Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Synthesis of 3,3-disubstituted α-tetralones by rhodium-catalysed reaction of 1-(2-haloaryl)cyclobutanols

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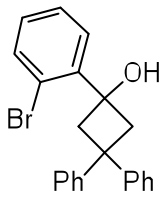
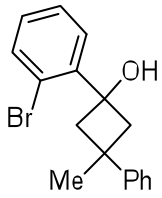
General Methods. All reactions were carried out under a nitrogen atmosphere unless otherwise noted. Infrared spectra were recorded on a Shimadzu FTIR-8400 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury vx400 (^{1}H at 400 MHz and ^{13}C at 100 MHz) spectrometer using $CHCl_3$ (^{1}H, $\delta = 7.26$) and $CDCl_3$ (^{13}C, $\delta = 77.0$) as an internal standard unless otherwise noted. High-resolution mass spectra were recorded on a Thermofisher EXACTIVE (APCI and ESI). Optical rotation was measured by a JASCO P-1020 polarimeter with a sodium lamp. HPLC analysis was performed by 4.6 x 250 mm column. Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9204. Recycling preparative HPLC was carried out with a Japan Analytical Industry LC-9110 NEXT SERIES. Flash column chromatography was performed with silica gel 60 N (Kanto). Preparative thin-layer chromatography was performed on silica gel plates with PF254 indicator (Merck).

Materials. 1,4-dioxane was distilled from sodium/benzophenone ketyl. $[Rh(OH)(cod)]_2$ was prepared according to the literature procedure.[1] The cyclobutanones were prepared by [2+2] cycloaddition of the corresponding olefins with dichloroketene and subsequent dechlorination with zinc dust in acetic acid.[2] Cyclobutanol **1b** was prepared according to the literature procedure.[3] All other commercially available chemical reagents were used as received without further purification.

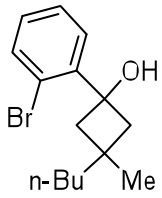


1-(2-bromophenyl)-3,3-diphenylcyclobutanol (1a). To a stirred solution of 2-bromoiodobenzene (2.97 g, 10.5 mmol) in THF (15 ml) at –78°C was added *i*-PrMgBr in THF (0.84 M, 12.5 ml, 10.5 mmol) slowly. After stirring for 2 h, a solution of 3,3-diphenylcyclobutanone (1.55 g, 7.0 mmol) in THF (5 ml) was added dropwise to the reaction mixture at –78°C. The mixture was stirred at room temperature for 11 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. Purification by flash column chromatography on silica gel (hexane:AcOEt = 5:1) afforded **1a**, which still contained only a small amount of unidentified impurities. After further purification with GPC and recrystalisation (DCM and hexane), **1a** was obtained in a pure form (861 mg, 2.27 mmol, 32%). ^{1}H NMR: $\delta = 2.66$ (s, 1H), 3.55 (s, 4H), 7.04-7.11 (m, 2H), 7.15-7.25 (m, 6H), 7.31-7.35 (m, 3H), 7.50-7.56 (m, 3H); ^{13}C NMR: $\delta = 44.3$, 48.5, 74.9, 121.7, 125.5, 125.7, 125.9, 126.5, 127.3, 127.6, 128.3, 128.5, 129.1, 134.0, 143.3, 148.9, 149.9; IR (neat): 3553, 2986, 762, 710, 696 cm^{-1}; HRMS (APCI)

Calcd for $C_{22}H_{19}BrOCl$ $(M + Cl)^-$ 413.0302, found 413.0311.

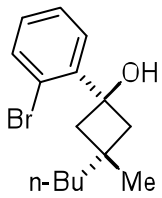


1-(2-bromophenyl)-3-methyl-3-phenylcyclobutanol (1c). To a stirred solution of 2-bromoiodobenzene (8.55 g, 30.0 mmol) in THF (10 ml) at –78 °C was added *i*-PrMgBr in THF (1.0 M, 30.0 ml, 30.0 mmol) slowly. After stirring for 2 h, a solution of 3-methyl-3-phenylcyclobutanone (3.20 g, 20.0 mmol) in THF (10 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 12 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by flash column chromatography on silica gel (hexane:AcOEt = 5:1) and GPC, **1c** was obtained (2.38 g, 7.5 mmol, 38%) as a diastereomer mixture. ^{1}H NMR: δ = 1.31 (s, 3H*), 1.77 (s, 3H), 2.83-2.87 (m, 1H* + 3H), 3.04-3.12 (m, 4H* + 2H), 7.08-7.40 (m, 7H* + 8H), 7.54-7.56 (m, 1H), 7.58-7.61 (m, 1H*), 7.63-7.65 (m, 1H*); ^{13}C NMR: δ = 31.9, 32.2*, 34.8*, 36.4, 47.3, 48.3*, 73.7*, 74.6, 121.5, 122.3*, 124.9, 125.27 125.30*, 125.4*, 127.3, 127.35*, 127.43, 127.6*, 128.2, 128.3*, 129.0, 129.2*, 133.9, 134.4*, 143.7*, 144.3, 151.1*, 152.0; IR (neat): 3422, 2951, 1026, 754, 729, 698 cm^{-1}; HRMS (APCI) Calcd for $C_{17}H_{17}BrOCl$ $(M + Cl)^-$ 351.0146, found 351.0155.

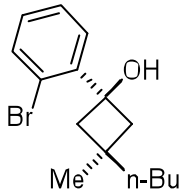


1-(2-bromophenyl)-3-*n*-butyl-3-methylcyclobutanol (1d). To a stirred solution of 2-bromoiodobenzene (2.15 g, 7.6 mmol) in THF (7 ml) at –78 °C was added *i*-PrMgBr in THF (0.90 M, 8.5 ml, 7.7 mmol) slowly. After stirring for 2 h, a solution of 3-*n*-butyl-3-methylcyclobutanone (0.87 g, 6.2 mmol) in THF (3 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 4 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by flash column chromatography on silica gel (hexane:AcOEt = 20:1) and GPC, **1d** was obtained as a diastereomer mixture. ^{1}H NMR: δ = 0.86 (t, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H*), 0.96 (s, 3H), 1.15-1.38 (m, 9H + 4H*), 1.65-1.69 (m, 2H*), 2.30-2.41 (m, 2H + 2H*), 2.49-2.54 (m, 2H + 2H*), 2.75-2.78 (m, 1H + 1H*), 7.10-7.15 (m, 1H + 1H*), 7.27-7.33 (m, 1H + 1H*), 7.36-7.38 (m, 1H), 7.43-7.45 (m, 1H*), 7.54-7.58 (m, 1H + 1H*); ^{13}C NMR: δ = 14.1, 14.2*, 23.2, 23.3*, 26.4, 26.7, 26.8*, 27.0*, 30.4*, 31.2, 42.4*, 43.4, 46.9, 47.0*, 73.9*, 74.3, 121.8, 122.1*, 127.3*, 127.35, 127.43, 127.5*, 128.89, 128.92*, 134.1, 134.2*, 144.6*, 144.8; IR (neat): 3422, 2924, 1003, 754, 727 cm^{-1}; HRMS (APCI) Calcd for $C_{15}H_{21}BrOCl$ $(M + Cl)^-$ 331.0459, found 331.0467.

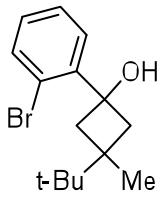
After purification by recycling preparative HPLC, *trans*-**1d** was obtained (217 mg, 0.73 mmol, 12%), and *cis*-**1d** was obtained (330 mg, 1.11 mmol, 18%).



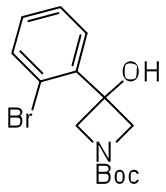
trans-**1d:** ^{1}H NMR: δ = 0.86 (t, *J* = 6.8 Hz, 3H), 1.14-1.30 (m, 6H), 1.35 (s, 3H), 2.31-2.35 (m, 2H), 2.49-2.53 (m, 2H), 2.74 (s, 1H), 7.10-7.14 (m, 1H), 7.27-7.32 (m, 1H), 7.36-7.38 (m, 1H), 7.54-7.57 (m, 1H); ^{13}C NMR: δ = 14.1, 23.2, 26.4, 26.7, 31.2, 43.4, 46.9, 74.3, 121.8, 127.36, 127.43, 128.9, 134.1, 144.8; IR (neat): 3422, 2924, 1001, 754, 727 cm^{-1}; HRMS (APCI) Calcd for $C_{15}H_{21}BrOCl$ $(M + Cl)^-$ 331.0459, found 331.0464.



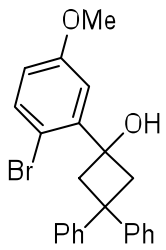
cis-**1d:** ^{1}H NMR: δ = 0.94 (t, *J* = 7.2 Hz, 3H), 0.96 (s, 3H), 1.25-1.38 (m, 4H), 1.65-1.69 (m, 2H), 2.37-2.41 (m, 2H), 2.50-2.54 (m, 2H), 2.78 (s, 1H), 7.11-7.15 (m, 1H), 7.28-7.32 (m, 1H), 7.43-7.45 (m, 1H), 7.56-7.58 (m, 1H); ^{13}C NMR: δ = 14.2, 23.3, 26.8, 27.0, 30.4, 42.4, 47.0, 73.9, 122.1, 127.3, 127.5, 128.9, 134.2, 144.6; IR (neat): 3422, 2926, 1005, 907, 754, 727 cm^{-1}; HRMS (APCI) Calcd for $C_{15}H_{21}BrOCl$ $(M + Cl)^-$ 331.0459, found 331.0471.



1-(2-bromophenyl)-3-*tert*-butyl-3-methylcyclobutanol (1e). To a stirred solution of 2-bromoiodobenzene (3.97 g, 14.0 mmol) in THF (15 ml) at –78 °C was added *i*-PrMgBr in THF (0.91 M, 15.4 ml, 14.0 mmol) slowly. After stirring for 2 h, a solution of 3-*tert*-butyl-3-methylcyclobutanone (1.64 g, 11.7 mmol) in THF (15 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 9 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by flash column chromatography on silica gel (hexane:AcOEt = 20:1) and GPC, **1e** was obtained (1.17 g, 3.94 mmol, 29%) as a diasteromer mixture. ^{1}H NMR: δ = 0.78 (s, 9H), 0.93 (s, 3H*), 0.94 (s, 9H*), 1.44 (s, 3H), 2.08-2.11 (m, 2H), 2.43-2.46 (m, 2H*), 2.60-2.63 (m, 2H*), 2.75-2.81 (m, 3H + 1H*), 7.09-7.16 (m, 1H + 1H*), 7.27-7.34 (m, 1H + 1H*), 7.37-7.40 (m, 1H), 7.55-7.58 (m, 1H + 1H*), 7.59-7.61 (m, 1H*); ^{13}C NMR: δ = 24.3, 24.4*, 25.0, 25.2*, 28.7*, 33.9, 35.3*, 37.2, 42.1, 42.8*, 71.8*, 73.0, 121.8, 122.6*, 127.2, 127.27*, 127.35, 127.5*, 128.85, 128.95*, 134.2, 134.5*, 144.2, 144.4*; IR (neat): 3447, 2961, 1159, 1020, 750, 725 cm^{-1} HRMS (APCI) Calcd for $C_{15}H_{21}BrOCl$ $(M + Cl)^-$ 331.0459, found 331.0466.

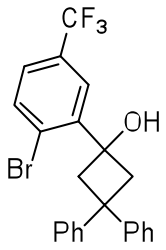


3-(2-bromophenyl)-1-*tert*-butyloxycarbonylazetidin-3-ol (1f). To a stirred solution of 2-bromoiodobenzene (843 mg, 3.0 mmol) in THF (5 ml) at –78 °C was added *i*-PrMgBr in THF (0.90 M, 3.3 ml, 3.0 mmol) slowly. After stirring for 2 h, a solution of 1-Boc-3-azetidinone (316 mg, 1.9 mmol) in THF (2 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 3 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by chromatography on silica gel (hexane:AcOEt = 2:1), **1f** was obtained (433 mg, 1.32 mmol, 66%); ^{1}H NMR: δ = 1.45 (s, 9H), 2.98 (s, 1H), 4.23-4.26 (m, 2H), 4.50-4.53 (m, 2H), 7.19-7.23 (m, 1H), 7.35-7.37 (m, 2H), 7.60-7.62 (m, 1H); ^{13}C NMR: δ = 28.4, 61.5, 73.6, 79.8, 121.9, 127.7, 127.8, 130.1, 134.2, 140.3, 156.3; IR (neat): 3350, 2976, 1678, 1433, 1111, 748 cm^{-1}; HRMS (APCI) Calcd for $C_{14}H_{18}BrNO_3Cl$ $(M + Cl)^-$ 362.0153, found 362.0163.

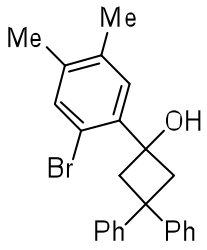


1-(2-bromo-5-methoxyphenyl)-3,3-diphenylcyclobutanol (1g). To a stirred solution of 2-iodo-4-methoxybromobenzene (1.40 g, 4.5 mmol), prepared according to the literature procedure [4], in THF (6 ml) at –78 °C was added *i*-PrMgBr in THF (0.84 M,

5.4 ml, 4.5 mmol) slowly. After stirring for 2 h, a solution of 3,3-diphenylcyclobutanone (0.67 g, 3.0 mmol) in THF (4 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 11 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by chromatography on silica gel (hexane:AcOEt = 5:1) and GPC, **1g** was obtained (404 mg, 0.99 mmol, 33%). ^{1}H NMR: δ = 2.74 (s, 1H), 3.53 (s, 4H), 3.74 (s, 3H), 6.63-6.66 (m, 1H), 6.87-6.88 (m, 1H), 7.05-7.09 (m, 1H), 7.15-7.24 (m, 5H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.49-7.51 (m, 2H); ^{13}C NMR: δ = 44.2, 48.4, 55.5, 74.7, 111.8, 114.0, 114.2, 125.5, 125.7, 125.9, 126.5, 128.3, 128.4, 134.6, 144.3, 148.9, 149.8, 158.8; IR (neat): 3545, 2939, 1464, 1292, 1228, 1026, 745, 694 cm^{-1} HRMS (APCI) Calcd for $C_{23}H_{21}BrO_2Cl$ $(M + Cl)^-$ 443.0408, found 443.0418.



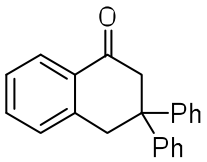
1-(2-bromo-5-trifluoromethylphenyl)-3,3-diphenylcyclobutanol (1h). To a stirred solution of 2-iodo-4-trifluoromethylbromobenzene (2.63 g, 7.5 mmol), prepared according to the literature procedure [5], in THF (10 ml) at –78 °C was added *i*-PrMgBr in THF (0.96 M, 7.8 ml, 7.5 mmol) slowly. After stirring for 2 h, a solution of 3,3-diphenylcyclobutanone (1.11 g, 5.0 mmol) in THF (5 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 13 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by flash column chromatography on silica gel (hexane:AcOEt = 5:1) and GPC, **1h** was obtained (327 mg, 0.73 mmol, 15%); ^{1}H NMR: δ = 2.67 (br, 1H), 3.58 (s, 4H), 7.07-7.12 (m, 1H), 7.19-7.27 (m, 5H), 7.34-7.39 (m, 3H), 7.52-7.57 (m, 3H), 7.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR = 44.3, 48.2, 74.7, 123.6 (q, *J* = 270.1 Hz), 124.7 (q, *J* = 3.7 Hz), 125.68, 125.71, 125.74, 125.8, 126.3, 128.4, 128.5, 129.6 (q, *J* = 32.9 Hz), 134.6, 144.1, 148.5, 149.2; IR (neat): 3566, 3024, 1329, 1167, 1124, 1082, 694 cm^{-1}; HRMS (APCI) Calcd for $C_{23}H_{18}BrF_3OCl$ $(M + Cl)^-$ 481.0176, found 481.0183.



