Aryl-Aryl Coupling via Directed Lithiation and Oxidation

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Supporting Information

General Information: ^{1}H NMR Spectra were recorded on Bruker DPX 400 or 500 spectrometers in deuterochloroform operating at 400 and 500 MHz respectively. ^{13}C NMR Spectra were recorded on a Bruker 400 or 500 operating at 100 and 125 MHz respectively. Chemical shifts are quoted relative to residual solvent (7.26 ppm for $CHCl_3$ and 77.0 ppm for ^{13}C of $CDCl_3$, 2.54 ppm for DMSO and 40.45 ppm for ^{13}C of d_6-DMSO) and coupling constants (*J*) are given in Hz. The following abbreviations are used to indicate the multiplicity of signals: s singlet, d doublet, t triplet, q quartet, dd doublet of doublets, dt doublet of triplets, m multiplet and b broad. NMR spectra were acquired at 300 K unless otherwise indicated. High resolution mass spectroscopic (HRMS) analyses were measured on a Micromass Q-TOF or a Micromass LCT Premier spectrometer at the Department of Chemistry, University of Cambridge or on a Finnigan MAT 900 XLT or a Finnigan MAT 95XP spectrometer at the EPSRC National Mass Spectrometry Service Centre, Swansea.

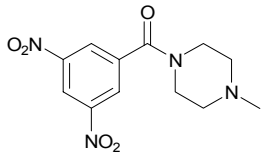
Infrared spectra were recorded on a Perkin Elmer 1 FT-IR Spectrometer fitted with an Attenuated Total Reflectance (ATR) sampling accessory as thin films or flattened solids. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}).

Optical rotations were recorded on a Perkin Elmer 343 polarimeter. $[\alpha]_D^{25}$ values are reported in 10^{-1} deg cm^2 g^{-1} at 589 nm, concentration (*c*) is given in $g(100mL)^{-1}$.

Melting points were determined on a Reichert hot stage apparatus and are uncorrected.

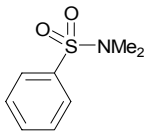
Full spectral data for all novel compounds are given below, all previously characterised compounds gave spectra consistent with the literature.

Except as otherwise indicated, reactions were carried out in oven-dried glassware under an atmosphere of nitrogen with dry, freshly distilled solvents. Tetrahydrofuran was distilled from $LiAlH_4$ with triphenylmethane as indicator. All chemicals were purchased from The Aldrich Chemical Company or Avocado. Copper(I) bromide-dimethyl sulfide complex was purified before use according to the procedure of House.[1] *i*PrMgCl solution was titrated with 1,10-phenanthroline and menthol before use. All flash chromatography was carried out using slurry-packed Merck 9385 Kieselgel 60 silca gel.

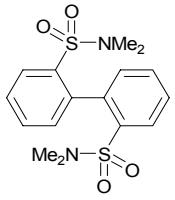


Synthesis of 3: 3,5-Dinitrobenzoic acid (21.2 g, 0.1 mol) was dissolved in thionyl chloride (100 mL), the solution heated at reflux for 10 h and then allowed to cool to 20 °C. Excess thionyl chloride was removed under reduced pressure and by azeotropic distillation with toluene. The residue was dissolved in chloroform (200 mL) and added dropwise to a stirred slurry of 1-methylpiperazine (12.0 g, 0.12 mol) and potassium carbonate (14 g, 0.1 mol) in chloroform (200 mL) at 0 °C. The reaction mixture was allowed to warm to 20 °C over 1 h and then washed with water (4 × 400 mL), dried (K_2CO_3) and the solvent removed under reduced pressure. The residue was recrystallized (hexanes) as yellow needles (20.4 g, 70%); mp 138-141 °C; ν_{max}(film)/cm^{-1} 1633, 1531, 1435, 1339, 1295, 1277, 1133, 995, 917,

908, 720, 681; δ_H (500 MHz; d_6-DMSO; 393 K) 8.87 (1 H, t, *J* 2.0), 8.56 (2 H, d, *J* 2.0), 3.54 (4 H, br), 2.42 (4 H, t, *J* 5.0), 2.27 (3 H, s); δ_C (125 MHz; d_6-DMSO; 393 K) 165.5, 149.1, 139.8, 127.6, 119.4, 54.7, 45.7; HRMS found ESI $[M+H]^+$ 295.1042, $[C_{12}H_{15}N_4O_5]^+$ requires 295.1043.

