The Neber Route to Substituted Indoles

Douglass F. Taber* and Weiwei Tian

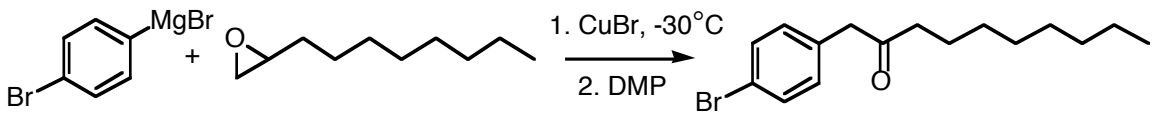
Department of Chemistry and Biochemistry, University of Delaware, Newark, DE 19716

Taberdf@udel.edu

Supporting Information

Contents:

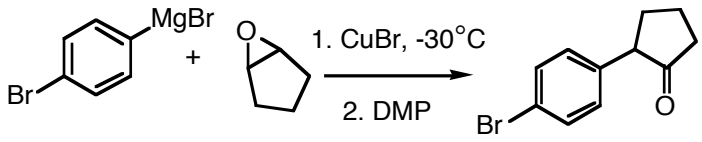
General. ^{1}H NMR and ^{13}C NMR spectra were recorded as solutions in deuteriochloroform ($CDCl_3$) unless otherwise indicated, at 400 MHz and 100 MHz, respectively. ^{13}C multiplicities were determined with the aid of a JVERT pulse sequence, differentiating the signals for methyl and methine carbons as "d" from methylene and quaternary carbons as "u". The infrared (IR) spectra were determined as neat oils. R_f values indicated refer to thin layer chromatography (TLC) on 2.5 x 10 cm, 250 μm analytical plates coated with silica gel GF, unless otherwise noted, and developed in the solvent system indicated. All glassware was oven dried and rinsed with dry solvent before use. Tetrahydrofuran (THF) was distilled from sodium metal/benzophenone ketyl under dry nitrogen. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride under dry nitrogen. Acetonitrile (MeCN) was treated with molecular sieve (4Å). MTBE is methyl *tert*-butyl ether and PE is petroleum ether. All reactions were conducted under N_2 and stirred magnetically.



4b

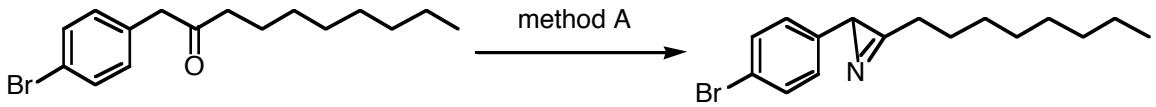
Ketone **4b**: In a round bottom flask, 1,4-dibromobenzene (14.16 g, 0.06 mol), Mg (1.44 g, 0.06 mol), iodine (trace) and 120 mL of THF were combined. The reaction was exothermic, reached reflux after 10 min. Then the reaction mixture was kept at reflux by heating until the Mg disappeared (30 min). After cooling to -30 °C, CuBr (0.75 g, 5.24 mmol) was added. After 3 min, 1, 2-epoxydecane (4.68 g, 0.03 mol) in THF (10 mL) was added dropwise over 10 min. The cooling bath was removed, and the mixture was stirred for 1 h. After quenching with saturated aqueous NH_4Cl (50 mL), the reaction mixture was partitioned between MTBE and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to afford the alcohol (4.23 g) as a white solid: TLC R_f (PE/MTBE = 9/1) = 0.28.

Dess-Martin periodinane (6.99 g, 16.5 mmol) was added at 0 °C to the alcohol (4.23 g) in 100 mL of CH_2Cl_2. The reaction was followed by TLC. After disappearance of the alcohol, saturated aqueous $Na_2S_2O_3 \cdot 5H_2O$ (10 mL) was added. The mixture was then partitioned between CH_2Cl_2 and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to afford the ketone **4b** (3.68 g, 11.8 mmol, 40% yield from the epoxide) as a white solid: mp 35-37 °C; TLC R_f (PE/MTBE = 9/1) = 0.60; ^{1}H NMR (400 MHz) 0.87 (3H, t, J = 7.0Hz), 1.22-1.28 (10H, m), 1.52-1.57(2H, m), 2.43 (2H, t, J = 7.4Hz), 3.60 (2H, s), 7.07 (2H, d, J = 8.4Hz), 7.44 (2H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz) δ u 22.8, 23.9, 29.3, 29.5, 32.0, 42.4, 49.4, 121.2, 133.5, 208.0; d 14.3, 131.3, 131.9; IR (film, cm^{-1}) 2920, 2848, 1708, 1413, 803; LRMS (CI) m/z (rel. intensity) 312 (1), 310 (1), 171 (20), 169 (20), 141 (100), 90 (14); HRMS calcd for $C_{16}H_{25}N^{79}Br$ (M+H) 311.1011, obsd 311.1008.



4e

Ketone **4e**: The ketone **4e** was prepared following the same procedure of synthesis of the ketone **4b** in 45% overall yield from cyclopentene oxide as a colorless oil: TLC R_f (PE/MTBE/CH_2Cl_2 = 6/2/2) = 0.32; ^{1}H NMR (400 MHz) 1.85-2.30 (4H, m), 2.41-2.49 (2H, m), 3.26 (1H, dd, J = 8.4, 11.6 Hz), 7.06 (2H, d, J = 8.4 Hz), 7.43 (2H, m); ^{13}C NMR (100 MHz) δ u 20.8, 31.5, 38.3, 120.9, 137.4, 217.3; d 54.7, 130.0, 131.7; IR (film, cm^{-1}) 1738, 1488, 1010; LRMS m/z (CI) (rel. intensity) 240 (92), 238 (92), 184 (100), 182 (100), 160 (55), 131 (38); HRMS calcd for $C_{11}H_{11}O^{79}Br$ (M) 237.9993, obsd 237.9990.



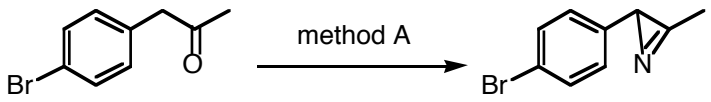
4b **5b**

Two procedures are developed for azirine synthesis.

Method A: Azirine **5b**: Methanol (20 mL) and water (1 mL) were added to a mixture of **4b** (0.631 g, 2.03 mmol), $NH_2OH{\cdot}HCl$ (0.212 g, 3.05 mmol) and sodium acetate (0.250 g, 3.05 mmol) in a round bottom flask. After stirring at rt for 4 h, the solvent was removed *in vacuo*. The reaction mixture was partitioned between MTBE and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4). Concentration led to the crude oxime (0.635 g), which was used directly in the next reaction.

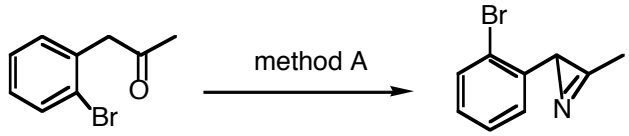
To a solution of the crude oxime (0.635 g) in 35 mL of THF was added triethylamine (296 mg, 2.93 mmol) and methanesulfonyl chloride (332 mg, 2.93 mmol) sequentially at rt. The solution got cloudy after the addition of methanesulfonyl chloride. After 30 min, DBU (890 mg, 5.86 mmol) was added over 1 min. After 30 min, the reaction mixture was passed through a pad of silica gel, washing with MTBE. The mixture was

concentrated *in vacuo* and the residue was chromatographed to give the azirine **5b** (437 mg, 1.42 mmol, 70% yield from the ketone) as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.69; ^{1}H NMR (400 MHz) 0.88 (3H, t, J = 6.8 Hz), 1.25-1.31 (8H, m), 1.38-1.42 (2H, m), 1.72-1.76 (2H, m), 2.80 (2H, t, J = 7.2 Hz), 2.82 (1H, s), 6.92 (2H, d, J = 8.4 Hz), 7.39 (2H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz) δ u 22.8, 24.5, 27.1, 29.2, 29.3, 29.4, 31.9, 120.5, 140.9, 167.5; d 14.2, 33.0, 127.2, 131.4; IR (film, cm^{-1}) 2927, 2855, 1765, 1487, 830; HRMS calcd for $C_{16}H_{22}N^{79}Br$ 307.0936, obsd 307.0943.



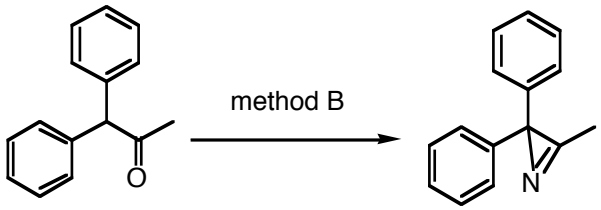
4a **5a**

Azirine **5a:** The azirine **5a** was prepared following method A in 78% yield as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.36; ^{1}H NMR (400 MHz) 2.48 (3H, s), 2.81 (1H, s), 6.91 (2H, d, J = 8.4 Hz), 7.38 (2H, d, J = 8.8 Hz); ^{13}C NMR (100 MHz) δ u 120.5, 140.4, 164.2; d 12.8, 32.8, 127.2, 131.3; IR (film, cm^{-1}) 3443, 2987, 1777, 1484, 830; HRMS calcd for $C_9H_9N^{79}Br$ (M+H) 207.9762, obsd 207.9764.



4d **5d**

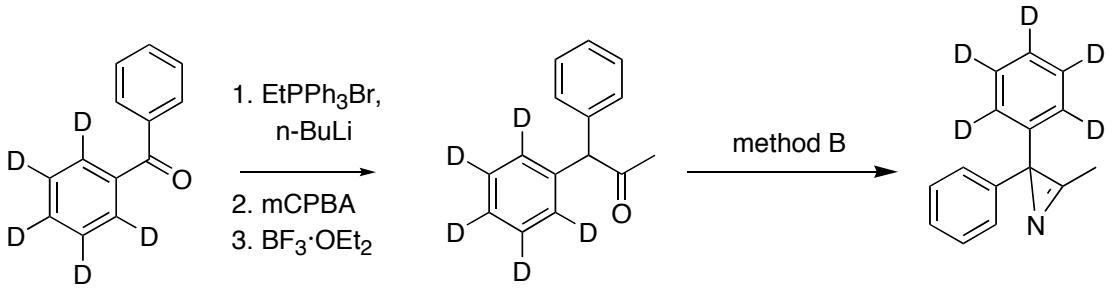
Azirine **5d:** The azirine **5d** was prepared following method A in 78% yield as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.48; ^{1}H NMR (400 MHz) δ 2.52 (3H, s), 3.23 (3H, s), 6.71 (1H, dd, J = 2.0, 8.0 Hz), 7.07 (1H, dt, J = 1.6, 7.6 Hz), 7.21 (1H, m), 7.52 (1H, dd, J = 0.8, 8.9 Hz); ^{13}C NMR (100 MHz) δ u 123.5, 140.0, 165.4; d 13.2, 32.9, 125.9, 127.4, 128.2, 132.8; IR (film, cm^{-1}) 2984, 1774, 1470, 1027, 757; HRMS calcd for $C_9H_9N^{79}Br$ (M+H) 207.9762, obsd 207.9752.



4c **5c**

Method B: Azirine **5c**[1]: The crude oxime was prepared by the same procedure described in method A.

The crude oxime (89 mg, 0.40 mmol) was suspended in 2 mL of MeCN. While stirring, a mixture of DIAD (0.258 g, 1.20 mmol) and tri-n-butylphosphine (0.243 g, 1.20 mmol) in MeCN (1 mL) was added over 5 min at rt. After 2 h, the reaction mixture was filtered through a short pad of silica gel, washing with MTBE. The organic solution was concentrated *in vacuo*. The residue was chromatographed to yield the azirine **5c** (75 mg, 0.36 mmol, 91% yield from the ketone) as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.43; ^{1}H NMR (400 MHz) 2.56 (3H, s), 7.19-7.32 (10H, m); ^{13}C NMR (100 MHz) δ u 42.9, 142.0, 167.6; d 13.0, 127.1, 128.1, 128.5.



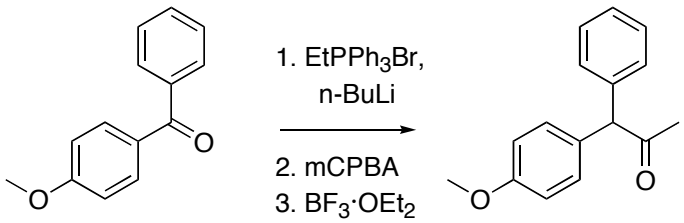
4c-d$_5$ **12**

Azirine **12**: To a THF (5 mL) solution of methyltriphenylphosphonium bromide (0.81 g, 2.19 mmol) was added a 1.92 M hexane solution of n-butyllithium (1.14 mL, 2.19 mmol) at 0 °C. After 1 h, a solution of benzophenone-2,3,4,5,6-d$_5$ (0.205 g, 1.09 mmol) in THF (5 mL) was added and the mixture was stirred at 0 °C for 2 h. The mixture was then partitioned between CH_2Cl_2 and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to afford the alkene (0.207 g) as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.78.

The alkene (0.207 g) was dissolved in CH_2Cl_2 (10 mL). $NaHCO_3$ (0.218 g, 2.6 mmol) and mCPBA (77% purity, 0.466 g, 2.08 mmol) were added sequentially at 0 °C. The reaction was monitored by TLC. After disappearance of the starting material on TLC, the reaction mixture was partitioned between MTBE and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to afford the epoxide (0.168 g) as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.63.

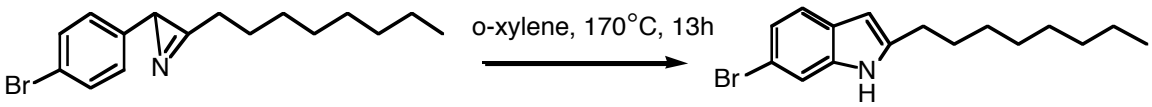
The epoxide (0.168 g) was dissolved in Et_2O (10 mL). $BF_3{\cdot}OEt_2$ (0.2 mL) was added at rt. After 1 min, the reaction mixture was partitioned between MTBE and, sequentially, water, saturated aqueous $NaHCO_3$ and brine. The combined organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed to afford the ketone **4c-d$_5$** (102 mg, 0.474 mmol, 43% yield from benzophenone-2,3,4,5,6-d_5) as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.45; ^{1}H NMR (400 MHz) 2.26 (3H, s), 5.14 (1H, s), 7.24-7.36 (5H, m); ^{13}C NMR (100 MHz) δ u 138.5, 206.7; d 30.3, 65.2, 127.5, 128.9, 129.2. IR (film, cm^{-1}) 1712, 1352, 1154, 746; LRMS (CI) m/z (rel. intensity) 216 (61), 139 (27), 172 (100), 156 (23); HRMS calcd for $C_{15}H_{10}D_5O$ (MH) 216.1437, obsd 216.1431.

The azirine **12** was prepared following method B in 73% yield from the ketone **4c-d$_5$** as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.46; ^{1}H NMR (400 MHz) 2.57 (3H, s), 7.20-7.33 (5H, m); ^{13}C NMR (100 MHz) δ u 42.9, 142.0, 167.6; d 13.1, 127.2, 128.1, 128.5; IR (film, cm^{-1}) 3026, 2271, 1764, 1493, 764; HRMS calcd for $C_{12}H_{10}D_5N$ 212.1362, obsd 212.1356.



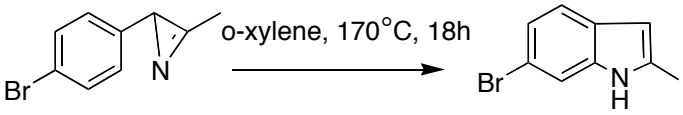
15

Ketone **15**[2]: The ketone **15** was prepared following the same procedure described in the synthesis of the ketone **4c-d$_5$** in 17% overall yield from 4-methoxybenzophenone as a colorless oil: TLC R_f (PE/MTBE = 8/2) = 0.36; ^{1}H NMR (400 MHz) 2.22 (3H, s), 3.77 (3H, s), 5.06 (1H, s), 6.86 (2H, d, J = 8.8 Hz), 7.14 (2H, d, J = 8.4 Hz), 7.19-7.34 (5H, m); ^{13}C NMR (100 MHz) δ u 130.5, 138.8, 158.9, 207.0; d 30.1, 55.4, 64.4, 114.3, 127.3, 128.9, 129.1, 130.2.



5b **6b**

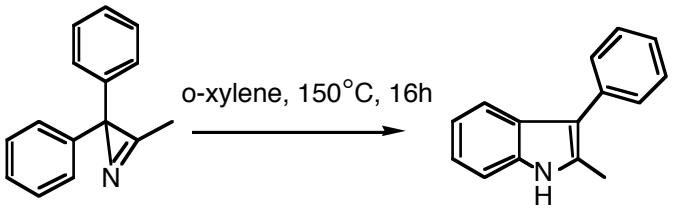
Indole **6b:** In a thick-wall tube, **5b** (120 mg, 0.390 mmol) and 2 mL of o-xylene were combined. The tube was then sealed and heated to 170 °C for 13 h. After cooling, the reaction mixture was chromatographed to yield the indole **6b** (103 mg, 0.334 mmol, 86% yield) as a white solid: mp 82-83 °C; TLC R_f (PE/MTBE = 95/5) = 0.32; ^{1}H NMR (400 MHz, acetone-d$_6$): 0.85-0.89 (3H, m), 1.27-1.38 (10H, m), 1.70-1.77 (2H, m), 2.77 (2H, t, J = 7.6Hz), 6.20-6.21 (1H, m), 7.08 (1H, dd, J = 1.6, 8.4 Hz), 7.37(1H, d, J = 8.4Hz), 7.47 (1H, m); ^{13}C NMR (100 MHz, acetone-d$_6$) δ u 23.4, 28.8, 30.0, 30.1, 30.1, 30.2, 32.7, 114.0, 129.0, 138.3, 142.5; d 14.4, 99.9, 114.2, 121.7, 122.7; IR (film, cm^{-1}) 3394, 2924, 1638, 809; LRMS (CI) m/z (rel. intensity) 309 (26), 307 (26), 280 (56), 278 (56), 266 (50), 264 (50), 252 (44), 254 (44), 224 (57), 210 (98), 184 (93), 130 (100), 89 (128); HRMS calcd for $C_{16}H_{22}N^{79}Br$ 307.0936, obsd 307.0932.



5a **6a**

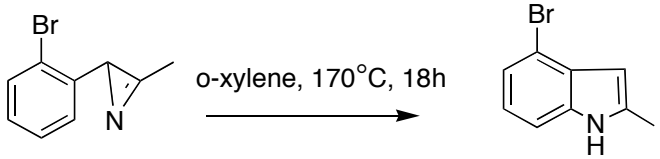
Indole **6a:** The indole **6a** was prepared following the procedure of synthesis of indole **6b** except that the sealed tube was heated to 170 °C for 18 h. The indole **6a** was isolated in 88% yield as a white solid: mp 123-124°C; TLC R_f (PE/MTBE = 80/20) = 0.31; ^{1}H

NMR (400 MHz) 2.39 (3H, d, J = 0.8 Hz), 6.16-6.18 (1H, m), 7.15 (1H, dd, J = 2.0, 8.4 Hz), 7.34-7.36 (2H, m), 7.73 (1H, bs); ^{13}C NMR (100 MHz) δ u 114.4, 128.1, 136.1, 137.0; d 13.9, 100.7, 113.3, 121.0, 123.0; IR (film, cm^{-1}) 3401, 1638, 1387, 809; HRMS calcd for $C_9H_8N^{79}Br$ 208.9840, obsd 208.9841.



5c **6c**

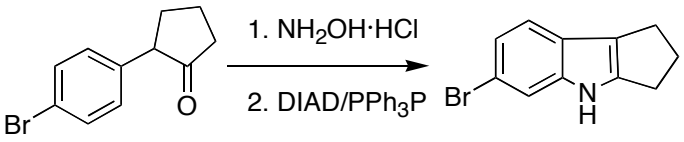
Indole **6c**[3]**:** The indole **6c** was prepared following the procedure of synthesis of indole **6b** except that the sealed tube was heated to 150 °C for 16 h. The indole **6c** was isolated in 89% yield as a white solid: mp 57-59 °C; TLC R_f (PE/MTBE = 8/2) = 0.30; ^{1}H NMR (400 MHz, acetone-d_6) 2.52 (3H, s), 7.02-7.12 (2H, m), 7.26-7.63 (7H, m), 10.20 (1H, bs); ^{13}C NMR (100 MHz, acetone-d_6) δ u 114.4, 128.7, 132.9, 136.8, 136.9; d 12.6, 111.5, 119.0, 120.3, 121.8, 126.3, 129.4, 130.0.



