Supporting Information for

A Novel Strategy To Assemble the β-Diketo Acid Pharmacophore of Integrase Inhibitors on Purine Nucleobase Scaffolds

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Contents for Supporting Information

Experimental Details.

General Methods. All synthetic procedures were performed under inert atmosphere of dry nitrogen unless stated otherwise. Commercial solvents and reagents were used without purification unless stated otherwise. ^{1}H NMR and ^{13}C NMR were recorded on a 500 MHz NMR spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane (TMS) and multiplicities as singlet (s), doublet (d), quartet (q) and multiplet (m). High resolution mass spectral data were obtained using a LCT TOF mass spectrometer. Melting points were recorded on an melting point apparatus and are uncorrected. Intermediates, **1a-e**, were synthesized according to literature procedures, which are cited.

Methyl 4-(9-benzyl-9*H*-purin-6-yl)-4-ethoxy-2-oxobut-3-enoate (3a). To a stirred solution of 9-benzyl-6-(1-ethoxyvinyl)purine, **2a**,[24] (0.2 g, 0.7 mmol) and pyridine (0.05 g, 2.1 mmol) in dry chloroform (10 mL) at 0°C was added dropwise, methyl chlorooxoacetate (0.07 g, 2.1 mmol) in dry chloroform (5 mL). The reaction mixture was allowed to stand in the refrigerator at 0°C for 48 h. It was then washed with water (2 x 10 mL), dried over anhydrous sodium sulfate and the solvent removed to give a dark red syrup from which pure product was isolated as a yellow oil by column chromatography on silica gel (EtOAc/hexane, 6:4). Yield 0.11 g (42 %); ^{1}H NMR ($CDCl_3$, 500 MHz): 1.53 (t, 3H, J = 6.5 Hz), 3.80 (s, 3H), 4.36 (q, 2H, J = 6.5 Hz), 5.49 (s, 2H), 6.72 (s, 1H, CH), 7.36 (m, 5H), 8.07 (s, 1H), 9.10 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 30.9, 47.4, 52.9, 67.0, 99.5, 128.0, 128.7, 129.2, 131.2, 134.7, 145.5, 152.0, 152.6, 162.4, 167.4, and 179.7. HRMS: $(M + H)^+$ calcd for $C_{19}H_{19}N_4O_4$ 367.1406, found 367.1406.

Methyl-4-(9-benzyl-9*H*-purin-6-yl)-2-hydroxy-4-oxobut-2-enoate (4a). A mixture of methyl 4-(9-benzyl-9*H*-purin-6-yl)-4-ethoxy-2-oxobut-3-enoate, **3a,** (0.10 g, 0.2 mmol) and $FeCl_3.6H_2O$ (0.125 g, 0.4 mmol) in CH_2Cl_2 (20 mL) was stirred at 40 °C for 12 h. The solvent was distilled off and the resulting residue was treated with 1 N HCl (50 mL) and stirred at RT for 1 h, extracted with EtOAc (4 x 20 mL), dried over anhydrous sodium sulfate, and the solvent distilled off to give a brown residue, which was purified by ion-exchange chromatography (DEAE sephadex anion exchange resin, CH_3CN/H_2O, 1:1) and recrystallized from methanol. Yield 0.038 g (42 %), yellow solid, mp 166-167 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.99 (s, 3H), 5.54 (s, 2H), 7.35-7.41 (m, 5H), 7.9 (s, 1H), 8.3 (s,1H), 9.19 (s,1H); ^{13}C NMR

($CDCl_3$, 125 MHz): δ 47.6, 53.3, 101.4, 127.9, 128.9, 129.3, 131.7, 134.5, 147.4, 147.5, 152.2, 154.3, 162.0, 172.8, and 185.7. FAB-HRMS: $(M + H)^+$ calcd for $C_{17}H_{15}N_4O_4$ 339.1093, found 339.1083.

9-benzyl-8-(1-ethoxyvinyl)purine, 2b A mixture of 9-benzyl-8-bromopurine **1b** (1.0 g, 3.4 mmol) bis(triphenylphosphine)palladium(II)chloride (0.24 g, 0.3 mmol) and ethoxyvinyl(tributyl)tin (1.49 g, 4.14 mmol) in dry DMF (50 mL) was heated under N_2 at 65 °C for 48 h. DMF was distilled off and the resulting residue redissolved in EtOAc (50 mL) and filtered through a pad of celite. EtOAc was distilled off and the residue obtained purified by flash chromatography on silica gel (EtOAc/hexane, 3:7). Yield 0.58 g, (60 %), yellow syrup. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.35 (t, 3H, *J* = 7.5 Hz), 3.95 (q, 2H, *J* = 13.7 Hz), 4.62 (d, 1H, *J* = 3Hz), 5.31 (d, 1H, *J* = 3 Hz), 5.77(s, 2H), 7.15-7.33 (m, 5H), 9.01 (s, 1H), 9.14 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 47.2, 64.2, 91.8, 126.8, 127.7, 128.6, 133.0, 136.4, 148.1, 151.2, 151.8, 152.8, and 153.0. HRMS: $(M + H)^+$ calcd for $C_{16}H_{17}N_4O$ 281.1402, found 281.1409.

Methyl 4-(9-benzyl-9*H*-purin-8-yl)-4-ethoxy-2-oxobut-3-enoate (3b). To a stirred solution of 9-benzyl-8-(1-ethoxyvinyl)purine, **2b,** (0.57 g, 2.0 mmol) and pyridine (0.50 g, 6.0 mmol) in dry chloroform (15 mL) at 0°C, was added (dropwise) methyl chlorooxoacetate (0.73, 6.0 mmol) in dry chloroform (10 mL). The reaction mixture was allowed to stand in the refrigerator for 15 h. It was then washed with water (2 x 20 mL), dried over anhydrous sodium sulfate and the solvent distilled off to give a dark reddish syrup from which pure product was isolated by column chromatography on silica gel (EtOAc/hexane, 1:1). Yield 0.54 g, (77 %), yellow oil; ^{1}H NMR

($CDCl_3$, 500 MHz): 1.27 (t, 3H, *J* = 6.5 Hz), 3.78 (s, 3H), 4.04 (q, 2H, *J* = 6.5 Hz), 5.45 (s, 2H), 6.57 (s, 1H), 7.22-7.34 (m, 5H), 9.11 (s, 1H), 9.19 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.7, 46.9, 53.2, 67.2, 102.1, 127.8, 128.3, 128.7, 132.8, 134.9, 148.0, 150.0, 152.3, 152.7, 161.9, 161.9 and 180.2. FAB-HRMS: $(M + H)^+$ calcd for $C_{19}H_{19}N_4O_4$ 367.1406, found 367.1158.

Methyl 4-(9-benzyl-9*H*-purin-8-yl)-2-hydroxy-4-oxobut-2-enoat (4b). A mixture of methyl 4-(9-benzyl-9*H*-purin-6-yl)-4-ethoxy-2-oxobut-3-enoate, **3b,** (0.21 mg, 0.5 mmol) and $FeCl_3.6H_2O$ (0.26 g, 0.9 mmol) in CH_2Cl_2 (60 mL) was stirred at 40 °C for 6 h. The solvent was then distilled off and the residue obtained was treated with 1 N HCl (50 mL), stirred at RT for 5 min, extracted with EtOAc (4 x 20 mL), dried over anhydrous sodium sulfate and concentrated. The resulting yellow residue was purified by ion exchange chromatography (DEAE sephadex anion exchange resin, CH_3CN/H_2O, 1:1) and then crystallized from methanol. Yield 0.14 g (74 %), yellow solid, mp 137-138 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): 3.98 (s, 3H,) 6.03 (s, 2H), 7.29-7.41 (m, 5H), 7.68 (s, 1H), 9.21 (s,1H), 9.39 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 47.6, 53.4, 102.2, 128.0, 128.1, 128.3, 128.8, 132.8, 135.9, 146.8, 151.6, 152.5, 155.2, 161.9, and 186.2. FAB-HRMS: $(M + H)^+$ calcd for $C_{17}H_{15}N_4O_4$ 339.1093, found 339.1099.

1, 9-dibenzyl-6,9-dihydro-6-oxo-8-(1-ethoxyvinyl)purine (2c). A mixture of 1,9-dibenzyl-6,9-dihydro-6-oxo-8-bromopurine, **1c,** (1.20 g, 3.04 mmol), bis(triphenylphosphine)palladium(II) chloride (0.21 g, 0.3 mmol) and ethoxyvinyl(tributyl)tin (2.19 g, 6.07 mmol) in dry DMF (50 mL) was heated under N_2 at 70 °C for 22 h. DMF was distilled off and the resulting residue was dissolved in EtOAc (100 mL) and filtered through a pad of celite and concentrated. The residue

obtained was purified by chromatography on silica gel (EtOAc/hexane, 6:4). Yield 0.98 g (88 %), white solid, mp 167-168 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.26 (t, 3H, *J* = 7.5 Hz), 3.86 (q, 2H, *J* = 7 Hz), 4.46 (d, 1H, *J* = 2.5 Hz), 5.27 (t, 2H, *J* = 3 Hz), 5.32 (d, 1H, *J* = 3 Hz), 5.60 (s, 2H), 7.10-7.37 (m, 10H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 47.5, 49.1, 63.8, 90.2, 123.4, 126.6, 127.5, 128.2, 128.5, 128.6, 128.9, 129.0, 136.1, 136.7, 146.2, 146.9, 148.9, 151.8, and 156.5. FAB-HRMS: $(M + H)^+$ calcd for $C_{23}H_{23}N_4O_2$ 387.1821, found 387.1815.

Methyl 4-(1,9-benzyl-6-9-dihydro-6-oxo-1*H*-purin-8-yl)-4-ethoxy-2-oxobut-3-enoate (3c). To a stirred solution of 1,9-dibenzyl-6,9-dihydro-6-oxo-8-(1-ethoxyvinyl)purine, **2c**, (0.62 g, 1.6 mmol) and pyridine (0.40 g, 4.8 mmol) in dry chloroform (30 mL) at 0 °C was added (dropwise) methyl chlorooxoacetate (0.58 g, 4.8 mmol) in dry chloroform (10 mL), the reaction mixture allowed to stand in the refrigerator for 48 h, then washed with water (2 x 100 mL), dried over anhydrous sodium sulfate and chloroform distilled off to give yellow syrup. Pure product was isolated by column chromatography on silica gel (EtOAc/hexane, 4:6). Yield 0.58 g, (77 %), yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): 1.14 (t, 3H, *J* = 6.5 Hz), 3.66 (s, 3H), 3.87 (q, 2H, *J* = 7 Hz), 5.19 (s, 2H), 5.23 (s, 2H), 6.25 (s, 1H), 7.09-7.28 (m, 10H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.7, 47.2, 49.1, 52.8, 66.5, 102.6, 127.4, 128.1, 128.5, 128.6, 129.0, 131.9, 131.9, 132.0, 132.1, 132.2, 133.0, 135.3, 135.9, 143.8, 147.8, 148.6, 156.3, 161.9, 162.6 and 181.2. FAB-HRMS: $(M + H)^+$ calcd for $C_{26}H_{25}N_4O_5$ 473.1825, found 473.1811

Methyl 4-(1,9-benzyl-6,9-dihydro-6-oxo-1*H*-purin-8-yl)-2-hydroxy-4-oxobut-2-enoate (4c). A mixture of methyl 4-(1,9-benzyl-6-9-dihydro-6-oxo-1*H*-purin-8-yl)-4-ethoxy-2-oxobut-3-

enoate, **3c**, (0.58 g, 1.2 mmol) and $FeCl_3.6H_2O$ (0.56 g, 2.1 mmol) in dichloroethane (150 mL) was stirred under reflux for 3 h. Dichloroethane was removed and the residue was treated with 1 N HCl (50 mL), stirred at RT for 5 min and extracted with EtOAc (4 x 20 mL). The organic layer was dried over anhydrous sodium sulfate, concentrated and the yellowish residue was purified by ion exchange chromatography (DEAE sephadex anion exchange resin, CH_3CN/H_2O, 1:1) and crystallized from methanol. Yield 0.50 g. (91 %), yellow solid, mp 178-179 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): 3.95 (s, 3H), 5.32 (s, 2H), 5.87 (s, 2H), 7.30-7.41 (m, 10H), 7.75 (s, 1H), 8.19 (s, 1H), 13.8 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 48.1, 49.5, 53.2, 102.4, 127.8, 128.2, 128.4, 128.6, 128.7, 129.2, 135.5, 135.8, 143.0, 149.3, 150.0, 156.7, 162.1, 162.2, 184.1, and 185.9. FAB-HRMS: $(M + H)^+$ calcd for $C_{24}H_{21}N_4O_5$ 445.1512, found 445.1520.

1,3,7-Tribenzyl-8-(1-ethoxyvinyl)-1*H*- purine-2,6(*3H*, *7H*)-dione (2d). A mixture of 8-bromo-1,3,7-tribenzyl-1*H*-purine-2,6(*3H*, *7H*)-dione **1d** (0.74 g, 1.48 mmol), bis(triphenylphosphine) palladium(II)chloride (0.104 g, 0.14 mmol) and ethoxyvinyl(tributyl)tin (0.81 g, 6.07 mmol) in anhydrous N-methylpyrrolidinone (10 mL) was heated under N_2 at 95 °C for 22 h. The NMP was distilled off and the resulting residue redissolved in EtOAc (100 mL) and filtered through a pad of celite. The solvent was removed and the residue obtained was purified by flash chromatography on silica gel (EtOAc:hexane, 6:4). Yield 0.54 g (75 %), oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.33 (t, 3H, *J* = 6.5 Hz), 3.94 (q, 2H, *J* = 7.5 Hz), 4.60 (d, 1H, *J* = 3.5 Hz), 5.20 (s, 2H), 5.25 (d, 1H, *J* = 2.5 Hz), 5.31 (s, 2H), 5.90 (s, 2H), 7.22-7.58 (m, 15H); ^{13}C NMR ($CDCl_3$, 125 MHz): 14.1, 44.4, 46.5, 49.7, 64.1, 91.5, 108.1, 126.9, 127.3, 127.6, 127.7, 128.3, 128.4, 128.5, 128.6, 128.9, 136.5, 137.1, 137.4, 147.1, 147.6, 149.9, 151.2, 151.6, and 155.0 HRMS:

$(M + H)^+$ calcd for $C_{30}H_{29}N_4O_3$ 493.2240, found 493.2240.

Methyl 4-(1,3,7-tribenzyl-2,3,6,7-tetrahydro-2,6-dioxo-1*H*-purin-8-yl)-4-ethoxy-2-oxobut-3-enoate (3d). To a stirred solution of 1,3,7-tribenzyl-8-(1-ethoxyvinyl)-*1H*-purine-2,6(*3H*, *7H*)-dione, **2d,** (0.45 g, 0.92 mmol) and pyridine (0.23 g, 2.7 mmol) in dry chloroform (15 mL) at 0 °C was added (dropwise) methyl chlorooxoacetate (0.33 g, 2.7 mmol) in dry chloroform (10 mL) and the reaction mixture was allowed to stand in the refrigerator for 3 days. It was then washed with water (2 x 100 mL), dried over anhydrous sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 9.5:0.5). Yield 0.16 g, (31 %), yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): 1.31 (t, 3H, J = 7.4 Hz), 3.78 (s, 3H), 4.03 (q, 2H, J = 7.1 Hz), 5.22 (s, 2H), 5.26 (s, 2H), 5.57 (s, 2H), 6.49 (s, 1H), 7.25-7.50 (m, 15H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.7, 44.5, 46.6, 49.5, 53.0, 66.8, 102.3, 108.1, 127.4, 127.6, 128.0, 128.3, 128.4, 128.5, 128.6, 128.7, 135.5, 136.2, 137.1, 144.8, 147.5, 151.1, 155.1, 160.9, 162.1 and 180.0 HRMS: $(M + H)^+$ calcd for $C_{33}H_{31}N_4O_6$ 579.2244, found 579.2232.

Methyl -4-(1,3,7-tribenzyl-2,3,6,7-tetrahydro-2,6-dioxo-1*H*-purin-8-yl)-2-hyroxyy-4-oxobut-3-enoate (4d). A mixture of methyl-4-(1,3,7-tribenzyl-2,3,6,7-4tetrahydro-2,6-dioxo-1*H*-purin-8-yl)-4-ethoxy-2-oxobut-3-enoate, **3d**, (0.32 g, 0.5 mmol) and $FeCl_3.6H_2O$ (0.26 g, 0.9 mmol) in dichloroethane (20 mL) was stirred at reflux for 8 h. Dichloroethane was distilled off and the residue obtained was treated with 1 N HCl (50 mL), stirred at RT for 5 min, extracted with EtOAc (2 x 20 mL), dried over anhydrous sodium sulfate, and concentrated. The residue was

purified by ion-exchange chromatography (DEAE sephadex anion exchange resin, CH_3CN/H_2O, 1:1) and crystallized from methanol. Yield 0.13 g. (46 %), yellow solid, mp 144-146 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): 4.00 (s, 3H), 5.29 (s, 2H), 5.33 (s, 2H), 6.17 (s, 2H), 7.30-7.57 (m, 16H), 13.97 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 44.8, 46.8, 50.2, 53.4, 102.5, 111.2, 127.7, 127.9, 128.1, 128.2, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 129.0, 136.0, 136.1, 136.8, 142.6, 146.9, 150.9, 155.33, 162.1, 163.7 and 185.1. HRMS: $(M + H)^+$ calcd for $C_{31}H_{27}N_4O_6$ 551.1931, found 551.1995.

