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Supporting Information

69451 Weinheim, Germany

Asymmetric Palladium-Catalyzed Intramolecular α-Arylation of Aldehydes.

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Supporting Information

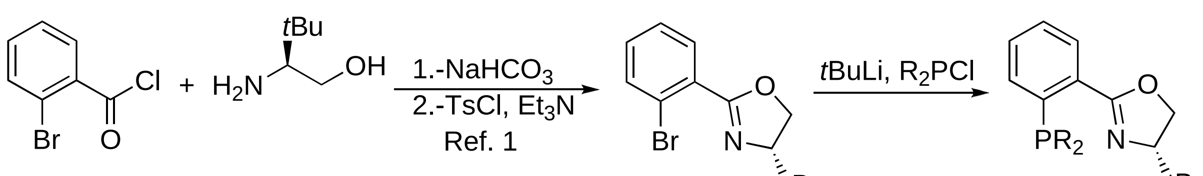
GENERAL CONSIDERATIONS

Reagents. All reactions were set up in the air (with no use of a glovebox) and carried out under an argon atmosphere in resealable screw-cap test tubes. $Pd(OAc)_2$ was a gift from BASF. Powdered Cs_2CO_3 was a gift from Chemetall. The bulk of the base was stored under nitrogen in a Vacuum Atmospheres glovebox. Small portions (~ 5 g) were removed from the glovebox in glass vials, stored in the air in a desiccator filled with anhydrous calcium sulfate, and weighed in the air. Anhydrous solvents were purchased from Aldrich in Sure/Seal™ bottles. All reagents were purchased from commercial sources and used as received. Flash chromatography was performed with EM Science silica gel 60 (230-400 mesh).

Analytical Methods. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR (where applicable), ^{31}P NMR (where applicable), IR spectroscopy and in most cases, elemental analysis. ^{1}H NMR and ^{13}C NMR spectra and melting points (where applicable) are included for all known compounds and for all new compounds not characterized by elemental analysis. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL 300 MHz. Infrared spectra were recorded on a Perkin-Elmer Model 2000 FT-IR using NaCl plates (thin film). The rotatory analyses were perfomed on Jacsco P-1010 polarimeter using Na lamp (589 nm). The concentration of the samples is given in g 100 mL^{-1}. HPLC analyses were carried out on an Agilent 1100 Series system with Daicel Chiralcel® or Chiralpak® columns (4.6 mm x 250 mm) in hexanes/*i*PrOH mixtures. Chiral GC analyses were performed on a Agilent 6850 Series system with a Chrompack capillary column (CP Chirasil-Dex CD, 25 m x 0.25 mm x 0.25

mm); Astec G-TA column (30 m x 0.25 mm) or Chiraldex capillary column (B-DA 30 m x 0.25 mm). Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA. All ^{1}H NMR spectra are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals for $CHCl_3$ (7.27 ppm). All ^{13}C NMR spectra were reported in ppm relative to residual $CHCl_3$ (77 ppm) and were obtained with ^{1}H decoupling. Melting points were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on Hewlett-Packard 6890 gas chromatography instrument with a FID detector using 25m x 0.20 mm capillary column with cross-linked methyl siloxane as the stationary phase. The yields reported in tables 3 and 4 refer to isolated yields and represent an average of at least two independent runs. The pure compounds are estimated to be ≥ 95% pure as determined by ^{1}H NMR and GC analysis and/or combustion analysis.

SYNTHESIS OF LIGANDS

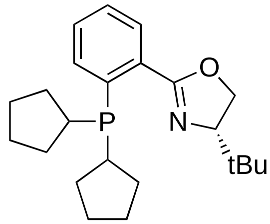


General procedure A for the preparation of the PHOX ligands (Table 2). To a solution of compound **S1**[1] (280 mg, 1.0 mmol) in Et_2O (5 mL) was added at −78 °C and under Ar *t*BuLi (705 µL, 1.2 mmol) dropwise. The mixture was stirred at −78 °C for 1 h, R_2PCl (1.2 mmol) was added. The reaction mixture was allowed to warm at RT and it was stirred at this temperature for 1 h. At this time it was poured into a separation funnel containing NH_4Cl aq. and it was extracted with Et_2O (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography or recrystallization.

General procedure B for the preparation of the PHOX ligands (Table 2). To a solution of compound **S1** (280 mg, 1.0 mmol) in Et_2O (5 mL) was added at −78 °C and under Ar *t*BuLi (705 µL, 1.2 mmol) dropwise. The mixture was stirred at −78 °C for 1 h, R_2PCl (1.2 mmol) was added. The reaction was allowed to warm at RT and it was stirred at this temperature for 1 h. Then, HBF_4 (48% in Et_2O, 530 µL, 2.0 mmol) was added and the mixture was stirred at RT for 30 min. The reaction was poured into a separation funnel containing H_2O and it was extracted with Et_2O (3 x 10 mL). The combined organic phases were dried over $MgSO_4$,

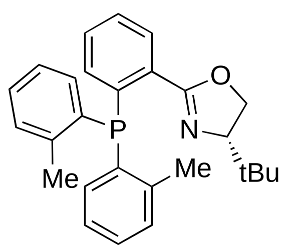
[1] K. Tani, D. C. Behenna, R. M. McFadden, B. M. Stoltz, *Org. Lett.* **2007**, *9*, 2529-2531.

filtered and concentrated under reduce pressure. The residue was subsequently purified by silica gel chromatography or recrystallization.



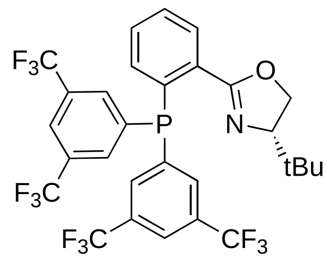
L9b

(*S*)-4-*tert*-butyl-2-(2-(dicyclopentylphosphino)phenyl)-4,5-dihydrooxazole L9b (Table 2, entry 1). General procedure A was followed using chlorodicyclopentylphosphine. Colorless solid; m.p. (88-90) °C; $[\alpha]_D$ –39.9 (*c* 0.382, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.60 (m, 2H), 7.43-7.26 (m, 2H), 4.38 (dd, *J* = 9.8, 8.7 Hz, 1H), 4.22 (t, *J* = 8.7 Hz, 1H), 4.08 (dd, *J* = 9.8, 8.7 Hz, 1H), 2.17 (m, 2H), 1.88 (m, 2H), 1.76-1.14 (m, 14H), 1.00 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 165.2, 140.1, 139.8, 136.1, 135.7, 132.2, 129.5, 129.2, 129.1, 128.2, 76.5, 68.7, 38.3, 38.2, 38.1, 38.0, 34.0, 31.2, 31.1, 30.9, 26.7, 26.6, 26.1, 25.7, 25.6, 25.5. ^{31}P NMR (121 MHz, $CDCl_3$) δ: –6.6. IR (neat, cm^{-1}): 2953, 2902, 2866, 1653, 1479, 1351, 1336, 1240, 1133, 1090, 1047, 965, 900, 745. Elemental analysis for $C_{23}H_{34}NOP$: C, 74.36; H, 9.22. Found: C, 74.20; H, 9.27.



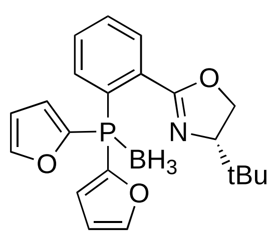
L9c

(*S*)-4-*tert*-butyl-2-(2-(di*o*-tolylphosphino)phenyl)-4,5-dihydrooxazole L9c (Table 2, entry 2). General procedure A was followed using chlorodi*o*-tolylphosphine. Colorless solid; m.p. (138-140) °C; $[\alpha]_D$ –74.5 (*c* 0.32, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.96 (dd, *J* = 7.5, 3.8 Hz, 1H), 7.39 (t, *J* = 7.5, 7.5 Hz, 1H), 7.34-7.15 (m, 7H), 7.06 (m, 2H), 6.92 (dd, *J* = 7.5, 3.3 Hz), 6.7 (m, 2H), 4.12 (dd, *J* = 10.0, 8.2 Hz, 1H), 4.04 (t, *J* = 8.2 Hz, 1H), 3.94 (dd, *J* = 10.0, 8.2 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 3H), 0.74 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 162.7, 142.6, 142.3, 142.2, 141.9, 137.5, 137.2, 136.5, 136.4, 136.3, 136.2, 134.2, 133.3, 132.9, 130.4, 129.9, 129.9, 129.8, 128.4, 128.2, 128.1, 126.1, 125.9, 76.7, 68.3, 33.6, 25.7, 21.4, 21.3, 21.0. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −20.9. IR (neat, cm^{-1}): 3056, 2956, 1652, 1588, 1468, 1353, 1305, 1248, 1133, 1092, 1025, 968, 909, 748. Elemental analysis for $C_{27}H_{30}NOP$: C, 78.05; H, 7.28. Found: C, 77.83; H, 7.41.



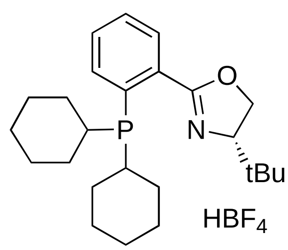
L9d

(*S*)-2-(2-(bis(3,5-bis(trifluoromethyl)phenyl)phosphino)phenyl)-4-*tert*-butyl-4,5-dihydrooxazole L9d (Table 2, entry 3). General procedure A was followed using bis(3,5-bis(trifluoromethyl)phenyl)chlorophosphine. Colorless solid; m.p. (115-118) °C; $[\alpha]_D$ −6.7 (*c* 0.304, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.05 (ddd, *J* = 7.7, 4.0, 1.2 Hz, 1H), 7.89 (s, 1H), 7.86 (s, 1H), 7.67 (s, 1H), 7.65 (s, 1H), 7.63 (s, 1H), 7.61 (s, 1H), 7.54 (dt, *J* = 7.7, 7.3, 1.3 Hz, 1H), 7.43 (dt, *J* = 7.7, 7.3, 1.3 Hz, 1H), 6.78 (ddd, *J* = 7.7, 4.0, 1.2 Hz, 1H), 4.29 (dd, *J* = 10.1, 8.6 Hz, 1H), 4.12 (t, *J* = 8.6, 8.6 Hz, 1H), 3.92 (dd, *J* = 10.1, 8.6 Hz, 1H), 0.68 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 161.3, 141.8, 141.7, 141.6, 134.9, 134.6, 134.0, 133.9 132.0, 131.9, 131.8, 131.6, 131.5, 131.3, 130.0, 130.0, 129.8, 124.9, 122.9, 122.7, 121.3, 77.1, 77.0, 68.6, 33.4, 25.5. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −6.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −63.38, −63.40. IR (neat, cm^{-1}): 2961, 1654, 1616, 1479, 1354, 1278, 1184, 1135, 1095, 1050, 966, 898, 844, 777, 744, 704, 682. Elemental analysis for $C_{29}H_{22}F_{12}NOP$: C, 52.82; H, 3.36. Found: C, 52.89; H, 3.44.



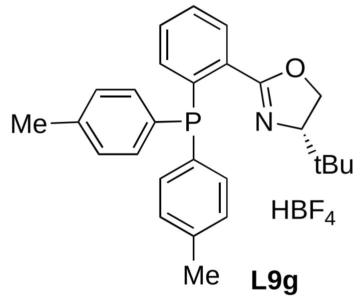
L9e

(*S*)-4-*tert*-butyl-2-(2-(difuran-2-ylphosphino)phenyl)-4,5-dihydrooxazole, borane complex L9e (Table 2, entry 4). General procedure B was followed using chlorodifuran-2-ylphosphine but BH_3 (10 M in dimethyl sulfide, 200 µL, 2.0 mmol) was added in lieu of HBF_4. White solid; m.p. (85-87) °C; $[\alpha]_D$ –52.3 (*c* 0.15, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.80 (m, 1H), 7.62 (m, 2H), 7.38 (m, 2H), 7.13 (m, 1H), 6.63 (ddd, *J* = 3.2, 1.5, 0.7 Hz, 1H), 6.52 (td, *J* = 3.2, 0.7 Hz, 1H), 6.41 (m, 2H), 4.21 (dd, *J* = 10.2, 8.3 Hz, 1H), 4.11 (t, *J* = 8.3 Hz, 1H), 3.97 (dd, *J* = 10.2, 8.3 Hz, 1H), 0.90 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 162.4, 162.4, 152.5, 152.4, 152.2, 152.1, 146.8, 146.6, 146.6, 136.6, 136.4, 133.3, 131.1, 130.8, 130.4, 129.7, 129.6, 128.4, 120.6, 120.3, 120.1, 119.9, 110.7, 76.8, 76.8, 68.4, 33.7, 25.9. ^{31}P NMR (121 MHz, $CDCl_3$) δ: –50.3. IR (neat, cm^{-1}): 2955, 1654, 1478, 1355, 1307, 1252, 1210, 1152, 1095, 1040, 1006, 965, 902, 742.



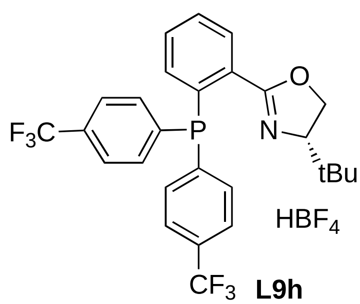
L9f

(*S*)-4-*tert*-butyl-2-(2-(dicyclohexylphosphino)phenyl)-4,5-dihydrooxazole, tetrafluoroborate salt L9f (Table 2, entry 5). General procedure B was followed using chlorodicyclohexyl phosphine. White foam; $[\alpha]_D$ –37.6 (*c* 0.922, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.63 (ddd, *J* = 7.5, 3.0, 2.0 Hz, 1H), 7.54 (td, *J* = 7.3, 1.8 Hz, 1H), 7.37 (m, 2H), 4.38 (dd, *J* = 10.0, 8.3 Hz, 1H), 4.23 (t, *J* = 8.3 Hz, 1H), 4.09 (dd, *J* = 10.0, 8.3 Hz, 1H), 1.98-1.48 (m, 12H), 1.34-1.04 (m, 10H), 0.99 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 165.1, 165.0, 136.9, 136.8, 136.5, 136.5, 132.6, 132.5, 129.7, 129.6, 129.1, 128.2, 76.5, 68.7, 34.7, 34.5, 34.4, 34.2, 33.9, 30.2, 30.0, 29.9, 29.9, 29.8, 29.7, 27.3, 27.2, 27.2, 27.1, 27.1, 26.4, 26.3, 26.1 ^{31}P NMR (121 MHz, $CDCl_3$) δ: –4.4. IR (neat, cm^{-1}): 2924, 2849, 1659, 1447, 1023.



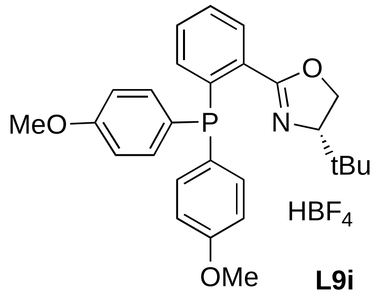
L9g

(*S*)-4-*tert*-butyl-2-(2-(di*p*-tolylphosphino)phenyl)-4,5-dihydrooxazole, tetrafluoroborate salt L9g (Table 2, entry 6). General procedure B was followed using chlorodi*p*-tolylphosphine. White solid; m.p. (85-87) °C; $[\alpha]_D$ −58.4 (*c* 0.248, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.93 (ddd, *J* = 7.6, 3.8, 1.3 Hz, 1H), 7.33 (m, 2H), 7.24-7.07 (m, 8H), 6.90 (ddd, *J* = 7.0, 3.8, 1.3 Hz, 1H), 4.09 (dd, *J* = 10.2, 8.2 Hz, 1H), 4.01 (t, *J* = 8.2 Hz, 1H), 3.88 (dd, *J* = 10.2, 8.2 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H), 0.76 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 139.6, 139.3, 138.5, 138.1, 134.8, 134.7, 134.6, 134.5, 134.4, 134.1, 133.9, 133.7, 133.5, 131.6, 131.4, 130.4, 130.0, 130.0, 129.3, 129.2, 129.0, 127.9, 76.2, 68.5, 33.6, 25.7, 21.3. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −6.5. IR (neat, cm^{-1}): 2954, 1653, 1496, 1478, 1353, 1306, 1248, 1090, 1038, 967, 908, 806, 732.



L9h

(*S*)-4-*tert*-butyl-2-(2-(di*p*-tolylphosphino)phenyl)-4,5-dihydrooxazole, tetrafluoroborate salt L9h (Table 2, entry 7). General procedure B was followed using chlorobis(4-(trifluoromethyl)phenyl)phosphine. White solid; m.p. (66-69) °C; $[\alpha]_D$ −23.4 (*c* 0.154, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ: 8.06 (ddd, *J* = 7.6, 3.9, 1.2 Hz, 1H), 7.60 (s, 1H), 7.57 (s, 2H), 7.54 (s, 1H), 7.46 (dt, *J* = 7.7, 7.6, 1.2 Hz, 1H), 7.40-7.28 (m, 5H), 6.83 (ddd, *J* = 7.6, 3.9, 1.2 Hz, 1H), 4.22 (dd, *J* = 10.0, 8.4 Hz, 1H), 4.07 (t, *J* = 8.4 Hz, 1H), 3.94 (dd, *J* = 10.0, 8.4 Hz, 1H), 0.69 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 161.9, 143.1, 136.9, 136.5, 134.5, 134.2, 133.8, 133.6, 132.0, 131.7, 130.8, 130.7, 130.4, 130.2, 129.9, 129.9, 128.9, 125.8, 125.3, 125.2, 125.1, 125.0, 122.2, 76.9, 68.4, 33.6, 25.6. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −6.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −63.13, −63.18. IR (neat, cm^{-1}): 2959, 1654, 1606, 1479, 1396, 1355, 1324, 1252, 1166, 1127, 1106, 1061, 1017, 966, 908, 832, 777, 735, 700. Elemental analysis for $C_{27}H_{24}F_6NOP$: C, 61.95; H, 4.62. Found: C, 61.59; H, 4.67.



L9i

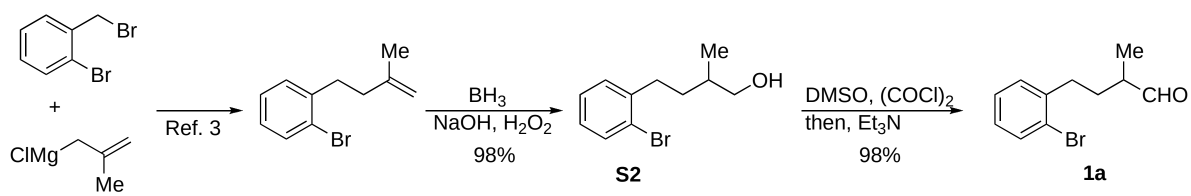
(*S*)-2-(2-(bis(4-methoxyphenyl)phosphino)phenyl)-4-*tert*-butyl-4,5-dihydrooxazole, tetrafluoroborate salt L9i (Table 2, entry 8). General procedure B was followed using chlorobis(4-methoxyphenyl)phosphine. White solid; m.p. (109-112) °C; $[\alpha]_D$ −63.4 (*c* 0.334, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.92 (ddd, *J* = 7.5, 3.6, 1.5 Hz, 1H), 7.38-7.14 (m, 6H), 6.86 (m, 5H), 4.06 (dd, *J* = 10.2, 8.2 Hz, 1H), 4.00 (t, *J* = 8.2 Hz), 3.85 (dd, *J* = 10.2, 8.2 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 0.76 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: Due to the complexity of the spectra all the peaks are listing without take into consideration C-P couplings. 163.1, 163.0, 160.0, 159.8, 140.0, 139.6, 135.8, 135.5, 135.1, 134.8, 133.6, 131.6, 131.4, 130.2, 130.0, 129.9, 129.5, 129.3, 129.3, 129.2, 127.7, 114.1, 114.0, 113.9, 76.4, 68.3, 55.1, 55.0, 33.6, 25.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ: −7.7. IR (neat, cm^{-1}): 2956, 2903, 2836, 1652, 1595, 1798, 1463, 1441, 1354, 1305, 1284, 1247, 1177, 1092, 1031, 966, 909, 826, 797, 733.

SYNTHESIS OF ALDEHYDES.[2]

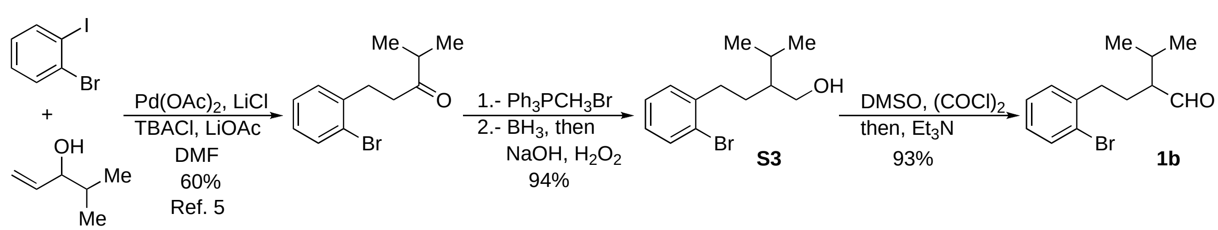
General procedure C for the oxidation of alcohols to aldehydes. To a solution of DMSO (170 µL, 2.4 mmol) in dichloromethane (10 mL) was added at −78 °C and under Ar oxalyl chloride (100 µL, 1.2 mmol) dropwise. The mixture was stirred for 5 min and a solution of alcohol (1.0 mmol) in dichloromethane (2 mL) was added. After stirring at −78 °C for 15 min,

[2] The use of freshly prepared aldehydes is important in order to achieve good reproducibility.

Et_3N (700 µL, 5.0 mmol) was added. The resulting reaction mixture was stirred at −78 °C for 30 min and at 0°C for 1 h. Then, it was poured into a separation funnel containing NH_4Cl aq. and it was extracted with dichloromethane (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue obtained was purified by column chromatography on silica gel (eluting with hexanes/diethylether or ethyl acetate mixtures).



4-(2-bromophenyl)-2-methylbutanal 1a. Following general procedure C using alcohol **S2**.[4] Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 9.66 (dd, J = 1.8, 0.3 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.28-7.18 (m, 2H), 7.07 (ddd, J = 8.1, 6.3, 2.7 Hz, 1H), 2.77 (m, 2H), 2.42 (app sixtd, J = 7.2, 1.8 Hz 1H), 2.04 (m, 1H), 1.68 (m, 1H), 1.18 (d, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 204.6, 140.7, 132.8, 130.3, 127.3, 127.5, 124.4, 45.8, 34.4, 30.5, 13.3. IR (neat, cm^{-1}): 3057, 2965, 2931, 2864, 2812, 2713, 1725, 1567, 1471, 1457, 1440, 1023, 751, 659.



2-(2-bromophenethyl)-3-methylbutanal 1b. Following general procedure C using alcohol **S3**.[6] Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 9.71 (d, J = 3.0 Hz, 1H), 7.52 (d, J = 8.1 Hz, 1H), 7.28-7.18 (m, 2H), 7.07 (ddd, J = 8.1, 6.6, 3.0 Hz, 1H), 2.67 (m, 2H), 2.16 (m, 1H), 2.05 (m, 1H), 1.93 (m, 1H), 1.77 (m, 1H), 0.97 (t, J = 6.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ:

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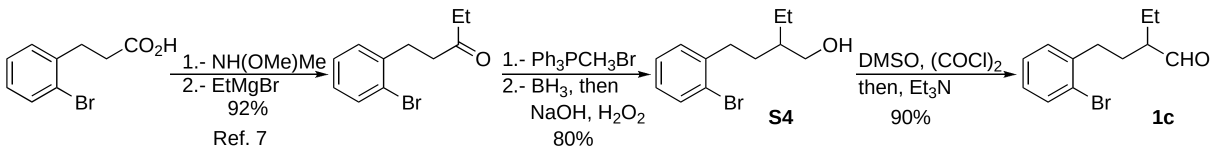
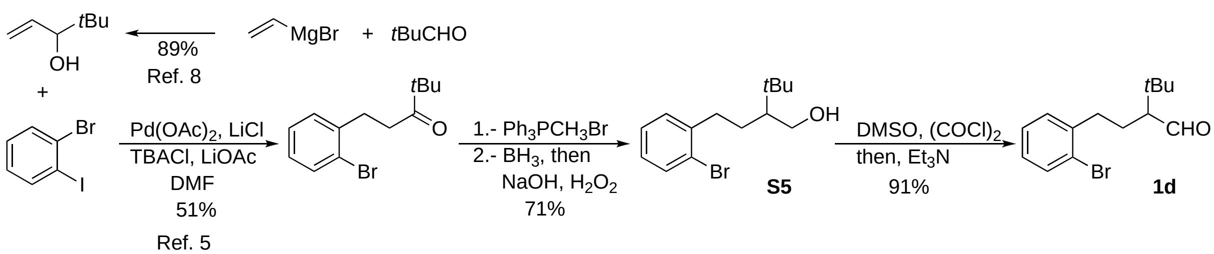
[3] According to O. M. Ghoneim, J. A. Legere, A. Golbraikh, A. Tropsha, R. G. Booth, *Bioorg. Med. Chem.* **2006**, *14*, 6640-6658.
[4] Prepared by hydroboration/oxidation of the olefin according to P. Beak, G. W. Selling, *J. Org. Chem.* **1989**, *54*, 5574-5580.
[5] According to R. C. Larock, W. Leung, S. Stolz-Dunn, *Tetrahedron Lett.* **1989**, *30*, 6629-6632.
[6] Prepared by olefination/hydroboration/oxidation of the ketone according to D. K. Barma, A. Bandyopadhyay, J. H. Capdevila, J. R. Falck, *Org. Lett.* **2003**, *5*, 4755-4757.

205.4, 141.0, 132.8, 130.4, 127.8, 127.5, 124.2, 57.7, 34.3, 28.3, 26.0, 20.2, 19.6. IR (neat, cm^{-1}): 2961, 2872, 1723, 1471, 1024, 751, 659.

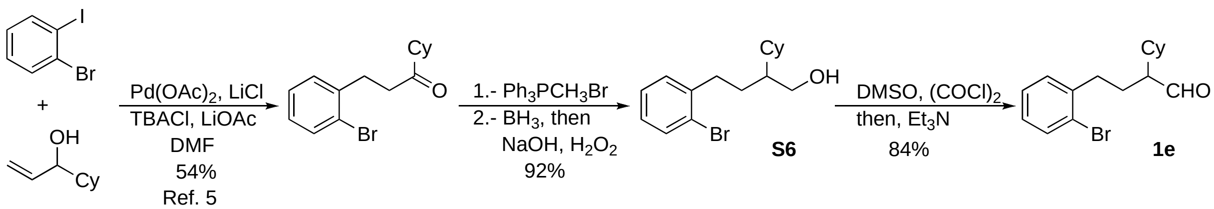


4-(2-bromophenyl)-2-ethylbutanal 1c. Following general procedure C using alcohol **S4.**[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.65 (d, *J* = 3.0 Hz, 1H), 7.53 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.28-7.18 (m, 2H), 7.07 (ddd, *J* = 8.0, 6.2, 3.0 Hz, 1H), 2.73 (m, 2H), 2.28 (dqd, *J* = 10.7, 5.5, 2.7 Hz, 1H), 1.96 (dddd, *J* = 14.1, 9.7, 8.0, 6.5 Hz, 1H), 1.75 (m, 2H), 1.63 (dqd, *J* = 14.6, 7.4, 5.5, 1H), 0.95 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 204.9, 140.8, 132.8, 130.3, 127.8, 127.5, 124.2, 52.8, 33.6, 28.4, 21.7, 11.3. IR (neat, cm^{-1}): 2964, 2933, 2875, 2709, 1725, 1471, 1456, 1440, 1383, 1024, 751.

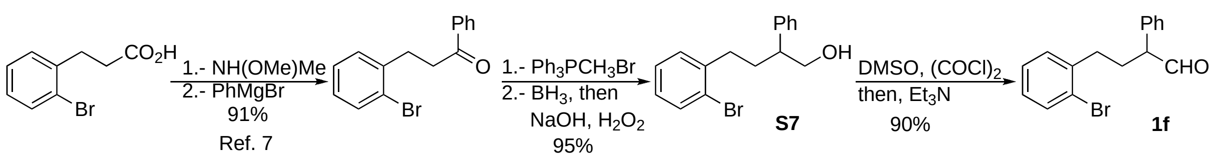


2-(2-bromophenethyl)-3,3-dimethylbutanal 1d. Following general procedure C using alcohol **S5.**[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.81, (d, *J* = 4.2 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.28-7.18 (m, 2H), 7.07 (ddd, *J* = 7.8, 6.9, 2.7 Hz, 1H), 2.62 (m, 2H), 2.69 (ddd, *J* = 13.3, 10.8, 4.9 Hz, 1H), 2.56 (ddd, *J* = 13.3, 9.6, 6.5 Hz, 1H), 2.12-1.90 (m, 2H), 1.82 (m, 1H), 1.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 206.2, 140.9, 132.8, 130.5, 127.8, 127.5, 124.2, 61.5, 34.7, 33.4, 27.9, 25.0. IR (neat, cm^{-1}): 2962, 2869, 1721, 1471, 1370, 1228, 1023, 752.

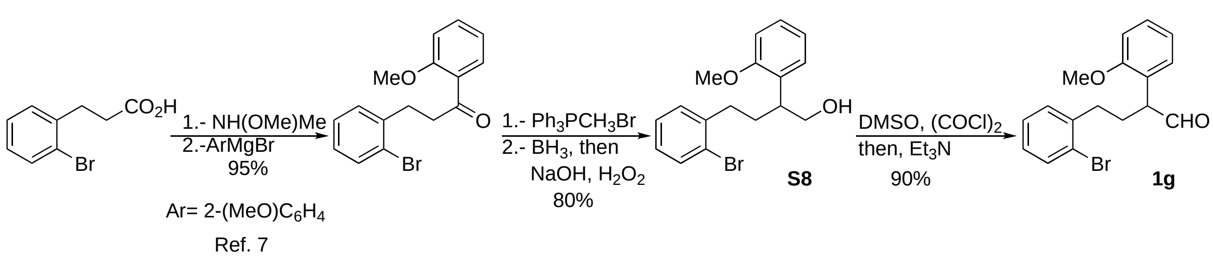
[7] According to M. Kim, J. Y. Kim, K. Song, J. Kim, J. Lee, *Tetrahedron*, **2007**, *63*, 12845-12852.
[8] According to D. Craig, M. W. Pennington, P. Warner, *Tetrahedron*, **1999**, *55*, 13495-13512.



4-(2-bromophenyl)-2-cyclohexylbutanal 1e. Following general procedure C using alcohol **S6**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.67 (d, *J* = 3.3 Hz, 1H), 7.51 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.28-7.18 (m, 2H), 7.07 (ddd, *J* = 8.0, 6.4, 2.9 Hz, 1H), 2.67 (m, 2H), 2.17 (tdd, *J* = 7.0, 5.5, 3.5 Hz, 1H), 1.94 (dtd, *J* = 15.2, 9.9, 5.5 Hz, 1H), 1.87-1.60 (m, 7H), 1.35-0.98 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.5, 141.0, 132.8, 130.4, 127.7, 127.5, 124.2, 57.2, 38.2, 34.2, 30.7, 30.0, 26.4, 26.2, 26.1. IR (neat, cm^{-1}): 2926, 2853, 1723, 1567, 1471, 1449, 1023, 751, 659.

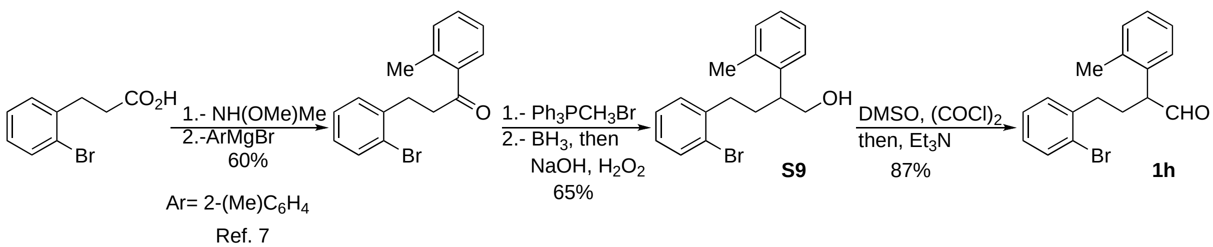


4-(2-bromophenyl)-2-phenylbutanal 1c. Following general procedure C using alcohol **S7**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.71 (d, *J* = 1.5 Hz, 1H), 7.53 (d, *J* = 7.8, 1H), 7.48-7.12 (m, 7H), 7.07 (dt, *J* = 7.8, 2.0 Hz, 1H), 3.59 (ddd, *J* = 8.3, 6.6, 1.5 Hz, 1H), 2.72 (t, *J* = 7.8 Hz, 2H), 2.42 (tdd, *J* = 14.9, 8.7, 6.6 Hz), 2.07 (td, *J* = 14.9, 8.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.3, 140.6, 135.7, 132.8, 130.4, 129.1, 128.9, 127.8, 127.7, 127.4, 124.3, 58.5, 33.6, 29.5. IR (neat, cm^{-1}): 2930, 2815, 1723, 1492, 1471, 1452, 1440, 1077, 1024, 753, 701, 659, 529.

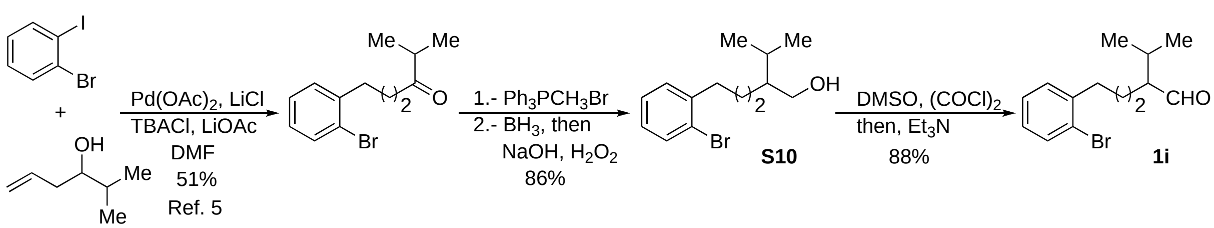


4-(2-bromophenyl)-2-(2-methoxyphenyl)butanal 1g. Following general procedure C using alcohol **S8**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.71 (d, *J* = 0.9 Hz, 1H), 7.51 (dd, *J* = 8.4, 0.9, 1H), 7.31 (ddd, *J* = 8.1, 7.5, 1.8 Hz, 1H), 7.26-7.12 (m, 3H), 7.08-6.90 (m, 3H), 3.87

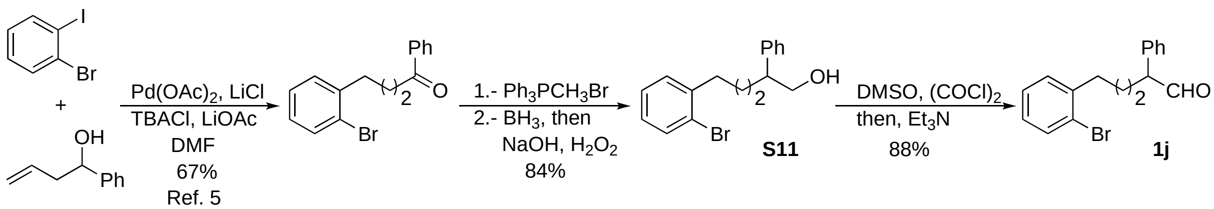
(dd, J = 8.2, 6.1 Hz, 1H), 3.82 (s, 3H), 2.70 (m, 2H), 2.42 (tdd, J = 12.2, 9.7, 6.2 Hz, 1H), 2.03 (dddd, J = 13.2, 9.7, 8.2, 6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 201.2, 157.4, 141.0, 132.7, 130.3, 129.9, 128.9, 127.6, 127.3, 124.9, 124.4, 120.9, 110.8, 55.4, 52.6, 33.7, 28.3. IR (neat, cm^{-1}): 2930, 2713, 2362, 1721, 1494, 1455, 1437, 1248, 1049, 1024, 822, 752.



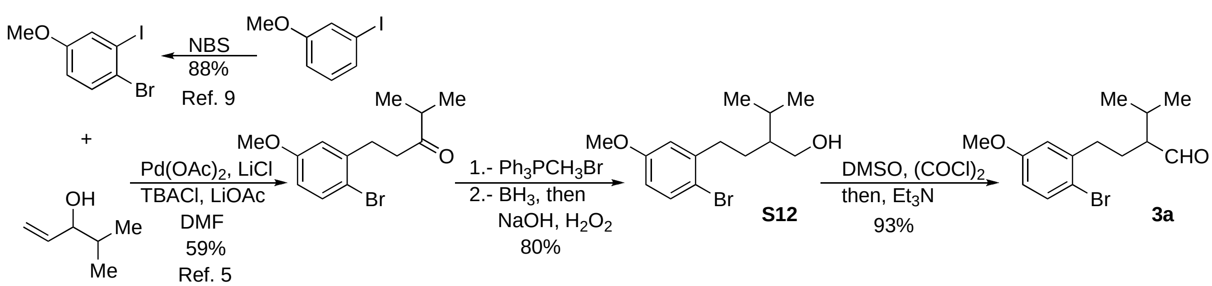
4-(2-bromophenyl)-2-*o*-tolylbutanal 1h. Following general procedure C using alcohol **S9**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.71 (dd, J = 1.5, 0.6 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.32-7.02 (m, 7H), 3.84 (dt, J = 7.1, 1.4 Hz 1H), 2.76 (m, 2H), 2.42 (m, 1H), 2.32 (s, 3H), 2.02 (tdd, J = 13.7, 9.7, 6.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.2, 140.7, 137.1, 134.2, 132.8, 131.0, 130.4, 127.8, 127.5, 127.4, 126.6, 124.3, 54.2, 33.7, 29.5, 19.7. IR (neat, cm^{-1}): 2925, 2357, 2336, 1721, 1558, 1492, 1455, 1047, 1024, 822, 754.



5-(2-bromophenyl)-2-isopropylpentanal 1i. Following general procedure C using alcohol **S10**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.62 (d, J = 3.3 Hz, 1H), 7.50 (dd, J = 8.1, 0.9 Hz, 1H), 7.24-7.14 (m, 2H), 7.03 (ddd, J = 8.1, 6.3, 2.7 Hz, 1H), 2.72 (m, 2H), 2.09 (m, 1H), 1.99 (qd, J = 13.4, 6.7 Hz), 1.80-1.45 (m, 4H), 0.96 (d, J = 1.7 Hz, 3H), 0.94 (d, J = 1.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.6, 141.1, 132.6, 130.1, 127.5, 127.3, 124.2, 57.9, 36.0, 28.1, 27.8, 25.5, 20.1, 19.7. IR (neat, cm^{-1}): 2960, 2870, 2710, 1723, 1470, 1440, 1389, 1371, 1022, 751, 659.

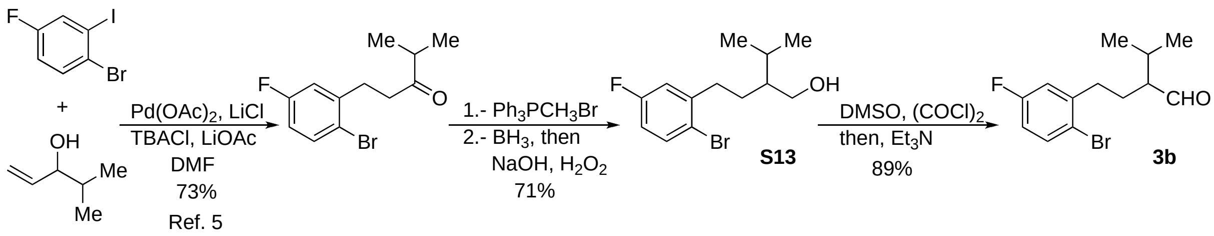


5-(2-bromophenyl)-2-isopropylpentanal 1j. Following general procedure C using alcohol **S11**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.69 (d, *J* = 2.1 Hz, 1H), 7.52 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.44-7.28 (m, 3H), 7.28-7.14 (m, 4H), 7.05 (ddd, *J* = 8.1, 7.0, 2.2 Hz, 1H), 3.56 (ddd, *J* = 8.3, 6.5, 1.8 Hz, 1H), 2.77 (m, 2H), 2.19 (m, 1H), 1.85 (m, 1H), 1.72-1.52 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.5, 141.0, 136.0, 132.7, 130.2, 129.0, 128.7, 127.5, 127.3, 124.3, 58.9, 35.8, 29.1, 27.2. IR (neat, cm^{-1}): 3061, 3028, 2938, 2862, 2816, 2714, 1723, 1600, 1566, 1492, 1471, 1553, 1439, 1024, 753, 701, 658.

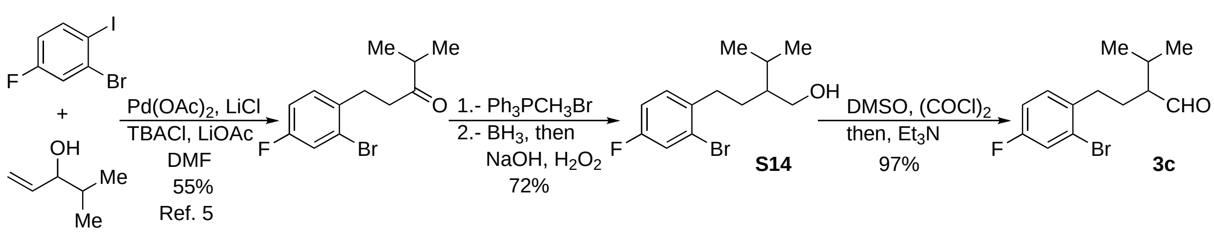


2-(2-bromo-5-methoxyphenethyl)-3-methylbutanal 3a. Following general procedure C using alcohol **S12**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.71 (d, *J* = 3.0, Hz, 1H), 7.40 (d, *J* = 8.7, 1H), 6.77 (d, *J* = 3.0, 1H), 6.64 (dd, *J* = 8.7, 3.2 Hz, 1H). 3.78 (s, 3H), 2.64 (m, 2H), 2.16 (tt, *J* = 10.8, 3.8 Hz, 1H), 2.12-1.86 (m, 2H), 1.76 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.4, 158.9, 141.9, 133.3, 116.0, 114.6, 113.3, 57.7, 55.4, 34.4, 28.3, 25.9, 20.2, 19.6. IR (neat, cm^{-1}): 2961, 2936, 2872, 1723, 1595, 1572, 1473, 1291, 1278, 1241, 1163, 1054, 1015, 867, 806.

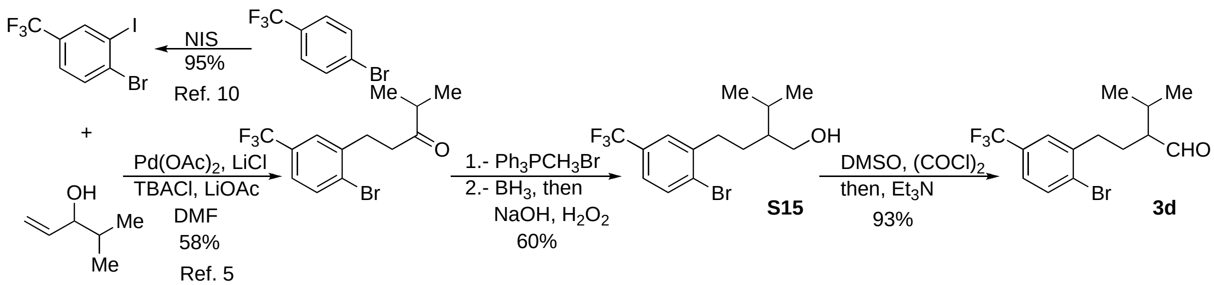
[9] According to H. Chang, S. Datta, A. Das, A. Odedra, R. Liu, *Angew. Chem.*, **2007**, *119*, 4828-4831; *Angew. Chem. Int. Ed.*, **2007**, *46*, 4744-4747.



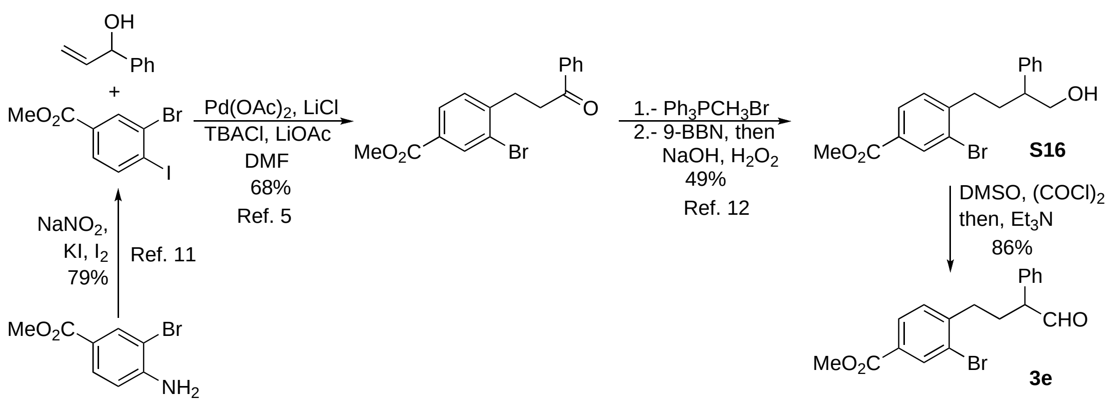
2-(2-bromo-5-fluorophenethyl)-3-methylbutanal 3b. Following general procedure C using alcohol **S13**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.72 (d, *J* = 2.7 Hz, 1H), 7.47 (dd, *J* = 8.7, 5.3 Hz, 1H), 6.96 (dd, *J* = 9.4, 3.0 Hz, 1H), 6.81 (td, *J* = 8.7, 3.0 Hz, 1H), 2.66 (m, 2H), 2.17 (tdd, *J* = 11.8, 5.8, 2.7 Hz, 1H), 2.12-1.86 (m, 2H), 1.73 (ddt, *J* = 16.5, 7.9, 4.8 Hz), 0.99 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.1, 161.9 (d, *J* = 246.8 Hz), 143.1 (d, *J* = 7.4 Hz), 133.8 (d, *J* = 8.1 Hz), 118.2 (d, *J* = 3.1 Hz), 117. 1 (dd, *J* = 22.4, 3.0 Hz), 114.9 (dd, *J* = 22.4, 2.1 Hz), 57.6, 34.3, 28.2, 25.6, 21.2, 19.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −115.39. IR (neat, cm^{-1}): 2962, 2873, 2713, 1724, 1606, 1580, 1470, 1409, 1272, 1235, 1155, 1105, 1031, 869, 810.