5d **6d**

Indole **6d:** The indole **6d** was prepared following the procedure of synthesis of indole **6a**. The indole **6d** was isolated in 84% yield as pale-red oil: TLC R_f (PE/MTBE = 9/1) = 0.26; ^{1}H NMR (400 MHz, acetone-d_6) δ 2.45 (3H, d, J = 0.4 Hz), 6.20 (1H, t, J = 0.8 Hz), 6.94 (1H, t, J = 7.8 Hz), 7.16 (1H, d, J = 7.2 Hz), 7.31 (1H, d, J = 8.0Hz), 10.33 (1H, bs); ^{13}C NMR (100 MHz, acetone-d_6) δ u 113.5, 130.6, 137.7, 137.8; d 13.6, 100.6, 110.8,

122.2, 122.6; IR (film, cm^{-1}) 3405, 1551, 1430, 1178, 762; HRMS calcd for $C_9H_9N^{79}Br$ (M+H) 207.9762, obsd 207.9763.

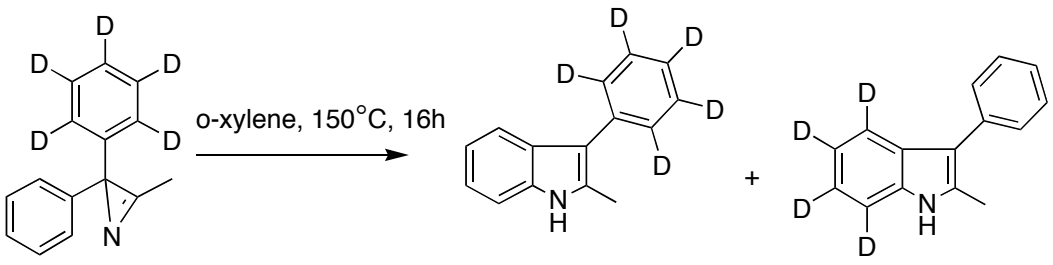


4e **6e**

Indole **6e:** The crude oxime was prepared by the same procedure described in method A of the azirine synthesis.

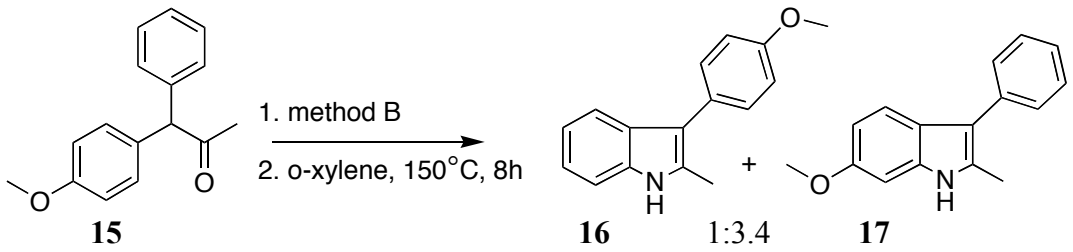
The indole **6e** was prepared by a modified method B of the azirine synthesis:

To a solution of the crude oxime (54 mg, 0.213 mmol) in 10 mL of CH_2Cl_2, a mixture of DIAD (137 mg, 0.64 mmol), triphenylphosphine (167 mg, 0.64 mmol) and CH_2Cl_2 (1 mL) were added in 10 min at the refluxing temperature of CH_2Cl_2. The reaction was monitored by TLC. After disappearance of the starting material (about 40 min), the reaction mixture was cooled to rt, then filtered through a short pad of silica gel, washing with MTBE. The organic solution was concentrated *in vacuo*. The residue was chromatographed to yield the indole **6e** (19 mg, 0.081 mmol, 41% yield from the ketone **4e**) as a white solid: mp 190-200 °C (decomposed); TLC R_f (PE/MTBE = 6/4) = 0.64; ^{1}H NMR (400 MHz, bezene-d_6): 2.18-2.22 (2H, m), 2.28-2.32 (2H, m), 2.57-2.62 (2H, m), 6.26 (1H, bs), 7.17 (1H, s), 7.24 (1H, t, J = 0.8 Hz), 7.28-7.31 (1H, dd, J = 1.6, 8.4 Hz); ^{13}C NMR (100 MHz, benzene-d_6) δ u 24.8, 26.1, 29.1, 114.5, 120.0, 124.5, 142.5, 144.5; d 114.9, 120.3, 123.3; IR (film, cm^{-1}) 3403, 1423, 1364, 803; LRMS (CI) m/z (rel. intensity) 237 (97), 235 (100), 208 (12), 155 (37), 154 (37), 128 (14); HRMS calcd for $C_{11}H_{10}N^{79}Br$ (M) 234.9997, obsd 234.9992.



12 S-10 **13** **14**

Indoles **13** and **14**: The indoles **13** and **14** were isolated as a 1.10:1.00 mixture (81% yield from the azirine **12**) following the procedure of synthesis of indole **6c**. The ratio was determined by integrating peaks at 7.08-7.18 ppm (indole), 7.43-7.52 ppm (phenyl) and 7.67 ppm (indole), then corrected for the same integrals of the indole **6c**: TLC R_f (PE/MTBE = 8/2) = 0.30; ^{1}H NMR (400 MHz) 2.44 (6H, s), 7.08-7.18 (2H, m), 7.25-7.31 (2H, m), 7.43-7.47 (2H, m), 7.49-7.52 (2H, m), 7.67 (1H, d, J = 8.0 Hz), 7.80 (2H, bs); ^{13}C NMR (100 MHz) δ u 114.6, 128.0, 131.6, 135.4, 135.6; d 12.7, 110.5, 119.0, 120.1, 121.7, 126.0, 128.7, 129.6.



15 **16** 1:3.4 **17**

Indoles **16**[4] and **17**[5]: The azirine was prepared following method B except that the azirine was not purified after concentration, but was used crude in the next reaction.

The indoles **16** and **17** were prepared following the procedure of synthesis of indole **6c** except that the sealed tube was heated to 150 °C for 8 h. The isolated yield for indole **16** was 11% from the ketone **15** and the isolated yield for **17** was 35% from the ketone **15**. The ratio was determined by integrating the singlets at 3.79 and 3.84 ppm in the crude product.

For the indole **16** (yellow oil): TLC R_f (PE/MTBE = 6/4) = 0.48; ^{1}H NMR (400 MHz, acetone-d_6) 2.48 (3H, s), 3.84 (3H,s), 6.98-7.08 (4H, m), 7.33-7.35 (1H, m), 7.42 (2H, d, J = 8.8 Hz), 7.54 (1H, d, J = 8.0 Hz), 10.13 (1H, bs); ^{13}C NMR (100 MHz, acetone-d_6) δ u 114.1, 128.9, 129.1, 132.4, 136.8, 158.8; d 12.5, 55.6, 111.5, 114.9, 119.0, 120.1, 121.7, 131.2.

For the indole **17** (white solid): mp 155-156 °C; TLC R_f (PE/MTBE = 6/4) = 0.37; ^{1}H

NMR (400 MHz, acetone-d_6) 2.47 (3H, s), 3.79 (3H, s), 6.71 (1H, dd, J = 2.4, 4.8 Hz), 6.91 (1H, d, J = 2.4 Hz), 7.23-7.28 (1H, m), 7.42-7.52 (5H, m), 10.02 (1H, bs); ^{13}C NMR (100 MHz, acetone-d_6) δ u 114.2, 123.0, 131.4, 137.1, 137.5, 157.0; d 12.6, 55.8, 95.3, 109.9, 119.6, 126.2, 129.4, 129.9;

References

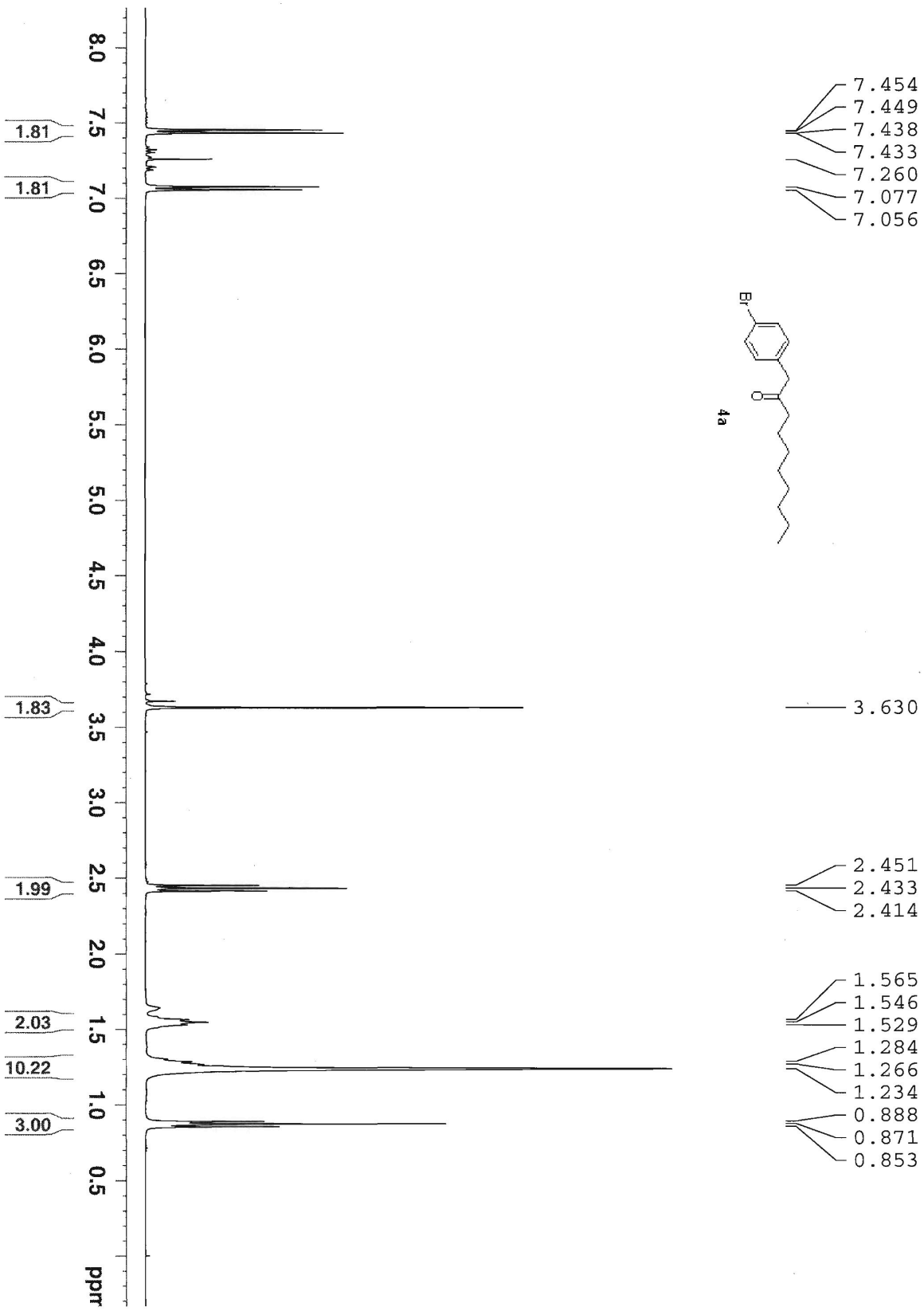
[1] Padwa, Albert; Rosenthal, Robert J.; Dent, William; Filho, Pedro; Turro, Nicholas J.; Hrovat, David A.; Gould, Ian R. *J. Org. Chem.* **1984**, 49, 3174.

[2] Katritzky, Alan R.; Toader, Dorin; Xie Lingong *J. Org. Chem.* **1996**, 61, 7571.

[3] Fuerstner, Alois; Jumbam, Denis N. *Tetrahedron* **1992**, 48, 5991.

[4] Baccolini, Grazieno; Dalpozzo, Renato; Todesco, Paolo E. *J. Chem. Soc. Perkin Trans. 1* **1988**, 971.