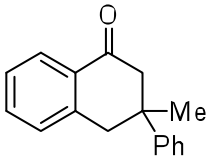
1-(2-bromo-4,5-dimethylphenyl)-3,3-diphenylcyclobutanol (1i). To a stirred solution of 4,5-dibromo-*o*-xylene (950 mg, 3.6 mmol) in THF (6 ml) at –78 °C was added *i*-PrMgCl in THF (0.82 M, 4.4 ml, 3.6 mmol) slowly. After stirring for 3 h, a solution of 3,3-diphenylcyclobutanone (665 mg, 3.0 mmol) in THF (4 ml) was added dropwise to the reaction mixture at –78 °C. The mixture was stirred at room temperature for 17 h, and saturated NH_4Cl aq was added. The mixture was extracted with Et_2O, washed with water and brine, dried over Na_2SO_4, and evaporated. After purification by chromatography on silica gel (hexane:AcOEt = 5:1) and GPC, **1i** was obtained (82 mg, 0.20 mmol, 7%); ^{1}H NMR: δ = 2.19 (s, 3H), 2.21 (s, 3H), 2.63 (br, 1H), 3.56 (s, 4H), 7.07-7.11 (m, 2H), 7.18-7.28 (m, 5H), 7.34-7.39 (m, 3H), 7.54-7.57 (m, 2H); ^{13}C NMR: δ = 18.9, 19.2, 44.3, 48.6, 74.6, 118.0, 125.4, 125.6, 125.9, 126.5, 128.2, 128.4, 128.8, 134.6, 135.6, 137.8, 140.6, 148.9, 150.1; IR (neat): 3566, 2980, 2359, 1447, 1265, 1088, 733, 700 cm^{-1}; HRMS (APCI) Calcd for $C_{24}H_{23}BrOCl$ $(M + Cl)^-$ 441.0615, found 441.0627.

4b. A mixture containing $[Rh(OH)(cod)]_2$ (2.2 mg, 5.0 μmol, 5.0 mol%), DPPB (4.7 mg, 11 μmol, 11 mol%), K_3PO_4 (23.3 mg, 0.11 mmol), PhBr (18.8 mg, 0.12 mmol) and **1b** (30.0 mg, 0.10 mmol) in 1,4-dioxane (0.50 ml) was stirred at 120 °C for 24 h. After being cooled to room temperature, the reaction mixture was diluted with water and extracted with AcOEt (three times). The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$ and evaporated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 10:1) to afford **4b**.

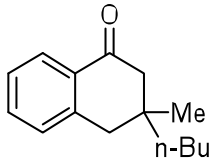
A typical procedure for the rhodium-catalysed reaction of **1a**: A mixture containing $[Rh(OH)(cod)]_2$ (2.3 mg, 5.0 μmol, 5.0 mol %), DPPB (4.7 mg, 11 μmol, 11 mol %), K_3PO_4 (23.3 mg, 0.11 mmol) and **1a** (37.9 mg, 0.10 mmol) in 1,4-dioxane (0.50 ml) was stirred at 120 °C for 15 h. After being cooled to room temperature, the reaction mixture was diluted with H_2O and extracted with AcOEt (three times). The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$ and evaporated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 10:1) to afford **2a** (28.7 mg, 0.096 mmol, 96%)



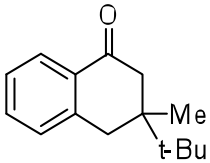
2a: ^{1}H NMR: δ = 3.46 (s, 2H), 3.78 (s, 2H), 7.11-7.16 (m, 2H), 7.19-7.33 (m, 10H), 7.45-7.49 (m, 1H), 7.91-7.94 (m, 1H); ^{13}C NMR: δ = 42.3, 48.6, 51.0, 126.4, 126.80, 126.83, 126.9, 128.5, 128.9, 132.4, 134.1, 142.1, 145.9, 197.0; IR (neat): 3024, 1676, 758, 694 cm^{-1}; HRMS (APCI) Calcd for $C_{22}H_{19}O$ (M^+ + H) 299.1430, found 299.1421.



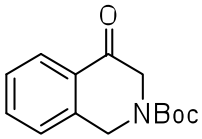
2c: ^{1}H NMR: δ = 1.42 (s, 3H), 2.87 (d, *J* = 16.4 Hz, 1H), 3.16-3.25 (m, 2H), 3.48 (d, *J* = 16.4 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.26-7.30 (m, 5H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.46-7.50 (m, 1H); ^{13}C NMR: δ = 29.5, 40.7, 42.8, 51.3, 125.5, 126.3, 126.7, 126.8, 128.5, 129.1, 131.9, 133.9, 142.3, 146.4, 197.7; IR (neat): 2920, 1678, 1285, 1028, 768, 698 cm^{-1}; HRMS (APCI) Calcd for $C_{17}H_{17}O$ (M^+ + H) 237.1274, found 237.1268.



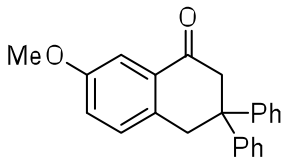
2d: ^{1}H NMR: δ = 0.86-0.89 (m, 3H), 1.01 (s, 3H), 1.23-1.38 (m, 6H), 2.44-2.49 (m, 1H), 2.52-2.56 (m, 1H), 2.77 (d, *J* = 16.4 Hz, 1H), 2.91 (d, *J* = 16.4 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.46-7.50 (m, 1H), 7.99-8.01 (m, 1H); ^{13}C NMR: δ = 14.0, 23.3, 24.9, 25.9, 36.3, 40.9, 41.9, 51.1, 126.5, 126.6, 129.3, 132.0, 133.7, 142.6, 198.7; IR (neat): 2928, 1682, 1288, 760 cm^{-1}; HRMS (APCI) Calcd for $C_{15}H_{21}O$ (M^+ + H) 217.1587, found 217.1582.



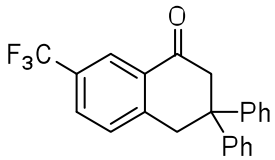
2e: ^{1}H NMR: δ = 0.92 (s, 3H), 0.99 (s, 9H), 2.51-2.71 (m, 3H), 3.19 (d, *J* = 16.4 Hz, 1H), 7.22-7.30 (m, 2H), 7.45-7.49 (m, 1H), 7.97-8.00 (m, 1H); ^{13}C NMR: δ = 18.5, 25.2, 35.7, 36.5, 41.0, 46.1, 126.3, 126.4, 129.7, 131.8, 133.6, 143.1, 199.7; IR (neat): 2964, 1682, 1296, 756 cm^{-1}; HRMS (APCI) Calcd for $C_{15}H_{21}O$ (M^+ + H) 217.1587, found 217.1582.



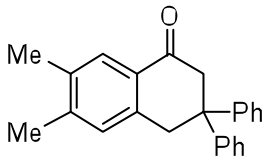
2f: ^{1}H NMR: δ = 1.47 (s, 9H), 4.33 (s, 2H), 4.76 (s, 2H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR: δ = 28.3, 44.9, 53.2, 81.0, 126.2, 127.2, 127.6, 127.8, 128.9, 130.4, 134.2, 140.8, 154.2, 192.9; IR (neat): 2980, 1736, 1693, 1418, 1367, 1229, 1159, 1123, 1045, 895, 764, 731 cm^{-1}; HRMS (ESI) Calcd for $C_{14}H_{18}NO_3$ (M^+ + H) 248.1281, found 248.1278.



2g: ^{1}H NMR: δ = 3.44 (s, 2H), 3.72 (s, 2H), 3.78 (s, 3H), 7.04-7.07 (m, 1H), 7.12-7.16 (m, 2H), 7.20-7.25 (m, 9H), 7.407-7.414 (m, 1H); ^{13}C NMR: δ = 41.5, 48.8, 50.8, 55.4, 108.9, 122.3, 126.3, 126.9, 128.5, 130.0, 133.2, 134.6, 146.0, 158.4, 197.0; IR (neat): 2924, 1678, 1495, 1285, 1032, 756, 694 cm^{-1}; HRMS (APCI) Calcd for $C_{23}H_{21}O_2$ (M^+ + H) 329.1536, found 329.1528.



2h: ^{1}H NMR: δ = 3.49 (s, 2H), 3.84 (s, 2H), 7.14-7.27 (m, 10H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.69-7.72 (m, 1H), 8.20 (s, 1H); ^{13}C NMR: δ = 42.1, 48.5, 50.9, 123.6 (q, *J* = 270.9 Hz), 124.0 (q, *J* = 3.7 Hz), 126.6, 126.8, 128.6, 129.7, 130.2 (q, *J* = 3.7 Hz), 132.7, 145.3, 145.6, 195.7; IR (neat): 2924, 1688, 1331, 1256, 1121, 696 cm^{-1}; HRMS (APCI) Calcd for $C_{23}H_{18}F_3O$ (M^+ + H) 367.1304, found 367.1298.



2i: ^{1}H NMR: δ = 2.21 (s, 3H), 2.27 (s, 3H), 3.40 (s, 2H), 3.70 (s, 2H), 7.07 (s, 1H), 7.11-7.15 (m, 2H), 7.20-7.24 (m, 8H), 7.68 (s, 1H); ^{13}C NMR: δ = 19.3, 20.2, 41.7, 48.7, 50.9, 126.2, 126.9, 127.5, 128.4, 129.9, 130.3, 135.3, 139.7, 143.9, 146.2, 197.1; IR (neat): 2918, 1670, 700 cm^{-1}; HRMS (APCI) Calcd for $C_{24}H_{23}O$ (M^+ + H) 327.1743, found 327.1735.

Asymmetric synthesis of (+)-2d. A mixture containing $[Rh(OH)(cod)]_2$ (2.2 mg, 5.0 μmol, 5.0 mol%), (*R*)-tol-BINAP (7.4 mg, 11 μmol, 11 mol%), K_3PO_4 (23.3 mg, 0.11 mmol), and *cis*-**1d** (29.7 mg, 0.10 mmol) in 1,4-dioxane (0.50 ml) was stirred at 120 °C for 24 h. After being cooled to room temperature, the reaction mixture was diluted with water and extracted with AcOEt (three times). The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$ and evaporated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 10:1) to afford (+)-**2d** (15.7 mg, 0.072 mmol, 72%). The enantiomeric excess was determined to be 87% by chiral HPLC [Daicel CHIRALPAK® AS-H column, hexane:*i*-PrOH = 98:2, 0.4 ml/min, retention times: t_1 = 6.7 min (major); t_2 = 7.0 min (minor)].

Transformation of (+)-2d to (+)-5d. The CH_2Cl_2 (1.0 ml), propane-1,3-dithiol (40.0 μL, 0.40 mmol) and boron trifluoride diethyl etherate (48.0 μl, 0.38 mmol) were added to the (-)-**2d** (31.5 mg, 0.14 mmol) in the schlenk and the mixture was stirred for 14 h at 23°C. The reaction mixture was quenched with 2 M

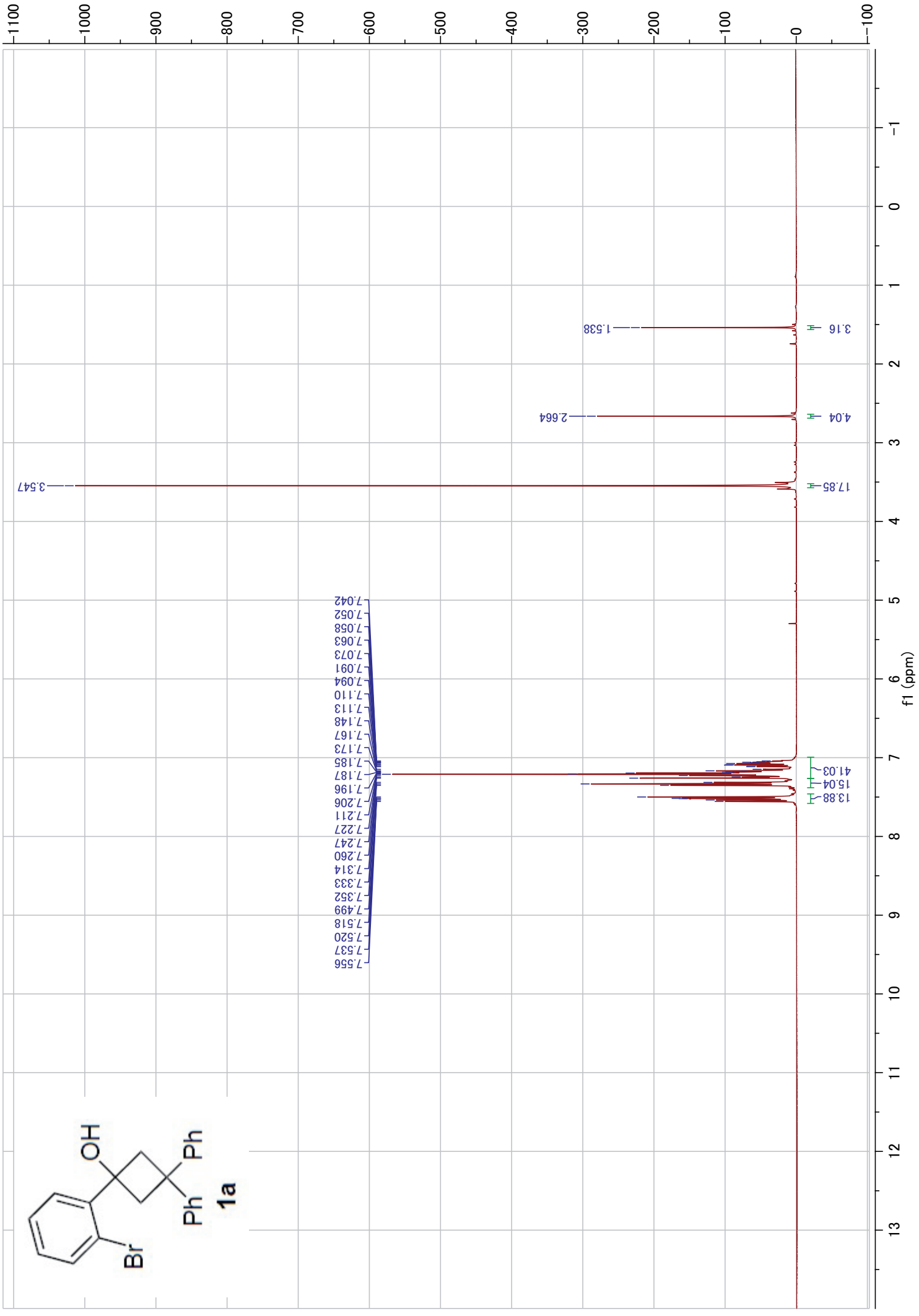
aq. NaOH and extracted with Et_2O. The organic layer was washed with water and brine, dried over $MgSO_4$ and evaporated. The residue was purified preparative thin-layer chromatography of silica gel (hexane:AcOEt = 20:1) to give dithiane. A solution of this dithiane in EtOH (1.0 mL) was added to a suspension of Raney-Ni (1 g) in MeOH (1.00 mL) and stirred for 10 h at room temperature. The mixture was filtered over celite. Hexane was added and the organic layer washed with water and brine, and evaporated. The residue was purified preparative thin-layer chromatography of silica gel (hexane only) to give (+)-**5d**. (14.7 mg, 0.073 mmol, 52 % over 2 steps). $[\alpha]_D$ = +1.2.

Asymmetric synthesis of (–)-2d. A mixture containing $[Rh(OH)(cod)]_2$ (2.2 mg, 5.0 μmol, 5.0 mol%), (*R*)-tol-BINAP (7.4 mg, 11 μmol, 11 mol%), K_3PO_4 (23.3 mg, 0.11 mmol), and *trans*-**1d** (29.7 mg, 0.10 mmol) in 1,4-dioxane (0.50 ml) was stirred at 120 °C for 24 h. After being cooled to room temperature, the reaction mixture was diluted with water and extracted with AcOEt (three times). The combined organic phase was washed with H_2O and brine, dried over $MgSO_4$ and evaporated. The residue was purified by preparative thin-layer chromatography of silica gel (hexane:AcOEt = 10:1) to afford (-)-**2d** (15.0 mg, 0.069 mmol, 69%). The enantiomeric excess was determined to be 81% by chiral HPLC [Daicel CHIRALPAK® AS-H column, hexane:*i*-PrOH = 98:2, 0.4 ml/min, retention times: t_1 = 7.4 min (minor); t_2 = 7.0 min (major)].

Transformation of (–)-2d to (–)-5d. The CH_2Cl_2 (1.0 ml), propane-1,3-dithiol (40.0 μL, 0.40 mmol) and boron trifluoride diethyl etherate (48.0 μl, 0.38 mmol) were added to the (–)-**2d** (30.0 mg, 0.13 mmol) in the shrenk and the mixture was stirred for 14 h at 23°C. The reaction mixture was quenched with 2 M aq. NaOH and extracted with Et_2O. The organic layer was washed with water and brine, dried over $MgSO_4$ and evaporated. The residue was purified preparative thin-layer chromatography of silica gel (hexane:AcOEt = 20:1) to give dithiane. A solution of this dithiane in EtOH (1.0 mL) was added to a suspension of Raney-Ni (1 g) in EtOH (1.0 mL) and stirred for 10 h at room temperature. The mixture was filtered over celite. Hexane was added and the organic layer washed with water and brine, and evaporated. The residue was purified preparative thin-layer chromatography of silica gel (hexane only) to give (–)-**5d**. (11.8 mg, 0.059 mmol, 45 % over 2 steps). $[\alpha]_D$ = -1.3.