2-(2-bromo-4-fluorophenethyl)-3-methylbutanal 3c. Following general procedure C using alcohol **S14**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.68 (d, *J* = 2.9 Hz, 1H), 7.24 (dd, *J* = 8.3, 2.6 Hz, 1H), 7.16 (dd, *J* = 8.5, 6.1 Hz, 1H), 6.93 (dt, *J* = 8.5, 8.3, 2.6 Hz, 1H), 2.62 (m, 2H), 2.18-1.98 (m, 2H), 1.90 (dtd, *J* = 15.0, 9.7, 5.3 Hz, 1H), 1.70 (m, 1H), 0.96 (d, *J* = 7.5 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.1, 160.7 (d, *J* = 248.7 Hz), 136.8 (d, *J* = 3.5 Hz), 130.9 (d, *J* = 8.2 Hz), 123.8 (d, *J* = 9.4 Hz), 119. 7 (dd, *J* = 24.3, 2.5 Hz), 114.4 (dd, *J* = 20.7, 1.5 Hz), 57.5, 33.3, 28.1, 25.9, 20.1, 19.4. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −115.20 (q, J = 8.7 Hz). IR (neat, cm^{-1}): 2962, 2873, 1724, 1600, 1587, 1487, 1464, 1390, 1372, 1264, 1228, 1182, 1032, 883, 859, 820, 674.



2-(2-bromo-5-(trifluoromethyl)phenethyl)-3-methylbutanal 3d. Following general procedure C using alcohol **S15**.[6] Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) d: 9.71 (J = 2.8 Hz, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.45 (d, J = 2.3 Hz, 1H), 7.28 (dd, J = 8.3, 2.8 Hz, 1H), 2.71 (m, 2H), 2.17 (ddd, J = 12.3, 6.0, 3.2 Hz, 1H), 2.12-1.86 (m, 2H), 1.73 (dddd, J = 14.1, 10.9, 6.0, 3.2 Hz, 1H), 0.98 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) d: Due to the complexity of the spectra all the peaks are listing without take into consideration C-F couplings. 204.8, 142.1, 133.3, 130.6, 130.1, 129.7, 129.3, 129.1, 128.1, 128.0, 126.8, 126.8, 125.5, 124.4, 124.3, 121.9, 57.7, 34.2, 28.2, 25.5, 20.1, 19.4. ^{19}F NMR (282 MHz, $CDCl_3$) d: –63.06. IR (neat, cm^{-1}): 2964, 2873, 2713, 1725, 1604, 1467, 1409, 1372, 1331, 1278, 1169, 1128, 1083, 1028, 891, 825, 745.



Methyl 3-bromo-4-(4-oxo-3-phenylbutyl)benzoate 3a. Following general procedure C using alcohol **S16**.[12] White solid; m.p. (44-46) °C ^{1}H NMR (300 MHz, $CDCl_3$) d: 9.70 (d, J = 1.5 Hz, 1H), 8.19 (d, J = 1.8 Hz, 1H), 7.88 (dd, J = 8.0, 1.7 Hz, 1H), 7.45-7.30 (m, 3H), 7.23 (m, 3H), 3.91 (s, 3H), 3.58 (ddd, J = 8.1, 6.6, 1.5 Hz, 1H), 2.75 (m, 2H), 2.41 (m, 1H), 2.06 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.0, 165.6, 145.9, 135.4, 133.9, 130.2, 129.8, 129.2,

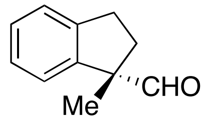
[10] P. Blurton, F. Burkamp, I. Churcher, T. Harrison, J. Neduvelil, patent WO 2006008558, **2006**.
[11] Acording to S. Tanaka, H. Katagiri, N. Morohashi, T. Hattori, S. Miyano, *Tetrahedron Lett.* **2007**, *48*, 5293-5296.
[12] Prepared by olefination/hydroboration/oxidation of the ketone according to Ref. 6 but 9-BBN (1.5 equiv) was used in lieu of borane.

128.9, 128.5, 127.8, 124.2, 58.5, 52.3, 33.7, 29.2. IR (neat, cm^{-1}): 3427, 3063, 3029, 2952, 2818, 2717, 1951, 1724, 1602, 1561, 1493, 1454, 1435, 1391, 1287, 1258, 1193, 1115, 1041, 972, 904, 846, 762, 701.

ASYMMETRIC Pd-CATALYZED α-ARYLATION OF ALDEHYDES.

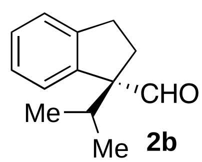
General procedure D for the Pd-catalyzed intramolecular α-arylation of aldehydes with a borane-complex catalyst L9e (Table 2, entry 4). An oven-dried resealable test tube containing a stirring bar was charged with $Pd(OAc)_2$ (0.7 mg, 3.0 mol%), **L9e** (3.4 mg, 9.00 mol%) and DABCO (1.5 mg, 13.5 mol%). The test tube fitted with a screw cap with a pierceable teflon septum was then evacuated and back-filled with dry argon (this sequence was repeated three times) and *t*BuOH (1 mL) was added by syringe. The mixture was stirred in a pre-heated oil bath (80 °C) for 5 min. and the resulting solution was cannulated into an oven-dried resealable test tube (fitted with a screw cup and a teflon seal) containing a stirring bar and Cs_2CO_3 (39 mg, 0.12 mmol), previously evacuated and back-filled with dry argon three times. The aldehyde[2] (21 µL, 26.9 mg, 0.1 mmol) was added by syringe and the mixture was stirred in a pre-heated oil bath (80 °C) for 15 h. The mixture was then allowed to cool to room temperature, diluted with dichloromethane (5 mL) and filtered through a Celite® plug and injected into the GC using dodecane as an internal standard.

General procedure E for the Pd-catalyzed intramolecular α-arylation of aldehydes (Table 3 and 4). An oven-dried resealable test tube containing a stirring bar was charged with $Pd(OAc)_2$ (3.4 mg, 15 µmol, 3.0 mol%), **L9i** (24 mg, 45 µmol, 9.00 mol%) and Cs_2CO_3 (210 mg, 0.65 mmol). The test tube fitted with a screw cap with a pierceable teflon septum was then evacuated and back-filled with dry argon (this sequence was repeated three times). Then, *t*BuOH (5 mL) and freshly prepared[2] aldehyde were added by syringe. The mixture was stirred in a pre-heated oil bath (80 °C) for 24 h. The mixture was then allowed to cool to room temperature, diluted with dichloromethane (5 mL) and filtered through a Celite® plug, eluting with additional dichlorometane (10 mL). The filtrate was concentrated and purified by column chromatography on silica gel (eluting with hexanes/diethylether or ethyl acetate mixtures).



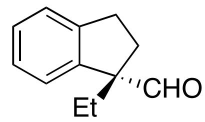
2a

(*S*)-1-methyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2a (Table 3, entry 1). General procedure E was followed using 4-(2-bromophenyl)-2-methylbutanal **1a** (95 μL, 120 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 51 mg (64% yield). Enantioselectivity: 87% *ee*, Chiral GC B-DA column, 85 °C to 115 °C at 0.85 °C min^{-1}; t_{minor}= 32.38 min, t_{major}= 32.61 min; $[\alpha]_D$ −72.3 (*c* 0.82, $CHCl_3$, 87% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.56 (s, 1H), 7.34-7.21 (m, 3H), 7.21-7.12 (m, 1H), 3.05 (d, *J* = 7.5 Hz, 1H), 3.03 (d, *J* = 7.2 Hz, 1H), 2.62 (dt, *J* = 13.4, 7.2 Hz, 1H), 1.95 (dt, *J* = 13.4, 7.5 Hz, 1H), 1.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 201.2, 144.4, 143.2, 128.0, 126.8, 125.0, 123.8, 59.5, 33.9, 30.7, 20.3. IR (neat, cm^{-1}): 2929, 1723, 1477, 1455, 758. Elemental analysis for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.12; H, 7.72.



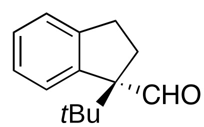
2b

(*R*)-1-isopropyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2b (Table 3, entry 2). General procedure E was followed using 2-(2-bromophenethyl)-3-methylbutanal **1b** (105 μL, 135 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 81 mg (86% yield). Enantioselectivity: 94% *ee*, Chiral GC G-TA column, 85 °C to 170 °C at 1.5°C min^{-1}; t_{minor}= 33.63 min, t_{major}= 35.63 min; $[\alpha]_D$ +33.6 (*c* 1.038, $CHCl_3$, 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.55 (d, *J* = 0.9 Hz, 1H), 7.32-7.16 (m, 4H), 2.95 (m, 2H), 2.68-2.47 (m, 2H), 1.99 (dtd, *J* = 13.5, 8.2, 0.9 Hz, 1H), 0.93 (d, *J* = 6.9 Hz, 3 H), 0.77 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.9, 145.1, 140.8, 127.8, 126.5, 125.0, 124.2, 68.2, 30.4, 30.0, 24.1, 18.1, 16.5. IR (neat, cm^{-1}): 2966, 2935, 2854, 1722, 1477, 1456, 1382, 1022, 785, 756. Elemental analysis for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.89; H, 8.64.



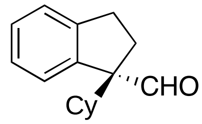
2c

(*S*)-1-ethyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2c (Table 3, entry 3). General procedure E was followed using 4-(2-bromophenyl)-2-ethylbutanal **1c** (95 μL, 128 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 55 mg (63% yield). Enantioselectivity: 88% *ee*, Chiral HPLC OD-H column, Hexanes:*i*PrOH 99:1, 1 mL min^{-1}; t_{minor}= 7.98 min, t_{major}= 7.08 min; $[\alpha]_D$ –6.0 (*c* 0.146, $CHCl_3$, 88% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.55 (s, 1H), 7.32-7.16 (m, 4H), 3.00 (d, *J* = 6.9 Hz, 1H), 2.98 (d, *J* = 7.8 Hz, 1H), 2.62 (dq, *J* = 7.2, 6.9 Hz, 1H), 2.16-1.93 (m, 2H), 1.81 (m, 1H), 0.88 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 201.2, 144.9, 141.7, 128.0, 126.6, 125.0, 124.1, 64.2, 30.8, 29.9, 27.1, 8.8. IR (neat, cm^{-1}): 2966, 2935, 2854, 1722, 1477, 1456, 1382, 1022, 785, 756.



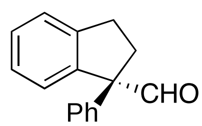
2d

(*R*)-1-*tert*-butyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2d (Table 3, entry 4). General procedure E was followed using 2-(2-bromophenethyl)-3,3-dimethylbutanal **1d** (110 μL, 142 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 89 mg (88% yield). Enantioselectivity: 96% *ee*, Chiral GC Chirasil-Dex CB column, 85 °C to 170 °C at 1.5°C min^{-1}; t_{minor}= 39.26 min, t_{major}= 38.69 min; $[\alpha]_D$ +125.0 (*c* 1.440, $CHCl_3$, 96% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.95 (s, 1H), 7.54-7.47 (m, 1H), 7.30-7.18 (m, 3H), 3.04-2.78 (m, 2H), 3.55 (ddd, *J* = 13.5, 9.3, 7.8 Hz, 1H), 2.20 (ddd, *J* = 13.5, 8.8, 4.4 Hz, 1H), 0.88 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 203.1, 145.6, 140.5, 127.7, 126.5, 125.8, 124.9, 69.2, 37.6, 31.1, 27.9, 26.4. IR (neat, cm^{-1}): 2959, 2874, 1720, 1477, 1456, 1394, 1368, 1218, 756. Elemental analysis for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.88; H, 9.07.



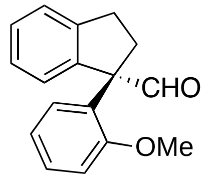
2e

(*R*)-1-cyclohexyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2e (Table 3, entry 5). General procedure E was followed using 4-(2-bromophenyl)-2-cyclohexylbutanal **1e** (120 μL, 155 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 99 mg (87% yield). Enantioselectivity: 96% *ee*, Chiral GC G-TA column, 120 °C to 180 °C at 1.5 °C min^{-1}; t_{minor}= 38.79 min, t_{major}= 39.40 min; $[\alpha]_D$ +28.5 (*c* 0.98, $CHCl_3$, 96% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 9.52 (s, 1H), 7.23 (m, 4H), 2.94 (m, 2H), 2.55 (ddd, *J* = 13.2, 7.6, 5.5 Hz, 1H), 2.22 (tt, *J* = 12.1, 2.9 Hz, 1H), 2.03 (dt, *J* = 13.2, 8.6, 2H), 1.85-1.53 (m, 4H), 1.44-0.87 (m, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 201.1, 145.2, 140.4, 127.8, 126.4, 125.1, 124.3, 68.1, 40.6, 30.9, 28.7, 26.5, 26.4, 26.3, 25.4. IR (neat, cm^{-1}): 2926, 2852, 1722, 1477, 1451, 1021, 999, 780, 757, 717. Elemental analysis for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.19; H, 8.91.



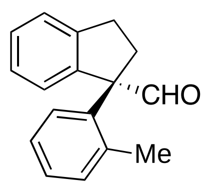
2f

(*R*)-1-phenyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2f (Table 3, entry 6). General procedure E was followed using 4-(2-bromophenyl)-2-phenylbutanal **1f** (110 μL, 152 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 90 mg (81% yield). Enantioselectivity: 98% *ee*, Chiral GC B-DA column, 120 °C to 180 °C at 4.0 °C min^{-1}; t_{minor}= 29.51 min, t_{major}= 29.02 min; $[\alpha]_D$ −103.9 (*c* 0.992, $CHCl_3$, 98% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 9.78 (d, *J* = 0.9 Hz, 1H), 7.43-7.26 (m, 7H), 7.18-7.12 (m, 2H), 3.15-2.96 (m, 3H), 2.18 (dddd, *J* = 12.3, 8.7, 6.9, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 197.2, 145.7, 141.1, 140.2, 128.9, 128.4, 127.5, 127.3, 126.7, 125.9, 125.4, 69.2, 35.7, 30.7. IR (neat, cm^{-1}): 2938, 1723, 1600, 1447, 1384, 1020, 755, 700. Elemental analysis for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.23; H, 6.42.



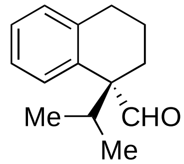
2g

(*S*)-1-(2-methoxyphenyl)-2,3-dihydro-1*H*-indene-1-carbaldehyde 2g (Table 3, entry 7). General procedure E was followed using 4-(2-bromophenyl)-2-(2-methoxyphenyl)butanal **1g** (120 μL, 167 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/ethyl acetate. Colorless crystalline solid; m.p. (106-107) °C; yield: 92 mg (73% yield). Enantioselectivity: 98% *ee*, Chiral HPLC OD-H column, Hexanes:*i*PrOH 99:1, 1 mL min^{-1}; t_{minor}= 8.43 min, t_{major}= 9.89 min; $[\alpha]_D$ –329.1 (*c* 0.444, $CHCl_3$, 98% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.81 (s, 1H), 7.31 (m, 5H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.89 (td, *J* = 7.5, 0.9 Hz, 1H), 6.81 (dd, *J* = 7.5, 1.7 Hz, 1H), 3.85 (s, 3H), 3.23-2.89 (m, 3H), 2.19 (ddd, *J* = 10.2, 8.2, 4.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 199.1, 156.4, 145.9, 140.6, 131.4, 128.8, 128.7, 128.1, 126.5, 126.2, 125.3, 120.7, 111.0, 66.4, 55.4, 34.3, 30.9. IR (neat, cm^{-1}): 2936, 1725, 1598, 1488, 1462, 1384, 1240, 1124, 1025, 755.



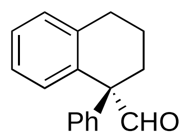
2h

(*R*)-1-*o*-tolyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 2h (Table 3, entry 8). General procedure E was followed using 4-(2-bromophenyl)-2-*o*-tolylbutanal **1h** (115 μL, 159 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless crystalline solid; m.p. (125-127) °C; yield: 32 mg (27% yield), 43 mg (37% yield when 5 mol% $Pd(OAc)_2$ and 15 mol% of **L9i** were used). Enantioselectivity: 98% *ee*, Chiral HPLC AD-H column, Hexanes:*i*PrOH 99:1, 1 mL min^{-1}; t_{minor}= 6.05 min, t_{major}= 5.67 min; $[\alpha]_D$ –282.0 (*c* 0.396, $CHCl_3$, 98% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.82 (s, 1H), 7.41-7.15 (m, 6 H), 7.10 (m, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 3.20 (m, 1H), 3.05 (m, 2H), 2.20 (ddd, *J* = ~14, 8.1, 6.0 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 198.2, 145.7, 140.3, 140.0, 136.3, 132.0, 128.5, 128.4, 127.5, 126.7, 126.6, 125.9, 125.6, 69.7, 33.3, 31.0, 21.4. IR (neat, cm^{-1}): 3019, 2941, 2710, 1722, 1478, 1454, 1384, 1093, 1018, 756, 728. Elemental analysis for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.24; H, 6.82.



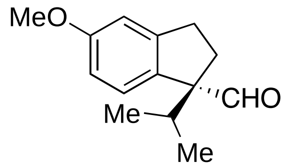
2i

(*R*)-1-isopropyl-1,2,3,4-tetrahydronaphthalene-1-carbaldehyde 2i (Table 3, entry 9). General procedure E was followed using 5-(2-bromophenyl)-2-isopropylpentanal **1i** (115 μL, 142 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 70 mg (69% yield). Enantioselectivity: 53% *ee*, Chiral GC G-TA column, 85 °C to 170 °C at 1.5 °C min^{-1}; t_{minor}= 43.50 min, t_{major}= 44.72 min; ^1H NMR (300 MHz, $CDCl_3$) δ: 9.61 (d, *J* = 1.2 Hz, 1H), 7.39 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.25 (tt, *J* = 6.9, 3.0, 1.8 Hz, 1H), 7.21-7.09 (m, 2H), 2.71 (m, 2H), 2.62 (dddd, *J* = 13.6, 6.8, 6.8, 6.8 Hz, 1H), 2.27 (m, 1H), 1.92 (m, 1H), 1.73-1.48 (m, 2H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.68 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 202.5, 139.9, 134.5, 129.6, 127.6, 126.4, 126.3, 56.3, 32.2, 30.2, 22.0, 20.3, 17.2, 16.4. IR (neat, cm^{-1}): 3059, 3022, 2939, 2870, 2712, 1724, 1598, 1491, 1446, 1032, 755, 736, 701, 657.



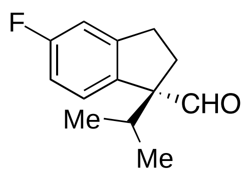
2j

(*R*)-1-phenyl-1,2,3,4-tetrahydronaphthalene-1-carbaldehyde 2j (Table 3, entry 10). General procedure E was followed using 5-(2-bromophenyl)-2-phenylpentanal **1j** (120 μL, 159 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 63 mg (53% yield). Enantioselectivity: 63% *ee*, Chiral GC B-DA column, 85 °C to 170 °C at 1.5 °C min^{-1}; t_{minor}= 42.43 min, t_{major}= 41.33 min. ^1H NMR (300 MHz, $CDCl_3$) δ: 9.88 (s, 1H), 7.39-7.18 (m, 6H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.03 (m, 2H), 2.88 (m, 2H), 2.60 (ddd, *J* = 13.1, 7.1, 3.8 Hz, 1H), 1.93 (m, 1H), 1.78 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.1, 144.1, 139.6, 133.5, 130.6, 130.0, 128.5, 128.2, 127.3, 126.9, 126.1, 60.2, 33.9, 29.8, 19.5. IR (neat, cm^{-1}): 2962, 2938, 2703, 1722, 1488, 1449, 1389, 1370, 1026, 840, 756, 736, 637.



4a

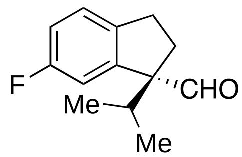
(*R*)-1-isopropyl-5-methoxy-2,3-dihydro-1*H*-indene-1-carbaldehyde 4a (Table 4, entry 1). General procedure E was followed using 2-(2-bromo-5-methoxyphenethyl)-3-methylbutanal **3a** (110 μL, 150 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/ethyl acetate. Colorless oil; yield: 62 mg (57% yield), 79 mg (72% yield when 5 mol% $Pd(OAc)_2$ and 15 mol% of **L9i** were used). Enantioselectivity: 93% *ee*, Chiral HPLC AD-H column, Hexanes:*i*PrOH 99:1, 1 mL min^{-1}; t_{minor}= 8.70 min, t_{major}= 7.70 min;. $[\alpha]_D$ +45.9 (*c* 1.09, $CHCl_3$, 93% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 9.47 (s, 1H), 7.08 (m, 1H), 6.78 (m, 1H), 3.78 (s, 3H), 2.90 (m, 2H), 2.50 (m, 2H), 1.97 (ddd, *J* = 13.3, 8.8, 8.8 Hz, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.9, 159.9, 146.8, 132.9, 124.9, 112.7, 110.3, 67.4, 55.3, 30.9, 30.0, 24.6, 18.2, 16.5. IR (neat, cm^{-1}): 2961, 2696, 1720, 1604, 1585, 1490, 1466, 1310, 1258, 1174, 1144, 1102, 1089, 1037, 846, 816. Elemental analysis for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.92; H, 8.41.



4b

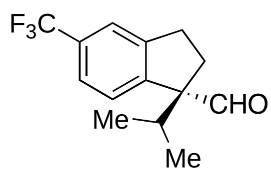
(*R*)-5-fluoro-1-isopropyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 4b (Table 4, entry 2). General procedure E was followed using 2-(2-bromo-5-fluorophenethyl)-3-methylbutanal **3b** (105 μL, 144 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 85 mg (82% yield). Enantioselectivity: 95% *ee*, Chiral GC B-DA column, 85 °C to 170 °C at 1.5 °C min^{-1}; t_{minor}= 41.82 min, t_{major}= 41.32 min; $[\alpha]_D$ +32.2 (*c* 1.3, $CHCl_3$, 95% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 9.48 (d, *J* = 0.7 Hz, 1H), 7.12 (dd, *J* = 9.0, 5.2 Hz, 1H), 6.97-6.86 (m, 2H), 2.91 (m, 2H), 2.51 (m, 2H), 1.99 (dddd, *J* = 13.3, 8.4, 8.5, 0.7 Hz, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.75 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.8, 162.9 (d, *J* = 245.4 Hz), 147.4 (d, *J* = 8.2 Hz), 136.4 (d, *J* = 2.5 Hz), 125.2 (d, *J* = 9.2 Hz), 113.7 (d, *J* = 22.8 Hz), 112.1 (d, *J* = 22.8 Hz) , 67.5, 30.7, 30.2, 24.7, 18.1, 16.5. ^{19}F NMR

(282 MHz, $CDCl_3$) δ: −115.34 (m). IR (neat, cm^{-1}): 2963, 2875, 1723, 1607, 1483, 1246, 1086, 931, 864, 816. Elemental analysis for $C_{13}H_{15}FO$: C, 75.70; H, 7.33. Found: C, 75.51; H, 7.40.



4c

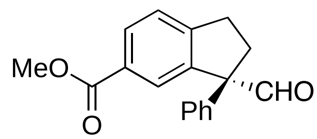
(*R*)-6-fluoro-1-isopropyl-2,3-dihydro-1*H*-indene-1-carbaldehyde 4c (Table 4, entry 3). General procedure E was followed using 2-(2-bromo-4-fluorophenethyl)-3-methylbutanal **3c** (105 μL, 144 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 80 mg (78% yield). Enantioselectivity: 93% *ee*, Chiral GC T-GA column, 85 °C to 170 °C at 1.5 °C min^{-1}; t_{minor}= 34.97 min, t_{major}= 35.49 min; $[\alpha]_D$ +31.7 (*c* 1.72, $CHCl_3$, 93% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.51 (d, *J* = 0.9 Hz, 1H), 7.15 (ddd, *J* = 7.8, 5.2, 0.9 Hz, 4H), 6.92 (m, 2H), 2.89 (m, 2H), 2.54 (m, 2H), 2.02 (dddd, *J* = 13.3, 8.6, 8.6, 0.9 Hz, 1H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.6, 162.1 (d, *J* = 243.7 Hz), 143.1 (d, *J* = 7.3 Hz), 140.3 (d, *J* = 2.5 Hz), 125.9 (d, *J* = 8.8 Hz), 114.9 (dd, *J* = 22.4, 2.4 Hz), 111.2 (dd, *J* = 22.4, 3.6 Hz), 68.3 (d, *J* = 1.9 Hz), 30.3 (d, *J* = 1.6 Hz), 30.1 (d, *J* = 1.6 Hz), 24.9, 18.0, 16.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −116.93 (dd, *J* = 8.8, 14.2 Hz). IR (neat, cm^{-1}): 2964, 1724, 1596, 1489, 1260, 1176, 865, 817.



4d

(*R*)-1-isopropyl-5-(trifluoromethyl)-2,3-dihydro-1*H*-indene-1-carbaldehyde 4d (Table 4, entry 4). General procedure E was followed using 2-(2-bromo-5-(trifluoromethyl) phenethyl)-3-methylbutanal **3d** (120 μL, 169 mg, 0.50 mmol), (5.7 mg, 5 mol%) of $Pd(OAc)_2$ and (40 mg, 15 mol%) of **L9i**. Column chromatography: silica gel, 95:5 hexanes/diethyl ether. Colorless oil; yield: 111 mg (87% yield). Enantioselectivity: 94% *ee*, Chiral GC T-GA column, 85 °C to 170 °C at 1.5 °C min^{-1}; t_{minor}= 37.20 min, t_{major}= 36.92 min; $[\alpha]_D$ +32.8 (*c* 0.936, $CHCl_3$, 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.54 (d, *J* = 0.9 Hz, 1H), 7.50 (m, 2H), 7.32 (d, *J* = 7.8 Hz, 1H), 2.99 (m, 2H), 2.59 (m, 2H), 2.04 (dddd, *J* = 13.4, 8.5, 8.4, 0.9 Hz, 1H), 0.93 (d, *J* = 6.6

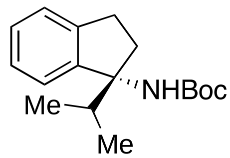
Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 200.5, 146.0, 145.1, 131.1, 130.5, 130.1, 129.7, 129.6, 126.0, 124.6, 123.8, 123.8, 122.4, 122.0, 122.0, 68.4, 30.7, 30.6, 30.5, 24.5, 18.0, 16.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −62.6 (s). IR (neat, cm^{-1}): 2966, 2877, 1725, 1432, 1332, 1310, 1162, 1124, 1065, 889, 831. Elemental analysis for $C_{14}H_{15}F_3O$: C, 65.62; H, 5.90. Found: C, 65.17; H, 5.84.



4e

(*R*)-methyl 3-formyl-3-phenyl-2,3-dihydro-1*H*-indene-5-carboxylate 4d (Table 4, entry 5). General procedure E was followed using methyl 3-bromo-4-(4-oxo-3-phenylbutyl) benzoate **3e** (181 mg, 0.50 mmol). Column chromatography: silica gel, 95:5 hexanes/ethyl acetate. Colorless oil; yield: 65 mg (46% yield), 81 mg (58% yield when 5 mol% $Pd(OAc)_2$ and 15 mol% of **L9i** were used). Enantioselectivity: 97% *ee*, Chiral HPLC OD-H column, Hexanes:*i*PrOH 95:5, 1 mL min^{-1}; t_{minor}= 10.54 min, t_{major}= 7.98 min;. $[\alpha]_D$ −106.7 (*c* 1.24, $CHCl_3$, 97% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.78 (d, J = 0.8 Hz, 1H), 8.04 (dd, J = 7.9, 1.5 Hz, 1H), 7.97 (s, 1H), 7.45-7.29 (m, 4H), 7.11 (m, 2H), 3.90 (s, 3H), 3.16-2.98 (m, 3H), 2.20 (dddd, J = 11.9, 8.2, 7.1, 0.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 196.7, 166.8, 151.3, 140.9, 140.5, 130.1, 129.1, 127.5, 127.4, 127.1, 125.4, 68.9, 52.1, 35.7, 30.9. IR (neat, cm^{-1}): 2950, 1721, 1609, 1493, 1436, 1288, 1233, 1109, 761, 701. Elemental analysis for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.00; H, 5.85.

SYNTHESIS OF DERIVATIVES.

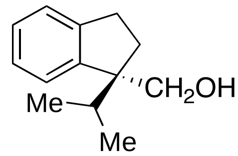


5

(*R*)-*tert*-butyl 1-isopropyl-2,3-dihydro-1*H*-inden-1-ylcarbamate 5 (Scheme 2). To a solution of **2b** (130 mg, 0.69 mmol) in *t*BuOH (15 mL) was added at RT 2-methyl-2-butene (3.5 mL), NaH_2PO_4 (525 mg, 3.8 mmol) in H_2O (6 mL) and $NaClO_2$ (625 mg, 6.9 mmol) in H_2O (3 mL). The resulting mixture was stirred at RT for 16 h. After this time the reaction mixture was poured into a separation funnel containing HCl (0.1 M) and it was extracted with EtOAc (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

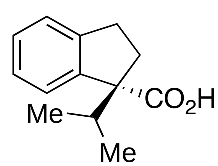
To a solution of the crude acid obtained above in toluene (10 mL) was added at RT and under Ar Et_3N (145 µL, 1.04 mmol) and diphenylphosphoryl azide (225 µL, 1.04 mmol). The mixture was stirred at reflux for 2 h. After cooling to RT, the solvent was removed under reduced pressure. The crude material so obtained was redissolved in diethyl ether (20 mL) and it was washed with H_2O (2 x 15 mL). The ethereal phase was dried over $MgSO_4$, filtered and the solvent was removed to dryness.

The crude isocyanate obtained above was redisolved in *t*BuOH (10 mL) and NaO*t*Bu (995 mg, 10.35 mmol) was added. The mixture was stirred at reflux for 16 h. After cooling to RT, the reaction mixture was poured into a separation funnel containing NH_4Cl aq. and it was extracted with diethyl ether (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified on silica gel. Column chromatography 9:1 hexanes/ethyl acetate. Colorless oil; yield: 132 mg (70% overall yield). Enantioselectivity: 94% *ee*, Chiral HPLC AD-H column, Hexanes:*i*PrOH 98:2, 1 mL min^{-1}; t_{minor}= 9.48 min, t_{major}= 7.40 min; $[\alpha]_D$ +7.2 (*c* 1.32, $CHCl_3$, 94% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.20 (m, 4H), 5.02 (br s, 1H), 3.01 (m, 1H), 2.84 (td, *J* = 16.3, 8.1 Hz, 1H), 2.53 (m, 1H), 2.38 (m, 2H), 1.37 (br s, 9H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.2, 144.8, 143.6, 127.4, 125.9, 124.5, 123.5, 78.8, 69.8, 34.5 (this signal appears as a mixture of two rotamers at 34.8 and 34.3 ppm), 30.6, 28.2 17.5, 17.1. IR (neat, cm^{-1}): 3282, 2973, 2925, 1721 1694, 1480, 1390, 1365, 1254, 1167, 1102, 762. Elemental analysis for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15. Found: C, 74.38; H, 9.11.



6

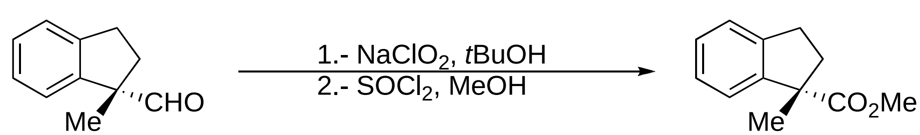
(*R*)-(1-isopropyl-2,3-dihydro-1*H*-inden-1-yl)methanol 6 (Scheme 2). An oven-dried resealable test tube containing a stirring bar was charged with $Pd(OAc)_2$ (3.4 mg, 15 µmol, 3.0 mol%), **L9i** (24 mg, 45 µmol, 9.00 mol%) and Cs_2CO_3 (210 mg, 0.65 mmol). The test tube fitted with a screw cap with a pierceable teflon septum was then evacuated and back-filled with dry argon (this sequence was repeated three times). Then, *t*BuOH (5 mL) and freshly prepared 2-(2-bromophenethyl)-3-methylbutanal **1b** (105 µL, 135 mg, 0.50 mmol) was added by syringe. The mixture was stirred in a pre-heated oil bath (80 °C) for 24 h. After cooling to RT, MeOH (15 mL) and $NaBH_4$ (38 mg, 1.0 mmol) were added and the mixture was stirred at RT for 30 min more. After this time, the reaction mixture was poured into a separation funnel containing NH_4Cl aq. and it was extracted with dichloromethane (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified on silica gel. Column chromatography: silica gel, 85:15 hexanes/ethyl acetate. Colorless oil; yield: 87 mg (91% yield). Enantioselectivity: 94% *ee*, chiral HPLC OD-H column, Hexanes:*i*PrOH 95:5, 1 mL min^{-1}; t_{minor}= 7.65 min, t_{major}= 6.59 min; $[\alpha]_D$ –38.5 (*c* 0.704, $CHCl_3$, 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.28-7.13 (m, 4H), 3.77 (d, *J* = 11.1 Hz, 1H), 3.60 (d, *J* = 11.1 Hz, 1H), 2.91 (m, 2H), 2.20 (td, *J* = 14.1, 7.0 Hz, 1H), 2.06 (ddd, *J* = 13.3, 8.8, 7.0 Hz, 1H), 1.87 (ddd, *J* = 13.3, 8.8, 5.9 Hz, 1H), 1.32 (br s, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.72 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 146.1, 145.1, 127.0, 126.1, 124.7, 123.7, 68.3, 57.2, 31.6, 31.0, 28.1, 18.3, 17.6. IR (neat, cm^{-1}): 3377, 2956, 2873, 1478, 1385, 1033, 760.



7

(*R*)-1-isopropyl-2,3-dihydro-1*H*-indene-1-carboxylic acid 7 (Scheme 2). An oven-dried resealable test tube containing a stirring bar was charged with $Pd(OAc)_2$ (3.4 mg, 15 µmol, 3.0 mol%), **L9i** (24 mg, 45 µmol, 9.00 mol%) and Cs_2CO_3 (210 mg, 0.65 mmol). The test tube fitted with a screw cap with a pierceable teflon septum was then evacuated and back-filled with dry argon (this sequence was repeated three times). Then, *t*BuOH (5 mL) and freshly prepared 2-(2-bromophenethyl)-3-methylbutanal **1b** (105 μL, 135 mg, 0.50 mmol) was added by syringe. The mixture was stirred in a pre-heated oil bath (80 °C) for 24 h. The mixture was allowed to cool to room temperature and it was filtered through a Celite® plug, eluting with additional *t*BuOH (5 mL). To this solution was added 2-methyl-2-butene (2.6 mL), NaH_2PO_4 (370 mg, 2.75 mmol) in H_2O (5 mL) and $NaClO_2$ (445 mg, 5.0 mmol) in H_2O (3 mL). The resulting mixture was stirred at RT for 16 h. Then it was poured into a separation funnel containing NaOH (0.5 M) and it was washed with dichloromethane (30 mL). The phases were separated, the aqueous one was acidified with HCl (3 M) and it was extracted with dichloromethane (3 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure providing carboxylic acid **7** that was enantiomerically pure as judged by GC and NMR. White solid; m.p. (53-55) °C; yield: 97 mg (95% yield). Enantioselectivity: 94% *ee*, Chiral HPLC OD-H column, Hexanes:*i*PrOH 95:5, 1 mL min^{-1}; t_{minor}= 5.58 min, t_{major}= 4.94 min; $[\alpha]_D$ –34.2 (*c* 1.662, $CHCl_3$, 94% ee). ^1H NMR (300 MHz, $CDCl_3$) δ: 11.75 (br s, 1H), 7.45 (m, 1H), 7.24 (m, 3H), 3.1 (td, *J* = 16.5, 8.4 Hz, 1H), 2.92 (m, 1H), 2.76 (td, J = 13.5, 6.8 Hz, 1H), 2.63 (ddd, J = 13.0, 8.9, 3.7 Hz, 1H), 2.05 (ddd, *J* = 13.0, 9.20, 7.9 Hz, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 182.4, 144.4, 142.9, 127.7, 126.4, 125.1, 124.5, 63.7, 33.5, 31.0, 27.2, 18.6, 17.1. IR (neat, cm^{-1}): 2963, 1693, 1476, 1389, 1281, 940, 763.

DERIVATIZATION OF 2a



2a

S17

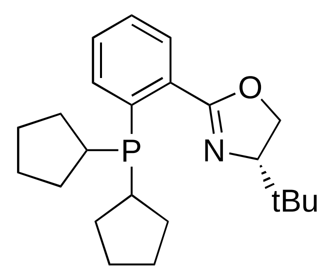
(*S*)-methyl 1-methyl-2,3-dihydro-1*H*-indene-1-carboxylate S17. To a solution of **2a** (135 mg, 0.57 mmol) in *t*BuOH (10 mL) was added at RT 2-methyl-2-butene (2.8 mL), NaH_2PO_4 (435 mg, 3.14 mmol) in H_2O (4 mL) and $NaClO_2$ (515 mg, 5.7 mmol) in H_2O (2 mL). The resulting mixture was stirred at RT for 16 h. After this time the reaction mixture was poured into a separation funnel containing HCl (0.1 M) and it was extracted with EtOAc (3 x 15 mL).

The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

To a solution of the crude acid prepared above in MeOH (10 mL) was added at −78 °C and under Ar, $SOCl_2$ (170 µL, 2.3 mmol). The mixture was allowed to warm to RT and was stirred for 16 h. After this time was concentrated on under reduced pressure and it was purified on silica gel. Column chromatography 9:1 hexanes/diethyl ether. Colorless oil; yield: 106 mg (98% overall yield). $[\alpha]_D$ −12.0 (*c* 0.14, $CHCl_3$, 87 % ee; lit.[13] $[\alpha]_D$ +19 (*c* 0.15, $CHCl_3$ for *R* isomer). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.34 (m, 1H), 7.24 (m, 3H), 3.68 (s, 3H), 3.11 (td, *J* = 15.7, 7.5 Hz, 1H), 2.96 (ddd, *J* = 15.7, 8.5, 4.8 Hz, 1H), 2.76 (ddd, *J* = 13.0, 8.5, 4.8 Hz, 1H), 1.98 (ddd, *J* = 13.0, 8.5, 7.5 Hz, 1H), 1.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.5, 145.9, 143.5, 127.4, 126.5, 124.5, 123.7, 54.4, 52.1, 37.6, 30.8, 24.9. IR (neat, cm^{-1}): 2950, 1730, 1459, 1237, 1157, 1095, 758.

[13] H. Abbayes, M. A. Boudeville, *Tetrahedron Lett.* **1976**, *25*, 2137-2140.

