Supporting Information

Exploring the Synthesis of Deceptively Simple Biginelli Products through N-CN Bond Cleavage

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General Methods:

All commercial reagents and solvents were used as received without further purification. Analytical thin-layer chromatography was performed on precoated Kieselgel 60F254 plates; spots were located using UV (254 and 366 nm) and iodine. All melting points were measured with a Fisher-Johns apparatus and remain uncorrected. ^{1}H and ^{13}C NMR spectra were obtained in DMSO-d_6 or $CDCl_3$ using a 300 MHz spectrometer. Chemical shifts (δ) are expressed in ppm relative to the tetramethylsilane peak used as an internal standard. The J values are in Hertz, and the splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; and *bs*, broad singlet. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. Mass spectra (MS) and high-resolution mass spectra (HRMS) were obtained using an MStation JMS-700 spectrometer. Elemental analyses were performed using an Elemental Vario EL III.

Representative procedure for the synthesis of *N*-(5-ethoxycarbonyl-6-methyl-4-phenyl-1,4-dihydropyrimidin-2-yl)carbamimidic formic anhydride (2a). One mmol of 2-cyanoimino-5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydro-1*H*-pyrimidine **1a** in 5 mL of HCO_2H was heated at ~101 °C for 10 min. The crude product was processed according to procedure A (*vide infra*) to give **2a**. Yield 95%; mp 142-145 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.08 (t, J = 7.20 Hz, 3H), 2.28 (s, 3H), 4.00 (q, J = 7.20 Hz, 2H), 5.38 (s, 1H), 6.33 (s, 2H), 7.04 (bs, 1H), 7.04-7.42 (m, 5H), 8.24 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.6, 19.1, 52.4, 59.3, 100.4, 126.4, 127.5, 128.5, 144.6, 149.2, 152.3, 162.7, 164.4, 165.3; IR (KBr) 774, 1594 (HCO_2), 1690 (C=N), 1715 [-NHC(=NH)-O-], 1710 (C=O), 1643, 3428 (NH) cm^{-1}; HRMS (EI+) Calcd for $C_{16}H_{18}N_4O_4$, 330.1328; Found, 330.1330. Anal. Calcd for $C_{16}H_{18}N_4O_4 \bullet CHO_2H$: C, 54.25; H, 5.36; N, 14.89. Found: C, 54.92; H, 5.86; N, 15.50.

General procedure for the synthesis of heterocyclic guanidine (3a-j).

Method A. 2-Cyanoimino-3,4-dihydro-1*H*-pyrimidine **1a-j** (1 mmol) was refluxed in 5 mL of formic acid for 24 h. After the starting material was consumed, the reaction mixture was poured into 10 mL of cold water, and then a saturated aqueous solution of sodium carbonate was added dropwise to adjust the pH of the system to 3-4. The precipitate was collected and dried to afford spectroscopically pure **3a-j**, and thus, further purification was not required.

Method B. Following method A, the reaction of 2-ureido-1,4-dihydropyrimidine **5a** (1 mmol) with formic acid afforded the cyclic guanidine **3a** in quantitative yield.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-iminium formate (3a). Yield 90 %; mp 155-158 °C; ^{1}H NMR (300 MHz; $CDCl_3$/TMS): δ 1.09 (t, *J* = 7.20 Hz, 3H), 2.31 (s, 3H),4.02 (q, *J* = 7.20 Hz, 2H), 5.33 (s, 1H), 7.12-7.30 (m, 5H), 8,05 (bs,1H), 8.37 (s, 1H), 10.02 (bs, 1H), 11.62 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 14.0, 17.7, 53.3, 60.3, 103.1, 126.5, 128.3, 128.9, 141.9, 143.9, 152.0, 164.8, 170.1; IR (KBr) 774, 1603 (HCO_2^-), 1603, 3320 (NH), 1652 (C=N), 1707 (C=O), 1494, 2830 ($=NH_2^+$) c.m^{-1}; HRMS (EI+) *m/z* 260.1402 (260.1399 calcd for $C_{14}H_{18}O_2N_3^+$). Anal. Calcd for $C_{15}H_{19}O_4N_3$: C, 59.01; H, 6.27; N, 13.76. Found: C, 58.51; H, 6.127; N, 13.18.

5-Oxo-4-phenyl-3,4,5,6,7,8-hexahydroquinazolin-2(1*H*)-iminium formate (3b). Yield 89%; mp 126-130 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.69-2.00 (m, 2H), 2.15-2.30 (m, 2H), 4.14 (bs, 2H), 5.29 (s, 1H), 7.20-7.36 (m, 5H), 8.33 (s, 1H), 8.78 (bs, 2H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 20.7, 27.2, 36.4, 49.9, 109.1, 126.3, 127.4, 128.5, 143.8, 153.5, 156.6, 167.2, 193.2; IR (KBr) 771, 1599 (HCO_2^-), 1649, 3336 (NH), 1668 (C=N), 1701 (C=O), 1525, 2797 ($=NH_2^+$) cm^{-1}; HRMS (EI+) Calcd for $C_{14}H_{16}N_3O^+$, 242.1293; Found, 242.1278. Anal. Calcd for $C_{15}H_{17}N_3O_3 \cdot H2O$: C, 50.13; H, 7.01; N, 11.69; Found: C, 50.63; H, 6.09; N, 11.18.

4-(Benzo[*d*][1,3]dioxol-4-yl)-5-(ethoxycarbonyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-iminium formate (3c). Yield 91%; mp 181-184 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.10 (t, J = 7.0 Hz, 3H), 2.32 (s, 3H), 4.01 (q, J = 7.0 Hz, 2H), 5.23 (s, 1H), 6.00 (s, 2H), 6.45-7.00 (m, 3H), 8.36 (s, 1H), 9.38 (bs, 3H); δ ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.0, 17.8, 51.7, 59.5, 101.0, 106.8, 108.2, 119.6, 137.3, 146.7, 147.4, 152.3, 164.9, 167.9; IR (KBr) 924 (C-O-C), 773, 1590 (HCO_2^-), 1604, 3337 (NH), 1664 (C=N), 1710 (C=O), 2782 (O-CH_2-O), 1502, 2987 (=NH_2^+) cm^{-1}; HRMS (EI+) Calcd for $C_{15}H_{18}N_3O_4^+$, 304.1297; Found, 304.1297; Anal. Calcd for $C_{16}H_{19}N_3O_6{\cdot}H_2O$: C, 52.31; H, 5.76; N, 11.44. Found: C, 52.69; H, 5.14; N, 10.98.

5-(Ethoxycarbonyl)-6-methyl-4-(thiophen-2-yl)-3,4-dihydropyrimidin-2(1*H*)-iminium formate (3d). Yield 85%; mp 118-122 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.15 (t, J = 7.2 Hz, 3H), 2.18 (s, 3H), 4.00 (q, J = 7.2 Hz, 2H), 5.48 (s, 1H), 6.86 (d, J = 3.3, 1H), 6.91 (t, J = 4.5, 1H), 7.30 (d, 1H), 7.40 (s, 1H), 8.43 (s, 1H), 8.64 (s, 1H); δ ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.4, 22.3, 48.1, 58.5, 98.2, 122.9, 124.3, 126.4, 150.5, 155.1, 160.9, 165.7, 167.4; IR (KBr) 771, 1608 (HCO_2^-), 1615, 3300 (NH), 1668 (C=N), 1711 (C=O), 1517, 2984 (=NH_2^+) cm^{-1}; HRMS (EI+) Calcd for $C_{12}H_{16}N_3O_2S^+$, 266.0963; Found, 266.0920.

5-(Methoxycarbonyl)-6-methyl-4-(2-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-iminium formate (3e). Yield 98%; mp 172-174 °C (dec); ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 2.35 (s, 3H), 3.40 (s, 3H), 5.82 (s, 1H), 6.52 (bs, 2H), 7.50-7.60 (m, 2H), 7.62-7.80 (m, 2H), 7.88 (d, J = 8.4, 1H), 8.31 (s,1H), 9.44 (bs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 17.8, 47.5, 51.0, 99.6, 124.1, 129.2, 129.4, 134.4, 137.4, 147.5, 148.7, 152.3 164.8, 166.0; IR (KBr) 774, 1610 (HCO_2^-), 1361 (Ar-NO_2), 1603, 3315 (NH), 1680 (C=N), 1703 (C=O), 1530, 2830 (=NH_2^+) cm^{-1}; HRMS (FAB+) *m/z* 291.1090 (291.1093 calcd for $C_{13}H_{15}O_4N_4^+$).

5-Ethoxycarbonyl-6-methyl-4-(2-clorophenyl)-3,4-dyhidropyrimidin-2(1*H*)-iminium formate (3f). Yield 41%; mp 202-205 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 0.95 (t, J = 7.20 Hz, 3H), 2.27 (s, 3H), 3.80 (q, J = 7.20 Hz, 2H), 5.62 (s, 1H), 6.39 (s, 2H), 7.20-7.38 (m, 3H), 7.39 (d, J = 7.2 Hz, 1H), 7.72 (bs, 1H), 8.44 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.1, 23.2, 49.7, 58.1, 95.3, 127.6, 128.7, 128.8, 129.1, 131.1, 142.6, 154.8, 165.7, 166.5; IR (KBr), 774, 1600 (HCO_2^-), 1089 (Ar-*o*-Cl), 1595, 3432 (NH), 1658 (C=N), 1709 (C=O), 1478, 2983 (=NH_2^+) cm^{-1}; HRMS (EI+) Calcd for $C_{14}H_{17}ClN_3O_2^+$, 294.1009; Found, 294.1001.

4-(4-Bromophenyl)-5-(ethoxycarbonyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-iminium formate (3g). Yield 99%; mp 170-173 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.08 (t, J = 7.20 Hz, 3H), 2.31 (s, 3H), 3.99 (q, J = 7.20 Hz, 2H), 5.28 (s, 1H), 7.20 (d, J = 8.10 Hz, 2H), 7.54 (d, J = 8.10 Hz, 2H), 8.35 (s,1H), 9.48 (bs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.0, 17.8, 51.5, 59.6, 100.5, 120.9, 128.7, 131.6, 142.8, 147.7, 152.5, 164.8, 167.7; IR (KBr) 774, 1589 (HCO_2^-), 1089 (Ar-*p*Br), 1603, 3345 (NH), 1658 (C=N), 1705 (C=O), 1521, 2828 (=NH_2^+) cm^{-1}; HRMS (FAB+) Calcd for $C_{14}H_{17}BrN_3O_2^+$, 338.0504; Found, 338.0506.

4-(2-Trifluoromethylphenyl)-5-(ethoxycarbonyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-iminium formate (3h). Yield 80%; mp 153-156 °C; ^{1}H NMR (300 MHz; $CDCl_3$/TMS): δ 0.97 (t, J = 7.2 Hz, 3H), 2.47 (s, 3H), 3.97 (q, J = 7.2 Hz, 2H), 5.81 (s, 1H), 7.36-7.46 (m, 2H), 7. 48-7.60 (m, 1H), 7.62-7.67 (m, 1H), 8.33 (s, 1H), 8.85 (bs, 2H), 12.31 (bs, 1H); δ ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 13.6, 17.4, 49.2, 60.3, 101.6, 122.3 ($^{1}J_{CF}$ = 273.7 Hz), 126. 2 ($^{3}J_{CF}$ = 5.6 Hz), 127. 2 ($^{2}J_{CF}$ = 30.8 Hz), 133.2, 139.9, 145.9, 151.6, 164.2, 169.7; IR (KBr) 768 (CF_3), 773, 1587 (HCO_2^-), 1631, 3420 (NH), 1664 (C=N), 1703 (C=O), 1541, 2980 (=NH_2^+) cm^{-1}; HRMS (FAB+) Calcd for $C_{15}H_{17}F_3N_3O2^+$, 328.1273; Found, 328.1276.

4-[2-(Difluoromethoxy)phenyl]-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1H)-iminium formate (3i). Yield 84%; mp 93-96 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ1.00 (t, J = 6.9 Hz, 3H), 2.34 (s, 3H), 3.92 (q, J = 6.9 Hz, 2H), 5.61 (s, 1H), 7.14-7.45 (m, 4H), 7.2 (t, $^{2}J_{HF}$ = 73.9 Hz, 1H), 8.33 (s, 1H), 9.10 (bs, 2H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 13.8, 17.7, 47.2, 59.4, 99.3, 116.7 (t, $^{1}J_{CF}$ = 255.1 Hz), 117.9, 125.5, 129.0, 129.6, 133.4, 147.8, 148.4, 152.0, 164.6, 168.0; IR (KBr) 774, 1588 (HCO_2^-), 1238 (Ar-O-C), 1603, 3368 (NH), 1667 (C=N), 1705 (C=O), 1496, 2989 ($=NH_2^+$) cm^{-1}; HRMS (EI+) Calcd for $C_{15}H_{18}F_2N_3O_3^+$, 326.1316; Found, 326.1341.

4-(3-Fluorophenyl)-5-(ethoxycarbonyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-iminium formate (3j). Yield 99%; mp 154-156 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.09 (t, J = 6.9 Hz, 3H), 2.33 (s, 3H), 4.0 (q, J = 6.9 Hz, 2H), 5.36 (s, 1H), 6.98-7.19 (m, 3H), 7.35-7.49 (m, 1H), 8.35 (s, 1H), 9.15 (bs, 2H); δ ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.0, 17.8, 51.6, 59.7, 100.8, 113.3 (d, $^{2}J_{CF}$ = 21.5 Hz), 114.7 (d, $^{2}J_{CF}$ = 21.5 Hz), 122.4, 130.9 (d, $^{3}J_{CF}$ = 7.9 Hz), 146.0 (d, $^{3}J_{CF}$ = 5.7 Hz), 147.5, 152.1,, 162.2 (d, $^{1}J_{CF}$ = 242.7 Hz), 164.7, 168.1; IR (KBr), 773, 1588 (HCO_2^-), 1598, 3358 (NH), 1650 (C=N), 1706 (C=O), 1496, 2809 ($=NH_2^+$) cm^{-1}; HRMS (FAB+) Calcd for $C_{14}H_{17}FN_3O_2^+$, 278.1305; Found, 278.1308.

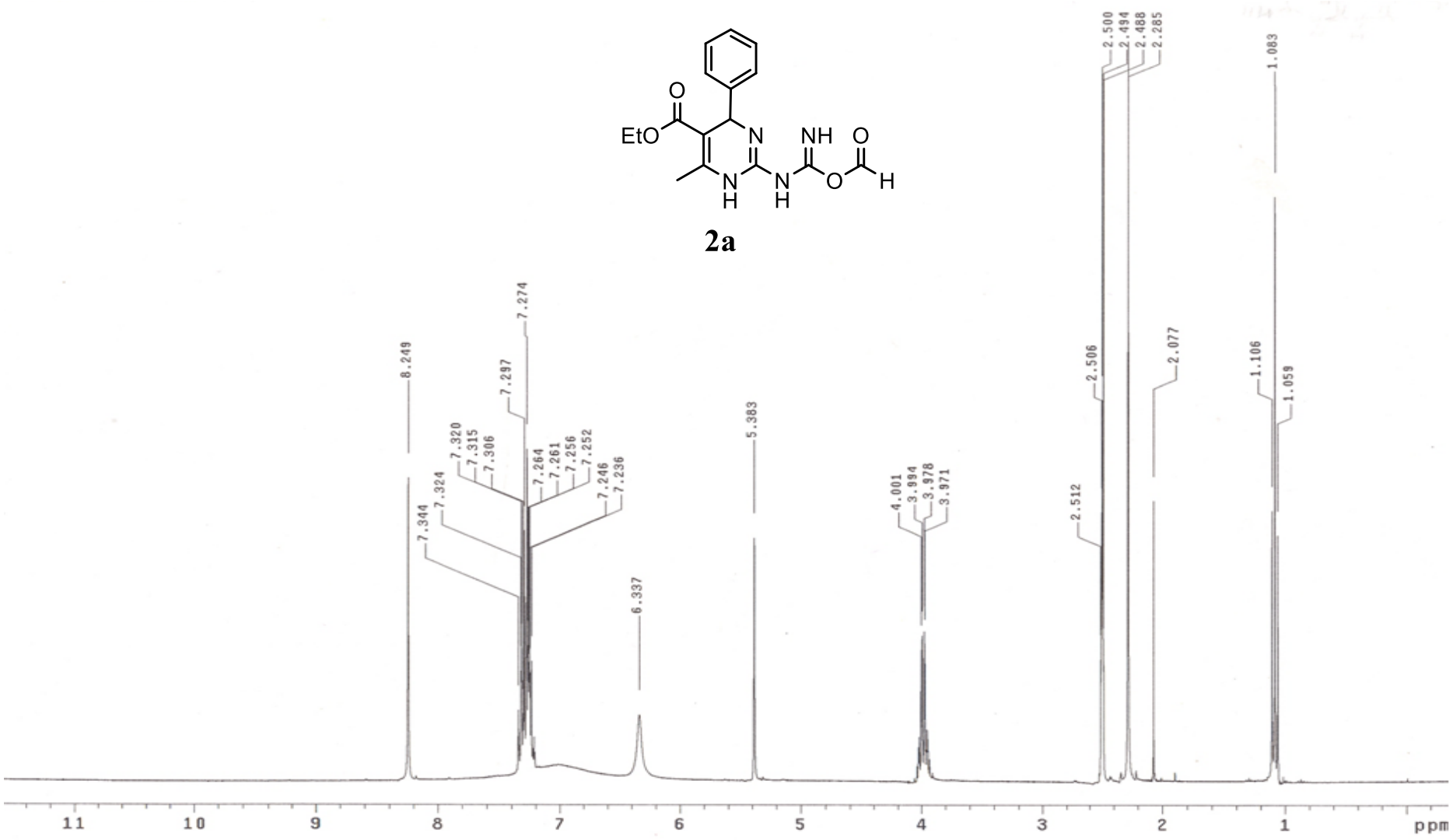
Representative procedure for the synthesis of 5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-iminium acetate (4a). One mmol of 2-cyanoimino-5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydro-1*H*-pyrimidine **1a** was refluxed in 5 mL of $MeCO_2H$ for 24 h. The crude product was processed according to procedure A to afford **4a**.. Yield 48%; mp 184-188 °C (dec); ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.09 (t, J = 7.20 Hz, 3H), 1.69 (s, 3H), 2.28 (s, 3H), 3.98 (q, J = 7.20 Hz, 2H), 4.60 (bs, 2H), 5.22 (s, 1H), 7.20-7.34 (m, 5H), 9.47 (bs, 2H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.1, 18.5, 24.2, 51.9, 59.2, 100.0, 126.3, 127.4, 128.5, 144.3, 149.7, 153.4, 165.2, 175.7; IR (KBr) 926 (ACO_2^-), 1603, 3432 (NH), 1652 (C=N), 1711 (C=O), 2981 ($=NH_2^+$) cm^{-1}; HRMS (FAB+) Calcd for $C_{14}H_{18}N_3O_2^+$, 260.1399; Found, 260.1402.

Representative procedure for the synthesis of 5-ethoxycarbonyl-6-methyl-4-phenyl-2-(*N*-carbamoylamino)-1,4-dihydropyrimidine (5a). 2-Cyanoimino-5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydro-1*H*-pyrimidine **1a** (10.2 mmol) was stirred and refluxed for 5 min in 15 mL of conc. HCl (37%). The mixture was cooled on crushed ice, diluted with 10 mL of water and treated with a 15% aqueous solution of Na_2CO_3 until it reached pH 5-6. The resulting insoluble solid was filtered, and washed with 10 mL of water and dried to afford **5a** as a slightly yellow granular solid. Yield 88%; mp 167-170 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.07 (t, J = 6.80 Hz, 3H), 2.35 (s, 3H), 4.01 (q, J = 6.80 Hz, 2H), 5.61 (s, 1H), 7.31-7.40 (m, 5H), 7.64 (s, 2H), 10.69 (bs, 1H), 11.55 (bs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.2, 17.7, 52.8, 61.0, 104.8, 127.2, 129.1, 129.4, 141.4, 143.3, 148.5, 153.7, 164.6; IR (KBr) 1573 (C=N), 1636 (H_2NC=O, amide II), 1679 (C=O), 1690 (H_2NC=O, amide I), 3212 (NH), 3357, 3367 (NH_2-amide) cm^{-1}; HRMS (EI+) Calcd for $C_{15}H_{18}N_4O_3$, 302.1379; Found, 302.1379; Anal. Calcd for $C_{15}H_{18}N_4O_3$•$2H_2OCl$: C, 44.02; H, 5.42; N, 13.53. Found: C, 44.67; H, 5.14; N, 13.12.

Representative procedure for the synthesis of 2-aminodyhidropyrimidine (6a-b). Following either method A or B, the free base was obtained by adjusting the reaction mixture to pH≥10 with a saturated aqueous solution of Na_2CO_3. The product was isolated according to method A.

2-Amino-5-ethoxycarbonyl-6-methyl-4-phenyl-1,4-dihydropyrimidine (6a). Yield 89%; mp 123-126 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.08 (t, J = 7.2 Hz, 3H), 2.27 (s, 3H), 3.76 (bs, 2H), 4.00 (q, J = 7.2 Hz, 2H), 5.36 (s, 1H), 6.27 (s, 2H), 7.20-7.40 (m, 5H), 9.54 (bs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 14.1, 19.2, 52.3, 59.1, 100.2, 126.2, 127.3, 128.4, 144.7, 152.4, 162.9, 165.3; IR (KBr) 1635 (C=O), 1578, 3356 (NH_2), 1595 (C=N), 3436 (NH), 3340 (NH_2) cm^{-1}; HRMS (EI+) Calcd for $C_{14}H_{17}N_3O_2$, 259.1321; Found, 259.1324.

