An Improved Palladium-Catalyzed Conversion of Aryl and Vinyl Triflates to Bromides and Chlorides

Jun Pan, Xinyan Wang, Yong Zhang and Stephen L. Buchwald*

Department of Chemistry, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139

Supporting Information

General Reagent Information

All reactions were carried out under an argon atmosphere. 1,4-Dioxane (anhydrous) in Sureseal® bottles and KF (spray-dried) were purchased from Aldrich Chemical Co. and used as received. KBr (ACS reagent) and KCl (ACS reagent) were purchased from Aldrich and ground into a fine powder prior to use. *t*-BuBrettPhos was prepared as reported by Fors.[1] $Pd_2(dba)_3$ was purchased from STREM and used as received. Flash chromatography was performed using a Biotage SP4 instrument with prepacked silica cartridges.

General Analytical Information

All compounds were characterized by ^1H NMR, ^{13}C NMR, IR spectroscopy, as well as, in most instances, elemental analysis. Copies of the ^1H and ^{13}C spectra can be found at the end of the supporting information. NMR spectra were recorded on a Bruker AMX 400 spectrometer and were calibrated using residual solvent as an internal reference ($CDCl_3$: 7.26 ppm for ^1H NMR and 77.16 ppm for ^{13}C NMR). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, ovrlp = overlapping. IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer using KBr plates (thin film). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on a Agilent 6890 gas chromatography with an FID detector

using a J & W DB-1 column (10 m, 0.1 mm I.D.). Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA.

Preparation of Trifluoromethanesulfonates

4-Acetylphenyl trifluoromethanesulfonate, 6-quinolinyl trifluoromethanesulfonate, 9*H*-carbazol-2-yl trifluoromethanesulfonate and 2-naphthyl trifluoromethanesulfonate were purchased from Aldrich and used as received. 4-Methoxyphenyl trifluoromethanesulfonate was purchased from TCI America and used as received. Ethyl 4-[[(trifluoromethyl)sulfonyl]oxy]benzoate,[2] 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl trifluoromethanesulfonate,[3] benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate,[4] 6-bromonaphthalen-2-yl trifluoromethanesulfonate,[5] 5-(trifluoromethylsulfonyloxy)indole,[6] isoquinolin-7-yl trifluoromethanesulfonate,[7] 2-methylbenzo[*d*]thiazol-5-yl trifluoromethanesulfonate,[8] 1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate,[9] 1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethanesulfonate,[10] 1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl trifluoromethanesulfonate,[11] 1*H*-inden-2-yl trifluoromethanesulfonate,[12] (8*R*,9*S*,13*S*,14*S*)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl trifluoromethanesulfonate,[13] (8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*] phenanthrene-17,2'-[1,3]dioxolan]-3-yl trifluoromethanesulfonate,[14] (*R*)-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl trifluoromethanesulfonate,[15] (8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*] phenanthren-3-yl trifluoromethanesulfonate[16] were prepared according to literature procedures.

General Procedures for Examples Described in Table 1

To a screw-cap test tube equipped with a magnetic stir bar was added KBr (119 mg, 1.0 mmol, 2.0 equiv), KF (14.5 mg, 0.25 mmol, 0.5 equiv) and 4-methoxyphenyl trifluoromethanesulfonate (128 mg, 0.5 mmol, 1.0 equiv). The tube was sealed with a Teflon-lined septum, evacuated and backfilled with argon (this process was repeated a total of three times).

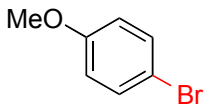
To another screw-cap test tube equipped with a magnetic stir bar was added $Pd_2(dba)_3$ (6.9 mg, 1.5 mol%) and *t*-BuBrettPhos (10.9 mg, 4.5 mol%). The tube was sealed with a Teflon-lined septum, evacuated and backfilled with argon (this process was repeated a total of three times). 1,4-Dioxane (0.5 mL) was added via syringe, and the mixture was heated at 120 °C in a preheated oil bath for 3 min. After the catalyst solution was cooled to room temperature, it was added to the reaction tube containing KBr, KF, and ArOTf via syringe, followed by addition of dioxane (1.5 mL). The resulting mixture was stirred vigorously at 130 °C in a preheated oil bath for 16 h, and then cooled to room temperature. Decane was then added as an internal standard. The mixture was filtered through a small plug of silica gel, eluted with diethyl ether and analyzed by GC.

General Procedures for Examples Described in Figure 2 and 3

To a screw-cap test tube equipped with a magnetic stir bar was added KBr or KCl (2.0 mmol, 2.0 equiv), KF (29.1 mg, 0.5 mmol, 0.5 equiv) and aryl triflate (1.0 mmol, 1.0 equiv). The tube was sealed with a Teflon-lined septum, evacuated and backfilled with argon (this process was repeated a total of three times).

To another screw-cap test tube equipped with a magnetic stir bar was added $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%). The tube was sealed with a Teflon-lined septum, evacuated and backfilled with argon (this process was repeated a total of three times). 1,4-Dioxane (1 mL) was added via syringe, and the mixture was heated at 120 °C in a preheated oil bath for 3 min. After the catalyst solution was cooled to room temperature, it was added to the reaction tube containing KBr or KCl, KF, and ArOTf via syringe, followed by addition of dioxane (3 mL). The resulting mixture was stirred vigorously at 130 °C in a preheated oil bath for 16 h and then cooled to room temperature, filtered through a pad of silica gel (eluted with EtOAc) and concentrated under reduced pressure. The crude material was purified via the Biotage SP4 (silica-packed 50g snap cartridge).

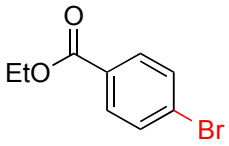
Experimental Procedures for Examples Described in Figure 2 and 3



2a

1-Bromo-4-methoxybenzene:[8]

The title compound was prepared according to the general procedure with 4-methoxyphenyl trifluoromethanesulfonate (256 mg, 1.0 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a colorless oil (146 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 9.0 Hz, 1H), 6.79 (d, *J* = 9.0 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 132.4, 115.9, 112.9, 55.6; IR (thin film): 2958, 1579, 1490, 1462, 1290, 1247, 1171, 1072, 1034, 822 cm^{-1}.

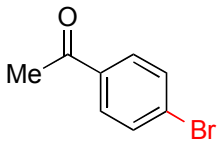


2b

Ethyl 4-bromobenzoate:[17]

The title compound was prepared according to the general procedure with ethyl 4-[[(trifluoromethyl)sulfonyl]oxy]benzoate (298 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a colorless oil (183 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.6 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 131.8, 131.2, 129.5, 128.0, 61.4, 14.4; IR

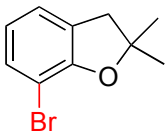
(thin film): 2982, 1721, 1591, 1398, 1272, 1173, 1103, 1069, 1013, 757 cm^{-1}; Anal. Calcd. for $C_9H_9BrO_2$: C, 47.19; H, 3.96. Found: C, 47.45; H, 4.05.



2c

1-(4-Bromophenyl)ethanone:[18]

The title compound was prepared according to the general procedure with 4-acetylphenyl trifluoromethanesulfonate (268 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (157 mg, 79%), m.p. = 50.6 – 51.0 ºC (lit. 50 – 51 °C).[18] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 8.6, 2H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 135.9, 132.0, 130.0, 128.4, 26.7; IR (thin film): 2924, 1689, 1588, 1396, 1266, 1078, 1103, 1010, 1013, 821 cm^{-1}; Anal. Calcd. for C_8H_7BrO: C, 48.27; H, 3.54. Found: C, 48.52; H, 3.42.

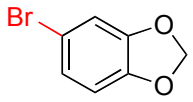


2d

7-Bromo-2,2-dimethyl-2,3-dihydrobenzofuran:

The title compound was prepared according to the general procedure with 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl trifluoromethanesulfonate (296 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes)

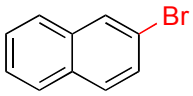
to provide the title compound as a pale yellow oil (191 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 1H), 7.06 (m, 1H), 6.69 (t, J = 7.5 Hz, 1H), 3.09 (s, 2H), 1.52 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 131.2, 128.6, 124.2, 121.3, 102.8, 87.8, 43.8, 28.3; IR (thin film): 2975, 1604, 1452, 1371, 1293, 1264, 1123, 1101, 1053, 877 cm^{-1}; Anal. Calcd. for $C_{10}H_{11}BrO$: C, 52.89; H, 4.88. Found: C, 53.17; H, 4.88.



2e

5-Bromobenzo[*d*][1,3]dioxole:[19]

The title compound was prepared according to the general procedure with 2 benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (270 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a colorless oil (163 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.93 (d, J = 2.0 Hz, 1H), 6.68 (dd, J = 6.3 Hz, 1.1 Hz, 1H), 5.97 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 147.1, 124.4, 113.2, 112.4, 109.7, 101.7; IR (thin film): 2896, 1501, 1473, 1417, 1234, 1158, 1105, 1039, 936, 876 cm^{-1}; Anal. Calcd. for $C_7H_5BrO_2$: C, 41.82; H, 2.51. Found: C, 41.87; H, 2.45.

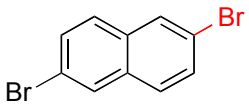


2f

2-Bromonaphthalene:[20]

The title compound was prepared according to the general procedure with 2-naphthyl trifluoromethanesulfonate (276 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4

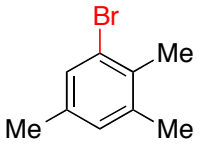
(silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (168 mg, 81%), m.p. = 55.0 – 55.4 °C (lit. 55 – 57 °C).[20] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.8 Hz, 1H), 7.83-7.81 (m, 1H), 7.77-7.71 (m, 2H), 7.57-7.49 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 132.0, 130.1, 129.7, 129.4, 128.0, 127.1, 127.0, 126.4, 119.9; IR (thin film): 3057, 1625, 1587, 1501, 1345, 1130, 1062, 908, 813, 734 cm^{-1}.



2g

2,6-Dibromonaphthalene:[21]

The title compound was prepared according to the general procedure with 6-bromonaphthalen-2-yl trifluoromethanesulfonate (355 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (235 mg, 82%), m.p. = 160.3 – 161.3 °C (lit. 158 – 159 °C).[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 2.0 Hz, 2H), 7.64-7.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.0, 130.5, 130.1, 128.8, 120.4; IR (thin film): 1569, 1482, 1133, 1064, 964, 885, 853, 816, 627 cm^{-1}; Anal. Calcd. for $C_{10}H_6Br_2$: C, 42.00; H, 2.11. Found: C, 42.27; H, 1.99.

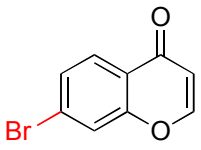


2h

1-Bromo-2,3,5-trimethylbenzene:[22]

The title compound was prepared according to the general procedure with 2,3,5-trimethylphenyl trifluoromethanesulfonate (268 mg, 1 mmol), KBr (238 mg, 2.0 mmol),

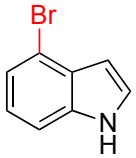
KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a colorless oil (159 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 1H), 6.91 (s, 1H), 2.33 (s, 3H), 2.30 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 136.7, 133.0, 130.7, 130.0, 125.4, 21.4, 20.6, 19.0; IR (thin film): 2920, 1610, 1556, 1476, 1444, 1383, 1262, 1006, 848, 803 cm^{-1}.



2i

7-Bromo-4*H*-benzopyran-4-one:[23]

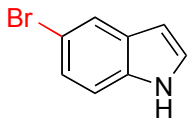
The title compound was prepared according to the general procedure with 4-oxo-4*H*-1-benzopyran-7-yl trifluoromethanesulfonate (294 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a white solid (185 mg, 82%), m.p. = 153.0 – 155.2 °C (lit. 147 – 149 °C).[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 6.0 Hz, 1H), 7.64 (d, *J* = 1.6 Hz, 1H), 7.51 (dd, *J* = 6.8, 1.7 Hz, 1H), 6.33 (d, *J* = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 156.7, 155.4, 129.1, 128.2, 127.4, 123.9, 121.5, 113.5; IR (thin film): 1643, 1601, 1428, 1338, 1299, 1179, 1134, 1021, 862, 810 cm^{-1}; Anal. Calcd. for $C_9H_5BrO_2$: C, 48.03; H, 2.24. Found: C, 48.29; H, 2.18.



2j

4-Bromo-1*H*-indole:[24]

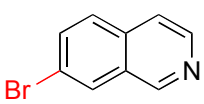
The title compound was prepared according to the general procedure with 4-(trifluoromethylsulfonyloxy)indole (265 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a pale yellow oil (145 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (br, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.26-7.23 (m, 1H), 7.07 (t, J = 7.8 Hz, 1H), 6.64-6.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 128.8, 124.9, 123.0, 122.9, 114.8, 110.4, 103.1; IR (thin film): 3425, 1611, 1564, 1478, 1429, 1413, 1334, 1179, 891, 747 cm^{-1}.



2k

5-Bromo-1*H*-indole:[25]

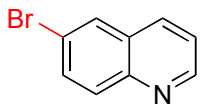
The title compound was prepared according to the general procedure with 5-(trifluoromethylsulfonyloxy)indole (265 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a white solid (147 mg, 75%), m.p. = 88.6 – 89.6 °C (lit. 90 – 92 °C).[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (br, 1H), 7.78 (d, J = 0.7 Hz, 1H), 7.28-7.25 (m, 2H), 7.22-7.20 (m, 1H), 6.61-6.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 129.8, 125.5, 125.0, 123.4, 113.2, 112.6, 102.5; IR (thin film): 3413, 1412, 1314, 1263, 1243, 1091, 1006, 884, 799, 763 cm^{-1}; Anal. Calcd. for C_8H_6BrN: C, 49.01; H, 3.08. Found: C, 49.22; H, 2.99.



2l

7-Bromoisoquinoline:[26]

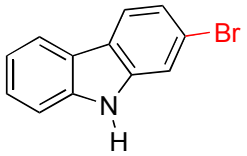
The title compound was prepared according to the general procedure with isoquinolin-7-yl trifluoromethanesulfonate (277 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a white solid (162 mg, 78%), m.p. = 71.3 – 72.0 °C (lit. 67 – 69 °C).[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.56 (d, *J* = 5.7 Hz, 1H), 8.14-8.13 (m, 1H), 7.78-7.70 (m, 2H), 7.63 (d, *J* = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 143.7, 134.3, 134.0, 129.9, 129.7, 128.4, 121.0, 120.4; IR (thin film): 3061, 1581, 1492, 1267, 1243, 1060, 946, 879, 844, 837 cm^{-1}; Anal. Calcd. for C_9H_6BrN: C, 51.96; H, 2.91. Found: C, 52.18; H, 2.86.



2m

6-Bromoquinoline:[27]

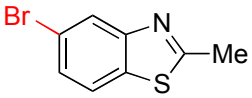
The title compound was prepared according to the general procedure with 6-quinolinyl trifluoromethanesulfonate (277 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a pale yellow oil (158 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (dd, *J* = 2.6, 1.6 Hz, 1H), 8.05 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.98-7.96 (m, 2H), 7.76 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.39 (dd, *J* = 8.1, 4.2 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 146.9, 135.1, 133.0, 131.3, 129.9, 129.4, 122.0, 120.6; IR (thin film): 3036, 1589, 1566, 1489, 1317, 1182, 1120, 1060, 847, 829 cm^{-1}; Anal. Calcd. for C_9H_6BrN: C, 51.96; H, 2.91. Found: C, 52.08; H, 2.89.



2n

2-Bromo-9*H*-carbazole: [28]

The title compound was prepared according to the general procedure with 9*H*-carbazol-2-yl trifluoromethanesulfonate (315 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (204 mg, 83%), m.p. = 251.1 – 253.1 °C (lit. 250 – 251 °C).[28] ^{1}H NMR (400 MHz, DMSO-d^6) δ 11.4 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 1.5 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.42 (t, J = 7.1 Hz, 1H), 7.29 (dd, J = 6.6, 1.7 Hz, 1H), 7.18 (t, J = 7.7 Hz, 1H), ^{13}C NMR (100 MHz, DMSO-d^6) δ 140.6, 139.9, 126.1, 121.9, 121.8, 121.6, 121.3, 120.4, 119.1, 118.1, 113.5, 111.2; IR (thin film): 3392, 1600, 1448, 1436, 1327, 1054, 854, 809, 755 cm^{-1}; Anal. Calcd. for $C_{12}H_8BrN$: C, 58.56; H, 3.28. Found: C, 58.81; H, 3.23.

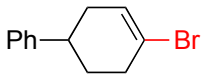


2o

5-Bromo-2-methylbenzo[*d*]thiazole:[29]

The title compound was prepared according to the general procedure with 2-methylbenzo[*d*]thiazol-5-yl trifluoromethanesulfonate (297 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (189 mg, 83%), m.p. = 77.8 – 78.4 °C (lit. 84 – 85 °C).[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 1.7 Hz, 1H), 7.67 (d, J = 8.5

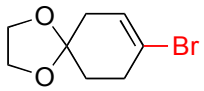
Hz, 1H), 7.45 (dd, J = 6.7, 1.8 Hz, 1H), 2.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 154.7, 134.6, 127.9, 125.5, 122.5, 119.6, 20.3; IR (thin film): 3061, 1519, 1413, 1300, 1171, 1067, 885, 800, 645 cm^{-1}; Anal. Calcd. for C_8H_6BrNS: C, 42.12; H, 2.65. Found: C, 42.28; H, 2.55.



2p

4-Bromo-1,2,3,6-tetrahydro-1,1'-biphenyl:[8]

The title compound was prepared according to the general procedure with 1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl trifluoromethanesulfonate (306 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (175 mg, 74%), m.p. = 58.0 – 58.6 °C (lit. 44 – 45.5 °C).[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.25-7.21 (m, 3H), 6.13 (m, 1H), 2.93-2.83 (m, 1H), 2.73-2.53 (m, 2H), 2.42-2.22 (m, 2H), 2.03-1.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 128.7, 128.6, 126.9, 126.5, 122.1, 38.9, 35.7, 35.4, 31.6; IR (thin film): 2921, 1651, 1602, 1494, 1452, 1433, 1042, 1030, 963, 756 cm^{-1}; Anal. Calcd. for $C_{12}H_{13}Br$: C, 60.78; H, 5.53. Found: C, 61.02; H, 5.52.

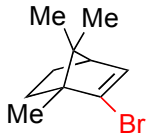


2q

8-Bromo-1,4-dioxaspiro[4.5]dec-7-ene: [30]

The title compound was prepared according to the general procedure with 1,4-dioxaspiro[4.5]dec-7-en-8-yl trifluoromethanesulfonate (288 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos

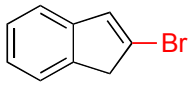
(21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a pale yellow oil (158 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91-5.89 (m, 1H), 3.98 (s, 4H), 2.65-2.61 (m, 2H), 2.30-2.29 (m, 2H), 1.85 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.2, 121.3, 106.5, 64.7, 37.7, 34.3, 32.8. IR (thin film): 2930, 1652, 1430, 1368, 1333, 1255, 1118, 1061, 1025, 929 cm^{-1}.



2r

2-Bromo-1,7,7-trimethylbicyclo[2.2.1]hept-2-ene:[31]

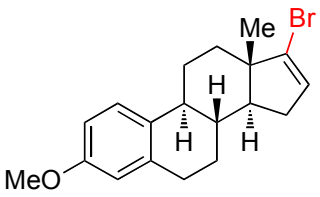
The title compound was prepared according to the general procedure with 1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl trifluoromethanesulfonate (284 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; hexanes) to provide the title compound as a colorless oil (151 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 (d, *J* = 3.5 Hz, 1H), 2.38 (t, *J* = 3.6 Hz, 1H), 1.89-1.82 (m, 1H), 1.57-1.51 (m, 1H), 1.12-1.08 (m, 2H), 1.01 (s, 3H), 0.86 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 130.9, 57.4, 56.6, 53.1, 31.0, 25.6, 20.3, 19.5, 12.7. IR (thin film): 2956, 1582, 1462, 1387, 1377, 1366, 1289, 1106, 1029, 973 cm^{-1}; Anal. Calcd. for $C_{10}H_{15}Br$: C, 55.83; H, 7.03. Found: C, 55.60; H, 7.00.



2s

2-Bromo-1*H*-indene:[32]

The title compound was prepared according to the general procedure with 1*H*-inden-2-yl trifluoromethanesulfonate (264 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; hexanes) to provide the title compound as a white soild (142 mg, 73%), m.p. = 35.2 – 36.3 °C (lit. 37 – 38 °C).[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.33 (m, 1H), 7.30-7.27 (m, 1H), 7.25-7.20 (m, 1H), 7.18-7.13 (m, 1H), 6.91 (s, 1H), 3.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 142.8, 133.1, 126.9, 125.0, 124.9, 123.3, 120.3, 45.6; IR (thin film): 2901, 1556, 1458, 1389, 1268, 1013, 912, 837, 741, 709 cm^{-1}; Anal. Calcd. for C_9H_7Br: C, 55.42; H, 3.62. Found: C, 55.69; H, 3.68.

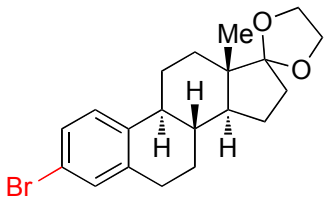


2t

(8R,9S,13S,14S)-17-bromo-3-methoxy-13-methyl-7,8,9,11,12,13,14,15-octahydro-6H-cyclopenta[*a*]phenanthrene: [8]

The title compound was prepared according to the general procedure with (8*R*,9*S*,13*S*,14*S*)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl trifluoromethanesulfonate (416 mg, 1.0 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white soild (323 mg, 93%), m.p. = 130.8 – 133.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 1H), 6.73 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.65 (d, *J* = 2.6 Hz, 1H), 5.88 (dd, *J* = 3.2, 1.6 Hz, 1H), 3.79 (s, 3H), 2.91-2.89 (m, 2H), 2.43-2.39 (m, 1H), 2.33-2.20 (m, 2H), 2.03-1.85 (m, 3H), 1.78-1.70 (m, 1H), 1.67-1.40 (m, 4H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 137.9, 135.9, 132.6, 129.1, 126.2, 114.0, 111.6, 55.3, 55.0, 49.1, 44.3, 37.7, 34.7, 31.7, 29.8,

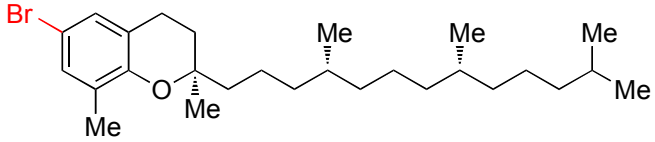
27.4, 26.4, 15.4. IR (thin film): 2930, 1609, 1499, 1453, 1281, 1256, 1154, 1049, 995, 810 cm^{-1}. Anal. Calcd. for $C_{19}H_{23}BrO$: C, 65.71; H, 6.68. Found: C, 65.90; H, 6.75.



2u

(8*R*,9*S*,13*S*,14*S*)-3-bromo-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane]:[8]

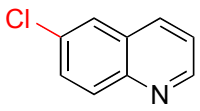
The title compound was prepared according to the general procedure with (8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolan]-3-yl trifluoromethanesulfonate (446 mg, 1.0 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white soild (283 mg, 75%), m.p. = 100.9 – 103.7 °C (lit. 98.5 – 101.5 °C).[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.14 (m, 3H), 3.98-3.90 (m, 4H), 2.85-2.80 (m, 2H), 2.36-2.18 (m, 2H), 2.08-1.96 (m, 1H), 1.90-1.72 (m, 4H), 1.62-1.24 (m, 6H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 139.3, 131.7, 128.6, 127.3, 119.43, 119.41, 65.4, 64.7, 49.5, 46.2, 43.9, 38.7, 34.3, 30.7, 29.4, 26.8, 26.0, 22.5, 14.4. IR (thin film): 2938, 1589, 1481, 1380, 1308, 1180, 1162, 1106, 1044, 962 cm^{-1}; Anal. Calcd. for $C_{20}H_{25}BrO_2$: C, 63.66; H, 6.68. Found: C, 63.67; H, 6.69.



2v

(*R*)-6-Bromo-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman:[8]

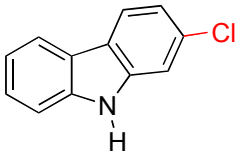
The title compound was prepared according to the general procedure with (*R*)-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl trifluoromethanesulfonate (535 mg, 1 mmol), KBr (238 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; hexanes) to provide the title compound as a colorless oil (331 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 1H), 7.02 (s, 1H), 2.72 (t, *J* = 6.4 Hz, 2H), 2.13 (s, 3H), 1.83-1.72 (m, 2H), 1.60-1.07 (m, 24H), 0.89-0.84 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 131.0, 129.4, 128.8, 122.7, 110.9, 76.5, 40.1, 39.5, 37.6, 37.5, 37.4, 33.0, 32.8, 31.1, 28.1, 25.0, 24.6, 24.3, 22.9, 22.8, 22.3, 21.1, 19.9, 19.8, 16.0; IR (thin film): 2927, 2868, 1468, 1379, 1300, 1219, 1153, 936, 858, 728 cm^{-1}. Anal. Calcd. for $C_{27}H_{45}BrO$: C, 69.66; H, 9.74. Found: C, 69.93; H, 9.83.



3a

6-Chloroquinoline:[33]

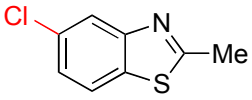
The title compound was prepared according to the general procedure with quinolin-6-yl trifluoromethanesulfonate (277 mg, 1 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-20% EtOAc/hexanes) to provide the title compound as a pale yellow solid (123 mg, 75%), m.p. = 38.9 – 39.6 °C (lit. 40 – 41 °C).[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 2.6, 1.6 Hz, 1H), 8.07-8.02 (m, 2H), 7.79 (d, *J* = 2.3 Hz, 1H), 7.64 (dd, *J* = 6.5, 2.4 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 146.8, 135.2, 132.4, 131.2, 130.5, 128.9, 126.5, 122.0; IR (thin film): 3038, 1592, 1566, 1491, 1320, 1184, 1120, 1075, 864, 831 cm^{-1}; Anal. Calcd. for C_9H_6ClN: C, 66.07; H, 3.70. Found: C, 65.91; H, 3.65.



3b

2-Chloro-9*H*-carbazole:[34]

The title compound was prepared according to the general procedure with 9*H*-carbazol-2-yl trifluoromethanesulfonate (315 mg, 1 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (157 mg, 78%), m.p. = 243.3 – 244.4 °C (lit. 242 – 244 °C).[34] ^{1}H NMR (400 MHz, DMSO-d^6) δ 11.4 (s, 1H), 8.12 (d, J = 8.2 Hz, 2H), 7.54-7.49 (m, 2H), 7.43-7.38 (m, 1H), 7.21-7.15 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d^6) δ 140.3, 140.1, 129.9, 126.0, 121.8, 121.6, 121.3, 120.3, 119.1, 118.7, 111.2, 110.6; IR (thin film): 3394, 1601, 1438, 1384, 1329, 1240, 1069, 854, 812, 753 cm^{-1}; Anal. Calcd. for $C_{12}H_8ClN$: C, 71.47; H, 4.00. Found: C, 71.23; H, 3.93.

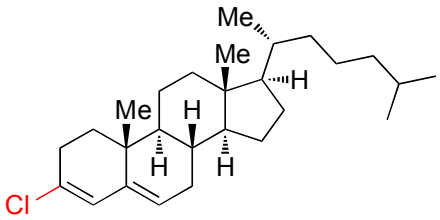


3c

5-Chloro-2-methylbenzo[*d*]thiazole:[35]

The title compound was prepared according to the general procedure with 2-methylbenzo[*d*]thiazol-5-yl trifluoromethanesulfonate (297 mg, 1 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (154 mg, 84%), m.p. = 68.1 – 69.1 °C (lit. 68 – 69 °C).[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 2.0 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.32 (dd, J = 6.5, 2.0 Hz, 1H), 2.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

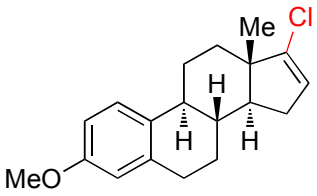
169.1, 154.4, 134.0, 132.1, 125.3, 122.4, 122.2, 20.4; IR (thin film): 3063, 1546, 1521, 1438, 1409, 1302, 1173, 1146, 886, 804 cm^{-1}; Anal. Calcd. for C_8H_6ClNS: C, 52.32; H, 3.29. Found: C, 52.53; H, 3.28.



3d

(8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-chloro-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*]phenanthrene:[8]

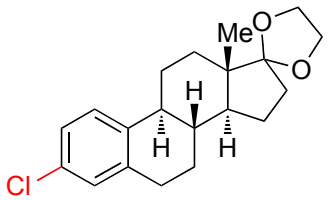
The title compound was prepared according to the general procedure with (8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1*H*-cyclopenta[*a*] phenanthren-3-yl trifluoromethanesulfonate (517 mg, 1 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; hexanes) to provide the title compound as a pale yellow solid (339 mg, 84%), m.p. = 59.6 – 62.4 °C (lit. 64 – 66 °C).[8] ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.05 (d, *J* = 2.2 Hz, 1H), 5.42-5.39 (m, 1H), 2.54-2.45 (m, 1H), 2.38-2.28 (m, 1H), 2.21-2.11 (m, 1H), 2.06-1.99 (m, 1H), 1.90-1.82 (m, 2H), 1.70-0.98 (m, 20H), 0.96 (s, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.7, 130.4, 127.2, 124.5, 56.9, 56.3, 48.1, 42.6, 39.8, 39.7, 36.3, 35.9, 35.0, 34.6, 31.9, 31.8, 30.9, 28.4, 28.2, 24.3, 24.0, 23.0, 22.7, 21.3, 19.0, 18.9, 12.1; IR (thin film): 2946, 2867, 1620, 1467, 1376, 1033, 890 cm^{-1}.



3e

(8*R*,9*S*,13*S*,14*S*)-17-chloro-3-methoxy-13-methyl-7,8,9,11,12,13,14,15-octahydro-6H-cyclopenta[*a*]phenanthrene:[36]

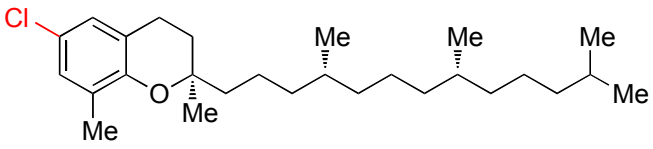
The title compound was prepared according to the general procedure with (8*R*,9*S*,13*S*,14*S*)-3-methoxy-13-methyl-7,8,9,11,12,13,14,15-octahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl trifluoromethanesulfonate (416 mg, 1.0 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (288 mg, 95%), m.p. = 108.7 – 111.0 °C (lit. 114 – 115 °C).[36] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 1H), 6.73 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.66 (d, *J* = 2.6 Hz, 1H), 5.67 (dd, *J* = 2.8, 1.5 Hz, 1H), 3.79 (s, 3H), 2.93-2.89 (m, 2H), 2.45-2.39 (m, 1H), 2.33-2.22 (m, 2H), 2.10-2.01 (m, 1H), 1.98-1.90 (m, 2H), 1.79-1.70 (m, 1H), 1.68-1.41 (m, 4H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 145.0, 138.0, 132.5, 126.2, 124.7, 114.0, 111.6, 55.3, 55.2, 48.0, 44.2, 44.4, 37.5, 33.9, 30.5, 29.8, 27.4, 26.4, 15.3. IR (thin film): 2931, 1607, 1499, 1451, 1372, 1236, 1047, 904, 859, 813 cm^{-1}. Anal. Calcd. for $C_{19}H_{23}ClO$: C, 75.35; H, 7.66. Found: C, 75.61; H, 7.58.