SELECTED SPECTRA



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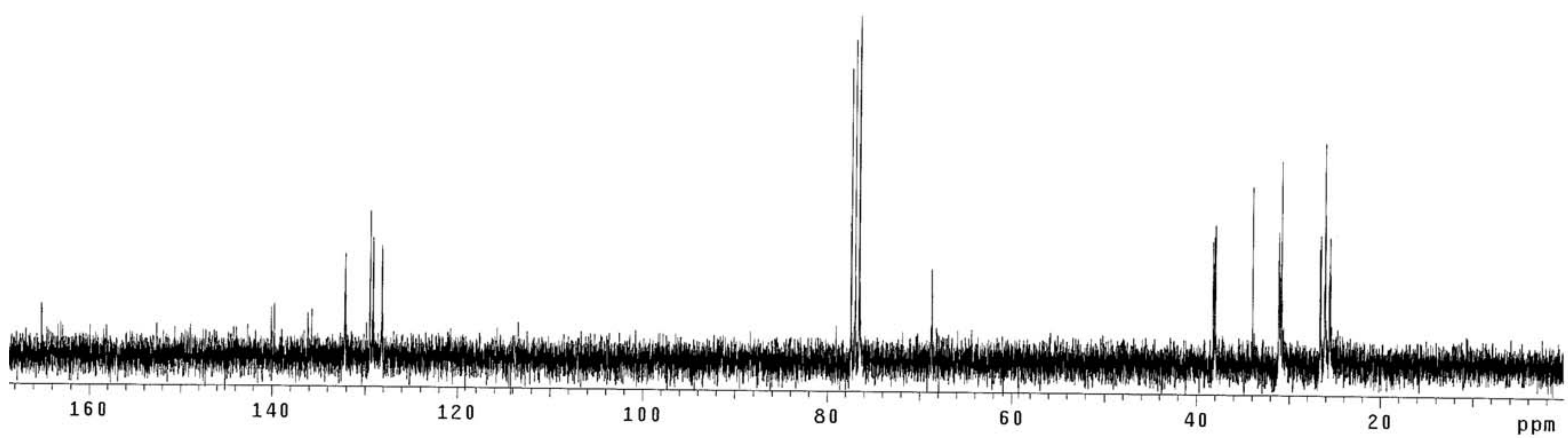

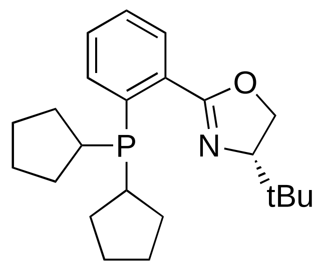

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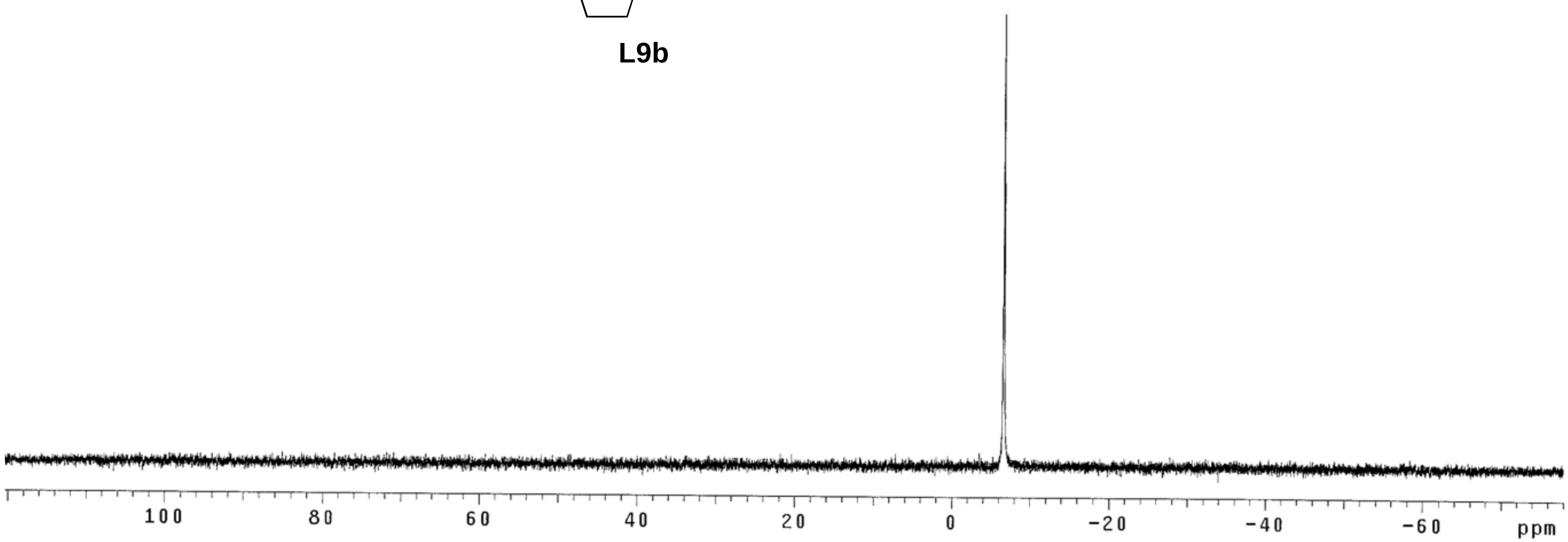

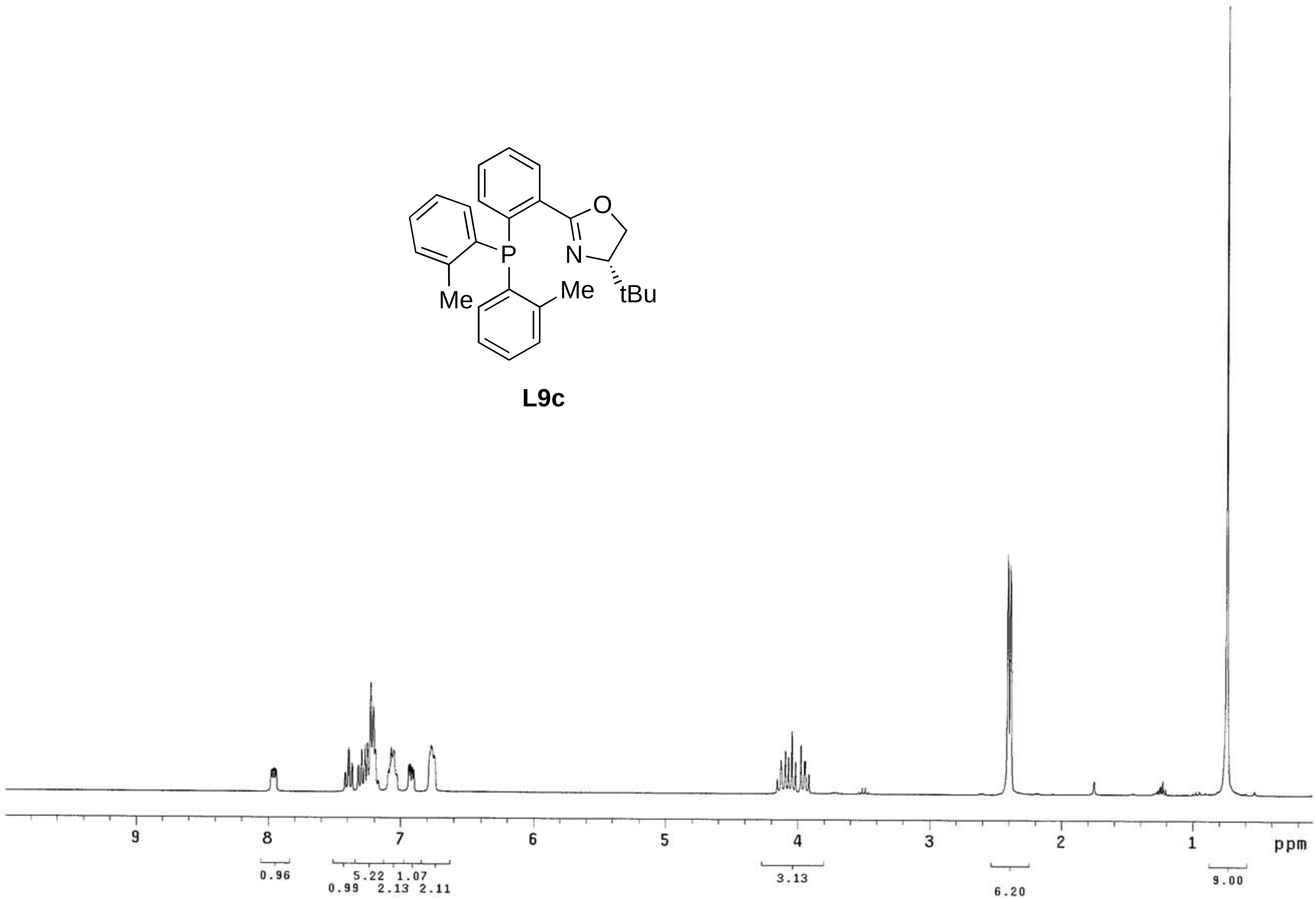

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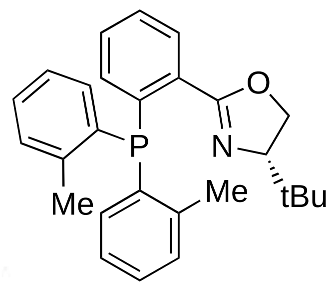

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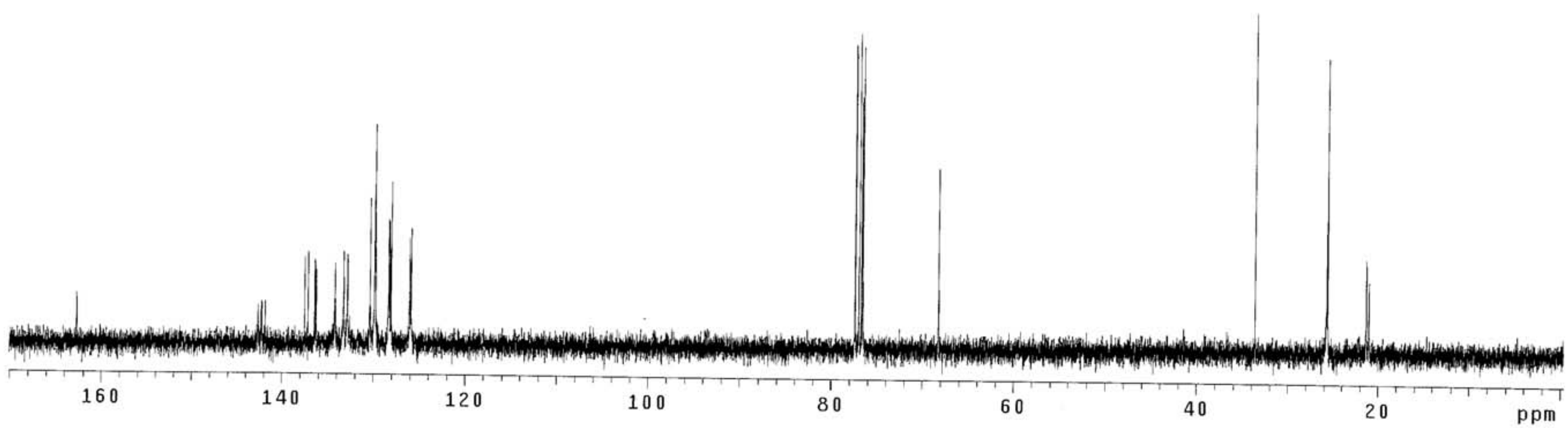

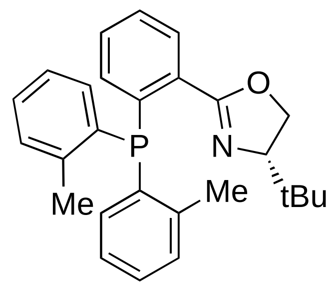

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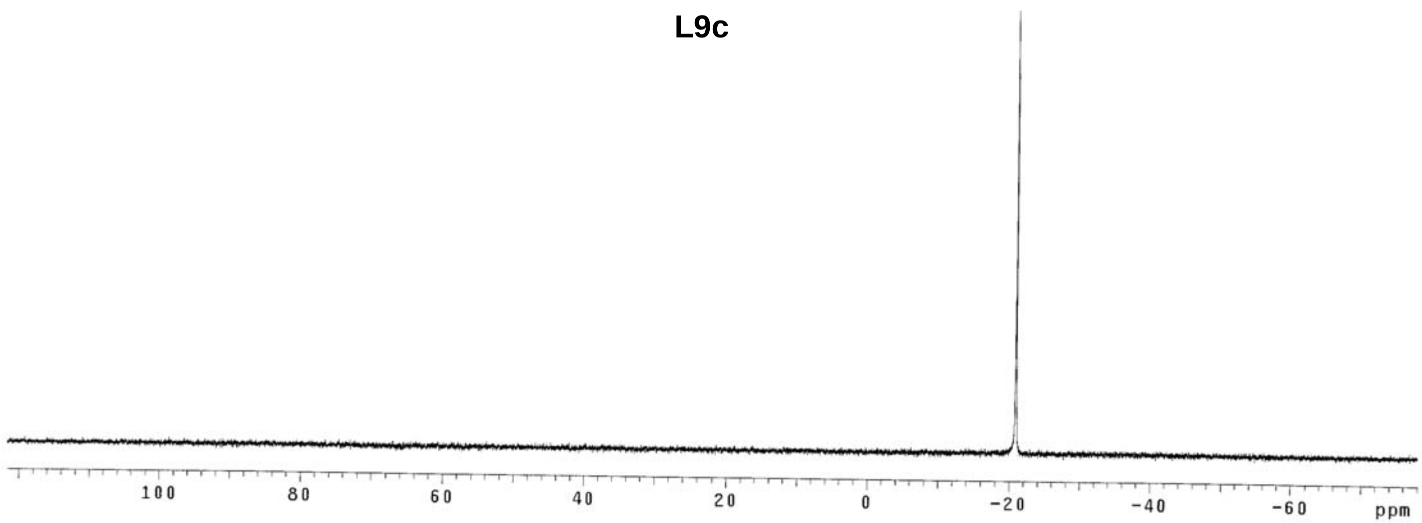

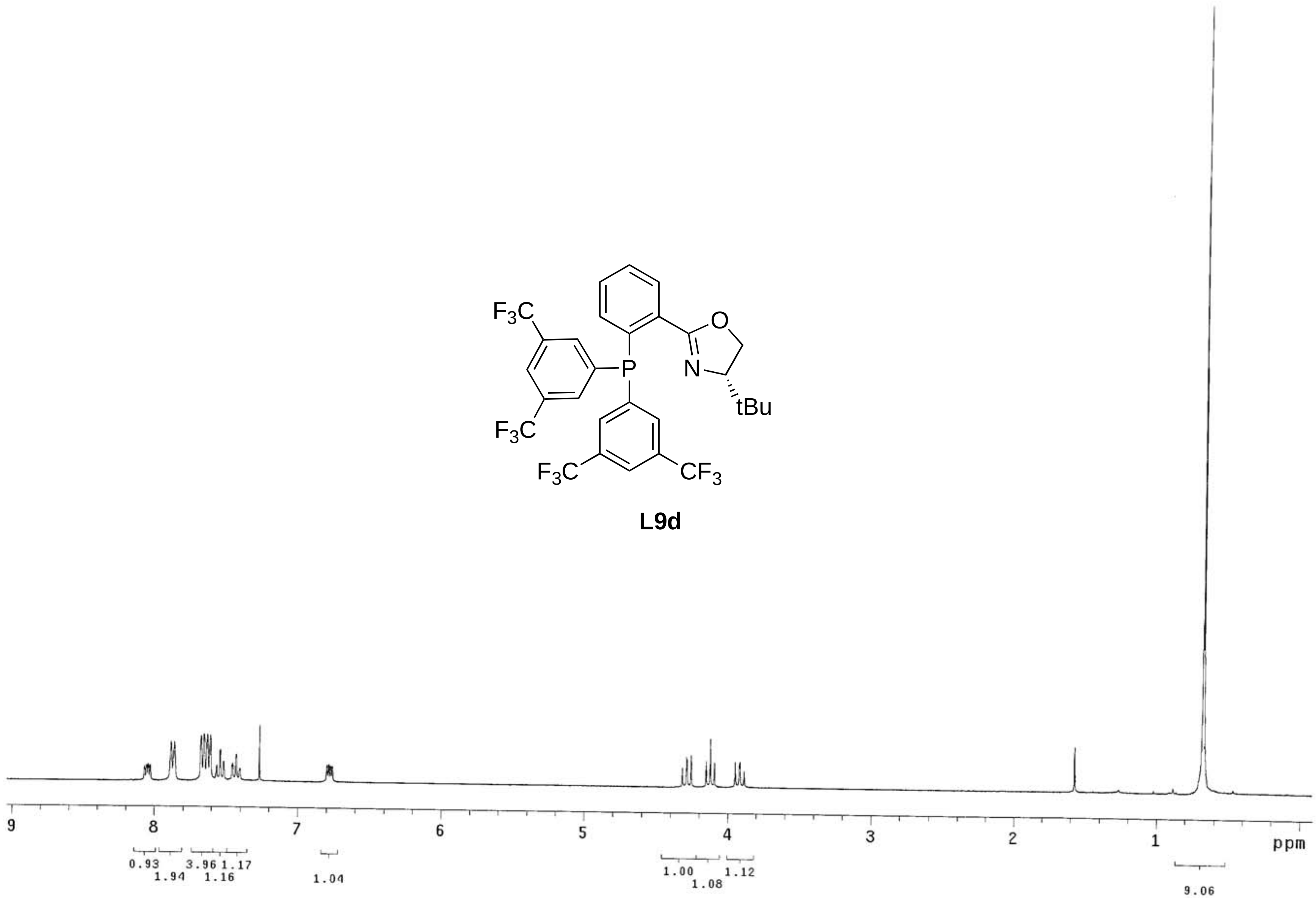

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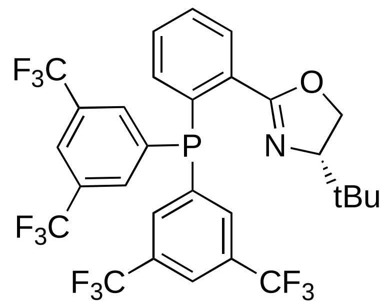

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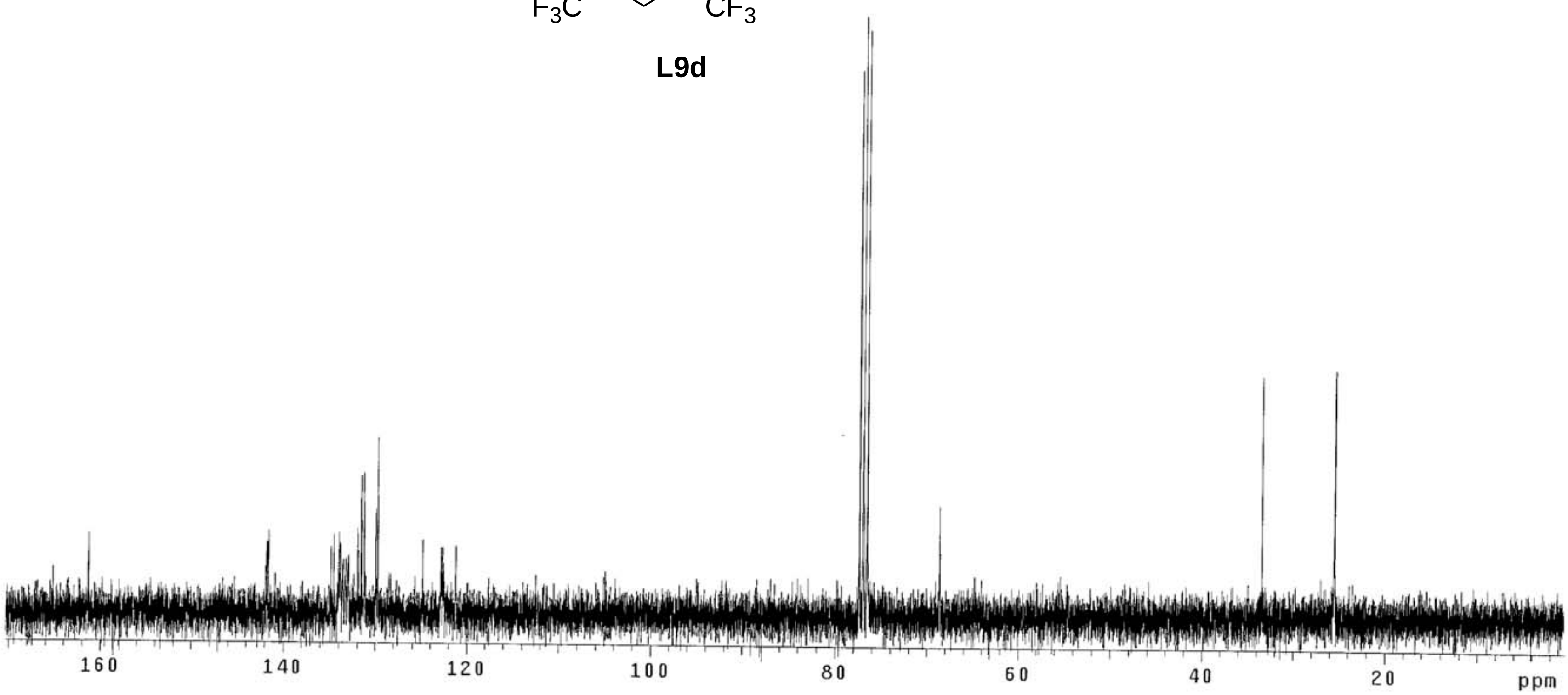

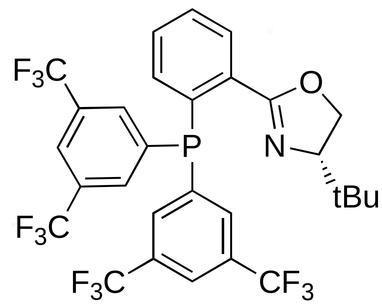

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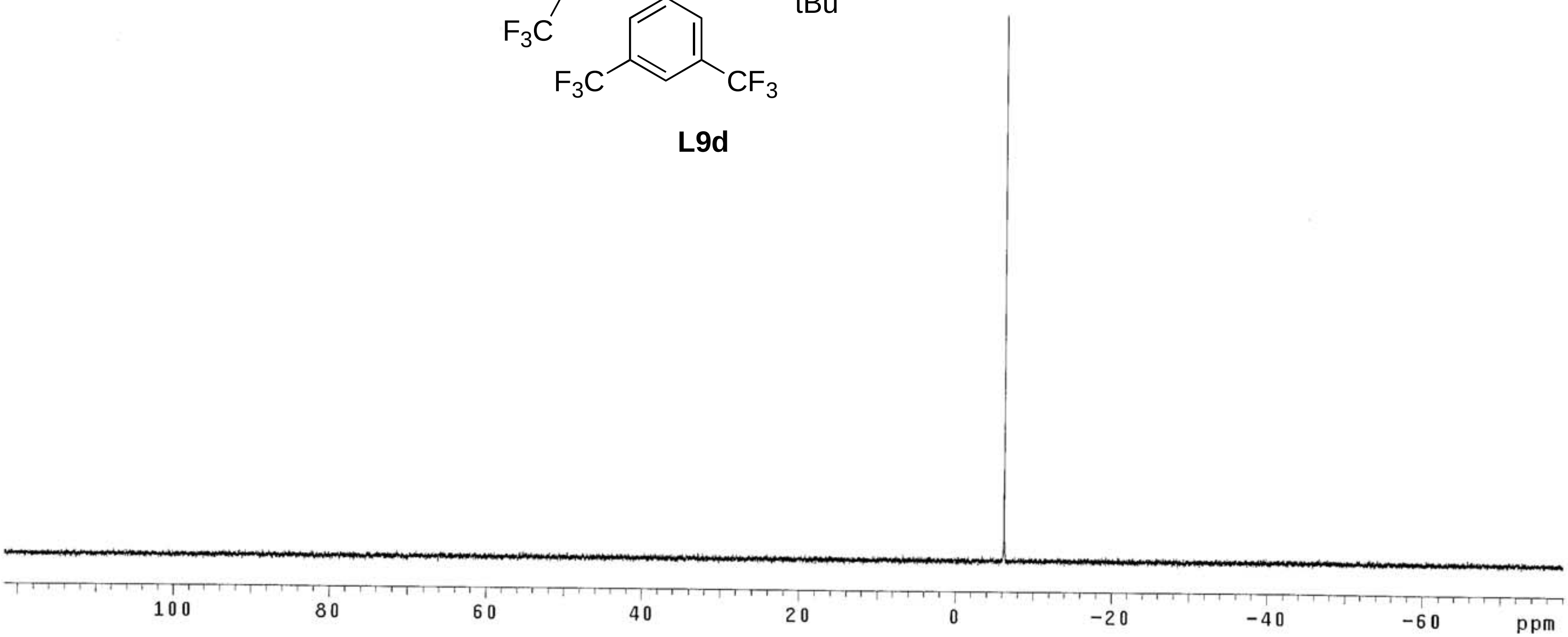

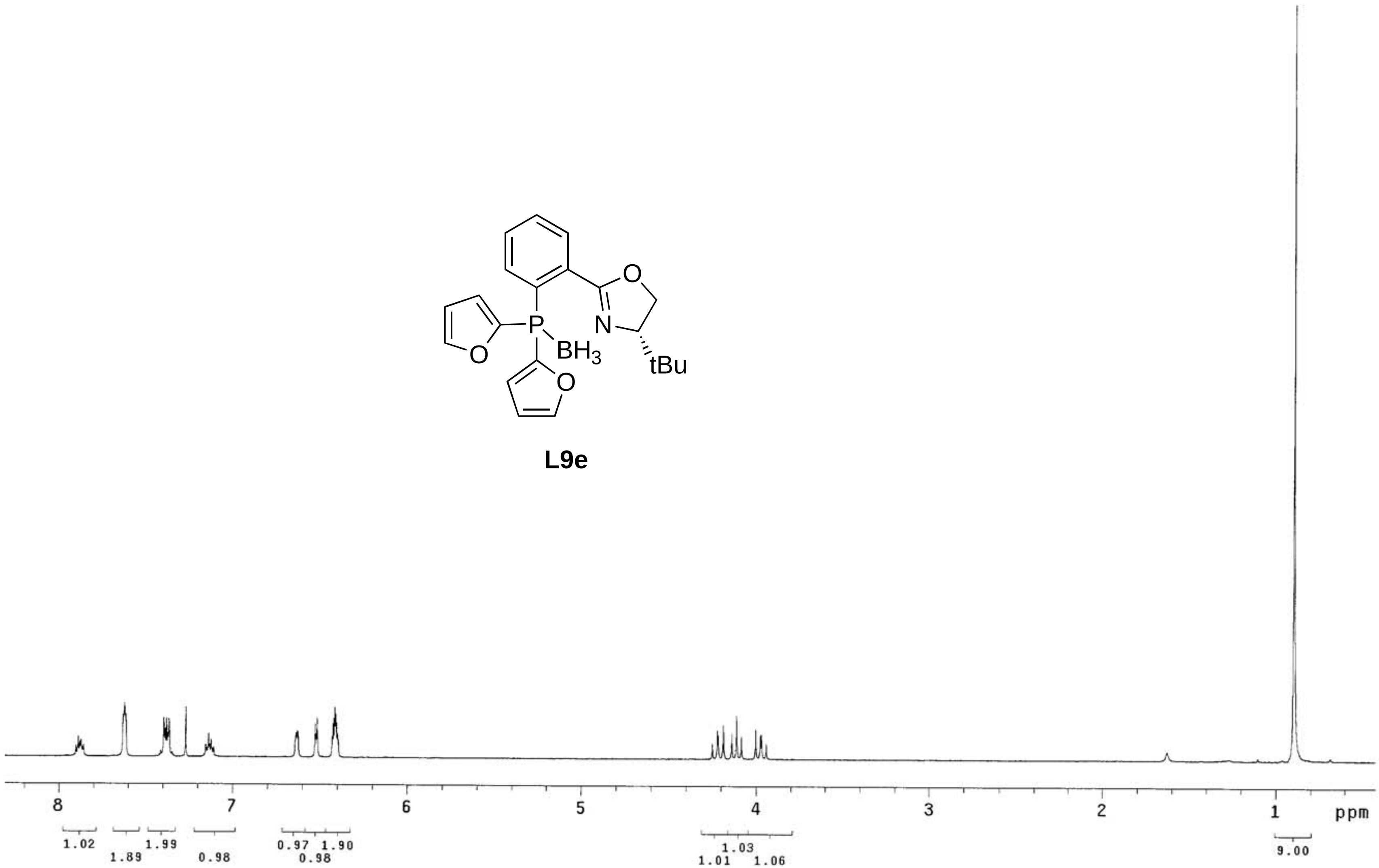
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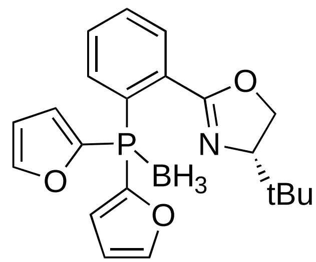

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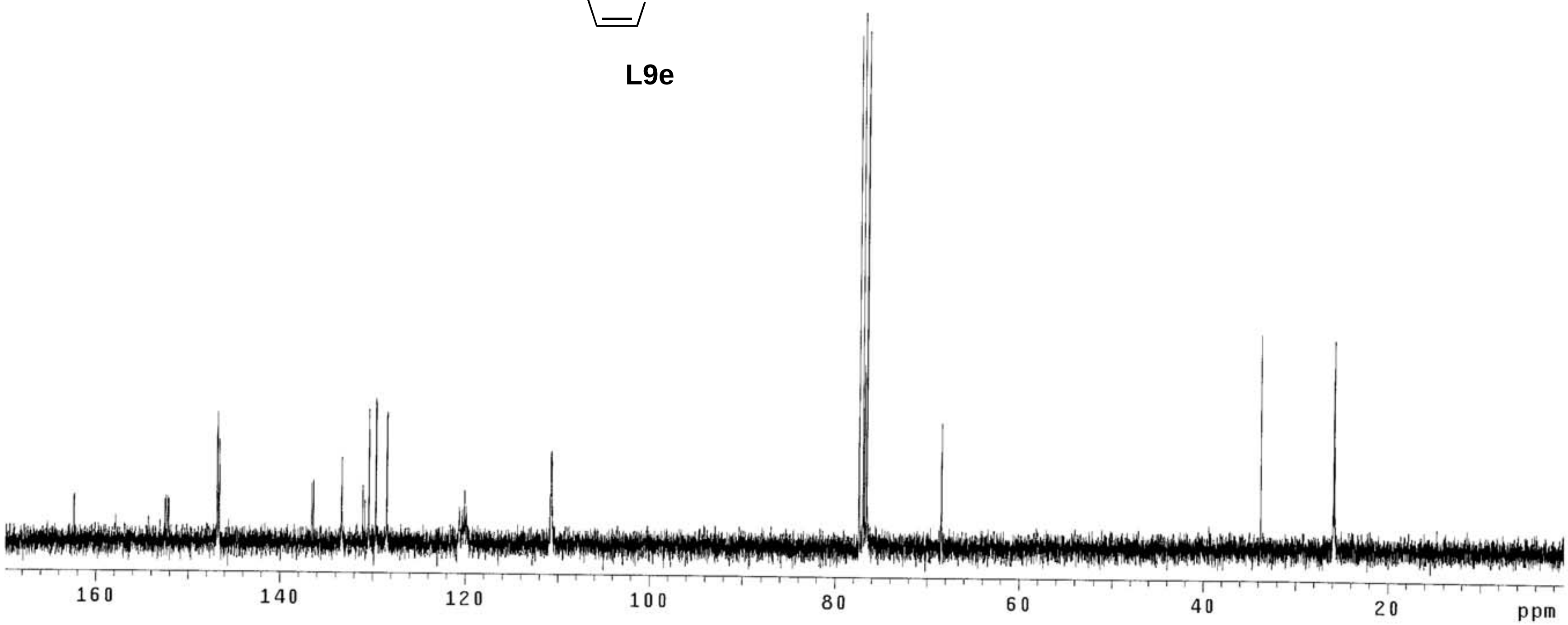

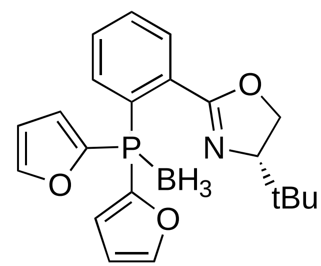

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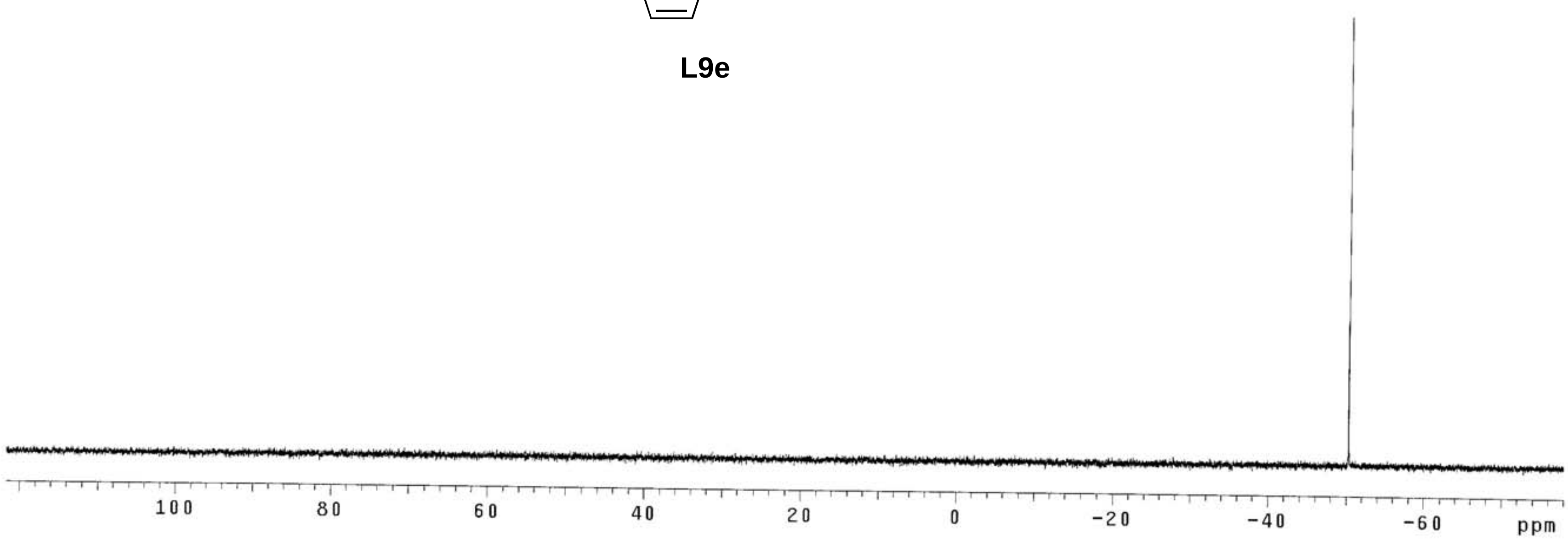

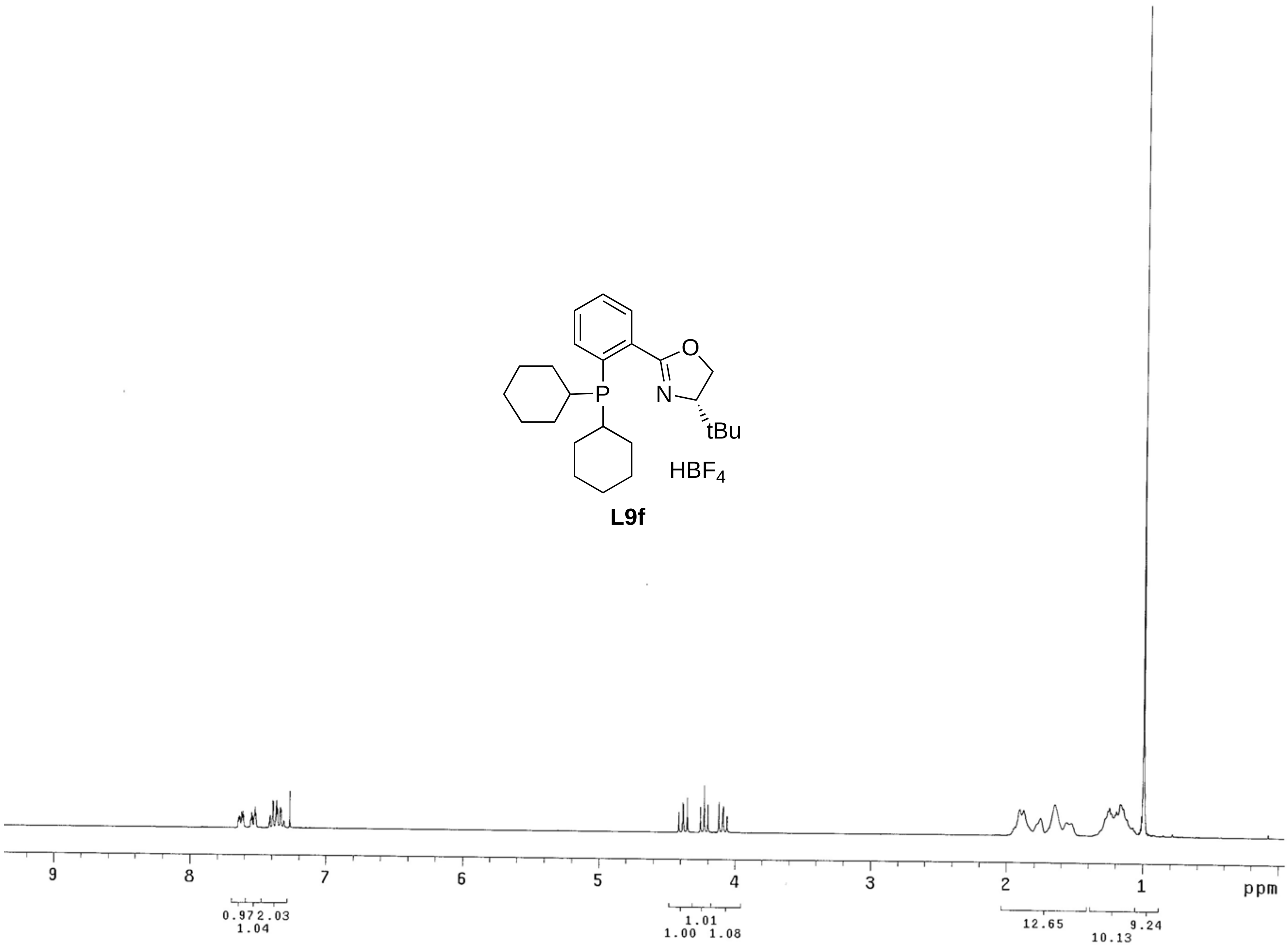
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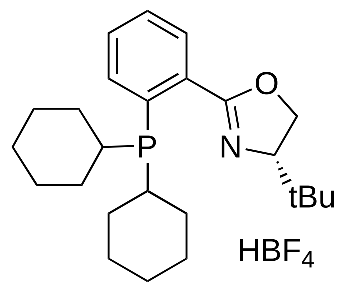

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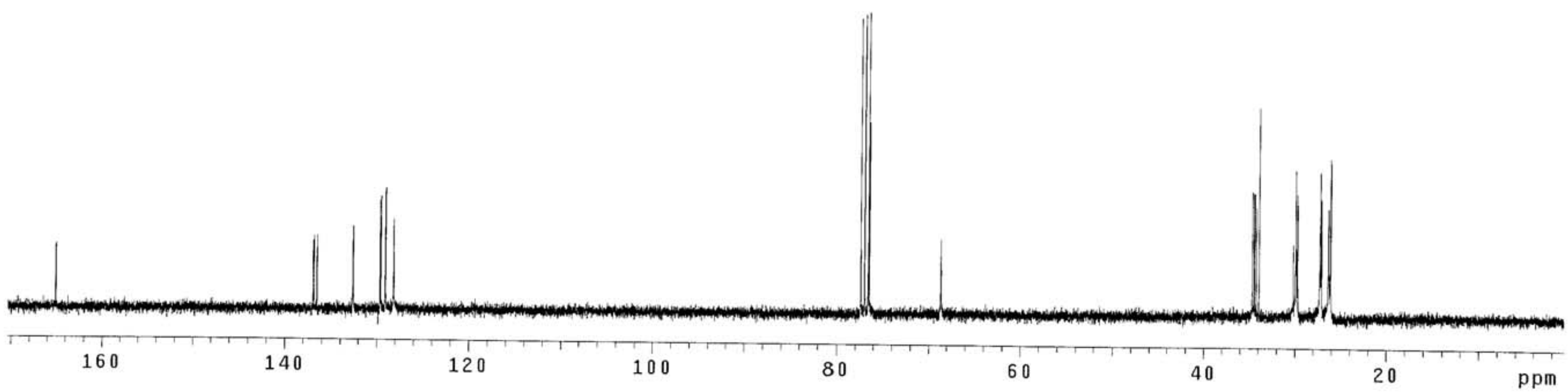

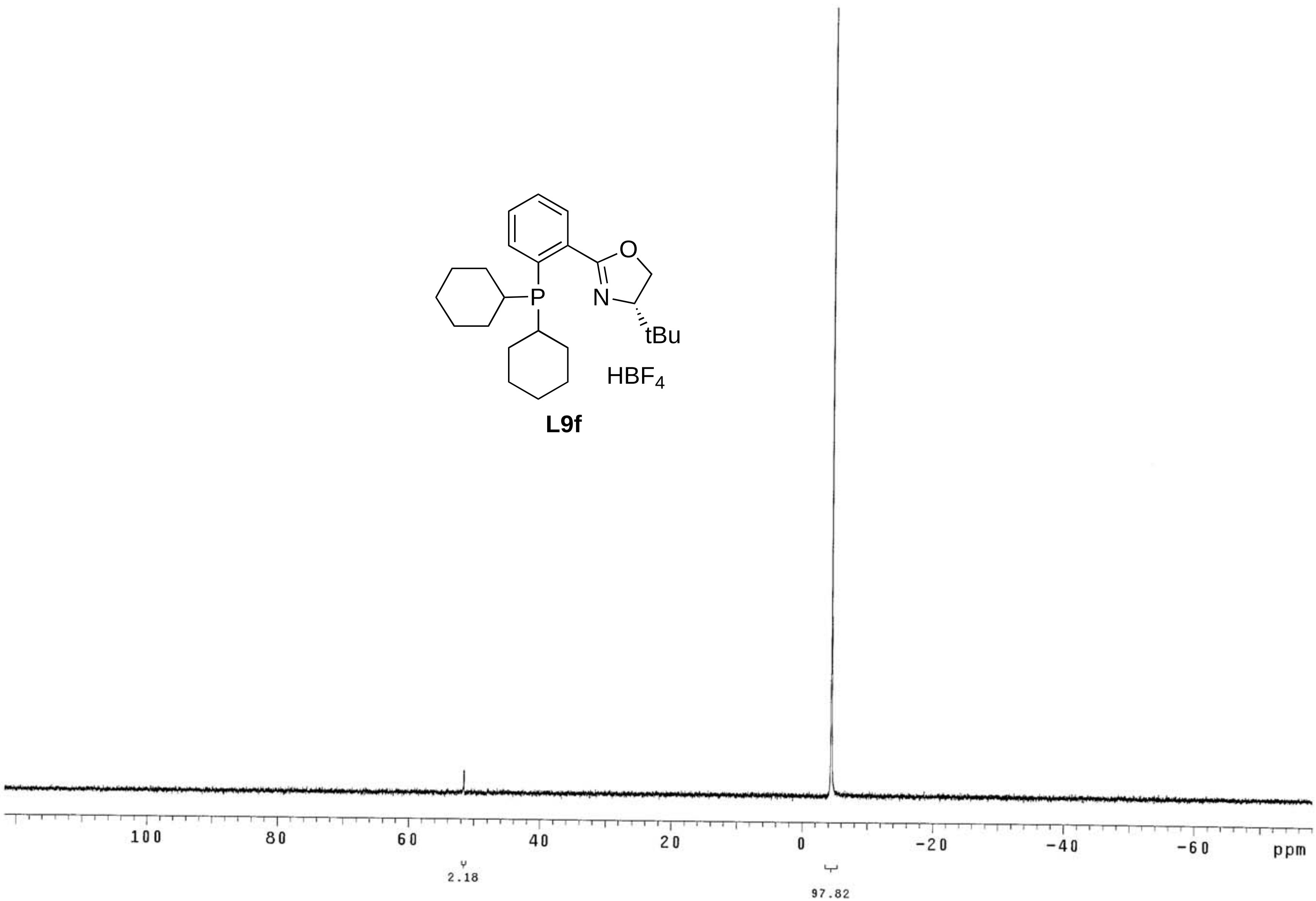
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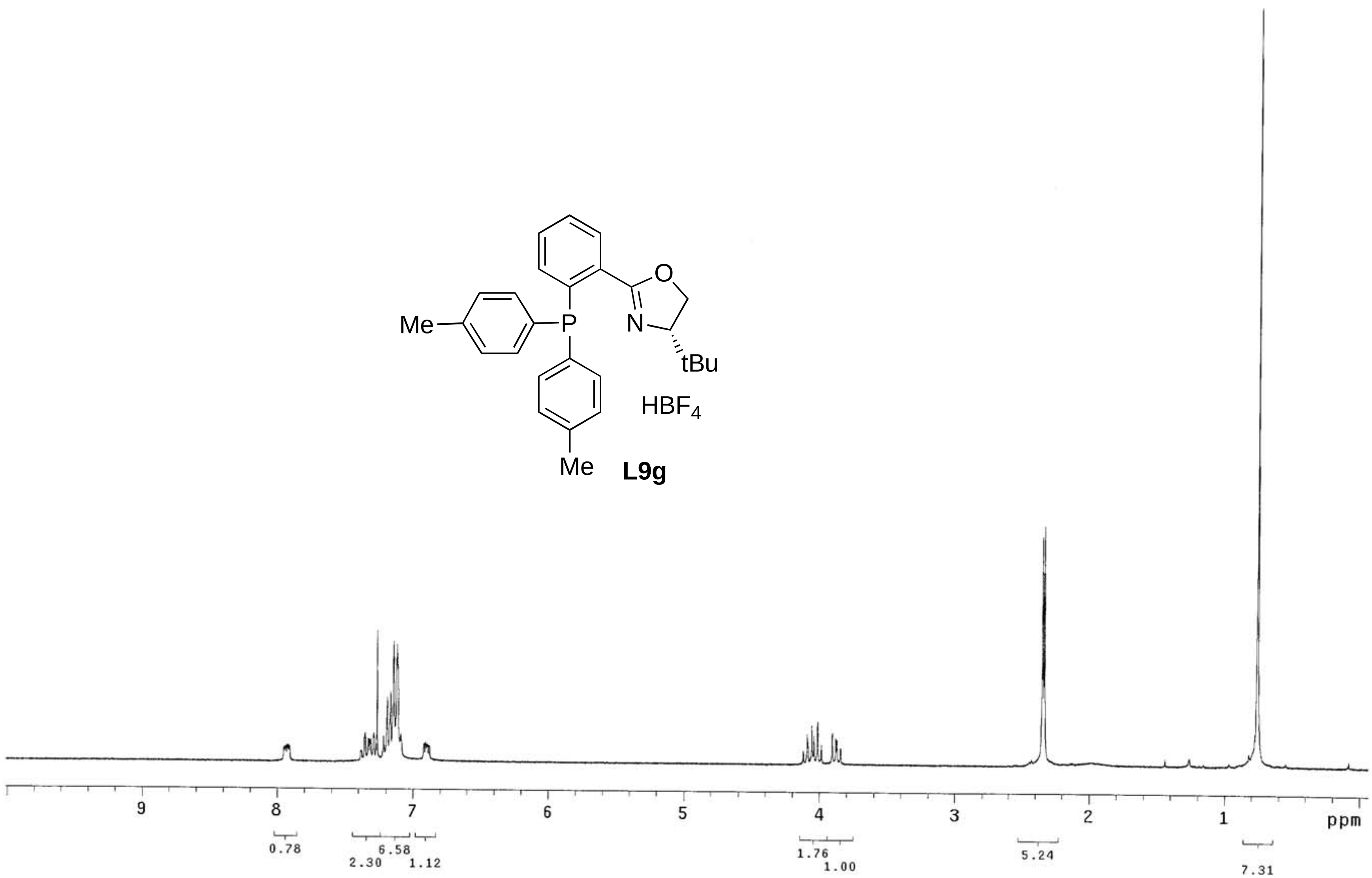

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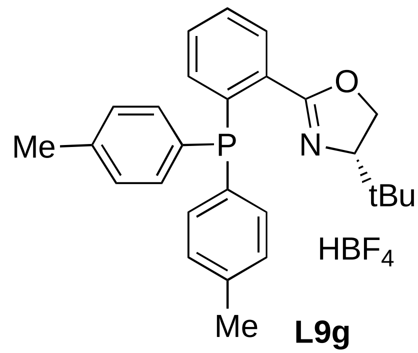

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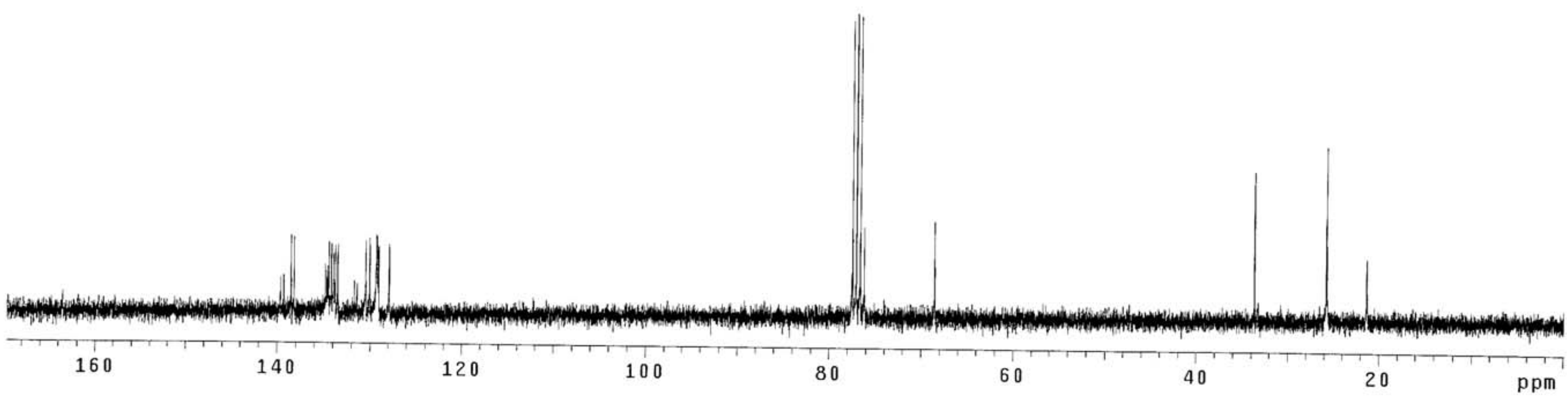

