Effect of Ester on Rhodium-Catalyzed Intermolecular [5 + 2] Cycloaddition of 3-Acyloxy-1,4-enynes and Alkynes

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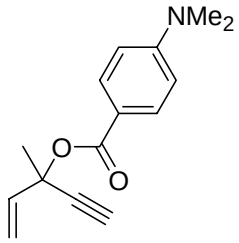
General Methods. All reactions were conducted under a positive pressure of dry argon in glassware that had been oven dried prior to use. Anhydrous solutions of reaction mixtures were transferred via an oven dried syringe or cannula. All solvents were dried prior to use unless noted otherwise. ^{1}H and ^{13}C nuclear magnetic resonance spectra (NMR) were obtained on 400 MHz or 500 MHz recorded in ppm (δ) downfield of TMS (δ = 0) in $CDCl_3$. Signal splitting patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint),or multiplet (m), with coupling constants (*J*) in hertz. High resolution mass spectra (HRMS) were performed on an Electron Spray Injection (ESI) mass spectrometer.

Procedure for the formation of ester 5c.

To a stirred solution of 4-(dimethylamino)-benzoic acid (9.4 g, 57 mmol) in dry toluene (250 ml) was added thionyl chloride (7.0 eq, 29.6 ml, 408 mmol). The mixture was stirred at reflux for 6 h. The solvent was removed under reduced pressure and the crude residue was used for the next step without further purification. To a stirred solution of 3-methyl-1-penten-4-yn-3-ol (1.76 ml, 3.0 eq, 16 mmol) in dry THF (25 ml) under argon was added nBuLi (2.5M, 2.0 eq, 4.4 ml) dropwise at -78 °C. The mixture was stirred at this temperature for 20 minutes before the crude 4-(dimethylamino)-benzoyl chloride was added. The reaction was then allowed to warm to room temperature and stirred overnight. After the reaction was determined complete, the solvent was removed under reduced pressure, and the residue was diluted with ethyl acetate, washed with H_2O, brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was then purified by silica gel chromatography (10:1 Hex/EtOAc) to afford **5c** (966 mg) in 65% yield over two steps as white solid.

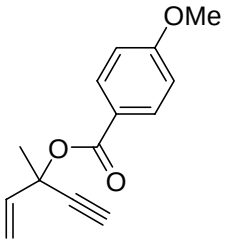


5c

5c: 966 mg, 65% yield over 2 steps; white solid. m.p. = 66-68 ^{o}C, R_f = 0.39 (4:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 9.2 Hz, 2H), 6.63 (d, *J* = 9.1 Hz, 2H), 6.10 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.65 (dd, *J* = 17.1, 0.8 Hz, 1H), 5.27 (dd, *J* = 10.4, 0.8 Hz, 1H), 3.03 (s, 6H), 2.70 (s, 1H), 1.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.17, 153.55, 139.31, 131.58, 117.42, 115.40, 110.82, 82.94, 74.73, 73.76, 40.24, 28.96. IR (film): ν 3300, 2987, 2934, 1704, 1605, 1526, 1482, 1445, 1407, 1369, 1315, 1278, 1234, 1182, 1090, 1060, 986, 945, 925, 895, 825, 768, 736, 696, 664. HRMS

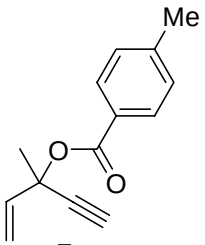
(ESI+) for $C_{15}H_{17}NO_2$ (M+Na) calculated 266.1126, found 266.1139.

Esters 5a, 5b, 5d, 5e, 5f, 5g, 5h, 5i and 10b were prepared according to our previous procedures. (Shu, X.-Z.; Li, X.; Shu, D.; Huang, S.; Schienebeck, C. M.; Zhou, X.; Robichaux, P. J.; Tang, W. *J. Am. Chem. Soc.* 2012, *134*, 5211.) The yield and characterization data for esters 5a, 5b, 5f, and 5i have been reported previously.



5d

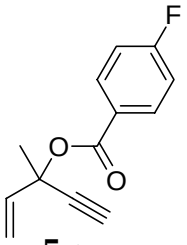
5d: 172.9mg, 71% yield; clear oil. R_f = 0.16 (10:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.82 (m, 2H), 6.99 – 6.75 (m, 2H), 6.07 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.64 (dd, *J* = 17.1, 0.7 Hz, 1H), 5.26 (dd, *J* = 10.4, 0.7 Hz, 1H), 3.80 (s, 3H), 2.71 (s, 1H), 1.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.28, 163.46, 138.71, 131.72, 122.94, 115.72, 113.62, 82.33, 75.07, 74.25, 55.44, 28.69. IR (film): ν 3299, 2918, 2849, 1717, 1605, 1581, 1510, 1460, 1420, 1369, 1316, 1276, 1254, 1167, 1141, 1095, 1061, 1028, 1009, 985, 931, 895, 847, 792, 769, 736, 695. HRMS (ESI+) for $C_{14}H_{14}O_3$ (M+Na) calculated 253.0835, found 253.0832.



5e

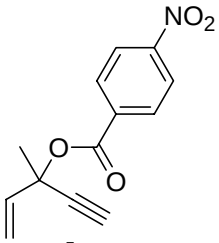
5e: 157.5mg, 66% yield; clear oil. R_f = 0.29 (10:1, hexanes / ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.18 (m, 2H), 6.10 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.67 (dd, *J* = 17.1, 0.7

Hz, 1H), 5.30 (dd, *J* = 10.4, 0.7 Hz, 1H), 2.72 (s, 1H), 2.40 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.83, 143.89, 138.78, 129.92, 129.24, 128.03, 116.00, 82.42, 75.21, 74.57, 28.85, 21.90. IR (film): ν 3297, 2991, 1722, 1611, 1446, 1408, 1369, 1272, 1244, 1177, 1143, 1094, 1061, 1020, 984, 932, 894, 840, 752, 689. HRMS (ESI+) for $C_{14}H_{14}O_2$ (M+Na) calculated 237.0886, found 237.0882.



5g

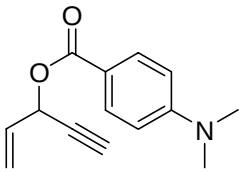
5g: 170mg, 73% yield; clear oil. R_f = 0.24 (10:1, hexanes / ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 – 8.00 (m, 2H), 7.10 (t, *J* = 8.6 Hz, 2H), 6.09 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.68 (dd, *J* = 17.1, 0.6 Hz, 1H), 5.32 (dd, *J* = 10.4, 0.7 Hz, 1H), 2.74 (s, 1H), 1.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.01 (d, ^1J = 254.5 Hz), 163.77, 138.47 , 132.42 (d, ^3J = 9.3 Hz), 126.99 (d, ^4J = 3.0 Hz), 116.31 , 115.68 (d, ^2J = 22.7 Hz), 82.12 , 75.48 , 75.01 , 28.79 . IR (film): ν 3305, 1727, 1604, 1506, 1447, 1410, 1370, 1271, 1238, 1186, 1153, 1102, 1088, 1060, 1014, 984. 933, 893, 853, 810, 766, 685. HRMS (ESI+) for $C_{13}H_{11}FO_2$ (M+Na) calculated 241.0635, found 241.0630.



5h

5h: 104.5mg, 40% yield; white solid, m.p. = 88-91 °C R_f = 0.18 (10:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.21 (m, 2H), 8.20 – 8.13 (m, 2H), 6.08 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.69 (d, *J* = 17.1 Hz, 1H), 5.33 (d, *J* = 10.4 Hz, 1H), 2.77 (s, 1H), 1.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

162.69, 150.68, 137.77, 136.06, 130.88, 123.63, 116.93, 81.45, 76.05, 75.99, 28.58. IR (film): ν 3297, 3115, 2926, 2852, 1731, 1607, 1522, 1453, 1408, 1370, 1347, 1322, 1275, 1242, 1171, 1151, 1098, 1057, 1010, 985, 931, 888, 874, 842, 784, 736, 715, 677. HRMS (ESI+) for $C_{13}H_{11}NO_4$ (M+Na) calculated 268.0580, found 268.0568.

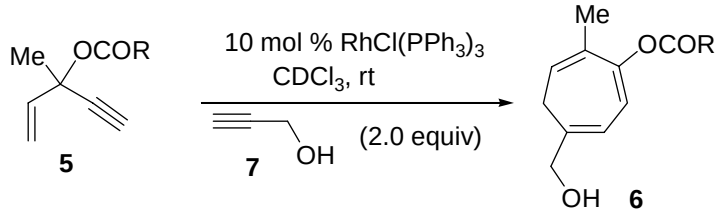


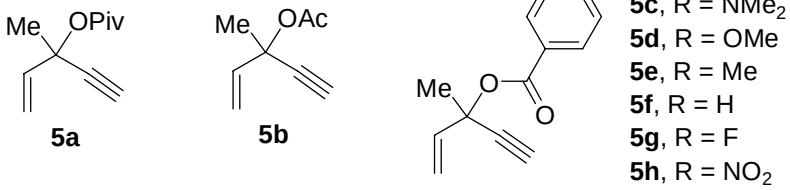
10b

10b: 117 mg, 42% yield, white powder, mp = 60-62 °C, R_f = 0.22 (10:1, hexanes / ethyl acetate). ^{1}H NMR (500 MHz, Chloroform-d) δ 8.00 – 7.89 (m, 2H), 6.71 – 6.58 (m, 2H), 6.11 (ddd, *J* = 5.2, 2.4, 1.2 Hz, 1H), 6.02 (ddd, *J* = 17.0, 10.1, 5.4 Hz, 1H), 5.64 (dt, *J* = 17.0, 1.2 Hz, 1H), 5.36 (dt, *J* = 10.2, 1.2 Hz, 1H), 3.04 (s, 6H), 2.58 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.73, 153.76, 133.33, 131.84, 118.83, 116.31, 110.87, 79.95, 75.03, 63.82, 40.25. IR (film): ν 2364, 2336, 1704, 1607, 1529, 1483, 1446, 1371, 1318, 1264, 1232, 1183, 1092, 963, 945, 829, 769, 738, 700, 668 cm^{-1}. HRMS (ESI+) for $C_{14}H_{15}NO_2$ (M+Na) calculated 252.0995, found 252.0994.

General procedure for the measure of rates of Rh-catalyzed cycloaddition of 5 and 7:

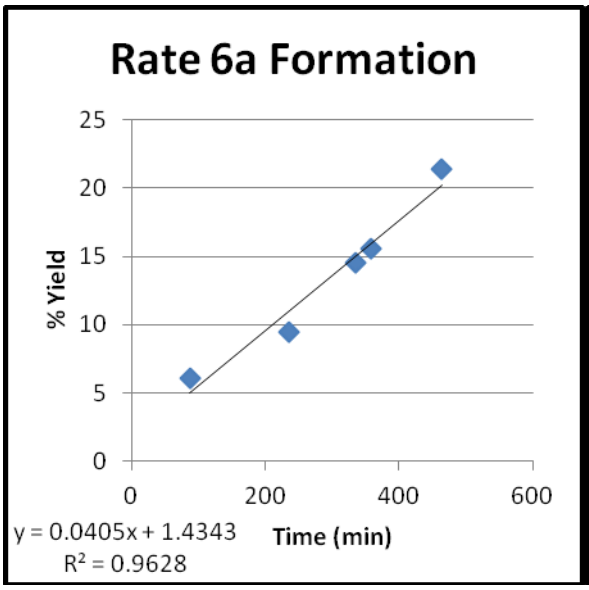
To a vial containing 3-acyloxy-1,4-ennye **5** (0.05 mmol, 1.0 equiv) and alkyne **7** (0.1 mmol, 2.0 equiv) was added $RhCl(PPh_3)_3$ (4.6 mg, 0.005 mmol, 0.1 equiv) and $CDCl_3$ (0.5 mL). The vial was flushed with argon and allowed to stir at rt. The rate of reaction was then monitored by ^1H NMR.

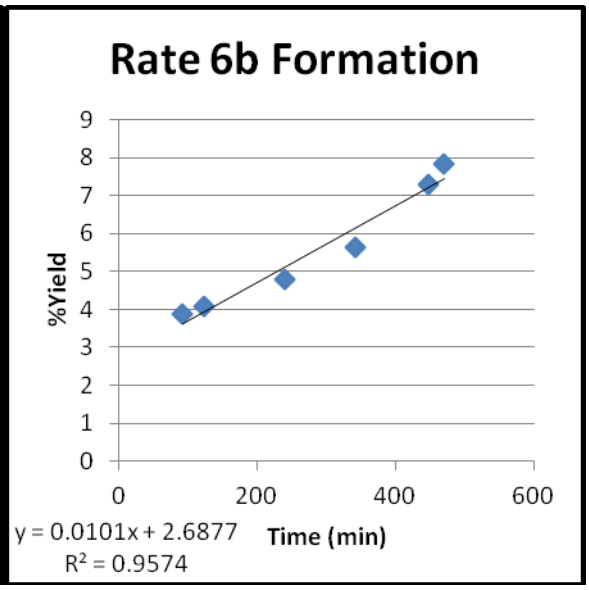


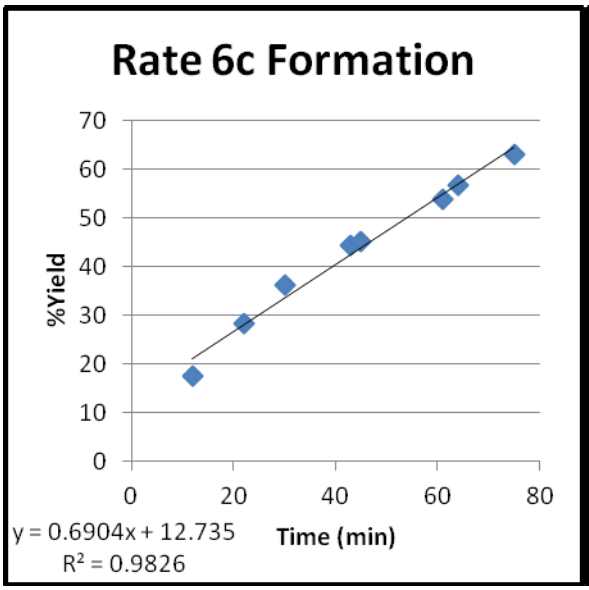


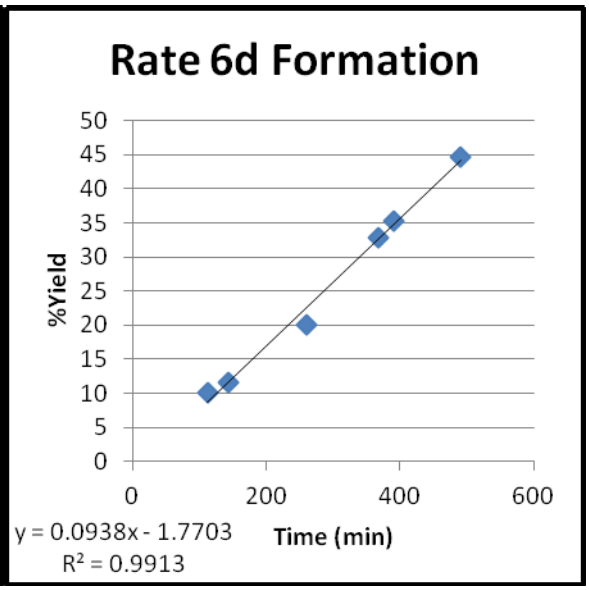
Ester	Initial rate[a,b] (min^{-1})	Ratio of rates **5/5f**	σ^c
5a	4.05	2.72	-
5b	1.01	0.68	-
5c	69.0	46.3	-0.83
5d	9.38	6.30	-0.27
5e	3.09	2.07	-0.17
5f	1.49	1.00	0.00
5g	1.80	1.21	0.06
5h	2.78	1.87	0.78

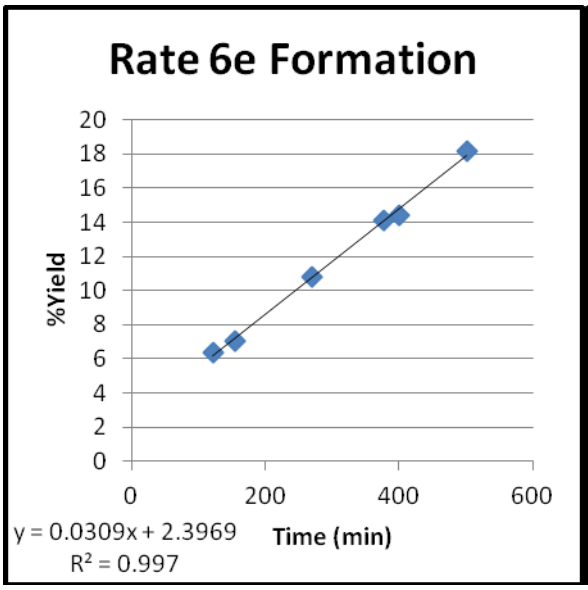
[a] rate = %yield/time, [b] $MeNO_2$ was used as internal standard, [c] Hammet sigma constant (Hammett, L. P. *Journal of the American Chemical Society* **1937**, *59*, 96.).

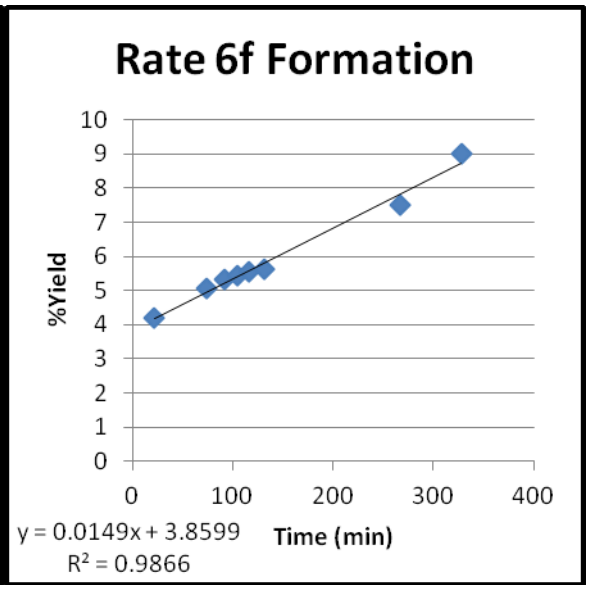

Rate 6a Formation
% Yield
Time (min)
y = 0.0405x + 1.4343
R² = 0.9628

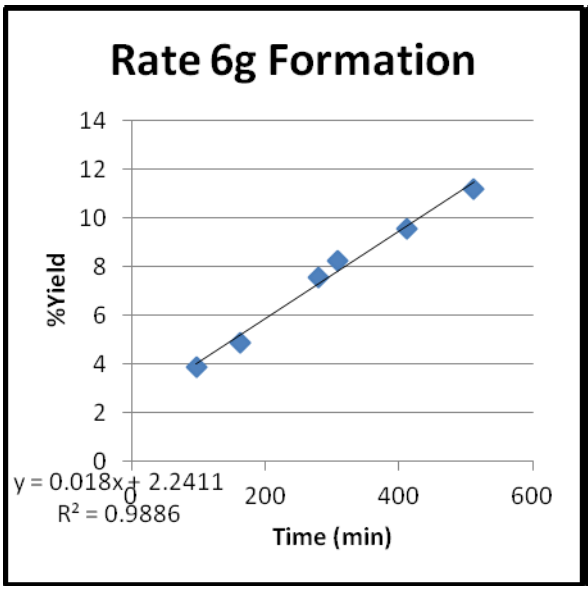

Rate 6b Formation
%Yield
Time (min)
y = 0.0101x + 2.6877
R² = 0.9574

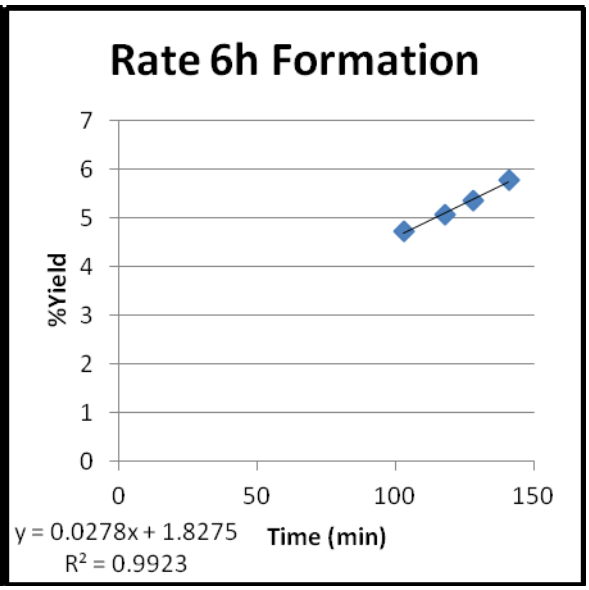

Rate 6c Formation
%Yield
Time (min)
y = 0.6904x + 12.735
R² = 0.9826


Rate 6d Formation
%Yield
Time (min)
y = 0.0938x - 1.7703
R² = 0.9913


Rate 6e Formation
%Yield
Time (min)
y = 0.0309x + 2.3969
R² = 0.997

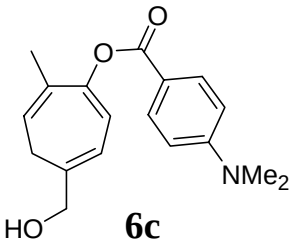

Rate 6f Formation
%Yield
Time (min)
y = 0.0149x + 3.8599
R² = 0.9866


Rate 6g Formation
%Yield
Time (min)
y = 0.018x + 2.2411
R² = 0.9886


Rate 6h Formation
%Yield
Time (min)
y = 0.0278x + 1.8275
R² = 0.9923

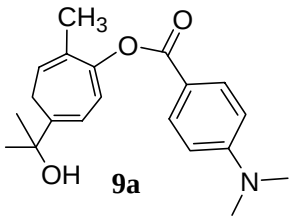
General procedure for the Rh-catalyzed [5+2] cycloaddition of 5 and alkynes:

To a flask containing ACE **5c** (1 equiv.) and alkyne (1.1 equiv) was added $RhCl(PPh_3)_3$ (0.5 mol %) and chloroform (0.4M). The flask was flushed with argon and allowed to stir at 50 ^oC. Reaction was monitored by TLC until **5c** was completely consumed (24h). The solvent was evaporated under vacuum and the resulting residue was purified via flash chromatography on silica gel (hexanes / ethyl acetate) to yield the cycloaddition product.



