

Rhodium-catalyzed Methylthio Transfer Reaction Between Ketone α -Positions

Reversible Single Bond Metathesis of C-S and C-H Bonds

Mieko Arisawa, Katsunori Suwa, and Masahiko Yamaguchi^{*†}

Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences,

Tohoku University, Aoba, Sendai, 980-8578, Japan

[†]*WPI Advanced Institute for Materials Research, Tohoku University, Aoba, Sendai, Japan*

Supplementary Materials

¹H-NMR, ¹³C-NMR spectra were recorded on a Varian Mercury (400 MHz) and JEOL JNM-ECA600 (600 MHz). IR spectra were measured on a JASCO FT/IR-410 spectrophotometer. Melting points were determined with a Yanagimoto micro melting point apparatus without correction. High- and low-resolution mass spectra were measured on a JEOL JMS-DX-303 or a JEOL JMS-AX-500. Merck silica gel 60 (63-200 mm) was employed for flash column chromatography.

Substrates

(2*R,4*S**)-4-(*t*-Butyl)-2-phenylthiocyclohexanone *ax*-1**¹ Under an argon atmosphere, to a stirred solution of diisopropylamine (55 mmol, 7.8 mL) in THF (80 mL) at -78°C was added dropwise a solution of 1.6 M butyllithium in hexane (48 mmol, 30 mL), and the mixture was stirred at the temperature for 30 min. The mixture was warmed to 0 °C, and stirred for additional 30 min at 0°C. After cooled to -78 °C, a solution of 4-(*t*-butyl)cyclohexanone (40 mmol, 6.17 g) in THF (10 mL) was added. The mixture was stirred for 30 min, and then diphenyl disulfide (42 mmol, 9.17 g) in THF (20 mL) was added at -78°C. The mixture was warmed to room temperature, and stirred overnight. The reaction was quenched with saturated aqueous NH₄Cl, and the organic materials were extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated. The residue was purified by flash column chromatography (hexane / ethyl acetate = 50) to give *ax*-1 (4.46 g, 43%). Colorless crystals. Mp 51-52°C (hexane). ¹H-NMR (400 MHz, CDCl₃) δ 0.925 (9H, s), 1.40-1.51 (1H, ddd, *J* = 4.0, 12.4, 13.6 Hz, 5ax), 1.87 (1H, tt, *J* = 2.8, 12.4 Hz, 4ax), 1.94 (1H, dt, *J* = 4.8, 12.8 Hz, 3ax), 2.07-2.14 (1H, m, 5eq), 2.23-2.28 (1H, dq, *J* = 14.4, 2.0 Hz, 6eq), 2.28-2.34 (1H, dq, *J* = 14.0, 2.8 Hz, 3eq), 3.13 (1H, dt, *J* = 6.4, 14.4 Hz, 6ax), 3.75 (1H, quintet, broad, *J* = 2.0 Hz, 2eq), 7.22-7.31 (3H, m), 7.39 (2H, d, *J* = 7.2 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 27.5, 27.9, 32.2, 33.8, 36.6, 41.6, 54.7, 127.5, 129.1, 131.4, 133.9, 208.8. IR (KBr) 3394, 3074, 2951, 2862, 1710, 1583, 1482, 1438, 1366, 1327, 1252, 1219, 1143, 1085, 1026, 943, 746, 689 cm⁻¹. MS (EI) *m/z* 262 (M⁺, 100%), 205 (M⁺-C₄H₉, 24%). HRMS Calcd for C₁₆H₂₂OS: 262.1390. Found: 262.1371.

(1-Adamantyl) phenylthiomethyl ketone² Colorless crystals. Mp 60-62°C (hexane). Lit. 59-60°C. ¹H-NMR (400 MHz, CDCl₃) δ 1.67-1.77 (6H, quatlet, broad, *J* = 12.4 Hz), 1.86 (6H, s, broad), 2.05 (3H, s, broad, *J* = 2.4, 12.4 Hz), 3.93 (2H, s), 7.20 (1H, dt, *J* = 1.2, 6.8 Hz), 7.27 (2H, dt, *J* = 2.0, 6.8 Hz), 7.36 (2H, dd, *J* = 1.2, 7.2 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 27.8, 36.4, 38.4, 40.2, 46.5, 126.6, 128.9, 129.9, 135.6, 208.9. IR (KBr) 3054, 2903, 2846, 1691, 1580, 1478, 1402, 1343, 1278, 1152, 1092, 1010, 735, 688 cm⁻¹. MS (EI) *m/z* 286 (M⁺, 25%), 135 (M⁺-C₈H₇OS, 100%). HRMS Calcd for C₁₈H₂₂OS: 286.1390. Found: 286.1385.

***t*-Butyl phenylthiomethyl ketone**³ Colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 1.19 (9H, s), 3.96 (2H, s), 7.21 (1H, t, *J* = 7.2 Hz), 7.29 (2H, t, *J* = 7.2 Hz), 7.37 (2H, d, *J* = 7.2 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.6, 40.6, 44.3, 126.8, 129.0, 130.2, 135.5, 209.5. IR (neat) 2967, 1707, 1479, 1059, 740 cm⁻¹. MS (EI) *m/z* 208 (M⁺, 100%), 57 (M⁺-C₈H₇OS, 84%). HRMS Calcd for C₁₂H₁₆OS: 208.0922. Found: 208.0910.

1-Methylcyclohexyl α -phenylthiomethyl ketone Colorless crystals. Mp 35.5-36.5°C (hexane). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.12 (3H, s), 1.33-1.46 (6H, m), 1.52-1.57 (2H, m), 1.93-1.98 (2H, m), 1.98 (2H, s), 7.21 (1H, t, J = 8.0 Hz), 7.28 (2H, td, J = 8.0, 1.2 Hz), 7.38 (2H, dd, J = 1.2, 8.0 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 22.7, 24.7, 25.7, 34.7, 40.9, 48.4, 126.6, 128.9, 130.1, 135.7, 209.4. IR (neat) 3059, 2931, 2856, 1704, 1456, 1013 cm^{-1} . MS (EI) m/z 248 (M^+ , 40%), 97 ($\text{M}^+ - \text{C}_8\text{H}_7\text{OS}$, 100%). HRMS Calcd for $\text{C}_{15}\text{H}_{20}\text{OS}$: 248.1235. Found: 248.1223.

***p*-Methoxyphenyl phenylthiomethyl ketone 7⁴** Colorless crystals. Mp 87-88°C (hexane). Lit. 85-85.5°C. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.88 (3H, s), 4.24 (2H, s), 6.93 (2H, ddd, J = 2.0, 2.8, 9.2 Hz), 7.22 (1H, t, J = 7.6 Hz), 7.28 (2H, t, J = 6.8 Hz), 7.39 (2H, d, J = 7.2 Hz), 7.93 (2H, ddd, J = 2.0, 2.8, 8.8 Hz). $^{13}\text{C-NMR}$ (150 MHz, CDCl_3) δ 41.0, 55.5, 113.9, 127.0, 128.4, 129.0, 130.4, 131.1, 135.1, 163.8, 192.7. IR (neat) 3060, 2925, 2846, 1670, 1599, 1575, 1509, 1260, 1172, 1024, 831, 740, 690 cm^{-1} . MS (EI) m/z 258 (M^+ , 7%), 135 ($\text{M}^+ - \text{C}_7\text{H}_7\text{S}$, 100%). HRMS Calcd for $\text{C}_{15}\text{H}_{14}\text{O}_2\text{S}$: 258.0714. Found: 258.0700.

***p*-Cyano- α -methylthioacetophenone 2a** To a stirred solution of diisopropylamine (55 mmol, 7.8 mL) in THF (80 mL) was added dropwise a solution of 1.6 M butyllithium in hexane (48 mmol, 30 mL), and the mixture was stirred for 30 min at the temperature. The mixture was warmed to 0 °C, and stirred for additional 30 min. After cooled to -78 °C, a solution of *p*-cyanoacetophenone (40 mmol, 5.84 g) in THF (10 mL) was added at -78°C. The mixture was stirred for 30 min, and then dimethyl disulfide (42 mmol, 3.78 mL) and HMPA (80 mmol, 13.9 mL) were added at -78°C. The mixture was warmed to room temperature, and stirred overnight. The reaction was quenched with saturated aqueous NH_4Cl , and the organic materials were extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated. The residue was purified by flash column chromatography (hexane / ethyl acetate = 10) to give **2a** (3.65 g, 48%). Colorless crystals. Mp 47-48°C (hexane). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.12 (3H, s), 3.75 (2H, s), 7.78 (2H, ddd, J = 1.6, 2.0, 8.4 Hz), 8.07 (2H, ddd, J = 1.6, 2.0, 8.4 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.7, 38.9, 116.5, 117.8, 129.2, 132.5, 138.2, 192.1. IR (KBr) 3326, 3093, 3076, 2989, 2929, 2231, 1672, 1604, 1562, 1423, 1402, 1272, 1142, 852, 774, 669 cm^{-1} . MS (EI) m/z 191 (M^+ , 52%), 130 ($\text{M}^+ - \text{C}_2\text{H}_5\text{S}$, 100%). HRMS Calcd for $\text{C}_{10}\text{H}_9\text{NOS}$: 191.0404. Found: 191.0377.

***p*-Trifluoromethyl- α -methylthioacetophenone 2b⁶** Colorless oil. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.13 (3H, s), 3.77 (2H, s), 7.74 (2H, d, J = 8.0 Hz), 8.09 (2H, d, J = 8.0 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.8, 39.0, 123.5 (q, J = 271.3 Hz), 125.7 (q, J = 3.0 Hz), 129.1, 134.5 (q, J = 32.6 Hz), 137.8, 192.7. IR (neat) 2923, 1682, 1328, 1130, 1067 cm^{-1} . MS (EI) m/z 234 (M^+ , 33%), 173 ($\text{M}^+ - \text{C}_2\text{H}_5\text{S}$, 100%). HRMS Calcd for $\text{C}_{10}\text{H}_9\text{F}_3\text{OS}$: 234.0326. Found: 234.0313.

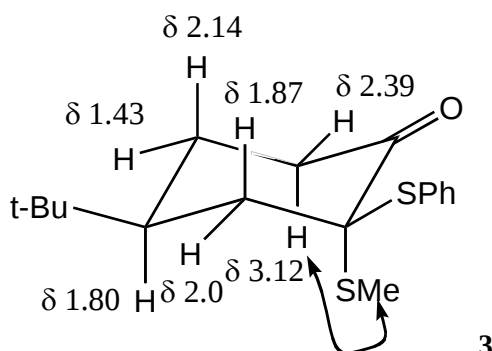
***p*-Chloro- α -methylthioacetophenone 2c⁷** Colorless oil. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.12 (3H, s), 3.72 (2H, s), 7.43 (2H, ddd, J = 2.0, 2.4, 9.2 Hz), 7.92 (2H, ddd, J = 2.0, 2.4, 8.8 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.7, 38.8, 128.8, 130.1, 133.3, 139.6, 192.6. IR (neat) 3066, 2981, 2919, 1674, 1588, 1420, 1398, 1273, 1092, 1011, 845, 763, 526 cm^{-1} . MS (EI) m/z 200 (M^+ , 25%), 139 ($\text{M}^+ - \text{C}_2\text{H}_5\text{S}$, 100%). HRMS Calcd for $\text{C}_9\text{H}_9\text{ClOS}$: 200.0062. Found: 200.0035.

α -Methylthioacetophenone 2d⁴ Colorless oil. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.13 (3H, s), 3.76 (2H, s), 7.47 (2H, t, J = 7.6 Hz), 7.57 (1H, t, J = 7.6 Hz), 7.98 (2H, d, J = 7.6 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.8, 38.9, 128.56, 128.65, 133.2, 135.1, 193.9. IR (neat) 3060, 2980, 2918, 1673, 1579, 1447, 1278, 1199, 1020, 688 cm^{-1} . MS (EI) m/z 166 (M^+ , 30%), 105 ($\text{M}^+ - \text{C}_2\text{H}_5\text{S}$, 100%). HRMS Calcd for $\text{C}_9\text{H}_{10}\text{OS}$: 166.0452. Found: 166.0442.

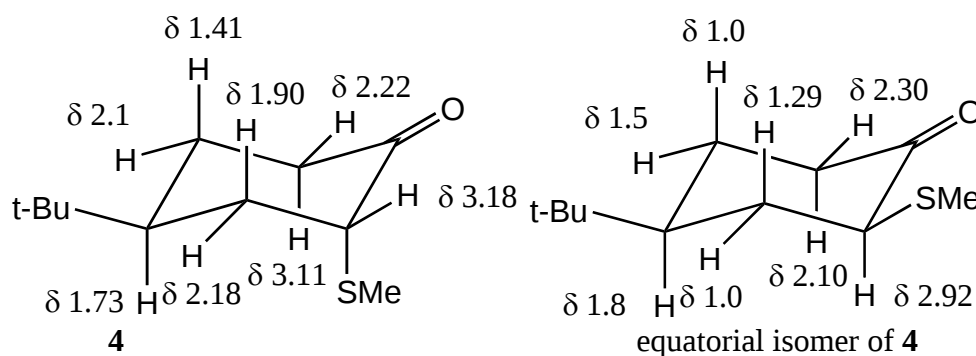
***p*-Methoxy- α -methylthioacetophenone 2e⁴** Colorless oil. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.14 (3H, s), 3.72 (2H, s), 3.87 (3H, s), 6.94 (2H, ddd, J = 2.0, 2.8, 9.6 Hz), 7.95 (2H, ddd, J = 2.0, 2.8, 9.6 Hz). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 15.8, 38.8, 55.4, 113.7, 128.1, 131.0, 163.6, 192.8. IR (neat) 2968, 2918, 2839, 1666, 1600, 1575, 1511, 1422, 1312, 1283, 1259, 1173, 1024, 845, 557 cm^{-1} . MS (EI) m/z 196 (M^+ , 10%), 135 ($\text{M}^+ - \text{C}_2\text{H}_5\text{S}$, 100%). HRMS Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$: 196.0557. Found: 196.0541.

Typical procedures for methylthiolation In a two-necked flask equipped with a reflux condenser were placed tetrakis(triphenylphosphine)hydriderrhodium (4 mol%, 5.8 mg), 1,2-bis(diphenylphosphino)ethane (8

mol%, 4.0 mg), *p*-cyano- α -methylthioacetophenone **2a** (0.125 mmol, 23.9 mg), and (2*R**,4*S**)-4-(*t*-butyl)-2-phenylthiocyclohexanone **ax-1** (0.625 mmol, 162.6 mg) in THF (0.5 mL) under an argon atmosphere, and the solution was heated at 90 °C for 4 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel giving (2*R**,4*S**)-4-(*t*-butyl)-2-methylthio-2-phenylthiocyclohexanone **3** (16.6 mg, 43%), **ax-1** (90.5 mg, 55%), **eq-1** (59.3 mg, 37%), *p*-cyanoacetophenone **5a** (15.3 mg, 84%), 4-(*t*-butyl)-2-methylthiocyclohexanone **4** (0.9 mg, 1%), *p*-cyanophenyl di(methylthio)methyl ketone **6a** (1.2 mg, 4%), and **2a** (2.6 mg, 11%). **3**: Colorless crystals. Mp 100-102°C (hexane). ¹H-NMR (400 MHz, CDCl₃) δ 0.774 (9H, s), 1.43 (1H, dq, *J* = 13.2, 4.4 Hz), 1.80 (1H, tt, *J* = 2.8, 12.4 Hz), 1.87 (1H, td, *J* = 3.2, 10.8 Hz), 1.98-2.05 (1H, m), 2.05 (1H, dd, *J* = 12.8, 14.0 Hz), 2.14 (3H, s), 2.39 (1H, ddd, *J* = 2.8, 4.4, 15.2 Hz), 3.12 (1H, dt, *J* = 6.0, 15.2 Hz), 7.32-7.42 (3H, m), 7.51 (2H, dd, *J* = 1.6, 6.4 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 13.0, 27.0, 27.3, 32.2, 36.6, 41.5, 42.4, 69.7, 128.4, 129.1, 130.2, 137.3, 203.3. IR (KBr) 3053, 2959, 2872, 1696, 1471, 1438, 1411, 1304, 1267, 1232, 1147, 752, 694 cm⁻¹. MS (EI) *m/z* 308 (M⁺, 8%), 199 (M⁺-C₆H₅S, 100%). HRMS Calcd for C₁₇H₂₄OS₂: 308.1269. Found: 308.1274. NOE was observed between the axial 6-proton (δ 3.12) and SMe protons (δ 2.14). **eq-1**: Colorless crystals. Mp 77-80°C (hexane). ¹H-NMR (400 MHz, benzene-d₆) δ 0.57 (9H, s), 0.99 (1H, dt, *J* = 4.0, 12.8 Hz, 4ax), 1.02 (1H, tt, *J* = 2.4, 10.8 Hz, 5eq), 1.36 (1H, q, *J* = 12.8 Hz, 3ax), 1.44-1.51 (1H, m, 5eq), 1.78-1.87 (1H, m, 5ax), 2.23 (1H, ddd, *J* = 3.2, 5.6, 12.8 Hz, 3eq), 2.30 (1H, ddd, *J* = 3.2, 4.0, 14.0 Hz, 5ax), 3.66 (1H, ddd, *J* = 1.2, 5.6, 12.8 Hz, 2ax), 6.94 (1H, tdd, *J* = 1.2, 7.2, 7.6 Hz), 7.03 (2H, t, *J* = 7.6 Hz), 7.44 (2H, dd, *J* = 1.2, 7.2 Hz). ¹³C-NMR (100 MHz, benzene-d₆) δ 27.4, 27.9, 32.2, 36.2, 41.0, 47.2, 57.4, 126.9, 129.1, 132.1, 135.6, 204.8. IR (KBr) 3396, 3052, 2965, 2865, 1706, 1581, 1478, 1438, 1364, 1315, 1224, 1133, 1068, 800, 753, 688, 553, 483 cm⁻¹. MS (EI) *m/z* 262 (M⁺, 100%), 205 (M⁺-C₄H₉, 24%). HRMS Calcd for C₁₆H₂₂OS: 262.1390. Found: 262.1393. The configuration of the 2-phenylthio group was determined by observing the coupling constant *J* = 12.8 Hz of the 2-axial proton (δ 3.66) and 3-axial proton (δ 1.36). **6a**: Colorless crystals. Mp 72-73°C (hexane-diethyl ether). ¹H-NMR (400 MHz, CDCl₃) δ 2.13 (6H, s), 5.26 (1H, s), 7.78 (2H, dd, *J* = 2.0, 6.8 Hz), 8.10 (2H, dd, *J* = 2.0, 6.8 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 12.4, 57.3, 116.5, 117.7, 129.2, 132.4, 137.7, 189.1. IR (neat) 2917, 2853, 2230, 1679, 1404, 1279, 1203, 1006, 855 cm⁻¹. MS (EI) *m/z* 237 (M⁺, 2%), 107 (M⁺-C₈H₄NO, 100%). HRMS Calcd for C₁₁H₁₁NOS₂: 237.0281. Found: 237.0254. **(2*R**,4*S**)-2-Methylthio-4-(*t*-butyl)cyclohexanone **4****: Colorless crystals. Mp 32-34°C (hexane). ¹H-NMR (400 MHz, CDCl₃) δ 0.902 (9H, s), 1.41 (1H, dq, *J* = 13.2, 4.0 Hz), 1.73 (1H, tt, *J* = 2.8, 12.4 Hz), 1.90 (1H, dt, *J* = 4.8, 13.6 Hz), 2.01-2.08 (1H, m), 2.05 (3H, s), 2.18 (1H, dq, *J* = 13.6, 2.8 Hz), 2.22 (1H, dq, *J* = 14.8, 2.4 Hz), 3.11 (1H, dt, *J* = 6.0, 14.4 Hz), 3.18 (1H, td, *J* = 2.4, 4.8 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 15.4, 27.4, 27.6, 32.1, 33.2, 35.8, 41.5, 53.0, 208.3. IR (neat) 2960, 2918, 2869, 1708, 1480, 1438, 1420, 1396, 1367, 1330, 1230, 1147, 668 cm⁻¹. MS (EI) *m/z* 200 (M⁺, 100%), 154 (M⁺-CH₃S, 42%). HRMS Calcd for C₁₁H₂₀OS: 200.1234. Found: 200.1242. **(2*S**,4*S**)-2-Methylthio-4-(*t*-butyl)cyclohexanone, equatorial isomer of **4****: Colorless oil. ¹H-NMR (400 MHz, benzene-d₆) δ 0.624 (9H, s), 0.98-1.07 (2H, m), 1.29 (1H, quartet, *J* = 12.8 Hz), 1.43-1.49 (1H, m), 1.72-1.81 (1H, m), 1.95 (3H, s), 2.10 (1H, dq, *J* = 12.8, 2.8 Hz), 2.30 (1H, dtd, *J* = 1.2, 4.4, 14.0 Hz), 2.92 (1H, ddd, *J* = 1.2, 5.2, 12.4 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 14.2, 27.5, 27.8, 32.6, 35.2, 40.6, 47.2, 54.9, 207.3. IR (neat) 2959, 2869, 1718, 1474, 1444, 1366, 1326, 1223, 1132, 1075, 959, 804, 551 cm⁻¹. MS (EI) *m/z* 200 (M⁺, 100%), 154 (M⁺-CH₃S, 78%). HRMS Calcd for C₁₁H₂₀OS: 200.1234. Found: 200.1216.



