

Supporting Information

Base-mediated one-pot synthesis of 1,2,4-oxadiazoles from nitriles, aldehydes and hydroxylamine using aldehydes as both substrates and oxidants

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General experimental procedures

The first step reaction is carried out in air and the second step under nitrogen atmosphere. Reagents were purchased and used without further purification. Reactions were monitored by thin layer chromatography (TLC) and the products were obtained by column chromatography on silica gel or by preparative thin layer chromatography (pTLC). Mass spectra were measured on a Bruker AmaZon SL mass spectrometer. Elemental analyses were performed with an Elementar Vario EL cube micro-analyzer instrument. NMR spectra were recorded on Bruker AVANCE III HD 400MHz; Proton and carbon magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of CDCl_3 as the internal standard (^1H NMR: TMS at 0.00 ppm, CHCl_3 at 7.26 ppm; ^{13}C NMR: CDCl_3 at 77.16 ppm) or were recorded using tetramethylsilane (TMS) in the solvent of $\text{DMSO}-d_6$ as the internal standard (^1H NMR: TMS at 0.00 ppm, DMSO at 2.50 ppm; ^{13}C NMR: DMSO at 39.51 ppm)

Synthesis of 1,2,4-oxadiazoles from corresponding 4,5-dihydro-1,2,4-oxadiazoles

4,5-dihydro-1,2,4-oxadiazoles were prepared by the literature.¹ The 4,5-dihydro-1,2,4-oxadiazole (**I-2** or **I-3**) (0.45 mmol), aldehyde (**2**) (0.5 mmol), Cs_2CO_3 (1 mmol, 326 mg), DMSO (1.0 mL) were added to the Schlenk tube, and the mixture was stirred at 100 °C for another 24 h under N_2 balloon (1 bar). The resulting solution was concentrated by a rotary evaporator, and the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to give the desired 1,2,4-oxadiazole **3** and corresponding by-product of arylmethanol (**4a** or **4b**) (Figure S1). Moreover, BnOH (**4a**) was hard to isolated due to the lower boiling point of BnOH (205 °C), and easy to lose under reduced pressure.

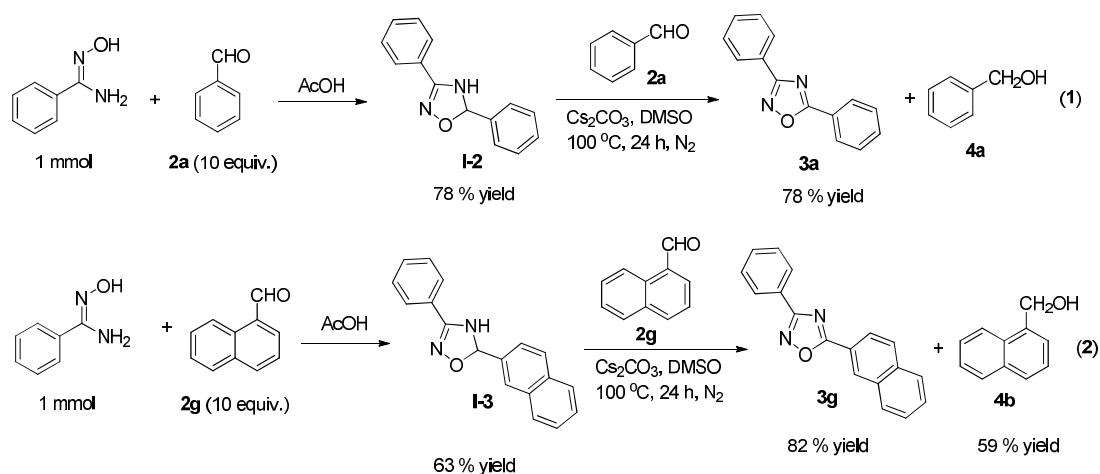
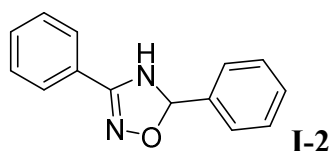
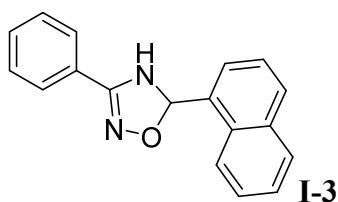


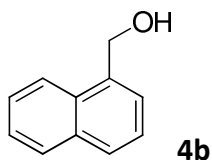
Figure S1. Aldehyde-oxidized synthesis of 3a and 3g under basic condition.



3,5-diphenyl-4,5-dihydro-1,2,4-oxadiazole (I-2).¹ Eluent: petroleum ether/ethyl acetate (5:1). Yield 175 mg (78 %). White solid, m.p. 93.2-94.1°C (lit.¹ m.p. 94-96 °C). ¹H NMR (*d*₆-DMSO, 400 MHz, 25 °C) δ 8.08 (s, 1H), 7.75 (m, 2H), 7.47 (m, 8H), 6.54 (s, 1H). ¹³C NMR (*d*₆-DMSO, 100 MHz, 25 °C) δ 155.8, 140.5, 131.1, 129.7, 129.2, 129.0, 127.1, 126.7, 125.8, 93.3. APCI-MS [M+H]⁺ m/z 225.1.



5-(naphthalen-1-yl)-3-phenyl-4,5-dihydro-1,2,4-oxadiazole (I-3): Eluent: petroleum ether/ethyl acetate (5:1). Yield 173 mg (63%). White solid, m.p. 88.0-90 .1°C . ¹H NMR (*d*₆-DMSO, 400 MHz, 25 °C) δ 8.31-8.17 (m, 2H), 8.07-7.96 (m, 2H), 7.89-7.74 (m, 3H), 7.68-7.45 (m, 6H), 7.25 (d, *J* = 2.8 Hz, 1H). ¹³C NMR (*d*₆-DMSO, 100 MHz, 25 °C) δ 156.1, 135.2, 134.0, 131.2, 130.9, 130.1, 129.2, 129.0, 126.9, 126.4, 125.9, 125.6, 125.0, 124.4, 92.0. APCI-MS [M+H]⁺ m/z 275.2.

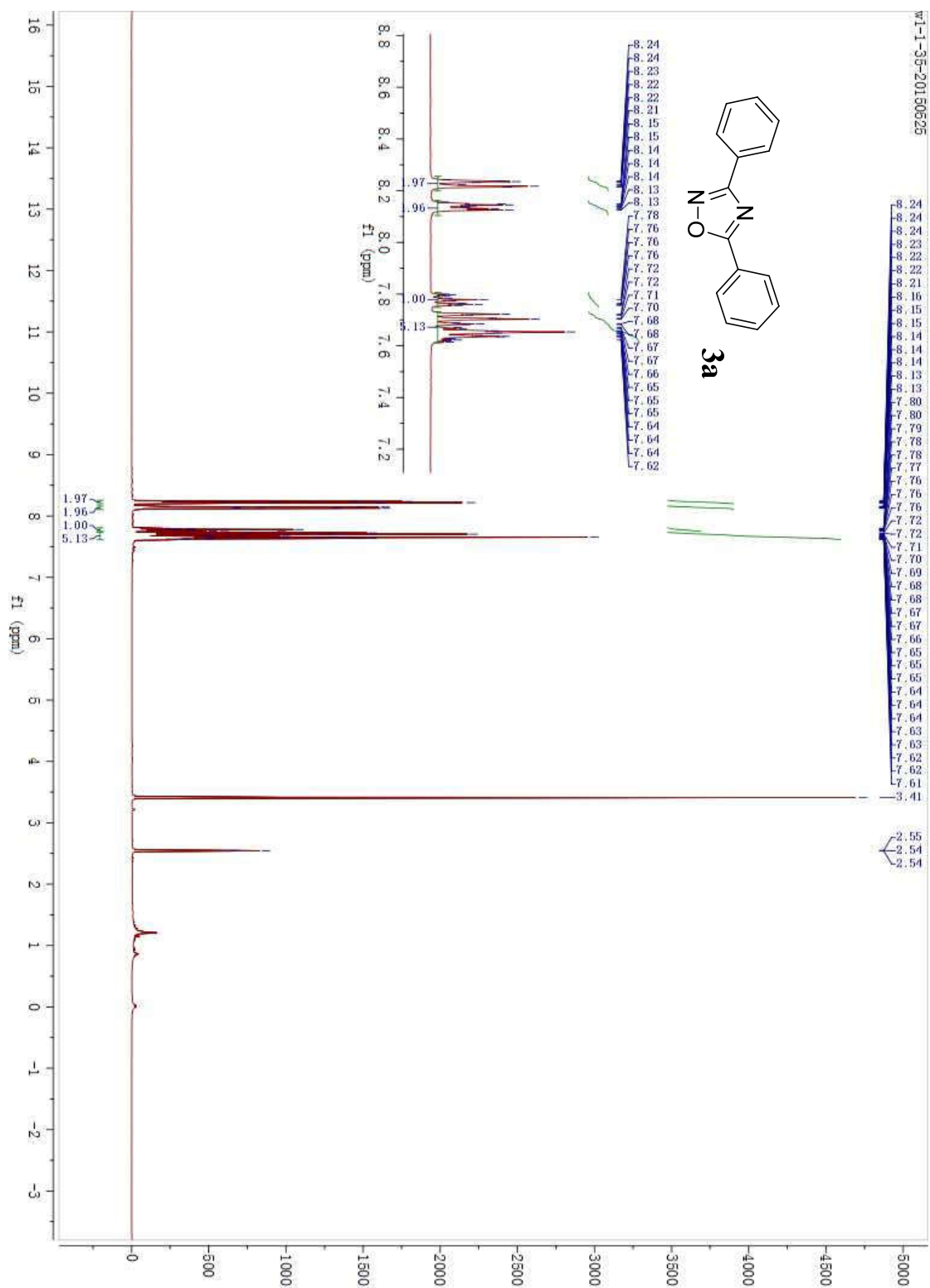


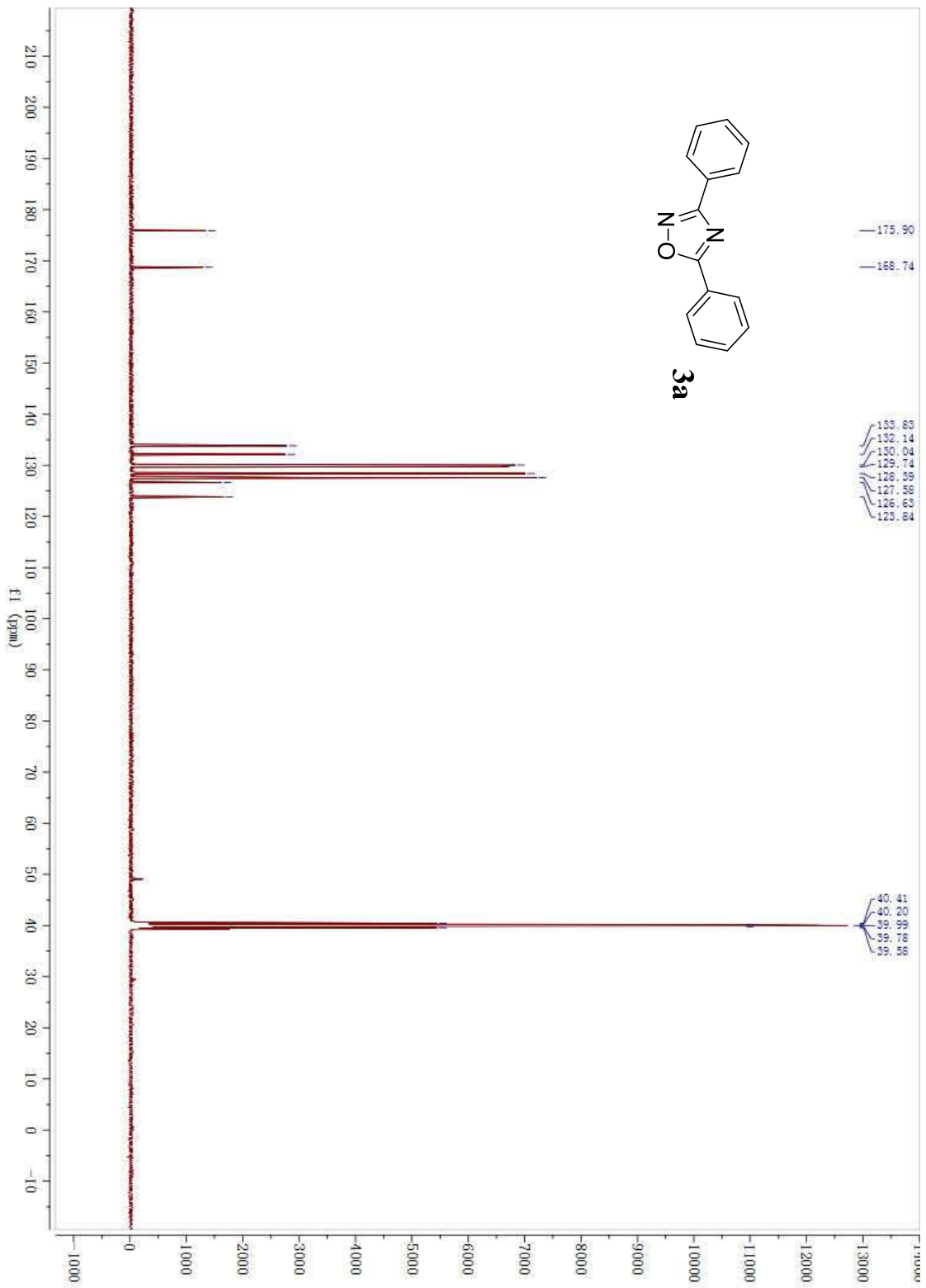
1-Naphthalenemethanol(4b):² Eluent: petroleum ether/ethyl acetate (1:1). Yield 42 mg (59 %). White solid, mp 62.1-64.0 °C (lit.² mp 62-63 °C). ¹H NMR (CDCl₃, 400 MHz, 25 °C) δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.79-7.64 (m, 2H), 7.46-7.26 (m, 4H), 4.95 (s, 2H), 2.21 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 135.1, 132.6, 130.1, 127.5, 127.4, 125.2, 124.7, 124.3, 124.2, 122.5, 62.4. APCIMS [M-H]⁻ m/z157.0.

