

Supporting Information

Copper-Mediated Oxysulfonylation of Alkenyl Oximes with Sodium Sulfinates: A Facile Synthesis of Isoxazolines Featuring a Sulfone Substituent

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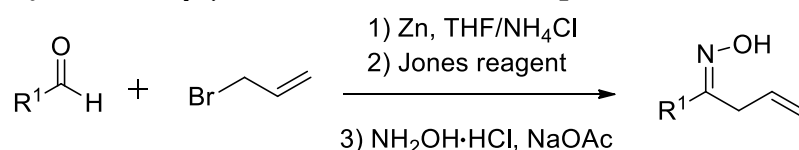
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General experimental procedures

Reaction progress was monitored via thin layer chromatography (TLC) performed on GF254 silica gel plates. Column chromatography was carried out with silica gel (200-300 mesh). Unless stated otherwise, all reactions were carried out under an argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^1H NMR spectra were recorded on 600 MHz in CDCl_3 or acetone- d_6 , ^{13}C NMR spectra were recorded on 150 MHz in CDCl_3 or acetone- d_6 . Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as: s (singlet), d (doublet), t (triplet), dd (doublet of doublets), or m (multiplet). IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported in cm^{-1} . Melting points were determined on a microscopic apparatus and were uncorrected. All products were further characterized by high resolution MS (ESI ionization sources); copies of their ^1H NMR and ^{13}C NMR spectra are provided in the Supporting Information. Commercially available reagents were used without further purification.

Starting materials

Method A: Synthesis of β,γ -unsaturated oximes 1a-q



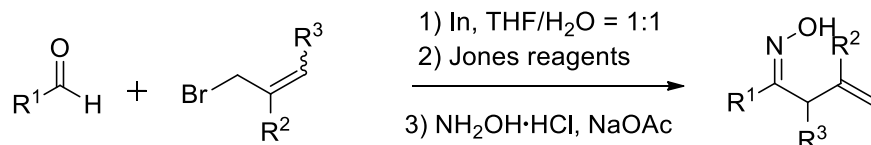
1) To a solution of the allylbromide (2.0 equiv) in anhydrous THF was slowly added the zinc dust (2.0 equiv) at 0°C . Aldehyde (1.0 equiv) was dissolved in anhydrous THF and added to the solution. The resulting suspension was stirred overnight at this temperature. The reaction was quenched with NH_4Cl (aq.) carefully at 0°C , filtered and extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated in *vacuo*. The crude homoallylic alcohol product was directly used in the next step without further purification.¹

2) A solution of the homoallylic alcohol in diethyl ether was stirred at 0°C while Jones reagent (2.0-4.0 equiv) was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred for 1 hour. The diethyl ether layer was then separated from the aqueous layer, which was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated in *vacuo*. The crude ketone product was directly used in the next step without further purification.²

3) To a solution of sodium acetate (7.0 equiv) in ethanol hydroxylamine hydrochloride (5.0 equiv, dissolved in H_2O) was added. The mixture was stirred at room temperature while the ketone (dissolved in ethanol) was added. The mixture was stirred overnight and then, extracted with ethyl acetate 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated in *vacuo*. The crude material was purified by flash chromatography on silica gel to afford the

corresponding oxime **1**.³

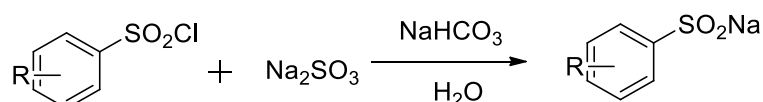
Method B: Synthesis of β,γ -unsaturated oximes **1r-s**



1) A round bottomed flask charged with a solution of the 3-bromo-2-methylprop-1-ene (1.1 equiv) or its analogue and indium (1.1 equiv) in THF/H₂O (1:1) was kept at room temperature with stirring. The aldehyde (1.0 equiv) was added to the solution and the resulting suspension was stirred for 10-24 h. Saturated ammonium chloride or 1 N hydrochloride solution was added at 0 °C. The THF layer was separated from the aqueous layer, which was extracted with diethyl ether for 3 times. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was directly used in the next step without further purification.⁴

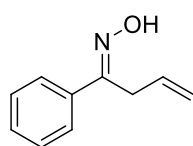
Steps 2) and 3) are same as above-mentioned.

Method C: Synthesis of sodium sulfinates **2e-h**



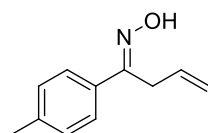
Add sodium sulfite (2.50 g, 20 mmol), sodium bicarbonate (1.68 g, 20 mmol) and 4-methoxybenzenesulphonyl chloride (2.06 g, 10 mmol) to 10 mL H₂O. After stirred at 80 °C for 4 h. Water was removed by rotary evaporator. Then the remaining solid was extracted and recrystallized by ethanol to get a white solid---the required compound. Other sodium sulfinate was prepared through similar method from their corresponding sulphonyl chlorides.

Characterization Data of **1a-s**



1a

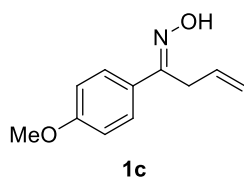
1-phenylbut-3-en-1-one oxime 1a. Colorless solid. ¹H NMR (CDCl₃, 600 MHz) δ 9.40 (s, 1H), 7.64-7.62 (m, 2H), 7.38-7.37 (m, 3H), 5.98-5.91 (m, 1H), 5.19-5.10 (m, 2H), 3.61-3.59 (m, 2H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.9, 135.6, 132.1, 129.3, 128.5, 126.4, 117.1, 31.1.



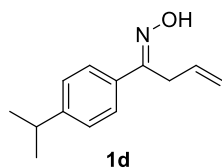
1b

1-(p-tolyl)but-3-en-1-one oxime 1b. Light yellow solid. ¹H NMR (CDCl₃, 600 MHz) δ 7.52 (d, *J* = 8.4Hz, 2H), 7.17 (d, *J* = 7.8Hz, 2H), 5.97-5.90 (m, 1H), 5.18-5.08 (m, 2H), 3.58 (d, *J* = 6.6Hz, 3H), 2.35 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.7, 139.3, 132.7, 129.2, 126.2, 117.0, 31.0.

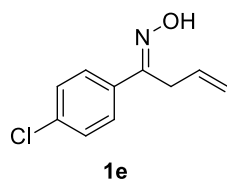
21.2.



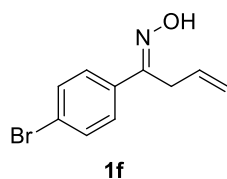
1-(4-methoxyphenyl)but-3-en-1-one oxime 1c. Light yellow solid. ^1H NMR (CDCl_3 , 600 MHz) δ 9.13 (s, 1H), 7.59 (d, $J = 9.0\text{Hz}$, 2H), 6.90 (d, $J = 9.0\text{Hz}$, 4H), 5.97-5.91 (m, 1H), 5.18-5.09 (m, 2H), 3.82 (s, 3H), 3.58 (d, $J = 6.0\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 160.5, 156.3, 132.3, 128.0, 127.7, 117.0, 113.9, 55.3, 30.9.



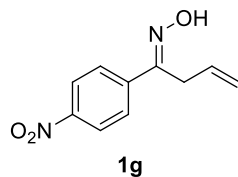
1-(4-isopropylphenyl)but-3-en-1-one oxime 1d. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 8.89 (s, 1H), 7.57 (d, $J = 7.8\text{Hz}$, 2H), 7.24 (d, $J = 8.4\text{Hz}$, 2H), 5.98-5.92 (m, 1H), 5.19-5.10 (m, 2H), 3.58 (d, $J = 6.0\text{Hz}$, 2H), 2.94-2.89 (m, 1H), 1.25 (d, $J = 7.2\text{Hz}$, 6H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.8, 150.2, 133.1, 132.3, 126.6, 126.3, 117.0, 33.9, 31.0, 23.8.



1-(4-chlorophenyl)but-3-en-1-one oxime 1e. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 79.75 (s, 1H), 7.56-7.54 (m, 2H), 7.35-7.33 (m, 2H), 5.94-5.87 (m, 1H), 5.17-5.10 (m, 2H), 3.56 (dd, $J = 4.8\text{Hz}$, $J = 1.2\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.0, 135.4, 133.9, 131.7, 128.8, 127.6, 117.4, 31.0.

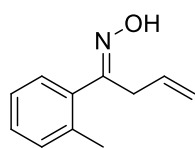


1-(4-bromophenyl)but-3-en-1-one oxime 1f. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 8.56 (s, 1H), 7.51 (s, 4H), 5.94-5.88 (m, 1H), 5.16-5.11 (m, 2H), 3.56 (m, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.1, 134.4, 131.8, 131.7, 127.9, 123.6, 117.3, 30.7.



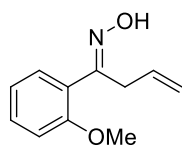
1-(4-nitrophenyl)but-3-en-1-one oxime 1g. Light yellow solid. ^1H NMR (CDCl_3 , 600 MHz) δ 8.82 (s, 1H), 8.24 (d, $J = 9.0\text{Hz}$, 2H), 7.81 (d, $J = 9.0$, 2H), 5.95-5.89 (m, 1H), 5.19-5.15 (m, 2H), 3.62 (d, $J = 6.0\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 155.5, 148.2, 141.6, 131.2, 127.2, 123.7,

117.8, 30.6.



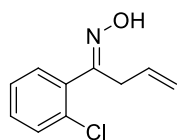
1h

1-(o-tolyl)but-3-en-1-one oxime 1h. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.27-7.24 (m, 1H), 7.21-7.17 (m, 3H), 5.81-5.75 (m, 1H), 5.10-5.02 (m, 2H), 3.47 (d, $J = 6.6\text{Hz}$, 1H), 2.32 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 158.9, 136.1, 136.0, 131.5, 130.5, 128.6, 128.6, 125.6, 117.7, 34.4, 20.0.



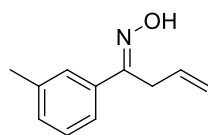
1i

1-(2-methoxyphenyl)but-3-en-1-one oxime 1i. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 9.19 (s, 1H), 7.35-7.32 (m, 1H), 7.28-7.26 (m, 1H), 6.96-6.90 (m, 2H), 5.84-5.78 (m, 1H), 5.09-4.99 (m, 2H), 3.83 (s, 3H), 3.55-3.54 (m, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 158.0, 157.3, 132.5, 130.2, 130.1, 125.5, 120.5, 116.9, 110.9, 55.3, 33.3.



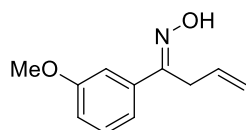
1j

1-(2-chlorophenyl)but-3-en-1-one oxime 1j. Light yellow liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 8.35 (s, 1H), 7.40 (d, $J = 7.8\text{Hz}$, 1H), 7.33-7.26 (m, 3H), 5.80-5.73 (m, 1H), 5.11-5.02 (m, 2H), 3.56 (d, $J = 6.6\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.8, 135.3, 132.7, 131.2, 130.7, 130.0, 129.8, 126.7, 117.9, 33.7.



1k

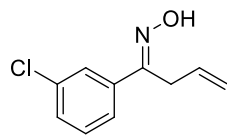
1-(m-tolyl)but-3-en-1-one oxime 1k. Light yellow liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.44-7.41 (m, 2H), 7.26 (t, $J = 7.8\text{Hz}$, 1H), 7.18 (d, $J = 7.8\text{Hz}$, 3H), 5.97-5.91 (m, 1H), 5.19-5.09 (m, 2H), 3.59 (d, $J = 6.6\text{Hz}$, 2H), 2.37 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.0, 138.1, 135.5, 132.1, 130.1, 128.4, 127.0, 123.5, 117.1, 31.2, 21.5.



1l

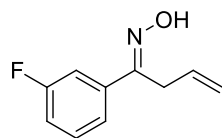
1-(3-methoxyphenyl)but-3-en-1-one oxime 1l. Light yellow liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 8.96 (s, 1H), 7.29 (t, $J = 7.8\text{Hz}$, 1H), 7.22-7.20 (m, 2H), 6.94-6.92 (m, 1H), 5.97-5.91 (m, 1H),

5.19-5.10 (m, 2H), 3.83 (s, 3H), 3.58 (d, $J = 6.0\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.6, 156.8, 137.0, 132.1, 129.5, 118.9, 117.1, 115.1, 111.7, 55.3, 31.1.



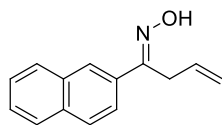
1m

1-(3-chlorophenyl)but-3-en-1-one oxime 1m. Light yellow liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 9.68 (s, 1H), 7.61 (t, $J = 1.8\text{Hz}$, 1H), 7.51-7.49 (m, 1H), 7.35-7.28 (m, 2H), 5.94-5.88 (m, 1H), 5.18-5.11 (m, 2H), 3.57-3.55 (m, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.0, 137.3, 134.5, 131.5, 129.7, 129.3, 126.5, 124.5, 117.4, 31.0.



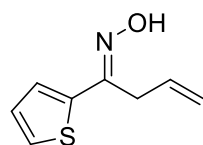
1n

1-(3-fluorophenyl)but-3-en-1-one oxime 1n. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 9.27 (s, 1H), 7.42-7.41 (m, 1H), 7.36-7.33 (m, 2H), 7.09-7.06 (m, 1H), 5.96-5.89 (m, 1H), 5.19-5.12 (m, 2H), 3.58-3.57 (m, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 163.6, 162.0, 156.0, 156.0, 137.8, 137.7, 131.7, 130.1, 130.0, 122.1, 122.0, 117.4, 116.3, 116.2, 113.4, 113.3, 31.0.



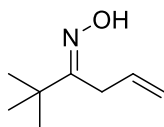
1o

1-(naphthalen-2-yl)but-3-en-1-one oxime 1o. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 9.35 (s, 1H), 8.04 (s, 1H), 7.87-7.81 (m, 4H), 7.50-7.48 (m, 2H), 6.04-5.98 (m, 1H), 5.23 (dd, $J = 16.8\text{Hz}$, $J = 1.8\text{Hz}$, 1H), 5.13 (dd, $J = 16.2\text{Hz}$, $J = 1.2\text{Hz}$, 1H), 3.72 (d, $J = 6.0\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.8, 133.7, 133.1, 132.9, 132.2, 128.5, 128.5, 128.3, 128.2, 127.8, 127.6, 127.0, 126.7, 126.4, 126.3, 123.6, 117.2, 30.8.



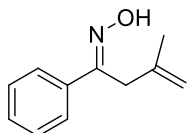
1p

1-(thiophen-2-yl)but-3-en-1-one oxime 1p. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.93 (s, 1H), 7.29-7.26 (m, 2H), 7.03 (dd, $J = 5.4\text{Hz}$, $J = 3.6\text{Hz}$, 1H), 5.98-5.91 (m, 1H), 5.21 (dd, $J = 17.4\text{Hz}$, $J = 1.8\text{Hz}$, 1H), 5.13 (dd, $J = 10.2\text{Hz}$, $J = 1.2\text{Hz}$, 1H), 3.58 (d, $J = 6.0\text{Hz}$, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 152.7, 139.1, 131.7, 127.2, 126.9, 126.8, 117.4, 31.2.



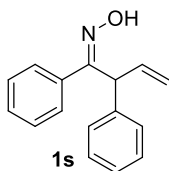
1q

2,2-dimethylhex-5-en-3-one oxime 1q. Light yellow liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 5.99-5.92 (m, 1H), 5.10 (dd, $J = 17.4\text{Hz}$, $J = 1.8\text{Hz}$, 1H), 5.05 (dd, $J = 10.2\text{Hz}$, $J = 1.2\text{Hz}$, 1H), 3.14 (d, $J = 6.6\text{Hz}$, 2H), 1.14 (s, 9H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 164.7, 133.1, 116.5, 37.7, 30.4, 27.8.



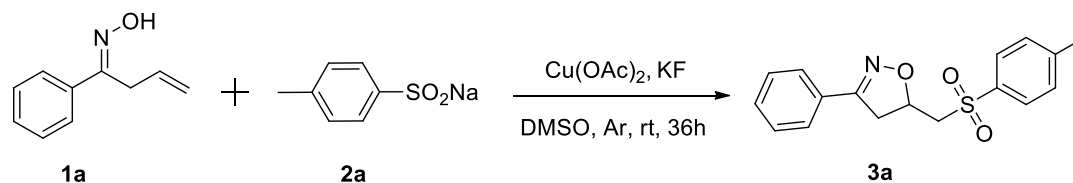
1r

3-methyl-1-phenylbut-3-en-1-one oxime 1r. Colorless liquid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.63 (t, $J = 3.0\text{Hz}$, 2H), 7.36 (t, $J = 2.4\text{Hz}$, 3H), 4.83 (s, 1H), 4.74 (s, 1H), 3.55 (s, 2H), 1.82 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.1, 140.4, 135.8, 129.2, 128.4, 126.3, 112.2, 34.2, 23.0.



1s

1,2-diphenylbut-3-en-1-one oxime 1s. White solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.96 (t, $J = 1.2\text{Hz}$, 2H), 7.49 (t, $J = 7.2\text{Hz}$, 1H), 7.39 (t, $J = 7.8\text{Hz}$, 2H), 7.31-7.30 (m, 4H), 7.24-7.21 (m, 1H), 6.39-6.33 (m, 1H), 5.29 (d, $J = 7.8\text{Hz}$, 1H), 5.22 (d, $J = 10.2\text{Hz}$, 1H), 5.09 (d, $J = 17.4\text{Hz}$, 1H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 198.5, 138.4, 137.2, 136.4, 133.0, 129.0, 128.8, 128.5, 128.3, 127.2, 117.1, 58.0.

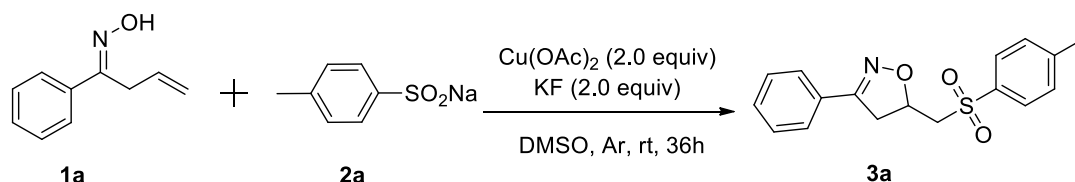
Table S1. Optimization of the reaction conditions^a

Entry	[Cu] (equiv.)	Base (equiv.)	oxidant (equiv.)	solvent	yield (%) ^b
1	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	DMSO	35
2	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	DMF	18
3	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	CH ₃ CN	0
4	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	toluene	0
5	CuI (0.2)	NaOAc (1.2)	-	DMSO	24
6	Cu(CF ₃ SO ₃) ₂ (0.2)	NaOAc (1.2)	-	DMSO	24
7	CuBr ₂ (0.2)	NaOAc (1.2)	-	DMSO	26
8	Cu ₂ O (0.2)	NaOAc (1.2)	-	DMSO	0
9	CuCl (0.2)	NaOAc (1.2)	-	DMSO	0
10 ^c	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	DMSO	15
11 ^d	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	-	DMSO	0
12	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	DTBP (2.0)	DMSO	31
13	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	DCP (2.0)	DMSO	30
14	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	K ₂ S ₂ O ₈ (2.0)	DMSO	0
15	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	PhI(OAc) ₂ (2.0)	DMSO	0
16	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	Mn(OAc) ₃ ·2H ₂ O (2.0)	DMSO	45
17	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	Mn(OAc) ₃ ·2H ₂ O (3.0)	DMSO	24
18	Cu(OAc) ₂ (0.2)	NaOAc (1.2)	Mn(OAc) ₃ ·2H ₂ O (1.0)	DMSO	29
19	-	NaOAc (1.2)	Mn(OAc) ₃ ·2H ₂ O (2.0)	DMSO	0
20	Cu(OAc) ₂ (1.0)	NaOAc (1.2)	-	DMSO	50
21	Cu(OAc) ₂ (2.0)	NaOAc (1.2)	-	DMSO	64
22	Cu(OAc) ₂ (3.0)	NaOAc (1.2)	-	DMSO	67
23 ^e	Cu(OAc) ₂ (2.0)	NaOAc (1.2)	-	DMSO	55
24 ^f	Cu(OAc) ₂ (2.0)	NaOAc (1.2)	-	DMSO	53
25	Cu(OAc) ₂ (2.0)	<i>t</i> -BuOK (1.2)	-	DMSO	52
26	Cu(OAc) ₂ (2.0)	NEt ₃ (1.2)	-	DMSO	57
27	Cu(OAc) ₂ (2.0)	KF (1.2)	-	DMSO	68
28	Cu(OAc) ₂ (2.0)	KF (0.2)	-	DMSO	67
29	Cu(OAc) ₂ (2.0)	KF (0.5)	-	DMSO	67
30	Cu(OAc) ₂ (2.0)	KF (1.5)	-	DMSO	71
31	Cu(OAc) ₂ (2.0)	KF (2.0)	-	DMSO	76
32	Cu(OAc) ₂ (2.0)	KF (2.5)	-	DMSO	66
33	Cu(OAc) ₂ (2.0)	-	-	DMSO	0
34 ^g	Cu(OAc) ₂ (2.0)	KF (2.0)	-	DMSO	80
35 ^h	Cu(OAc) ₂ (2.0)	KF (2.0)	-	DMSO	80

36 ⁱ	Cu(OAc) ₂ (2.0)	KF (2.0)	-	DMSO	66
37	-	KF (2.0)	-	DMSO	0

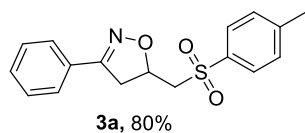
^aAll reactions were carried out by using **1a** (0.2 mmol), **2a** (1.5 equiv), copper salts (2.0 equiv), base (2.0 equiv), and solvent (2 mL) under argon and stirred at room temperature for 36 h, except as noted. ^bIsolated yield. ^cAt 60°C. ^dAt 100°C. ^eUnder air. ^fUnder oxygen. ^g2.0 equiv of **2a** was used. ^h2.5 equiv of **2a** was used. ⁱ1.2 equiv of **2a** was used

Typical procedure for the preparation of product 3a

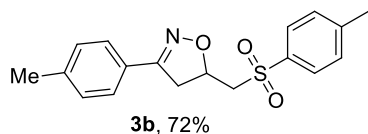


DMSO was added to 0.2 mmol **1a**, 0.4 mmol sodium *p*-toluenesulfonate **2a**, 0.4 mmol Cu(OAc)₂ and 0.4 mmol KF 2 mL under Argon. The mixture was stirred for 36 h at room temperature. After the reaction finished as indicated by TLC, The reaction mixture was diluted with water and extracted with ethyl acetate for 3 times. The combined organic layers were washed with water, saturated brine, dried over Na₂SO₄, concentrated in *vacuo* and purified by chromatography on silica gel (elute: EtOAc/Petroleum ether 1/10 - 1/5, v/v) to give the desired product **3a** (80%).

Characterization Data of 3a-3r, 3ab-3af and 3ag-3ai

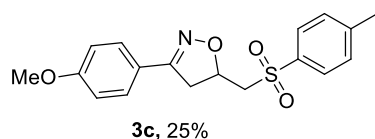


3-phenyl-5-(tosylmethyl)-4,5-dihydroisoxazole 3a. white solid, mp 106-108°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.82 (d, *J* = 8.4Hz, 2H), 7.64 (dd, *J* = 7.8Hz, *J* = 1.2Hz, 2H), 7.43-7.38 (m, 5H), 5.12-5.07 (m, 5H), 3.62-3.58 (m, 2H), 3.45 (dd, *J* = 17.4Hz, *J* = 7.2Hz, 1H), 3.36 (dd, *J* = 14.4Hz, *J* = 8.4Hz, 1H), 2.46 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.8, 145.3, 136.4, 130.5, 130.1, 128.8, 128.7, 128.0, 126.8, 59.8, 40.3, 21.7. IR (neat, cm⁻¹): 2954, 2918, 2850, 1736, 1596, 1447, 1357, 1314, 1150, 1086, 903, 817, 761, 694, 673, 631, 564, 517. HRMS (ESI) Calcd for C₁₇H₁₇NO₃S: [M+H]⁺ = 316.1010 Found: 316.1002.

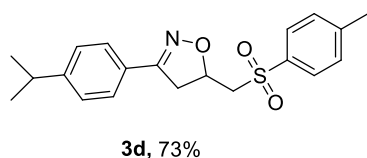


3-(p-tolyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3b. White solid, mp 118-120°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.82 (d, *J* = 8.4Hz, 2H), 7.53 (d, *J* = 8.4Hz, 2H), 7.38 (d, *J* = 7.8Hz, 2H), 7.20 (d, *J* = 7.8Hz, 2H), 5.09-5.04 (m, 1H), 3.60-3.55 (m, 2H), 3.42 (dd, *J* = 17.4Hz, *J* = 7.2Hz, 1H), 3.35 (dd, *J* = 14.4Hz, *J* = 8.4Hz, 1H), 2.46 (s, 3H), 2.37 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.7, 145.2, 140.7, 136.3, 130.0, 129.4, 128.0, 126.7, 125.9, 59.8, 40.4, 21.6, 21.4. IR (neat, cm⁻¹): 3034, 2957, 2923, 2869, 1724, 1597, 1516, 1494, 1441, 1379, 1303, 1185, 1151, 1087, 1018, 954, 905, 816, 745, 659, 633, 600, 563, 517, 476. HRMS (ESI) Calcd for C₁₈H₁₉NO₃S:

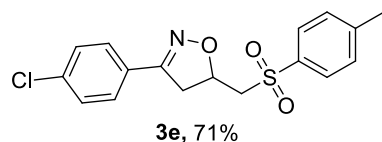
$[M+H]^+ = 330.1169$ Found: 330.1158.



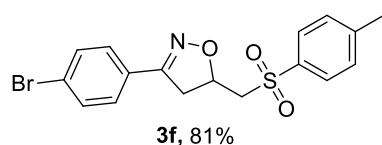
3-(4-methoxyphenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3c. Light yellow solid, mp 130-132°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.59 (d, $J = 8.4\text{Hz}$, 2H), 7.39 (d, $J = 7.8\text{Hz}$, 2H), 6.92 (d, $J = 9.0\text{Hz}$, 2H), 5.09-5.04 (m, 1H), 3.84 (s, 3H), 3.61-3.56 (m, 2H), 3.44 (dd, $J = 17.4\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.35 (dd, $J = 13.8\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 2.47 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 161.4, 156.4, 145.3, 136.4, 130.1, 128.4, 128.1, 121.3, 114.2, 59.9, 55.4, 40.6, 21.7. IR (neat, cm^{-1}): 2957, 2925, 2854, 1728, 1607, 1516, 1461, 1420, 1357, 1306, 1254, 1178, 1150, 1086, 1041, 1020, 900, 833, 745, 658, 633, 563, 517. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_4\text{S}$: $[M+H]^+ = 346.1116$ Found: 346.1108.



