Supporting Information

An Inexpensive Radical Methylation and Related Alkylations of Heteroarenes

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General Experimental Methods

All reactions were carried out under dry, oxygen free nitrogen. Acrylic acid was purified by vacuum distillation and was freshly used. Other commercially available reagents were used as received without further purification. Thin Layer Chromatography (TLC) was performed on alumina plates precoated with silica gel (Merck silica gel, 60 F_{254}), which were visualized by the quenching of UV fluorescence when applicable (max = 254 nm and/or 366 nm) and/or by staining with anisadehyde in acidic ethanol solution and/or $KMnO_4$ in basic water followed by heating. Flash chromatography was carried out on Kieselgel 60 (40-63 μm). Petroleum ether refers to the fraction of petroleum boiling between 40 ℃ and 60 ℃. Infrared spectra were recorded on a Perkin-Elmer Spectrum Two. Absorption maxima (υ_{max}) are reported in wavenumbers (cm^{-1}). Nuclear magnetic resonance spectra were recorded at ambient temperature on a Bruker Avance DPX 400 instrument. Proton magnetic resonance spectra (^{1}H NMR) were recorded at 400 MHz and coupling constants (J) are reported to ± 0.5 Hz. The following abbreviations were utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Carbon magnetic resonance spectra (^{13}C NMR) were recorded at 100 MHz. Chemical shifts (H, C) are quoted in parts per million (ppm) and are referenced to the residual solvent peak ($CDCl_3$: δ_H= 7.27 and δ_C= 77.1; DMSO: δ_H = 2.50 and δ_C = 39.5; CD_3COCD_3, δ_H = 2.05 and δ_C = 29.8; CD_3OD: δ_H = 3.31 and δ_C = 49.0). High-resolution mass spectra were recorded by electron impact ionization (EI) on a JMS-GCmateII mass spectrometer. The quoted masses are accurate to ± 5 ppm. Microwave-assisted decarboxylation was performed using an Anton Paar® Monowave 300 microwave reactor.

General Procedures

General procedure A for the radical alkylkation

A solution of xanthate (3.0 equiv) and heteroarene (1.0 equiv) in a ethyl acetate or 1,2-dichloroethane (1.0 M according to xanthate) was refluxed under nitrogen for 10 min. DLP was added portionwise (20 mol % per hour) until the total consumption of the heterocycle [for substrates that were not completely consumed in 6 h, a seconde addition of xanthate was performed at room temperature, followed by heating at reflux for 15 min and portionwise addition of DLP (20 mol % per hour) was performed]. The reaction mixture was then cooled down to room temperature, concentrated under reduced pressure and purified by flash chromatography on silica gel or triturated in the appropriate solvent.

General procedure B for microwave-assisted decarboxylation

A solution of the carboxylic acid in *N*,*N*-dimethylacetamide (0.1 M) in a sealed tube was irradiated in a microwave reactor at 180 ℃ for 10 min and the reaction was monitored by TLC plate. In cases that the starting material was not totally consumed, the reaction temperature was increased by 10-20 ℃ and irradiated for another 10 min. And this procedure was repeated several times until the total consumption of the starting material. Upon cooling to room temperature, *N*,*N*-dimethylacetamide was removed under reduced pressure by azeotropic evaporation with toluene. The residue was purified by flash chromatography on silica gel.

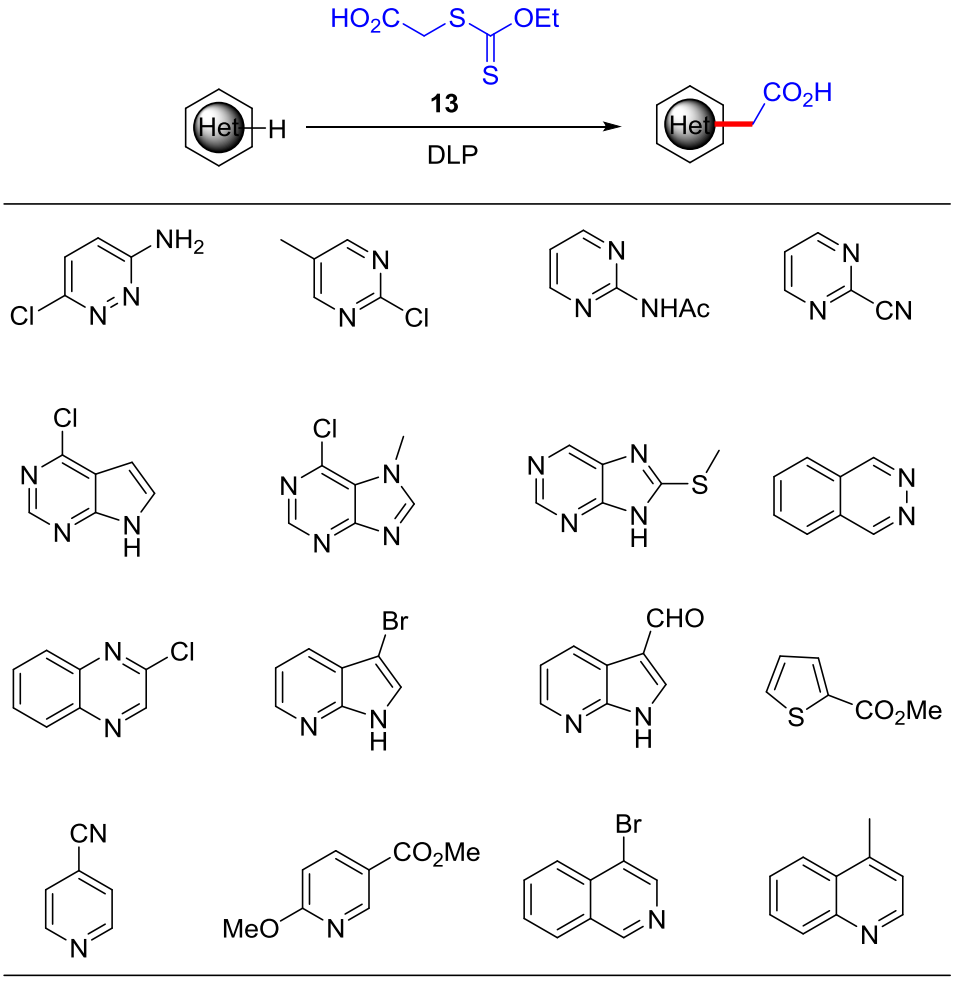
General procedure C for microwave-assisted decarboxylation

A solution of the carboxylic acid (x mmol) in *N*-methyl-2-pyrrolidone (10x mL) in a sealed tube was irradiated in a microwave reactor at 220 ℃ and the reaction was monitored by TLC plate. In cases that the starting material was not totally consumed, the reaction temperature was increased by 20 ℃ and irradiated for another 10 min. And this procedure was repeated several times until the total consumption of the starting material. Upon cooling to room temperature, the reaction mixture was poured

into water (50x mL) and extracted with ethyl acetate (3 × 50x mL). The combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by flash chromatography on silica gel.

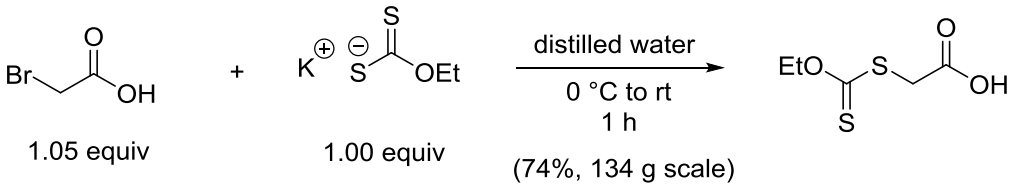
Limitations of the Scope of Heteroarenes

The following heteroarenes showed low or even no reactivity towards the reaction with xanthylacetic acid **13** under standard reaction conditions, including pyridazine, pyrimidine, quinoxaline, pyridine, quinoline, etc.

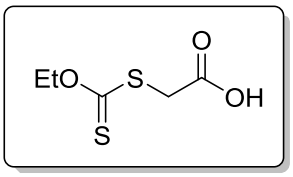


Experimental Procedures and Spectroscopic Data

2-((Ethoxycarbonothioyl)thio)acetic acid (13)



A solution of 2-bromoacetic acid (145.9 g, 1.05 mol, 1.05 equiv) in distilled water (500 mL) in 1 L Erlenmeyer was cooled to 0 ℃. Potassium *O*-ethylxanthate (160.0 g, 1.00 mol, 1.00 equiv) was added portionwise. The ice bath was then removed and the reaction mixture was stirred for 1 h. The reaction mixture was then cooled down to 0 ℃ and was kept at 0 ℃ until no oil present in the mixture (3 h, if necessary, some crystals of the product could be added to promote crystallization). The crystals were then filtered, washed with cold water and dried above filtration paper in a crystallizer to afford the desired product (143.5 g, 80% yield), which could be recrystallized from ethyl acetate/cyclohexane (30 mL/500 mL) at 55 ℃ (temperature of oil bath) to give the desired product **13** as white crystals (134.2 g, 0.74 mol, 74% yield). The spectra data are in agreement with the literature report.[1]



Chemical Formula: $C_5H_8O_3S_2$
Molecular Weight: 180,24

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.84 (br, 1H), 4.66 (q, J = 7.1 Hz, 2H), 3.96 (s, 2H), 1.43 (t, J = 7.2 Hz, 3H).

^{13}C NMR (δ, ppm) (100 MHz, $CDCl_3$) 212.4, 173.8, 71.0, 37.9, 13.8.

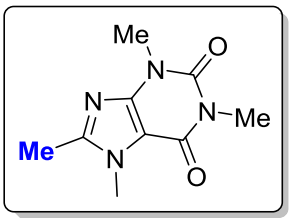
IR (ν, cm^{-1}, $CDCl_3$) 2990, 2940, 2902, 1719, 1416, 1365, 1298, 1239, 1113, 1051.

HRMS (EI+) calculated for $C_5H_8O_3S_2$: 179.9915; Found: 179.9923.

mp: 52-53 ℃.

[1] Auty, S. E. R.; Andren, O.; Malkoch, M.; Rannard, S. P. *Chem. Commun.* **2014**, 6574.

1,3,7,8-Tetramethyl-3,7-dihydro-1*H*-purine-2,6-dione (21)



Chemical Formula: $C_9H_{12}N_4O_2$
Molecular Weight: 208,22

According to the general procedure A, the reaction was carried out with caffeine 3 (97 mg, 0.50 mmol, 1.0 equiv) and xanthate 13 (271 mg, 1.50 mmol, 3.0 equiv) in ethyl acetate (1.5 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/methanol = 1:0 to 20:1) afforded the desired product 21 as a white solid (68 mg, 0.33 mmol, 65% yield). The spectra data are in agreement with the literature report.[2]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 3.91 (s, 3H), 3.56 (s, 3H), 3.40 (s, 3H), 2.46 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 155.3, 151.8, 150.8, 148.0, 107.6, 32.0, 29.8, 28.0, 13.2.

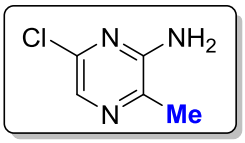
IR (ν, cm^{-1}, $CDCl_3$) 2954, 1701, 1654, 1549, 1502, 1469, 1457, 1435, 1397, 1342, 1291, 1220, 1041, 978.

HRMS (EI+) calculated for $C_9H_{12}N_4O_2$: 208.0960; Found: 208.0966.

mp: 211-212 ℃ (lit.: 189-191 ℃).

[2] Gui, J.; Zhou, Q.; Pan, C.-M.; Yabe, Y.; Burns, A. C.; Collins, M. R.; Ornelas, M. A.; Ishihara, Y.; Baran, P. S. *J. Am. Chem. Soc.* **2014**, *136*, 4853.

6-Chloro-3-methylpyrazin-2-amine (23)



Chemical Formula: $C_5H_6ClN_3$
Molecular Weight: 143,57

According to the general procedure A, the reaction was carried out with 2-amino-6-chloropyrazine **22** (130 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 3:1 to 2:1) afforded the desired product **23** as a white solid (46 mg, 0.32 mmol, 32% yield).

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.83 (s, 1H), 4.67 (br, 2H), 2.37 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 152.4, 144.5, 137.4, 131.8, 19.7.

IR (ν, cm^{-1}, $CDCl_3$) 3520, 3413, 1609, 1559, 1542, 1438, 1377, 1268, 1241, 1213, 1033, 990.

HRMS (EI+) calculated for $C_5H_6ClN_3$: 143.0250; Found: 143.0257.

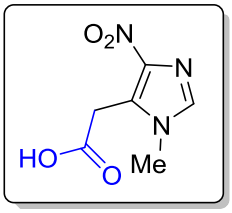
mp: 144-145 ℃.

2-(1-Methyl-4-nitro-1*H*-imidazol-5-yl)acetic acid (30)

Entry 1: According to the general procedure, the reaction was carried out with imidazole **29** (127 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate was added and needed 5 h for the reaction to go to completion. After removal of the solvent, the residue was triturated from diethyl ether to give product **30** (74 mg, 0.40 mmol, 40% yield) as a black powder. The filtrate was concentrated under reduced pressure and flash chromatography on silica gel (gradient of dichloromethane/ethyl acetate = 4:1 to 7:3) afforded product **31** as a white solid (6 mg, 0.04 mmol, 4% yield).

Entry 2: A solution of imidazole (163 mg, 1.28 mmol, 1.0 equiv) and xanthate (693 mg, 3.84 mmol, 3.0 equiv) in ethyl acetate (3.8 mL) was refluxed under nitrogen for 10 min. The solution was then cooled down to 60 ℃ (temperature of oil bath) and DLP (100 mol %) was then added. After 12 h, DLP (50 mol %) was added and took another 12 h for the reaction to go to completion. The reaction mixture was then cooled down to room temperature, concentrated under reduced pressure and triturated with diethyl ether to give the desired product **30** as an orange powder (163 mg, 0.88 mmol, 68% yield).

The spectra data of **30** and **31** are in agreement with the literature report.[3]



Chemical Formula: $C_6H_7N_3O_4$
Molecular Weight: 185,14

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.71 (s, 1H), 4.18 (s, 2H), 3.74 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 171.5, 145.8, 137.7, 129.8, 32.9, 30.9.

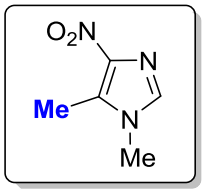
IR (ν, cm^{-1}, neat) 3153, 2796, 2712, 2506, 1705, 1575, 1506, 1441, 1418, 1361, 1332, 1297, 1254, 1221, 1195, 1178, 1042, 989, 924.

HRMS (EI+) calculated for $C_6H_7N_3O_4$: 185.0437, M-CO_2, $C_5H_7N_3O_2$: 141.0538; Found: 141.0544.

[3] Godt Jr., H. C.; Blicke, F. F. *J. Org. Chem.* **1969**, *34*, 2008.

mp: decomposed at 160 ℃ (lit.: 144 ℃ decomposition).

1,2-Dimethyl-4-nitro-1*H*-imidazole (31)



Chemical Formula: $C_5H_7N_3O_2$
Molecular Weight: 141,13

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.34 (s, 1H), 3.65 (s, 3H), 2.63 (s, 3H).

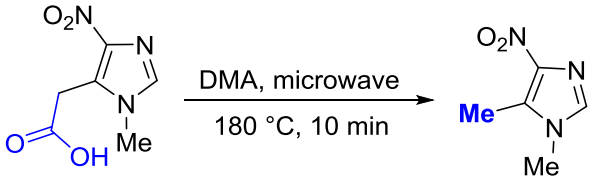
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 145.0, 134.9, 130.8, 32.4, 10.3.

IR (ν, cm^{-1}, $CDCl_3$) 2959, 2928, 1576, 1504, 1379, 1358, 1289, 1235, 1189, 1058.

HRMS (EI+) calculated for $C_5H_7N_3O_2$: 141.0538; Found: 141.0541.

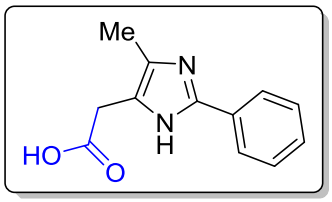
mp: 156-158 ℃ (lit.[3] = 160-161 ℃).

Preparation of imidazole 31 by decarboxylation:



According to the general procedure B, the reaction was carried out with acid **30** (56 mg, 0.30 mmol) in *N*,*N*-dimethylacetamide (3.0 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (gradient of dichloromethane/ethyl acetate = 7:3 to 3:2) afforded product **31** (34 mg, 0.24 mmol, 80% yield) as a white solid.

2-(4-Methyl-2-phenyl-1*H*-imidazol-5-yl)acetic acid (33)



Chemical Formula: $C_{12}H_{12}N_2O_2$
Molecular Weight: 216,24

According to the general procedure A, the reaction was carried out with 4-methyl-2-phenylimidazole **32** (158 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate was added and needed 5 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of dichloromethane/methanol = 4:1 to 2:1, with acetic acid (1%) as additive) afforded product **33** (98 mg, 0.45 mmol, 45% yield) as a light yellow powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.89 – 7.79 (m, 2H), 7.54 (dd, J = 5.2, 2.0 Hz, 3H), 3.58 (s, 2H), 2.29 (s, 3H).

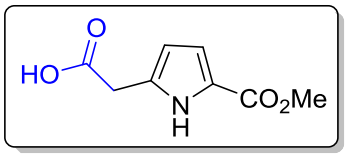
^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 175.4, 144.1, 131.9, 130.5, 128.6, 128.0, 126.9, 126.6, 33.1, 9.4.

IR (ν, cm^{-1}, Nujol) 1748, 1663, 1574, 1455, 1236.

HRMS (EI+) calculated for $C_{12}H_{11}N_2O_2$: 216.0899; Found: not found.

mp: decomposed at 201 ℃.

2-(5-(Methoxycarbonyl)-1*H*-pyrrol-2-yl)acetic acid (35)



Chemical Formula: $C_8H_9NO_4$
Molecular Weight: 183,16

According to the general procedure A, the reaction was carried out with pyrrole **34** (250 mg, 2.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 1.5 equiv) in 1,2-dichloroethane (3.0 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 5:1 to 7:3, then dichloromethane/methanol = 10:1, with acetic acid (1%) as additive) afforded product **35** (139 mg, 0.76 mmol, 38% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 6.79 (d, J = 3.7 Hz, 1H), 6.06 (d, J = 3.8 Hz, 1H), 3.80 (s, 3H), 3.64 (s, 2H).

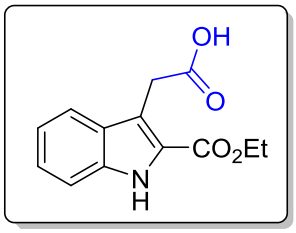
^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 174.0, 163.2, 132.3, 122.8, 117.1, 110.6, 51.6, 34.0.

IR (v, cm^{-1}, $CDCl_3$) 3443, 3275, 2955, 1719, 1602, 1493, 1441, 1337, 1233, 1125, 1042, 1007.

HRMS (EI+) calculated for $C_8H_9NO_4$: 183.0532; Found: 183.0523.

mp: 168-170 ℃.

2-(2-(Ethoxycarbonyl)-1*H*-indol-3-yl)acetic acid (37)



Chemical Formula: $C_{13}H_{13}NO_4$
Molecular Weight: 247,25

According to the general procedure A, the reaction was carried out with indole **36** (1.89 g, 10.0 mmol, 1.0 equiv) and xanthate **13** (2.70 g, 15.0 mmol, 1.5 equiv) in ethyl acetate (30 mL), and needed 5 h for the reaction to go to completion. After removal of the solvent, the residue was triturated with diethyl ether to give a white solid. Subsequent recrystallization from methanol/ethyl acetate gave the desired product **37** as a white powder (1.42 g, 5.7 mmol, 57% yield).

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.63 (dt, J = 8.2, 1.1 Hz, 1H), 7.43 (dt, J = 8.4, 1.0 Hz, 1H), 7.27 (ddd, J = 8.2, 6.9, 1.1 Hz, 1H), 7.09 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 4.14 (s, 2H), 1.41 (t, J = 7.1 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 175.6, 163.6, 137.9, 129.1, 126.2, 125.8, 121.1, 121.0, 116.9, 113.2, 61.7, 31.1, 14.7.

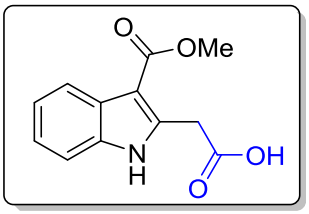
IR (ν, cm^{-1}, neat) 3308, 2986, 2901, 1698, 1678, 1542, 1478, 1465, 1409, 1382, 1332, 1255, 1206, 1193, 1128, 1104, 1025.

HRMS (EI+) calculated for $C_{13}H_{13}NO_4$: 247.0845; Found: 247.0841.

mp: 207-209 ℃ (lit.[4]: 208-210 ℃).

[4] Keller, H.; Langer, E.; Lehner, H. *Monatshefte fuer Chemie*, **1977**, *108*, 123.

2-(3-(Methoxycarbonyl)-1*H*-indol-2-yl)acetic acid (39)



Chemical Formula: $C_{12}H_{11}NO_4$
Molecular Weight: 233,22

A solution of indole **38** (175 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL) was refluxed under nitrogen for 10 min. The solution was then cooled down to 60 ℃ (temperature of oil bath) and DLP (100 mol %) was then added. It took 18 h for the reaction to go to completion. The reaction mixture was then cooled down to room temperature, concentrated under reduced pressure and purified by flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 2:1 to 1:1, with acetic acid (1%) as additive) afforded **39** as a light brown powder (67 mg, 0.29 mmol, 29% yield).

^{1}H NMR (δ, ppm) (400 MHz, CD_3CN) 10.04 (br, 1H), 8.08 – 7.98 (m, 1H), 7.49 – 7.40 (m, 1H), 7.28 – 7.16 (m, 2H), 4.19 (s, 2H), 3.87 (s, 3H).

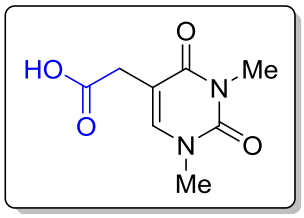
^{13}C NMR (δ, ppm) (101 MHz, CD_3CN) 171.1, 167.0, 141.0, 136.0, 127.4, 123.7, 122.6, 121.9, 112.5, 105.6, 51.4, 33.8.

IR (ν, cm^{-1}, $CDCl_3$) 3286, 2970, 2946, 2880, 2843, 1698, 1658, 1555, 1497, 1456, 1378, 1345, 1270, 1208, 1118, 1094.

HRMS (EI+) calculated for $C_{12}H_{11}NO_4$: 233.0688; Found: 233.0686.

mp: decomposed at 179 ℃.

2-(1,3-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acetic acid (41)



Chemical Formula: $C_8H_{10}N_2O_4$
Molecular Weight: 198,18

According to the general procedure A, the reaction was carried out with 1,3-dimethyluracil **40** (140 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (360 mg, 2.00 mmol, 2.0 equiv) in 1,2-dichloroethane (2.0 mL). After 6 h, another 2.0 equiv of xanthate **13** was added and the reaction needed 5 h to go to completion. Flash chromatography on silica gel (gradient of dichloromethane/methanol = 20:1 to 10:1, with acetic acid (1%) as additive) afforded product **41** (77 mg, 0.39 mmol, 39% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.56 (s, 1H), 3.39 (s, 3H), 3.32 (d, J = 0.8 Hz, 2H), 3.30 (s, 3H).

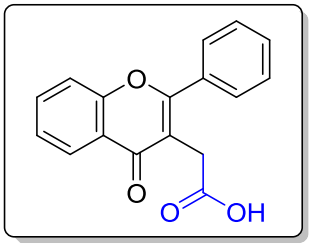
^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 174.7, 165.3, 153.4, 144.3, 108.2, 37.2, 33.1, 28.3.

IR (ν, cm^{-1}, neat) 3096, 1723, 1689, 1660, 1621, 1478, 1434, 1410, 1400, 1375, 1343, 1320, 1211, 1184, 1086, 1050, 932.

HRMS (EI+) calculated for $C_8H_{10}N_2O_4$: 198.0641; Found: 198.0638.

mp: 161-162 ℃.

2-(4-Oxo-2-phenyl-4*H*-chromen-3-yl)acetic acid (43)



Chemical Formula: $C_{17}H_{12}O_4$
Molecular Weight: 280,28

According to the general procedure A, the reaction was carried out with flavone **42** (222 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate was added and the reaction needed 4 h to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:4 to 1:2, with acetic acid (1%) as additive) afforded product **43** (78 mg, 0.28 mmol, 28% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) COO*H* not observed, 8.27 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.77 – 7.70 (m, 3H), 7.60 – 7.55 (m, 3H), 7.55 – 7.51 (m, 1H), 7.46 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 3.62 (s, 2H).

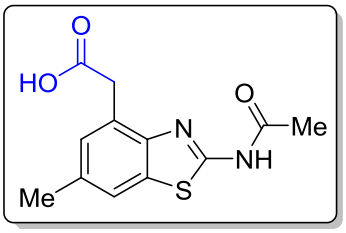
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 179.6, 174.4, 164.5, 156.4, 134.6, 132.1, 131.4, 129.2, 129.0, 126.1, 125.7, 122.3, 118.2, 114.9, 33.5.

IR (ν, cm^{-1}, $CDCl_3$) 3513, 3068, 2929, 2739, 1751, 1714, 1622, 1609, 1587, 1563, 1482, 1469, 1428, 1396, 1306, 1240, 1222, 1161, 1150, 1121.

HRMS (EI+) calculated for $C_{17}H_{12}O_4$: 280.0736, M-CO_2: $C_{16}H_{12}O_2$: 236.0837; Found: 236.0837.

mp: 180-181 ℃.

2-(2-Acetamido-6-methylbenzo[*d*]thiazol-4-yl)acetic acid (45)



Chemical Formula: $C_{12}H_{12}N_2O_3S$
Molecular Weight: 264,30

According to the general procedure A, the reaction was carried out with benzothiazole **44**[5] (206 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in methyl benzoate (3.0 mL) at 80 ℃. After 6 h, another 3.0 equiv of xanthate was added and xanthate was totally consumed in 4 h. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 2:3, with acetic acid (1%) as additive) afforded the desired product **45** as a white powder (70 mg, 0.26 mmol, 26% yield), and 75 mg (0.36 mmol) of **44** was recovered.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.56 (s, 1H), 7.15 (s, 1H), 3.97 (s, 2H), 2.43 (s, 3H), 2.22 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 175.6, 171.3, 158.1, 147.3, 134.9, 133.6, 129.7, 128.1, 120.9, 38.1, 22.8, 21.4.

IR (ν, cm^{-1}, Nujol) 3185, 1694, 1568, 1311, 1269, 1240.

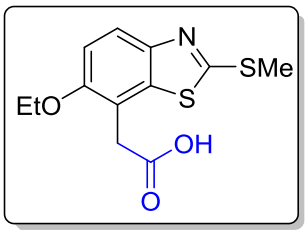
HRMS (EI+) calculated for $C_{12}H_{12}N_2O_3S$: 264.0569; Found: not found.

mp: >250 ℃.

[5] Glennon, R. A.; Gaines, J. J.; Rogers, M. E. *J. Med. Chem.* **1981**, *24*, 766.

2-(6-Ethoxy-2-(methylthio)benzo[*d*]thiazol-7-yl)acetic acid (47)

According to the general procedure A, the reaction was carried out with benzothiazole **46**[6] (225 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in 1,2-dichloroethane (3.0 mL). After 6 h, another 3.0 equiv of xanthate **13** was added and needed 5 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:10 to 3:2, with acetic acid (1%) as additive) afforded product **47** (47 mg, 0.17 mmol, 17% yield) as a white powder, and product **48** (16 mg, 0.05 mmol, 5% yield) as a white powder.



Chemical Formula: $C_{12}H_{13}NO_3S_2$
Molecular Weight: 283,36

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.74 (d, J = 8.8 Hz, 1H), 7.02 (d, J = 8.9 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.83 (s, 2H), 2.76 (s, 3H), 1.41 (t, J = 7.0 Hz, 3H).

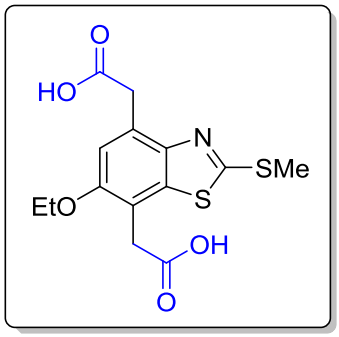
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 176.0, 153.8, 147.8, 138.1, 121.0, 114.9, 111.5, 65.1, 35.8, 16.2, 15.0.

IR (ν, cm^{-1}, $CDCl_3$) 3512, 2984, 2933, 1747, 1714, 1596, 1576, 1470, 1403, 1394, 1315, 1261, 1129, 1112, 1059, 1043, 997, 962.

HRMS (EI+) calculated for $C_{12}H_{13}NO_3S_2$: 283.0337; Found: 283.0332.

mp: 170-172 ℃ (ethyl acetate).

2,2'-(6-Ethoxy-2-(methylthio)benzo[*d*]thiazole-4,7-diyl)diacetic acid (48)



Chemical Formula: $C_{14}H_{15}NO_5S_2$
Molecular Weight: 341,40

[6] Brown, D. J.; Grigg, G. W.; Iwai, Y.; McAndrew, K. N.; Nagamatsu, T. Van Heeswyck, R. *Austral. J. Chem.* **1979**, *32*, 2713.

^{1}H NMR (δ, ppm) (400 MHz, acetone-d_6) 10.84 (s, 2H), 7.17 (s, 1H), 4.15 (q, J = 6.9 Hz, 2H), 4.08 (s, 2H), 3.79 (s, 2H), 2.79 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H).

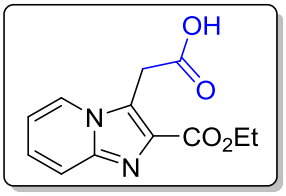
^{13}C NMR (δ, ppm) (101 MHz, acetone-d_6) 172.3, 171.3, 164.9, 154.7, 147.6, 138.4, 128.3, 116.1, 114.2, 65.8, 37.7, 35.6, 15.9, 15.2.

IR (ν, cm^{-1}, Nujol) 1698, 1590, 1494, 1343, 1319, 1245, 1121, 1110, 1048.

HRMS (EI+) calculated for $C_{14}H_{15}NO_5S_2$: 341.0392; Found: 341.0376.

mp: 246-247 ℃.

2-(2-(Ethoxycarbonyl)imidazo[1,2-*a*]pyridin-3-yl)acetic acid (50)



Chemical Formula: $C_{12}H_{12}N_2O_4$
Molecular Weight: 248,24

According to the general procedure A, the reaction was carried out with imidazopyridine **49**[7] (190 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (541 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL), and needed 4 h for the reaction to go to completion. After removal of the solvent, the residue was triturated with diethyl ether to give a brown solid. Subsequent recrystallization from methanol/ethyl acetate gave the desired product **50** as a white powder (224 mg, 0.90 mmol, 90% yield).

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 8.35 (dt, J = 7.0, 1.1 Hz, 1H), 7.61 (dt, J = 9.2, 1.1 Hz, 1H), 7.44 (ddd, J = 9.2, 6.7, 1.2 Hz, 1H), 7.06 (td, J = 6.9, 1.2 Hz, 1H), 4.46 (s, 2H), 4.42 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 172.4, 164.6, 145.7, 133.6, 128.5, 126.3, 125.6, 118.4, 115.1, 62.1, 30.4, 14.6.

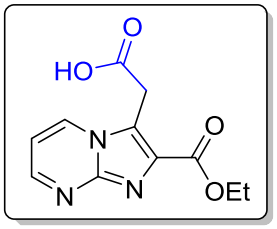
IR (ν, cm^{-1}, Nujol) 3371, 1710, 1694, 1578, 1319, 1297, 1275, 1247, 1223, 1169, 1108, 1028.

HRMS (EI+) calculated for $C_{12}H_{12}N_2O_4$: 248.0797; Found: 248.0799.

mp: decomposed at 164 ℃.

[7] Aginagalde, M.; Vara, Y.; Arrieta, A.; Zangi, R.; Cebolla, V. L.; Delgado-Camon, A.; Coss ́o, F. P. *J. Org. Chem.* **2010**, *75*, 2776.

2-(2-(Ethoxycarbonyl)imidazo[1,2-*a*]pyrimidin-3-yl)acetic acid (52)



Chemical Formula: $C_{11}H_{11}N_3O_4$
Molecular Weight: 249,23

According to the general procedure A, the reaction was carried out with imidazopyrimidine **51**[8] (191 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (270 mg, 1.50 mmol, 1.5 equiv) in 1,2-dichloroethane (1.5 mL), and needed 5 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of dichloromethane/methanol = 10:1 to 5:1, with acetic acid (1%) as additive) afforded product **52** (40 mg, 0.16 mmol, 16% yield) as a pink powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 8.84 (dd, J = 7.0, 1.9 Hz, 1H), 8.70 (dd, J = 4.1, 1.9 Hz, 1H), 7.15 (dd, J = 7.0, 4.1 Hz, 1H), 4.45 (s, 2H), 4.43 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) $\underline{C}$OOH not observed, 164.5, 154.4, 148.5, 135.2, 134.3, 124.7, 111.2, 62.3, 30.3, 14.6.

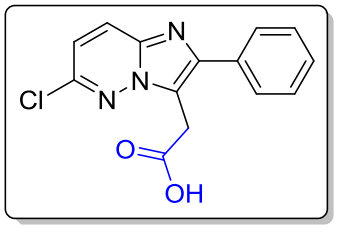
IR (ν, cm^{-1}, Nujol) 1709, 1625, 1574, 1509, 1351, 1311, 1267, 1241, 1206, 1181, 1156, 1099.

HRMS (EI+) calculated for $C_{11}H_{11}N_3O_4$: 249.0750; Found: not found.

mp: decomposed at 162 ℃.

[8] Abignente, E.; Sacchi, A.; Laneri, S.; Rossi, F.; Amico, M D.; Berrinoz, L.; Calderaroz, V.; Parrillo, C. *Eur. J. Med. Chem.* **1994**, *29*, 279.

2-(6-Chloro-2-phenylimidazo[1,2-*b*]pyridazin-3-yl)acetic acid (54)



Chemical Formula: $C_{14}H_{10}ClN_3O_2$
Molecular Weight: 287,70

According to the general procedure A, the reaction was carried out with imidazopyrimidine **53**[9] (230 mg, 1.00 mmol, 1.0 equiv) and xanthate **13** (540 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL), and needed 3 h for the reaction to go to completion. After removal of the solvent, the residue was triturated with diethyl ether to give a white solid. Subsequent recrystallization from methanol/ethyl acetate gave the desired product **54** as a white powder (166 mg, 0.58 mmol, 58% yield).

^{1}H NMR (δ, ppm) (400 MHz, DMSO-d_6) 12.85 (br, 1H), 8.28 (d, J = 9.4 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.52 (dd, J = 8.4, 6.8 Hz, 2H), 7.46 – 7.40 (m, 2H), 4.17 (s, 2H).

^{13}C NMR (δ, ppm) (101 MHz, DMSO-d_6) 170.4, 146.0, 143.6, 136.8, 133.4, 128.9, 128.3, 127.5, 127.3, 119.9, 119.0, 29.7.

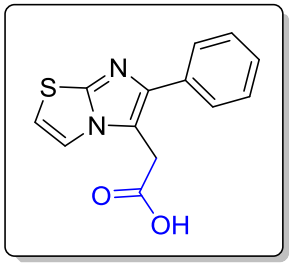
IR (ν, cm^{-1}, Nujol) 1707, 1526, 1355, 1337, 1215, 1201, 1170, 1144, 1109.

HRMS (EI+) calculated for $C_{14}H_{10}ClN_3O_2$: 287.0462; Found: 287.0457.

mp: decomposed at 175 ℃.

[9] El Akkaoui, A.; Koubachi, J.; El Kazzouli, S.; Berteina-Raboin, S.; Mouaddib, A.; Guillaumet, G. *Tetrahedron Lett.* **2008**, *49*, 2472.

2-(6-Phenylimidazo[2,1-*b*]thiazol-5-yl)acetic acid (56)



Chemical Formula: $C_{13}H_{10}N_2O_2S$
Molecular Weight: 258,30

According to the general procedure A, the reaction was carried out with imidazo[2,1-*b*]thiazole **55**[10] (2.00 g, 10.0 mmol, 1.0 equiv) and xanthate **13** (5.41 g, 30.0 mmol, 3.0 equiv) in 1,2-dichloroethane (30 mL), and needed 2.5 h for the reaction to go to completion. After removal of the solvent, the residue was triturated with diethyl ether. The desired product **56** was obtained by recrystallization from acetic acid/ethyl acetate as a white powder (2.06 g, 8.0 mmol, 80% yield). The spectra data are in agreement with the literature report.[10]

^{1}H NMR (δ, ppm) (400 MHz, DMSO-d_6) 12.74 (br, 1H), 7.93 (d, J = 4.5 Hz, 1H), 7.73 – 7.60 (m, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.6 Hz, 1H), 7.28 (d, J = 4.5 Hz, 1H), 4.04 (s, 2H).

^{13}C NMR (δ, ppm) (101 MHz, DMSO-d_6) 171.1, 147.6, 143.3, 134.5, 128.6, 127.0, 126.8, 119.2, 116.2, 112.8, 30.9.

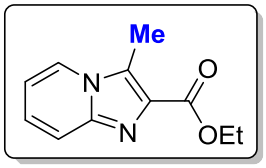
IR (ν, cm^{-1}, neat) 3110, 2988, 2346, 1695, 1542, 1491, 1470, 1441, 1423, 1377, 1340, 1288, 1266, 1137, 1077, 1048.

HRMS (EI+) calculated for $C_{13}H_{10}N_2O_2S$: 258.0463; Found: 258.0454.

mp: decomposed at 180 ℃ (lit.: 238-240 ℃).

[10] Palagiano, F.; Arenare, L.; Luraschil, E. ; de Caprariis, P.; Abignente, E.; D'Amico, M.; Filippelli, W.; Rossi, F. *Eur. J. Med. Chem.* **1995**, *30*, 901.

Ethyl 3-methylimidazo[1,2-*a*]pyridine-2-carboxylate (57)



Chemical Formula: $C_{11}H_{12}N_2O_2$
Molecular Weight: 204,23

According to the general procedure B, the reaction was carried out with acid **50** (124 mg, 0.50 mmol) in *N*,*N*-dimethylacetamide (5 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 1:3 to 1:5) afforded product **57** (90 mg, 0.44 mmol, 88% yield) as a white solid. The spectra data are in agreement with the literature report.[2]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.90 (dt, J = 7.0, 1.2 Hz, 1H), 7.65 (dt, J = 9.1, 1.2 Hz, 1H), 7.22 (ddd, J = 9.2, 6.7, 1.3 Hz, 1H), 6.89 (td, J = 6.8, 1.2 Hz, 1H), 4.46 (q, J = 7.2 Hz, 2H), 2.79 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H).

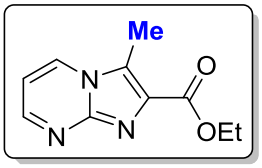
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 164.4, 144.0, 126.4, 125.4, 123.4, 119.2, 113.5, 61.0, 14.6, 9.5.

IR (ν, cm^{-1}, $CDCl_3$) 2983, 2929, 2857, 1709, 1567, 1507, 1445, 1405, 1377, 1362, 1277, 1259, 1227, 1162, 1097, 1058.

HRMS (EI+) calculated for $C_{11}H_{12}N_2O_2$: 204.0899; Found: 204.0905.

mp: 34-36 ℃.

Ethyl 3-methylimidazo[1,2-*a*]pyrimidine-2-carboxylate (58)



Chemical Formula: $C_{10}H_{11}N_3O_2$
Molecular Weight: 205,22

According to the general procedure B, the reaction was carried out with acid **52** (43 mg, 0.17 mmol) in *N*,*N*-dimethylacetamide (1.7 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (gradient of dichloromethane/methanol = 20:1 to 15:1) afforded product **58** (25 mg, 0.12 mmol, 72% yield) as a light green solid.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.64 (dd, J = 4.0, 2.0 Hz, 1H), 8.27 (dd, J = 6.9, 2.0 Hz, 1H), 6.96 (dd, J = 6.9, 4.0 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 2.80 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H).

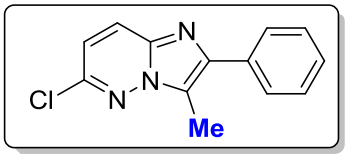
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 164.1, 151.5, 146.8, 133.5, 131.3, 124.9, 109.6, 61.3, 14.5, 9.1.

IR (ν, cm^{-1}, $CDCl_3$) 2984, 2940, 1710, 1623, 1558, 1530, 1503, 1444, 1409, 1386, 1374, 1345, 1299, 1247, 1227, 1153, 1089, 1061, 1020.

HRMS (EI+) calculated for $C_{10}H_{11}N_3O_2$: 205.0851; Found: 205.0837.

mp: 182-184 ℃.

6-Chloro-3-methyl-2-phenylimidazo[1,2-*b*]pyridazine (59)



Chemical Formula: $C_{13}H_{10}ClN_3$
Molecular Weight: 243,69

According to the general procedure B, the reaction was carried out with acid **54** (99 mg, 0.40 mmol) in *N*,*N*-dimethylacetamide (4.0 mL) and heated at 180 ℃ for 20 min and then 200 ℃ for 50 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:3) afforded product **59** (57 mg, 0.23 mmol, 58% yield) as a yellow solid.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.89 (d, J = 9.3 Hz, 1H), 7.87 – 7.83 (m, 2H), 7.52 – 7.46 (m, 2H), 7.42 – 7.36 (m, 1H), 7.02 (d, J = 9.3 Hz, 1H), 2.77 (s, 3H).

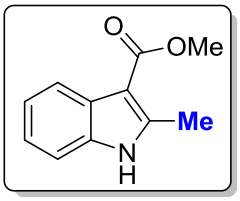
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 146.4, 143.7, 137.0, 134.2, 128.9, 128.2, 128.1, 126.3, 122.6, 117.6, 9.7.

IR (ν, cm^{-1}, $CDCl_3$) 3065, 1713, 1602, 1579, 1548, 1520, 1485, 1443, 1401, 1348, 1313, 1295, 1219, 1171, 1134, 1116, 1082.

HRMS (EI+) calculated for $C_{13}H_{10}ClN_3$: 243.0563; Found: 243.0563.

mp: 131-133 ℃.

Methyl 2-methyl-1*H*-indole-3-carboxylate (60)



Chemical Formula: $C_{11}H_{11}NO_2$
Molecular Weight: 189,21

According to the general procedure B, the reaction was carried out with acid **39** (47 mg, 0.20 mmol) in *N*,*N*-dimethylacetamide (2.0 mL) and heated at 180 ℃ for 10 min and 200 ℃ for 10 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:5 to 1:4) afforded product **60** (30 mg, 0.16 mmol, 79% yield) as a white powder. The spectra data are in agreement with the literature report.[11]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.43 (br, 1H), 8.16 – 8.06 (m, 1H), 7.34 – 7.28 (m, 1H), 7.25 – 7.17 (m, 2H), 3.94 (s, 3H), 2.75 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 166.7, 144.1, 134.6, 127.2, 122.5, 121.9, 121.4, 110.6, 104.6, 50.9, 14.4.

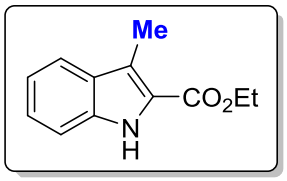
IR (ν, cm^{-1}, $CDCl_3$) 3459, 3061, 2996, 2951, 1691, 1602, 1554, 1460, 1444, 1421, 1271, 1233, 1200, 1118, 1093.

HRMS (EI+) calculated for $C_{11}H_{11}NO_2$: 189.0790; Found: 189.0781.

mp: 163-165 ℃ (lit.[12] = 161-163 ℃).

[11] Tanimori, S. ; Ura, H. ; Kirihata, M. *Eur. J. Org. Chem.* **2007**, *24*, 3977.
[12] Nguyen, H. H.; Kurth, M. J. *Org. Lett.* **2013**, *15*, 362.

Ethyl 3-methyl-1*H*-indole-2-carboxylate (61)



Chemical Formula: $C_{12}H_{13}NO_2$
Molecular Weight: 203,24

Entry 1: According to the general procedure B, the reaction was carried out with acid **37** (99 mg, 0.40 mmol) in *N*,*N*-dimethylacetamide (4.0 mL) and heated at 220 ℃ for 30 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:5 to 2:1) afforded product **61** (32 mg, 0.16 mmol, 39% yield) as a white powder, and side-product **62** (48 mg, 0.17 mmol, 44% yield) as a white powder.

Entry 2: According to the general procedure C, the reaction was carried out with acid **37** (99 mg, 0.40 mmol) in *N*-methyl-2-pyrrolidone (4.0 mL) and was heated at 230 ℃ for 70 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:4) afforded product **61** (54 mg, 0.27 mmol, 66% yield) as a white powder.

The spectra data of **61** are in agreement with the literature report.[13]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.74 (br, 1H), 7.67 (dq, J = 8.1, 1.0 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.15 (ddd, J = 8.0, 6.7, 1.3 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 2.62 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 162.8, 136.0, 128.7, 125.7, 123.6, 120.9, 120.3, 120.0, 111.7, 60.8, 14.6, 10.1.

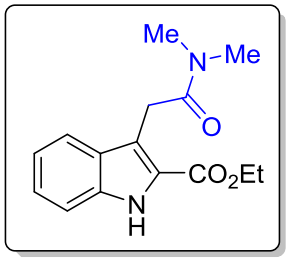
IR (ν, cm^{-1}, $CDCl_3$) 3464, 3064, 2985, 2939, 1693, 1580, 1560, 1450, 1380, 1334, 1322, 1311, 1244, 1188, 1130, 1093, 1057, 1017.

HRMS (EI+) calculated for $C_{12}H_{13}NO_2$: 203.0946; Found: 203.0949.

mp: 134-135 ℃ (lit.: 130-132 ℃).

[13] Yang, Q.-Q.; Marchini, M.; Xiao, W.-J.; Ceroni, P.; Bandini, M. *Chem. - Eur. J.* **2015**, *21*, 18052.

Ethyl 3-(2-(dimethylamino)-2-oxoethyl)-1*H*-indole-2-carboxylate (62)



Chemical Formula: $C_{15}H_{18}N_2O_3$
Molecular Weight: 274,32

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.85 (br, 1H), 7.80 (dd, J = 8.1, 1.0 Hz, 1H), 7.38 – 7.27 (m, 2H), 7.13 (ddd, J = 8.1, 6.7, 1.3 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 4.27 (s, 2H), 3.10 (s, 3H), 2.97 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H).