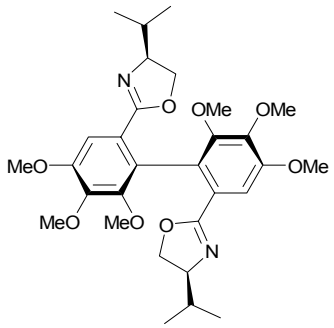


1d: Benzenesulfonyl chloride (20 mml, 2.6 mL) was added to a vigorously stirred solution of dimethylamine (22 mmol, 11 mL of 2 M solution in THF) in THF (10 mL) and water (10 mL) at 0 °C. The solution was allowed to warm to ambient temperature, the organic layer separated, washed with water and brine, dried ($MgSO_4$) and the solvent removed under reduced pressure. The residue was purified by recrystallization from hexane/toluene to yield the sulfonamide as white plates mp 45-47 °C (lit.,[2] 51-52 °C); ν_{max}(film)/cm^{-1} 1445, 133.2, 1164, 1090, 949, 731, 693, 682; δ_H (500 MHz; $CDCl_3$) 7.79 (2 H, dd, *J* 6.0, 1.0), 7.60 (1 H, td, *J* 6.0,1.5), 7.56 (2 H, td, *J* 6.5, 1.5), 2.72 (6 H, s); δ_C (125 MHz; $CDCl_3$) 135.5, 132.7, 129.0, 127.7, 37.9; HRMS found ESI $[M+H]^+$ 186.0583, $[C_8H_{11}O_2NS]^+$ requires 186.0583.



2d: mp 133-135 °C; ν_{max}(film)/cm^{-1} 1456, 1341, 1318, 1258, 1155, 1084, 1064, 953, 782, 772, 750, 734, 705, 680, 666; δ_H (500 MHz; $CDCl_3$) 7.91 (2 H, dd, *J* 8.0, 1.5), 7.50 (2 H, td, *J* 7.5, 1.5), 7.45 (2 H, td, *J* 7.5, 1.5), 7.29 (2 H, dd, *J* 7.5, 1.5), 2.52

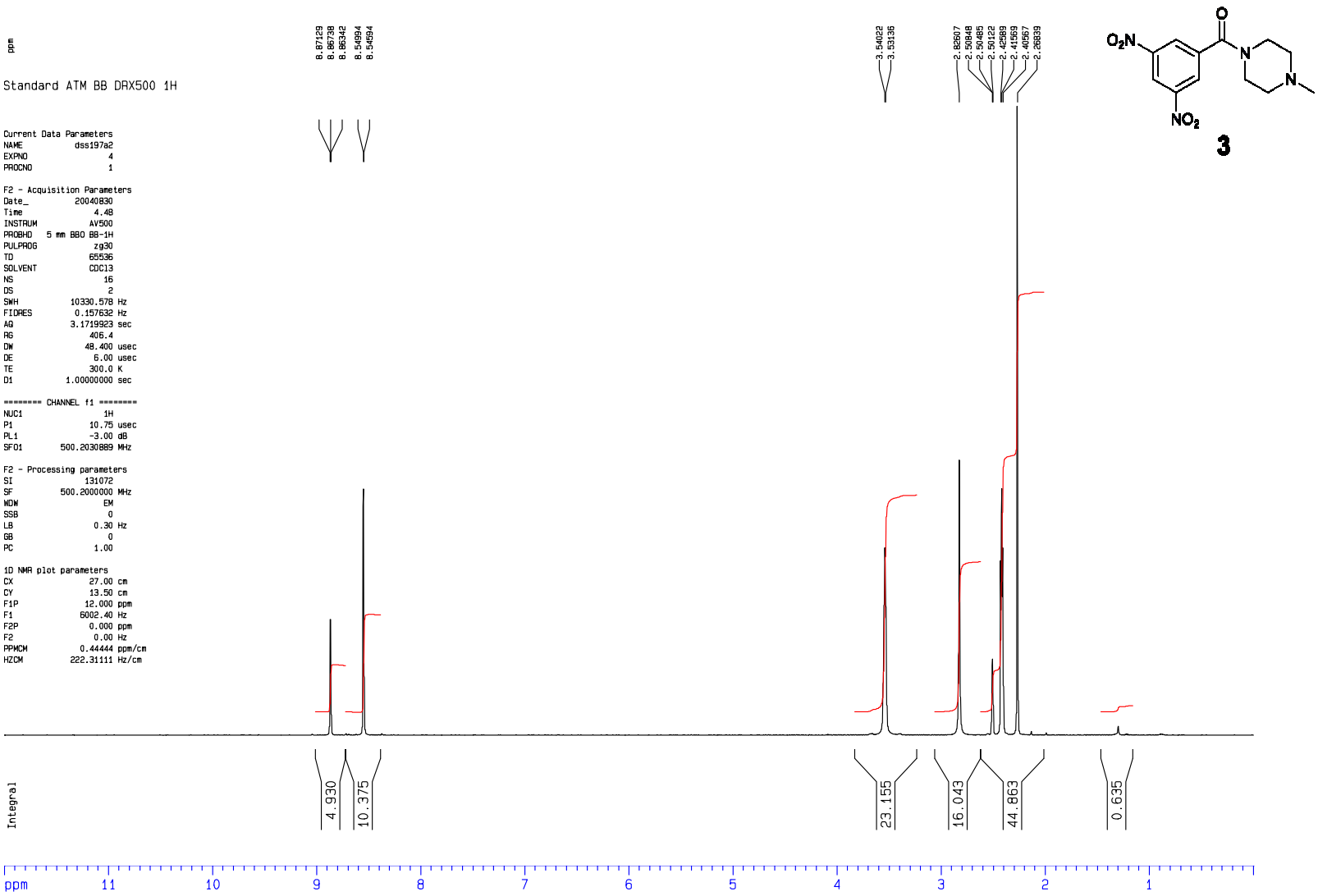
(12 H, s); δ_C (125 MHz; $CDCl_3$) 138.3, 137.2, 132.6, 131.2, 129.2, 128.1, 36.8; HRMS found ESI $[M+Na]^+$ 391.0746, $[C_{16}H_{20}O_4NaN_2S_2]^+$ requires 391.0757.