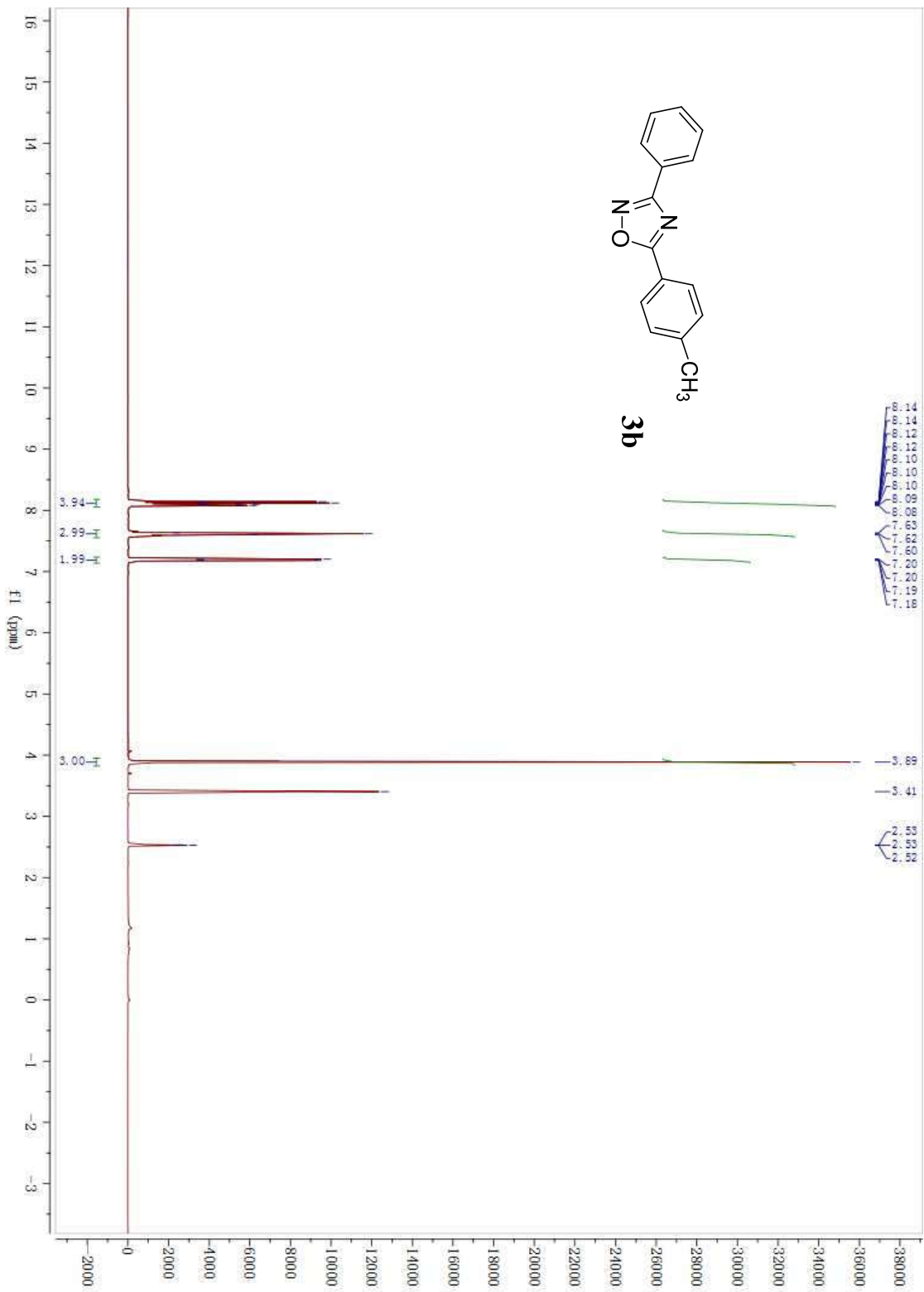
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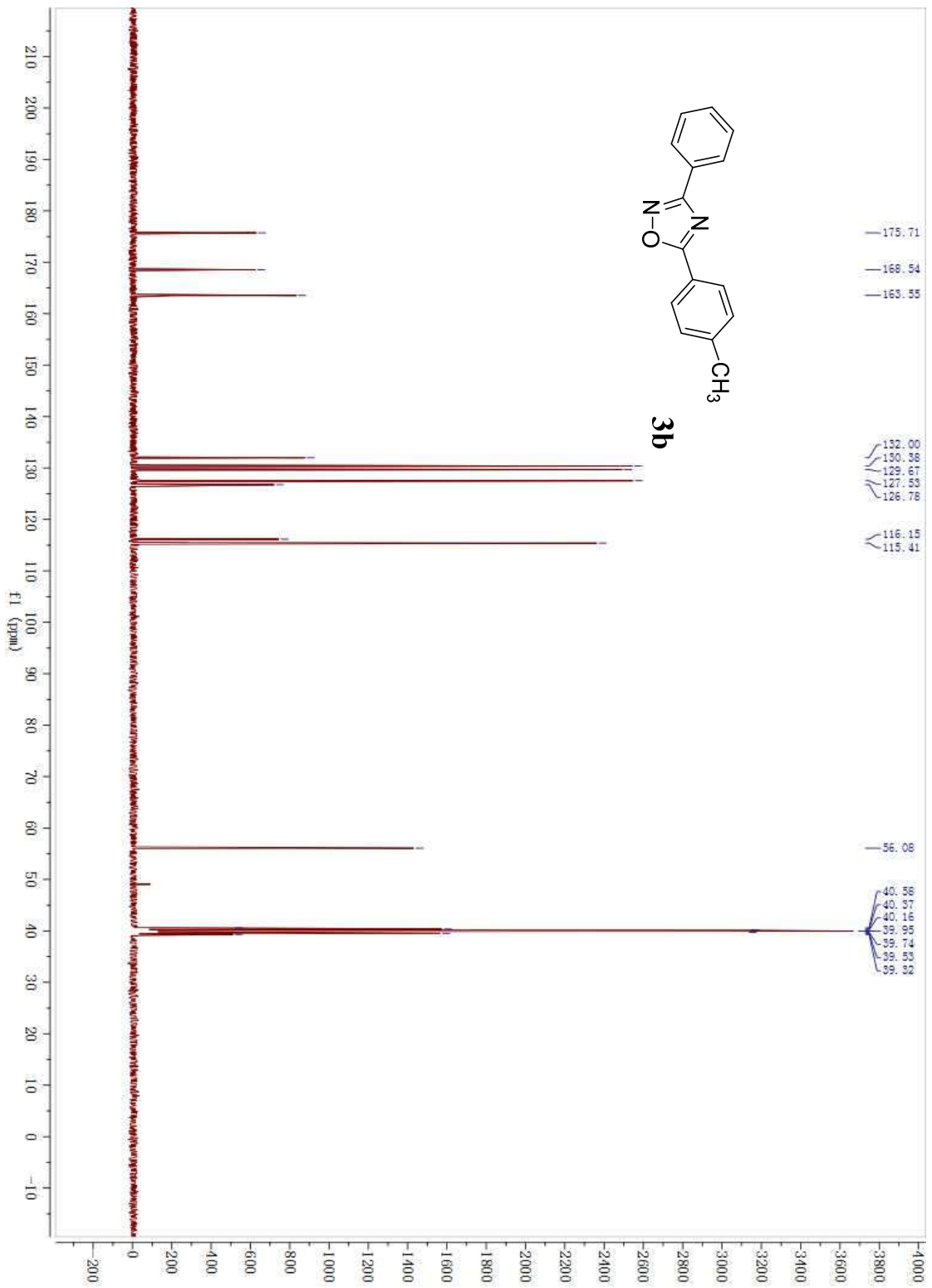
- (1) Wang, Y. -F.; Zhang, F. -L.; Chiba, S. *Org. Lett.* **2013**, *15*, 2842.
- (2) Zeynizadeh, B. Z. *Naturforsch. B* **2004**, *59*, 704.

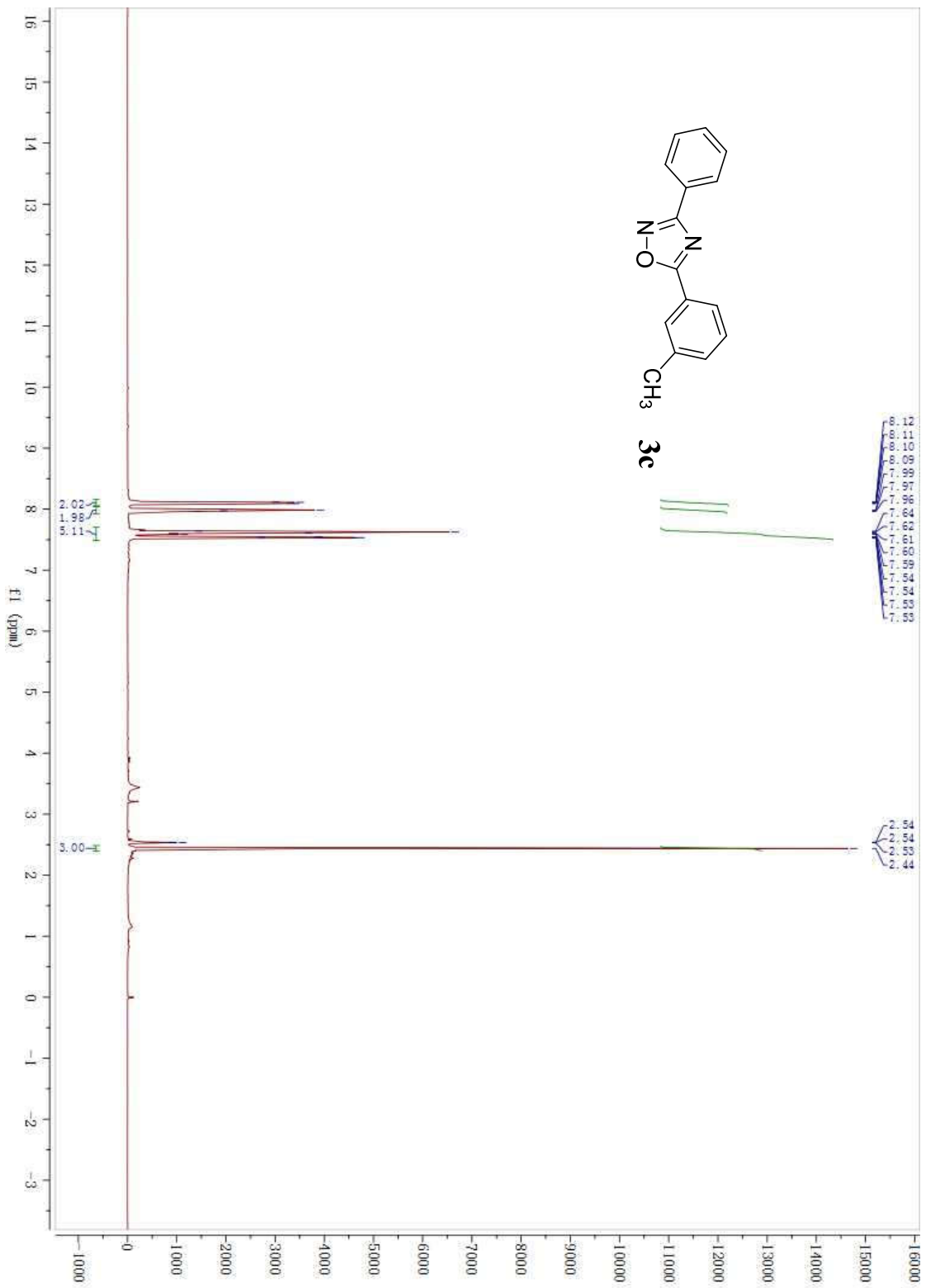
The ^1H and ^{13}C NMR spectra of compounds 3a-w, I-2, I-3, 4b