References

(1) Uson, R; Oro, L.A.; Cabeza, J. A. *Inorg, Synth*. **1985**, *23*, 129.
(2) Hyatt, J. A; Raynolds, P. W. *Org. React*. **1994**, *45*, 159.
(3) Seiser, T; Roth, O. A; Cramer, N. *Angew. Chem., Int. Ed*. **2009**, *48*, 6320.
(4) Bhunia, S; Wang, K. C.; Liu, R. S. *Angew. Chem., Int. Ed.* **2008**, *47*, 5063.
(5) PCT Int. Appl., 2006008558, 26 Jan 2006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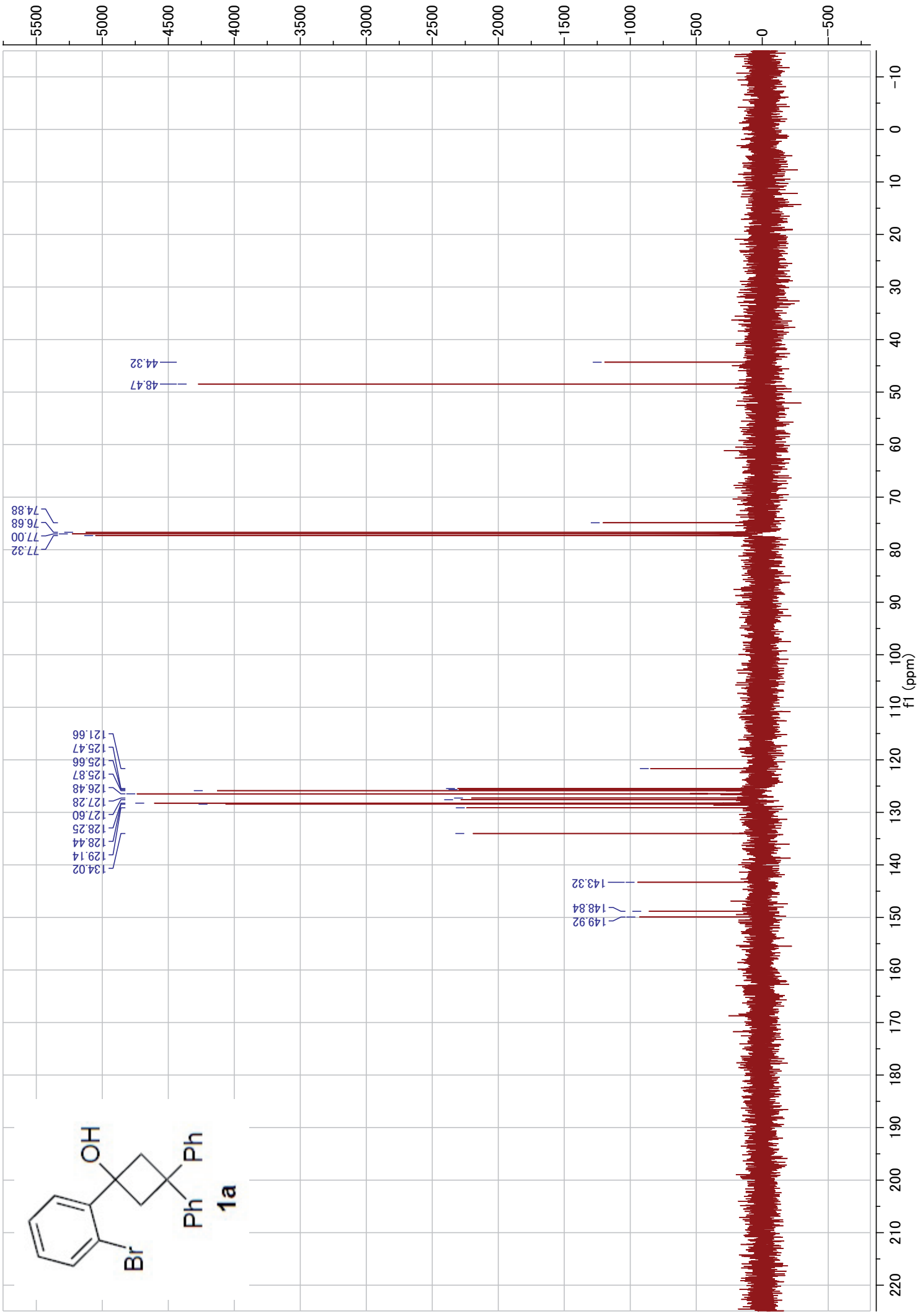
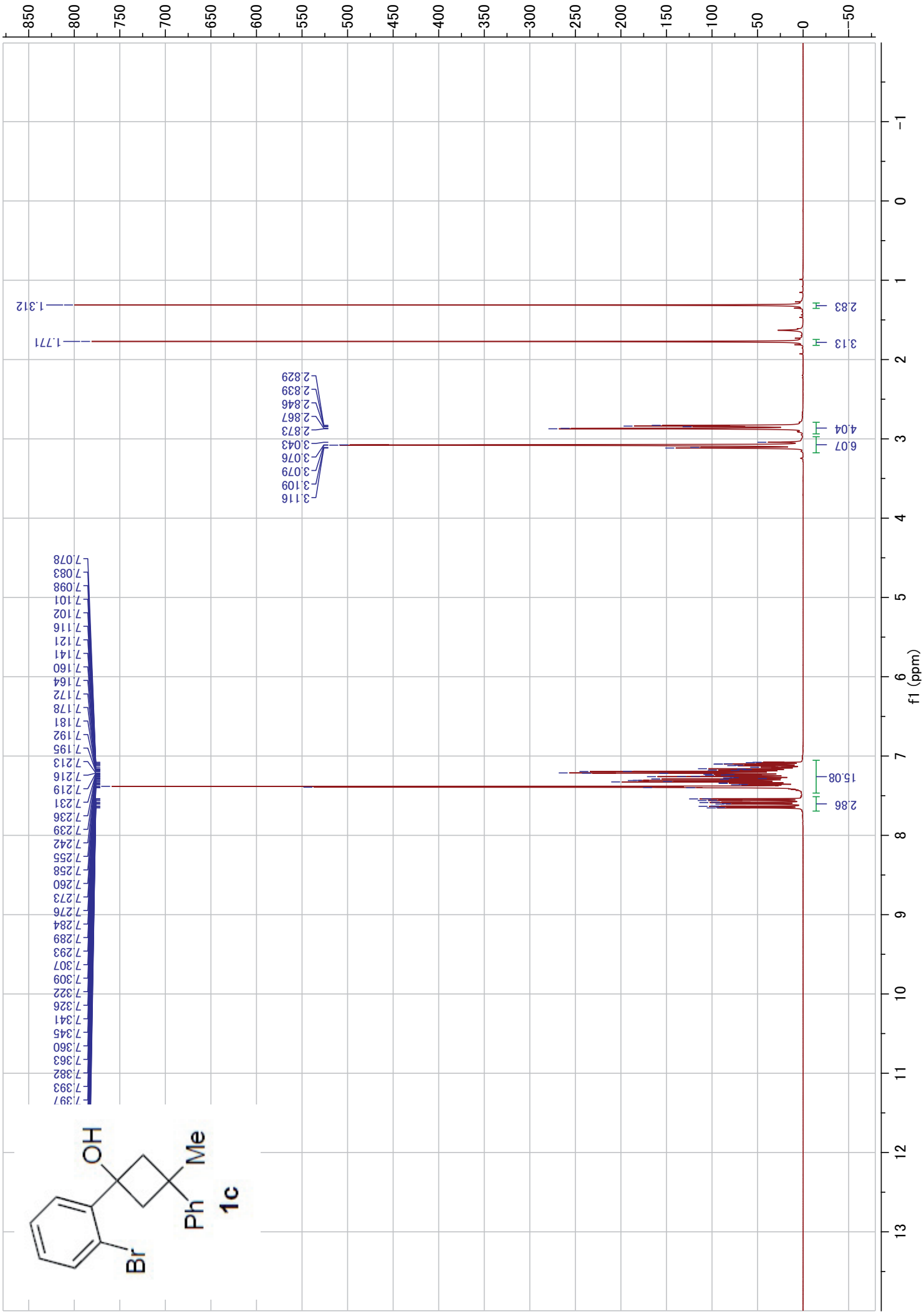
Ph
Br
1a