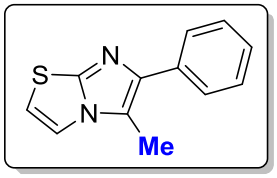
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 170.8, 162.0, 136.0, 128.3, 125.9, 123.6, 121.7, 120.7, 117.8, 111.8, 61.0, 37.6, 35.9, 31.1, 14.5.

IR (ν, cm^{-1}, $CDCl_3$) 3465, 2984, 2938, 1705, 1644, 1602, 1555, 1448, 1399, 1326, 1314, 1238, 1180, 1130, 1093, 1024.

HRMS (EI+) calculated for $C_{15}H_{18}N_2O_3$: 274.1317; Found: 274.1316.

mp: 151-152 ℃.

5-Methyl-6-phenylimidazo[2,1-*b*]thiazole (63)



Chemical Formula: $C_{12}H_{10}N_2S$
Molecular Weight: 214,29

Entry 1: According to the general procedure B, the reaction was carried out with acid **56** (103 mg, 0.40 mmol) in *N*,*N*-dimethylacetamide (4.0 mL) and heated at 200 ℃ for 70 min and 220 ℃ for 10 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 3:7 to 1:0) afforded product **63** (37 mg, 0.17 mmol, 43% yield) as a white powder, and side-product **64** (53 mg, 0.19 mmol, 46% yield) as light yellow oil.

Entry 2: According to the general procedure C, the reaction was carried out with acid **56** (103 mg, 0.40 mmol) in *N*-methyl-2-pyrrolidone (4.0 mL) and was heated at 220 ℃ for 10 min and then at 240 ℃ for 10 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:4) afforded product **64** (81 mg, 0.38 mmol, 94% yield) as a white powder.

The spectra data of **63** are in agreement with the literature report.[14]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.75 – 7.68 (m, 2H), 7.43 (dd, J = 8.4, 7.0 Hz, 2H), 7.32 – 7.27 (m, 2H), 6.82 (d, J = 4.5 Hz, 1H), 2.60 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 147.6, 143.3, 135.2, 128.6, 127.4, 126.9, 117.7, 116.8, 112.3, 10.9.

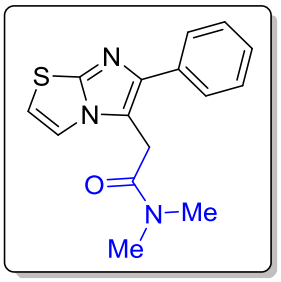
IR (ν, cm^{-1}, $CDCl_3$) 3119, 3064, 2921, 1603, 1542, 1494, 1484, 1471, 1388, 1367, 1320, 1258, 1142, 1073, 1016.

HRMS (EI+) calculated for $C_{12}H_{10}N_2S$: 214.0565; Found: 214.0566.

mp: 125-126 ℃ (lit.: 109-111 ℃).

[14] Wu, F.; Hou, R.; Wang, H.; Kang, I.; Chen, L. *J. Chin. Chem. Soc.* **2011**, *58*, 663.

N,*N*-Dimethyl-2-(6-phenylimidazo[2,1-*b*]thiazol-5-yl)acetamide (64)



Chemical Formula: $C_{15}H_{15}N_3OS$
Molecular Weight: 285,37

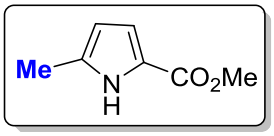
^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.67 (d, J = 4.5 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.46 – 7.40 (m, 2H), 7.36 – 7.30 (m, 1H), 6.78 (d, J = 4.5 Hz, 1H), 4.04 (s, 2H), 2.91 (s, 3H), 2.78 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 168.5, 149.5, 144.8, 134.8, 128.8, 128.1, 127.6, 119.3, 115.6, 111.9, 37.6, 35.9, 31.0.

IR (ν, cm^{-1}, $CDCl_3$) 3120, 3034, 2935, 1643, 1605, 1541, 1492, 1468, 1444, 1401, 1370, 1324, 1261, 1119.

HRMS (EI+) calculated for $C_{15}H_{15}N_3OS$: 285.0936; Found: 285.0934.

Methyl 5-methyl-1*H*-pyrrole-2-carboxylate (65)



Chemical Formula: $C_7H_9NO_2$
Molecular Weight: 139,15

According to the general procedure C, the reaction was carried out with acid **35** (37 mg, 0.20 mmol) in *N*-methyl-2-pyrrolidone (2.0 mL) and was heated at 220 ℃ for 30 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:4 to 1:2) afforded product **65** (26 mg, 0.19 mmol, 93% yield) as white needles. The spectra data are in agreement with the literature report.[15]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 9.04 (br, 1H), 6.88 – 6.77 (m, 1H), 5.95 (ddq, *J* = 3.5, 2.5, 0.8 Hz, 1H), 3.83 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 161.8, 134.0, 121.2, 116.3, 109.1, 51.4, 13.3.

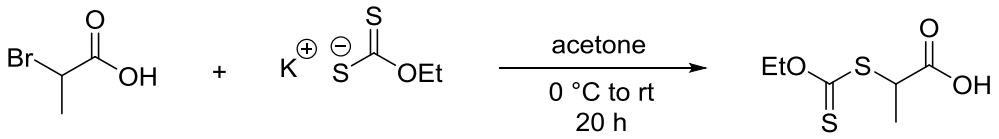
IR (*v*, cm^{-1}, $CDCl_3$) 3292, 2950, 1666, 1488, 1438, 1373, 1326, 1263, 1221, 1194, 1139, 1040, 1006, 992, 927.

HRMS (EI+) calculated for $C_7H_9NO_2$: 139.0633; Found: 139.0634.

mp: 98-99 ℃ (lit. = 93-94 ℃).

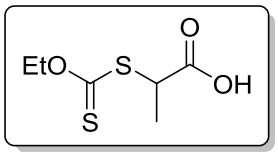
[15] Dong, H.; Shen, M.; Redford, J. E.; Stokes, B. J.; Pomphrey, A. L.; Driver, T. G. *Org. Lett.* **2007**, *9*, 5191.

2-((Ethoxycarbonothioyl)thio)propanoic acid (66)



(44%, 14 g scale)

Potassium *O*-ethylxanthate (28.4 g, 0.177 mol, 1.05 equiv) was added portionwise to a solution of 2-bromopropionic acid (25.7 g, 0.168 mol, 1.00 equiv) in acetone (170 mL) at 0 ℃ and the mixture was allowed to warm up to room temperature and stirred for 20 h. The solid formed was then filtered off and the filtrate was evaporated to driness. The residue was dissolved in 50 mL dichloromethane and washed with water (100 mL). The aqueous phase was extracted with dichloromethane (50 mL × 2). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The desired product **66** precipitated upon addition of pentane at 0 ℃ as a white powder (14.2 g, 0.073 mol, 44% yield). The spectra data are in agreement with the literature report.[16]



Chemical Formula: $C_6H_{10}O_3S_2$
Molecular Weight: 194,26

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 10.42 (br, 1H), 4.63 (qd, J = 7.1, 0.8 Hz, 2H), 4.38 (q, J = 7.4 Hz, 1H), 1.57 (d, J = 7.4 Hz, 3H), 1.41 (t, J = 7.1 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 212.2, 177.6, 70.5, 47.7, 17.0, 13.8.

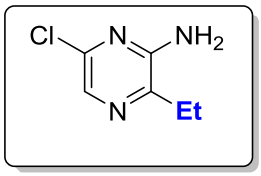
IR (ν, cm^{-1}, $CDCl_3$) 3507, 2987, 2933, 2900, 1752, 1714, 1602, 1453, 1412, 1365, 1292, 1238, 1150, 1113, 1048, 1001.

HRMS (EI+) calculated for $C_6H_{10}O_3S_2$: 194.0071; Found: 194.0062.

mp: 41-42 ℃.

[16] Nguyen, T. H.; Paluck, S. J.; McGahran, A. J.; Maynard, H. D. *Biomacromolecules* **2015**, *16*, 2684.

6-Chloro-3-ethylpyrazin-2-amine (67)



Chemical Formula: $C_6H_8ClN_3$
Molecular Weight: 157,60

According to the general procedure A, the reaction was carried out with 2-amino-6-chloropyrazine **22** (130 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/diethyl ether = 3:2 to 1:1) afforded the desired product **67** as a light yellow solid (116 mg, 0.74 mmol, 74% yield).

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.86 (s, 1H), 4.76 (br, 2H), 2.62 (q, J = 7.5 Hz, 2H), 1.31 (t, J = 7.4 Hz, 3H).

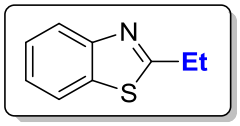
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 151.9, 144.2, 141.6, 131.7, 25.9, 10.6.

IR (ν, cm^{-1}, $CDCl_3$) 3520, 3412, 2978, 2940, 2878, 1608, 1558, 1538, 1464, 1431, 1288, 1212, 1150, 1042, 972.

HRMS (EI+) calculated for $C_6H_8ClN_3$: 157.0407; Found: 157.0411.

mp: 99-100 ℃.

2-Ethylbenzo[*d*]thiazole (69)



Chemical Formula: C_9H_9NS
Molecular Weight: 163,24

According to the general procedure A, the reaction was carried out with benzothiazole **68** (135 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (1.5 mL). After 6 h, another 3.0 equiv of xanthate 66 was added and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of diethyl ether/petroleum ether = 1:10 to 1:8) afforded the desired product **69** as a colorless oil (36 mg, 0.22 mmol, 22% yield) and 76 mg (0.56 mmol) of the starting material was recovered. The spectra data are in agreement with the literature report.[17]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.00 – 7.94 (m, 1H), 7.84 (ddd, J = 8.0, 1.3, 0.7 Hz, 1H), 7.45 (ddd, J = 8.2, 7.2, 1.3 Hz, 1H), 7.34 (ddd, J = 8.3, 7.2, 1.2 Hz, 1H), 3.15 (q, J = 7.6 Hz, 2H), 1.48 (t, J = 7.6 Hz, 3H).

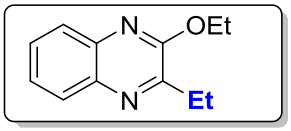
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 173.7, 153.4, 135.2, 126.0, 124.7, 122.6, 121.6, 27.9, 14.0.

IR (ν, cm^{-1}, $CDCl_3$) 3069, 2979, 2938, 1599, 1518, 1457, 1438, 1311, 1279, 1239, 1173, 1157, 1068, 1015.

HRMS (EI+) calculated for C_9H_9NO: 163.0456; Found: 163.0464.

[17] Nguyen, T. B.; Ermolenko, L.; Dean, W. A.; Al-Mourabit, A. *Org. Lett.* **2012**, *14*, 5948.

2-Ethoxy-3-ethylquinoxaline (71)



Chemical Formula: $C_{12}H_{14}N_2O$
Molecular Weight: 202,26

According to the general procedure A, the reaction was carried out with quinoxaline **70** (174 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate **66** was added and it took 4 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/diethyl ether = 20:1 to 10:1) afforded product **71** (107 mg, 0.53 mmol, 53% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.97 – 7.92 (m, 1H), 7.78 (ddd, J = 8.2, 1.5, 0.5 Hz, 1H), 7.58 (ddd, J = 8.3, 7.0, 1.6 Hz, 1H), 7.51 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 2.99 (q, J = 7.5 Hz, 2H), 1.48 (t, J = 7.1 Hz, 3H), 1.36 (t, J = 7.5 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 156.2, 152.6, 140.0, 138.6, 128.8, 128.3, 126.8, 126.2, 62.3, 27.1, 14.6, 11.7.

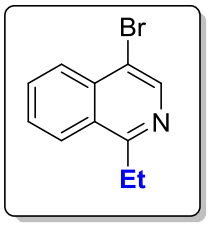
IR (ν, cm^{-1}, $CDCl_3$) 3068, 2982, 2939, 1582, 1461, 1423, 1378, 1327, 1314, 1265, 1225, 1183, 1161, 1139, 1050, 1032.

HRMS (EI+) calculated for $C_{12}H_{14}N_2O$: 202.1106; Found: 202.1104.

mp: 66-67 ℃ (lit.[18] = 66-67 ℃).

[18] Eiden, F.; Bachmann, G. *Arch. Pharmaz.* **1972**, *305*, 580.

4-Bromo-1-ethylisoquinoline (73)



Chemical Formula: $C_{11}H_{10}BrN$
Molecular Weight: 236,11

According to the general procedure A, the reaction was carried out with 4-bromoisoquinoline **72** (208 mg, 1.00 mmol, 1.0 equiv), xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) and TFA (137 mg, 92 μL, 1.2 mmol, 1.2 equiv) in 1,2-dichloroethane (3.0 mL). After 6 h, another 3.0 equiv of xanthate was added and it took 4 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 10:1 to 4:1) afforded product **73** (80 mg, 0.34 mmol, 34% yield) as a colorless oil.

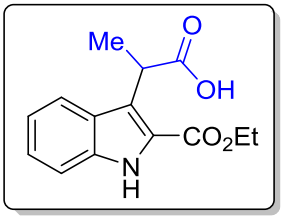
^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.62 (s, 1H), 8.22 – 8.12 (m, 2H), 7.78 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.65 (ddd, J = 8.3, 6.9, 1.3 Hz, 1H), 3.30 (q, J = 7.5 Hz, 2H), 1.43 (t, J = 7.6 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 162.9, 143.7, 134.9, 131.1, 128.1, 128.0, 126.9, 125.7, 117.9, 28.5, 13.6.

IR (ν, cm^{-1}, $CDCl_3$) 3075, 2977, 2937, 2878, 1617, 1568, 1497, 1465, 1386, 1312, 1264, 1242, 1183, 1058, 1015.

HRMS (EI+) calculated for $C_{11}H_{10}BrN$: 234.9997; Found: 234.9980.

2-(2-(Ethoxycarbonyl)-1*H*-indol-3-yl)propanoic acid (74)



Chemical Formula: $C_{14}H_{15}NO_4$
Molecular Weight: 261,28

According to the general procedure A, the reaction was carried out with ethyl indole-2-carboxylate **36** (189 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (233 mg, 1.20 mmol, 1.2 equiv) in 1,2-dichloroethane (1.2 mL). After 6 h, another 1.2 equiv of xanthate was added and it took 3 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 4:1 to 2:1, with acetic acid (1%) as additive) afforded product **74** (210 mg, 0.80 mmol, 80% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.98 (s, 1H), 7.73 (dq, J = 8.2, 0.9 Hz, 1H), 7.39 (dt, J = 8.3, 1.0 Hz, 1H), 7.32 (ddd, J = 8.2, 6.8, 1.1 Hz, 1H), 7.12 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 4.89 (q, J = 7.2 Hz, 1H), 4.45 – 4.36 (m, 2H), 1.63 (d, J = 7.2 Hz, 3H), 1.39 (t, J = 7.2 Hz, 3H).

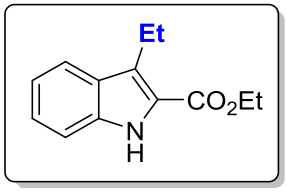
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 179.5, 162.2, 136.0, 126.5, 125.9, 123.3, 122.0, 121.5, 120.7, 112.2, 61.4, 36.4, 17.3, 14.5.

IR (ν, cm^{-1}, $CDCl_3$) 3463, 2987, 1747, 1708, 1602, 1546, 1435, 1380, 1325, 1238, 1153, 1105, 1061.

HRMS (EI+) calculated for $C_{14}H_{15}NO_4$: 261.1001; Found: 261.0999.

mp: 131-133 ℃.

Ethyl 3-ethyl-1*H*-indole-2-carboxylate (75)



Chemical Formula: $C_{13}H_{15}NO_2$
Molecular Weight: 217,27

According to the general procedure C, the reaction was carried out with acid **74** (56 mg, 0.21 mmol) in *N*-methyl-2-pyrrolidone (2.1 mL) and heated at 260 ℃ for 60 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:5) afforded product **75** (28 mg, 0.13 mmol, 61% yield) as colorless needle. The spectra data are in agreement with the literature report.[19]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.72 (br, 1H), 7.70 (dq, J = 8.1, 0.9 Hz, 1H), 7.38 (dt, J = 8.3, 1.0 Hz, 1H), 7.32 (ddd, J = 8.2, 6.8, 1.1 Hz, 1H), 7.14 (ddd, J = 8.0, 6.8, 1.1 Hz, 1H), 4.43 (q, J = 7.2 Hz, 2H), 3.14 (q, J = 7.5 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.5 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 162.6, 136.0, 127.8, 127.0, 125.6, 122.9, 120.9, 120.0, 111.8, 60.8, 18.2, 15.6, 14.6.

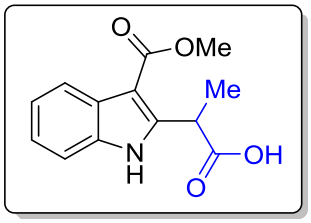
IR (ν, cm^{-1}, $CDCl_3$) 3463, 2975, 2934, 2873, 1711, 1693, 1577, 1555, 1464, 1452, 1380, 1328, 1312, 1266, 1240, 1185, 1132, 1097, 1085, 1019.

HRMS (EI+) calculated for $C_{13}H_{15}NO_2$: 217.1103; Found: 217.1101.

mp: 119-121 ℃ (lit.[20]: 112-114 ℃).

[19] Du, X.; Ghosh, A.; Stanley, L. M. *Org. Lett.* **2014**, *16*, 4036.
[20] Piscitelli, F.; Ligresti, A.; La Regina, G.; Coluccia, A.; Morera, L.; Allara, M.; Novellino, E.; Di Marzo, V.; Silvestri, R. *J. Med. Chem.* **2012**, *55*, 5627.

2-(3-(Methoxycarbonyl)-1*H*-indol-2-yl)propanoic acid (76)



Chemical Formula: $C_{13}H_{13}NO_4$
Molecular Weight: 247,25

According to the general procedure A, the reaction was carried out with indole **38** (175 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (291 mg, 1.50 mmol, 1.5 equiv) in 1,2-dichloroethane (1.5 mL). After 6 h, another 1.5 equiv of xanthate was added and the reaction needed 6 h to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:4 to 1:2, with acetic acid (1%) as additive) afforded product **76** (145 mg, 0.59 mmol, 59% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 9.70 (br, 1H), 8.08 – 7.98 (m, 1H), 7.41 (ddd, J = 7.2, 3.7, 2.2 Hz, 1H), 7.26 (dd, J = 6.1, 3.1 Hz, 2H), 4.91 (q, J = 7.2 Hz, 1H), 4.02 (s, 3H), 1.67 (d, J = 7.2 Hz, 3H).

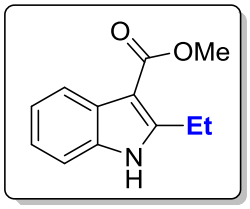
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 175.8, 168.6, 144.0, 135.0, 126.1, 123.6, 122.5, 121.6, 111.7, 104.8, 52.1, 38.2, 16.6.

IR (ν, cm^{-1}, $CDCl_3$) 3454, 3308, 2990, 2953, 1757, 1691, 1636, 1536, 1457, 1389, 1363, 1332, 1285, 1265, 1206, 1137, 1121, 1066.

HRMS (EI+) calculated for $C_{13}H_{13}NO_4$: 247.0845; Found: 247.0852.

mp: 137-138 ℃.

Methyl 2-ethyl-1*H*-indole-3-carboxylate (77)



Chemical Formula: $C_{12}H_{13}NO_2$
Molecular Weight: 203,24

According to the general procedure B, the reaction was carried out with acid **76** (99 mg, 0.40 mmol) in *N*,*N*-dimethylacetamide (4.0 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:4) afforded product **77** (66 mg, 0.32 mmol, 81% yield) as a colorless needle. The spectra data are in agreement with the literature report.[21]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.50 (br, 1H), 8.11 (ddt, J = 6.9, 1.5, 0.7 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.26 – 7.18 (m, 2H), 3.94 (s, 3H), 3.21 (q, J = 7.6 Hz, 2H), 1.35 (t, J = 7.6 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 166.5, 149.8, 134.6, 127.3, 122.5, 121.9, 121.6, 110.8, 103.7, 50.9, 21.5, 13.4.

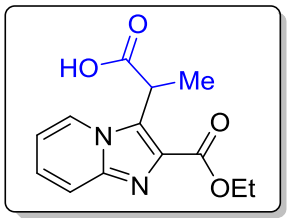
IR (ν, cm^{-1}, $CDCl_3$) 3459, 3061, 2979, 2951, 2876, 1692, 1548, 1490, 1461, 1447, 1363, 1343, 1329, 1270, 1226, 1196, 1118, 1097, 1058.

HRMS (EI+) calculated for $C_{12}H_{13}NO_2$: 203.0946; Found: 203.0938.

mp: 74-55 ℃ (lit. = 72-73 ℃).

[21] Kaneko, C; Fujii, H; Kawai, S.; Yamamoto, A.; Hashiba, K.; Kimata, T.; Hayashi, R.; Somei, M. *Chem. Pharm. Bull.* **1980**, *28*, 1157.

2-(2-(Ethoxycarbonyl)imidazo[1,2-*a*]pyridin-3-yl)propanoic acid (78)



Chemical Formula: $C_{13}H_{14}N_2O_4$
Molecular Weight: 262,26

A solution of imidazopyridine **49** (190 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate was added and it took 4 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:1 to dichloromethane/methanol = 10:1, with acetic acid (1%) as additive) afforded product **78** (118 mg, 0.45 mmol, 45% yield) as a yellow powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.10 (dd, J = 7.1, 1.2 Hz, 1H), 7.79 (d, J = 9.2 Hz, 1H), 7.30 – 7.23 (m, 1H), 6.87 (td, J = 6.9, 1.2 Hz, 1H), 5.37 (q, J = 7.4 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 1.62 (d, J = 7.4 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H).

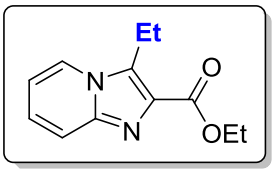
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 175.2, 163.6, 144.2, 131.5, 128.6, 126.7, 125.1, 118.9, 114.1, 61.3, 35.4, 14.3, 14.1.

IR (ν, cm^{-1}, $CDCl_3$) 3508, 2986, 2941, 1749, 1710, 1602, 1557, 1403, 1383, 1280, 1266, 1210, 1173, 1062, 1032.

HRMS (EI+) calculated for $C_{13}H_{14}N_2O_4$: 262.0954; Found: 262.0954.

mp: 90-92 ℃.

Ethyl 3-ethylimidazo[1,2-*a*]pyridine-2-carboxylate (79)



Chemical Formula: $C_{12}H_{14}N_2O_2$
Molecular Weight: 218,26

According to the general procedure B, the reaction was carried out with acid **78** (105 mg, 0.40 mmol) in *N*,*N*-dimethylacetamide (4.0 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 7:3 to 3:1) afforded product **79** (63 mg, 0.29 mmol, 72% yield) as a light brown oil.

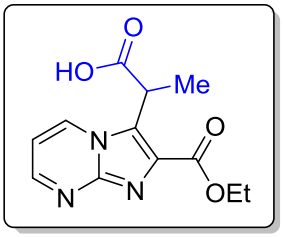
^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.96 (dt, J = 7.0, 1.2 Hz, 1H), 7.66 (dt, J = 9.2, 1.1 Hz, 1H), 7.21 (ddd, J = 9.2, 6.7, 1.2 Hz, 1H), 6.87 (td, J = 6.8, 1.2 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 3.32 (q, J = 7.5 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.5 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 164.2, 144.0, 132.2, 131.8, 125.3, 123.3, 119.4, 113.4, 61.0, 17.1, 14.6, 12.2.

IR (ν, cm^{-1}, $CDCl_3$) 2982, 2937, 2877, 1709, 1602, 1560, 1508, 1462, 1401, 1384, 1364, 1279, 1219, 1163, 1100, 1090, 1058, 1019.

HRMS (EI+) calculated for $C_{12}H_{14}N_2O_2$: 218.1055; Found: 218.1046.

2-(2-(Ethoxycarbonyl)imidazo[1,2-*a*]pyrimidin-3-yl)propanoic acid (80)



Chemical Formula: $C_{12}H_{13}N_3O_4$
Molecular Weight: 263,25

According to the general procedure A, the reaction was carried out with imidazopyrimidine **51** (191 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in 1,2-dichloroethane (3.0 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of dichloromethane/methanol = 50:1 to 20:1, with acetic acid (1%) as additive) afforded product **80** (87 mg, 0.33 mmol, 33% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 8.84 (dd, J = 7.1, 1.9 Hz, 1H), 8.69 (dd, J = 4.0, 1.9 Hz, 1H), 7.15 (dd, J = 7.1, 4.0 Hz, 1H), 5.09 (q, J = 7.4 Hz, 1H), 4.42 (qd, J = 7.1, 1.0 Hz, 2H), 1.63 (d, J = 7.4 Hz, 3H), 1.42 (t, J = 7.1 Hz, 3H).

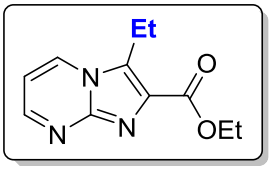
^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 174.7, 164.5, 154.3, 148.3, 135.3, 133.5, 129.4, 111.3, 62.4, 36.3, 15.0, 14.6.

IR (ν, cm^{-1}, Nujol) 3104, 1917, 1710, 1620, 1566, 1505, 1421, 1321, 1256, 1233, 1214, 1159, 1110, 1075, 1064, 1023.

HRMS (EI+) calculated for $C_{12}H_{13}N_3O_4$: 263.0906; Found: not found.

mp: decomposed at 160 ℃.

Ethyl 3-ethylimidazo[1,2-*a*]pyrimidine-2-carboxylate (81)



Chemical Formula: $C_{11}H_{13}N_3O_2$
Molecular Weight: 219,24

According to the general procedure B, the reaction was carried out with acid **80** (79 mg, 0.30 mmol) in *N*,*N*-dimethylacetamide (3.0 mL) and heated at 180 ℃ for 10 min. Flash chromatography on silica gel (dichloromethane/methanol = 20:1) afforded product **81** (47 mg, 0.21 mmol, 71% yield) as a light brown powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.65 (dd, J = 4.0, 2.0 Hz, 1H), 8.30 (dd, J = 7.0, 2.0 Hz, 1H), 6.95 (dd, J = 6.9, 3.9 Hz, 1H), 4.47 (q, J = 7.1 Hz, 2H), 3.32 (q, J = 7.6 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.6 Hz, 3H).

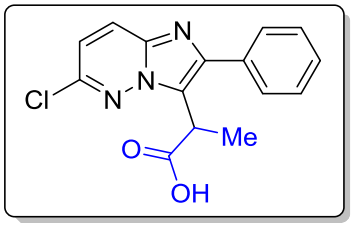
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 163.9, 151.5, 146.8, 132.9, 131.2, 130.7, 109.6, 61.3, 16.8, 14.5, 12.4.

IR (ν, cm^{-1}, $CDCl_3$) 2983, 2938, 2878, 1710, 1623, 1602, 1552, 1504, 1434, 1408, 1351, 1268, 1220, 1152, 1094, 1058, 1019.

HRMS (EI+) calculated for $C_{11}H_{13}N_3O_2$: 219.1008; Found: 219.1007.

mp: 145-147 ℃.

2-(6-Chloro-2-phenylimidazo[1,2-*b*]pyridazin-3-yl)propanoic acid (82)



Chemical Formula: $C_{15}H_{12}ClN_3O_2$
Molecular Weight: 301,73

According to the general procedure A, the reaction was carried out with imidazopyrimidine **53** (230 mg, 1.00 mmol, 1.0 equiv) and xanthate **66** (583 mg, 3.00 mmol, 3.0 equiv) in ethyl acetate (3.0 mL). After 6 h, another 3.0 equiv of xanthate **66** was added and it took 3 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:4 to 1:2, with acetic acid (1%) as additive) afforded product **82** (105 mg, 0.35 mmol, 35% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, DMSO-d_6) 12.66 (br, 1H), 8.26 (d, J = 9.4 Hz, 1H), 7.78 – 7.70 (m, 2H), 7.56 – 7.48 (m, 2H), 7.46 – 7.41 (m, 1H), 7.39 (d, J = 9.4 Hz, 1H), 4.49 (q, J = 7.3 Hz, 1H), 1.54 (d, J = 7.2 Hz, 3H).

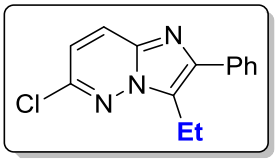
^{13}C NMR (δ, ppm) (101 MHz, DMSO-d_6) 172.5, 145.6, 143.1, 136.6, 133.6, 128.8, 128.3, 128.1, 127.4, 125.0, 118.7, 34.9, 13.8.

IR (ν, cm^{-1}, neat) 3087, 2993, 2981, 2937, 2480, 1699, 1902, 1699, 1547, 1521, 1487, 1448, 1384, 1352, 1318, 1254, 1187, 1109, 1090, 1035, 952.

HRMS (EI+) calculated for $C_{15}H_{12}ClN_3O_2$: 301.0618; Found: 301.0605.

mp: decomposed at 246 ℃.

6-Chloro-3-ethyl-2-phenylimidazo[1,2-*b*]pyridazine (83)



Chemical Formula: $C_{14}H_{12}ClN_3$
Molecular Weight: 257,72

According to the general procedure C, the reaction was carried out with acid **82** (60 mg, 0.20 mmol) in *N*-methyl-2-pyrrolidone (2.0 mL) and heated at 260 ℃ for 10 min. Flash chromatography on silica gel (ethyl acetate/petroleum ether = 1:3) afforded product **83** (40 mg, 0.16 mmol, 78% yield) as a light yellow powder.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.91 (d, J = 9.4 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.55 – 7.48 (m, 2H), 7.45 – 7.38 (m, 1H), 7.04 (d, J = 9.3 Hz, 1H), 3.25 (q, J = 7.5 Hz, 2H), 1.41 (t, J = 7.4 Hz, 3H).

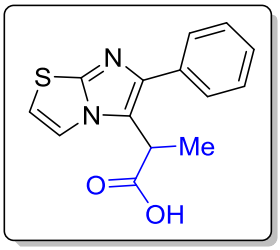
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 146.4, 143.1, 136.8, 134.2, 128.9, 128.2, 128.0 (CH and C), 126.3, 117.8, 17.2, 12.2.

IR (ν, cm^{-1}, neat) 3031, 2975, 2938, 2910, 1605, 1544, 1517, 1487, 1459, 1441, 1422, 1356, 1291, 1279, 1255, 1213, 1168, 1139, 1123, 1091, 1073, 942, 910.

HRMS (EI+) calculated for $C_{14}H_{12}ClN_3$: 257.0720; Found: 257.0722.

mp: 136-138 ℃.

2-(6-Phenylimidazo[2,1-*b*]thiazol-5-yl)propanoic acid (84)



Chemical Formula: $C_{14}H_{12}N_2O_2S$
Molecular Weight: 272,32

According to the general procedure A, the reaction was carried out with imidazo[2,1-*b*]thiazole **59** (200 mg, 1.00 mmol, 1.0 equiv) and xanthate 66 (583 mg, 3.00 mmol, 3.0 equiv) in 1,2-dichloroethane (3.0 mL), and needed 4 h to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 3:2 to dichloromethane/methanol = 20:1, with acetic acid (1%) as additive) afforded product **84** (176 mg, 0.65 mmol, 65% yield) as a white powder.

^{1}H NMR (δ, ppm) (400 MHz, CD_3OD) 7.82 (d, J = 4.5 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.49 – 7.43 (m, 2H), 7.41 – 7.35 (m, 1H), 7.18 (d, J = 4.5 Hz, 1H), 4.29 (q, J = 7.4 Hz, 1H), 1.55 (d, J = 7.4 Hz, 3H).

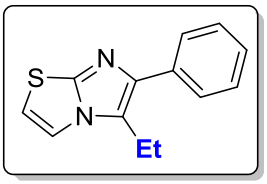
^{13}C NMR (δ, ppm) (101 MHz, CD_3OD) 175.7, 150.9, 145.2, 135.2, 129.63, 129.60, 128.9, 122.9, 120.9, 114.0, 37.6, 16.1.

IR (ν, cm^{-1}, Nujol) 3107, 1704, 1338, 1308, 1247, 1222, 1137, 1098, 1078, 1068.

HRMS (EI+) calculated for $C_{14}H_{12}N_2O_2S$: 272.0619; Found: 272.0622.

mp: decomposed at 180 ℃.

5-Ethyl-6-phenylimidazo[2,1-*b*]thiazole (85)



Chemical Formula: $C_{13}H_{12}N_2S$
Molecular Weight: 228,31

According to the general procedure C, the reaction was carried out with acid **84** (55 mg, 0.20 mmol) in *N*-methyl-2-pyrrolidone (2.0 mL) and heated at 250 ℃ for 60 min. Flash chromatography on silica gel (gradient of ethyl acetate/petroleum ether = 1:2 to 1:1) afforded product **85** (34 mg, 0.15 mmol, 74% yield) as a light brown oil.

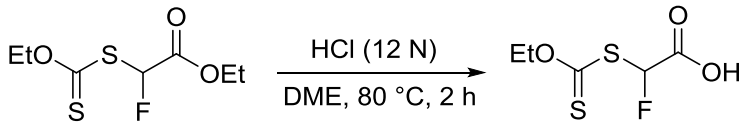
^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 7.73 – 7.66 (m, 2H), 7.45 – 7.40 (m, 2H), 7.33 (d, J = 4.5 Hz, 1H), 7.30 (ddt, J = 8.0, 6.8, 1.3 Hz, 1H), 6.81 (d, J = 4.5 Hz, 1H), 3.01 (q, J = 7.6 Hz, 2H), 1.33 (t, J = 7.6 Hz, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 147.8, 142.8, 135.2, 128.6, 127.4, 127.0, 123.9, 116.9, 112.4, 18.4, 13.6.

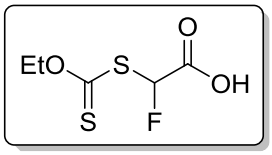
IR (ν, cm^{-1}, neat) 2970, 2901, 1538, 1467, 1441, 1394, 1369, 1066, 1057.

HRMS (EI+) calculated for $C_{13}H_{12}N_2S$: 228.0721; Found: 228.0722.

2-((Ethoxycarbonothioyl)thio)-2-fluoroacetic acid (89)



Into a solution of ethyl ethoxythiocarbonylsulfanylfluoroacetate **88**[22] (3.93 g, 17.4 mmol) in dimethoxyethane (17 mL) was added slowly 12 N HCl (17 mL). The mixture was heated in an open flask at 80 ℃ for 2 h (88% of conversion of starting material by ^{1}H NMR of the crude product). The solution was then cooled down to room temperature and concentrated to half volume and was then extracted twice with dichloromethane. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 6:1 to 2:3, with acetic acid (1%) as additive) afforded **89** as a yellow oil (2.28 g, 11.5 mmol, 66% yield).



Chemical Formula: $C_5H_7FO_3S_2$
Molecular Weight: 198,23

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 10.56 (s, 1H), 6.79 (d, J = 49.6 Hz, 1H), 4.73 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H).

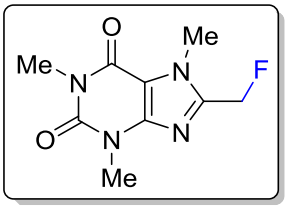
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 206.4 (d, J = 1.7 Hz), 171.0 (d, J = 27.8 Hz), 93.0 (d, J = 233.4 Hz), 72.0, 13.7.

IR (ν, cm^{-1}, $CDCl_3$) 3504, 2989, 1760, 1735, 1369, 1254, 1112, 1042.

HRMS (EI+) calculated for $C_5H_7FO_3S_2$: 197.9821; Found: 197.9809.

[22] Jean-Baptiste, L.; Yemets, S.; Legay, R.; Lequeux, T. *J. Org. Chem.* **2006**, *71*, 2352.

8-(Fluoromethyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (90)



Chemical Formula: $C_9H_{11}FN_4O_2$
Molecular Weight: 226,21

According to the general procedure A, the reaction was carried out with caffeine **3** (69 mg, 0.35 mmol, 1.0 equiv) and xanthate **89** (210 mg, 1.06 mmol, 3.0 equiv) in ethyl acetate (1.1 mL). After 6 h, another 3.0 equiv of xanthate **89** was added and after 3 h, the reaction didn't evolve. Flash chromatography on silica gel (gradient of ethyl acetate/diethyl ether = 1:1 to 3:2) afforded product **90** (23 mg, 0.10 mmol, 29% yield) as a white powder, and 20 mg (0.10 mmol) of caffeine **3** was recovered. The spectra data are in agreement with the literature report.[23]

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 5.49 (d, J = 47.9 Hz, 2H), 4.07 (d, J = 1.6 Hz, 3H), 3.57 (s, 3H), 3.41 (s, 3H).

^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 155.6, 151.6, 147.4, 146.5 (d, J = 18.9 Hz), 109.1, 75.5 (d, J = 168.7 Hz), 32.5 (d, J = 1.8 Hz), 29.9, 28.1.

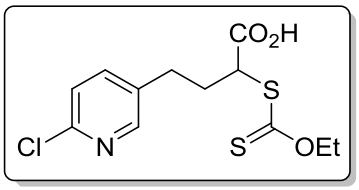
IR (ν, cm^{-1}, $CDCl_3$) 2955, 1706, 1660, 1607, 1550, 1467, 1451, 1428, 1407, 1357, 1346, 1294, 1221, 1044, 1013, 991, 980.

HRMS (EI+) calculated for $C_9H_{11}FN_4O_2$: 226.0866; Found: 226.0862.

mp: 165-167 ℃ (lit.: 155-157 ℃).

[23] Fujiwara, Y.; Dixon, J. A.; Fionn O'Hara, Daa Funder, E.; Dixon, D. D.; Rodriguez, R. A.; Baxter, R. D.; Herlé, B.; Sach, N.; Collins, M. R.; Ishihara, Y.; Baran, P. S. *Nature*, **2012**, *492*, 95.

4-(6-Chloropyridin-3-yl)-2-((ethoxycarbonothioyl)thio)butanoic acid (92)



Chemical Formula: $C_{12}H_{14}ClNO_3S_2$
Molecular Weight: 319,82

A solution of xanthate **91**[24] (2.22 g, 9.00 mmol, 3.0 equiv) and acrylic acid (216 mg, 3.00 mmol, 1.0 equiv) in ethyl acetate (9.0 mL) was refluxed under nitrogen for 10 min. DLP was added portionwise (2.5 mol % per hour) and it took 5 h for the total consumption of the olefin. The reaction mixture was then cooled down to room temperature, concentrated under reduced pressure and purified by flash chromatography on silica gel (gradient of petroleum ether/ethyl acetate = 4:1 to 5:2, with acetic acid (1%) as additive) afforded xanthate **92** as a light yellow oil (311 mg, 0.97 mmol, 32% yield).

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 9.22 (br, 1H), 8.33 – 8.25 (m, 1H), 7.55 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.29 (dd, *J* = 8.2, 0.7 Hz, 1H), 4.64 (qd, *J* = 7.1, 1.1 Hz, 2H), 4.43 (t, *J* = 7.1 Hz, 1H), 2.82 (ddd, *J* = 8.9, 6.7, 2.2 Hz, 2H), 2.34 (ddt, *J* = 14.1, 8.7, 7.0 Hz, 1H), 2.19 (ddt, *J* = 14.0, 8.9, 7.1 Hz, 1H), 1.41 (t, *J* = 7.1 Hz, 3H).

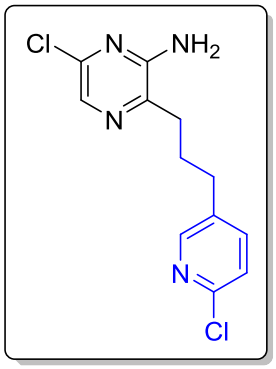
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 211.4, 174.8, 149.4, 149.3, 139.6, 135.0, 124.5, 71.0, 51.6, 32.4, 29.7, 13.8.

IR (ν, cm^{-1}, neat) 2927, 2524, 1713, 1588, 1566, 1458, 1385, 1214, 1144, 1106, 1040.

HRMS (EI+) calculated for $C_{12}H_{14}ClNO_3S_2$: 319.0104; Found: 319.0101.

[24] Ferjancic, Z.; Quiclet-Sire, B.; Zard, S. Z. *Synthesis* **2008**, 2996.

6-Chloro-3-(3-(6-chloropyridin-3-yl)propyl)pyrazin-2-amine (93)



Chemical Formula: $C_{12}H_{12}Cl_2N_4$
Molecular Weight: 283,16

According to the general procedure A, the reaction was carried out with 2-amino-6-chloropyrazine 22 (40 mg, 0.31 mmol, 1.0 equiv) and xanthate 92 (295 mg, 0.92 mmol, 3.0 equiv) in ethyl acetate (0.9 mL), and needed 6 h for the reaction to go to completion. Flash chromatography on silica gel (gradient of petroleum ether/diethyl ether = 1:1 to 3:7) afforded the desired product 93 as a white powder (46 mg, 0.16 mmol, 52% yield) and 7 mg (0.05 mmol) of starting material 22 was recovered.

^{1}H NMR (δ, ppm) (400 MHz, $CDCl_3$) 8.24 (d, J = 2.4 Hz, 1H), 7.87 (s, 1H), 7.51 (dd, J = 8.1, 2.5 Hz, 1H), 7.26 (d, J = 8.1 Hz, 1H), 4.68 (br, 2H), 2.76 – 2.68 (m, 2H), 2.60 (m, 2H), 2.11 (m, 2H).

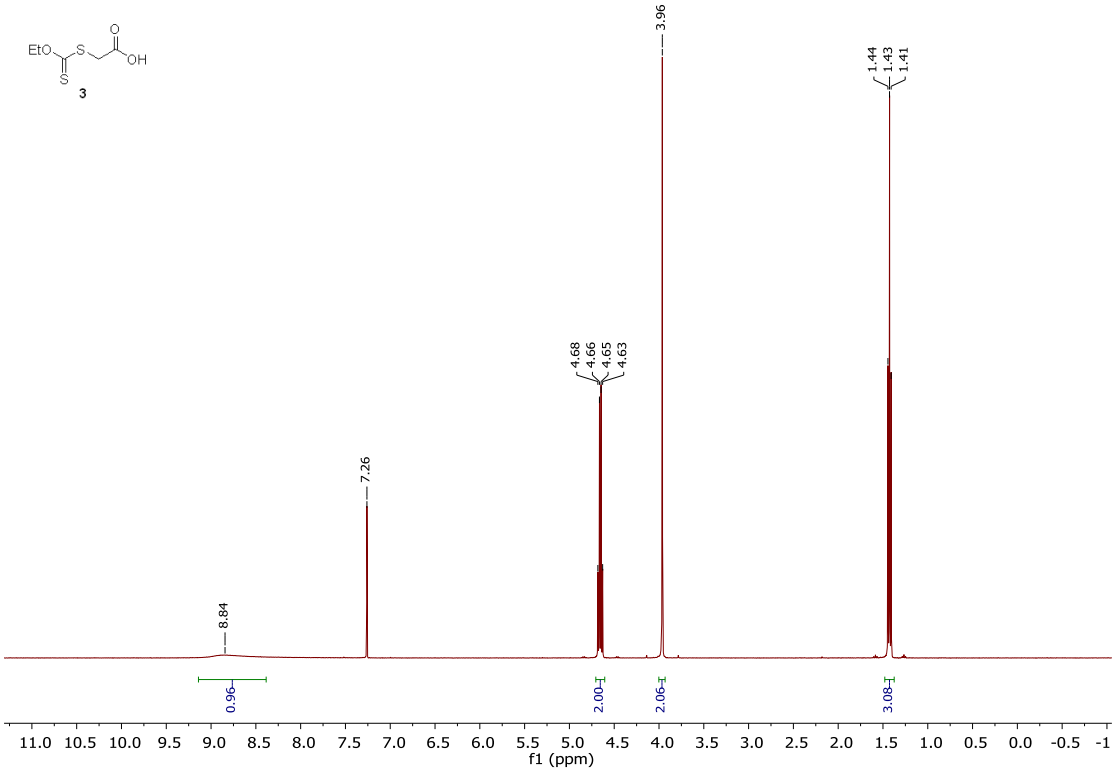
^{13}C NMR (δ, ppm) (101 MHz, $CDCl_3$) 152.0, 149.7, 149.4, 144.5, 139.3, 139.0, 135.9, 131.9, 124.2, 31.7, 31.4, 27.2.

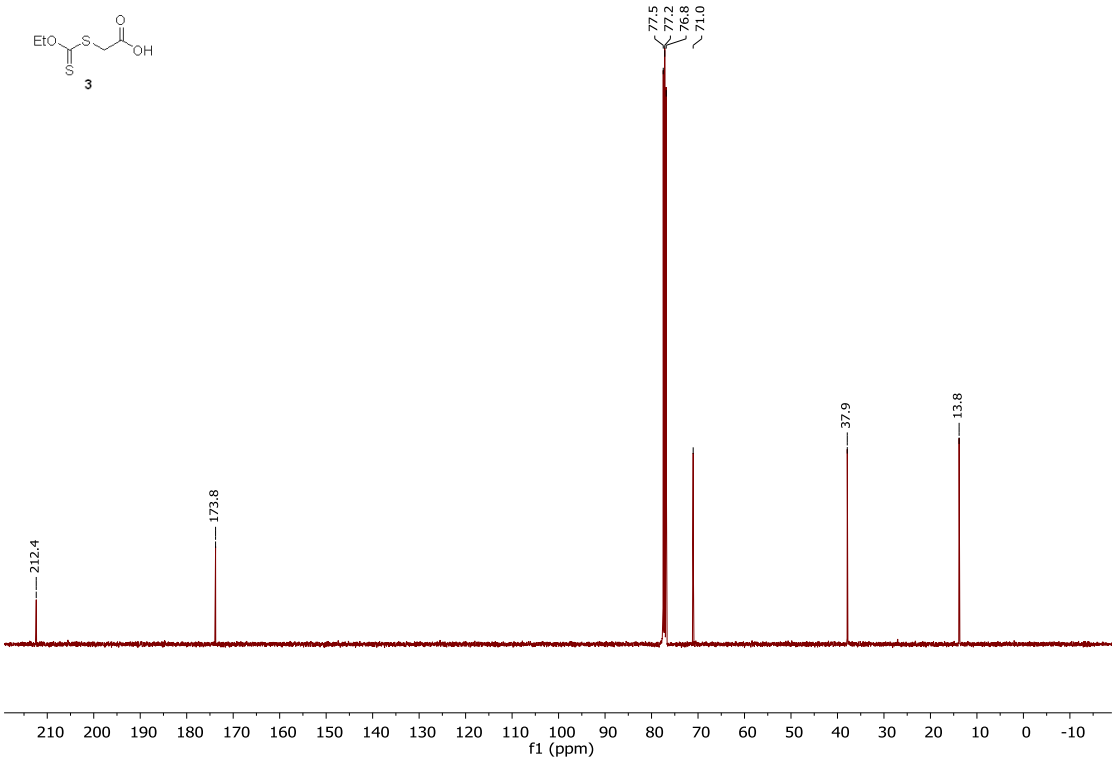
IR (ν, cm^{-1}, neat) 3325, 3182, 1650, 1589, 1560, 1462, 1434, 1388, 1284, 1198, 1175, 1126, 1106, 1030, 970.