6c

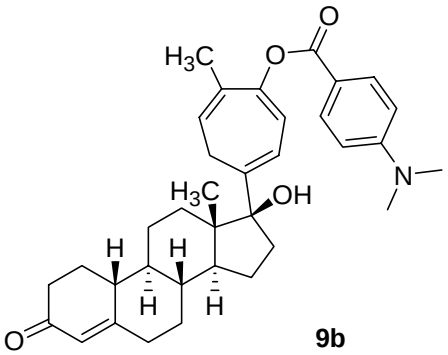
6c: 95 mg, 97%; yellow oil. R_f = 0.24 (1:1, hexanes / ethyl acetate). ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.98 (m, 2H), 6.71 – 6.66 (m, 2H), 6.35 (d, *J* = 6.3 Hz, 1H), 6.13 (dt, *J* = 6.2, 1.4 Hz, 1H), 5.32 (tq, *J* = 7.3, 1.6 Hz, 1H), 4.27 (dt, *J* = 1.4, 0.7 Hz, 2H), 3.07 (s, 6H), 2.50 (d, *J* = 7.3 Hz, 2H), 1.82 – 1.80 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.65, 153.87, 152.42, 136.94, 132.04, 131.71, 120.29, 119.54, 118.73, 116.17, 110.99, 66.32, 40.28, 29.19, 18.08. IR (film): ν 3436, 2919, 2360, 1711, 1602, 1528, 1444, 1369, 1317, 1273, 1231, 1180, 1118, 1065, 1002, 945, 908, 869, 825, 802, 764, 728, 696. HRMS (ESI+) for $C_{18}H_{21}NO_3$ (M+Na) calculated 322.1414, found 322.1410.



9a

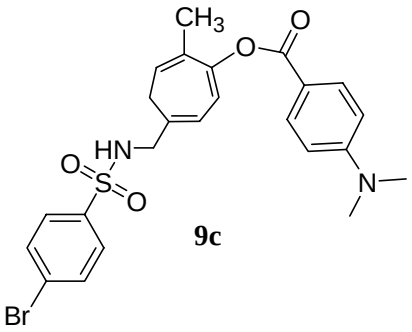
9a, 82.6 mg, 87%; white solid, m.p. = 138-140 °C. R_f = 0.22 (3:1, hexanes / ethyl acetate). ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 9.0 Hz, 2H), 6.59 (d, J = 9.0 Hz, 2H), 6.28 (d, J = 6.4 Hz, 1H), 6.12 (d,

J = 6.5 Hz, 1H), 5.21 (t, J = 8.0 Hz, 1H), 2.97 (s, 6H), 2.41 (d, J = 7.4 Hz, 2H), 1.72 (s, 3H), 1.35 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.72, 153.86, 151.95, 145.10, 132.04, 131.25, 120.66, 119.72, 116.24, 115.63, 111.00, 72.96, 40.28, 30.00, 28.93, 17.93. IR (film): ν 3450, 2974, 2918, 2362, 2342, 1704, 1604, 1529, 1369, 1274, 1182, 1167, 1115, 1061, 907, 827, 784, 766, 727, 696 cm^{-1}. HRMS (ESI+) for $C_{20}H_{25}NO_3$ (M+Na) calculated 350.1727, found 350.1728.



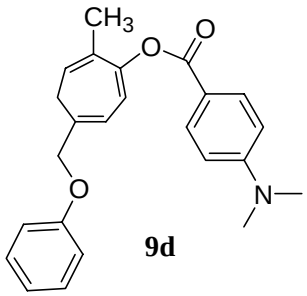
9b

9b: 86 mg, 89%; light yellow oil. R_f = 0.23 (1:2, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 2H), 6.69 (d, *J* = 6.8 Hz, 2H), 6.36 (d, *J* = 6.4 Hz, 1H), 5.89 (d, *J* = 6.8 Hz, 1H), 5.81 (s, 1H), 5.31 (t, *J* = 8.4 Hz, 1H), 3.06 (s, 6H), 2.46 – 1.11 (m, 26H), 1.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.22, 166.96, 165.74, 153.88, 152.22, 144.05, 132.03, 131.24, 124.75, 121.28, 120.67, 119.68, 116.14, 111.00, 109.99, 86.34, 49.26, 48.30, 47.42, 42.76, 41.40, 40.29, 38.82, 36.71, 35.74, 33.96, 30.97, 30.89, 26.74, 26.57, 23.86, 17.93, 14.81. IR (film): ν 3435, 2929, 2870, 2360, 1714, 1662, 1604, 1529, 1449, 1369, 1332 1273, 1231, 1181, 1137, 1118, 1063, 1006, 945, 910, 881, 862, 828, 765, 731, 697. HRMS (ESI+) for $C_{35}H_{43}NO_4$ (M+Na) calculated 564.3084, found 564.3078.



9c

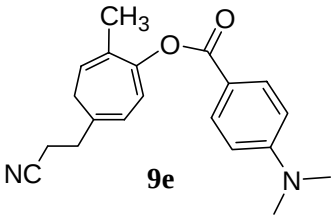
9c, 130 mg, 95%; white solid, m.p. = 171-175 °C. R_f = 0.14 (3:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 9.0 Hz, 2H), 7.72 (d, J = 8.6 Hz, 2H), 7.64 (d, J = 8.6 Hz, 2H), 6.67 (d, J = 9.0 Hz, 2H), 6.23 (d, J = 6.3 Hz, 1H), 5.96 (d, J = 6.4 Hz, 1H), 5.22 (t, J = 6.5 Hz, 1H), 4.86 (t, J = 6.3 Hz, 1H), 3.73 (d, J = 6.1 Hz, 2H), 3.06 (s, 6H), 2.37 (d, J = 7.3 Hz, 2H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.56, 153.93, 153.00, 139.31, 132.62, 132.06, 131.95, 131.30, 128.87, 127.89, 121.34, 120.42, 119.17, 115.92, 111.00, 48.77, 40.28, 29.70, 18.05. IR (film): ν 3266, 2918, 2361, 2342, 1705, 1604, 1575, 1525, 1469, 1431, 1368, 1330, 1278, 1232, 1177, 1158, 1123, 1088, 1070, 1043, 1010, 945, 911, 865, 829, 766, 741, 695, 663 cm^{-1}. HRMS (ESI+) for $C_{24}H_{25}BrN_2O_4S$ (M+Na) calculated 539.0611, found 539.0610.



9d

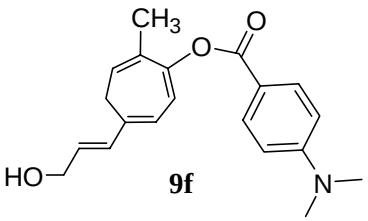
9d: 93 mg, 96%; light yellow oil. R_f = 0.25 (1:4, hexanes / ethyl acetate). (isomeric ratio = 17:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.27 (dd, *J* = 8.8, 3.2 Hz, 2H), 6.93 – 6.97 (m, 3H), 6.68 (d, *J* = 9.6 Hz, 2H), 6.36 (d, *J* = 6.4 Hz, 1H), 6.23 (d, *J* = 6.4 Hz, 1H), 5.33 (t, *J* = 8.4 Hz, 1H), 4.64 (s, 2H), 3.05 (s, 6H), 2.56 (d, *J* = 7.6 Hz, 2H), 1.82 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.64,

158.92, 153.90, 152.76, 132.30, 132.07, 131.83, 129.66, 121.18, 120.63, 120.32, 119.47, 116.15, 115.20, 111.01, 70.90, 40.29, 29.06, 18.12. IR (film): ν 3433, 2919, 2868, 2360, 1714, 1604, 1529, 1494, 1370, 1274, 1237, 1181, 1125, 1069, 909, 828, 755, 731, 693. HRMS (ESI+) for $C_{24}H_{25}NO_3$ (M+Na) calculated 398.1727, found 398.1725.



9e

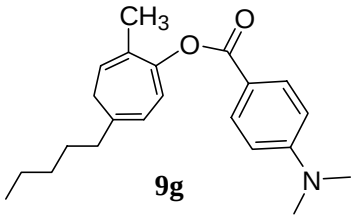
9e: 69 mg, 74%; white solid, m.p. = 129-132 °C. R_f = 0.10 (5:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.32 (d, *J* = 6.4 Hz, 1H), 5.98 (d, *J* = 6.0 Hz, 1H), 5.31 (t, *J* = 7.2 Hz, 1H), 3.06 (s, 6H), 2.61 (t, *J* = 6.8 Hz, 2H), 2.51 (t, *J* = 6.8 Hz, 2H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.63, 153.92, 152.54, 133.59, 132.06, 131.97, 120.68, 119.68, 119.41, 119.28, 116.07, 111.02, 40.29, 33.40, 31.86, 18.00, 17.66. IR (film): ν 2918, 2360, 2342, 2250, 1709, 1603, 1528, 1445, 1370, 1317, 1273, 1232, 1180, 1119, 1066, 945, 908, 864, 828, 765, 727, 696. HRMS (ESI+) for $C_{20}H_{22}N_2O_2$ (M+Na) calculated 345.1573, found 345.1572.



9f

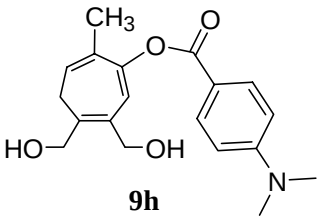
9f: 53 mg, 58%; yellow solid, m.p. = 147-157 °C. R_f = 0.41 (1:1, hexanes / ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.9 Hz, 2H), 6.39-6.35 (m, 2H), 6.16-6.10 (m, 2H), 5.33 (t, *J* = 7.2 Hz, 1H), 4.26 (d, *J* = 5.7 Hz, 2H), 3.06 (s, 6H), 2.70 (d, *J* = 7.4 Hz, 2H), 1.81 (s, 3H),

1.25 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.73, 153.96, 152.84, 132.51, 132.39, 132.28, 132.12, 129.39, 123.73, 121.15, 120.36, 116.16, 111.06, 63.95, 40.34, 27.85, 18.10. IR (film): ν 3481, 2920, 2853, 2362, 2343, 1707, 1604, 1530, 1444, 1371, 1318, 1276, 1232, 1182, 1124, 1092, 965, 945, 907, 828, 765, 730, 697, 669. HRMS (ESI+) for $C_{20}H_{23}NO_3$ (M+H) calculated 326.1751, found 326.1751.



9g

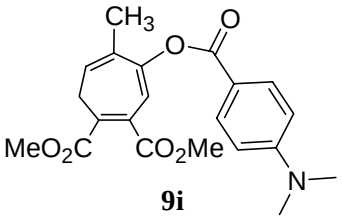
9g: 73 mg, 77%; yellow oil. (isomeric ratio = 8:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 9.1 Hz, 2H), 6.68 (d, J = 9.1 Hz, 2H), 6.30 (d, J = 6.3 Hz, 1H), 5.89 (d, J = 6.4 Hz, 1H), 5.24 (t, J = 7.3 Hz, 1H), 3.05 (s, 6H), 2.42 (d, J = 7.3 Hz, 2H), 2.28 – 2.20 (m, 2H), 1.80 (s, 3H), 1.56 – 1.39 (m, 2H), 1.39 – 1.18 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.79, 153.81, 151.25, 139.50, 132.01, 131.06, 120.14, 119.50, 118.42, 116.45, 110.99, 40.29, 38.10, 32.41, 31.75, 29.19, 22.74, 18.00, 14.28. IR (film): ν 2954, 2925, 2856, 2362, 2342, 1714, 1604, 1527, 1483, 1445, 1368, 1317, 1271, 1232, 1179, 1124, 1089, 1061, 1001, 945, 898, 863, 827, 801, 764, 732, 695. HRMS (ESI+) for $C_{22}H_{29}NO_2$ (M+Na) calculated 362.2091, found 362.2088.



9h

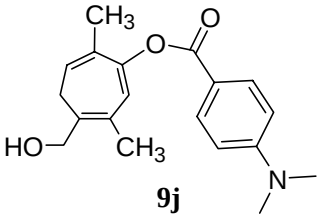
9h: 59 mg, 82%; yellow oil. R_f = 0.35 (1:2, hexanes / ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 8.6 Hz, 2H), 6.44 (s, 1H), 5.40 (t, J = 6.7 Hz, 1H), 4.28 (s, 4H), 3.05 (s, 6H), 2.49 (d, J = 6.8 Hz, 2H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.02, 154.01, 152.61, 133.03, 132.19, 132.03, 130.94, 123.03, 121.19, 115.90, 111.07, 62.93, 62.34, 40.33, 31.73, 17.81. IR

(film): ν 3379, 2943, 2927, 2900, 2864, 2360, 2343, 2252, 1703, 1605, 1530, 1438, 1371, 1278, 1183, 1149, 1095, 1062, 1002, 946, 905, 829, 725. HRMS (ESI+) for $C_{19}H_{23}NO_4$ (M+H) calculated 330.1700, found 330.1715.



9i

9i, 50.6mg, 89%; yellow solid, m.p. = 107-110 °C. R_f = 0.17 (4:1, hexanes / ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.9 Hz, 2H), 6.76 – 6.57 (m, 3H), 5.01 (t, J = 7.3 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.04 (s, 6H), 2.49 (d, J = 6.4 Hz, 2H), 1.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.78, 167.72, 165.02, 154.05, 153.65, 132.46, 132.14, 132.09, 131.27, 119.24, 115.24, 111.00, 109.04, 52.69, 52.66, 40.23, 26.40, 17.70. IR (film): ν 2951, 2361, 2342, 2256, 1716, 1604, 1531, 1435, 1371, 1321, 1262, 1163, 1122, 1069, 1000, 945, 907, 828, 764, 727, 697 cm^{-1}. HRMS (ESI+) for $C_{21}H_{23}NO_6$ (M+Na) calculated 408.1418, found 408.1414.



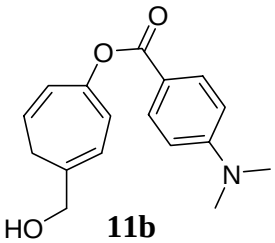
9j

9j, 67 mg, 77%; pale yellow oil. (isomeric ratio = 5:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 9.1 Hz, 2H), 6.67 (d, J = 9.0 Hz, 2H), 6.29 (s, 1H), 5.44 (t, J = 7.3 Hz, 1H), 4.25 (s, 2H), 3.04 (s, 6H), 2.53 (d, J = 7.1 Hz, 2H), 1.90 (s, 3H), 1.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.72, 153.88, 151.59, 132.03, 130.58, 130.12, 127.56, 124.84, 122.22, 116.12, 111.01, 62.85, 40.27, 30.55, 17.91, 17.79. IR

(film): ν 3414, 2916, 2849, 2360, 2342, 1710, 1603, 1528, 1367, 1273, 1223, 1180, 1150, 1087, 1000, 945, 829, 766, 734, 697 cm^{-1}. HRMS (ESI+) for $C_{19}H_{23}NO_3$ (M+Na) calculated 336.1571, found 336.1579.

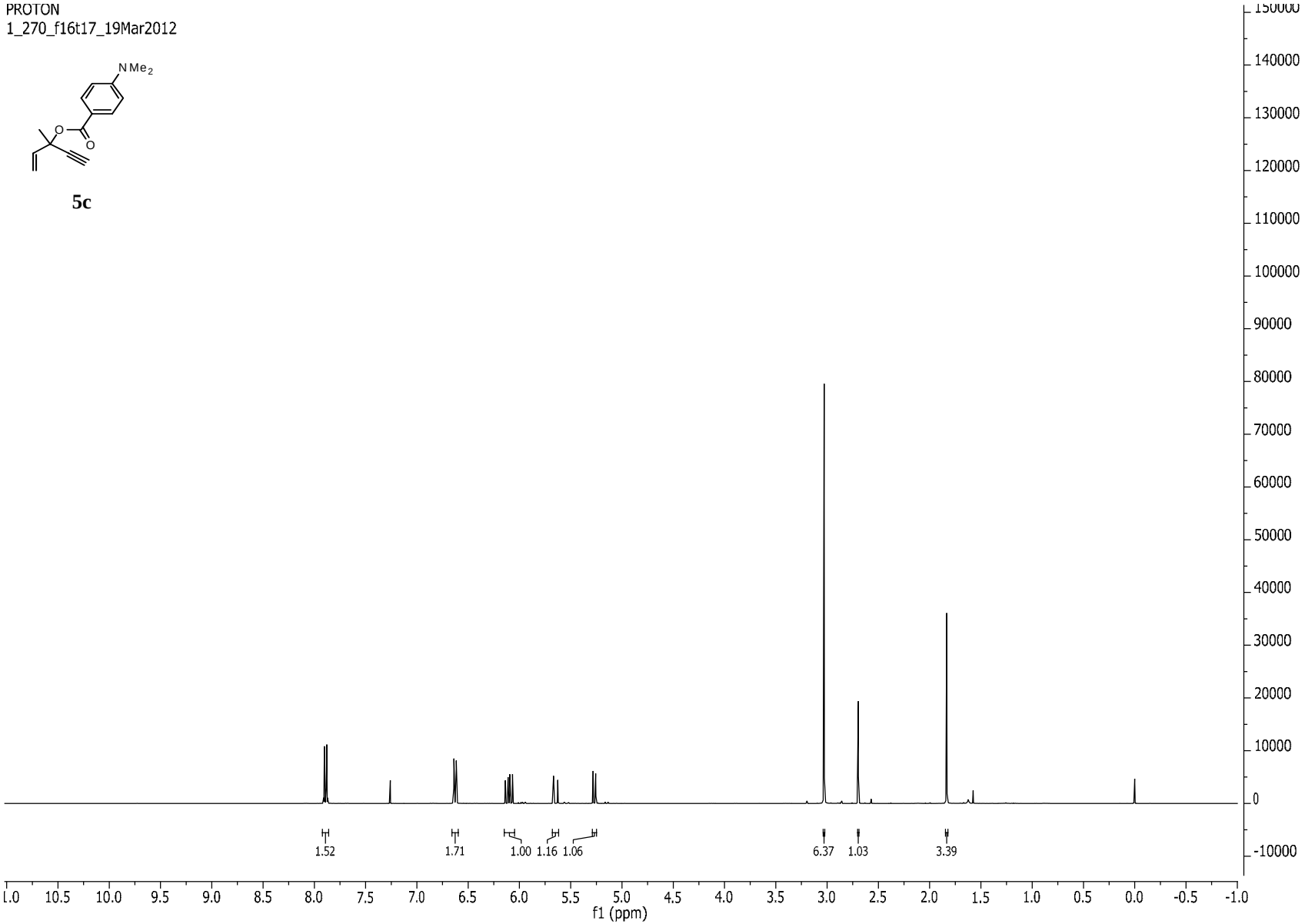
Procedure for the Rh-catalyzed [5+2] cycloaddition of 10b and 7:

To a flask containing ene-yne **10b** (70 mg, 3 mmol, 1 equiv.) and alkyne **7** (34 mg, 6 mmol, 2 equiv) was added $[Rh(COD)Cl]_2$ (7.5 mg, 0.15 mmol, 5 mol %) and $(p\text{-}CF_3C_6H_4)_3P$ (42.7 mg, 0.9 mmol, 30 mol %) and chloroform (3 mL, 0.1 M). The flask was flushed with argon and allowed to stir at 70 °C. Reaction was monitored by TLC until **10b** was completely consumed (10 h). The solvent was evaporated under vacuum and the resulting residue was purified via flash chromatography on silica gel (hexanes / ethyl acetate; R_f = 0.28 (60:40, hexanes / ethyl acetate)) to yield 45.3 mg (53% yield) of a yellow solid **11b**.