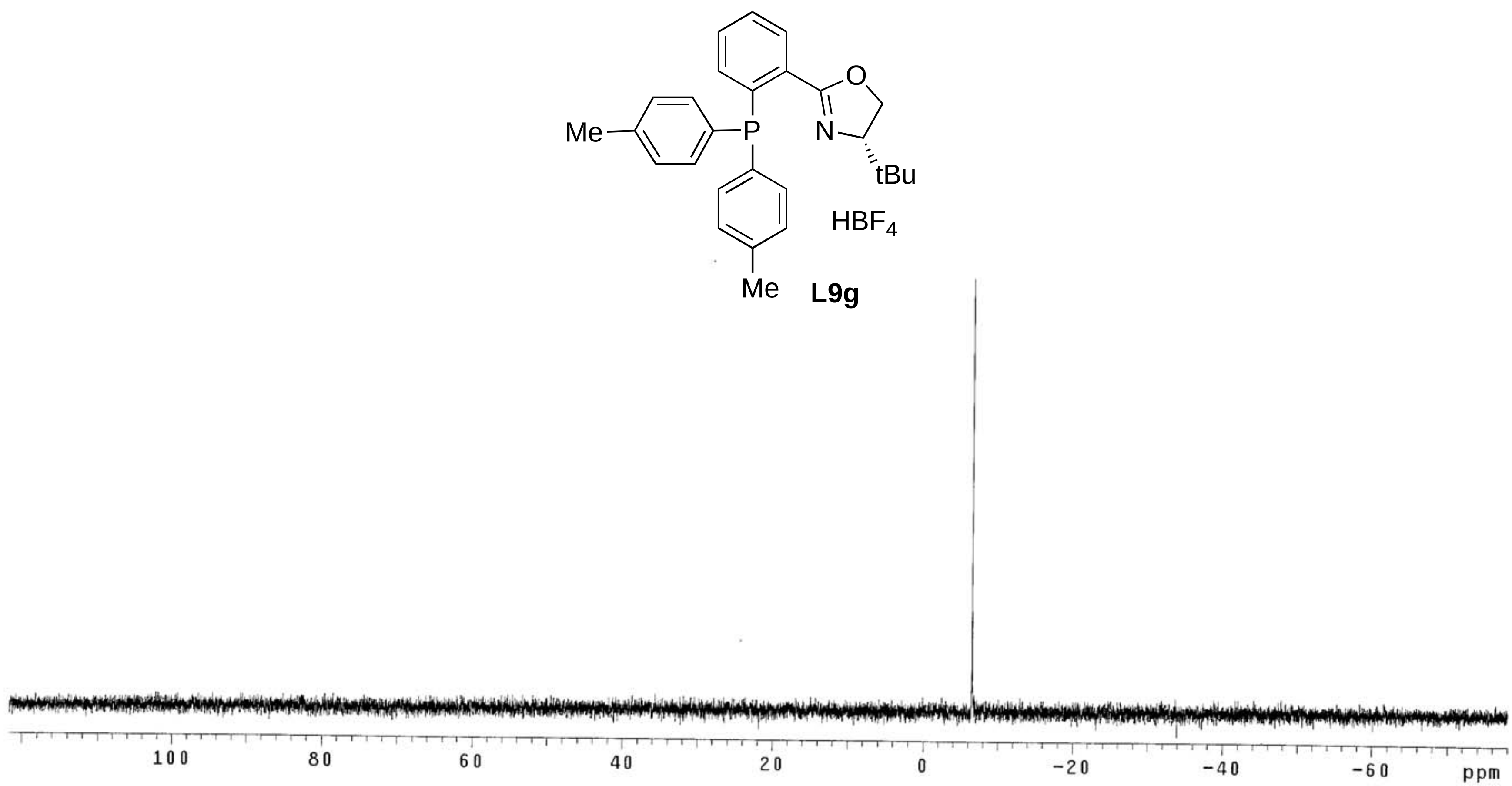

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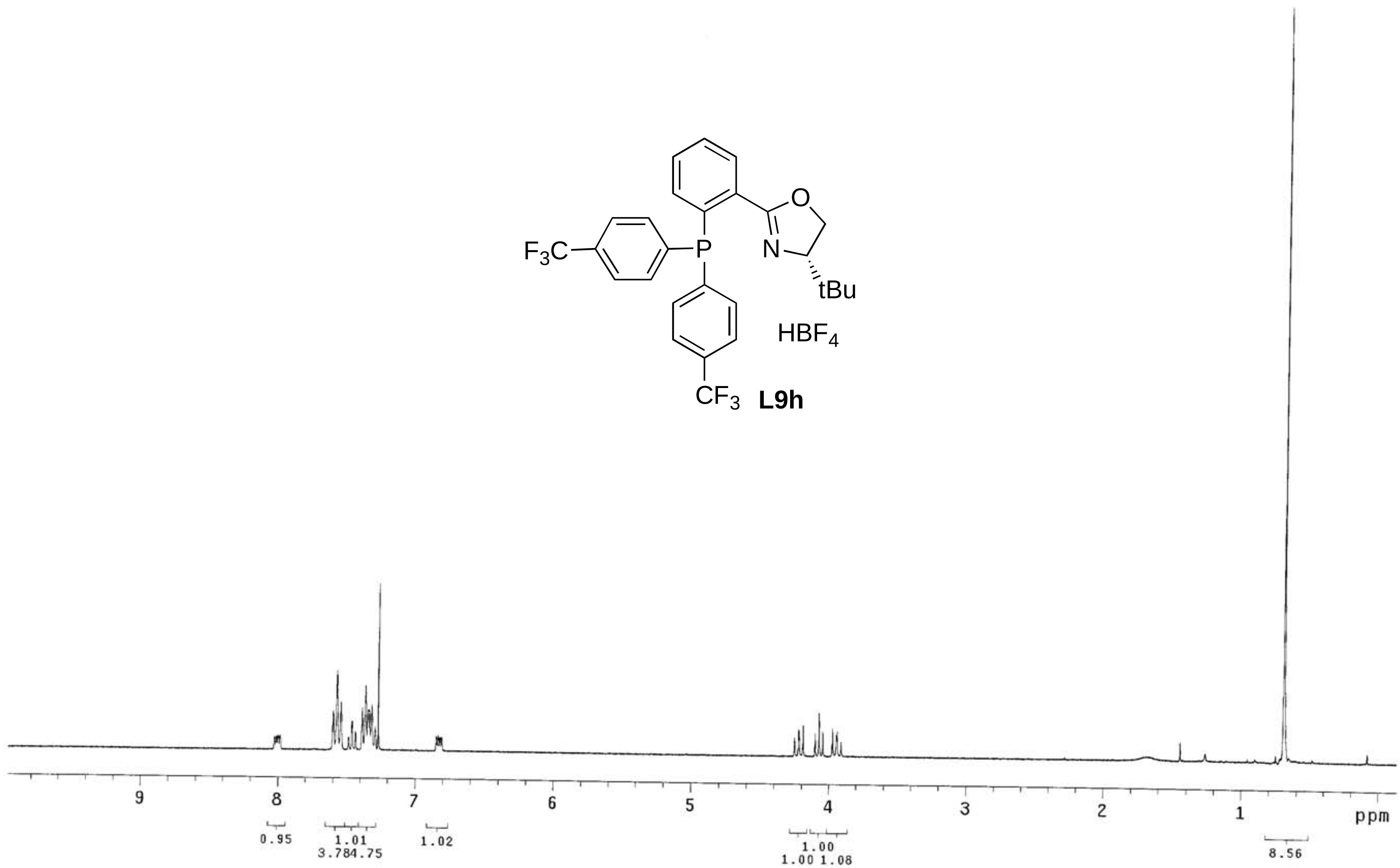

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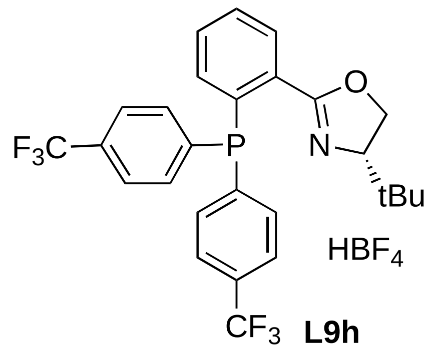

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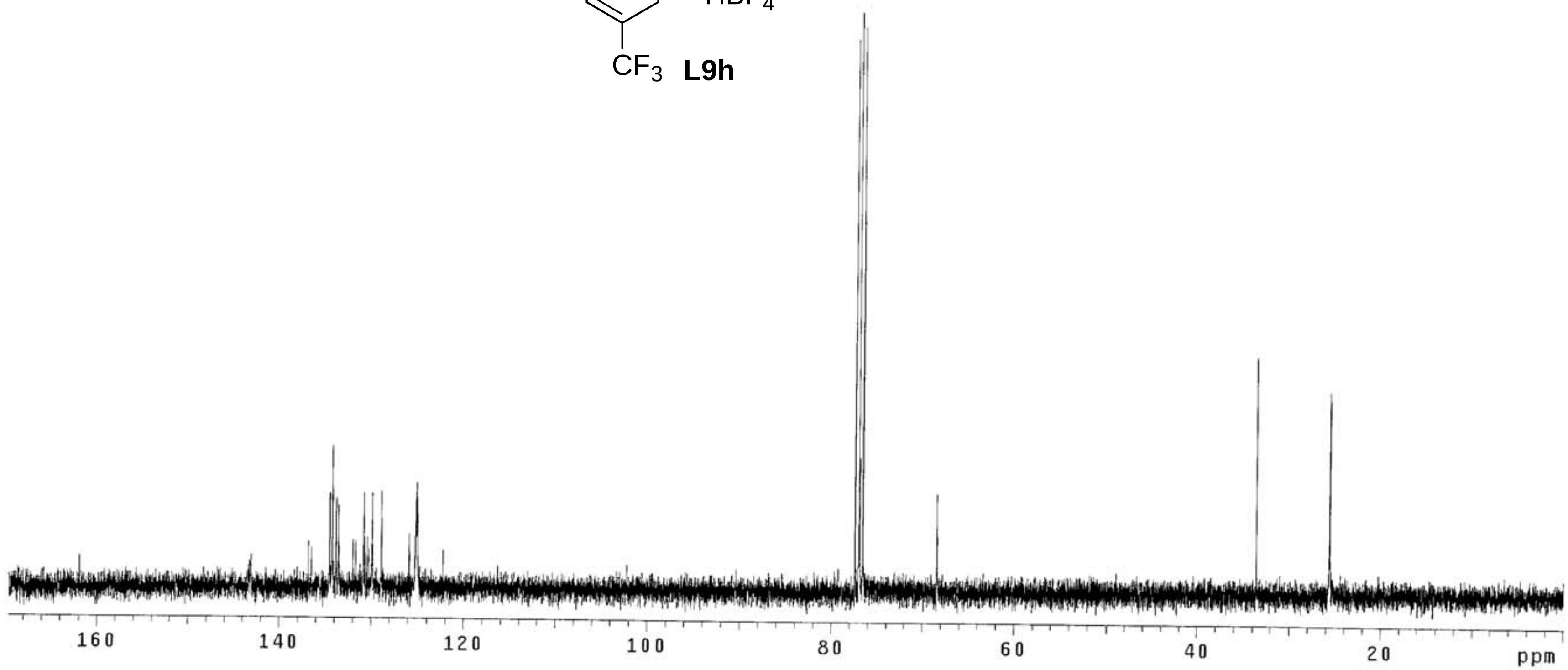

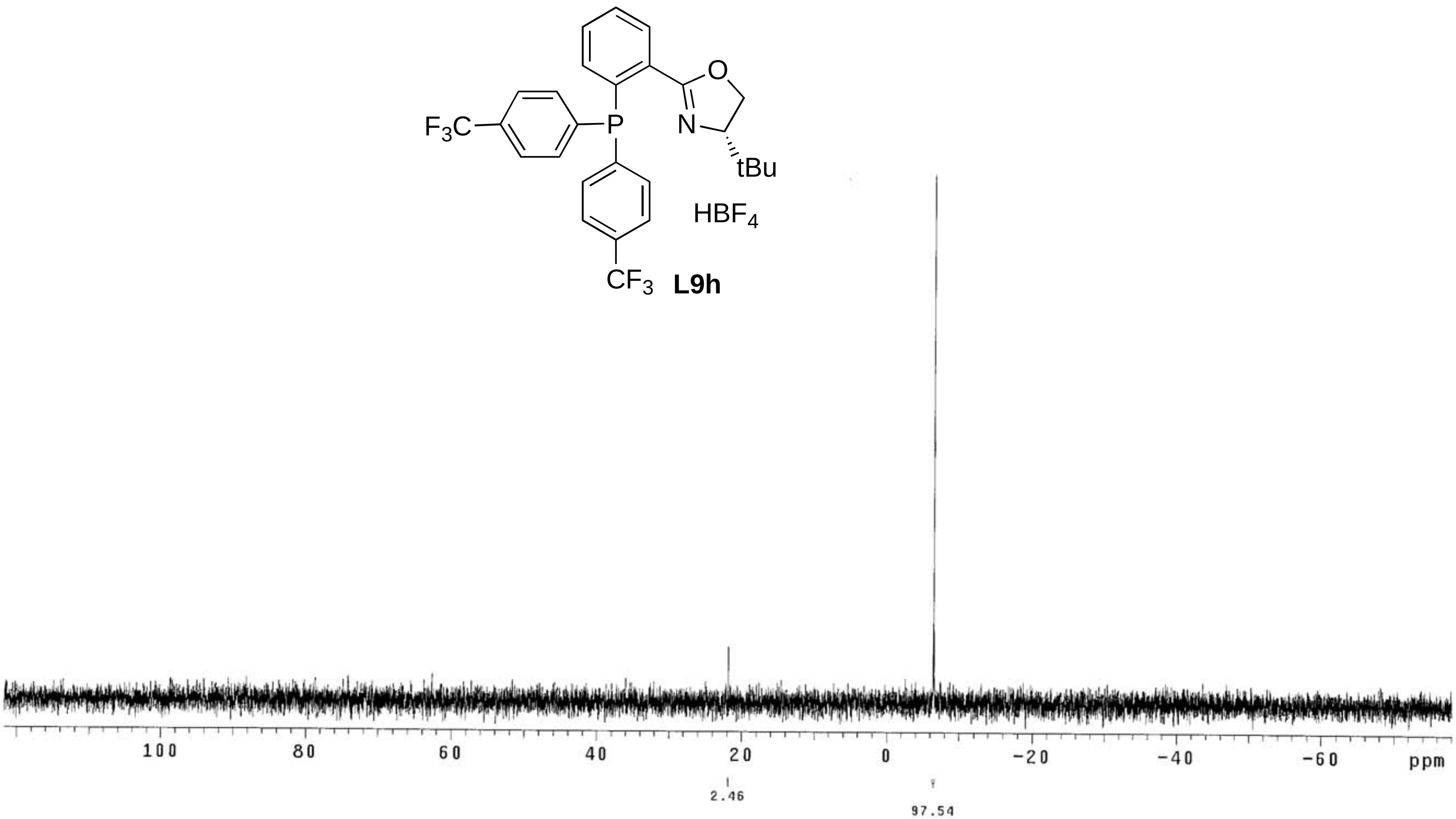

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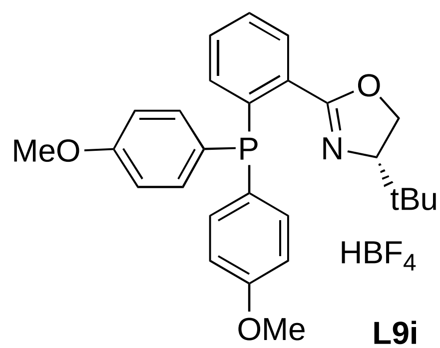
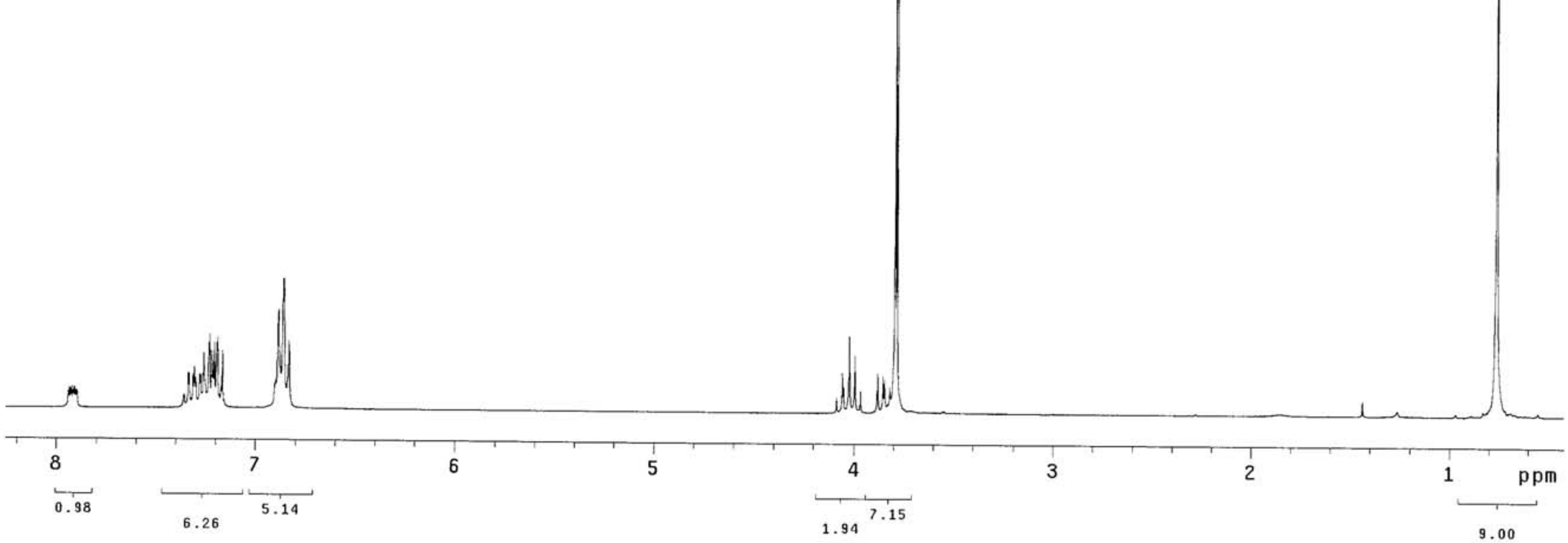
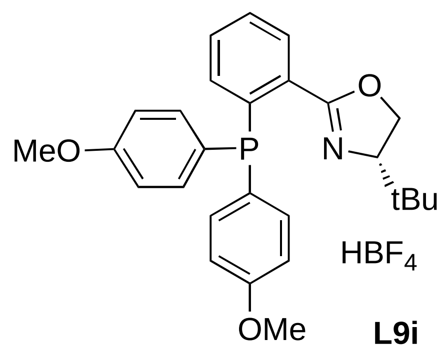


L9i





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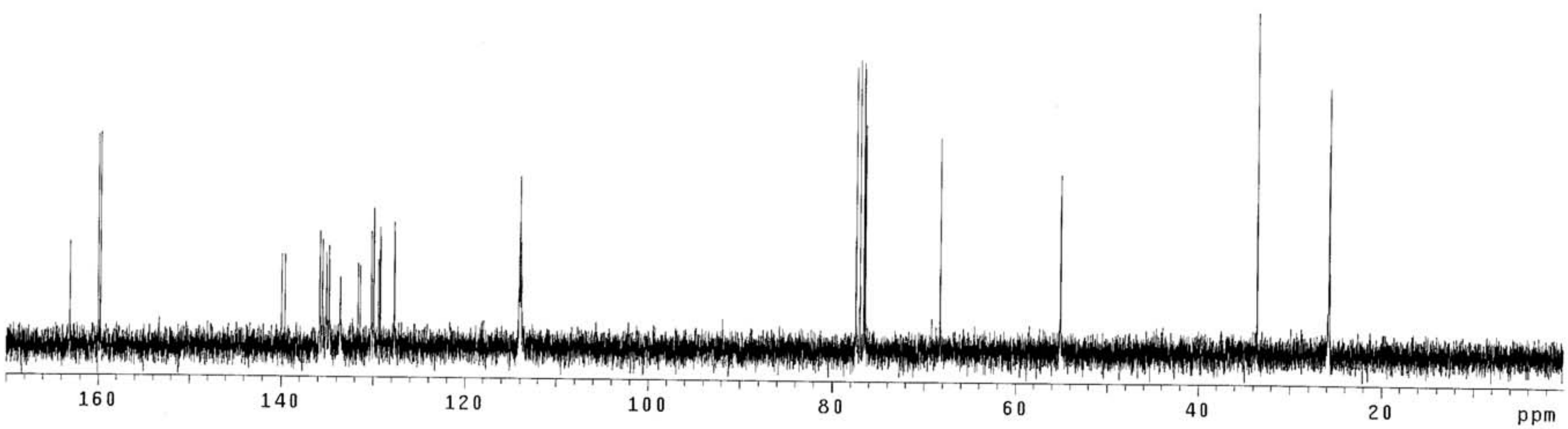

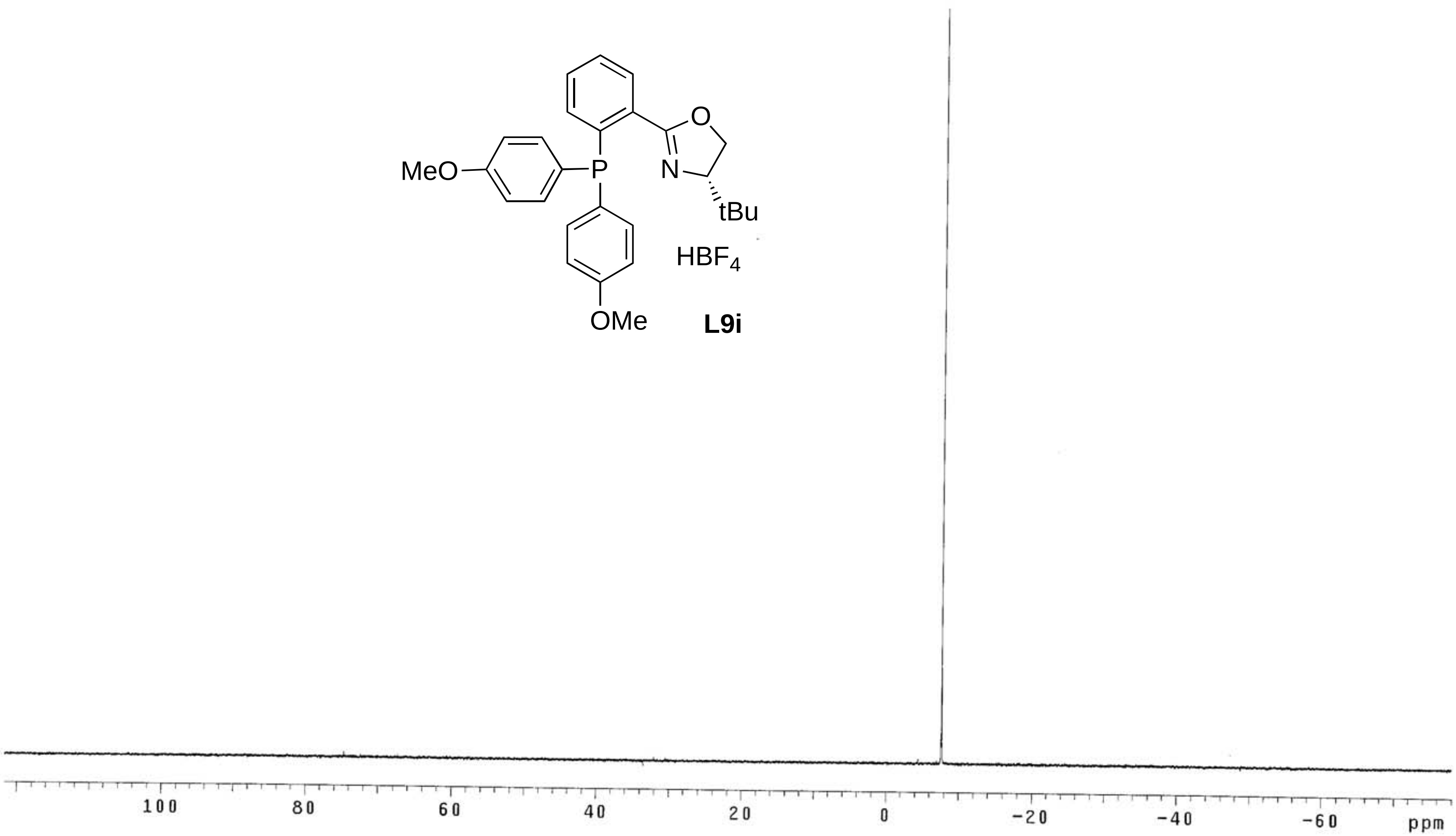
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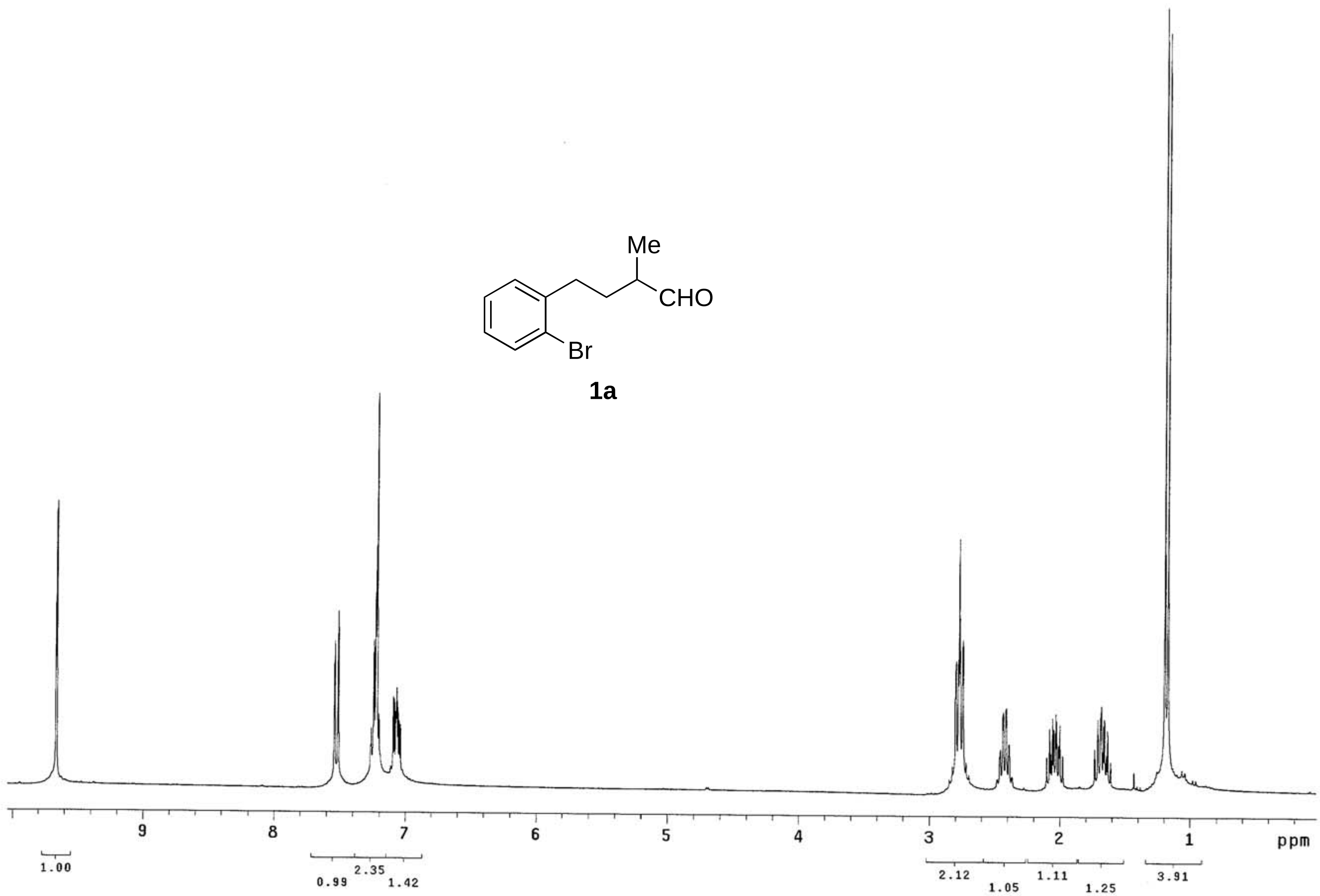

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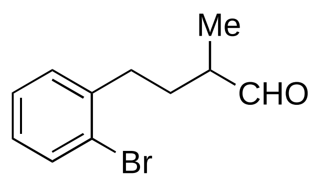

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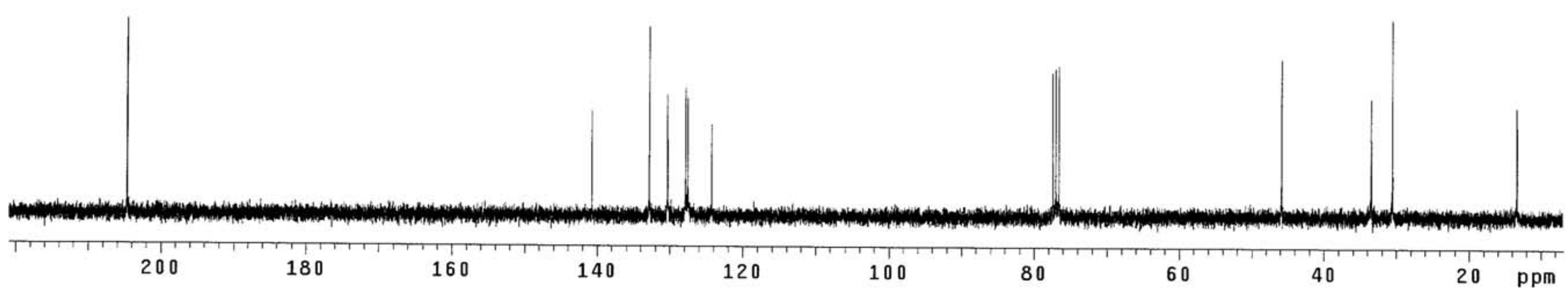

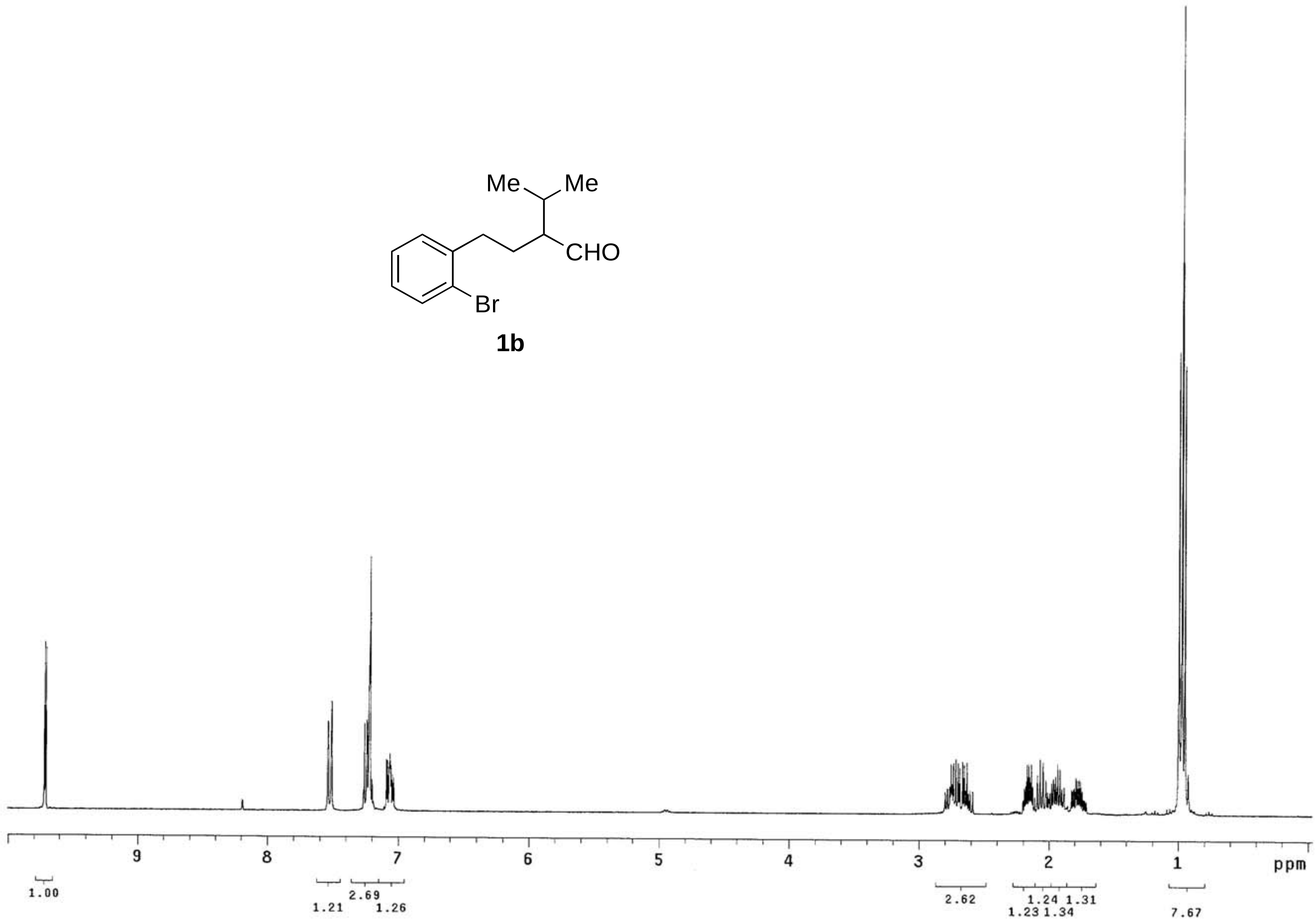
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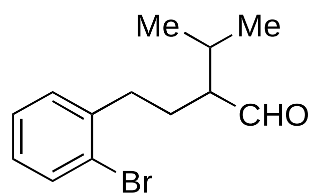

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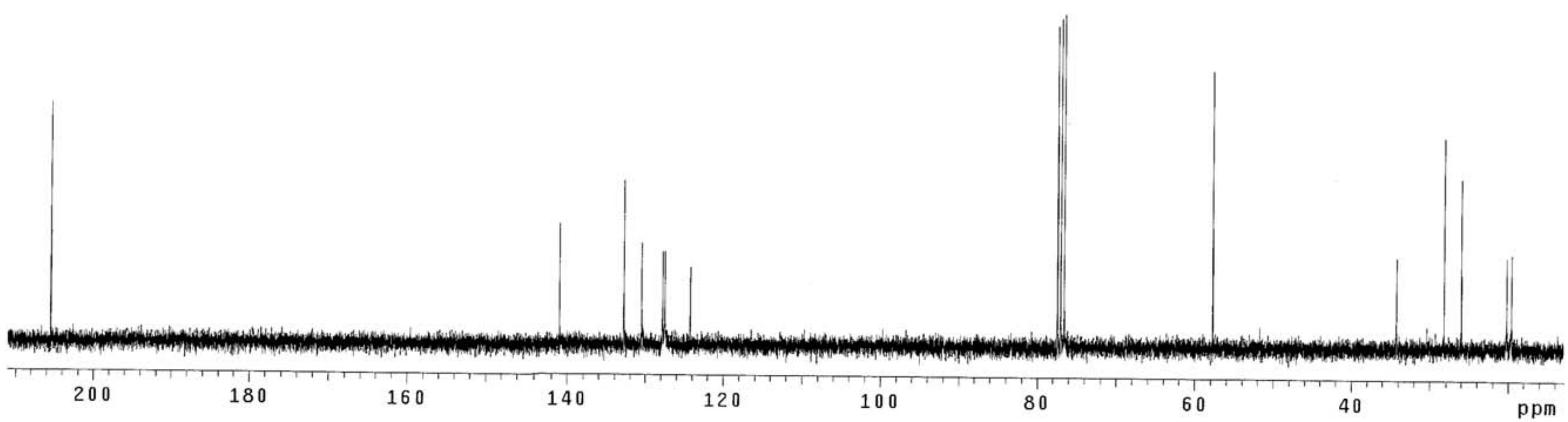

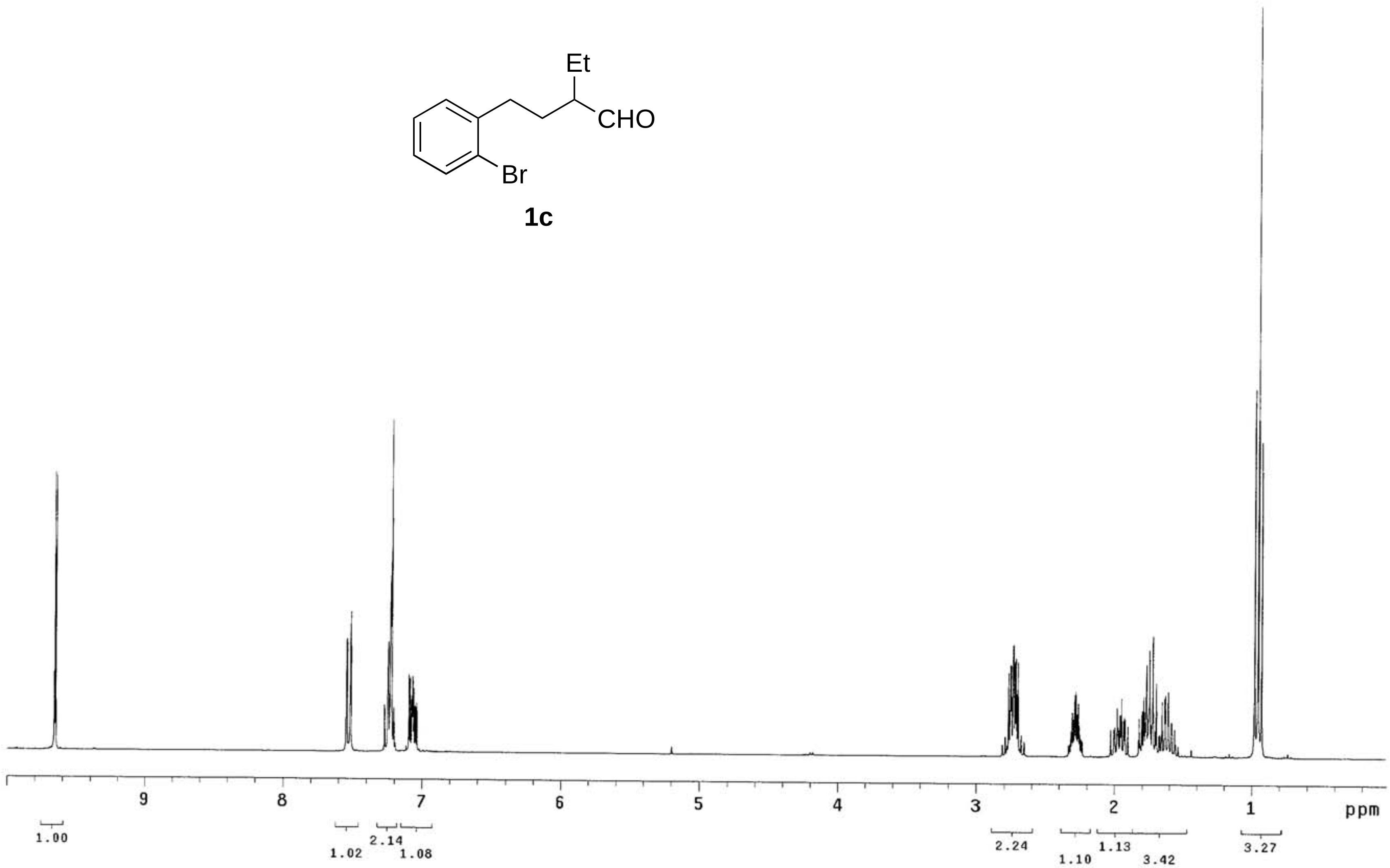

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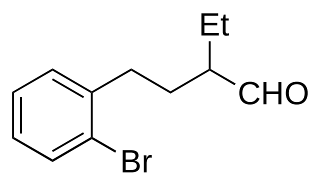

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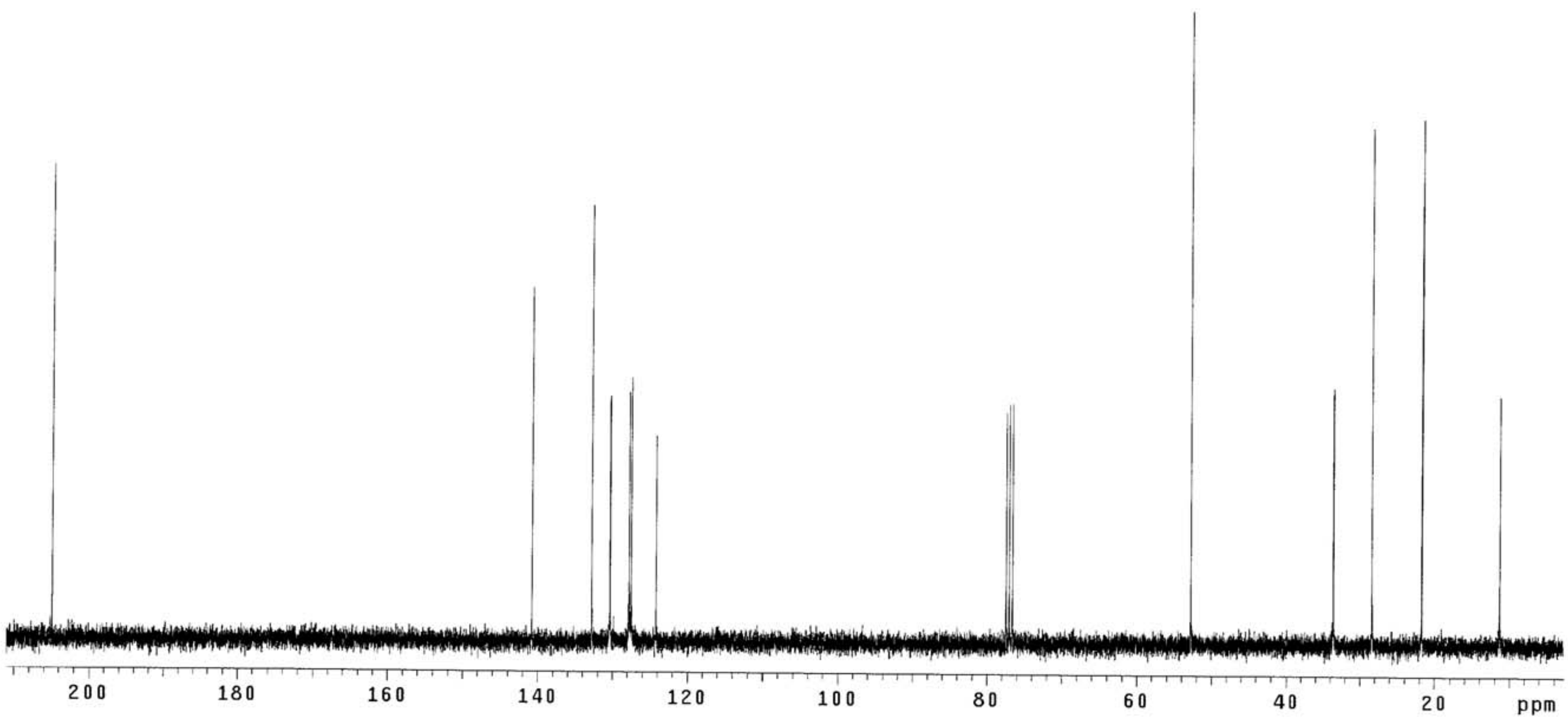

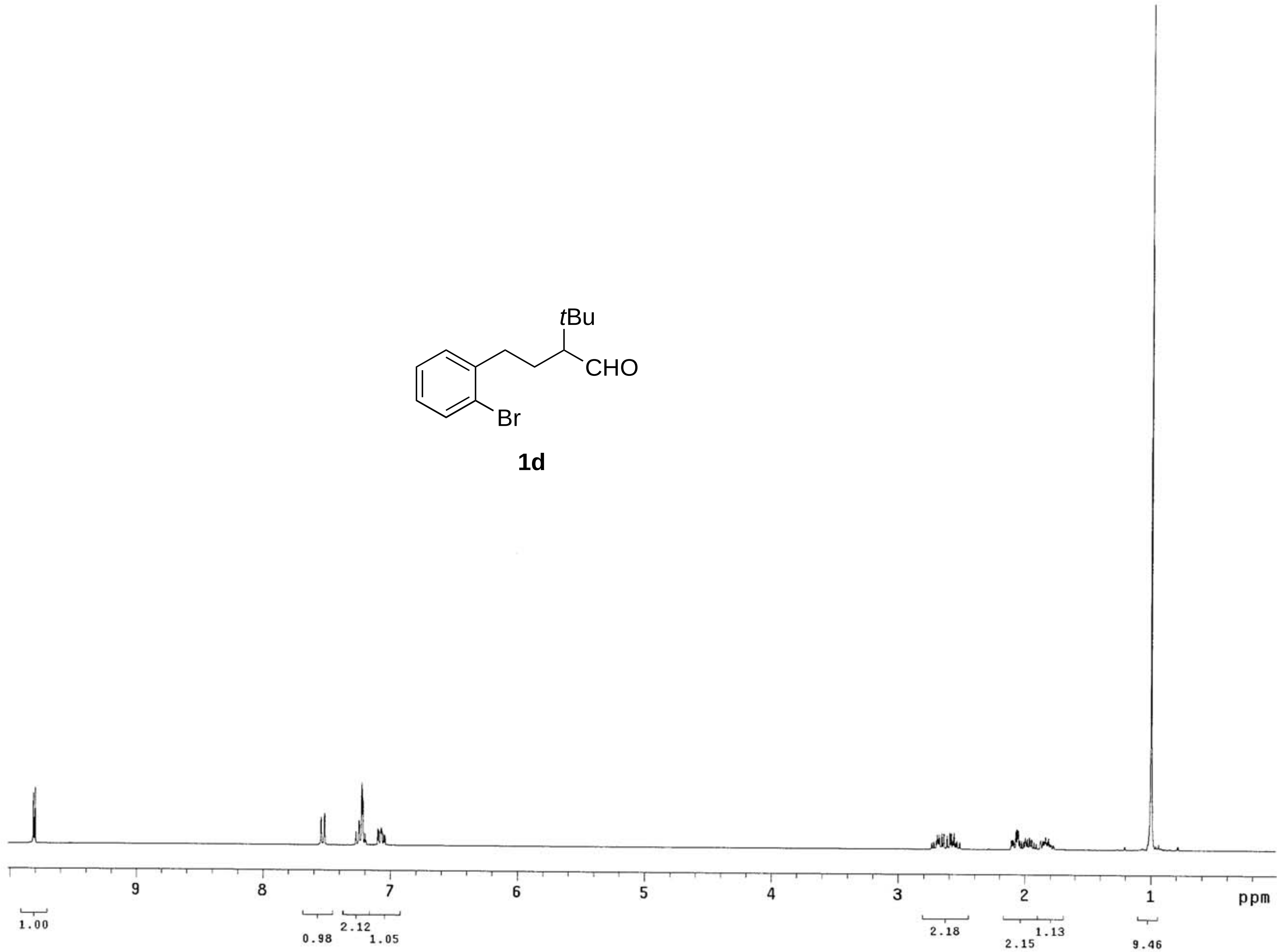

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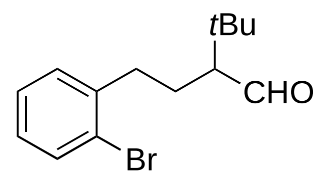