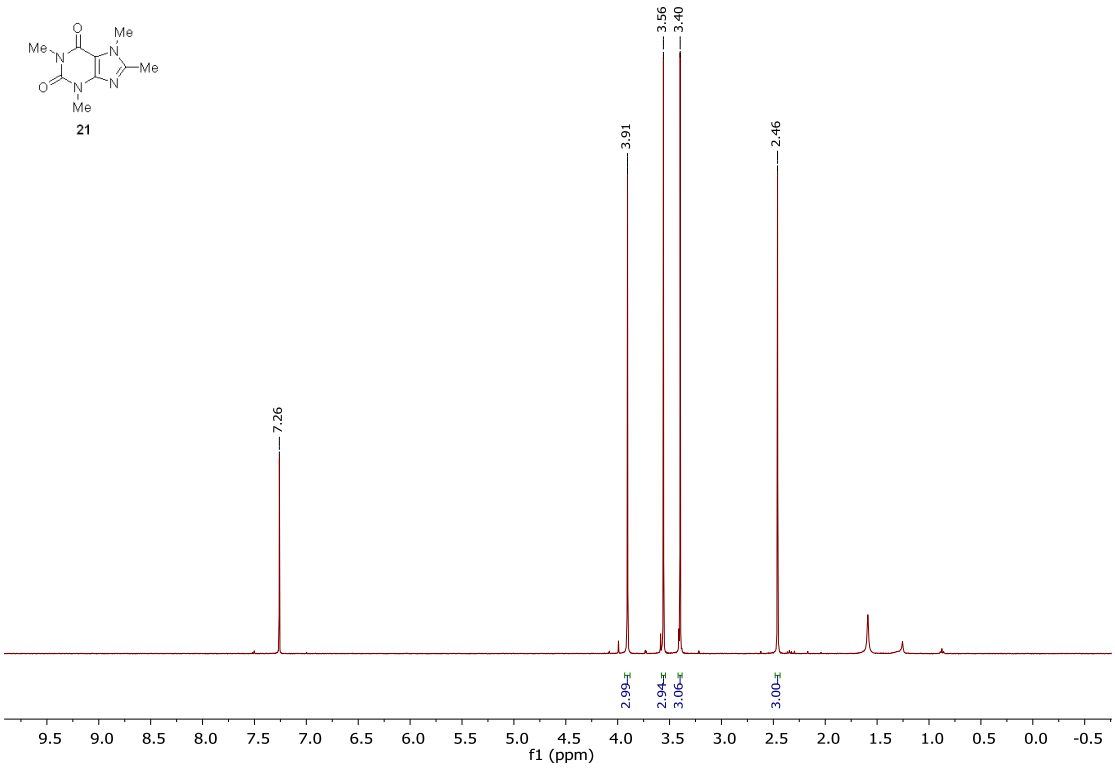
HRMS (EI+) calculated for $C_{12}H_{12}Cl_2N_4$: 282.0439; Found: 282.0436.

mp: 144-146 ℃.

Copies of NMR spectra



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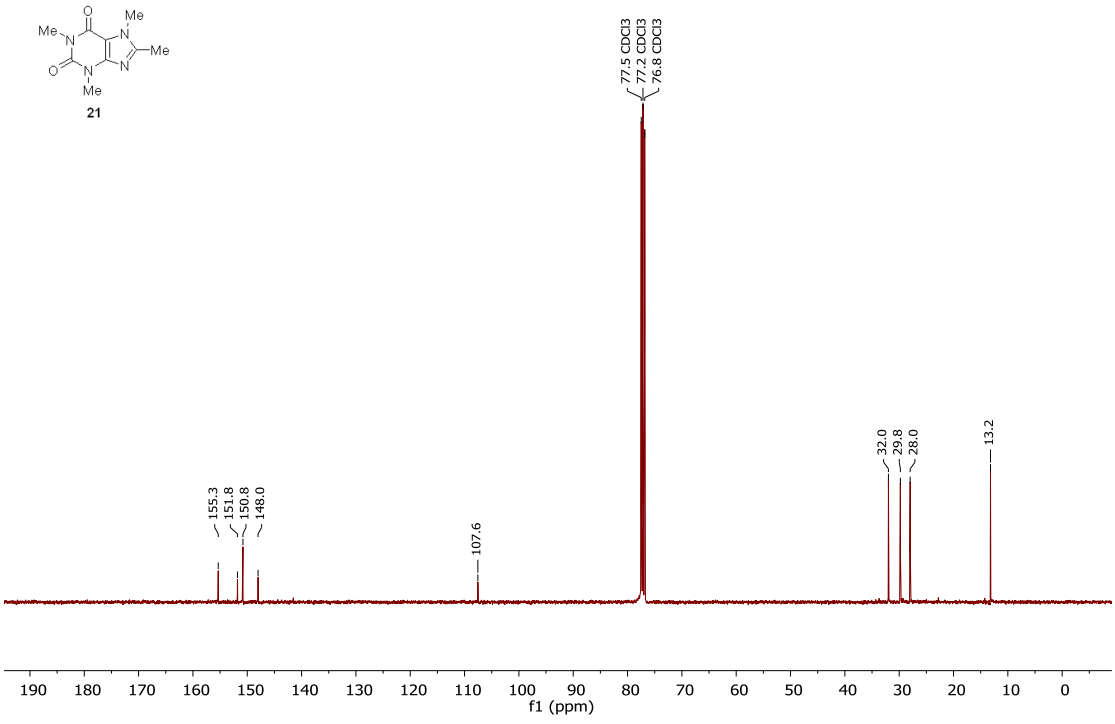
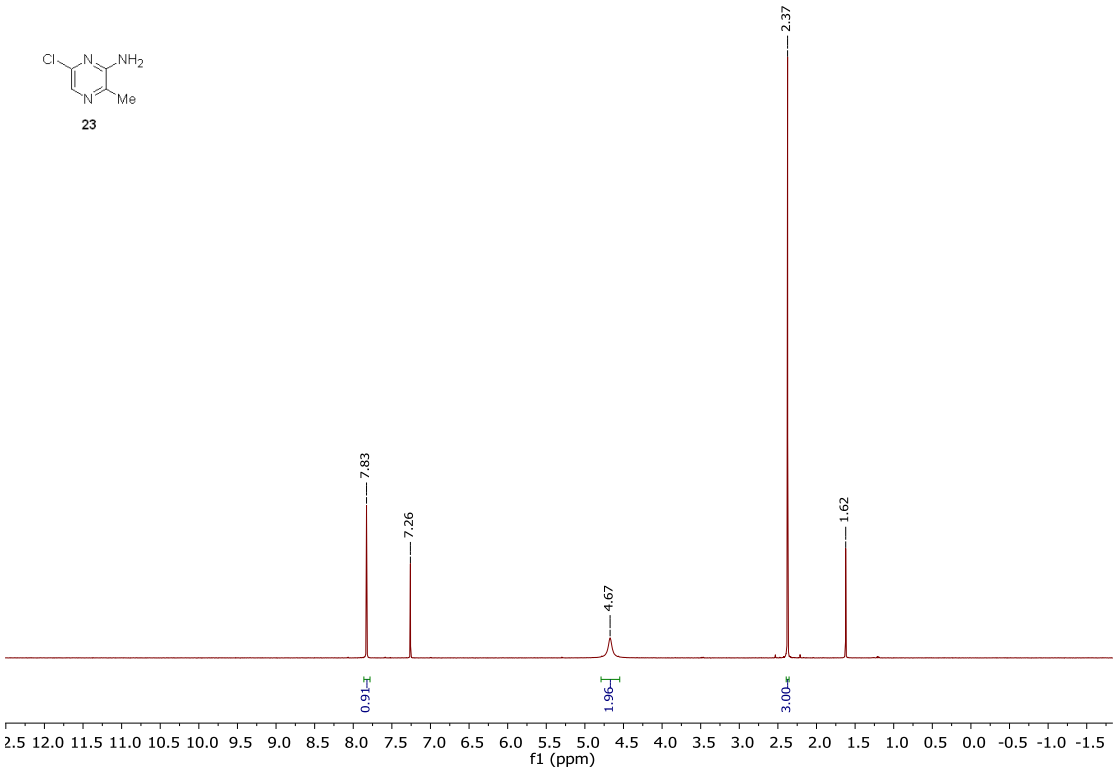
3.56
3.40
2.46
2.99
2.94
3.06
3.00
f1 (ppm)


21
77.5 CDCl3
77.2 CDCl3
76.8 CDCl3
155.3
151.8
150.8
148.0
107.6
32.0
29.8
28.0
13.2
f1 (ppm)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N
Me
23
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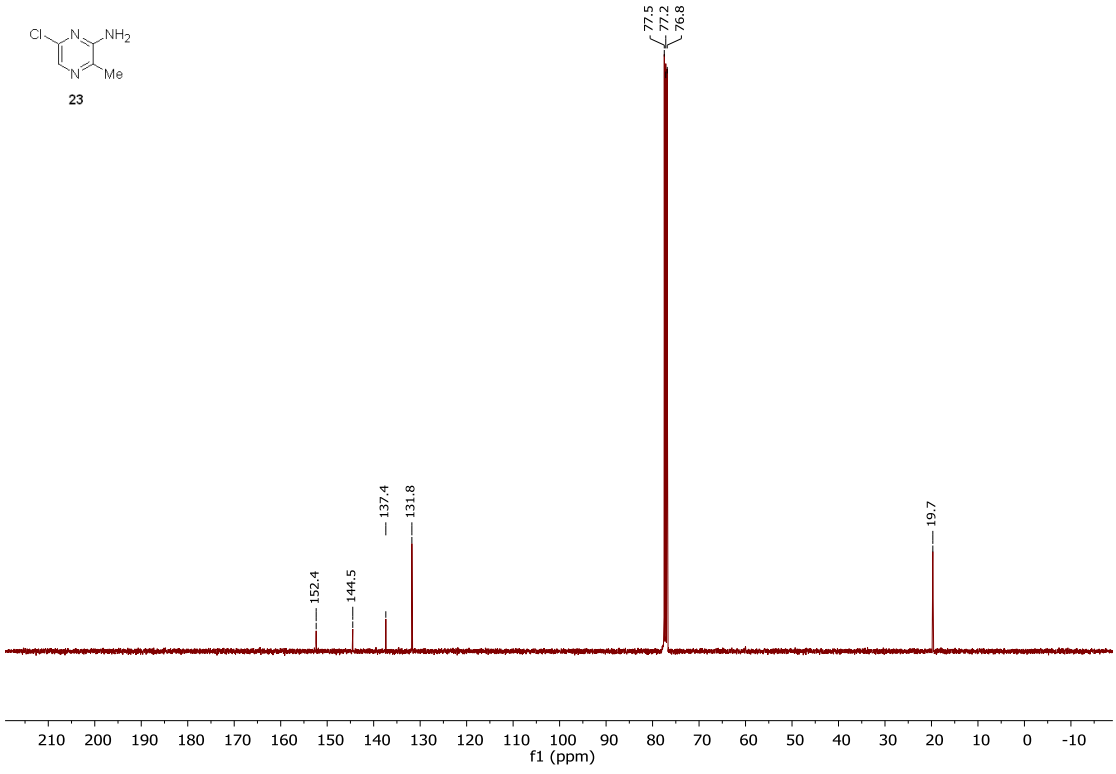
7.26
4.67
1.62
0.91
1.96
3.00
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)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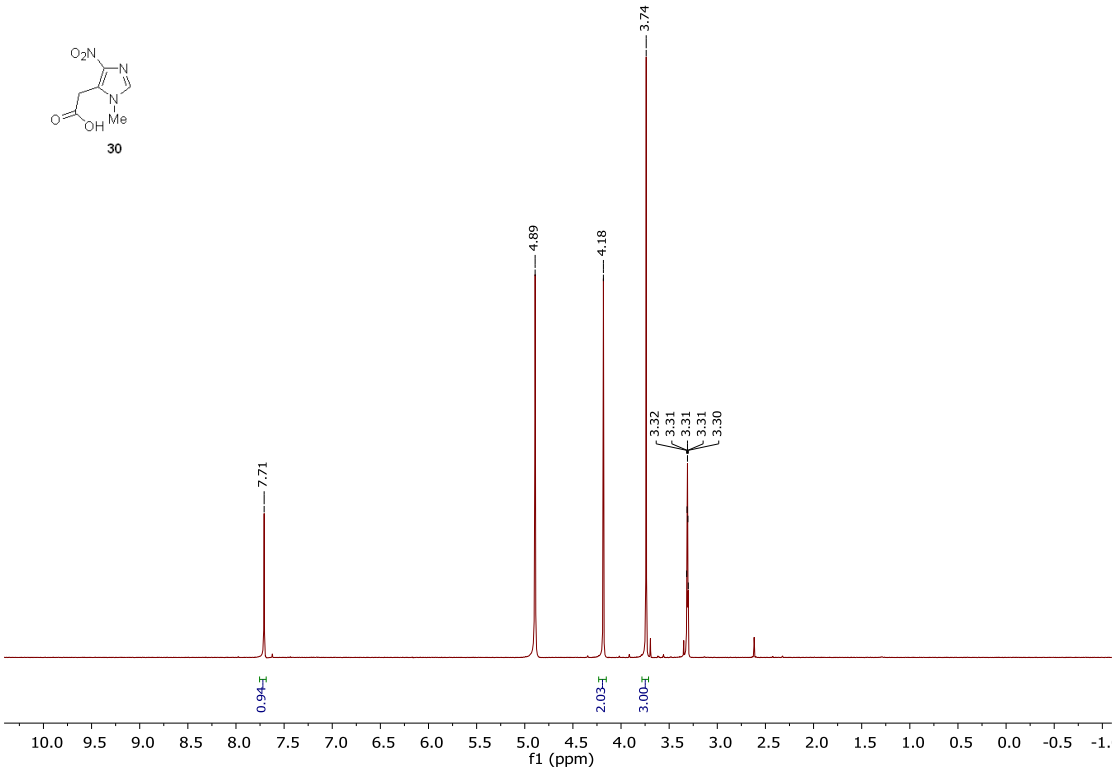
N
NH2
N
Me
23
77.5
77.2
76.8
137.4
131.8
152.4
144.5
19.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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3.74
3.32
3.31
3.31
3.31
3.30
0.94
2.03
3.00
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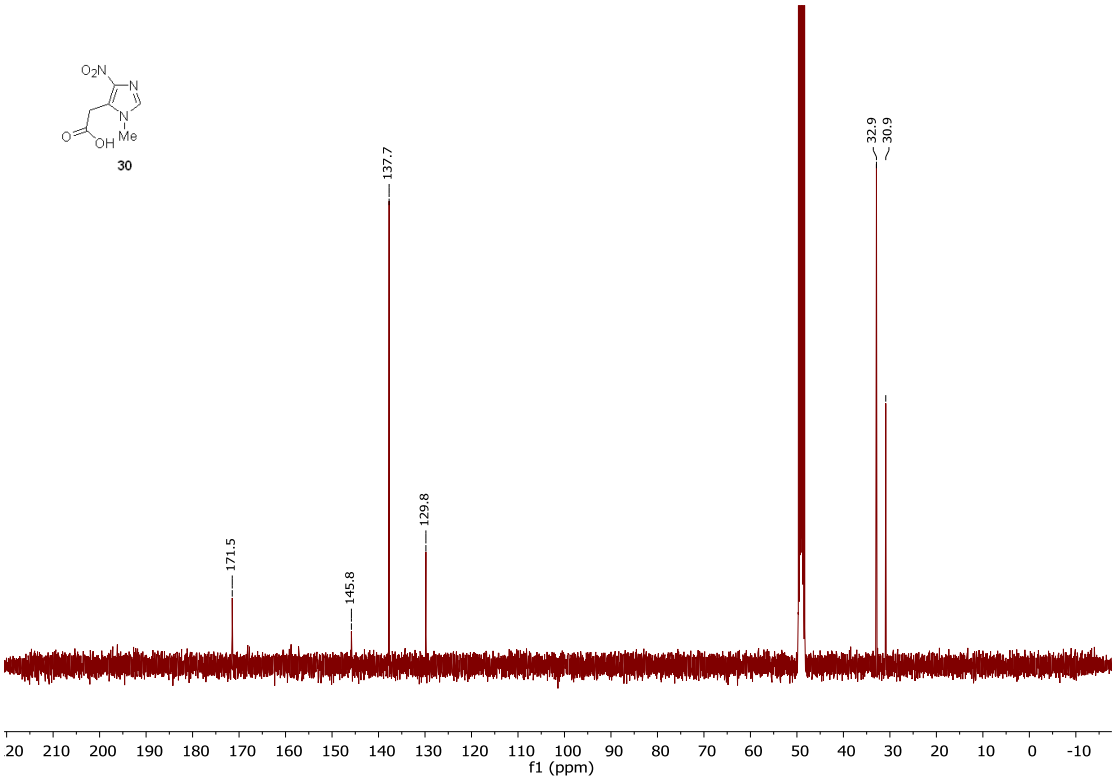
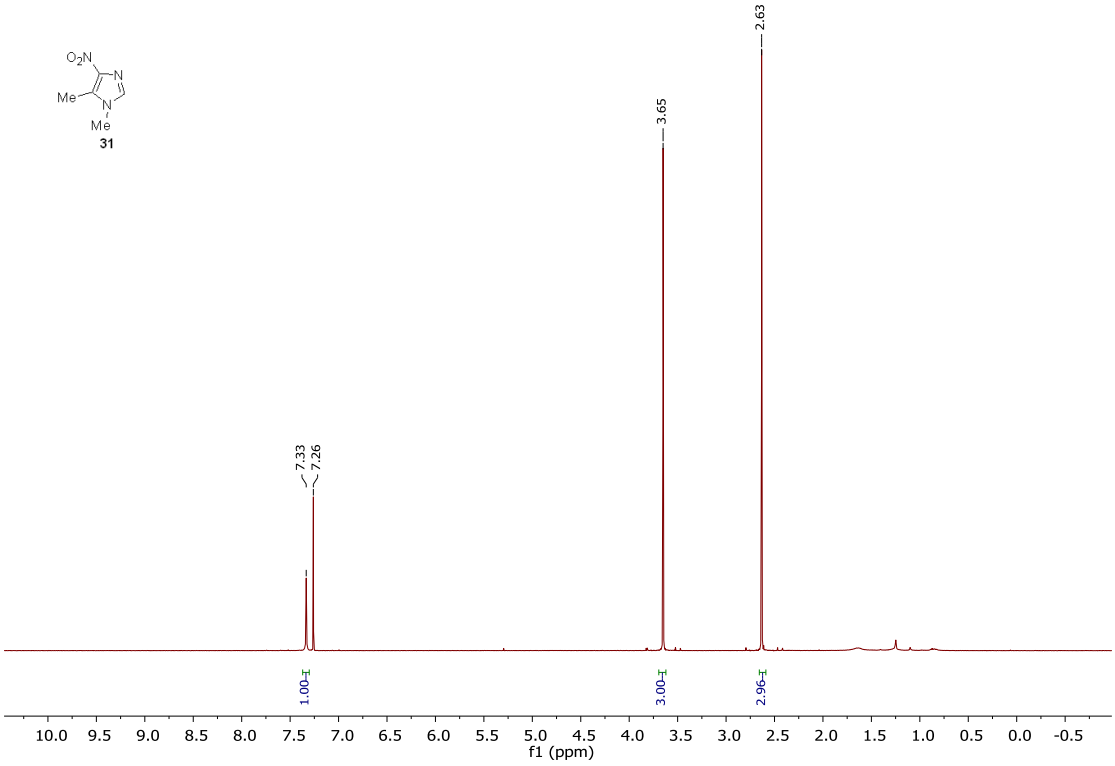
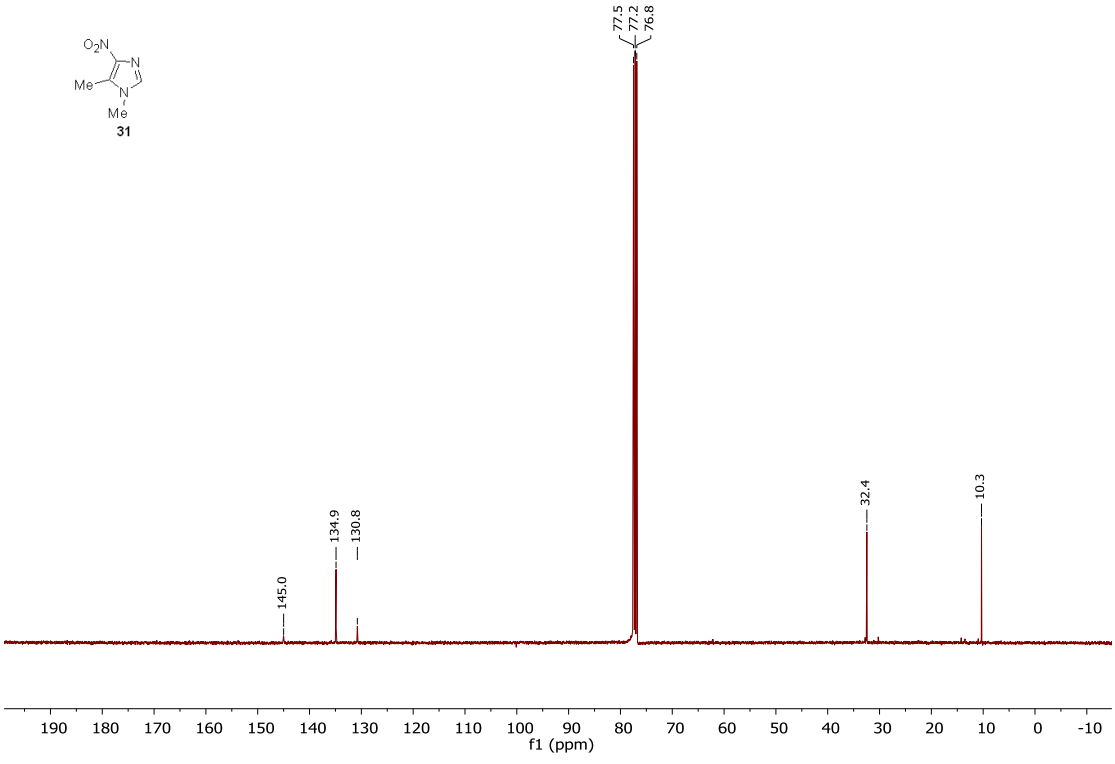

30
171.5
145.8
137.7
129.8
32.9
30.9
f1 (ppm)


O2N
Me
N
N
Me
31
2.63
3.65
7.33
7.26
1.00
3.00
2.96
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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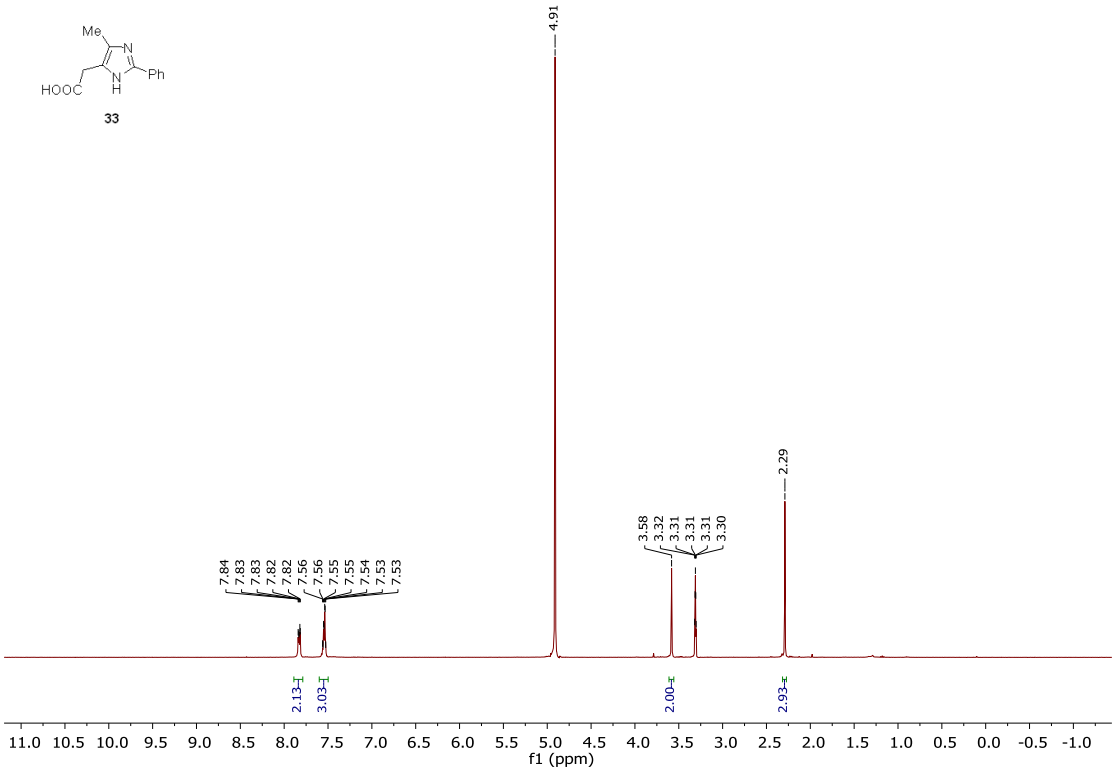
Me
N
N
Me
31
77.5
77.2
76.8
145.0
134.9
130.8
32.4
10.3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Me
N
Ph
HOOC
N
H
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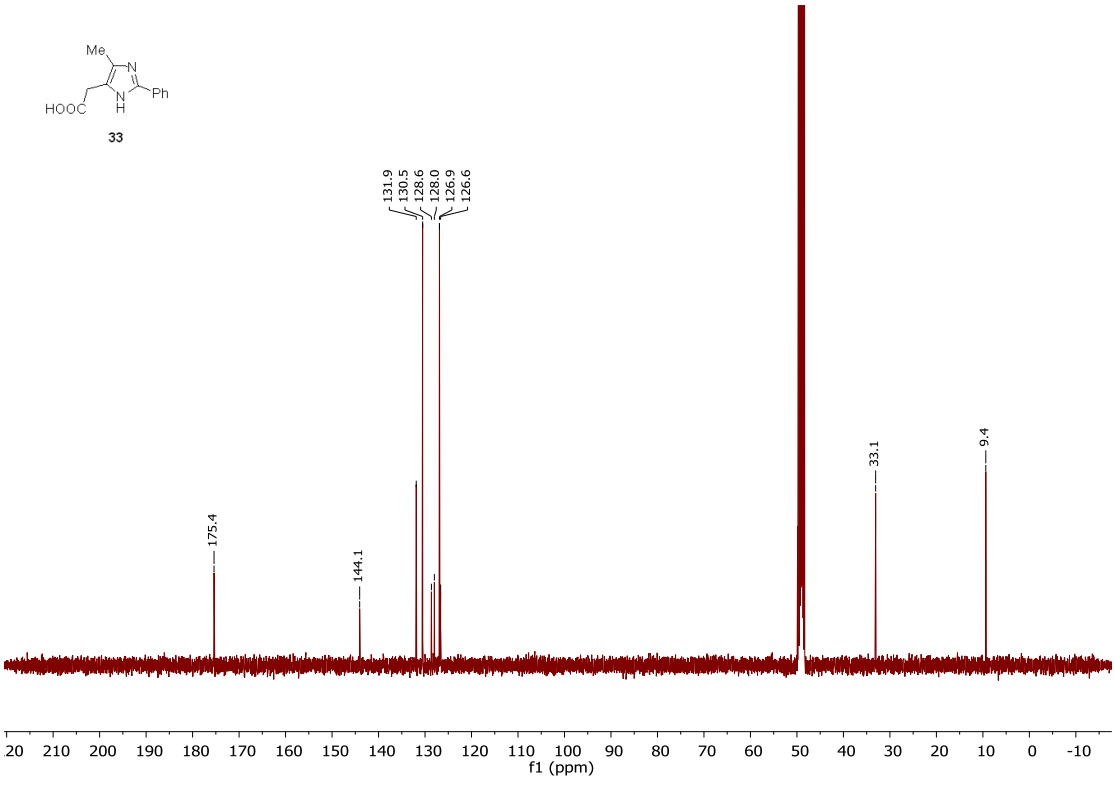
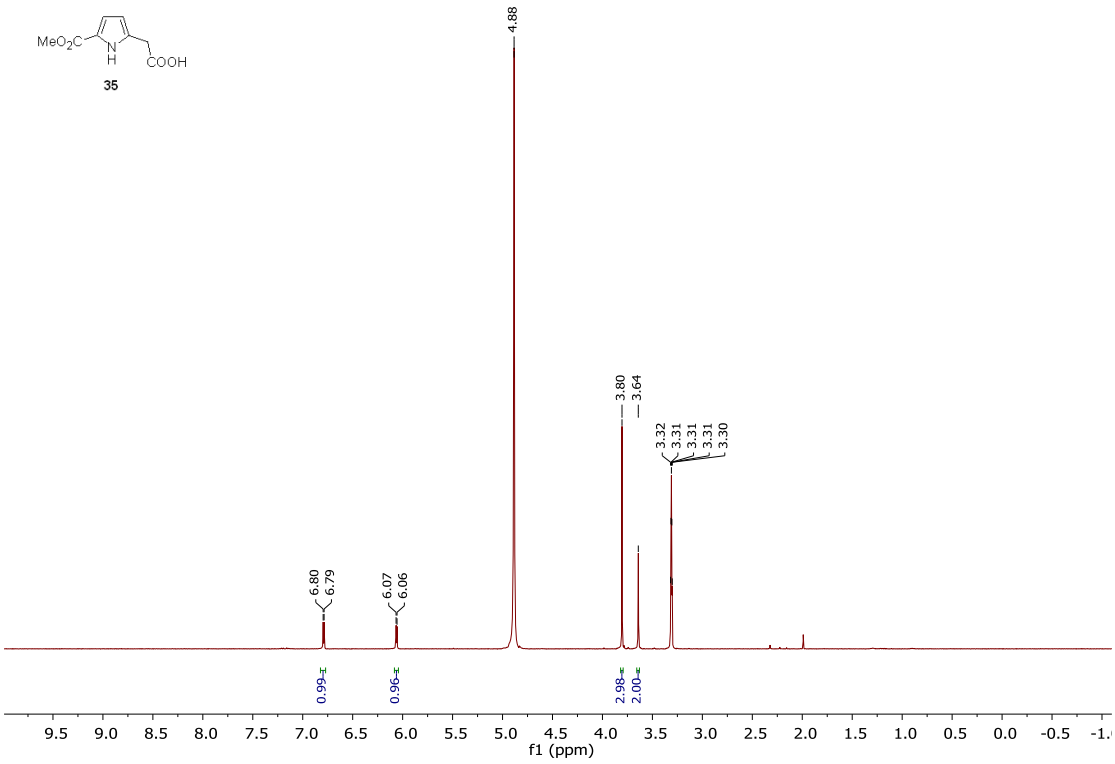
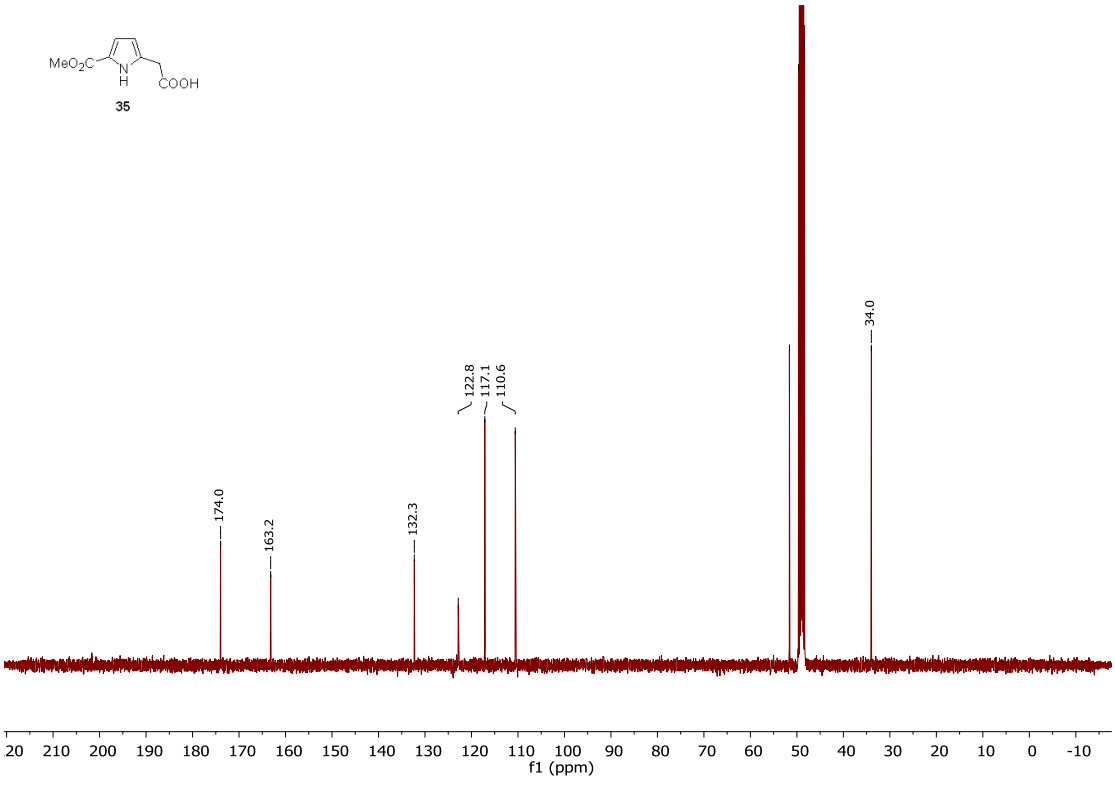
2.29
3.58
3.32
3.31
3.31
3.31
3.30
7.84
7.83
7.83
7.82
7.82
7.56
7.56
7.55
7.55
7.54
7.53
7.53
2.13
3.03
2.00
2.93
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


Me
N
Ph
HOOC
N
H
33
131.9
130.5
128.6
128.0
126.9
126.6
175.4
144.1
33.1
9.4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


MeO2C
N
H
COOH
35
4.88
3.80
3.64
3.32
3.31
3.31
3.31
3.30
6.80
6.79
6.07
6.06
0.99
0.96
2.98
2.00
f1 (ppm)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N
H
COOH
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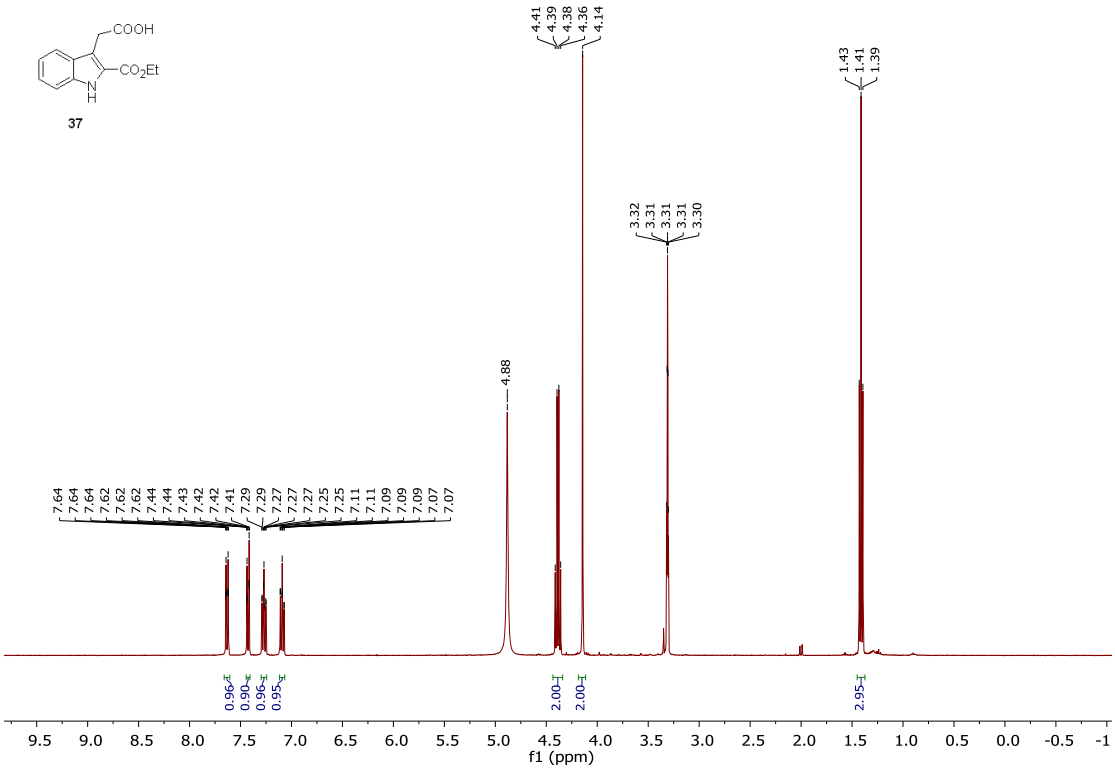
163.2
132.3
122.8
117.1
110.6
34.0
f1 (ppm)


COOH
CO2Et
N
H
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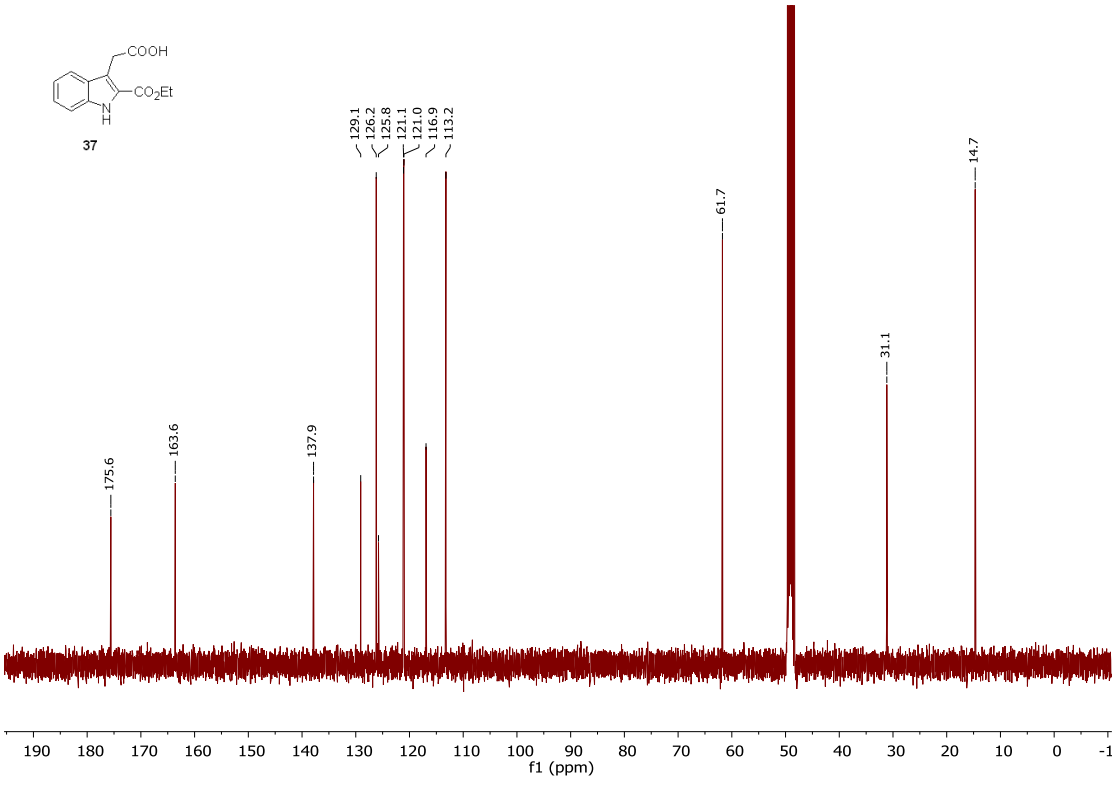
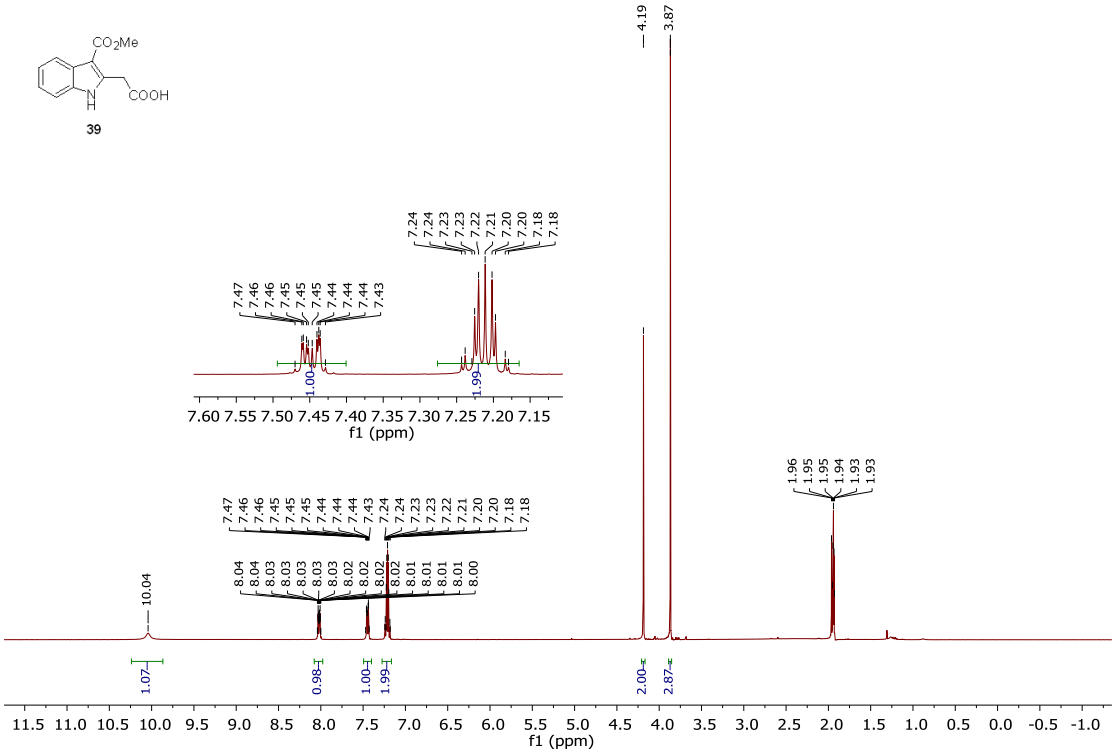
4.41
4.39
4.38
4.36
4.14
1.43
1.41
1.39
3.32
3.31
3.31
3.31
3.30
4.88
7.64
7.64
7.64
7.62
7.62
7.62
7.44
7.44
7.43
7.42
7.42
7.41
7.29
7.29
7.27
7.27
7.27
7.25
7.25
7.11
7.09
7.09
7.09
7.07
7.07
0.96
0.90
0.96
0.95
2.00
2.00
2.95
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