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7.121
7.141
7.160
7.164
7.172
7.178
7.181
7.192
7.195
7.213
7.216
7.219
7.231
7.236
7.239
7.242
7.255
7.258
7.260
7.273
7.276
7.284
7.289
7.293
7.307
7.309
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7.382
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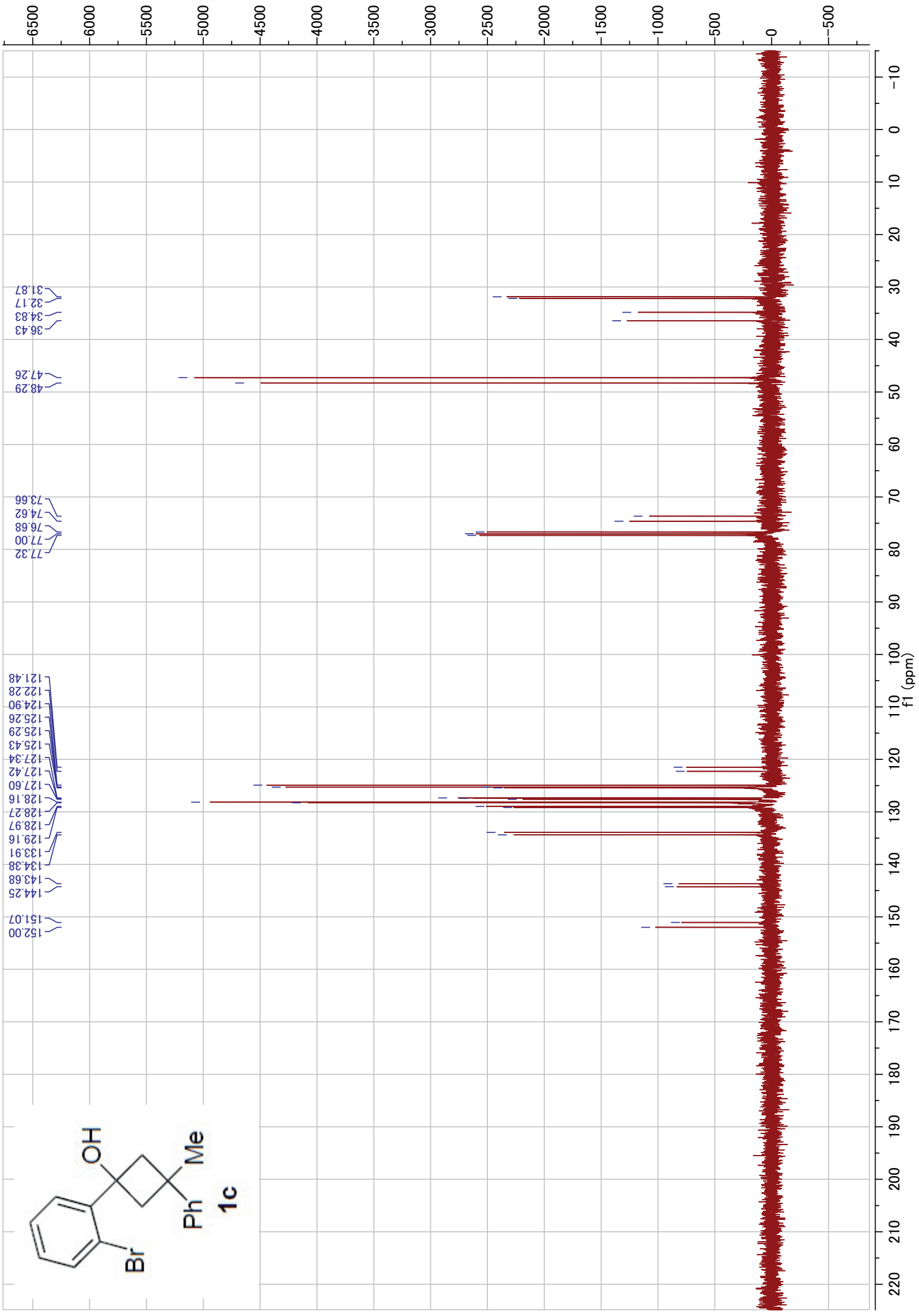
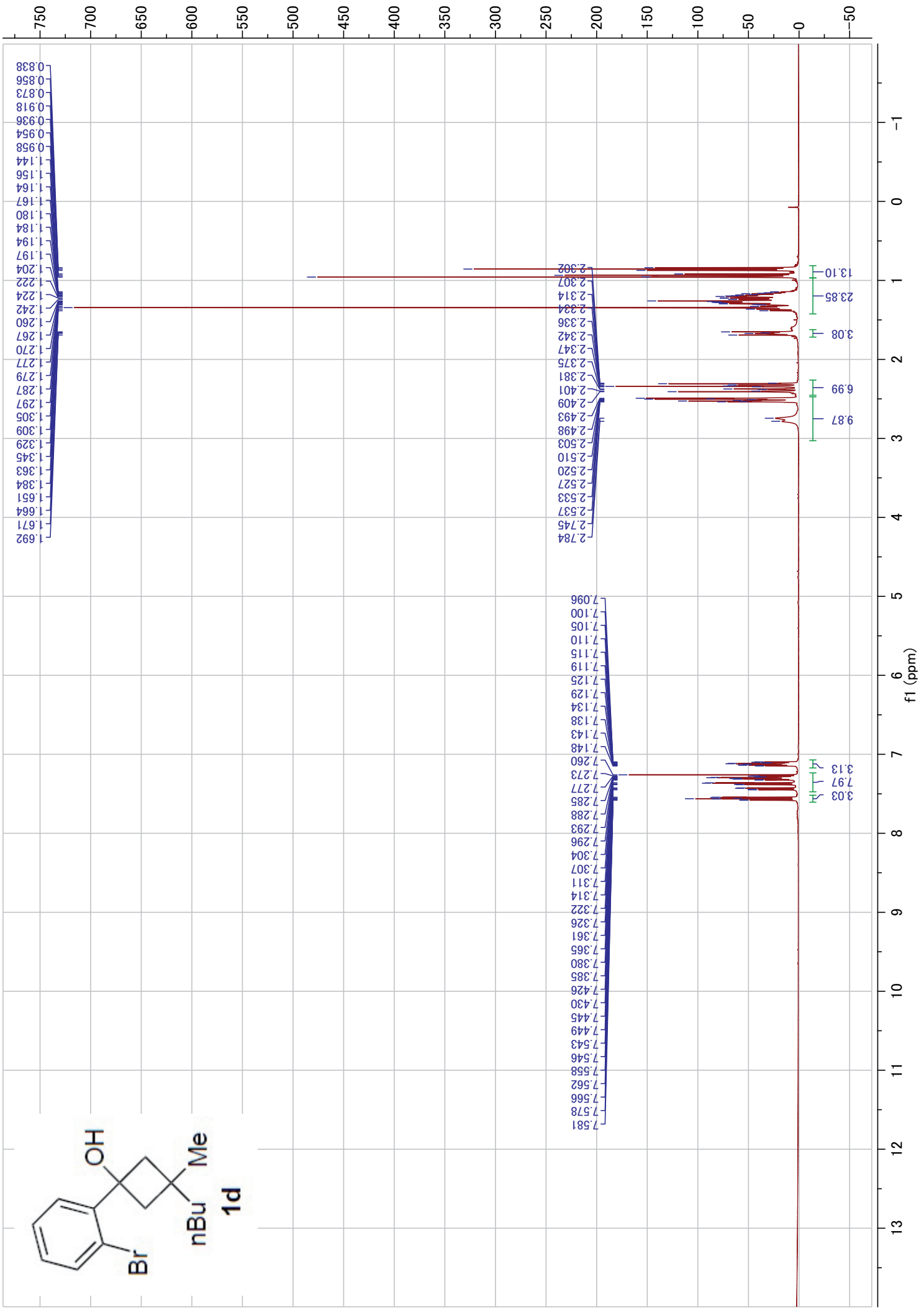
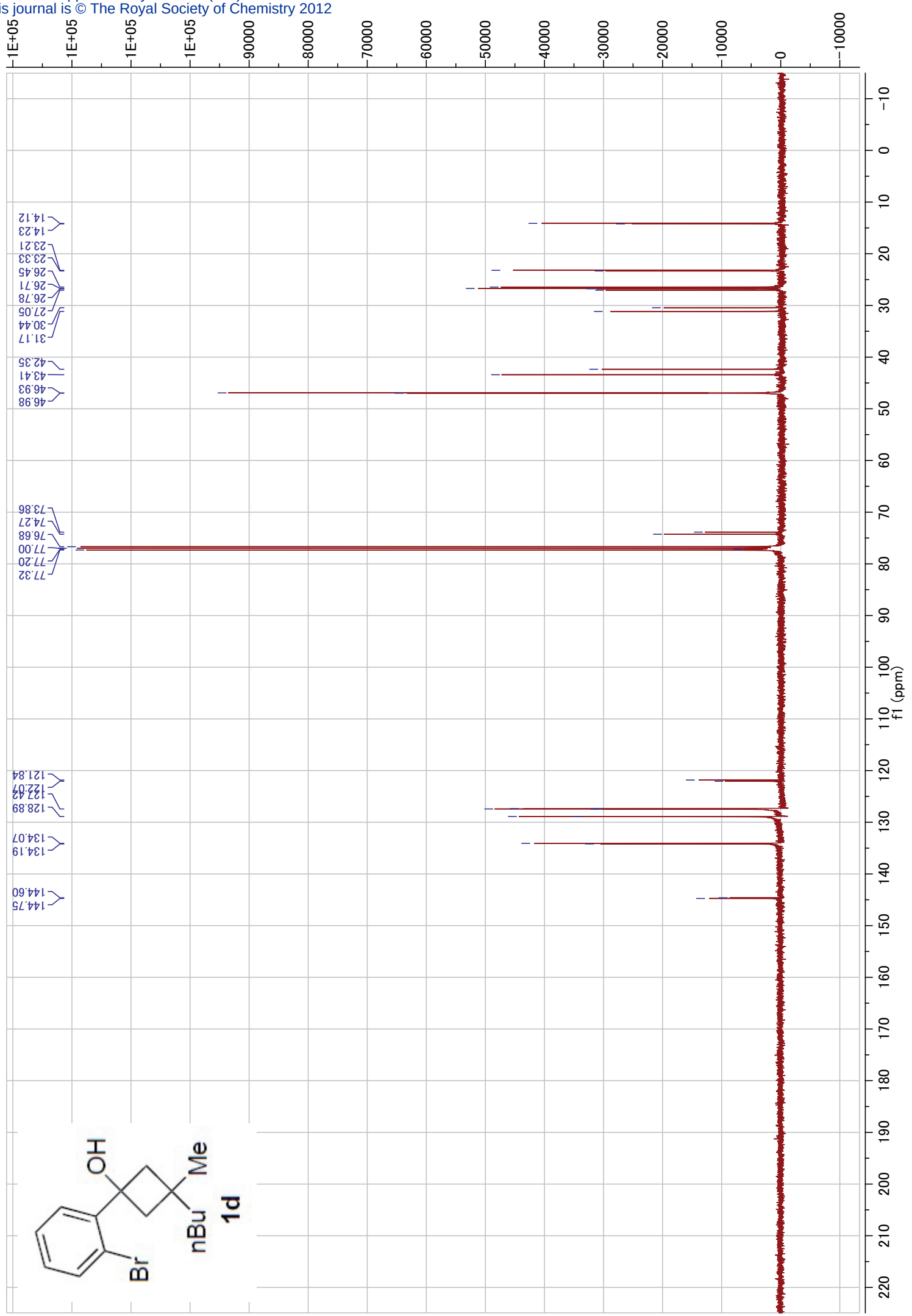
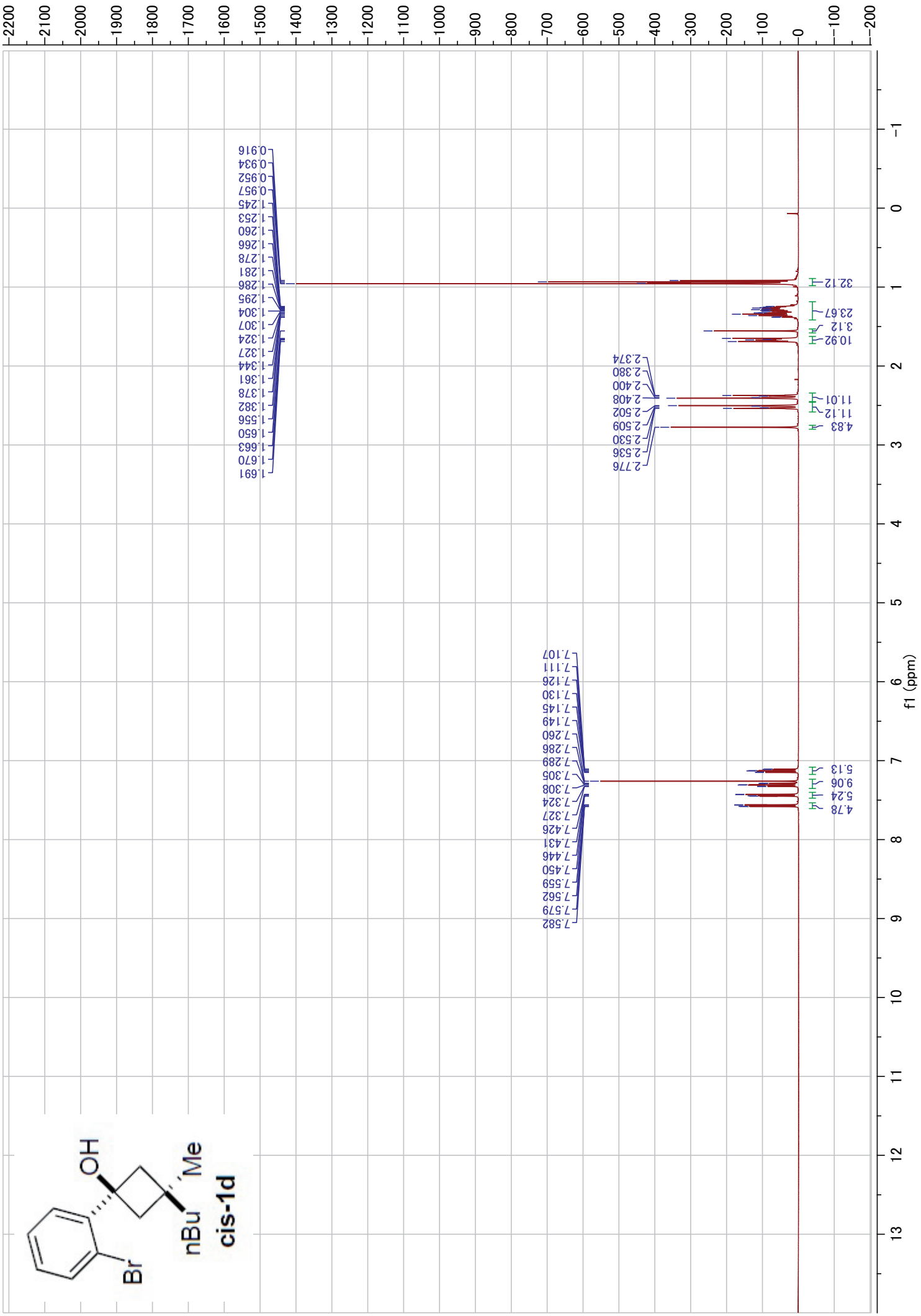
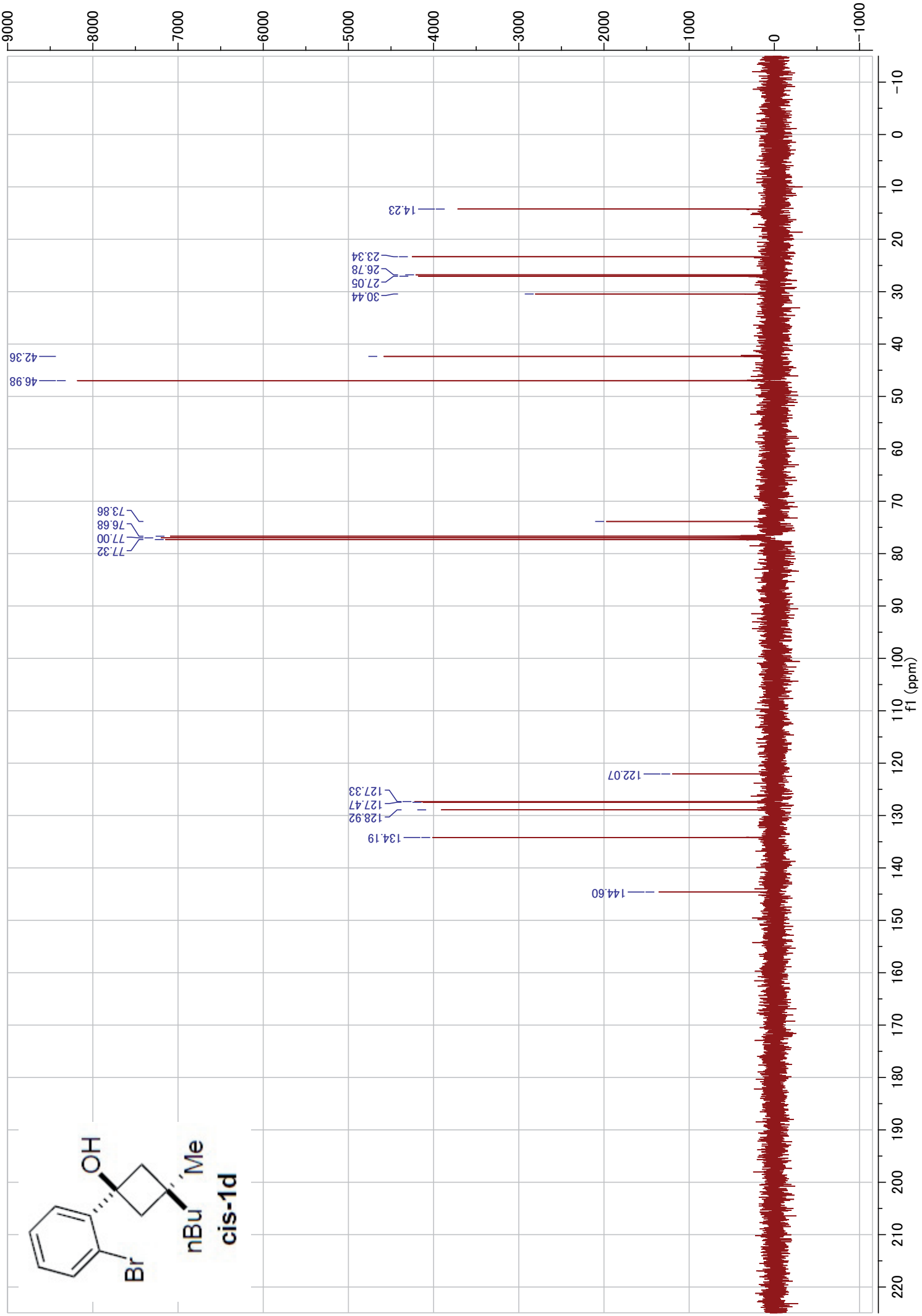
3.13
4.04
6.07
15.08
2.86
f1 (ppm)
OH
Me
Ph
Br
1c