3



***p*-Cyanoacetophenone 5a⁹** Colorless crystals. Mp 57.5-58°C (Hexane). Lit. 58-60°C. ¹H-NMR (400 MHz, CDCl₃) δ 2.66 (3H, s), 7.80 (2H, ddd, *J* = 2.0, 2.4, 8.4 Hz), 8.06 (2H, ddd, *J* = 2.0, 2.4, 8.4 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.7, 116.3, 117.9, 128.6, 132.5, 139.8, 196.5. IR (KBr) 3354, 3095, 2228, 1687, 1402, 1357, 1263, 961, 832, 593, 535 cm⁻¹. MS (EI) *m/z* 145 (M⁺, 27%), 130 (M⁺-CH₃, 100%). HRMS Calcd for C₉H₇NO: 145.0527. Found: 145.0549.

***p*-Trifluoromethylacetophenone 5b¹⁰** Colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 2.65 (3H, s), 7.74 (2H, dd, *J* = 0.8, 8.0 Hz), 8.07 (2H, dd, *J* = 0.8, 8.0 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.7, 123.6 (q, *J* = 270.5), 125.6 (q, *J* = 3.8 Hz), 128.6, 133.4 (q, *J* = 32.6 Hz), 139.6, 197.0. IR (neat) 3066, 3014, 1695, 1411, 1329, 1264, 1170, 1129, 844, 719, 609 cm⁻¹. MS (EI) *m/z* 188 (M⁺, 15%), 173 (M⁺-CH₃, 100%). HRMS Calcd for C₉H₇F₃O: 188.0449. Found: 188.0441.

***p*-Chloroacetophenone 5c⁹** Colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 2.59 (3H, s), 7.43 (2H, ddd, *J* = 2.0, 2.4, 8.8 Hz), 7.90 (2H, ddd, *J* = 2.0, 2.4, 8.8 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.5, 128.8, 129.6, 135.3, 139.5, 196.7. IR (neat) 3066, 3007, 1686, 1589, 1396, 1358, 1260, 1094, 1012, 957, 828, 761 cm⁻¹. MS (EI) *m/z* 154 (M⁺, 39%), 139 (M⁺-CH₃, 100%). HRMS Calcd for C₈H₇ClO: 154.0185. Found: 154.0176.

Acetophenone 5d⁹ Colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 2.60 (3H, s), 7.46 (2H, t, *J* = 7.6 Hz), 7.56 (2H, tt, *J* = 1.2, 7.6 Hz), 7.96 (2H, dd, *J* = 1.6, 7.6 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.5, 128.2, 128.5, 133.0, 137.0, 198.1. IR (neat) 3066, 3007, 1685, 1599, 1449, 1360, 1266, 760, 690, 589 cm⁻¹. MS (EI) *m/z* 120 (M⁺, 35%), 105 (M⁺-CH₃, 100%). HRMS Calcd for C₈H₈O: 120.0575. Found: 120.0558.

***p*-Methoxyacetophenone 5e¹¹** Colorless crystals. Mp 35-35.5°C (Hexane). Lit. 37-39°C. ¹H-NMR (400 MHz, CDCl₃) δ 2.56 (3H, s), 3.87 (3H, s), 6.93 (2H, d, *J* = 8.8 Hz), 7.94 (2H, d, *J* = 8.8 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 26.3, 55.4, 113.6, 130.3, 130.5, 163.4, 196.7. IR (KBr) 3317, 2965, 2843, 1674, 1602, 1509, 1359, 1259, 1173, 1023, 834 cm⁻¹. MS (EI) *m/z* 150 (M⁺, 53%), 135 (M⁺-CH₃, 100%). HRMS Calcd for C₉H₁₀O₂: 150.0680. Found: 150.0694.

***p*-Chlorophenyl di(methylthio)methyl ketone 6c¹²** Colorless crystals. Mp 65-67°C (chloroform-hexane). Lit. 56-57°C. ¹H-NMR (400 MHz, CDCl₃) δ 2.13 (6H, s), 5.26 (1H, s), 7.44 (2H, ddd, *J* = 2.0, 2.4, 9.2 Hz), 7.95 (2H, ddd, *J* = 2.0, 2.4, 9.2 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 12.5, 57.2, 129.0, 130.2, 132.7, 139.9, 189.7. IR (neat) 2982, 2917, 2853, 1672, 1587, 1569, 1488, 1399, 1275, 1190, 1092, 1004, 847, 781 cm⁻¹. MS (EI) *m/z* 246 (M⁺, 3%), 107 (M⁺-C₇H₄ClO, 100%). HRMS Calcd for C₁₀H₁₁ClOS₂: 245.9939. Found: 245.9943.

***t*-Butyl (methylthio)(phenylthio)methyl ketone** Colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 1.21 (9H, s), 2.19 (3H, s), 5.04 (1H, s), 7.33-7.35 (3H, m), 7.53 (2H, dd, *J* = 3.6, 7.2 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 11.6, 27.1, 44.1, 56.4, 128.5, 128.7, 129.0, 133.8, 205.4. IR (neat) 2965, 1694, 1475, 1056 cm⁻¹. MS (EI) *m/z* 254 (M⁺, 6%), 169 (M⁺-C₅H₉O, 100%). HRMS Calcd for C₁₃H₁₈OS₂: 254.0799. Found: 254.0807.

1-Adamantyl (methylthio)(phenylthio)methyl ketone Colorless crystals. Mp 90-92°C (hexane). ¹H-NMR (400 MHz, CDCl₃) δ 1.65-1.75 (6H, dt, broad, *J* = 10.4, 12.4 Hz), 1.81-1.86 (3H, broad dq, *J* = 2.4, 12.0 Hz), 1.91-1.96 (3H, dq, *J* = 2.4, 12.4 Hz), 2.01-2.08 (3H, m), 2.16 (3H, s), 5.07 (1H, s), 7.31-7.35 (3H, m), 7.53 (2H, dd, *J* = 2.0, 7.6 Hz). ¹³C-NMR (100 MHz, CDCl₃) δ 11.5, 27.9, 36.3, 38.7, 46.2, 55.9, 128.3, 129.0,

133.3, 133.7, 204.5. IR (neat) 3072, 2973, 2899, 2849, 2677, 1680, 1471, 1449, 1270, 1100, 1014, 804, 741, 495 cm^{-1} . MS (EI) m/z 332 (M^+ , 8%), 169 ($\text{M}^+ - \text{C}_{11}\text{H}_{15}\text{O}$, 100%). HRMS Calcd for $\text{C}_{19}\text{H}_{24}\text{OS}_2$: 332.1269. Found: 332.1243.

***p*-Methoxyphenyl (phenylthio)(methylthio)methyl ketone 8** Colorless oil. ^1H -NMR (400 MHz, CDCl_3) δ 2.21 (3H, s), 3.88 (3H, s), 5.54 (1H, s), 6.93 (2H, d, J = 8.8 Hz), 7.32-7.34 (3H, m), 7.53 (2H, dd, J = 2.0, 7.2 Hz), 7.98 (2H, d, J = 8.8, 7.2 Hz). ^{13}C -NMR (100 MHz, CDCl_3) δ 12.4, 55.5, 59.4, 113.9, 127.0, 128.4, 129.0, 131.3, 133.1, 133.6, 163.9, 189.7. IR (neat) 2919, 2840, 1666, 1600, 1262, 1173 cm^{-1} . MS (EI) m/z 304 (M^+ , 8%), 135 ($\text{M}^+ - \text{C}_8\text{H}_9\text{S}_2$, 100%). HRMS Calcd for $\text{C}_{16}\text{H}_{16}\text{O}_2\text{S}_2$: 304.0592. Found: 304.0582.

α -Phenylthioacetophenone¹³ Colorless crystals. Mp 52.0-52.5°C (hexane). Lit. 51-52°C. ^1H -NMR (400 MHz, CDCl_3) δ 4.28 (2H, s), 7.22 (1H, t, J = 7.2 Hz), 7.28 (2H, t, J = 7.2 Hz), 7.39 (2H, d, J = 7.2 Hz), 7.46 (2H, t, J = 7.2 Hz), 7.58 (1H, t, J = 7.2 Hz), 7.94 (2H, d, J = 7.2 Hz). ^{13}C -NMR (100 MHz, CDCl_3) δ 41.2, 127.1, 128.7, 128.7, 129.0, 130.5, 133.5, 134.7, 135.4, 194.0. IR (KBr) 3073, 1671, 1278 cm^{-1} . MS (EI) m/z 228 (M^+ , 66%), 105 ($\text{M}^+ - \text{C}_7\text{H}_7\text{S}$, 100%). HRMS Calcd for $\text{C}_{14}\text{H}_{12}\text{OS}$: 228.0609. Found: 228.0597.

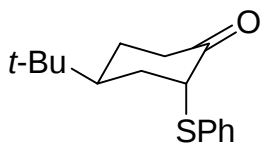
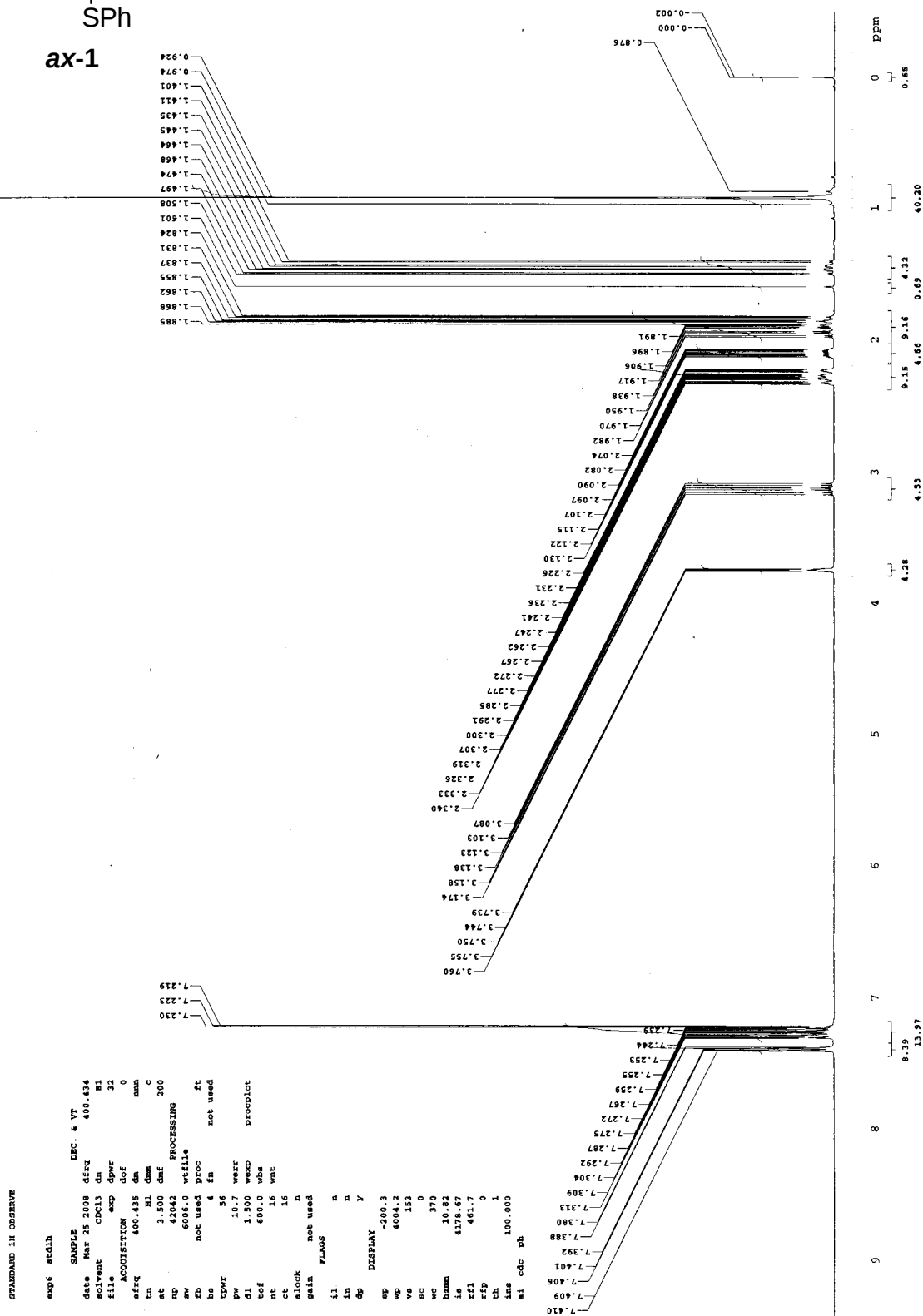
1-Methylcyclohexyl α -methylthio- α -phenylthiomethyl ketone Colorless oil. ^1H -NMR (400 MHz, CDCl_3) δ 1.20 (3H, s), 1.33-1.43 (4H, m), 1.47-1.53 (4H, m), 1.85-1.96 (2H, m), 2.21 (3H, s), 5.04 (1H, s), 7.33-7.35 (3H, m), 7.53 (2H, dd, J = 2.0, 7.6 Hz). ^{13}C -NMR (100 MHz, CDCl_3) δ 11.6, 22.66, 22.70, 24.7, 25.7, 34.7, 35.1, 48.2, 56.4, 128.5, 129.0, 133.3, 133.9, 205.9. IR (neat) 2927, 2856, 1693, 1439 cm^{-1} . MS (EI) m/z 294 (M^+ , 3%), 169 ($\text{M}^+ - \text{C}_8\text{H}_{13}\text{O}$, 100%). HRMS Calcd for $\text{C}_{16}\text{H}_{22}\text{OS}_2$: 294.1112. Found: 294.1138.

Reverse reaction In a two-necked flask equipped with a reflux condenser were placed tetrakis(triphenylphosphine)hydriderrhodium (4 mol%, 5.8 mg), 1,2-bis(diphenylphosphino)ethane (8 mol%, 4.0 mg), **3** (0.125 mmol, 38.6 mg), and *p*-cyanoacetophenone **5a** (0.125 mmol, 18.1mg) in THF (0.5 mL) under an argon atmosphere, and the solution was heated at 90°C for 4 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel giving **3** (11.0 mg, 29%), *ax*-**1** (10.7 mg, 33%), **4** (3.5 mg, 14%), *eq*-**1** (9.2 mg, 28%), **6a** (2.8 mg, 9%), **2a** (4.0 mg, 17%), *p*-cyano- α -phenylthioacetophenone (0.4 mg, 1%), and **5a** (14.4 mg, 80%).

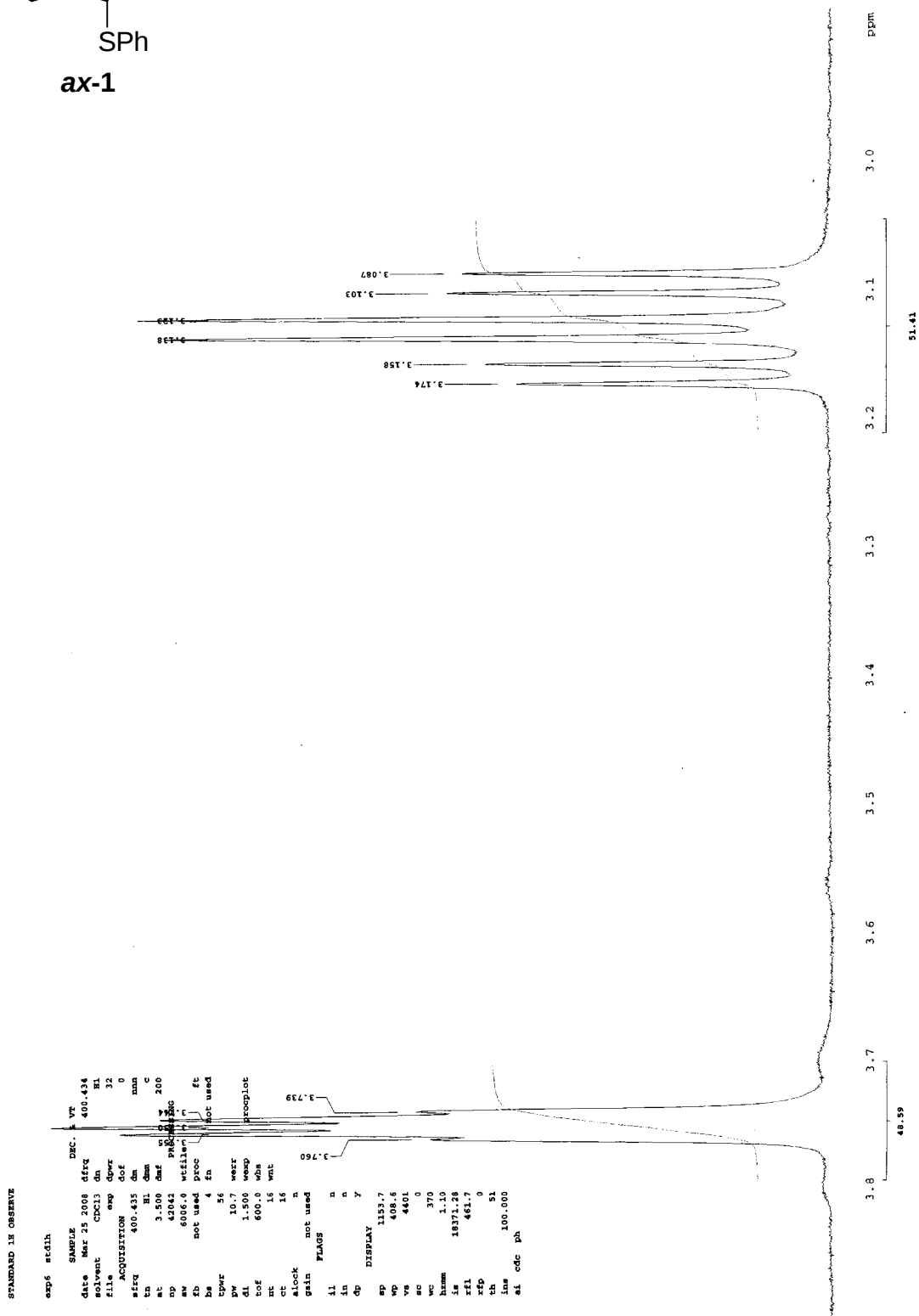
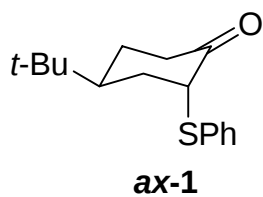
Equilibrium experiment of *ax*-1 In a two-necked flask equipped with a reflux condenser were placed tetrakis(triphenylphosphine)hydriderrhodium (4 mol%, 5.8 mg), *ax*-**1** (0.125 mmol, 32.5 mg) in THF (0.5 mL) under an argon atmosphere, and the solution was heated at 90°C for 4 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel giving *ax*-**1** (19.5 mg, 60%) and *eq*-**1** (13.2 mg, 41%).