Ethyl 1-benzyl-5-(1-ethoxyvinyl)-1*H*-imidazole-4-carboxylate (2e). A mixture of ethyl-5-iodo-1-benzylimidazole-4-carboxylate, **1e,** (1g, 3.0 mmol), bis(triphenylphosphine)palladium(II) chloride (0.25 g, 0.3 mmol) and ethoxyvinyl(tributyl)tin (2.22 g, 6.1 mmol) in dry DMF (50 mL) was heated under N_2 at 65 °C for 12 h. DMF was distilled off and the residue dissolved in EtOAc (100 mL) and filtered through a pad of celite followed by washing with fresh portions of EtOAc (2 x 50 mL). The combined EtOAc portions were concentrated and the crude product was purified by chromatography on silica gel (EtOAc/Hexane, 1:1). Yield 0.88 g, (97 %), yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.28 (t, 3H, *J* = 7 Hz), 1.38 (t, 3H, *J* = 7 Hz), 3.86 (q, 2H, *J* = 7 Hz), 4.35 (q, 2H, *J* = 7.5 Hz), 4.47 (d, 1H, *J* = 2 Hz), 4.61 (d, 1H, *J* = 2 Hz), 5.14 (s, 2H), 7.13-7.35 (m, 5H), 7.44 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ14.2, 14.3, 49.4, 60.4, 63.7, 91.9, 127.2, 128.2, 128.5, 128.8, 132.0, 135.6, 137.2, 149.4, 162.5 HRMS: $(M + H)^+$ calcd for $C_{17}H_{21}N_2O_3$ 301.1552, found 301.1555.

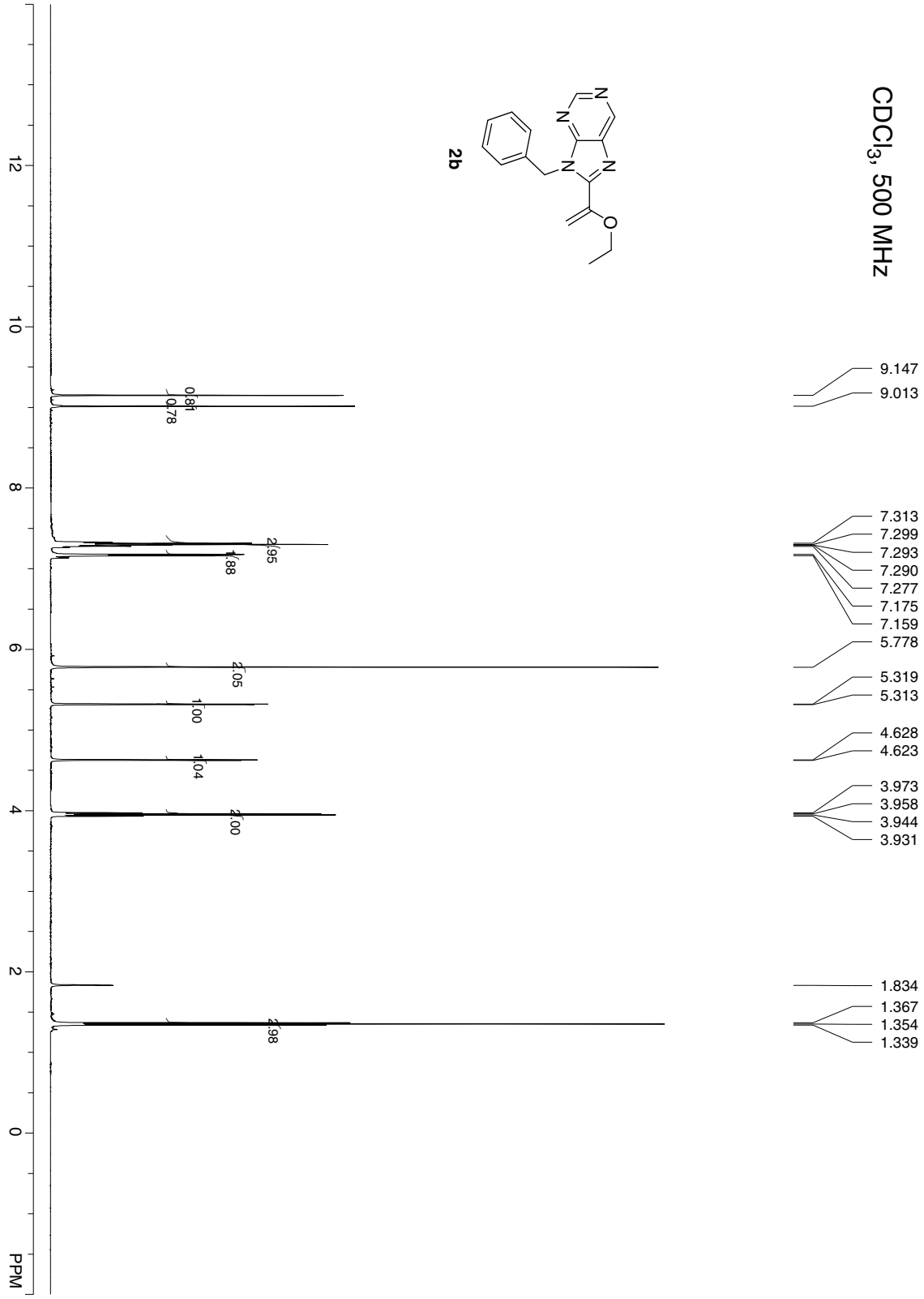
Methyl-4-(1-benzyl-4-ethylcarboxylate-*1H*-imidazol-5-yl)-4-ethoxy-2-oxo-but-3enoate (3e). To a stirred solution of ethyl 1-benzyl-5-(1-ethoxyvinyl)-*1H*-imidazole-*4*-carboxylate, **2e**, (0.91 g, 3.0 mmol) and pyridine (0.75 g, 9.0 mmol) in dry chloroform (50 mL) at 0 °C was added (dropwise) methyl chlorooxoacetate (1.10 g 9.0 mmol) in dry chloroform (10 mL) and reaction mixture allowed to stand at 0 °C in the refrigerator for 48 h. It was then washed with water (2 x 50 mL), dried over anhydrous sodium sulfate, concentrated and the residue was purified by column chromatography (EtOAc/Hexane, 1:1). Yield 0.85 g, (72 %), yellow oil;p ^{1}H NMR ($CDCl_3$, 500 MHz): 1.23 (t, 3H, *J* = 3 Hz), 1.32 (t, 3H, *J* = 3 Hz) 3.77 (s, 3H), 3.88 (m, 2H), 4.02 (m, 2H), 4.29 (m, 2H), 4.89 (d, 1H, J = 15.5 Hz), 5.08 (d, 1H, *J* = 15.5 Hz), 6.47 (s, 1H), 7.15-7.34 (m, 6H), 7.51 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): 13.7, 14.2, 49.8, 52.9, 60.6, 66.5, 102.0, 127.9, 128.4, 128.5, 128.8, 132.1, 134.6, 138.2, 161.8, 162.8, 180.4 and 184.1. HRMS: $(M + H)^+$ calcd for $C_{20}H_{23}N_2O_6$ 387.1556, found 387.1507.

Methyl-4-(1-benzyl-4-ethylcarboxylate-1*H*-imidazol-5-yl)-2-hydroxy-4-oxo-but-2enoate (4e). A mixture of methyl-4-(1-benzyl-4-ethylcarboxylate-1*H*-imidazol-5-yl)-4-ethoxy-2-oxo-but-3enoate, **3e**, (0.85 g, 2.2 mmol) and $FeCl_3.6H_2O$ (1.02 g, 3.7 mmol) in dichloroethane (20 mL) was stirred at reflux 10 h. The solvent was distilled off and the residue obtained was treated with 1N HCl (50 mL), stirred at RT for 1 h, extracted with EtOAc (4 x 20 mL), dried over anhydrous sodium sulfate and concentrated. The resulting brownish residue was purified by ion-exchange chromatography (DEAE sephadex anion exchange resin, CH_3CN/H_2O, 1:1) and crystallized from methanol. Yield 0.61 g (78 %), yellow oil; ^{1}H NMR ($CDCl_3$, 500 MHz): 1.40 (t, 3H, *J* = 7 Hz), 3.89 (s, 3H), 4.43 (q, 2H, *J* = 6.5 Hz), 5.42 (s, 2H), 7.10-7.34 (m, 6H), 7.66 (s,

1H). ^{13}C NMR ($CDCl_3$, 125 MHz): 14.1, 50.9, 53.1, 61.7, 105.3, 127.3, 127.6, 128.5, 128.7, 129.0, 135.0, 140.9, 162.2, 163.8, 163.8 and 186.6. HRMS: $(M + H)^+$ calcd for $C_{18}H_{19}N_2O_6$ 359.1243, found 359.1208.

Hydrolysis of Enol Ester 4c.

4-(1,9-benzyl-6-9-dihydro-6-oxo-1H-purine-8-yl)-2-hydroxy-4-oxobut-2-enoic acid. To a stirred solution of methyl 4-(1,9-benzyl-6-9-dihydro-6-oxo-1H-purine-8-yl)-2-hydroxy-4-oxobut-2-enoate **4c** (0.11 g, 0.24 mmol) in MeOH (10 mL) at 0 °C was added a solution of 1N NaOH (2 mL) and reaction mixture allowed to stir at 0 °C for 30 min and further stirred at ambient temperature for 1 h. The reaction mixture was neutralized with 1 N HCl when a solid separated out which was filtered dried and triturated with diethyl ether to give yellow solid. Yield 91 mg (86 %), mp 167 decomposes. ^{1}H NMR (DMSO, 500 MHz): 5.27 (s, 2H), 5.80 (s, 2H), 7.25 (s, 1H), 7.27-7.37 (m, 10H), 8.77 (s,1H). ^{13} C NMR ($CDCl_3$, 125 MHz): δ 47.9, 49.3, 101.3, 123.9, 127.4, 127.4, 127.5, 127.5, 128.1, 128.2,128.6, 128.9, 129.1, 137.1, 137.2, 150.4, 151.5, 156.4, 163.8, 175.9, 179.5. FAB-HRMS: $[M + H]^+$ calcd for $C_{23}H_{19}N_4O_5$ 431.1355, found 431.1374.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5.313
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3.944
3.931
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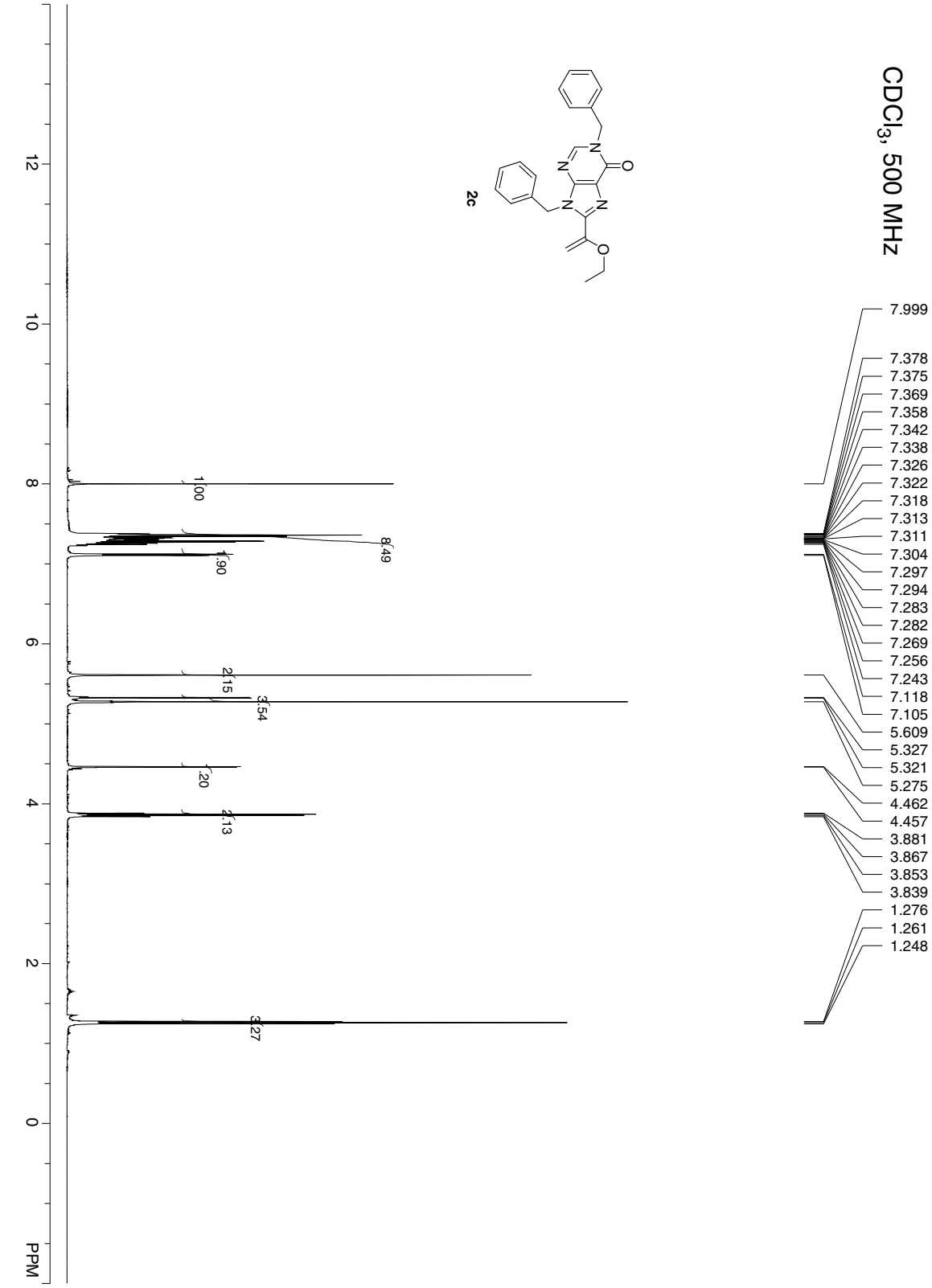
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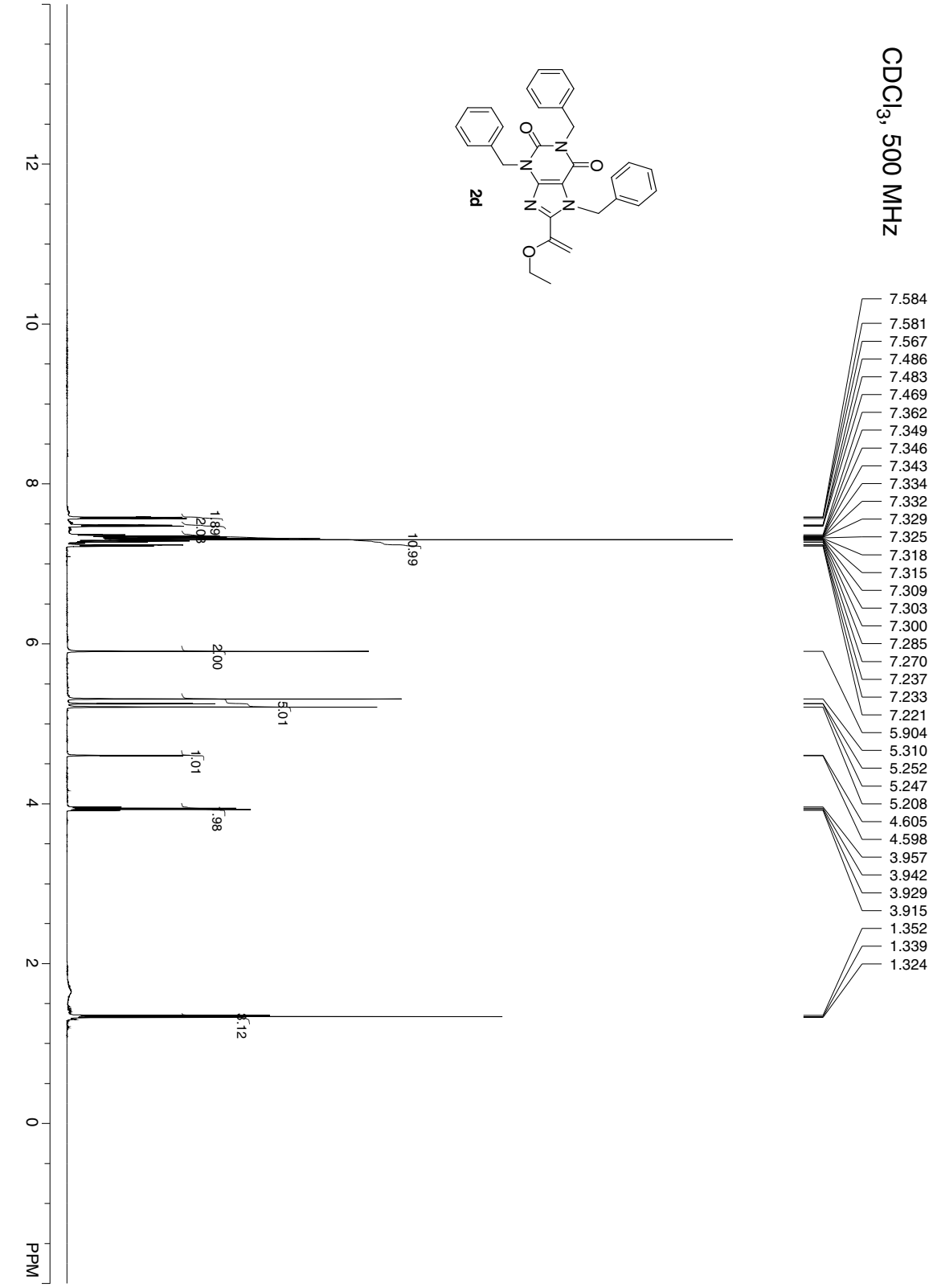
CDCl3, 500 MHz
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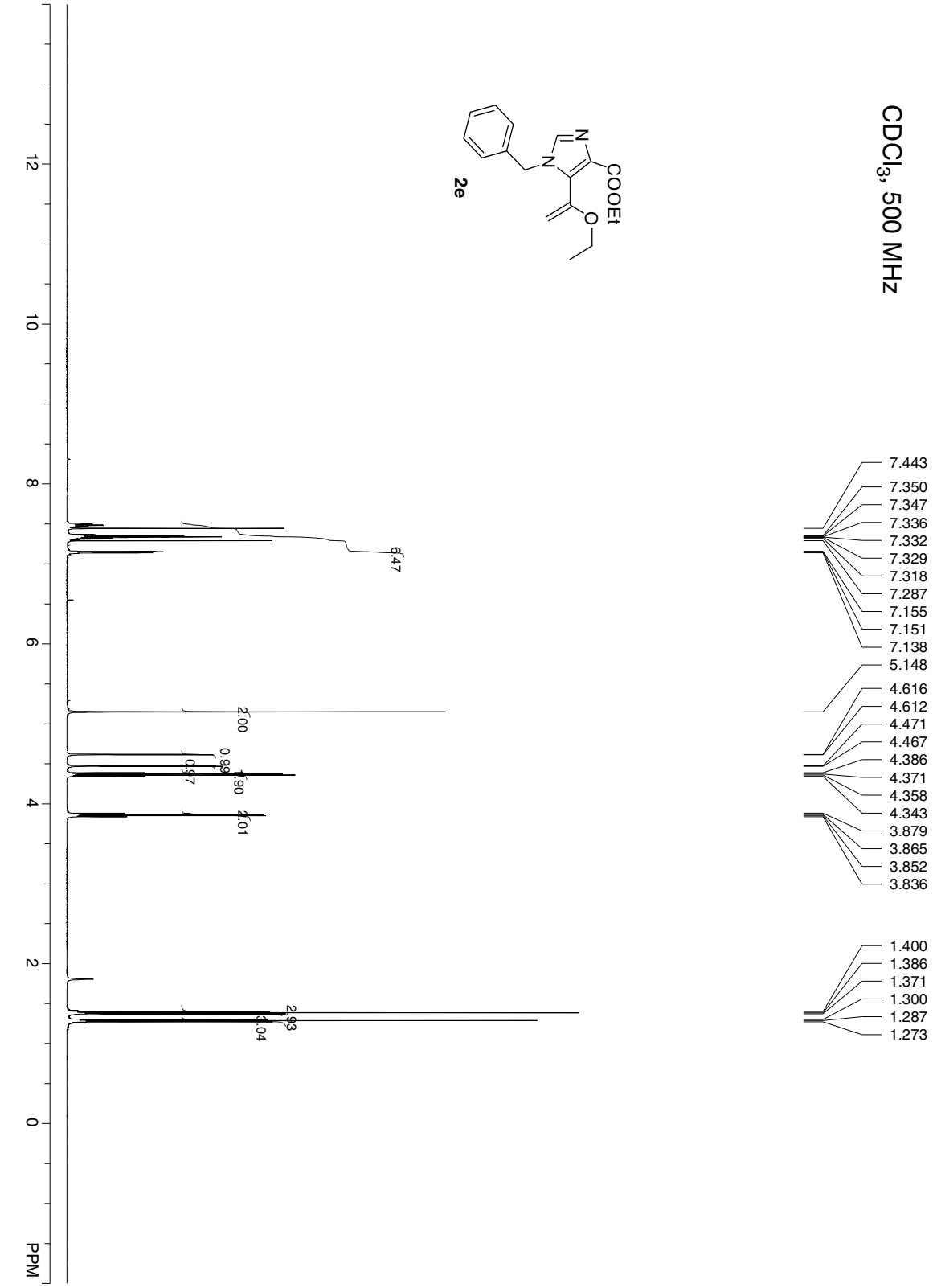
7.486
7.483
7.469
7.362
7.349
7.346
7.343
7.334
7.332
7.329
7.325
7.318
7.315
7.309
7.303
7.300
7.285
7.270
7.237
7.233
7.221
5.904
5.310
5.252
5.247
5.208
4.605
4.598
3.957
3.942
3.929
3.915
1.352
1.339
1.324
1.89
2.03
10.99
2.00
5.01
1.01
1.98
9.12
12
10
8
6
4
2
0
PPM