(*M*)-**5**:[3] $[\alpha]_D^{25}$ =−26.8 (*c* = 3.3, $CHCl_3$); ν_{max}(film)/cm^{-1} 2956, 1651, 1594, 1488, 1462, 1392, 1358, 1242, 1207, 1167, 1101, 1026, 1006, 983, 923, 751; δ_H (500 MHz; $CDCl_3$) 7.14 (2 H, s), 4.03 (2 H, t, *J* 8.0), 3.91 (6 H, s), 3.90 (6 H, s), 3.77 (2 H, m), 3.74 (2 H, q, *J* 7.5), 3.69 (6 H, s), 1.54 (2 H, septet, *J* 6.5), 0.74 (6 H, d, *J* 7.0), 0.73 (6 H, d, *J* 7.0);δ_C (125 MHz; $CDCl_3$) 163.4, 152.3, 152.0, 143.9, 125.4, 123.4, 107.9, 72.5, 70.0, 60.7, 60.4, 56.0, 31.9, 18.7, 18.2; HRMS found ESI $[M+Na]^+$ 579.2682, $[C_{30}H_{40}O_8NaN_2]^+$ requires 579.2785.

References

1. H. O. House, C.-Y. Chu, J. M. Wilkins, M. J. Umen, *J. Org. Chem.*, **1975**, *40*, 1460.
2. V. I. Naddaka, K. V. Avanesyan, M. L. Cherkinskaya, V. I. Minkin, *J. Org. Chem. USSR*, **1987**, *23*, 801.
3. For spectral data of the diastereoisomer see T. D. Nelson, A. I. Meyers, *J. Org. Chem.*, **1994**, *59*, 2577.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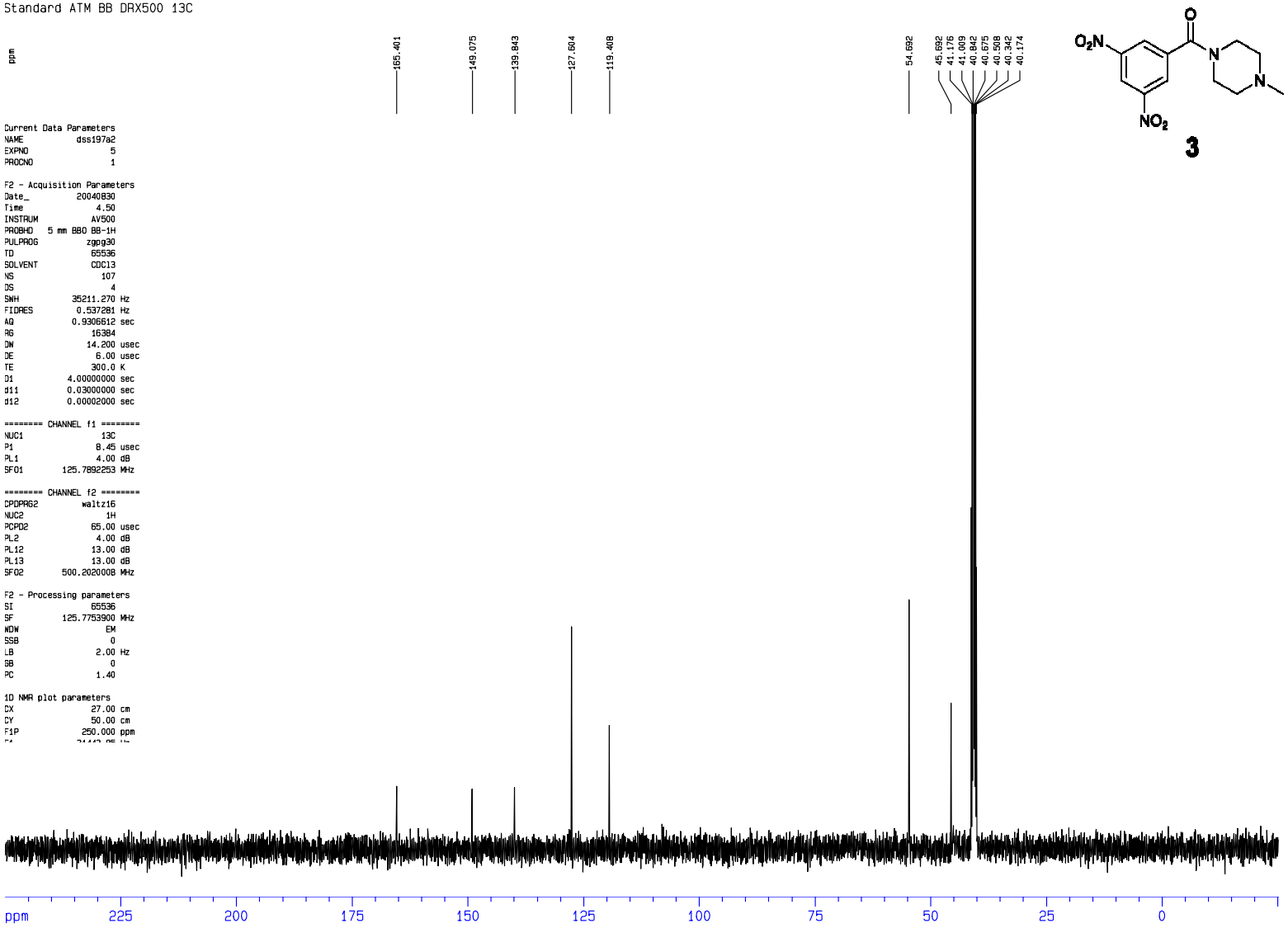