[5] Ikuta, Shunichi; Shiro, Miyoshi; Ogawa, Kohei WO0183451. US Patent App US2003/0191174A1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O
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1.565
1.546
1.529
1.284
1.266
1.234
0.888
0.871
0.853
1.81
1.81
1.83
1.99
2.03
10.22
3.00
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
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2.0
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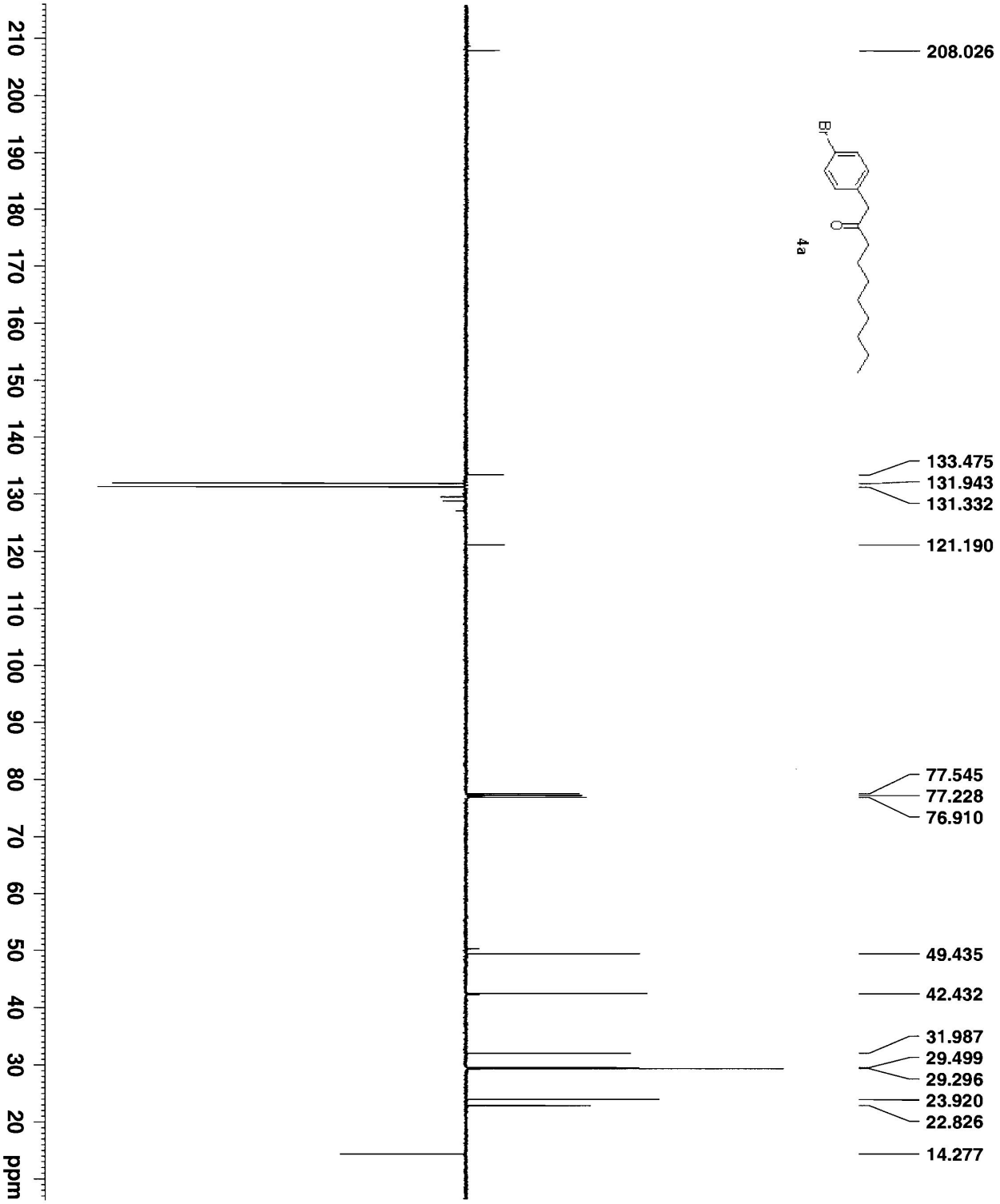
ppm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29.499
29.296
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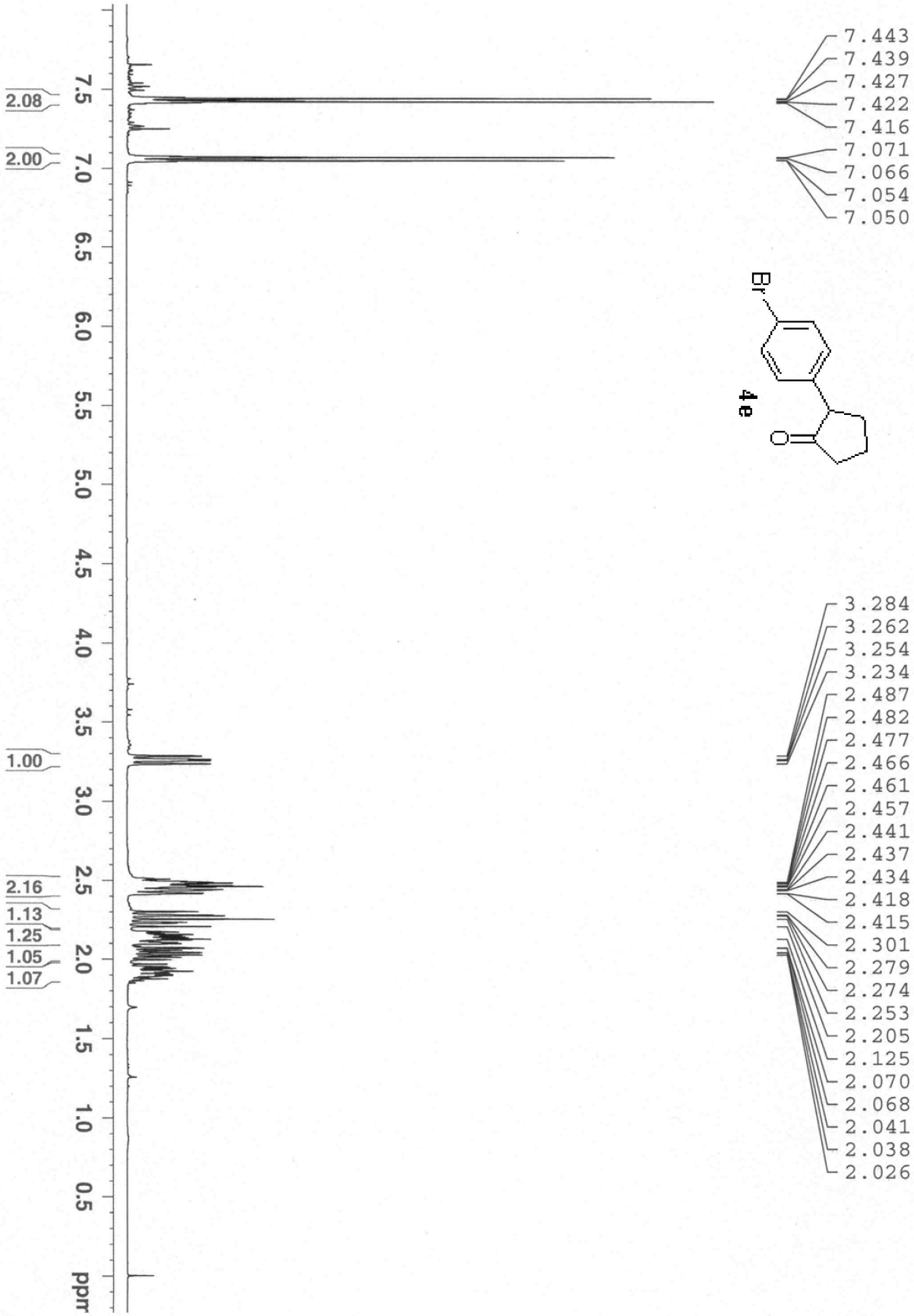
22.826
14.277
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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4e
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3.254
3.234
2.487
2.482
2.477
2.466
2.461
2.457
2.441
2.437
2.434
2.418
2.415
2.301
2.279
2.274
2.253
2.205
2.125
2.070
2.068
2.041
2.038
2.026
2.08
2.00
1.00
2.16
1.13
1.25
1.05
1.07
7.5
7.0
6.5
6.0
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4.5
4.0
3.5
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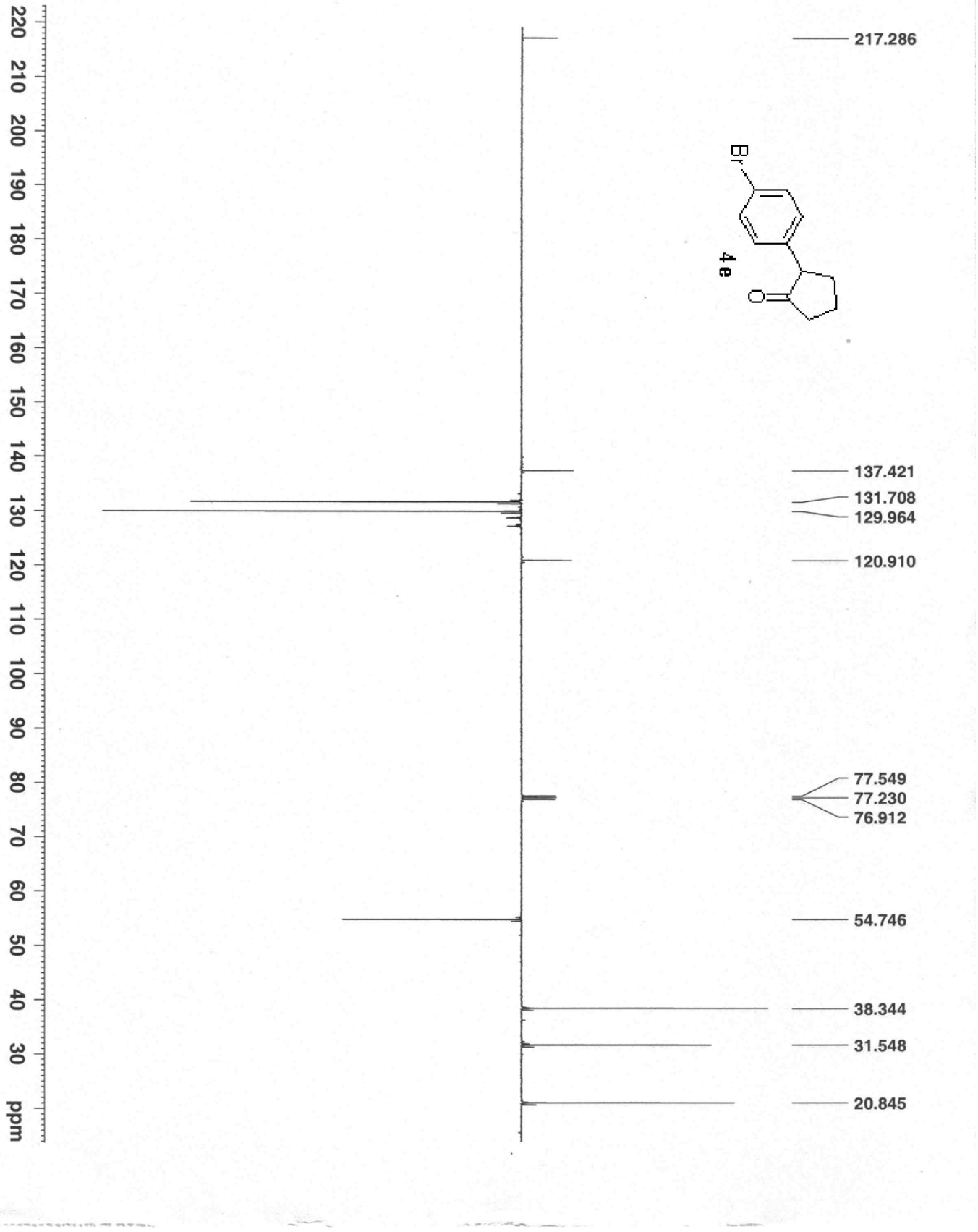
2.0
1.5
1.0
0.5
ppm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O
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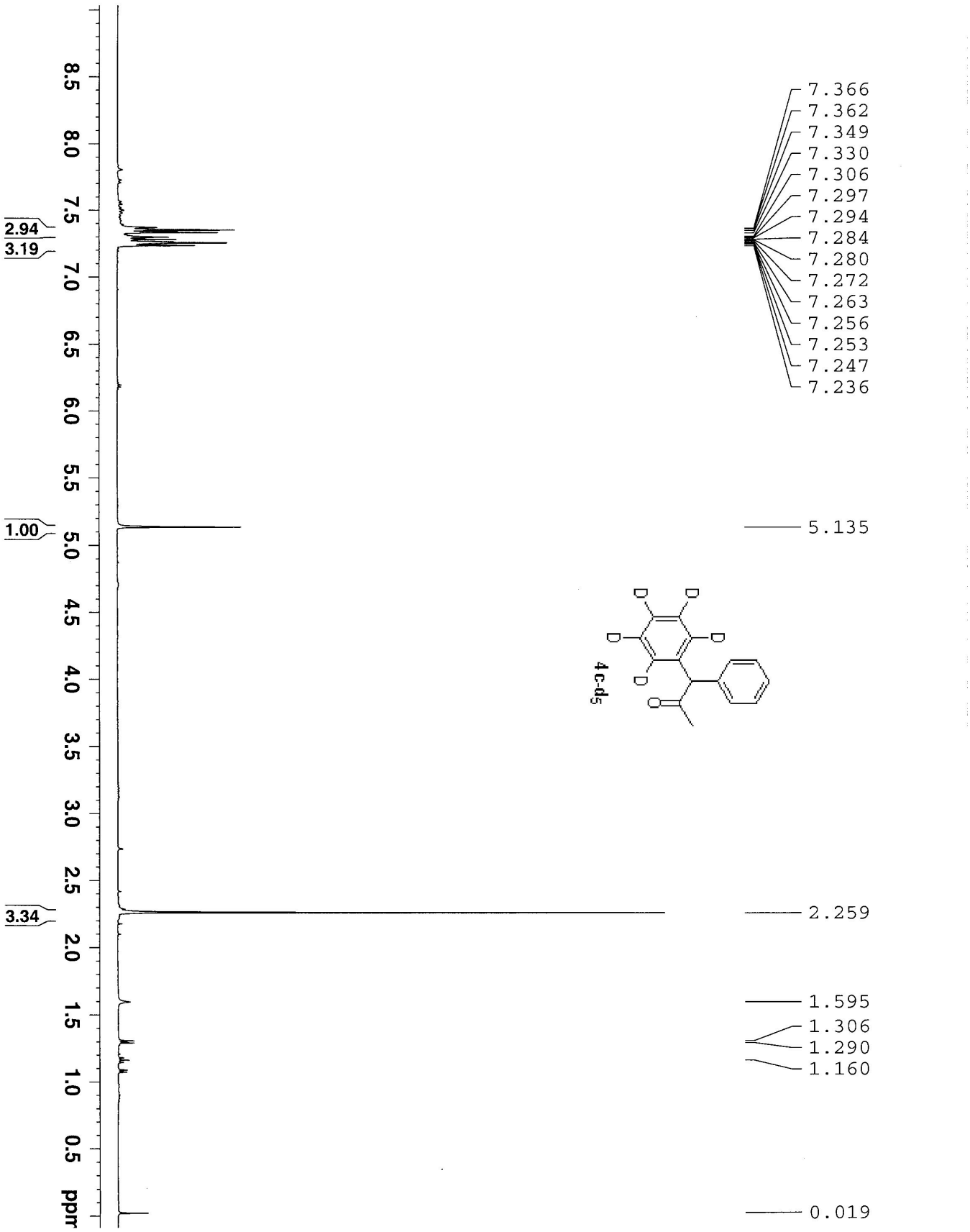
20.845
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 ppm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7.272
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7.253
7.247
7.236
5.135
2.259
1.595
1.306
1.290
1.160
0.019
2.94
3.19
1.00
3.34
4c-d5
D
O
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
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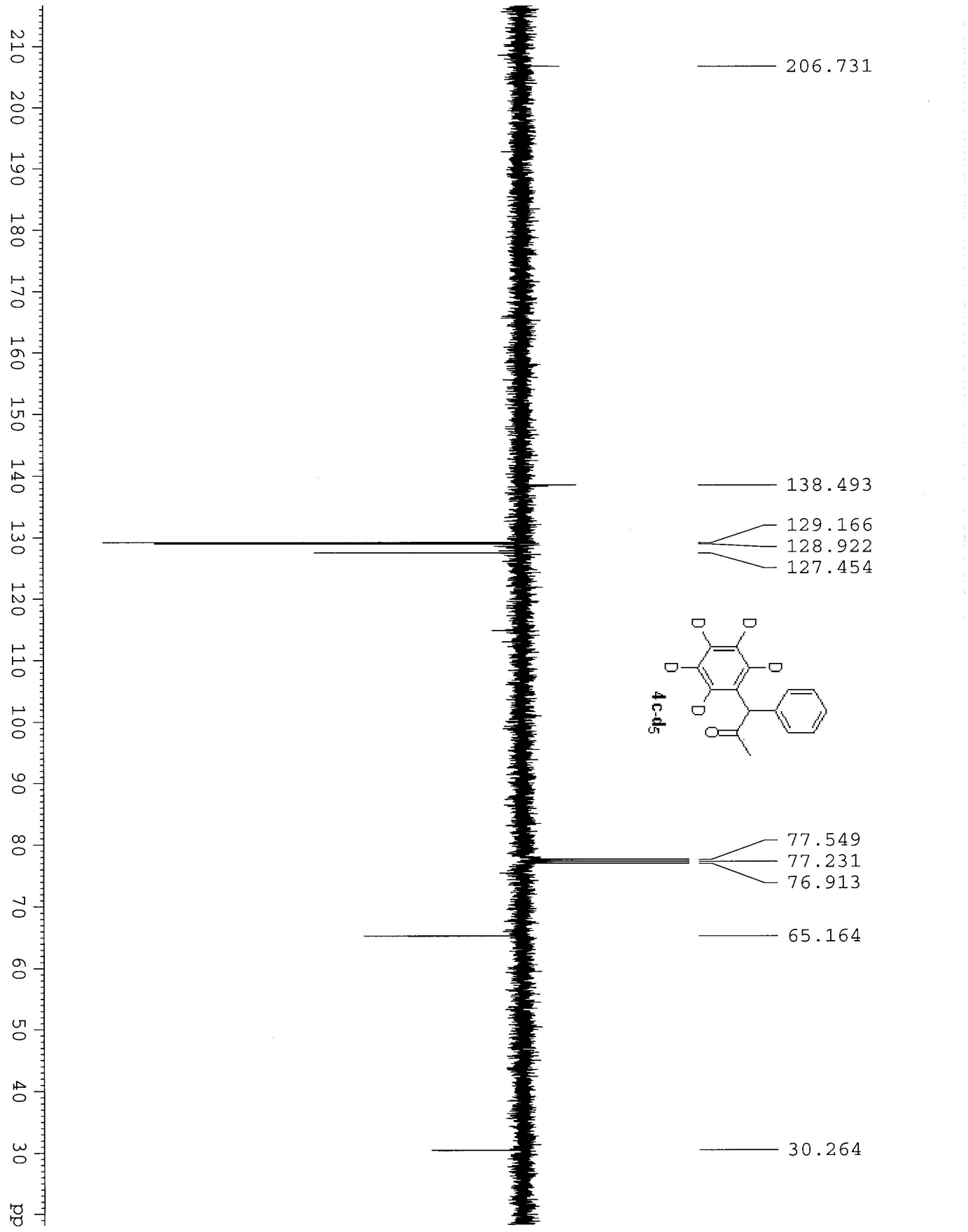
0.5
ppm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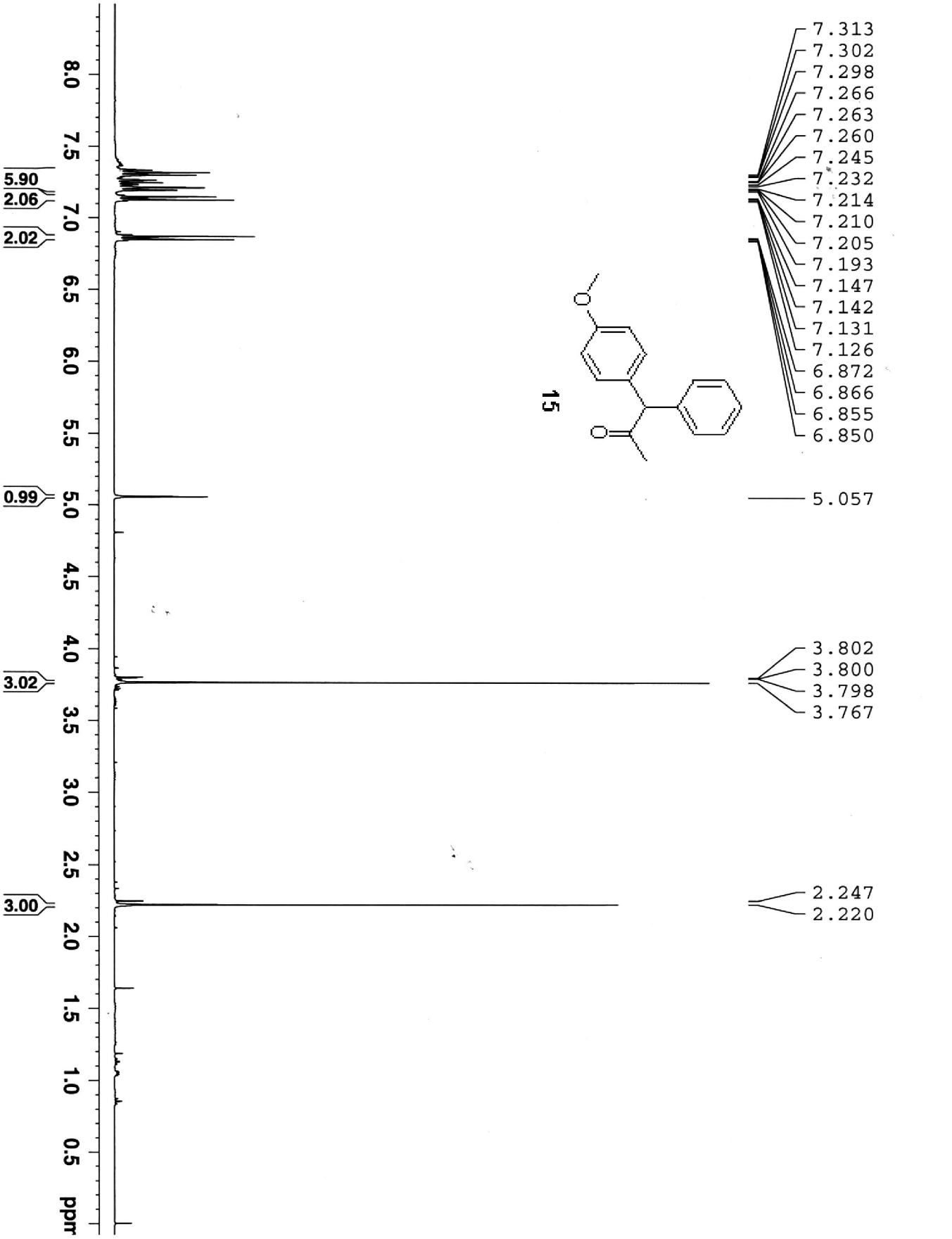
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7.260
7.245
7.232
7.214
7.210
7.205
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7.147
7.142
7.131
7.126
6.872
6.866
6.855
6.850
5.057
3.802
3.800
3.798
3.767
2.247
2.220