2-Amino-4-phenyl-4,6,7,8-tetrahydroquinazolin-5(1*H*)-one (6b). Yield 88%; mp 132-135 °C; ^{1}H NMR (300 MHz; DMSO-d_6/TMS): δ 1.65-1.90 (m, 2H), 2.10-2.20 (m, 2H), 2.28-2.37 (m, 2H), 5.27 (s, 1H), 6.52 (s, 2H), 7.10-7.36 (m, 5H), 7.49 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6/TMS): δ 21.4, 31.4, 36.7, 50.3, 108.0, 126.2, 126.8, 128.1, 146.2, 156.4, 166.8, 192.1; IR (KBr) 1625 (C=O), 1571, 3336 (NH_2), 1598 (C=N), 3420 (NH), cm^{-1}; HRMS (EI+) Calcd for $C_{14}H_{15}N_3O$, 241.1215; Found, 241.1213; Anal. Calcd for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.41. Found: C, 66.19; H, 6.50; N, 16.75.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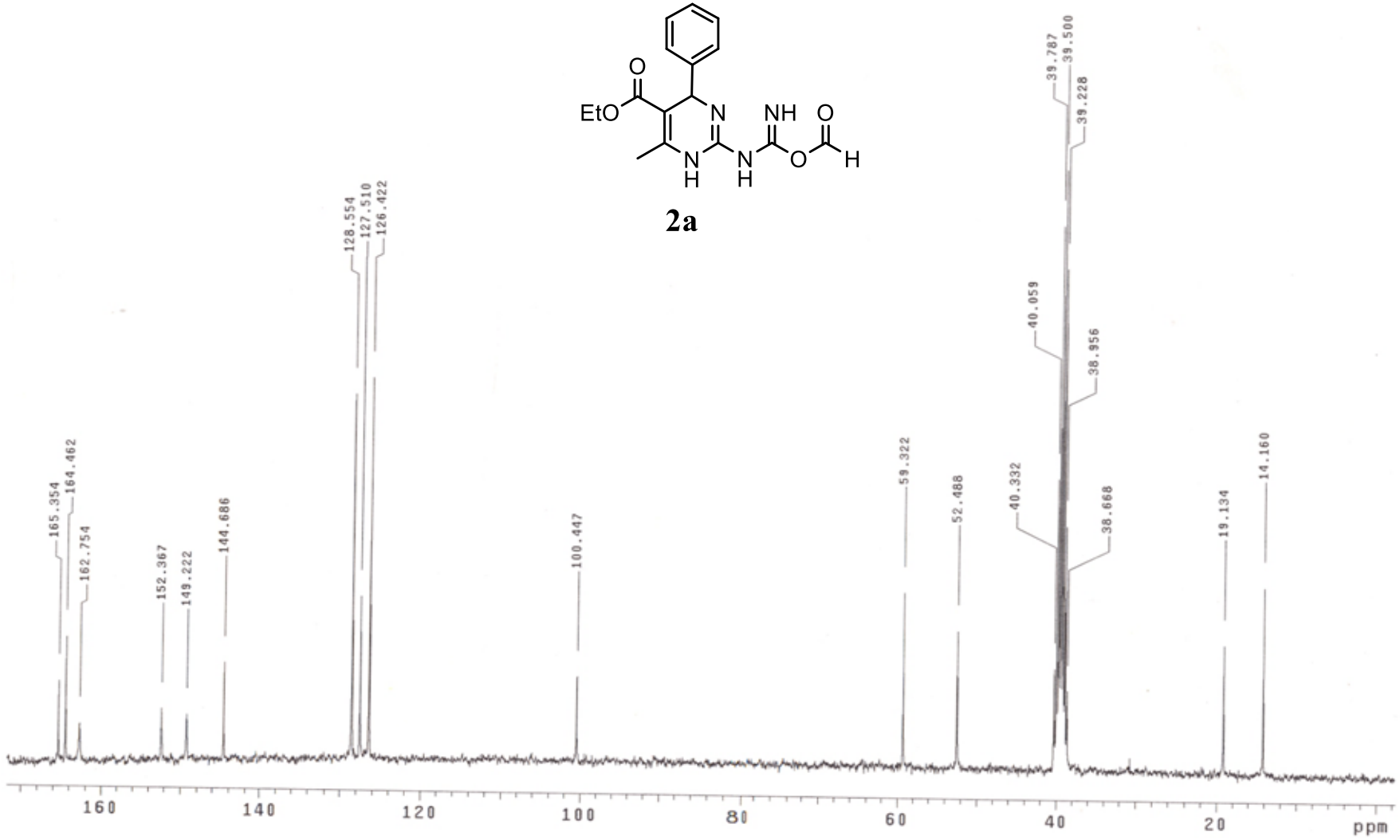
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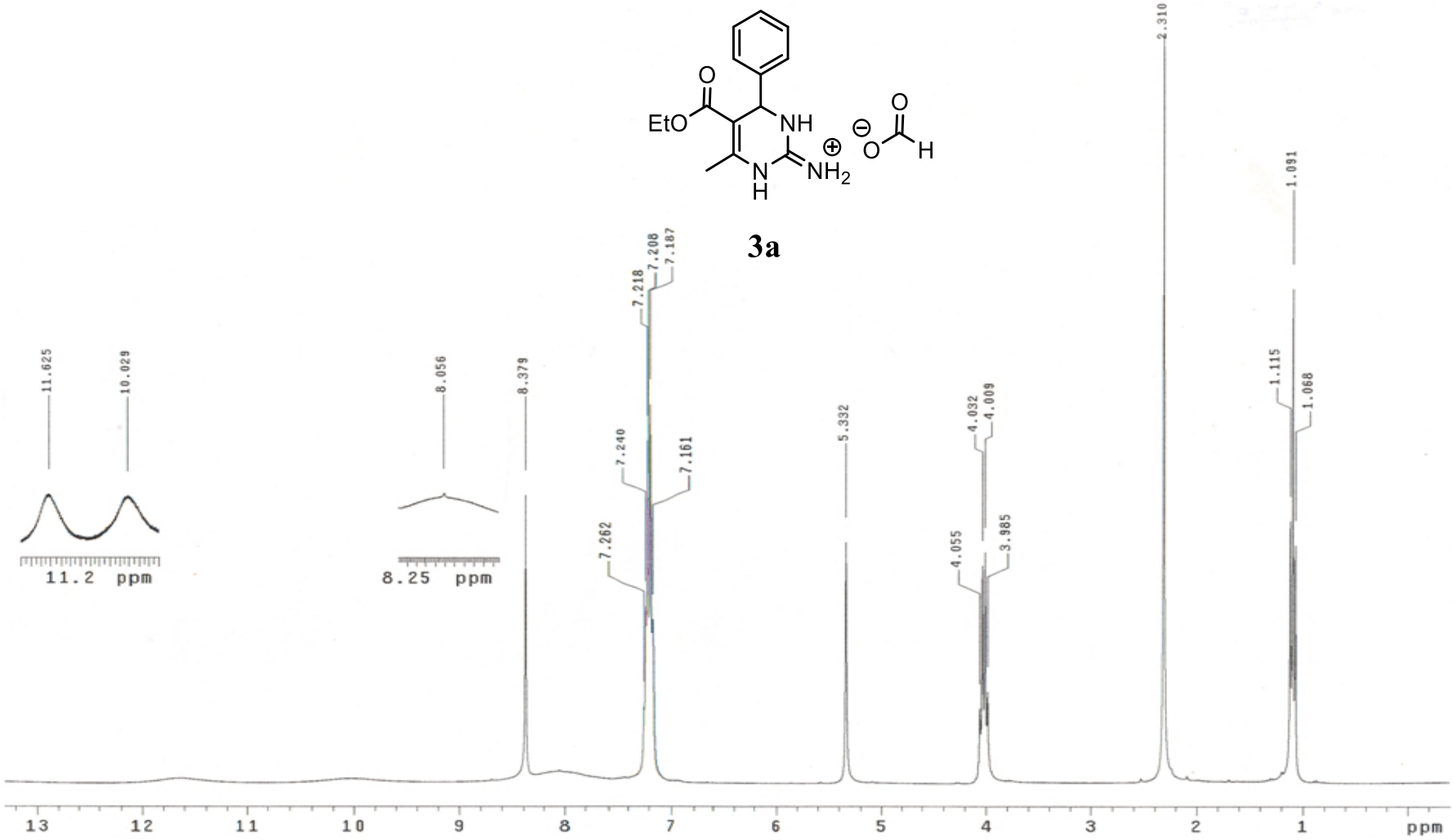
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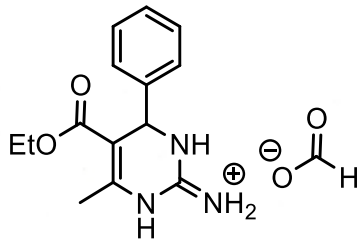
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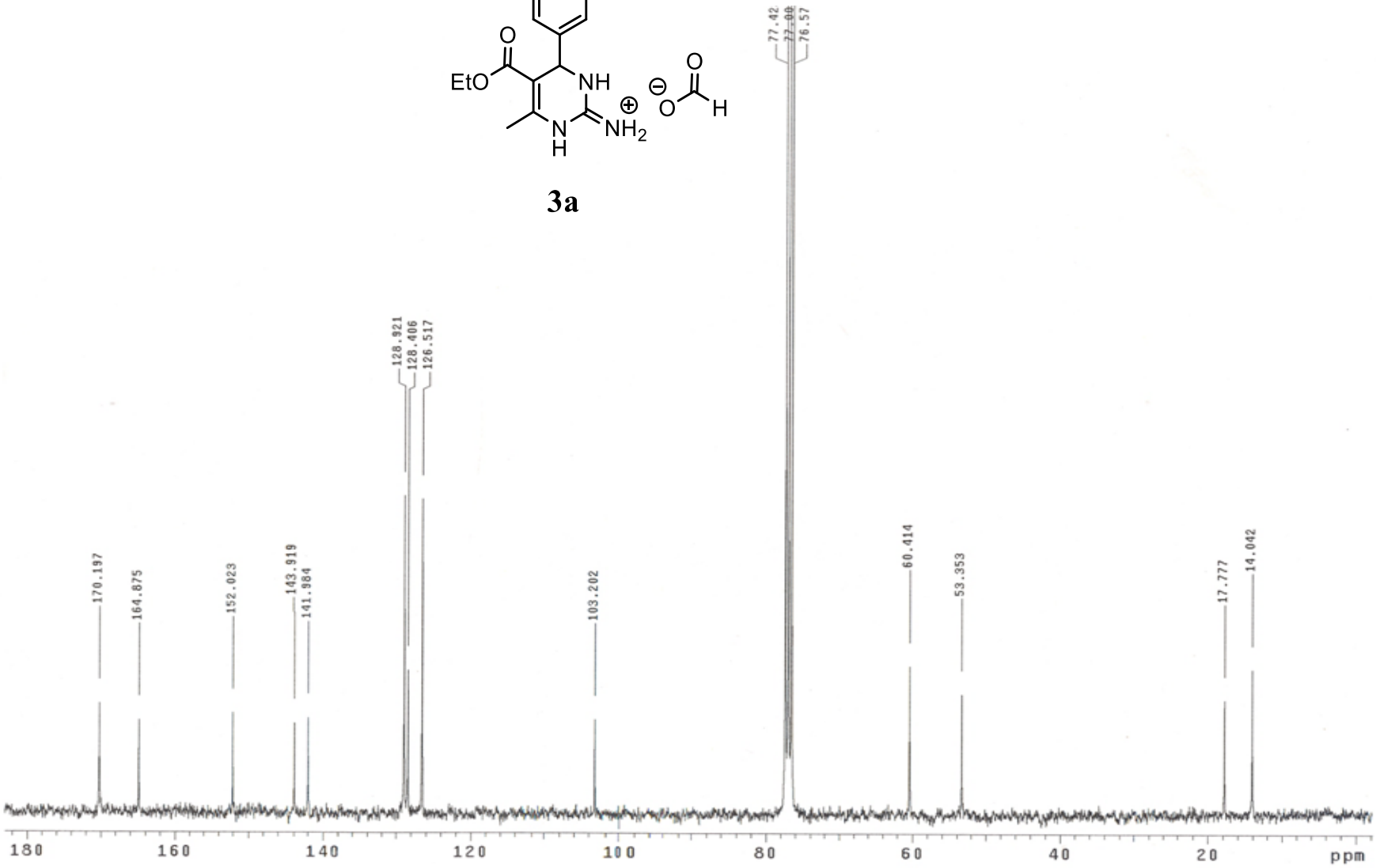
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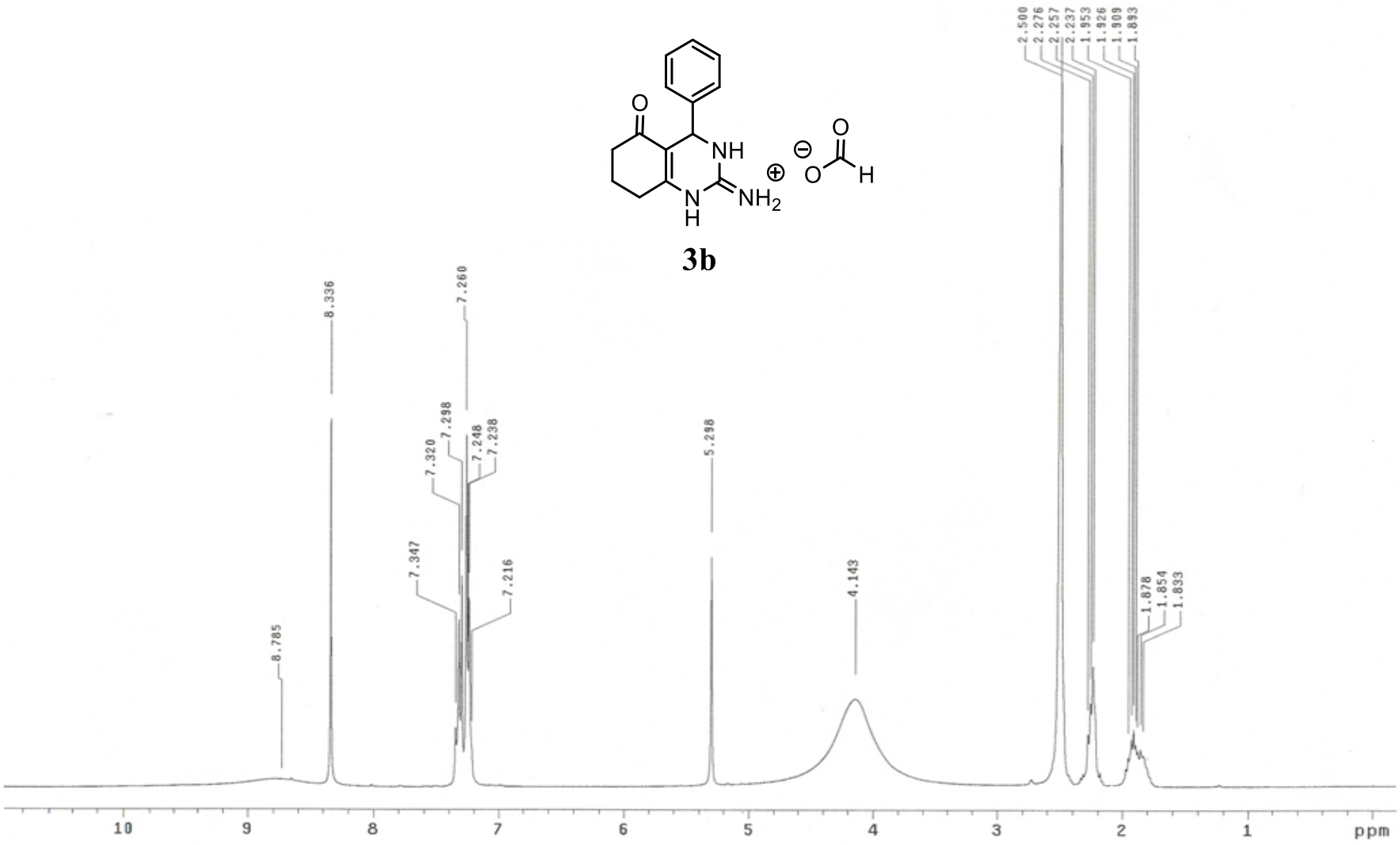
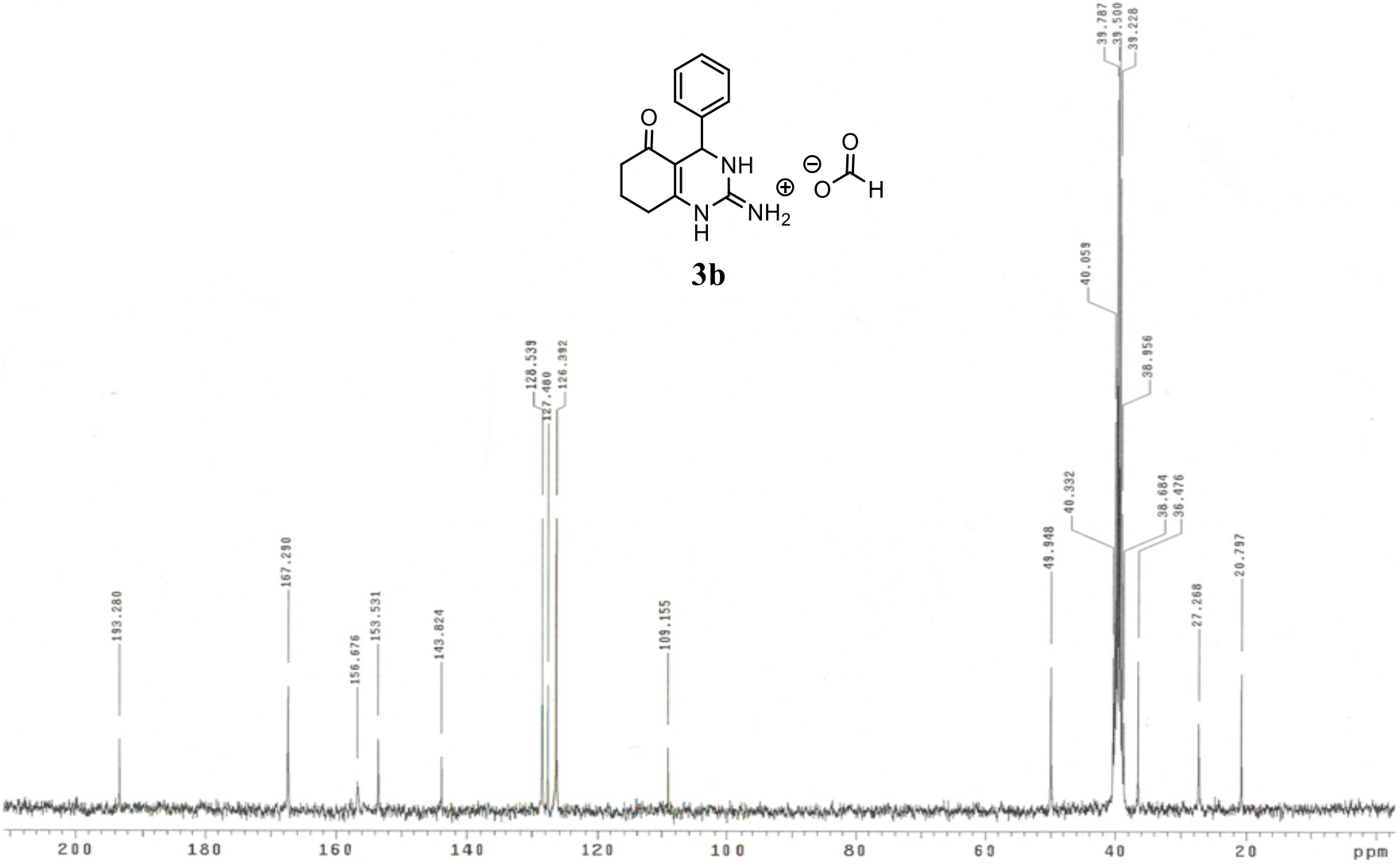
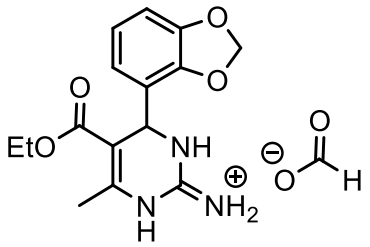
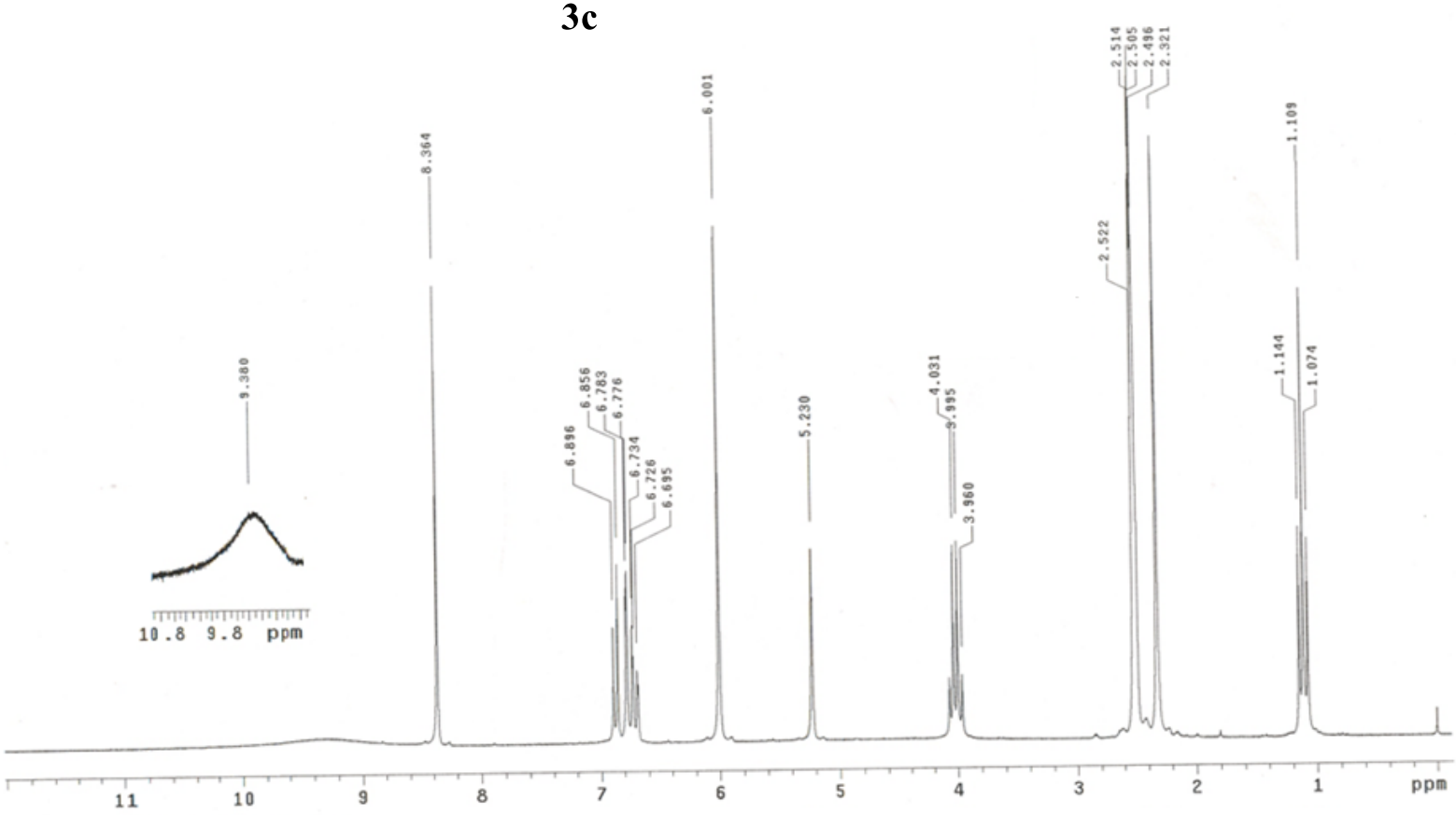
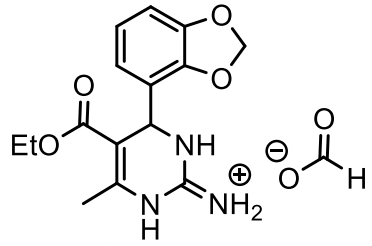

O
NH
N
H
NH2
O
O
H
3b
8.785
8.336
7.347
7.320
7.298
7.260
7.248
7.238
7.216
5.298
4.143
2.500
2.276
2.257
2.237
1.953
1.926
1.909
1.893
1.878
1.854
1.833
10
9
8
7
6
5
4
3
2
1
ppm


O
NH
N
H
NH2
O
O
H
3b
193.280
167.290
156.676
153.531
143.824
128.539
127.480
126.392
109.155
49.948
40.332
40.059
39.787
39.500
39.228
38.956
38.684
36.476
27.268
20.797
200
180
160
140
120
100
80
60
40
20
ppm