3-(4-isopropylphenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3d. White solid, mp 143-145°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.57 (d, $J = 8.4\text{Hz}$, 2H), 7.38 (d, $J = 7.8\text{Hz}$, 2H), 7.26 (d, $J = 7.8\text{Hz}$, 2H), 5.10-5.05 (m, 1H), 3.61-3.56 (m, 2H), 3.43 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36-3.32 (m, 1H), 2.96-2.89 (m, 1H), 2.46 (s, 3H), 1.25 (d, $J = 7.2\text{Hz}$, 6H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.7, 151.7, 145.2, 136.4, 130.1, 128.0, 126.9, 126.2, 74.6, 59.8, 40.4, 34.0, 23.7, 21.6. IR (neat, cm^{-1}): 3033, 2961, 2926, 2870, 1730, 1597, 1461, 1357, 1316, 1241, 1152, 1087, 1058, 1017, 904, 834, 817, 737, 659, 633, 602, 565, 515. HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{S}$: $[M+H]^+ = 358.1479$ Found: 358.1471.

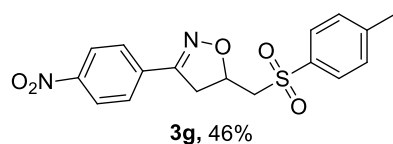


3-(4-chlorophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3e. White solid, mp 135-137°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.81 (d, $J = 8.4\text{Hz}$, 2H), 7.57 (d, $J = 9.0\text{Hz}$, 2H), 7.39 (d, $J = 8.4\text{Hz}$, 2H), 7.37 (d, $J = 9.0\text{Hz}$, 2H), 5.13-5.08 (m, 1H), 3.61-3.55 (m, 2H), 3.43 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 14.4\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 2.46 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 155.9, 145.3, 136.4, 136.3, 130.1, 129.0, 128.0, 128.0, 127.2, 75.0, 59.7, 40.1, 21.6. IR (neat, cm^{-1}): 3001, 2947, 2922, 2855, 1733, 1595, 1492, 1406, 1350, 1300, 1221, 1150, 1088, 1013, 903, 830, 815, 763, 699, 650, 568, 547, 523, 502, 434. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{16}\text{ClNO}_3\text{S}$: $[M+H]^+ = 350.0628$ Found: 350.0612.

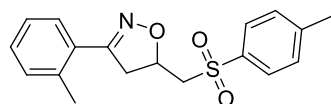


3-(4-bromophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3f. Light yellow solid, mp 151-153°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.81 (d, $J = 8.4\text{Hz}$, 2H), 7.53-7.49 (m, 4H), 7.38 (d, $J = 8.4\text{Hz}$, 2H), 5.12-5.07 (m, 1H), 3.61-3.55 (m, 2H), 3.42 (dd, $J = 17.4\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 13.8\text{Hz}$,

$J = 8.4\text{Hz}$, 1H), 2.46 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.0, 145.3, 136.2, 131.9, 130.1, 128.2, 127.9, 127.6, 124.7, 75.0, 59.6, 40.0, 21.6. IR (neat, cm^{-1}): 2993, 2947, 2922, 2855, 1733, 1590, 1491, 1401, 1380, 1300, 1259, 1151, 1118, 1086, 1009, 904, 856, 827, 763, 691, 647, 568, 546, 480. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{16}\text{BrNO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 394.0117$ Found: 394.0107.

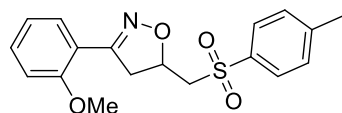


3-(4-nitrophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3g. Light yellow solid, mp 188-190°C. ^1H NMR (acetone- d_6 , 600 MHz) δ 8.32-8.30 (m, 2H), 7.95 (dd, $J = 7.2\text{Hz}$, $J = 1.8\text{Hz}$, 2H), 7.88 (d, $J = 8.4\text{Hz}$, 2H), 7.50 (d, $J = 7.8\text{Hz}$, 2H), 5.22-5.17 (m, 1H), 3.81-3.76 (m, 2H), 3.70 (dd, $J = 14.4\text{Hz}$, $J = 6.6\text{Hz}$, 1H), 3.51 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 2.48 (s, 3H). ^{13}C NMR (acetone- d_6 , 150 MHz) δ 156.7, 145.8, 138.4, 136.6, 130.8, 129.1, 128.6, 124.7, 77.3, 60.5, 40.4, 21.5. IR (neat, cm^{-1}): 2957, 2929, 2871, 1720, 1576, 1516, 1458, 1344, 1289, 1149, 1117, 1085, 908, 847, 814, 691, 648, 521. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_5\text{S}$: $[\text{M}+\text{H}]^+ = 361.0859$ Found: 361.0853.



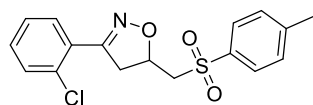
3h, 37%

3-(o-tolyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3h. White solid, mp 95-97°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.38 (d, $J = 8.4\text{Hz}$, 2H), 7.39 (d, $J = 7.8\text{Hz}$, 2H), 7.34-7.29 (m, 2H), 7.27-7.23 (m, 2H), 5.06-5.01 (m, 1H), 3.66-3.59 (m, 2H), 3.50 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 13.8\text{Hz}$, $J = 9.0\text{Hz}$, 1H), 2.52 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.7, 145.3, 138.1, 136.4, 131.6, 130.1, 129.7, 129.0, 128.0, 127.8, 125.9, 73.7, 59.7, 42.8, 22.9, 21.7. IR (neat, cm^{-1}): 3063, 2958, 2924, 2855, 1719, 1597, 1494, 1455, 1316, 1291, 1151, 1087, 1018, 818, 718, 632, 566, 457. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 330.1169$ Found: 330.1158.



3i, 69%

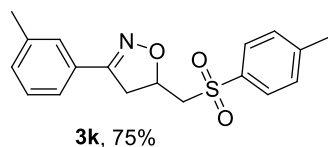
3-(3-methoxyphenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3i. Light yellow solid, mp 92-94°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.66 (dd, $J = 7.2\text{Hz}$, $J = 1.2\text{Hz}$, 1H), 7.38 (d, $J = 7.8\text{Hz}$, 3H), 6.97-6.92 (m, 2H), 5.07-5.02 (m, 1H), 3.84 (s, 3H), 3.66 (dd, $J = 17.4\text{Hz}$, $J = 10.2\text{Hz}$, 1H), 3.57 (dd, $J = 13.8\text{Hz}$, $J = 4.2\text{Hz}$, 1H), 3.48 (dd, $J = 18\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 14.4\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 2.46 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.5, 156.4, 145.1, 136.4, 131.6, 130.0, 129.3, 128.0, 120.7, 117.9, 111.3, 74.7, 60.0, 55.4, 42.9, 21.6. IR (neat, cm^{-1}): 2957, 2925, 2840, 1723, 1560, 1492, 1437, 1350, 1290, 1150, 1087, 1029, 903, 867, 757, 633, 563. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_4\text{S}$: $[\text{M}+\text{H}]^+ = 346.1116$ Found: 346.1108.



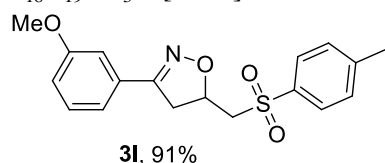
3j, 34%

3-(3-chlorophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3j. Light yellow liquid. ^1H NMR (CDCl_3 , 400 MHz) δ 7.75 (d, $J = 8.4\text{Hz}$, 2H), 7.49 (dd, $J = 7.8\text{Hz}$, $J = 1.2\text{Hz}$, 1H), 7.35-7.27 (m, 4H), 7.23-7.19

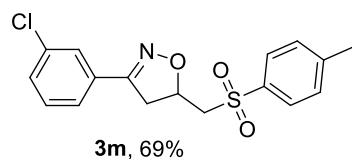
(m, 1H), 5.08-5.03 (m, 1H), 3.61 (dd, $J = 17.4\text{Hz}$, $J = 10.2\text{Hz}$, 1H), 3.54 (dd, $J = 13.8\text{Hz}$, $J = 4.8\text{Hz}$, 1H), 3.47 (dd, $J = 17.4\text{Hz}$, $J = 6.6\text{Hz}$, 1H), 3.33 (dd, $J = 13.8\text{Hz}$, $J = 7.8\text{Hz}$, 1H), 2.39 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.8, 145.3, 136.3, 132.8, 131.1, 130.6, 130.5, 130.1, 128.2, 128.1, 127.0, 75.4, 58.7, 42.6, 21.6. IR (neat, cm^{-1}): 3065, 2924, 2855, 1718, 1596, 1435, 1316, 1151, 1087, 1018, 867, 817, 760, 714, 632, 566, 459. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{16}\text{ClNO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 350.0628$ Found: 350.0612.



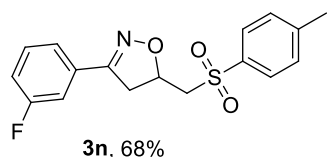
3-(m-tolyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3k. White solid, mp 109-111 °C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.47 (s, 1H), 7.43 (d, $J = 7.2\text{Hz}$, 1H), 7.38 (d, $J = 7.8\text{Hz}$, 2H), 7.29 (t, $J = 7.8\text{Hz}$, 1H), 7.23 (d, $J = 7.8\text{Hz}$, 1H), 5.10-5.05 (m, 1H), 3.61-3.56 (m, 2H), 3.44 (dd, $J = 17.4\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.35 (dd, $J = 13.8\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 2.46 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.9, 145.2, 138.5, 136.3, 131.2, 130.1, 128.6, 128.6, 128.0, 127.4, 123.9, 74.6, 59.8, 40.3, 21.6, 21.2. IR (neat, cm^{-1}): 3041, 2955, 2924, 2857, 1727, 1597, 1442, 1380, 1316, 1242, 1087, 1017, 817, 745, 669, 564, 447. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 330.1169$ Found: 330.1158.



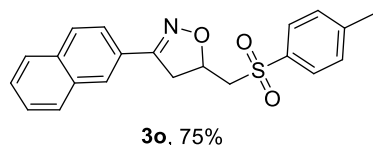
3-(3-methoxyphenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3l. Light yellow solid, mp 80-82 °C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.38 (d, $J = 7.8\text{Hz}$, 2H), 7.30 (t, $J = 8.4\text{Hz}$, 1H), 7.23 (t, $J = 1.8\text{Hz}$, 1H), 7.16 (d, $J = 7.2\text{Hz}$, 1H), 6.97 (dd, $J = 8.4\text{Hz}$, $J = 2.4\text{Hz}$, 1H), 5.11-5.06 (m, 1H), 3.81 (s, 3H), 3.61-3.56 (m, 2H), 3.42 (dd, $J = 17.4\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 13.8\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 2.46 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.7, 156.8, 145.3, 136.3, 130.1, 129.9, 129.8, 128.0, 119.4, 116.8, 111.3, 74.8, 59.8, 55.3, 40.3, 21.6. IR (neat, cm^{-1}): 3064, 2956, 2924, 2854, 1724, 1599, 1494, 1434, 1361, 1218, 1087, 1032, 817, 745, 667, 564, 459. HRMS (ESI) Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_4\text{S}$: $[\text{M}+\text{H}]^+ = 346.1116$ Found: 346.1108.



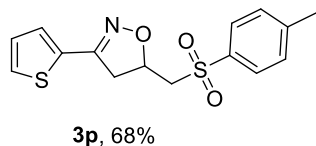
3-(3-chlorophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3m. White solid, mp 125-127 °C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (d, $J = 8.4\text{Hz}$, 2H), 7.64 (s, 1H), 7.52 (d, $J = 7.8\text{Hz}$, 1H), 7.39 (d, $J = 7.8\text{Hz}$, 3H), 7.34 (t, $J = 7.8\text{Hz}$, 1H), 5.14-5.09 (m, 1H), 3.62-3.56 (m, 2H), 3.43 (dd, $J = 17.4\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 13.8\text{Hz}$, $J = 7.8\text{Hz}$, 1H), 2.47 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 155.8, 145.4, 136.2, 134.8, 130.5, 130.4, 130.1, 130.0, 128.0, 126.7, 124.8, 75.1, 59.7, 40.0, 21.6. IR (neat, cm^{-1}): 3065, 2957, 2924, 1727, 1597, 1442, 1380, 1316, 1242, 1151, 1017, 908, 789, 694, 633, 524. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{16}\text{ClNO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 350.0628$ Found: 350.0612.



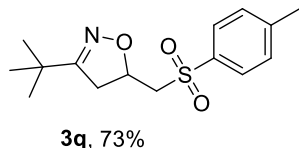
3-(3-fluorophenyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3n. Light yellow solid, mp 102-104°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.82 (d, *J* = 8.4Hz, 2H), 7.40-7.36 (m, 5H), 7.14-7.10 (m, 1H), 5.14-5.09 (m, 1H), 3.62-3.56 (m, 2H), 3.43 (dd, *J* = 17.4Hz, *J* = 7.2Hz, 1H), 3.36 (dd, *J* = 14.4Hz, *J* = 9.0Hz, 1H), 2.47 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 163.5, 161.9, 156.0, 156.0, 145.4, 136.3, 130.8, 130.8, 130.4, 130.4, 130.1, 128.0, 122.6, 122.7, 117.5, 117.3, 113.6, 113.5, 75.1, 59.7, 40.1, 21.6. IR (neat, cm⁻¹): 3068, 2956, 2925, 1725, 1598, 1494, 1452, 1361, 1303, 1151, 1018, 914, 746, 667, 565, 475. HRMS (ESI) Calcd for C₁₇H₁₆FNO₃S: [M+Na]⁺ = 356.0720 Found: 356.0727.



3-(naphthalen-2-yl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3o. White solid, mp 139-141°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.91 (d, *J* = 9.0Hz, 2H), 7.86-7.82 (m, 5H), 7.55-7.51 (m, 2H), 7.39 (d, *J* = 8.4Hz, 2H), 5.17-5.12 (m, 1H), 3.72 (dd, *J* = 16.8Hz, *J* = 10.2Hz, 1H), 3.65-3.57 (m, 2H), 3.39 (dd, *J* = 13.8Hz, *J* = 8.4Hz, 1H), 2.46 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 157.0, 145.3, 136.3, 134.1, 132.9, 130.1, 128.6, 128.4, 128.0, 127.8, 127.3, 126.8, 126.3, 123.3, 74.9, 59.8, 40.3, 21.6. IR (neat, cm⁻¹): 3058, 2957, 2856, 1725, 1598, 1439, 1375, 1316, 1196, 1086, 1016, 951, 861, 747, 658, 563, 477. HRMS (ESI) Calcd for C₂₁H₁₉NO₃S: [M+H]⁺ = 366.1169 Found: 366.1158.

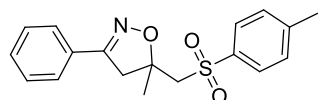


3-(thiophen-2-yl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3p. Light yellow solid, mp 117-119°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.82 (d, *J* = 8.4Hz, 2H), 7.41-7.38 (m, 3H), 7.23-7.22 (m, 1H), 7.07 (dd, *J* = 6.8Hz, *J* = 4.8Hz, 1H), 5.11-5.06 (m, 1H), 3.64-3.58 (m, 2H), 3.46 (dd, *J* = 16.8Hz, *J* = 6.6Hz, 1H), 3.36 (dd, *J* = 13.8Hz, *J* = 8.4Hz, 1H), 2.46 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 152.6, 145.3, 136.3, 131.0, 130.1, 129.1, 128.8, 128.0, 127.4, 75.0, 59.7, 41.1, 21.6. IR (neat, cm⁻¹): 3106, 2957, 2856, 1730, 1596, 1438, 1357, 1315, 1233, 1151, 1018, 966, 904, 816, 660, 534, 518, 471. HRMS (ESI) Calcd for C₁₅H₁₅NO₃S₂: [M+H]⁺ = 322.0576 Found: 322.0566.



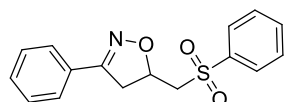
3-(tert-butyl)-5-(tosylmethyl)-4,5-dihydroisoxazole 3q. Colorless solid, mp 93-95°C. ¹H NMR (CDCl₃, 400 MHz) δ 7.80 (d, *J* = 8.4Hz, 2H), 7.38 (d, *J* = 7.8Hz, 2H), 4.90-4.84 (m, 1H), 3.51 (dd, *J* = 14.4Hz, *J* = 4.8Hz, 1H), 3.26-3.19 (m, 2H), 3.04 (dd, *J* = 17.4Hz, *J* = 7.2Hz, 1H), 2.46 (s, 3H), 1.19 (s, 9H). ¹³C NMR (CDCl₃, 150 MHz) δ 166.4, 145.2, 136.3, 130.0, 128.0, 73.9, 59.7, 39.7, 33.0, 27.9, 21.6. IR (neat, cm⁻¹): 3031, 2967, 2929, 2871, 1725, 1597, 1479, 1398, 1367, 1261, 1151, 1087, 955, 873, 748, 632, 564, 473. HRMS (ESI) Calcd for C₁₅H₂₁NO₃S: [M+H]⁺ =

296.1322 Found: 296.1315.



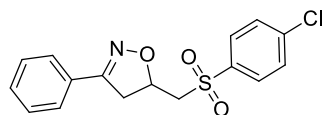
3r, 54%

5-methyl-3-phenyl-5-(tosylmethyl)-4,5-dihydroisoxazole 3r. White solid, mp 111-113°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.79 (d, *J* = 7.8Hz, 2H), 7.66-7.65 (m, 2H), 7.40 (d, *J* = 7.2Hz, 3H), 7.35 (d, *J* = 7.8Hz, 2H), 3.97 (d, *J* = 17.4Hz, 1H), 3.51 (s, 2H), 3.22 (d, *J* = 17.4Hz, 1H), 2.44 (s, 3H), 1.71 (s, 3H). ¹³C NMR (CDCl₃, 150 MHz) δ 157.2, 144.9, 137.5, 130.2, 129.9, 129.2, 128.7, 127.7, 12.6, 84.0, 62.9, 44.8, 26.1, 21.6. IR (neat, cm⁻¹): 3061, 2979, 1722, 1597, 1496, 1447, 1360, 1319, 1151, 1087, 1019, 916, 870, 761, 694, 633, 548, 517, 477. HRMS (ESI) Calcd for C₁₈H₁₉NO₃S: [M+H]⁺ = 330.1157 Found: 330.1158.



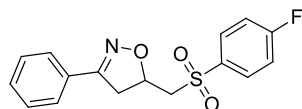
3ab, 80%

3-phenyl-5-((phenylsulfonyl)methyl)-4,5-dihydroisoxazole 3ab. White solid, mp 124-126°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.96-7.94 (m, 2H), 7.72-7.68 (m, 1H), 7.64-7.30 (m, 2H), 7.61-7.59 (m, 2H), 7.44-7.38 (m, 3H), 5.13-5.09 (m, 1H), 3.63-3.58 (m, 2H), 3.46-3.36 (m, 2H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.8, 139.3, 134.2, 130.5, 129.5, 128.8, 128.7, 128.0, 126.8, 74.7, 59.8, 40.3. IR (neat, cm⁻¹): 2978, 2967, 2925, 1723, 1446, 1384, 1355, 1282, 1199, 1136, 1082, 952, 897, 829, 756, 677, 569, 529, 492. HRMS (ESI) Calcd for C₁₆H₁₅NO₃S : [M+H]⁺ = 302.0854 Found: 302.0845.



3ac, 49%

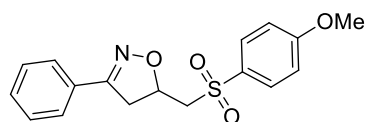
5-(((4-chlorophenyl)sulfonyl)methyl)-3-phenyl-4,5-dihydroisoxazole 3ac. White solid, mp 138-140°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.89 (dd, *J* = 6.6Hz, *J* = 1.8Hz, 2H), 7.64-7.63 (m, 2H), 7.57 (dd, *J* = 7.2Hz, *J* = 1.8Hz, 2H), 7.43-7.39 (m, 3H), 5.17-5.12 (m, 1H), 3.64-3.59 (m, 2H), 3.44-3.37 (m, 2H). ¹³C NMR (CDCl₃, 150 MHz) δ 156.8, 141.0, 137.8, 130.6, 129.8, 129.6, 128.8, 128.6, 126.8, 74.6, 60.0, 40.4. IR (neat, cm⁻¹): 3090, 2959, 2925, 2854, 1719, 1583, 1476, 1395, 1317, 1153, 1089, 1013, 903, 869, 761, 669, 576, 550, 464. HRMS (ESI) Calcd for C₁₆H₁₄ClNO₃S : [M+H]⁺ = 336.0464 Found: 336.0456.



3ad, 58%

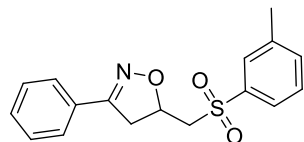
5-(((4-fluorophenyl)sulfonyl)methyl)-3-phenyl-4,5-dihydroisoxazole 3ad. Light yellow solid, mp 96-98°C. ¹H NMR (CDCl₃, 600 MHz) δ 7.99-7.97 (m, 2H), 7.65-7.64 (m, 2H), 7.45-7.39 (m, 3H), 7.28 (d, *J* = 8.4Hz, 2H), 5.18-5.13 (m, 1H), 3.65-3.59 (m, 2H), 3.45-3.37 (m, 2H). ¹³C NMR (CDCl₃, 150 MHz) δ 166.9, 165.2, 156.8, 135.4, 131.1, 131.0, 130.6, 128.8, 128.6, 126.8, 116.9, 116.7, 74.7, 60.1, 40.4. IR (neat, cm⁻¹): 3103, 3066, 2989, 2936, 1718, 1591, 1494, 1356, 1313, 1290, 1150, 1084, 907, 825, 754, 676, 567, 519, 472. HRMS (ESI) Calcd for C₁₆H₁₄FNO₃S :

$[M+H]^+ = 320.0759$ Found: 320.0751.



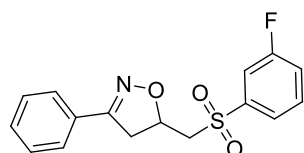
3ae, 88%

5-(((4-methoxyphenyl)sulfonyl)methyl)-3-phenyl-4,5-dihydroisoxazole 3ae. Light yellow solid, mp 107-109°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.88-7.86 (m, 2H), 7.65 (dd, $J = 7.8\text{Hz}$, $J = 1.2\text{Hz}$, 2H), 7.44-7.39 (m, 3H), 7.04 (d, $J = 8.4\text{Hz}$, 2H), 5.13-5.07 (m, 1H), 3.89 (s, 3H), 3.62-3.57 (m, 2H), 3.45 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.36 (dd, $J = 13.8\text{Hz}$, $J = 8.4\text{Hz}$, 1H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 164.1, 156.8, 130.8, 130.5, 130.2, 128.8, 128.7, 126.8, 114.6, 74.8, 60.0, 55.7, 40.3. IR (neat, cm^{-1}): 3066, 3025, 2986, 2917, 2843, 1727, 1595, 1444, 1360, 1294, 1206, 1137, 1024, 910, 836, 767, 694, 565, 491. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_4\text{S}$: $[M+H]^+ = 332.0959$ Found: 332.0951.



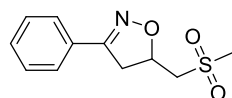
3ag, 82%

3-phenyl-5-((m-tolylsulfonyl)methyl)-4,5-dihydroisoxazole 3ag. Light yellow solid, mp 108-110°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.75-7.74 (m, 2H), 7.65 (dd, $J = 7.8\text{Hz}$, $J = 1.2\text{Hz}$, 2H), 7.50-7.47 (m, 2H), 7.44-7.39 (m, 3H), 5.13-5.08 (m, 1H), 3.64-3.59 (m, 2H), 3.47 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.37 (dd, $J = 13.8\text{Hz}$, $J = 9.0\text{Hz}$, 1H), 2.46 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 156.8, 139.8, 139.1, 135.0, 130.5, 129.3, 128.8, 128.7, 128.2, 126.8, 125.1, 74.7, 59.7, 40.3, 21.3. IR (neat, cm^{-1}): 3056, 2972, 2924, 1971, 1724, 1601, 1482, 1447, 1319, 1244, 1146, 1019, 898, 768, 692, 551, 493. HRMS (ESI) Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3\text{S}$: $[M+H]^+ = 316.1010$ Found: 316.1002.



3ah, 60%

5-(((3-fluorophenyl)sulfonyl)methyl)-3-phenyl-4,5-dihydroisoxazole 3ah. White solid, mp 129-131°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (d, $J = 7.8\text{Hz}$, 1H), 7.67-7.59 (m, 4H), 7.45-7.39 (m, 4H), 5.17-5.12 (m, 1H), 3.66-3.61 (m, 2H), 3.46-3.38 (m, 2H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 163.3, 161.6, 156.8, 141.3, 141.3, 131.4, 131.4, 130.6, 128.8, 128.6, 126.8, 123.9, 123.9, 121.6, 121.5, 115.6, 115.4, 74.5, 59.8, 40.4. IR (neat, cm^{-1}): 3072, 2961, 2926, 1718, 1593, 1475, 1435, 1357, 1303, 1271, 1225, 1145, 1083, 892, 762, 693, 677, 534, 510. HRMS (ESI) Calcd for $\text{C}_{16}\text{H}_{14}\text{FNO}_3\text{S}$: $[M+H]^+ = 320.0759$ Found: 320.0751.



3ai, 84%

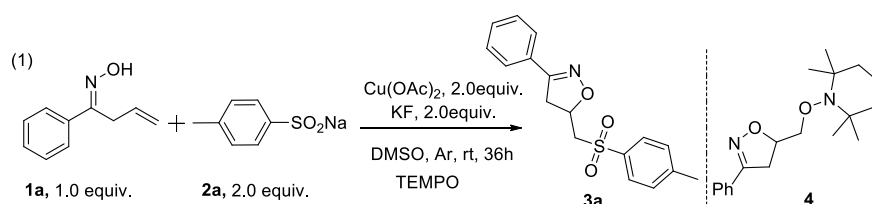
5-(((methylsulfonyl)methyl)-3-phenyl-4,5-dihydroisoxazole 3ai. White solid, mp 130-132°C. ^1H NMR (CDCl_3 , 600 MHz) δ 7.67-7.65 (m, 2H), 7.47-7.41 (m, 3H), 5.30-5.25 (m, 1H), 3.66 (dd, $J =$

16.8Hz, $J = 10.8\text{Hz}$, 1H), 3.51 (dd, $J = 15.0\text{Hz}$, $J = 8.4\text{Hz}$, 1H), 3.30 (dd, $J = 16.8\text{Hz}$, $J = 7.2\text{Hz}$, 1H), 3.20 (dd, $J = 14.4\text{Hz}$, $J = 3.6\text{Hz}$, 1H), 3.10 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 157.0, 130.7, 128.9, 128.5, 126.8, 75.0, 59.0, 42.8, 40.4. IR (neat, cm^{-1}): 3038, 2969, 2928, 1720, 1448, 1359, 1326, 1282, 1156, 1129, 1069, 945, 876, 796, 703, 666, 522, 473. HRMS (ESI) Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_3\text{S}$: $[\text{M}+\text{H}]^+ = 240.0698$ Found: 240.0689.

