

Supporting Information

Cycloadditions of Non-Complementary Substituted 1,2,3-Triazines

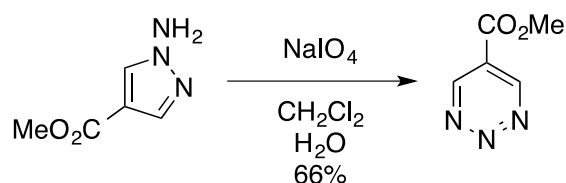
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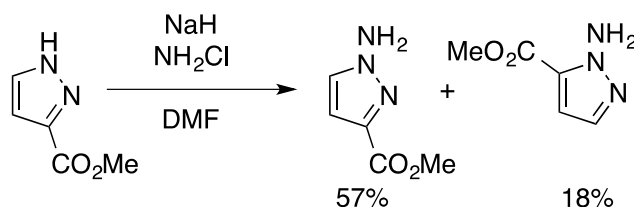
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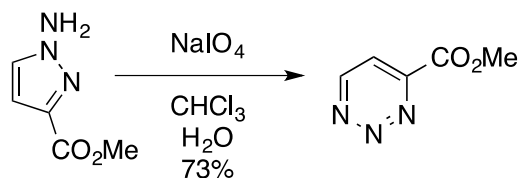
I. Synthesis of Substituted 1,2,3-Triazines



Methyl 1,2,3-Triazine-5-carboxylate (3). A mechanically stirred solution of methyl 1-amino-1*H*-pyrazole-4-carboxylate¹ (6.50 g, 46.1 mmol) in 1 L of dichloromethane at 0 °C was treated with a 0 °C solution of sodium periodate (19.70 g, 92.10 mmol) in 1 L of distilled water over 2 min. Stirring was intensified to yield a fine emulsion and the mixture was allowed to react for 15 min. The organic layer was separated and the aqueous layer was washed with dichloromethane (2 × 200 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. Flash chromatography (SiO₂ 50% Et₂O/hexanes) afforded **3** (4.22 g, 66%) as a light yellow solid: mp 45–46 °C; ¹H NMR (CDCl₃, 400 MHz) δ 9.45 (d, *J* = 2.5 Hz, 2H), 4.05 (s, 3H); ¹³C (acetone-*d*₆, 125 MHz) δ 178.7, 149.8, 130.1, 54.8; IR (film) ν_{max} 2953, 1712 cm⁻¹; HRESI-TOF *m/z* 140.0454 (C₅H₅N₃O₂ + H⁺ requires 140.0454).

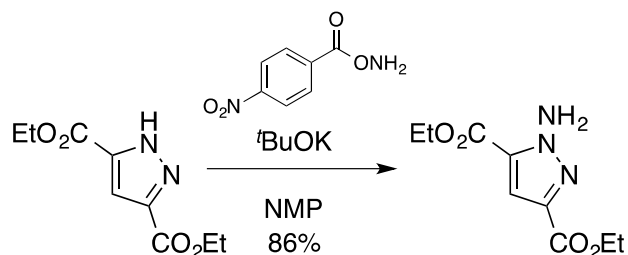


Methyl 1-Amino-1*H*-pyrazole-3-carboxylate (S1) & Methyl 1-Amino-1*H*-pyrazole-5-carboxylate (S2). A solution of 3-carbomethoxypyrazole² (1.26 g, 10.0 mmol) in DMF (20 mL) was treated with sodium hydride (60% in mineral oil) (480 mg, 12.0 mmol). The reaction mixture was stirred for 45 min at room temperature and then a 0.15 M solution of monochloramine³ in diethyl ether (83 mL, 12.0 mmol) was added. The reaction mixture was stirred at room temperature for 1 h. After 1 h, saturated aqueous Na₂S₂O₃ (70 mL), H₂O (70 mL), and EtOAc (150 mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc (150 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated on a rotary evaporator. Flash chromatography (SiO₂, 20% EtOAc/toluene) provided the title products as an off-white crystalline solid (**S1**, 809 mg, 57%) and as a pale yellow oil (**S2**, 257 mg, 18%): For **S1**: mp 97–99 °C; ¹H NMR (CDCl₃, 400 MHz) δ 7.44 (d, *J* = 2.4 Hz, 1H), 6.74 (d, *J* = 2.4 Hz, 1H), 5.41 (bs, 2H), 3.93 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 162.2, 140.3, 130.5, 107.5, 51.8; IR (film) ν_{max} 3308, 3207, 3127, 3107, 1727, 1651, 1273, 1148, 767 cm⁻¹; ESI-TOF HRMS *m/z* 142.0611 ([M + H]⁺, C₅H₇N₃O₂ + H⁺ requires 142.0611). For **S2**: ¹H NMR (CDCl₃, 400 MHz) δ 7.30 (d, *J* = 2.0 Hz, 1H), 6.73 (d, *J* = 2.4 Hz, 1H), 6.27 (bs, 2H), 3.89 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 160.7, 134.1, 127.0, 109.2, 52.1; IR (film) ν_{max} 3338, 1716, 1519, 1320, 1260, 1092, 758 cm⁻¹; HRESI-TOF *m/z* 142.0611 (C₅H₇N₃O₂ + H⁺ requires 142.0611).

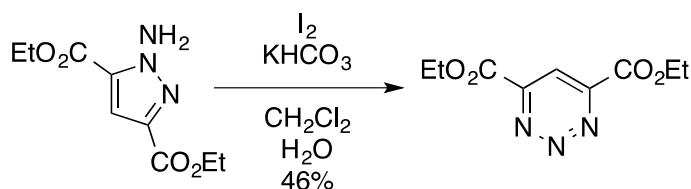


Methyl 1,2,3-Triazine-4-carboxylate (5). A solution of NaIO₄ (1.02 g, 4.79 mmol) in 40 mL of distilled water was added to a stirring solution of methyl 1-amino-1*H*-pyrazole-3-carboxylate (**S1**, 340 mg, 2.35 mmol) in 40 mL of dichloromethane at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred at room temperature for 2 h. After 2 h, the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (10 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated on a rotary

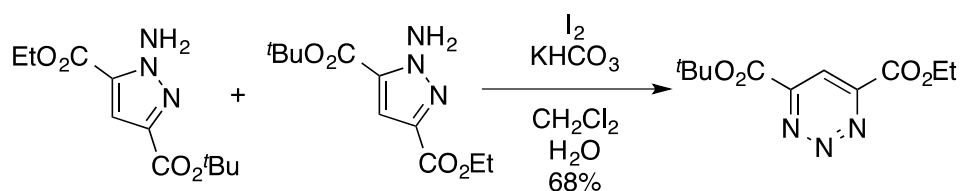
evaporator. Flash chromatography (SiO₂ 5% acetone/toluene) provided **5** (180 mg, 54%; 50–73%) as an off-white solid: mp 85–90 °C (hexanes); ¹H NMR (CDCl₃, 400 MHz) δ 9.34 (d, *J* = 6.0 Hz, 1H), 8.03 (d, *J* = 6.0 Hz, 1H), 4.13 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 163.2, 151.4, 148.8, 117.5, 54.0; IR (film) ν_{max} 1731, 1439, 1312, 1267, 1196, 1158, 1123, 1059, 998, 958, 924, 892, 8378, 804, 778, 764, 735, 709 cm⁻¹; HRESI-TOF *m/z* 140.0453 (C₅H₅N₃O₂ + H⁺ requires 140.0455).



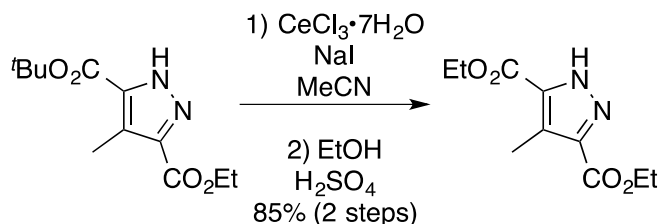
Diethyl 1-Amino-1*H*-pyrazole-3,5-dicarboxylate (S3). A solution of ^tBuOK (775 mg, 6.91 mmol) in NMP (6.9 mL) was added to a stirred solution of 3,5-dicarboethoxypyrazole⁴ (1.33 g, 6.28 mmol) in NMP (8.1 mL). The reaction mixture was stirred for 20 min at room temperature and then a solution of *O*-4-nitrobenzoylhydroxylamine⁵ (1.14 g, 6.28 mmol) in NMP (4.3 mL) was added dropwise while keeping the internal reaction temperature below 25 °C. The reaction mixture was stirred at room temperature for 1 h. After 1 h, 10% aqueous NaCl (25 mL) and EtOAc (25 mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted EtOAc (25 mL). The combined organic extracts were washed with 5% aqueous NaHCO₃ (15 mL) and H₂O (3 × 15 mL), dried over Na₂SO₄, and concentrated on a rotary evaporator. Flash chromatography (SiO₂ 30% EtOAc/hexanes) provided the title compound (1.22 g, 86%) as an off-white solid: mp 63–64 °C; ¹H NMR (CDCl₃, 600 MHz) δ 7.18 (s, 1H), 6.84 (bs, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.31 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 161.2, 159.8, 137.4, 127.54, 127.49, 111.89, 111.84, 61.8, 61.2, 14.3, 14.1; IR (film) ν_{max} 1714, 1532, 1270, 1218, 1200, 1160, 1109, 1078, 998, 960, 926, 853, 757, 718 cm⁻¹; HRESI-TOF *m/z* 228.0980 (C₉H₁₃N₃O₄ + H⁺ requires 228.0979).



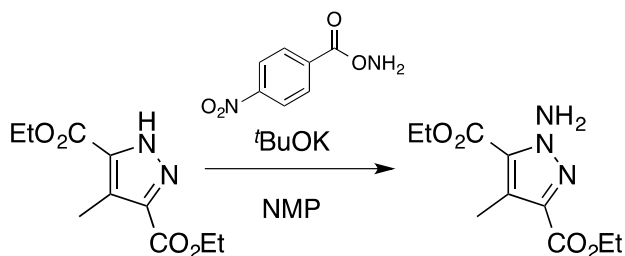
Diethyl 1,2,3-Triazine-4,6-dicarboxylate (6). Diethyl 1-amino-1*H*-pyrazole-3,5-dicarboxylate (**S3**, 340 mg, 1.50 mmol) was dissolved in CH₂Cl₂–20% aqueous KHCO₃ (15 mL, 1:1), cooled in an ice bath, and stirred while I₂ (570 mg, 2.25 mmol) in CH₂Cl₂ (15 mL) was added by an addition funnel. The reaction mixture was stirred at room temperature for 1 h. After 1 h, saturated aqueous Na₂SO₃ was added to quench the reaction mixture and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (2 × 25 mL). The combined organic layers were washed with H₂O (25 mL), dried over Na₂SO₄ and concentrated on a rotary evaporator. Flash chromatography (SiO₂, 3% acetone/toluene) provided **6** (142 mg, 42%; 40–46%) as a yellow solid: mp 85 °C (hexanes); ¹H NMR (CDCl₃, 400 MHz) δ 8.55 (s, 1H), 4.61 (q, *J* = 7.2 Hz, 4H), 1.51 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.6, 151.4, 117.7, 64.3, 14.6; IR (film) ν_{max} 1721, 1384, 1368, 1351, 1263, 1092, 1014, 957, 857, 803, 761, 718 cm⁻¹; HRESI-TOF *m/z* 226.0822 (C₉H₁₁N₃O₄ + H⁺ requires 226.0822).



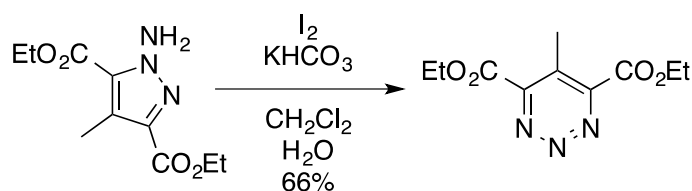
4-(*tert*-Butyl) 6-Ethyl 5-Methyl-1,2,3-Triazine-4,6-dicarboxylate (7). Compound 7 was prepared as described elsewhere.³



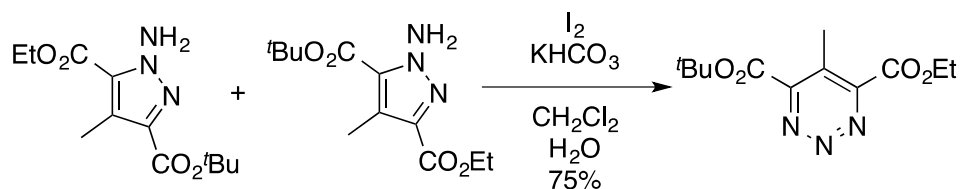
Diethyl 4-Methyl-1*H*-pyrazole-3,5-dicarboxylate (S4). Compound S4 can be prepared as described elsewhere.⁷ Alternatively, $CeCl_3 \cdot 7H_2O$ (2.08 g, 5.57 mmol) was added to a stirred solution of 5-(*tert*-butyl) 3-ethyl 4-methyl-1*H*-pyrazole-3,5-dicarboxylate⁸ (944 mg, 3.71 mmol) and NaI (723 mg, 4.82 mmol) in $MeCN$ (35 mL). The resulting reaction mixture was warmed to 82 °C and stirred at 82 °C for 1 h. After 1 h the reaction mixture was diluted with Et_2O (50 mL) and treated with 0.5 M HCl (50 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3×75 mL). The combined organic layers were washed with saturated aqueous $NaCl$ (2×50 mL), dried over Na_2SO_4 and concentrated on a rotary evaporator. The crude extract was warmed at 80 °C in $EtOH$ (15 mL) with H_2SO_4 (6 drops) for 12 h. After 12 h, the reaction mixture was concentrated. Flash chromatography (SiO_2 , 40% $EtOAc$ /hexanes) provided the title compound (714 mg, 85%) as an off-white solid: mp 80–85 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 4.35 (q, $J = 6.8$ Hz, 4H), 2.52 (s, 3H), 1.34 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 137.1, 124.5, 61.0, 14.0, 9.3; IR (film) ν_{max} 1717, 1448, 1381, 1292, 1261, 1232, 1199, 1130, 1063, 1017, 964, 848, 786, 639 cm^{-1} ; HRESI-TOF m/z 227.1025 ($C_{10}H_{14}N_2O_4 + H^+$ requires 227.1025).



Diethyl 1-Amino-4-methyl-1*H*-pyrazole-3,5-dicarboxylate (S5). A solution of $tBuOK$ (818 mg, 7.29 mmol) in NMP (7.3 mL) was added to a stirred solution of 3,5-dicarboethoxy-4-methyl-1*H*-pyrazole (S4, 1.51 g, 6.63 mmol) in NMP (11 mL). The reaction mixture was stirred for 20 min at room temperature and then a solution of *O*-4-nitrobenzoylhydroxylamine⁵ (1.21 g, 6.63 mmol) in NMP (5.2 mL) was added dropwise while keeping the internal reaction temperature below 25 °C. The reaction mixture was stirred at room temperature for 1 h. After 1 h, 10% aqueous $NaCl$ (25 mL) and $EtOAc$ (25 mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted $EtOAc$ (25 mL). The combined organic extracts were washed with 5% aqueous $NaHCO_3$ (15 mL) and H_2O (3×15 mL), dried over Na_2SO_4 , and concentrated on a rotary evaporator to provide the title product. The crude material was carried on to the next step without further purification.

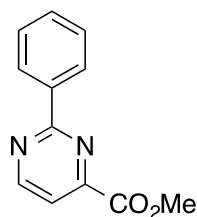


Diethyl 5-Methyl-1,2,3-triazine-4,6-dicarboxylate (8). Diethyl 1-amino-4-methyl-1*H*-pyrazole-3,5-dicarboxylate (**S5**, 1.45 g, 6.01 mmol) was dissolved in CH₂Cl₂–20% aqueous KHCO₃ (60 mL, 1:1), cooled in an ice bath, and stirred while I₂ (3.05 g, 12.0 mmol) in CH₂Cl₂ (140 mL) was added by an addition funnel. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. After 1 h, saturated aqueous Na₂SO₃ was added to quench the reaction mixture and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (75 mL). The combined organic layers were washed with H₂O (75 mL), dried over Na₂SO₄ and concentrated on a rotary evaporator. Flash chromatography (SiO₂, 15–20% EtOAc/hexanes) provided **8** (950 mg, 66%) as a light yellow oil: ¹H NMR (CDCl₃, 600 MHz) δ 4.55 (q, *J* = 7.2 Hz, 4H), 2.66 (s, 3H), 1.47 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 163.0, 152.3, 127.7, 63.3, 14.1, 13.7; IR (film) ν_{max} 1731, 1424, 1381, 1275, 1150, 1096, 1050, 1016 cm⁻¹; HRESI-TOF *m/z* 240.0977 (C₁₀H₁₃N₃O₄ + H⁺ requires 240.0979).

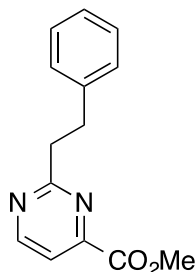


4-(*tert*-Butyl) 6-Ethyl 5-Methyl-1,2,3-Triazine-4,6-dicarboxylate (9). Compound **9** was prepared as described elsewhere.³

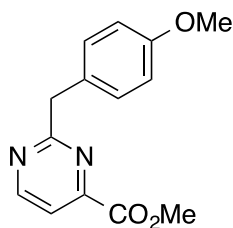
II. Reaction of 1,2,3-Triazines with Amidines



Methyl 2-Phenylpyrimidine-4-carboxylate (11a). A solution of **5** (11.0 mg, 0.08 mmol, 1.5 equiv) in CH₃CN (170 μ L) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10a** (6.3 mg, 0.053 mmol, 1.0 equiv) in CH₃CN (175 μ L) at room temperature. The reaction mixture was stirred for 1 h, at which time the mixture was purified by preparative TLC (50% EtOAc/hexanes) to provide **11a** (8.1 mg, 71%): ¹H NMR (CDCl₃, 500 MHz) δ 9.03 (d, J = 5.0 Hz, 1H), 8.57–8.47 (m, 2H), 7.85 (d, J = 4.9 Hz, 1H), 7.56–7.47 (m, 3H), 4.05 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 165.5, 165.2, 159.4, 155.4, 136.9, 131.4, 128.8 (2C), 128.7 (2C), 118.5, 53.4; IR (film) ν_{\max} 2954, 1752, 1728, 1561, 1459, 1427, 1329, 1386, 1309, 1279, 1197, 1154, 1084, 864, 740, 691, 645 cm⁻¹; HRESI-TOF m/z 215.0816 (C₁₂H₁₀N₂O₂ + H⁺ requires 215.0815).

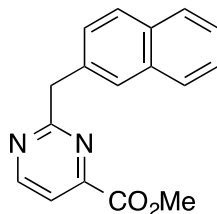


Methyl 2-(2-Phenylethyl)pyrimidine-4-carboxylate (11b). A solution of **5** (11.0 mg, 0.08 mmol, 2.0 equiv) in CH₃CN (170 μ L) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10b** (6.0 mg, 0.04 mmol, 1.0 equiv) in CH₃CN (135 μ L) at room temperature. The reaction mixture was stirred for 1 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **11b** (8.1 mg, 84%): ¹H NMR (CDCl₃, 500 MHz) δ 8.91 (d, J = 4.9 Hz, 1H), 7.82 (d, J = 4.9 Hz, 1H), 7.31–7.23 (m, 4H), 7.22–7.15 (m, 1H), 4.03 (s, 3H), 3.45–3.37 (m, 2H), 3.23–3.16 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.5, 165.0, 159.2, 155.2, 141.2, 128.59 (2C), 128.55 (2C), 126.2, 118.3, 53.6, 41.1, 34.7; IR (film) ν_{\max} 3027, 2953, 1730, 1603, 1564, 1496, 1433, 1396, 1317, 1199, 1150, 1074, 999, 865, 769, 701, 684 cm⁻¹; HRESI-TOF m/z 243.1129 (C₁₄H₁₄N₂O₂ + H⁺ requires 243.1128).

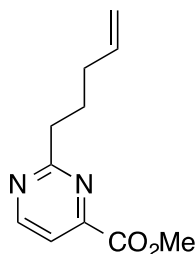


Methyl 2-(4-Methoxybenzyl)pyrimidine-4-carboxylate (11c). A solution of **5** (11.0 mg, 0.08 mmol, 2.0 equiv) in CH₃CN (170 μ L) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10c** (6.5 mg, 0.04 mmol, 1.0 equiv) in CH₃CN (135 μ L) at room temperature. The reaction mixture was stirred for 1 h, at which time the mixture was purified by preparative TLC (50% EtOAc/hexanes) to provide **11c** (10.1 mg, 98%): ¹H NMR (CDCl₃, 500 MHz) δ 8.90 (d, J = 4.9 Hz, 1H), 7.80 (d, J = 4.9 Hz, 1H), 7.30 (d, J = 8.2 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 4.36 (s, 2H), 4.03 (s, 3H), 3.77 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.2, 165.0, 159.6, 158.6, 155.3, 130.4 (2C), 130.0, 118.3, 114.1 (2C), 55.4, 53.6, 45.1; IR (film) ν_{\max} 2953, 2836,

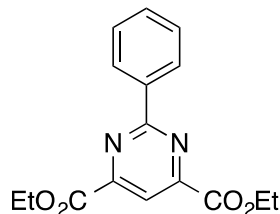
1749, 1731, 1611, 1563, 1511, 1433, 1390, 1319, 1299, 1246, 1205, 1179, 1150, 1109, 1033, 995, 808, 781, 727, 683, 630 cm^{-1} ; HRESI-TOF m/z 259.1076 ($\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3 + \text{H}^+$ requires 259.1077).



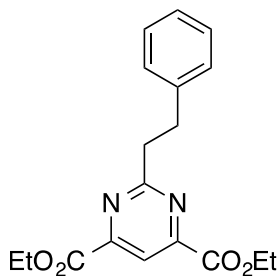
Methyl 2-(Naphthalen-2-ylmethyl)pyrimidine-4-carboxylate (11d). A solution of **5** (11.0 mg, 0.08 mmol, 1.5 equiv) in CH_3CN (171 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10d** (6.5 mg, 0.053 mmol, 1.0 equiv) in CH_3CN (177 μL) at room temperature. The reaction mixture was stirred for 1 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **11d** (10.0 mg, 68%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.84 (d, $J = 4.9$ Hz, 1H), 8.19–8.13 (m, 1H), 7.88–7.81 (m, 1H), 7.80–7.75 (m, 2H), 7.52–7.41 (m, 4H), 4.88 (s, 2H), 4.04 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 171.0, 165.0, 159.6, 155.2, 134.4, 134.0, 132.3, 128.8, 128.0, 127.8, 126.2, 125.8, 125.7, 124.6, 118.2, 53.6, 43.7; IR (film) ν_{max} 3040, 2950, 1750, 1731, 1562, 1510, 1432, 1388, 1322, 1293, 1202, 1150, 994, 795, 780, 685, 515 cm^{-1} ; HRESI-TOF m/z 279.1131 ($\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2 + \text{H}^+$ requires 279.1128).



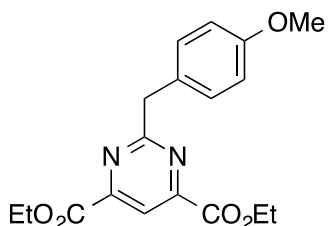
Methyl 2-(Pent-4-en-1-yl)pyrimidine-4-carboxylate (11e). A solution of **5** (11.0 mg, 0.08 mmol, 1.5 equiv) in CH_3CN (171 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10e** (5.9 mg, 0.053 mmol, 1.0 equiv) in CH_3CN (177 μL) at room temperature. The reaction mixture was stirred for 1 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **11e** (7.7 mg, 71%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.90 (d, $J = 4.9$ Hz, 1H), 7.81 (d, $J = 5.0$ Hz, 1H), 5.84 (ddt, $J = 17.0$, 10.1, 6.7 Hz, 1H), 5.03 (dd, $J = 17.4$, 1.6 Hz, 1H), 4.97 (dd, $J = 10.3$, 1.1 Hz, 1H), 4.02 (s, 3H), 3.14–3.06 (m, 2H), 2.16 (q, $J = 7.2$ Hz, 2H), 1.96 (p, $J = 7.6$ Hz, 2H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 172.4, 165.1, 159.2, 155.0, 138.2, 118.1, 115.2, 53.5, 39.1, 33.6, 28.1; IR (film) ν_{max} 2954, 2934, 2854, 1752, 1732, 1640, 1564, 1434, 1398, 1316, 1200, 1151, 995, 913, 795, 769, 683 cm^{-1} ; HRESI-TOF m/z 207.1133 ($\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_2 + \text{H}^+$ requires 207.1128).



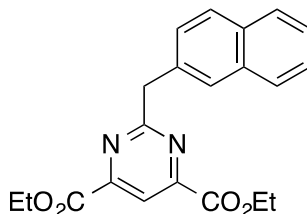
Diethyl 2-Phenylpyrimidine-4,6-dicarboxylate (12a). A solution of **6** (20.0 mg, 0.09 mmol, 2.0 equiv) in CH_3CN (193 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10a** (5.4 mg, 0.045 mmol, 1.0 equiv) in CH_3CN (150 μL) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **12a** (4.1 mg, 30%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.60 (dt, $J = 7.6$, 1.9 Hz, 2H), 8.43 (s, 1H), 7.56–7.50 (m, 3H), 4.54 (q, $J = 7.2$ Hz, 4H), 1.49 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 166.2 (2C), 164.1, 158.0 (2C), 136.3, 131.9, 129.1 (2C), 128.9 (2C), 117.9, 63.0 (2C), 14.7 (2C); IR (film) ν_{max} 2923, 1741, 1556, 1379, 1331, 1225, 1194, 1100, 1022, 741 cm^{-1} ; HRESI-TOF m/z 301.1184 ($\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_4 + \text{H}^+$ requires 301.1183).



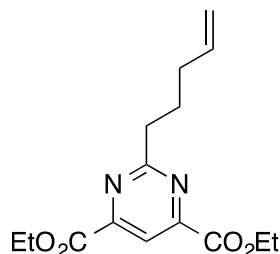
Diethyl 2-(2-Phenylethyl)pyrimidine-4,6-dicarboxylate (12b). A solution of **6** (20.0 mg, 0.09 mmol, 2.0 equiv) in CH₃CN (193 μ L) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10b** (6.7 mg, 0.045 mmol, 1.0 equiv) in CH₃CN (150 μ L) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **12b** (9.1 mg, 61%): ¹H NMR (CDCl₃, 500 MHz) δ 8.38 (s, 1H), 7.30–7.21 (m, 4H), 7.16 (td, *J* = 6.5, 2.9 Hz, 1H), 4.50 (q, *J* = 7.1 Hz, 4H), 3.56–3.43 (m, 2H), 3.21 (dd, *J* = 9.4, 6.9 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 172.4 (2C), 163.9, 157.7 (2C), 141.1, 128.7 (2C), 128.5 (2C), 126.2, 117.8, 63.0 (2C), 41.0, 34.5, 14.4 (2C); IR (film) ν_{max} 2982, 2932, 1750, 1729, 1555, 1496, 1453, 1383, 1247, 1199, 1102, 1023, 916, 861, 756, 722, 701 cm⁻¹; HRESI-TOF *m/z* 329.1501 (C₁₈H₂₀N₂O₄ + H⁺ requires 329.1496).



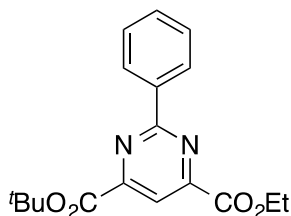
Diethyl 2-(4-Methoxybenzyl)pyrimidine-4,6-dicarboxylate (12c). A solution of **6** (20.0 mg, 0.09 mmol, 2.0 equiv) in CH₃CN (193 μ L) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10c** (7.4 mg, 0.045 mmol, 1.0 equiv) in CH₃CN (150 μ L) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **12c** (9.4 mg, 61%): ¹H NMR (CDCl₃, 500 MHz) δ 8.38 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 4.50 (q, *J* = 7.2 Hz, 4H), 4.45 (s, 2H), 3.76 (s, 3H), 1.45 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.9 (2C), 163.8, 158.6 (2C), 157.9, 130.4 (2C), 129.7, 117.8, 114.1 (2C), 63.0 (2C), 55.4, 44.9, 14.3; IR (film) ν_{max} 2980, 2929, 1730, 1612, 1554, 1512, 1466, 1375, 1300, 1248, 1203, 1096, 1024, 859, 777, 722 cm⁻¹; HRESI-TOF *m/z* 345.1448 (C₁₈H₂₀N₂O₅ + H⁺ requires 345.1445).



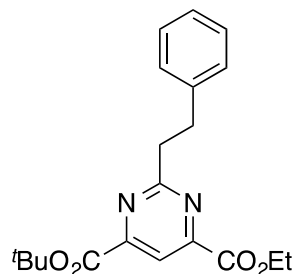
Diethyl 2-(Naphthalen-2-yl-methyl)pyrimidine-4,6-dicarboxylate (12d). A solution of **6** (20.0 mg, 0.09 mmol, 2.0 equiv) in CH₃CN (343 μ L) stirring with crushed 4 Å molecule sieves was treated with **10d** (8.3 mg, 0.045 mmol, 1.0 equiv) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **12d** (8.3 mg, 51%): ¹H NMR (CDCl₃, 500 MHz) δ 8.37 (s, 1H), 8.35 (s, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.54–7.47 (m, 1H), 7.49–7.37 (m, 3H), 4.96 (s, 2H), 4.47 (q, *J* = 7.2 Hz, 4H), 1.42 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.6 (2C), 163.8, 157.8 (2C), 134.2, 134.0, 132.3, 128.7, 127.9, 127.8, 126.2, 125.74, 125.71, 124.7, 117.8, 62.9 (2C), 43.3, 14.3 (2C); IR (film) ν_{max} 2982, 2930, 1750, 1729, 1574, 1553, 1466, 1445, 1369, 1249, 1203, 1100, 1021, 795, 780, 724 cm⁻¹; HRESI-TOF *m/z* 365.1497 (C₂₁H₂₀N₂O₄ + H⁺ requires 365.1496).



Diethyl 2-(Pent-4-en-1-yl)pyrimidine-4,6-dicarboxylate (12e). A solution of **6** (20.0 mg, 0.09 mmol, 2.0 equiv) in CH₃CN (193 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10e** (5.1 mg, 0.045 mmol, 1.0 equiv) in CH₃CN (150 μL) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **12e** (7.2 mg, 56%): ¹H NMR (CDCl₃, 500 MHz) δ 8.39 (s, 1H), 5.83 (ddt, *J* = 17.0, 10.1, 6.8 Hz, 1H), 5.04 (d, *J* = 17.2 Hz, 1H), 4.97 (d, *J* = 10.1 Hz, 1H), 4.52 (q, *J* = 7.2 Hz, 4H), 3.22–3.15 (m, 2H), 2.18 (q, *J* = 7.3 Hz, 2H), 2.02–1.95 (m, 2H), 1.45 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 173.4 (2C), 164.0, 157.6 (2C), 138.2, 117.6, 115.3, 63.0 (2C), 39.1, 33.6, 28.3, 14.4 (2C); IR (film) ν_{max} 2981, 2935, 1752, 1731, 1556, 1446, 1385, 1348, 1264, 1247, 1200, 1172, 1098, 1022, 914, 722 cm⁻¹; HRESI-TOF *m/z* 293.1502 (C₁₅H₂₀N₂O₄ + H⁺ requires 293.1496).

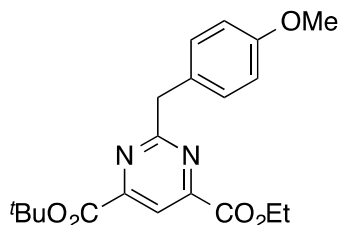


4-(tert-Butyl) 6-Ethyl 2-Phenylpyrimidine-4,6-dicarboxylate (13a). A solution of **7** (0.090 mmol, 22.7 mg) in anhydrous CH₃CN (200 μL) at 25 °C was treated with a solution of **10a** (0.066 mmol, 8.0 mg) in anhydrous CH₃CN (200 μL). The reaction mixture was stirred at 60 °C for 16 h, upon which time the mixture was cooled to 25 °C, filtered through Celite, and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 15% EtOAc/hexanes) to yield **13a** as a clear oil (12.7 mg, 49%): ¹H NMR (CDCl₃, 500 MHz) δ 8.61–8.59 (m, 2H), 8.35 (s, 1H), 7.55–7.50 (m, 3H), 4.54 (q, *J* = 7.1 Hz, 2H), 1.68 (s, 9H), 1.49 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 166.0, 164.3, 162.8, 159.0, 157.8, 136.4, 131.8, 129.0 (2C), 128.8 (2C), 117.6, 84.0, 62.9, 28.2 (3C), 14.4; IR (neat) ν_{max} 2981, 2930, 1746, 1727, 1555, 1458, 1377, 1279, 1256, 1216, 1187, 159, 1104, 1020, 845, 737, 694 cm⁻¹; HRESI-TOF *m/z* 329.1497 (C₁₈H₂₀N₂O₄ + H⁺ requires 329.1496).