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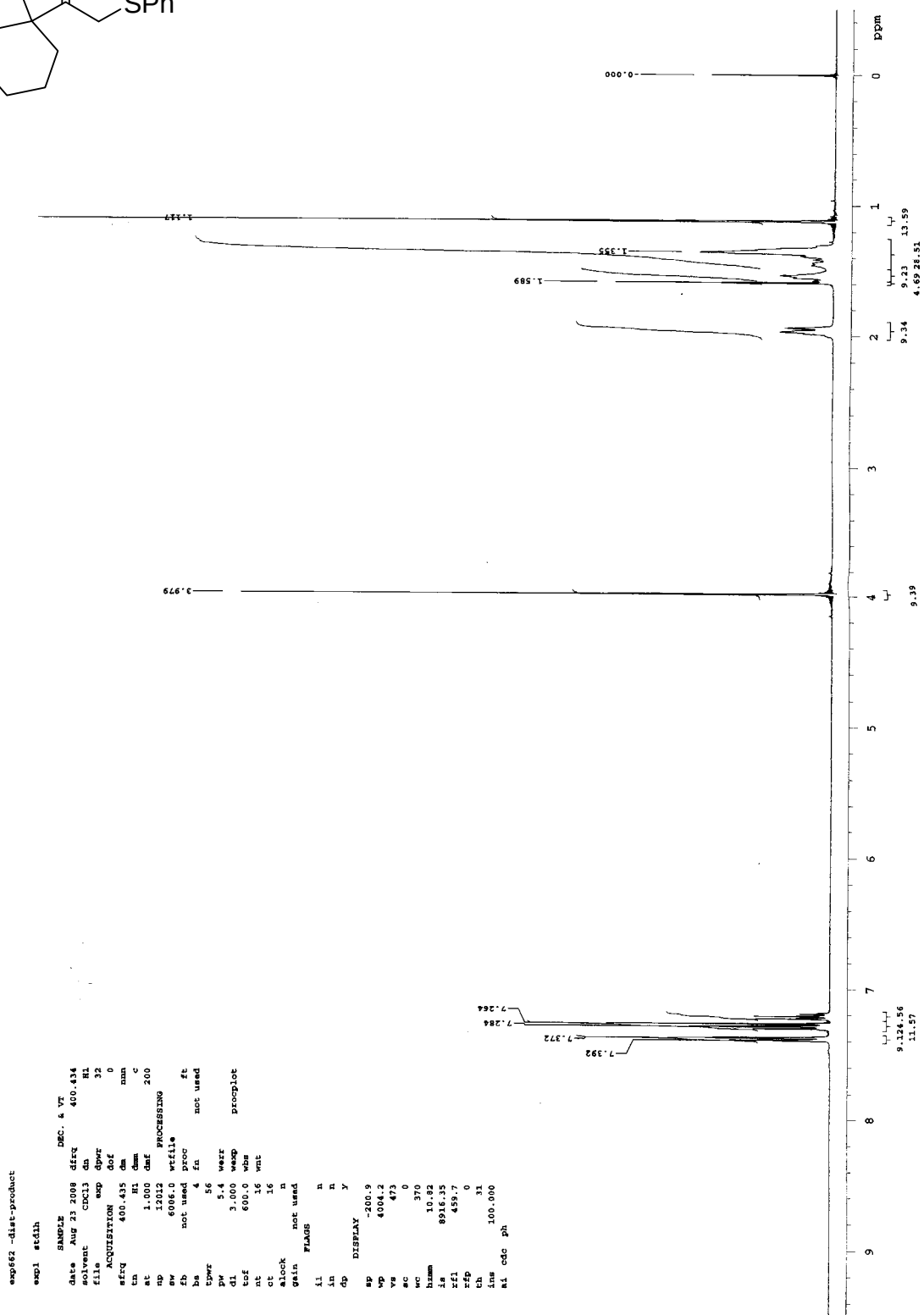
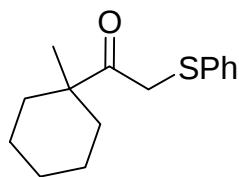
¹H-NMR (CDCl₃, 400MHz)
$$ax-1$$


$^1\text{H-NMR}$ (CDCl_3 , 400MHz)



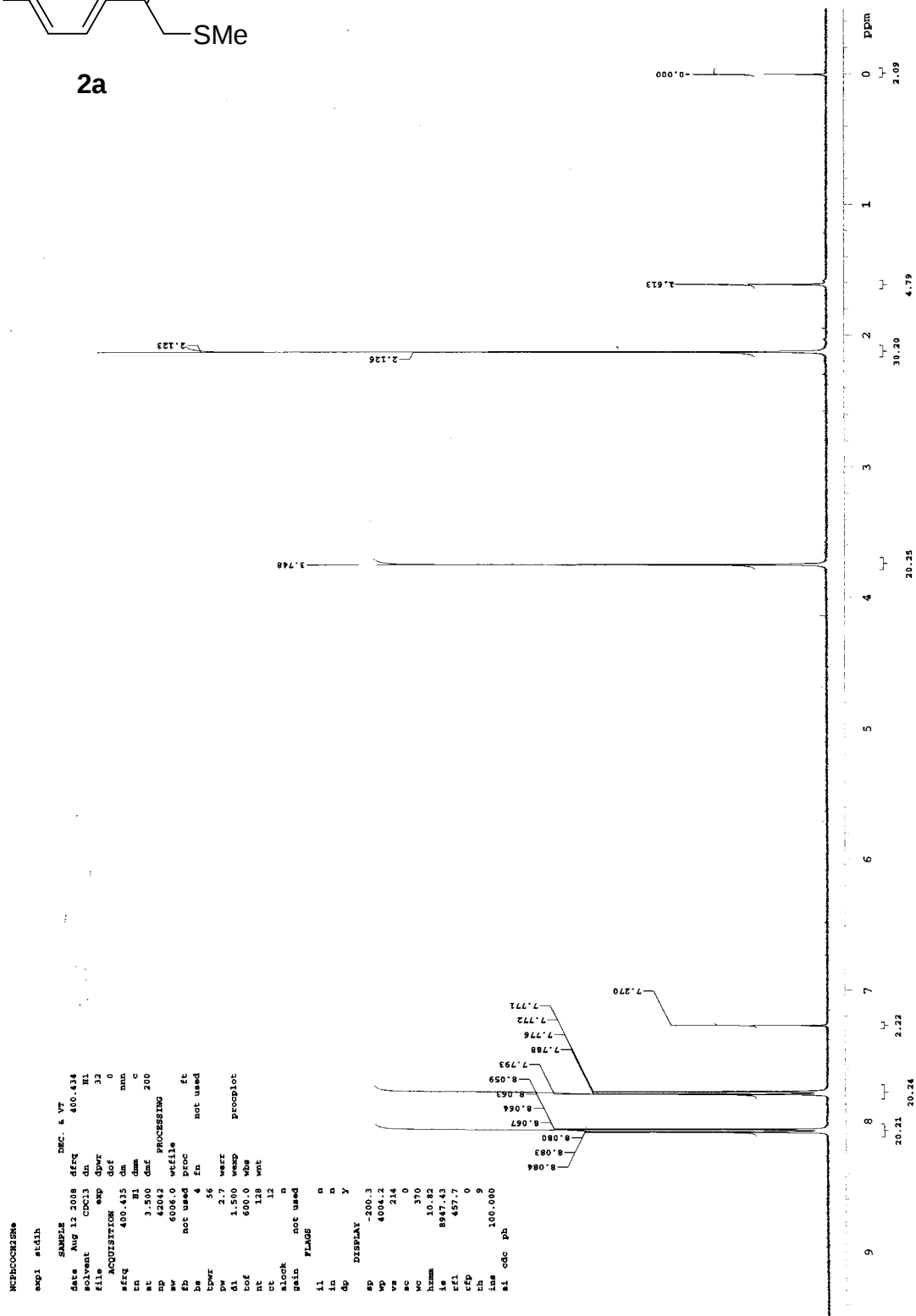
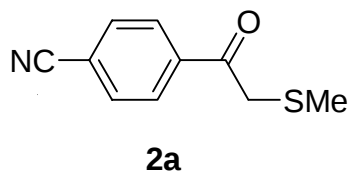
1-Methylcyclohexyl α -phenylthiomethyl ketone

$^1\text{H-NMR}$ (CDCl_3 , 400MHz)

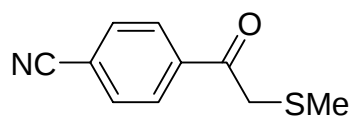


p-Cyano- α -methylthioacetophenone **2a**

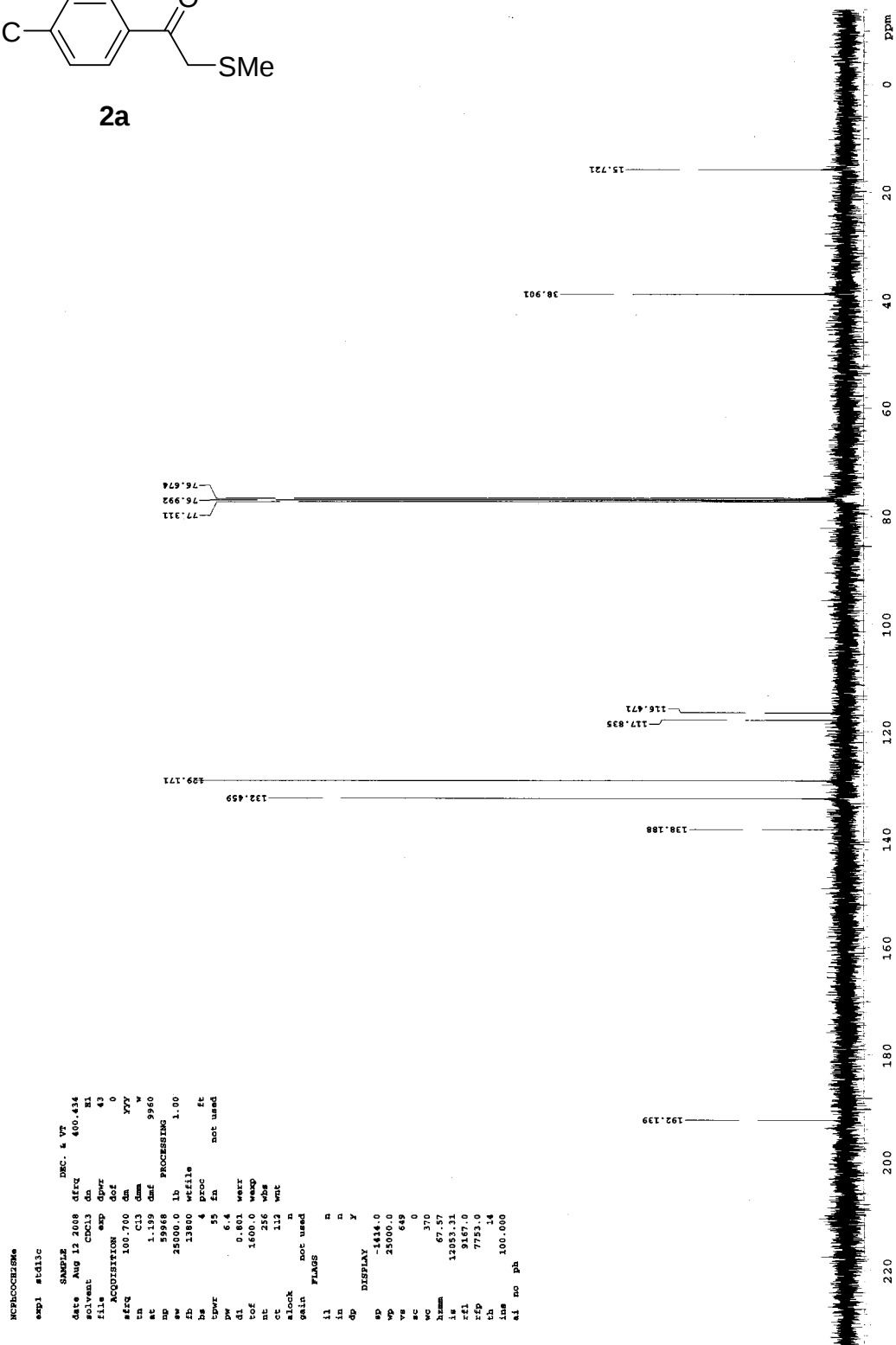
$^1\text{H-NMR}$ (CDCl_3 , 400MHz)



^{13}C -NMR (CDCl_3 , 100MHz)

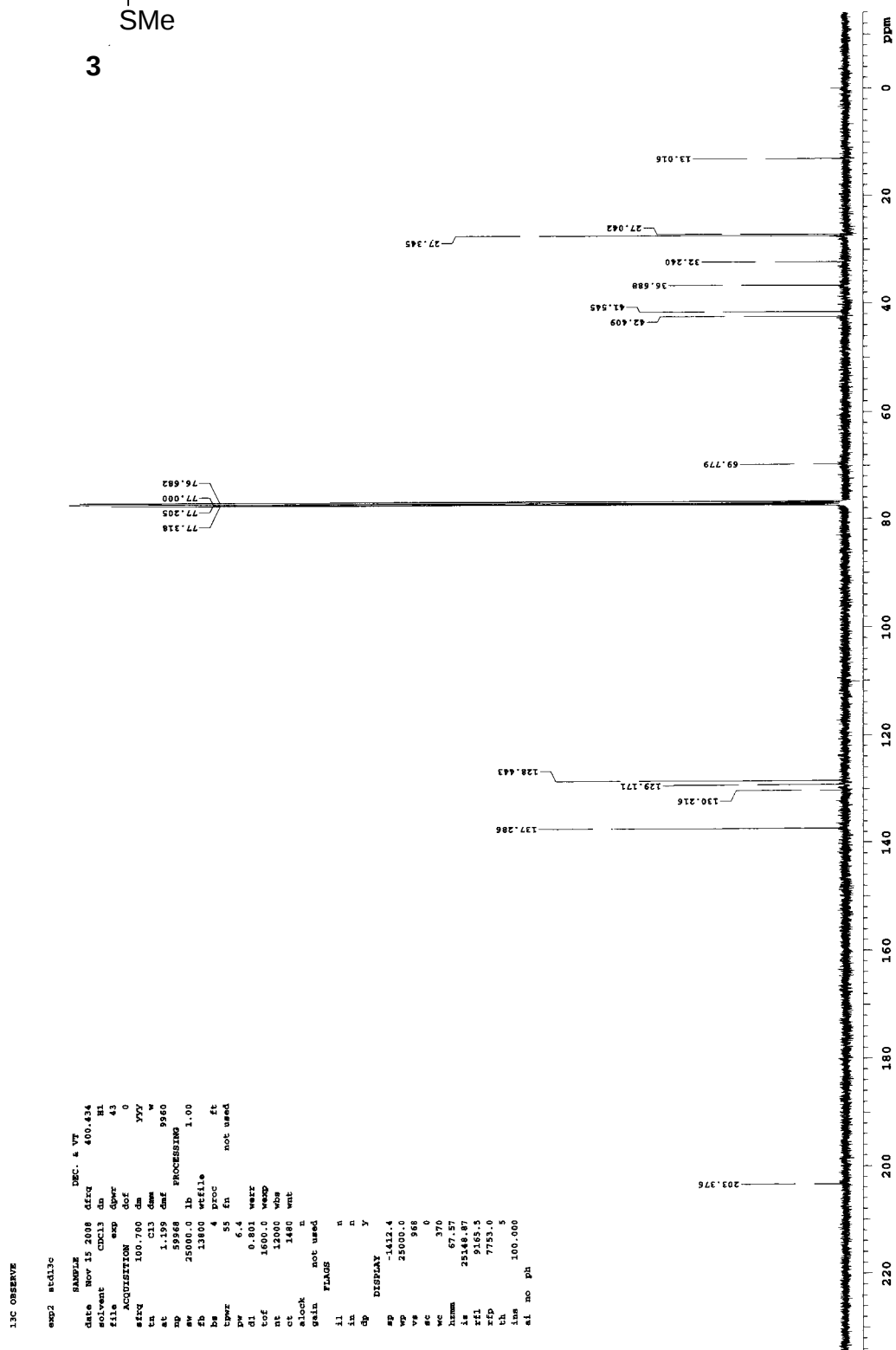
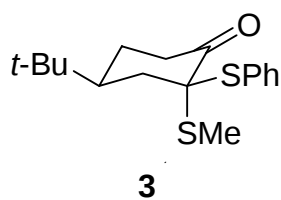


2a

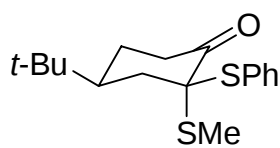


¹H-NMR (CDCl₃, 400MHz)

^{13}C -NMR (CDCl_3 , 100MHz)



^{13}C -NMR (CDCl_3 , 100MHz)



3

13C OBSERVE

exp2 std13c

SAMPLE Date Nov 13 2008 dfrq 400.414

SOLVENT CDCl3 ch 1

PROB 43

ACQ 100.780 dm 120

NUC1 C13 dm 120

AT 1.159 dm 9960

MP 59968

NR 25000.0 lb PROCESSING

EB 13800 wfile 1.00

HE 4 proc ft

DP 55 in not used

PR 6.4

CH 0.84

RG 1500.0 wpr

RG 1200.0 wpr

RG 1484 wnt

ALOOK not used

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FLAG

il n

in n

dp y

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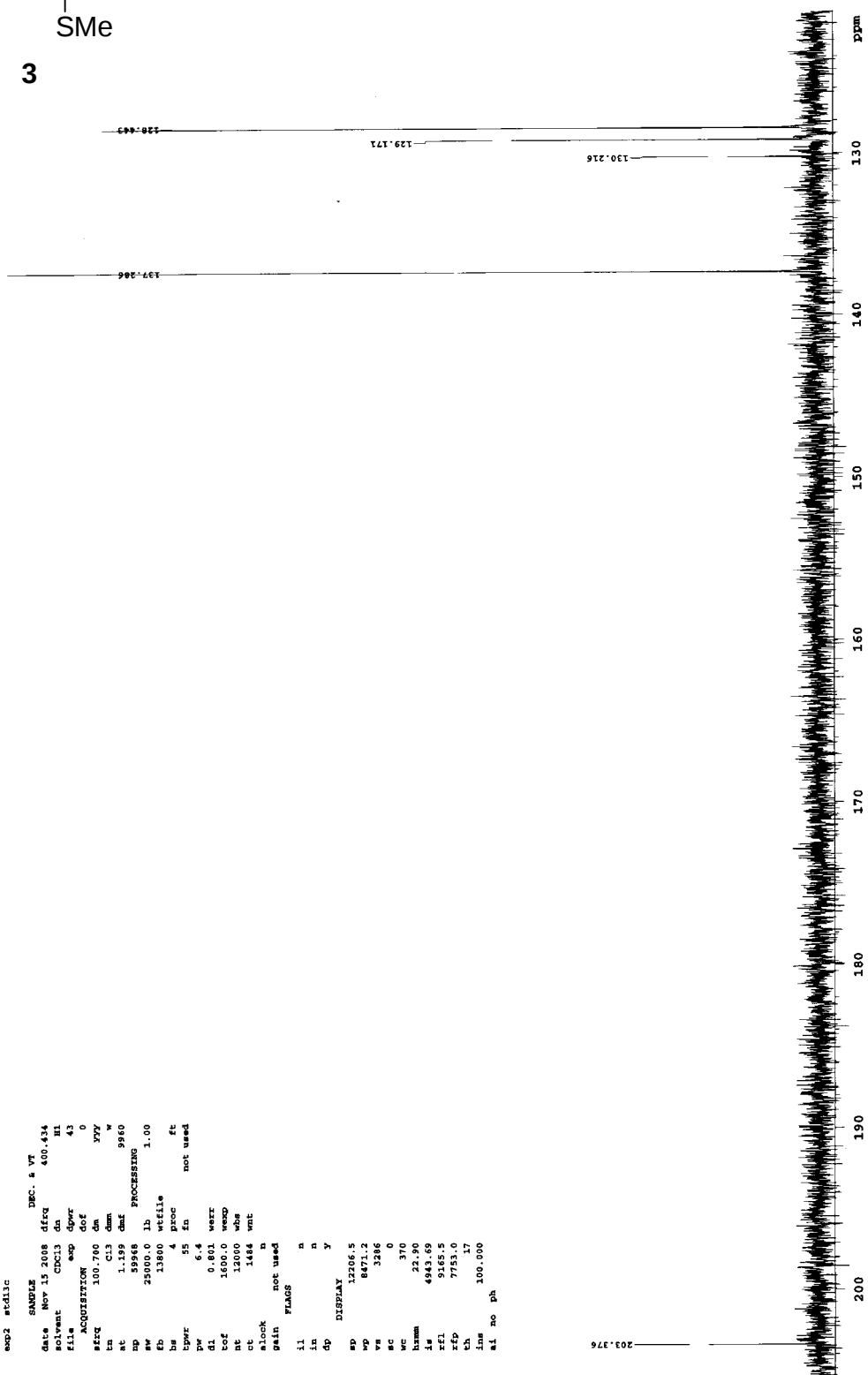
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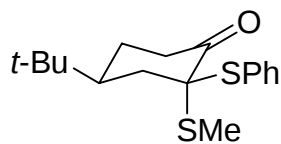
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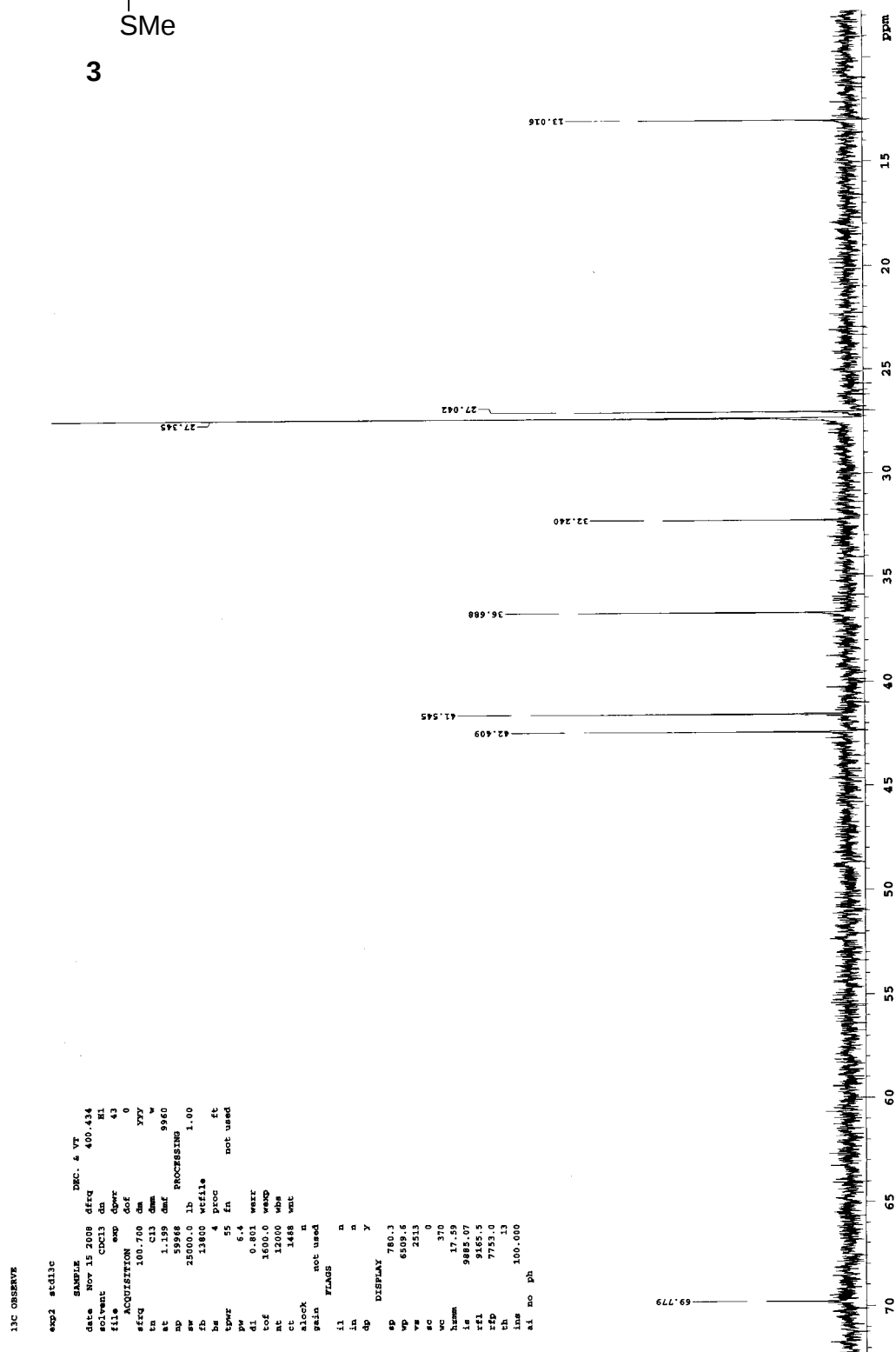
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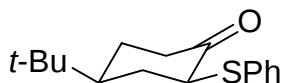