CDCl3, 500 MHz
2e
COOEt
7.443
7.350
7.347
7.336
7.332
7.329
7.318
7.287
7.155
7.151
7.138
5.148
4.616
4.612
4.471
4.467
4.386
4.371
4.358
4.343
3.879
3.865
3.852
3.836
1.400
1.386
1.371
1.300
1.287
1.273
6.47
2.00
0.99
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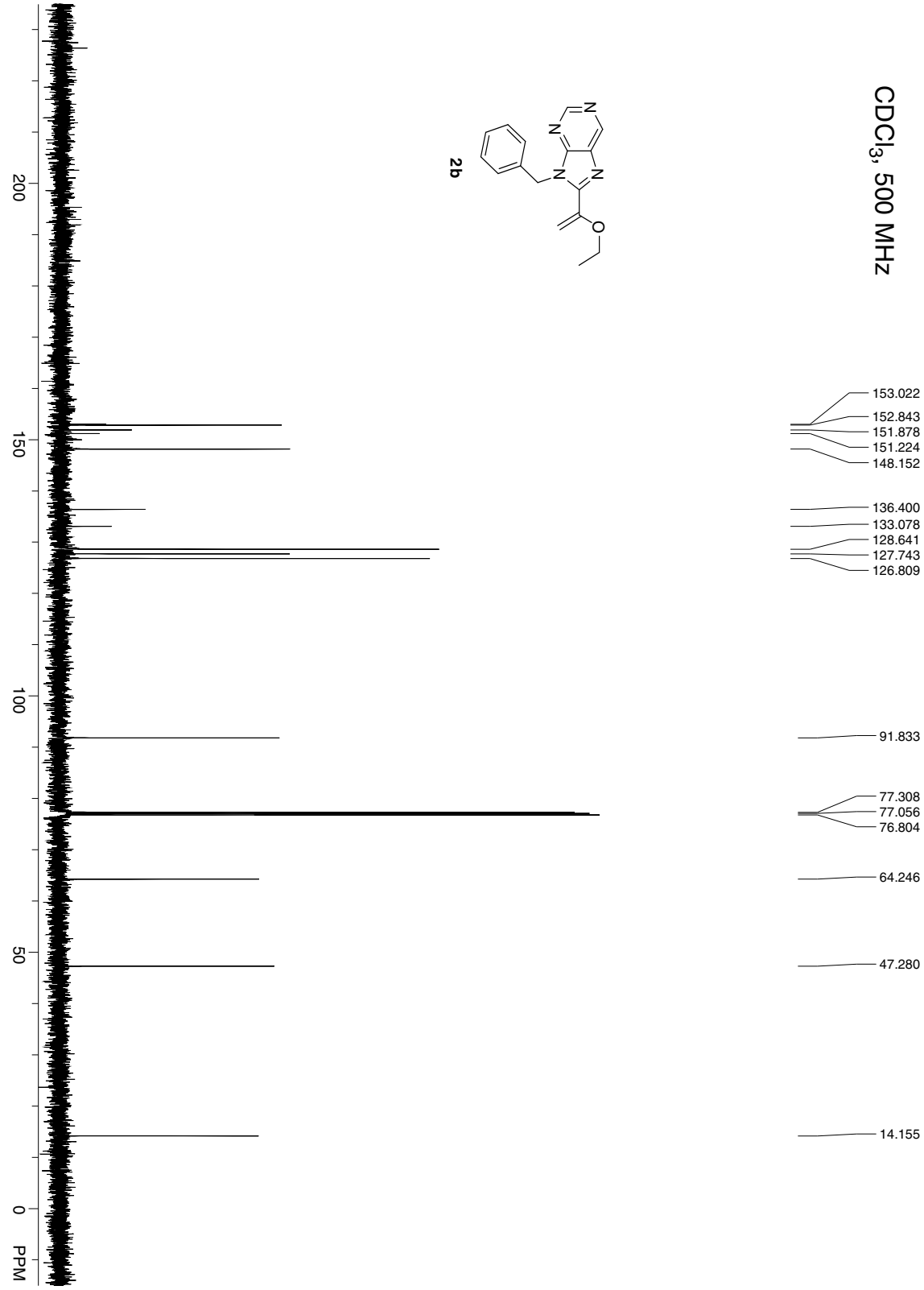
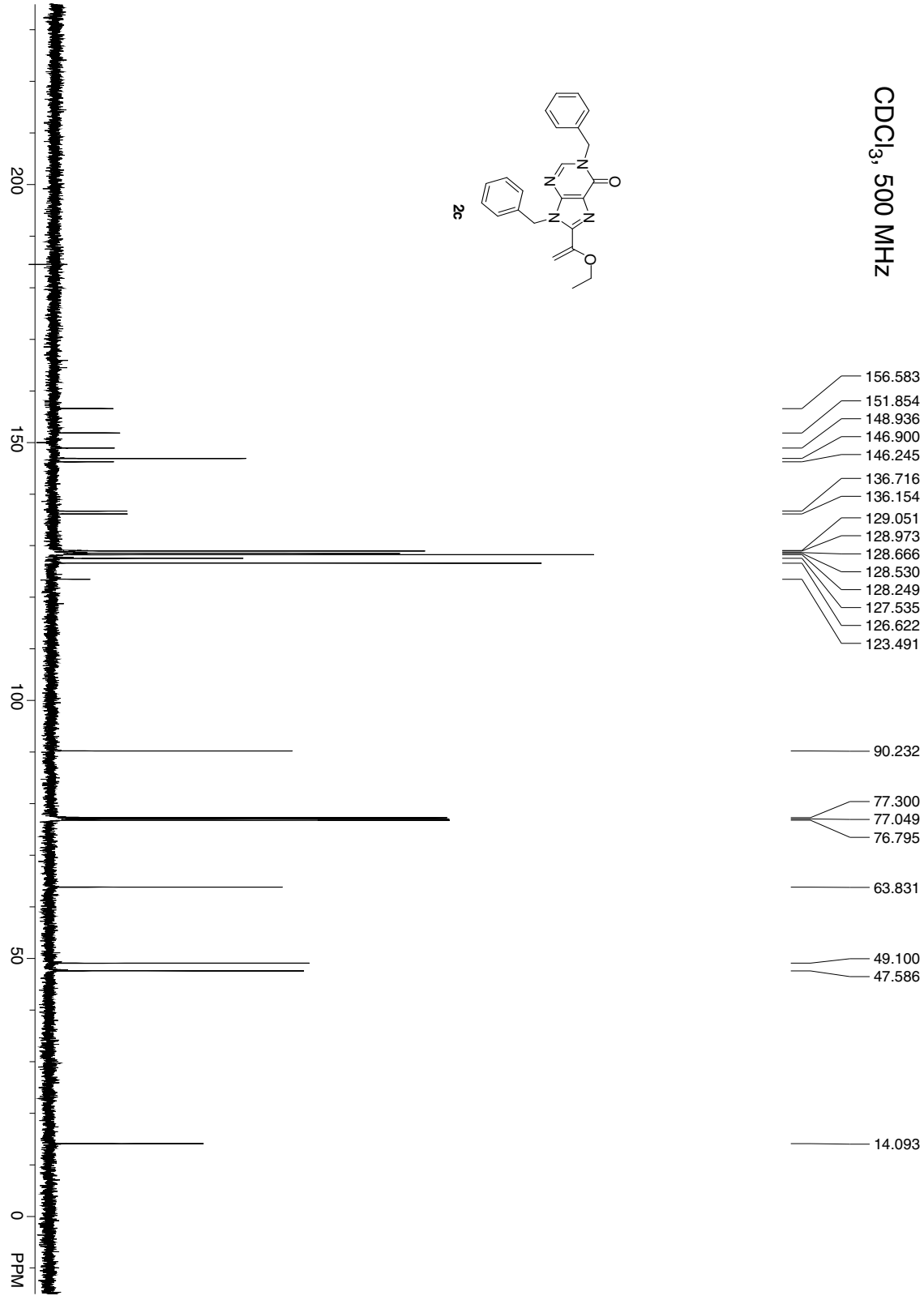
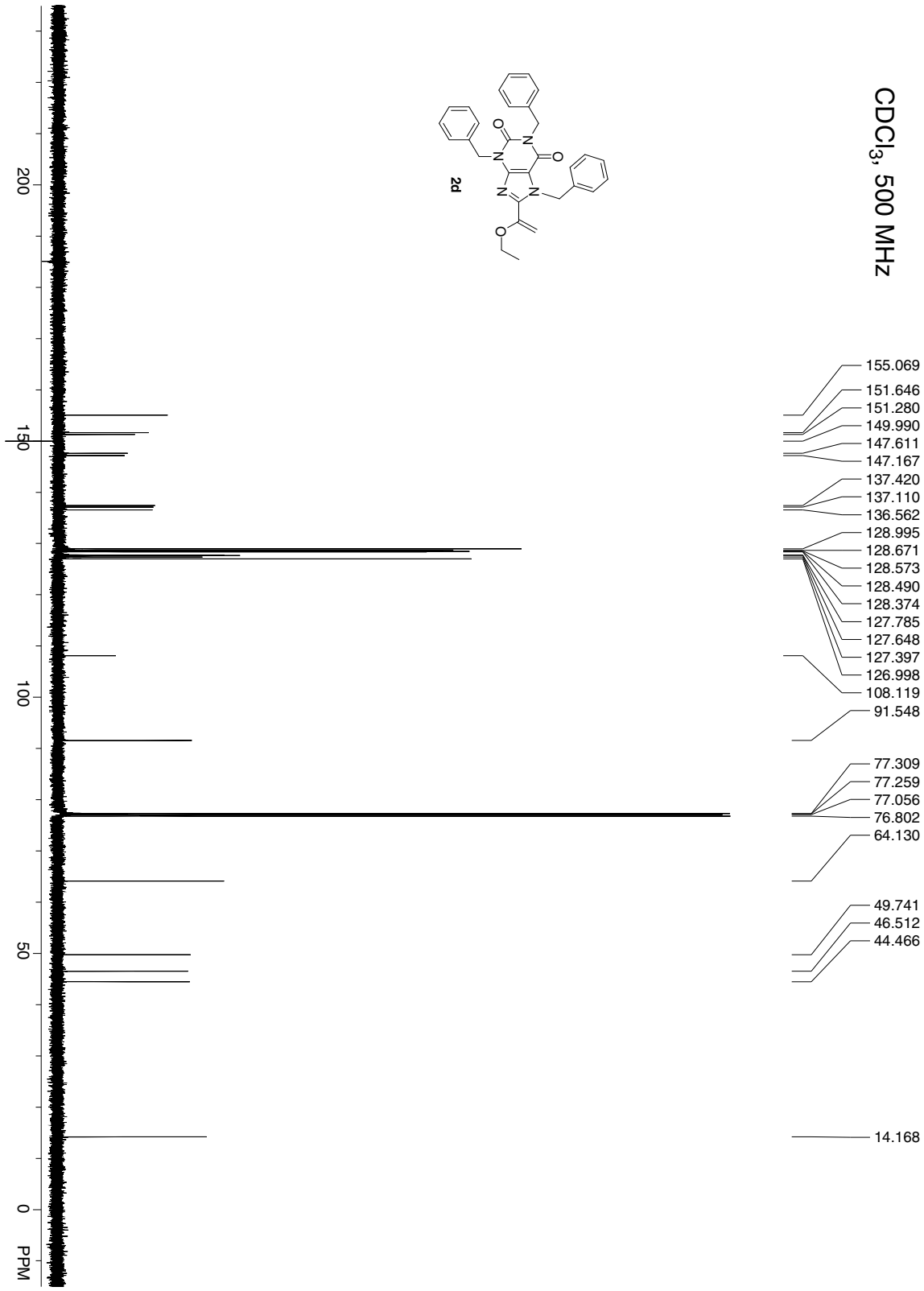
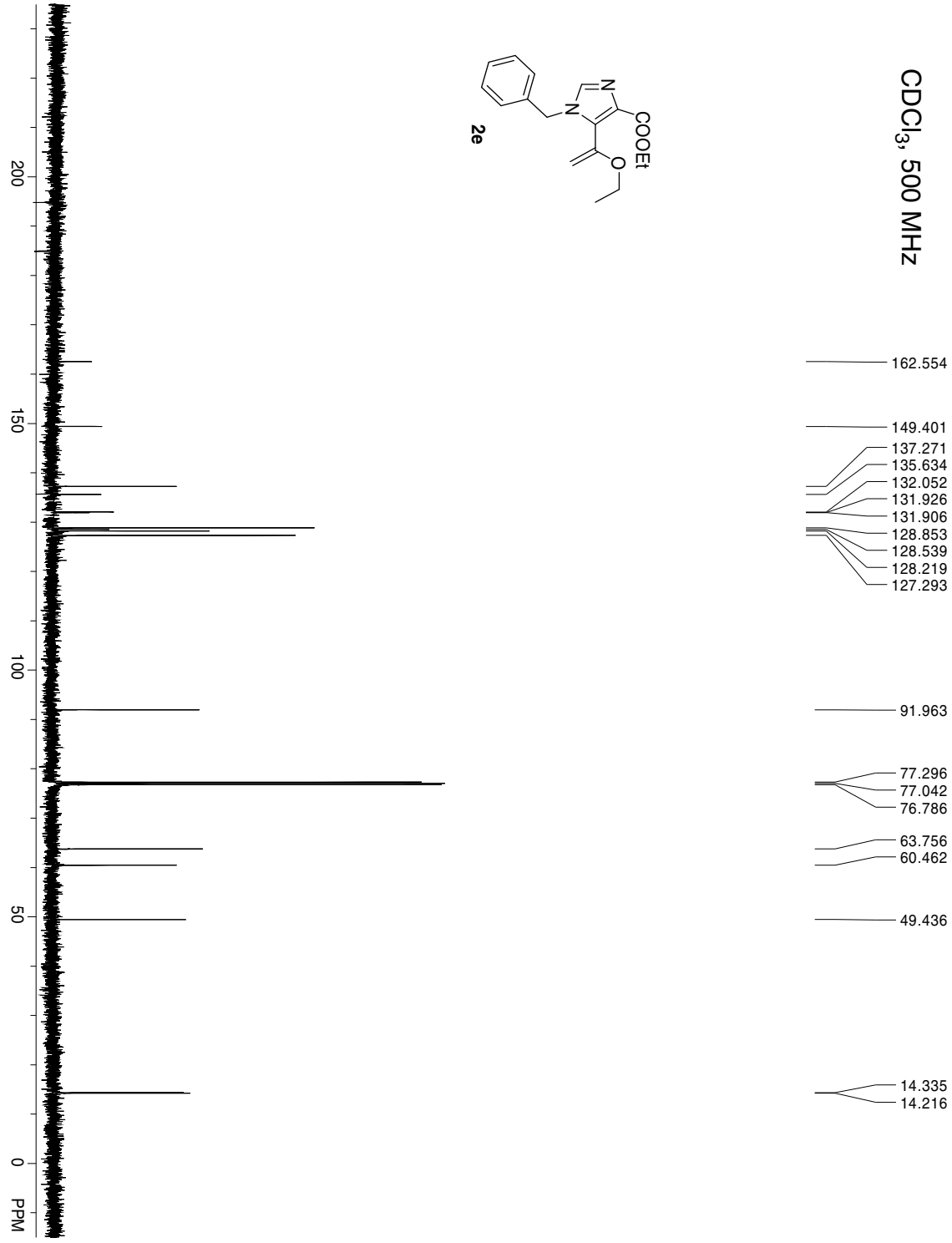
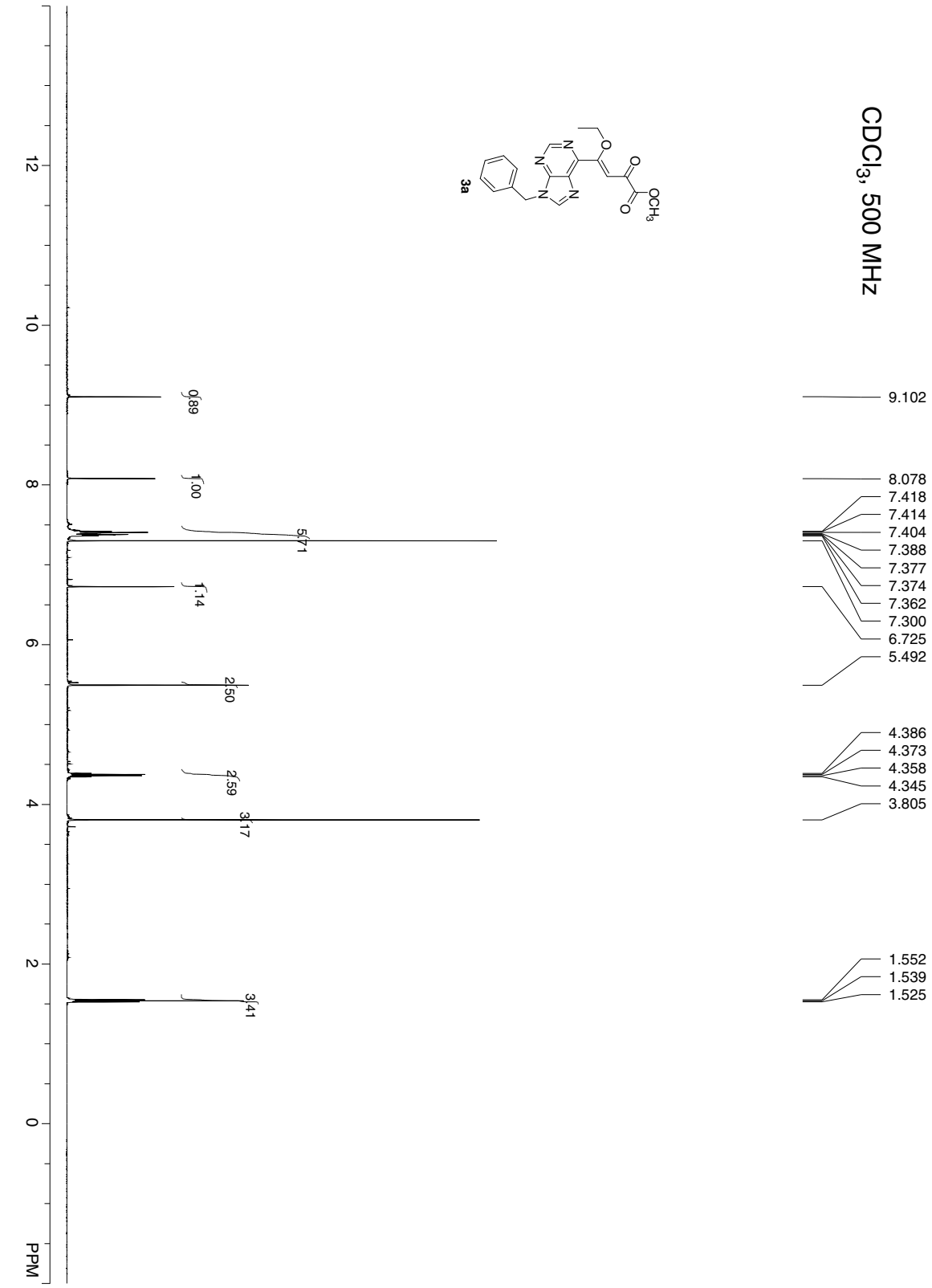
1.90
2.01
2.93
3.04
12
10
8
6
4
2
0
PPM

