

Synthesis of 2-Mercaptobenzothiazoles *via* DBU-promoted Tandem Reaction of
o-Haloanilines and Carbon Disulfide

Fei Wang, Shangjun Cai, Zhipeng Wang, Chanjuan Xi*

Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology (Ministry
of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China

State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin
300071, China

List of the contents:

1. General Procedures and Experimental Section.....	S2
2. Copies of ¹H and ¹³C NMR Spectra.....	S6
3. References.....	S30

1. General Procedures and Experimental Section

General Comments

All the reactions were carried out in pre-dried a screwcapped tube with a Teflon-lined septum under N₂ atmosphere. Unless otherwise indicated, all materials were obtained from commercial sources and used as received. DMF, toluene, 1,4-dioxane, and DMSO were fresh distilled. Column chromatography was performed on silica gel (particle size 10-40 μ m, Ocean Chemical Factory of Qingdao, China). ¹H NMR and ¹³C NMR spectra were recorded on a JEOL AL-300MHz, JEOL AL-600MHz and Bruker 400M NMR spectrometer at ambient temperature with DMSO-*d*₆ as the solvent. Chemical shifts (δ) were given in ppm, referenced to the residual proton resonance of DMSO, to the carbon resonance of DMSO-*d*₆ (39.52). Coupling constants (*J*) were given in Hertz (Hz). The term m, d, s referred to multiplet, doublet, singlet. The melting points were measured on X-4 digital melting point apparatus and were uncorrected. Mass spectra were obtained using Bruker Esquire ion trap mass spectrometer in positive mode. The reaction progress was monitored by ¹H NMR. ¹H NMR yields, using trichloroethene as internal standard, were obtained in proportion to the integral area of trichloroethene signal.

Experimental Section

General procedure for the synthesis of 2-Mercaptobenzothiazoles 2

A sealed tube was charged with the mixture of *o*-haloaniline **1** (0.5 mmol), DBU (1.0 mmol, 149 μ L), carbon disulfide (1.0 mmol), then stirred in toluene (1 mL) at room temperature under nitrogen atmosphere. Half an hour later, the tube was sealed

and the mixture was allowed to stir at 80-100 °C for indicated time. After completion, the mixture was cooled to room temperature, then H₂O (5 mL) was added and the mixture was extracted with EtOAc (5 mL x 3), dried by anhydrous Na₂SO₄. Evaporation of the solvent followed by purification on silica gel (petroleum ether/ethyl acetate = 5/1) provided the corresponding product **2**.

2-Mercaptobenzothiazole (2a)¹: White solid, 68 mg (82% yield), mp: 189-190 °C; ¹H NMR (DMSO-*d*₆, 300 MHz): δ 7.24-7.31 (m, 2H), 7.37 (d, *J*_{H-H} = 7.4 Hz, 1H), 7.67 (d, *J*_{H-H} = 7.8 Hz, 1H), 13.76 (brs, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 112.5, 121.8, 124.3, 127.2, 129.4, 141.3, 189.9; ESI-MS: [M+H]⁺ *m/z* 167.8.

6-Methyl-2-mercaptobenzothiazole (2b)¹: White solid, 68 mg (76% yield), mp: 178-179 °C; ¹H NMR (DMSO-*d*₆, 300 MHz): δ 2.31 (s, 3H, CH₃), 7.19 (s, 2H), 7.45 (s, 1H), 13.68 (brs, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 20.8, 112.2, 121.6, 128.1, 129.5, 133.9, 139.2, 189.2; ESI-MS: [M+Na]⁺ *m/z* 205.1.

6-Fluoro-2-mercaptobenzothiazole (2c)¹: White solid, 82 mg (89% yield), mp: 216-217 °C; ¹H NMR (DMSO-*d*₆, 300 MHz): δ 7.21-7.31 (m, 2 H), 7.64 (dd, *J*_{F-H} = 8.2 Hz, *J*_{H-H} = 1.8 Hz, 1H), 13.82 (brs, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 109.0 (d, *J*_{F-C} = 28.0 Hz), 113.5 (d, *J*_{F-C} = 9.3 Hz), 114.8 (d, *J*_{F-C} = 24.4 Hz), 130.8 (d, *J*_{F-C} = 10.8 Hz), 138.1, 159.2 (d, *J*_{F-C} = 239.5 Hz), 190.0; ESI-MS: [M+H]⁺ *m/z* 186.6.

6-Bromo-2-mercaptobenzothiazole (2d)¹: White solid, 70 mg (57% yield), mp: 265-266 °C; ¹H NMR (DMSO-*d*₆, 300 MHz): δ 7.21 (d, *J*_{H-H} = 8.2 Hz, 1H), 7.54 (d, *J*_{H-H} = 8.7 Hz, 1H), 7.95 (s, 1H), 13.88 (brs, 1H); ¹³C NMR (DMSO-*d*₆, 75 MHz): δ 113.9, 116.5, 124.2, 130.1, 131.5, 140.6, 190.1; ESI-MS: [M+H]⁺ *m/z* 246.4.

4-Bromo-2-mercaptobenzothiazole (2e): White solid, 76 mg (62% yield), mp: 184-185 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.20 (m, 1H), 7.58 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 7.68 (d, $J_{\text{H-H}} = 7.8$ Hz, 1H), 13.72 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 103.7, 121.0, 125.5, 130.5, 131.9, 140.2, 190.9; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 246.8; HRMS calcd for $\text{C}_7\text{H}_4\text{BrNS}_2$: 245.9041 ($\text{M}+\text{H})^+$, found: 245.9044.

6-Methoxycarbonyl-2-mercaptobenzothiazole (2f): White solid, 87 mg (78% yield), mp: 265-266 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 3.85 (s, 3H, CH_3), 7.37 (d, $J_{\text{H-H}} = 8.7$ Hz, 1H), 7.96 (d, $J_{\text{H-H}} = 8.7$ Hz, 1H), 8.32 (s, 1H), 13.92 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz): δ 52.3, 112.2, 123.3, 125.3, 128.4, 129.8, 144.8, 165.6, 191.9; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 226.1; HRMS calcd for $\text{C}_9\text{H}_7\text{NO}_2\text{S}_2$: 225.9991 ($\text{M}+\text{H})^+$, found: 225.9986.

6-Cyano-2-mercaptobenzothiazole (2g): White solid, 62 mg (65% yield), mp: 272-274 °C; ^1H NMR (DMSO- d_6 , 600 MHz): δ 7.39 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 7.80 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 8.20 (s, 1H), 13.94 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 150 MHz): δ 106.4, 113.0, 118.6, 126.0, 130.3, 131.2, 144.5, 191.7; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 193.1; HRMS calcd for $\text{C}_8\text{H}_4\text{N}_2\text{S}_2$: 192.9889 ($\text{M}+\text{H})^+$, found: 192.9891.

6-Trifluoromethoxy-2-mercaptobenzothiazole (2h): White solid, 100 mg (79% yield), mp: 234-235 °C; ^1H NMR (DMSO- d_6 , 400 MHz): δ 7.34-7.41 (m, 2H), 7.84 (s, 1H), 13.90 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz): δ 113.3, 115.2, 120.1 (d, $J_{\text{F-C}} = 191.2$ Hz), 120.6, 130.8, 140.4, 144.7, 190.9; ESI-MS: $[\text{M}+\text{Na}]^+$ m/z 275.1; HRMS calcd for $\text{C}_8\text{H}_4\text{F}_3\text{NOS}_2$: 251.9759 ($\text{M}+\text{H})^+$, found: 251.9760.

4,6-Dibromo-2-mercaptobenzothiazole (2i): White solid, 87 mg (54% yield), mp:

251-252 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.78 (s, 1 H), 7.94 (s, 1 H), 13.86 (brs, 1 H); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 104.4, 116.5, 123.3, 132.2, 133.5, 139.9, 191.0; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 326.8; HRMS calcd for $\text{C}_7\text{H}_3\text{Br}_2\text{NS}_2$: 323.8146 ($\text{M}+\text{H})^+$, found: 323.8149.

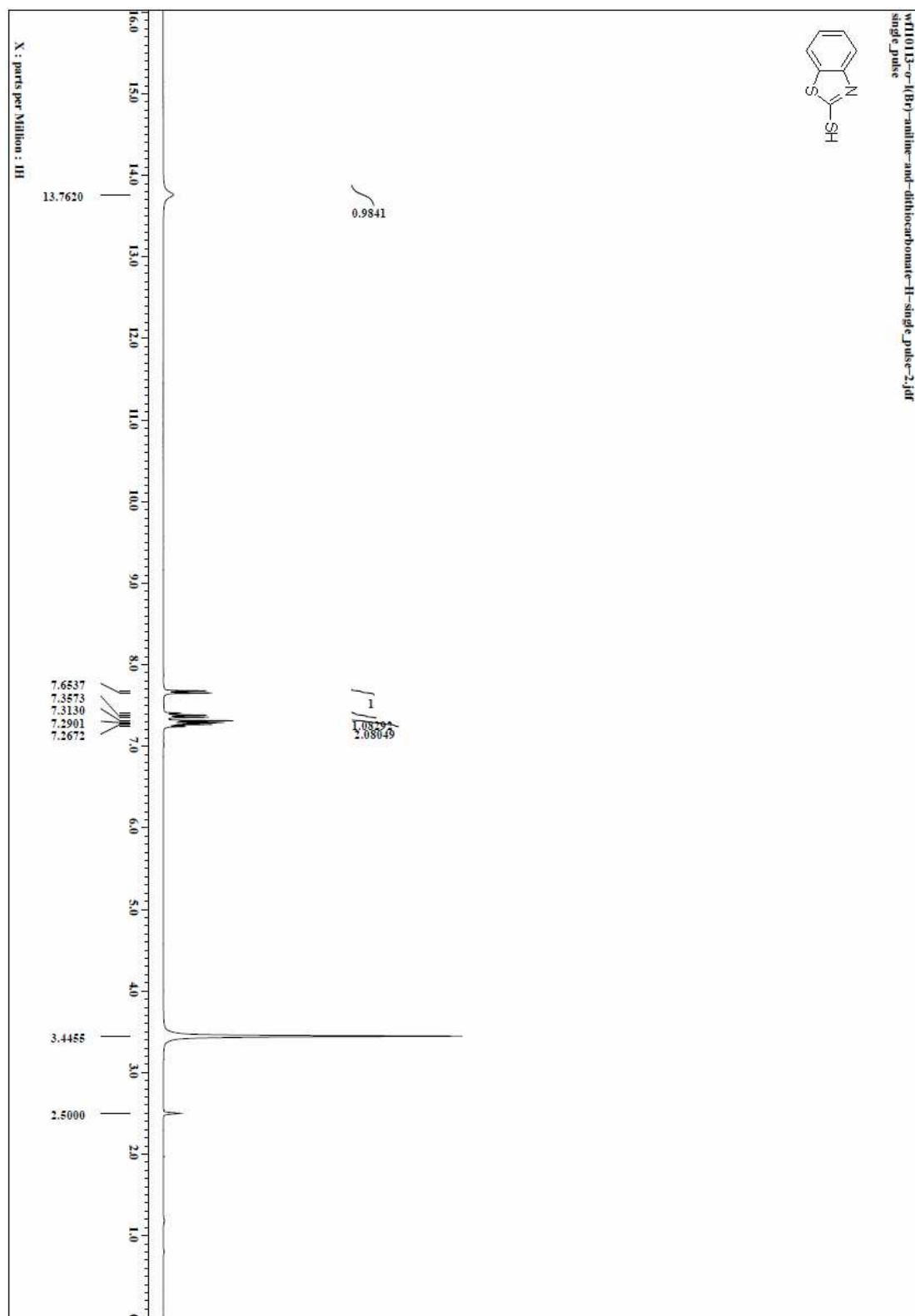
4-Bromo-6-methyl-2-mercaptobenzothiazole (2j): White solid, 78 mg (60% yield), mp: 219-220 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.43 (s, 1H), 7.47 (s, 1H), 13.72 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 20.3 (s, CH_3), 103.3, 121.0, 130.5, 131.1, 135.6, 138.1, 190.4; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 260.2; HRMS calcd for $\text{C}_8\text{H}_6\text{BrNS}_2$: 259.9198 ($\text{M}+\text{H})^+$, found: 259.9194.

6-Chloro-4-fluoro-2-mercaptobenzothiazole (2k): White solid, 90 mg (82% yield), mp: 210-211 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.48-7.70 (m, 1H), 7.72-7.90 (m, 1H), 14.13 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 114.1 (d, $J_{\text{F-C}} = 20.8$ Hz), 117.7, 120.7, 128.7 (d, $J_{\text{F-C}} = 8.6$ Hz), 129.1, 129.7, 133.1 (d, $J_{\text{F-C}} = 65.2$ Hz), 190.8; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 219.1; HRMS calcd for $\text{C}_7\text{H}_3\text{ClFNS}_2$: 219.9452 ($\text{M}+\text{H})^+$, found: 219.9457.