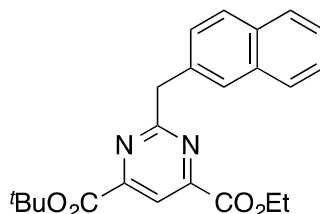


4-(tert-Butyl) 6-Ethyl 2-Phenethylpyrimidine-4,6-dicarboxylate (13b). A solution of **7** (0.079 mmol, 20 mg) in anhydrous CH₃CN (170 μL) at 25 °C was treated with a solution of **10b** (0.04 mmol, 6.0 mg) in anhydrous CH₃CN (135 μL). The reaction mixture was stirred at 25 °C for 4 h, upon which time the mixture was filtered through Celite and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 20% EtOAc/hexanes) to yield **13b** as a clear oil (12.7 mg, 89%): ¹H NMR (CDCl₃, 600 MHz) δ 8.30 (s, 1H), 7.32–7.23 (m, 4H), 7.21–7.16 (m, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 3.54–3.45 (m, 2H), 3.27–3.17 (m, 2H), 1.65 (s, 9H), 1.46 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz) δ 172.3, 164.1, 162.6, 158.8, 157.5, 141.2, 128.7 (2C), 128.5 (2C), 126.2, 117.5, 84.1, 63.0, 41.0, 34.4, 28.1 (3C), 14.4; IR (neat) ν_{max} 2980, 2931, 1746, 1727, 1555,

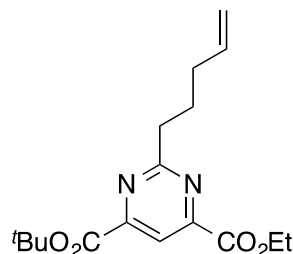
1386, 1454, 1386, 1370, 1276, 1256, 1202, 1157, 1103, 1025, 844, 756, 701 cm^{-1} ; HRESI-TOF m/z 357.1816 ($\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_4 + \text{H}^+$ requires 357.1809).



4-(tert-Butyl) 6-Ethyl 2-(4-Methoxybenzyl)pyrimidine-4,6-dicarboxylate (13c). A solution of **7** (20.0 mg, 0.08 mmol, 2.0 equiv) in CH_3CN (174 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10c** (6.5 mg, 0.04 mmol, 1.0 equiv) in CH_3CN (133 μL) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **13c** (12.7 mg, 85%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.27 (s, 1H), 7.37 (d, $J = 8.3$ Hz, 2H), 6.82 (d, $J = 8.4$ Hz, 2H), 4.50 (q, $J = 7.1$ Hz, 2H), 4.43 (s, 2H), 3.76 (s, 3H), 1.63 (s, 9H), 1.44 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 171.8, 164.1, 162.5, 159.0, 158.6, 157.7, 130.5 (2C), 129.8, 117.5, 114.0 (2C), 84.0, 62.9, 55.4, 44.9, 28.1 (3C), 14.3; IR (film) ν_{max} 2981, 2933, 1745, 1726, 1612, 1553, 1512, 1462, 1371, 1251, 1202, 1157, 1096, 1029, 844, 817, 779 cm^{-1} ; HRESI-TOF m/z 373.1758 ($\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_5 + \text{H}^+$ requires 373.1758).

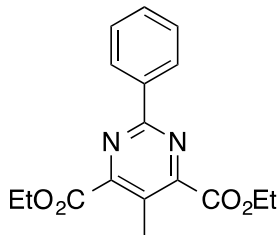


4-(tert-Butyl) 6-Ethyl 2-(Naphthalen-2-ylmethyl)pyrimidine-4,6-dicarboxylate (13d). A solution of **7** (30.0 mg, 0.118 mmol, 2.0 equiv) in CH_3CN (454 μL) stirring with crushed 4 Å molecule sieves was treated with **10d** (10.9 mg, 0.059 mmol, 1.0 equiv) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **13d** (12.5 mg, 54%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.39 (d, $J = 8.3$ Hz, 1H), 8.27 (s, 1H), 7.83 (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 8.2$ Hz, 1H), 7.55–7.38 (m, 4H), 4.94 (s, 2H), 4.47 (q, $J = 7.1$ Hz, 2H), 1.60 (s, 9H), 1.42 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 171.4, 164.0, 162.6, 159.0, 157.7, 134.3, 134.0, 132.3, 128.7, 127.9, 127.7, 126.1, 125.72, 125.69, 124.9, 117.5, 83.9, 62.9, 43.3, 28.1, 14.3; IR (film) ν_{max} 2980, 2935, 1746, 1726, 1573, 1552, 1511, 1457, 1395, 1369, 1277, 1256, 1202, 1157, 1102, 1021, 845, 795, 781, 708 cm^{-1} ; HRESI-TOF m/z 393.1811 ($\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_4 + \text{H}^+$ requires 393.1809).

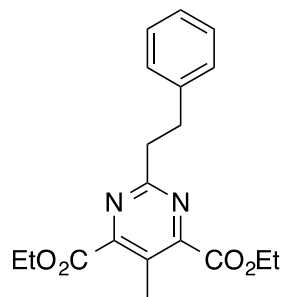


4-(tert-Butyl) 6-Ethyl 2-(Pent-4-en-1-yl)pyrimidine-4,6-dicarboxylate (13e). A solution of **7** (30.0 mg, 0.118 mmol, 2.0 equiv) in CH_3CN (257 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10e** (6.7 mg, 0.059 mmol, 1.0 equiv) in CH_3CN (197 μL) at room temperature. The reaction mixture was stirred for 4 h, at which time the mixture was purified by preparative TLC (40% EtOAc/hexanes) to provide **13e** (13.6 mg, 72%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.27 (s, 1H), 5.89–5.78 (m, 1H), 5.03 (d, $J = 17.2$ Hz, 1H), 4.96 (dd, $J = 10.2, 1.0$ Hz, 1H), 4.51 (q, $J = 7.1$ Hz, 2H), 3.20–3.13 (m, 2H), 2.17 (q, $J = 7.2$ Hz, 2H), 1.98 (p, $J = 7.6, 7.1$ Hz, 2H), 1.64 (s, 9H), 1.45 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 173.2, 164.2,

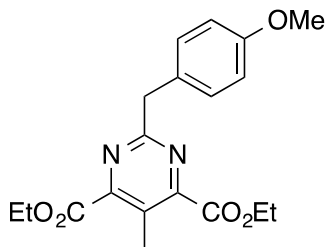
162.7, 158.7, 157.4, 138.3, 117.3, 115.2, 84.0, 63.0, 39.0, 33.6, 28.13 (3C), 28.08, 14.3; IR (film) ν_{\max} 2980, 2935, 1747, 1727, 1555, 1457, 1387, 1370, 1277, 1255, 1202, 1158, 1100, 1023, 913, 845, 756 cm^{-1} ; HRESI-TOF m/z 321.1811 ($\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_4 + \text{H}^+$ requires 321.1809).



Diethyl 5-Methyl-2-phenylpyrimidine-4,6-dicarboxylate (14a). A solution of **8** (20.0 mg, 0.084 mmol, 2.0 equiv) in CH_3CN (182 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10a** (5.0 mg, 0.042 mmol, 1.0 equiv) in CH_3CN (140 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **14a** (2.5 mg, 19%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.51–8.43 (m, 2H), 7.54–7.44 (m, 3H), 4.51 (q, $J = 7.2$ Hz, 4H), 2.53 (s, 3H), 1.46 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 165.5 (2C), 162.4, 159.0 (2C), 136.3, 131.3, 128.7 (2C), 128.6 (2C), 124.5, 62.6 (2C), 14.4 (3C); IR (film) ν_{\max} 2925, 2853, 1739, 1557, 1398, 1378, 1291, 1245, 1180, 1044 cm^{-1} ; HRESI-TOF m/z 315.1340 ($\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_4 + \text{H}^+$ requires 315.1339).

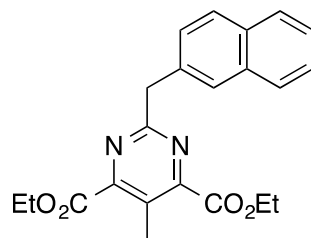


Diethyl 5-Methyl-2-(2-phenylethyl)pyrimidine-4,6-dicarboxylate (14b). A solution of **8** (20.0 mg, 0.084 mmol, 2.0 equiv) in CH_3CN (182 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10b** (6.2 mg, 0.042 mmol, 1.0 equiv) in CH_3CN (140 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **14b** (2.8 mg, 20%): ^1H NMR (CDCl_3 , 500 MHz) δ 7.34–7.21 (m, 4H), 7.23–7.15 (m, 1H), 4.49 (q, $J = 7.2$ Hz, 4H), 3.34 (dd, $J = 9.9, 6.5$ Hz, 2H), 3.16 (dd, $J = 9.9, 6.6$ Hz, 2H), 2.47 (s, 3H), 1.44 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 168.2 (2C), 165.3, 158.7 (2C), 141.3, 128.7 (2C), 128.5 (2C), 126.2, 124.1, 62.7 (2C), 40.5, 34.4, 14.32 (2C), 14.29; IR (film) ν_{\max} 2921, 2857, 1739, 1556, 1401, 1245, 1134, 1044, 703 cm^{-1} ; HRESI-TOF m/z 343.1654 ($\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_4 + \text{H}^+$ requires 343.1652).

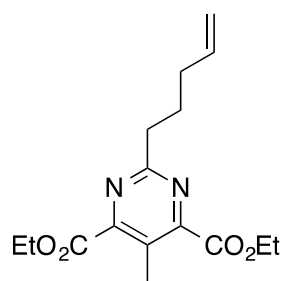


Diethyl 2-(4-Methoxybenzyl)-5-methylpyrimidine-4,6-dicarboxylate (14c). A solution of **8** (20.0 mg, 0.084 mmol, 2.0 equiv) in CH_3CN (182 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10c** (6.9 mg, 0.042 mmol, 1.0 equiv) in CH_3CN (140 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **14c** (3.8 mg, 25%): ^1H NMR (CDCl_3 , 500 MHz) δ 7.29 (d, $J = 8.5$ Hz, 2H), 6.82 (d, $J = 8.6$ Hz, 2H), 4.46 (q, $J = 7.2$ Hz, 4H), 4.28 (s, 2H), 3.77 (s, 3H), 2.44 (s, 3H), 1.42 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 167.8 (2C), 165.3, 161.9, 159.0 (2C), 158.6, 130.3 (2C), 114.0 (2C), 99.8, 62.6 (2C), 55.4, 44.4, 14.3

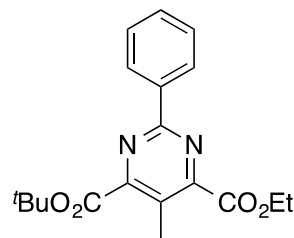
(2), 14.2; IR (film) ν_{\max} 2925, 2854, 1738, 1612, 1556, 1512, 1445, 1397, 1299, 1246, 1137, 1089, 1042, 859, 801 cm^{-1} ; HRESI-TOF m/z 359.1601 ($\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_5 + \text{H}^+$ requires 359.1601).



Diethyl 5-Methyl-2-(naphthalen-2-ylmethyl)pyrimidine-4,6-dicarboxylate (14d). A solution of **8** (20.0 mg, 0.084 mmol, 2.0 equiv) in CH_3CN (182 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10d** (7.7 mg, 0.042 mmol, 1.0 equiv) in CH_3CN (140 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **14d** (3.5 mg, 22%): ^1H NMR (CDCl_3 , 500 MHz) δ 8.31 (d, $J = 8.3$ Hz, 1H), 7.83 (d, $J = 8.1$ Hz, 1H), 7.77–7.71 (m, 1H), 7.54–7.42 (m, 2H), 7.43–7.37 (m, 2H), 4.80 (s, 2H), 4.44 (q, $J = 7.1$ Hz, 4H), 2.44 (s, 3H), 1.39 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 167.4 (2C), 165.2, 158.8 (2C), 134.3, 134.0, 132.3, 128.6, 127.7, 127.6, 126.1, 125.7 (2C), 124.8, 124.4, 62.5 (2C), 42.8, 14.3 (2C), 14.2; IR (film) ν_{\max} 2982, 2933, 1737, 1555, 1445, 1397, 1297, 1243, 1136, 1095, 1043, 1019, 793, 713 cm^{-1} ; HRESI-TOF m/z 379.1653 ($\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_4 + \text{H}^+$ requires 379.1652).

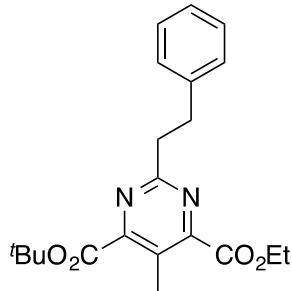


Diethyl 5-Methyl-2-(pent-4-en-1-yl)pyrimidine-4,6-dicarboxylate (14e). A solution of **8** (20.0 mg, 0.084 mmol, 2.0 equiv) in CH_3CN (182 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10e** (4.7 mg, 0.042 mmol, 1.0 equiv) in CH_3CN (140 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **14e** (3.2 mg, 25%); ^1H NMR (CDCl_3 , 500 MHz) δ 5.89–5.78 (m, 1H), 5.03 (d, $J = 17.0$ Hz, 1H), 4.97 (d, $J = 10.2$ Hz, 1H), 4.48 (q, $J = 7.3$ Hz, 4H), 3.06–2.98 (m, 2H), 2.46 (s, 3H), 2.15 (q, $J = 7.2$ Hz, 2H), 1.93 (p, $J = 7.7$ Hz, 2H), 1.43 (t, $J = 7.1$ Hz, 6H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 169.1 (2C), 165.4, 158.7 (2C), 138.3, 123.9, 115.2, 62.6 (2C), 38.4, 33.6, 28.0, 14.30 (2C), 14.25; IR (film) ν_{\max} 2982, 2930, 2872, 1739, 1558, 1447, 1407, 1379, 1243, 1165, 1135, 1097, 1044, 913, 862, 717 cm^{-1} ; HRESI-TOF m/z 307.1654 ($\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}_4 + \text{H}^+$ requires 307.1652).

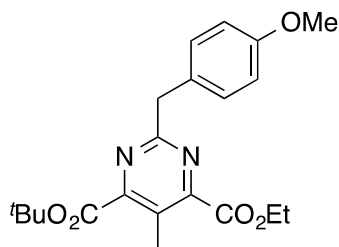


4-(tert-Butyl) 6-Ethyl 5-Methyl-2-phenylpyrimidine-4,6-dicarboxylate (15a). A solution of **9** (0.094 mmol, 25 mg) in anhydrous CH_3CN (200 μL) at 25 °C was treated with a solution of **10a** (0.062 mmol, 7.5 mg) in anhydrous CH_3CN (200 μL). The reaction mixture was stirred at 60 °C for 16 h, upon which time the mixture was cooled to 25 °C, filtered through Celite, and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2 , 10% EtOAc/hexanes) to yield **15a** as a clear oil (13.2 mg, 62%): ^1H NMR (CDCl_3 , 400

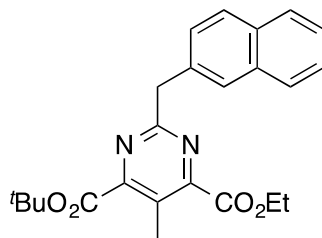
MHz) δ 8.54–8.39 (m, 2H), 7.54–7.39 (m, 3H), 4.50 (q, $J = 7.1$ Hz, 2H), 2.49 (s, 3H), 1.66 (s, 9H), 1.46 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 165.5, 164.8, 162.4, 160.5, 158.4, 136.4, 131.2, 128.64 (2C), 128.59 (2C), 123.5, 84.3, 62.5, 28.3 (3C), 14.4, 14.3; IR (neat) ν_{max} 2981, 2930, 1736, 1555, 1454, 1397, 1373, 1292, 1254, 1161, 1134, 1095, 1044, 846, 748, 721, 695 cm^{-1} ; HRESI-TOF m/z 343.1658 ($\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_4 + \text{H}^+$ requires 343.1652).



4-(tert-Butyl) 6-Ethyl 5-Methyl-2-phenethylpyrimidine-4,6-dicarboxylate (15b). A solution of **9** (0.075 mmol, 20 mg) in anhydrous CH_3CN (160 μL) at 25 $^\circ\text{C}$ was treated with a solution of free-based 3-phenylpropanimidamide (0.037 mmol, 5.5 mg) in anhydrous CH_3CN (125 μL). The reaction mixture was stirred at 25 $^\circ\text{C}$ for 16 h, upon which time the mixture was filtered through Celite and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2 , 10% EtOAc/hexanes) to yield **15b** as a clear oil (9.0 mg, 66%): ^1H NMR (CDCl_3 , 600 MHz) δ 7.31–7.23 (m, 4H), 7.20–7.17 (m, 1H), 4.48 (q, $J = 7.1$ Hz, 2H), 3.36–3.29 (m, 2H), 3.19–3.12 (m, 2H), 2.44 (s, 3H), 1.64 (s, 9H), 1.43 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 168.1, 165.4, 164.7, 160.3, 158.1, 141.4, 128.7 (2C), 128.5 (2C), 126.1, 123.0, 84.4, 62.6, 40.4, 34.4, 28.3 (3C), 14.3, 14.2; IR (neat) ν_{max} 2977, 2927, 1736, 1556, 1453, 1406, 1370, 1253, 1224, 1163, 1135, 1045, 845, 751, 700 cm^{-1} ; HRESI-TOF m/z 371.1963 ($\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_4 + \text{H}^+$ requires 371.1965).

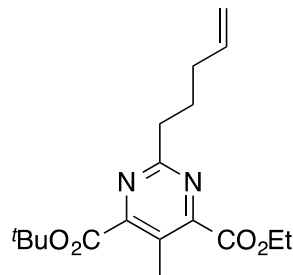


4-(tert-Butyl) 6-Ethyl 2-(4-Methoxybenzyl)-5-methylpyrimidine-4,6-dicarboxylate (15c). A solution of **9** (30.0 mg, 0.112 mmol, 2.0 equiv) in CH_3CN (244 μL) stirring with crushed 4 \AA molecule sieves was treated dropwise with a solution of **10c** (9.2 mg, 0.056 mmol, 1.0 equiv) in CH_3CN (187 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **15c** (10.7 mg, 50%): ^1H NMR (CDCl_3 , 500 MHz) δ 7.31 (d, $J = 8.6$ Hz, 2H), 6.81 (d, $J = 8.7$ Hz, 2H), 4.45 (q, $J = 7.1$ Hz, 2H), 4.26 (s, 2H), 3.77 (s, 3H), 2.41 (s, 3H), 1.62 (s, 9H), 1.41 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 167.7, 165.3, 164.6, 160.4, 158.5, 158.4, 130.3 (2C), 130.1, 123.1, 113.9 (2C), 84.3, 62.5, 55.4, 44.3, 28.3 (3C), 14.3, 14.1; IR (film) ν_{max} 2979, 2932, 1734, 1555, 1512, 1460, 1396, 1371, 1299, 1249, 1163, 1037, 844, 800 cm^{-1} ; HRESI-TOF m/z 387.1916 ($\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_5 + \text{H}^+$ requires 387.1914).



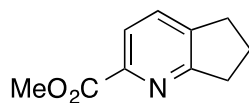
4-(tert-Butyl) 6-Ethyl 5-Methyl-2-(naphthalen-2-yl-methyl)pyrimidine-4,6-dicarboxylate (15d). A solution of **9** (30.0 mg, 0.112 mmol, 2.0 equiv) in CH_3CN (431 μL) stirring with crushed 4 \AA molecule sieves was treated with **10d** (10.3 mg, 0.056 mmol, 1.0 equiv) at room temperature. The reaction mixture was stirred for

16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **15d** (11.2 mg, 49%): $^1\text{H NMR}$ (CDCl_3 , 500 MHz) δ 8.34 (d, $J = 8.5$ Hz, 1H), 7.85–7.81 (m, 1H), 7.76–7.71 (m, 1H), 7.52–7.37 (m, 4H), 4.78 (s, 2H), 4.43 (q, $J = 7.1$ Hz, 2H), 2.41 (s, 3H), 1.59 (s, 9H), 1.39 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 125 MHz) δ 167.3, 165.3, 164.6, 160.2, 158.3, 134.4, 134.0, 132.4, 128.6, 127.7, 127.6, 126.0, 125.7, 125.6, 124.9, 123.3, 84.2, 62.4, 42.7, 28.2 (3C), 14.3, 14.1; IR (film) ν_{max} 2981, 2930, 1734, 1555, 1452, 1395, 1371, 1297, 1223, 1161, 1135, 1045, 846, 791 cm^{-1} ; HRESI-TOF m/z 407.1967 ($\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_4 + \text{H}^+$ requires 407.1965).

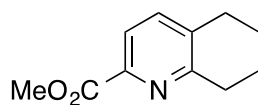


4-(tert-Butyl) 6-Ethyl 5-Methyl-2-(pent-4-en-1-yl)pyrimidine-4,6-dicarboxylate (15e). A solution of **9** (30.0 mg, 0.112 mmol, 2.0 equiv) in CH_3CN (244 μL) stirring with crushed 4 Å molecule sieves was treated dropwise with a solution of **10e** (6.3 mg, 0.056 mmol, 1.0 equiv) in CH_3CN (187 μL) at room temperature. The reaction mixture was stirred for 16 h, at which time the mixture was purified by preparative TLC (30% EtOAc/hexanes) to provide **15e** (6.7 mg, 36%): $^1\text{H NMR}$ (CDCl_3 , 500 MHz) δ 5.83 (ddt, $J = 17.0, 10.2, 6.7$ Hz, 1H), 5.03 (dd, $J = 17.1, 1.8$ Hz, 1H), 4.99–4.94 (m, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 3.03–2.97 (m, 2H), 2.42 (s, 3H), 2.20–2.10 (m, 2H), 1.98–1.88 (m, 2H), 1.63 (s, 9H), 1.42 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 125 MHz) δ 169.0, 165.5, 164.8, 160.3, 158.1, 138.4, 122.7, 115.1, 84.4, 62.5, 38.4, 33.6, 28.3 (3C), 28.0, 14.3, 14.1; IR (film) ν_{max} 2979, 2930, 1736, 1557, 1407, 1252, 1224, 1159, 1135, 1044 cm^{-1} ; HRESI-TOF m/z 335.1966 ($\text{C}_{18}\text{H}_{26}\text{N}_2\text{O}_4 + \text{H}^+$ requires 335.1965).

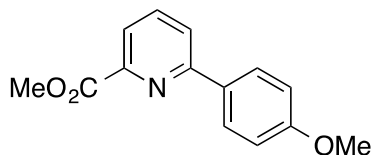
III. Reaction of 1,2,3-Triazines with Enamines



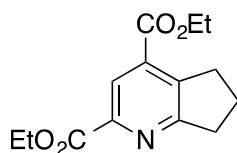
Methyl 6,7-Dihydro-5H-cyclopenta[b]pyridine-2-carboxylate (17a). Pyrrolidino-1-cyclopentene (**16a**, 19 μL , 0.13 mmol, 1.2 equiv) was added to a stirred solution of **5** (15.8 mg, 0.11 mmol) and 4 Å molecular sieves (16 mg) in CHCl_3 (1.1 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile and rapid N_2 evolution was observed. After 15 min, the reaction mixture was warmed to 60 °C and stirred for 30 min at 60 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 40% EtOAc/hexanes) to provide **17a** (13.6 mg, 68%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 7.91 (d, $J = 8.0$ Hz, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 3.98 (s, 3H), 3.10 (t, $J = 8.0$ Hz, 2H), 2.99 (t, $J = 7.6$ Hz, 2H), 2.17 (q, $J = 7.6$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 166.5, 166.2, 146.0, 141.6, 132.4, 123.2, 52.7, 34.2, 30.8, 23.2; IR ν_{max} 2949, 1708, 1441, 1426, 1335, 1285, 1191, 1163, 1119, 970, 860, 783 cm^{-1} ; HRESI-TOF m/z 200.0685 ($\text{C}_{10}\text{H}_{11}\text{NO}_2 + \text{Na}^+$ requires 200.0683).



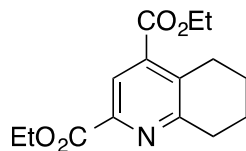
Methyl 5,6,7,8-Tetrahydroquinoline-2-carboxylate (17b). 1-Pyrrolidino-1-cyclohexene (**16b**, 43 μL , 0.26 mmol, 1.2 equiv) was added to a stirred solution of **5** (30 mg, 0.21 mmol) and 4 Å molecular sieves (30 mg) in CHCl_3 (2.1 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile and rapid N_2 evolution was observed. After 15 min, the reaction mixture was warmed to 60 °C and stirred for 2 h at 60 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 40% EtOAc/hexanes) to provide **17b** (21.8 mg, 53%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 7.87 (d, $J = 8.0$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 1H), 3.98 (s, 3H), 3.02 (t, $J = 6.4$ Hz, 2H), 2.84 (t, $J = 6.4$ Hz, 2H), 1.91-1.93 (m, 2H), 1.82-1.85 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 166.1, 158.0, 145.0, 137.5, 136.8, 122.5, 52.8, 32.7, 29.0, 22.8, 22.3; IR ν_{max} 2940, 1738, 1434, 1426, 1365, 1268, 1197, 1163, 1133 cm^{-1} ; HRESI-TOF m/z 192.1017 ($\text{C}_{11}\text{H}_{13}\text{NO}_2 + \text{H}^+$ requires 192.1019).



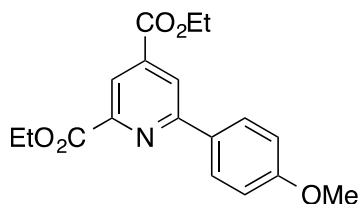
Methyl 6-(4-Methoxyphenyl)picolinate (17c). 1-(1-(4-methoxyphenyl)vinyl)pyrrolidine (**16c**,⁹ 24 mg, 0.12 mmol, 1.2 equiv) was added to a stirred solution of **5** (14 mg, 0.10 mmol) and 4 Å molecular sieves (15 mg) in CHCl_3 (1.0 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile. After 30 min, the reaction mixture was warmed to 60 °C and stirred for 8 h at 60 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 10% EtOAc/hexanes) to provide **17c** (10.2 mg, 53%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.02 (d, $J = 8.8$ Hz, 2H), 7.99 (d, $J = 8.0$ Hz, 1H), 7.85 (d, $J = 3.2$ Hz, 1H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.00 (d, $J = 8.8$ Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 166.1, 160.8, 157.4, 147.9, 137.5, 131.1, 128.5, 122.9, 122.6, 114.2, 55.3, 52.8; IR ν_{max} 2946, 1731, 1608, 1452, 1386, 1214, 1077, 1046, 1018 cm^{-1} ; HRESI-TOF m/z 244.0970 ($\text{C}_{14}\text{H}_{13}\text{NO}_3 + \text{H}^+$ requires 244.0968).



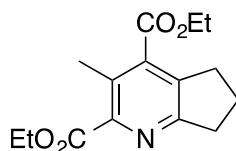
Diethyl 6,7-Dihydro-5H-cyclopenta[*b*]pyridine-2,4-dicarboxylate (18a). 1-Pyrrolidino-1-cyclopentene (**16a**, 30 μ L, 0.20 mmol, 1.2 equiv) was added to a stirred solution of **6** (39 mg, 0.17 mmol) and 4 Å molecular sieves (39 mg) in CHCl_3 (1.7 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile and rapid N_2 evolution was observed. After 15 min, the reaction mixture was warmed to 60 °C and stirred for 4 h at 60 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 40% EtOAc/hexanes) to provide **18a** (23.6 mg, 52%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.41 (s, 1H), 4.49 (q, $J = 7.2$ Hz, 2H), 4.42 (q, $J = 7.2$ Hz, 2H), 3.35 (t, $J = 7.6$ Hz, 2H), 3.16 (t, $J = 7.6$ Hz, 2H), 2.21–2.17 (m, 2H), 1.46–1.41 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 169.5, 165.7, 156.5, 147.7, 142.8, 123.1, 100.0, 62.4, 62.2, 34.6, 32.3, 31.3, 14.8, 14.7; IR ν_{max} 2977, 1724, 1441, 1369, 1201, 1177, 1096, 1026 cm^{-1} ; HRESI-TOF m/z 264.1227 ($\text{C}_{14}\text{H}_{15}\text{NO}_4 + \text{H}^+$ requires 264.1230).



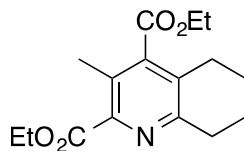
Diethyl 5,6,7,8-Tetrahydroquinoline-2,4-dicarboxylate (18b). 1-Pyrrolidino-1-cyclopentene (**16b**, 31 μ L, 0.19 mmol, 1.0 equiv) was added to a stirred solution of **6** (42 mg, 0.19 mmol) and 4 Å molecular sieves (42 mg) in CHCl_3 (1.9 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile. After 1 h, the reaction mixture was treated with *m*-CPBA (68 mg, 0.28 mmol, 1.5 equiv) and stirred for 2 h at room temperature. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 40% EtOAc/hexanes) to provide **18b** (21.8 mg, 41%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.22 (s, 1H), 4.48 (q, $J = 7.2$ Hz, 2H), 4.40 (q, $J = 7.2$ Hz, 2H), 3.08–3.12 (m, 4H), 1.88–1.94 (m, 2H), 1.80–1.86 (m, 2H), 1.40–1.46 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 166.0, 165.0, 160.0, 145.4, 138.6, 136.3, 122.3, 62.0, 61.8, 33.6, 27.3, 22.2, 14.3, 14.2; IR ν_{max} 2938, 1730, 1447, 1373, 1234, 1096, 1042, 1018 cm^{-1} ; HRESI-TOF m/z 278.1390 ($\text{C}_{14}\text{H}_{19}\text{NO}_4 + \text{H}^+$ requires 278.1387).



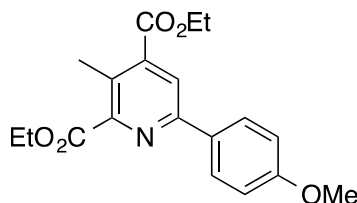
Diethyl 6-(4-Methoxyphenyl)pyridine-2,4-dicarboxylate (18c). 1-(1-(4-methoxyphenyl)vinyl)pyrrolidine (**16c**,⁹ 29 mg, 0.14 mmol, 1.0 equiv) was added to a stirred solution of **6** (33 mg, 0.14 mmol) and 4 Å molecular sieves (33 mg) in CHCl_3 (1.4 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile. After 30 min, the reaction mixture was warmed to 60 °C and stirred for 12 h at 60 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 10% EtOAc/hexanes) to provide **18c** (6.9 mg, 15%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.46 (s, 1H), 8.40 (s, 1H), 8.10 (d, $J = 8.8$ Hz, 2H), 7.01 (d, $J = 8.8$ Hz, 2H), δ 4.49 (q, $J = 7.2$ Hz, 2H), 4.44 (q, $J = 7.2$ Hz, 2H), 3.87 (s, 3H), 1.42–1.48 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 165.0, 164.8, 161.2, 158.3, 149.2, 139.7, 130.3, 128.7, 121.9, 121.6, 114.3, 62.2, 62.1, 55.4, 14.3, 14.2; IR ν_{max} 2937, 1740, 1611, 1429, 1362, 1234, 1083, 1018 cm^{-1} ; HRESI-TOF m/z 330.1441 ($\text{C}_{18}\text{H}_{19}\text{NO}_5 + \text{H}^+$ requires 330.1336).



Diethyl 3-Methyl-6,7-dihydro-5H-cyclopenta[*b*]pyridine-2,4-dicarboxylate (19a). Pyrrolidino-1-cyclopentene (**16a**, 47 μ L, 0.30 mmol, 1.2 equiv) was added to a stirred solution of **8** (60 mg, 0.25 mmol) and 4 Å molecular sieves (60 mg) in CHCl_3 (2.5 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile. After 45 min, the reaction mixture was cooled to 0 °C and treated with *m*-CPBA (93 mg, 0.37 mmol, 1.5 equiv) and stirred for 1 h at 0 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 20% EtOAc/hexanes) to provide **19a** (53 mg, 78%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 4.43 (q, $J = 7.2$ Hz, 2H), 4.39 (q, $J = 7.2$ Hz, 2H), 3.05 (t, $J = 7.6$ Hz, 2H), 2.99 (t, $J = 7.6$ Hz, 2H), 2.46 (s, 3H), 2.11–2.15 (m, 2H), 1.36–1.41 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 166.9, 166.7, 164.0, 148.1, 138.4, 137.4, 128.0, 61.8, 61.6, 33.9, 30.4, 22.9, 14.8, 16.0, 14.2; IR ν_{max} 2977, 1721, 1423, 1294, 1254, 1096, 1041, 1026 cm^{-1} ; HRESI-TOF m/z 278.1396 ($\text{C}_{15}\text{H}_{19}\text{NO}_4 + \text{H}^+$ requires 278.1387).