3f

(8*R*,9*S*,13*S*,14*S*)-3-chloro-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*]phenanthrene-17,2'-[1,3]dioxolane]:[8]

The title compound was prepared according to the general procedure with (8*R*,9*S*,13*S*,14*S*)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydrospiro[cyclopenta[*a*] phenanthrene-17,2'-[1,3]dioxolan]-3-yl trifluoromethanesulfonate (446 mg, 1.0 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; 0-10% EtOAc/hexanes) to provide the title compound as a white solid (256mg, 77%), m.p. = 104.2 – 106.9 °C (lit. 104 – 106 °C).[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.3 Hz, 1H), 7.12-7.05 (m, 2H), 4.01-3.88 (m, 4H), 2.90-2.82 (m, 2H), 2.36-2.22 (m, 2H), 2.10-2.00 (m, 1H), 1.95-1.74 (m, 4H), 1.71-1.27 (m, 6H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.9, 131.2, 128.8, 126.9, 125.7, 119.5, 65.4, 64.7, 49.5, 46.2, 43.9, 38.8, 34.3, 30.8, 29.5, 26.8, 26.1, 22.5, 14.4. IR (thin film): 2938, 2873, 1483, 1455, 1308, 1180, 1163, 1108, 1045, 882 cm^{-1}; Anal. Calcd. for $C_{20}H_{25}ClO_2$: C, 72.17; H, 7.57. Found: C, 72.42; H, 7.52.



3g

(*R*)-6-chloro-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman:[8]

The title compound was prepared according to the general procedure with (*R*)-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl trifluoromethanesulfonate (535 mg, 1 mmol), KCl (149 mg, 2.0 mmol), KF (29.1 mg, 0.5 mmol), $Pd_2(dba)_3$ (13.7 mg, 1.5 mol%) and *t*-BuBrettPhos (21.8 mg, 4.5 mol%) in 1,4-dioxane (4.0 mL) at 130 °C for 16h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap cartridge; hexanes) to provide the title compound a colorless oil (295 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, *J* = 2.2 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 2.74-2.71 (m, 2H), 2.13 (s, 3H), 1.88-1.73 (m, 2H), 1.62-1.09 (m, 24H), 0.95-0.88 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 128.2, 128.1, 126.4, 123.4, 122.1, 76.4, 40.1, 39.5, 37.6, 37.5, 37.4, 32.9, 32.8, 31.1, 28.1, 25.0, 24.6, 24.3, 22.9, 22.8, 22.4, 21.1, 19.9, 19.8, 16.1;

IR (thin film): 2927, 2868, 1469, 1378, 1301, 1220, 1153, 1104, 938, 864 cm^{-1}. Anal. Calcd. for $C_{27}H_{45}ClO$: C, 77.01; H, 10.77. Found: C, 77.26; H, 10.96.

References:

(1) Fors, B. P.; Dooleweerdt, K.; Zeng, Q. L.; Buchwald, S. L. *Tetrahedron* **2009**, *65*, 6576.

(2) Park, N. S.; Jung, Y. S.; Park, C. H.; Seong, C. M.; Lim, H. J. *Bull. Korean Chem. Soc.* **2001**, *22*, 139.

(3) Plobeck, N.; Delorme, D.; Wei, Z.-Y.; Yang, H.; Zhou, F.; Schwarz, P.; Gawell, L.; Gagnon, H. l. n.; Pelcman, B.; Schmidt, R.; Yue, S. Y.; Walpole, C.; Brown, W.; Zhou, E.; Labarre, M.; Payza, K.; St-Onge, S.; Kamassah, A.; Morin, P.-E.; Projean, D.; Ducharme, J.; Roberts, E. *J. Med. Chem.* **2000**, *43*, 3878.

(4) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.

(5) Tam, V. K.; Liu, Q.; Tor, Y. *Chem. Commun.* **2006**, 2684.

(6) Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 1137.

(7) Kuduk, S. D.; Di Marco, C. N.; Bodmer-Narkevitch, V.; Cook, S. P.; Cato, M. J.; Jovanovska, A.; Urban, M. O.; Leitl, M.; Sain, N.; Liang, A.; Spencer, R. H.; Kane, S. A.; Hartman, G. D.; Bilodeau, M. T. *ACS Chem. Neurosci.* **2009**, *1*, 19.

(8) Shen, X.; Hyde, A. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 14076.

(9) Mee, S. P. H.; Lee, V.; Baldwin, J. E. *Chem. Eur. J.* **2005**, *11*, 3294.

(10) Carreno, M. C.; Garcia-Cerrada, S.; Urbano, A. *Chem. Eur. J.* **2003**, *9*, 4118.

(11) Tessier, P. E.; Nguyen, N.; Clay, M. D.; Fallis, A. G. *Org. Lett.* **2005**, *7*, 767.

(12) Okitsu, T.; Iwatsuka, K.; Wada, A. *Chem. Commun.* **2008**, 6330.

(13) Holt, D. A.; Levy, M. A.; Oh, H. J.; Erb, J. M.; Heaslip, J. I.; Brandt, M.; Lan-Hargest, H. Y.; Metcalf, B. W. *J. Med. Chem.* **1990**, *33*, 943.

(14) Sengupta, S.; Leite, M.; Raslan, D. S.; Quesnelle, C.; Snieckus, V. *J. Org. Chem.* **1992**, *57*, 4066.

(15) Furuya, T.; Strom, A. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 1662.

(16) Cacchi, S.; Morera, E.; Ortar, G. *Org. Synth.* **1990**, *68*, 138.

(17) Hu, Y.; Liu, J.; LuÃà, Z.; Luo, X.; Zhang, H.; Lan, Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 3153.

(18) Qian, W. X.; Jin, E. L.; Bo, W. L.; Zhang, Y. M. *Tetrahedron* **2006**, *62*, 556.

(19) Wang, J. B.; Mo, F. Y.; Yan, J. M.; Qiu, D.; Li, F.; Zhang, Y. *Angew. Chem. Int. Ed.* **2010**, *49*, 2028.

(20) Parham, W. E.; Reiff, H. E.; Swartzentruber, P. *J. Am. Chem. Soc.* **1956**, *78*, 1437.

(21) Nelsen, S. F.; Konradsson, A. E.; Weaver, M. N.; Guzei, I. A.; Goebel, M.; Wortmann, R.; Lockard, J. V.; Zink, J. I. *J. Phys. Chem. A* **2005**, *109*, 10854.

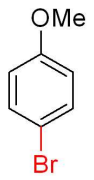
(22) Carpenter, M. S.; Easter, W. M. *J. Org. Chem.* **1954**, *19*, 77.

(23) Patonay, T.; Vasas, A.; Kiss-Szikszai, A.; Silva, A. M. S.; Cavaleiro, J. A. S. *Aust. J. Chem.* **2010**, *63*, 1582.

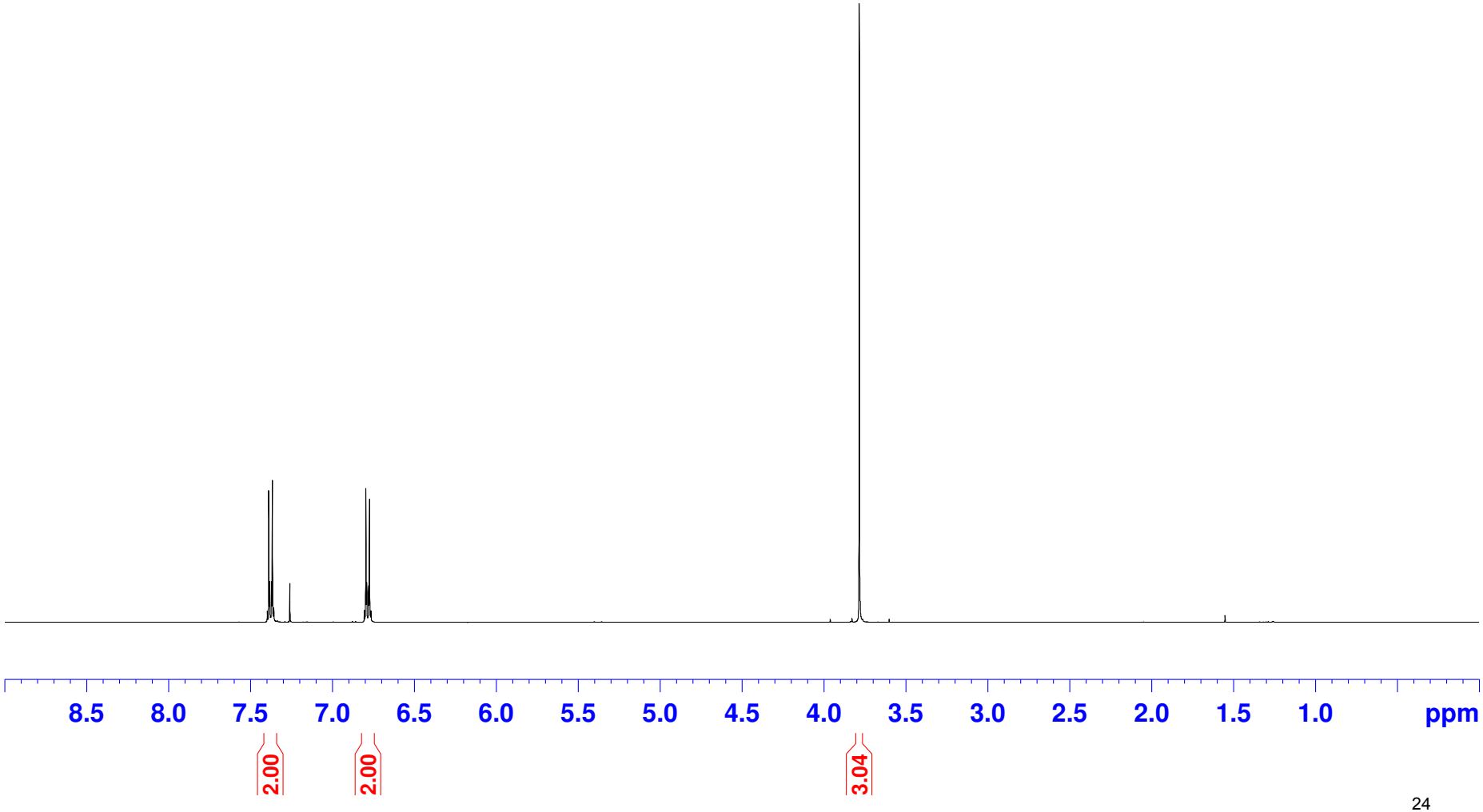
(24) Guilarte, V.; Castroviejo, M. P.; Garcia-Garcia, P.; Fernandez-Rodriguez, M. A.; Sanz, R. *J. Org. Chem.* **2011**, *76*, 3416.

(25) Xu, H.; Fan, L. L. *Eur. J. Med. Chem.* **2011**, *46*, 364.
(26) Miller, R. B.; Frincke, J. M. *J. Org. Chem.* **1980**, *45*, 5312.
(27) Woods, K. W.; Fischer, J. P.; Claiborne, A.; Li, T.; Thomas, S. A.; Zhu, G. D.; Diebold, R. B.; Liu, X. S.; Shi, Y.; Klinghofer, V.; Han, E. K.; Guan, R.; Magnone, S. R.; Johnson, E. F.; Bouska, J. J.; Olson, A. M.; de Jong, R.; Oltersdorf, T.; Luo, Y.; Rosenberg, S. H.; Giranda, V. L.; Li, Q. *Bioorg. Med. Chem.* **2006**, *14*, 6832.
(28) Barclay, B. M.; Campbell, N. *J. Chem. Soc.* **1945**, 530.
(29) Mylari, B. L.; Larson, E. R.; Beyer, T. A.; Zembrowski, W. J.; Aldinger, C. E.; Dee, M. F.; Siegel, T. W.; Singleton, D. H. *J. Med. Chem.* **1991**, *34*, 108.
(30) Shirakawa, E.; Imazaki, Y.; Hayashi, T. *Chem. Commun.* **2009**, 5088.
(31) Spaggiari, A.; Vaccari, D.; Davoli, P.; Torre, G.; Prati, F. *J. Org. Chem.* **2007**, *72*, 2216.
(32) Adamczyk, M.; Watt, D. S.; Netzel, D. A. *J. Org. Chem.* **1984**, *49*, 4226.
(33) Benito, Y.; Canoira, L.; Rodriguez, J. G. *Appl. Organomet. Chem.* **1987**, *1*, 535.
(34) Kikugawa, Y.; Aoki, Y.; Sakamoto, T. *J. Org. Chem.* **2001**, *66*, 8612.
(35) Xian, H.; Jing, T. *Tetrahedron* **2003**, *59*, 4851.
(36) Johns, W. F. *J. Org. Chem.* **1961**, *26*, 4583.

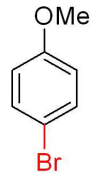
jp3-102-CDCl3-401-1H-2011-07-05



2a

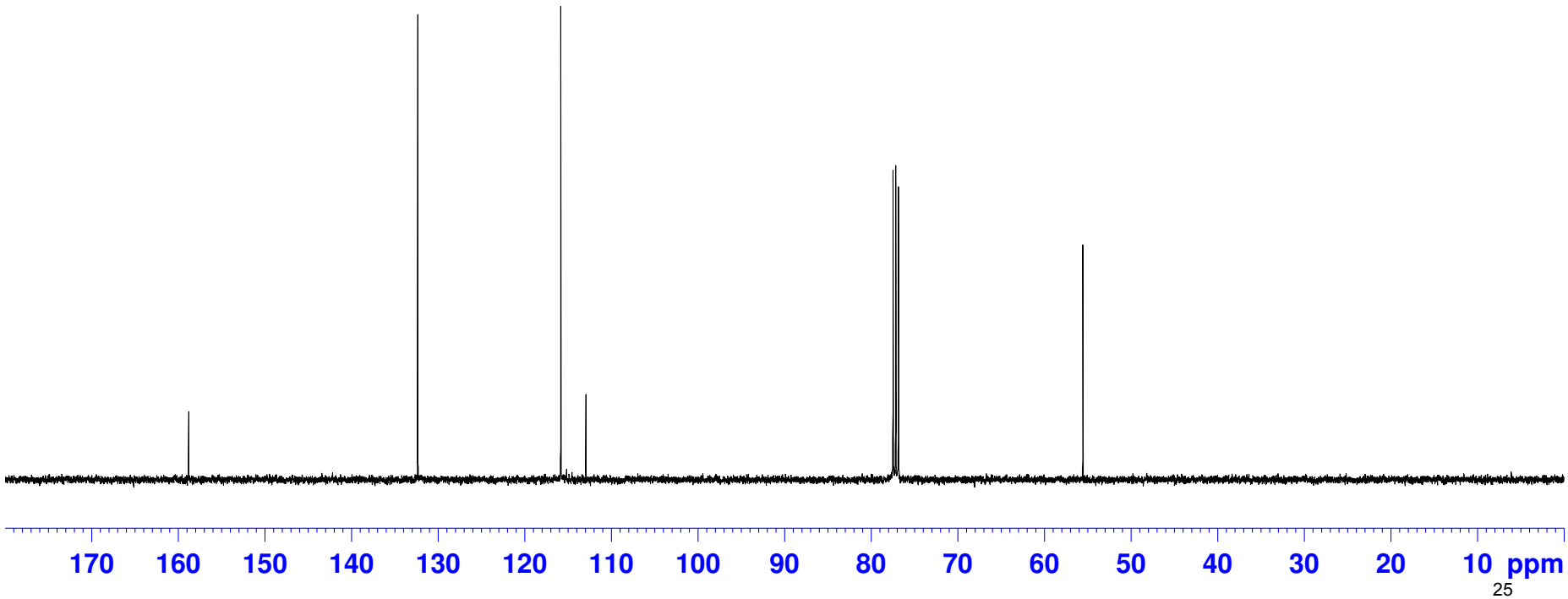


jp3-102-prod-CDCl3-400-13C

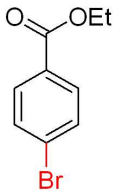


2a

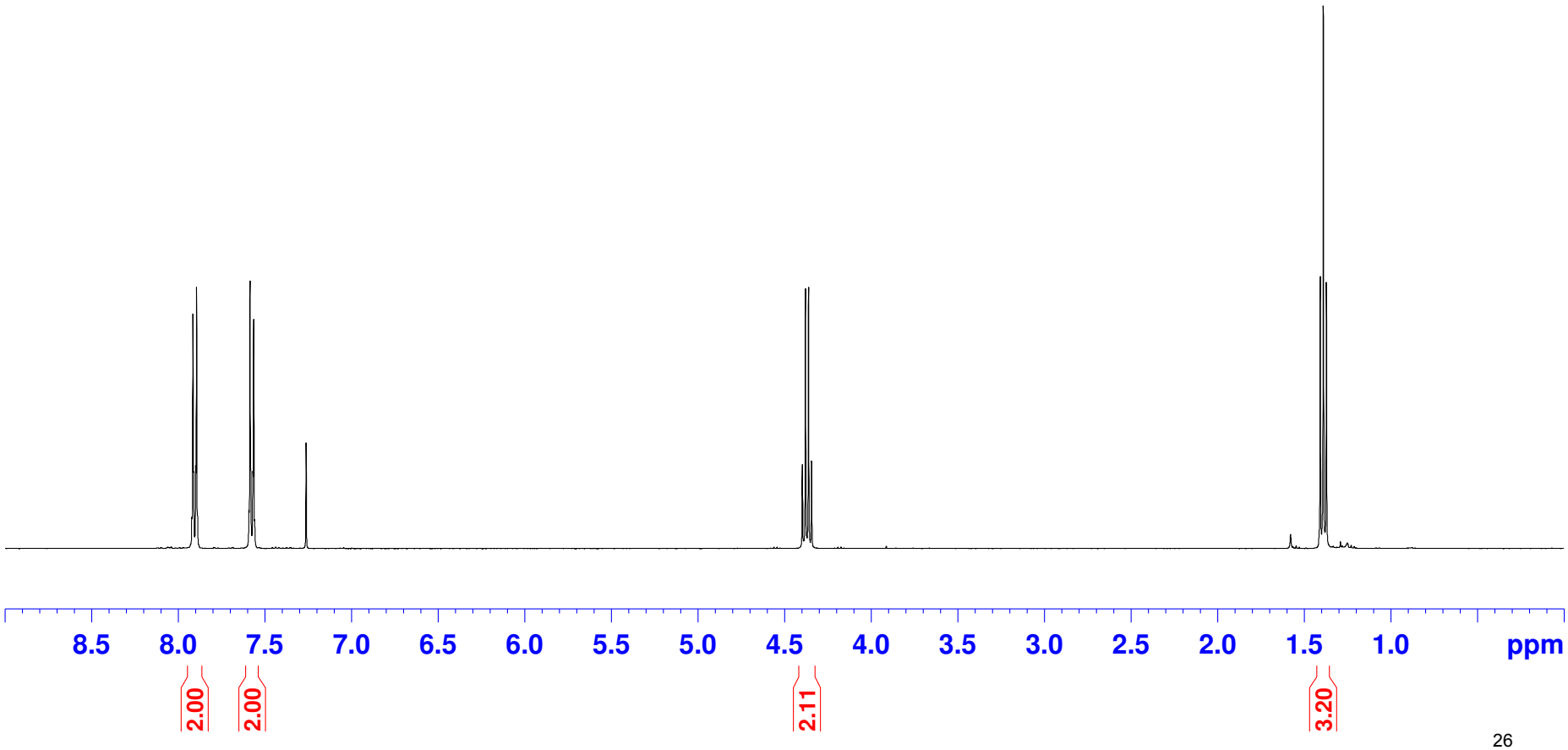
158.81
132.36
115.85
112.94
77.48
77.16
76.85
55.57



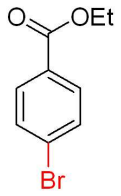
jp3-wxy-06-prod-CDCl3-400-1H-1



2b

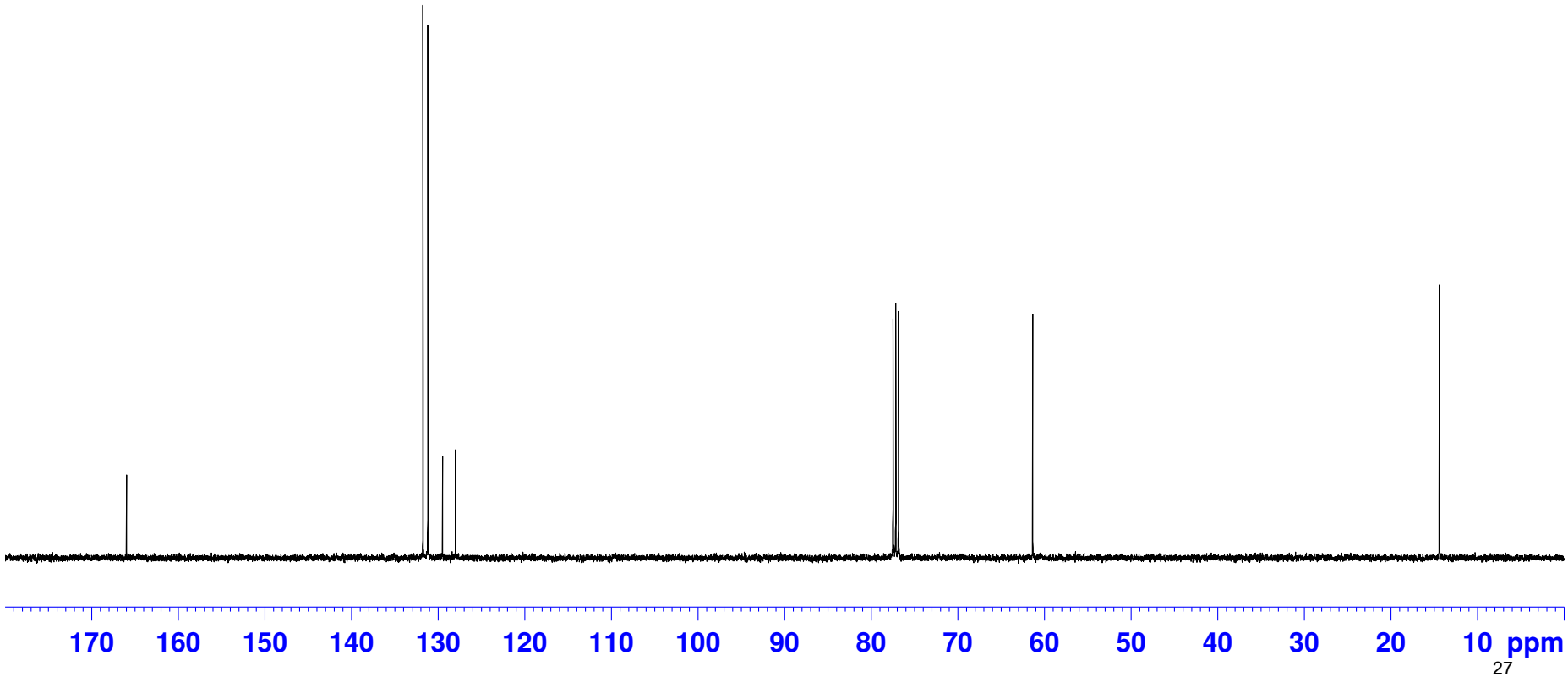


jp3-103-prod-CDCl3-400-13C

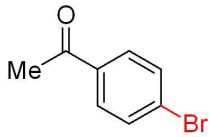


2b

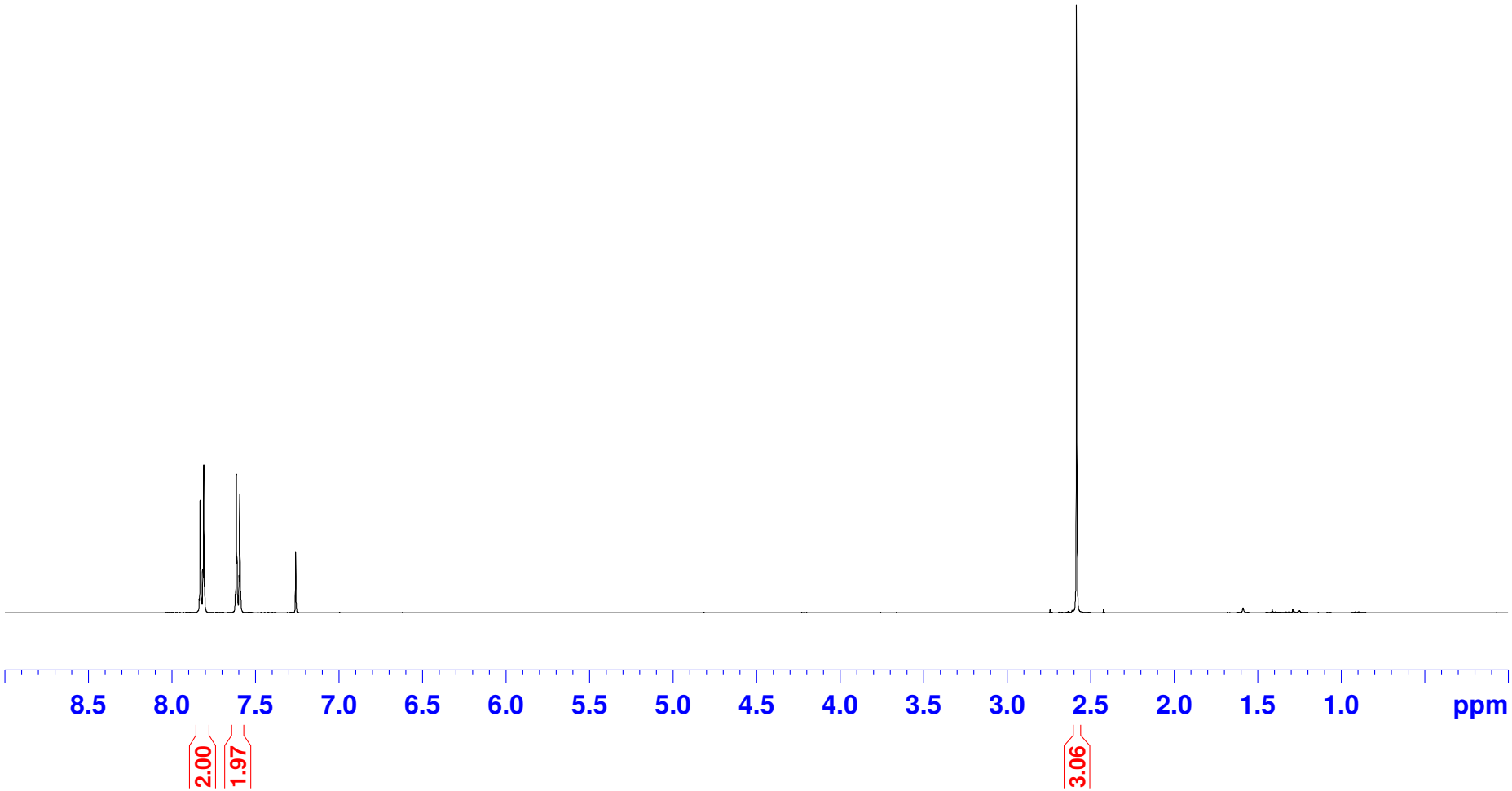
165.98
131.76
131.20
129.49
128.01
77.48
77.16
76.85
61.35
14.41



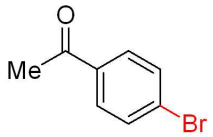
jp3-037-prod-CDCl3-400-1H-1



2c

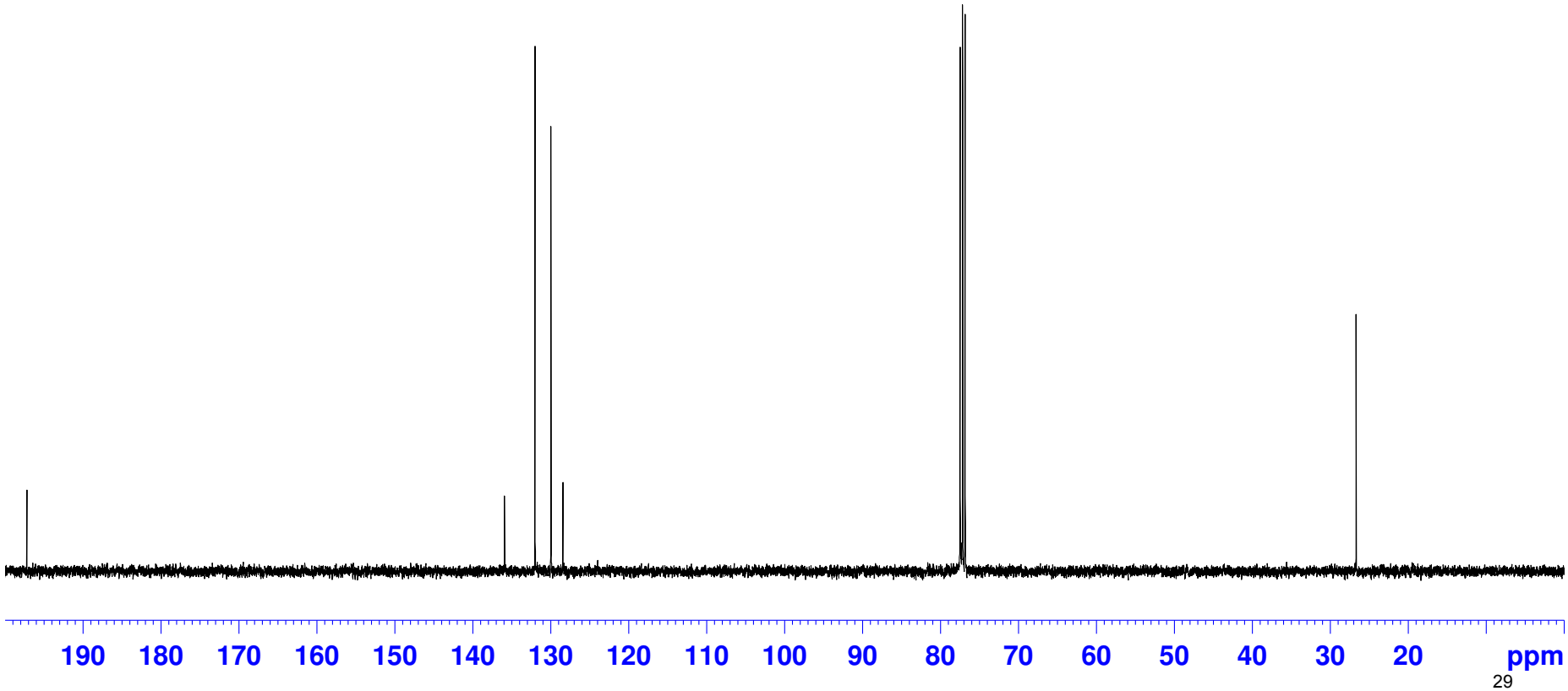


jp3-104-prod-CDCl3-400-13C

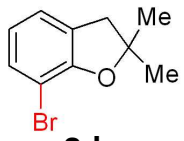


2c

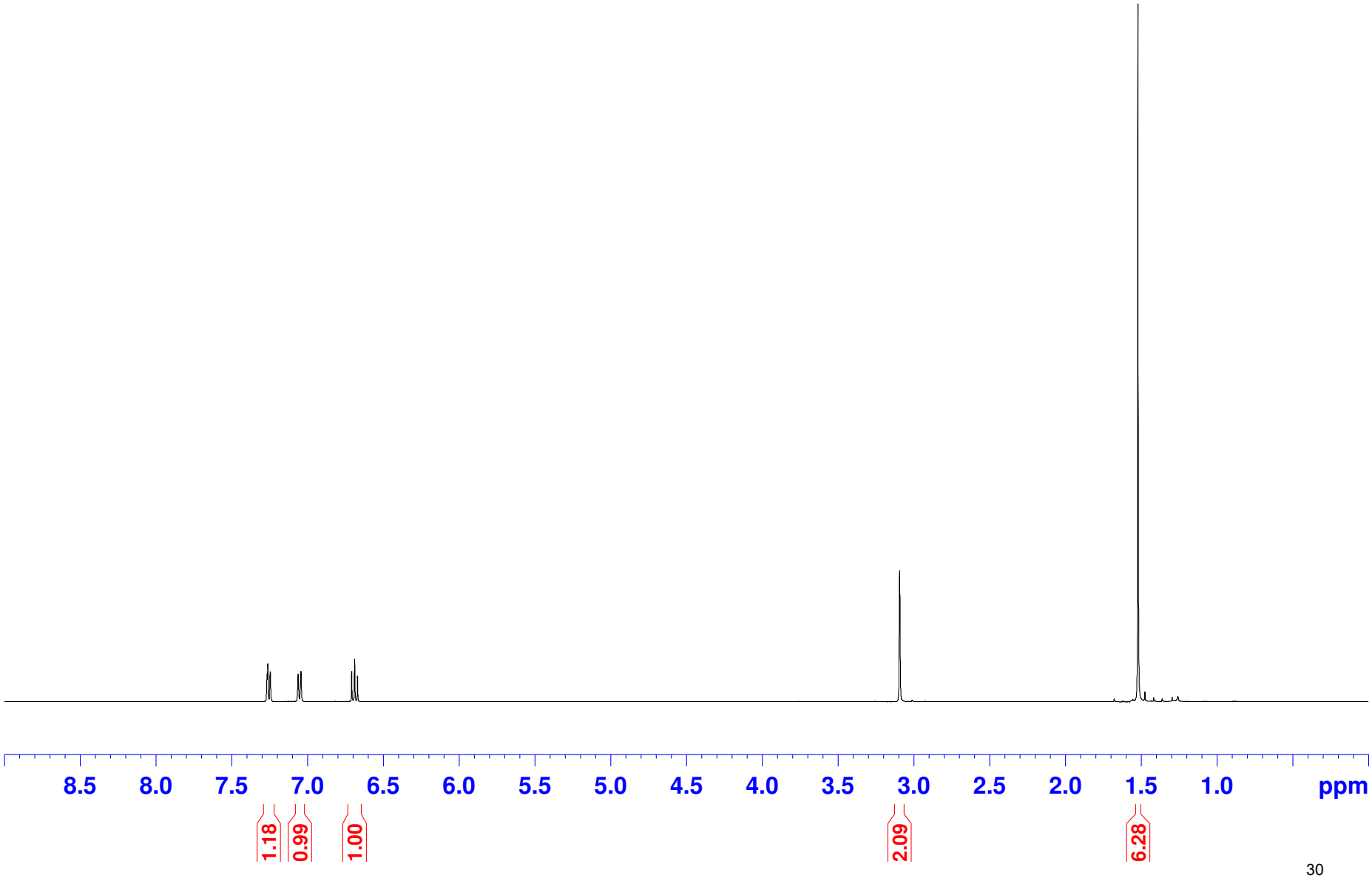
197.15
135.94
132.02
129.98
128.44
77.48
77.16
76.84
26.69