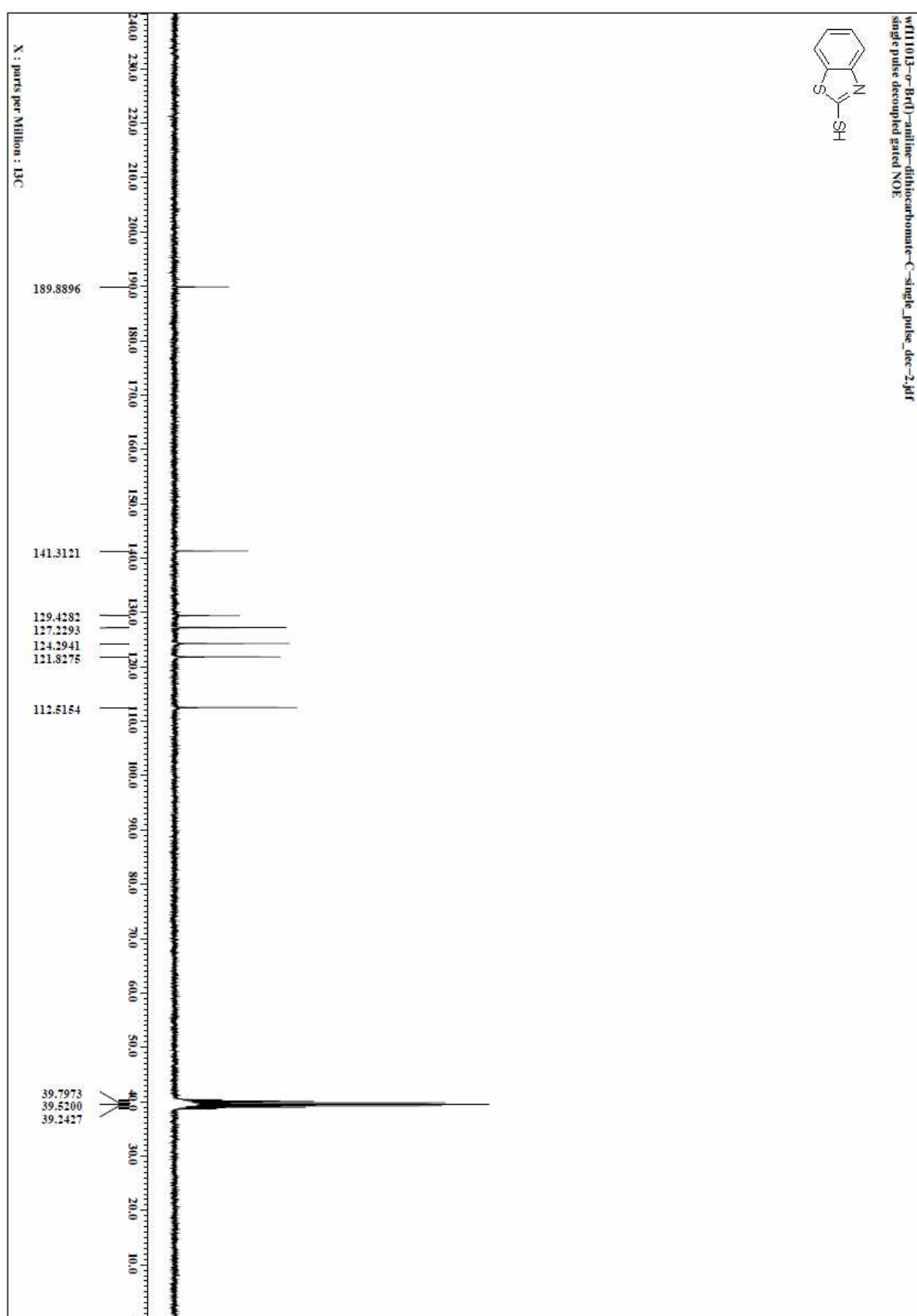
4,6-Difluoro-2-mercaptobenzothiazole (2l)²: White solid, 87 mg (86% yield), mp: 185-186 °C; ^1H NMR (DMSO- d_6 , 300 MHz): δ 7.35-7.66 (m, 2H), 13.94 (brs, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz): δ 102.9 (d, $J_{\text{F-C}} = 22.2$ Hz), 105.0 (d, $J_{\text{F-C}} = 27.2$ Hz), 108.2 (d, $J_{\text{F-C}} = 27.2$ Hz), 134.6 (d, $J_{\text{F-C}} = 459.6$ Hz), 158.6 (d, $J_{\text{F-C}} = 243.8$ Hz), 190.6; ESI-MS: $[\text{M}+\text{H}]^+$ m/z 203.3.