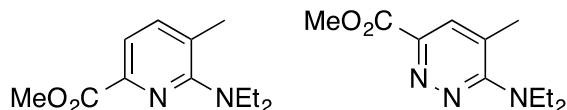


Diethyl 3-Methyl-5,6,7,8-tetrahydroquinoline-2,4-dicarboxylate (19b). Pyrrolidino-1-cyclohexene (**16b**, 56 μ L, 0.36 mmol, 1.2 equiv) was added to a stirred solution of **8** (72 mg, 0.30 mmol) and 4 Å molecular sieves (72 mg) in CHCl_3 (3.0 mL) at room temperature. The reaction mixture turned from yellow to red with the addition of the dienophile. After 4 h, the reaction mixture was cooled to 0 °C and treated with *m*-CPBA (100 mg, 0.45 mmol, 1.5 equiv) and stirred for 1 h at 0 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 20% EtOAc/hexanes) to provide **19b** (51 mg, 58%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 4.44 (q, $J = 7.2$ Hz, 2H), 4.39 (q, $J = 7.2$ Hz, 2H), 2.96 (t, $J = 6.4$ Hz, 2H), 2.71 (t, $J = 6.4$ Hz, 2H), 2.37 (s, 3H), 1.80–1.88 (m, 4H), 1.36–1.41 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 167.7, 166.5, 155.4, 146.5, 143.5, 130.4, 126.4, 61.7, 61.6, 32.5, 26.1, 22.5, 22.1, 15.7, 14.2; IR ν_{max} 2938, 1730, 1447, 1373, 1234, 1096, 1042, 1018 cm^{-1} ; HRESI-TOF m/z 292.1558 ($\text{C}_{16}\text{H}_{21}\text{NO}_4 + \text{H}^+$ requires 292.1549).

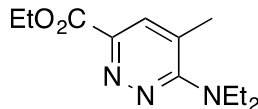


Diethyl 6-(4-Methoxyphenyl)-3-methylpyridine-2,4-dicarboxylate (19c). 1-(1-(4-Methoxyphenyl)vinyl)pyrrolidine (**16c**,⁹ 97 mg, 0.48 mmol, 1.2 equiv) was added to a stirred solution of **8** (92 mg, 0.40 mmol) and 4 Å molecular sieves (92 mg) in CHCl_3 (4.0 mL) at room temperature. After 2 h, the reaction mixture was cooled to 0 °C and treated with *m*-CPBA (133 mg, 0.60 mmol, 1.5 equiv) and stirred for 1 h at 0 °C. The reaction mixture was evaporated under vacuum and the residue was purified by flash chromatography (SiO_2 , 10% EtOAc/hexanes) to provide **19c** (80.7 mg, 58%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 8.04 (s, 1H), 7.98 (d, $J = 8.8$ Hz, 2H), 6.98 (d, $J = 8.8$ Hz, 2H), δ 4.46 (q, $J = 7.2$ Hz, 2H), 4.40 (q, $J = 7.2$ Hz, 2H), 3.85 (s, 3H), 2.59 (s, 3H), 1.40–1.46 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 167.1, 166.4, 160.8, 154.7, 151.9, 140.5, 130.3, 128.5, 128.2, 120.5, 114.1, 61.9, 61.8, 55.3, 15.8, 14.2; IR ν_{max} 2980, 1726, 1608, 1440, 1372, 1234, 1077, 1042, 1018 cm^{-1} ; HRESI-TOF m/z 344.1498 ($\text{C}_{19}\text{H}_{21}\text{NO}_5 + \text{H}^+$ requires 344.1495).

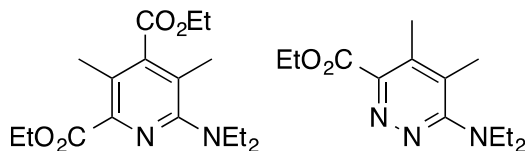
IV. Reaction of 1,2,3-Triazines with Ynamines



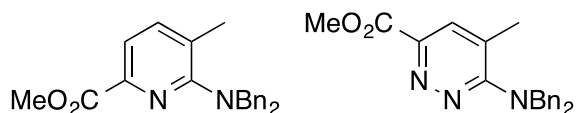
Methyl 6-(Diethylamino)-5-methylpicolinate (24a) & Methyl 6-(Diethylamino)-5-methylpyridazine-3-carboxylate (23a). Compound **22a** (7 μ L, 0.25 mmol, 1.0 equiv) was added to a stirred solution of **5** (34.6 mg, 0.25 mmol) in CHCl₃ (2.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO₂, 40% EtOAc/hexanes) to afford **24a** (5.7 mg, 10%) as a yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 7.57 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 3.93 (s, 3H), 3.28 (q, J = 7.2 Hz, 4H), 2.30 (s, 3H), 1.21 (t, J = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 166.5, 161.2, 143.4, 139.6, 118.2, 99.5, 52.4, 44.8, 19.4, 13.5; IR ν_{\max} 1742, 1468, 1435, 1210, 1134 cm⁻¹; HRESI-TOF m/z 223.1451 (C₁₂H₁₈N₂O₂ + H⁺ requires 223.1441) and **23a** (47.4 mg, 85%) as a yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 7.69 (s, 1H), 3.95 (s, 3H), 3.50 (q, J = 6.8 Hz, 4H), 2.31 (s, 3H), 1.17 (t, J = 6.8 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 165.3, 162.7, 144.2, 130.4, 126.5, 104.6, 52.5, 44.5, 20.1, 13.2; IR ν_{\max} 1740, 1532, 1426, 1379, 1164 cm⁻¹; HRESI-TOF m/z 224.1403 (C₁₁H₁₇N₃O₂ + H⁺ requires 224.1393).



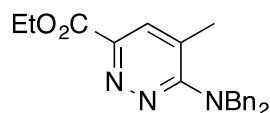
Ethyl 6-(Diethylamino)-5-methylpyridazine-3-carboxylate (25a). Compound **22a** (17 μ L, 0.15 mmol, 1.0 equiv) was added to a stirred solution of **6** (33.0 mg, 0.15 mmol) in CHCl₃ (1.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO₂, 40% EtOAc/hexanes) to afford **25a** (27.7 mg, 80%) as an oil: ¹H NMR (CDCl₃, 400 MHz) δ 7.71 (s, 1H), 4.43 (q, J = 7.2 Hz, 2H), 3.51 (q, J = 6.8 Hz, 4H), 2.32 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 6.8 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 164.9, 162.7, 144.6, 130.4, 126.6, 61.6, 44.5, 20.0, 14.3, 13.2; IR ν_{\max} 1737, 1531, 1403, 1379, 1166, 1102, 1023 cm⁻¹; HRESI-TOF m/z 238.1551 (C₁₂H₁₉N₃O₂ + H⁺ requires 238.1550).



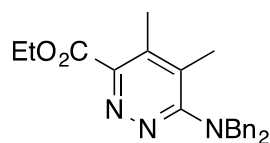
Diethyl 6-(Diethylamino)-3,5-dimethylpyridine-2,4-dicarboxylate (27a) & Ethyl 6-(Diethylamino)-4,5-dimethylpyridazine-3-carboxylate (26a). Compound **22a** (31 μ L, 0.28 mmol, 1.0 equiv) was added to a stirred solution of **8** (66.5 mg, 0.28 mmol) in CHCl₃ (3.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO₂, 40% EtOAc/hexanes) to afford **27a** (10.6 mg, 12%) as a yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 4.44–4.37 (m, 4H), 3.17 (q, J = 7.2 Hz, 4H), 2.32 (s, 3H), 2.20 (s, 3H), 1.41–1.36 (m, 6H), 1.08 (t, J = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 168.4, 166.9, 159.1, 145.6, 144.0, 123.8, 121.8, 61.5, 61.1, 45.1, 15.7, 15.2, 14.2, 13.2; IR ν_{\max} 1740, 1454, 1420, 1379, 1337, 1307, 1172, 1067, 1037 cm⁻¹; HRESI-TOF m/z 323.1968 (C₁₇H₂₆N₂O₄ + H⁺ requires 323.1965) and **26a** (50.4 mg, 79%) as a yellow oil: ¹H NMR (CDCl₃, 400 MHz) δ 4.43 (q, J = 7.2 Hz, 2H), 3.35 (q, J = 7.2 Hz, 4H), 2.41 (s, 3H), 2.21 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ 166.1, 163.3, 147.2, 137.7, 128.8, 61.5, 44.8, 15.1, 14.8, 14.1, 12.8; IR ν_{\max} 1740, 1548, 1448, 1419, 1381, 1175, 1083, 1056 cm⁻¹; HRESI-TOF m/z 252.1713 (C₁₃H₂₁N₃O₂ + H⁺ requires 252.1706).



Methyl 6-(Dibenzylamino)-5-methylpicolinate (24b) & Methyl 6-(Dibenzylamino)-5-methylpyridazine-3-carboxylate (23b). Compound **22b** (22 μ L, 0.09 mmol, 1.0 equiv) was added to a stirred solution of **5** (13.0 mg, 0.09 mmol) in CHCl_3 (1.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO_2 , 40% EtOAc/hexanes) to afford **24b** (1.0 mg, 3%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 7.62 (d, $J = 7.6$ Hz, 1H), 7.47 (d, $J = 7.6$ Hz, 1H), 7.38–7.21 (m, 10H), 4.41 (s, 4H), 3.94 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 140.0, 139.0, 128.51, 128.49, 128.2, 126.8, 119.4, 112.4, 107.7, 54.5, 52.4, 19.2; IR ν_{max} 1740, 1454, 1357, 1315, 1264, 1201, 1135, 700, 426 cm^{-1} ; HRESI-TOF m/z 347.1755 ($\text{C}_{22}\text{H}_{22}\text{N}_2\text{O}_2 + \text{H}^+$ requires 347.1754) and **23b** (21.3 mg, 66%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 7.80 (d, $J = 0.8$ Hz, 1H), 7.33–7.25 (m, 10H), 4.71 (s, 4H), 4.00 (s, 3H), 2.41 (d, $J = 0.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 165.1, 163.6, 145.5, 137.6, 130.9, 128.5, 128.0, 127.6, 127.3, 53.4, 52.7, 19.8; IR ν_{max} 1740, 1583, 1531, 1494, 1438, 1417, 1388, 1361, 1264, 1227, 1173, 1113, 741, 699 cm^{-1} ; HRESI-TOF m/z 348.1789 ($\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_2 + \text{H}^+$ requires 348.1710).



Ethyl 6-(Dibenzylamino)-5-methylpyridazine-3-carboxylate (25b). Compound **22b** (26 μ L, 0.11 mmol, 1.0 equiv) was added to a stirred solution of **6** (25.0 mg, 0.11 mmol) in CHCl_3 (1.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO_2 , 40% EtOAc/hexanes) to afford **25b** (27.9 mg, 70%) as a yellow oil: ^1H NMR (CDCl_3 , 400 MHz) δ 7.93 (s, 1H), 7.47–7.37 (m, 10H), 4.84 (s, 4H), 4.60 (q, $J = 7.2$ Hz, 2H), 2.55 (s, 3H), 1.58 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 164.7, 163.6, 145.8, 137.6, 130.9, 128.5, 127.9, 127.6, 127.3, 61.9, 53.4, 19.8, 14.3; IR ν_{max} 1740, 1531, 1452, 1404, 1358, 1227, 1172, 1109, 1026, 744, 699 cm^{-1} ; HRESI-TOF m/z 362.1867 ($\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2 + \text{H}^+$ requires 362.1863).

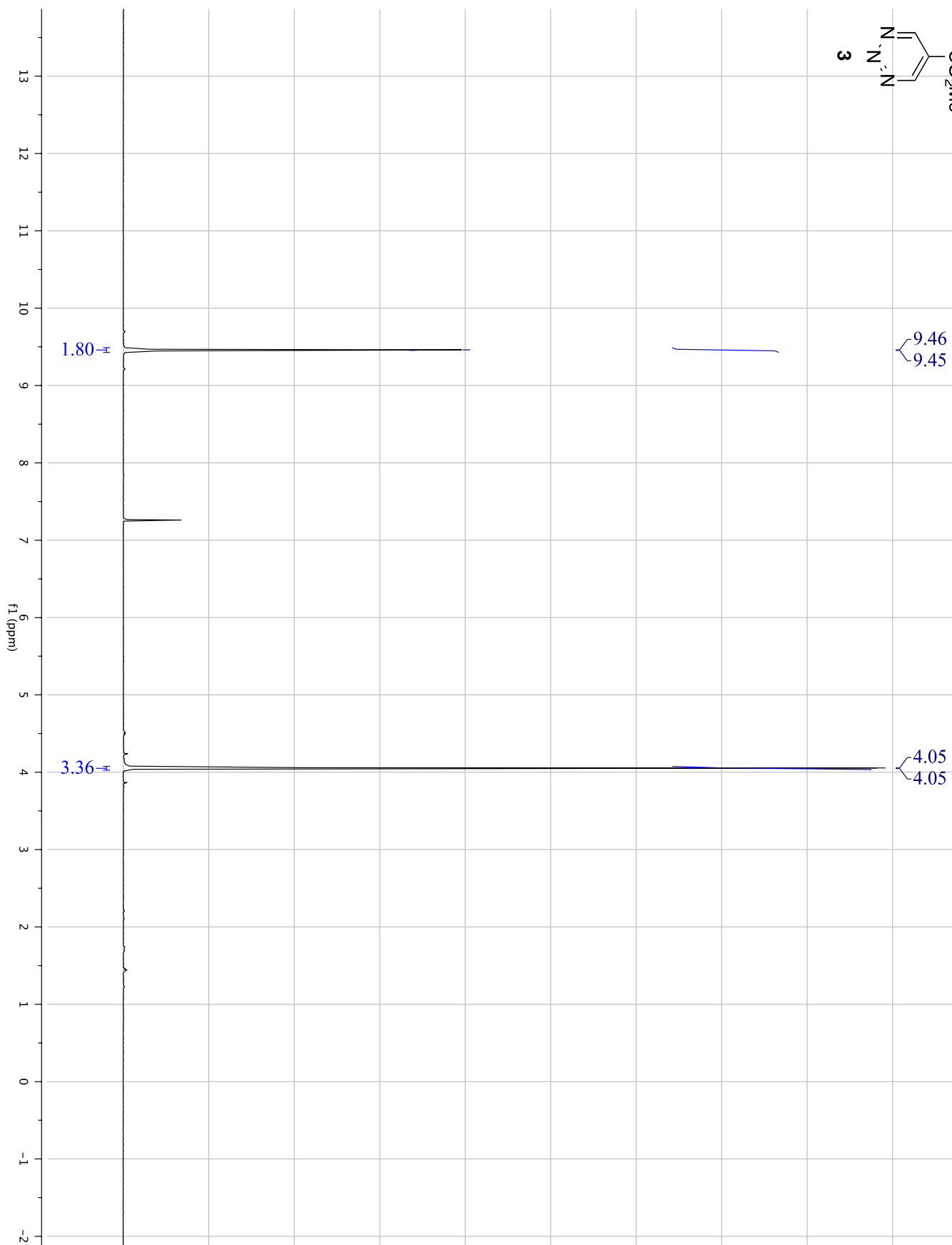
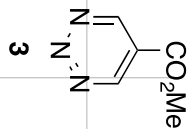


Ethyl 6-(Dibenzylamino)-4,5-dimethylpyridazine-3-carboxylate (26b). Compound **22b** (49 μ L, 0.21 mmol, 1.0 equiv) was added to a stirred solution of **8** (49.0 mg, 0.21 mmol) in CHCl_3 (2.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h, concentrated and purified by column chromatography (SiO_2 , 40% EtOAc/hexanes) to afford **26b** (62.8 mg, 81%) as a white solid: ^1H NMR (CDCl_3 , 400 MHz) δ 7.27–7.25 (m, 10 H), 4.49 (s, 4H), 4.47 (q, $J = 7.2$ Hz, 2H), 2.43 (s, 3H), 2.36 (s, 3H), 1.44 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 165.9, 163.7, 148.2, 140.2, 138.3, 137.8, 129.4, 129.0, 128.4, 128.3, 128.2, 128.1, 127.1, 126.9, 125.2, 61.8, 54.4, 53.1, 15.2, 14.7, 14.2; IR ν_{max} 1740, 1449, 1410, 1364, 1219, 1140, 1094, 1056, 1026, 738, 697 cm^{-1} ; HRESI-TOF m/z 376.2019 ($\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_2 + \text{H}^+$ requires 376.2019).

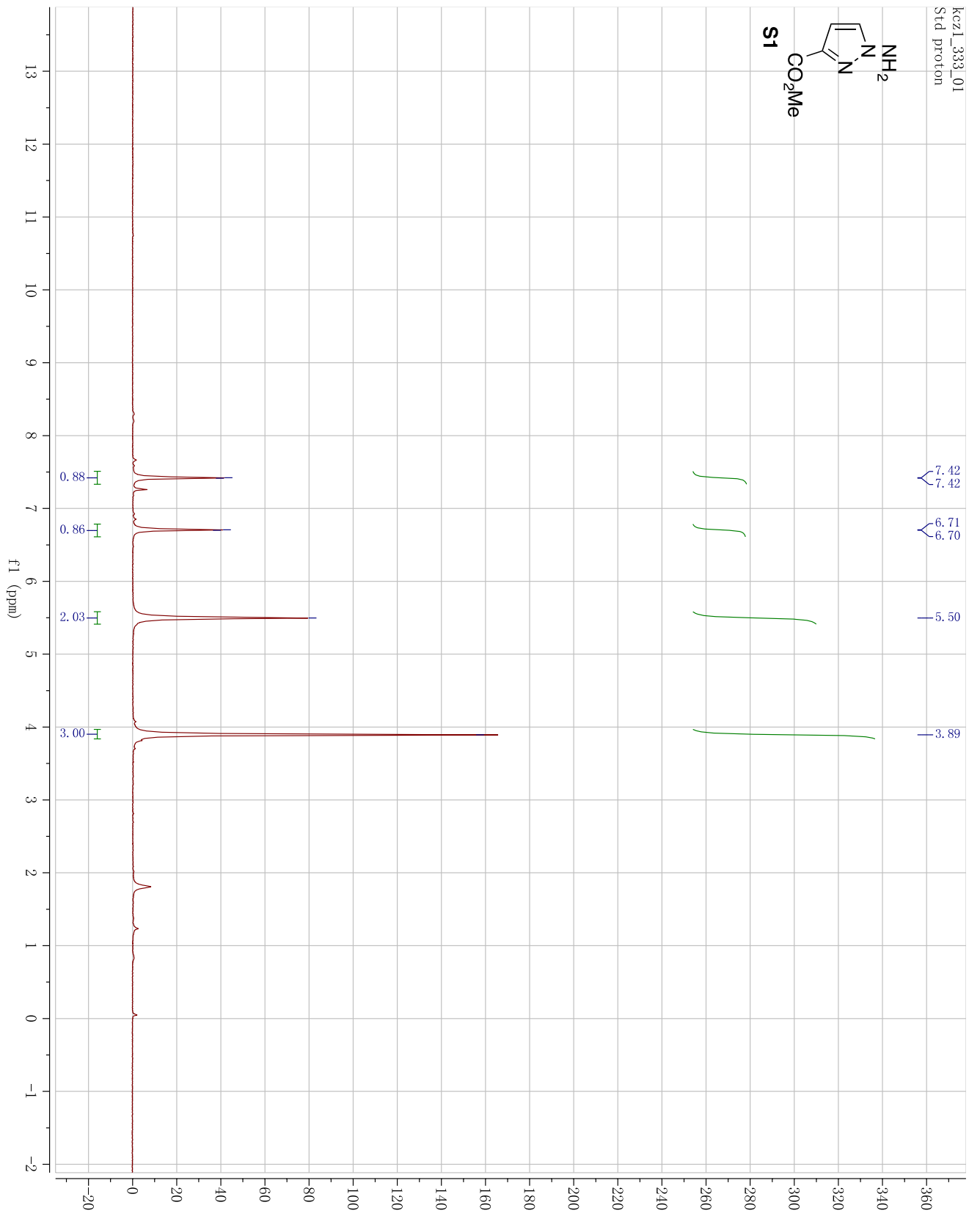
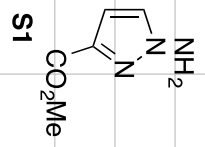
V. References

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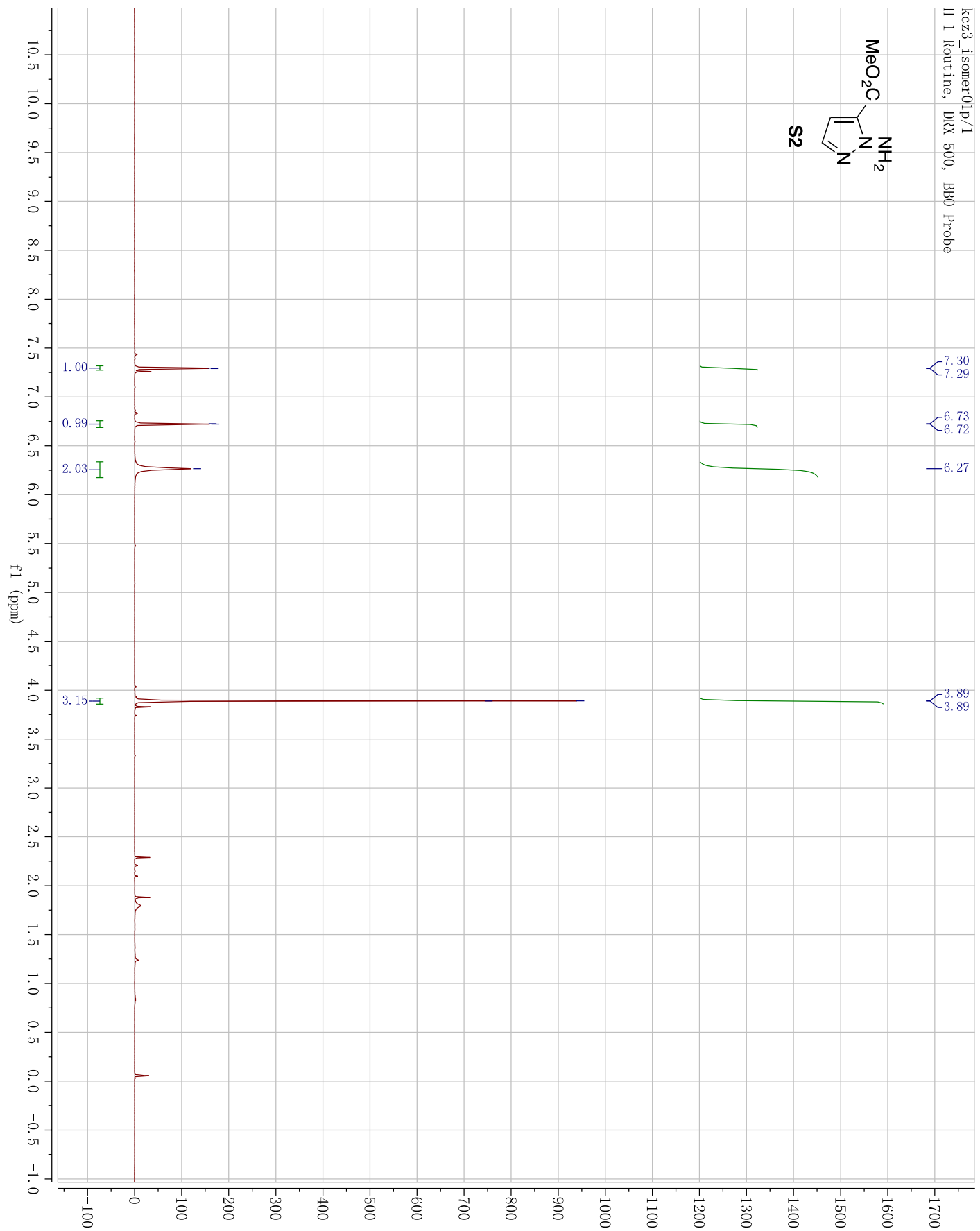
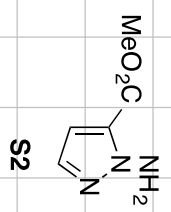
VI. ^1H NMR Spectra

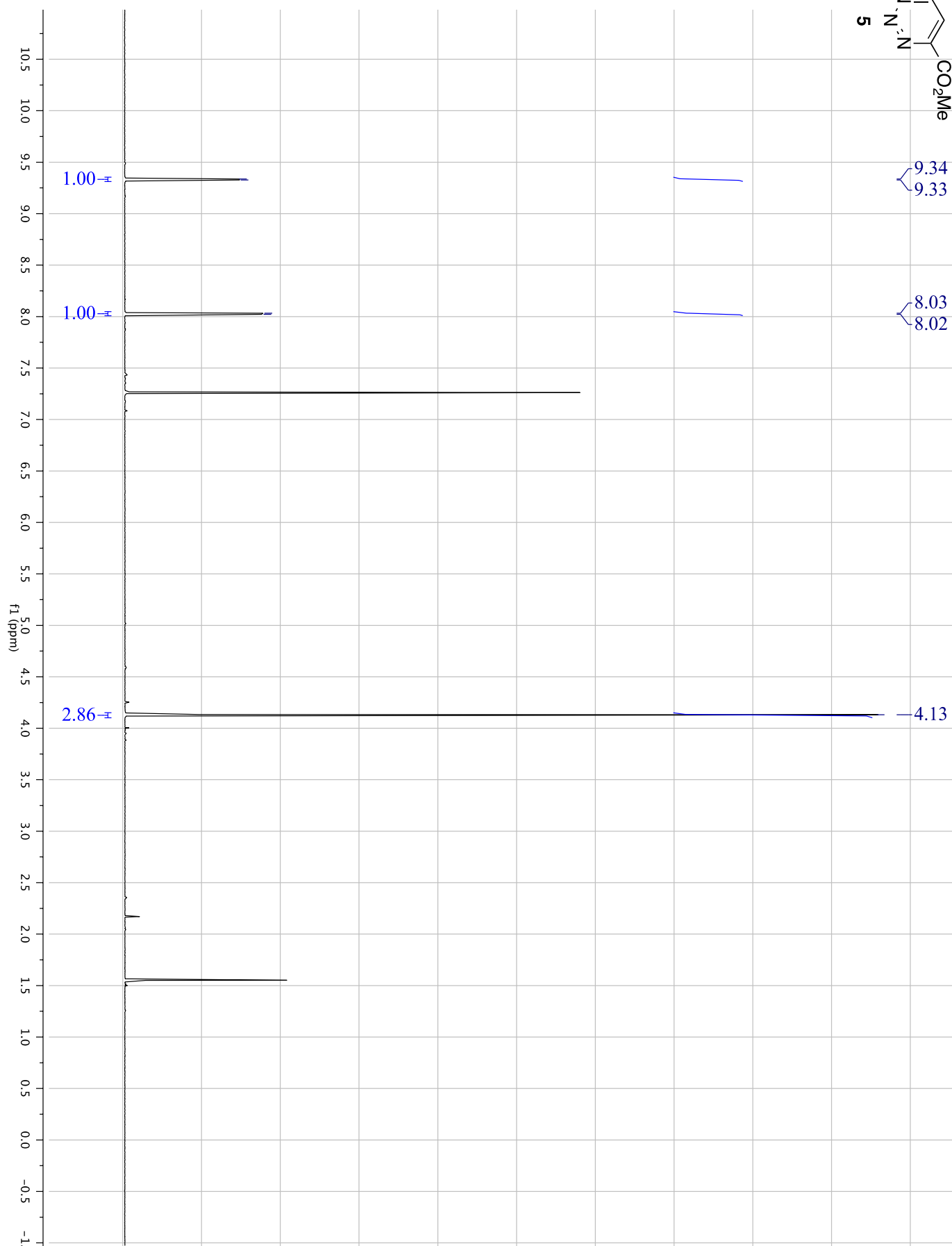
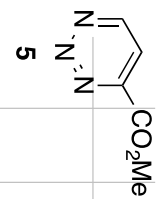


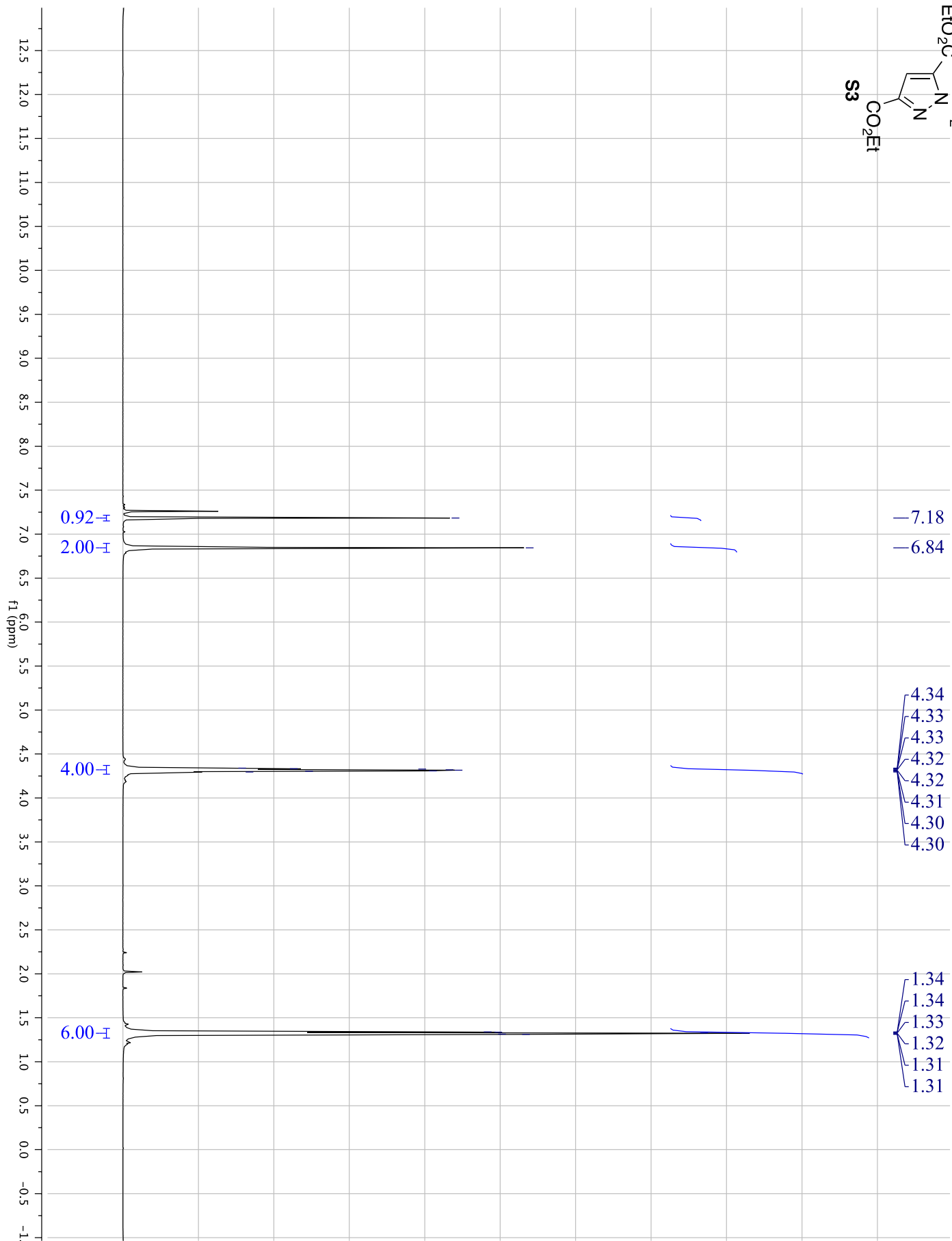
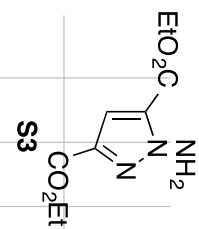
kezl_333_01
Std. proton

