Electronic Supporting Information

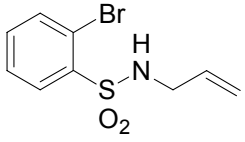
Selective Generation of Quaternary All-Carbon-Centres Through Heck-Cyclisations: Application to the Total Synthesis of Mesembrane

Johannes E. M. N. Klein, Kimberly Geoghegan, Nicolas Méral and Paul Evans*

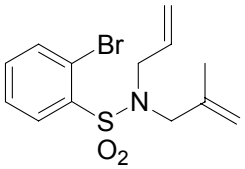
Centre for Synthesis and Chemical Biology, School of Chemistry and Chemical Biology, University College Dublin, Dublin 4, Ireland. E-mail: paul.evans@ucd.ie

General Directions:

Reactions with anhydrous solvents were carried out under an atmosphere of N_2. Glassware was either dried in an oven or by heat-gun before use, assembled hot and cooled to room temperature under a stream of N_2. Anhydrous tetrahydrofuran (THF) was freshly distilled from sodium-benzophenone prior to use, anhydrous dichloromethane (DCM) and acetonitrile (MeCN) were freshly distillted from CaH_2, anhydrous dimethylformamide (DMF) was purchased from Fluka. Reagents were purchased from Acros or Aldrich, and used without further purification. Thin layer chromatography (TLC) was carried out on Merck silica gel aluminum sheets (60 F254). Merck silica gel (60, 0.040-0.063 mm) was used for flash column chromatography. NMR spectra were recorded on Varian 300 MHz, 400 MHz and 500 MHz spectrometers and calibrated using tetramethylsilane (TMS) or the residual non-deuterated solvent signal as an internal standard. IR spectra were recorded on a Varian 3100 FT-IR spectrometer. High Resolution Mass Spectra (HRMS) were recorded using either a Waters Corp, Micromass LCT (ESI), or a Waters Corp, Micromass GCT Premier (EI) spectrometer. Melting points were determined in an open capillary on a Gallenkamp melting point apparatus and are uncorrected.



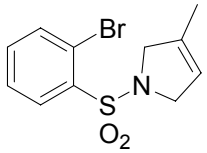
***N*-Allyl-2-bromobenzenesulfonamide S1:**[1] A mixture of 2-bromobenzenesulfonyl chloride (1.63 g, 6.37 mmol, 1 eq.) and triethylamine (1.80 cm^3, 12.91 mmol, 2.0 eq.) in DCM (75 cm^3) was treated with allylamine (0.53 cm^3, 7.01 mmol, 1.1 eq.) in a dropwise fashion at 0 °C. Stirring was continued for 15 h and the reaction gradually warmed to room temperature. The solvent was removed under reduced pressure and Et_2O (100 cm^3) and H_2O (100 cm^3) were added. The resultant aqueous layer was further extracted with Et_2O (2 x 100 cm^3) and the combined ethereal extracts were dried over $MgSO_4$. Filtration followed by solvent removal *in vacuo* afforded the *title compound* **S1** (1.37 g, 78%) as a colourless solid. M.p. 66-68 °C; IR (KBr, dep from DCM) 3316, 3087, 2988, 2922, 2855, 1647, 1575, 1448, 1427, 1332, 1253, 1163, 1127, 1103, 1020 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ = 3.57 (2H, t, *J* = 6.0 Hz, CH_2), 5.08-5.21 (3H, m, CH_2, NH), 5.64-5.77 (1H, m, CH), 7.39-7.51 (2H, m, ArH), 7.74 (1H, dd, *J* = 1.75, 7.5 Hz, ArH), 8.14 (1H, dd, *J* = 1.75, 7.5 Hz, ArH); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ = 45.9 (CH_2), 118.2 (CH_2), 119.7 (C), 127.8 (CH), 131.6 (CH), 132.5 (CH), 133.7 (CH), 135.0 (CH), 138.9 (C).



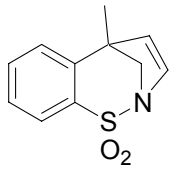
***N*-Allyl-*N*-2-methylallyl-2-bromobenzenesulfonamide S2:** *N*-Allyl-2-bromo-benzenesulfonamide **S1** (342 mg, 1.24 mmol, 1 eq.) was dissolved in DMF (15 cm^3) and cooled to 0

[1] C. Bressy, C. Menant and O. Piva, *Synlett*, 2005, 577-582.

°C. Sodium hydride (60% w/w in mineral oil, 65 mg, 1.625 mmol, 1.3 eq.) was added and the mixture was stirred for a 0.5 h. 3-Chloro-2-methylprop-1-ene (0.225 g, 2.48 mmol, 2 eq.) was dissolved in DMF (2 cm^3) and was added in a dropwise fashion. Stirring was continued for 17 h during which period room temperature was reached. Et_2O (20 cm^3) and H_2O (20 cm^3) were added and the phases were separated. The aqueous phase was further extracted with Et_2O (2 x 20 cm^3). The combined organic phases were dried over $MgSO_4$. The crude product, obtained after solvent removal and filtration, was purified by column chromatography (Pentane-EtOAc, 12:1) which gave *the title compound* **S2** (299 mg, 73%) as a viscous colourless oil. R_f = 0.60 (Pentane-EtOAc; 12:1); IR (KBr, dep from DCM) 3082, 2976, 2919, 2851, 1575, 1446, 1434, 1342, 1280, 1255, 1160, 1125, 1102, 1078, 1027 cm^{-1}; HRMS (ESI): calcd for $[(C_{13}H_{16}NO_2{}^{79}BrS)+H]^+$ 330.0163; found 330.0179; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ = 1.62 (3H, s, CH_3), 3.86 (2H, d, *J* = 6.5 Hz, CH_2), 3.91 (2H, s, CH_2), 4.90 (1H, s, CH_2), 4.93 (1H, s, CH_2), 5.07-5.14 (2H, m, CH_2), 5.49-5.63 (1H, m, CH), 7.37 (1H, dt, *J* = 1.75, 7.5 Hz, ArH), 7.44 (1H, dt, *J* = 1.75, 7.5 Hz, ArH), 7.73 (1H, dd, *J* = 1.75, 7.6 Hz, ArH), 8.17 (1H, dd, *J* = 1.75, 7.5 Hz, ArH); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ = 19.5 (CH_3), 48.4 (CH_2), 52.8 (CH_2), 114.7 (CH_2), 119.2 (CH_2), 120.3 (C), 127.3 (CH), 131.9 (CH), 132.2 (CH), 133.3 (CH), 135.3 (CH), 139.5 (C), 139.7 (C).

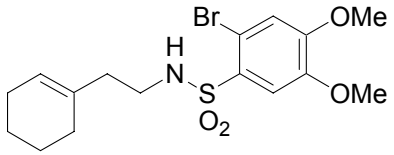


1-(2-Bromobenzenesulfonyl)-2,5-dihydro-3-methyl-1*H*-pyrrole 1: Under N_2, a degassed solution of **S2** (1.88 g, 5.69 mmol, 1 eq.) in DCM (100 cm^3) was treated with the Hoyveda-Grubbs catalyst (149 mg, 0.238 mmol, 4 mol%). Stirring was continued at 50 °C for 3 h and the solvent was removed under reduced pressure. Purification by flash column chromatography (Pentane-EtOAc; 12:1) gave **1** (1.41 g, 82%) as a viscous oil. R_f = 0.30 (Pentane-EtOAc; 12:1), 0.70 (Pentane-EtOAc; 4:1); IR (KBr, dep from DCM) 3075, 2918, 2858, 1631, 1574, 1431, 1334, 1256, 1165, 1130, 1107, 1088, 1023 cm^{-1}; HRMS (ESI): calcd for $[(C_{11}H_{12}NO_2{}^{79}BrS)+H]^+$ 301.9850; found 301.9863; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ = 1.74 (3H, s, CH_3), 4.11-4.15 (2H, m, CH_2), 4.21-4.26 (2H, m, CH_2), 5.34-5.38 (1H, m, CH), 7.38 (1H, dt, *J* = 1.5, 8.0 Hz, ArH), 7.44 (1H, dt, *J* = 1.5, 8.0 Hz, ArH), 7.75 (1H, dd, *J* = 1.5, 8.0 Hz, ArH), 8.04 (1H, dd, *J* = 1.5, 8.0 Hz, ArH); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ = 14.1 (CH_3), 55.2 (CH_2), 57.7 (CH_2), 118.9 (CH), 120.4 (C), 127.5 (CH), 131.5 (CH), 133.4 (CH), 134.9 (C), 135.7 (CH), 138.7 (C).

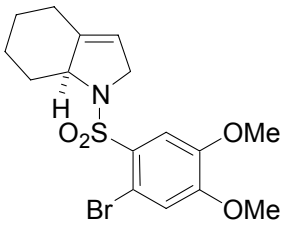


1-Methyl-8-thia-9-azatricyclo[7.2.1.0^{2,7}]dodeca-2(7),3,5,10-tetraene-8,8-dioxide 3: Under N_2, a mixture of **1** (365 mg, 1.21 mmol, 1 eq.), $Pd(OAc)_2$ (27 mg, 0.12 mmol, 10 mol%), PPh_3 (63 mg, 0.24 mmol, 20 mol%) and K_2CO_3 (334 mg, 2.42 mmol, 2 eq.) in DMF (10 cm^3) was heated to 110 °C for 18 h. The reaction mixture was cooled and Et_2O (50 cm^3) and H_2O (50 cm^3) were added. The resultant aqueous layer was further extracted with Et_2O (2 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure gave the crude product which was purified by flash column chromatography (Pentane-EtOAc; 4:1) affording the Heck product **3** (241 mg, 90%) as a colourless solid. M.p. 128-134 °C; R_f = 0.35 (Pentane-EtOAc; 4:1); IR (KBr, dep from DCM) 3086, 2935, 2883, 1840, 1723, 1591, 1463, 1439, 1386, 1329, 1277, 1243, 1207, 1166, 1112, 1053, 1027 cm^{-1}; HRMS (EI): calcd for $[C_{11}H_{11}NO_2{}^{79}BrS]^+$ 221.0511; found 221.0520; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ = 1.47 (3H, s, CH_3), 3.81 (1H, d, *J* = 11.75 Hz, CH_2), 4.45 (1H, d, *J* = 11.75 Hz, CH_2), 6.23 (1H, d, *J* = 3.5 Hz, CH), 6.38 (1H, d, *J* = 3.5, CH), 7.22 (1H, dd, *J* = 1.5, 8.0 Hz, ArH), 7.44 (1H, dt, *J* = 1.5, 8.0 Hz, ArH),

7.49 (1H, dt, J = 1.5, 8.0 Hz, ArH), 7.72 (1H, dd, J = 1.5, 8.0 Hz, ArH); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ = 16.0 (CH_3), 43.9 (C), 67.5 (CH_2), 121.8 (CH), 126.3 (CH), 128.7 (CH), 130.7 (CH), 132.4 (C), 132.5 (CH), 139.5 (CH), 141.6 (C).



2-Bromo-*N*-(2-cyclohex-1-enylethyl)-4,5-dimethoxybenzenesulfonamide 13: To a solution of 2-bromo-4,5-dimethoxybenzene-1-sulfonyl chloride **12**[2] (5.00 g, 15.94 mmol, 1 equiv.) and triethylamine (4.44 cm^3, 31.86 mmol, 2 equiv.) in dichloromethane (300 cm^3) was added 2-cyclohex-1-enylethylamine **11** (3.33 cm^3, 23.91 mmol, 1.5 equiv.) at 0°C in a dropwise fashion. The mixture was stirred for 16 h during which period room temperature was reached. The solution was poured into 1 M HCl solution (200 cm^3) and extracted with Et_2O (3 x 200 cm^3). Combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 2:1) gave **13** (5.46 g, 85% yield) as a white solid. Recrystallisation was performed using industrial methylated spirit (IMS). M.p. 69 °C (IMS); R_f = 0.45 (cyclohexane-EtOAc; 1:1); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 1.50-1.61 (4H, m, CH_2), 1.76 (2H, s(br), CH_2), 1.97 (2H, s(br), CH_2), 2.11 (2H, t, J = 6.0 Hz, CH_2), 2.93 (2H, q, J = 6.0 Hz, CH_2), 3.92 (3H, s, CH_3), 3.93 (3H, s, CH_3), 5.05 (1H, t, J = 6.0 Hz, NH), 5.46 (1H, s(br), CH), 7.12 (1H, s, ArH), 7.60 (1H, s, ArH); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 22.2 (CH_2), 22.6 (CH_2) 25.2 (CH_2), 27.5 (CH_2), 37.1 (CH_2), 40.6 (CH_2), 56.4 (CH_3), 56.5 (CH_3), 110.9 (C), 114.0 (CH), 116.9 (CH), 125.0 (CH), 130.2 (C), 133.3 (C), 148.0 (C), 152.2 (C); IR (KBr, dep from DCM) 3318, 3111, 3089, 3057, 2999, 2928, 2839, 1585, 1503, 1360, 1159 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{22}NO_4{}^{79}BrS)+H]^+$ 404.0531; found 404.0515.



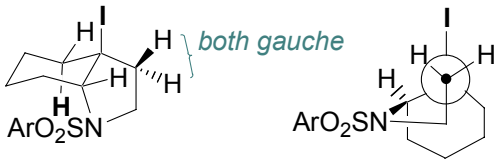
1-(2-Bromo-4,5-dimethoxybenzenesulfonyl)-2,4,5,6,7,7a-hexahydro-1*H*-indole 14:[3] A solution of **13** (786 mg, 1.95 mmol, 1 equiv.) in MeCN (25 cm^3) was treated with powdered K_2CO_3 (807 mg, 5.85 mmol, 3 equiv.) the mixture was stirred for 1 h at room temperature. Solid I_2 (1.480 g, 5.85 mmol, 3 equiv.) was then added and the mixture stirred for 18 h. A saturated solution of Na_2SO_3 (50 cm^3) was added and the combined mixture was extracted with EtOAc (3 x 50 cm^3). The combined extracts were dried over $MgSO_4$ and filtration and solvent removal in vacuo afforded the crude iodide. The crude material was directly dissolved in DCM (25 cm^3) and treated at room temperature with DBU (600 mg, 3.94 mmol, 2 equiv.). Stirring was maintained for 2 h before a 1 M solution of HCl (15 cm^3) was added. The resultant aqueous layer was further extracted with DCM (2 x 20 cm^3). The organic layers were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (cyclohexane-EtOAc; 6:1 → 4:1) afforded the alkene **14** (587 mg, 75%) as a viscous yellow oil. R_f = 0.20 (cyclohexane-EtOAc; 4:1); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 1.18-1.34 (3H, m, CH_2), 1.61-1.79 (2H, m, CH_2), 1.92-2.00 (1H, m, CH_2), 2.14-2.19 (1H, m, CH_2), 2.45-2.51 (1H, m, CH_2), 3.88 (3H, s, CH_3), 3.92 (3H, CH_3), 4.19-4.24 (1H, m, CH_2), 4.28-4.35 (2H, m, CH, CH_2), 5.26 (1H, s(br), CH), 7.16 (1H, s,

[2]P. Evans, T. McCabe, B. S. Morgan and S. Reau, *Org. Lett.*, 2005, **7**, 43-46.
[3]For method see: A. D. Jones, D. W. Knight and D. E. Hibbs, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1182-1203.