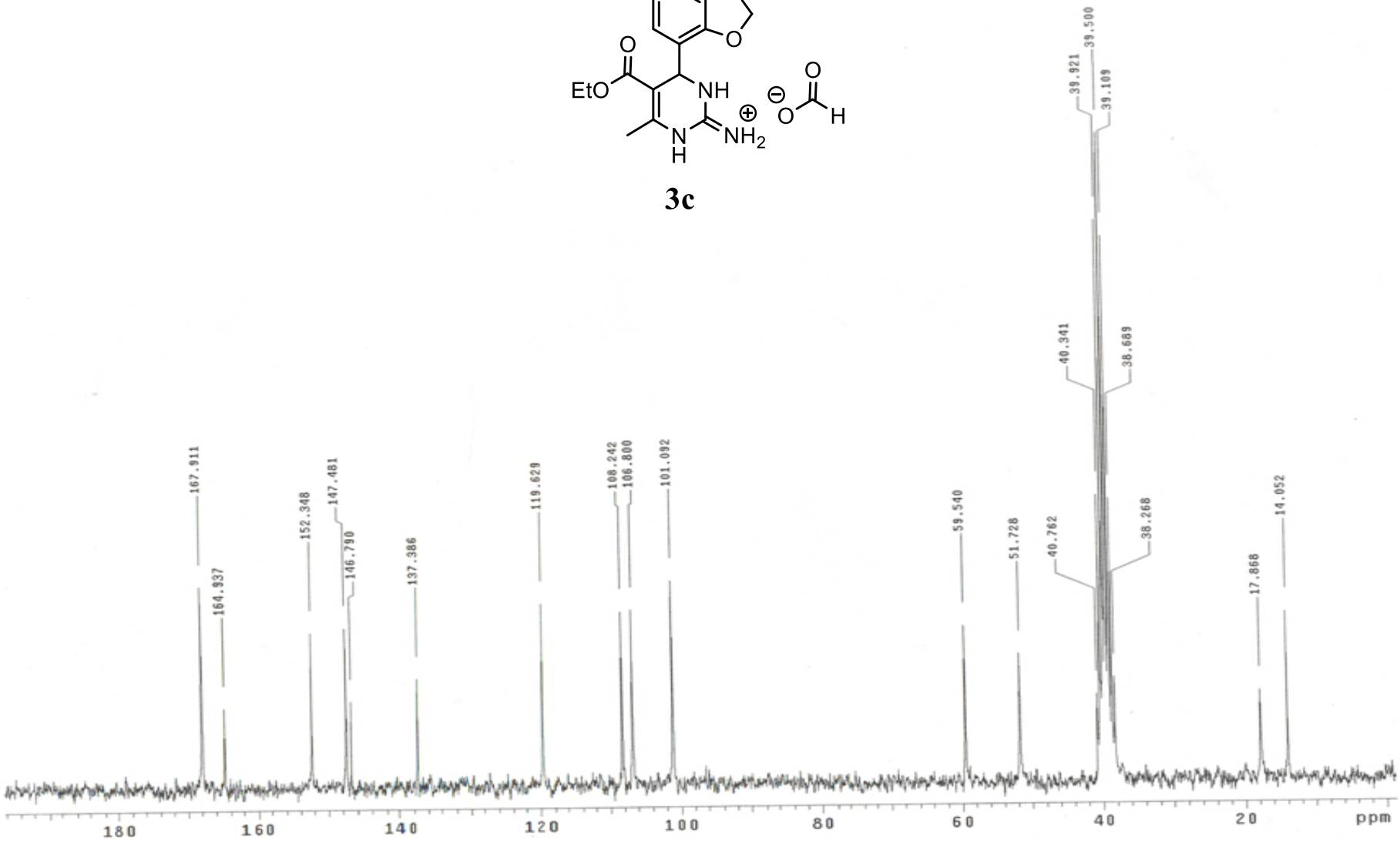

O
O
O
EtO
NH
O
H
N
H
NH2

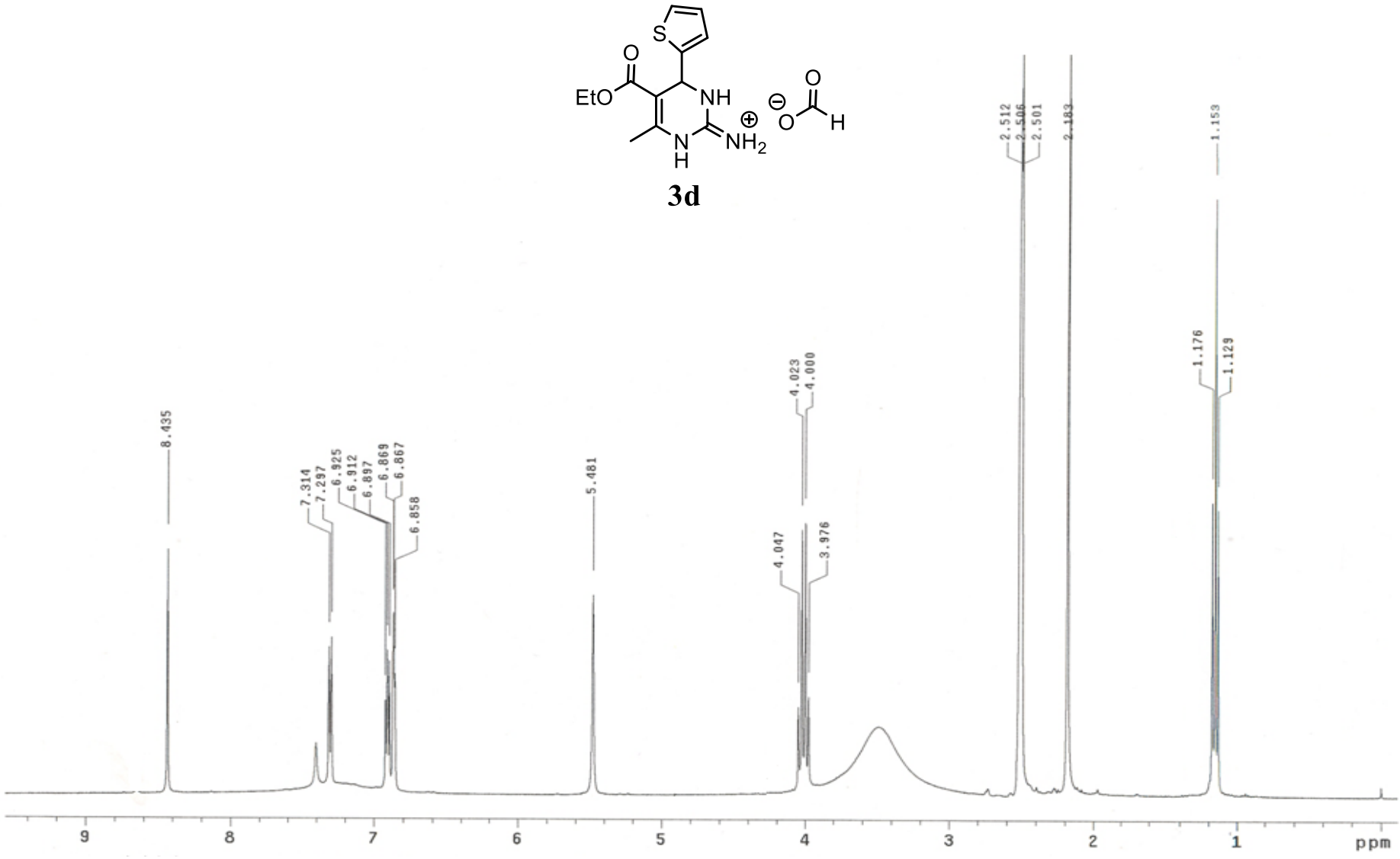
3c


9.380
8.364
6.896
6.856
6.783
6.776
6.734
6.726
6.695
6.001
5.230
4.031
3.995
3.960
2.522
2.514
2.505
2.496
2.321
1.144
1.109
1.074
10.8 9.8 ppm
11 10 9 8 7 6 5 4 3 2 1 ppm


O
O
O
EtO
NH
O
H
NH2
N
H

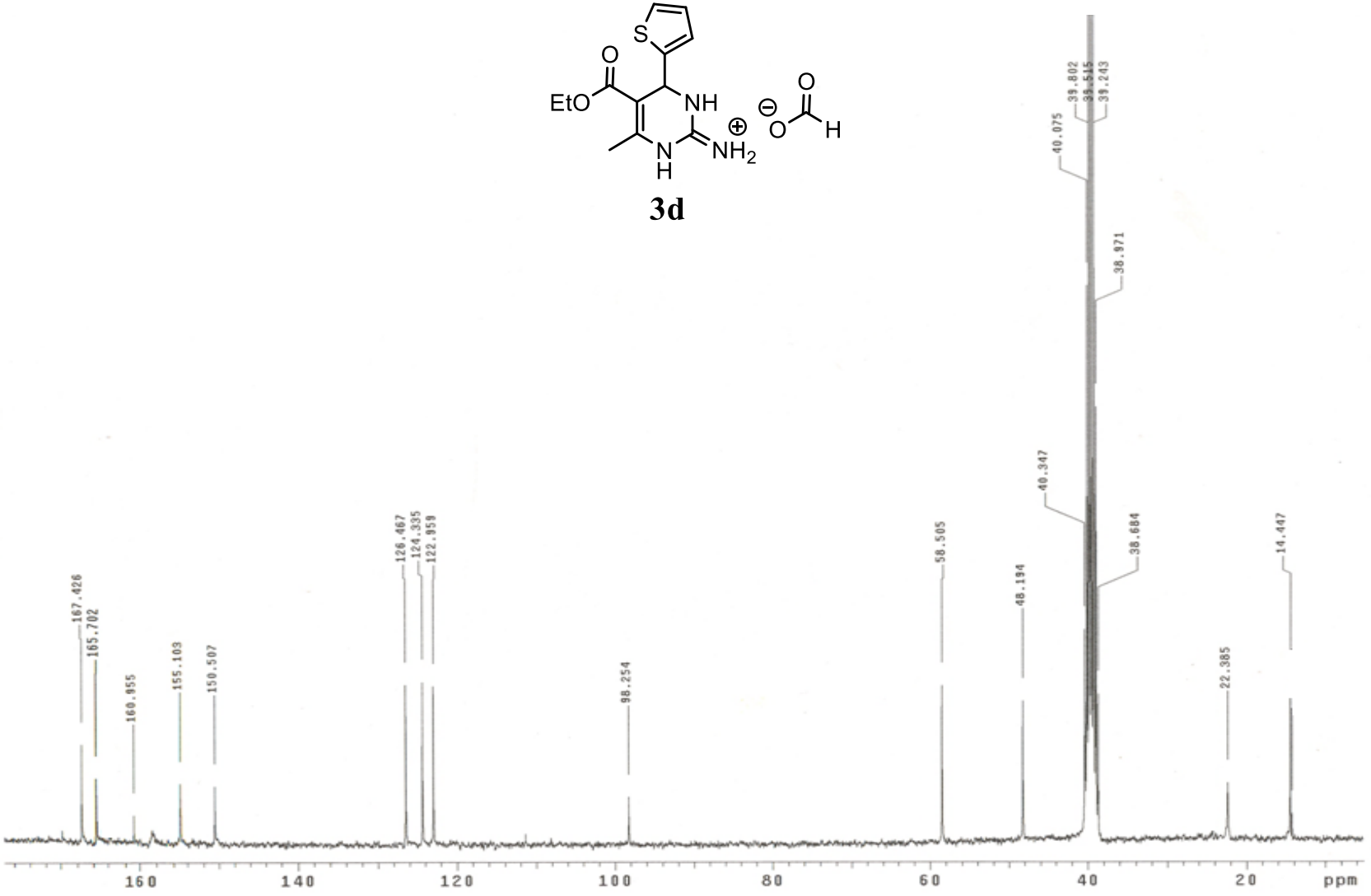
3c

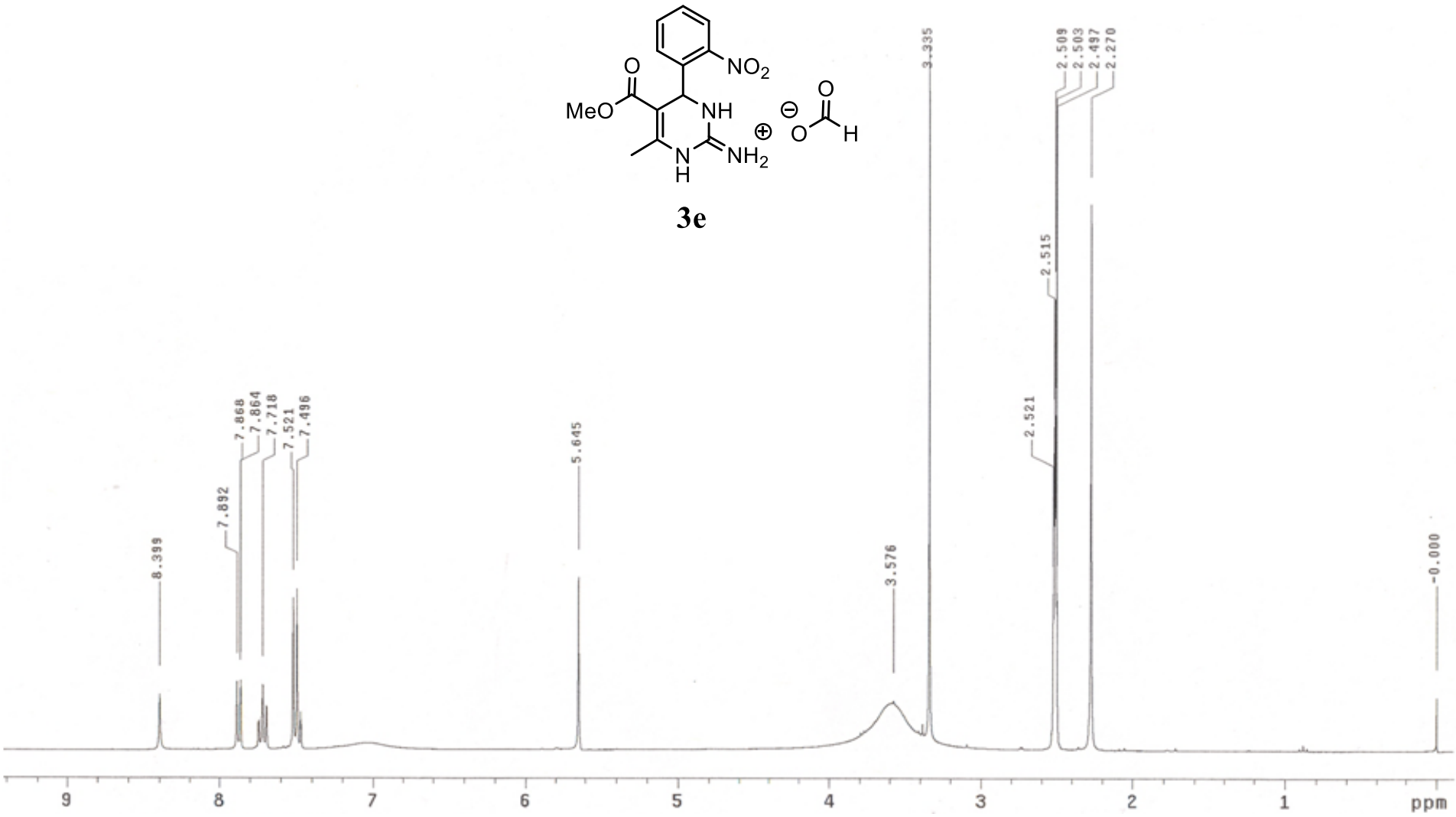

167.911
164.937
152.348
147.481
146.790
137.386
119.629
108.242
106.800
101.092
59.540
51.728
40.762
40.341
39.921
39.500
39.109
38.689
38.268
17.868
14.052
180
160
140
120
100
80
60
40
20
ppm


S
O
EtO
NH
N
H
NH2
O
O
H
3d
8.435
7.314
7.297
6.925
6.912
6.897
6.869
6.867
6.858
5.481
4.047
4.023
4.000
3.976
2.512
2.506
2.501
2.183
1.176
1.153
1.129
9
8
7
6
5
4
3
2
1
ppm

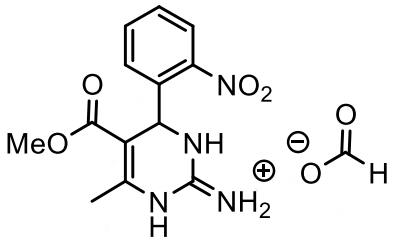
S
O
EtO
NH
N
H
NH2
O
O
H

3d

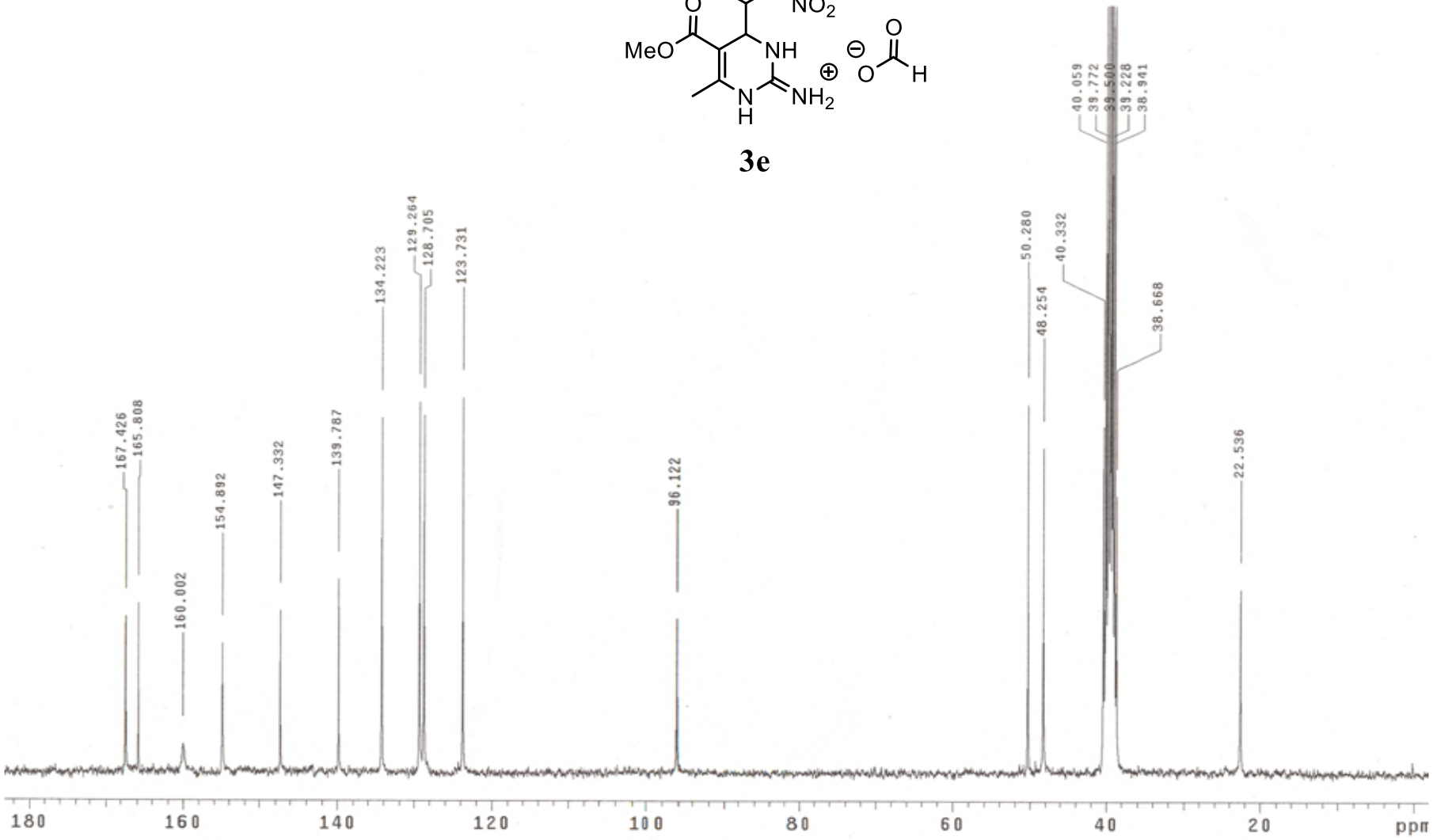

167.426
165.702
160.955
155.103
150.507
126.467
124.335
122.959
98.254
58.505
48.194
40.347
40.075
39.802
39.515
39.243
38.971
38.684
22.385
14.447
160
140
120
100
80
60
40
20
ppm

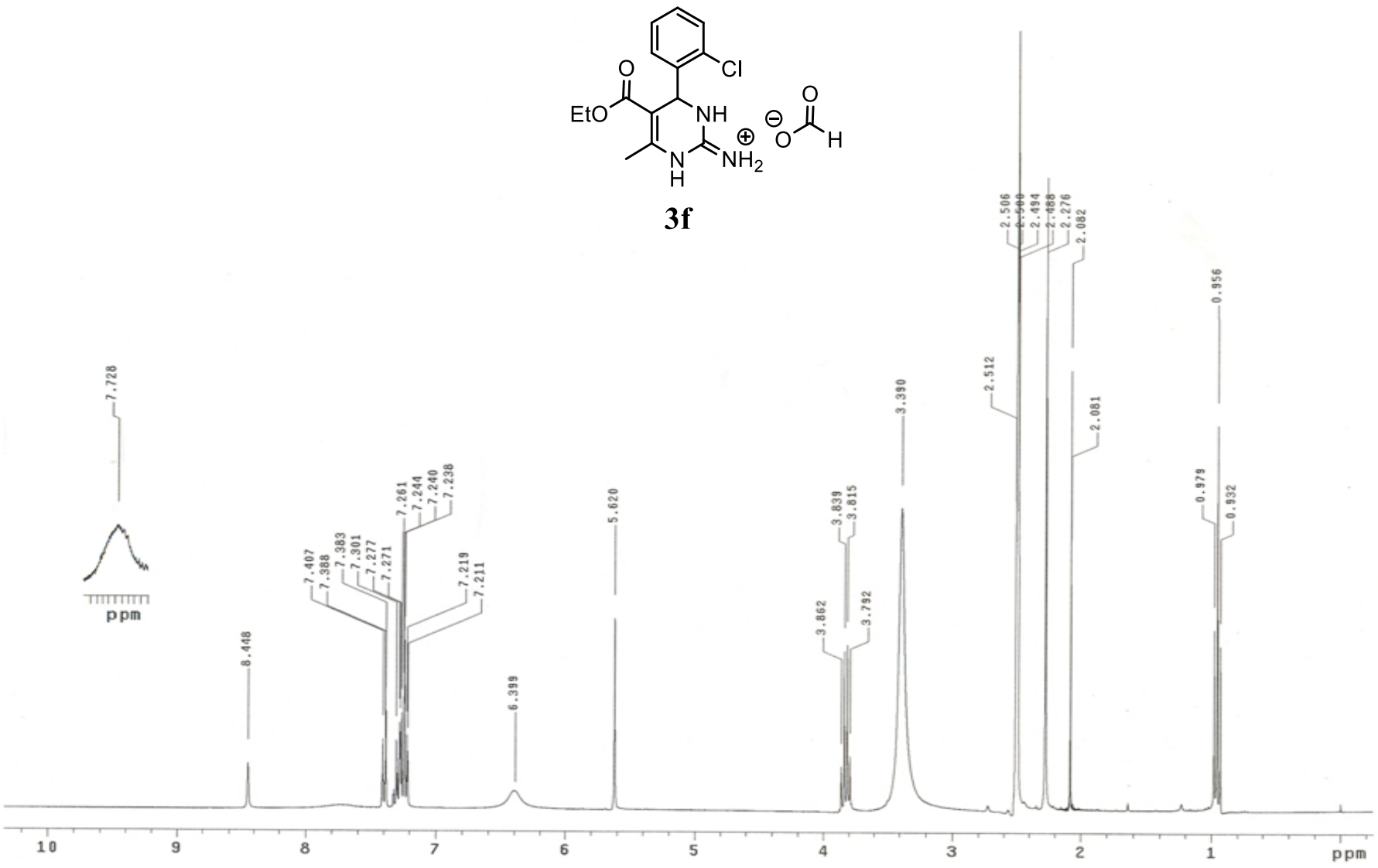

NO2
O
MeO
NH
N
H
NH2
O
O
H
8.399
7.892
7.868
7.864
7.718
7.521
7.496
5.645
3.576
3.335
2.521
2.515
2.509
2.503
2.497
2.270
-0.000
9
8
7
6
5
4
3
2
1
ppm