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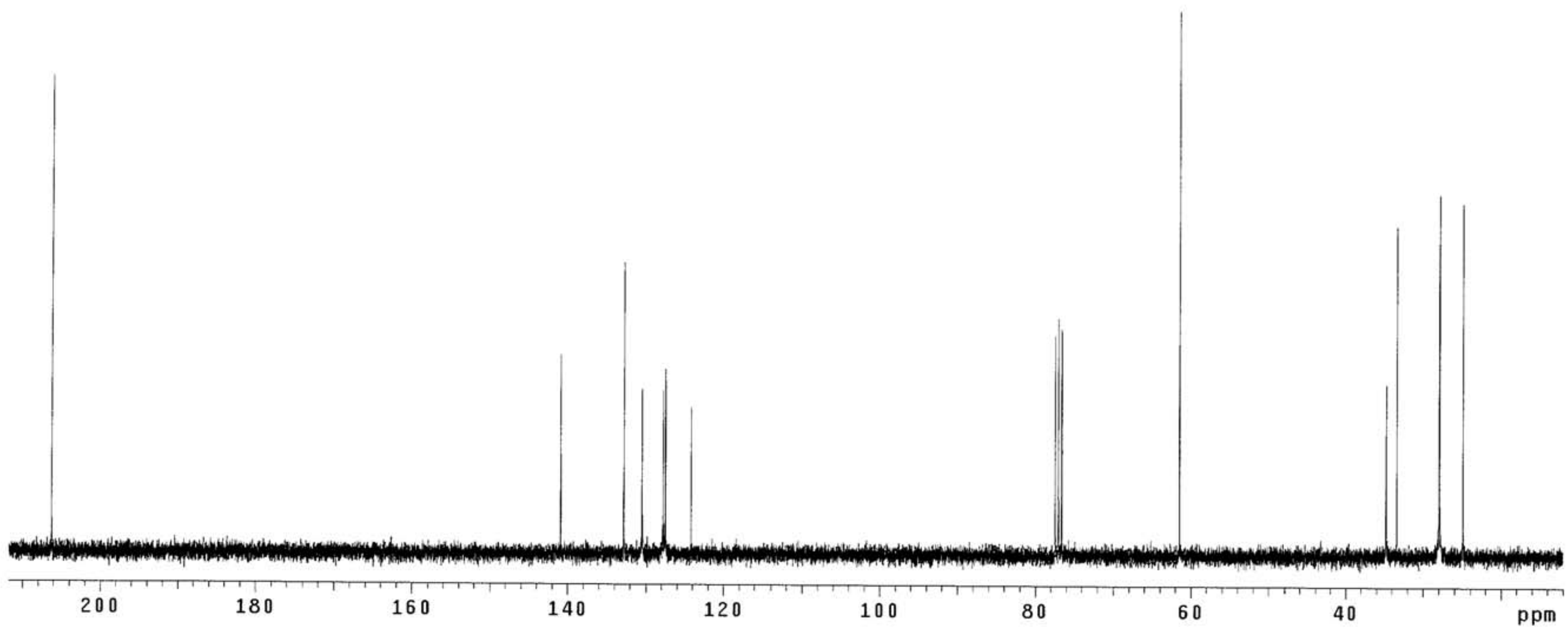

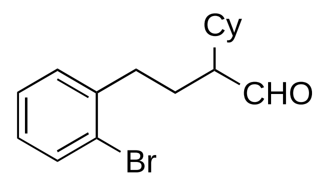

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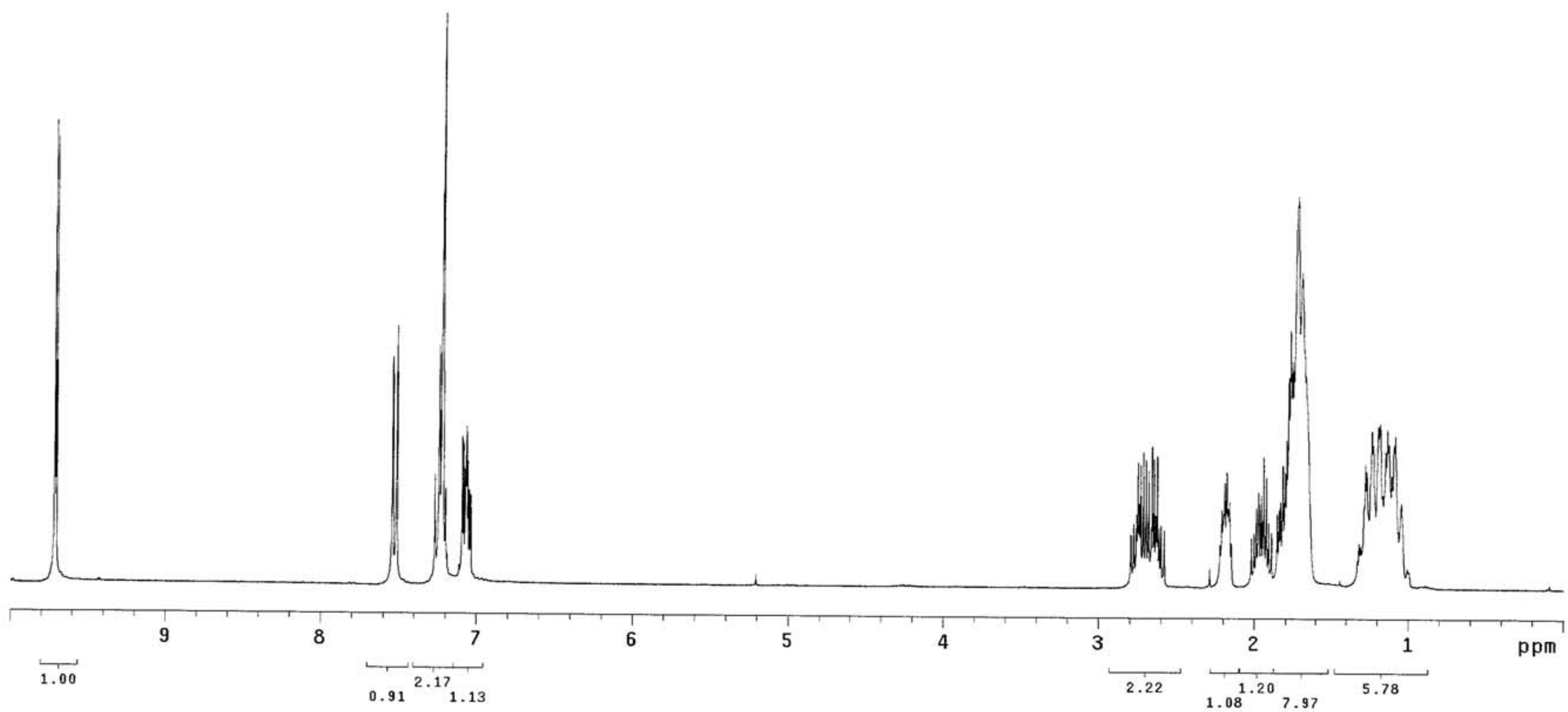

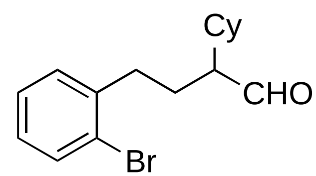

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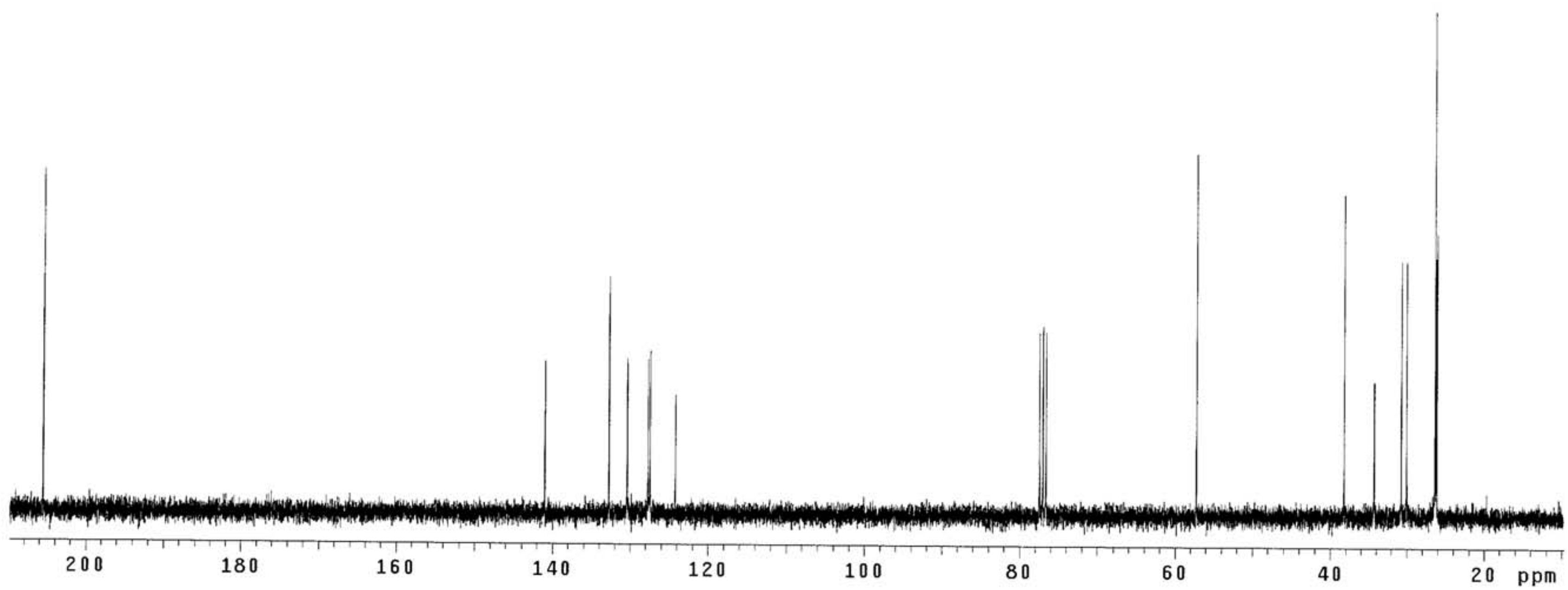

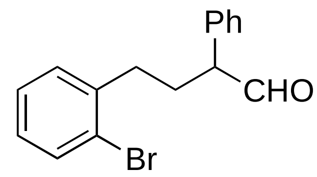

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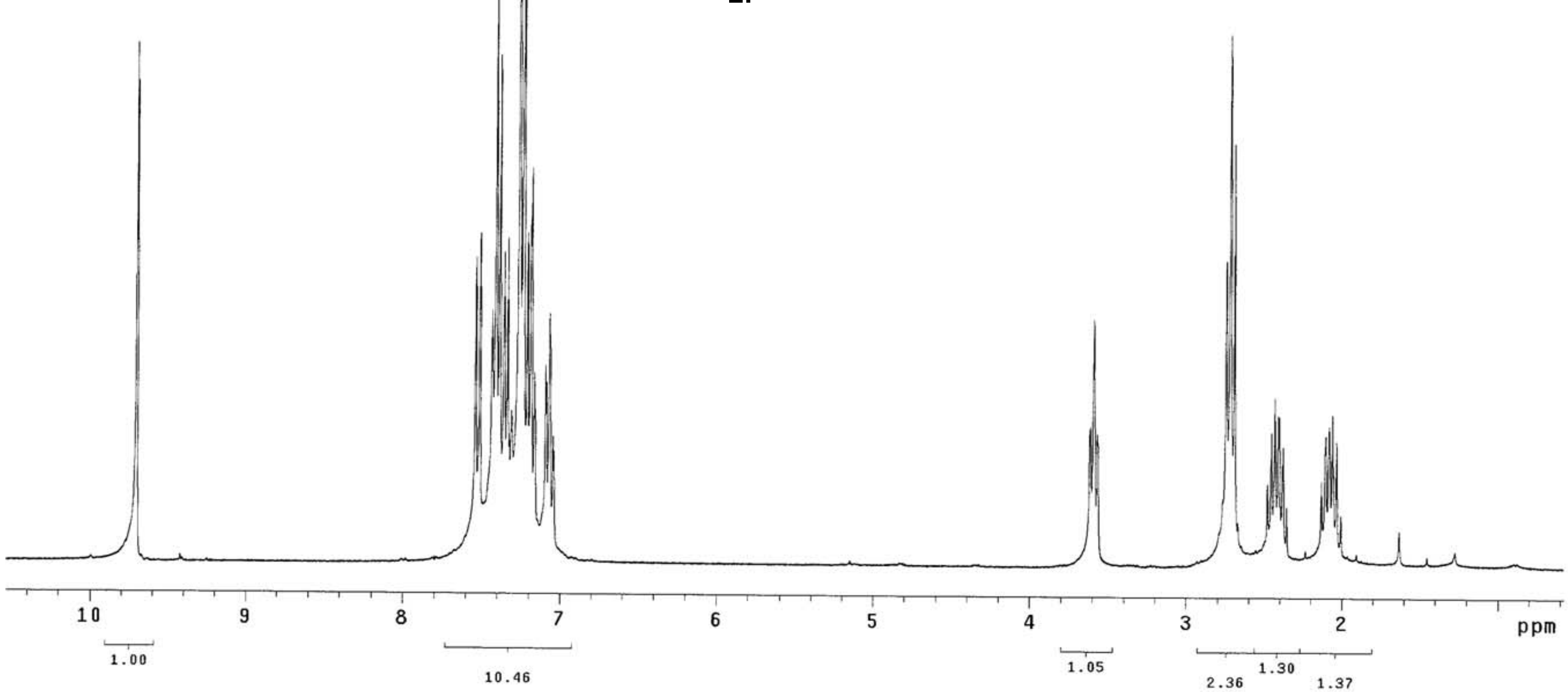

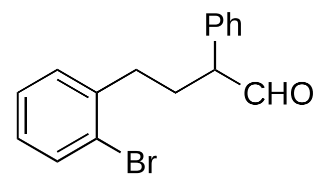

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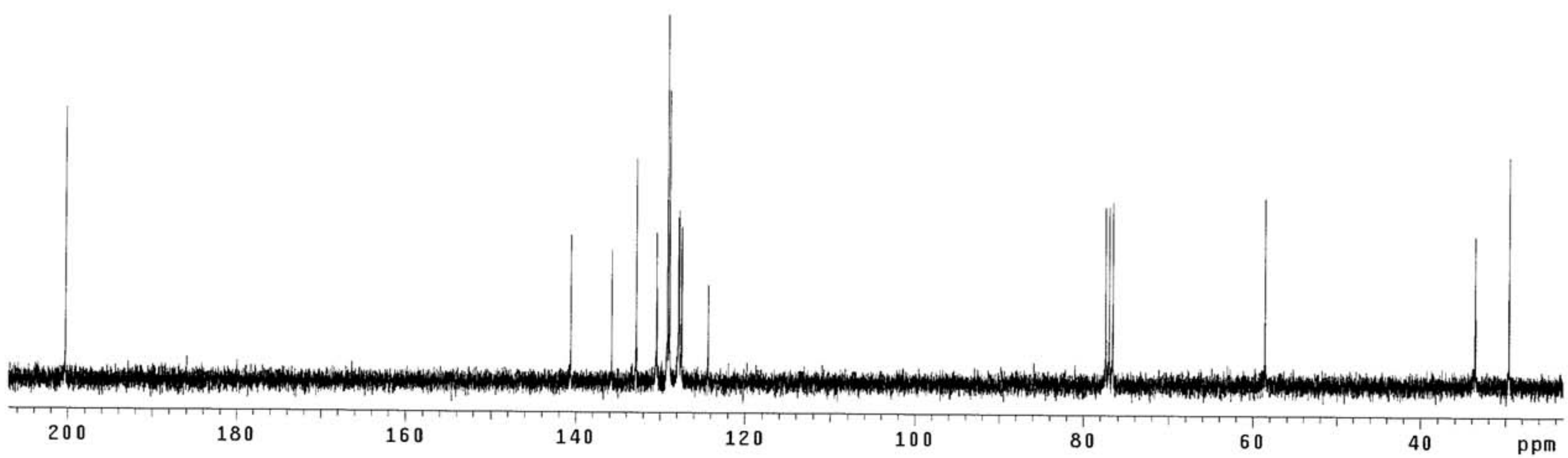

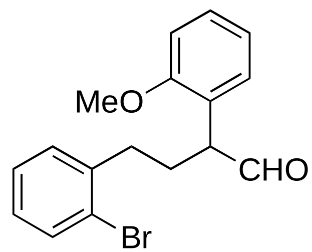

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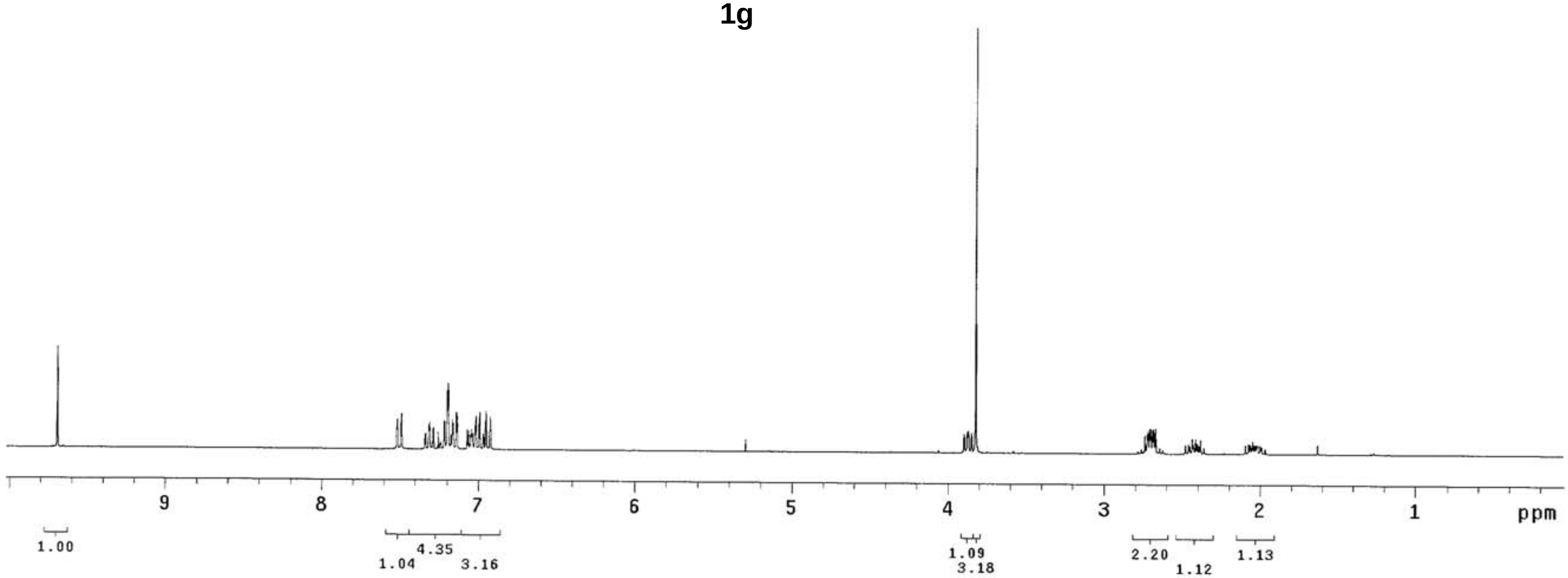

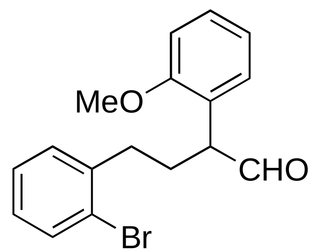

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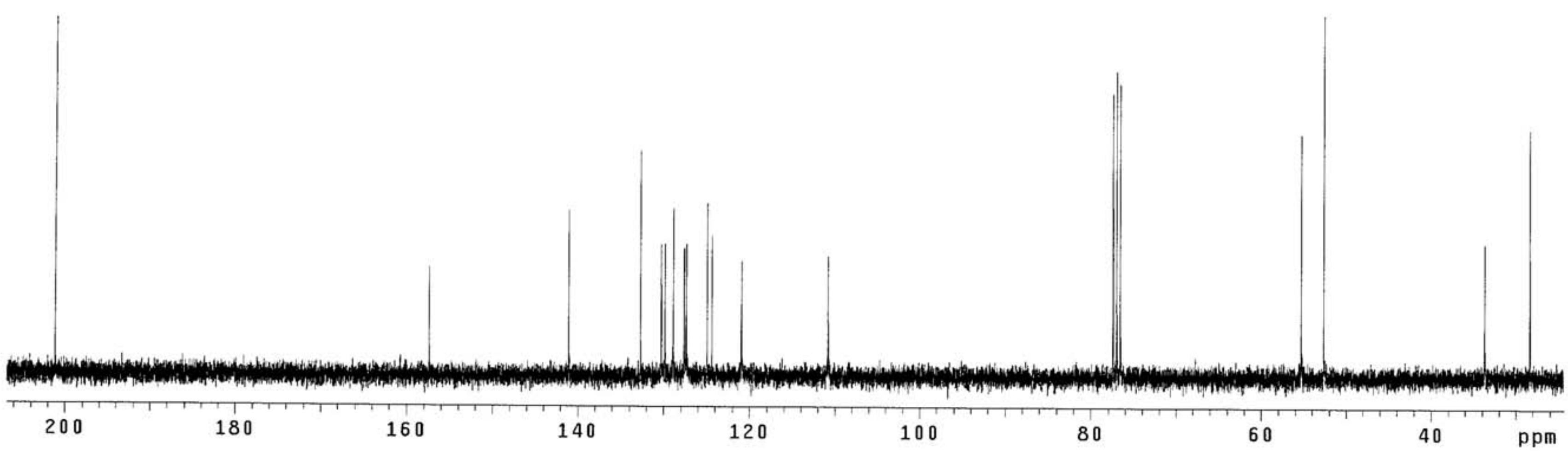

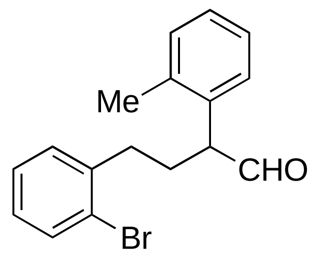

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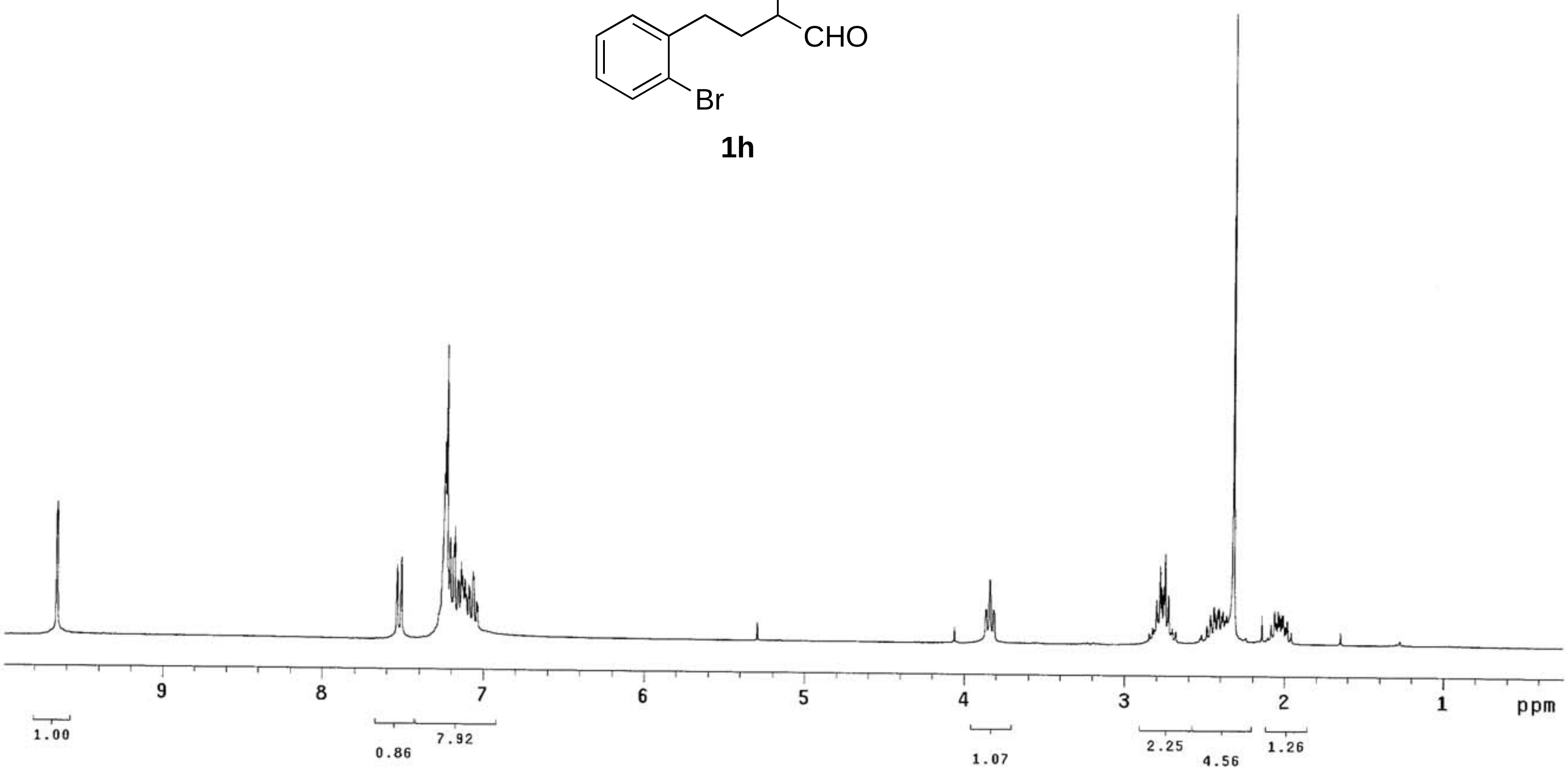

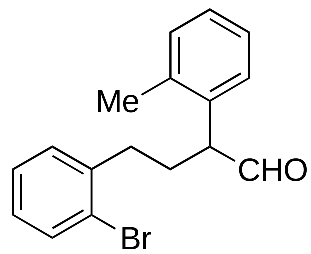

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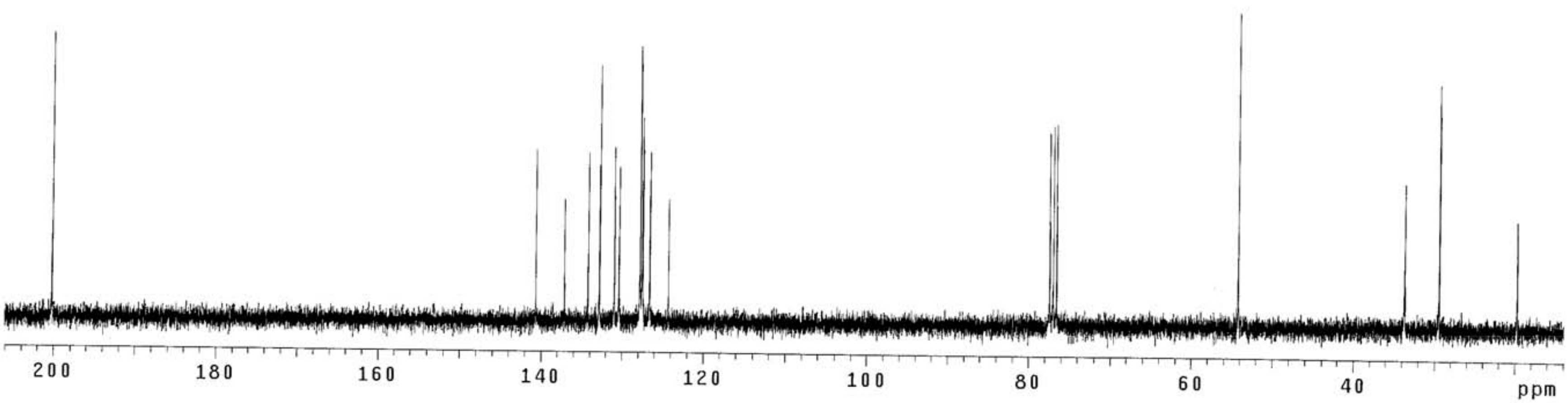

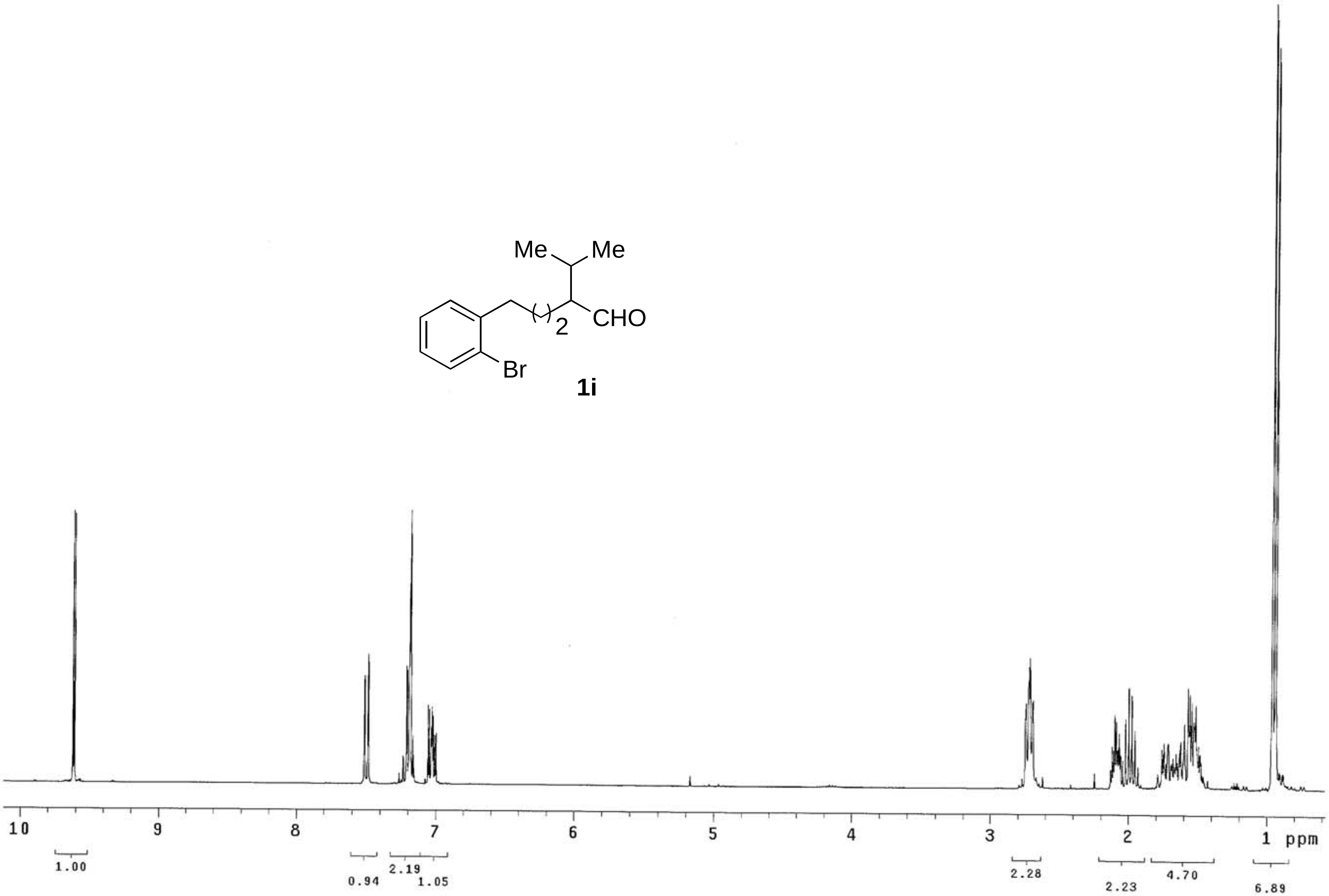

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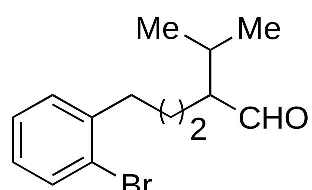

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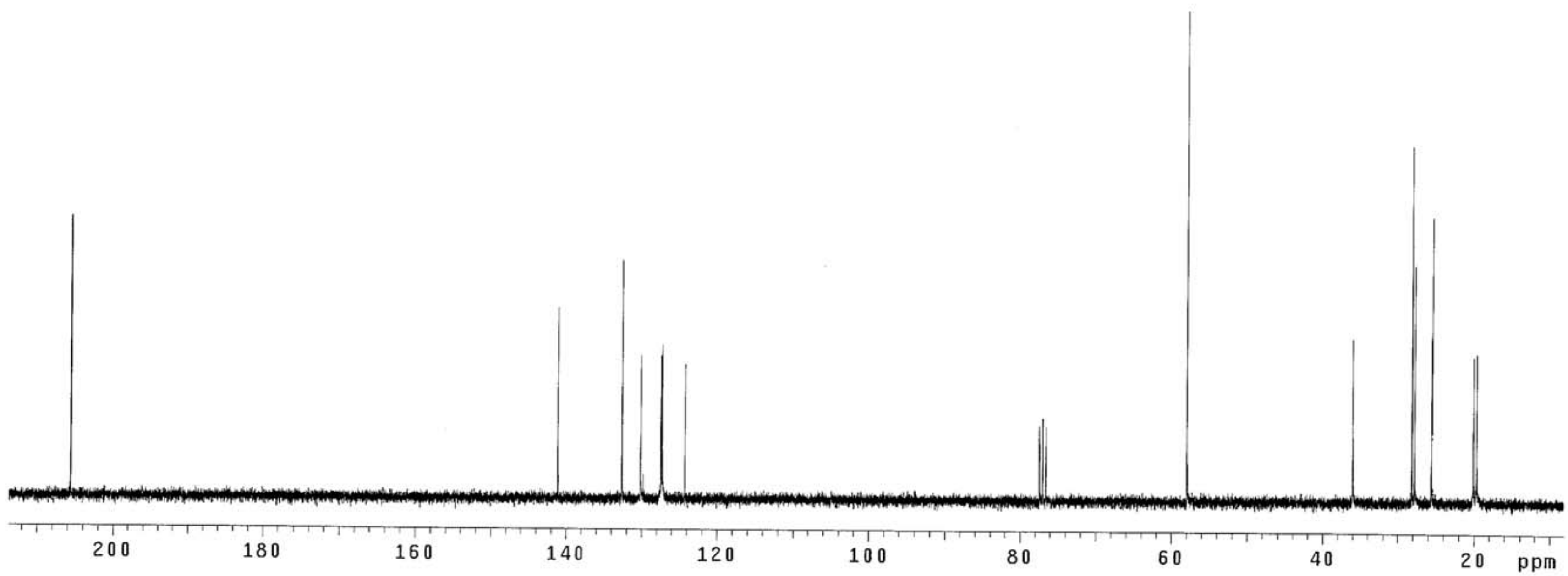

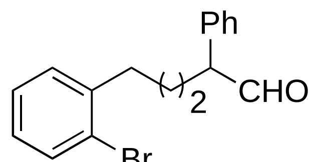

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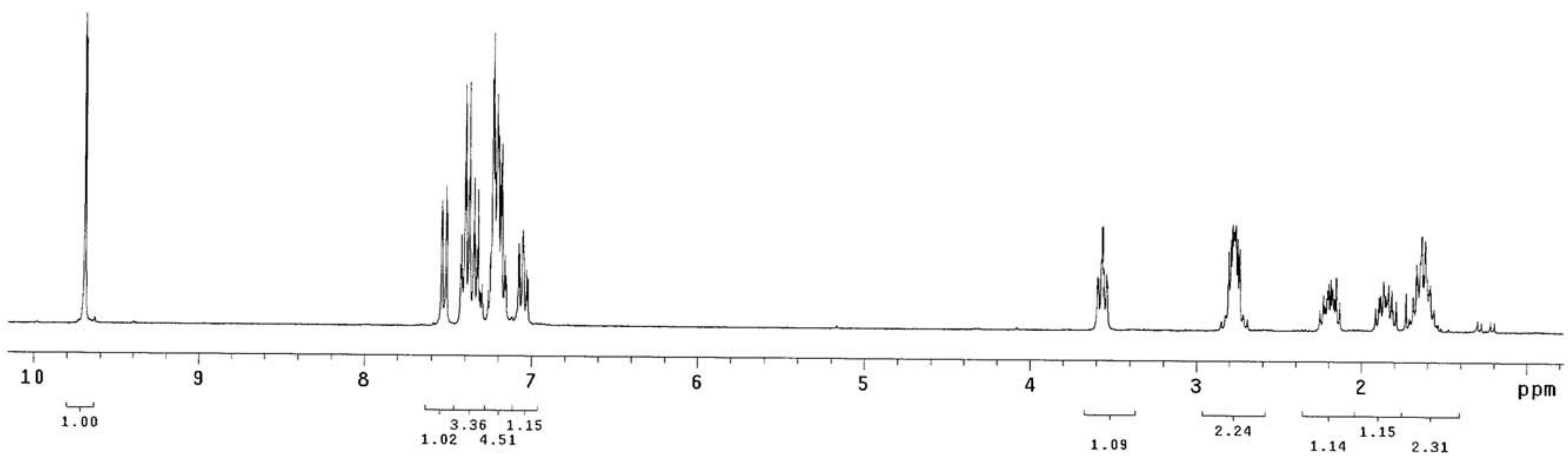
Br

1j



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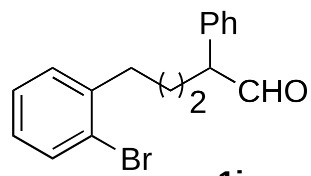

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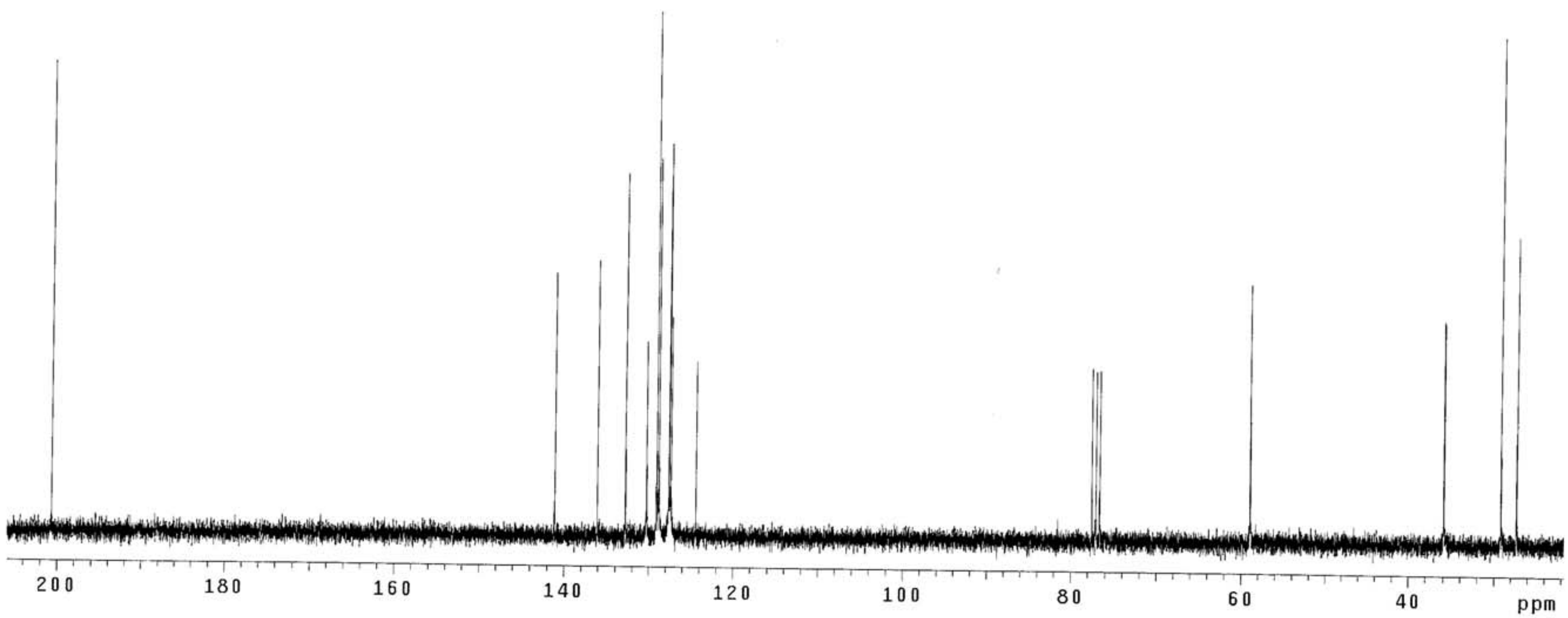

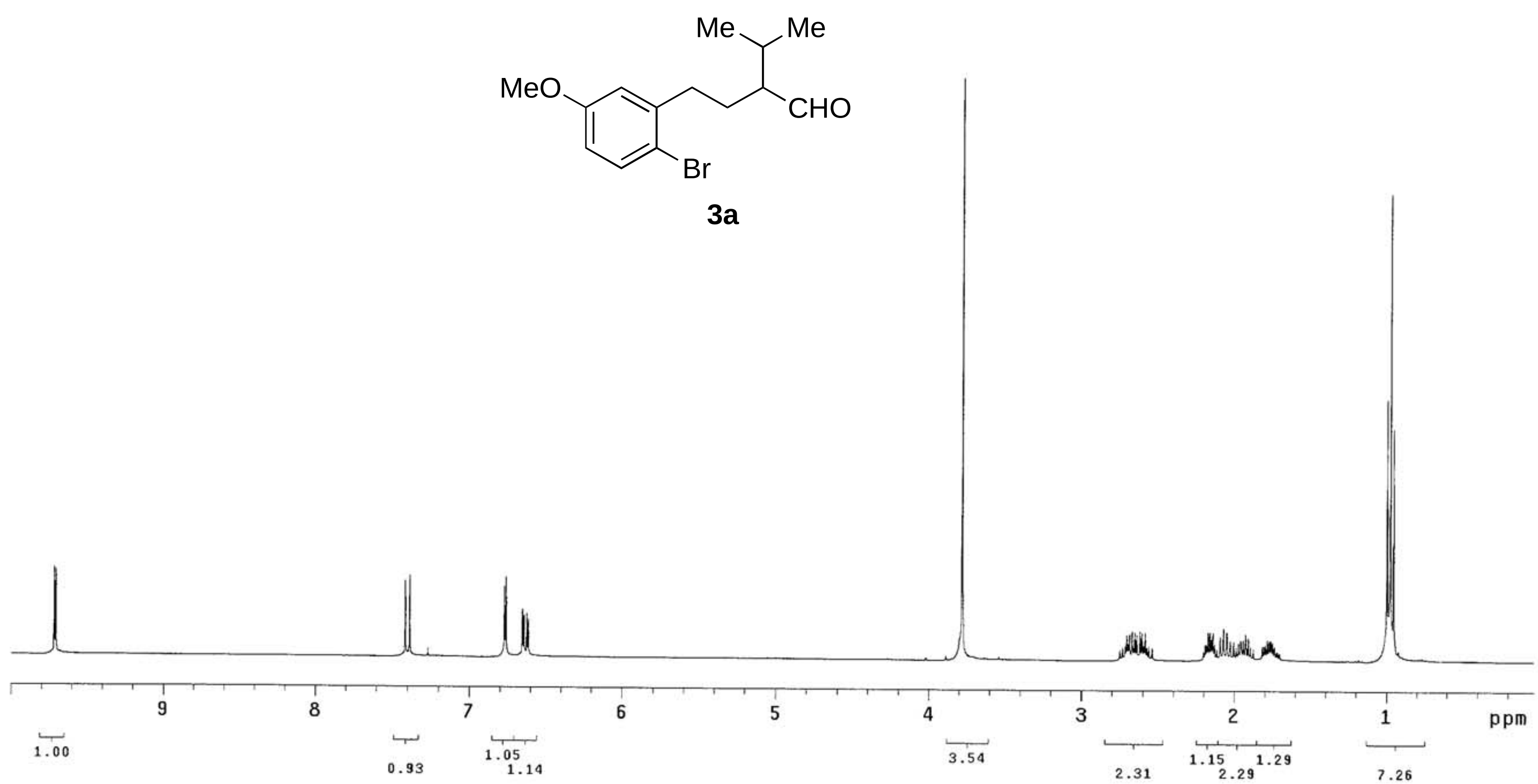

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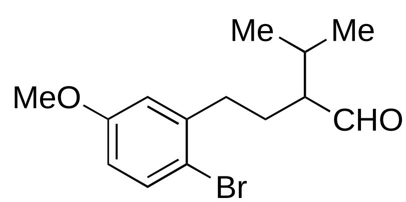