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127.47
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f1 (ppm)
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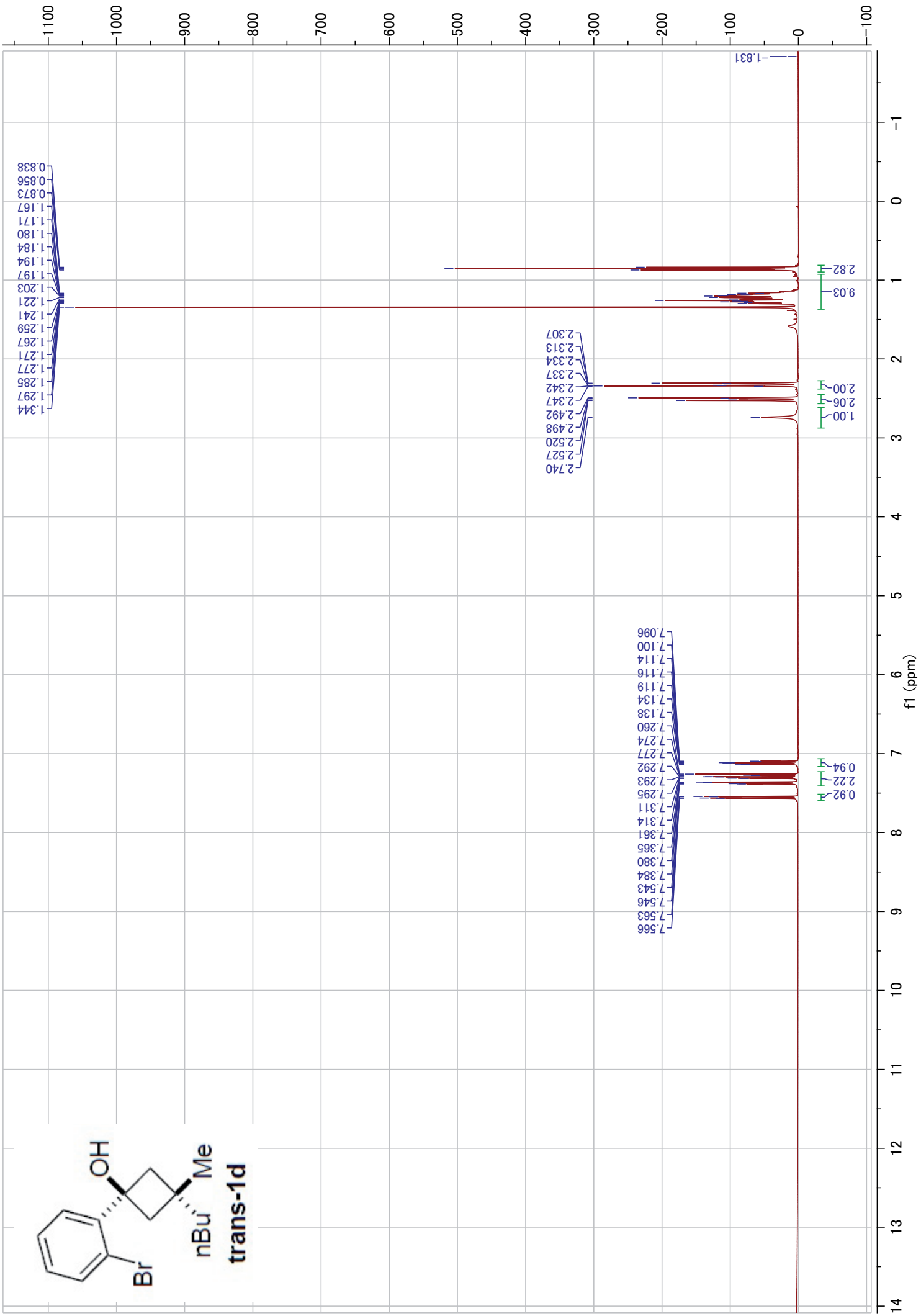
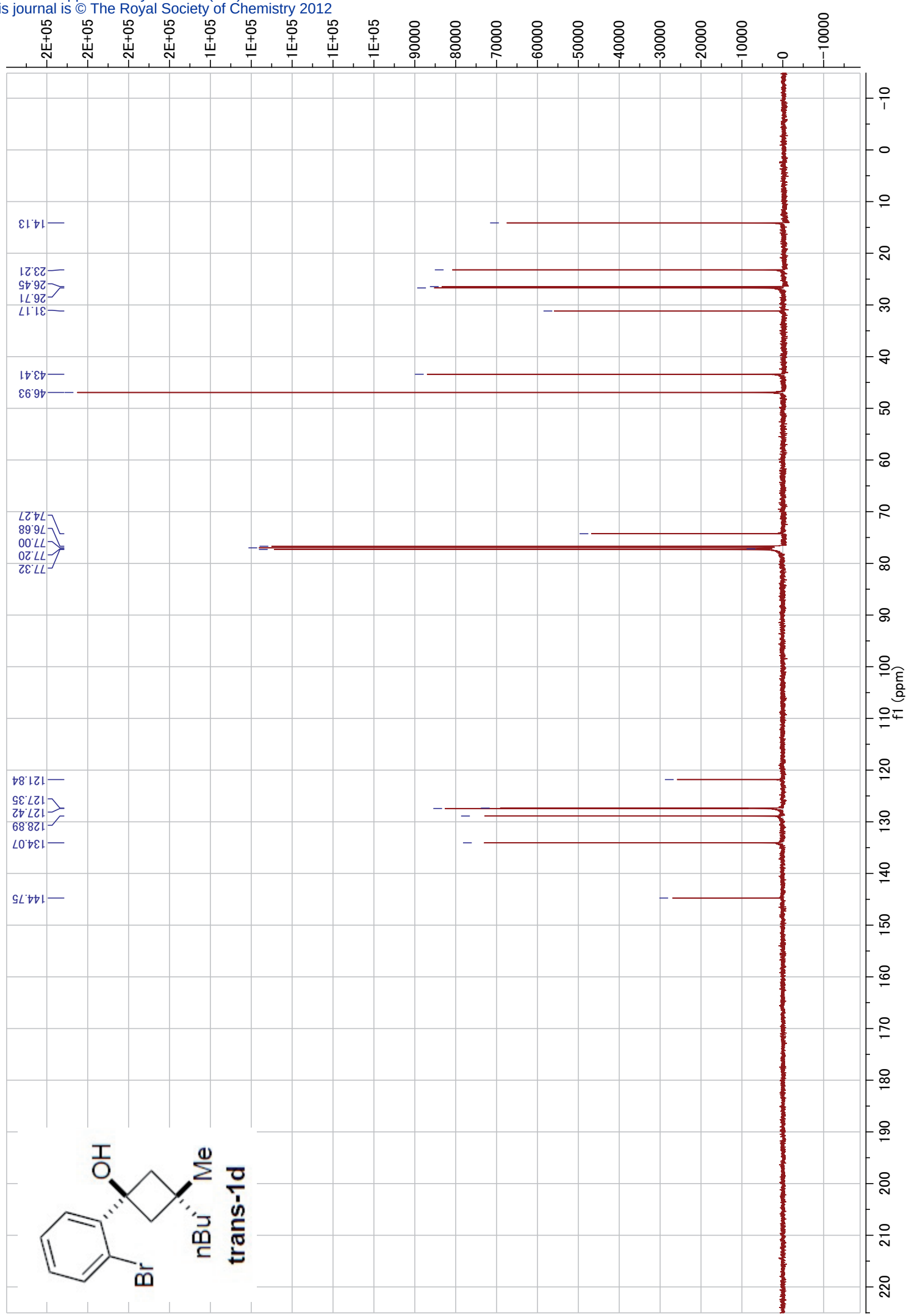
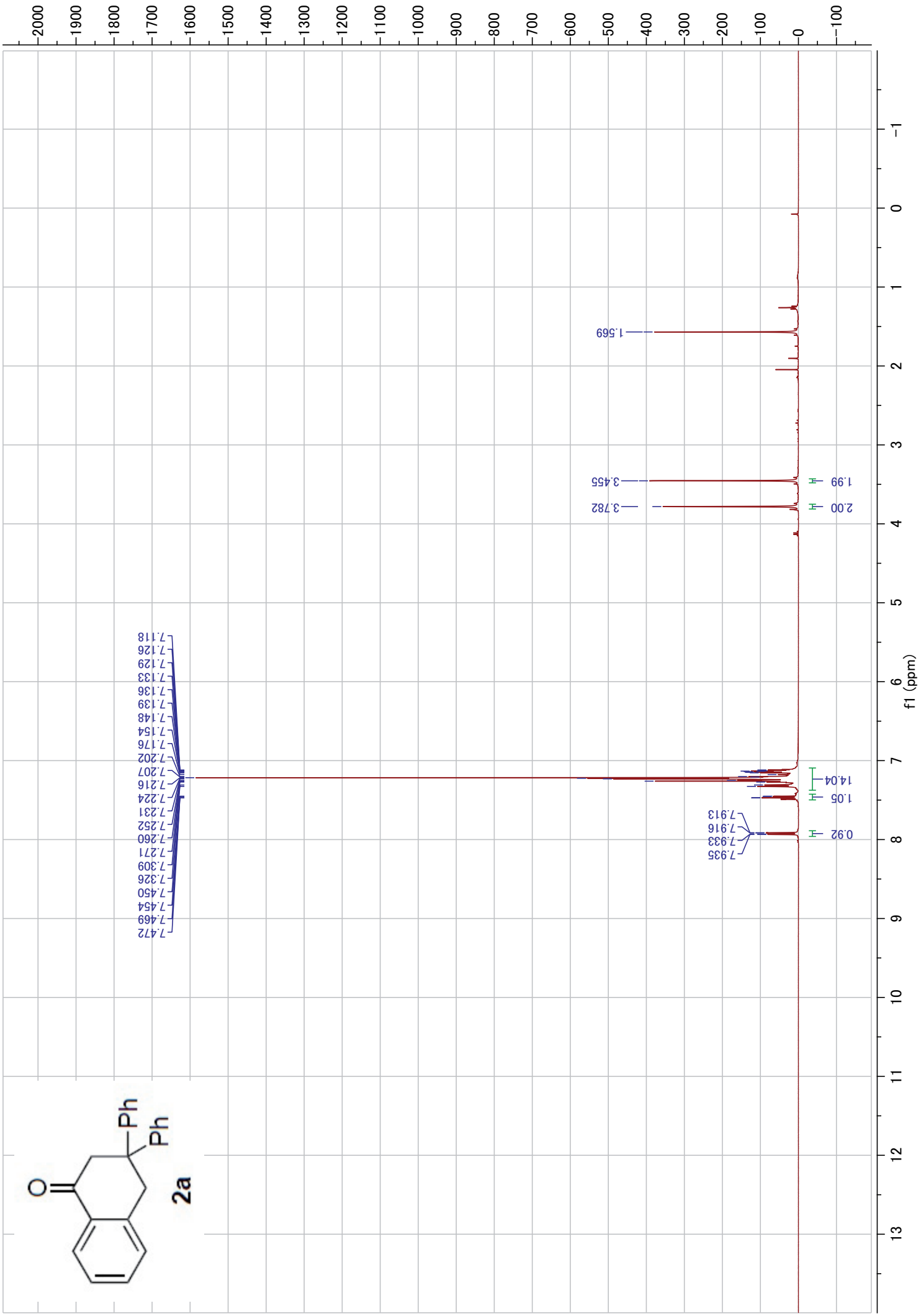
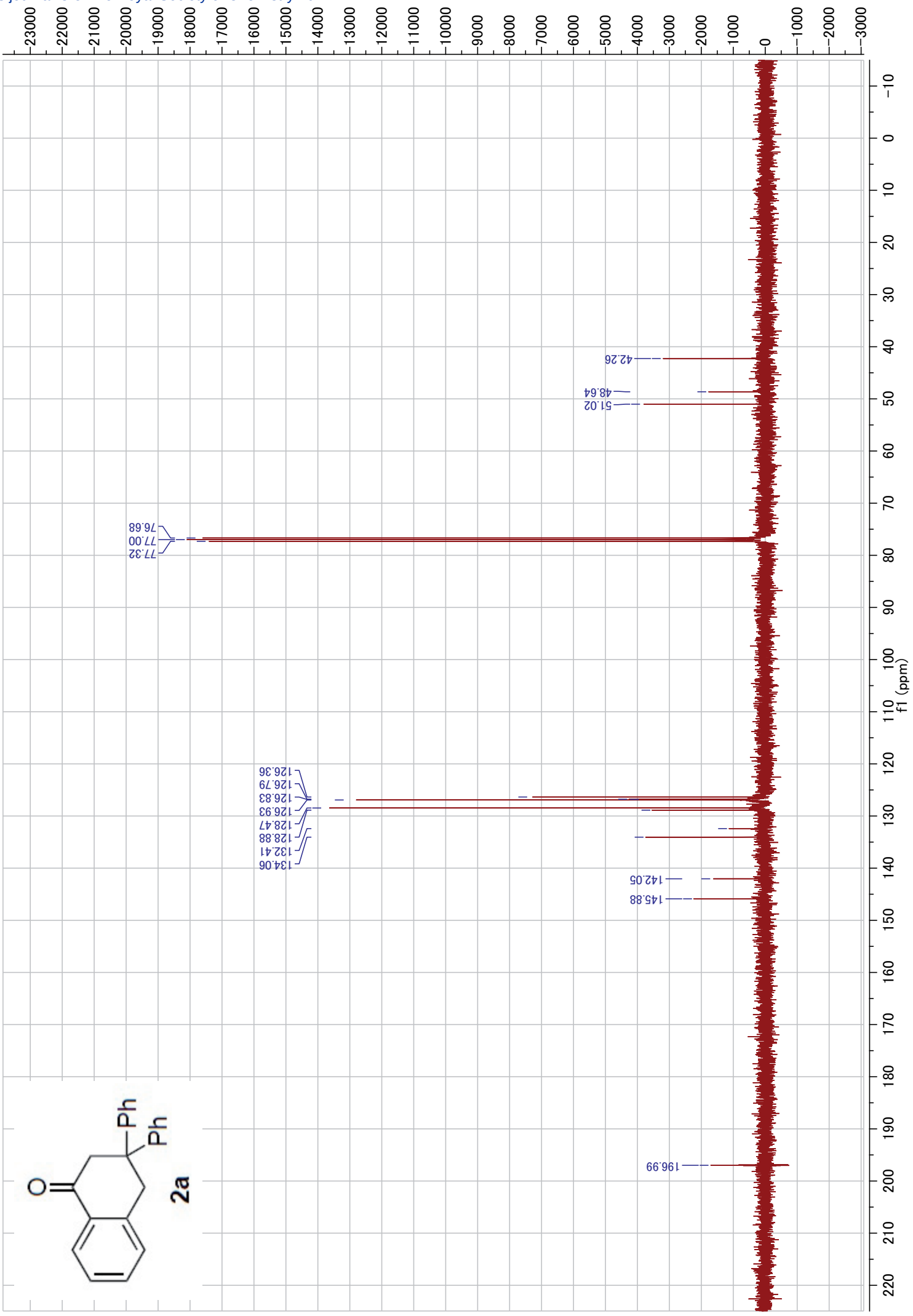
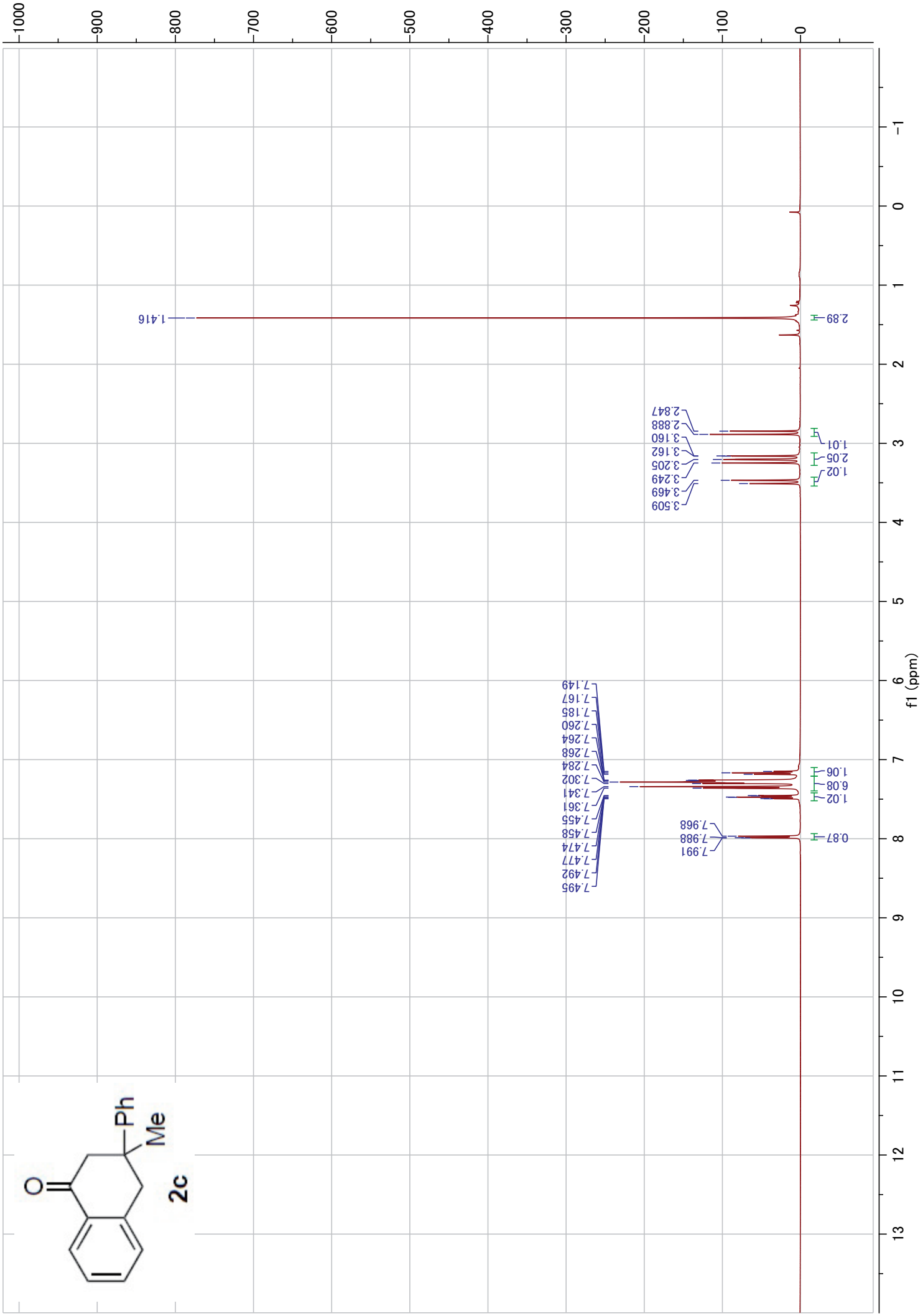
Me
nBu
Br
cis-1d







