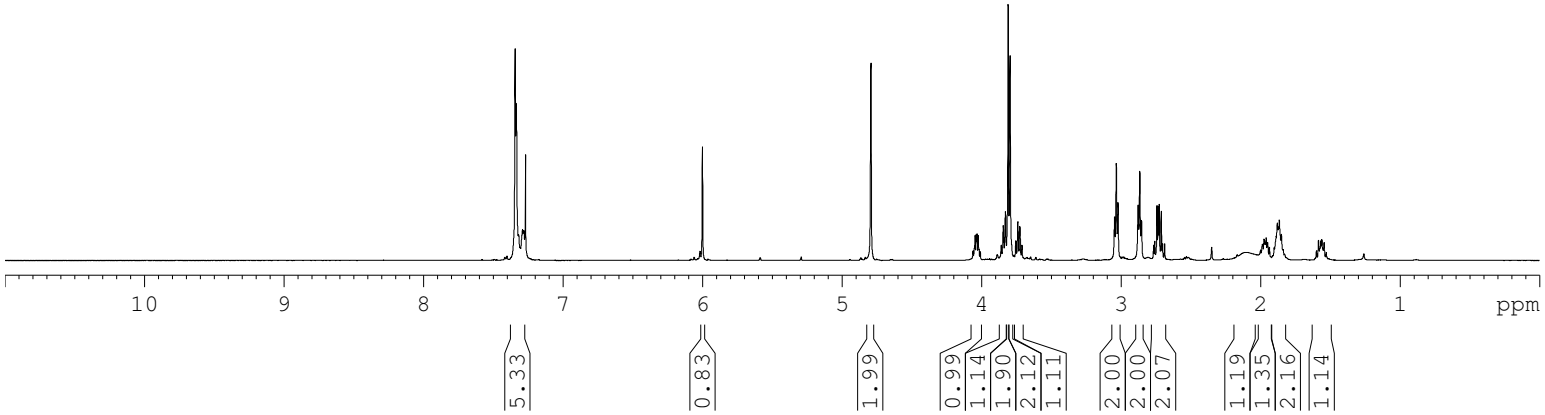

7.353
7.344
7.341
7.329
7.319
7.309
7.300
7.298
7.292
7.287
7.269
6.066
6.059
5.999
5.875
5.873
5.868
5.866
4.805
3.805
3.789
3.772
3.061
3.046
3.031
2.891
2.876
2.861
2.278
2.268
NH
N
N
O
Me
N
Ph
47
10
9
8
7
6
5
4
3
2
1
ppm
5.82
0.83
0.86
1.08
2.00
1.99
1.62
1.66
2.00
2.03
2.91
1.59

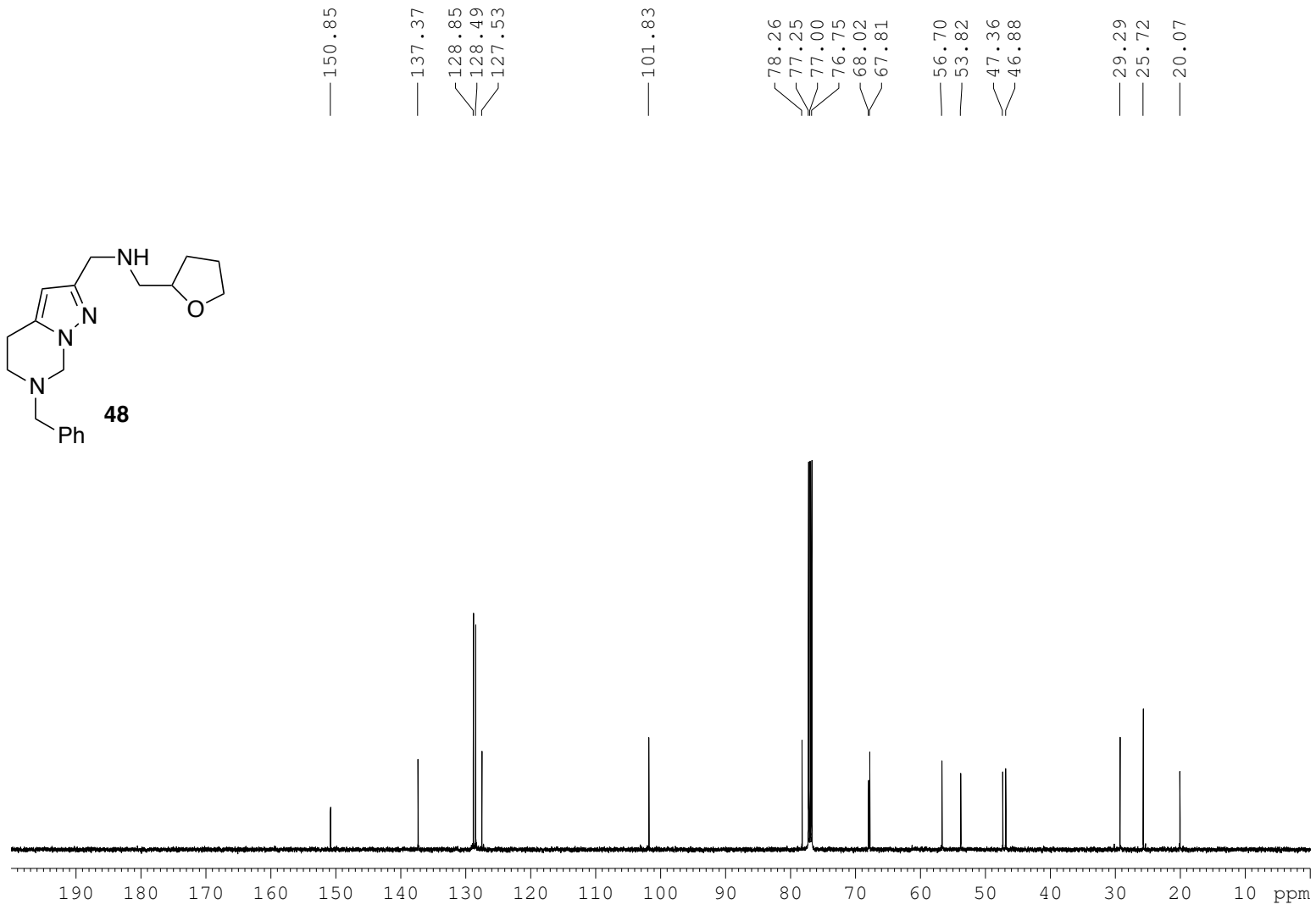

151.90
151.34
150.68
137.40
137.35
128.86
128.51
127.55
107.79
105.86
101.95
77.32
77.00
76.68
68.02
56.69
46.86
46.29
45.77
20.04
13.55
NH
N
N
N
O
Me
Ph
47
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

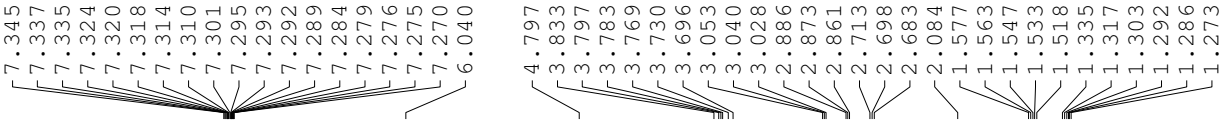

7.345
7.338
7.322
7.319
7.292
7.288
7.284
7.281
7.270
6.002
4.794
4.053
4.047
4.039
4.033
4.025
4.019
3.860
3.846
3.830
3.810
3.797
3.755
3.741
3.726
3.711
3.047
3.035
3.023
2.878
2.866
2.854
2.767
2.759
2.743
2.735
2.727
2.712
2.703
2.688
1.988
1.976
1.967
1.960
1.953
1.950
1.937
1.903
1.889
1.881
1.875
1.871
1.866
1.852
1.840
1.585
1.568
1.561
1.553
1.545

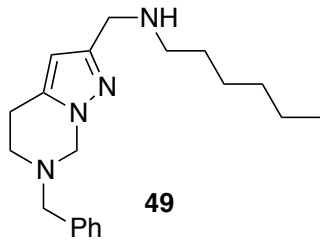

NH
O
N
N
N
Ph

48

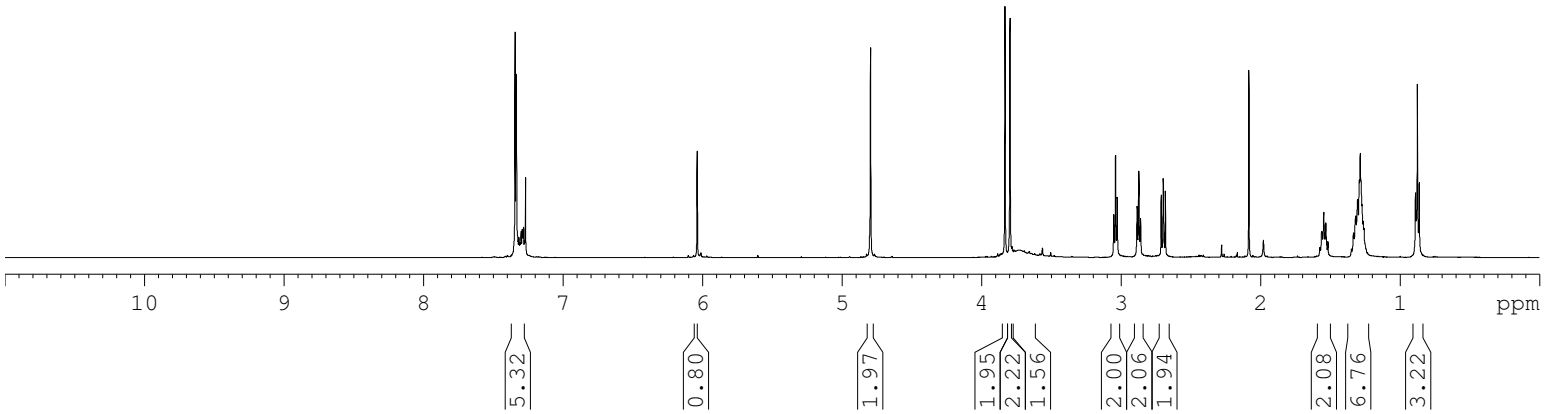

10
9
8
7
6
5
4
3
2
1
ppm
5.33
0.83
1.99
0.99
1.14
1.90
2.12
1.11
2.00
2.00
2.07
1.19
1.35
2.16
1.14

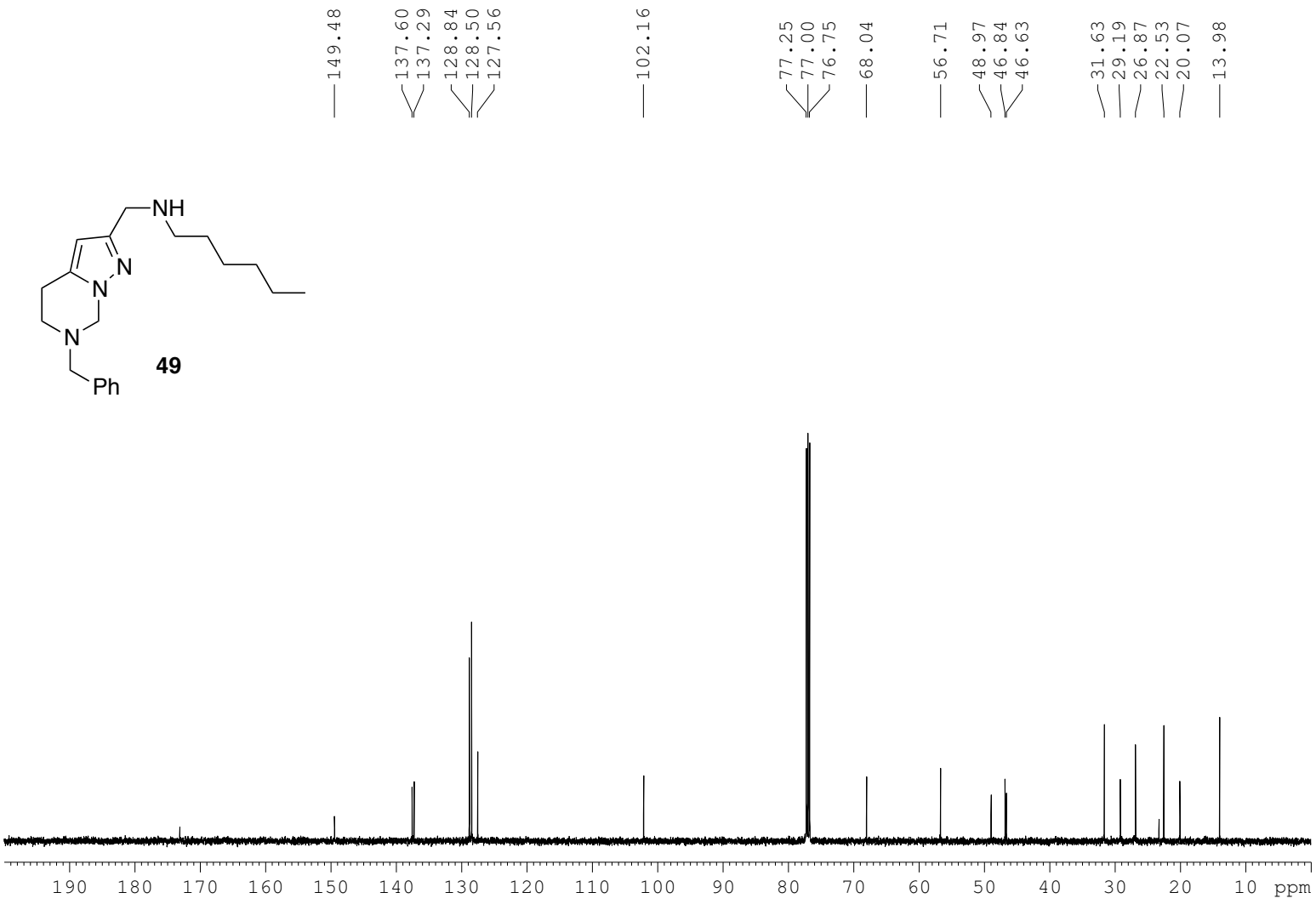

150.85
137.37
128.85
128.49
127.53
101.83
78.26
77.25
77.00
76.75
68.02
67.81
56.70
53.82
47.36
46.88
29.29
25.72
20.07
NH
O
N
N
N
Ph
48
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