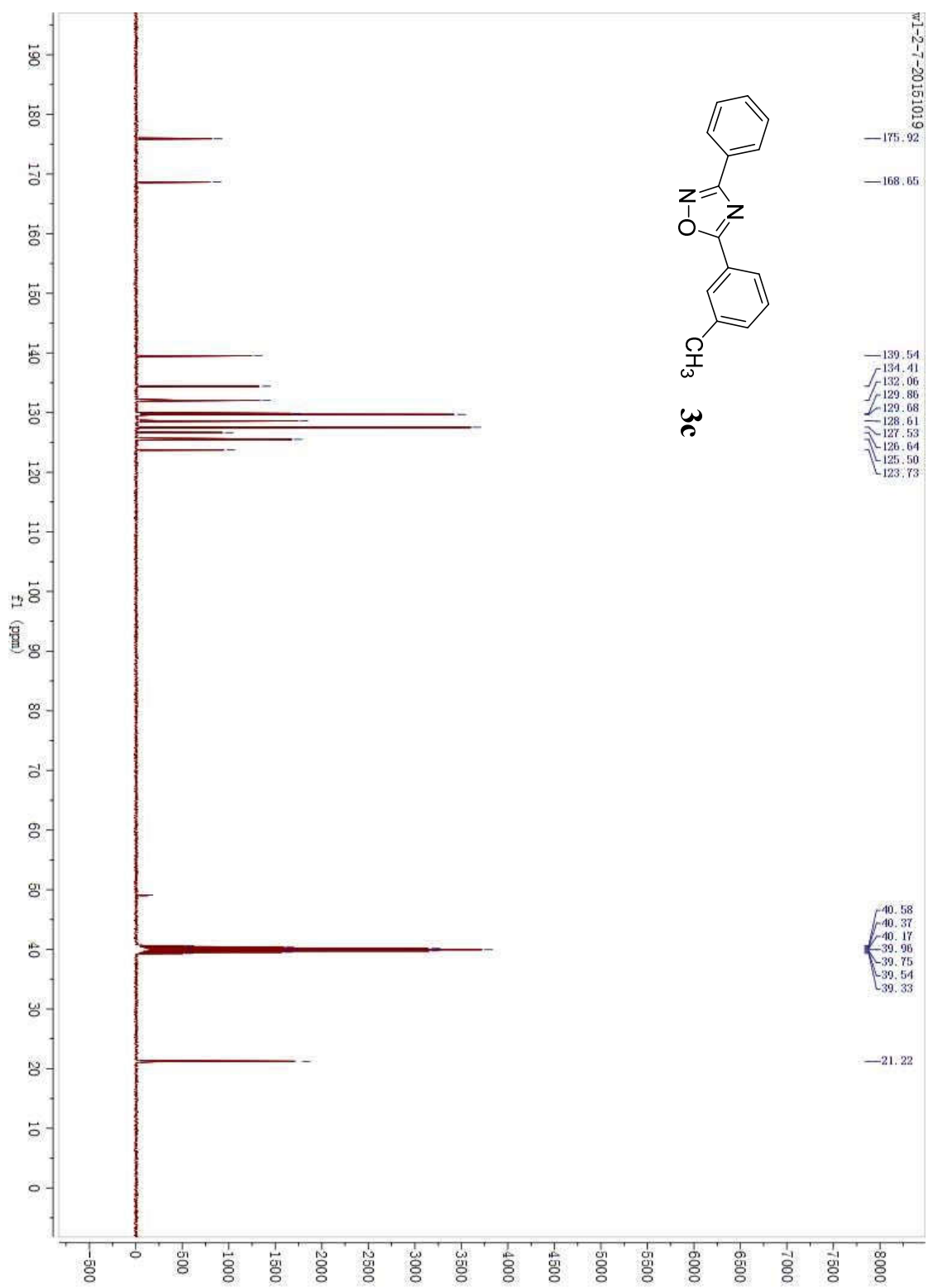


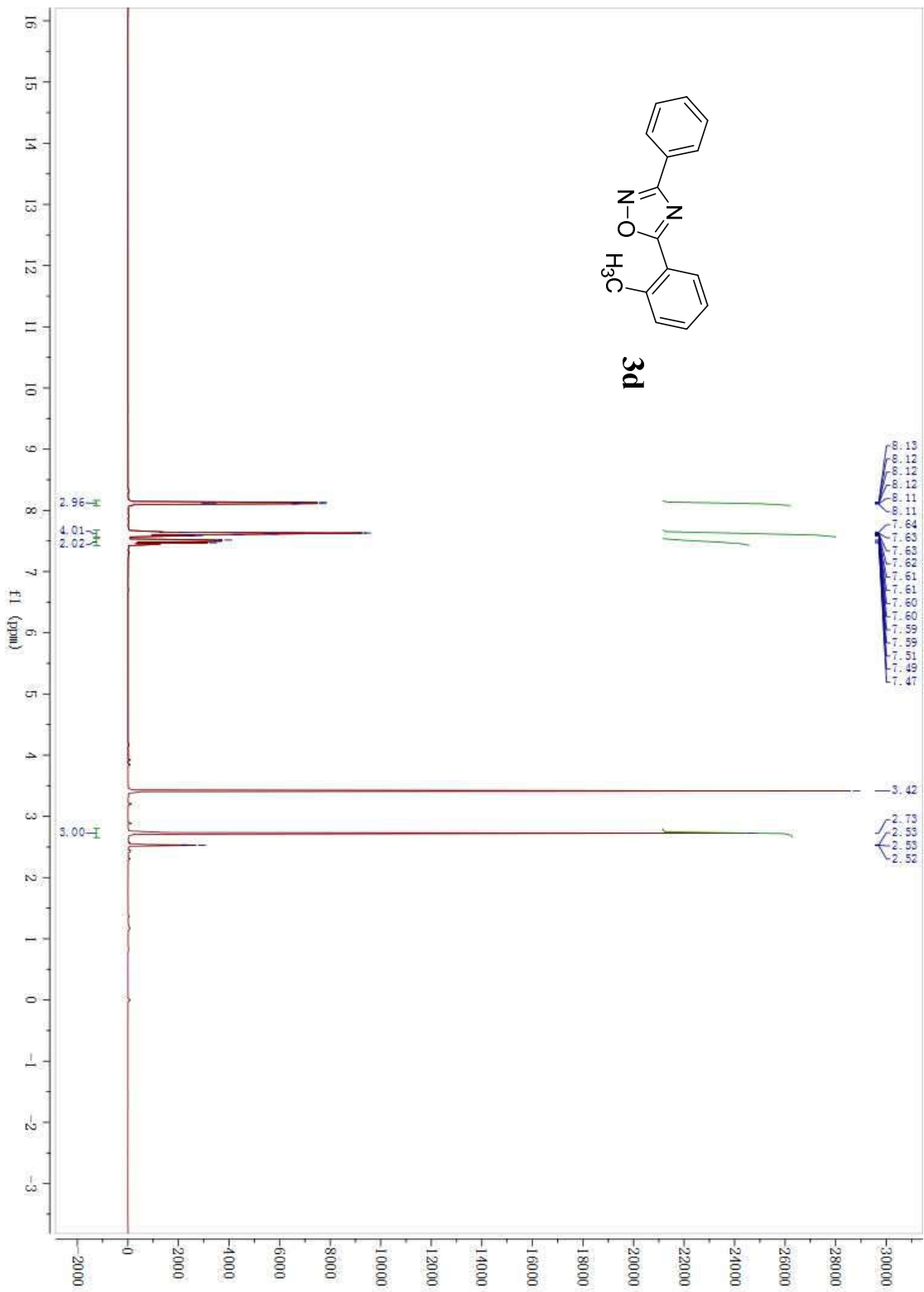


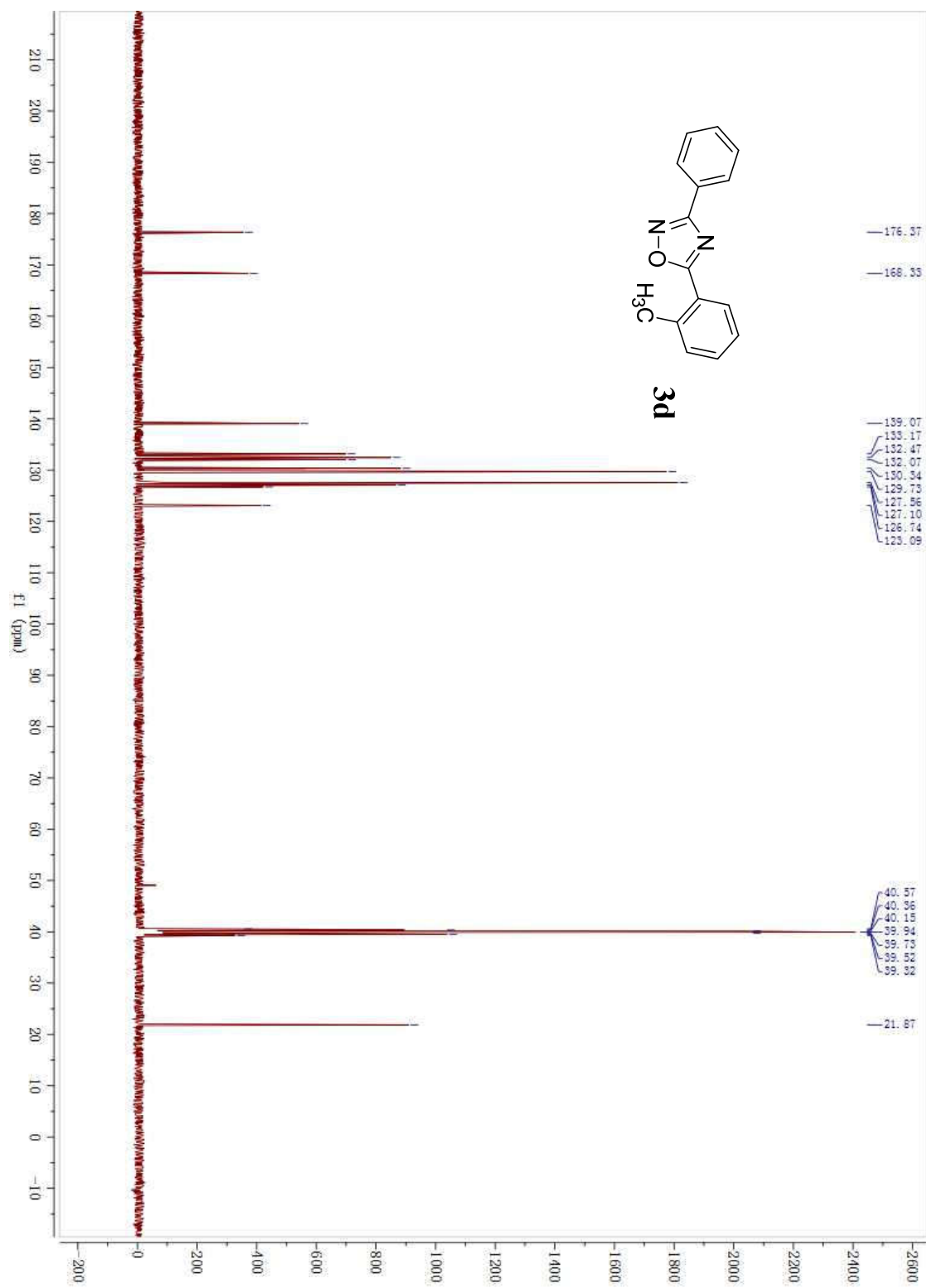


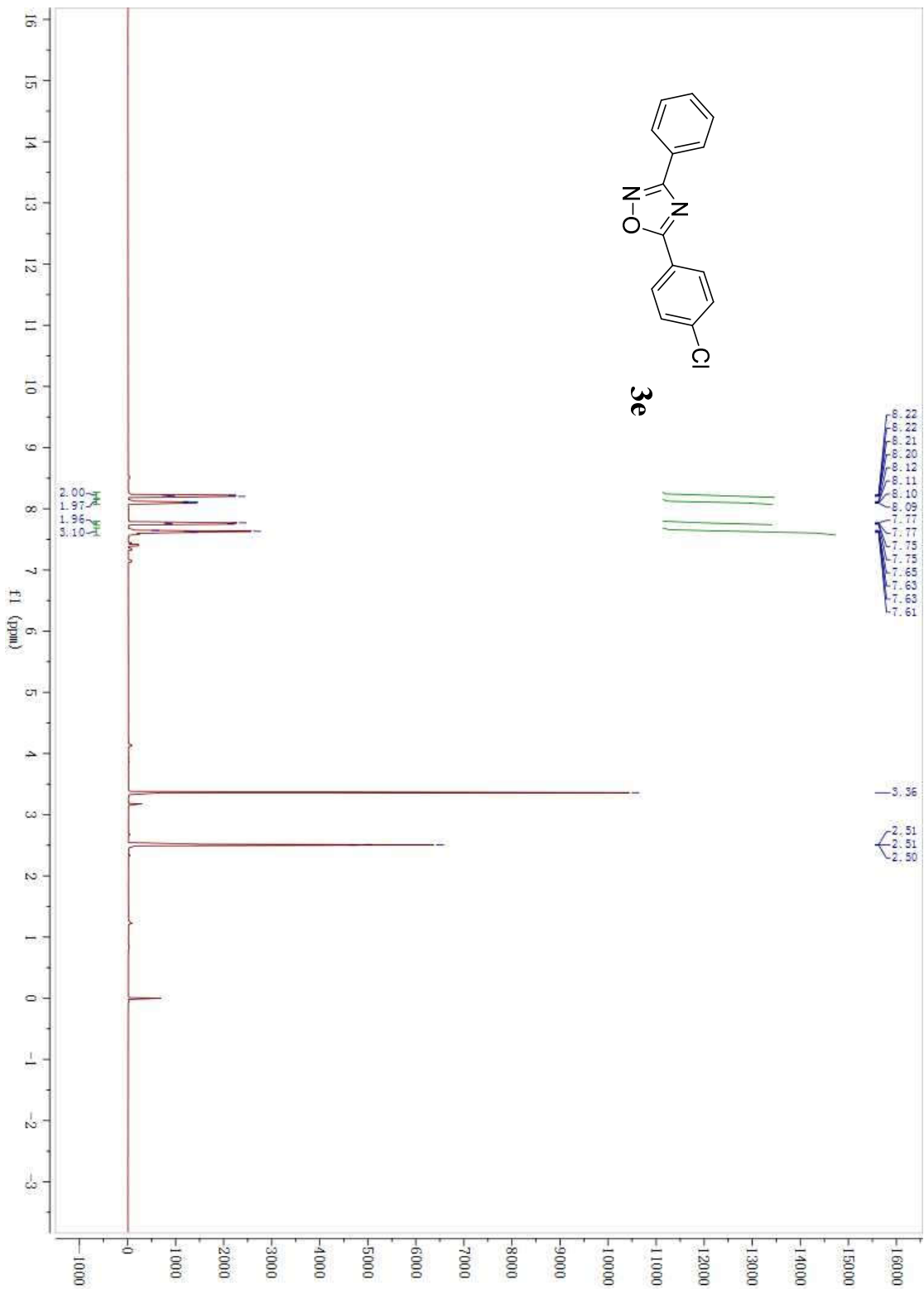


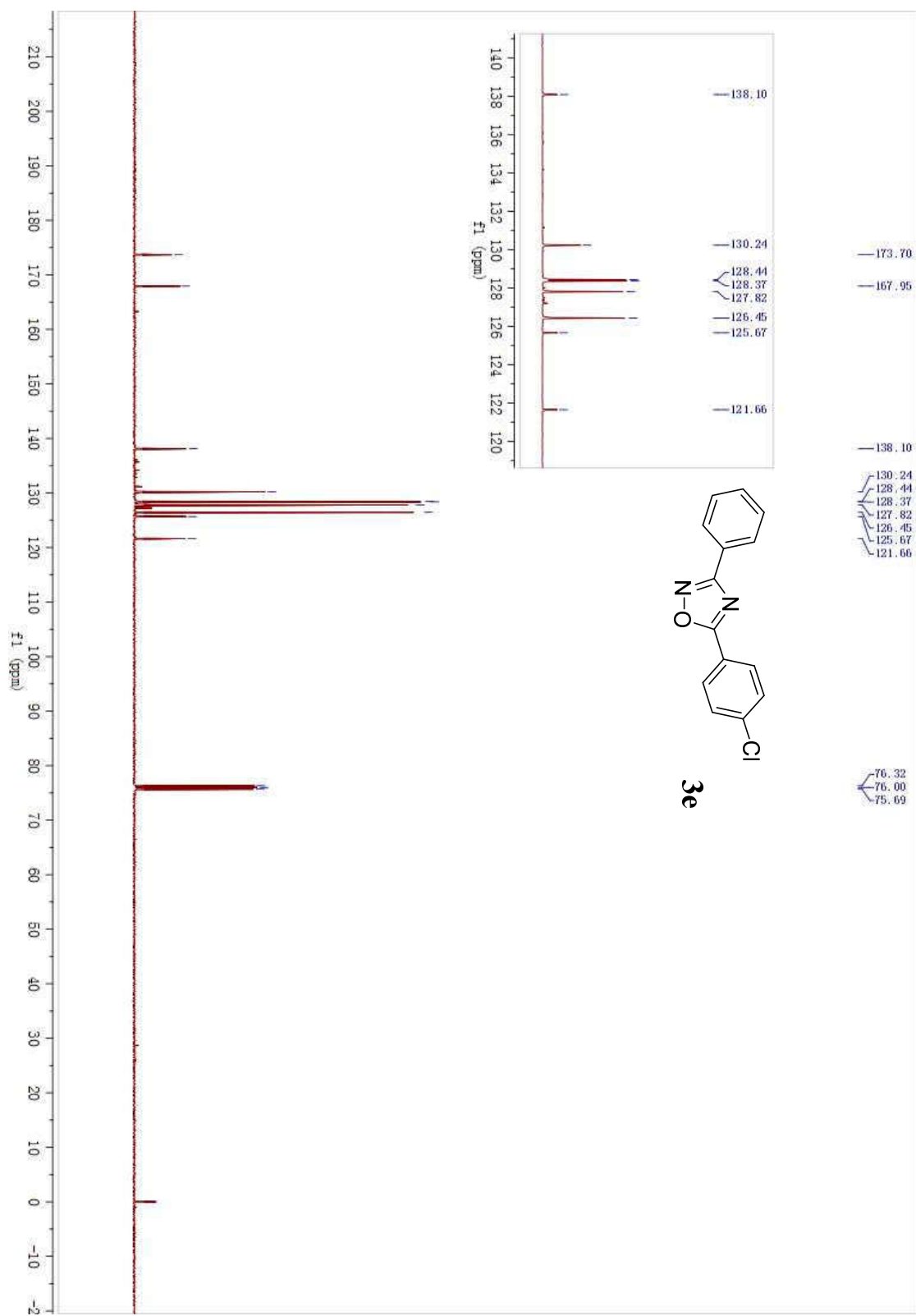