COOH
CO2Et
N
H
37
129.1
126.2
125.8
121.1
121.0
116.9
113.2
175.6
163.6
137.9
61.7
31.1
14.7
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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COOH
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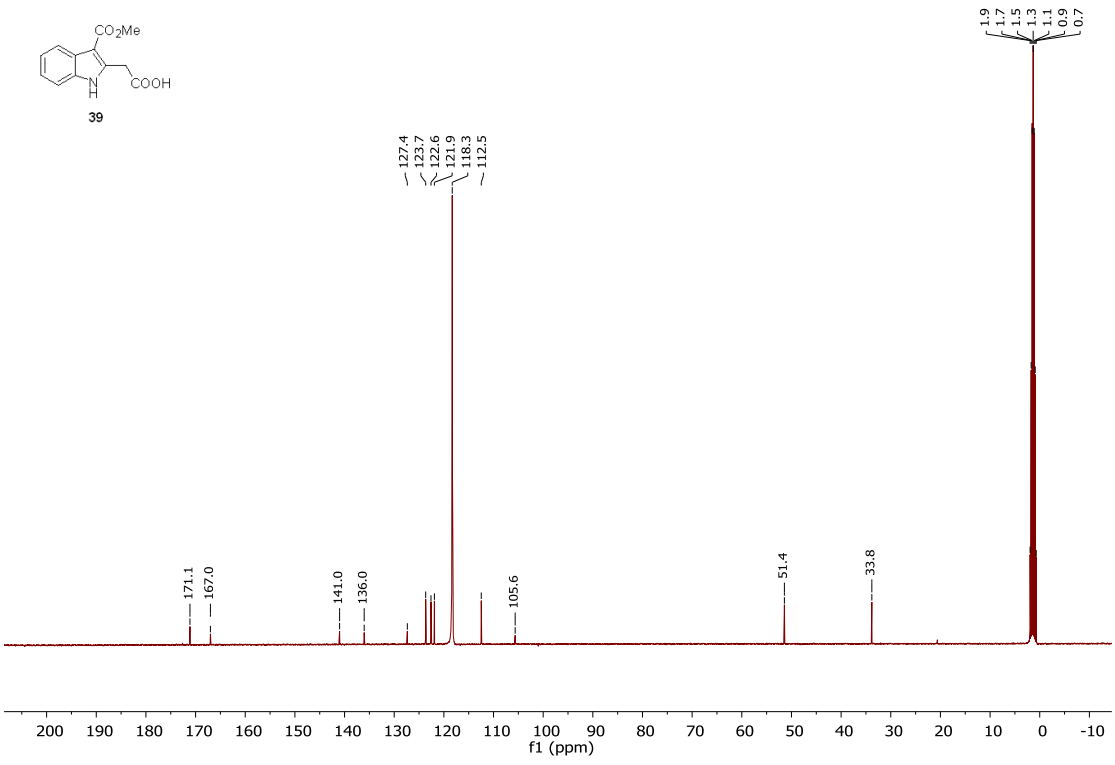
7.24
7.24
7.23
7.23
7.22
7.21
7.20
7.20
7.18
7.18
7.47
7.46
7.46
7.45
7.45
7.45
7.44
7.44
7.44
7.43
1.00
1.99
7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15
f1 (ppm)
1.96
1.95
1.95
1.94
1.93
1.93
7.47
7.46
7.46
7.45
7.45
7.45
7.44
7.44
7.44
7.43
7.24
7.24
7.23
7.23
7.22
7.21
7.20
7.20
7.18
7.18
8.04
8.04
8.03
8.03
8.03
8.03
8.02
8.02
8.02
8.02
8.01
8.01
8.01
8.01
8.00
10.04
1.07
0.98
1.00
1.99
2.00
2.87
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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COOH
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1.7
1.5
1.3
1.1
0.9
0.7
127.4
123.7
122.6
121.9
118.3
112.5
171.1
167.0
141.0
136.0
105.6
51.4
33.8
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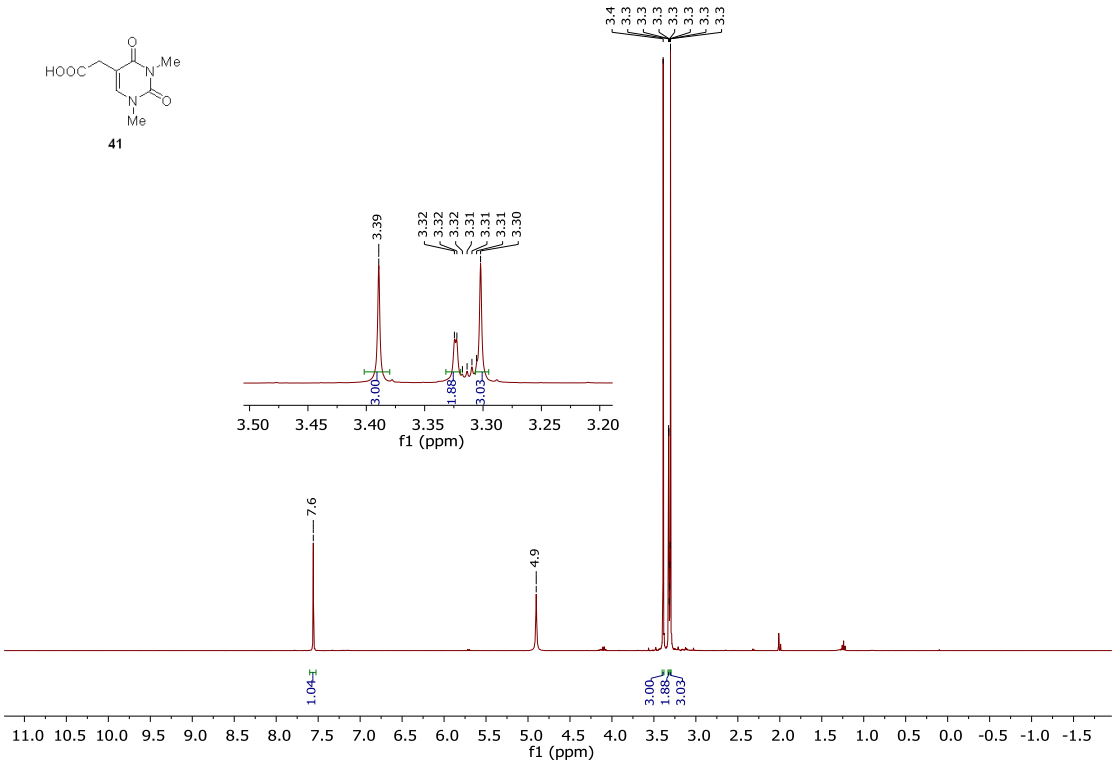
f1 (ppm)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Me
Me
41
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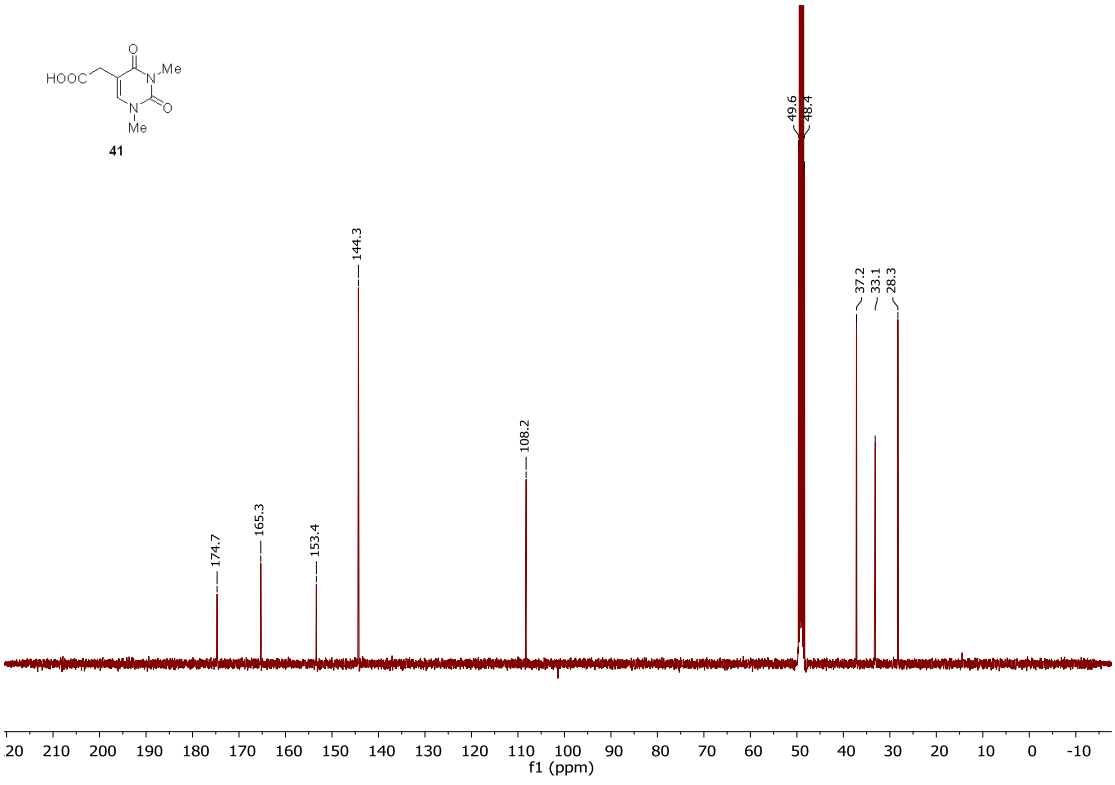
3.3
3.3
3.3
3.3
3.3
3.3
3.3
3.39
3.32
3.32
3.32
3.31
3.31
3.31
3.30
3.00
1.88
3.03
3.50 3.45 3.40 3.35 3.30 3.25 3.20
f1 (ppm)
7.6
4.9
1.04
3.00
1.88
3.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


HOOC
Me
Me
41
49.6
48.4
144.3
37.2
33.1
28.3
108.2
174.7
165.3
153.4
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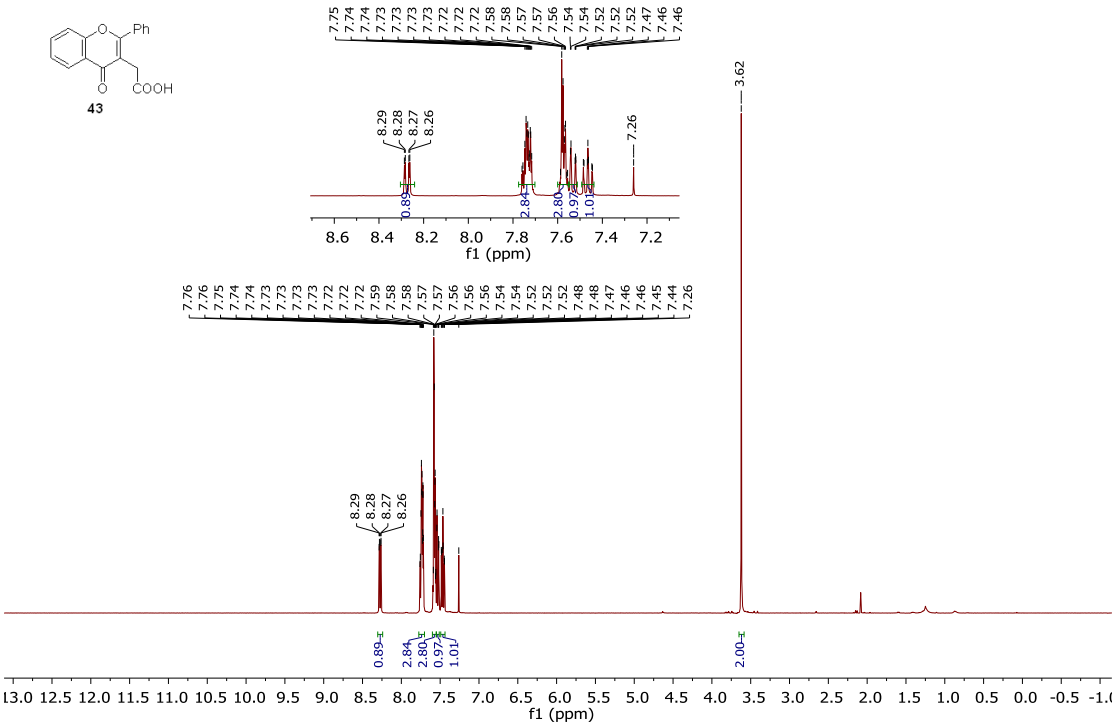
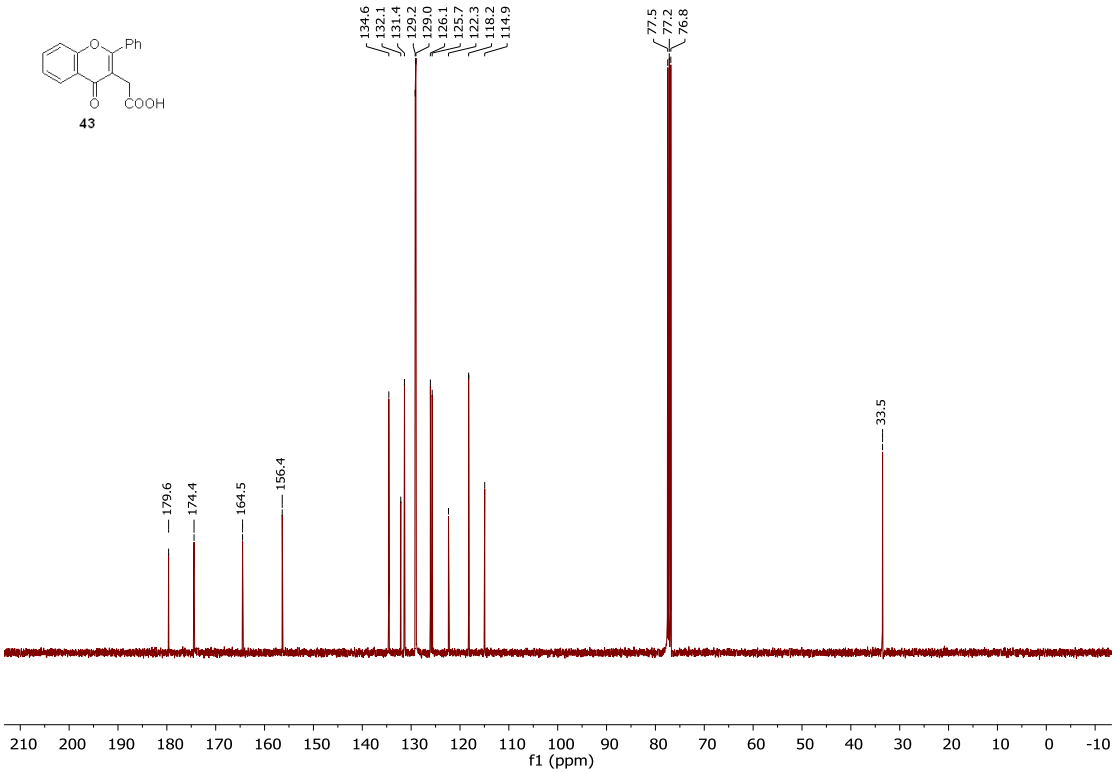
f1 (ppm)


Ph
O
O
COOH
43
f1 (ppm)


Ph
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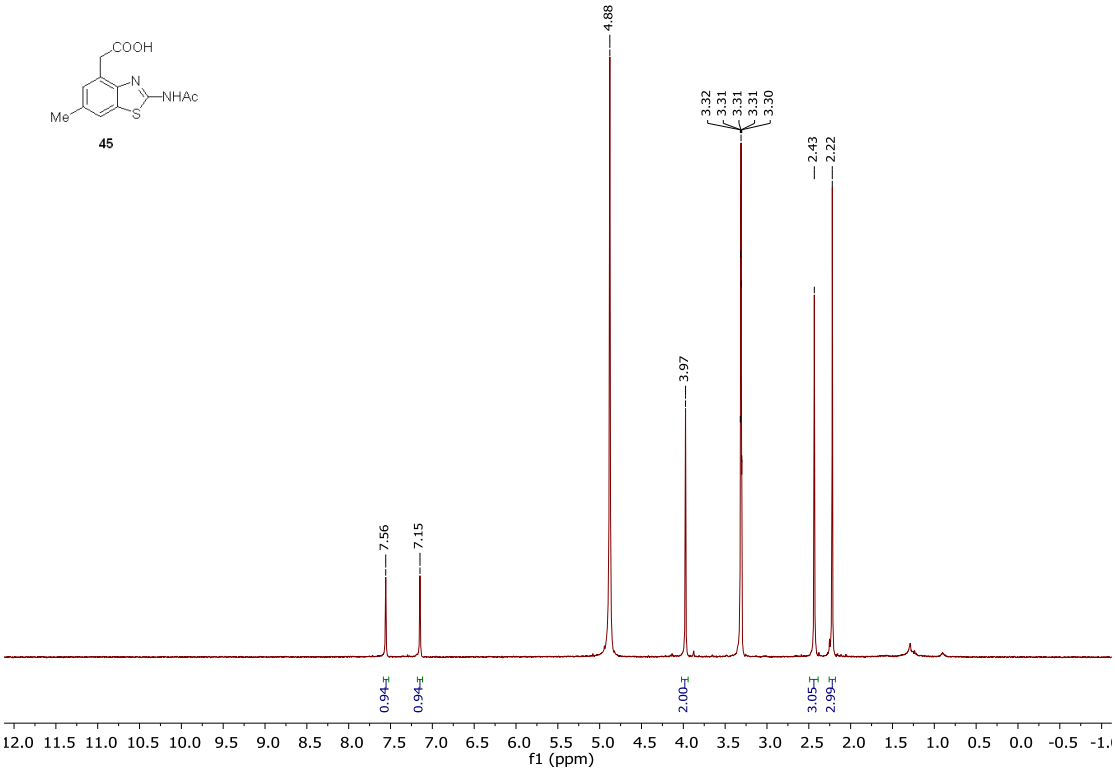
O
COOH
43
f1 (ppm)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NHAc
S
Me
45
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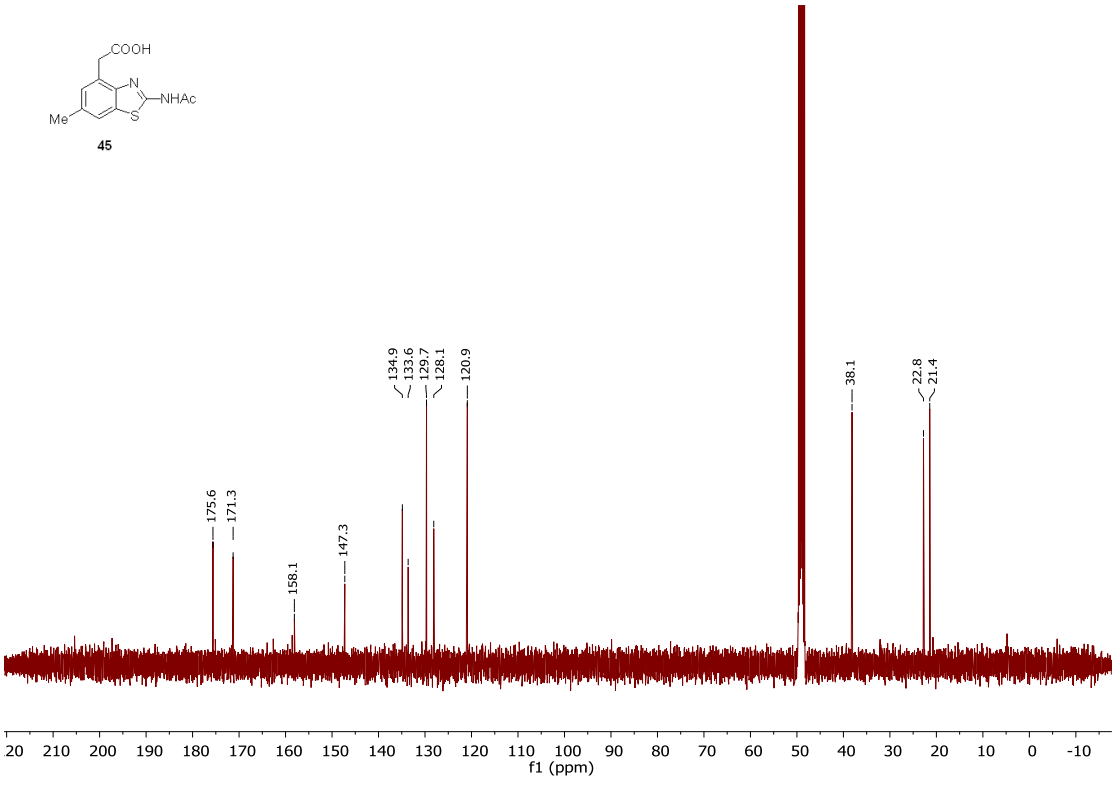
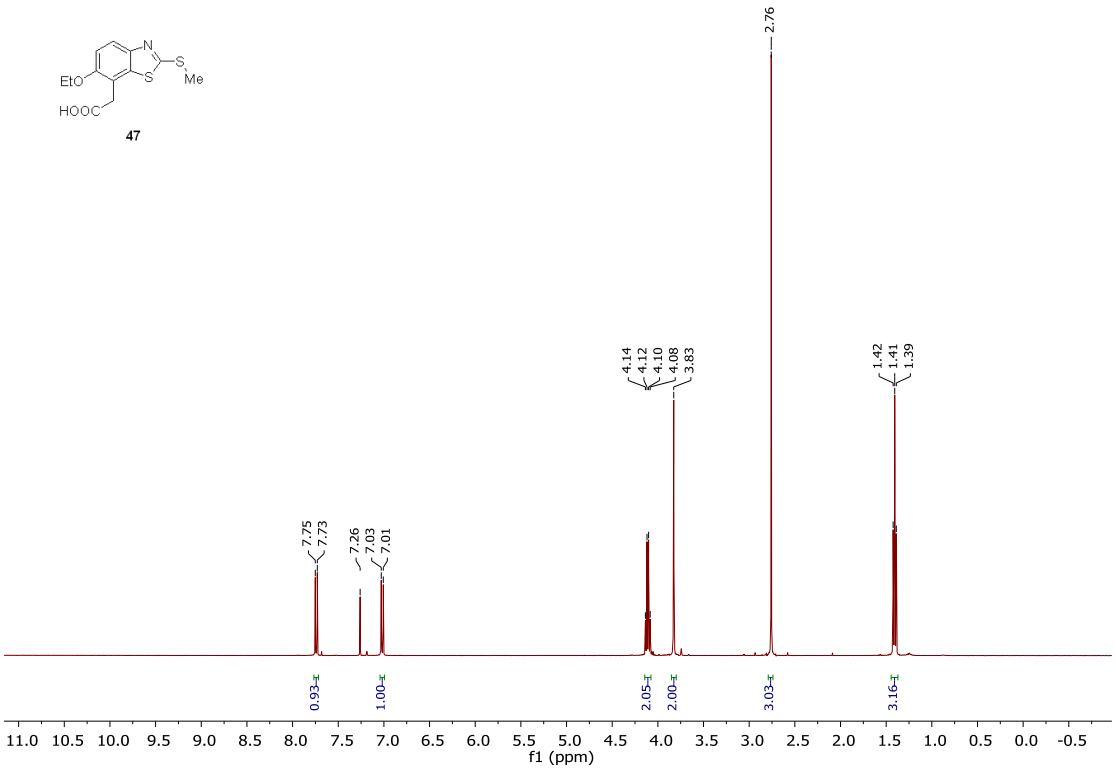
3.32
3.31
3.31
3.31
3.30
2.43
2.22
3.97
7.56
7.15
0.94
0.94
2.00
3.05
2.99
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


COOH
N
NHAc
S
Me
45
134.9
133.6
129.7
128.1
120.9
38.1
22.8
21.4
175.6
171.3
158.1
147.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


EtO
HOOC
N
S
S
Me
47
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4.14
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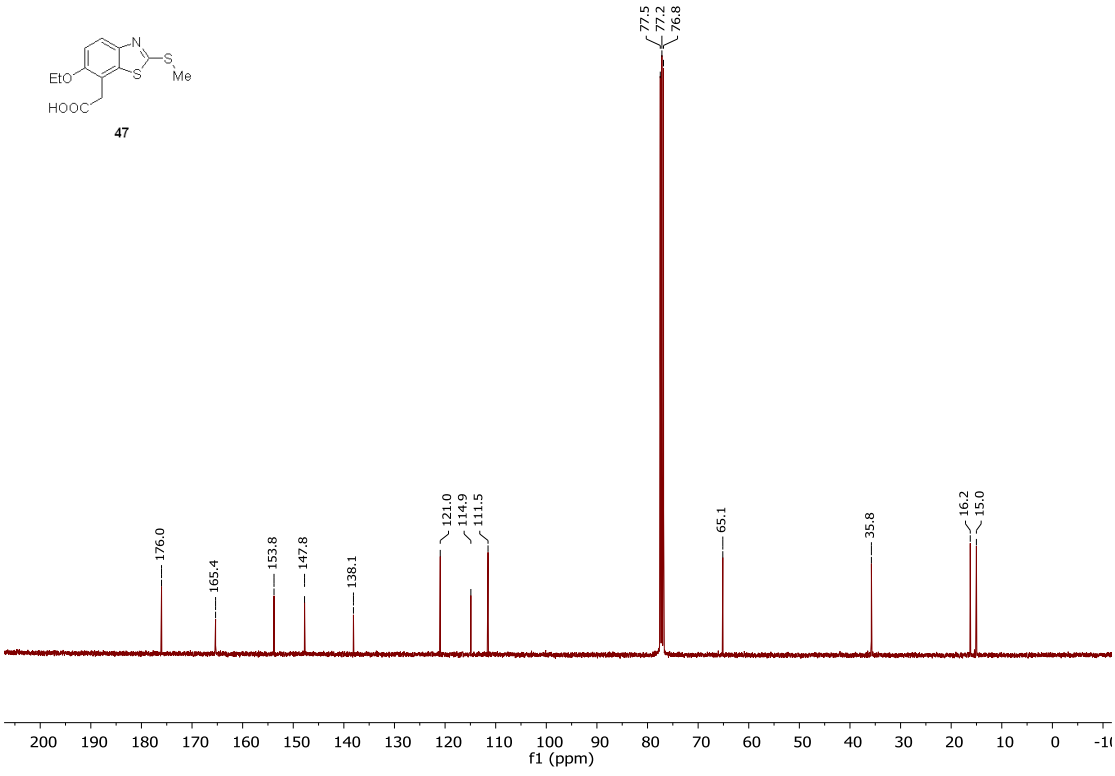
4.10
4.08
3.83
1.42
1.41
1.39
7.75
7.73
7.26
7.03
7.01
0.93
1.00
2.05
2.00
3.03
3.16
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


EtO
HOOC
N
S
S
Me
47
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77.2
76.8
176.0
165.4
153.8
147.8
138.1
121.0
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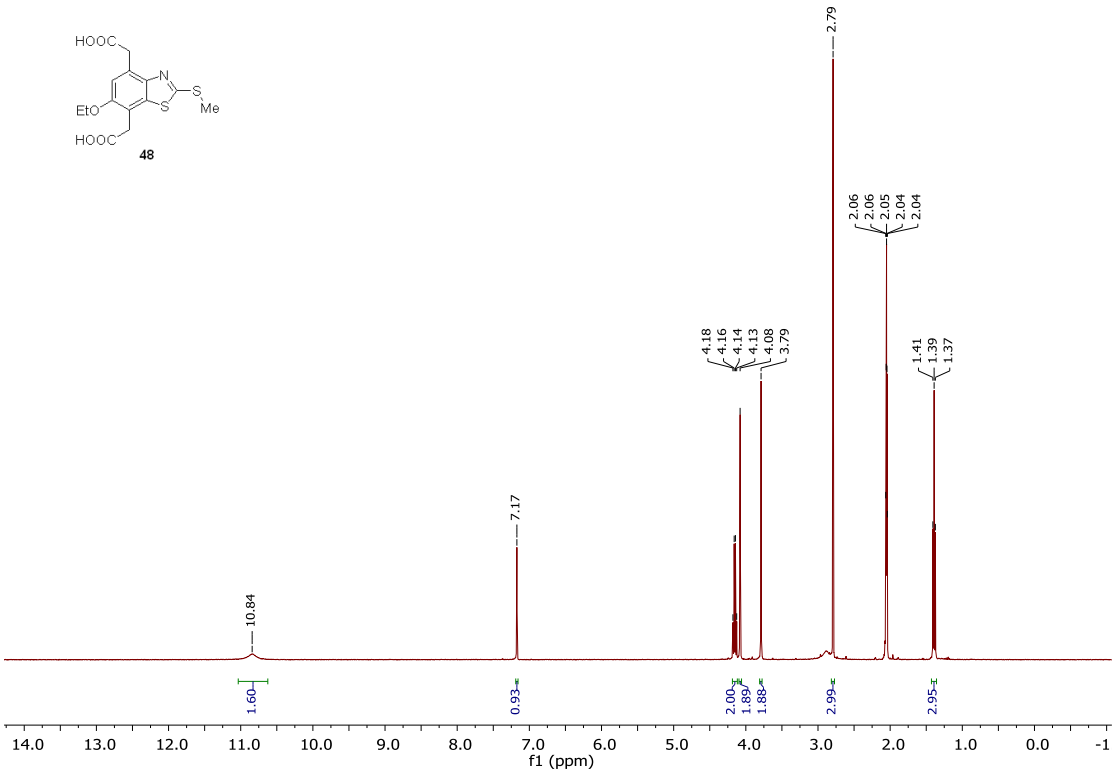
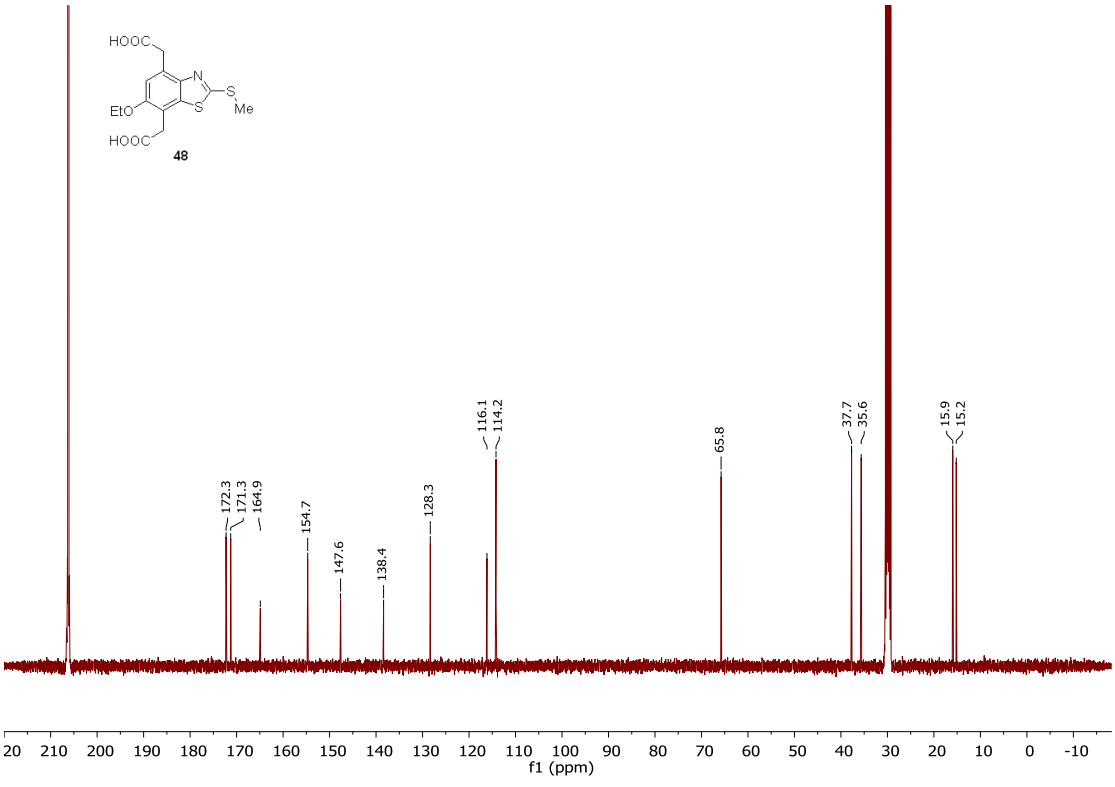
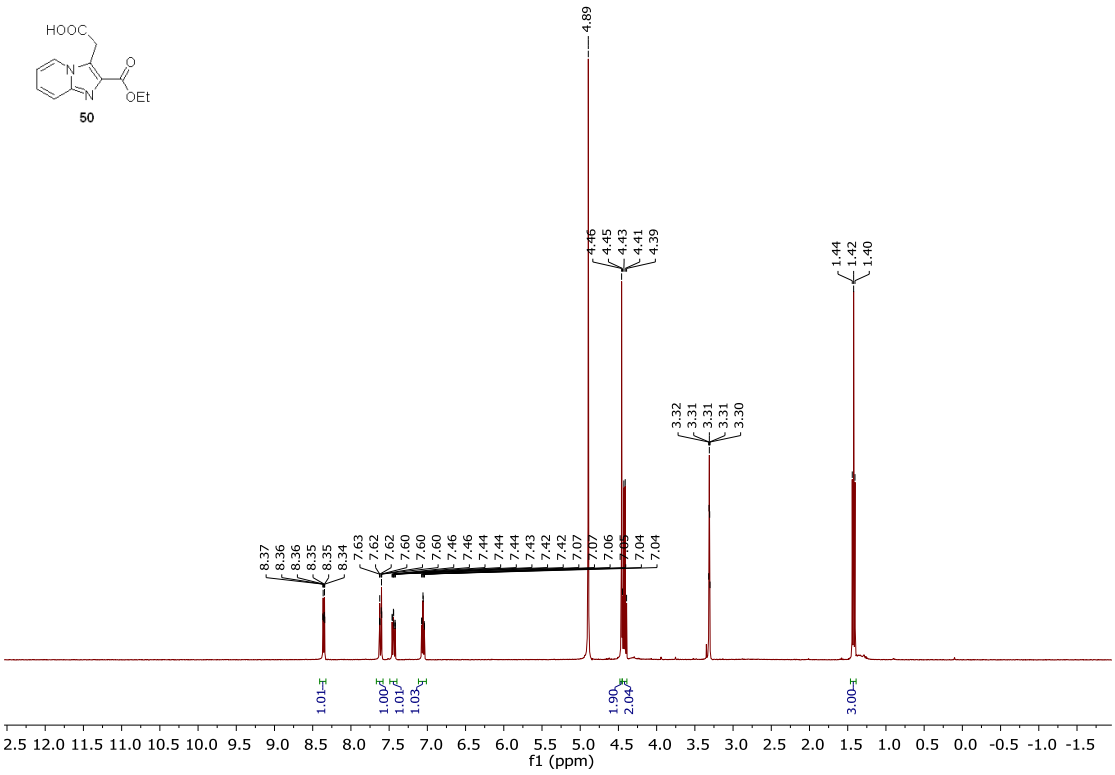
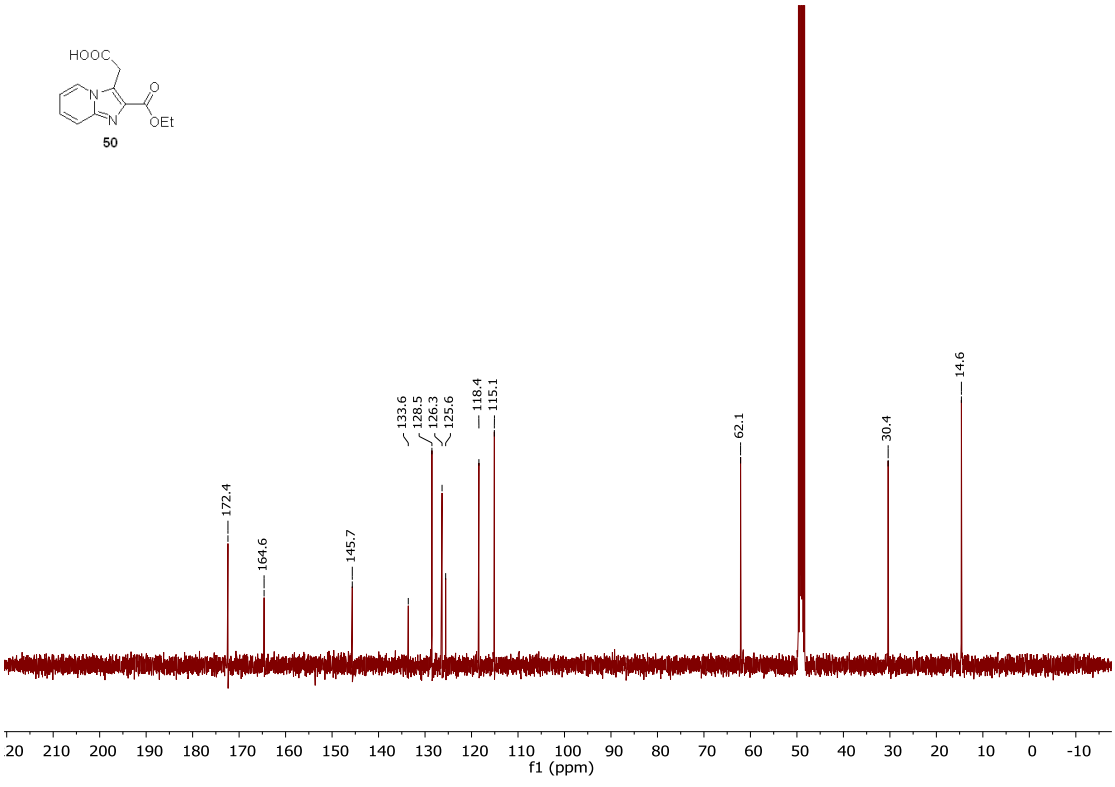
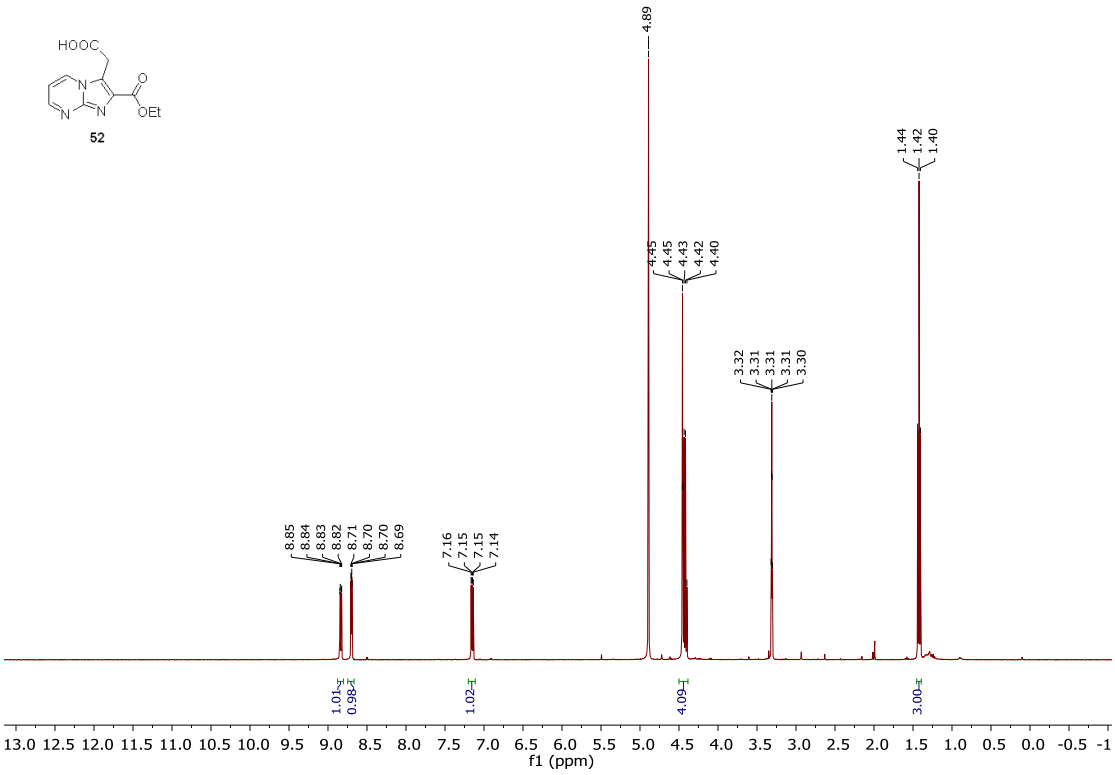
111.5
65.1
35.8
16.2
15.0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

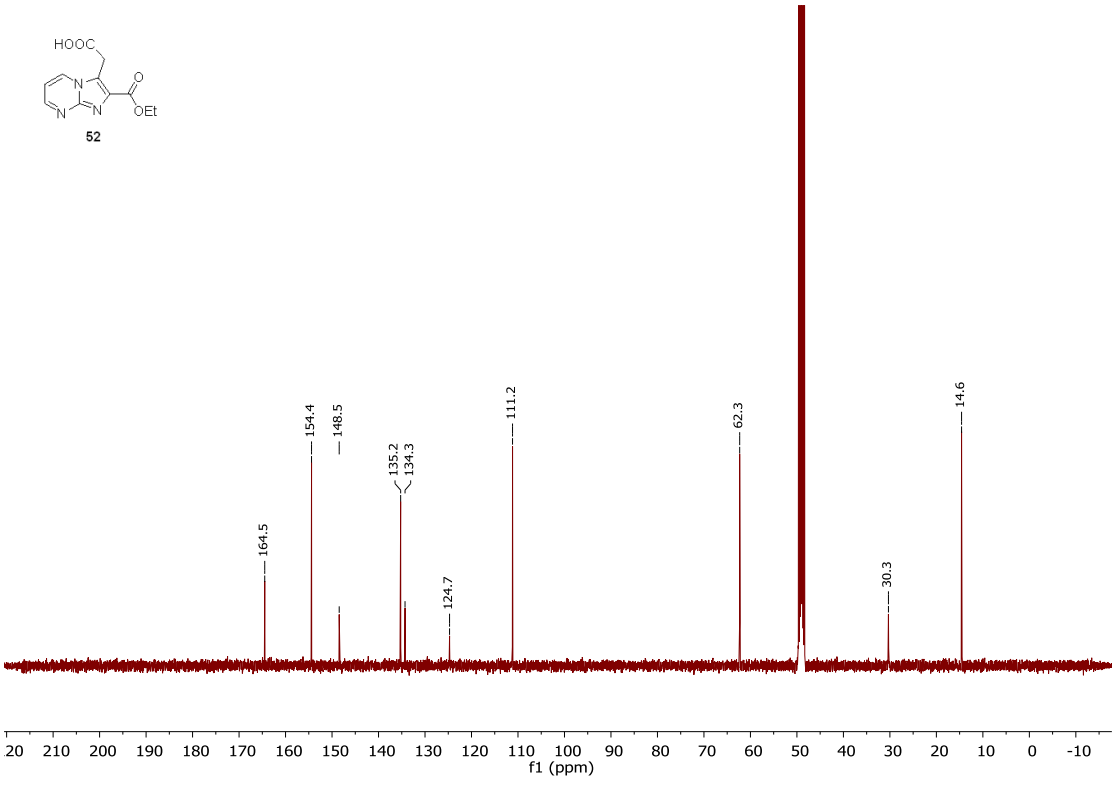

HOOC
EtO
HOOC
N
S
S
Me
48
10.84
7.17
4.18
4.16
4.14
4.13
4.08
3.79
2.79
2.06
2.06
2.05
2.04
2.04
1.41
1.39
1.37
1.60
0.93
2.00
1.89
1.88
2.99
2.95
f1 (ppm)

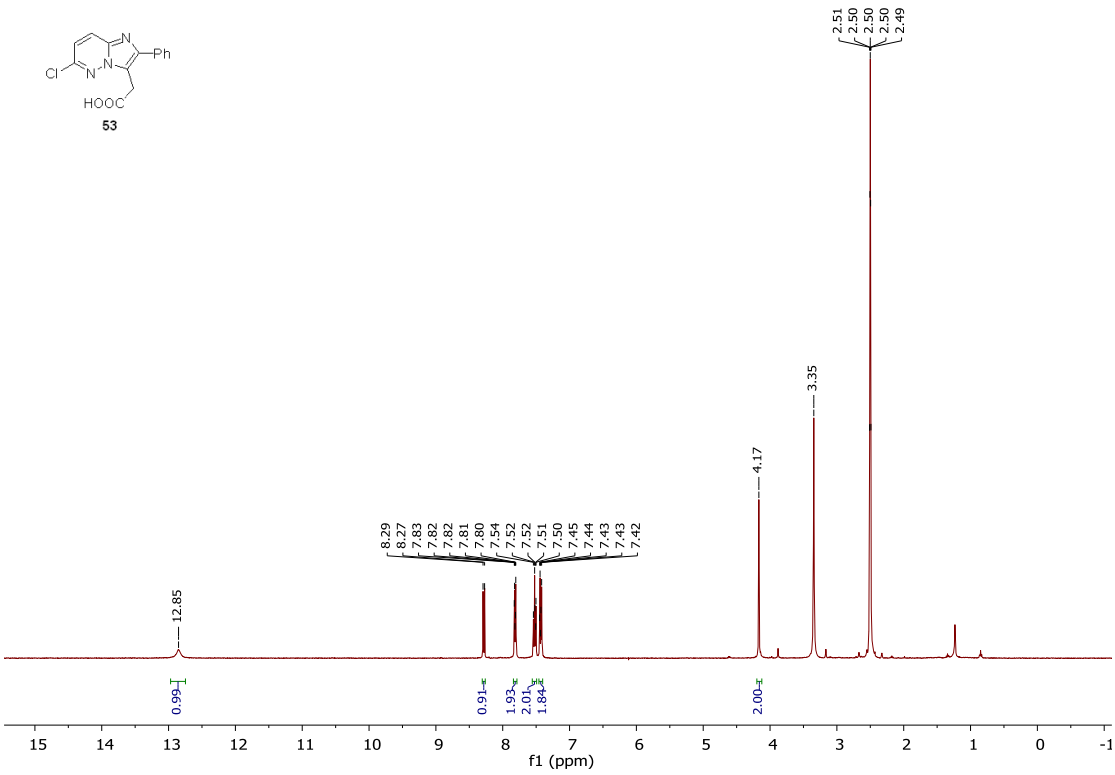

HOOC
EtO
HOOC
N
S
S
Me
48
172.3
171.3
164.9
154.7
147.6
138.4
128.3
116.1
114.2
65.8
37.7
35.6
15.9
15.2
f1 (ppm)

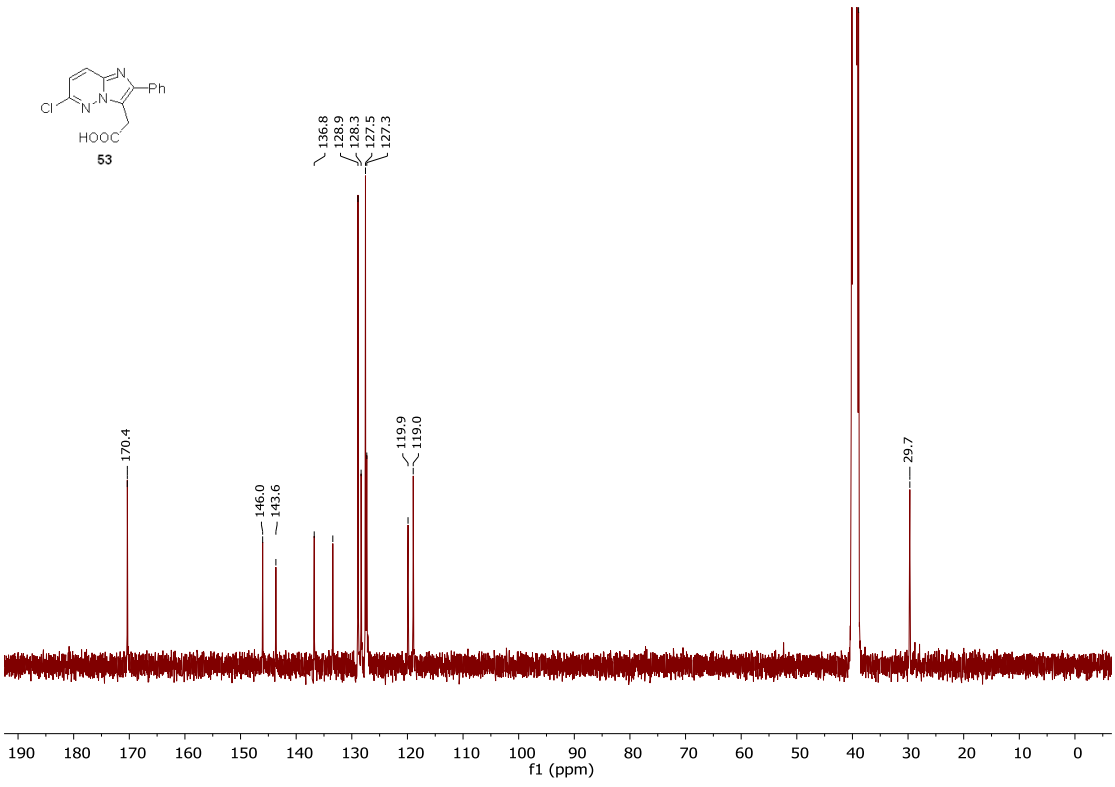

HOOC
O
OEt
N
N
50
4.89
4.46
4.45
4.43
4.41
4.39
1.44
1.42
1.40
3.32
3.31
3.31
3.31
3.30
8.37
8.36
8.36
8.35
8.35
8.34
7.63
7.62
7.62
7.60
7.60
7.60
7.46
7.46
7.44
7.44
7.44
7.43
7.42
7.42
7.07
7.07
7.06
7.04
7.04
7.04
1.01
1.00
1.01
1.03
1.90
2.04
3.00
2.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