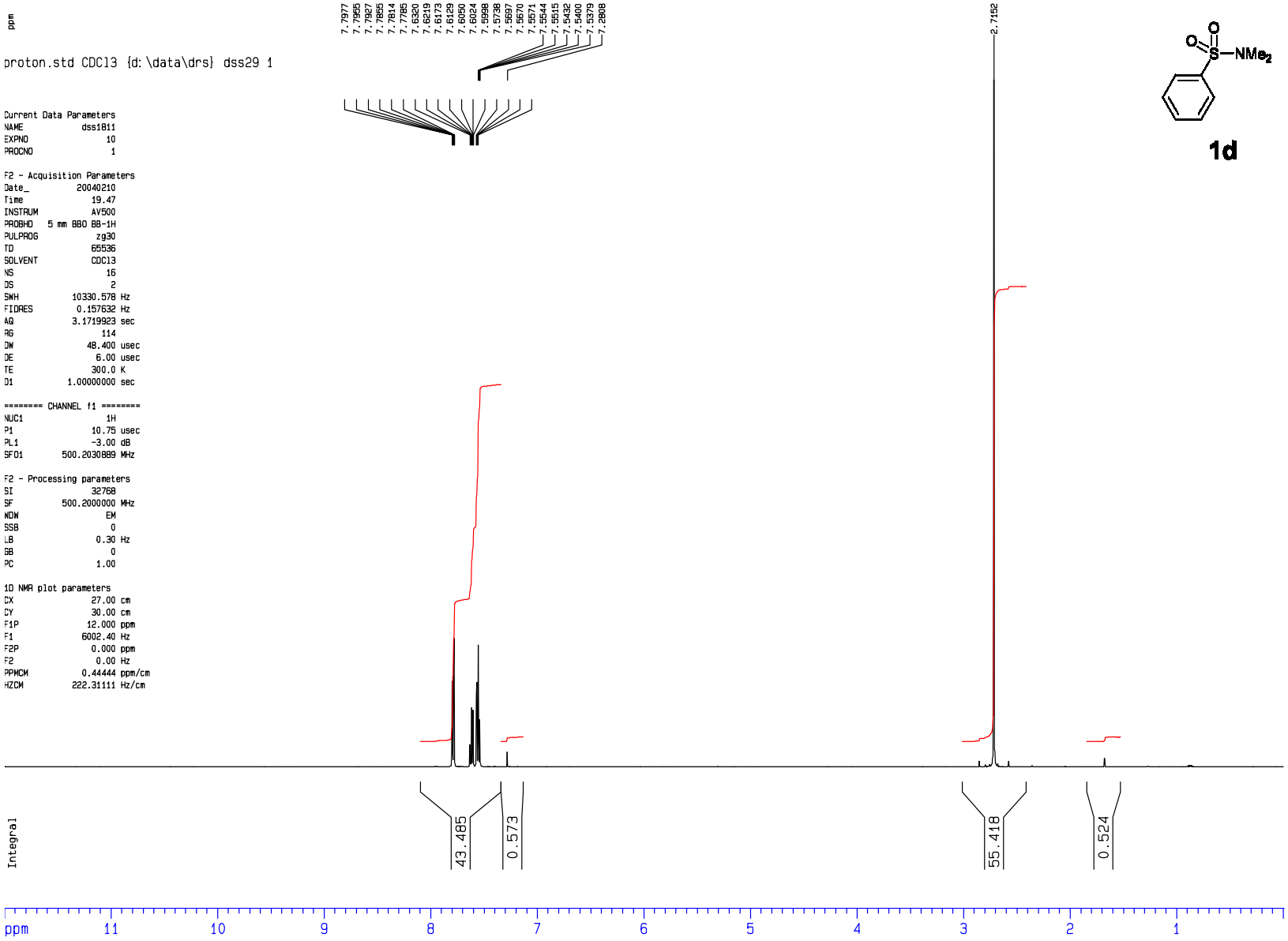
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