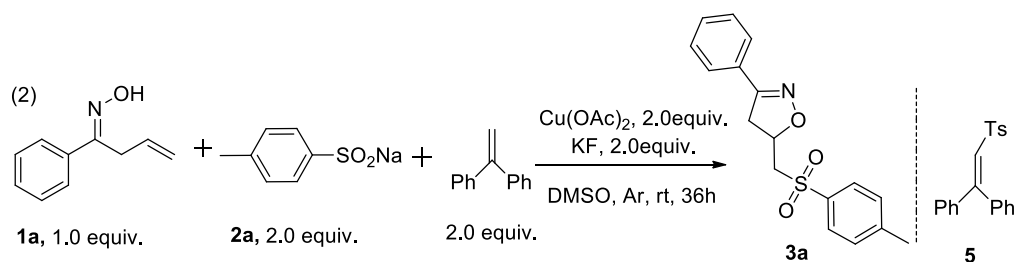
References

- (1) Dam, J. H.; Fristrup, P.; Madsen, R. *J. Org. Chem.*, **2008**, *73*, 3228.
- (2) Jiang, D.; Peng, J.; Chen, Y. *Org. Lett.*, **2008**, *10*, 1695.
- (3) Garzan, A.; Jaganathan, A.; MarziJarani, N. S.i; Yousefi, R.; Whitehead, D. C.; Jackson, J. E.; Borhan, B. *Chem. Eur. J.* **2013**, *19*, 9015.
- (4) M.-K. Zhu, J.-F. Zhao and T.-P. Loh, *J. Am. Chem. Soc.* 2010, **132**, 6284.

The mechanistic study



The reaction was carried out according to **Typical procedure for the preparation of product 3a**, except TEMPO (2.0 equiv) was used. The mixture was stirred for 36 h at room temperature. And then diluted with water and extracted with ethyl acetate for 3 times. The combined organic layers were washed with water, saturated brine, dried over Na₂SO₄, concentrated in *vacuo* and purified by chromatography on silica gel (elute: EtOAc/Petroleum ether 1/10 - 1/5, v/v) to give the desired product **3a** (17%). Meanwhile, **1a** was recovered in 26% yield. The product **4** was detected by ESI-HRMS measurement of the crude reaction mixture (HRMS (ESI): C₁₉H₂₈N₂O₂, [M+H]⁺, Calcd: 317.2231, Found: 317.2224). If we use 4.0 equiv of TEMPO, no product **3a** was detected and **1a** was recovered in 99% yield.



The reaction was carried out according to **Typical procedure for the preparation of product 3a**, except 1,1-diphenylethylene (2.0 equiv) was used. The mixture was stirred for 36 h at room temperature. And then diluted with water and extracted with ethyl acetate for 3 times. The combined organic layers were washed with water, saturated brine, dried over Na₂SO₄, concentrated in *vacuo* and purified by chromatography on silica gel (elute: EtOAc/Petroleum ether 1/10 - 1/5, v/v) to give the desired product **3a** (73%). The product **5** was detected by ESI-HRMS measurement of the crude reaction mixture (HRMS (ESI): C₂₁H₁₈O₂S, [M+H]⁺, Calcd: 335.1103, Found: 335.1100).

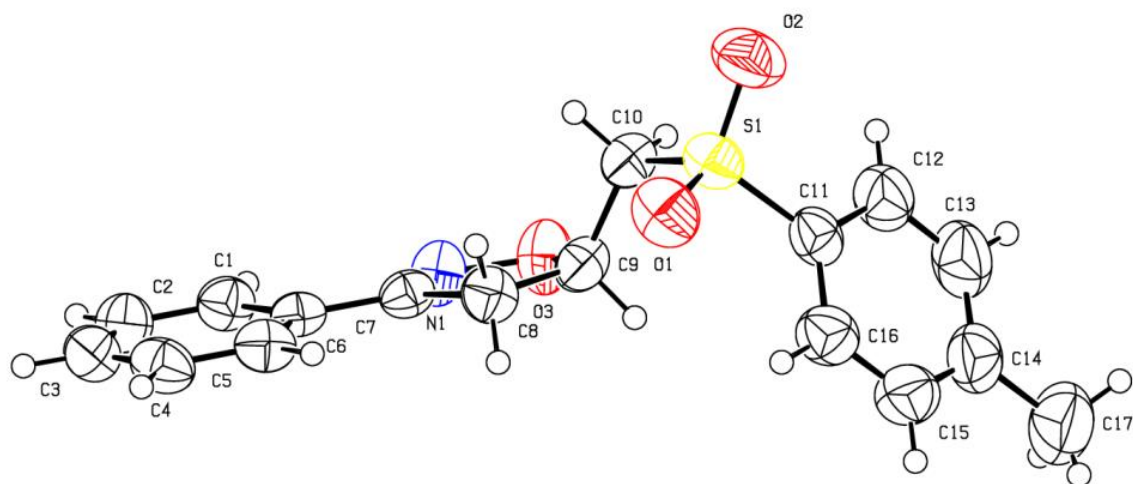


1,1-diphenylethylene was recovered in 65% yield

The reaction was carried out according to **Typical procedure for the preparation of product 3a**, except 1,1-diphenylethylene (2.0 equiv) was used in the absence of **1a**. The mixture was stirred for 36 h at room temperature. 1,1-Diphenylethylene could be recovered in 65% yield. And when we detected the crude reaction mixture by ESI-HRMS measurement, we could find the radical coupling product **5** (HRMS (ESI):

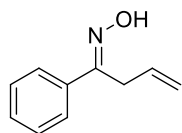
C₂₁H₁₈O₂S, [M+H]⁺, Calcd: 335.1103, Found: 335.1100) and another product **6** (HRMS (ESI): C₂₁H₂₀O₂S, [M+H]⁺, Calcd: 337.1259, Found: 337.1257).

X-ray diffraction analysis of compound **3a**

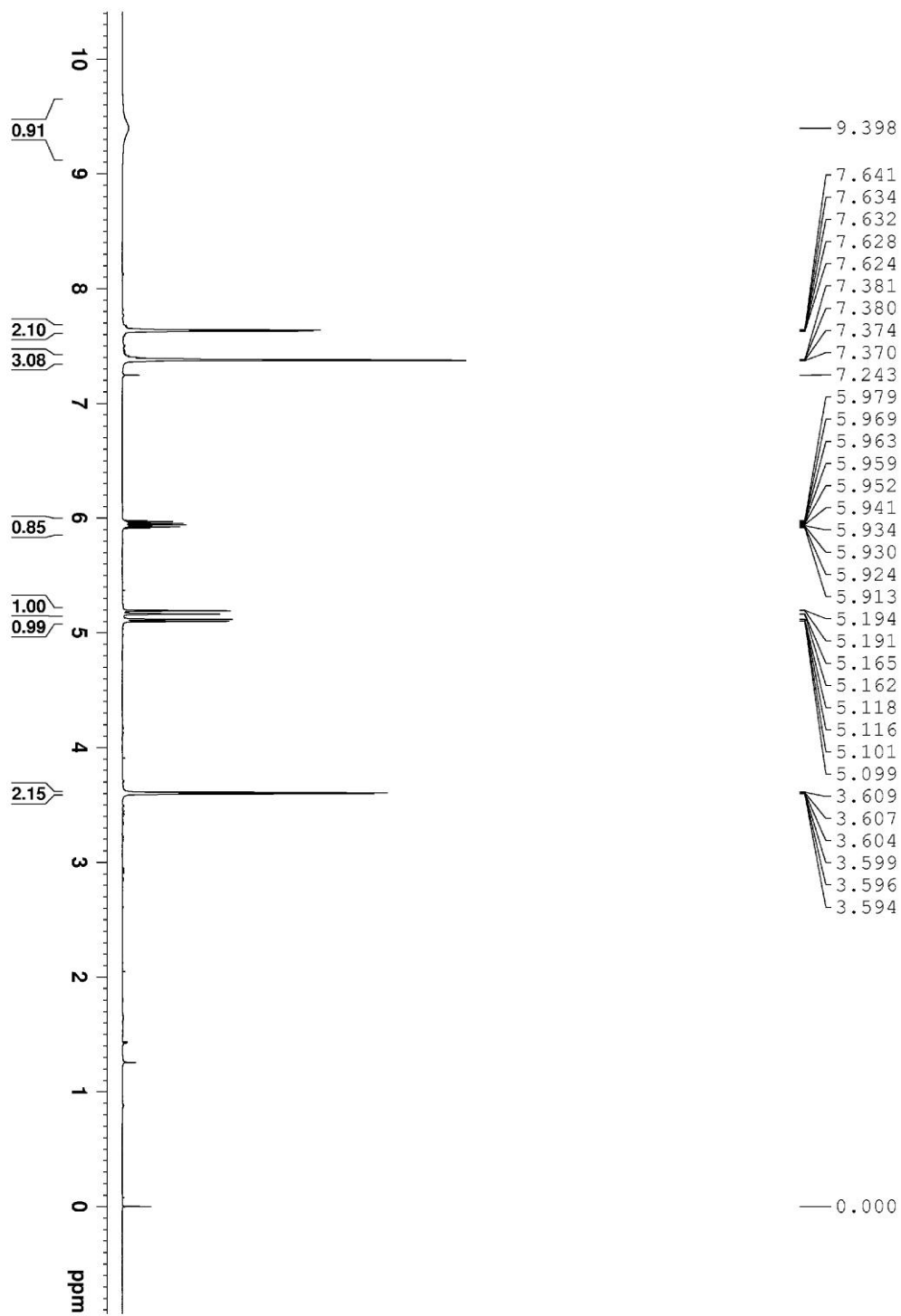


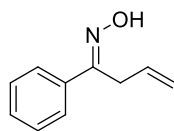
X-ray structure of **3a** (CCDC 1524458)

Bond precision: C-C = 0.0026 Å Wavelength=0.71073
Cell: a=18.0767(10) b=10.7938(6) c=8.1475(5)
alpha=90 beta=91.976(1) gamma=90
Temperature: 296 K
Calculated Reported
Volume 1588.77(16) 1588.76(16)
Space group P 21/c P2(1)/c
Hall group -P 2ybc ?
Moiety formula C17 H17 N O3 S ?
Sum formula C17 H17 N O3 S C17 H17 N O3 S
Mr 315.38 315.38
D_x, g cm⁻³ 1.319 1.318
Z 4 4
Mu (mm⁻¹) 0.215 0.215
F000 664.0 664.0
F000' 664.79
h, k, lmax 24, 14, 10 24, 14, 10
Nref 3966 3958
Tmin, Tmax 0.904, 0.981 0.906, 0.981
Tmin' 0.904
Correction method= # Reported T Limits: Tmin=0.906 Tmax=0.981
AbsCorr = MULTI-SCAN
Data completeness= 0.998 Theta(max)= 28.360
R(reflections)= 0.0423(2653) wR2(reflections)= 0.1211(3958)
S = 1.025 Npar= 200

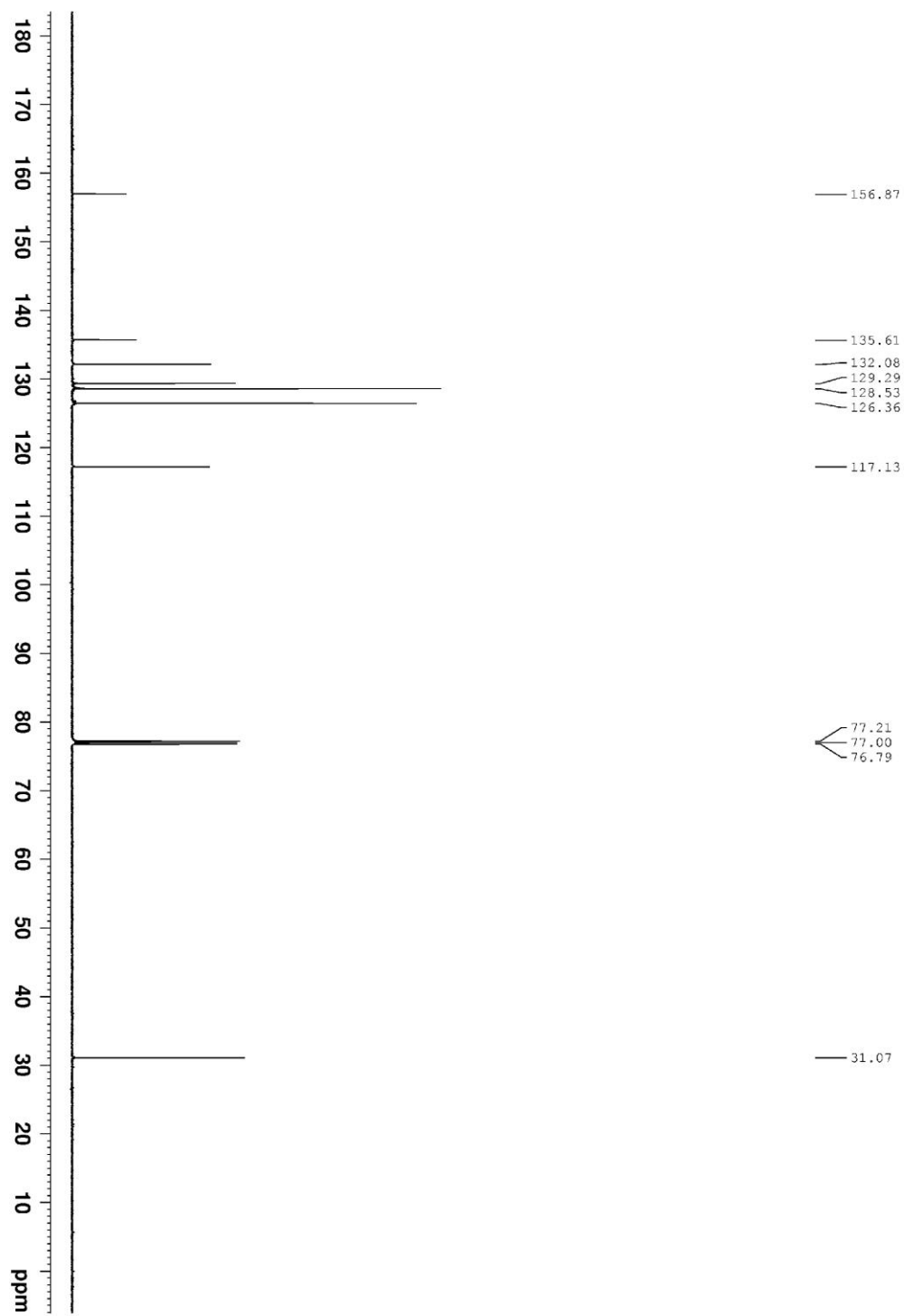


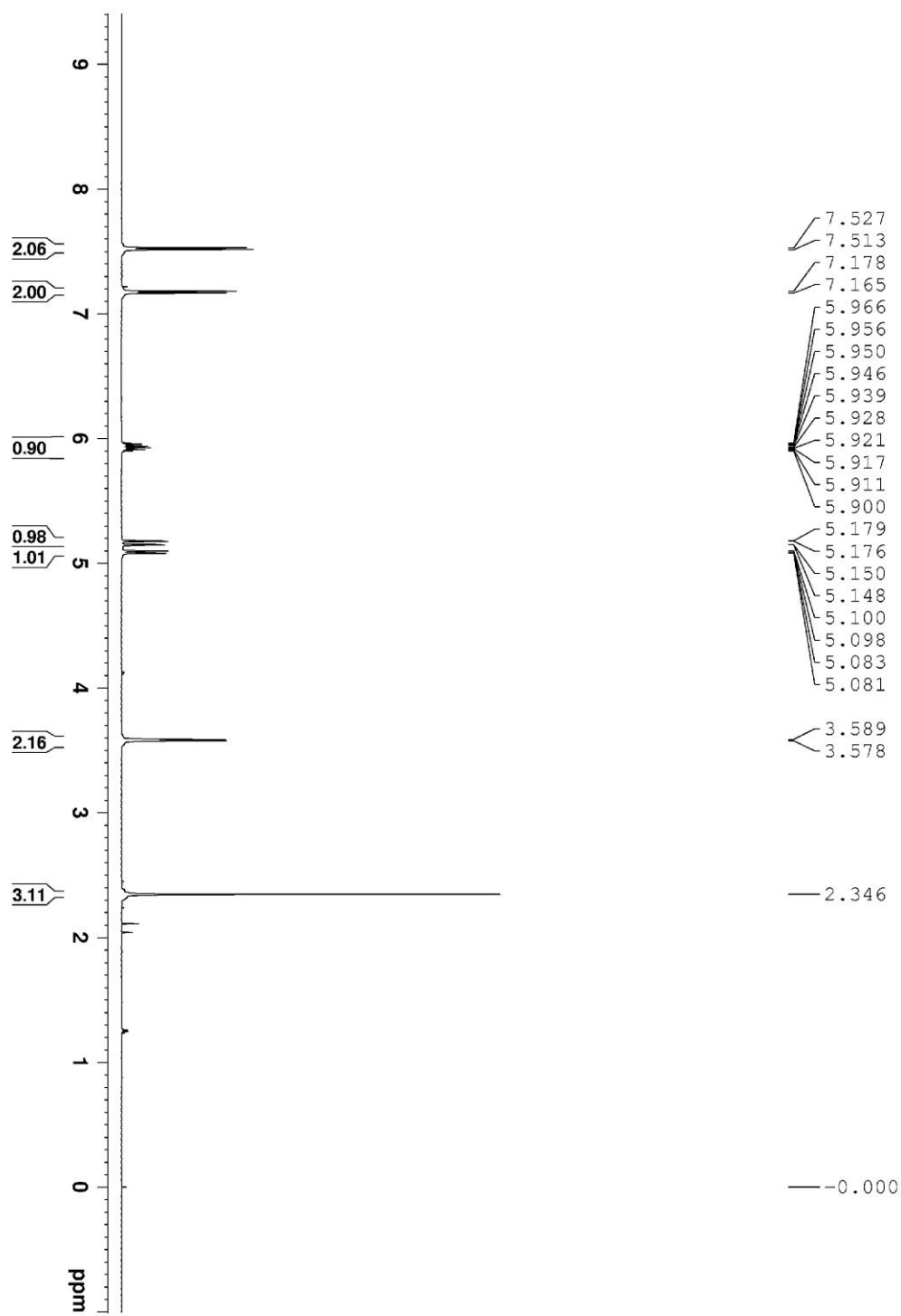
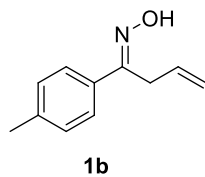
1a

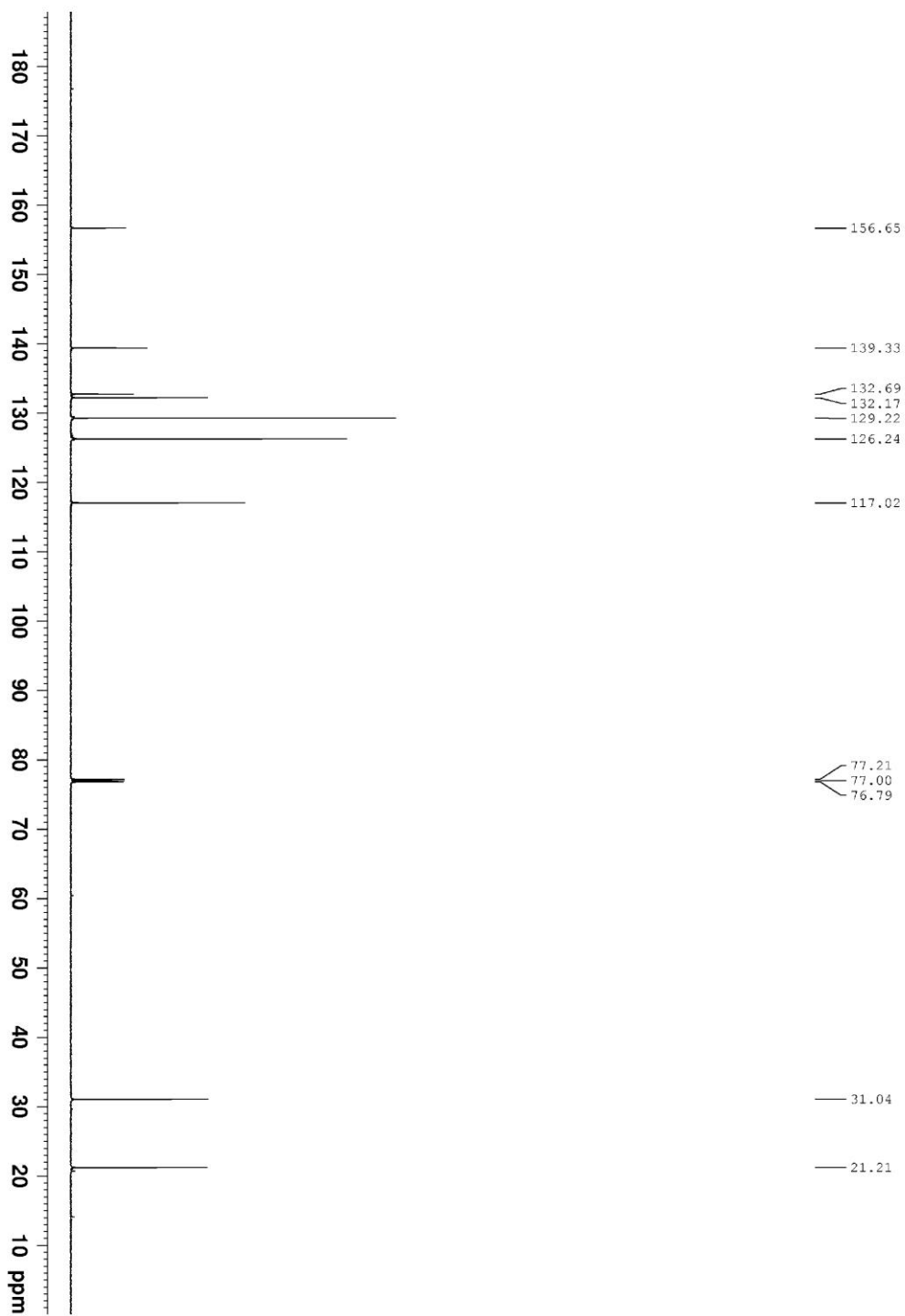
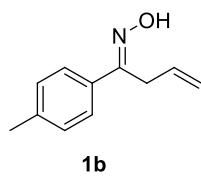


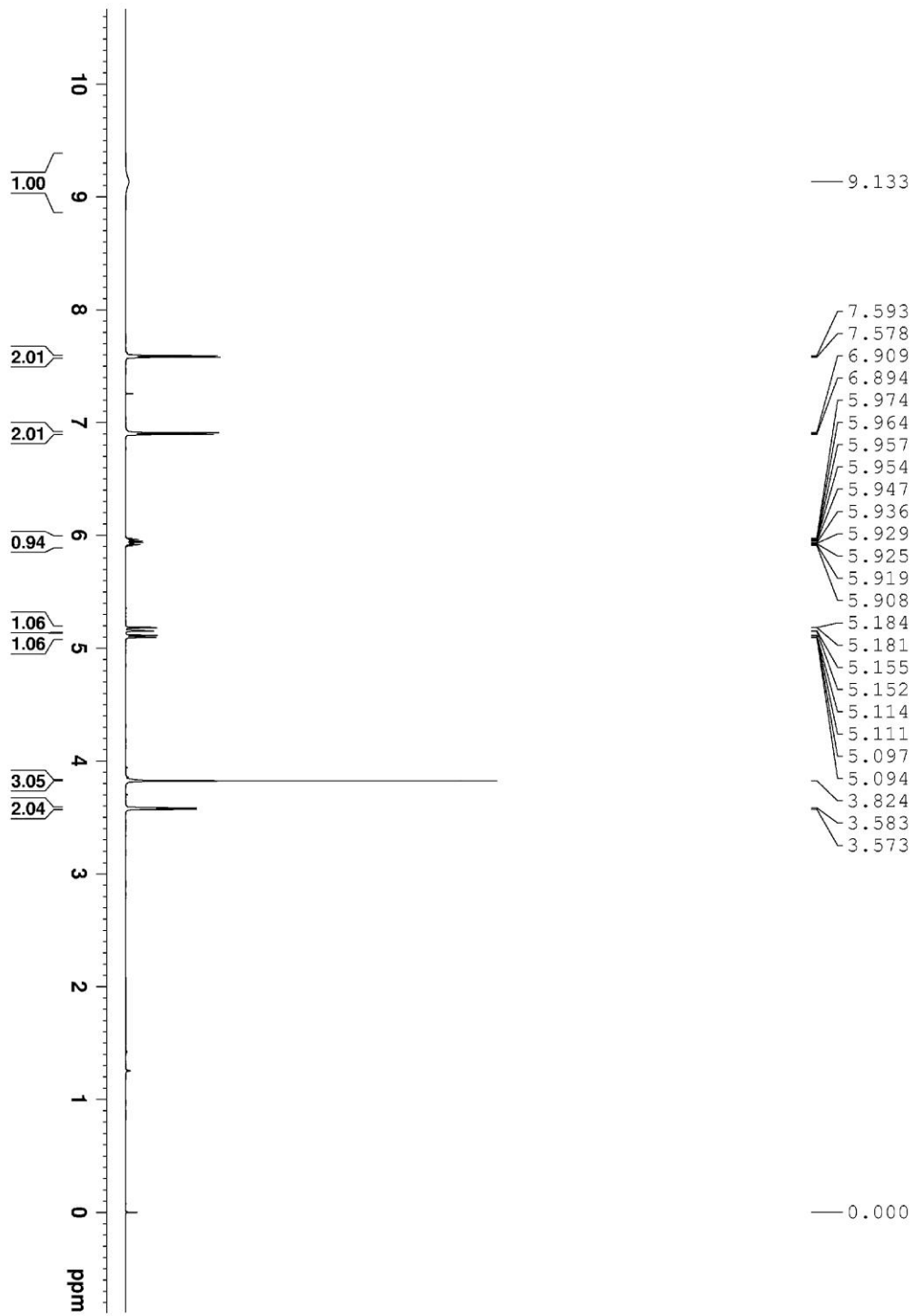
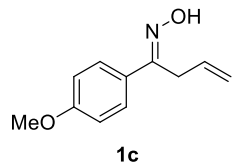