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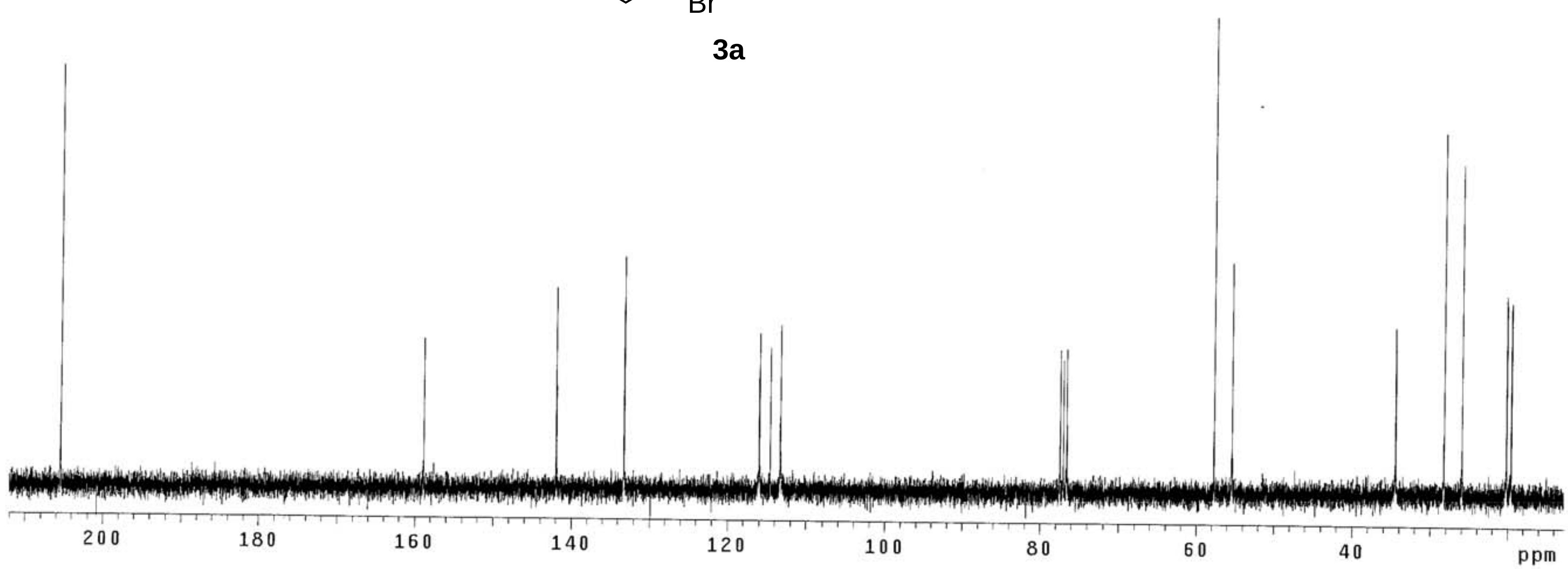

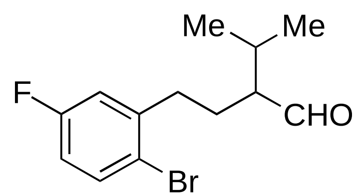

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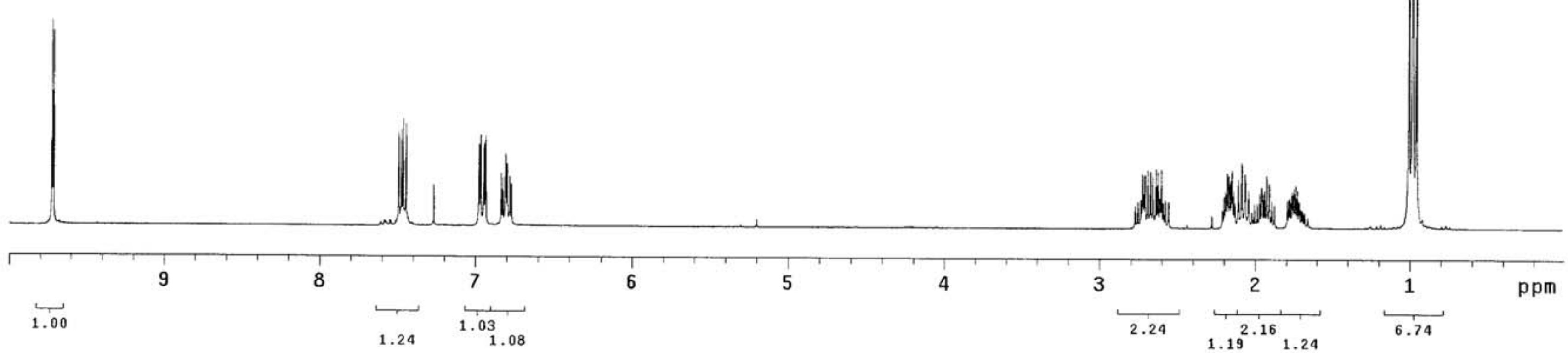

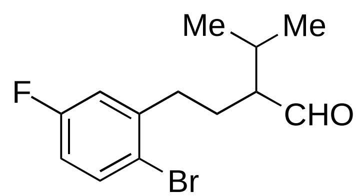

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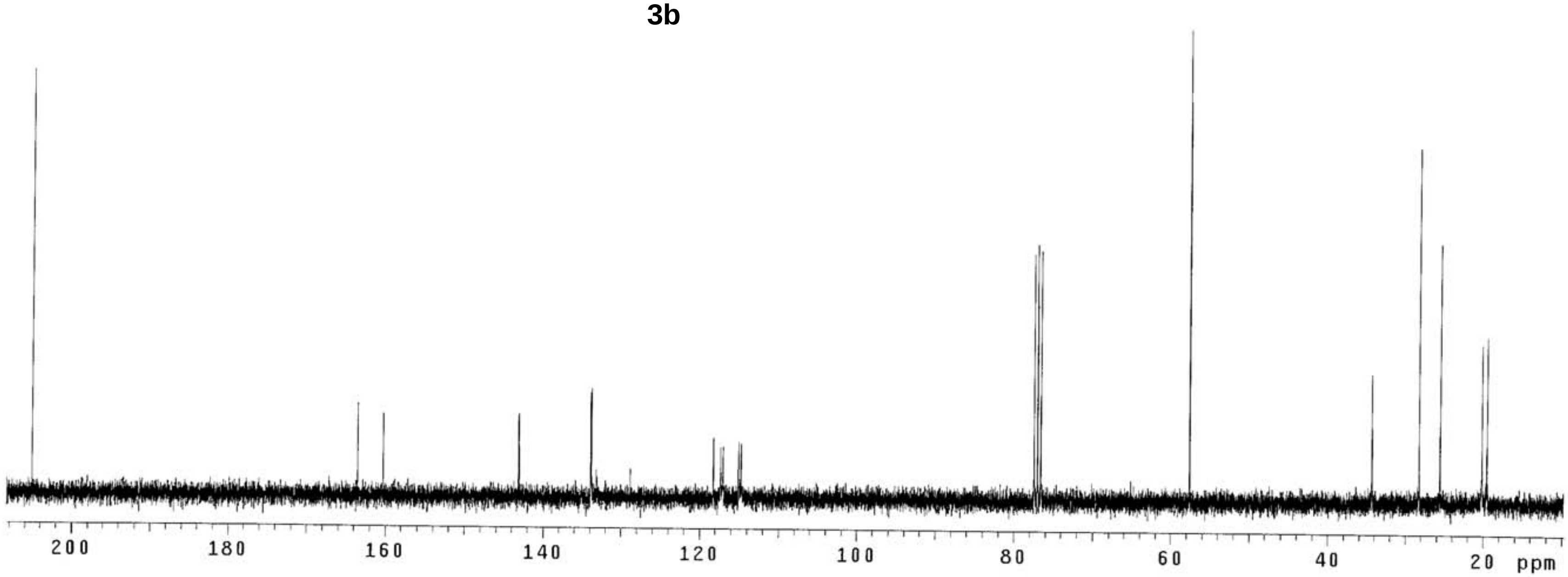

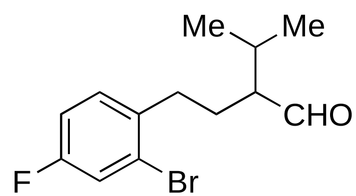

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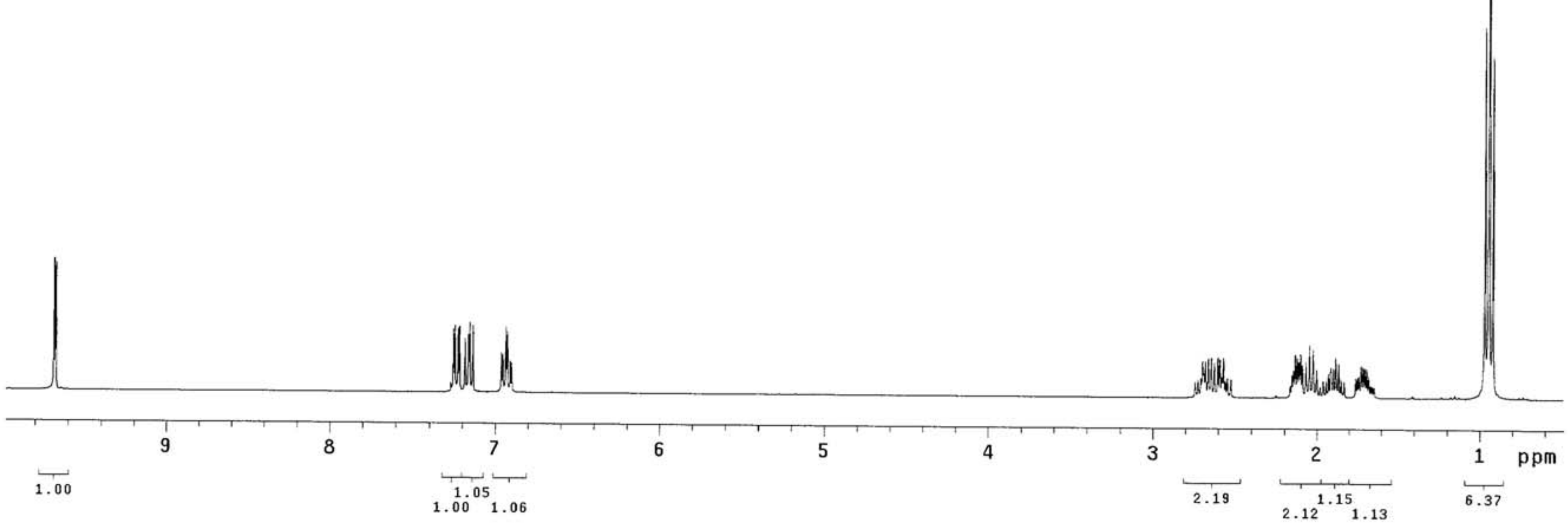

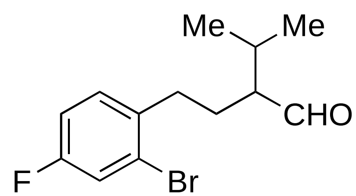

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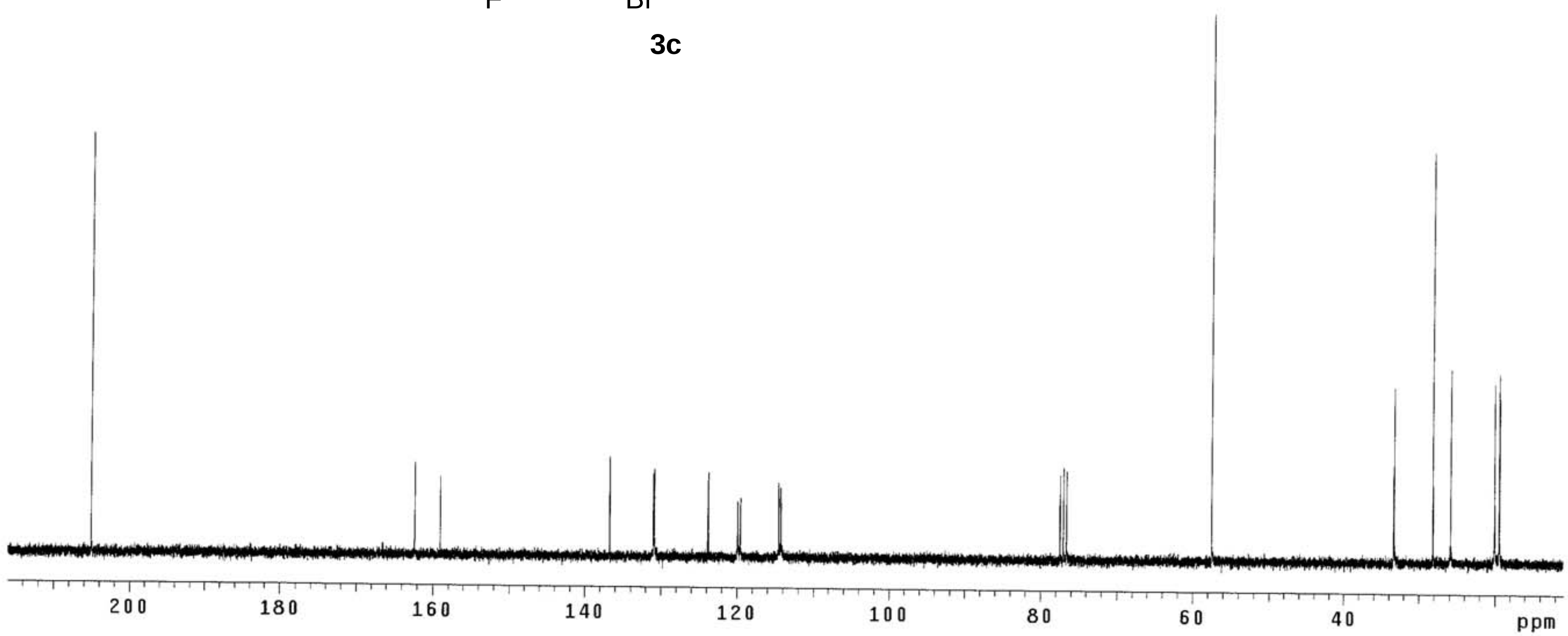

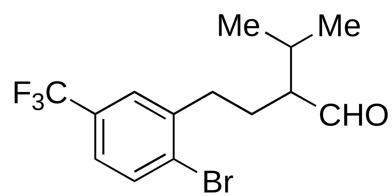
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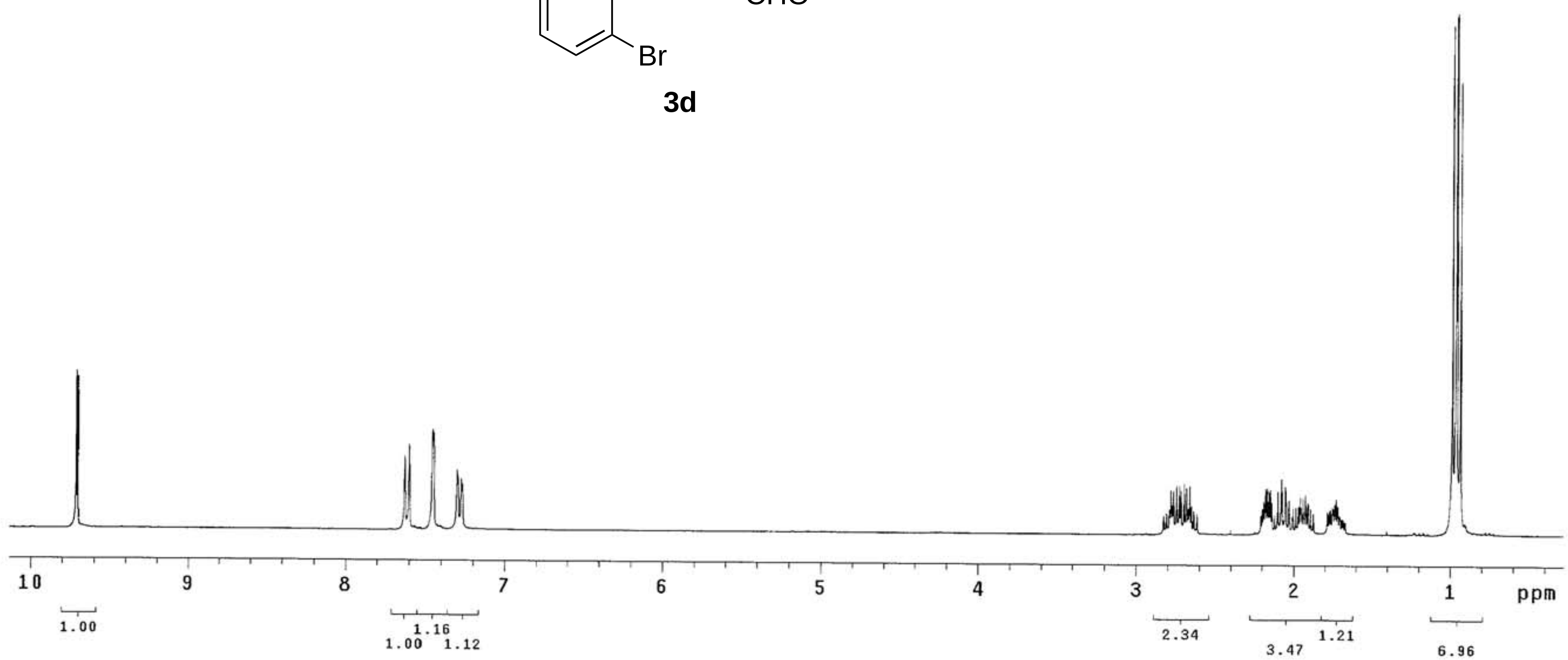
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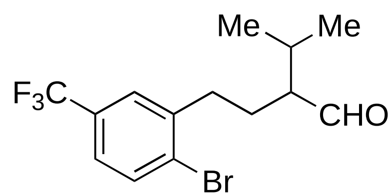

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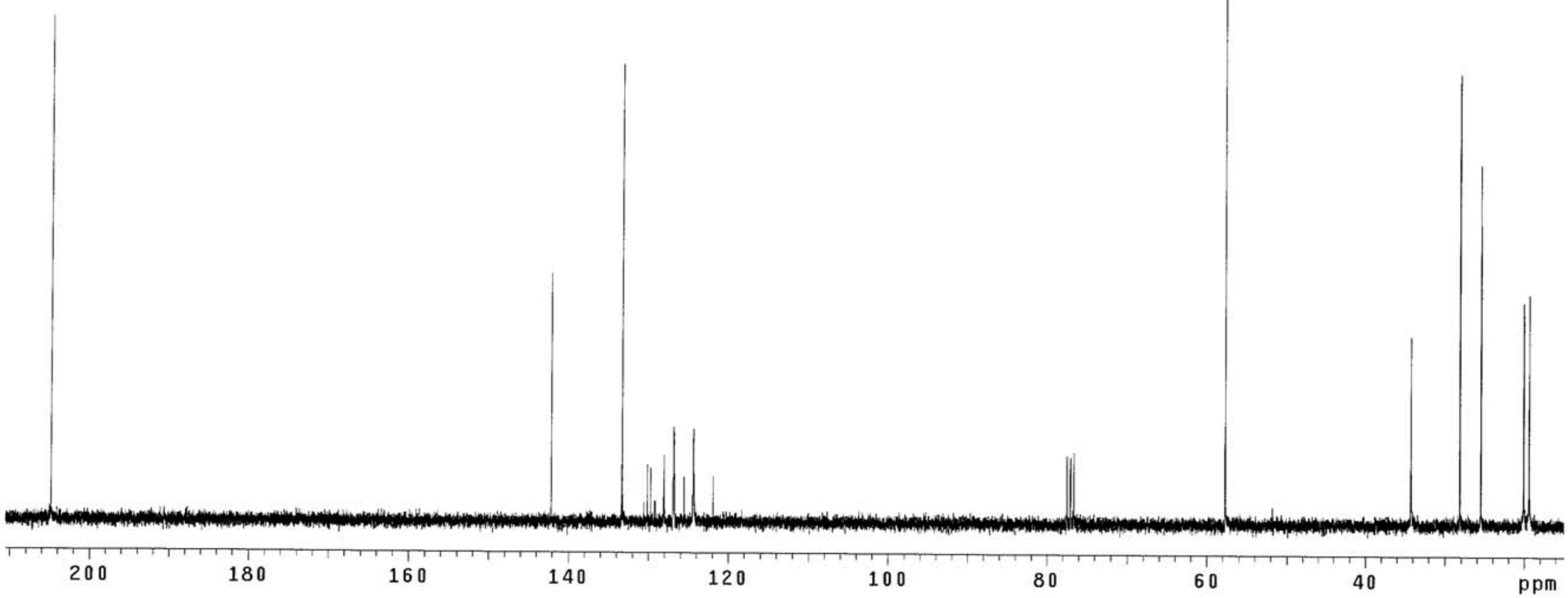

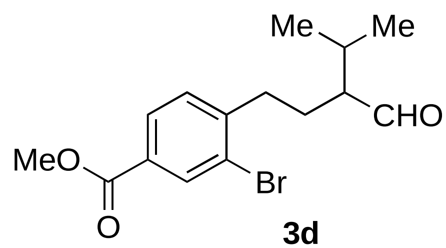

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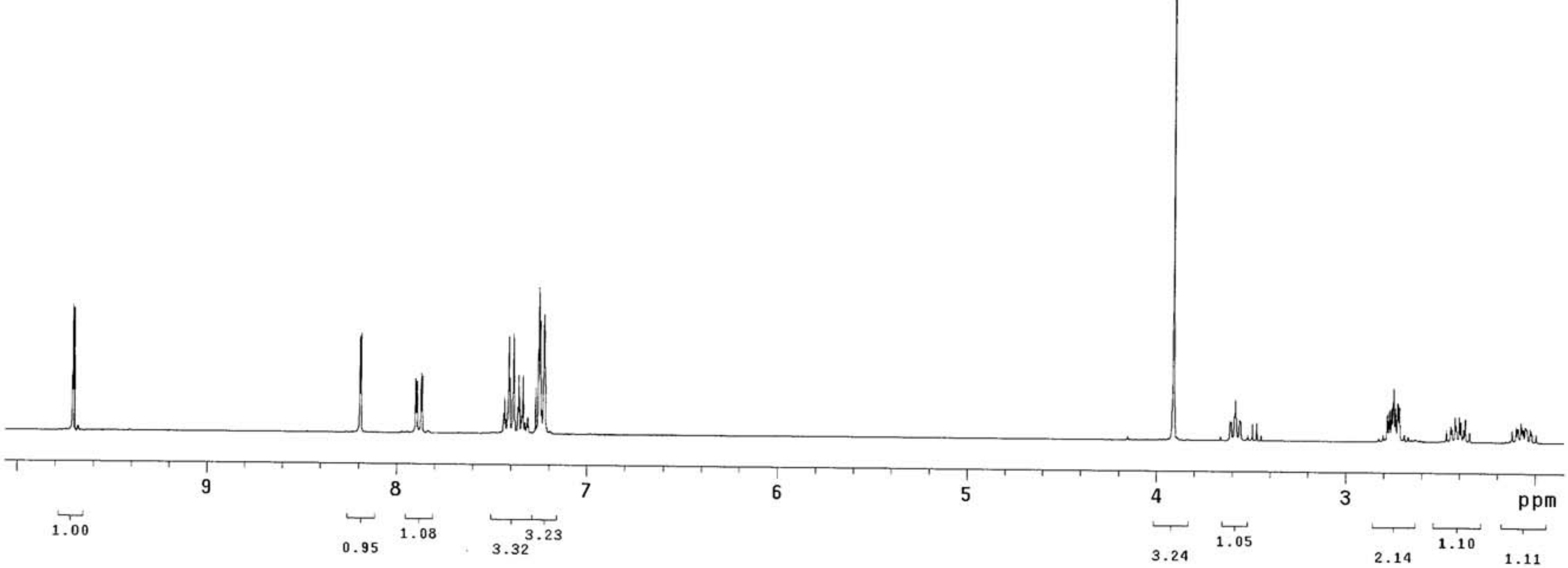

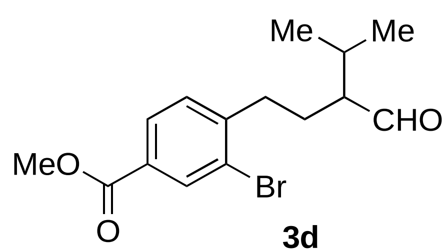

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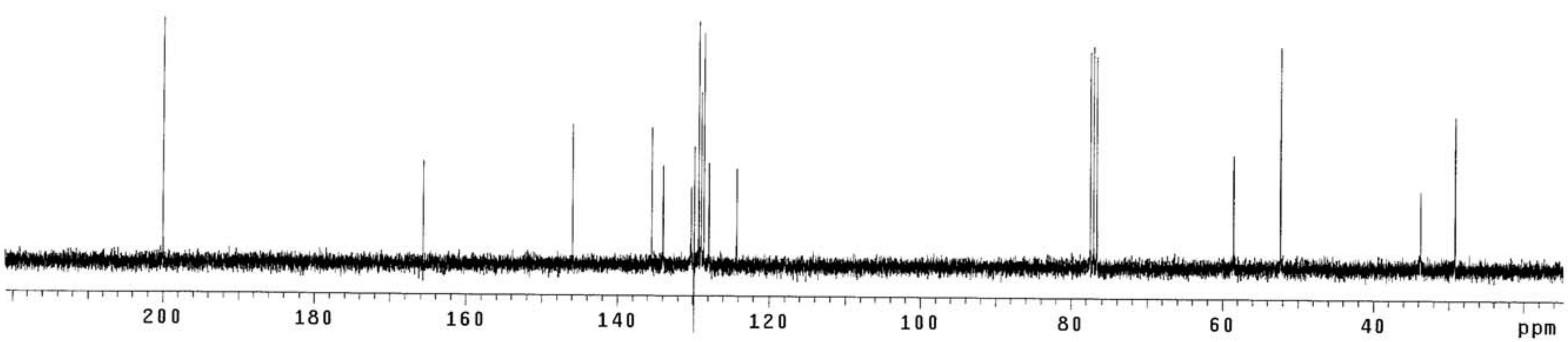

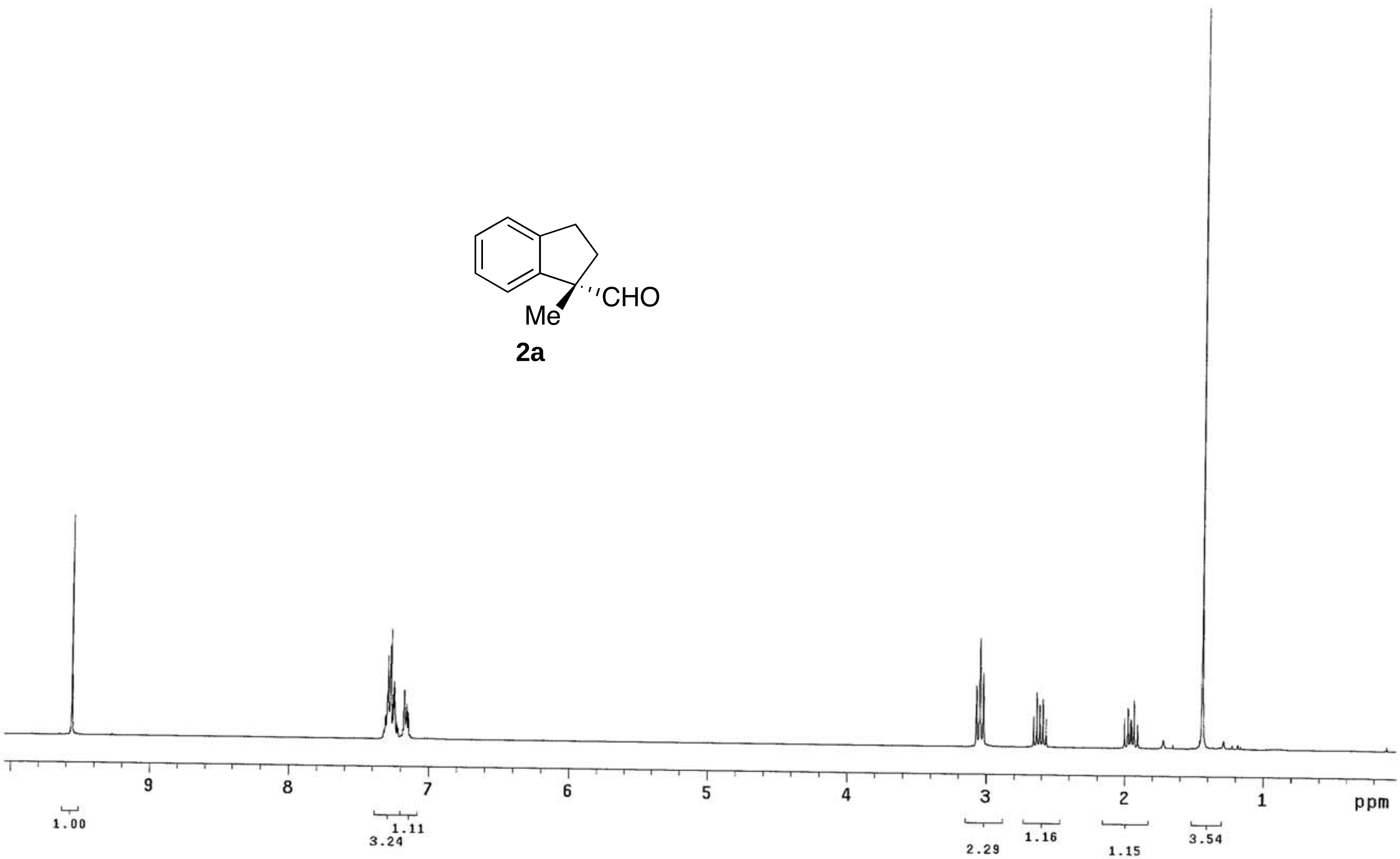

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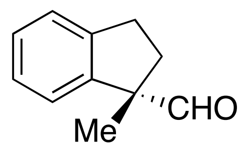

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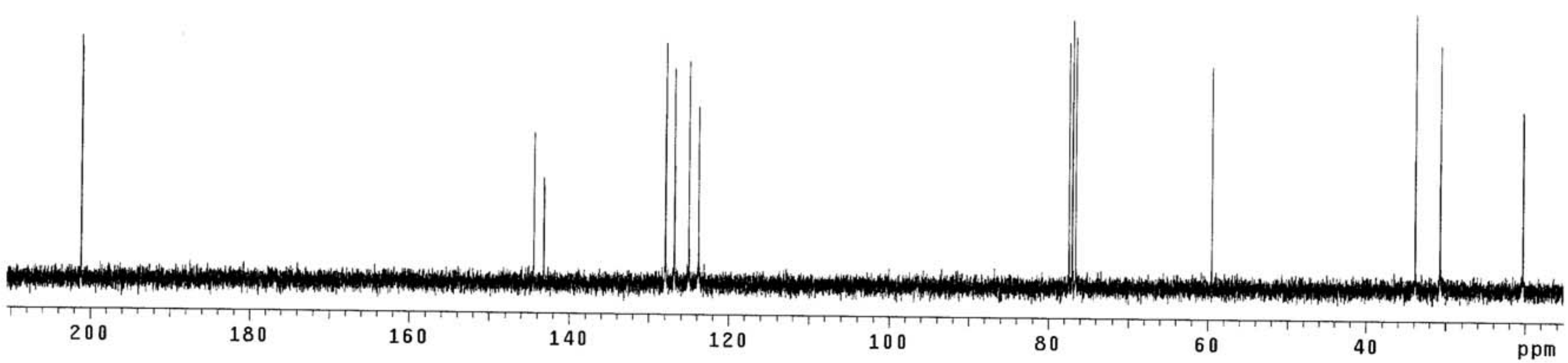

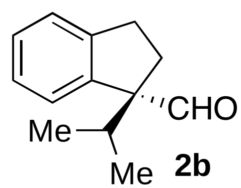

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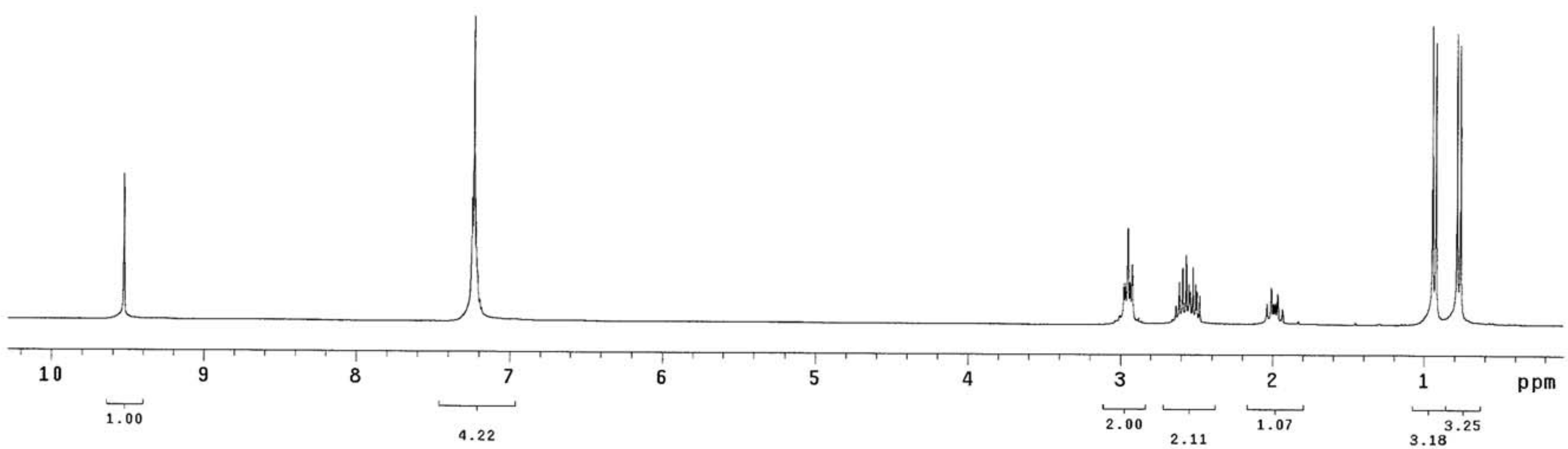

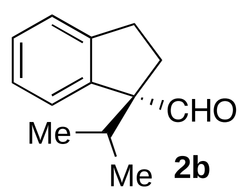

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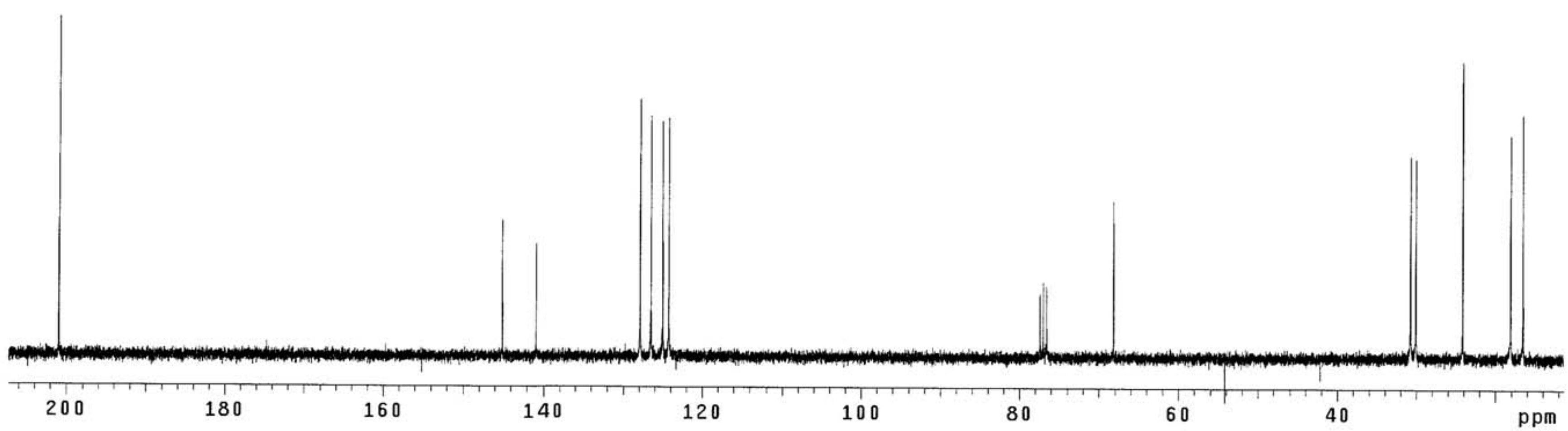

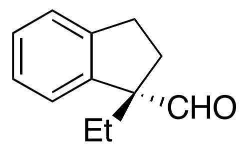

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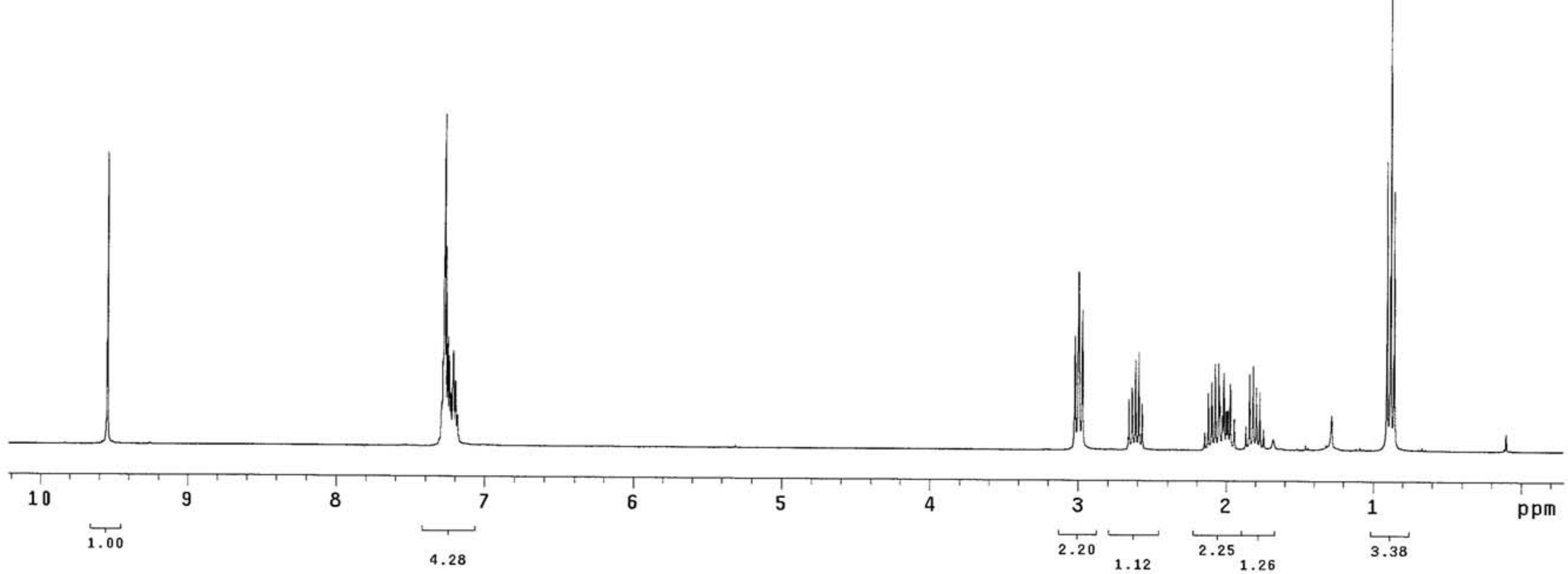

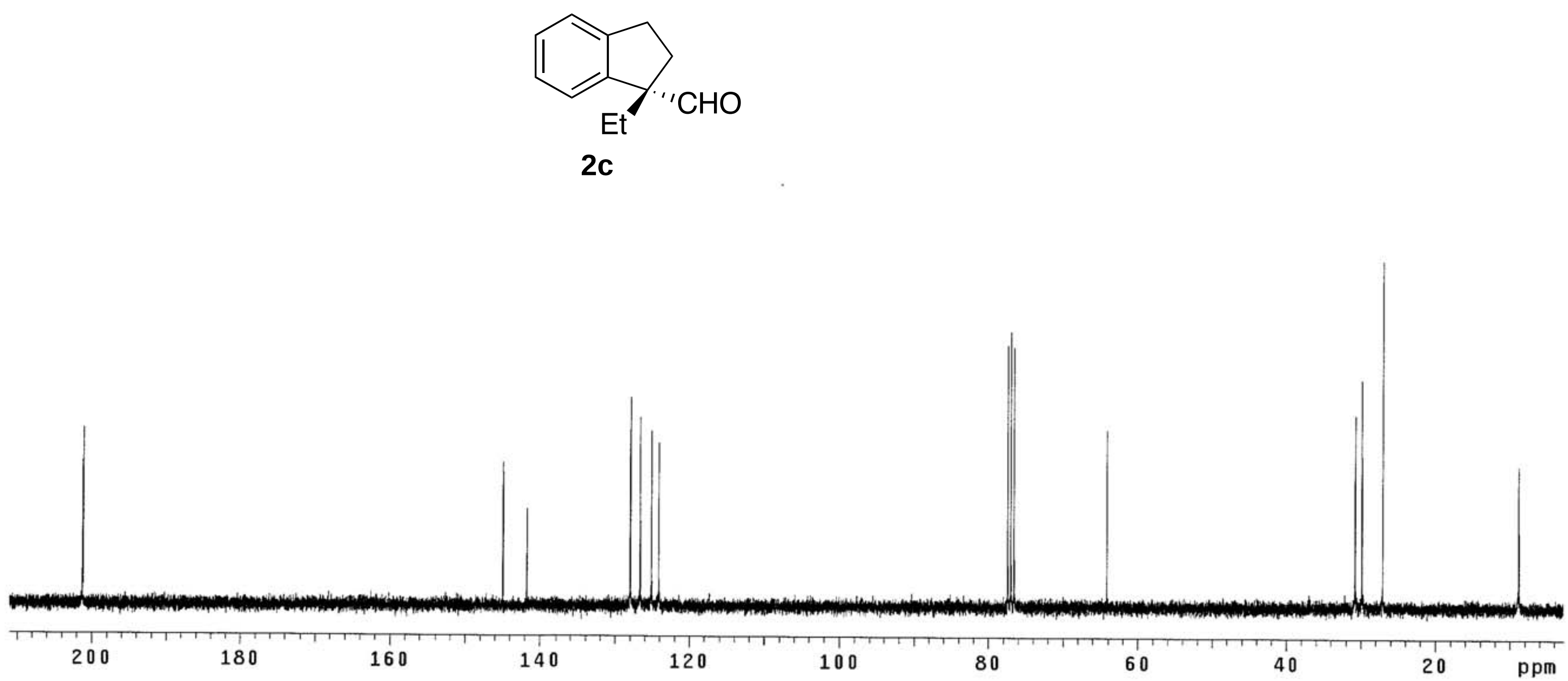
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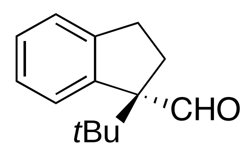

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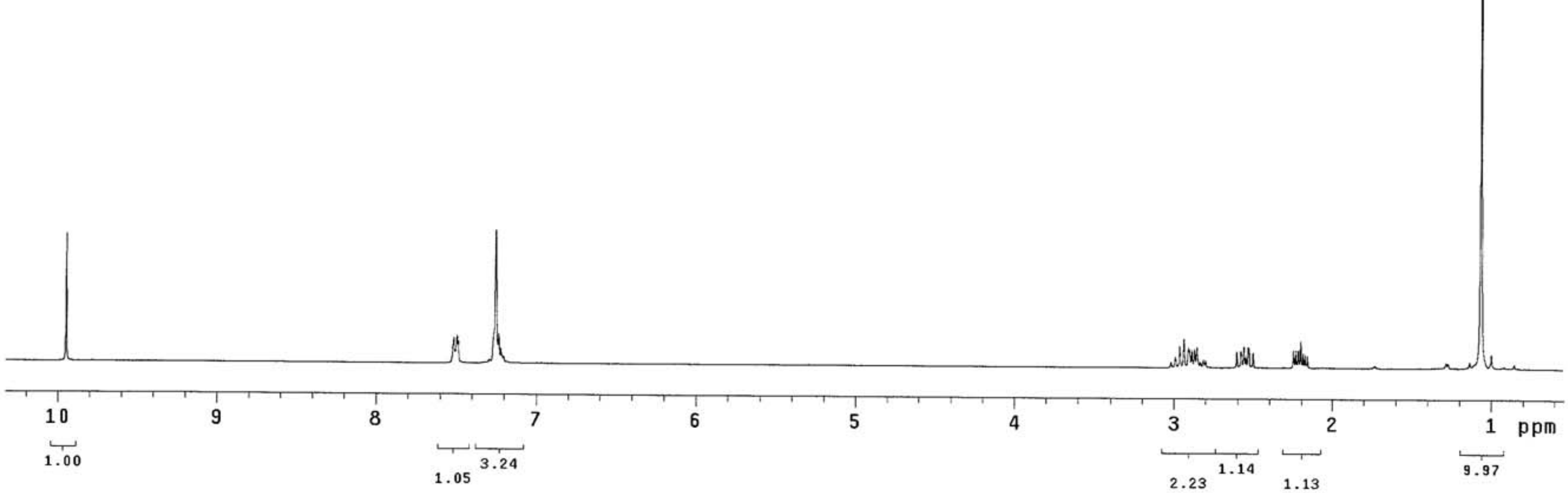