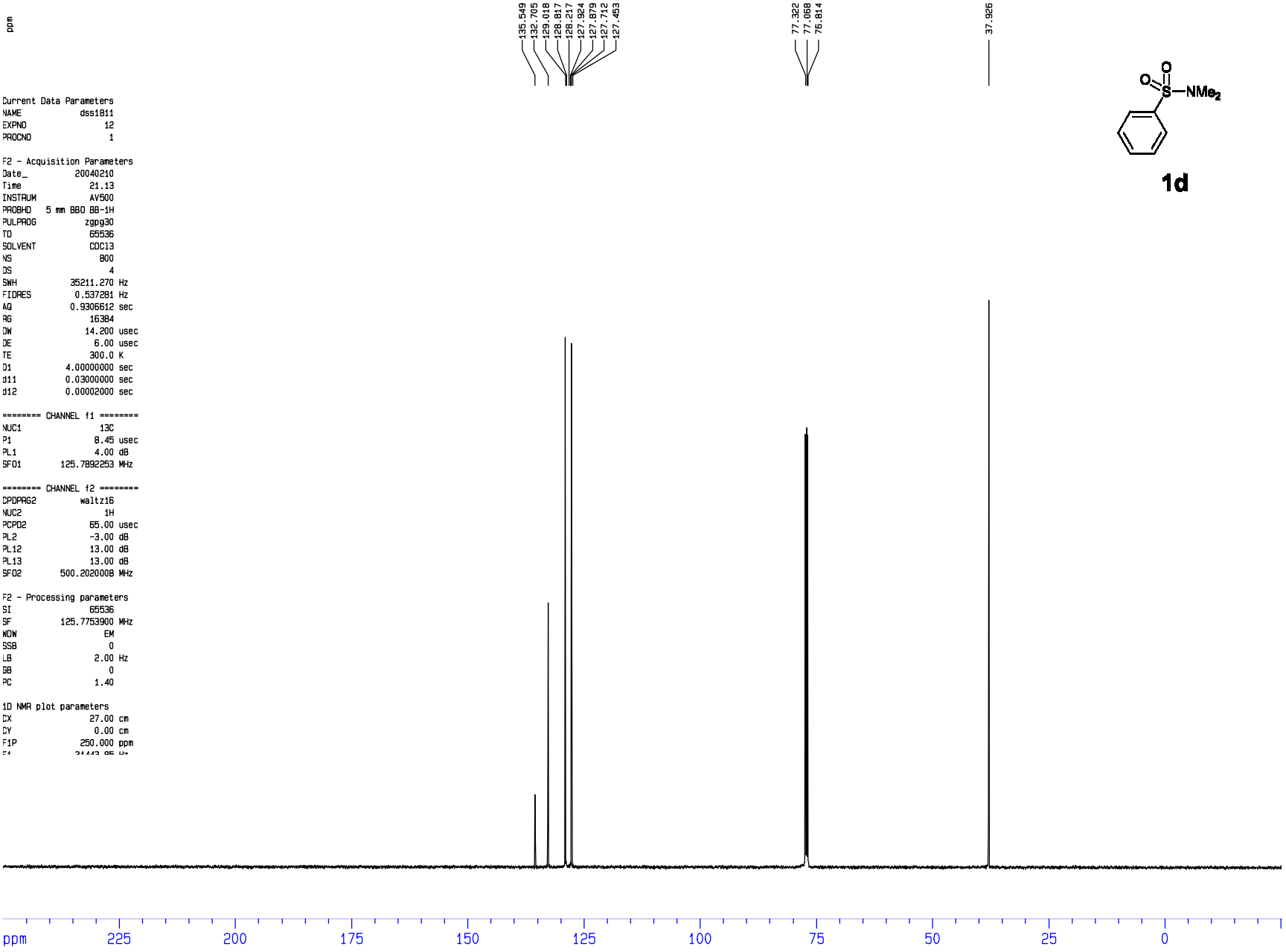