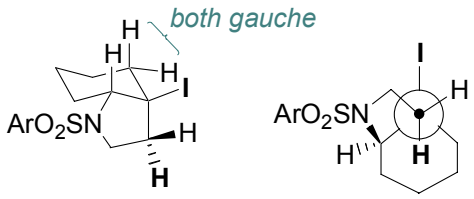
ArH), 7.58 (1H, s, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 23.9 (CH_2), 26.6 (CH_2), 28.5 (CH_2), 35.3 (CH_2), 55.2 (CH_2), 56.4 (CH_3), 56.5 (CH_3), 66.4 (CH), 112.2 (C), 114.1 (2 x CH), 117.7 (CH), 131.1 (C), 141.9 (C), 147.9 (C), 152.2 (C); IR (KBr, dep from DCM) 3113, 3090, 3062, 2935, 2858, 1585, 1503, 1438, 1360, 1323, 1261, 1216, 1158, 1117, 1023 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{20}NO_4{}^{79}BrS)+H]^+$ 402.0375; found 402.0359.

• ^{1}H-^{1}H COSY, TOCSY, HSQC and HMBC experiments were performed to aid the assignment of the given alkene regioisomer.

• A possible explanation for regioselectivity observed, based on the E2 elimination of the equatorial iodide conformer, is given below:

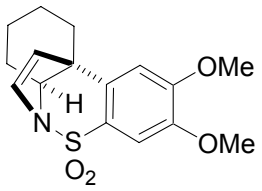


Axial Iodide Conformer:

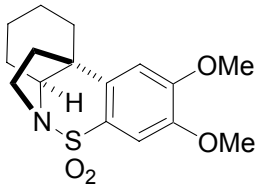


Equatorial Iodide Conformer:

Assuming an S_N2 process affords the iodide shown, the axial iodide conformer would be expected to afford the regioisomer not detected in which the alkene forms within the 6-membered ring. In contrast, the equatorial conformer would be expected to afford the product predominantly observed.

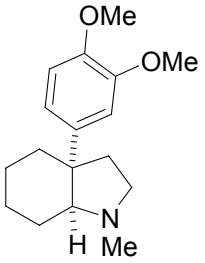


(±)-(4a*R*,10a*S*)-6,7-Dimethoxy-4a,10-etheno-2,3,4,4a,10,10a-hexahydro-1*H*-9-thia-10-aza-phenanthrene 9,9-dioxide 15: A solution of **14** (1.20 g, 2.985 mmol, 1 equiv.) in DMF (15 cm^3) was treated with $Pd(OAc)_2$ (33 mg, 0.149 mmol, 5 mol%), PPh_3 (78 mg, 0.299 mmol, 10 mol%) and K_2CO_3 (825 mg, 5.969 mmol, 2 equiv.). The mixture was degassed by passing a steady stream of N_2 through the solution (for 1 h) and then heated to 130 ºC (oil bath temperature) for 15 h. The mixture was cooled, water (25 cm^3) was added and then extracted with ether (4 x 15 cm^3). The combined ether extracts were dried over $MgSO_4$. Filtration and solvent removal under reduced pressure gave the crude material which was purified by flash column chromatography (cyclohexane-EtOAc; 6:1 → 1:1) to afford the Heck adduct **15** (816 mg, 85%) as a colourless solid. Recrystallisation from EtOAc gave crystals suitable for X–ray analysis. M.p. 186°C (EtOH); R_f = 0.10 (cyclohexane-EtOAc; 6:1); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 1.16-1.45 (2H, m, CH_2), 1.63-1.90 (4H, m, CH_2), 2.08-2.19 (1H, m, CH_2), 2.42 (1H, d, J = 13.5 Hz, CH_2), 3.90 (3H, s, CH_3), 3.91 (3H, s, CH_3), 4.50 (1H, dd, J = 6.0, 11.0 Hz, CH), 6.15 (1H, d, J = 3.5 Hz, CH), 6.22 (1H, d, J = 3.5 Hz, CH), 6.68 (1H, s, ArH), 7.17 (1H, s, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 21.6 (CH_2), 22.9 (CH_2) 27.6 (CH_2), 28.2 (CH_2), 48.2 (C), 56.1 (CH_3), 56.2 (CH_3), 72.5 (CH), 105.3 (CH), 109.3 (CH), 125.1 (C), 132.6 (CH), 138.3 (CH), 138.8 (C), 149.5 (C), 151.0 (C); IR (KBr, dep from DCM) 3088, 3008, 2937, 2859, 1599, 1568, 1505, 1451, 1332, 1268, 1152, 1054 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{19}NO_4S)+H]^+$ 322.1113; found 322.1100.



(±)-(4a*R*,10a*S*)-6,7-Dimethoxy-4a,10-ethano-2,3,4,4a,10,10a-hexahydro-1*H*-9-thia-10-aza-phenanthrene 9,9-dioxide 16: A mixture of **15** (595 mg, 1.854 mmol, 1 equiv.) and 10% w/w Pd/C (98 mg) in EtOAc (40 cm^3) was stirred under an atmosphere of hydrogen (1 atm.) for 19 h. The mixture was filtered through celite (washed with EtOAc 3 x 20 cm^3). Solvent removal under reduced pressure and recrystallisation from EtOH gave **16** (570 mg, 95%) as a colourless solid. M.p. 205°C (EtOH); R_f = 0.10 (cyclohexane-EtOAc; 6:1); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 1.23-1.43 (2H, m, CH_2), 1.49-1.62 (1H, m, CH_2), 1.65-1.77 (2H, m, CH_2), 1.79-1.88 (2H, m, CH_2), 1.91-1.96 (1H, m, CH_2), 2.35 (1H, ddd, *J* = 6.5, 10.0, 16.5 Hz, CH_2), 2.46 (1H, d, *J* = 13.5 Hz, CH_2), 3.60 (1H, ddd, *J* = 4.0, 10.0, 14.25 Hz, CH_2), 3.83 (1H, ddd, *J* = 6.5, 9.0, 14.25 Hz, CH_2), 3.91 (3H, s, CH_3), 3.92 (3H, s, CH_3), 4.07 (1H, dd, *J* = 5.5, 11.0 Hz, CH), 6.77 (1H, s, ArH), 7.24 (1H, s, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 21.3 (CH_2), 23.8 (CH_2) 27.4 (CH_2), 29.3 (CH_2), 33.2 (CH_2), 44.6 (C), 45.7 (CH_2), 56.1 (CH_3), 56.2 (CH_3), 67.5 (CH), 106.1 (CH), 107.9 (CH), 126.9 (C), 139.8 (C), 148.5 (C), 152.3 (C); IR (KBr, dep from DCM) 3061, 2936, 2859, 1601, 1568, 1508, 1465, 1329, 1261, 1158, 1045 cm^{-1}; HRMS (ESI): calcd for $[(C_{16}H_{21}NO_4S)+H]^+$ 324.1270; found 324.1283; Found C, 59.35; H, 6.52; N, 4.26%, $C_{16}H_{21}NO_4S$ requires C, 59.42; H, 6.54; N, 4.33%.

One pot procedure: A solution of **14** (346 mg, 0.861 mmol, 1 equiv.) in DMF (13 cm^3) was treated with $Pd(OAc)_2$ (19 mg, 0.085 mmol, 10 mol%), PPh_3 (45 mg, 0.172 mmol, 20 mol%) and K_2CO_3 (238 mg, 1.722 mmol, 2 equiv.). The mixture was degassed by passing a steady stream of N_2 through the solution (for 1 h) and then heated at 130ºC (oil bath temperature) for 18 h. On cooling the mixture was stirred under an atmosphere of H_2 for 23 h. Water (25 cm^3) was added and then extracted with EtOAc (4 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$ before filtration and solvent removal under reduced pressure gave the crude material. Purification by flash column chromatography (cyclohexane-EtOAc; 6:1 to 4:1) gave **16** (120 mg, 43%) as a colourless solid with data as above.



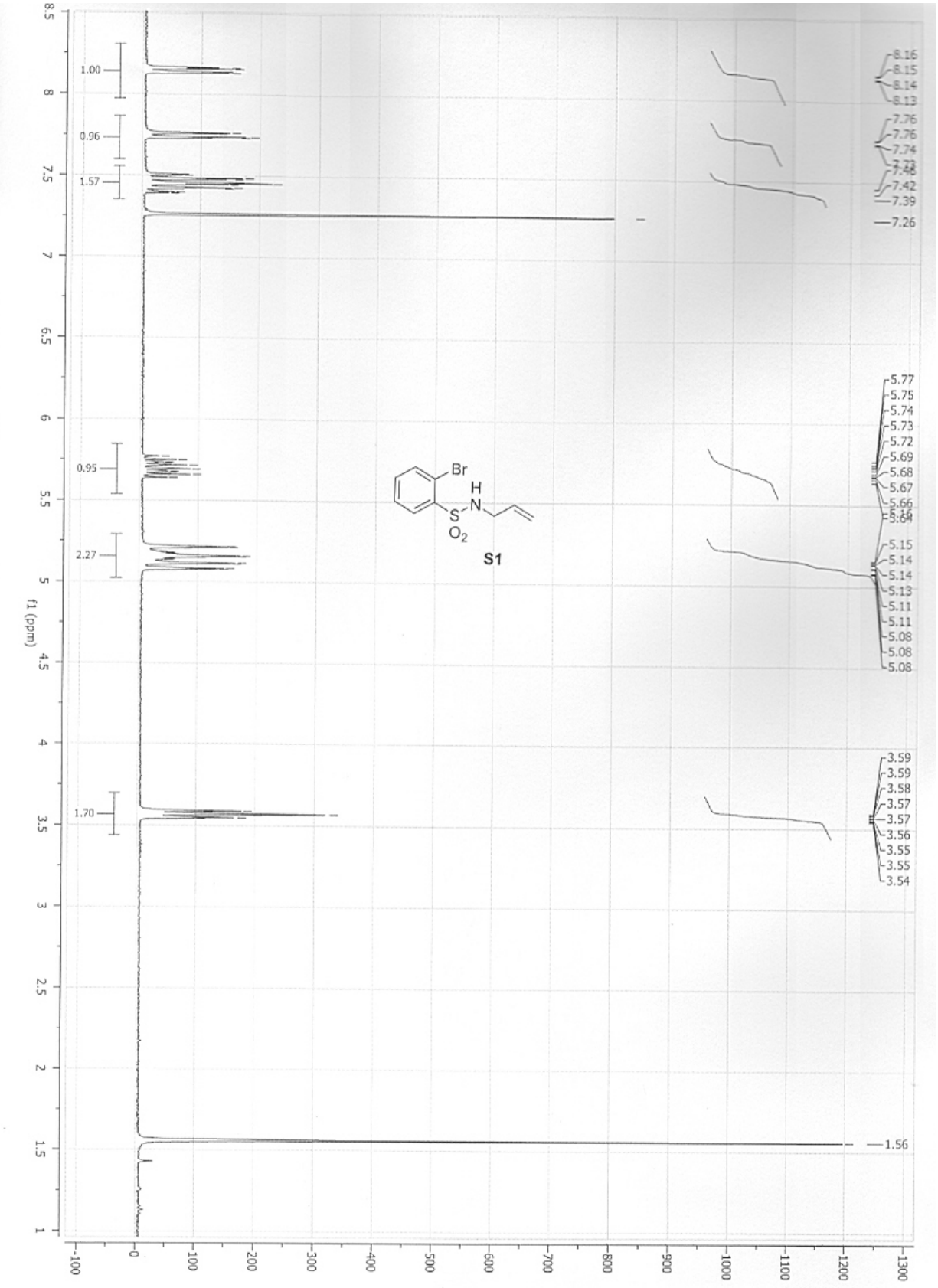
(±)-(3a*S*,7a*S*)-3a-(3,4-Dimethoxyphenyl)-1-methyloctahydroindole (Mesembrane) 7: Under N_2, small pieces of Li (15 mg, 2.143 mmol, 8.6 equiv.) were added to NH_3 (75 cm^3) at –78 ºC. The mixture was stirred for 45 min before a solution of **16** (80 mg, 0.248 mmol, 1 equiv.) in THF (15 cm^3 + 5 cm^3 to wash flask) was added in a dropwise fashion. Stirring was continued for 15 min at –78 ºC before addition of solid NH_4Cl (*ca.* 2 g). The NH_3 was allowed to evaporate on warming to room temperature and the residue was dissolved in dichloromethane (25 cm^3). A 1 M solution of NaOH solution (25 cm^3) was added and the resultant aqueous layer was further extracted with dichloromethane (3 x 25 cm^3). The combined organic layers were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure afforded a 1:1 mixture of 3a-(4-methoxyphenyl)octahydroindole and 3a-(3,4-dimethoxyphenyl)octahydroindole (72 mg) [3a-(4-methoxyphenyl)octahydroindole: HRMS (ESI): calcd for $[(C_{15}H_{21}NO)+H]^+$ 232.1701; found 232.1692; 3a-(3,4-dimethoxyphenyl)octahydroindole: HRMS (ESI): calcd for $[(C_{16}H_{23}NO2)+H]^+$