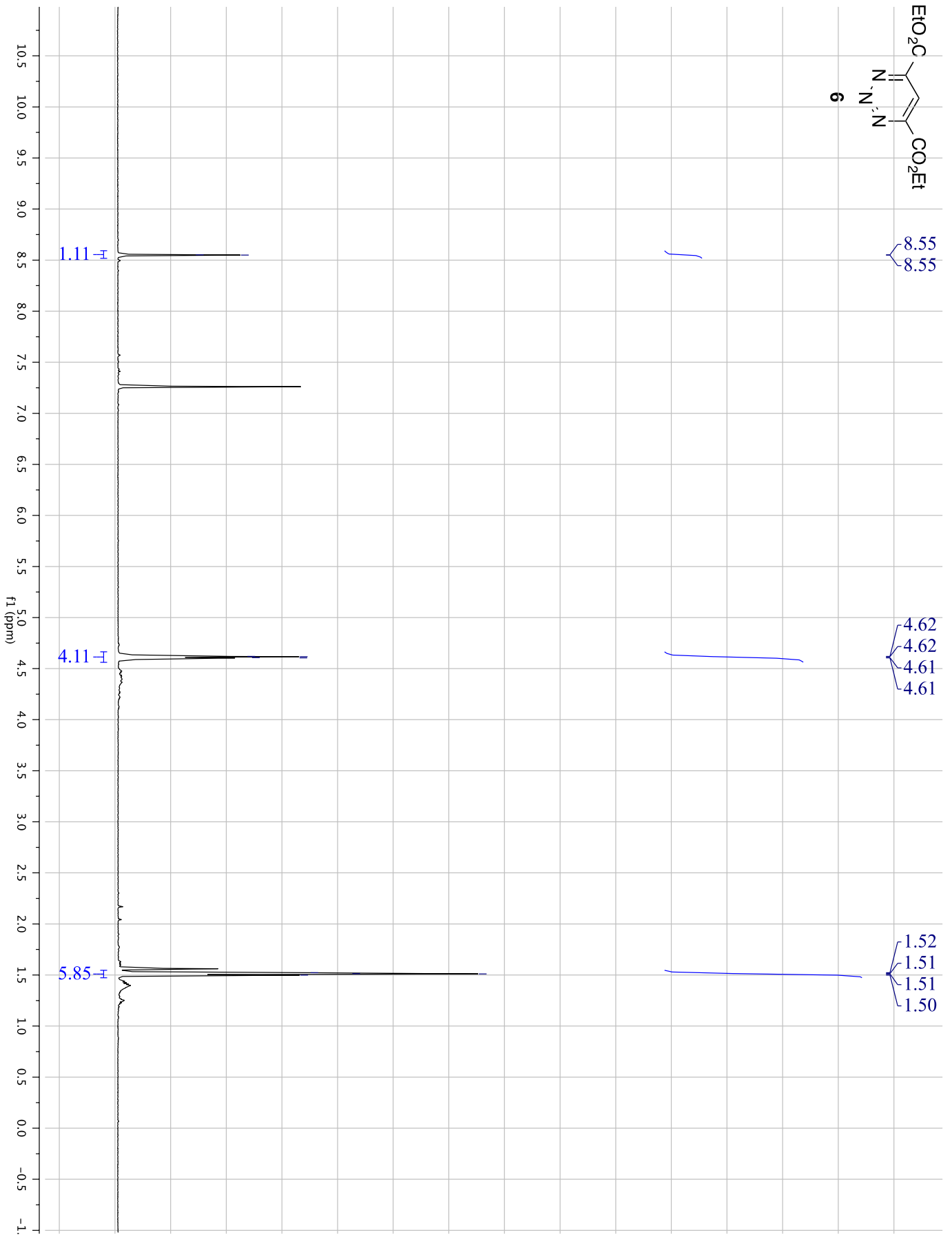
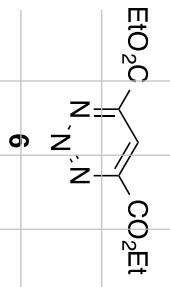


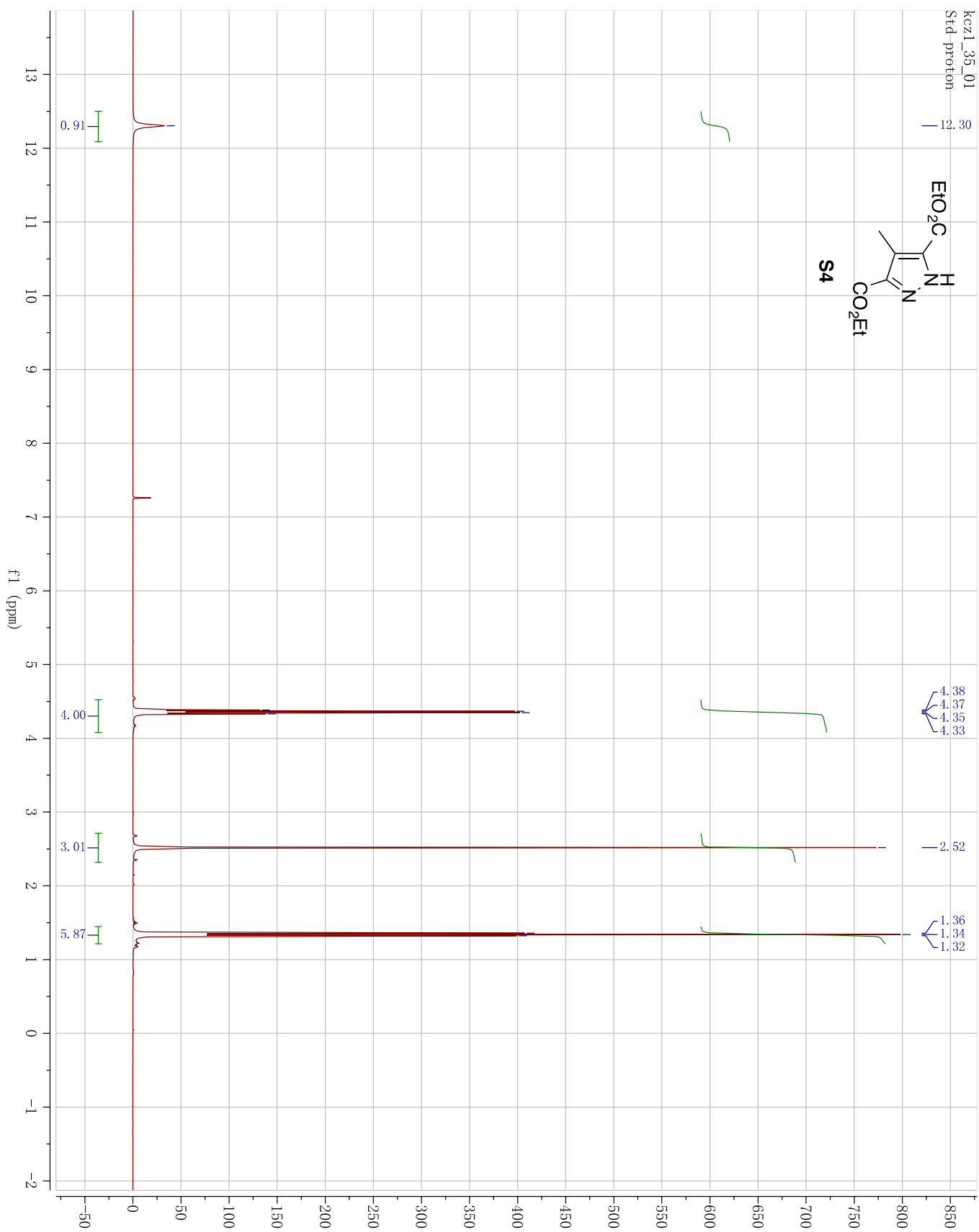
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H-1 Routine, DRX-500, BBO Probe

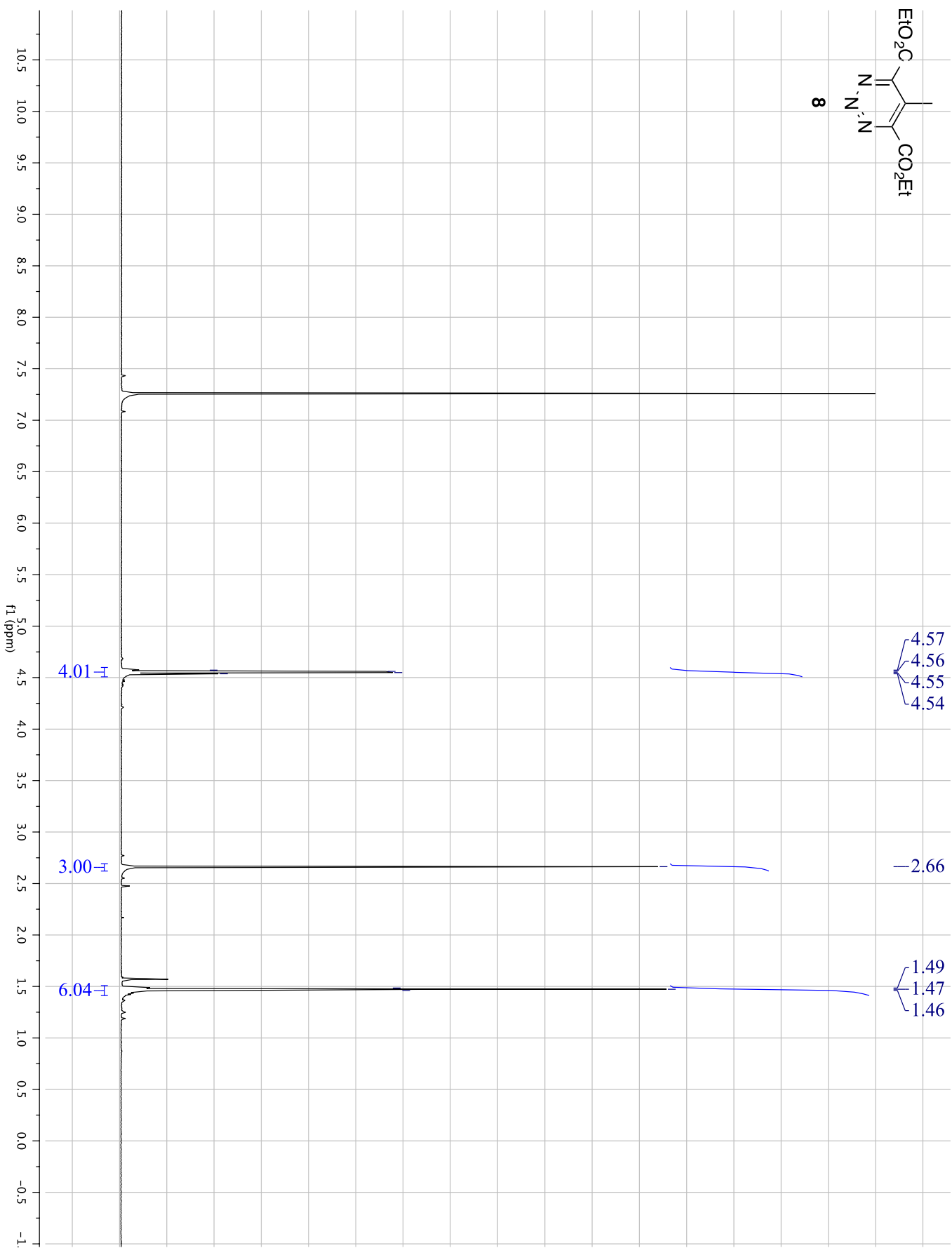


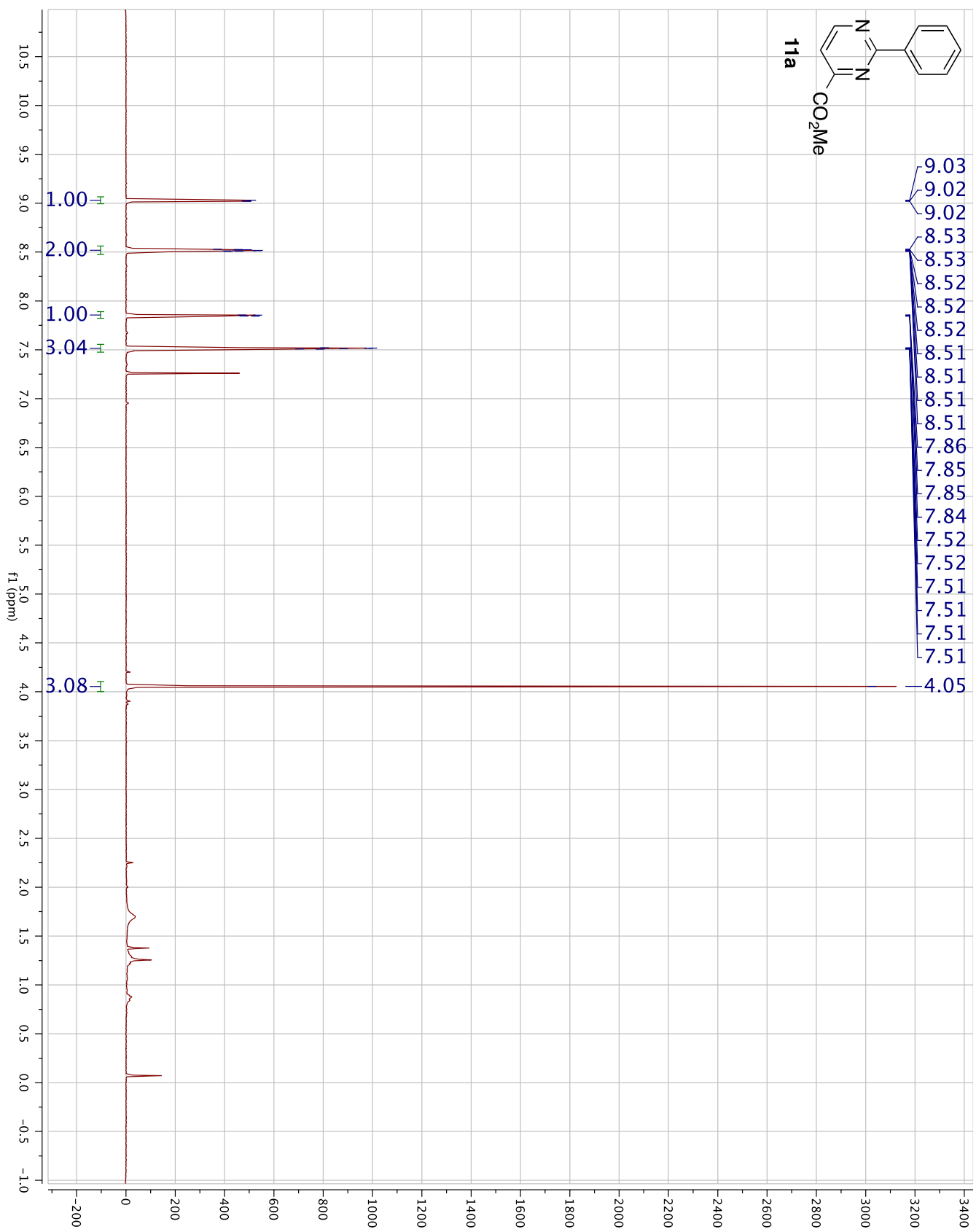


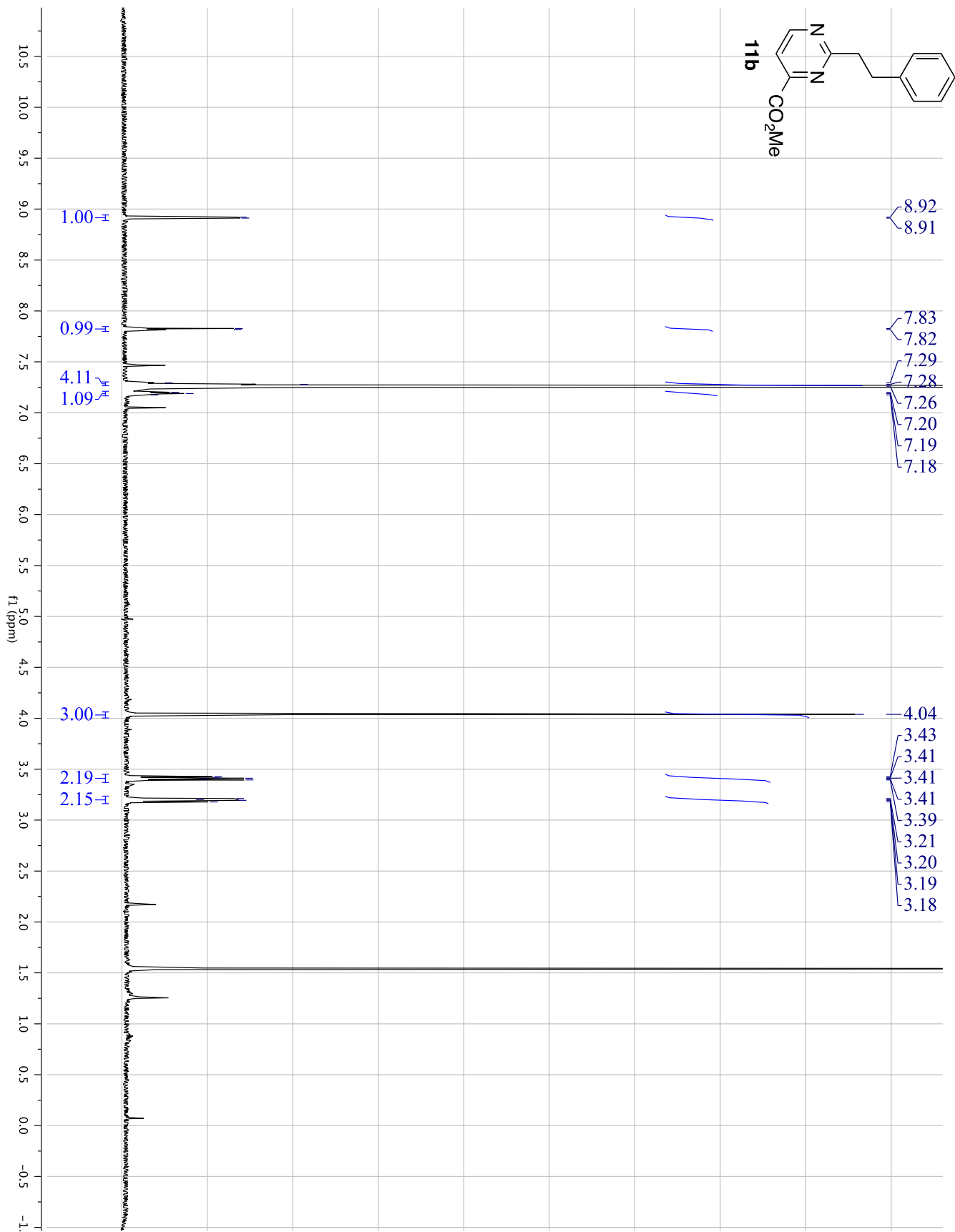


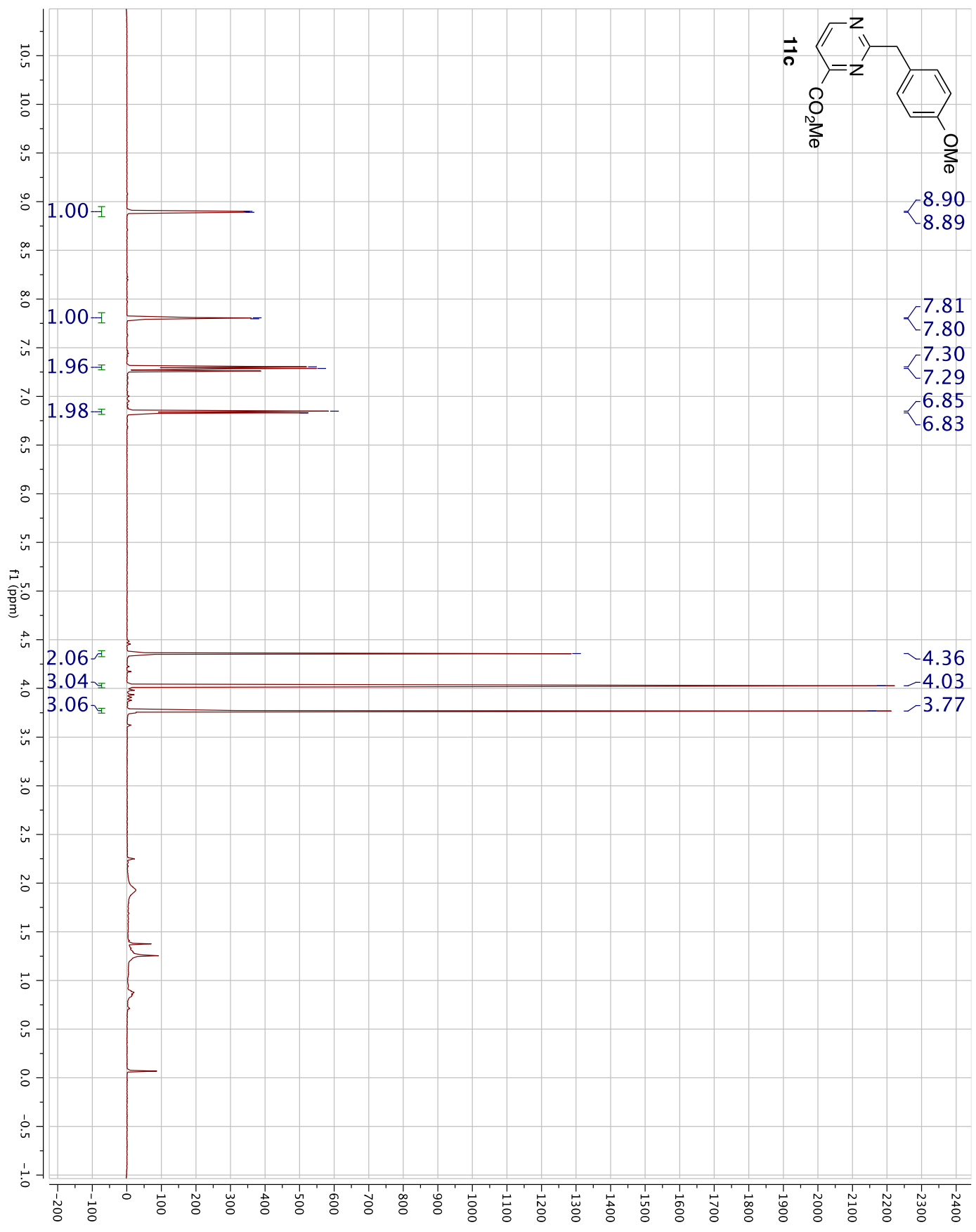
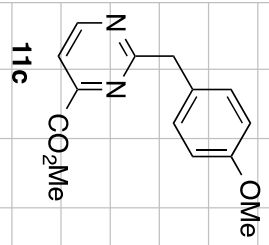


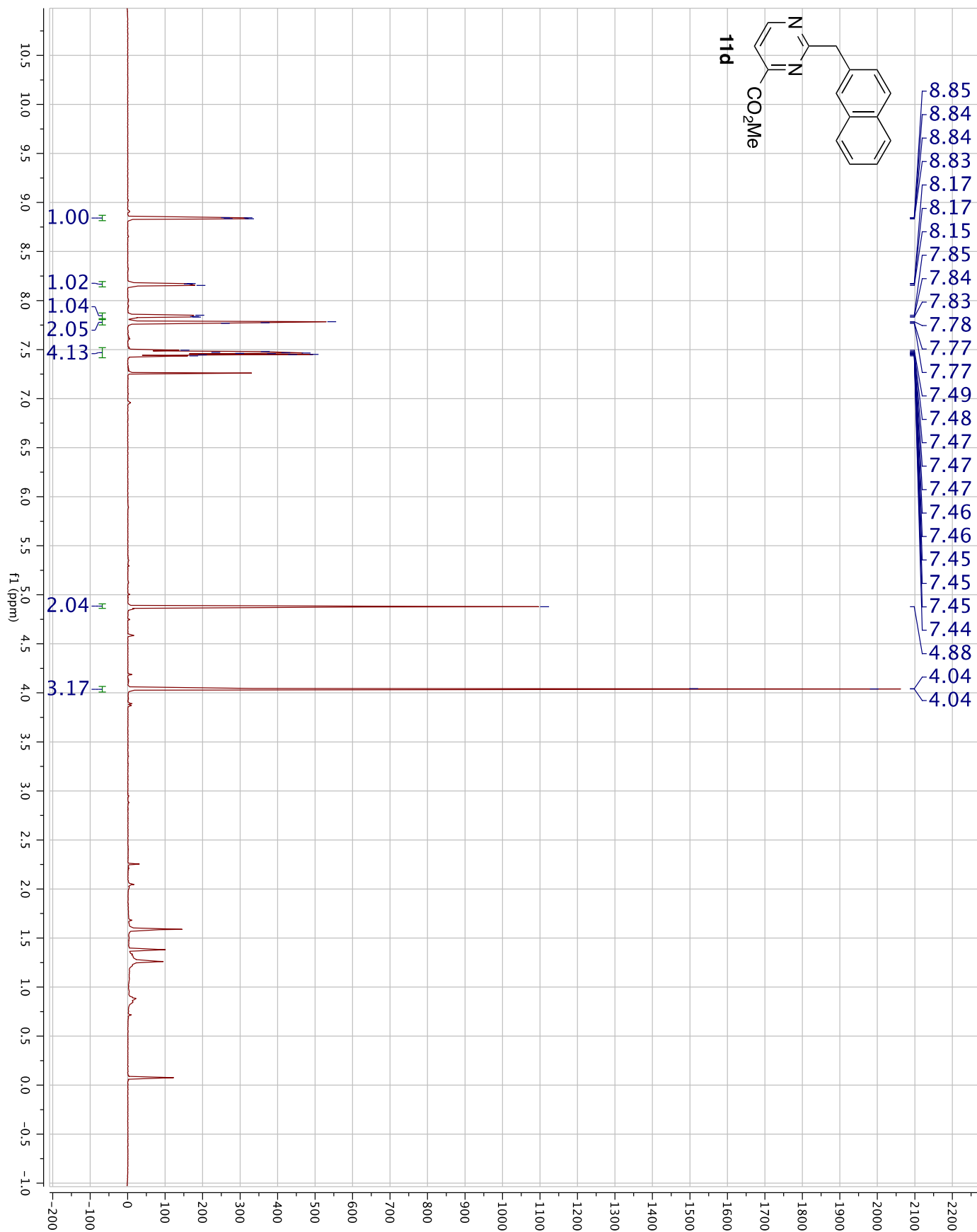


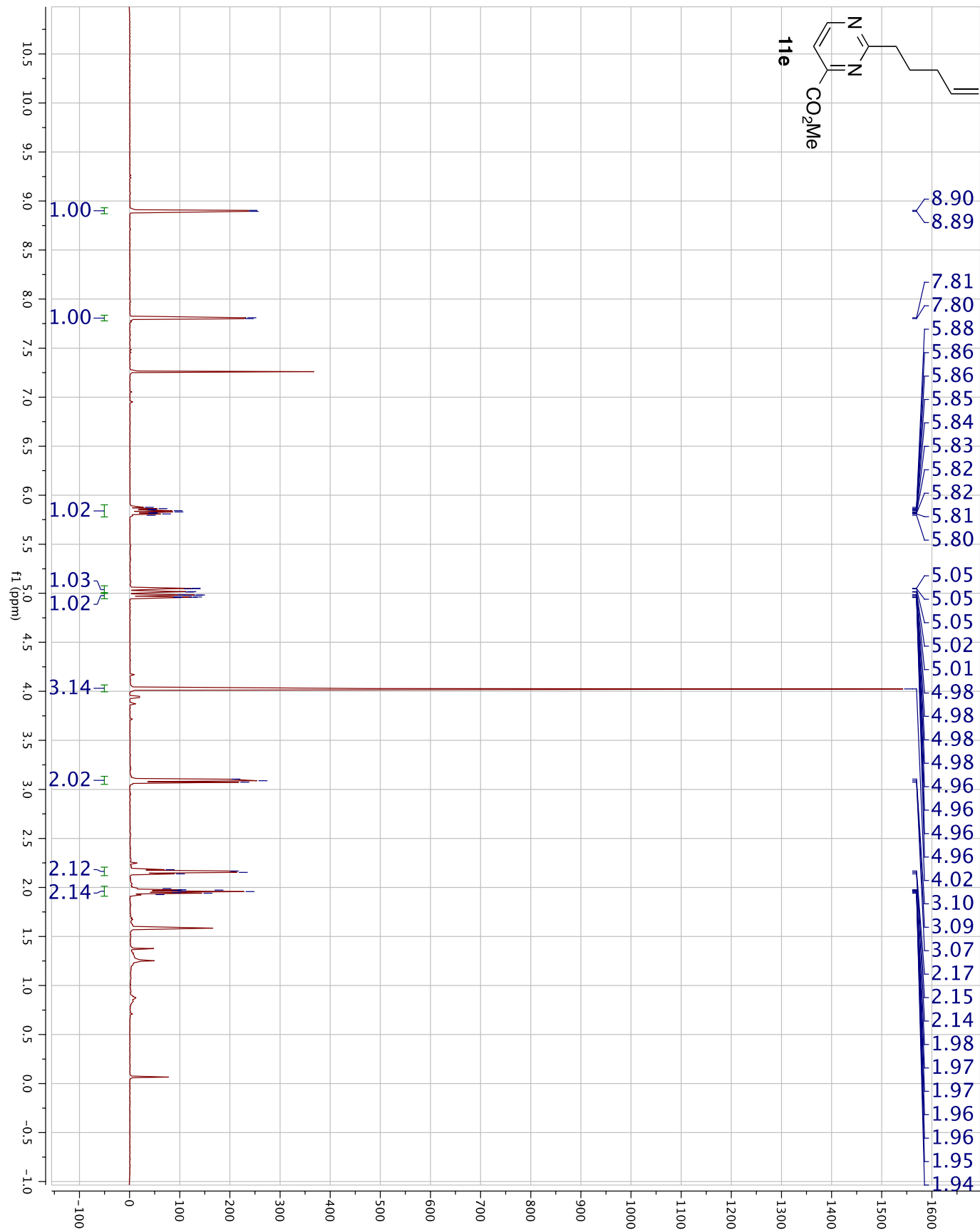


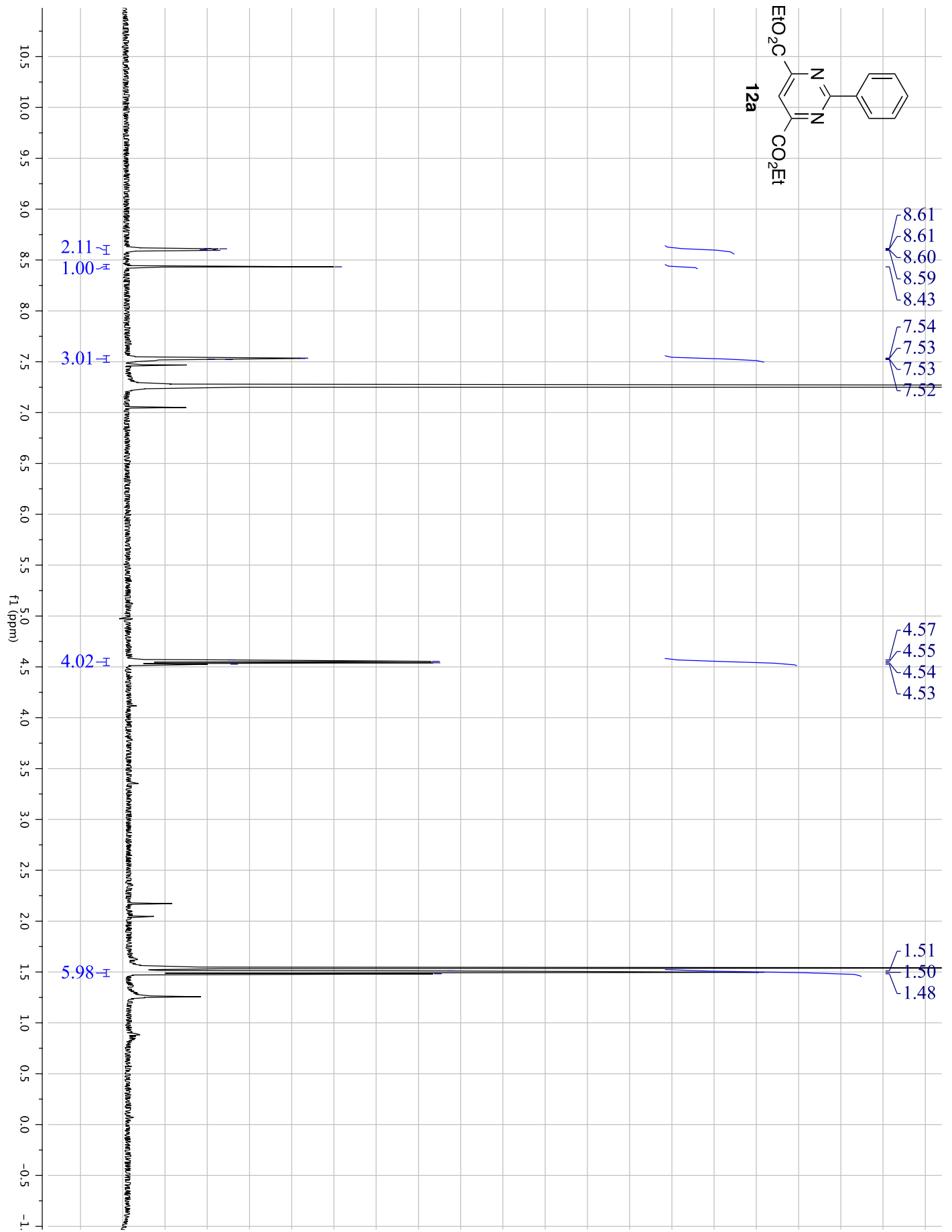
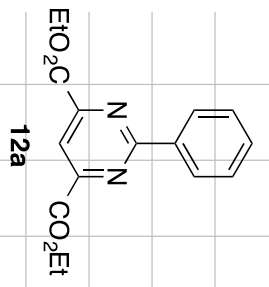


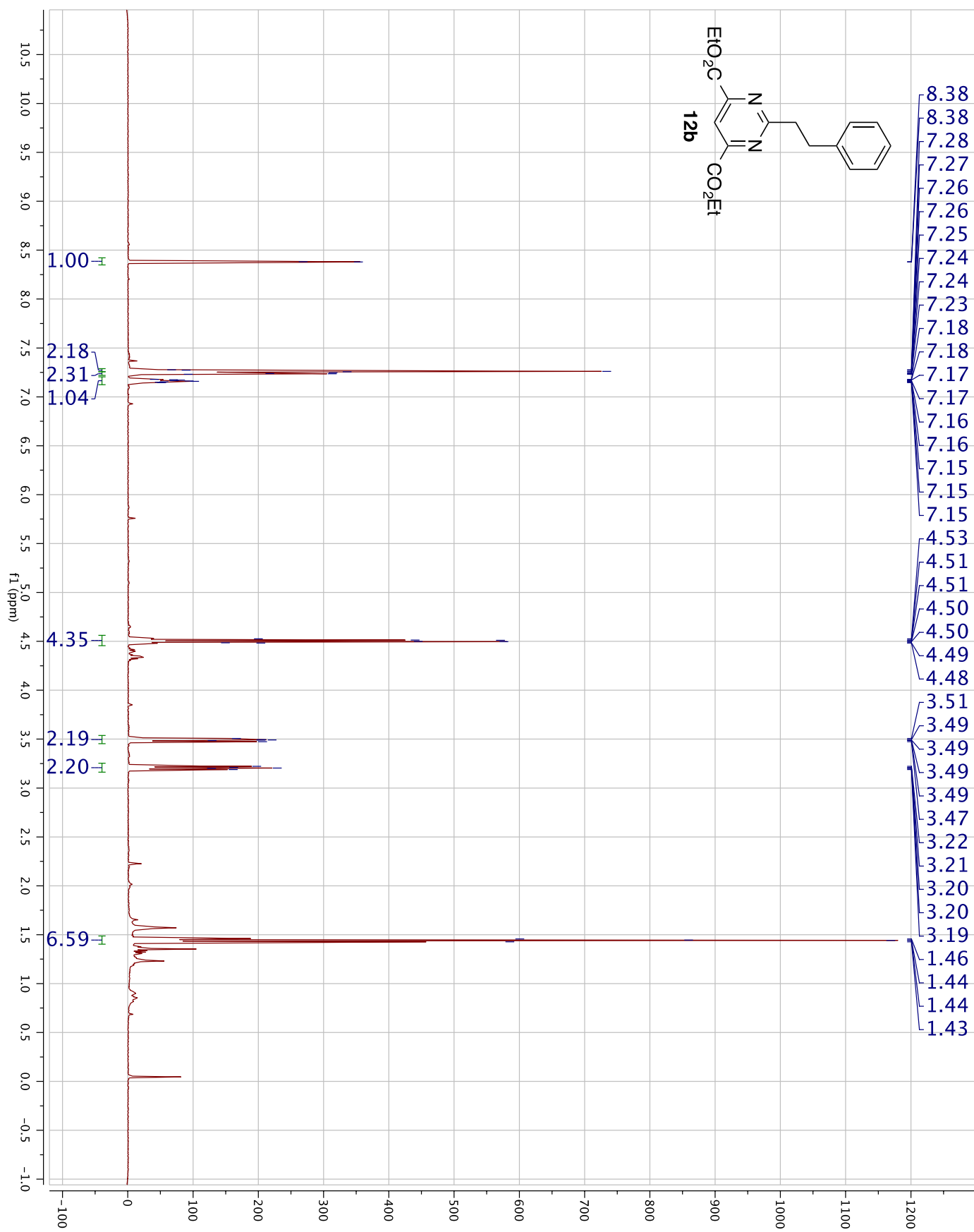


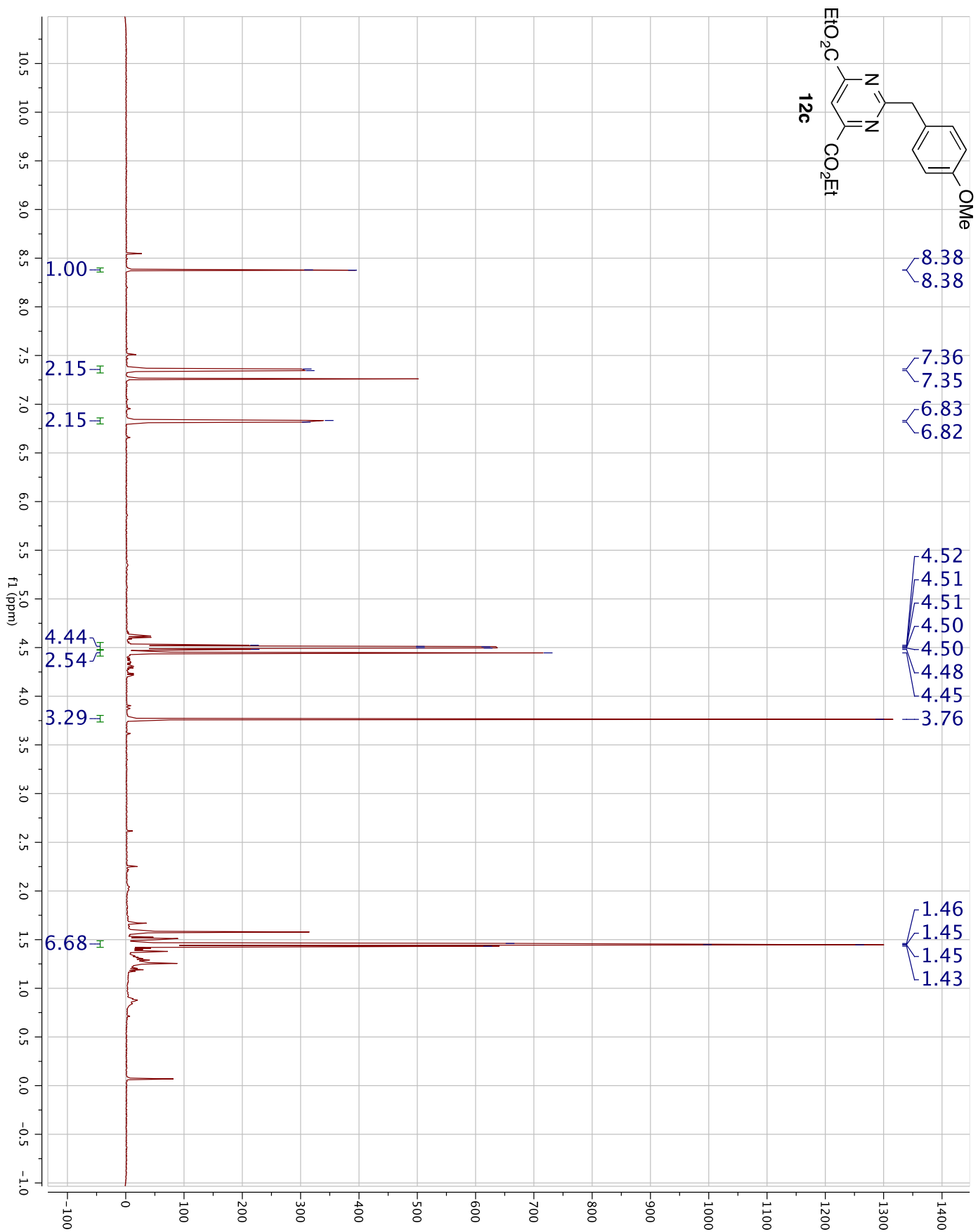


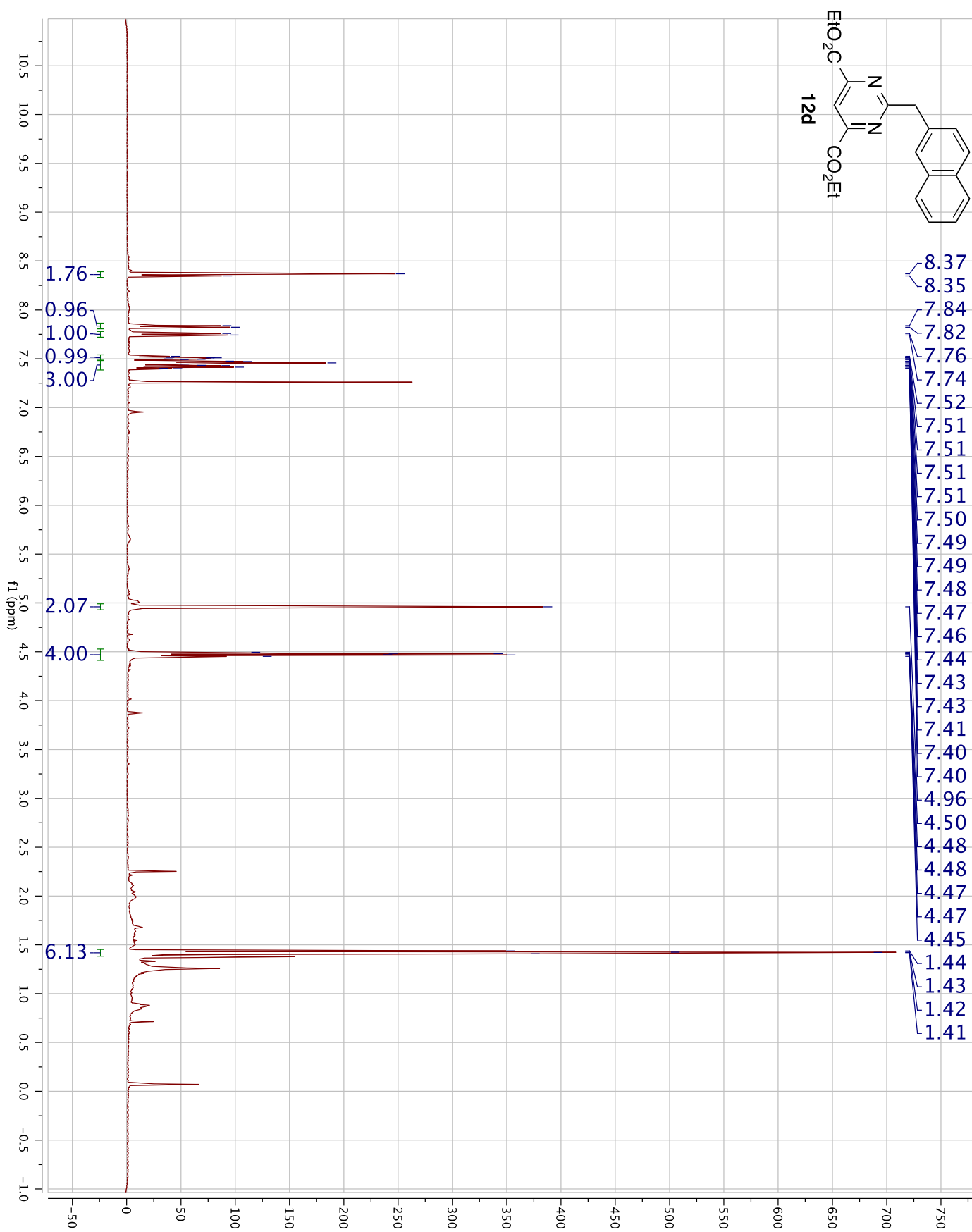


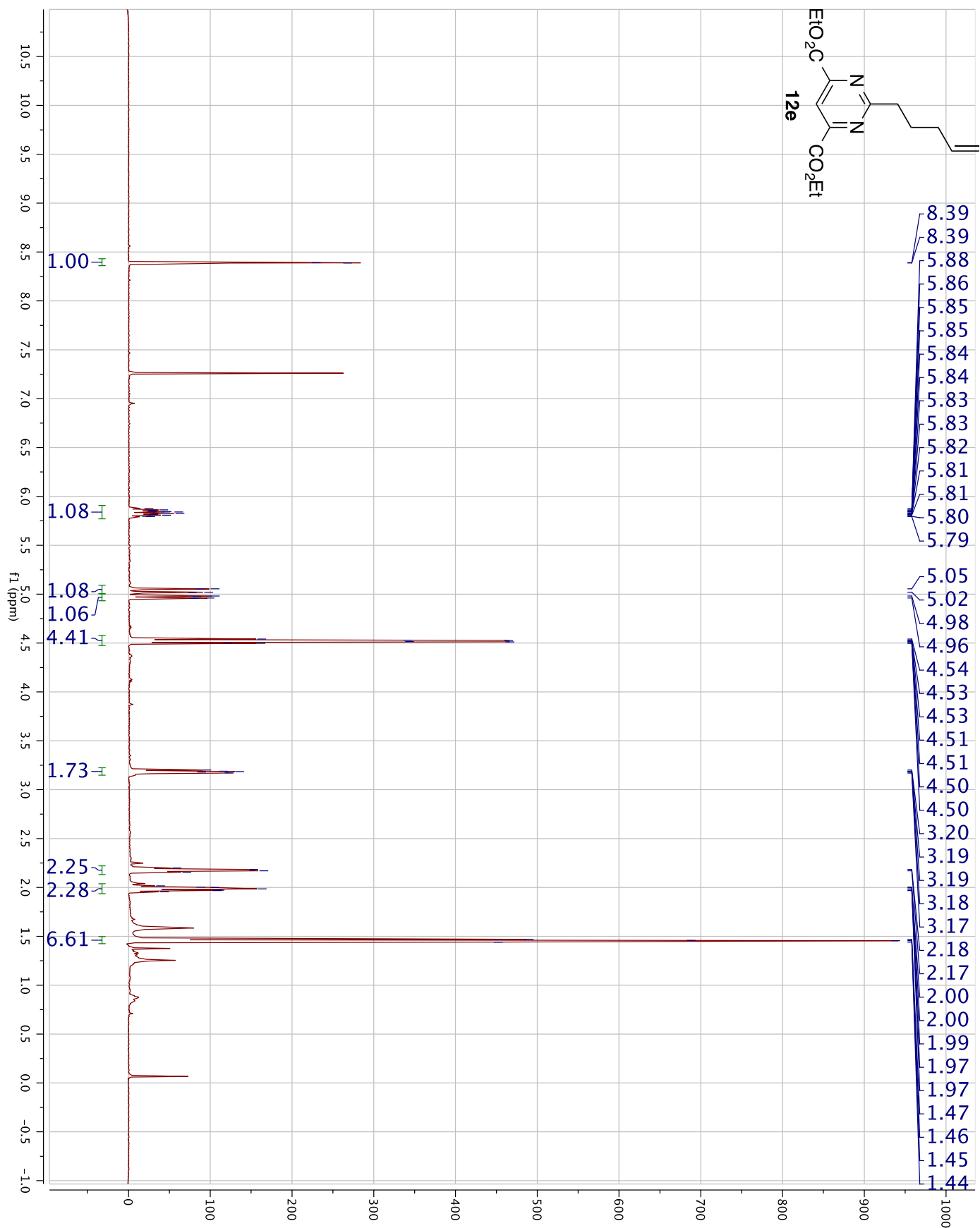


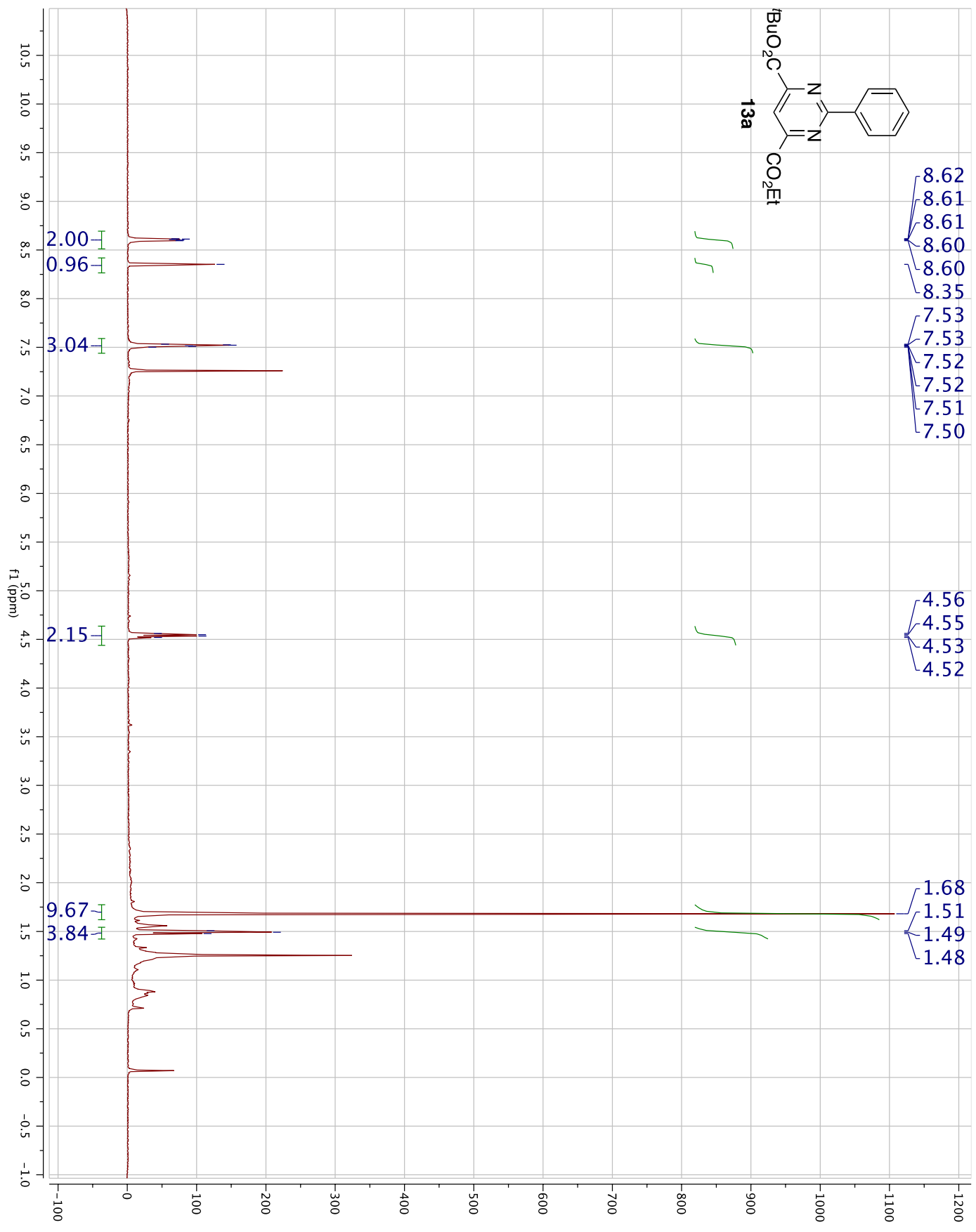


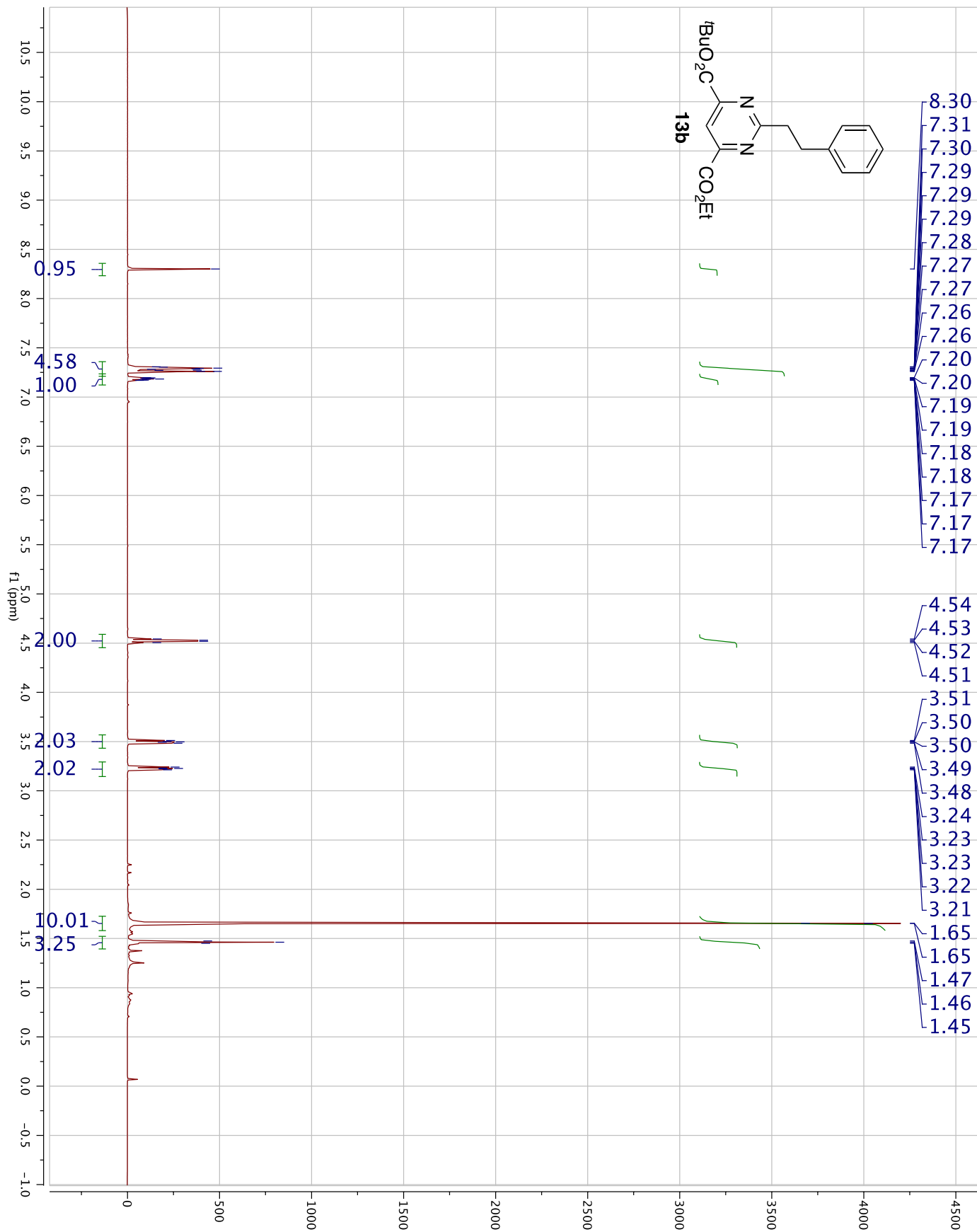


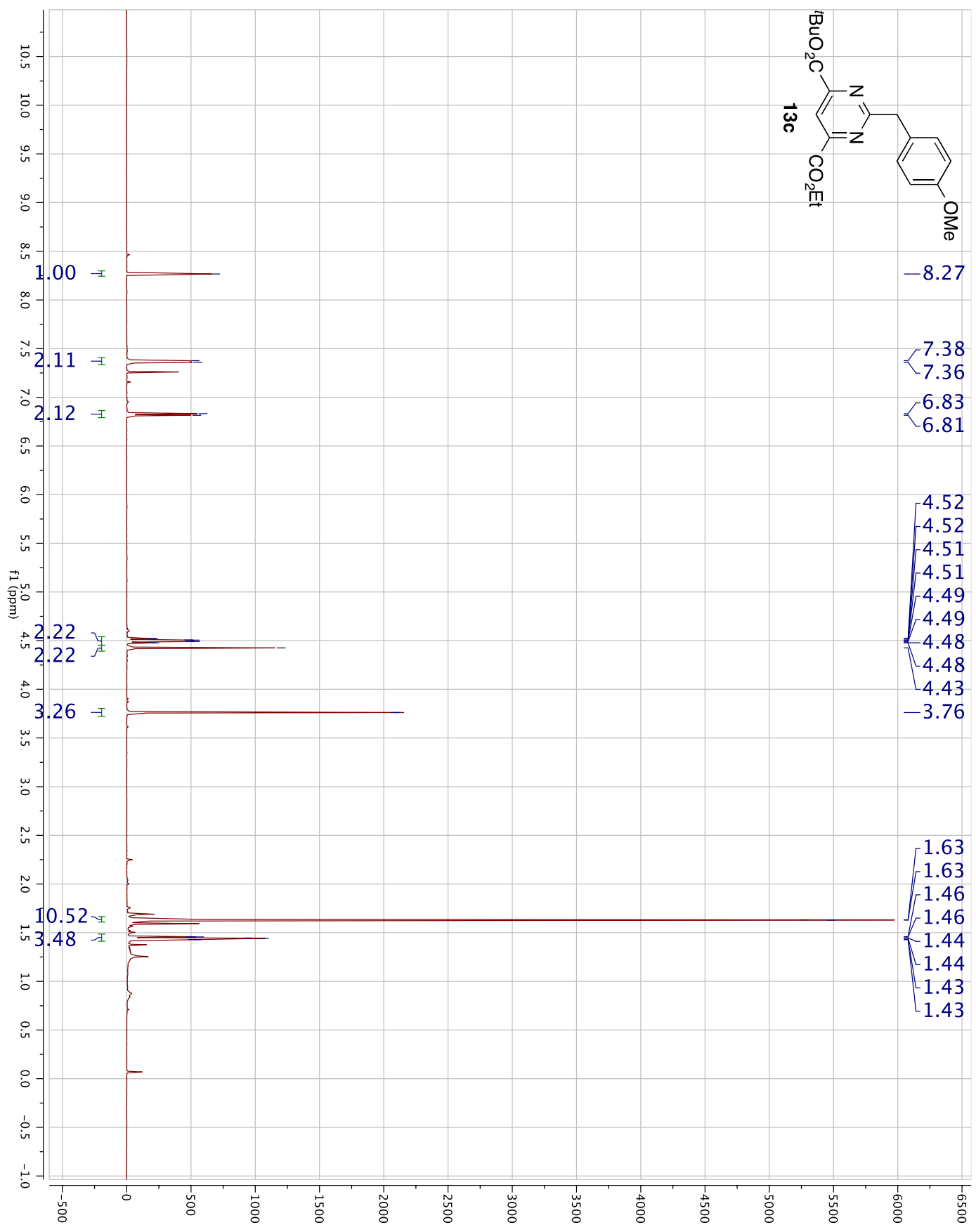
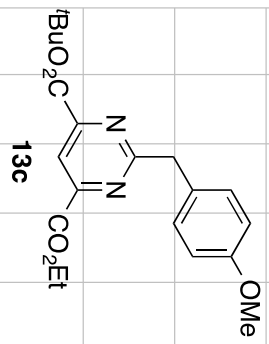