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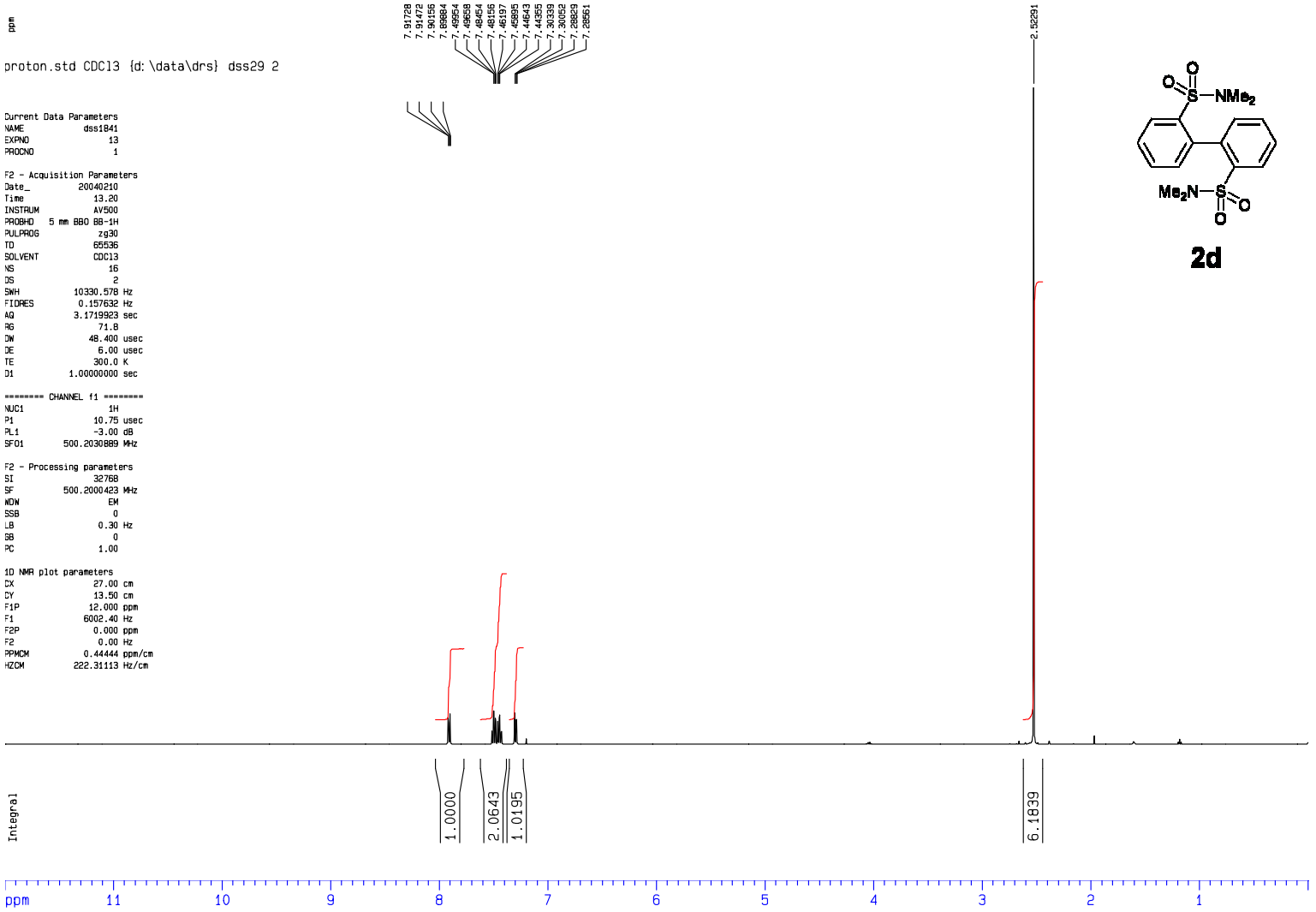