^{13}C -NMR (CDCl_3 , 100MHz)

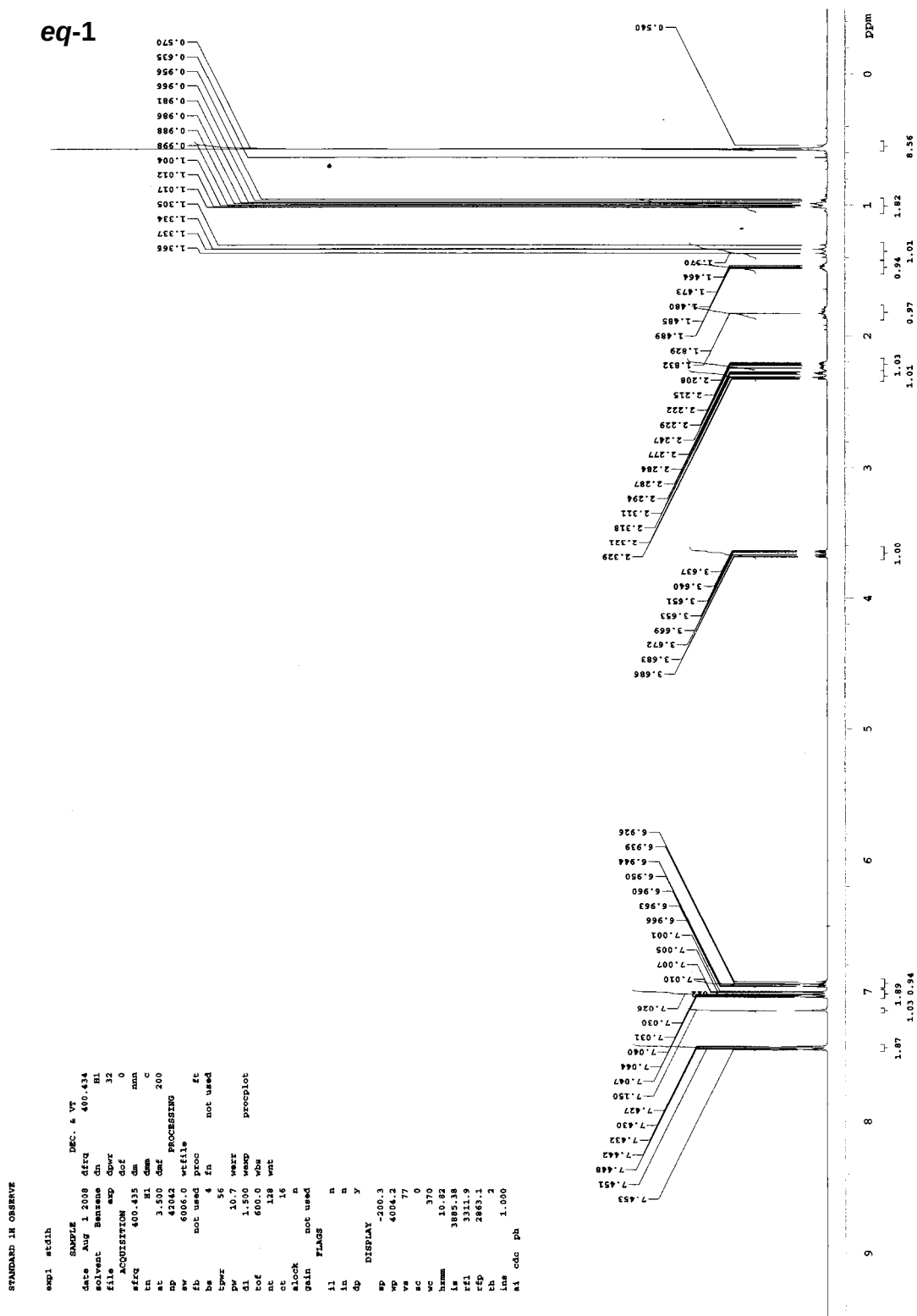


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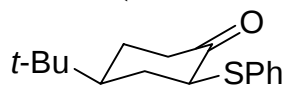


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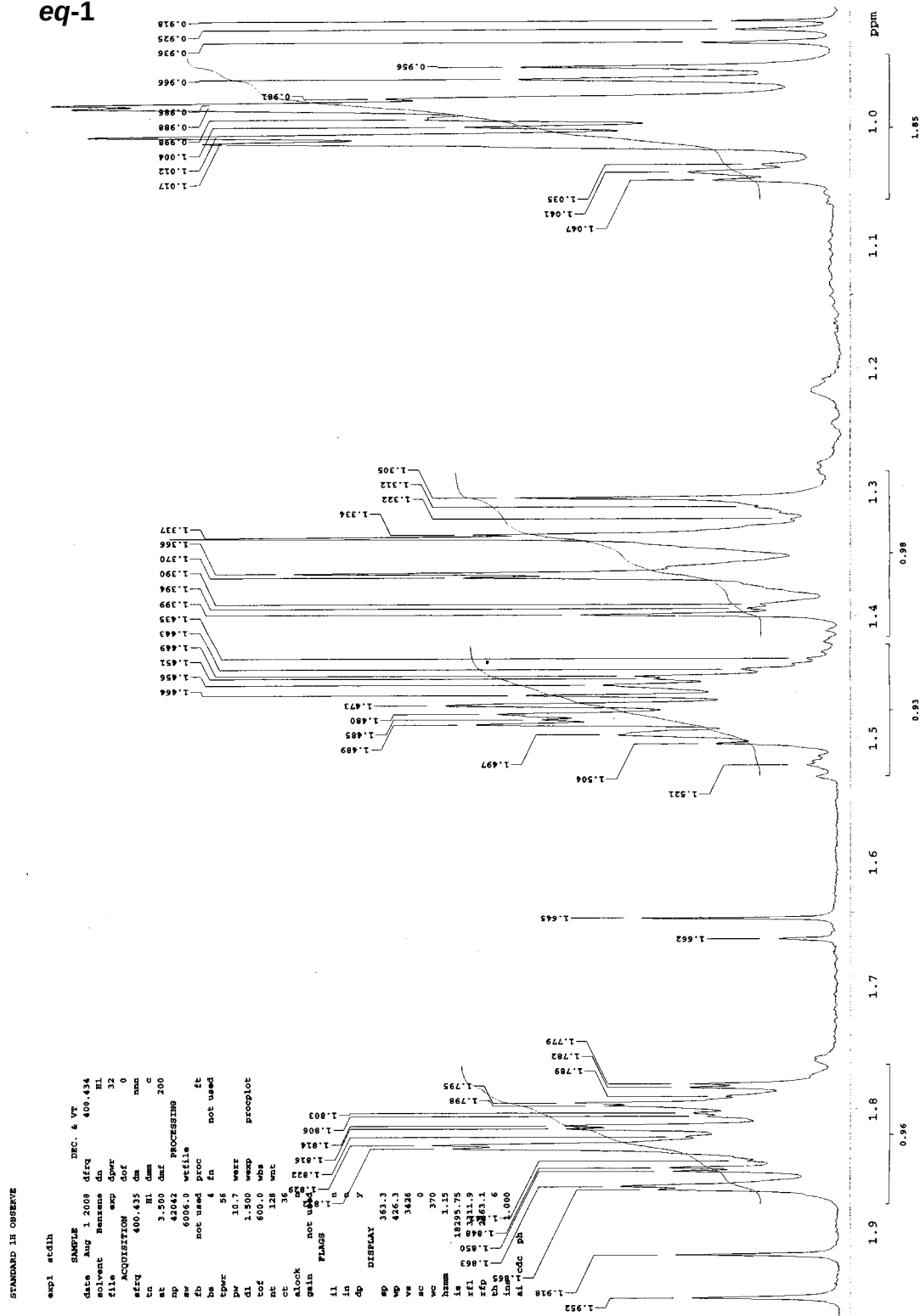
eq-1



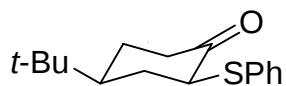
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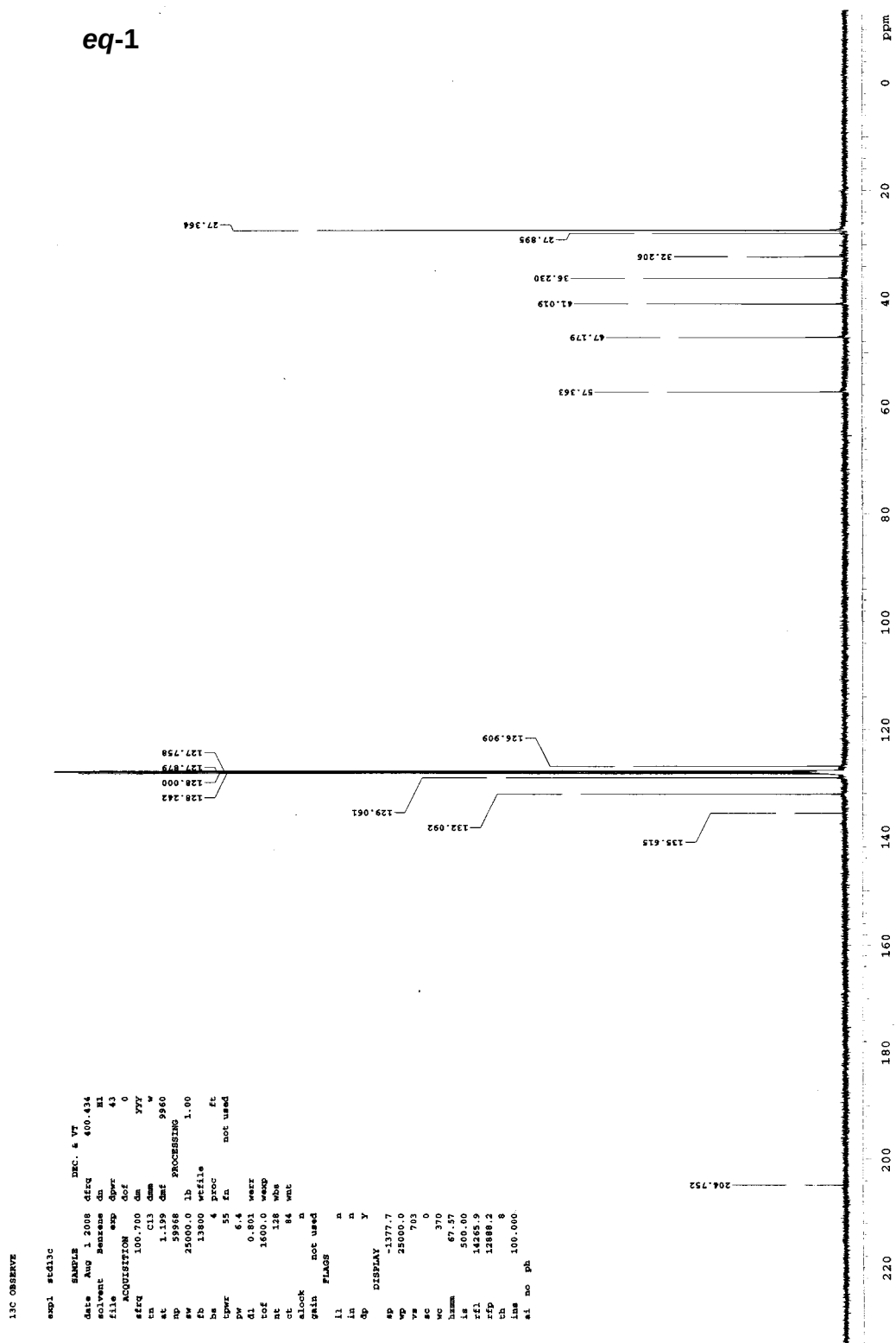
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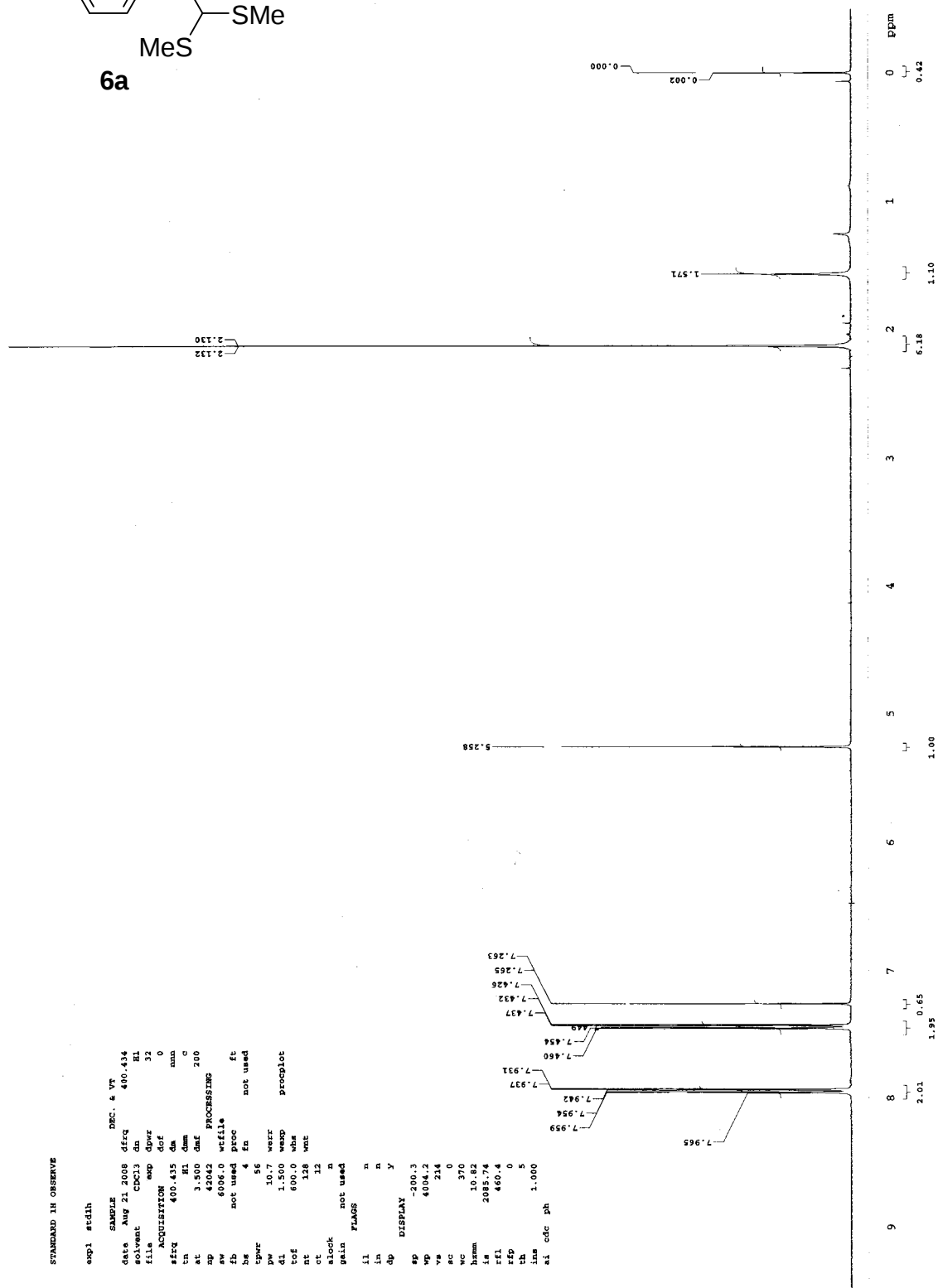
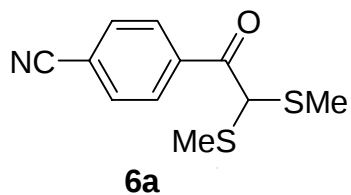


^{13}C -NMR (Benzene- d_6 , 100MHz)