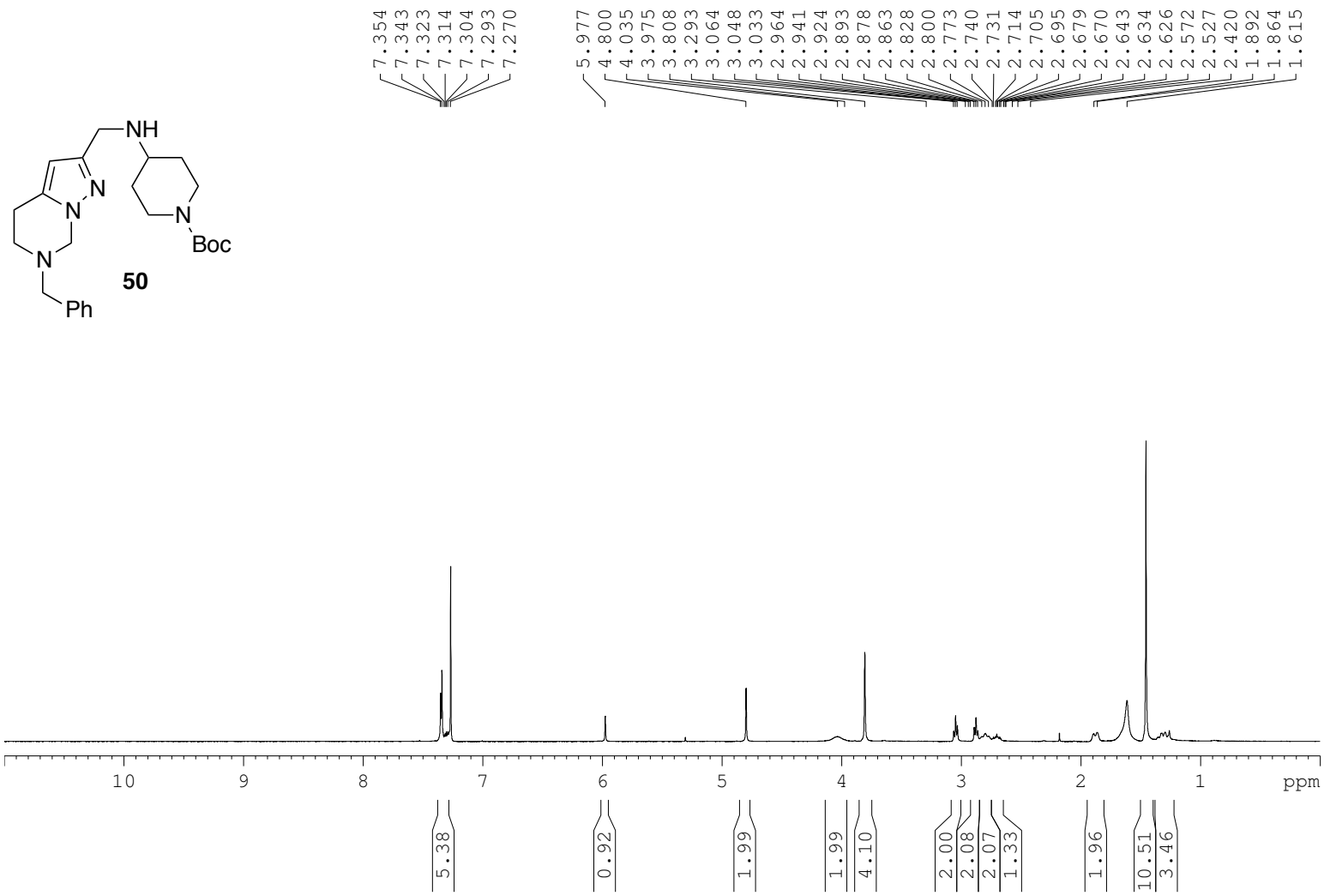

7.345
7.337
7.335
7.324
7.320
7.318
7.314
7.310
7.301
7.295
7.293
7.292
7.289
7.284
7.279
7.276
7.275
7.270
6.040
4.797
3.833
3.797
3.783
3.769
3.730
3.696
3.053
3.040
3.028
2.886
2.873
2.861
2.713
2.698
2.683
2.084
1.577
1.563
1.547
1.533
1.518
1.335
1.317
1.303
1.292
1.286
1.273

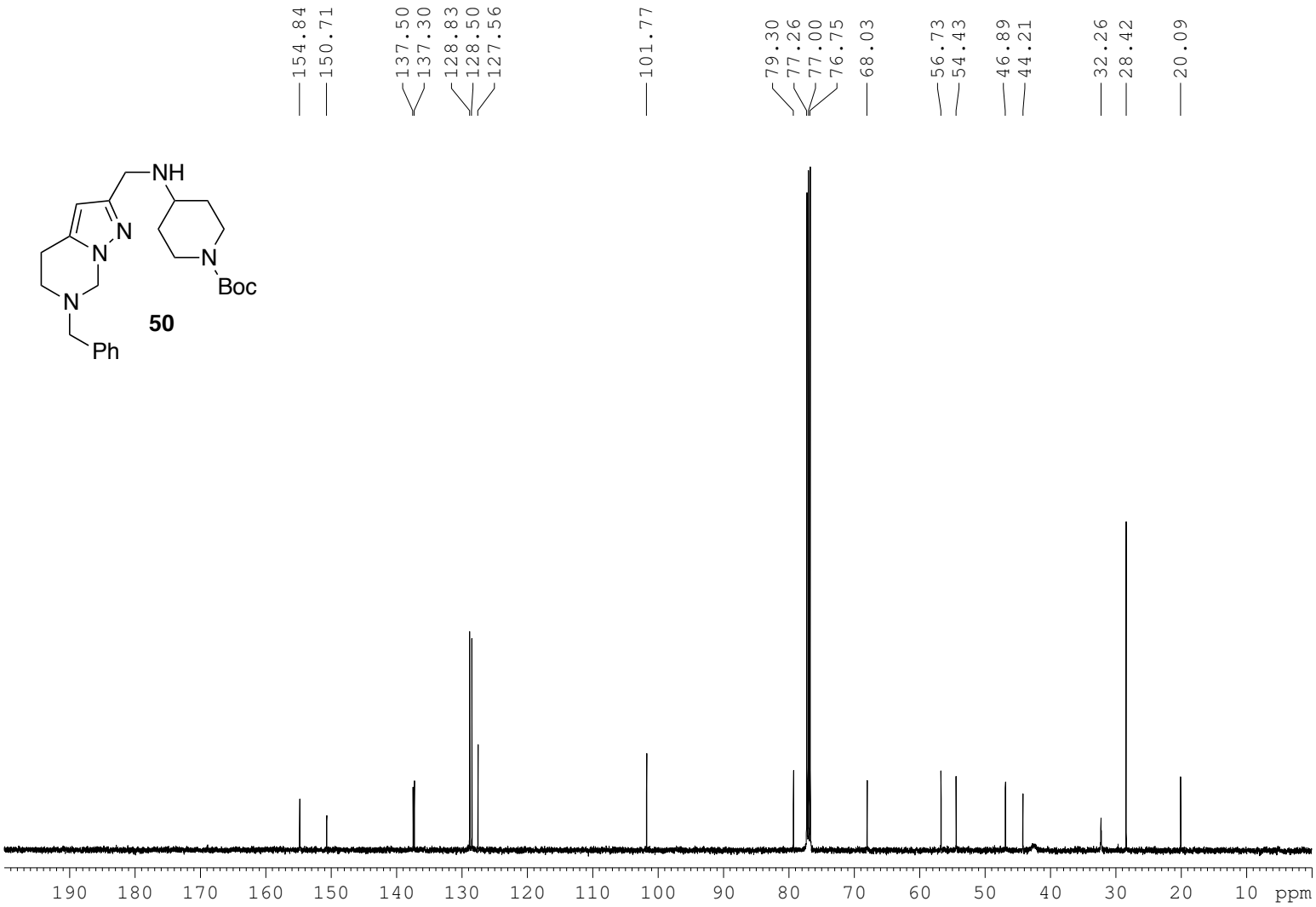

NH
N
N
N
Ph

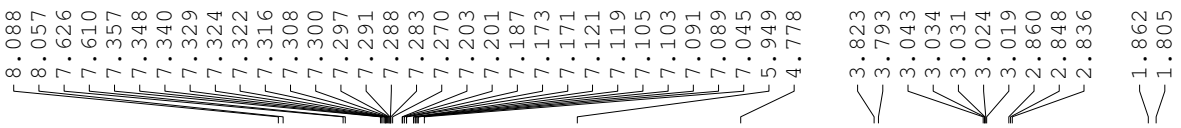
49

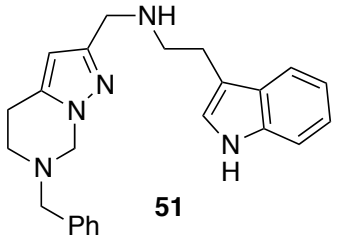

10
9
8
7
6
5
4
3
2
1
ppm
5.32
0.80
1.97
1.95
2.22
1.56
2.00
2.06
1.94
2.08
6.76
3.22


149.48
137.60
137.29
128.84
128.50
127.56
102.16
77.25
77.00
76.75
68.04
56.71
48.97
46.84
46.63
31.63
29.19
26.87
22.53
20.07
13.98
NH
N
N
N
Ph
49
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

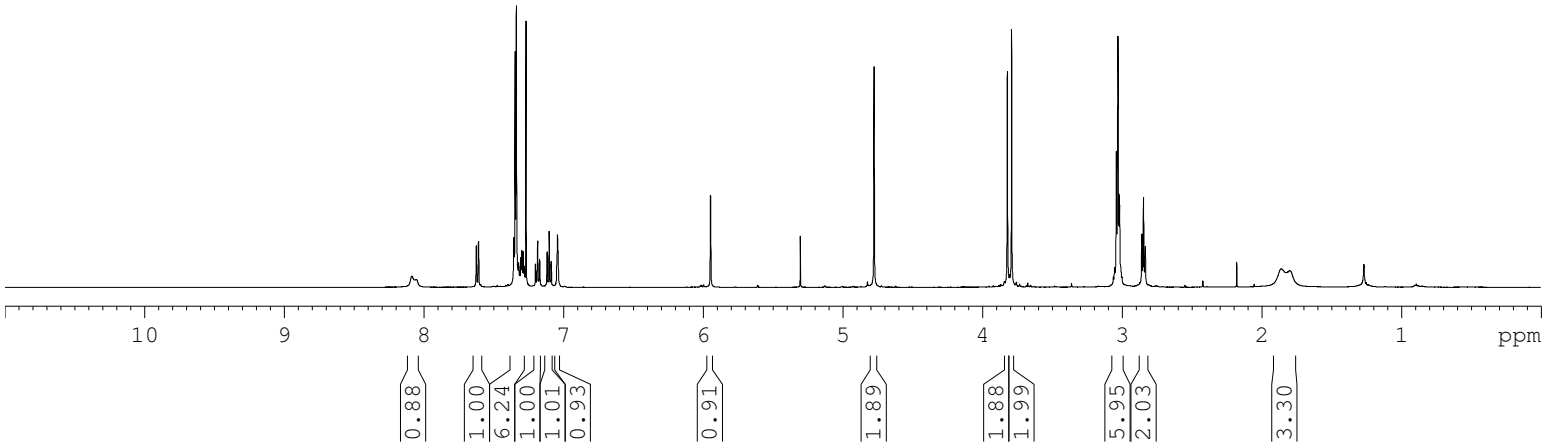

7.354
7.343
7.323
7.314
7.304
7.293
7.270
5.977
4.800
4.035
3.975
3.808
3.293
3.064
3.048
3.033
2.964
2.941
2.924
2.893
2.878
2.863
2.828
2.800
2.773
2.740
2.731
2.714
2.705
2.695
2.679
2.670
2.643
2.634
2.626
2.572
2.527
2.420
1.892
1.864
1.615
NH
N
N
N
Boc
Ph
50
10
9
8
7
6
5
4
3
2
1
ppm
5.38
0.92
1.99
1.99
4.10
2.00
2.08
2.07
1.33
1.96
10.51
3.46