11b

11b: 45.3 mg, 53% yield, yellow solid, mp = 118-120 °C, R_f = 0.28 (3:2, hexanes / ethyl acetate). ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.96 (m, 2H), 6.72 – 6.62 (m, 2H), 6.44 – 6.36 (m, 1H), 6.20 (dt, *J* = 6.5, 1.5 Hz, 1H), 6.12 (dd, *J* = 9.7, 1.7 Hz, 1H), 5.52 (dt, *J* = 9.7, 7.1 Hz, 1H), 4.33 – 4.21 (m, 2H), 3.06 (s, 6H), 2.58 (d, *J* = 7.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.88, 153.84, 151.53, 134.75, 132.05, 125.28, 122.70, 119.68, 119.28, 116.31, 110.95, 66.60, 40.28, 29.50. IR (film): ν 3514, 2922, 1686, 1611, 1532, 1447, 1378, 1319, 1293, 1283, 1233, 1187, 1127, 1071, 1026, 946, 868, 825, 761, 745, 699 cm^{-1}. HRMS (ESI+) for $C_{17}H_{19}NO_3$ (M+Na) calculated 308.1257, found 308.1248.


PROTON
1_270_f16t17_19Mar2012
NMe2
O
O
5c
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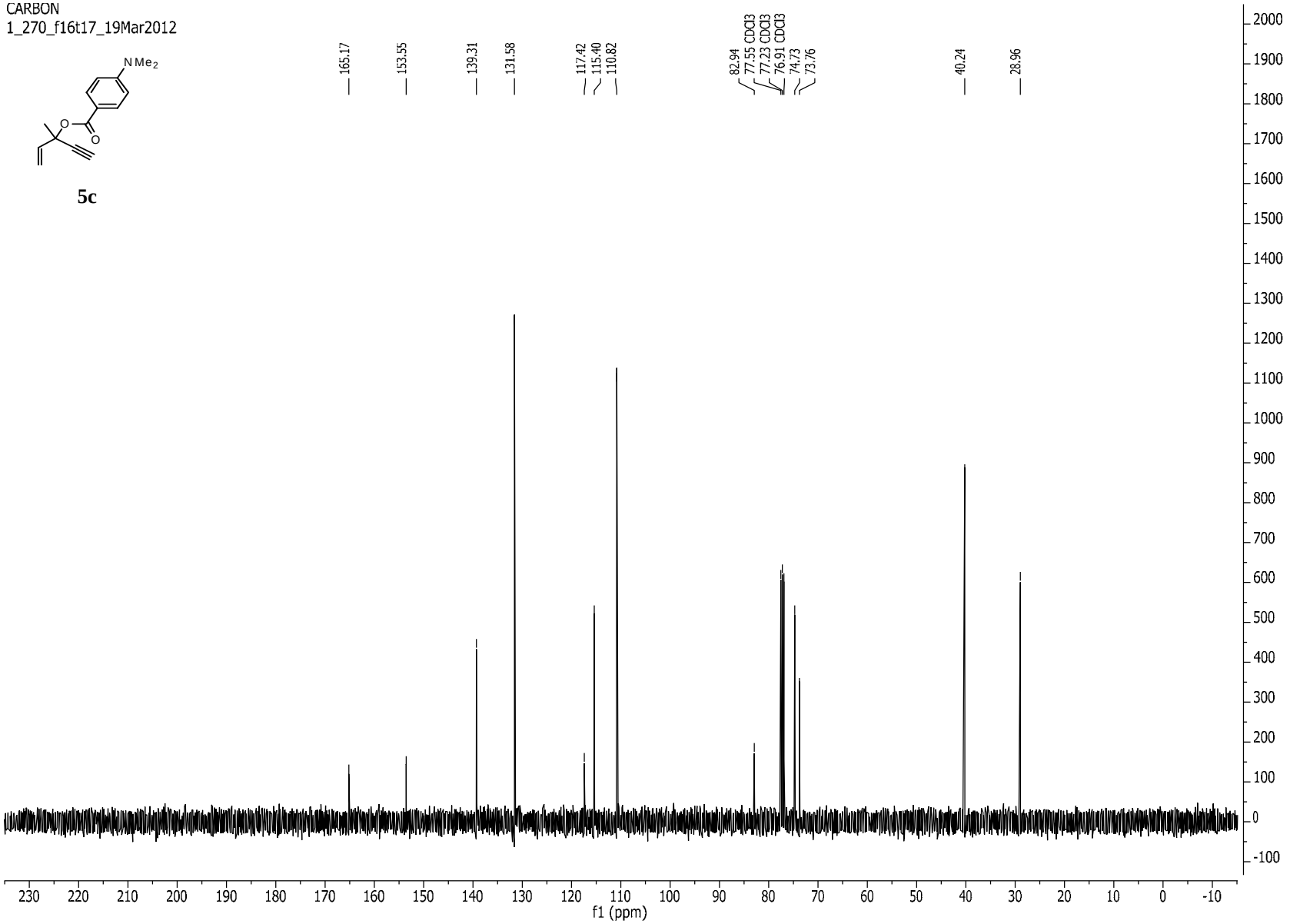
1.71
1.00
1.16
1.06
6.37
1.03
3.39
f1 (ppm)


CARBON
1_270_f16t17_19Mar2012
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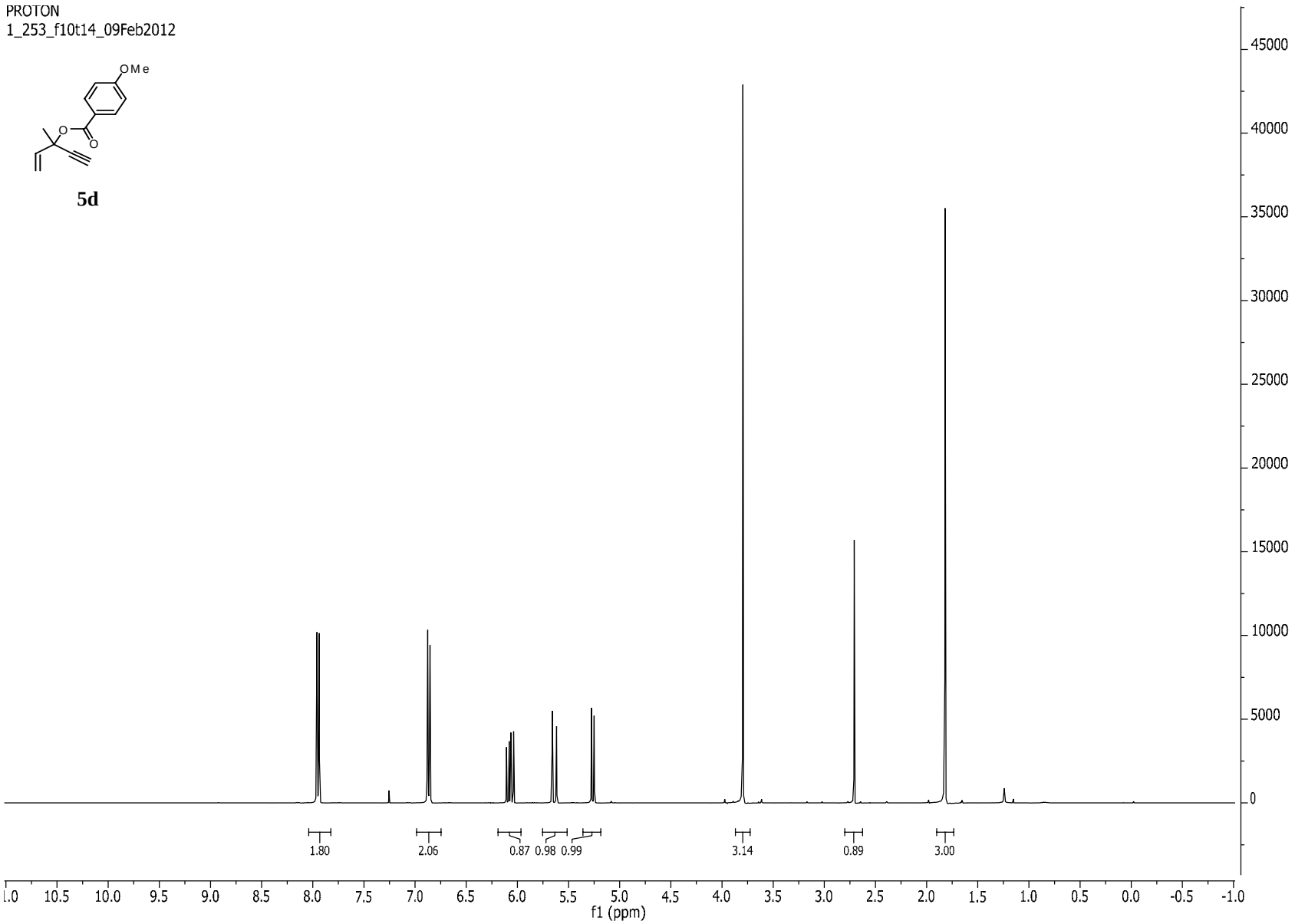
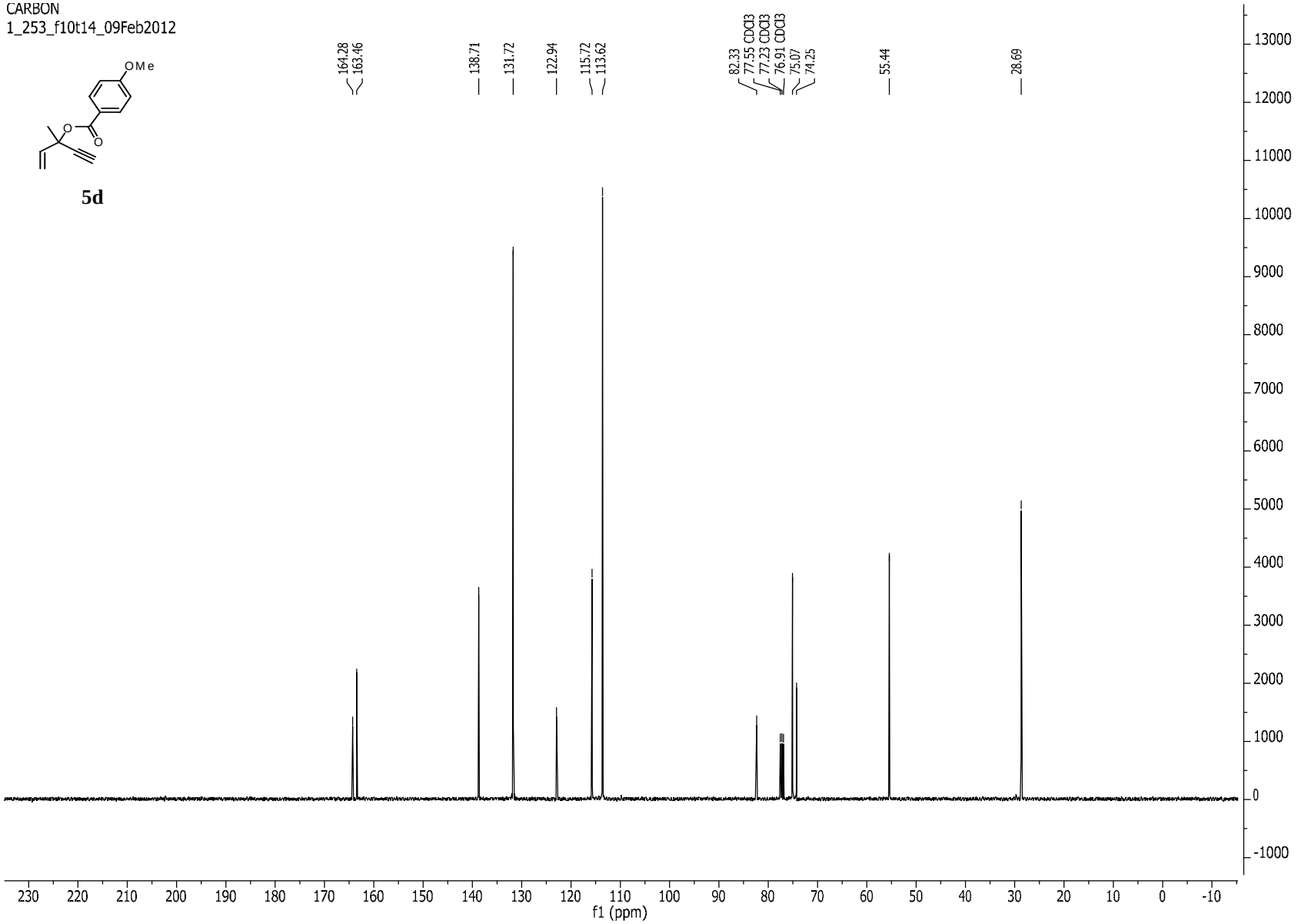
O
O
165.17
153.55
139.31
131.58
117.42
115.40
110.82
82.94
77.55 CDCl3
77.23 CDCl3
76.91 CDCl3
74.73
73.76
40.24
28.96
f1 (ppm)

5c




CARBON
1_253_f10t14_09Feb2012
OMe
O
O
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163.46
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131.72
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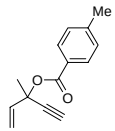
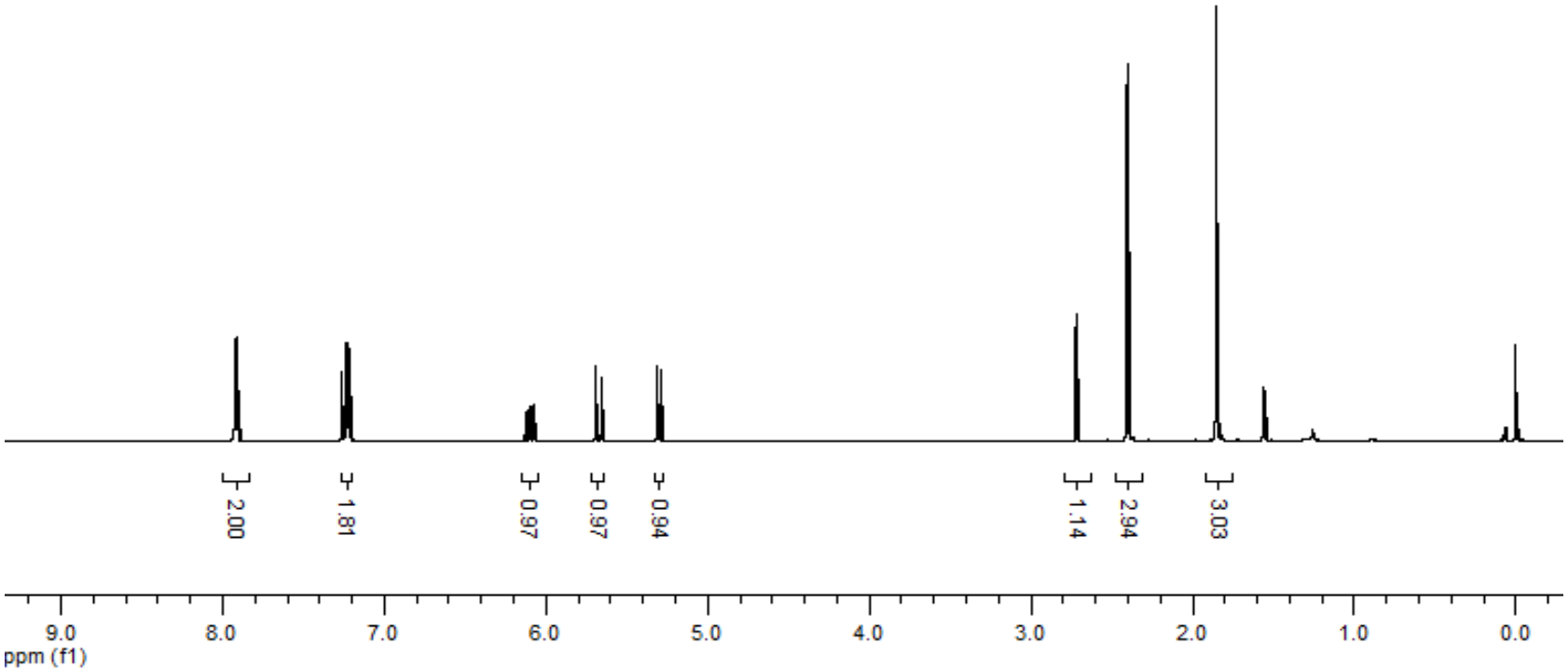
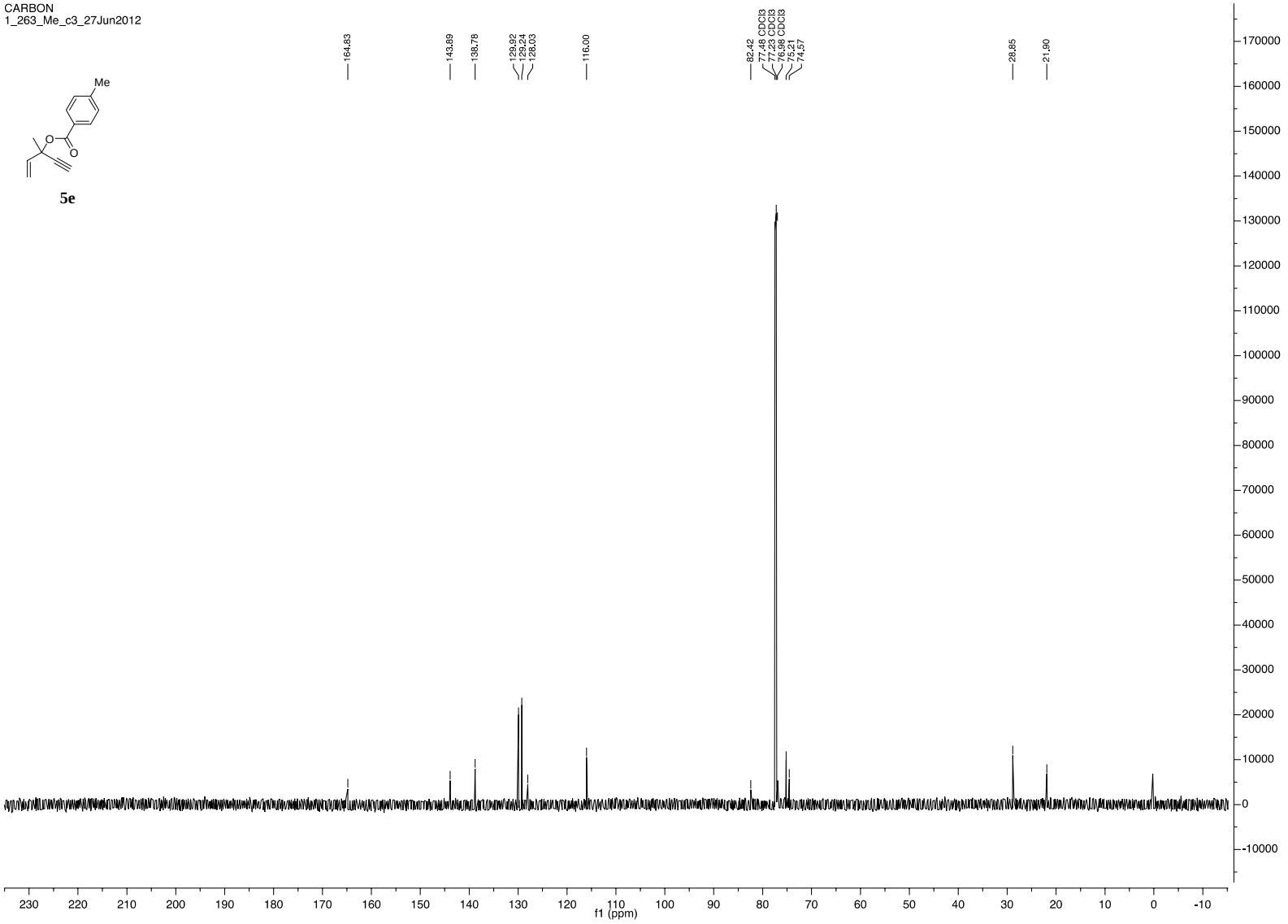
115.72
113.62
82.33
77.55 CDCl3
77.23 CDCl3
76.91 CDCl3
75.07
74.25
55.44
28.69
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