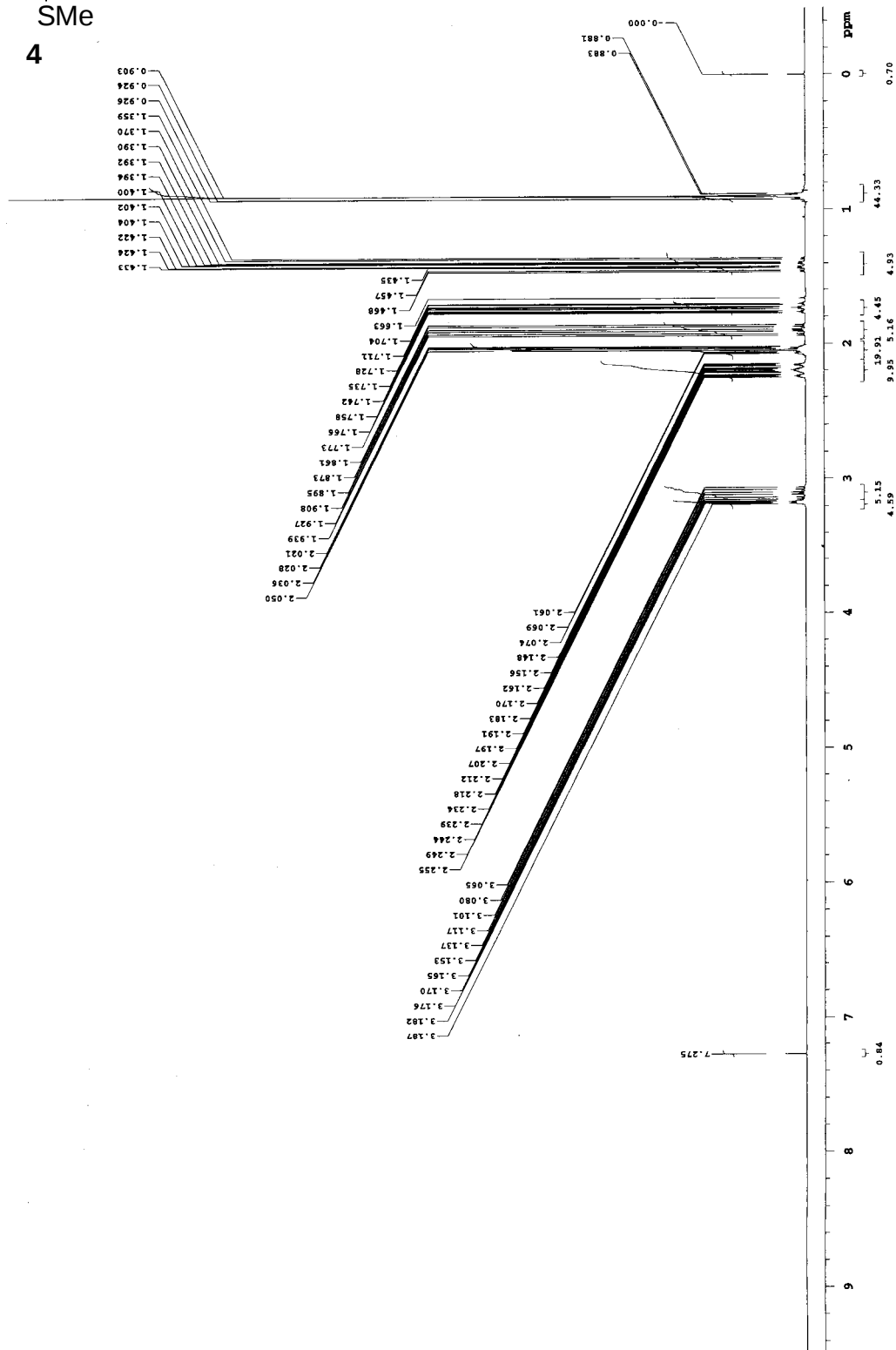
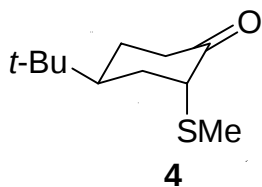
eq-1



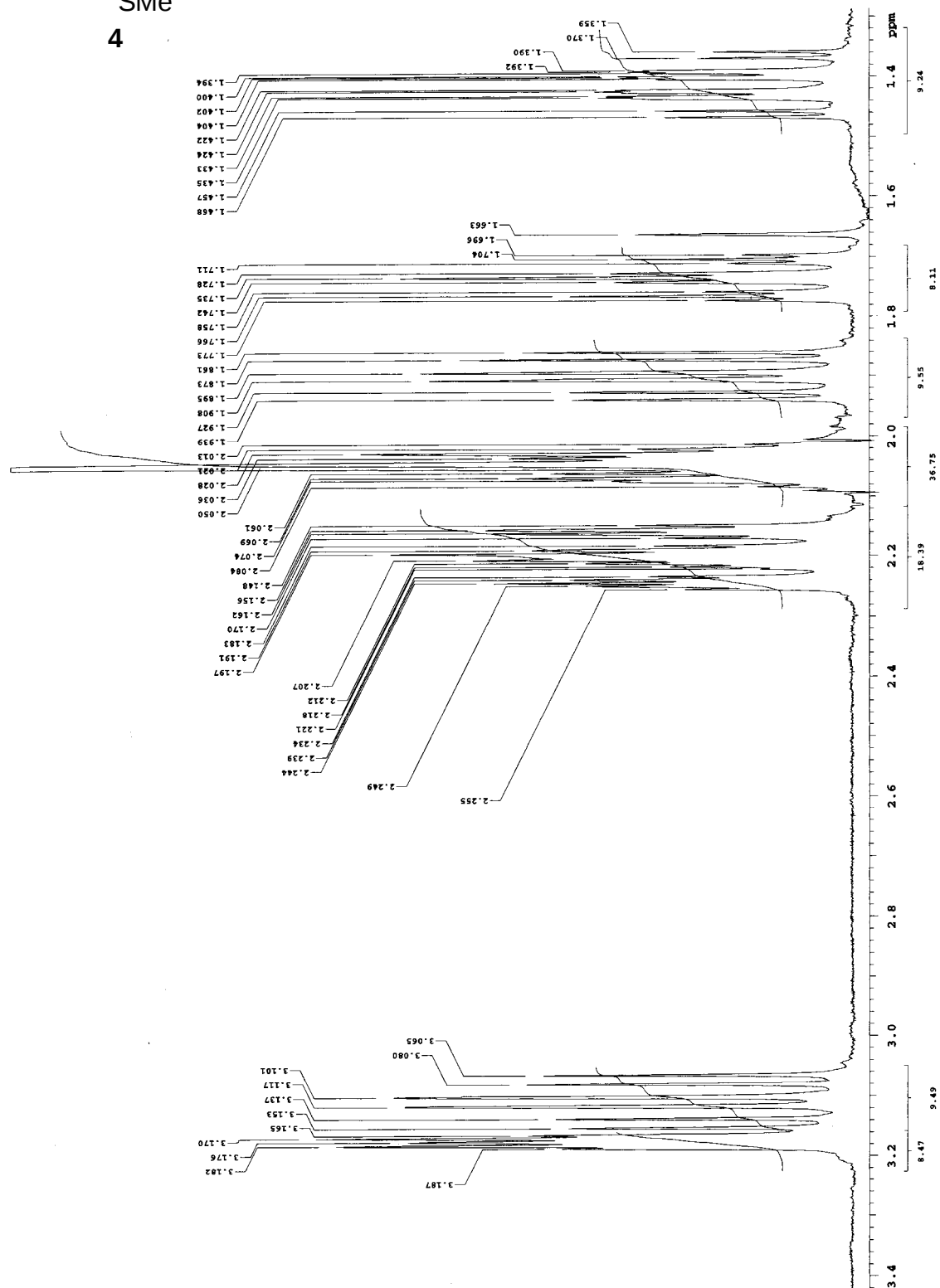
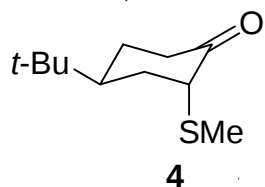
¹H-NMR (CDCl₃, 400MHz)

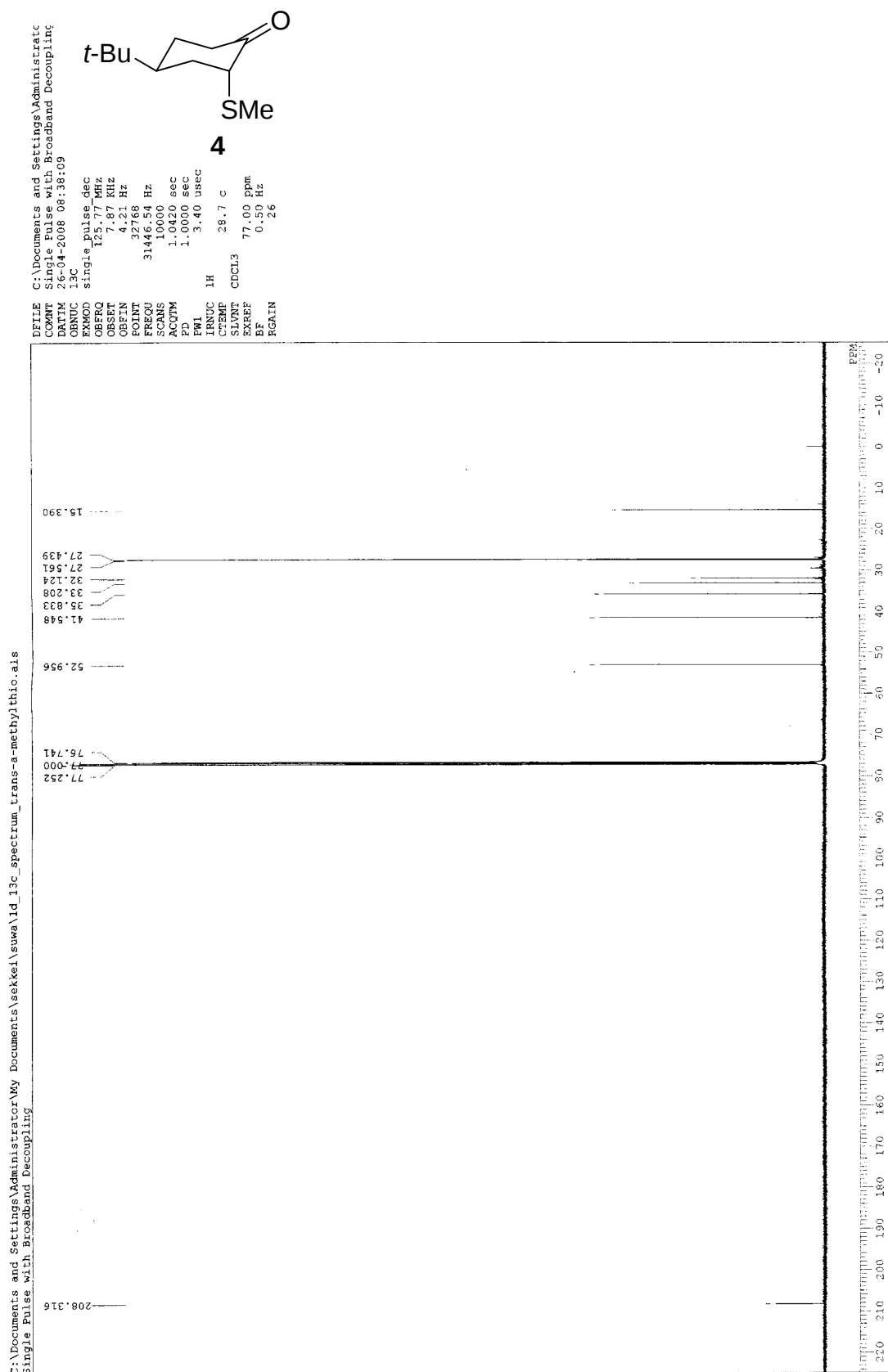
(2*R**,4*S**)-2-Methylthio-4-(*t*-butyl)cyclohexanone **4**

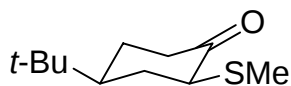
¹H-NMR (CDCl₃, 400MHz)



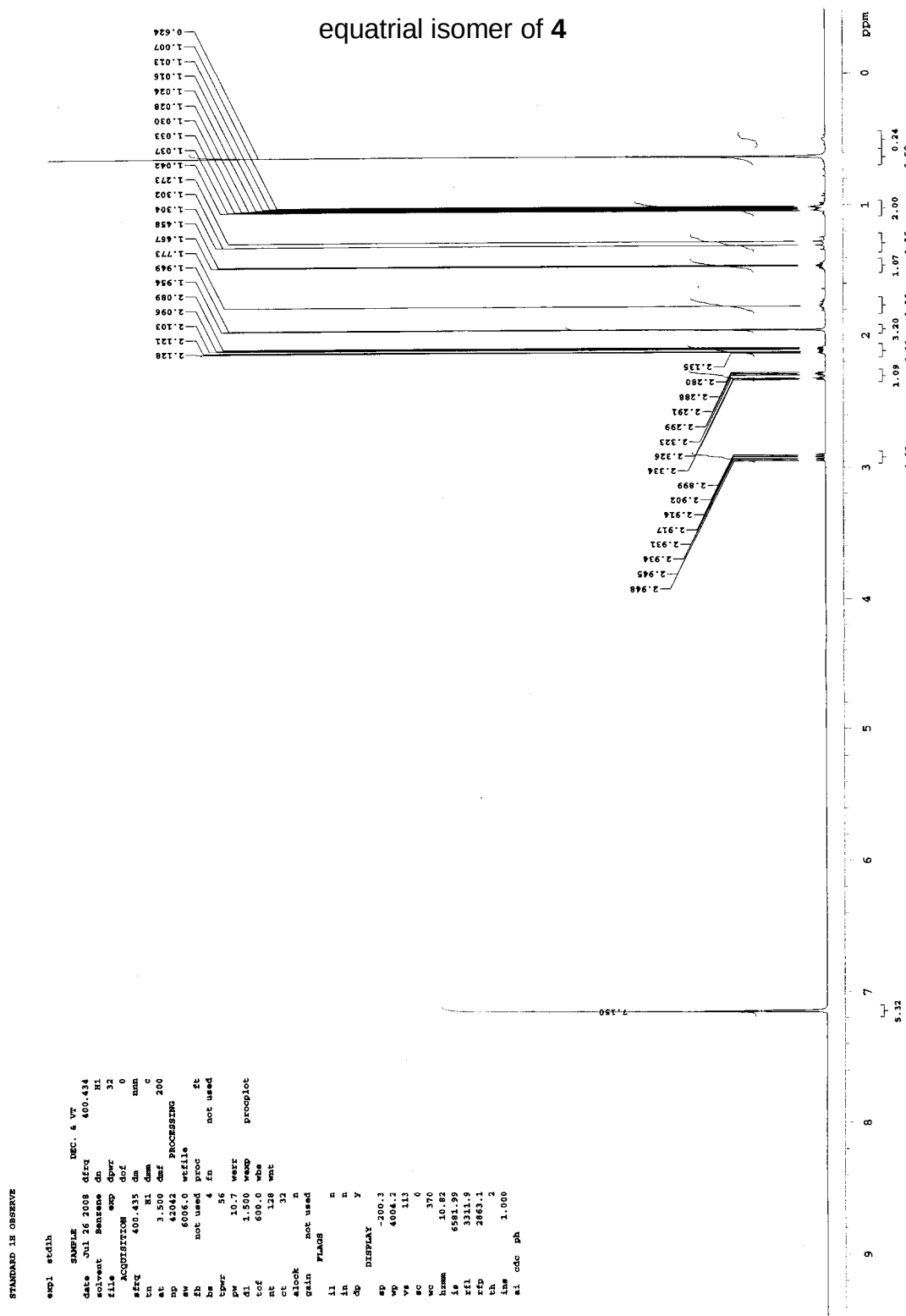
$^1\text{H-NMR}$ (CDCl_3 , 400MHz)



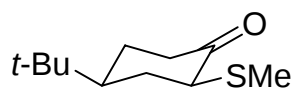
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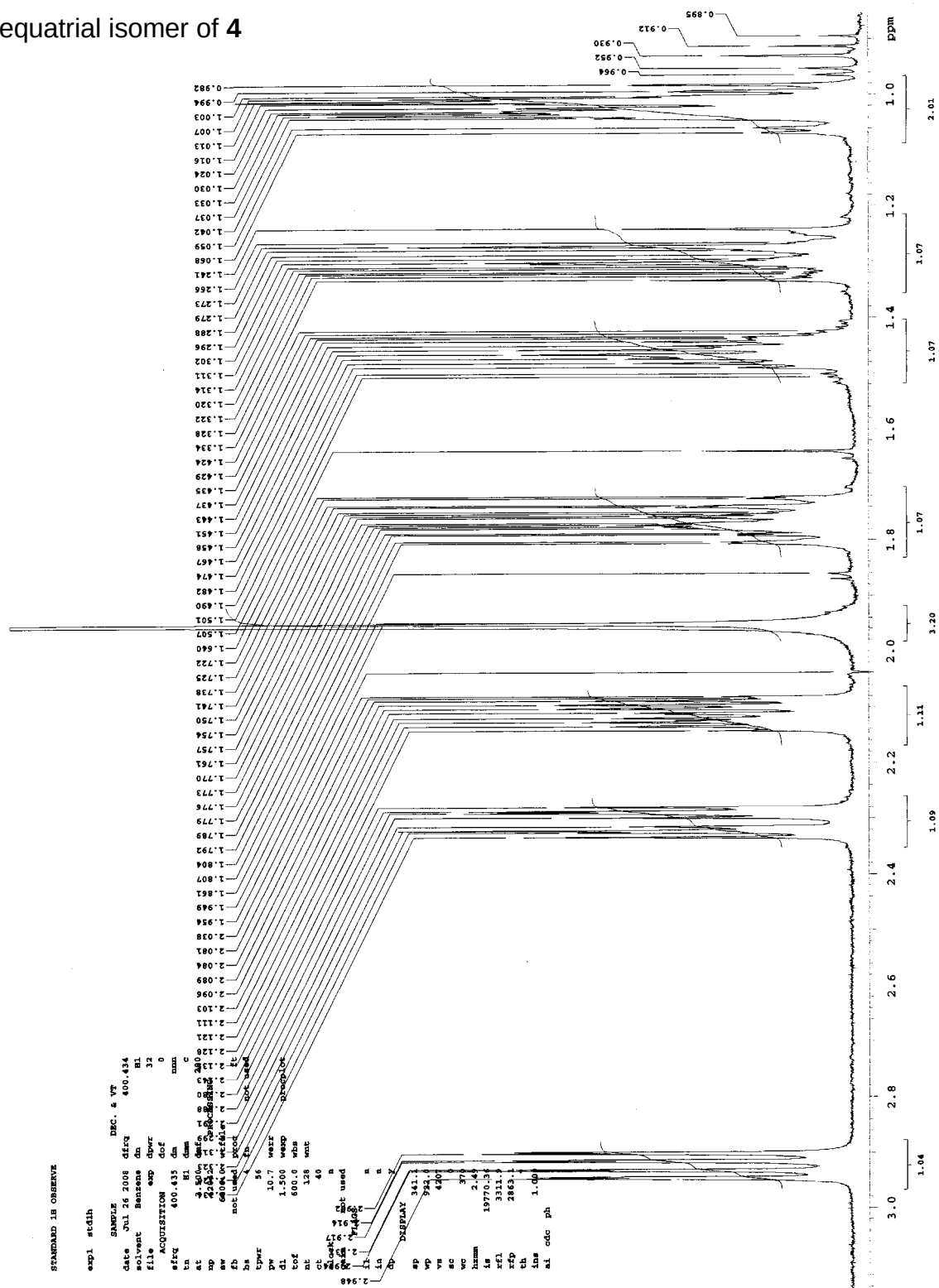
equatorial isomer of **4**



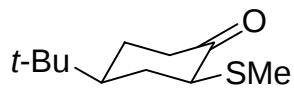
$^1\text{H-NMR}$ (Benzene- d_6 , 400MHz)