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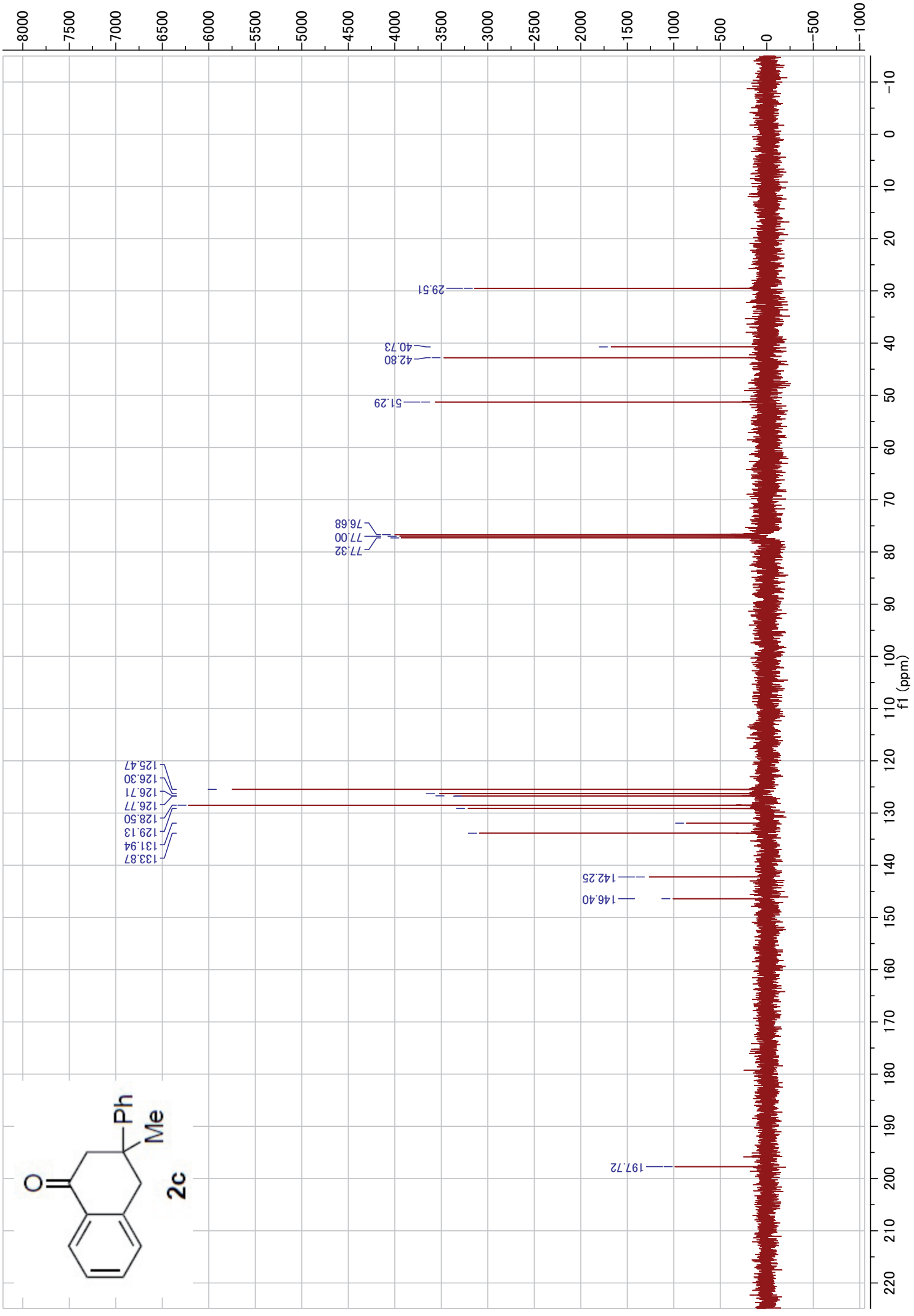
Ph
Me
O
2c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Me
O
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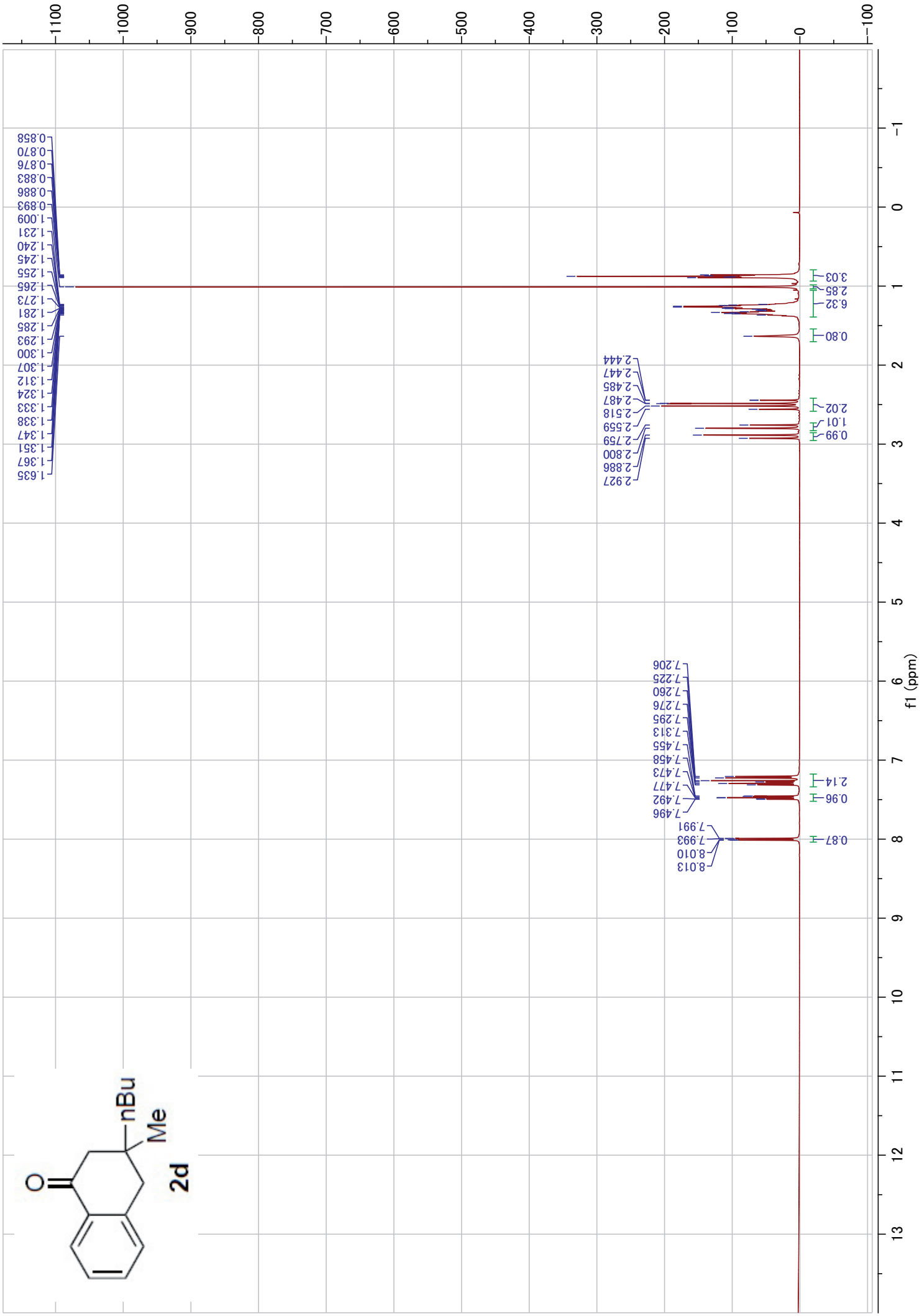