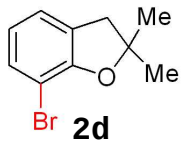
jp3-074-prod-CDCl3-400-1H-1



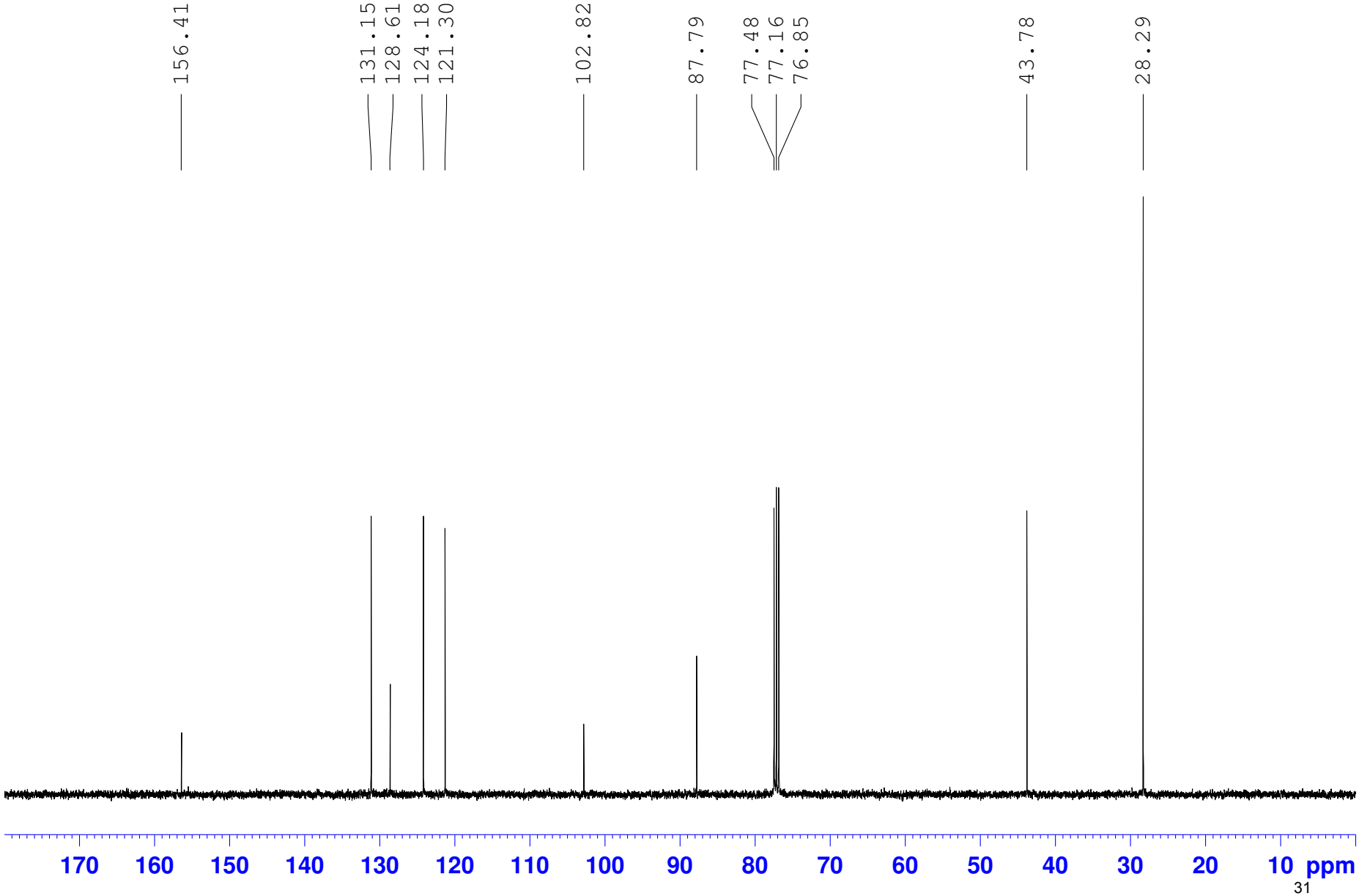
2d



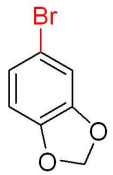
jp3-108-prod-CDCl3-400-13C



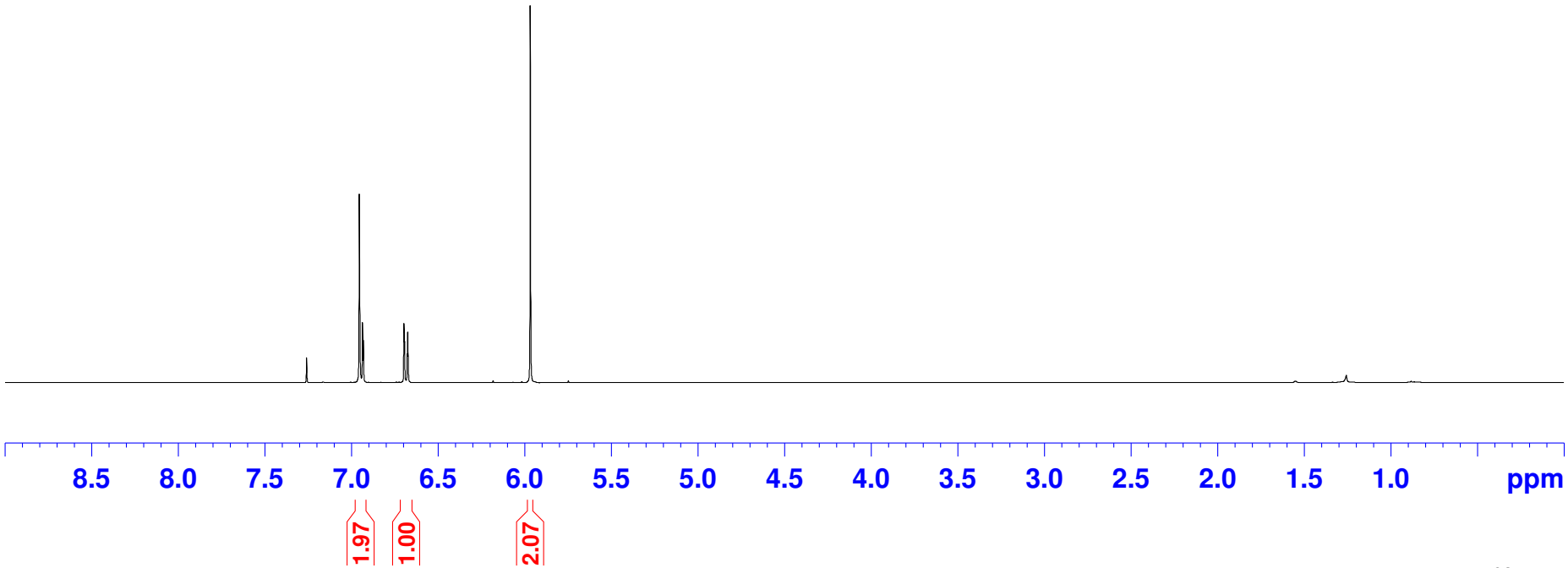
2d



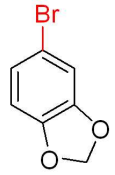
jp3-049-prod-CDCl3-400-1H-1



2e

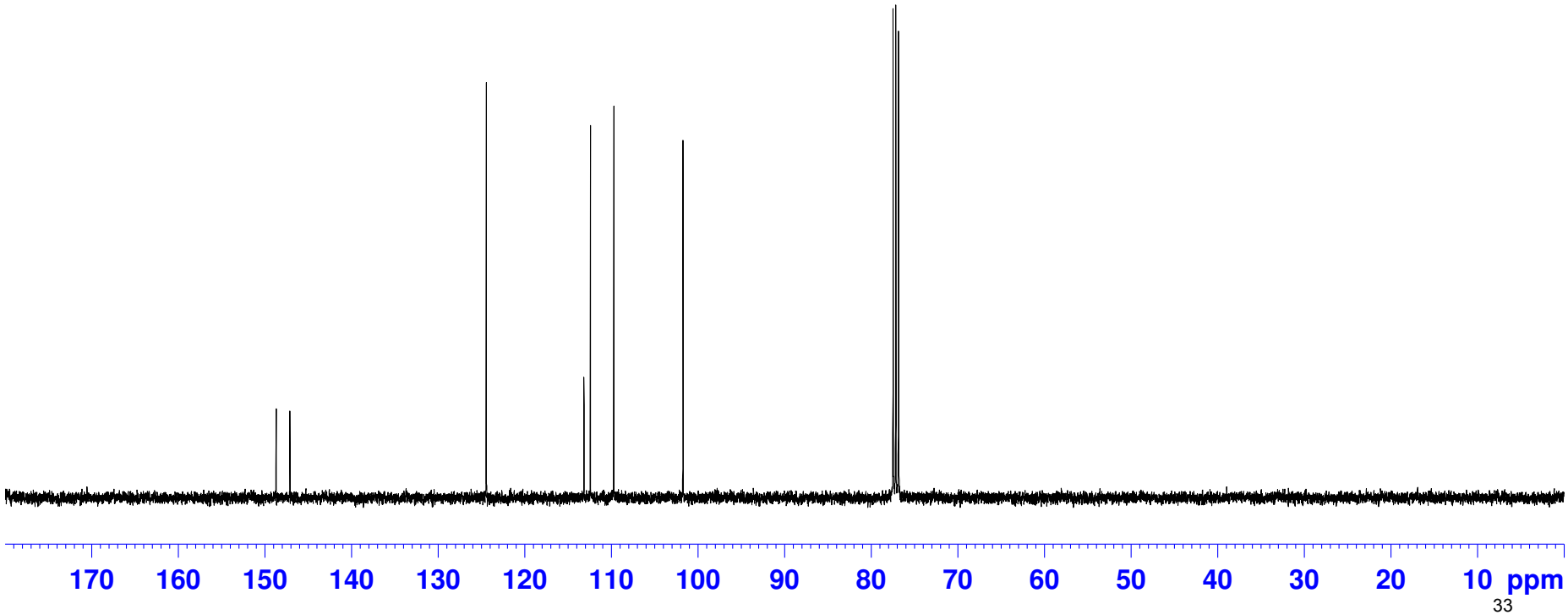


jp3-109-prod-CDCl3-400-13C

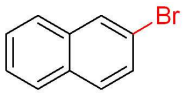


2e

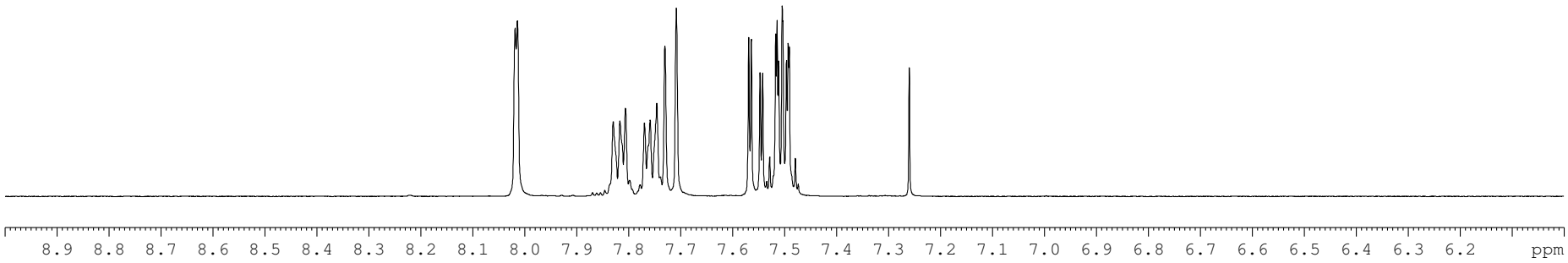
148.72
147.12
124.44
113.17
112.43
109.71
101.74
77.48
77.17
76.85

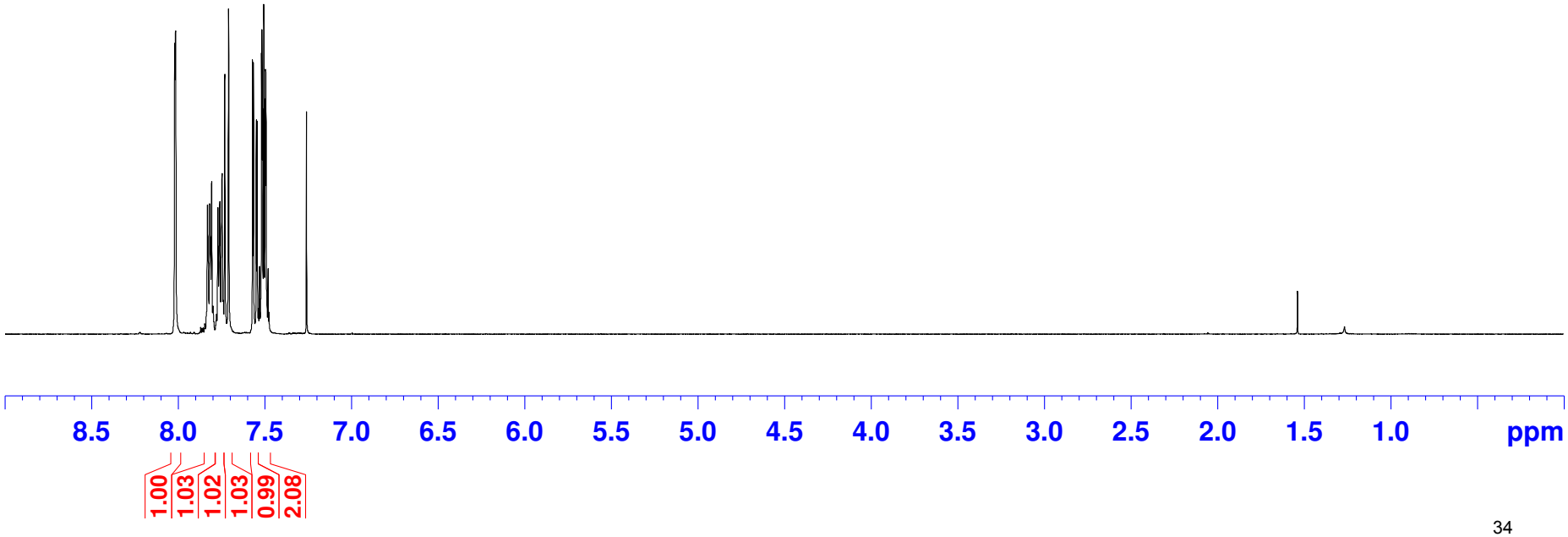


jp3-105-CDCl3-401-1H-2011-07-05

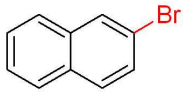


2f





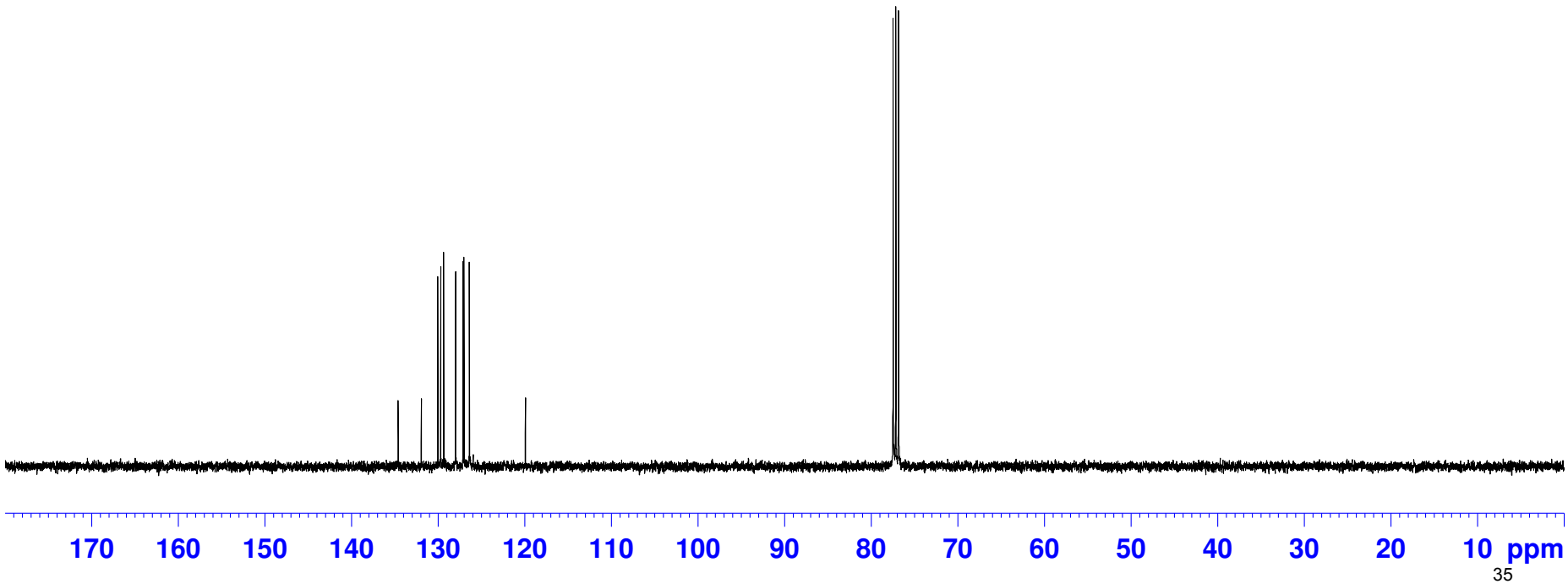
jp3-105-prod-CDCl3-400-13C-29



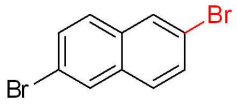
2f

134.62
131.95
130.05
129.71
129.37
127.99
127.14
127.02
126.40
119.93

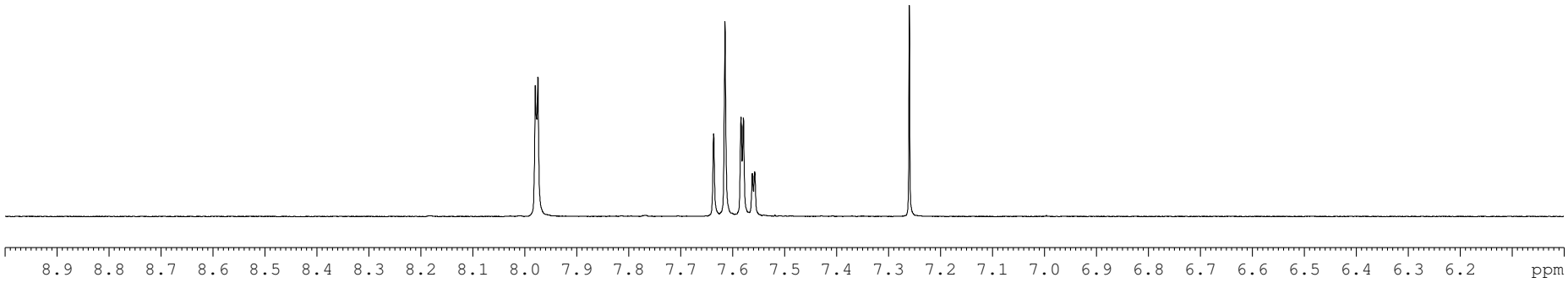
77.48
77.16
76.84

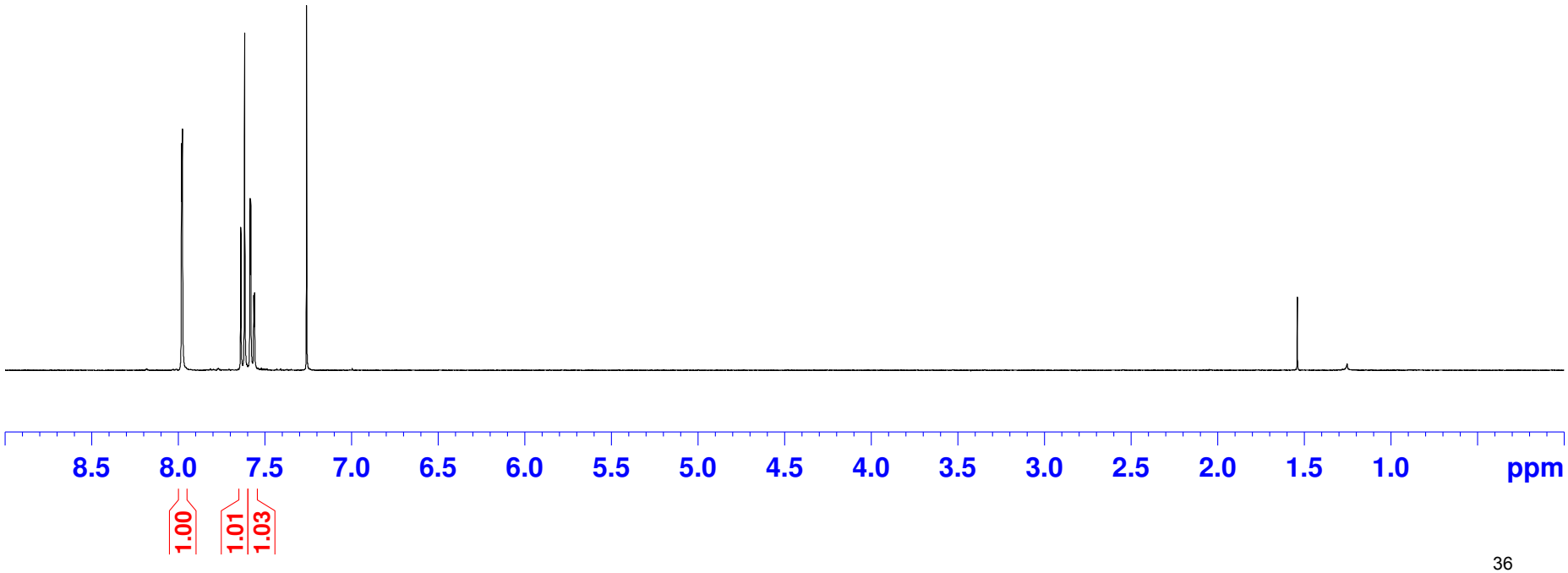


jp3-wxy-38-CDCl3-401-1H-2011-07-05

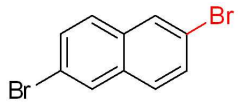


2g

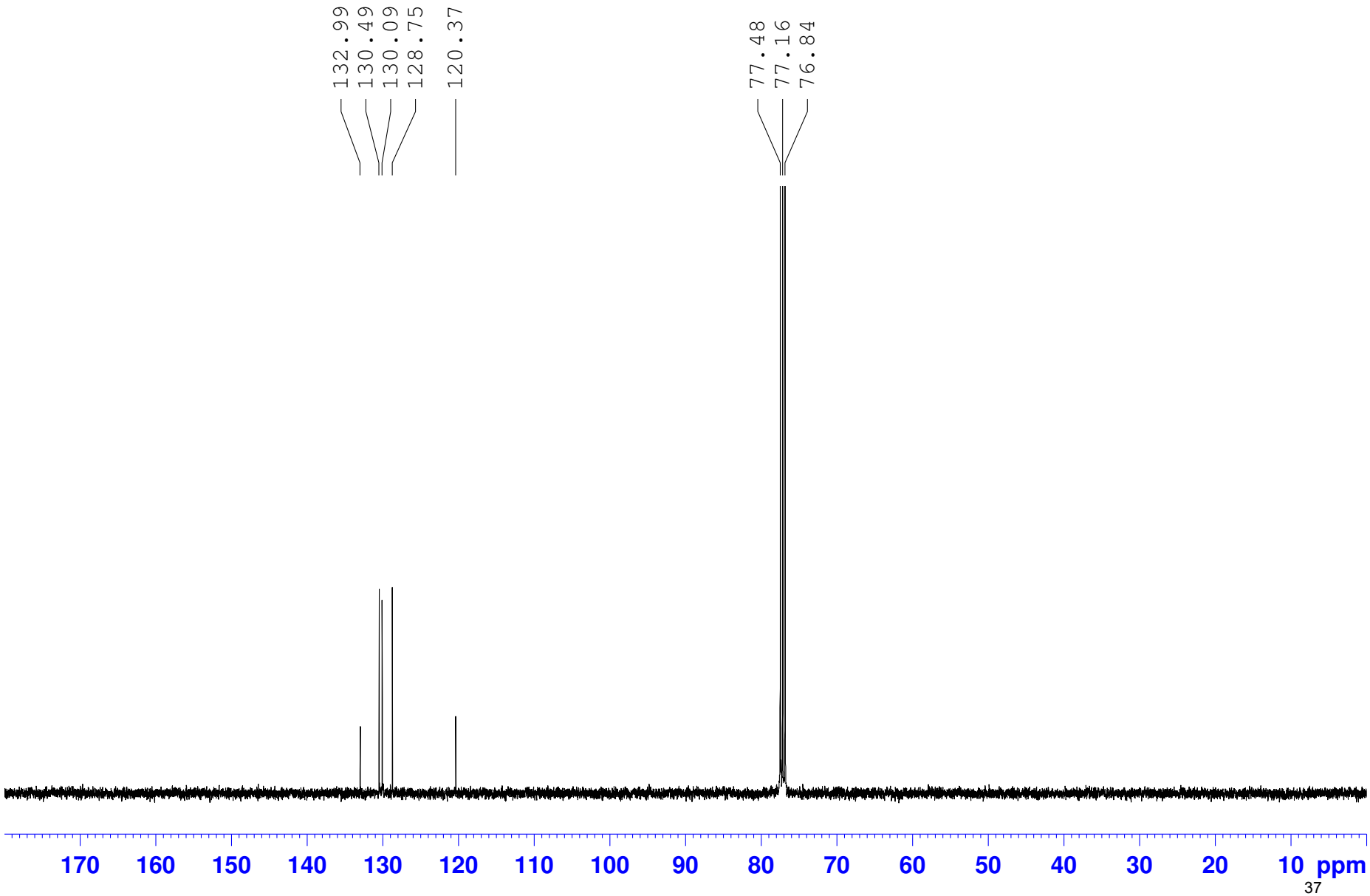




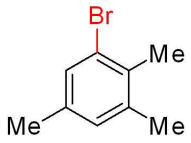
jp3-106-prod-CDCl3-400-13C



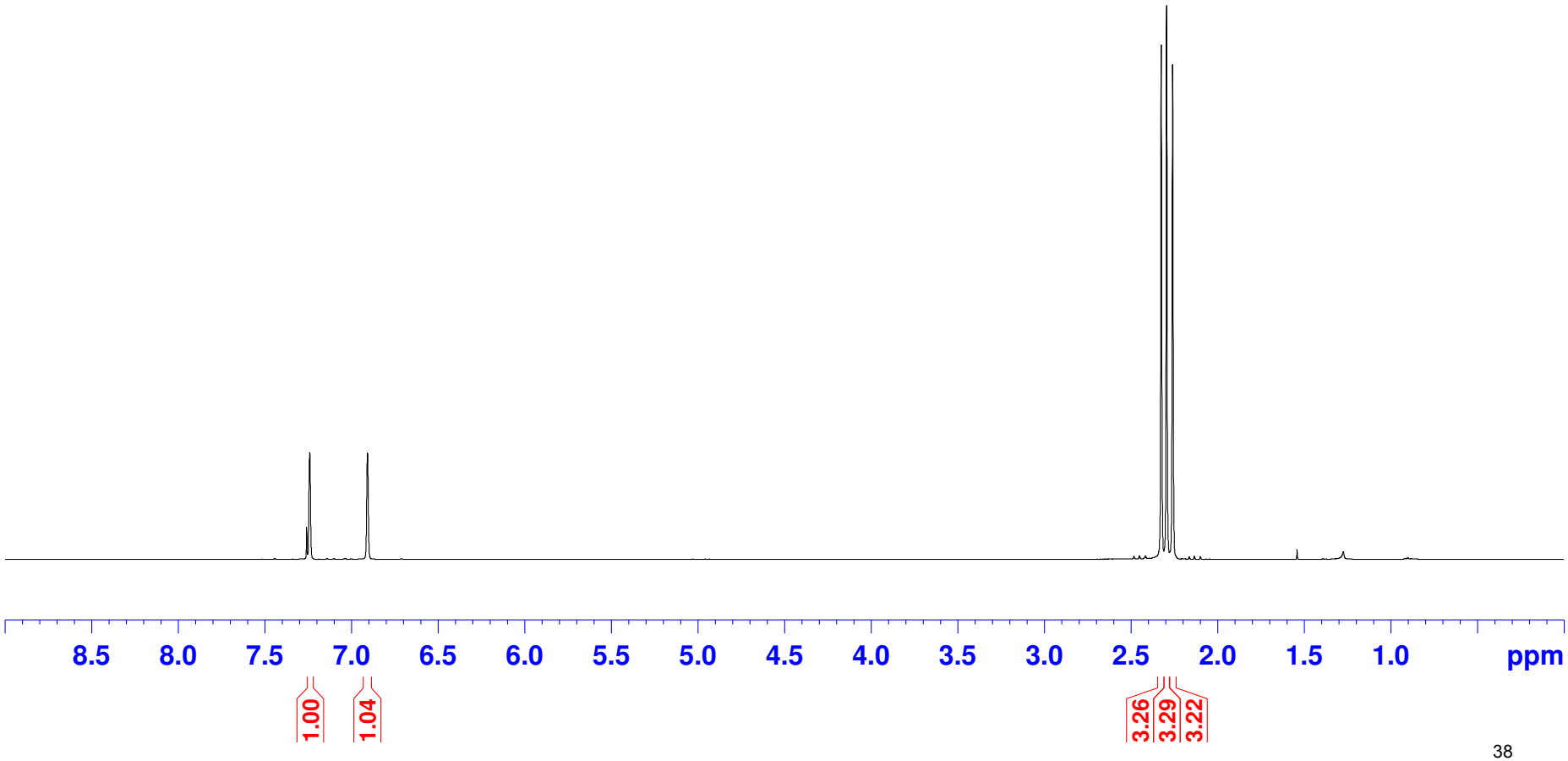
2g



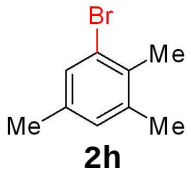
jp3-159-prod-CDCl3-400-1H



2h



jp3-159-prod-CDCl3-401-13C

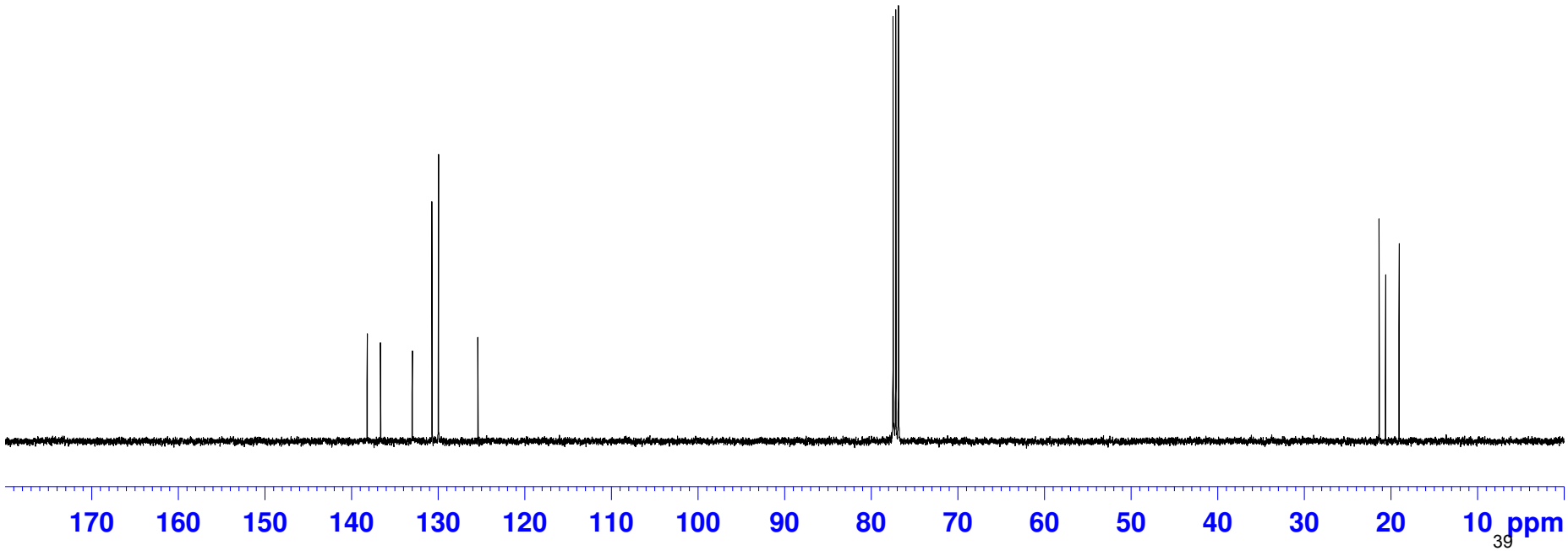


2h

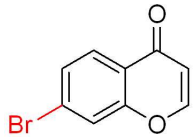
138.20
136.66
133.00
130.72
129.97
125.42