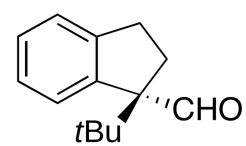

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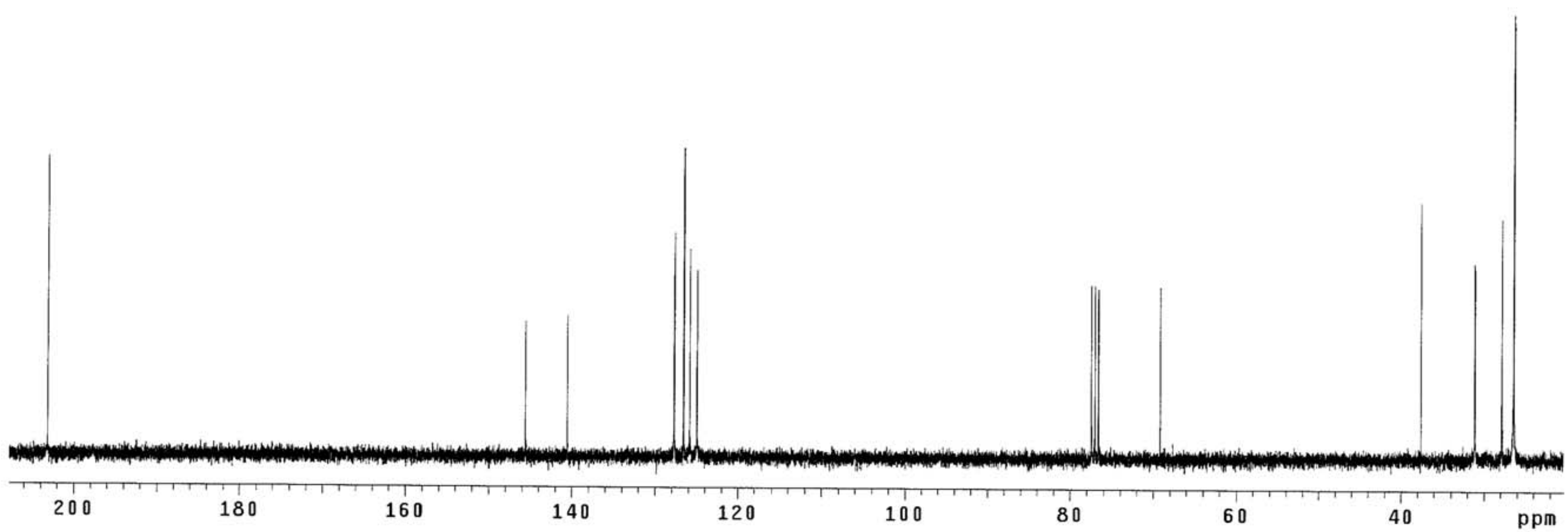

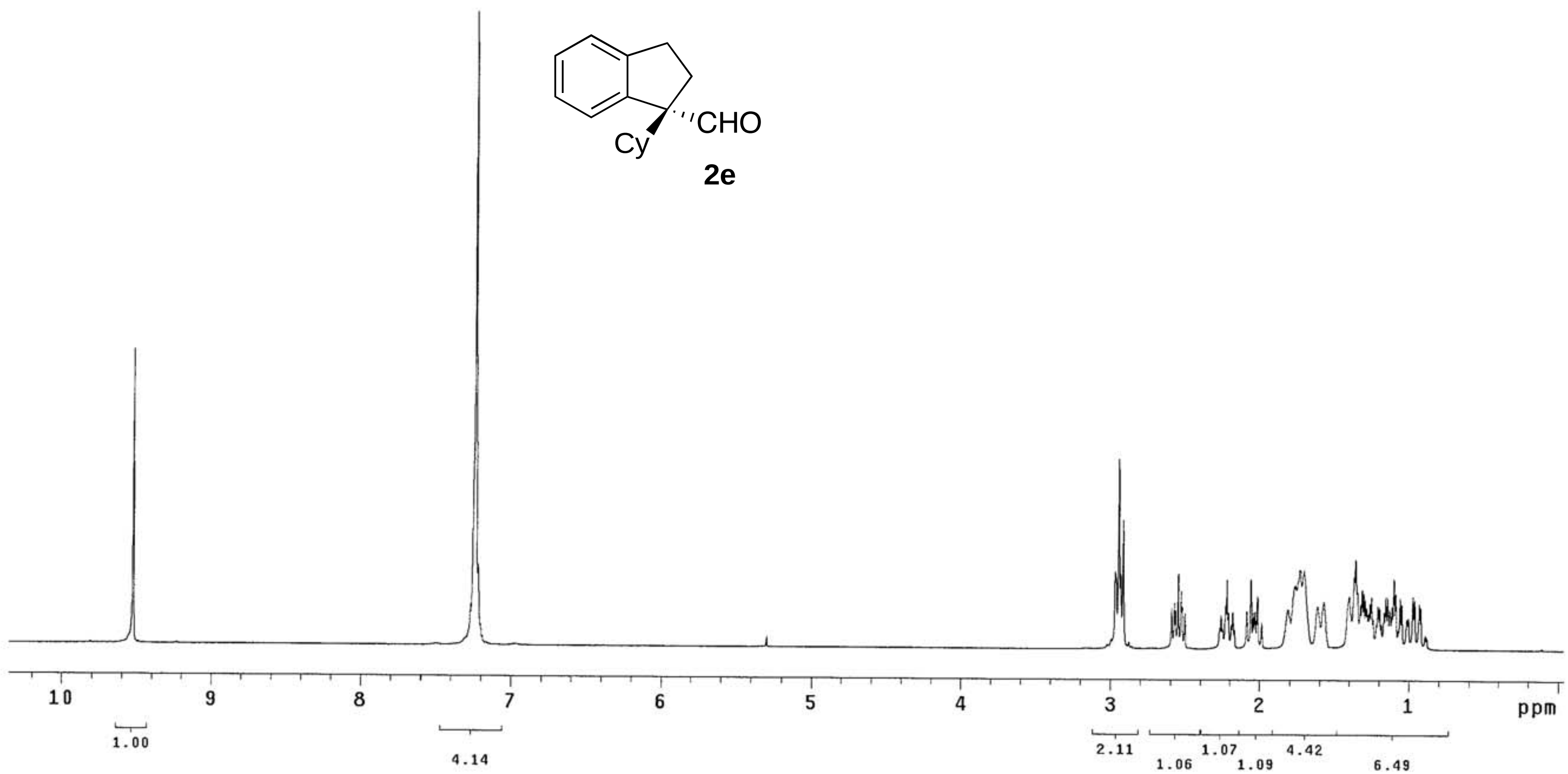
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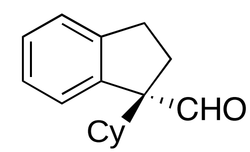

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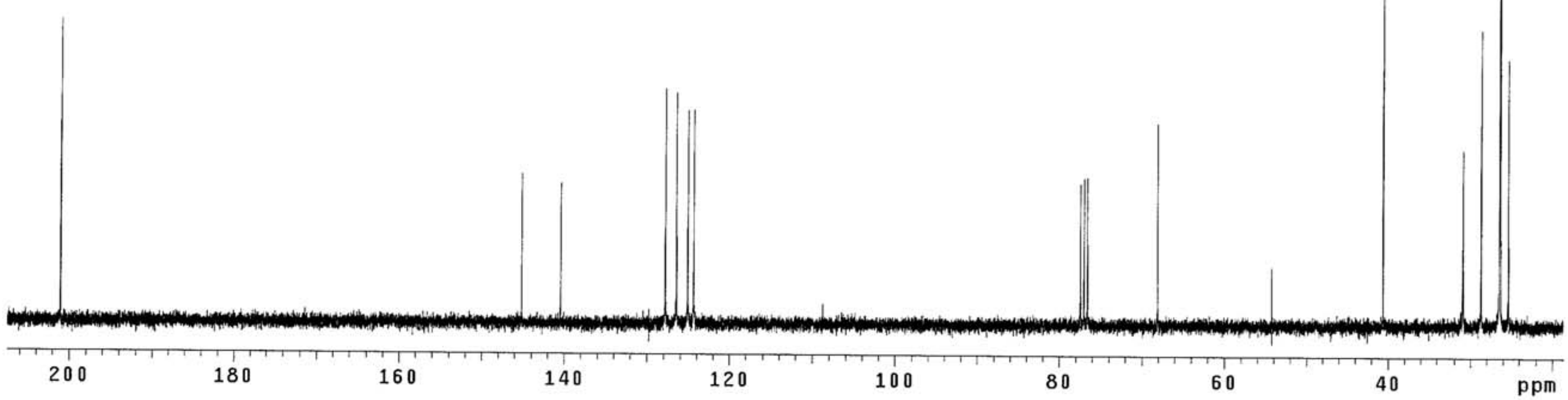

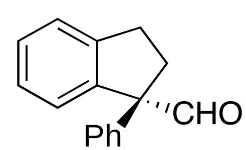

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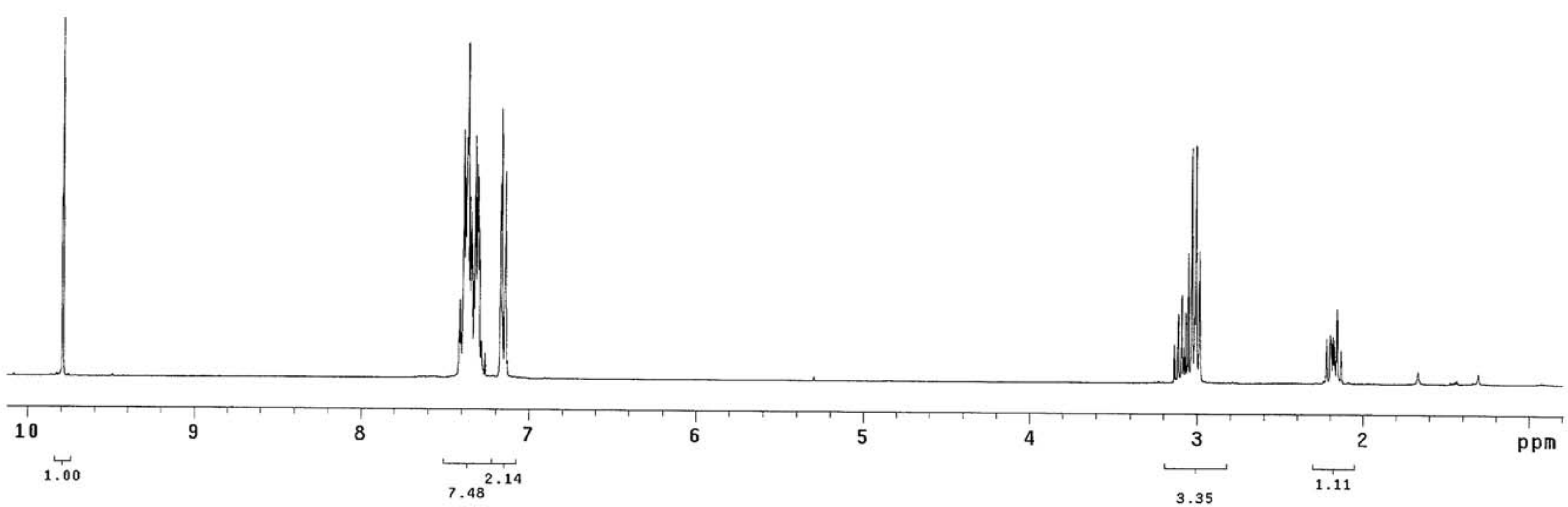

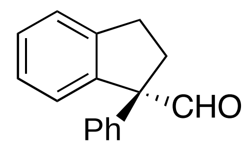

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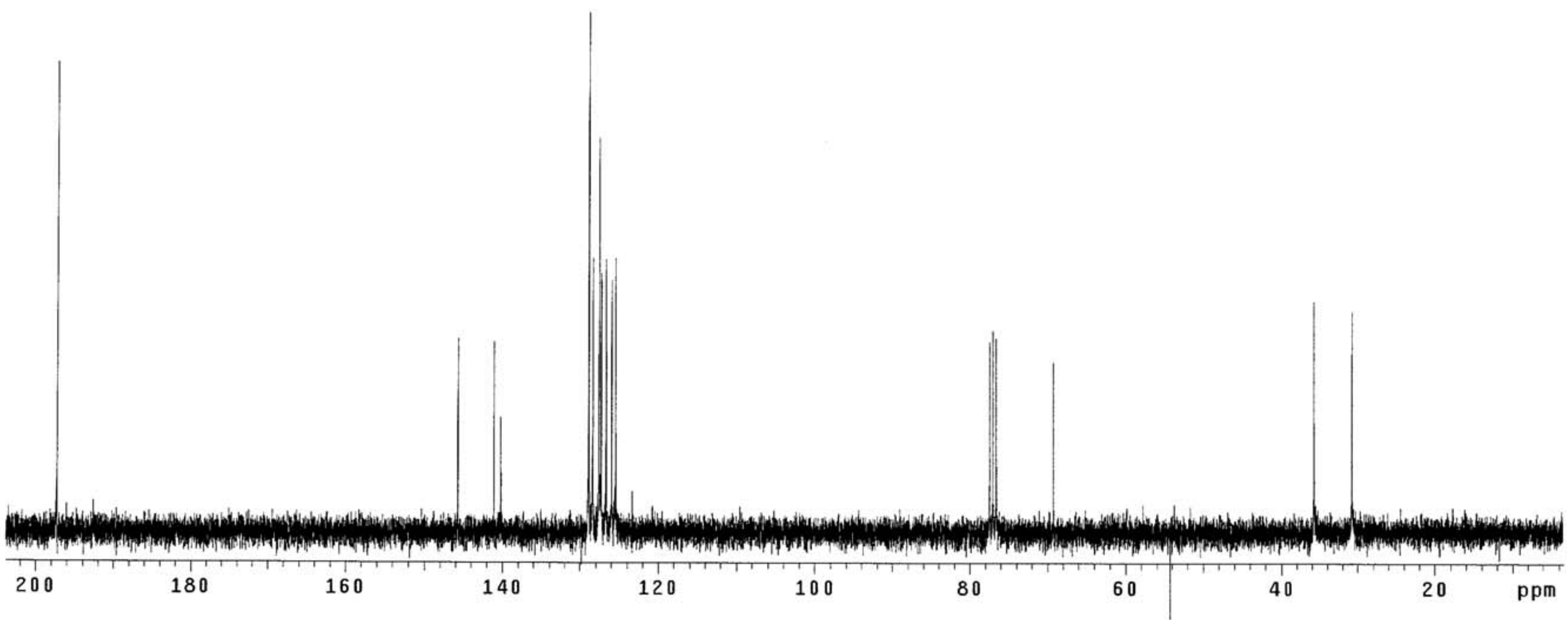

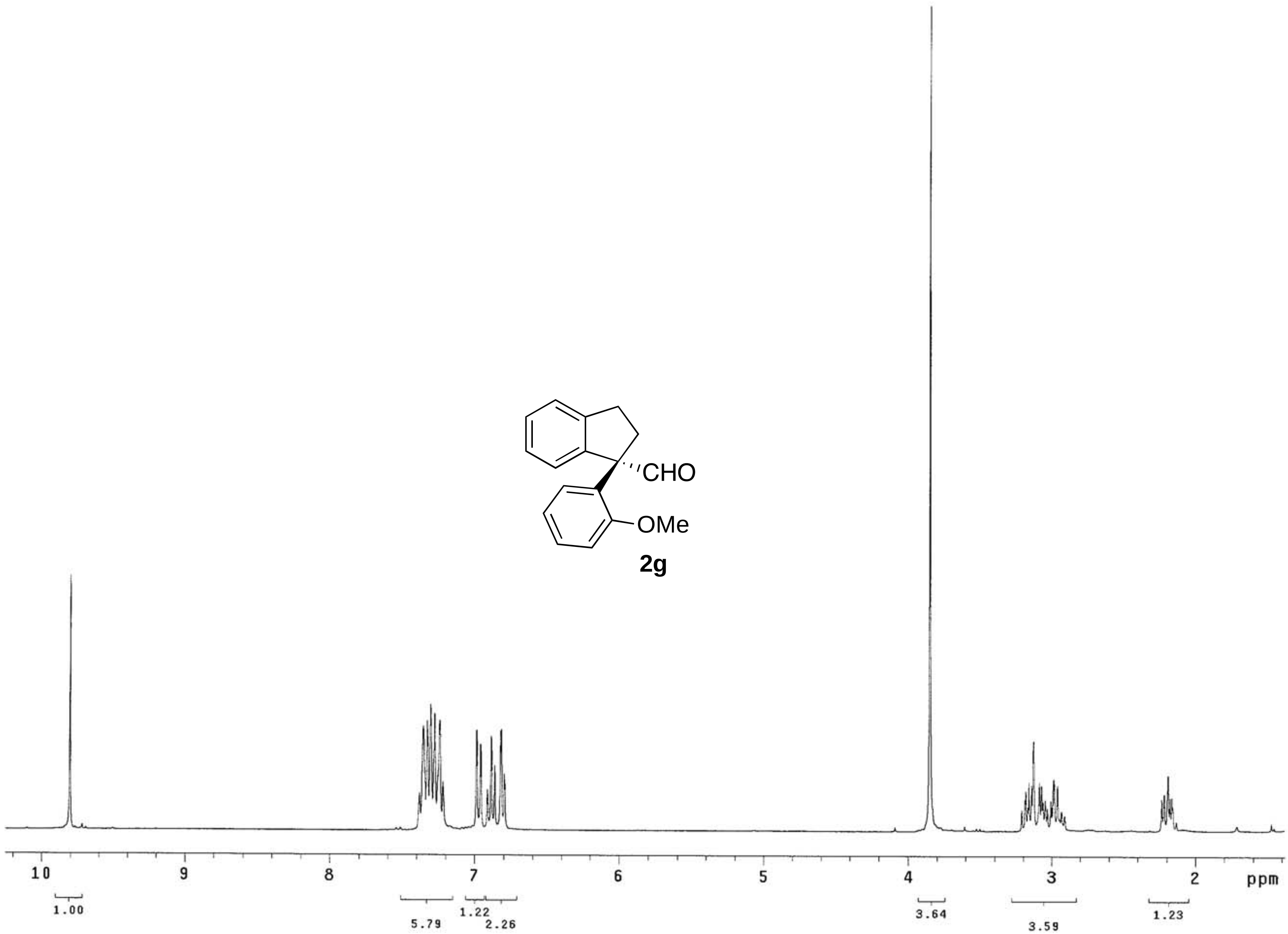
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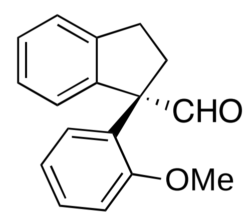

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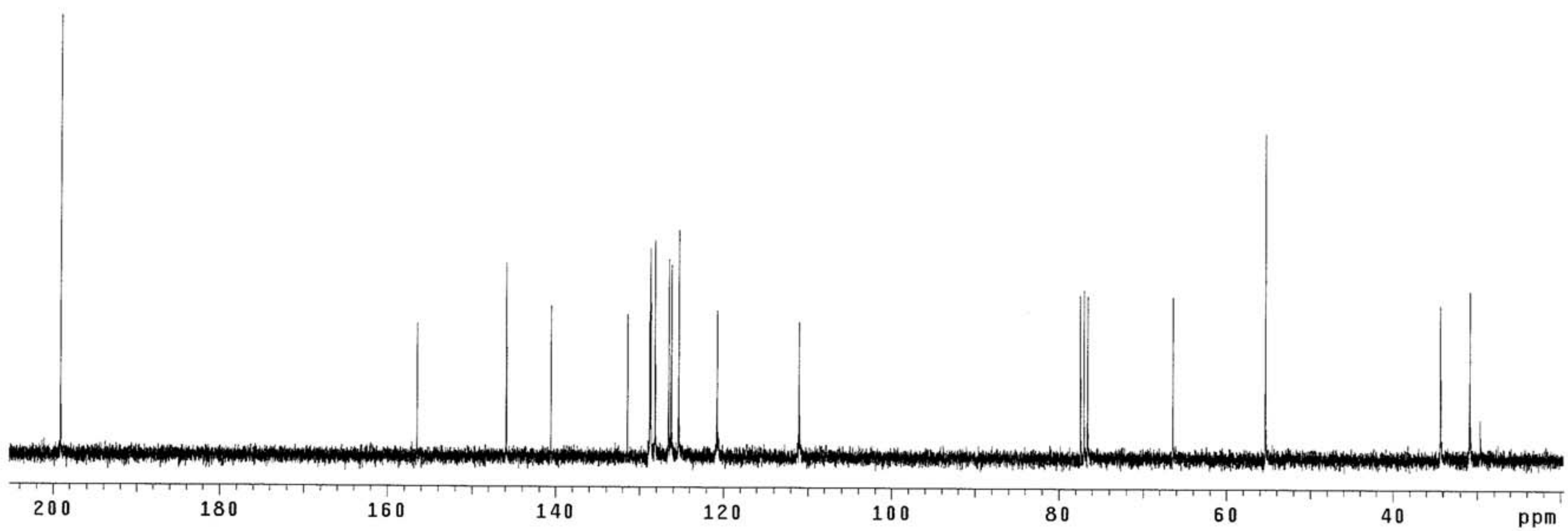

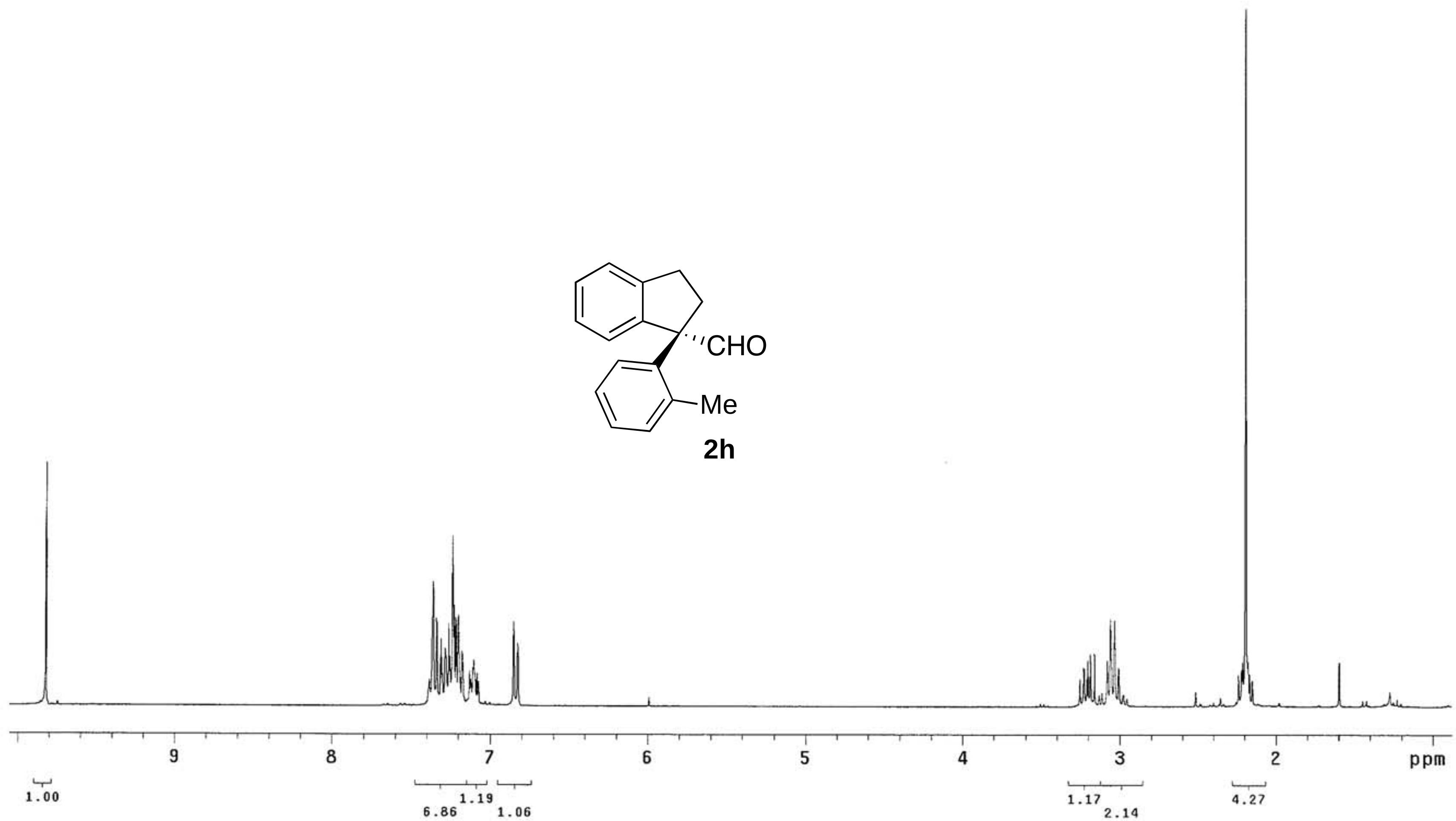
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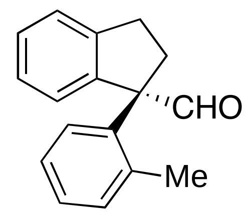

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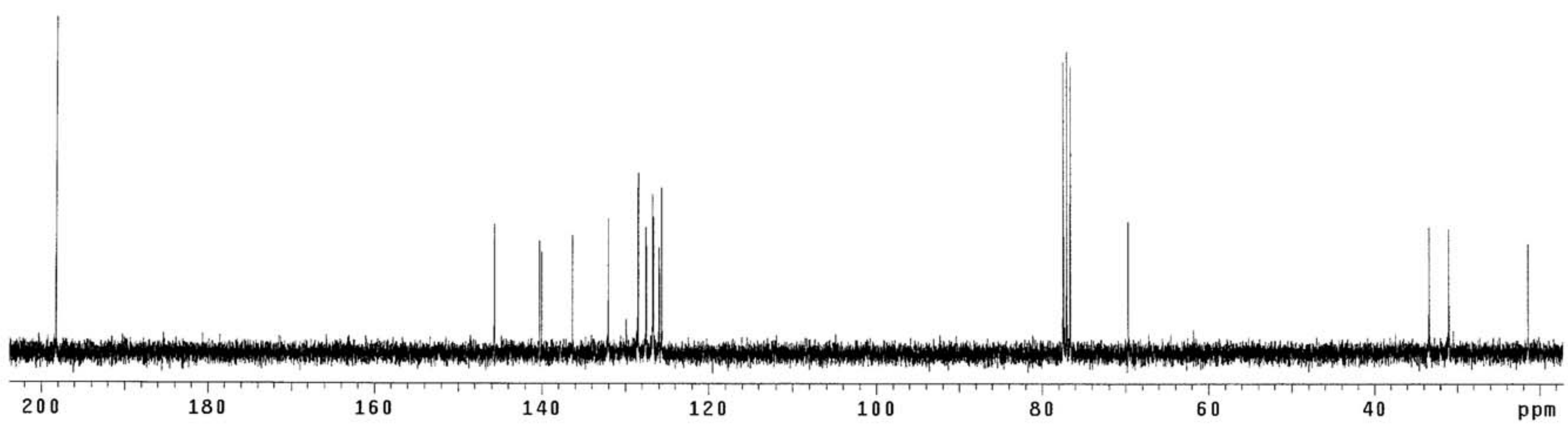

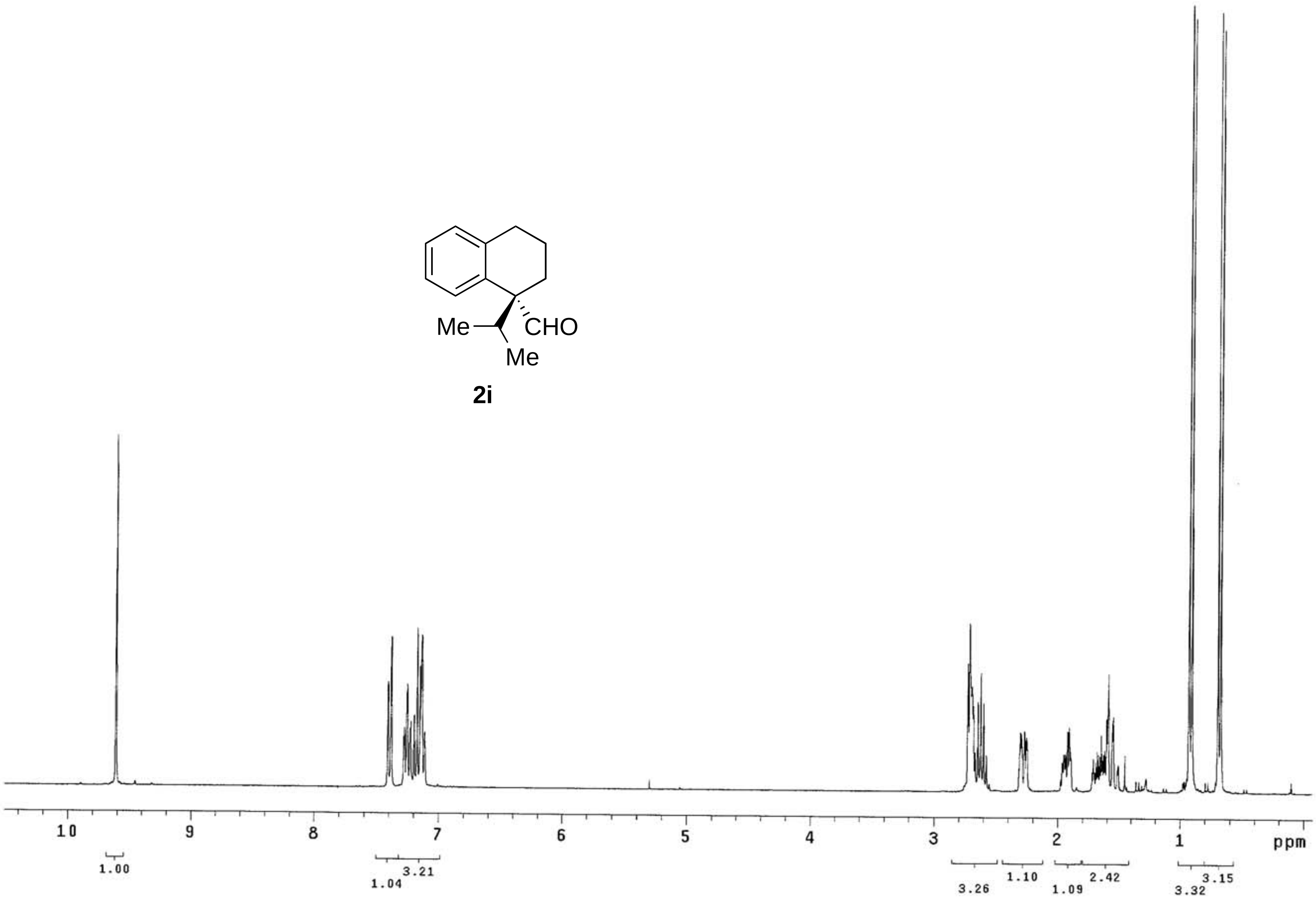
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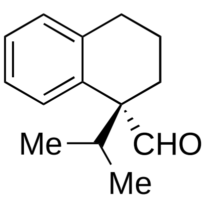
3.32
3.15



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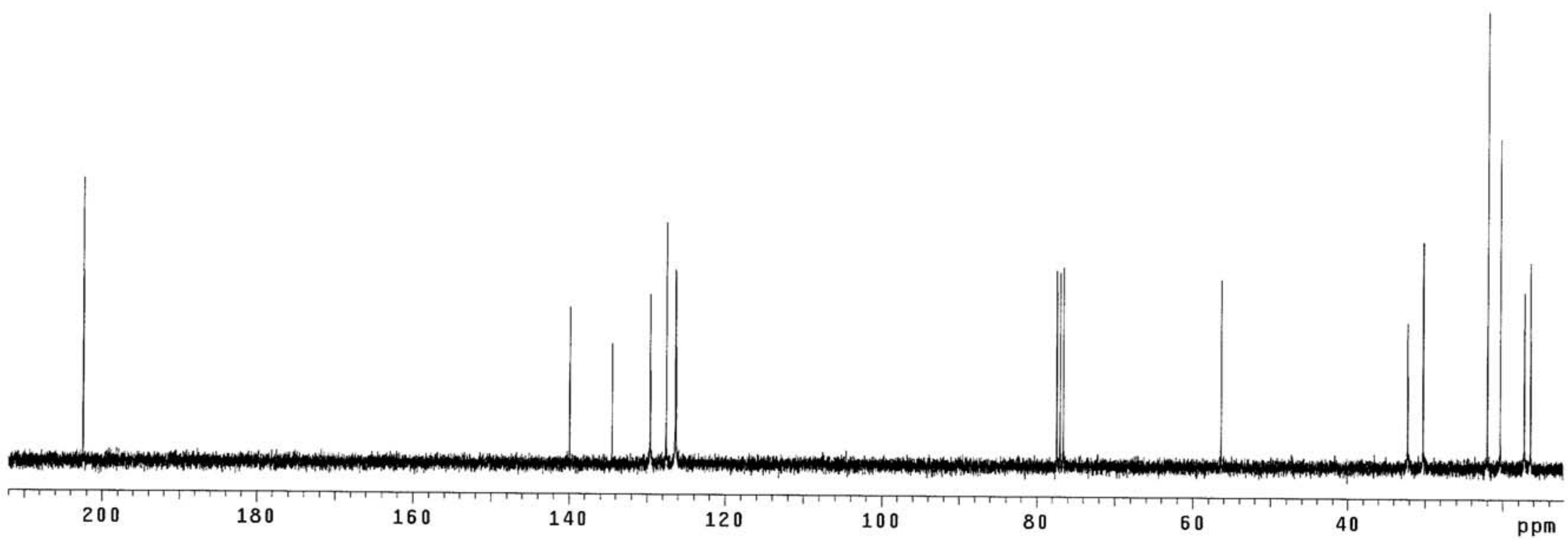

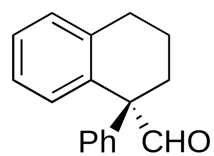

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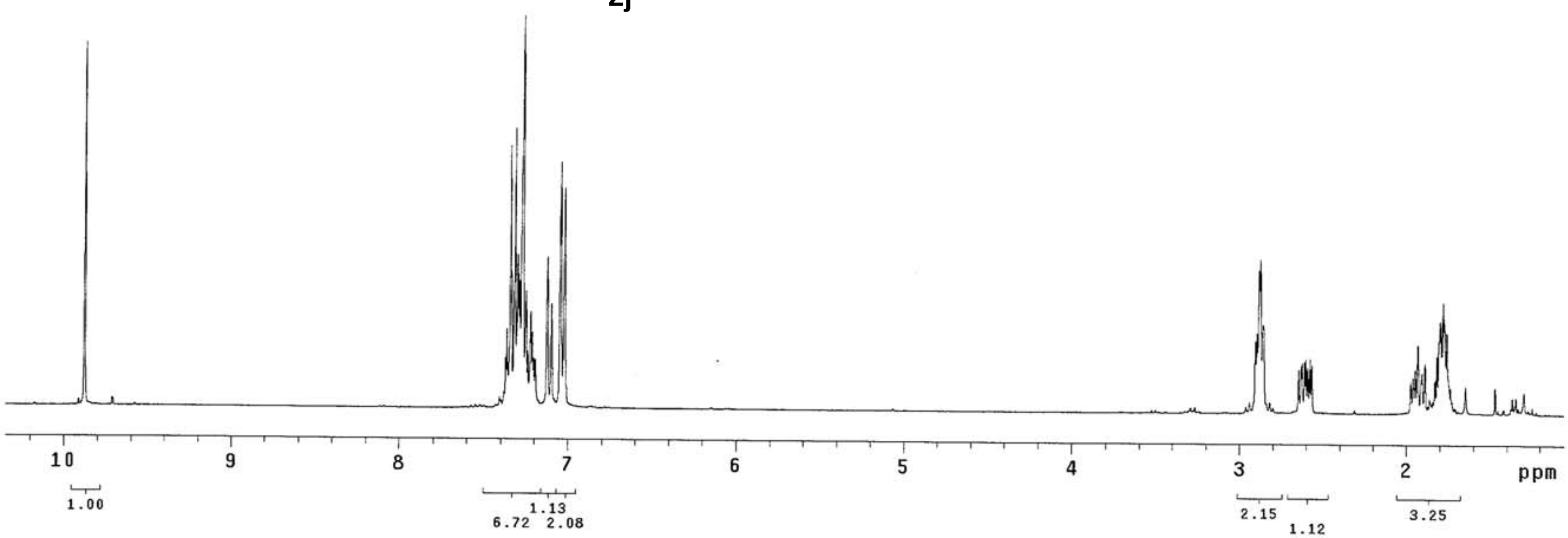

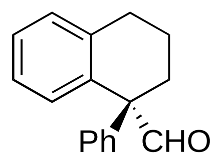

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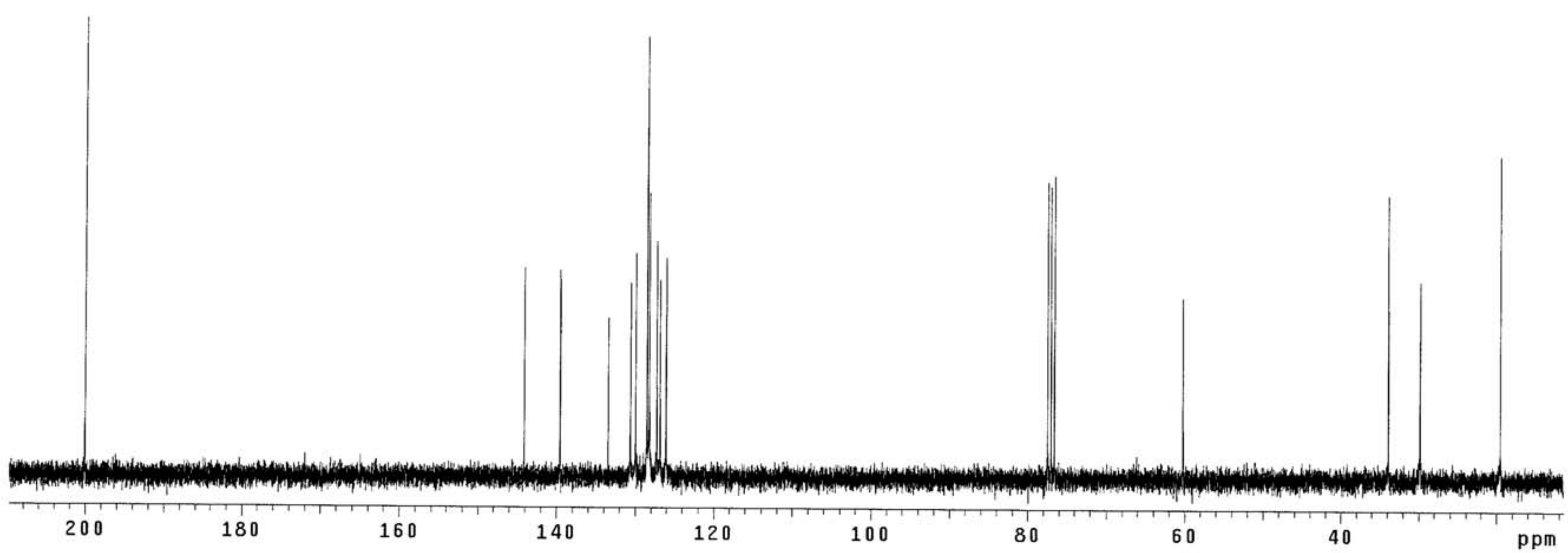

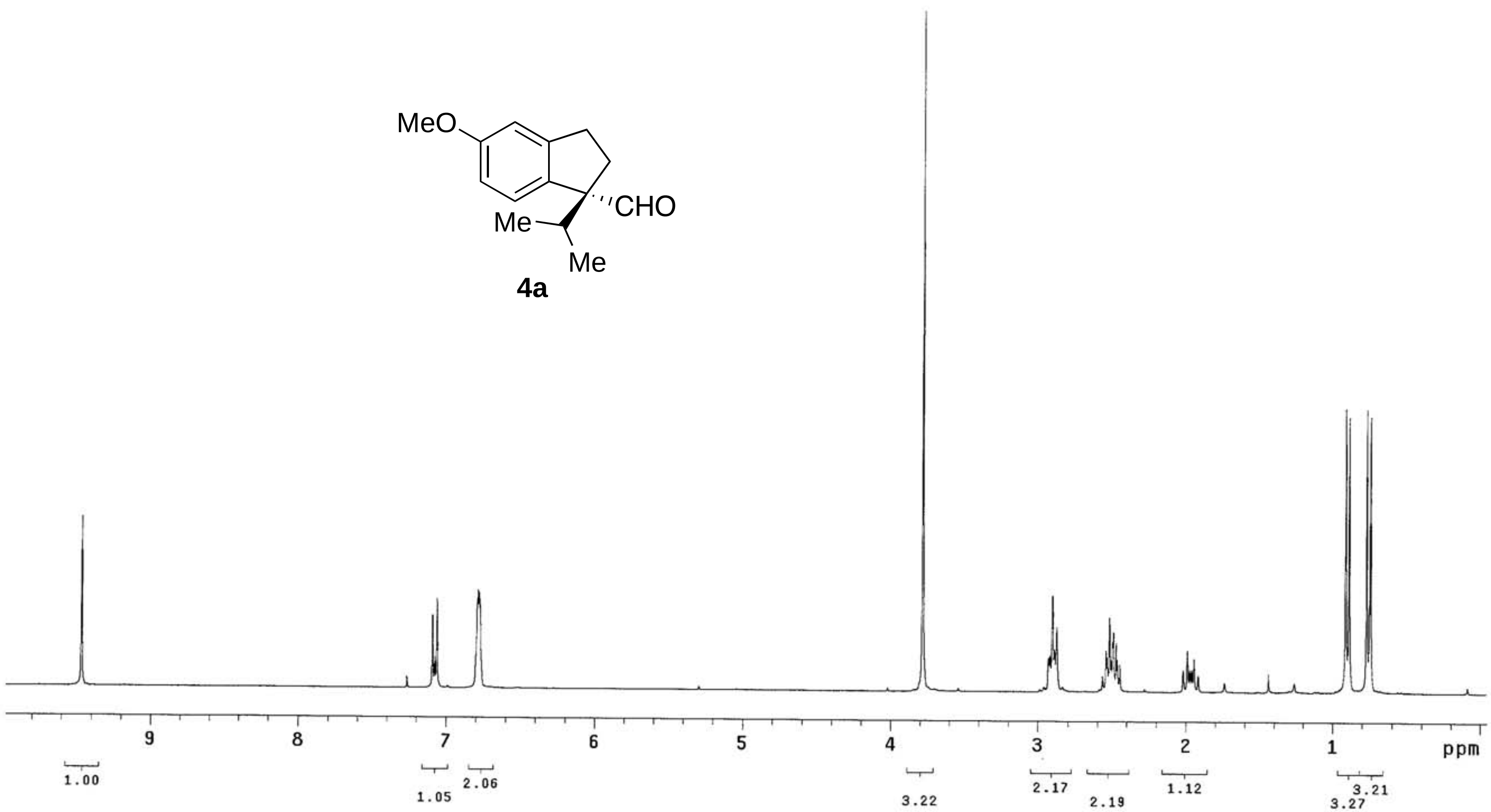
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ppm
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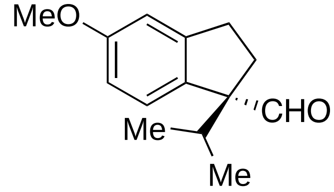
3.21
3.27



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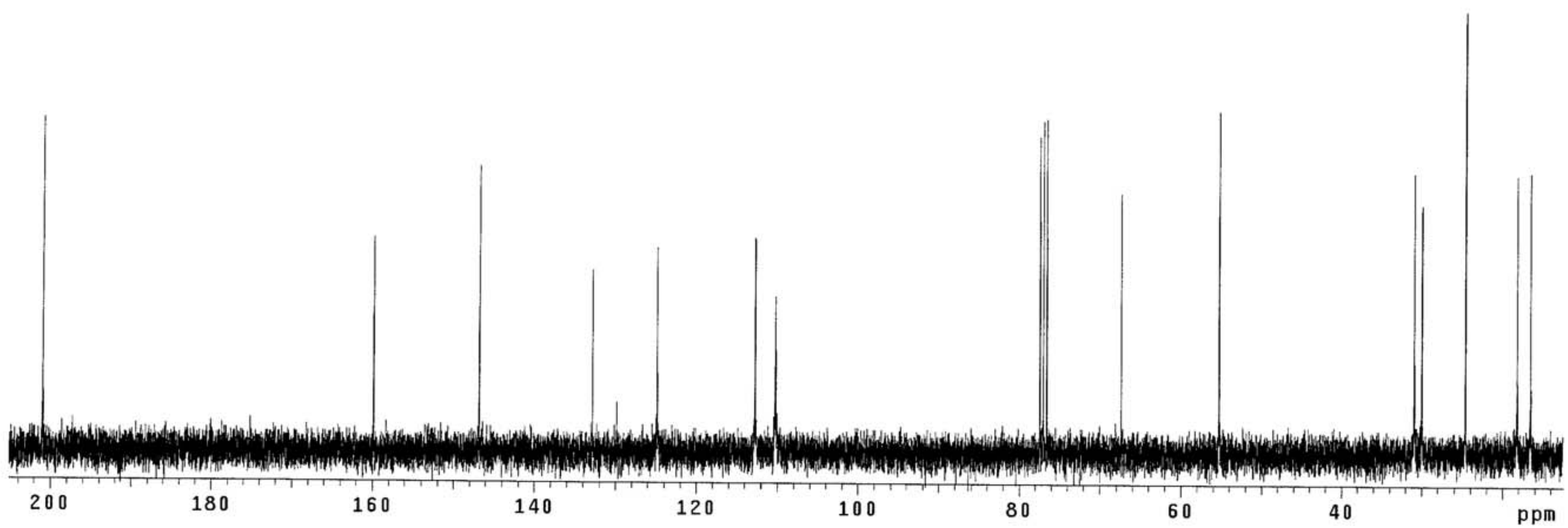