5.90
2.06
2.02
0.99
3.02
3.00
15
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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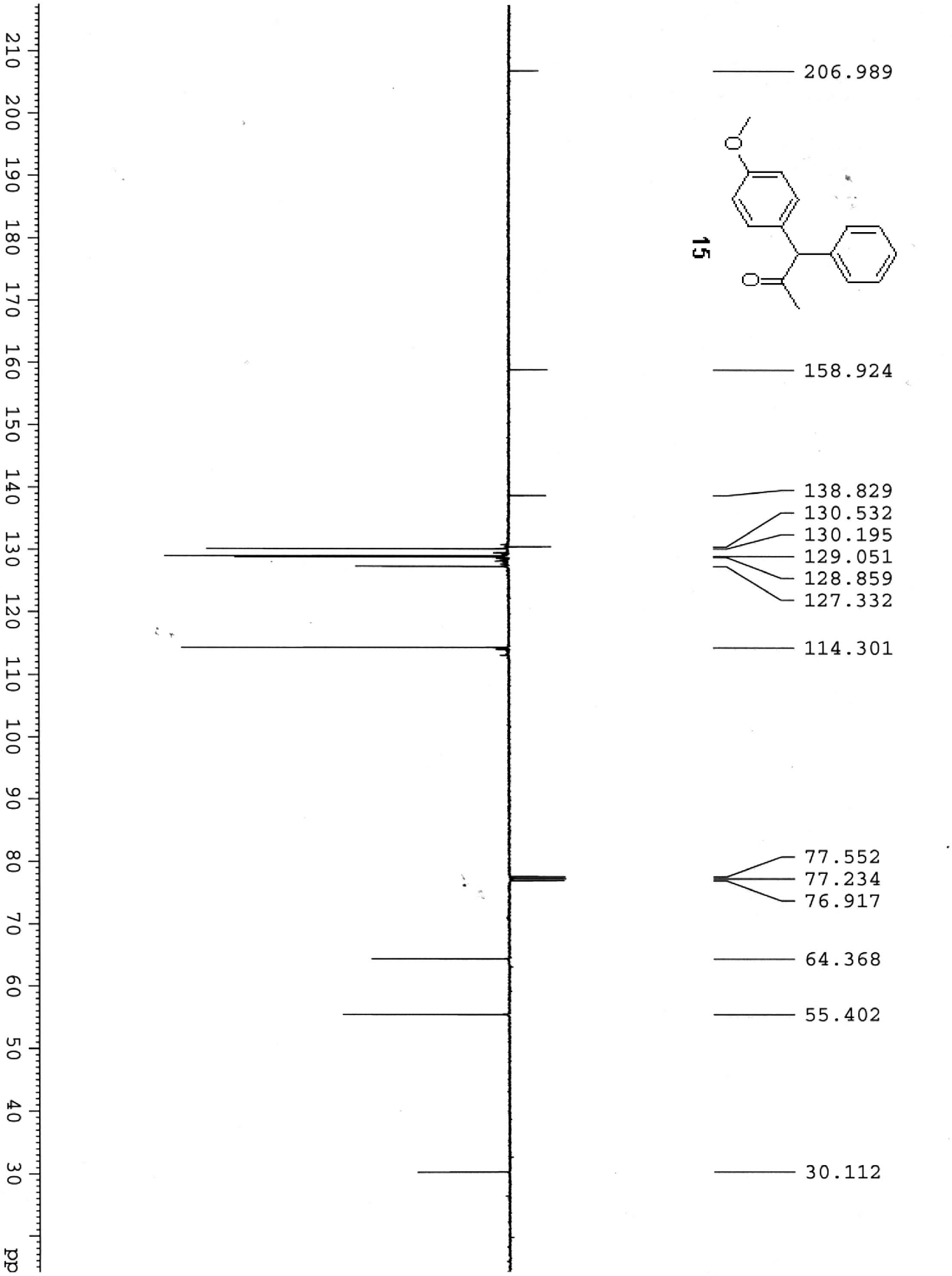
2.0
1.5
1.0
0.5
ppm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127.332
114.301
77.552
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64.368
55.402
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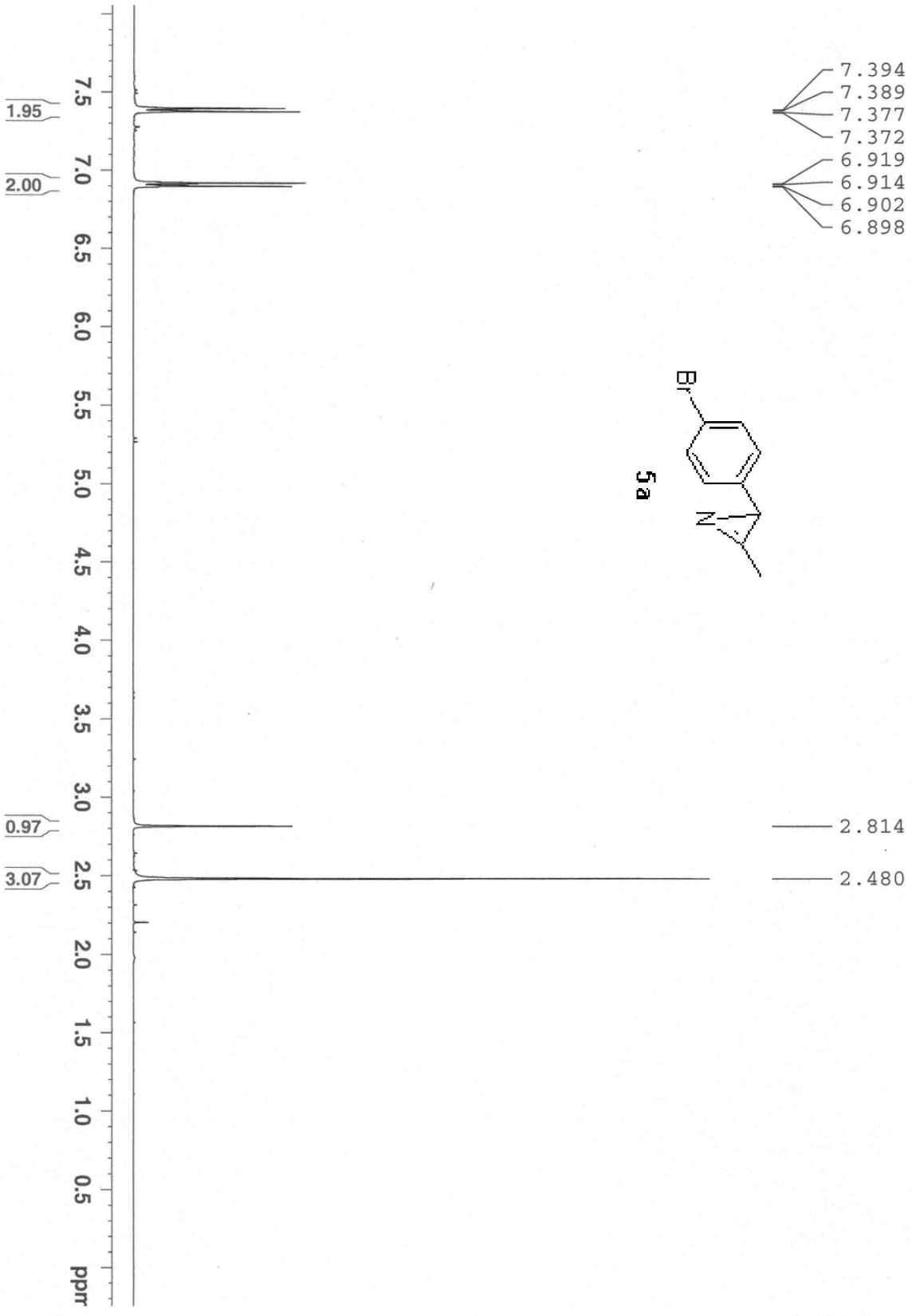
15
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
ppm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6.898
2.814
2.480
1.95
2.00
0.97
3.07
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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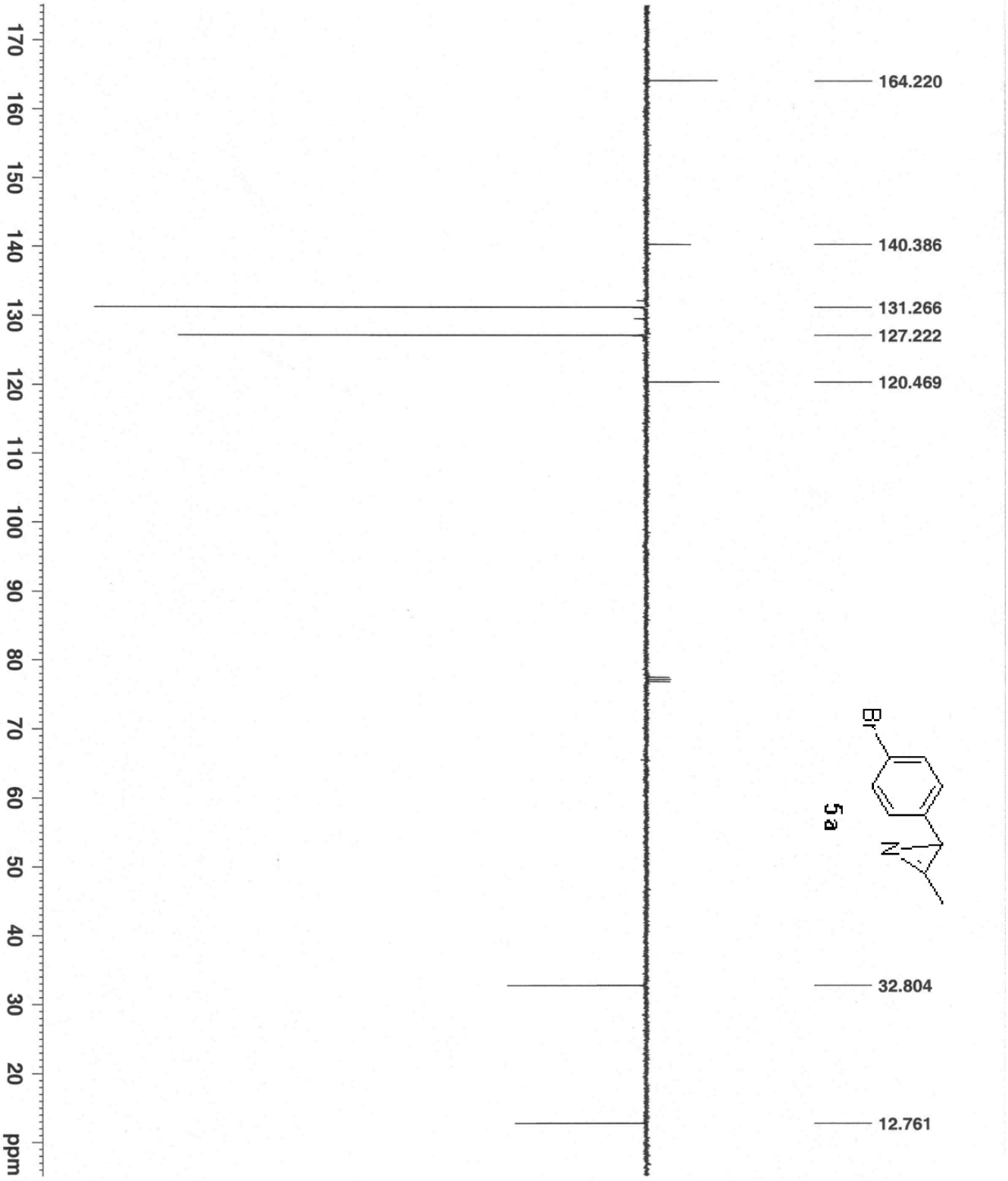
1.0
0.5
ppm
5a
Br
N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160
150
140
130
120
110
100
90
80
70
60
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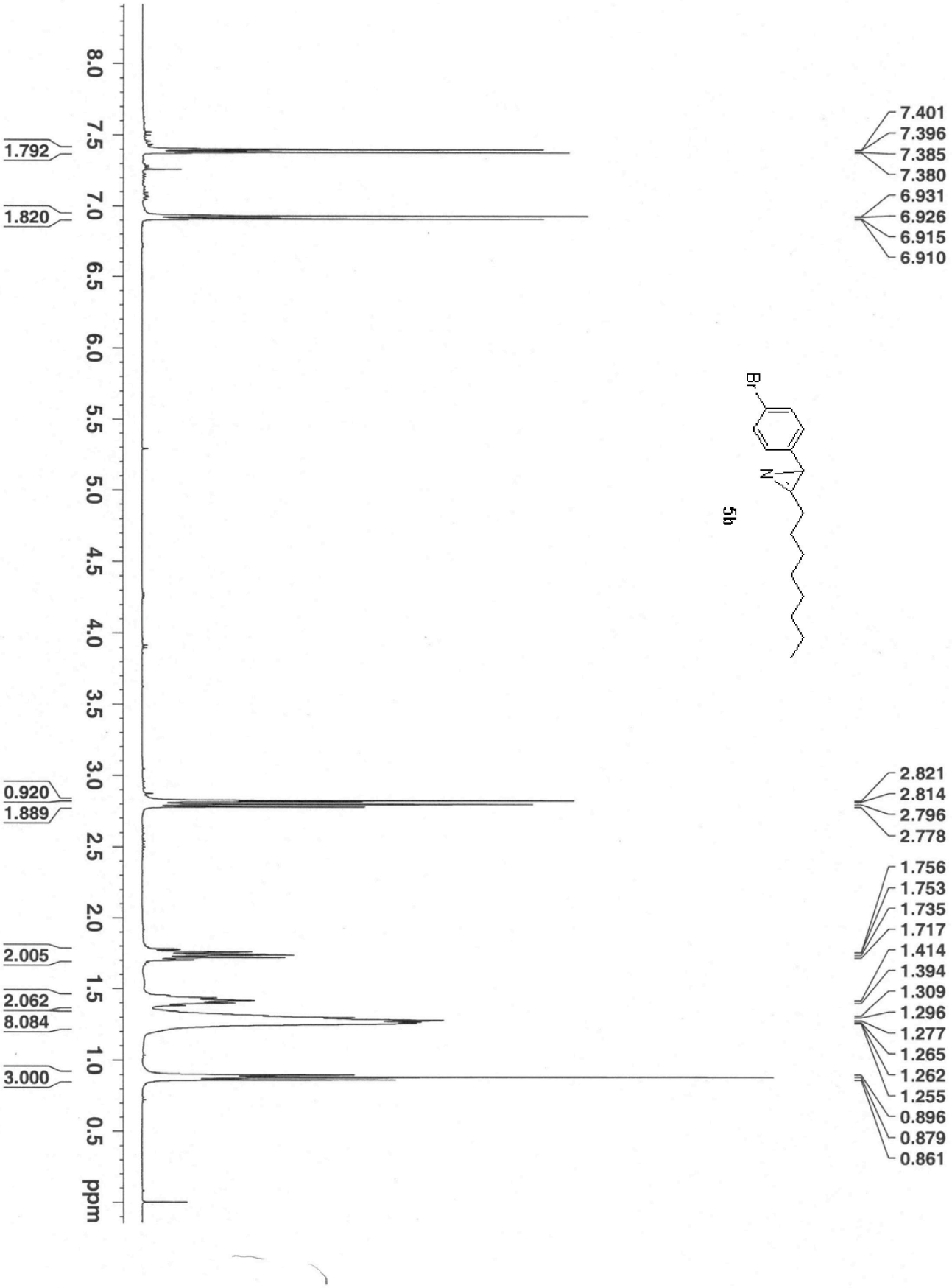
12.761
Br
N
5a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6.910
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2.778
1.756
1.753
1.735
1.717
1.414
1.394
1.309
1.296
1.277
1.265
1.262
1.255
0.896
0.879
0.861
1.792
1.820
0.920
1.889
2.005
2.062
8.084
3.000
8.0
7.5
7.0
6.5
6.0
5.5
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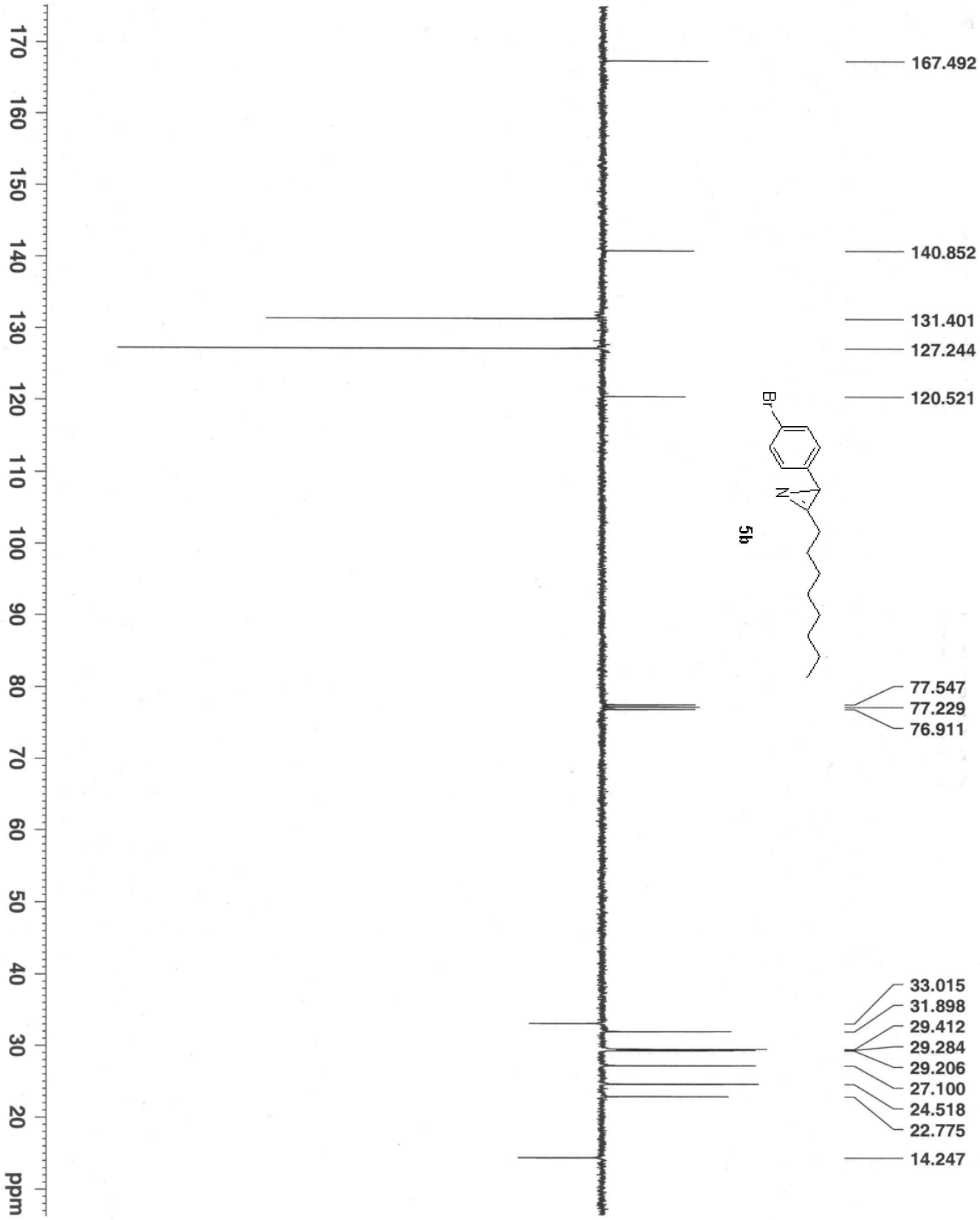
1.0
0.5
ppm
Br
N
5b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76.911
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29.206
27.100
24.518
22.775
14.247
Br
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5b
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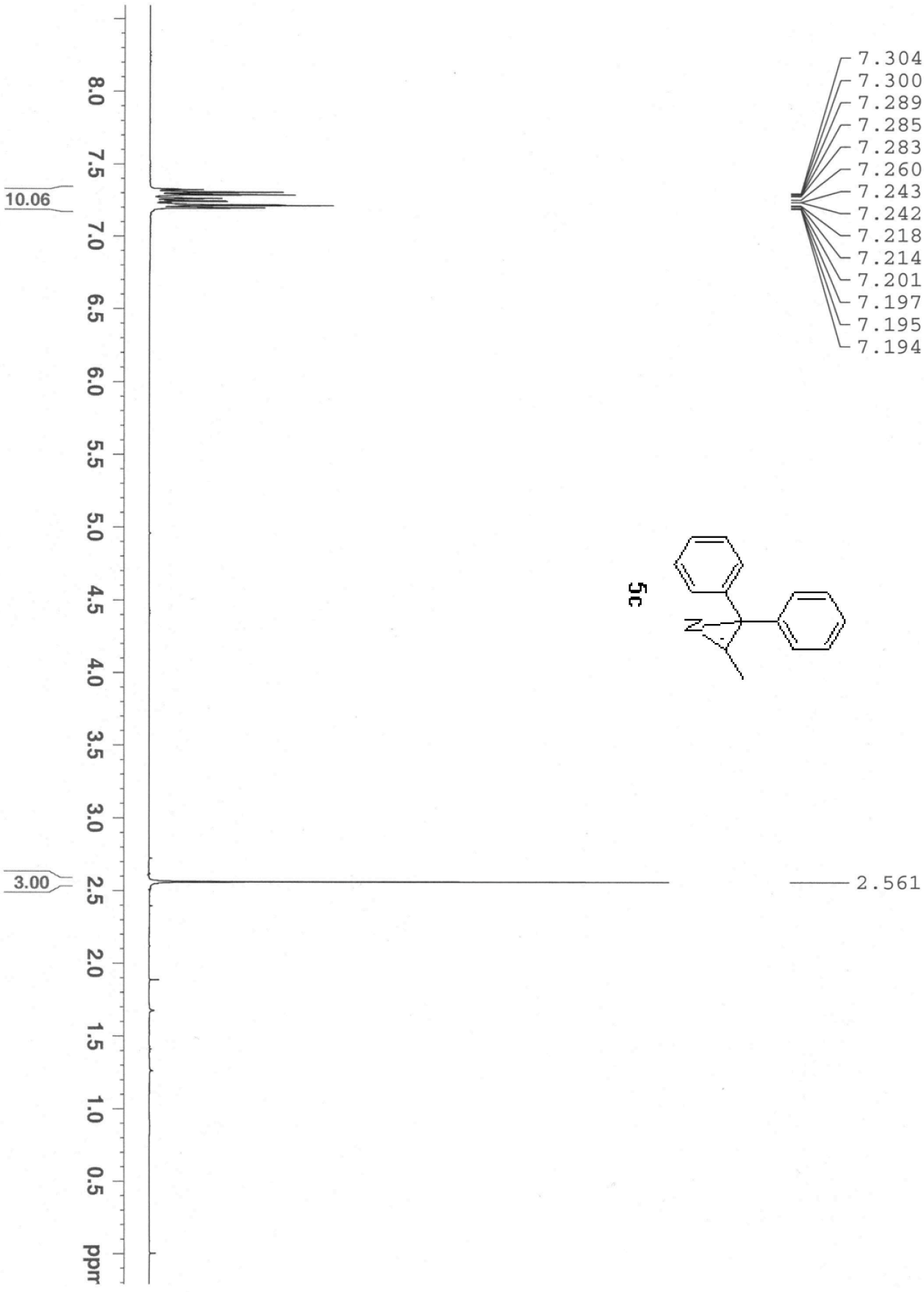
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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7.242
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7.214
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7.197
7.195
7.194
10.06
3.00
2.561
5c
8.0
7.5
7.0
6.5
6.0
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4.5
4.0
3.5
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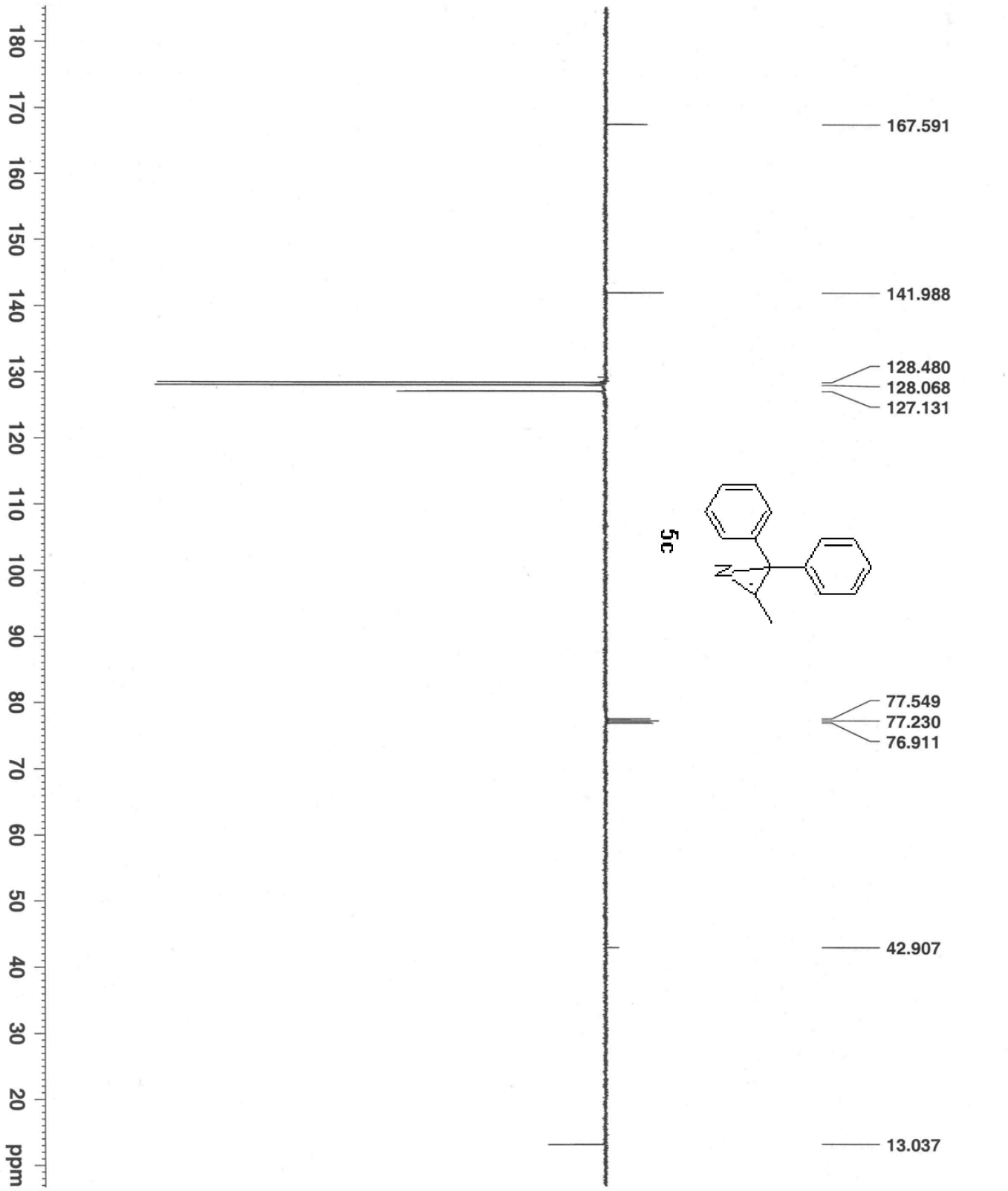
2.0
1.5
1.0
0.5
ppm