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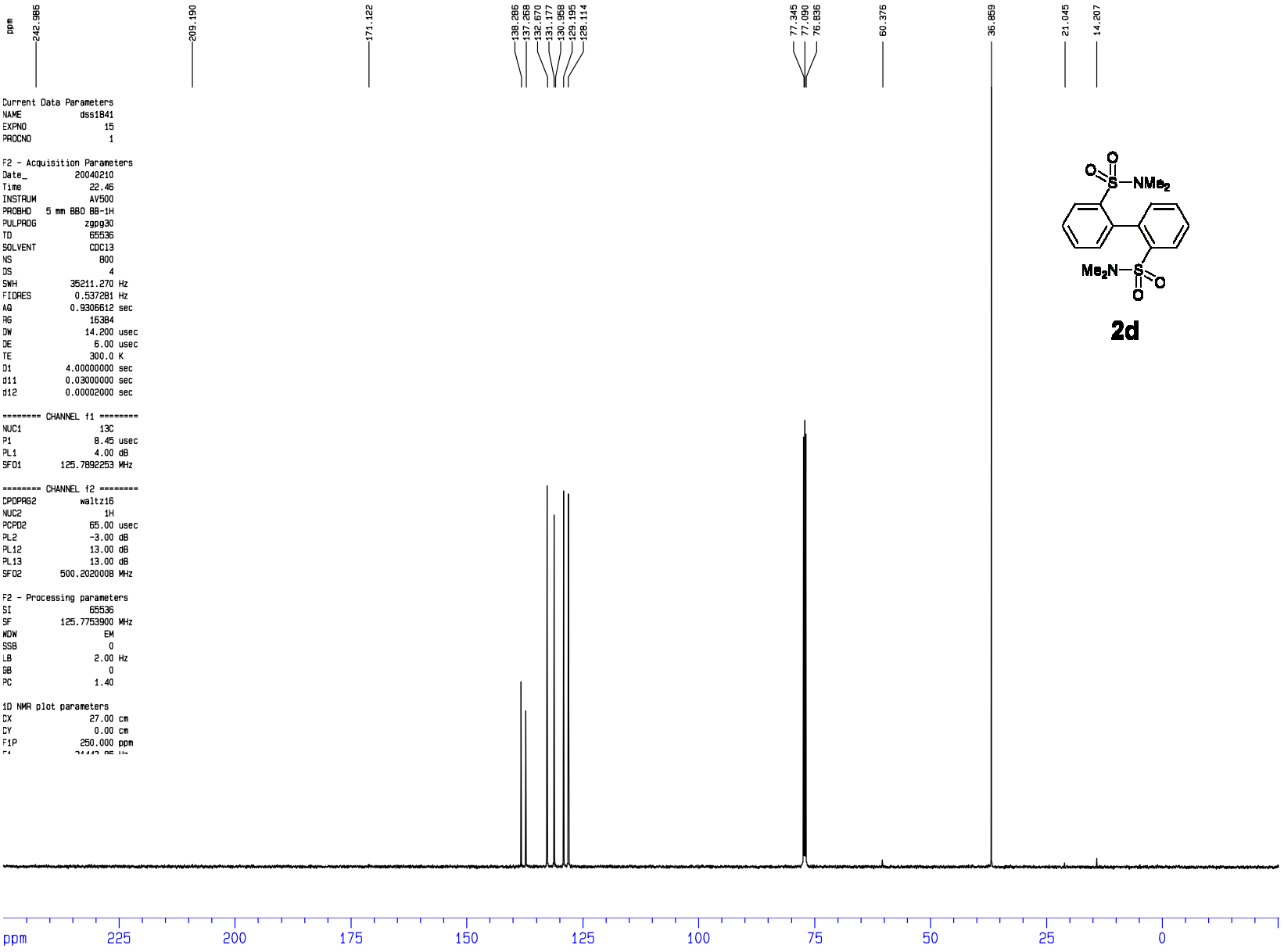