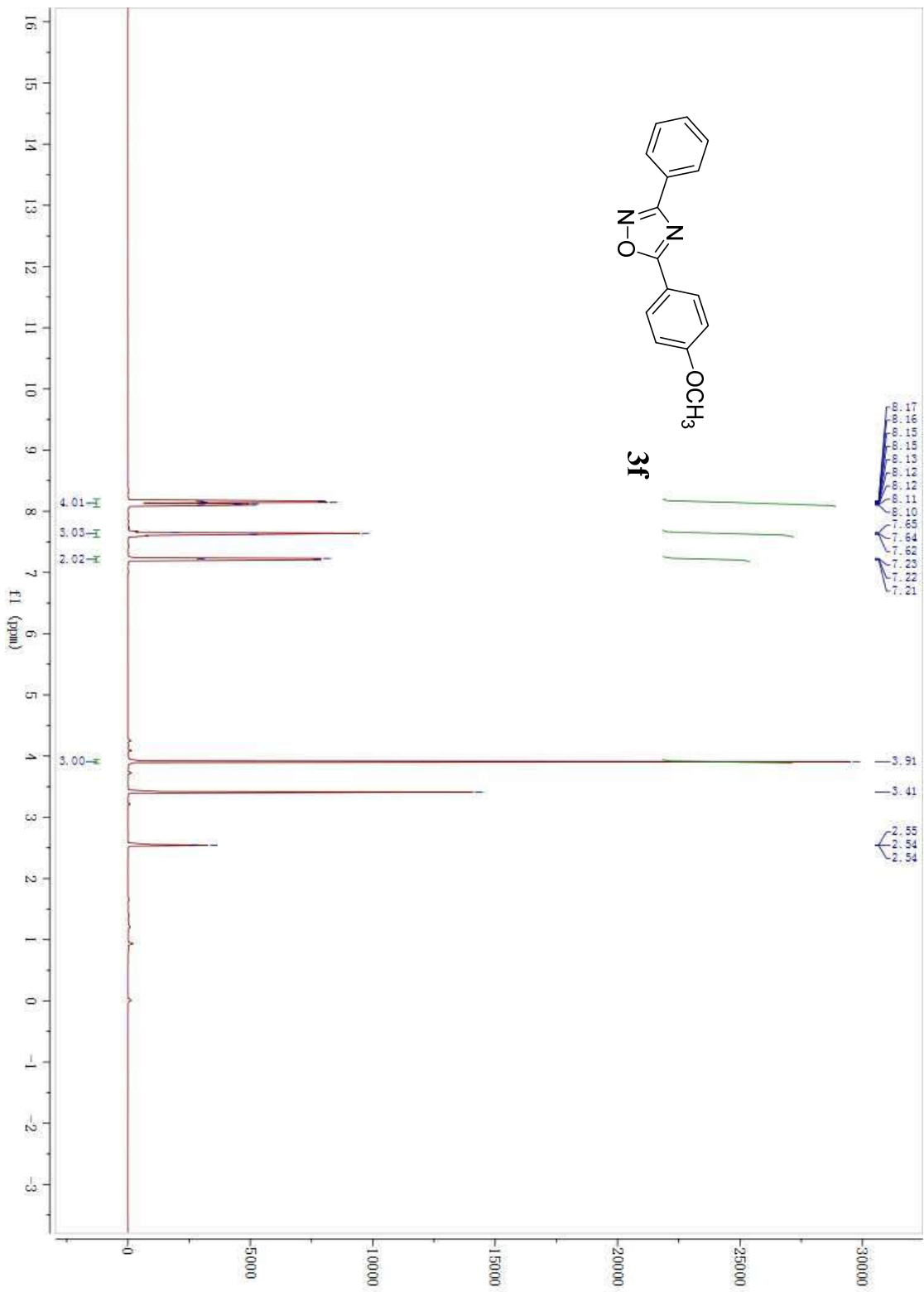


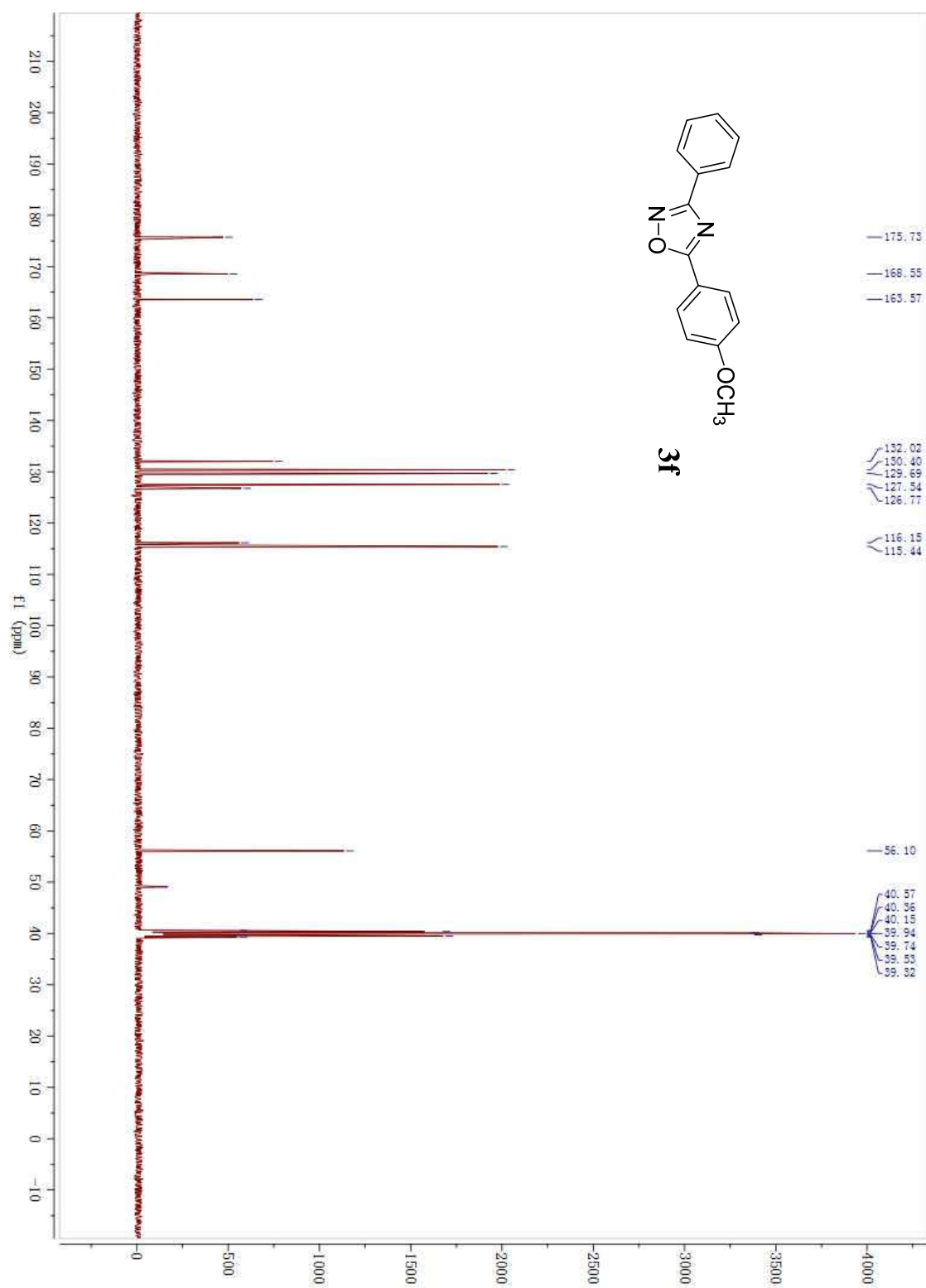


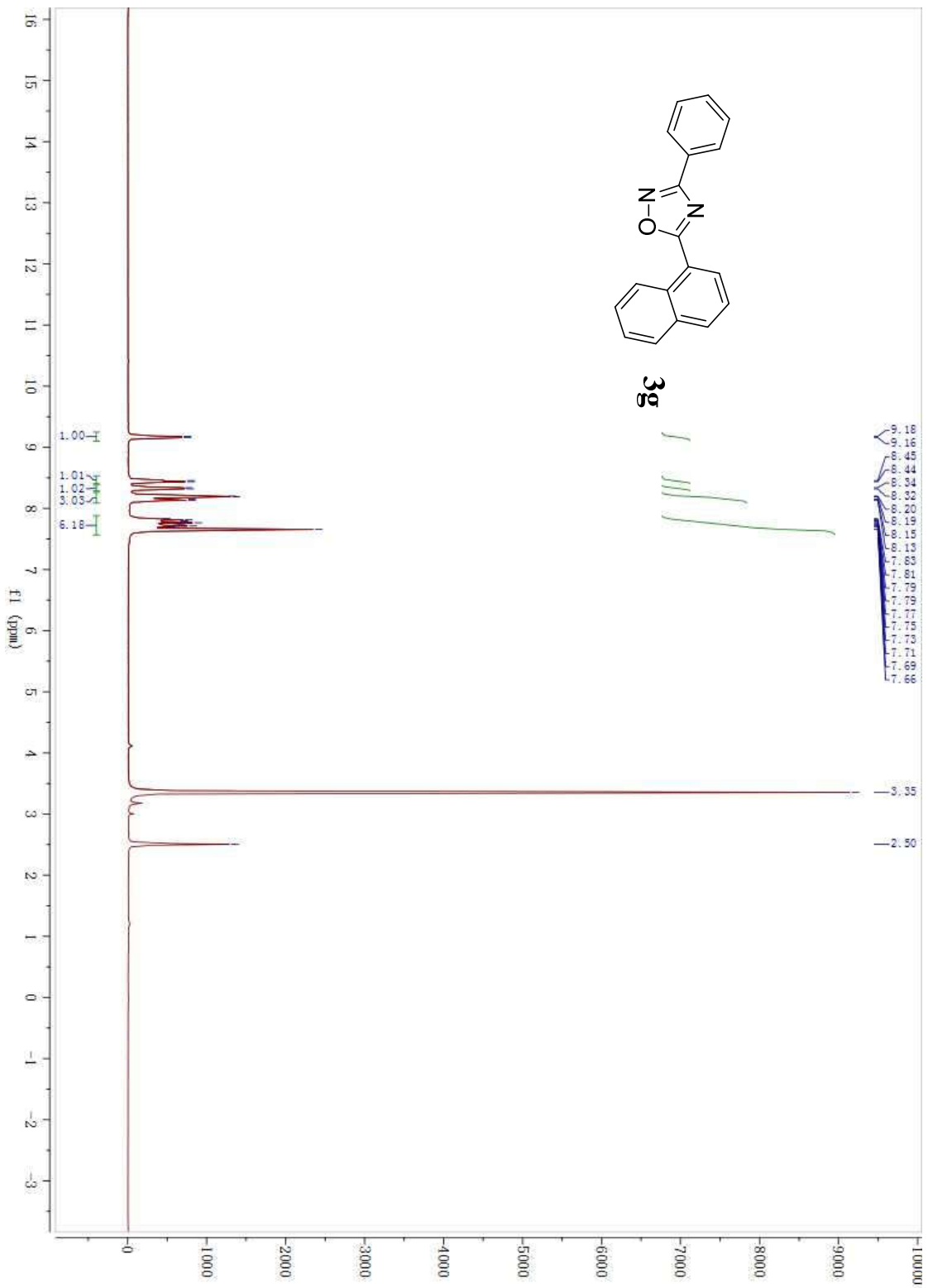


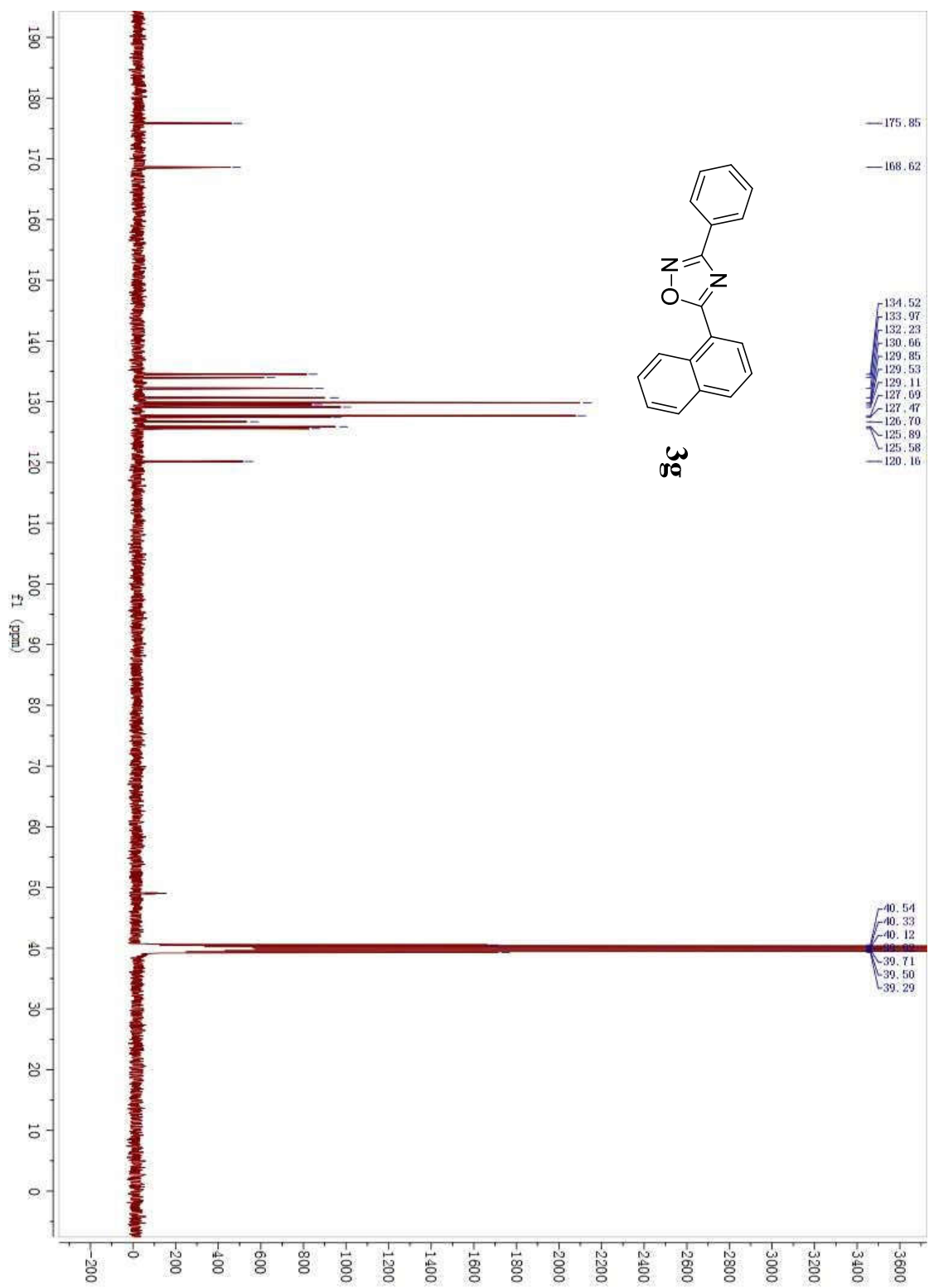


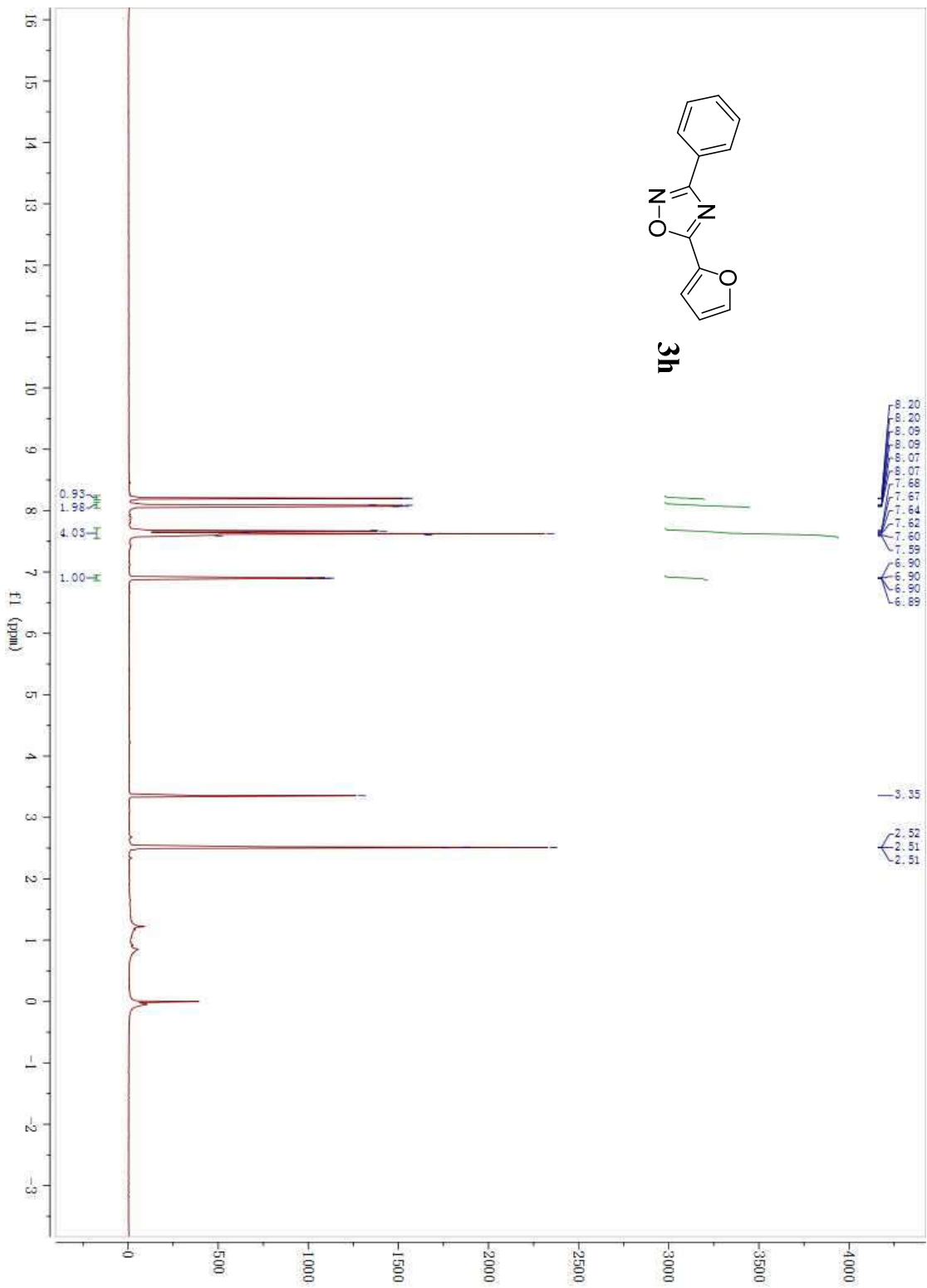