180
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160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
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128.480
128.068
127.131
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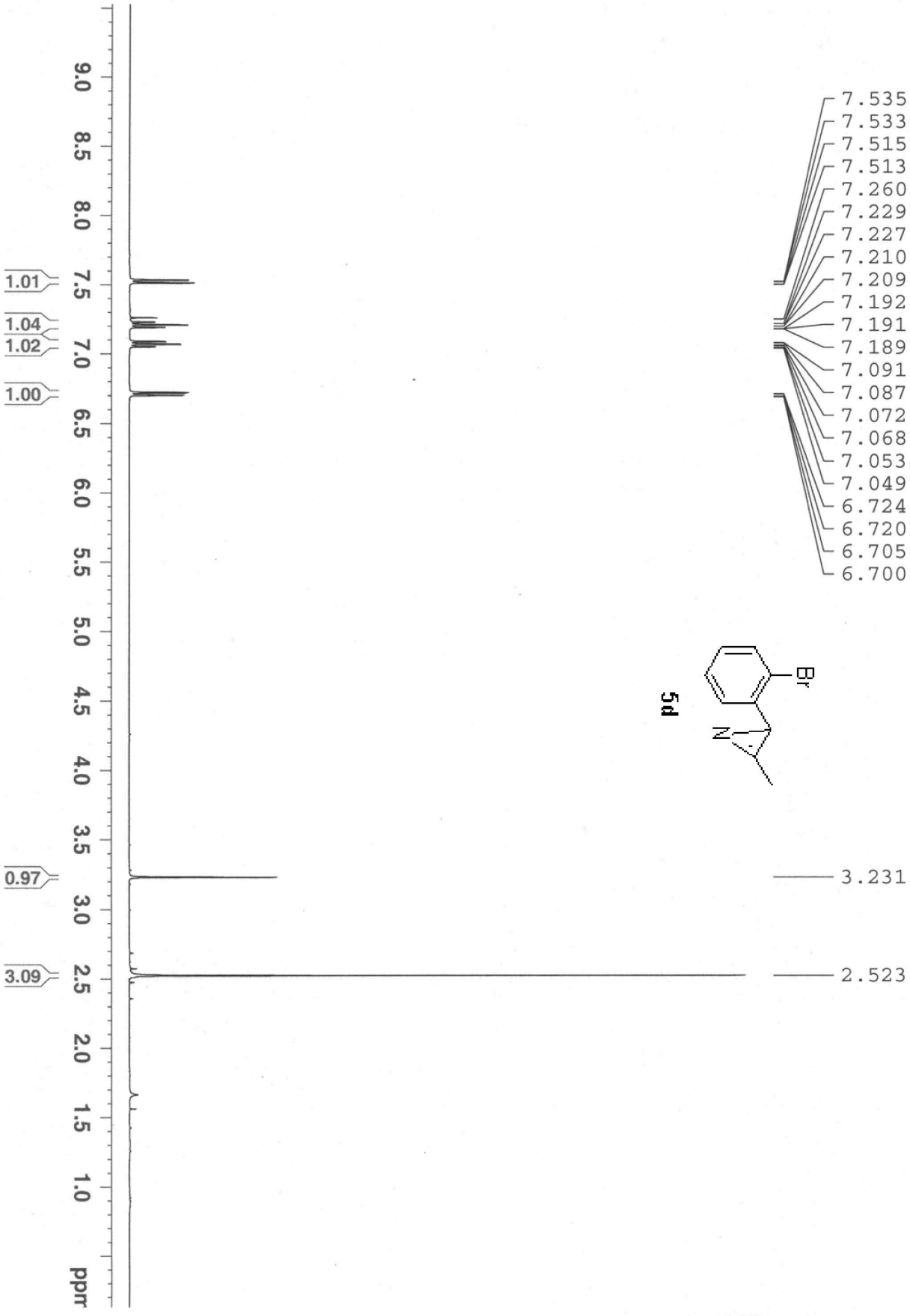
77.230
76.911
42.907
13.037
5c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7.515
7.513
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7.210
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7.192
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7.087
7.072
7.068
7.053
7.049
6.724
6.720
6.705
6.700
Br
N
5d
3.231
2.523
1.01
1.04
1.02
1.00
0.97
3.09
9.0
8.5
8.0
7.5
7.0
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5.0
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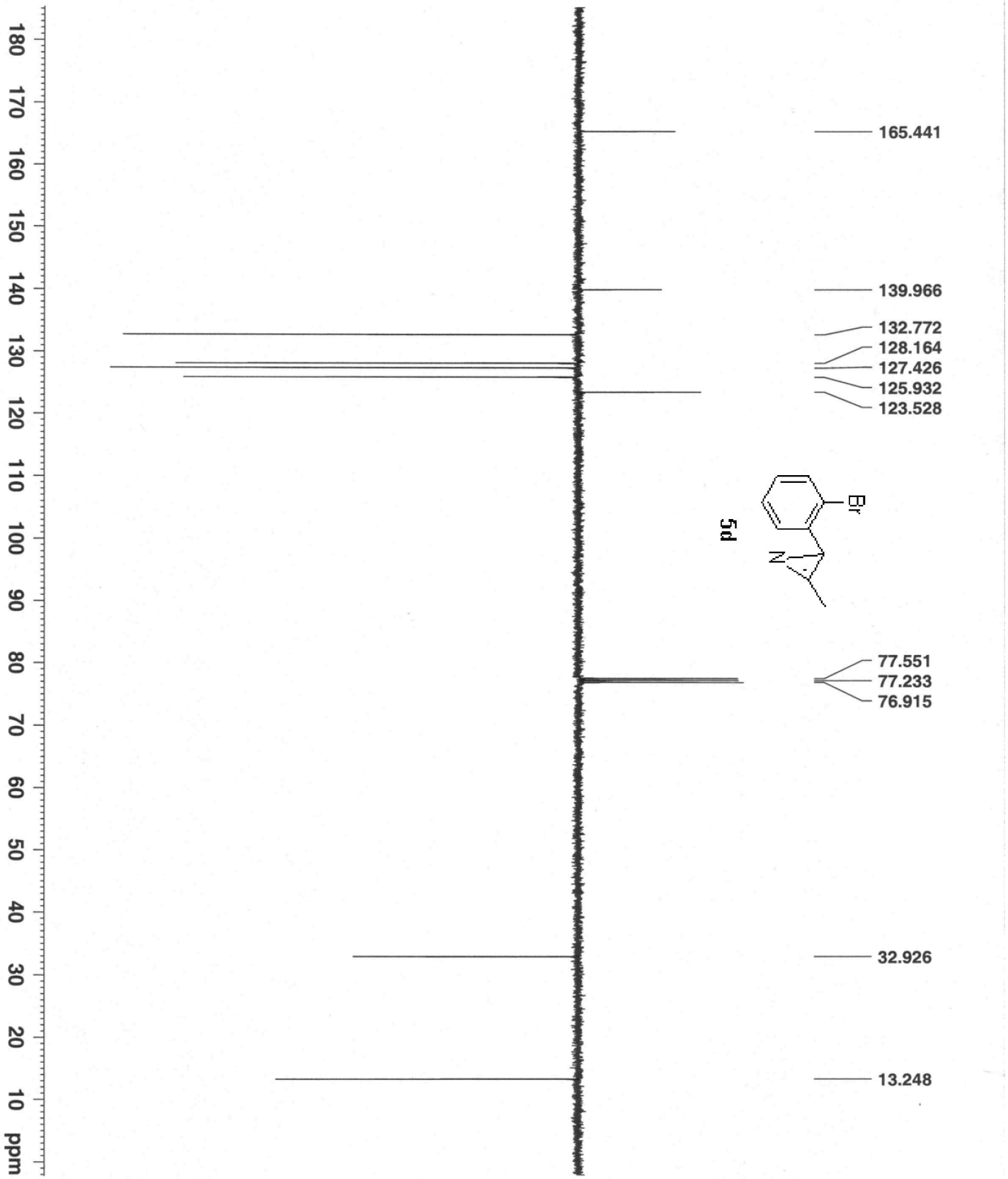
ppm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Br
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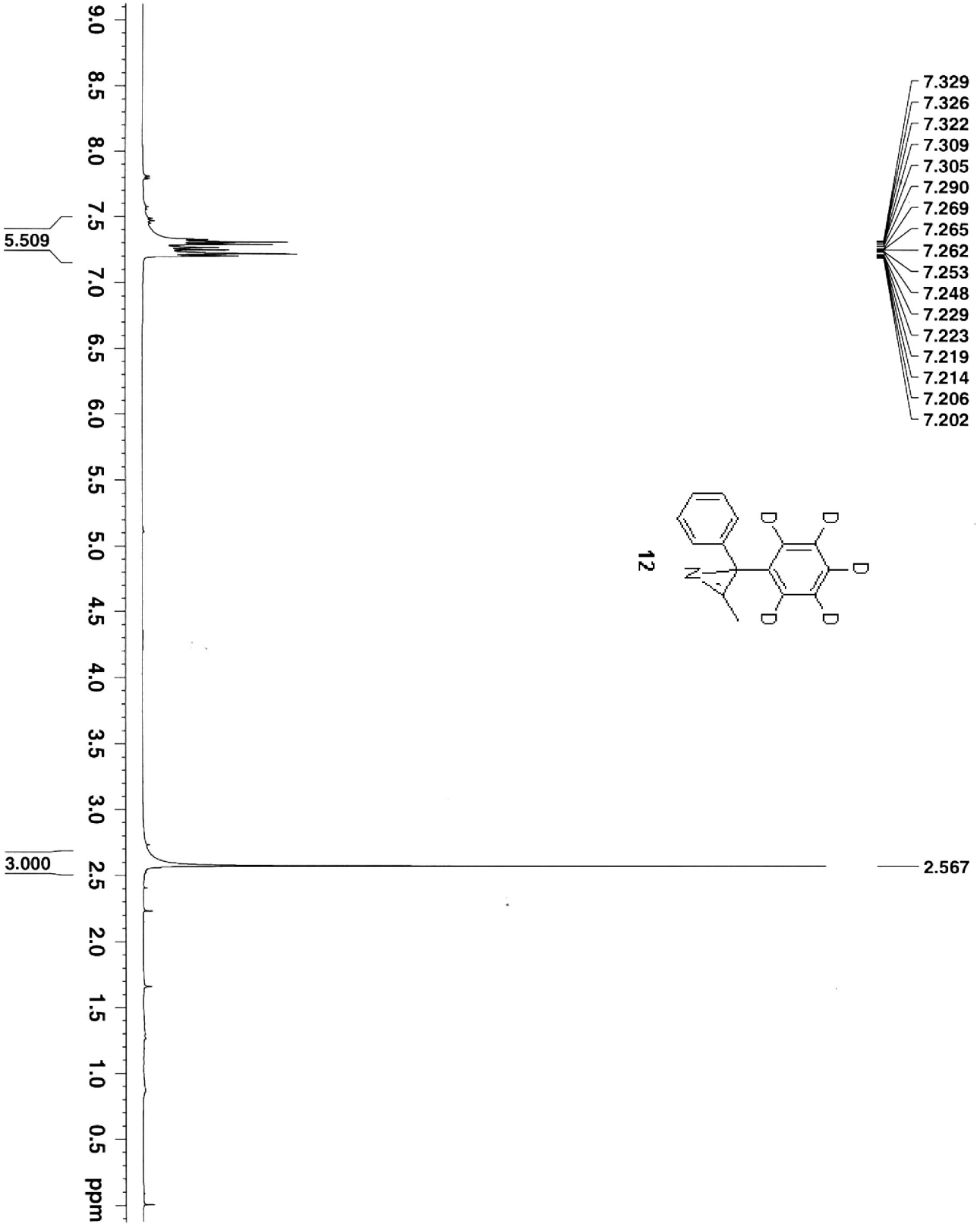
76.915
32.926
13.248
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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5.5
5.0
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3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.509
3.000
2.567
7.329
7.326
7.322
7.309
7.305
7.290
7.269
7.265
7.262
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7.202
12
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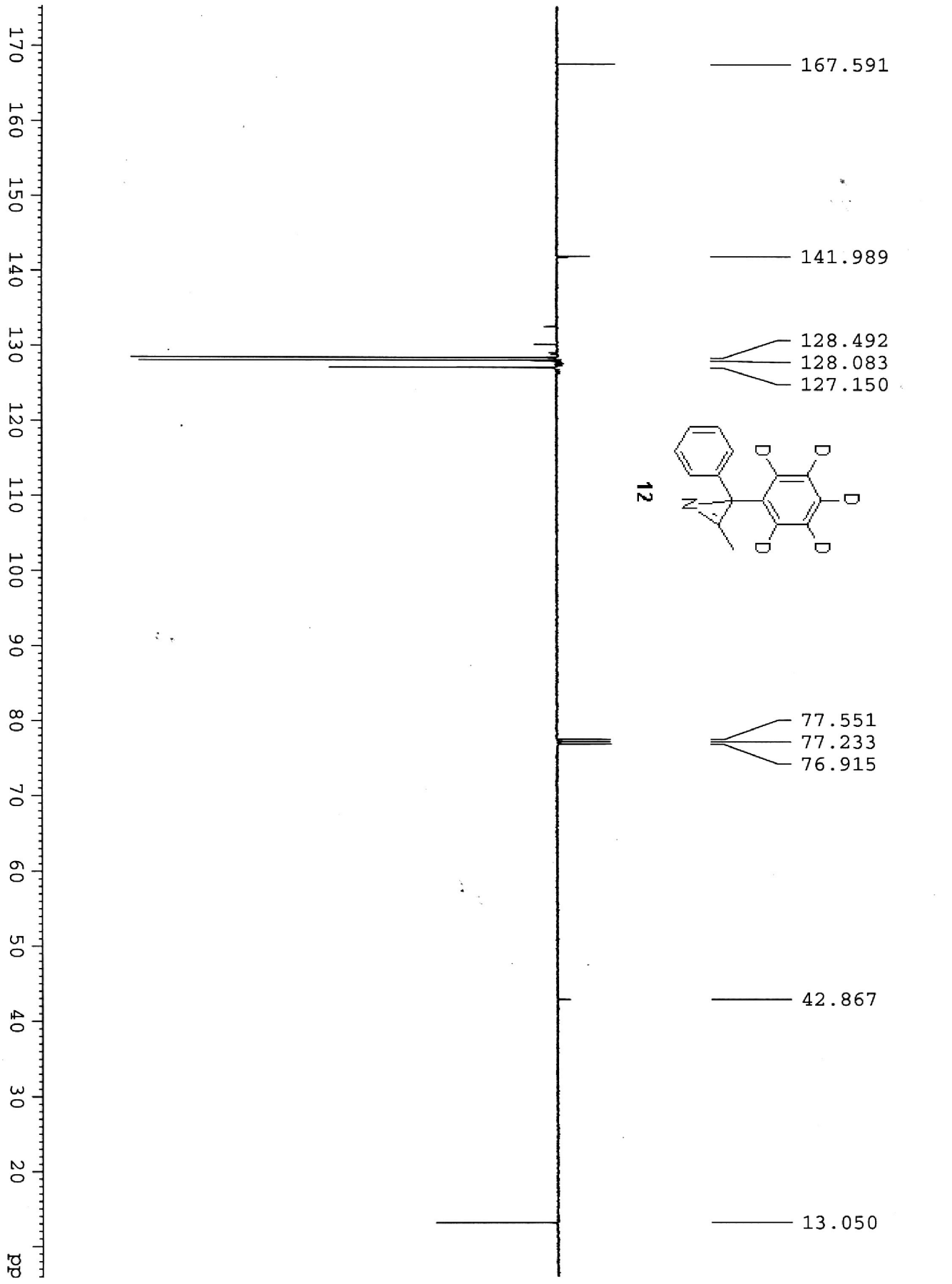
D
D
D
D
D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77.551
77.233
76.915
42.867
13.050
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D
D
D
D
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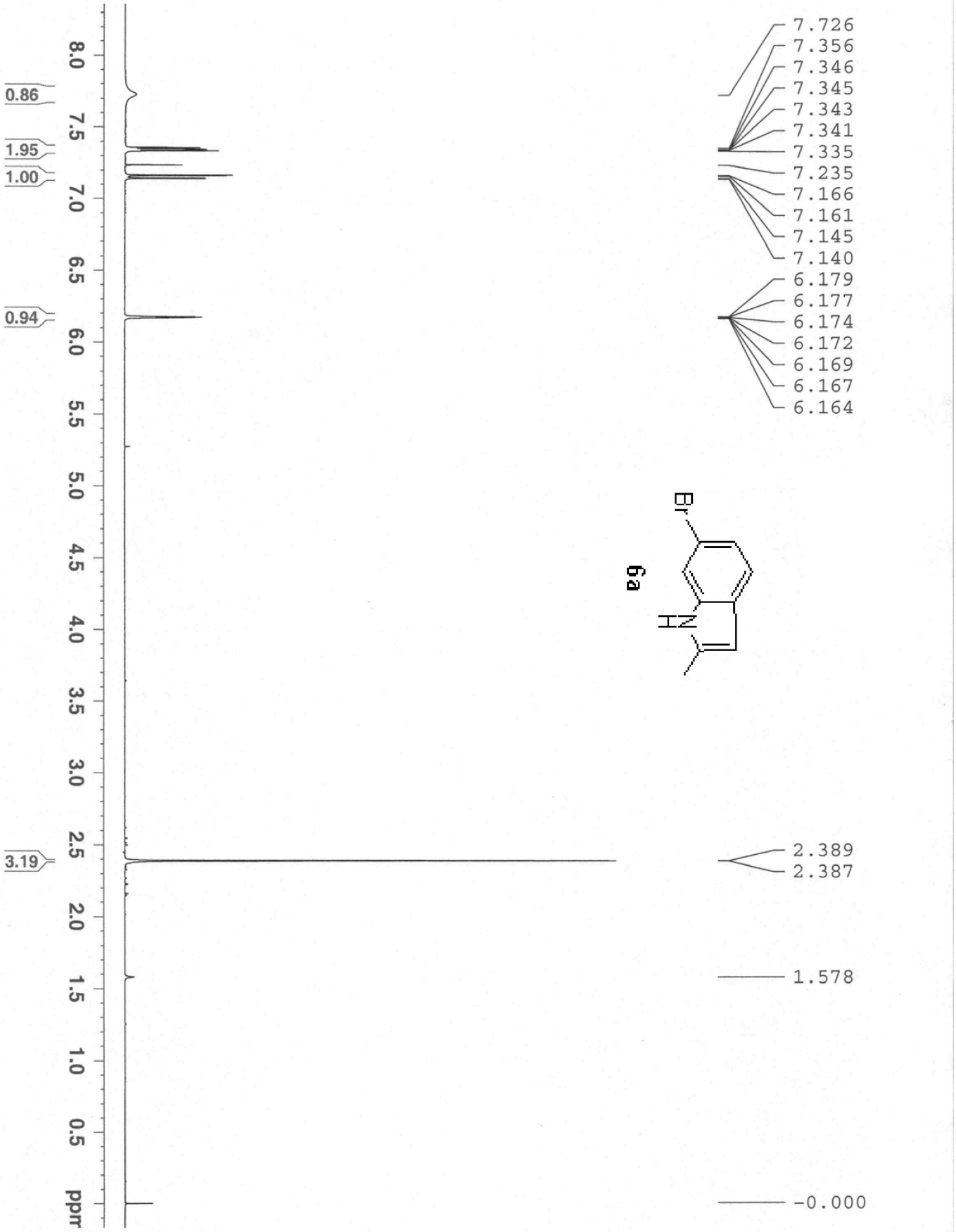
150
140
130
120
110
100
90
80
70
60
50
40
30
20
pp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7.335
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7.161
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7.140
6.179
6.177
6.174
6.172
6.169
6.167
6.164
0.86
1.95
1.00
0.94
3.19
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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ppm
Br
N
H