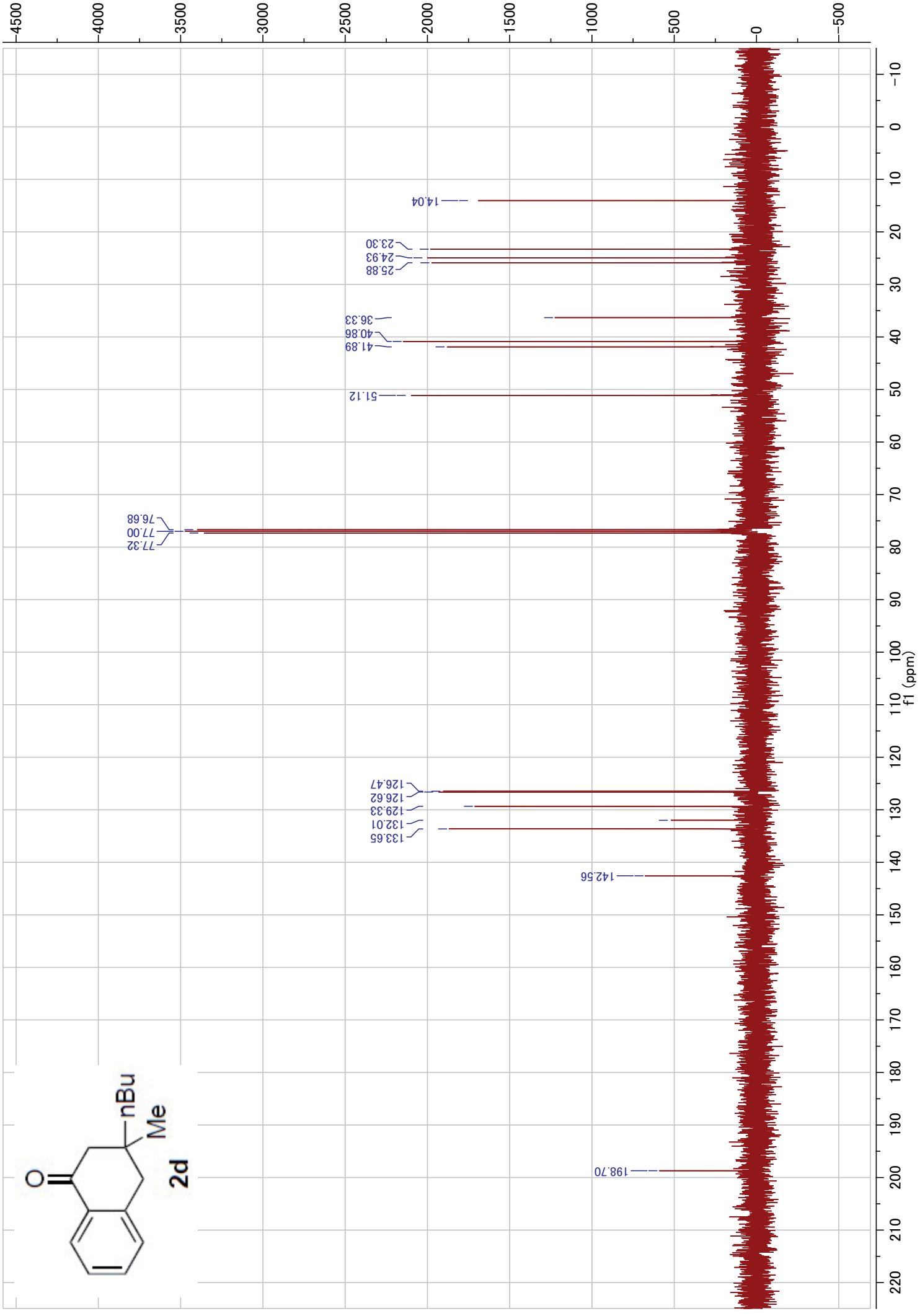

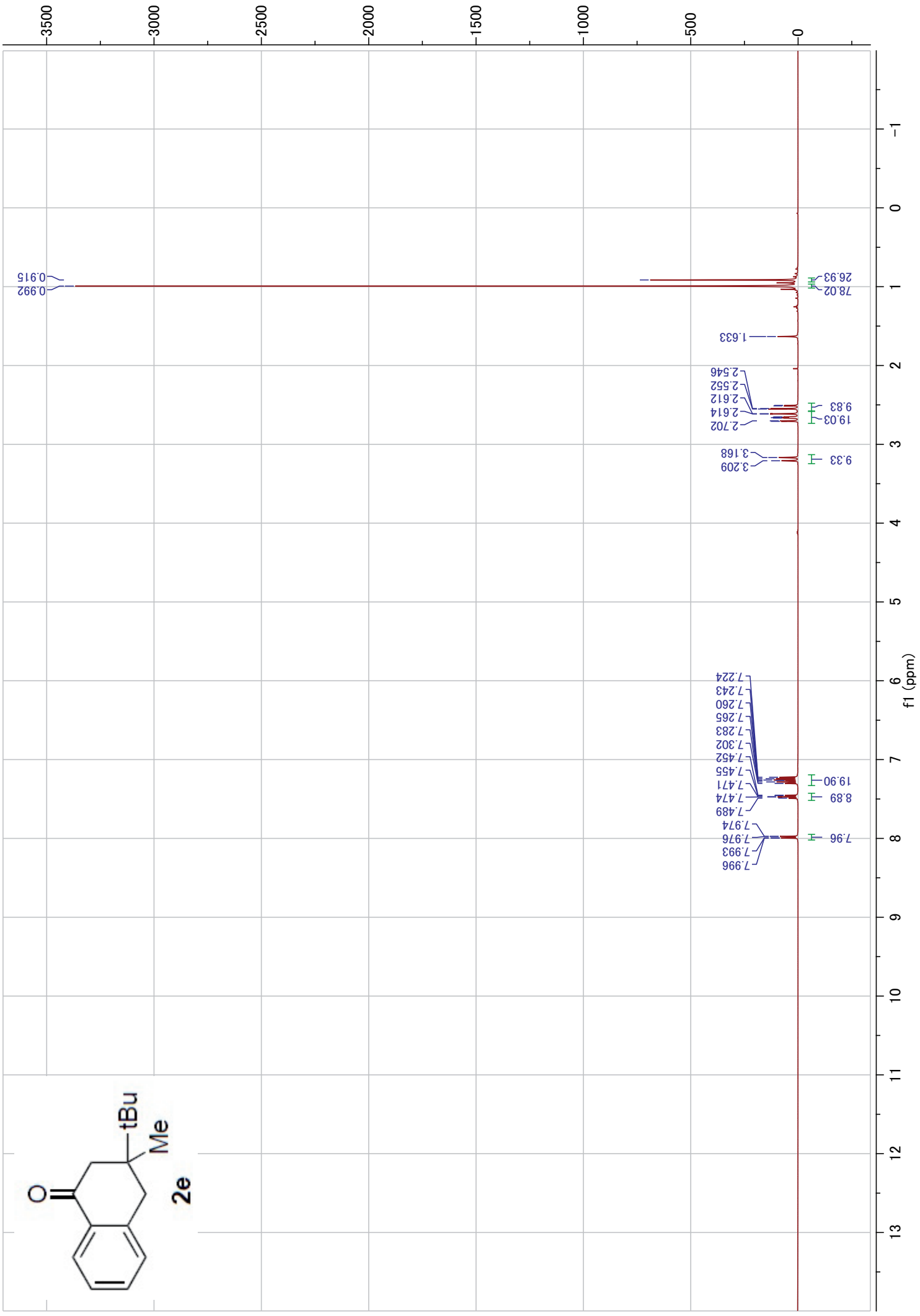

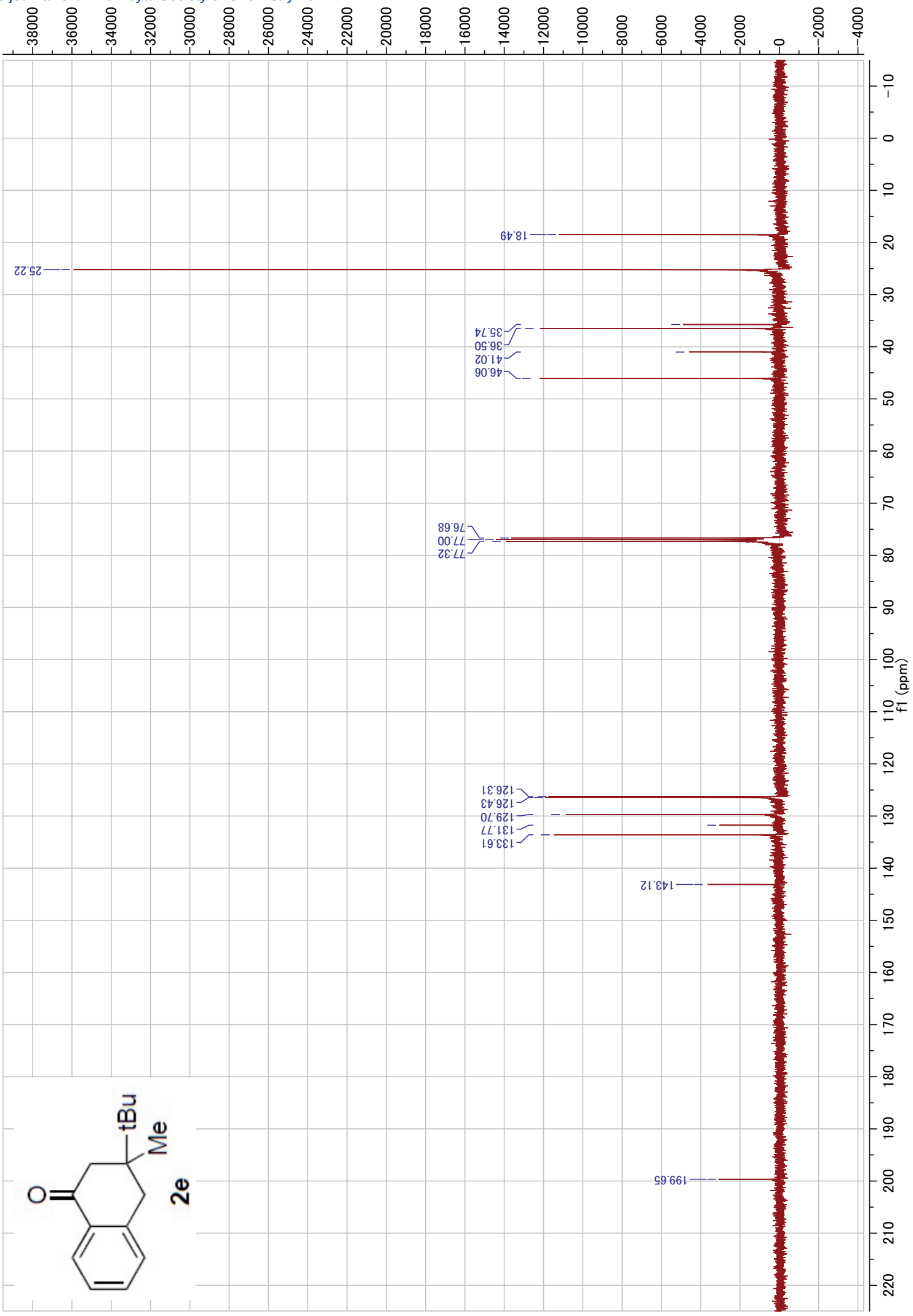

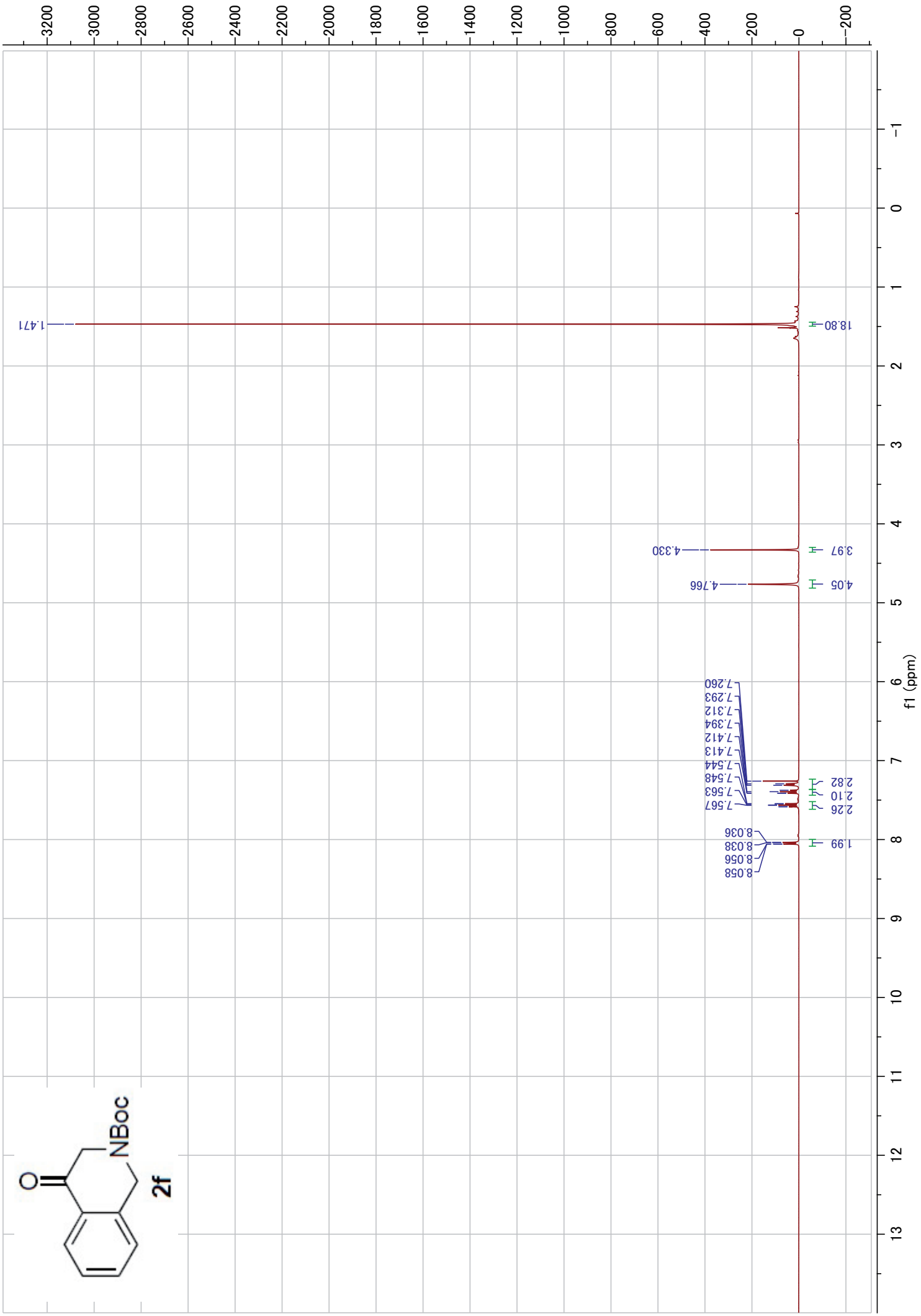
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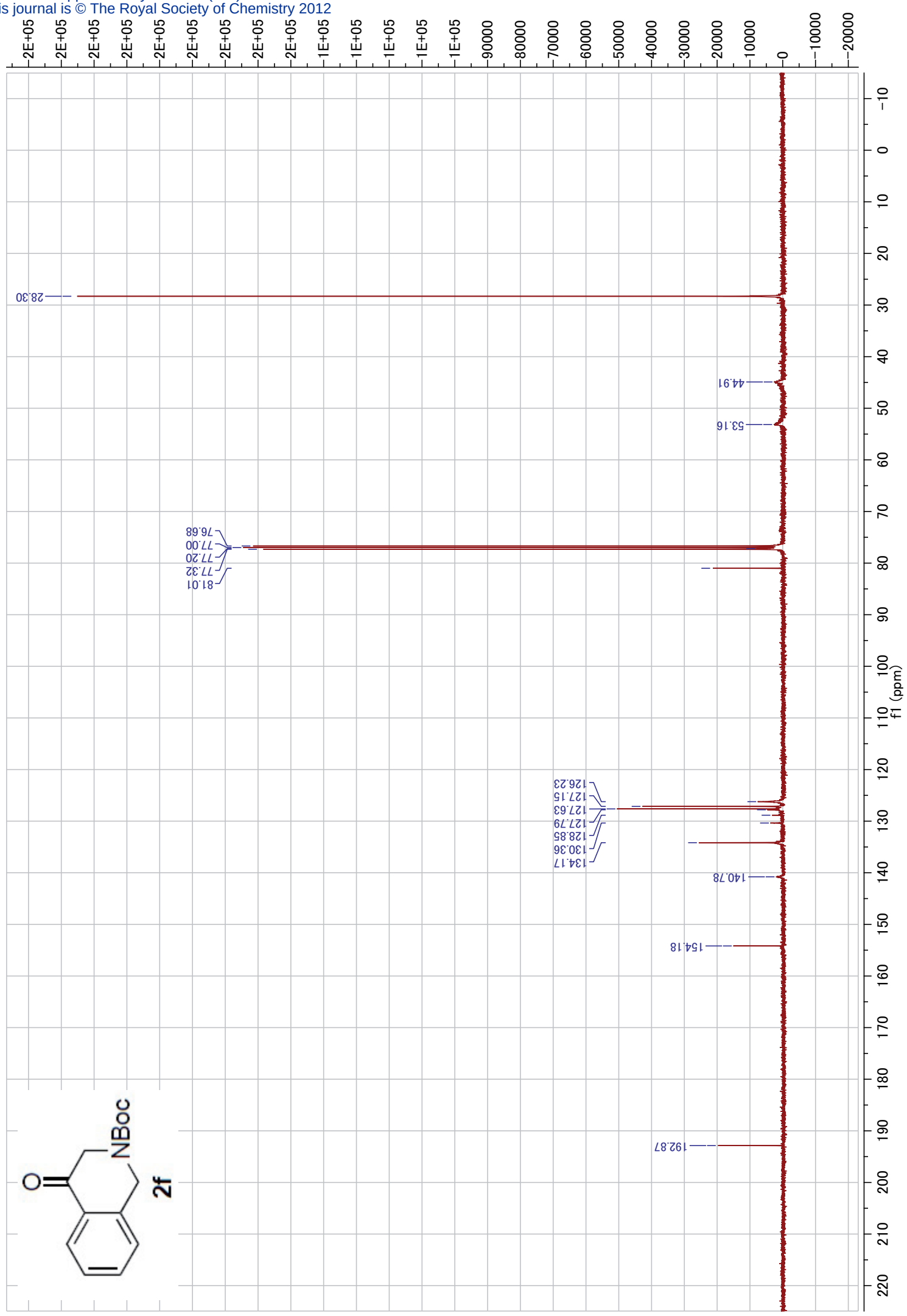
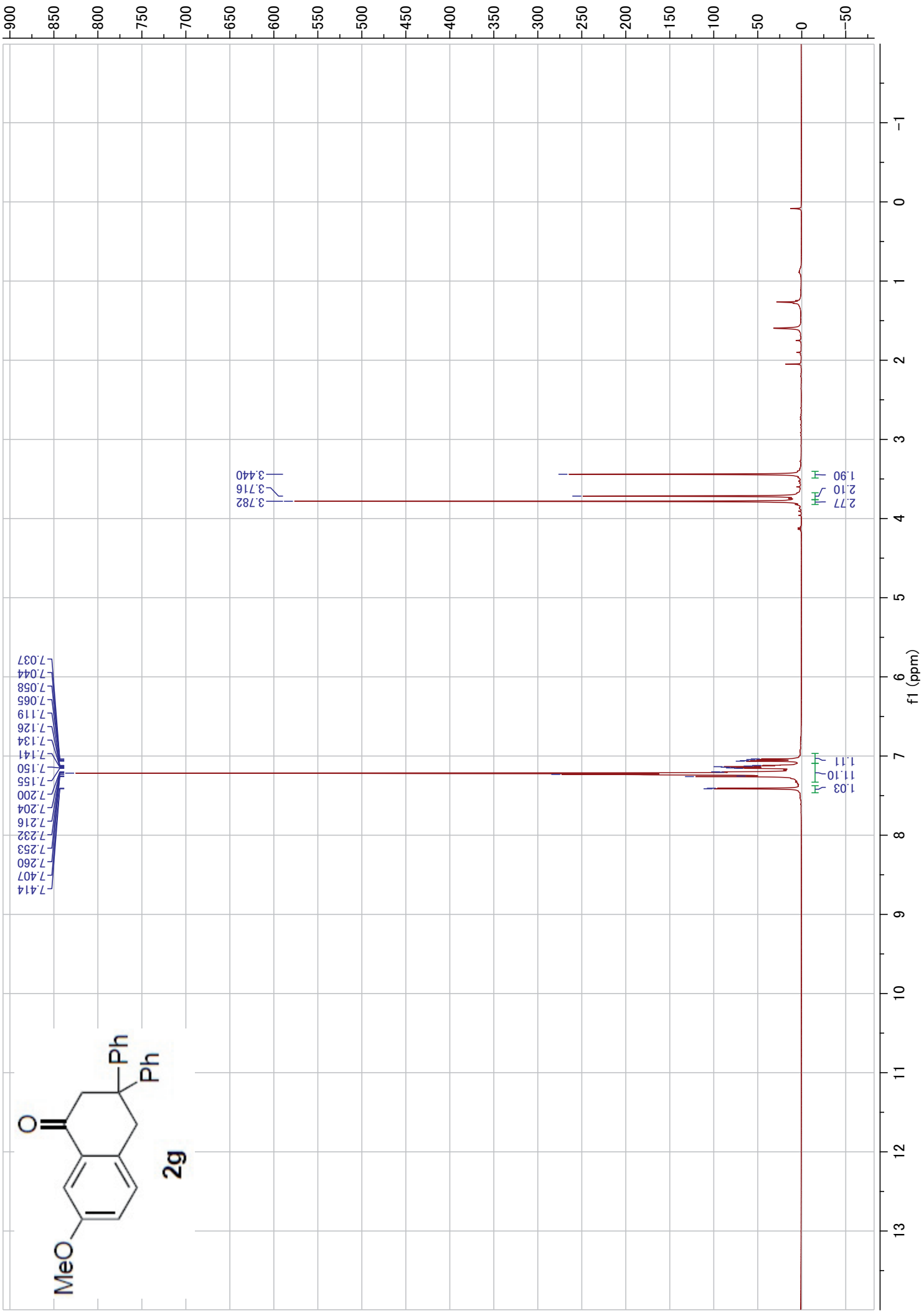
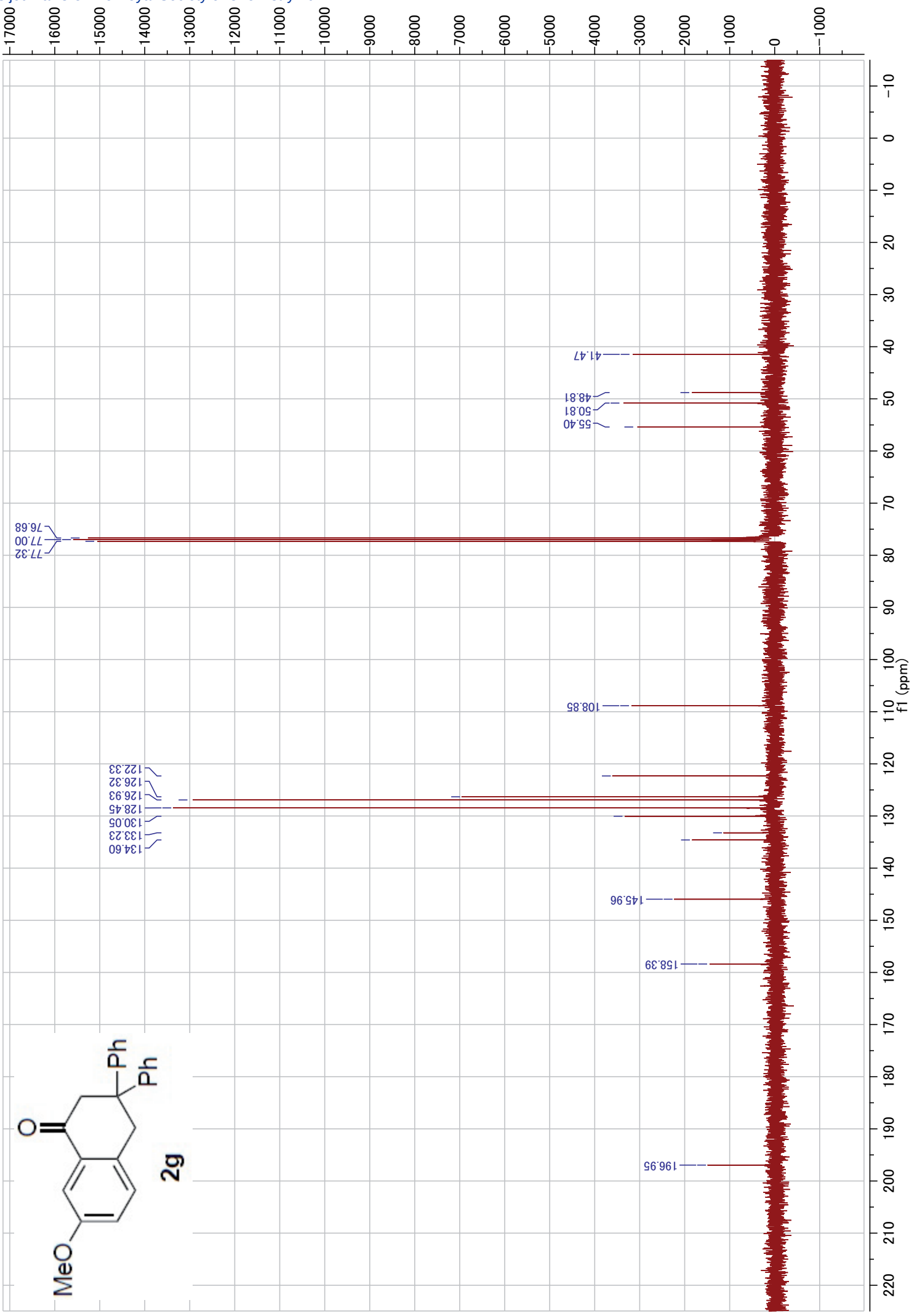
2f
f1 (ppm)