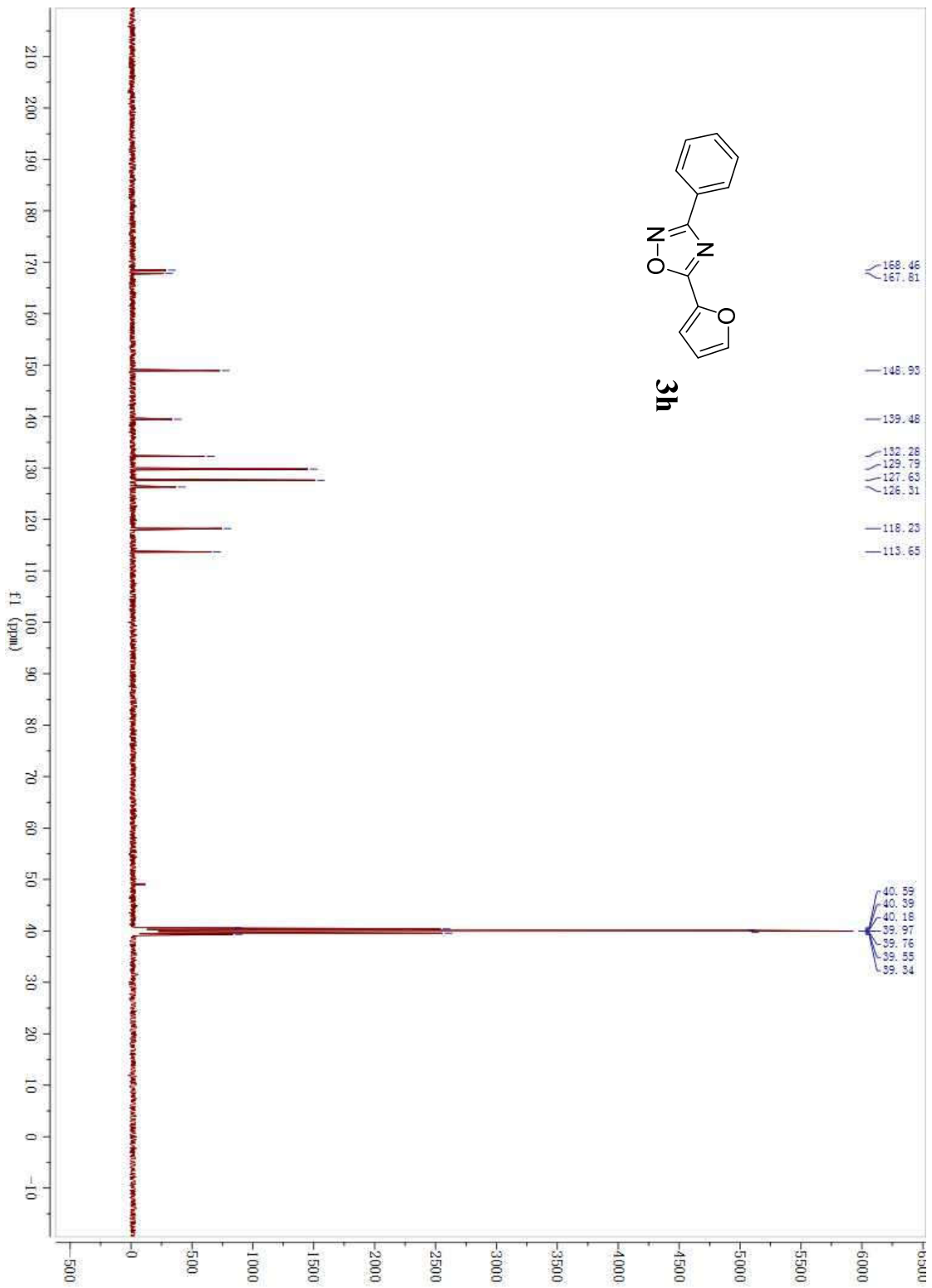


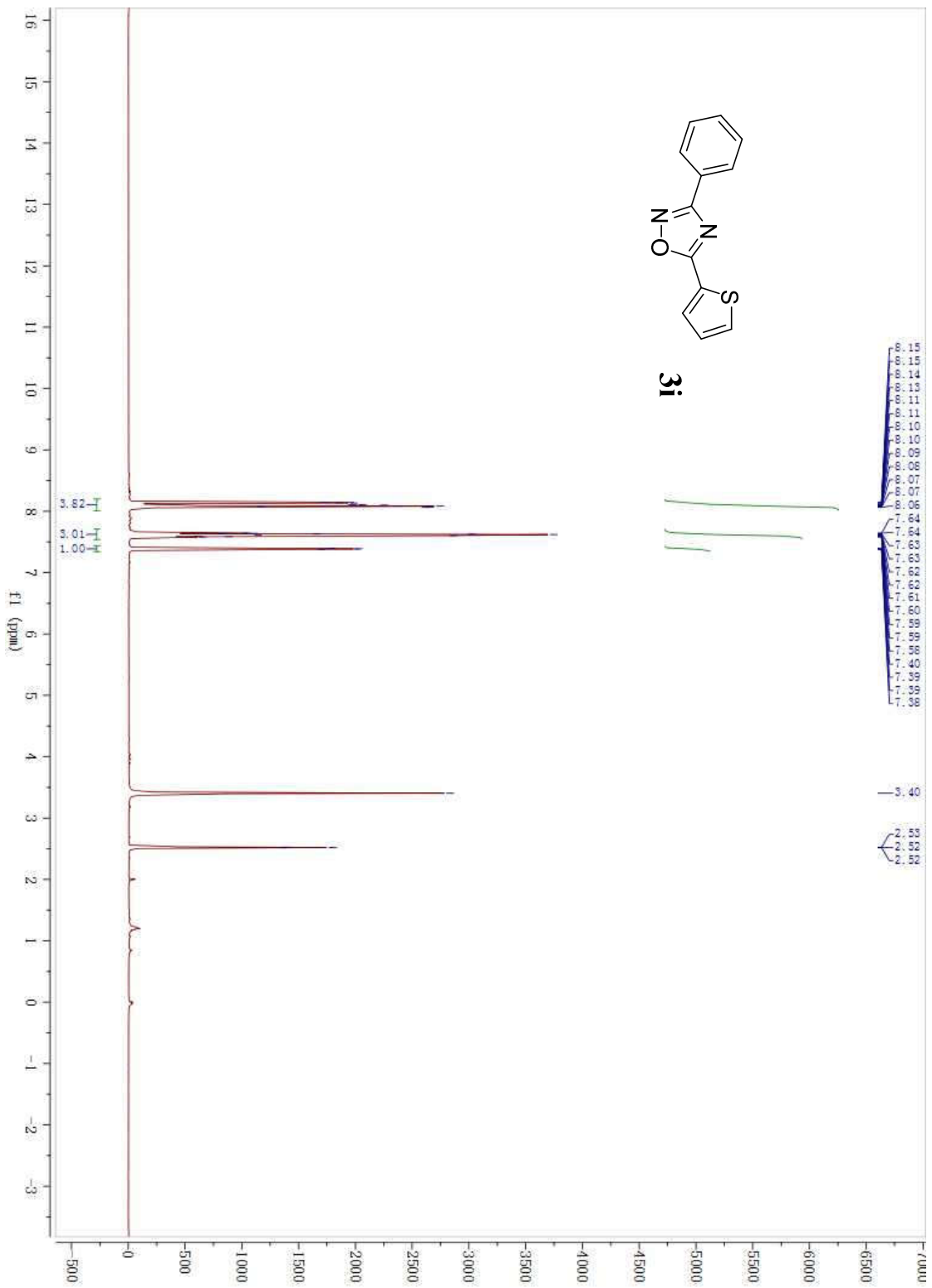


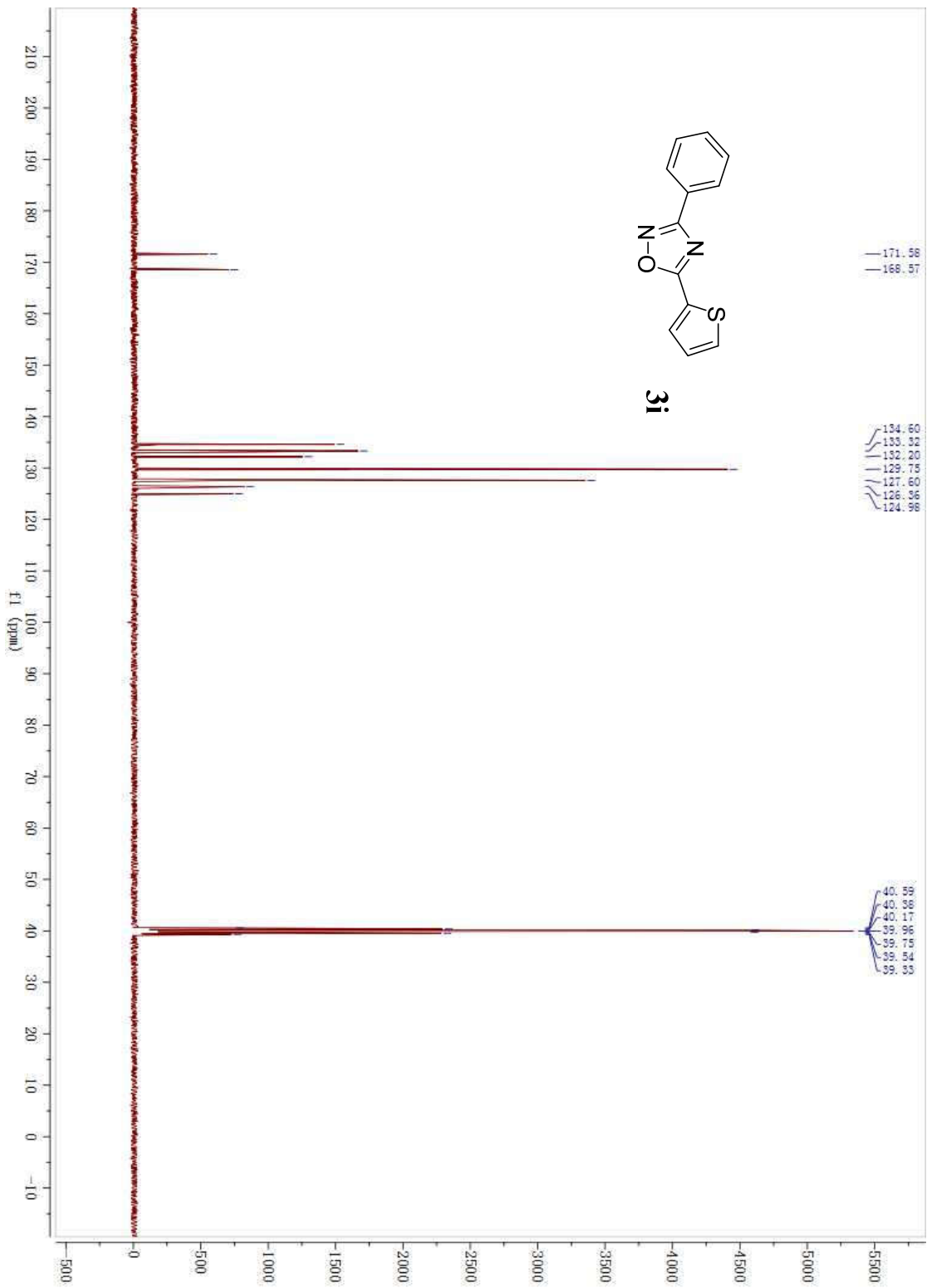


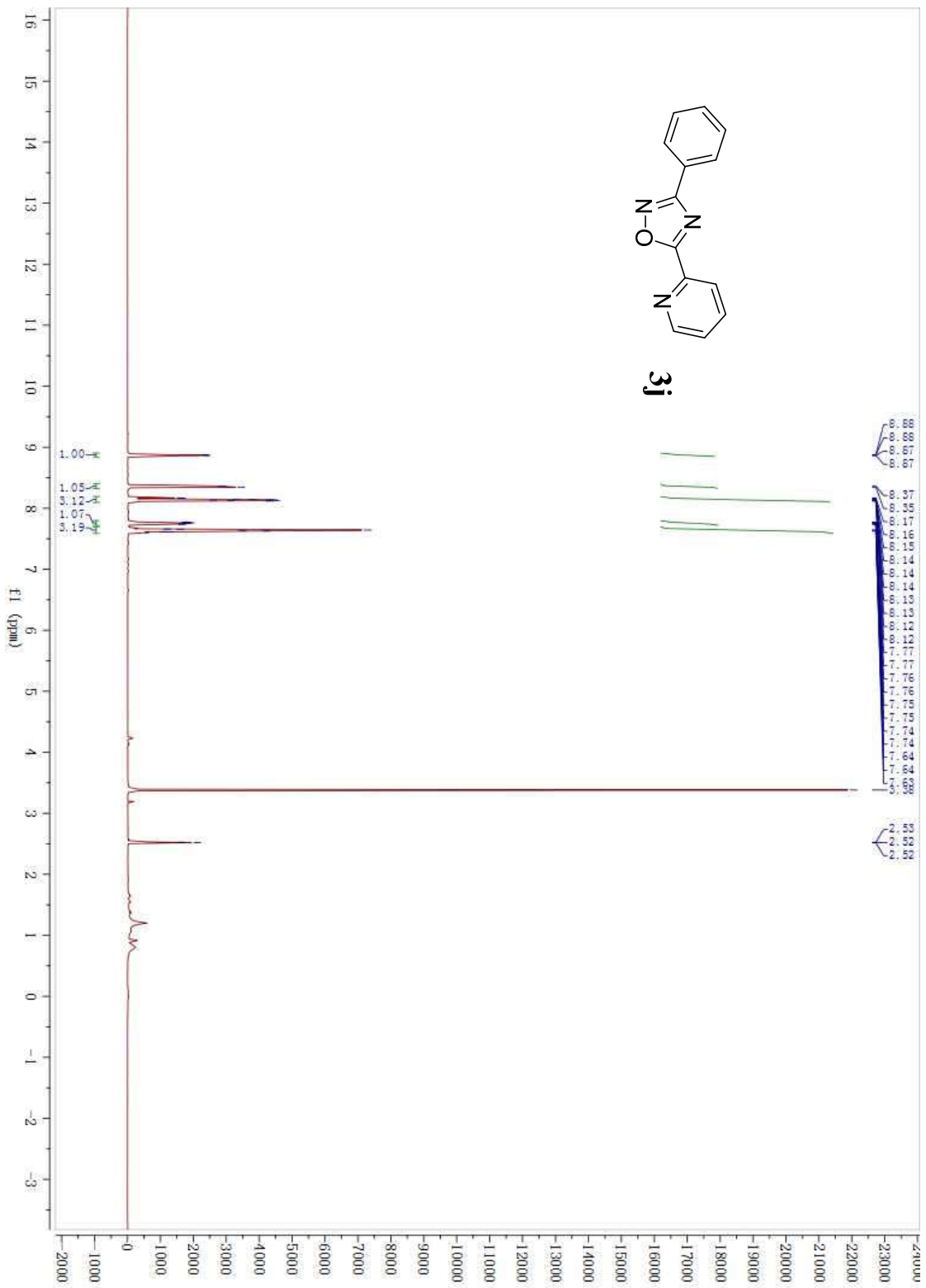


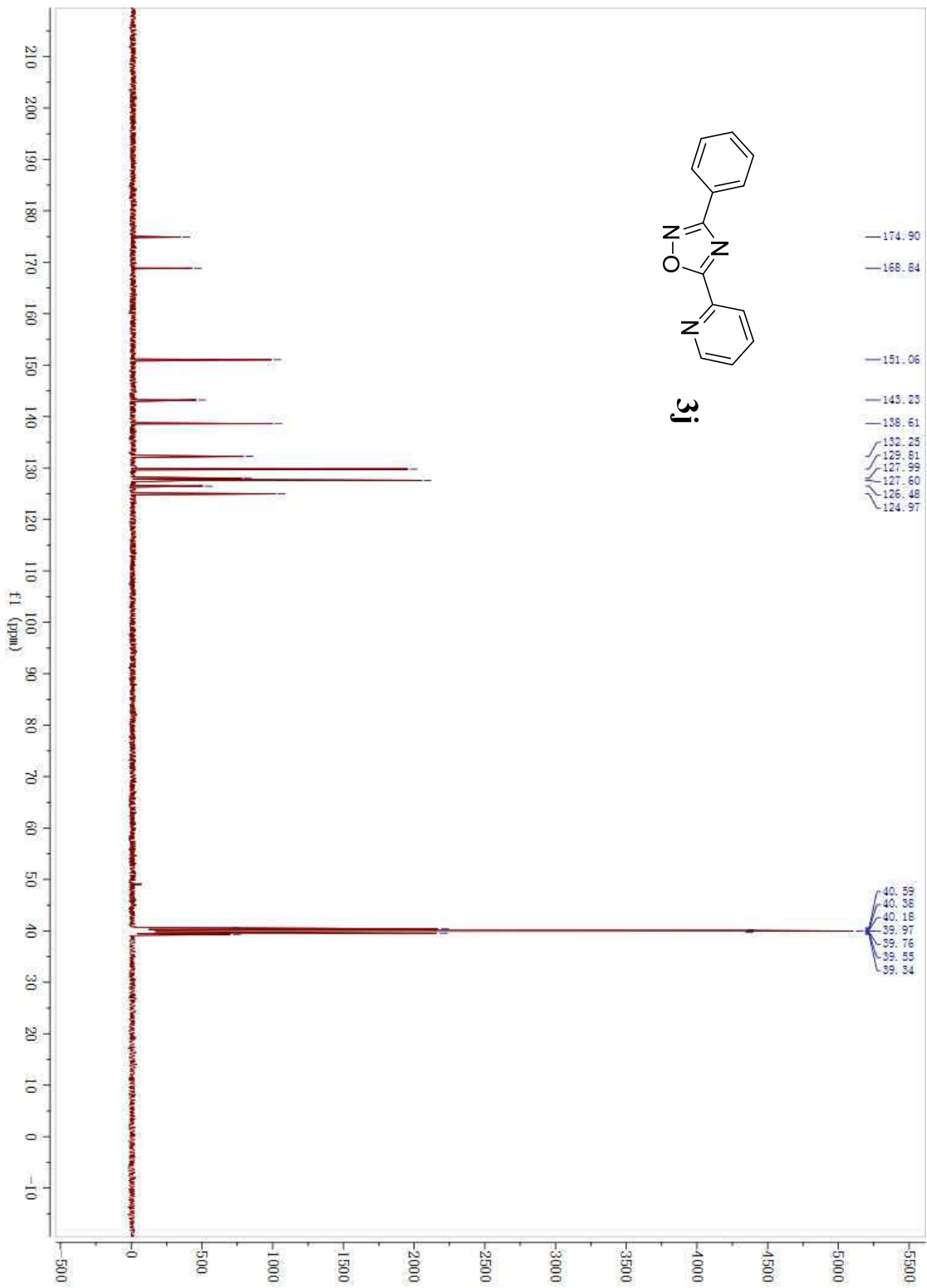