2. Copies of ^1H and ^{13}C NMR Spectra

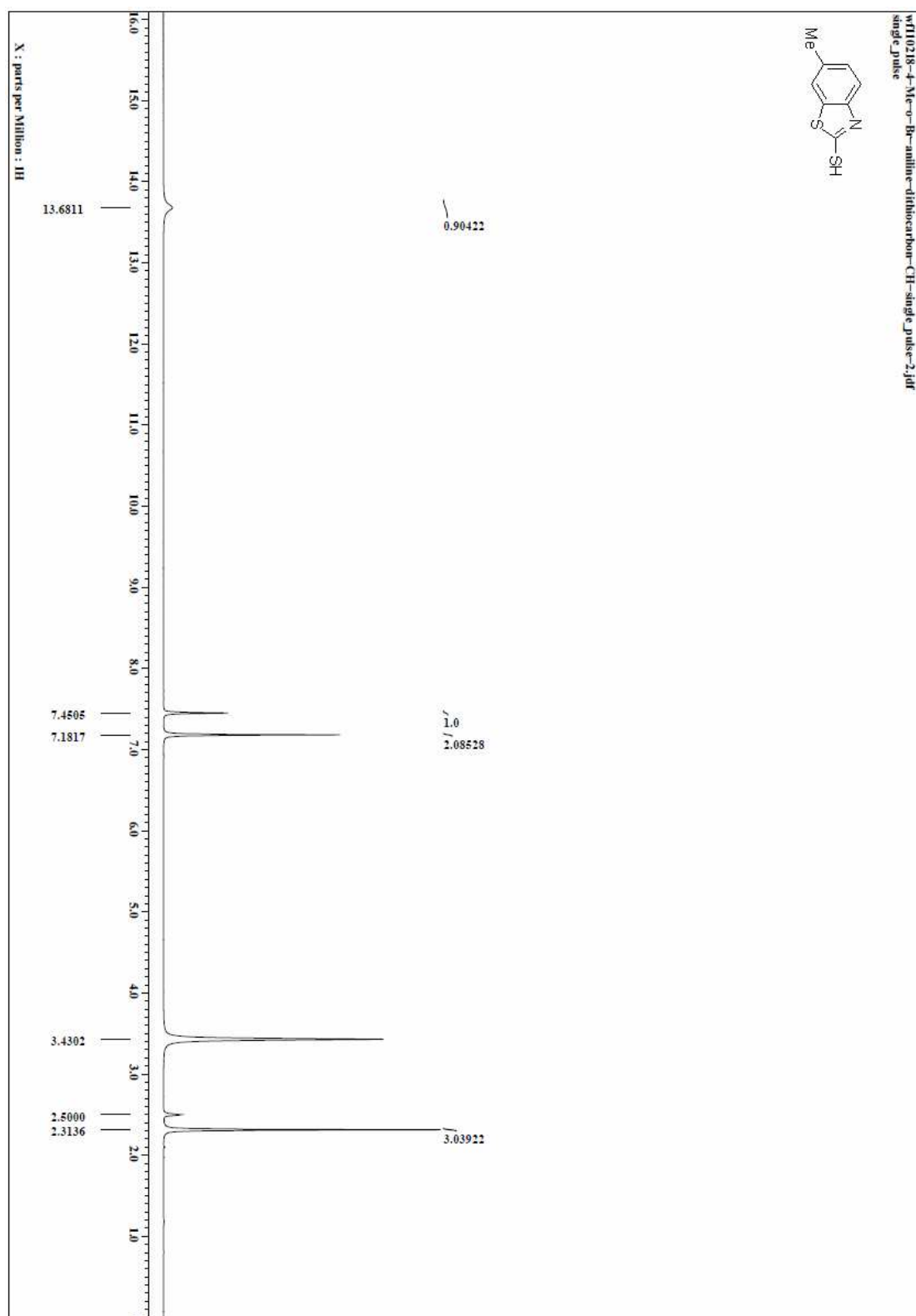
Compound 2a



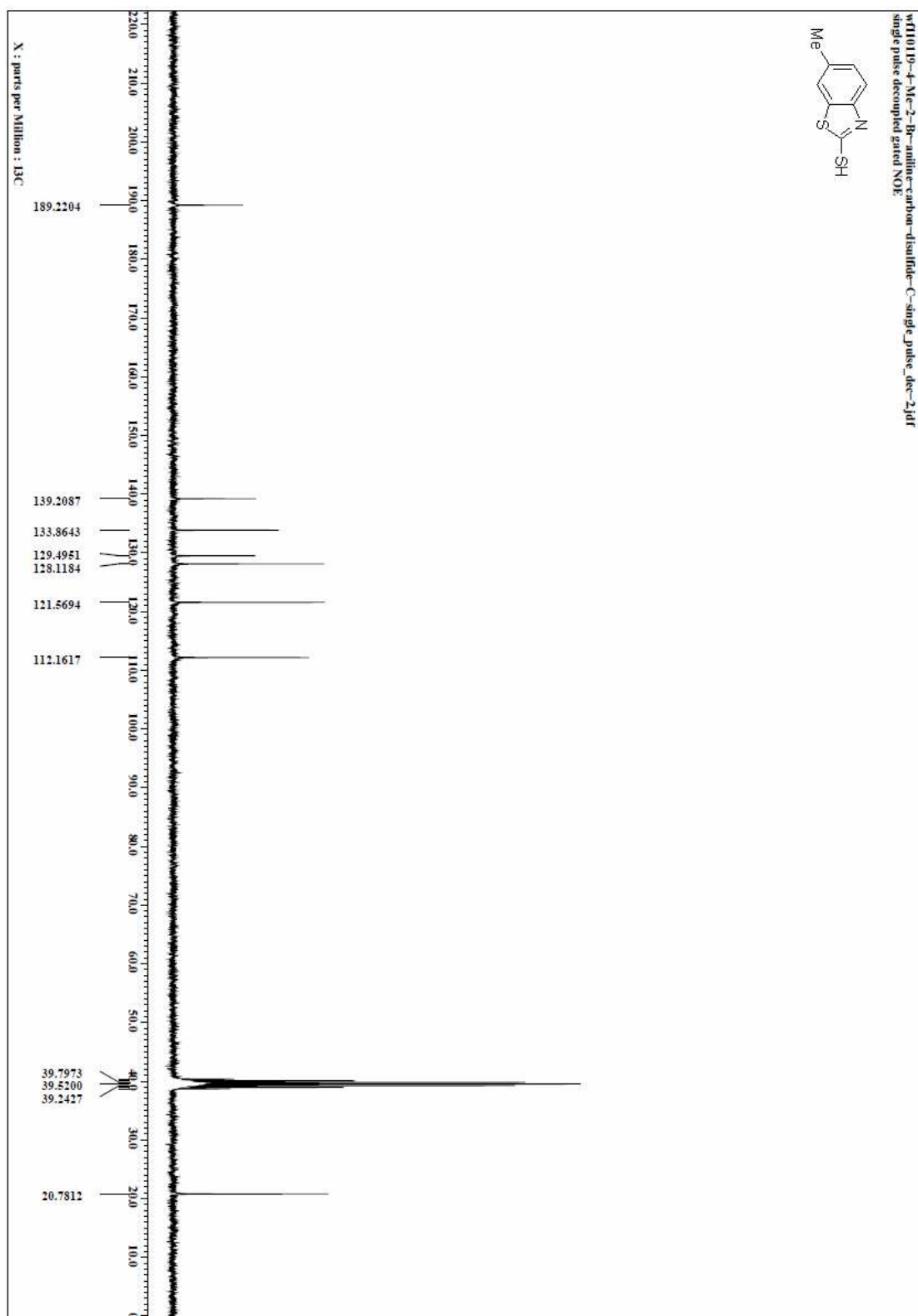
Compound 2a



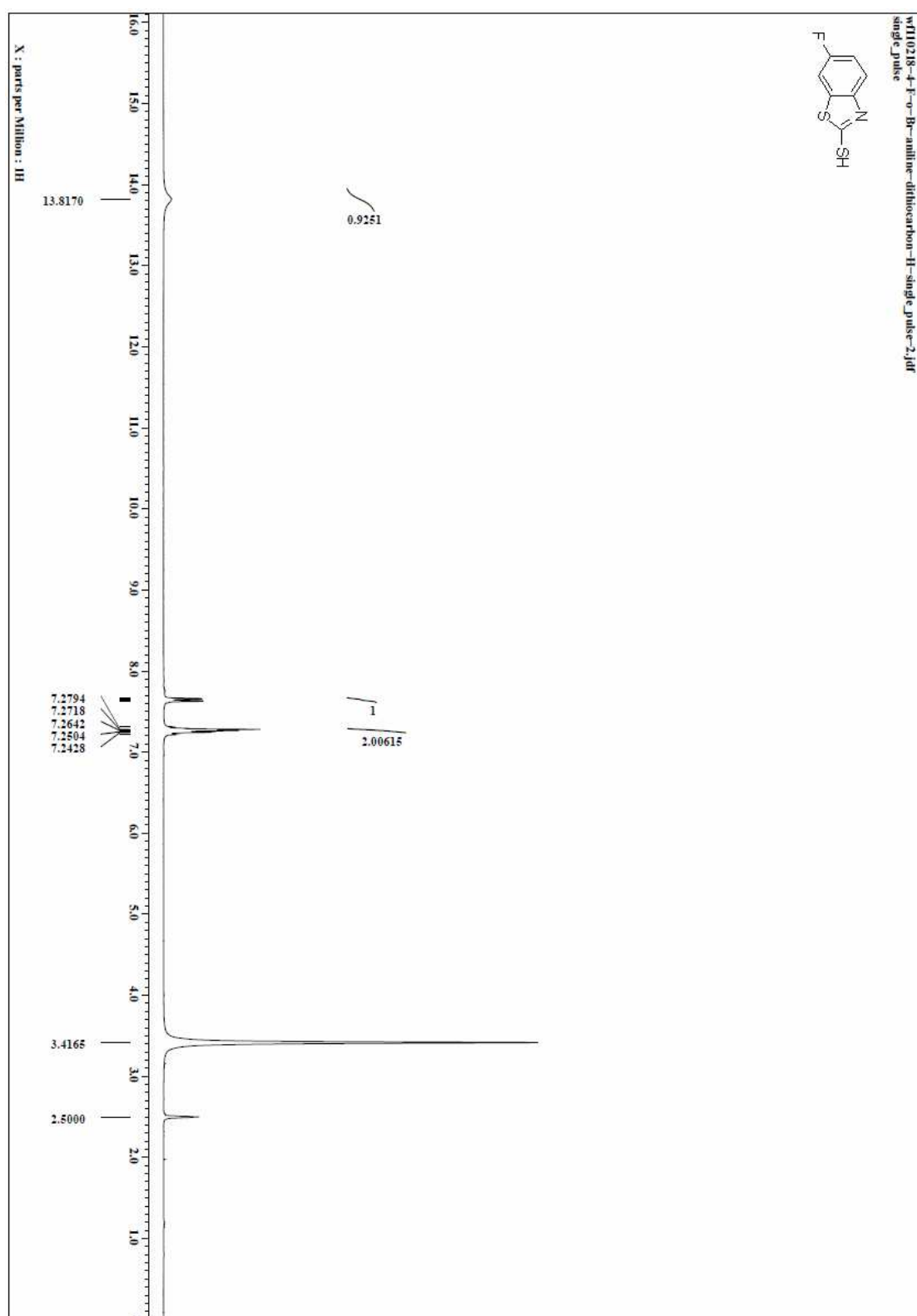
Compound 2b



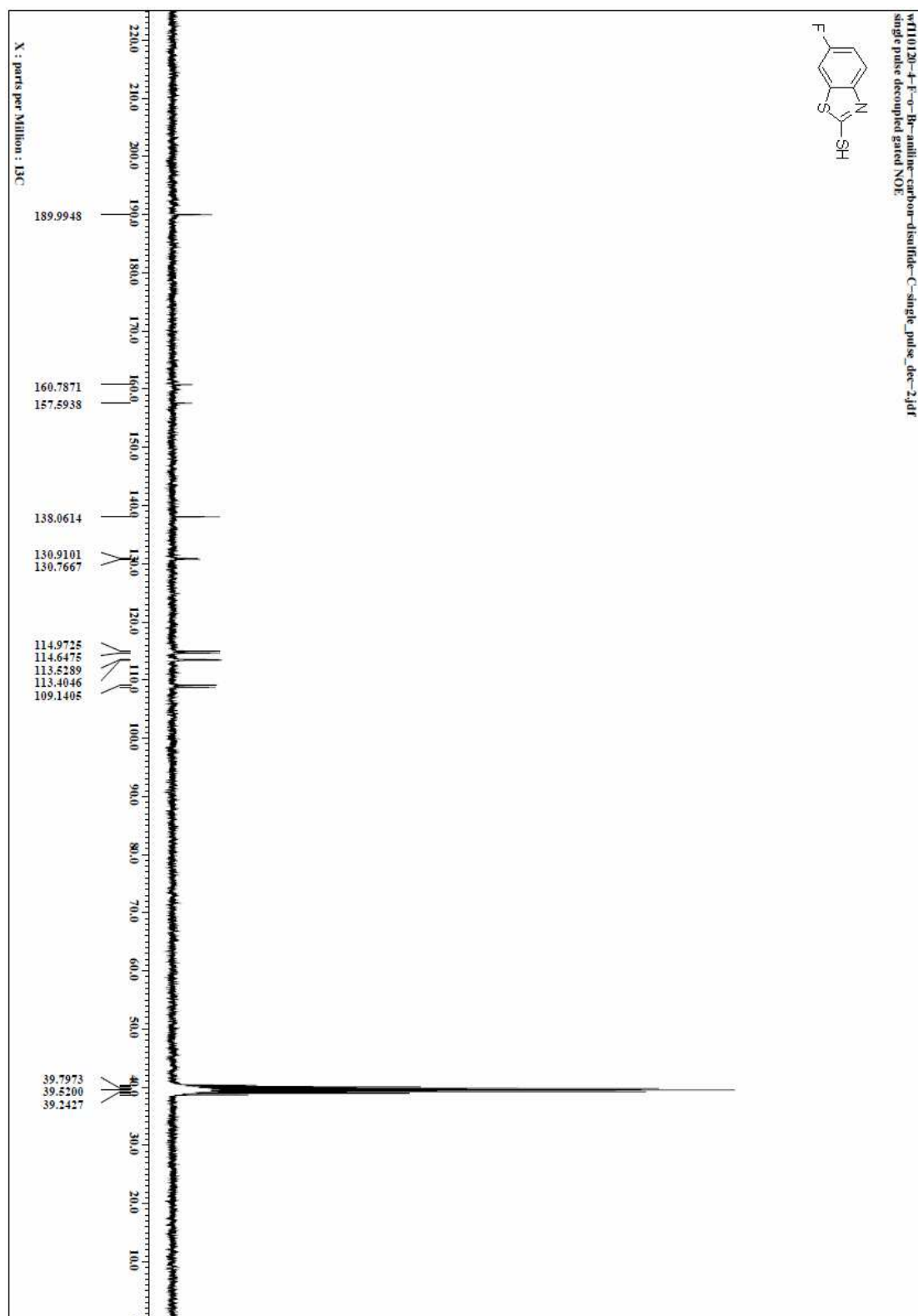