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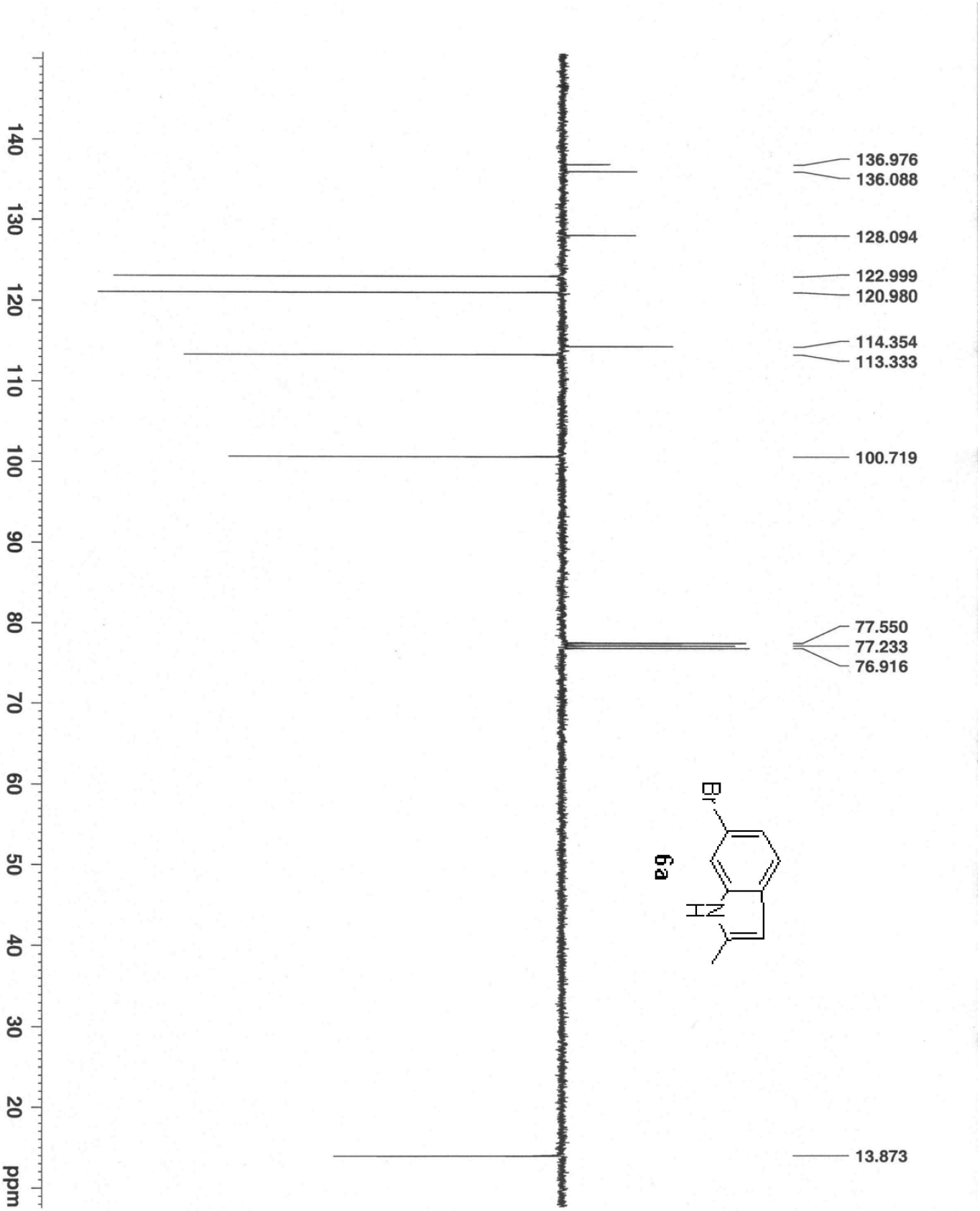
-0.000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77.233
76.916
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ppm
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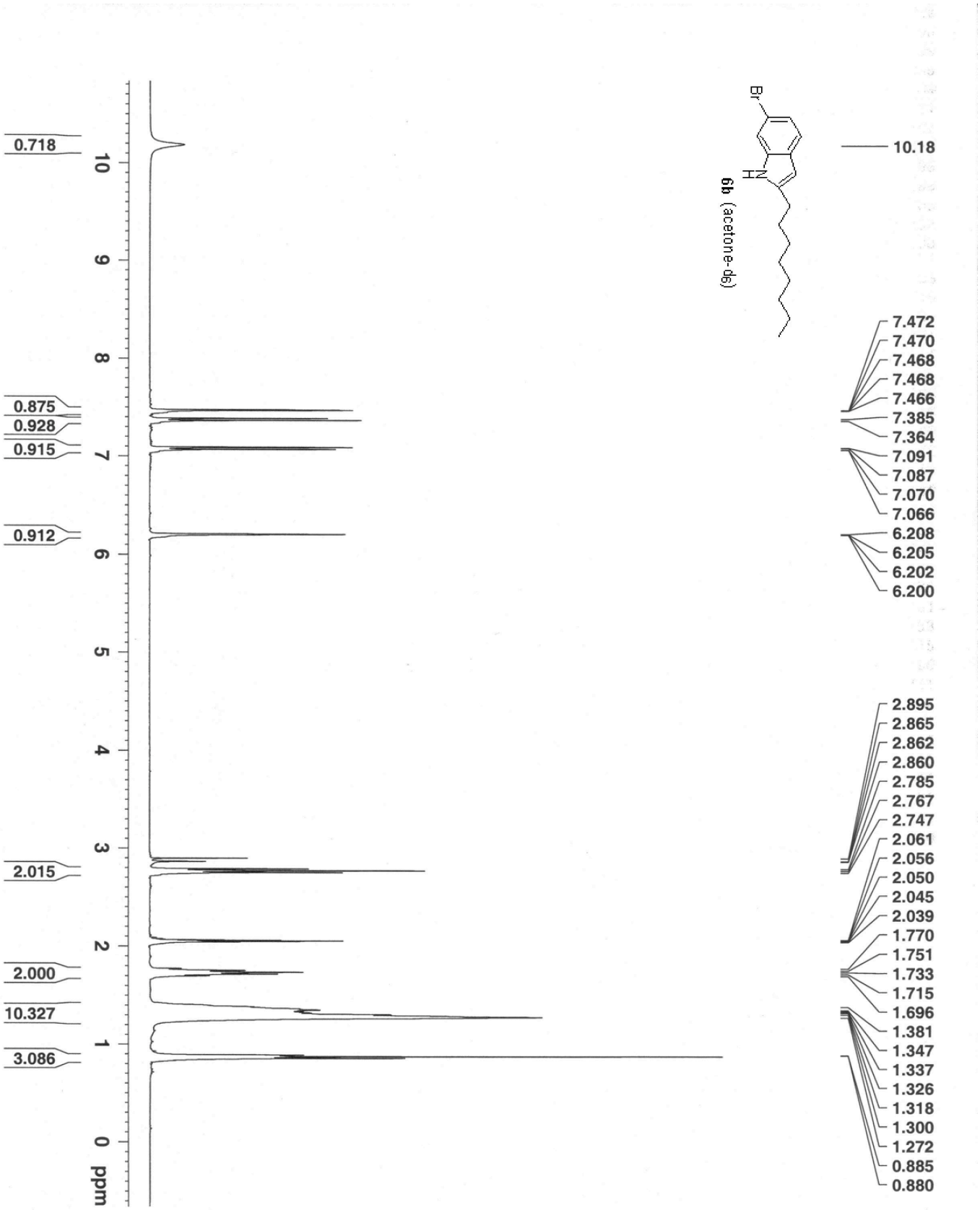
60
50
40
30
20
6a
Br
N
H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0.875
0.928
0.915
0.912
2.015
2.000
10.327
3.086
10 9 8 7 6 5 4 3 2 1 0 ppm
Br
N
H
6b (acetone-d6)
10.18
7.472
7.470
7.468
7.468
7.466
7.385
7.364
7.091
7.087
7.070
7.066
6.208
6.205
6.202
6.200
2.895
2.865
2.862
2.860
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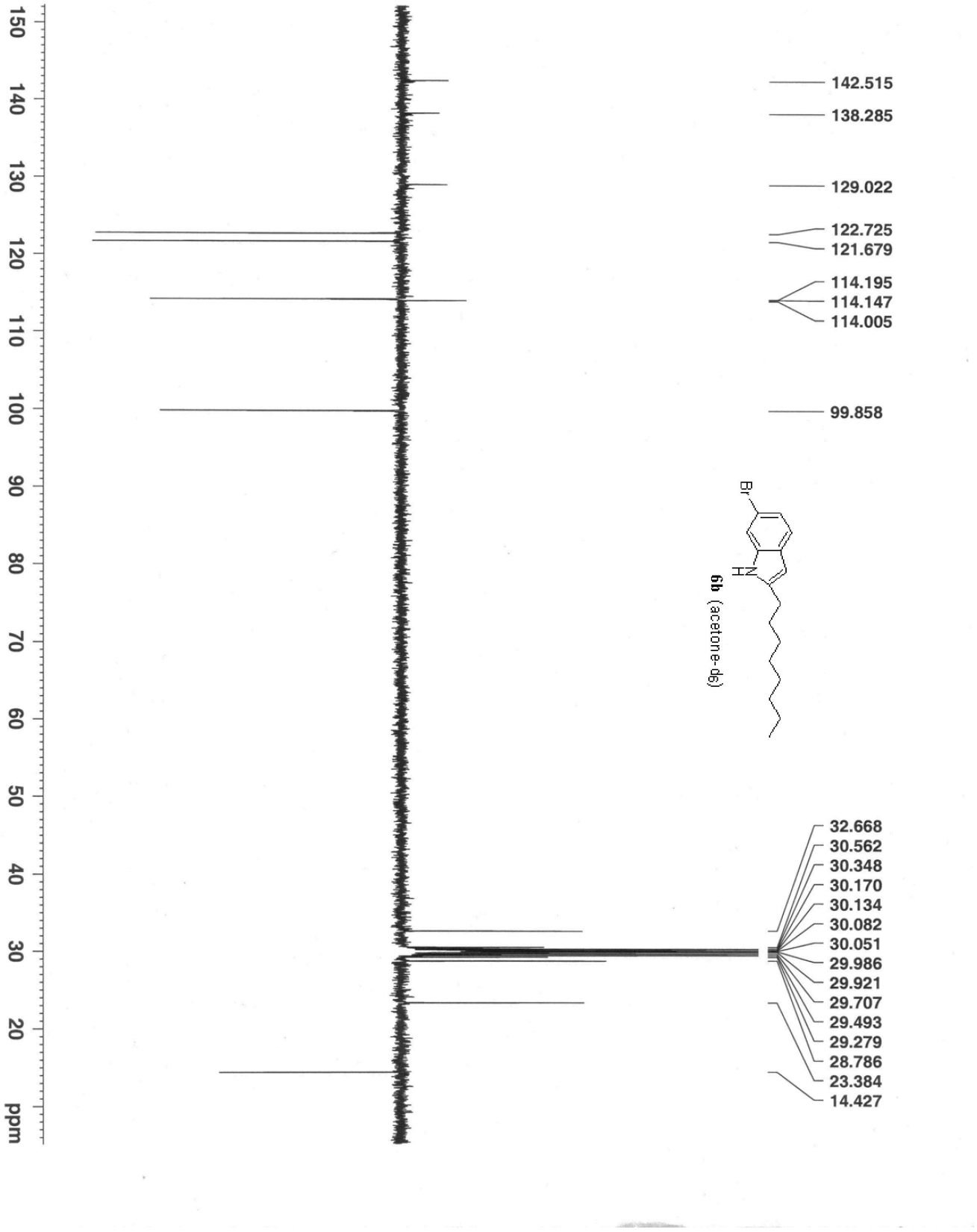
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121.679
114.195
114.147
114.005
99.858
Br
N
H
6b (acetone-d6)
32.668
30.562
30.348
30.170
30.134
30.082
30.051
29.986
29.921
29.707
29.493
29.279
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140
130
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110
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80
70
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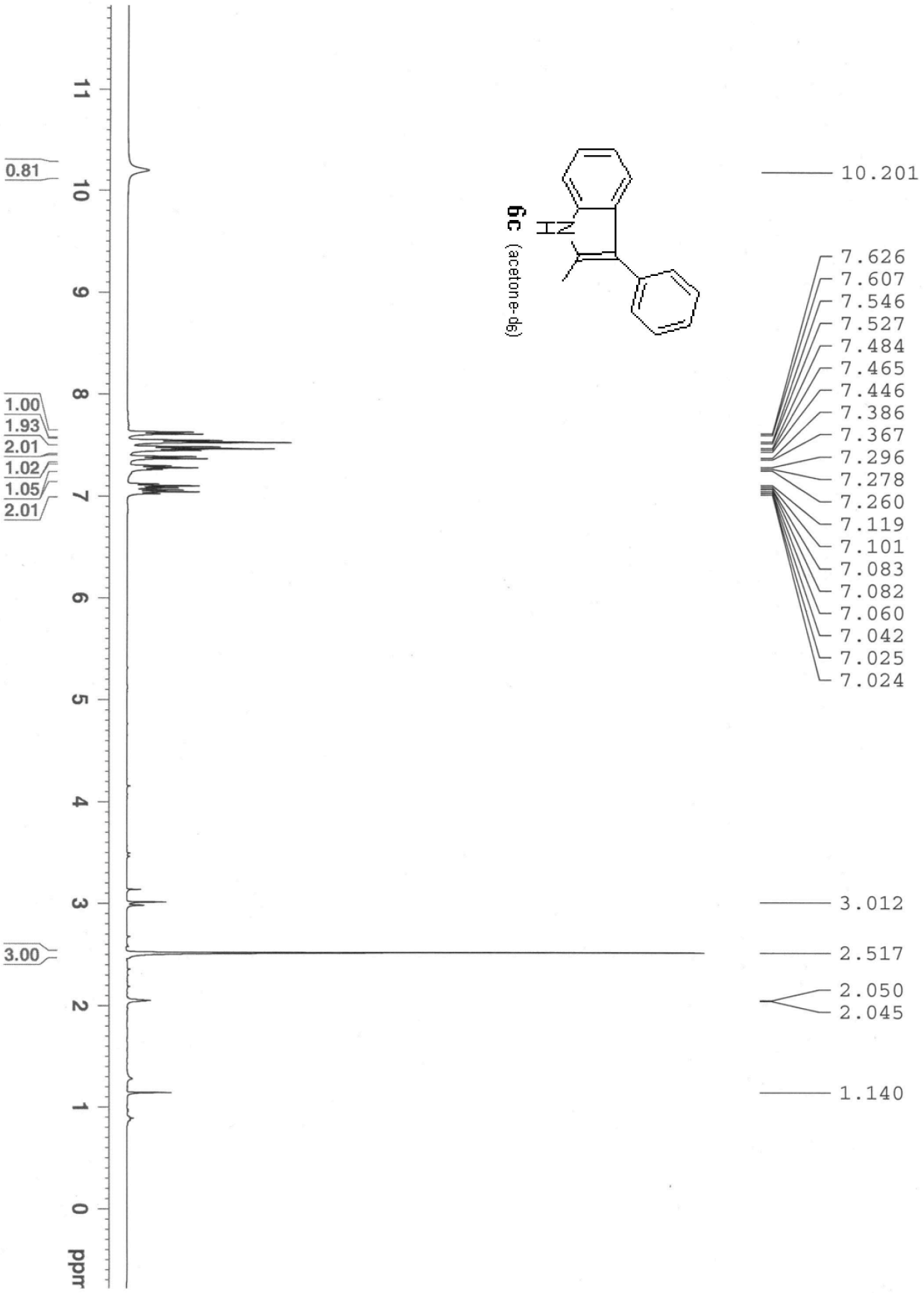
50
40
30
20
ppm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7.607
7.546
7.527
7.484
7.465
7.446
7.386
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7.260
7.119
7.101
7.083
7.082
7.060
7.042
7.025
7.024
3.012
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2.050
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1.00
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1.02
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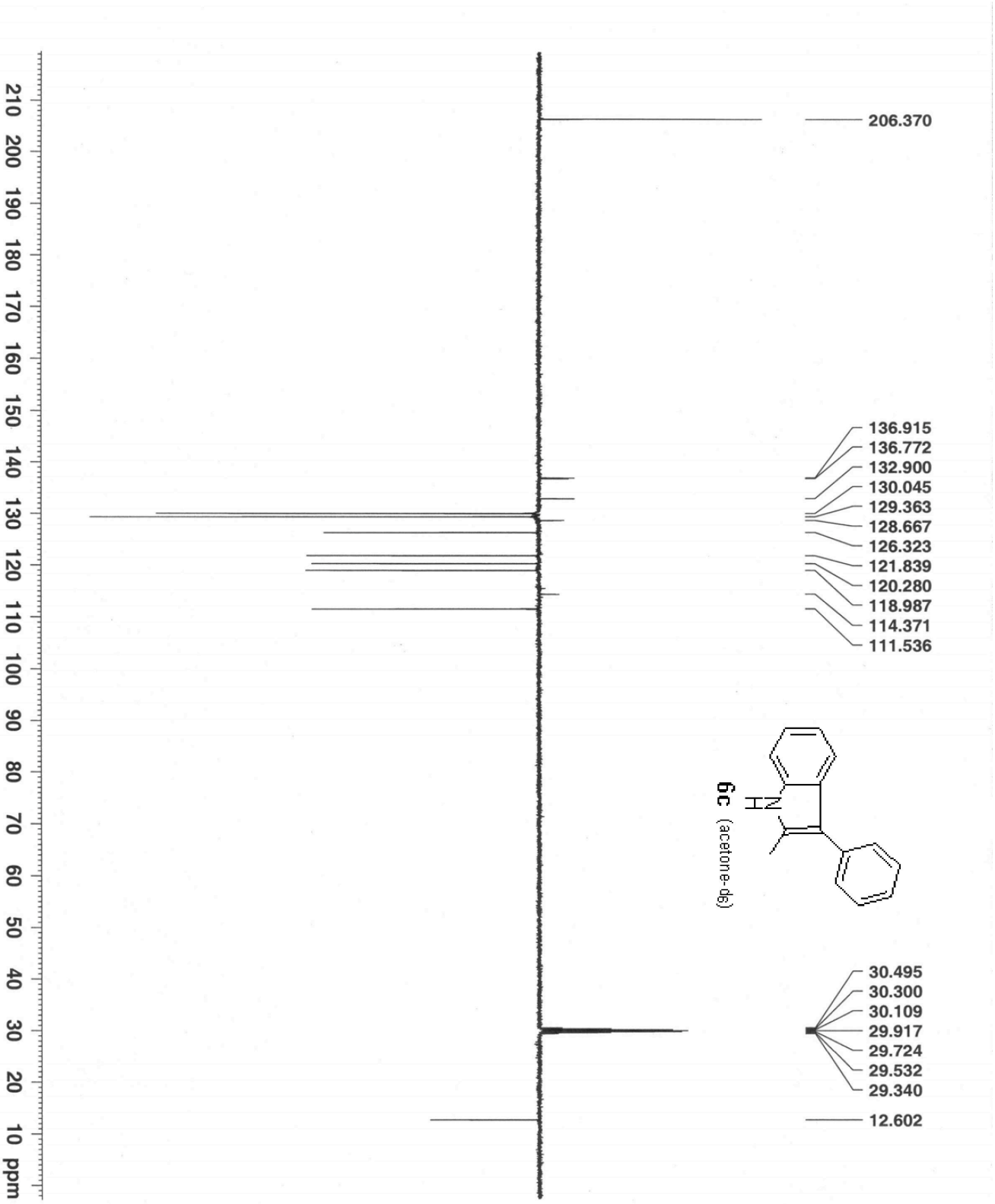
2.01
3.00
ppm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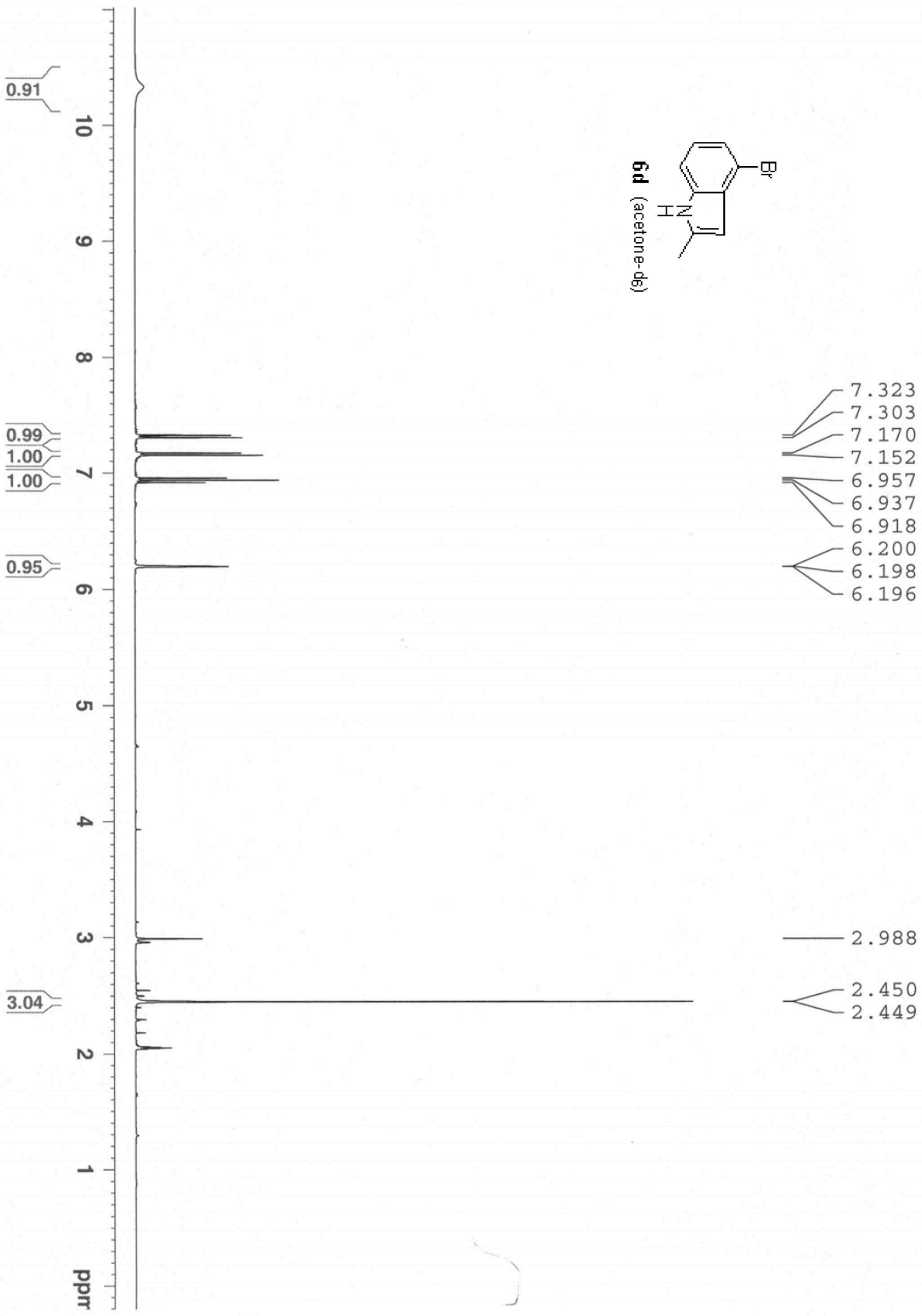
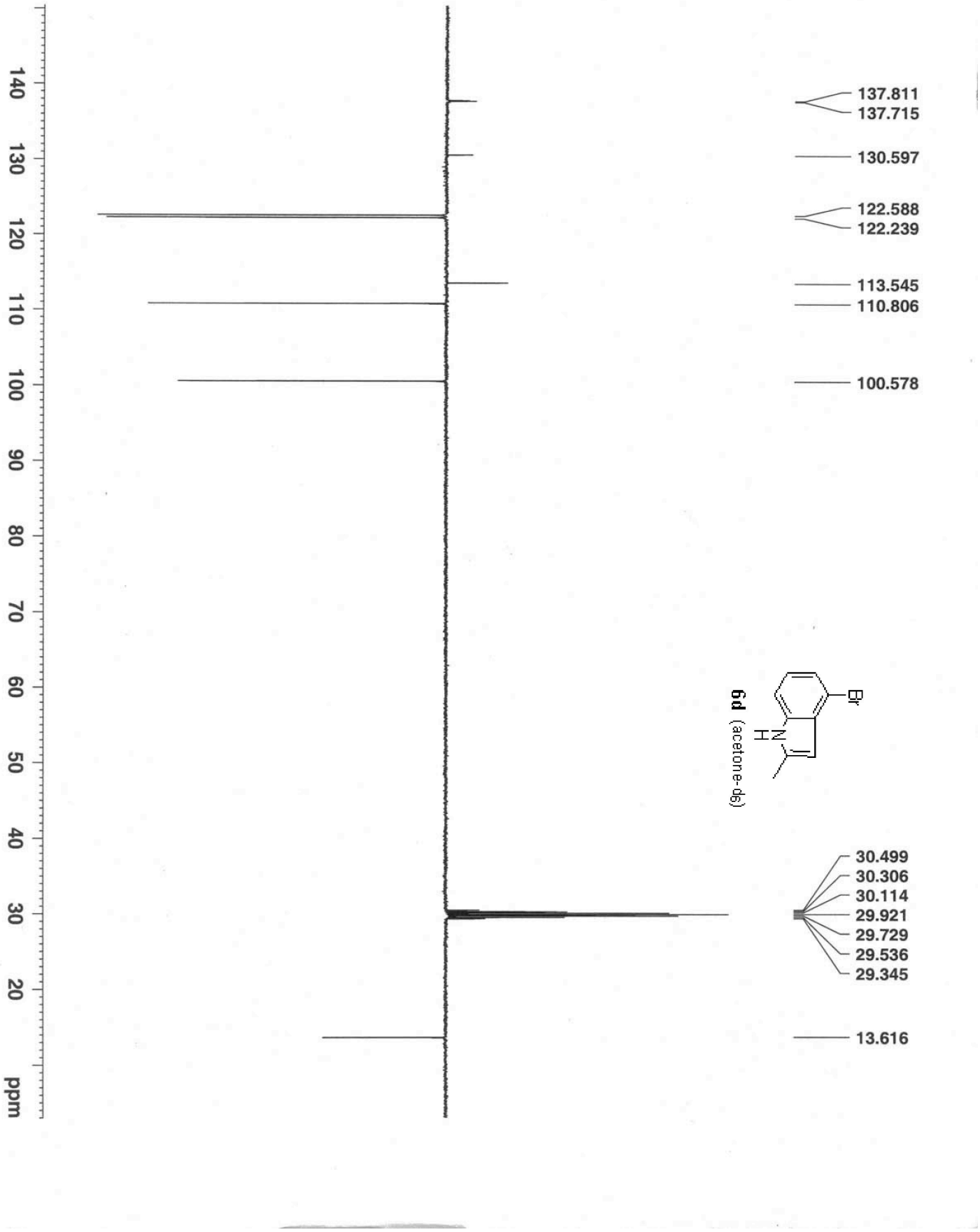
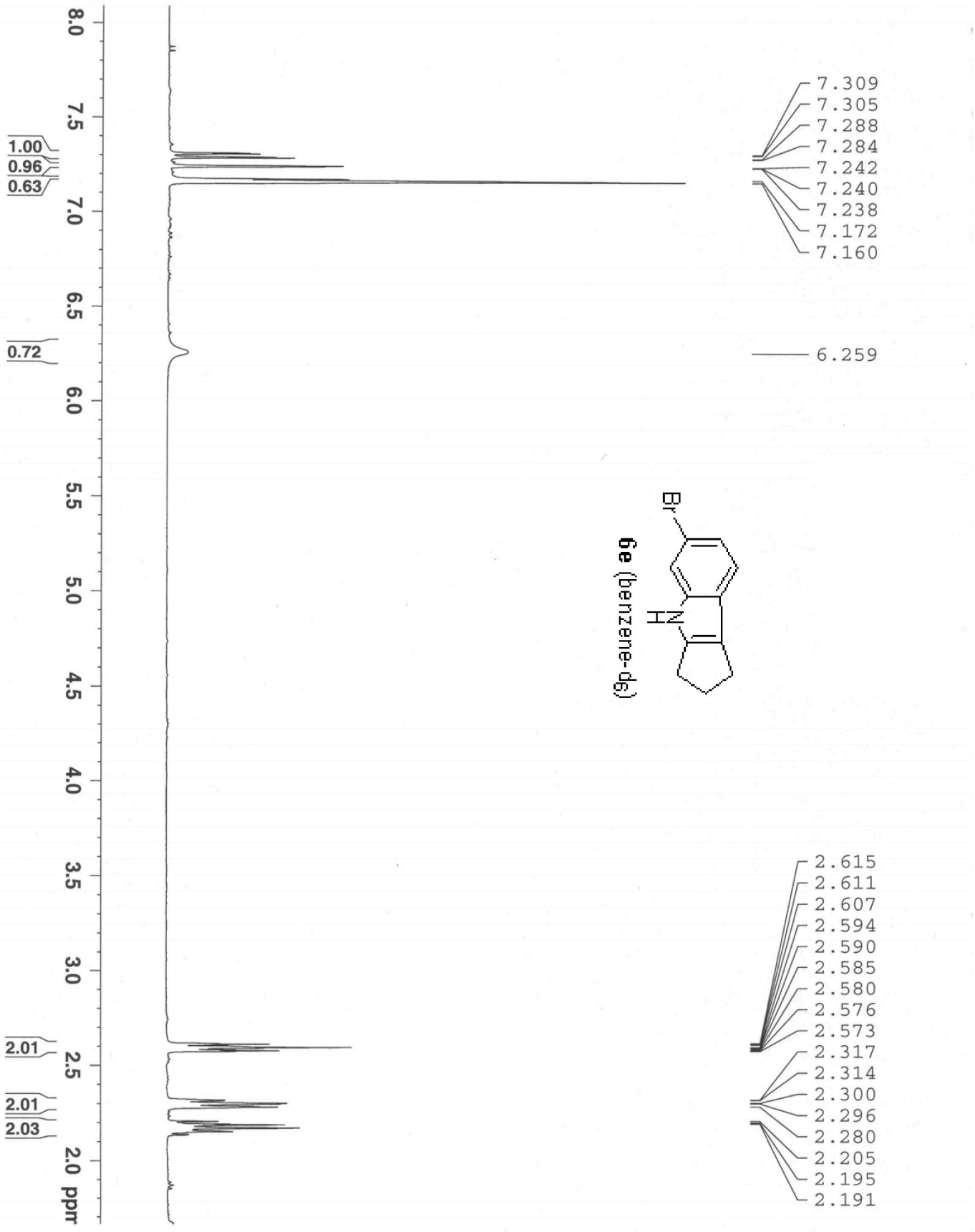
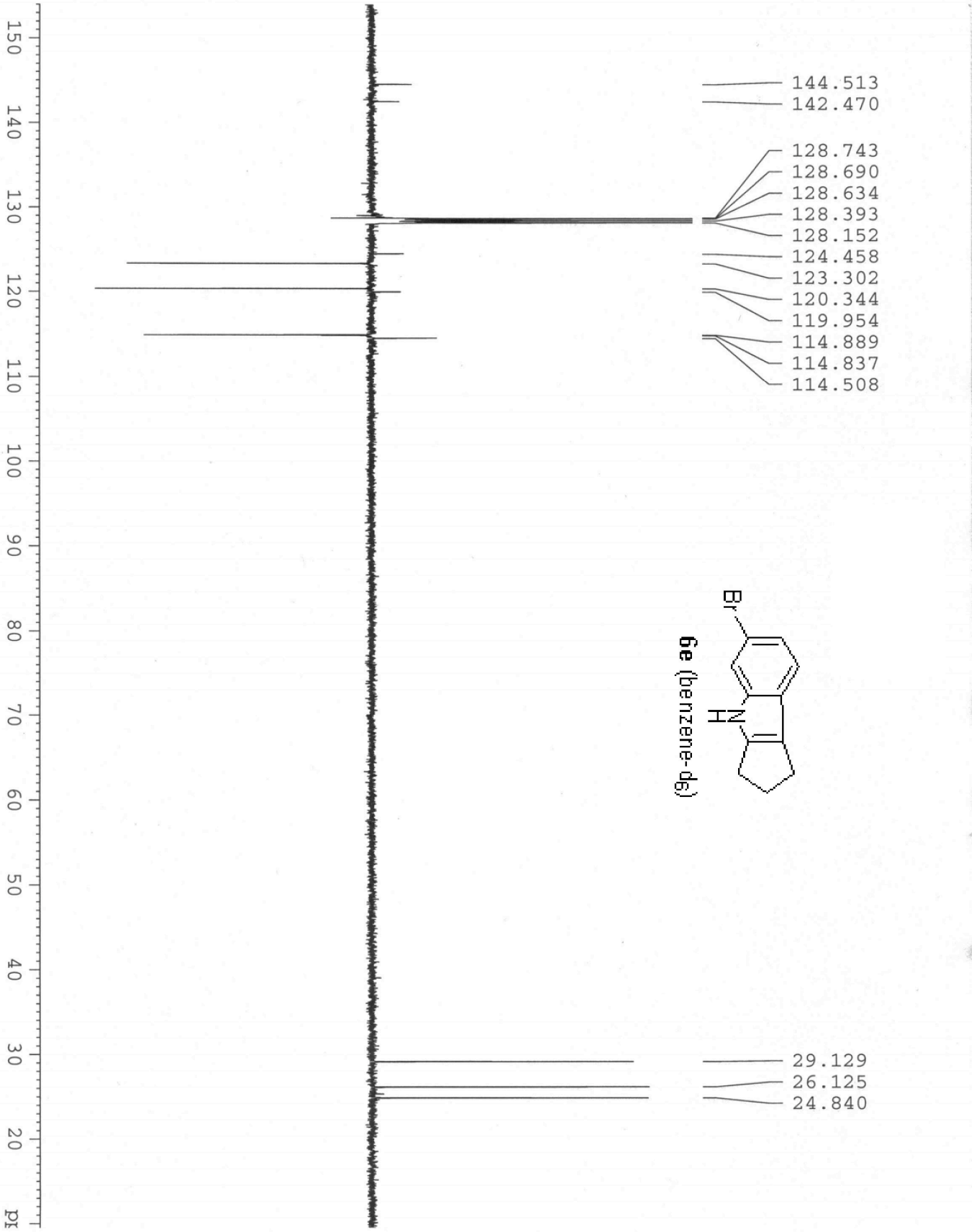
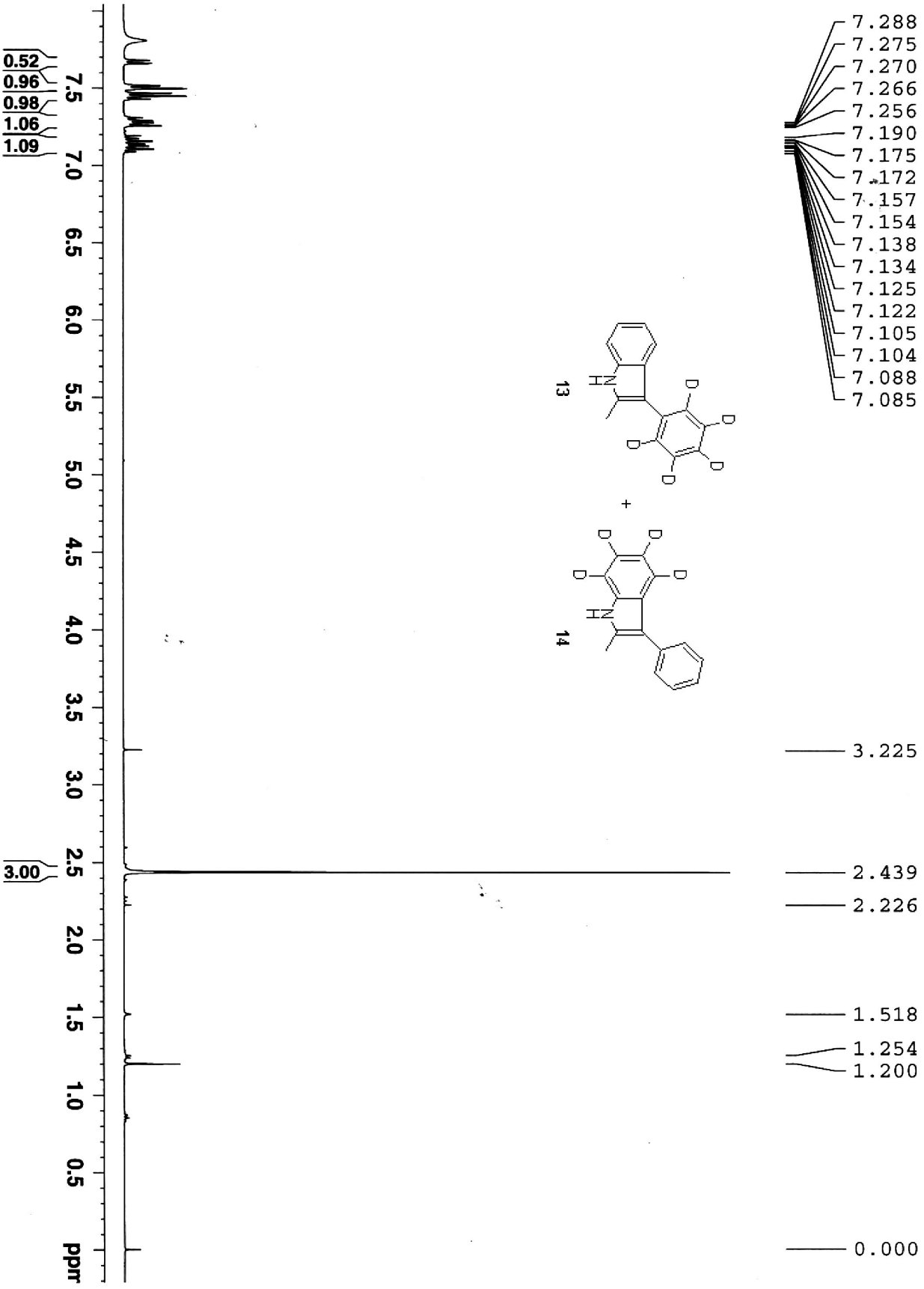
136.915
136.772
132.900
130.045
129.363
128.667
126.323
121.839
120.280
118.987
114.371
111.536
6c (acetone-d6)
30.495
30.300
30.109
29.917
29.724
29.532
29.340
12.602
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