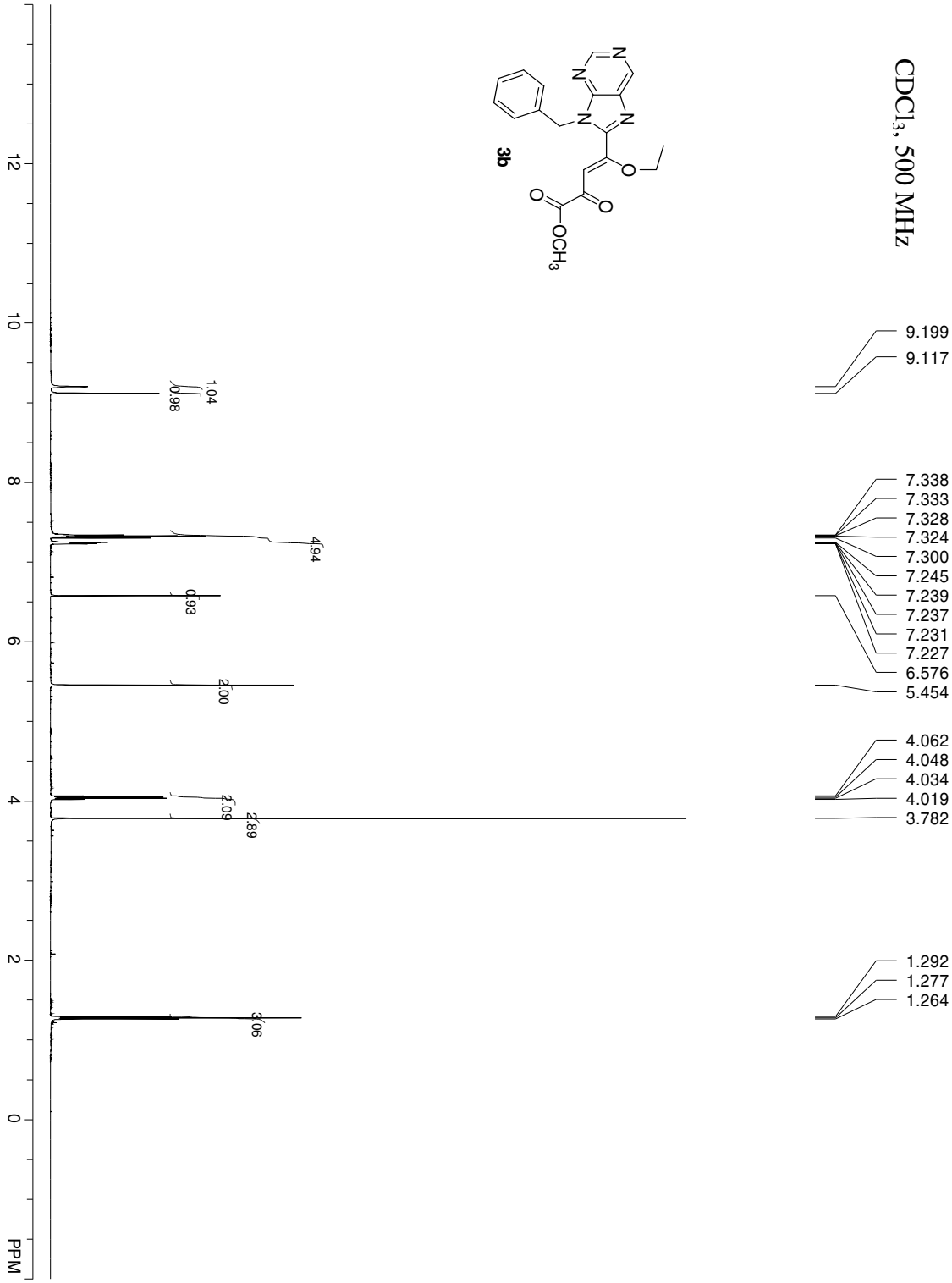

CDCl3, 500 MHz
2b
153.022
152.843
151.878
151.224
148.152
136.400
133.078
128.641
127.743
126.809
91.833
77.308
77.056
76.804
64.246
47.280
14.155
200
150
100
50
0
PPM

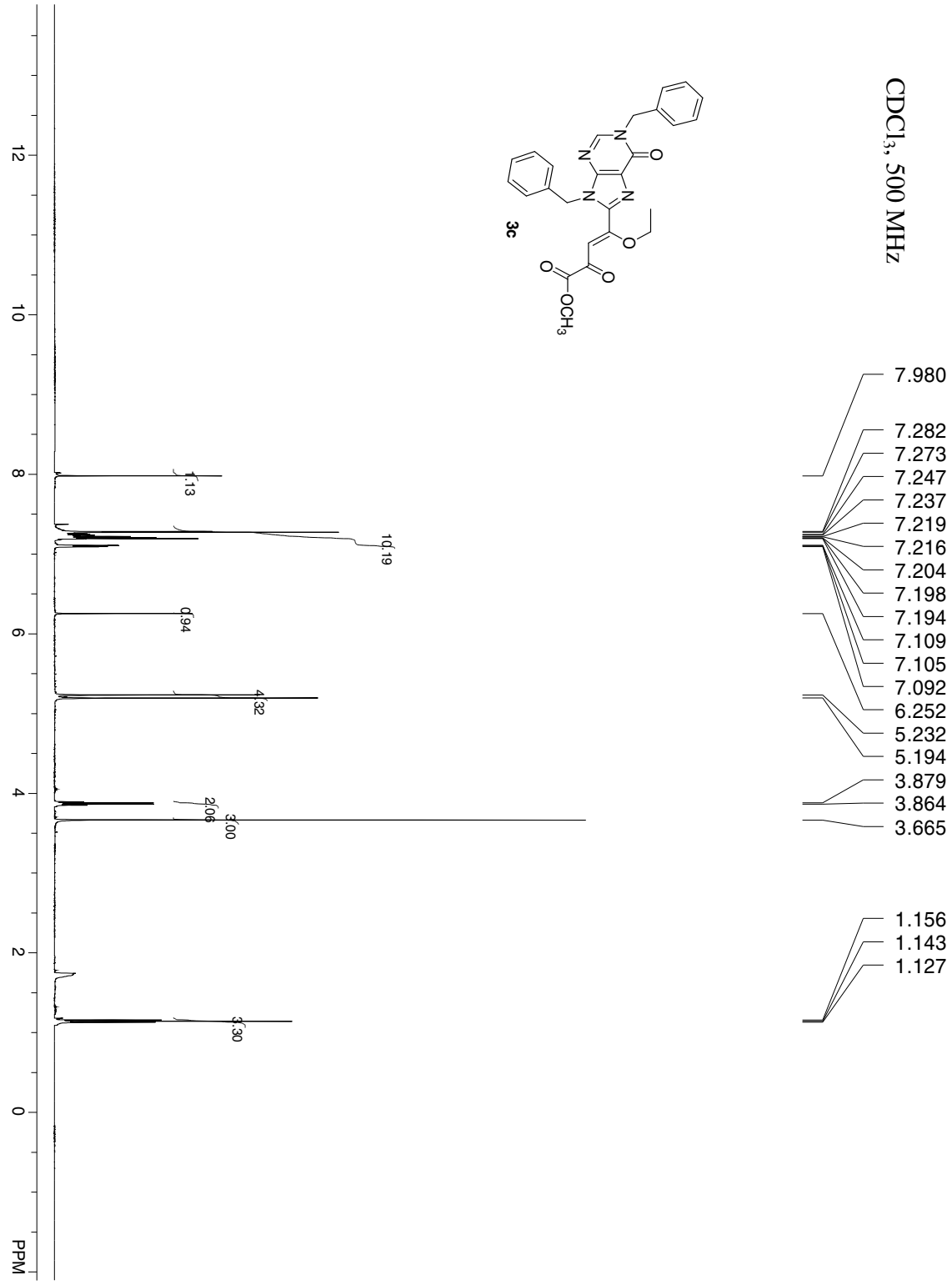

CDCl3, 500 MHz
2c
156.583
151.854
148.936
146.900
146.245
136.716
136.154
129.051
128.973
128.666
128.530
128.249
127.535
126.622
123.491
90.232
77.300
77.049
76.795
63.831
49.100
47.586
14.093
200
150
100
50
0
PPM


CDCl3, 500 MHz
2d
155.069
151.646
151.280
149.990
147.611
147.167
137.420
137.110
136.562
128.995
128.671
128.573
128.490
128.374
127.785
127.648
127.397
126.998
108.119
91.548
77.309
77.259
77.056
76.802
64.130
49.741
46.512
44.466
14.168
200
150
100
50
0
PPM

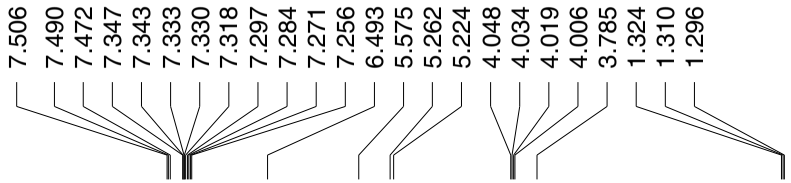

2e
COOEt
CDCl3, 500 MHz
162.554
149.401
137.271
135.634
132.052
131.926
131.906
128.853
128.539
128.219
127.293
91.963
77.296
77.042
76.786
63.756
60.462
49.436
14.335
14.216
200
150
100
50
0
PPM

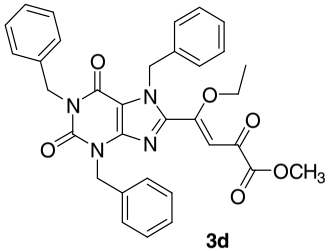

CDCl3, 500 MHz
3a
9.102
8.078
7.418
7.414
7.404
7.388
7.377
7.374
7.362
7.300
6.725
5.492
4.386
4.373
4.358
4.345
3.805
1.552
1.539
1.525
0.89
1.00
5.71
1.14
2.50
2.59
3.17
3.41
PPM