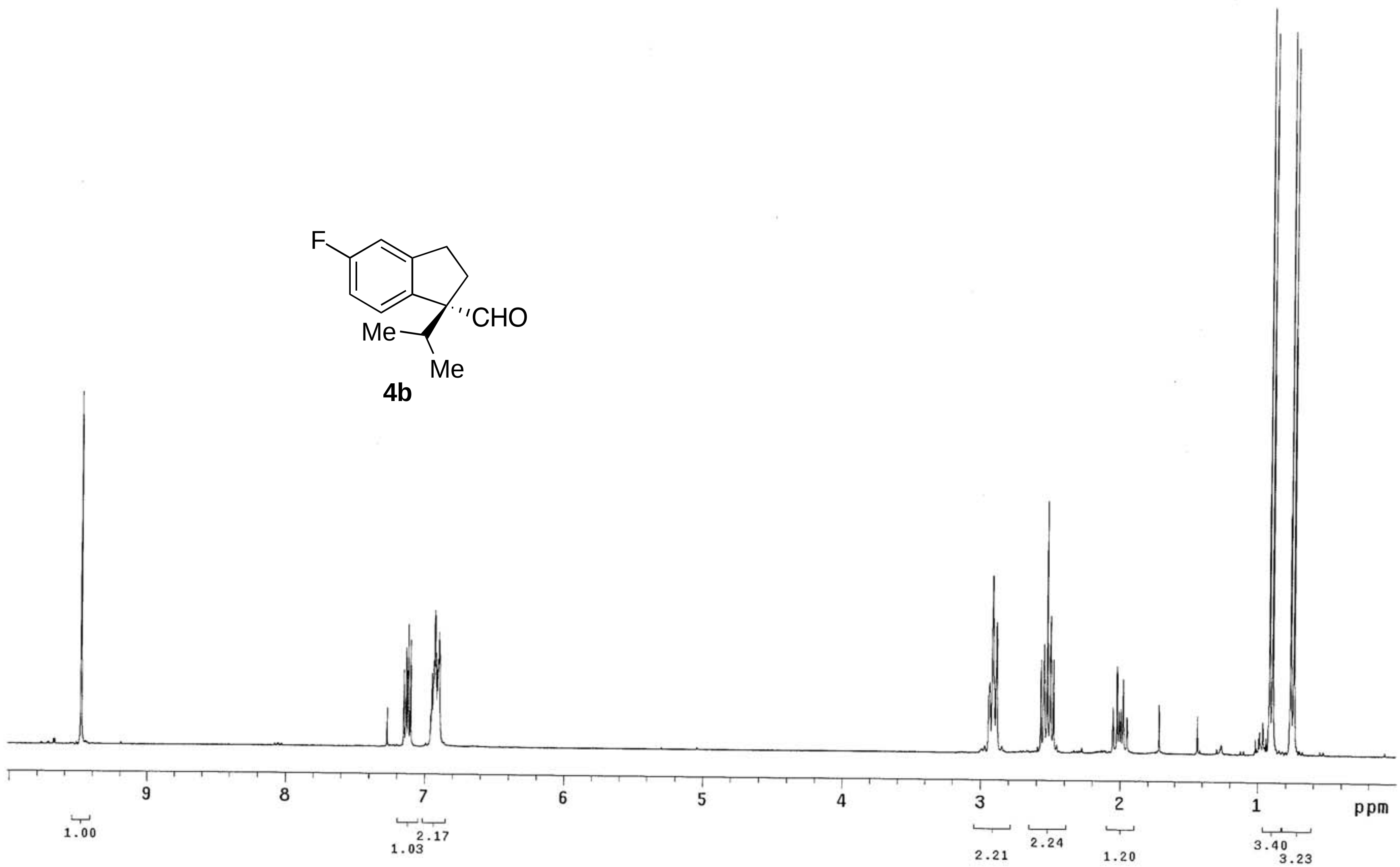
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4b
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ppm
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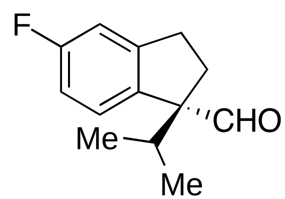
3.40
3.23



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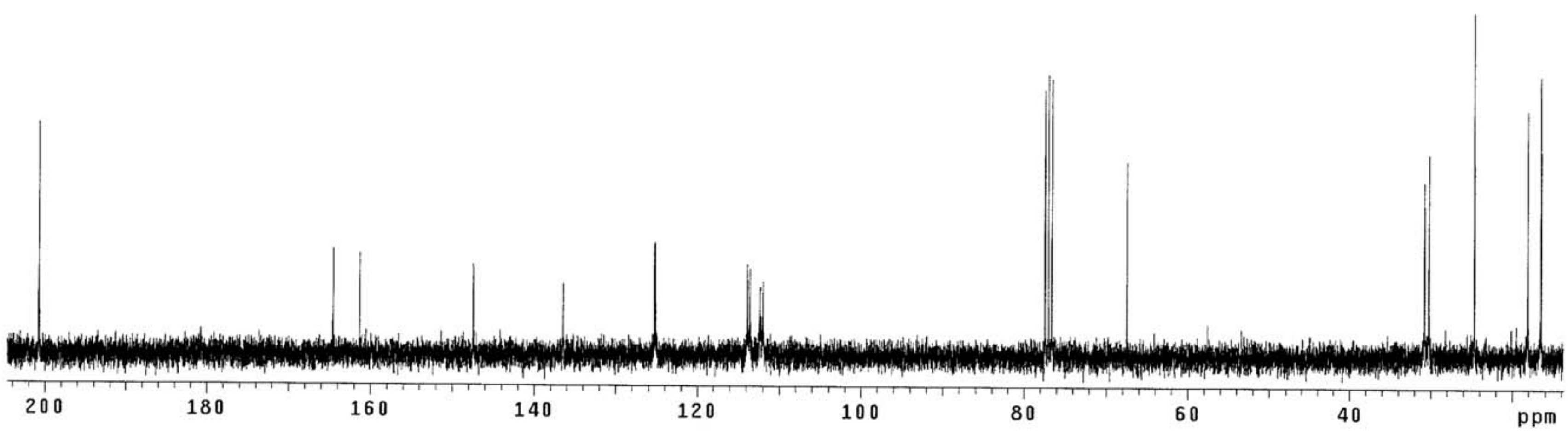

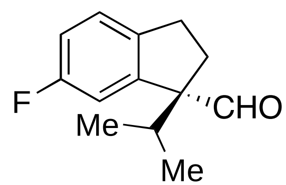

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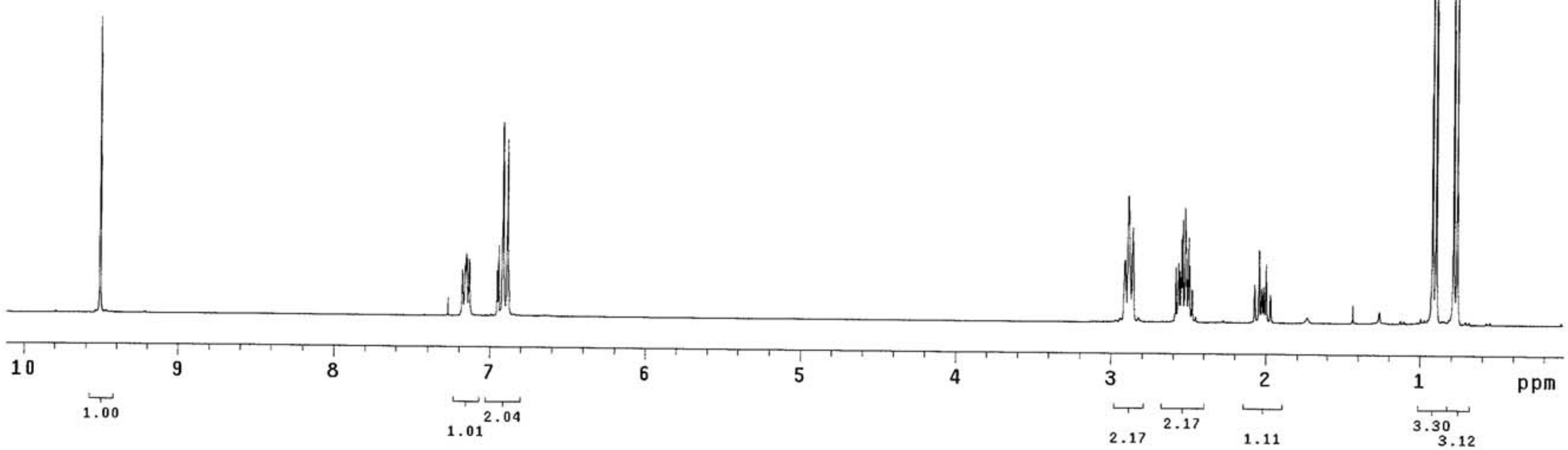

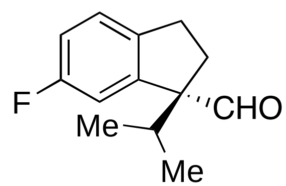

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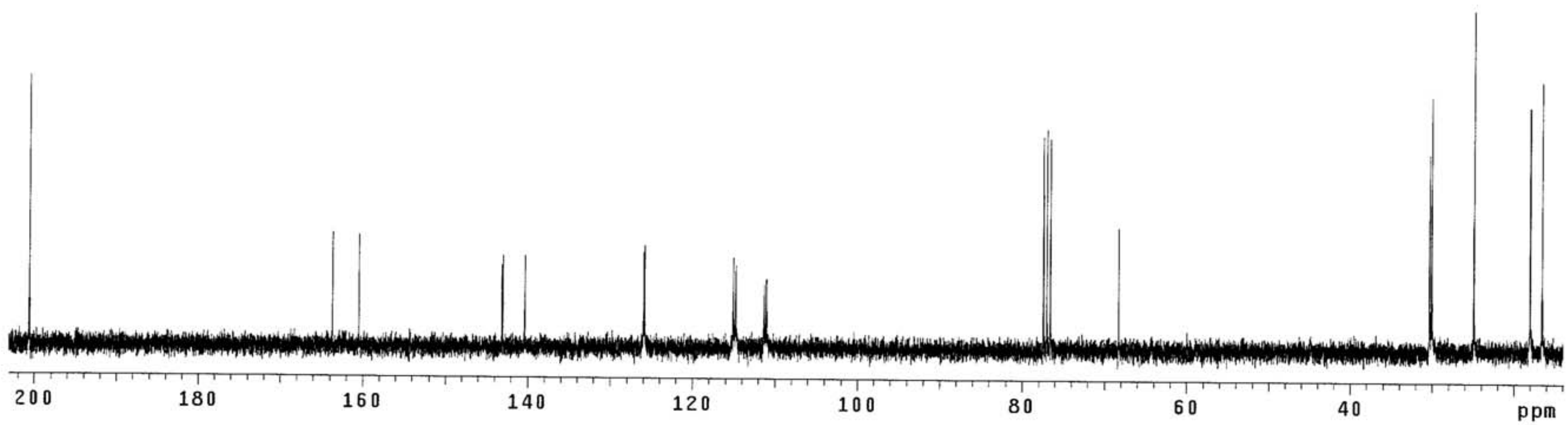

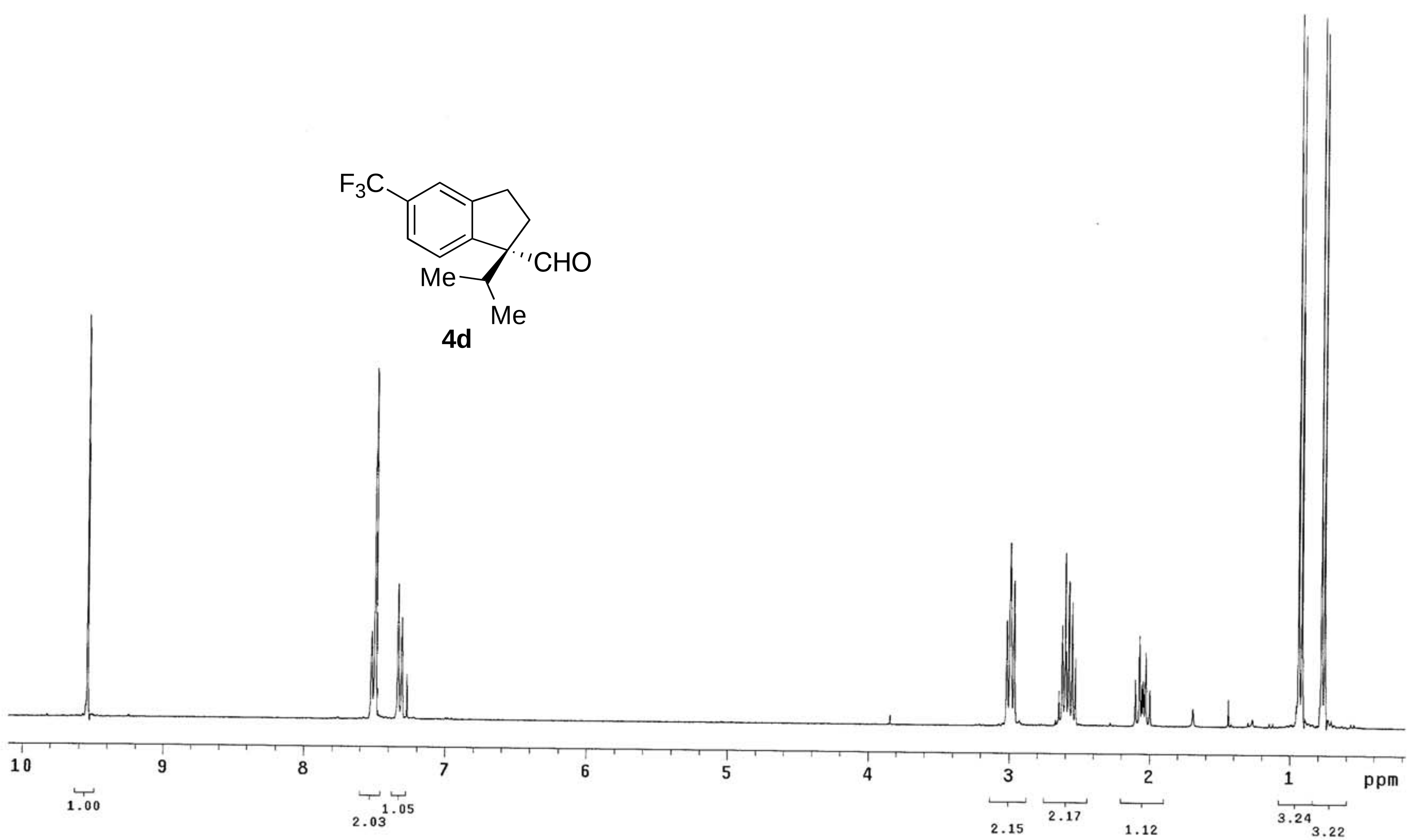
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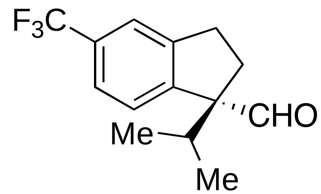
3.22



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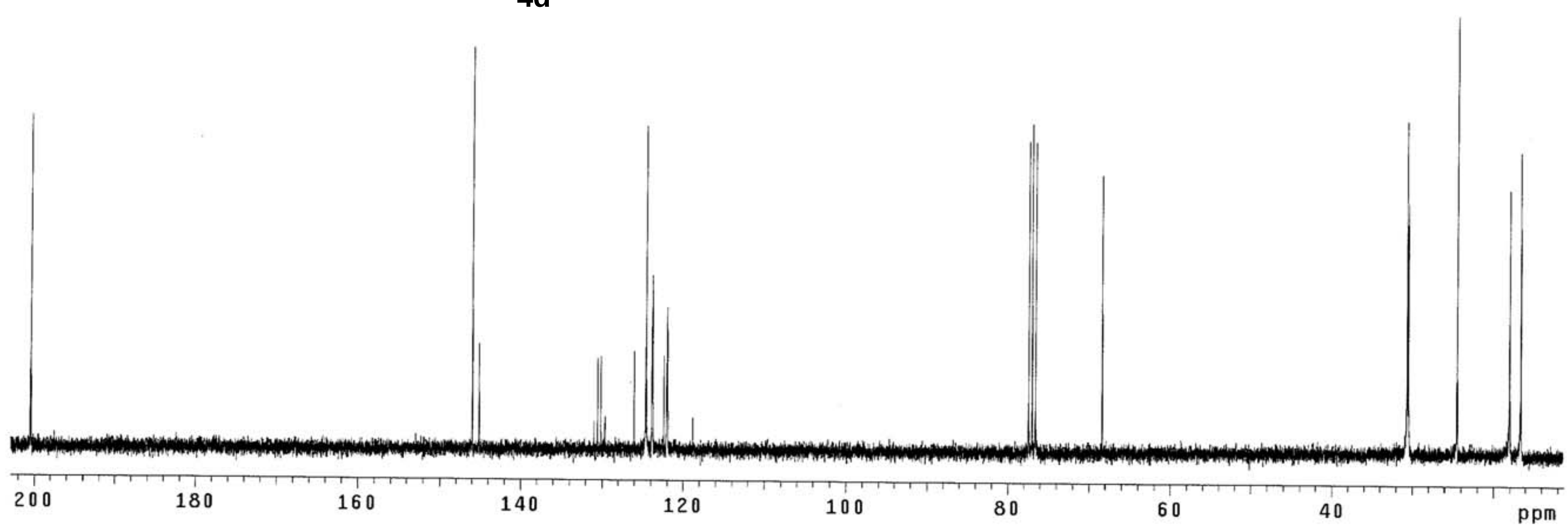

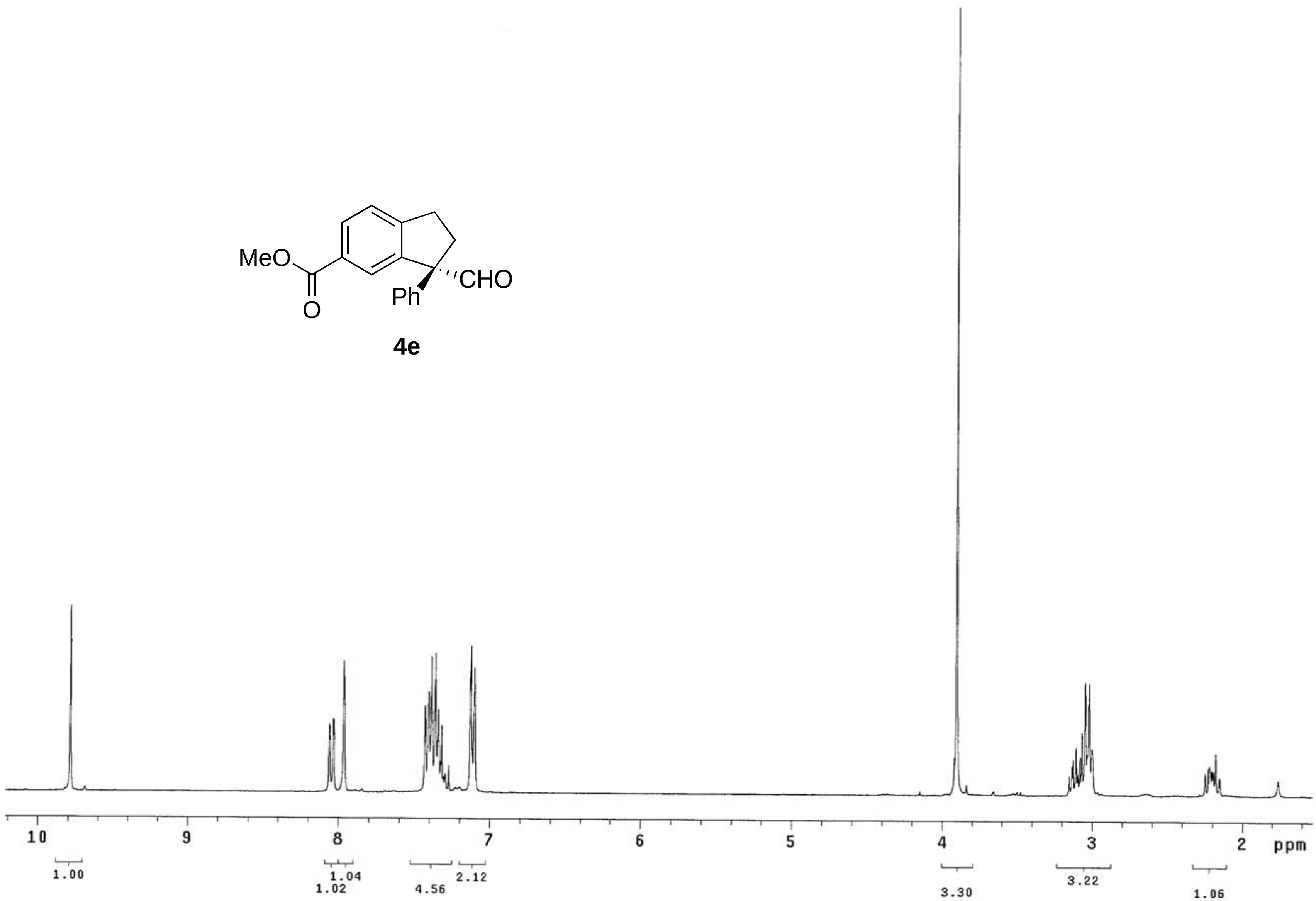

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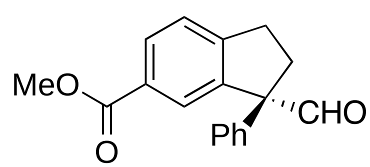

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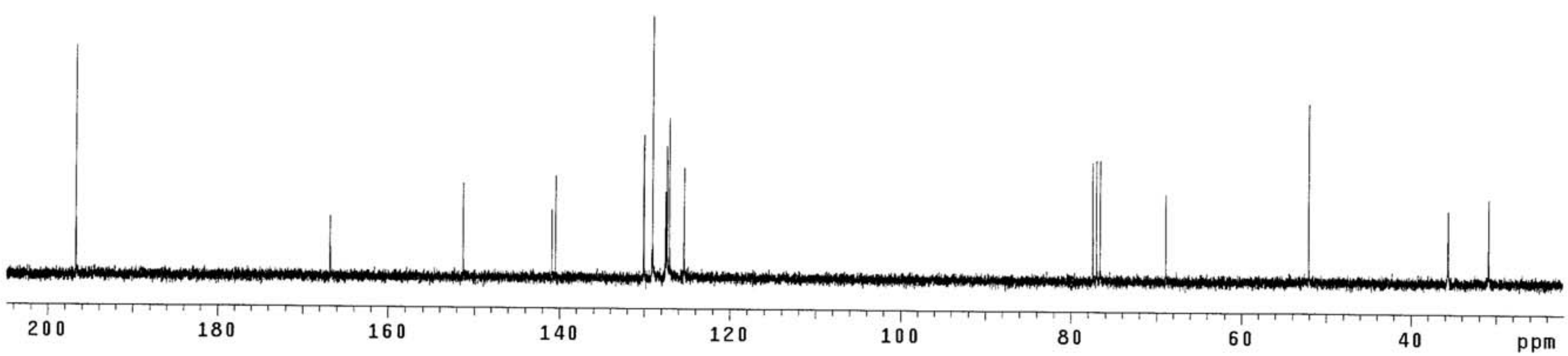

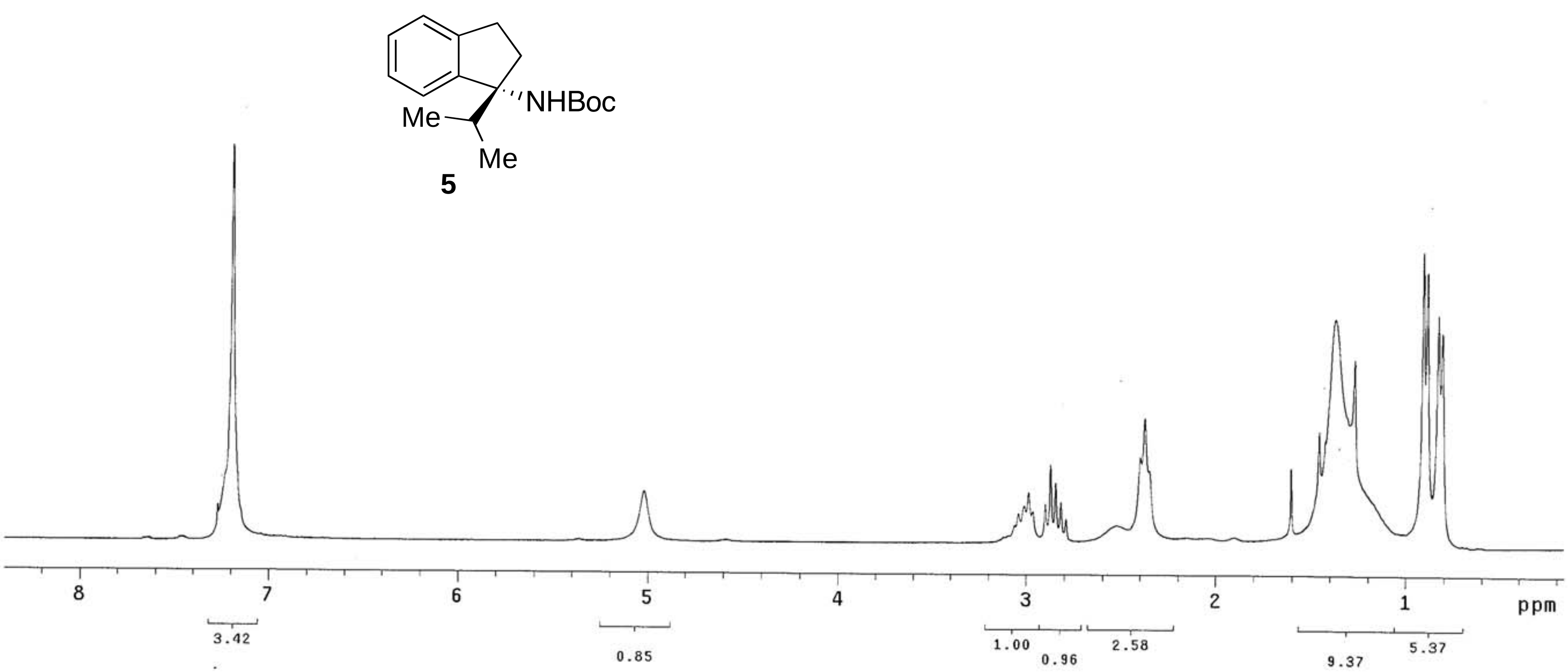

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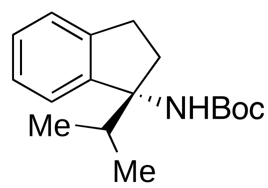

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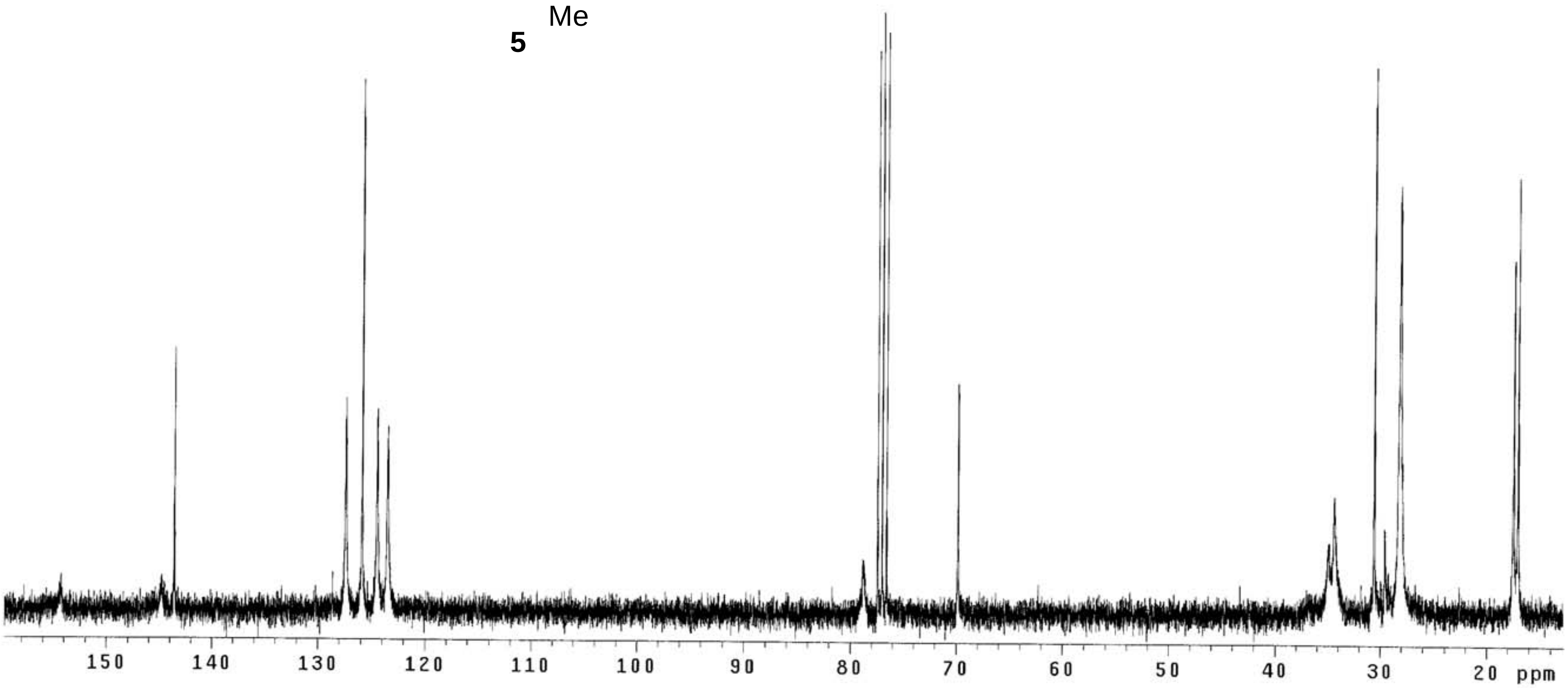

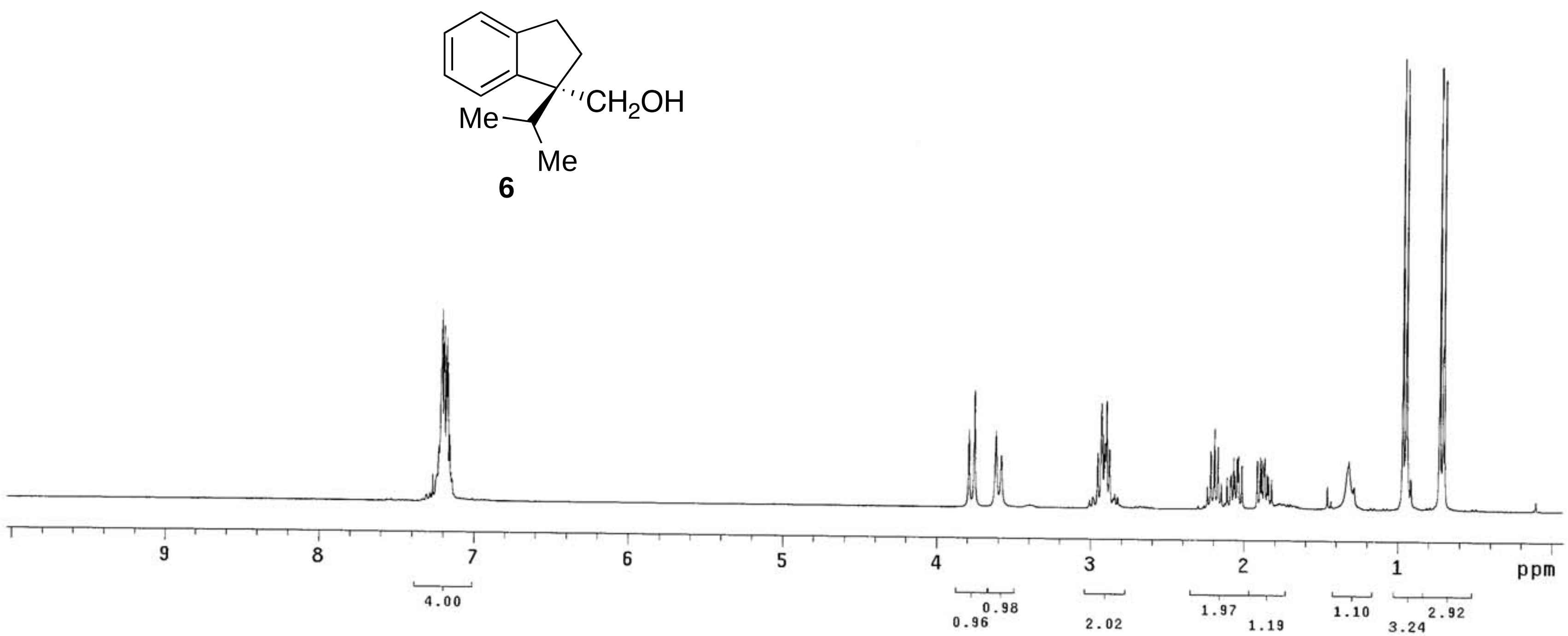

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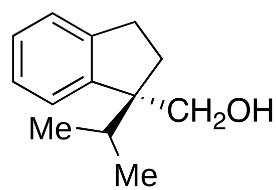

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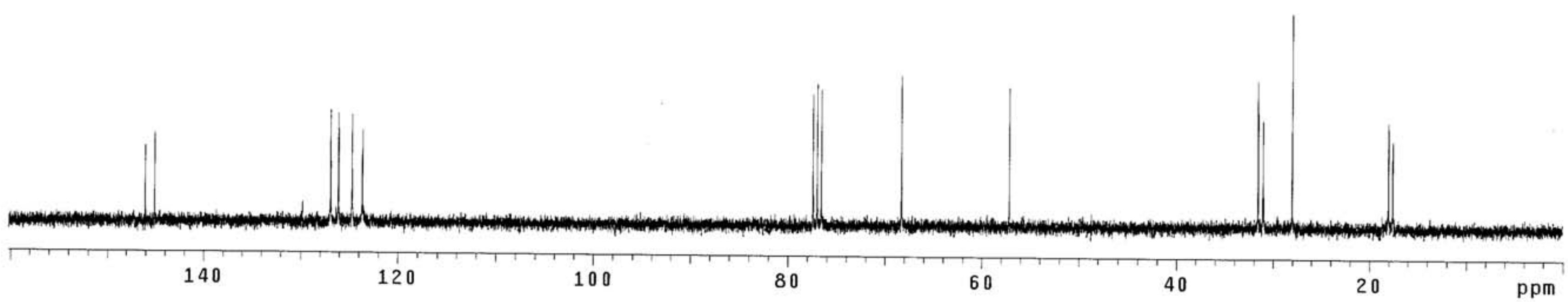

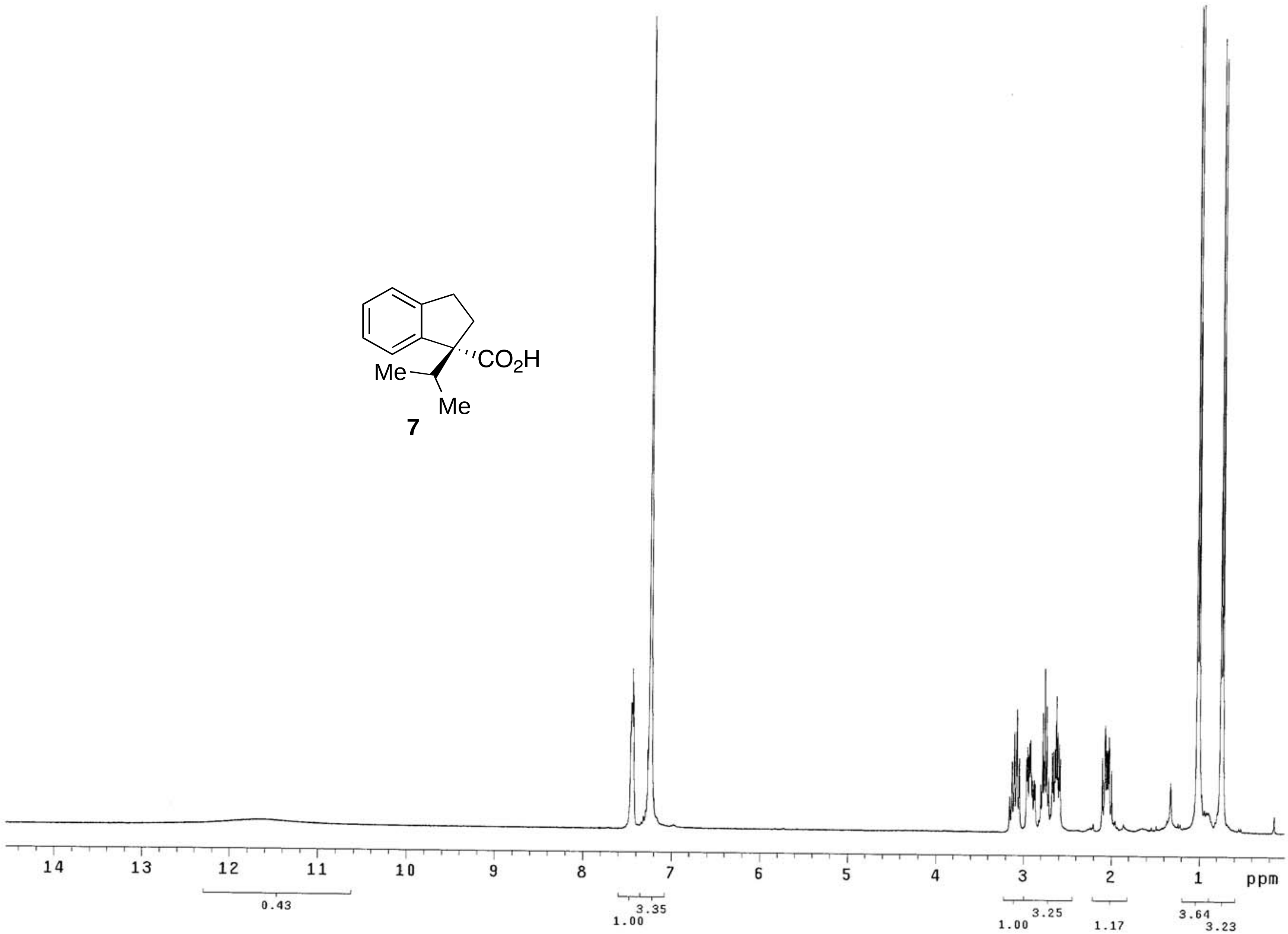
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Me
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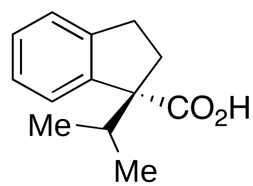

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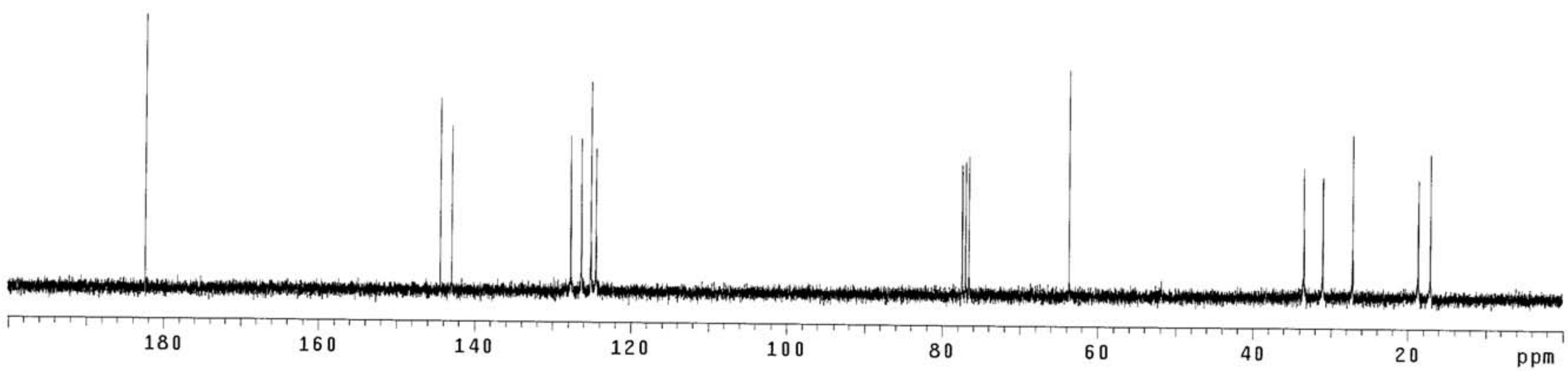

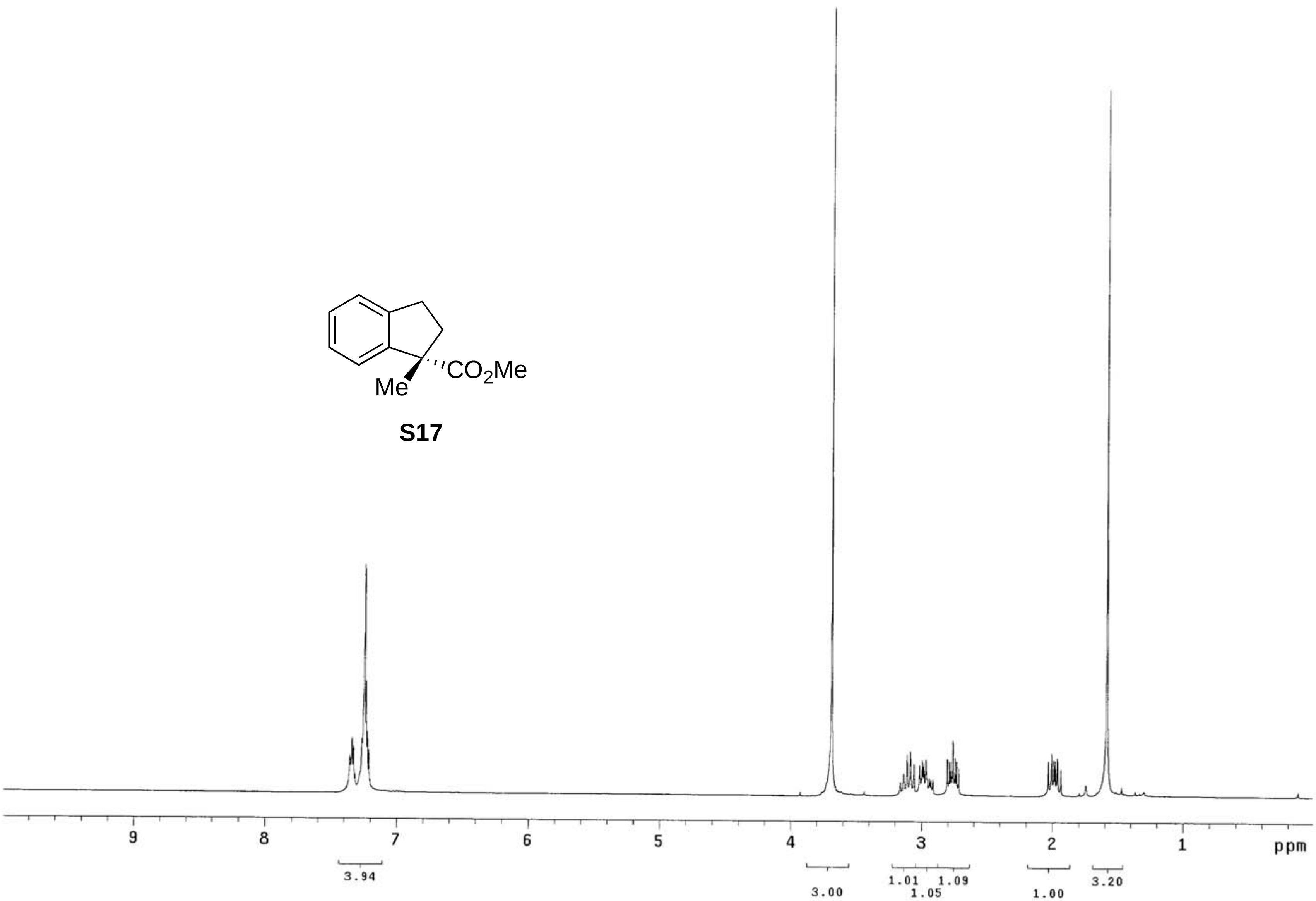
Me
CO2Me
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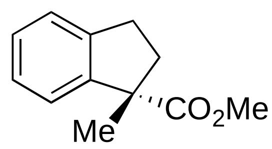
1.00
3.20



S17