77.48
77.16
76.84

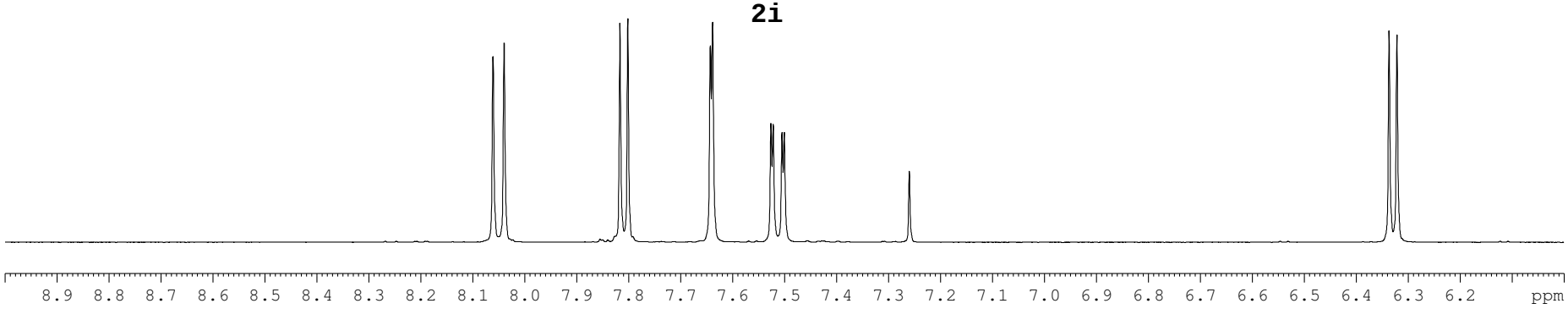
21.35
20.61
19.05

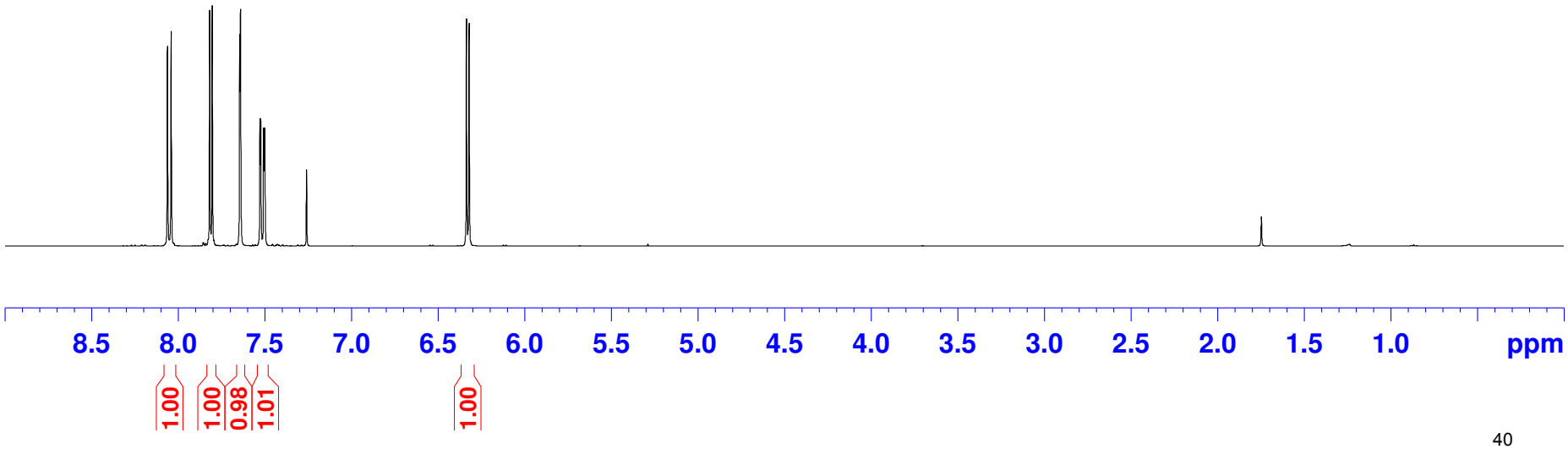


jp3-107-prod-CDCl3-400-1H-B

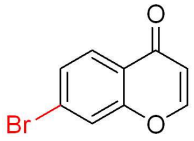


2i

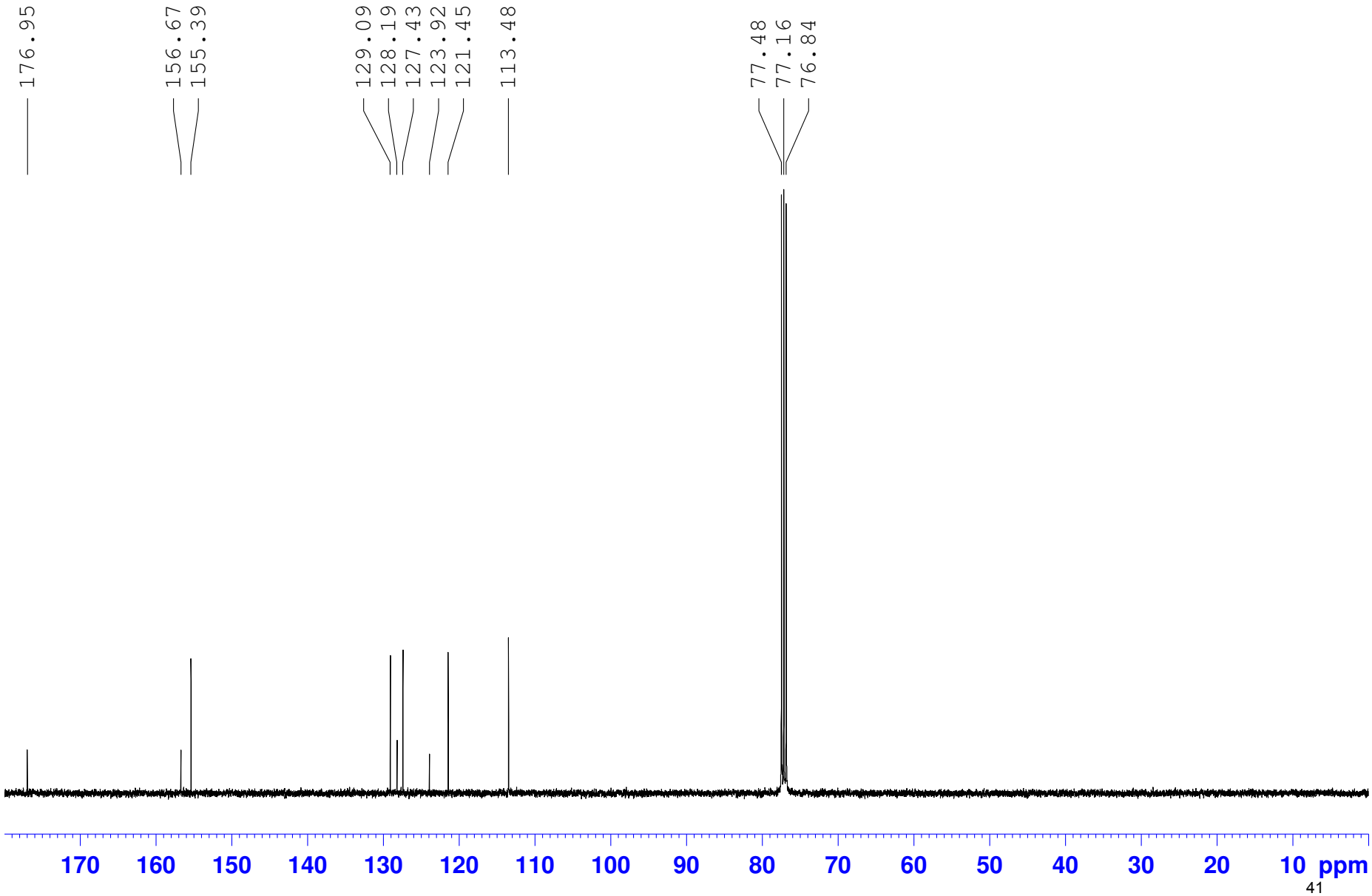




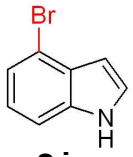
jp3-107-prod-CDCl3-400-13C



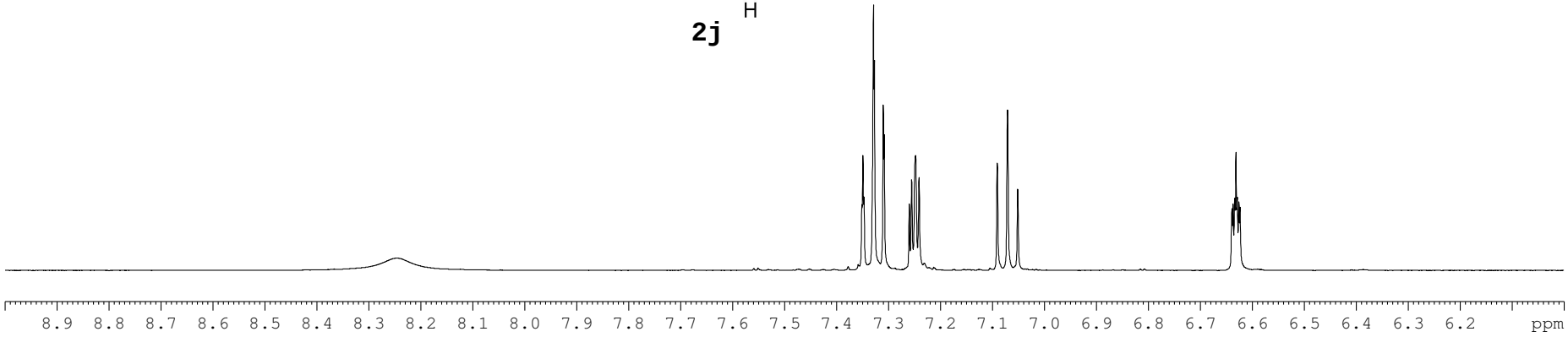
2i

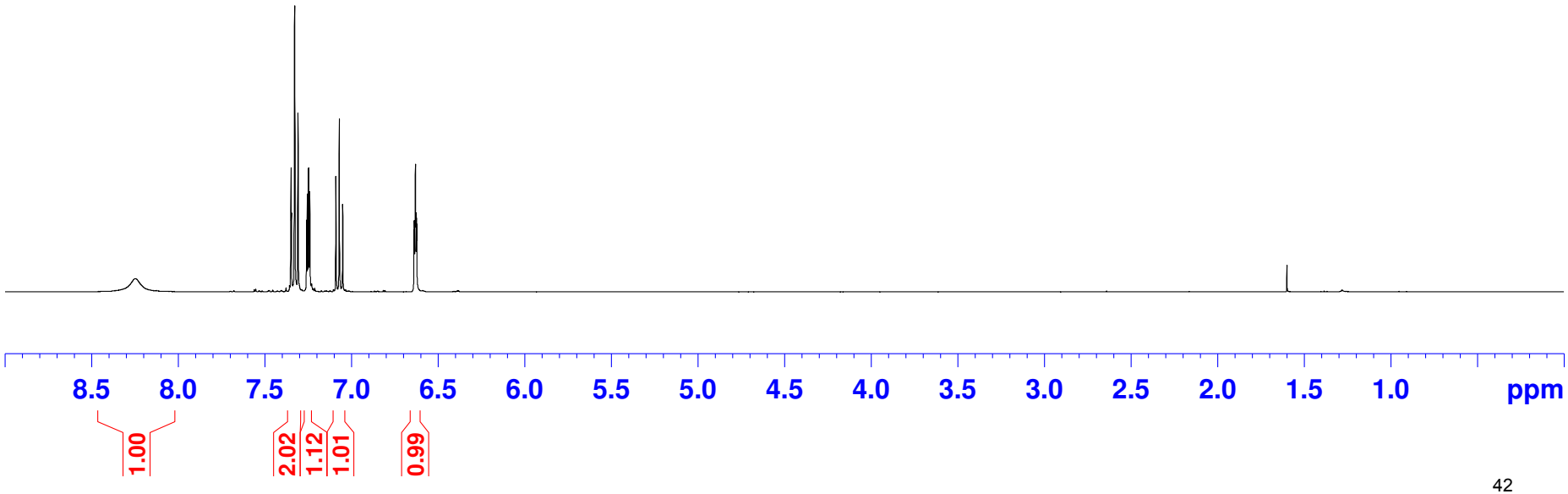


jp3-110-CDCl3-401-1H-2011-07-05

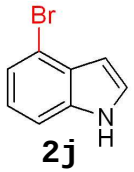


2j



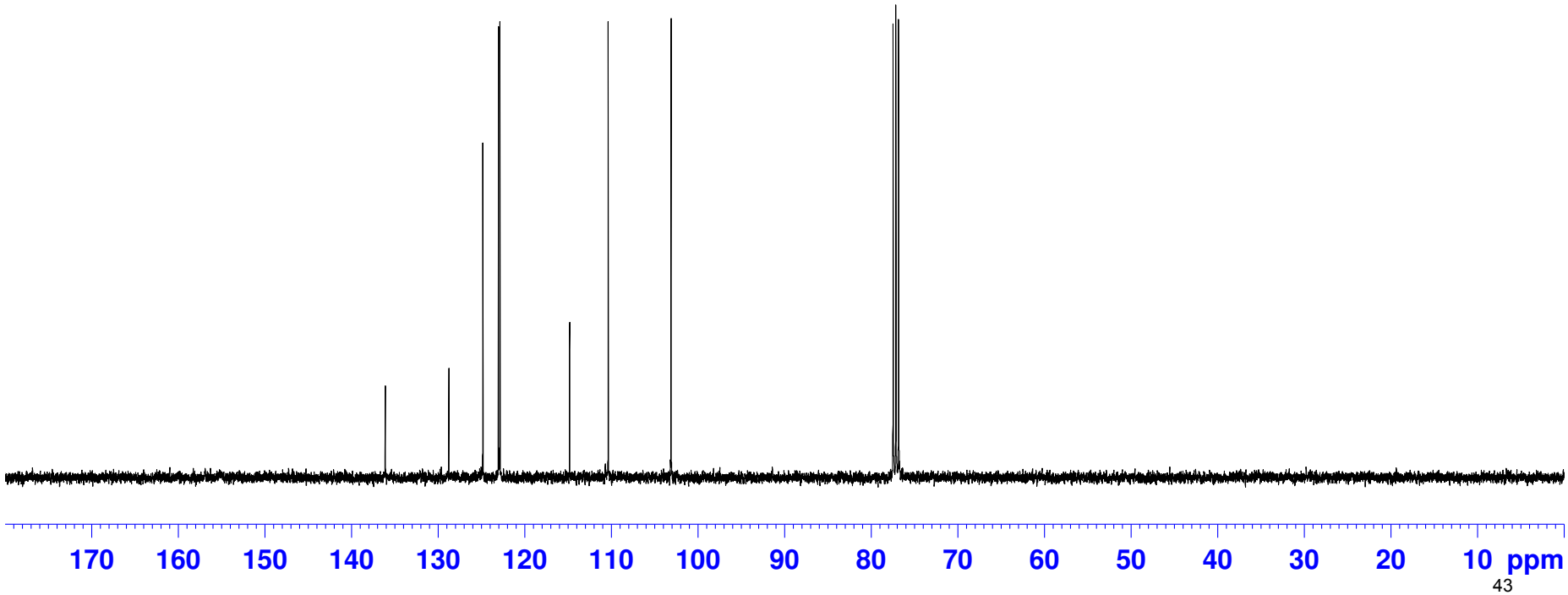


jp3-110-prod-CDCl3-400-13C-pan

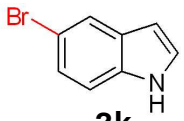


2j

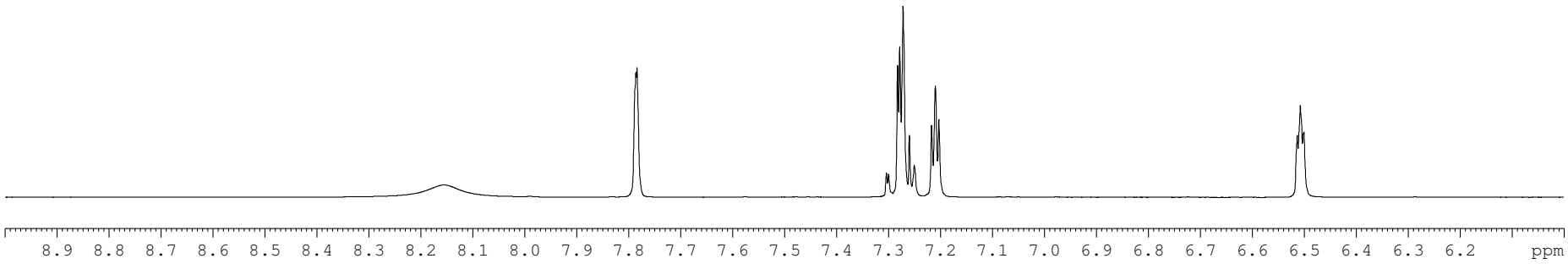
136.10
128.76
124.85
123.03
122.87
114.83
110.37
103.11
77.48
77.16
76.84