CDCl3, 500 MHz
3b
9.199
9.117
7.338
7.333
7.328
7.324
7.300
7.245
7.239
7.237
7.231
7.227
6.576
5.454
4.062
4.048
4.034
4.019
3.782
1.292
1.277
1.264
1.04
0.98
4.94
0.93
2.00
2.09
2.89
3.06
PPM

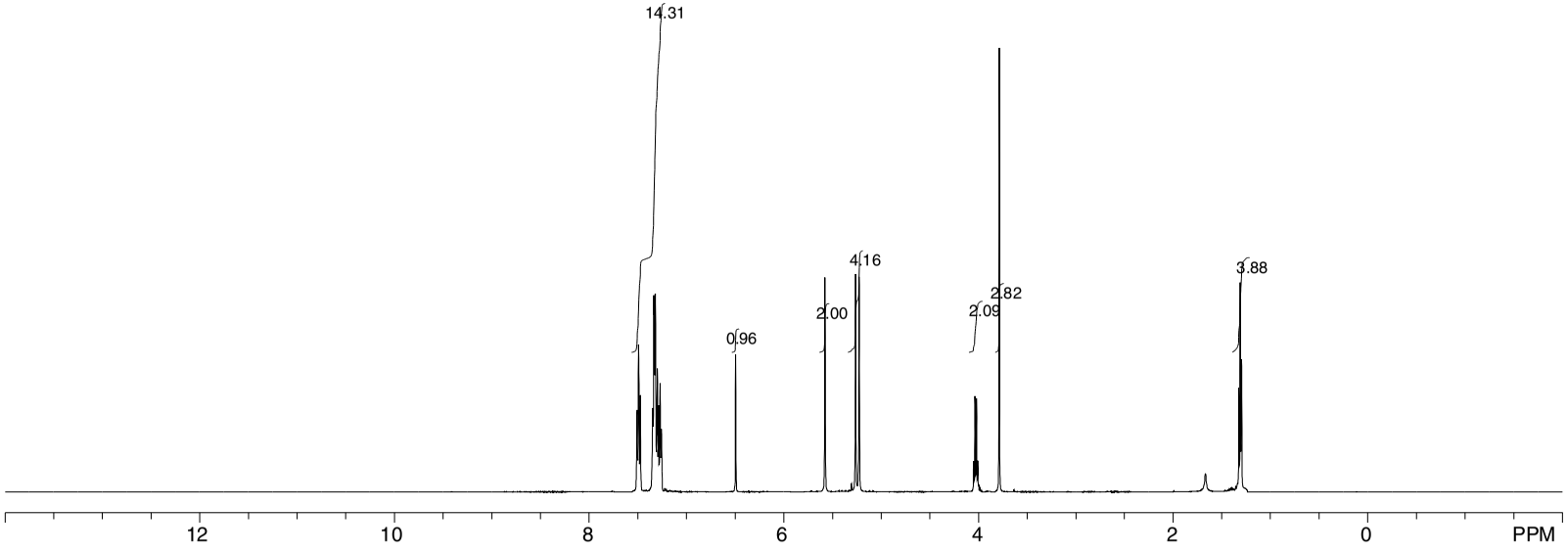

CDCl3, 500 MHz
7.980
7.282
7.273
7.247
7.237
7.219
7.216
7.204
7.198
7.194
7.109
7.105
7.092
6.252
5.232
5.194
3.879
3.864
3.665
1.156
1.143
1.127
3c
1.13
10.19
0.94
4.32
2.06
3.00
3.30
PPM