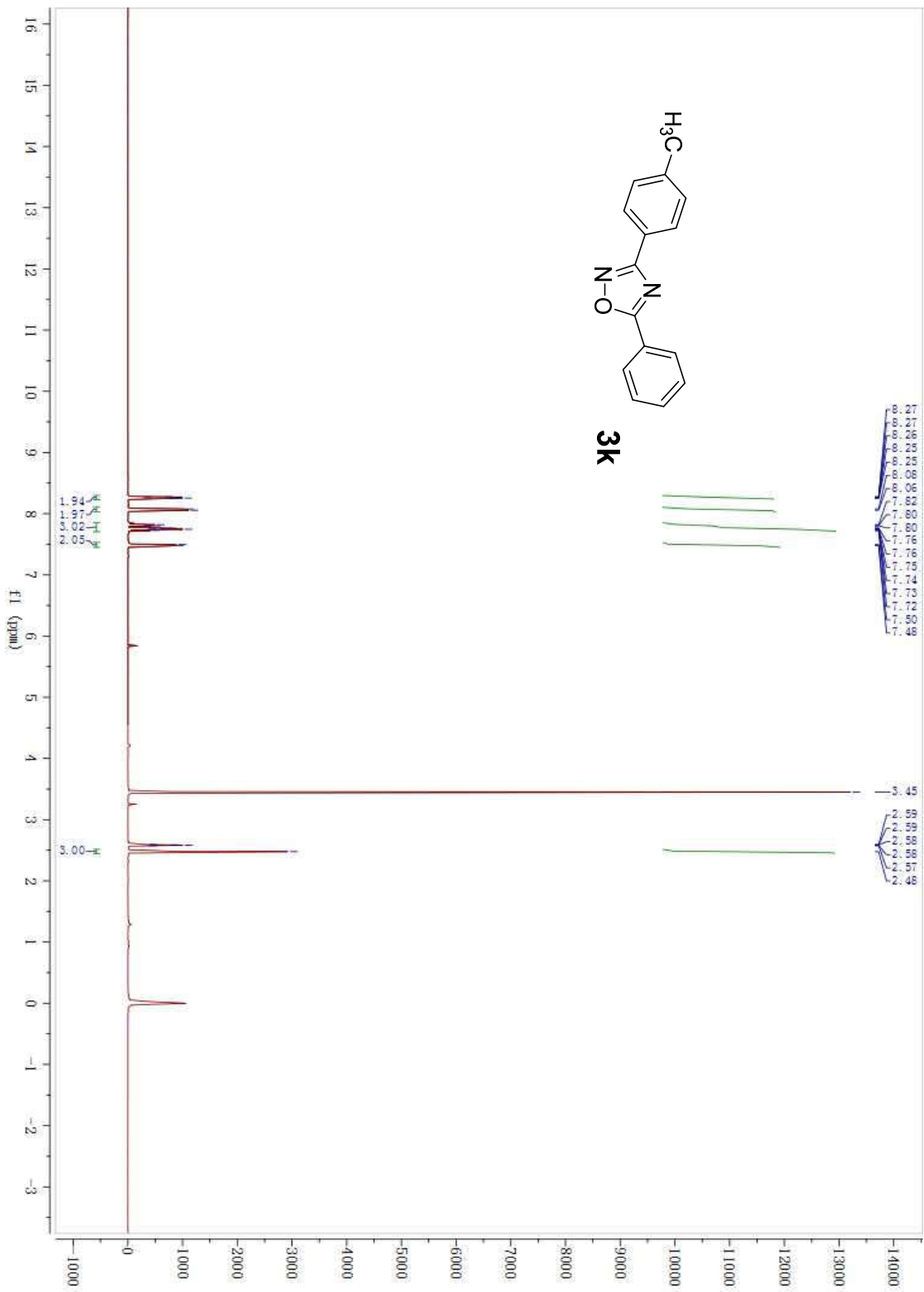


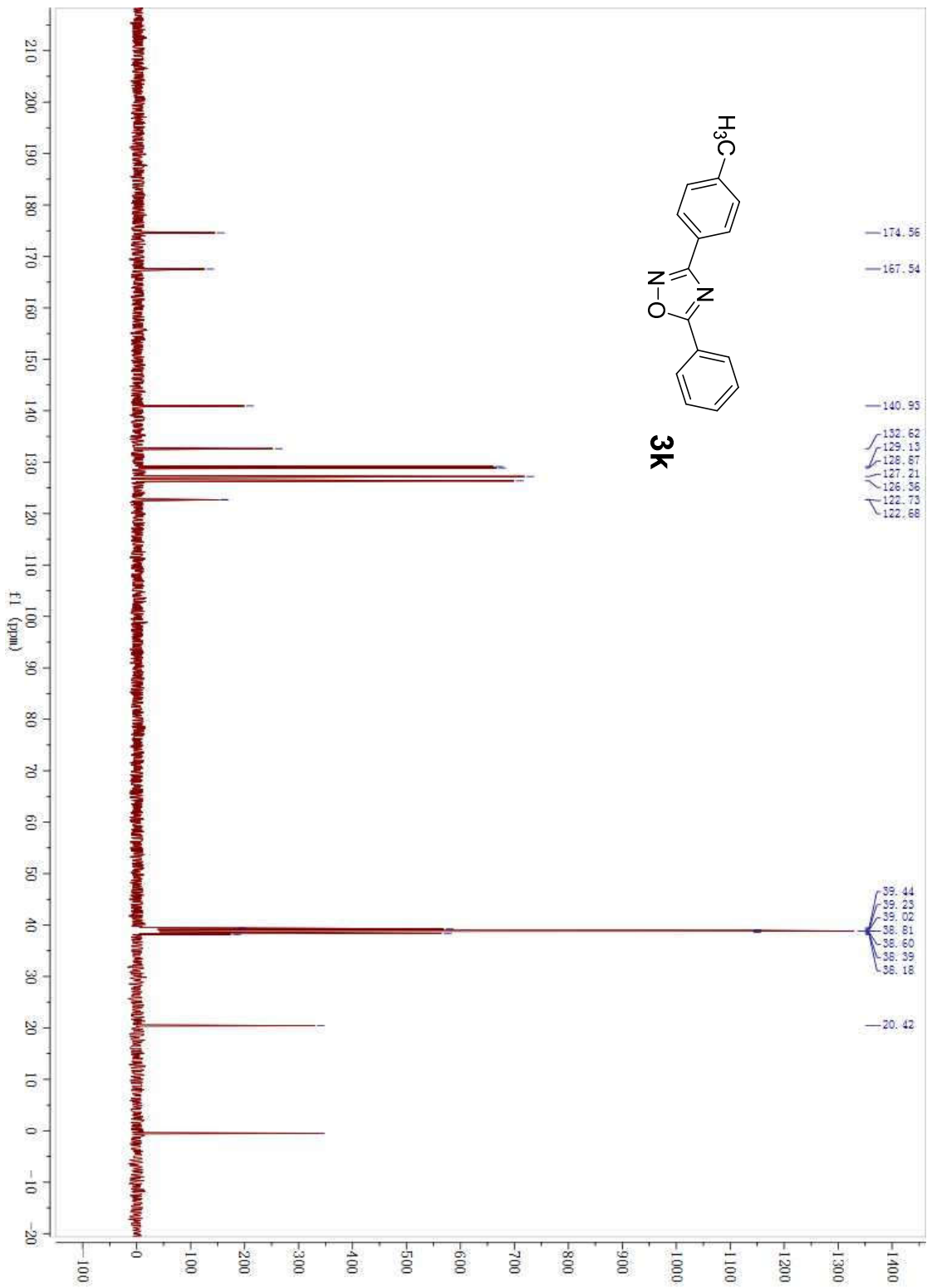


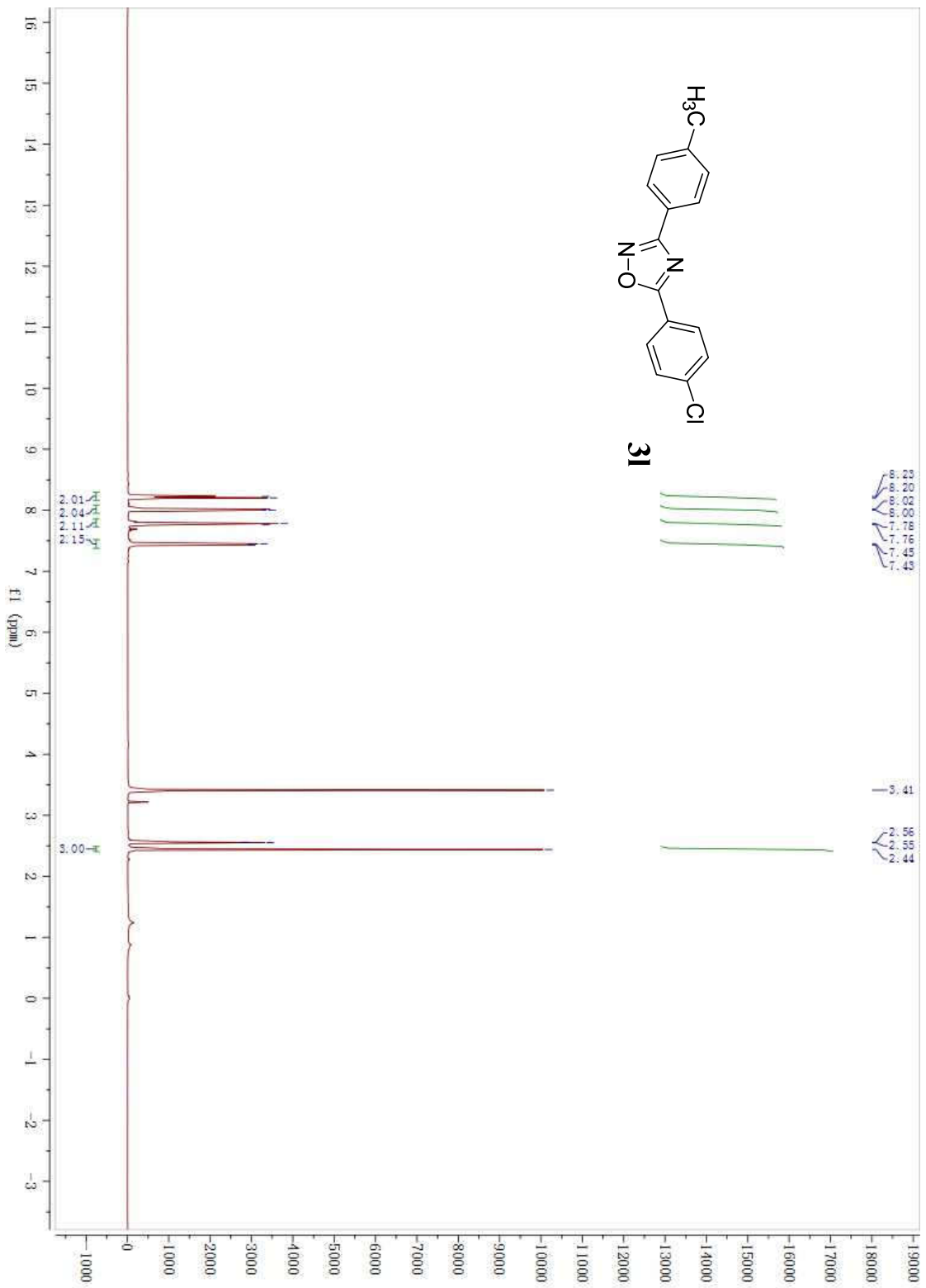


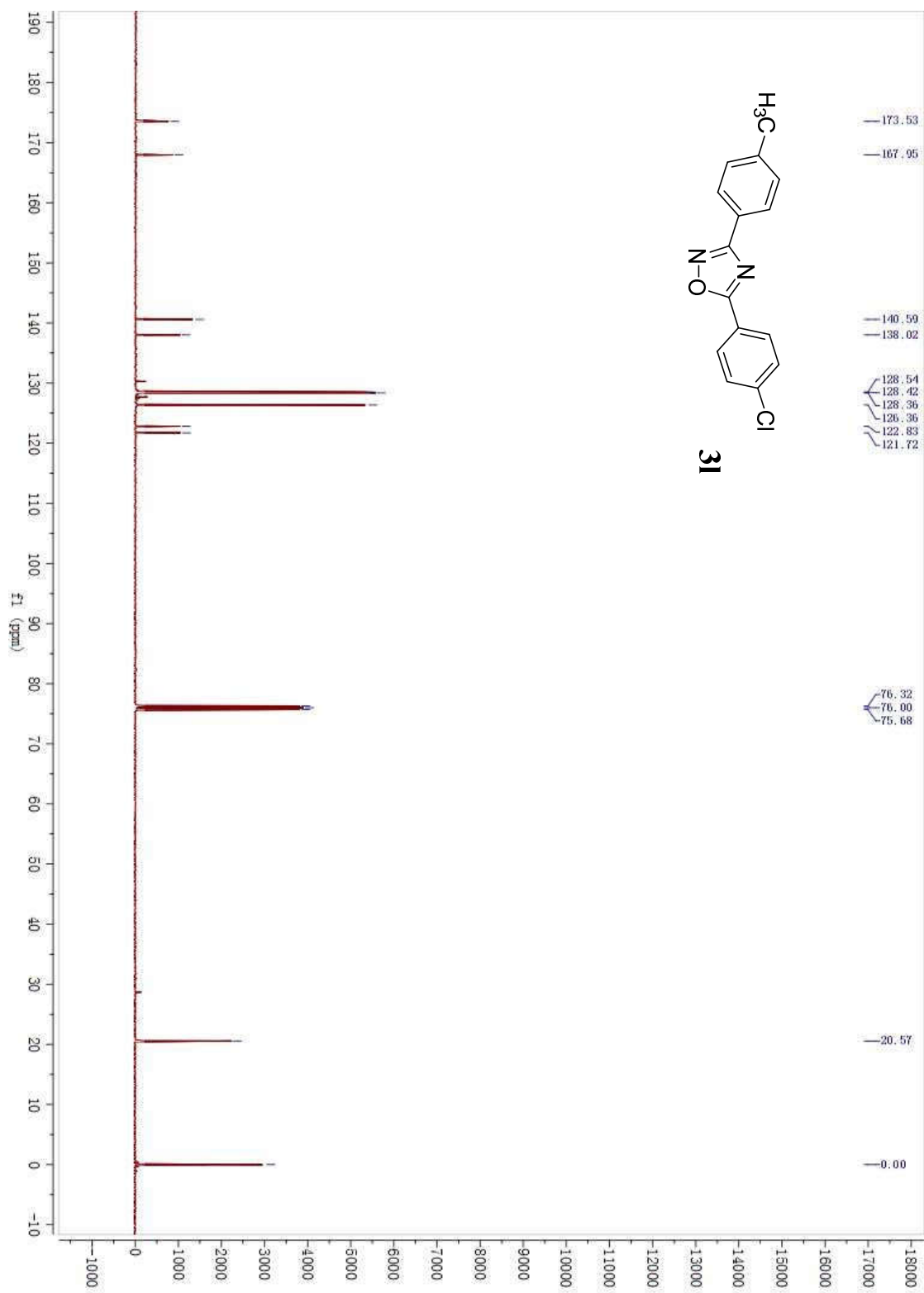


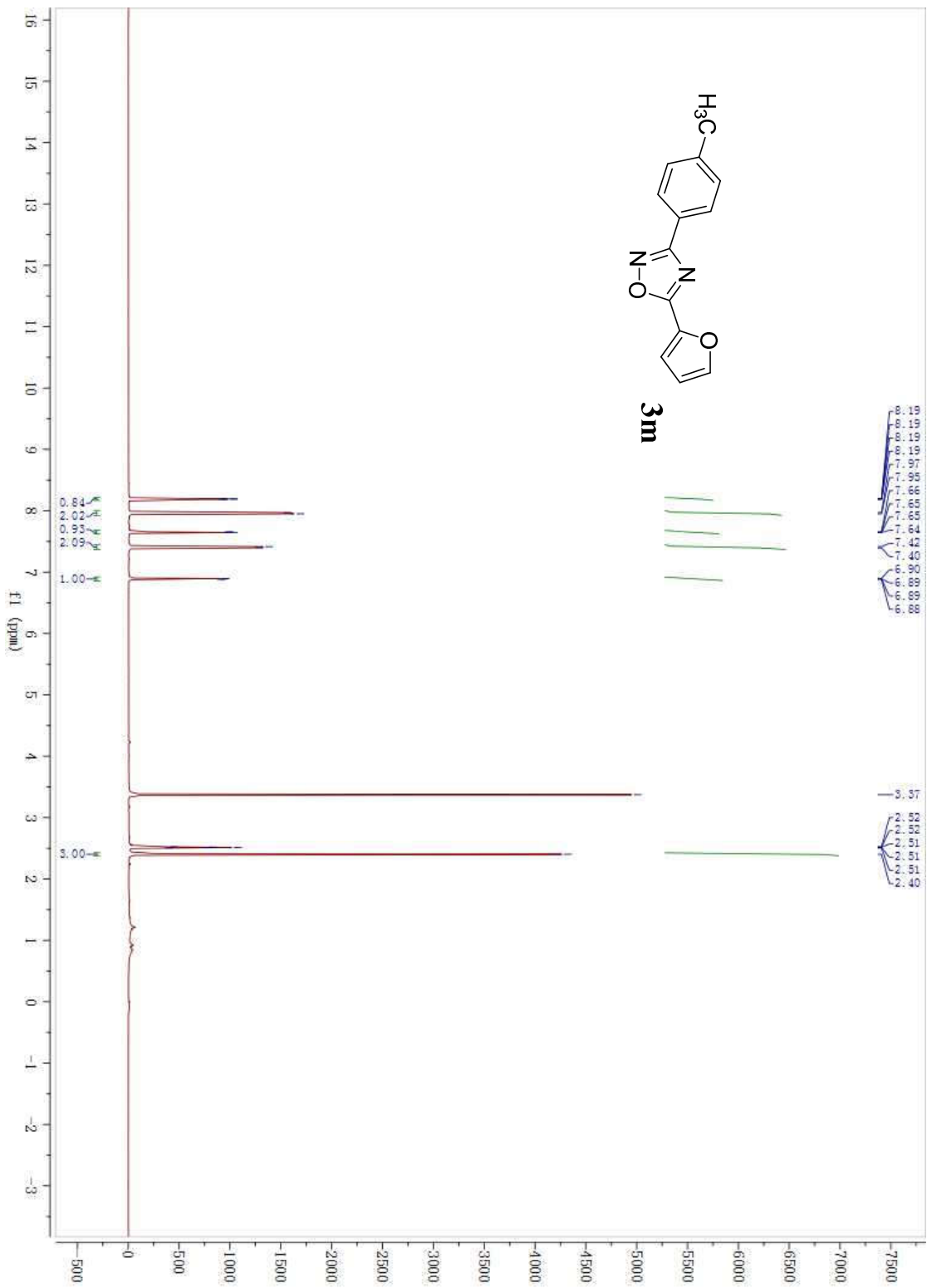