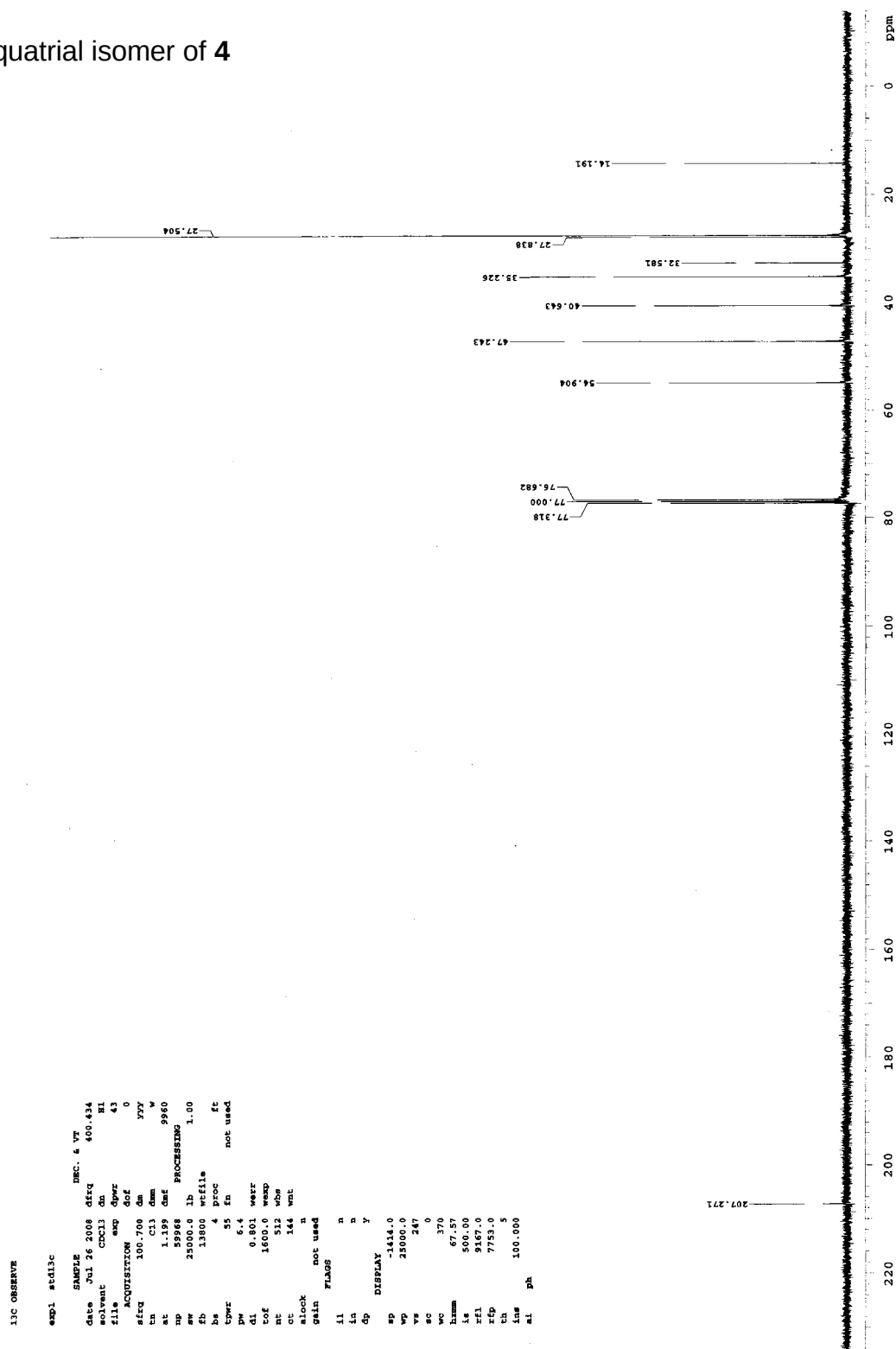
equatorial isomer of **4**



^{13}C -NMR (CDCl_3 , 100MHz)

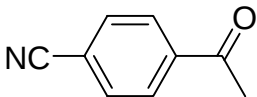


equatorial isomer of 4

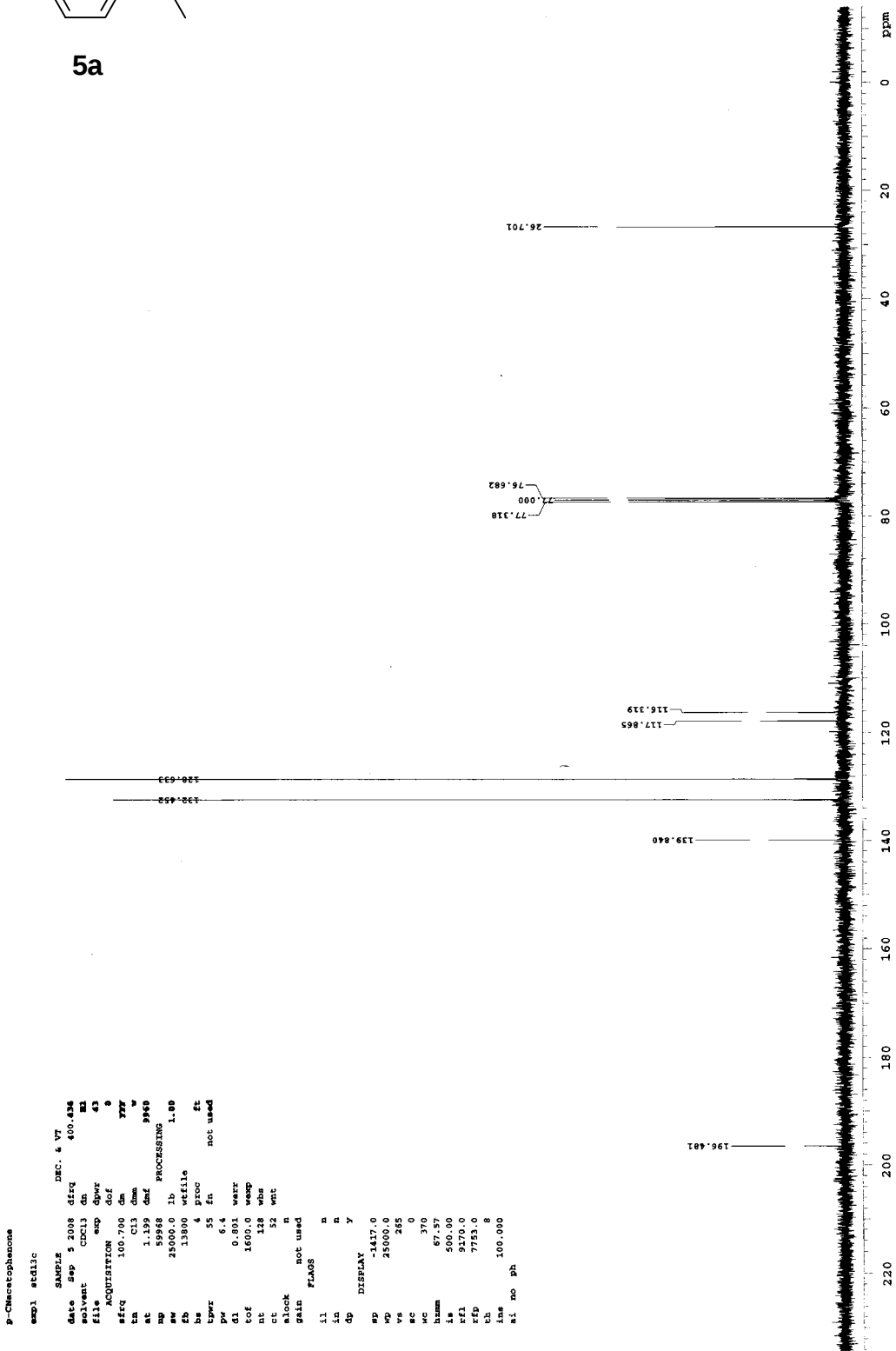


¹H-NMR (CDCl₃, 400MHz)

¹³C-NMR (CDCl₃, 100MHz)

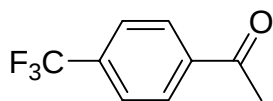


5a

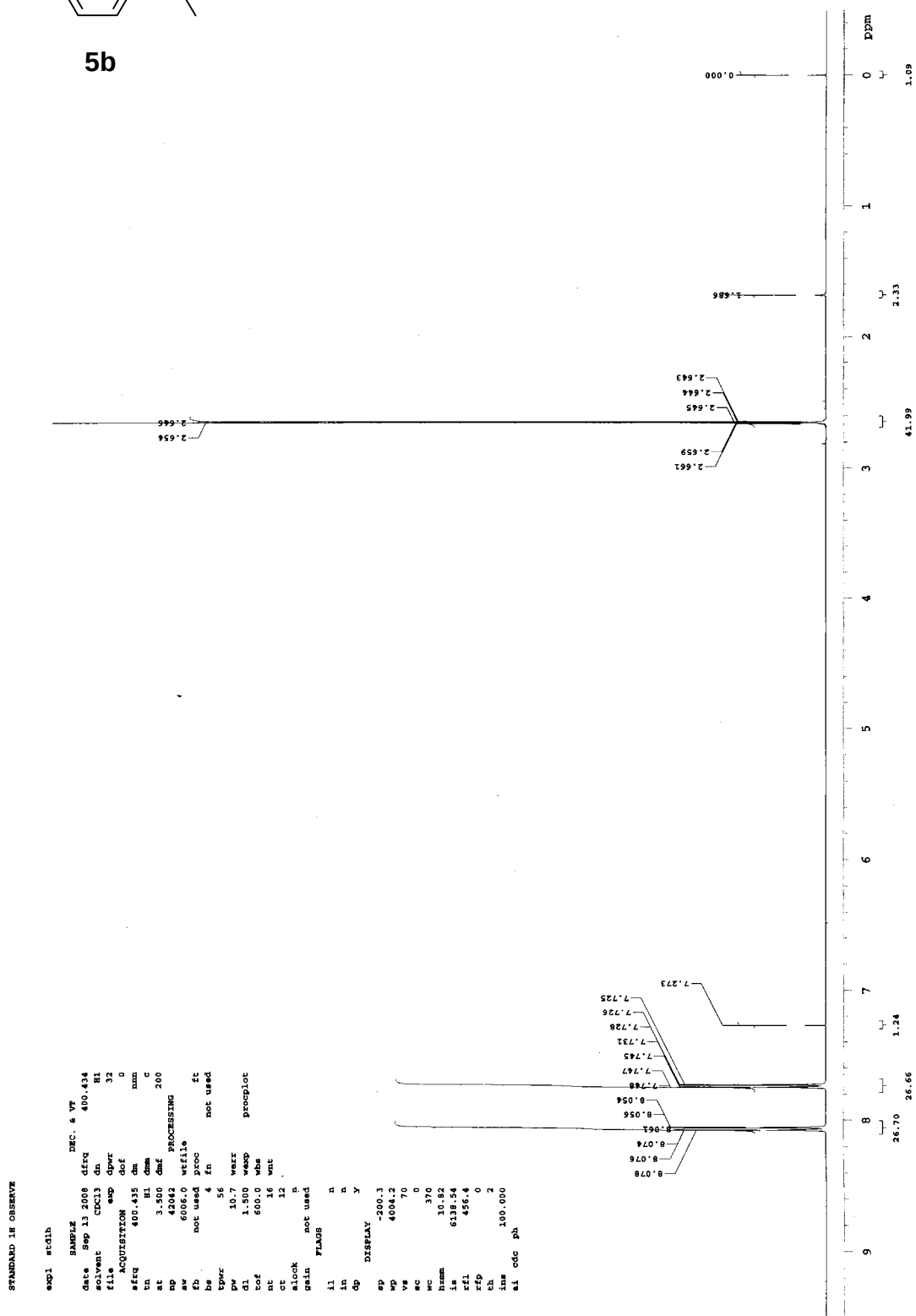


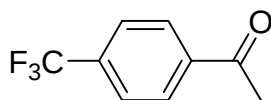
p-Trifluoromethylacetophenone **5b**

¹H-NMR (CDCl₃, 400MHz)

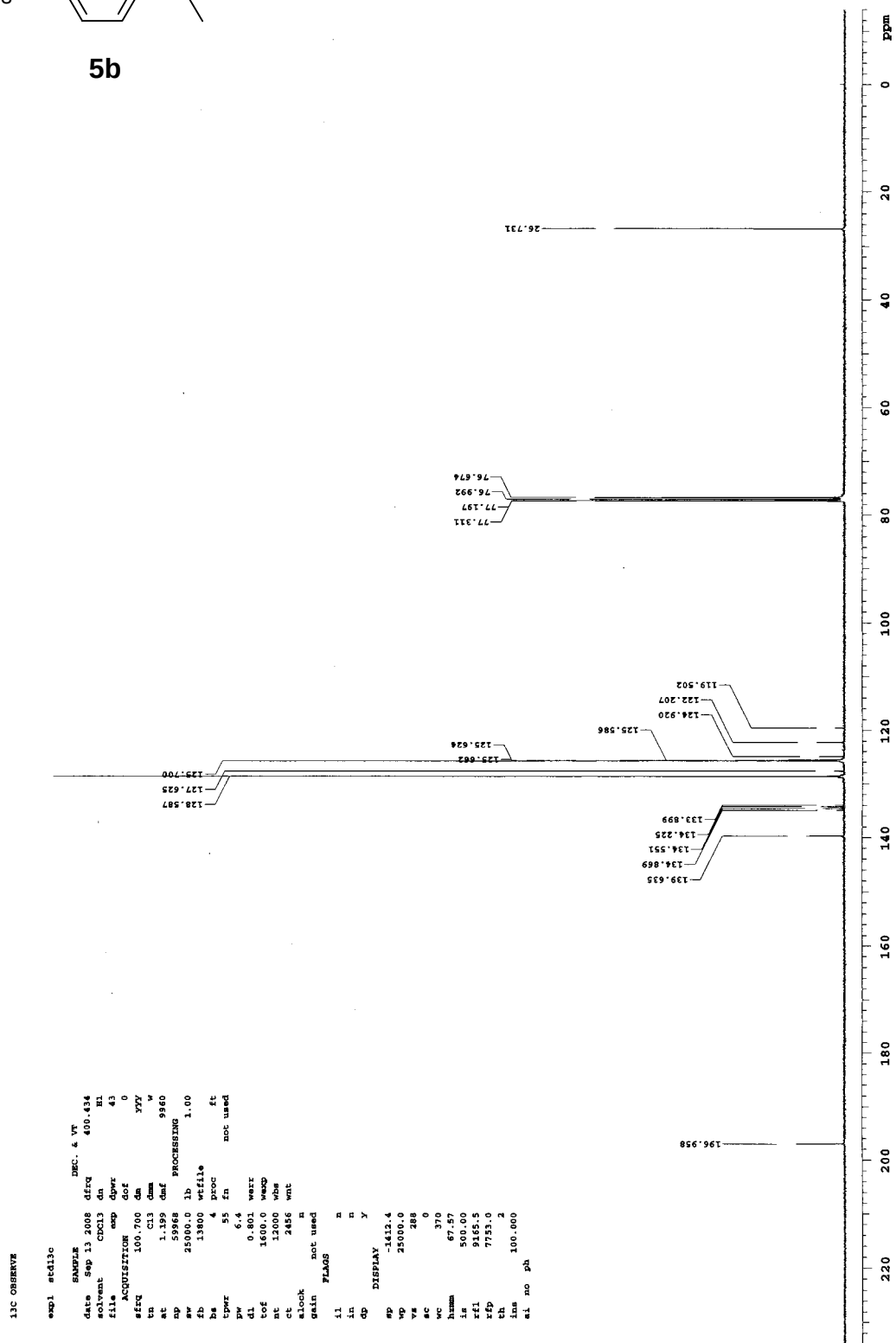


5b



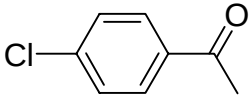
^{13}C -NMR (CDCl_3 , 100MHz)

5b

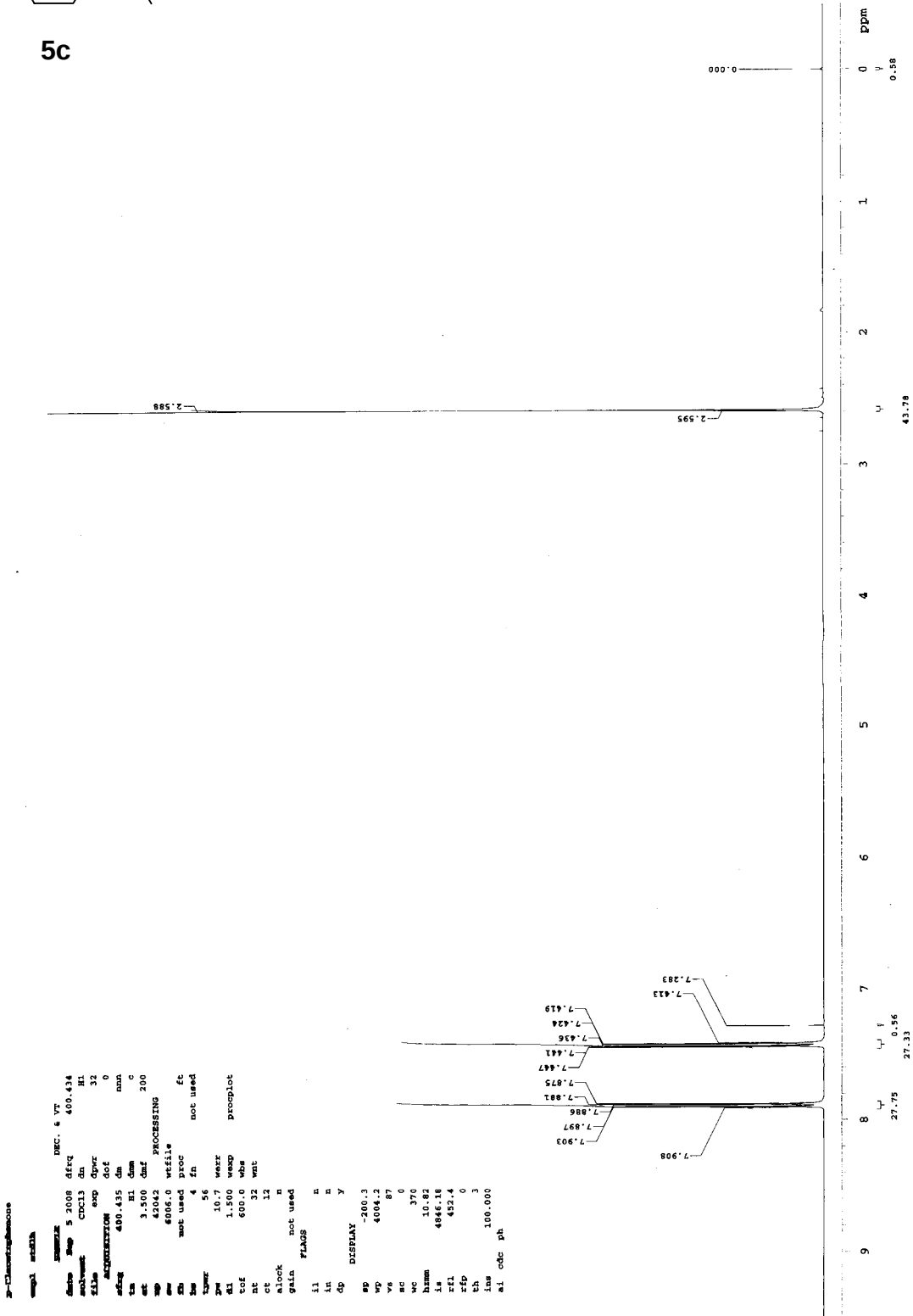


p-Chlorophenylacetophenone 5c

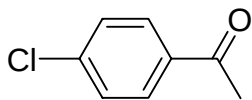
¹H-NMR (CDCl₃, 400MHz)



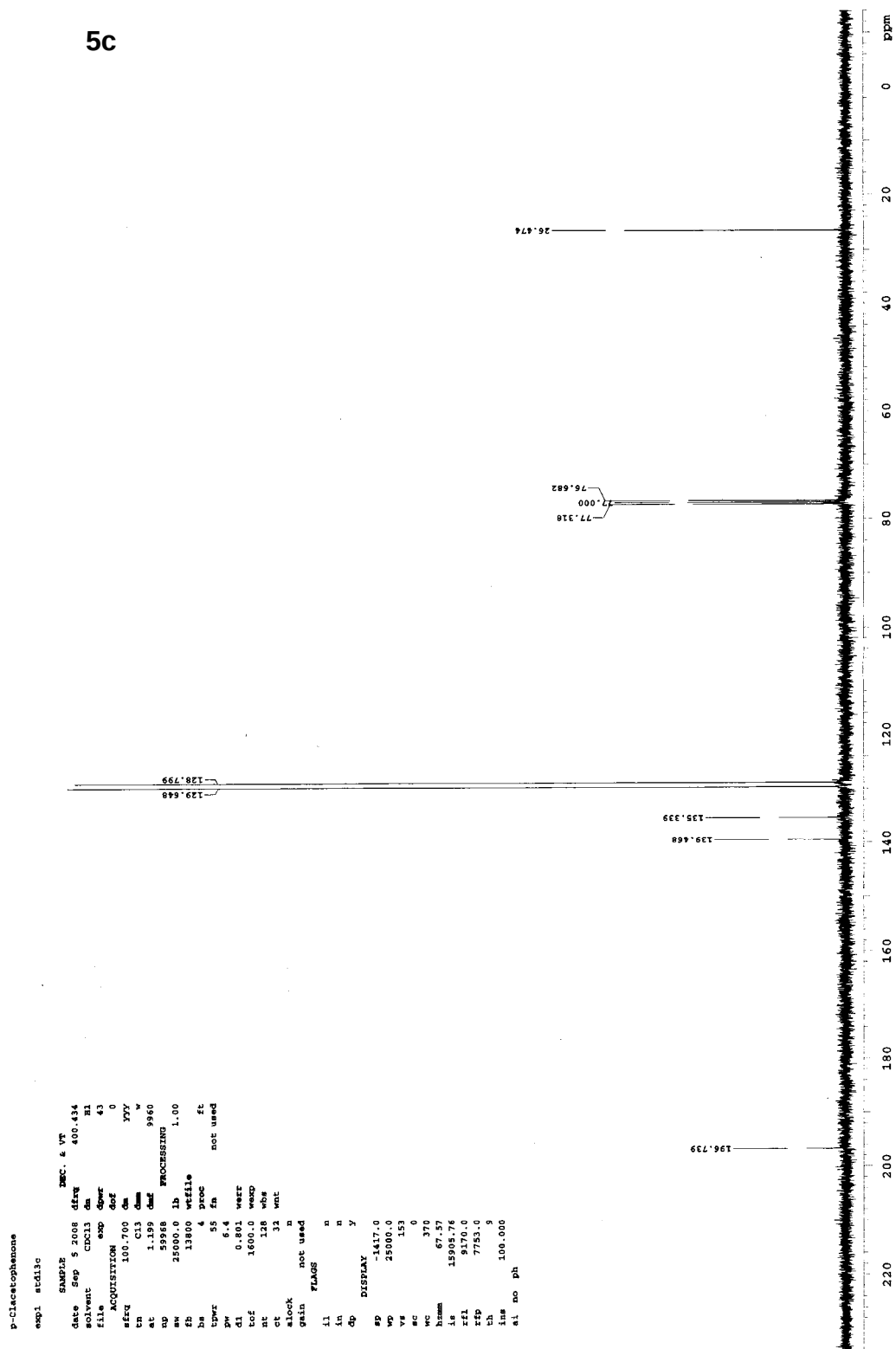
5c



^{13}C -NMR (CDCl_3 , 100MHz)