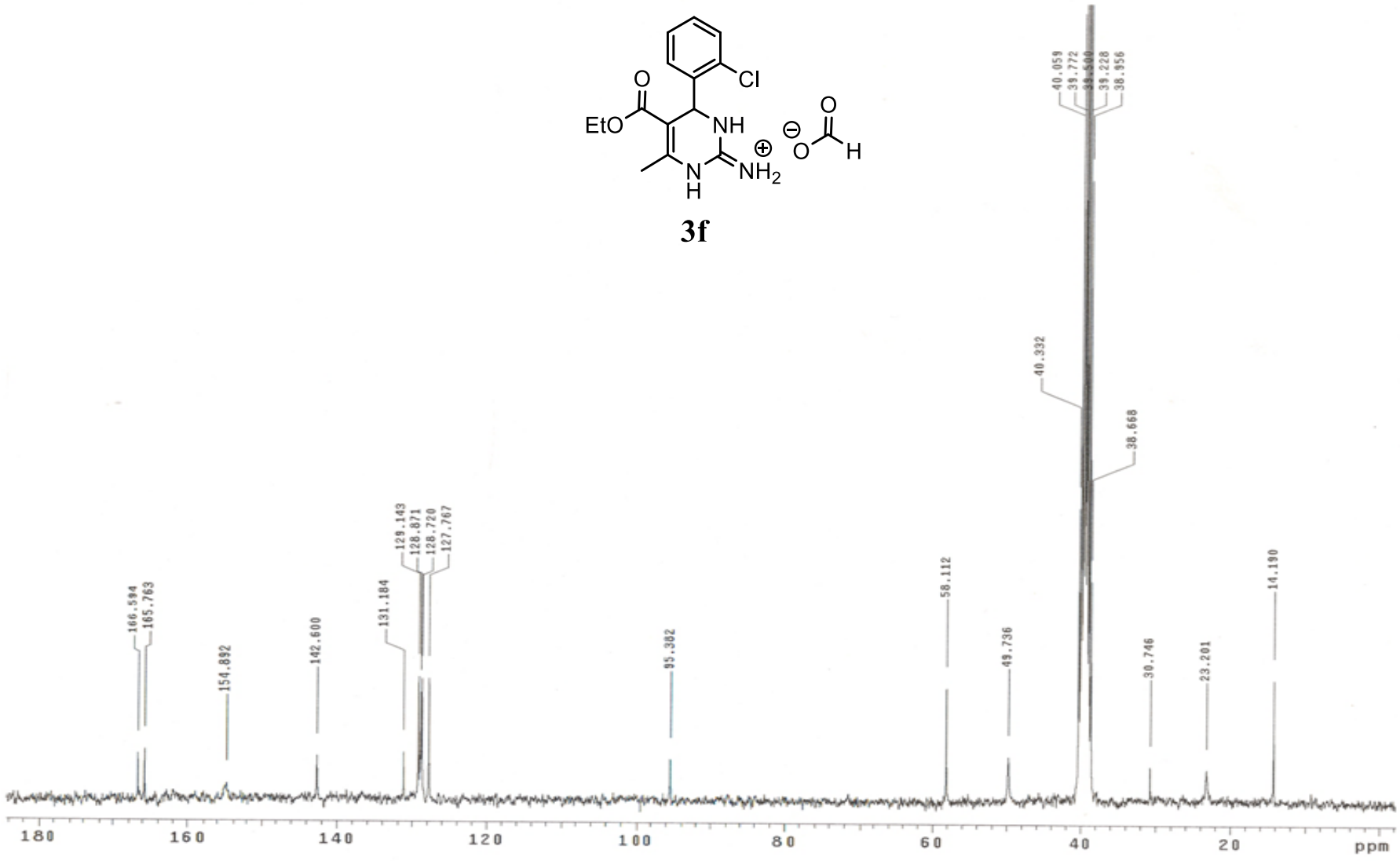
3e

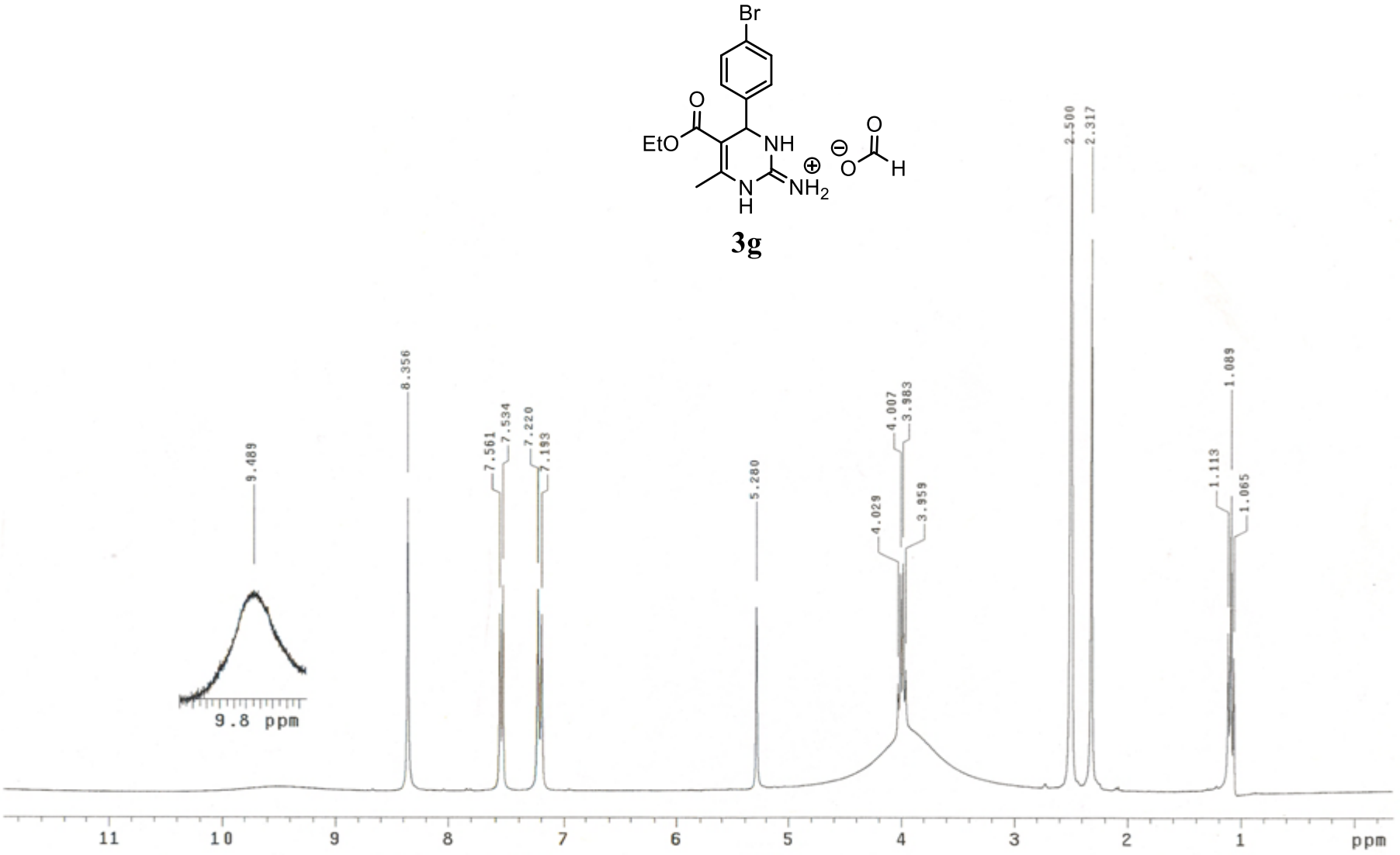

O
NO2
MeO
NH
O
O
H
N
H
NH2

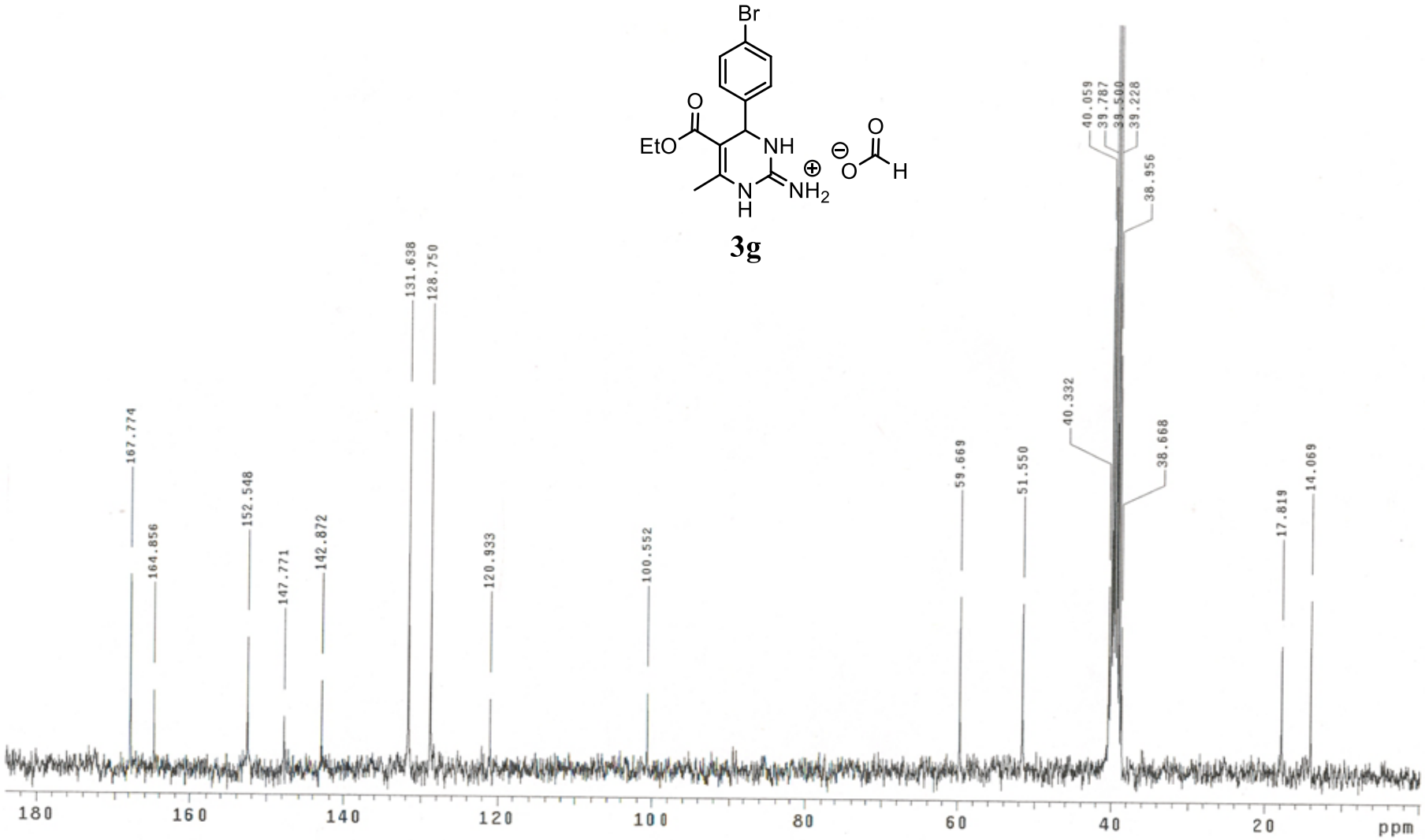
3e

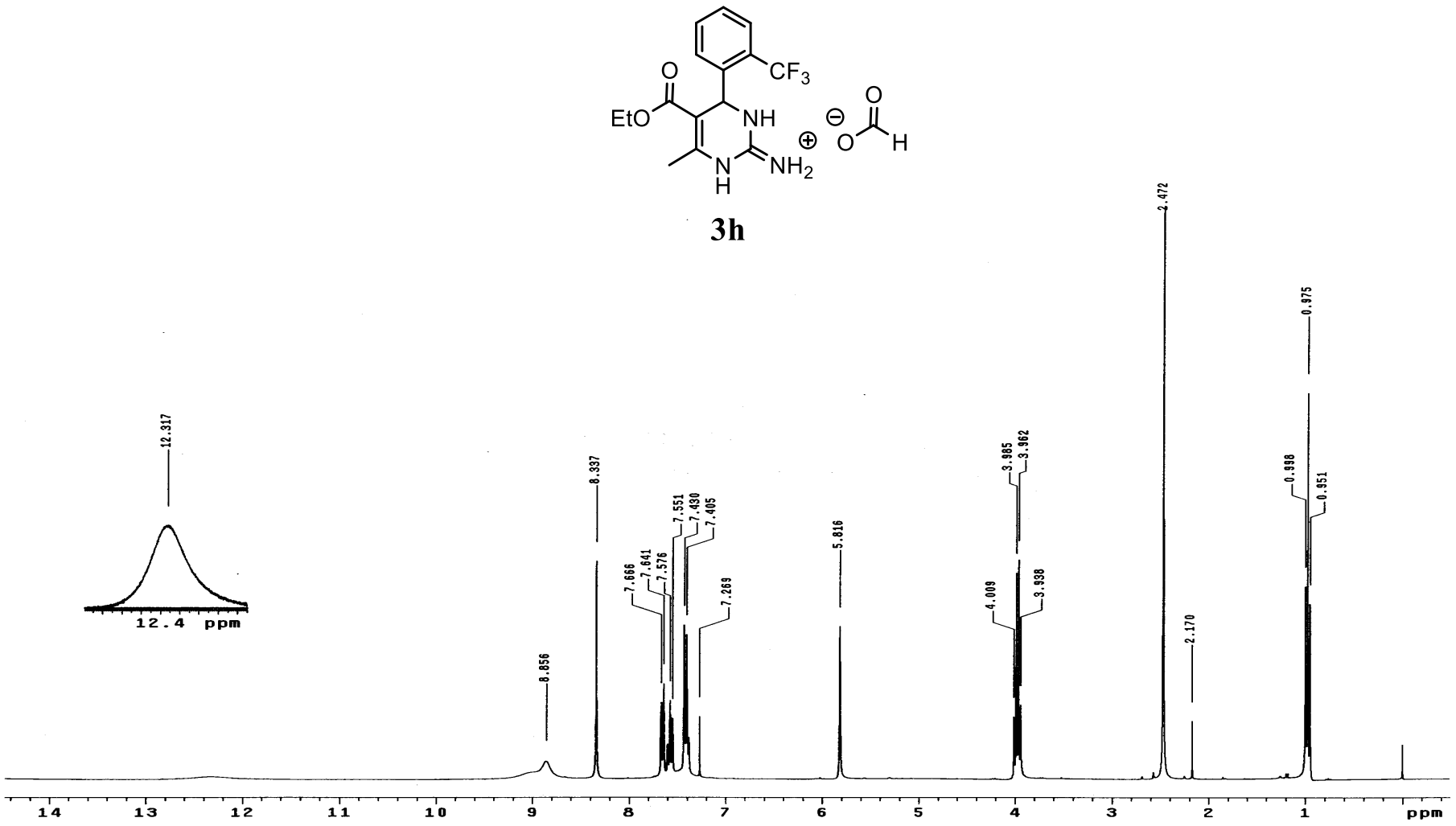

167.426
165.808
160.002
154.892
147.332
139.787
134.223
129.264
128.705
123.731
96.122
50.280
48.254
40.332
40.059
39.772
39.500
39.228
38.941
38.668
22.536
180
160
140
120
100
80
60
40
20
ppm

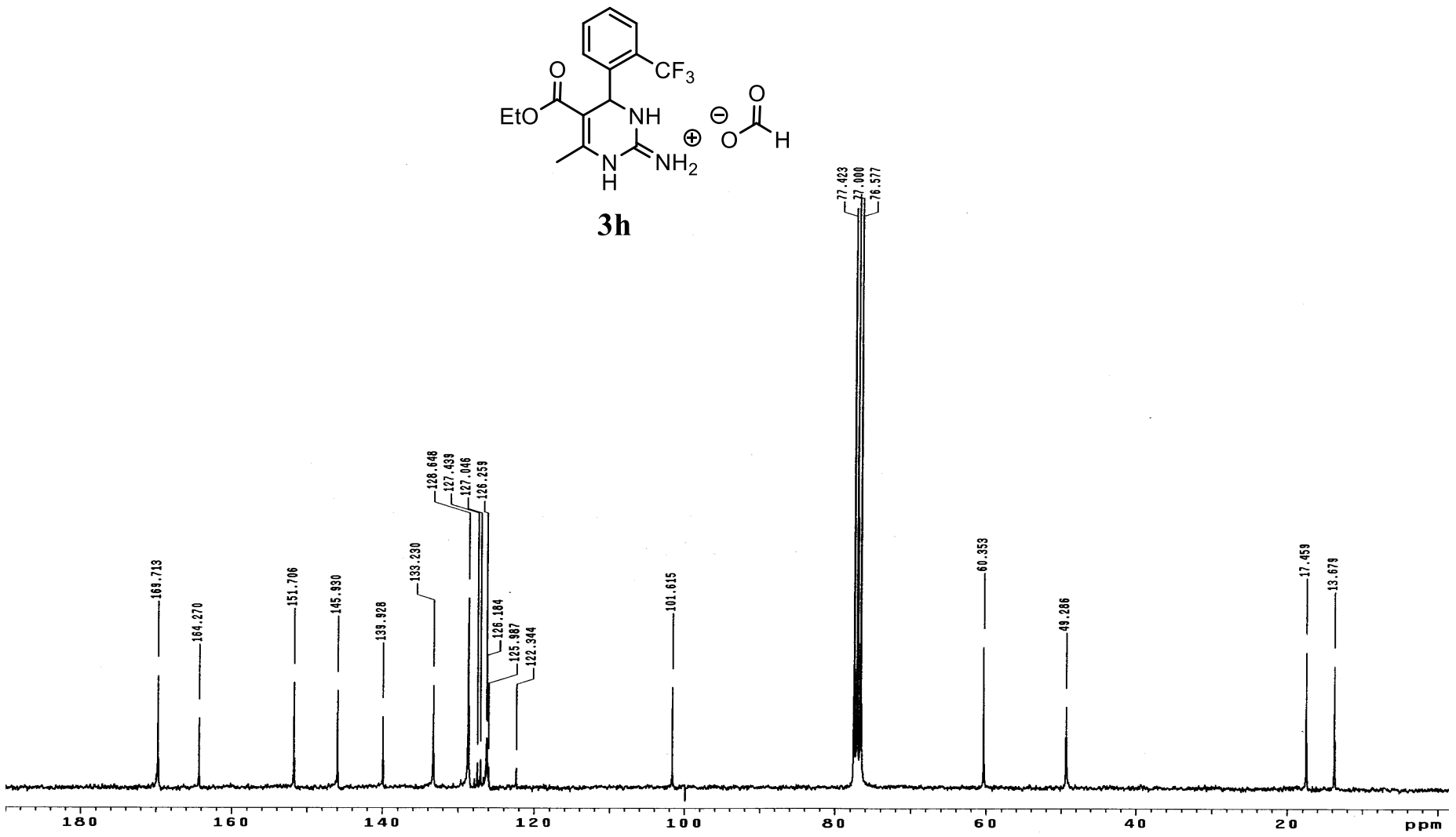

Cl
O
EtO
NH
O
H
N
H
NH2
3f
7.728
ppm
8.448
7.407
7.388
7.383
7.301
7.277
7.271
7.261
7.244
7.240
7.238
7.219
7.211
6.399
5.620
3.862
3.839
3.815
3.792
3.390
2.512
2.506
2.500
2.494
2.488
2.276
2.082
2.081
0.979
0.956
0.932
10
9
8
7
6
5
4
3
2
1
ppm

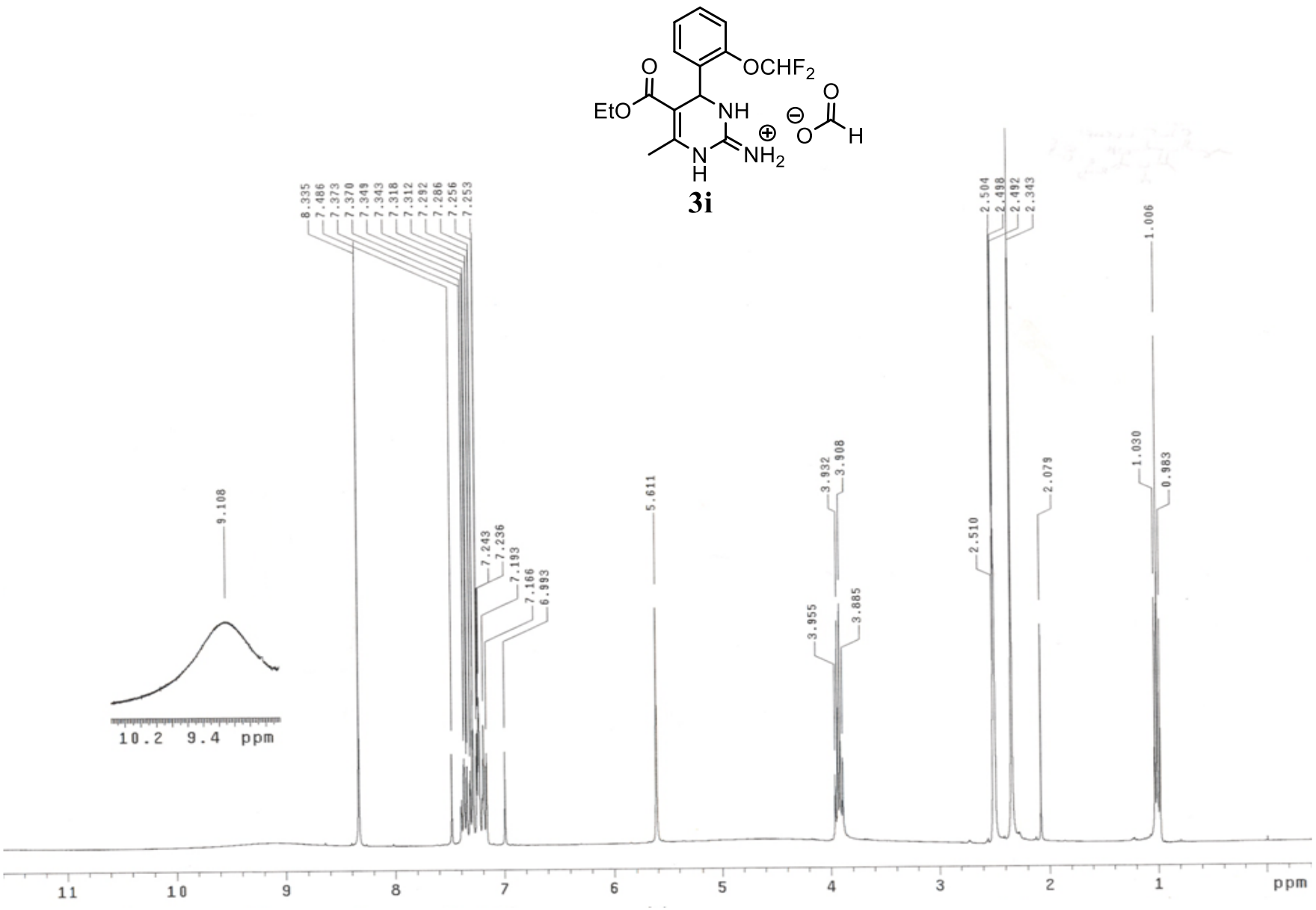

Cl
O
EtO
NH
O
O
H
N
H
NH2
3f
166.594
165.763
154.882
142.600
131.184
129.143
128.871
128.720
127.767
95.382
58.112
49.736
40.332
40.059
39.772
39.500
39.228
38.956
38.668
30.746
23.201
14.190
180
160
140
120
100
80
60
40
20
ppm

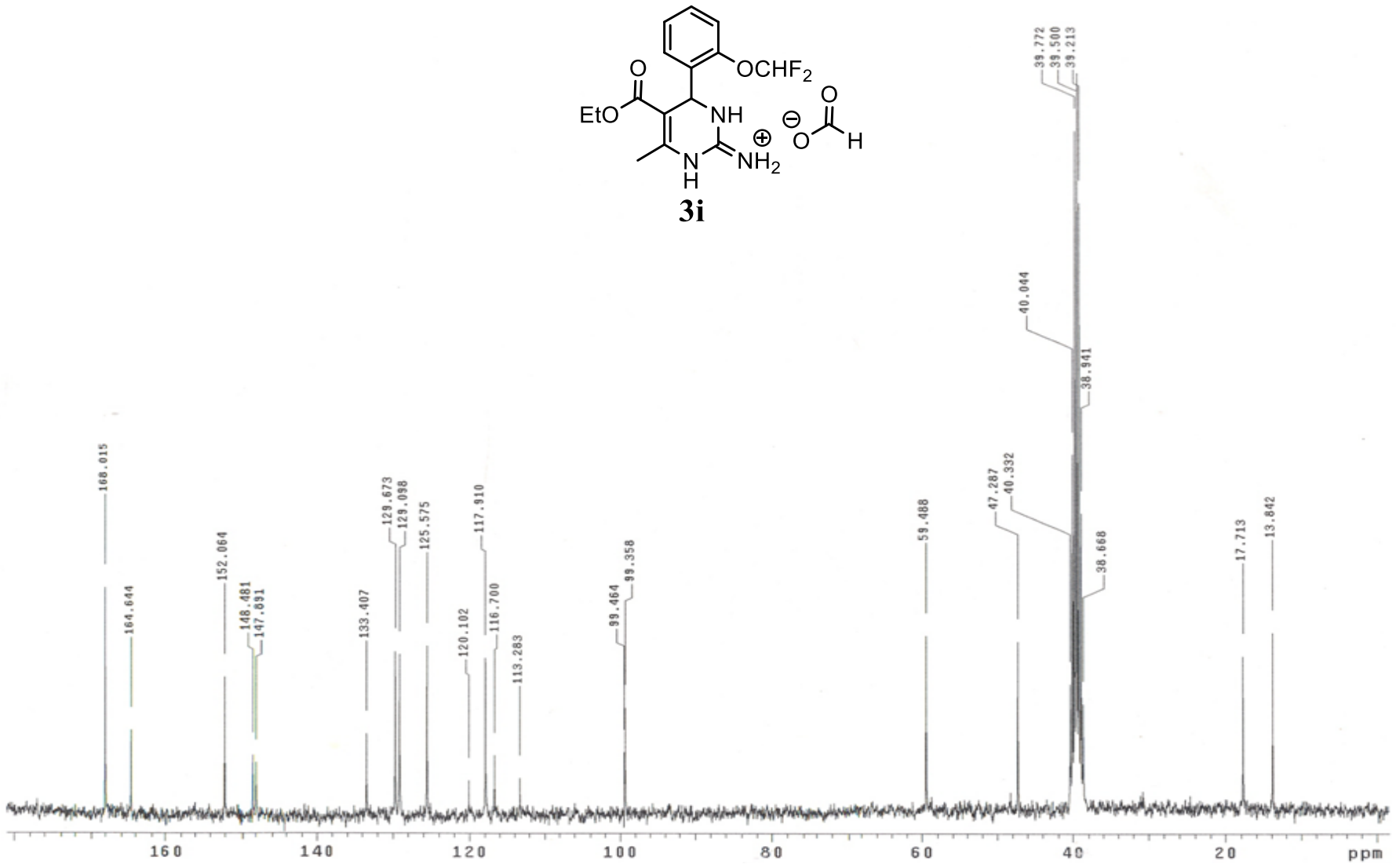

Br
O
EtO
NH
O
O
H
N
H
NH2
3g
9.489
8.356
7.561
7.534
7.220
7.193
5.280
4.029
4.007
3.983
3.959
2.500
2.317
1.113
1.089
1.065
9.8 ppm
11
10
9
8
7
6
5
4
3
2
1
ppm

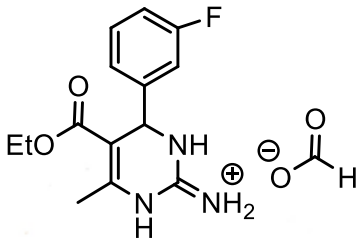

Br
O
EtO
NH
N
H
NH2
O
O
H
3g
167.774
164.856
152.548
147.771
142.872
131.638
128.750
120.933
100.552
59.669
51.550
40.332
40.059
39.787
39.500
39.228
38.956
38.668
17.819
14.069
180
160
140
120
100
80
60
40
20
ppm


3h
12.317
12.4 ppm
8.856
8.337
7.666
7.641
7.576
7.551
7.430
7.405
7.269
5.816
4.009
3.985
3.962
3.938
2.472
2.170
0.998
0.975
0.951
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

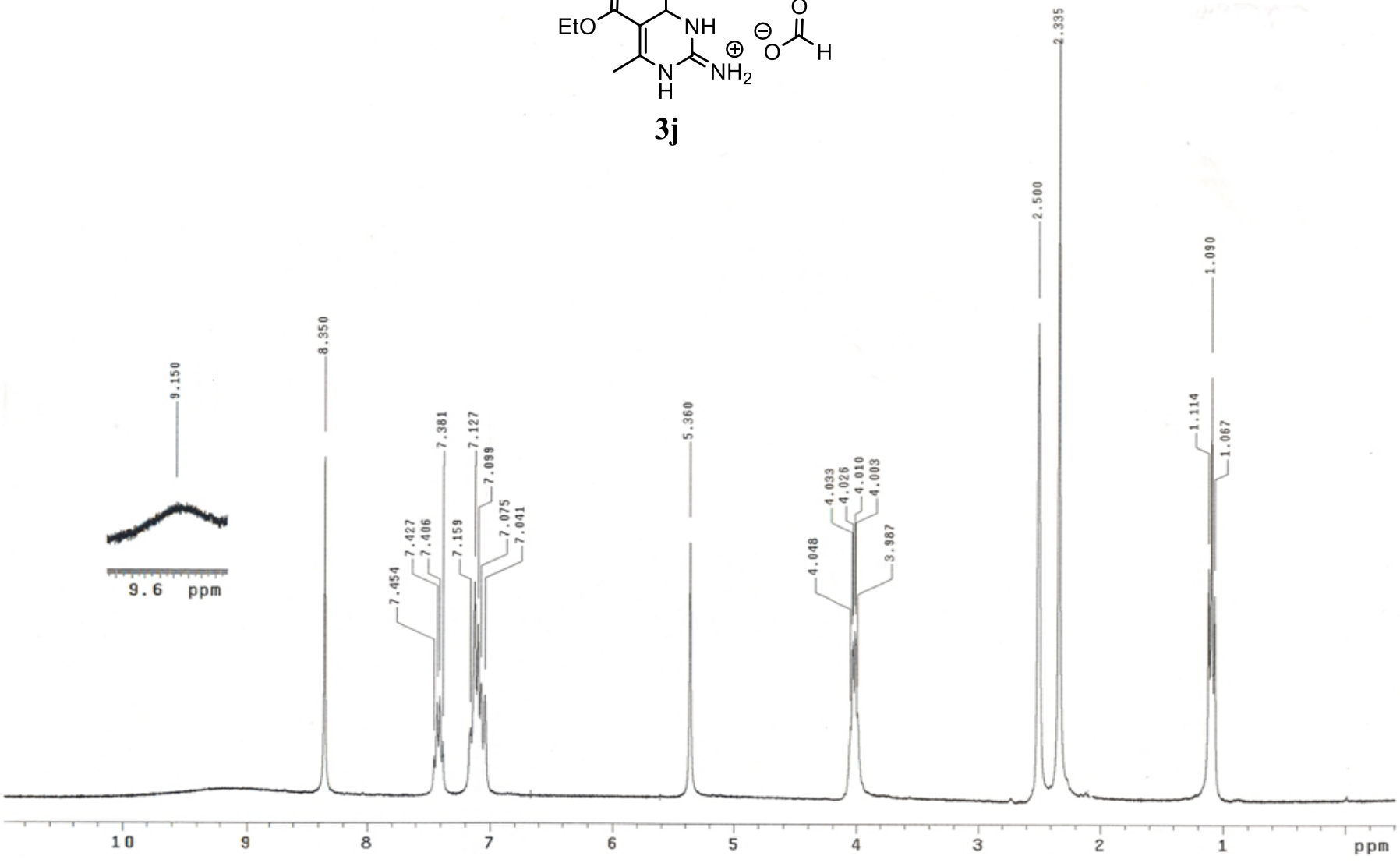

CF3
O
EtO
NH
NH2
N
H
O
O
H
3h
169.713
164.270
151.706
145.930
139.928
133.230
128.648
127.439
127.046
126.259
126.184
125.987
122.344
101.615
77.423
77.000
76.577
60.353
49.286
17.459
13.678
180
160
140
120
100
80
60
40
20
ppm

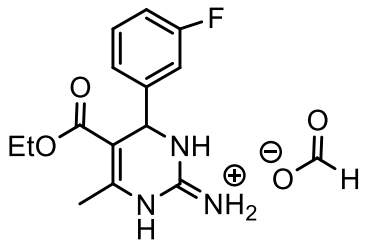

OCHF2
O
EtO
NH
O
O
H
N
H
NH2
3i
8.335
7.486
7.373
7.370
7.349
7.343
7.318
7.312
7.292
7.286
7.256
7.253
9.108
10.2 9.4 ppm
7.243
7.236
7.193
7.166
6.993
5.611
3.955
3.932
3.908
3.885
2.510
2.504
2.498
2.492
2.343
2.079
1.030
1.006
0.983
11 10 9 8 7 6 5 4 3 2 1 ppm


OCHF2
O
EtO
NH
O
O
H
N
H
NH2
3i
168.015
164.644
152.064
148.481
147.691
133.407
129.673
129.098
125.575
120.102
117.910
116.700
113.283
99.464
99.358
59.488
47.287
40.332
40.044
39.772
39.500
39.213
38.941
38.668
17.713
13.842
160
140
120
100
80
60
40
20
ppm

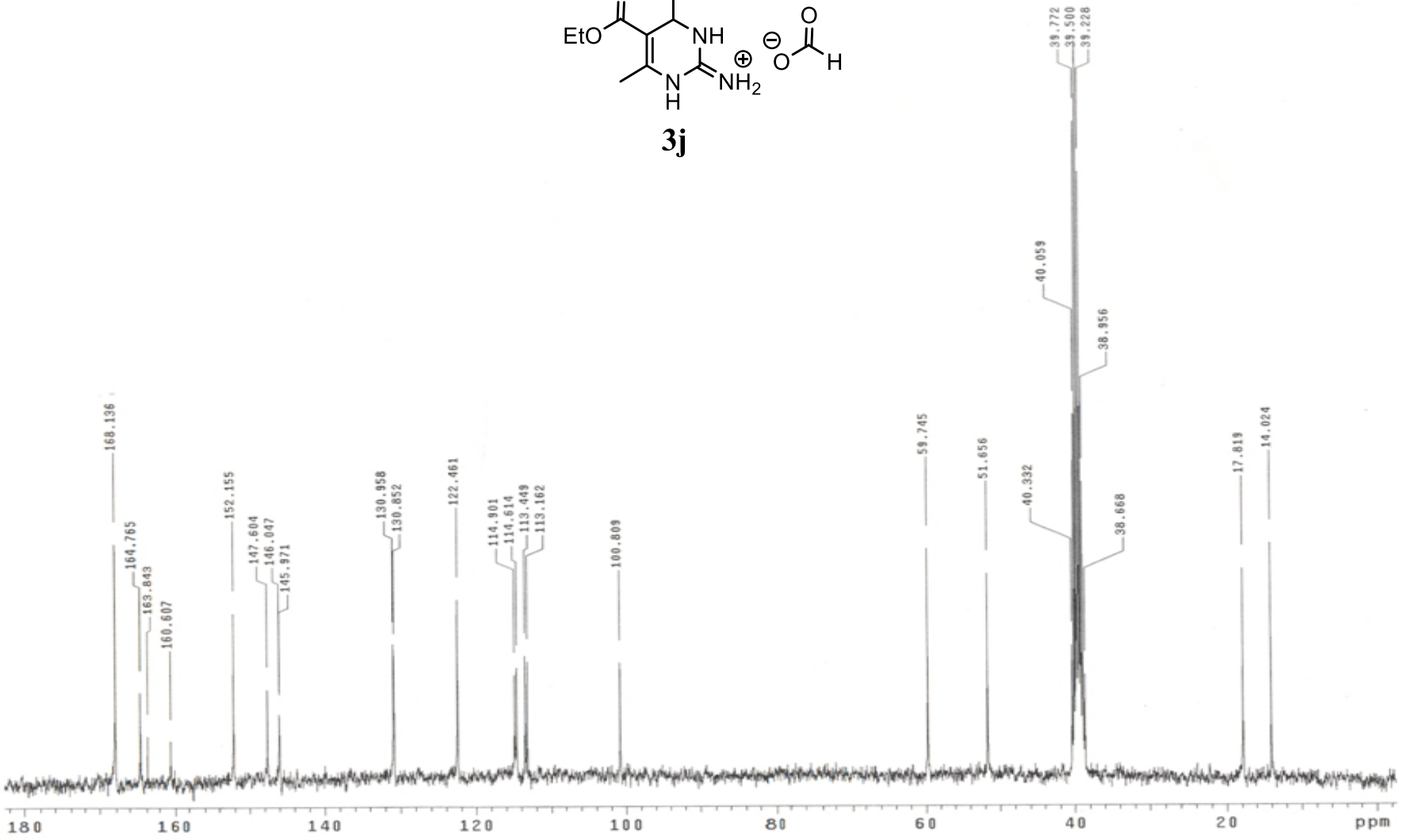

F
O
EtO
NH
O
O
H
N
H
NH2

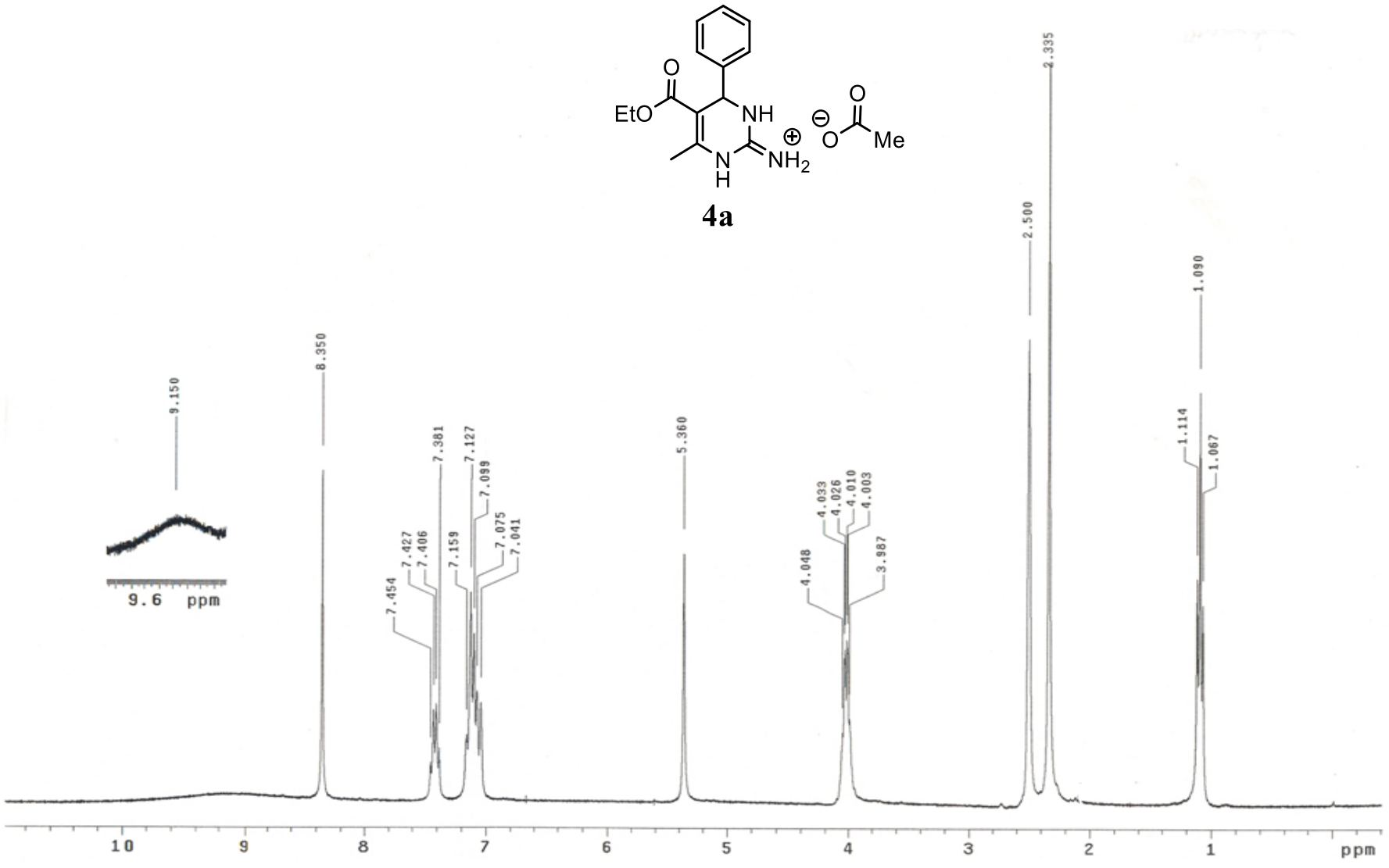
3j

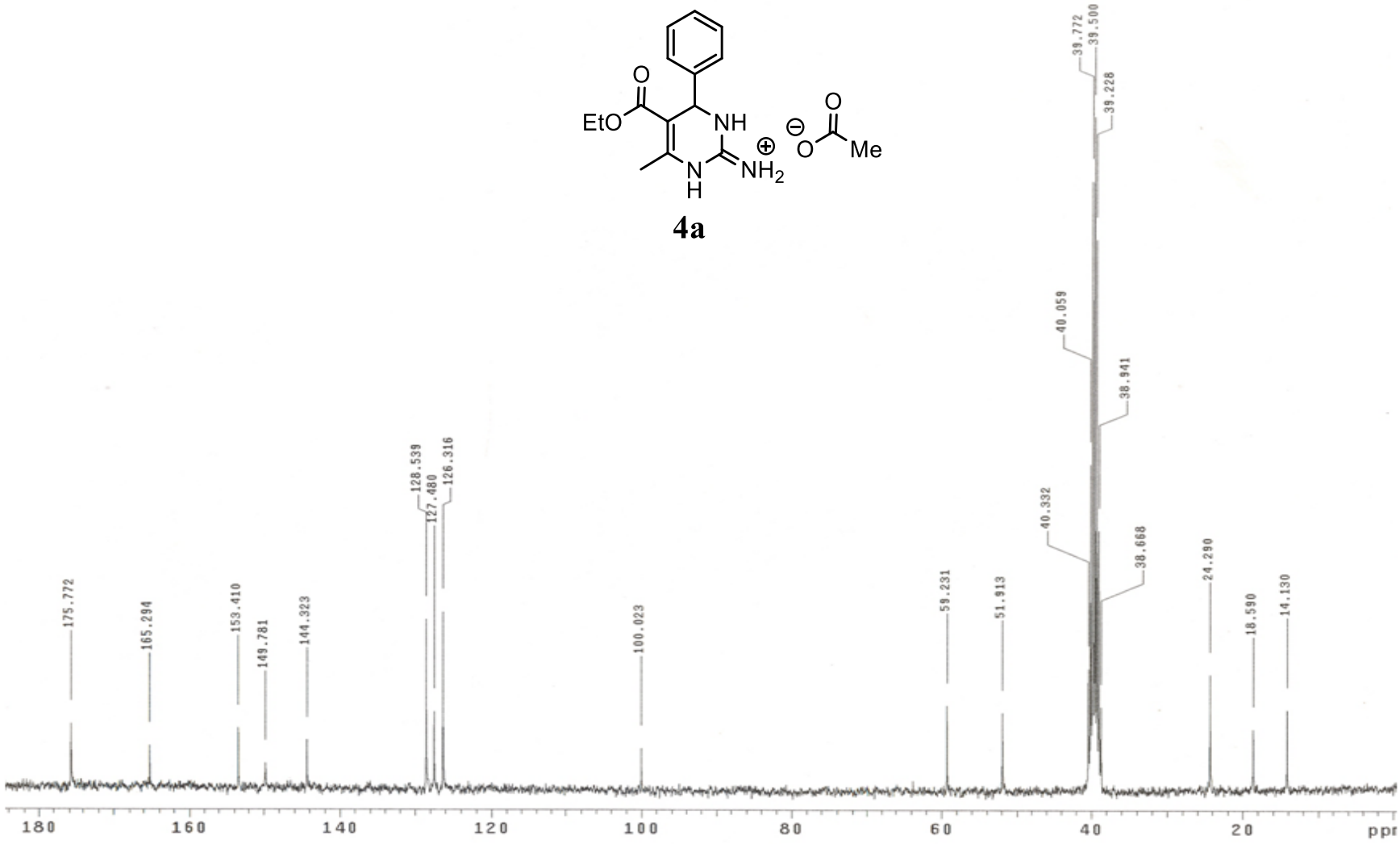

9.150
8.350
7.454
7.427
7.406
7.381
7.159
7.127
7.099
7.075
7.041
5.360
4.048
4.033
4.026
4.010
4.003
3.987
2.500
2.335
1.114
1.090
1.067
9.6 ppm
10
9
8
7
6
5
4
3
2
1
ppm

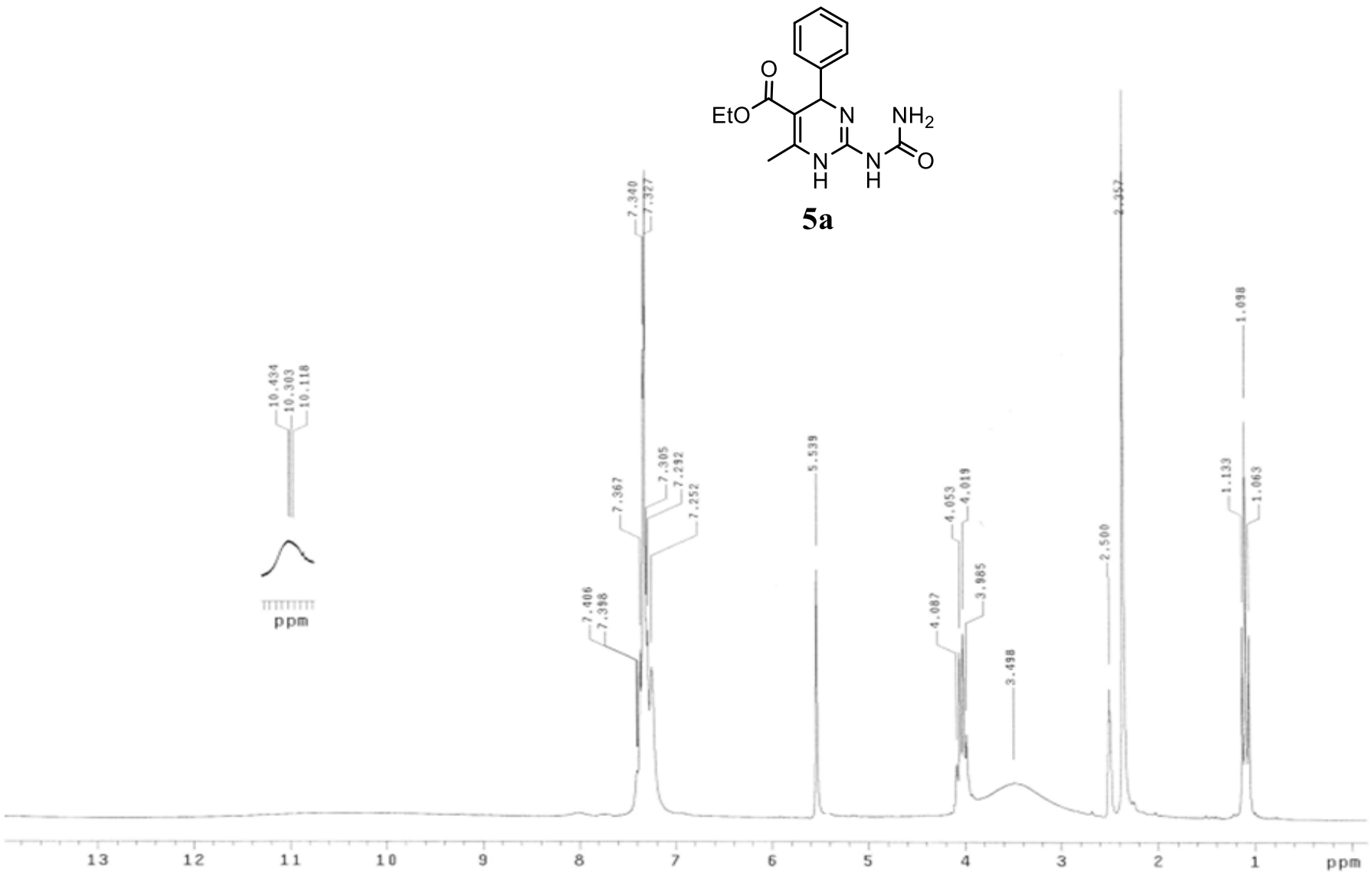

F
O
EtO
NH
O
O
H
N
H
NH2

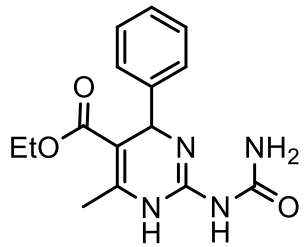
3j


168.136
164.765
163.843
160.607
152.155
147.604
146.047
145.971
130.958
130.852
122.461
114.901
114.614
113.449
113.162
100.809
59.745
51.656
40.332
40.059
39.772
39.500
39.228
38.956
38.668
17.819
14.024
180
160
140
120
100
80
60
40
20
ppm

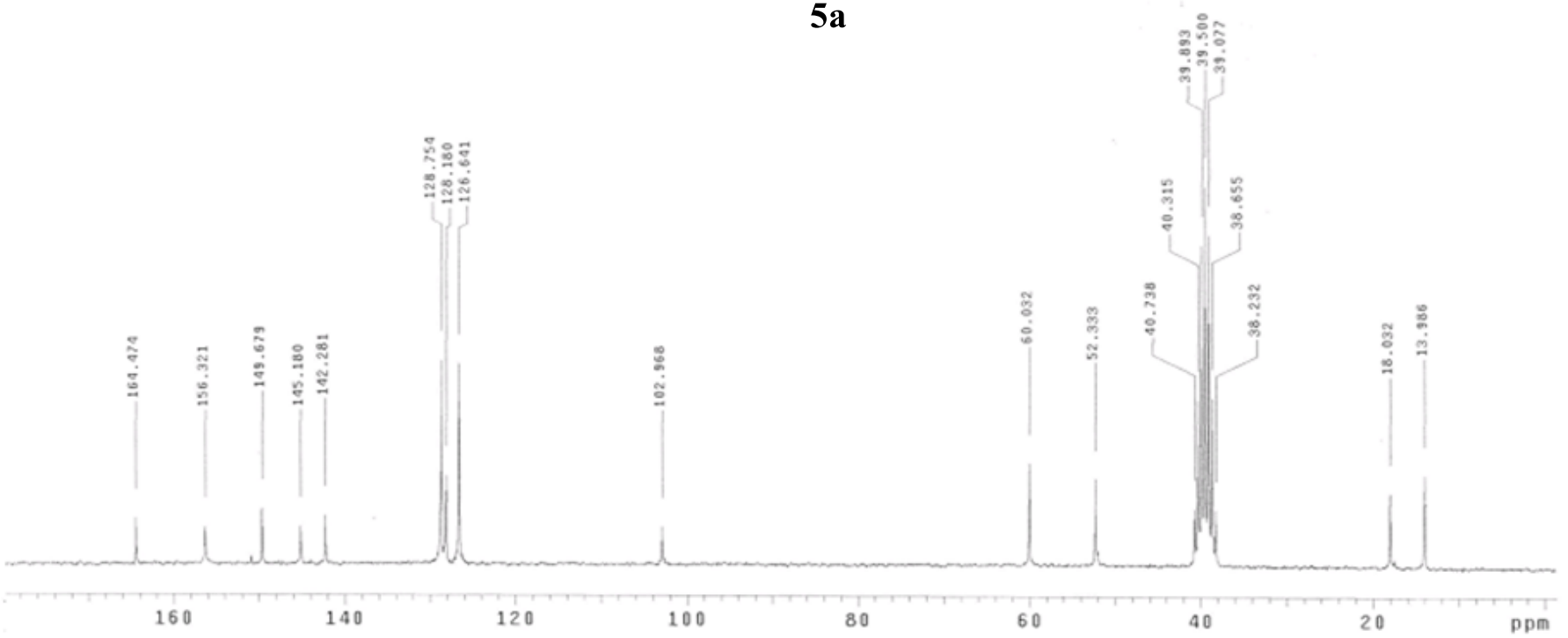

EtO
O
NH
N
H
NH2
O
O
Me
4a
9.150
8.350
7.454
7.427
7.406
7.381
7.159
7.127
7.099
7.075
7.041
5.360
4.048
4.033
4.026
4.010
4.003
3.987
2.500
2.335
1.114
1.090
1.067
9.6 ppm
10
9
8
7
6
5
4
3
2
1
ppm

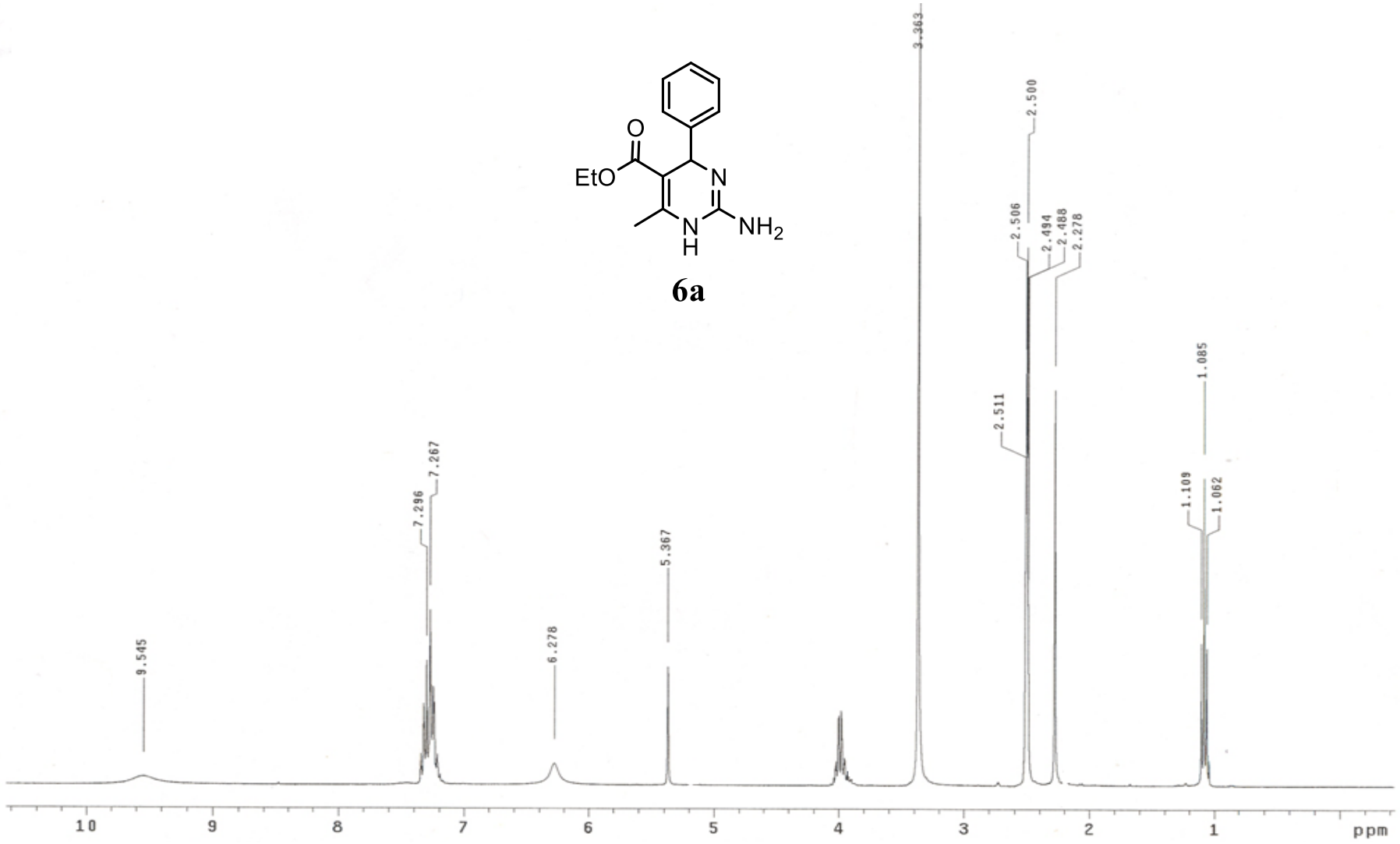

EtO
O
NH
N
H
NH2
O
O
Me
4a
175.772
165.294
153.410
149.781
144.323
128.539
127.480
126.316
100.023
59.231
51.913
40.332
40.059
39.772
39.500
39.228
38.941
38.668
24.290
18.590
14.130
180
160
140
120
100
80
60
40
20
ppm

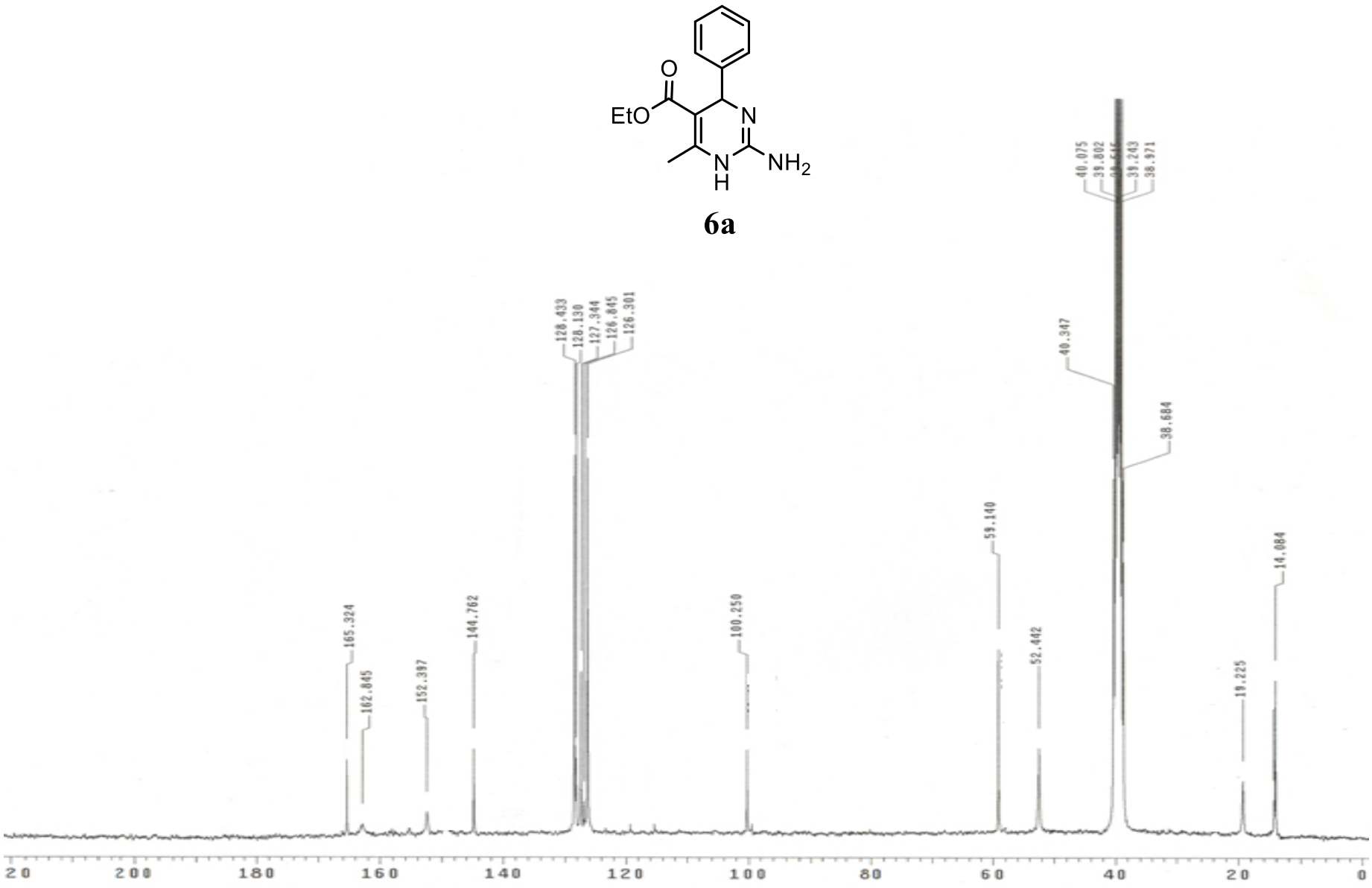

EtO
O
N
NH2
N
H
N
H
O
5a
10.434
10.303
10.118
ppm
7.406
7.398
7.367
7.340
7.327
7.305
7.292
7.252
5.539
4.087
4.053
4.019
3.985
3.498
2.500
2.352
1.133
1.098
1.063
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

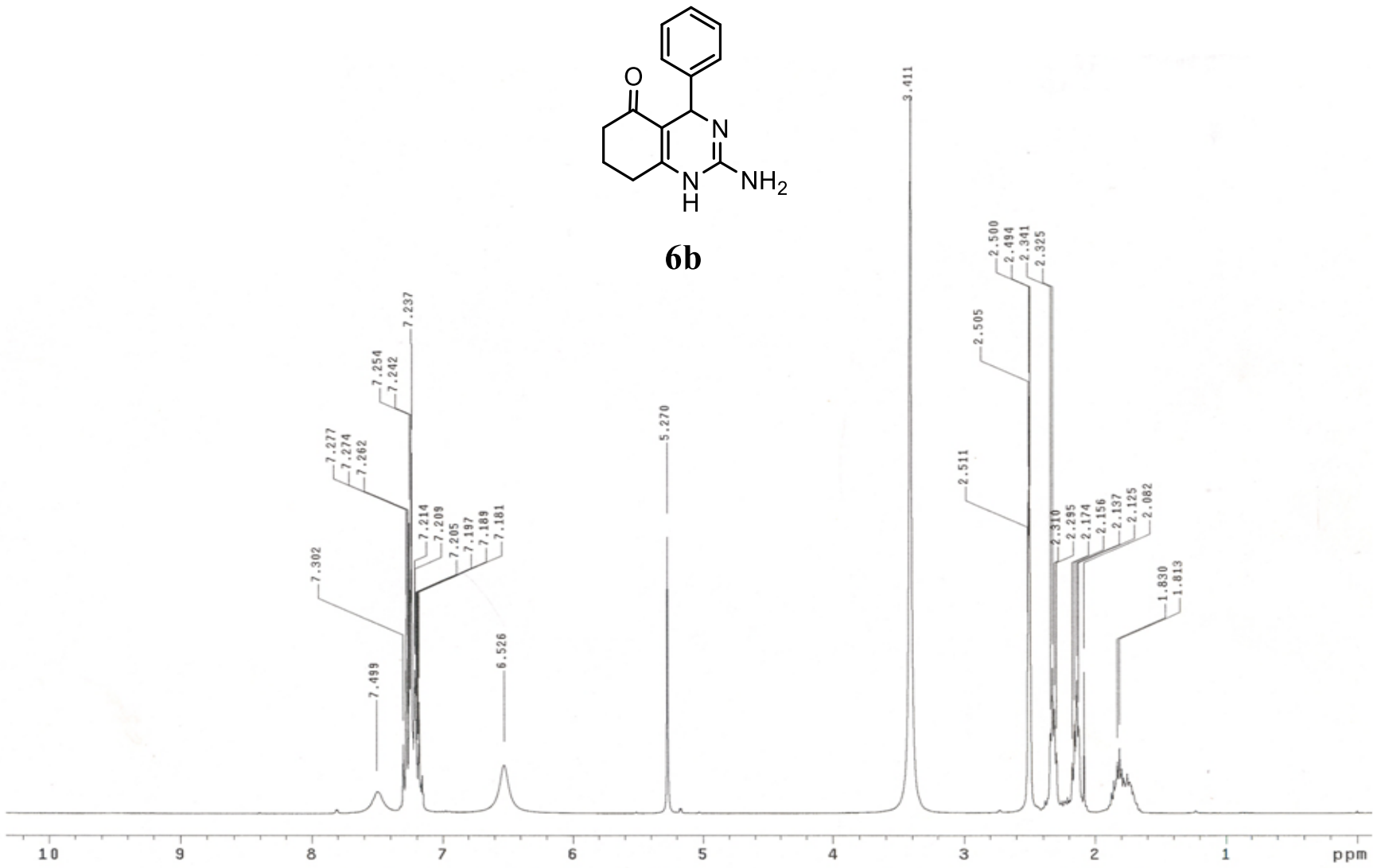

O
EtO
N
NH2
N
O
H
N
H

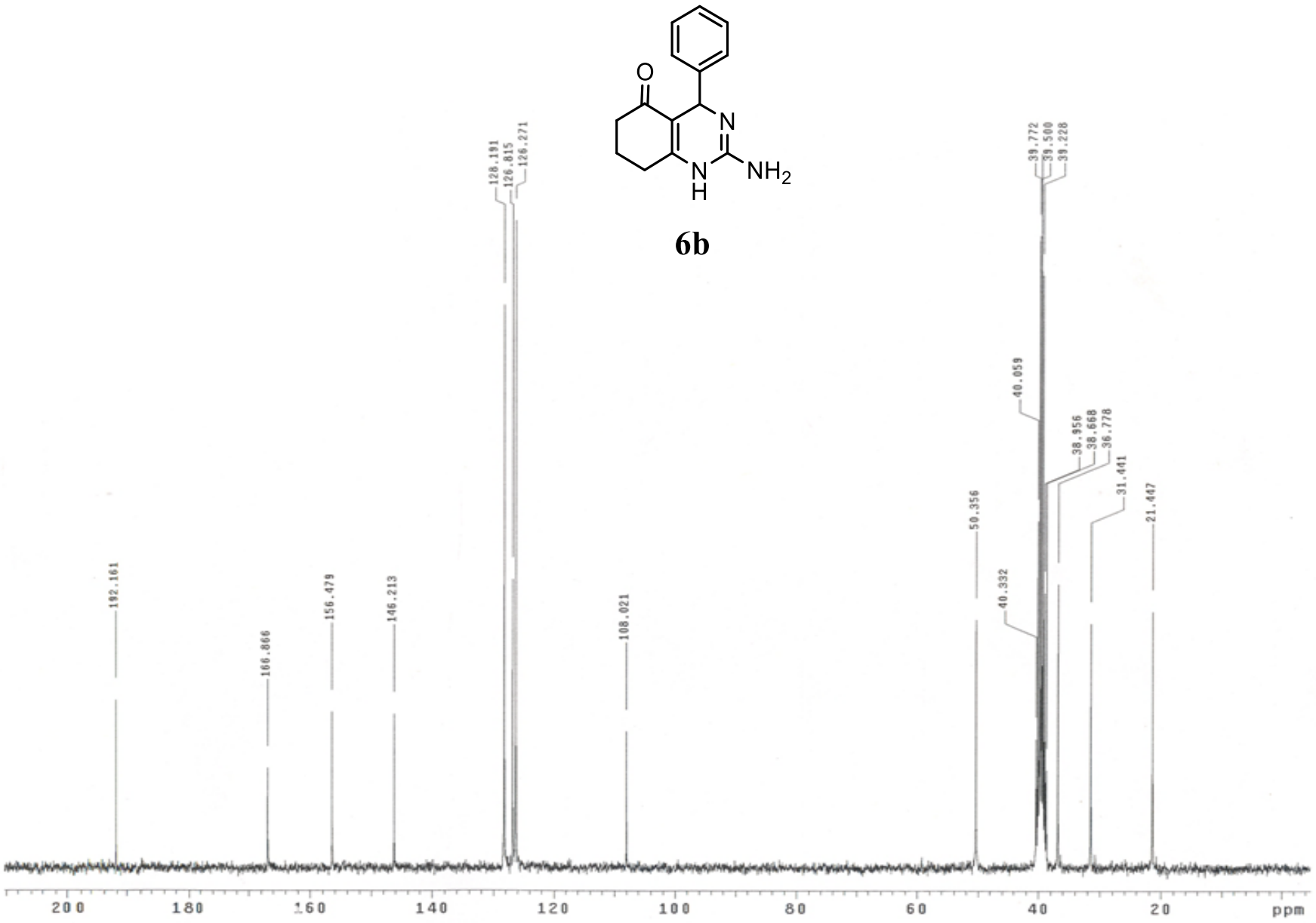
5a


164.474
156.321
149.679
145.180
142.281
128.754
128.180
126.641
102.968
60.032
52.333
40.738
40.315
39.893
39.500
39.077
38.655
38.232
18.032
13.986
160
140
120
100
80
60
40
20
ppm


O
EtO
N
N
H
NH2
6a
9.545
7.296
7.267
6.278
5.367
3.363
2.511
2.506
2.500
2.494
2.488
2.278
1.109
1.085
1.062
10
9
8
7
6
5
4
3
2
1
ppm


O
EtO
N
N
H
NH2
6a
165.324
162.845
152.397
144.762
128.433
128.130
127.344
126.845
126.301
100.250
59.140
52.442
40.347
40.075
39.802
39.243
38.971
38.684
19.225
14.084
20
200
180
160
140
120
100
80
60
40
20
0


O
N
N
H
NH2
6b
7.499
7.302
7.277
7.274
7.262
7.254
7.242
7.237
7.214
7.209
7.205
7.197
7.189
7.181
6.526
5.270
3.411
2.511
2.505
2.500
2.494
2.341
2.325
2.310
2.295
2.174
2.156
2.137
2.125
2.082
1.830
1.813
10
9
8
7
6
5
4
3
2
1
ppm

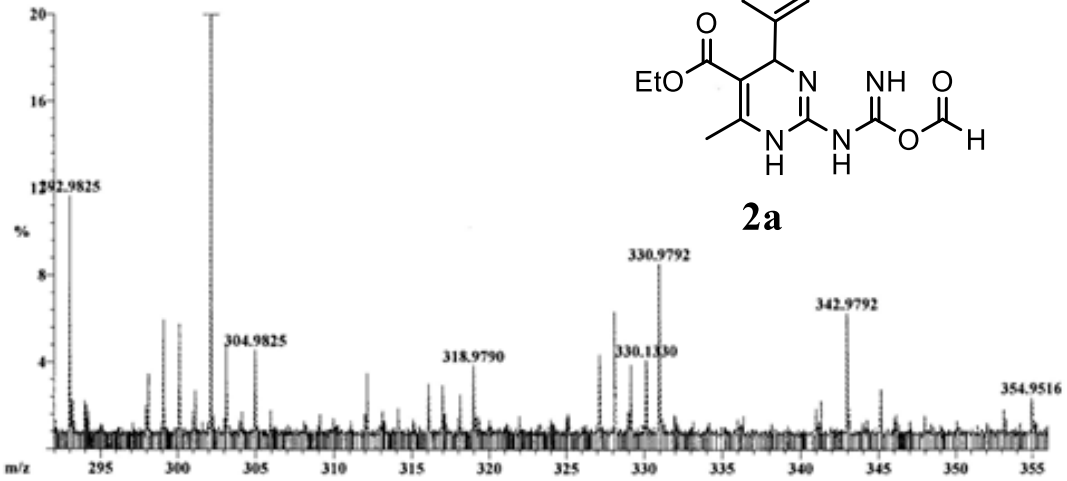

O
N
N
H
NH2
192.161
166.866
156.479
146.213
128.191
126.815
126.271
108.021
50.356
40.332
40.059
39.772
39.500
39.228
38.956
38.668
36.778
31.441
21.447
200
180
160
140
120
100
80
60
40
20
ppm

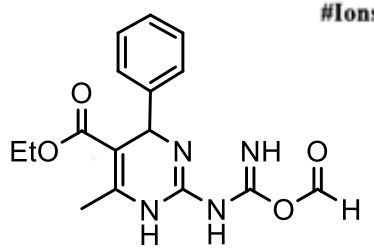
6b

Table of Contents

File: 19aP2
Sample: 19a
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 19-21 R.T.: .2
Base: m/z 259; 6.9%FS TIC: 1501170 #Ions: 1249





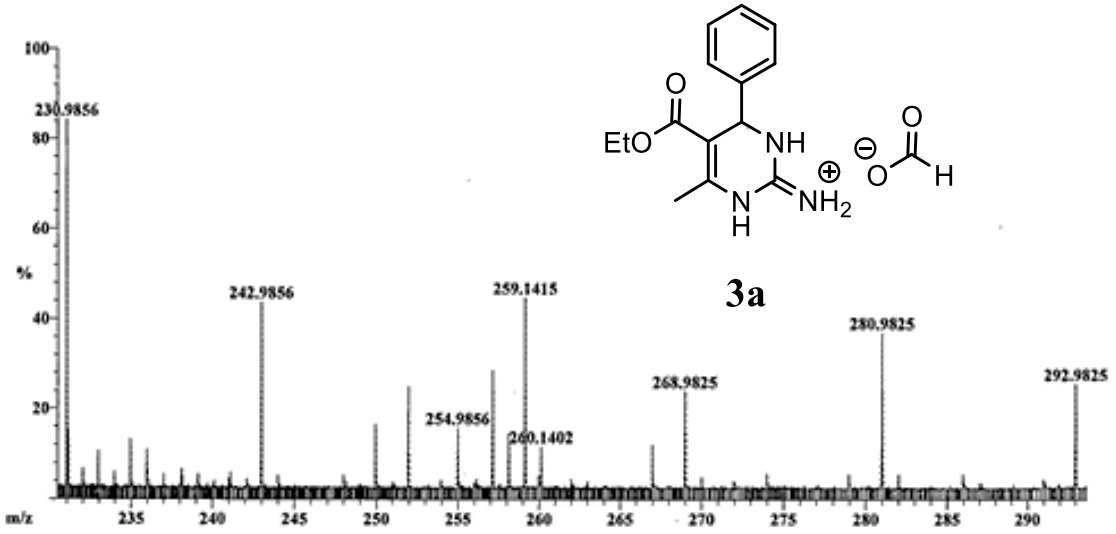
2a

Selected Isotopes : $N_{0-4}O_{0-4}C_{0-16}H_{0-18}$ Error Limit : 80 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
330.1330	4.1%	$C_{16}H_{18}N_4O_4$	330.1328	0.6

File: H5
Sample: H5
Instrument: JEOL GCmate
Inlet: Direct Probe **Ionization mode: EI+**

Scan: 53-61 **R.T.: .65**
Base: m/z 219; 1.9%FS TIC: 1064754 **#Ions: 1501**



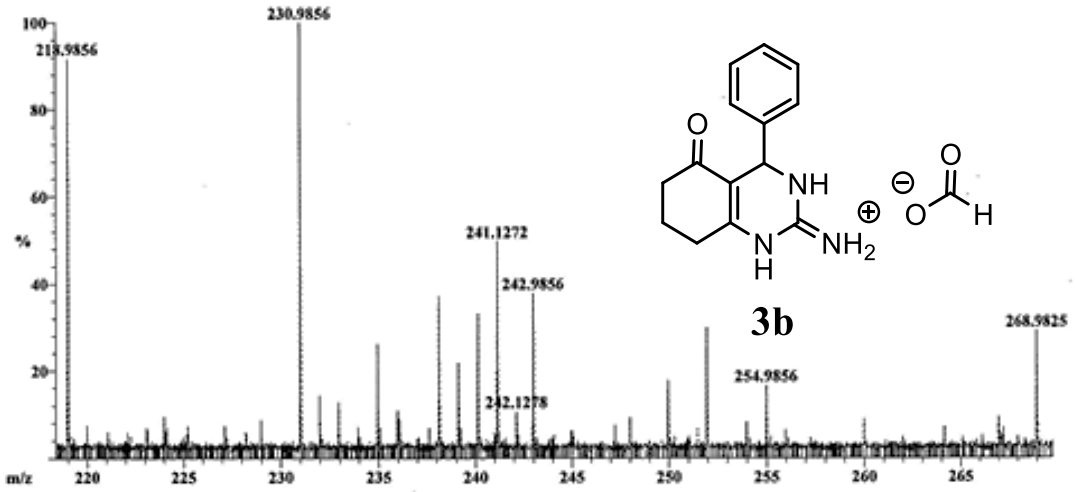
3a

Selected Isotopes : $N_{0-3}O_{0-2}C_{0-14}H_{0-18}$ **Error Limit : 50 ppm**

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
260.1402	11.6%	$C_{14}H_{18}N_3O_2$	260.1399	1.2

File: H2
Sample: H-2
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 130 R.T.: 1.49
Base: m/z 231; 2.6%FS TIC: 1456896 #Ions: 1355



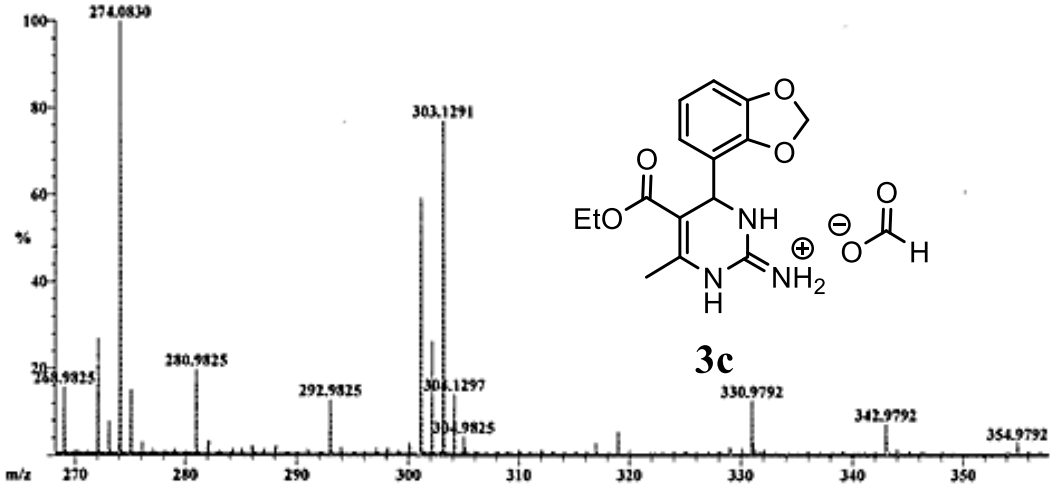
3b

Selected Isotopes : $N_{0-3}O_{0-1}C_{0-14}H_{0-16}$ Error Limit : 50 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
242.1278	10.7%	$C_{14}H_{16}N_3O$	242.1293	-6.4

File: 3
Sample: 3
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 56-58 R.T.: .57
Base: m/z 274; 11.6%FS TIC: 1658853 #Ions: 1182



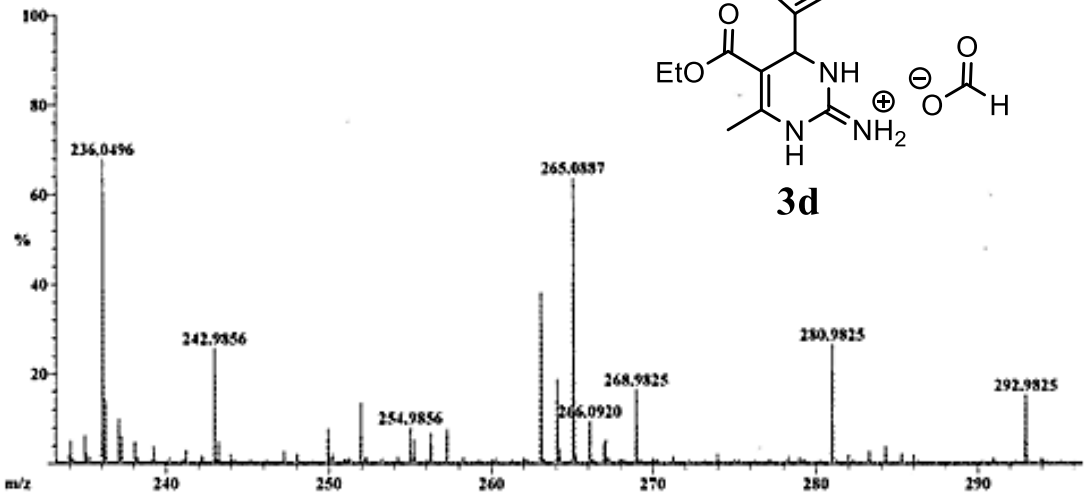
3c

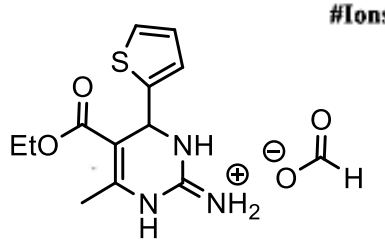
Selected Isotopes : $N_{0-3}O_{0-4}C_{0-15}H_{0-18}$ Error Limit : 20 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
304.1297	14.2%	$C_{15}H_{18}N_3O_4$	304.1297	-0.1

File: H-1
Sample: H-1
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 31-41 R.T.: .42
Base: m/z 218; 12.2%FS TIC: 1687362 #Ions: 1066



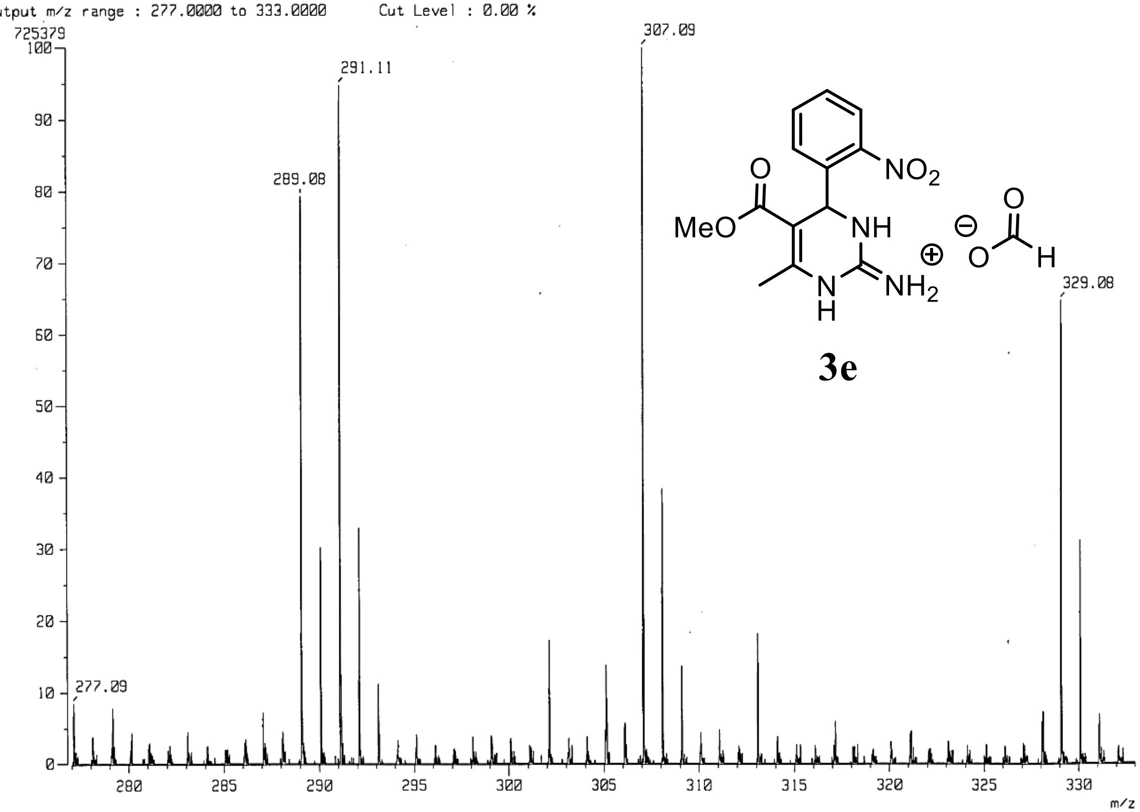


3d

Selected Isotopes : $N_{0-3}O_{0-2}C_{0-12}H_{0-16}S_{0-1}$ Error Limit : 20 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
266.0920	9.6%	$C_{12}H_{16}N_3O_2S$	266.0963	0.8

[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 42-STE-2507
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 8.74 min Scan# : 25
BP : m/z 307.0865 Int. : 69.18
Output m/z range : 277.0000 to 333.0000 Cut Level : 0.00 %

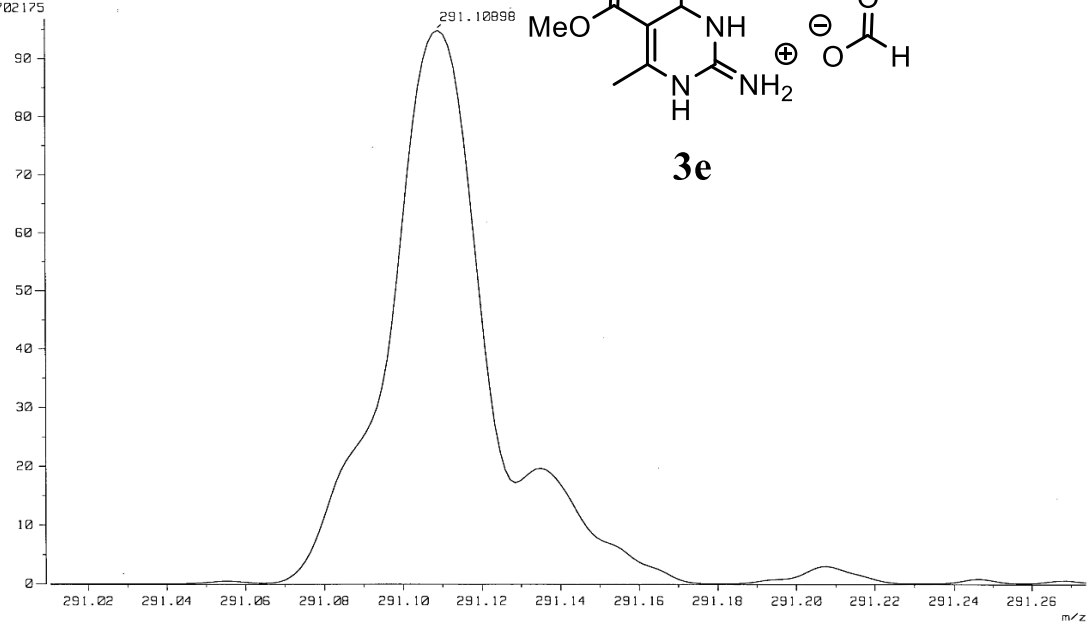


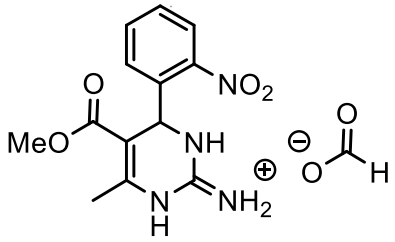
3e

[Elemental Composition]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 42-STE-2507
Note :
Inlet : Direct Ion Mode : FAB+
RT : 8.74 min Scan#: 25
Elements : C 40/0, H 49/0, O 5/1, N 4/1
Mass Tolerance : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z	Int%					
291.1090	94.8					
Estimated m/z	Error[ppm]	U.S.	C	H	O	N
291.1093	-1.2	8.5	13	15	4	4

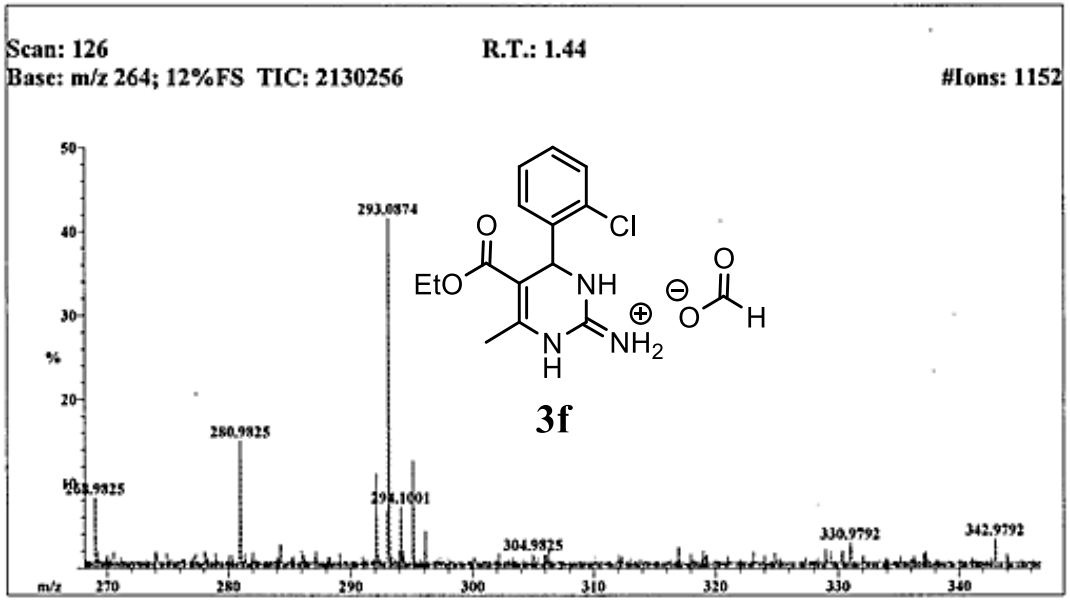
[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 42-STE-2507
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 8.74 min Scan# : 25
BP : m/z 307.0865 Int. : 69.18
Output m/z range : 291.0103 to 291.2737 Cut Level : 0.00 %





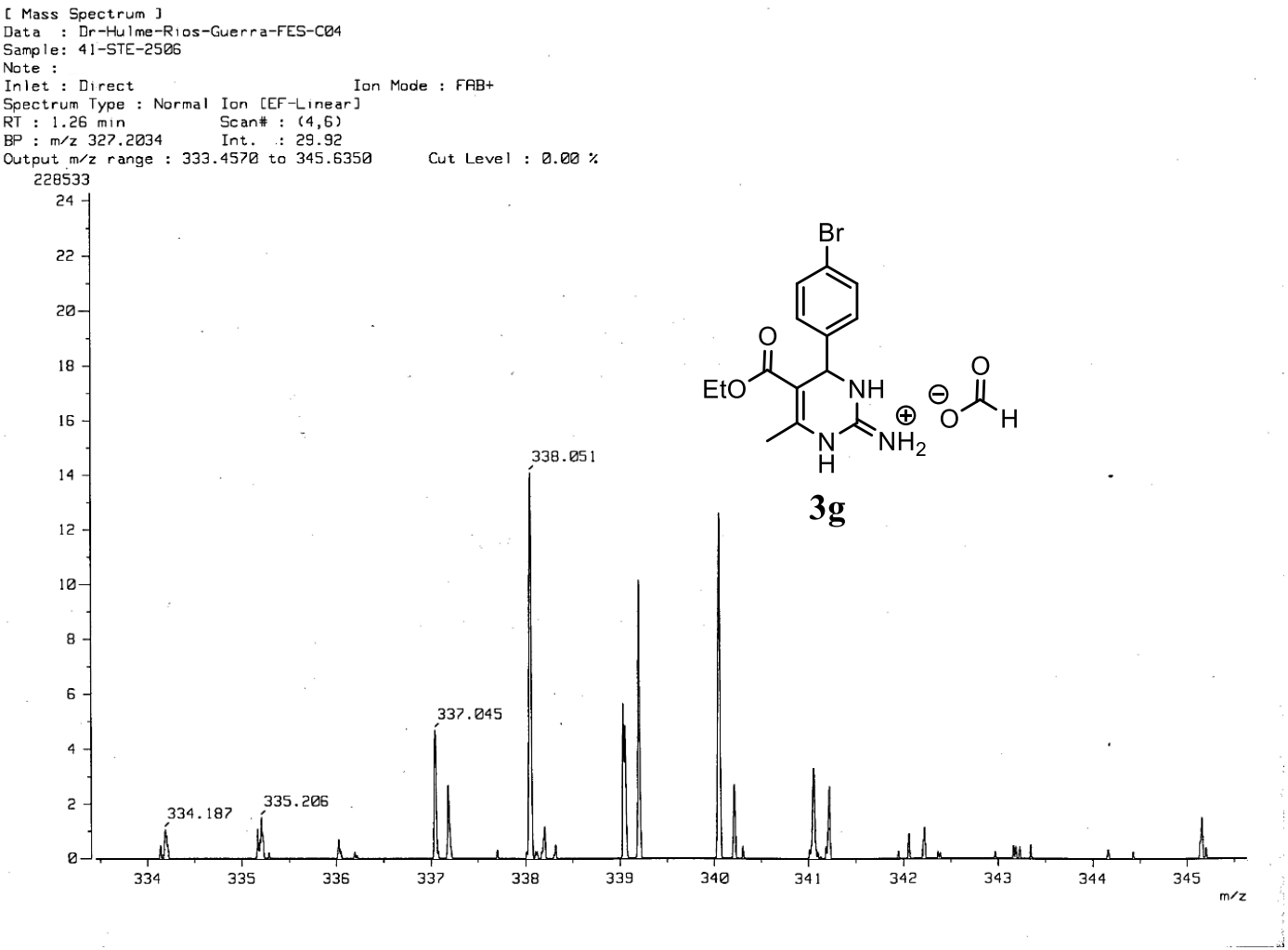
3e

File: A-P2
Sample: A
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+



Selected Isotopes : $N_{0-3}O_{0-2}Cl_{0-1}H_{0-17}C_{0-14}$ Error Limit : 50 ppm

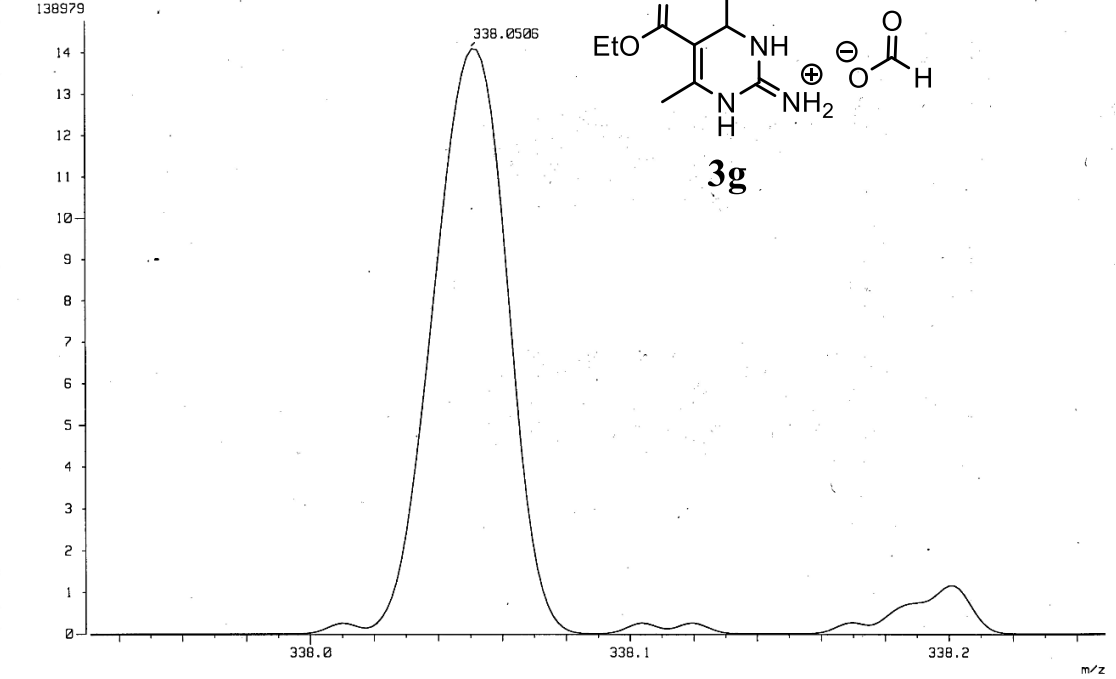
Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
294.1001	7.3%	$C_{14}H_{17}N_3O_2Cl$	294.1009	-2.8

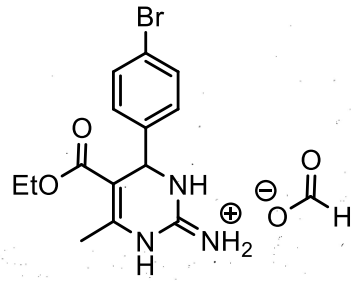

[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C04
Sample: 41-STE-2506
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 1.26 min Scan# : (4,6)
BP : m/z 327.2034 Int. : 29.92
Output m/z range : 333.4570 to 345.6350 Cut Level : 0.00 %
228533
338.051
337.045
335.206
334.187
m/z
Br
EtO
NH
NH2
3g

[Elemental Composition]
Data : Dr-Hulme-Rios-Guerra-FES-C04
Sample: 41-STE-2506
Note :
Inlet : Direct Ion Mode : FAB+
RT : 1.26 min Scan#: (4,6)
Elements : C 40/0, H 49/0, O 8/1, N 4/1, Br 2/0
Mass Tolerance : 1000ppm, 3mmu if m/z > 3
Unsaturation (U.S.) : 4.0 - 9.0

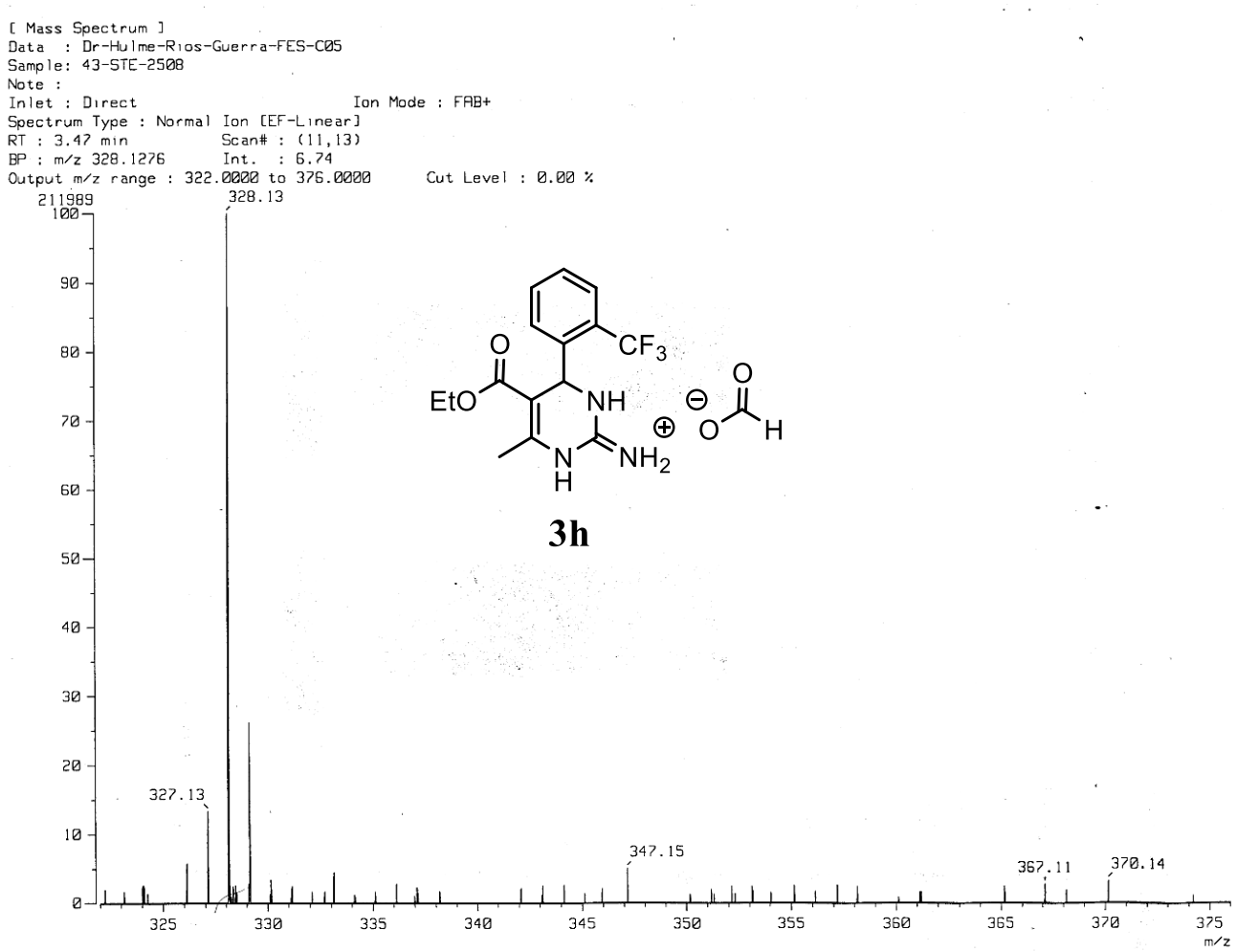
Observed m/z	Int%						
338.0506	14.1						
Estimated m/z	Error[ppm]	U.S.	C	H	O	N	Br
338.0504	+0.6	7.5	14	17	2	3	1

[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C04
Sample: 41-STE-2506
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 1.26 min Scan# : (4,6)
BP : m/z 327.2034 Int. : 29.92
Output m/z range : 337.9308 to 338.2488 Cut Level : 0.00 %





3g

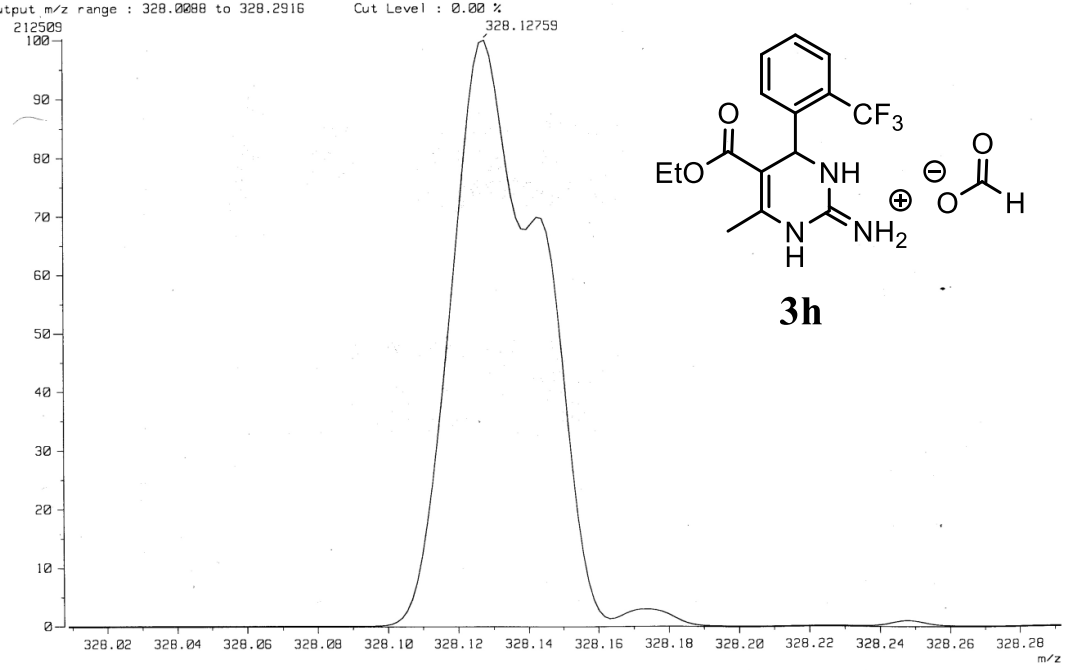

[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 43-STE-2508
Note :
Inlet : Direct
Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 3.47 min
Scan# : (11,13)
BP : m/z 328.1276
Int. : 6.74
Output m/z range : 322.0000 to 376.0000
Cut Level : 0.00 %
211989
328.13
327.13
347.15
367.11
370.14
m/z

3h

[Elemental Composition]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 43-STE-2508
Note :
Inlet : Direct Ion Mode : FAB+
RT : 3.47 min Scan#: (11,13)
Elements : C 40/0, H 49/0, O 5/1, N 4/1, F 4/0
Mass Tolerance : 1000ppm, 3mmu if m/z > 3
Unsaturation (U.S.) : 4.0 - 8.0

Observed m/z	Int%						
328.1276	100.0						
Estimated m/z	Error[ppm]	U.S.	C	H	O	N	F
328.1273	+0.9	7.5	15	17	2	3	3

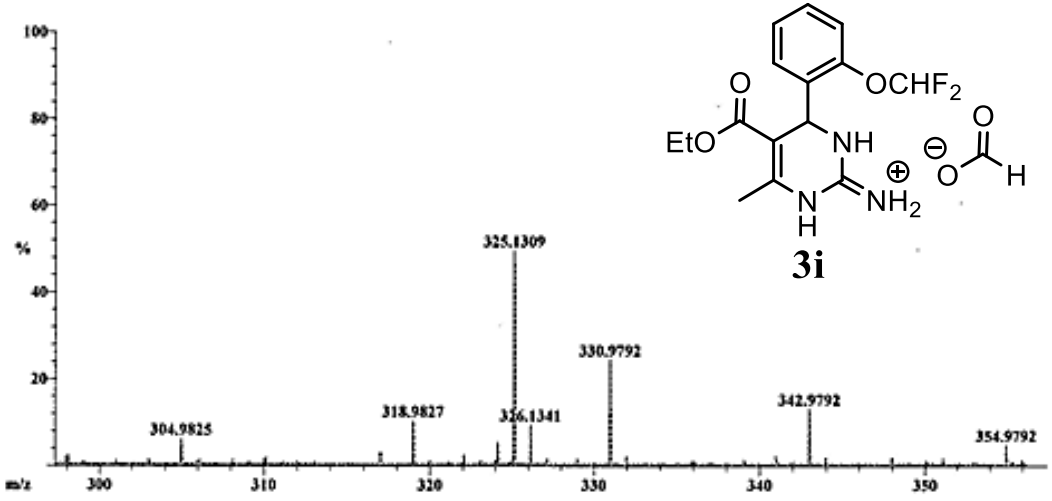
[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 43-STE-2508
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 3.47 min Scan# : (11,13)
BP : m/z 328.1276 Int. : 6.74
Output m/z range : 328.0088 to 328.2916 Cut Level : 0.00 %



3h

File: H-2
Sample: H-2
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 80 R.T.: .93
Base: m/z 296; 9.6%FS TIC: 908128 #Ions: 740

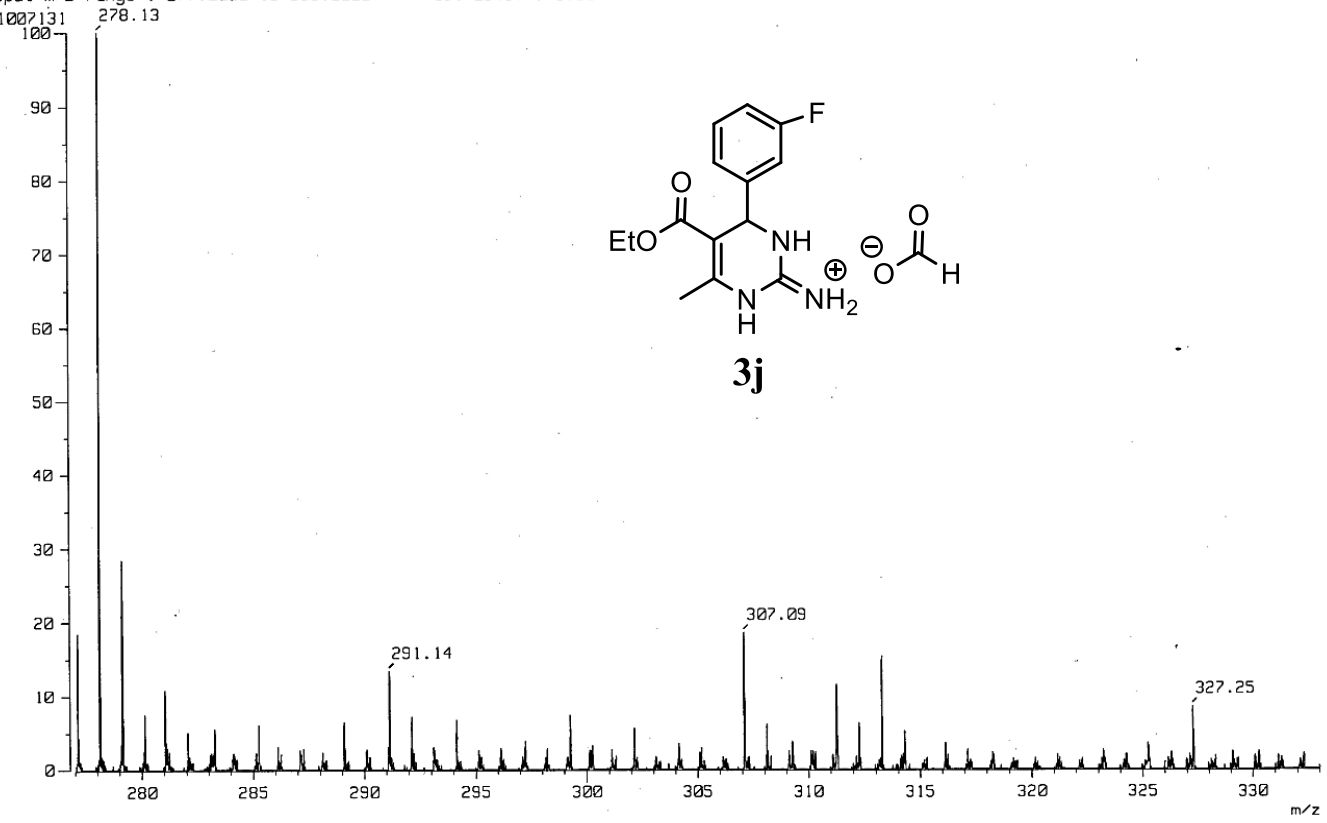


3i

Selected Isotopes : $N_{0-3}O_{0-3}C_{0-15}H_{0-18}F_{0-2}$ Error Limit : 20 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
326.1341	9.6%	$C_{15}H_{18}N_3O_3F_2$	326.1316	7.6

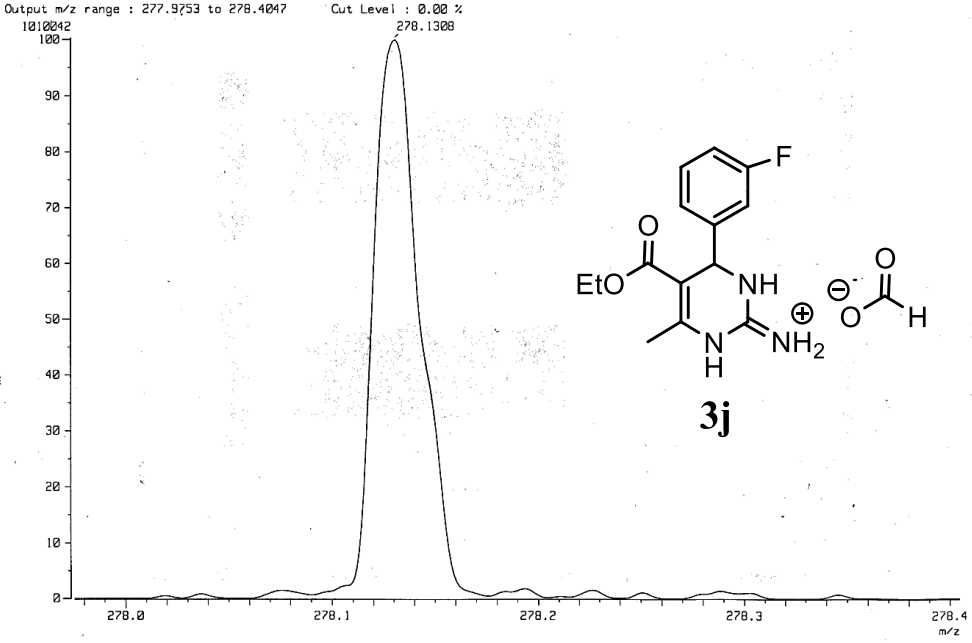
[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 44-STE-2509
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 6.19 min Scan# : 18
BP : m/z 278.1308 Int. : 96.05
Output m/z range : 277.0000 to 333.0000 Cut Level : 0.00 %



3j

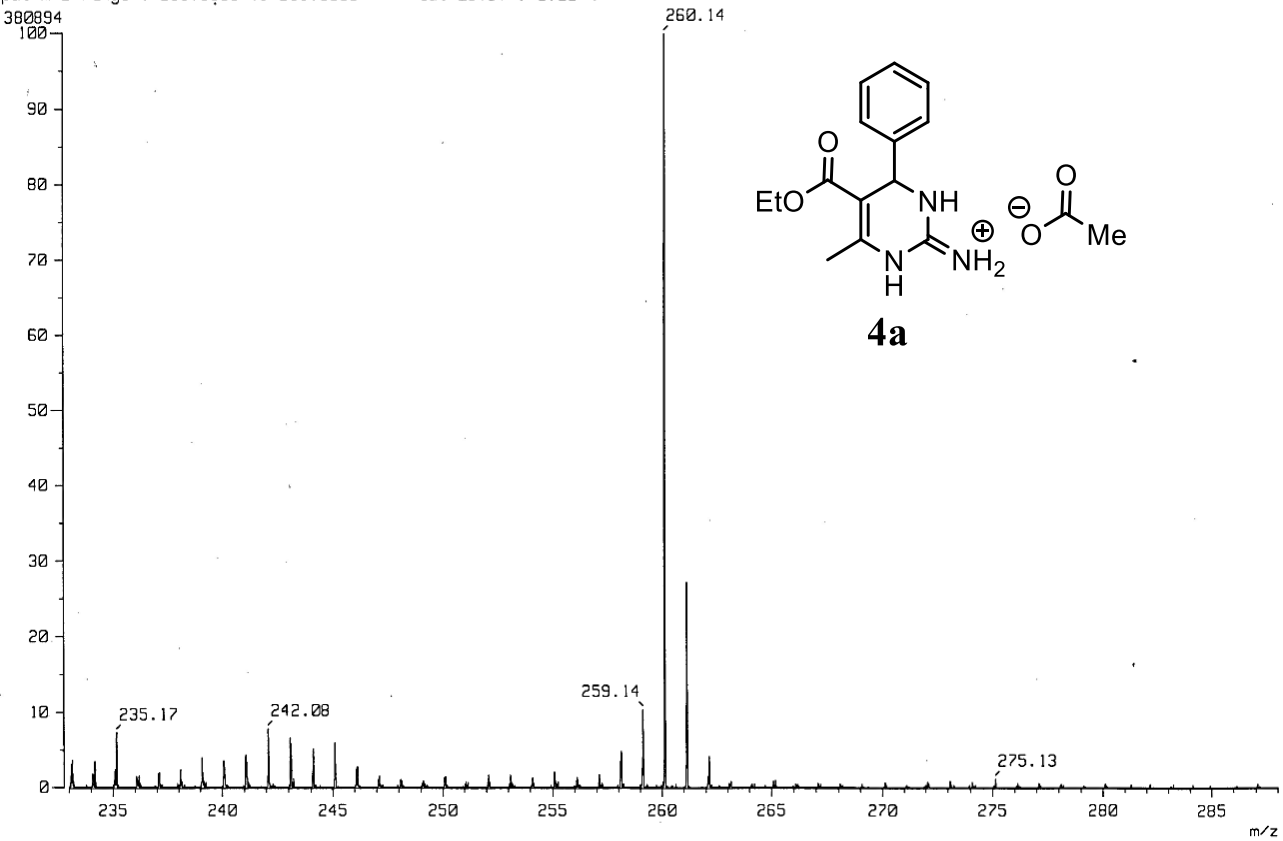
```
[ Elemental Composition ]
Data  : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 44-STE-2509
Note :
Inlet : Direct                          Ion Mode : FAB+
RT : 6.19 min                           Scan#: 18
Elements : C 40/0, H 49/0, O 5/1, N 4/1, F 2/1
Mass Tolerance       : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z    Int%
  278.1308      100.0
Estimated m/z  Error[ppm]  U.S.     C     H     O     N     F
  278.1305        +1.1       7.5    14    17     2     3     1
```

```
[ Mass Spectrum ]
Data  : Dr-Hulme-Rios-Guerra-FES-C05
Sample: 44-STE-2509
Note :
Inlet : Direct                    Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 6.19 min          Scan# : 18
BP : m/z 278.1308      Int.  : 96.05
Output m/z range : 277.9753 to 278.4047      Cut Level : 0.00 %
```



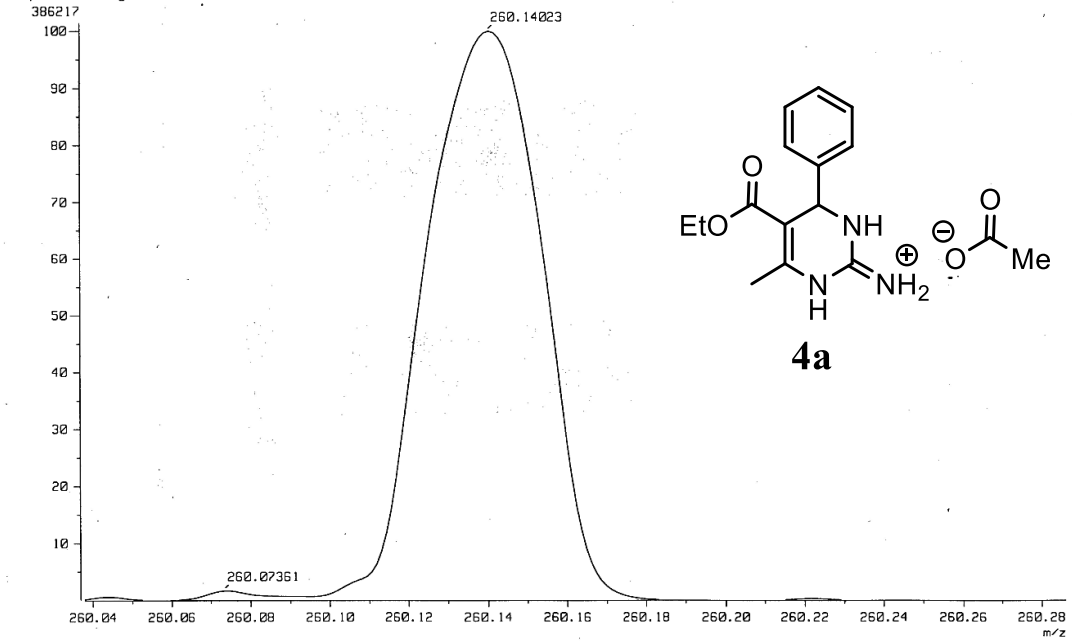
3j

[Mass Spectrum]
Data : Dr-Hulme-Rios-Guerra-FES-C06
Sample: 46-STE-2511
Note :
Inlet : Direct Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 0.41 min Scan# : (1,3)
BP : m/z 260.1402 Int. : 12.11
Output m/z range : 233.0000 to 288.0000 Cut Level : 0.00 %



4a

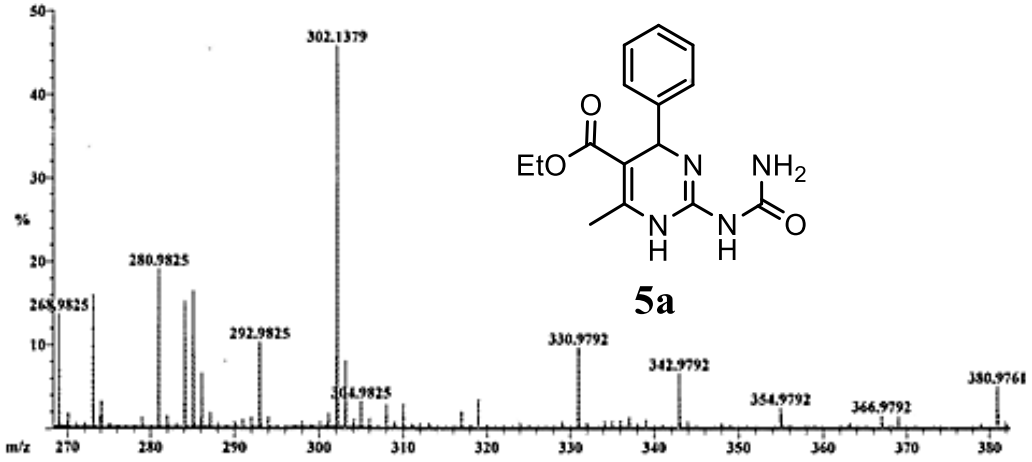
```
[ Elemental Composition ]
Data  : Dr-Hulme-Rios-Guerra-FES-C06
Sample: 46-STE-2511
Note :
Inlet : Direct                          Ion Mode : FAB+
RT : 0.41 min                           Scan#: (1,3)
Elements : C 40/0, H 49/0, O 5/1, N 4/1
Mass Tolerance       : 1000ppm, 1mmu if m/z > 1
Unsaturation (U.S.) : 4.0 - 15.0

Observed m/z   Int%
  260.1402     100.0
Estimated m/z  Error[ppm]  U.S.     C     H     O     N
  260.1399       +1.3       7.5    14    18     2     3

[ Mass Spectrum ]
Data  : Dr-Hulme-Rios-Guerra-FES-C06
Sample: 46-STE-2511
Note :
Inlet : Direct                          Ion Mode : FAB+
Spectrum Type : Normal Ion [EF-Linear]
RT : 0.41 min          Scan# : (1,3)
BP : m/z 260.1402      Int.  : 12.11
Output m/z range : 260.0379 to 260.2860      Cut Level : 0.03 %
```



4a

File: H-4
Sample: H-4
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 113-117 R.T.: 1.33
Base: m/z 259; 20.6%FS TIC: 1579298 #Ions: 1196



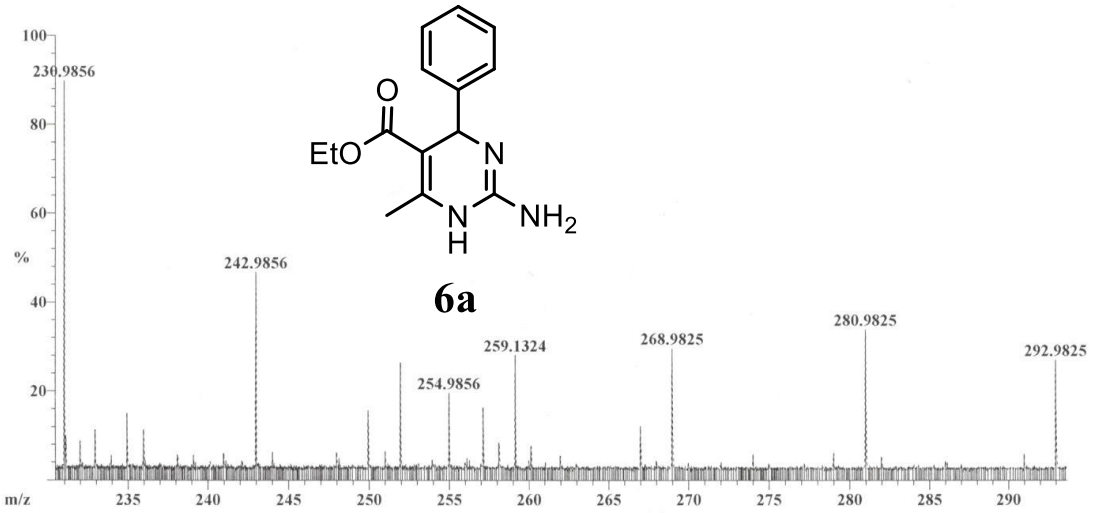
5a

Selected Isotopes : $N_{0-4}O_{0-4}C_{0-16}H_{0-18}$ Error Limit : 20 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
302.1379	45.9%	$C_{15}H_{18}N_4O_3$	302.1379	0.0

File: FDR-H5
Sample: FDR-H5
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 37-45 R.T.: .47
Base: m/z 219; 1.9%FS TIC: 1040898 #Ions: 1439



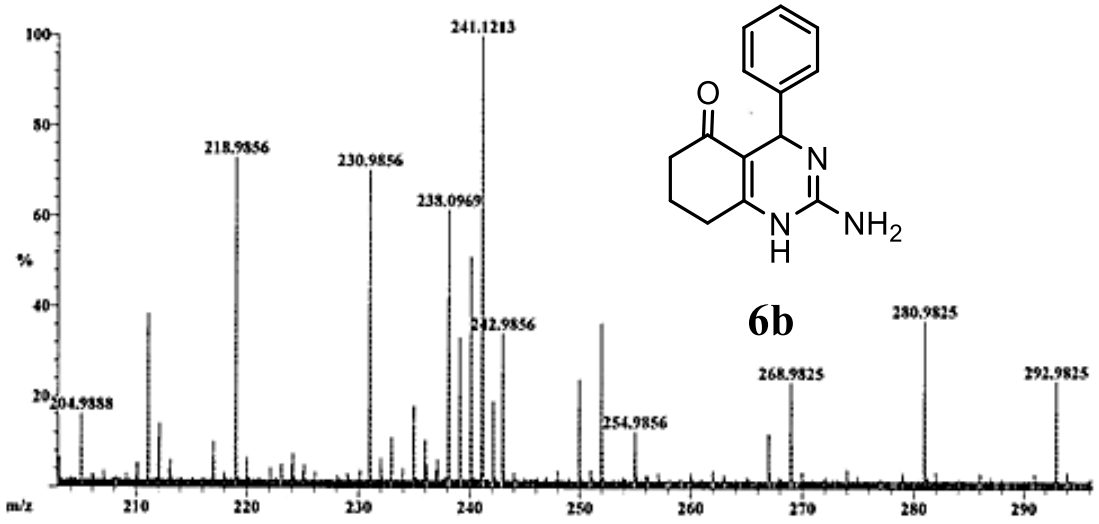
6a

Selected Isotopes : $N_{0-3}O_{0-2}C_{0-14}H_{0-18}$ Error Limit : 50 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
259.1324	28.2%	$C_{14}H_{17}N_3O_2$	259.1321	1.3

File: R-1
Sample: 1
Instrument: JEOL GCmate
Inlet: Direct Probe Ionization mode: EI+

Scan: 131-134 R.T.: 1.51
Base: m/z 241; 3.9%FS TIC: 1362548 #Ions: 1545



6b

Selected Isotopes : $N_{0-3}O_{0-1}C_{0-14}H_{0-15}$ Error Limit : 20 ppm

Measured Mass	*% Base*	*Formula*	*Calculated Mass*	*Error*
241.1213	100.0%	$C_{14}H_{15}N_3O$	241.1215	-0.9