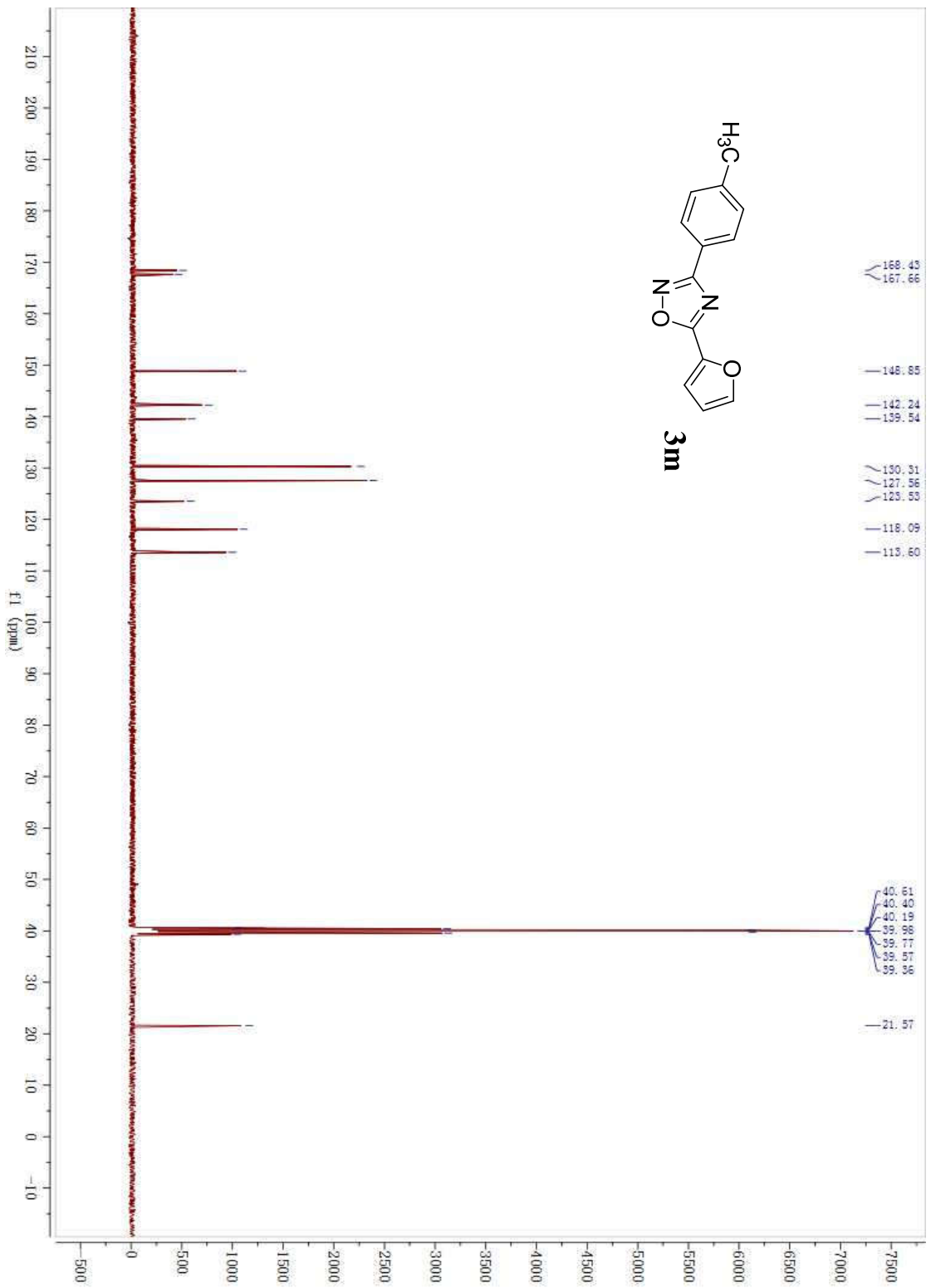


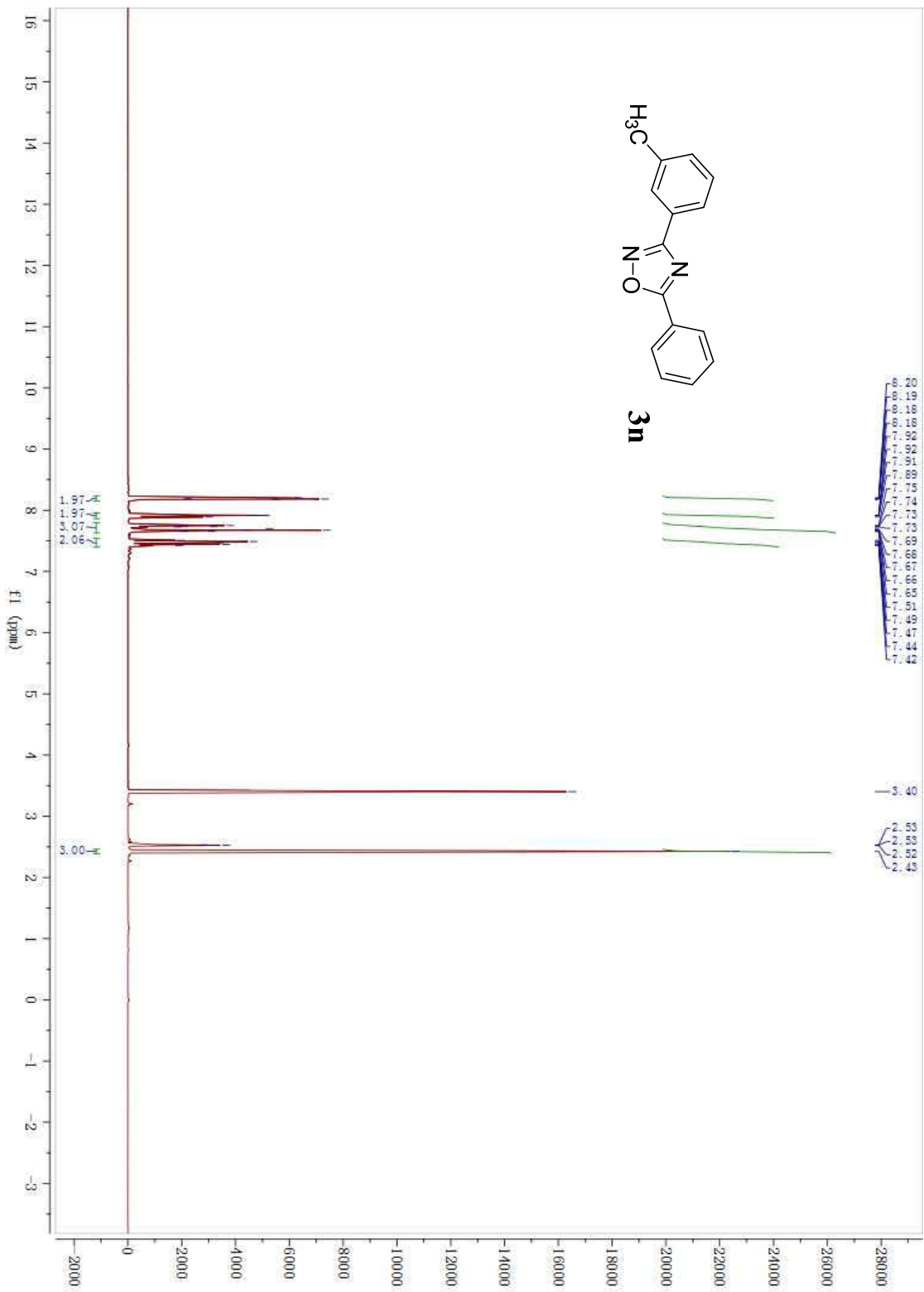


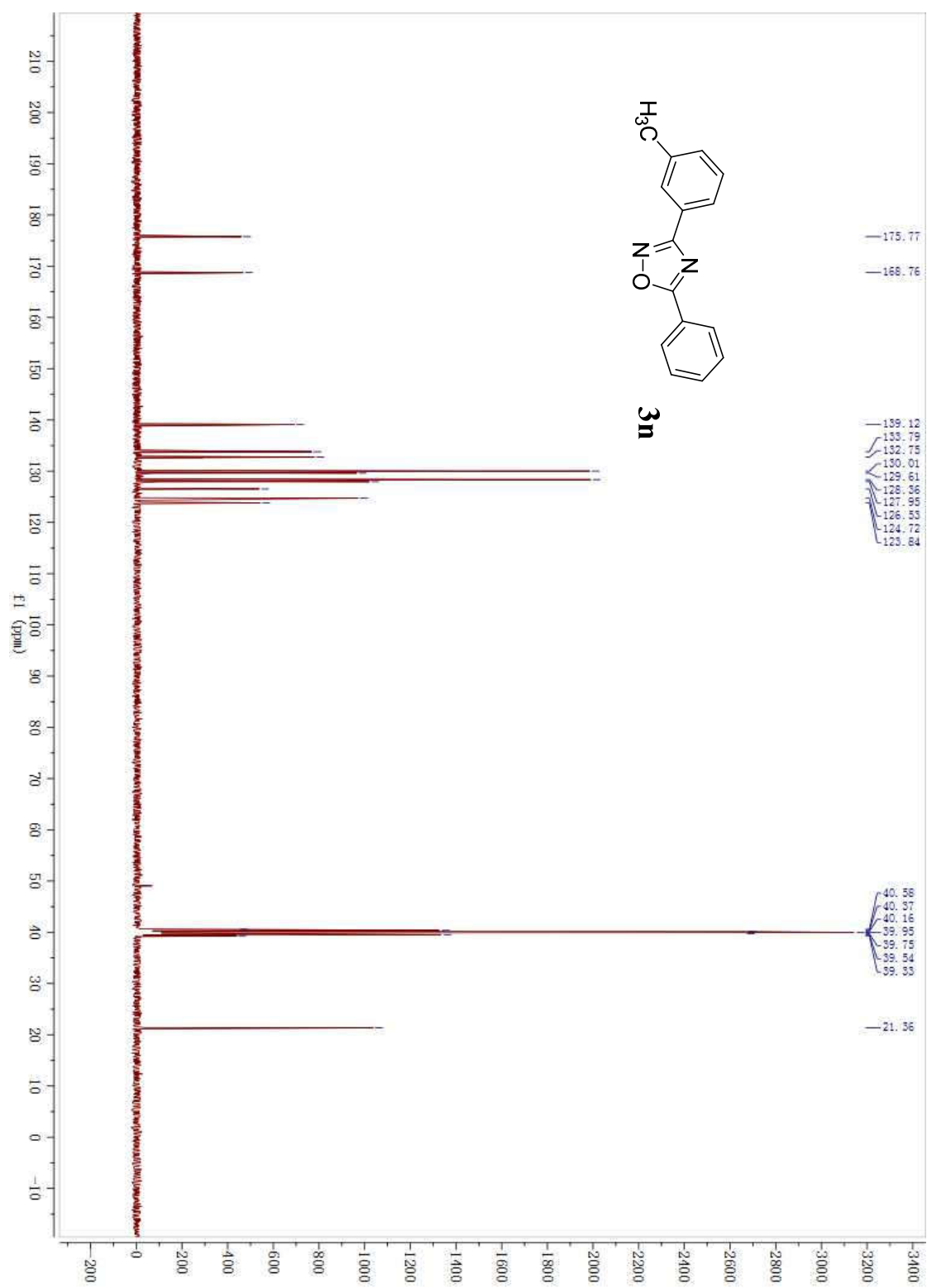


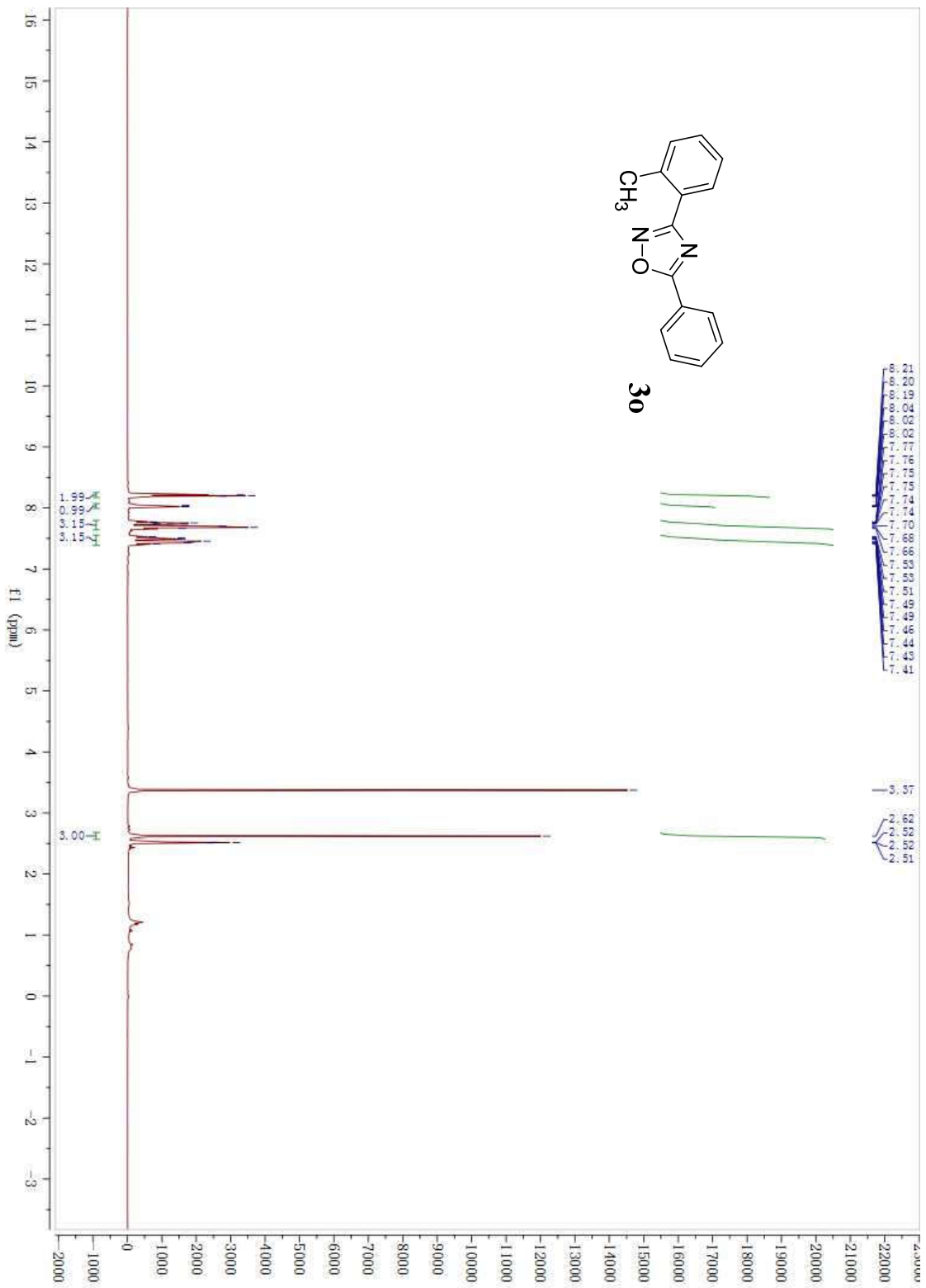


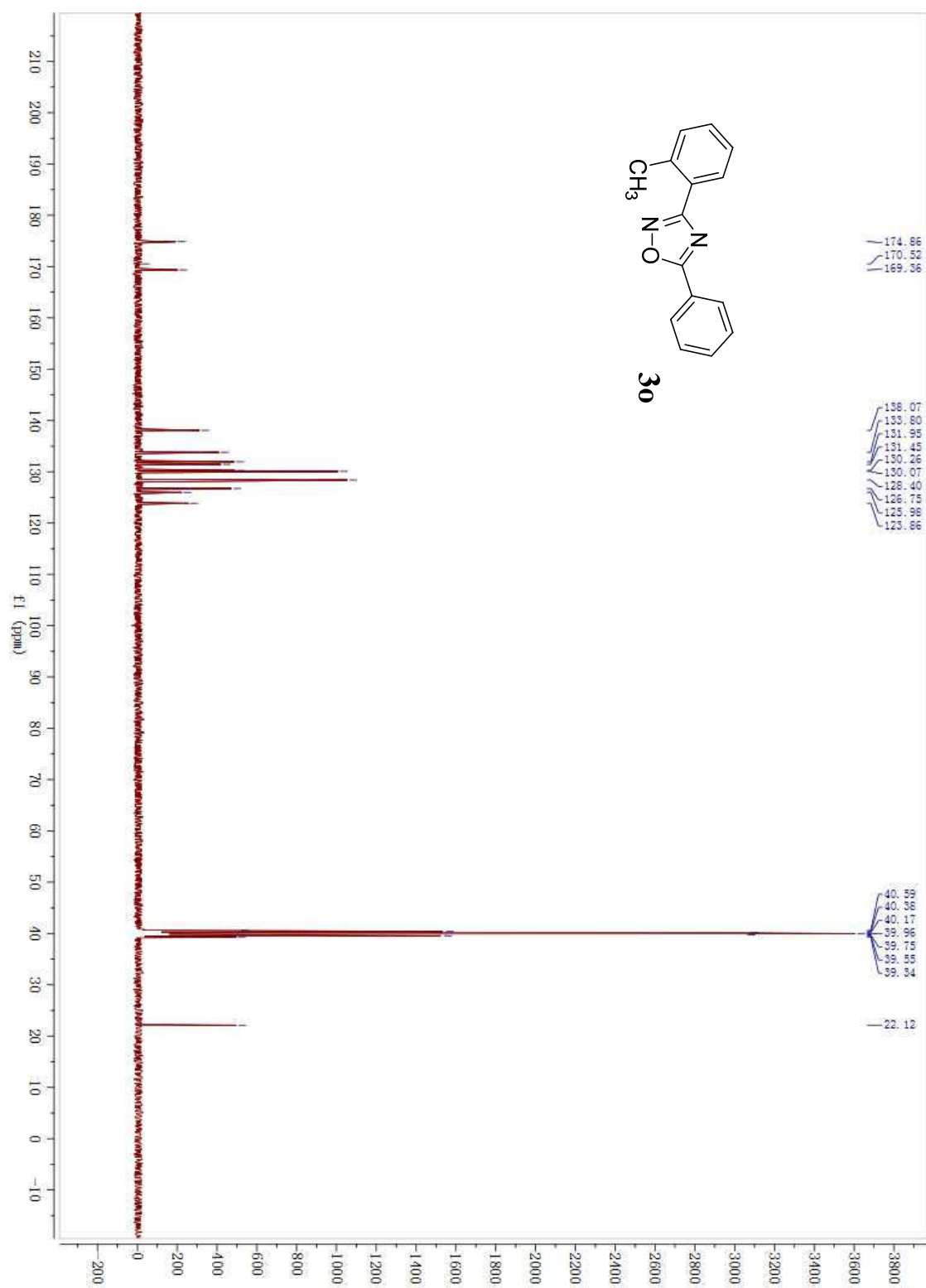