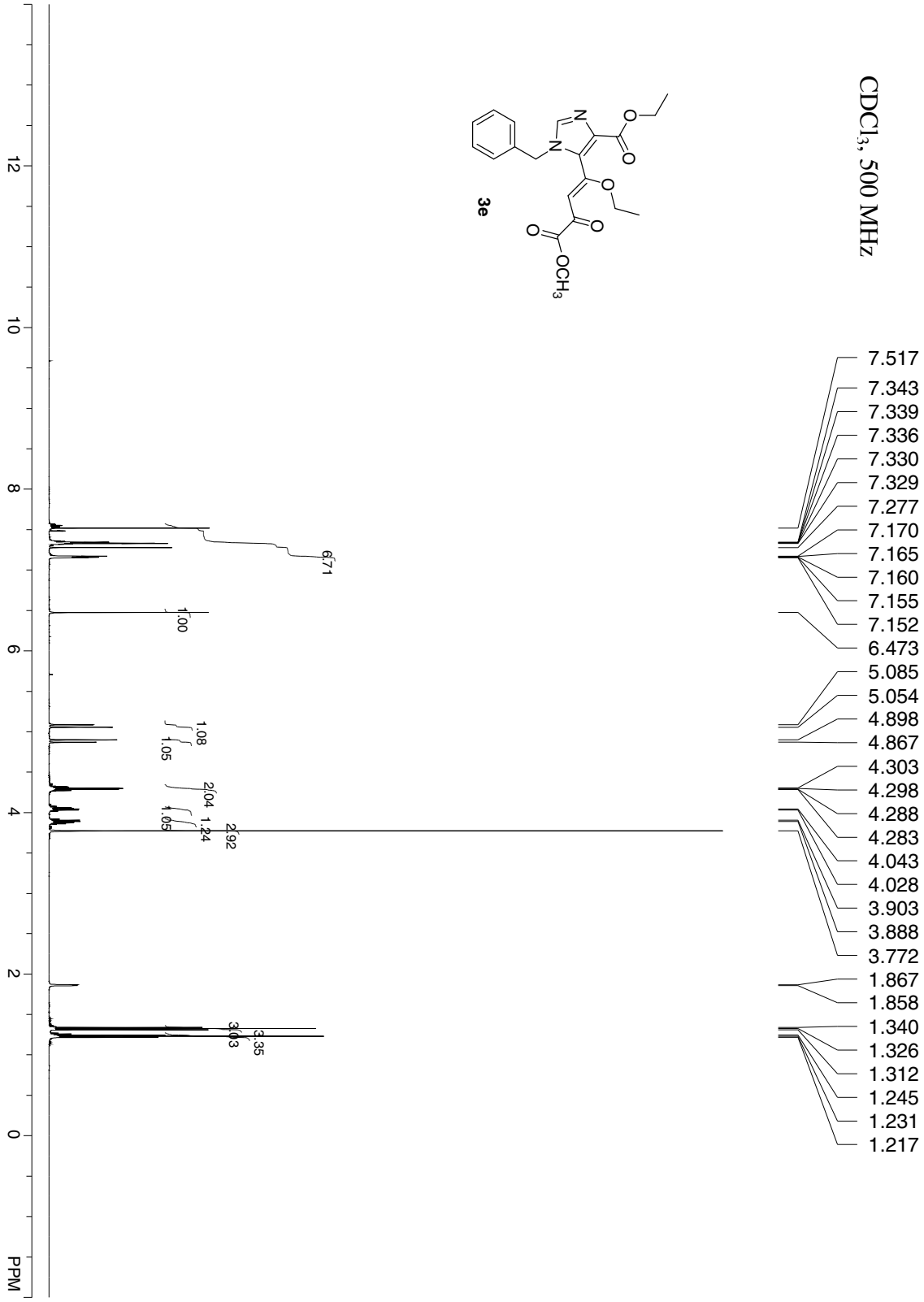
$CDCl_3$, 500 MHz

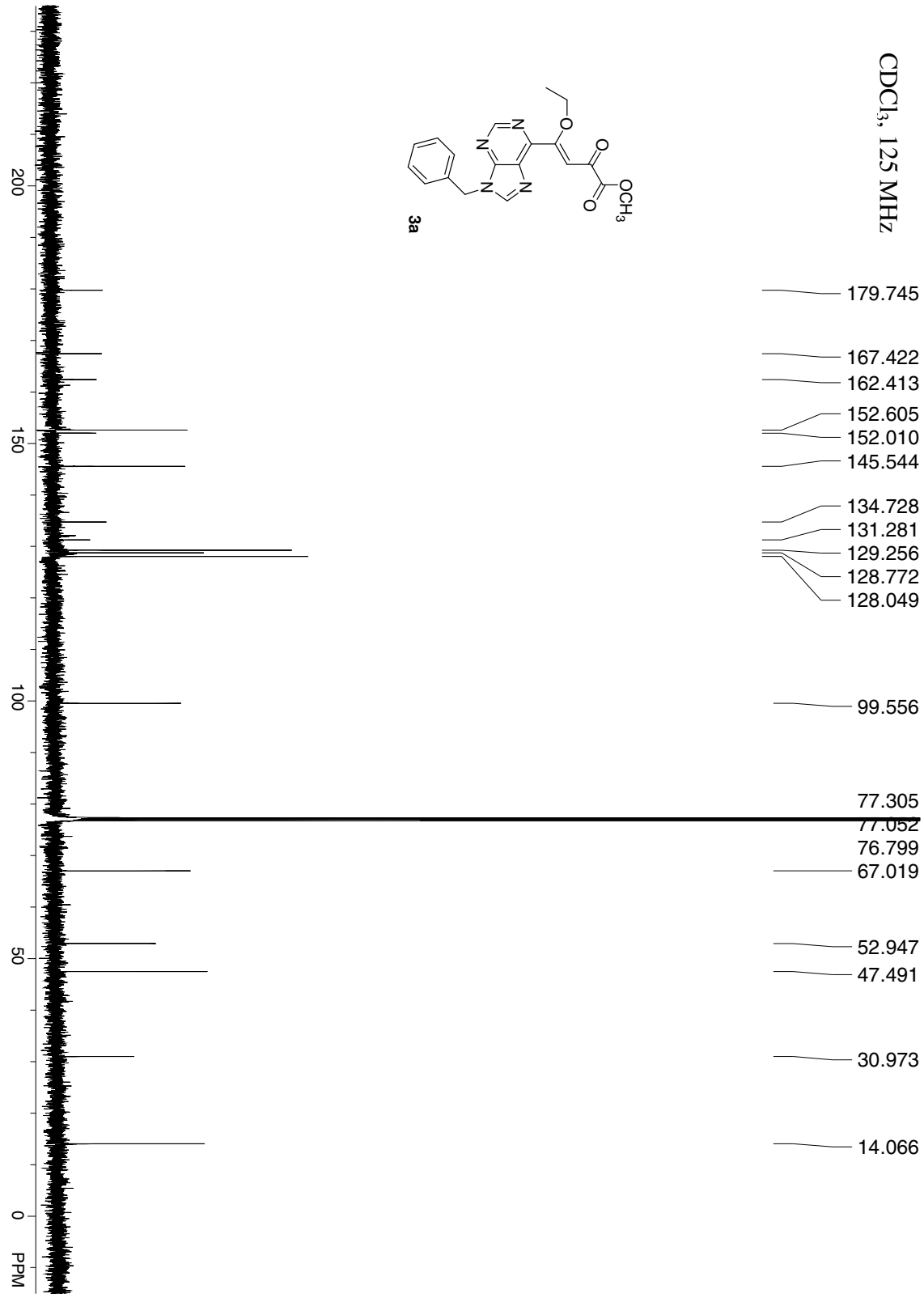


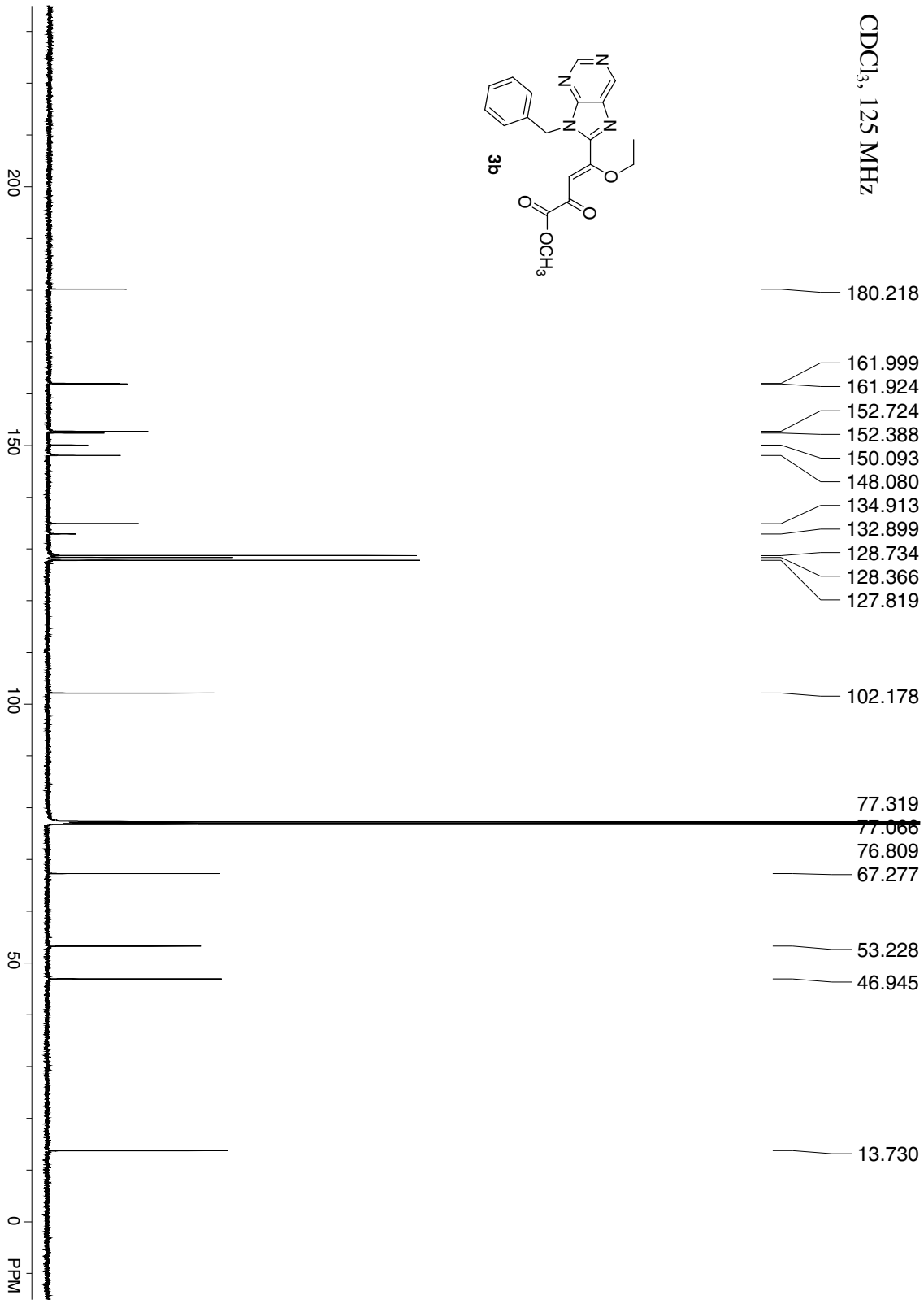


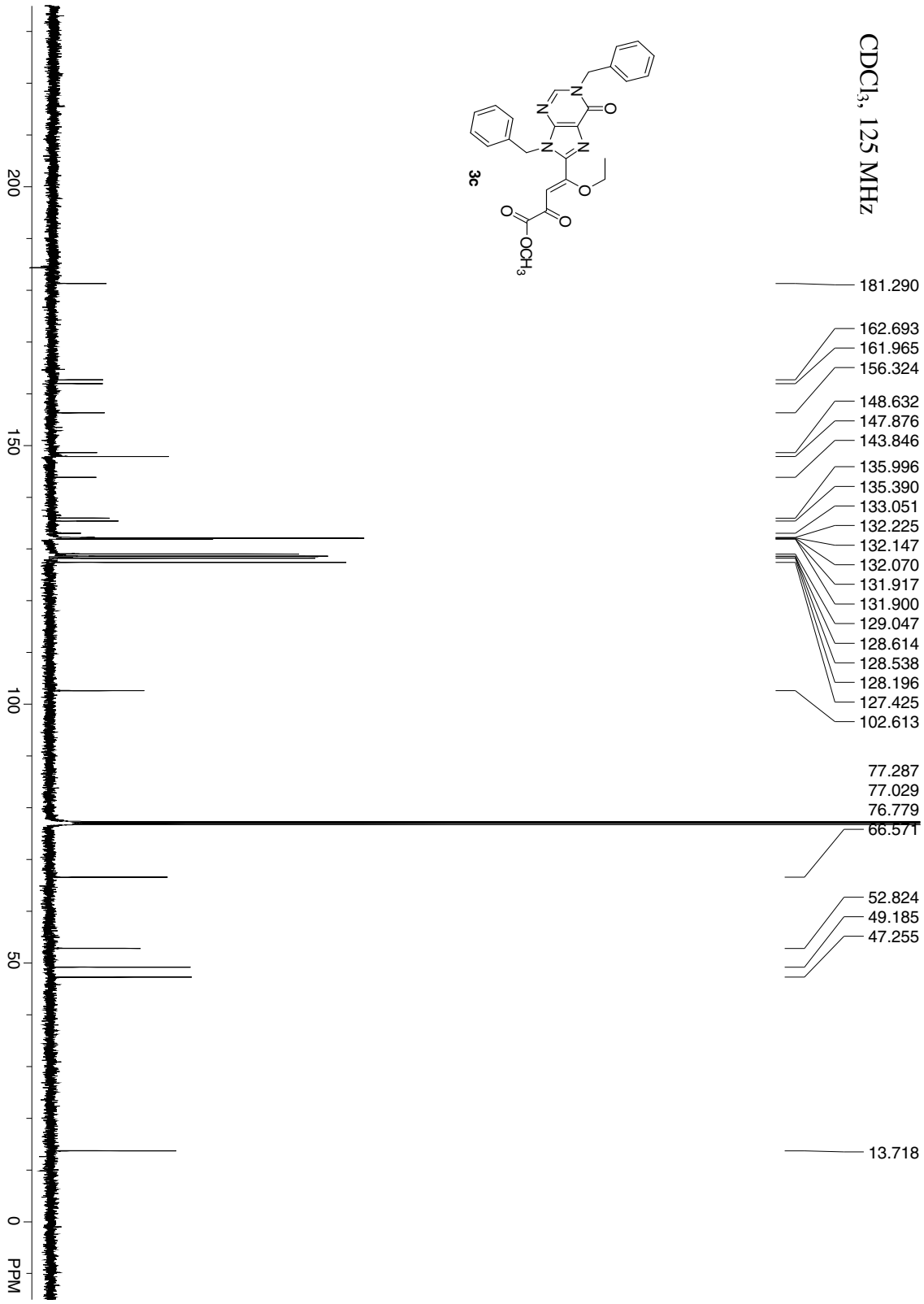
3d

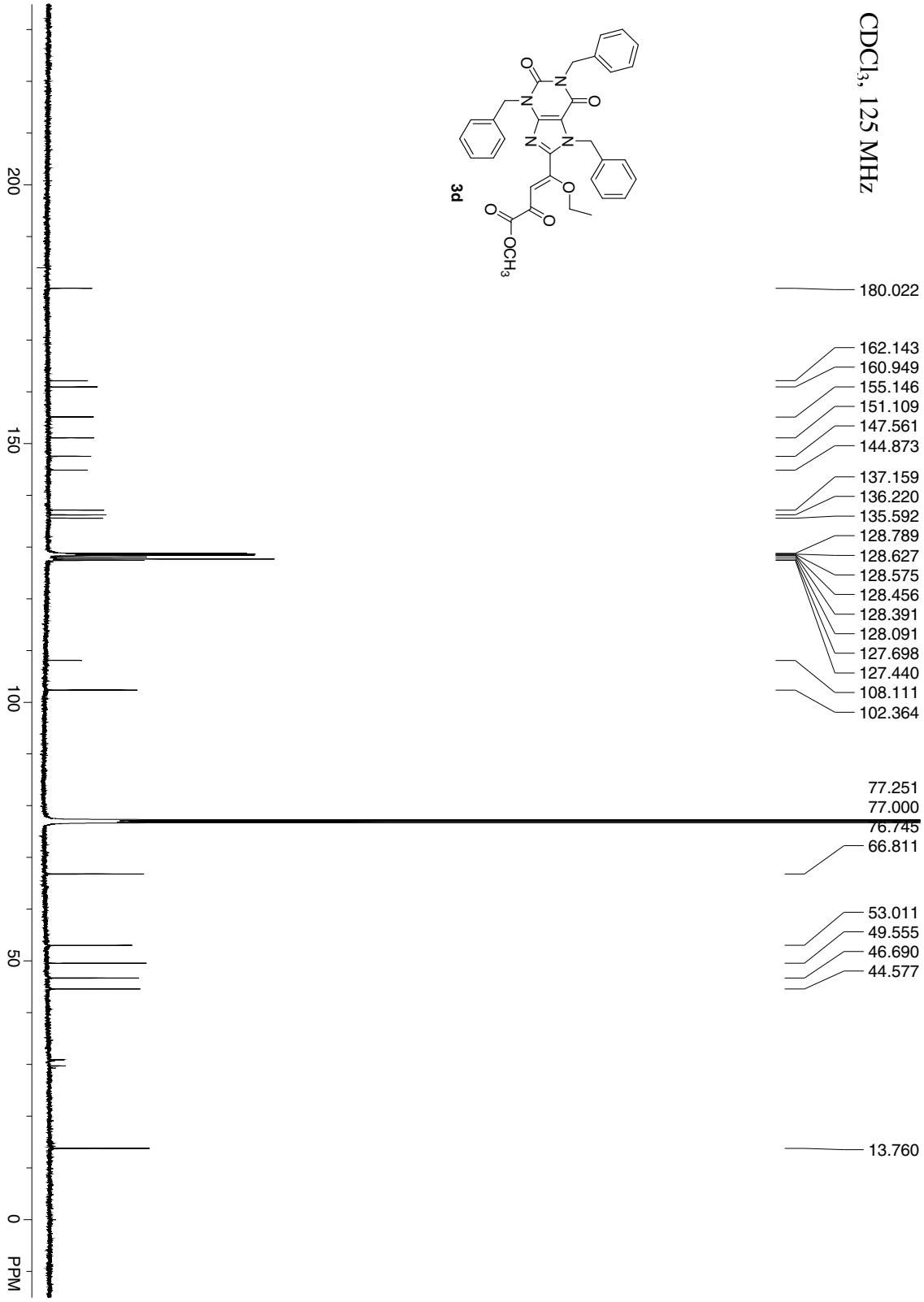


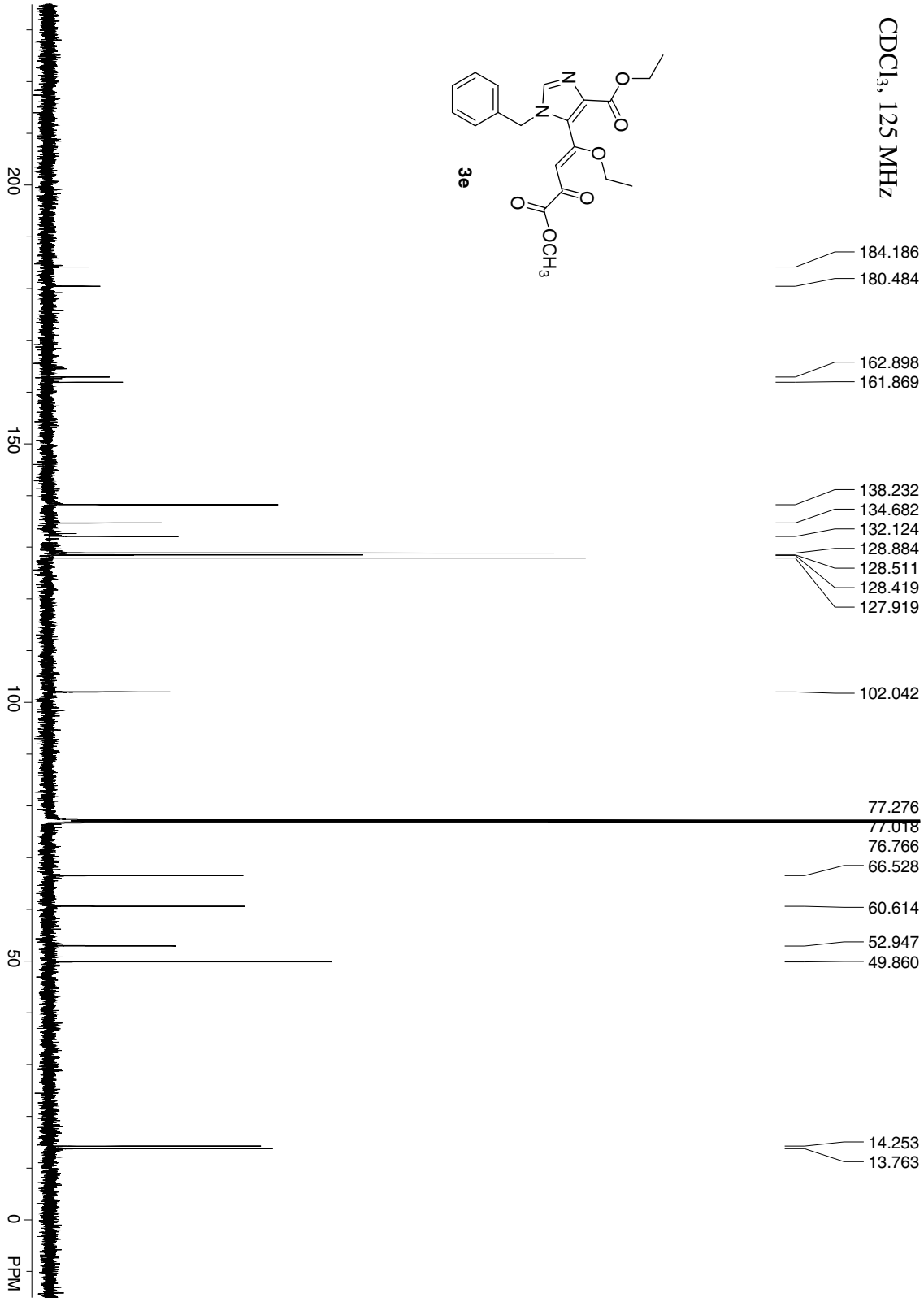

CDCl3, 500 MHz
3e
7.517
7.343
7.339
7.336
7.330
7.329
7.277
7.170
7.165
7.160
7.155
7.152
6.473
5.085
5.054
4.898
4.867
4.303
4.298
4.288
4.283
4.043
4.028
3.903
3.888
3.772
1.867
1.858
1.340
1.326
1.312
1.245
1.231
1.217
6.71
1.00
1.08
1.05
2.04
1.24
1.05
2.92
3.03
3.35
12
10
8
6
4
2
0
PPM

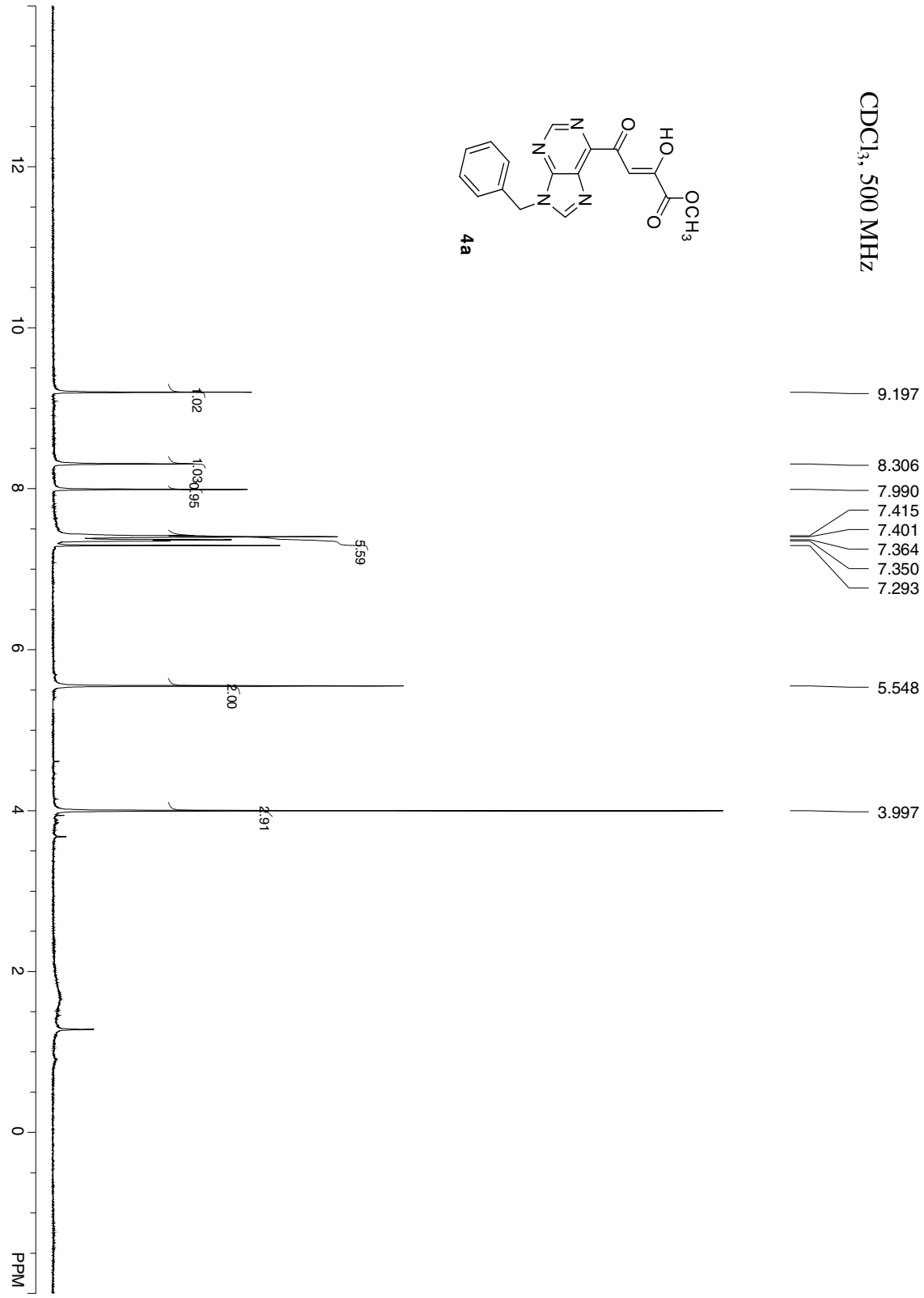

CDCl3, 125 MHz
3a
179.745
167.422
162.413
152.605
152.010
145.544
134.728
131.281
129.256
128.772
128.049
99.556
77.305
77.052
76.799
67.019
52.947
47.491
30.973
14.066
200
150
100
50
0
PPM

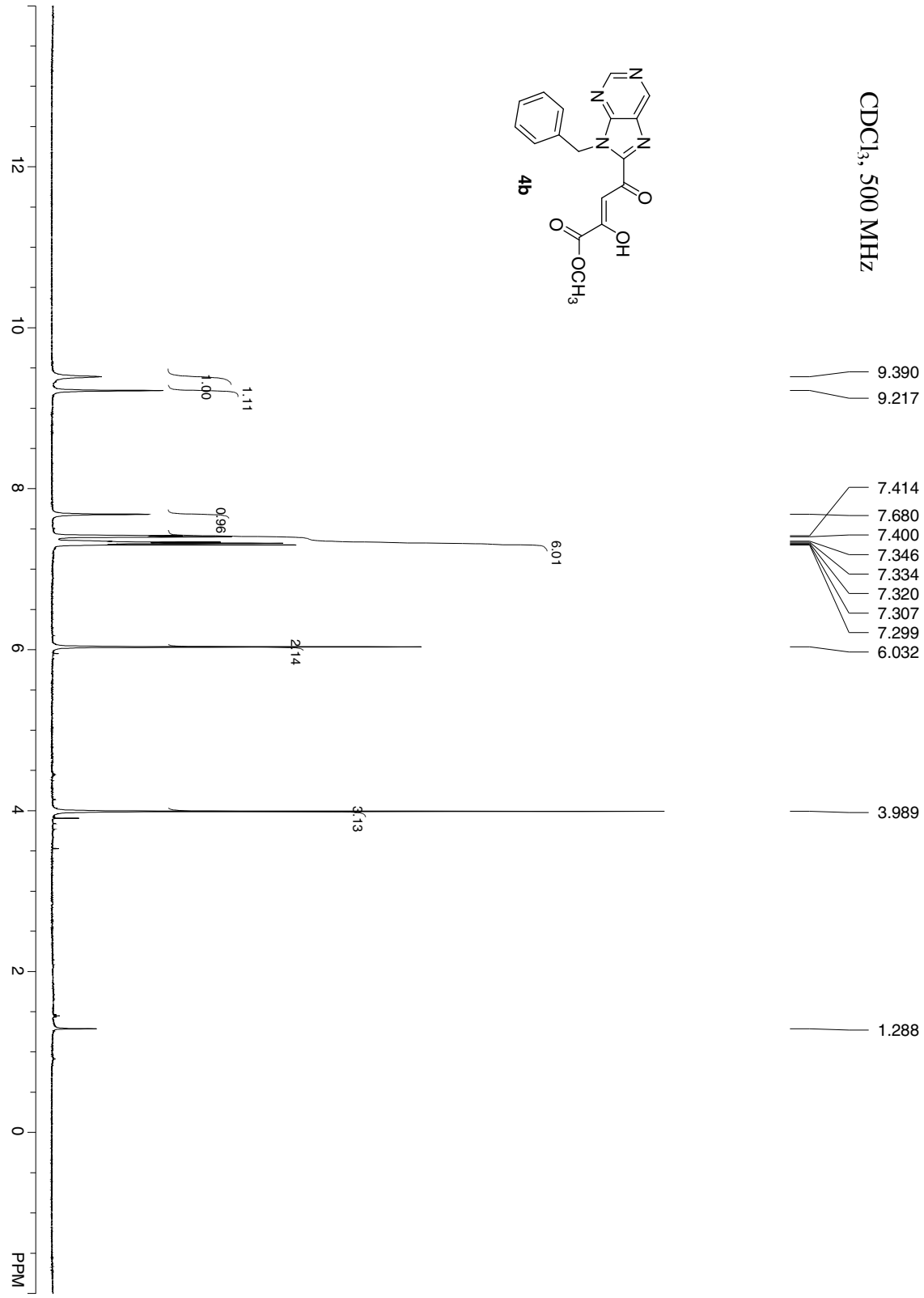

CDCl3, 125 MHz
3b
180.218
161.999
161.924
152.724
152.388
150.093
148.080
134.913
132.899
128.734
128.366
127.819
102.178
77.319
77.066
76.809
67.277
53.228
46.945
13.730
200
150
100
50
0
PPM