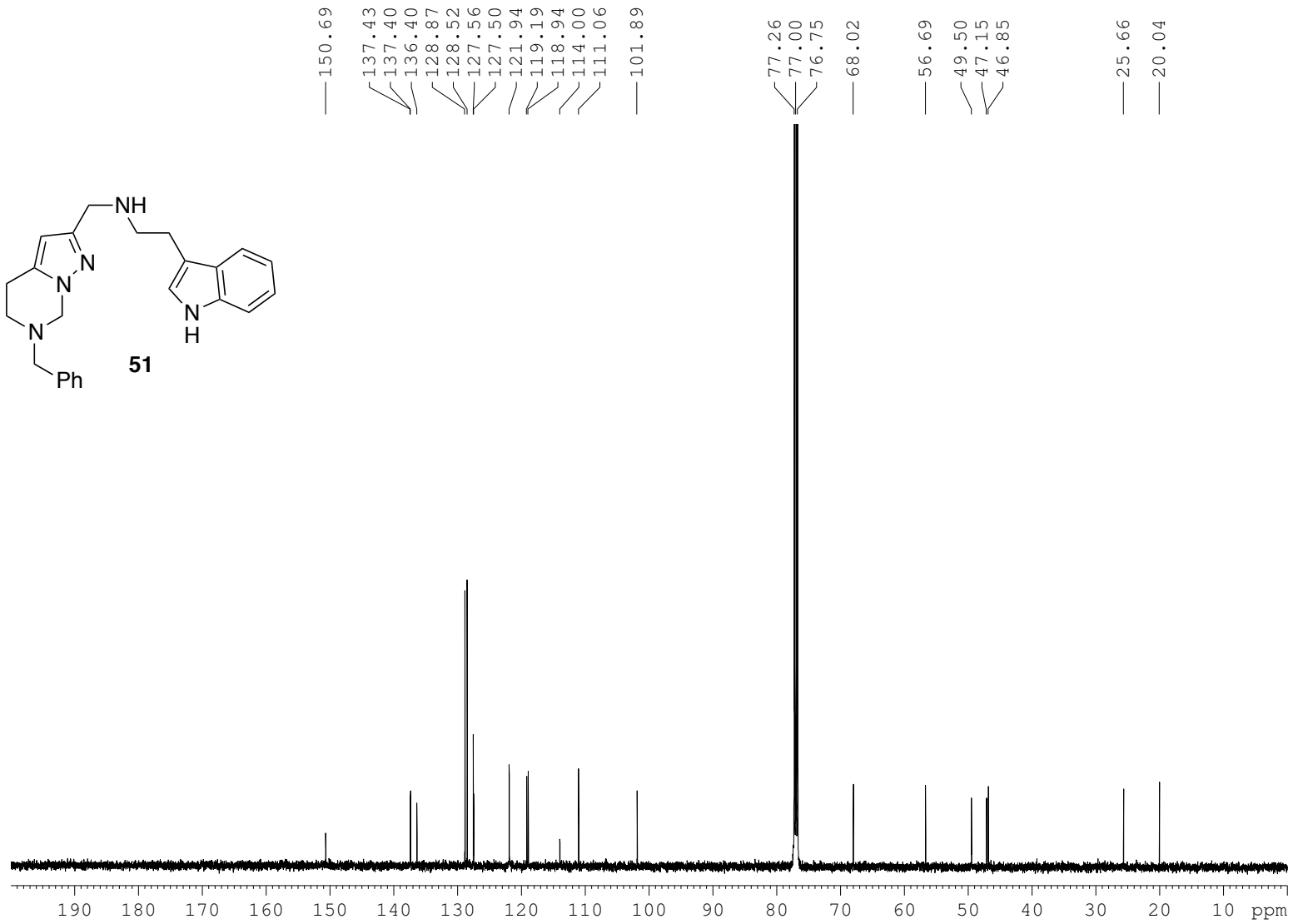

154.84
150.71
137.50
137.30
128.83
128.50
127.56
101.77
79.30
77.26
77.00
76.75
68.03
56.73
54.43
46.89
44.21
32.26
28.42
20.09
NH
N
N
N
N
Boc
Ph
50
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.088
8.057
7.626
7.610
7.357
7.348
7.340
7.329
7.324
7.322
7.316
7.308
7.300
7.297
7.291
7.288
7.283
7.270
7.203
7.201
7.187
7.173
7.171
7.121
7.119
7.105
7.103
7.091
7.089
7.045
5.949
4.778
3.823
3.793
3.043
3.034
3.031
3.024
3.019
2.860
2.848
2.836
1.862
1.805


NH
N
N
N
N
H
Ph

51


10
9
8
7
6
5
4
3
2
1
ppm
0.88
1.00
6.24
1.00
1.01
0.93
0.91
1.89
1.88
1.99
5.95
2.03
3.30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77.26
77.00
76.75
68.02
56.69
49.50
47.15
46.85
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NH
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N
Ph
N
H
51
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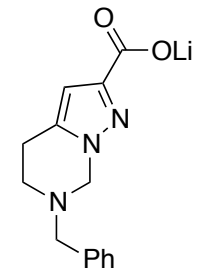
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OLi
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N
N
Ph

52

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7.301
7.297
7.292
7.287
7.280
6.440
5.033
4.803
3.820
3.318
3.314
3.310
3.306
3.302
3.114
3.099
3.083
2.948
2.933
2.917
10
9
8
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5
4
3
2
1
ppm
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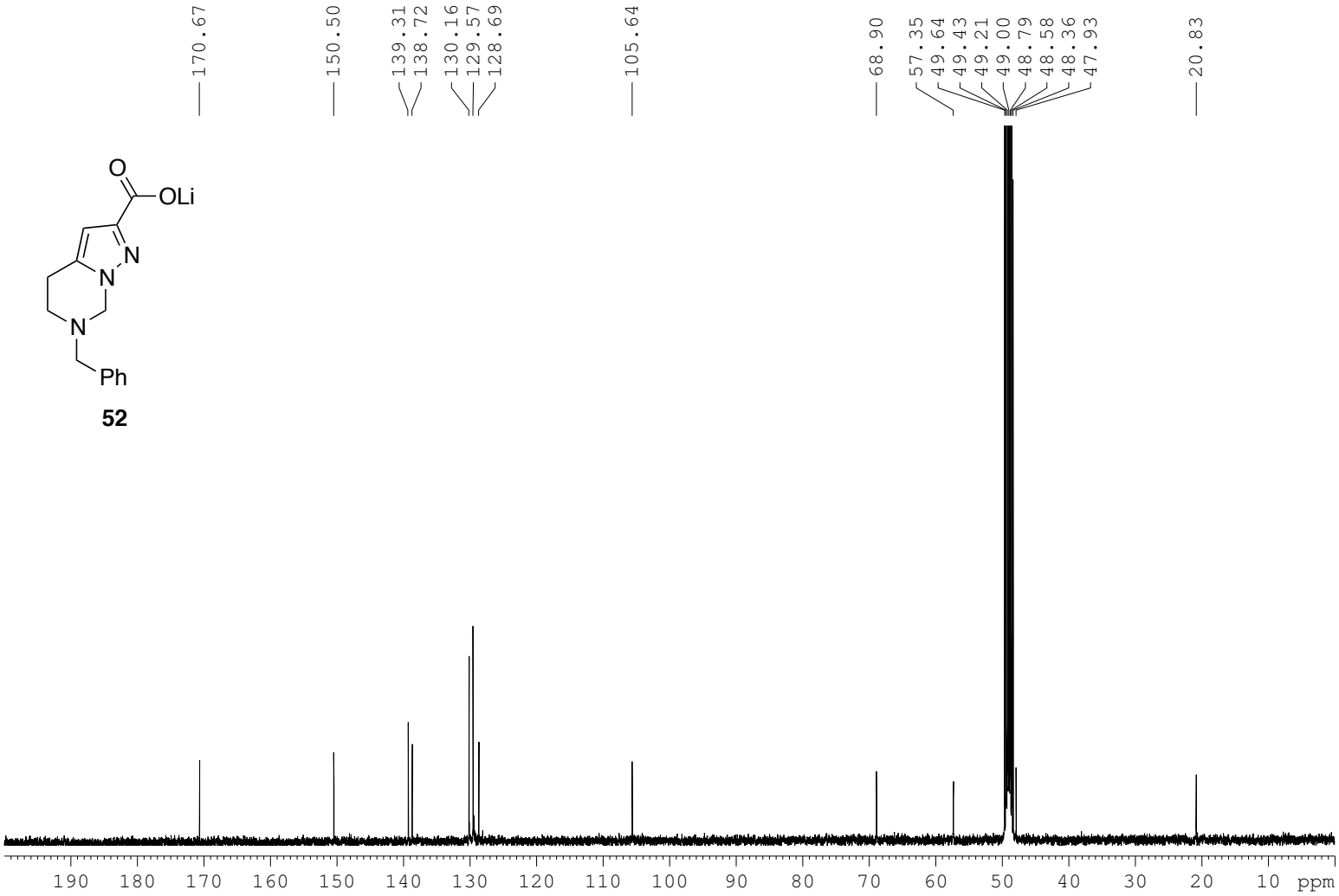
2.09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49.00
48.79
48.58
48.36
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20.83
O
OLi
N
N
N
Ph
52
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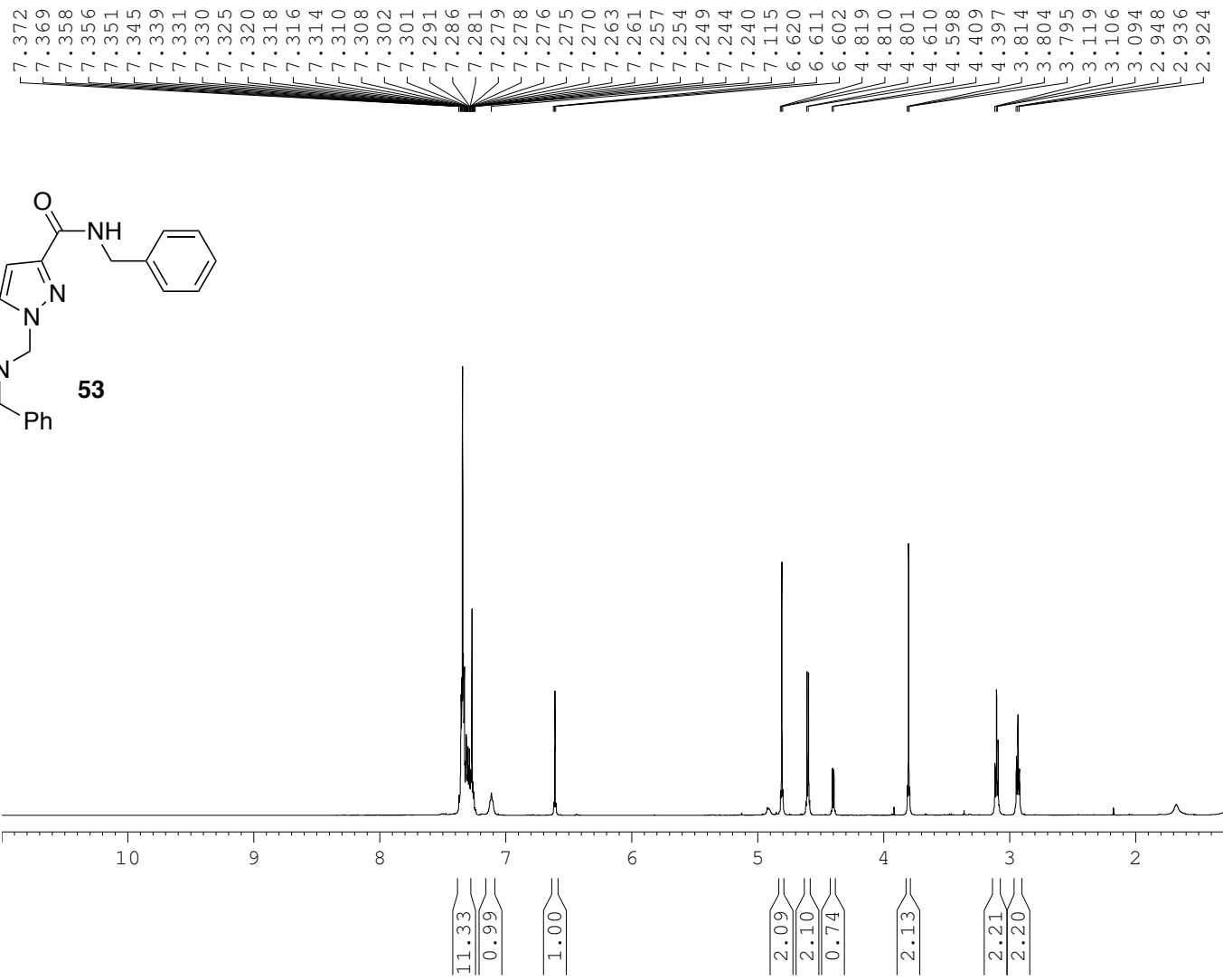
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7.314
7.310
7.308
7.302
7.301
7.291
7.286
7.281
7.279
7.278
7.276
7.275
7.270
7.263
7.261
7.257
7.254
7.249
7.244
7.240
7.115
6.620
6.611
6.602
4.819
4.810
4.801
4.610
4.598
4.409
4.397
3.814
3.804
3.795
3.119
3.106
3.094
2.948
2.936
2.924
O
NH
N
N
N
Ph
53
10
9
8
7
6
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ppm
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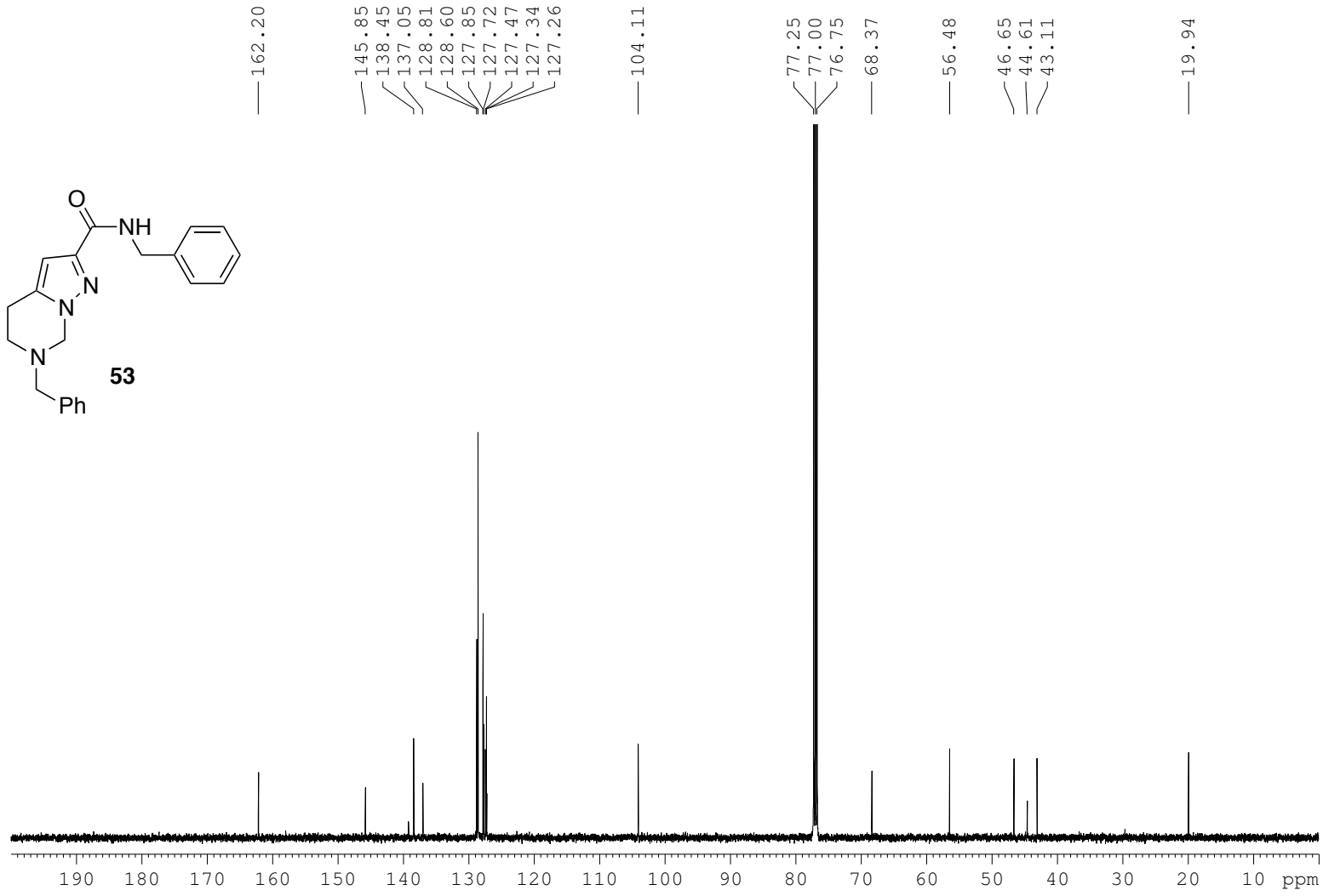
2.21
2.20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77.00
76.75
68.37
56.48
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19.94
O
NH
N
N
N
Ph
53
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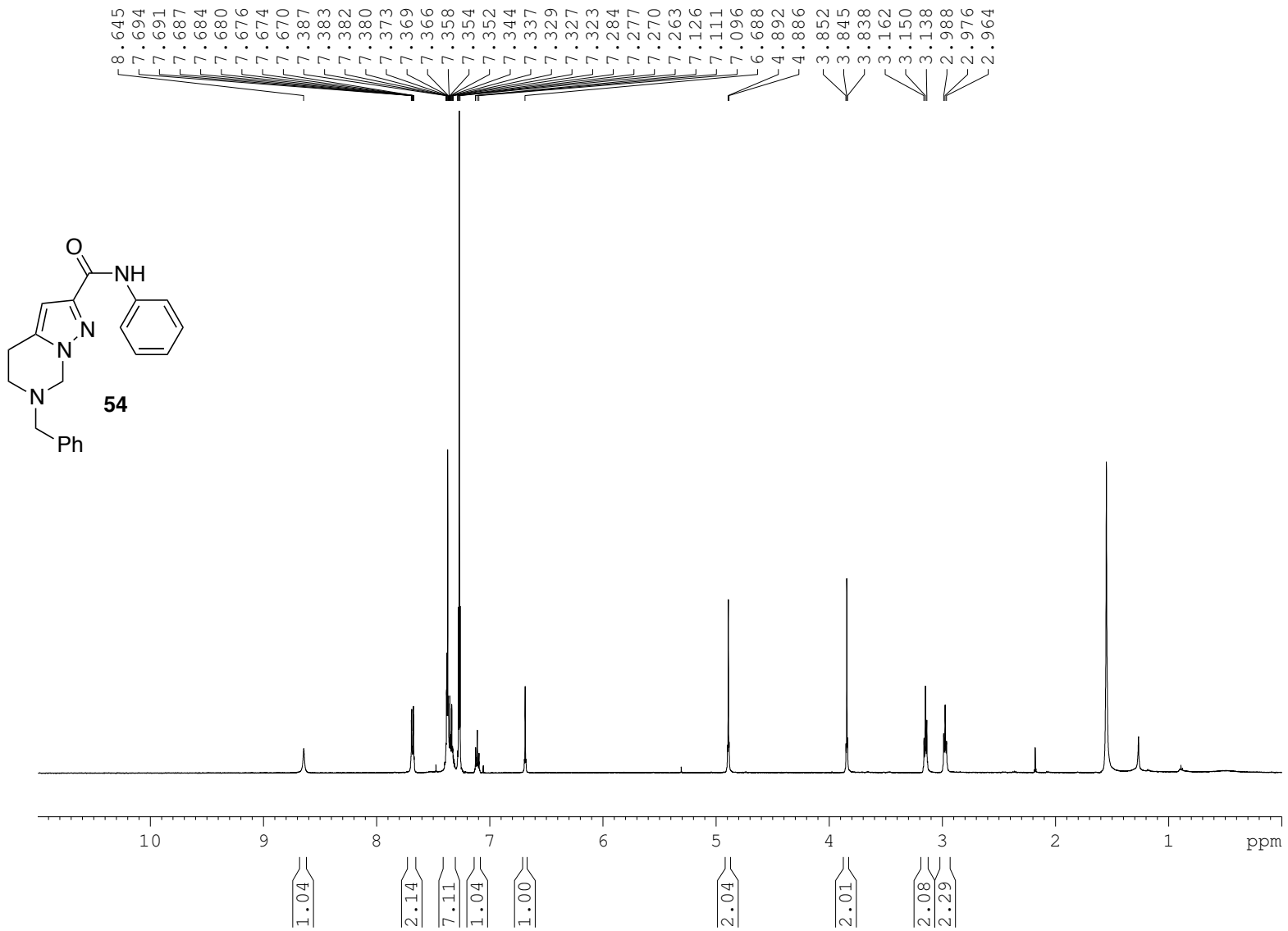
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7.380
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7.366
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7.354
7.352
7.344
7.337
7.329
7.327
7.323
7.284
7.277
7.270
7.263
7.126
7.111
7.096
6.688
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4.886
3.852
3.845
3.838
3.162
3.150
3.138
2.988
2.976
2.964
O
NH
N
N
N
Ph
54
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9
8
7
6
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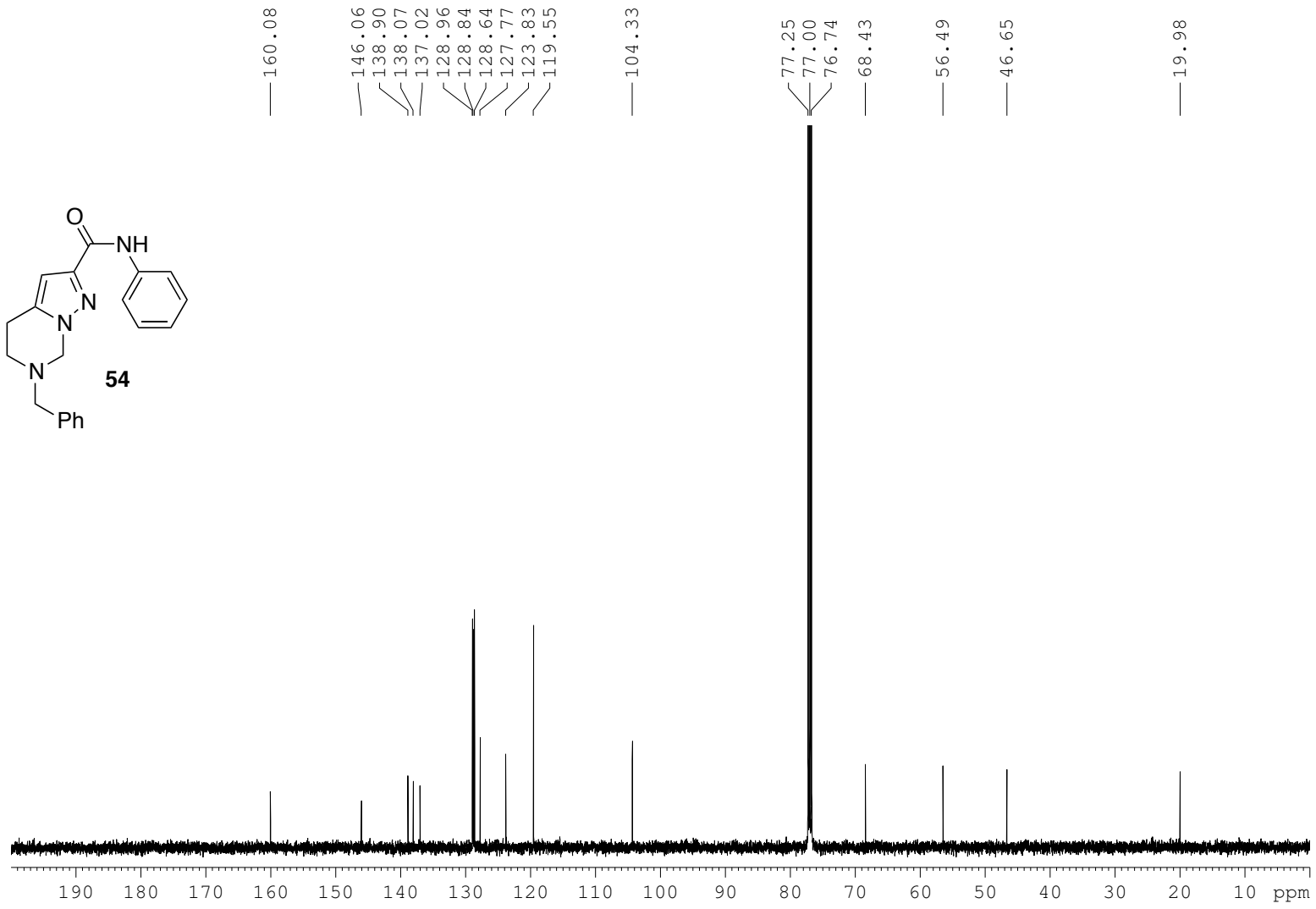