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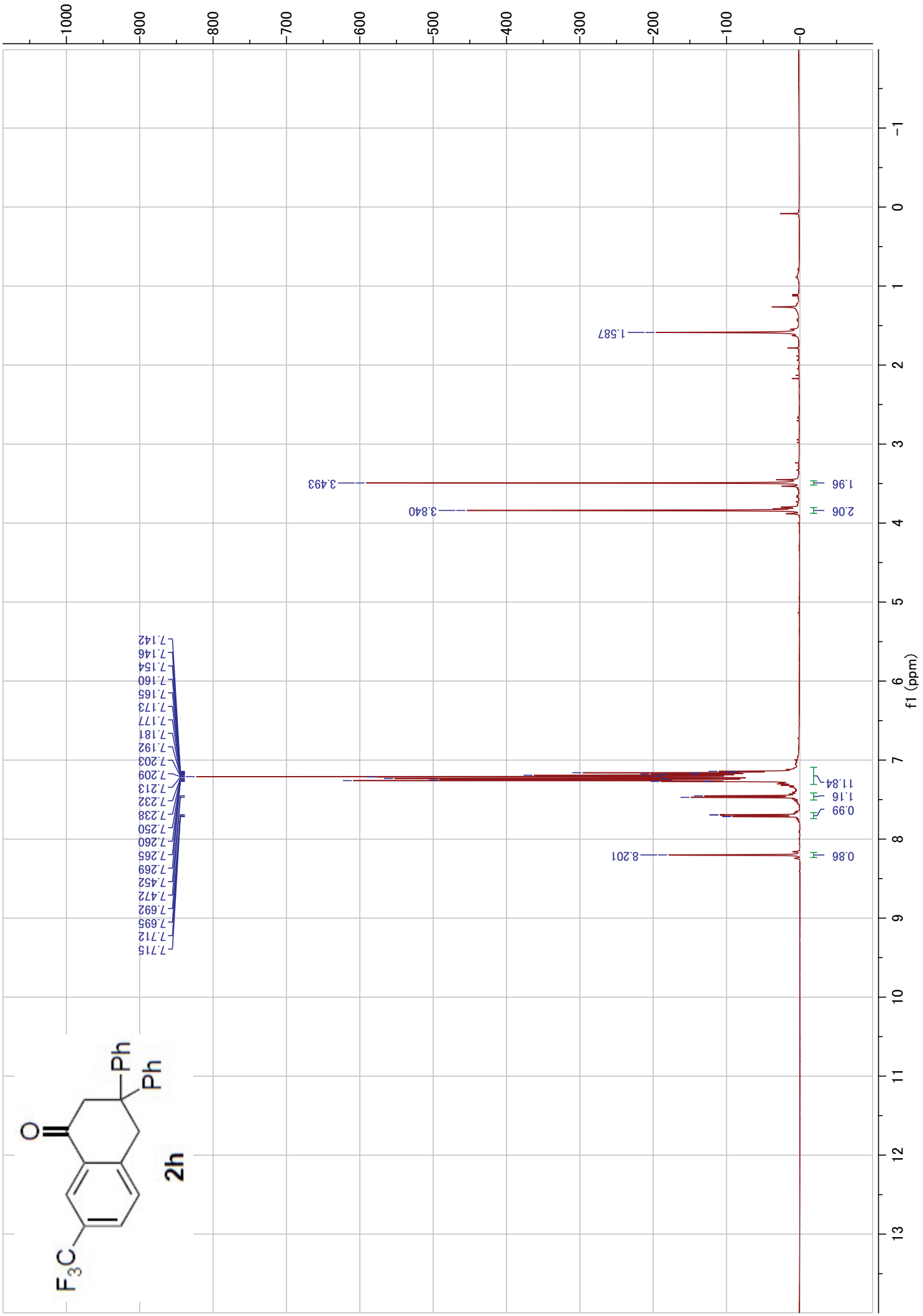
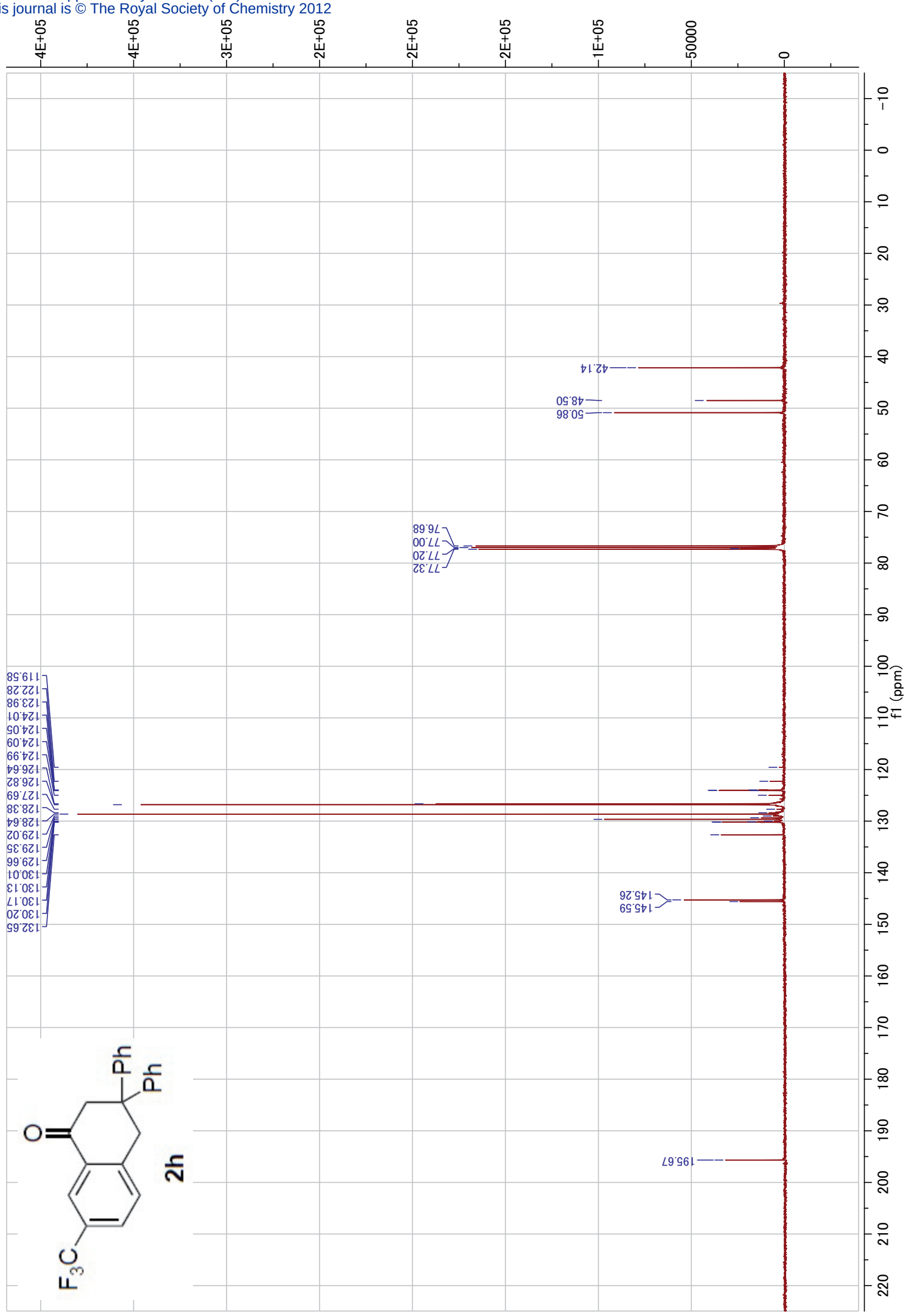
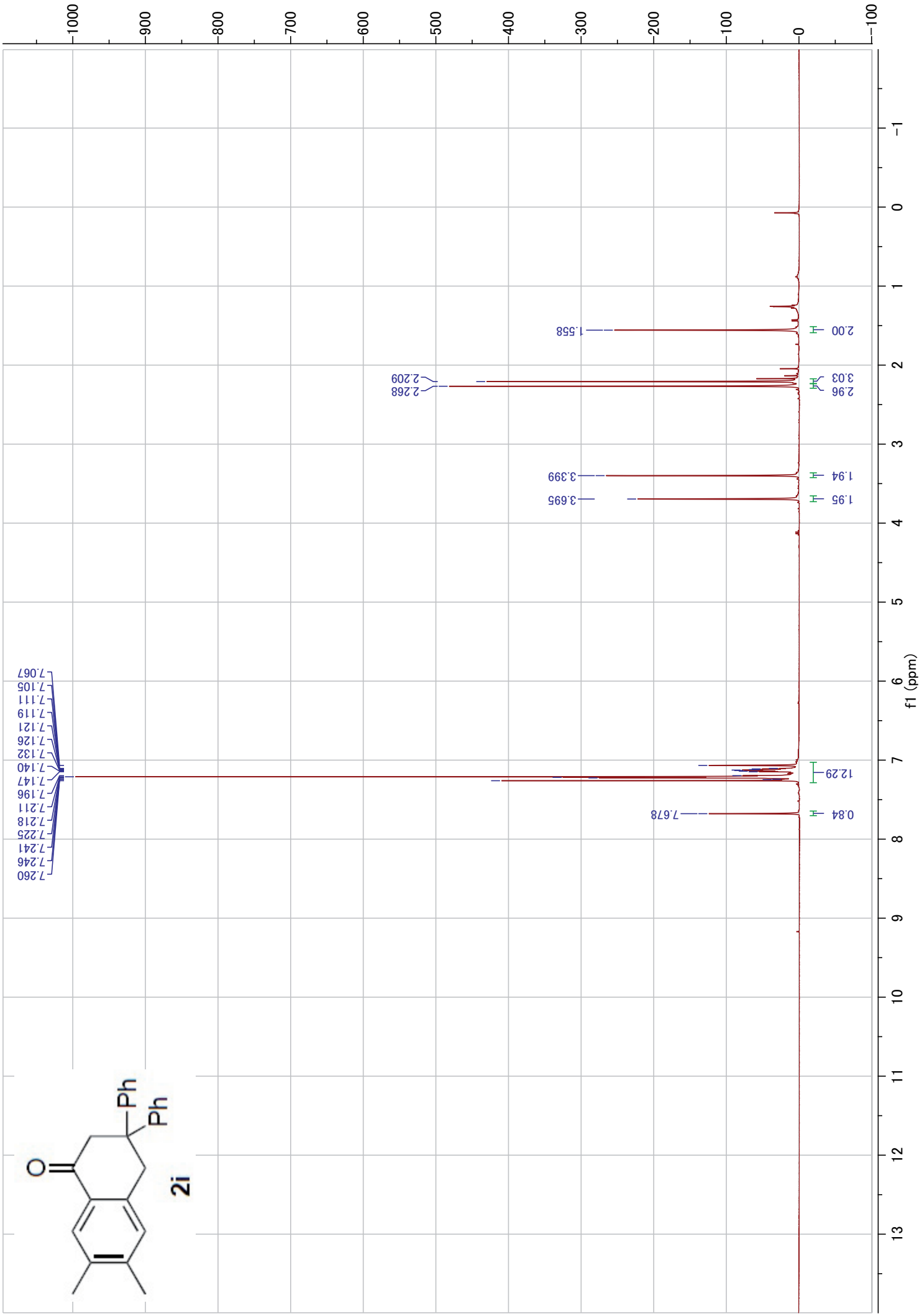
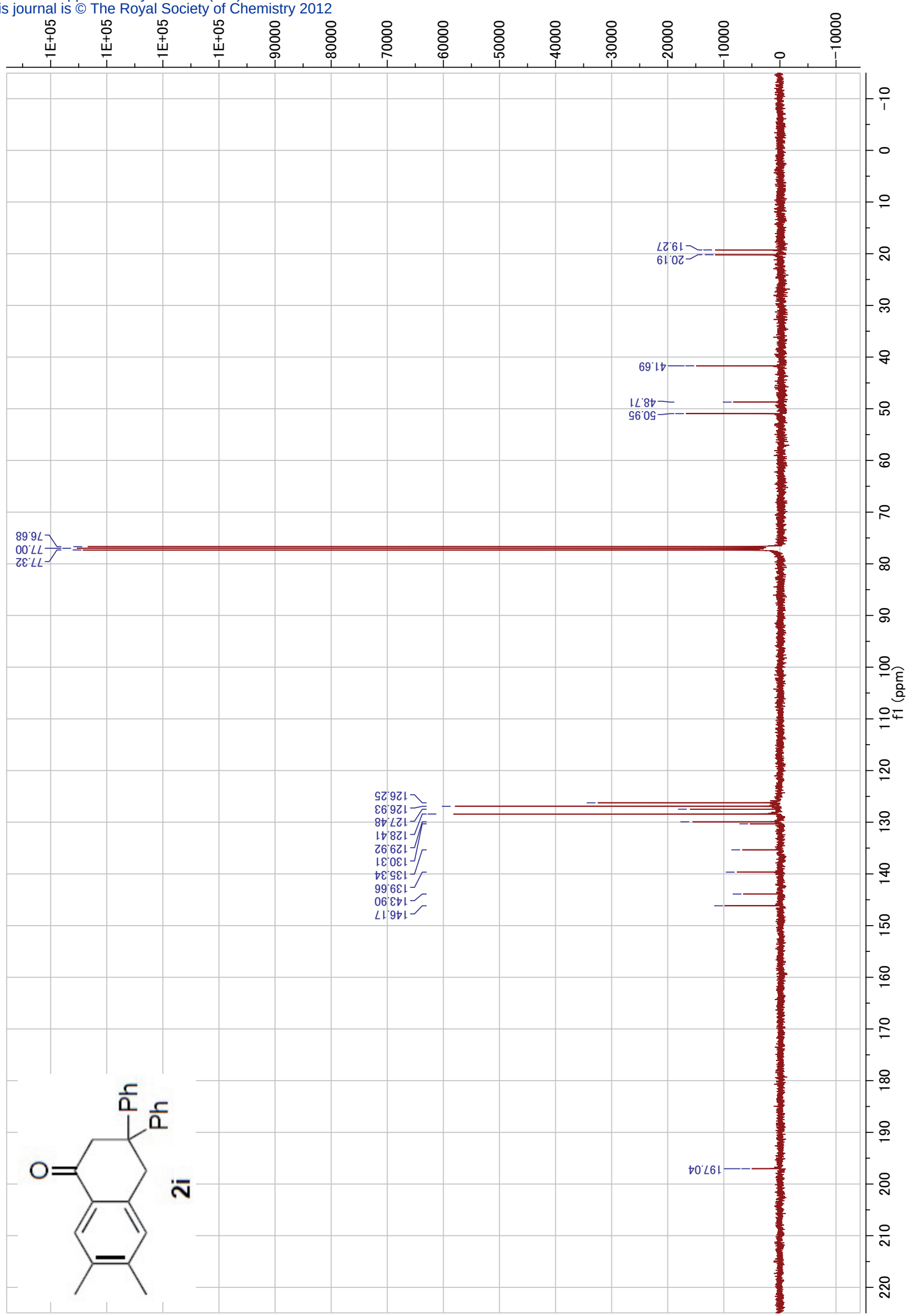
2g



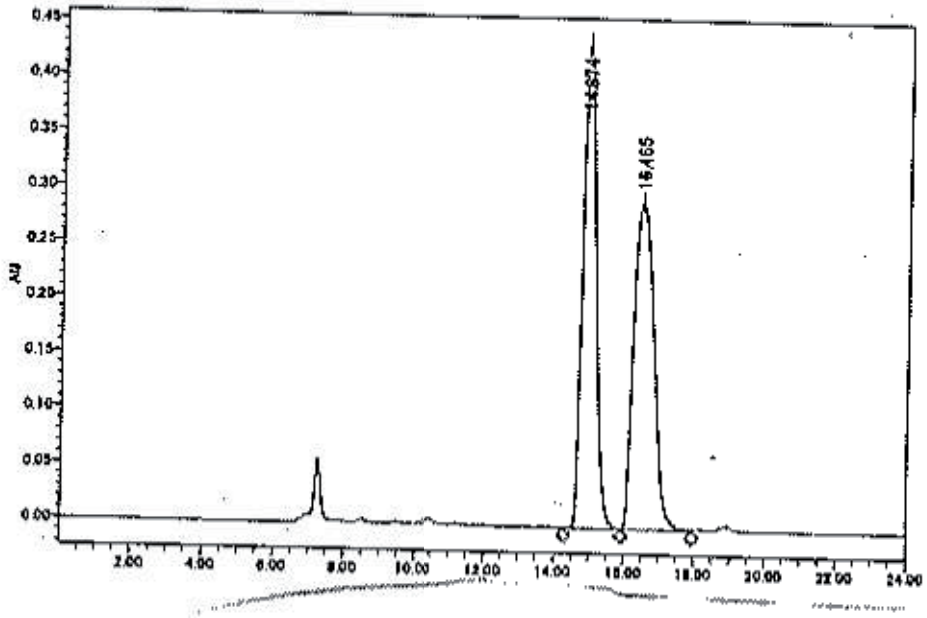


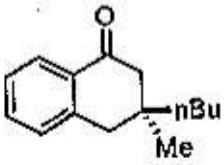



1E+05
1E+05
1E+05
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
−10000
19.27
20.19
41.69
48.71
50.95
76.68
77.00
77.32
126.25
126.93
127.48
128.41
129.92
130.31
135.34
139.66
143.90
146.17
197.04
f1 (ppm)
−10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
O
Ph
Ph
2i

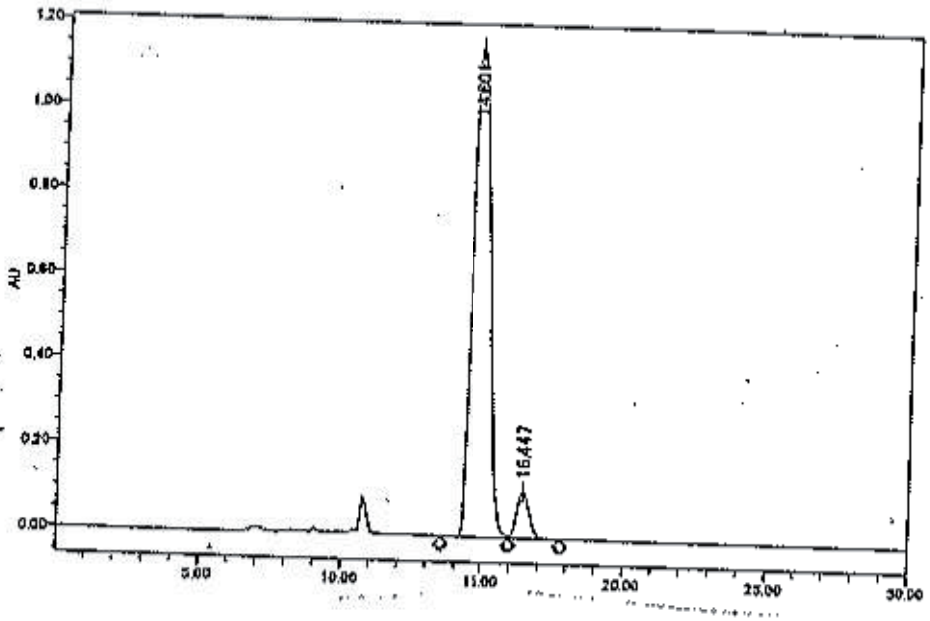
2d

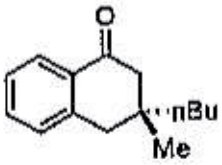
Ret time	Area	Area %
14.874	11638463	49.78
16.465	11741662	50.22





Ret time	Area	Area %
14.601	50312367	93.74
16.447	3357437	6.26





Ret time	Area	Area %
17.055	6071214	9.71
18.677	56424666	90.29