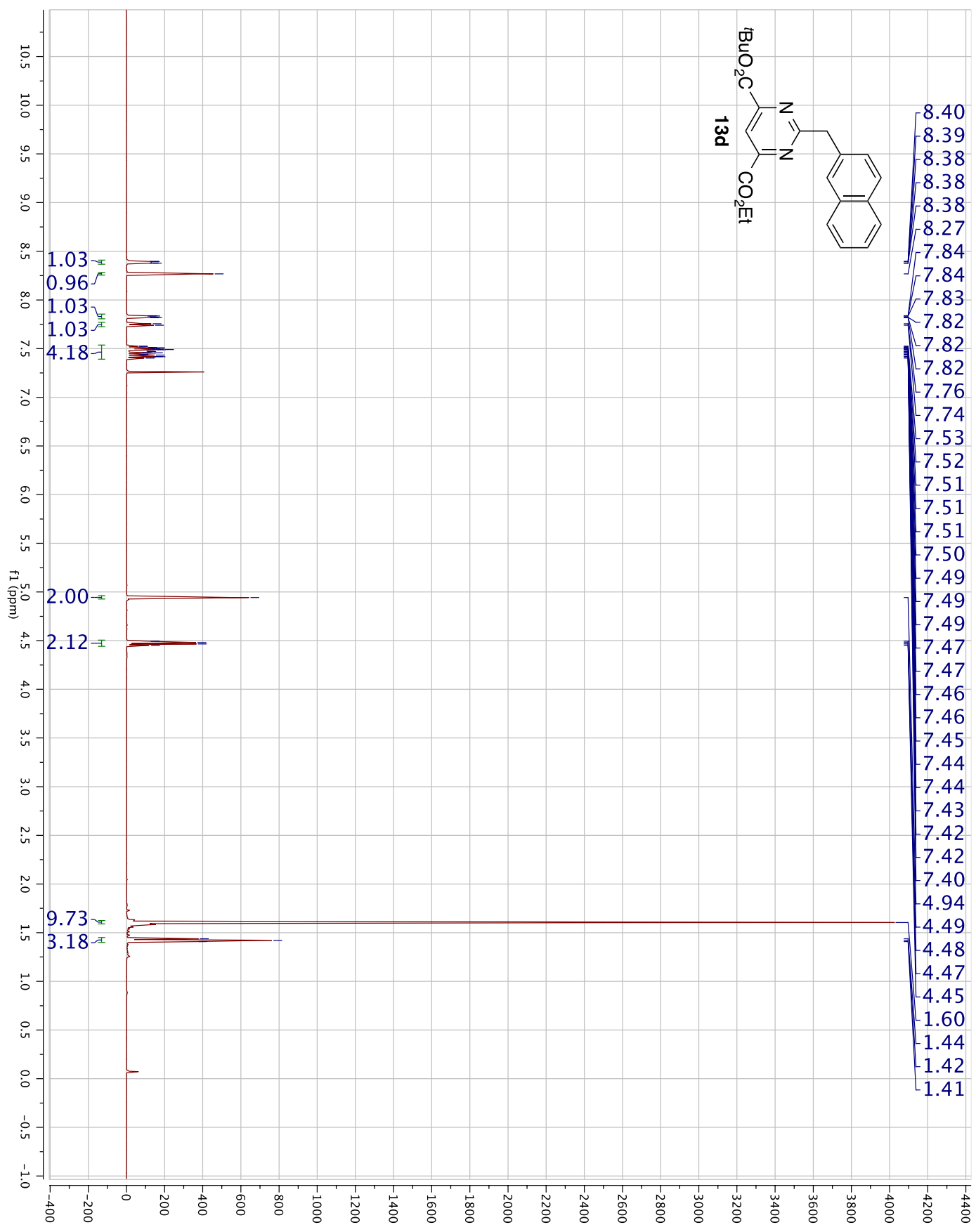


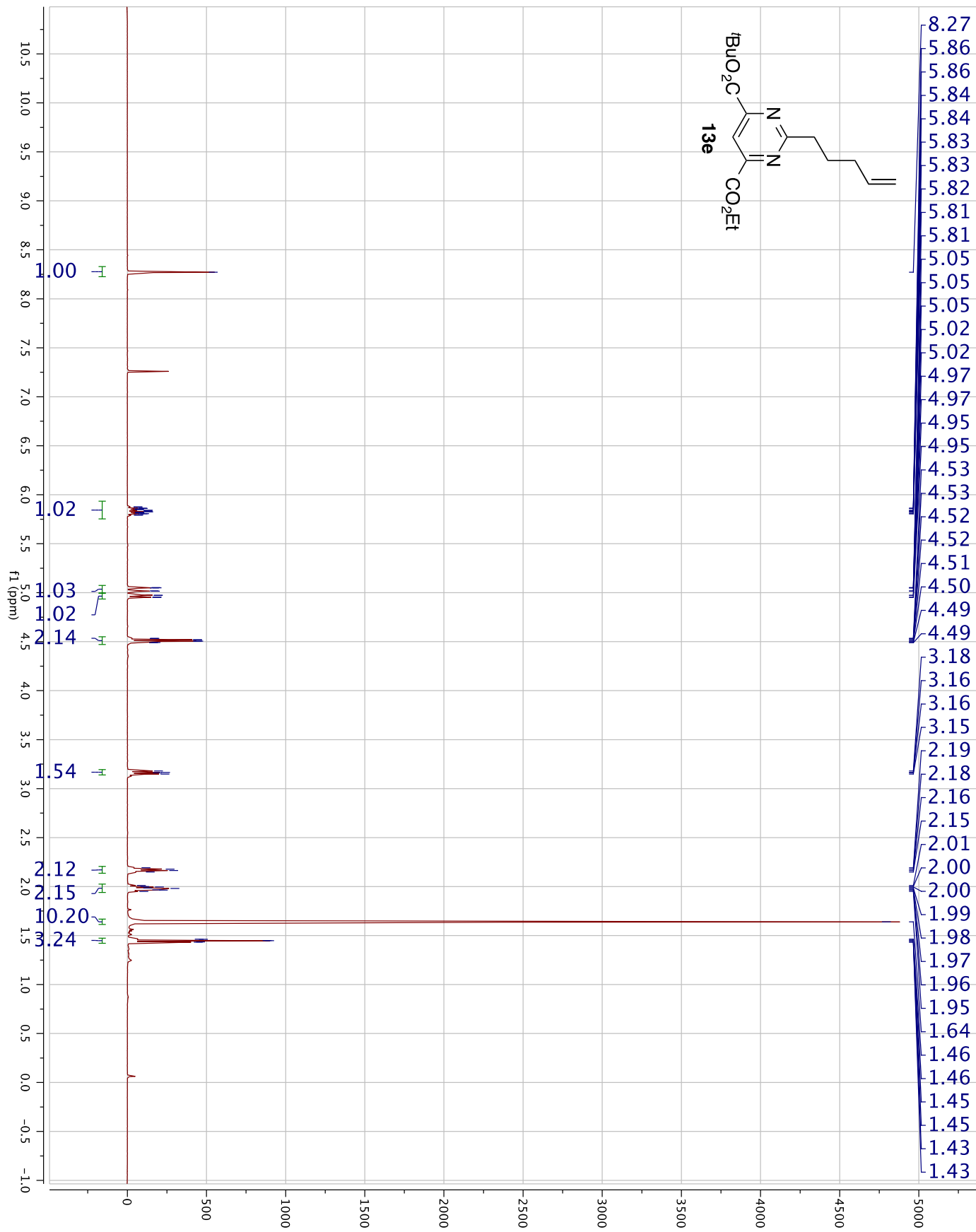


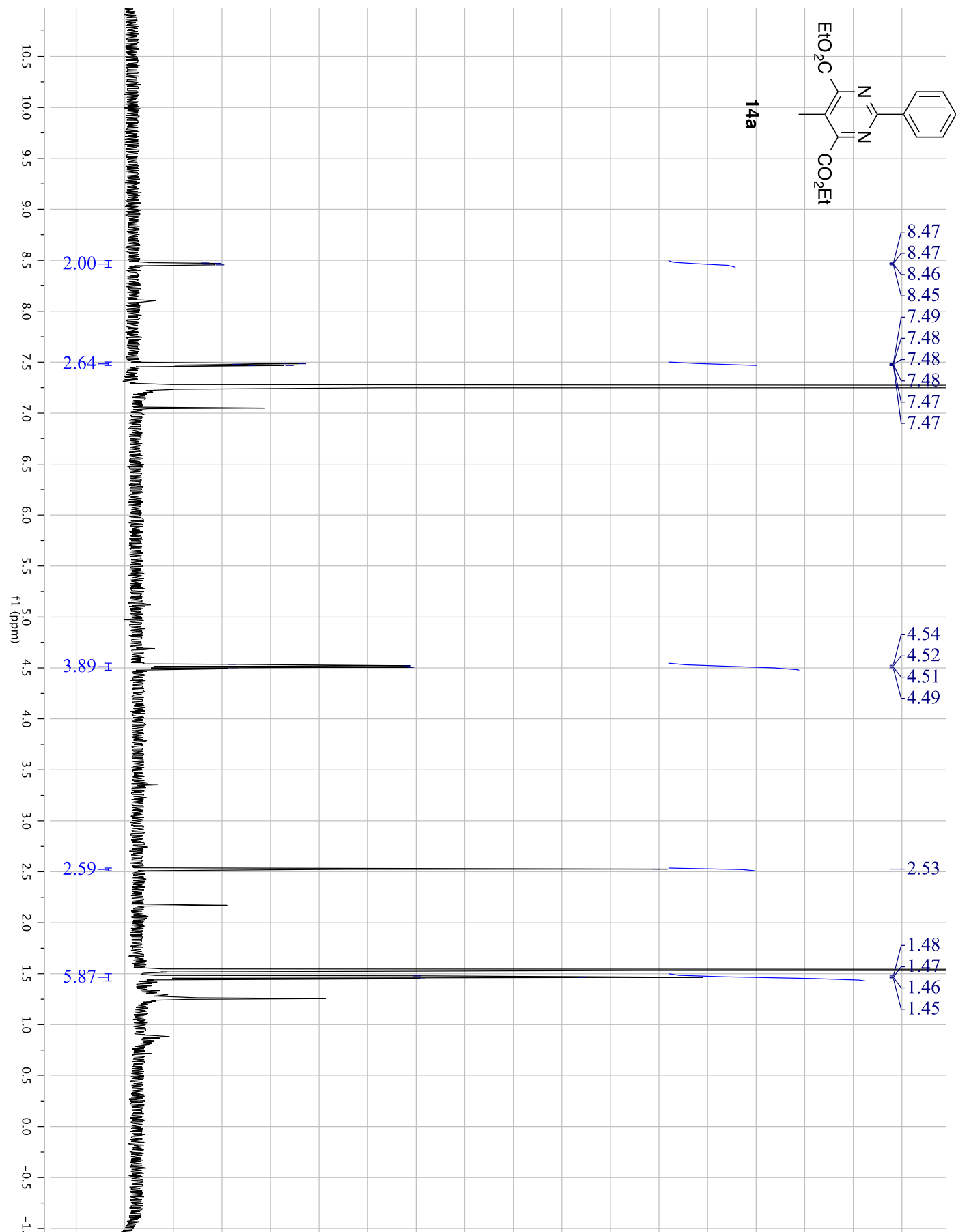


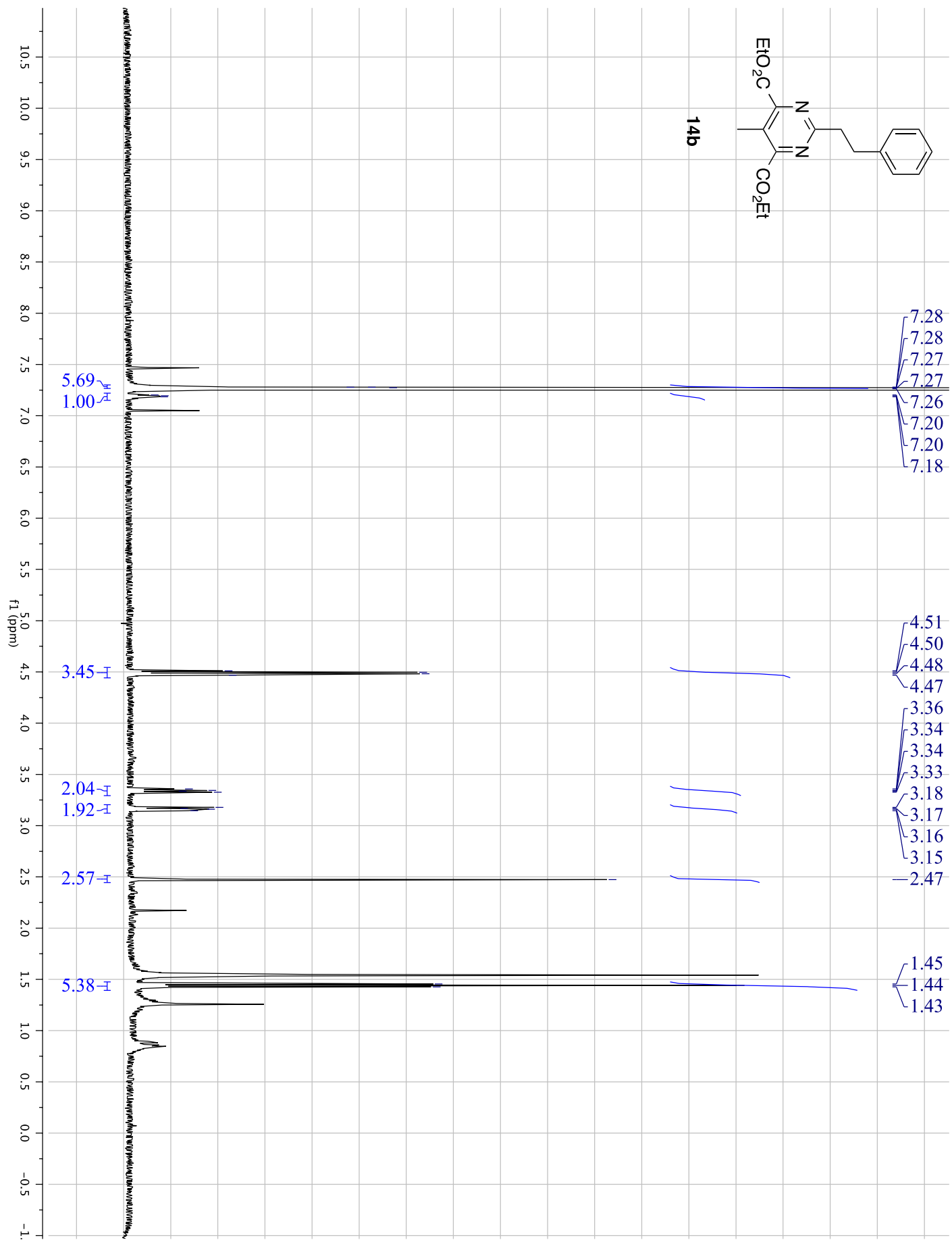


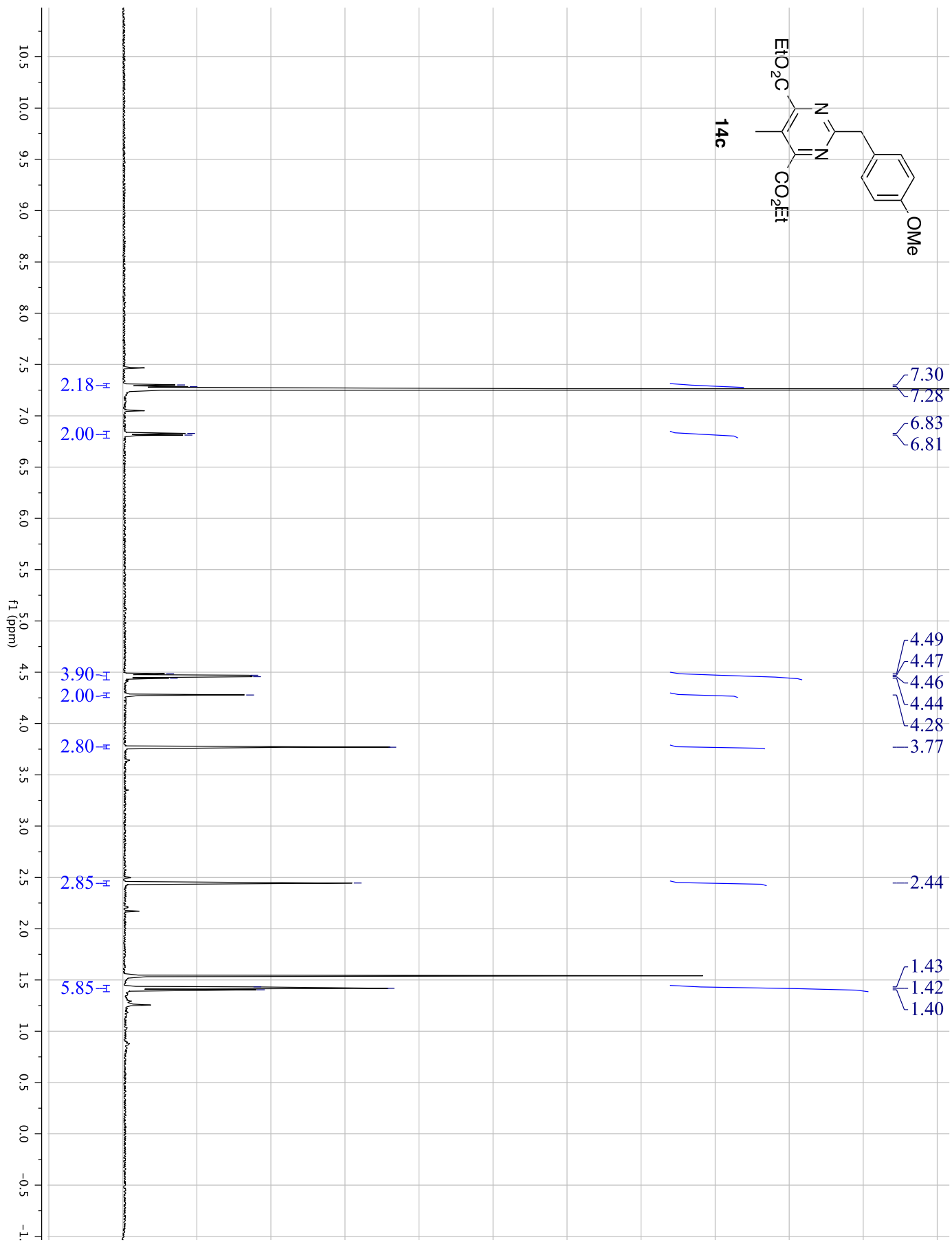


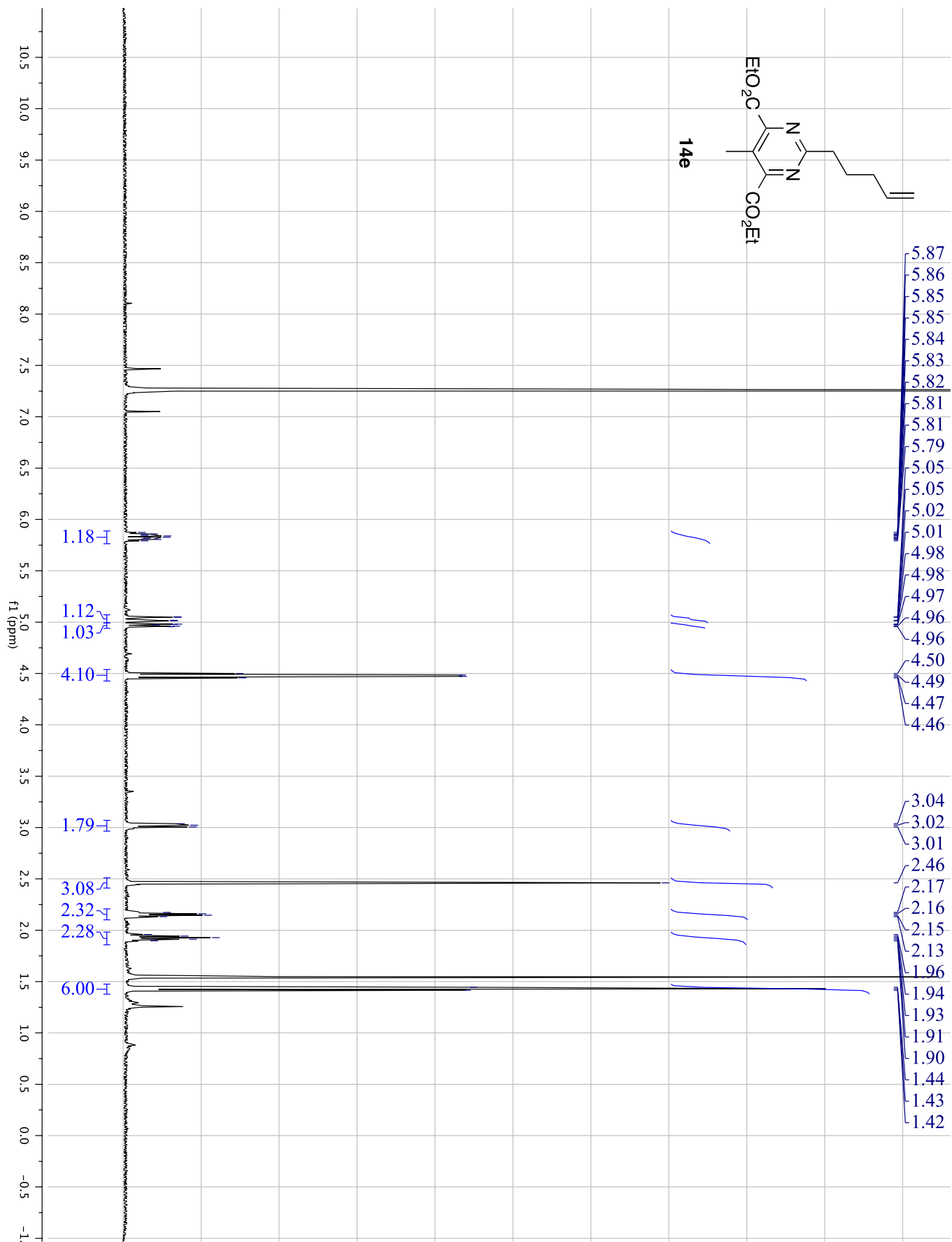


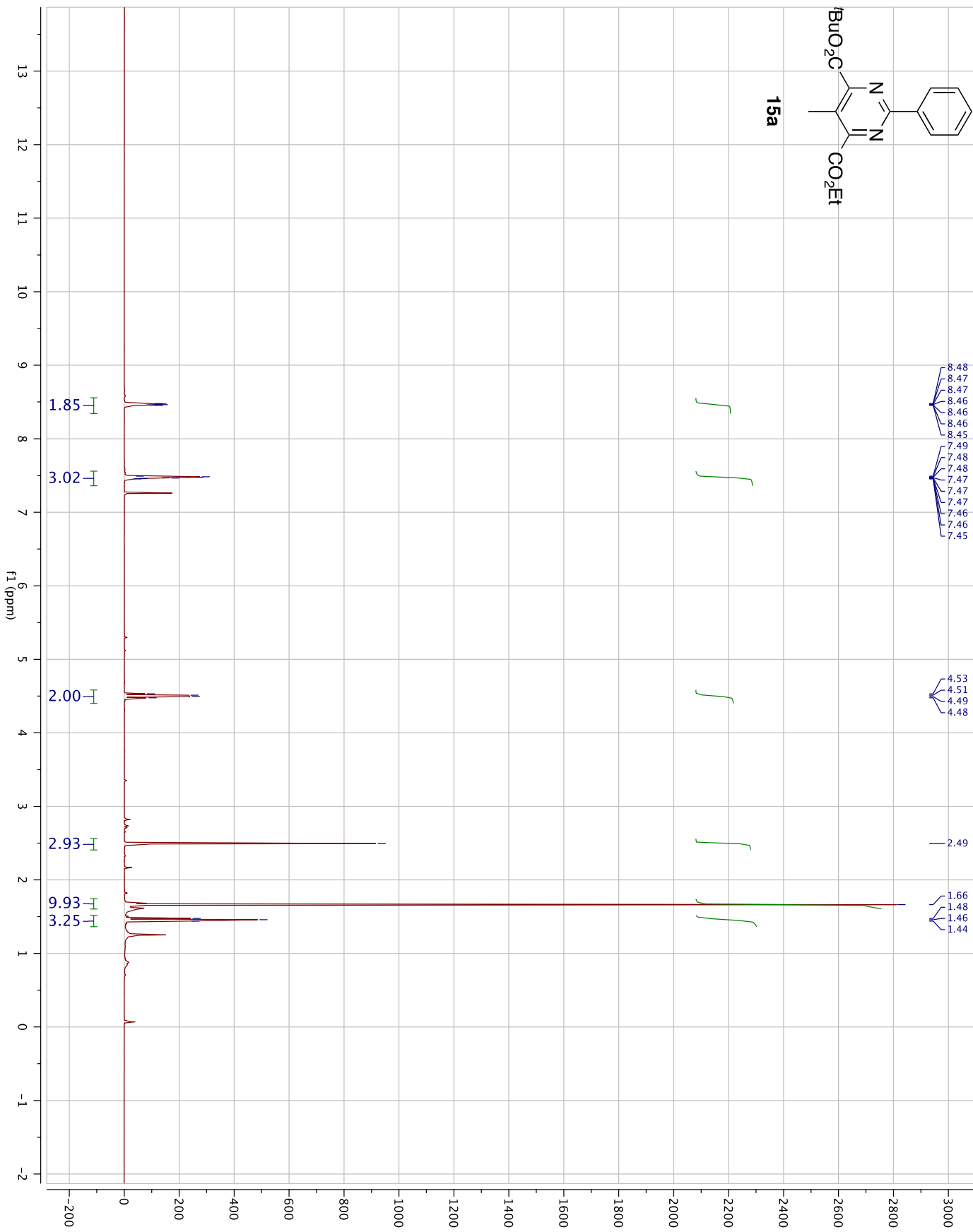


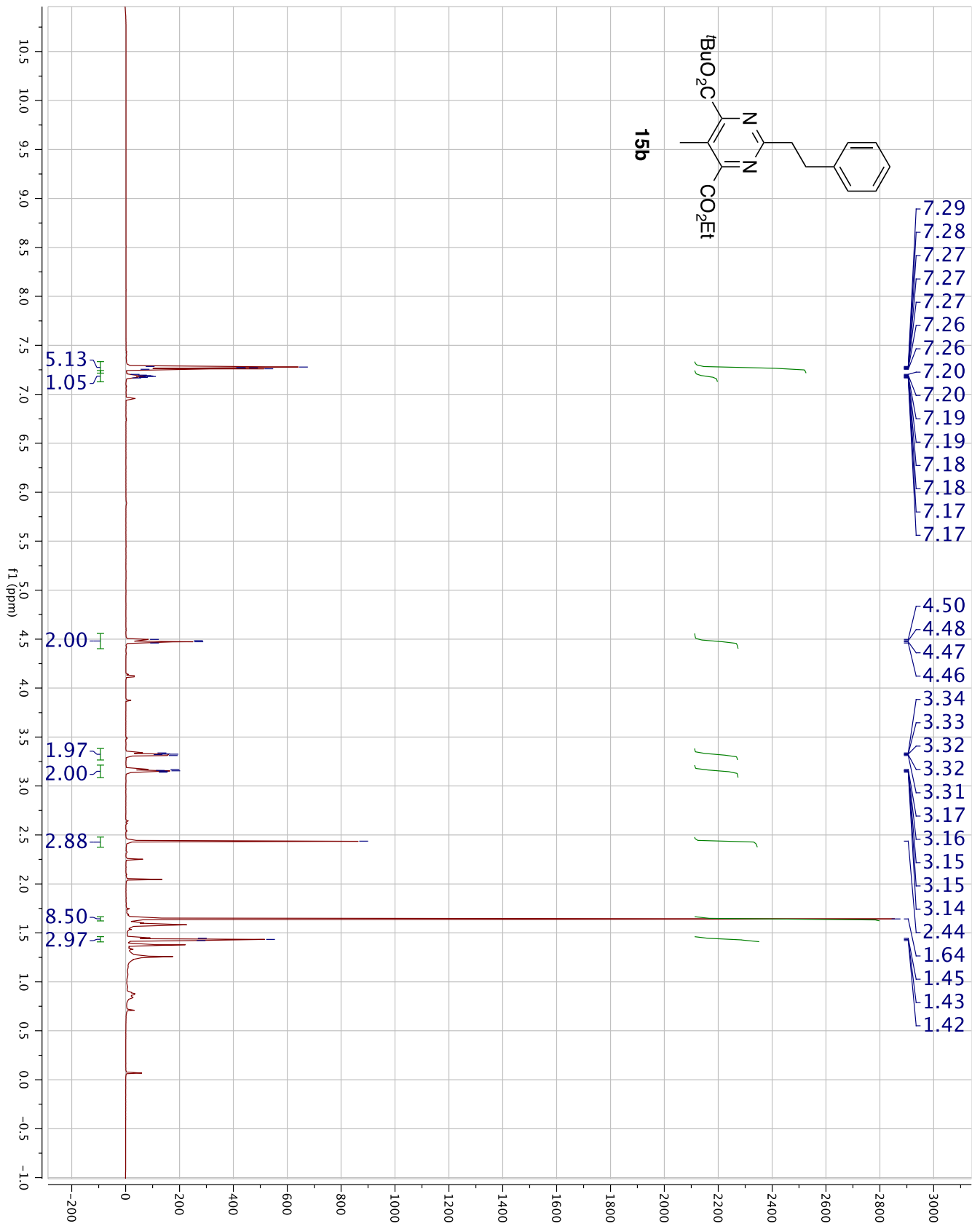


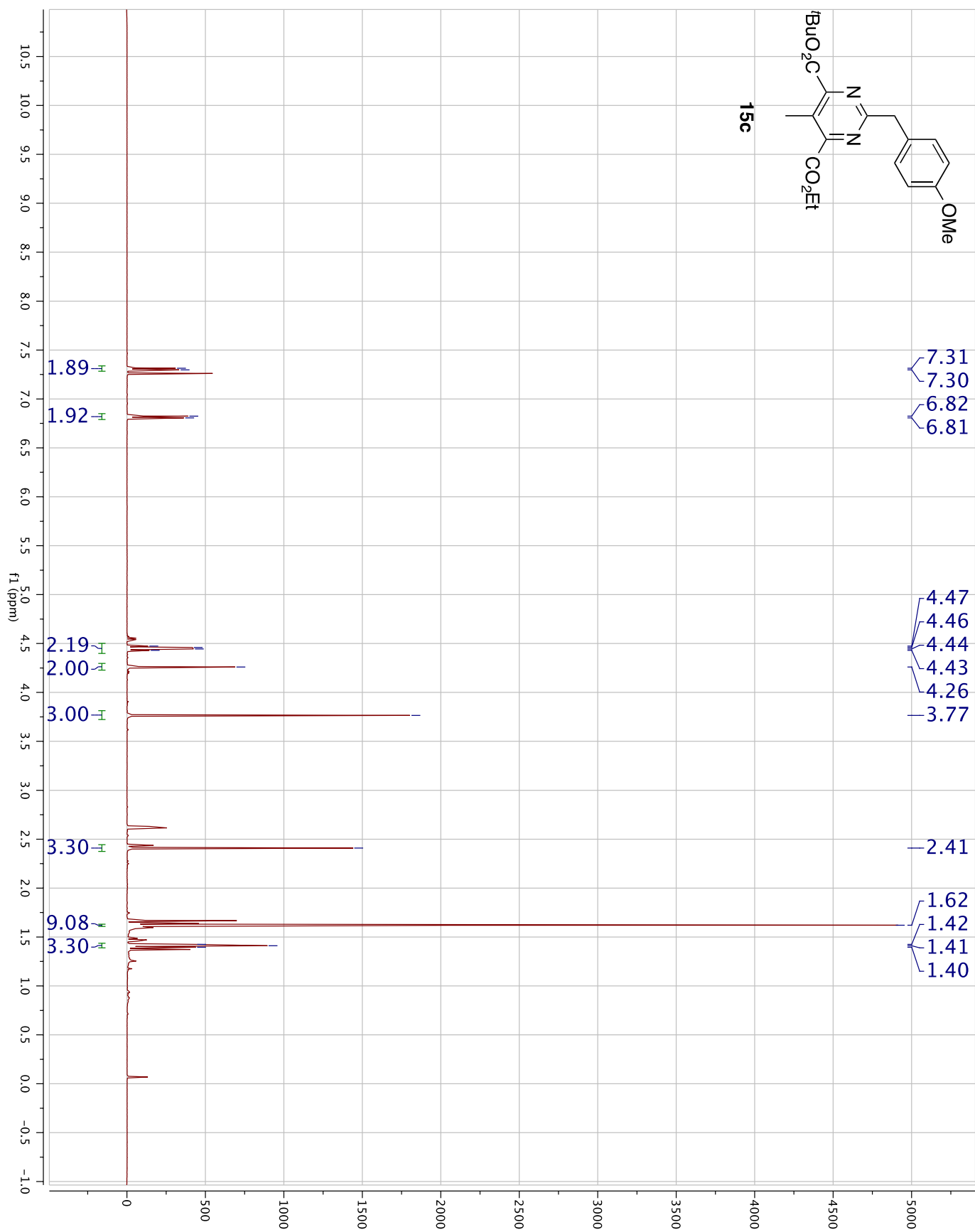
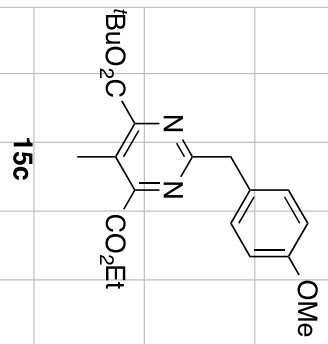


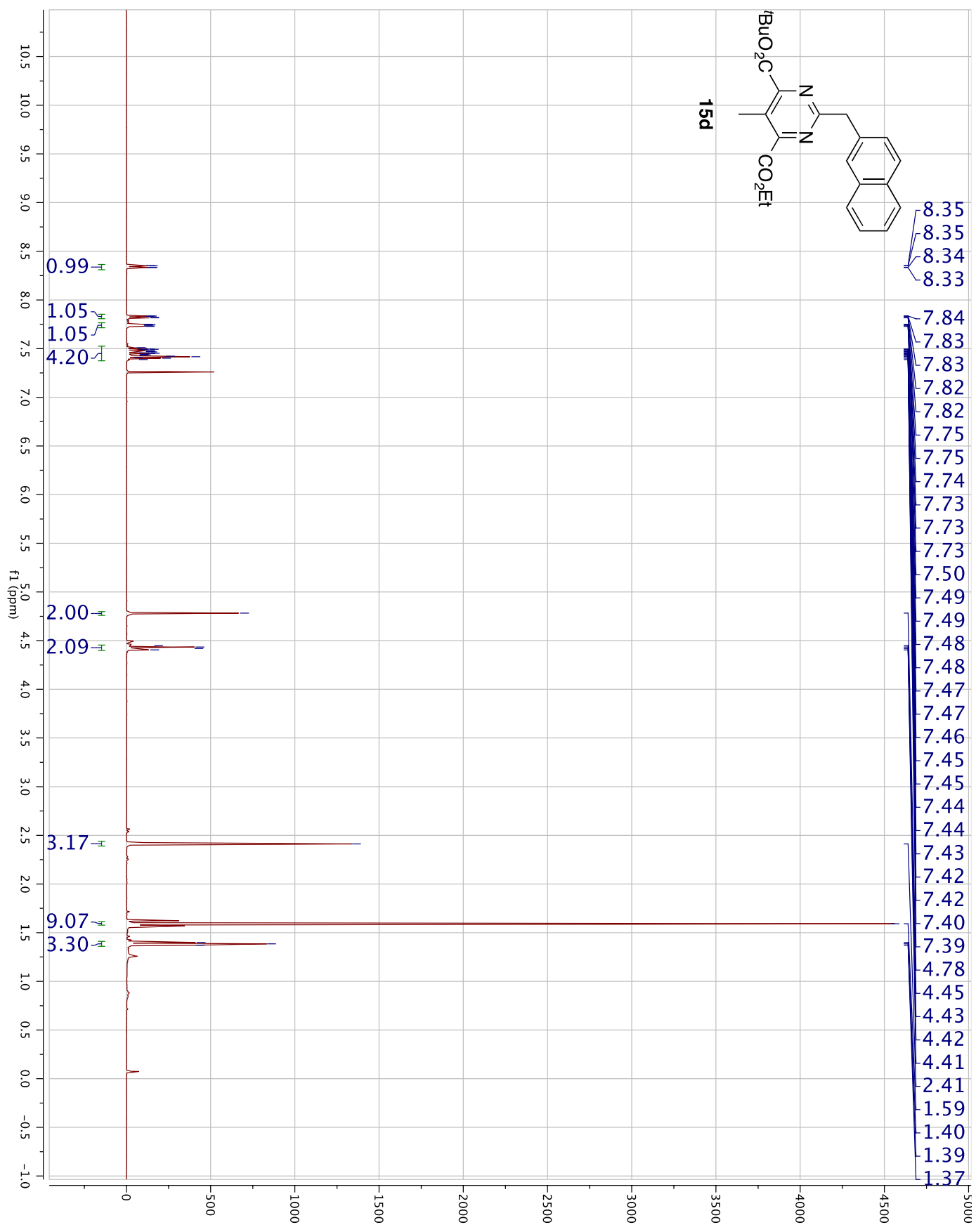


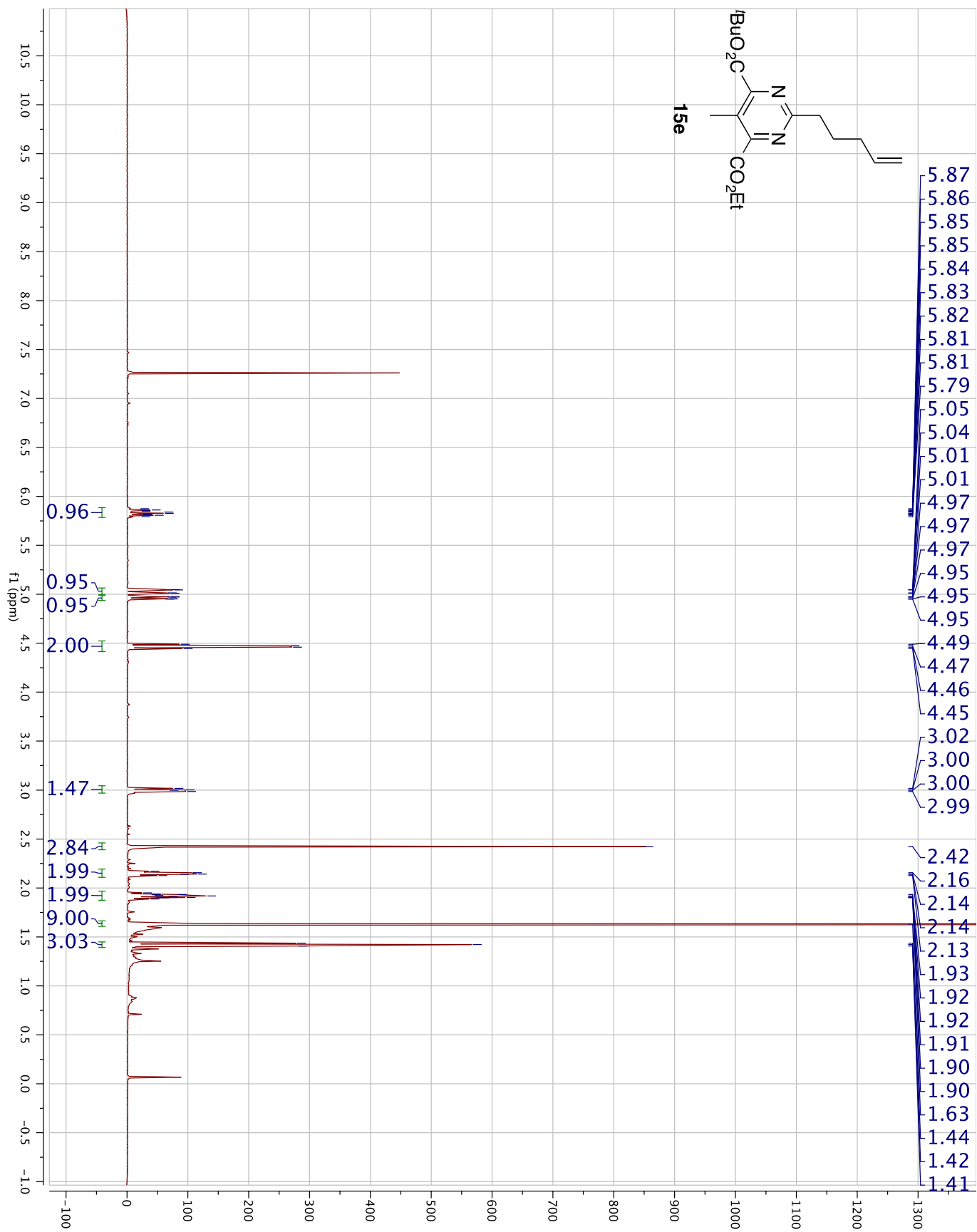




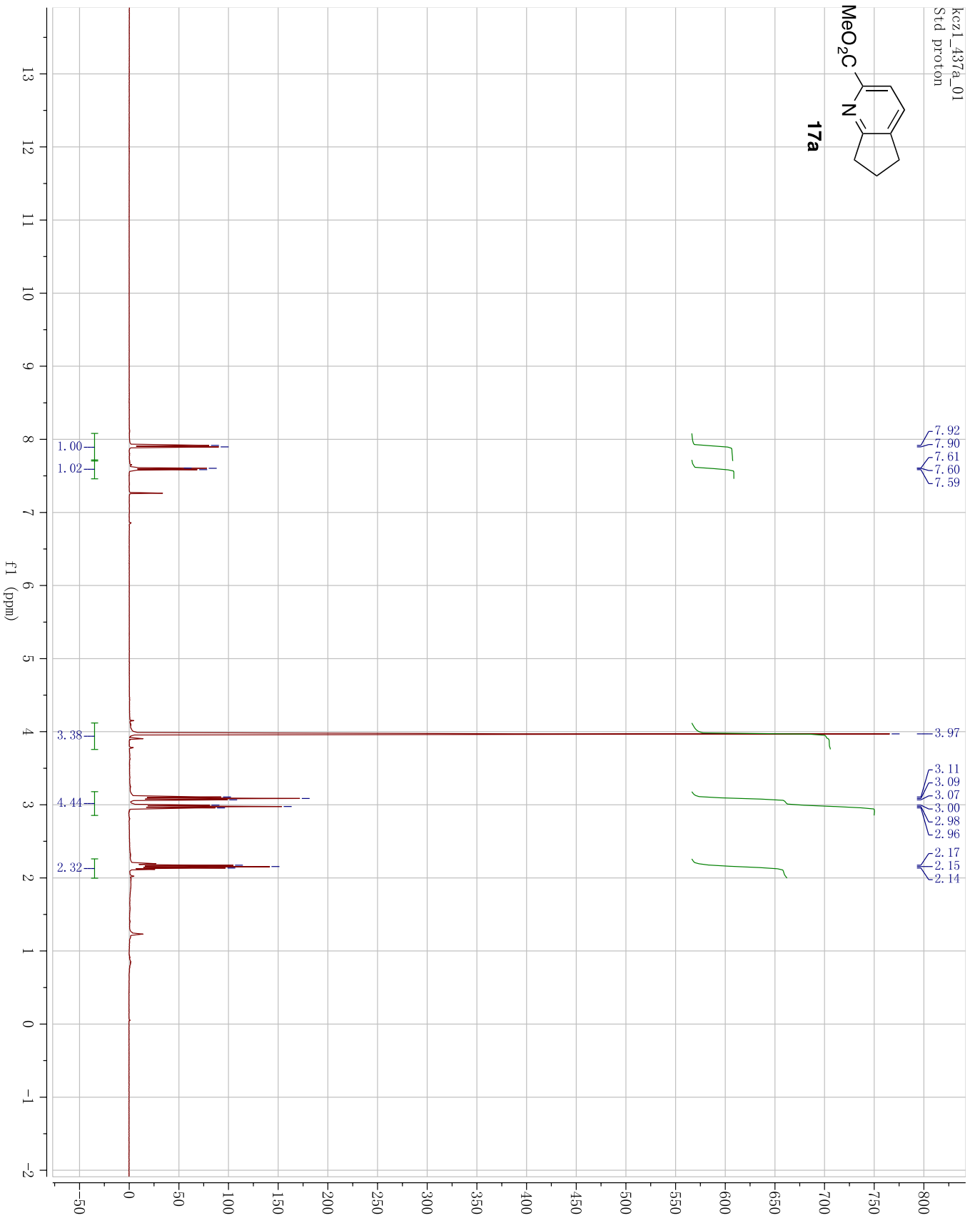
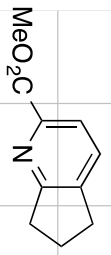


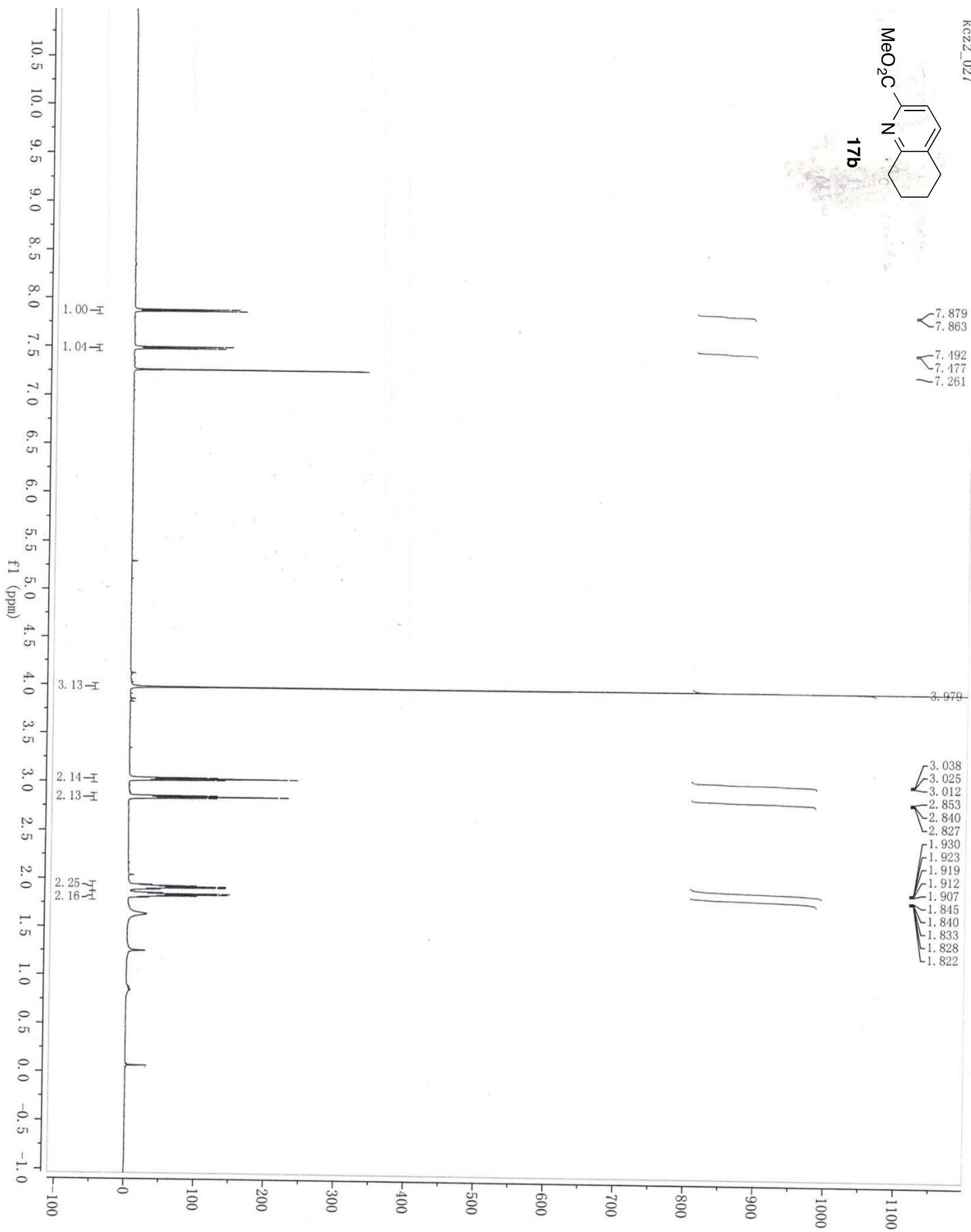
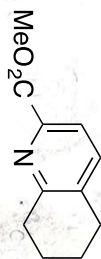




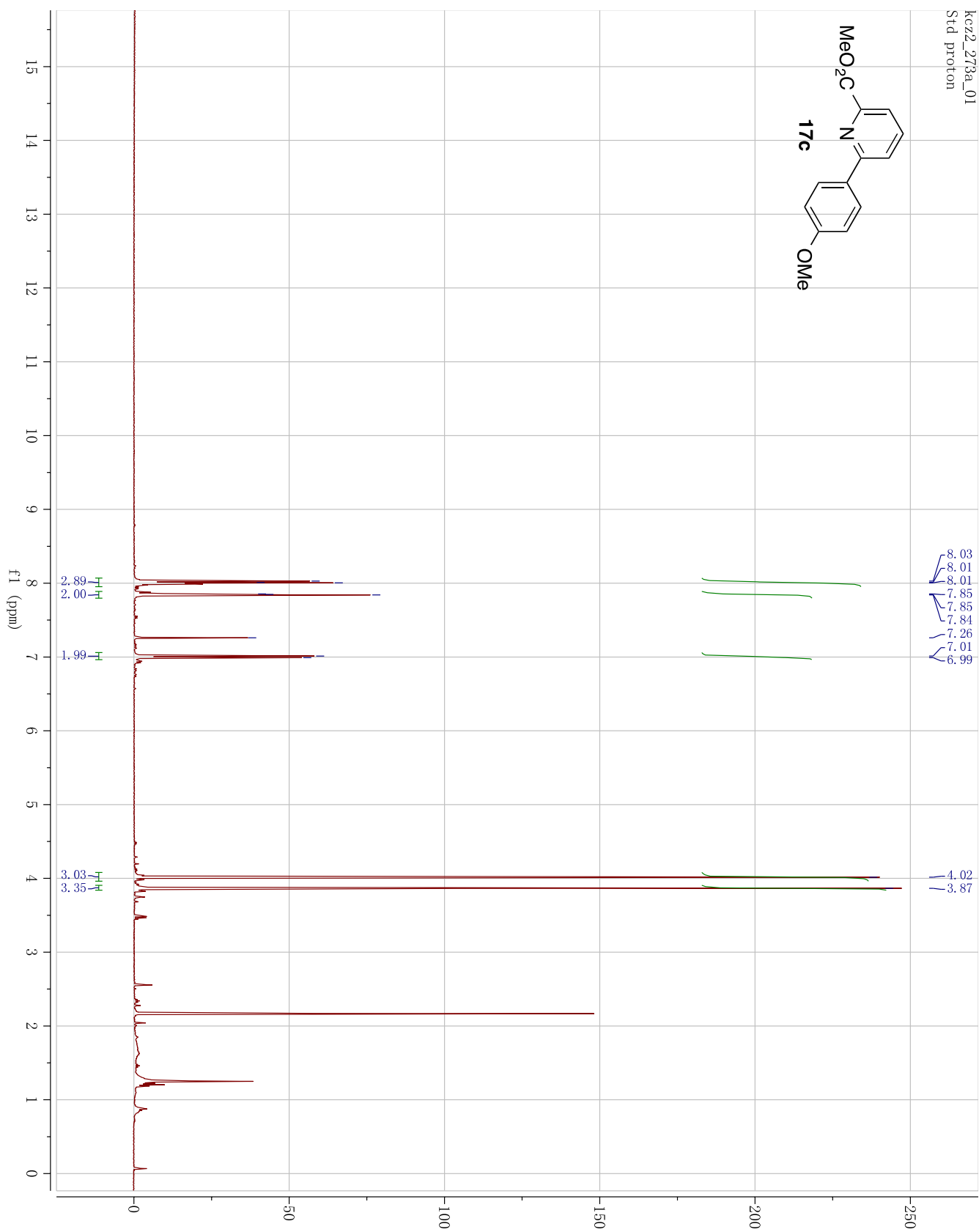
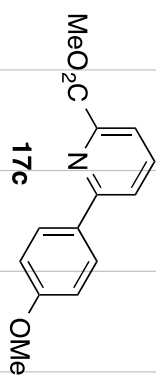


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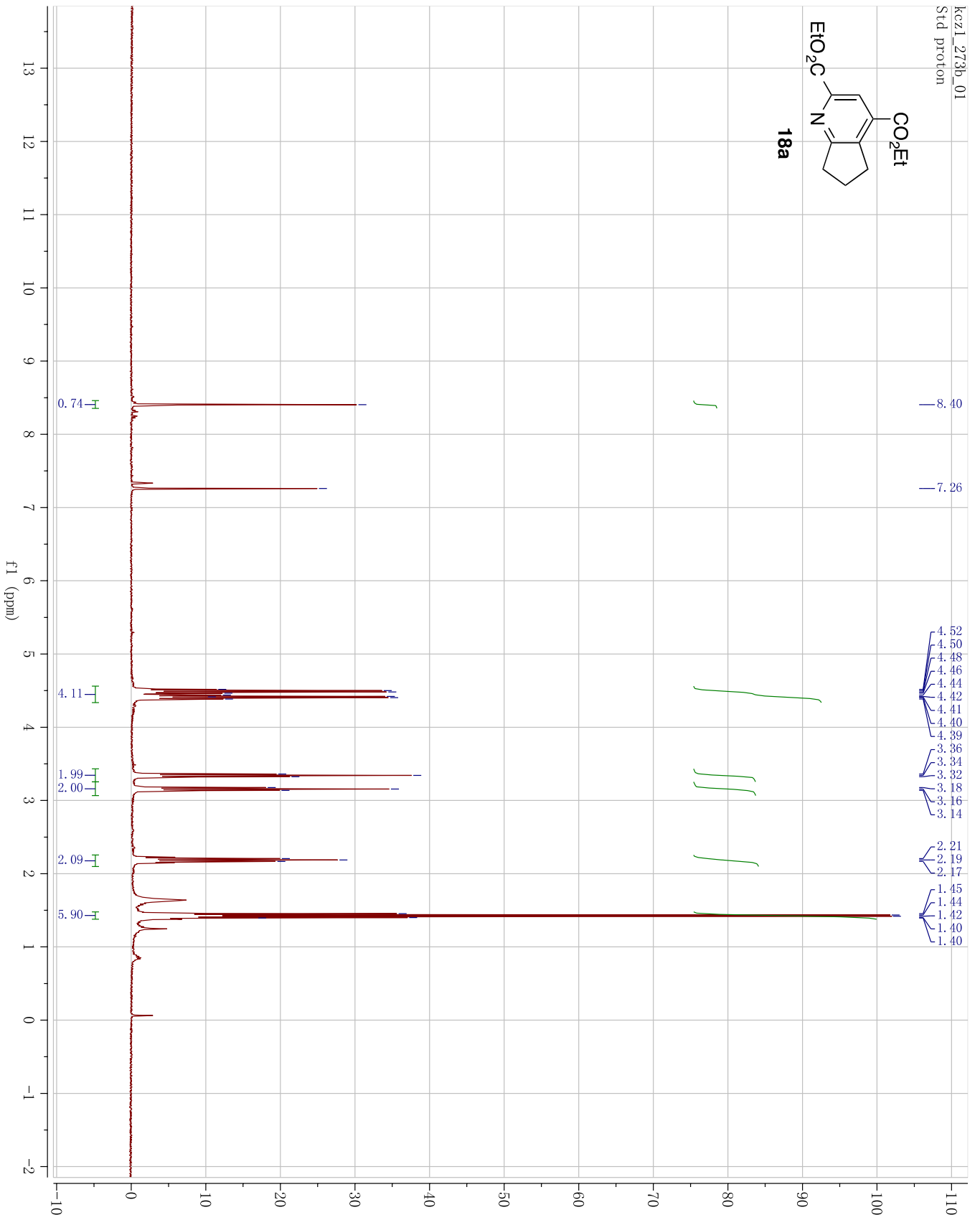
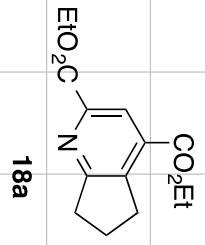




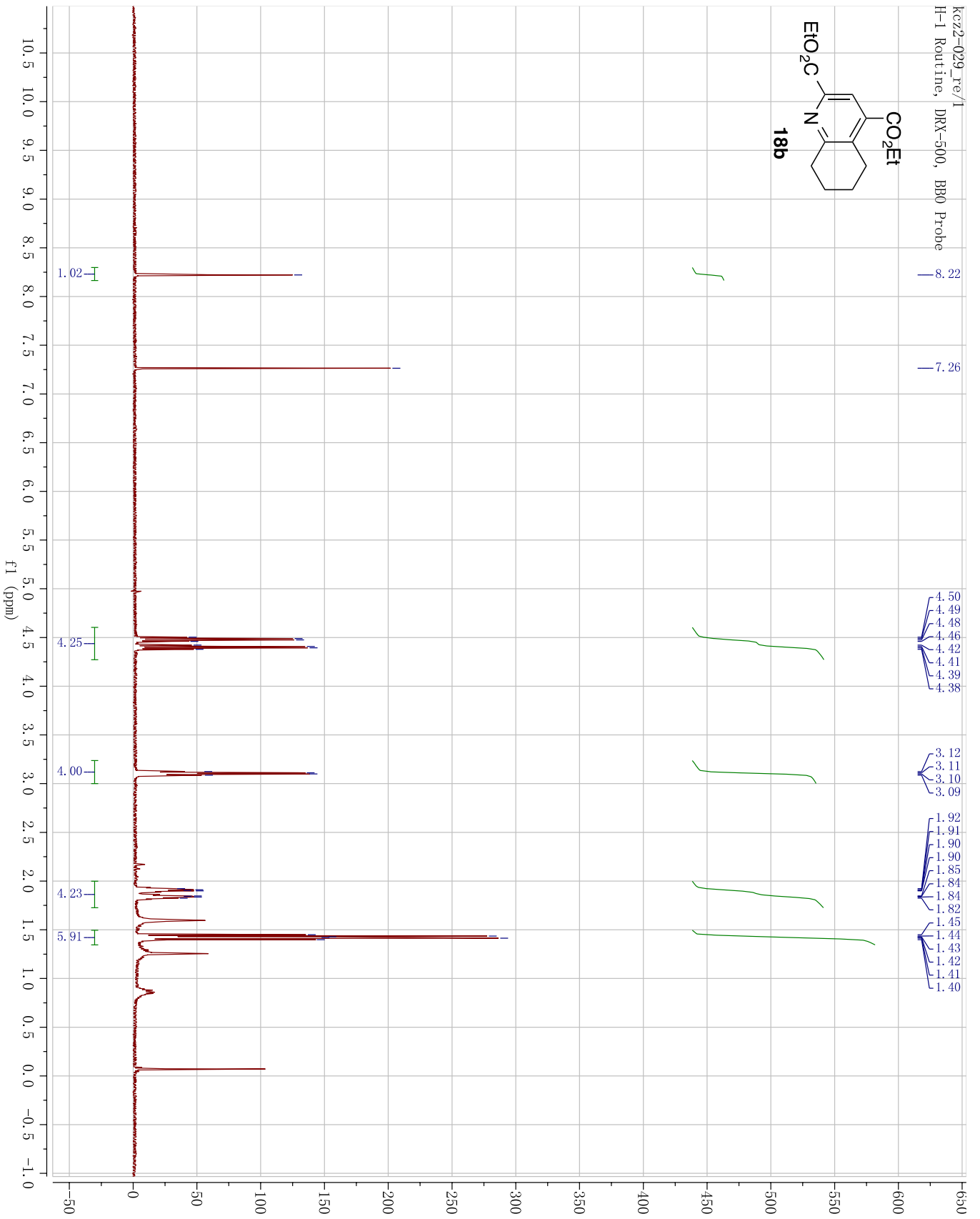
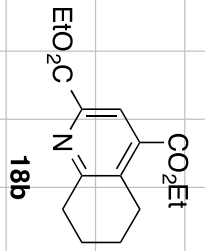
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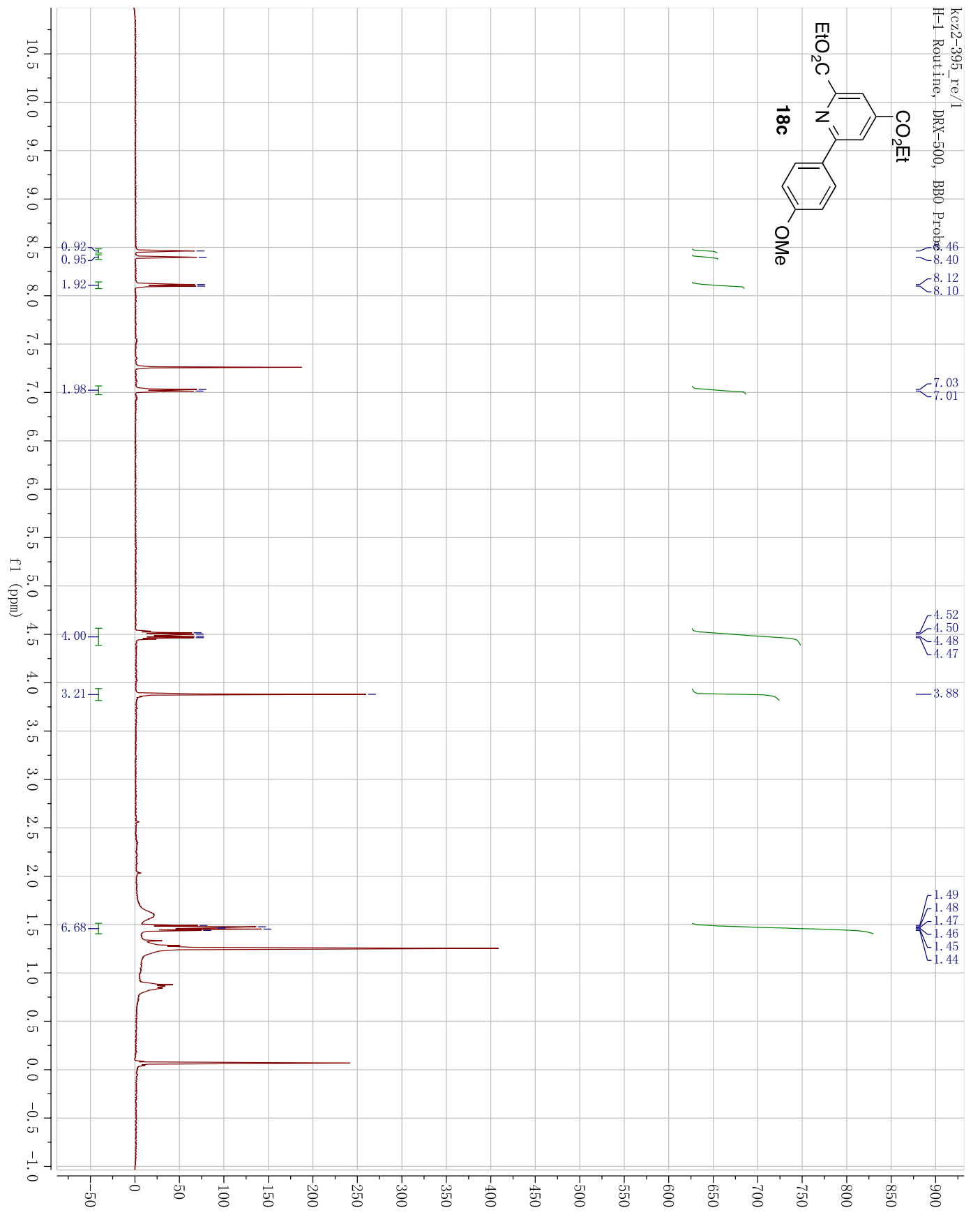


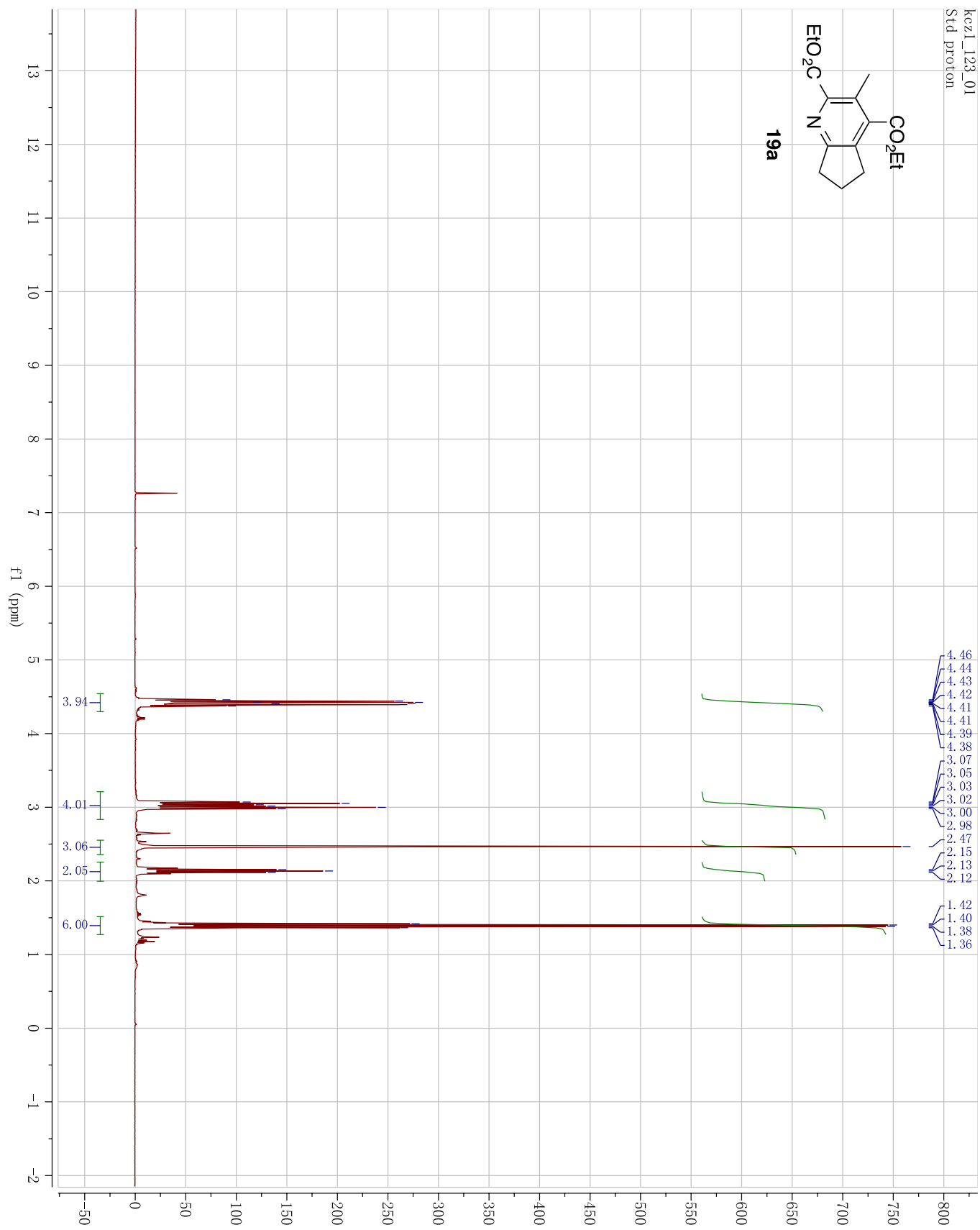
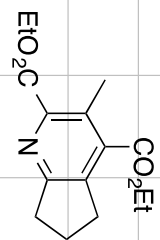
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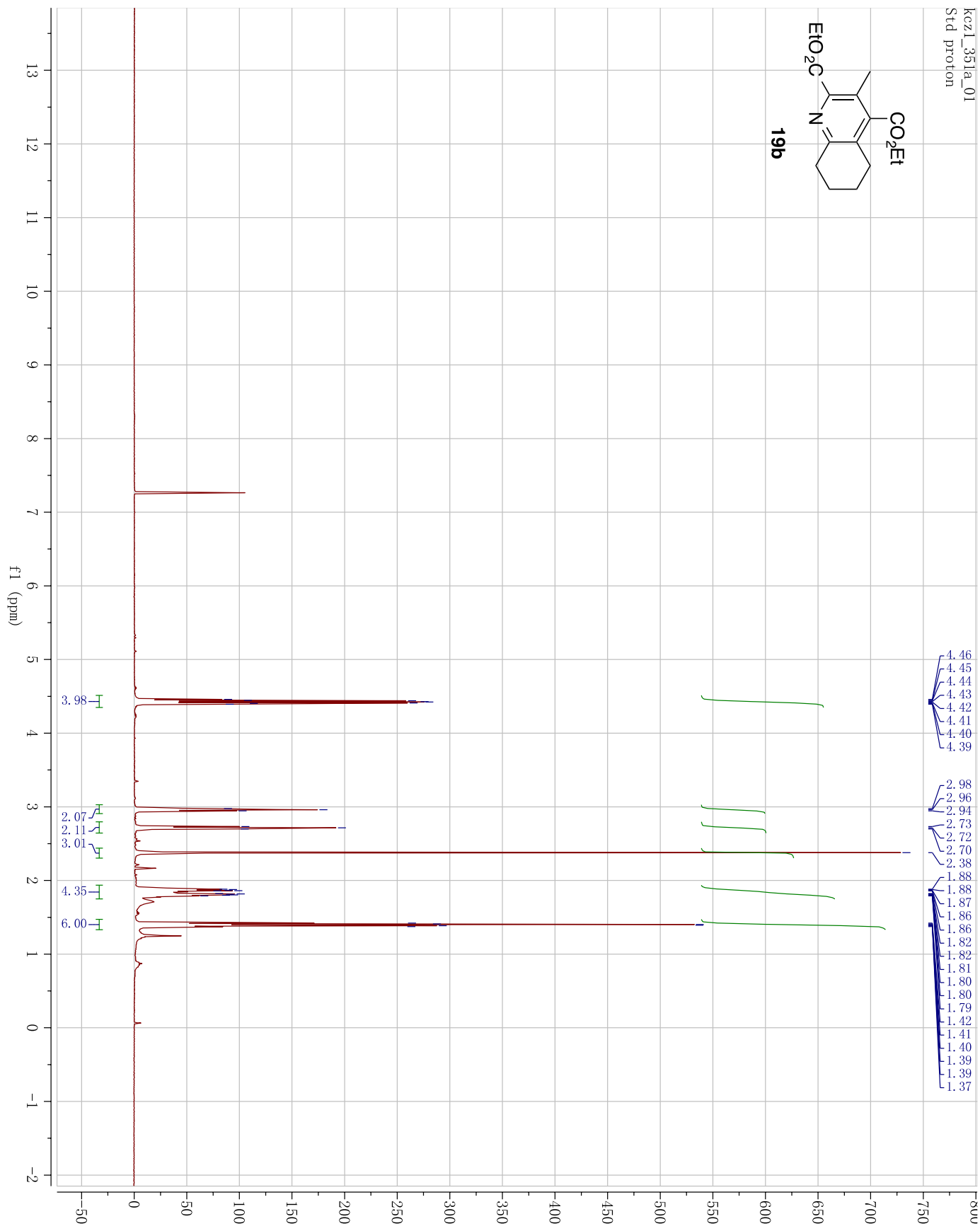
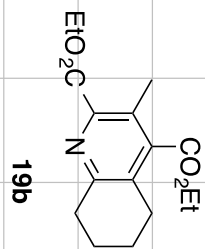