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128.64
127.77
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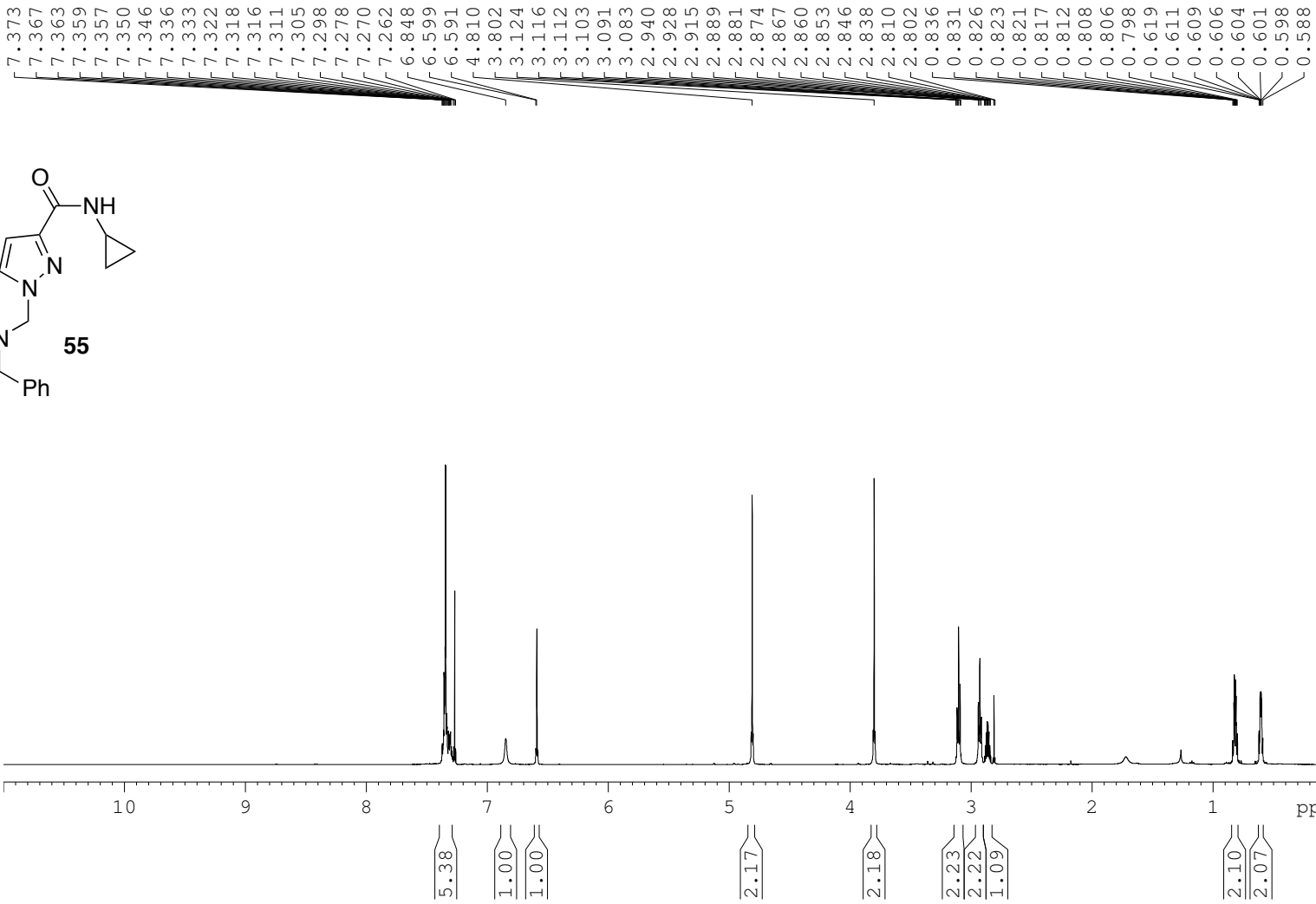
104.33
77.25
77.00
76.74
68.43
56.49
46.65
19.98
O
NH
N
N
N
Ph
54
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.322
7.318
7.316
7.311
7.305
7.298
7.278
7.270
7.262
6.848
6.599
6.591
4.810
3.802
3.124
3.116
3.112
3.103
3.091
3.083
2.940
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2.860
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2.846
2.838
2.810
2.802
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0.831
0.826
0.823
0.821
0.817
0.812
0.808
0.806
0.798
0.619
0.611
0.609
0.606
0.604
0.601
0.598
0.588
O
NH
N
N
N
Ph
55
10
9
8
7
6
5
4
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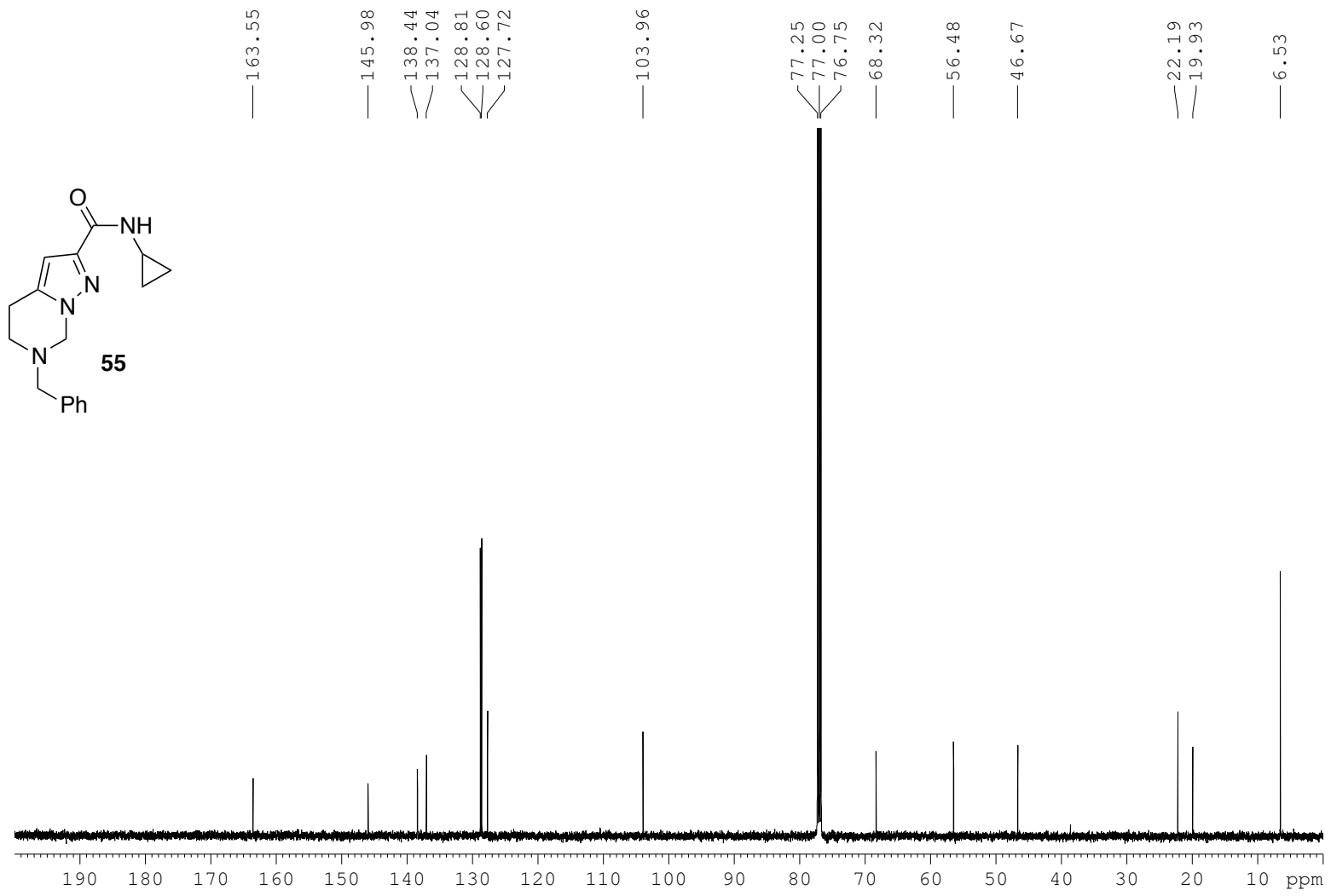
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77.00
76.75
68.32
56.48
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O
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N
N
N
Ph
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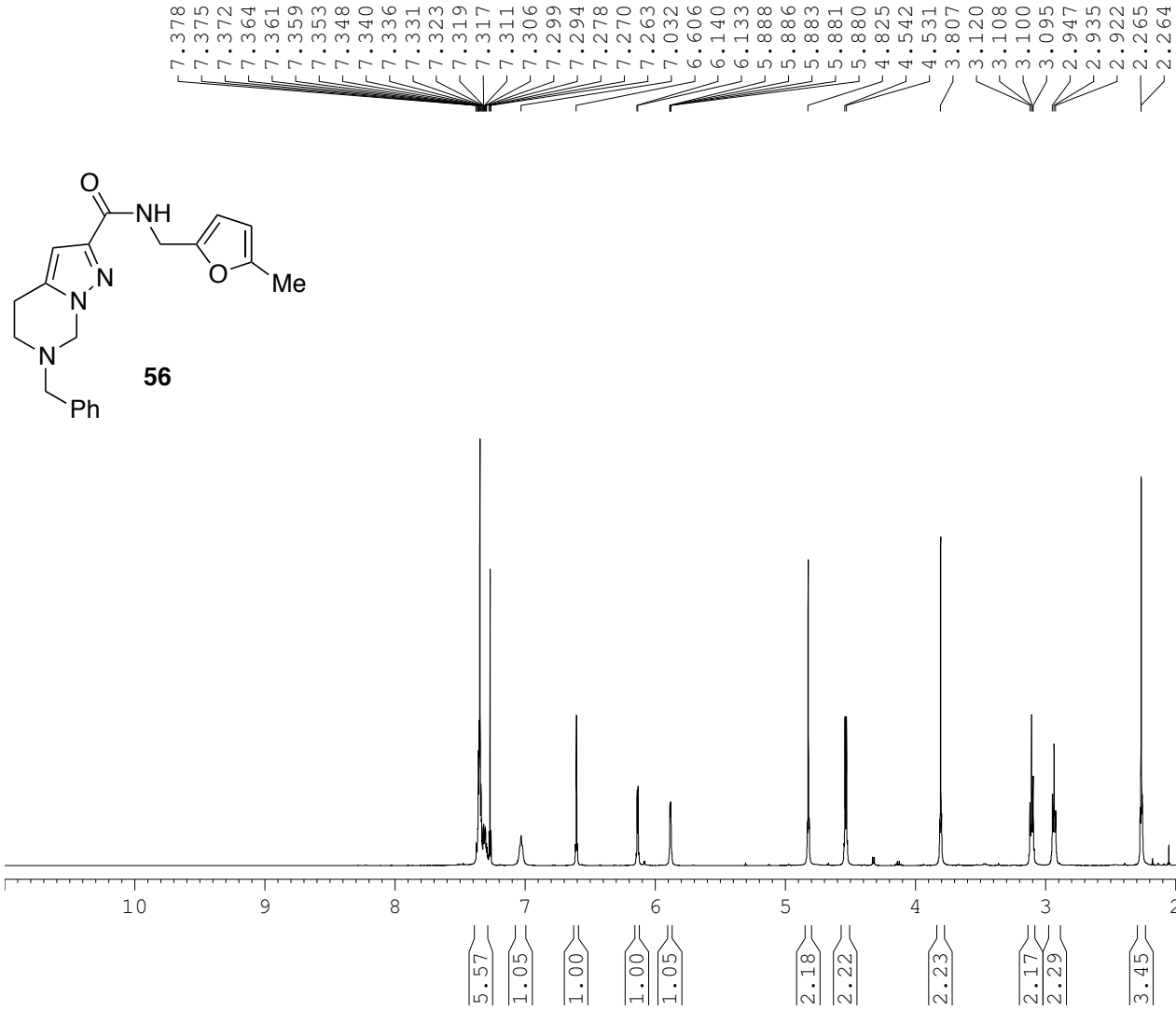
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7.317
7.311
7.306
7.299
7.294
7.278
7.270
7.263
7.032
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6.140
6.133
5.888
5.886
5.883
5.881
5.880
4.825
4.542
4.531
3.807
3.120
3.108
3.100
3.095
2.947
2.935
2.922
2.265
2.264
O
NH
N
N
O
Me
N
Ph
56
10
9
8
7
6
5
4
3
2
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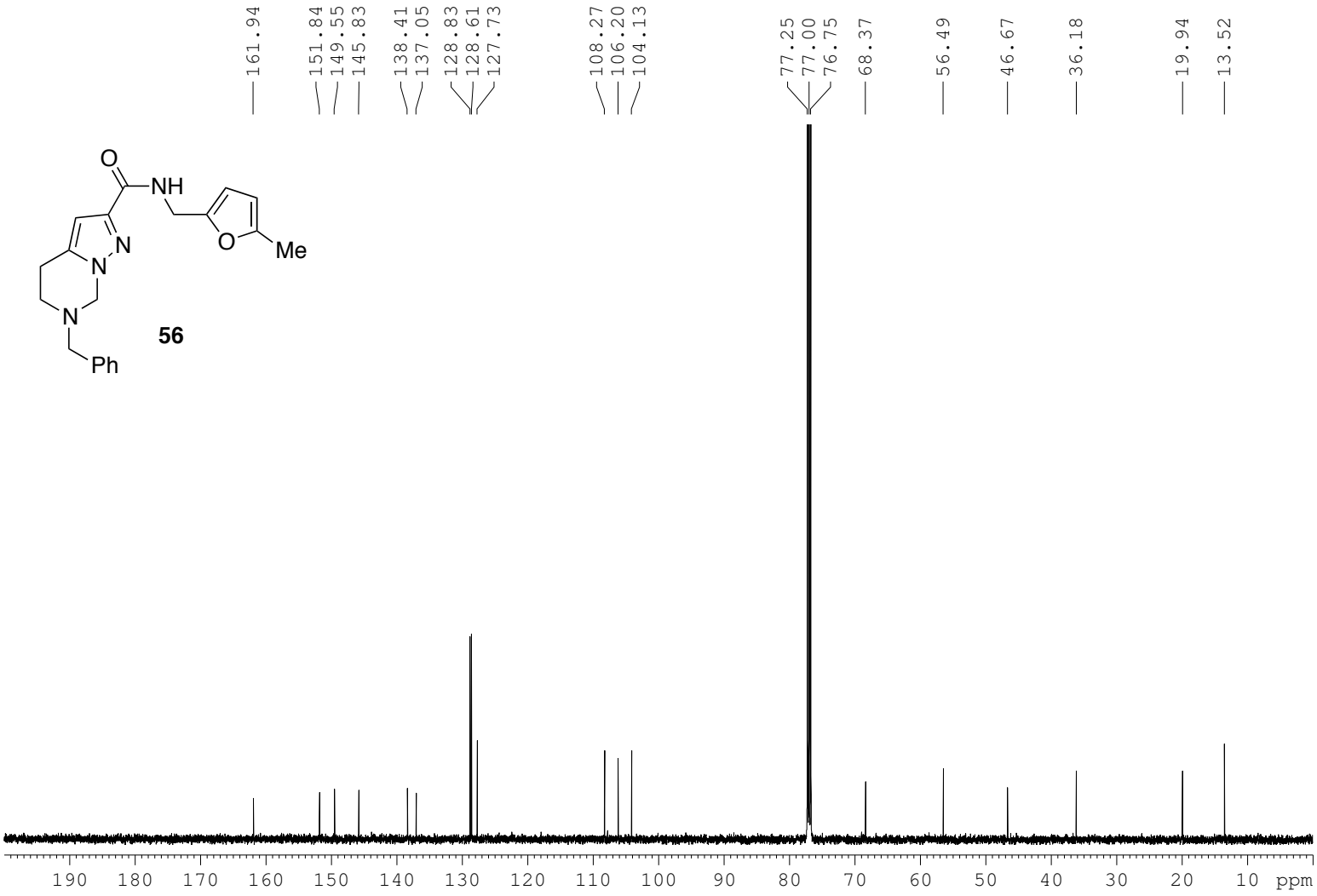
3.45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106.20
104.13
77.25
77.00
76.75
68.37
56.49
46.67
36.18
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O
NH
N
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O
Me
N
Ph
56
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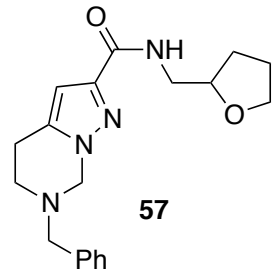
O
NH
O
N
N
N
Ph

57

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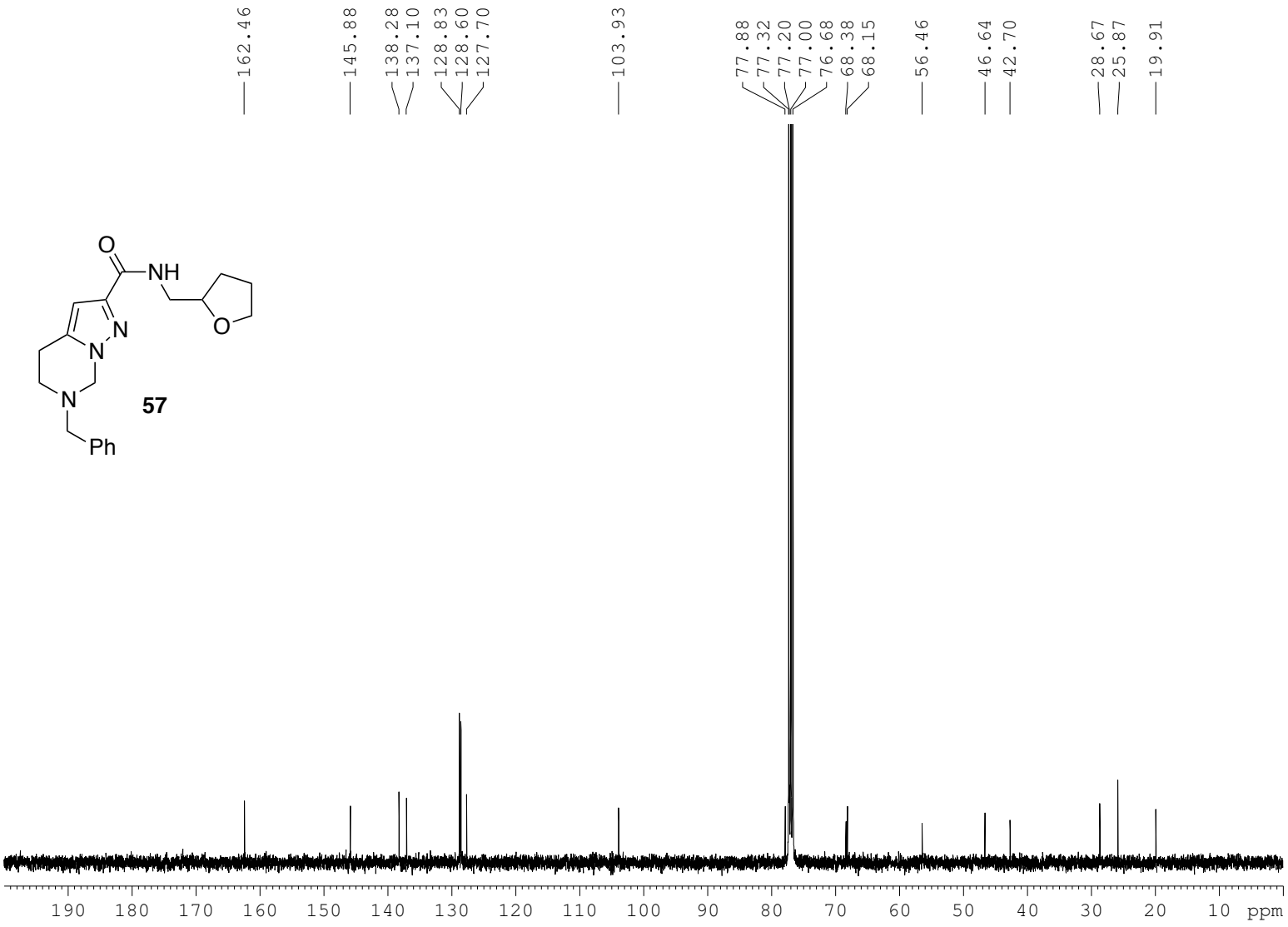
2.27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68.15
56.46
46.64
42.70
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O
NH
O
N
N
N
Ph
57
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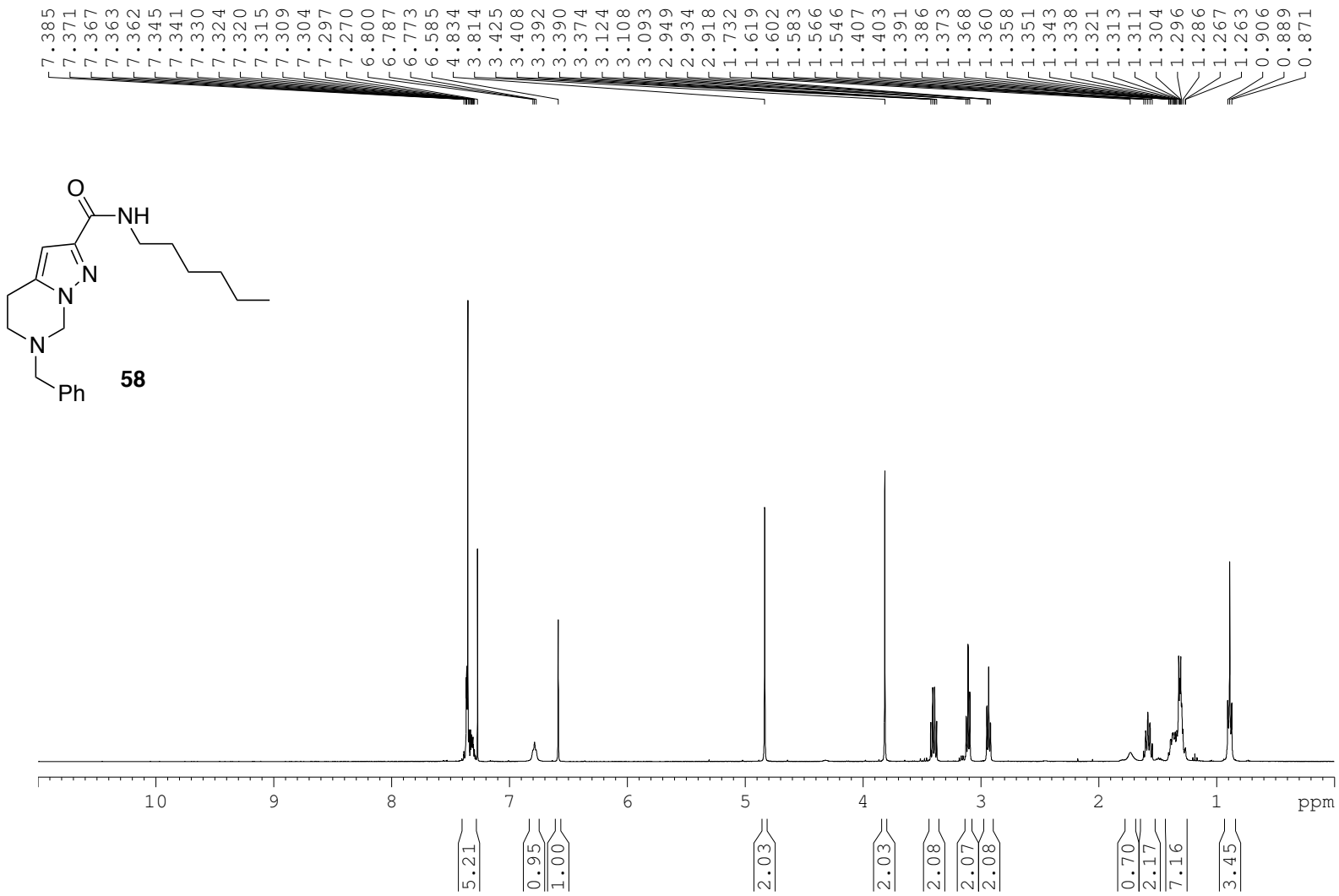
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Ph
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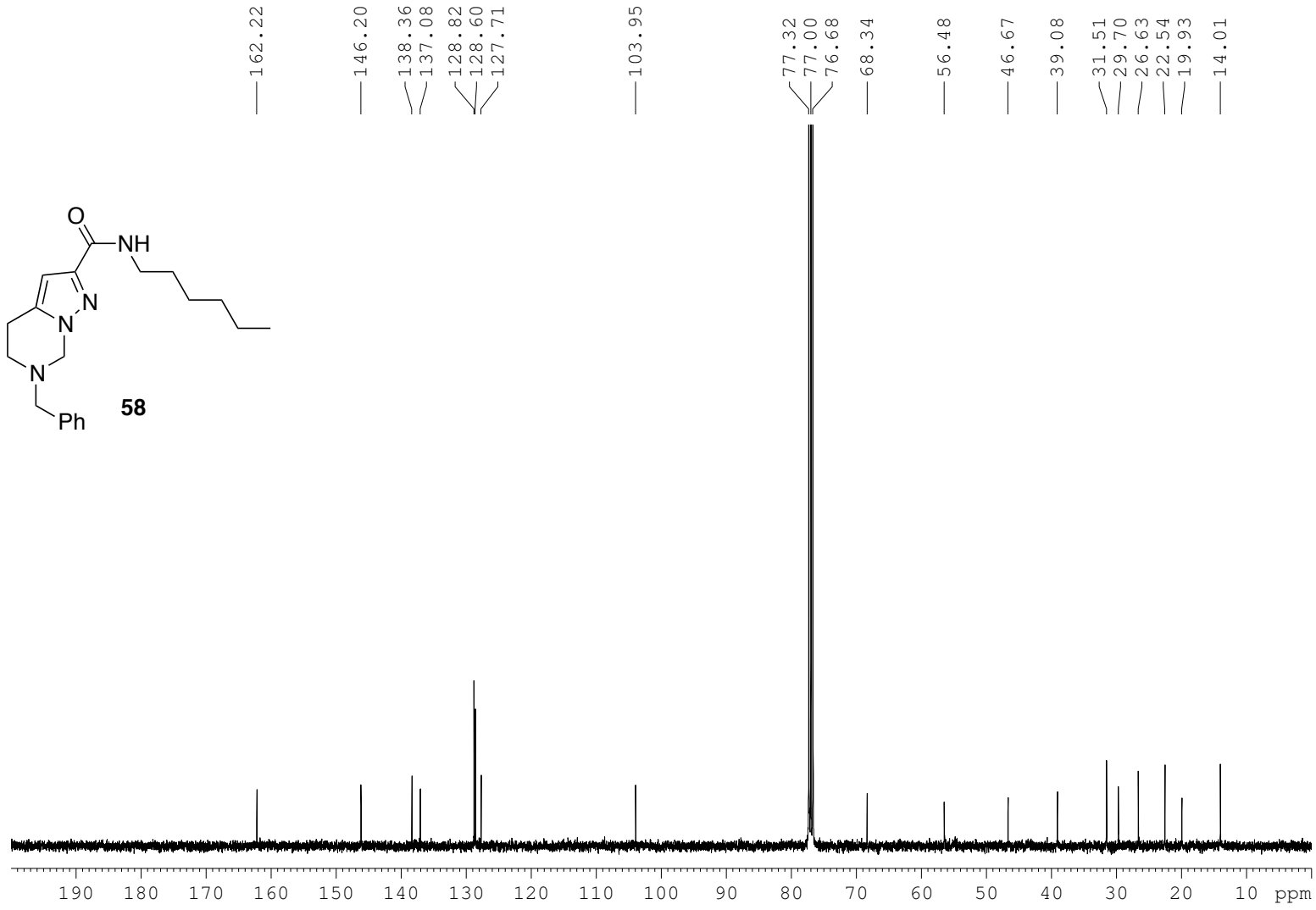
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29.70
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N
N
N
Ph
58
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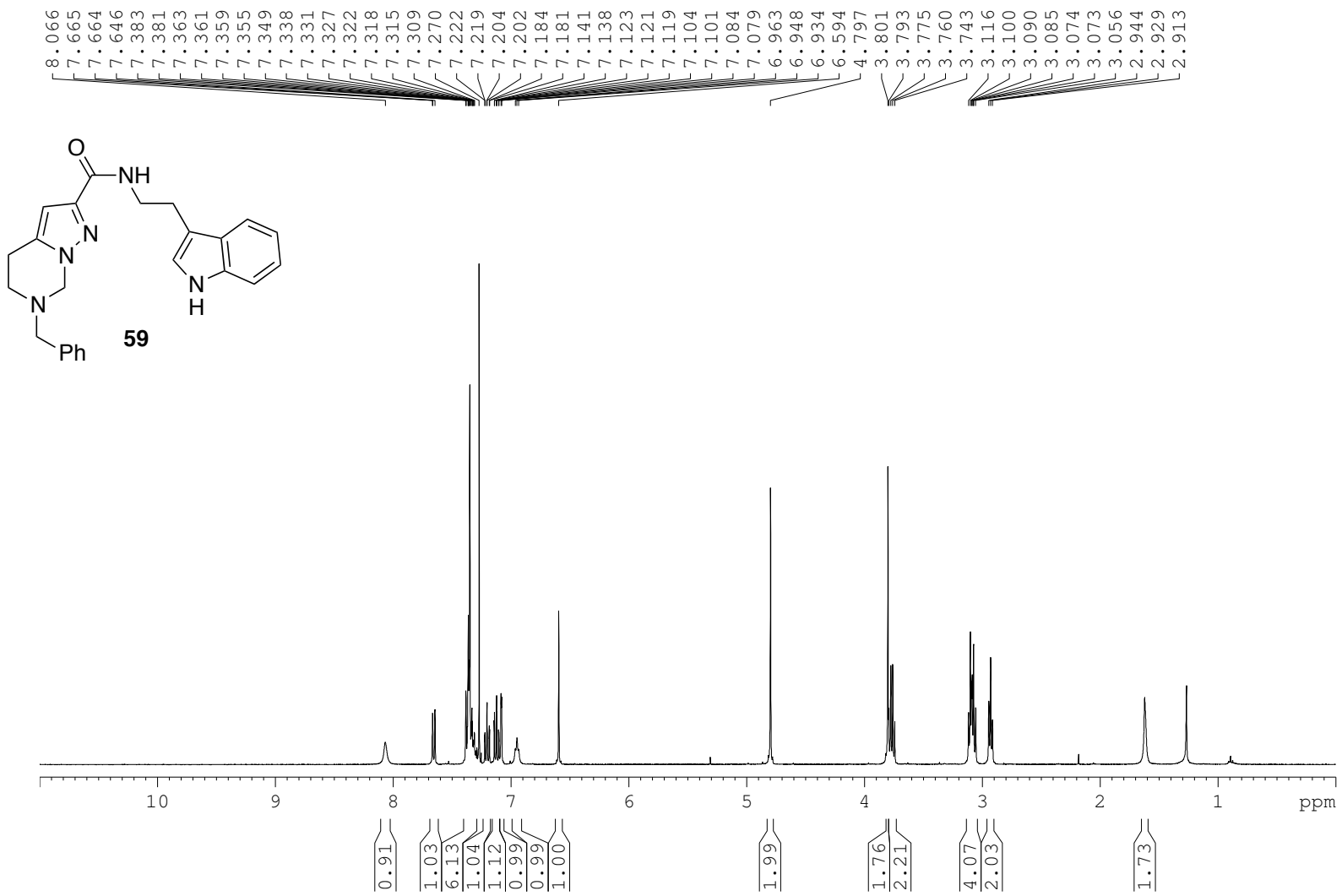
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N
H
Ph
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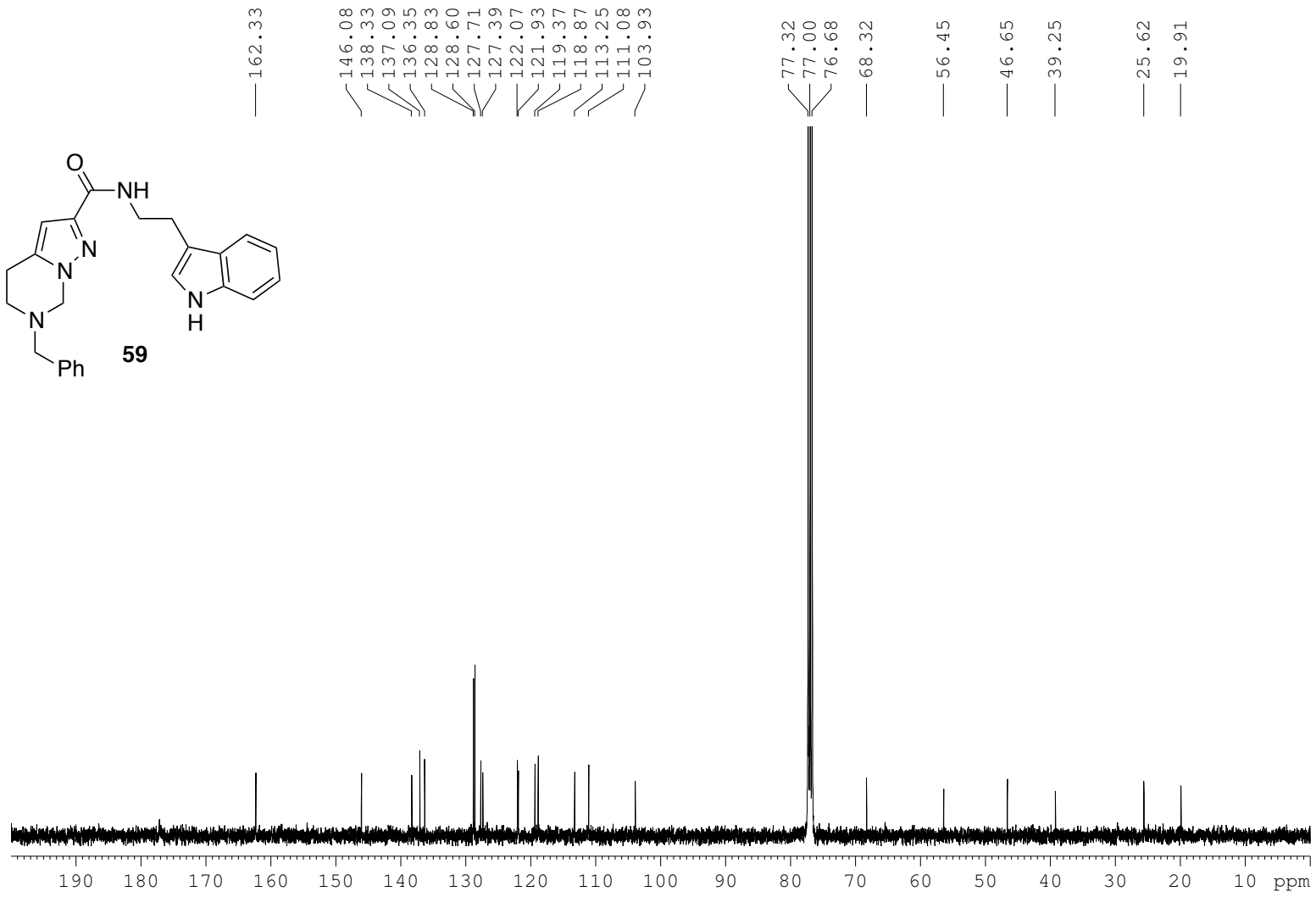
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111.08
103.93
77.32
77.00
76.68
68.32
56.45
46.65
39.25
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O
NH
N
N
N
Ph
N
H
59
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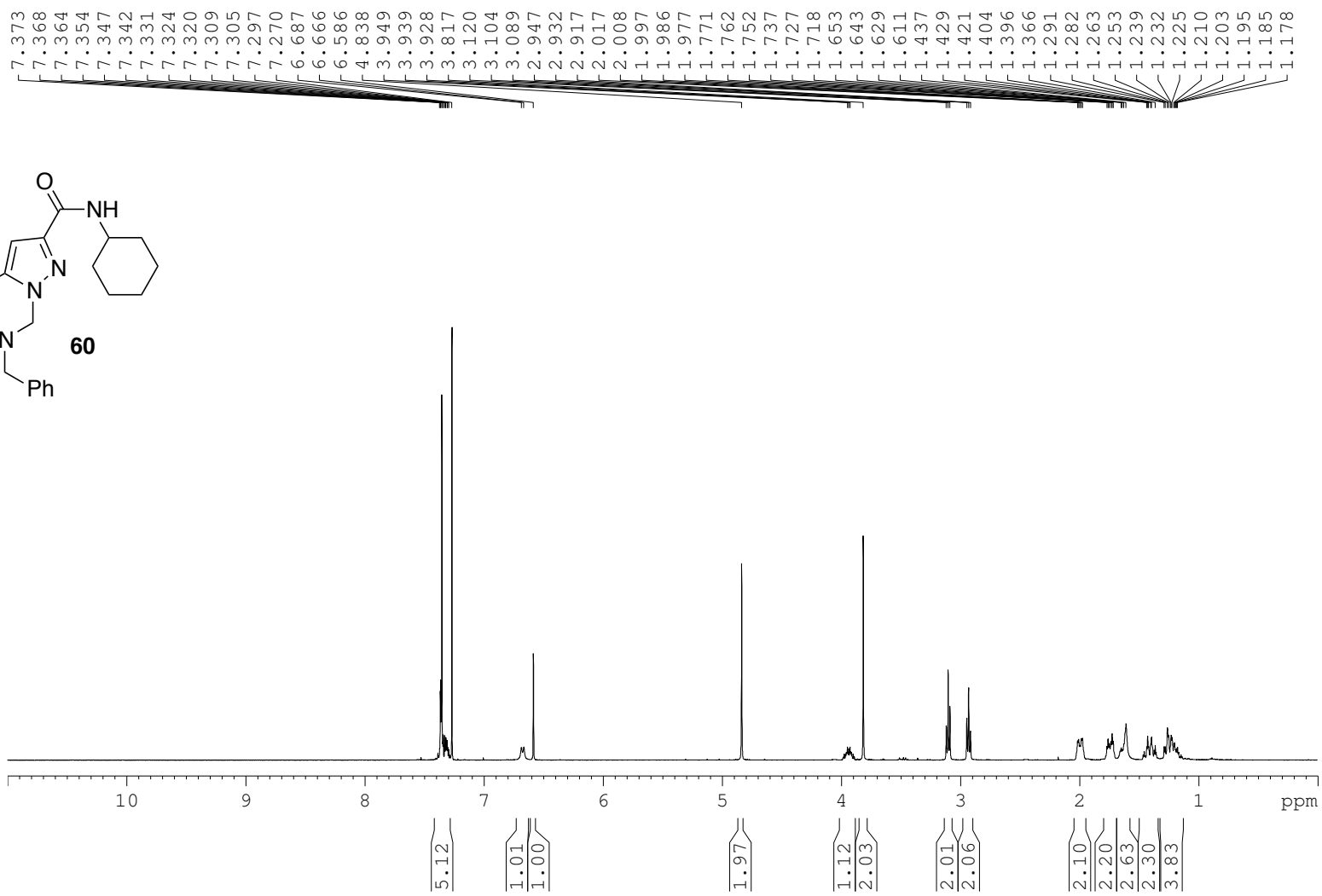
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6.586
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3.104
3.089
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2.932
2.917
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2.008
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N
N
Ph
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4
3
2
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ppm
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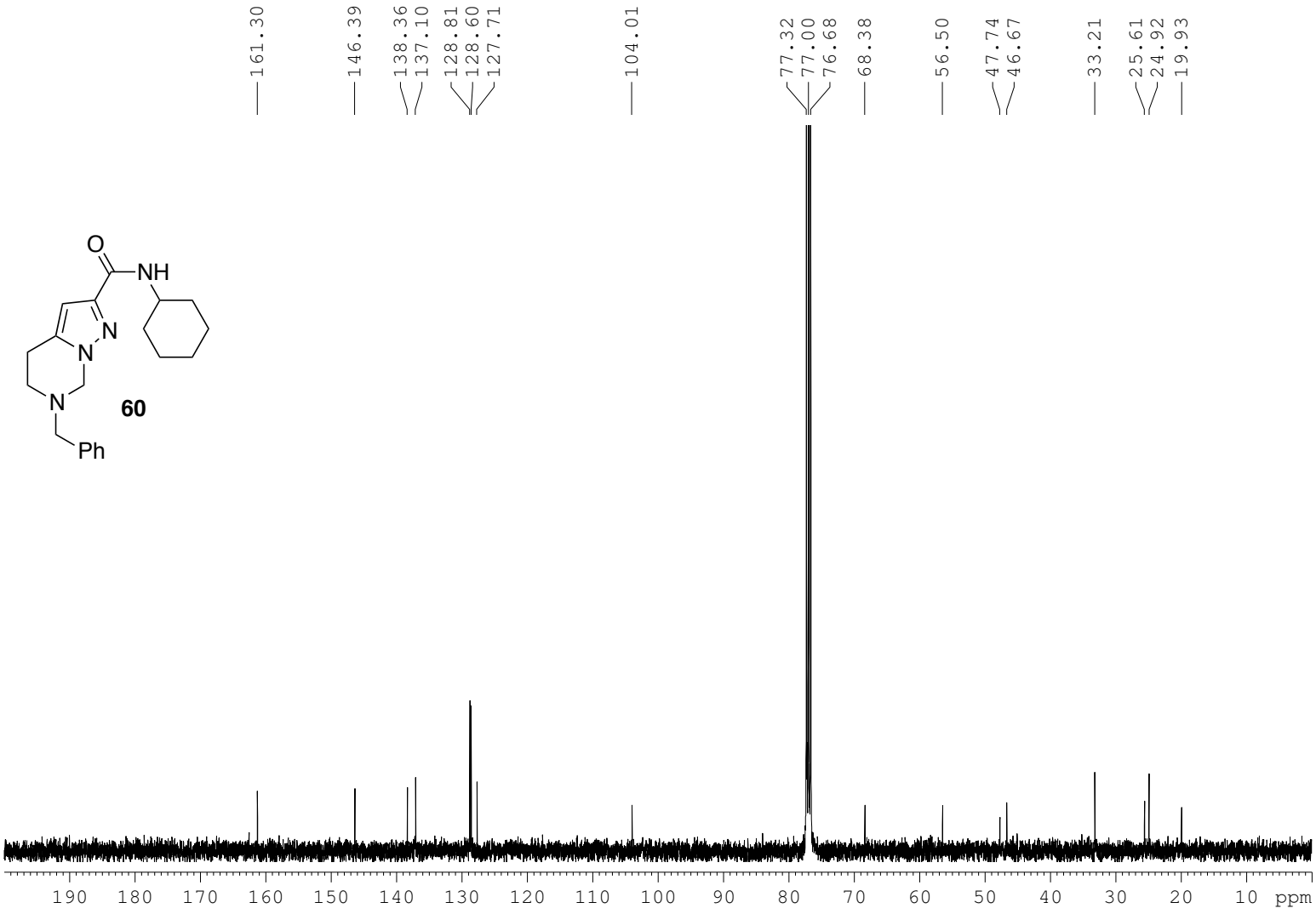
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47.74
46.67
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19.93
O
NH
N
N
N
Ph
60
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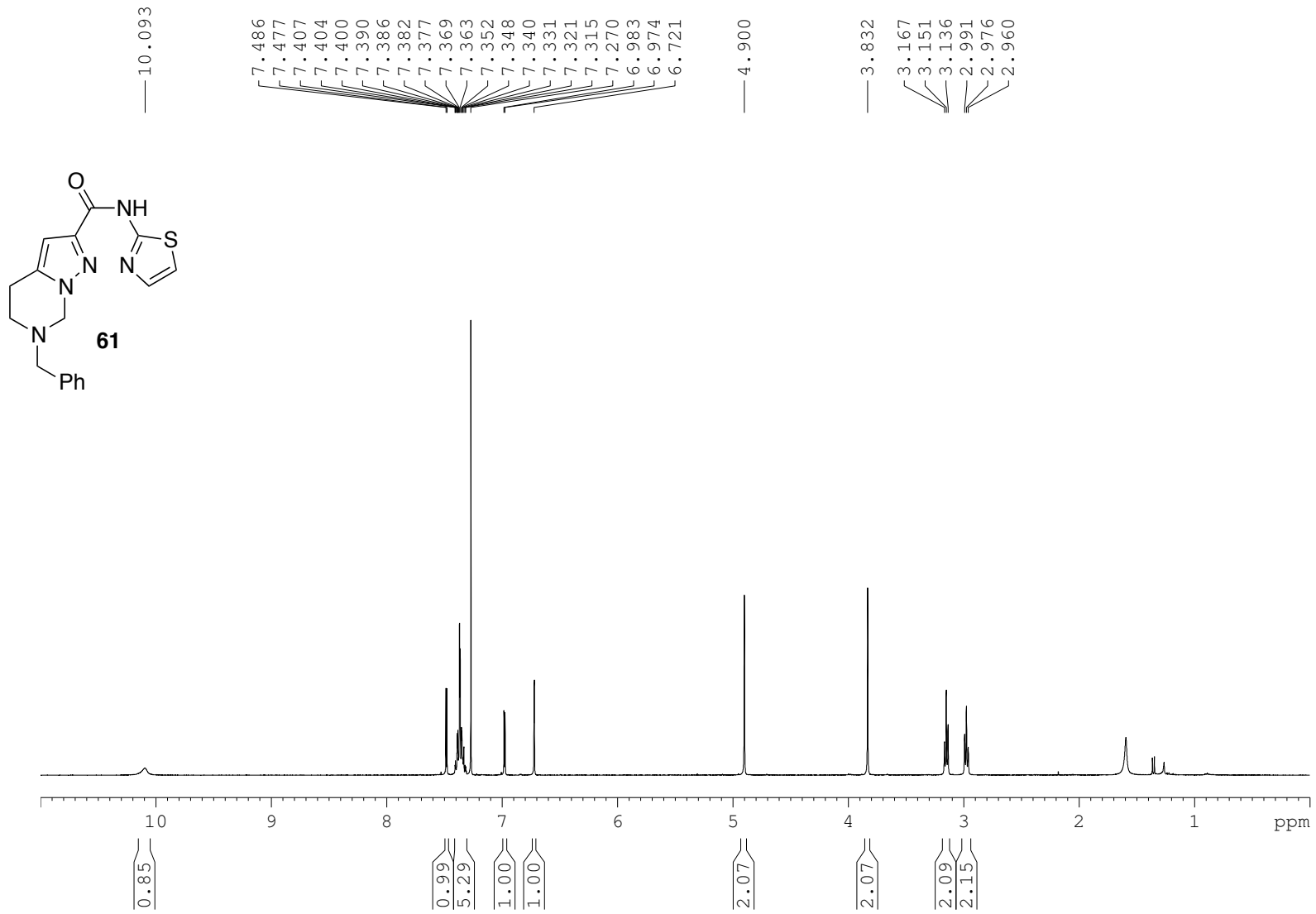
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7.270
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O
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S
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N
N
N
Ph
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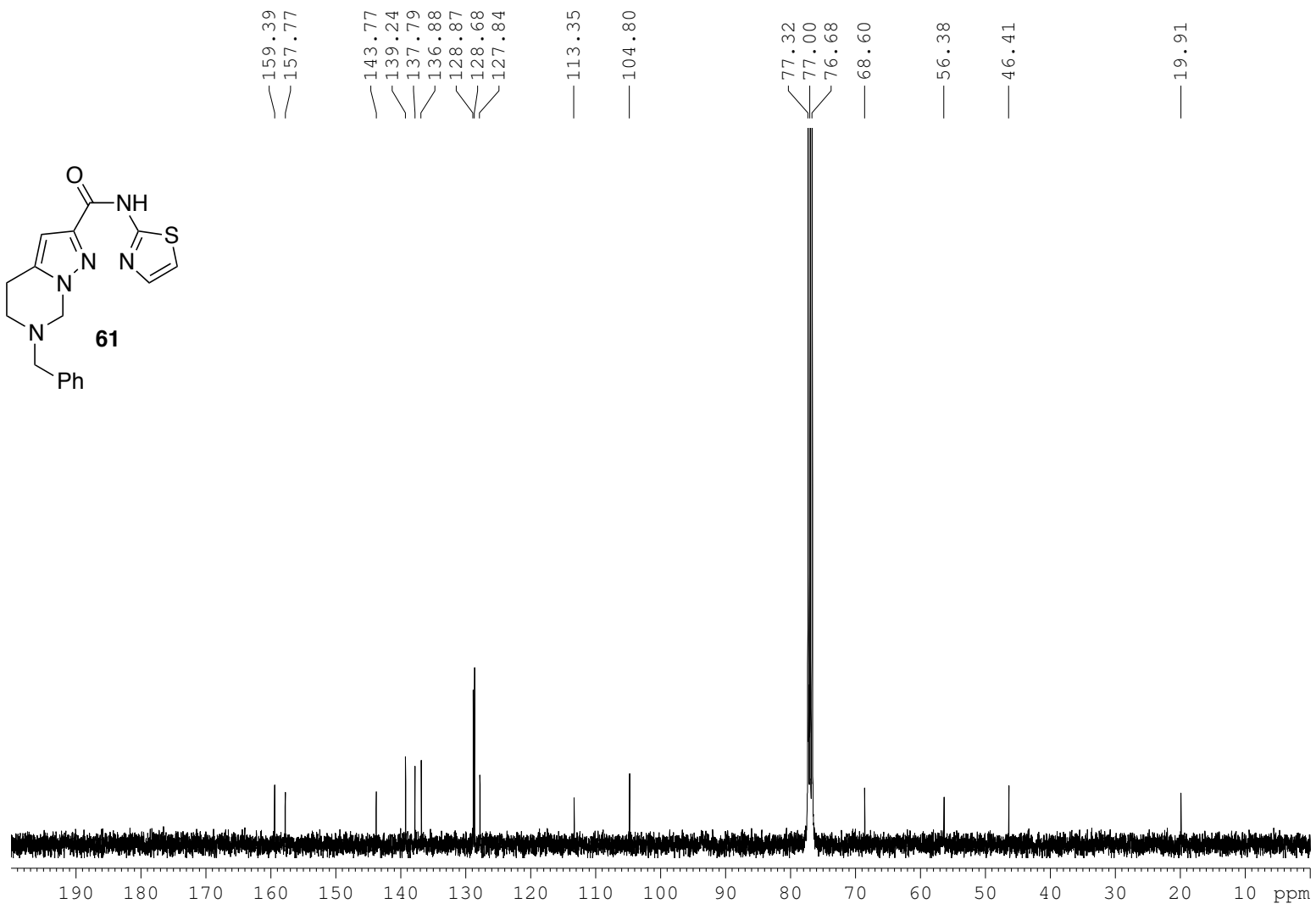
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68.60
56.38
46.41
19.91
O
NH
S
N
N
N
N
Ph
61
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


9.270
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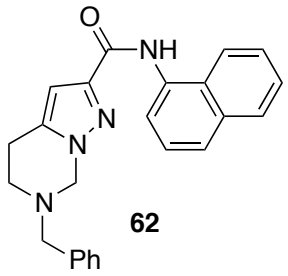
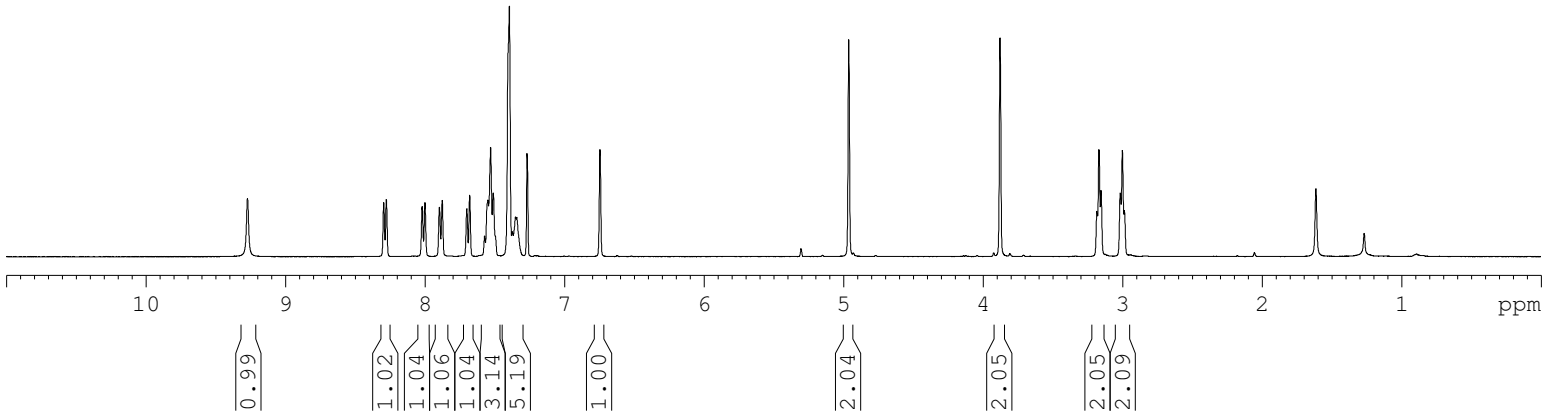
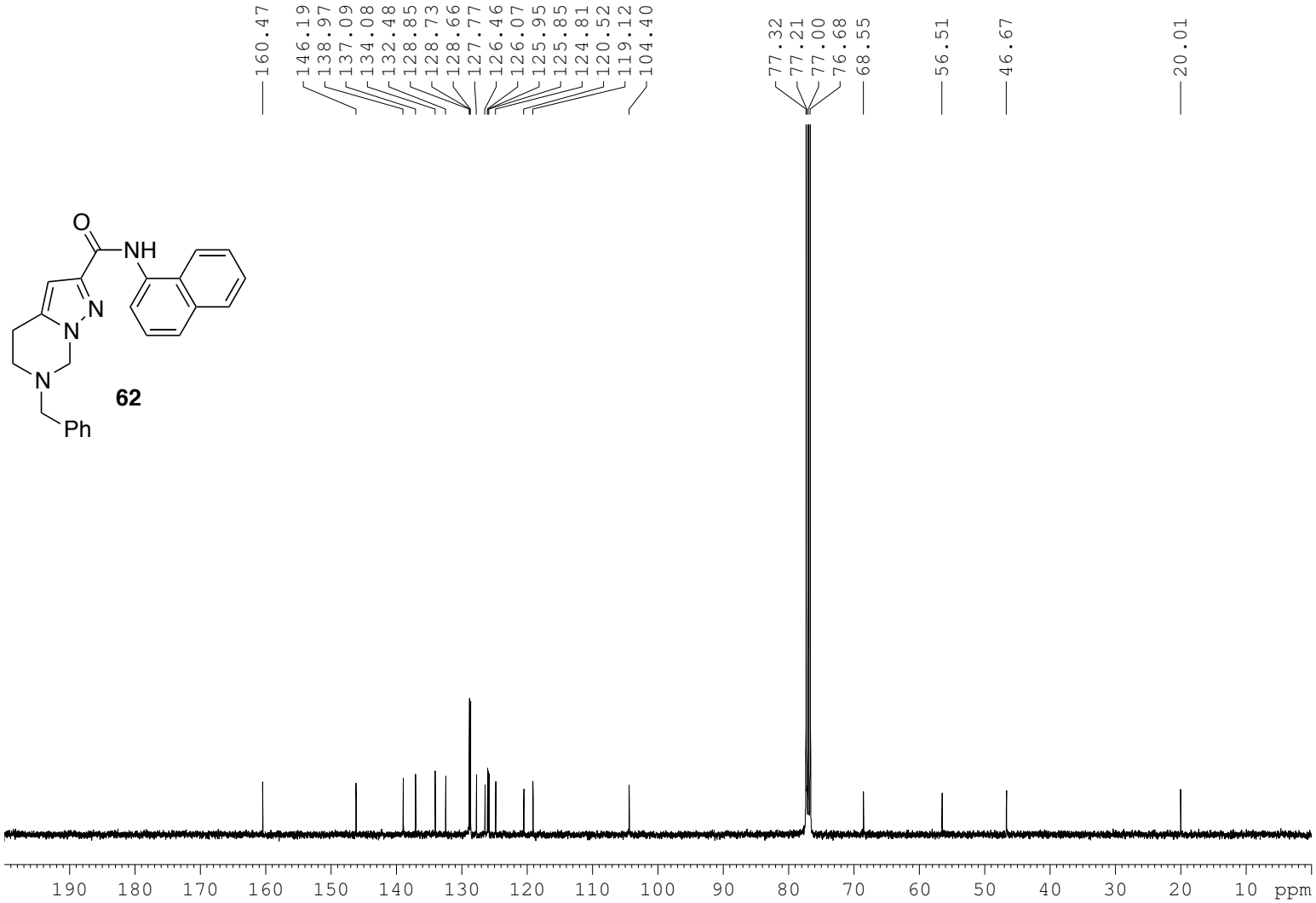
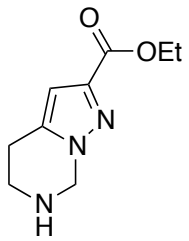
2.988


O
NH
N
N
N
Ph

62

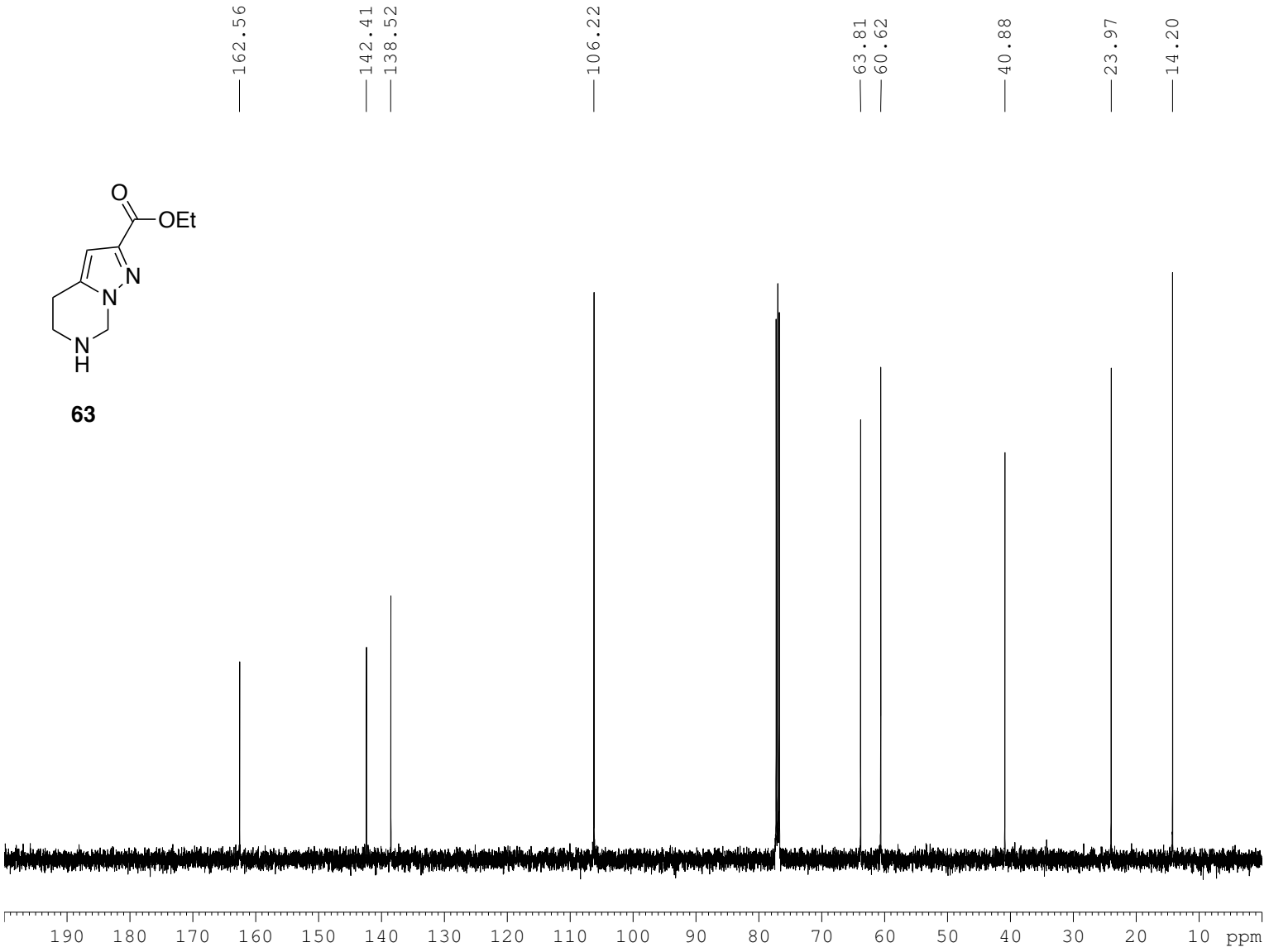

10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.02
1.04
1.06
1.04
3.14
5.19
1.00
2.04
2.05
2.05
2.09


160.47
146.19
138.97
137.09
134.08
132.48
128.85
128.73
128.66
127.77
126.46
126.07
125.95
125.85
124.81
120.52
119.12
104.40
77.32
77.21
77.00
76.68
68.55
56.51
46.67
20.01
O
NH
N
N
N
Ph
62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


O
OEt
N
N
N
H

63

6.490
6.489
6.487
5.012
4.335
4.321
4.307
4.293
3.156
3.144
3.132
2.805
2.793
2.781
1.335
1.321
1.307
10
9
8
7
6
5
4
3
2
1
ppm
0.91
1.97
2.01
2.07
2.09
3.01


162.56
142.41
138.52
106.22
63.81
60.62
40.88
23.97
14.20
O
OEt
N
N
N
H
63
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm