Regioselective and Enantiospecific Rhodium-Catalyzed Allylic Amination with Thymine: Synthesis of a New Conformationally Rigid Nucleoside

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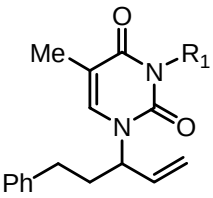
Representative Experimental Procedures and Supplemental Data

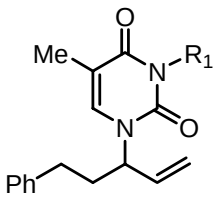
General Information. The chemical shifts of the ^{1}H NMR and ^{13}C NMR spectra were all recorded relative to chloroform. All ^{13}C NMR spectral data using the descriptors *o* and *e* refer to whether the peak is odd or even respectively, and correlate to an attached proton test (APT) experiment. HPLC analysis was carried out using an HP1100 HPLC. Optical rotations were recorded on a Perkin Elmer Mode 1343 polarimeter. All compounds were purified using flash column chromatography, and gave spectroscopic data consistent with being ≥95% the assigned structures. Analytical t.l.c. was carried out on precoated 0.2 mm thick Merck 60 F_{254} silica plates. Flash chromatography was carried out using Merck Silica Gel 60 (230–400 mesh).



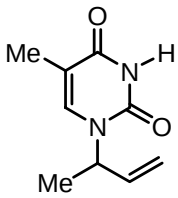
3-Benzoyl-5-methyl-1-[1-(2-phenylethyl)prop-2-en-1-yl]pyrimidine-2,4-(1*H*,3*H*)-dione (3a: R_1 = Bz). Trimethyl phosphite (12 μL, 0.102 mmol) was added directly to a red solution of Wilkinson's catalyst (23.1 mg, 0.025 mmol) in anhydrous THF (1 mL) at room temperature under an atmosphere of argon. The catalyst was allowed to form over *ca.* 15 minutes resulting in a light yellow homogeneous solution. Lithium hexamethyldisilylazide (475 μL, 0.475 mmol, 1.0 M solution in THF) was added to N^3-benzoyl thymine **1** (115.1 mg, 0.500 mmol) in anhydrous THF (3 mL) at 30 °C and the anion allowed to form over *ca.* 30 minutes. The catalyst was then added *via* Teflon cannula to the anion solution followed by addition of allylic carbonate **2a** (51.6 mg, 0.255 mmol) *via* a tared 100 μL syringe. The mixture was heated at 30 °C for *ca*. 12 hours (t.l.c. control). The reaction mixture was then quenched with saturated aqueous NH_4Cl solution at room temperature and partitioned between ethyl acetate and water. The organic layers were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 20–50% ethyl acetate/hexanes) furnished the *N*,*N*-

disubstituted thymine **3a** (R_1 = Bz; 69.3 mg, 73%) as a pale yellow oil: IR ($CDCl_3$) 2929 (m), 1747 (s), 1698 (s), 1652 (s), 1436 (s), 1260 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.4 Hz, 2H), 7.62 (dd, J = 7.6, 7.2 Hz, 1H), 7.47 (dd, J = 7.8, 7.8 Hz, 2H), 7.28 (dd, J = 7.6, 7.2 Hz, 1H), 7.24–7.15 (m, 3H), 6.98 (s, 1H), 5.90 (ddd, J = 16.7, 10.5, 5.7 Hz, 1H), 5.36 (dd, J = 10.6, 0.6 Hz, 1H), 5.30 (dd, J = 17.6, 1.1 Hz, 1H), 5.18–5.13 (m, 1H), 2.72 (ddd, A of ABXY, J_{AB} = 14.7 Hz, J_{AX} = 9.2 Hz, J_{AY} = 6.1 Hz, 1H), 2.61 (ddd, B of ABXY, J_{AB} = 14.8 Hz, J_{BX} = 9.0 Hz, J_{BY} = 6.6 Hz, 1H), 2.21–2.04 (m, 2H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.98 (e), 162.51 (e), 150.05 (e), 140.29 (e), 136.53 (o), 135.18 (o), 134.83 (o), 131.67 (e), 130.26 (o), 129.04 (o), 128.55 (o), 128.14 (o), 126.25 (o), 118.99 (e), 110.88 (e), 56.84 (o), 34.01 (e), 32.13 (e), 12.47 (o); HRMS (CI, $M+H^+$) calcd for $C_{23}H_{22}N_2O_2$ 375.1703, found 375.1697.

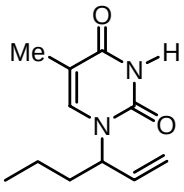
Representative Procedure for the Rhodium-Catalyzed Allylic Amination–Debenzoylation Sequence: Trimethyl phosphite (12 μL, 0.102 mmol) was added directly to a red solution of Wilkinson's catalyst (23.1 mg, 0.025 mmol) in anhydrous THF (1 mL) at room temperature under an atmosphere of argon. The catalyst was allowed to form over *ca.* 15 minutes resulting in a light yellow homogeneous solution. Lithium hexamethyldisilylazide (475 μL, 0.475 mmol, 1.0 M solution in THF) was added to N^3-benzoyl thymine **1** (115.1 mg, 0.500 mmol) in anhydrous THF (3 mL) at 30 °C and the anion allowed to form over *ca.* 30 minutes. The catalyst was then added *via* Teflon cannula to the anion solution followed by addition of allylic carbonate **2a** (54.2 mg, 0.246 mmol) *via* a tared 100 μL syringe. The mixture was heated at 30 °C for *ca*. 12 hours (t.l.c. control). The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and methanol at room temperature and partitioned between ethyl acetate and water. The organic layer were combined, washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford a crude oil. The residue was re-dissolved in methanol (15 mL) followed by addition of *c* NH_4OH (2.5 mL) at room temperature. After stirring at the same temperature for *ca*. 4 hours (t.l.c. control), the reaction mixture was concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 20–50% ethyl acetate/hexanes) furnished the N^1-alkylated thymine **3a** (R_1 = H; 65.1 mg, 98%) as a colorless oil.



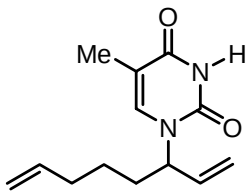
5-Methyl-1-[1-(2-phenylethyl)prop-2-en-1-yl]pyrimidine-2,4(1*H*,3*H*)-dione (3a: R_1 = H). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3508 (m), 3030 (s), 1656 (s), 1385 (s), 1256 (s), 1108 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (br s, 1H), 7.29–7.20 (m, 2H), 7.19–7.14 (m, 3H), 6.87 (s, 1H), 5.88 (ddd, *J* = 16.6, 10.5, 5.4 Hz, 1H), 5.33 (d, *J* = 10.8 Hz, 1H), 5.26 (d, *J* = 17.6 Hz, 1H), 5.25–5.20 (m, 1H), 2.72 (ddd, A of ABXY, J_{AB} = 14.7 Hz, J_{AX} = 9.6 Hz, J_{AY} = 5.8 Hz, 1H), 2.59 (ddd, B of ABXY, J_{AB} = 14.9 Hz, J_{BX} = 9.5 Hz, J_{BY} = 6.4 Hz, 1H), 2.20–2.11 (m, 1H), 2.08–1.89 (m, 1H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.94 (e), 151.37 (e), 140.45 (e), 136.65 (o), 135.58 (o), 128.45 (o), 128.11 (o), 126.14 (o), 118.38 (e), 110.98 (e), 56.27 (o), 34.08 (e), 32.08 (e), 12.48 (o); HRMS (CI, M^+) calcd for $C_{16}H_{18}N_2O_2$ 270.1368, found 270.1366.



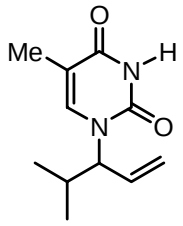
5-Methyl-1-(1-methylprop-2-en-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (3b). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3183 (s), 3043 (s), 1683 (s), 1472 (s), 1377 (s), 1255 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 6.95 (s, 1H), 5.88 (ddd, *J* = 17.4, 10.5, 4.4 Hz, 1H), 5.37–5.28 (m, 3H), 1.92 (s, 3H), 1.40 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.20 (e), 151.11 (e), 136.56 (o), 117.83 (e), 110.90 (e), 51.36 (o), 17.60 (o), 12.38 (o); HRMS (CI, M^+) calcd for $C_9H_{12}N_2O_2$ 180.0899, found 180.0900.



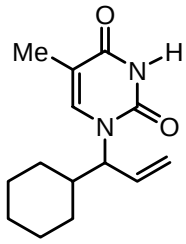
5-Methyl-1-(1-propylprop-2-en-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (3c). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3158 (s), 3032 (s), 2961 (s), 1694 (s), 1472 (s), 1257 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.19 (br s, 1H), 6.90 (s, 1H), 5.80 (dddd, *J* = 17.1, 10.5, 5.3, 3.0 Hz, 1H), 5.24 (dd, *J* = 10.5, 2.6 Hz, 1H), 5.18 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.15–5.13 (m, 1H), 1.87 (d, *J* = 2.8 Hz, 3H), 1.77–1.57 (m, 2H), 1.33-1.21 (m, 2H), 0.89 (dt, *J* = 7.3, 4.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.12 (e), 151.45 (e), 136.74 (o), 135.85 (o), 117.92 (e), 110.87 (e), 55.73 (o), 34.42 (e), 18.82 (e), 13 53 (o), 12.44 (o); HRMS (CI, M^+) calcd for $C_{11}H_{16}N_2O_2$ 208.1212, found 208.1209.



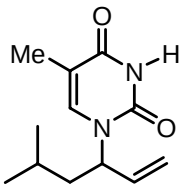
5-Methyl-1-(1-vinylhex-5-en-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (3d). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3179 (s), 3043 (s), 2930 (s), 1683 (s), 1471 (s), 1376 (s), 1256 (s), 912 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.11 (br s, 1H), 6.90 (s, 1H), 5.81 (dddd, *J* = 17.4, 10.5, 5.4, 1.6 Hz, 1H), 5.76–5.65 (m, 1H), 5.26 (d, *J* = 10.6 Hz, 1H), 5.20 (d, *J* = 17.3 Hz, 1H), 5.17–5.12 (m, 1H), 4.97 (d, *J* = 17.3 Hz, 1H), 4.93 (d, *J* = 11.3 Hz, 1H), 2.05 (q, *J* = 7.0 Hz, 2H), 1.89 (s, 3H), 1.81–1.73 (m, 1H), 1.68–1.59 (m, 1H), 1.46–1.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.11 (e), 151.42 (e), 137.67 (o), 136.66 (o), 135.69 (o), 118.14 (e), 115.18 (e), 110.97 (e), 55.86 (o), 32.98 (e), 31.64 (e), 24.72 (e), 12.48 (o); HRMS (CI, M^+) calcd for $C_{13}H_{18}N_2O_2$ 234.1368, found 234.1360.



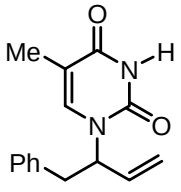
1-(1-Isopropylprop-2-en-1-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3e). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3149 (s), 3028 (s), 1683 (s), 1474 (s), 1371 (s), 1256 (s), 931 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.69 (br s, 1H), 6.94 (s, 1H), 5.88 (ddd, *J* = 17.3, 10.3, 7.2 Hz, 1H), 5.30 (dd, *J* = 10.5, 1.0 Hz, 1H), 5.26 (dd, *J* = 17.2, 1.0 Hz, 1H), 4.70 (dd, *J* = 9.7, 7.7 Hz, 1H), 2.04–1.95 (m, 1H), 1.91 (s, 3H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.92 (e), 151.43 (e), 137.35 (o), 134.29 (o), 120.00 (e), 110.77 (e), 63.51 (o), 30.82 (o), 19.67 (o), 18.98 (o), 12.54 (o); HRMS (CI, M^+) calcd for $C_{11}H_{16}N_2O_2$ 208.1212, found 208.1221.



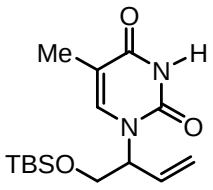
1-(1-Cyclohexylprop-2-en-1-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3f). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* = 58:1; IR ($CDCl_3$) 3168 (m), 3038 (m), 2929 (s), 1679 (s), 1470 (s), 1256 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.16 (br s, 1H), 6.93 (s, 1H), 5.88 (ddd, *J* = 17.2, 9.7, 7.7 Hz, 1H), 5.30 (d, *J* = 10.5 Hz, 1H), 5.26 (dd, *J* = 17.1, 1.0 Hz, 1H), 4.74 (dd, *J* = 8.4, 9.2 Hz, 1H), 1.93 (s, 3H), 1.84–1.65 (m, 5H), 1.52 (d, *J* = 12.6 Hz, 1H), 1.27–1.10 (m, 3H), 1.04–0.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.77 (e), 151.33 (e), 137.50 (o), 134.14 (o), 120.13 (e), 110.73 (e), 62.64 (o), 39.83 (o), 30.10 (e), 28.97 (e), 25.95 (e), 25.64 (e), 25.56 (e), 12.59 (o); HRMS (CI, M^+) calcd for $C_{14}H_{20}N_2O_2$ 248.1525, found 248.1532.



1-(1-Isobutylprop-2-en-1-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3g). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* = 32:1; IR ($CDCl_3$) 2958 (s), 1646 (s), 1470 (s), 1384 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.14 (br s, 1H), 6.90 (s, 1H), 5.80 (ddd, *J* = 16.5, 10.4, 5.2 Hz, 1H), 5.22 (d, *J* = 10.5 Hz, 1H), 5.17 (d, *J* = 17.6 Hz, 1H), 1.88 (s, 3H), 1.61–1.53 (m, 2H), 1.51–1.43 (m, 1H), 0.91 (dd, *J* = 6.4, 2.1 Hz, 3H), 0.89 (dd, *J* = 6.4, 2.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.20 (e), 151.32 (e), 136.74 (o), 136.12 (o), 117.65 (e), 110.87 (e), 54.11 (o), 41.34 (e), 24.42 (o), 22.78 (o), 21.88 (o), 12.46 (o); HRMS (CI, M^+) calcd for $C_{12}H_{18}N_2O_2$ 222.1368, found 222.1373.

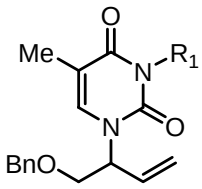


1-(1-Benzylprop-2-en-1-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3h). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* = 29:1; IR ($CDCl_3$) 3155 (m), 3029 (s), 1683 (s), 1473 (s), 1257 (s), 753 (s), 702 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (br s, 1H), 7.31–7.15 (m, 5H), 6.94 (d, *J* = 1.2 Hz, 1H), 5.98 (ddd, *J* = 17.2, 10.6, 5.2 Hz, 1H), 5.45–5.40 (m, 1H), 5.37 (d, *J* = 10.6 Hz, 1H), 5.29 (dd, *J* = 17.3, 1.5 Hz, 1H), 3.16 (dd, A of ABX, J_{AB} = 14.0 Hz, J_{AX} = 6.6 Hz, 1H), 3.01 (dd, B of ABX, J_{AB} = 14.0 Hz, J_{BX} = 8.9 Hz, 1H), 1.92 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.52 (e), 150.73 (e), 137.25 (o), 135.96 (e), 134.93 (o), 129.02 (o), 128.66 (o), 127.05 (o), 118.81 (e), 110.66 (e), 57.84 (o), 38.92 (e), 12.49 (o); HRMS (CI, M^+) calcd for $C_{15}H_{16}N_2O_2$ 256.1212, found 256.1200.

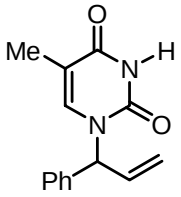


1-[1-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)prop-2-en-1-yl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3i). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3180 (s), 3045 (s), 2954 (s), 1696 (s), 1471 (s), 1254 (s), 1116 (s), 837 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.03 (br s, 1H), 7.17 (s, 1H), 5.91 (dddd, *J* = 17.3, 10.7, 5.3, 1.3 Hz, 1H), 5.36 (d, *J* = 11.8 Hz, 1H), 5.32 (d, *J* = 18.1 Hz, 1H), 5.17–5.16 (m, 1H), 3.90 (dd, A of ABX, J_{AB} = 10.4 Hz, J_{AX} = 3.7 Hz, 1H), 3.83 (dd, B of ABX, J_{AB} = 11.0 Hz, J_{BX} = 2.3 Hz, 1H), 1.86 (s, 3H), 0.82 (d, *J* = 1.5 Hz, 9H), 0.00 (d, *J* = 1.2 Hz, 3H), -0.04 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.27 (e), 151.33 (e), 139.47 (e), 132.60 (o), 120.05 (o), 109.37 (e), 63.16 (e), 57.53 (o), 25.56 (o), 17.95 (e), 12.31 (o), –5.74 (o), –5.83 (o); HRMS (CI, M+H^+) calcd for $C_{15}H_{27}N_2O_3Si$ 311.1791,

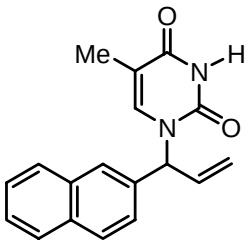
found 311.1790.



1-{1-[(Benzyloxy)methyl]prop-2-en-1-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3j, R_1 = H). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3184 (m), 3033 (m), 1683 (s), 1468 (s), 1264 (s), 1100 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.36–7.25 (m, 5H), 7.13 (d, *J* = 0.8 Hz, 1H), 5.91 (ddd, *J* = 17.2, 10.6, 5.4 Hz, 1H), 5.38 (dd, *J* = 10.6, 1.2 Hz, 1H), 5.35–5.28 (m, 2H), 4.56 (d, A of AB, *J* = 12.0, 1H), 4.49 (d, B of AB, *J* = 12.1 Hz, 1H), 3.78 (dd, A of ABX, J_{AB} = 10.5 Hz, J_{AX} = 5.8 Hz, 1H), 3.72 (dd, B of ABX, J_{AB} = 10.3 Hz, J_{BX} = 4.2 Hz, 1H), 1.89 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.21 (e), 151.36 (e), 138.58 (o), 137.21 (e), 132.47 (o), 128.34 (o), 127.82 (o), 127.62 (o), 119.69 (e), 110.01 (e), 73.08 (e), 69.49 (e), 55.89 (o), 12.37 (o); HRMS (CI, M^+) calcd for $C_{16}H_{18}N_2O_3$ 286.1317, found 286.1325.

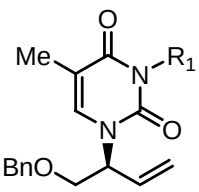


5-Methyl-1-(1-phenylprop-2-en-1-yl)pyrimidine-2,4(1*H*,3*H*)-dione (3k). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3178 (s), 3036 (s), 1683 (s), 1469 (s), 1374 (s), 1247 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.44 (br s, 1H), 7.39–7.24 (m, 5H), 6.88 (d, *J* = 0.8 Hz, 1H), 6.40 (d, *J* = 5.2 Hz, 1H), 6.13 (ddd, *J* = 16.5, 10.5, 5.3 Hz, 1H), 5.47 (dd, *J* = 10.7, 0.9 Hz, 1H), 5.18 (dd, *J* = 17.4, 1.1 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.88 (e), 151.14 (e), 137.61 (o), 136.96 (e), 134.09 (o), 129.05 (o), 128.55 (o), 128.02 (o), 120.00 (e), 110.87 (e), 59.60 (o), 12.57 (o); HRMS (CI, M^+) calcd for $C_{14}H_{14}N_2O_2$ 242.1055, found 242.1061.

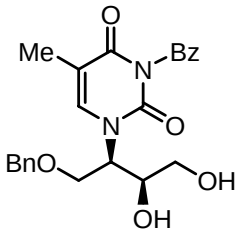


5-Methyl-1-[1-(2-naphthyl)prop-2-en-1-yl]pyrimidine-2,4(1*H*,3*H*)-dione (3l). Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°*:*1°* ≥ 99:1; IR ($CDCl_3$) 3055 (s), 2828 (s), 1668 (s), 1471 (s), 1373 (s), 1249 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (br s, 1H), 7.89–7.77 (m, 4H), 7.55–7.53 (m, 2H), 7.35 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.92 (d, *J* = 1.1 Hz, 1H), 6.58 (d, *J* = 5.1 Hz, 1H), 6.28 (ddd, *J* = 17.1, 10.5, 5.4 Hz, 1H), 5.57 (dd, *J* = 10.5, 0.9 Hz, 1H), 5.27 (dd, *J* = 17.2, 1.6 Hz, 1H), 1.84 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.18

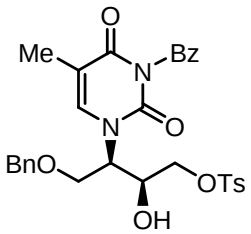
(e), 151.41 (e), 137.50 (o), 134.40 (e), 133.90 (o), 132.94 (e), 132.88 (e), 128.95 (o), 127.93 (o), 127.56 (o), 127.08 (o), 126.57 (o), 126.53 (o), 125.51 (o), 119.87 (e), 110.88 (e), 59.48 (o), 12.42 (o); HRMS (CI, M^+) calcd for $C_{18}H_{16}N_2O_2$ 292.1212, found 292.1220.



3-Benzoyl-1-{(1*S*)-1-[(benzyloxy)methyl]prop-2-en-1-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (*S*)-3j (R_1 = Bz). Trimethyl phosphite (142 μL, 1.2 mmol) was added directly to a red solution of Wilkinson's catalyst (278 mg, 0.3 mmol) in anhydrous THF (12 mL) at room temperature under an atmosphere of argon. The catalyst was allowed to form over *ca.* 15 minutes resulting in a light yellow homogeneous solution. Lithium hexamethyldisilylazide (5.7 mL, 5.70 mmol, 1.0 M solution in THF) was added to N^3-benzoyl thymine **1** (1.38 g, 5.99 mmol) in anhydrous THF (18 mL) at 0 °C and the anion allowed to form over *ca.* 30 minutes. The catalyst was then added *via* Teflon cannula to the anion solution followed by addition of allylic carbonate **(*S*)-2j** (681.8 mg, 2.89 mmol) *via* a tared 1000 μL syringe. The mixture was stirred at 0 °C for 24 hours. The reaction mixture was then quenched with saturated aqueous NH_4Cl aqueous solution at 0 °C and partitioned between ethyl acetate and water. The combined phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 20–40% ethyl acetate/hexanes) furnished the *N*,*N*-disubstituted thymine **(*S*)-3j** (900 mg, 80%) as a colorless oil: Racemic HPLC analysis (ZORBAX HPLC column 2276) *2°:1°* = 23:1; Chiral HPLC analysis (Chiralcel AD, 10% isopropanol in hexanes, 1.0 mL/min, 254 nm detector wavelength, retention time: t_{major} = 29.00 min and t_{minor} = 34.62 min) *cee* ≥ 99%; $[\alpha]_D^{22}$ –32.7 (*c* = 0.99, $CHCl_3$); IR ($CDCl_3$) 3066 (m), 2929 (s), 2866 (s), 1747 (s), 1696 (s), 1436 (s), 1260 (s), 1105 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90–7.88 (m, 2H), 7.64–7.60 (m, 1H), 7.46–7.42 (m, 2H), 7.38–7.24 (m, 5H), 5.95 (ddd, *J* = 16.7, 10.7, 5.6 Hz, 1H), 5.43 (d, *J* = 10.7 Hz, 1H), 5.36 (d, *J* = 17.1 Hz, 1H), 5.39–5.34 (m, 1H), 4.59 (d, A of AB, J_{AB} = 12.0 Hz, 1H), 4.52 (d, B of AB, J_{AB} = 12.0 Hz, 1H), 3.82 (dd, A of ABX, J_{AB} = 10.5 Hz, J_{AX} = 6.1 Hz, 1H), 3.76 (dd, B of ABX, J_{AB} = 10.5 Hz, J_{BX} = 3.9 Hz, 1H), 1.94 (d, *J* = 0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.05 (e), 162.76 (e), 150.12 (e), 138.35 (o), 137.29 (e), 134.84 (o), 132.20 (o), 131.66 (e), 130.39 (o), 129.08 (o), 128.53 (o), 128.02 (o), 127.74 (o), 120.33 (e), 110.16 (e), 73.28 (e), 69.65 (e), 56.32 (o), 12.51 (o); HRMS (EI, M^+) calcd for $C_{23}H_{22}N_2O_4$ 390.1580, found 390.1572.

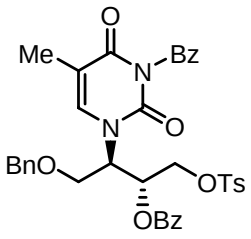


3-Benzoyl-1-{(1*R*,2*S*)-1-[(benzyloxy)methyl]-2,3-dihydroxypropyl}-5-methyl-pyrimidine-2,4(1*H*,3*H*)-dione (5). $(DHQ)_2PYR$ (203 mg, 0.230 mmol), $K_3Fe(CN)_6$ (4.55 g, 13.82 mmol), K_2CO_3 (1.91 g, 13.82 mmol), $K_2OsO_2(OH)_4$ (6.8 mg, 0.185 mmol) were suspended in a mixture of water and *tert*-butyl alcohol (1:1, 24 mL). Methanesulfonamide (219.3 mg, 2.31 mmol) was added and the mixture stirred at room temperature for 1 hour. The reaction mixture was then added to the alkene **(*S*)-3j** (114.4 mg, 0.29 mmol), and the heterogeneous slurry was stirred at room temperature for 8 hours (t.l.c. control). The reaction was quenched at 0 °C by addition of $Na_2S_2O_3$ (6.97 g) and the mixture stirred at room temperature for *ca.* 2 hours. The reaction mixture was then partitioned between ethyl acetate and water. The combined organic phases were dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 50–90% ethyl acetate/hexanes) furnished the diol **5** (961.9 mg, 96%) as a colorless oil: Chiral HPLC analysis (Chiralcel OD, 10% isopropanol in hexanes, 1.0 mL/min, 254 nm detector wavelength, retention time: t_{minor} = 65.15 min and t_{major} = 68.69 min) *ds* = 31:1; $[\alpha]_D^{23}$ –12.7 (*c* = 1.53, $CHCl_3$). IR ($CDCl_3$) 3460 (br s), 3089 (m), 2929 (s), 1747 (s), 1667 (s), 1445 (s), 1259 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 2H), 7.62–7.58 (m, 1H), 7.48–7.26 (m, 8H), 4.77 (br s, 1H), 4.53 (d, A of AB, *J* = 12.0 Hz, 1H), 4.46 (d, B of AB, *J* = 12.0 Hz, 1H), 3.98–3.96 (m, 1H), 3.87 (dd, A of ABX, J_{AB} = 10.6 Hz, J_{AX} = 7.3 Hz, 1H), 3.77 (dd, B of ABX, J_{AB} = 10.6 Hz, J_{BX} = 3.7 Hz, 1H), 3.52–3.43 (m, 3H), 3.13 (br s, 1H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.01 (e), 162.70 (e), 151.28 (e), 136.97 (e), 135.06 (o), 131.29 (e), 130.32 (o), 129.14 (o), 128.55 (o), 128.11 (o), 127.79 (o), 110.17 (e), 73.28 (e), 70.59 (o), 68.65 (e), 63.08 (e), 12.45 (o); HRMS (CI, M+H^+) calcd for $C_{23}H_{25}N_2O_6$ 425.1713, found 425.1700.

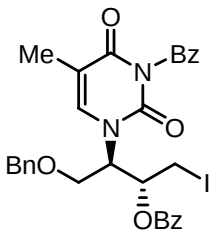


(2*S*,3*R*)-3-(3-Benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-4-(benzyl-oxy)-2-hydroxybutyl 4-methylbenzenesulfonate (6). To a solution of diol **5** (527.9 mg, 1.24 mmol) in anhydrous dichloromethane (3 mL) was added sequentially dibutyltin oxide (6.2 mg, 0.025 mmol), tosyl chloride (236 mg, 1.24 mmol) and triethylamine (173 μL, 1.24 mmol) at room temperature. The reaction was stirred at this temperature for *ca.* 3 hours, and then concentrated *in vacuo* to afford a crude oil. Purification by flash chromatography (eluting with

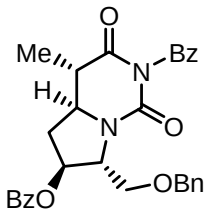
50–80% ethyl ether/pentane) furnished the tosylate **6** (143.2 mg, 86%) as a white solid: $[\alpha]_D^{23}$ –13.4 (*c* = 1.10, $CHCl_3$); IR ($CDCl_3$) 3452 (br s), 2956 (m), 1749 (s), 1698 (s), 1652 (s), 1442 (s), 1364 (s), 1258 (s), 1177 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.64–7.61 (m, 1H), 7.46–7.25 (m, 10H), 4.61 (br s, 1H), 4.53 (d, A of AB, *J* = 12.0 Hz, 1H), 4.48 (d, B of AB, *J* = 12.0 Hz, 1H), 4.24 (quintet, *J* = 5.5 Hz, 1H), 4.04–3.97 (m, 2H), 3.89–3.84 (m, 1H), 3.79–3.72 (m, 1H), 3.54 (br s, 1H), 2.42 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.56 (e), 162.52 (e), 151.01 (e), 145.45 (e), 136.92 (e), 134.98 (o), 131.91 (e), 131.33 (e), 130.36 (o), 130.02 (o), 129.16 (o), 128.60 (o), 128.16 (o), 127.90 (o), 127.74 (o), 110.68 (e), 73.38 (e), 70.27 (e), 68.36 (o), 67.92 (e), 21.62 (o), 12.48 (o); HRMS (EI, M^+) calcd for $C_{30}H_{30}N_2O_8S$, 578.1723, found 578.1719.



(1*R*,2*R*)-2-(3-Benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3-(benzyl-oxy)-1-({[(4-methylphenyl)sulfonyl]oxy}methyl)propyl-benzoate. The tosylate **6** (4.23 g, 7.31 mmol), triphenylphosphine (3.83 g, 14.61 mmol) and benzoic acid (1.79 g, 14.66 mmol) were dissolved in anhydrous THF (120 mL) and the mixture was cooled with stirring to 0 °C under an atmosphere of nitrogen. Diisopropyl azodicarboxylate (DIAD) (2.8 mL, 14.46 mmol) was added dropwise followed by stirring at room temperature for 6 hours (t.l.c. control). The solvent was removed *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 5–10% ethyl acetate/benzene) furnished the ester (4.14 g, 83%) as a white solid: $[\alpha]_D^{23}$ +11.6 (*c* = 0.90, $CHCl_3$); IR ($CDCl_3$) 3066 (m), 2928 (m), 1748 (s), 1699 (s), 1599 (s), 1436 (s), 1367 (s), 1260 (s), 1096 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94–7.88 (m, 4H), 7.69–7.59 (m, 4H), 7.49–7.41 (m, 4H), 7.28–7.19 (m, 8H), 5.78–5.76 (m, 1H), 4.86 (br s, 1H), 4.50 (d, A of AB, *J* = 11.8 Hz, 1H), 4.43 (d, B of AB, *J* = 11.8 Hz, 1H), 4.33 (dd, A of ABX, J_{AB} = 11.7 Hz, J_{AX} = 2.6 Hz, 1H), 4.23 (dd, B of ABX, J_{AB} = 11.4 Hz, J_{BX} = 3.7 Hz, 1H), 3.93 (br s, 1H), 3.71 (dd, *J* = 10.5, 3.2 Hz, 1H), 2.34 (s, 3H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.59 (e), 164.92 (e), 162.44 (e), 149.91 (e), 145.33 (e), 136.79 (e), 134.97 (o), 133.71 (o), 131.91 (e), 131.38 (e), 130.48 (o), 129.93 (o), 129.77 (o), 129.15 (o), 128.61 (e), 128.50 (o), 128.05 (o), 127.82 (o), 127.68 (o), 110.83 (e), 73.40 (e), 68.70 (o), 67.44 (e), 66.94 (e), 21.57 (o), 12.36 (o); HRMS (ESI, $M+Na^+$) calcd for $C_{37}H_{34}N_2NaO_9S$ 705.1883, found 705.1862.

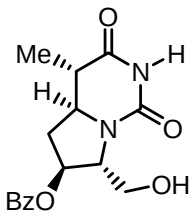


(1*R*,2*R*)-2-(3-Benzoyl-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl) -3-(benzyl-oxy)-1-(iodomethyl)propyl benzoate (7). Anhydrous *n*-tetra-butylammonium iodide (1.14 g, 3.09 mmol) was added to a solution of the tosylate (442.6 mg, 0.619 mmol) in anhydrous THF (6 mL). The flask was covered with aluminum foil and heated to reflux in an oil bath (90 °C) for 5 hours. The reaction mixture was then cooled to room temperature, diluted with ethyl acetate and water. The mixture was then partitioned between ethyl acetate and water. The combined phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 25–30% ethyl acetate/hexanes) afforded the iodide **7** (375.4 mg, 95%) as a colorless oil: $[\alpha]_D^{22}$ +23.5 (*c* = 0.89, $CHCl_3$); IR ($CDCl_3$) 3340 (m), 3066 (s), 2871 (s), 1755 (s), 1696 (s), 1600 (s), 1435 (s), 1250 (s), 1095 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.9 Hz, 2H), 7.94 (d, *J* = 7.7 Hz, 2H), 7.66–7.60 (m, 2H), 7.50–7.45 (m, 4H), 7.35–7.23 (m, 6H), 5.52 (dt, *J* = 8.2, 4.1 Hz, 1H), 4.98 (br s, 1H), 4.54 (d, A of AB, *J* = 11.8 Hz, 1H), 4.47 (d, B of AB, *J* = 11.8 Hz, 1H), 3.99 (dd, A of ABX, J_{AB} = 9.9 Hz, J_{AX} = 6.3 Hz, 1H), 3.79 (dd, B of ABX, J_{AB} = 10.6 Hz, J_{BX} = 3.0 Hz, 1H), 3.59 (dd, A of ABX, J_{AB} = 11.4 Hz, J_{AX} = 4.1 Hz, 1H), 3.36 (dd, B of ABX, J_{AB} = 11.4 Hz, J_{BX} = 5.0 Hz, 1H), 1.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.60 (e), 165.00 (e), 162.46 (e), 149.98 (e), 136.82 (e), 135.01 (o), 133.76 (o), 131.46 (e), 130.52 (o), 129.87 (o), 129.16 (o), 128.87 (e), 128.65 (o), 128.57 (o), 128.16 (o), 127.80 (o), 110.87 (e), 73.55 (e), 69.68 (o), 66.85 (e), 29.69 (e), 12.42 (o); HRMS (CI, $M+H^+$) calcd for $C_{30}H_{28}IN_2O_6$ 639.0992, found 639.1004.

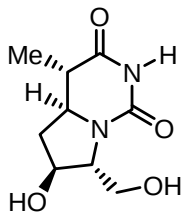


(4*S*,4a*S*,6*S*,7*R*)-2-Benzoyl-7-[(benzyloxy)methyl]-4-methyl-1,3-dioxoocta-hydro-pyrrolo[1,2-*c*]pyrimidin-6-yl benzoate (8). Tributyltin hydride (209 μL, 0.776 mmol) and 2,2'-azobisisobutyronitrile (AIBN) (9.5 mg, 58 μmol) in anhydrous benzene (9 mL) were added *via* syringe pump to a refluxing solution of the iodide **7** (247.6 mg, 0.388 mmol) in anhydrous benzene (30 mL) over *ca.* 3 hours under an atmosphere of argon. The reaction was refluxed for an additional *ca.* 2 hours (t.l.c. control), cooled to room temperature and concentrated *in vacuo* to afford a crude oil. Purification by flash column chromatography (eluting with 20% ethyl ether–15% dichloromethane/pentane) afforded the bicyclic compound **8** (169 mg, 85%) as a white solid: $[\alpha]_D^{23}$ –20.0 (*c* = 0.63, $CHCl_3$); IR ($CDCl_3$) 3064 (m), 2937 (m), 2868 (s), 1748 (s), 1683 (s),

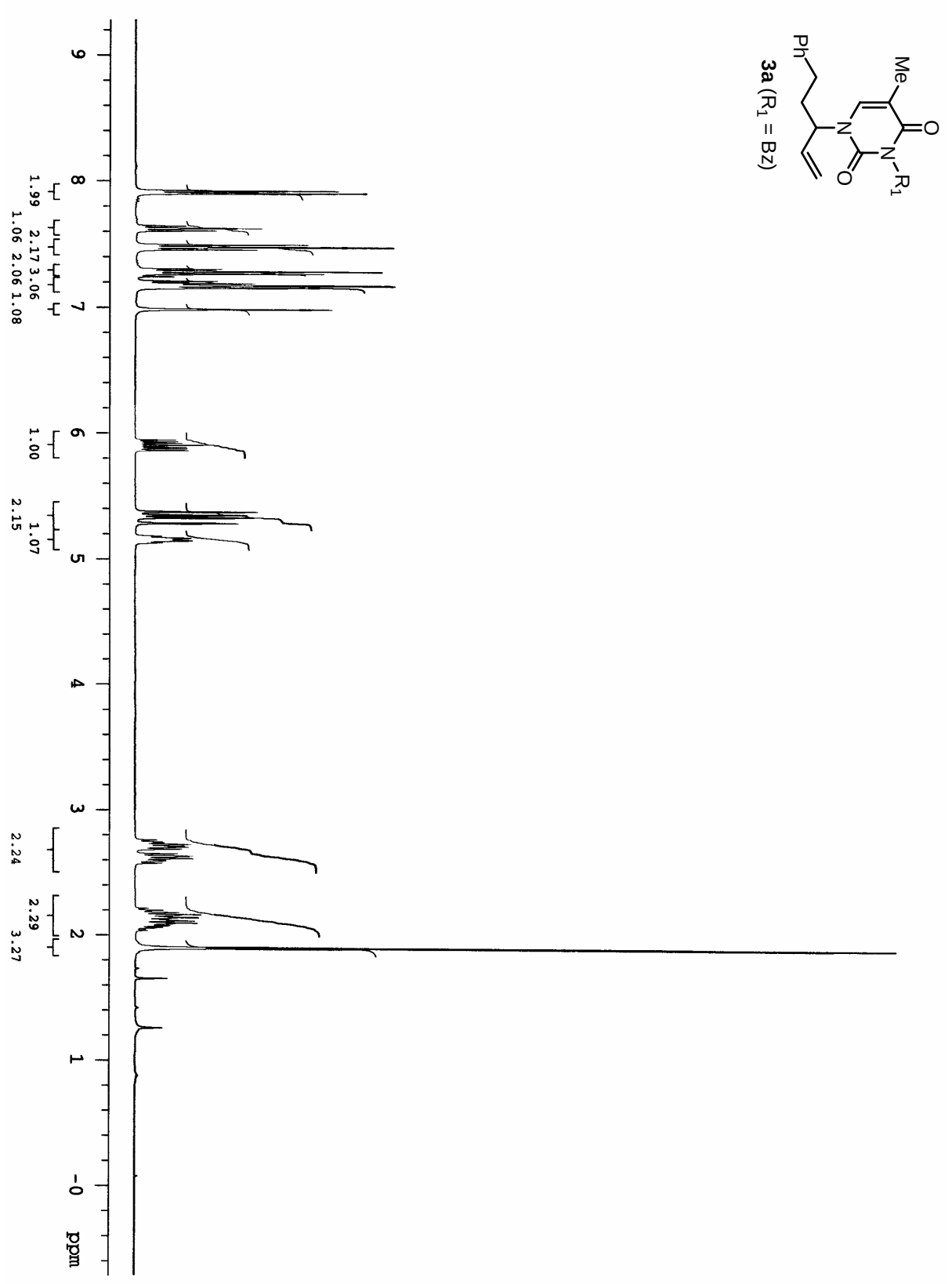
1600 (s), 1435 (s), 1271 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.3 Hz, 2H), 7.90 (d, J = 7.3 Hz, 2H), 7.64–7.59 (m, 2H), 7.51–7.32 (m, 9H), 5.64–5.61 (m, 1H), 4.59 (d, A of AB, J = 12.0 Hz, 1H), 4.56 (d, B of AB, J = 12.1 Hz, 1H), 4.46 (br s, 1H), 4.00 (dd, A of ABX, J_{AB} = 9.4 Hz, J_{AX} = 3.4 Hz, 1H), 3.97–3.91 (m, 1H), 3.83 (dd, B of ABX, J_{AB} = 9.8 Hz, J_{BX} = 2.1 Hz, 1H), 3.00 (dt, J = 14.4, 7.2 Hz, 1H), 2.72 (dq, J = 13.4, 6.7 Hz, 1H), 2.07 (ddd, J = 14.0, 6.0, 3.0 Hz, 1H), 1.29 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.25 (e), 169.69 (e), 165.93 (e), 149.70 (e), 137.69 (e), 134.45 (o), 133.50 (o), 132.55 (e), 130.01 (o), 129.56 (o), 129.30 (e), 128.89 (o), 128.53 (o), 128.51 (o), 127.80 (o), 127.35 (o), 75.65 (o), 73.55 (e), 69.00 (e), 64.20 (o), 58.47 (o), 42.56 (o), 37.03 (e), 11.11 (o); HRMS (EI, M^+) calcd for $C_{30}H_{28}N_2O_6$ 512.1947, found 512.1937.

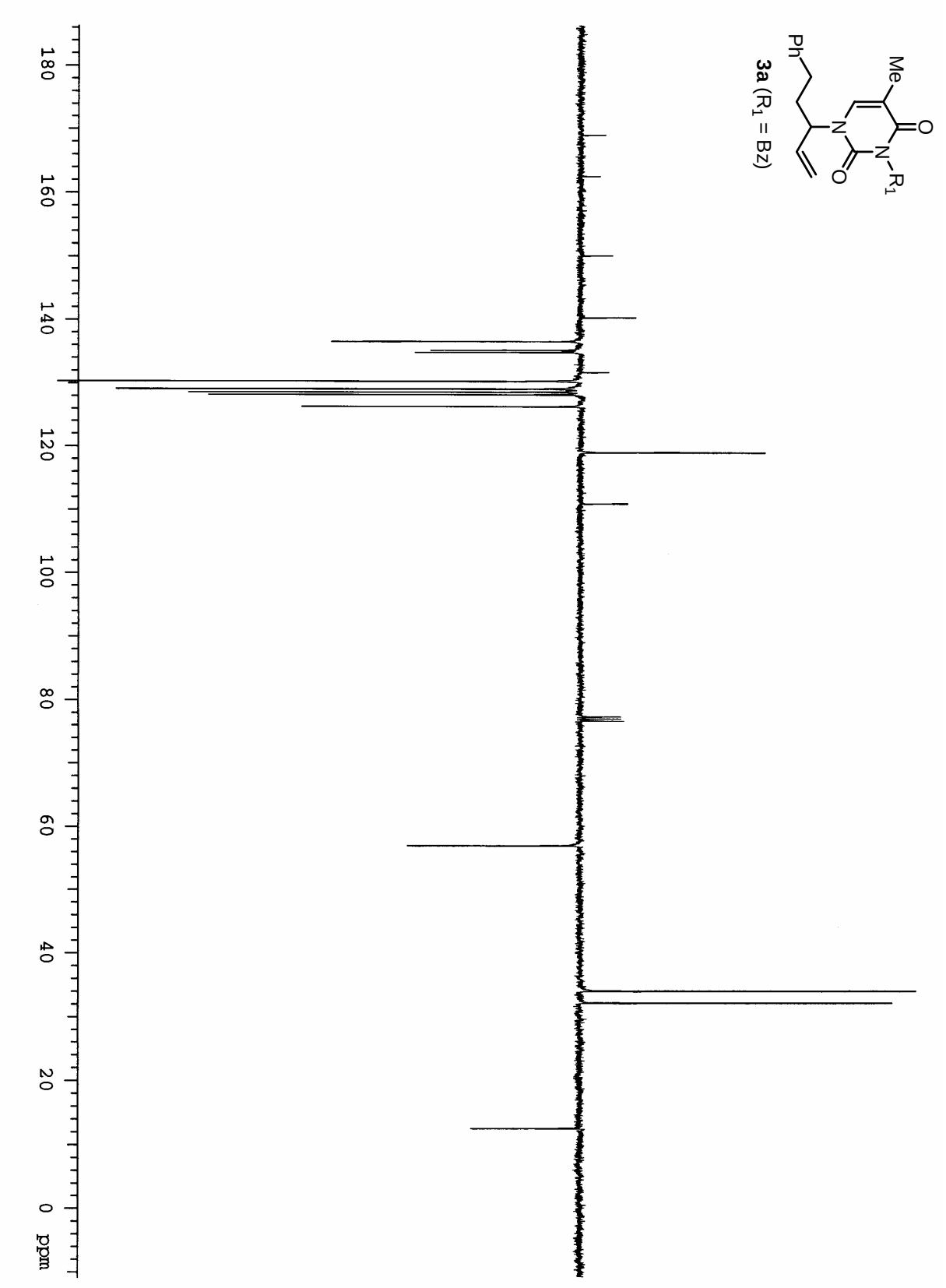


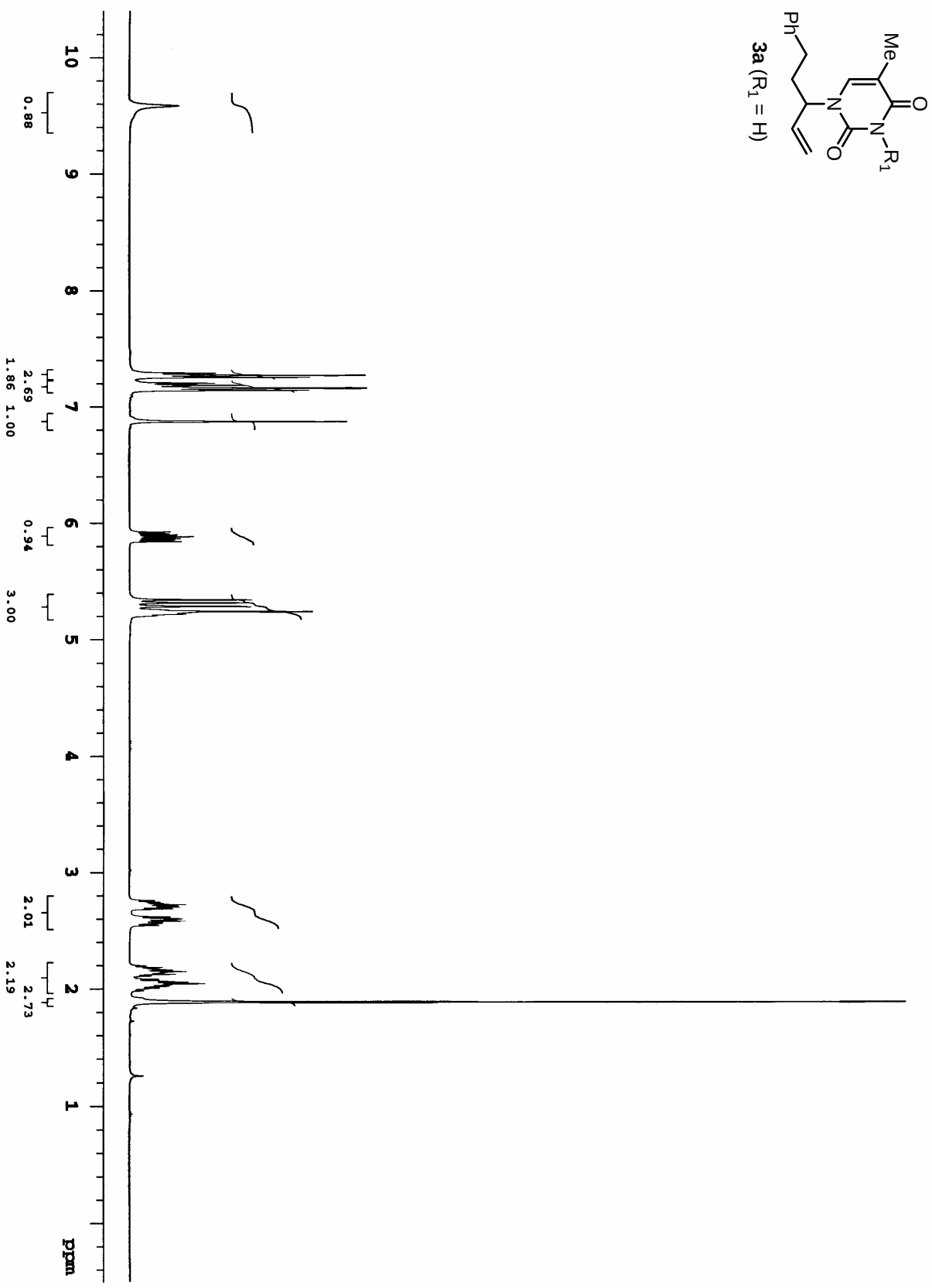
(4*S*,4a*S*,6*S*,7*R*)-7-(Hydroxymethyl)-4-methyl-1,3-dioxooctahydropyrrolo-[1,2-*c*]pyrimidin-6-yl benzoate (9). The azobicyclic compound **8** (45.2 mg, 0.088 mmol) was dissolved in a mixture of dioxane (2.4 mL) and water (1.2 mL). Acetic acid (50 μL) and 30% palladium on charcoal (47 mg, 0.132 mmol) were added. The reaction mixture was stirred under an atmosphere of hydrogen at room temperature for *ca*. 17 hours. The reaction mixture was filtered through a short pad of Celite, which was washed with dichloromethane and methanol. The filtration was washed with saturated aqueous $NaHCO_3$ solution, water and brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford a crude oil. Recrystallization in methanol afforded the primary alcohol **9** (25.1 mg, 90%) as a colorless crystalline solid: $[\alpha]_D^{23}$ –18.2 (c = 0.63, $CHCl_3$); IR ($CDCl_3$) 3419 (br s), 3213 (br s), 2939 (s), 1715 (s), 1602 (s), 1471 (s), 1453 (s), 1274 (s), 1071 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (br s, 1H), 8.00 (d, J = 7.3 Hz, 2H), 7.61–7.58 (m, 1H), 7.48–7.44 (m, 2H), 5.43–5.40 (m, 1H), 4.32 (d, J = 3.6 Hz, 1H), 4.08 (dd, A of ABX, J_{AB} = 11.5 Hz, J_{AX} = 3.1 Hz, 1H), 3.85 (dd, B of ABX, J_{AB} = 11.7 Hz, J_{BX} = 5.2 Hz, 1H), 3.78 (dt, J = 12.4, 7.5 Hz, 1H), 3.28 (br s, 1H), 2.90 (dt, J = 13.6, 7.0 Hz, 1H), 2.47 (dq, J = 13.6, 6.8 Hz, 1H), 1.95 (dt, J = 12.4, 7.1 Hz, 1H), 1.24 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.17 (e), 166.00 (e), 151.79 (e), 133.59 (o), 129.67 (o), 129.16 (e), 128.57 (o), 74.48 (o), 65.73 (o), 62.78 (e), 58.41 (o), 41.62 (o), 36.62 (e), 11.14 (o); HRMS (EI, M^+–CH_2OH) calcd for $C_{15}H_{15}N_2O_4$ 287.1032, found 287.1028.



(4*S*,4a*S*,6*S*,7*R*)-6-Hydroxy-7-(hydroxymethyl)-4-methyltetrahydropyrrolo-[1,2-*c*]-pyrimi-dine-1,3(2*H*,4*H*)-dione (10). The benzoate **9** (16.9 mg, 0.053 mmol) was dissolved in methanol (1.0 mL) and cooled with stirring to 0 °C. Potassium carbonate (73.4 mg, 0.513 mmol) was added, and the reaction mixture stirred at room temperature for 16 hours (t.l.c. control), before being concentrated *in vacuo* to afford the crude product. Purification by flash column chromatography (eluting with 20% methanol/dichloromethane with 1% triethylamine) afforded the unnatural nucleoside **10** (9.1 mg, 80%) as a colorless oil: $[\alpha]_D^{23}$ –50.0 (*c* = 0.25, MeOH); IR (neat) 3356 (br s), 1683 (s), 1463 (m), 1074 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 3.96–3.92 (m, 1H), 3.55 (dd, A of ABX, J_{AB} = 11.3 Hz, J_{AX} = 3.9 Hz, 1H), 3.51–3.47 (m, 1H), 3.35 (dd, B of ABX, J_{AB} = 11.3 Hz, J_{BX} = 4.3 Hz, 1H), 3.25 (dt, *J* = 12.5, 7.1 Hz, 1H), 2.21 (dt, *J* = 12.7, 6.4 Hz, 1H), 2.16 (dq, *J* = 13.5, 6.7 Hz, 1H), 1.41 (dt, *J* = 12.9, 7.0 Hz, 1H), 0.84 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD) δ 173.14 (e), 151.84 (e), 70.52 (o), 67.22 (o), 60.85 (e), 57.80 (o), 40.65 (o), 38.01 (e), 10.08 (o); HRMS (CI, M+H^+) calcd for $C_9H_{15}N_2O_4$ 215.1026, found 215.1027.


Me
O
N
R1
N
O
Ph
3a (R1 = Bz)
9
8
7
6
5
4
3
2
1
-0
ppm
1.99 2.17 3.06
1.06 2.06 1.08
1.00
1.07
2.15
2.24
2.29
3.27


Ph
Me
O
N
N
O
R_1
3a (R_1 = Bz)
180
160
140
120
100
80
60
40
20
0
ppm


Ph
Me
O
N
N
R1
O
3a (R1 = H)
10
9
8
7
6
5
4
3
2
1
ppm
0.88
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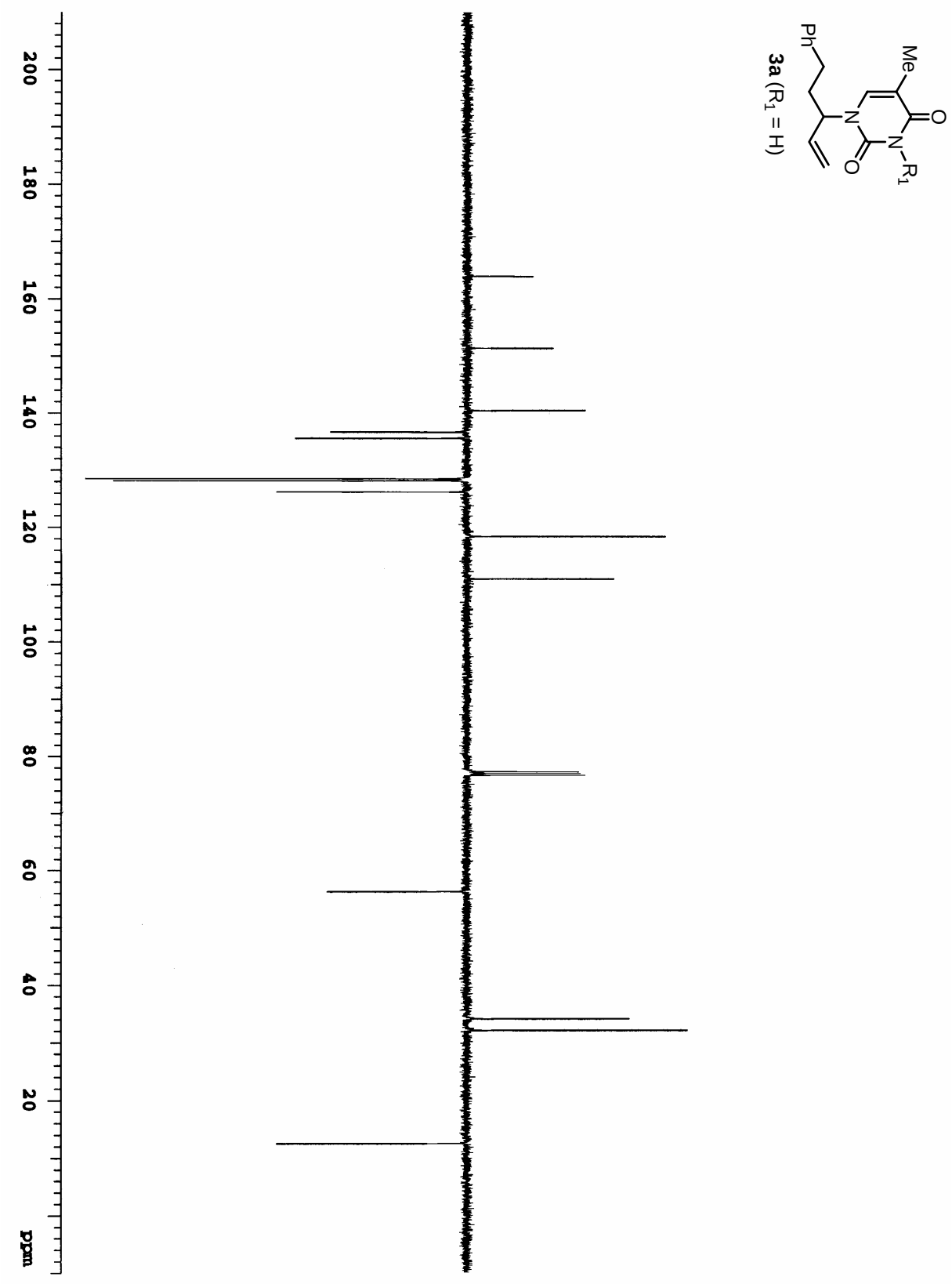
1.86
1.00
0.94
3.00
2.01
2.73
2.19


Ph
Me
O
N
N
R1
O
3a (R1 = H)
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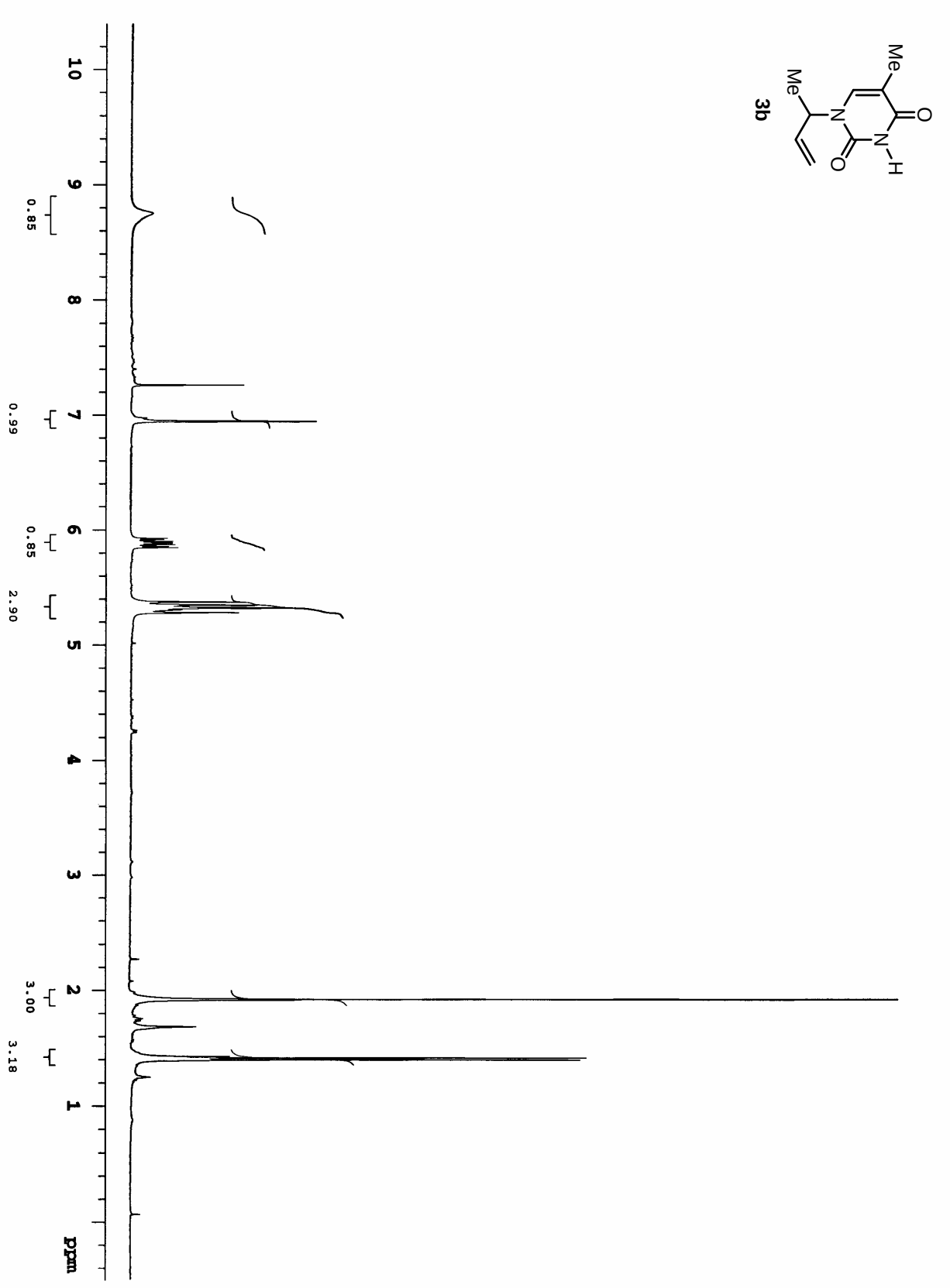
180
160
140
120
100
80
60
40
20
ppm


Me
Me
O
N
N
H
O
3b
10
9
8
7
6
5
4
3
2
1
ppm
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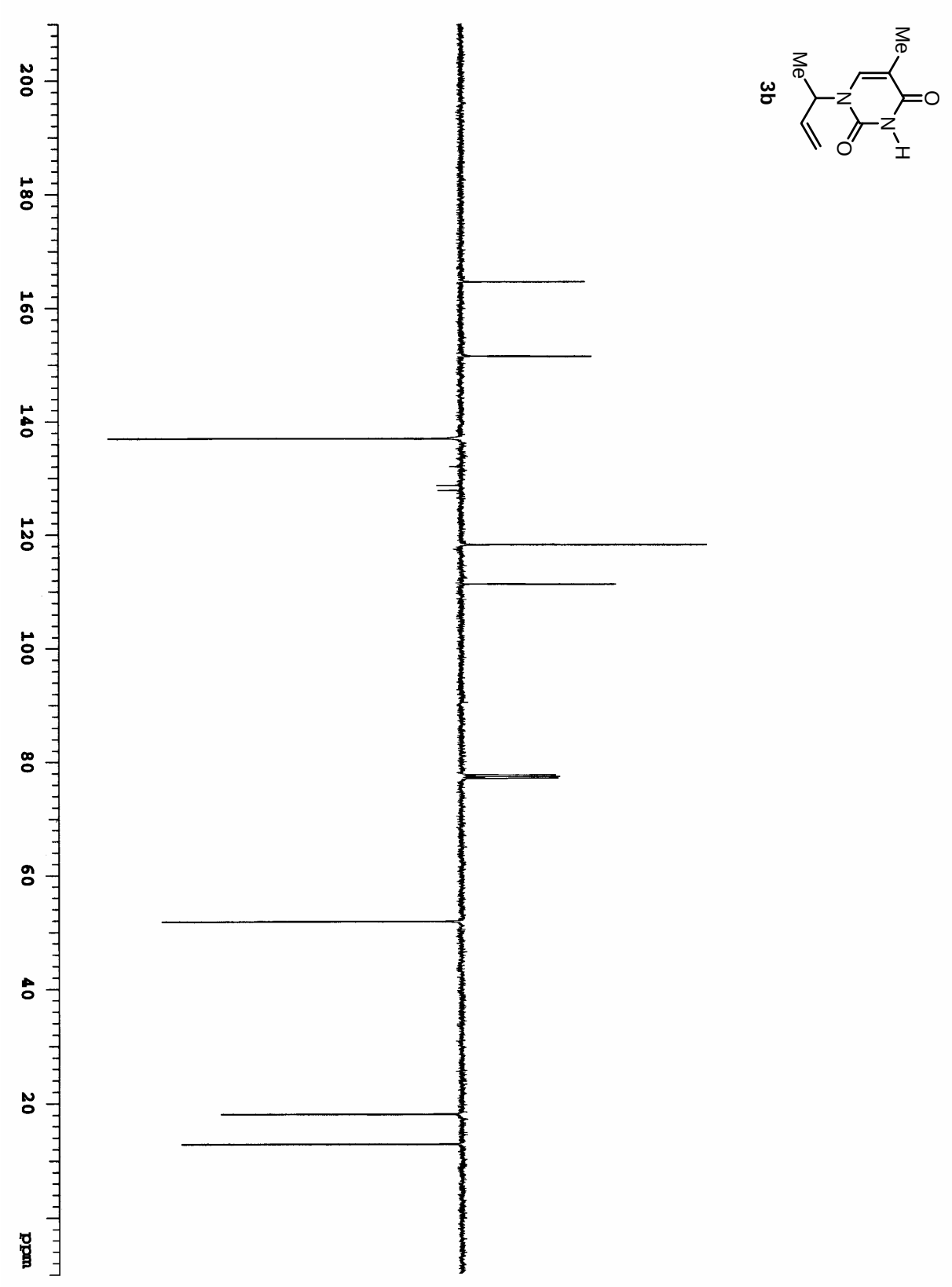
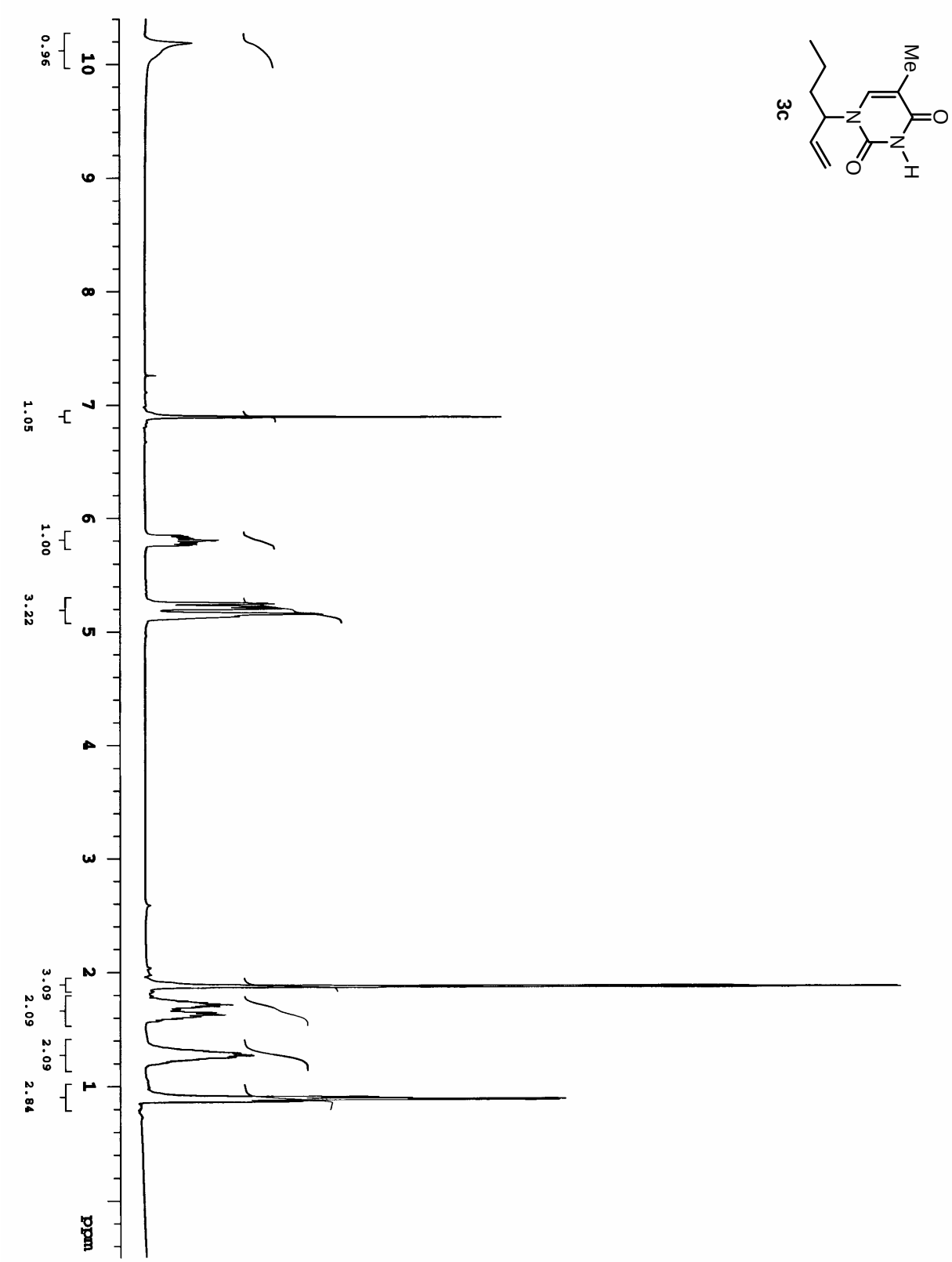
0.99
0.85
2.90
3.00
3.18


Me
Me
O
N
N
H
O
3b
200
180
160
140
120
100
80
60
40
20
ppm


3c
Me
O
N
N
H
O
10
9
8
7
6
5
4
3
2
1
ppm
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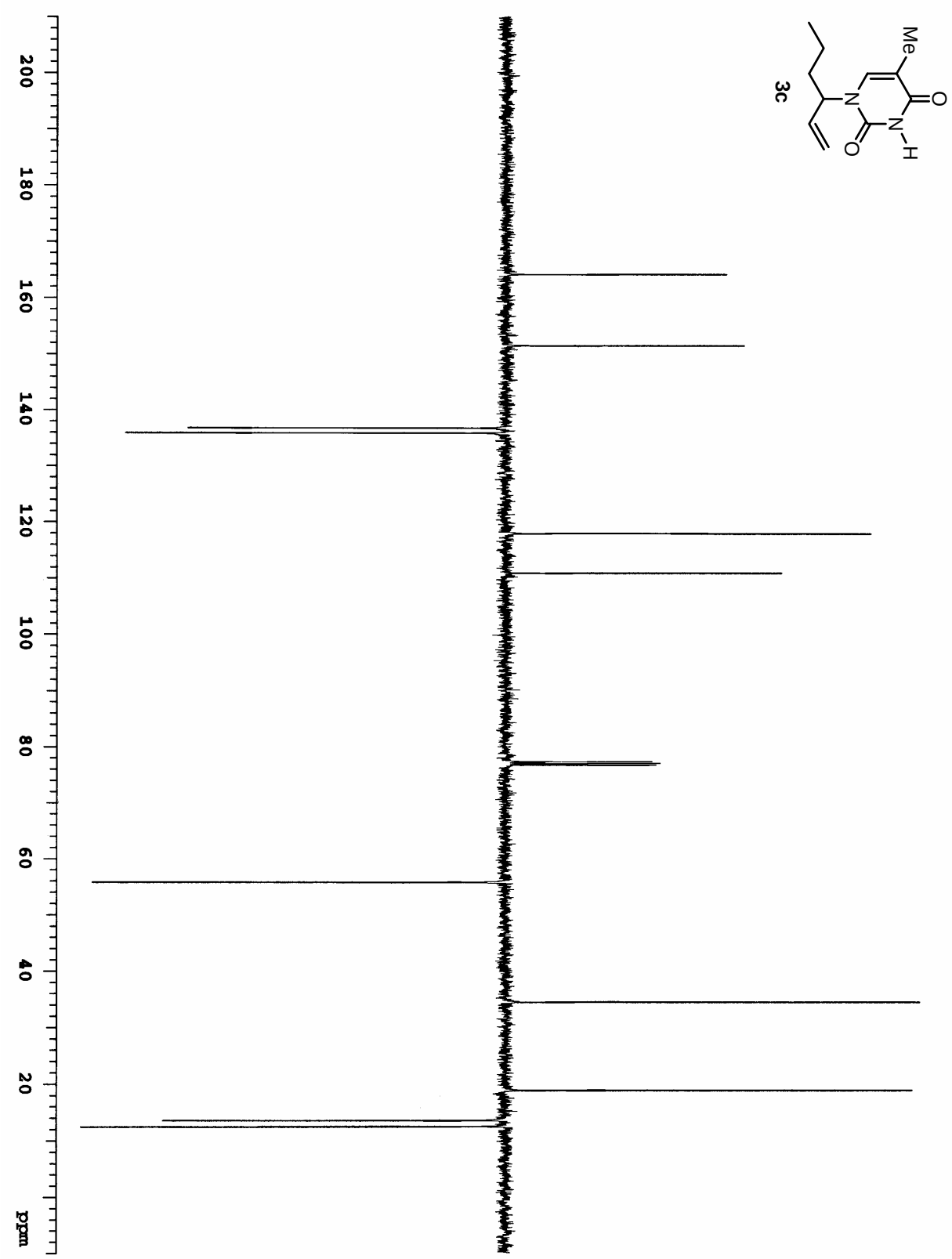
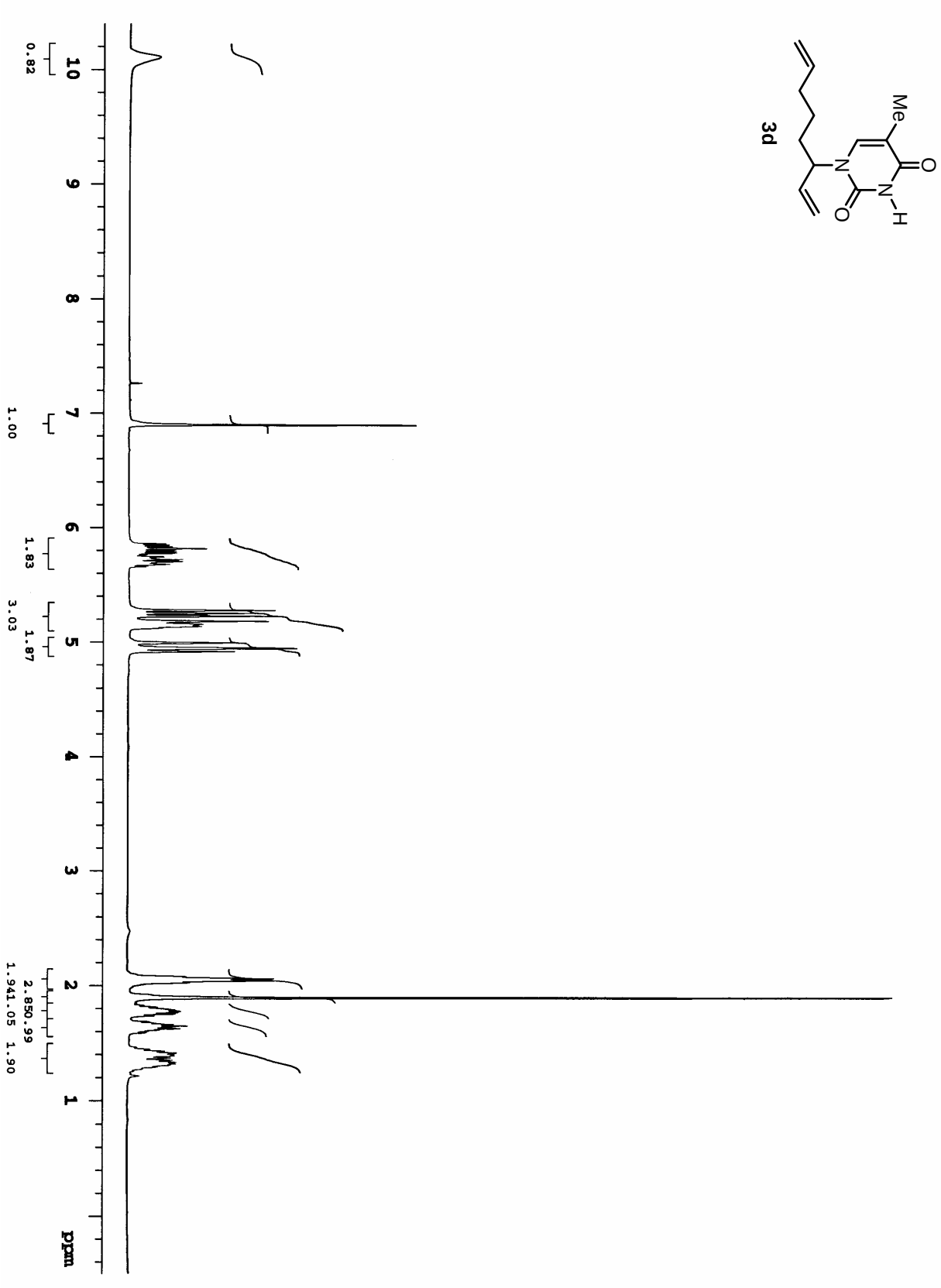
1.05
1.00
3.22
3.09
2.09
2.09
2.84


3c
Me
O
N
N
H
O
200
180
160
140
120
100
80
60
40
20
ppm


3d
Me
O
N
N
H
O
10
9
8
7
6
5
4
3
2
1
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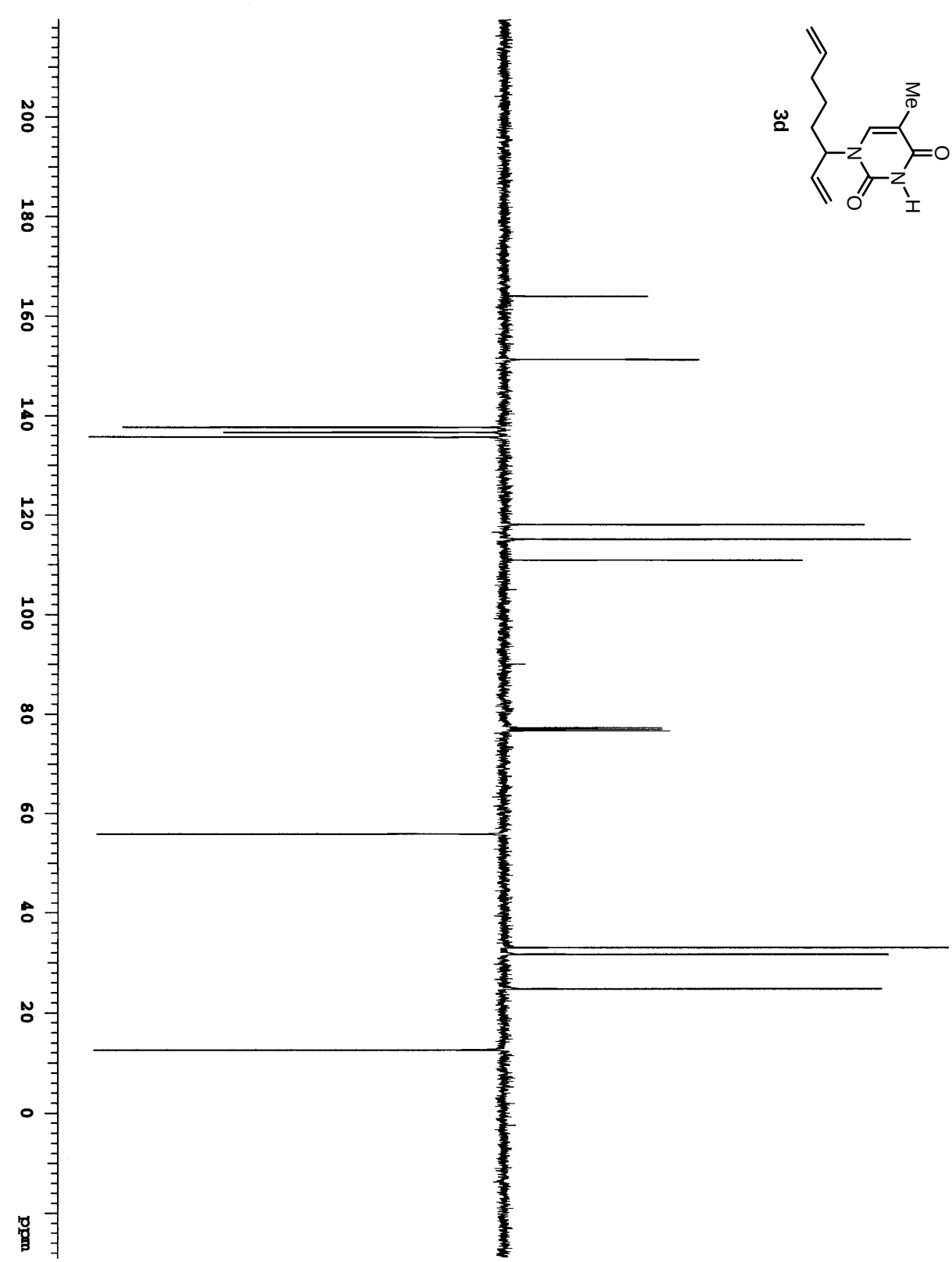
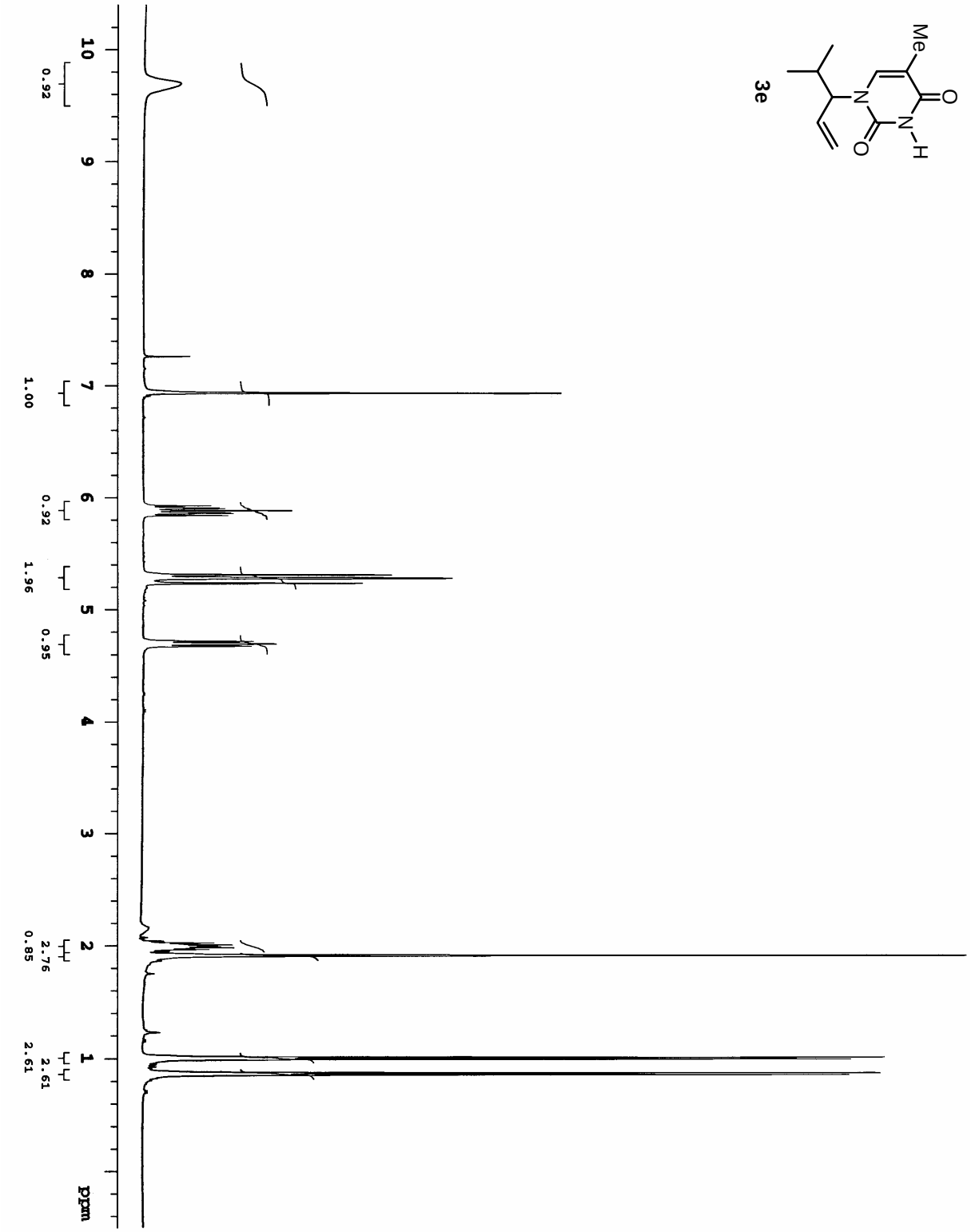
1.00
1.83
1.87
3.03
2.85
0.99
1.94
1.05
1.90


3d
Me
O
N
H
O
N
O
200
180
160
140
120
100
80
60
40
20
0
ppm


3e
Me
O
N
H
O
N
10
9
8
7
6
5
4
3
2
1
ppm
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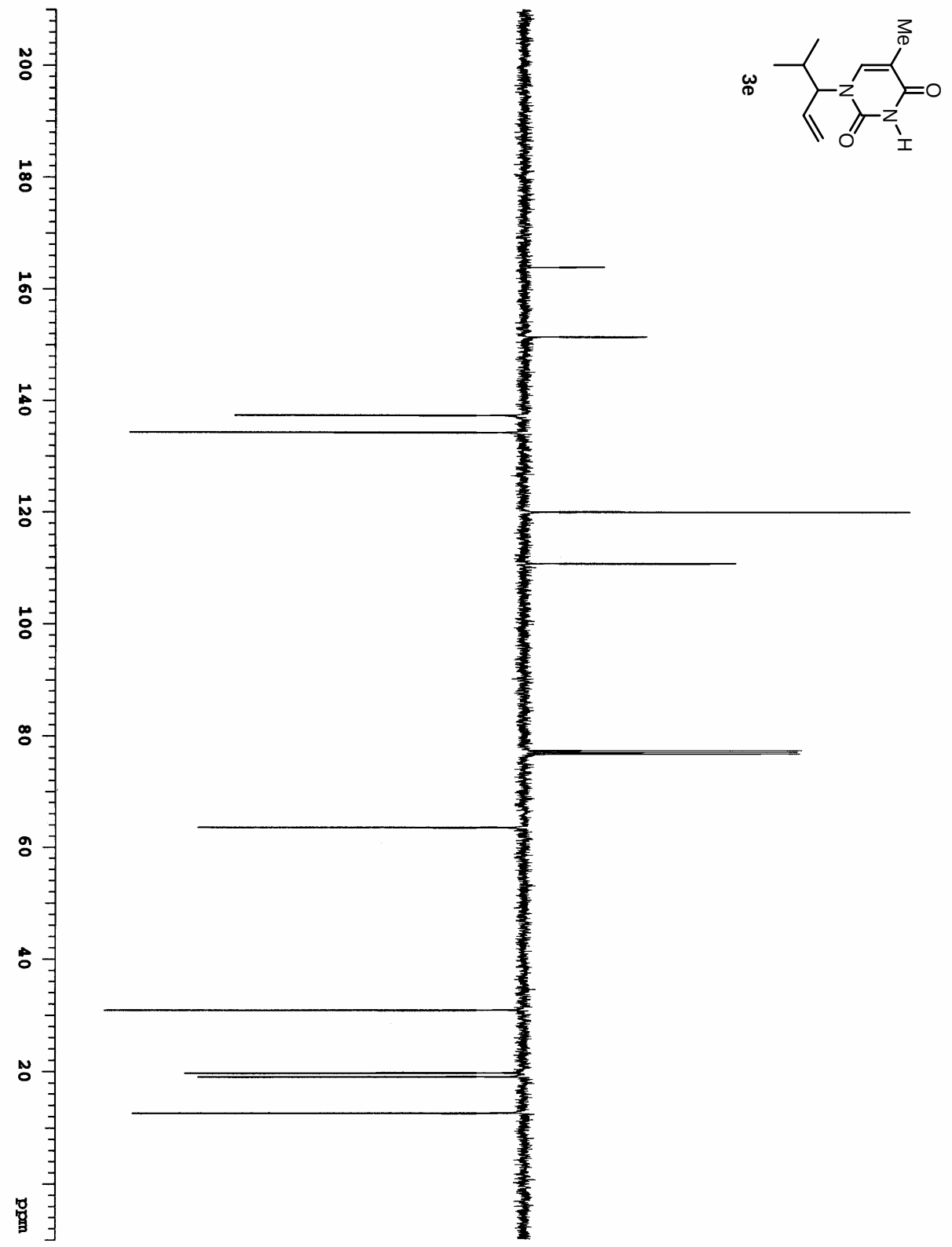
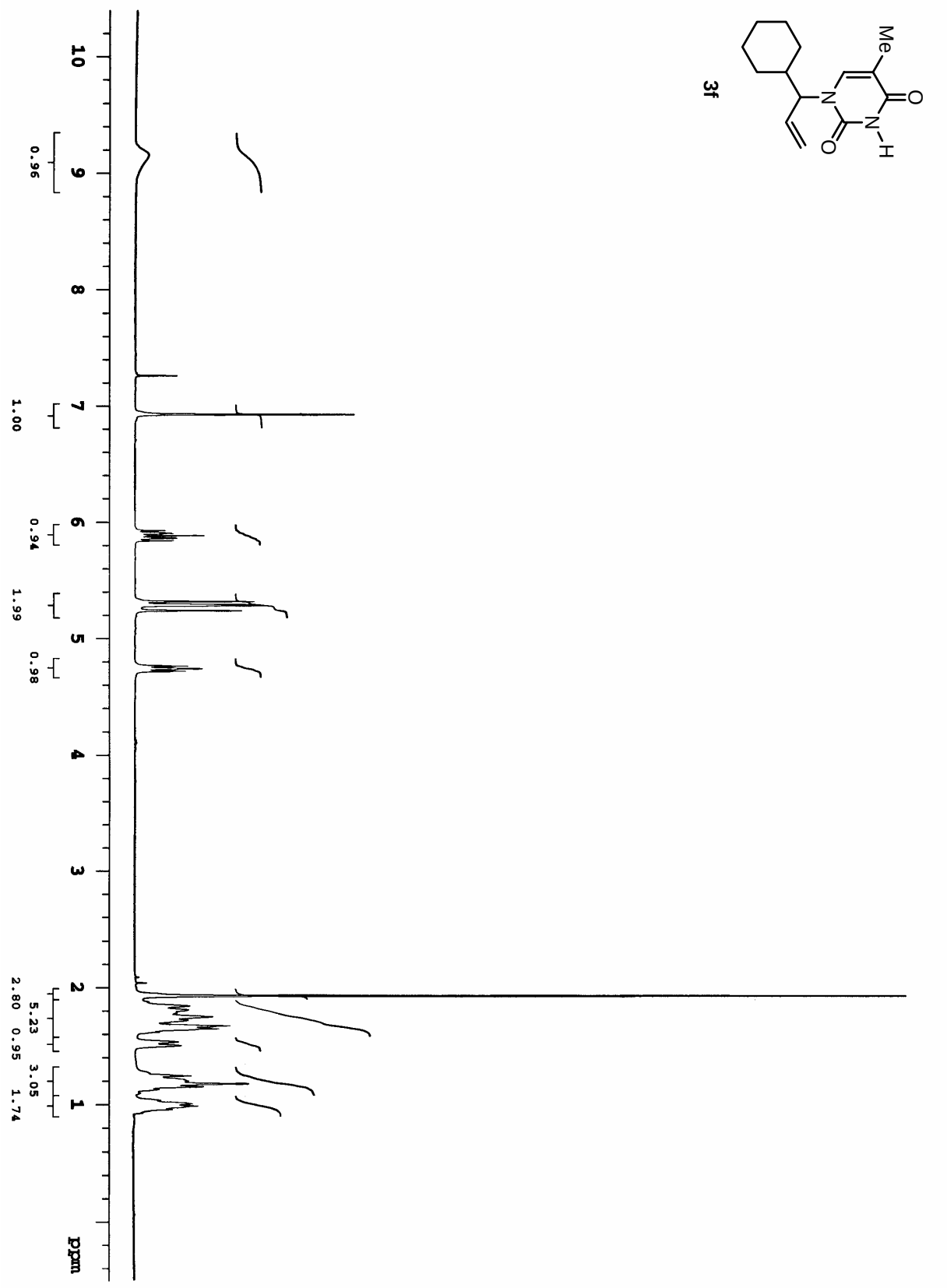
1.00
0.92
1.96
0.95
0.85
2.76
2.61
2.61


Me
O
N
H
O
N
3e
200
180
160
140
120
100
80
60
40
20
ppm


3f
Me
O
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N
H
O
10
9
8
7
6
5
4
3
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1
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0.94
1.99
0.98
5.23
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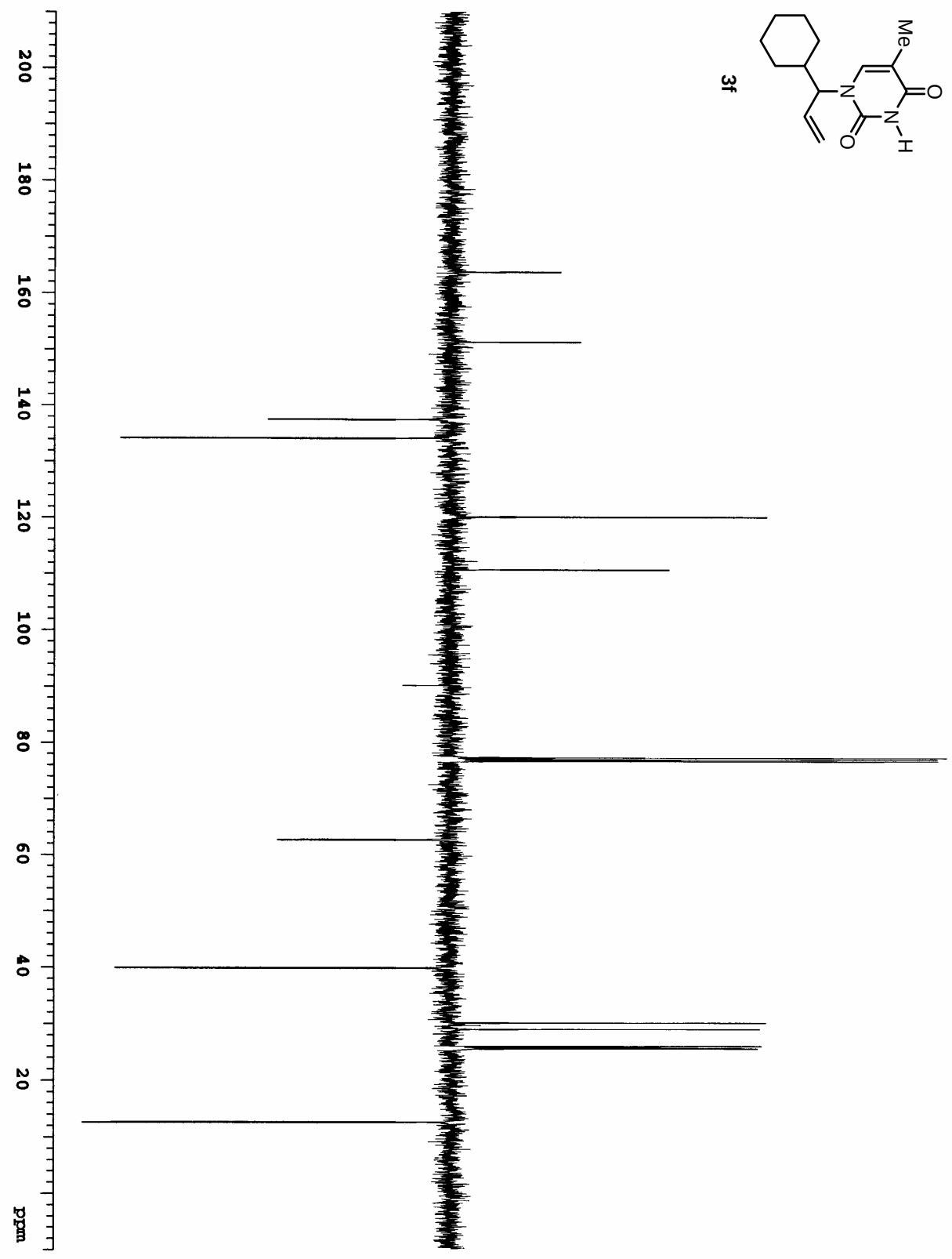
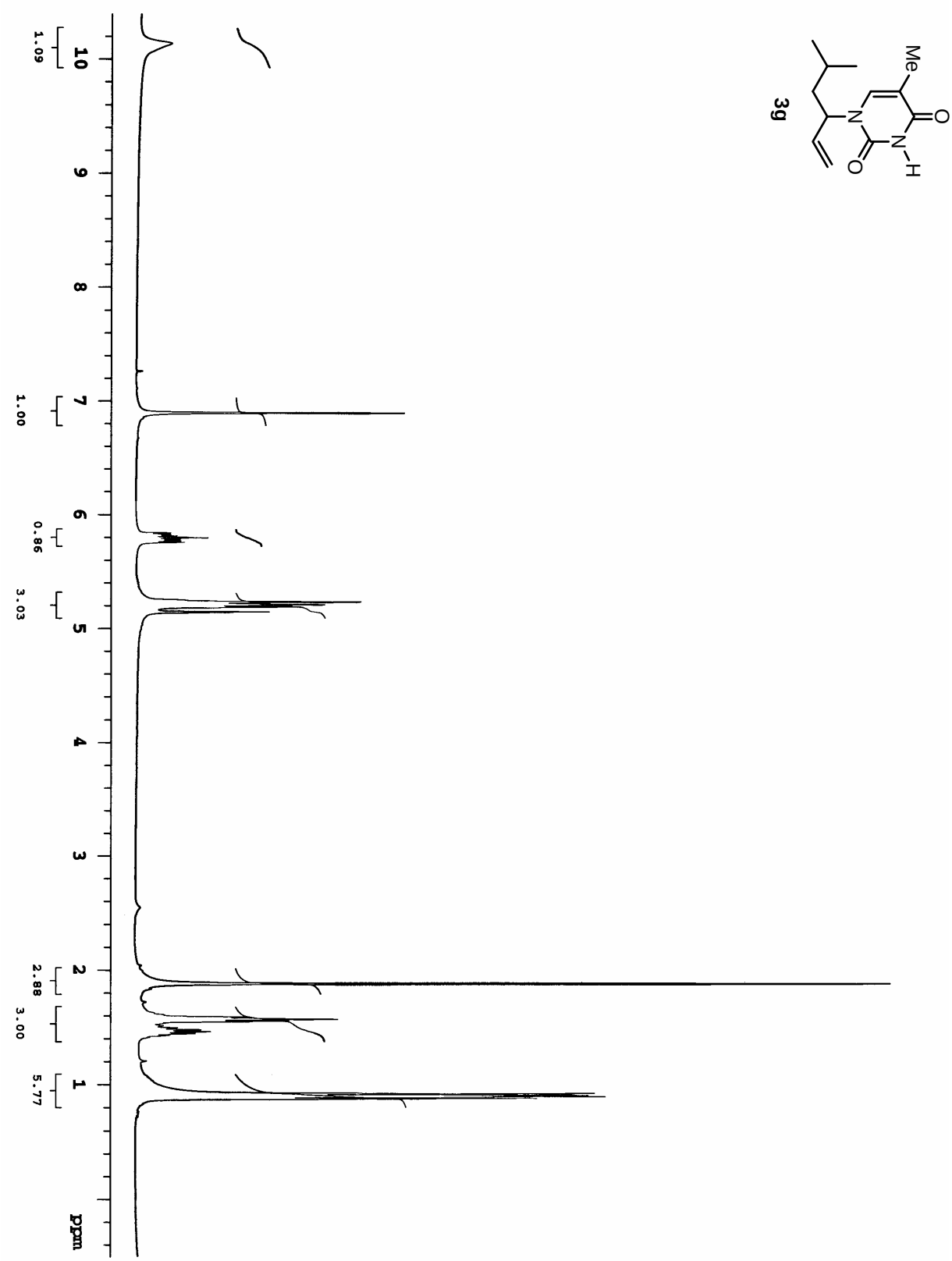
3.05
1.74


Me
O
N
N
H
O
3f
200
180
160
140
120
100
80
60
40
20
ppm


3g
Me
O
N
N
H
O
10
9
8
7
6
5
4
3
2
1
ppm
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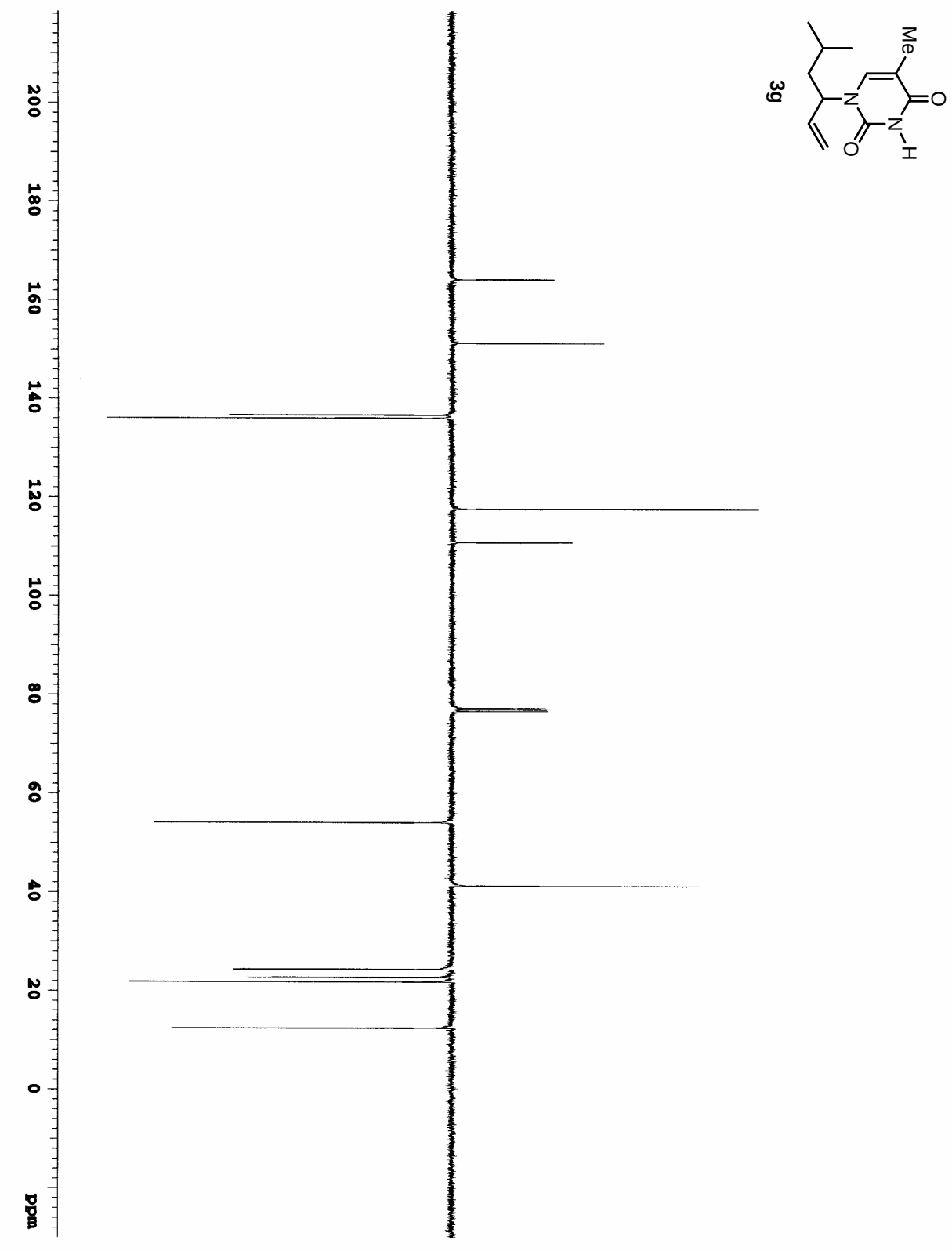
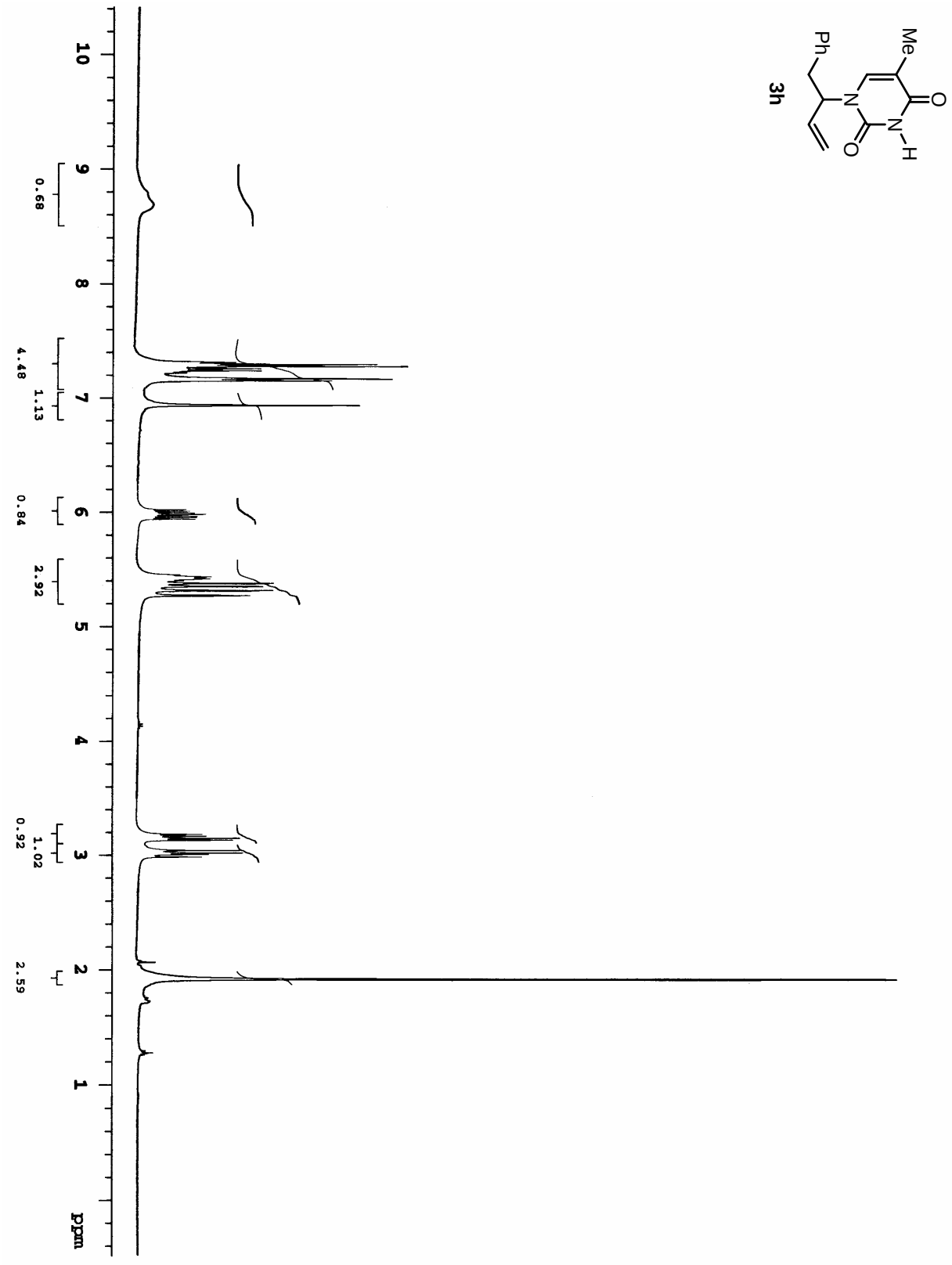
1.00
0.86
3.03
2.88
3.00
5.77


3g
Me
O
N
N
H
O
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
Ph
O
N
N
H
O
3h
10
9
8
7
6
5
4
3
2
1
ppm
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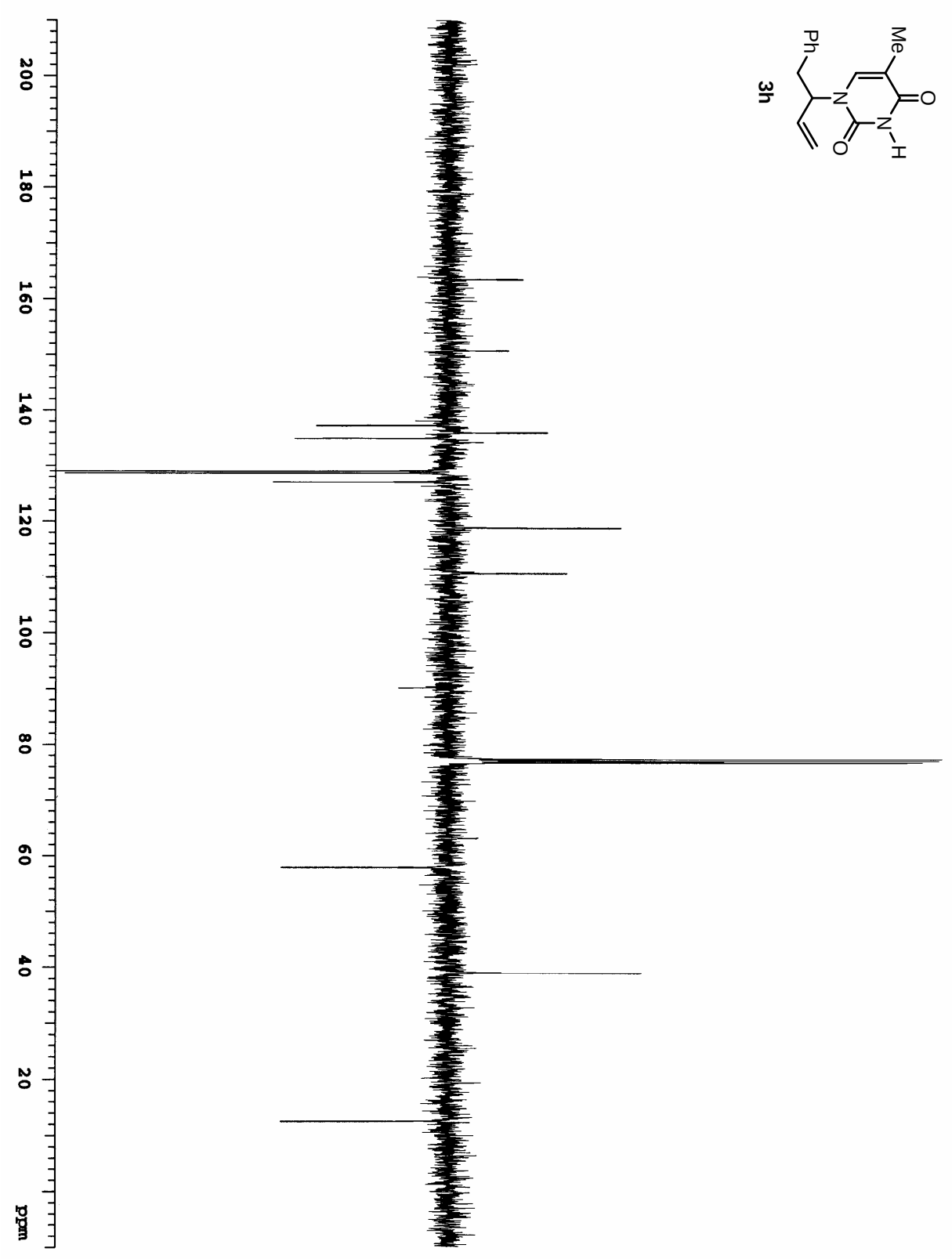
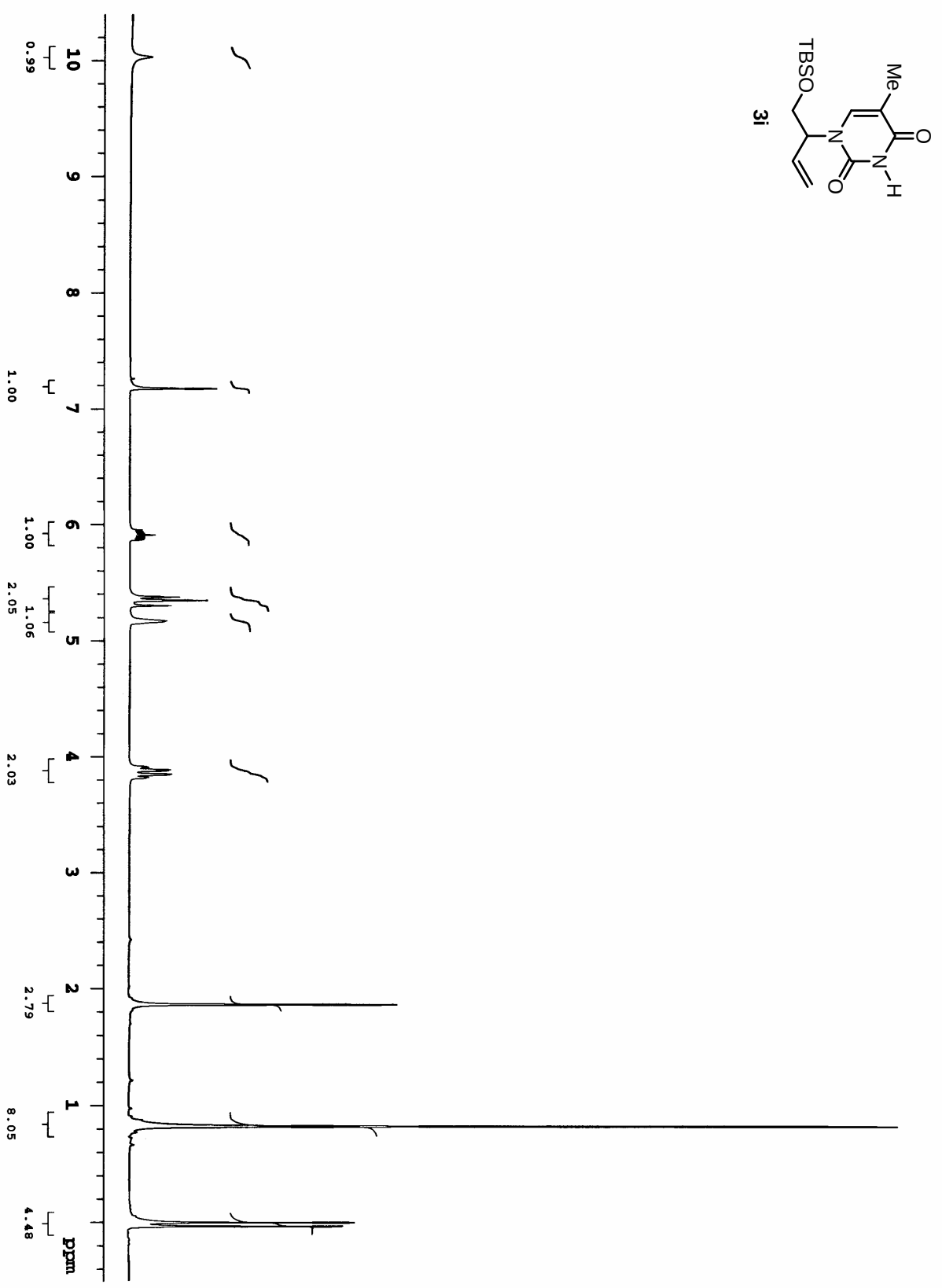
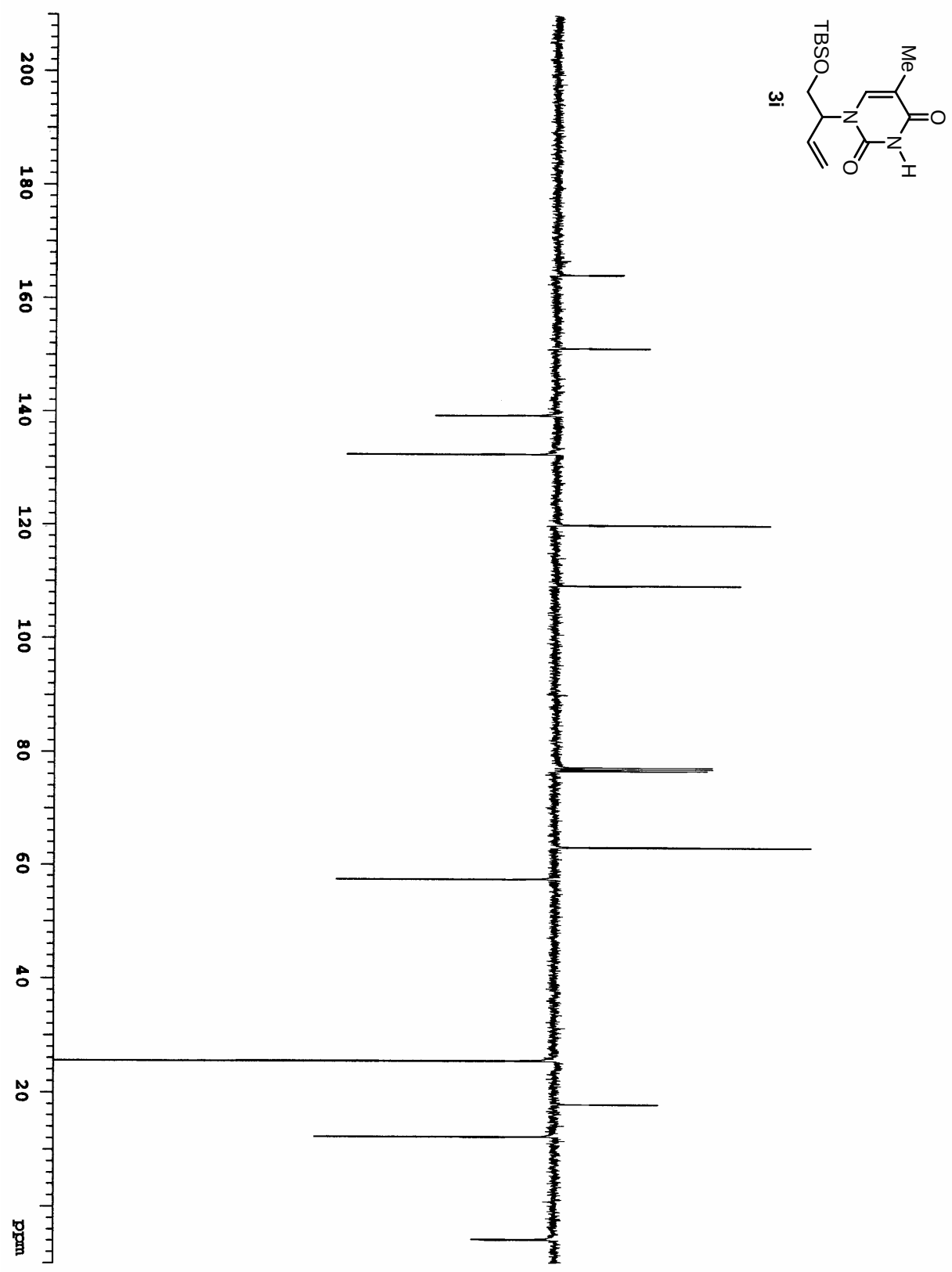
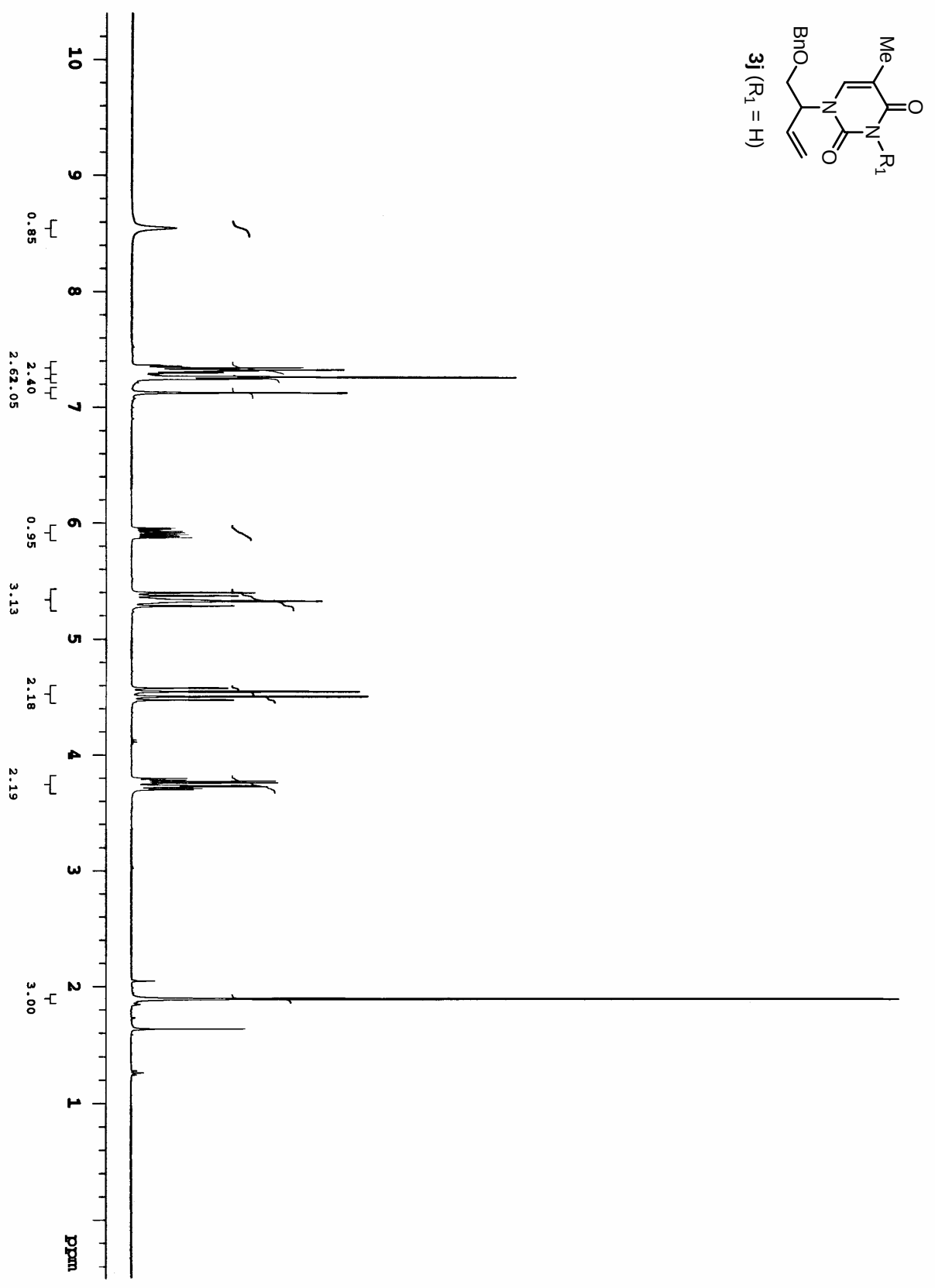
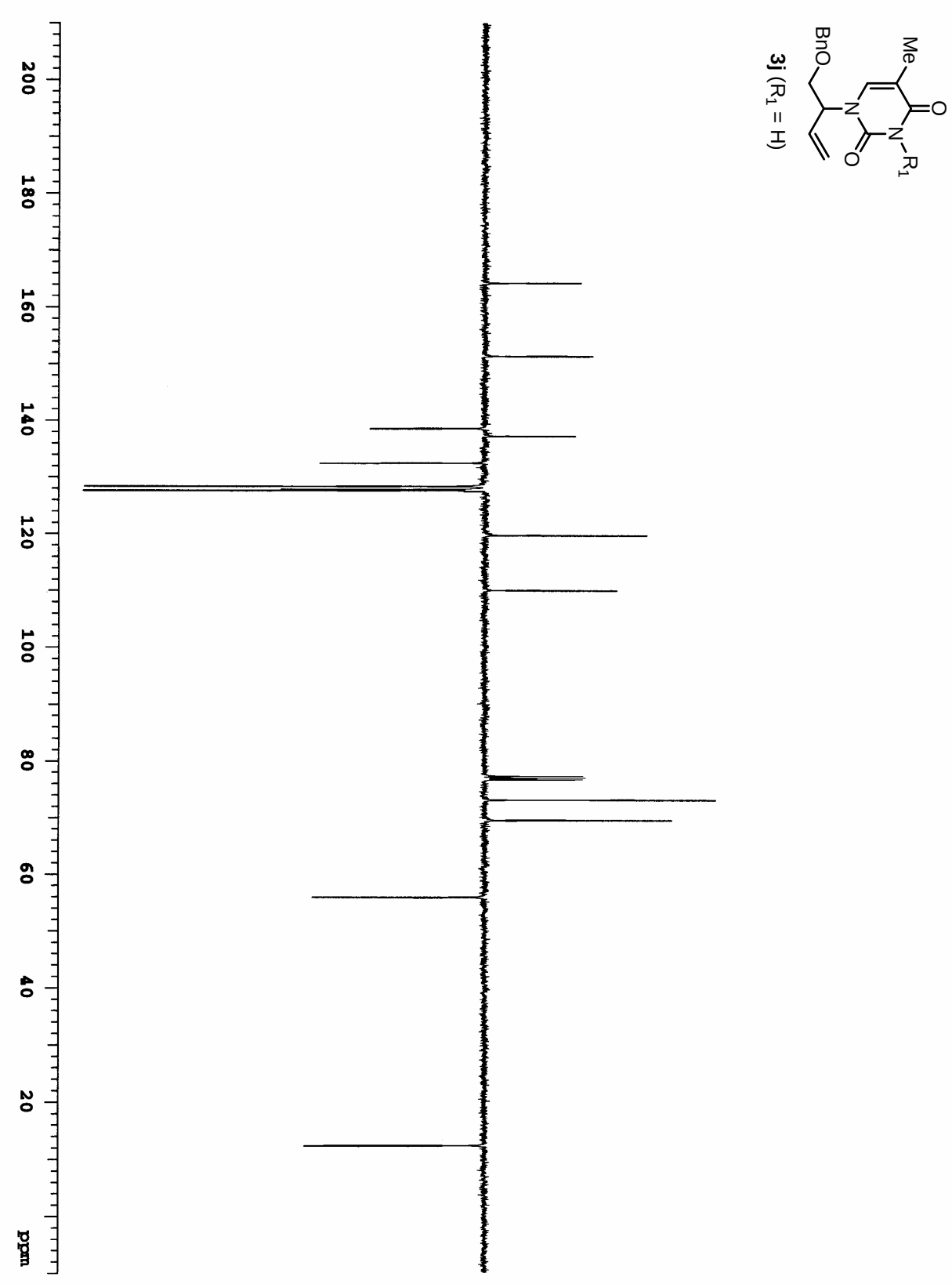
4.48
1.13
0.84
2.92
0.92
1.02
2.59

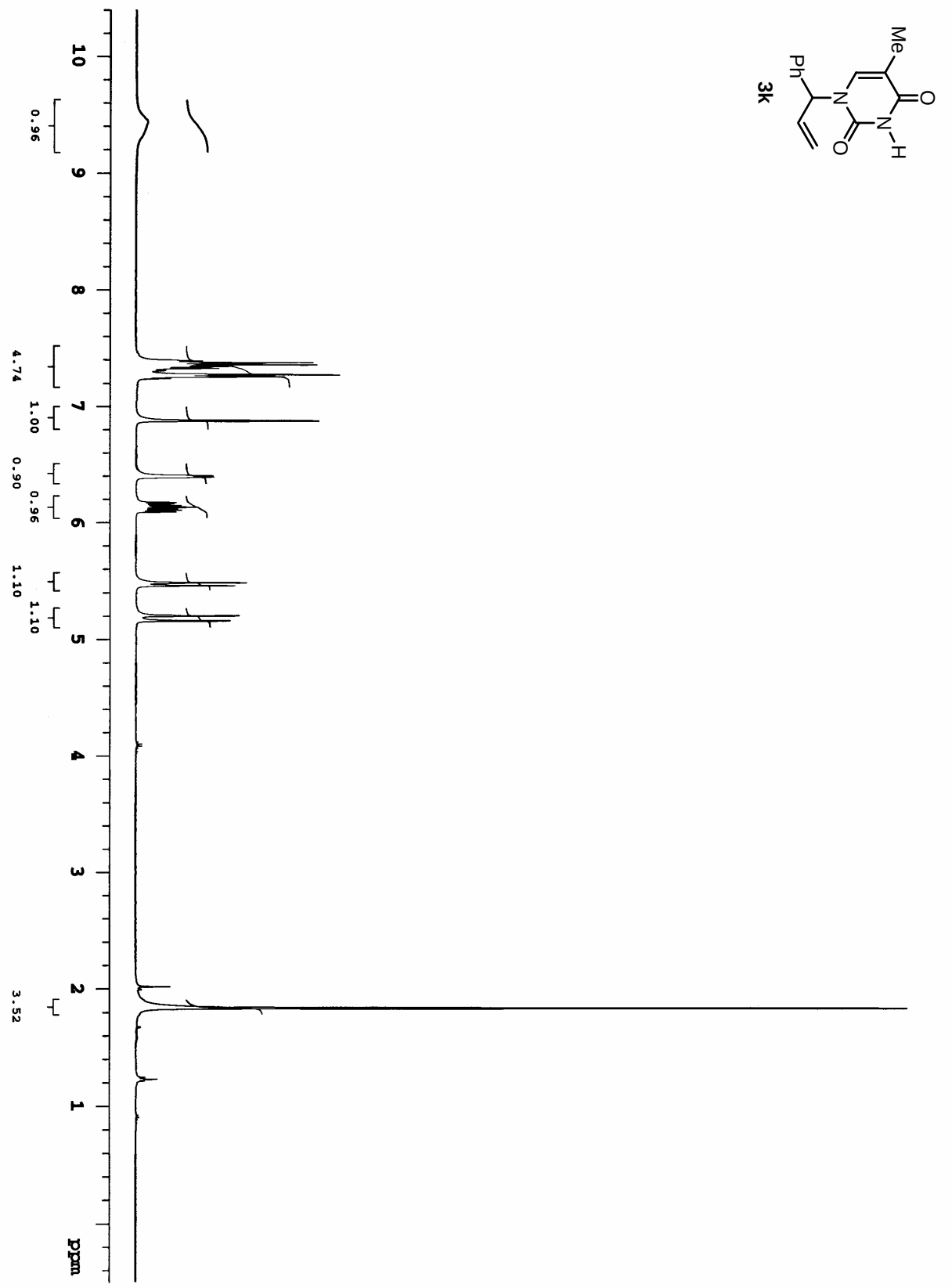

Ph
Me
O
N
N
H
O
3h
200
180
160
140
120
100
80
60
40
20
ppm


TBSO
Me
O
N
H
O
N
3i
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.00
1.00
1.06
2.05
2.03
2.79
8.05
4.48


TBSO
Me
O
N
N
H
O
3i
200
180
160
140
120
100
80
60
40
20
ppm


Me
O
BnO
N
N
R1
O
3j (R1 = H)
10
9
8
7
6
5
4
3
2
1
ppm
0.85
2.40
2.62.05
0.95
3.13
2.18
2.19
3.00


Me
O
BnO
N
N
R1
O
3j (R1 = H)
200
180
160
140
120
100
80
60
40
20
ppm


Me
Ph
O
N
N
H
O
3k
10
9
8
7
6
5
4
3
2
1
ppm
0.96
4.74
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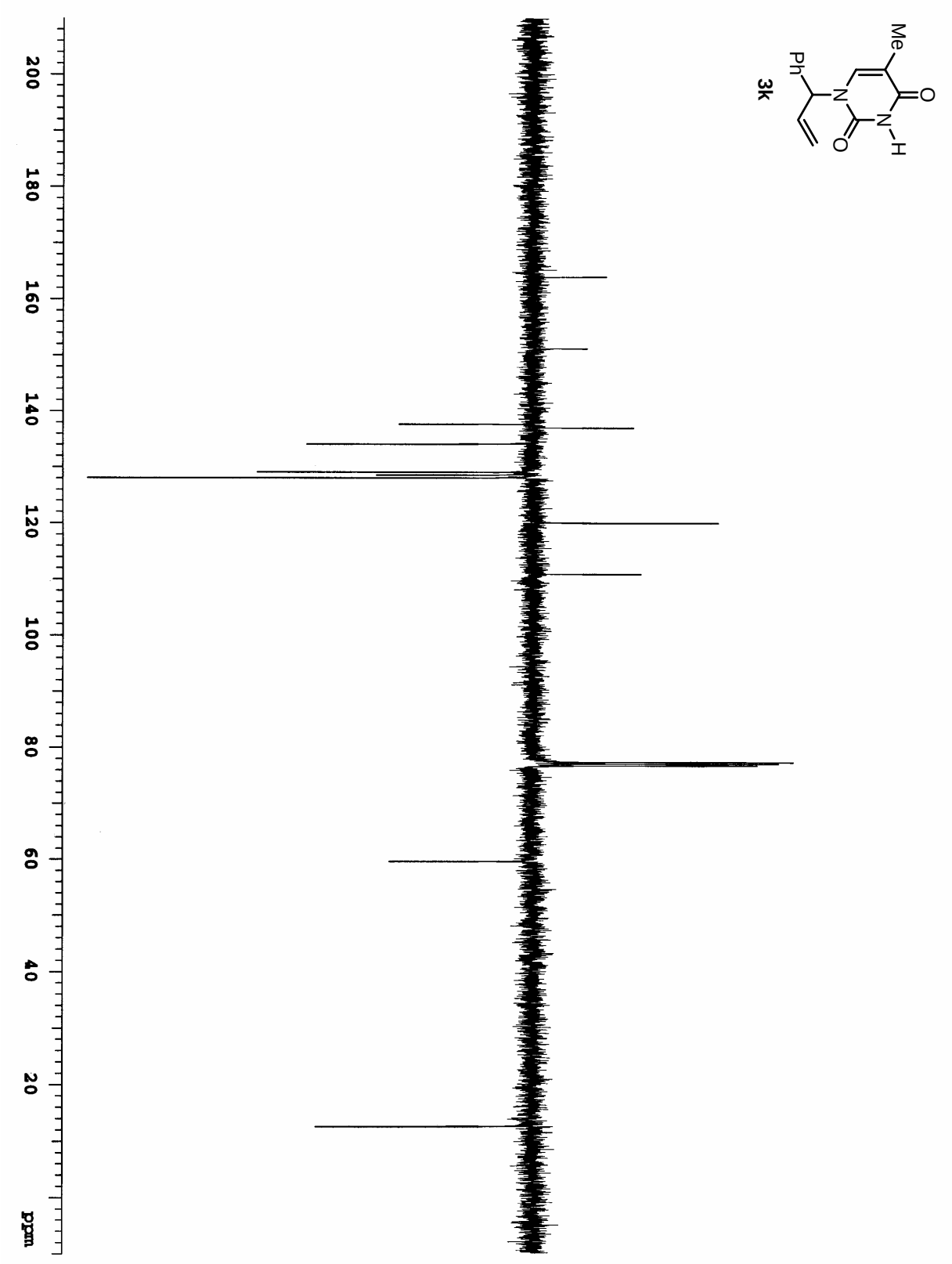
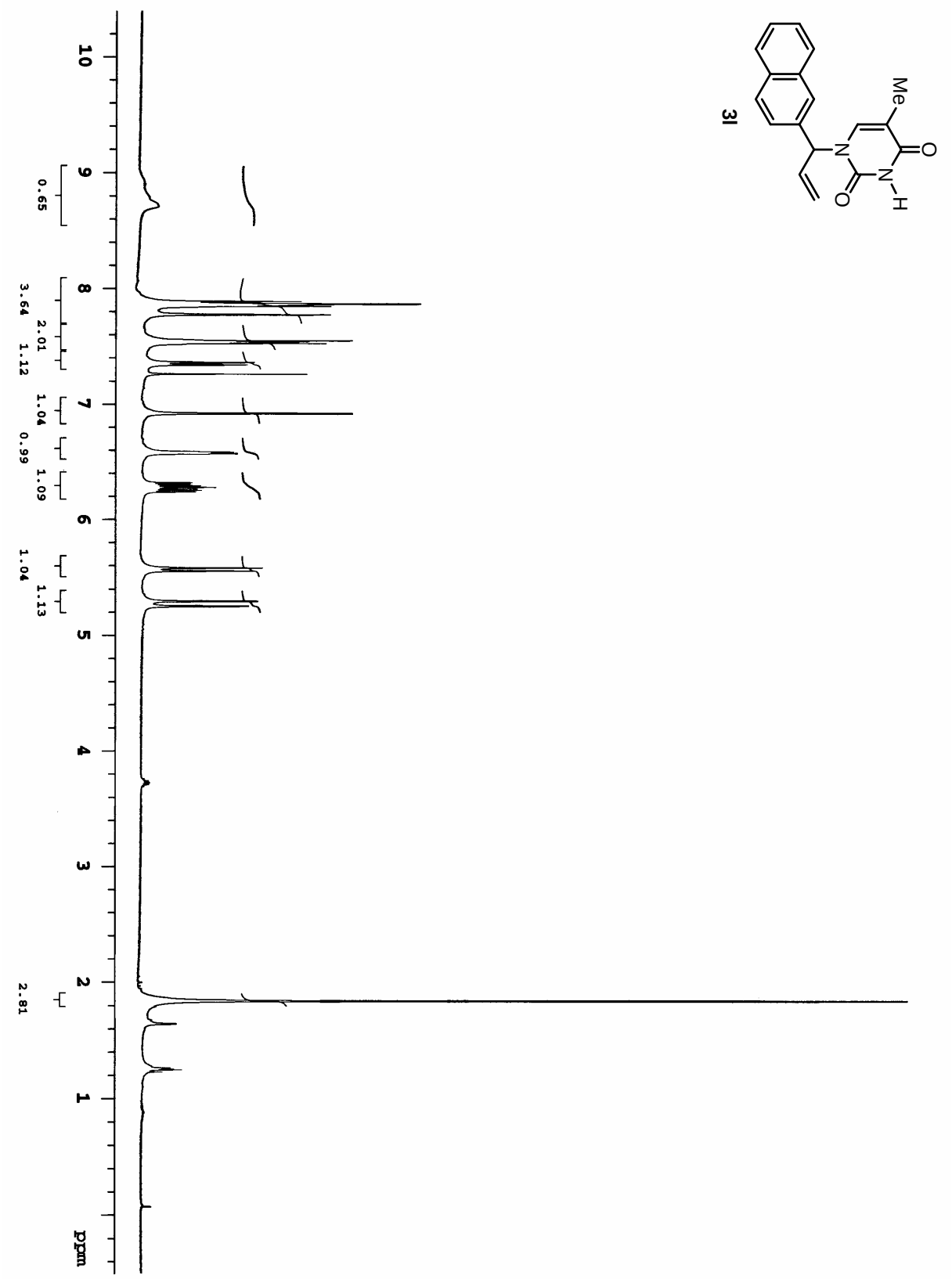
0.90
0.96
1.10
1.10
3.52


Me
Ph
O
N
H
O
3k
200
180
160
140
120
100
80
60
40
20
ppm


3l
Me
O
N
H
O
N
10
9
8
7
6
5
4
3
2
1
ppm
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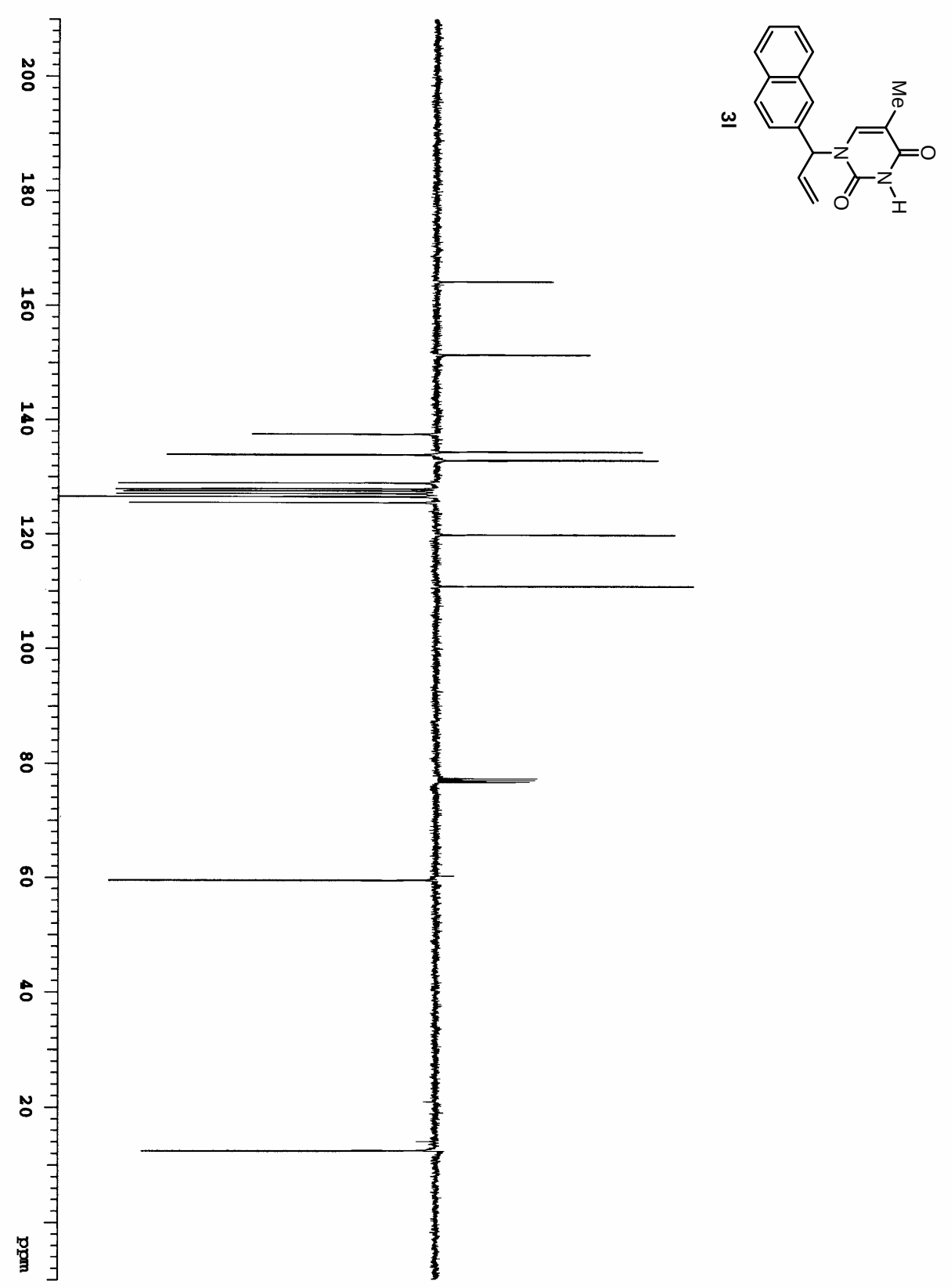
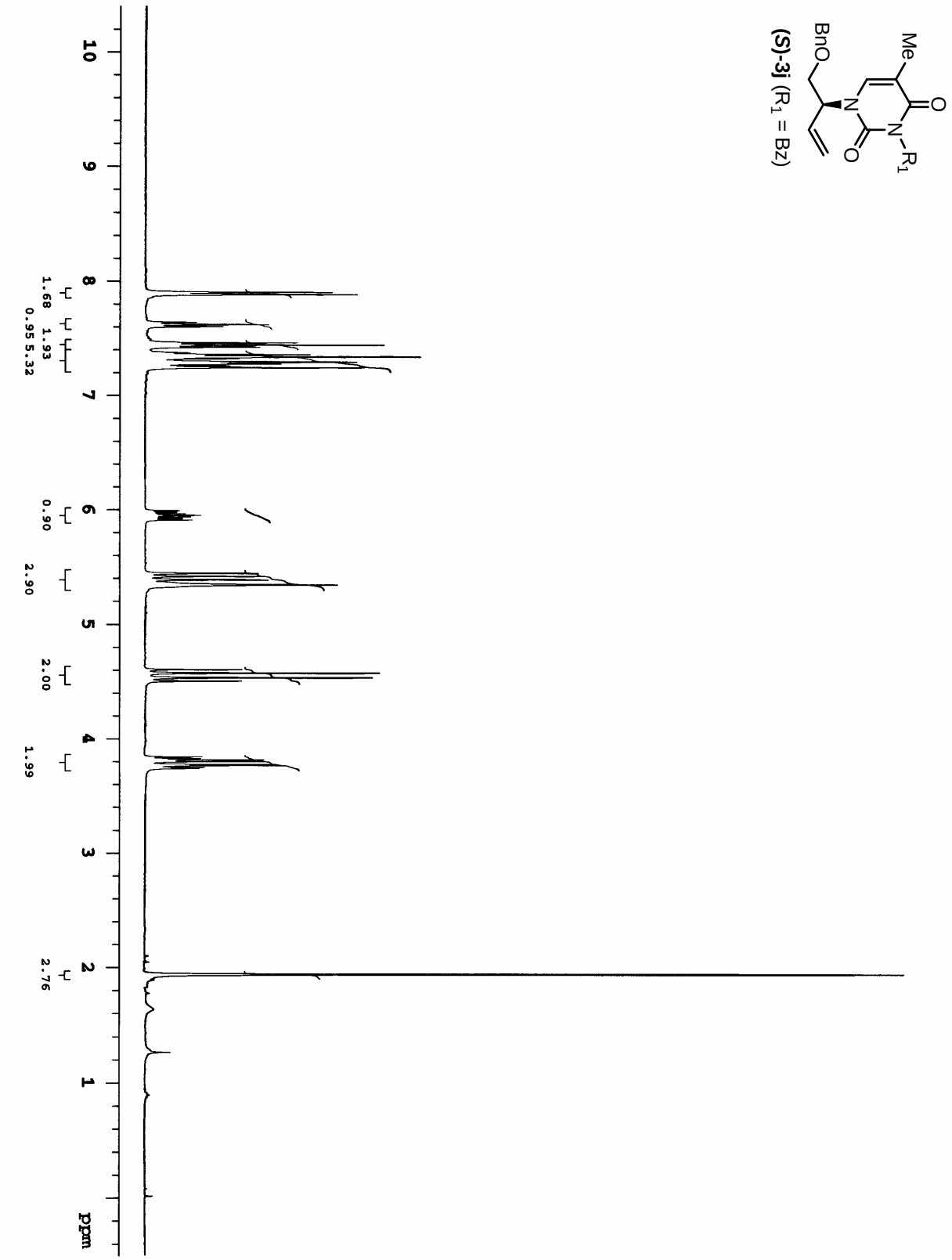
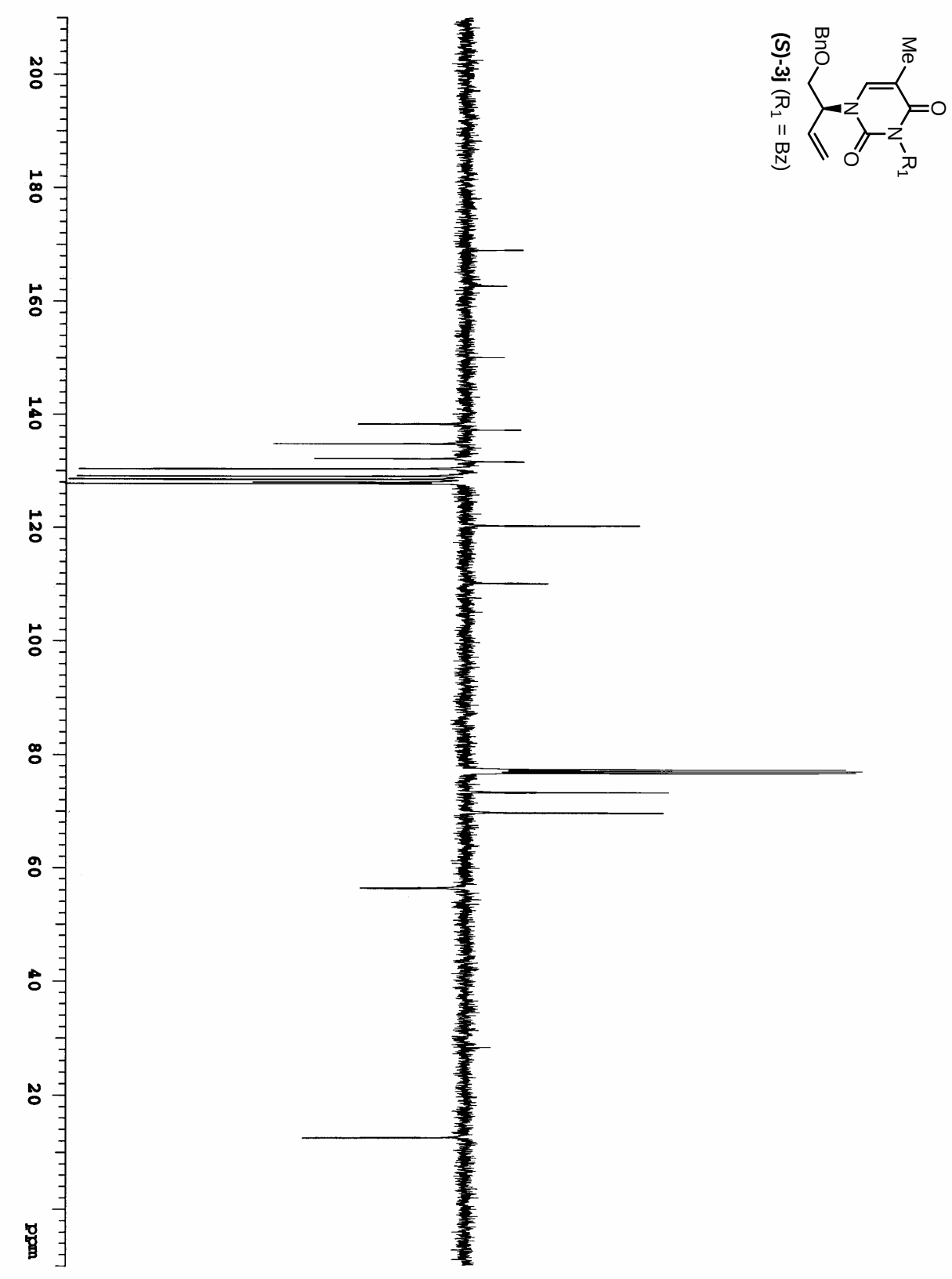
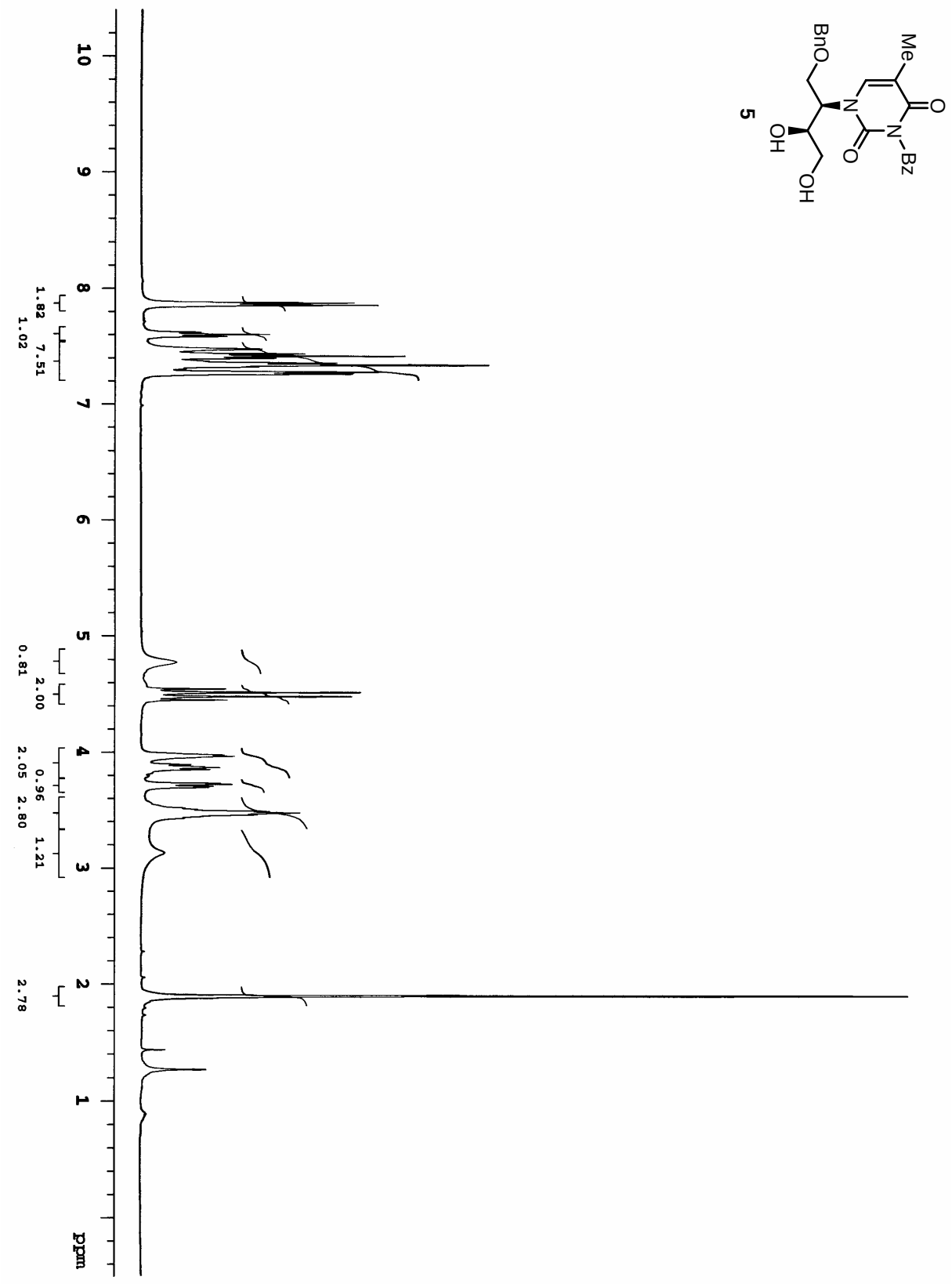
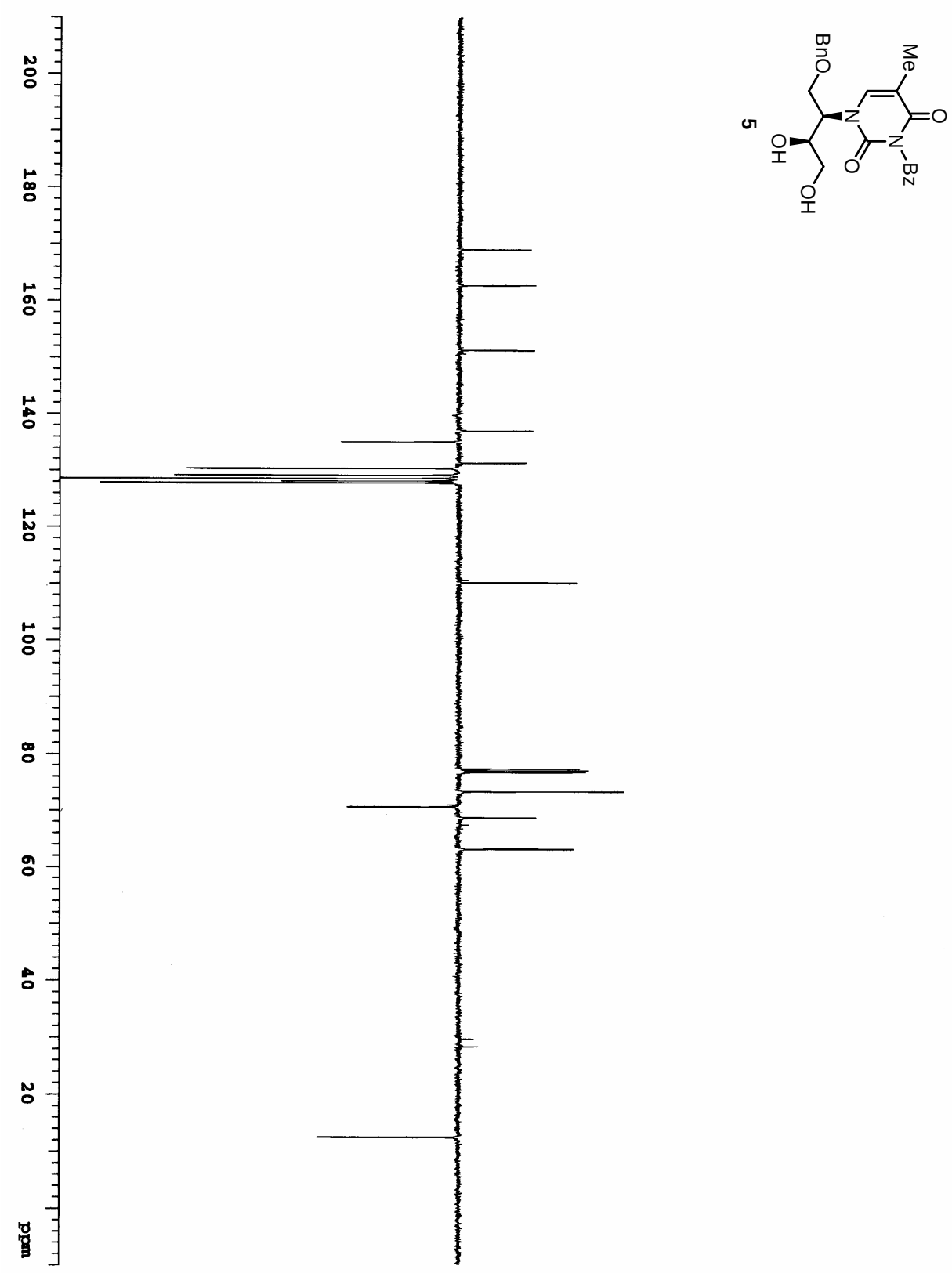
2.01
3.64
1.12
1.04
0.99
1.09
1.04
1.13
2.81

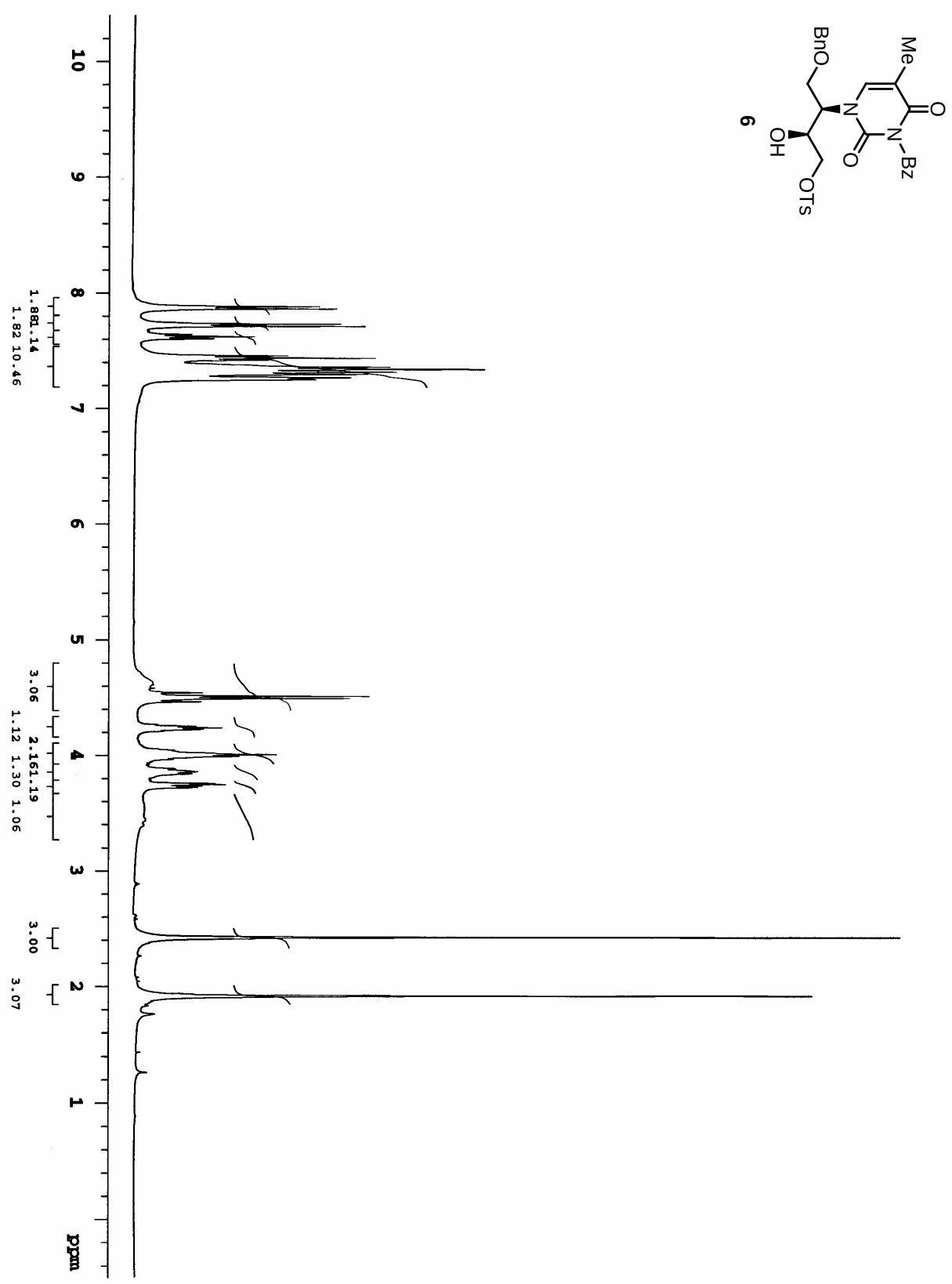

3l
Me
O
N
H
O
N
200
180
160
140
120
100
80
60
40
20
ppm

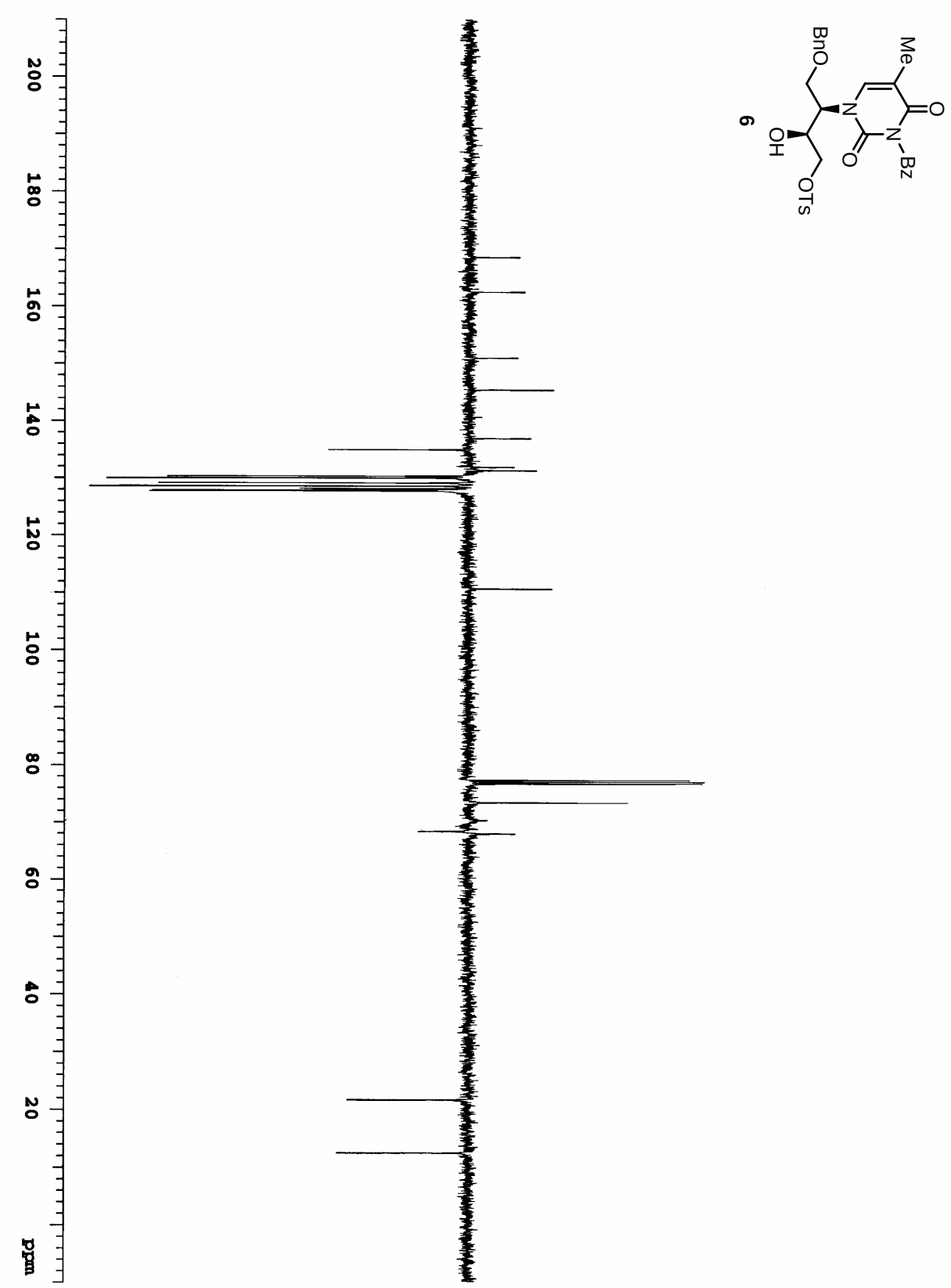

(S)-3j (R1 = Bz)
Me
BnO
O
N
N
O
R1
10
9
8
7
6
5
4
3
2
1
ppm
1.68
1.93
0.95
5.32
0.90
2.90
2.00
1.99
2.76

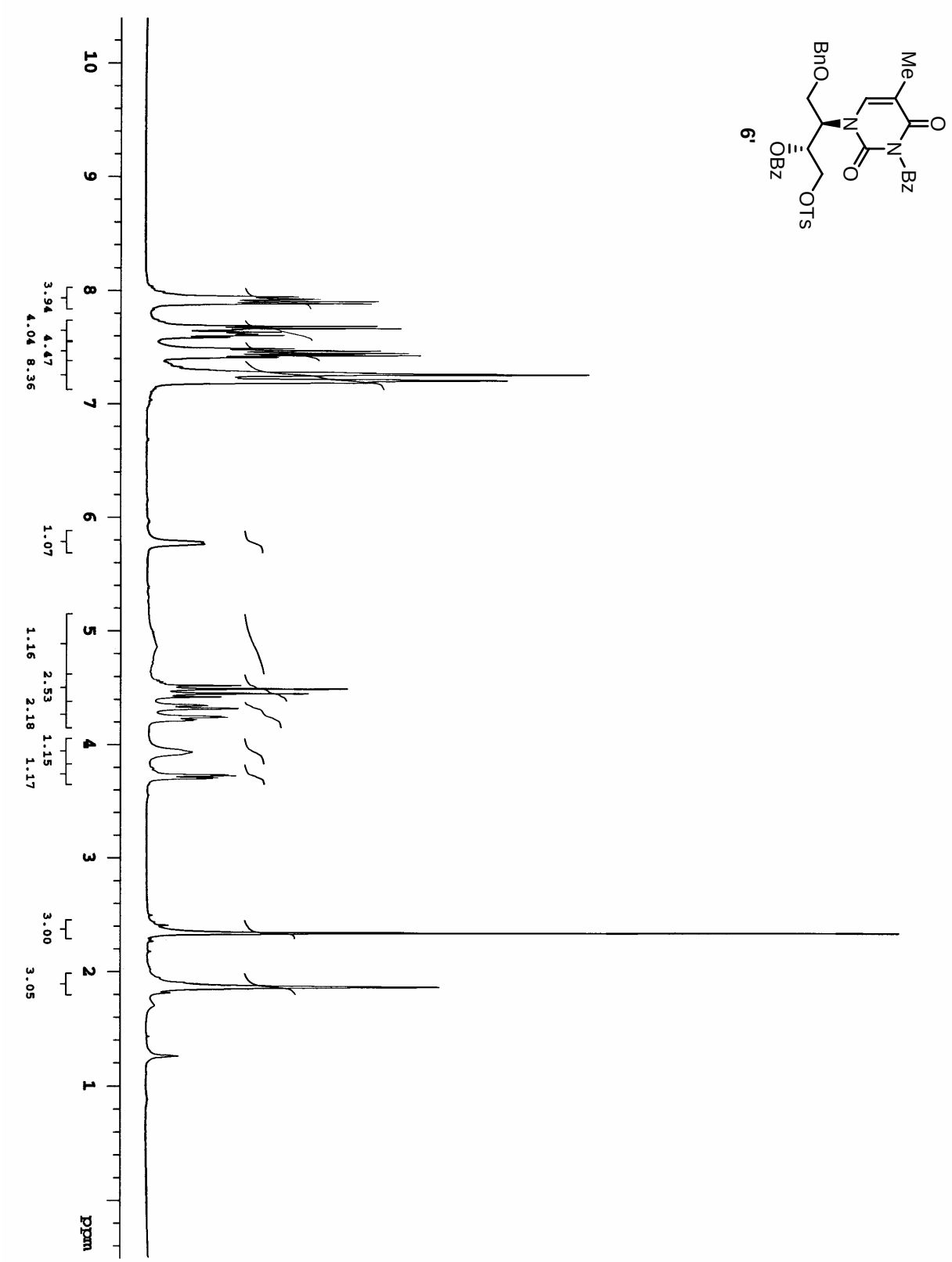

Me
O
N
R1
O
N
BnO
(S)-3j (R1 = Bz)
200
180
160
140
120
100
80
60
40
20
ppm

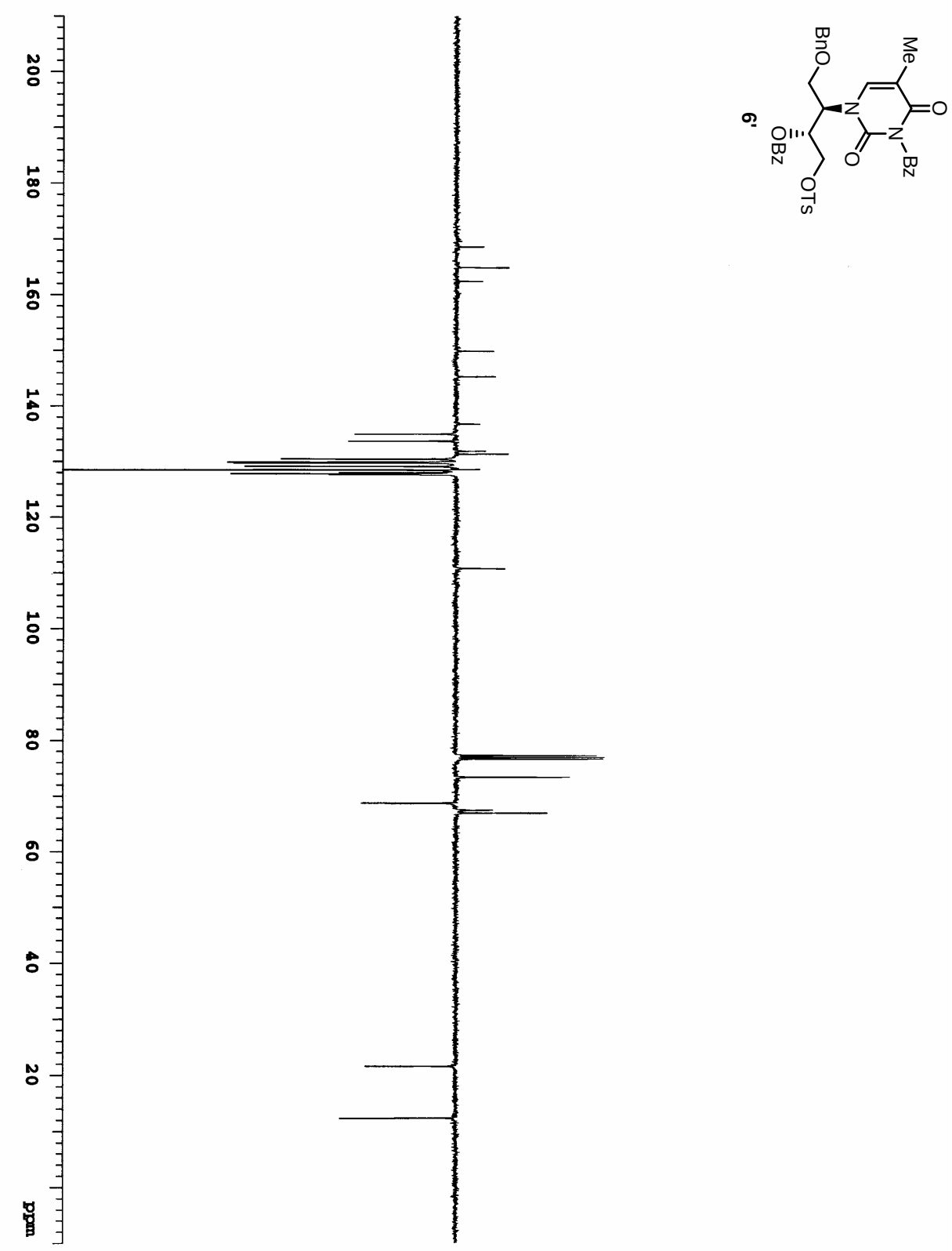

Me
O
N
N
Bz
O
BnO
OH
OH
5
10
9
8
7
6
5
4
3
2
1
ppm
1.82
7.51
1.02
0.81
2.00
0.96
1.21
2.05
2.80
2.78

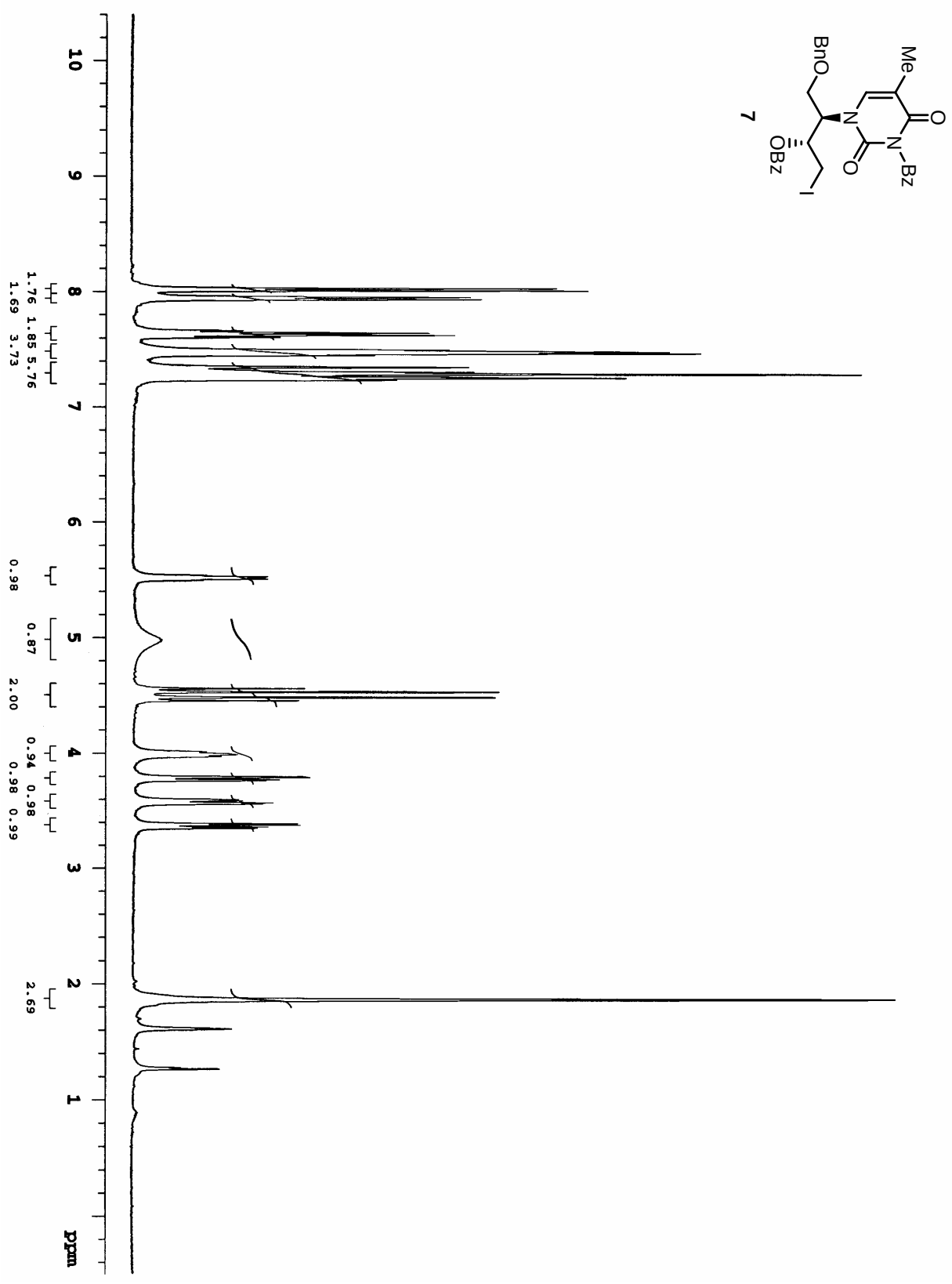

BnO
Me
O
N
N
Bz
O
OH
OH
5
200
180
160
140
120
100
80
60
40
20
ppm


Me
O
N
N
Bz
O
BnO
OH
OTs
6
10
9
8
7
6
5
4
3
2
1
ppm
1.88 1.14
1.82 10.46
3.06 2.16 1.19
1.12 1.30 1.06
3.00
3.07


Me
O
N
Bz
N
O
BnO
OH
OTs
6
200
180
160
140
120
100
80
60
40
20
ppm


Me
O
N
Bz
O
BnO
N
OTs
OBz
6'
10
9
8
7
6
5
4
3
2
1
ppm
3.94
4.47
4.04
8.36
1.07
1.16
2.53
2.18
1.15
1.17
3.00
3.05


Me
O
BnO
N
N
Bz
O
OBz
OTs
6'
200
180
160
140
120
100
80
60
40
20
ppm


7
BnO
OBz
I
Me
O
N
N
Bz
O
ppm
10
9
8
7
6
5
4
3
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1
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1.69 3.73
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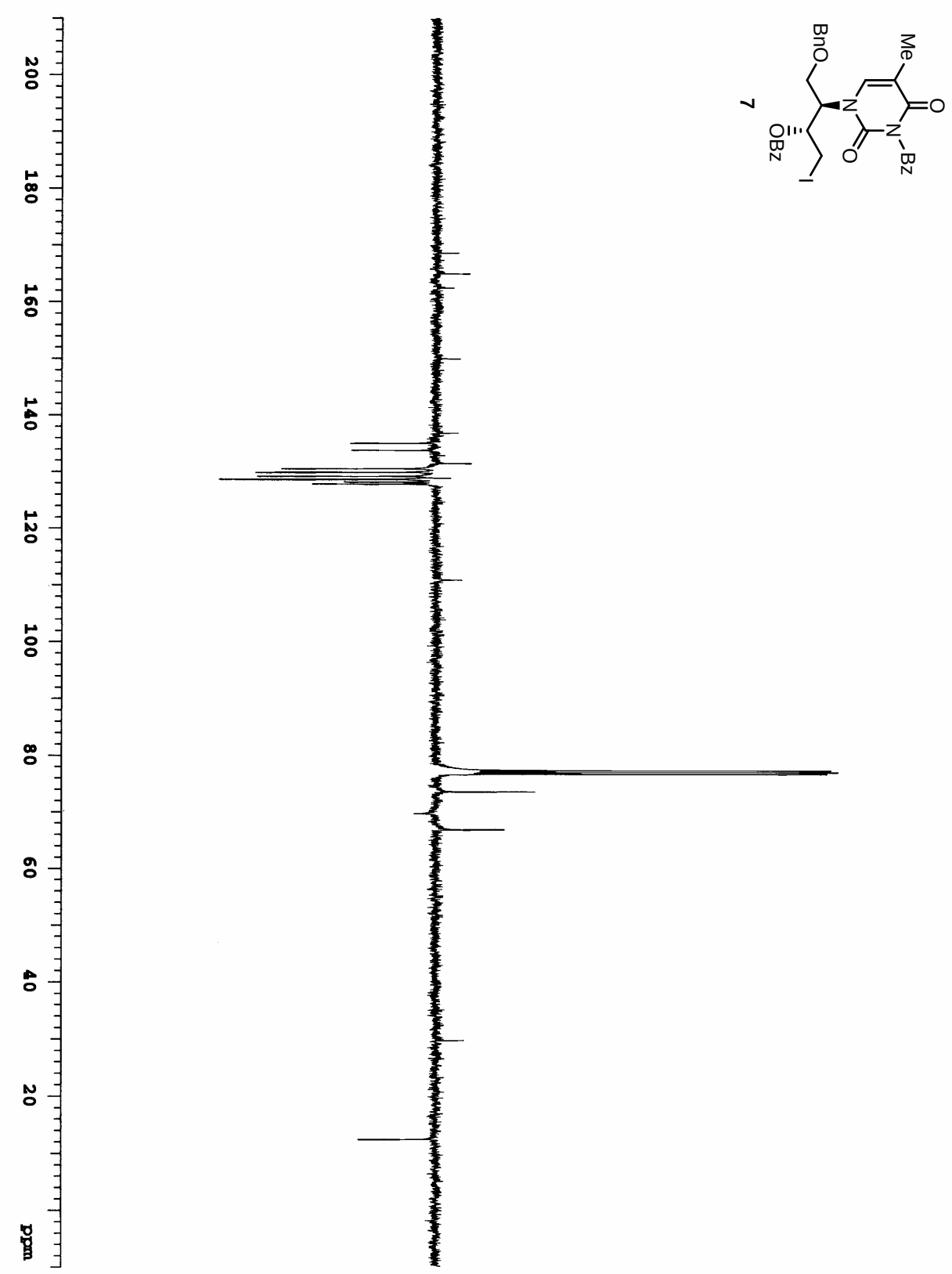
0.87
2.00
0.94 0.98
0.98 0.99
2.69


Me
O
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N
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Bz
O
OBz
I
7
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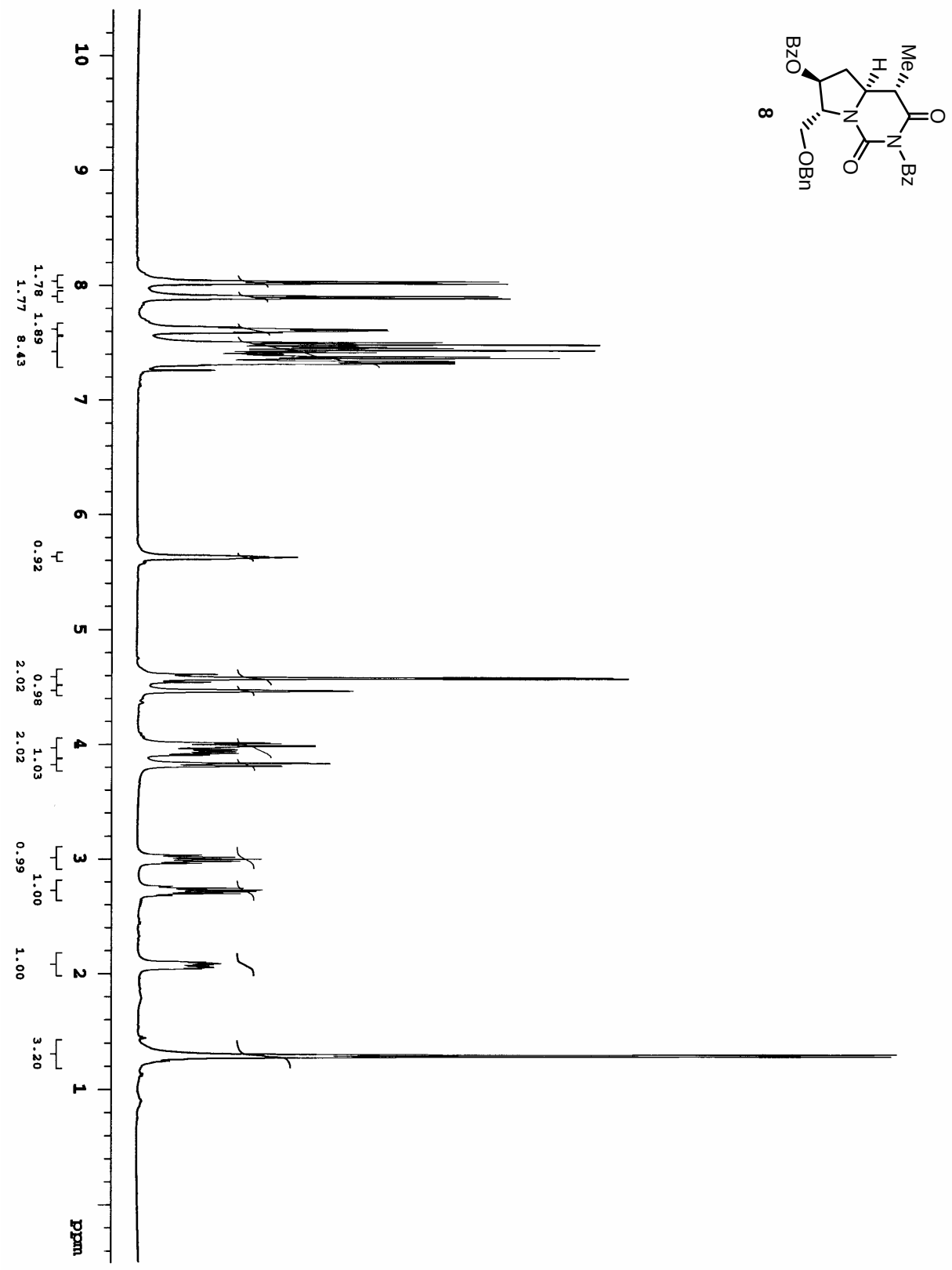
20
ppm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Bz
O
BzO
OBn
8
10
9
8
7
6
5
4
3
2
1
ppm
1.78
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8.43
0.92
0.98
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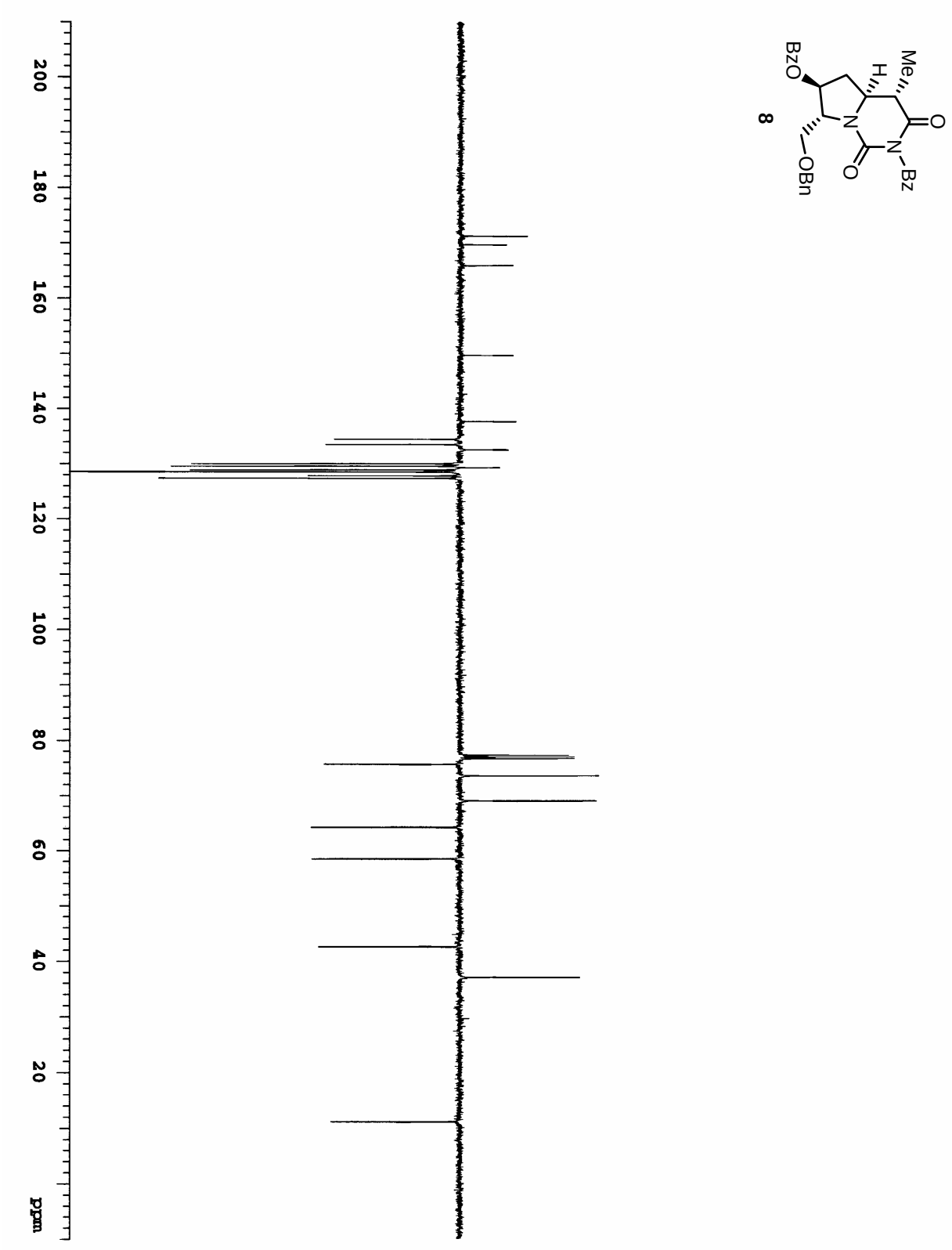
1.03
2.02
0.99
1.00
1.00
3.20


200
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60
40
20
ppm
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Me
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O
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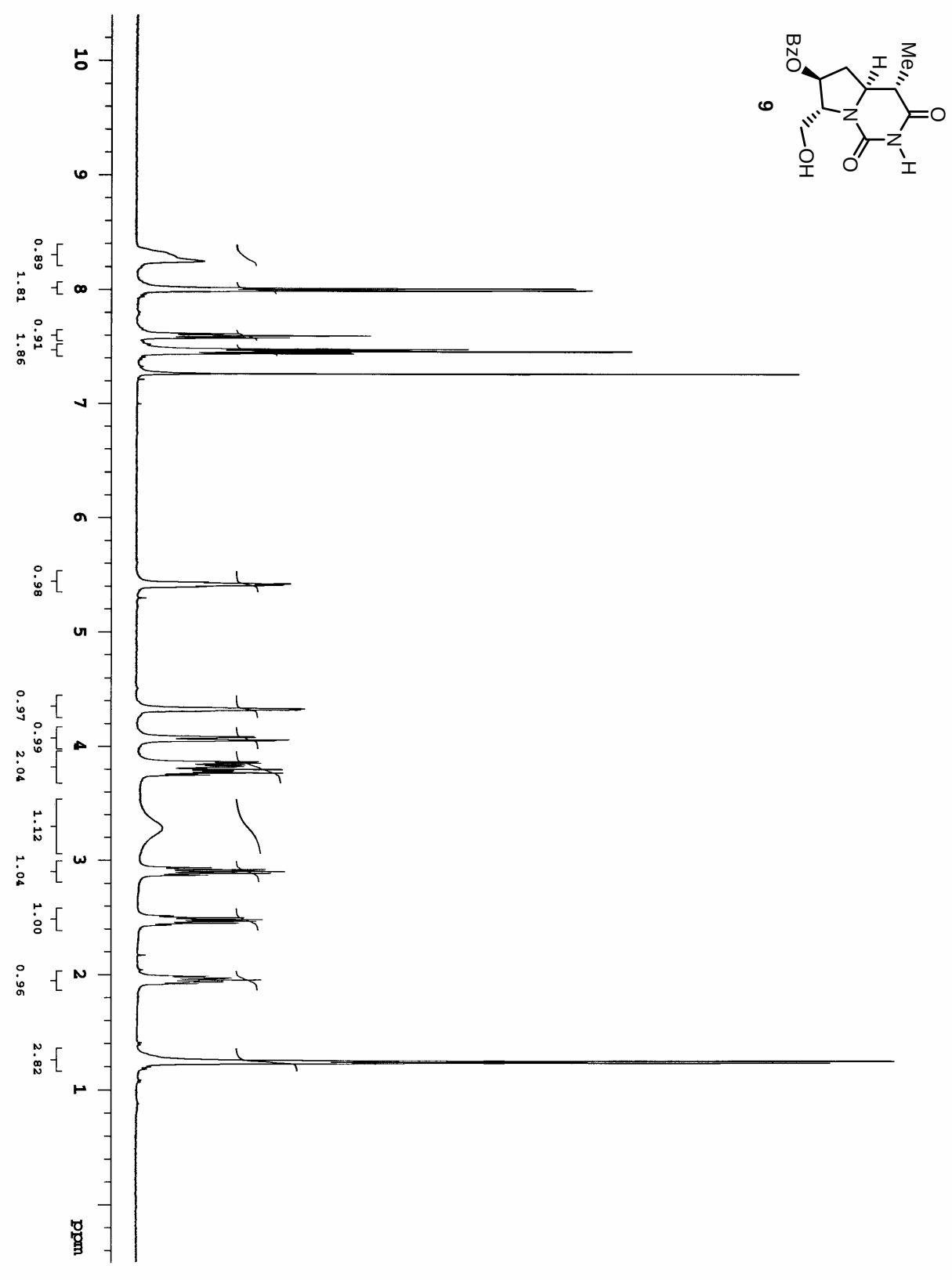
Bz
O
OBn
8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N
H
N
O
OH
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10
9
8
7
6
5
4
3
2
1
ppm
0.89
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0.91
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0.98
0.97
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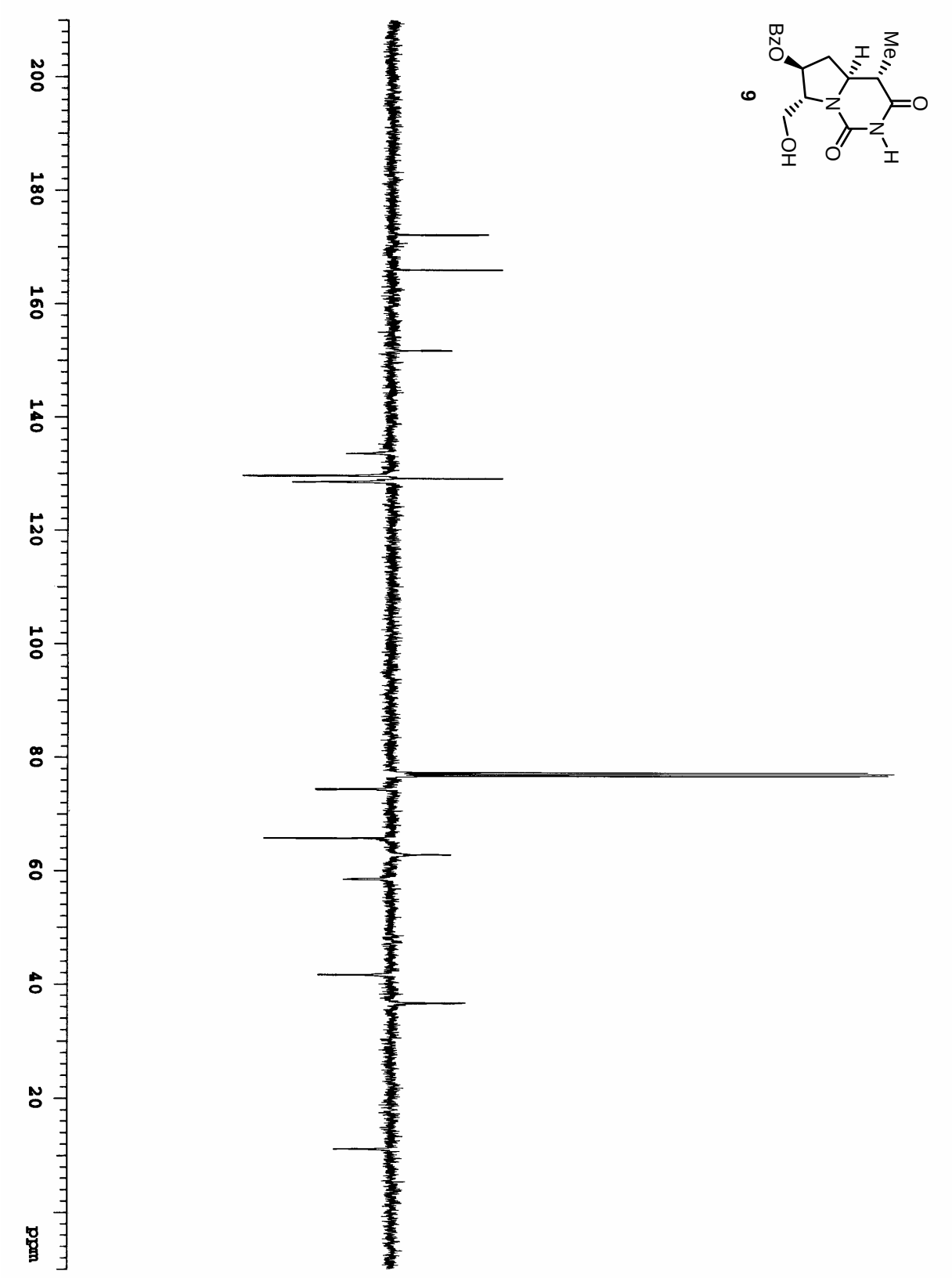
0.99
1.12
1.04
1.00
0.96
2.82


9
BzO
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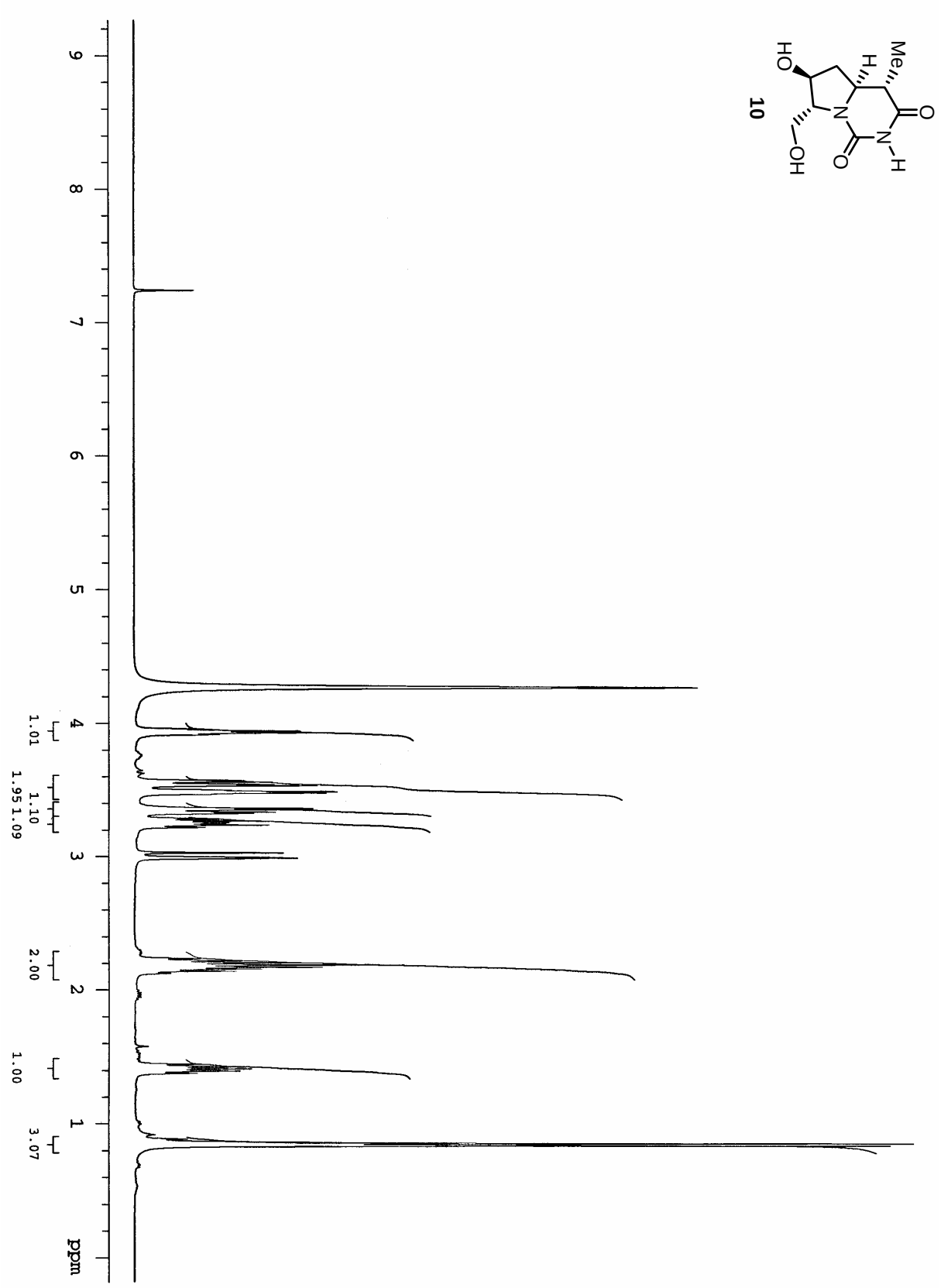
N
H
O
OH
200
180
160
140
120
100
80
60
40
20
ppm


Me
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HO
O
N
N
H
O
OH
10
9
8
7
6
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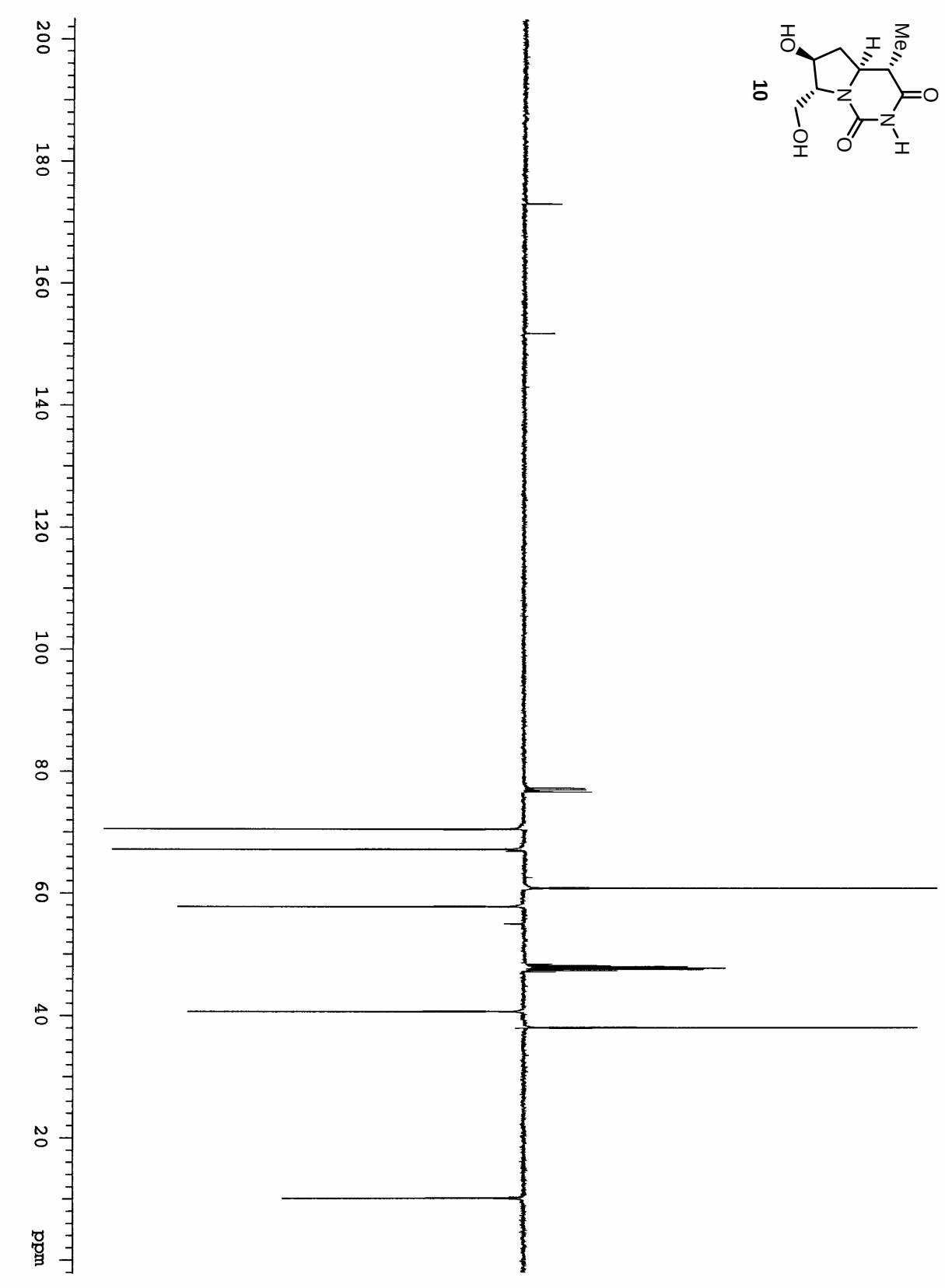
4
3
2
1
ppm
1.01
1.10
1.95
1.09
2.00
1.00
3.07


200
180
160
140
120
100
80
60
40
20
ppm
HO
Me
H
O
N
H
O
N
OH
10

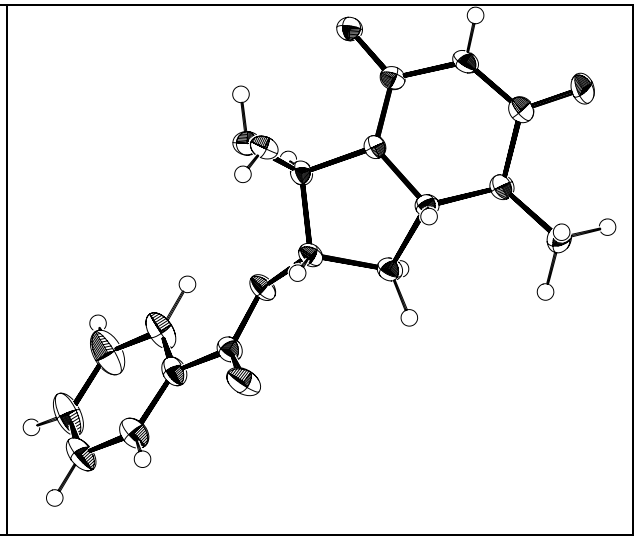
Indiana University Molecular Structure Center

Report 03254: $C_{16}H_{18}N_2O_5$

John C. Huffman

X-ray Structure of Compound 9

Empirical Formula:	C16H18N2O5
Color of Crystal:	colorless
Crystal System:	Monoclinic
Space Group:	P2(1)
Cell Dimensions (at 118(2) K; 808 data)	
a =	6.2583(7)
b =	7.3007(8)
c =	16.5882(16)
alpha =	90
beta =	98.717(3)
gamma =	90
Z (Molecules/cell):	2
Volume:	749.16(14)
Calculated Density:	1.411
Molecular Weight:	318.32
Linear Absorption Coefficient:	0.106
Final residuals are:	
R(F) (observed data) =	0.0367
Rw(F2) (refinement data) =	0.0851



The sample was submitted by Hai-Ren Zhang from the research group of Prof. P.A. Evans, Department of Chemistry, Indiana University. The crystals occur as transparent rectangular plates that tend to grow in clumps. Inert atmosphere techniques were used to place a fragment of one of the plates of approximate dimensions 0.30 × 0.30 × 0.30 mm onto the tip of a 0.1 mm diameter glass fiber which was subsequently mounted on a SMART6000 (Bruker) and cooled to 118(2) K.

Data collection

A preliminary set of cell constants was calculated from reflections obtained from three nearly orthogonal sets of 20 frames. The data collection was carried out using graphite monochromated Mo Kα radiation with a frame time of 2 seconds and a detector distance of 5.0 cm. A randomly oriented region of a sphere in reciprocal space was surveyed. Two sections of 606 frames were collected with 0.30º steps in ω at different ϕ settings with the detector set at –43° in 2θ. Final cell constants were calculated from the xyz centroids of 808 strong reflections from the actual data collection after integration (SAINT).

Structure solution and refinement

Intensity statistics and systematic absences suggested the noncentrosymmetric space group $P2_1$ and subsequent solution and refinement confirmed this choice. The structure was solved using SHELXS-97 and refined with SHELXL-97. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. There are two alternate positions for the –OH group, with the disorder being 50:50. All hydrogen atoms with the exception of the one obscured by the –OH disorder were located in subsequent Fourier maps and included as isotropic contributors in the final cycles of refinement.

Complete data are available at
http://bl-chem-iumsc110.chem.indiana.edu/recipnet/showsample.jsp?sampleId=59057831&sampleHistoryId=-1