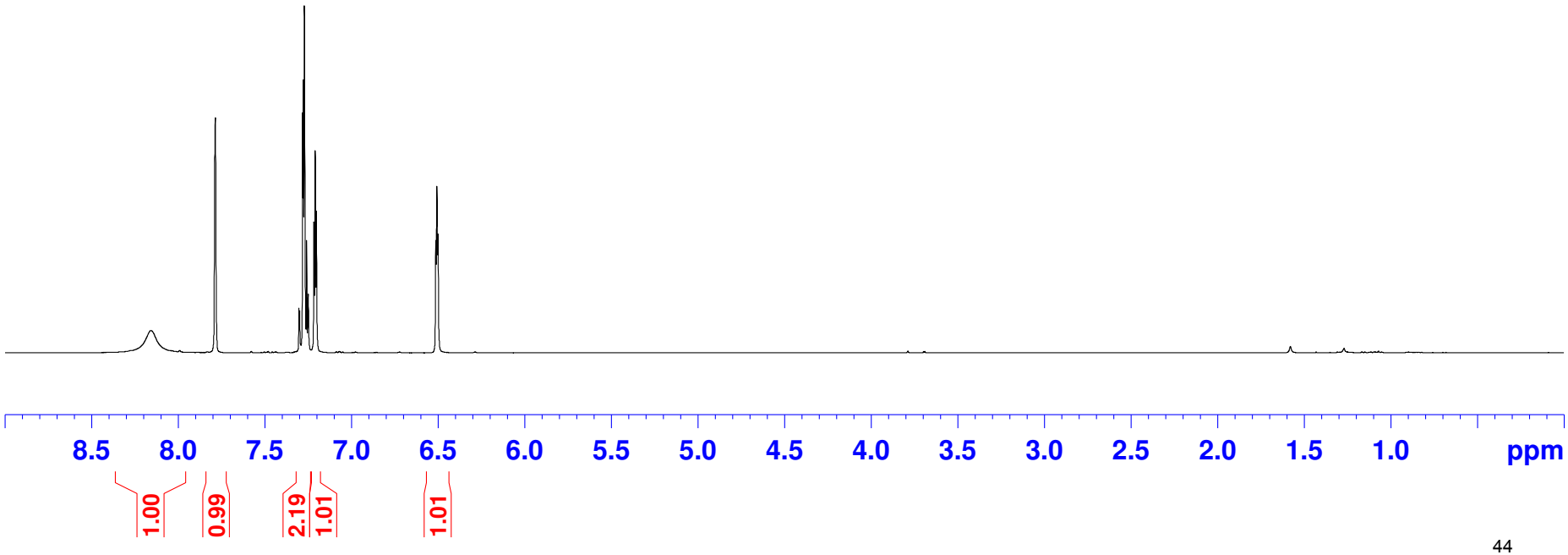


jp3-046-prod-CDCl3-400-1H-1

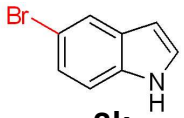


2k

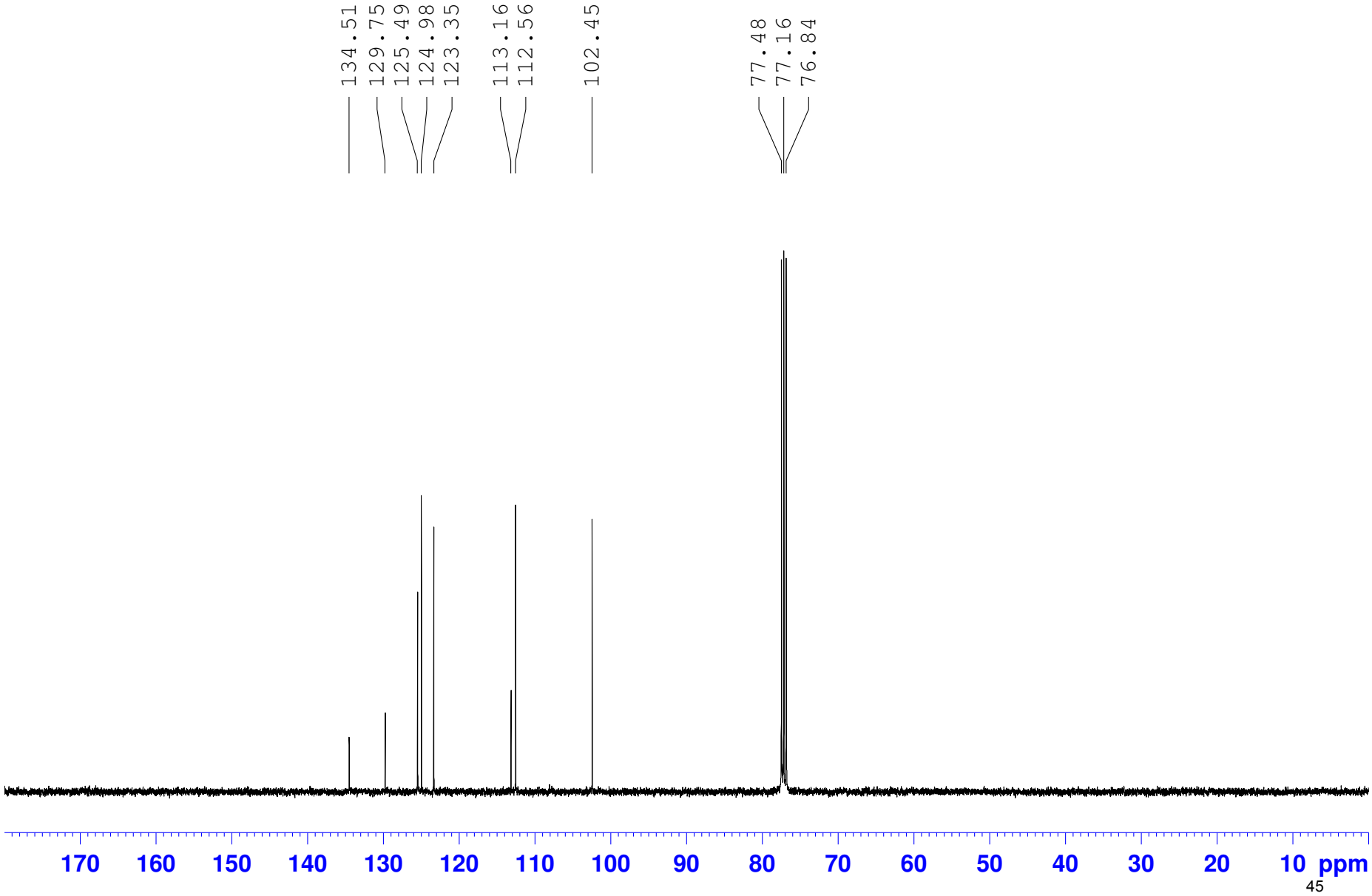




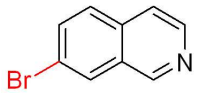
jp3-046-prod-CDCl3-400-13C



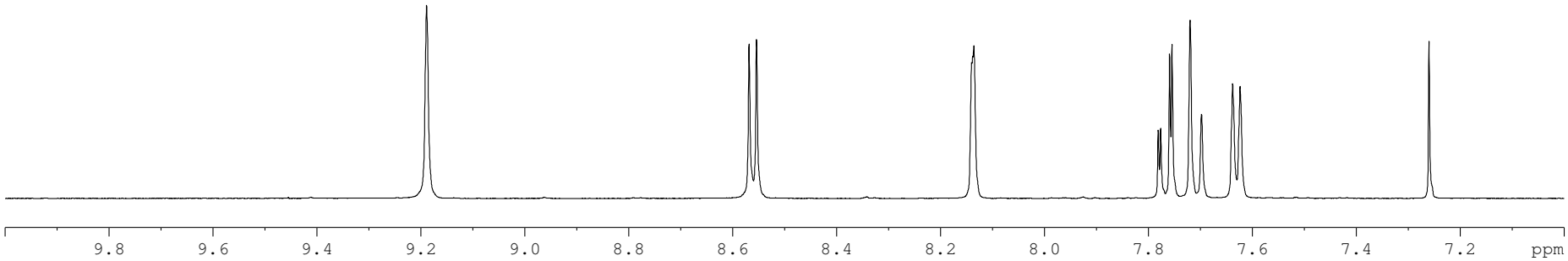
2k

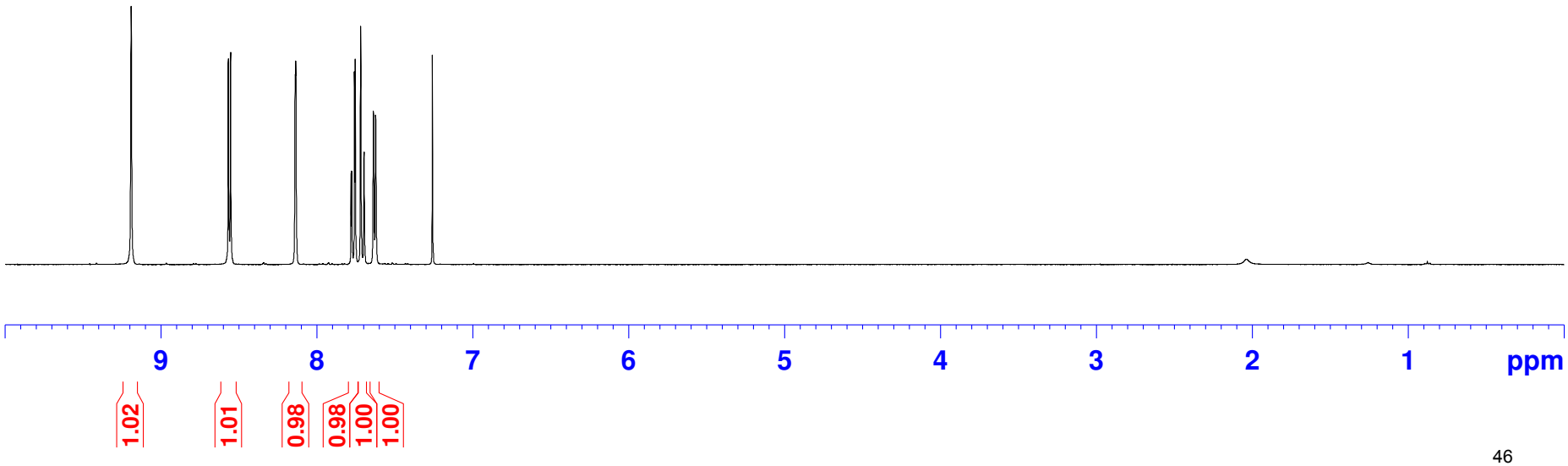


jp3-112-prod-CDCl3-400-1H-B

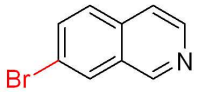


2l





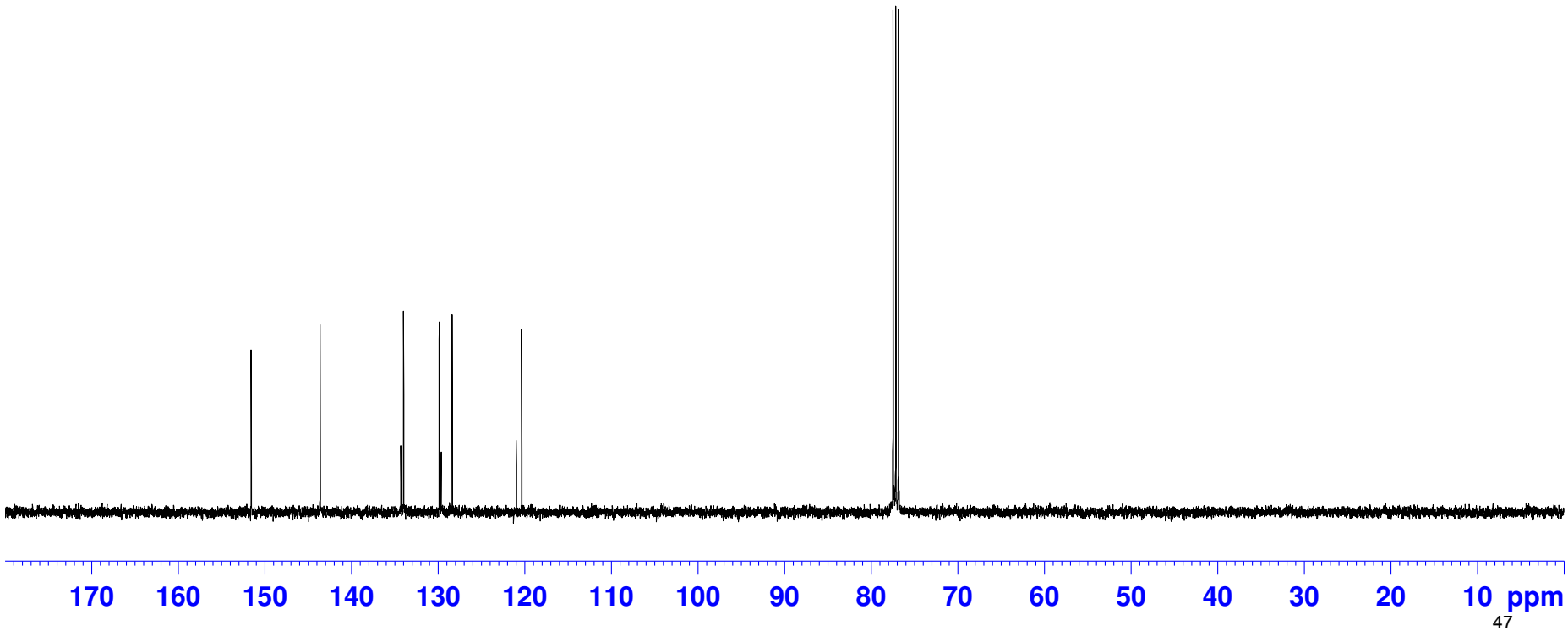
jp3-112-prod-CDCl3-400-13C



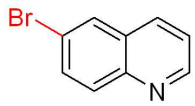
2l

151.59
143.65
134.31
134.00
129.88
129.65
128.39
120.98
120.36

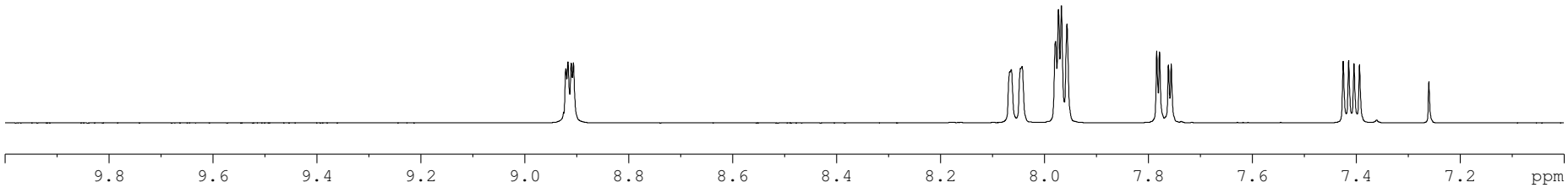
77.48
77.16
76.84

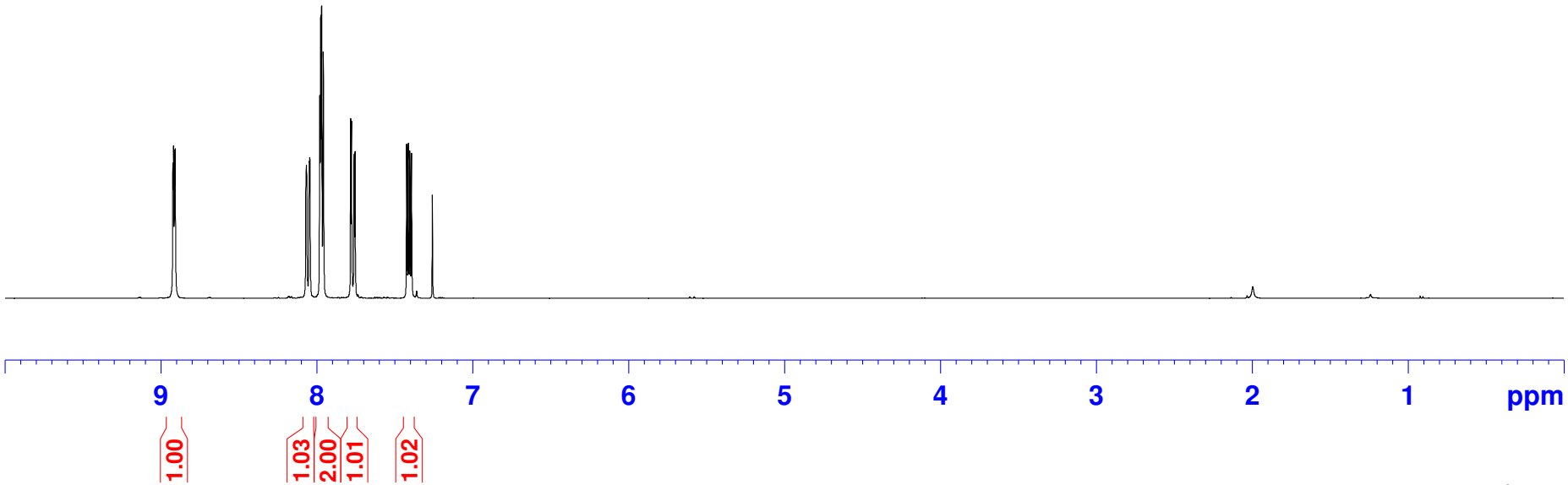


jp3-113-prod-CDCl3-400-1H-2011-07-01

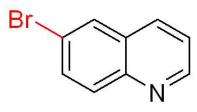


2m



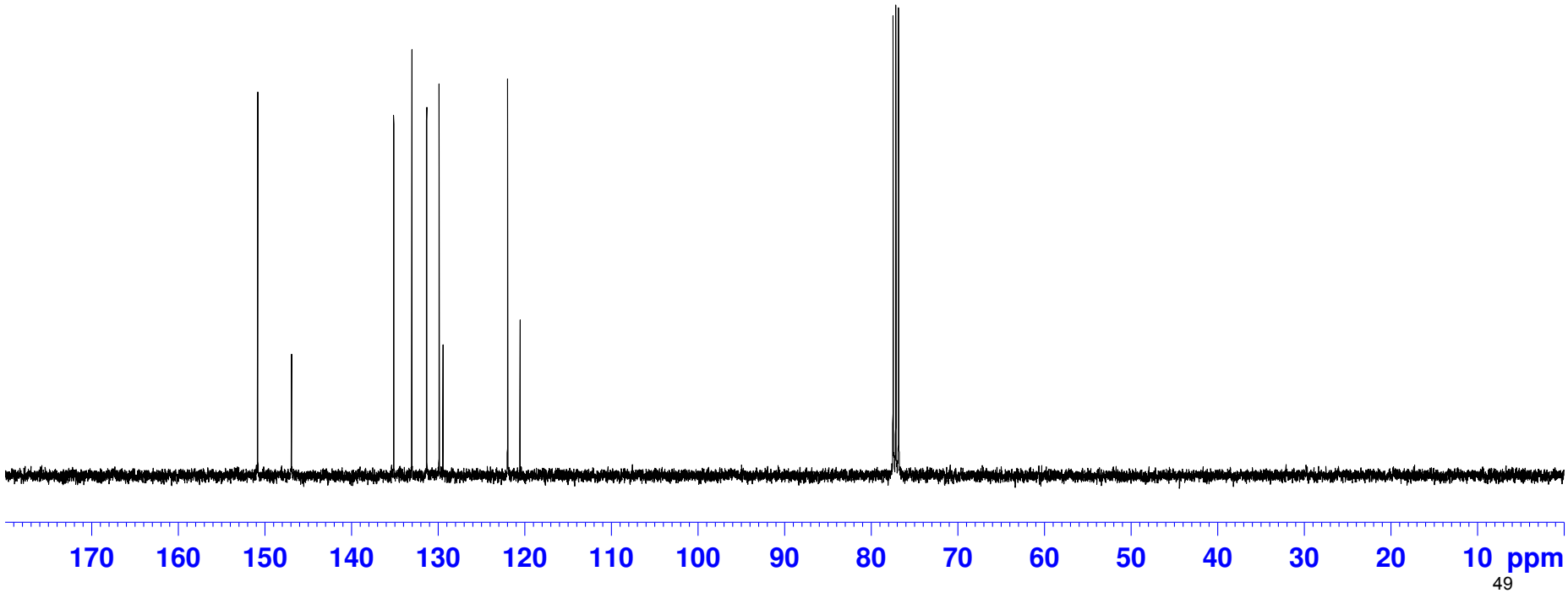


jp3-113-prod-CDCl3-400-13C

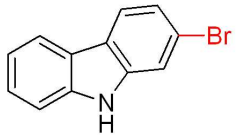


2m

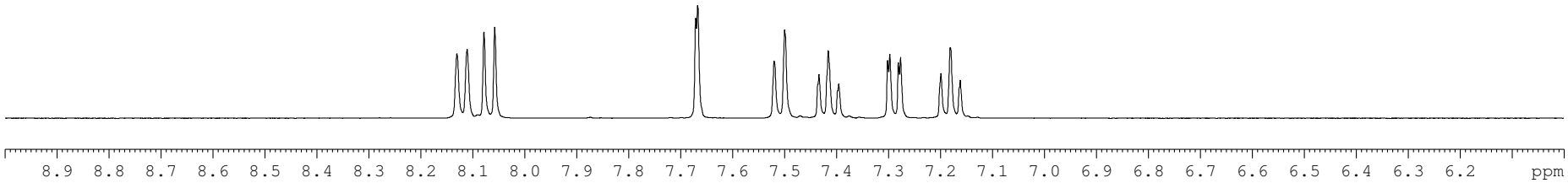
150.84
146.93
135.14
133.04
131.33
129.90
129.44
121.99
120.55
77.48
77.16
76.84