Compound 2b



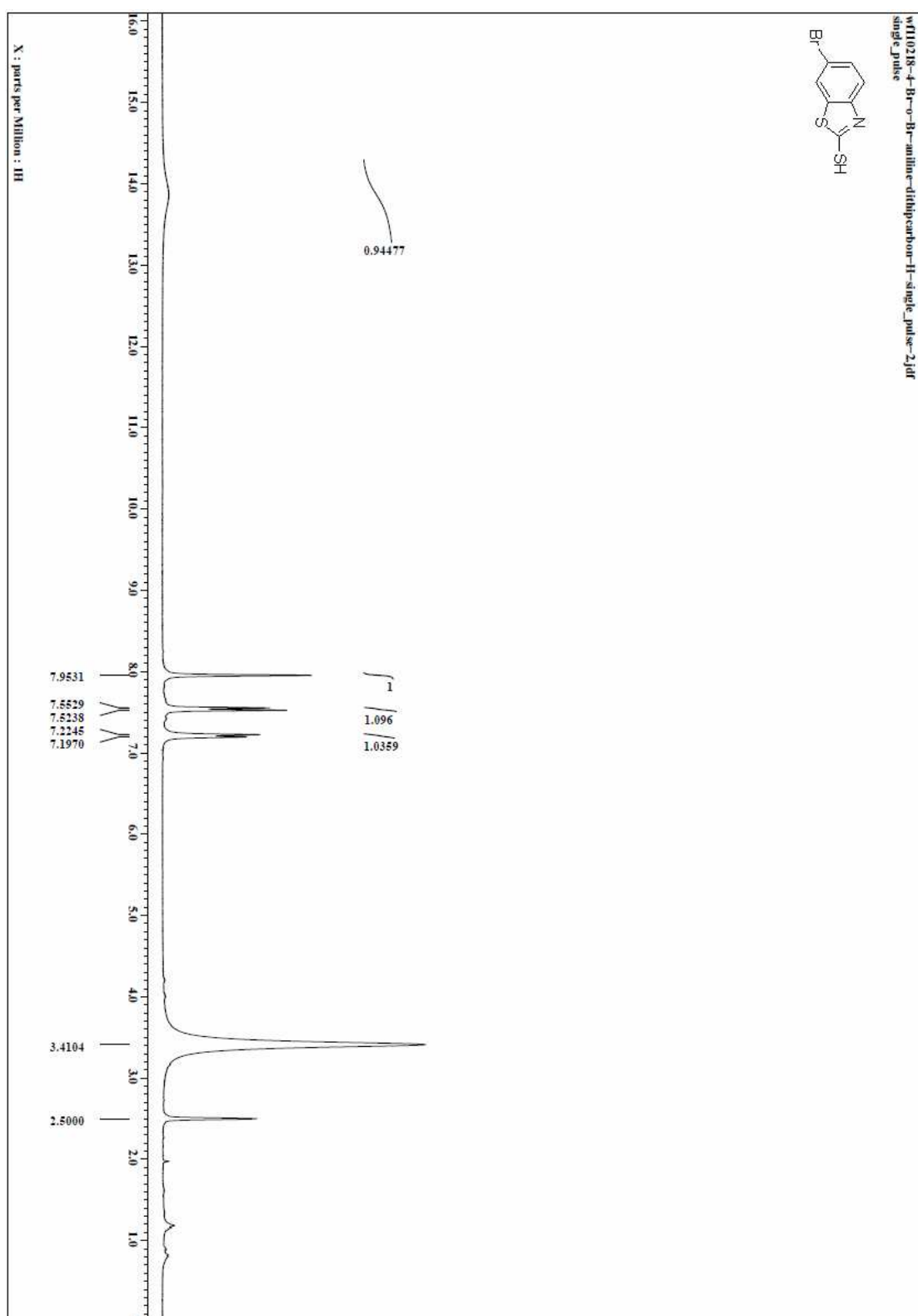
Compound 2c



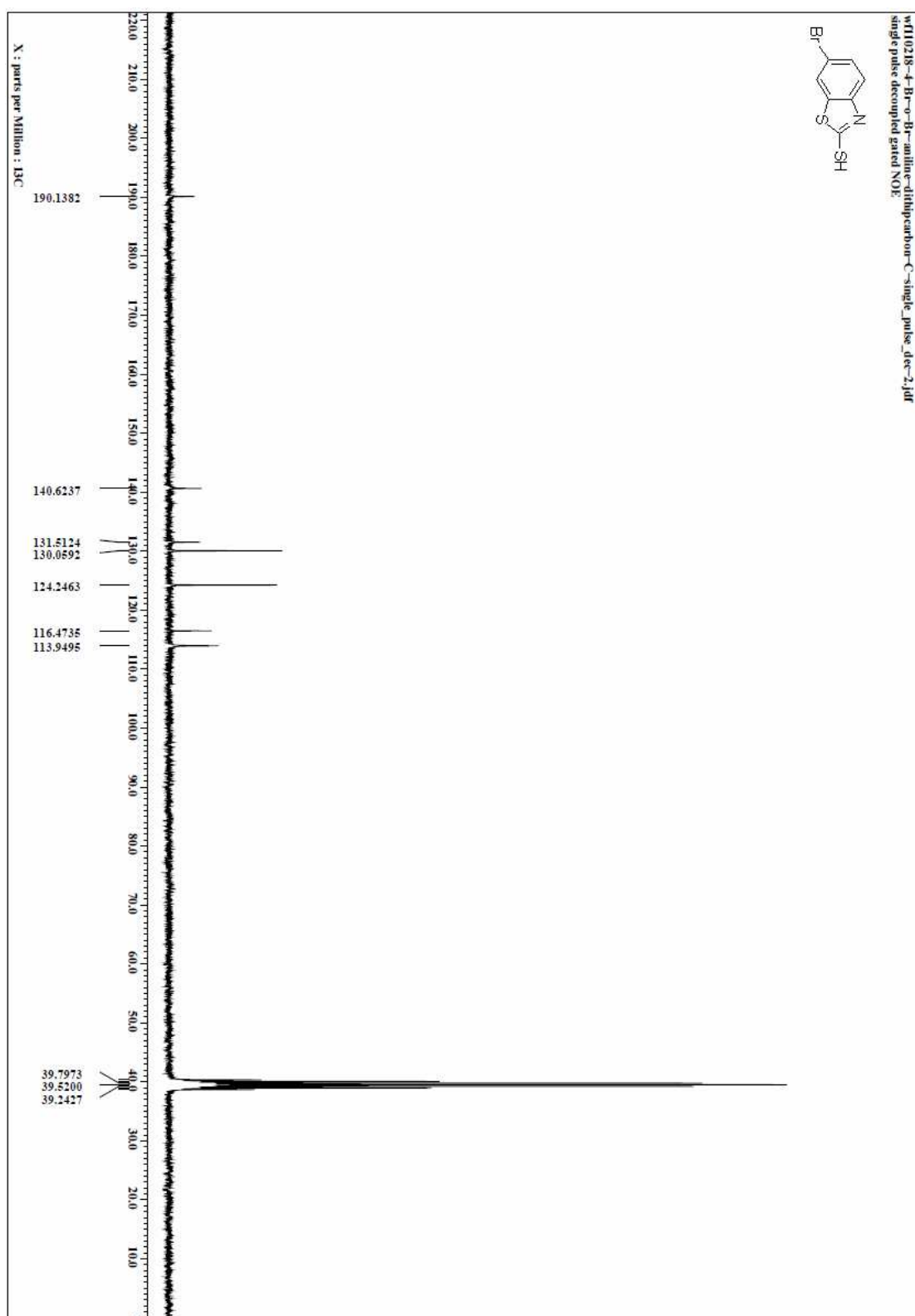
Compound 2c



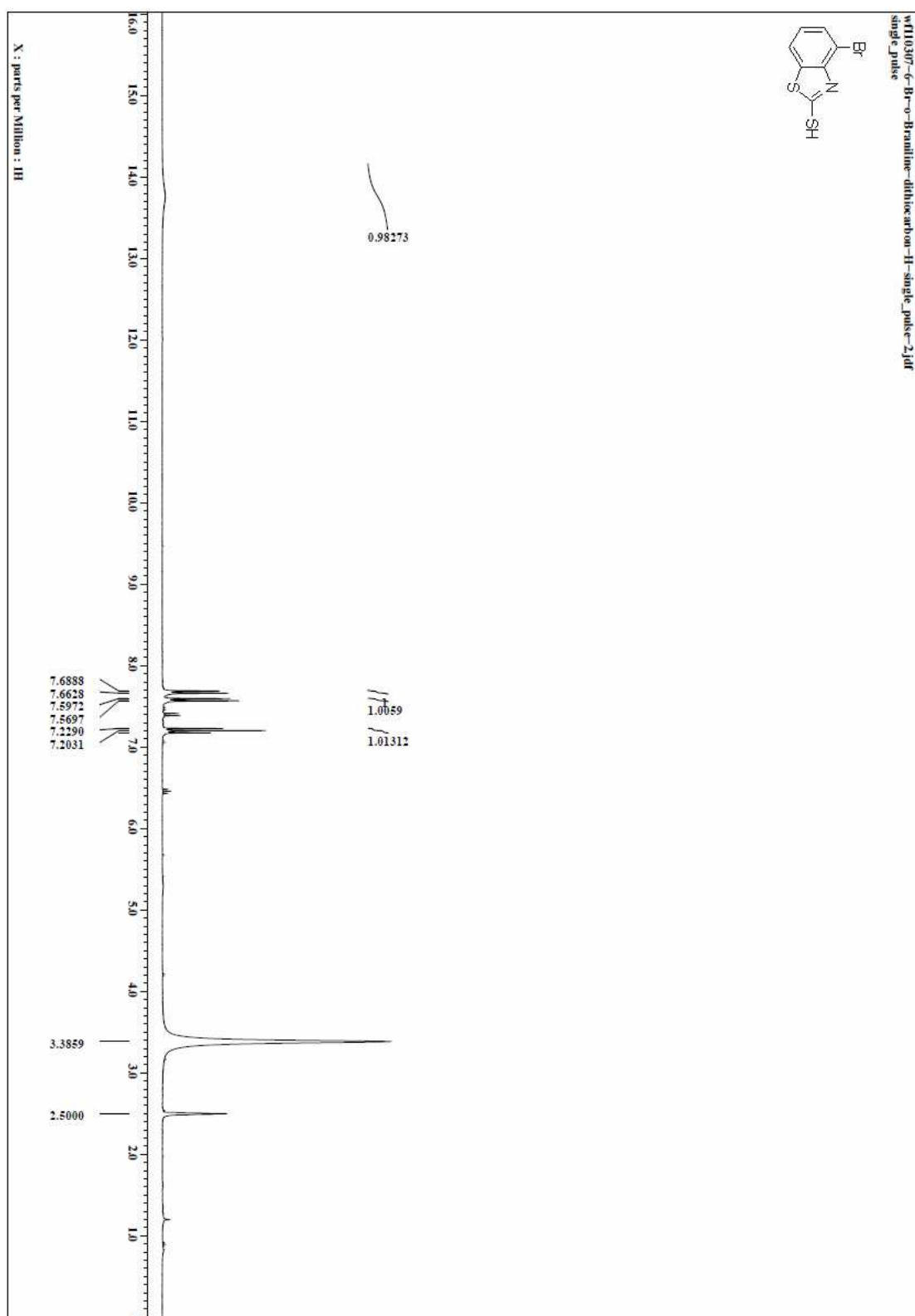
Compound 2d



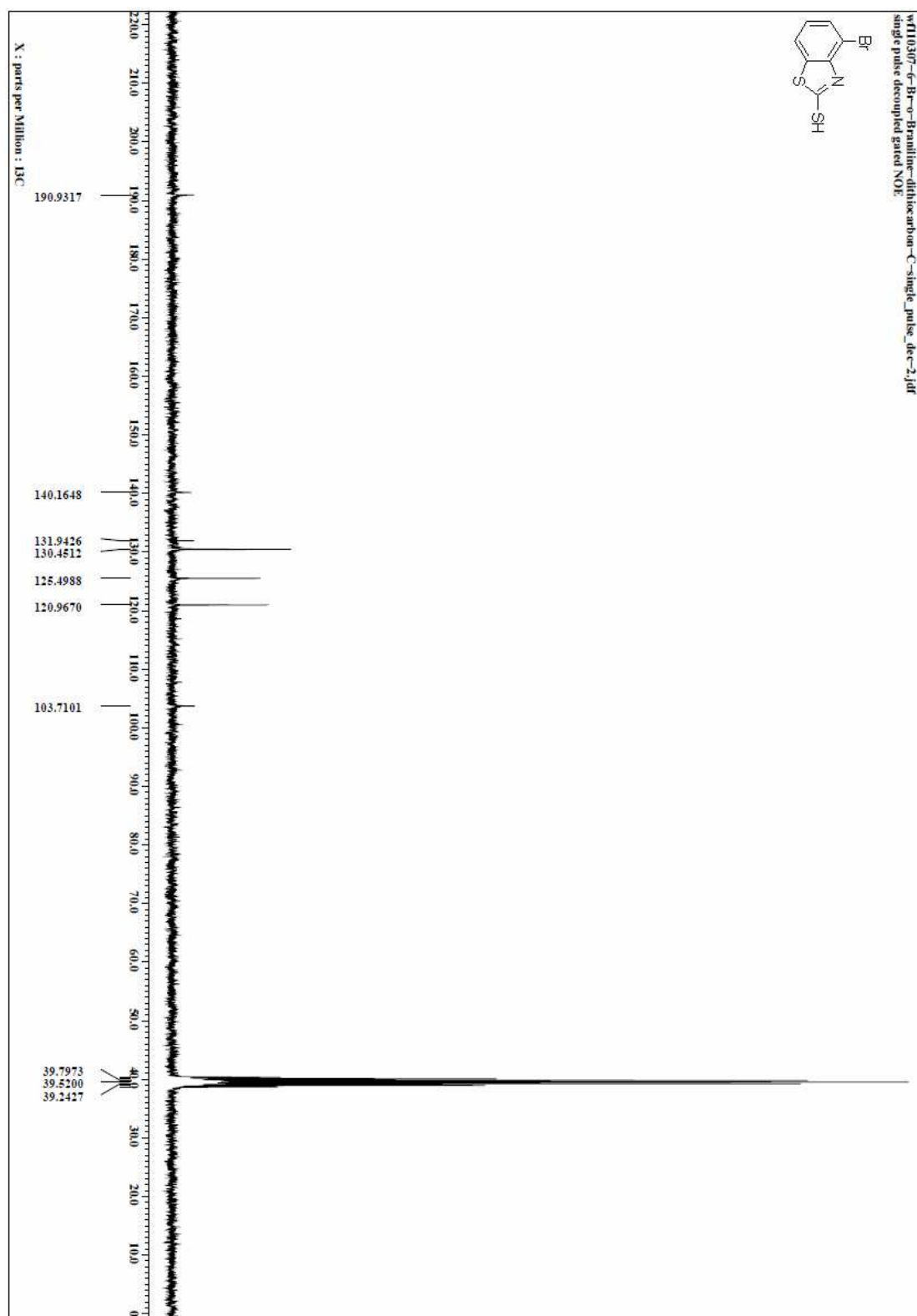
Compound 2d



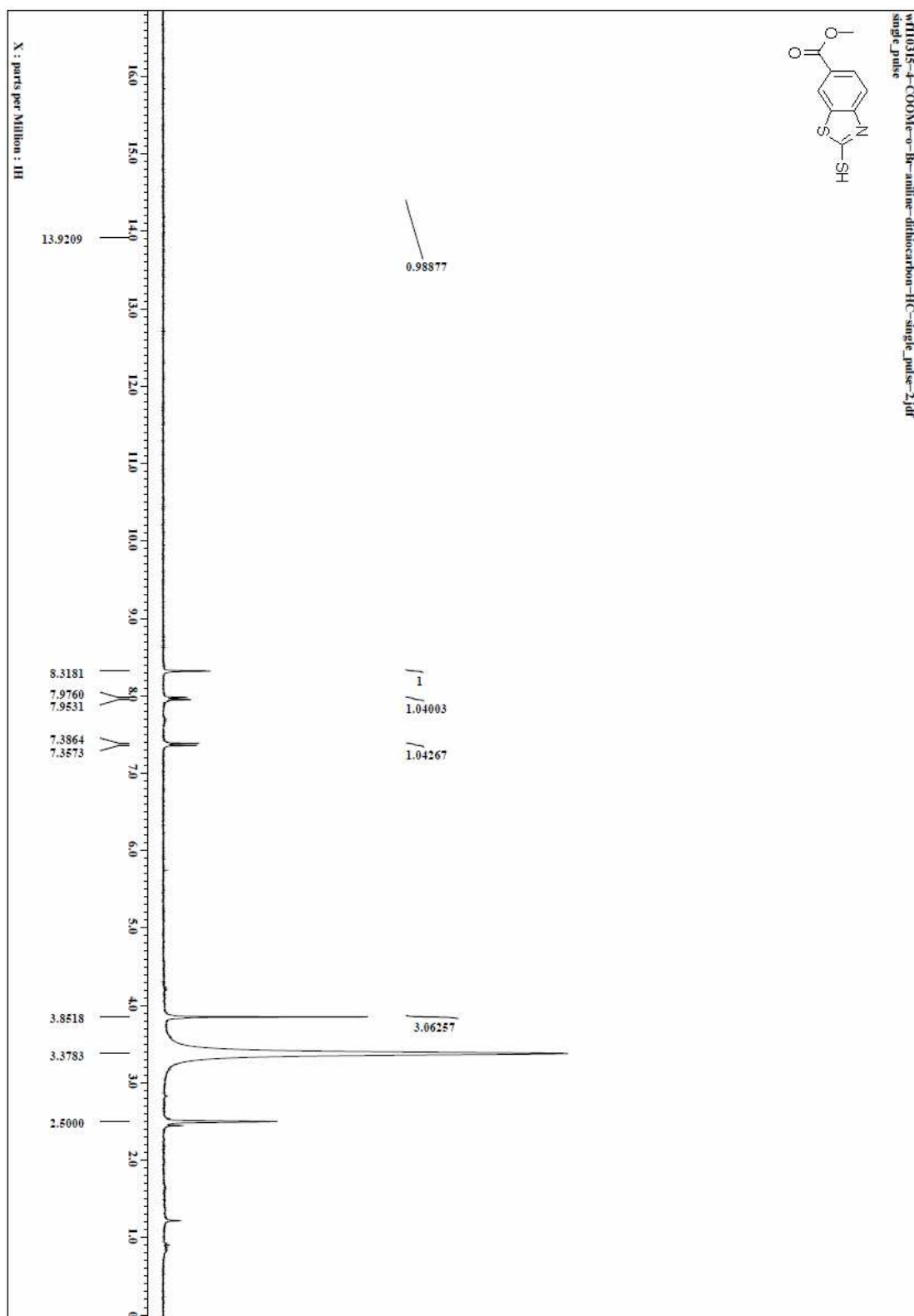
Compound 2e



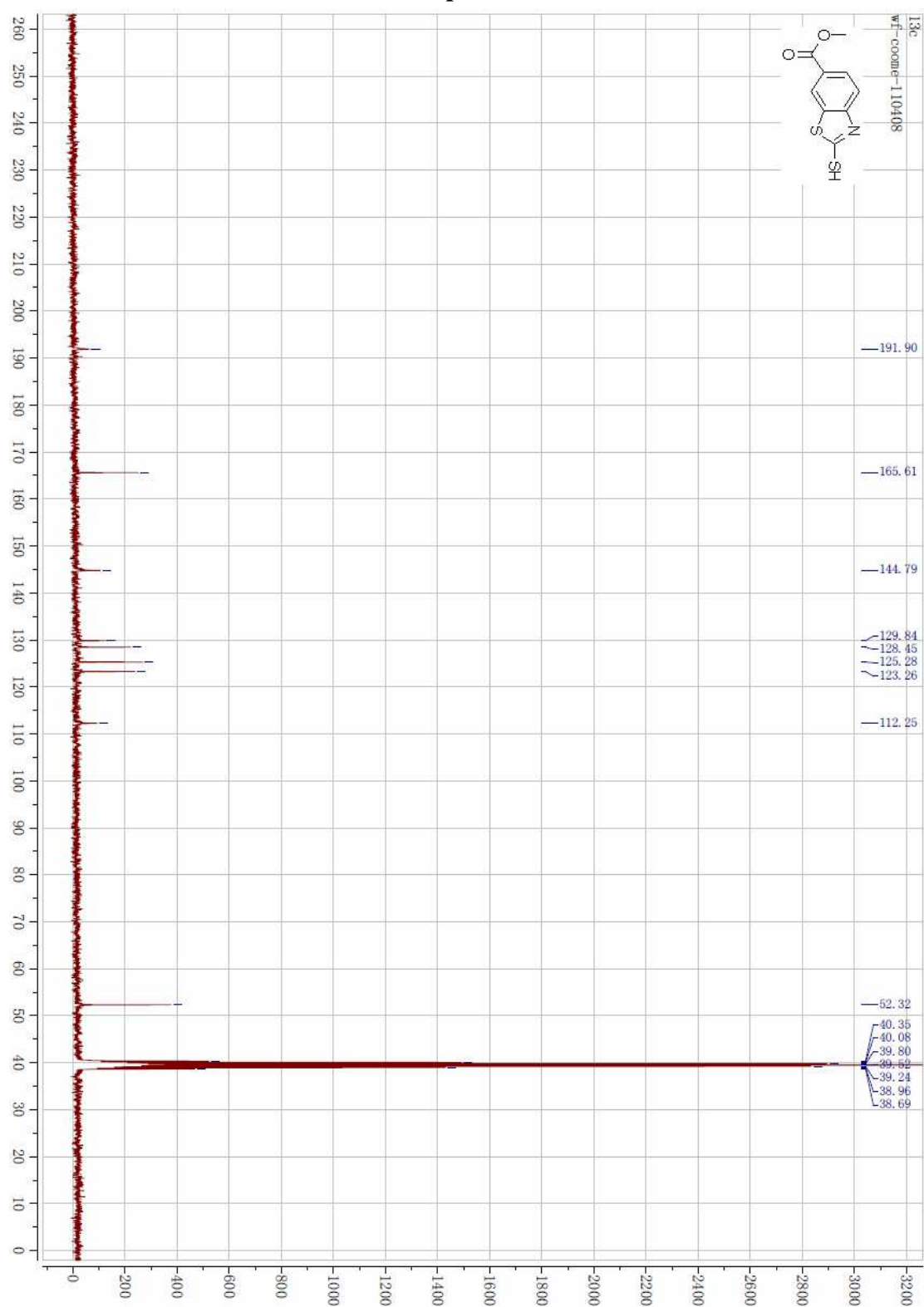
Compound 2e



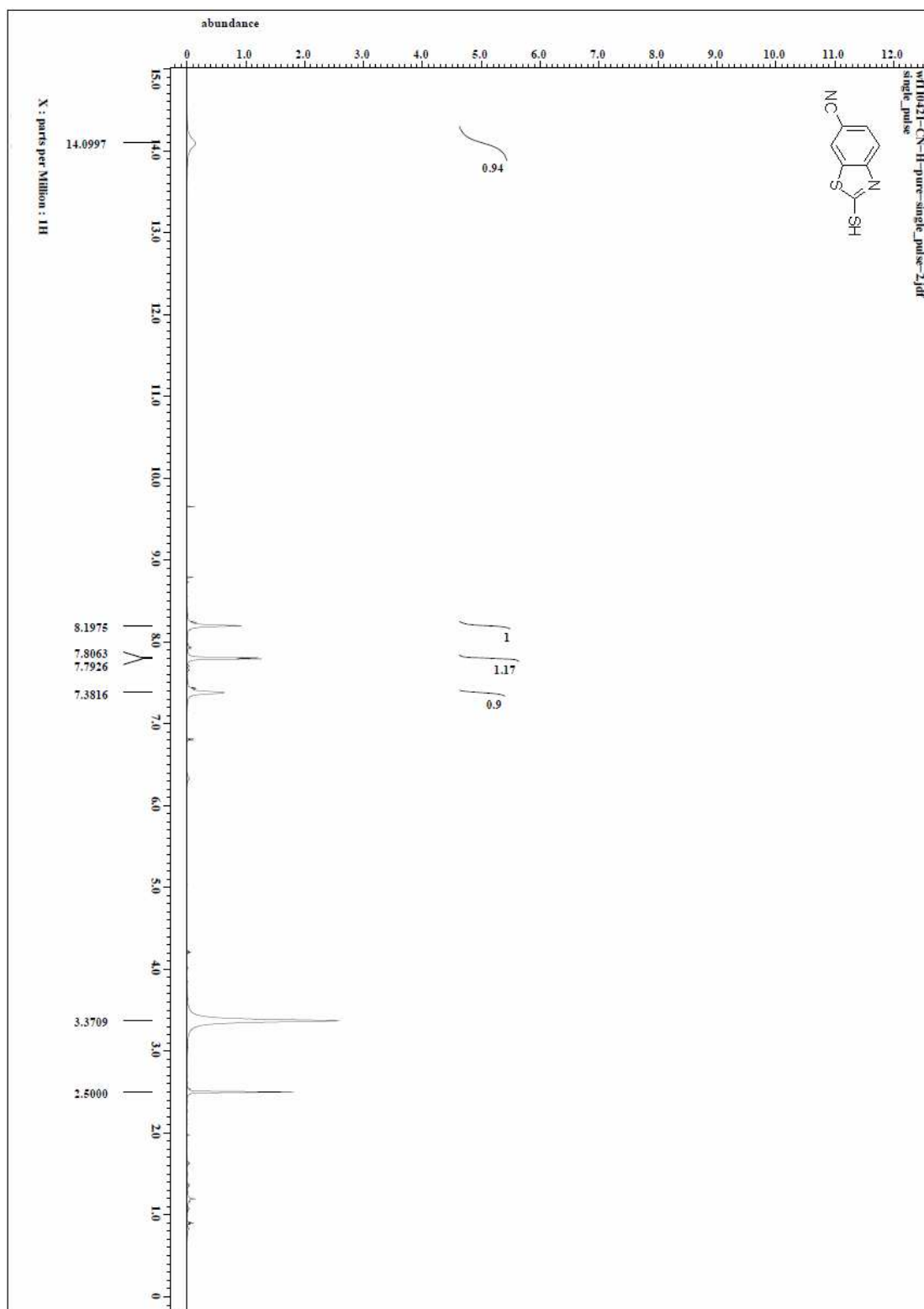
Compound 2f



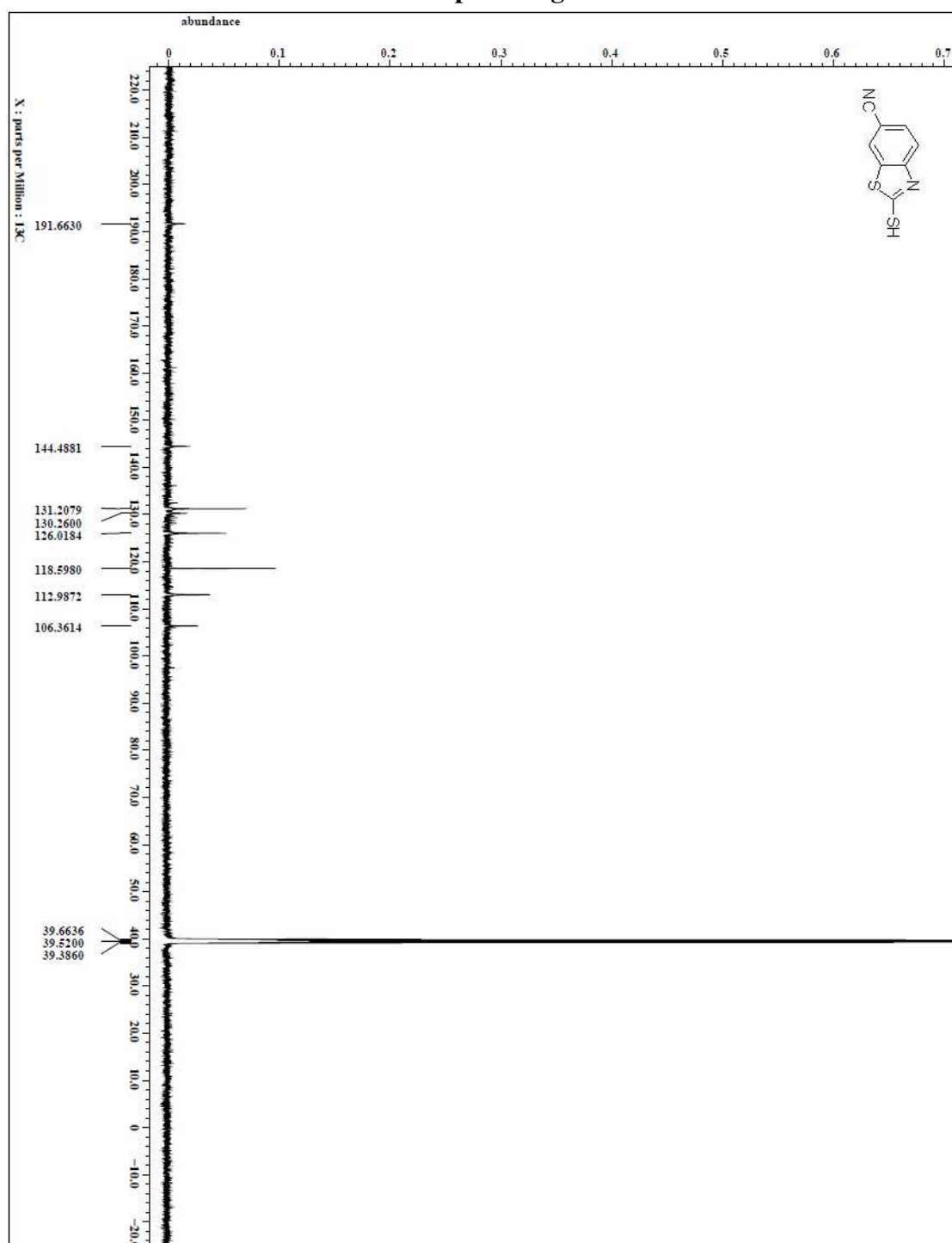
Compound 2f



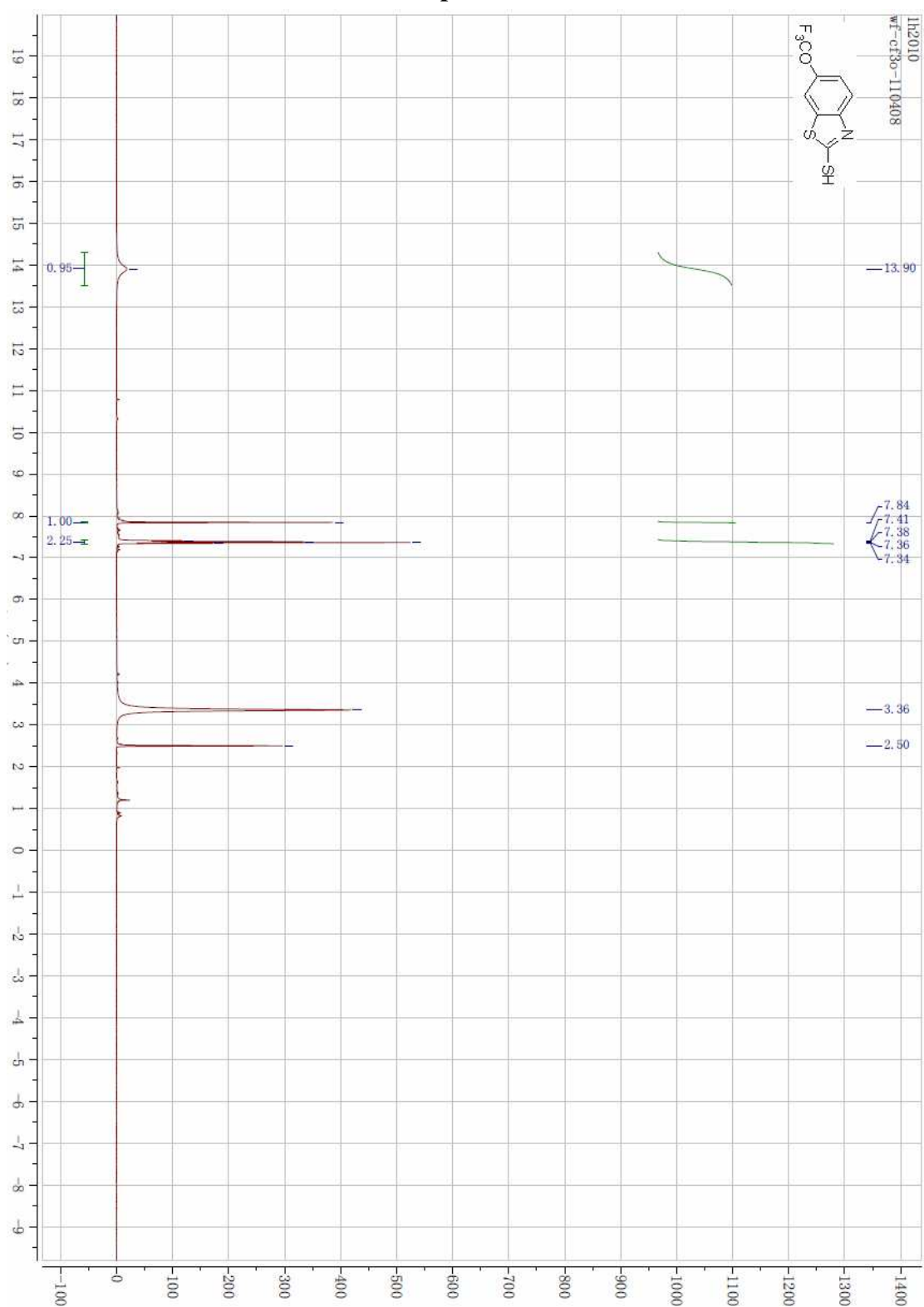
Compound 2g



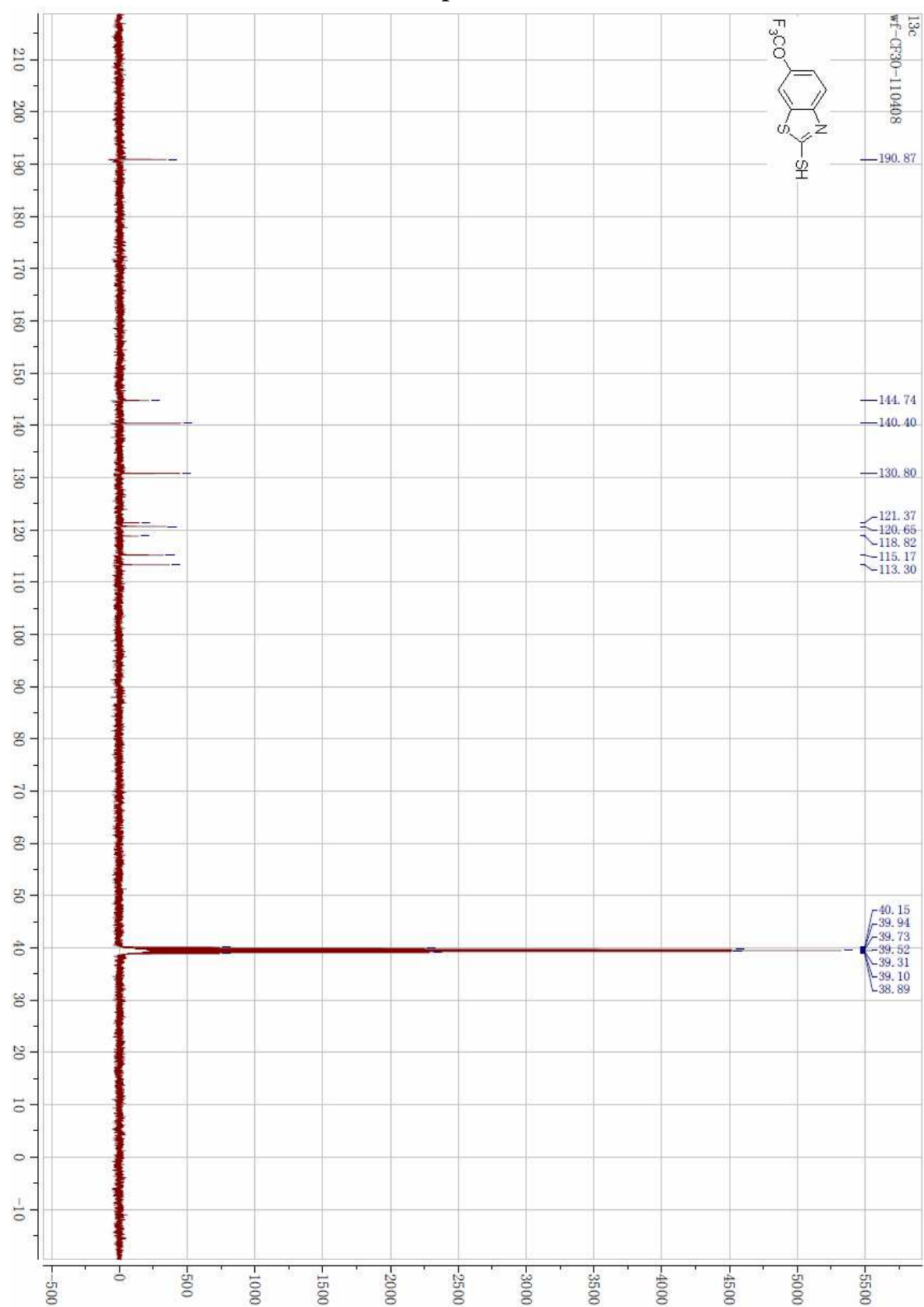
Compound 2g



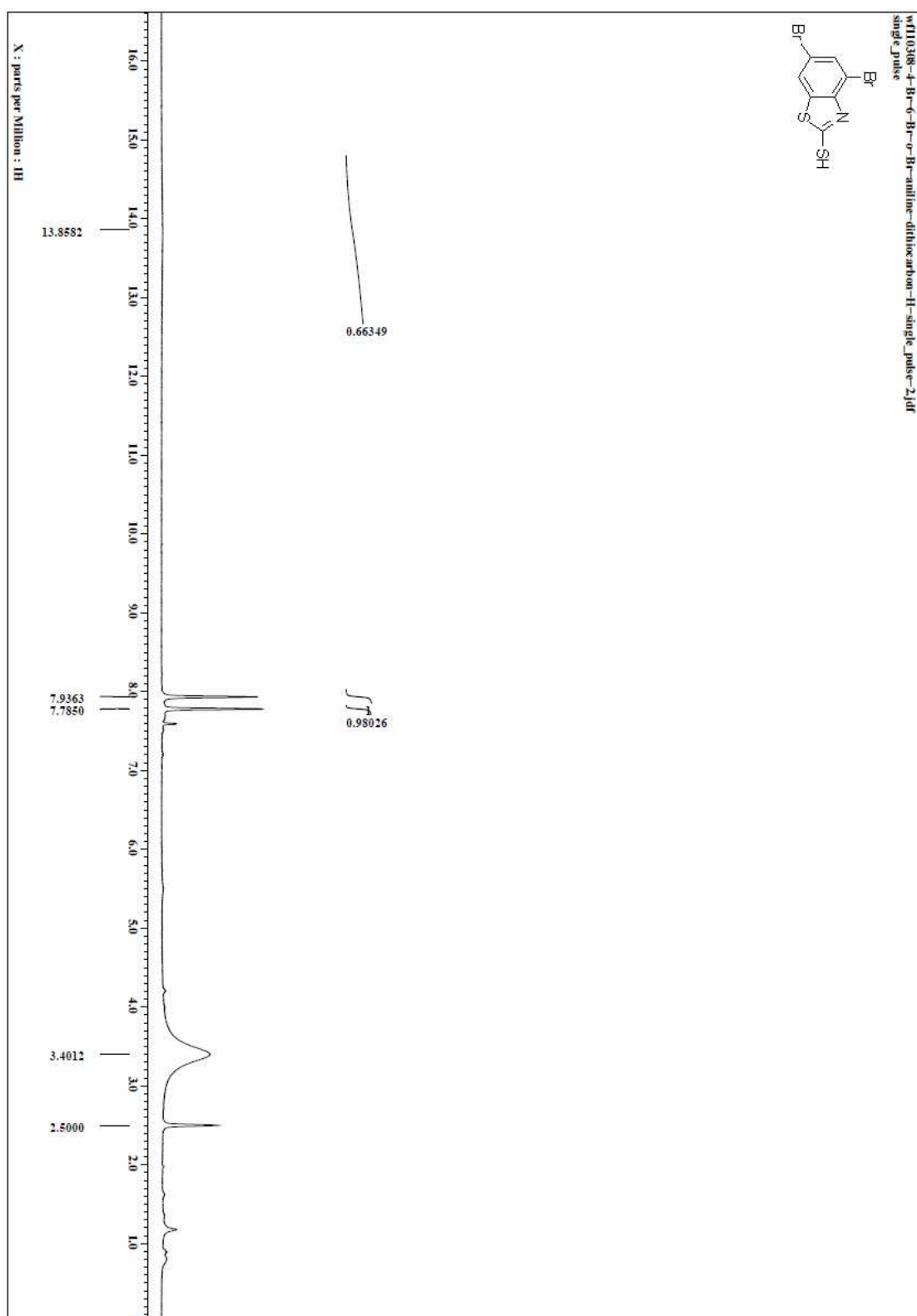
Compound 2h



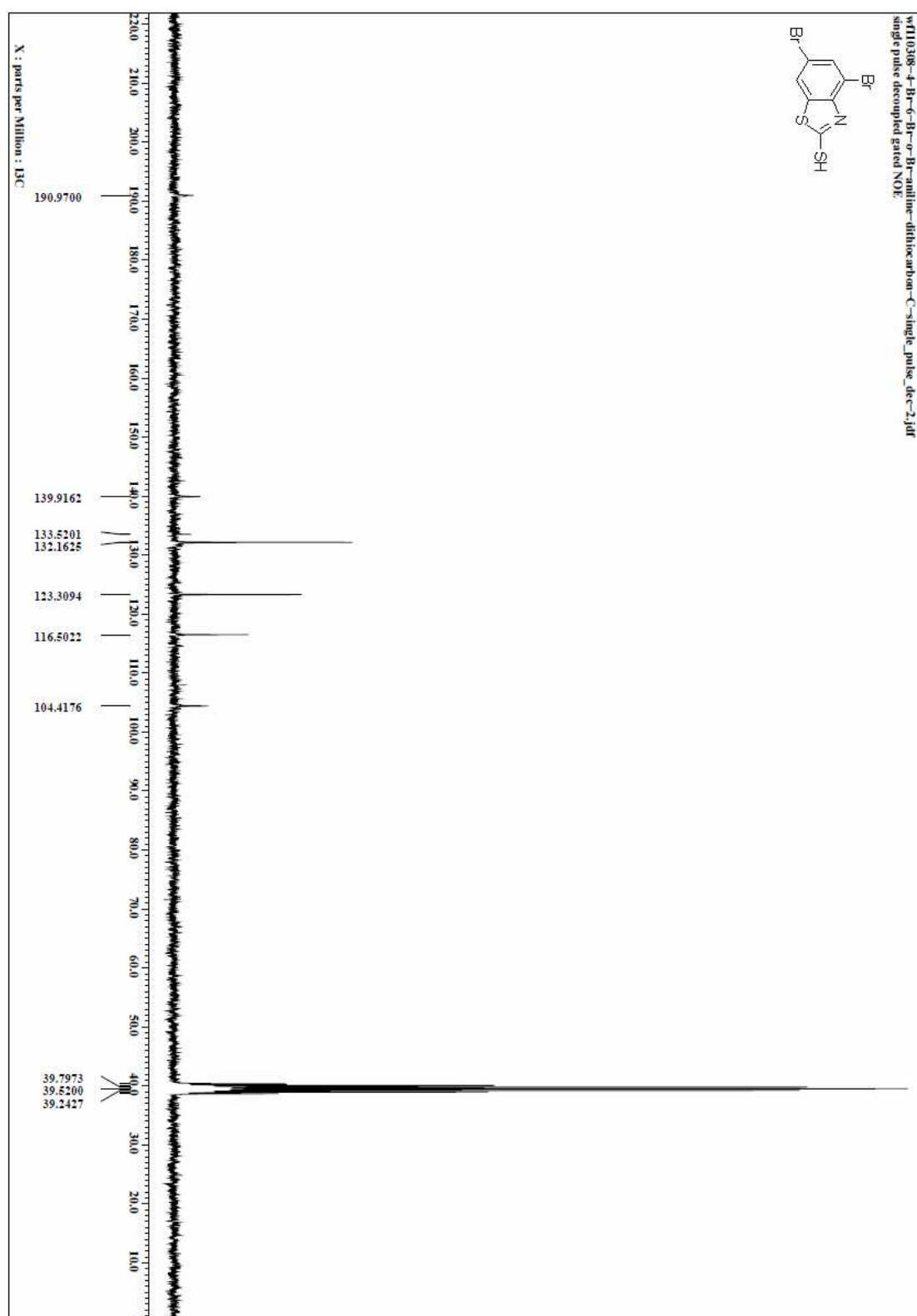
Compound 2h



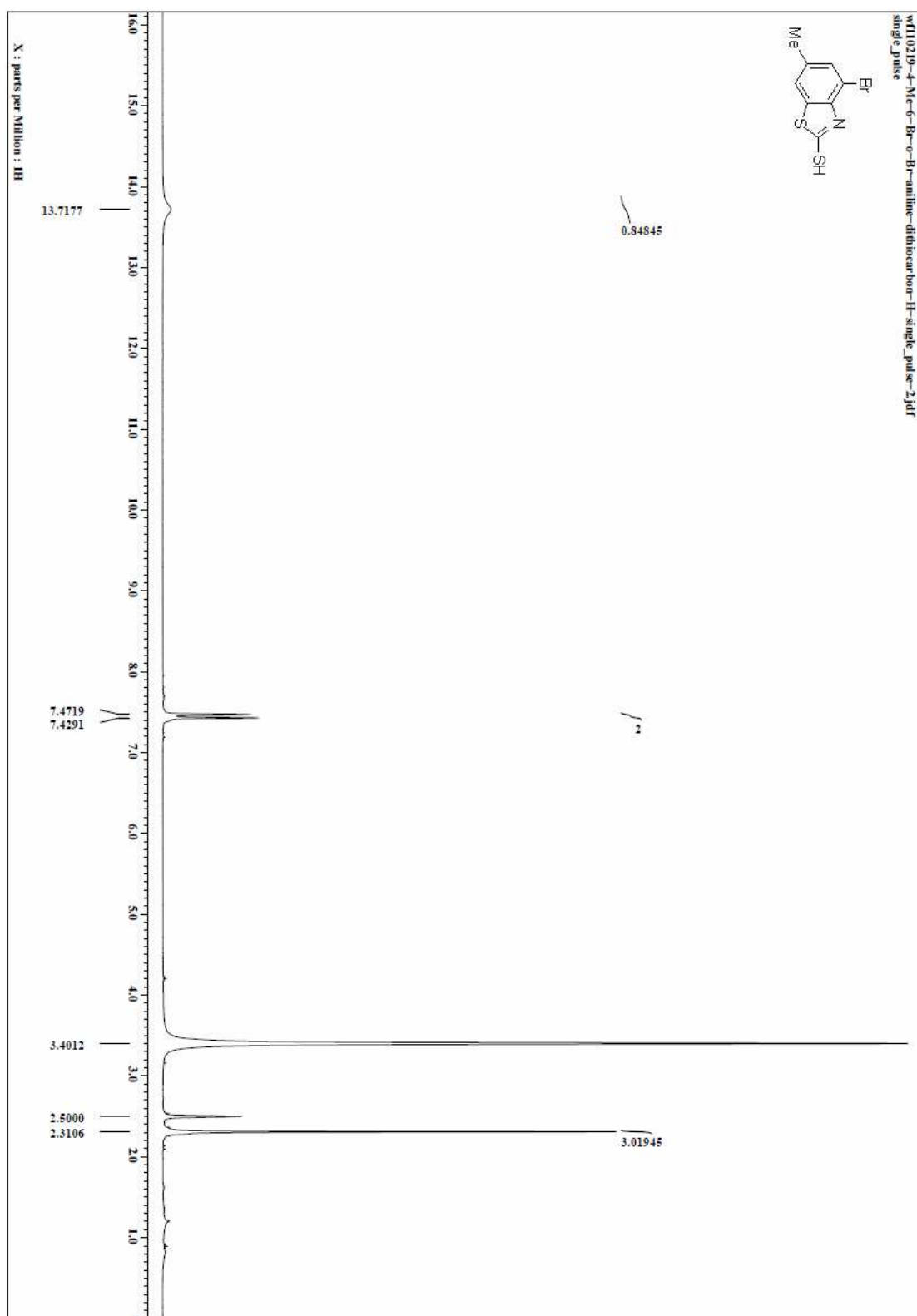
Compound 2i



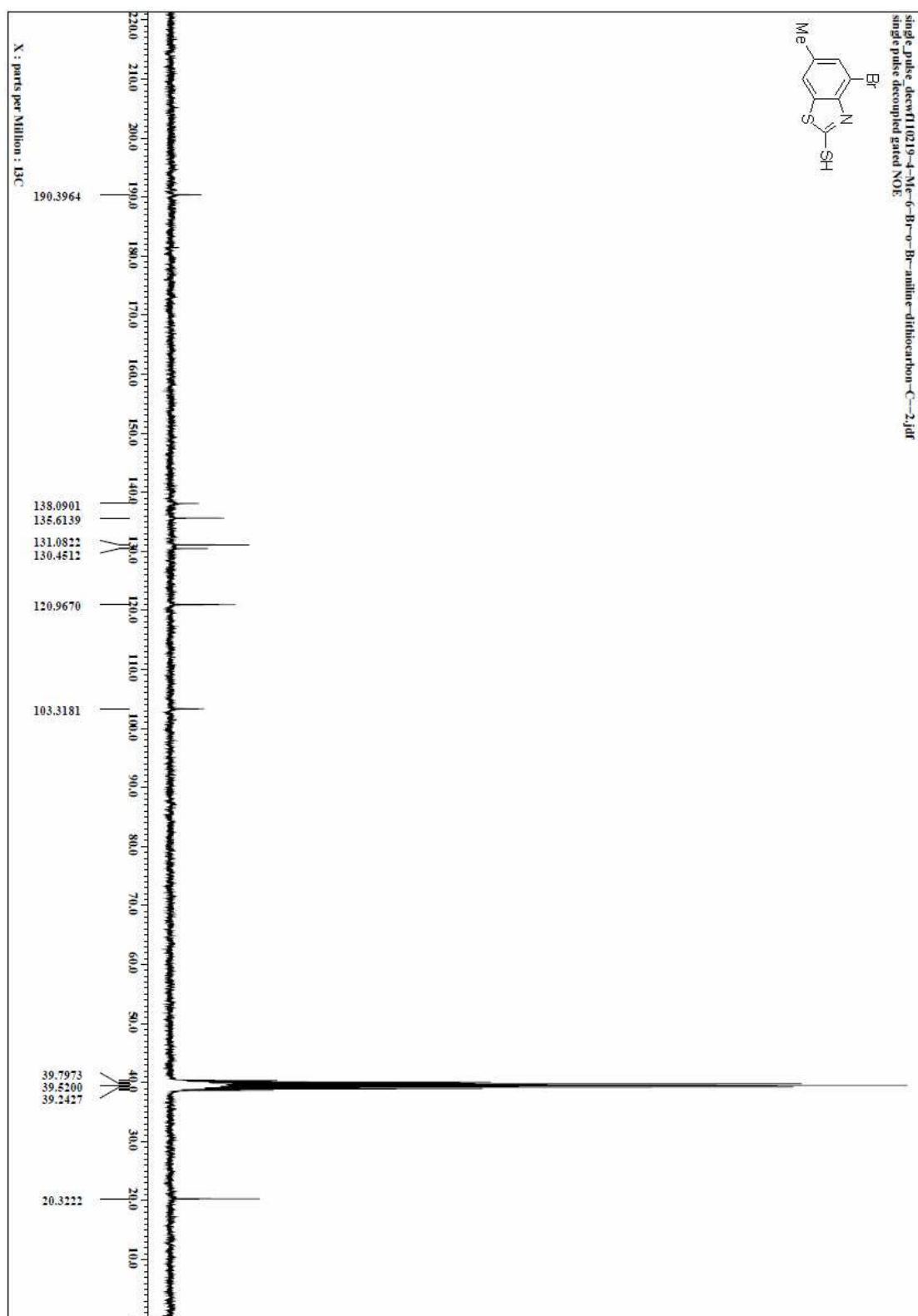
Compound 2i



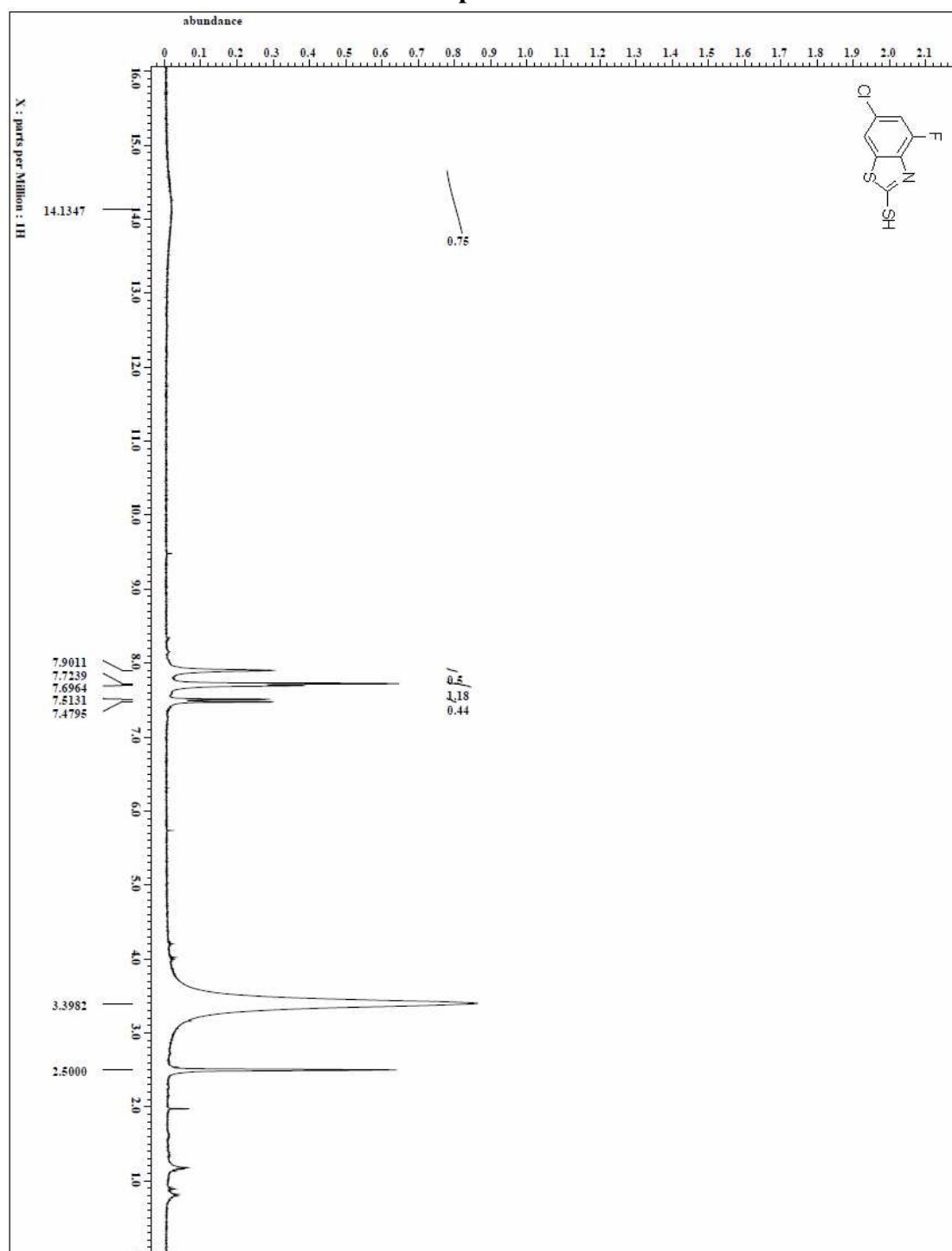
Compound 2j



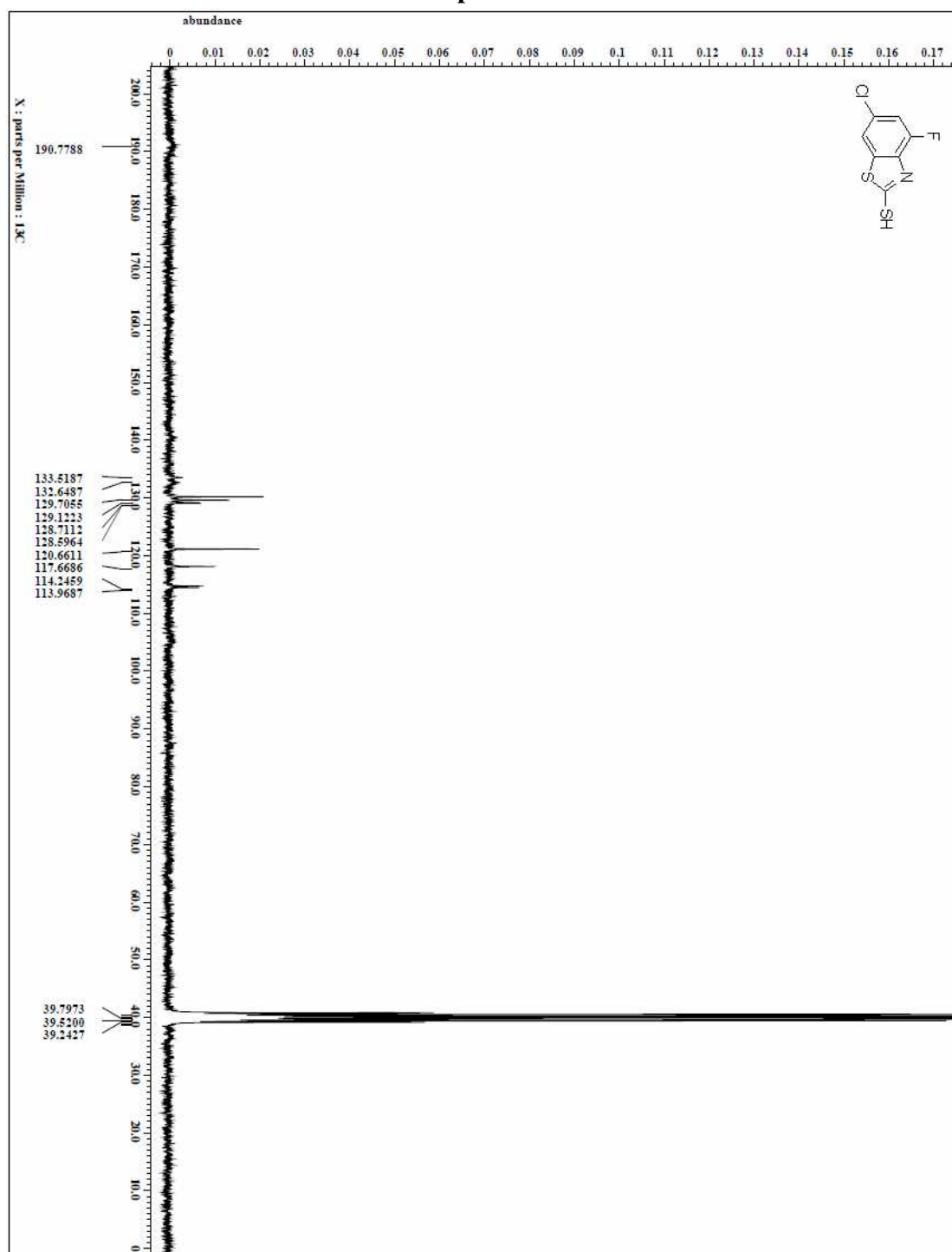
Compound 2j



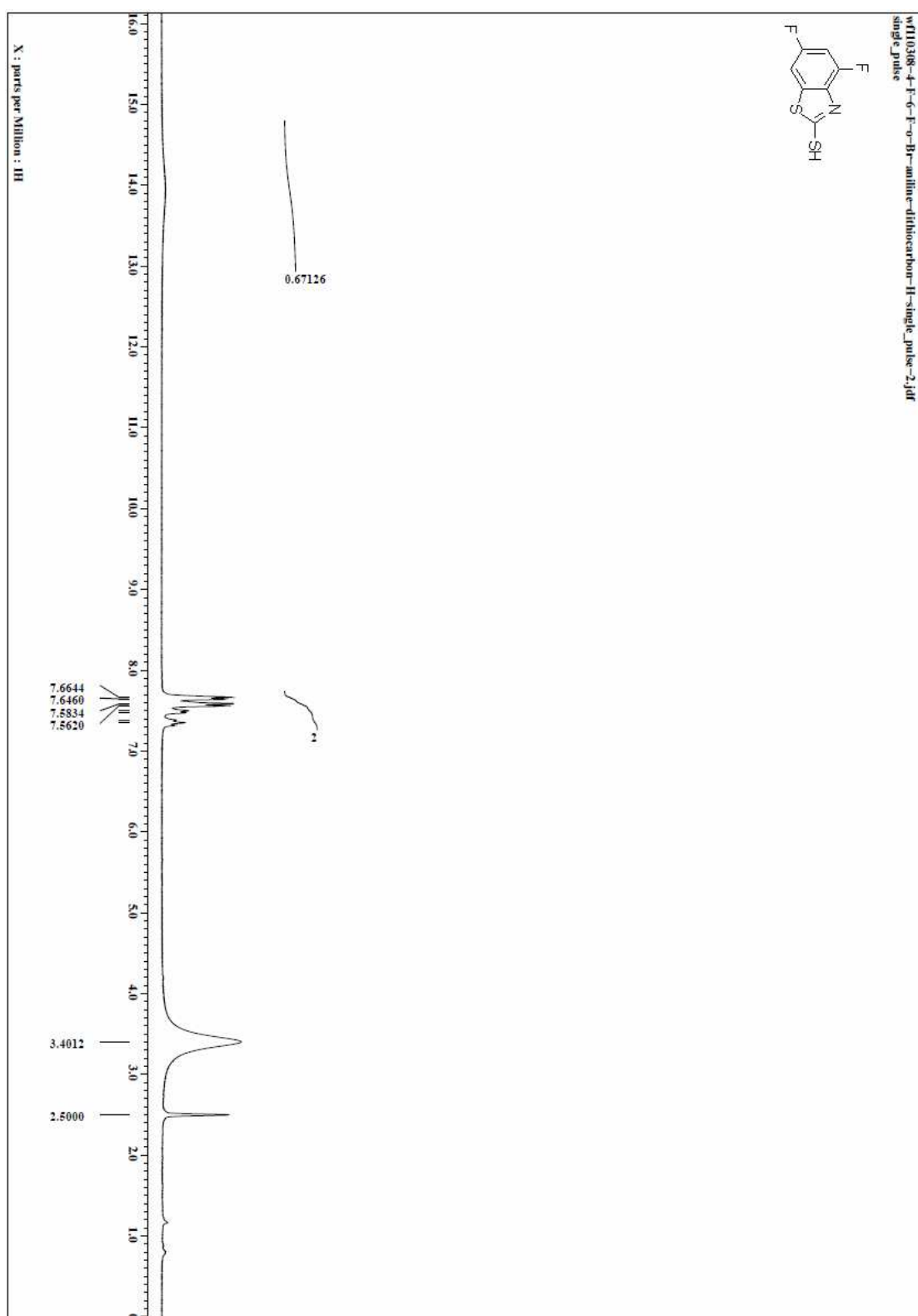
Compound 2k