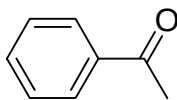


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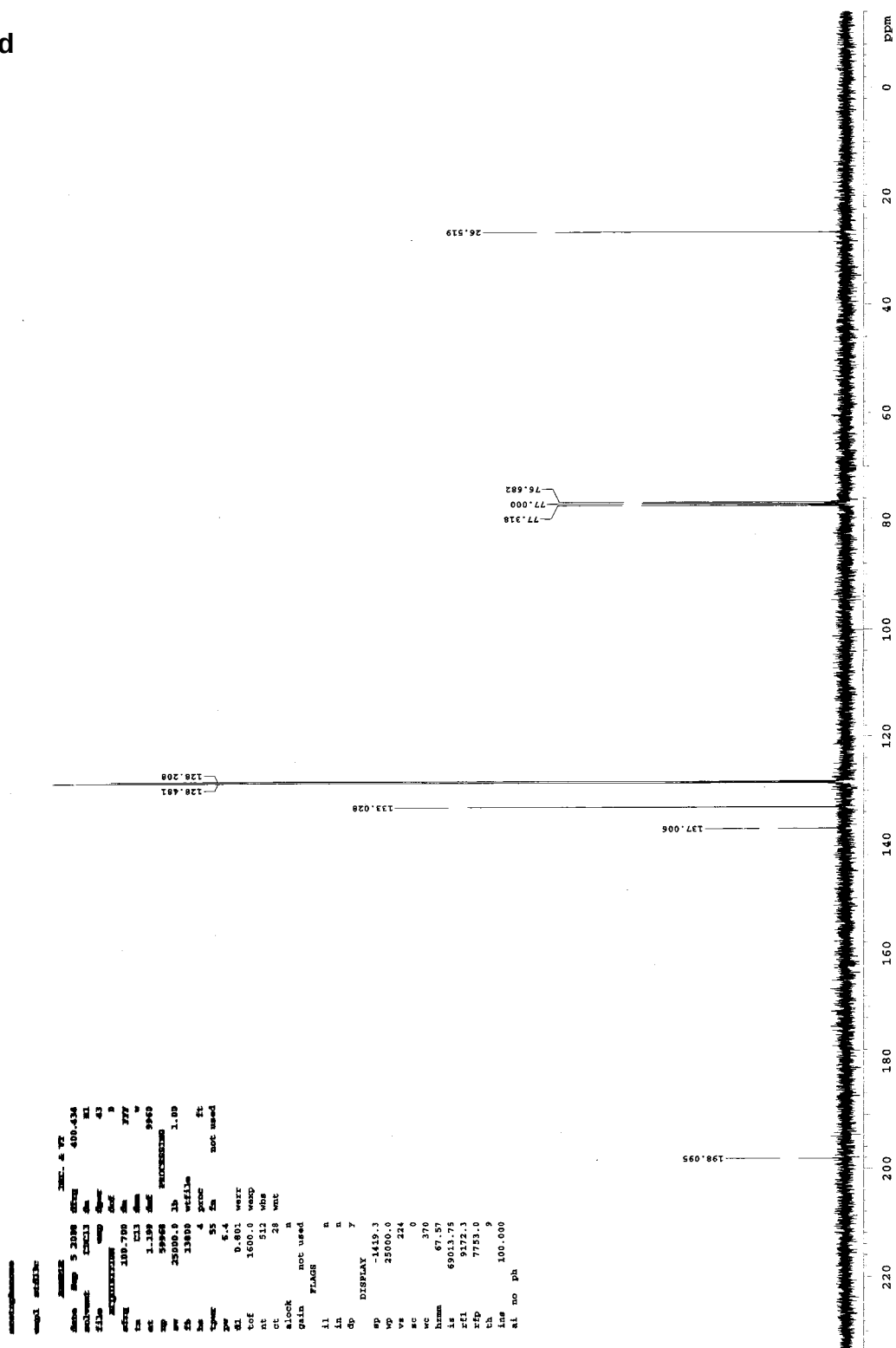


¹H-NMR (CDCl₃, 400MHz)

^{13}C -NMR (CDCl_3 , 100MHz)

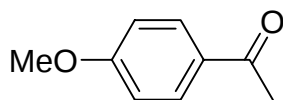


5d

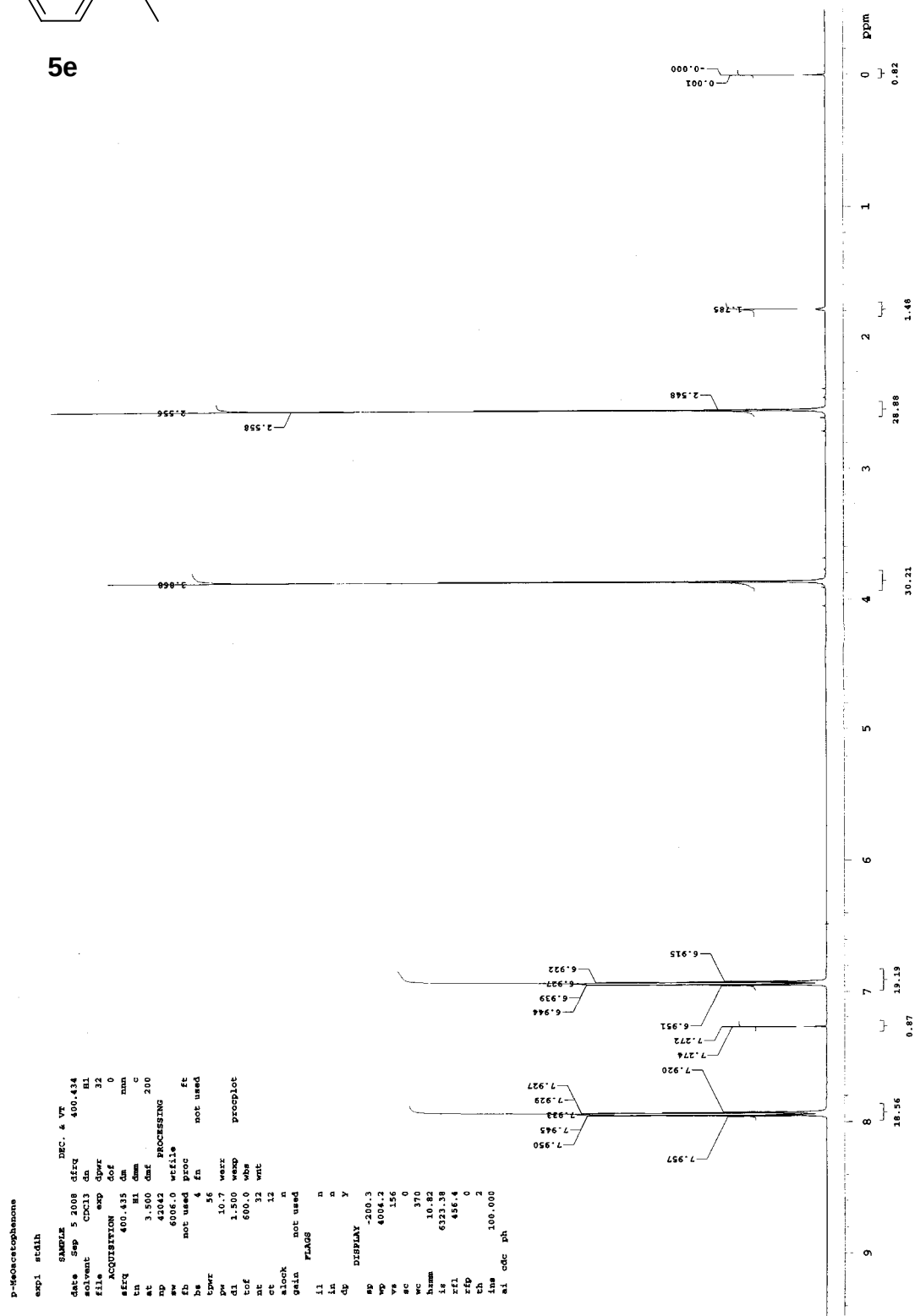


p-Methoxyacetophenone **5e**

¹H-NMR (CDCl₃, 400MHz)

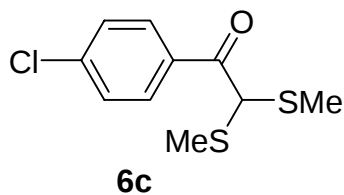


5e



p-Chlorophenyl di(methylthio)methyl ketone **6c**

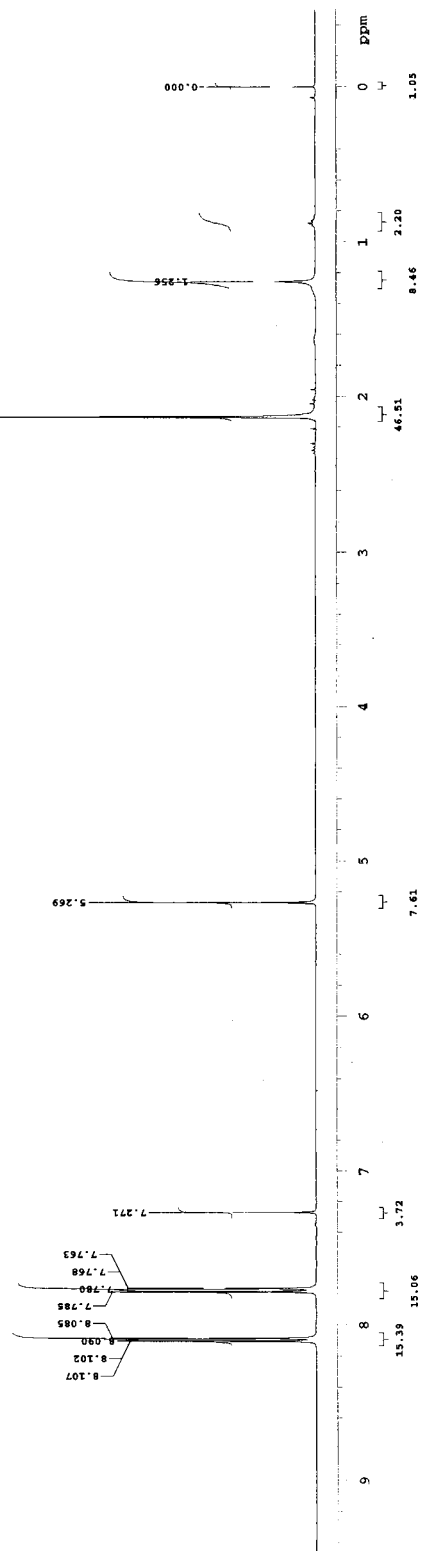
¹H-NMR (CDCl₃, 400MHz)

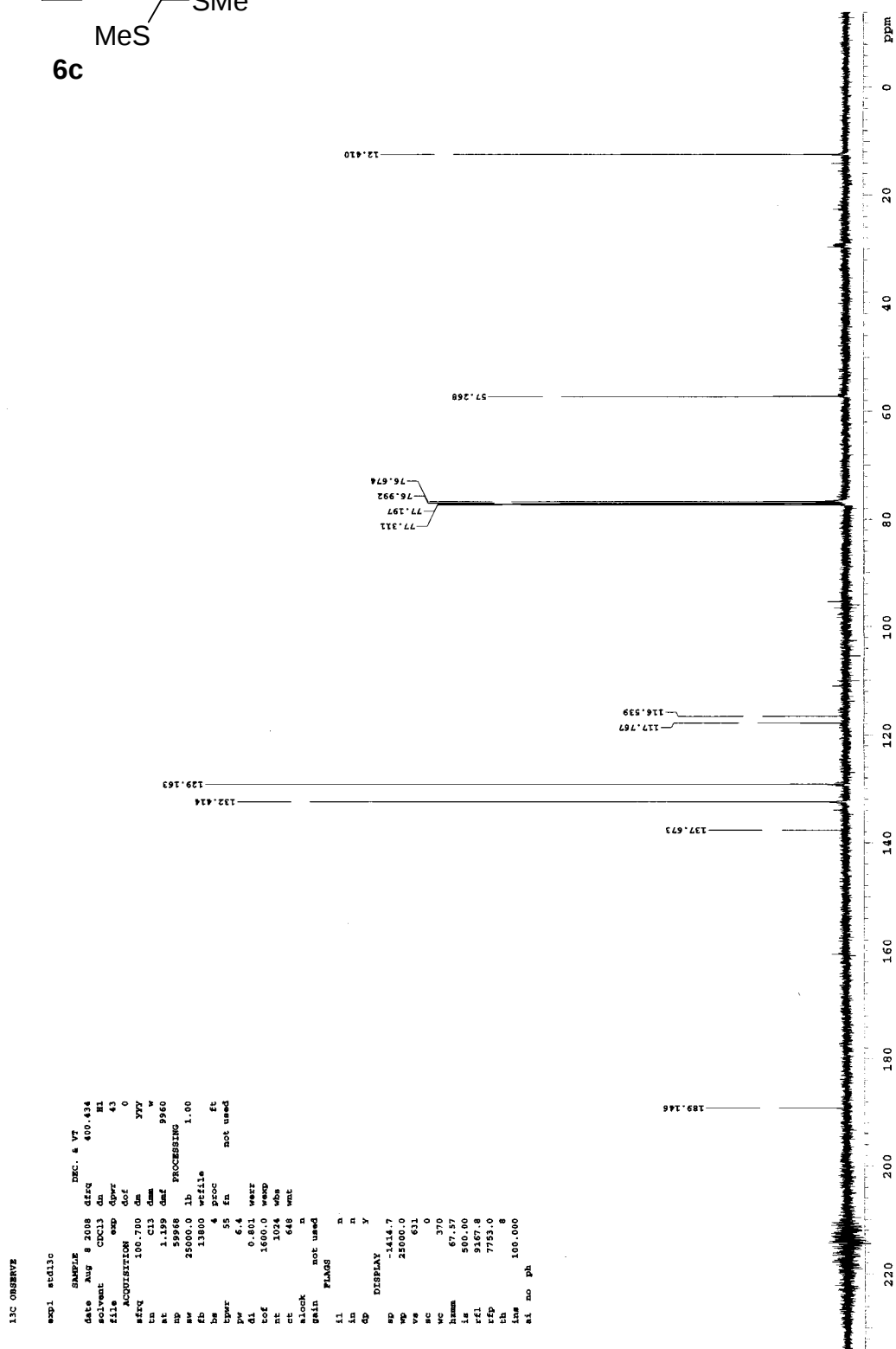
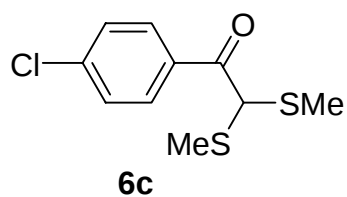


STANDARD IN OBSERVE

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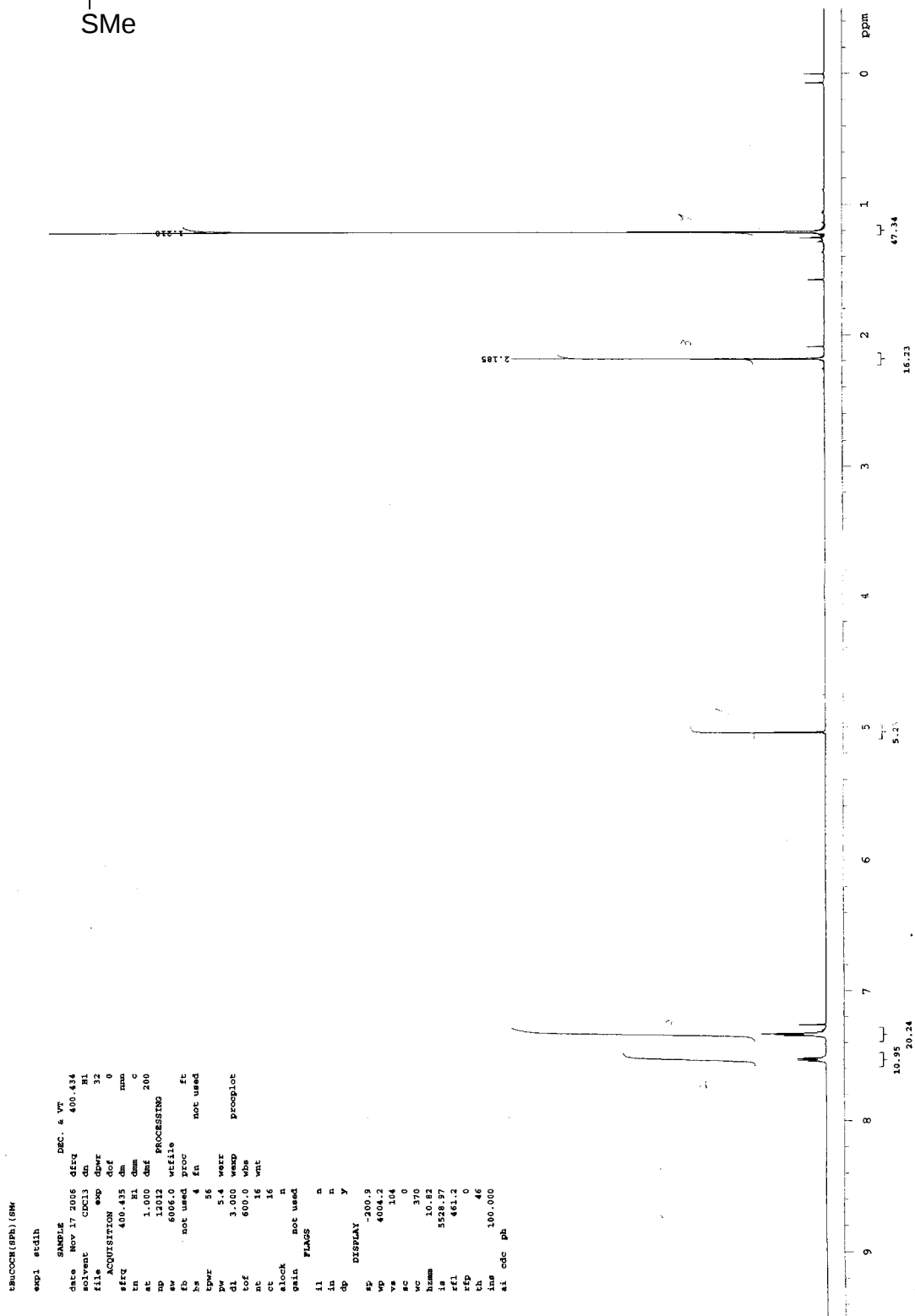
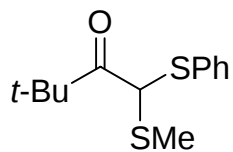
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NAME
data AUG 8 2008 DEC. 5 VT
solvent CDCl3 dn H1
file exp 32
ACQUISITION exp 32
sfreq 400.435 dm
in H1 dm
at 3.500 dmf PROCESSING
sw 42042
fo 8006.0 wfile
fo not used proc
cpwr 55
pw 10.7 warr
di 1.500 wexp
tof 600.0 wba
nt 32 wnt
ct 12
alock not used
gain not used
F1A0S
ll n
in n
op F
DP DISPLAY
pd -200.3
wp 4004.2
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rf2 0
tms 0
lms 100.000
xl cdc ph
  