5d



5e




CARBON
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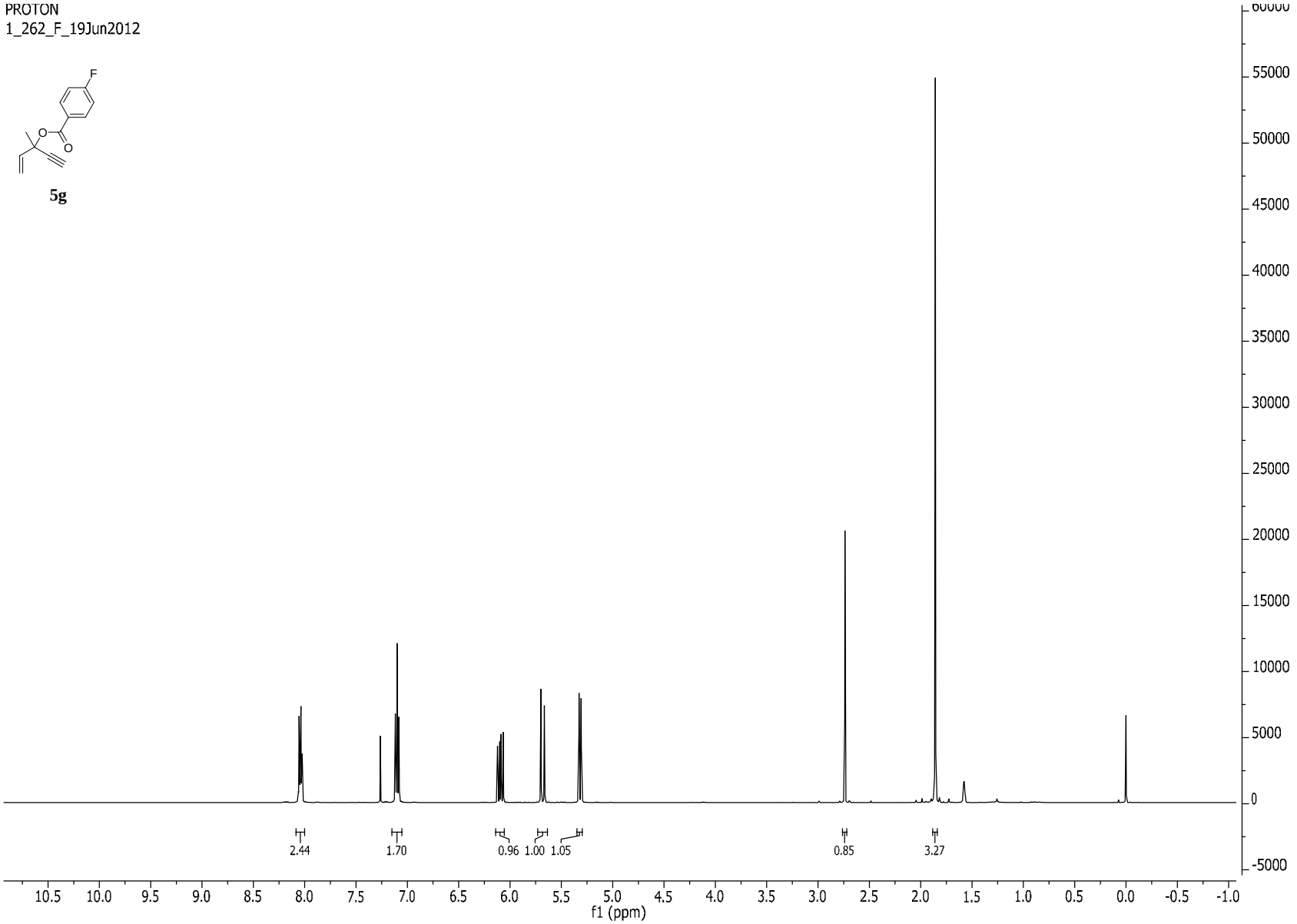
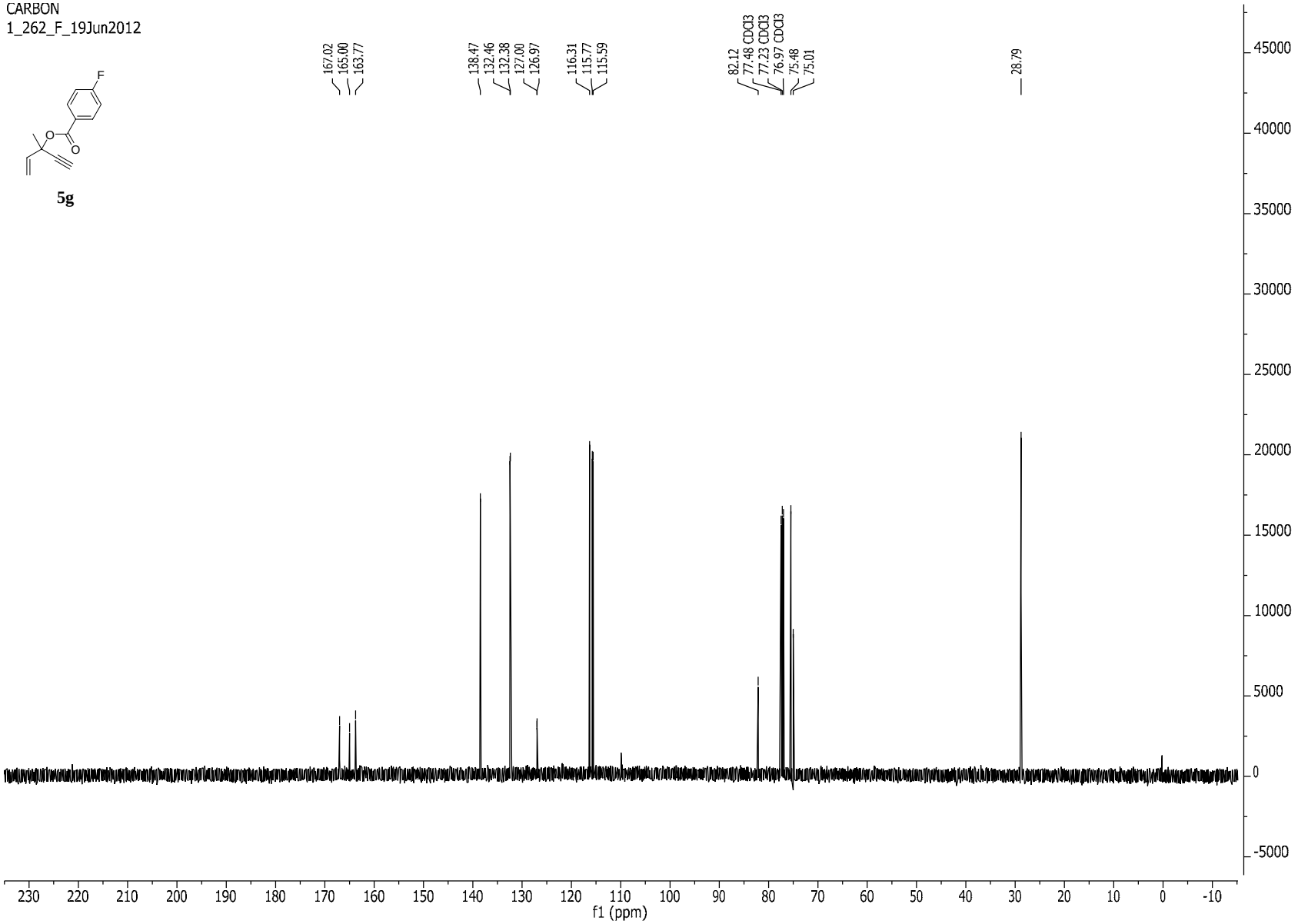
Me
O
O
5e
164.83
143.89
138.78
129.92
129.24
128.03
116.00
82.42
77.48 CDCl3
77.23 CDCl3
76.98 CDCl3
75.27
74.57
28.85
21.90
f1 (ppm)

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F
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O
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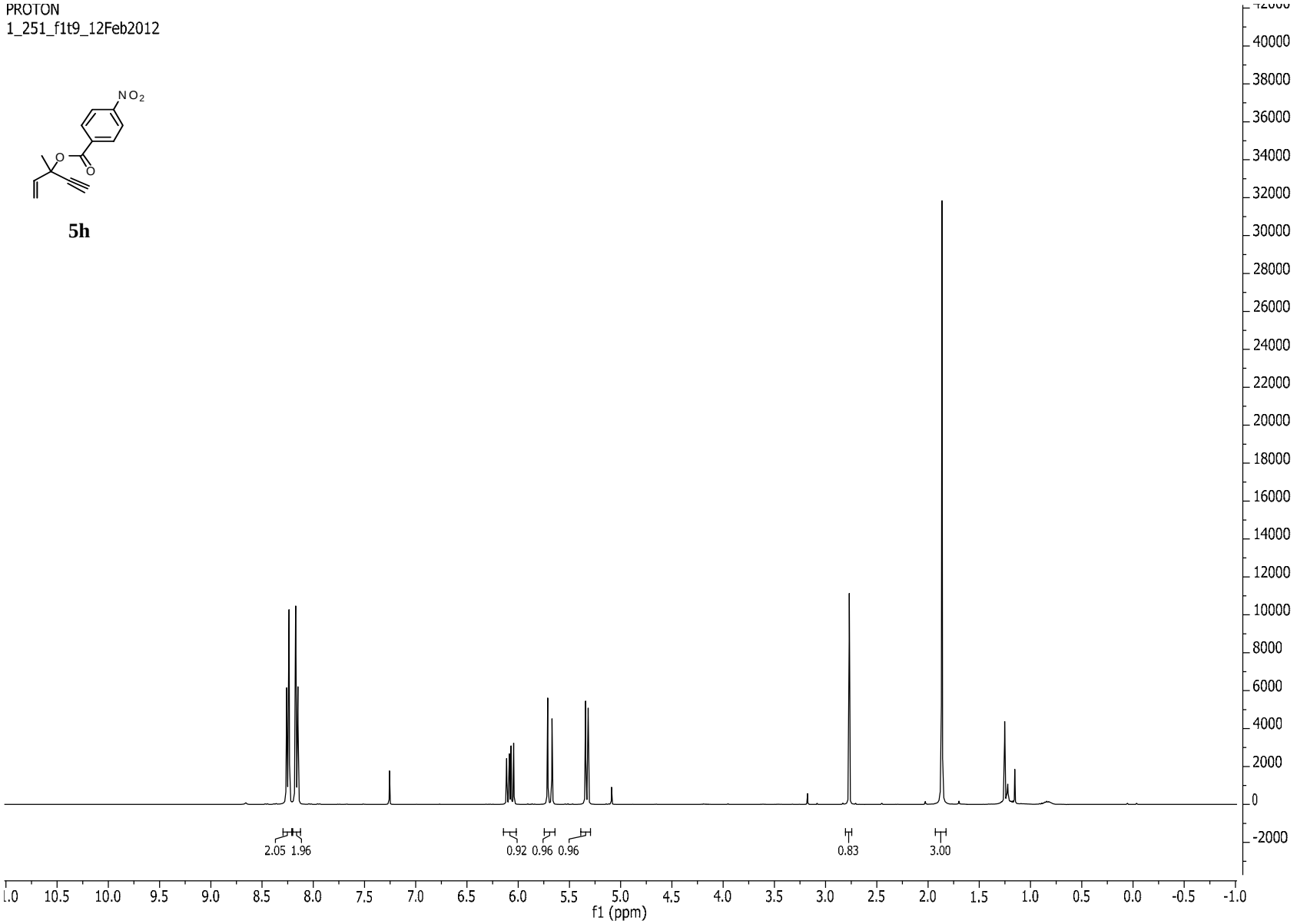
163.77
138.47
132.46
132.38
127.00
126.97
116.31
115.77
115.59
82.12
77.48 CDCl3
77.23 CDCl3
76.97 CDCl3
75.48
75.01
28.79
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


PROTON
1_251_f1t9_12Feb2012
NO2
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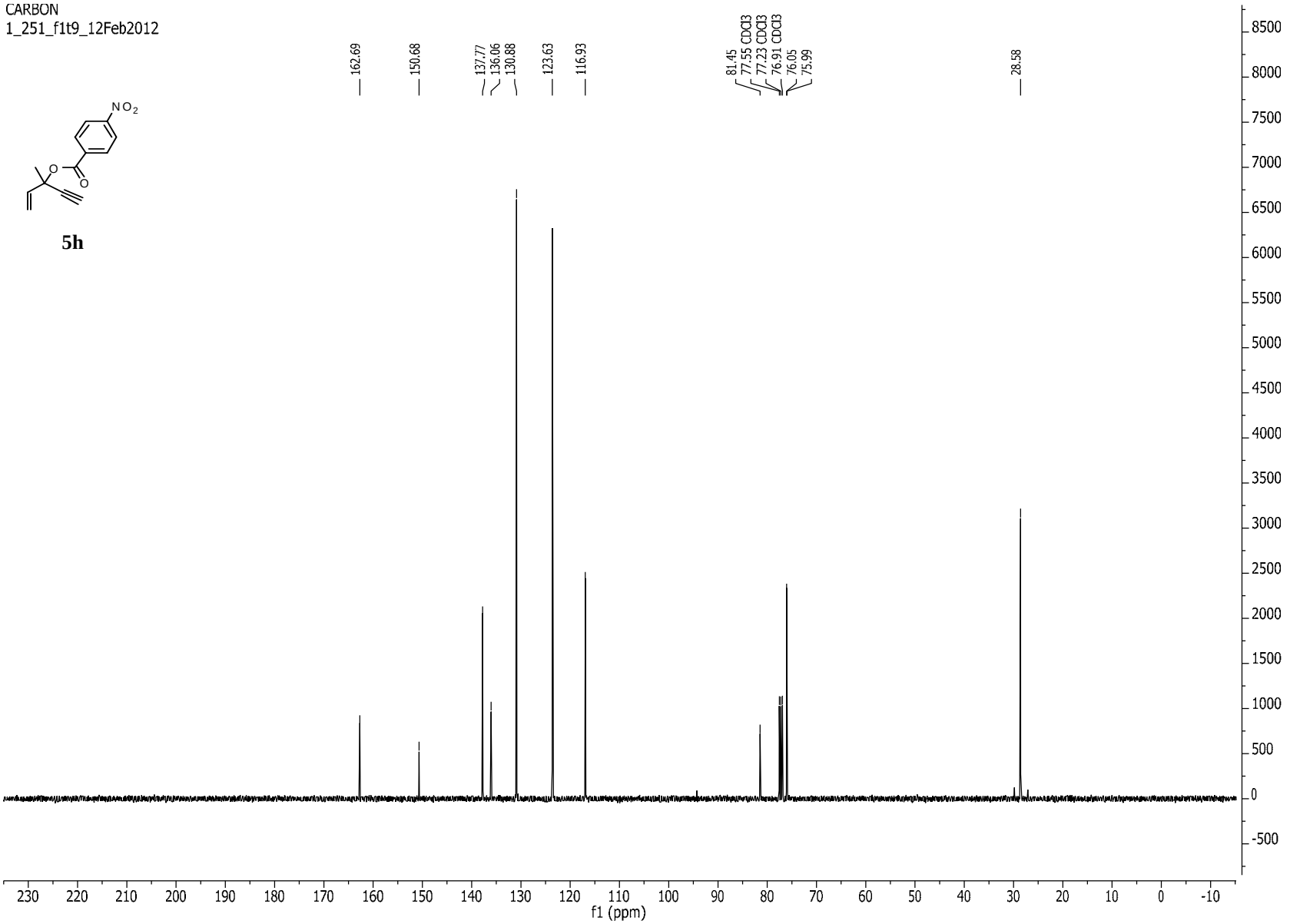
O
5h
2.05 1.96
0.92 0.96 0.96
0.83
3.00
f1 (ppm)


CARBON
1_251_f1t9_12Feb2012
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150.68
137.77
136.06
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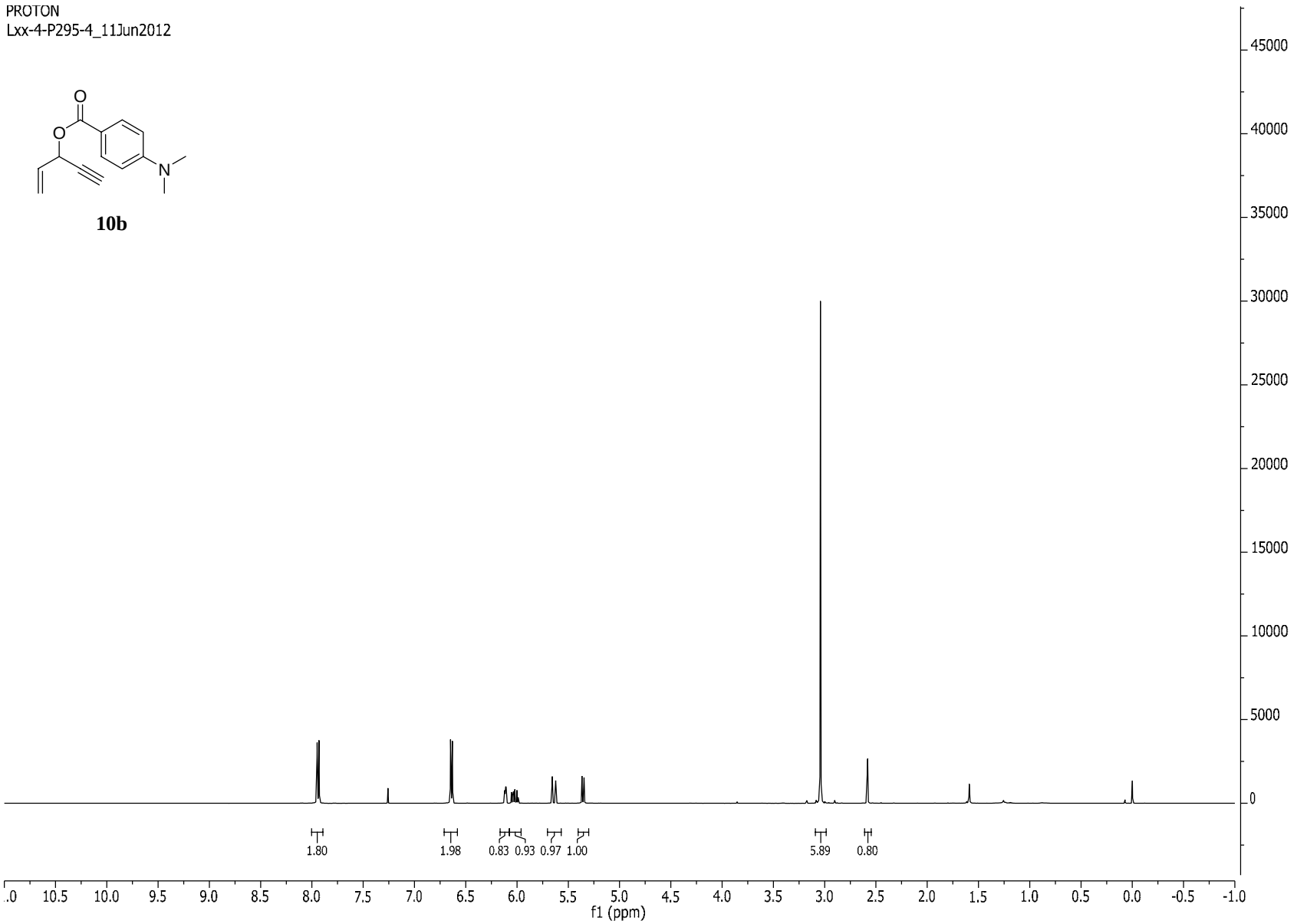
123.63
116.93
81.45
77.55 CDCl3
77.23 CDCl3
76.91 CDCl3
76.05
75.99
28.58
NO2
O
O
f1 (ppm)