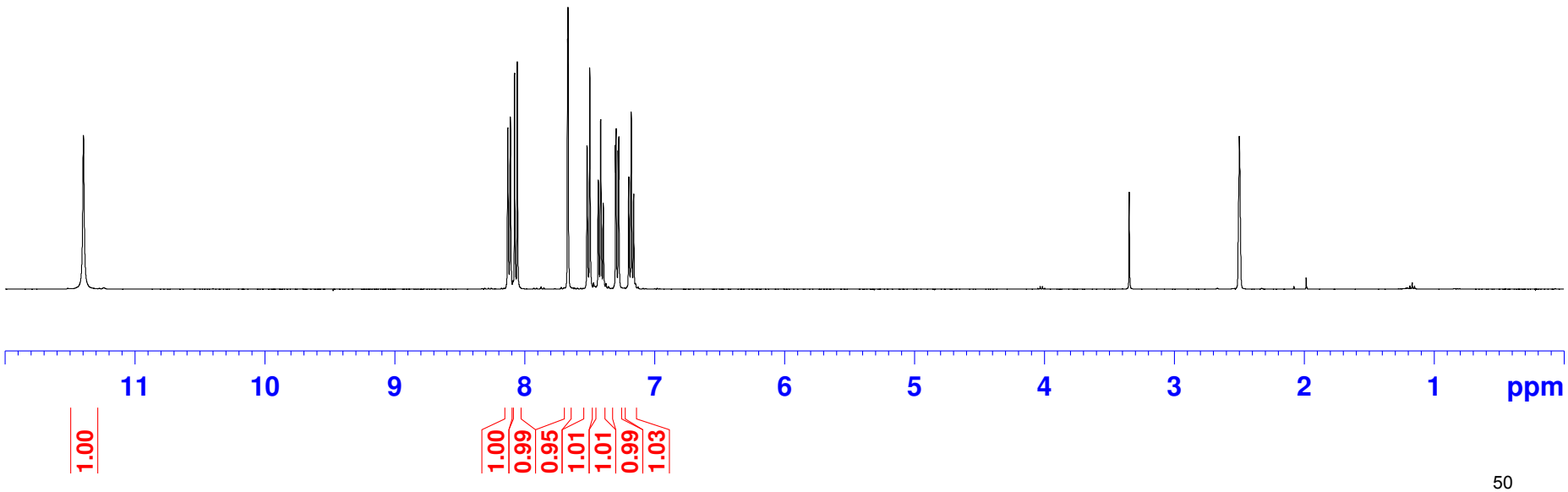


jp3-114-prod-DMSO-400-1H-29

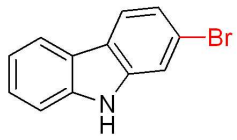


2n

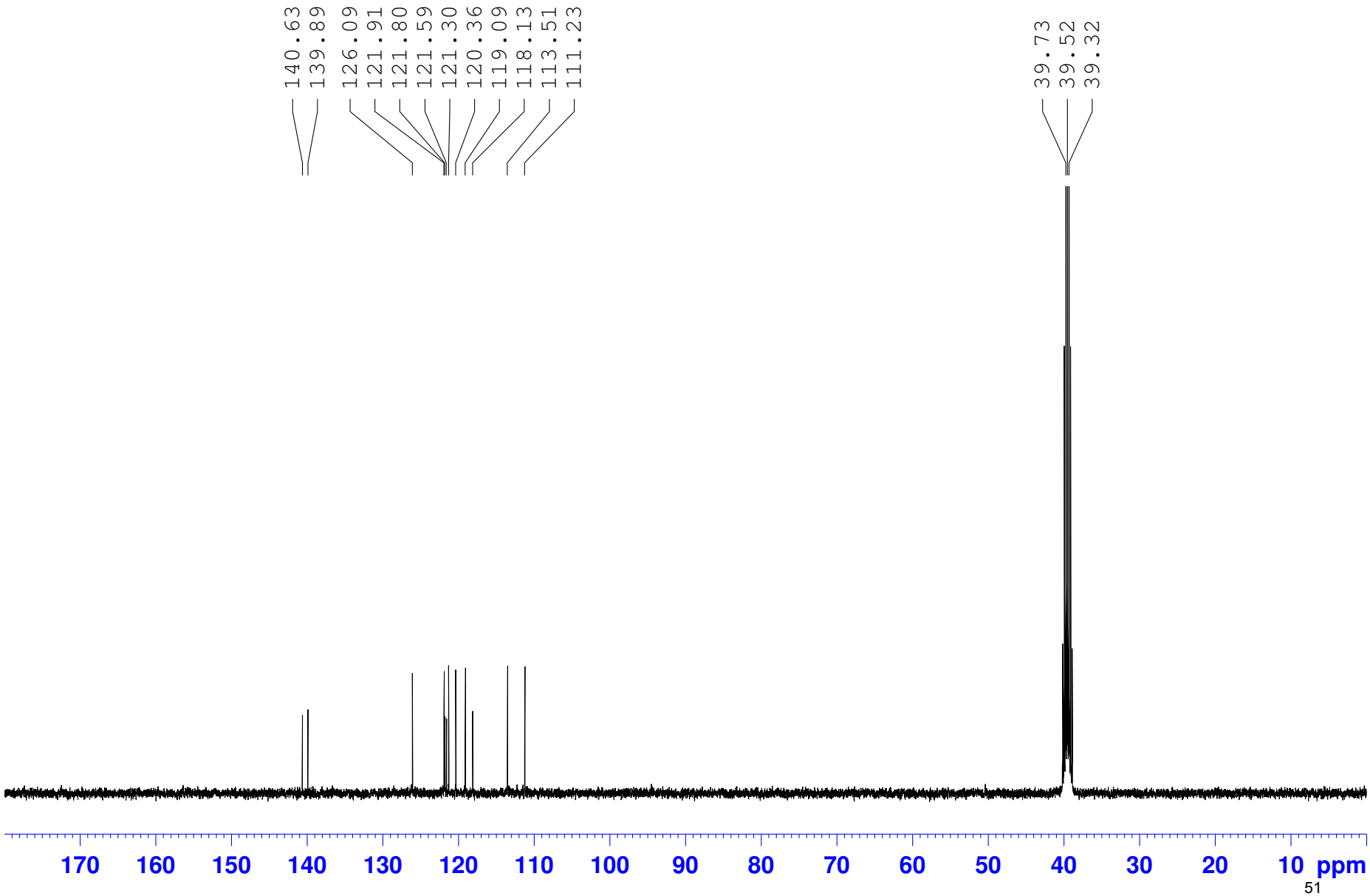




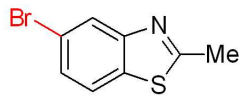
jp3-114-prod-DMSO-400-13C-29



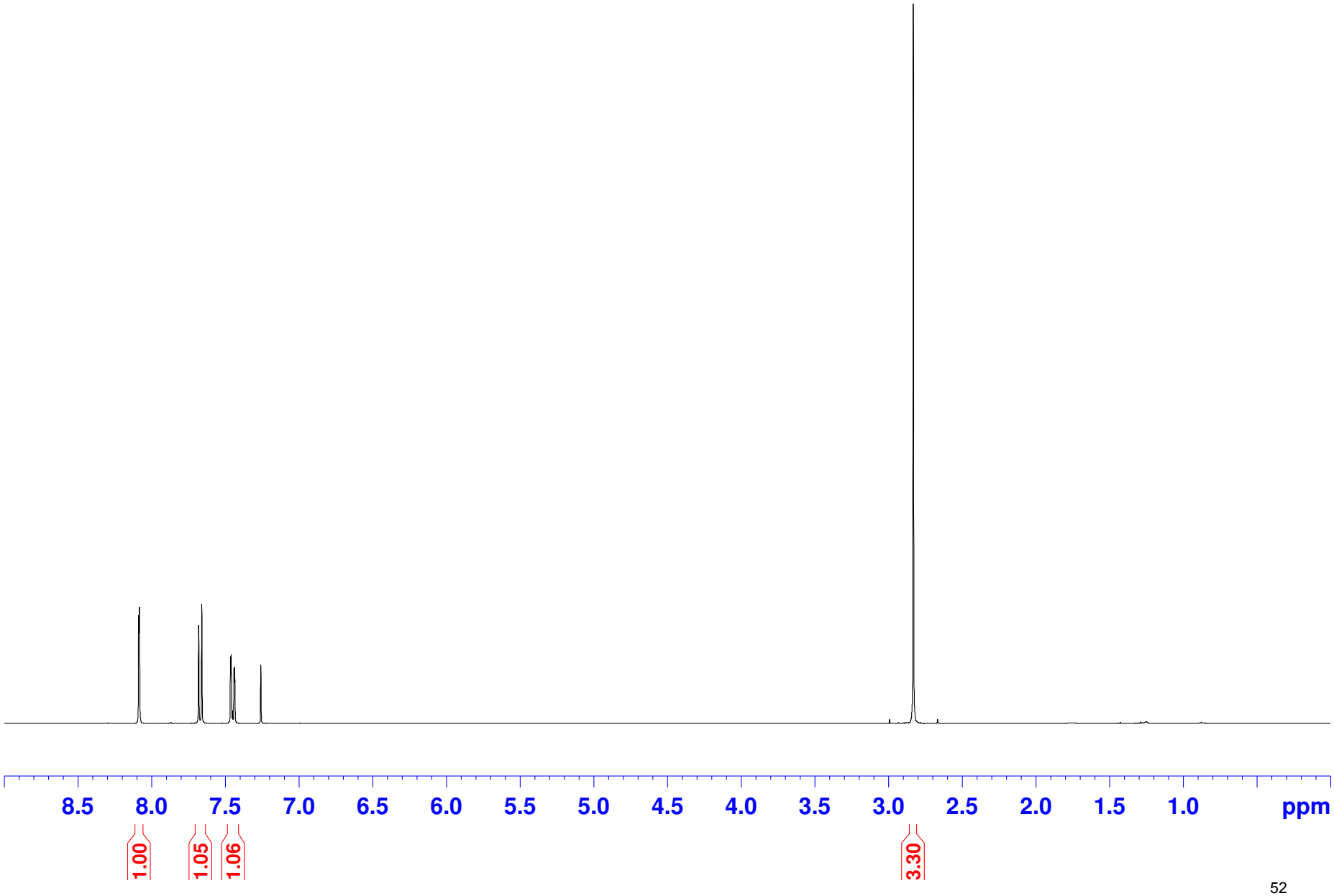
2n



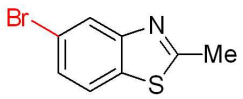
jp3-038-prod-CDCl3-400-1H-1



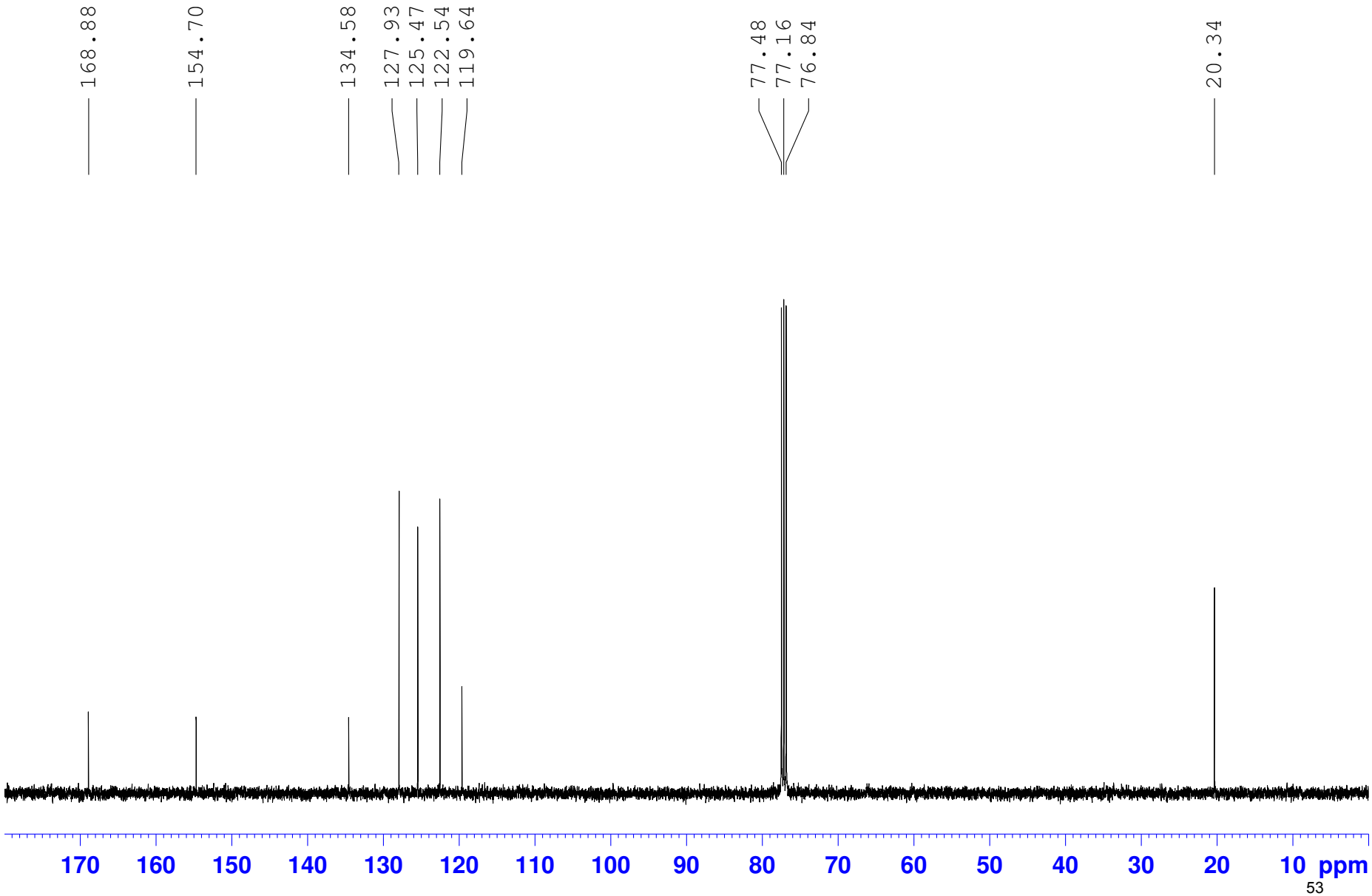
2o



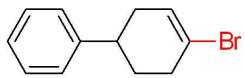
jp3-115-prod-CDCl3-400-13C



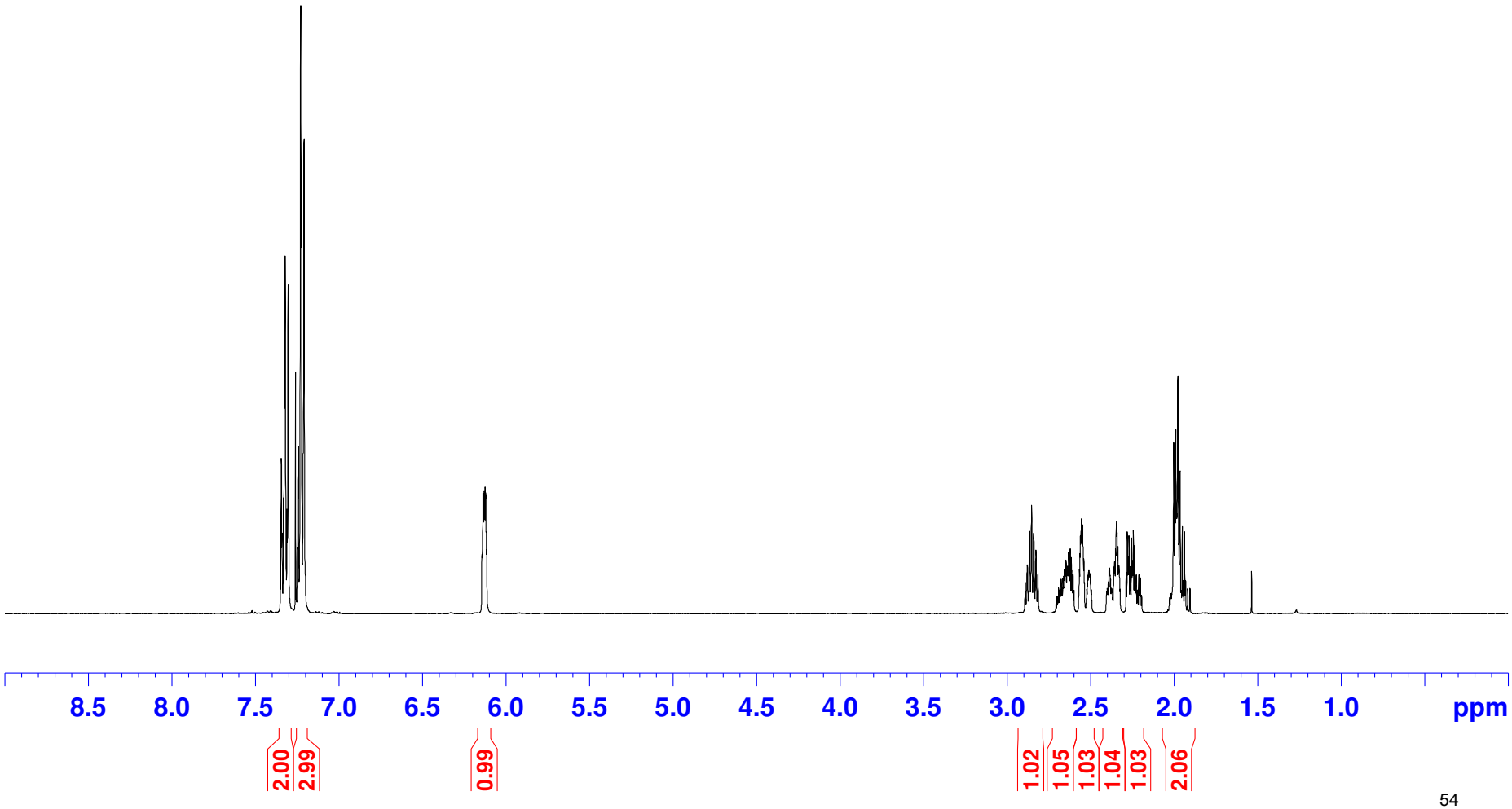
2o



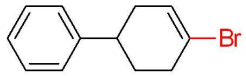
jp3-090-CDCl3-401-1H-2011-07-05



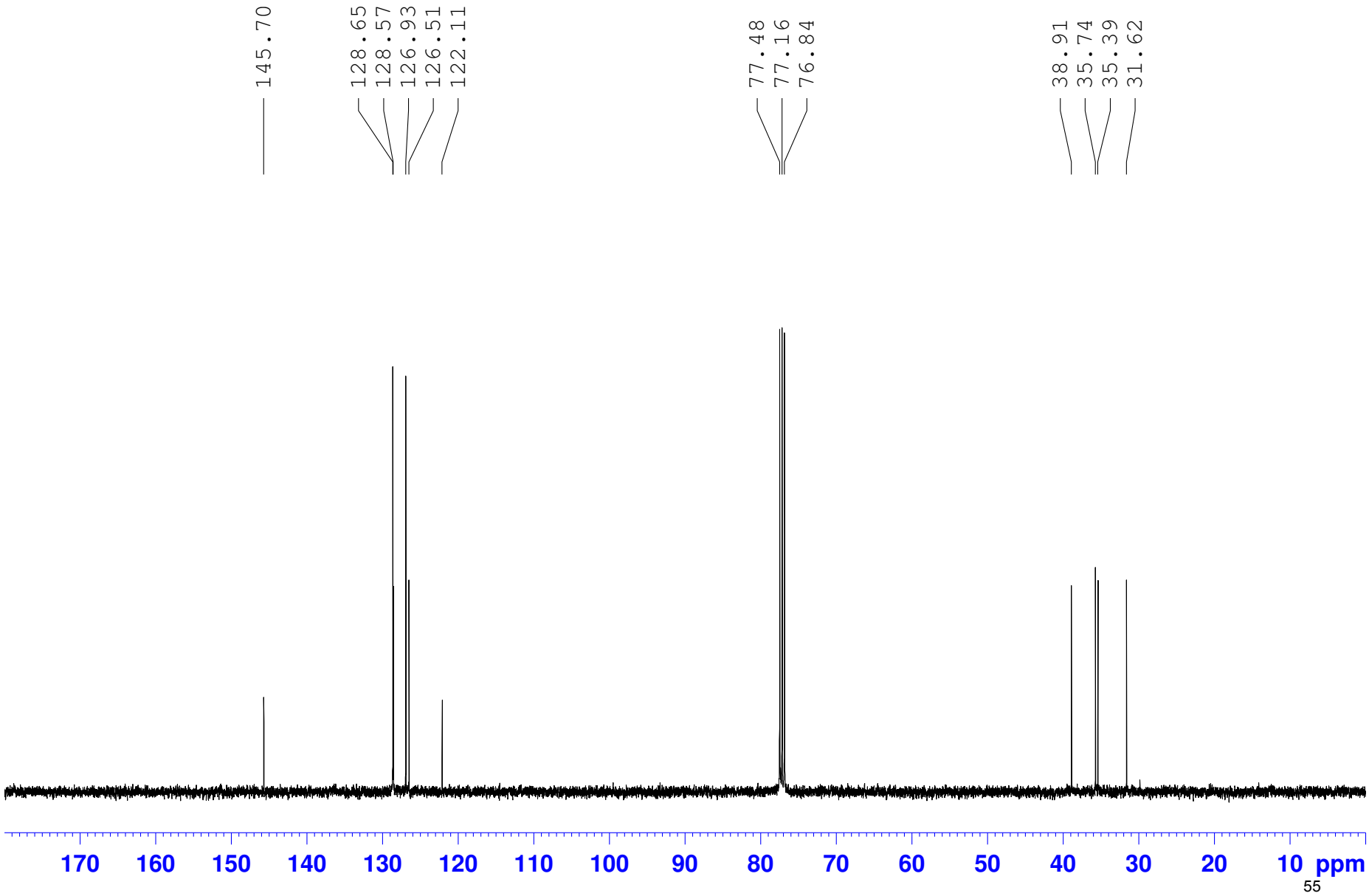
2p



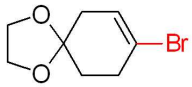
jp3-090-prod-CDCl3-400-13C-New



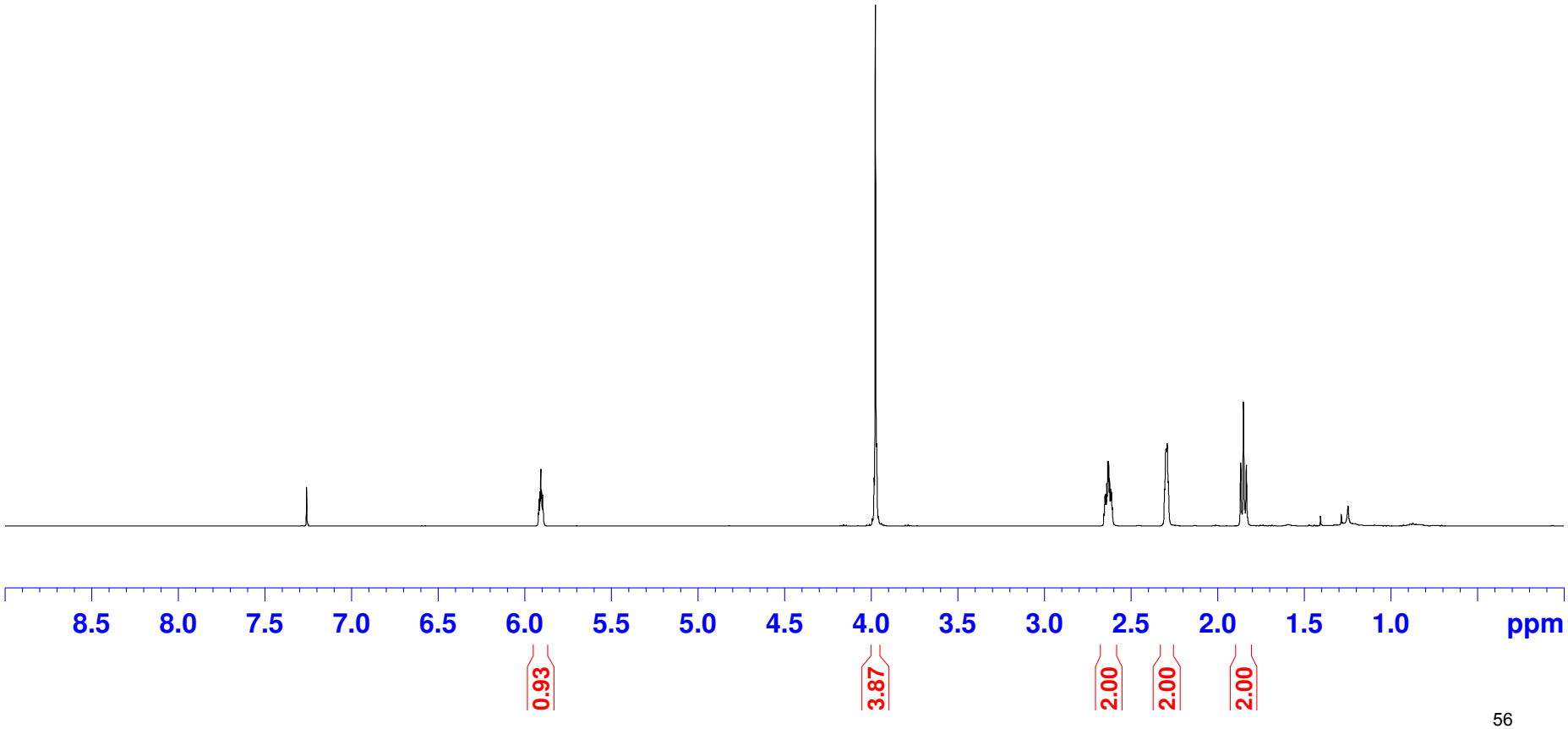
2p



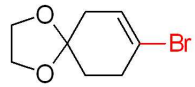
jp3-082-prod-CDCl3-400-1H-1



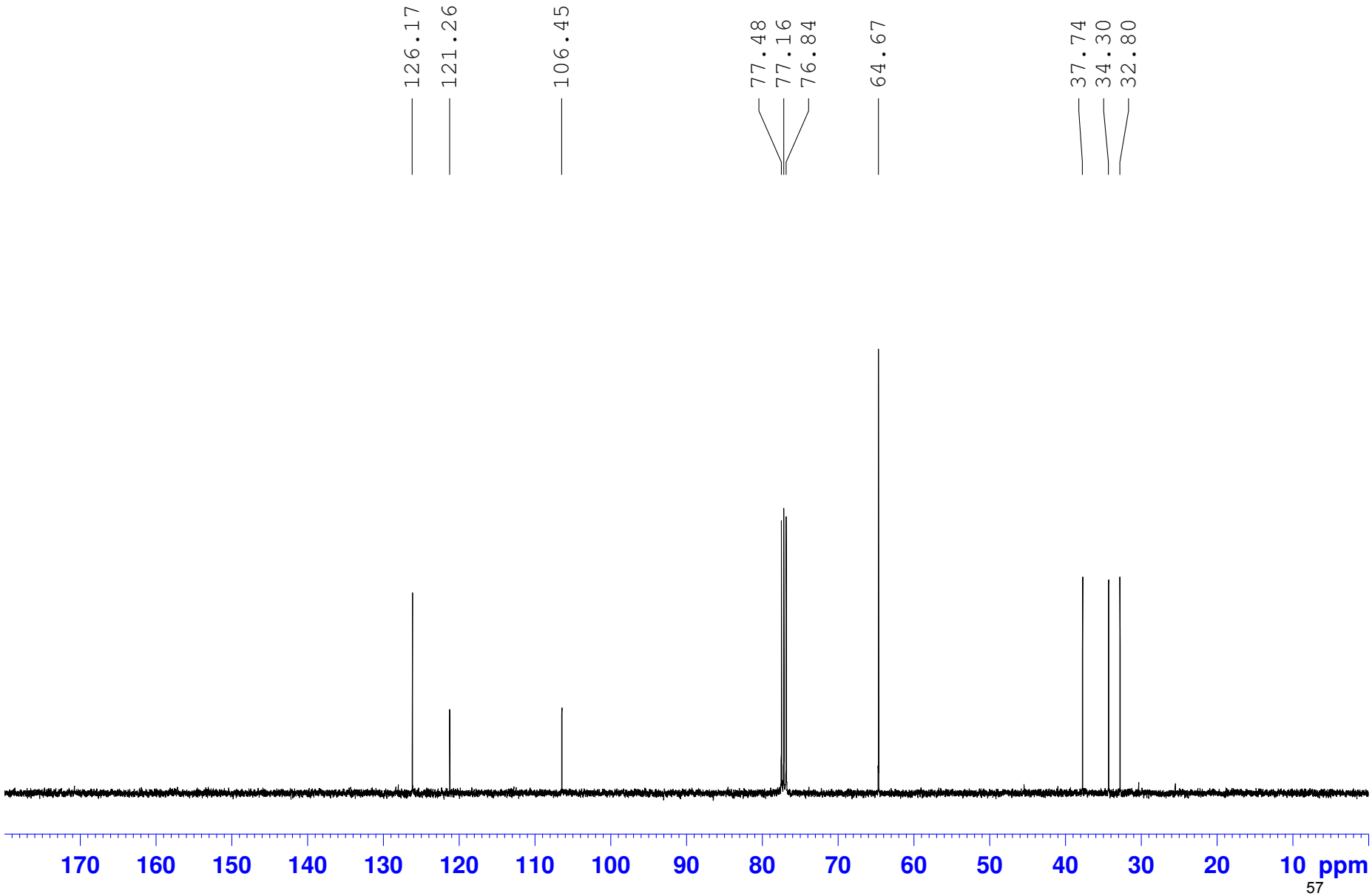
2q



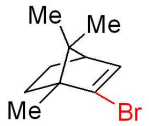
jp3-117-prod-CDCl3-400-13C



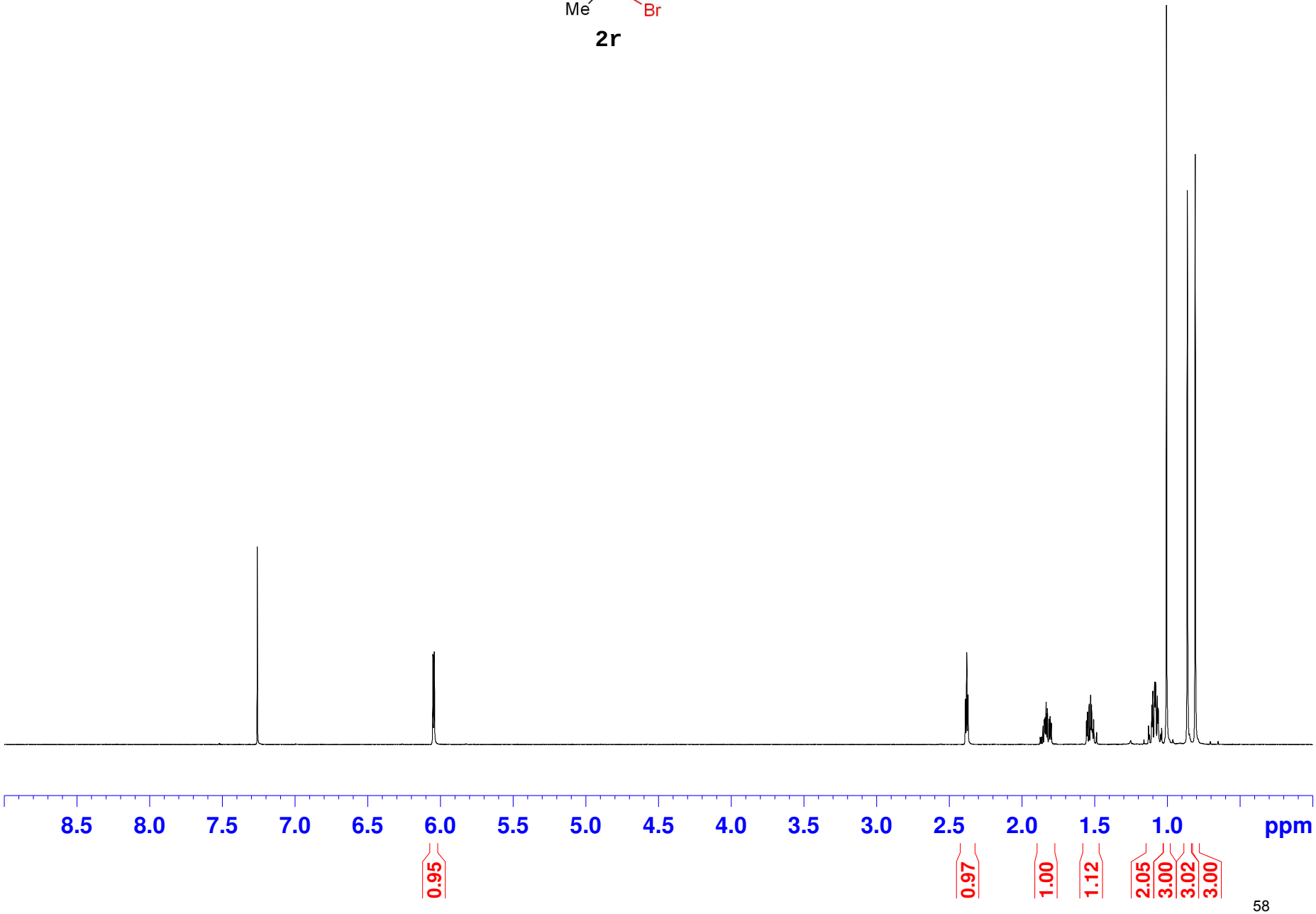
2q



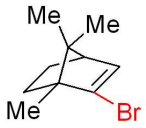
jp3-120-CDCl3-401-1H-2011-07-01



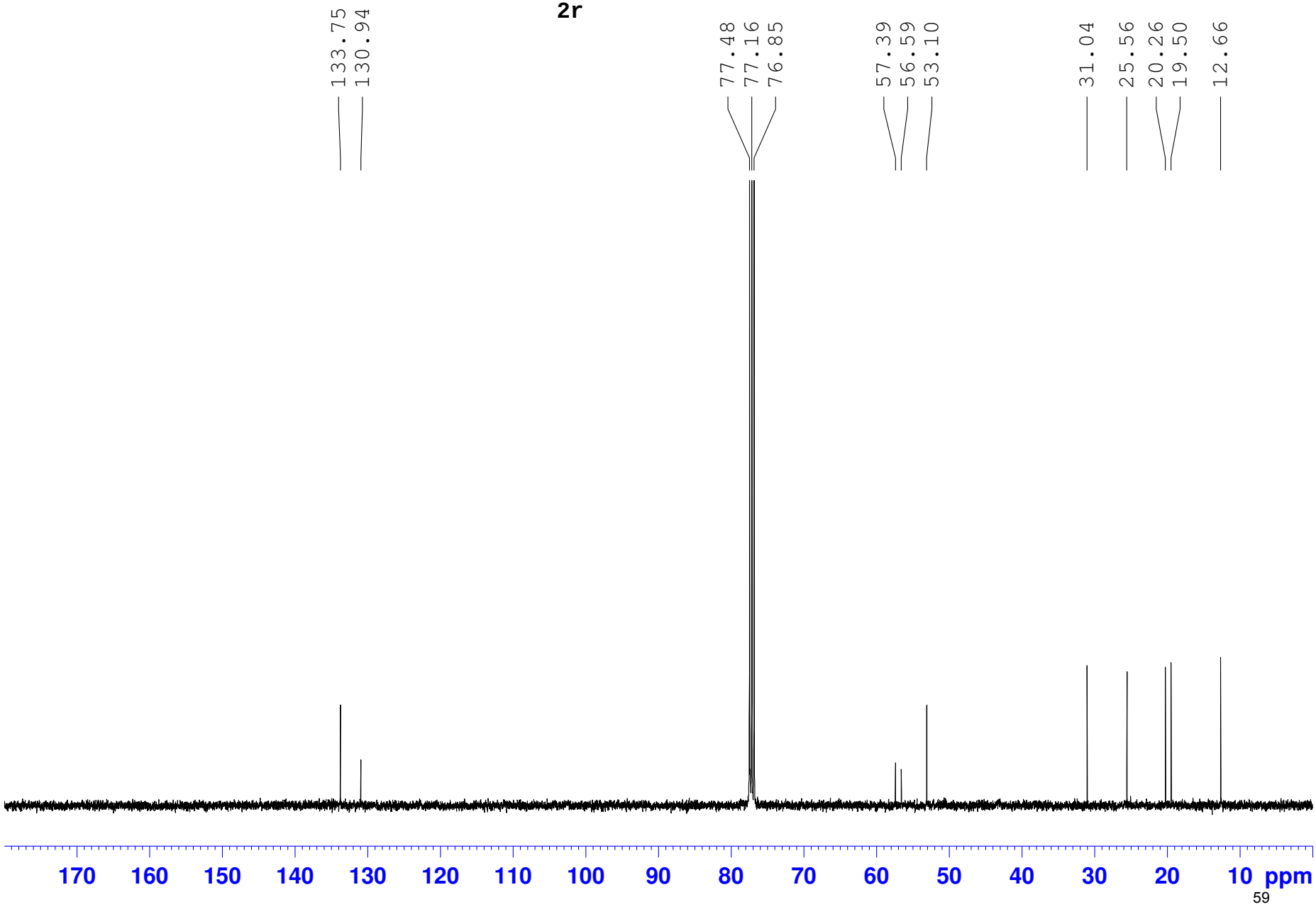
2r



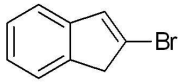
jp3-120-CDCl3-401-13C-2011-07-01



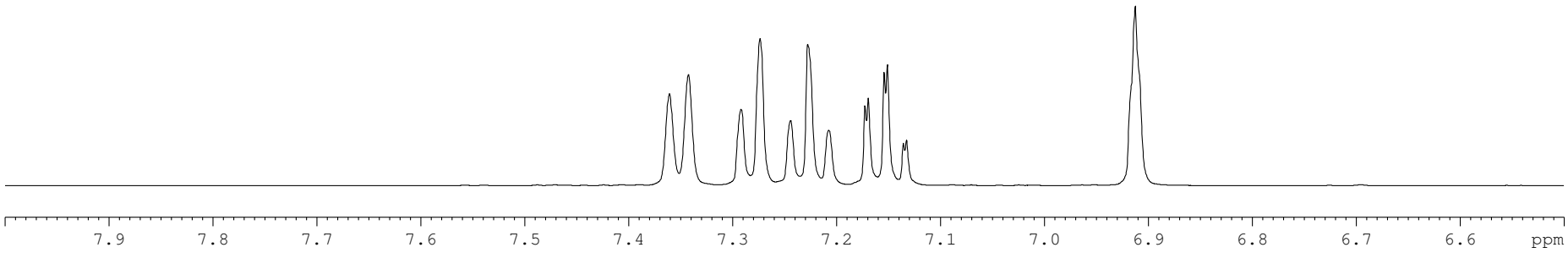
2r

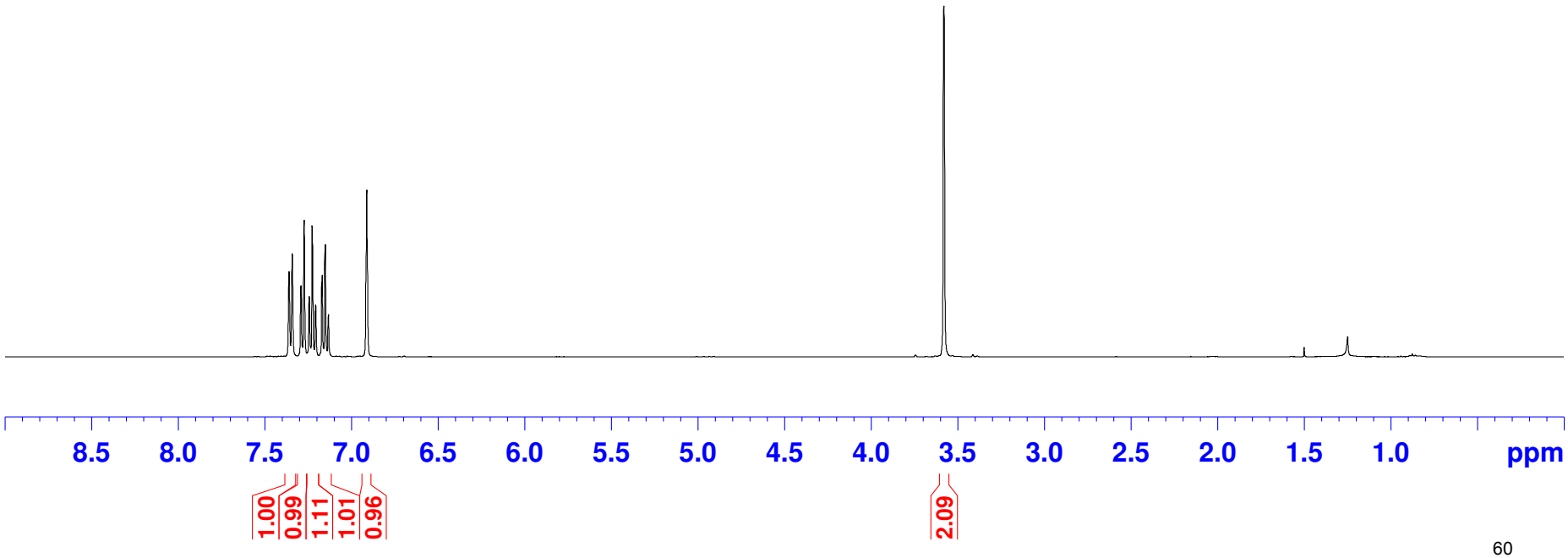


jp3-134-prod-CDCl3-400-1H

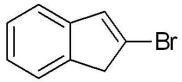


2s



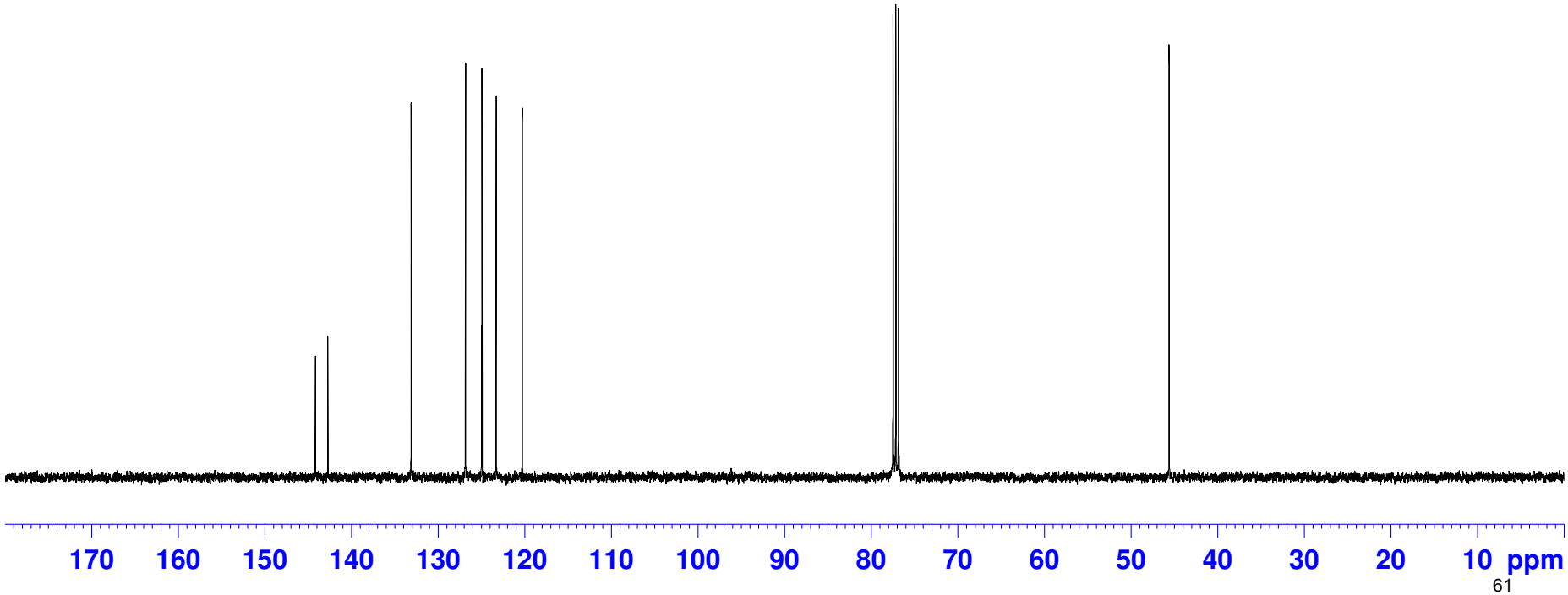


jp3-134-prod-CDCl3-400-13C

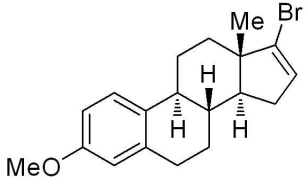


2s

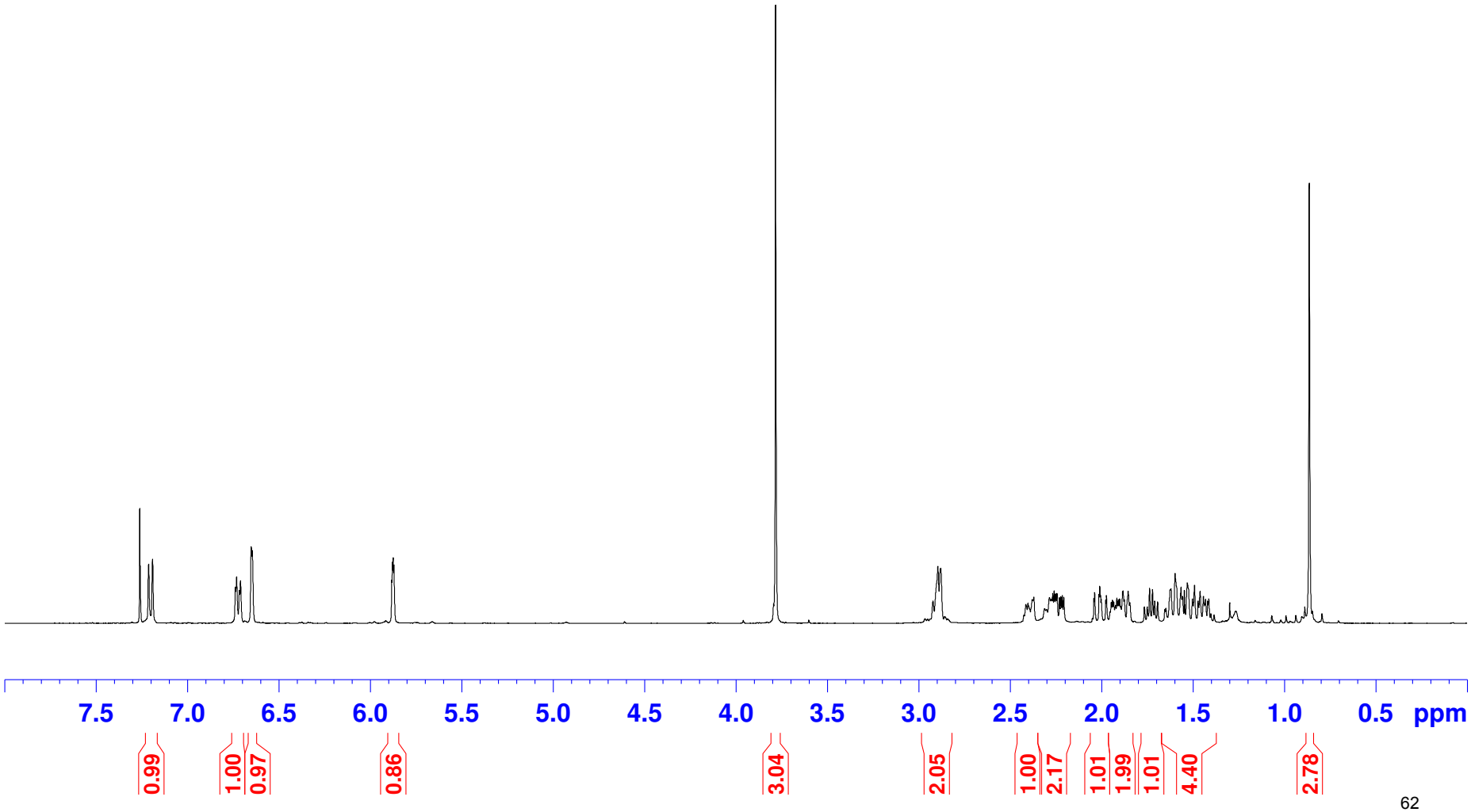
144.17
142.75
133.12
126.85
125.01
124.94
123.31
120.30
77.48
77.16
76.84
45.60



jp3-146-prod-CDCl3-400-1H

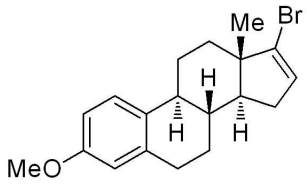


2t

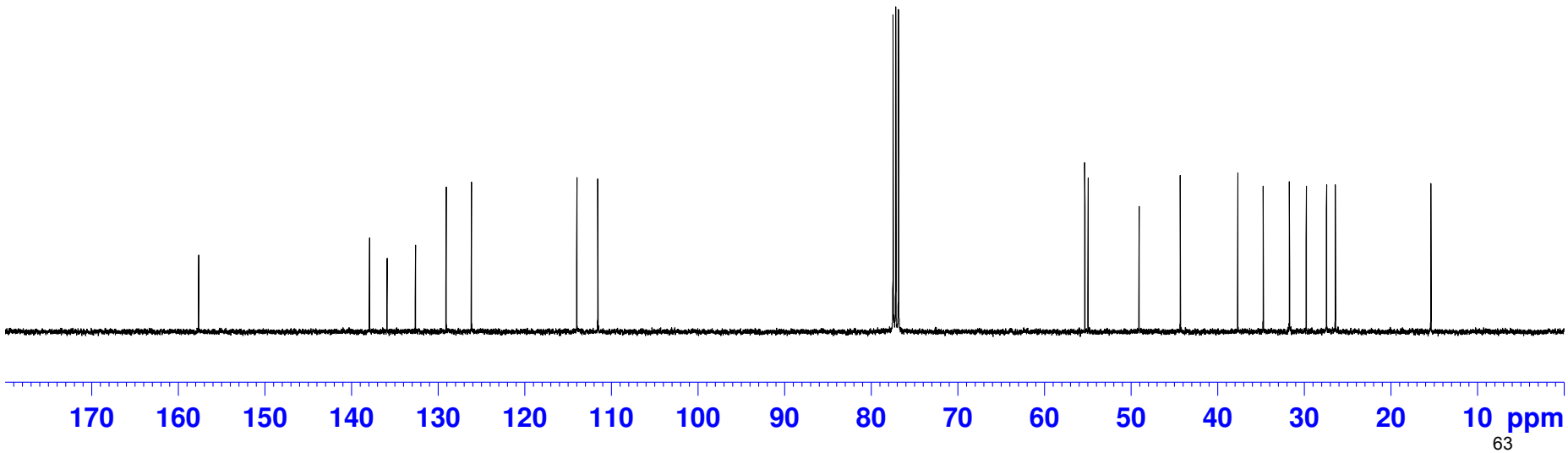


jp3-141-prod-CDCl3-400-13C

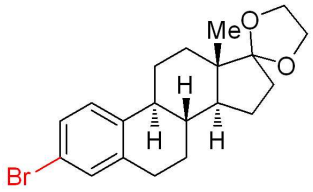
157.66
137.92
135.91
132.63
129.09
126.16
113.99
111.58
77.48
77.16
76.85
55.34
54.96
49.07
44.32
37.67
34.74
31.71
29.77
27.43
26.42
15.38