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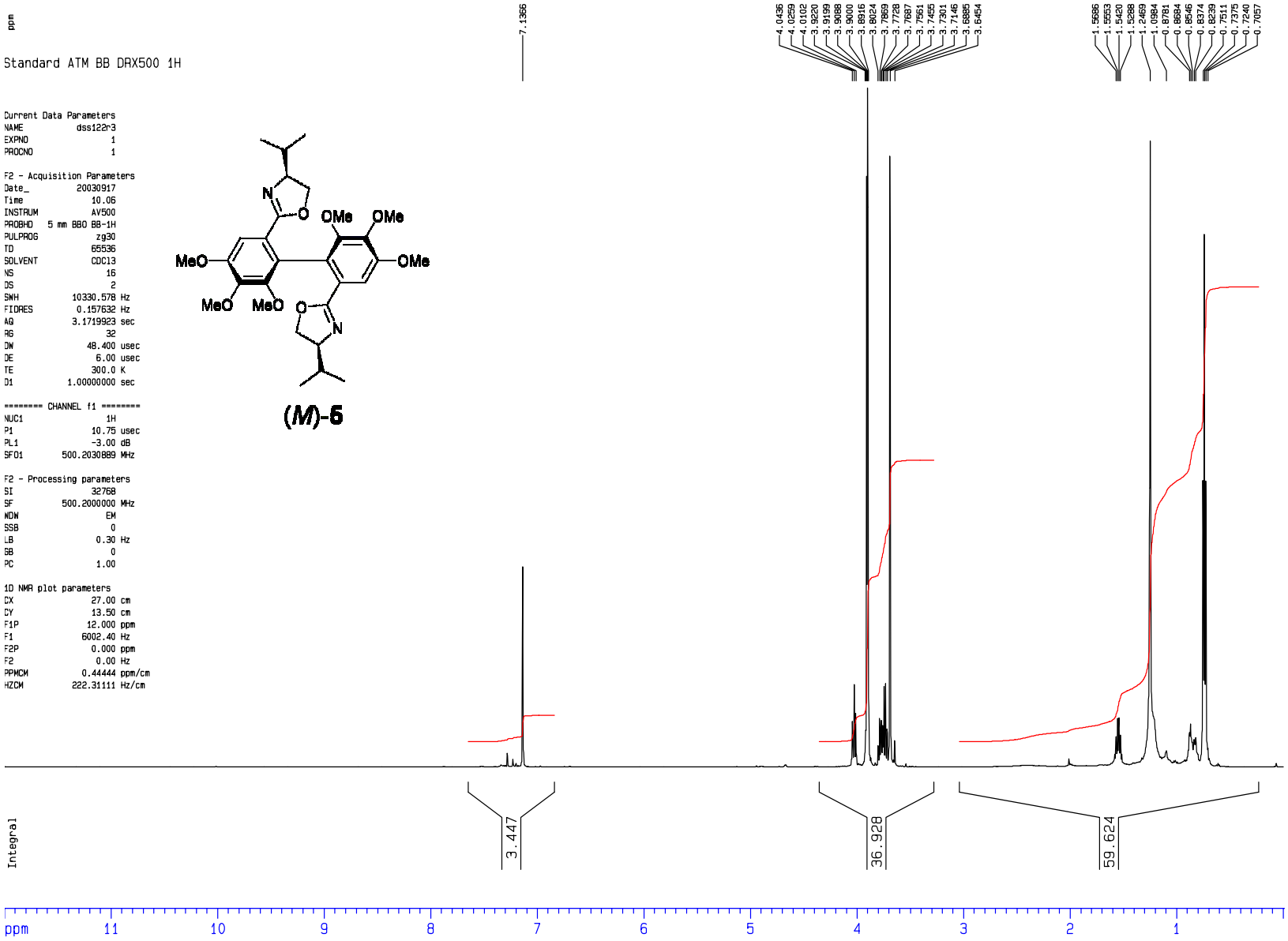
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