5h


PROTON
Lxx-4-P295-4_11Jun2012
O
O
N
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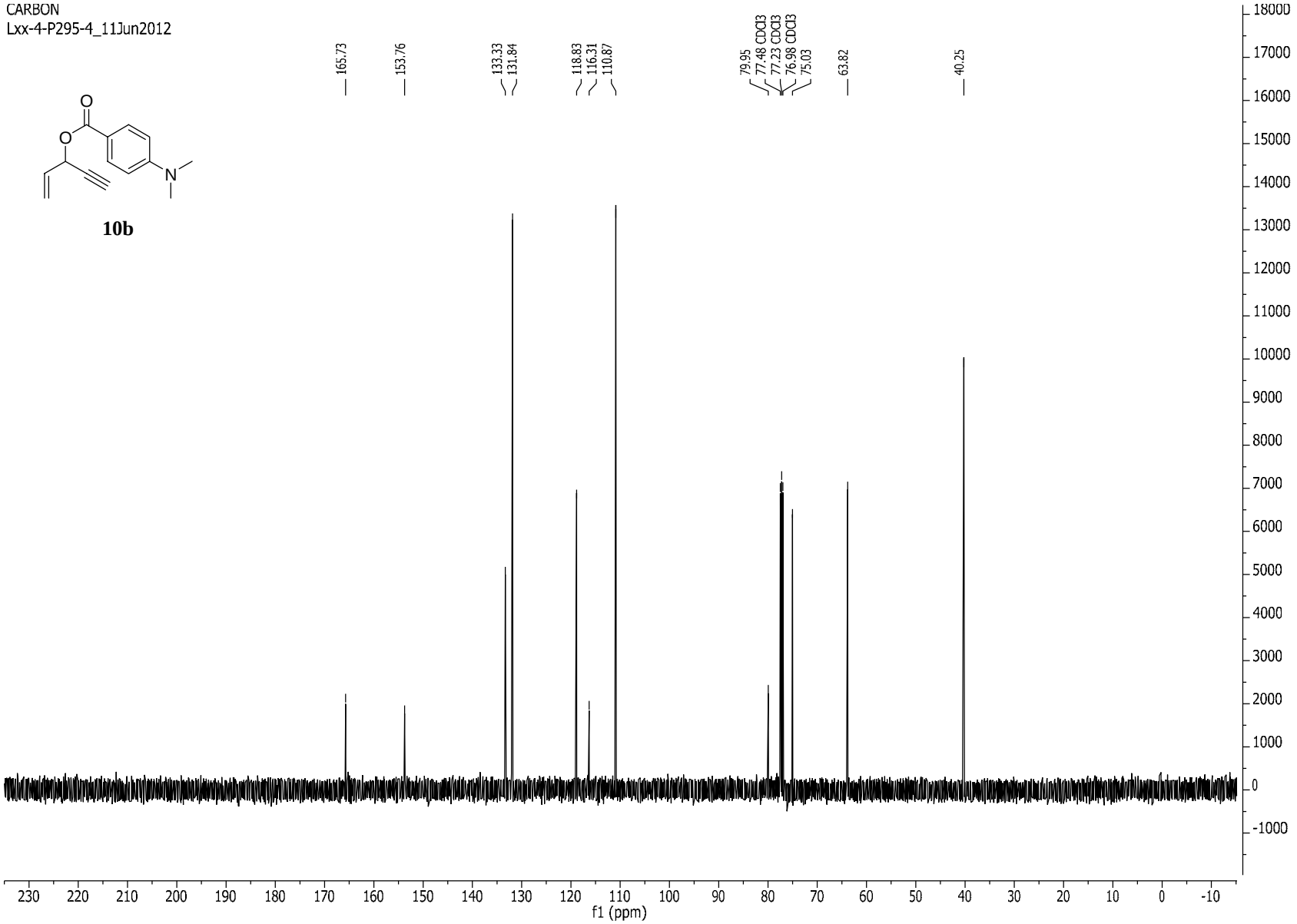
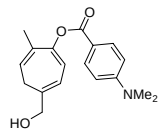
40000
35000
30000
25000
20000
15000
10000
5000
0
1.80
1.98
0.83
0.93
0.97
1.00
5.89
0.80
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

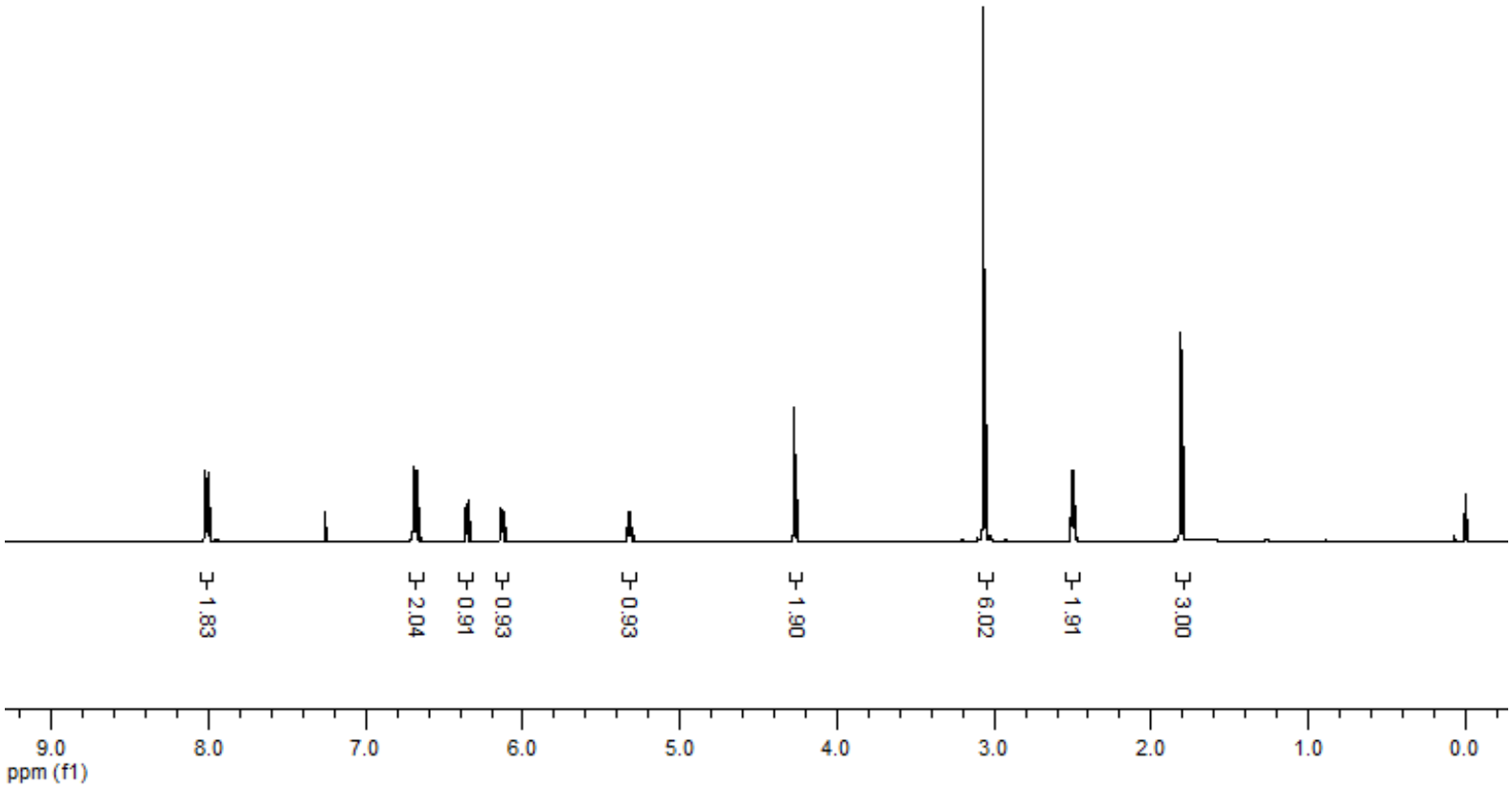
10b

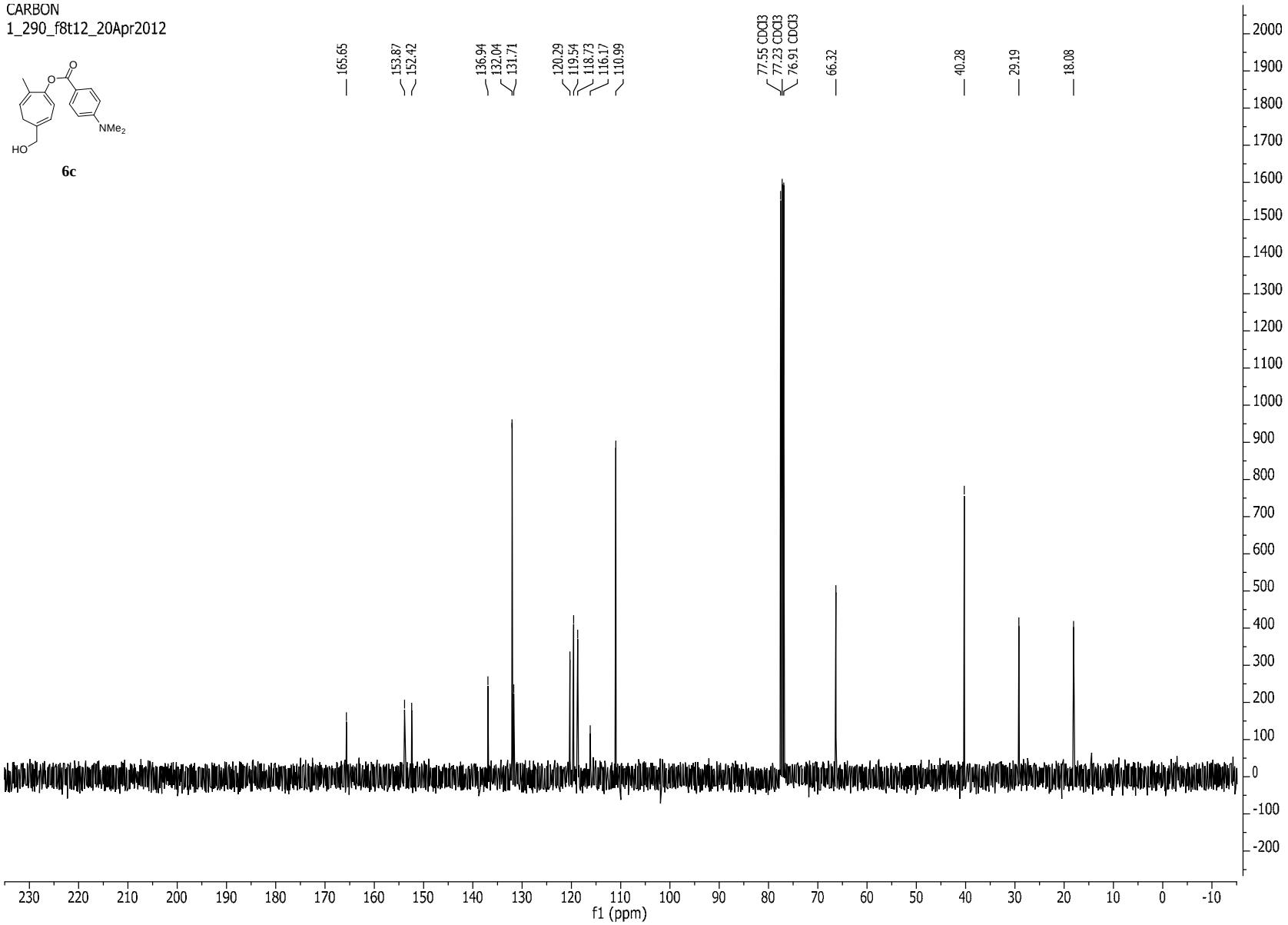

CARBON
Lxx-4-P295-4_11Jun2012
165.73
153.76
133.33
131.84
118.83
116.31
110.87
79.95
77.48 CDCl3
77.23 CDCl3
76.98 CDCl3
75.03
63.82
40.25
O
O
N
f1 (ppm)

10b

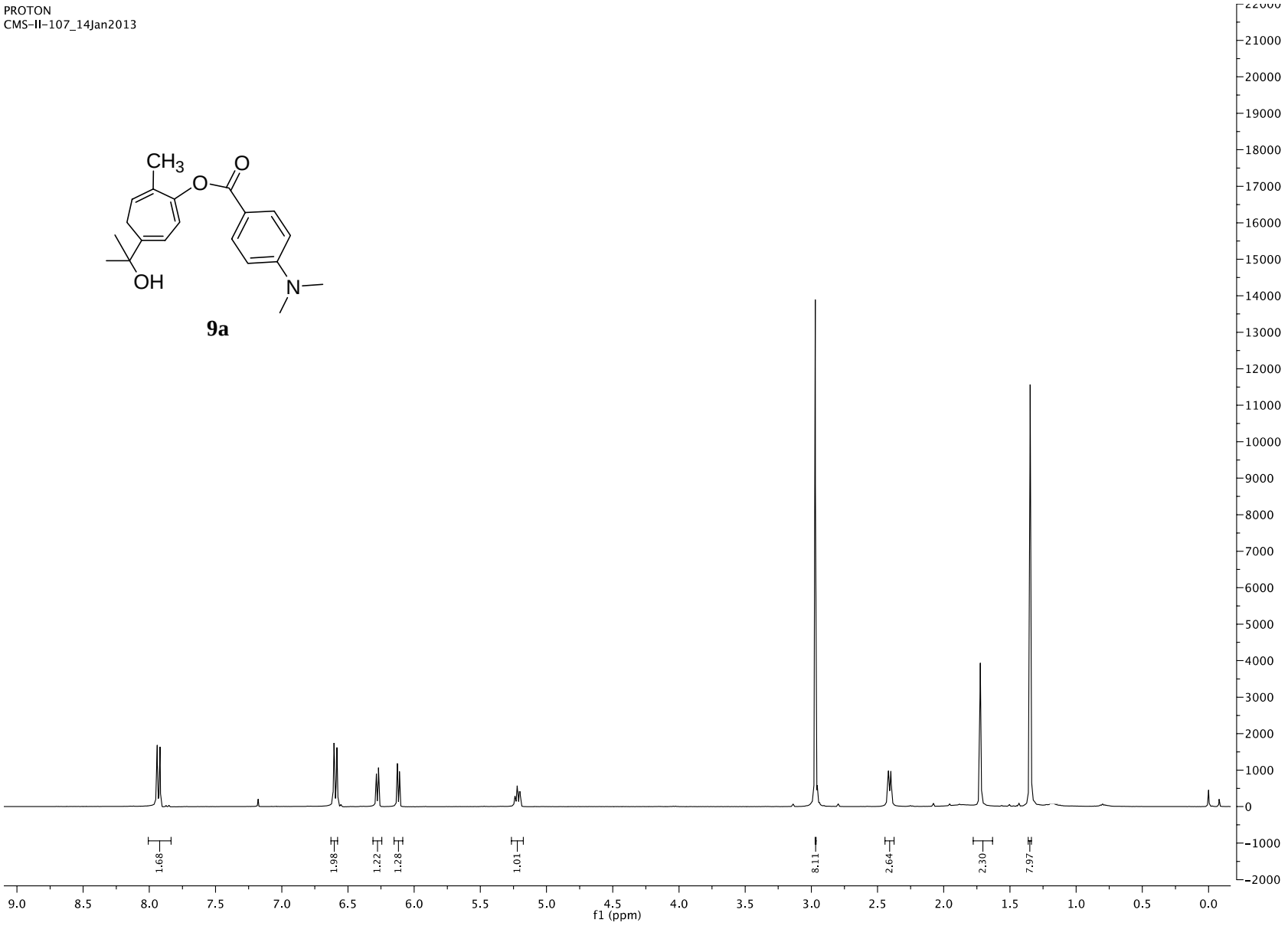


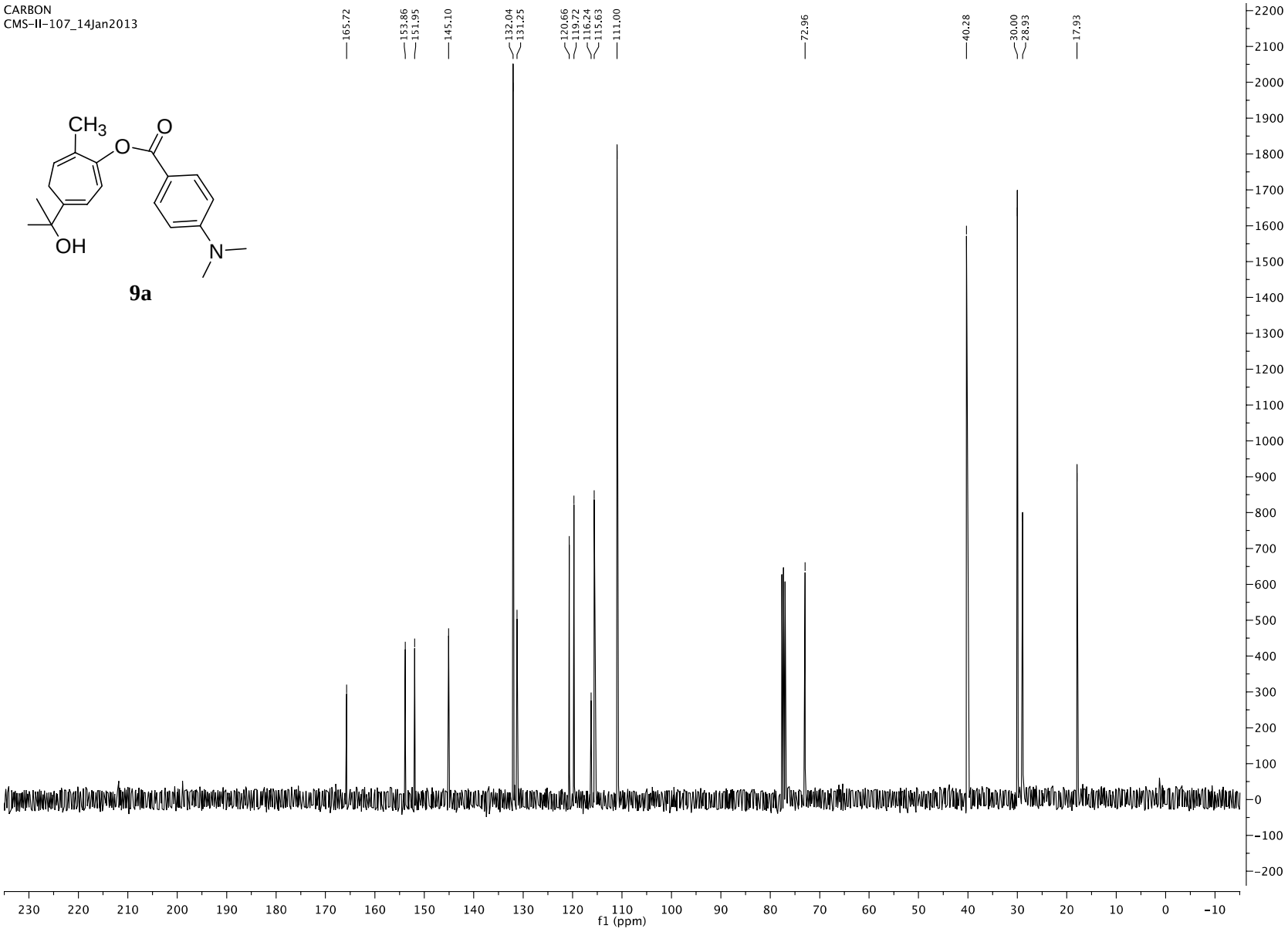
6c



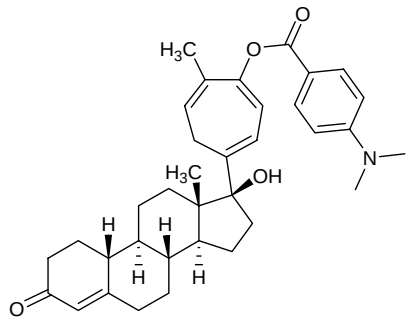

CARBON
1_290_f8t12_20Apr2012
165.65
153.87
152.42
136.94
132.04
131.71
120.29
119.54
118.73
116.17
110.99
77.55 CDCl3
77.23 CDCl3
76.91 CDCl3
66.32
40.28
29.19
18.08
NMe2
HO
f1 (ppm)

6c

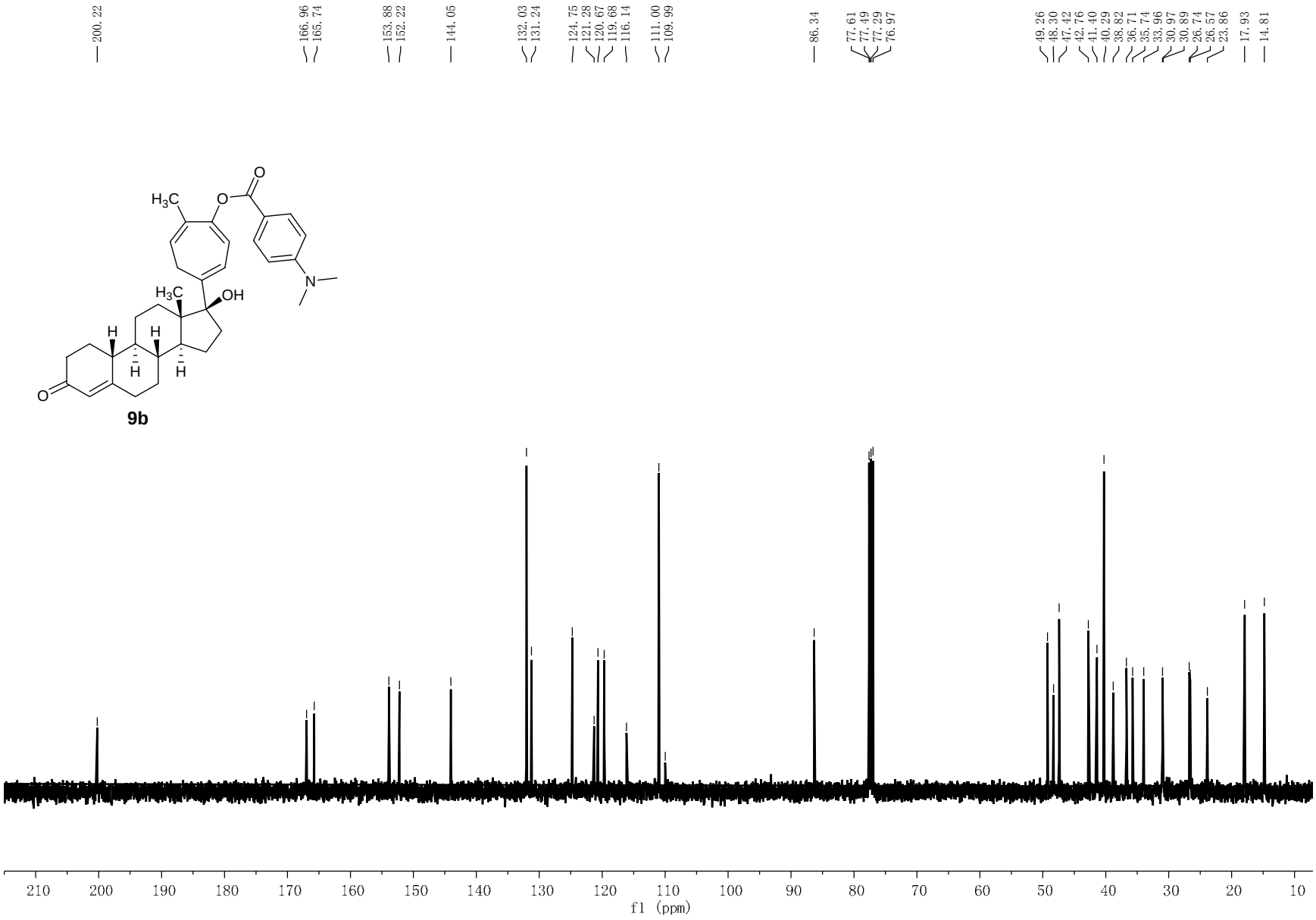

PROTON
CMS-II-107_14Jan2013
CH3
O
O
OH
N
9a
1.68
1.98
1.22
1.28
1.01
8.11
2.64
2.30
7.97
f1 (ppm)