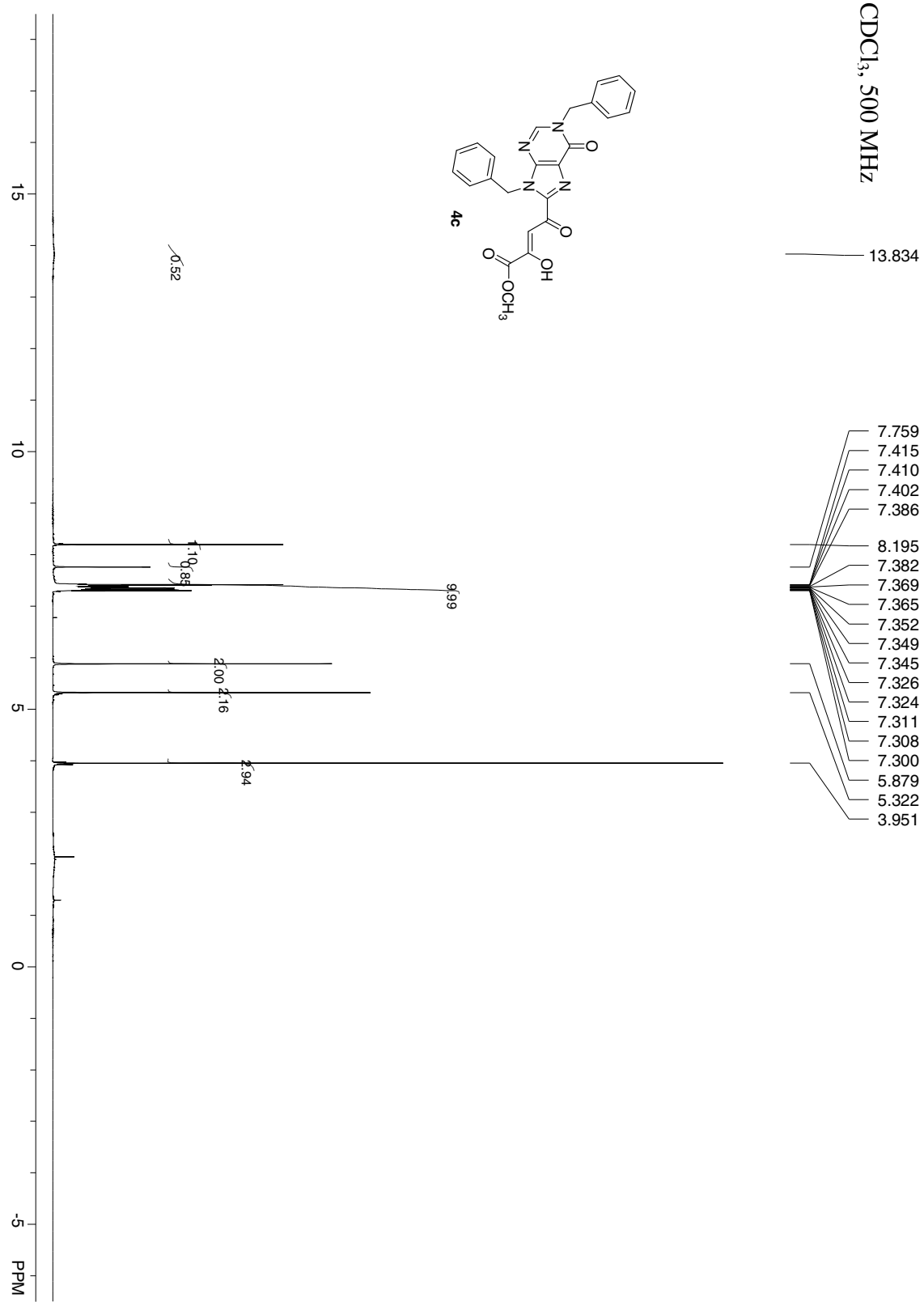

CDCl3, 125 MHz
3c
181.290
162.693
161.965
156.324
148.632
147.876
143.846
135.996
135.390
133.051
132.225
132.147
132.070
131.917
131.900
129.047
128.614
128.538
128.196
127.425
102.613
77.287
77.029
76.779
66.571
52.824
49.185
47.255
13.718
200
150
100
50
0
PPM

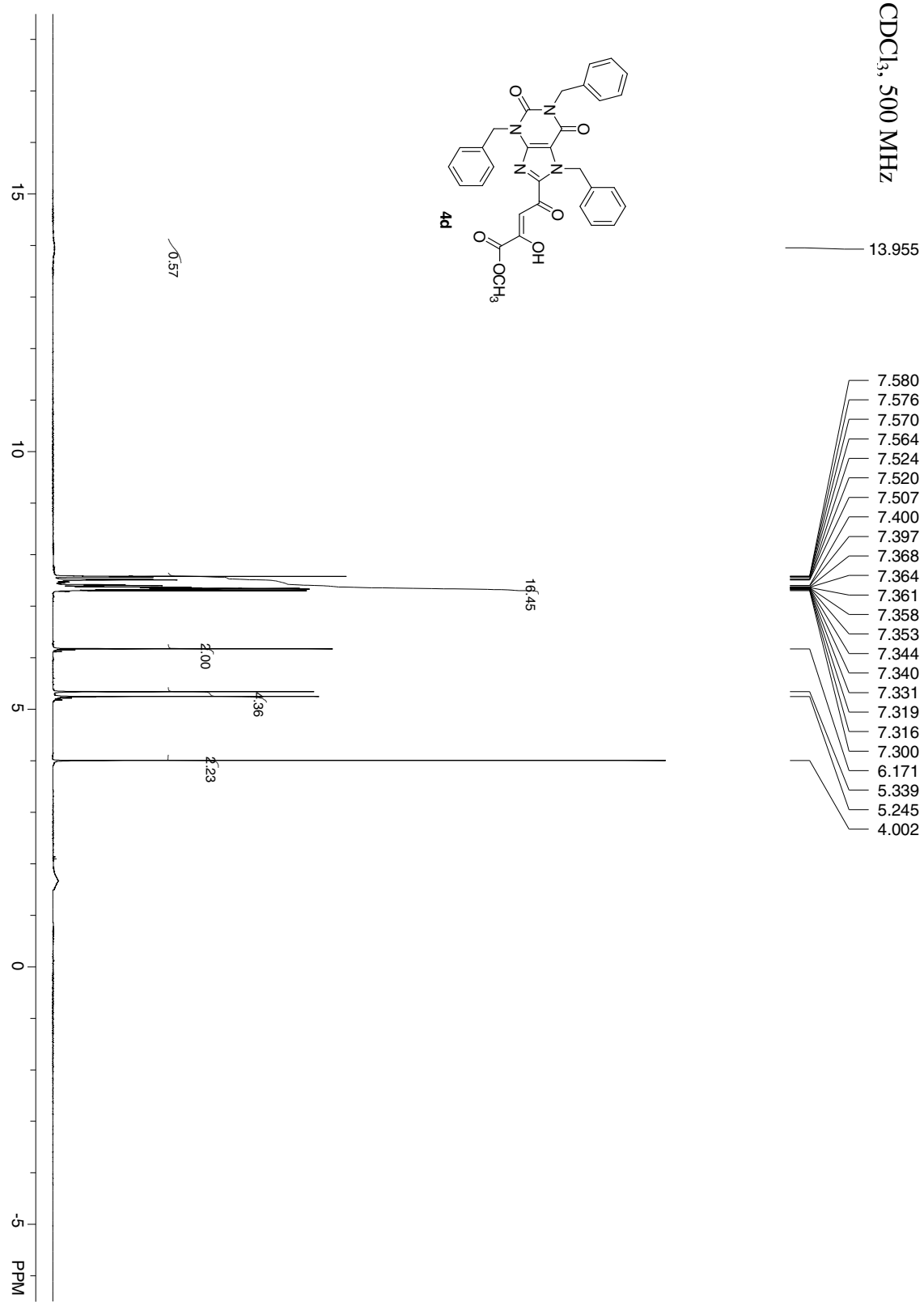

CDCl3, 125 MHz
3d
180.022
162.143
160.949
155.146
151.109
147.561
144.873
137.159
136.220
135.592
128.789
128.627
128.575
128.456
128.391
128.091
127.698
127.440
108.111
102.364
77.251
77.000
76.745
66.811
53.011
49.555
46.690
44.577
13.760
200
150
100
50
0
PPM

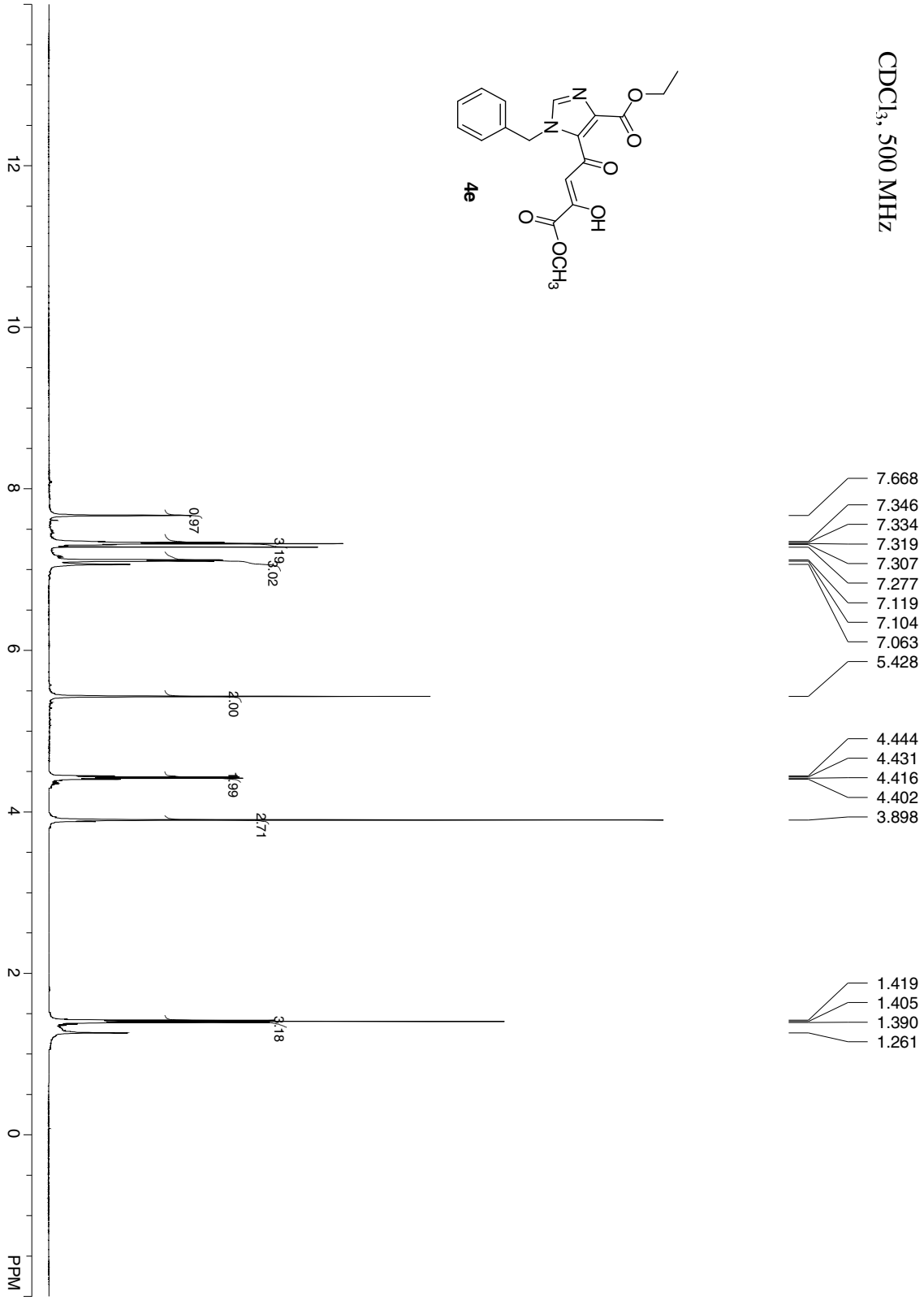

CDCl3, 125 MHz
3e
184.186
180.484
162.898
161.869
138.232
134.682
132.124
128.884
128.511
128.419
127.919
102.042
77.276
77.018
76.766
66.528
60.614
52.947
49.860
14.253
13.763
200
150
100
50
0
PPM

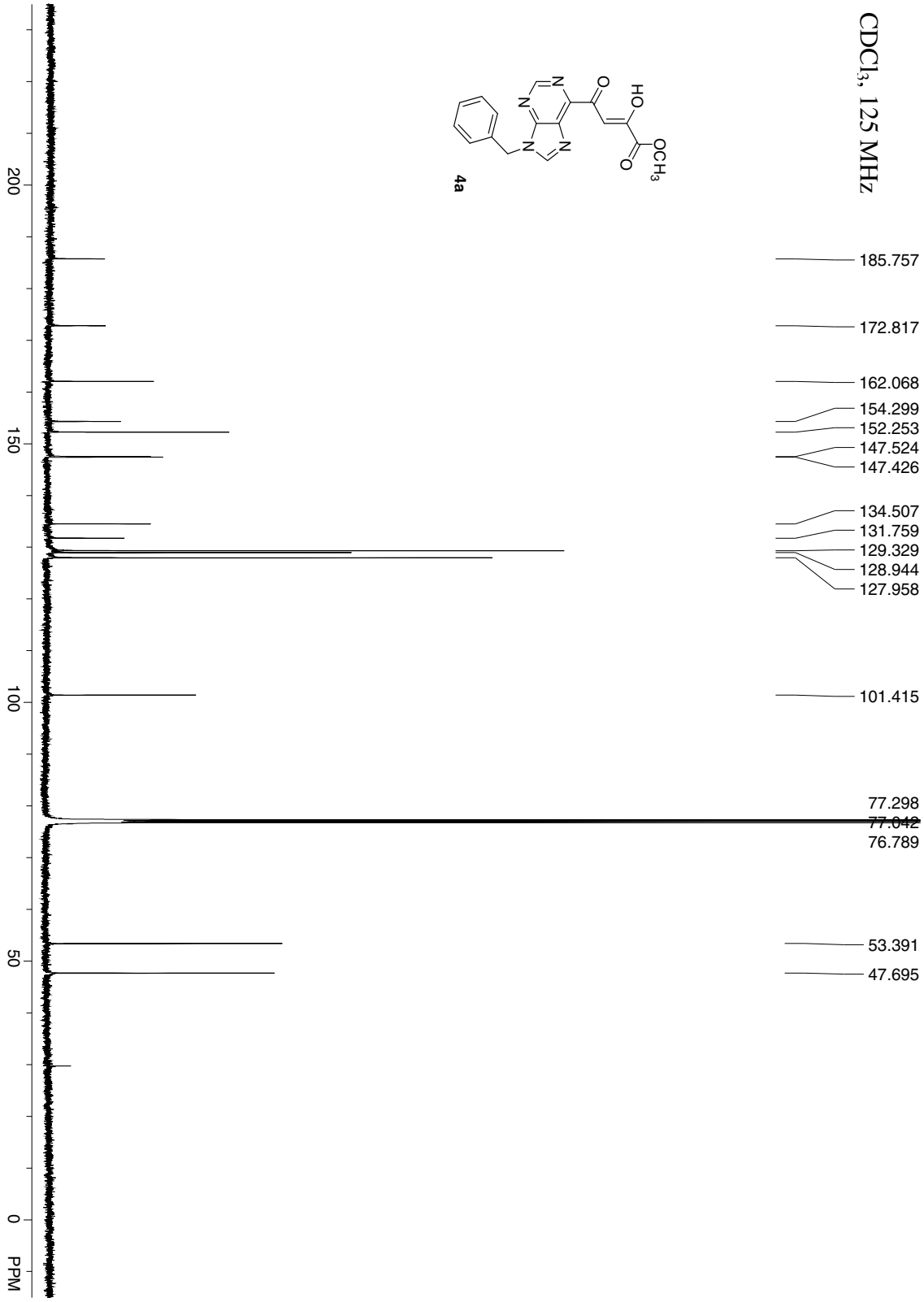

CDCl3, 500 MHz
4a
9.197
8.306
7.990
7.415
7.401
7.364
7.350
7.293
5.548
3.997
1.02
1.03
0.95
5.59
2.00
2.91
PPM