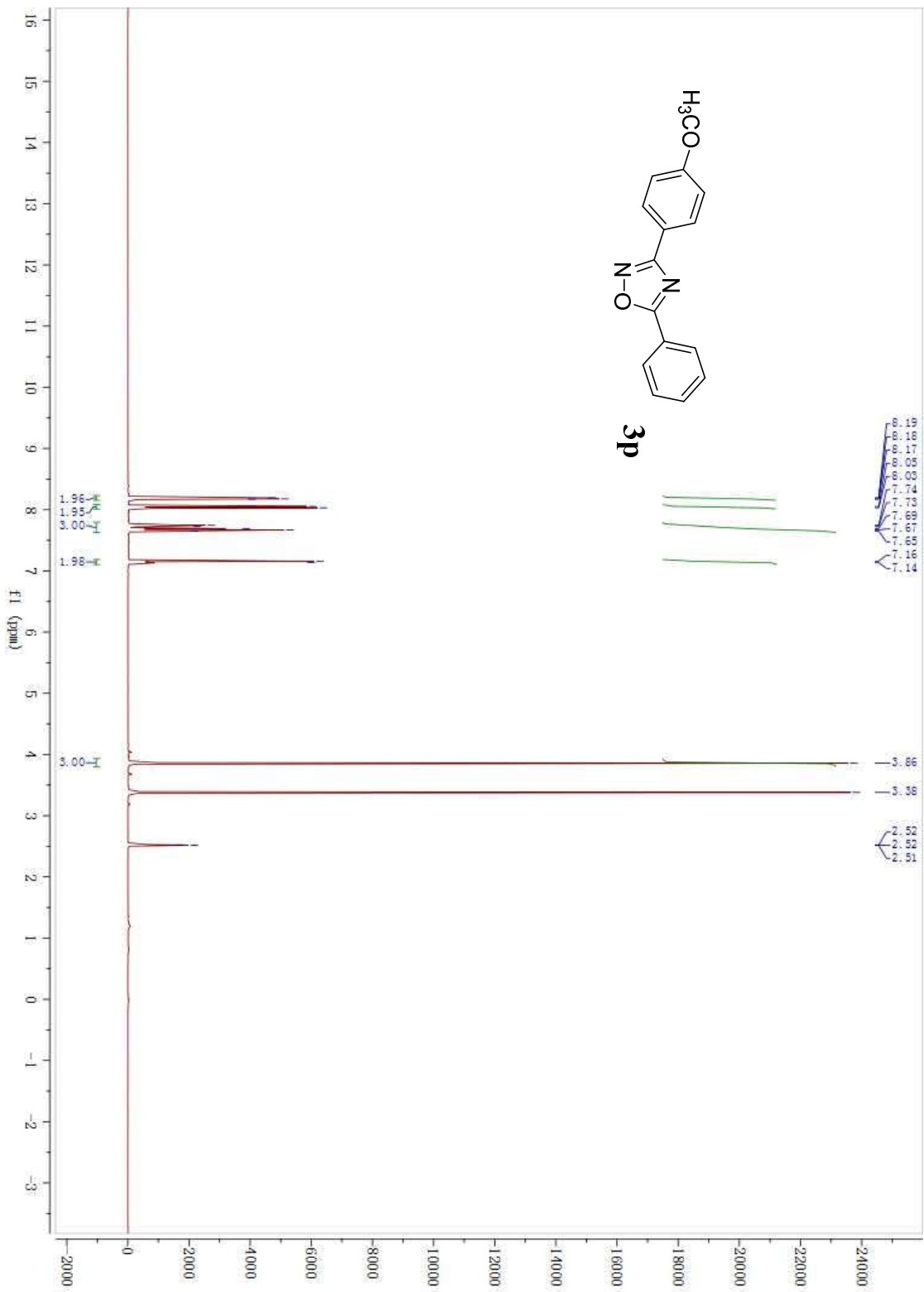


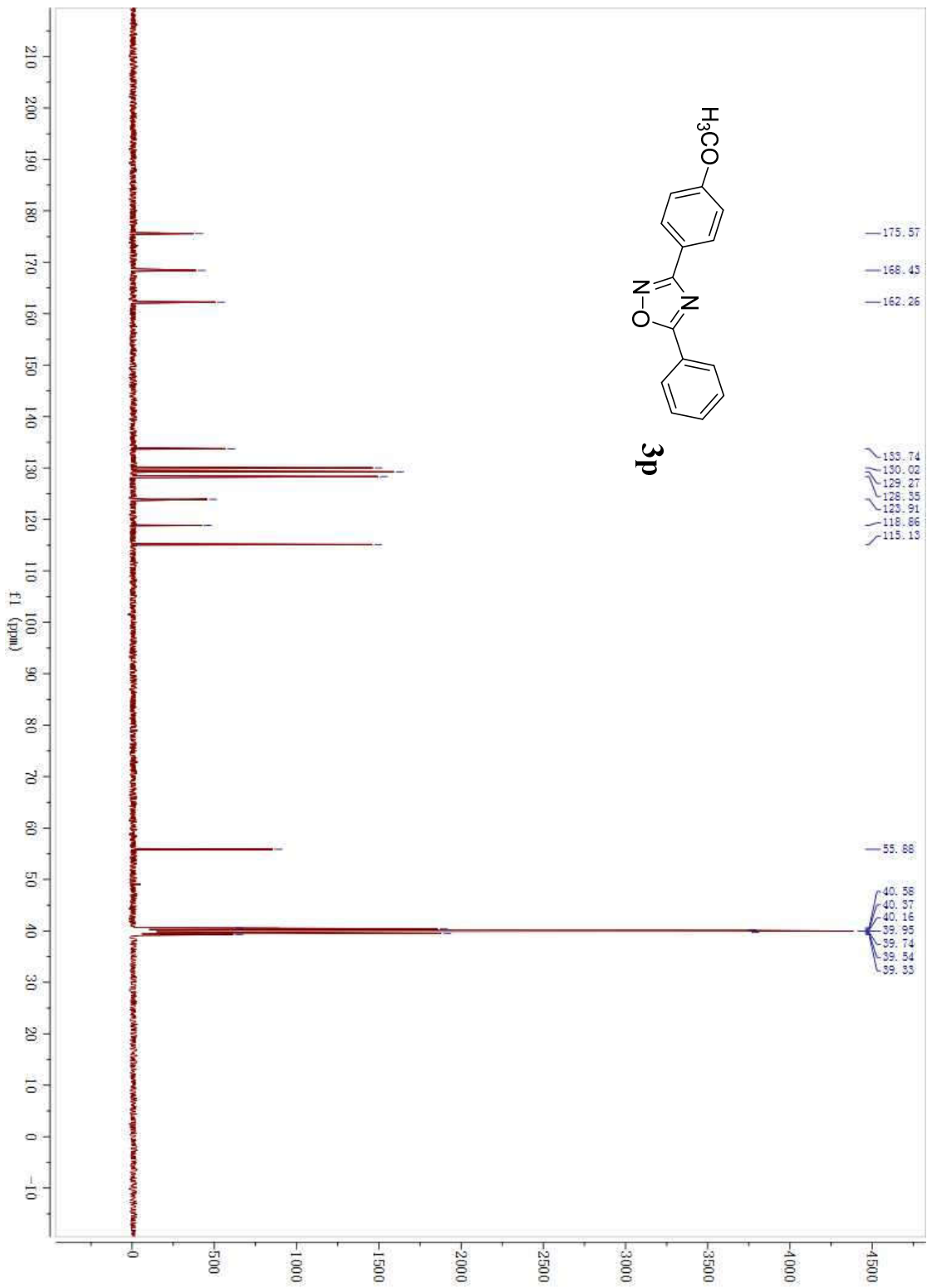


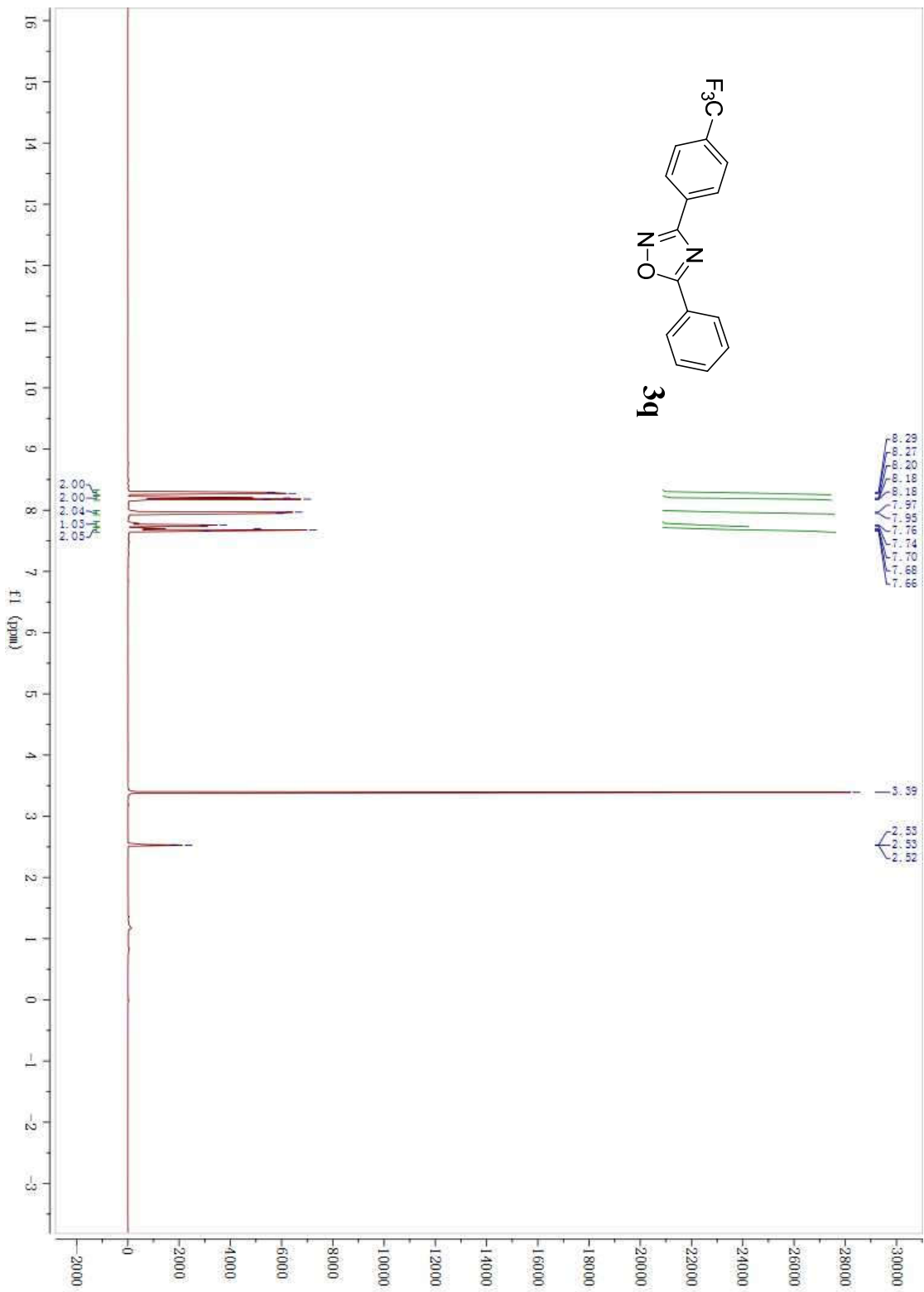












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