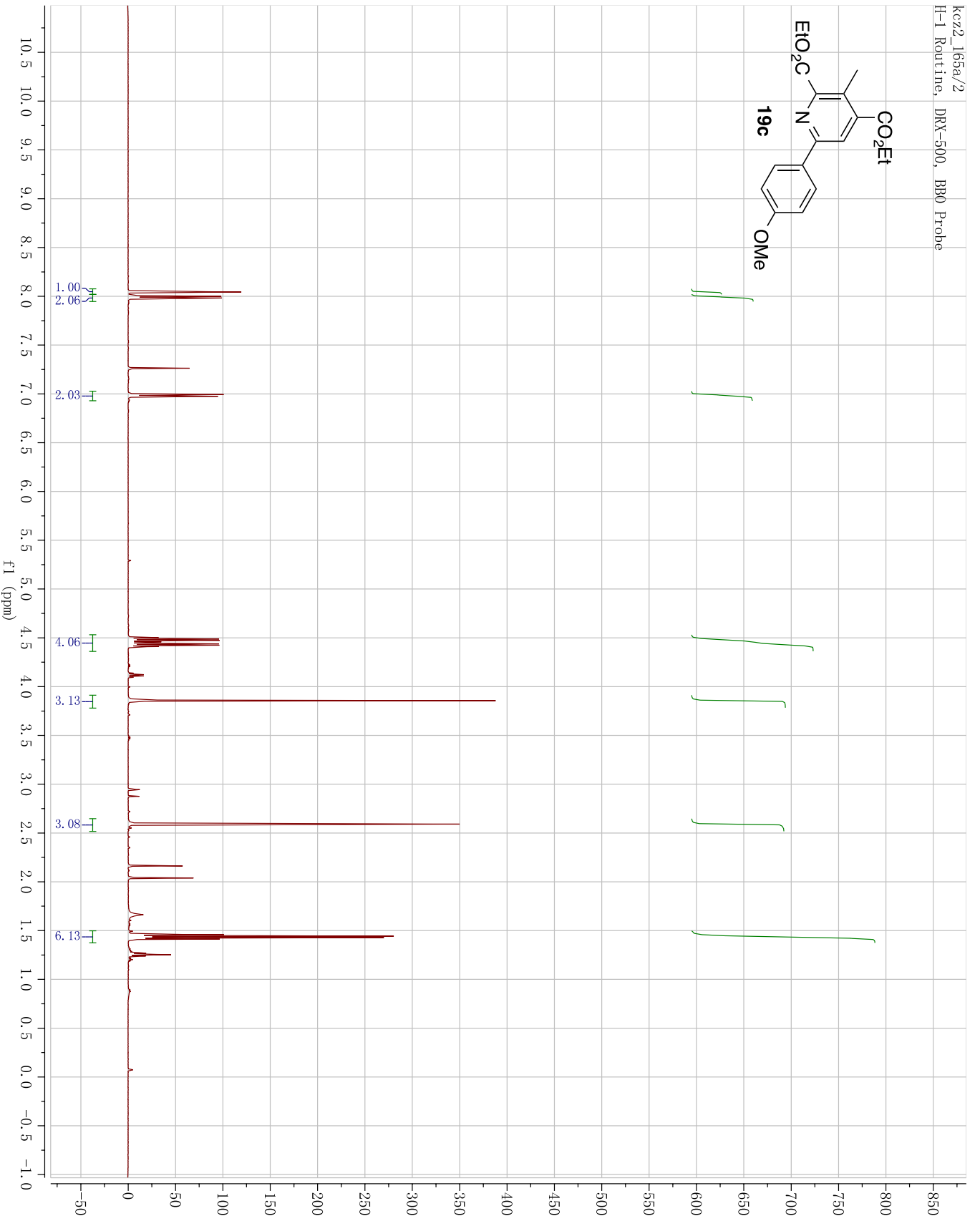
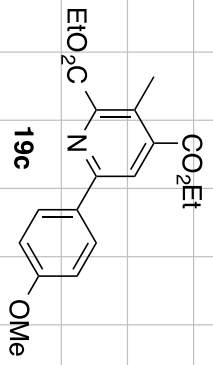
kc72-029_re/1
H-1 Routine, DRX-500, BBO Probe

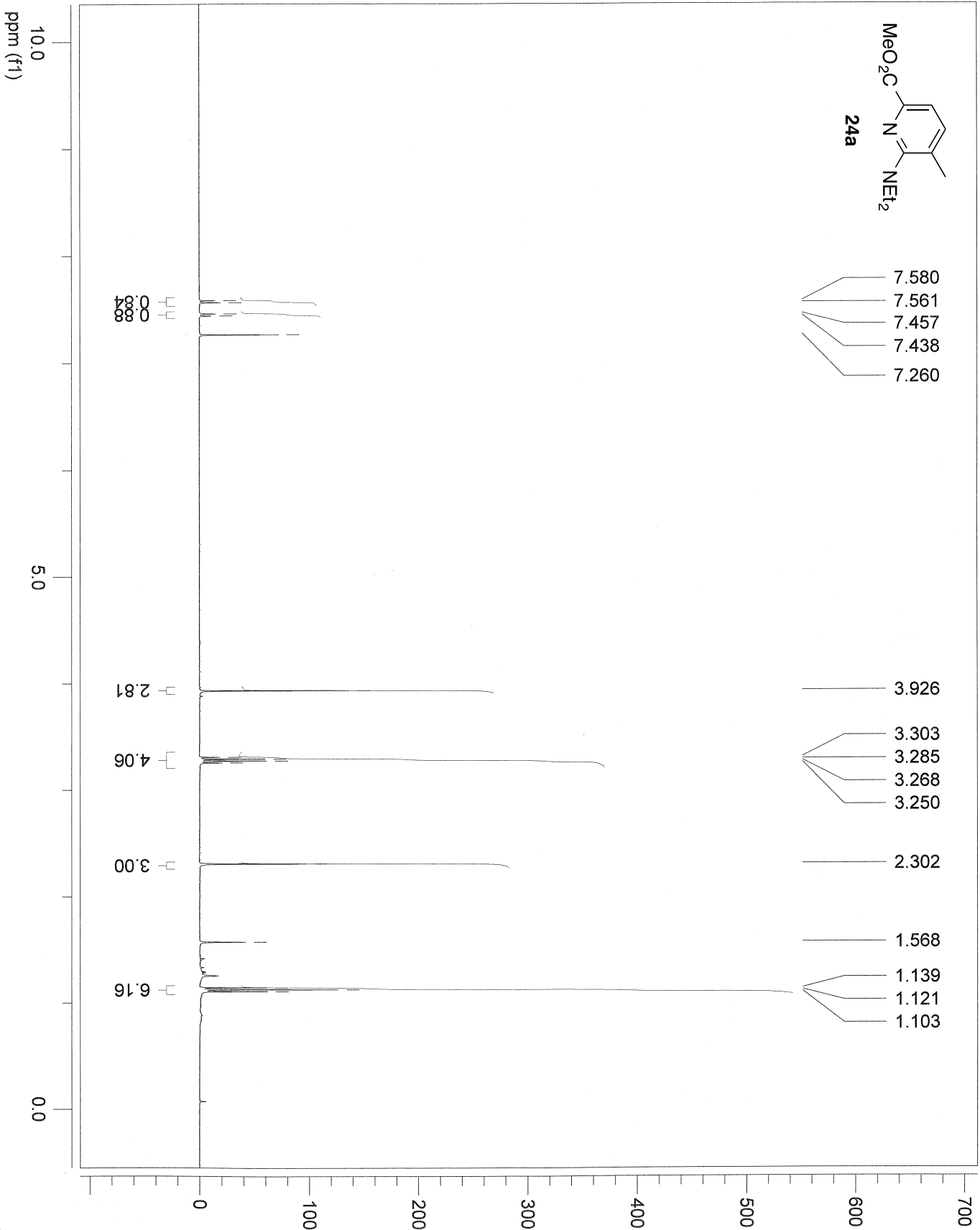
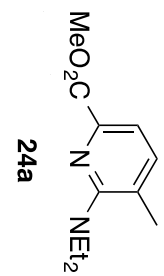




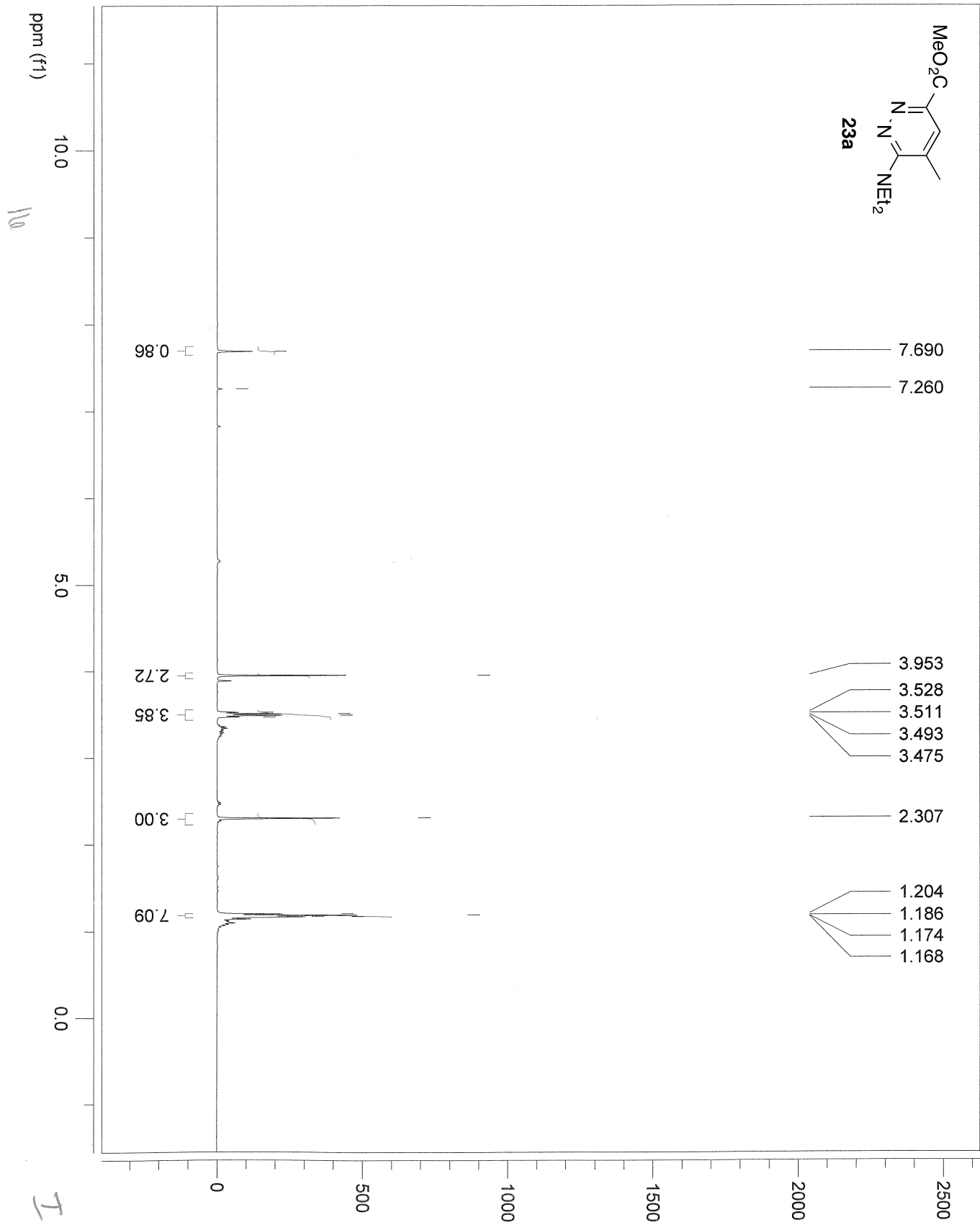


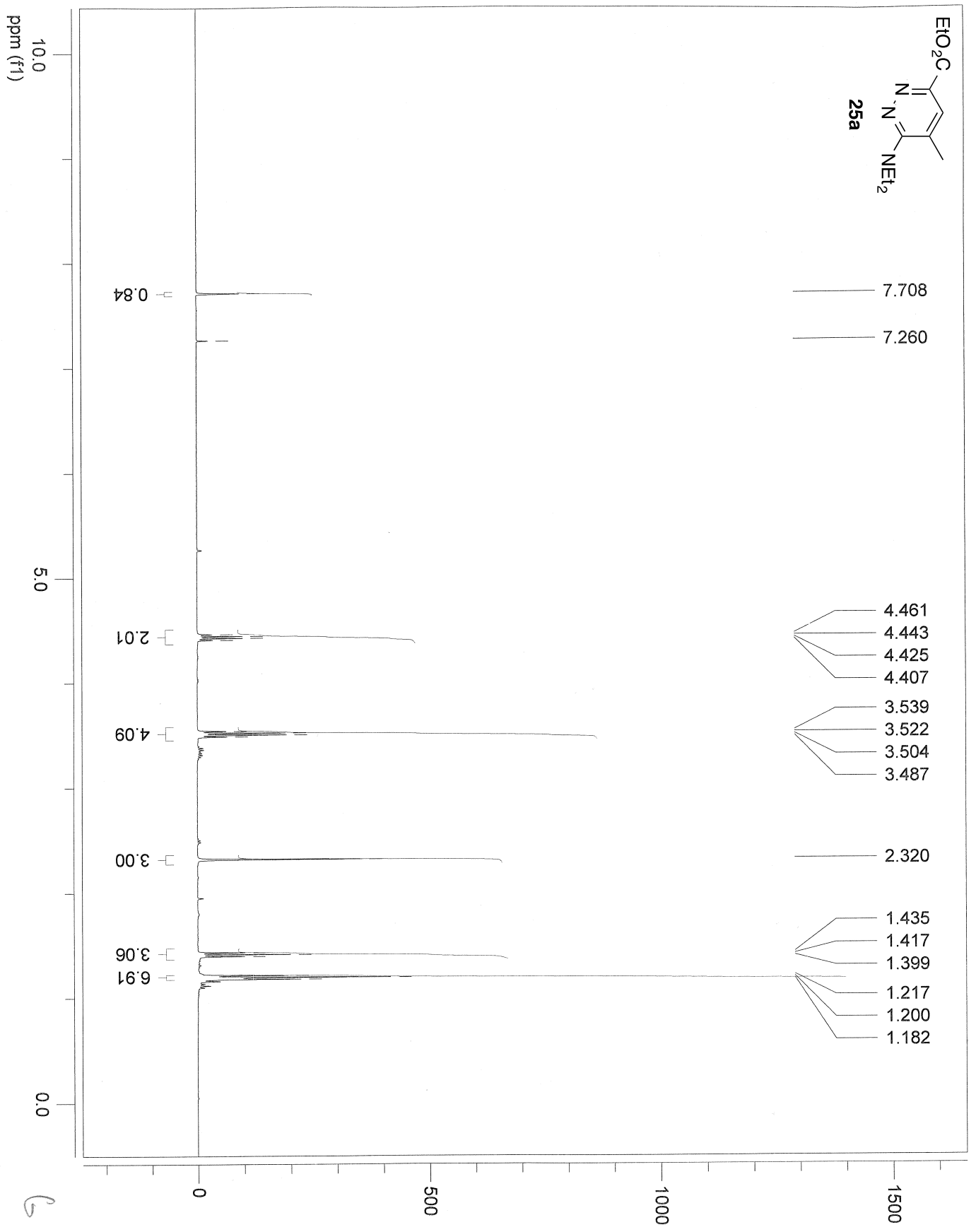
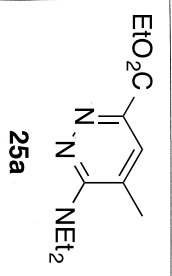


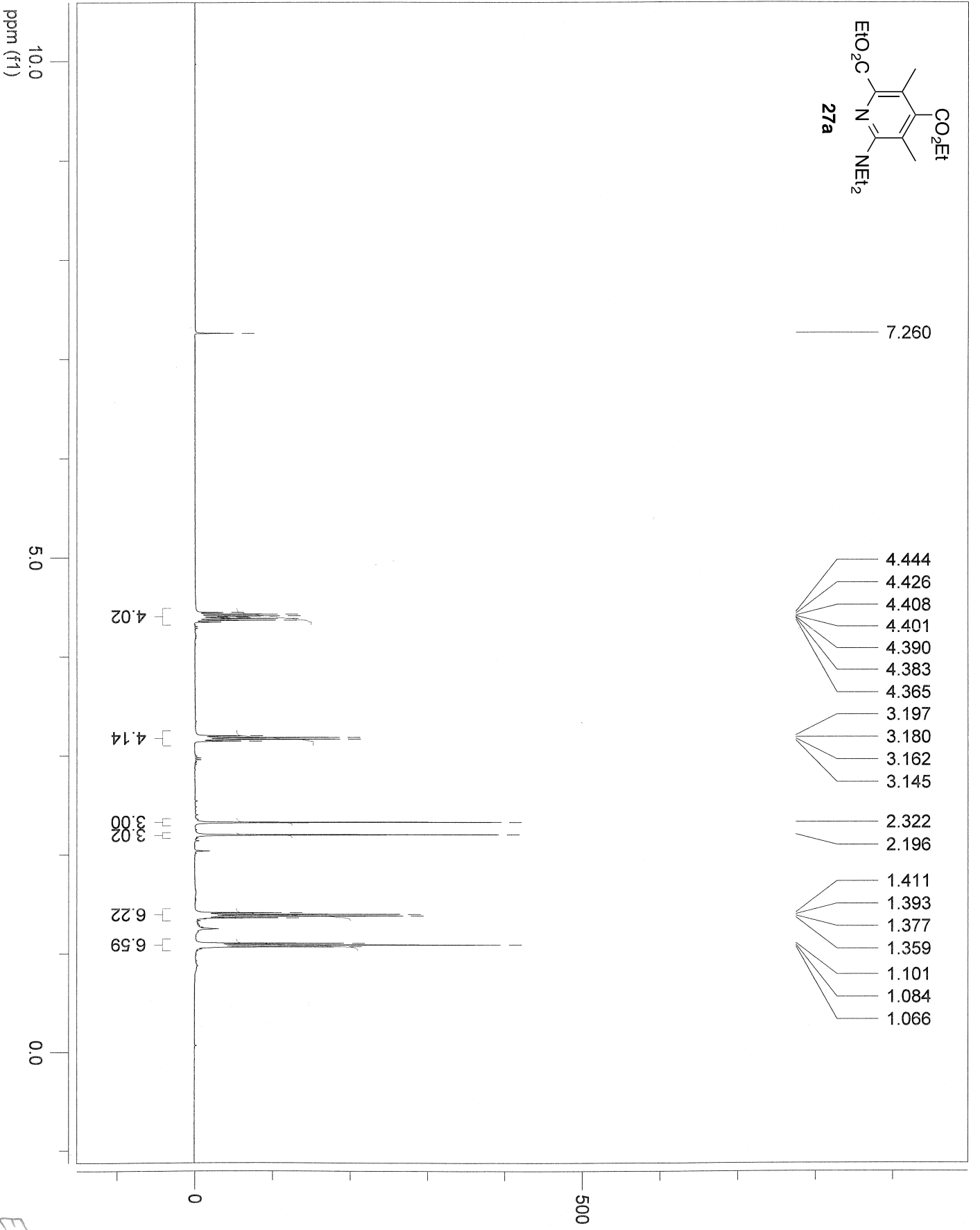
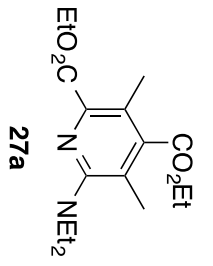


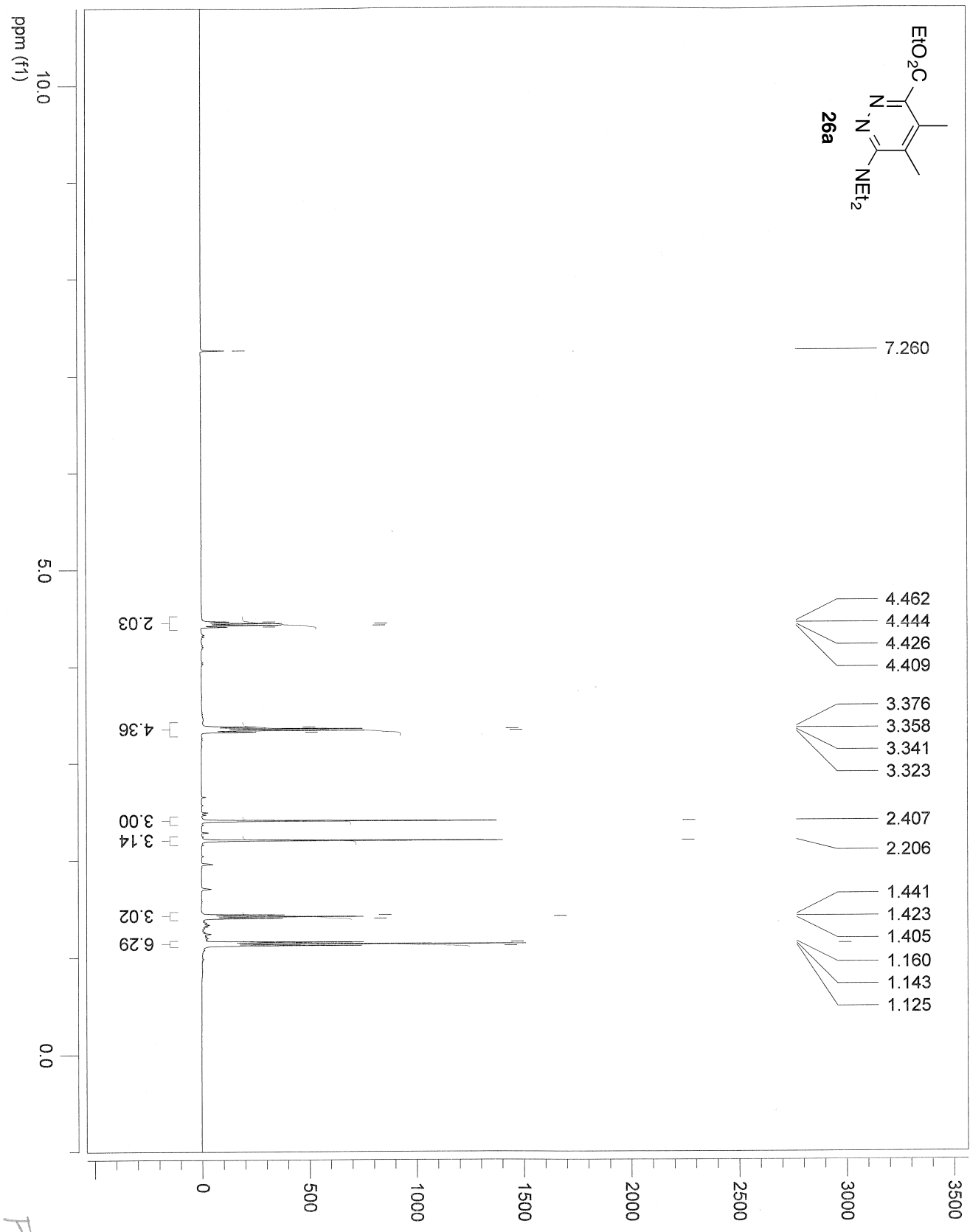


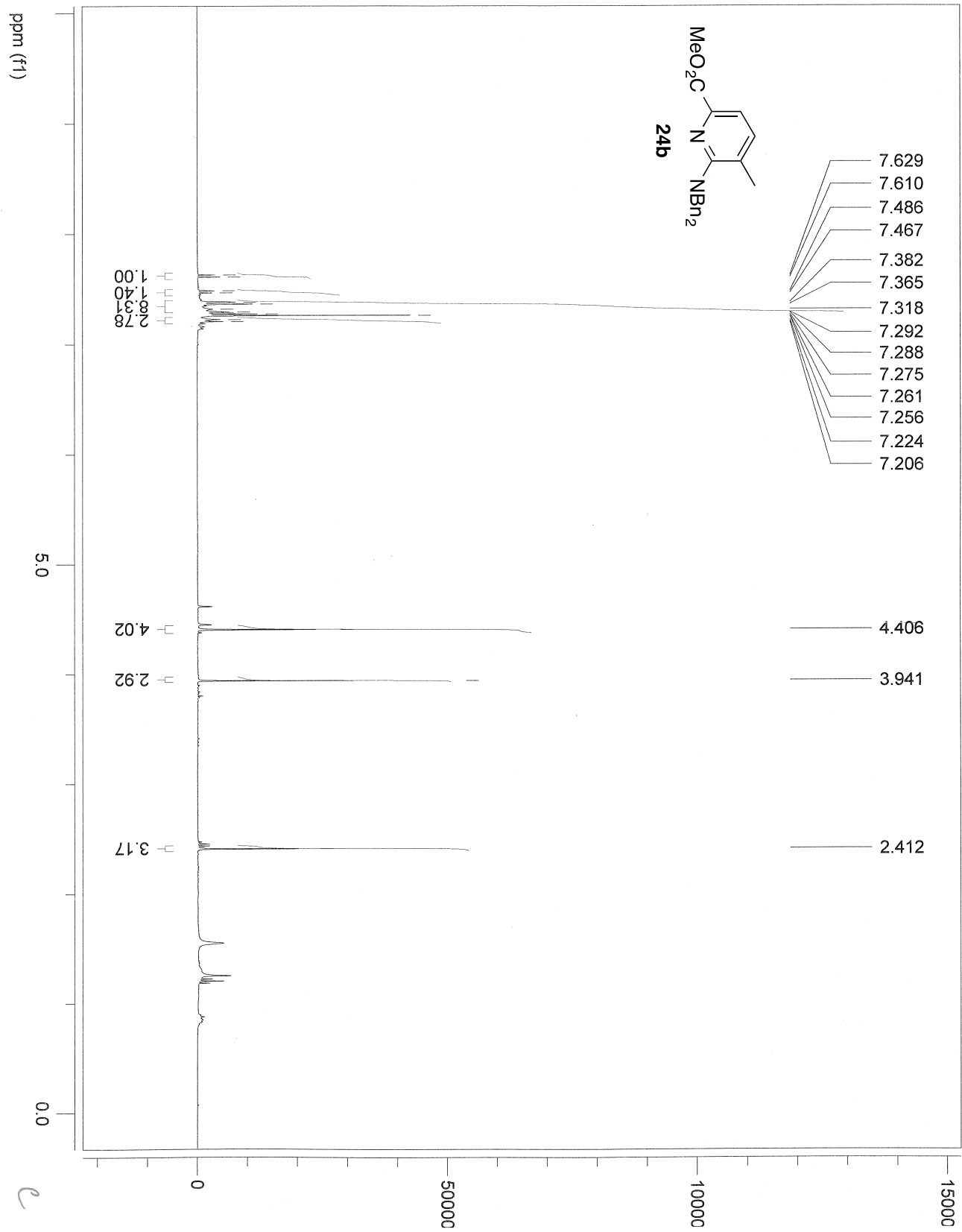
11

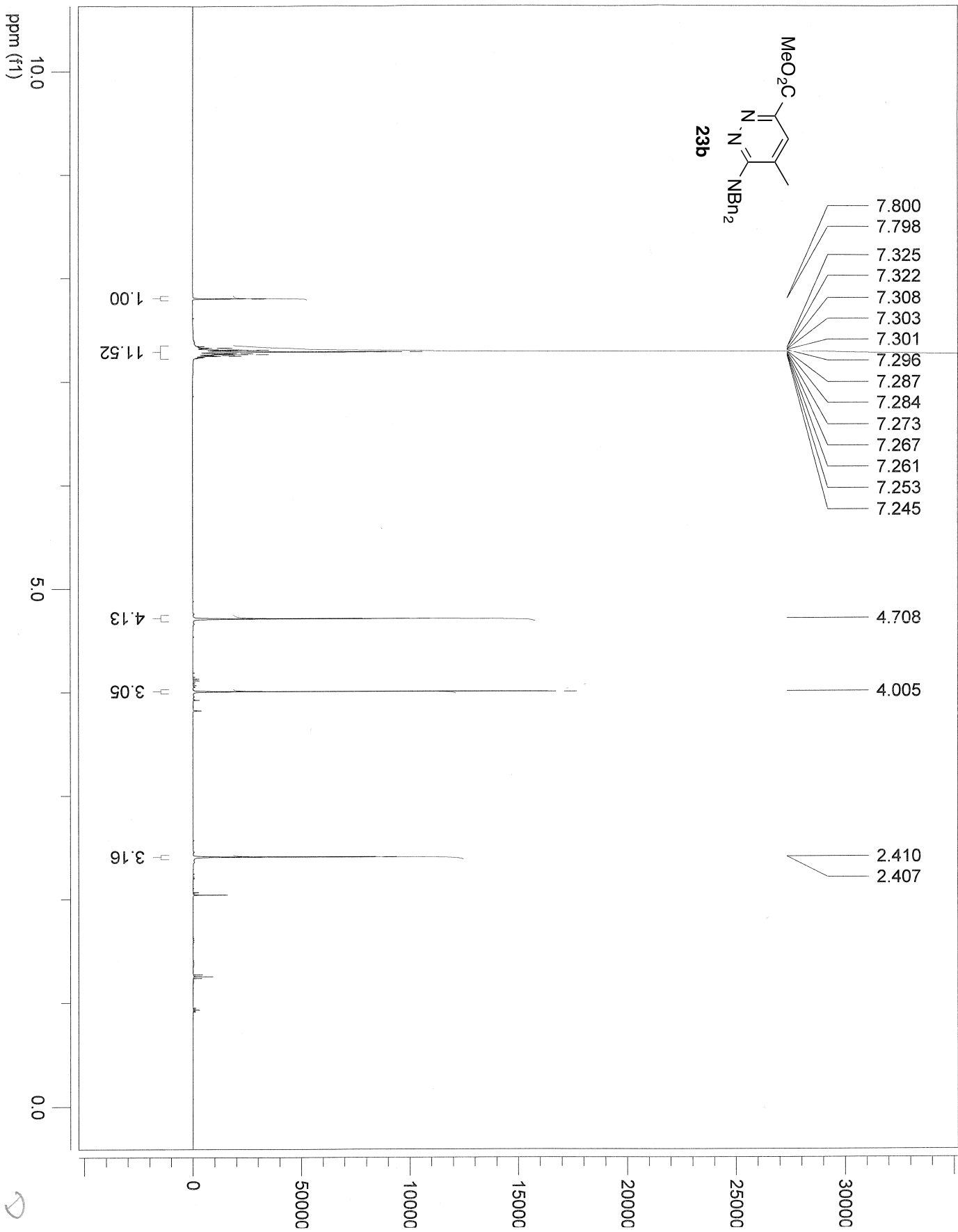


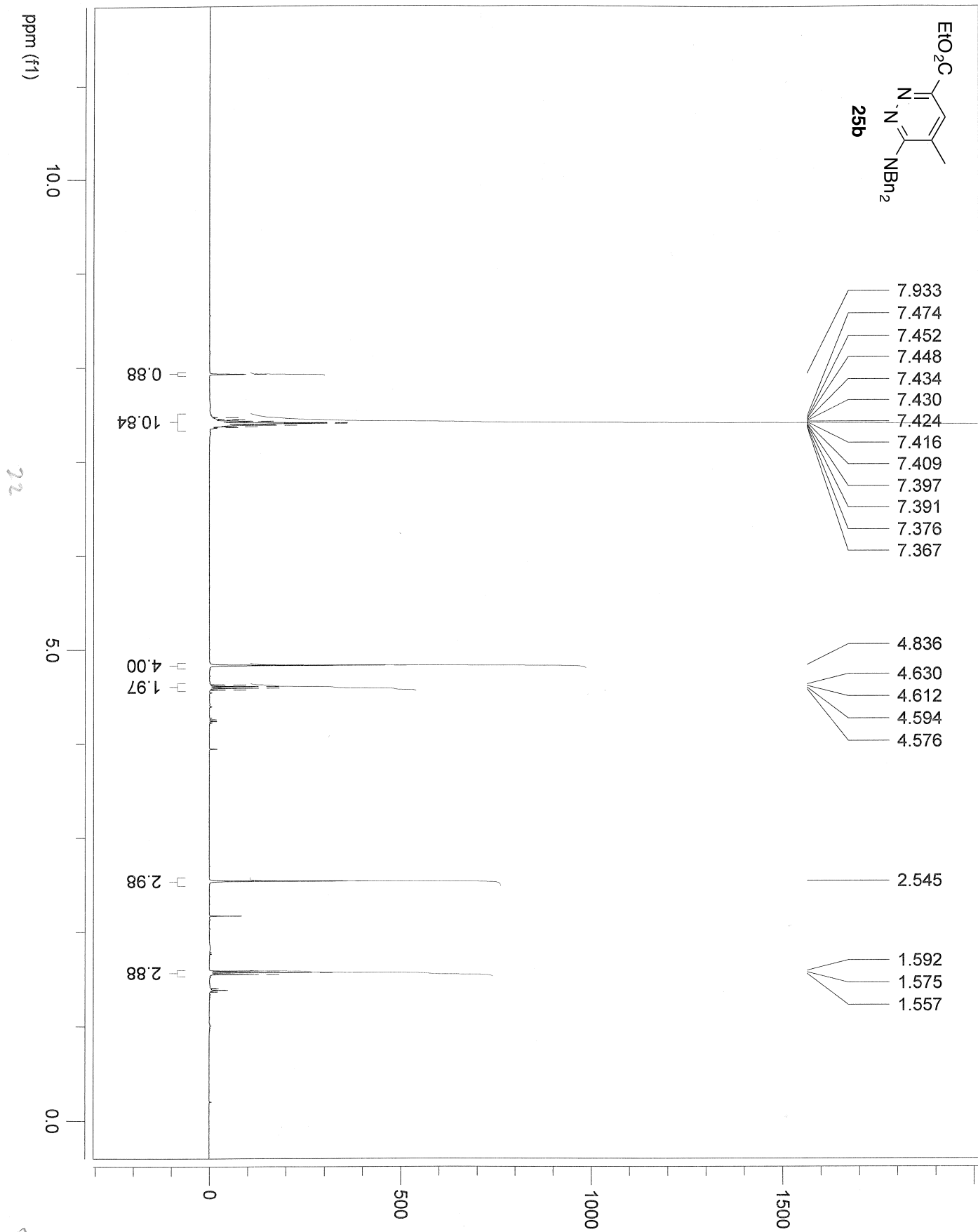
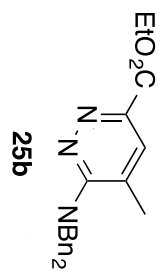












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