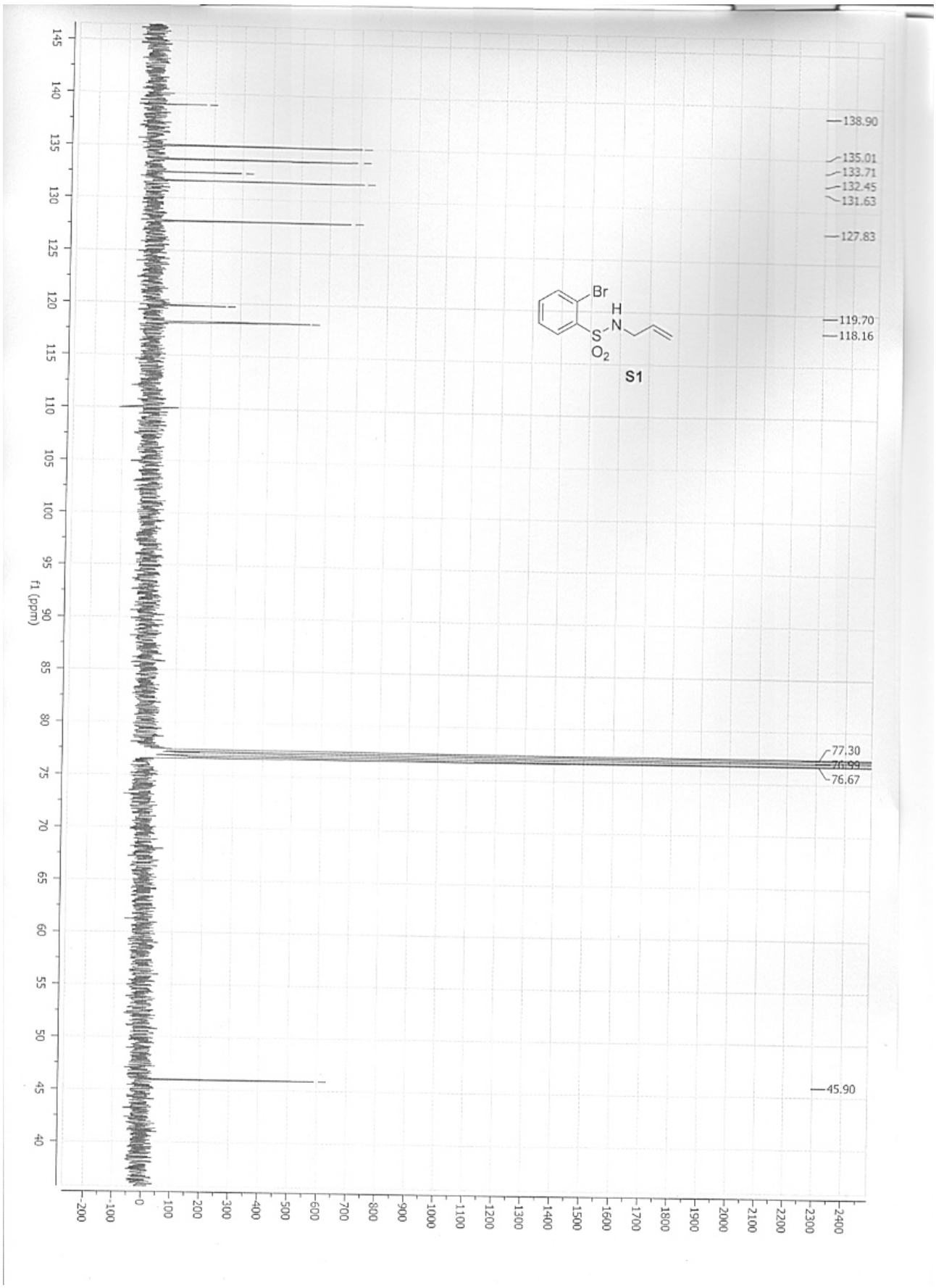
262.1807; found 262.1805]. This mixture was taken up in DCM (3 cm^3) and powdered K_2CO_3 (343 mg, 2.482 mmol, 10 equiv.) was added followed by benzyl chloroformate (63 mg, 0.369 mmol, 1.5 equiv.). Stirring was continued at room temperature for 4 hours before addition of silica (*ca.* 2 g) and solvent removal under reduced pressure. Purification by flash column chromatography gave **17** (37 mg, 41%) R_f = 0.2 (cyclohexane-EtOAc; 4:1); HRMS (ESI): calcd for $[(C_{23}H_{27}NO_3)+H]^+$ 366.2069; found 366.2077. Further elution gave **18** (32 mg, 33%) R_f = 0.1 (cyclohexane-EtOAc; 4:1).[4] Under N_2, **18** (32 mg, 0.081 mmol, 1 equiv.) in THF (5 cm^3) was treated with $LiAlH_4$ (10 mg, 0.263 mmol, 3.25 equiv.). The reaction mixture was heated to reflux for 2 h. On cooling EtOAc (20 cm^3) was gradually added follwed by 1 M NaOH solution (20 cm^3). The resultant aqueous layer was extracted with EtOAc (2 x 20 cm^3) and the combined organic extracts were dried over $MgSO_4$. Following filtration and solvent removal column chromatography ($CHCl_3$-MeOH; 19:1, 1 % Et_3N) afforded the title compound **7** (21 mg, 94%) as a colourless oil with data in accord to that reported.[5] R_f = 0.1 ($CHCl_3$-MeOH; 19:1, 1 % Et_3N); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 1.14-1.19 (1H, m, CH_2), 1.39-1.42 (1H, m, CH_2), 1.50 (1H, d, *J* = 12.25 Hz, CH_2), 1.58-1.69 (2H, m, CH_2), 1.81-1.88 (2H, m, CH_2), 1.89-1.97 (3H, m, CH_2), 2.33-2.40 (1H, m, CH_2), 2.39 (3H, s, CH_3), 2.60 (1H, s(br), CH), 3.34-3.39 (1H, m, CH_2), 3.87 (3H, s, CH_3), 3.89 (3H, s, CH_3), 6.81 (1H, d, *J* = 8.25 Hz, ArH), 6.88 (1H, d, *J* = 2.0 Hz, ArH), 6.91 (1H, dd, *J* = 2.0, 8.25 Hz, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 20.4 (CH_2), 22.7 (CH_2) 23.6 (CH_2), 35.7 (CH_2), 40.8 (CH_2 and CH_3), 47.6 (C), 54.3 (CH_2), 55.9 (CH_3), 56.0 (CH_3), 69.0 (CH), 110.8 (CH), 110.85 (CH), 118.8 (CH), 139.8 (C), 147.0 (C), 148.8 (C); IR (KBr, dep from DCM) 3054, 2929, 2852, 1516, 1456, 1253 cm^{-1}; HRMS (ESI): calcd for $[(C_{17}H_{25}NO_2)+H]^+$ 276.1964; found 276.1971.

Lithium Naphthalenide Method: Under nitrogen a solution of naphthalene (138 mg, 1.07 mmol, 7 equiv.) in THF (10 cm^3) was treated with small pieces of lithium metal (7.5 mg, 1.07 mmol, 7 equiv.) and sonicated for 0.5 h at rt. The reaction mixture was cooled to -78 °C and treated with a solution of **16** (49 mg, 0.15 mmol, 1 equiv.) in THF (10 cm^3). After 10 min the reaction was warmed to rt (*ca.* 30 min). NH_4Cl sat. (20 cm^3) was added and the mixture extracted with dichloromethane (20 cm^3) and washed with 1 M NaOH solution (3 x 20 cm^3). The organic layer was dried over $MgSO_4$ before filtration and evaporation under reduced pressure. The crude product was dissolved in dichloromethane (10 cm^3) and treated with K_2CO_3 (149 mg, 1.08 mmol, 7.2 equiv.) and benzyl chloroformate (0.2 cm^3, 1.40 mmol, 9.3 equiv.). Stirring was maintained for 4 h at rt. Water (20 cm^3) and dichloromethane (20 cm^3) were added and the resultant aqueous layer was further extracted with dichloromethane (2 x 20 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification by silica gel chromatography (*n*-Hexane:EtOAc; 4:1) afforded the product **18** (13 mg, 22%) as a viscous yellow oil. R_f = 0.35 (*n*-Hexane:EtOAc; 4:1); υ_{max} (KBr, dep from MeOH) 3037, 2930, 2859, 1697, 1594, 1414, 1358, 1258, 1096 cm^{-1}; HRMS (ESI): calcd for $[(C_{24}H_{29}NO_4)+H]^+$ 396.2175; found 396.2178.[4]

[4]NMR spectra for compounds **17** and **18** were complex due to presence of rotameric species.
[5]For spectroscopic data see: M. Saito, J. Matsuo and H. Ishibashi, *Tetrahedron*, 2007, **63**, 4865-4873.
[4]NMR spectra for compound **18** was complex due to presence of rotameric species.