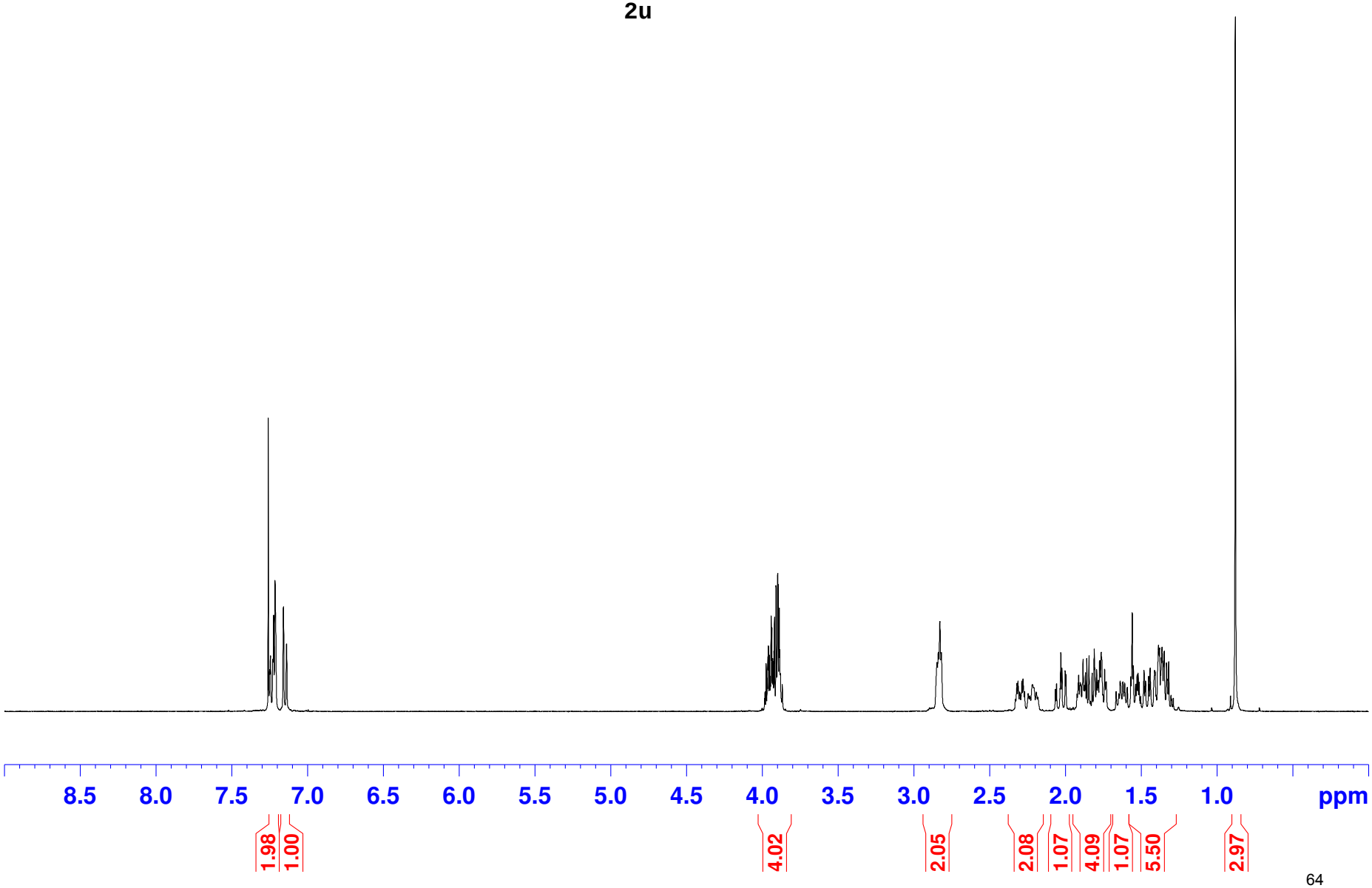
2t



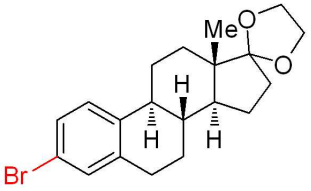
jp3-118-prod-CDCl3-400-1H-New



2u

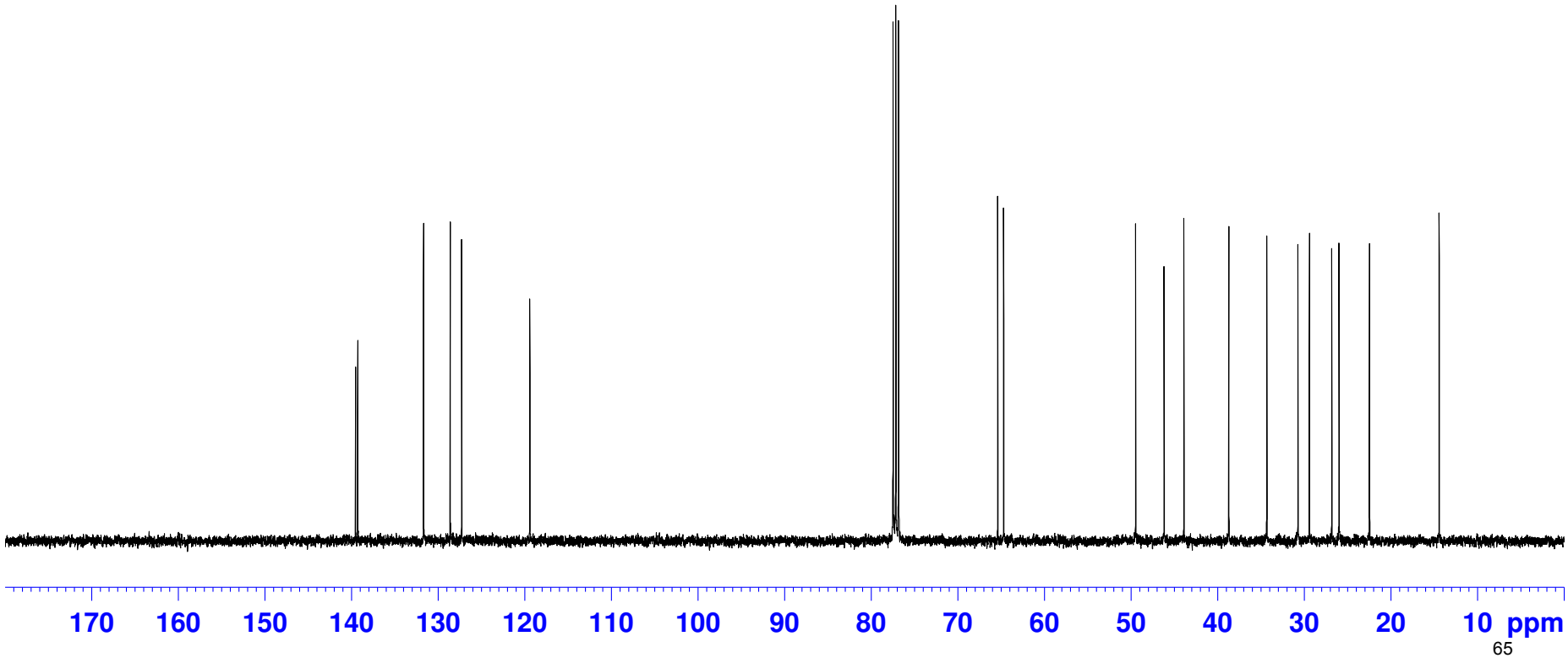


jp3-118-prod-CDCl3-400-13C

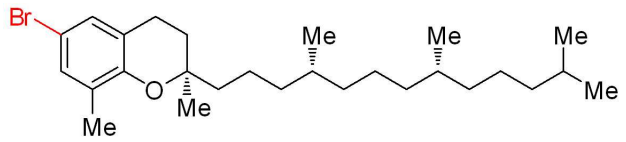


2u

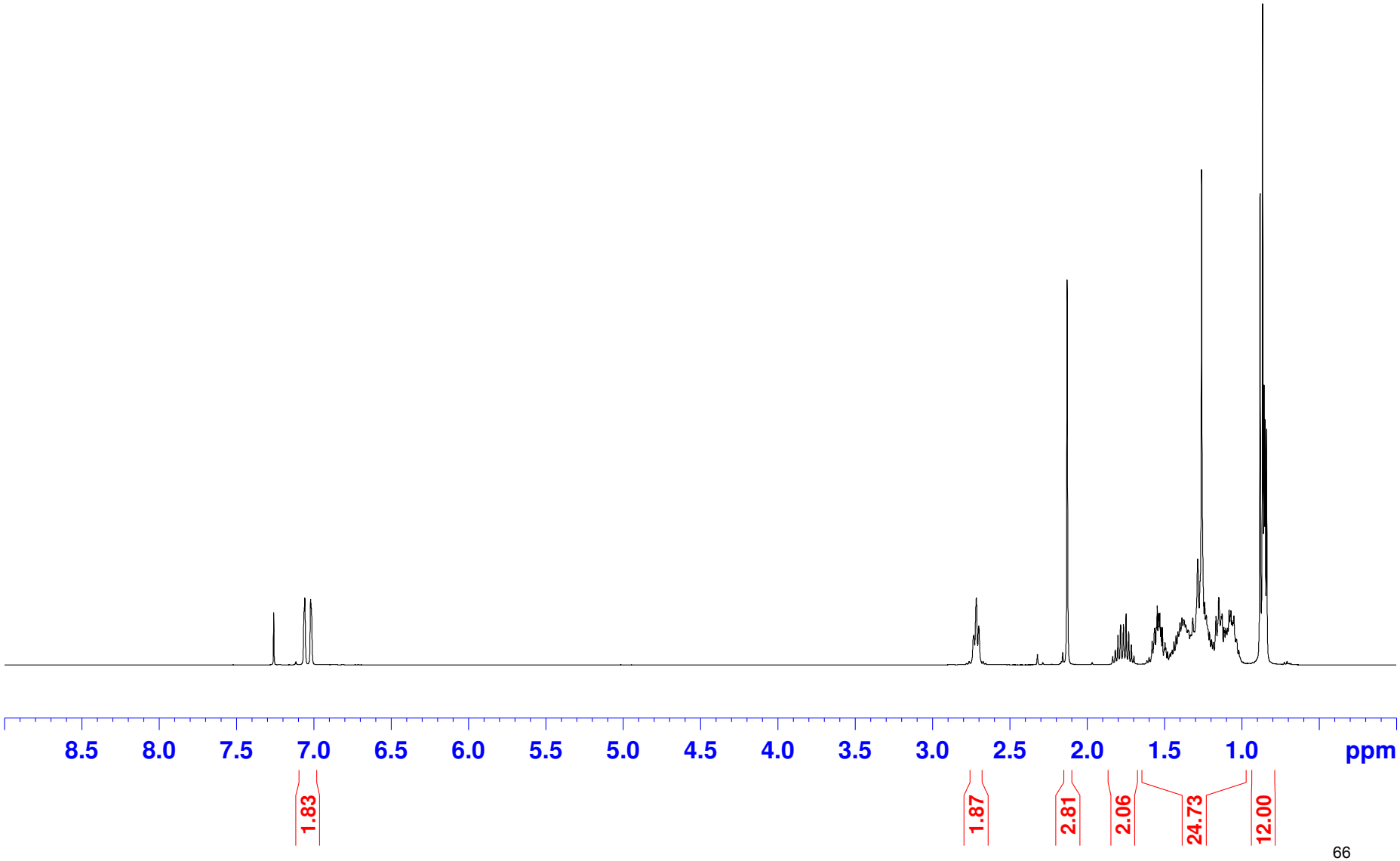
139.53
139.29
131.70
128.61
127.30
119.43
119.41
77.48
77.16
76.84
65.39
64.71
49.47
46.18
43.89
38.70
34.32
30.73
29.41
26.82
25.98
22.46
14.42



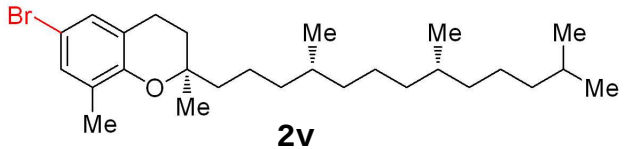
jp3-119-prod-CDCl3-400-1H-2



2v

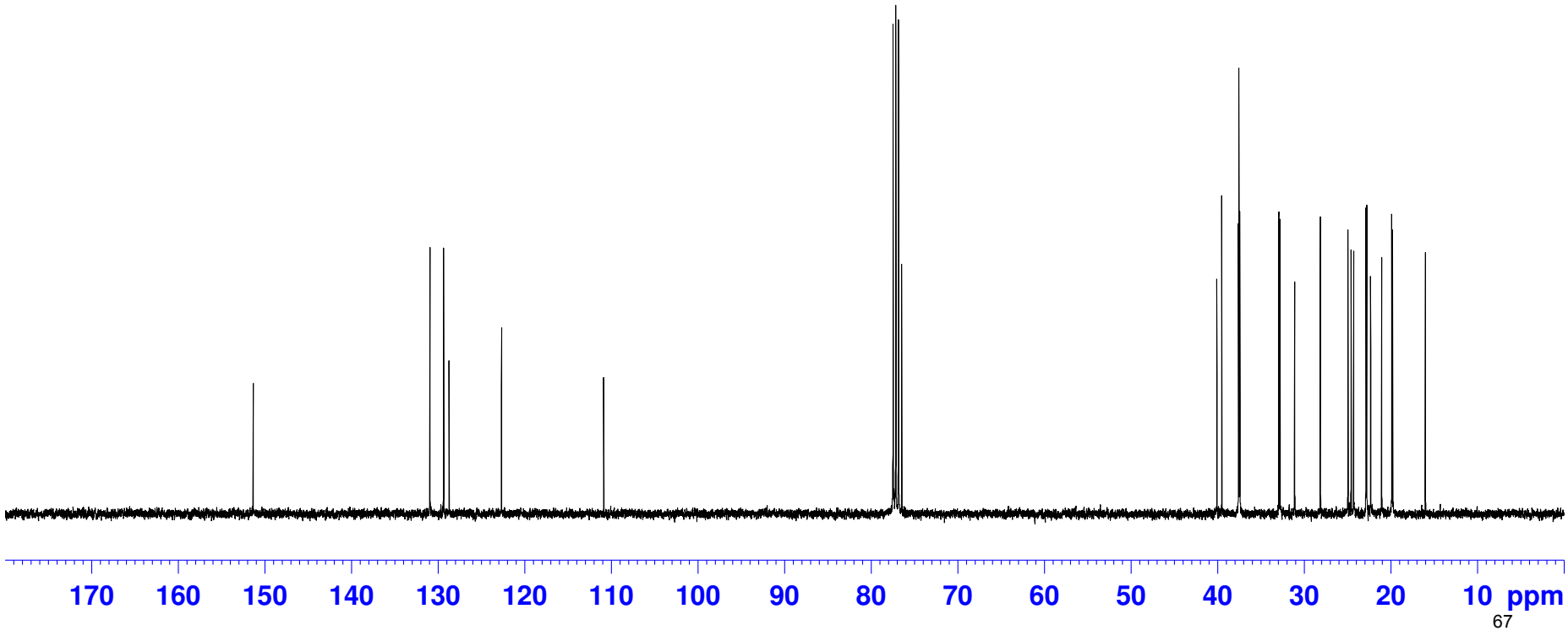


jp3-119-prod-CDCl3-400-13C

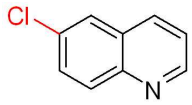


2v

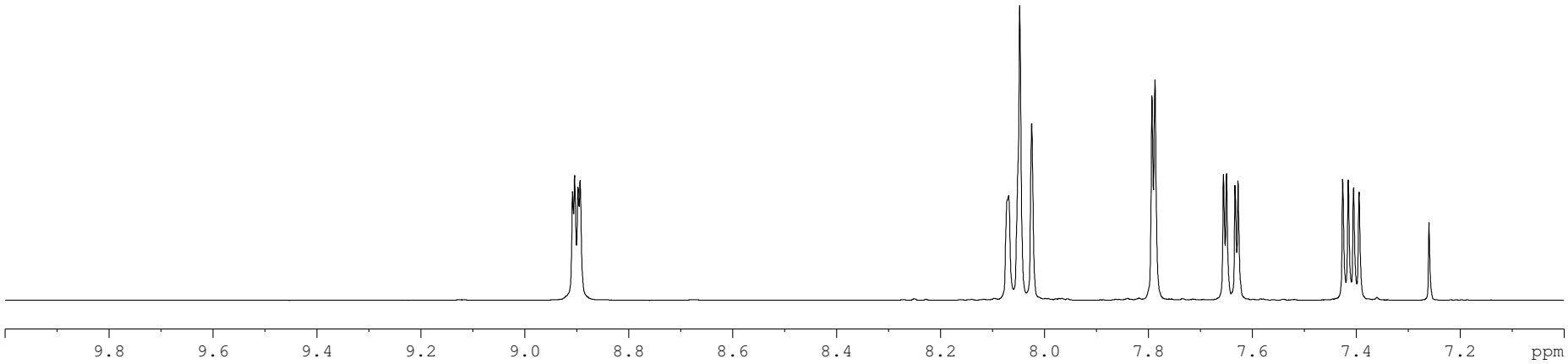
151.36
130.95
129.37
128.75
122.69
110.88
77.48
77.16
76.84
76.48
40.08
39.53
37.59
37.54
37.44
32.95
32.80
31.11
28.14
24.96
24.60
24.30
22.89
22.79
22.33
21.06
19.91

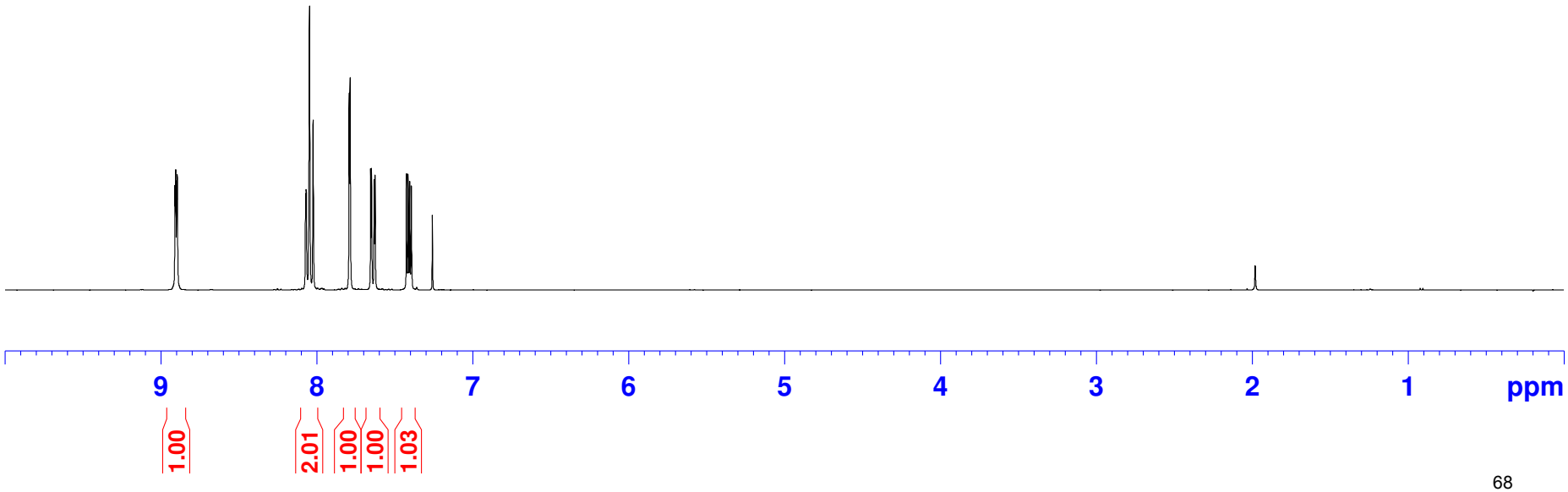


jp3-122-prod-CDCl3-400-1H-2011-07-01

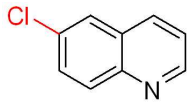


3a



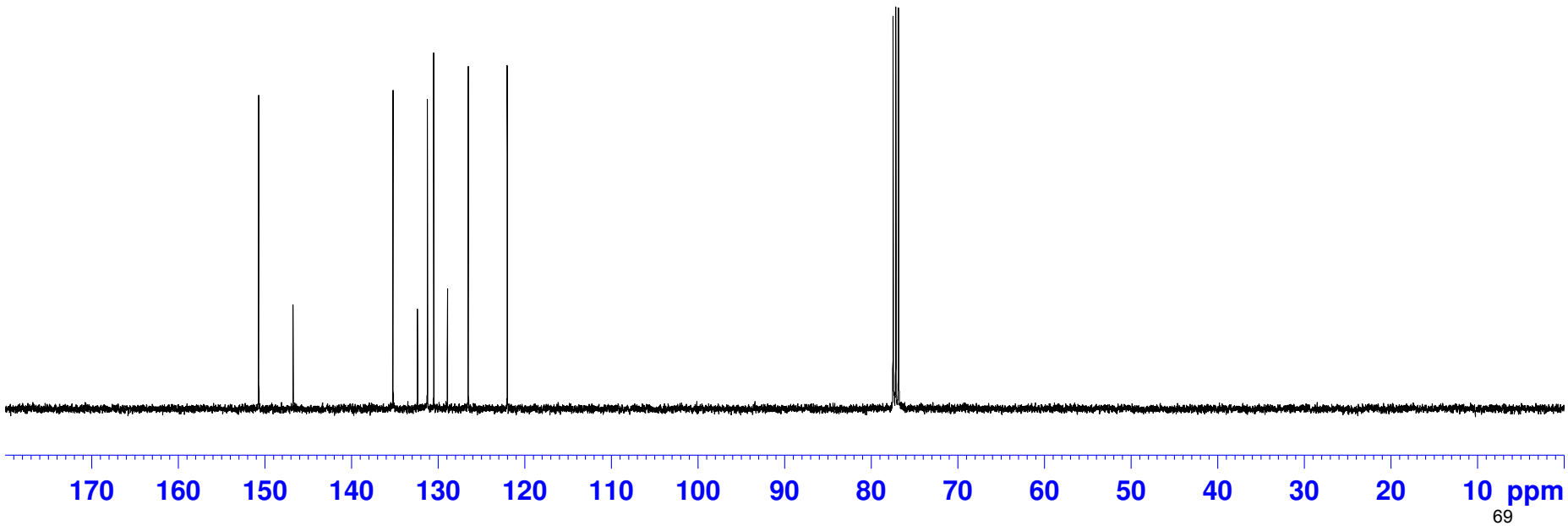


jp3-095-prod-CDCl3-400-13C

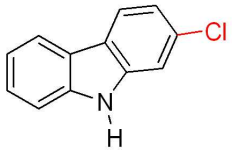


3a

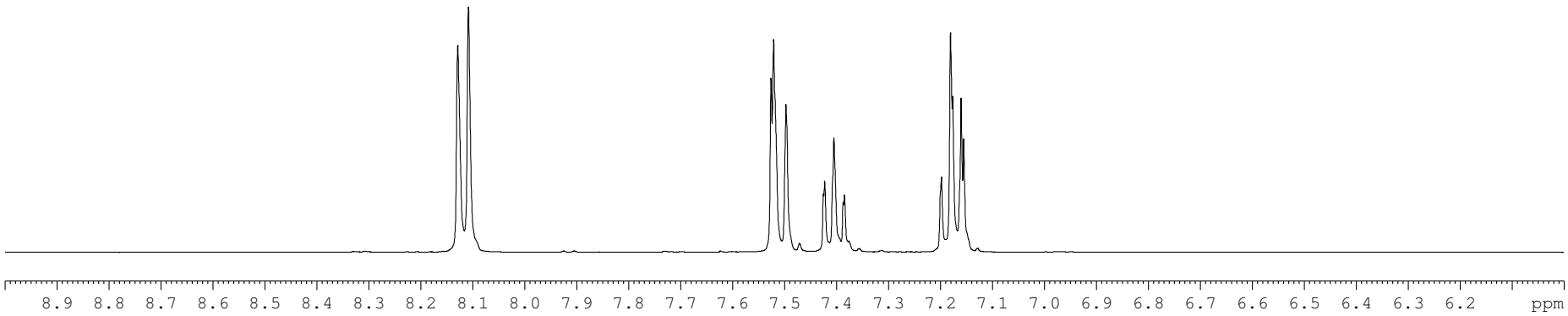
150.73
146.76
135.22
132.39
131.24
130.52
128.93
126.52
122.02
77.48
77.16
76.84