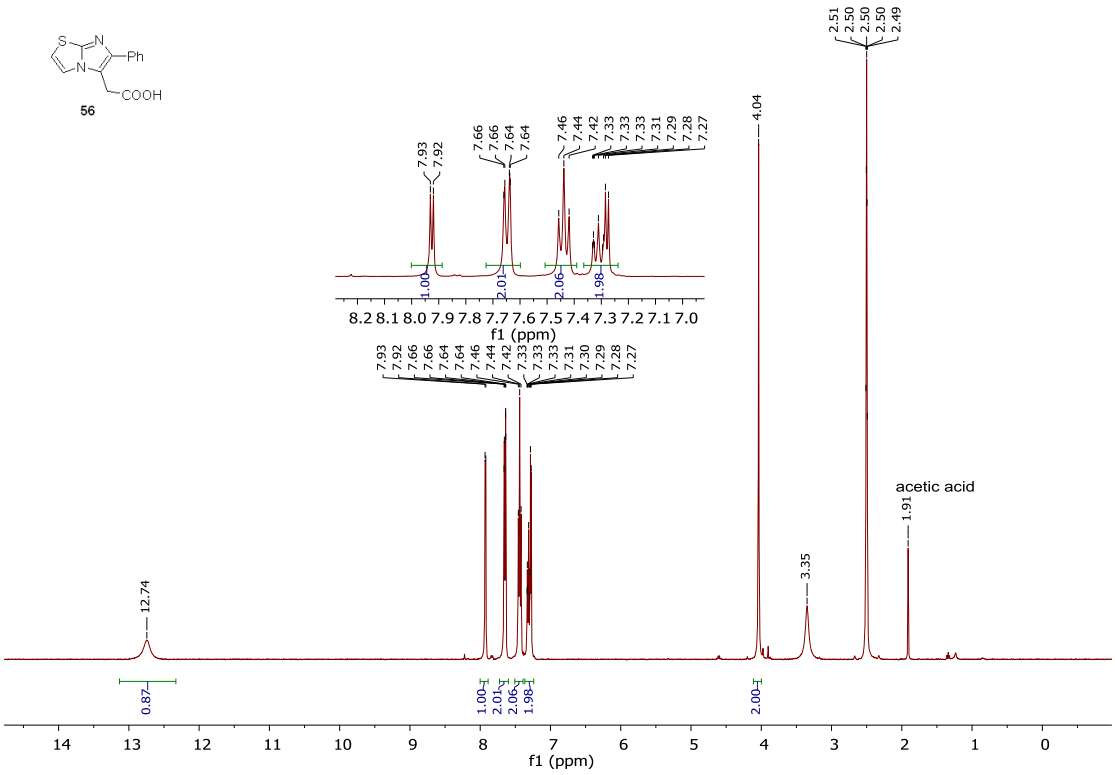

HOOC
O
OEt
N
N
50
172.4
164.6
145.7
133.6
128.5
126.3
125.6
118.4
115.1
62.1
30.4
14.6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

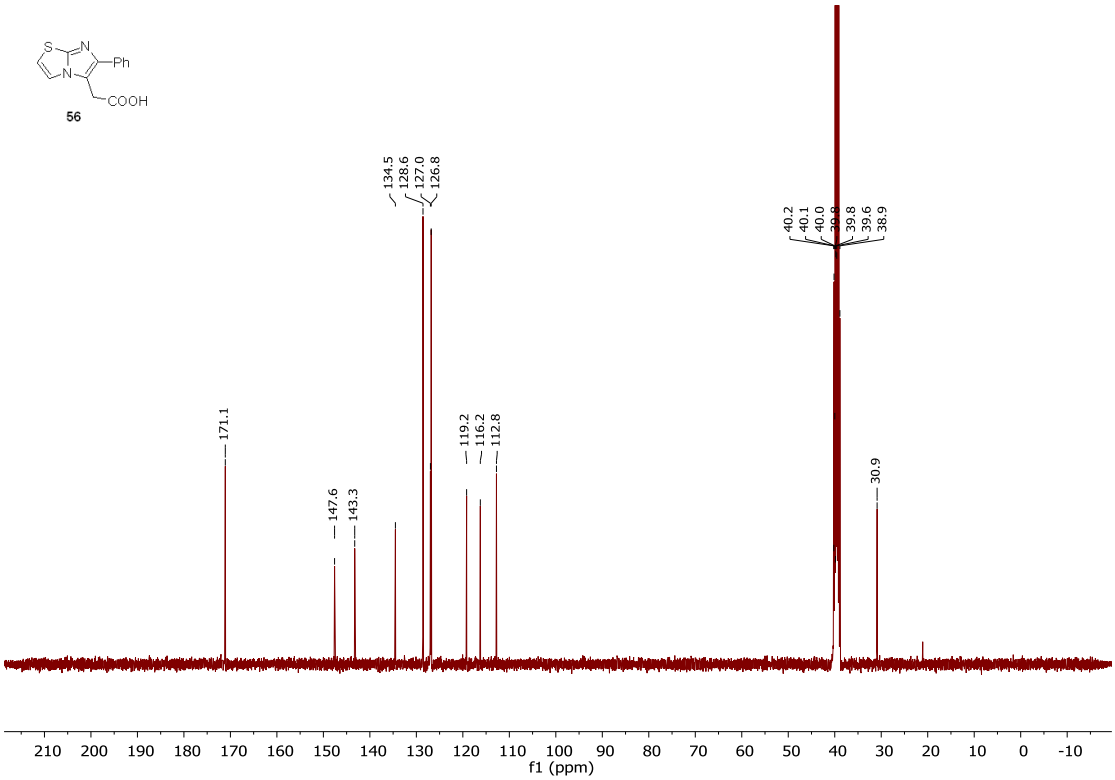

HOOC
O
OEt
N
N
52
4.89
4.45
4.45
4.43
4.42
4.40
1.44
1.42
1.40
3.32
3.31
3.31
3.31
3.30
8.85
8.84
8.83
8.82
8.71
8.70
8.70
8.69
7.16
7.15
7.15
7.14
1.01
0.98
1.02
4.09
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

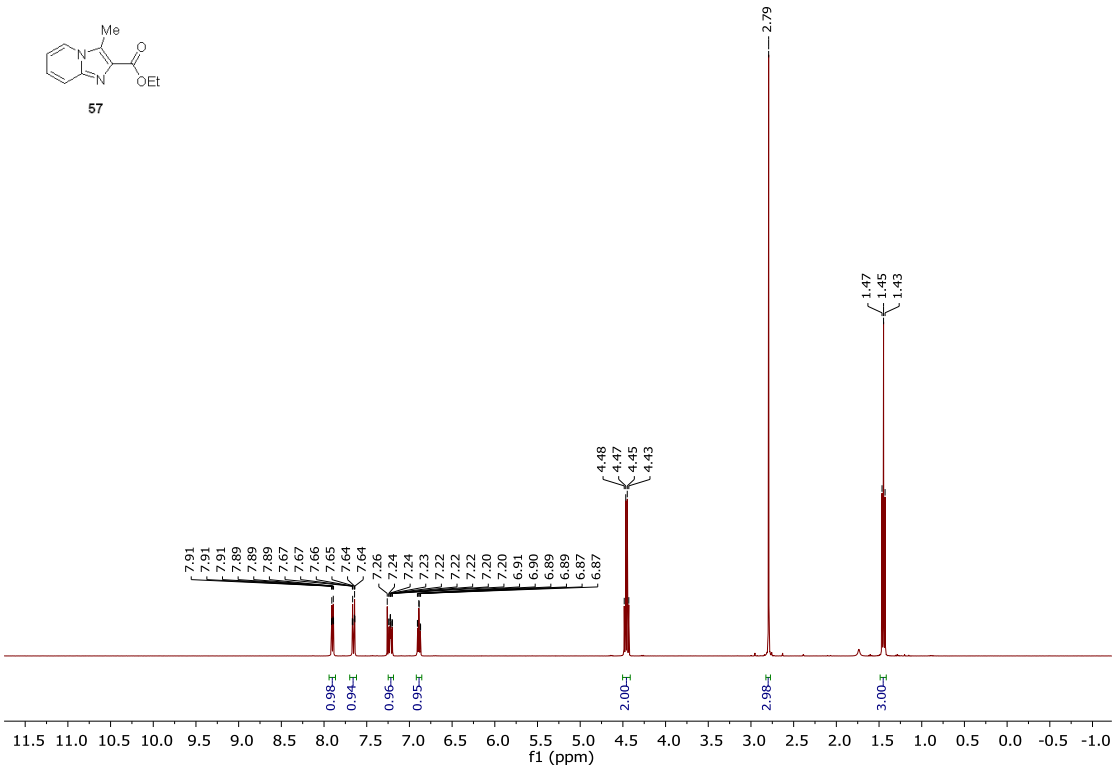

HOOC
O
OEt
N
N
52
164.5
154.4
148.5
135.2
134.3
124.7
111.2
62.3
30.3
14.6
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

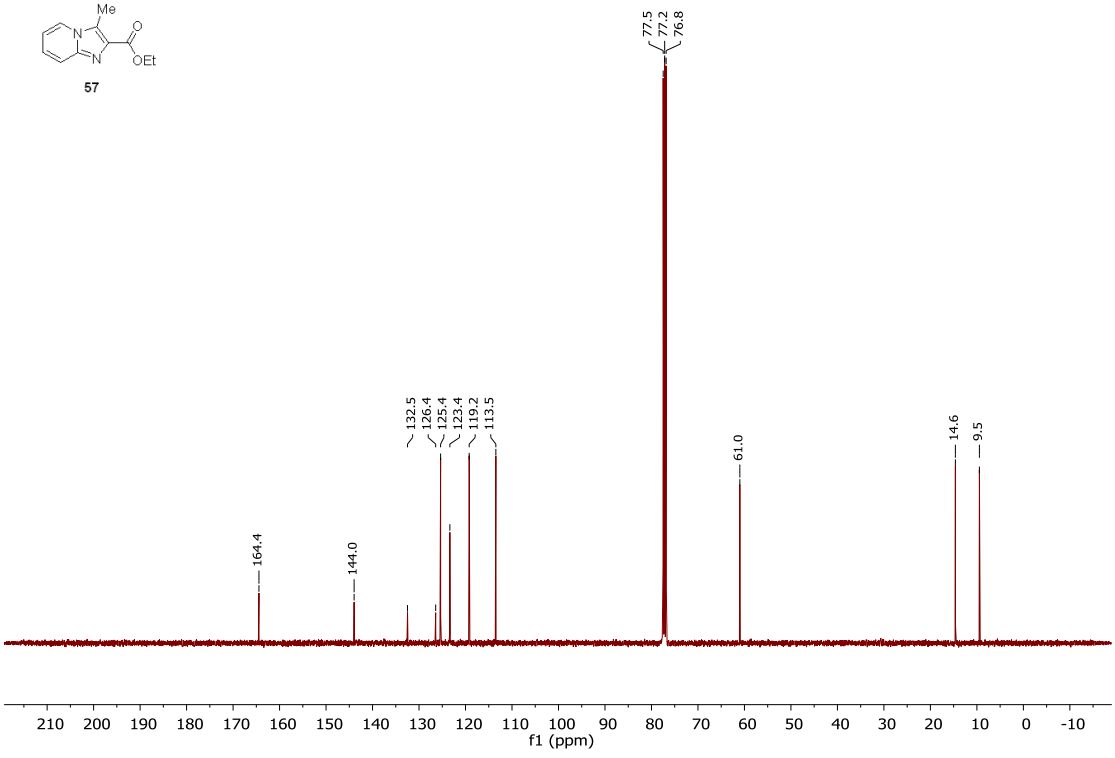

Cl
N
N
N
Ph
HOOC
53
2.51
2.50
2.50
2.50
2.49
3.35
4.17
8.29
8.27
7.83
7.82
7.82
7.81
7.80
7.54
7.52
7.52
7.51
7.50
7.45
7.44
7.43
7.43
7.42
12.85
0.99
0.91
1.93
2.01
1.84
2.00
f1 (ppm)

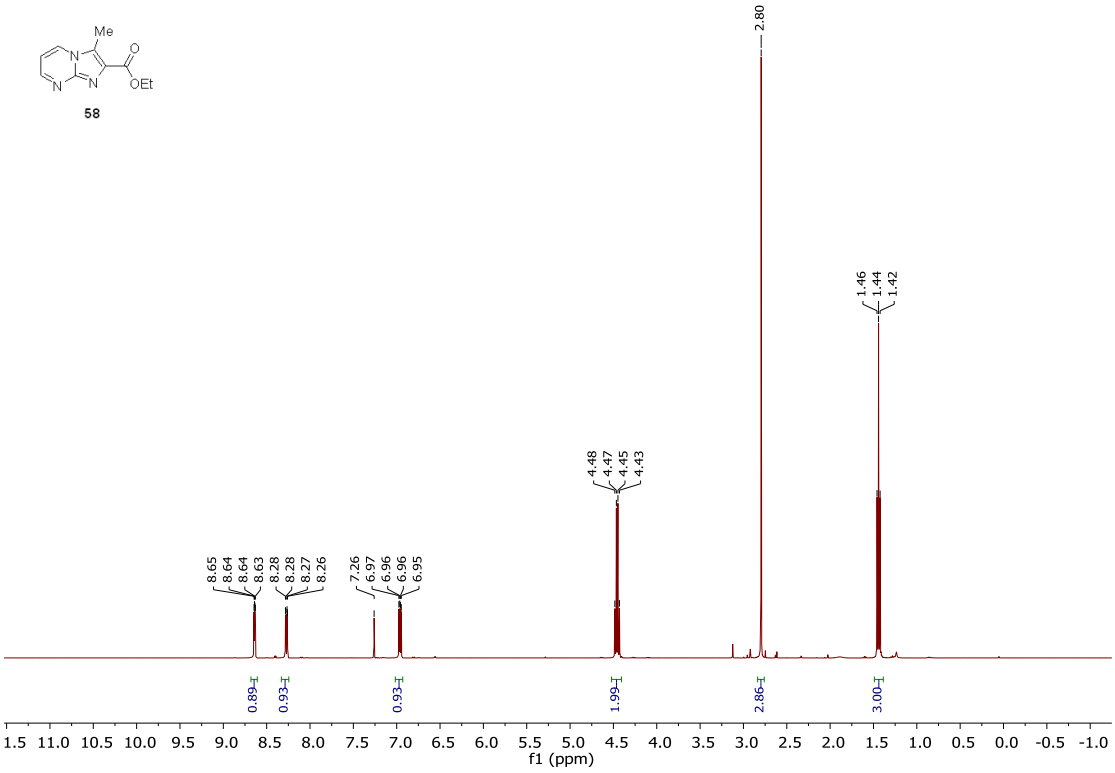

Cl
N
N
N
Ph
HOOC
53
136.8
128.9
128.3
127.5
127.3
170.4
146.0
143.6
119.9
119.0
29.7
f1 (ppm)

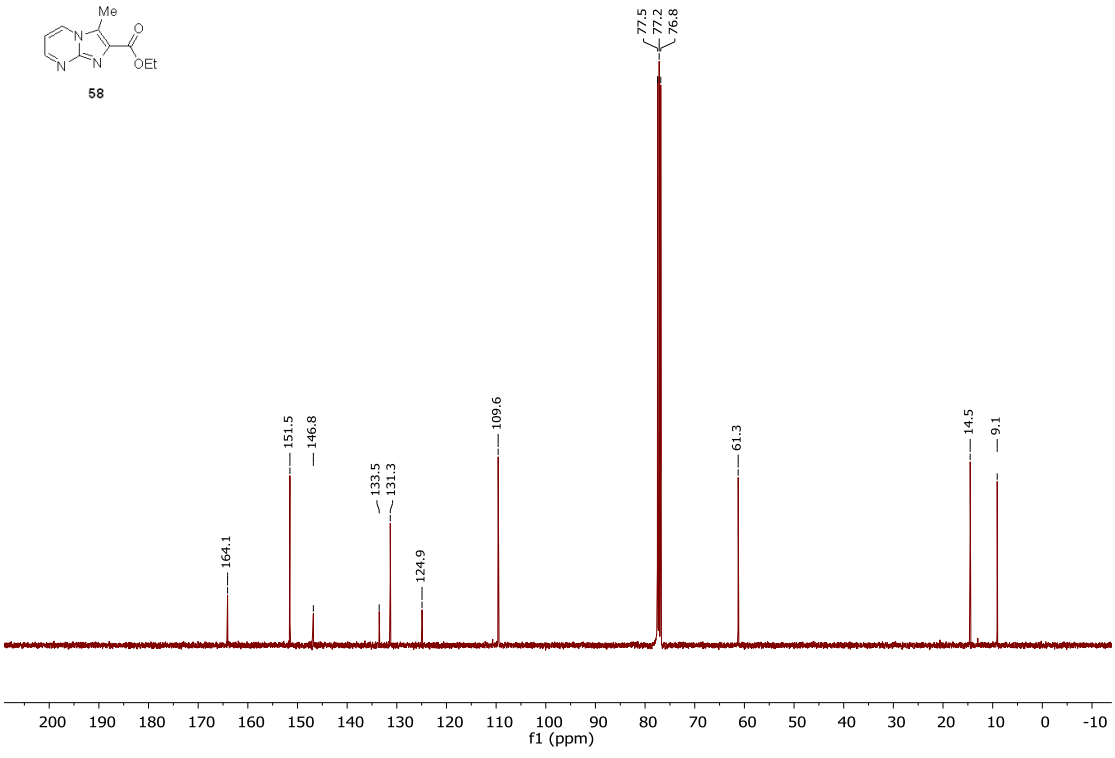

56
Ph
COOH
acetic acid
f1 (ppm)

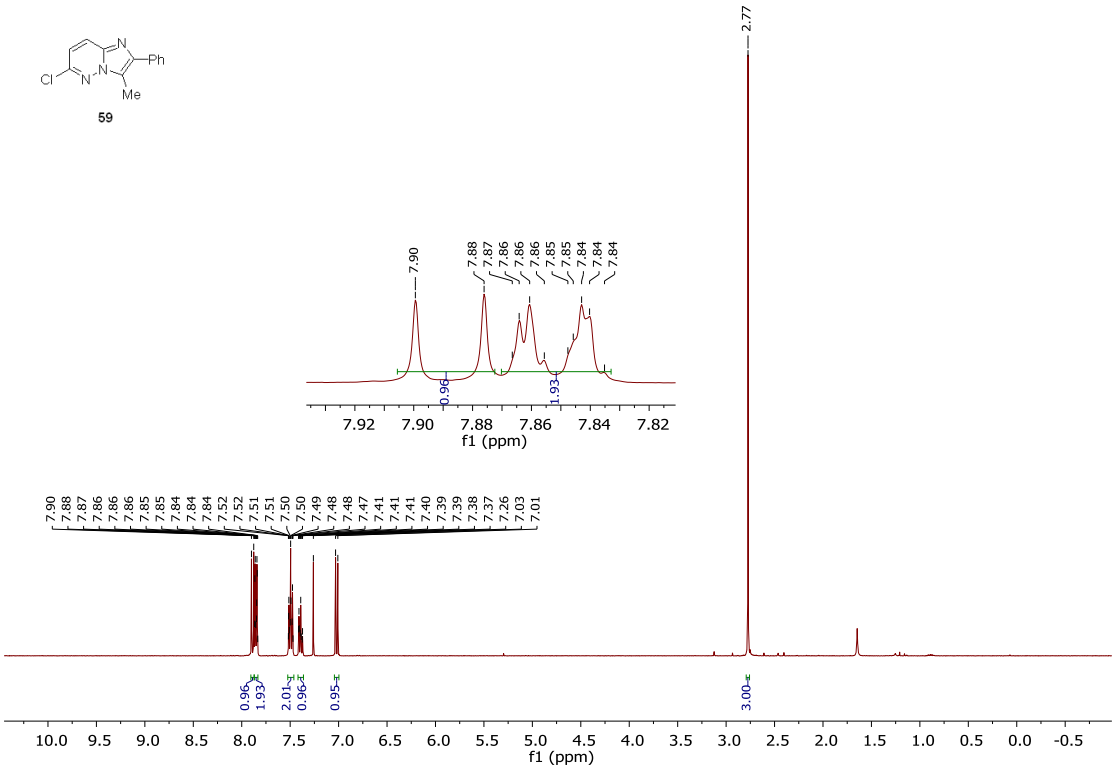

56
Ph
COOH
f1 (ppm)

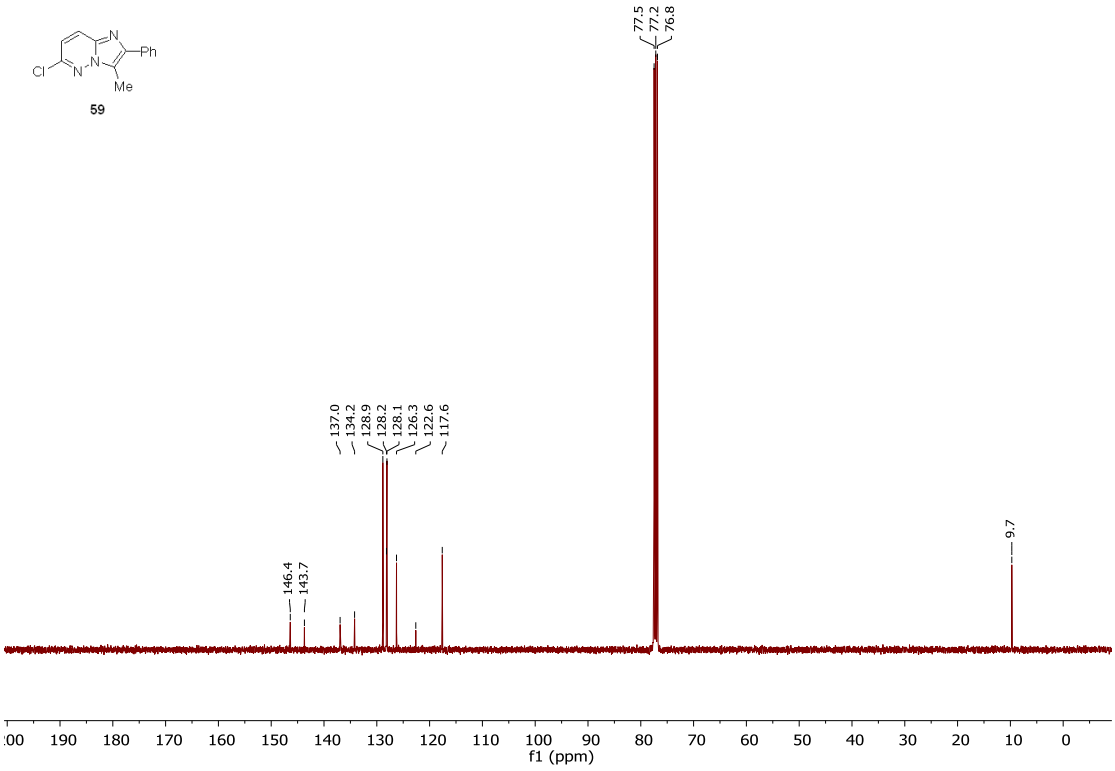

Me
O
OEt
57
2.79
1.47
1.45
1.43
4.48
4.47
4.45
4.43
7.91
7.91
7.91
7.89
7.89
7.89
7.67
7.67
7.66
7.65
7.64
7.64
7.26
7.24
7.24
7.24
7.23
7.22
7.22
7.22
7.20
7.20
6.91
6.90
6.89
6.89
6.87
6.87
0.98
0.94
0.96
0.95
2.00
2.98
3.00
f1 (ppm)

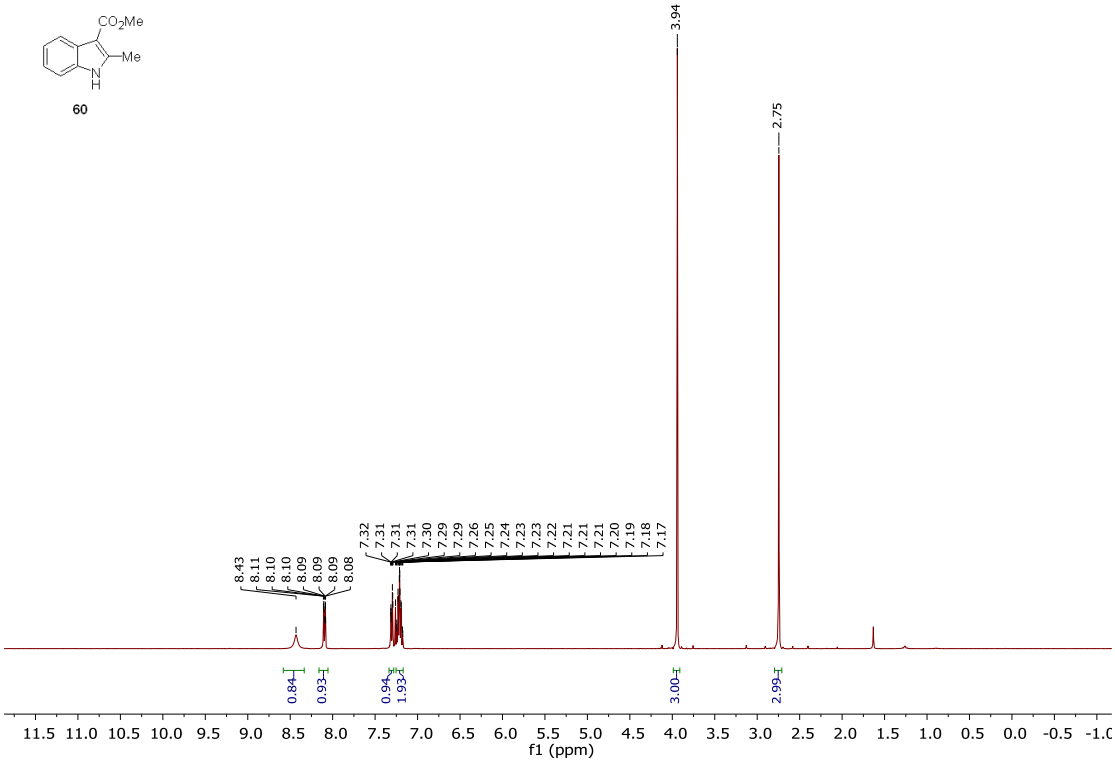

Me
O
OEt
57
77.5
77.2
76.8
132.5
126.4
125.4
123.4
119.2
113.5
164.4
144.0
61.0
14.6
9.5
f1 (ppm)

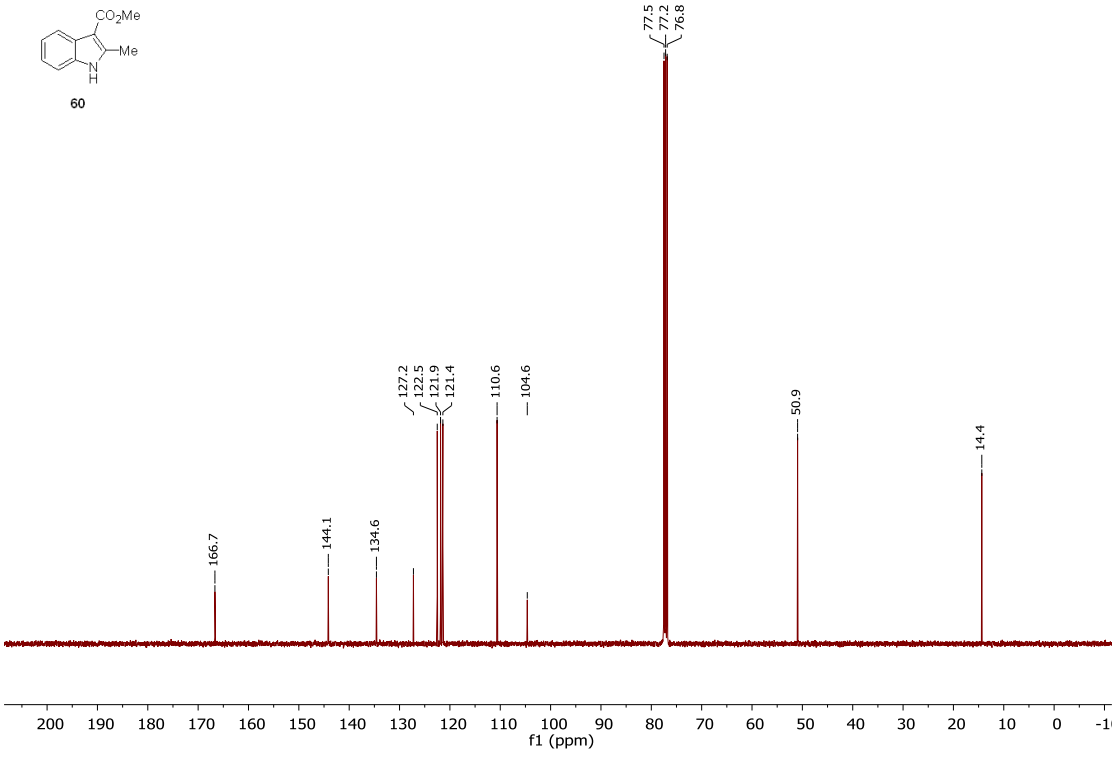

Me
O
OEt
N
N
58
2.80
1.46
1.44
1.42
4.48
4.47
4.45
4.43
8.65
8.64
8.64
8.63
8.28
8.28
8.27
8.26
7.26
6.97
6.96
6.96
6.95
0.89
0.93
0.93
1.99
2.86
3.00
1.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

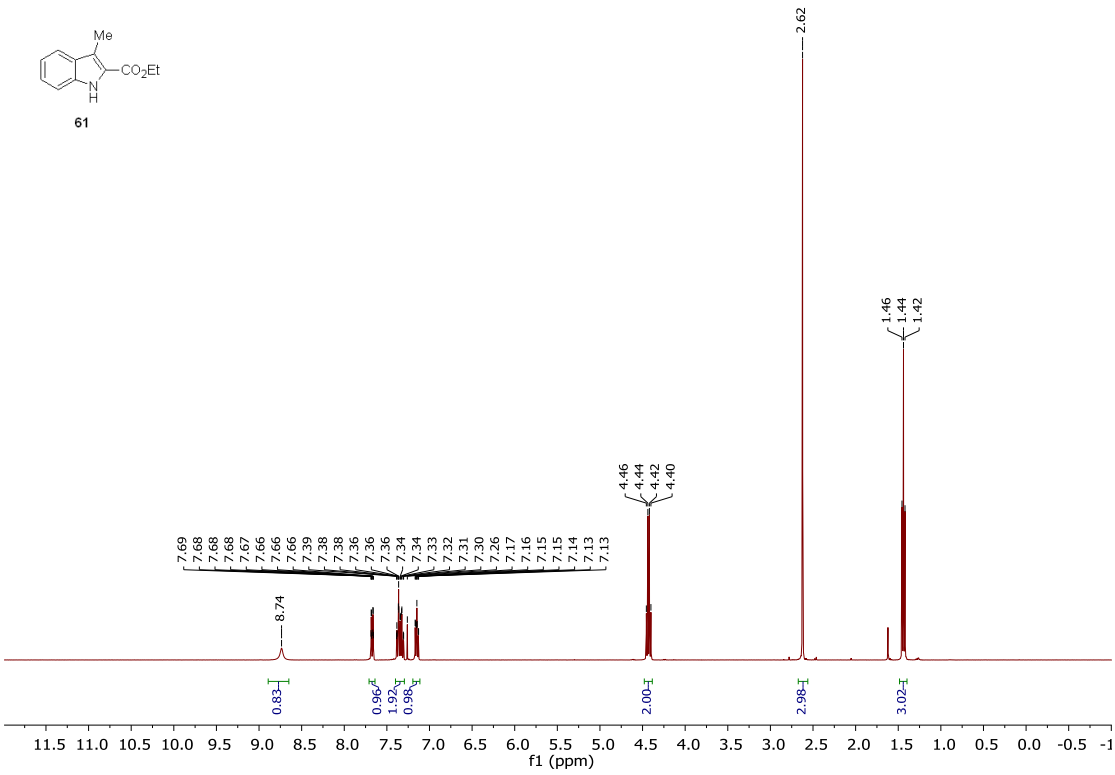

Me
O
OEt
N
N
58
77.5
77.2
76.8
164.1
151.5
146.8
133.5
131.3
124.9
109.6
61.3
14.5
9.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

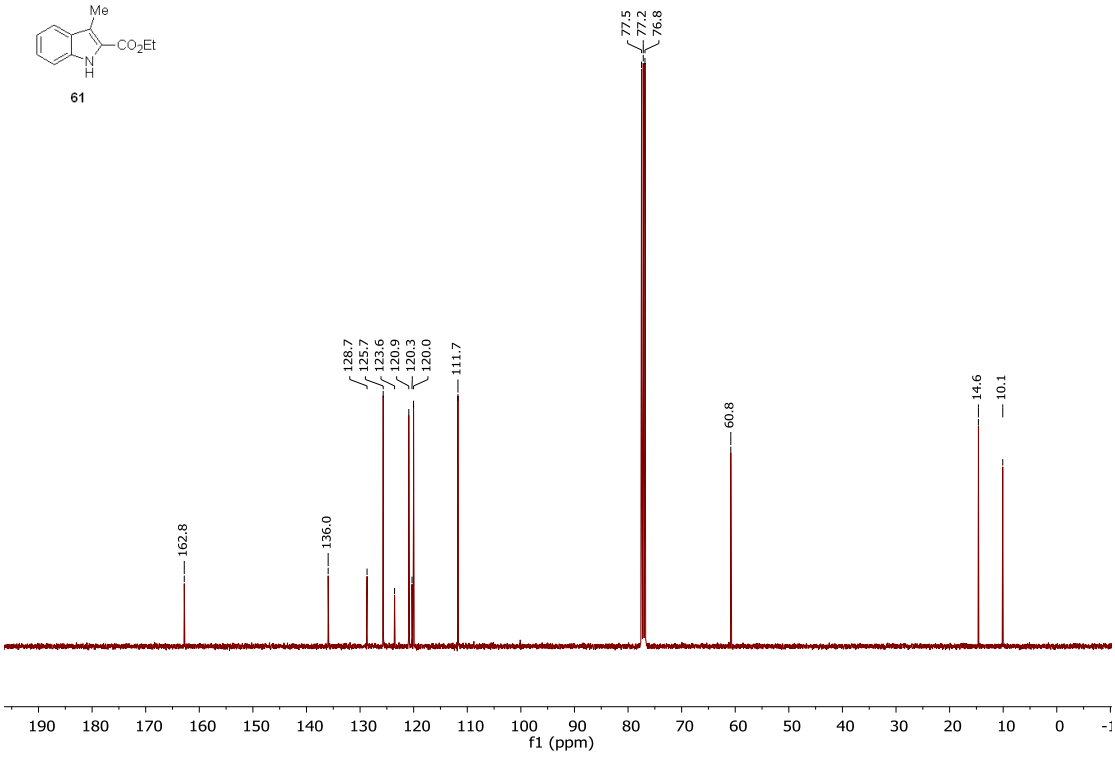

Cl
N
N
N
Ph
Me
59
2.77
7.90
7.88
7.87
7.86
7.86
7.85
7.84
7.84
7.52
7.51
7.51
7.50
7.50
7.49
7.48
7.48
7.47
7.41
7.41
7.41
7.40
7.39
7.39
7.38
7.37
7.26
7.03
7.01
0.96
1.93
2.01
0.96
0.95
3.00
f1 (ppm)

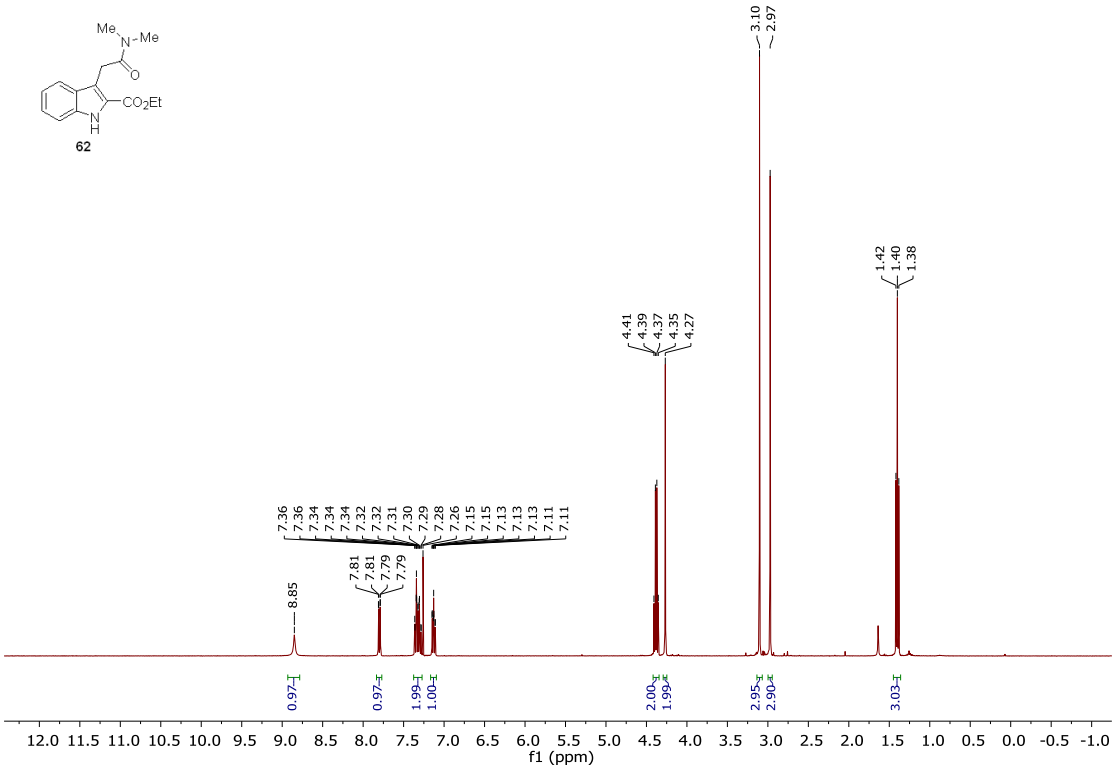

Cl
N
N
N
Ph
Me
59
77.5
77.2
76.8
137.0
134.2
128.9
128.2
128.1
126.3
122.6
117.6
146.4
143.7
9.7
f1 (ppm)

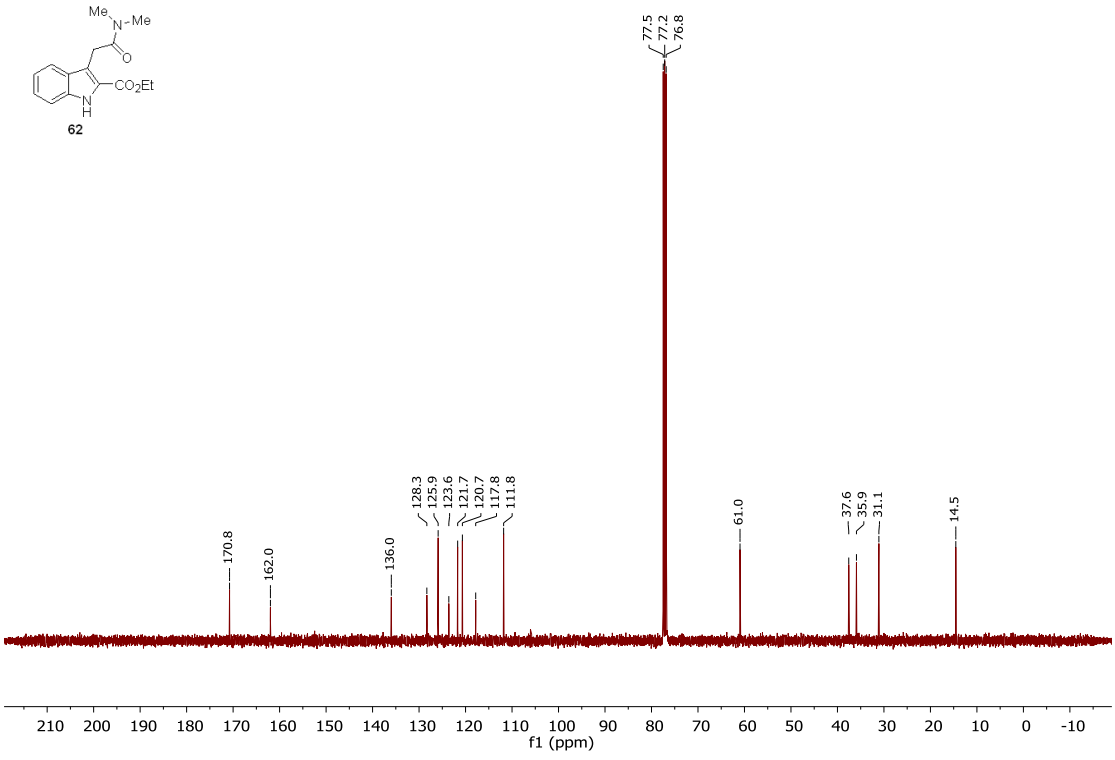

CO2Me
Me
N
H
60
3.94
2.75
8.43
8.11
8.10
8.10
8.09
8.09
8.09
8.08
7.32
7.31
7.31
7.31
7.30
7.29
7.29
7.26
7.25
7.24
7.23
7.23
7.22
7.21
7.21
7.21
7.20
7.19
7.18
7.17
0.84
0.93
0.94
1.93
3.00
2.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

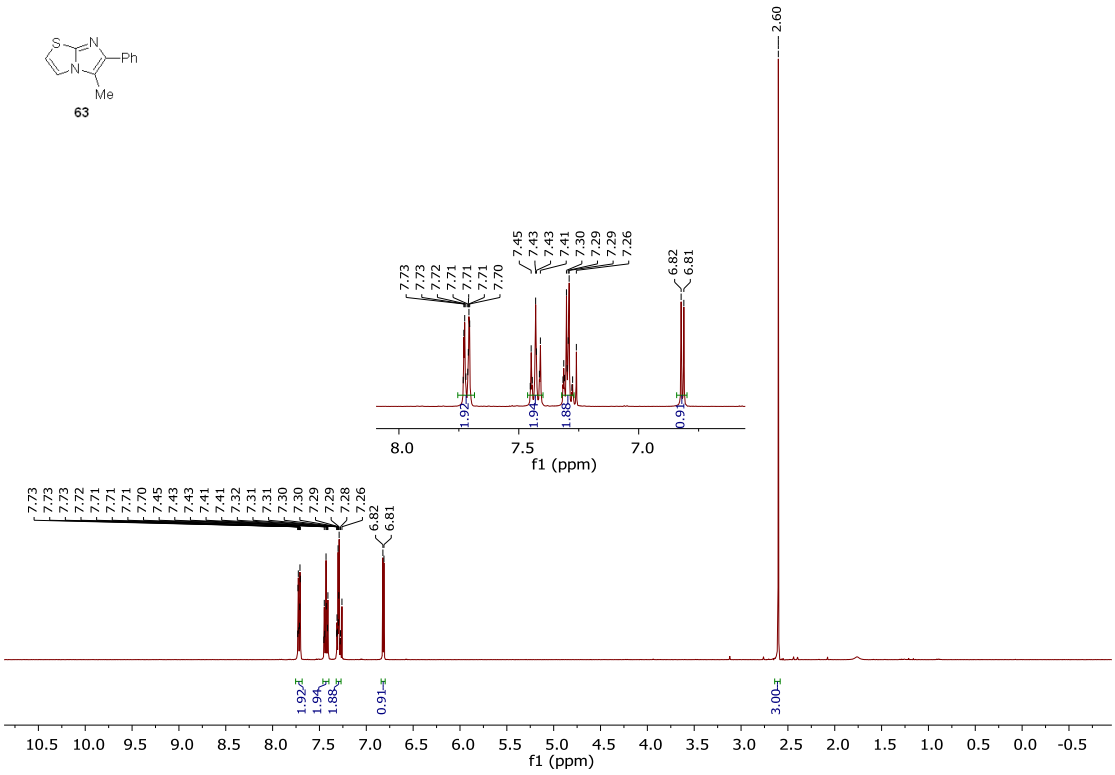

CO2Me
Me
N
H
60
77.5
77.2
76.8
127.2
122.5
121.9
121.4
110.6
104.6
50.9
14.4
166.7
144.1
134.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

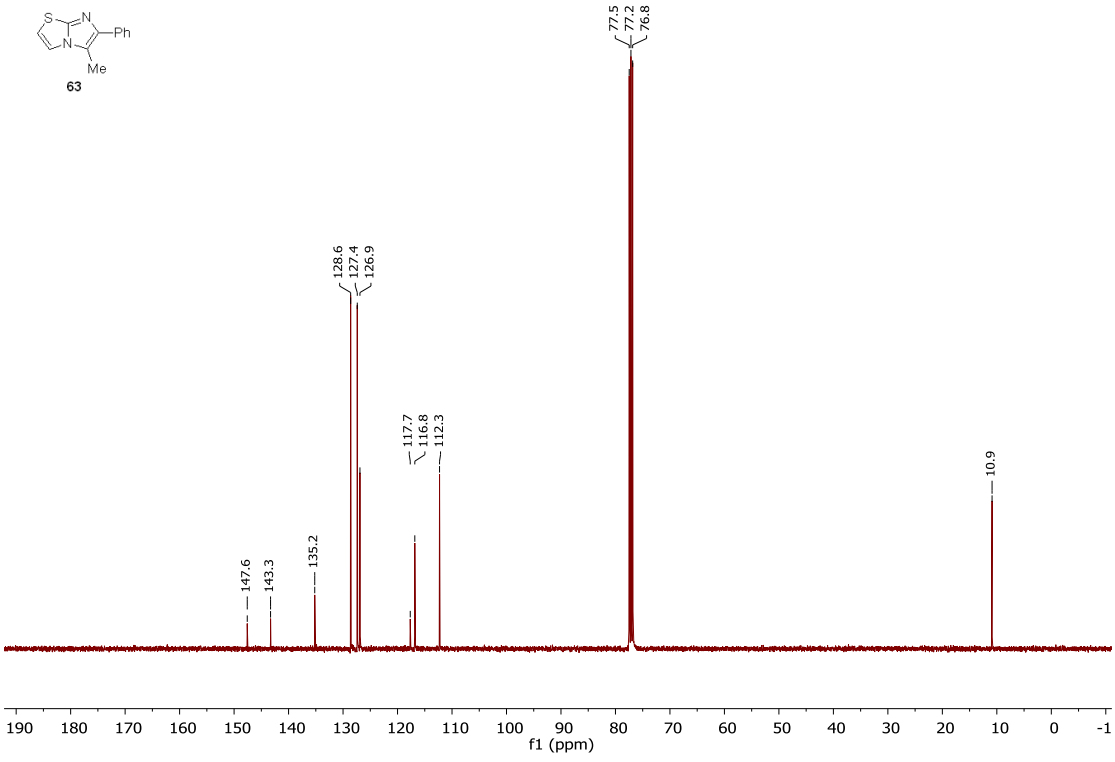

Me
CO2Et
N
H
61
2.62
1.46
1.44
1.42
4.46
4.44
4.42
4.40
7.69
7.68
7.68
7.68
7.67
7.66
7.66
7.66
7.39
7.38
7.38
7.36
7.36
7.36
7.34
7.34
7.33
7.32
7.31
7.30
7.26
7.17
7.16
7.15
7.15
7.14
7.13
7.13
8.74
0.83
0.96
1.92
0.98
2.00
2.98
3.02
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

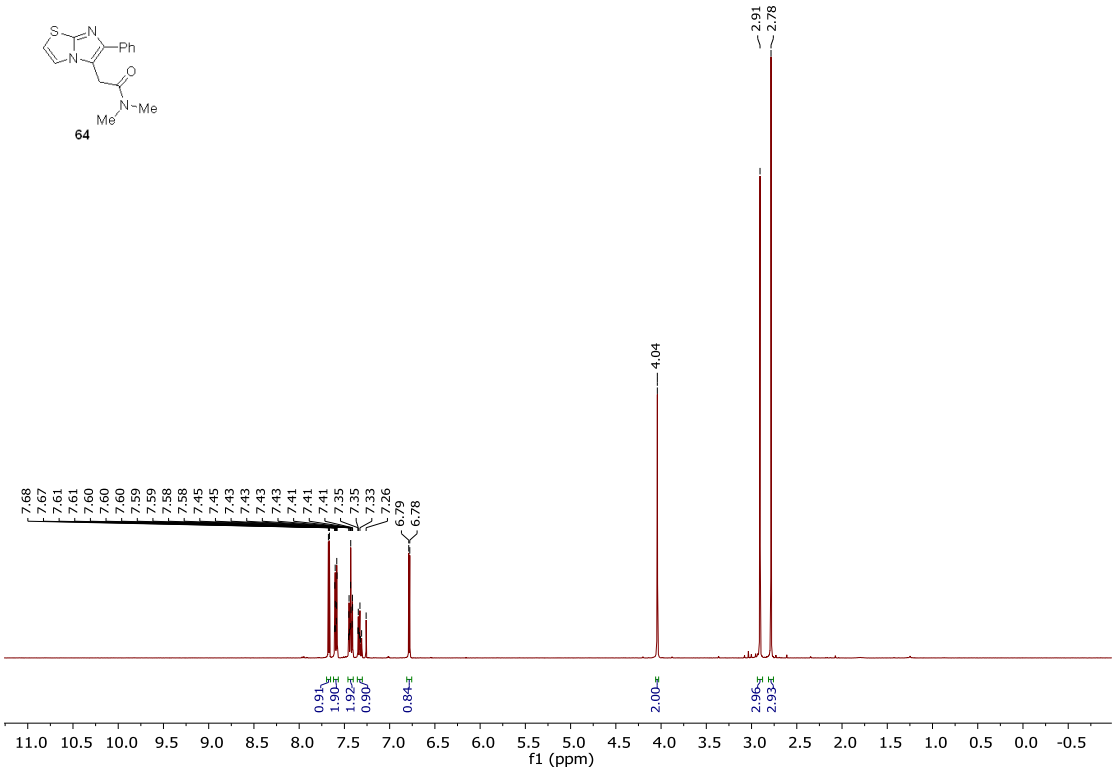

Me
CO2Et
N
H
61
77.5
77.2
76.8
128.7
125.7
123.6
120.9
120.3
120.0
111.7
162.8
136.0
60.8
14.6
10.1
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

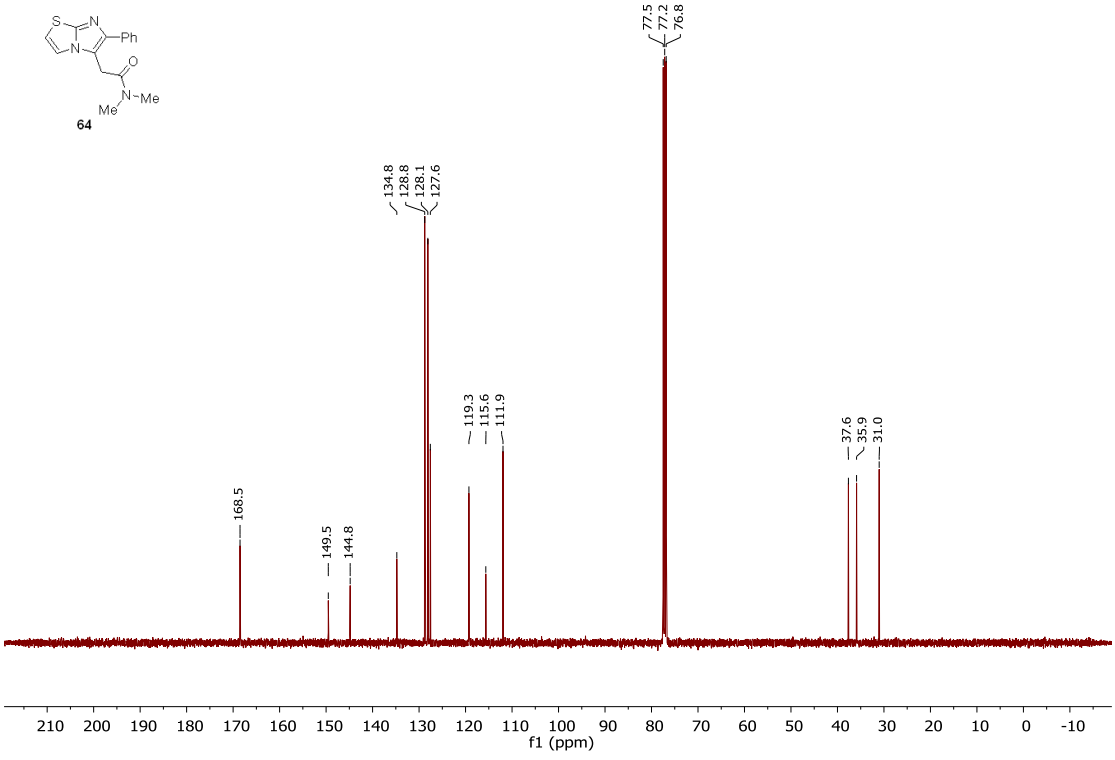

Me
N
Me
O
CO2Et
N
H
62
3.10
2.97
1.42
1.40
1.38
4.41
4.39
4.37
4.35
4.27
7.36
7.36
7.34
7.34
7.34
7.32
7.32
7.31
7.30
7.29
7.28
7.26
7.15
7.15
7.13
7.13
7.13
7.11
7.11
7.81
7.81
7.79
7.79
8.85
0.97
0.97
1.99
1.00
2.00
1.99
2.95
2.90
3.03
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

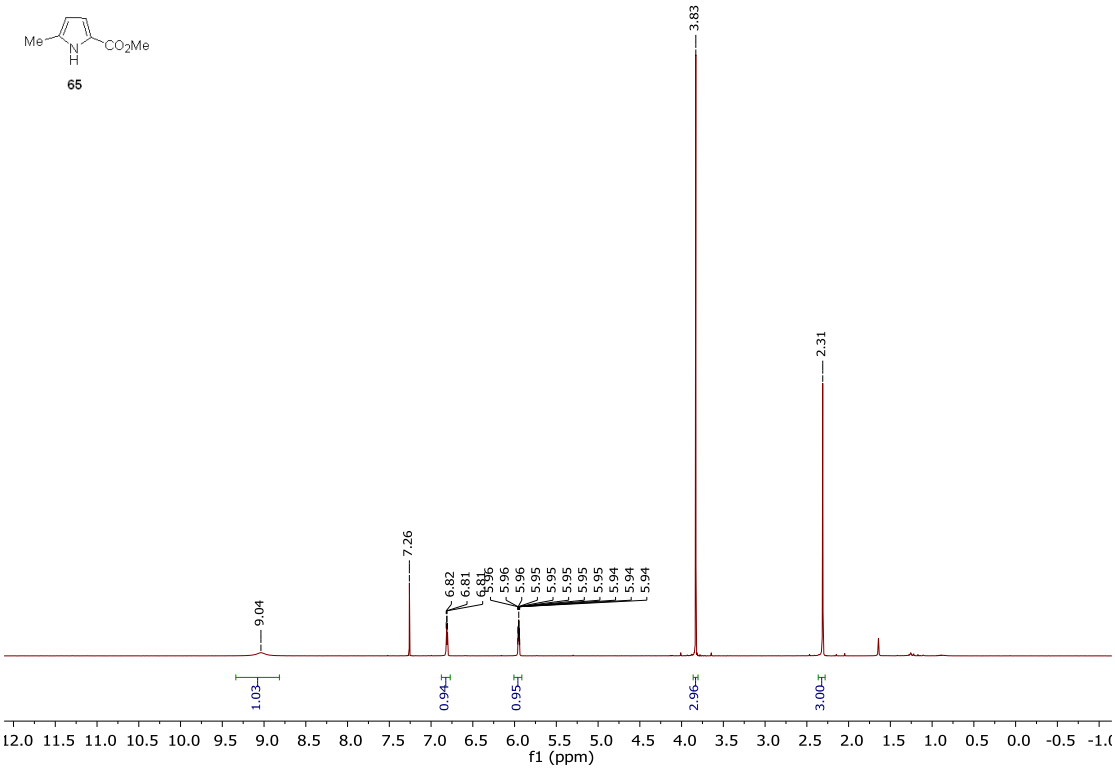

Me
N
Me
O
CO2Et
N
H
62
77.5
77.2
76.8
170.8
162.0
136.0
128.3
125.9
123.6
121.7
120.7
117.8
111.8
61.0
37.6
35.9
31.1
14.5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

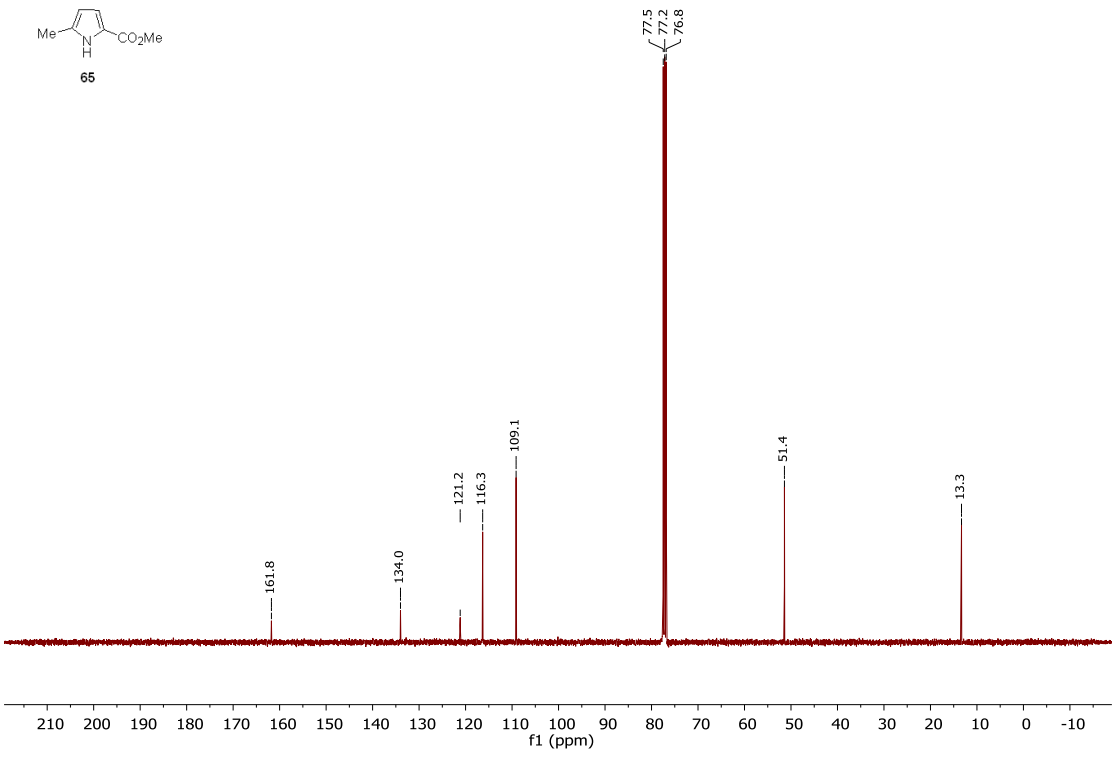

Ph
Me
63
2.60
7.73
7.73
7.73
7.72
7.71
7.71
7.71
7.70
7.45
7.43
7.43
7.41
7.41
7.32
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.26
6.82
6.81
1.92
1.94
1.88
0.91
3.00
f1 (ppm)

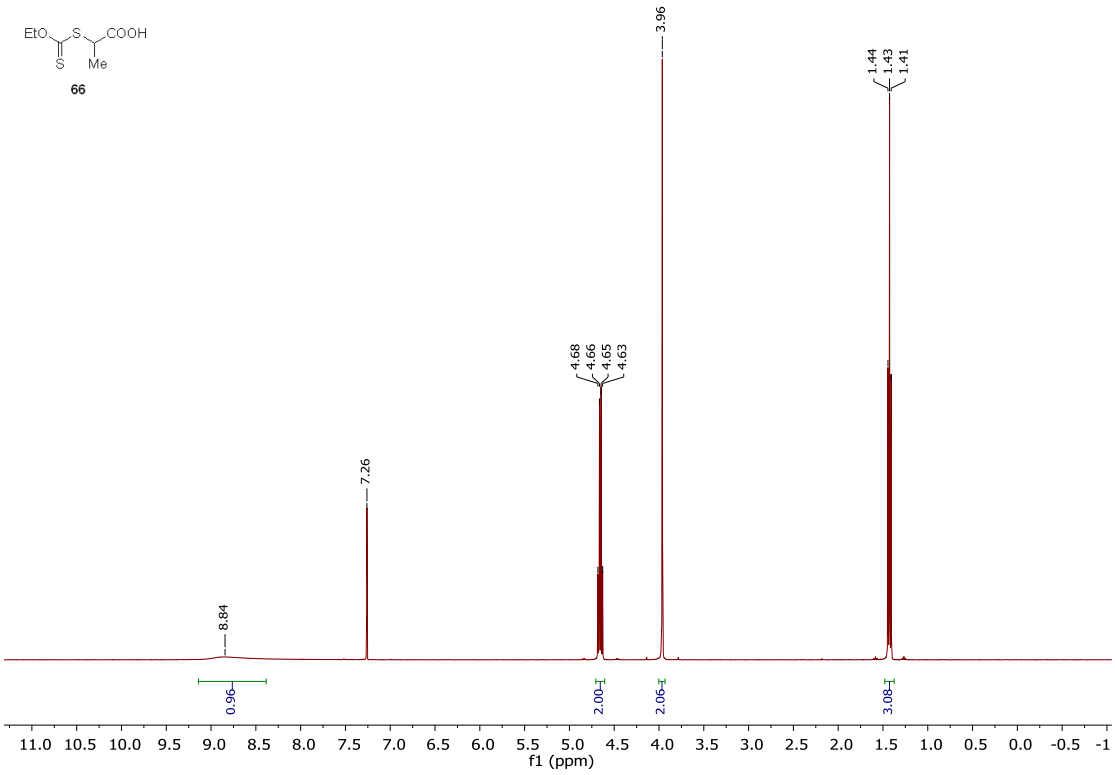

Ph
Me
63
77.5
77.2
76.8
128.6
127.4
126.9
117.7
116.8
112.3
147.6
143.3
135.2
10.9
f1 (ppm)

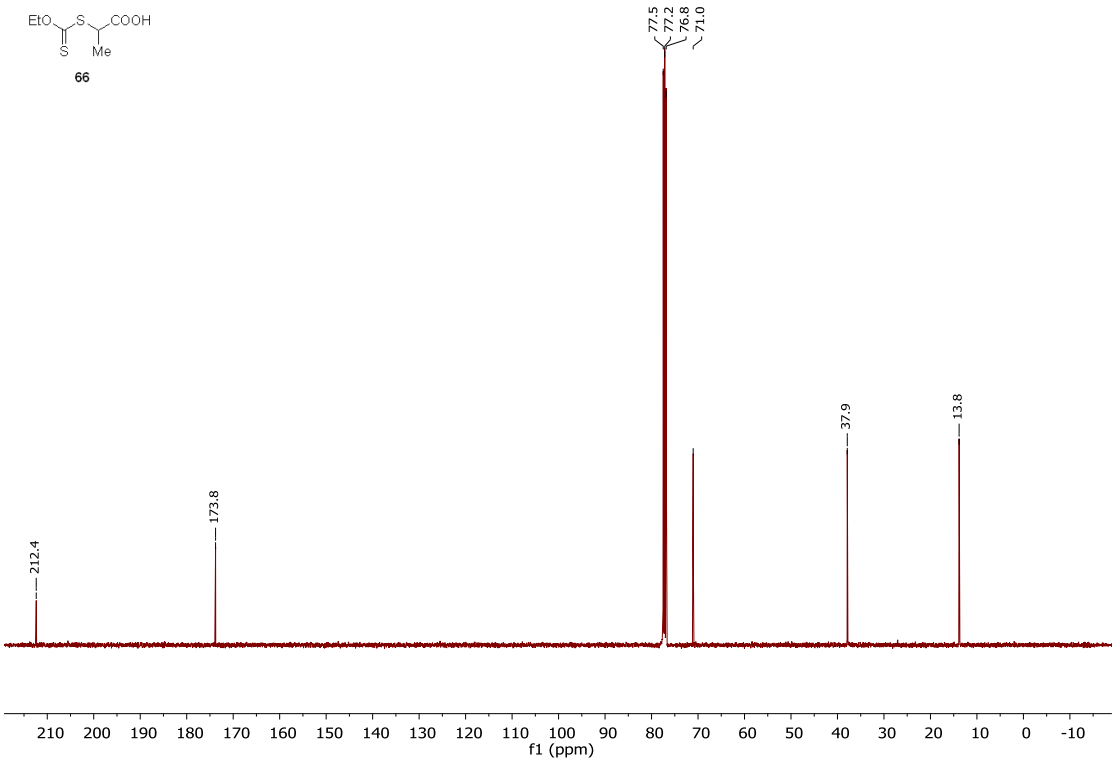

64
2.91
2.78
4.04
7.68
7.67
7.61
7.61
7.60
7.60
7.60
7.59
7.59
7.58
7.58
7.45
7.45
7.43
7.43
7.43
7.43
7.41
7.41
7.41
7.35
7.35
7.33
7.26
6.79
6.78
0.91
1.90
1.92
0.90
0.84
2.00
2.96
2.93
f1 (ppm)

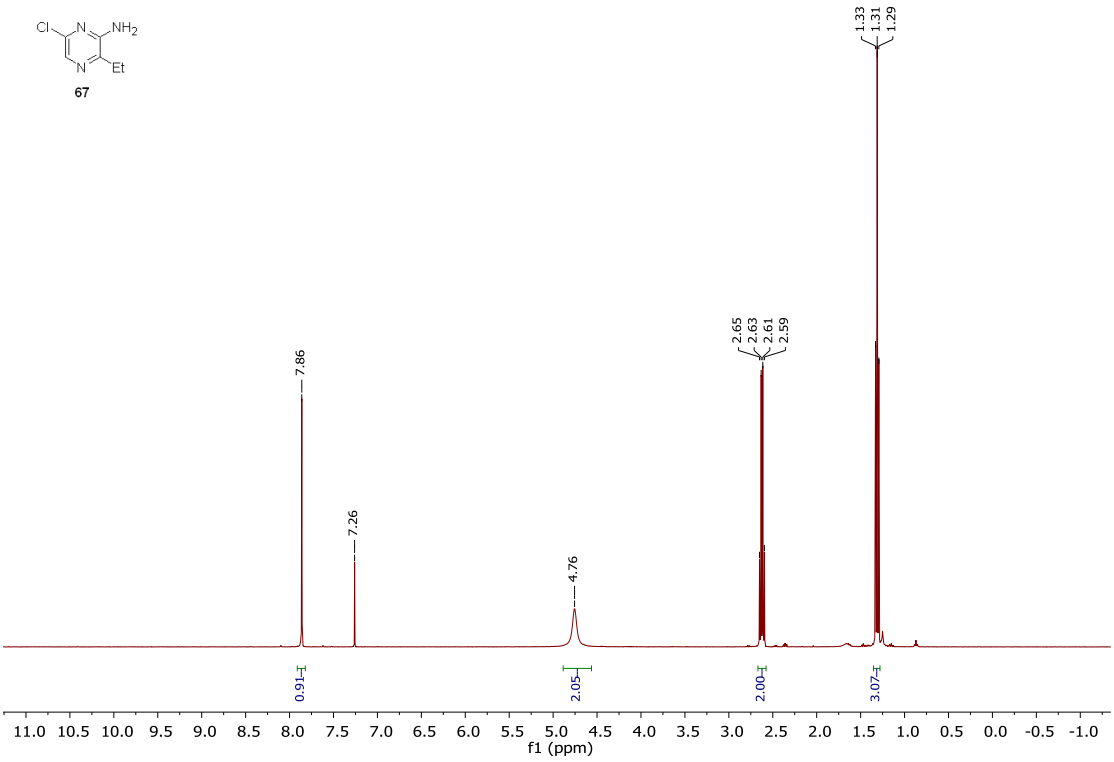

64
77.5
77.2
76.8
134.8
128.8
128.1
127.6
119.3
115.6
111.9
168.5
149.5
144.8
37.6
35.9
31.0
f1 (ppm)

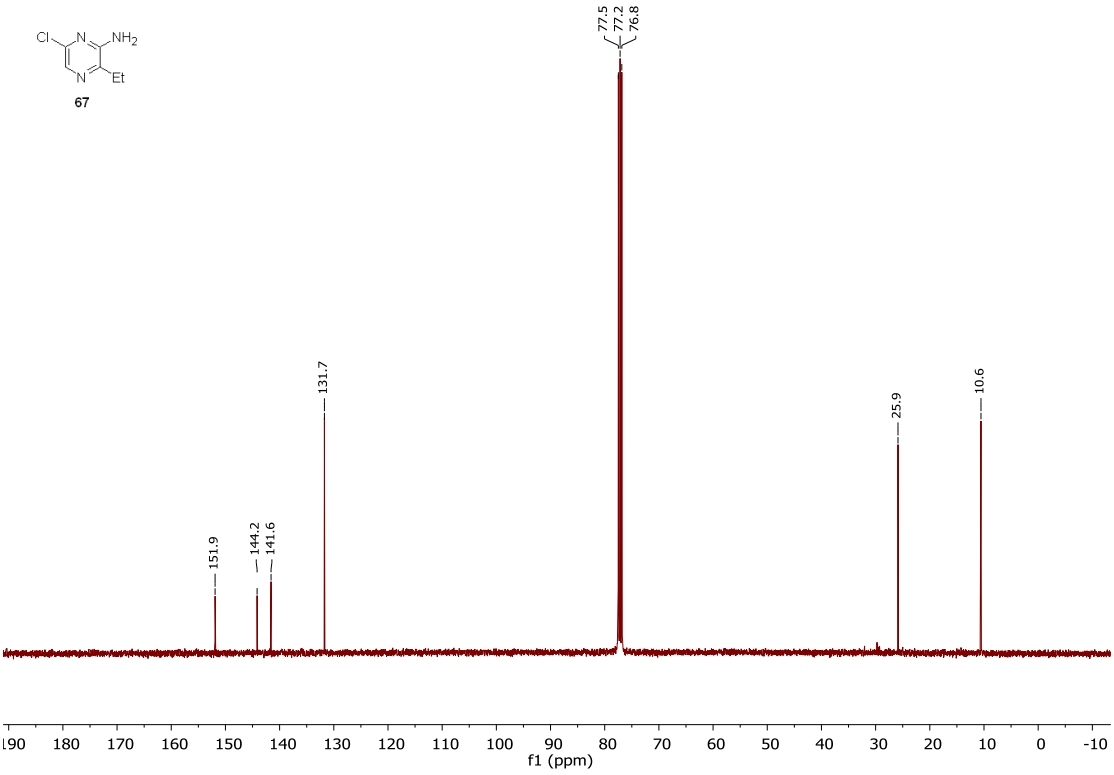

Me
CO2Me
65
3.83
2.31
7.26
6.82
6.81
5.96
5.95
5.94
9.04
1.03
0.94
0.95
2.96
3.00
f1 (ppm)

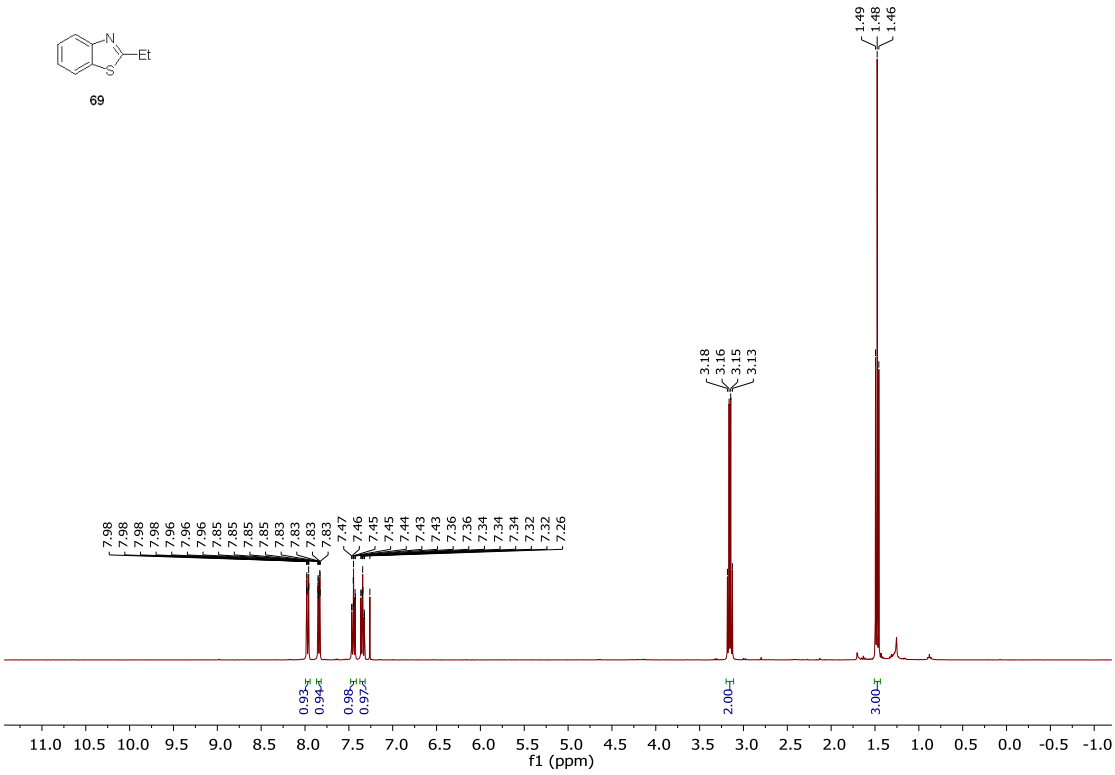

Me
CO2Me
65
77.5
77.2
76.8
161.8
134.0
121.2
116.3
109.1
51.4
13.3
f1 (ppm)

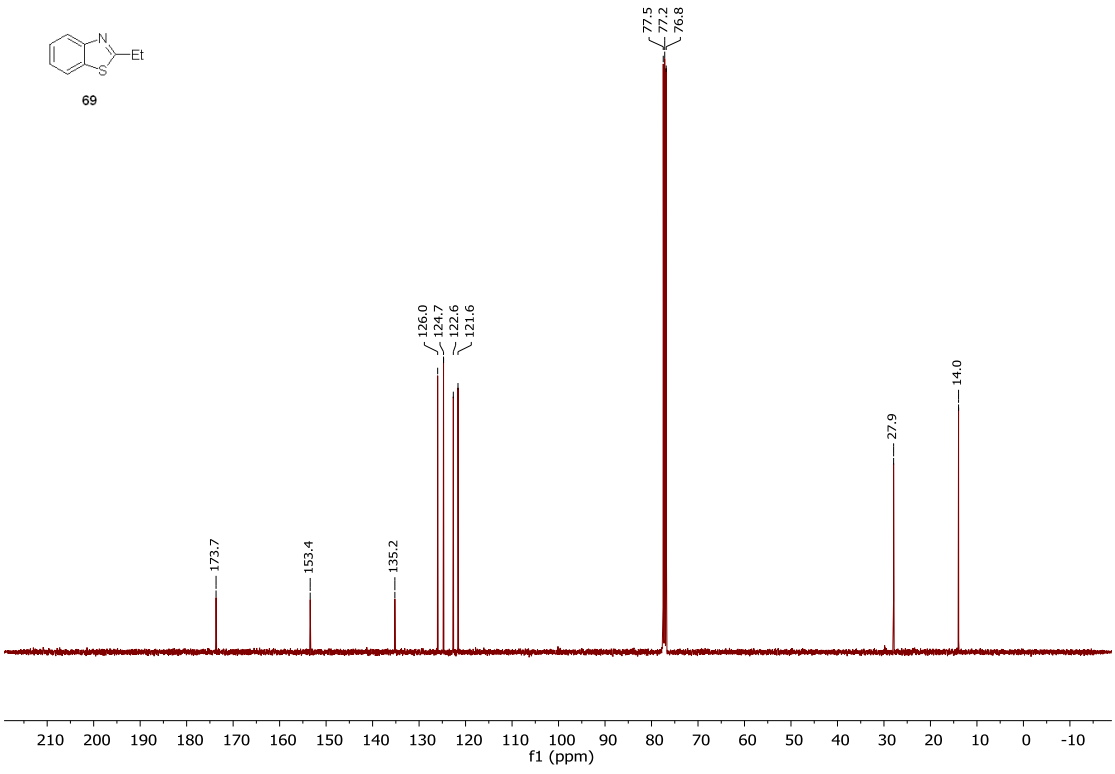

EtO
S
S
COOH
Me
66
3.96
1.44
1.43
1.41
4.68
4.66
4.65
4.63
7.26
8.84
0.96
2.00
2.06
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

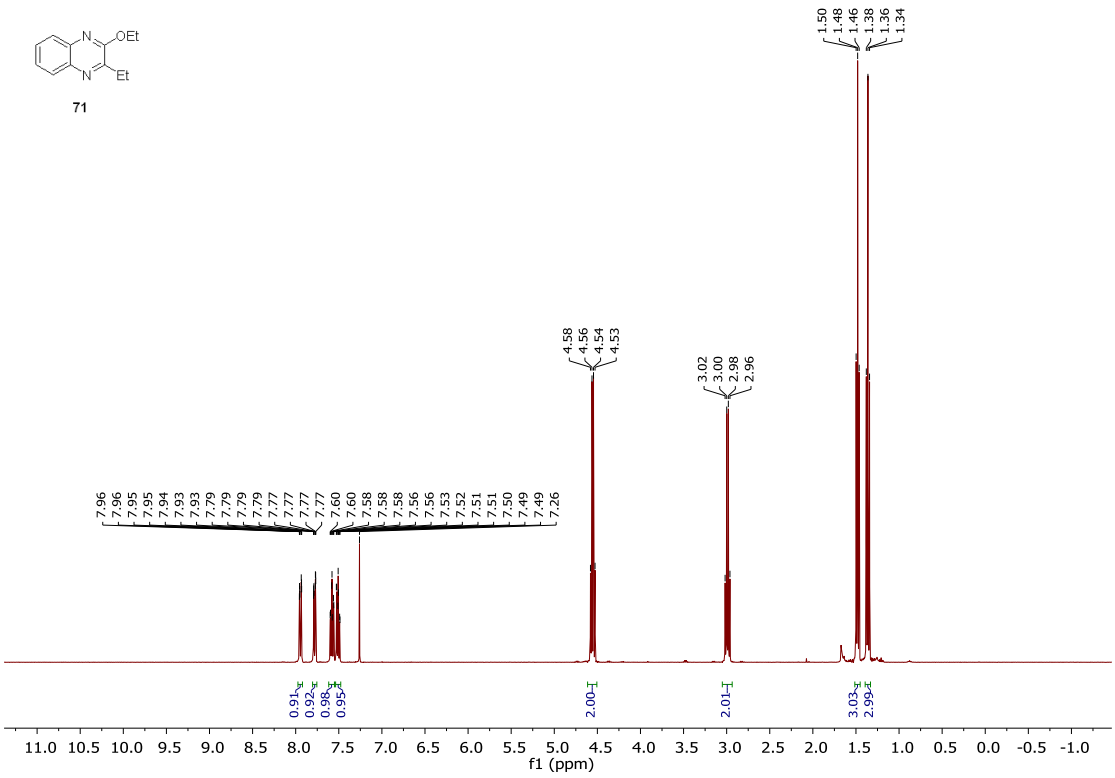

EtO
S
S
COOH
Me
66
77.5
77.2
76.8
71.0
37.9
13.8
212.4
173.8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

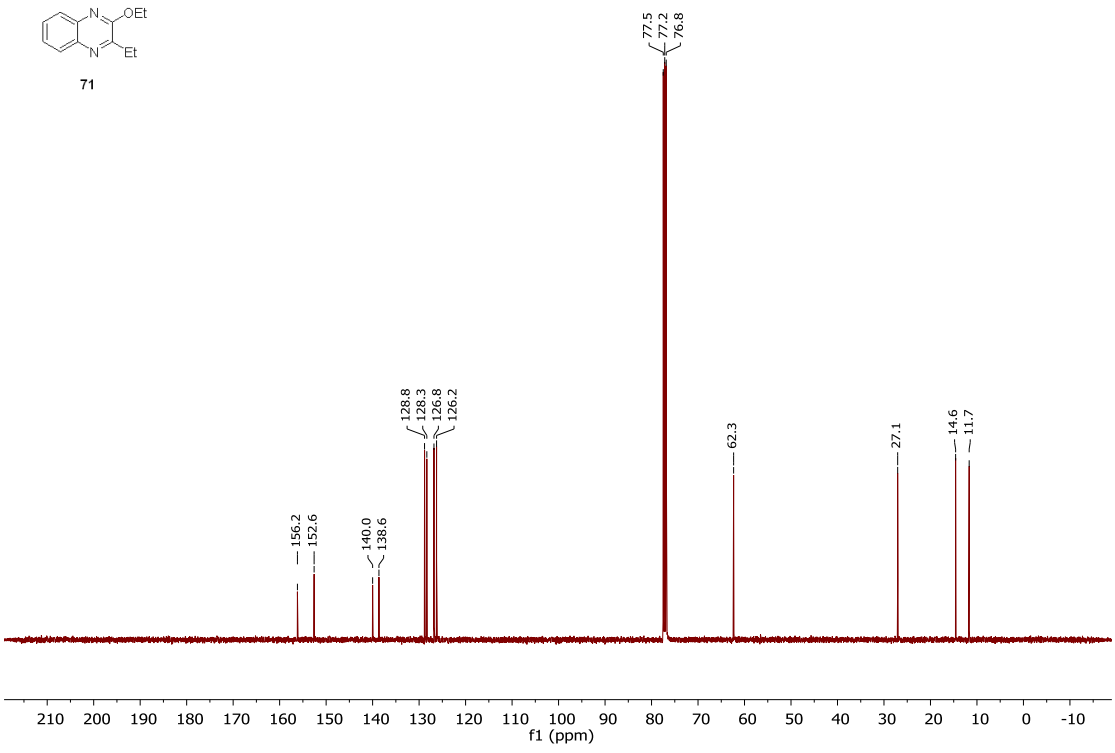

Cl
N
NH2
N
Et
67
1.33
1.31
1.29
2.65
2.63
2.61
2.59
7.86
7.26
4.76
0.91
2.05
2.00
3.07
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

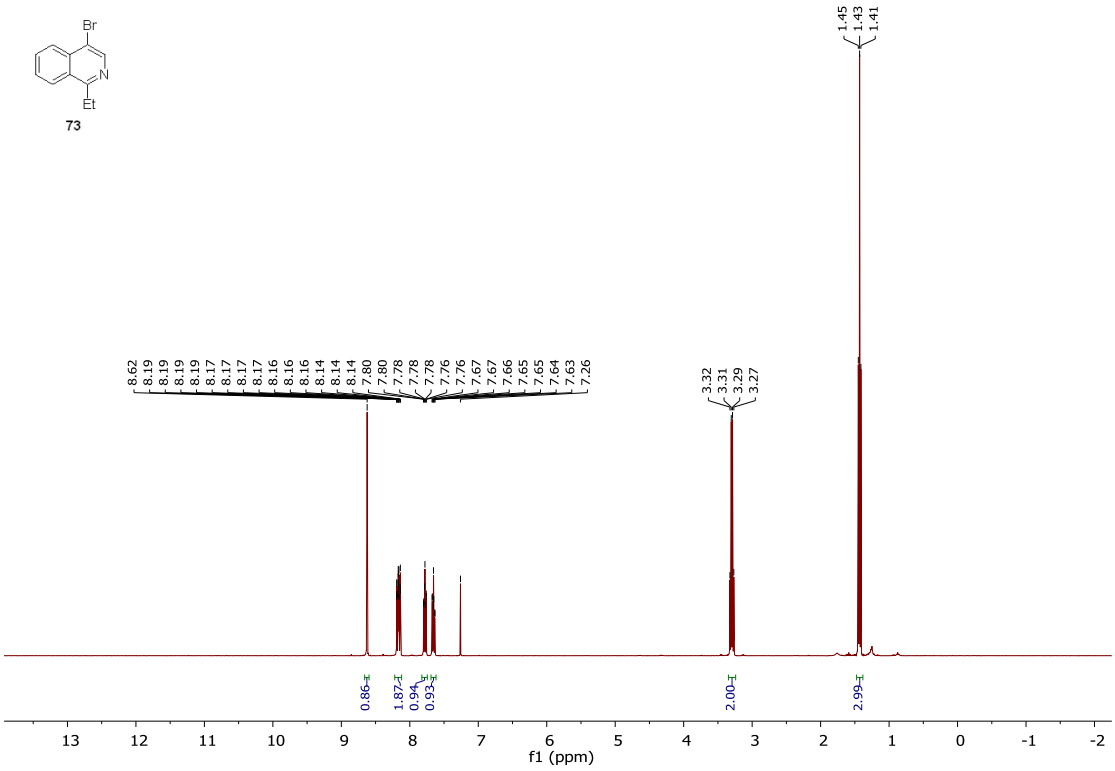

Cl
N
NH2
N
Et
67
77.5
77.2
76.8
131.7
151.9
144.2
141.6
25.9
10.6
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

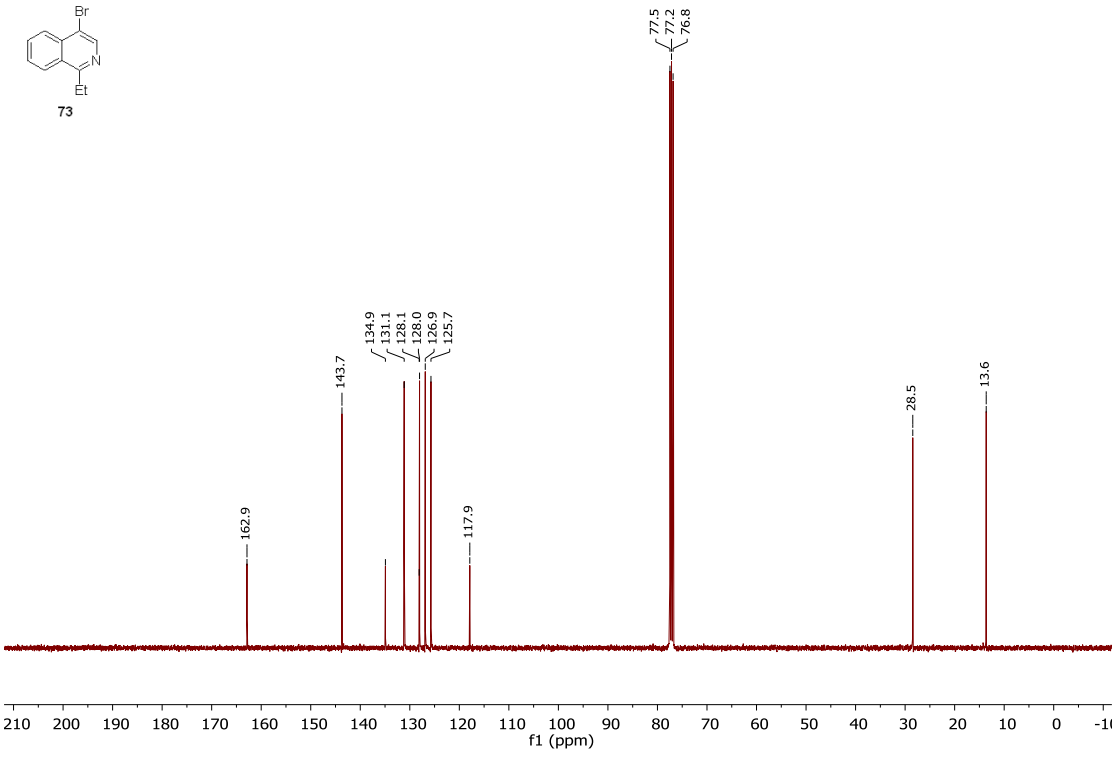

69
7.98
7.98
7.98
7.98
7.96
7.96
7.96
7.85
7.85
7.85
7.83
7.83
7.83
7.83
7.47
7.46
7.45
7.45
7.44
7.43
7.43
7.36
7.36
7.34
7.34
7.34
7.32
7.32
7.26
3.18
3.16
3.15
3.13
1.49
1.48
1.46
0.93
0.94
0.98
0.97
2.00
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

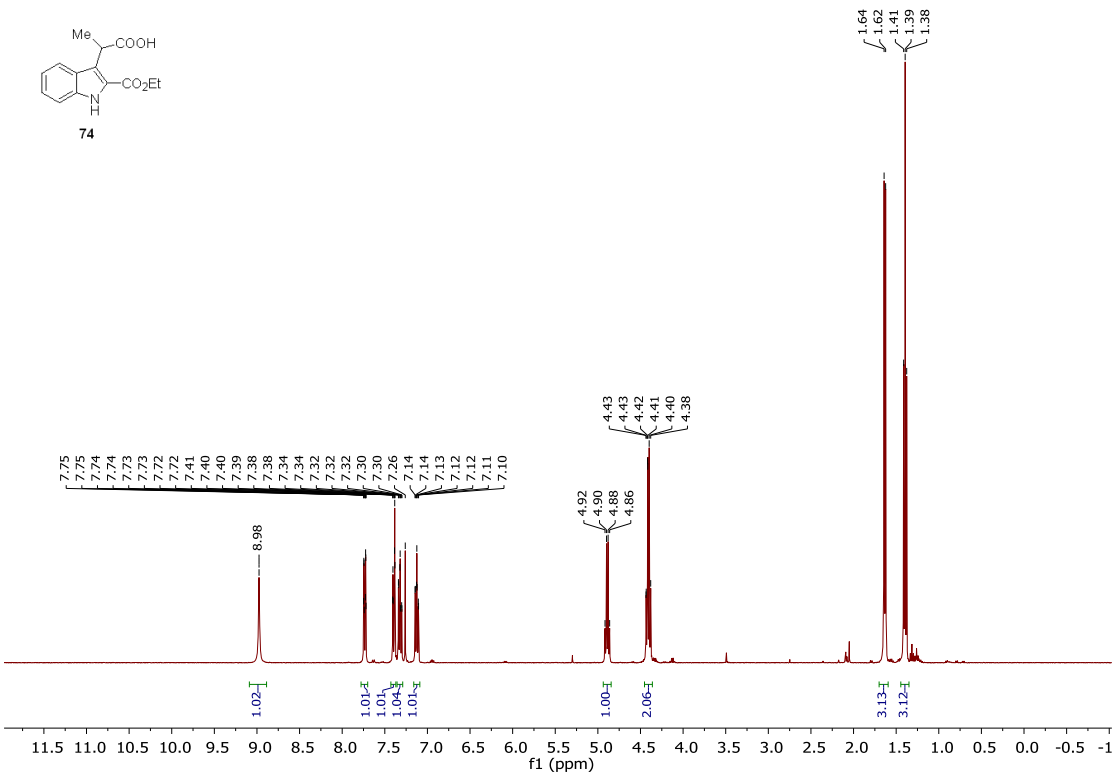

69
77.5
77.2
76.8
126.0
124.7
122.6
121.6
173.7
153.4
135.2
27.9
14.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

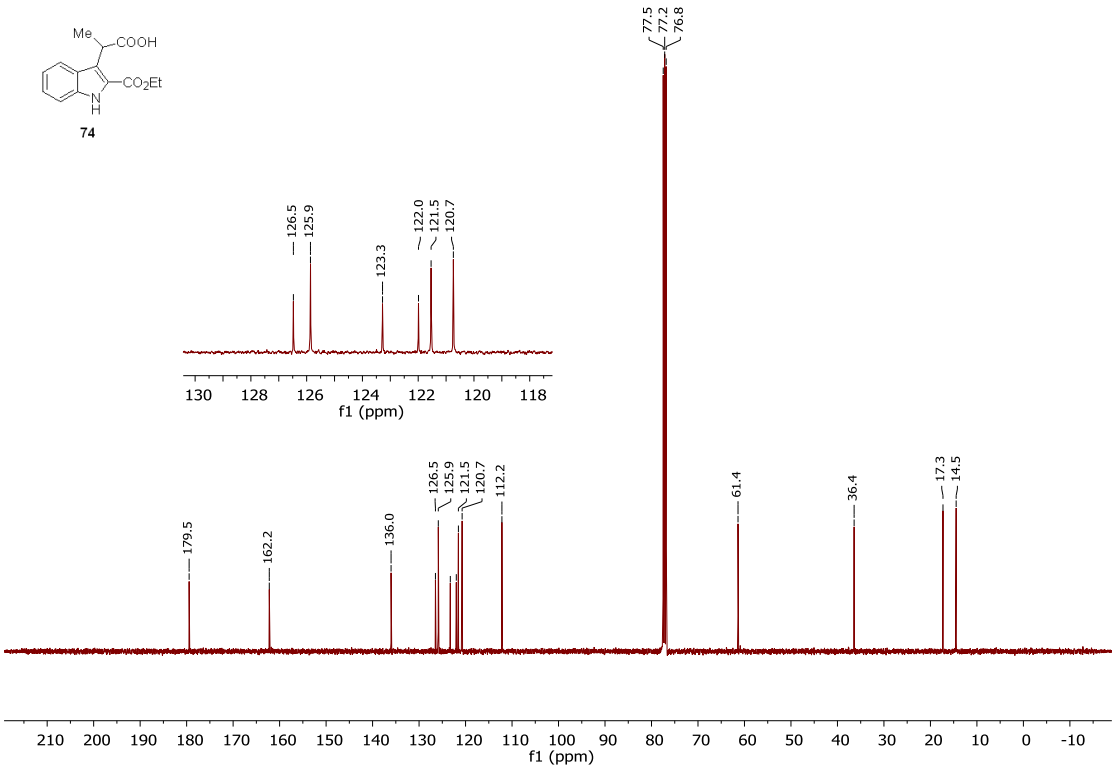

OEt
Et
71
1.50
1.48
1.46
1.38
1.36
1.34
4.58
4.56
4.54
4.53
3.02
3.00
2.98
2.96
7.96
7.96
7.95
7.95
7.94
7.93
7.93
7.79
7.79
7.79
7.79
7.77
7.77
7.77
7.77
7.60
7.60
7.58
7.58
7.58
7.56
7.56
7.53
7.52
7.51
7.51
7.50
7.49
7.49
7.26
0.91
0.92
0.98
0.95
2.00
2.01
3.03
2.99
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

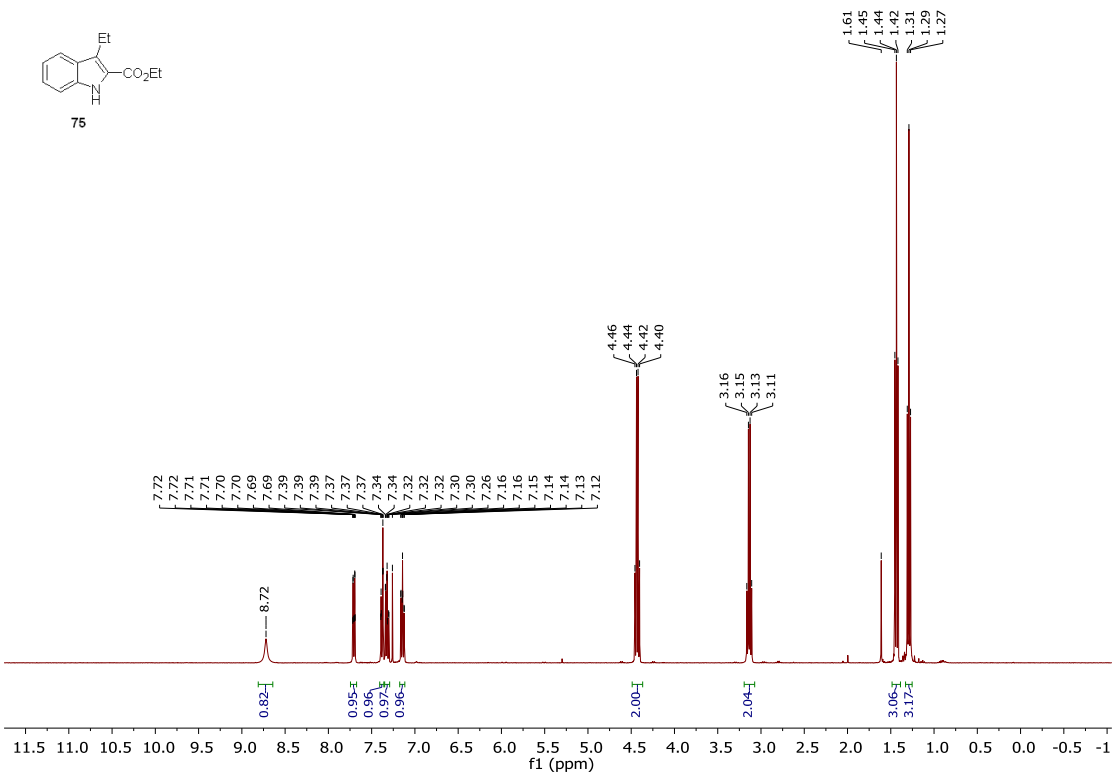

OEt
Et
71
77.5
77.2
76.8
128.8
128.3
126.8
126.2
156.2
152.6
140.0
138.6
62.3
27.1
14.6
11.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

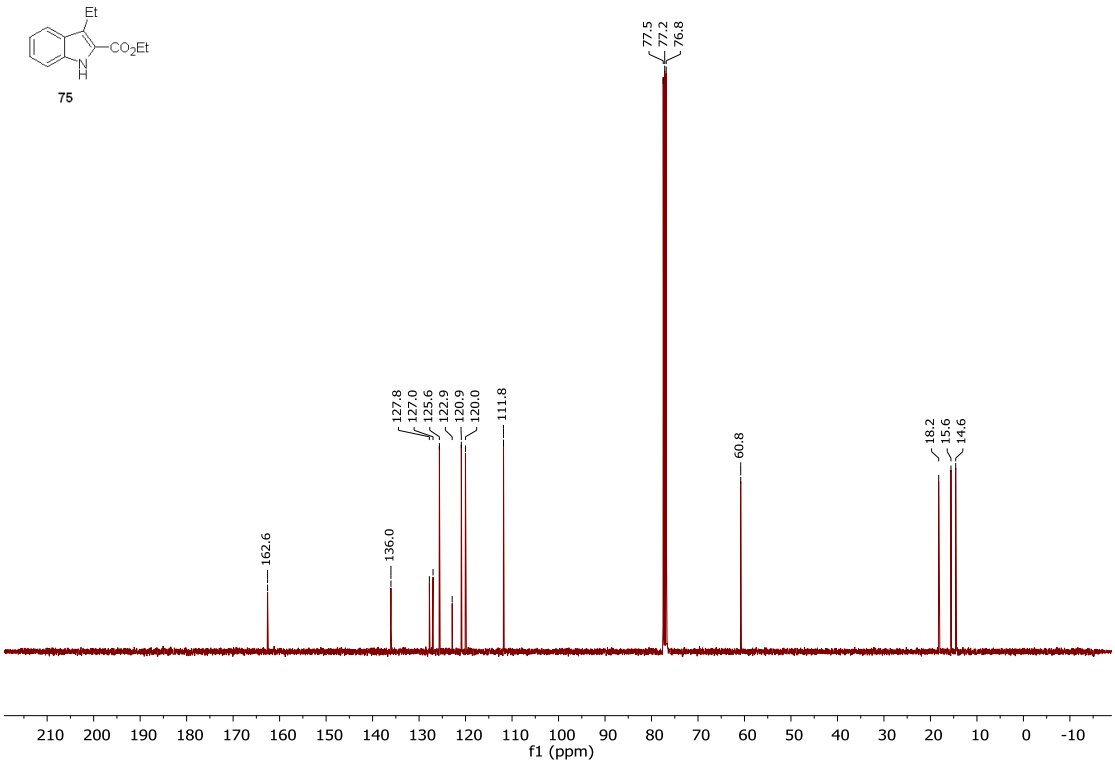

Br
N
Et
73
1.45
1.43
1.41
8.62
8.19
8.19
8.19
8.17
8.17
8.17
8.16
8.16
8.14
8.14
8.14
7.80
7.80
7.78
7.78
7.78
7.76
7.76
7.67
7.67
7.66
7.65
7.65
7.64
7.63
7.26
3.32
3.31
3.29
3.27
0.86
1.87
0.94
0.93
2.00
2.99
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

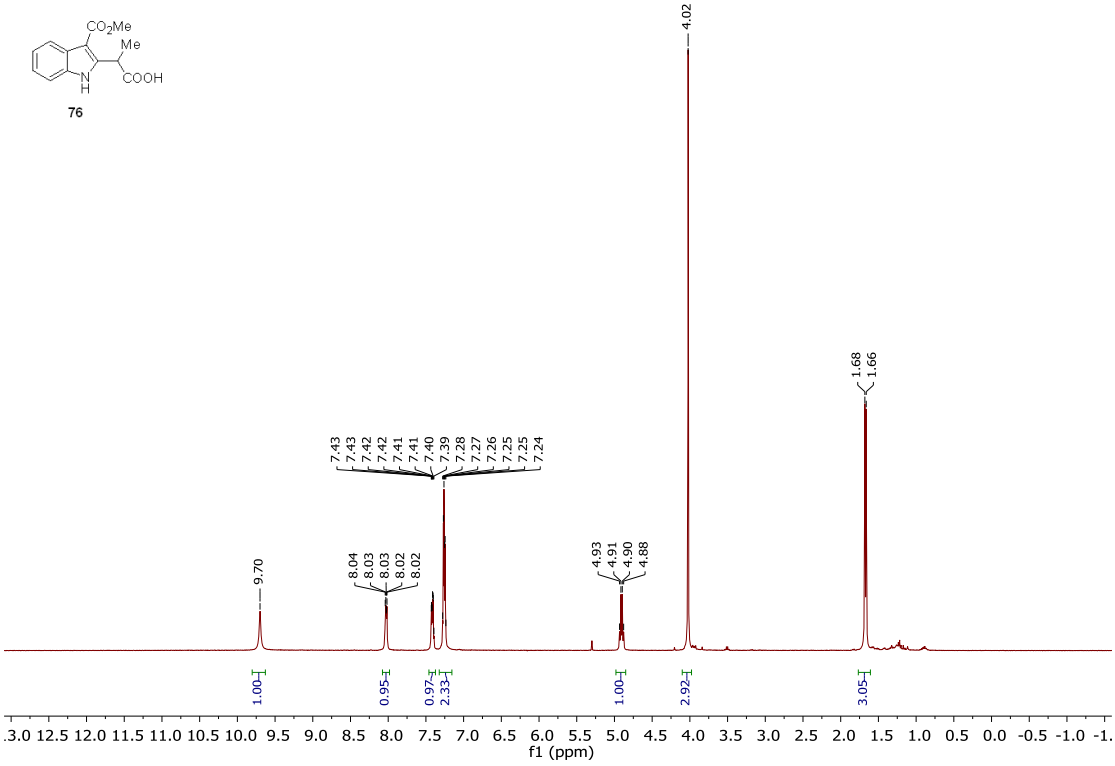

Br
N
Et
73
77.5
77.2
76.8
134.9
131.1
128.1
128.0
126.9
125.7
143.7
162.9
117.9
28.5
13.6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

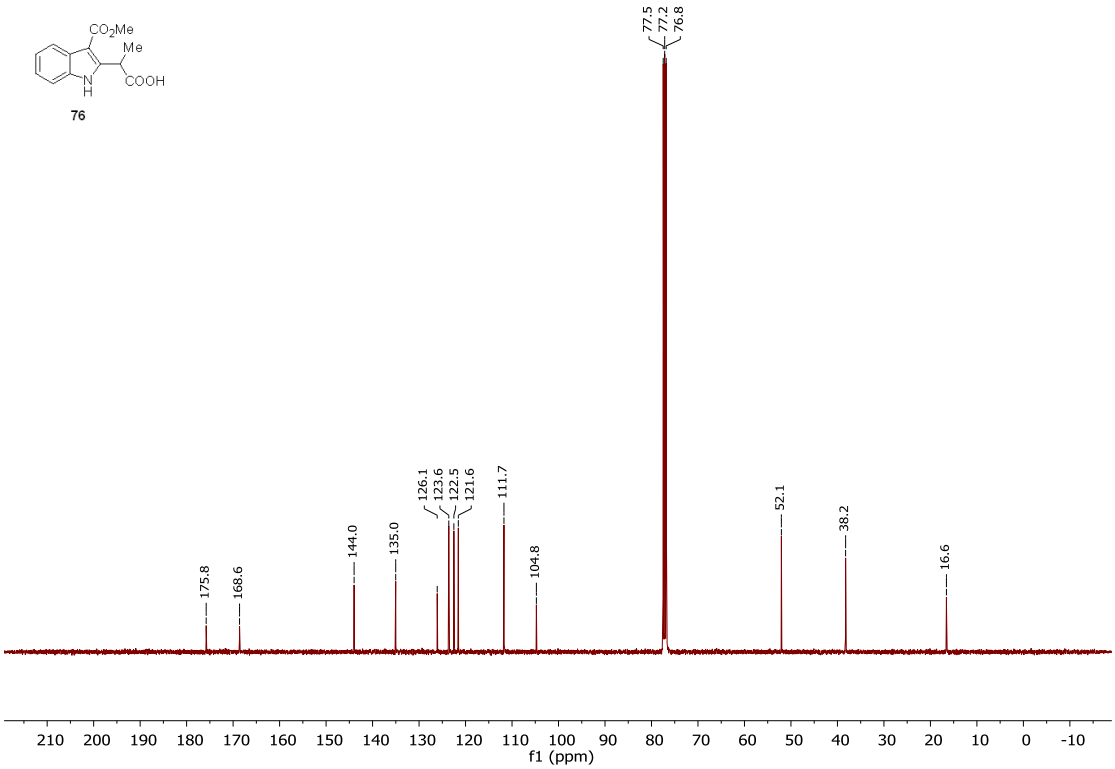

Me
COOH
CO2Et
N
H
74
1.64
1.62
1.41
1.39
1.38
4.43
4.43
4.42
4.41
4.40
4.38
4.92
4.90
4.88
4.86
8.98
1.02
1.01
1.01
1.04
1.01
1.00
2.06
3.13
3.12
f1 (ppm)

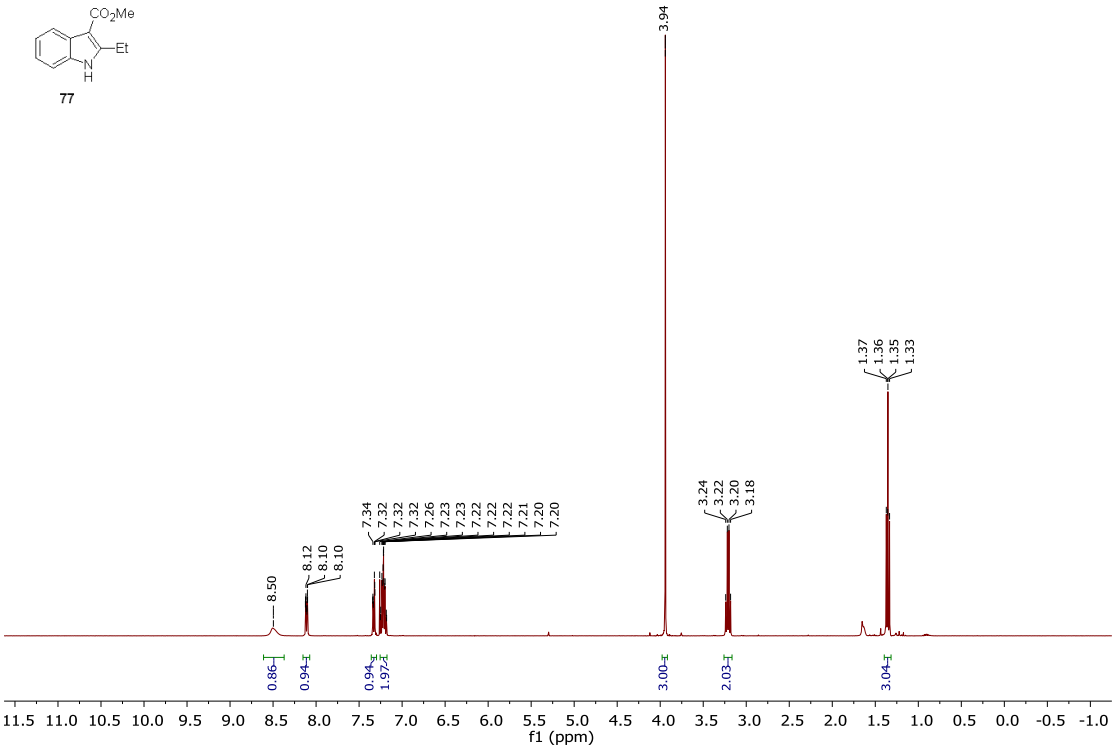

Me
COOH
CO2Et
N
H
74
77.5
77.2
76.8
126.5
125.9
123.3
122.0
121.5
120.7
f1 (ppm)
179.5
162.2
136.0
126.5
125.9
121.5
120.7
112.2
61.4
36.4
17.3
14.5
f1 (ppm)

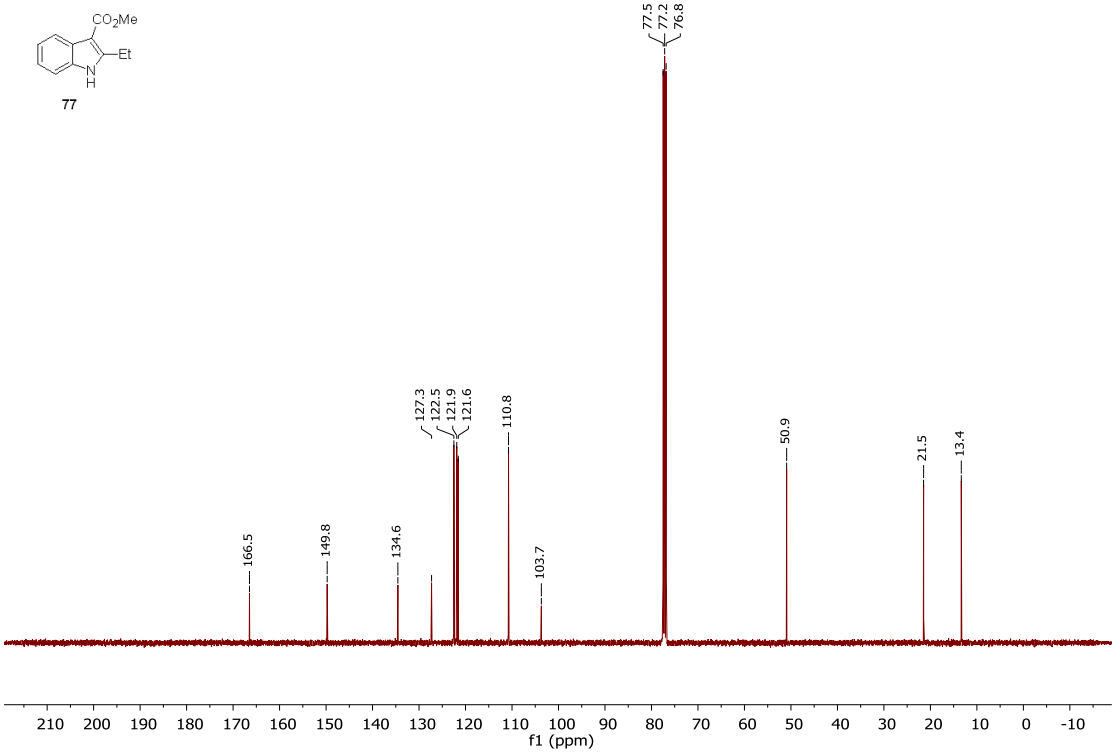

Et
CO2Et
N
H
75
1.61
1.45
1.44
1.42
1.31
1.29
1.27
4.46
4.44
4.42
4.40
3.16
3.15
3.13
3.11
7.72
7.72
7.71
7.71
7.70
7.70
7.69
7.69
7.39
7.39
7.39
7.37
7.37
7.37
7.34
7.34
7.32
7.32
7.32
7.30
7.30
7.26
7.16
7.16
7.15
7.14
7.14
7.13
7.12
8.72
0.82
0.95
0.96
0.97
0.96
2.00
2.04
3.06
3.17
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

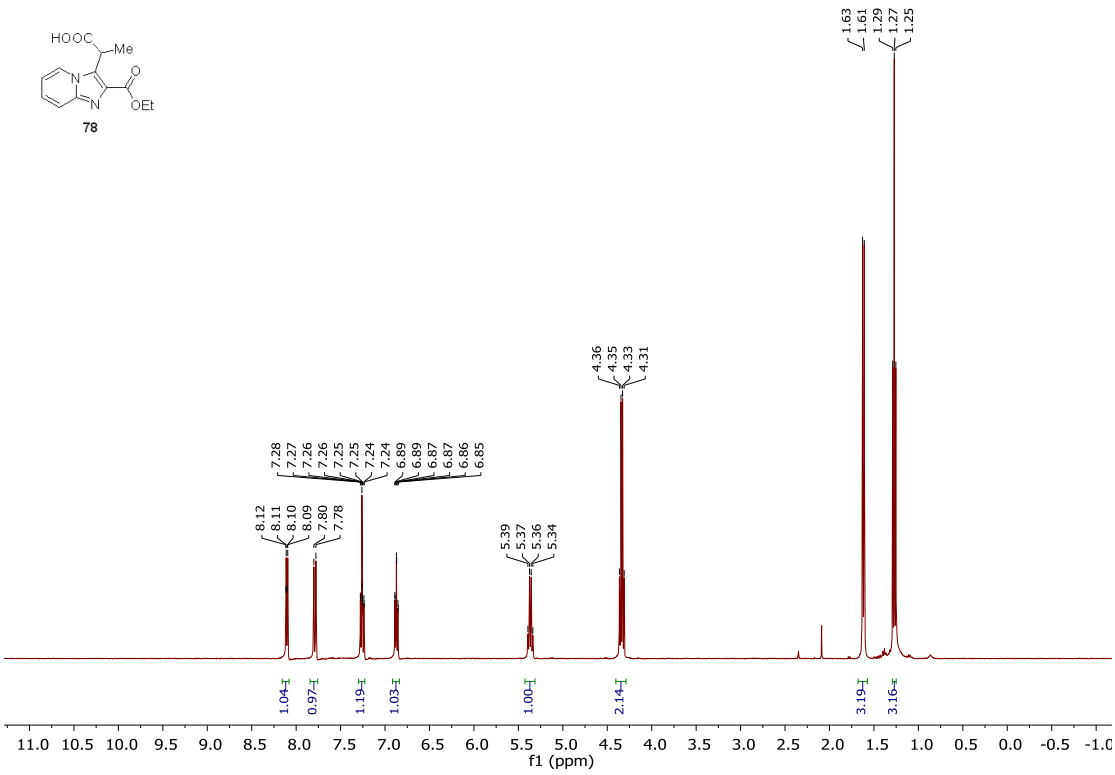

Et
CO2Et
N
H
75
77.5
77.2
76.8
127.8
127.0
125.6
122.9
120.9
120.0
111.8
60.8
18.2
15.6
14.6
162.6
136.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

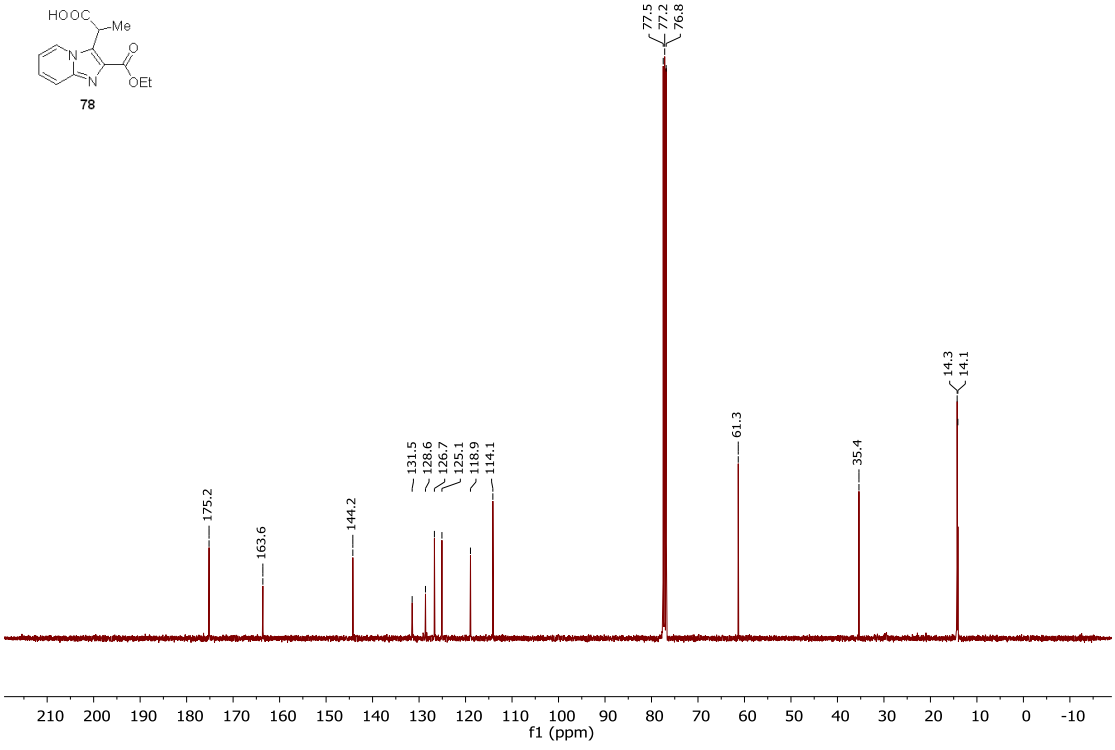

CO2Me
Me
COOH
N
H
76
9.70
8.04
8.03
8.03
8.02
8.02
7.43
7.43
7.42
7.42
7.41
7.41
7.40
7.39
7.28
7.27
7.26
7.25
7.25
7.24
4.93
4.91
4.90
4.88
4.02
1.68
1.66
1.00
0.95
0.97
2.33
1.00
2.92
3.05
f1 (ppm)

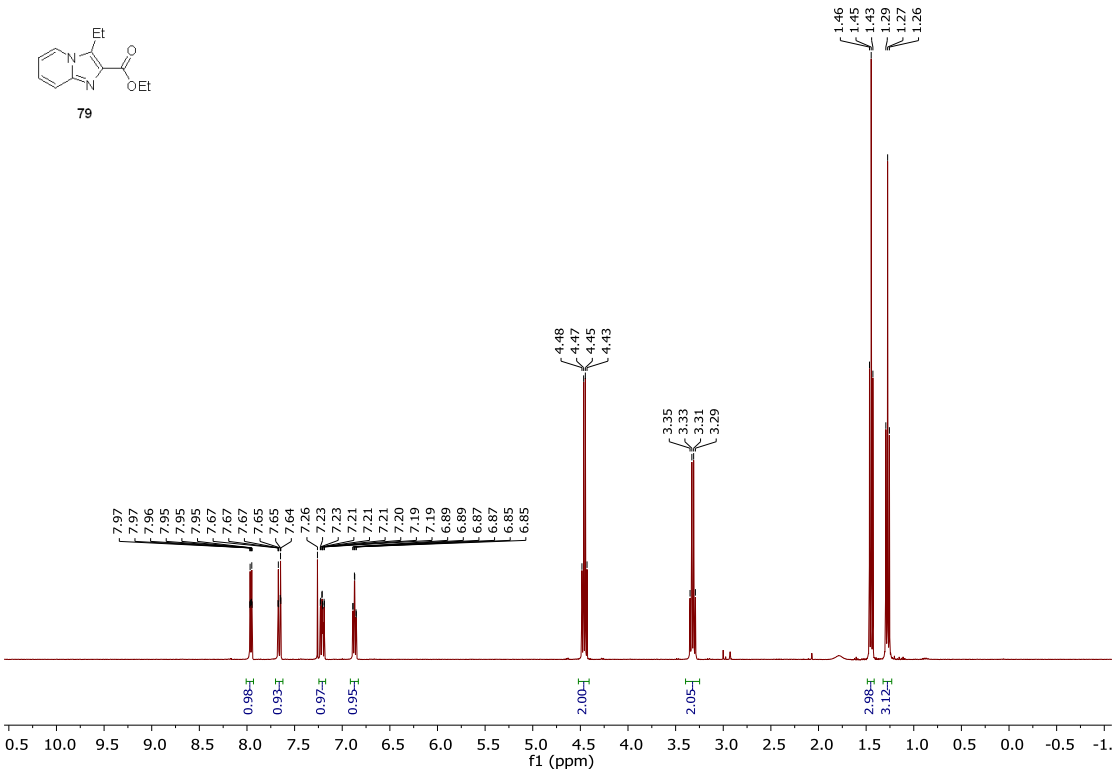

CO2Me
Me
COOH
N
H
76
77.5
77.2
76.8
175.8
168.6
144.0
135.0
126.1
123.6
122.5
121.6
111.7
104.8
52.1
38.2
16.6
f1 (ppm)

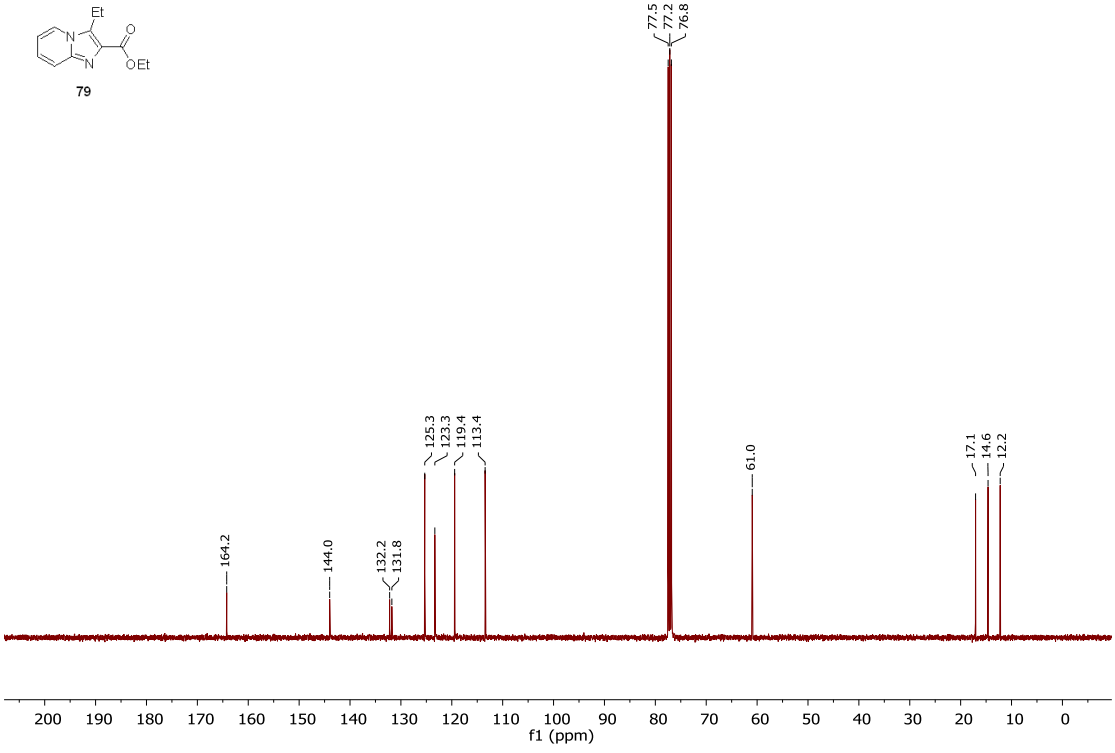

CO2Me
Et
N
H
77
3.94
1.37
1.36
1.35
1.33
3.24
3.22
3.20
3.18
7.34
7.32
7.32
7.32
7.26
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.20
8.12
8.10
8.10
8.50
0.86
0.94
0.94
1.97
3.00
2.03
3.04
f1 (ppm)

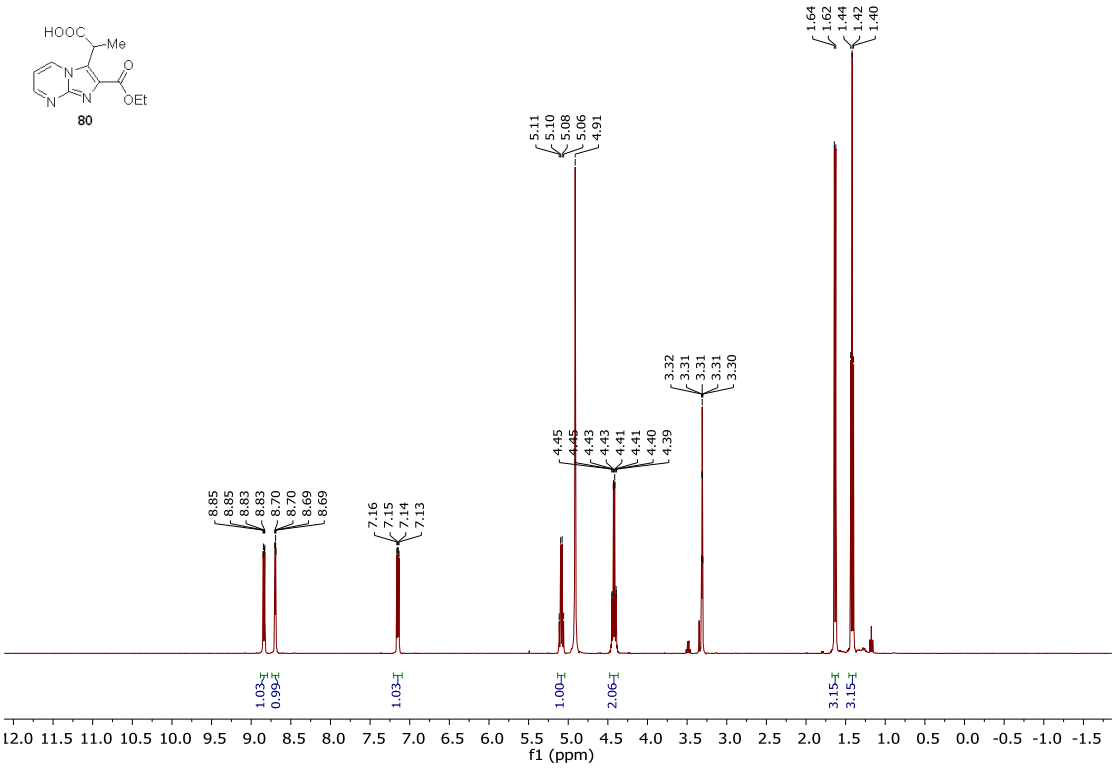

CO2Me
Et
N
H
77
77.5
77.2
76.8
127.3
122.5
121.9
121.6
110.8
50.9
21.5
13.4
166.5
149.8
134.6
103.7
f1 (ppm)

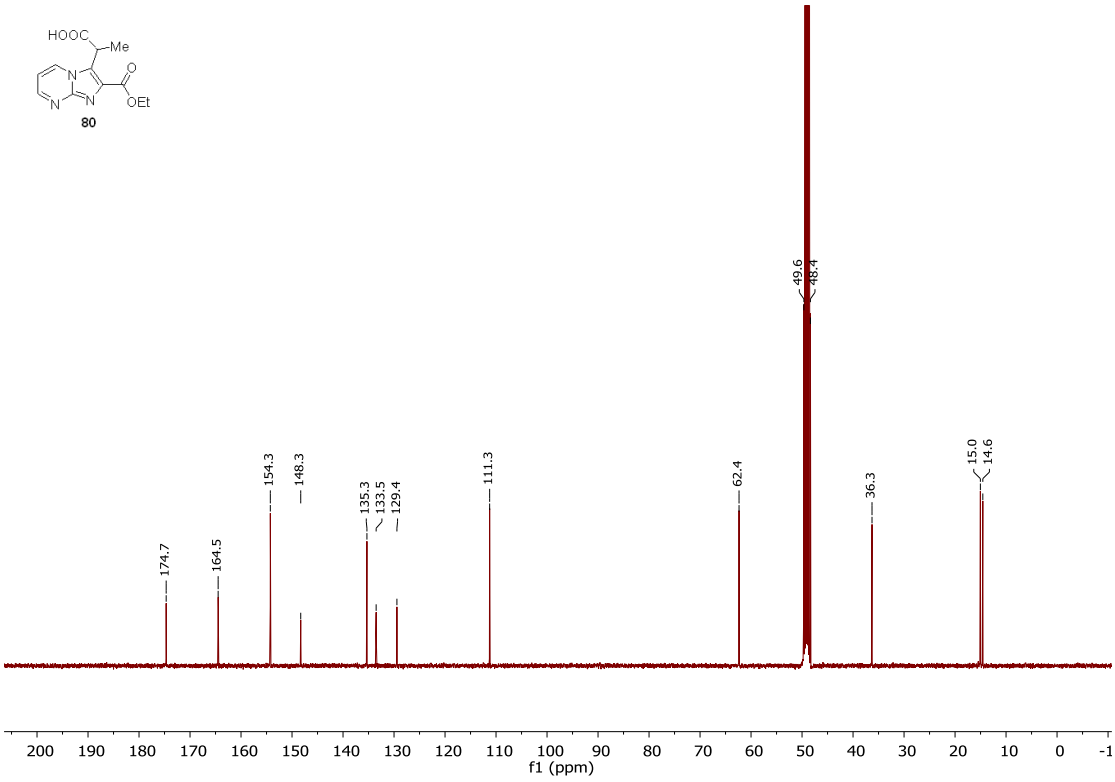

HOOC
Me
N
N
O
OEt
78
1.63
1.61
1.29
1.27
1.25
4.36
4.35
4.33
4.31
7.28
7.27
7.26
7.26
7.25
7.25
7.24
7.24
6.89
6.89
6.87
6.87
6.86
6.85
8.12
8.11
8.10
8.09
7.80
7.78
5.39
5.37
5.36
5.34
1.04
0.97
1.19
1.03
1.00
2.14
3.19
3.16
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

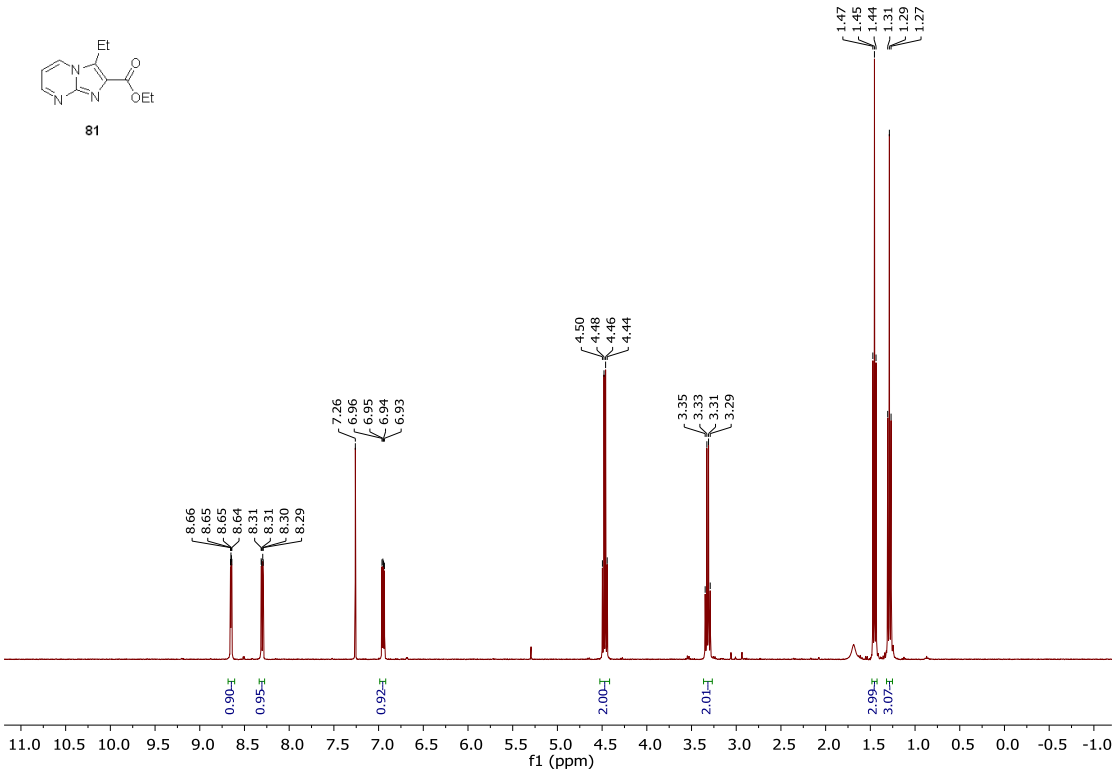

HOOC
Me
N
N
O
OEt
78
77.5
77.2
76.8
14.3
14.1
61.3
35.4
175.2
163.6
144.2
131.5
128.6
126.7
125.1
118.9
114.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

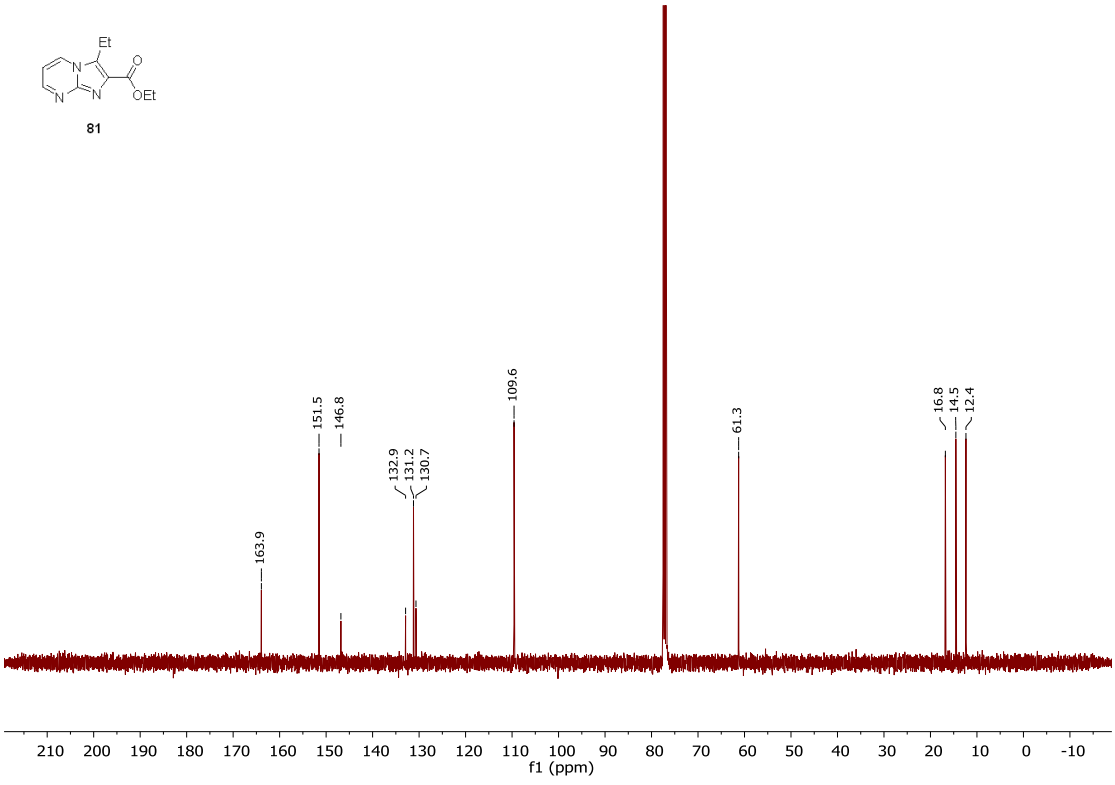

Et
O
N
OEt
79
1.46
1.45
1.43
1.29
1.27
1.26
4.48
4.47
4.45
4.43
3.35
3.33
3.31
3.29
7.97
7.97
7.96
7.95
7.95
7.67
7.67
7.65
7.65
7.64
7.26
7.23
7.23
7.21
7.21
7.21
7.20
7.19
7.19
6.89
6.89
6.87
6.87
6.85
6.85
0.98
0.93
0.97
0.95
2.00
2.05
2.98
3.12
f1 (ppm)

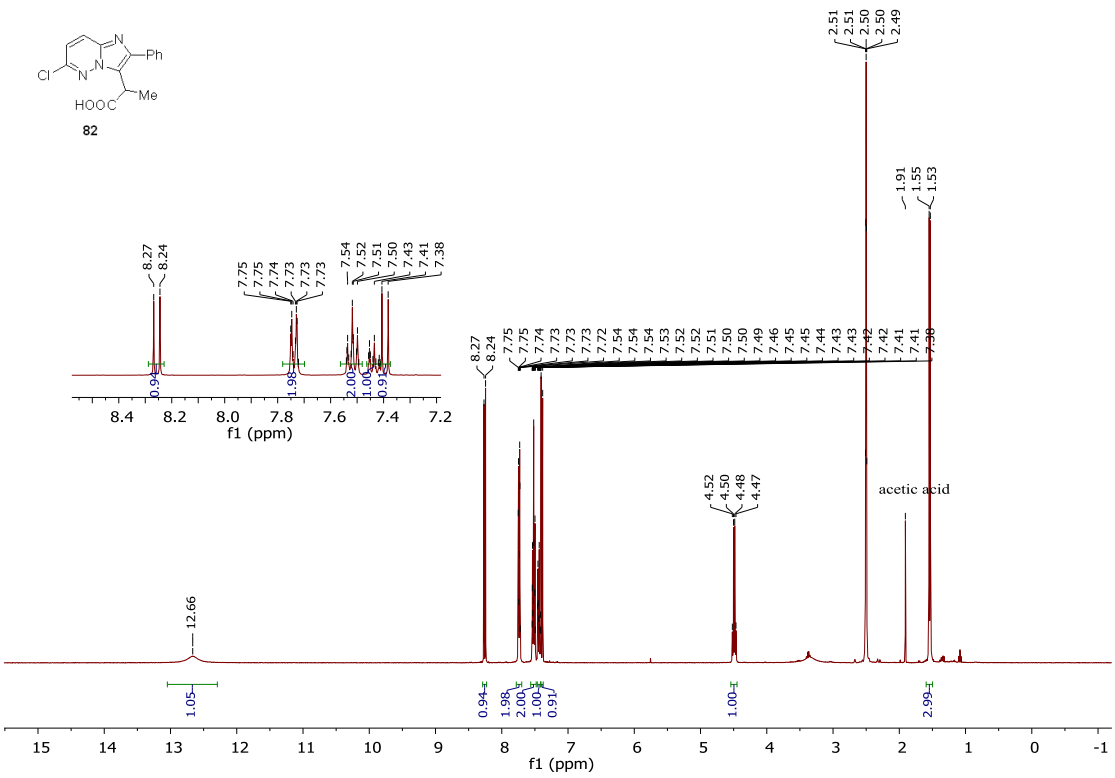

Et
O
N
OEt
79
77.5
77.2
76.8
125.3
123.3
119.4
113.4
61.0
17.1
14.6
12.2
164.2
144.0
132.2
131.8
f1 (ppm)

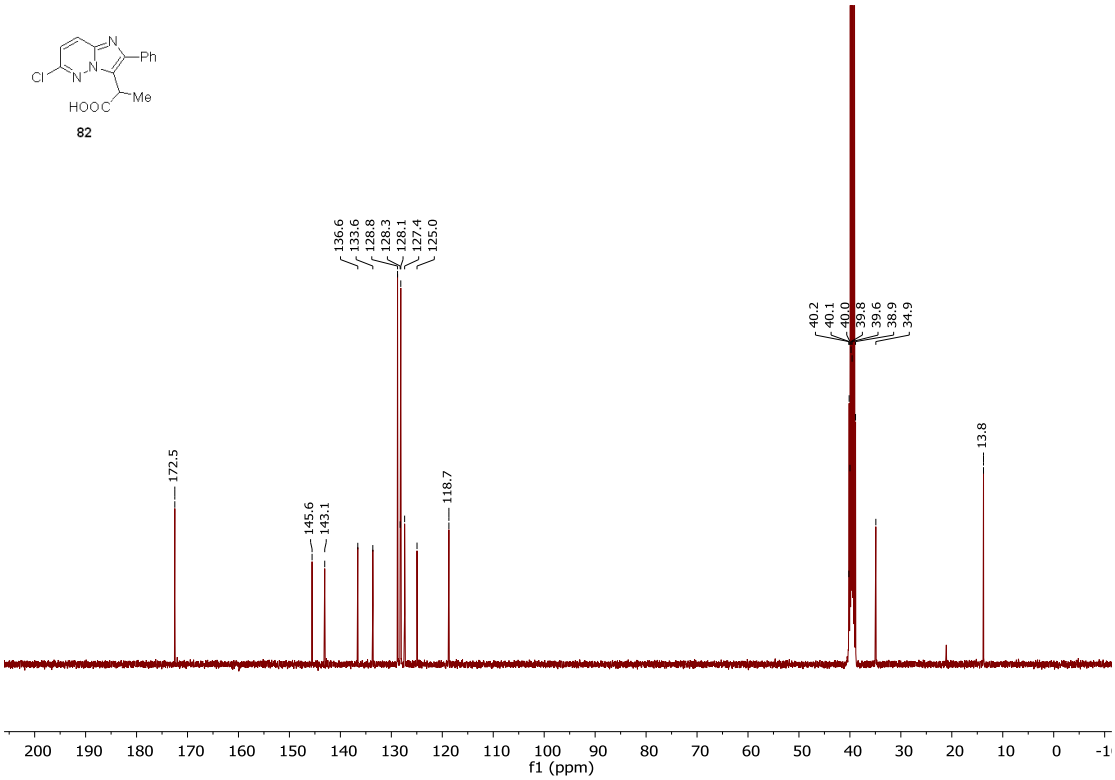

HOOC
Me
O
OEt
N
N
80
1.64
1.62
1.44
1.42
1.40
5.11
5.10
5.08
5.06
4.91
3.32
3.31
3.31
3.31
3.30
4.45
4.45
4.43
4.43
4.41
4.41
4.40
4.39
8.85
8.85
8.83
8.83
8.70
8.70
8.69
8.69
7.16
7.15
7.14
7.13
1.03
0.99
1.03
1.00
2.06
3.15
3.15
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

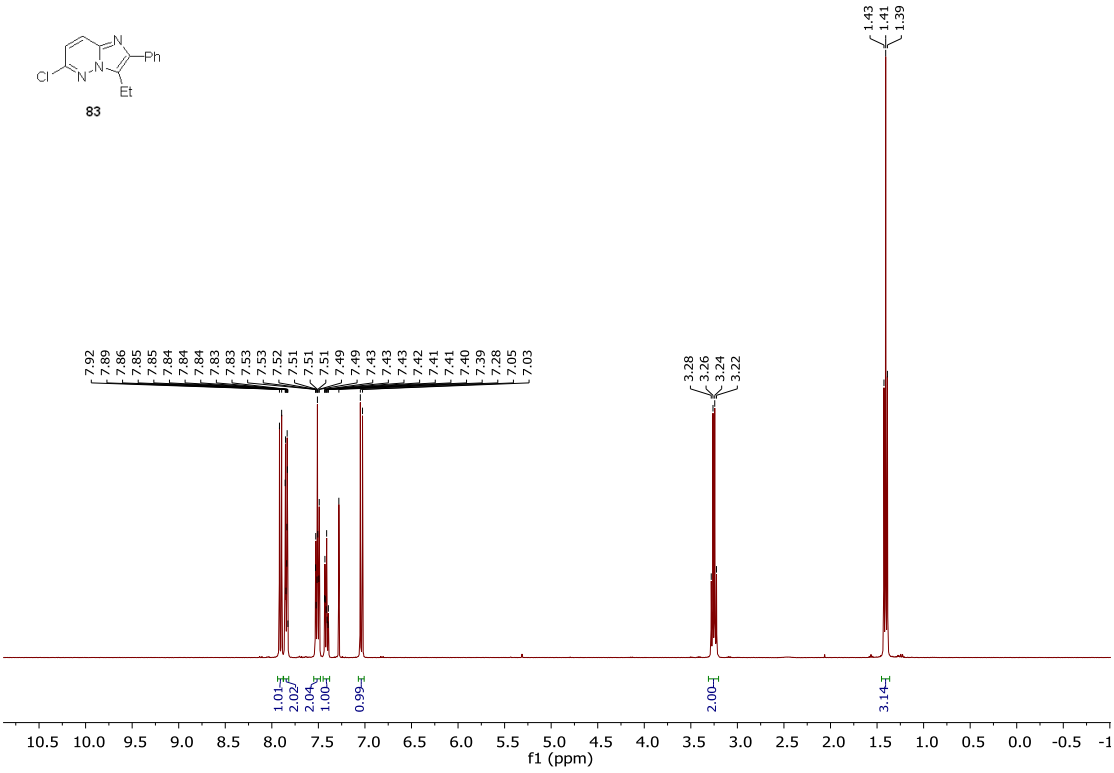

HOOC
Me
O
OEt
N
N
80
49.6
48.4
174.7
164.5
154.3
148.3
135.3
133.5
129.4
111.3
62.4
36.3
15.0
14.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

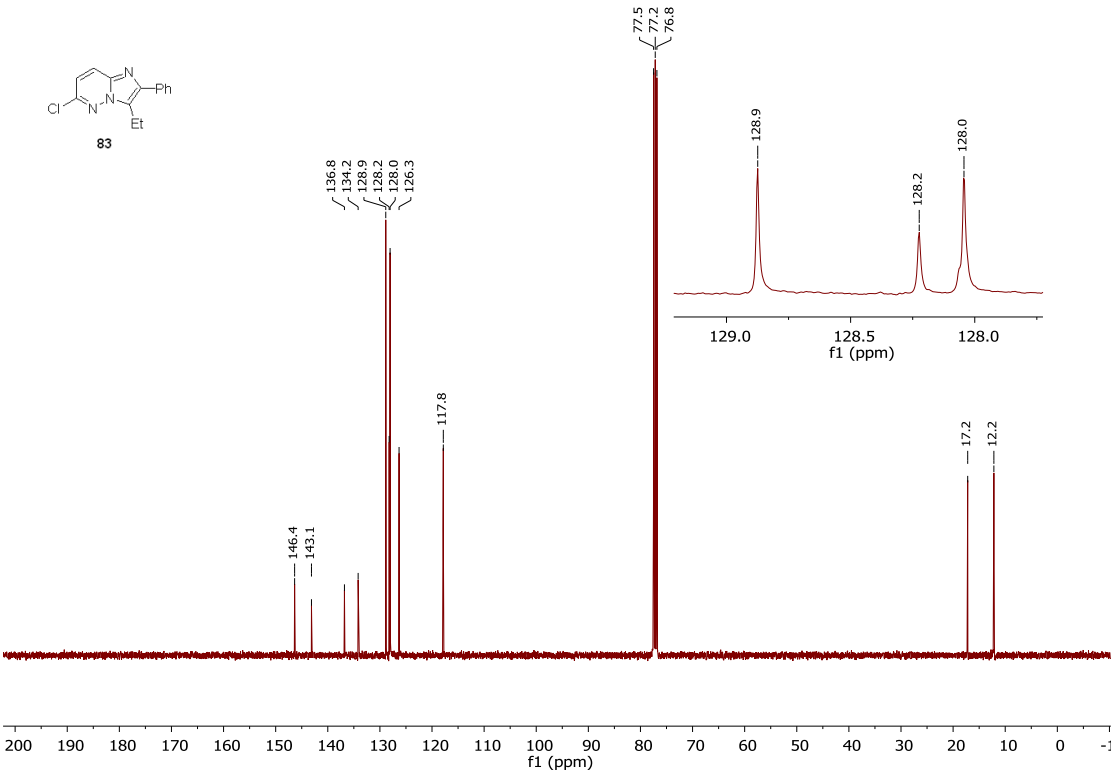

Et
O
OEt
N
N
81
1.47
1.45
1.44
1.31
1.29
1.27
4.50
4.48
4.46
4.44
3.35
3.33
3.31
3.29
7.26
6.96
6.95
6.94
6.93
8.66
8.65
8.65
8.64
8.31
8.31
8.30
8.29
0.90
0.95
0.92
2.00
2.01
2.99
3.07
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

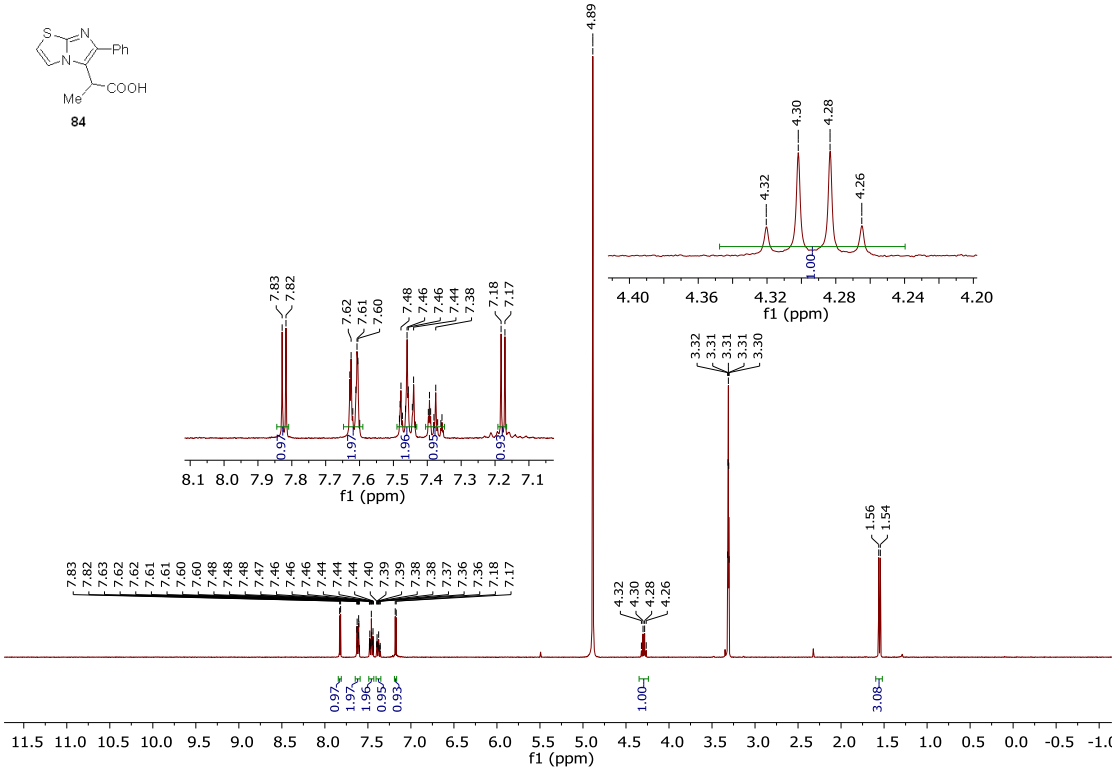

Et
O
OEt
N
N
81
163.9
151.5
146.8
132.9
131.2
130.7
109.6
61.3
16.8
14.5
12.4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

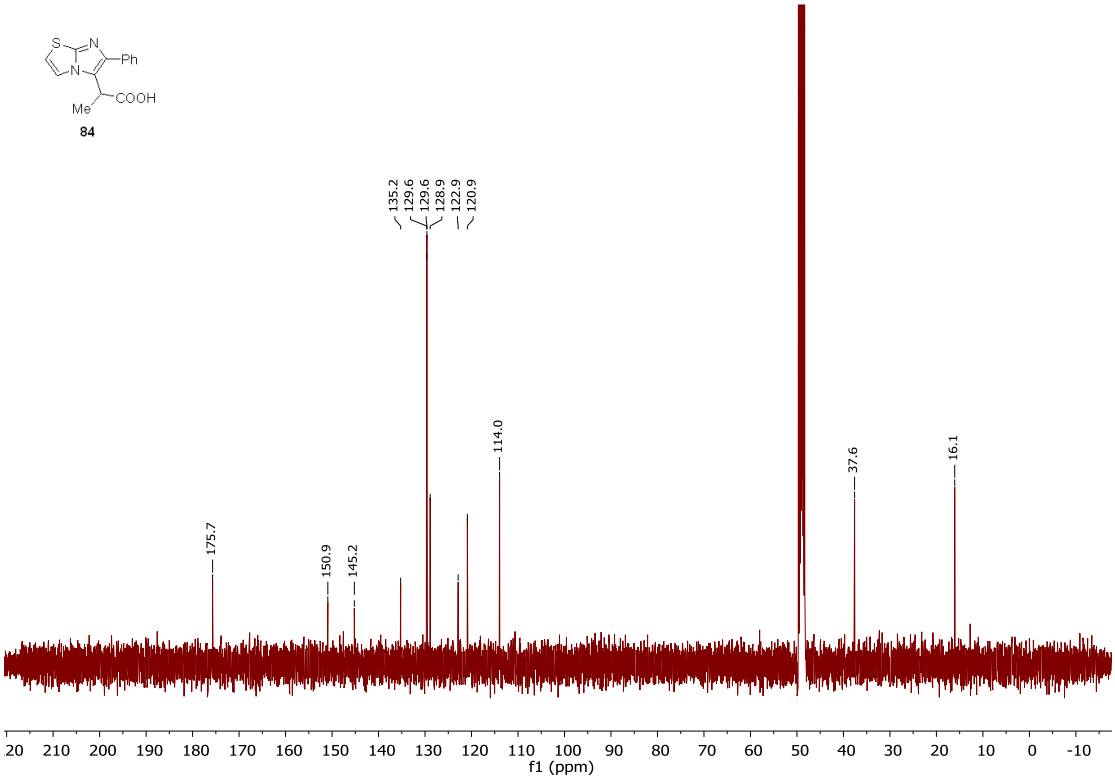

82
acetic acid
f1 (ppm)

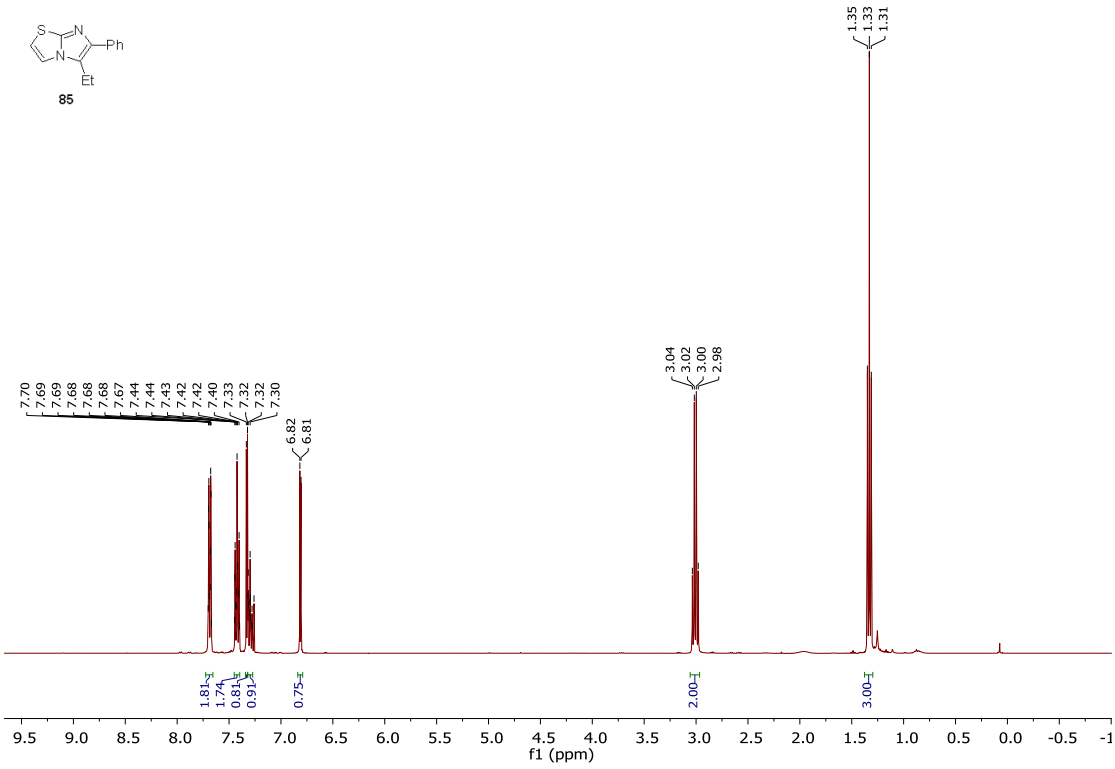

82
f1 (ppm)

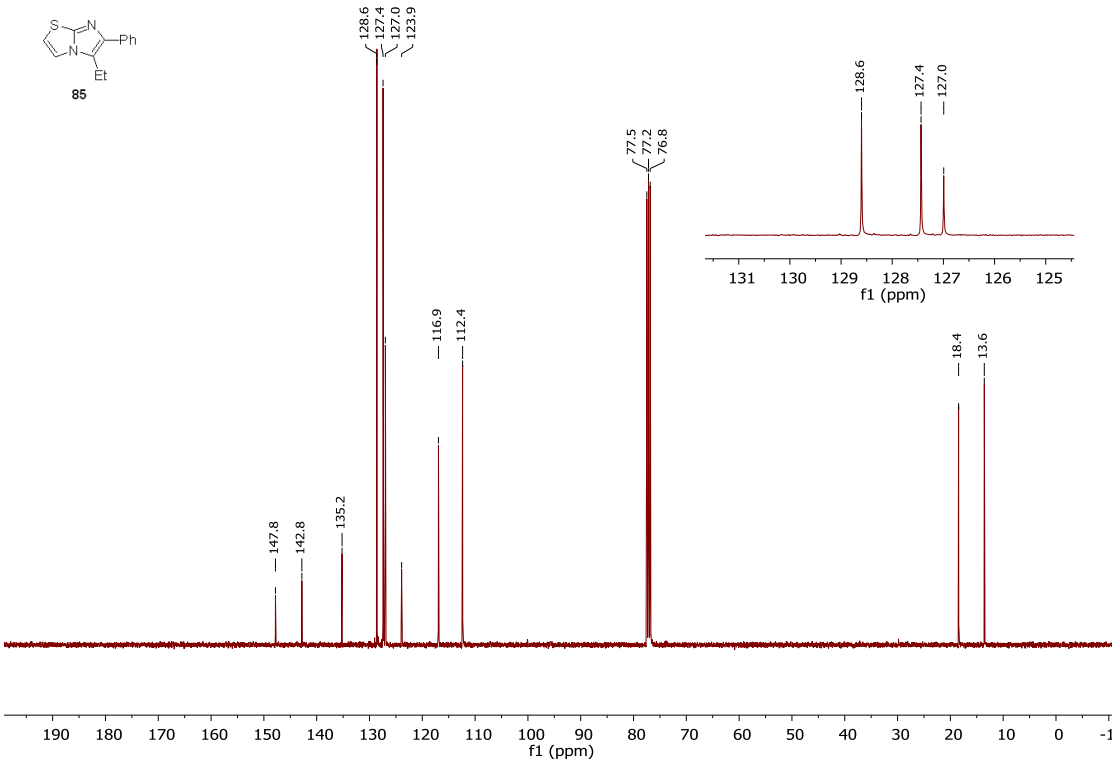

Cl
N
N
N
Ph
Et
83
7.92
7.89
7.86
7.85
7.85
7.84
7.84
7.84
7.83
7.83
7.53
7.53
7.52
7.51
7.51
7.51
7.49
7.49
7.43
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.28
7.05
7.03
3.28
3.26
3.24
3.22
1.43
1.41
1.39
1.01
2.02
2.04
1.00
0.99
2.00
3.14
f1 (ppm)

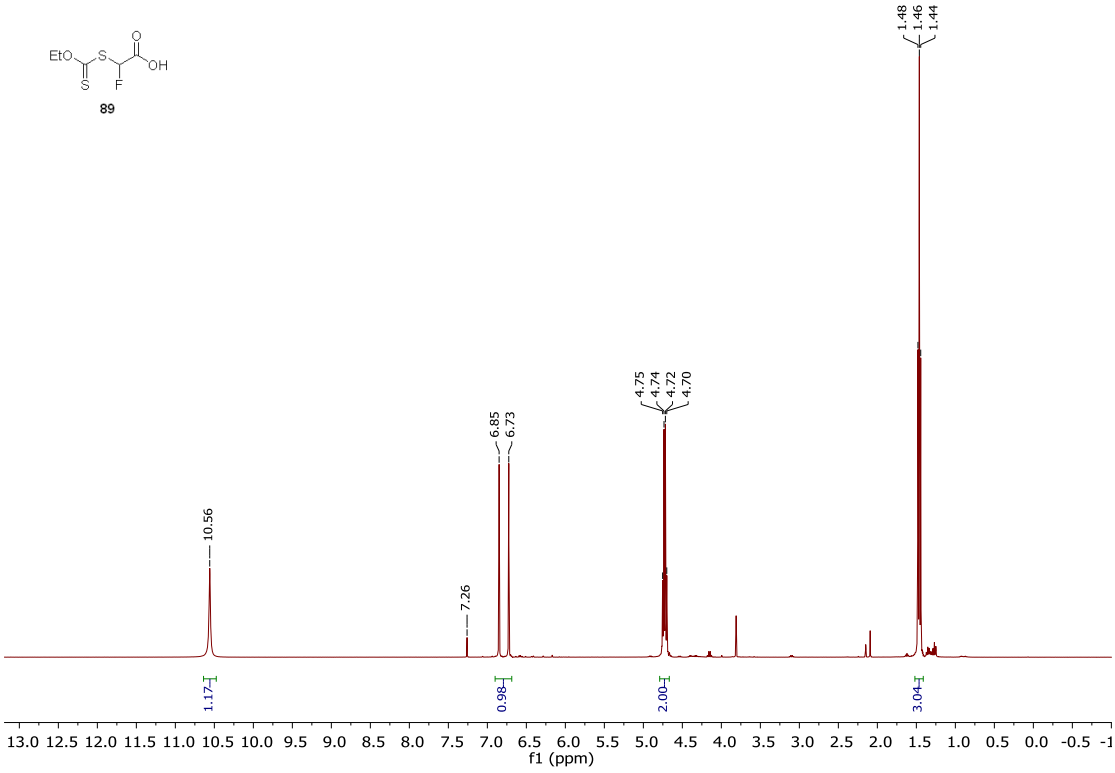

Cl
N
N
N
Ph
Et
83
136.8
134.2
128.9
128.2
128.0
126.3
117.8
146.4
143.1
77.5
77.2
76.8
128.9
128.2
128.0
17.2
12.2
129.0
128.5
128.0
f1 (ppm)
f1 (ppm)

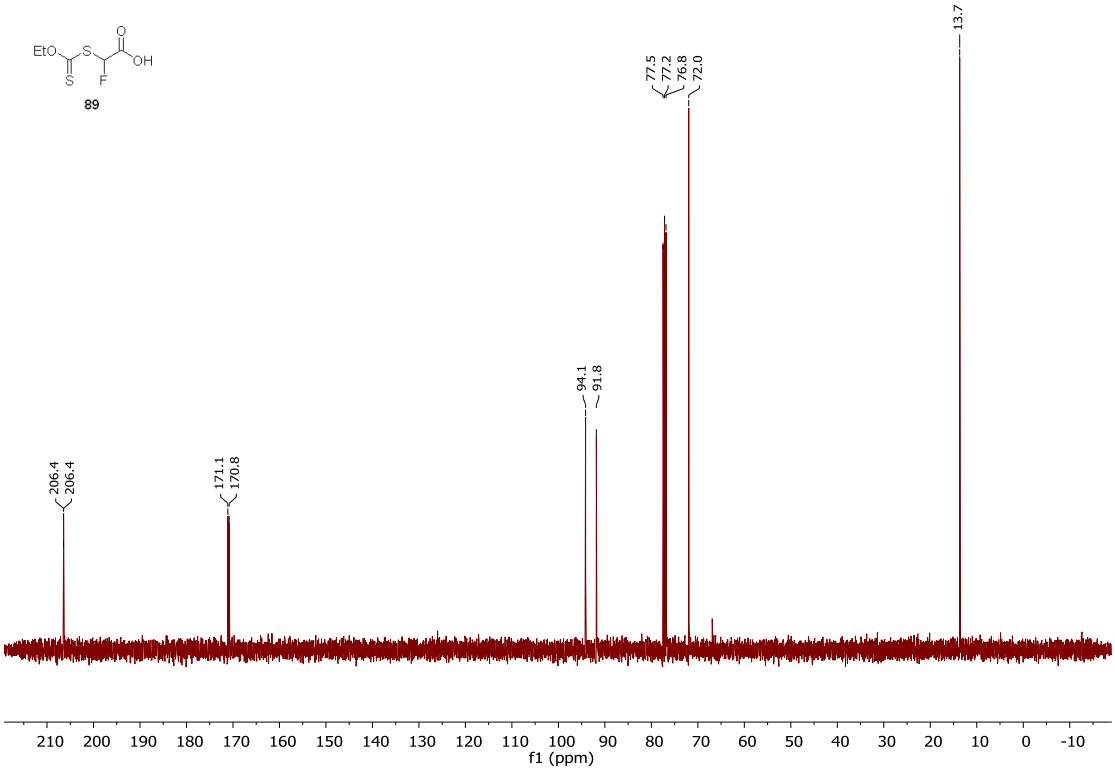

S
N
Ph
N
Me
COOH
84
4.89
4.32
4.30
4.28
4.26
1.00
7.83
7.82
7.62
7.61
7.60
7.48
7.46
7.46
7.44
7.38
7.18
7.17
0.97
1.97
1.96
0.95
0.93
3.32
3.31
3.31
3.31
3.30
1.56
1.54
3.08
f1 (ppm)

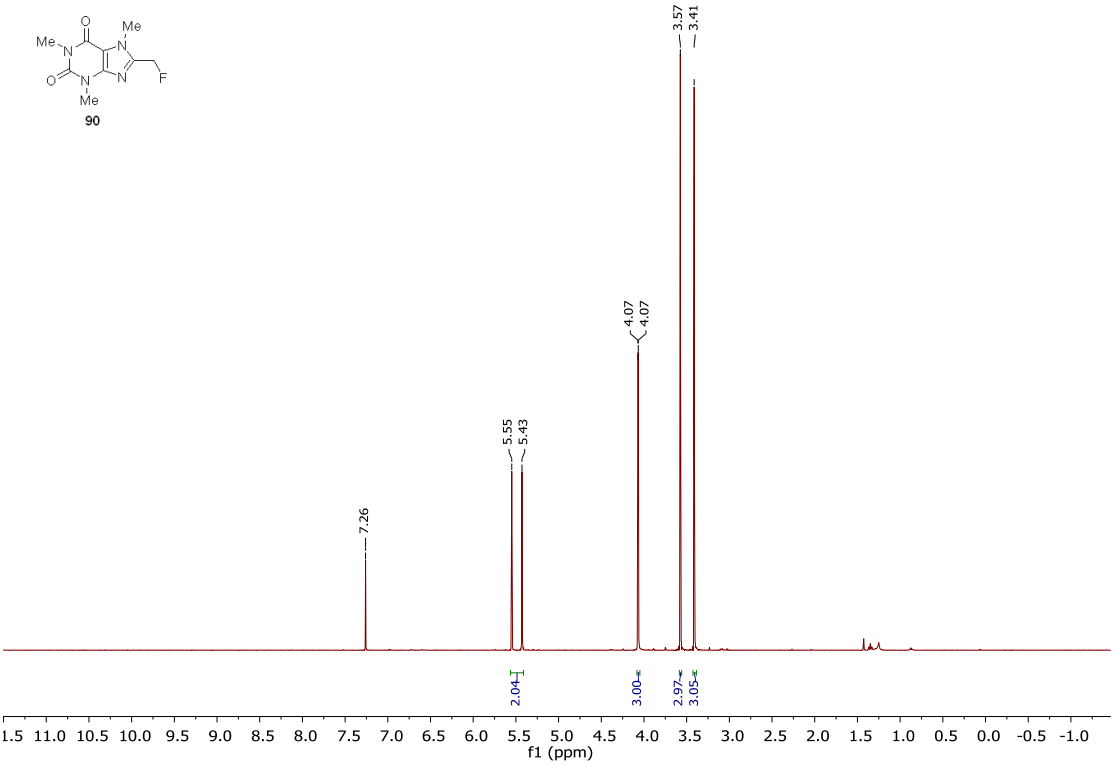

S
N
Ph
N
Me
COOH
84
135.2
129.6
129.6
128.9
122.9
120.9
175.7
150.9
145.2
114.0
37.6
16.1
f1 (ppm)

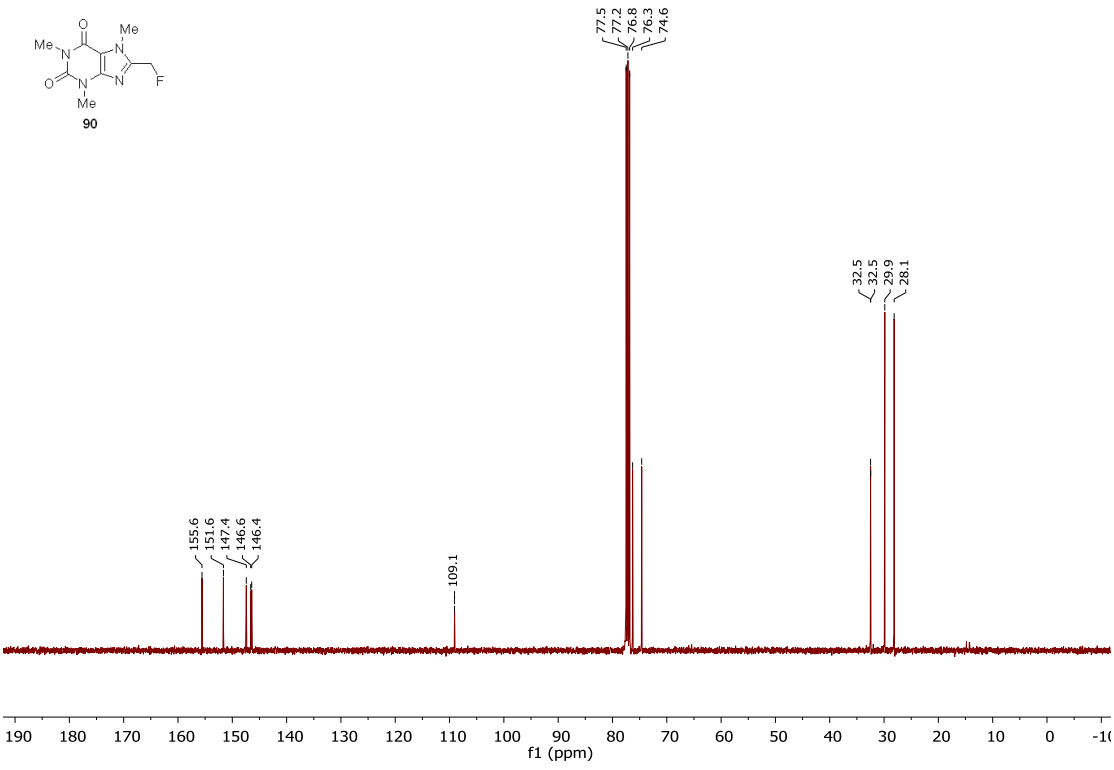

85
7.70
7.69
7.69
7.68
7.68
7.68
7.67
7.44
7.44
7.43
7.42
7.42
7.40
7.33
7.32
7.32
7.30
6.82
6.81
3.04
3.02
3.00
2.98
1.35
1.33
1.31
1.81
1.74
0.81
0.91
0.75
2.00
3.00
f1 (ppm)

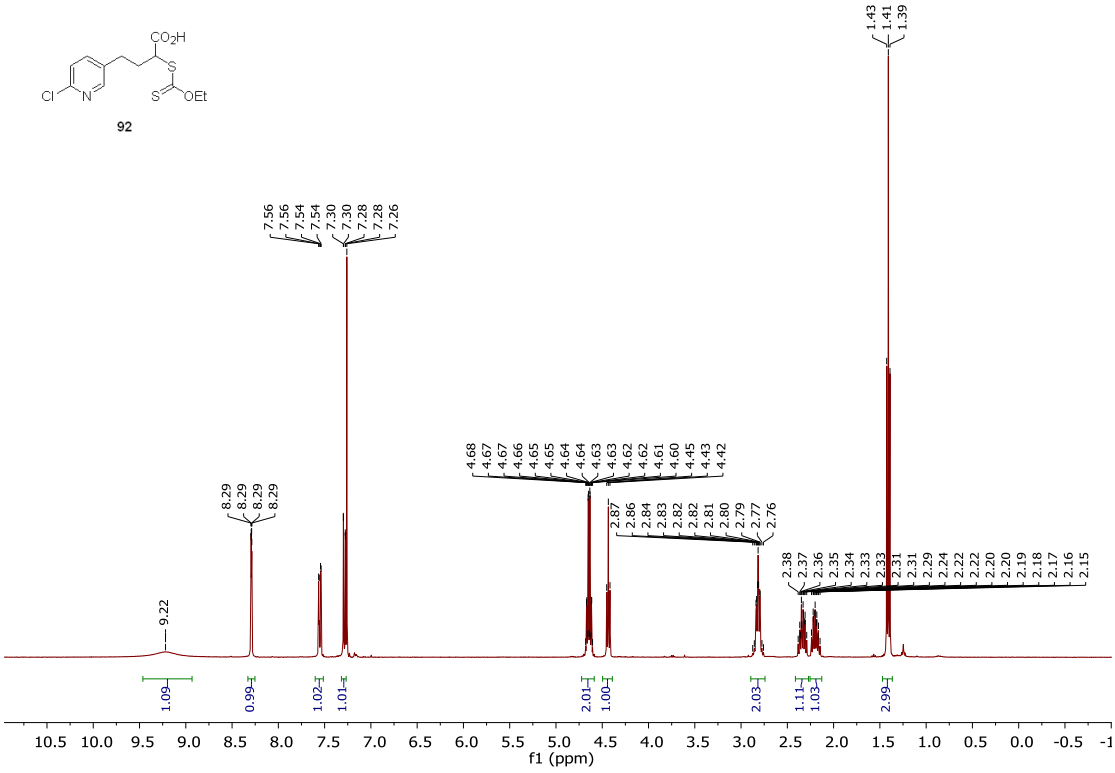

85
128.6
127.4
127.0
123.9
77.5
77.2
76.8
116.9
112.4
147.8
142.8
135.2
18.4
13.6
f1 (ppm)

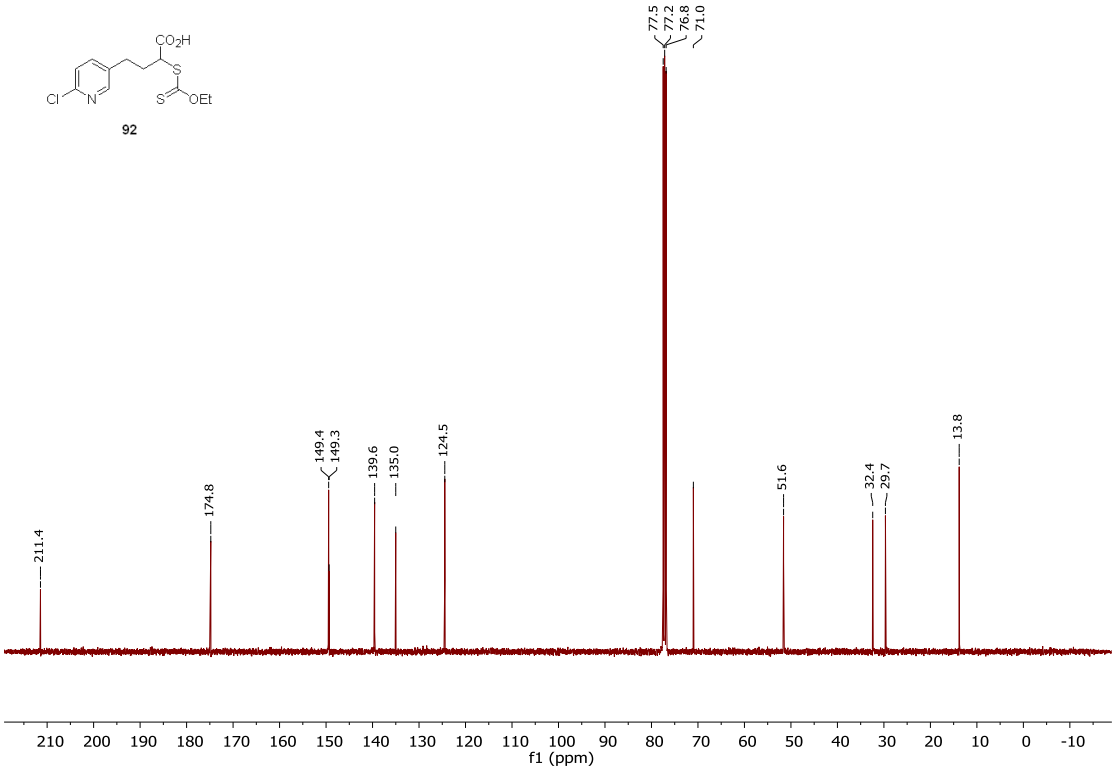

89
1.48
1.46
1.44
4.75
4.74
4.72
4.70
6.85
6.73
7.26
10.56
1.17
0.98
2.00
3.04
f1 (ppm)

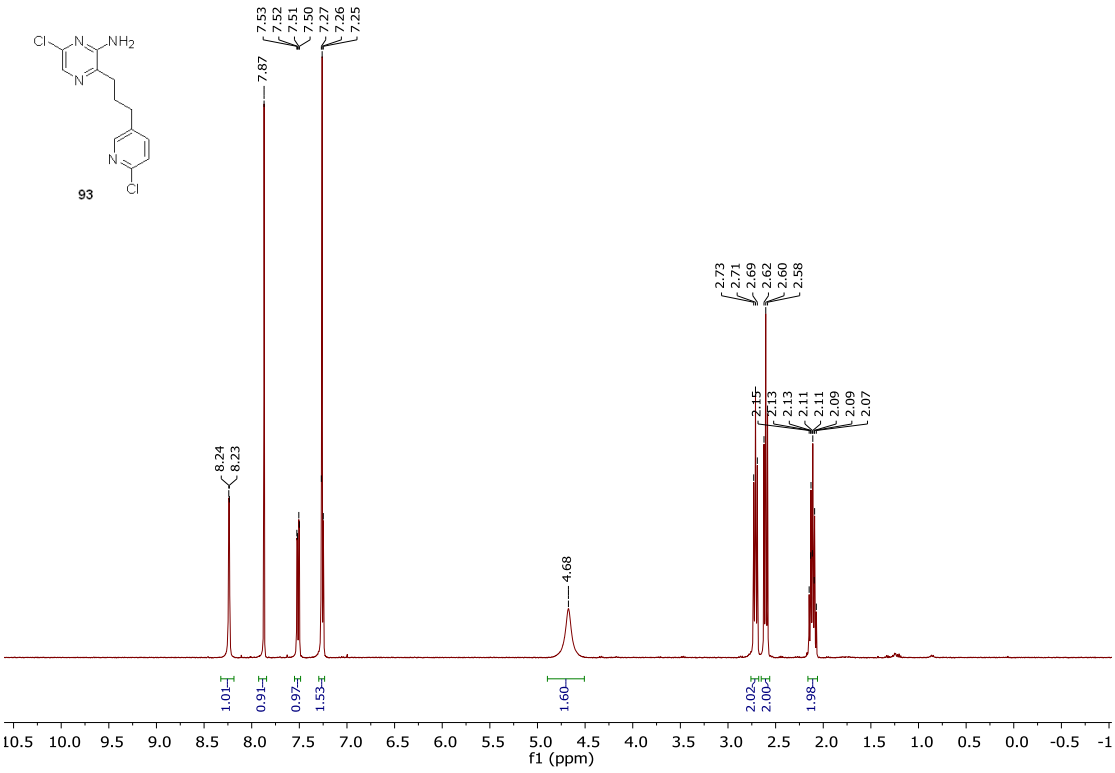

89
13.7
77.5
77.2
76.8
72.0
94.1
91.8
206.4
206.4
171.1
170.8
f1 (ppm)

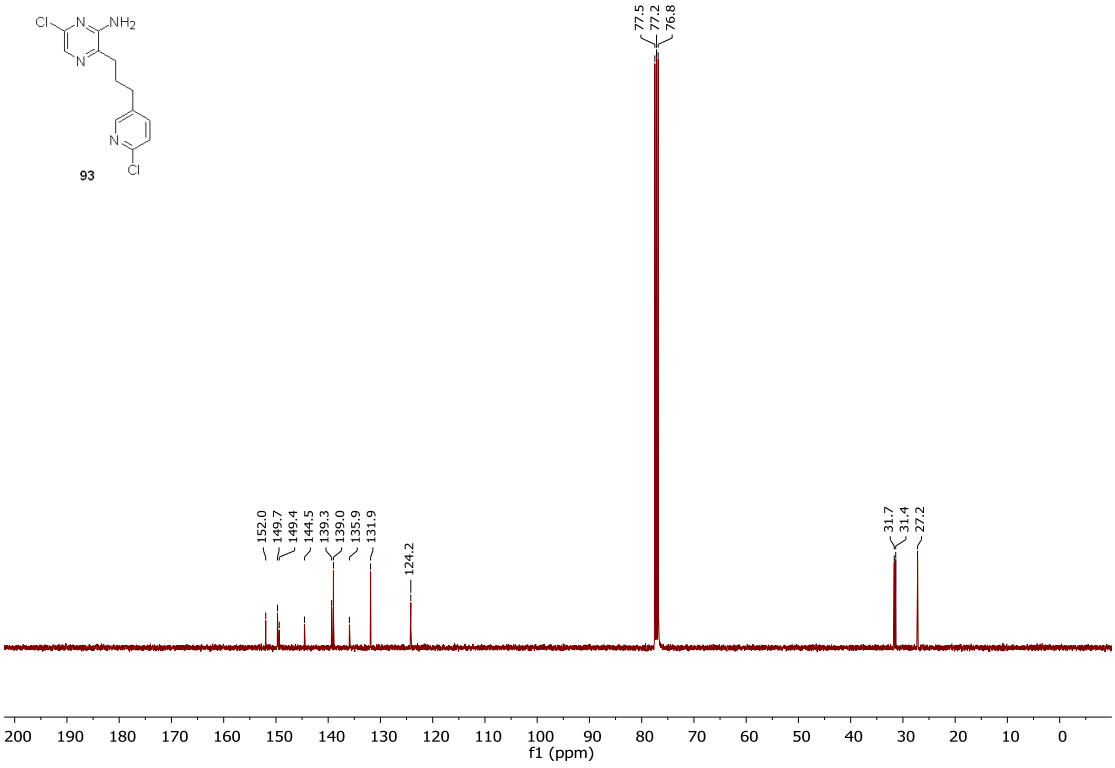

90
3.57
3.41
4.07
4.07
5.55
5.43
7.26
2.04
3.00
2.97
3.05
f1 (ppm)


90
77.5
77.2
76.8
76.3
74.6
32.5
32.5
29.9
28.1
155.6
151.6
147.4
146.6
146.4
109.1
f1 (ppm)


CO2H
S
Cl
N
S
OEt
92
1.43
1.41
1.39
7.56
7.56
7.54
7.54
7.30
7.30
7.28
7.28
7.26
4.68
4.67
4.67
4.66
4.65
4.65
4.64
4.64
4.63
4.63
4.62
4.62
4.61
4.60
4.45
4.43
4.42
8.29
8.29
8.29
8.29
2.87
2.86
2.84
2.83
2.82
2.82
2.81
2.80
2.79
2.77
2.76
2.38
2.37
2.36
2.35
2.34
2.33
2.33
2.31
2.31
2.29
2.24
2.22
2.22
2.20
2.20
2.19
2.18
2.17
2.16
2.15
9.22
1.09
0.99
1.02
1.01
2.01
1.00
2.03
1.11
1.03
2.99
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


CO2H
S
Cl
N
S
OEt
92
77.5
77.2
76.8
71.0
211.4
174.8
149.4
149.3
139.6
135.0
124.5
51.6
32.4
29.7
13.8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Cl
N
NH2
N
N
Cl
93
7.53
7.52
7.51
7.50
7.27
7.26
7.25
7.87
8.24
8.23
4.68
2.73
2.71
2.69
2.62
2.60
2.58
2.15
2.13
2.13
2.11
2.11
2.09
2.09
2.07
1.01
0.91
0.97
1.53
1.60
2.02
2.00
1.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


Cl
N
NH2
N
N
Cl
93
77.5
77.2
76.8
152.0
149.7
149.4
144.5
139.3
139.0
135.9
131.9
124.2
31.7
31.4
27.2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)