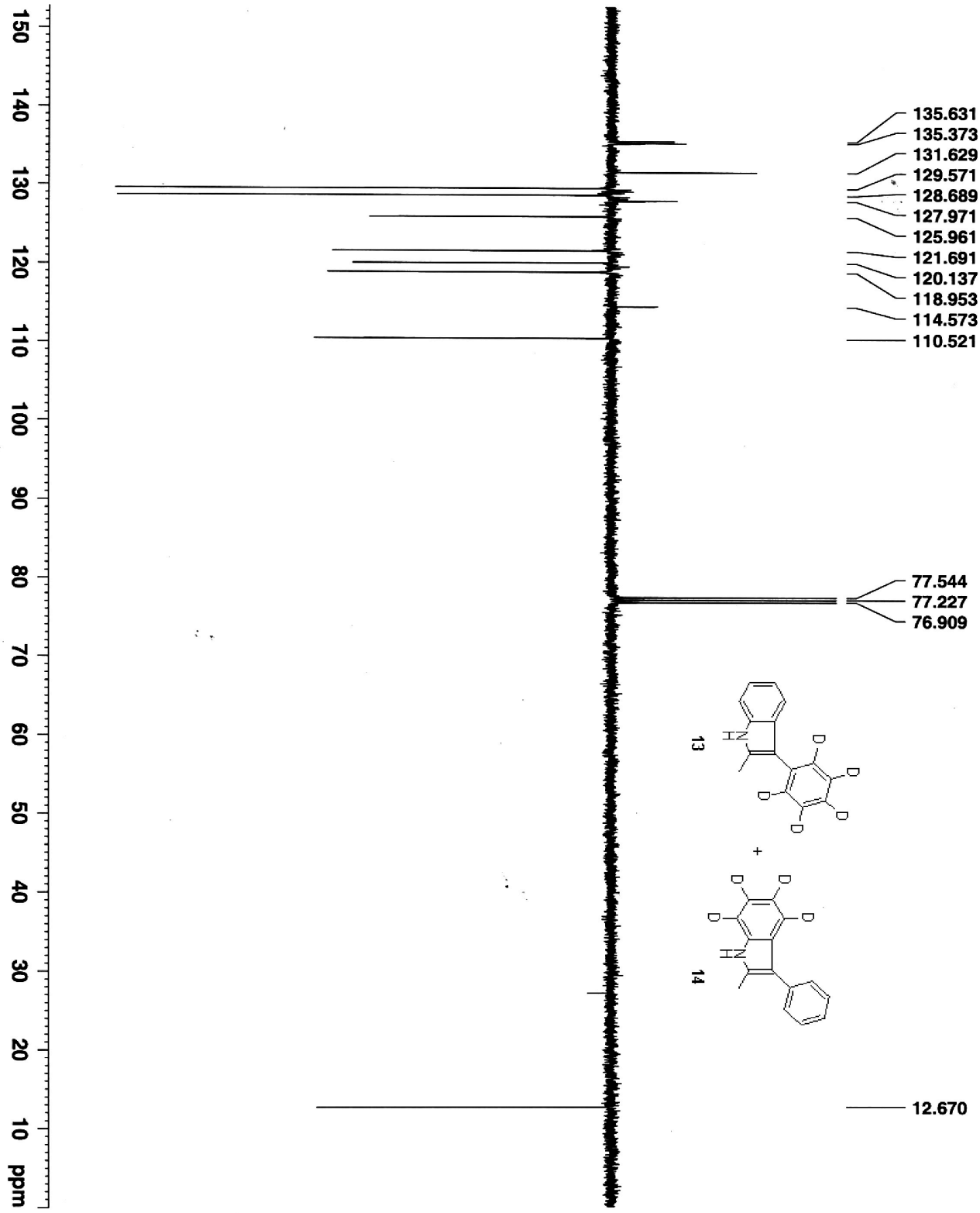

6d (acetone-d6)
Br
N
H
0.91
0.99
1.00
1.00
0.95
3.04
7.323
7.303
7.170
7.152
6.957
6.937
6.918
6.200
6.198
6.196
2.988
2.450
2.449
10
9
8
7
6
5
4
3
2
1
ppm