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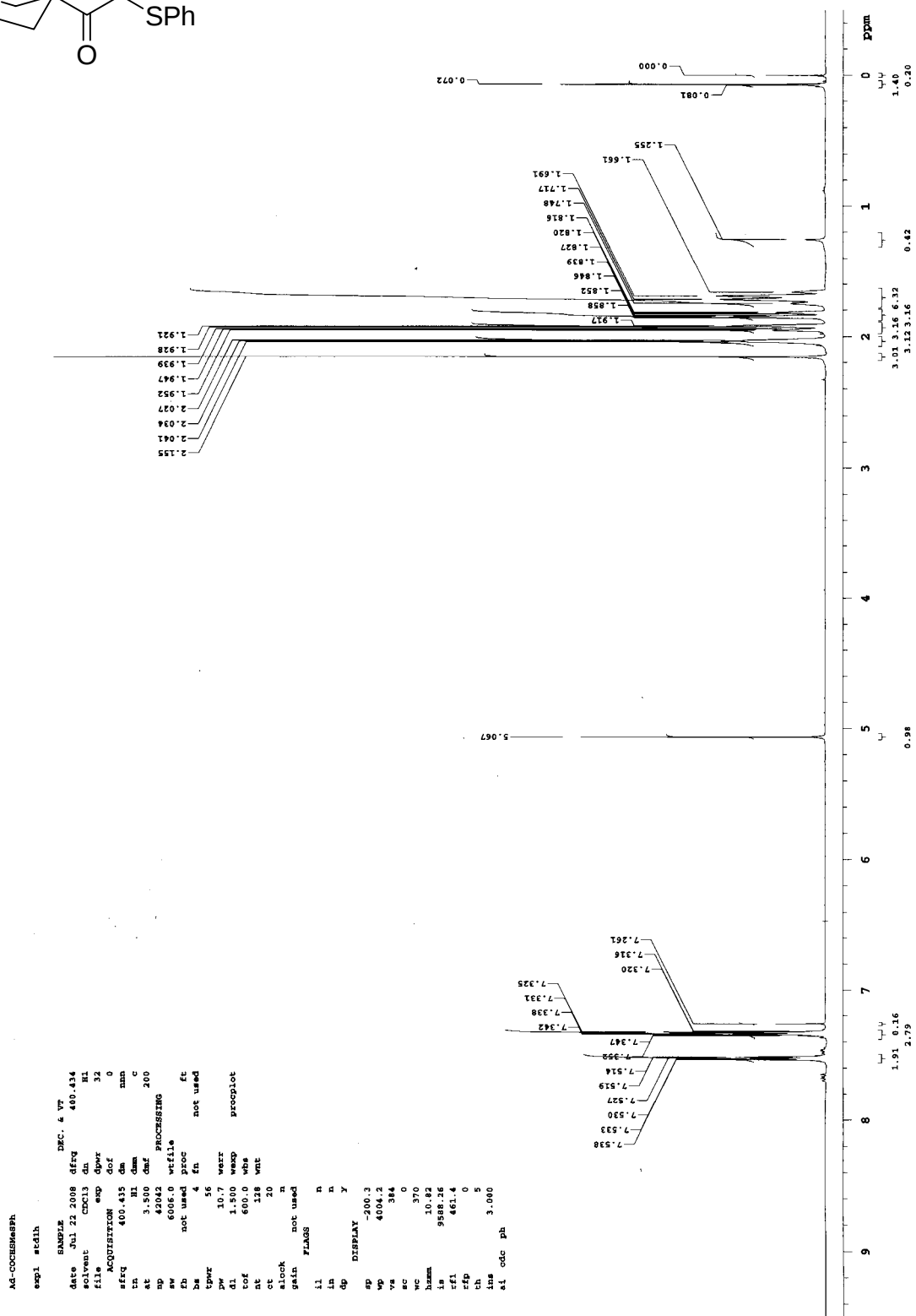
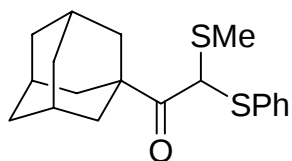


^{13}C -NMR (CDCl_3 , 100MHz)

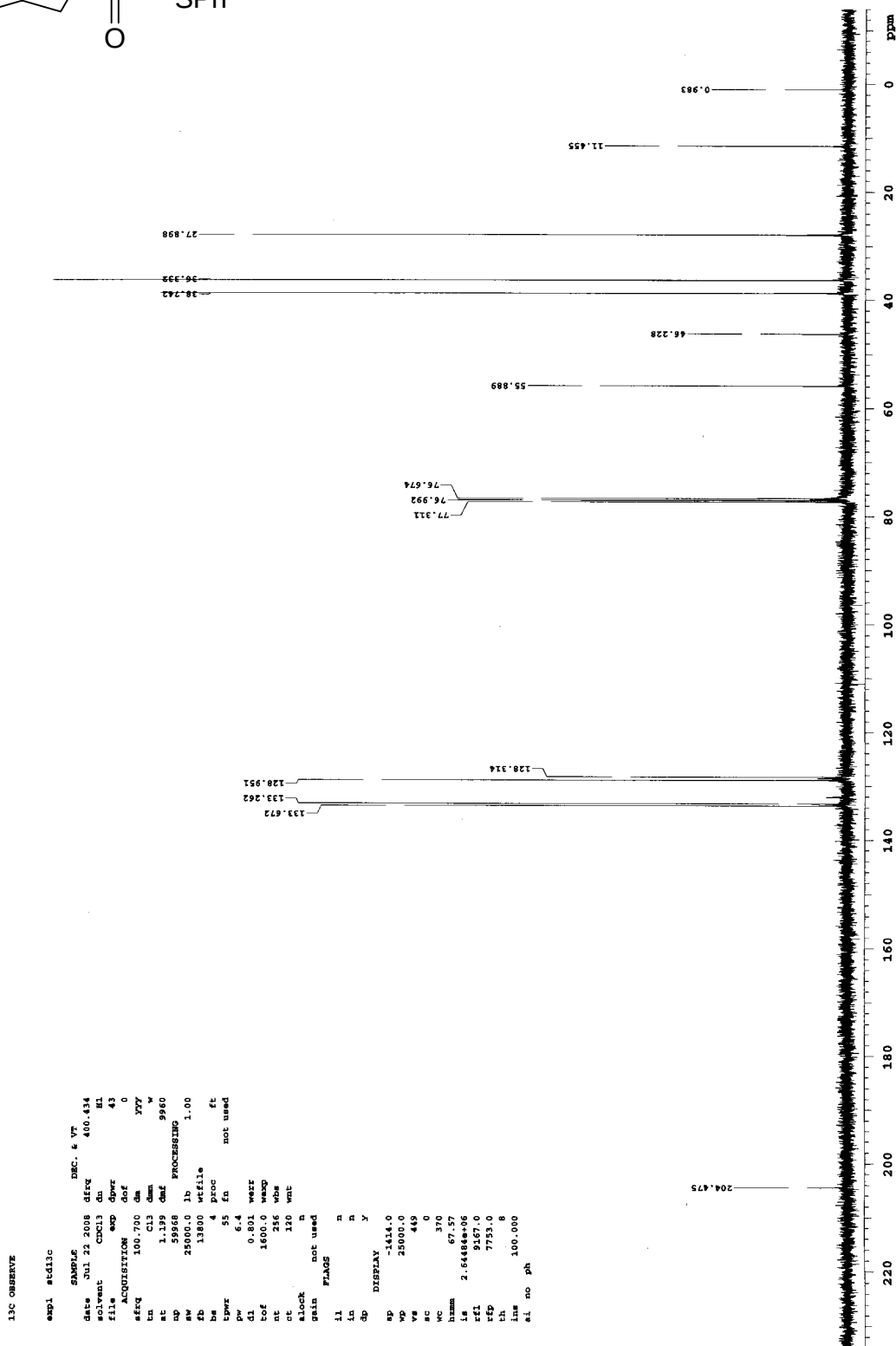
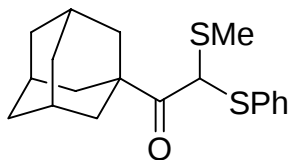
t-Butyl (methylthio)(phenylthio)methyl ketone

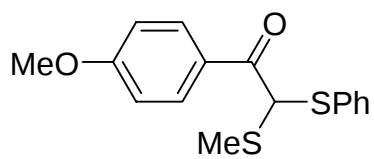
¹H-NMR (CDCl₃, 400MHz)



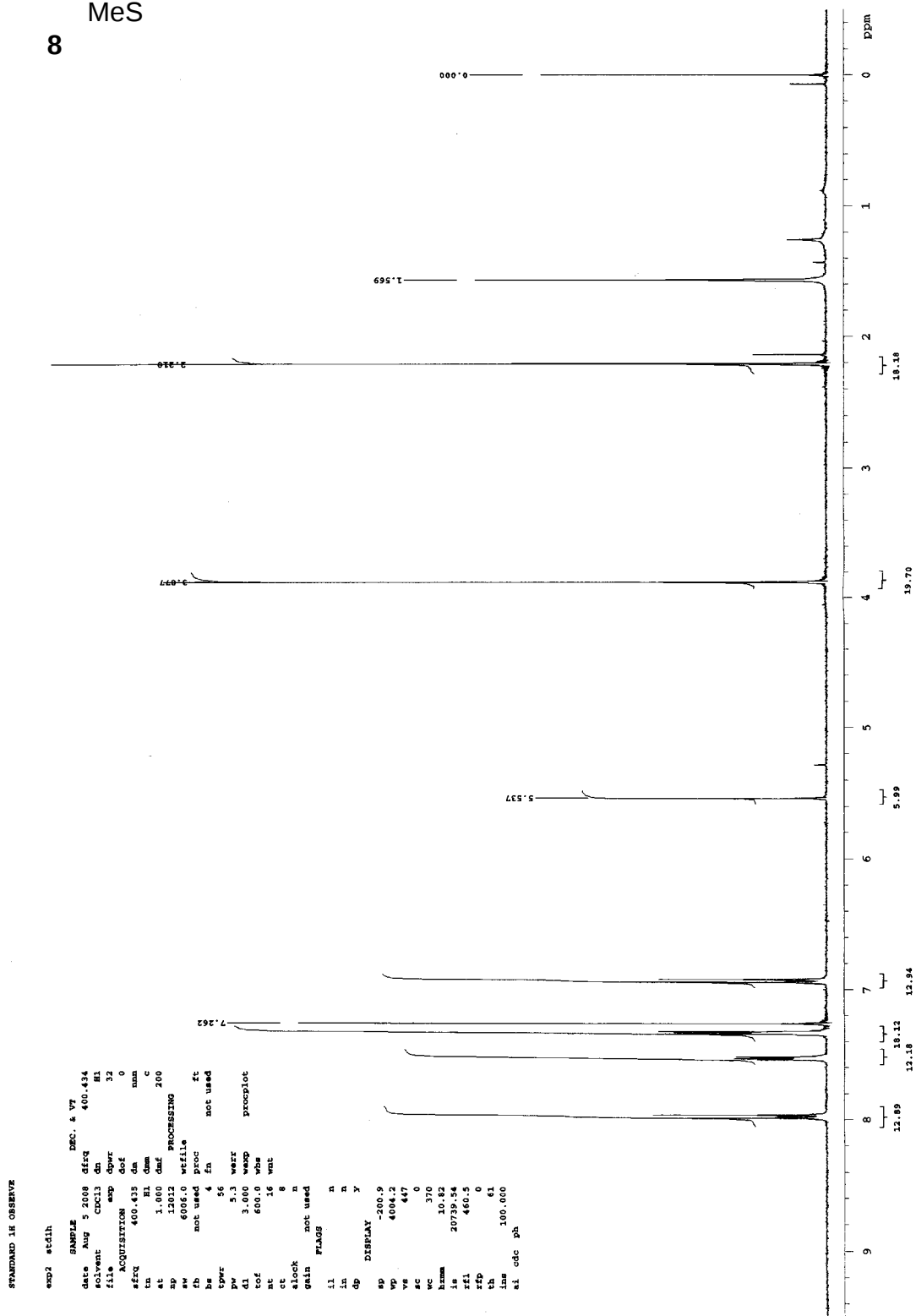
¹H-NMR (CDCl₃, 400MHz)

^{13}C -NMR (CDCl_3 , 100MHz)



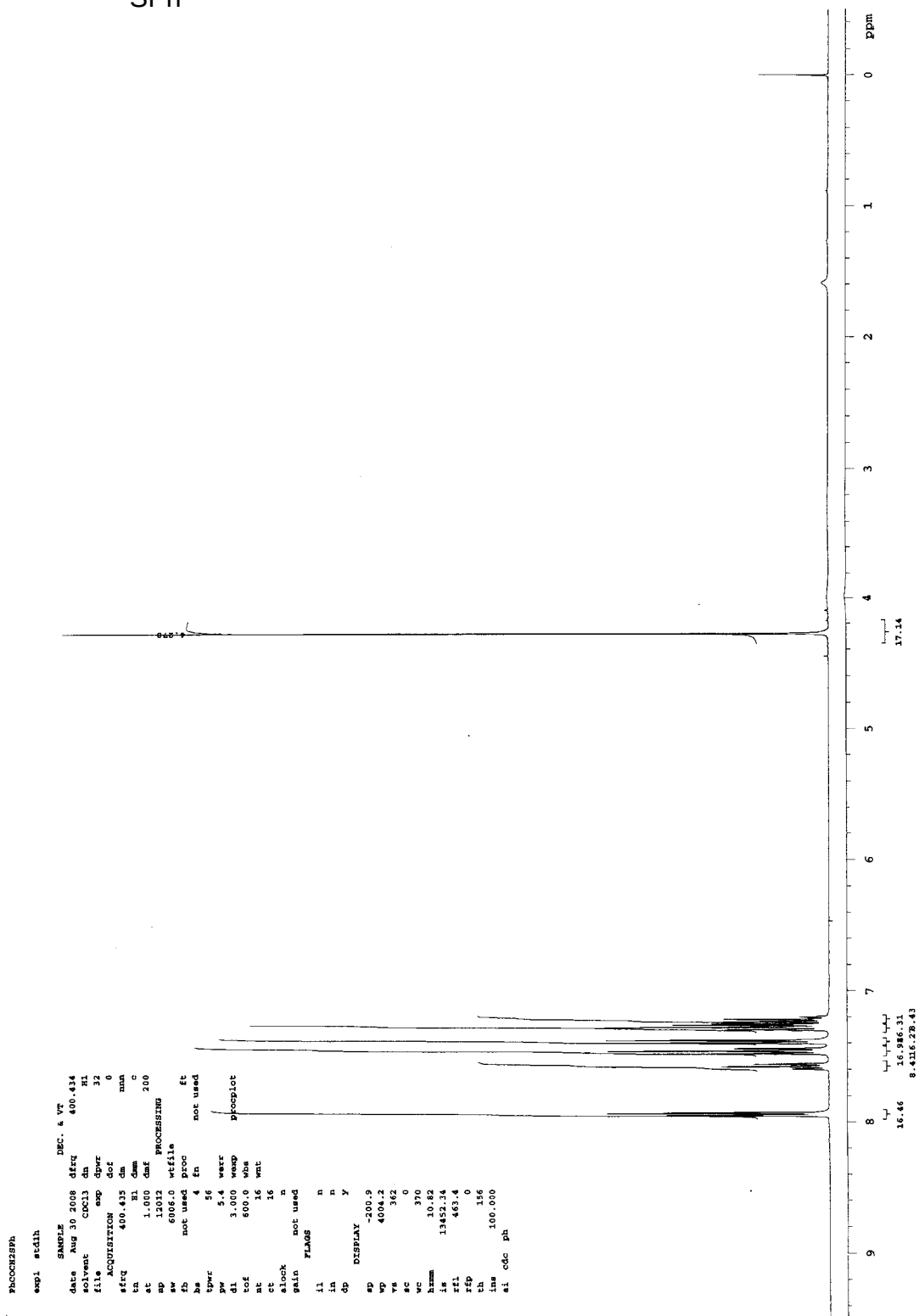
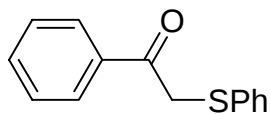
¹H-NMR (CDCl₃, 400MHz)

8



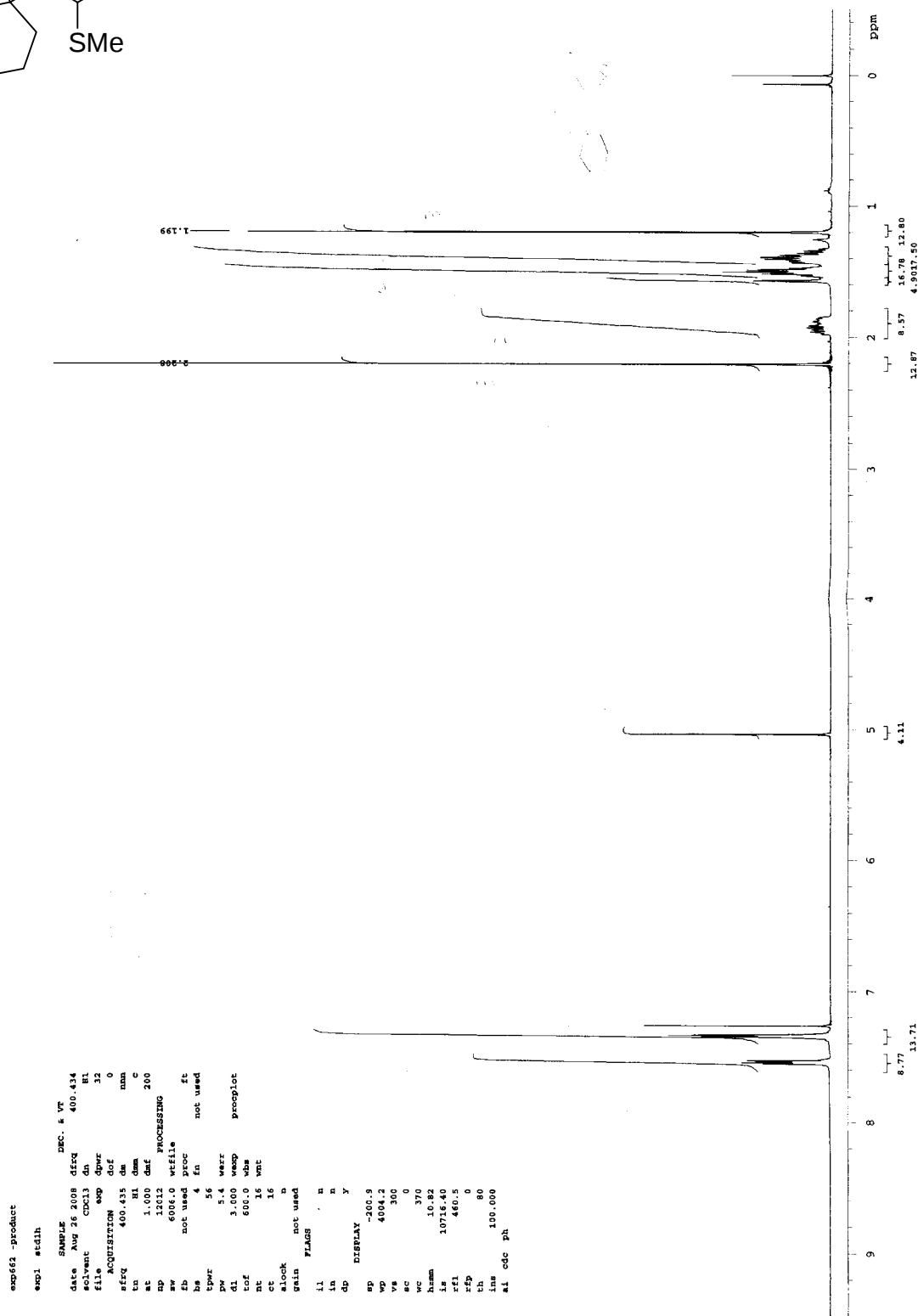
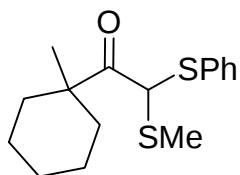
α -Phenylthioacetophenone

$^1\text{H-NMR}$ (CDCl_3 , 400MHz)



1-Methylcyclohexyl α -methylthio- α -phenylthiomethyl ketone

$^1\text{H-NMR}$ (CDCl_3 , 400MHz)



^{13}C -NMR (CDCl_3 , 100MHz)