Proton and Carbon NMR Spectra

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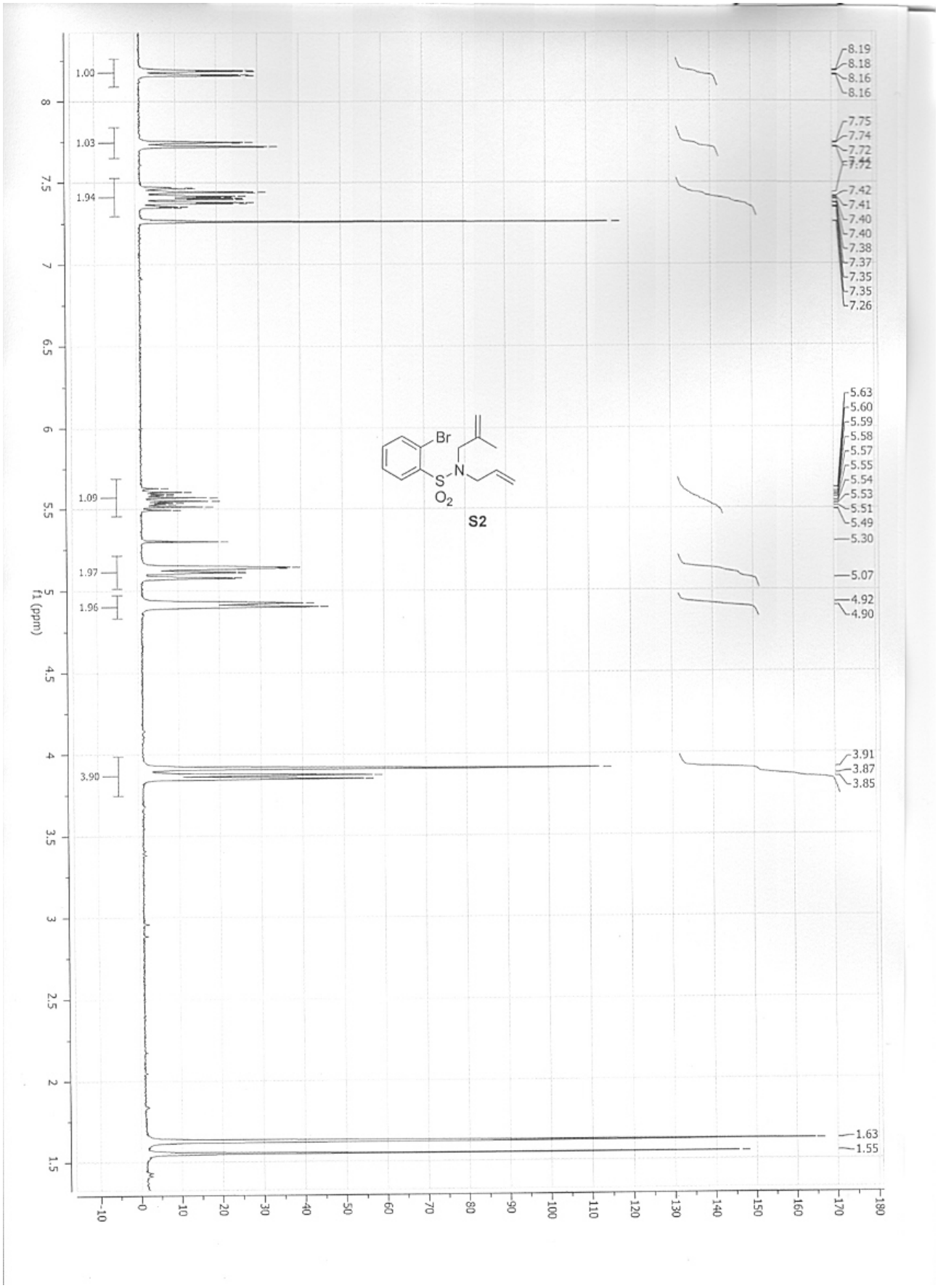
H
N
S
O2
S1
f1 (ppm)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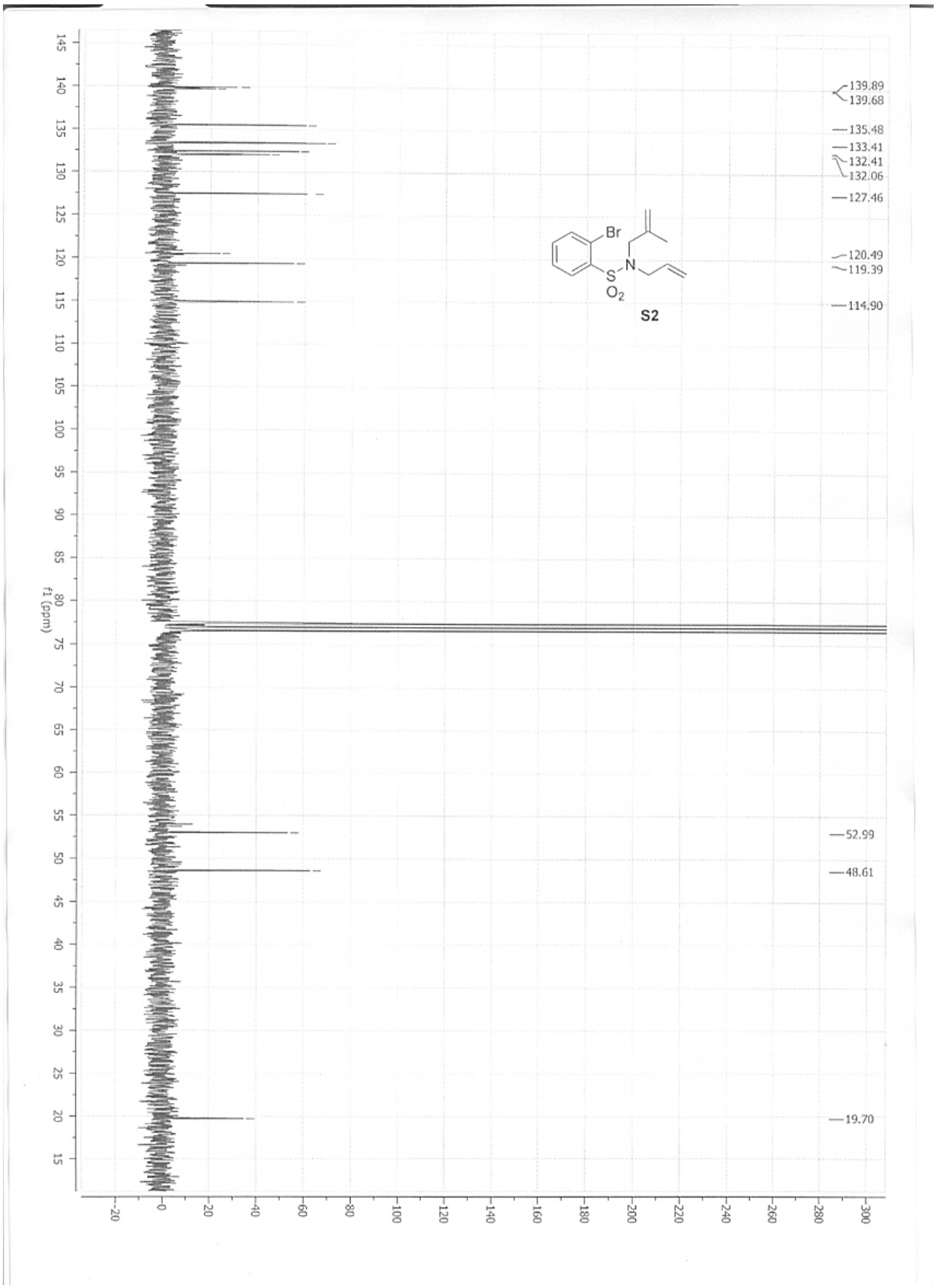
S2
f1 (ppm)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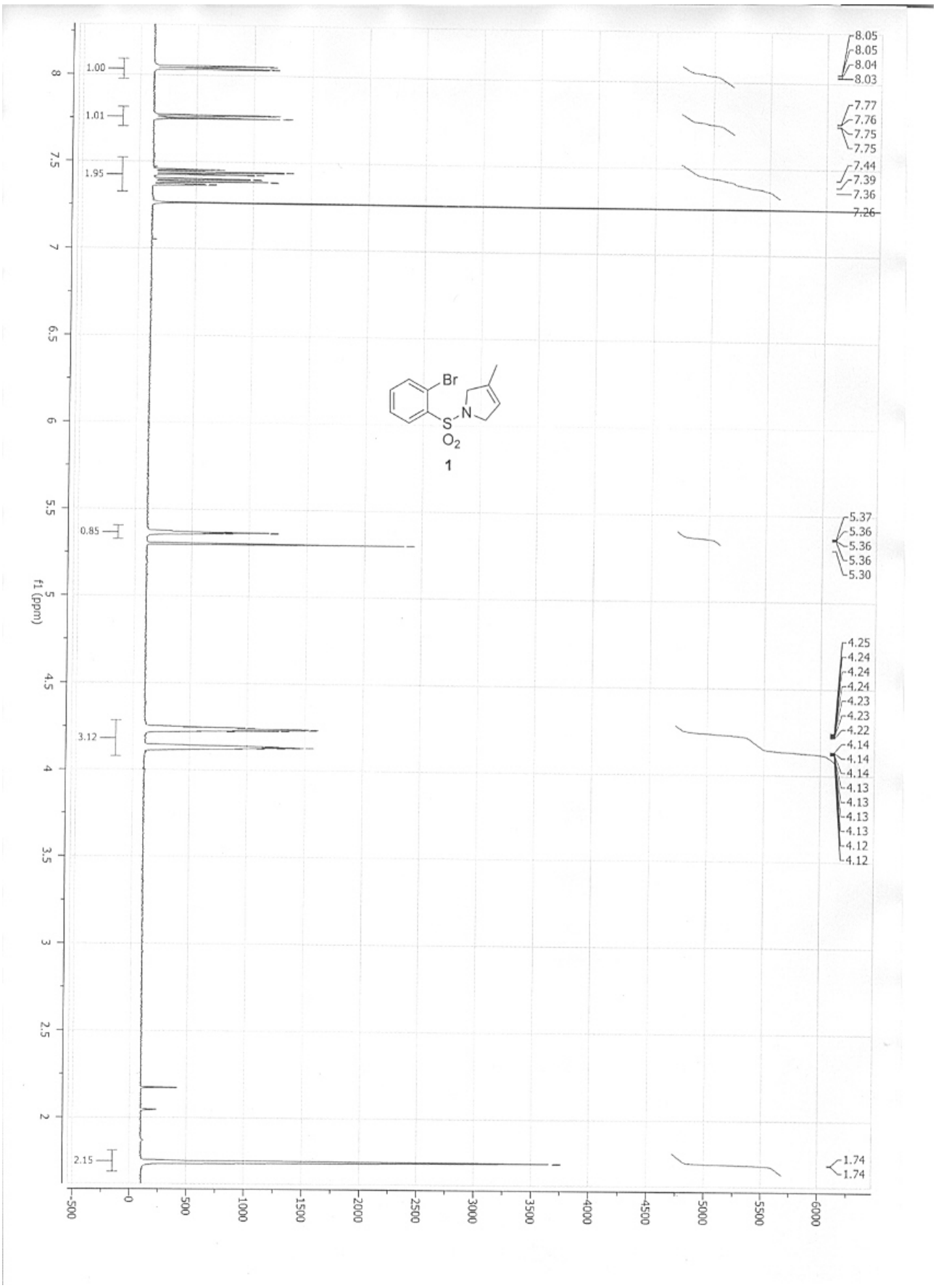
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O2
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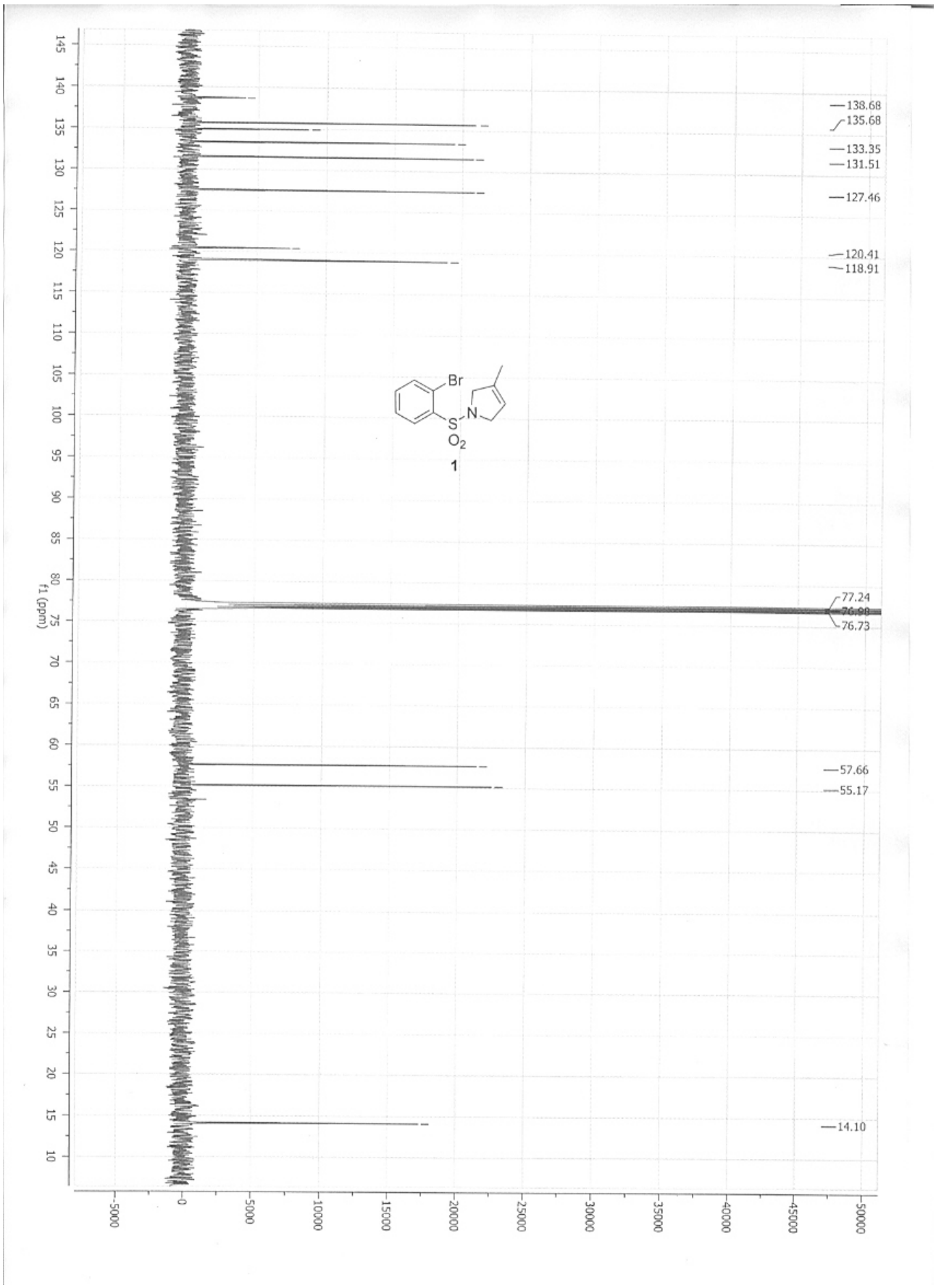