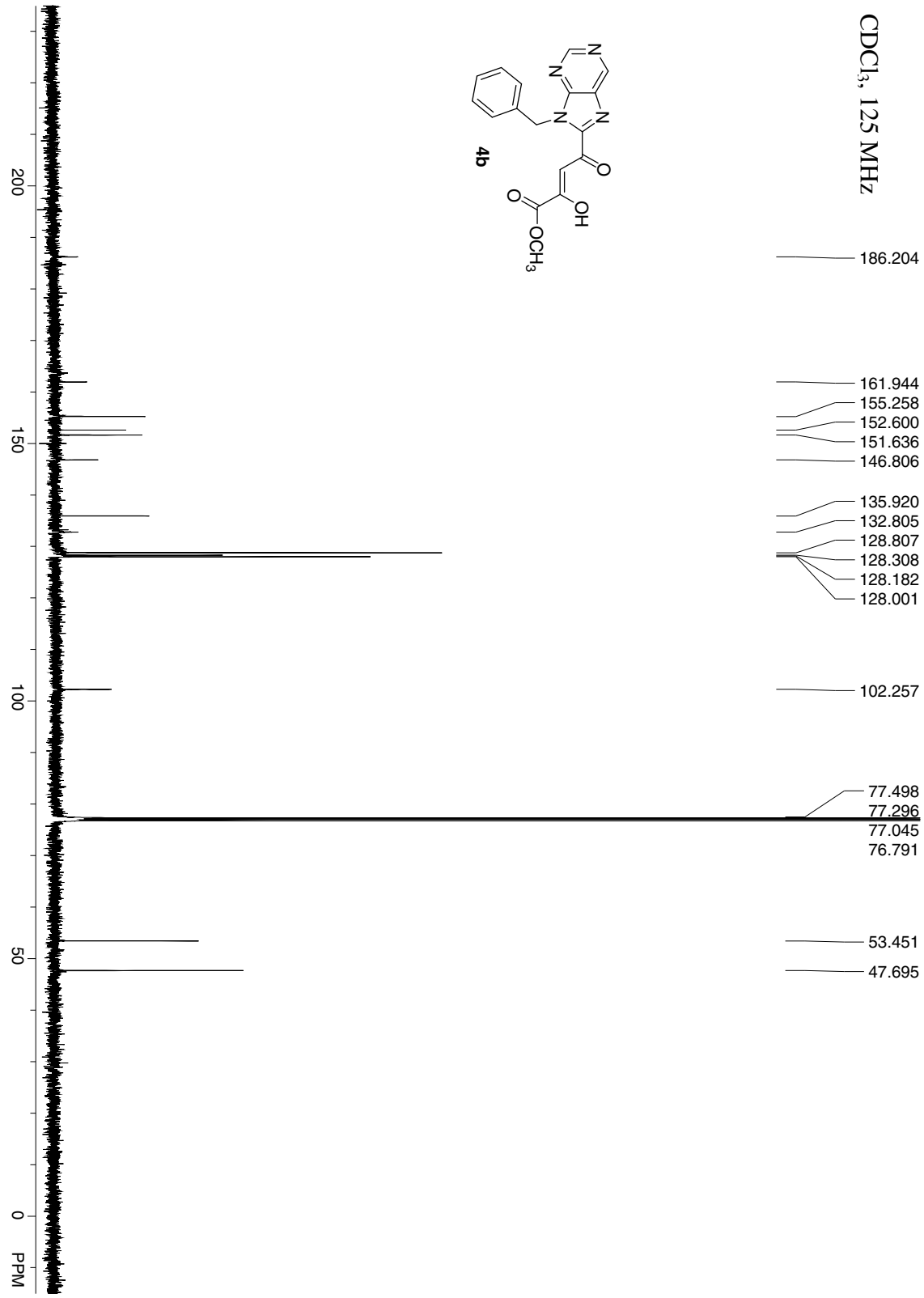

CDCl3, 500 MHz
4b
9.390
9.217
7.414
7.680
7.400
7.346
7.334
7.320
7.307
7.299
6.032
3.989
1.288
1.11
1.00
0.96
6.01
2.14
3.13
PPM

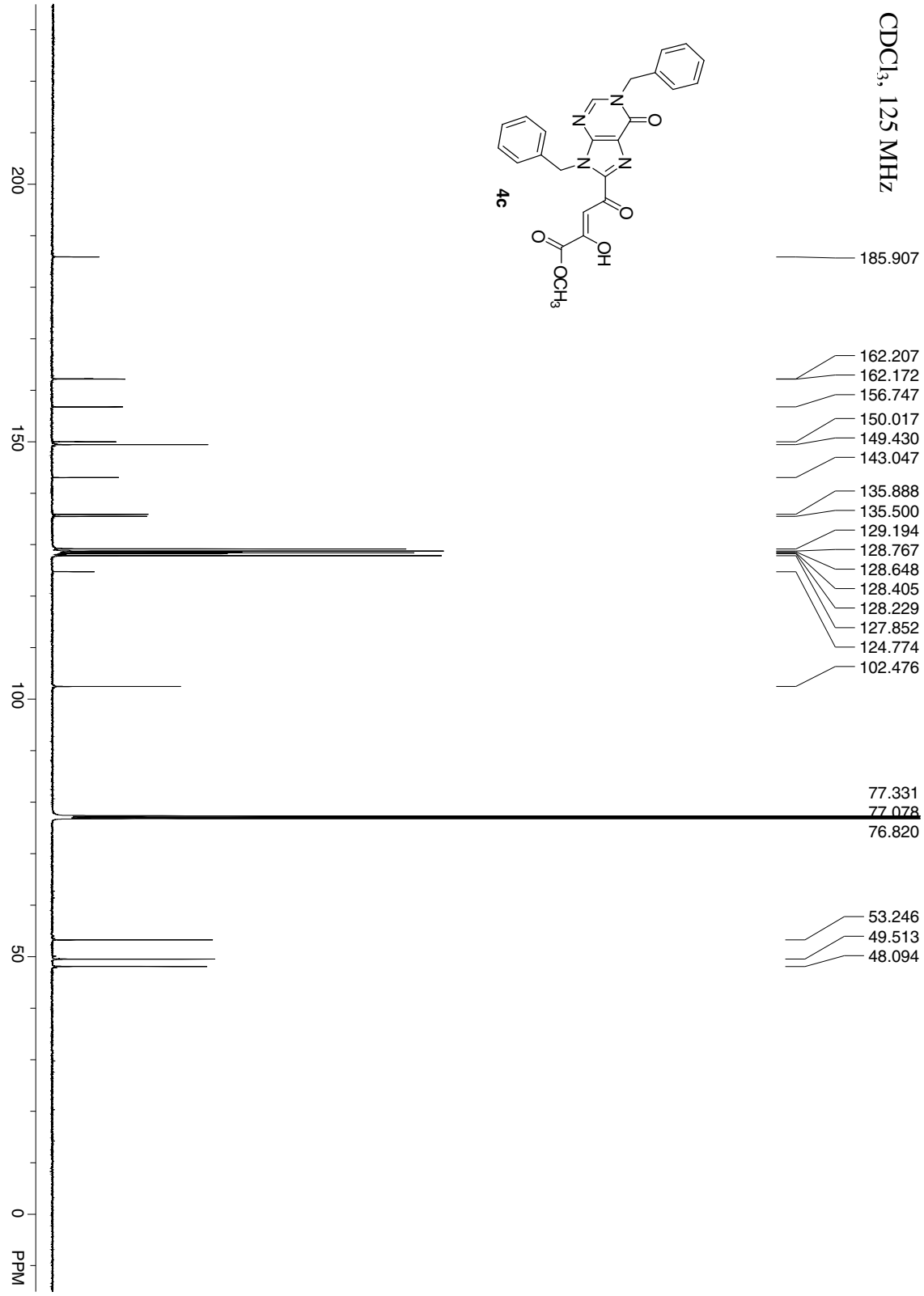

CDCl3, 500 MHz
4c
13.834
7.759
7.415
7.410
7.402
7.386
8.195
7.382
7.369
7.365
7.352
7.349
7.345
7.326
7.324
7.311
7.308
7.300
5.879
5.322
3.951
0.52
1.10
0.88
9.99
2.00
2.16
2.94
15
10
5
0
-5
PPM

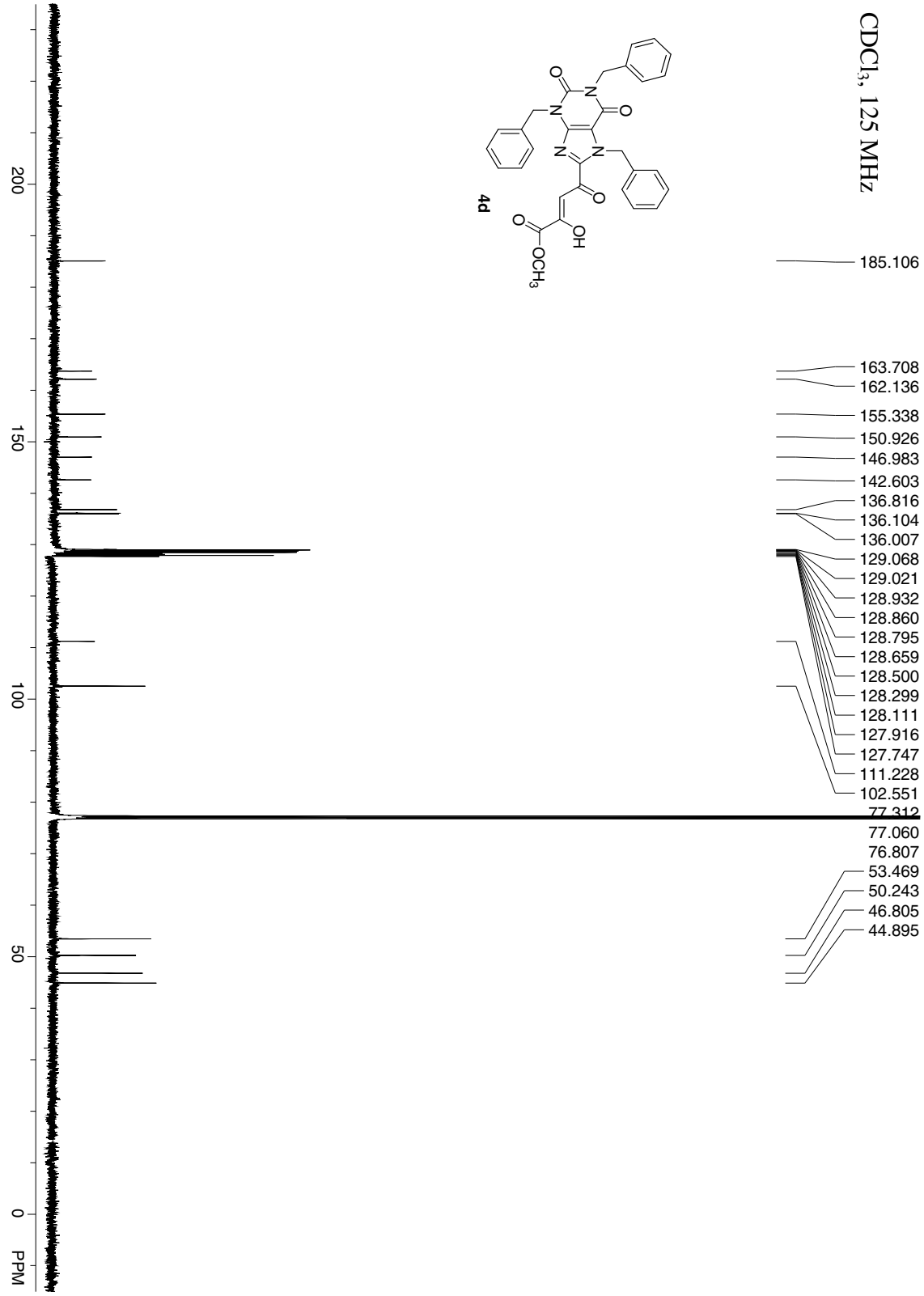

CDCl3, 500 MHz
13.955
7.580
7.576
7.570
7.564
7.524
7.520
7.507
7.400
7.397
7.368
7.364
7.361
7.358
7.353
7.344
7.340
7.331
7.319
7.316
7.300
6.171
5.339
5.245
4.002
4d
0.57
16.45
2.00
4.36
2.23
15
10
5
0
-5
PPM

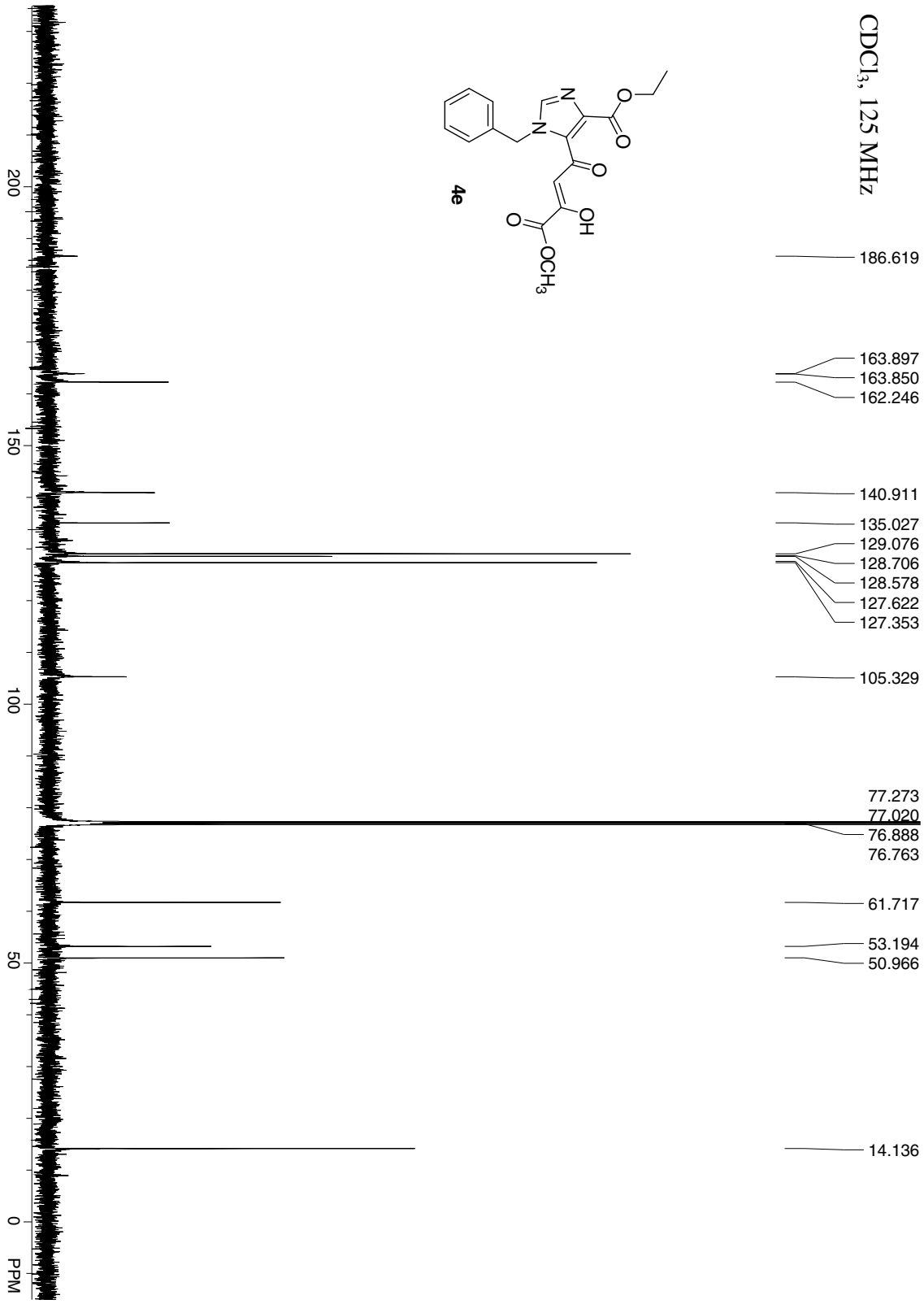

CDCl3, 500 MHz
4e
7.668
7.346
7.334
7.319
7.307
7.277
7.119
7.104
7.063
5.428
4.444
4.431
4.416
4.402
3.898
1.419
1.405
1.390
1.261
0.97
3.19
3.02
2.00
1.99
2.71
3.18
PPM


CDCl3, 125 MHz
4a
185.757
172.817
162.068
154.299
152.253
147.524
147.426
134.507
131.759
129.329
128.944
127.958
101.415
77.298
77.042
76.789
53.391
47.695
200
150
100
50
0
PPM


CDCl3, 125 MHz
4b
186.204
161.944
155.258
152.600
151.636
146.806
135.920
132.805
128.807
128.308
128.182
128.001
102.257
77.498
77.296
77.045
76.791
53.451
47.695
200
150
100
50
0
PPM


CDCl3, 125 MHz
4c
185.907
162.207
162.172
156.747
150.017
149.430
143.047
135.888
135.500
129.194
128.767
128.648
128.405
128.229
127.852
124.774
102.476
77.331
77.078
76.820
53.246
49.513
48.094
200
150
100
50
0
PPM


CDCl3, 125 MHz
4d
185.106
163.708
162.136
155.338
150.926
146.983
142.603
136.816
136.104
136.007
129.068
129.021
128.932
128.860
128.795
128.659
128.500
128.299
128.111
127.916
127.747
111.228
102.551
77.312
77.060
76.807
53.469
50.243
46.805
44.895
200
150
100
50
0
PPM


CDCl3, 125 MHz
4e
186.619
163.897
163.850
162.246
140.911
135.027
129.076
128.706
128.578
127.622
127.353
105.329
77.273
77.020
76.888
76.763
61.717
53.194
50.966
14.136
200
150
100
50
0
PPM