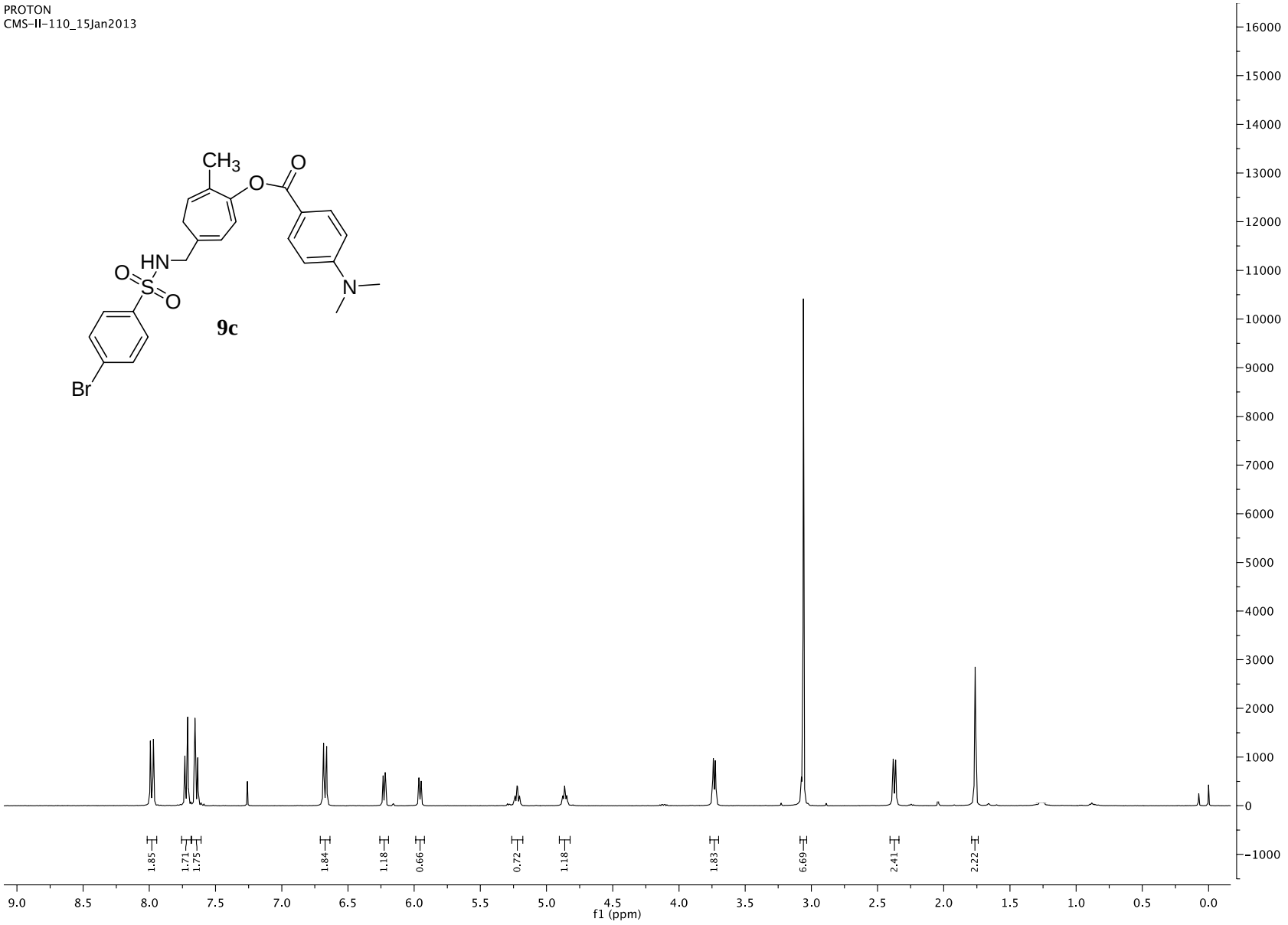

CARBON
CMS-II-107_14Jan2013
165.72
153.86
151.95
145.10
132.04
131.25
120.66
119.72
116.24
115.63
111.00
72.96
40.28
30.00
28.93
17.93
CH3
O
O
OH
N
f1 (ppm)

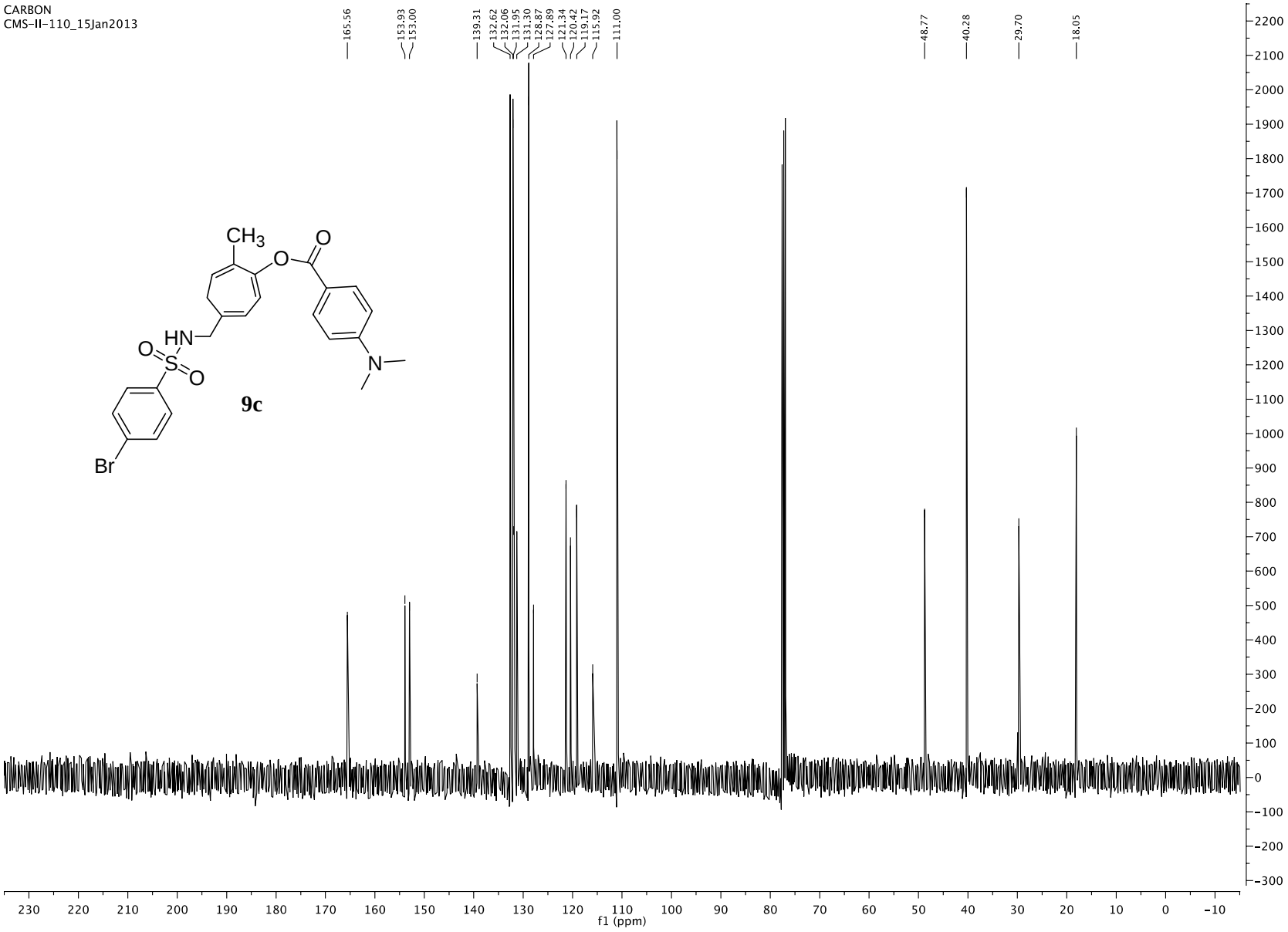
9a

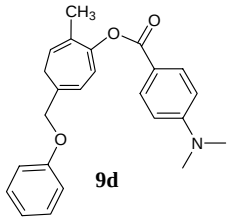


9b

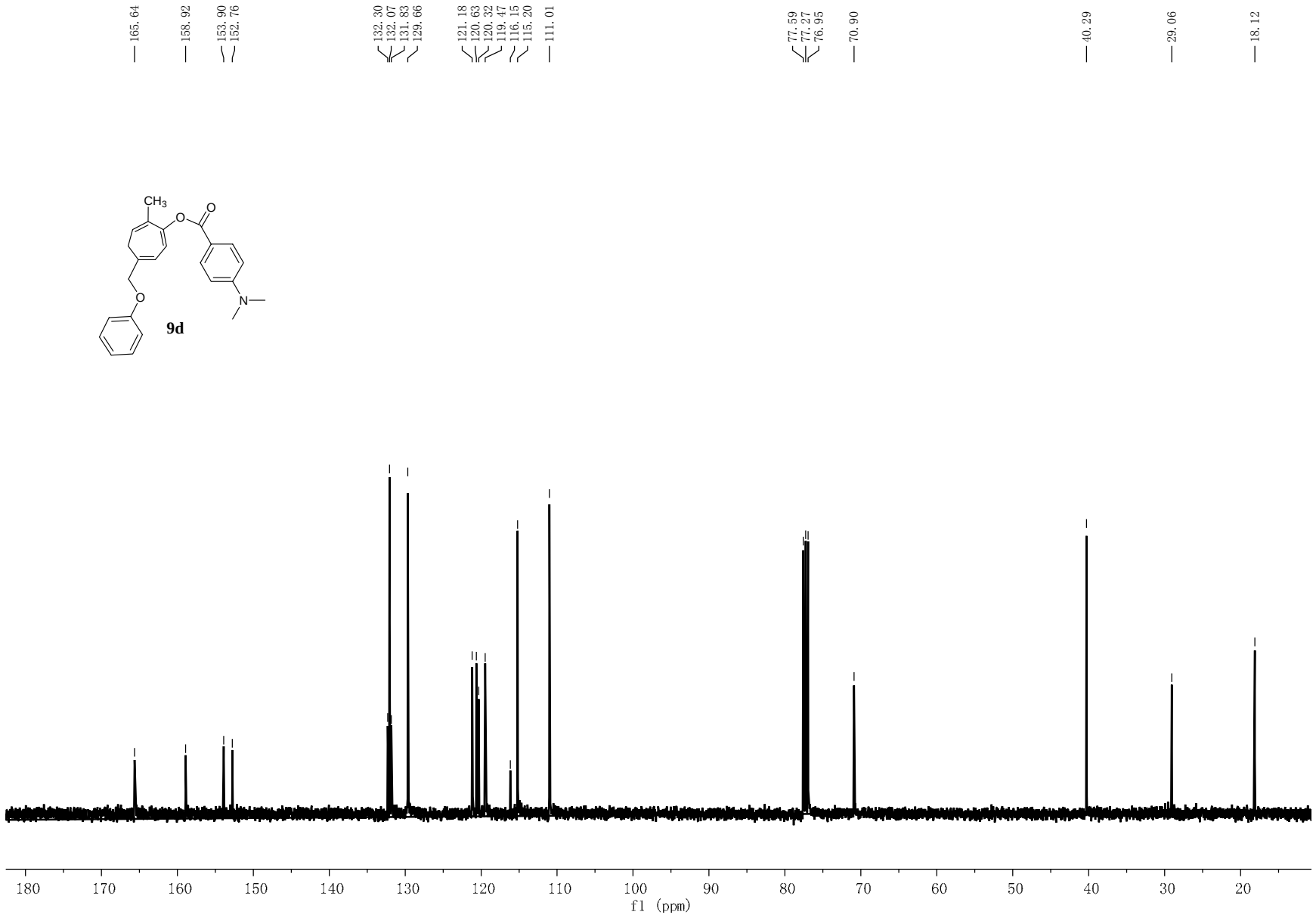

200.22
166.96
165.74
153.88
152.22
144.05
132.03
131.24
124.75
121.28
120.67
119.68
116.14
111.00
109.99
86.34
77.61
77.49
77.29
76.97
49.26
48.30
47.42
42.76
41.40
40.29
38.82
36.71
35.74
33.96
30.97
30.89
26.74
26.57
23.86
17.93
14.81
H3C
O
O
N
H3C
OH
H
H
H
H
O
9b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

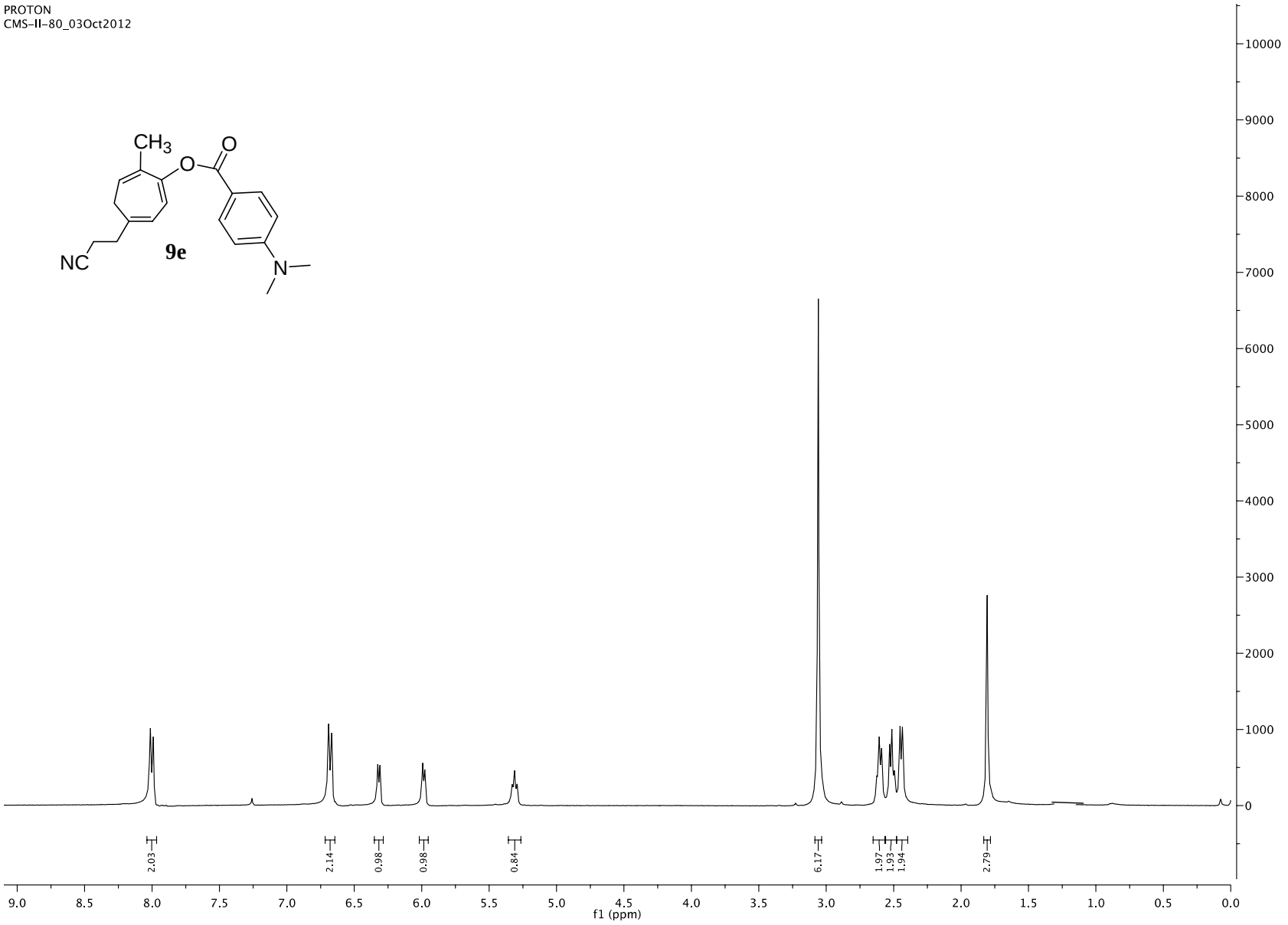

PROTON
CMS-II-110_15Jan2013
CH3
O
O
HN
O
S
O
N
Br
9c
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.85
1.71
1.75
1.84
1.18
0.66
0.72
1.18
1.83
6.69
2.41
2.22
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

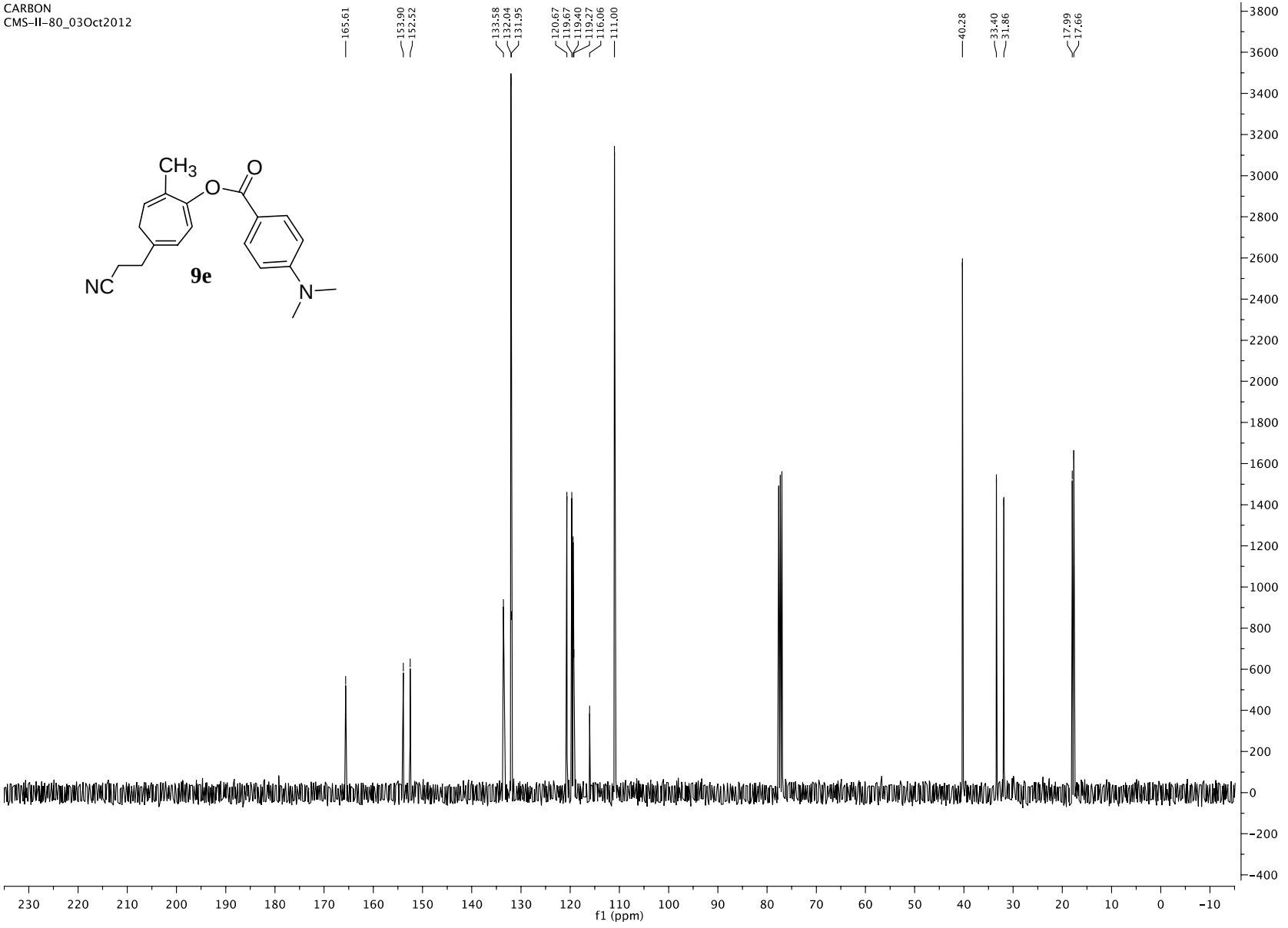

CARBON
CMS-II-110_15Jan2013
165.56
153.93
153.00
139.31
132.62
132.06
131.95
131.30
128.87
127.89
121.34
120.42
119.17
115.92
111.00
48.77
40.28
29.70
18.05
CH3
O
O
HN
O
S
O
N
Br
9c
f1 (ppm)

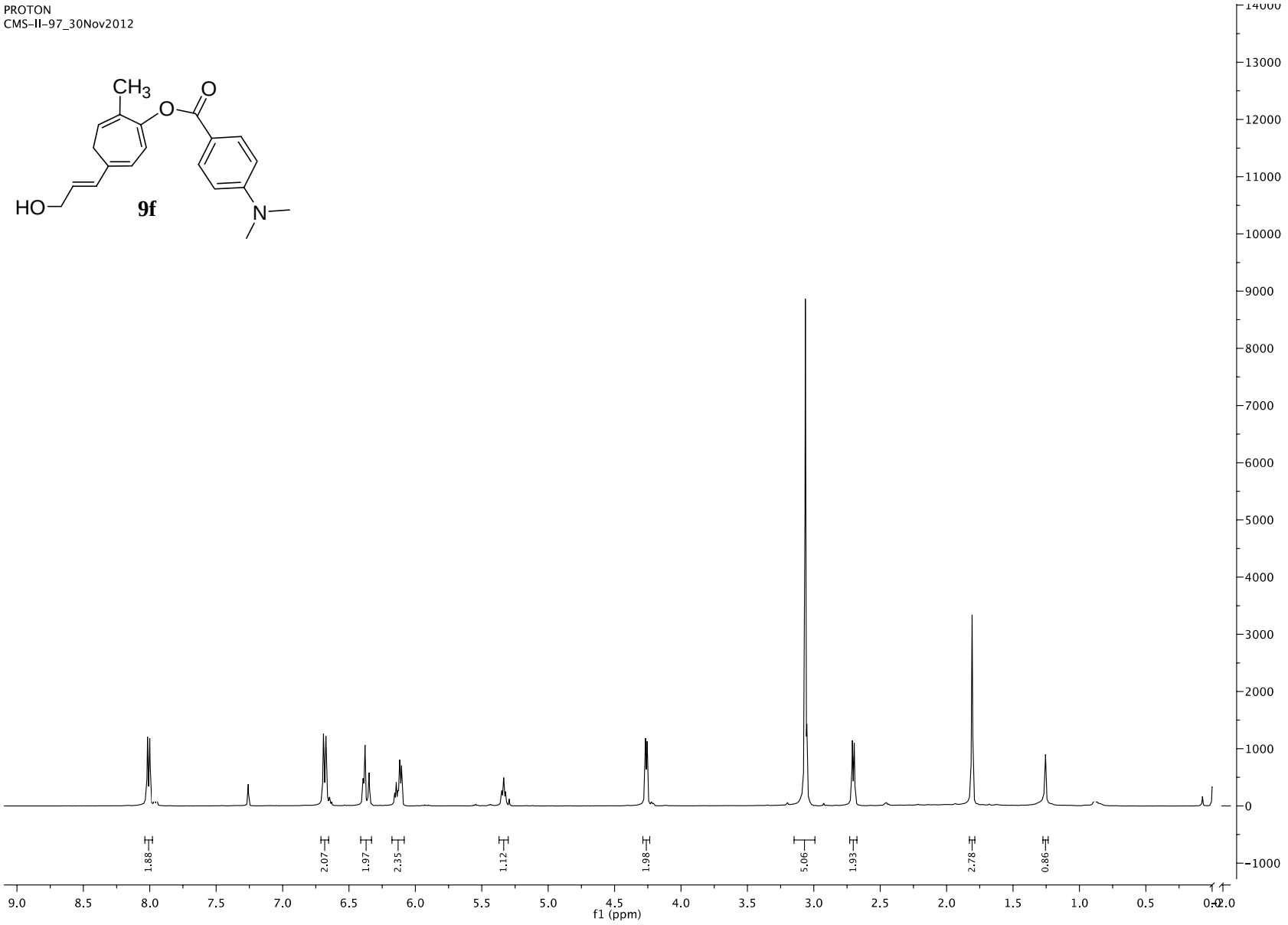


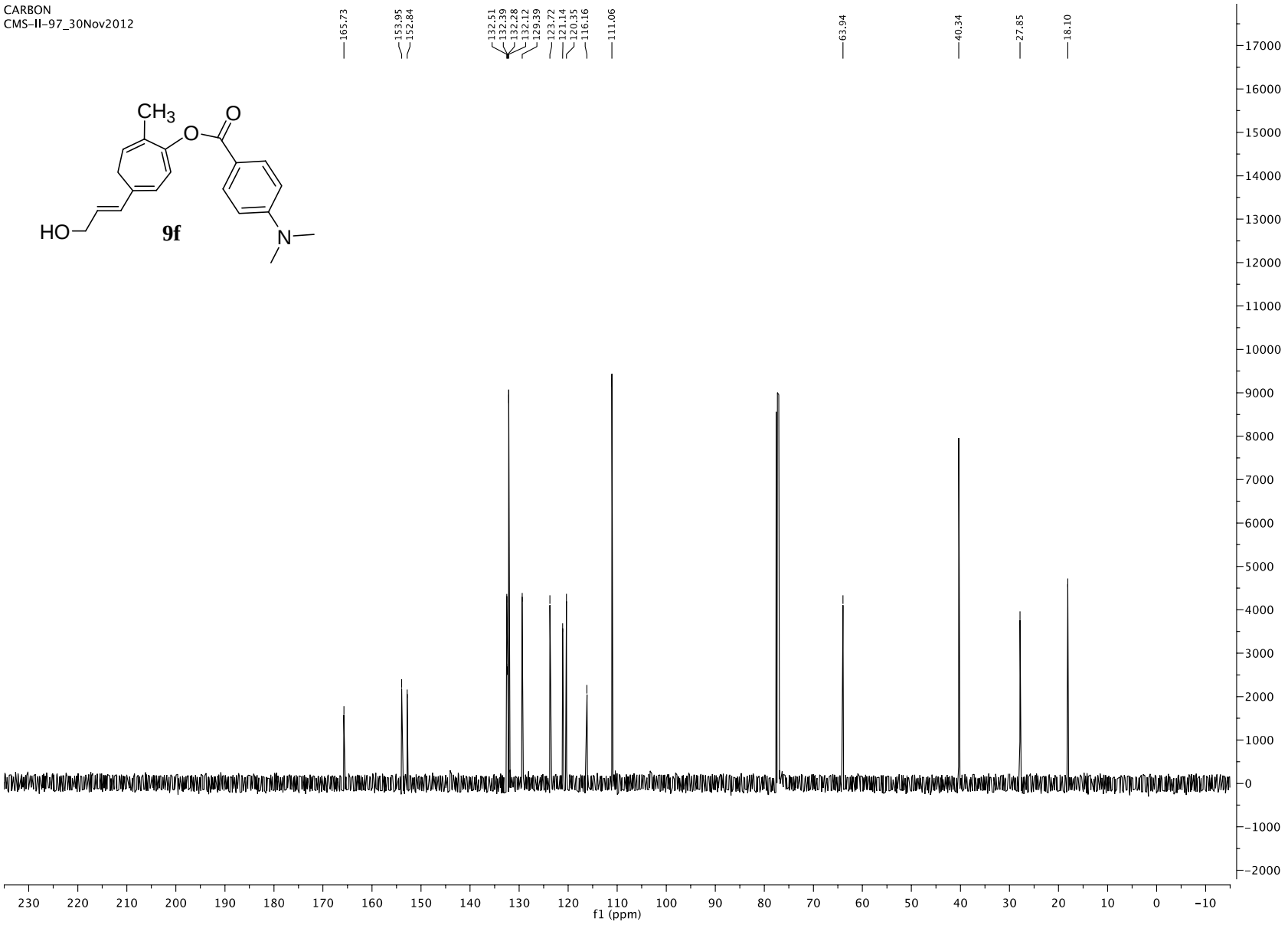
9d

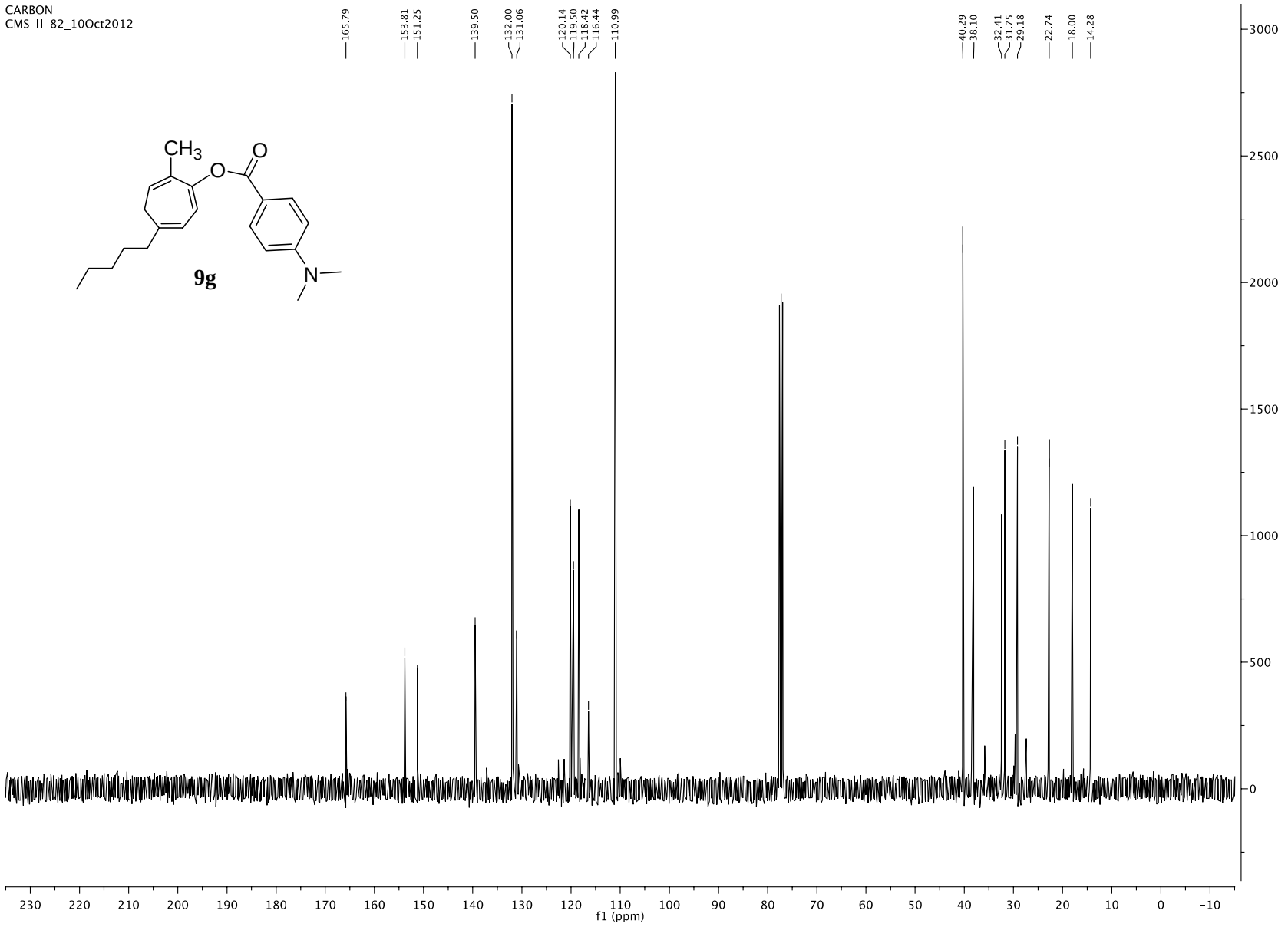


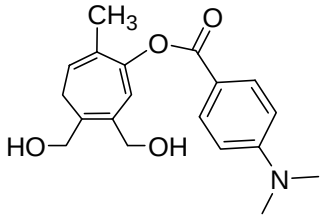

PROTON
CMS-II-80_03Oct2012
CH3
O
O
NC
9e
N
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2.03
2.14
0.98
0.98
0.84
6.17
1.97
1.93
1.94
2.79
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CARBON
CMS-II-80_03Oct2012
165.61
153.90
152.52
133.58
132.04
131.95
120.67
119.67
119.40
119.27
116.06
111.00
40.28
33.40
31.86
17.99
17.66
CH3
O
O
NC
9e
N
f1 (ppm)

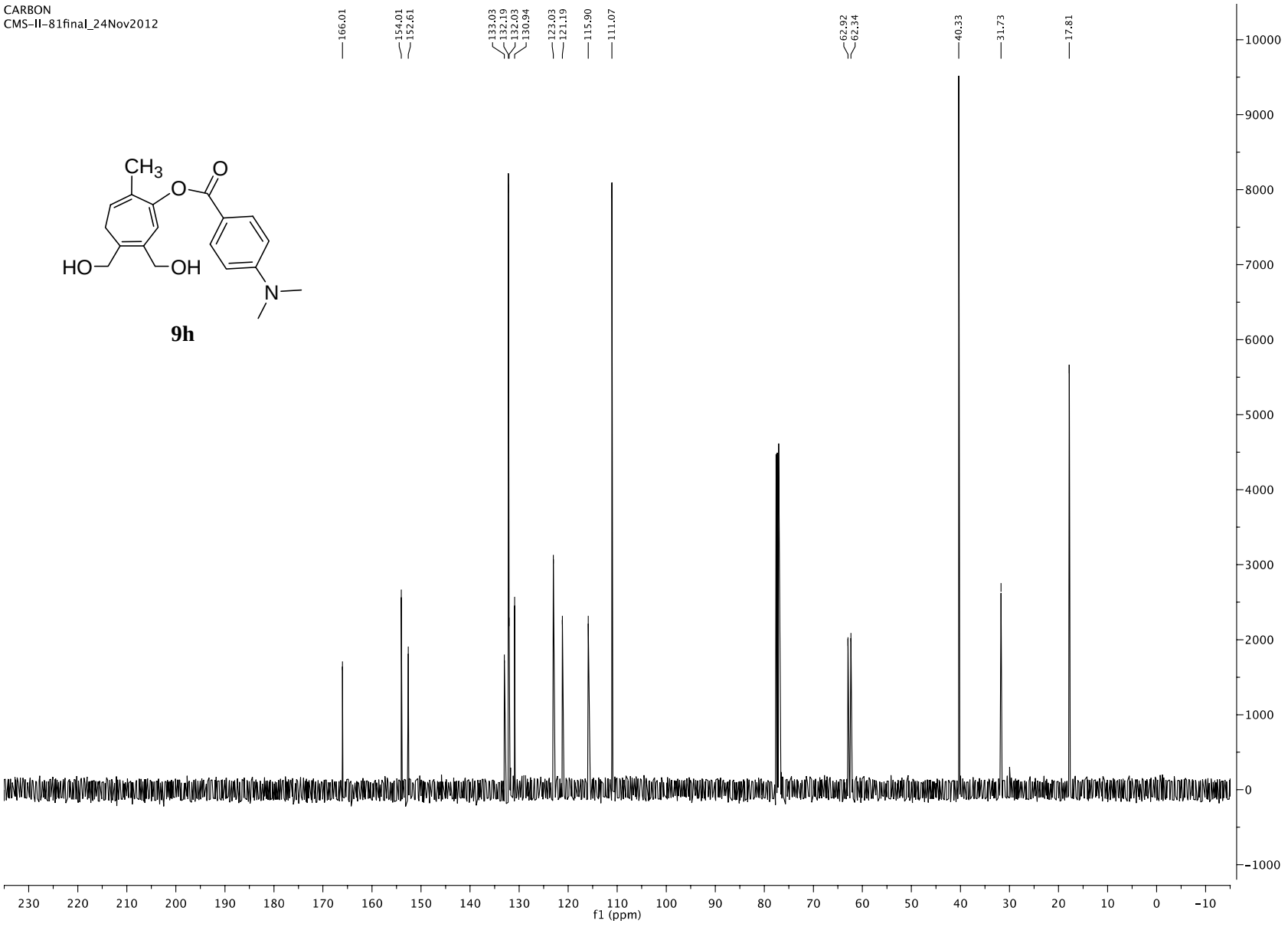

PROTON
CMS-II-97_30Nov2012
CH3
O
O
HO
9f
N
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.88
2.07
1.97
2.35
1.12
1.98
5.06
1.93
2.78
0.86
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

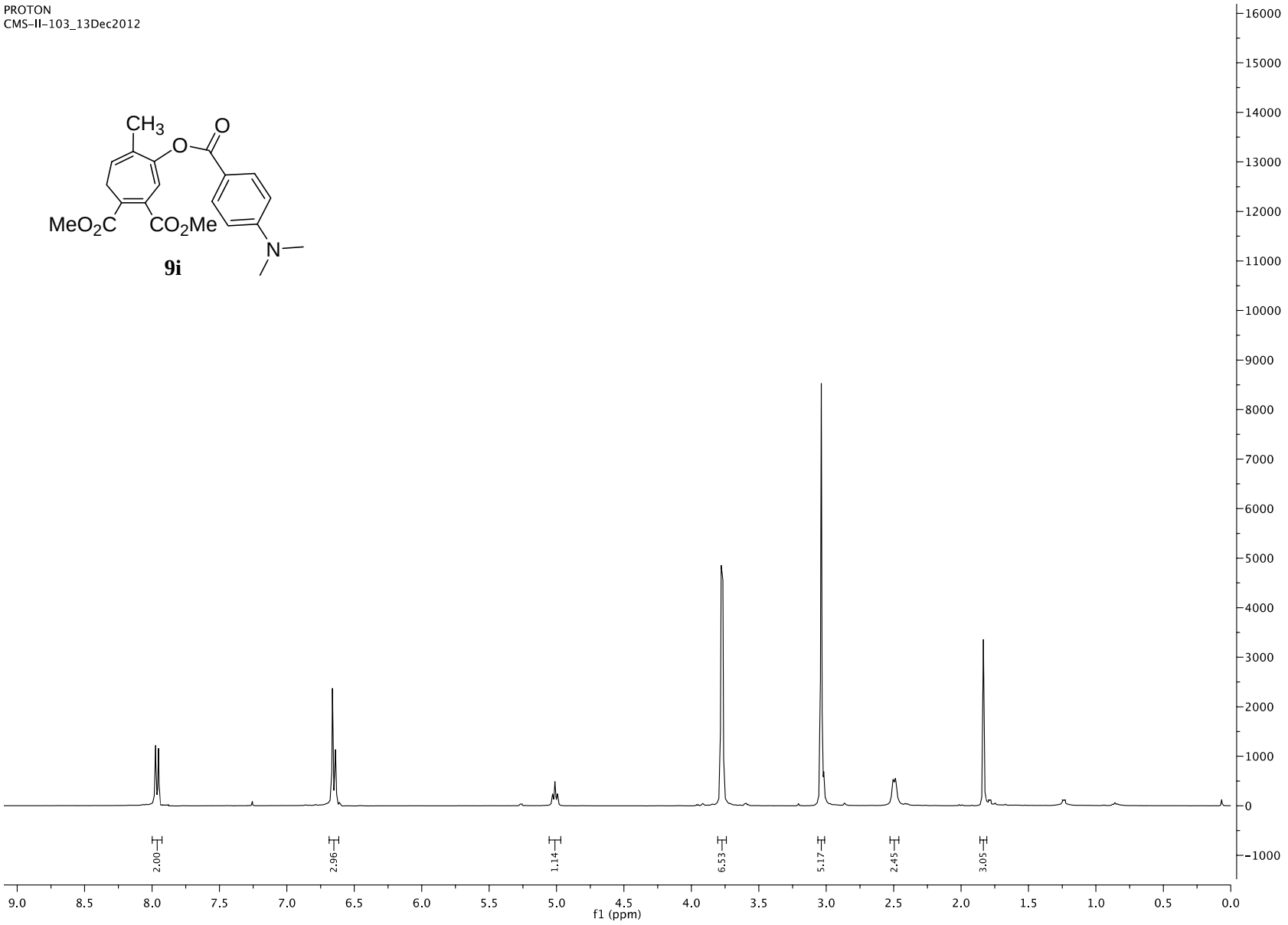

CARBON
CMS-II-97_30Nov2012
165.73
153.95
152.84
132.51
132.39
132.28
132.12
129.39
123.72
121.14
120.35
116.16
111.06
63.94
40.34
27.85
18.10
CH3
O
O
HO
N
9f
f1 (ppm)

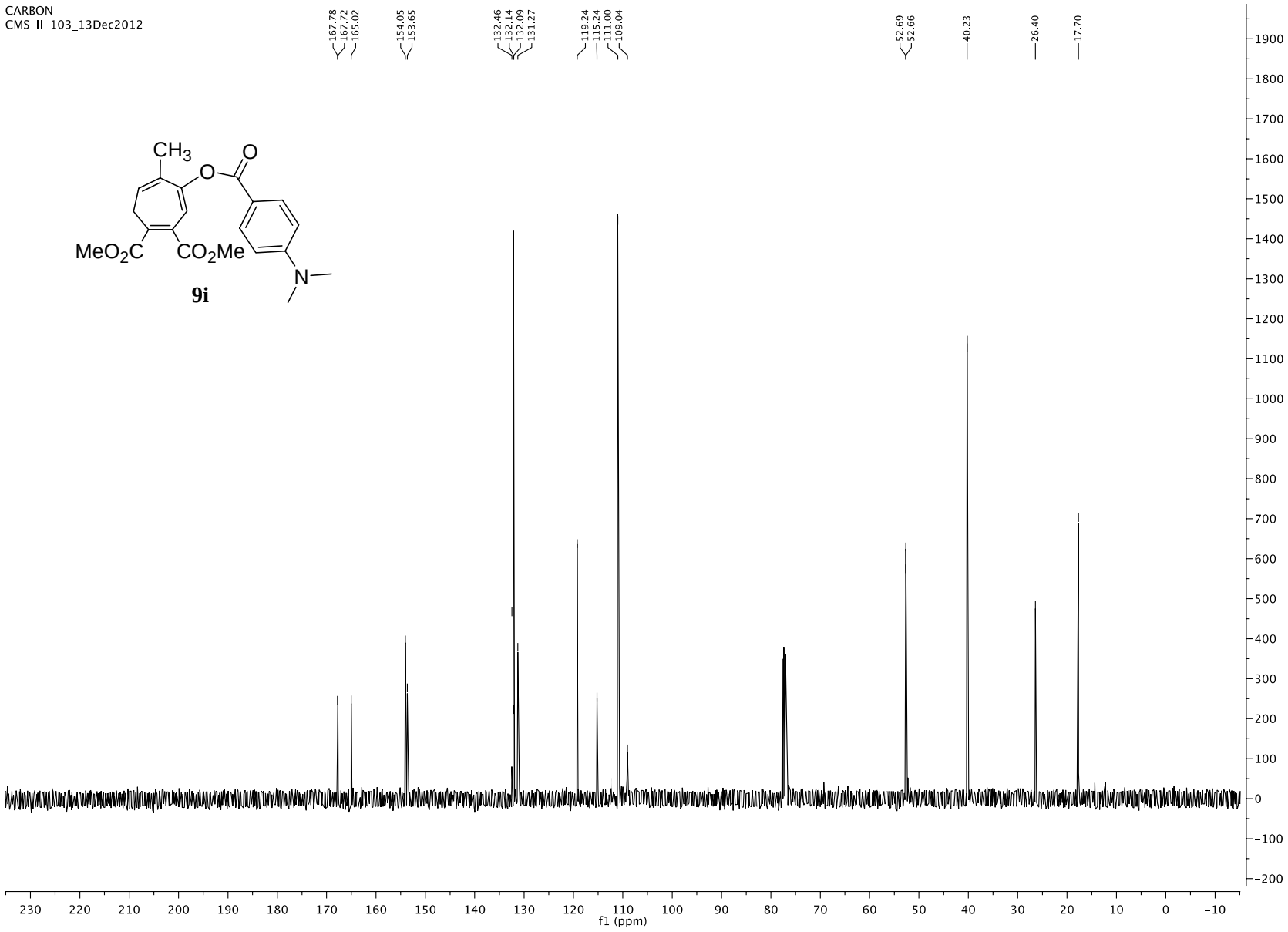

CARBON
CMS-II-82_10Oct2012
165.79
153.81
151.25
139.50
132.00
131.06
120.14
119.50
118.42
116.44
110.99
40.29
38.10
32.41
31.75
29.18
22.74
18.00
14.28
CH3
O
O
N
9g
3000
2500
2000
1500
1000
500
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

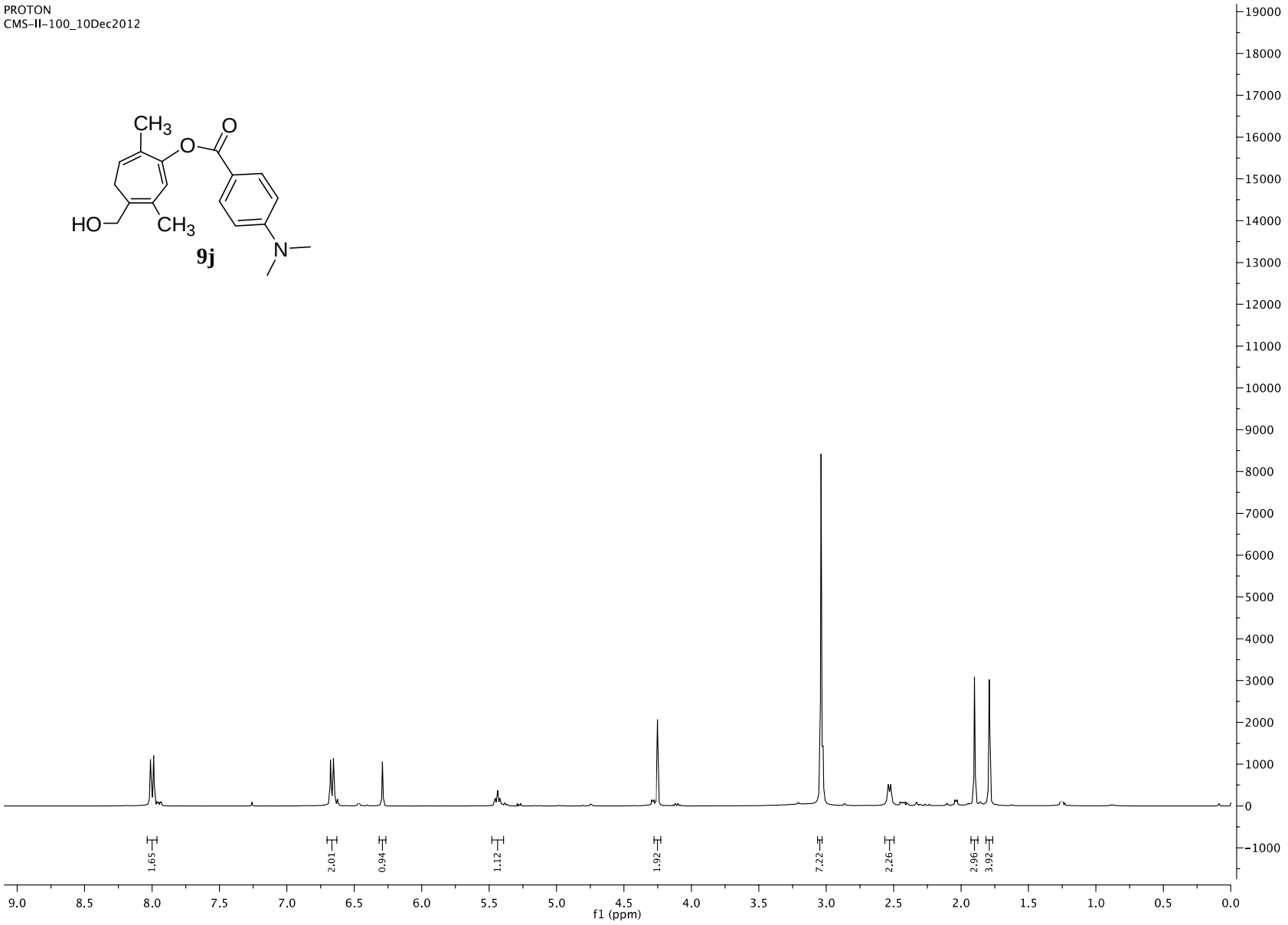


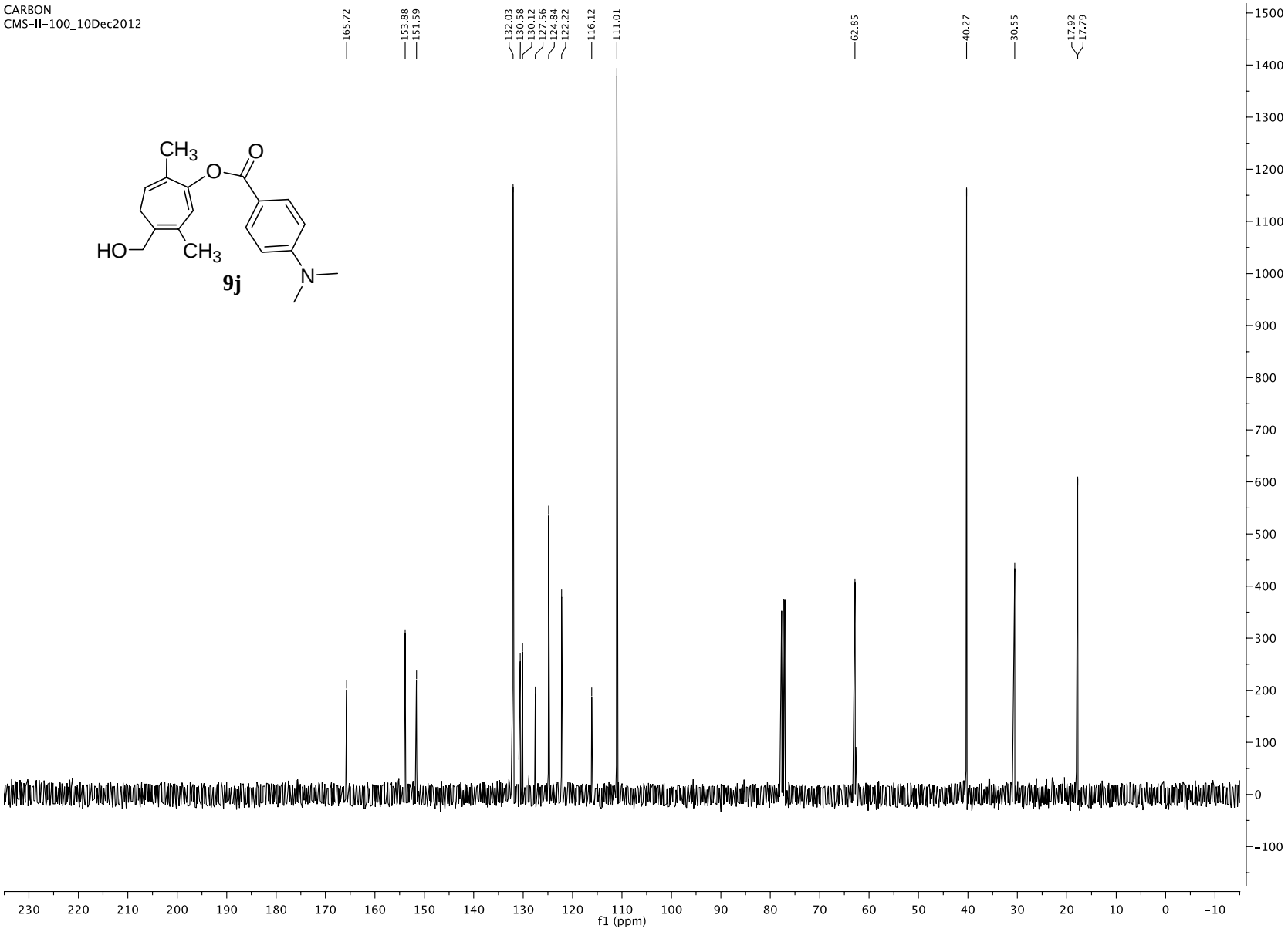
9h

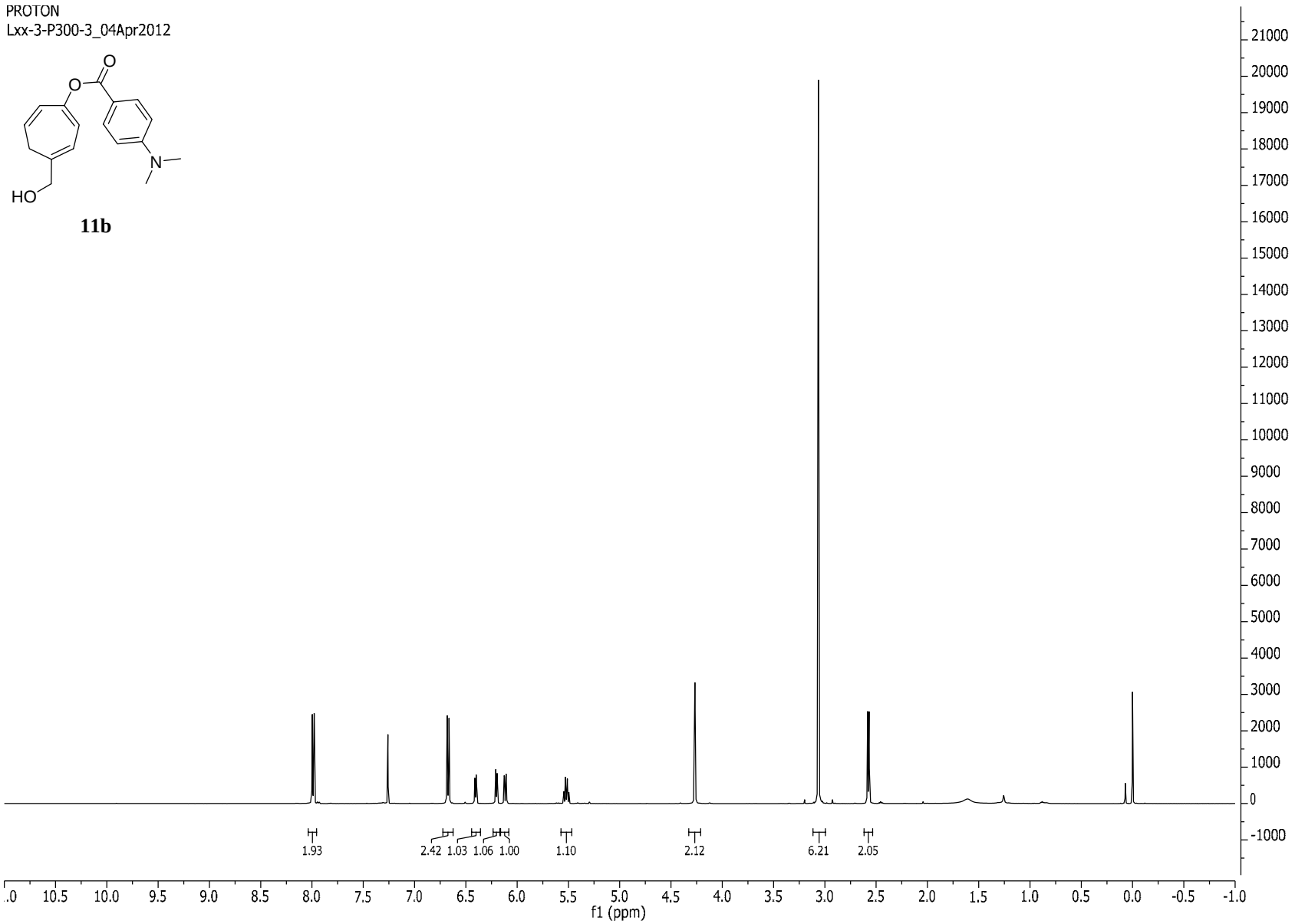



PROTON
CMS-II-103_13Dec2012
CH3
O
O
MeO2C
CO2Me
N
9i
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
2.00
2.96
1.14
6.53
5.17
2.45
3.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

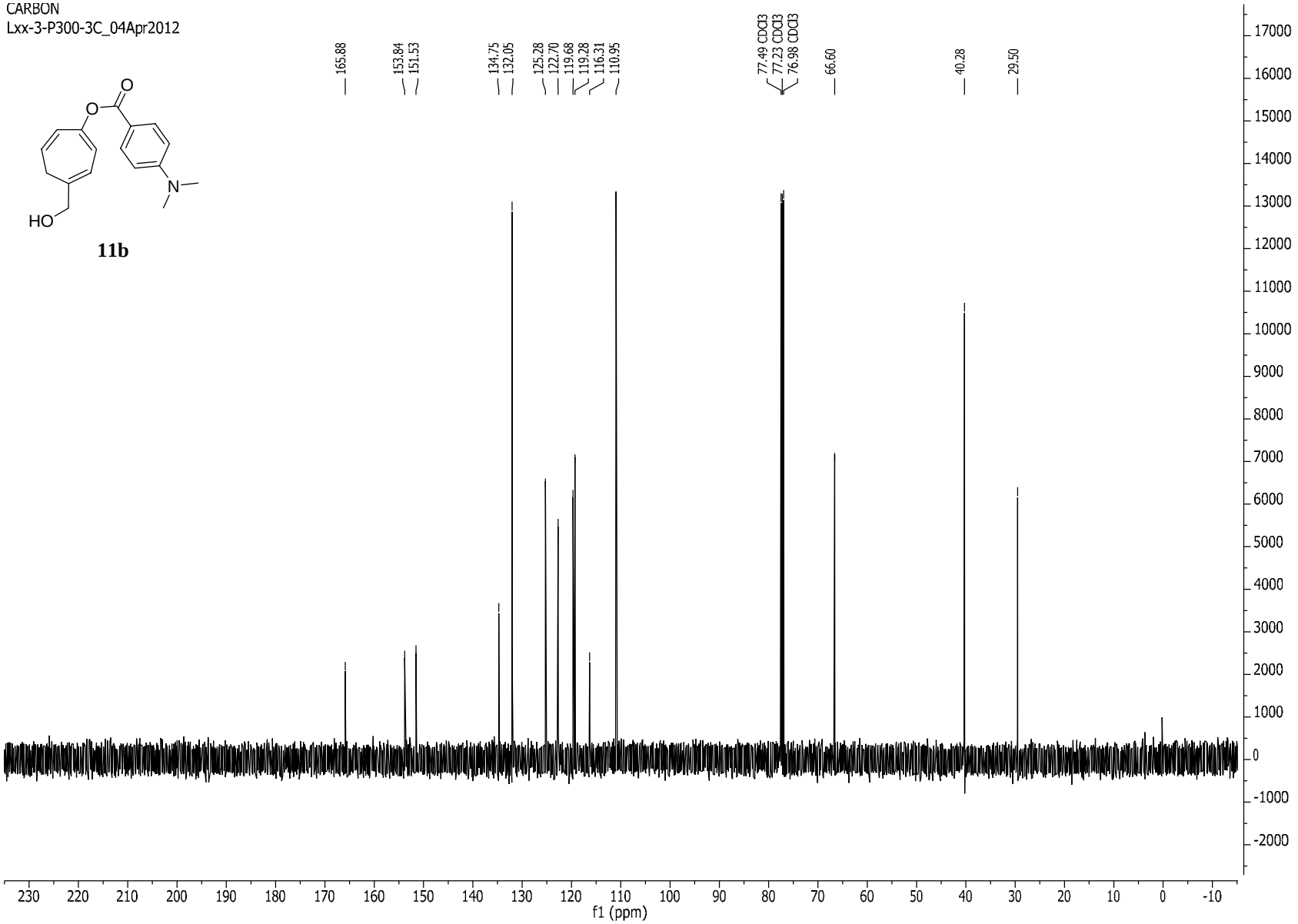

CARBON
CMS-II-103_13Dec2012
167.78
167.72
165.02
154.05
153.65
132.46
132.14
132.09
131.27
119.24
115.24
111.00
109.04
52.69
52.66
40.23
26.40
17.70
CH3
O
O
MeO2C
CO2Me
N
9i
f1 (ppm)


PROTON
CMS-II-100_10Dec2012
CH3
O
O
HO
CH3
N
9j
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1.65
2.01
0.94
1.12
1.92
7.22
2.26
2.96
3.92
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


CARBON
CMS-II-100_10Dec2012
165.72
153.88
151.59
132.03
130.58
130.12
127.56
124.84
122.22
116.12
111.01
62.85
40.27
30.55
17.92
17.79
CH3
O
O
HO
CH3
N
9j
f1 (ppm)


PROTON
Lxx-3-P300-3_04Apr2012
O
O
N
HO
1.93
2.42
1.03
1.06
1.00
1.10
2.12
6.21
2.05
f1 (ppm)

11b


CARBON
Lxx-3-P300-3C_04Apr2012
165.88
153.84
151.53
134.75
132.05
125.28
122.70
119.68
119.28
116.31
110.95
77.49 CDCl3
77.23 CDCl3
76.98 CDCl3
66.60
40.28
29.50
O
O
N
HO
f1 (ppm)

11b