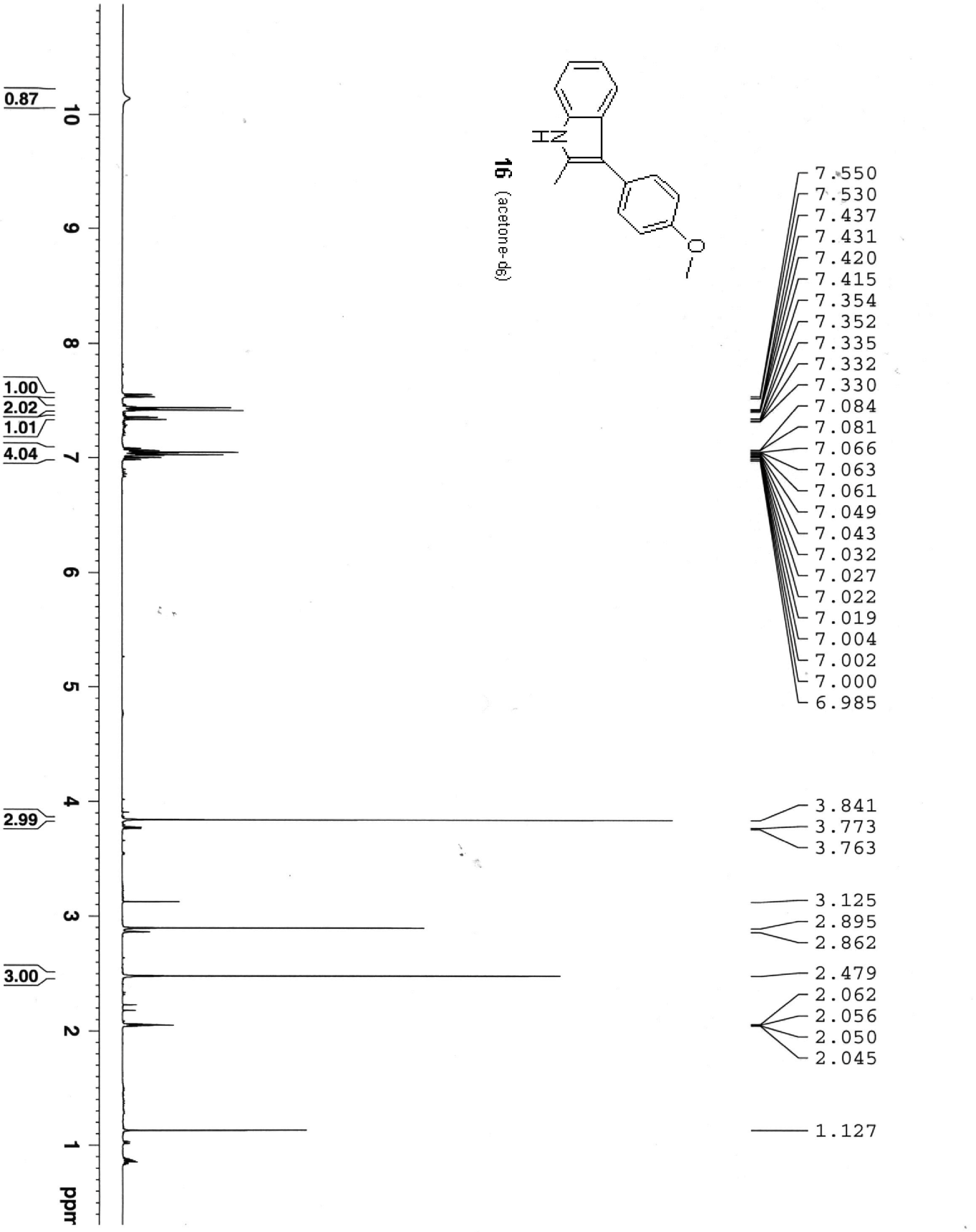

137.811
137.715
130.597
122.588
122.239
113.545
110.806
100.578
30.499
30.306
30.114
29.921
29.729
29.536
29.345
13.616
6d (acetone-d6)
Br
N
H
ppm

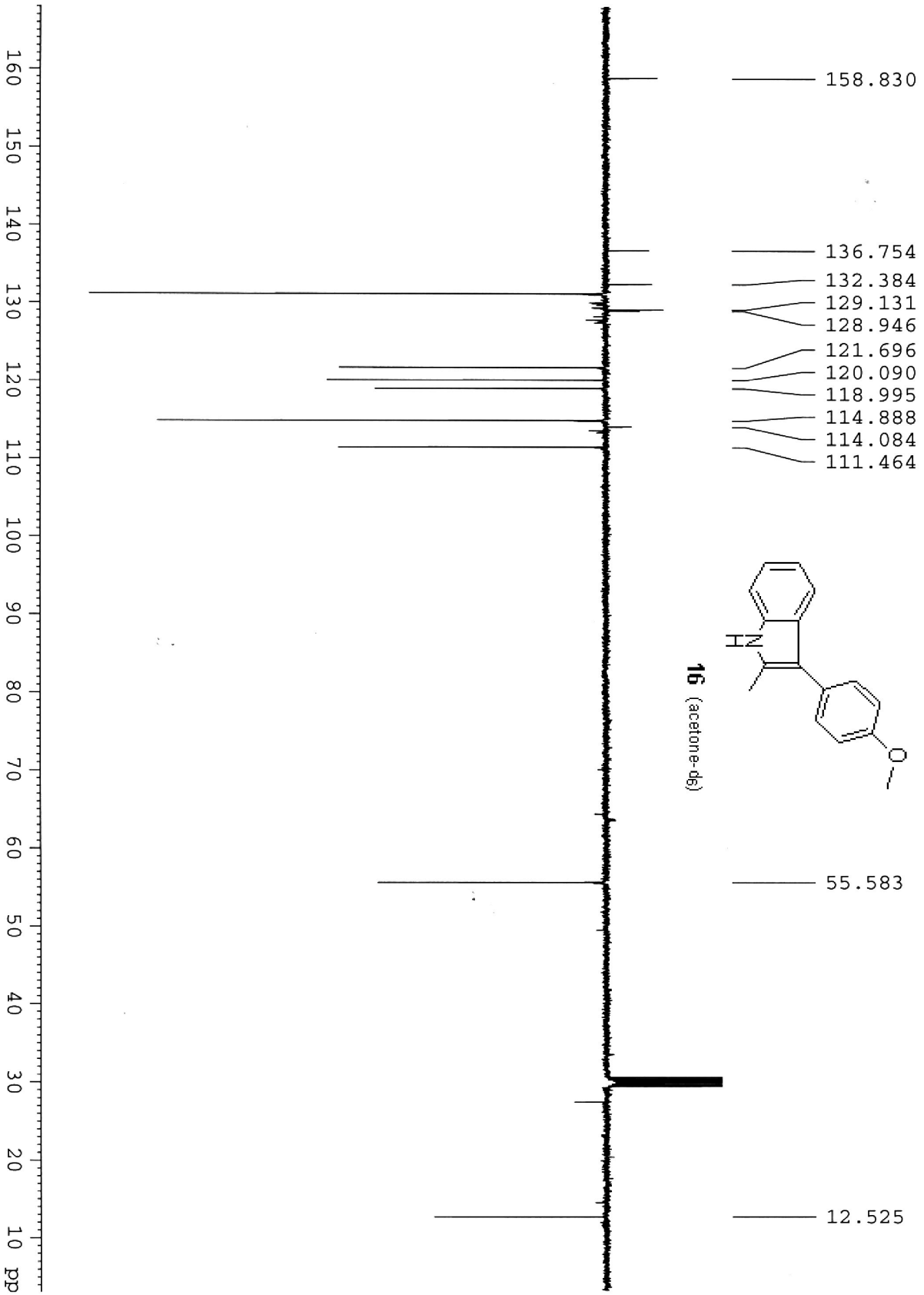

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0 ppm
1.00
0.96
0.63
0.72
2.01
2.01
2.03
7.309
7.305
7.288
7.284
7.242
7.240
7.238
7.172
7.160
6.259
2.615
2.611
2.607
2.594
2.590
2.585
2.580
2.576
2.573
2.317
2.314
2.300
2.296
2.280
2.205
2.195
2.191
Br
N
H
6e (benzene-d6)

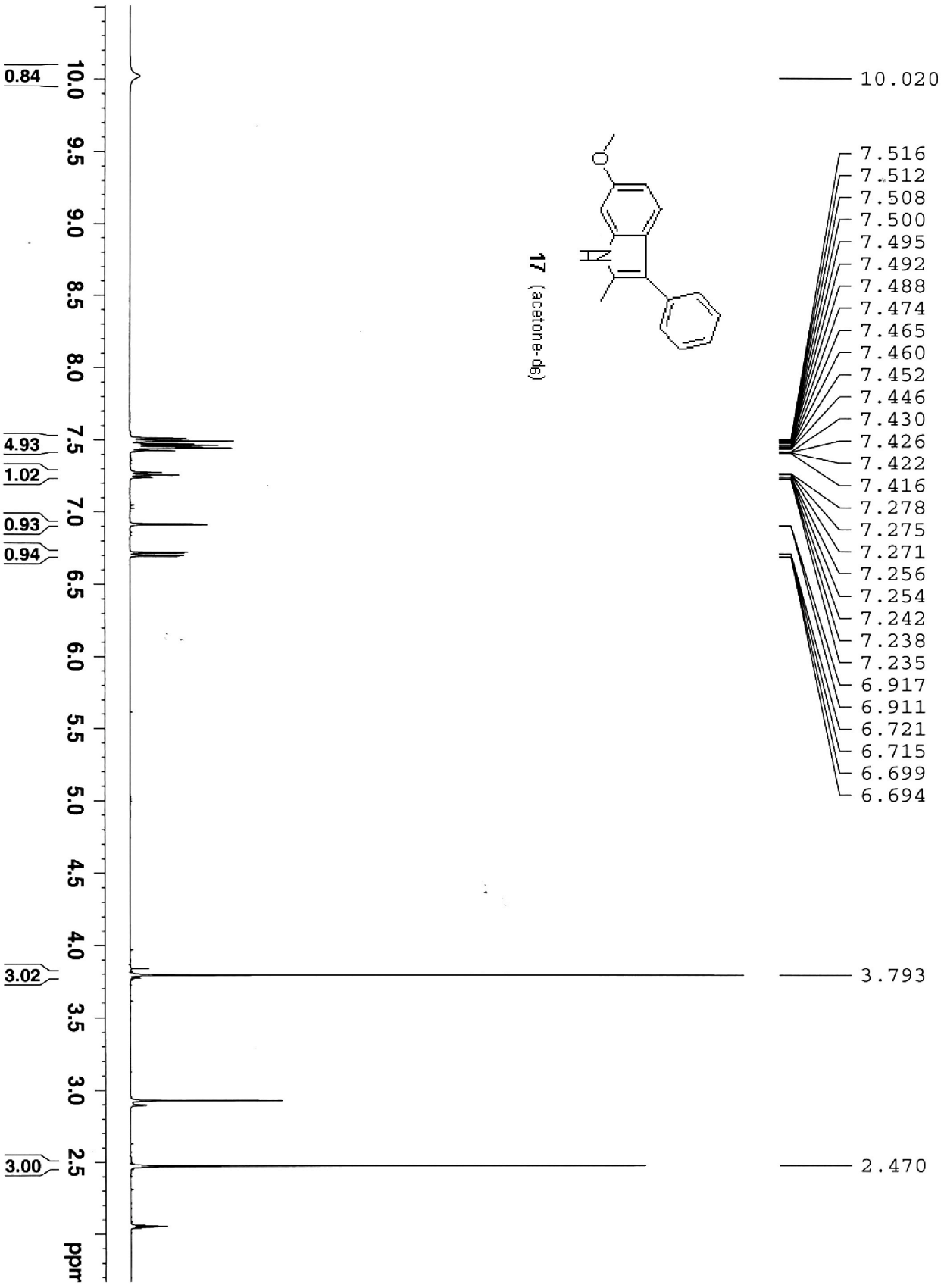

144.513
142.470
128.743
128.690
128.634
128.393
128.152
124.458
123.302
120.344
119.954
114.889
114.837
114.508
29.129
26.125
24.840
Br
N
H
6e (benzene-d6)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

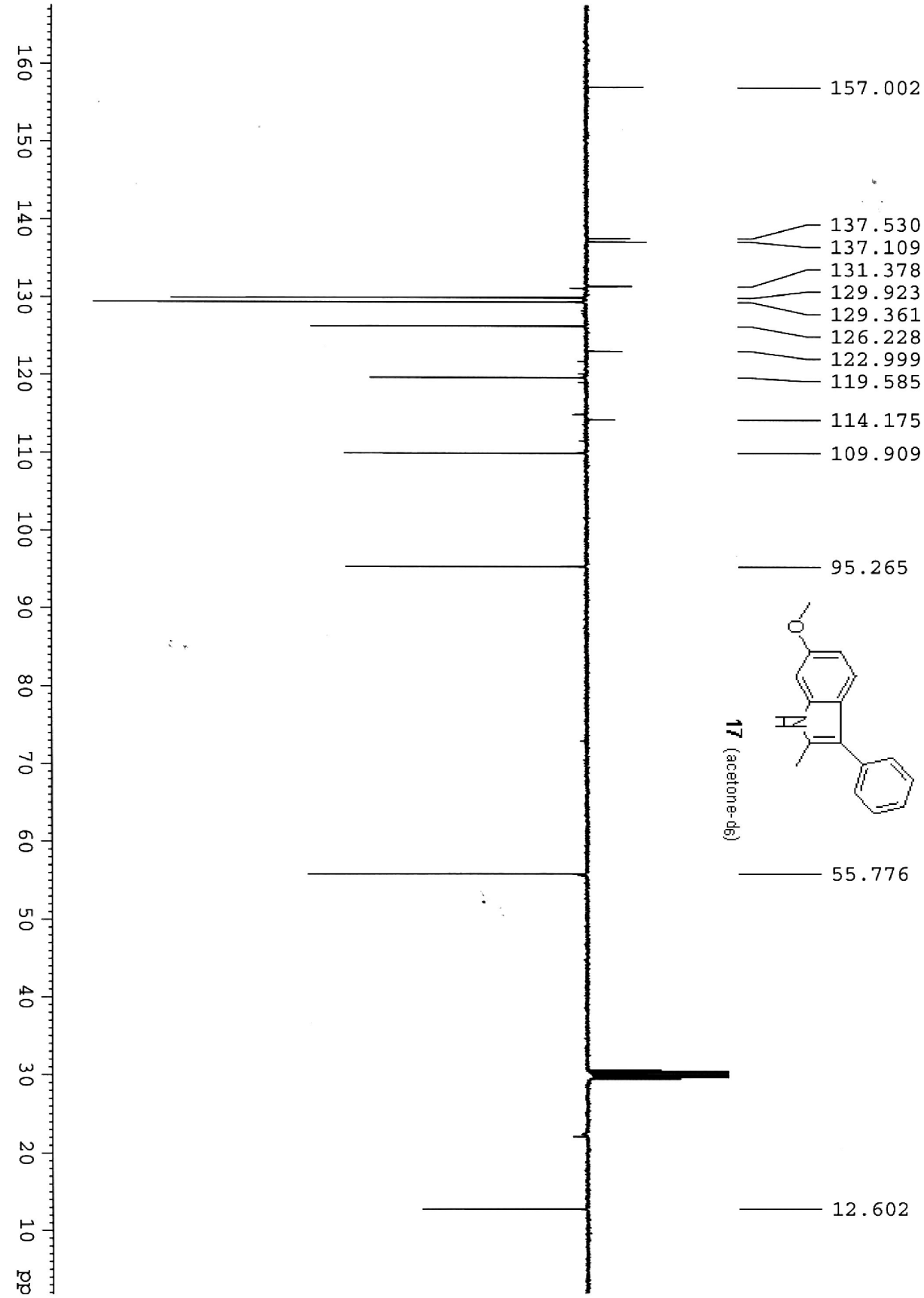

0.52
0.96
0.98
1.06
1.09
3.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
7.288
7.275
7.270
7.266
7.256
7.190
7.175
7.172
7.157
7.154
7.138
7.134
7.125
7.122
7.105
7.104
7.088
7.085
13
14
3.225
2.439
2.226
1.518
1.254
1.200
0.000


135.631
135.373
131.629
129.571
128.689
127.971
125.961
121.691
120.137
118.953
114.573
110.521
77.544
77.227
76.909
12.670
13
14
+
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


16 (acetone-d6)
0.87
1.00
2.02
1.01
4.04
2.99
3.00
7.550
7.530
7.437
7.431
7.420
7.415
7.354
7.352
7.335
7.332
7.330
7.084
7.081
7.066
7.063
7.061
7.049
7.043
7.032
7.027
7.022
7.019
7.004
7.002
7.000
6.985
3.841
3.773
3.763
3.125
2.895
2.862
2.479
2.062
2.056
2.050
2.045
1.127
ppm


158.830
136.754
132.384
129.131
128.946
121.696
120.090
118.995
114.888
114.084
111.464
55.583
12.525
16 (acetone-d6)
HN
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


10.020
7.516
7.512
7.508
7.500
7.495
7.492
7.488
7.474
7.465
7.460
7.452
7.446
7.430
7.426
7.422
7.416
7.278
7.275
7.271
7.256
7.254
7.242
7.238
7.235
6.917
6.911
6.721
6.715
6.699
6.694
3.793
2.470
0.84
4.93
1.02
0.93
0.94
3.02
3.00
ppm
17 (acetone-d6)


157.002
137.530
137.109
131.378
129.923
129.361
126.228
122.999
119.585
114.175
109.909
95.265
55.776
12.602
17 (acetone-d6)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm