

# Base-promoted Cyclization Reaction of *o*-Isothiocyanato Arylacetylenes and Aroylacetonitriles: Easy Access to Benzo[d][1,3]thiazines

*Jian Shen*<sup>a,b</sup>, *Shumin Li*<sup>a,b</sup>, *Zhenyu Yao*<sup>a,b</sup>, *Shenghui Lin*<sup>\*b</sup>, and *Xiuling Cui*<sup>\*a,b</sup>

<sup>a</sup> Engineering Research Centre of Molecular Medicine of Ministry of Education, Key Laboratory of Fujian Molecular Medicine, Key Laboratory of Precision Medicine and Molecular Diagnosis of Fujian Universities, Key Laboratory of Xiamen Marine and Gene Drugs, School of Biomedical Sciences, Huaqiao University, Xiamen 361021, P. R. China.

<sup>b</sup> School of Biomedical Sciences, Huaqiao University, Quanzhou 362021, P. R. China.

Corresponding Author: Xiuling Cui and Shenghui Lin

Email: [cuixl@hqu.edu.cn](mailto:cuixl@hqu.edu.cn); [lsh@hqu.edu.cn](mailto:lsh@hqu.edu.cn)

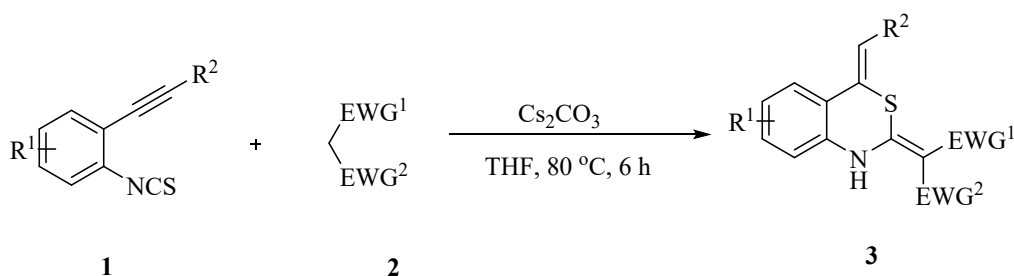
Tel & Fax: +86-592-6162996

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## General information

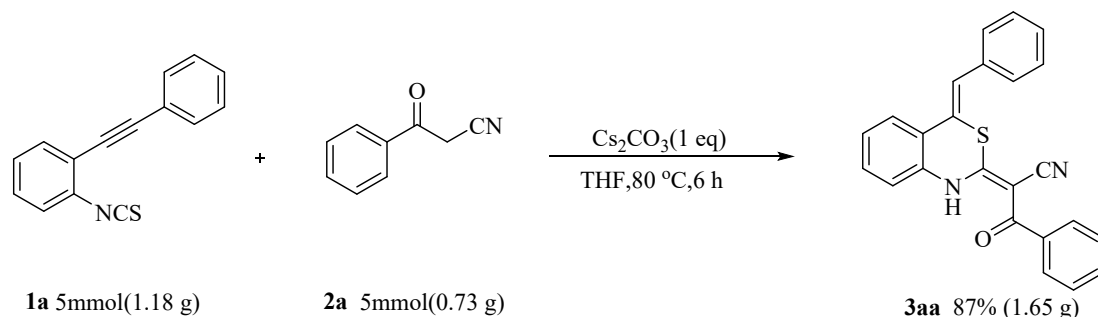
All manipulations were conducted under air atmosphere. Unless otherwise stated, all commercial materials and solvents were used directly without further purification. Commercially available chemicals were obtained from Energy Chemical, Admas, J&K.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured on a 400 MHz Bruker spectrometer ( $^1\text{H}$  400MHz,  $^{13}\text{C}$  100MHz,  $^{19}\text{F}$  NMR 376 MHz), using  $\text{CDCl}_3$  as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are reported in ppm using tetramethylsilane with the solvent resonance as the internal standard ( $\text{CDCl}_3$ :  $^1\text{H}$  d 7.26,  $^{13}\text{C}$  d 77.0). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. Column chromatography was performed on silica gel (70-230 mesh ASTM) using the reported eluent. Thin-layer chromatography (TLC) was carried out on  $4\times 5$  cm plates with a layer thickness of 0.2 mm (silica gel 60 F254). Starting materials **1**<sup>[1, 2]</sup> and **2**<sup>[3]</sup> were prepared according to the literatures.

## General procedure for the synthesis of **3**



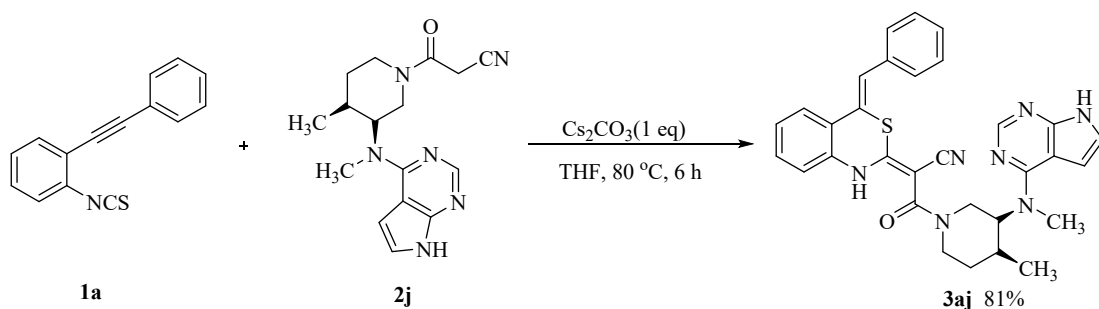
To a tube *o*-alkynylphenyl isothiocyanate **1** (0.2 mmol),  $\text{Cs}_2\text{CO}_3$  (1.0 equiv), aroylacetonitrile **2** (0.2 mmol), were added sequentially and dissolved in THF (2.0 mL) under air atmosphere. The mixture was heated at 80 °C in an oil bath and stirred for 6 h. After cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using ethyl acetate (EA)/petroleum ether (PE) (1: 25~2: 1) as eluent to afford the desired product **3**.

## Procedure for the synthesis of **3aa** on large scale



To a tube *o*-alkynylphenyl isothiocyanate **1a** (5.0 mmol),  $\text{Cs}_2\text{CO}_3$ (1.0 equiv), Aroylacetonitrile **2** (5.0 mmol), were added sequentially and dissolved in toluene (4.0 mL) under air atmosphere. The mixture was heated at 80 °C in an oil bath and stirred for 6 h. After cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using ethyl acetate (EA)/petroleum ether (PE) (1: 25~2: 1) as eluent to afford the desired product **3aa** (87%, 1.65 g).

## Procedure for post-modification of clinic drug



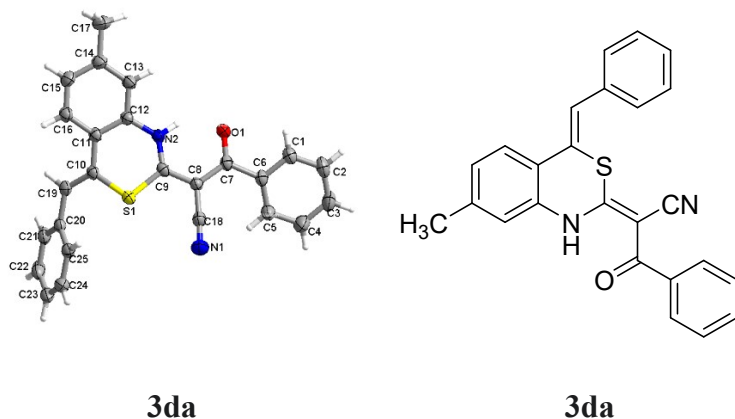
To a tube o-alkynylphenyl isothiocyanate **1a** (0.2 mmol),  $\text{Cs}_2\text{CO}_3$  (1.0 equiv), tofacitinib **2** (0.2 mmol), were added sequentially and dissolved in THF (2.0 mL) under air atmosphere. The mixture was heated at 80 °C in an oil bath and stirred for 6 h. After cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using ethyl acetate (EA)/petroleum ether (PE) (1: 5~2: 1) as eluent to afford the desired product **3aj**.

## References

- (1) Hao, W. Y.; Zeng, J. B.; Cai, M. Z., The copper(I)-catalyzed tandem reaction of o-alkynylphenyl isothiocyanates with isocyanides: a rapid synthesis of 5*H*-benzo d imidazo 5,1-*b* 1,3 thiazines. *Chem. Commun.* **2014**, 79, 11686-11689.
- (2) Xie, J. L.; Guo, Z. L.; Huang, Y. Q.; Qu, Y.; Song, H. J.; Song, H. B.; Liu, Y. X.; Wang, Q. M., One-pot copper-catalyzed cascade bicyclization strategy for synthesis of 2-(1*H*-indol-1-yl)-4,5-dihydrothiazoles and 2-(1*H*-indol-1-yl)thiazol-5-yl aryl ketones with molecular oxygen as an oxygen source. *Adv. Synth. Catal.* **2019**, 3, 490-495.
- (3) Yu, W. Q.; Du, Y. F.; Zhao, K., PIDA-mediated oxidative C-C bond formation: novel synthesis of indoles from *N*-aryl enamines. *Org. Lett.* **2009**, 11, 2417-2420

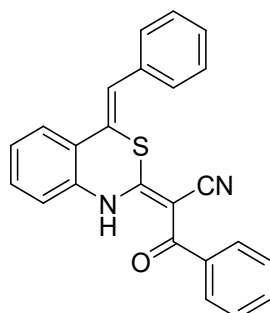
## X-ray structure of compound 3da

The single crystal of compound **3da** was prepared by the slow evaporation method for which 30 mg of the compound (**3da**) was dissolved in 1 mL of DCM in a clean and dry 10 mL glass vial. Then, pentane (2 mL) was added to this solution slowly with a dropper. The mixture was kept for slow evaporation at room temperature. The structures of **3da** was determined by the X-ray diffraction. Recrystallized from dichloromethane/pentane. Further information can be found in the CIF file. The crystal was deposited in the Cambridge Crystallographic Data Centre and assigned as CCDC 2144111. ORTEP view of complex Ellipsoids are represented at the 50% probability level.



## Characterization of products

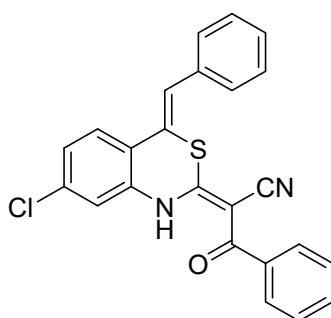
### (E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3aa)



light yellow solid, 72.3 mg, yield: 95%, m.p.: 248-250 °C, column chromatography eluent, EtOAc/PE=1:25→1:2;

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.83 (s, 1H), 7.85 (d,  $J = 7.6$  Hz, 2H), 7.61 (d,  $J = 7.9$  Hz, 1H), 7.57 – 7.36 (m, 10H), 7.32 (t,  $J = 7.6$  Hz, 1H), 7.11 (d,  $J = 7.9$  Hz, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.4, 166.4, 138.3, 134.3, 133.6, 131.8, 130.5, 130.4, 129.4, 128.8, 128.8, 128.3, 128.0, 127.1, 125.4, 122.3, 120.2, 119.8, 118.3, 81.1. **HRMS** (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{17}\text{N}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 381.1056, found: 381.1057.

### (E)-2-(4-((Z)-Benzylidene)-7-chloro-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ba)

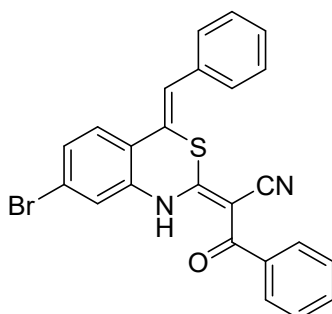


light yellow solid, 80.5 mg, yield: 97%, m.p.: 287-290 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.87 (s, 1H), 7.85 (d,  $J = 7.6$  Hz, 2H), 7.54 (t,  $J = 10.1$  Hz, 2H), 7.48 (d,  $J = 5.3$  Hz, 6H), 7.40 (d,  $J = 4.7$  Hz, 1H), 7.30 – 7.22 (m, 2H), 7.13 (s, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 166.7, 138.0, 136.2, 134.6, 134.0, 132.1, 130.9, 129.4, 129.0, 128.8, 128.3, 128.1, 127.1,

126.7, 120.8, 119.6, 119.3, 118.0, 81.6. **HRMS** (ESI, m/z) calcd for  $C_{24}H_{16}ClN_2OS^+$   $[M+H]^+$ : 415.0666, found: 415.0665

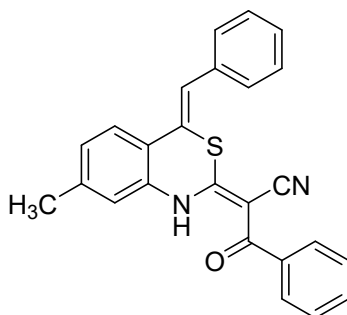
**(E)-2-(4-((Z)-Benzylidene)-7-bromo-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ca)**



light yellow solid, 88.2 mg, yield: 96%, m.p.: 248-251 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  14.87 (s, 1H), 7.85 (d,  $J = 7.4$  Hz, 2H), 7.58 – 7.51 (m, 1H), 7.51 – 7.37 (m, 9H), 7.29 (s, 1H), 7.25 (s, 1H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  191.5, 166.7, 138.1, 134.8, 134.0, 132.0, 130.9, 123.0, 129.4, 129.0, 128.9, 128.3, 128.1, 126.7, 124.0, 122.5, 121.3, 119.4, 118.0, 81.7. **HRMS** (ESI, m/z) calcd for  $C_{24}H_{15}BrN_2NaOS^+$   $[M+Na]^+$ : 480.9981, found: 480.9980

**(E)-2-(4-((Z)-Benzylidene)-7-methyl-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3da)**

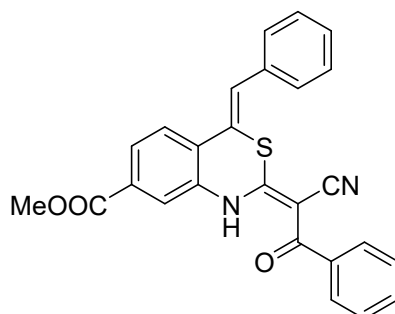


light yellow solid, 75.8 mg, yield: 96 %, m.p.: 193-194 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  14.77 (s, 1H), 7.89 – 7.81 (m, 2H), 7.55 – 7.44 (m, 8H), 7.42 – 7.34 (m, 1H), 7.23 (s, 1H), 7.11 (d,  $J = 8.1$  Hz, 1H), 6.90 (s, 1H), 2.38 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  191.3, 166.2, 141.2, 138.4, 134.4, 133.3, 131.8, 129.3, 129.0, 128.8, 128.6, 128.3, 128.2, 128.0, 125.1,

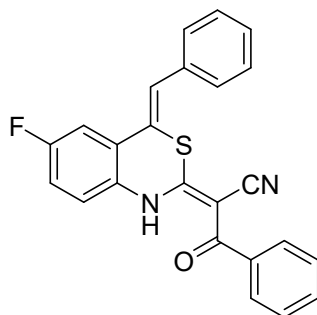
120.4, 120.2, 119.4, 118.4, 80.9, 21.1. **HRMS** (ESI, m/z) calcd for  $C_{25}H_{19}N_2OS^+$   $[M+H]^+$ : 395.1213, found: 395.1214

**Methyl (E)-4-((Z)-benzylidene)-2-(1-cyano-2-oxo-2-phenylethylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazine-7-carboxylate (3ea)**



light yellow solid, 84.2 mg, yield: 96 %, m.p.: 272-274 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  14.98 (s, 1H), 7.96 (d,  $J = 8.3$  Hz, 1H), 7.90 – 7.80 (m, 3H), 7.68 (d,  $J = 8.3$  Hz, 1H), 7.51 (q,  $J = 8.3, 7.7$  Hz, 7H), 7.42 (t,  $J = 5.5$  Hz, 1H), 7.36 (s, 1H), 3.98 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  191.5, 166.5, 165.4, 138.1, 133.9, 133.8, 132.4, 132.0, 132.0, 129.5, 129.3, 128.9, 128.3, 128.1, 127.6, 126.2, 125.6, 120.9, 119.5, 118.1, 81.5, 52.7. **HRMS** (ESI, m/z) calcd for  $C_{26}H_{19}N_2O_3S^+$   $[M+H]^+$ : 439.1111, found: 439.1111  
**(E)-2-(4-((Z)-Benzylidene)-6-fluoro-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3fa)**

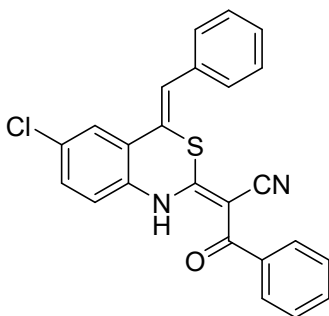


light yellow solid, 77.3 mg, yield: 97 %, m.p.: 290-293 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  14.98 (s, 1H), 7.84 (d,  $J = 7.6$  Hz, 2H), 7.57 – 7.38 (m,  $J = 6.8, 6.0$  Hz, 8H), 7.32 (d,  $J = 9.0$  Hz, 1H), 7.25 (s, 1H), 7.13 (p,  $J = 8.2$  Hz, 2H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  191.5, 165.9, 161.0(d,  $J_{C-F} = 247.9$  Hz), 138.2, 133.9, 131.9, 131.3, 130.0(d,  $J_{C-F} = 2.6$  Hz), 129.4, 129.1,

128.9, 128.3, 128.0, 124.0(d, $J_{C-F}$ =7.9 Hz), 121.4(d, $J_{C-F}$ =8.5 Hz), 119.4(d, $J_{C-F}$ =2.3 Hz), 118.2, 117.8, 117.5, 112.0(d, $J_{C-F}$ =24.7 Hz), 81.1.  **$^{19}\text{F}$  NMR** (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.5. **HRMS** (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{15}\text{FN}_2\text{NaOS}^+$   $[\text{M}+\text{Na}]^+$ : 421.0781, found: 421.0780

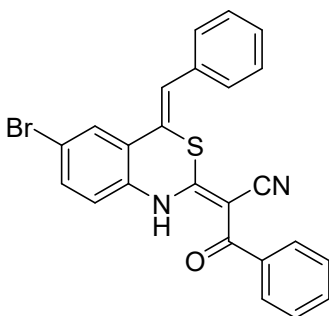
**(E)-2-(4-((Z)-Benzylidene)-6-chloro-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ga)**



light yellow solid, 79.7 mg, yield: 96 %, m.p.: 298-300 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.93 (s, 1H), 7.84 (d,  $J$  = 7.6 Hz, 2H), 7.59 (s, 1H), 7.57 – 7.36 (m, 9H), 7.27 (s, 1H), 7.07 (d,  $J$  = 8.6 Hz, 1H).  **$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 166.2, 138.1, 133.9, 132.4, 132.3, 132.0, 131.6, 130.4, 129.5, 129.2, 128.9, 128.3, 128.1, 125.3, 123.7, 120.9, 119.0, 118.1, 81.4. **HRMS** (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{16}\text{ClN}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 415.0666, found: 415.0666

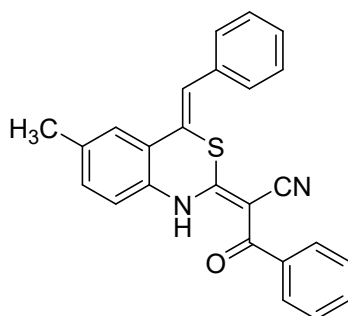
**(E)-2-(4-((Z)-Benzylidene)-6-bromo-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ha)**



light yellow solid, 97.3 mg, yield: 95 %, m.p.: 300 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;  **$^1\text{H}$  NMR** (400 MHz, Chloroform-*d*)  $\delta$  14.91 (s, 1H), 7.84 (d,  $J$  = 7.6 Hz, 2H), 7.73 (s, 1H), 7.53 (d,  $J$  = 8.1 Hz, 2H), 7.48 (d,  $J$  = 6.8 Hz, 6H), 7.42 (d,  $J$  = 6.0 Hz, 1H), 7.26 (s, 1H),

7.00 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 166.3, 138.1, 133.9, 133.2, 132.7, 132.0, 131.7, 129.5, 129.2, 128.9, 128.3, 128.2, 128.1, 124.0, 121.1, 119.9, 118.8, 118.1, 81.5. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{16}\text{BrN}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 459.0161, found: 459.0161

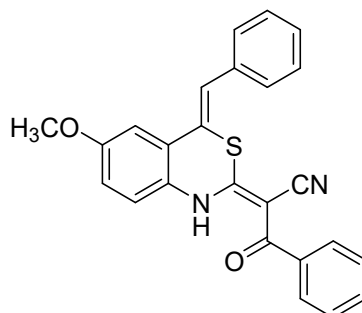
**(E)-2-(4-((Z)-Benzylidene)-6-methyl-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ia)**



light yellow solid, 62.3 mg, yield: 89 % , m.p.: 218-220 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.84 (s, 1H), 7.84 (d,  $J = 7.5$  Hz, 2H), 7.50 (dd,  $J = 16.6, 6.8$  Hz, 7H), 7.40 (d,  $J = 9.0$  Hz, 2H), 7.29 – 7.20 (m, 2H), 7.02 (d,  $J = 8.1$  Hz, 1H), 2.42 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.3, 165.8, 138.4, 137.3, 134.3, 131.8, 131.3, 131.3, 129.9, 129.4, 128.8, 128.7, 128.3, 128.0, 125.6, 122.0, 120.4, 119.7, 118.5, 80.7, 21.2. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{25}\text{H}_{18}\text{N}_2\text{NaOS}^+$   $[\text{M}+\text{Na}]^+$ : 417.1032, found: 417.1029

**(E)-2-(4-((Z)-Benzylidene)-6-methoxy-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ja)**



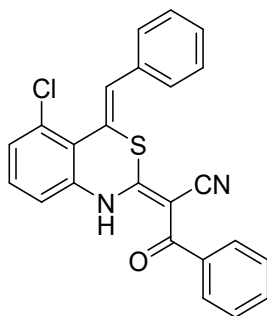
light yellow solid, 77.2 mg, yield: 94 % , m.p.: 252-254 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.94 (s, 1H), 7.84 (d,  $J = 7.9$  Hz, 2H), 7.55 – 7.35 (m, 8H), 7.27 (d,  $J = 2.0$  Hz, 1H), 7.10 (s, 1H), 7.04 (d,  $J = 6.7$  Hz, 1H),



6.97 (d,  $J = 8.7$  Hz, 1H), 3.86 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.1, 164.8, 158.6, 138.4, 134.2, 131.7, 130.1, 129.4, 128.8, 128.7, 128.2, 128.0, 127.2, 123.3, 121.1, 120.4, 118.6, 116.4, 109.9, 80.3, 55.8. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{25}\text{H}_{18}\text{N}_2\text{NaO}_2\text{S}^+$   $[\text{M}+\text{Na}]^+$ : 433.0981, found: 433.0982

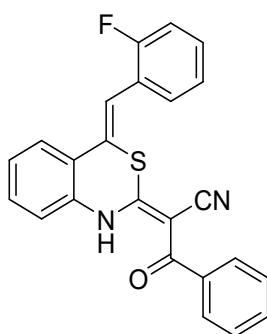
**(E)-2-(4-((Z)-Benzylidene)-5-chloro-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ka)**



light yellow solid, 78.8 mg, yield: 95 %, m.p.: 220-222 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.78 (s, 1H), 7.84 (d,  $J = 6.3$  Hz, 2H), 7.60 (s, 1H), 7.57 – 7.40 (m, 9H), 7.34 (t,  $J = 8.1$  Hz, 1H), 7.08 (d,  $J = 8.0$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 169.4, 142.3, 138.2, 136.8, 133.6, 132.0, 131.3, 130.0, 129.9, 129.1, 128.7, 128.7, 128.3, 128.1, 122.3, 118.2, 118.1, 113.8, 81.7. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{15}\text{ClN}_2\text{NaOS}^+$   $[\text{M}+\text{Na}]^+$ : 437.0486, found: 437.0485

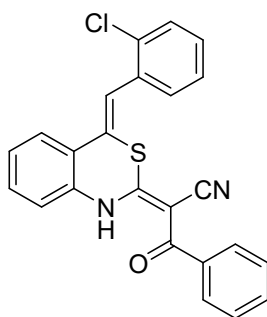
**(E)-2-(4-((Z)-2-Fluorobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3la)**



light yellow solid, 77.3 mg, yield: 97 %, m.p.: 246-247 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 14.88 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.55 (q, *J* = 8.0 Hz, 2H), 7.47 (q, *J* = 6.7, 6.2 Hz, 3H), 7.42 – 7.23 (m, 4H), 7.17 (t, *J* = 10.3 Hz, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 191.5, 166.1, 160.3(d, *J*<sub>C-F</sub> = 249.8 Hz), 138.3, 133.6, 131.9, 130.8, 130.8(d, *J*<sub>C-F</sub> = 8.3 Hz), 130.1(d, *J*<sub>C-F</sub> = 3.7 Hz), 128.3, 128.0, 127.2, 125.6, 124.4(d, *J*<sub>C-F</sub> = 3.7 Hz), 122.9, 122.7(d, *J*<sub>C-F</sub> = 13.6 Hz), 122.3(d, *J*<sub>C-F</sub> = 13.6 Hz), 121.9, 119.8, 118.3, 115.8(d, *J*<sub>C-F</sub> = 21.7 Hz), 81.1. **<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>) δ -113.2. **HRMS** (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>16</sub>FN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 399.0962, found: 399.0962

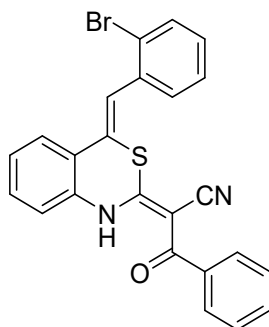
**(E)-2-(4-((Z)-2-Chlorobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ma)**



light yellow solid, 79.7 mg, yield: 96 %, m.p.: 250-253 °C, column chromatography eluent, EtOAc/PE= 1: 25 → 2: 1;

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 14.86 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 7.46 (d, *J* = 13.8 Hz, 7H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.21 (s, 1H), 7.14 (d, *J* = 8.2 Hz, 1H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 191.5, 165.9, 138.2, 134.7, 133.6, 132.7, 131.9, 130.7, 130.6, 129.1, 129.0, 128.3, 128.0, 127.2, 125.4, 122.0, 121.1, 119.8, 118.3, 81.2. **HRMS** (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>16</sub>ClN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 415.0666, found: 415.0666

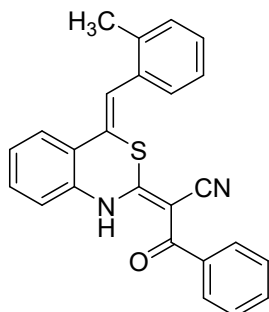
**(E)-2-(4-((Z)-2-Bromobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3na)**



light yellow solid, 86.4 mg, yield: 94% , m.p.: 257-260 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.88 (s, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.68 (t, *J* = 8.4 Hz, 2H), 7.48 (h, *J* = 9.3 Hz, 6H), 7.38 – 7.22 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.5, 166.0, 138.3, 134.3, 133.7, 133.2, 131.9, 130.9, 130.4, 130.4, 128.9, 128.3, 128.0, 127.7, 127.2, 125.5, 124.4, 122.9, 121.4, 119.9, 118.3, 81.1. HRMS (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>15</sub>BrN<sub>2</sub>NaOS<sup>+</sup> [M+Na]<sup>+</sup>: 480.9981, found: 480.9981

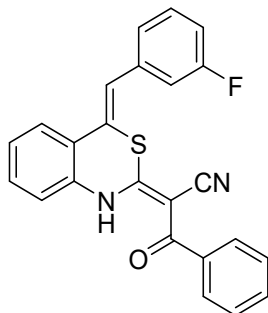
**(E)-2-(4-((Z)-2-Methylbenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3oa)**



light yellow solid, 75.0 mg, yield: 95%, m.p.: 265-268 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.88 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.46 (q, *J* = 7.5, 6.9 Hz, 3H), 7.32 (q, *J* = 11.1, 9.8 Hz, 6H), 7.14 (d, *J* = 8.0 Hz, 1H), 2.36 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.5, 166.9, 138.4, 136.9, 133.7, 133.3, 131.8, 130.6, 130.5, 129.2, 129.1, 129.0, 128.3, 128.0, 127.1, 126.2, 125.4, 121.9, 121.7, 119.8, 118.3, 81.0, 20.1. HRMS (ESI, *m/z*) calcd for C<sub>25</sub>H<sub>19</sub>N<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 395.1213, found: 395.1213

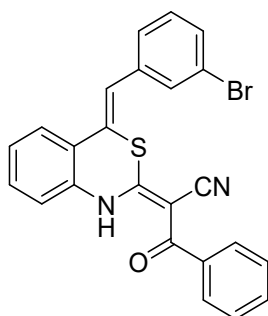
**(E)-2-(4-((Z)-3-Fluorobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3pa)**



light yellow solid, 76.5 mg, yield: 96 %, m.p.: 230-232 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 14.86 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.45 (dt, *J* = 13.8, 7.3 Hz, 4H), 7.36 – 7.26 (m, 2H), 7.21 (s, 1H), 7.16 (d, *J* = 9.8 Hz, 1H), 7.14 – 7.05 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4, 165.8, 162.7(d, *J*<sub>C-F</sub> = 247.3 Hz), 138.2, 136.3, 136.2, 133.6, 132.0, 130.8, 130.4(d, *J*<sub>C-F</sub> = 8.4 Hz), 128.7(d, *J*<sub>C-F</sub> = 2.5 Hz), 128.3, 128.1, 127.2, 125.3, 124.9(d, *J*<sub>C-F</sub> = 2.9 Hz), 121.9, 121.7, 119.9, 118.3, 116.2(d, *J*<sub>C-F</sub> = 22.2 Hz), 115.8(d, *J*<sub>C-F</sub> = 21.2 Hz), 81.1. <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -111.7. HRMS (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>16</sub>FN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 399.0962, found: 399.0962

**(E)-2-(4-((Z)-3-Bromobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3qa)**

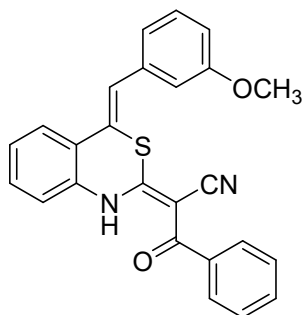


light yellow solid, 88.2 mg, yield: 96 % , m.p.: 207-210 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.85 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.48 (q, *J* = 10.4, 8.8 Hz, 6H), 7.33 (q, *J* = 7.9 Hz, 2H), 7.17 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4,

165.7, 138.2, 136.3, 133.6, 132.4, 132.0, 131.7, 130.9, 130.3, 128.3, 128.1, 127.4, 127.2, 125.3, 122.8, 122.1, 121.6, 119.9, 118.2, 81.2. **HRMS** (ESI, m/z) calcd for C<sub>24</sub>H<sub>16</sub>BrN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 459.1061, found: 459.1060

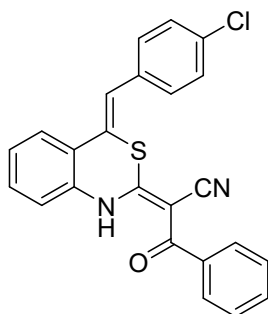
**(E)-2-(4-((Z)-3-Methoxybenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ra)**



light yellow solid, 80.5 mg, yield: 98 % , m.p.: 209-210 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.80 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 6.3 Hz, 1H), 7.50 – 7.26 (m, 5H), 7.23 (s, 1H), 7.14 – 7.03 (m, 3H), 6.94 (d, *J* = 8.3 Hz, 1H), 3.87 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4, 166.2, 159.7, 138.3, 135.5, 133.6, 131.9, 130.5, 130.1, 129.8, 128.3, 128.1, 127.2, 125.4, 122.2, 121.9, 120.4, 119.8, 118.4, 115.1, 114.2, 81.1, 55.4. **HRMS** (ESI, m/z) calcd for C<sub>25</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 411.1162, found: 411.1163

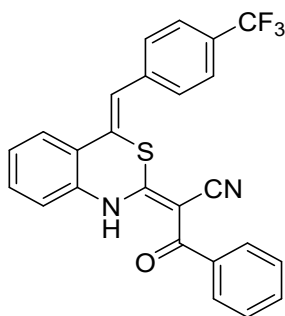
**(E)-2-(4-((Z)-4-Chlorobenzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3sa)**



light yellow solid, 78.0 mg, yield: 94 % , m.p.: 237-240 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.86 (s, 1H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 6.3 Hz, 1H), 7.46 (d, *J* = 12.6 Hz, 7H), 7.35

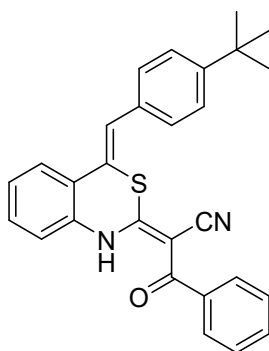
(d,  $J = 7.9$  Hz, 1H), 7.21 (s, 1H), 7.15 (d,  $J = 8.0$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.5, 165.9, 138.2, 134.7, 133.6, 132.7, 131.9, 130.7, 130.6, 129.1, 129.0, 128.3, 128.0, 127.2, 125.4, 122.0, 121.1, 119.8, 118.3, 81.2. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{24}\text{H}_{15}\text{ClN}_2\text{NaOS}^+$   $[\text{M}+\text{Na}]^+$ : 437.0486, found: 437.0486  
**(E)-3-Oxo-3-phenyl-2-(4-((Z)-4-(trifluoromethyl)benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)propanenitrile (3ta)**



light yellow solid, 87.0 mg, yield: 97 %, m.p.: 248-251 °C, column chromatography eluent, EtOAc/PE= 1: 25  $\rightarrow$  2: 1;

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.90 (s, 1H), 7.85 (d,  $J = 7.4$  Hz, 2H), 7.74 (d,  $J = 8.0$  Hz, 2H), 7.63 (dd,  $J = 14.4, 8.0$  Hz, 3H), 7.58 – 7.51 (m, 1H), 7.48 (t,  $J = 8.0$  Hz, 3H), 7.36 (t,  $J = 7.7$  Hz, 1H), 7.28 (s, 1H), 7.16 (d,  $J = 8.0$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.4, 165.4, 138.2, 137.7, 133.7, 132.0, 131.0, 130.4(q,  $J_{\text{C-F}} = 32.8$  Hz), 129.5, 128.3, 128.3, 128.1, 127.3, 125.8(q,  $J_{\text{C-F}} = 3.8$  Hz), 125.3, 123.9(q,  $J_{\text{C-F}} = 272.5$  Hz), 123.0, 121.5, 119.9, 118.2, 81.2.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.7. HRMS (ESI,  $m/z$ ) calcd for  $\text{C}_{25}\text{H}_{16}\text{F}_3\text{N}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 449.0930, found: 449.0931

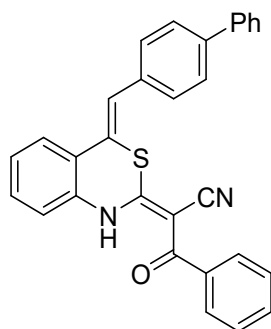
**(E)-2-(4-((Z)-4-(Tert-butyl)benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3ua)**



light yellow solid, 80.3 mg, yield: 92 %, m.p.: 218 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 14.84 (s, 1H), 7.85 (d, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.47 (dq, *J* = 17.0, 8.3, 7.7 Hz, 8H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.25 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 1.38 (s, 9H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.5, 166.8, 152.2, 138.4, 133.6, 131.8, 131.4, 130.6, 130.3, 129.3, 128.3, 128.0, 127.1, 125.8, 125.5, 122.6, 119.7, 119.1, 118.5, 81.0, 77.4, 77.3, 77.1, 76.7, 34.9, 31.2. HRMS (ESI, m/z) calcd for C<sub>28</sub>H<sub>25</sub>N<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 437.1682, found: 437.1682

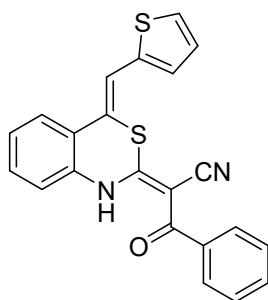
**(E)-2-((Z)-4-([1,1'-Biphenyl]-4-ylmethylene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3va)**



light yellow solid, 85.2 mg, yield: 90 %, m.p.: 273-275 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.83 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.66 (d, *J* = 7.5 Hz, 2H), 7.64 – 7.56 (m, 3H), 7.55 – 7.45 (m, 5H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 7.10 (d, *J* = 8.1 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4, 166.3, 141.4, 140.1, 138.3, 133.6, 133.2, 131.9, 130.5, 129.9, 128.9, 128.3, 128.1, 127.8, 127.4, 127.2, 127.2, 127.1, 125.4, 122.3, 120.0, 119.8, 118.4, 81.1. HRMS (ESI, m/z) calcd for C<sub>30</sub>H<sub>20</sub>N<sub>2</sub>NaOS<sup>+</sup> [M+Na]<sup>+</sup>: 479.1189, found: 479.1192

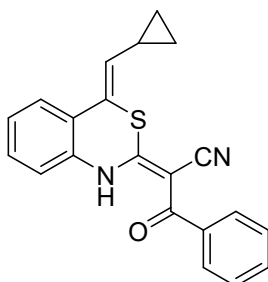
**(E)-3-Oxo-3-phenyl-2-((Z)-4-(thiophen-2-ylmethylene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)propanenitrile (3wa)**



light yellow solid, 73.4 mg, yield: 95 %, m.p.: 243-246 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.77 (s, 1H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.57 (dd, *J* = 16.8, 7.6 Hz, 2H), 7.50 (d, *J* = 6.6 Hz, 3H), 7.45 – 7.35 (m, 3H), 7.31 (t, *J* = 8.5 Hz, 1H), 7.14 (dd, *J* = 15.7, 5.9 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4, 165.7, 138.3, 137.8, 133.7, 132.0, 130.9, 130.2, 128.7, 128.3, 128.1, 127.6, 127.2, 124.7, 122.8, 122.3, 119.9, 118.4, 116.5, 81.5. HRMS (ESI, m/z) calcd for C<sub>22</sub>H<sub>15</sub>N<sub>2</sub>OS<sub>2</sub><sup>+</sup> [M+H]<sup>+</sup>: 387.0620, found: 387.0621

**(E)-2-((Z)-4-(Cyclopropylmethylene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-oxo-3-phenylpropanenitrile (3xa)**

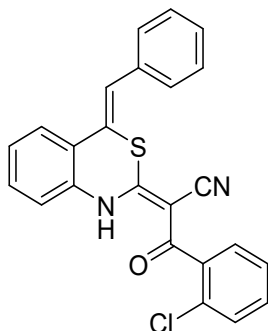


light yellow solid, 59.3 mg, yield: 86 %, m.p.: 168-170 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 14.65 (s, 1H), 7.93 – 7.82 (m, 2H), 7.59 – 7.44 (m, 3H), 7.40 – 7.31 (m, 2H), 7.29 (s, 1H), 7.23 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.66 (d, *J* = 9.9 Hz, 1H), 1.93 (dddd, *J* = 12.6, 9.5, 8.0, 4.6 Hz, 1H), 1.12 – 1.02 (m, 2H), 0.73 – 0.62 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.4, 167.4, 138.5, 136.2, 133.3, 131.8, 129.6, 128.3, 128.0, 127.0, 124.4, 122.3, 119.7, 118.9, 117.1, 81.3, 12.4, 8.4. HRMS (ESI, m/z) calcd for C<sub>21</sub>H<sub>17</sub>N<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 345.1056, found: 345.1057

**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-(2-chlorophenyl)-3-oxopropanenitrile (3ab)**

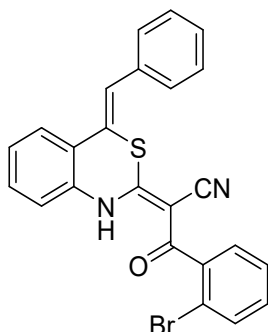




light yellow solid, 78.8 mg, yield: 95 %, m.p.: 250-253 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.43 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.32 (m, 11H), 7.29 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 190.8, 166.0, 138.2, 134.1, 133.4, 131.3, 130.8, 130.6, 130.6, 130.1, 129.3, 128.9, 128.8, 128.3, 127.4, 126.7, 125.5, 122.3, 119.9, 119.9, 117.0, 83.3. HRMS (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>16</sub>ClN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 415.0666, found: 415.0666

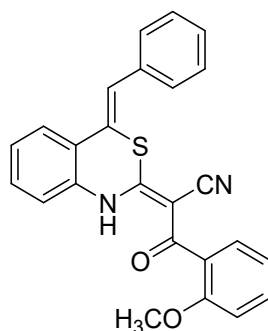
**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-(2-bromophenyl)-3-oxopropanenitrile (3ac)**



light yellow solid, 88.2 mg, yield: 96 %, m.p.: 257-261 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.40 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 4.2 Hz, 5H), 7.43 – 7.35 (m, 4H), 7.35 – 7.30 (m, 1H), 7.29 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.6, 166.0, 140.3, 134.1, 133.3, 133.2, 131.3, 130.7, 130.6, 129.3, 128.9, 128.8, 128.2, 127.5, 127.4, 125.5, 122.2, 119.9, 119.8, 119.1, 117.0, 83.0. HRMS (ESI, *m/z*) calcd for C<sub>24</sub>H<sub>16</sub>BrN<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 459.0161, found: 459.0160

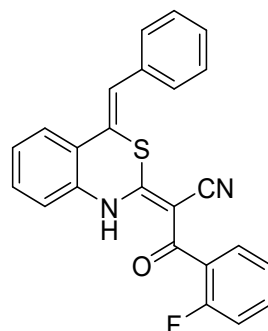
**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-(2-methoxyphenyl)-3-oxopropanenitrile (3ad)**



light yellow solid, 77.9 mg, yield: 95 %, m.p.: 278-280 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.56 (s, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 25.2 Hz, 6H), 7.38 (d, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.27 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.02 (dd, *J* = 19.7, 8.0 Hz, 2H), 3.92 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.9, 164.9, 156.4, 134.3, 133.6, 132.1, 130.5, 130.2, 129.4, 128.7, 128.7, 128.7, 127.0, 125.4, 122.1, 120.6, 120.3, 119.7, 117.8, 111.5, 84.1, 55.8. HRMS (ESI, *m/z*) calcd for C<sub>25</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 411.1162, found: 411.1160

**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-(2-fluorophenyl)-3-oxopropanenitrile (3ae)**

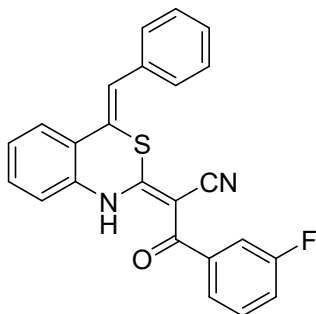


light yellow solid, 75.7 mg, yield: 95 %, m.p.: 246-247 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 14.88 (s, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.55 (q, *J* = 8.0 Hz, 2H), 7.47 (q, *J* = 6.6, 5.9 Hz, 3H), 7.42 – 7.24 (m, 4H), 7.17 (t, *J* = 10.5 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 191.5, 166.1, 160.3(d, *J*<sub>C-F</sub> = 249.8 Hz), 138.3, 133.6, 131.9, 130.8, 130.8(d,

$J_{C-F} = 8.4$  Hz), 130.1(d,  $J_{C-F} = 2.2$  Hz), 128.3, 128.0, 127.2, 125.6, 124.3(d,  $J_{C-F} = 3.7$  Hz), 122.9, 122.7(d,  $J_{C-F} = 4.8$  Hz), 122.3(d,  $J_{C-F} = 13.6$  Hz), 121.9, 119.8, 118.3, 115.8(d,  $J_{C-F} = 21.7$  Hz), 81.1  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.2. **HRMS** (ESI, m/z) calcd for  $\text{C}_{24}\text{H}_{16}\text{FN}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 399.0962, found: 399.0962

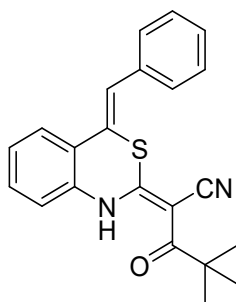
**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-3-(3-fluorophenyl)-3-oxopropanenitrile (3af)**



light yellow solid, 75.7 mg, yield: 95 %, m.p.: 265-266 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  14.86 (s, 1H), 7.85 (d,  $J = 7.5$  Hz, 2H), 7.60 (d,  $J = 8.0$  Hz, 1H), 7.57 – 7.50 (m, 1H), 7.45 (dt,  $J = 13.6, 7.3$  Hz, 4H), 7.36 – 7.27 (m, 2H), 7.21 (s, 1H), 7.16 (d,  $J = 9.6$  Hz, 1H), 7.14 – 7.05 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  191.4, 165.8, 162.7 (d,  $J_{C-F} = 247.3$  Hz), 138.2, 136.3(d,  $J_{C-F} = 7.8$  Hz), 133.6, 132.0, 130.8, 130.4(d,  $J_{C-F} = 8.4$  Hz), 128.7(d,  $J_{C-F} = 2.5$  Hz), 128.3, 128.1, 127.2, 125.3, 124.9(d,  $J_{C-F} = 2.9$  Hz), 121.9, 121.7, 119.9, 118.3, 116.2(d,  $J_{C-F} = 22.2$  Hz), 115.8(d,  $J_{C-F} = 21.2$  Hz), 81.1.  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -111.7. **HRMS** (ESI, m/z) calcd for  $\text{C}_{24}\text{H}_{16}\text{FN}_2\text{OS}^+$   $[\text{M}+\text{H}]^+$ : 399.0962, found: 399.0962

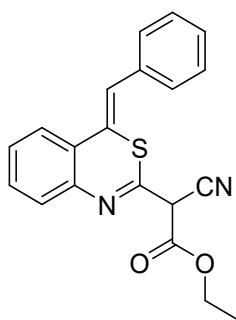
**(E)-2-(4-((Z)-Benzylidene)-1,4-dihydro-2H-benzo[d][1,3]thiazin-2-ylidene)-4,4-dimethyl-3-oxopentanenitrile (3ag)**



light yellow solid, 70.6 mg, yield: 98 %, m.p.: 223-225 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.65 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 7.0 Hz, 4H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.22 (s, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 1.39 (s, 9H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 203.9, 166.4, 134.4, 133.8, 130.3, 130.2, 129.4, 128.7, 128.7, 126.7, 125.3, 122.3, 120.6, 119.5, 118.8, 79.3, 44.0, 26.8. HRMS (ESI, m/z) calcd for C<sub>22</sub>H<sub>21</sub>N<sub>2</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 361.1369, found: 361.1371

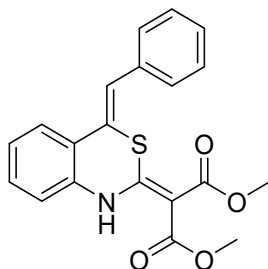
**Ethyl (Z)-2-(4-benzylidene-4H-benzo[d][1,3]thiazin-2-yl)-2-cyanoacetate (3ah)**



colorless solid, 66.2 mg, yield: 95 %, m.p.: 219-220 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 12.35 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 4.4 Hz, 4H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.9, 163.8, 134.4, 133.9, 130.4, 130.1, 129.4, 128.7, 126.1, 125.5, 121.7, 120.4, 118.7, 116.2, 71.5, 61.3, 14.4. HRMS (ESI, m/z) calcd for C<sub>20</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 349.1005, found: 349.1005

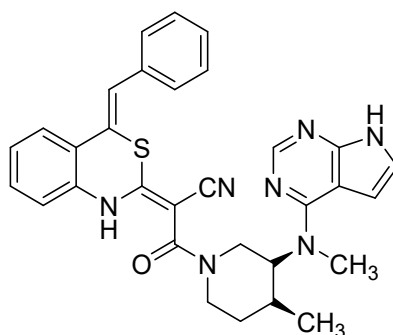
**Dimethyl (Z)-2-(4-benzylidene-4H-benzo[d][1,3]thiazin-2-yl)malonate (3ai)**



colorless liquid, 57.3 mg, yield: 78 %, 198-201 °C, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

<sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 12.96 (s, 1H), 7.53 (d, *J* = 7.4 Hz, 3H), 7.48 – 7.41 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 6.6 Hz, 1H), 7.16 (s, 1H), 7.01 (d, *J* = 5.5 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.3, 167.0, 162.1, 135.0, 134.9, 129.9, 129.7, 129.3, 128.4, 128.1, 125.1, 125.0, 123.6, 122.7, 118.6, 90.9, 51.9, 51.8. HRMS (ESI, *m/z*) calcd for C<sub>20</sub>H<sub>18</sub>NO<sub>4</sub>S<sup>+</sup> [M+H]<sup>+</sup>: 368.0951, found: 368.0952

**(Methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino)piperidin-1-yl)-3-oxopropanenitrile (3aj)**

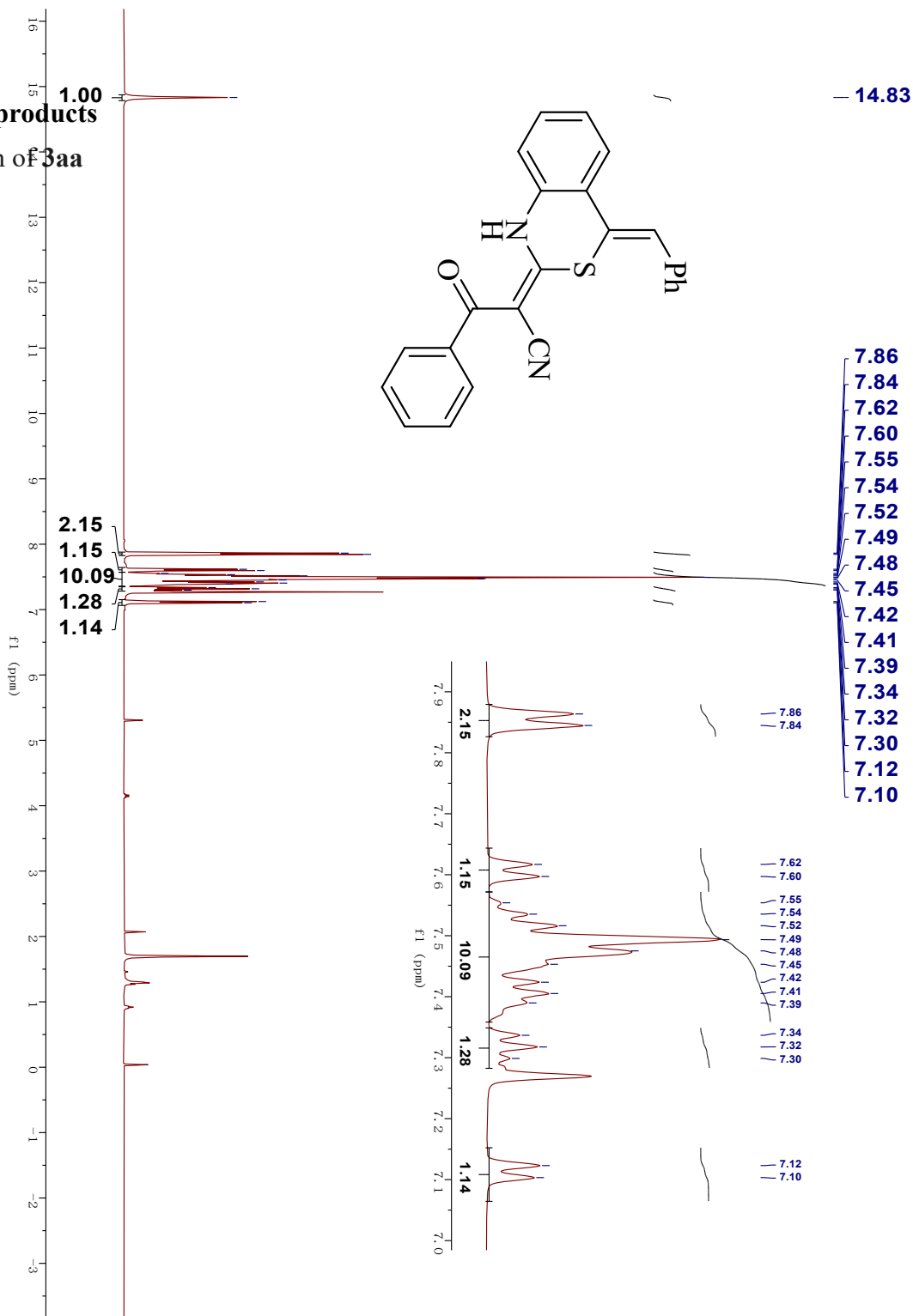


light yellow solid, 88.7 mg, yield: 81 %, column chromatography eluent, EtOAc/PE= 1: 25→ 2: 1;

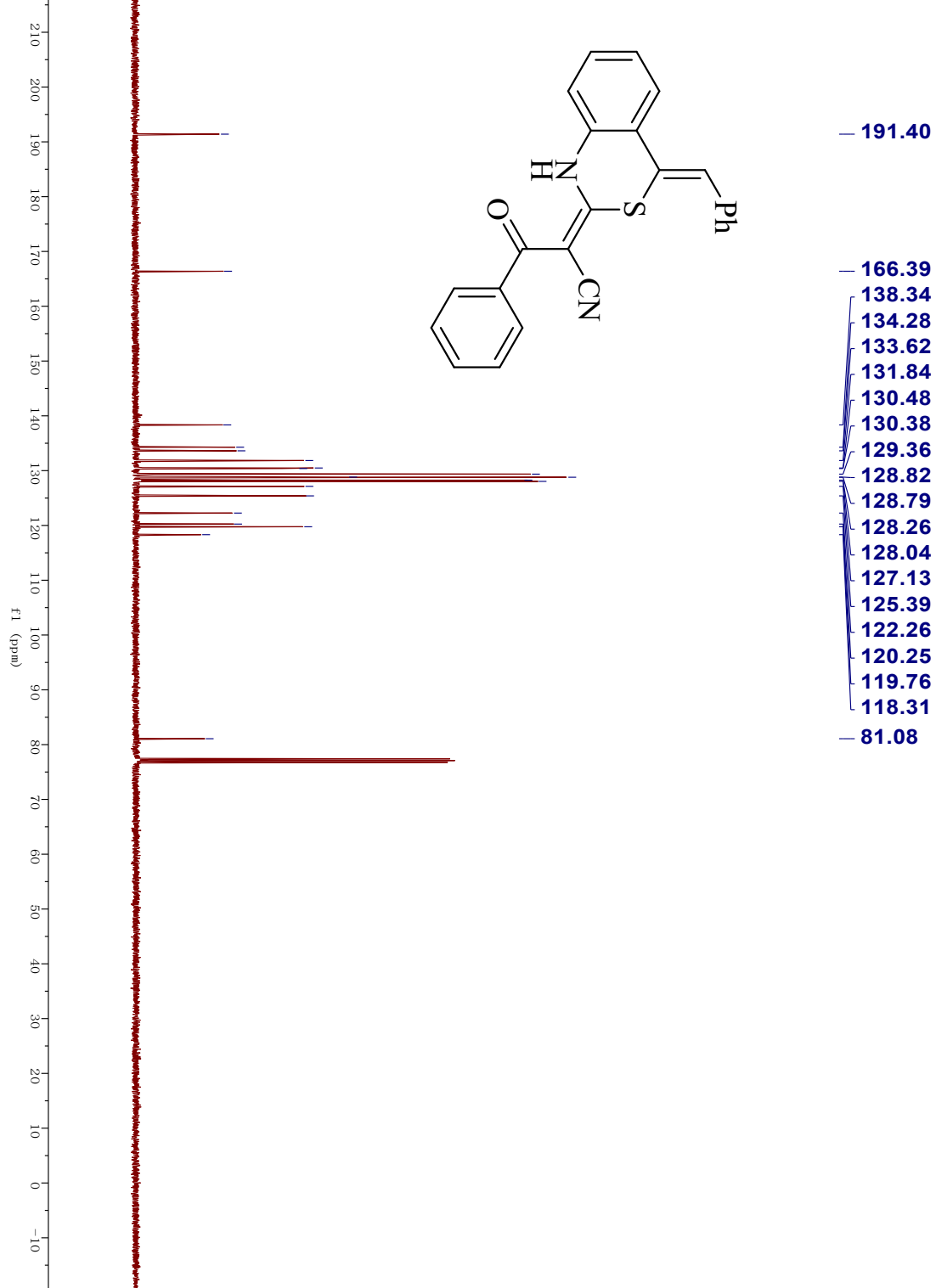
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.94 (s, 1H), 11.90 (s, 1H), 8.32 (d, *J* = 2.8 Hz, 1H), 7.53 (d, *J* = 6.6 Hz, 1H), 7.47 (t, *J* = 10.1 Hz, 4H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 3.9 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.53 (s, 1H), 5.16 (s, 1H), 4.01 (d, *J* = 12.5 Hz, 1H), 3.94 – 3.80 (m, 2H), 3.74 (d, *J* = 9.0 Hz, 1H), 3.42 (s, 3H), 2.54 (t, *J* = 7.5 Hz, 1H), 2.41 (s, 1H), 2.02 – 1.88 (m, 1H), 1.89 – 1.64 (m, 1H), 1.09 (d, *J* = 5.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.9, 163.7, 157.8, 151.9, 150.7, 134.6, 134.4, 130.2, 129.7, 129.4, 128.7, 128.6, 125.6, 125.3, 122.1, 121.1, 120.1, 118.9, 118.1, 103.0, 102.3, 71.3, 53.4, 45.4, 44.0, 34.6, 32.1, 31.1, 14.4. HRMS (ESI, *m/z*) calcd for C<sub>31</sub>H<sub>30</sub>N<sub>7</sub>OS<sup>+</sup> [M+H]<sup>+</sup>: 570.2047, found: 570.2051

**NMR spectra of products**

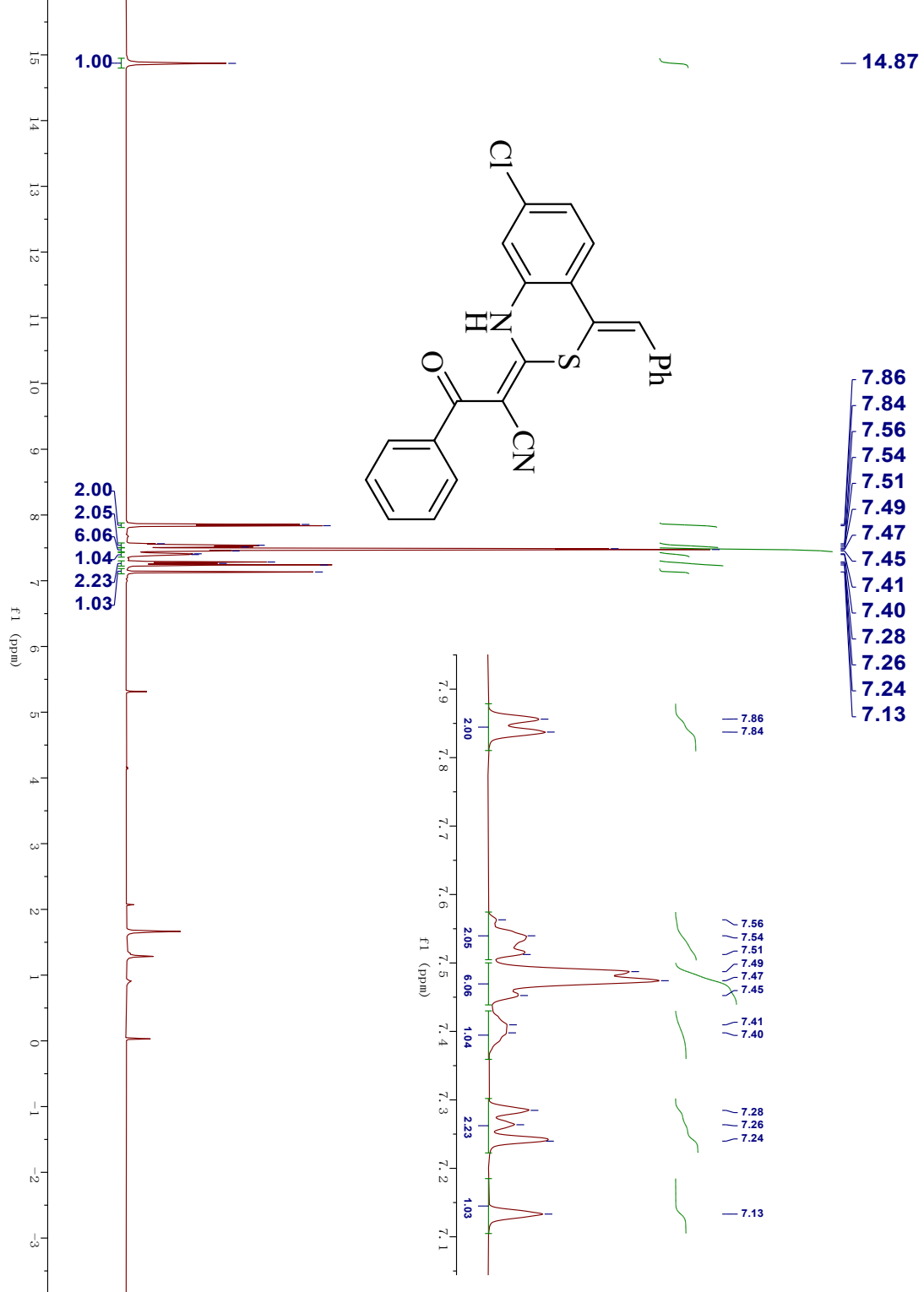
**<sup>1</sup>H NMR spectrum of 3aa**



**<sup>13</sup>C NMR spectrum of 3aa**

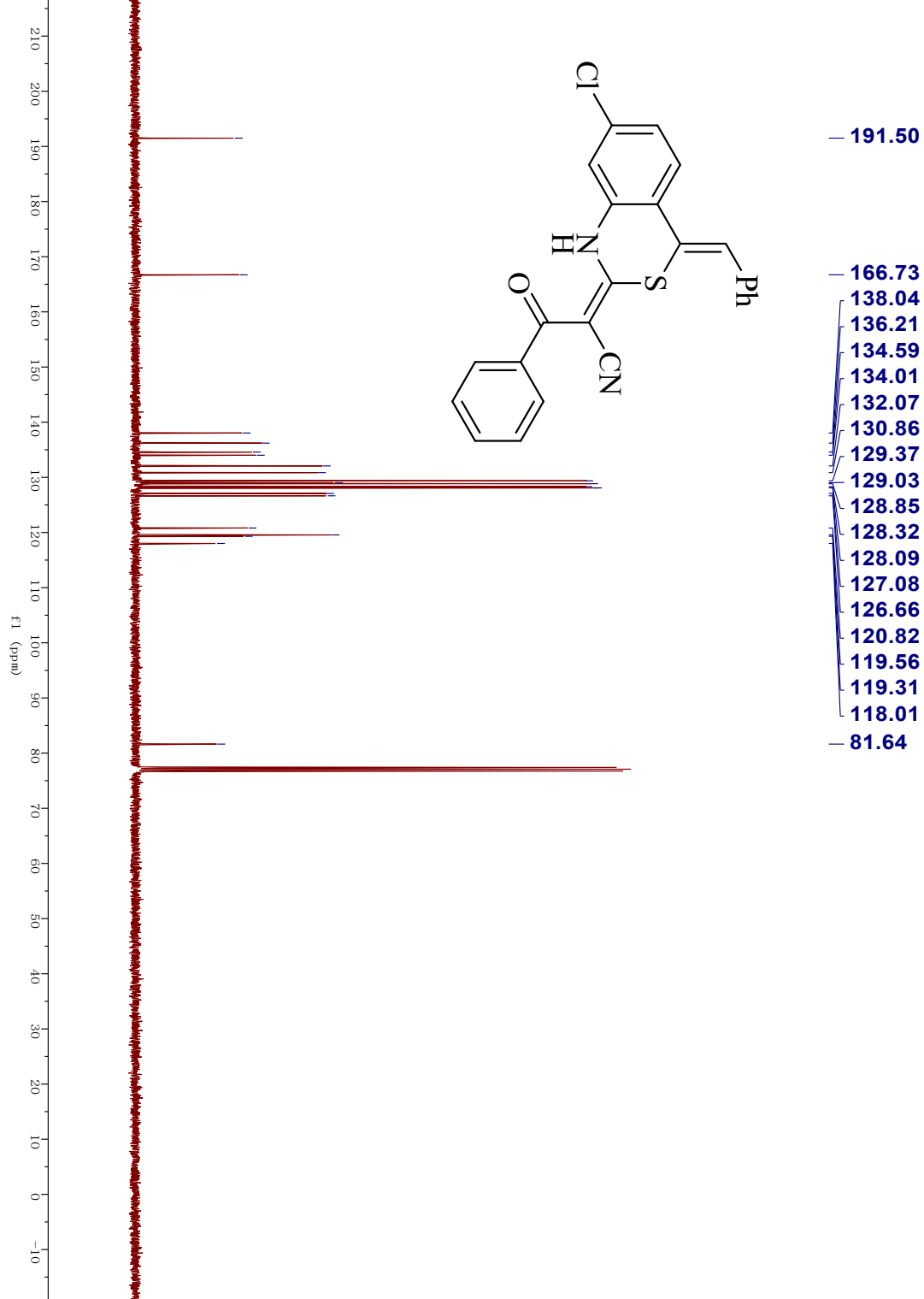


<sup>1</sup>H NMR spectrum of **3ba**

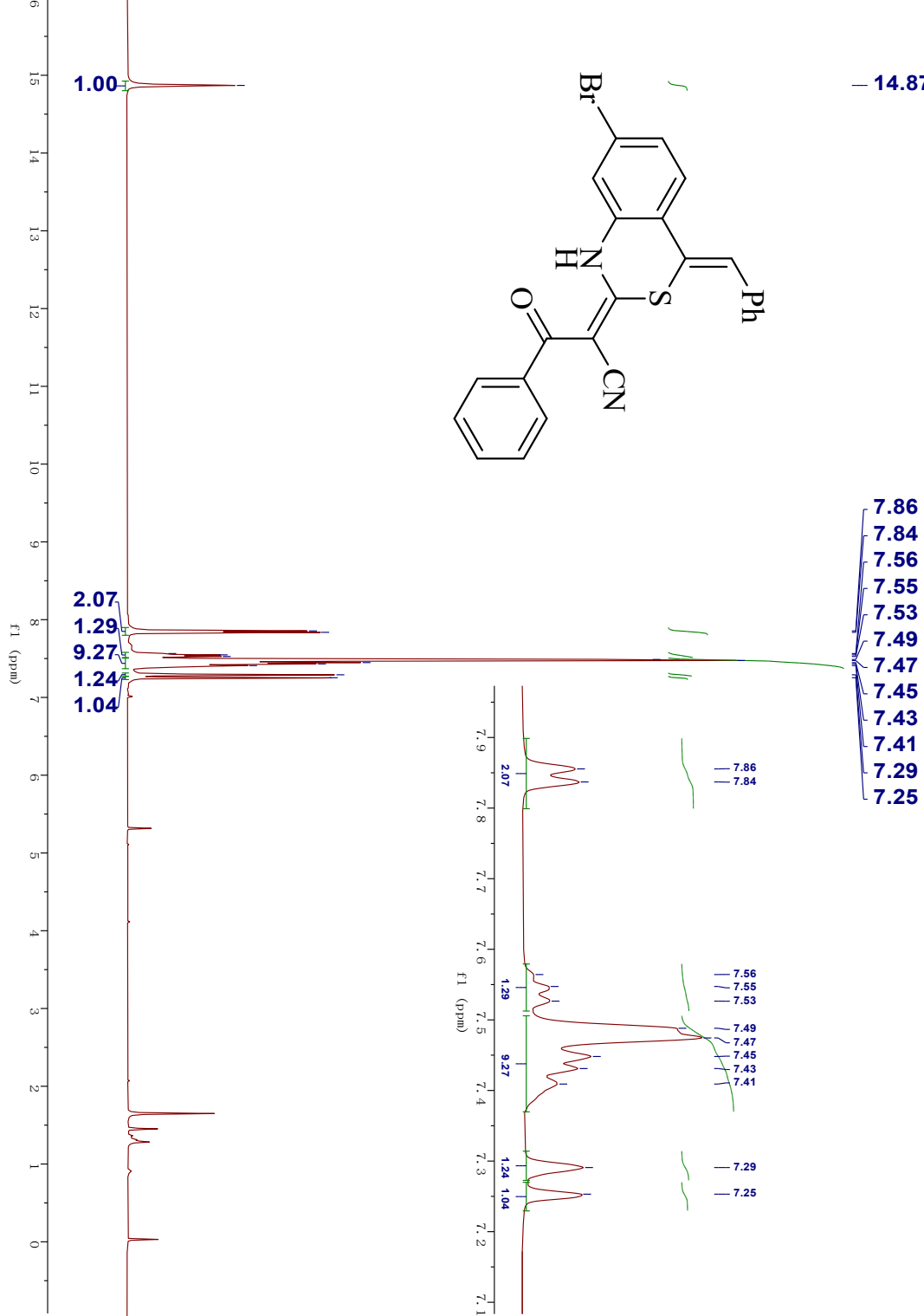


<sup>13</sup>C NMR spectrum of **3ba**

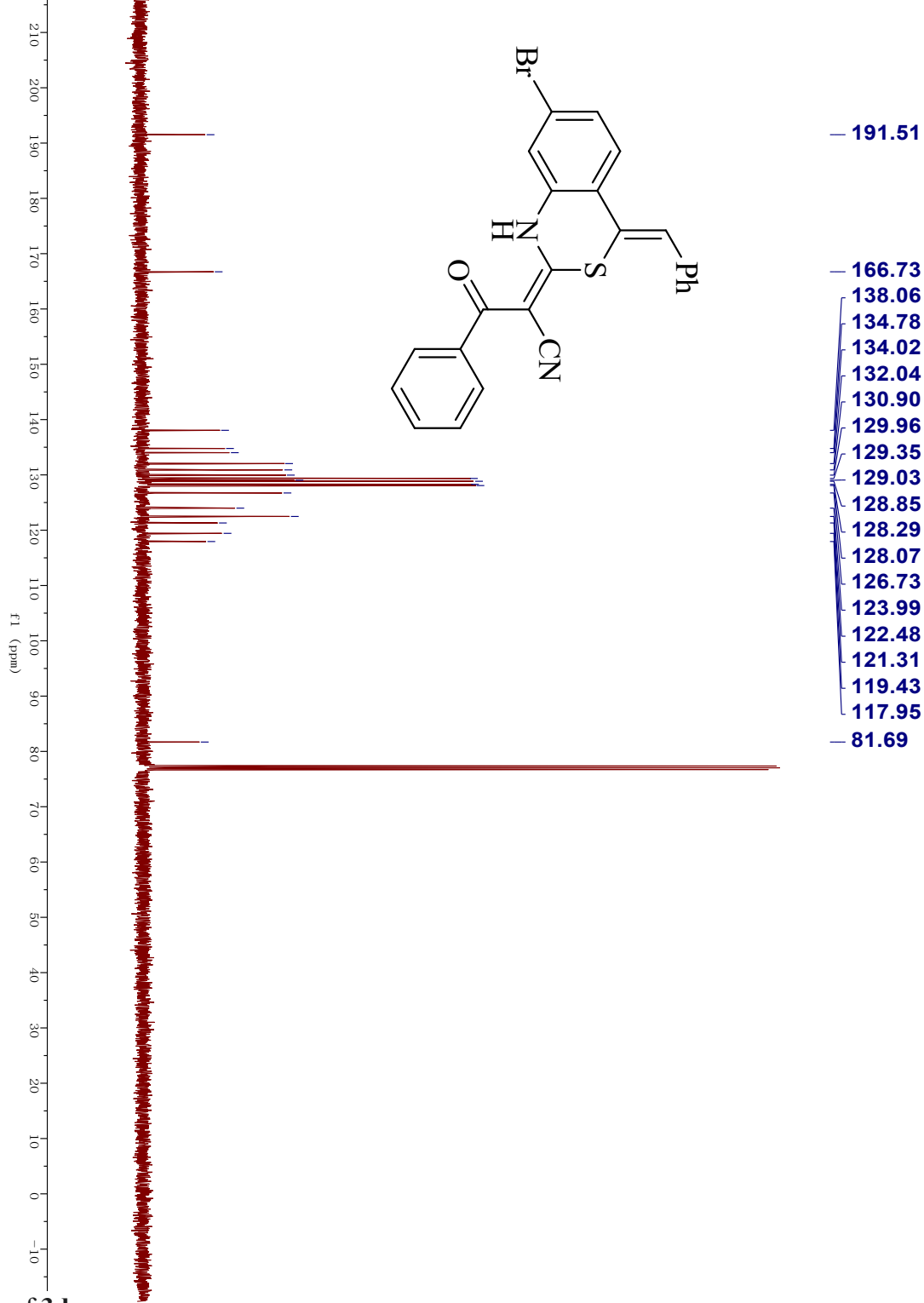




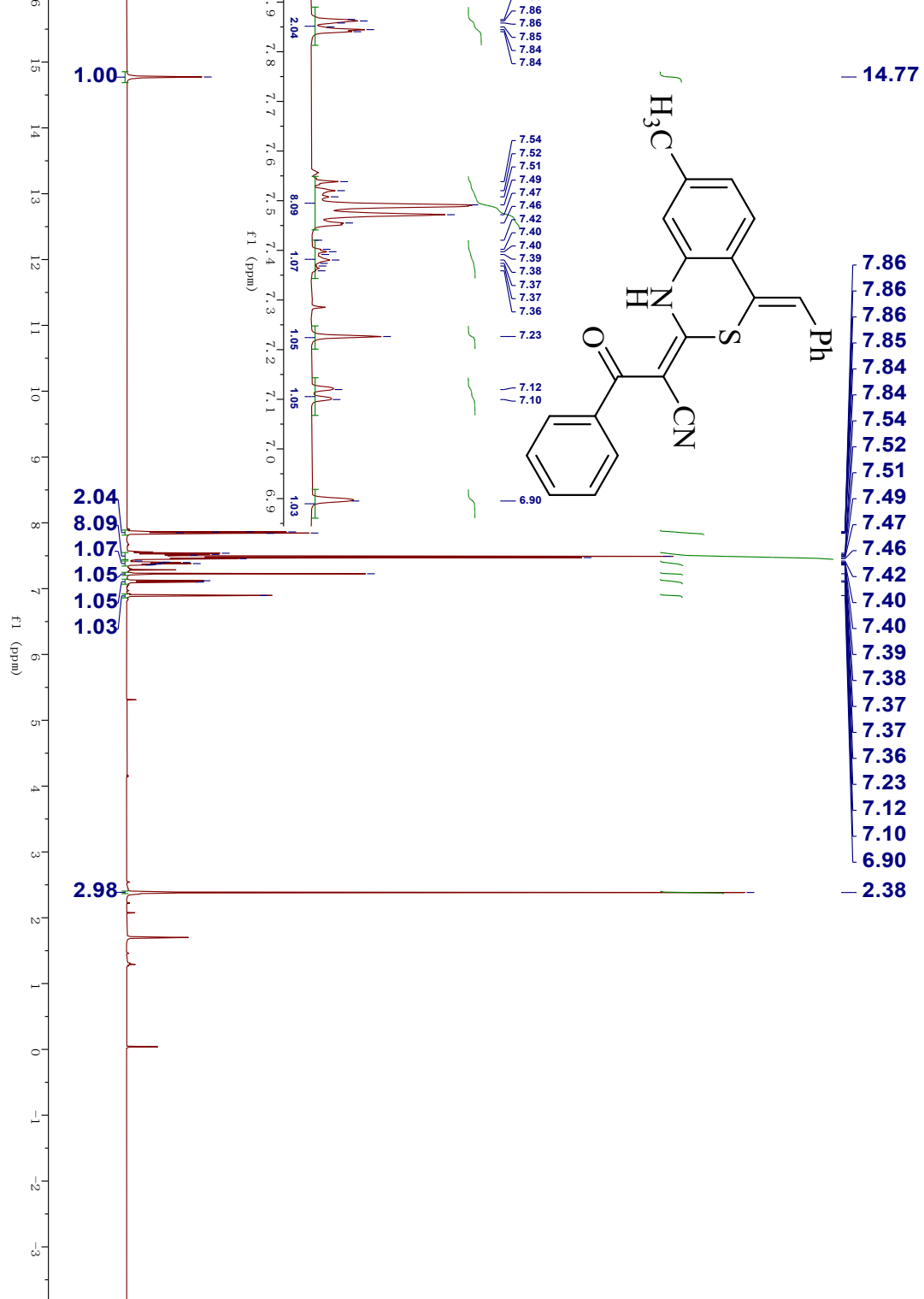
$^{13}\text{C}$  NMR spectrum of **3ca**



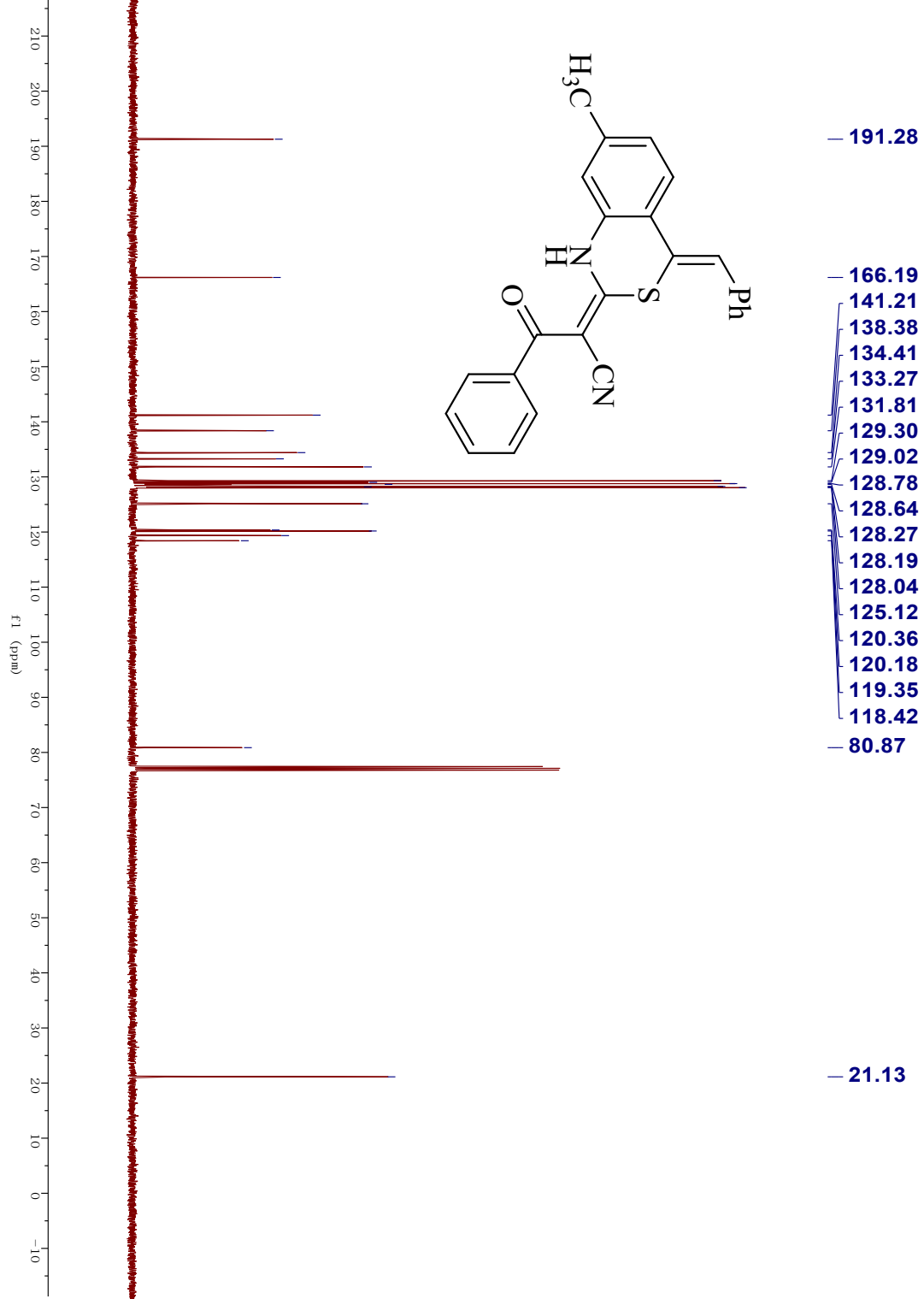
<sup>13</sup>C NMR spectrum of **3ca**



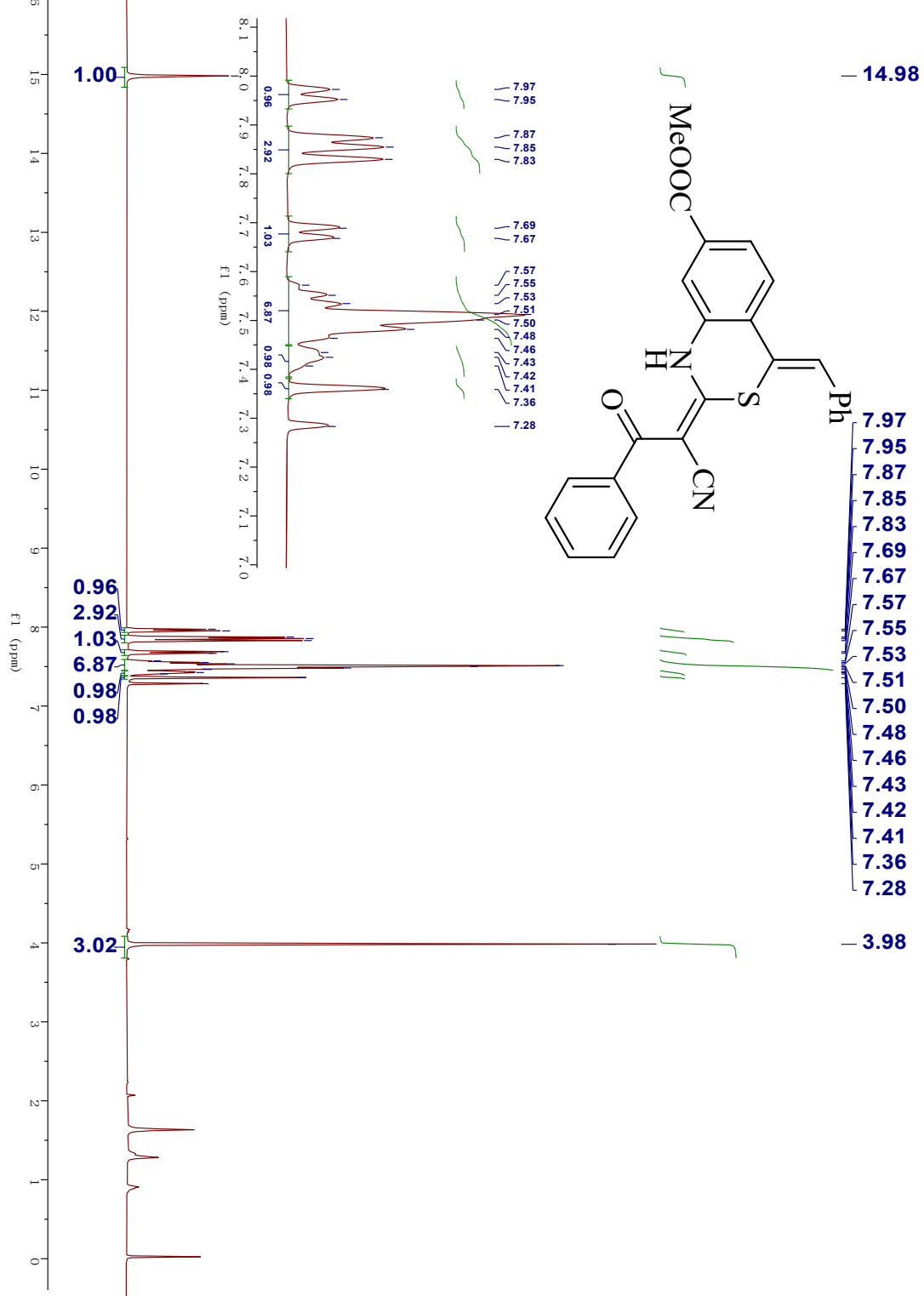
<sup>1</sup>H NMR spectrum of **3da**



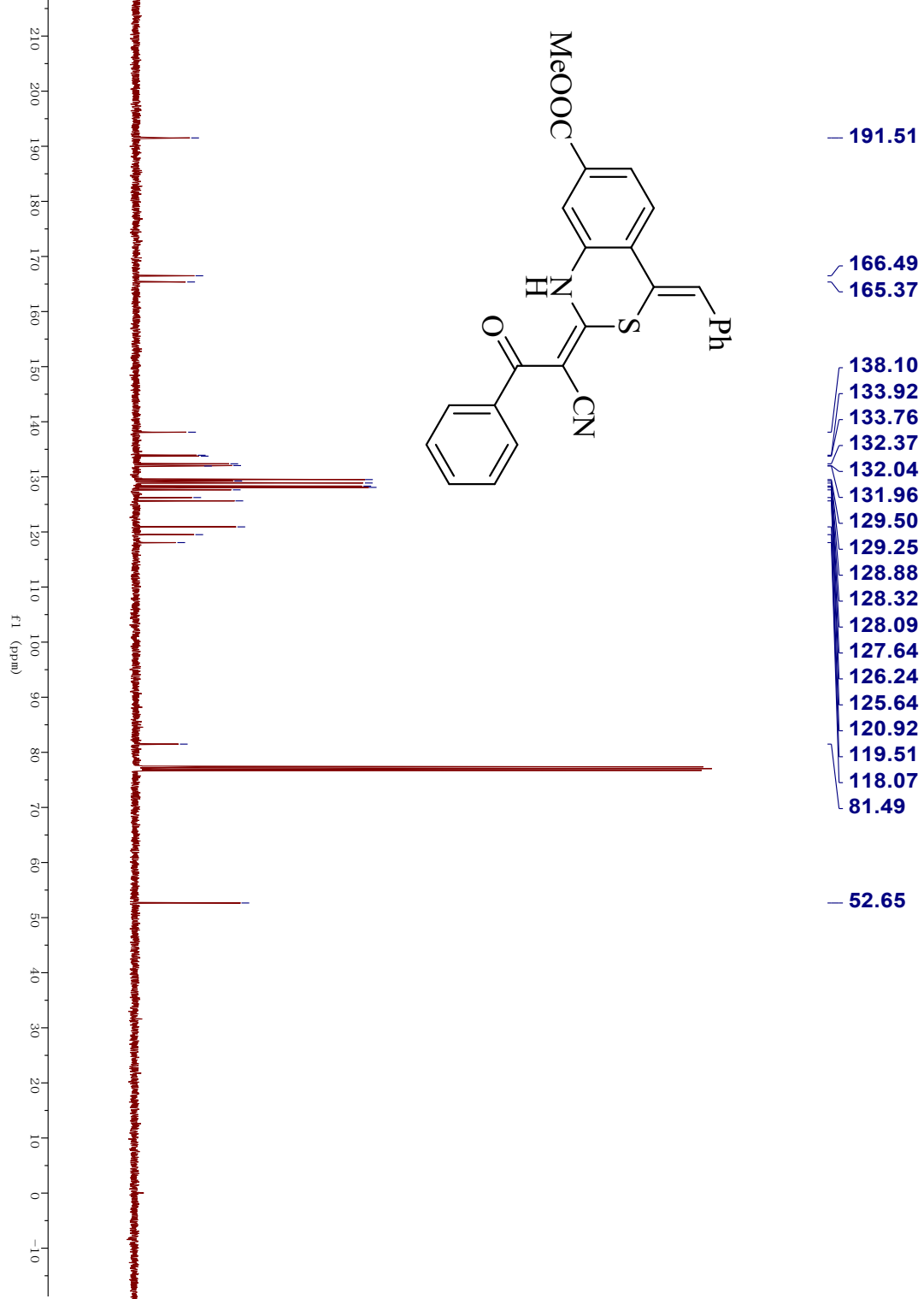
<sup>13</sup>C NMR spectrum of **3da**



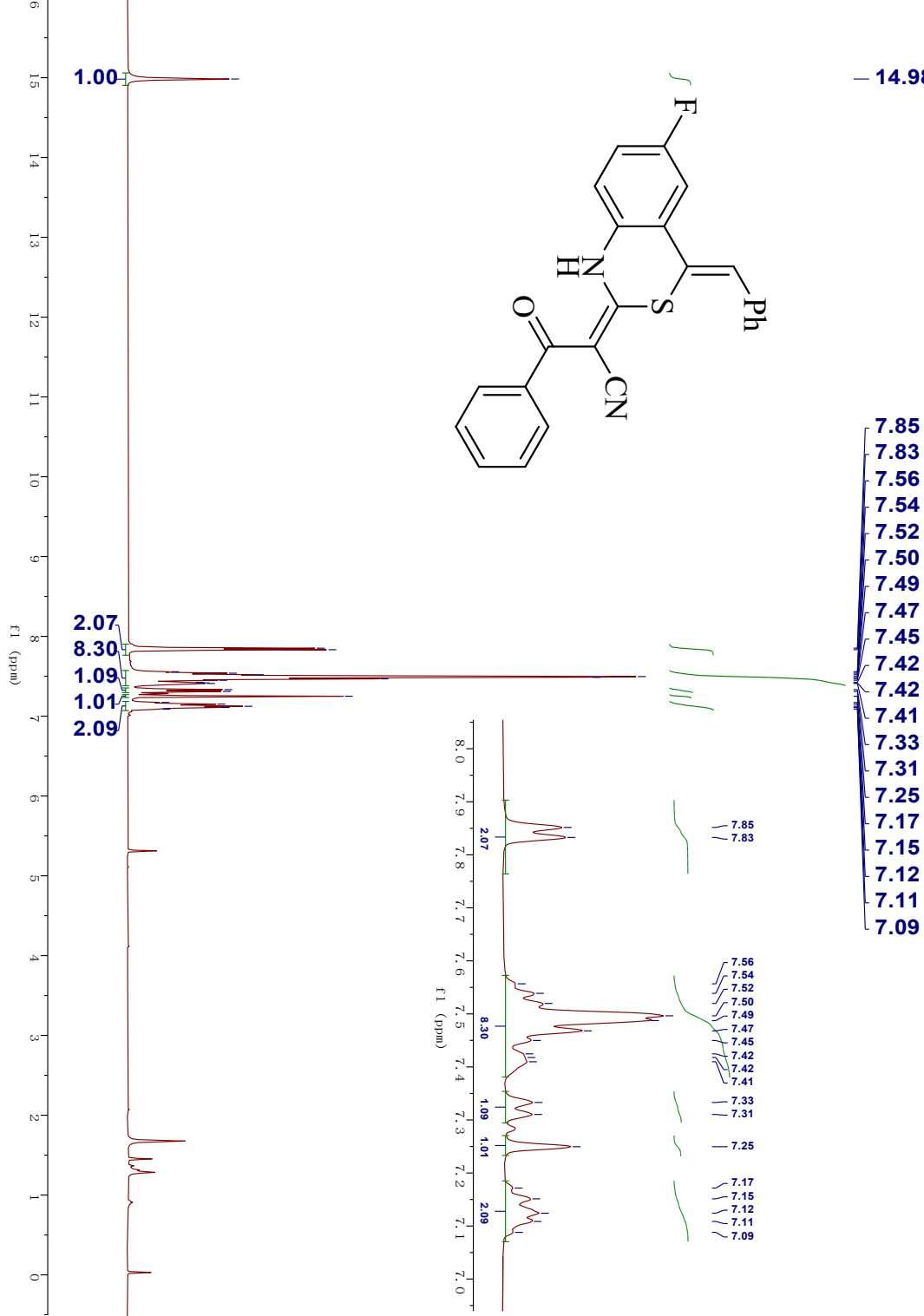
<sup>1</sup>H NMR spectrum of **3ea**



<sup>13</sup>C NMR spectrum of **3ea**

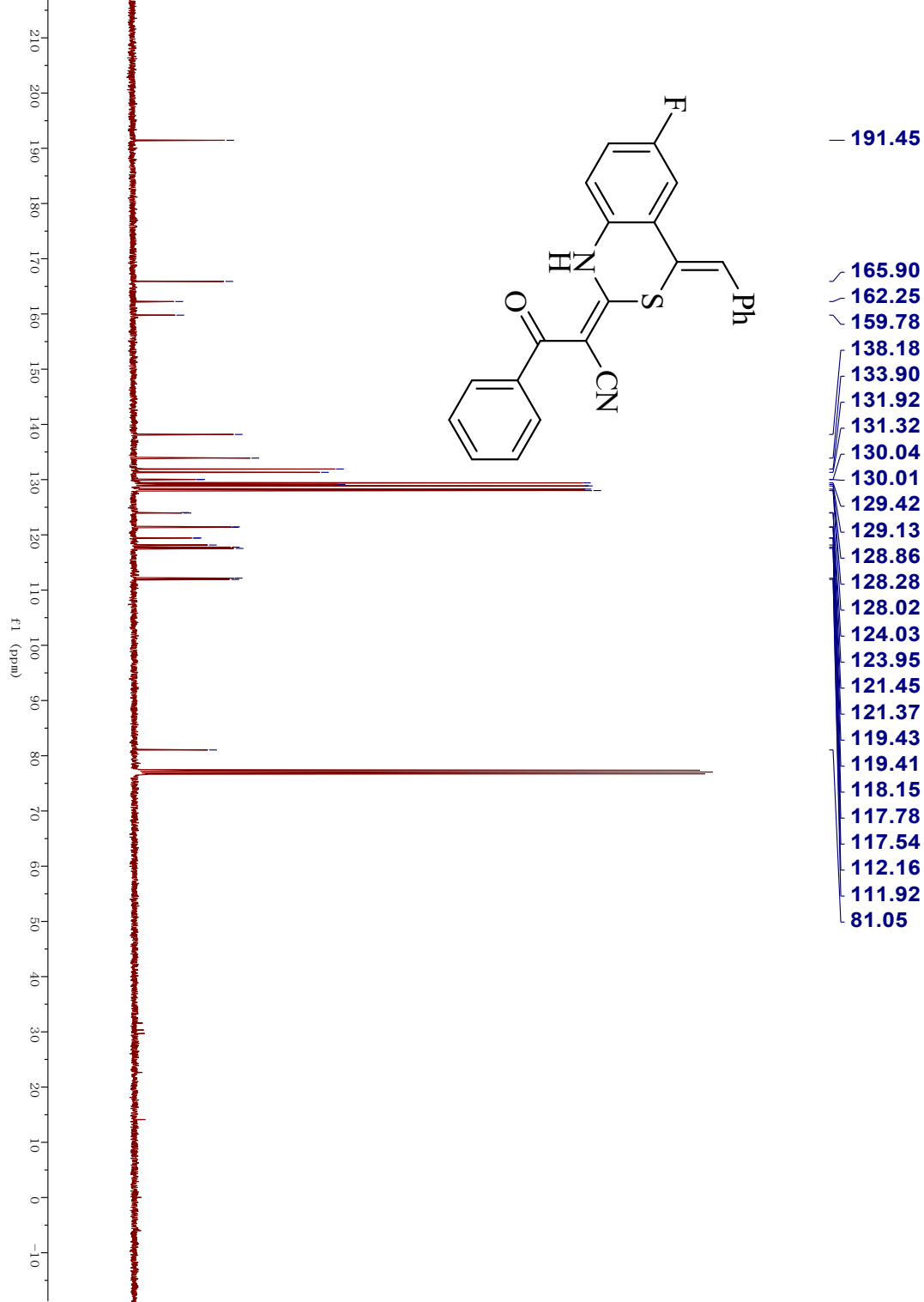


<sup>1</sup>H NMR spectrum of **3fa**

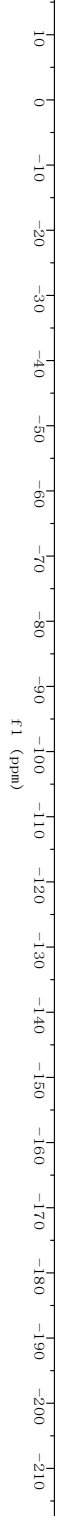
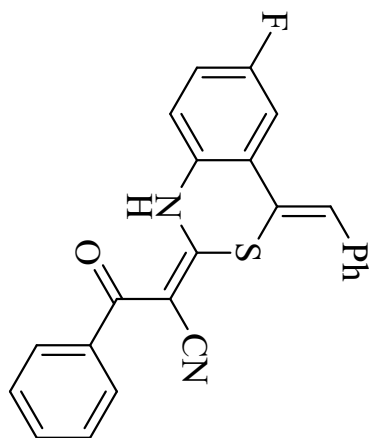


<sup>13</sup>C NMR spectrum of **3fa**



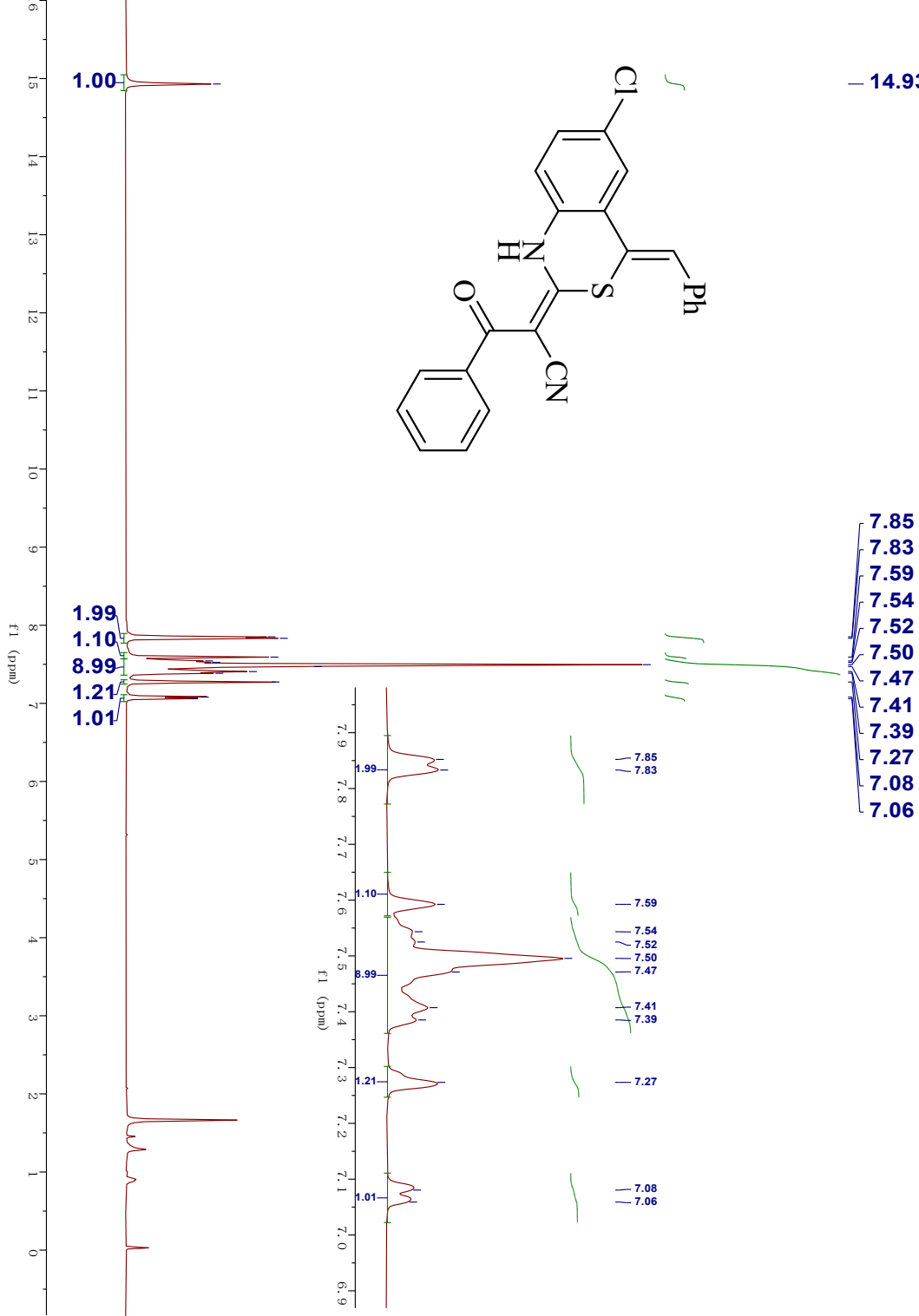


$^{19}\text{F}$  NMR spectrum of **3fa**

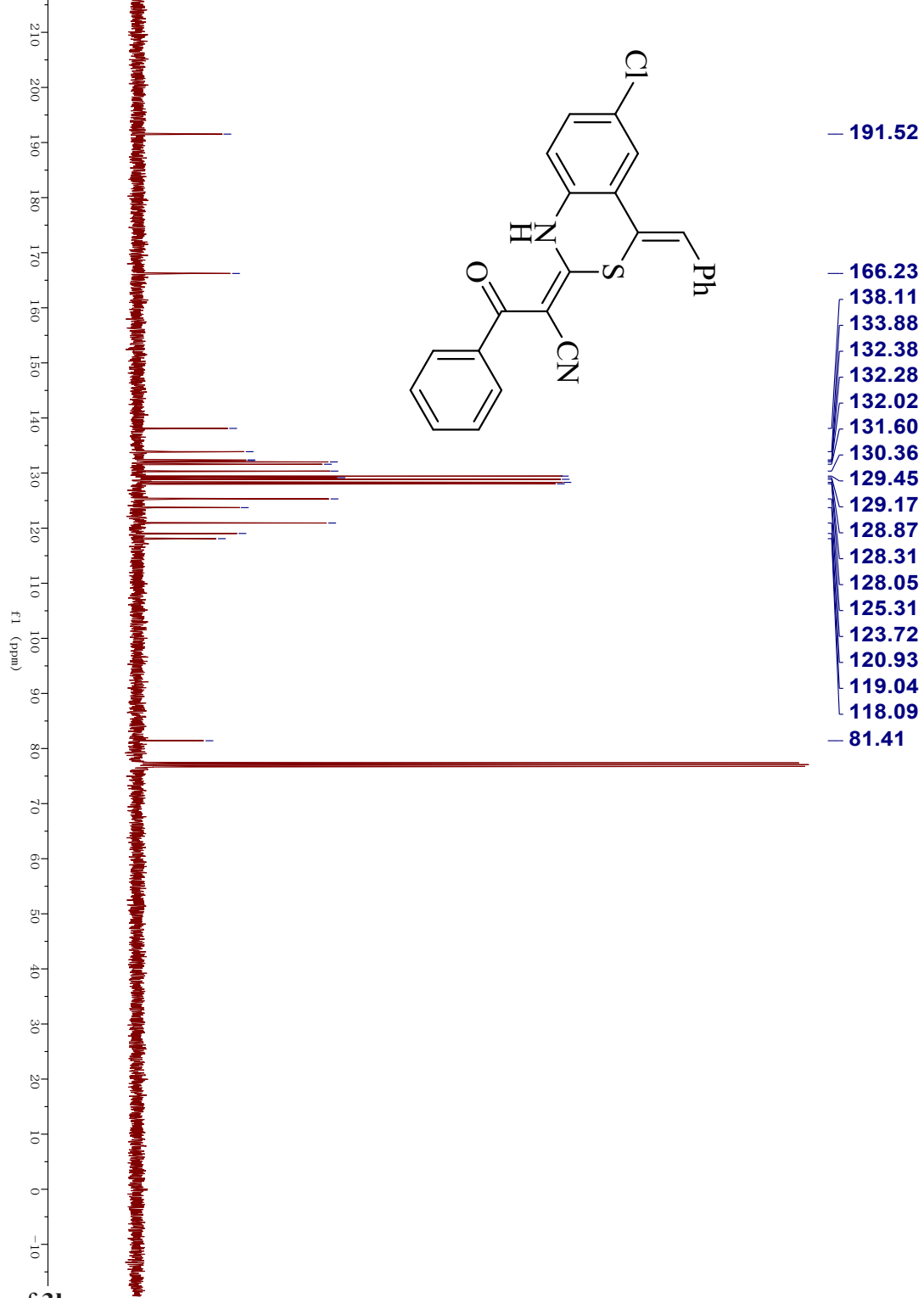


-113.46

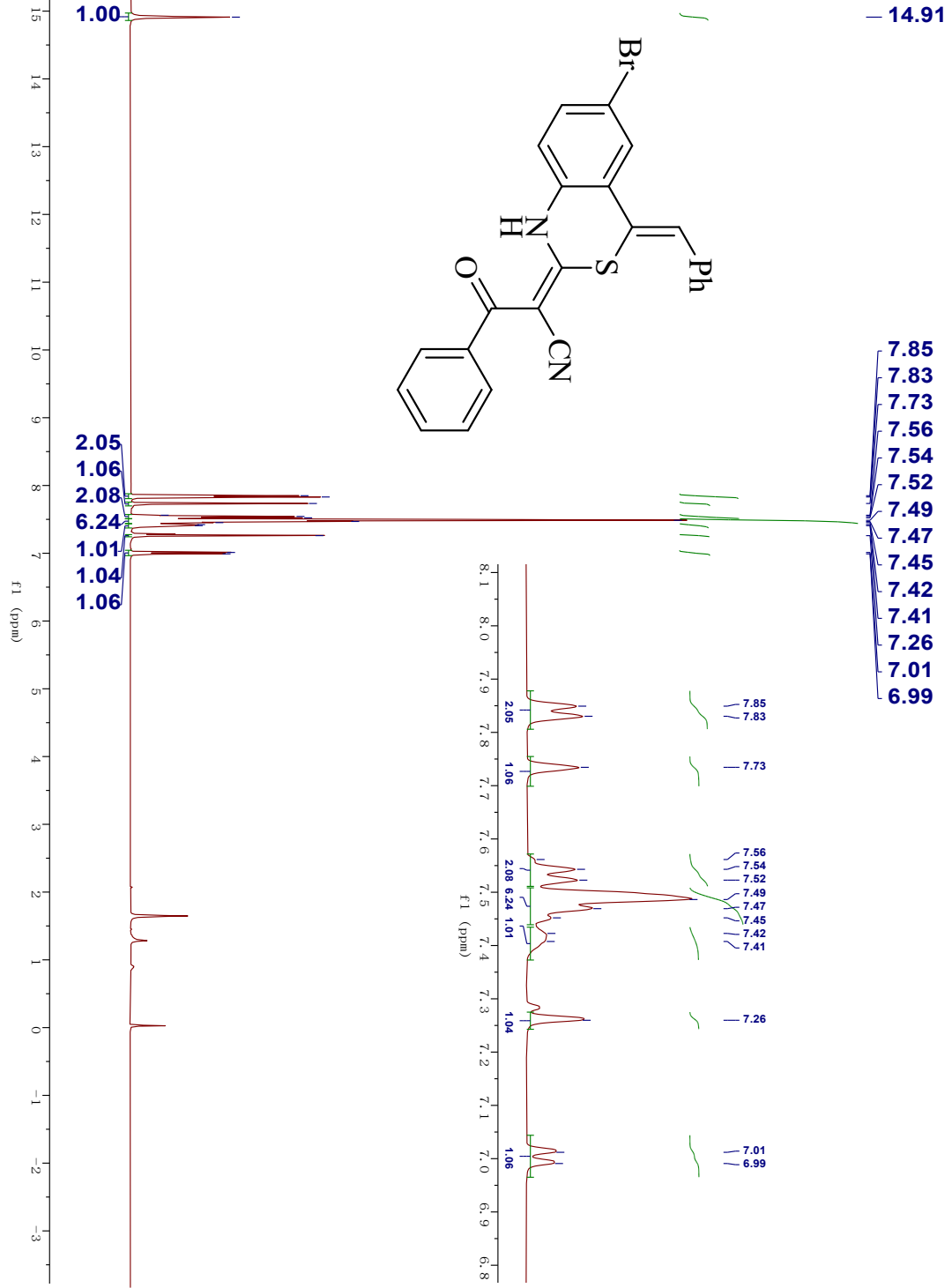
<sup>1</sup>H NMR spectrum of **3ga**



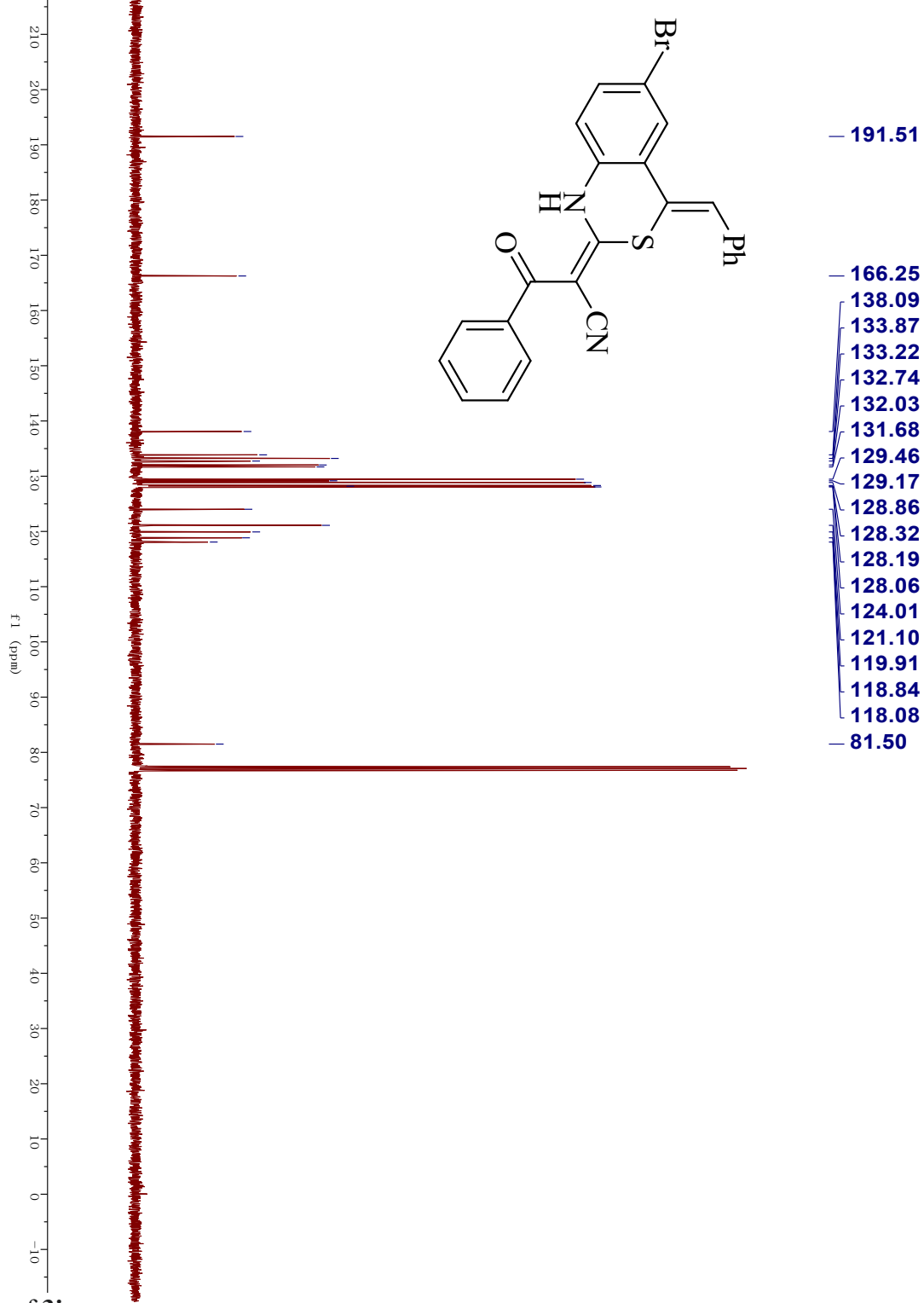
<sup>13</sup>C NMR spectrum of **3ga**



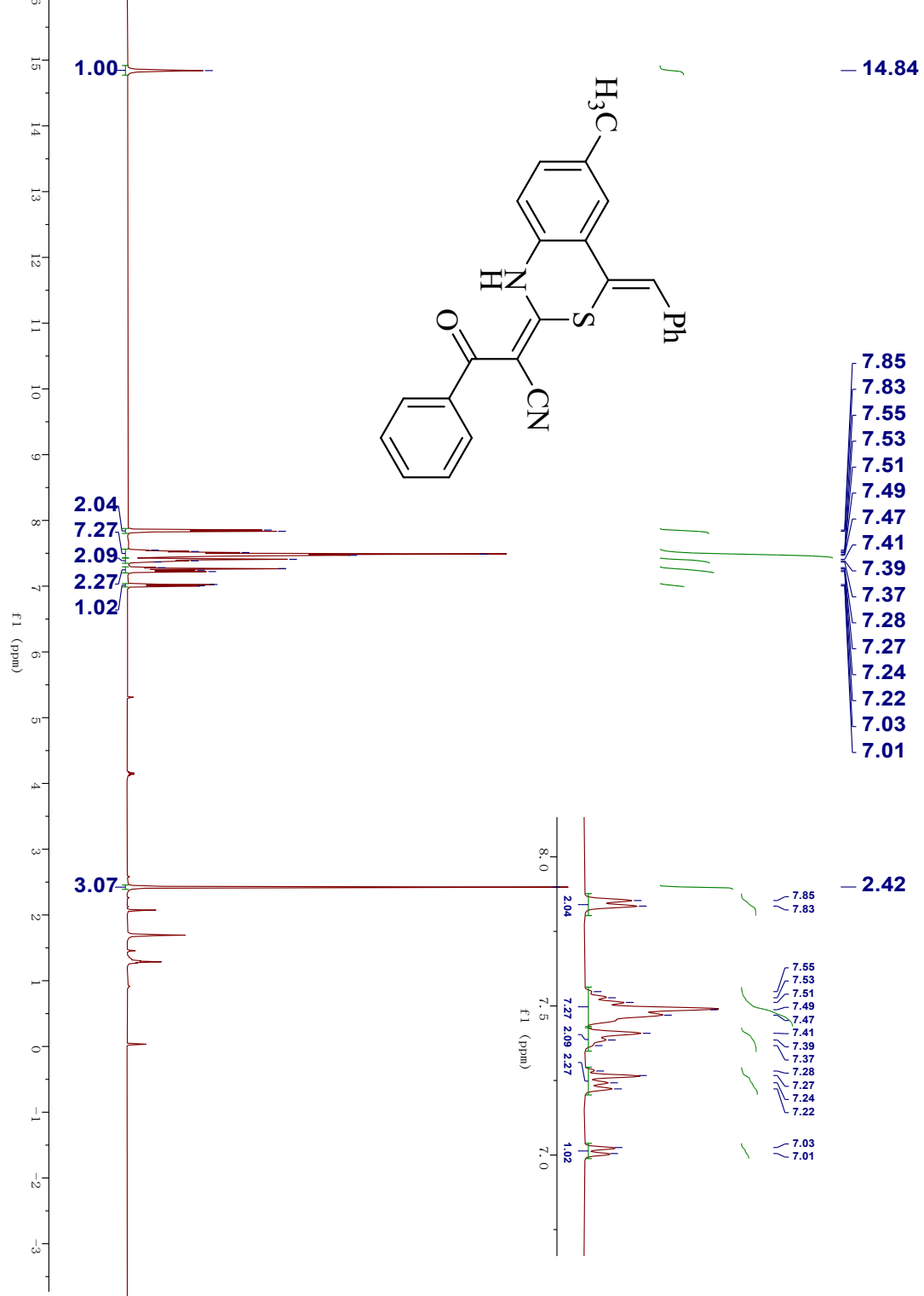
<sup>1</sup>H NMR spectrum of **3ha**



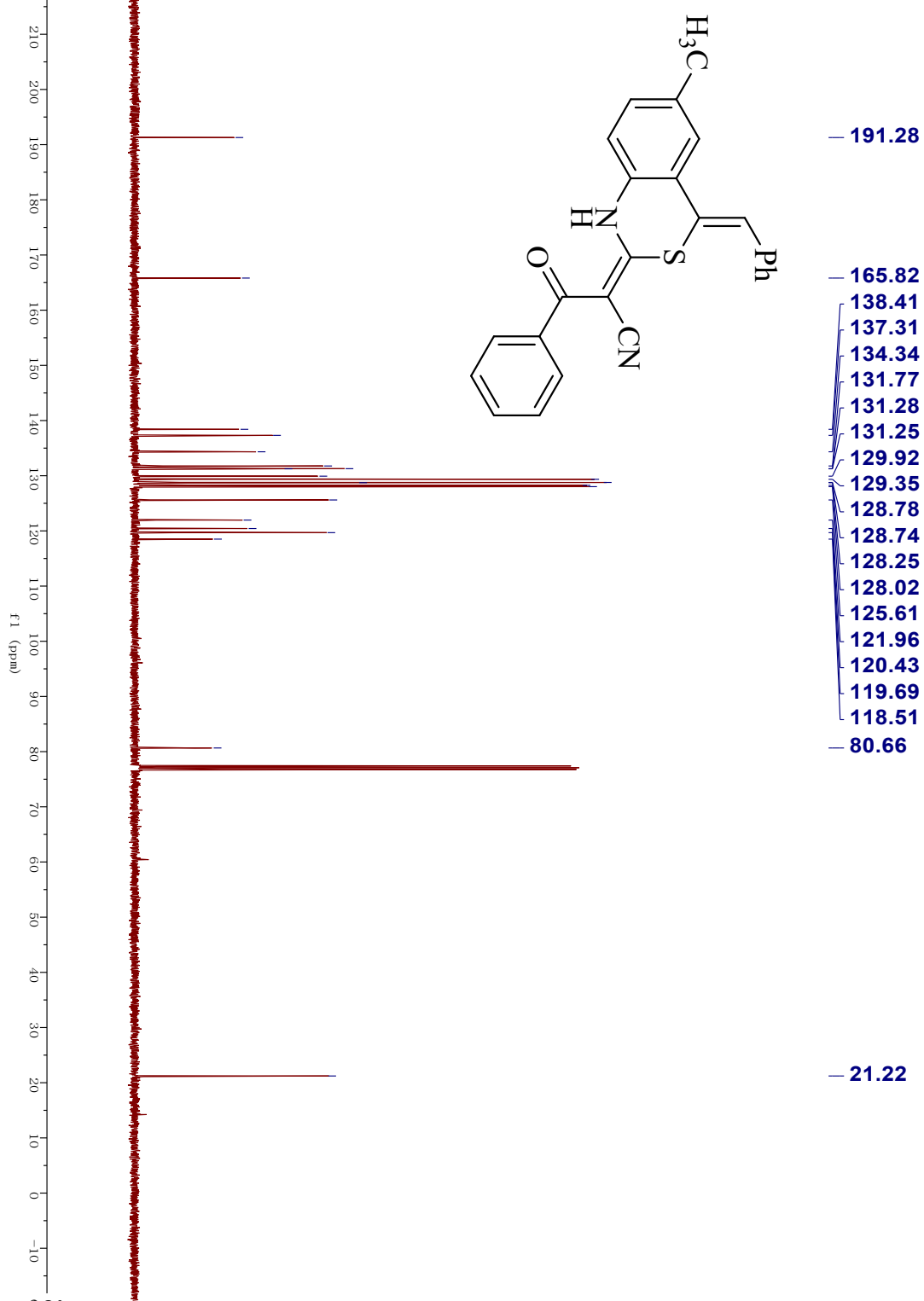
<sup>13</sup>C NMR spectrum of **3ha**



<sup>1</sup>H NMR spectrum of **3ia**

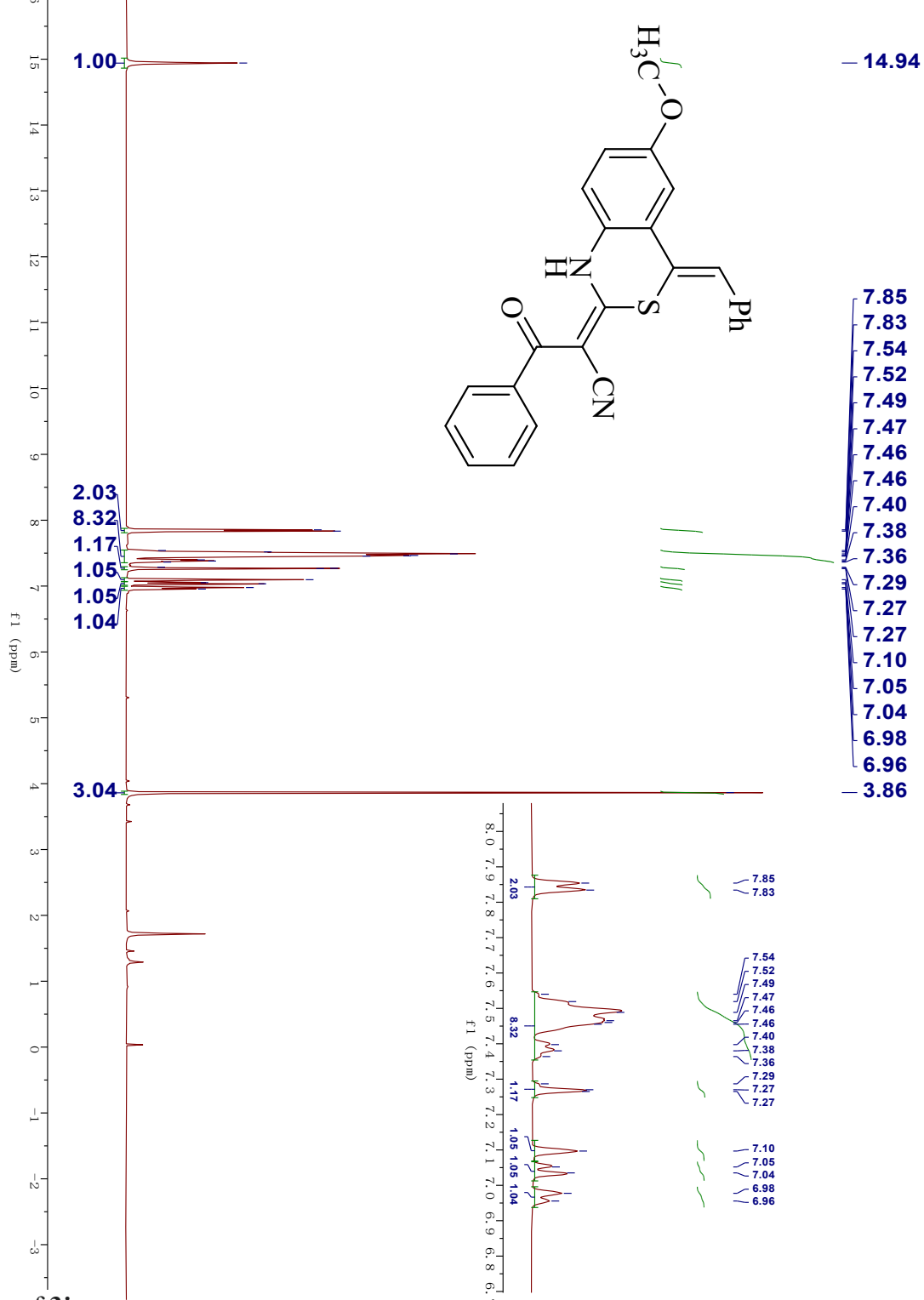


<sup>13</sup>C NMR spectrum of **3ia**

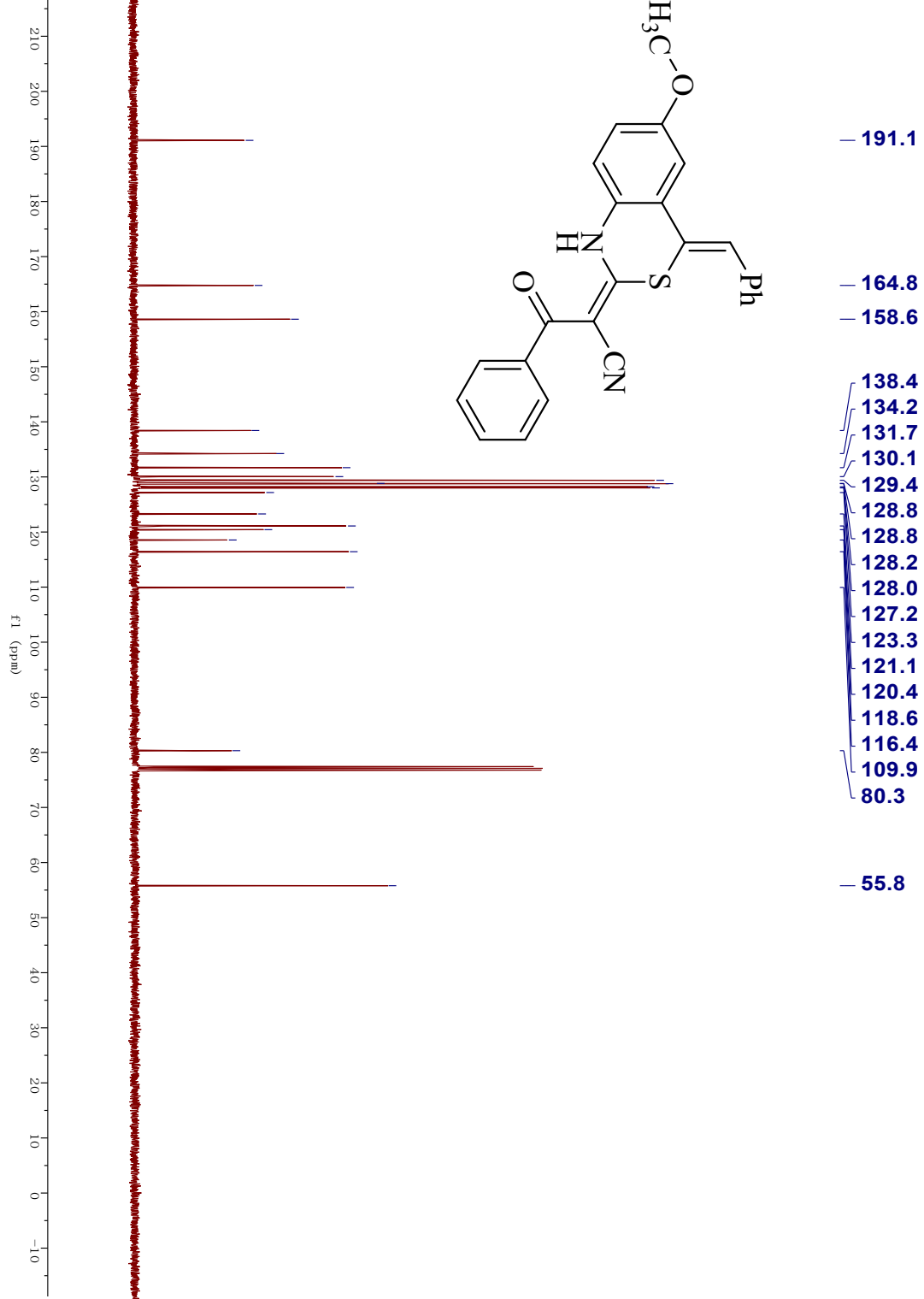


<sup>1</sup>H NMR spectrum of **3ja**

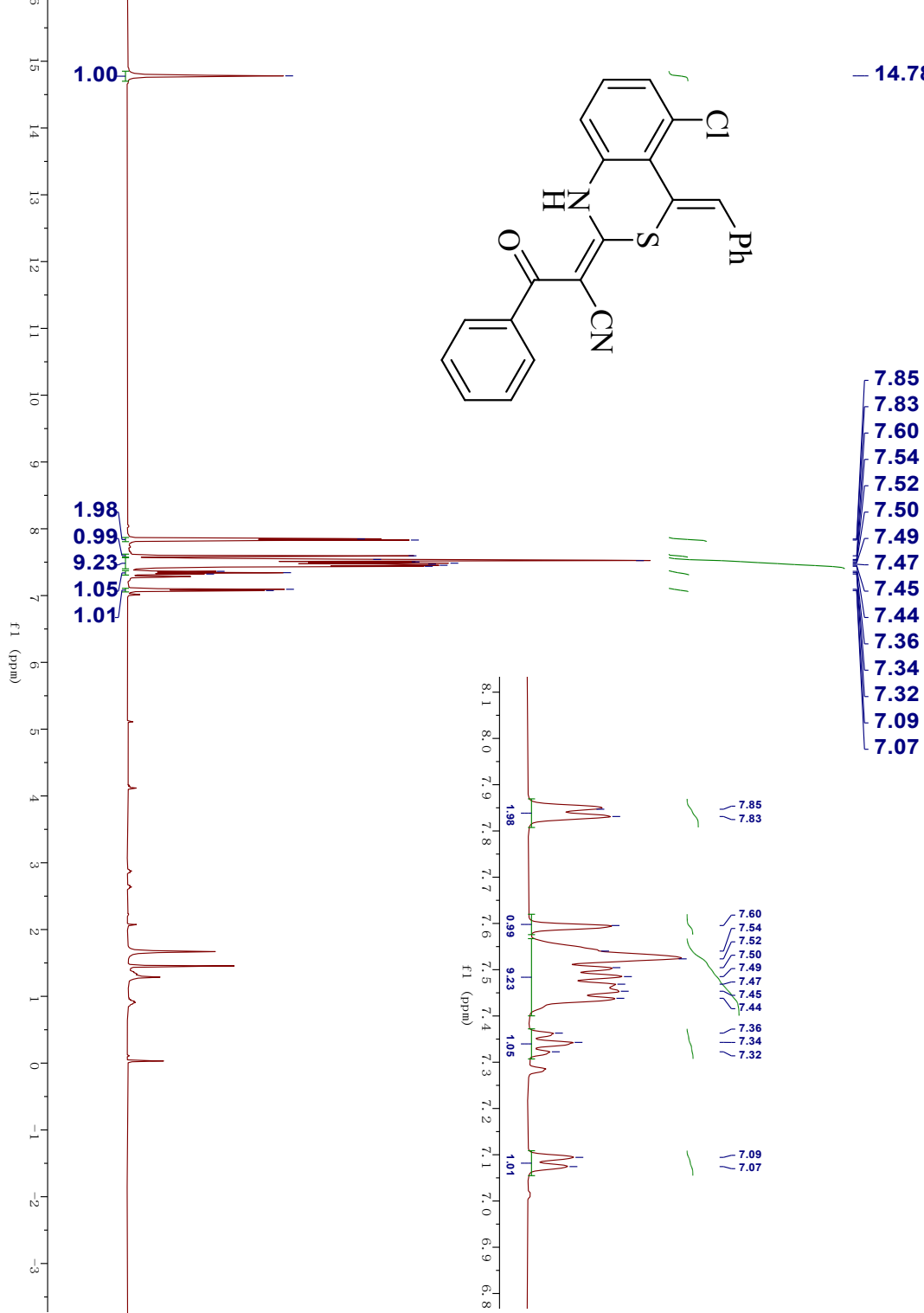




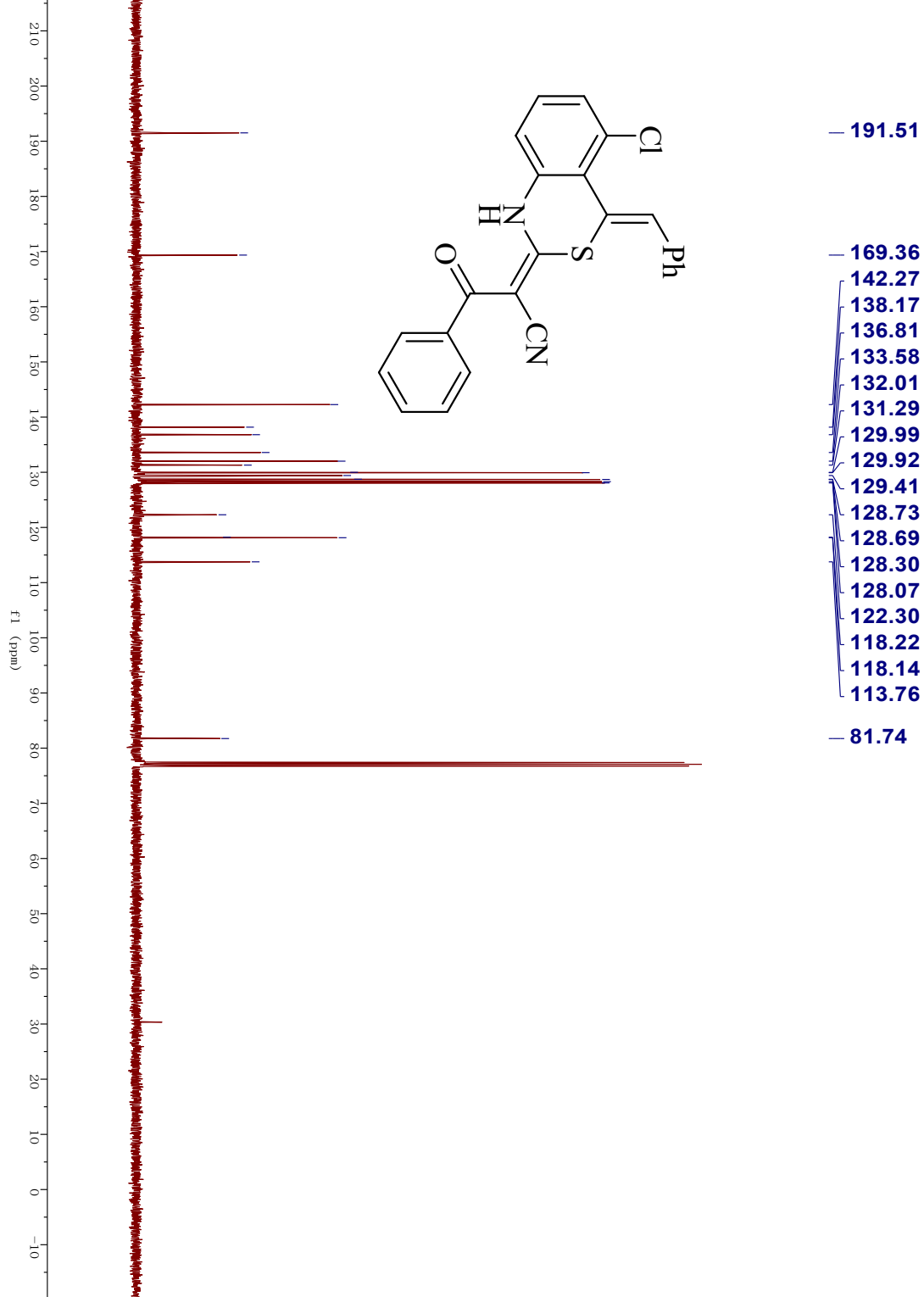
$^{13}\text{C}$  NMR spectrum of **3ja**



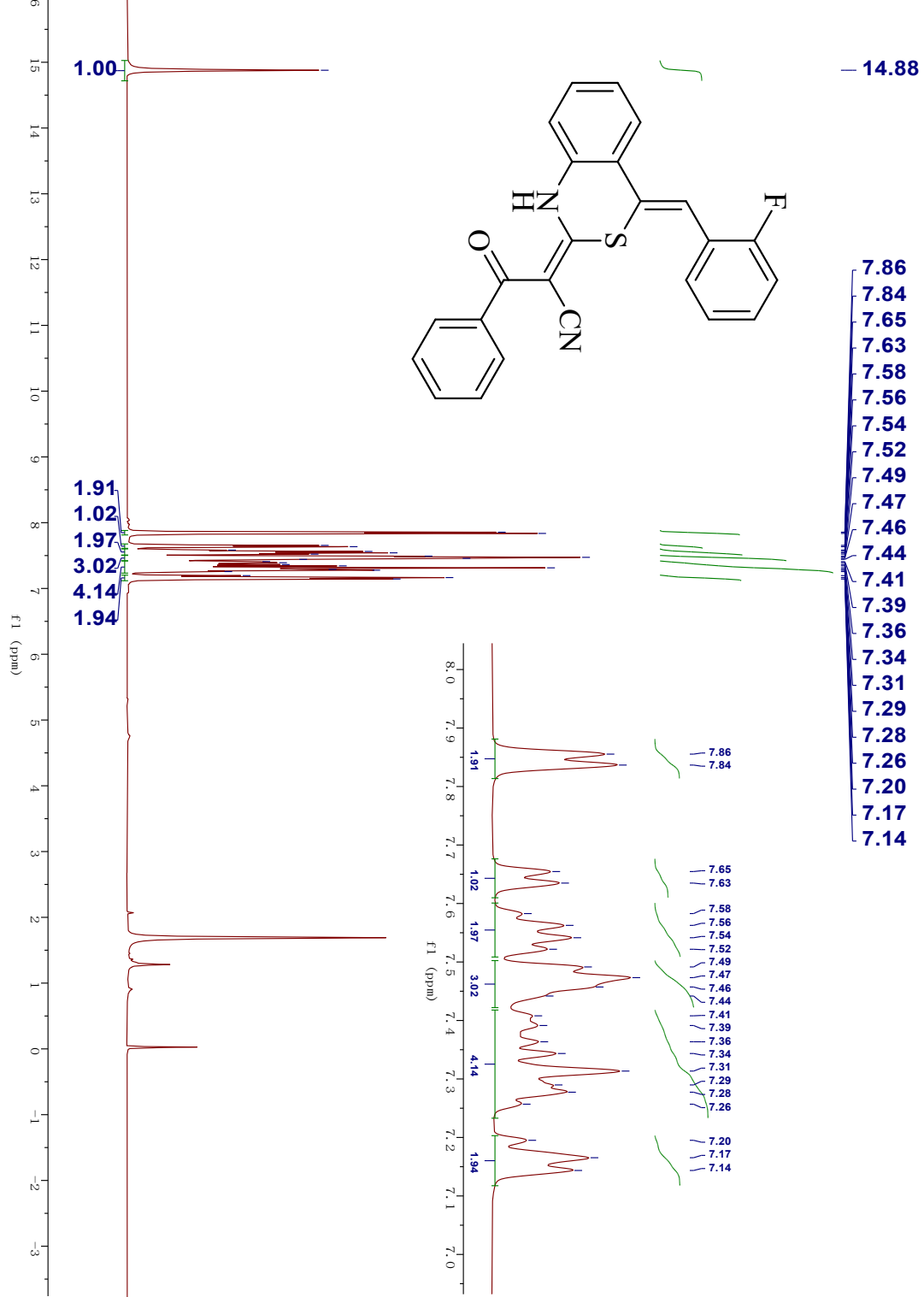
<sup>1</sup>H NMR spectrum of **3ka**



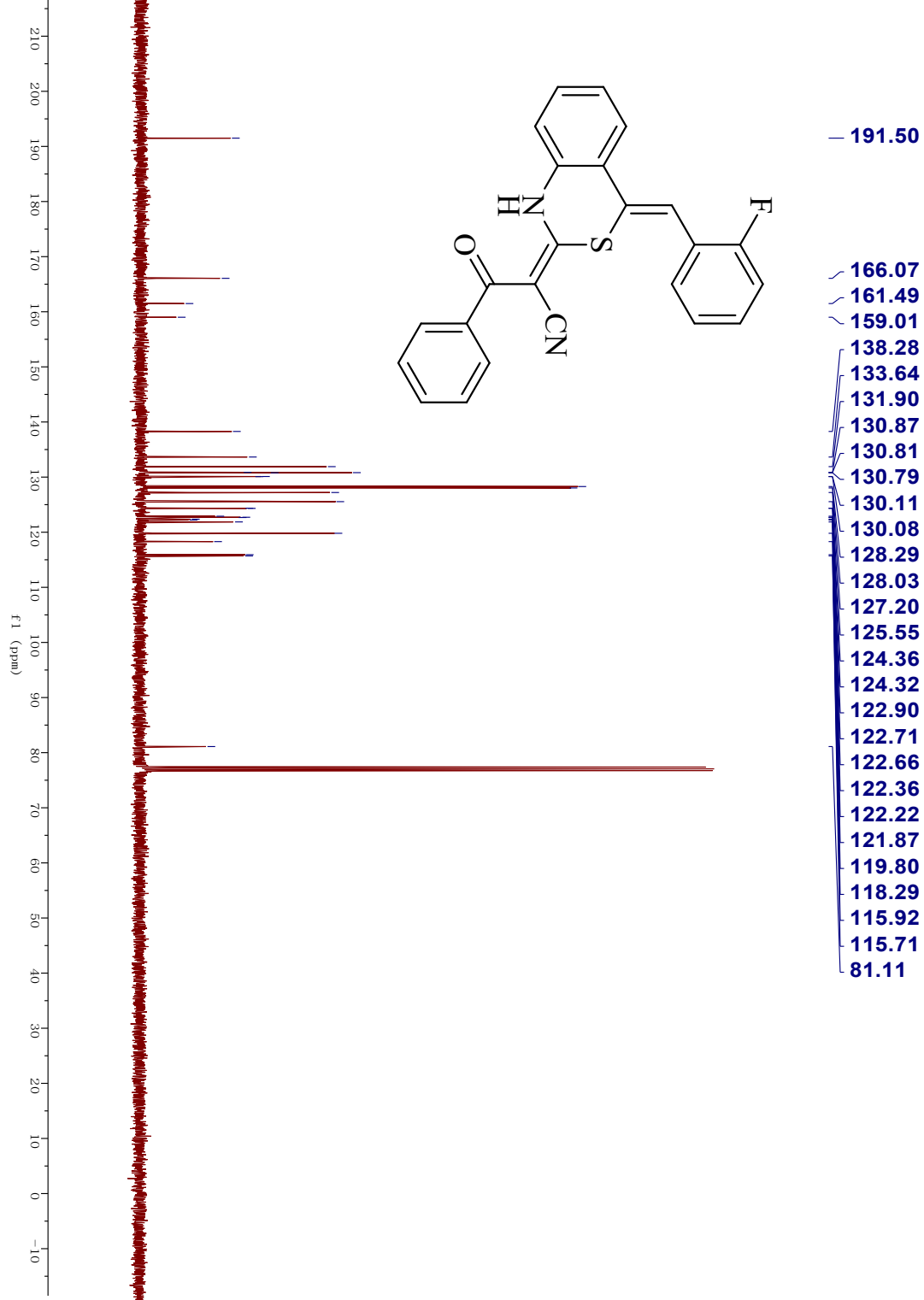
<sup>13</sup>C NMR spectrum of **3ka**



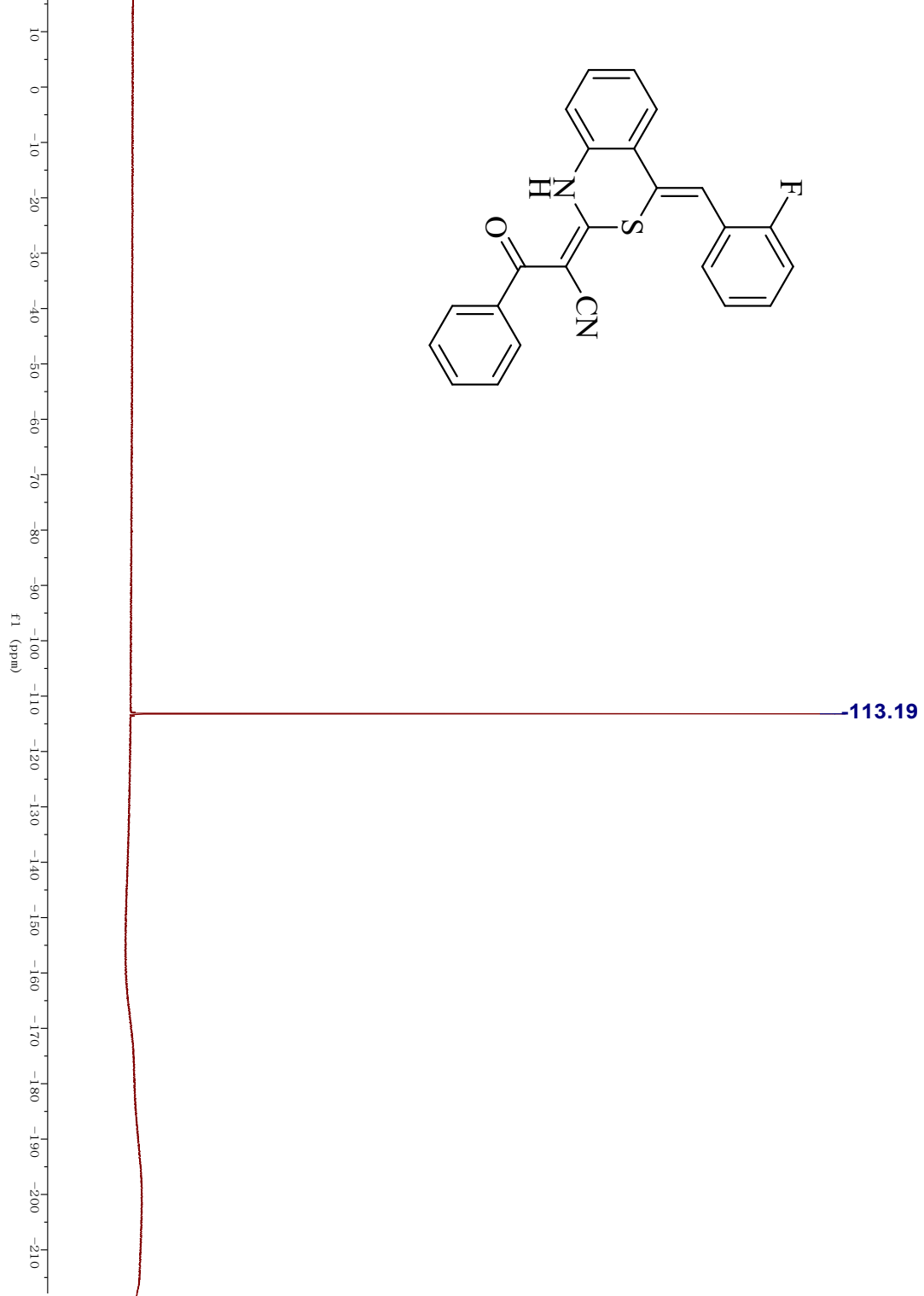
<sup>1</sup>H NMR spectrum of 3la



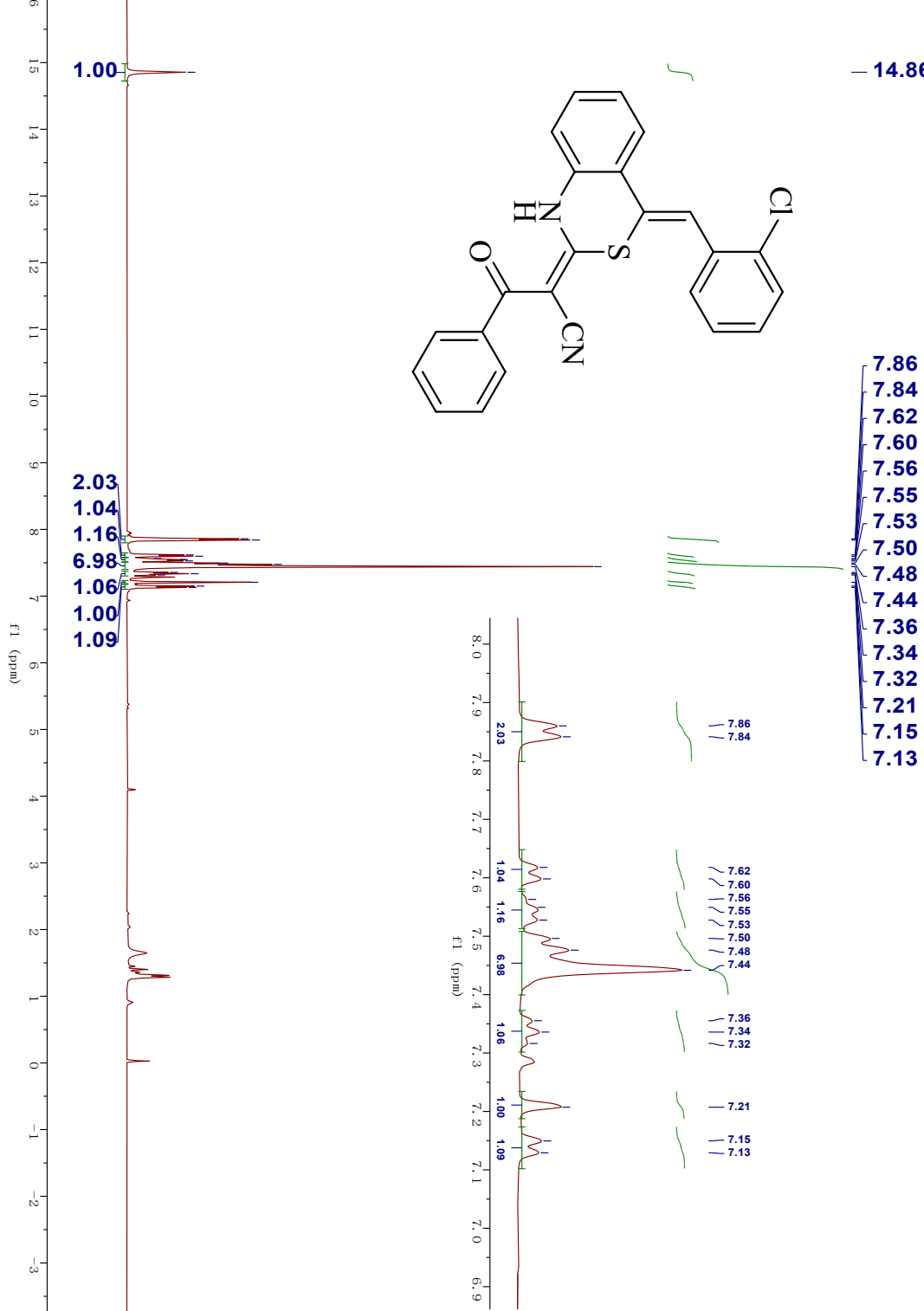
<sup>13</sup>C NMR spectrum of **31a**



<sup>19</sup>F NMR spectrum of **3la**

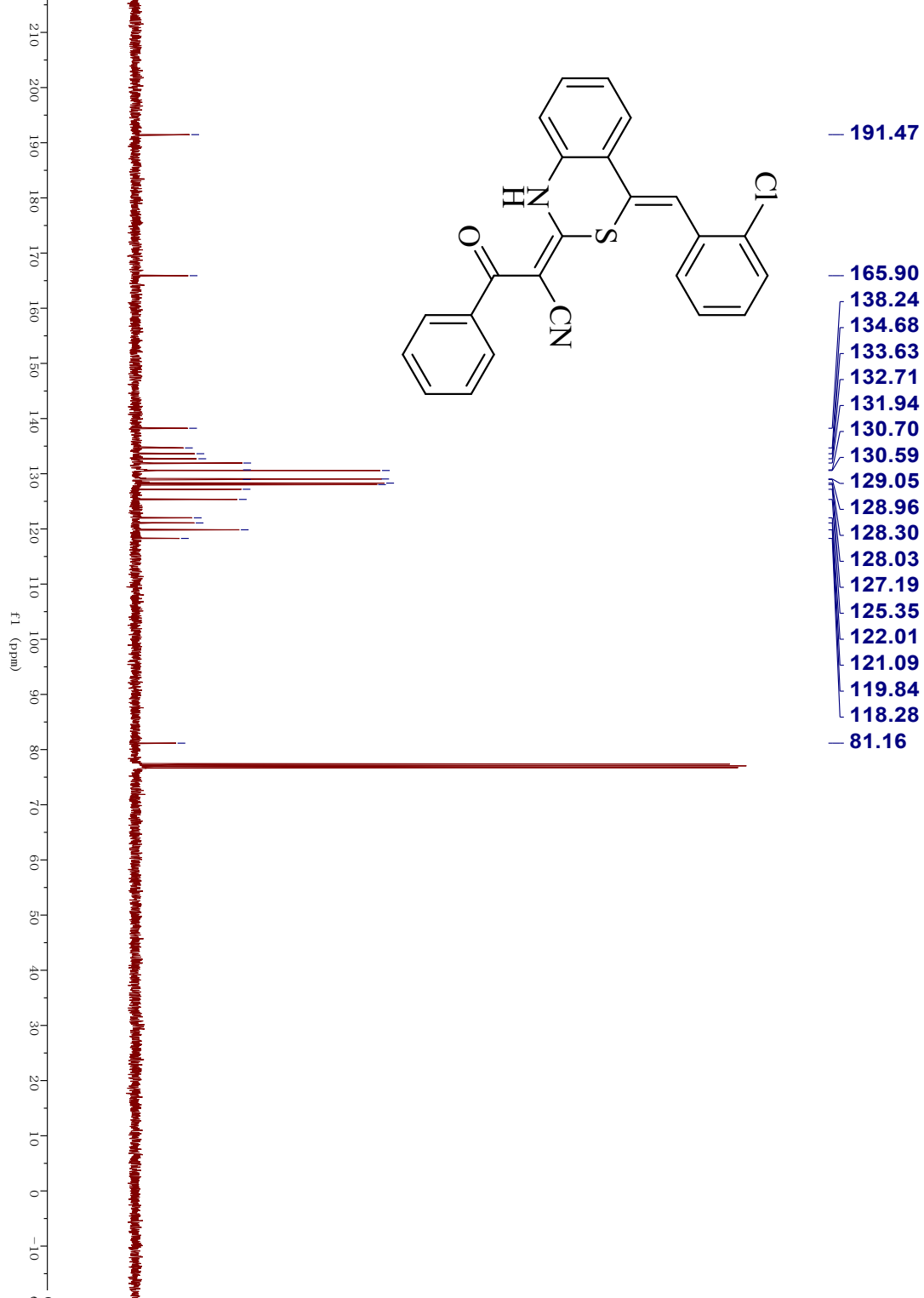


$^1\text{H}$  NMR spectrum of **3ma**

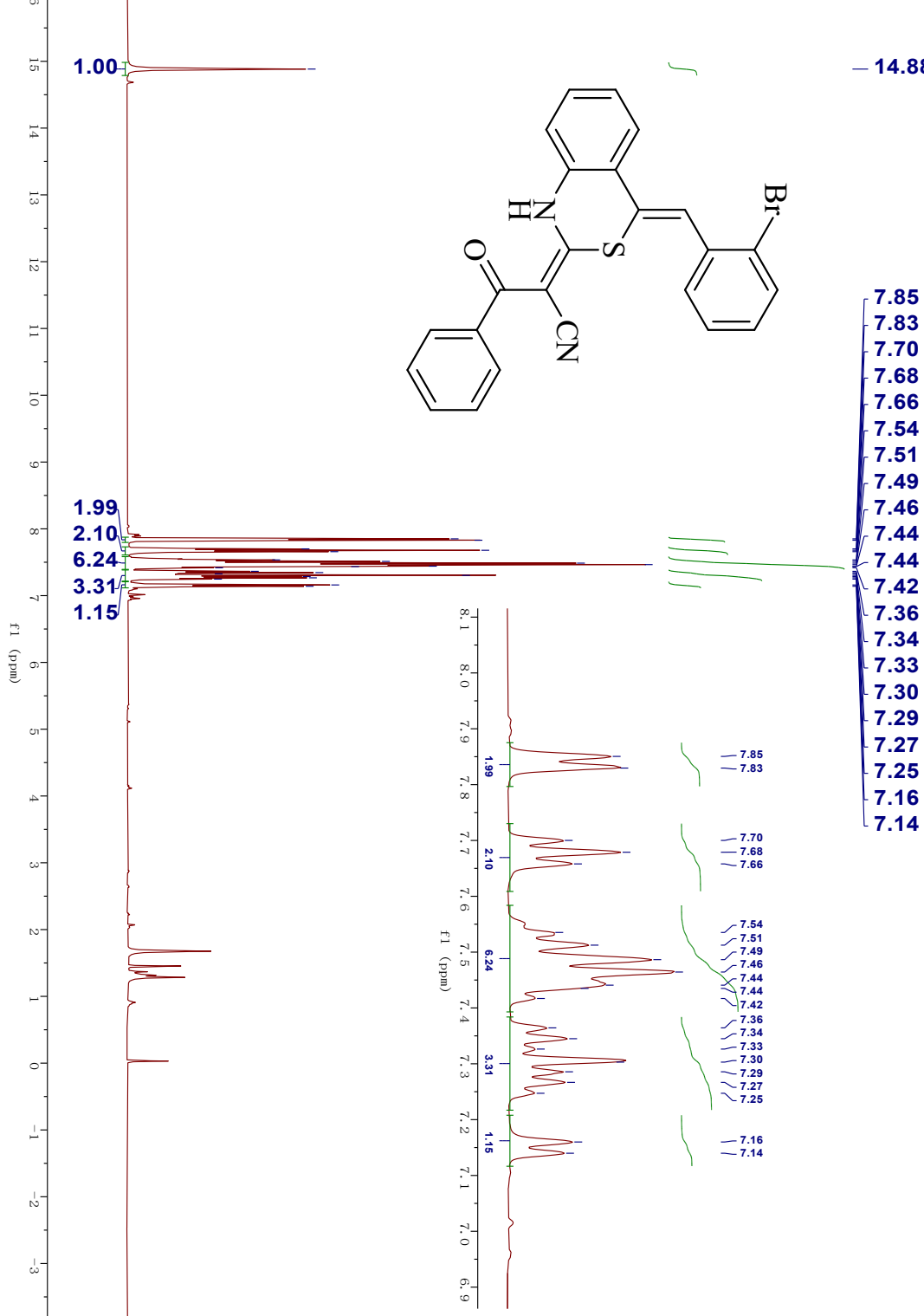


<sup>13</sup>C NMR spectrum of **3ma**

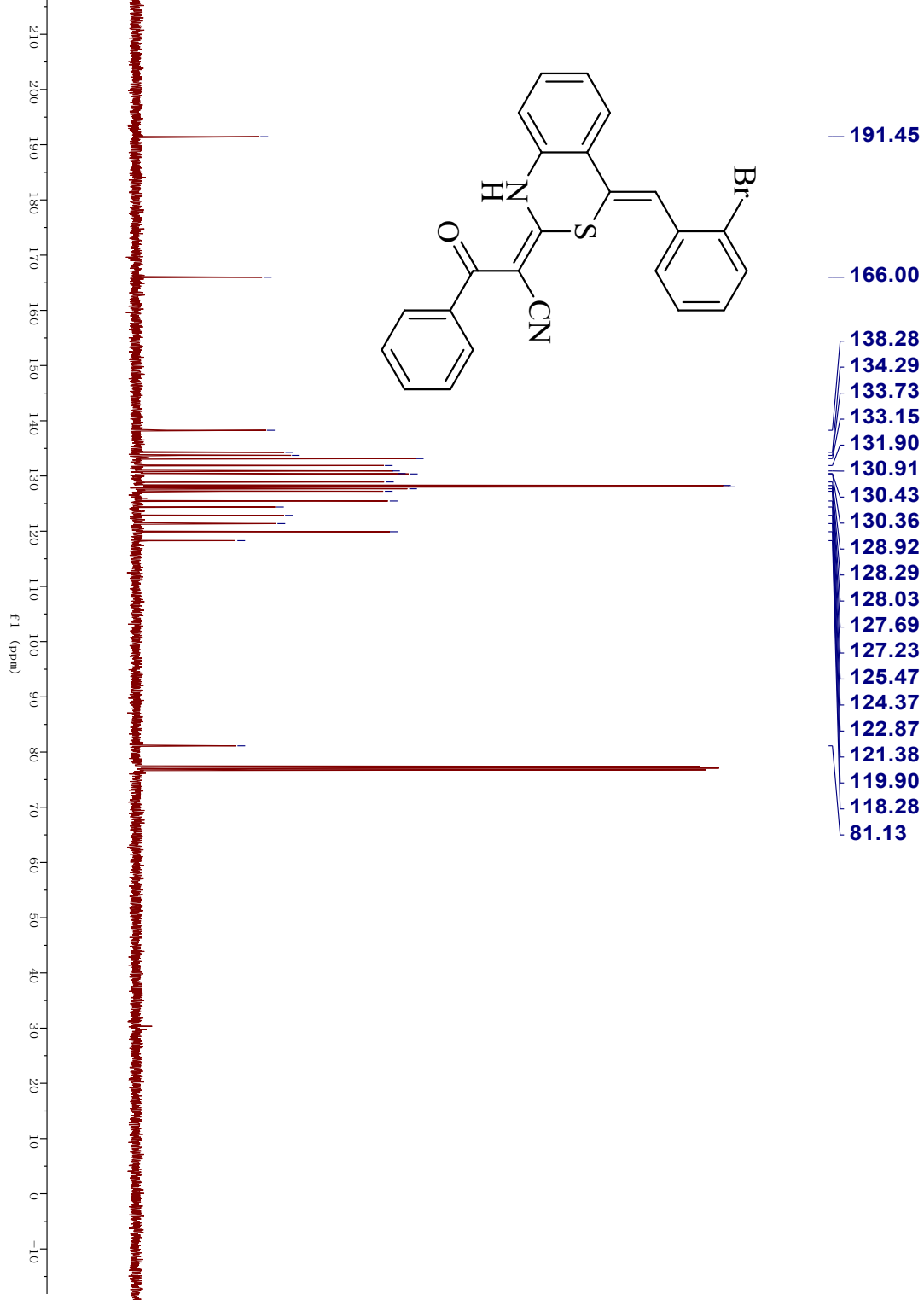




<sup>1</sup>H NMR spectrum of **3na**

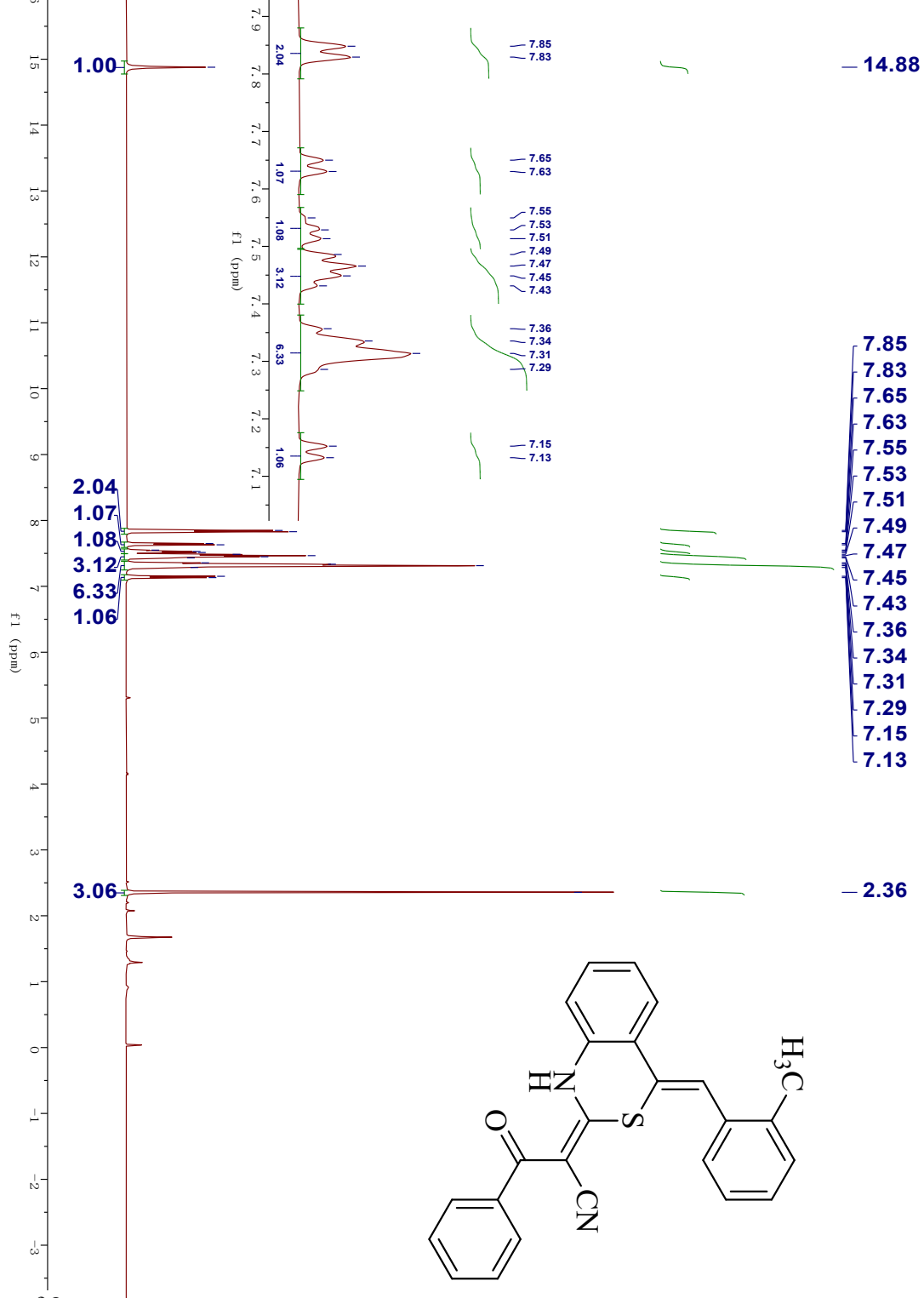


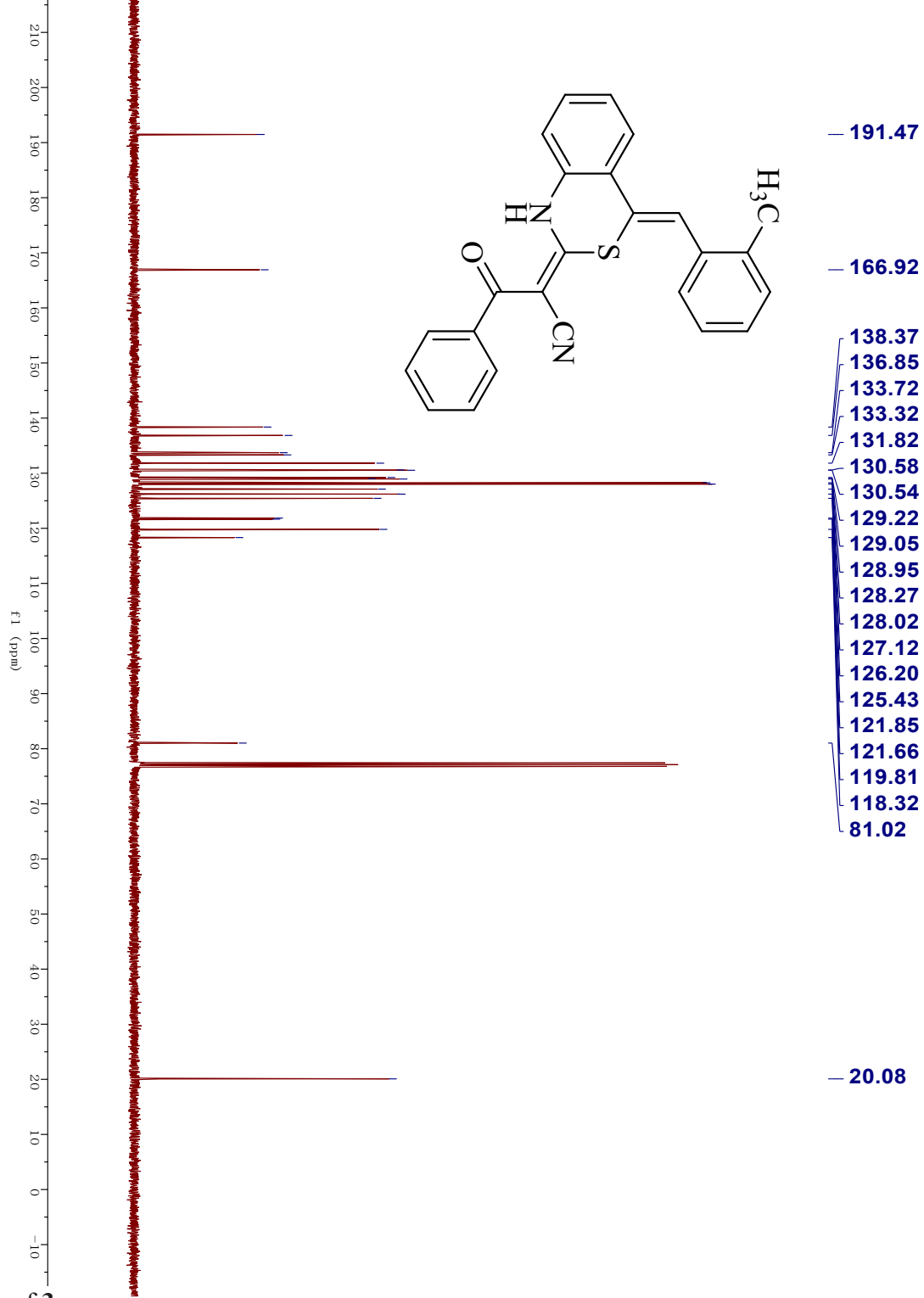
<sup>13</sup>C NMR spectrum of **3na**



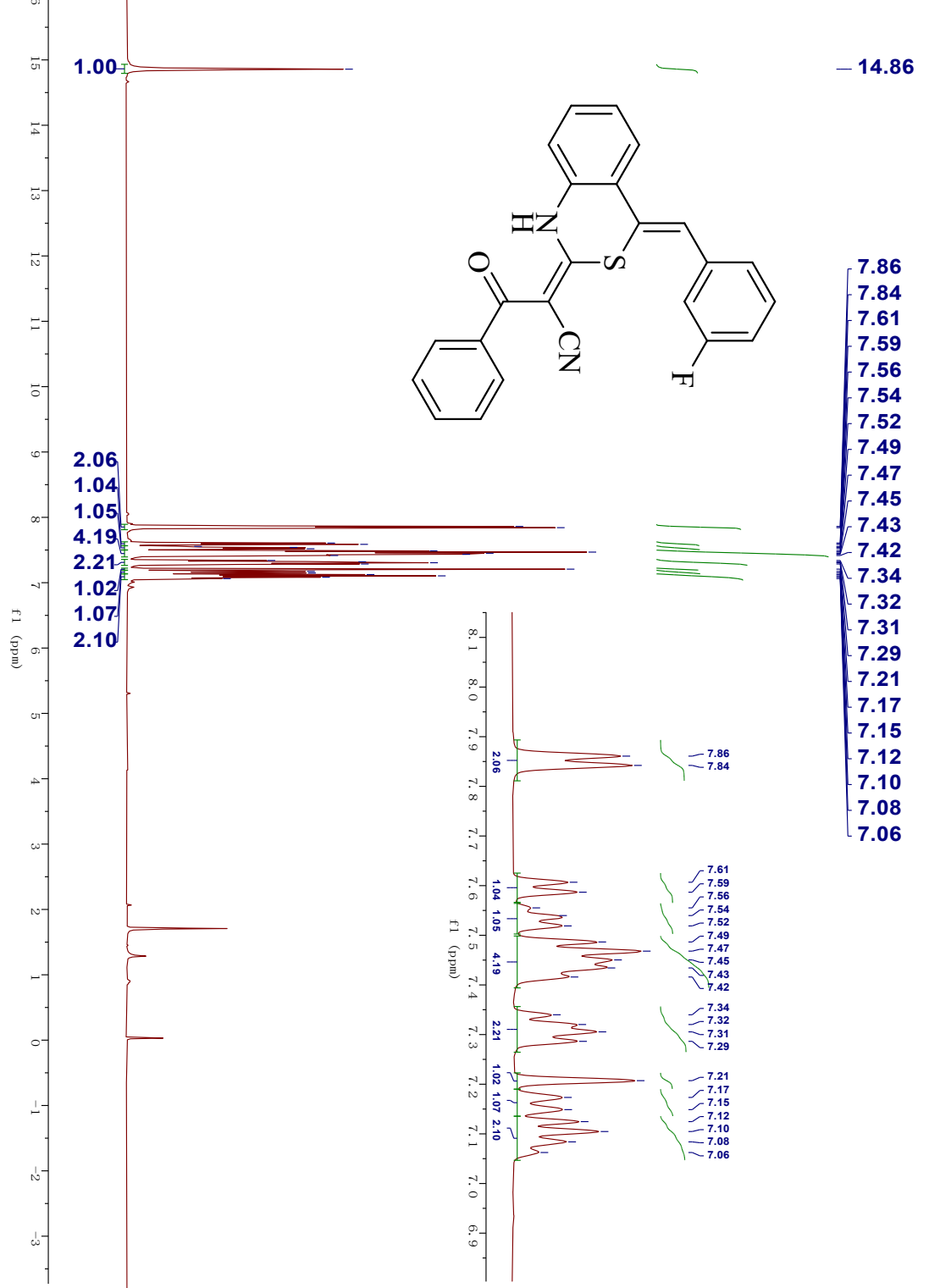
<sup>1</sup>H NMR spectrum of **30a**

<sup>13</sup>C NMR spectrum of **30a**

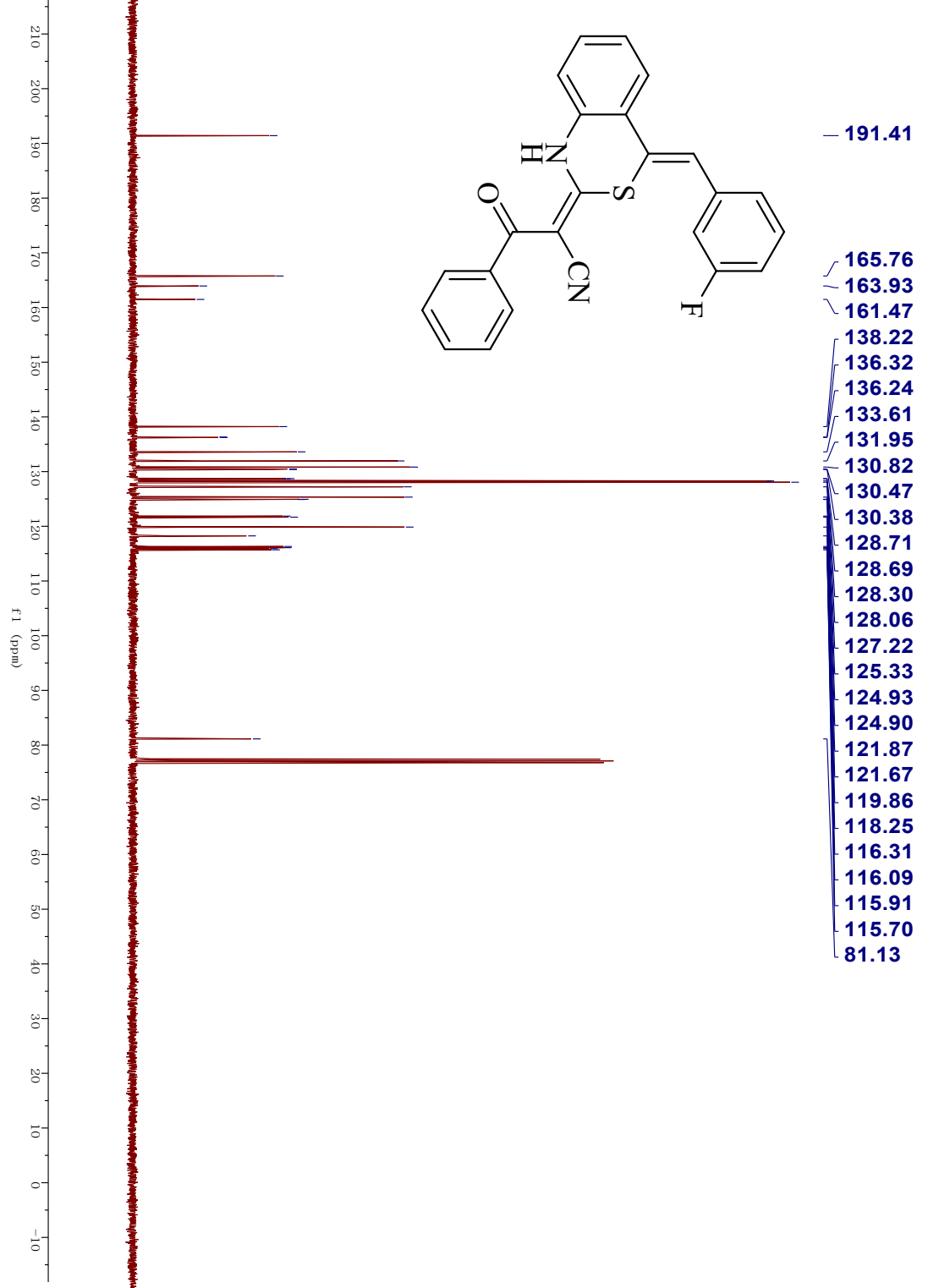




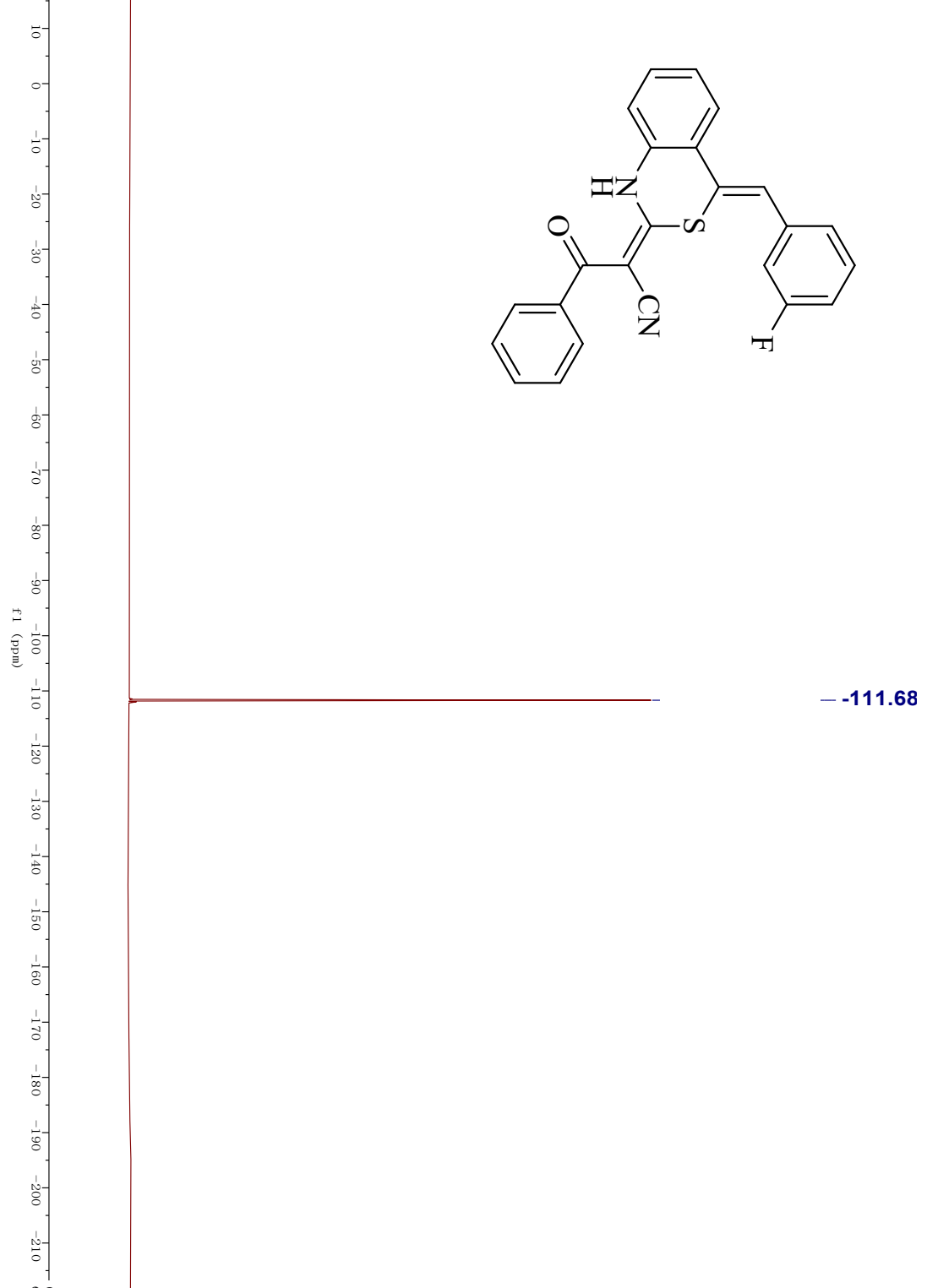
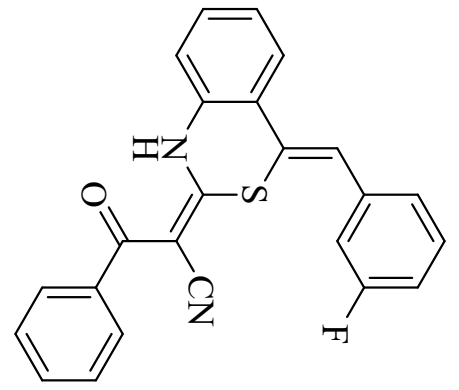
<sup>1</sup>H NMR spectrum of **3pa**



<sup>13</sup>C NMR spectrum of **3pa**

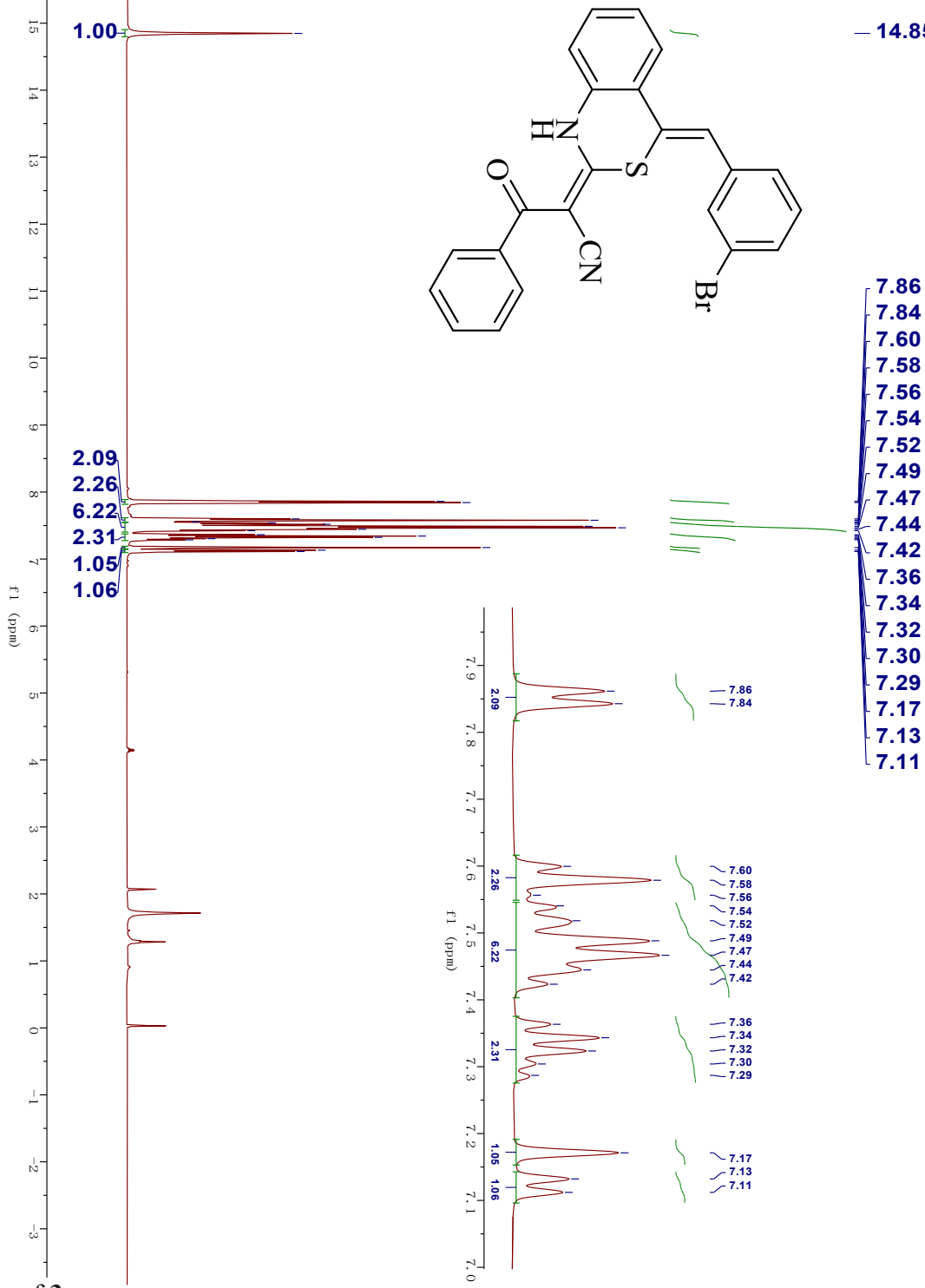


<sup>19</sup>F NMR spectrum of **3pa**

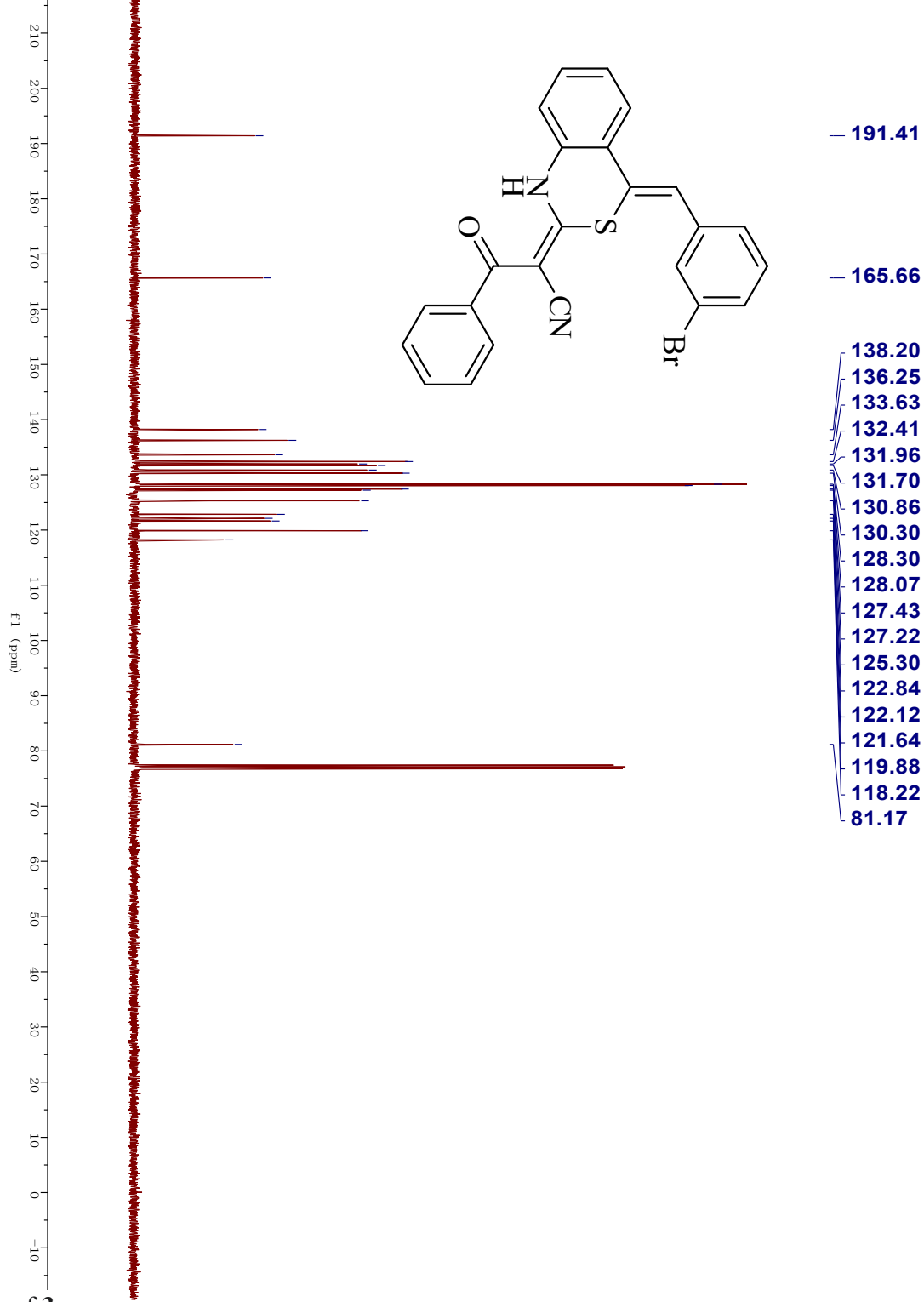


$^1\text{H}$  NMR spectrum of **3qa**

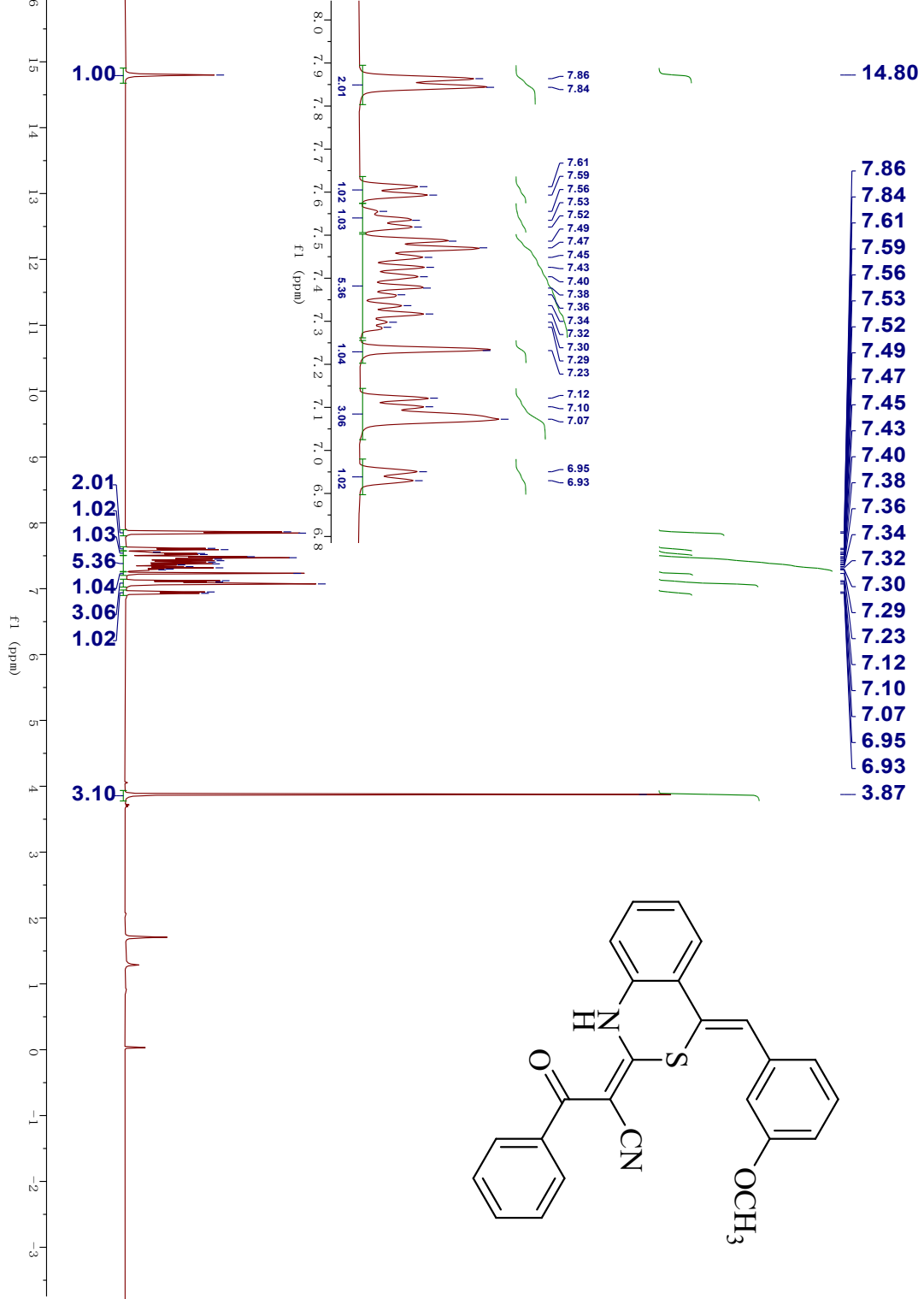




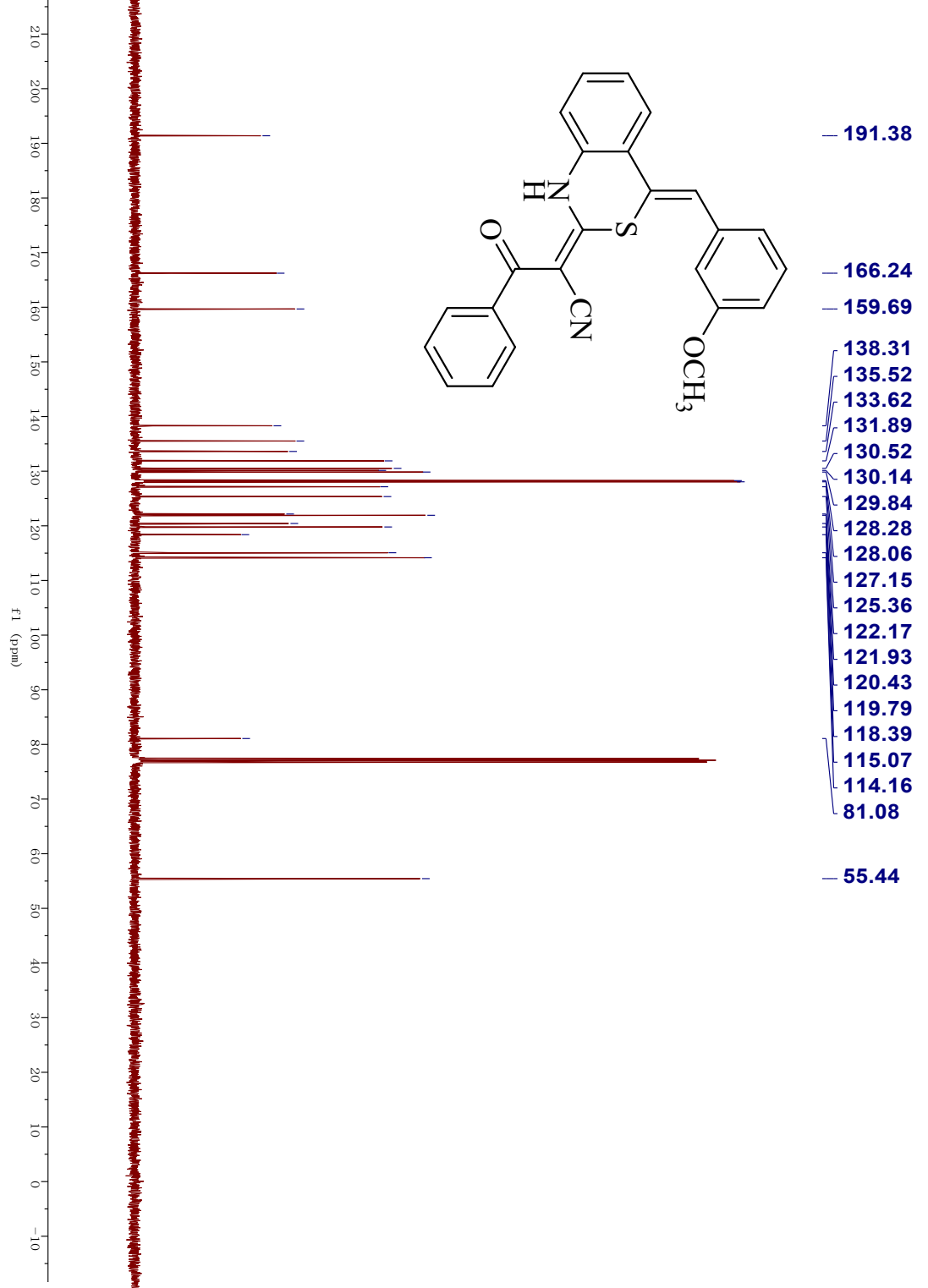
<sup>13</sup>C NMR spectrum of **3qa**



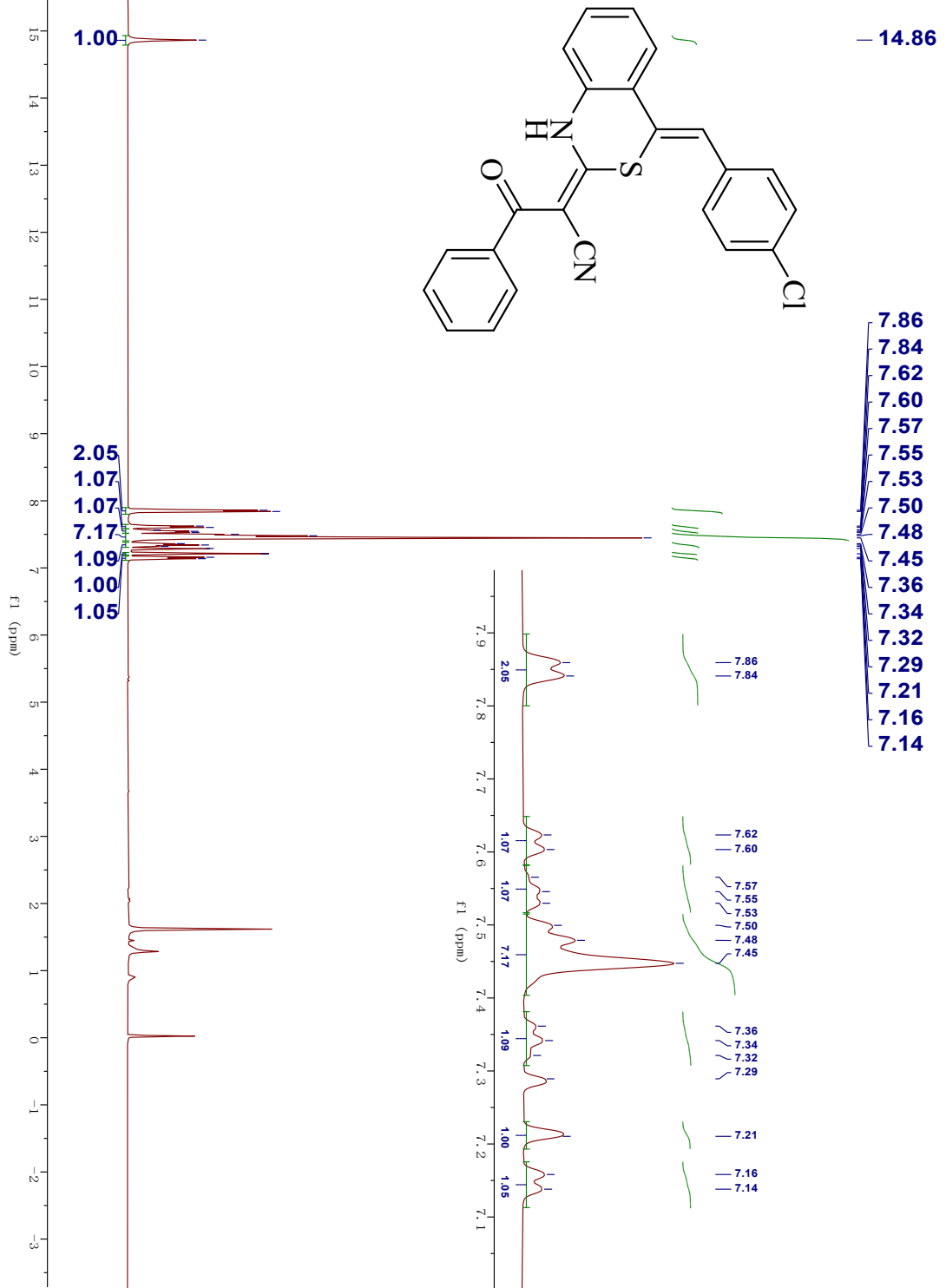
<sup>1</sup>H NMR spectrum of **3ra**



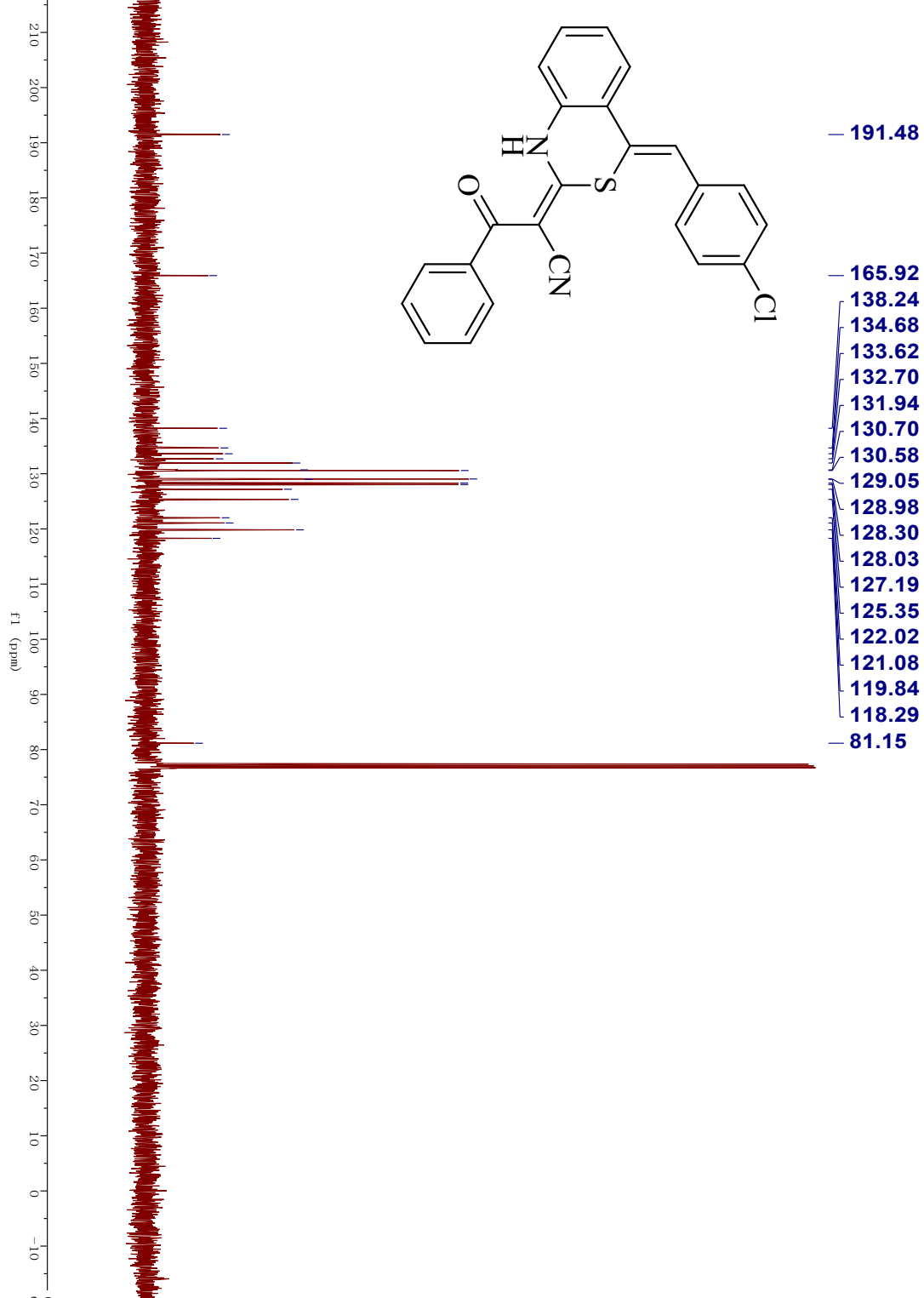
<sup>13</sup>C NMR spectrum of **3ra**



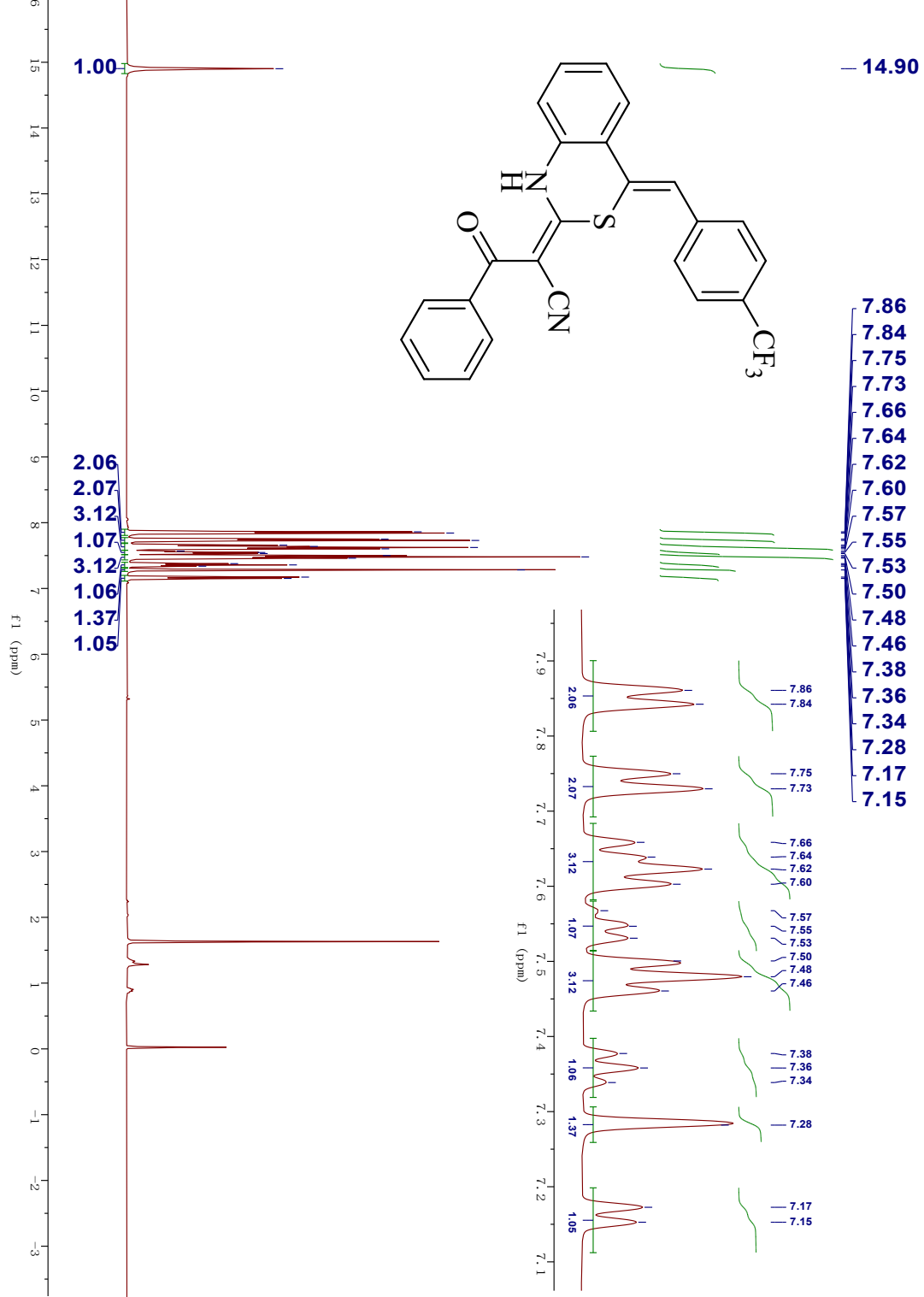
<sup>1</sup>H NMR spectrum of **3sa**



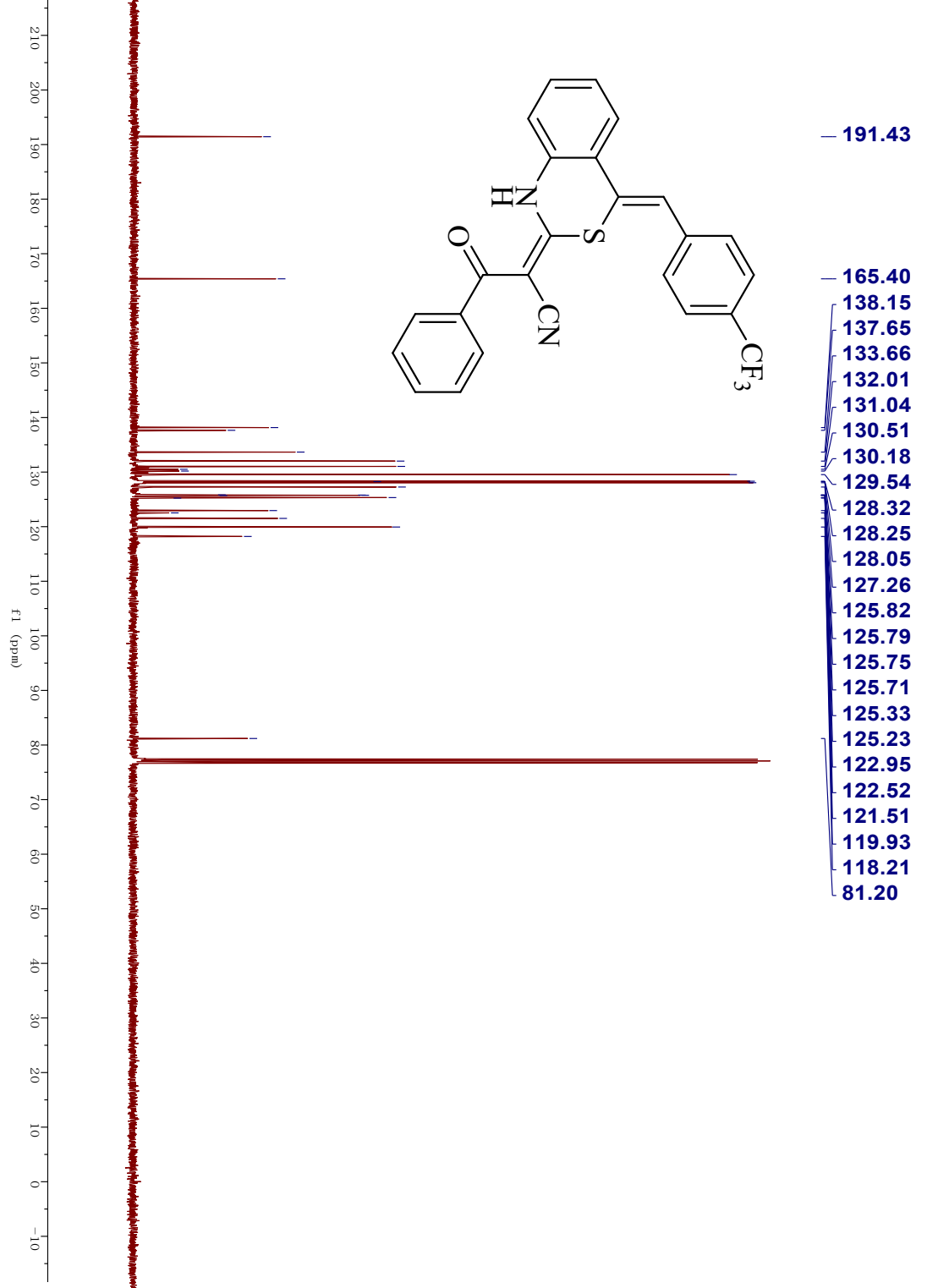
<sup>13</sup>C NMR spectrum of **3sa**



<sup>1</sup>H NMR spectrum of **3ta**

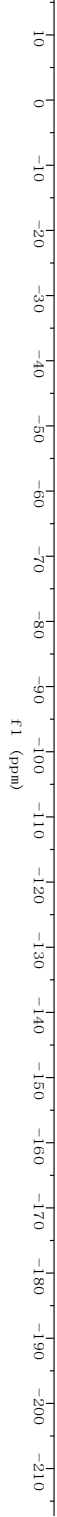
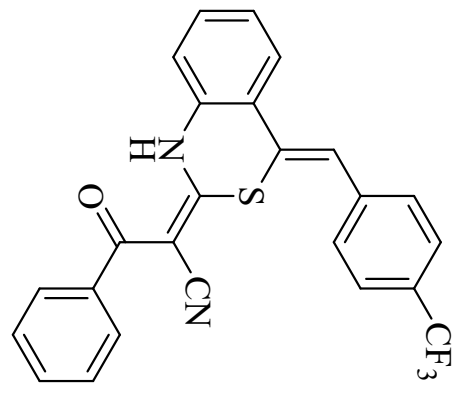


<sup>13</sup>C NMR spectrum of **3ta**



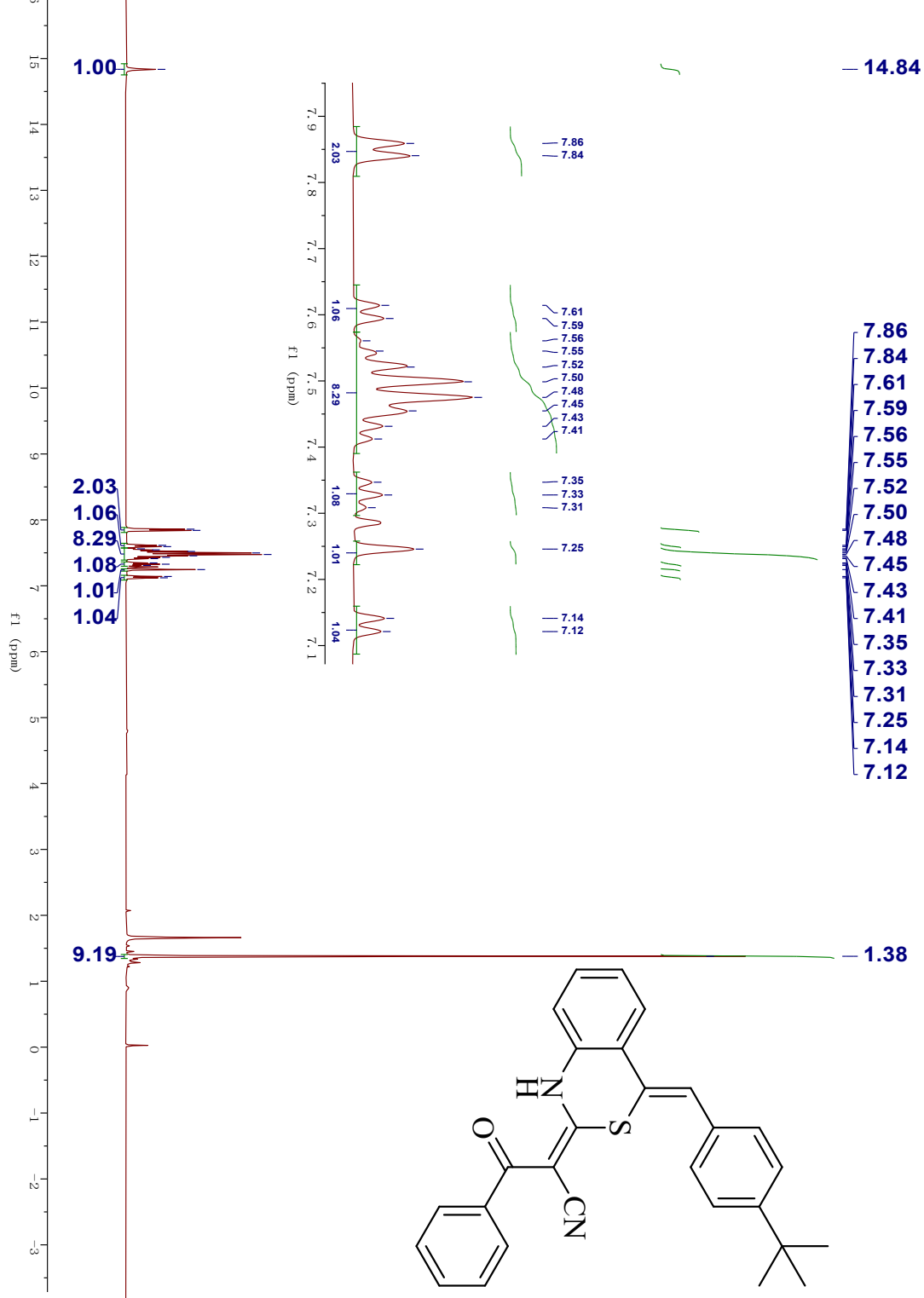
<sup>19</sup>F NMR spectrum of **3ta**



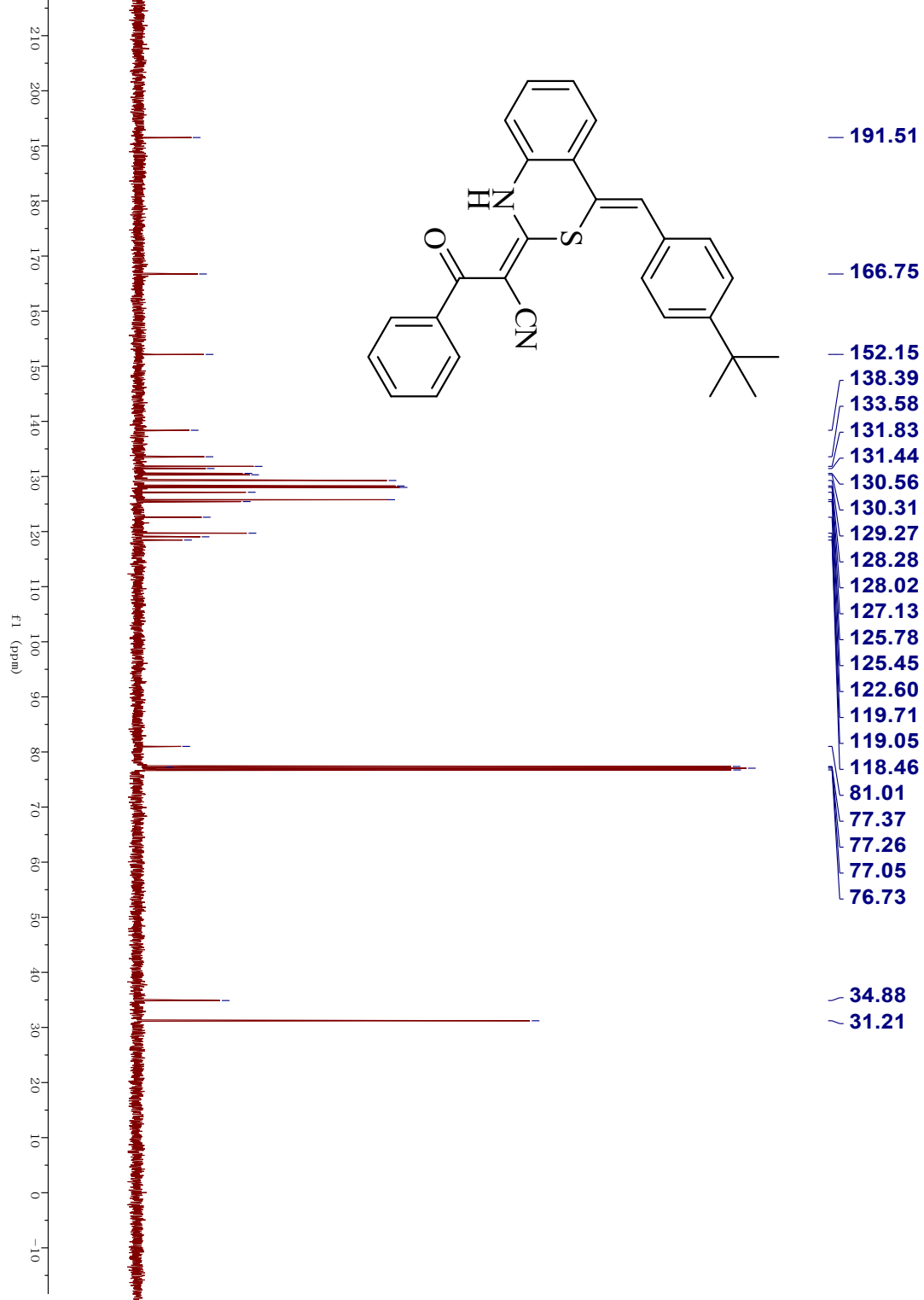


— -62.68

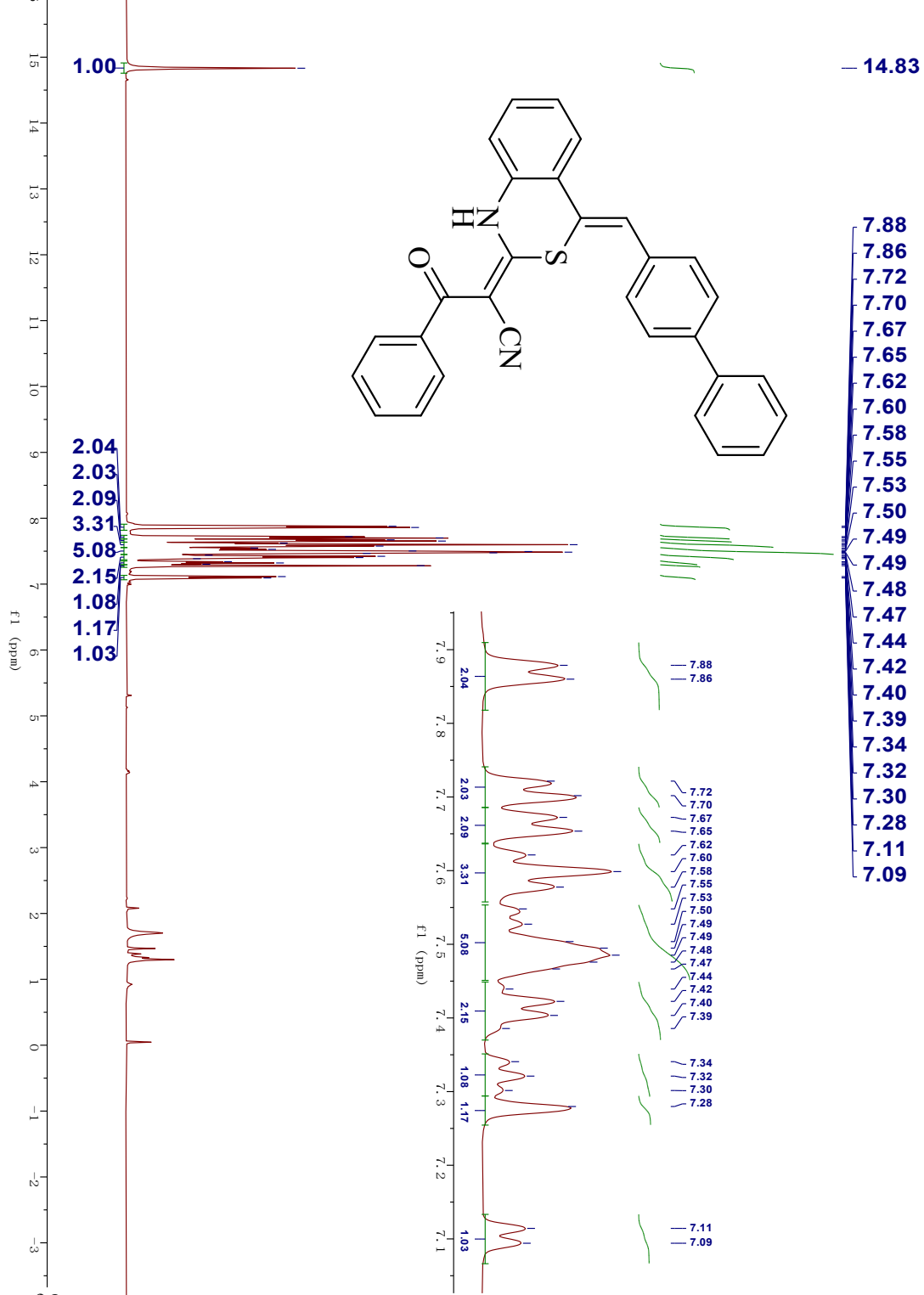
<sup>1</sup>H NMR spectrum of **3ua**



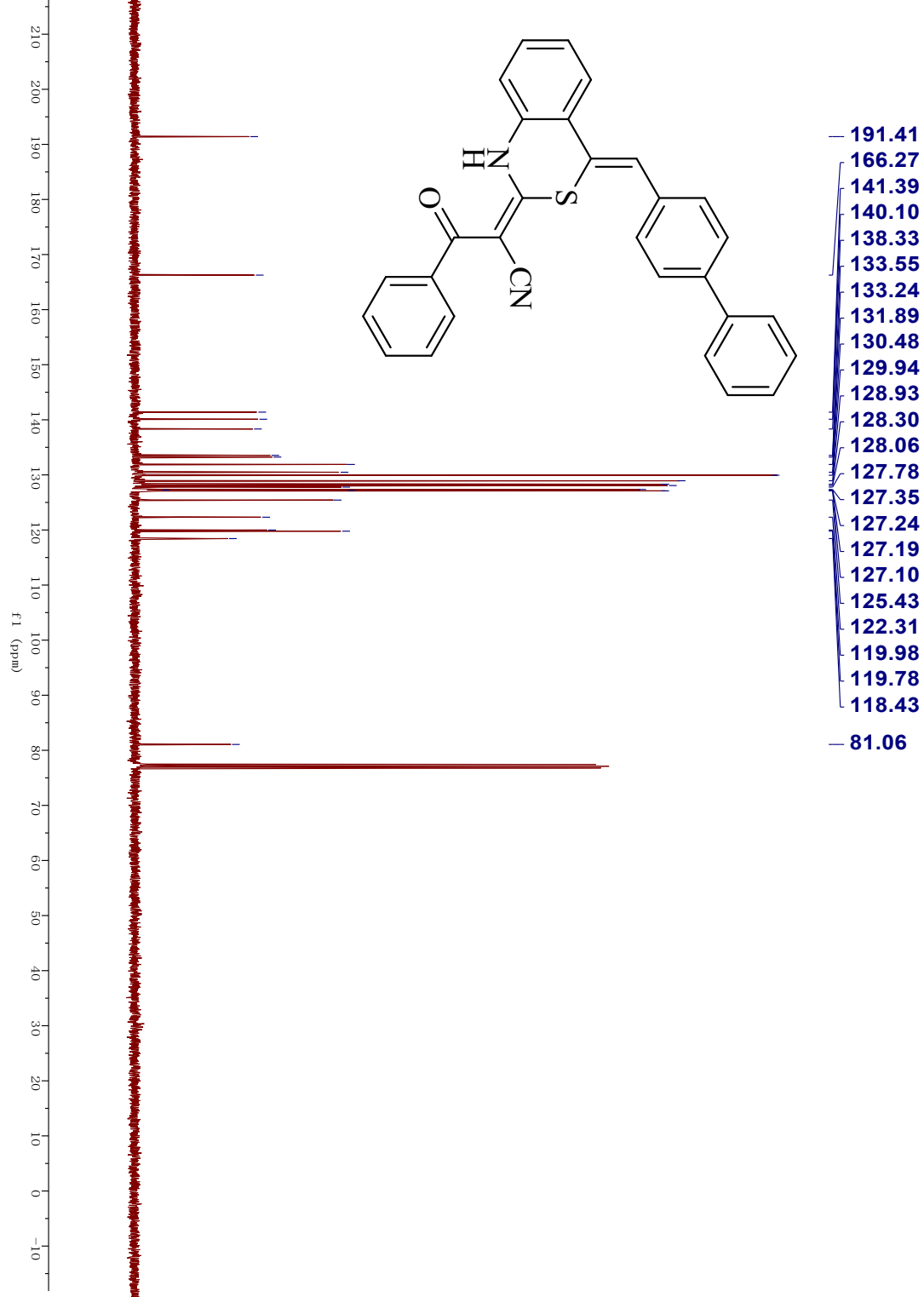
<sup>13</sup>C NMR spectrum of **3ua**



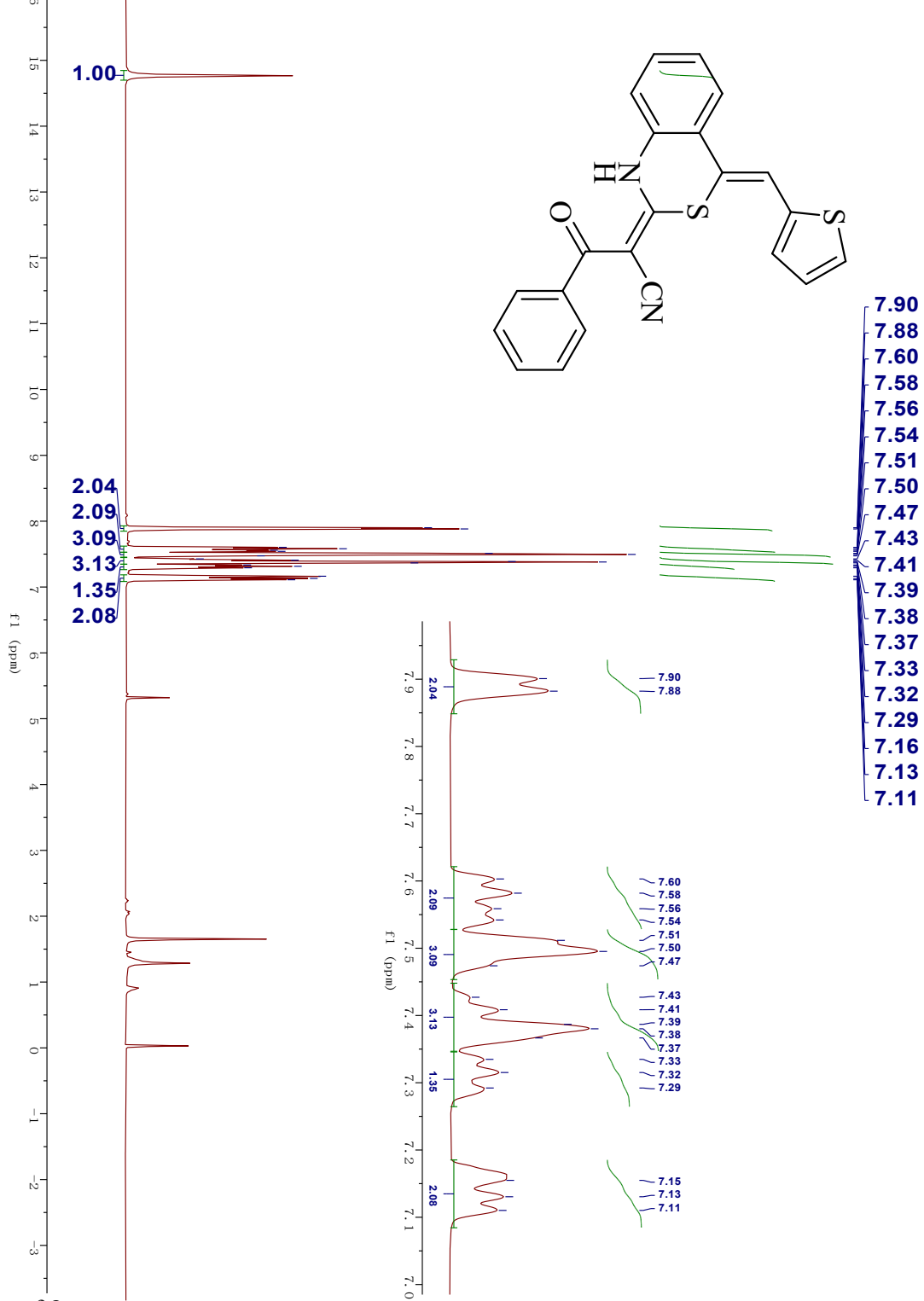
<sup>1</sup>H NMR spectrum of **3va**



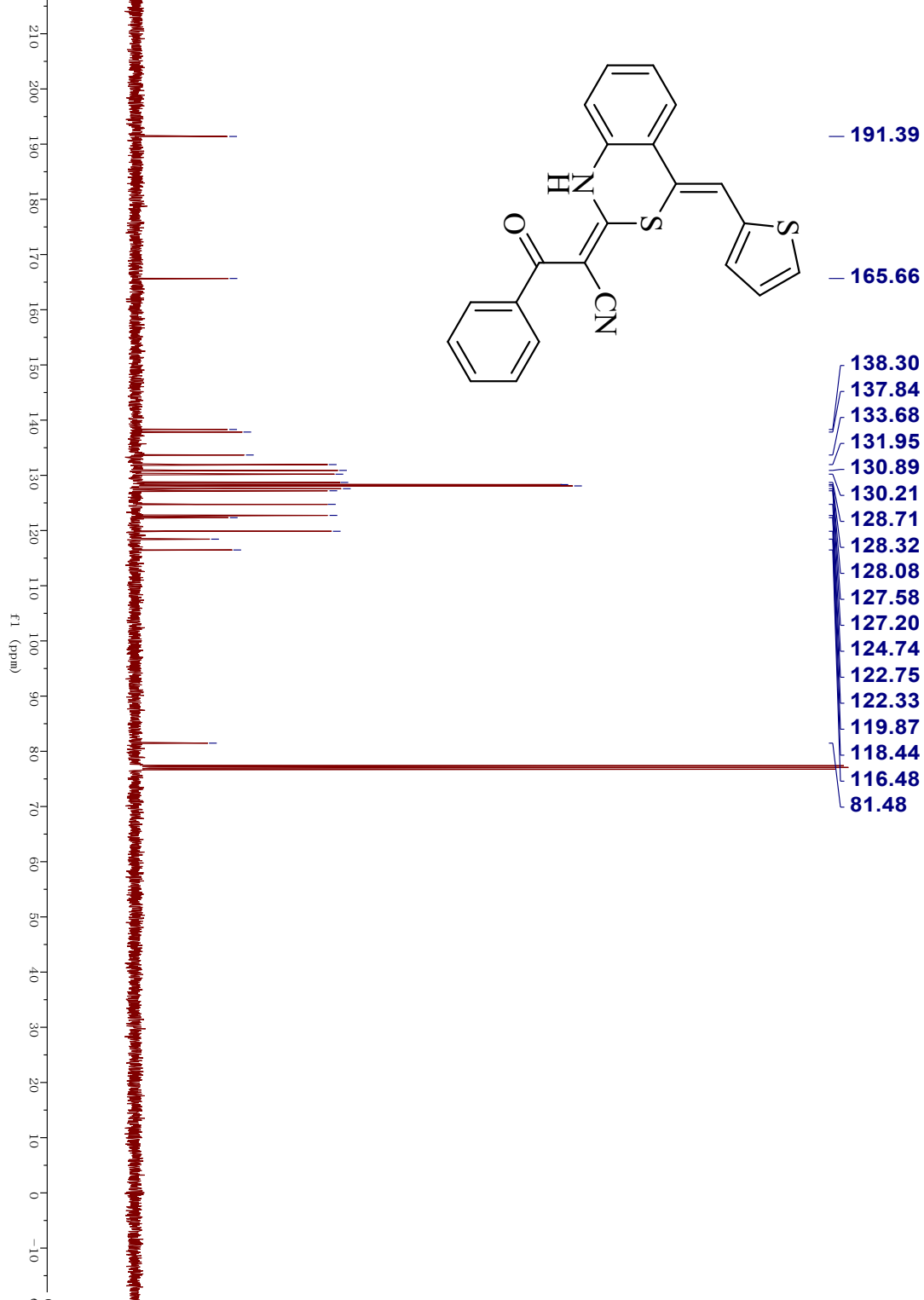
<sup>13</sup>C NMR spectrum of **3va**



$^1\text{H}$  NMR spectrum of **3wa**



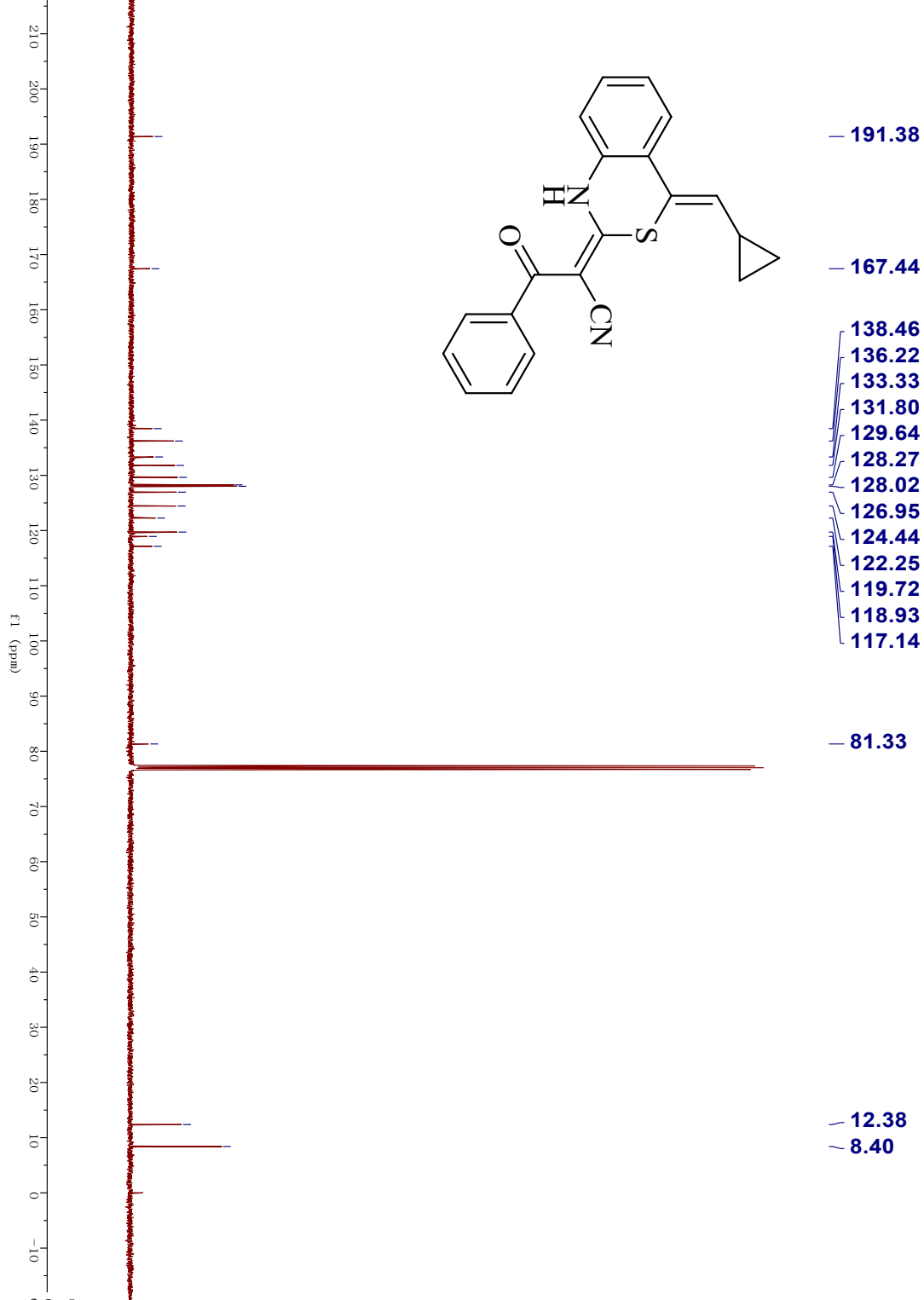
<sup>13</sup>C NMR spectrum of **3wa**



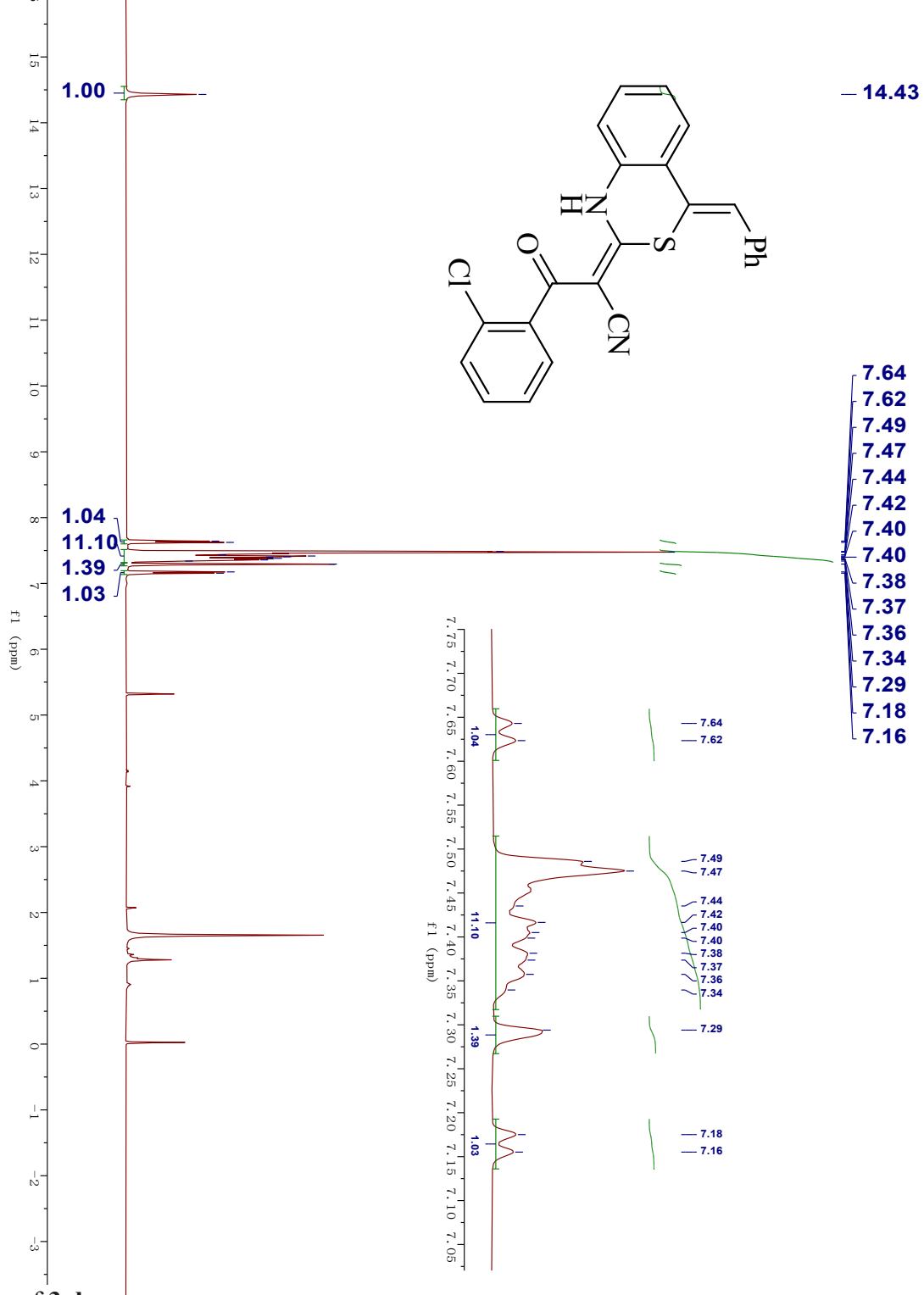
<sup>1</sup>H NMR spectrum of **3xa**



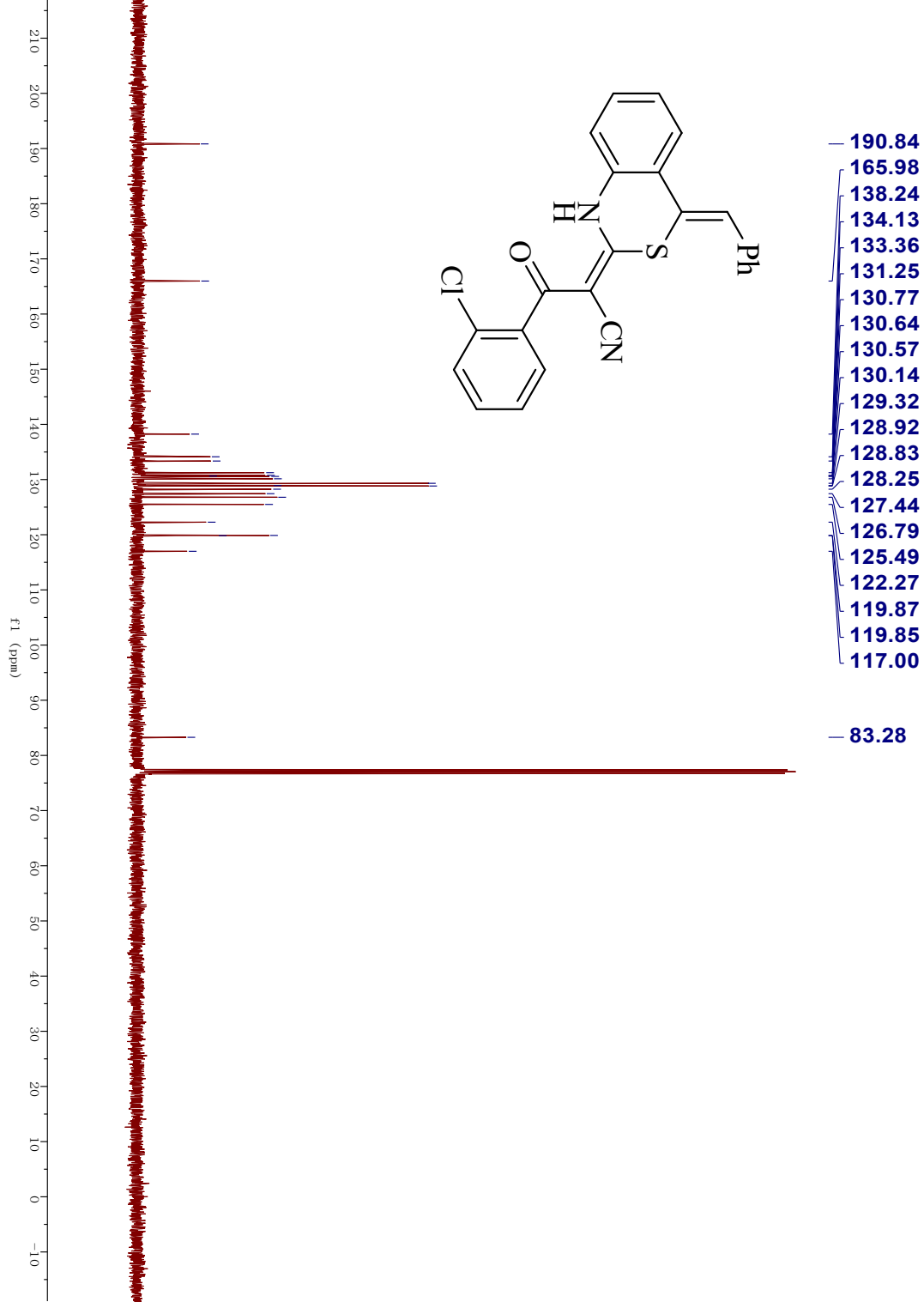




<sup>1</sup>H NMR spectrum of **3ab**

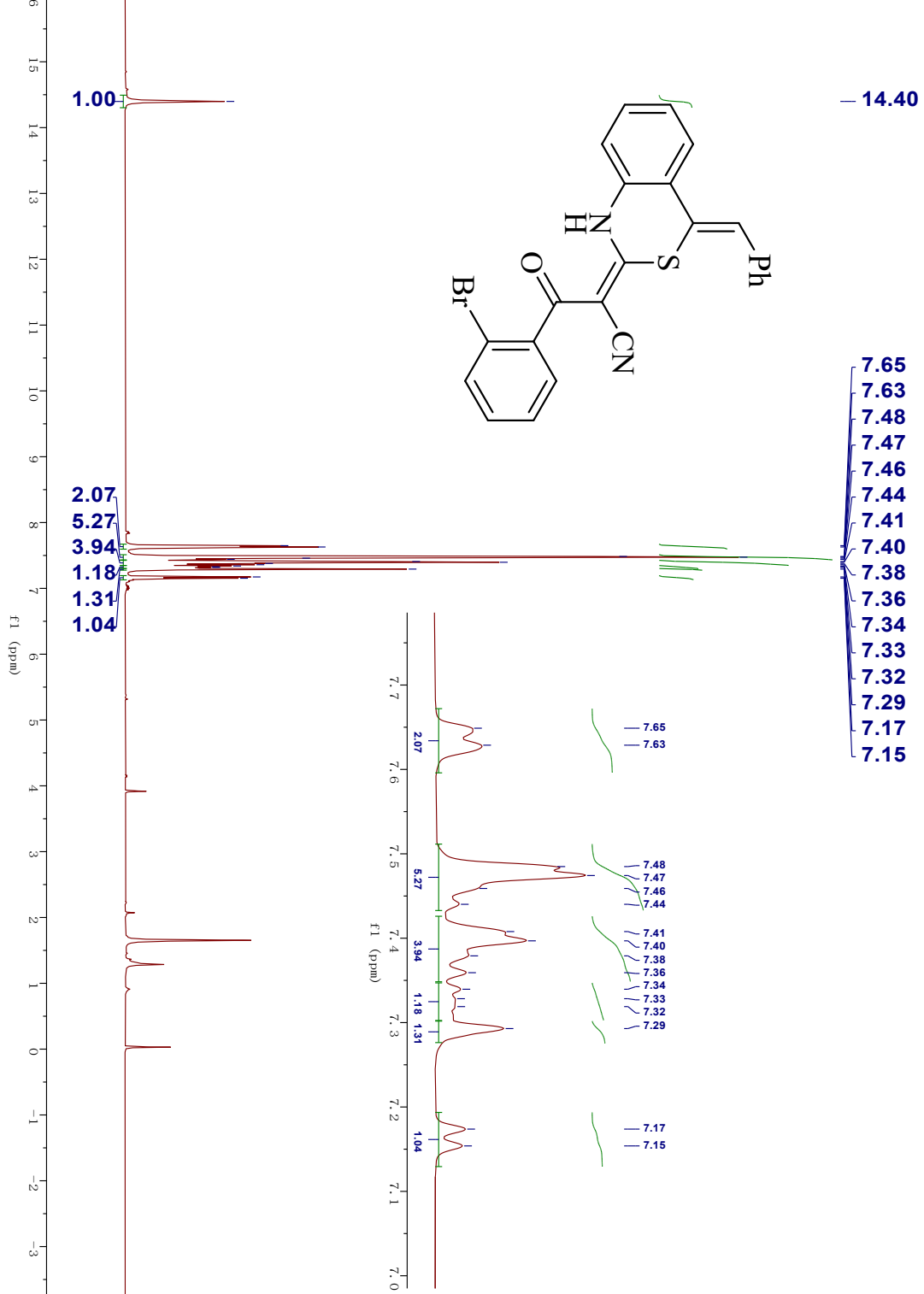


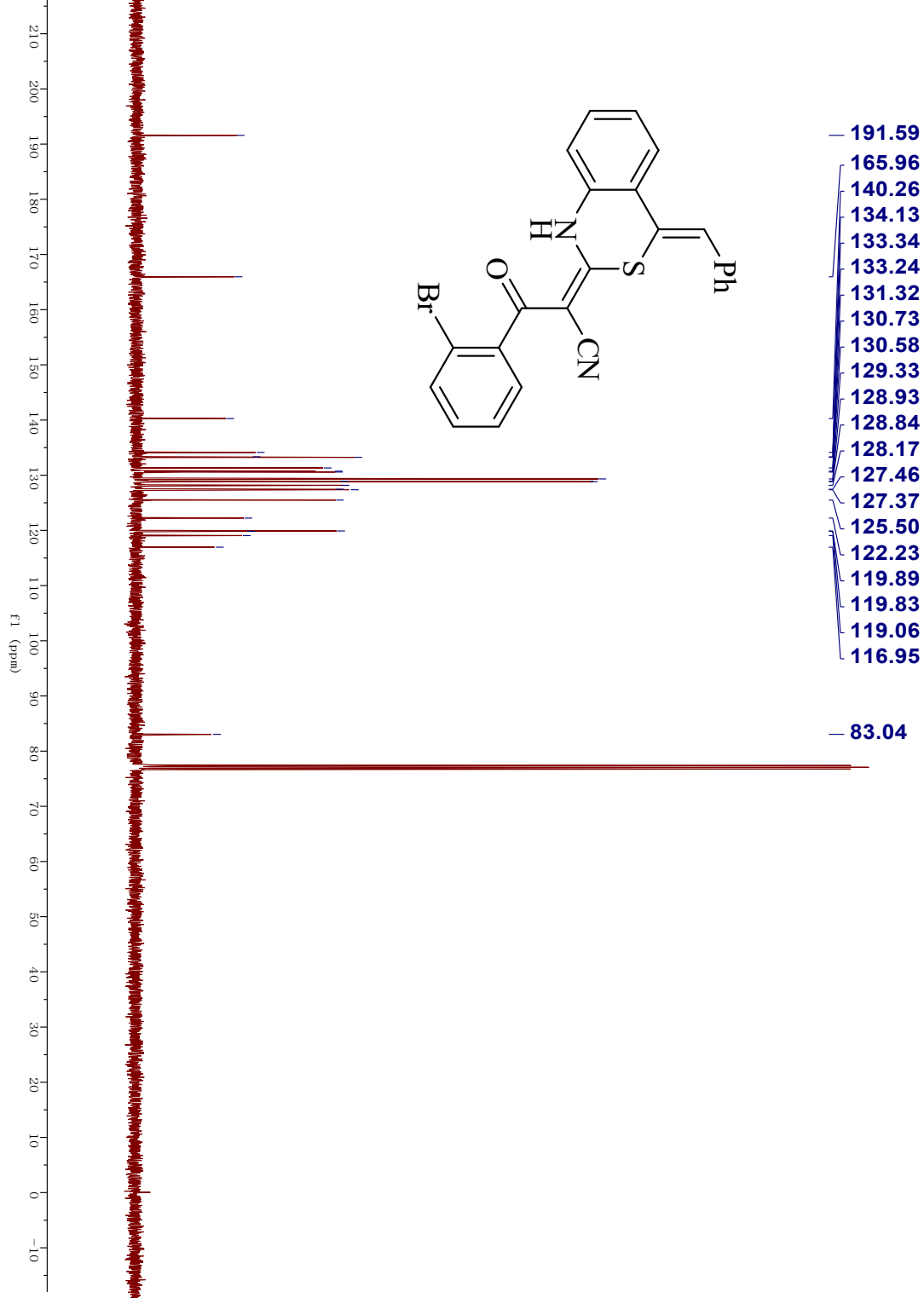
<sup>13</sup>C NMR spectrum of **3ab**



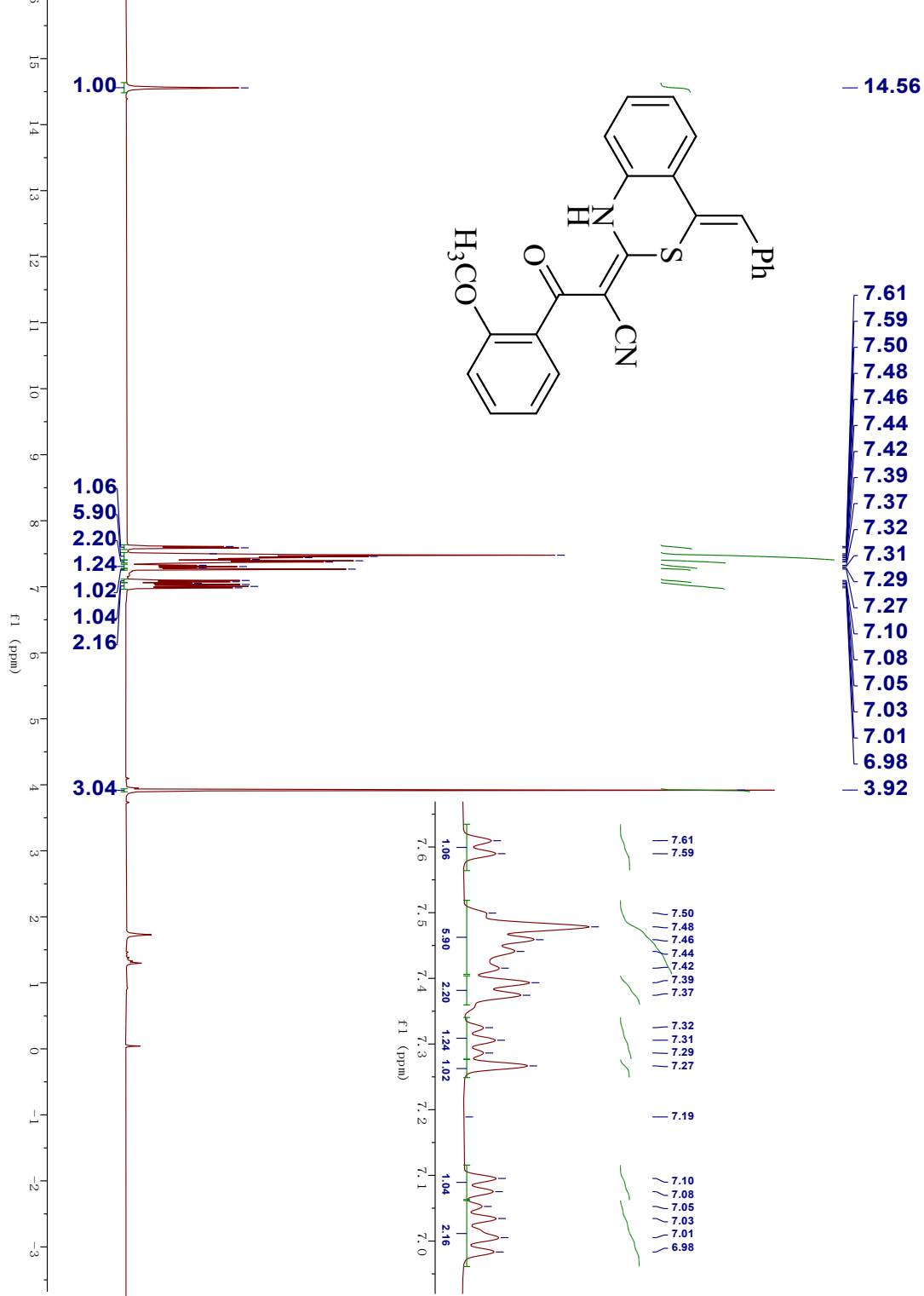
<sup>1</sup>H NMR spectrum of **3ac**

$^{13}\text{C}$  NMR spectrum of **3ac**

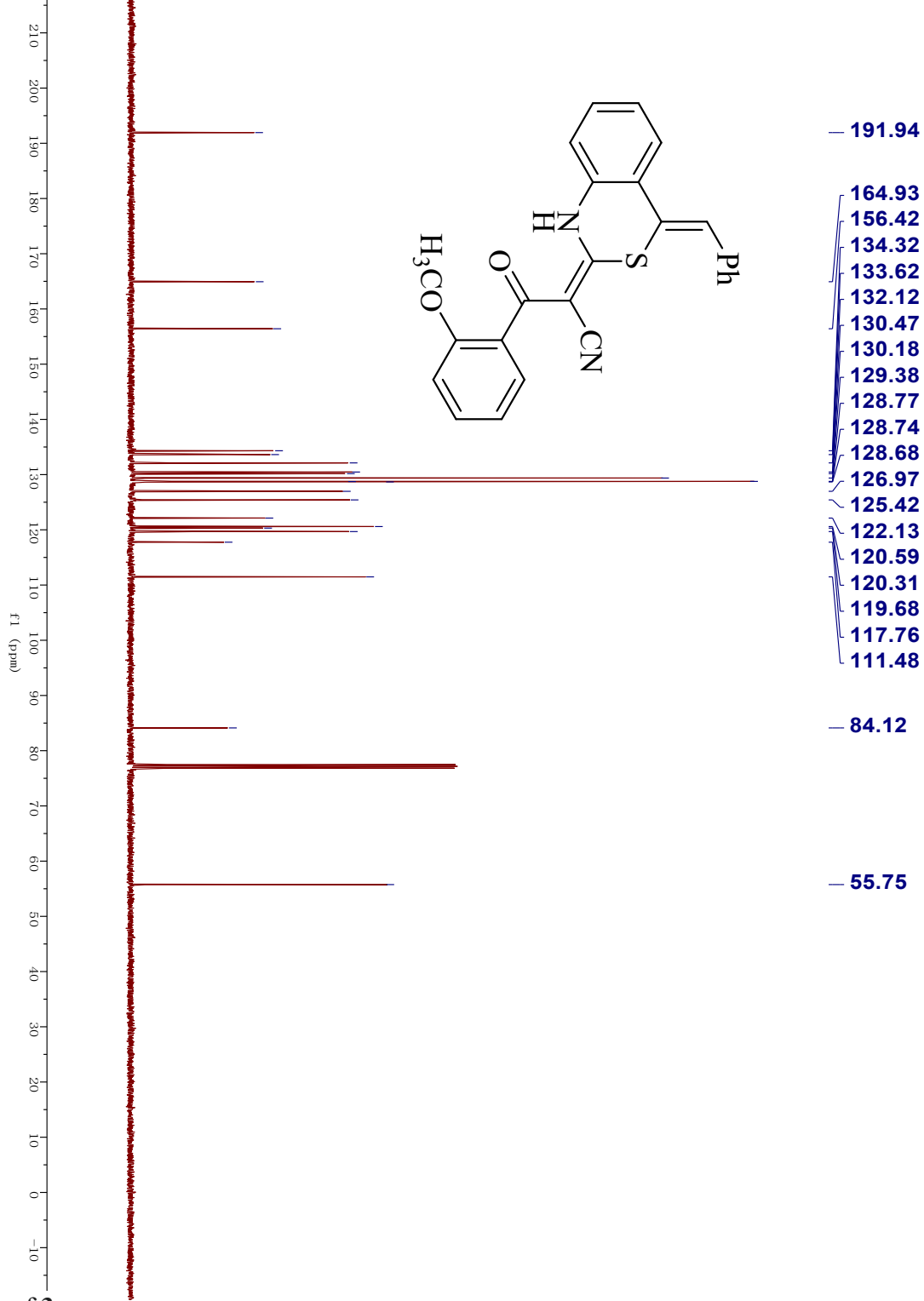




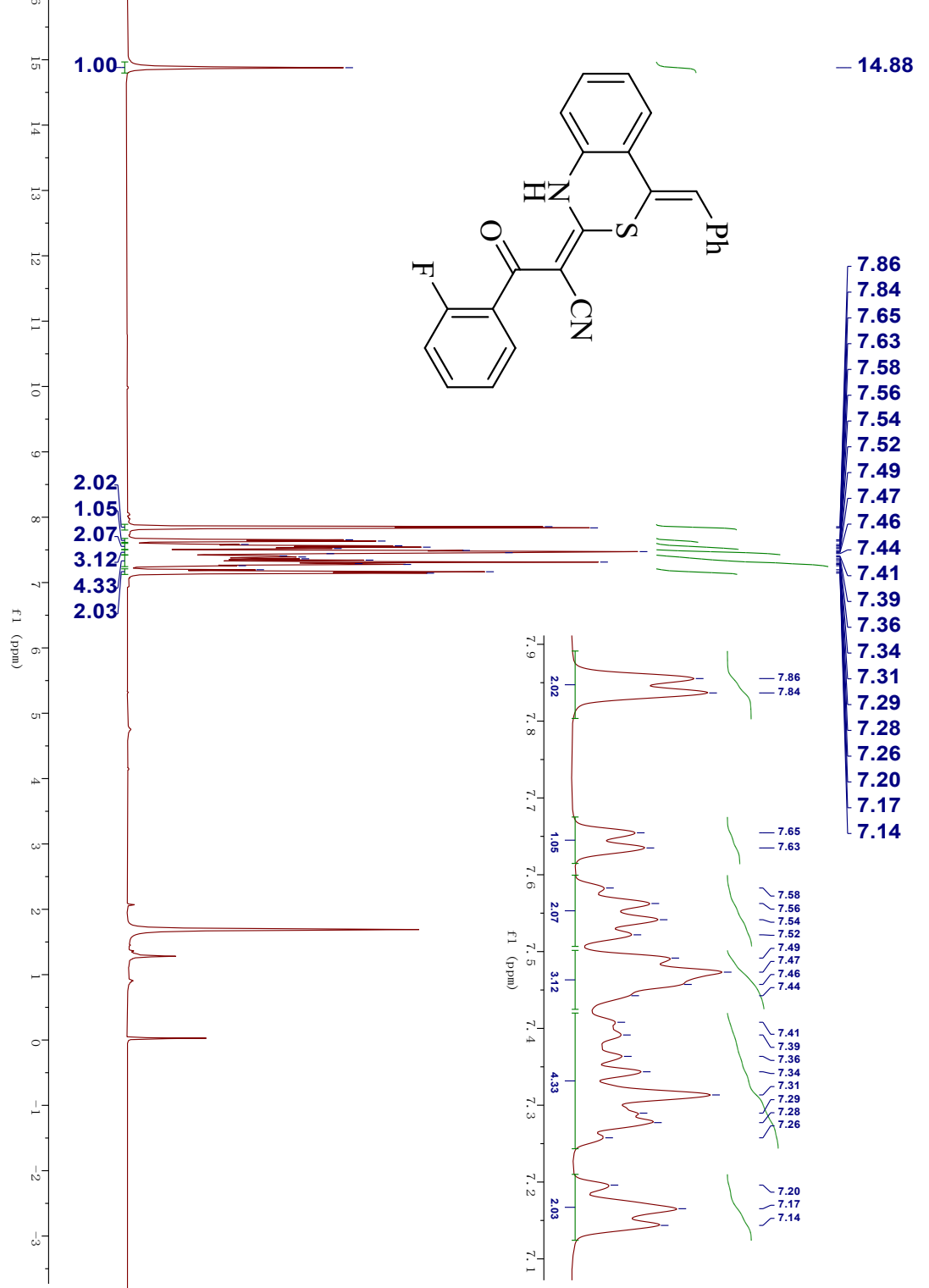
<sup>1</sup>H NMR spectrum of **3ad**



<sup>13</sup>C NMR spectrum of **3ad**

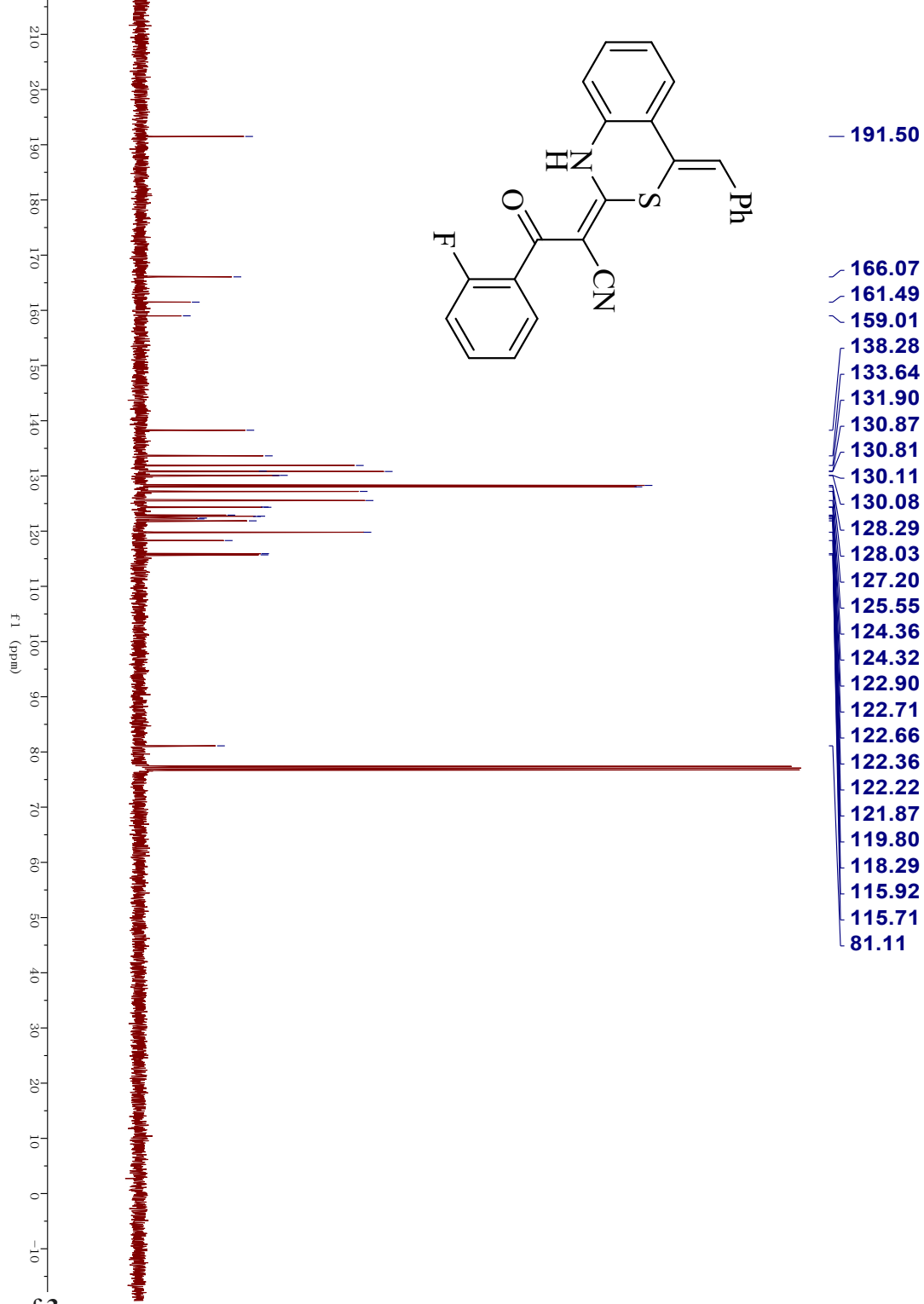


<sup>1</sup>H NMR spectrum of **3ae**

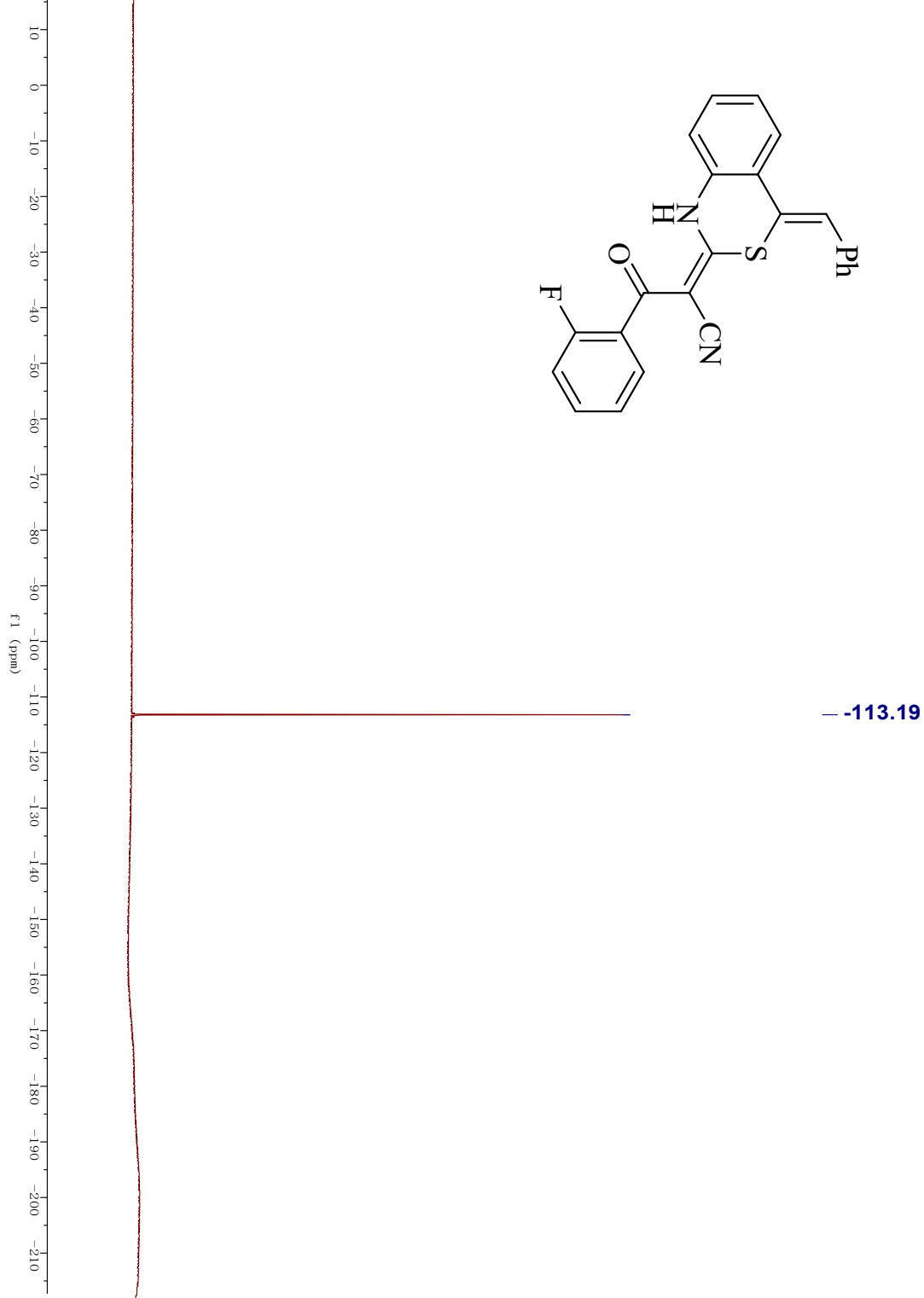
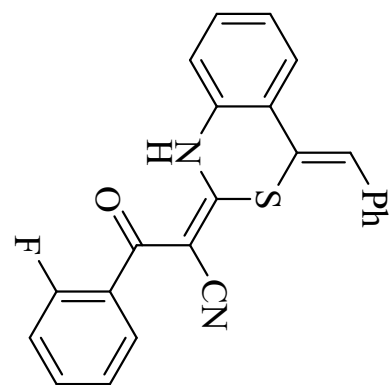


<sup>13</sup>C NMR spectrum of **3ae**

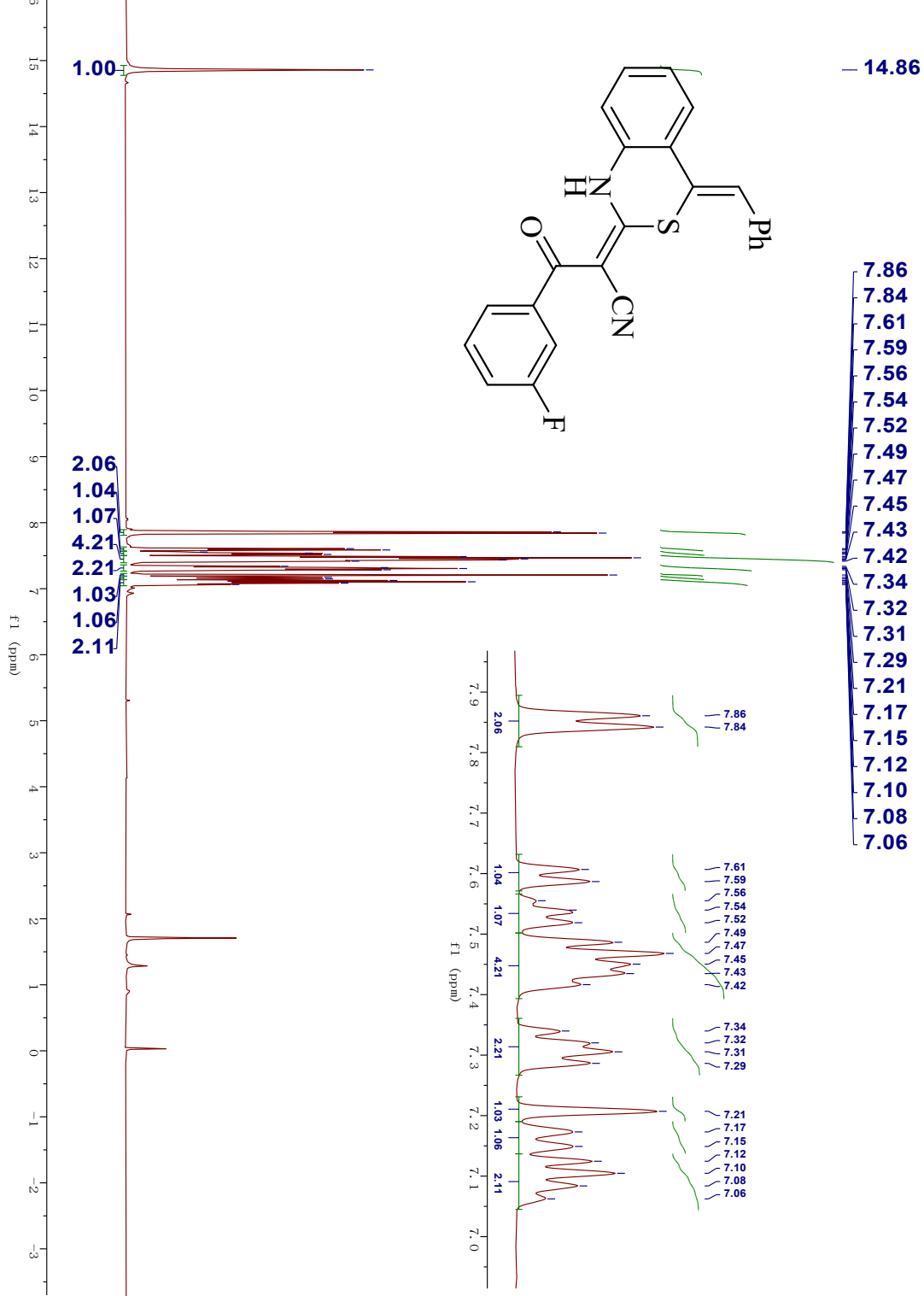




<sup>19</sup>F NMR spectrum of **3ae**

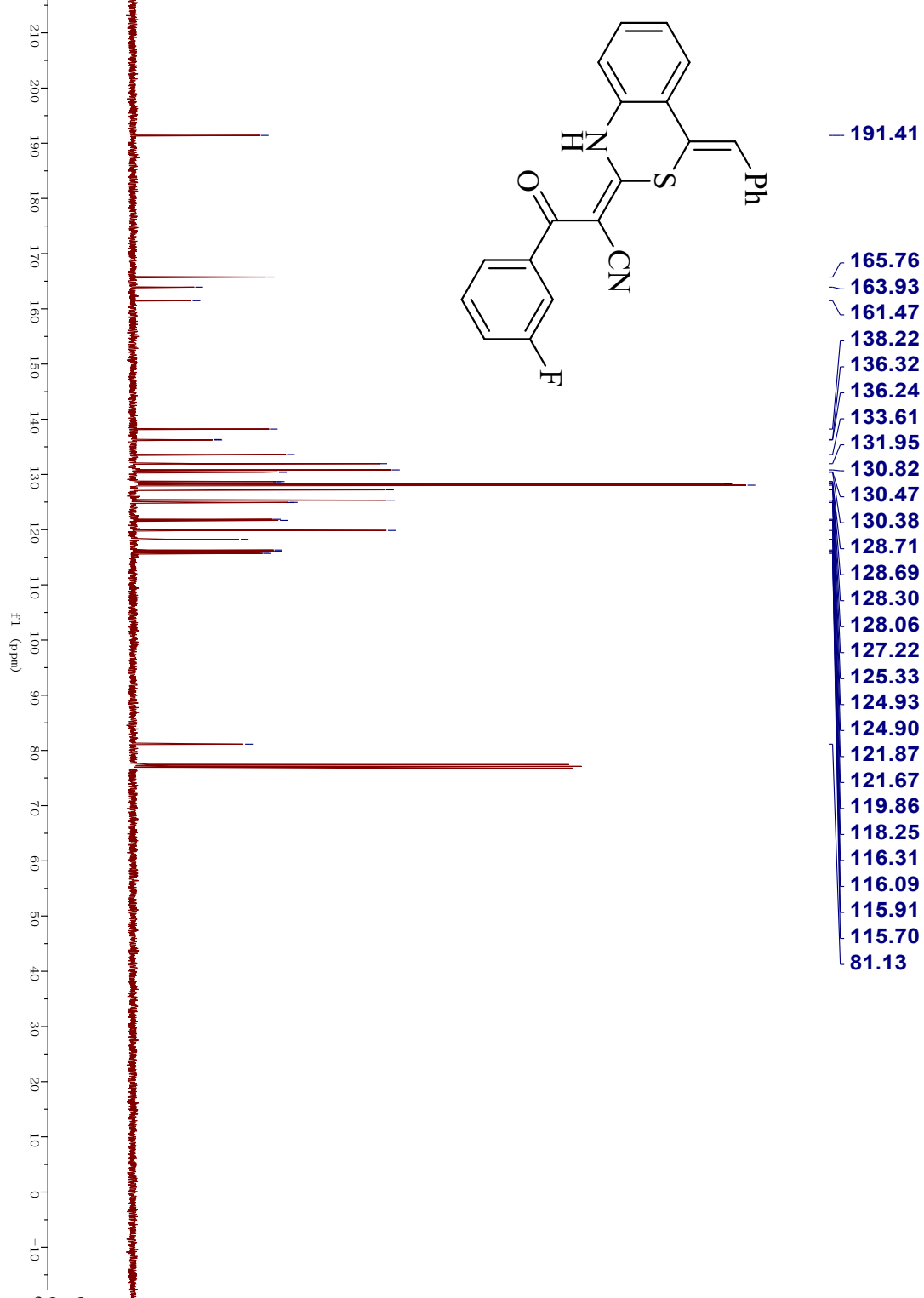


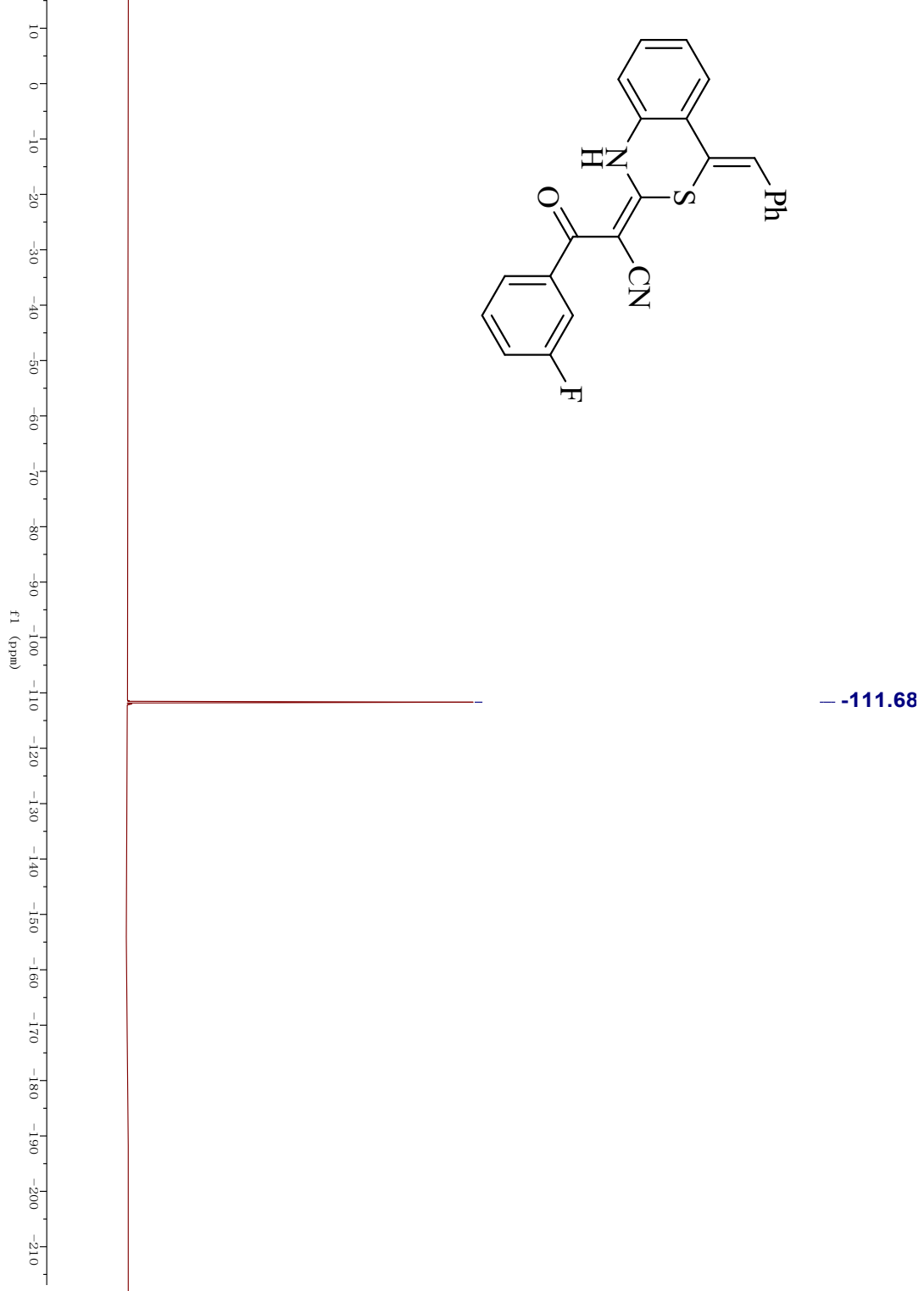
$^1\text{H}$  NMR spectrum of **3af**



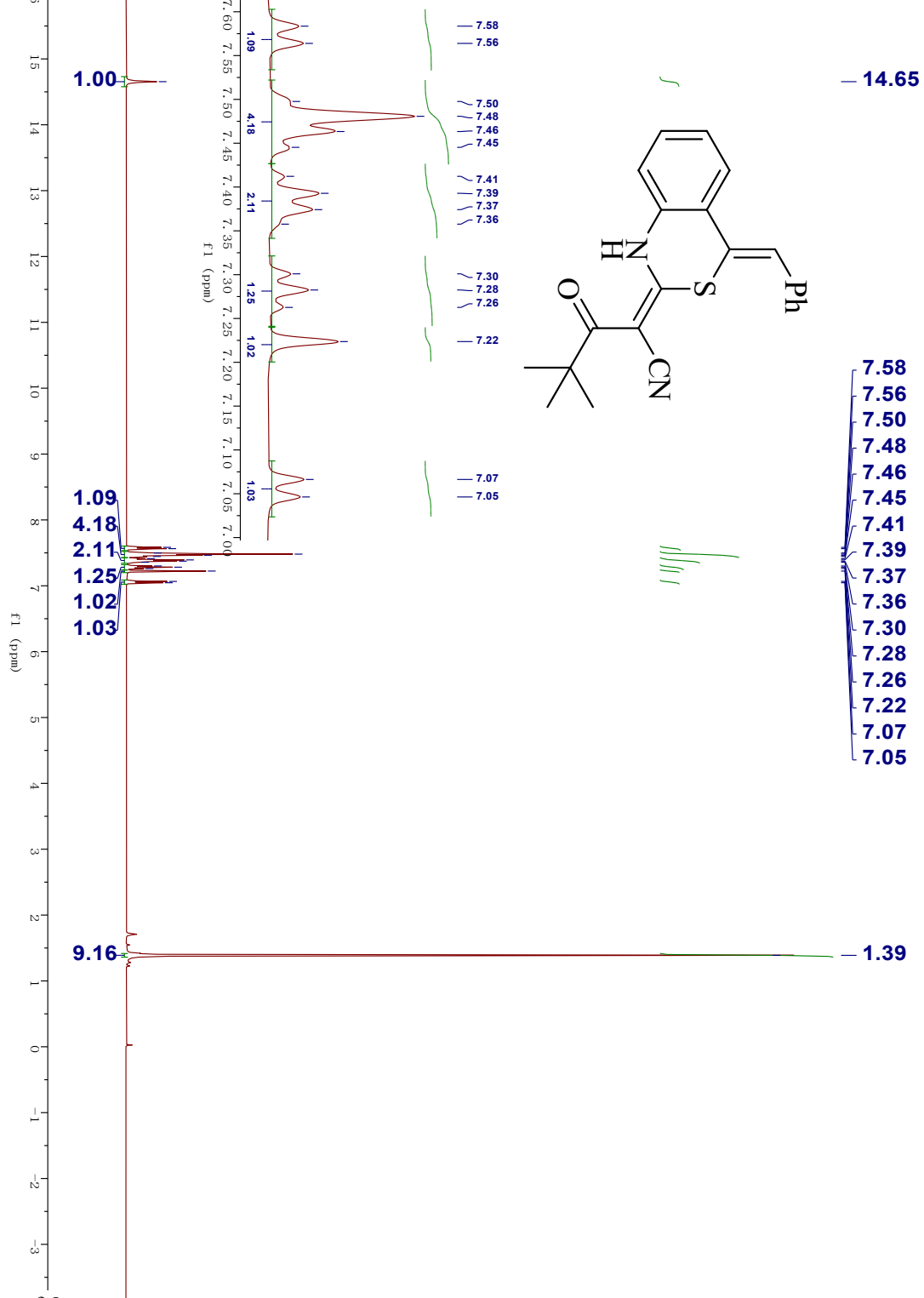
<sup>13</sup>C NMR spectrum of **3af**

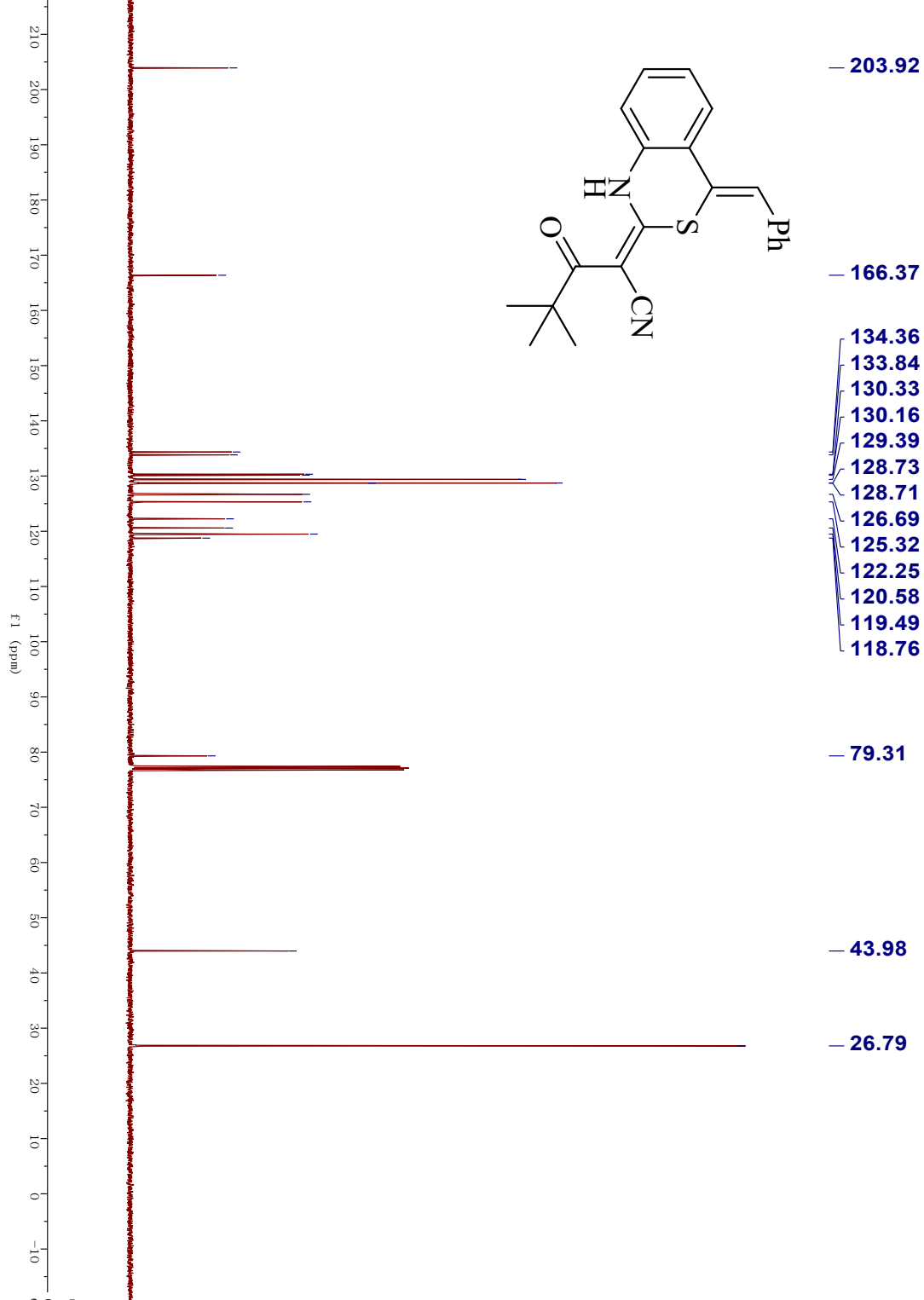
<sup>19</sup>F NMR spectrum of **3af**



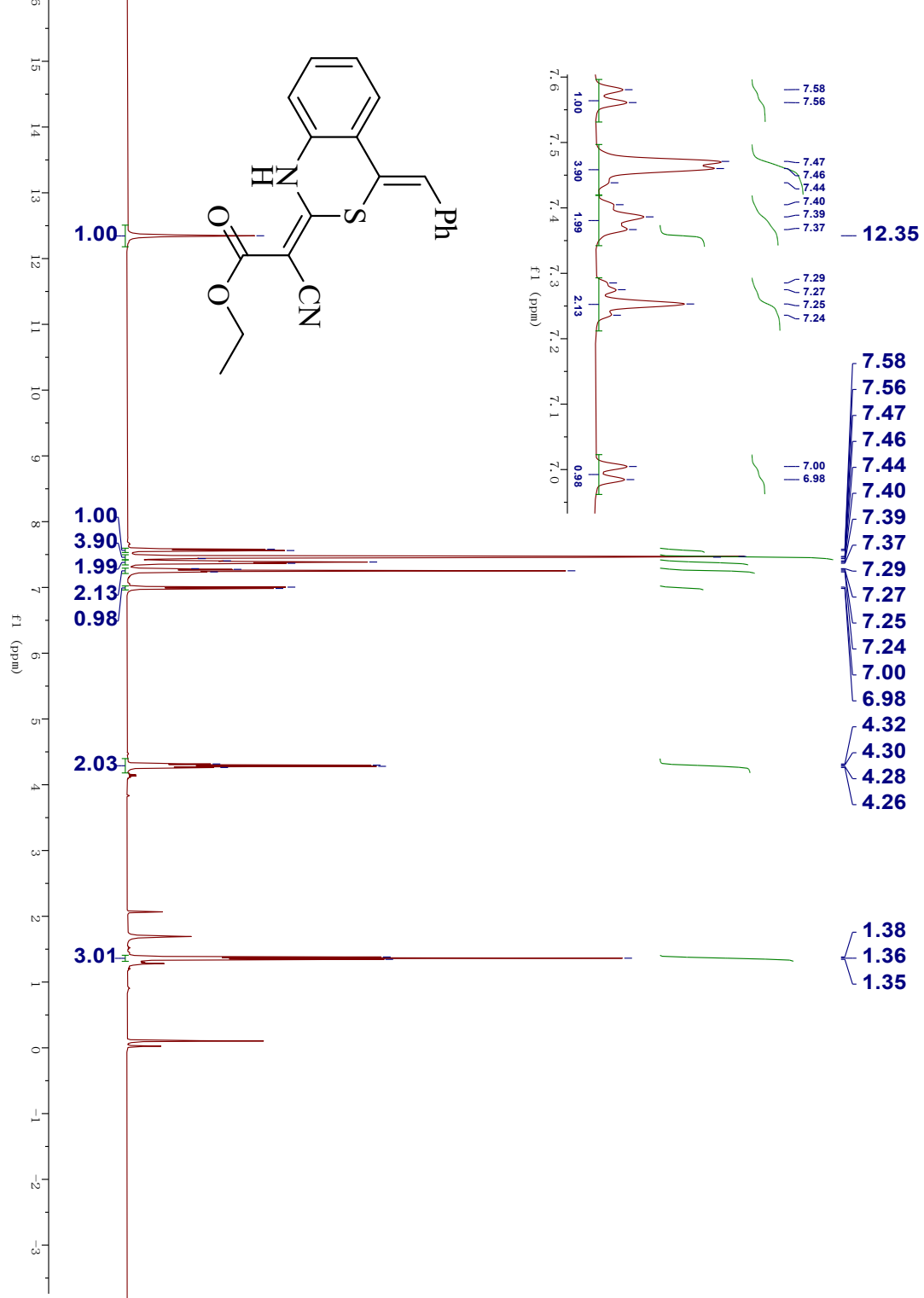


$^1\text{H}$  NMR spectrum of **3ag**



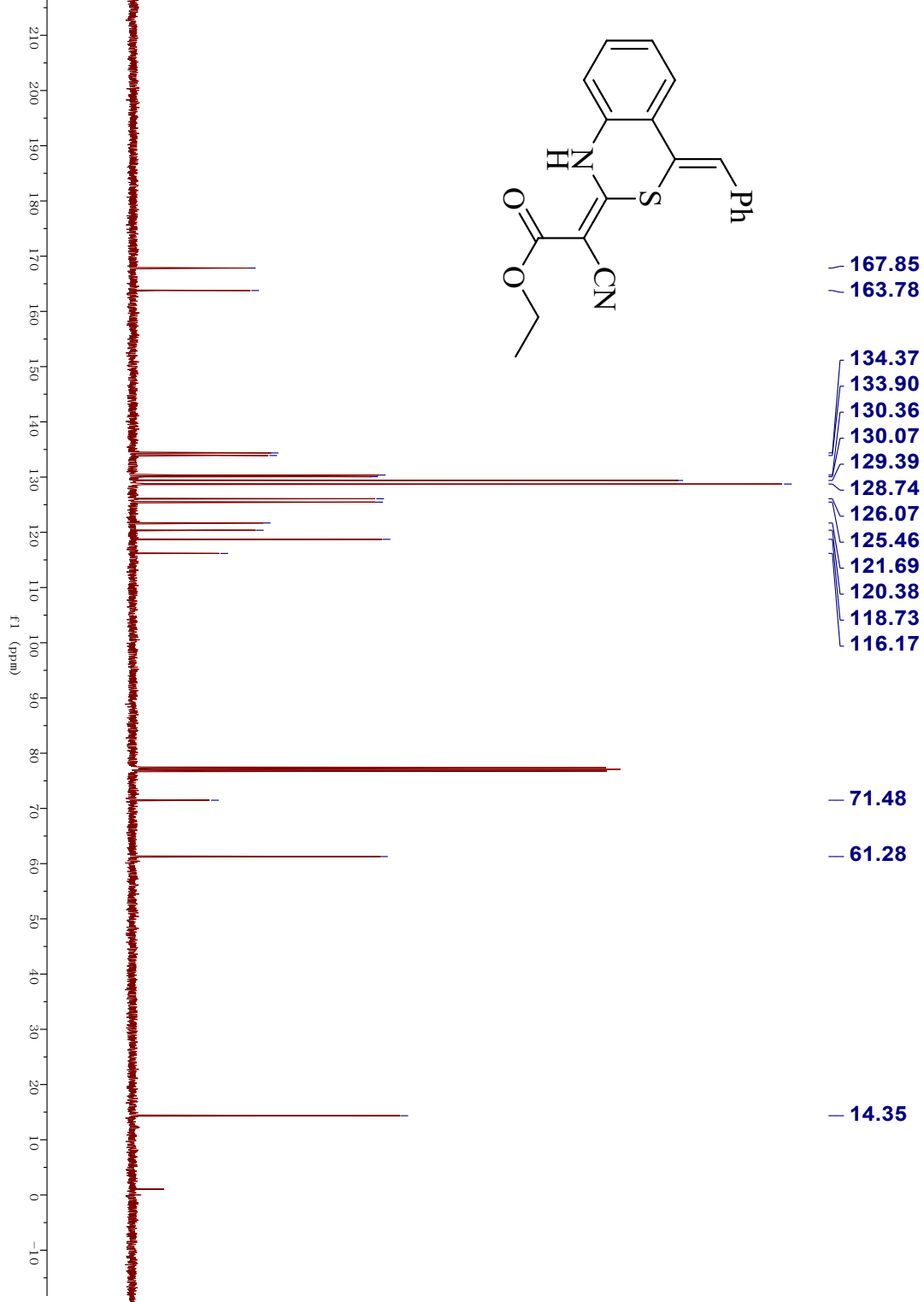


<sup>1</sup>H NMR spectrum of **3ah**

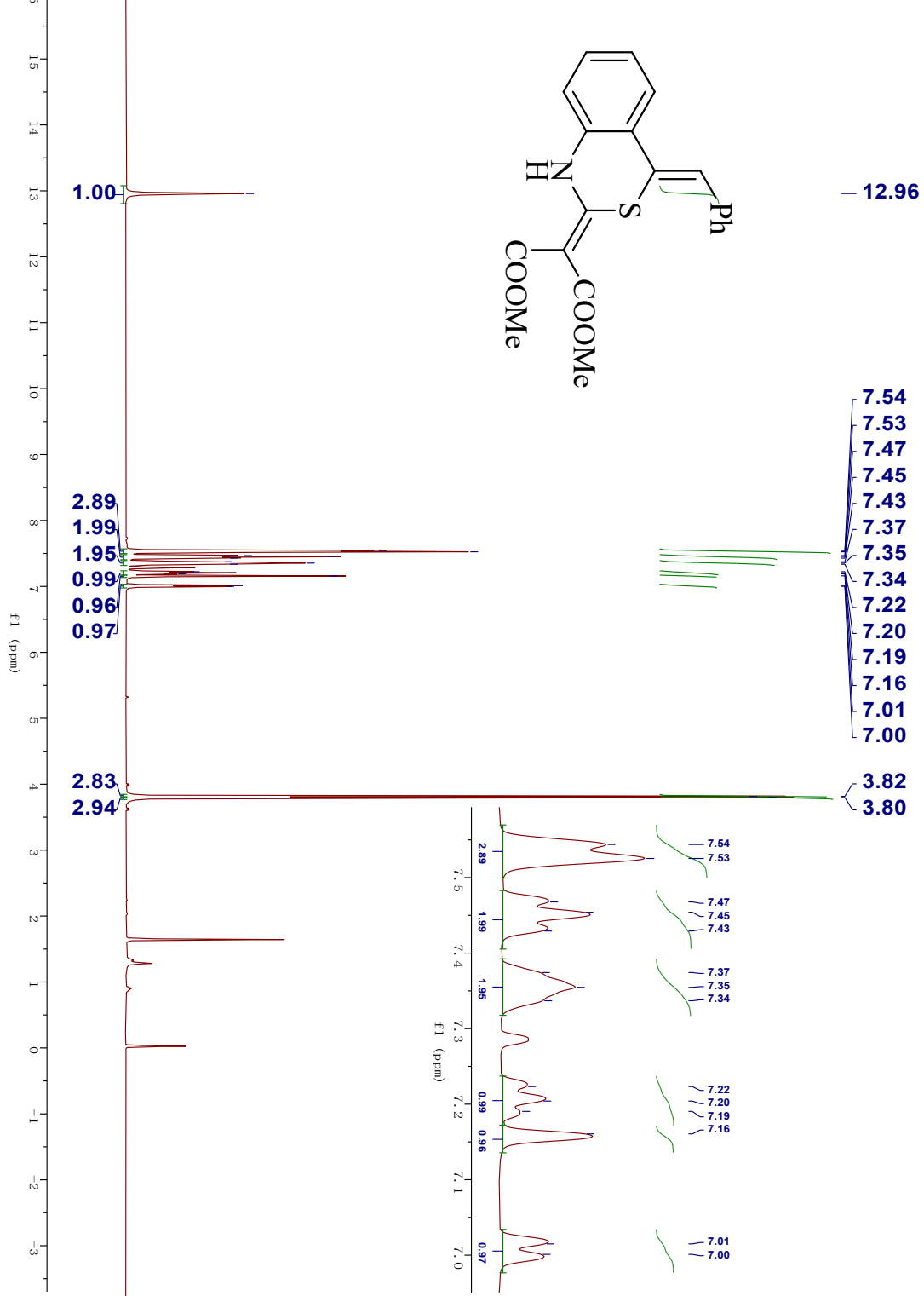


<sup>13</sup>C NMR spectrum of **3ah**

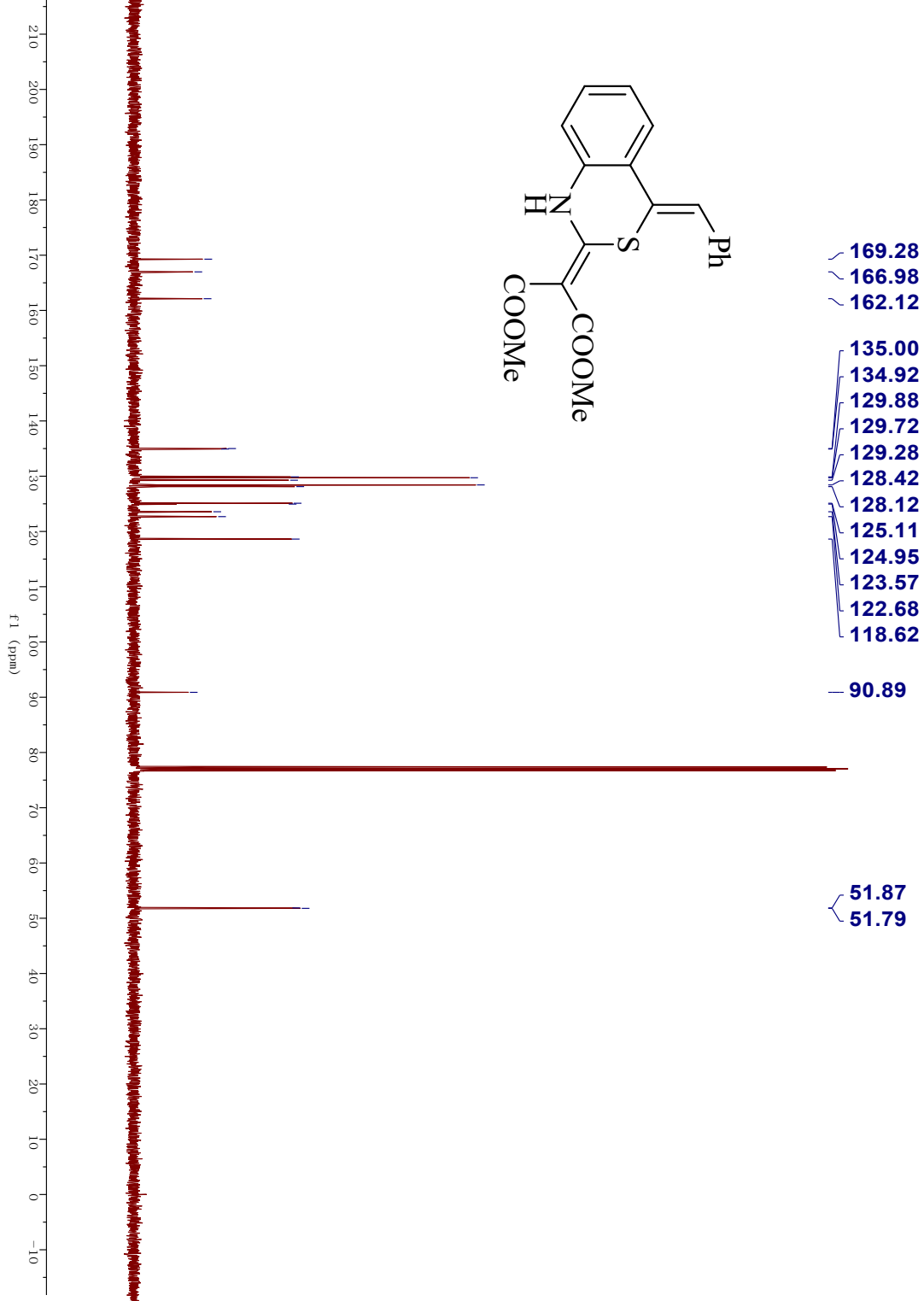




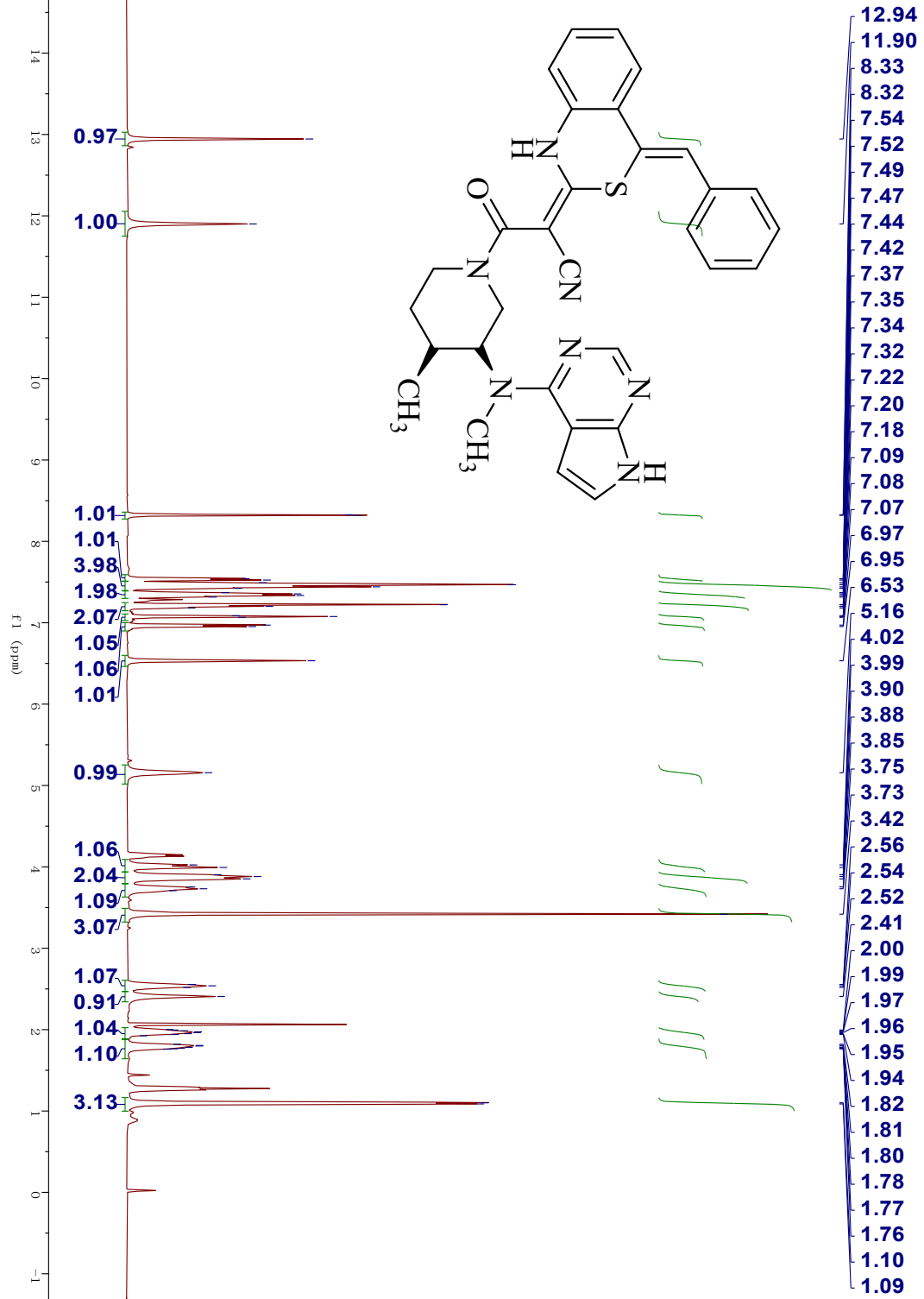
<sup>1</sup>H NMR spectrum of **3ai**



<sup>13</sup>C NMR spectrum of **3ai**



<sup>1</sup>H NMR spectrum of **3aj**



<sup>13</sup>C NMR spectrum of **3aj**