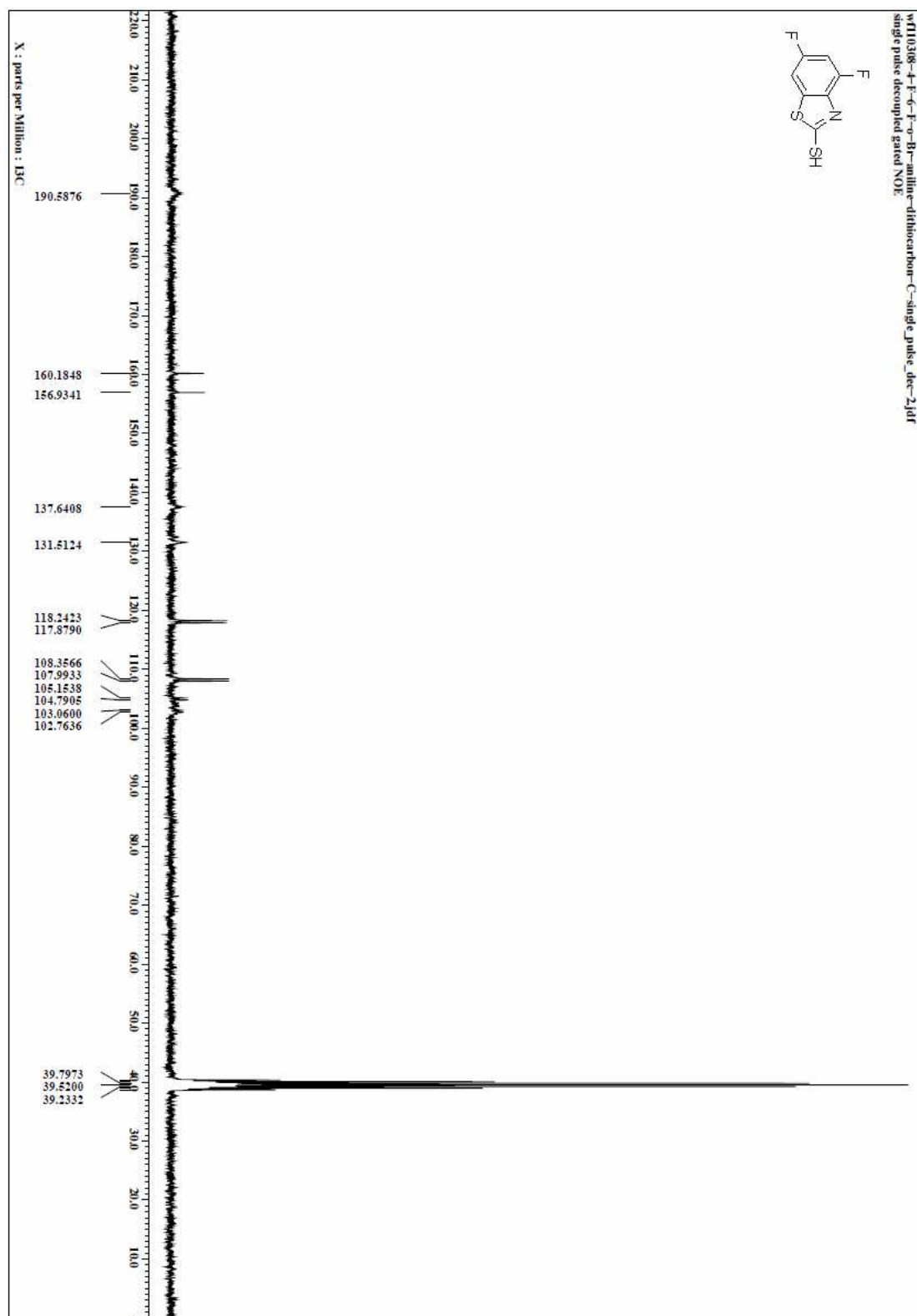
Compound 2k



Compound 2l



Compound 2l



3. References:

- (1) Zhu, L.; Zhang M.; Dai, M. *J. Heterocyclic Chem.* **2005**, 42, 727.
- (2) Zhu, L.; Zhang, M. *J. Org. Chem.* **2004**, 69, 7371.