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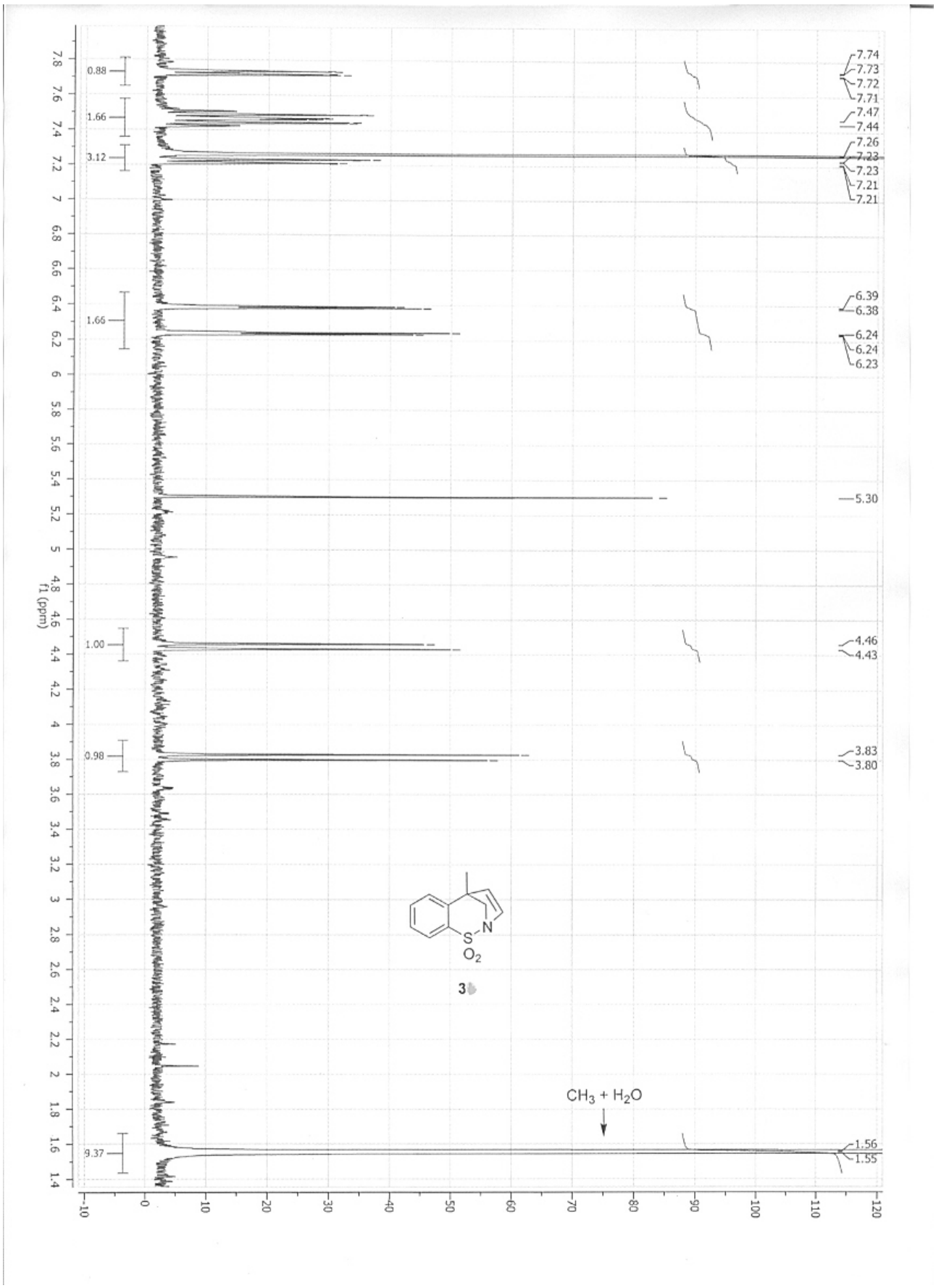
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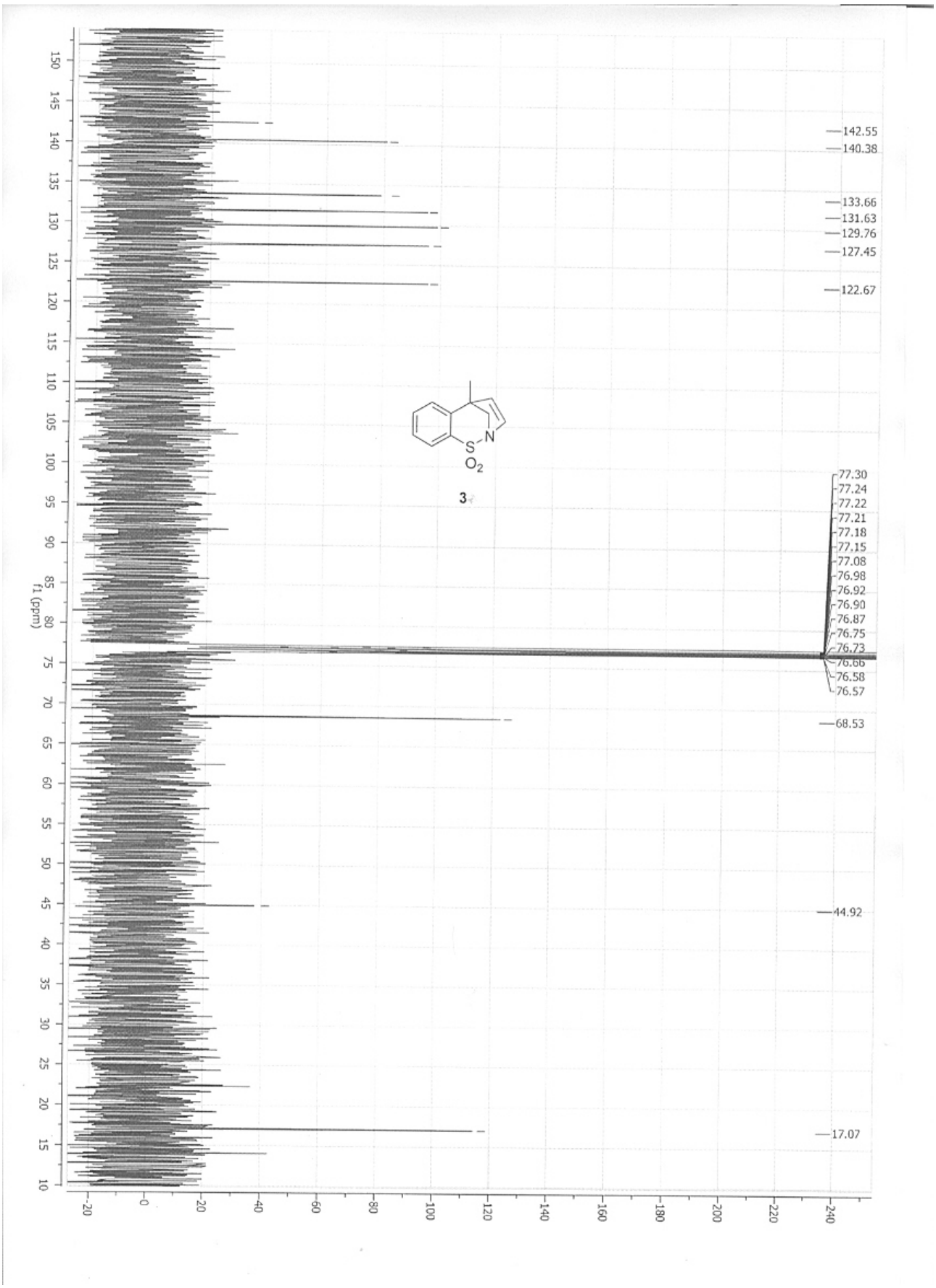
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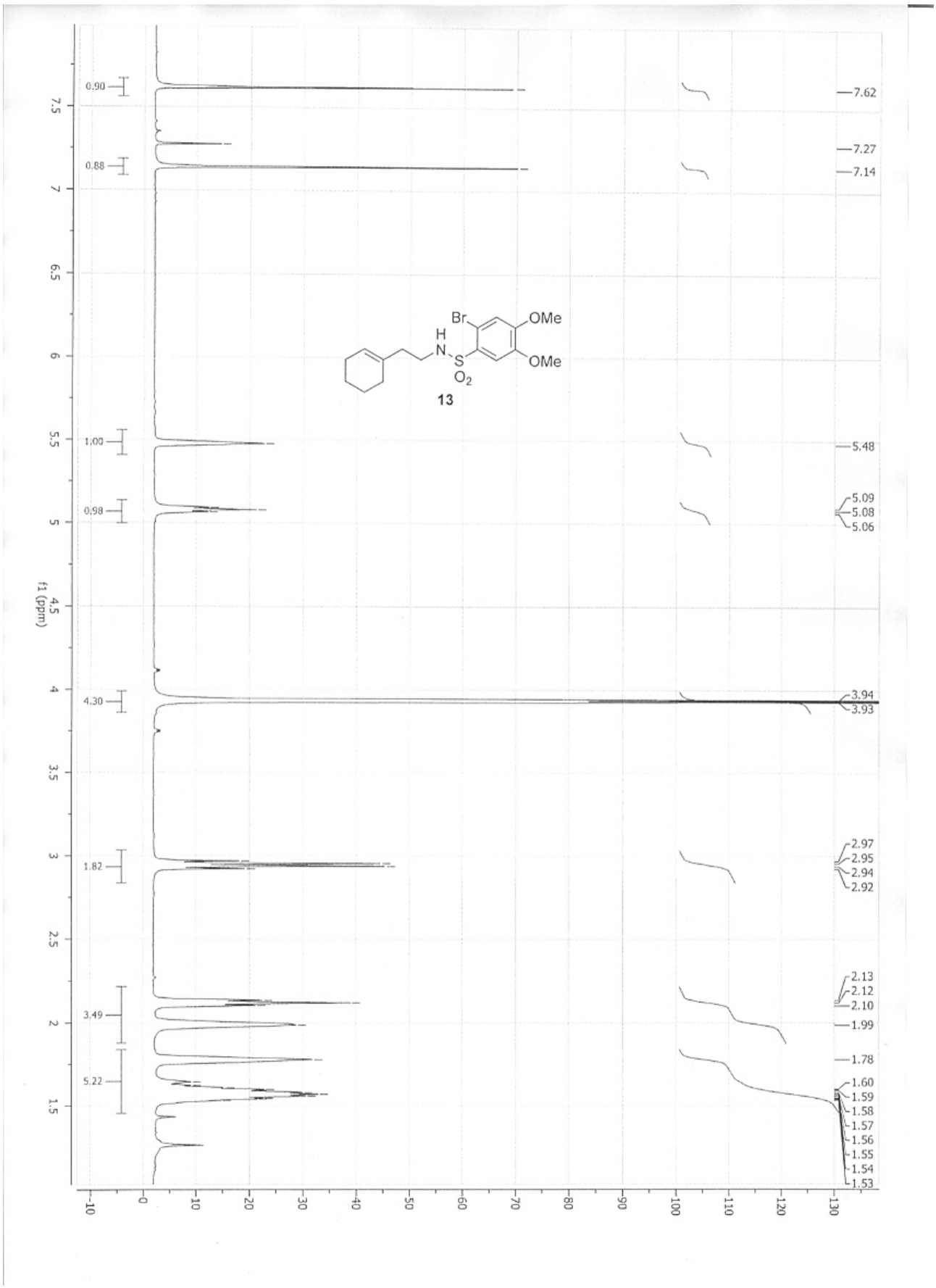
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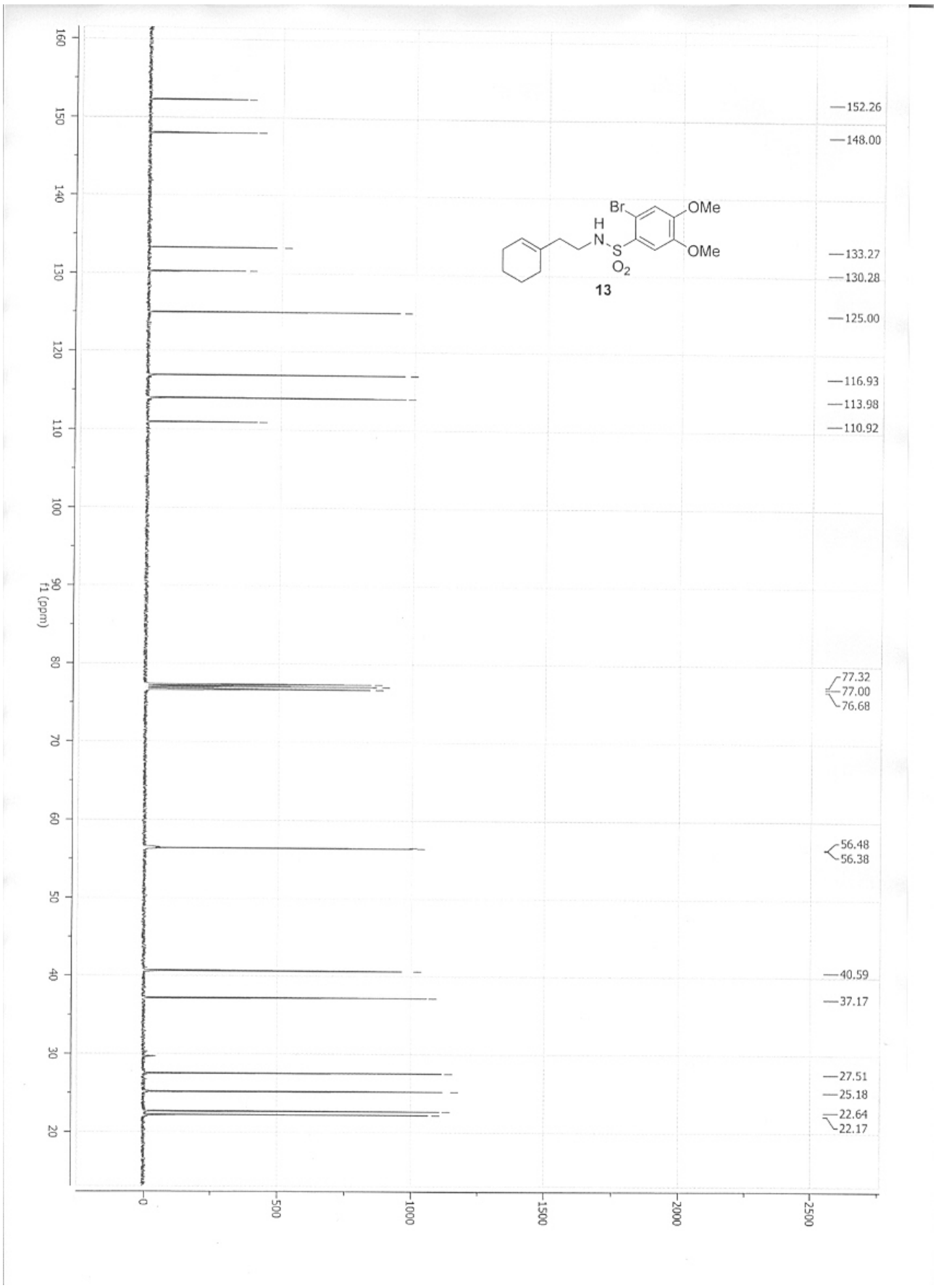
1.53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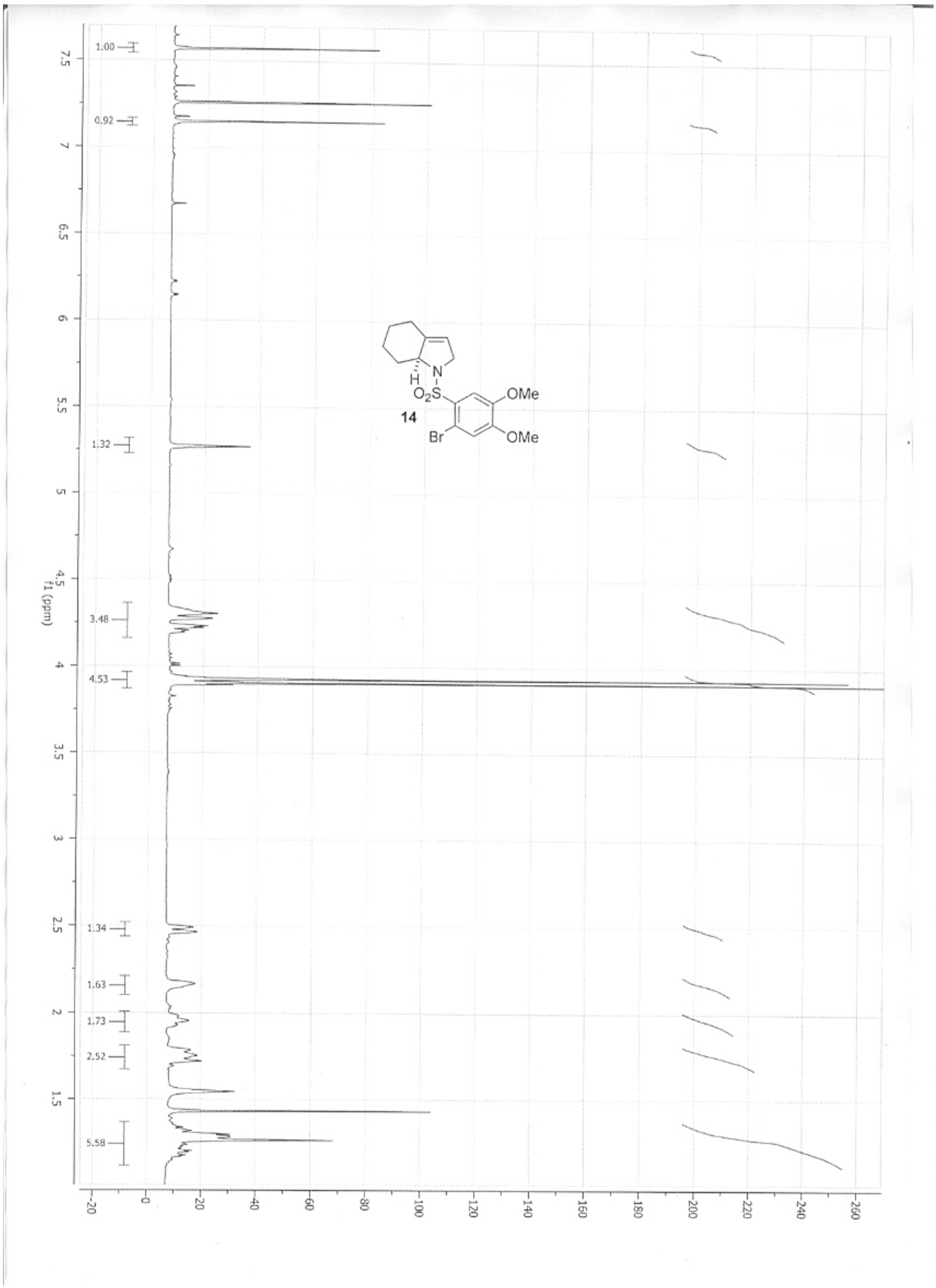
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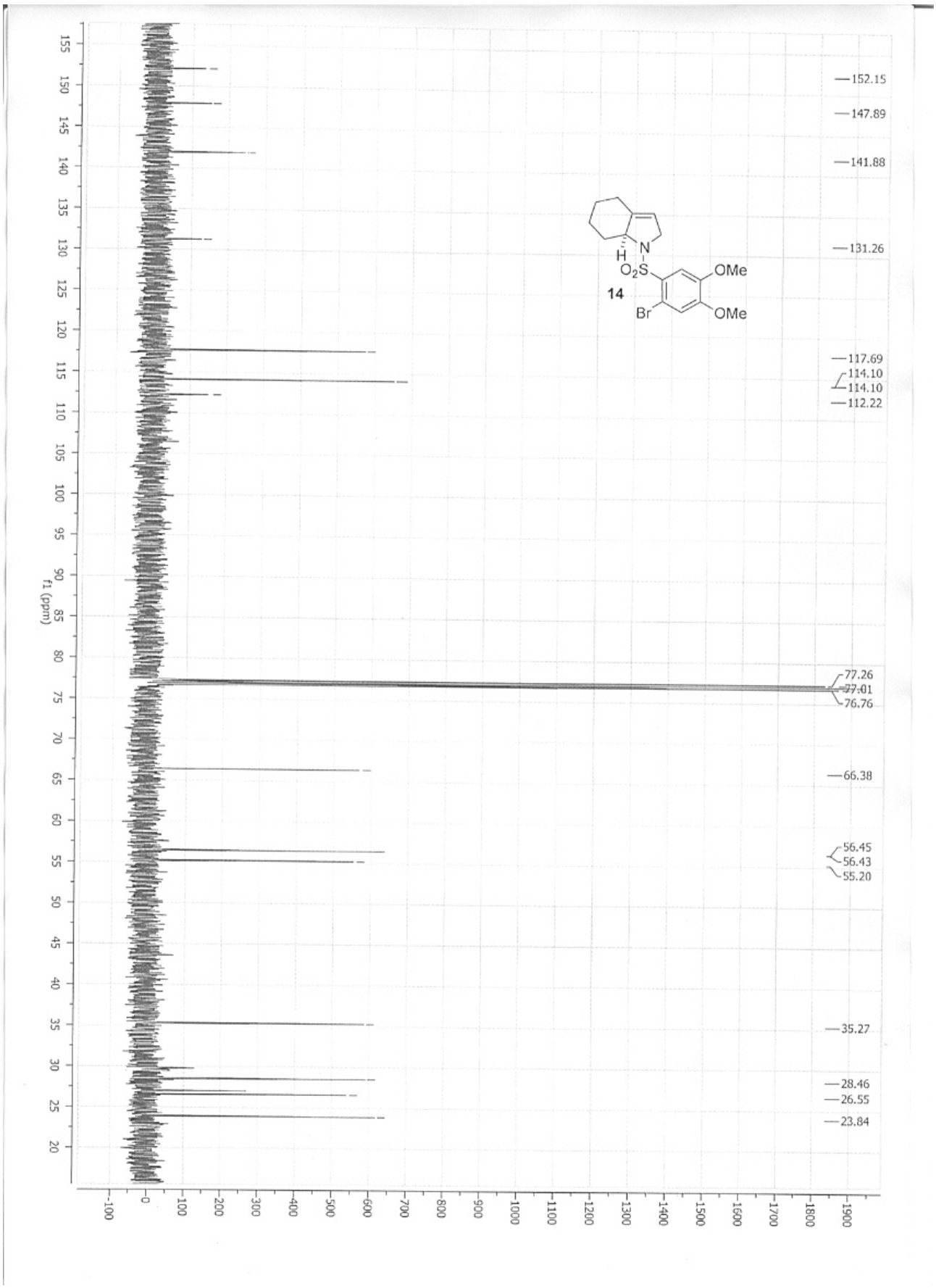
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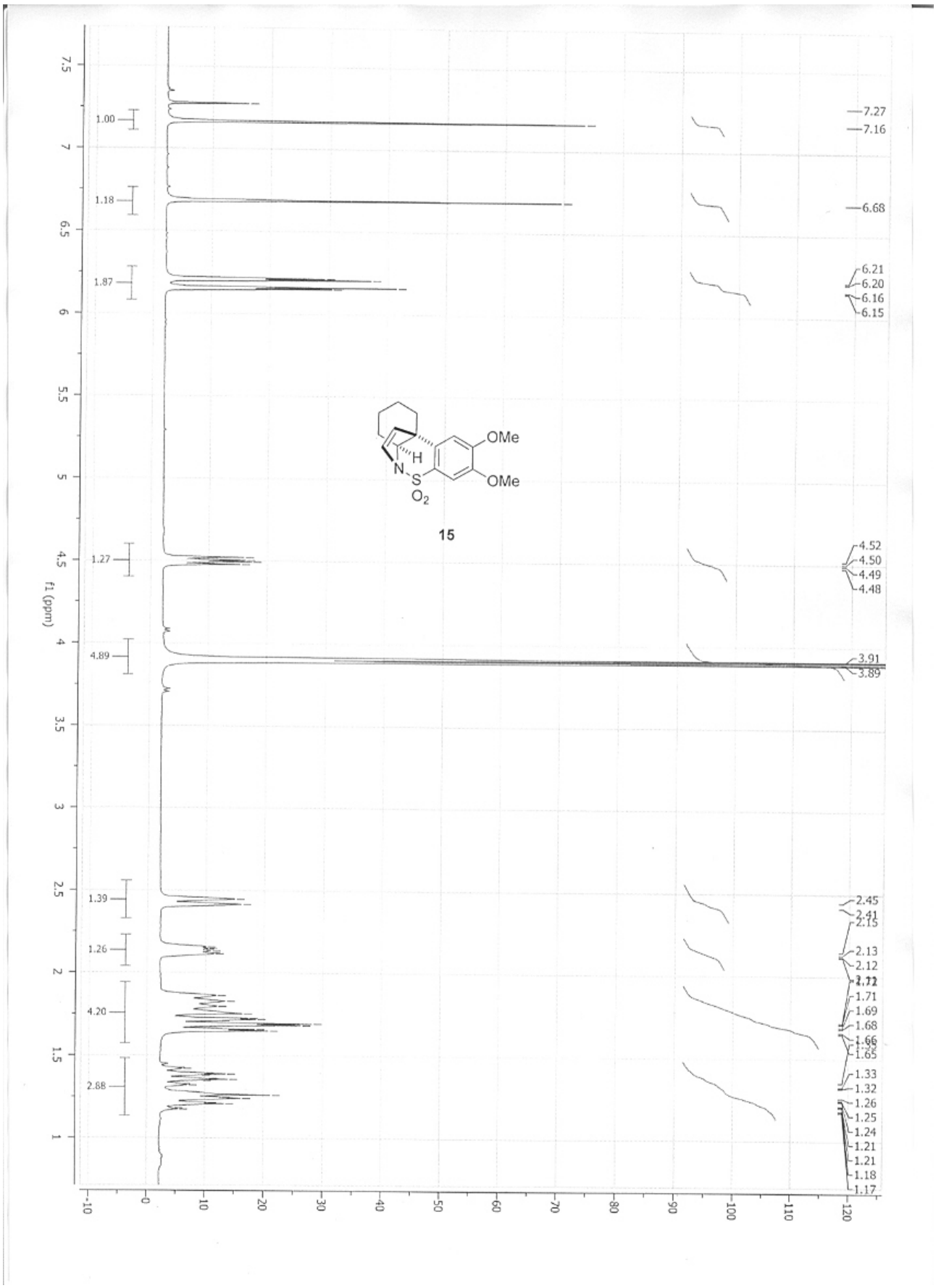
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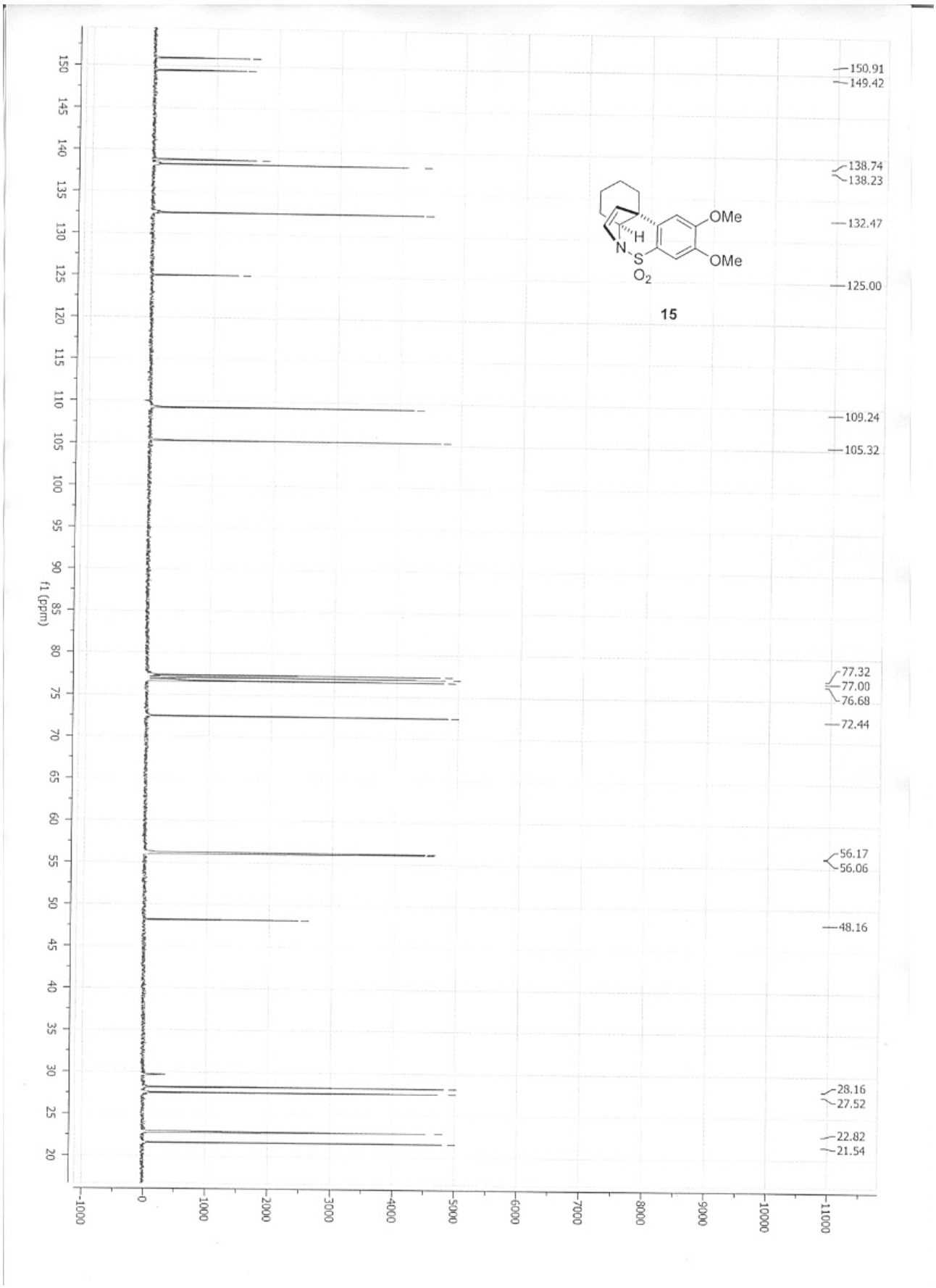
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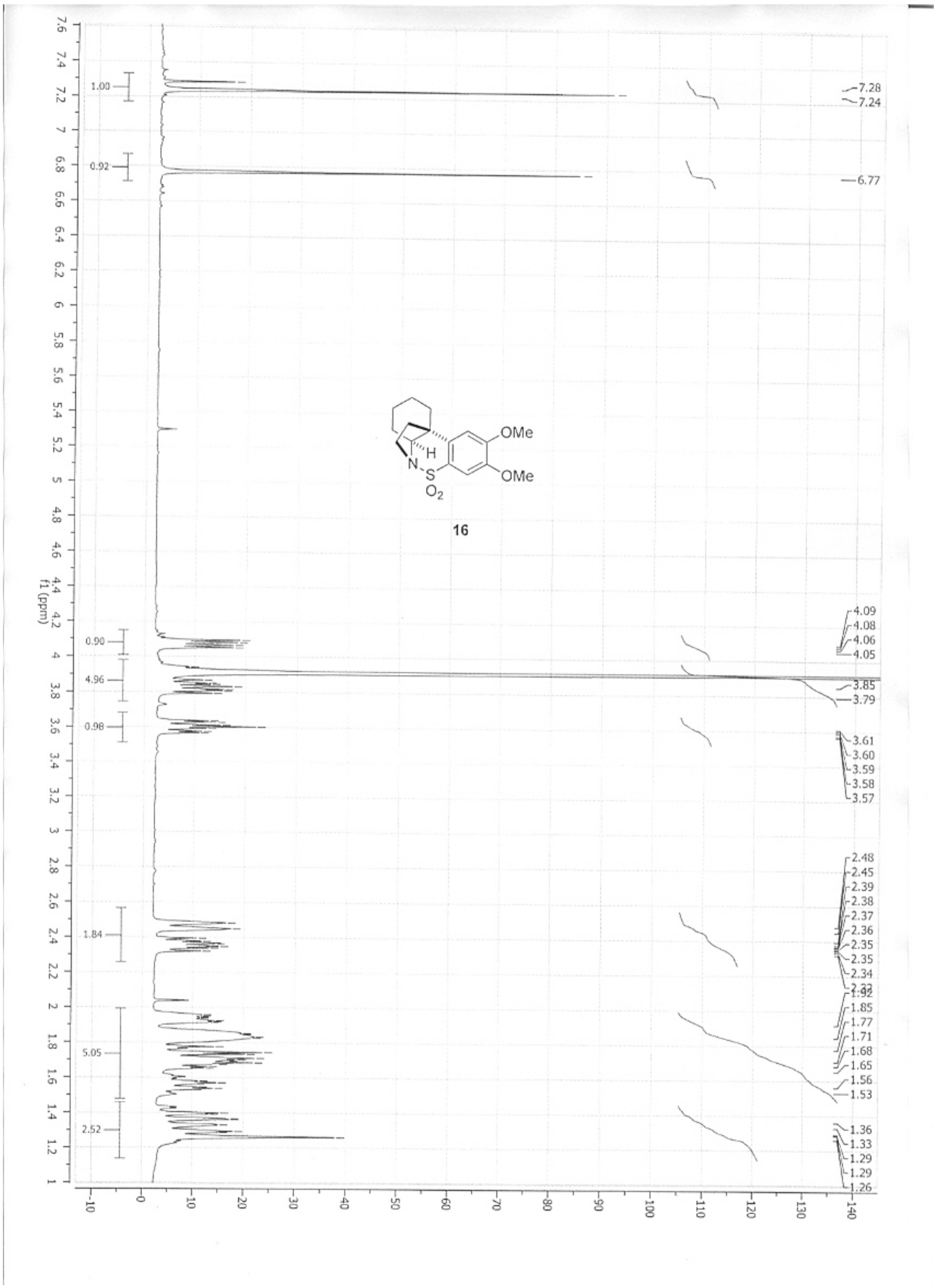
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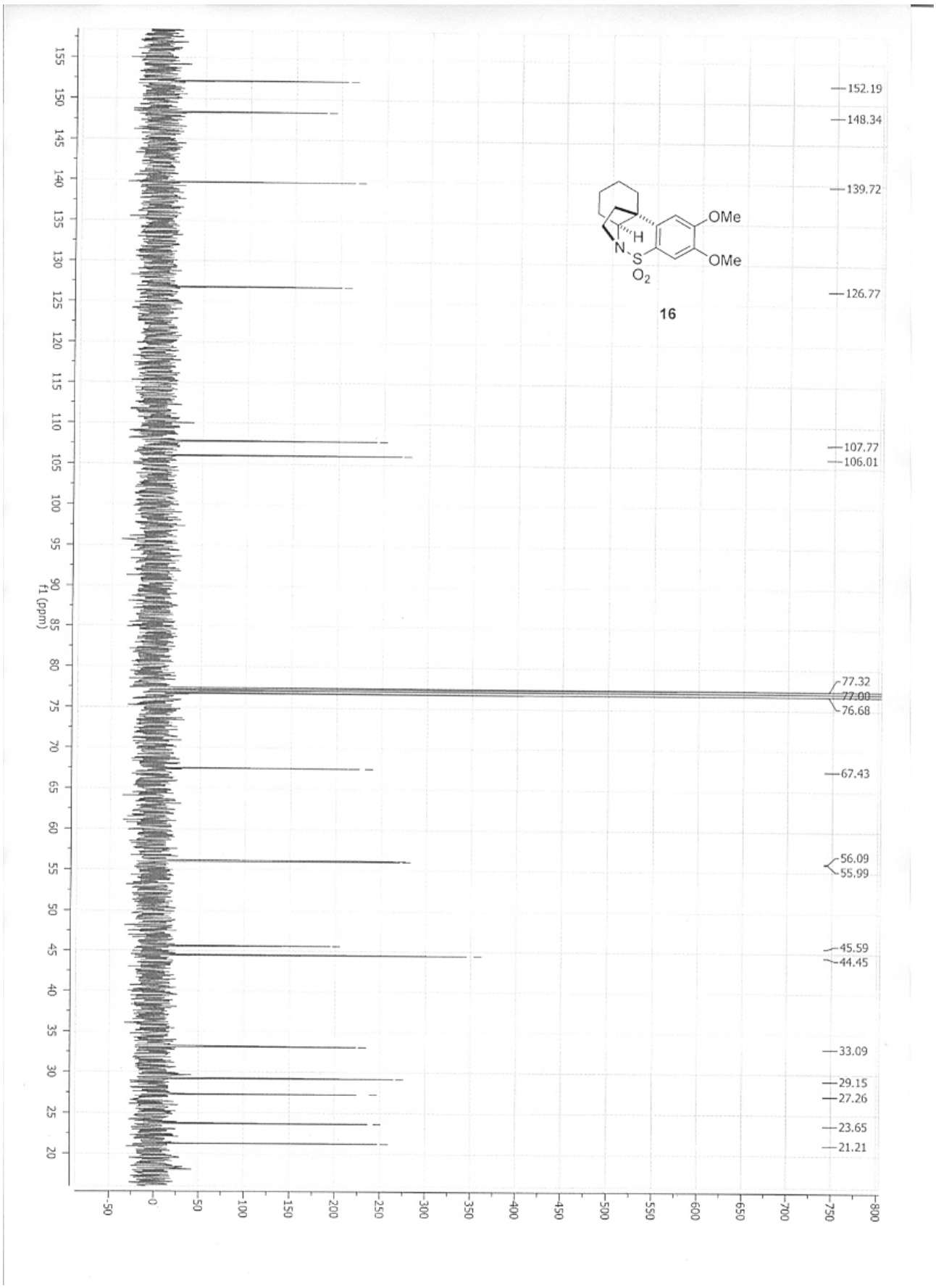
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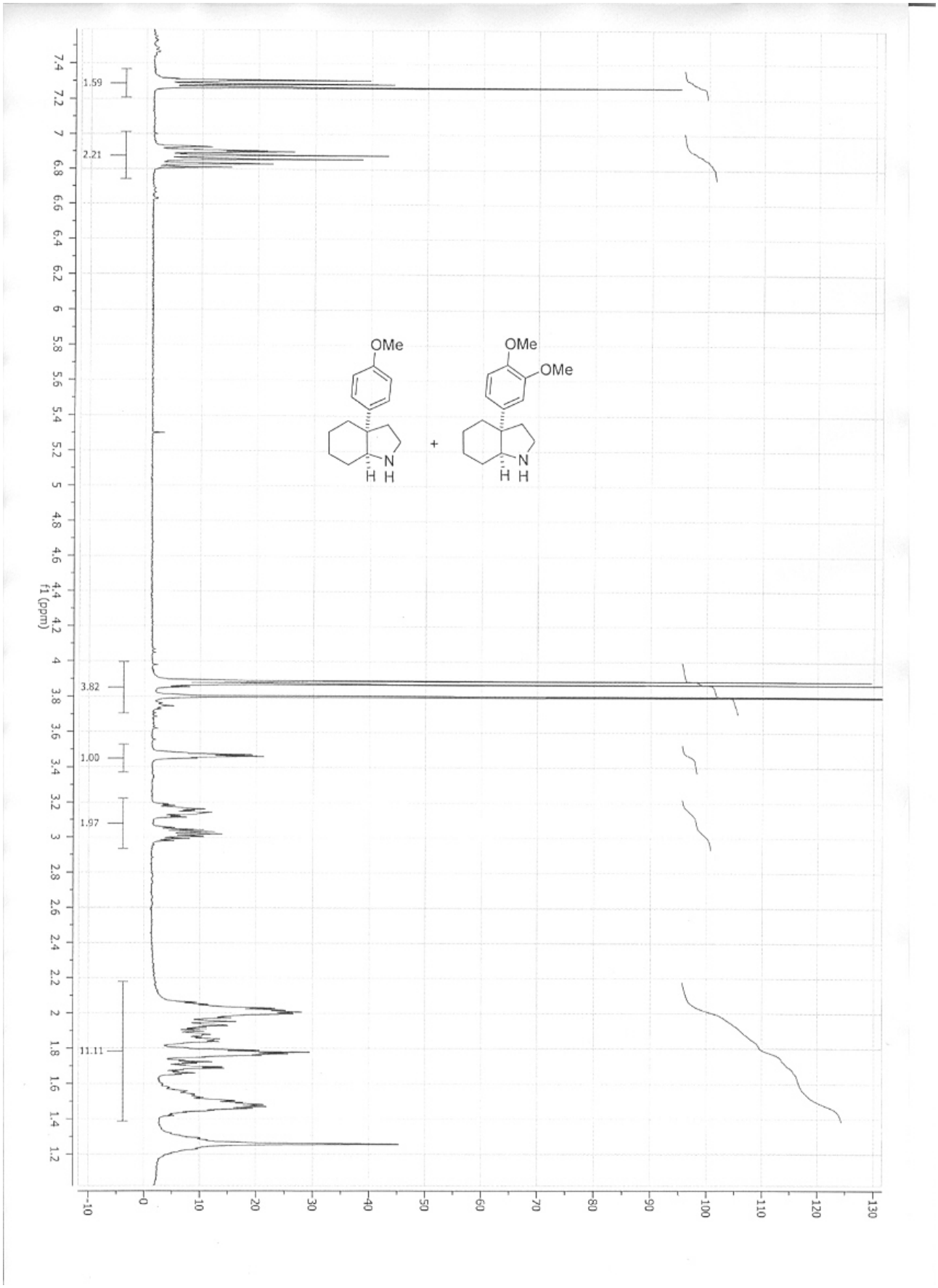
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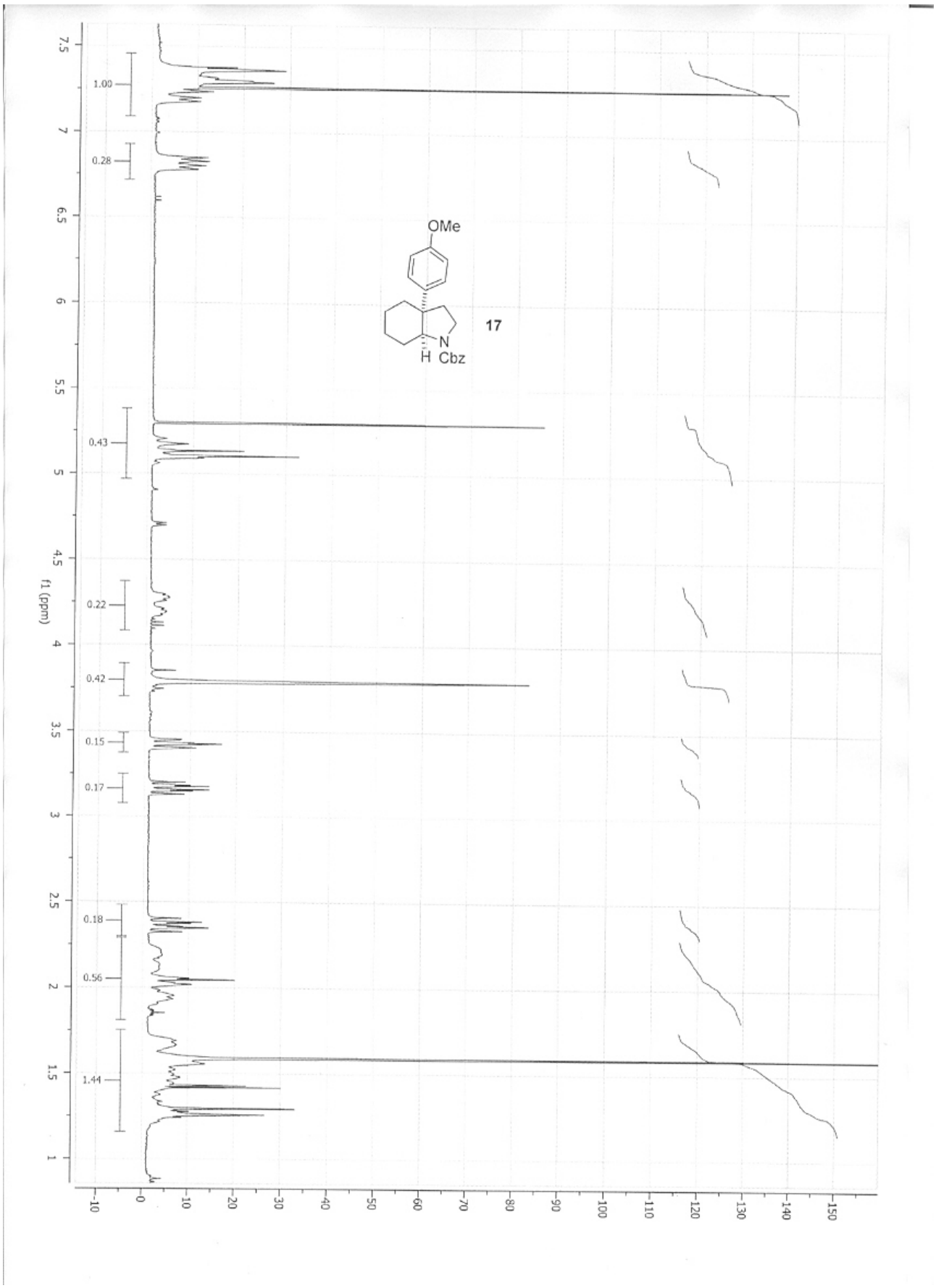
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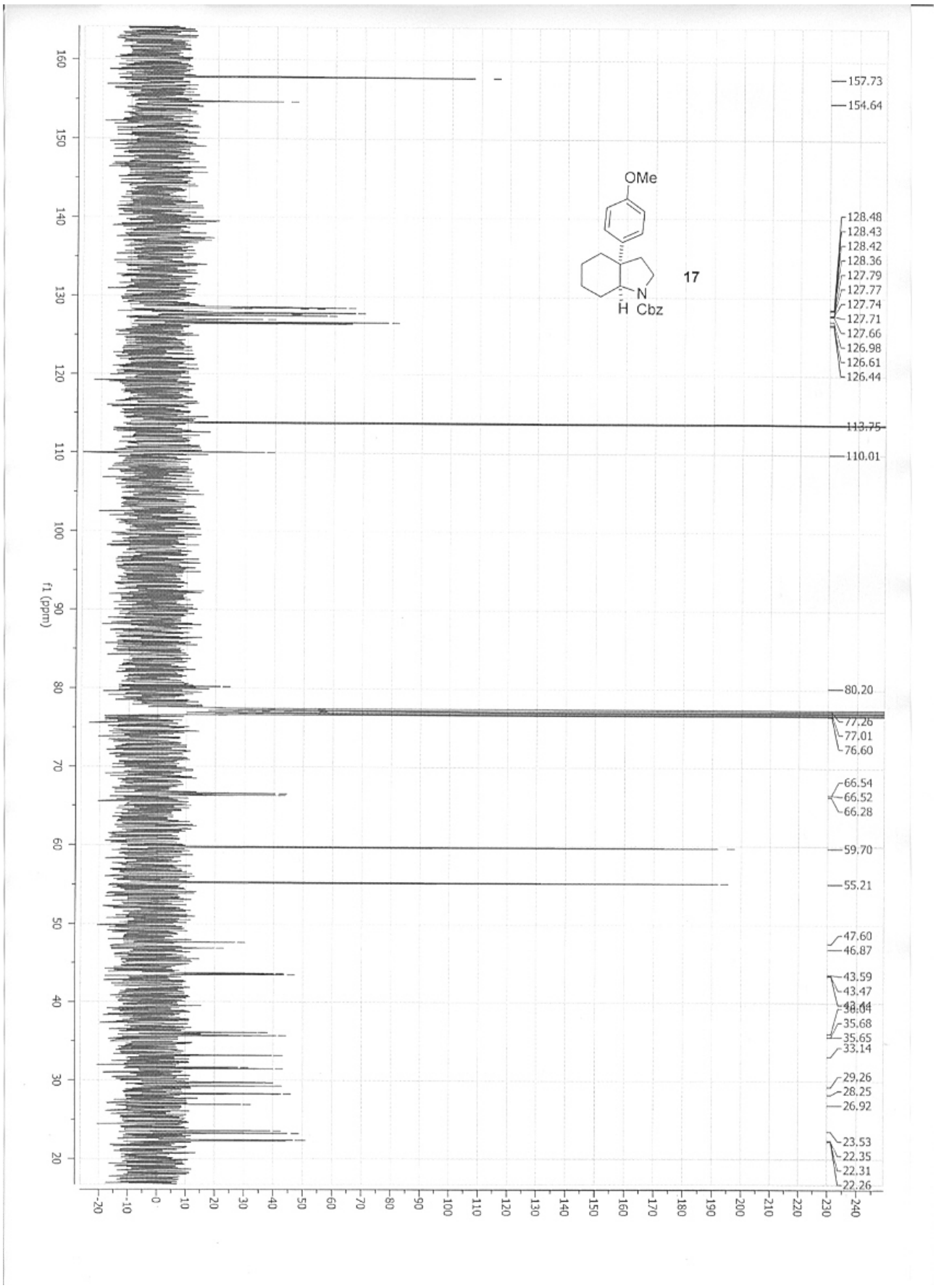
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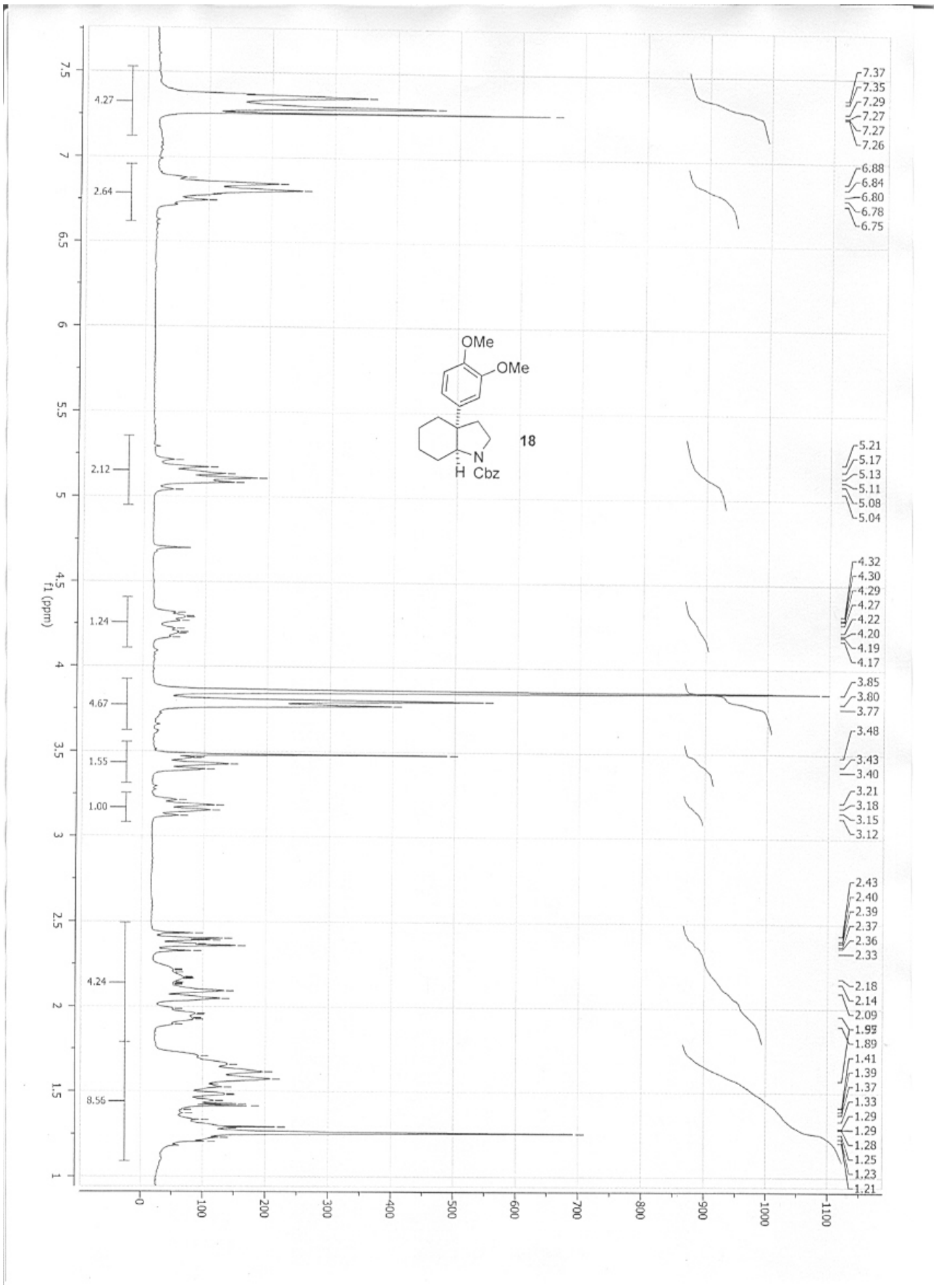
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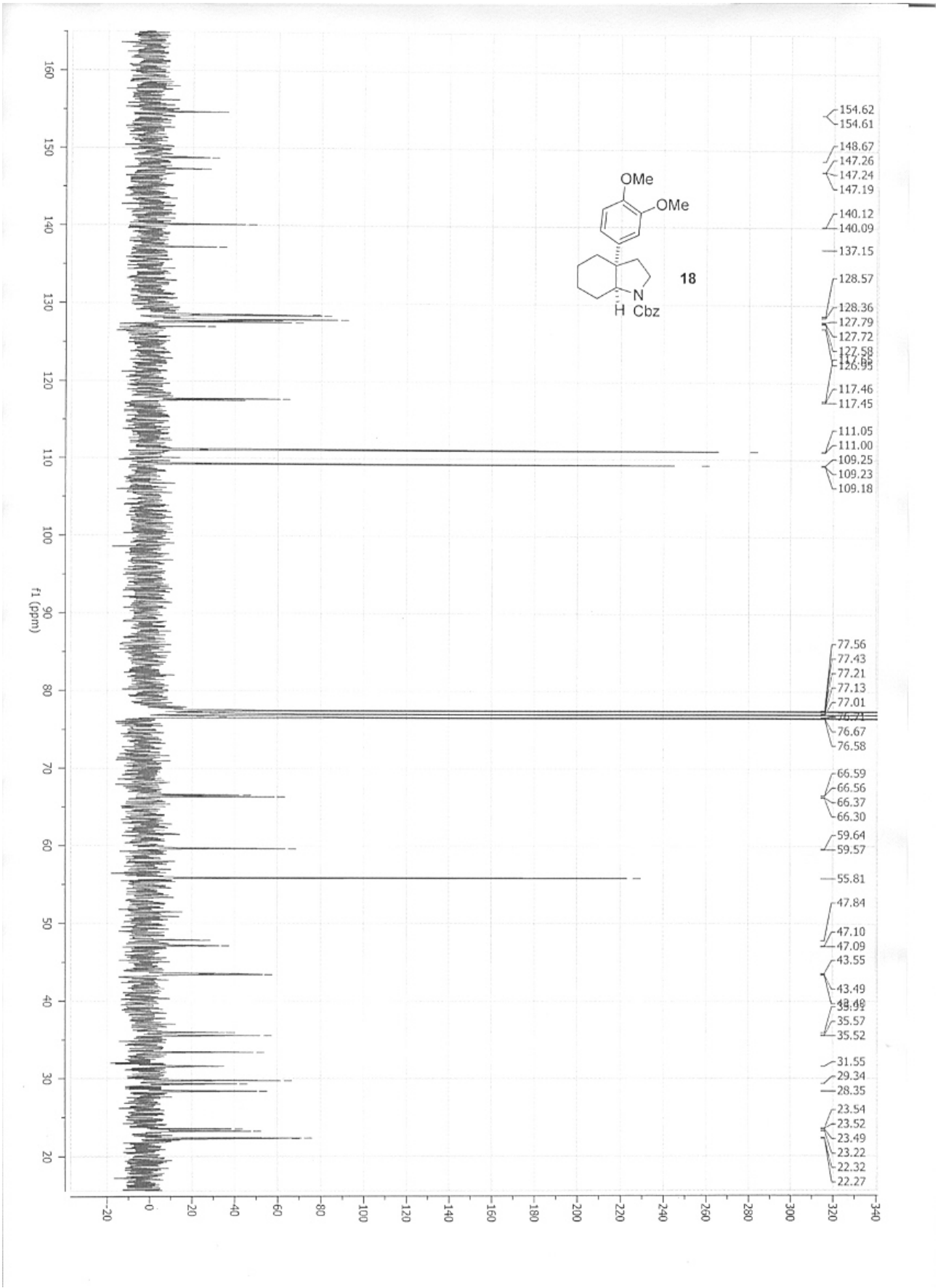
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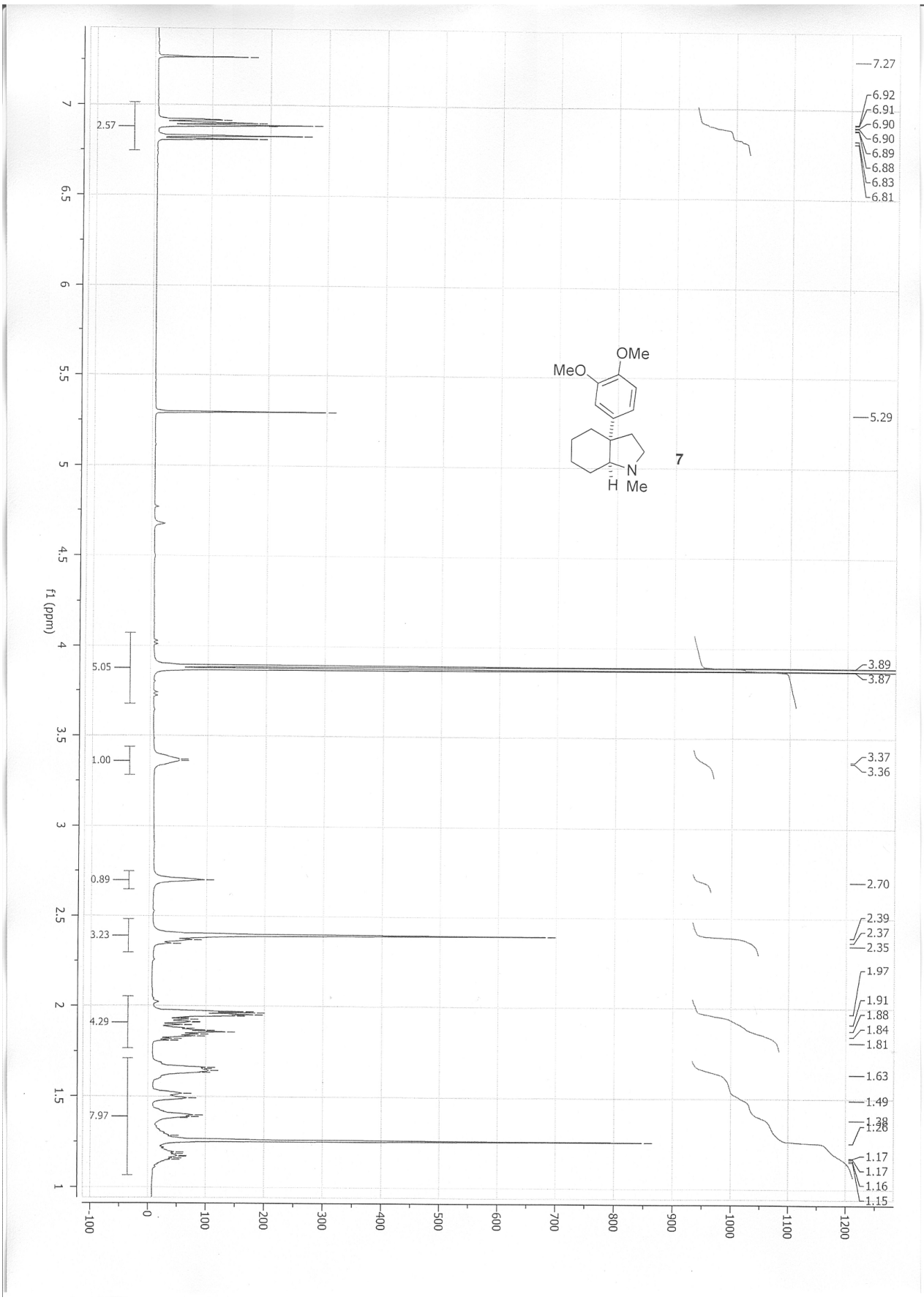
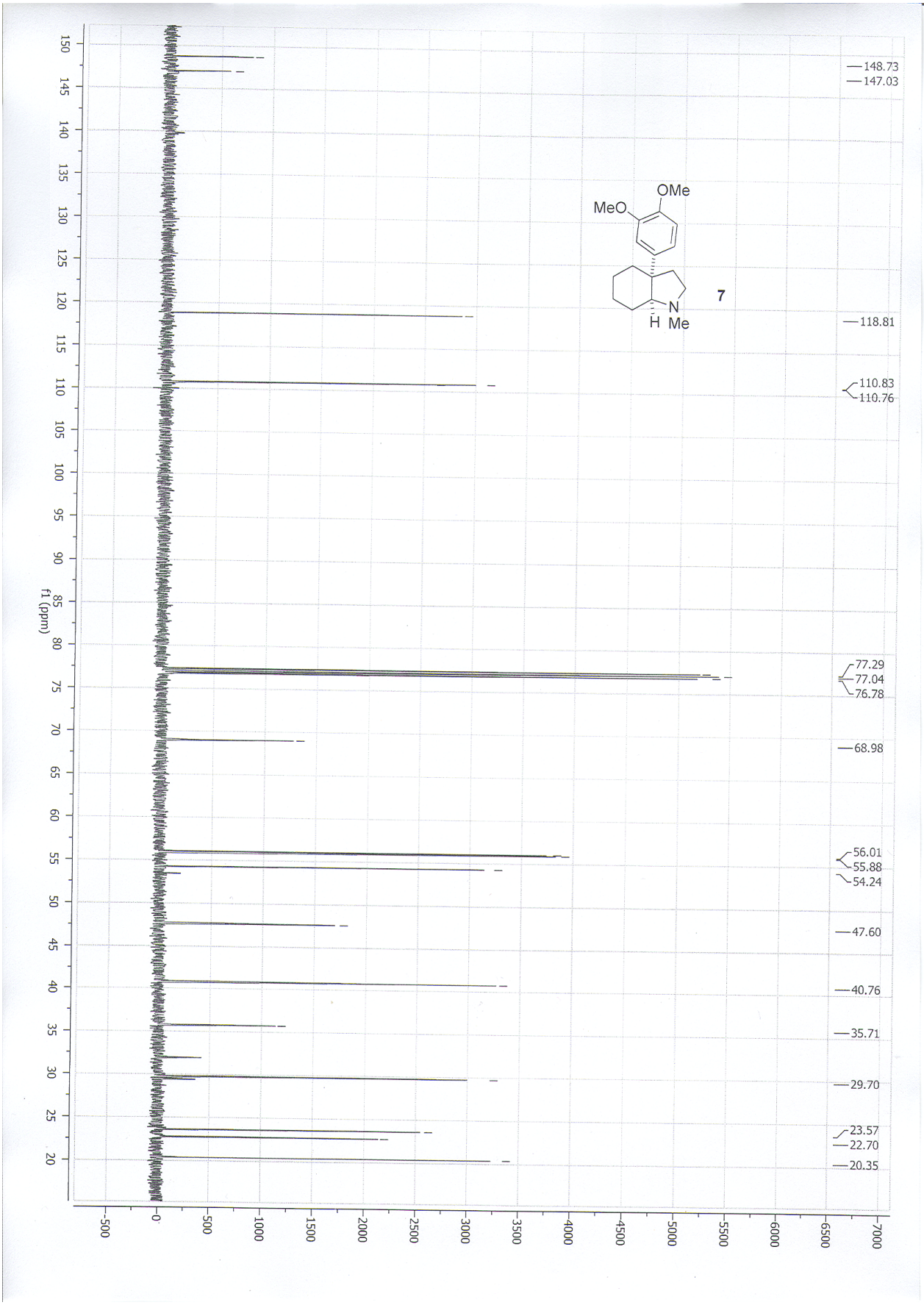
77.43
77.21
77.13
77.01
76.67
76.58
66.59
66.56
66.37
66.30
59.64
59.57
55.81
47.84
47.10
47.09
43.55
43.49
35.57
35.52
31.55
29.34
28.35
23.54
23.52
23.49
23.22
22.32
22.27
f1 (ppm)


7.27
6.92
6.91
6.90
6.90
6.89
6.88
6.83
6.81
5.29
3.89
3.87
3.37
3.36
2.70
2.39
2.37
2.35
1.97
1.91
1.88
1.84
1.81
1.63
1.49
1.38
1.26
1.17
1.17
1.16
1.15
2.57
5.05
1.00
0.89
3.23
4.29
7.97
OMe
MeO
N
H Me
7
f1 (ppm)


148.73
147.03
OMe
MeO
7
N
H Me
118.81
110.83
110.76
77.29
77.04
76.78
68.98
56.01
55.88
54.24
47.60
40.76
35.71
29.70
23.57
22.70
20.35
f1 (ppm)