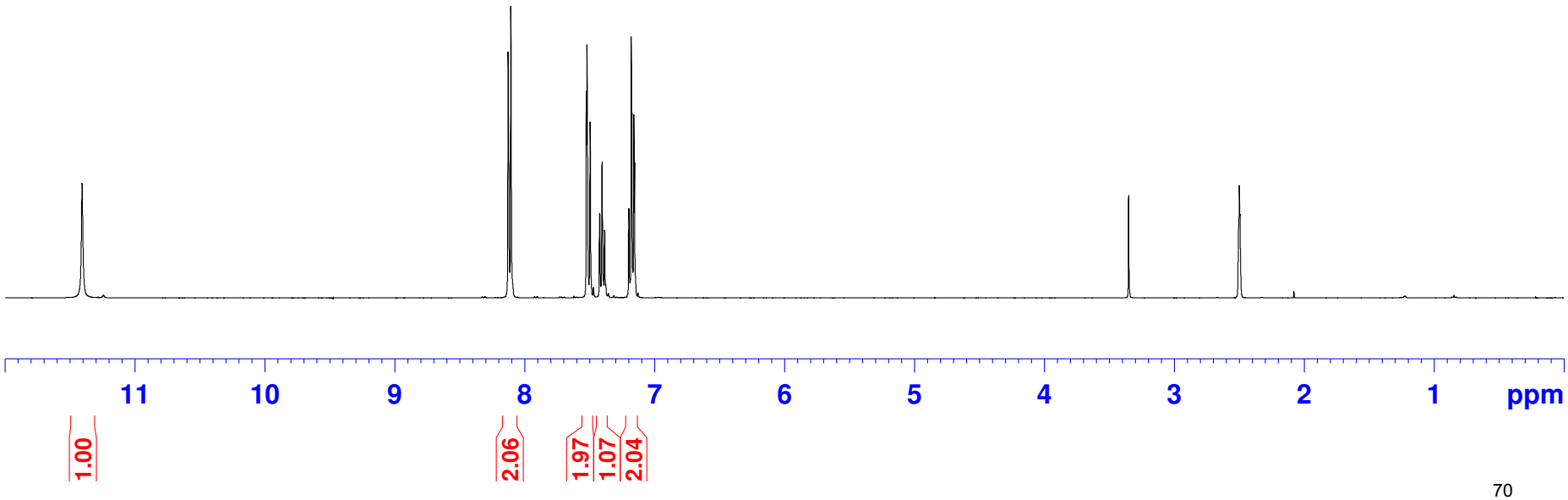


jp3-123-prod-DMSO-400-1H-29

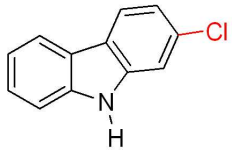


3b

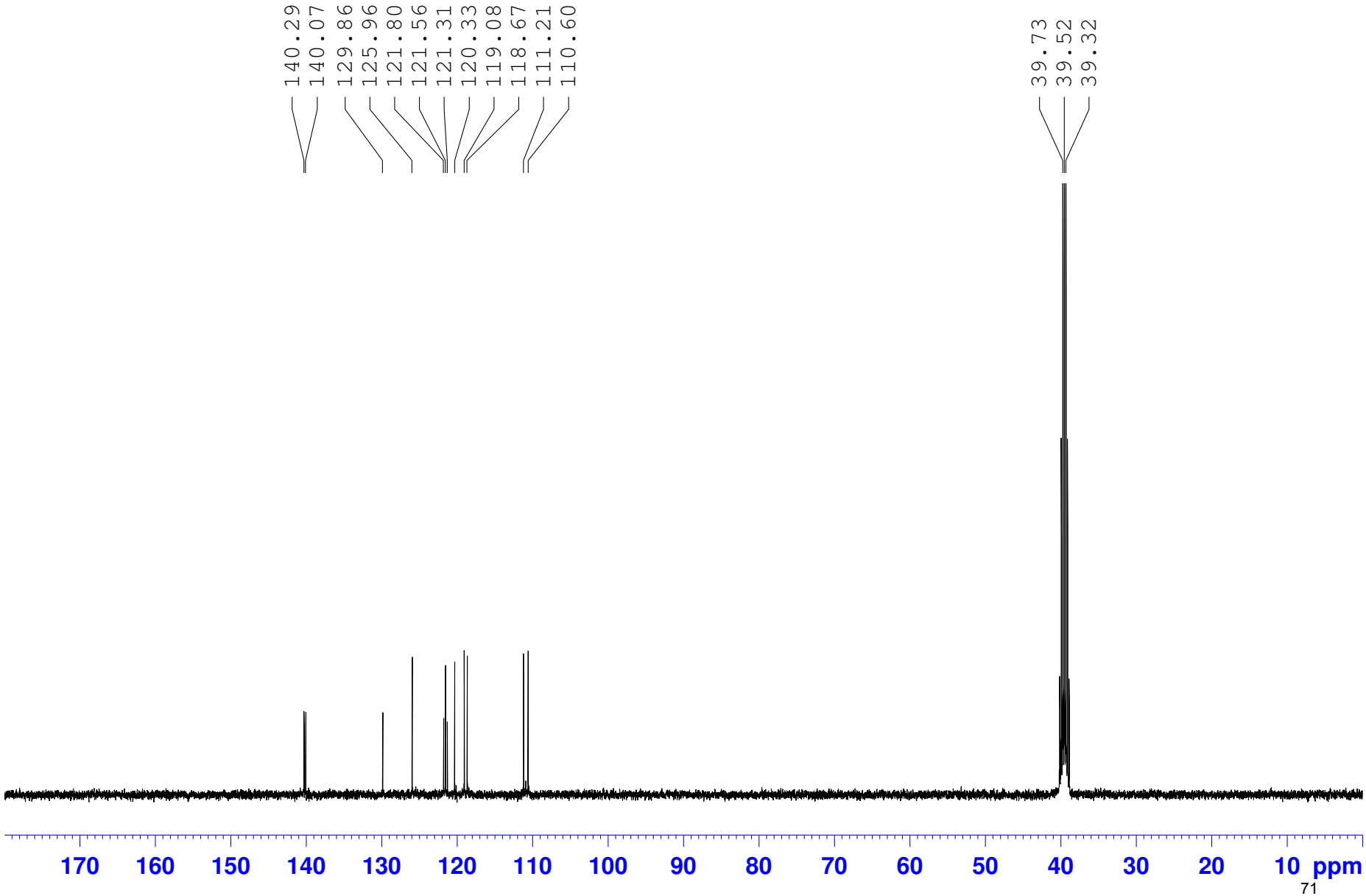




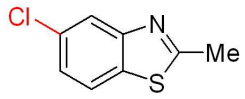
jp3-123-prod-DMSO-400-13C-29



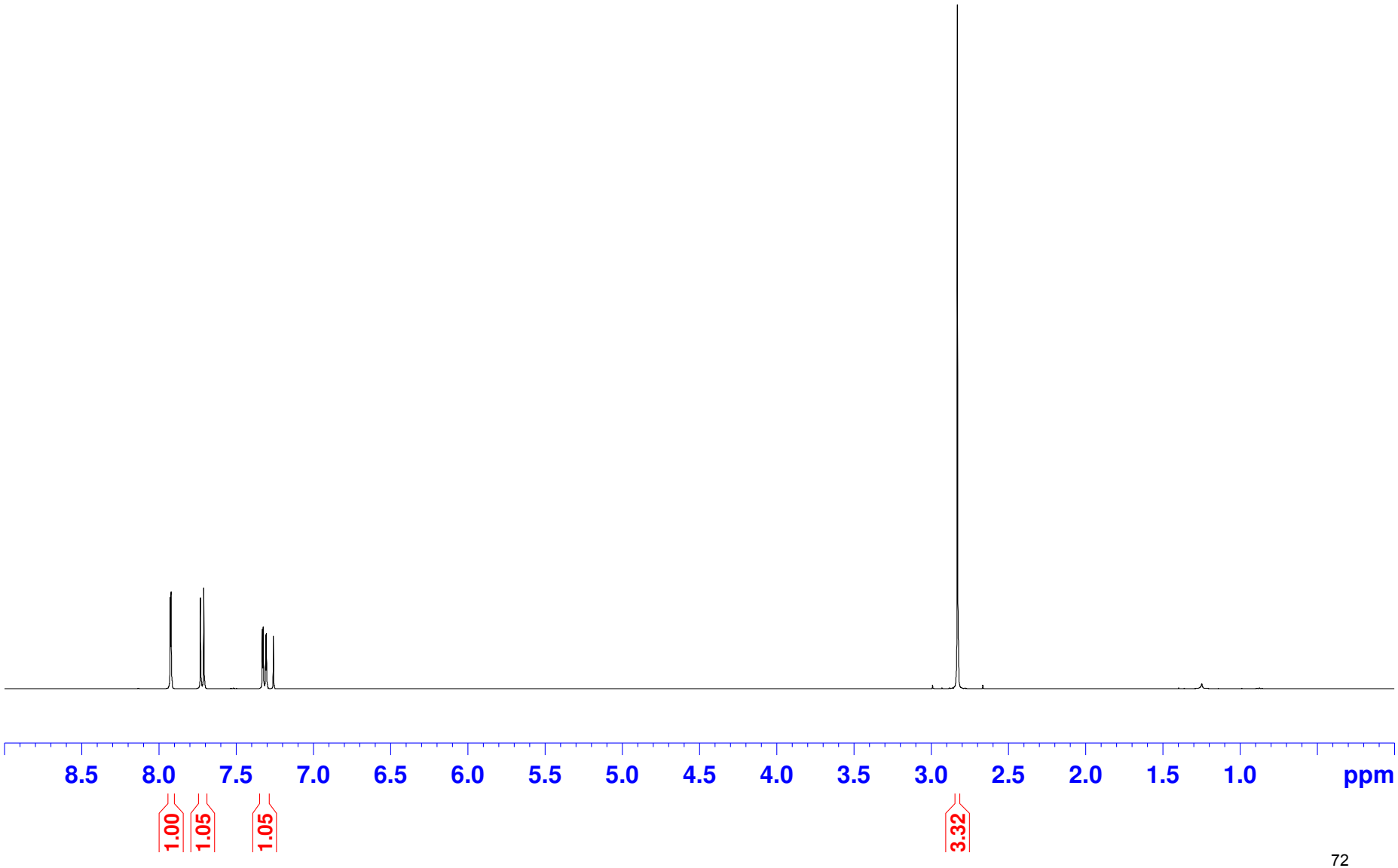
3b



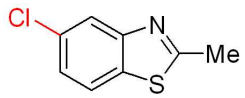
jp3-124-prod-CDCl3-400-1H-1



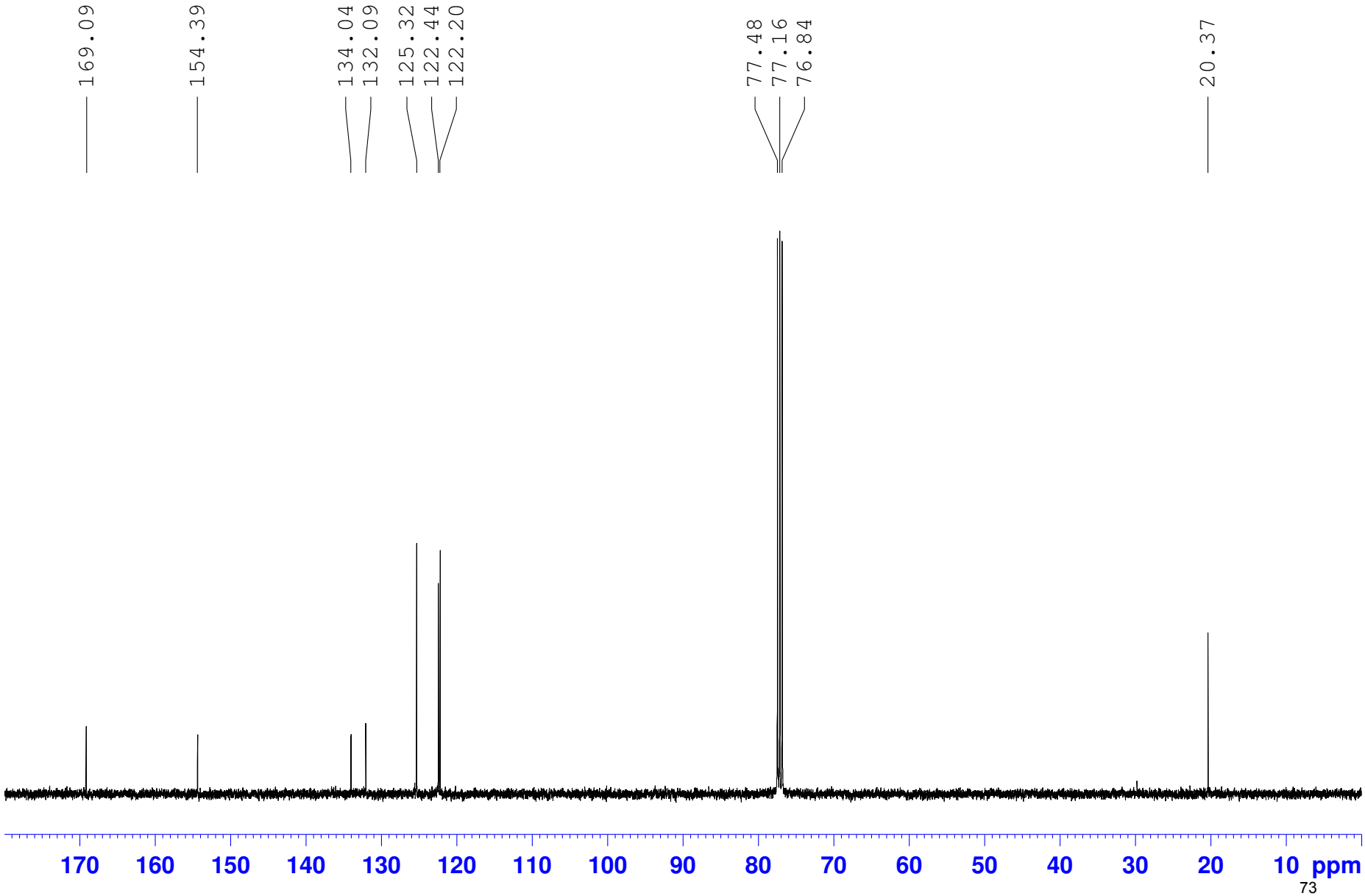
3c



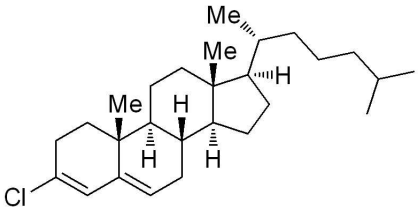
jp3-097-prod-CDCl3-400-13C



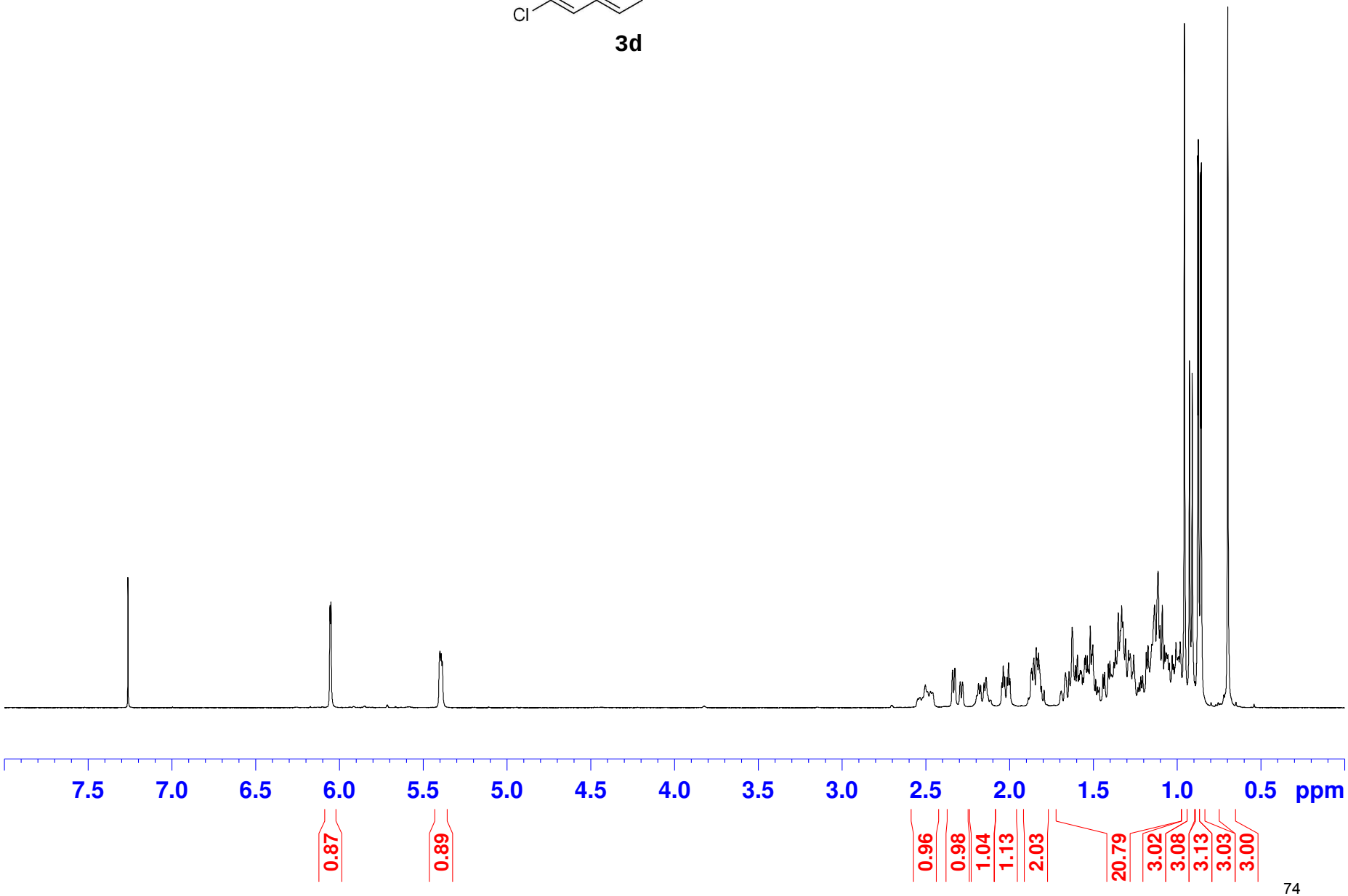
3c



jp3-140-prod-CDCl3-401-1H

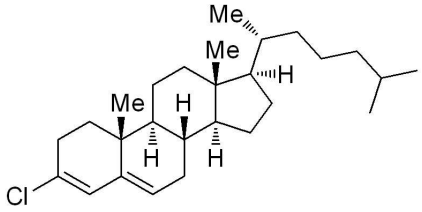


3d

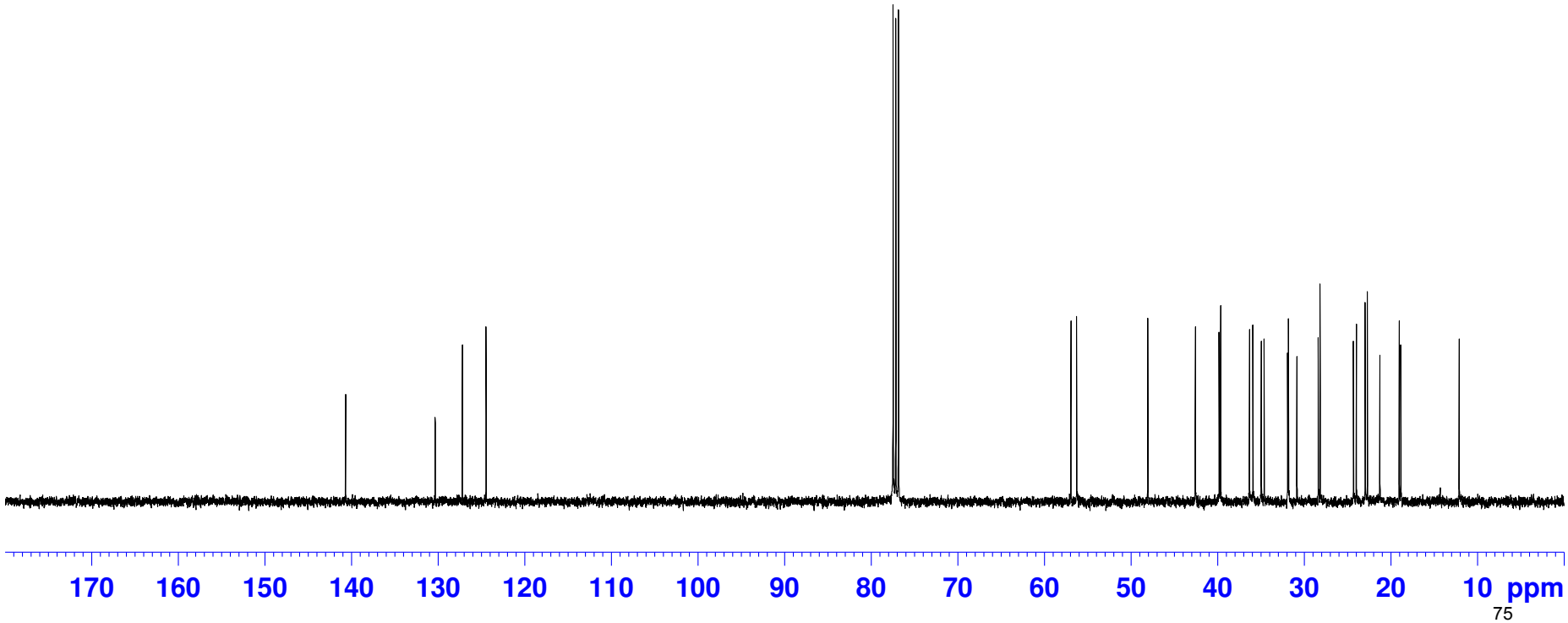


jp3-140-prod-CDCl3-401-13C

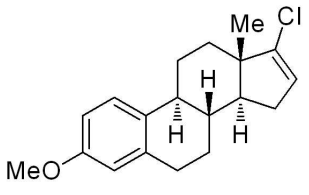
140.68
130.35
127.20
124.47
77.48
77.16
76.84
56.94
56.28
48.07
42.58
39.83
39.66
36.32
35.94
34.95
34.63
31.92
31.83
30.85
28.38
28.17
24.33
23.98
22.98
22.72
21.27
19.02



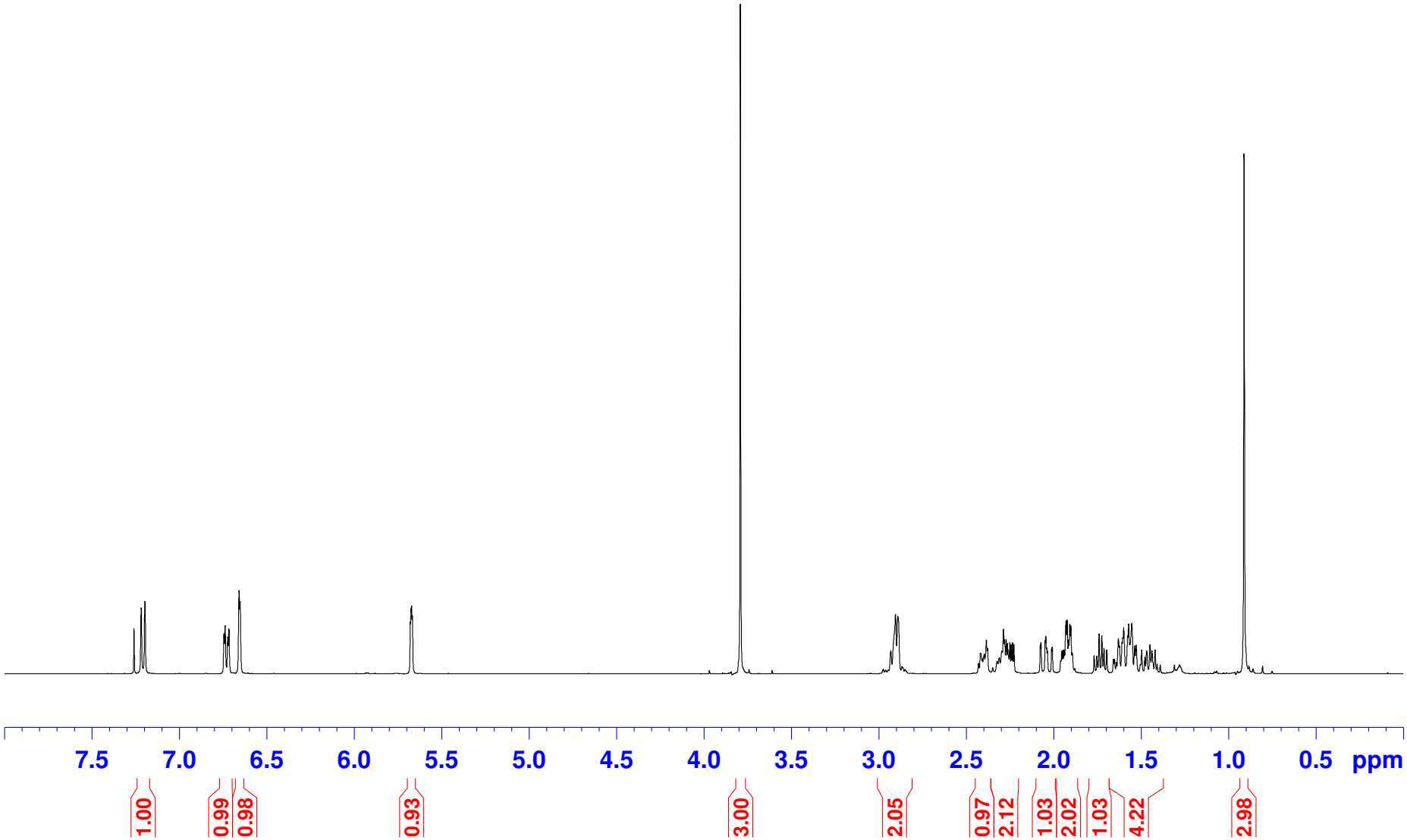
3d



jp3-142-prod-CDCl3-400-1H

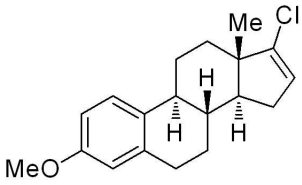


3e

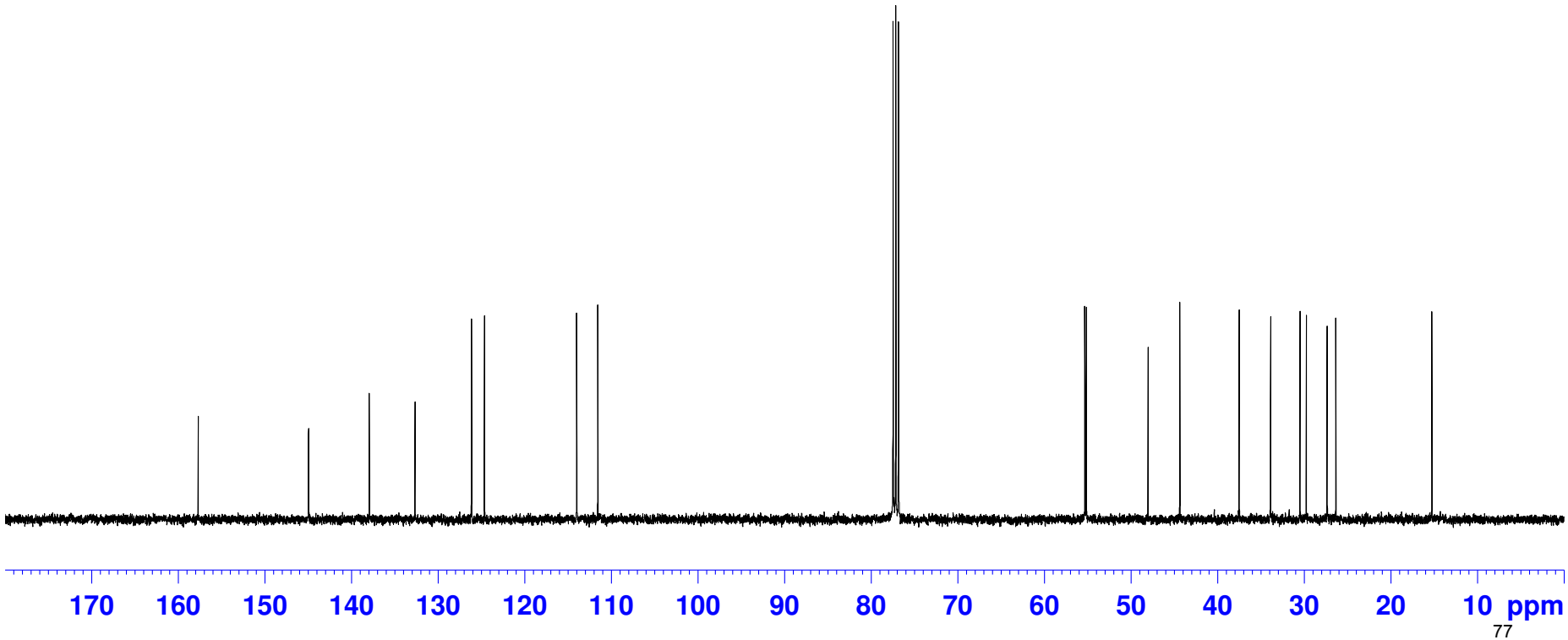


jp3-142-prod-CDCl3-400-13C

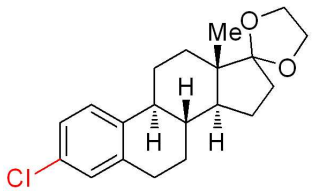
157.66
144.97
137.95
132.68
126.15
124.66
114.01
111.58
77.48
77.16
76.84
55.34
55.16
48.03
44.37
37.51
33.88
30.49
29.76
27.36
26.36
15.27



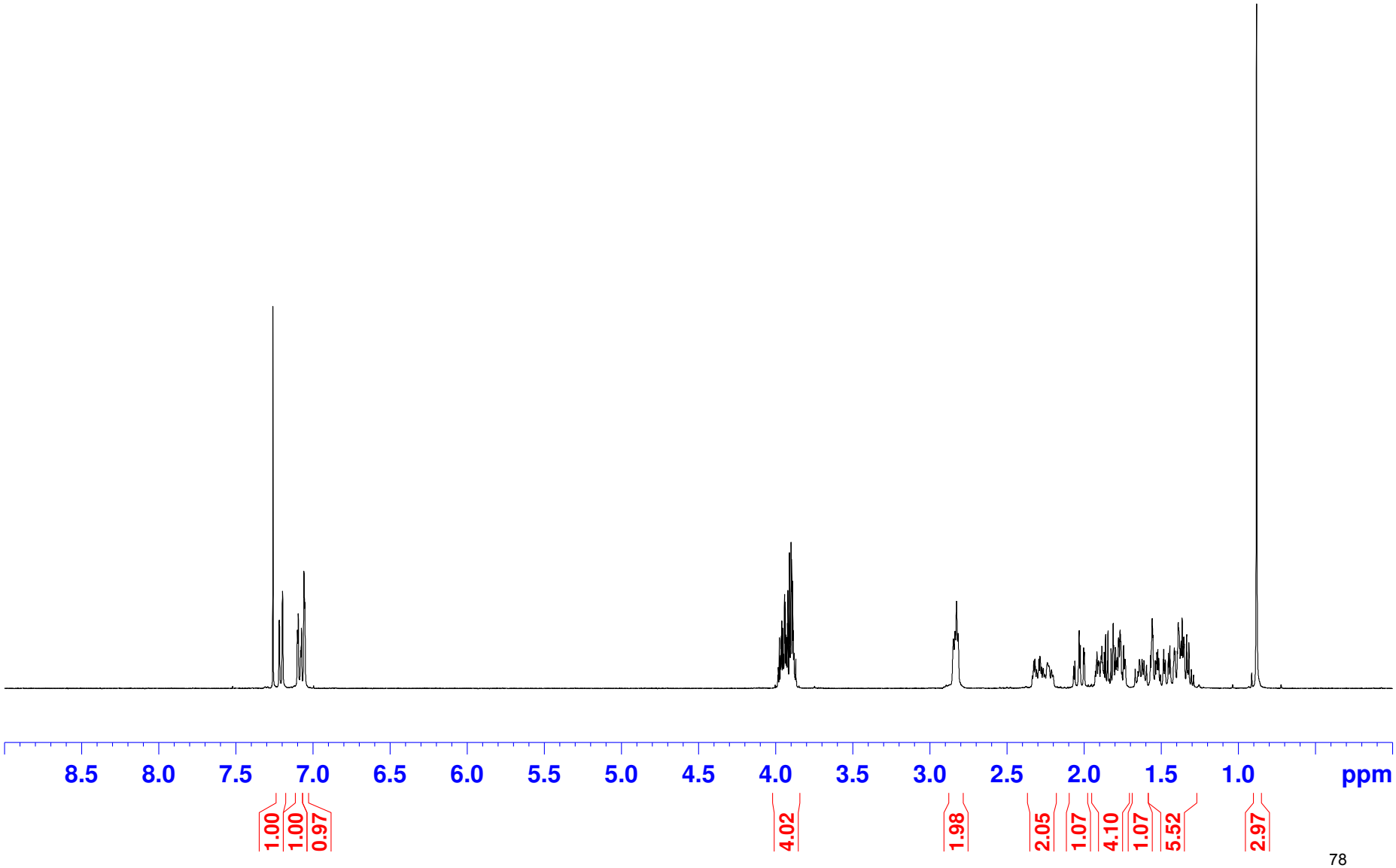
3e



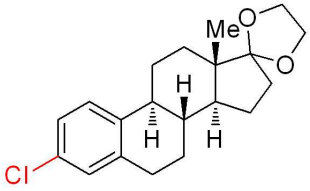
jp3-125-prod-CDCl3-400-1H-New



3f

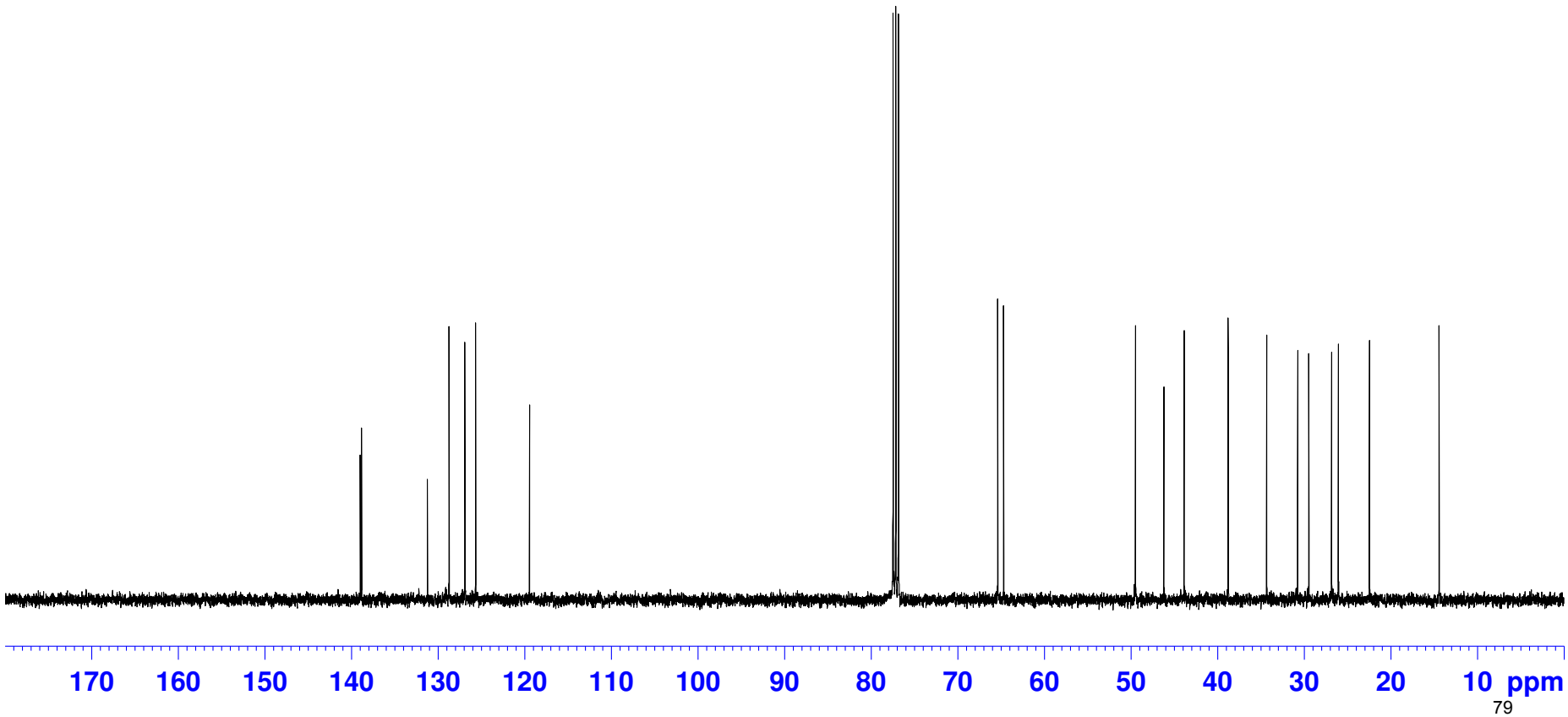


jp3-098-prod-CDCl3-400-13C

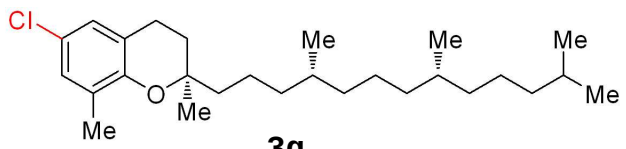


3f

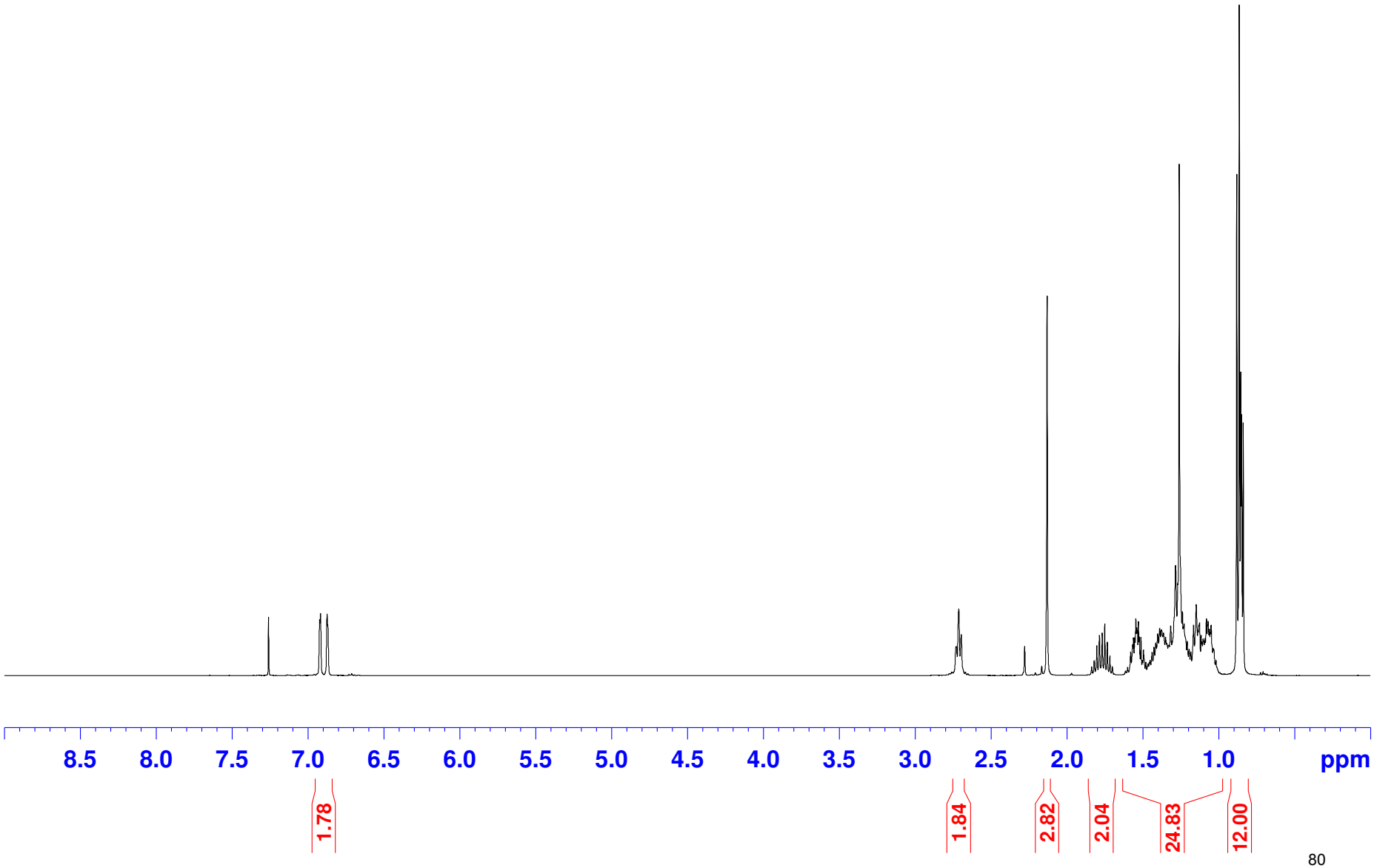
139.01
138.86
131.25
128.75
126.92
125.68
119.45
77.48
77.16
76.84
65.40
64.72
49.48
46.20
43.86
38.78
34.33
30.76
29.47
26.84
26.06
22.47
14.43



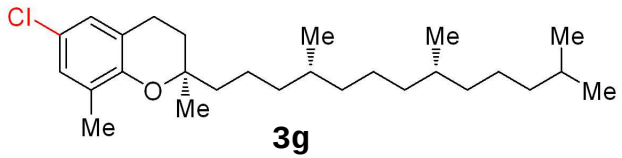
jp3-129-prod-CDCl3-400-1H-1



3g



jp3-129-prod-CDCl3-400-13C



3g

150.81
128.24
128.12
126.39
123.42
122.09
77.47
77.16
76.84
76.45
40.08
39.52
37.59
37.54
37.43
32.95
32.80
31.13
28.13
24.96
24.59
24.29
22.88
22.78
22.40
21.06
19.90