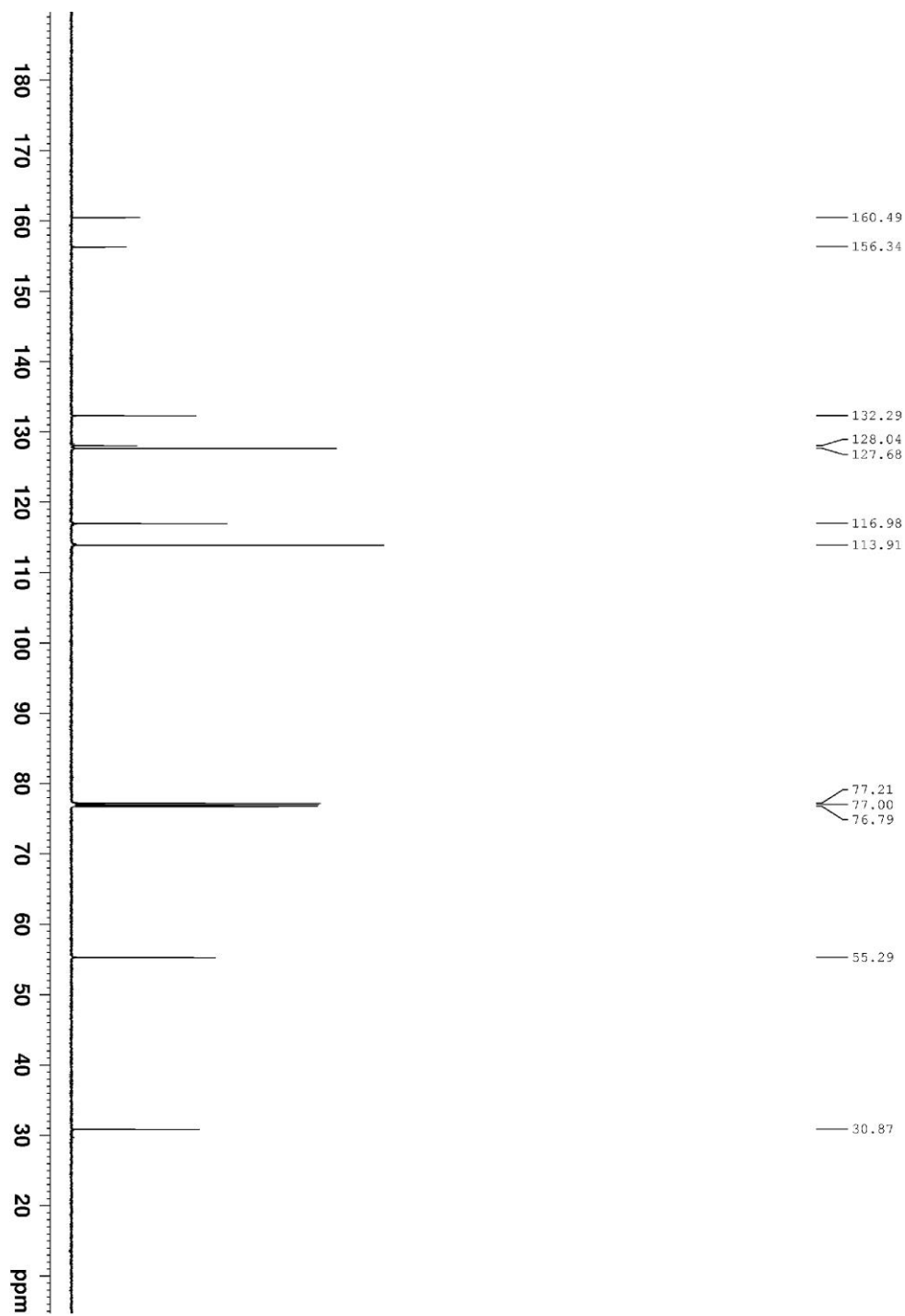
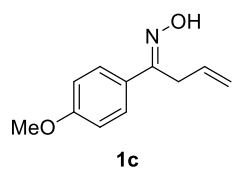
1a

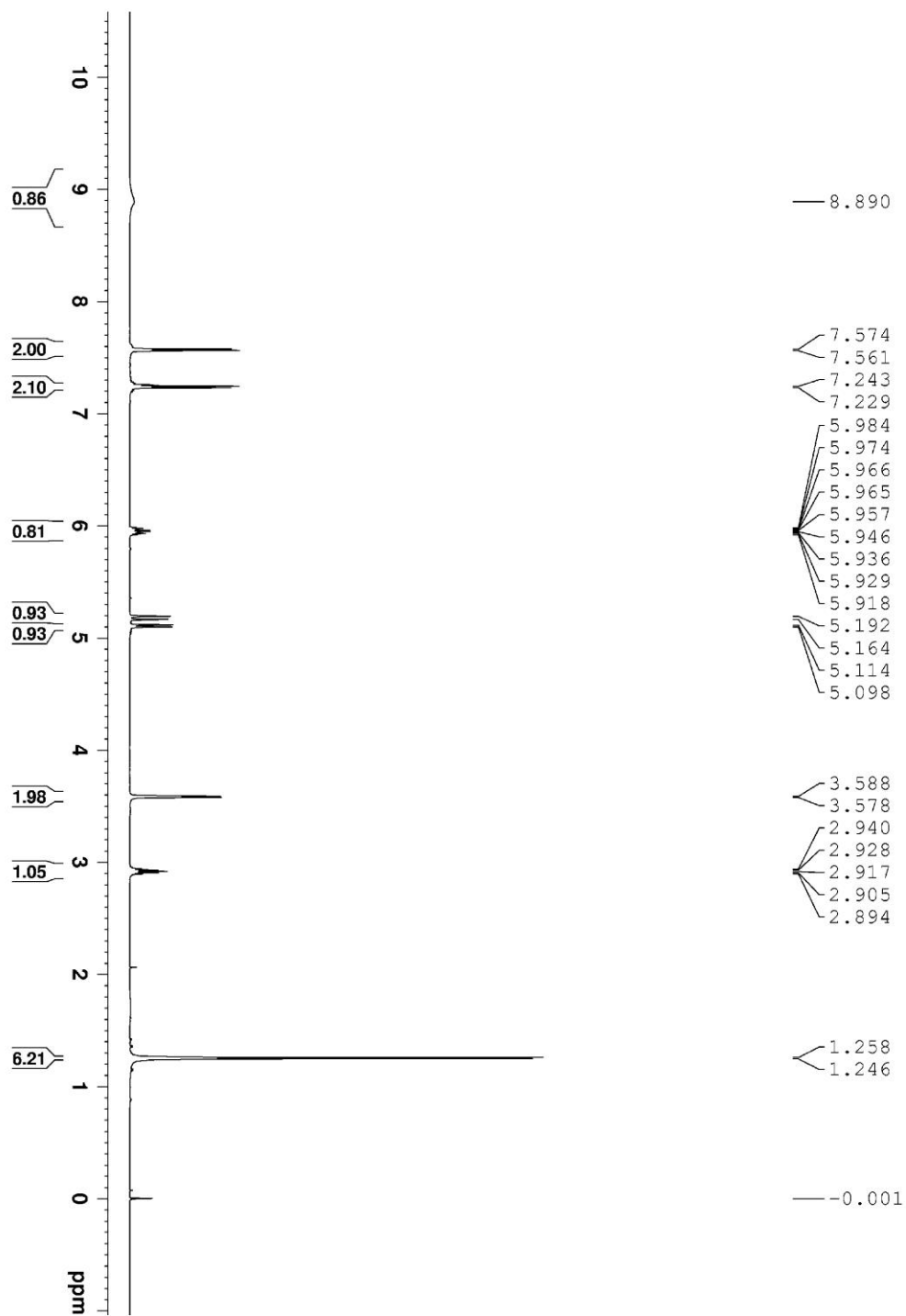
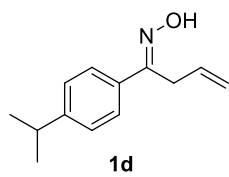


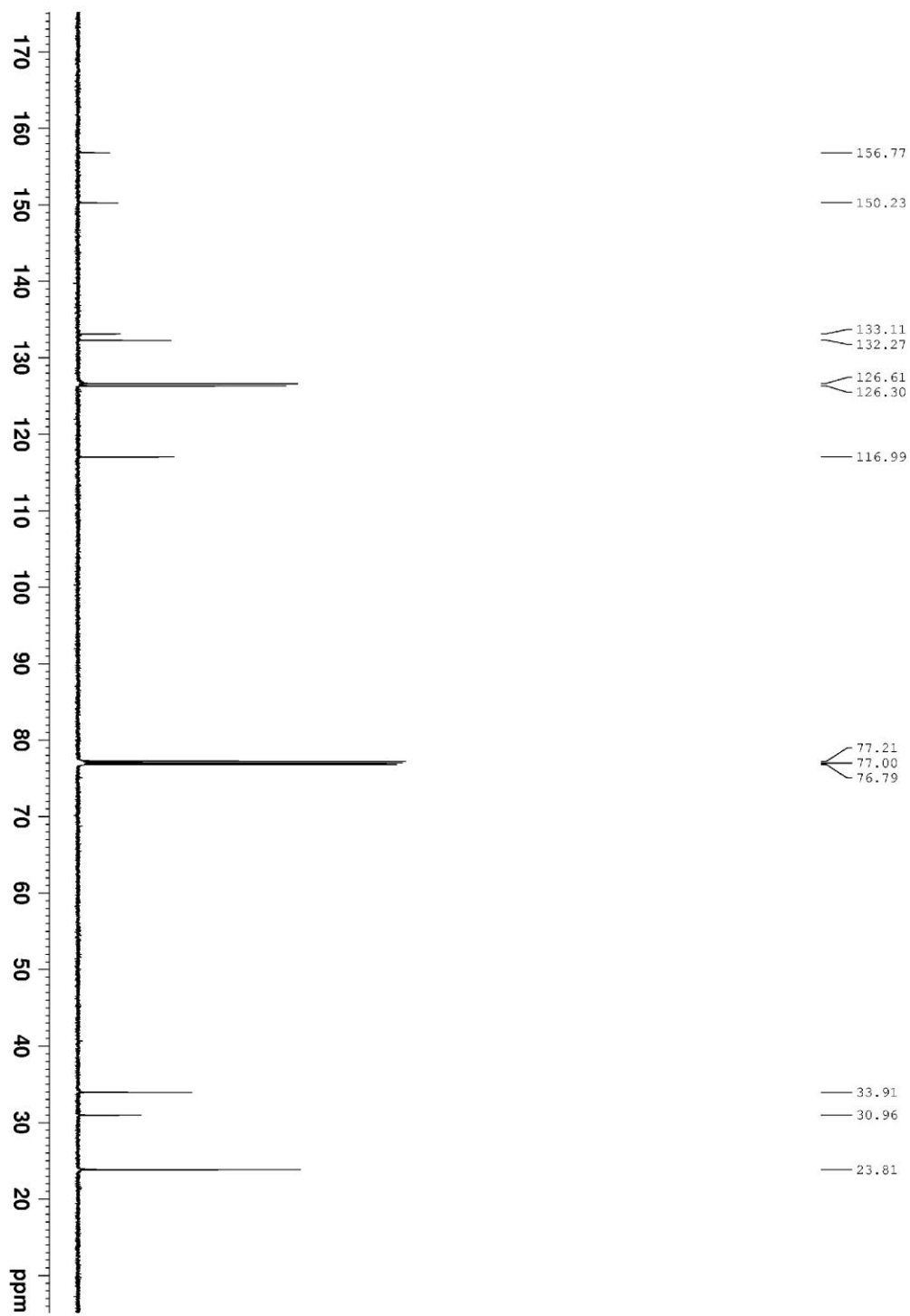
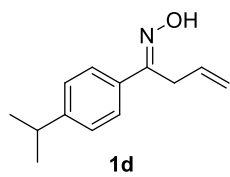


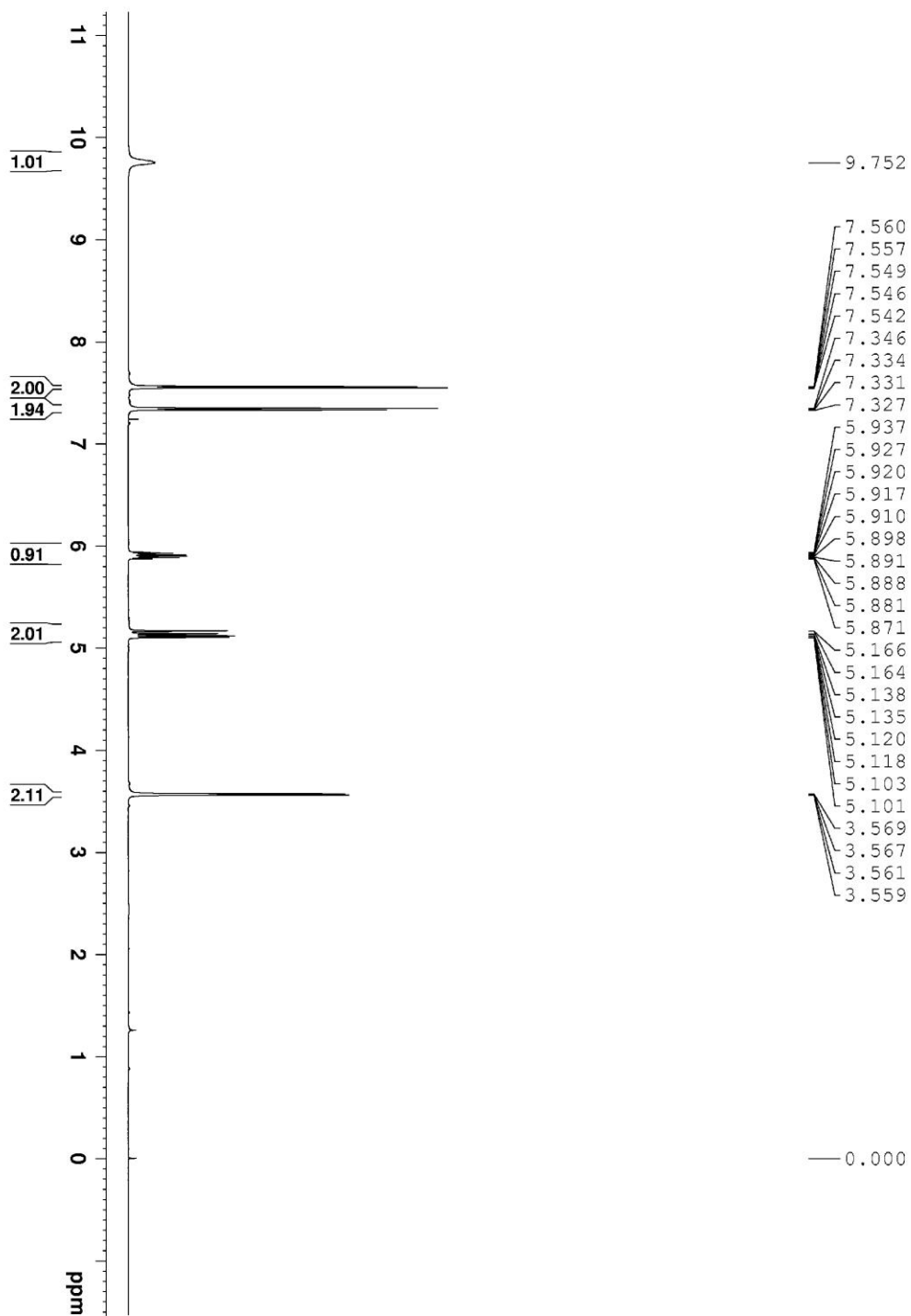
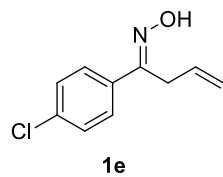


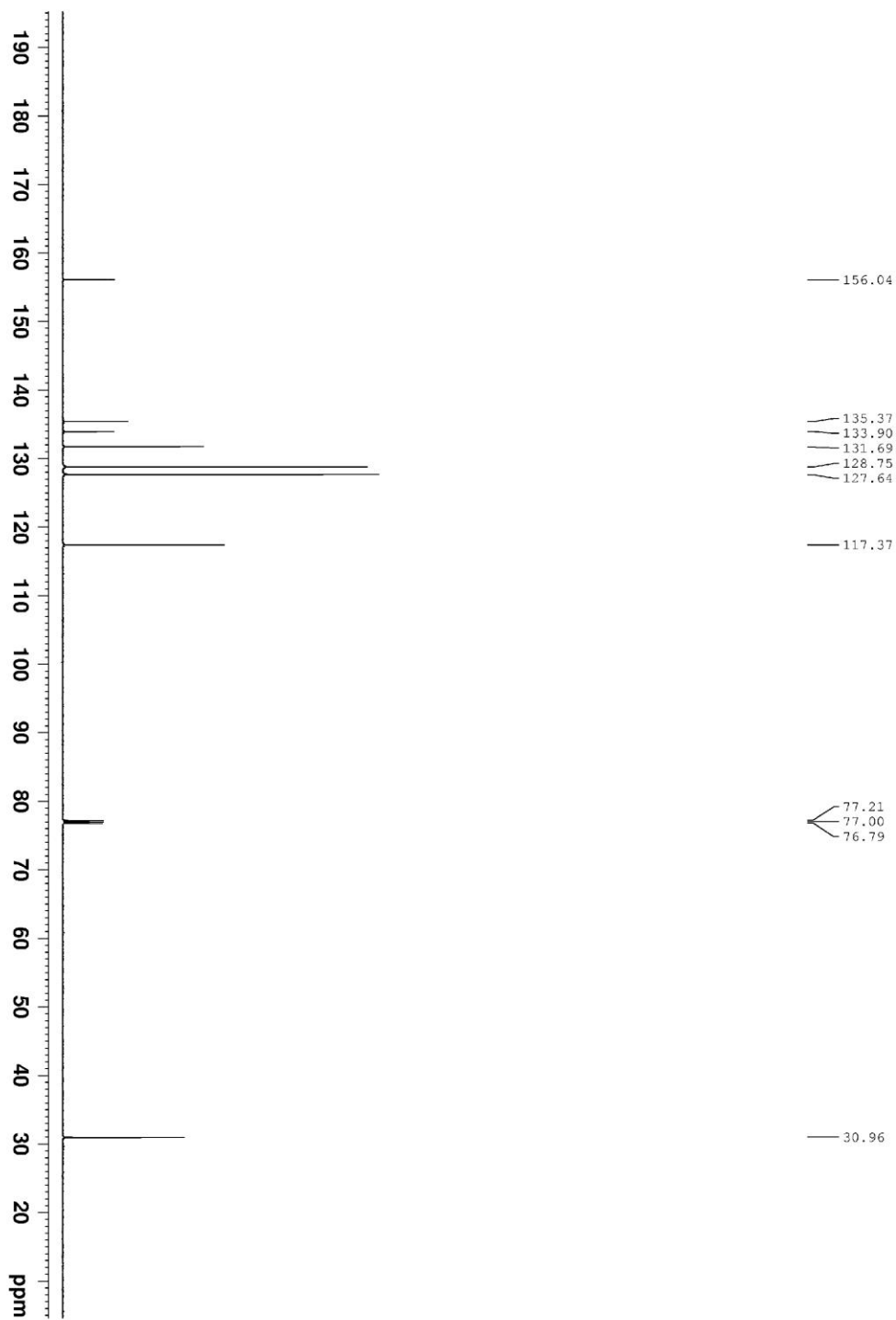
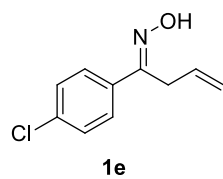


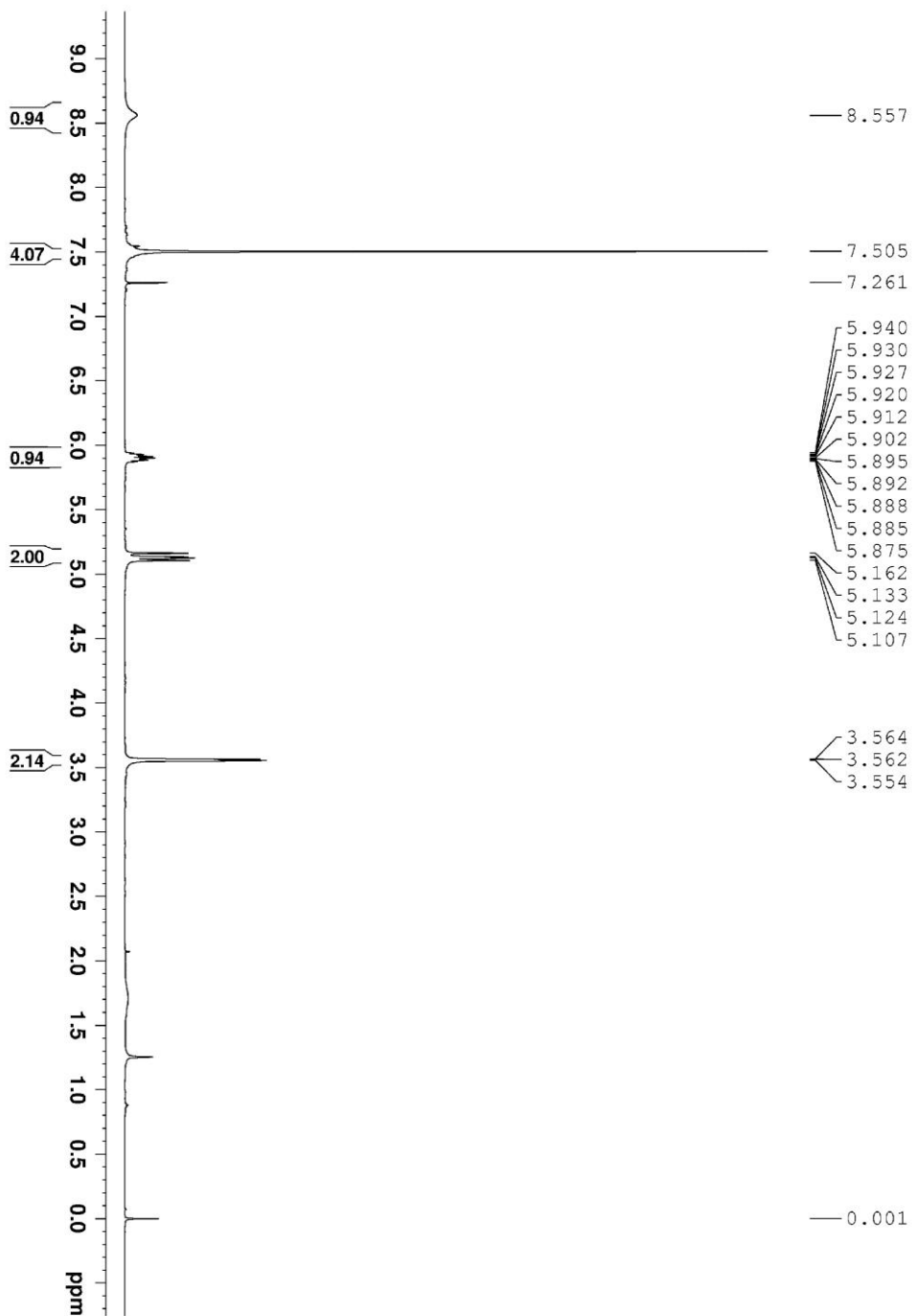
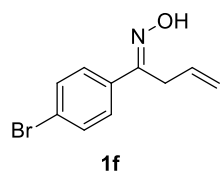


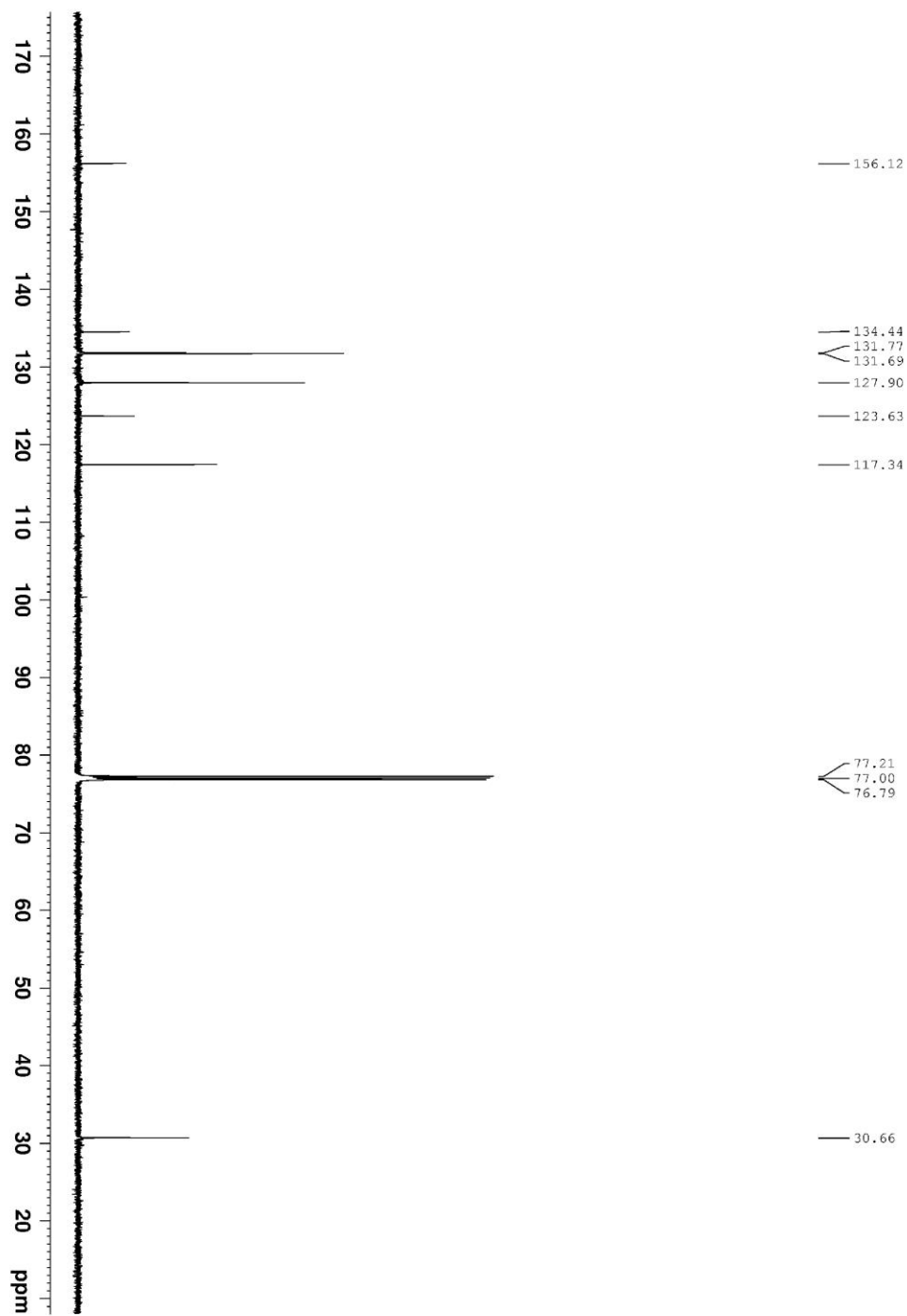
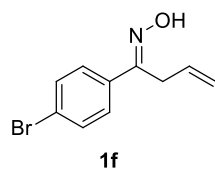


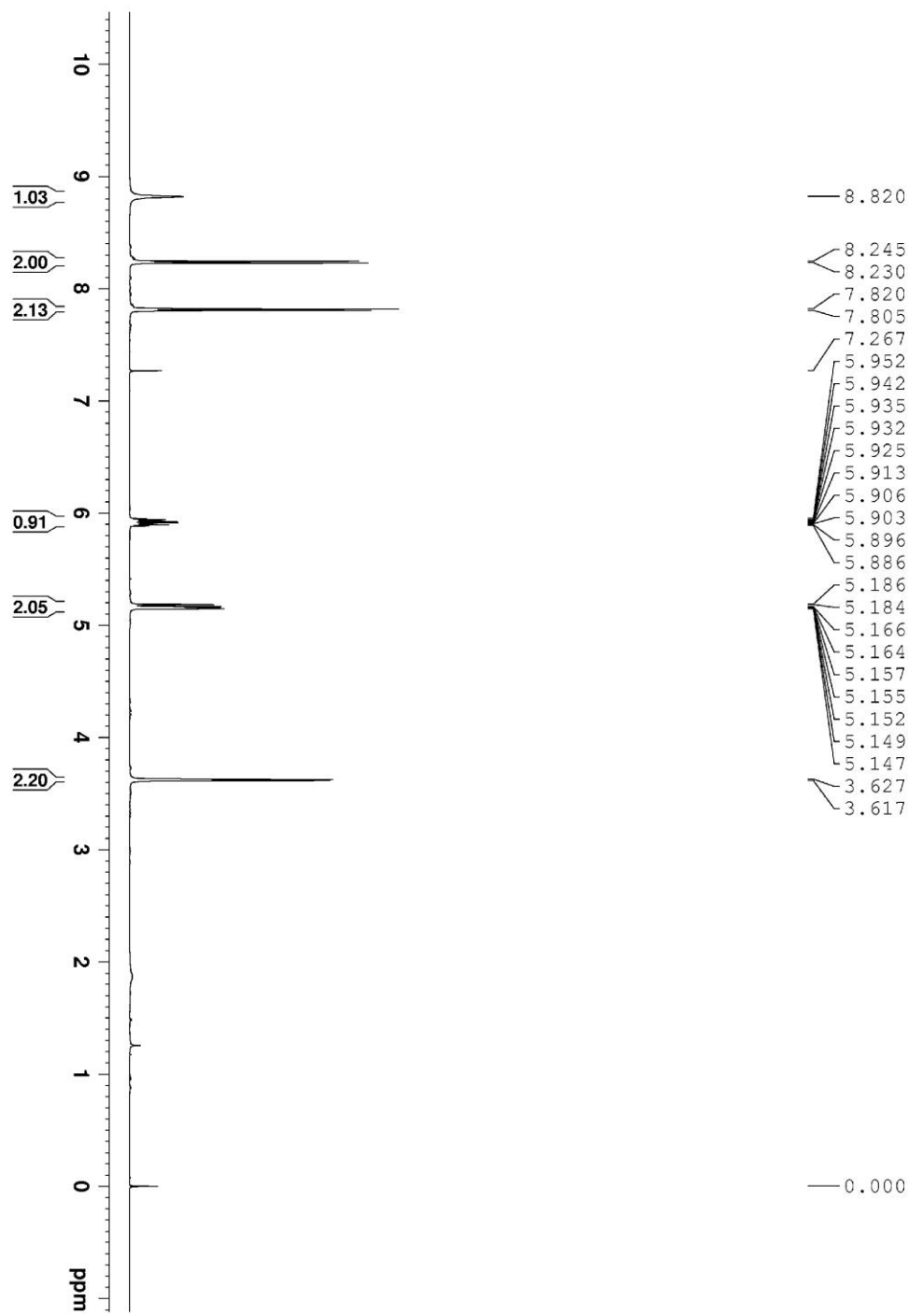
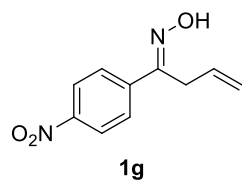


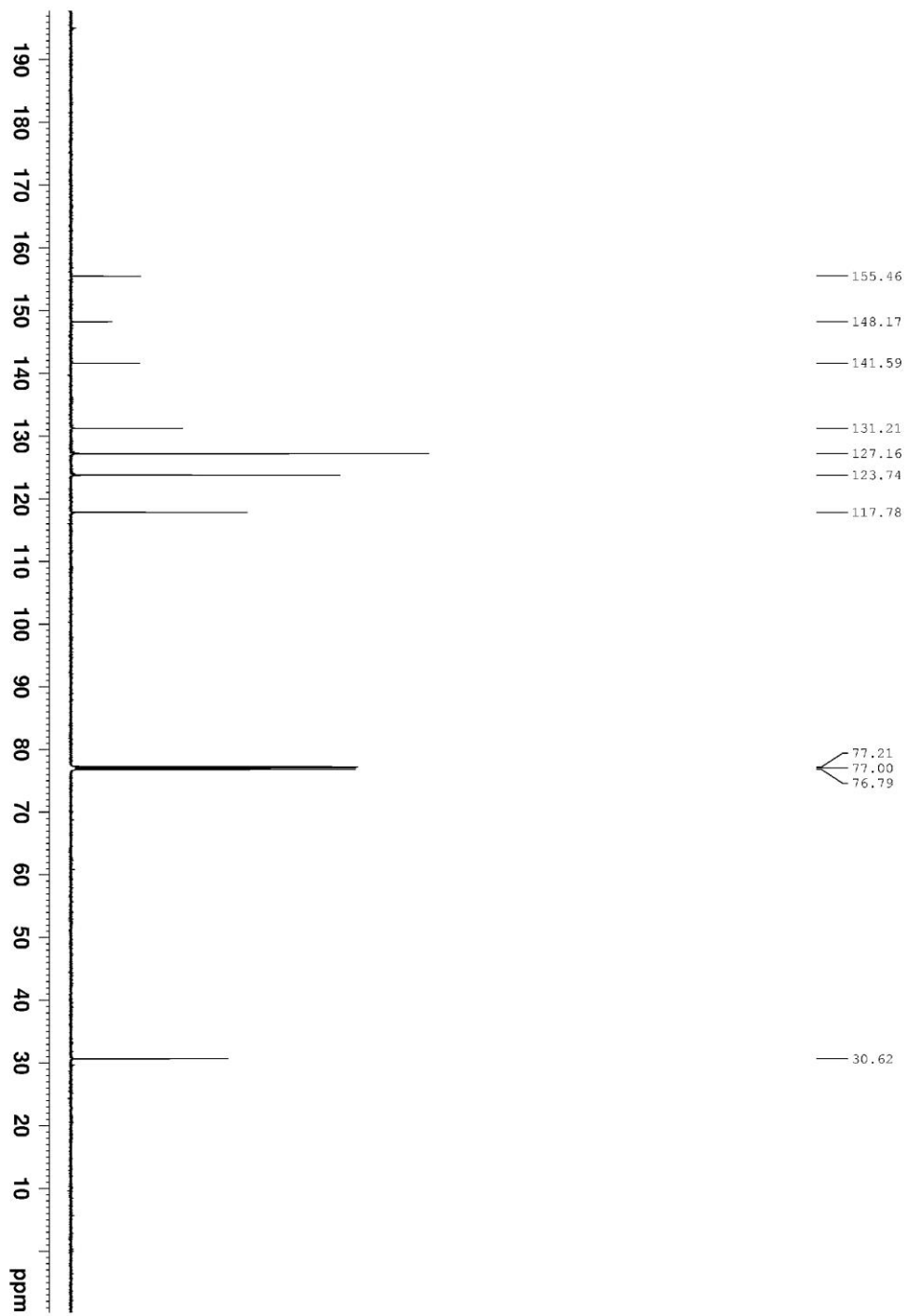
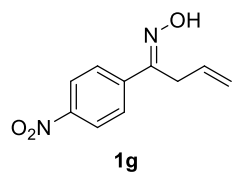


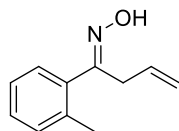




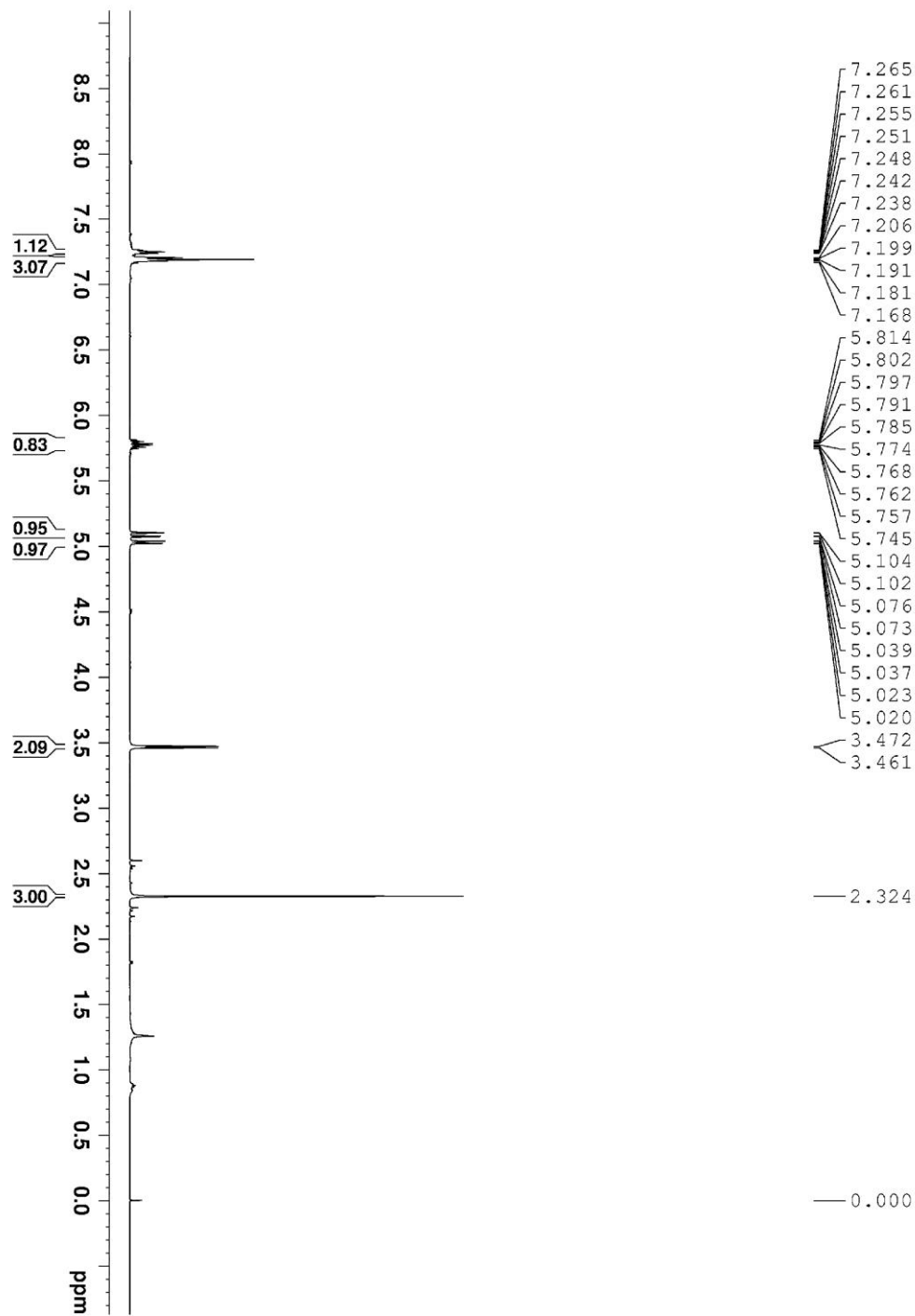


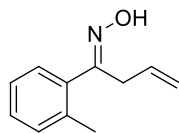




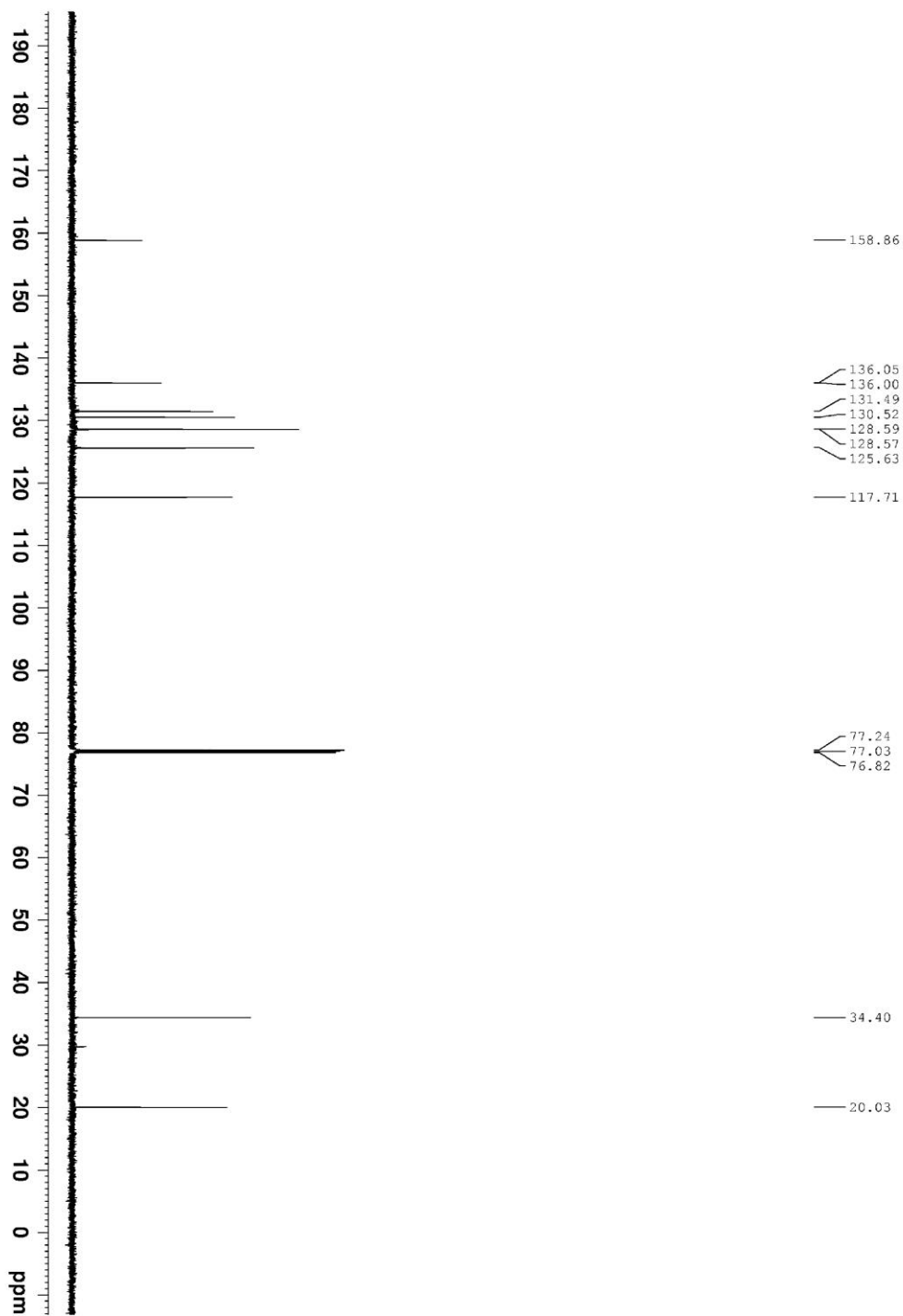


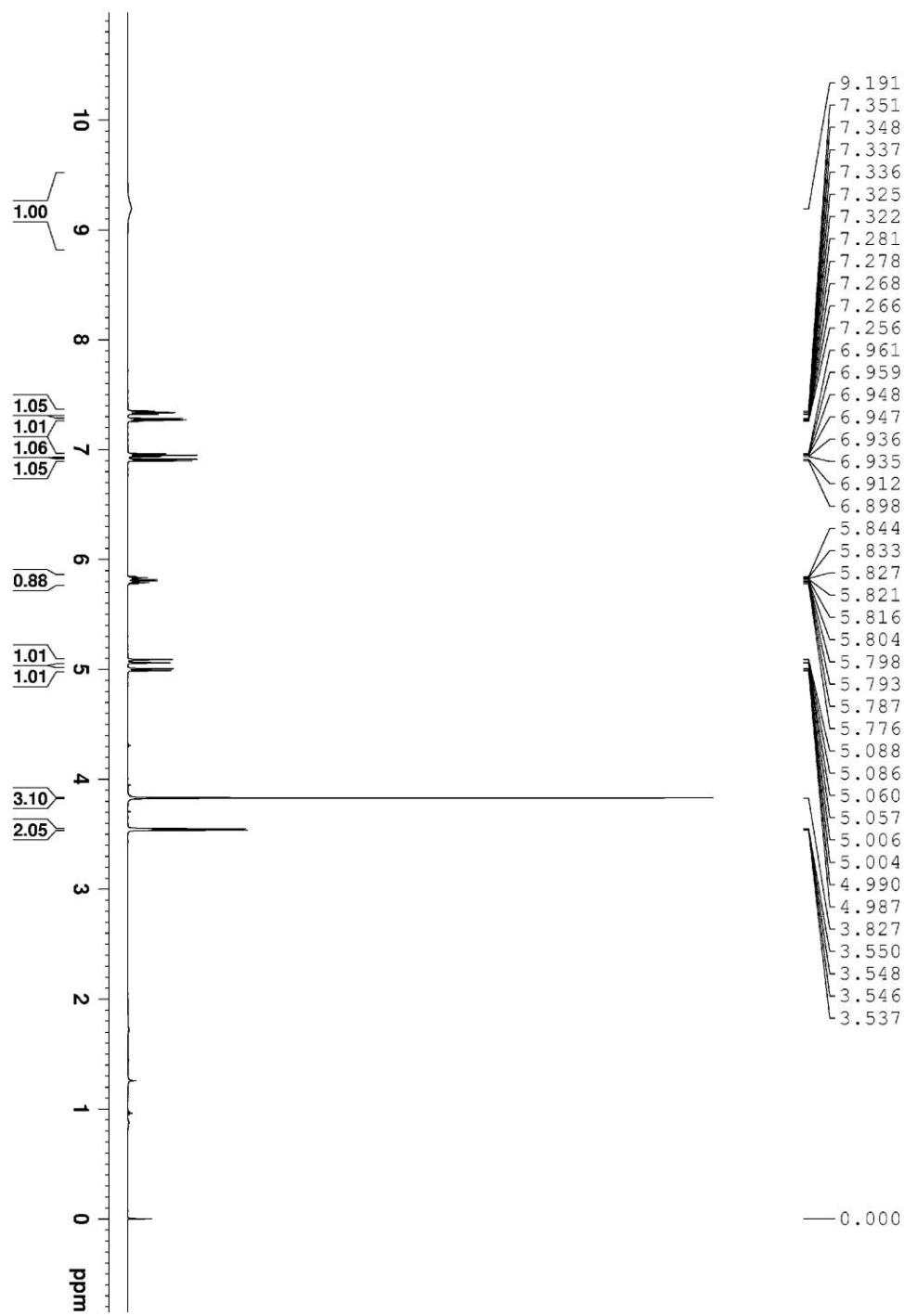
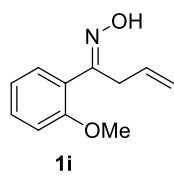
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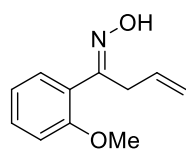




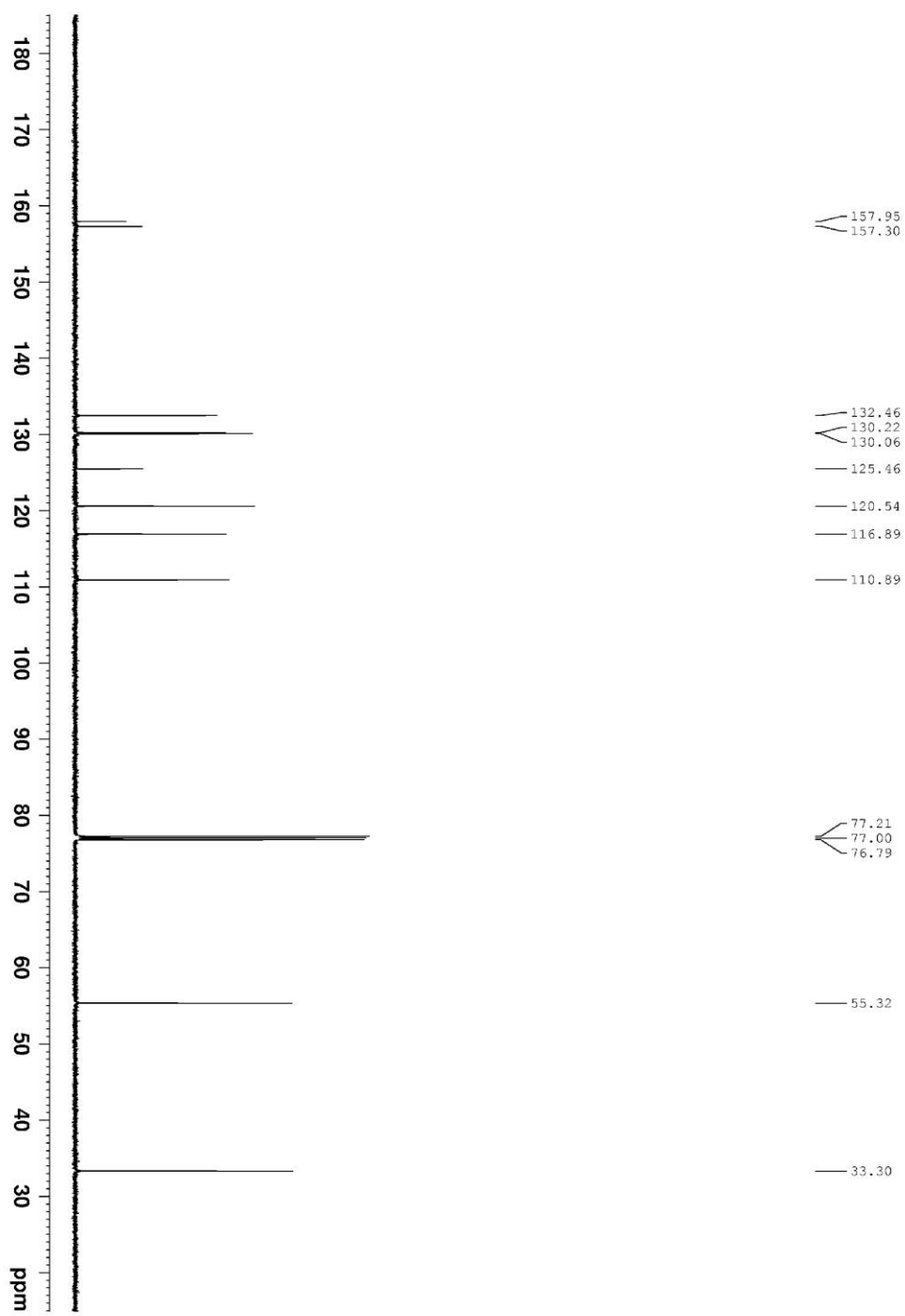
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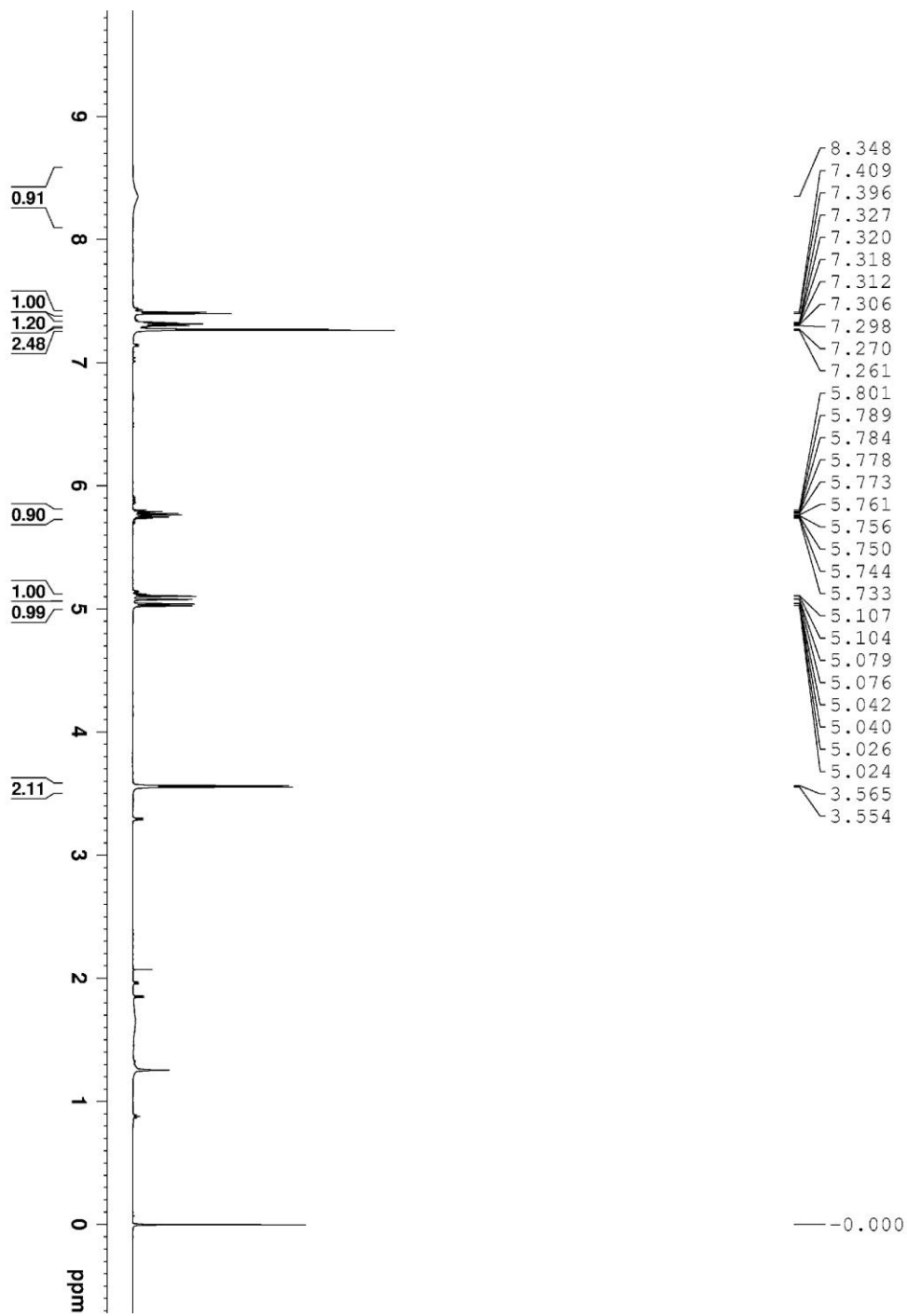
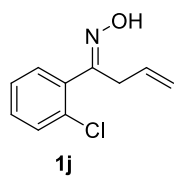


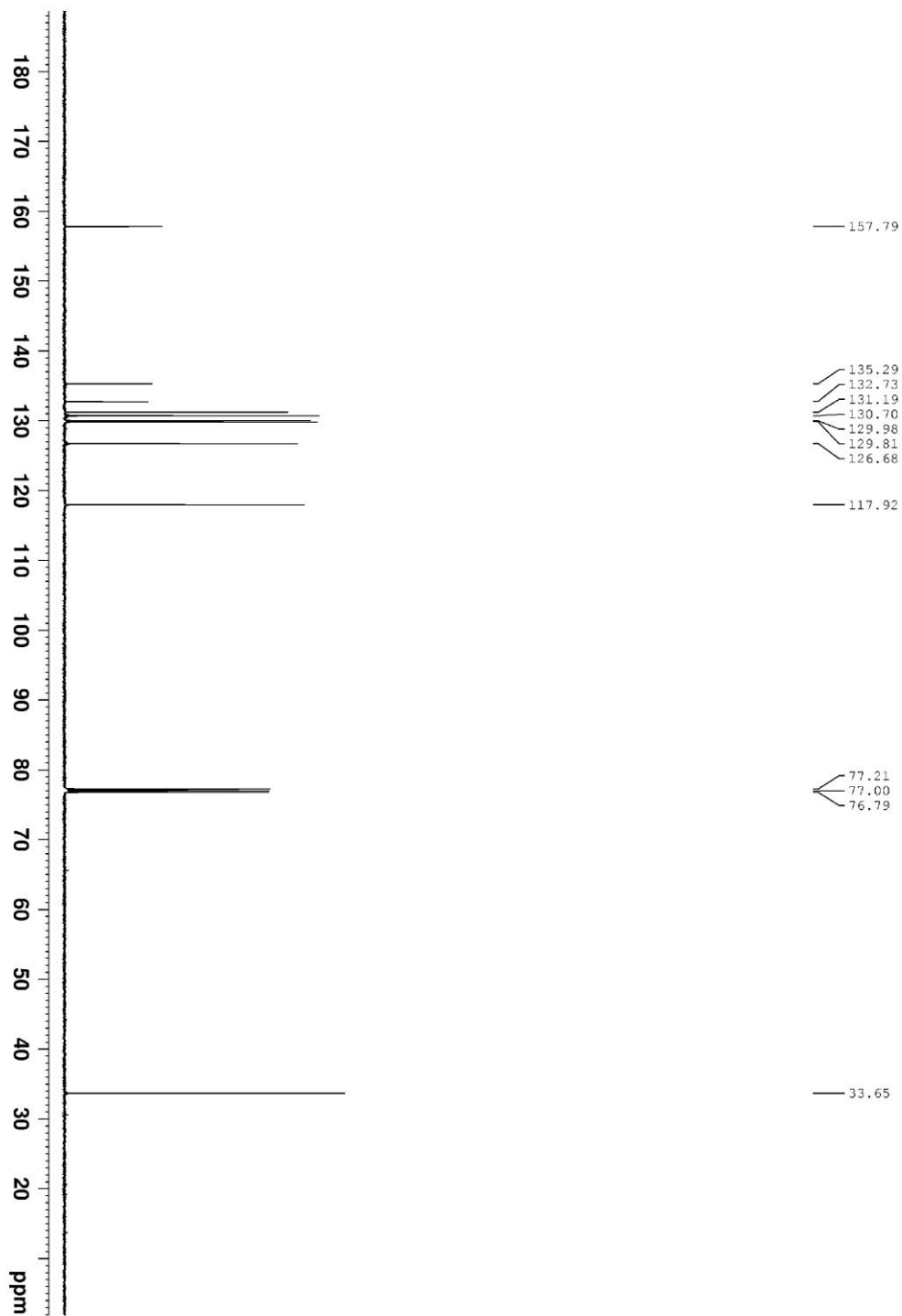
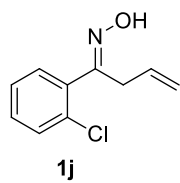


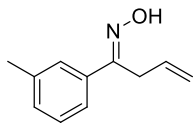


1i

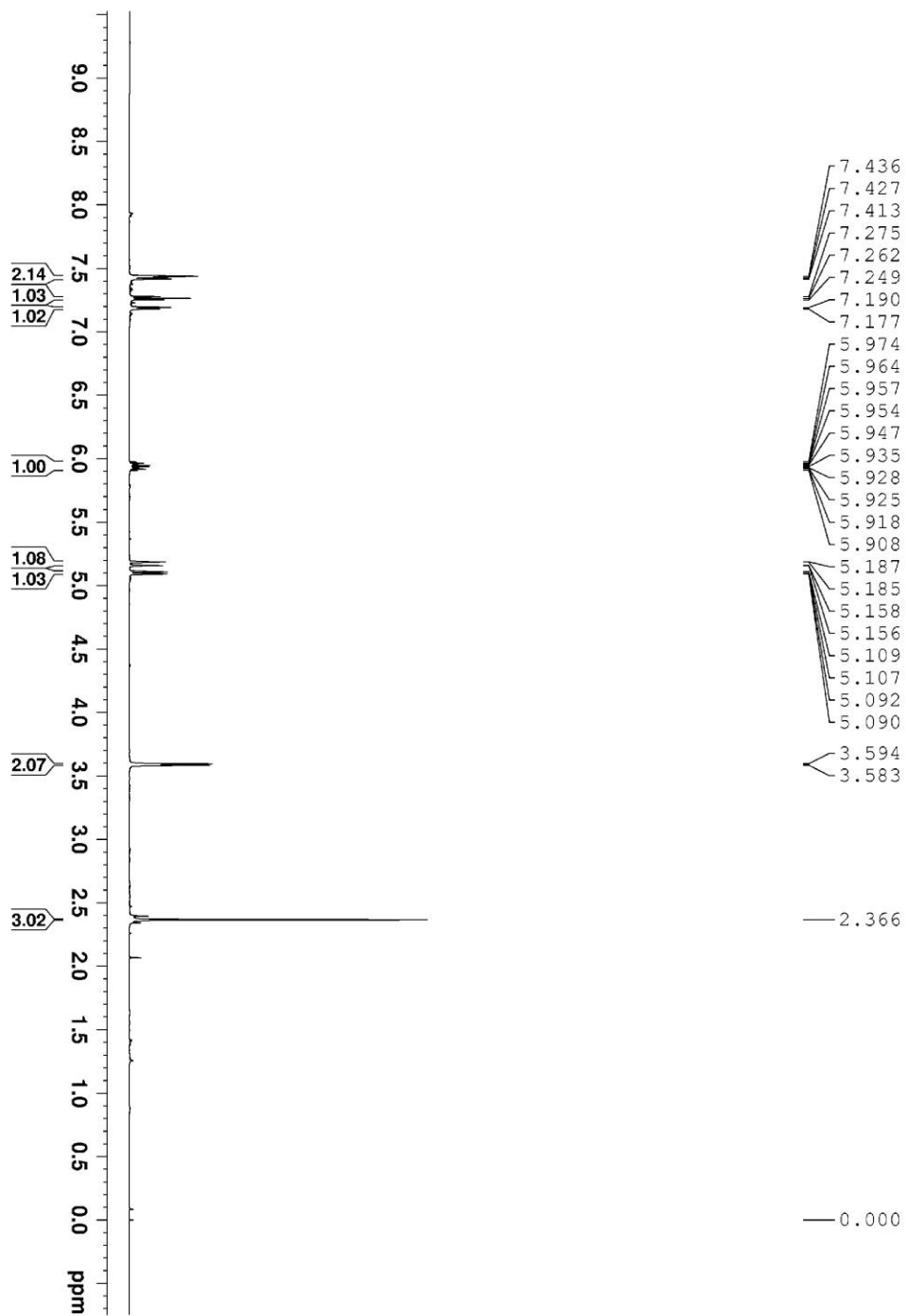


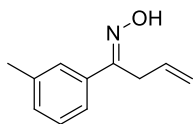




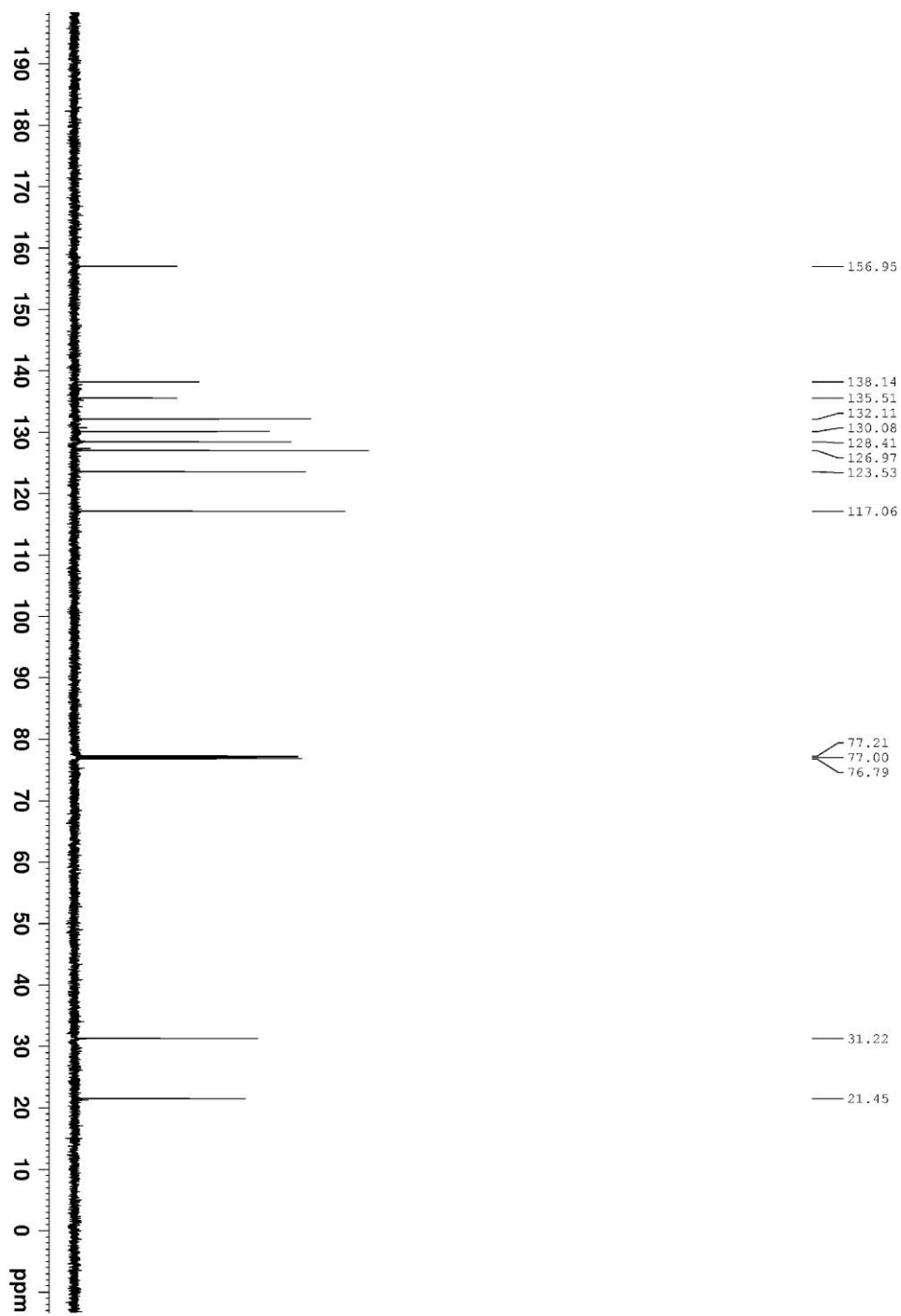


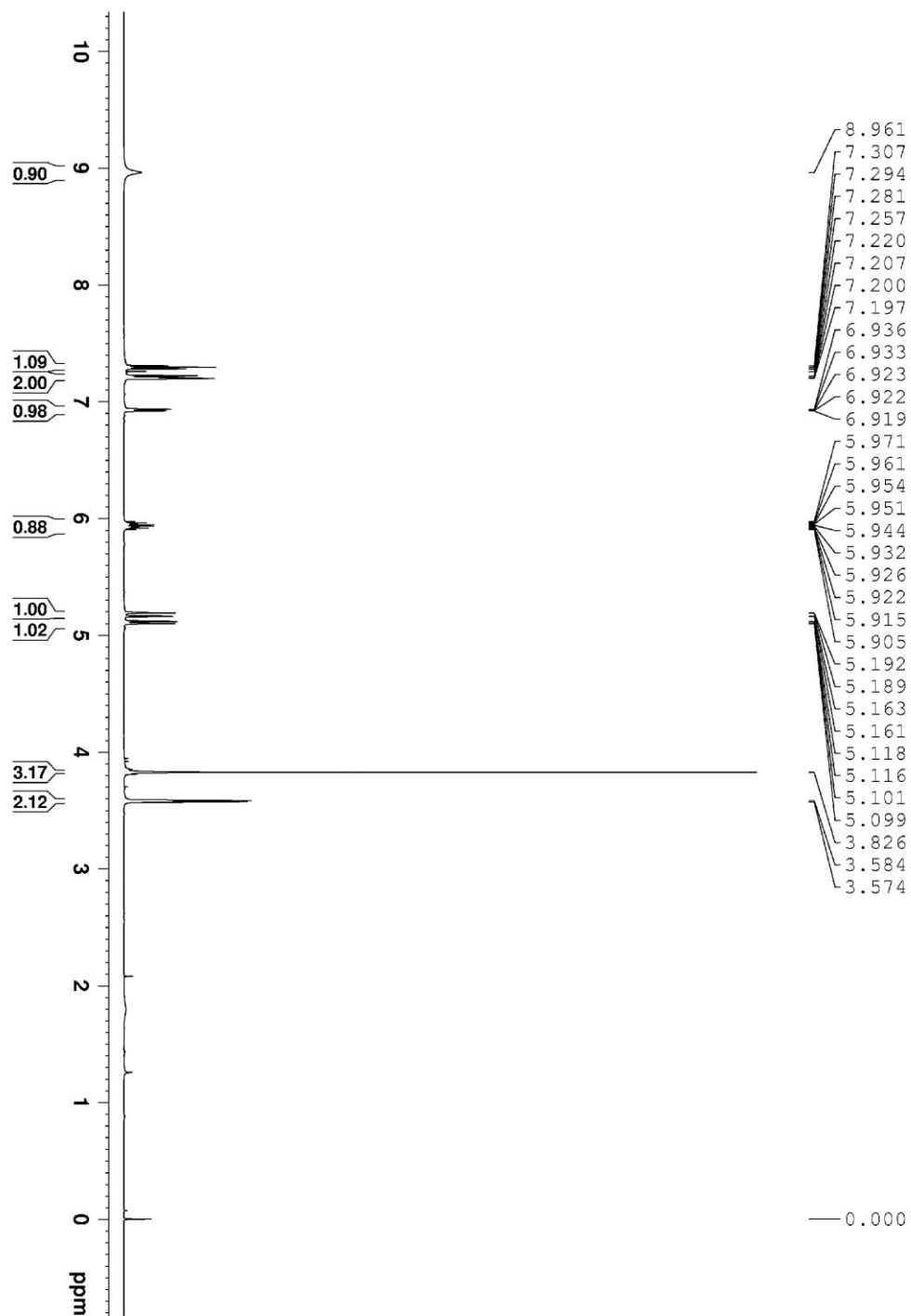
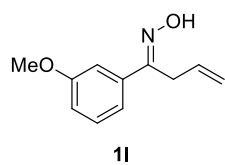
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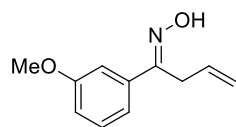




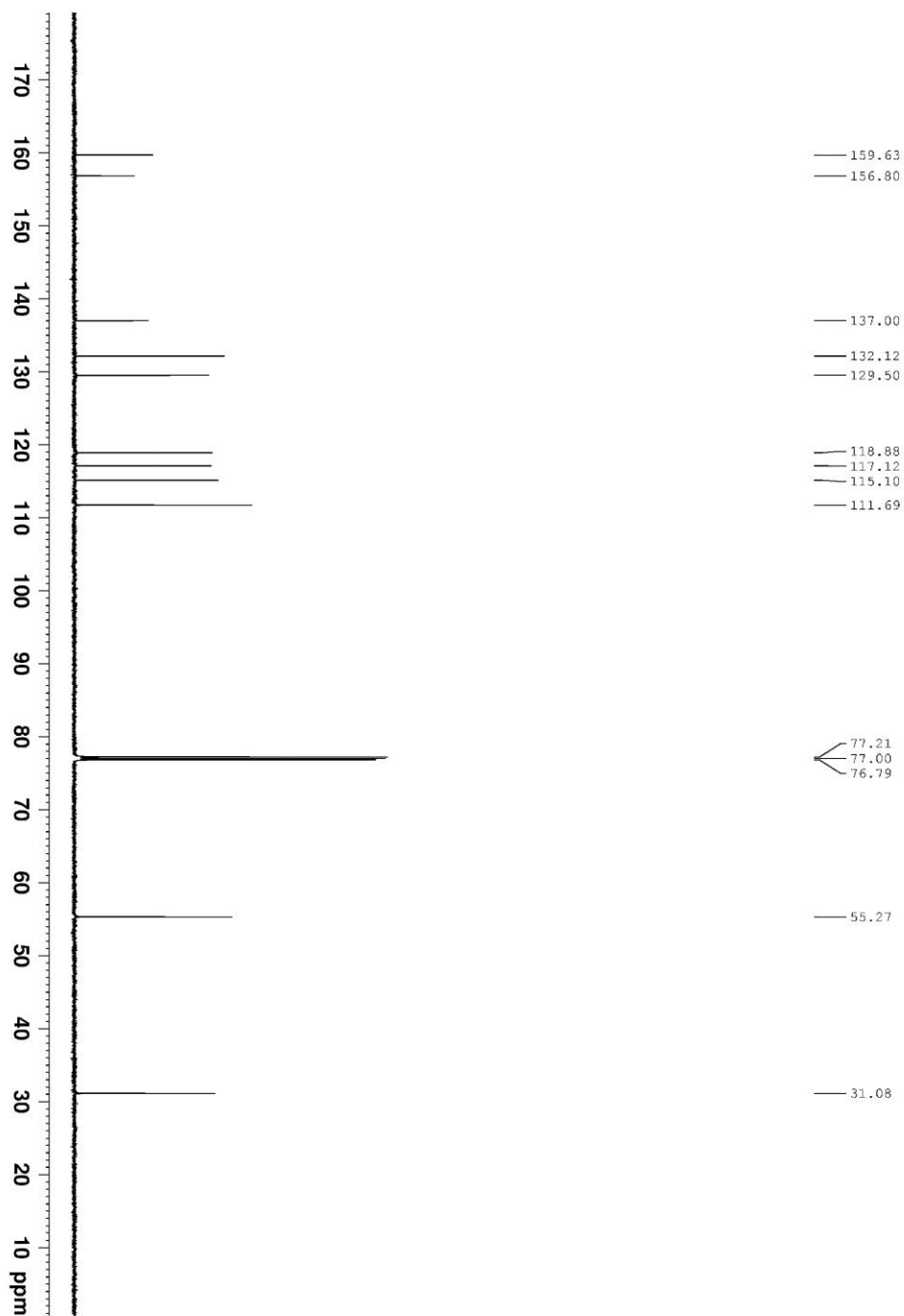
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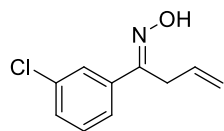




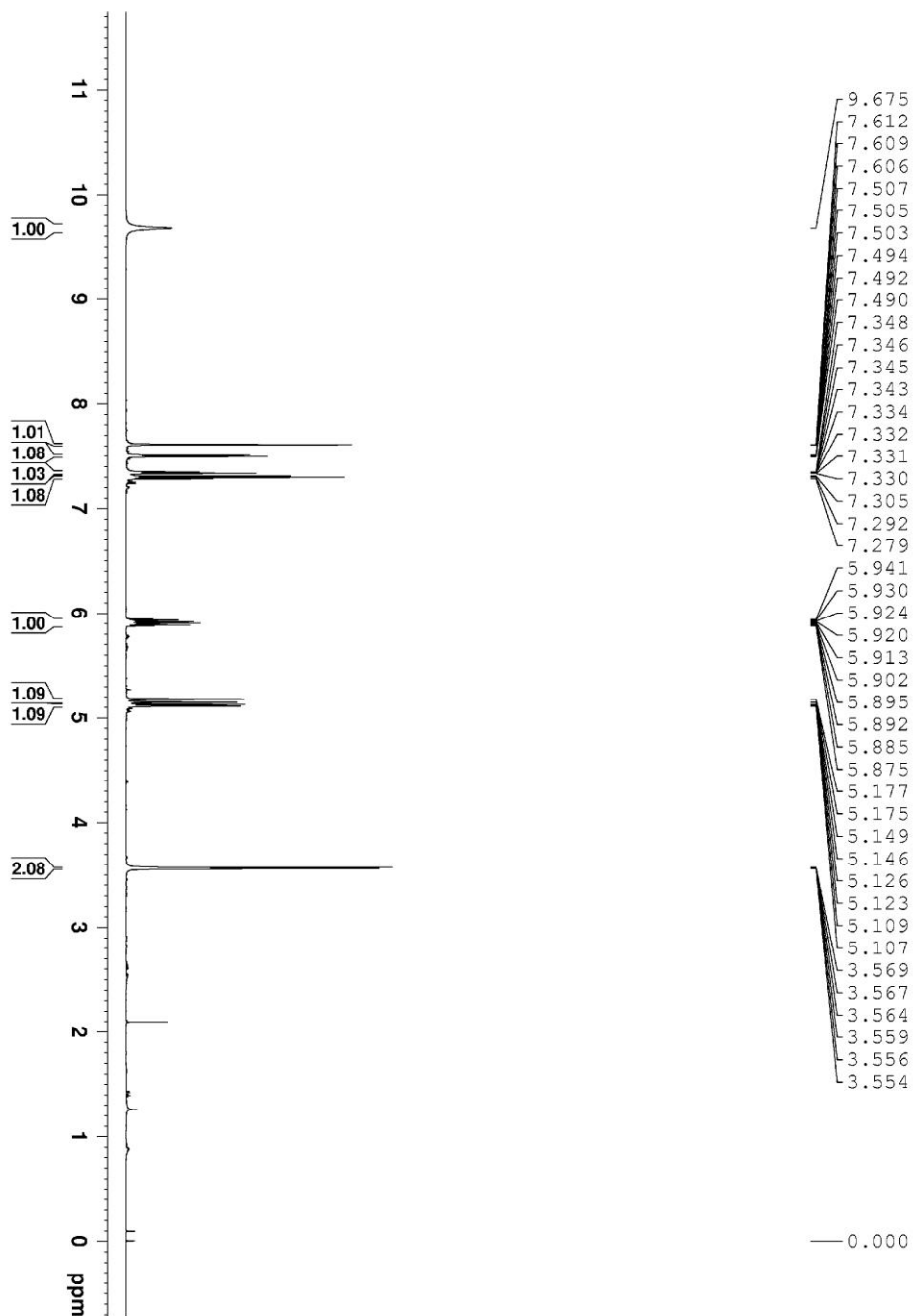


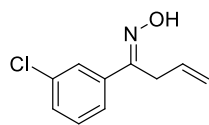
11



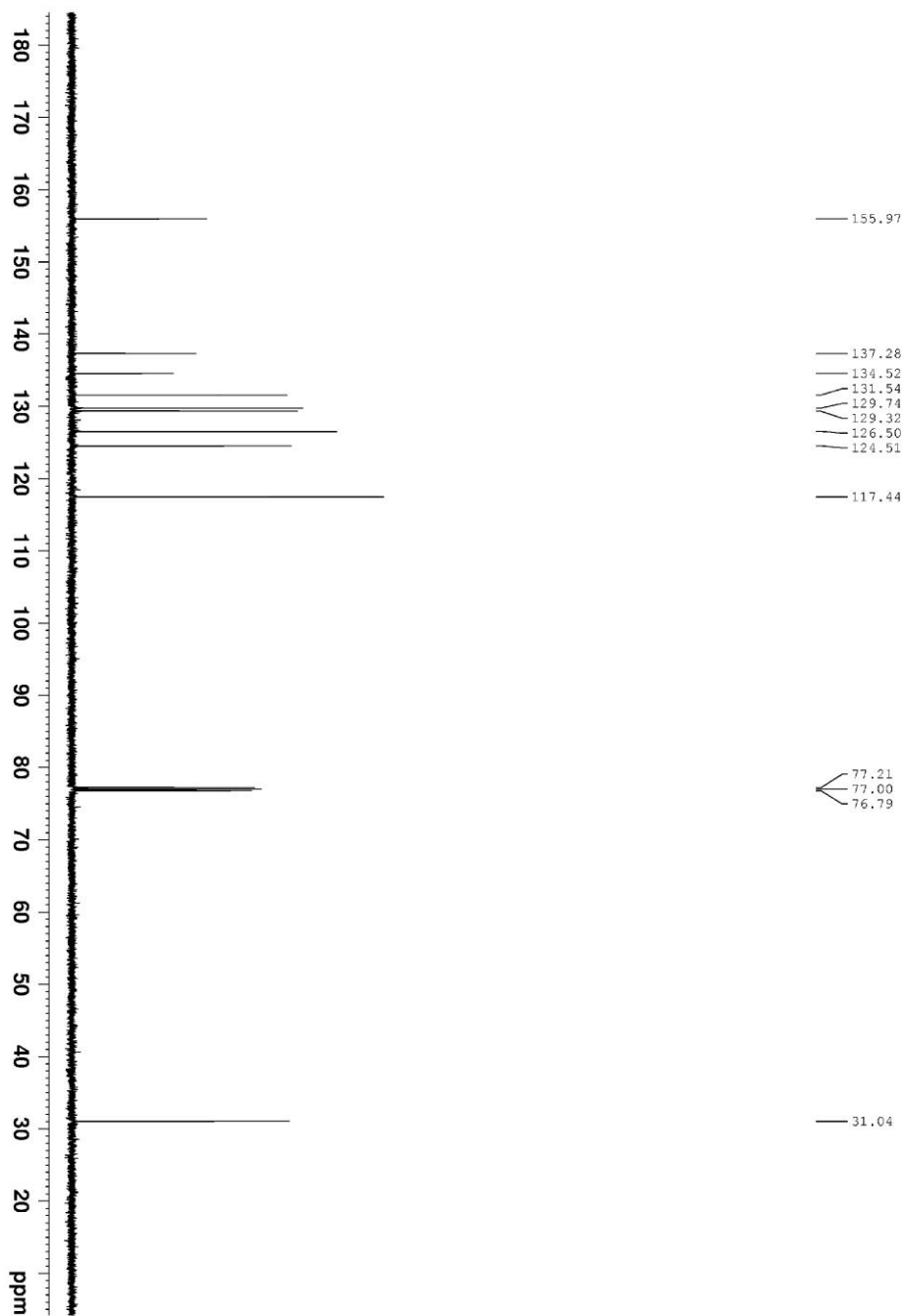


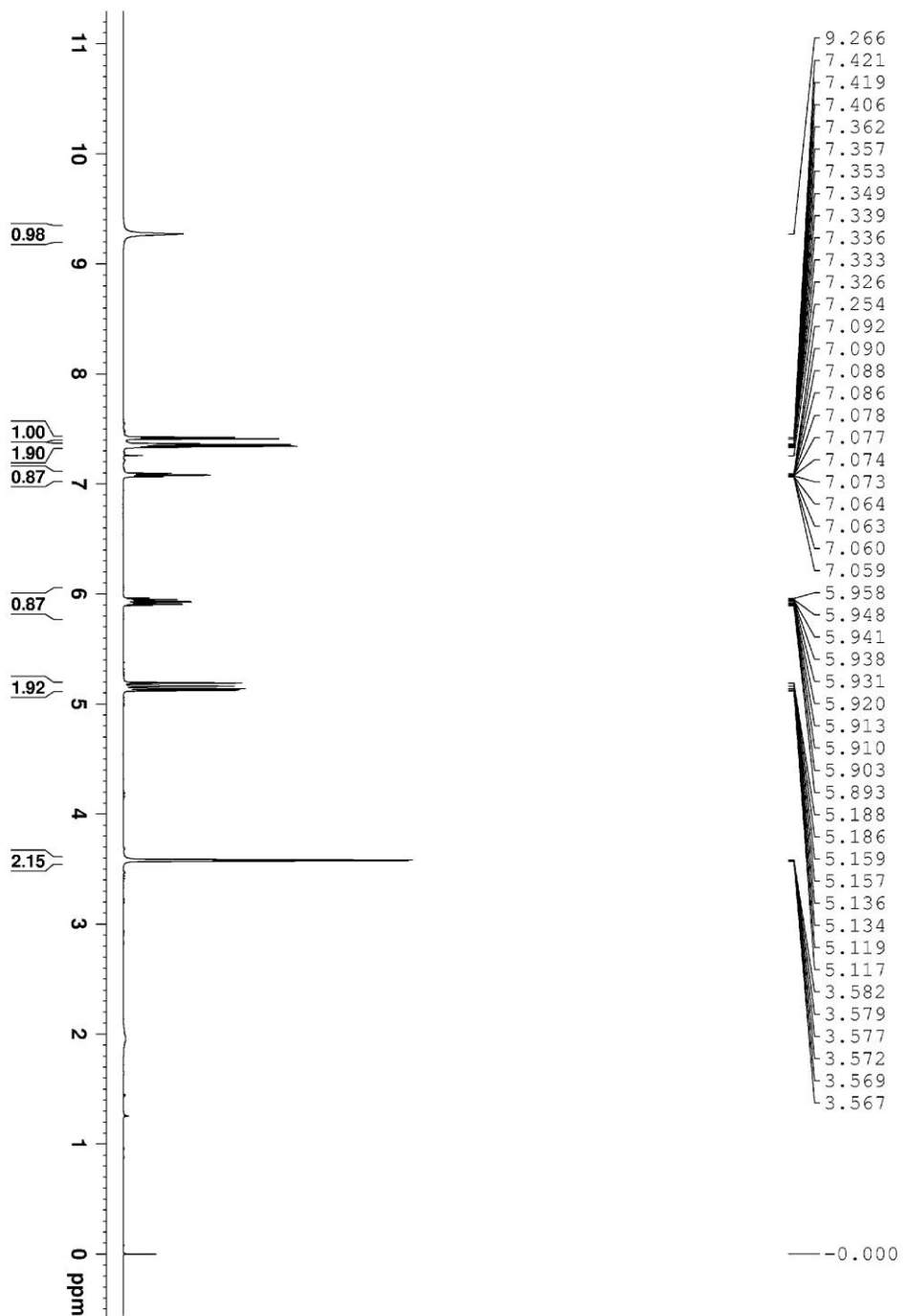
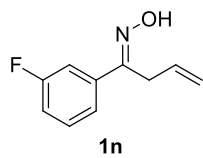
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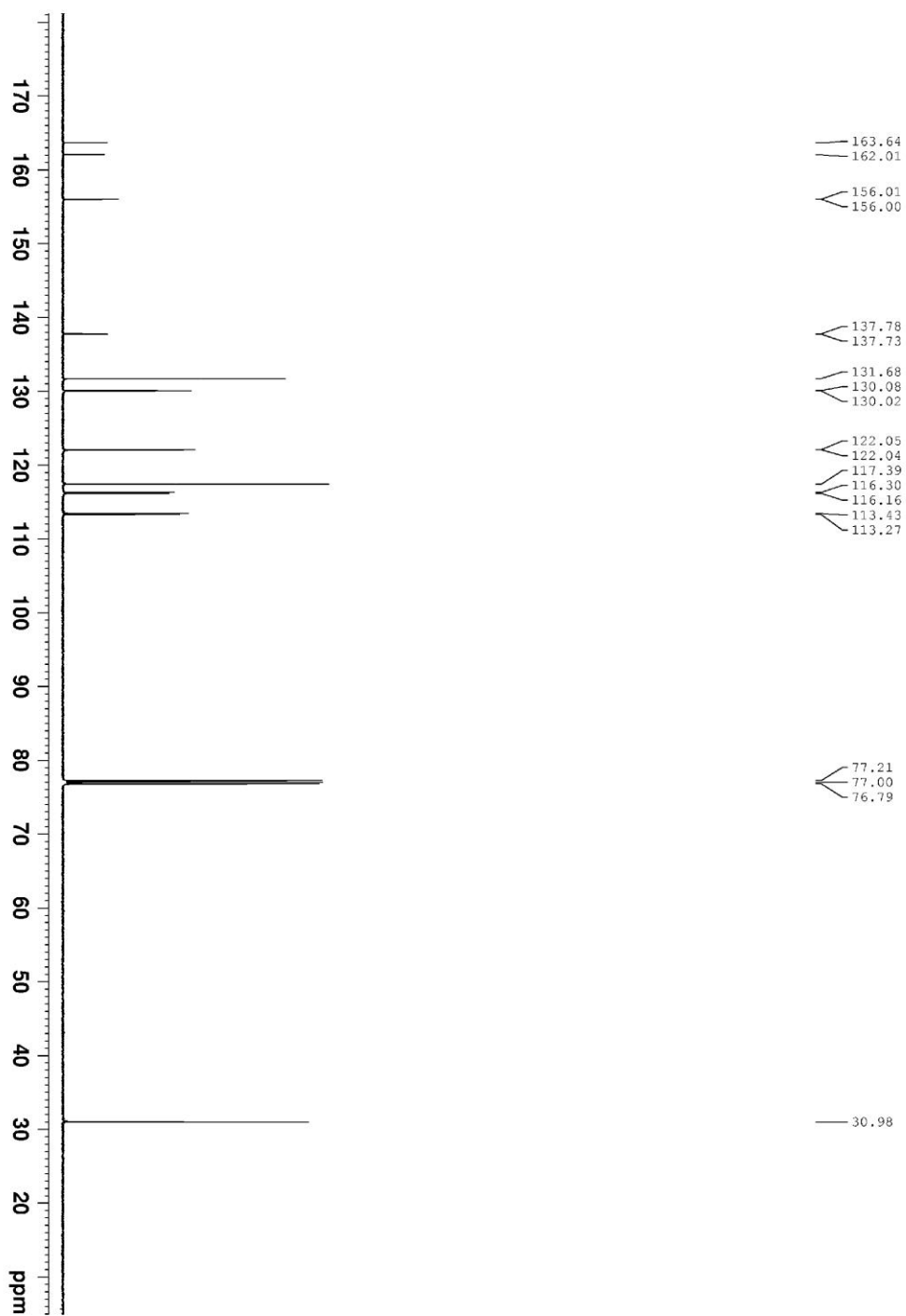
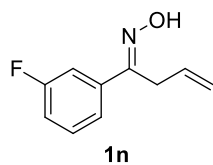


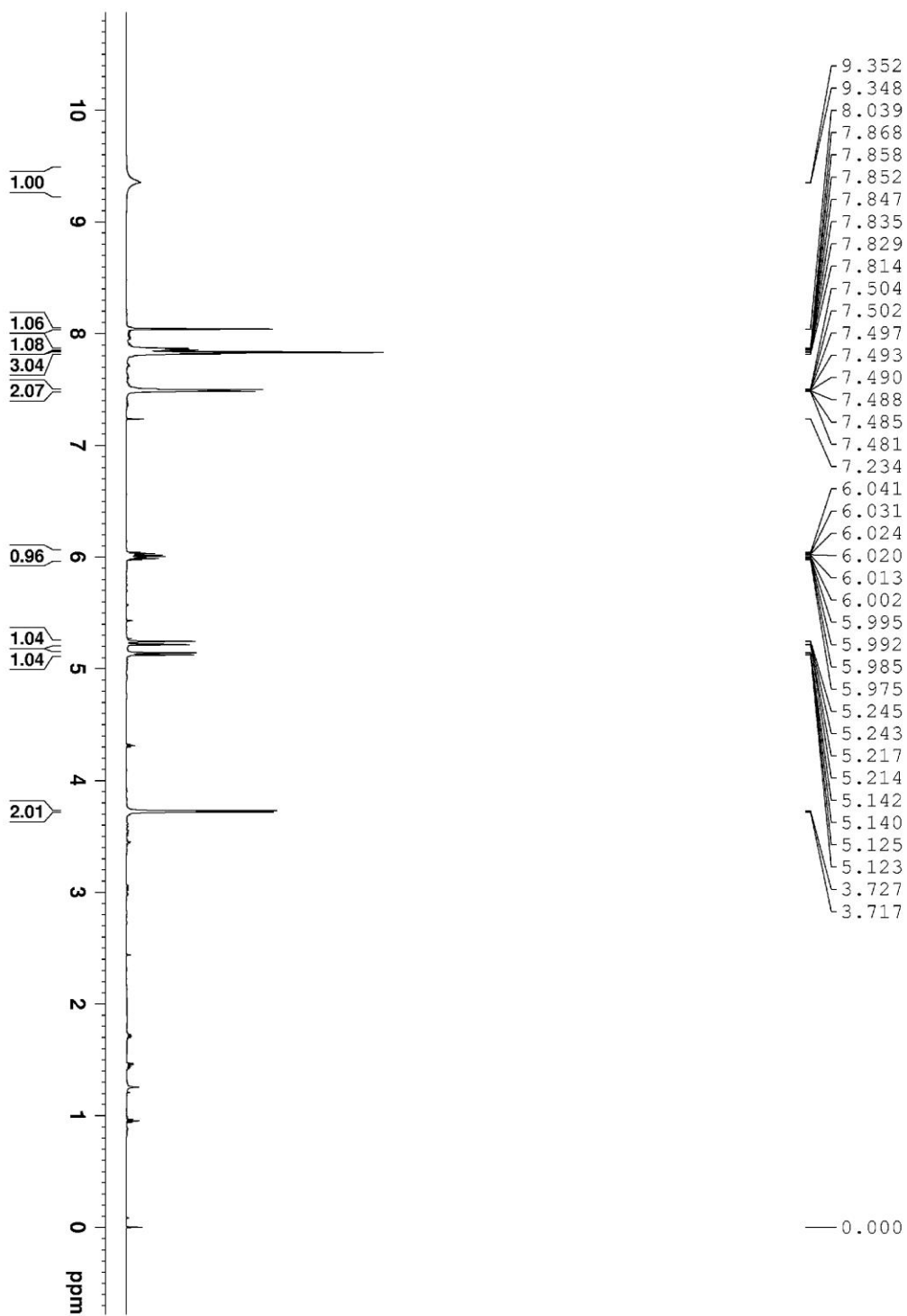
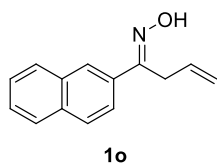


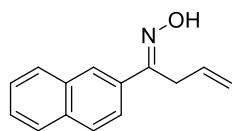
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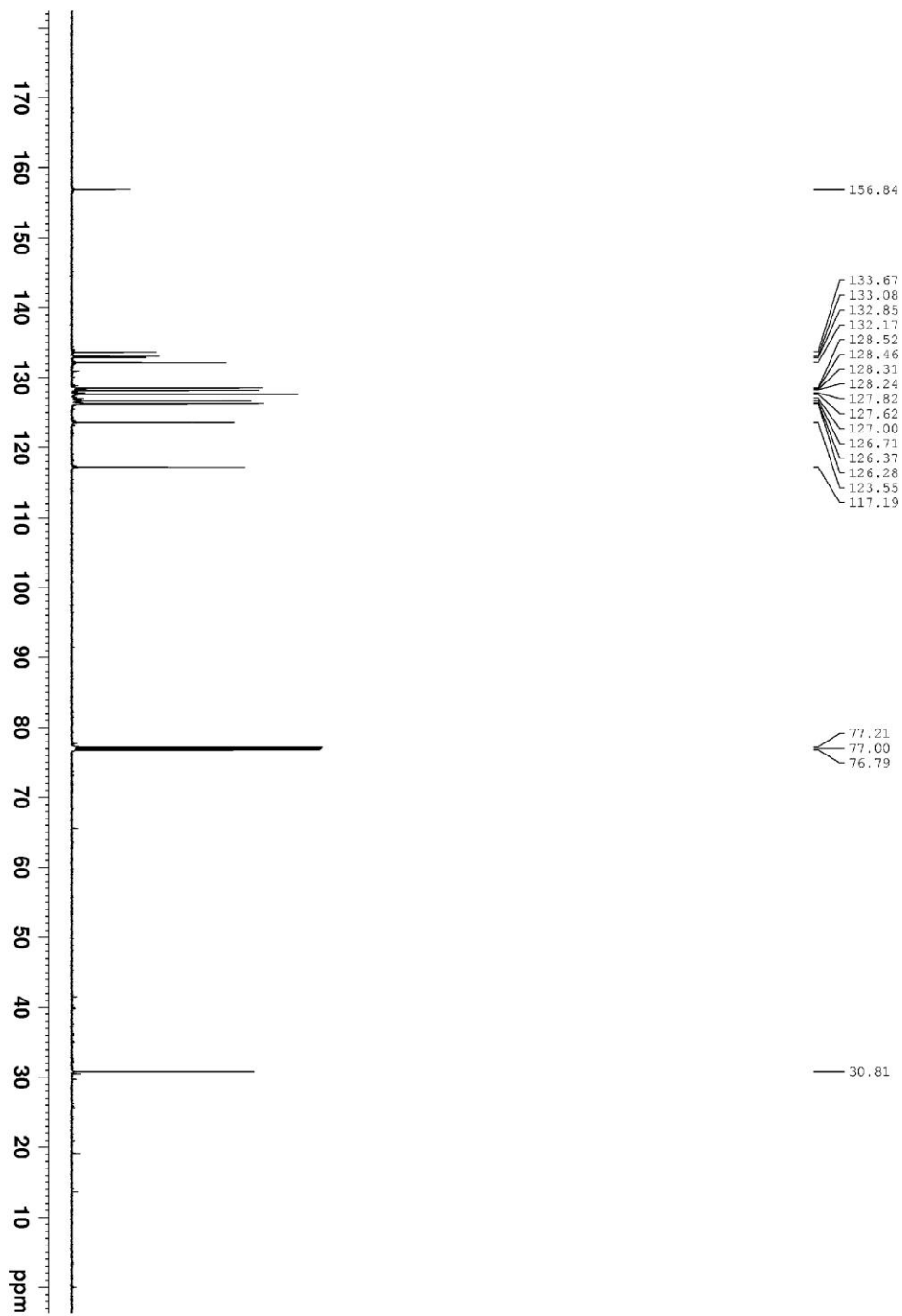


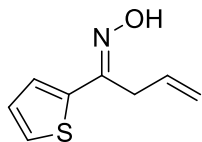




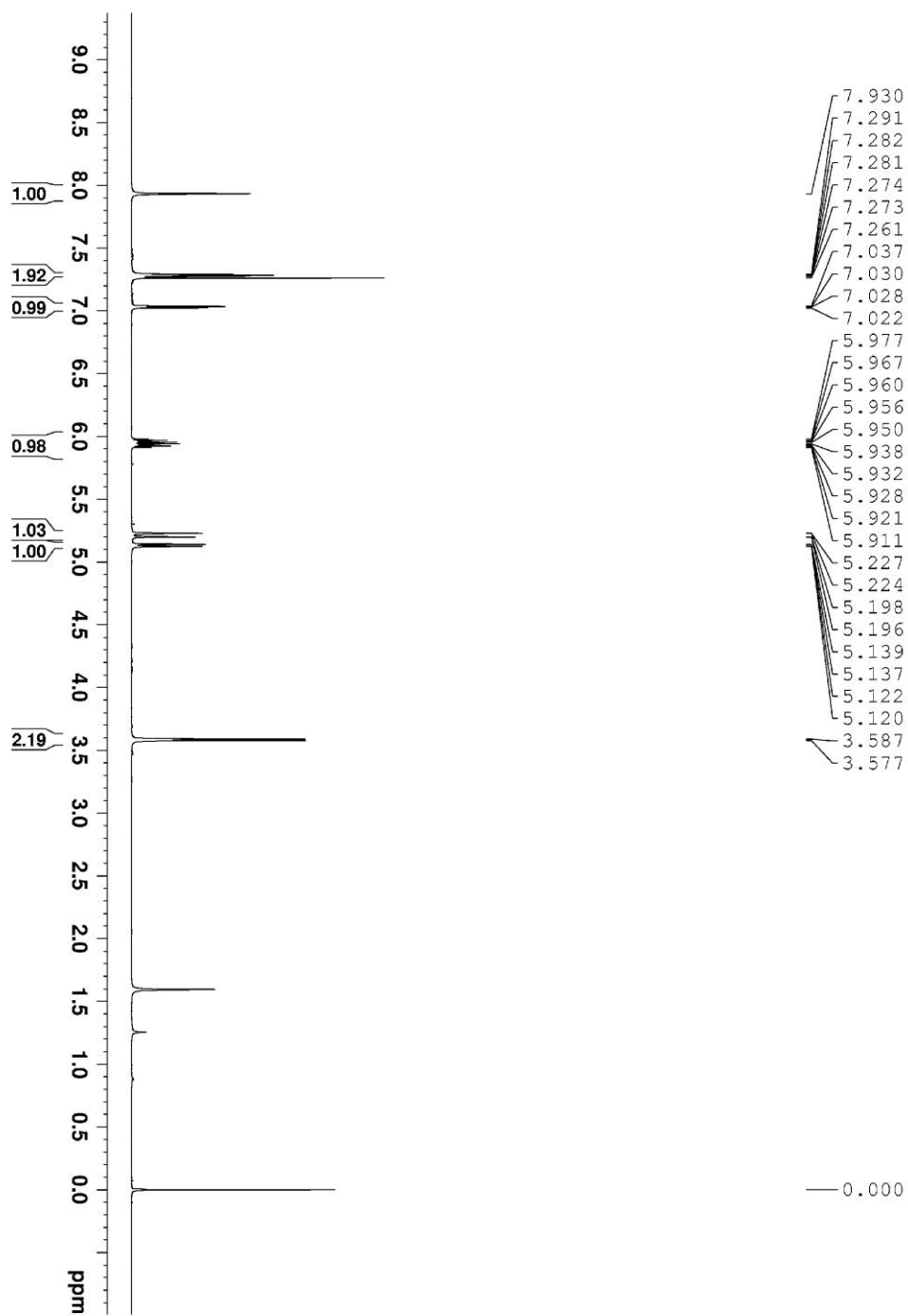


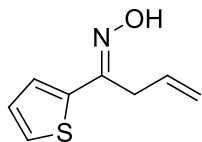
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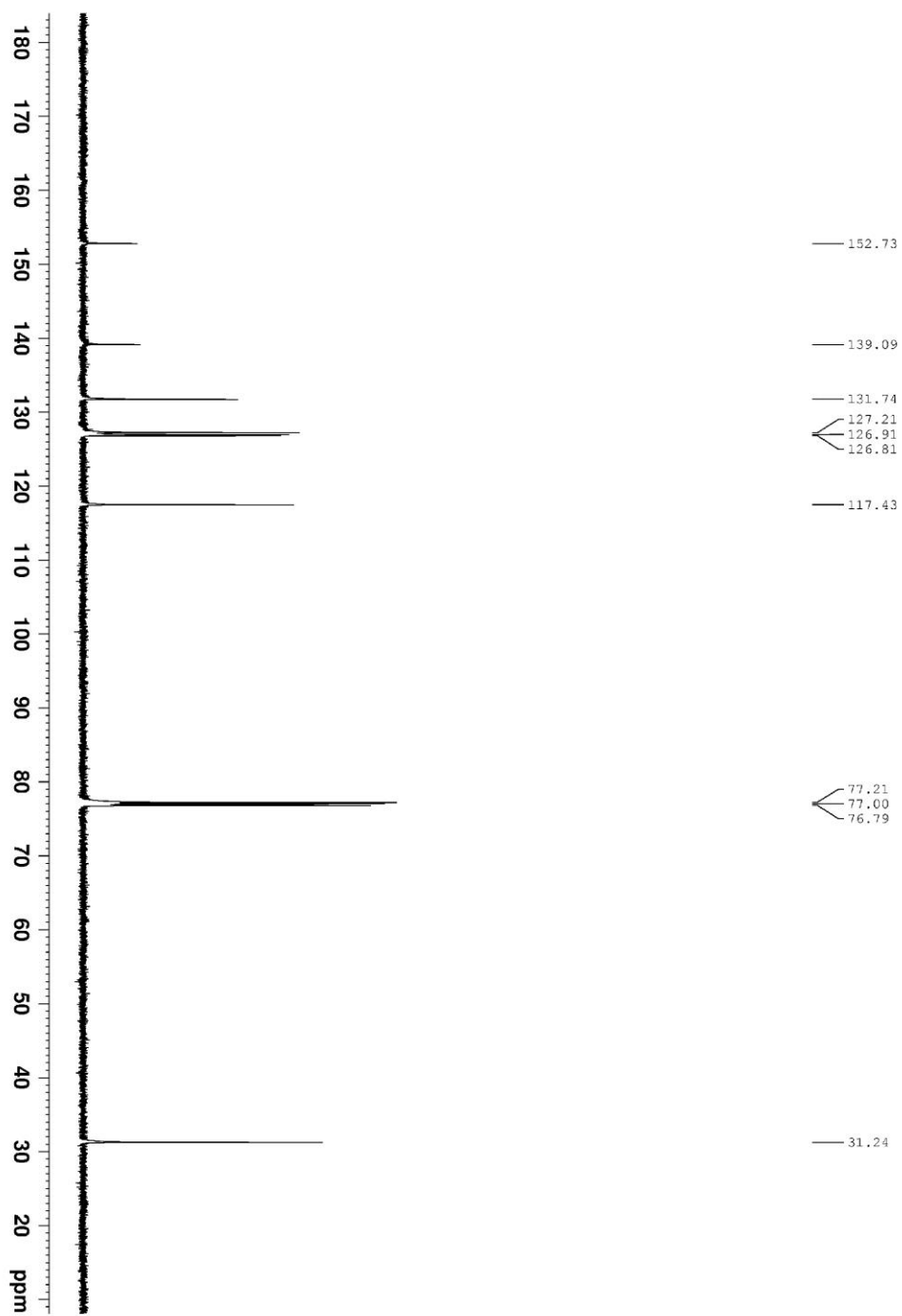


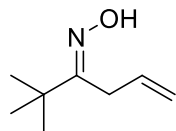
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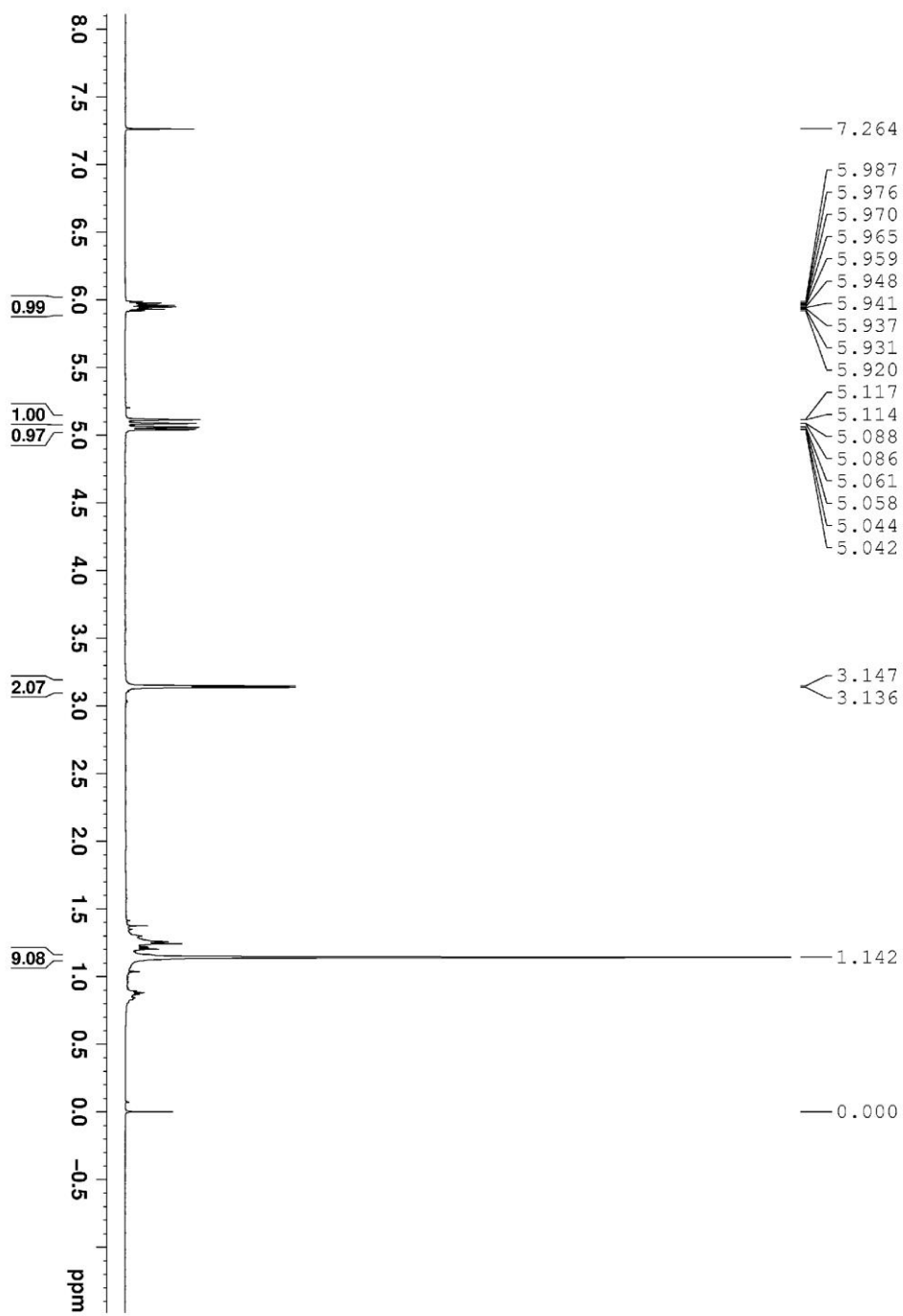


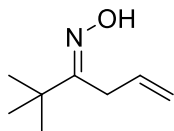
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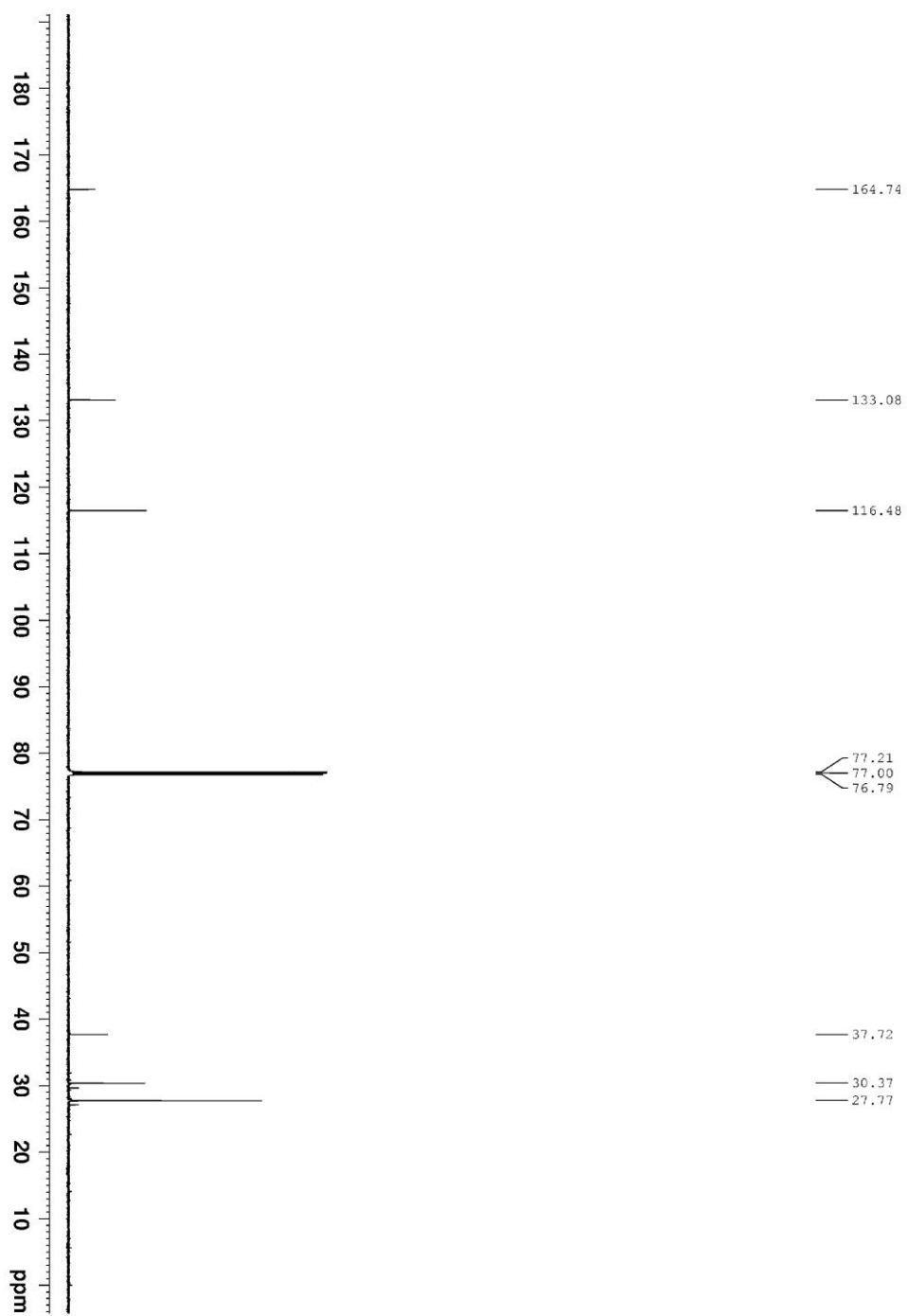


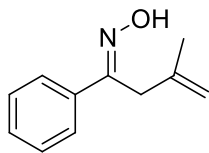
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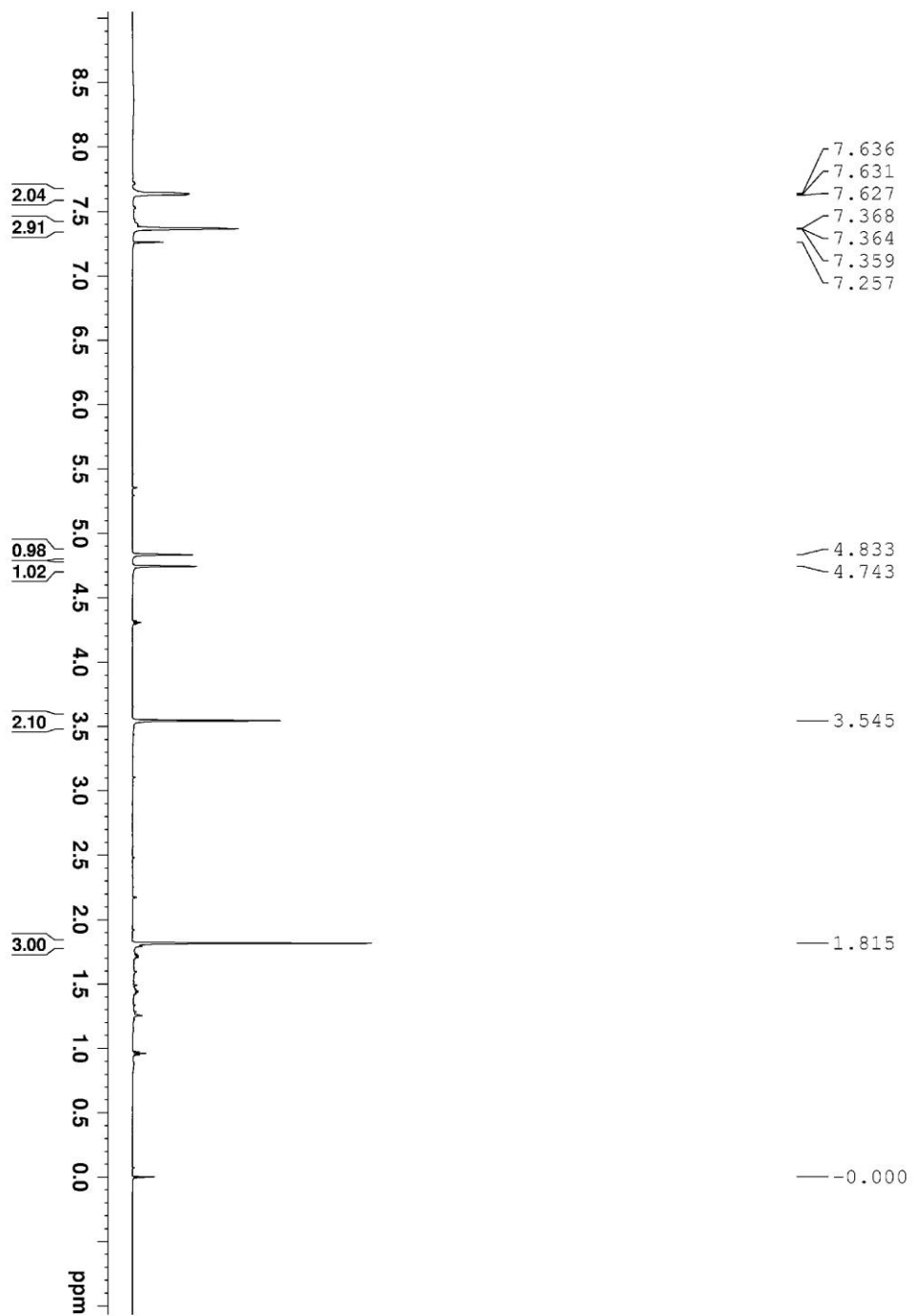


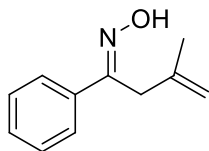
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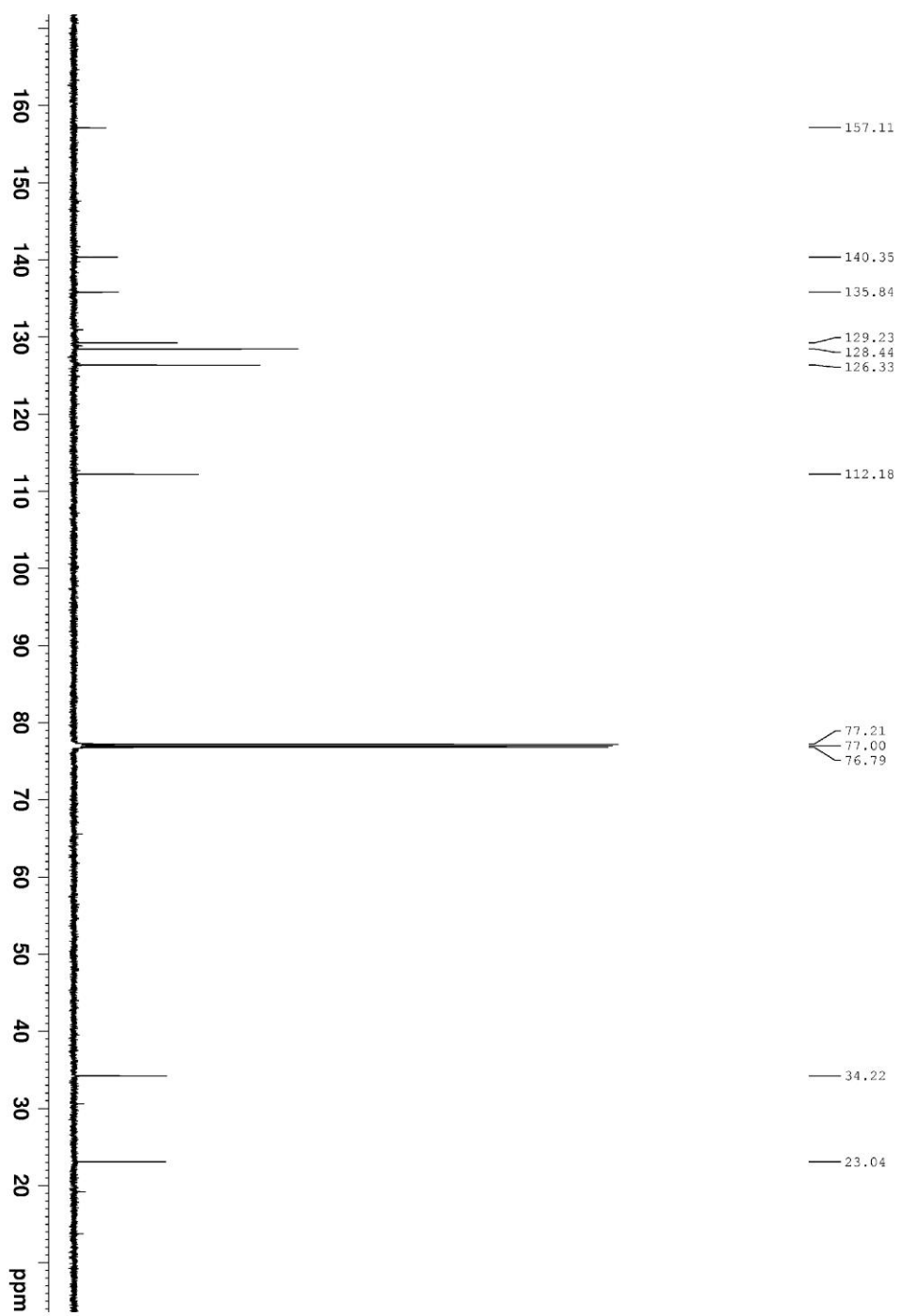


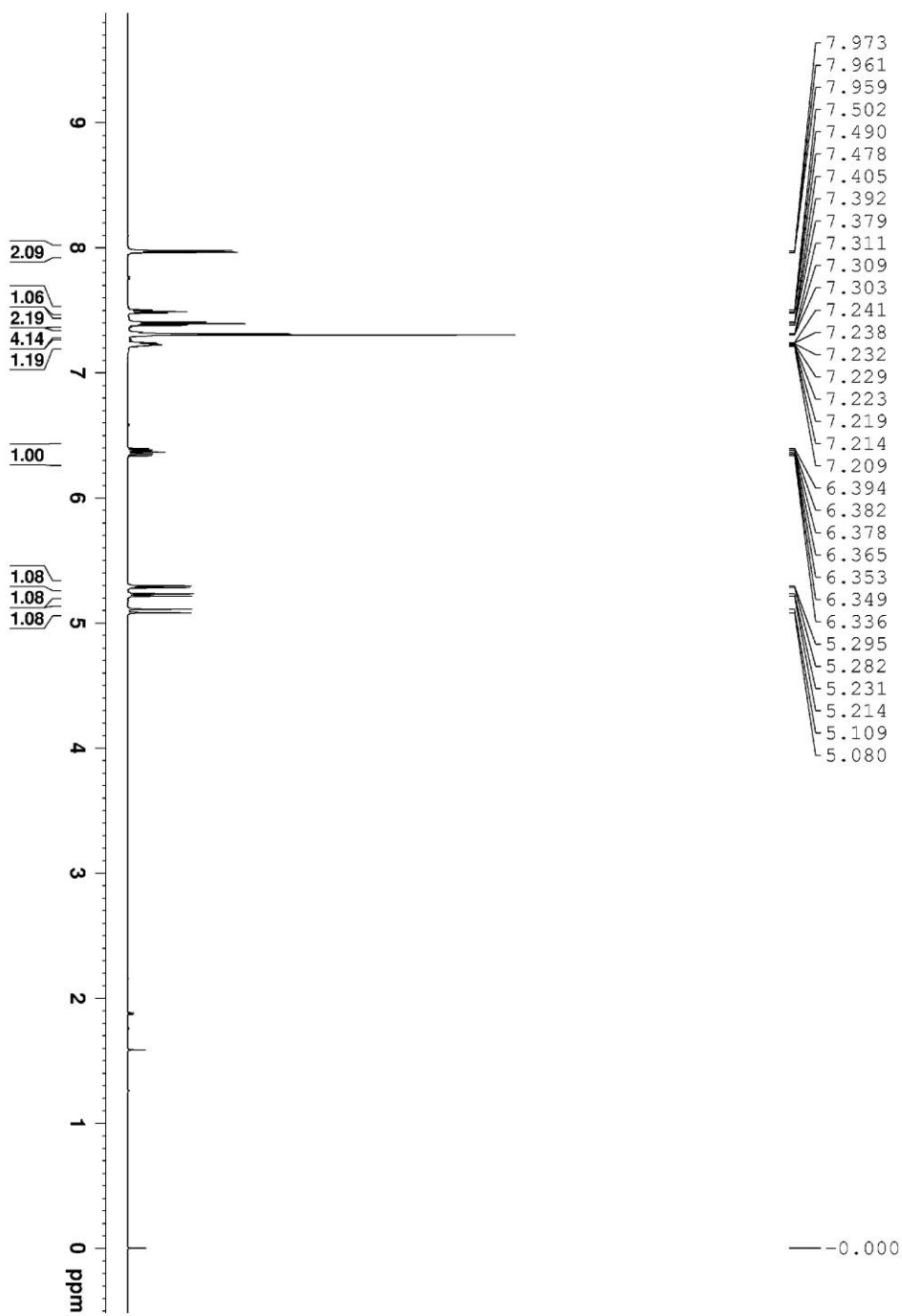
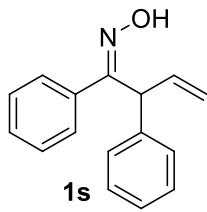
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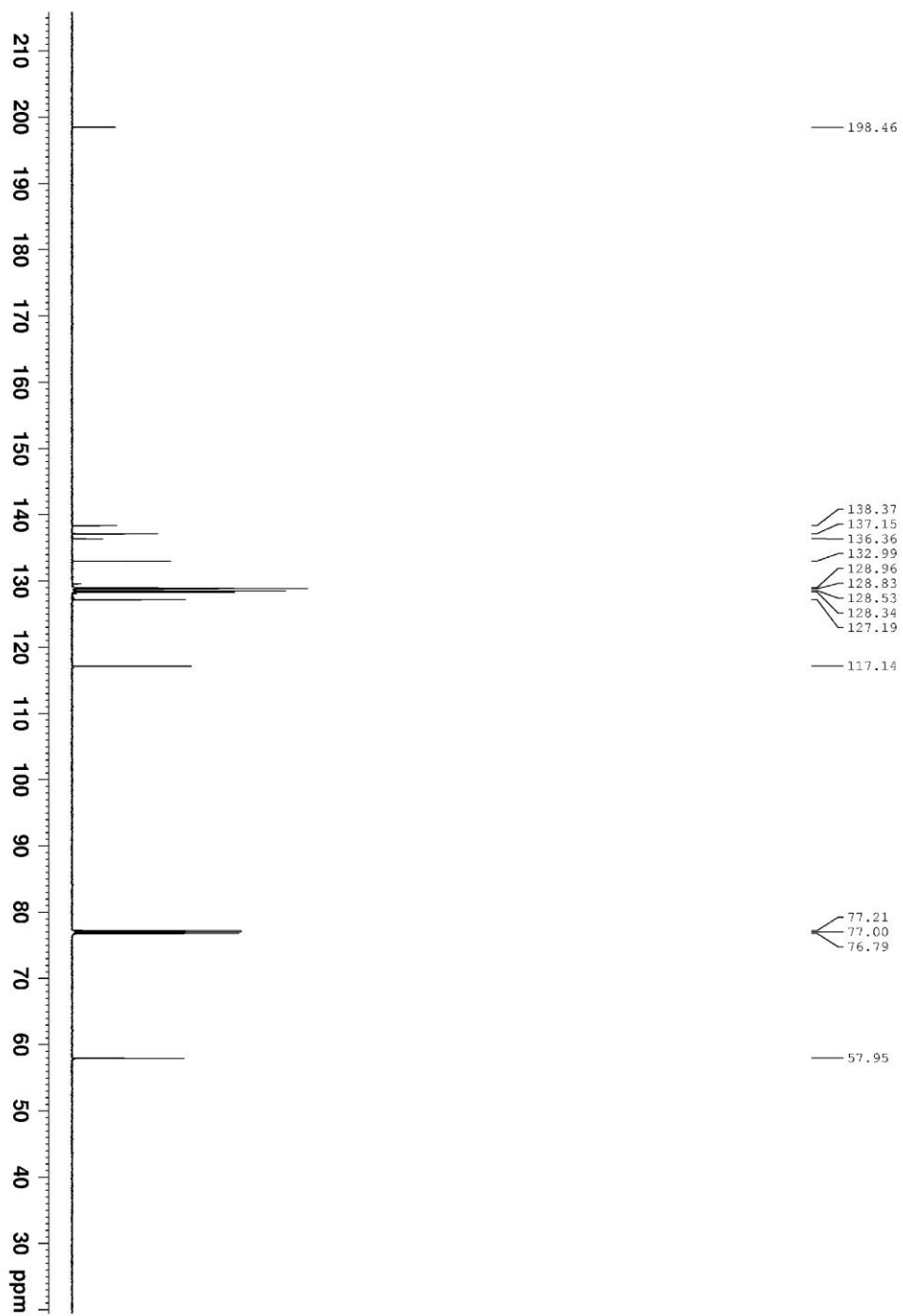
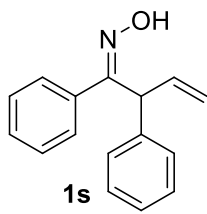


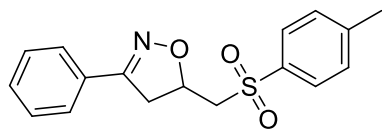


1r

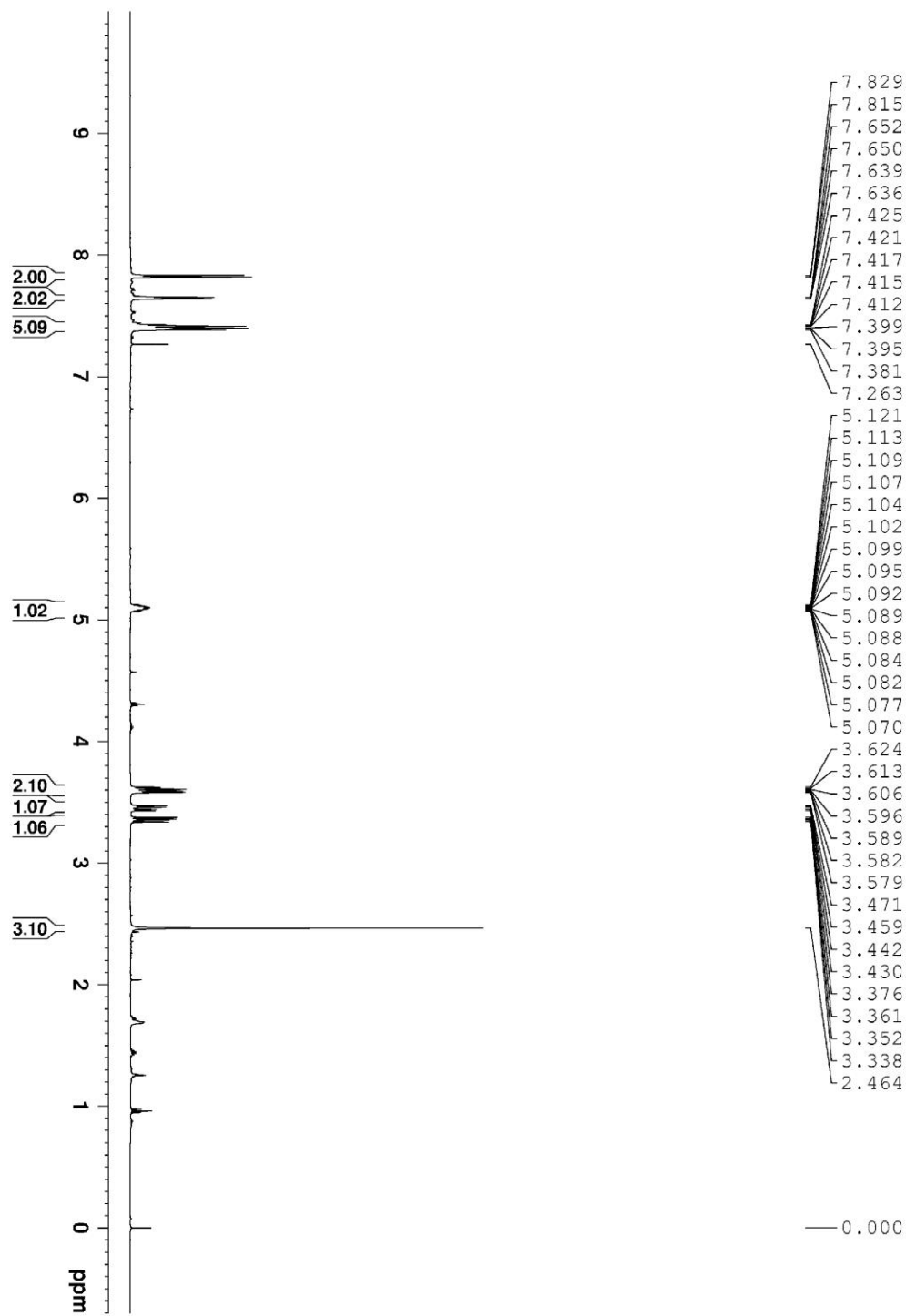


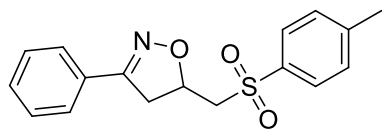




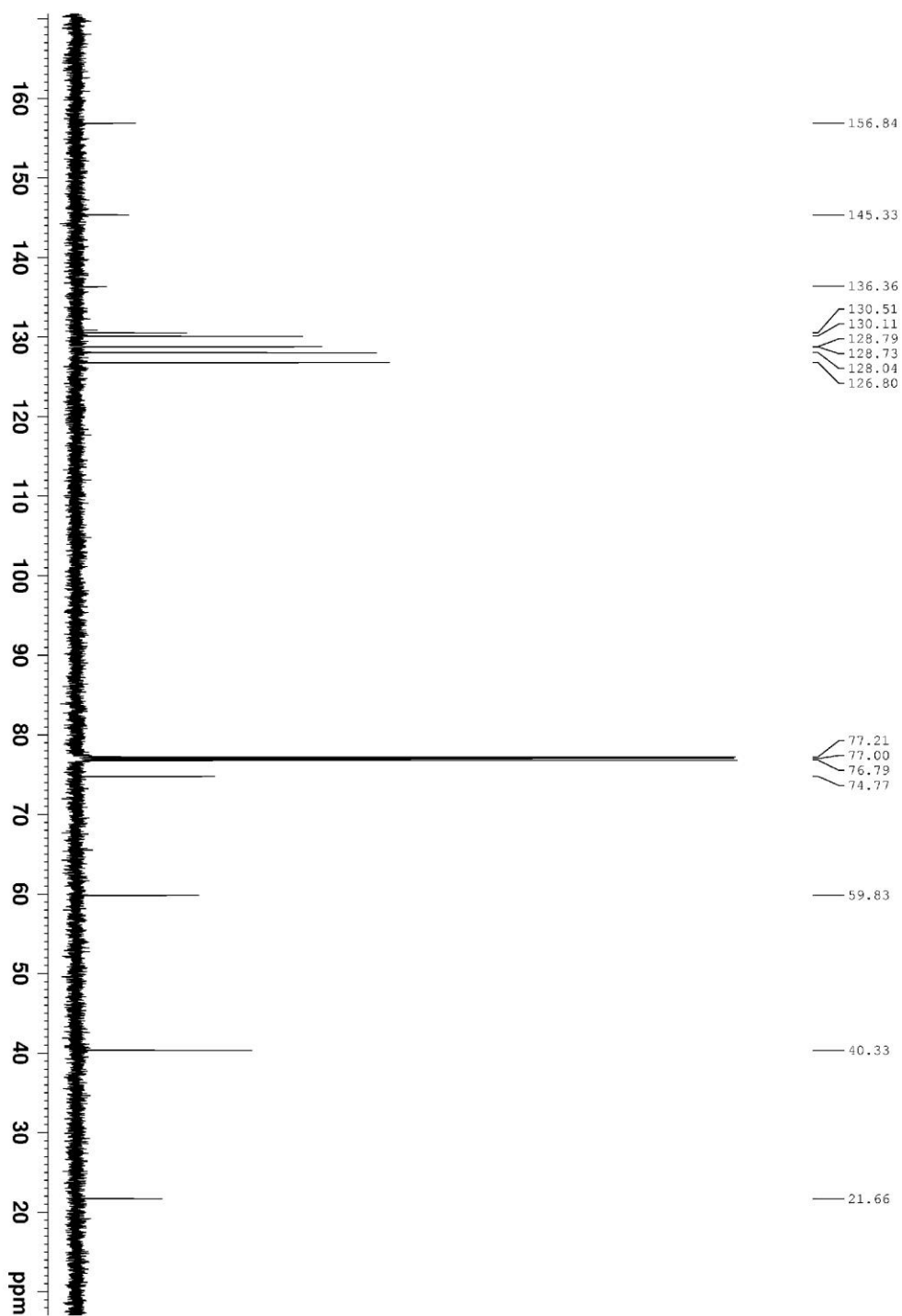


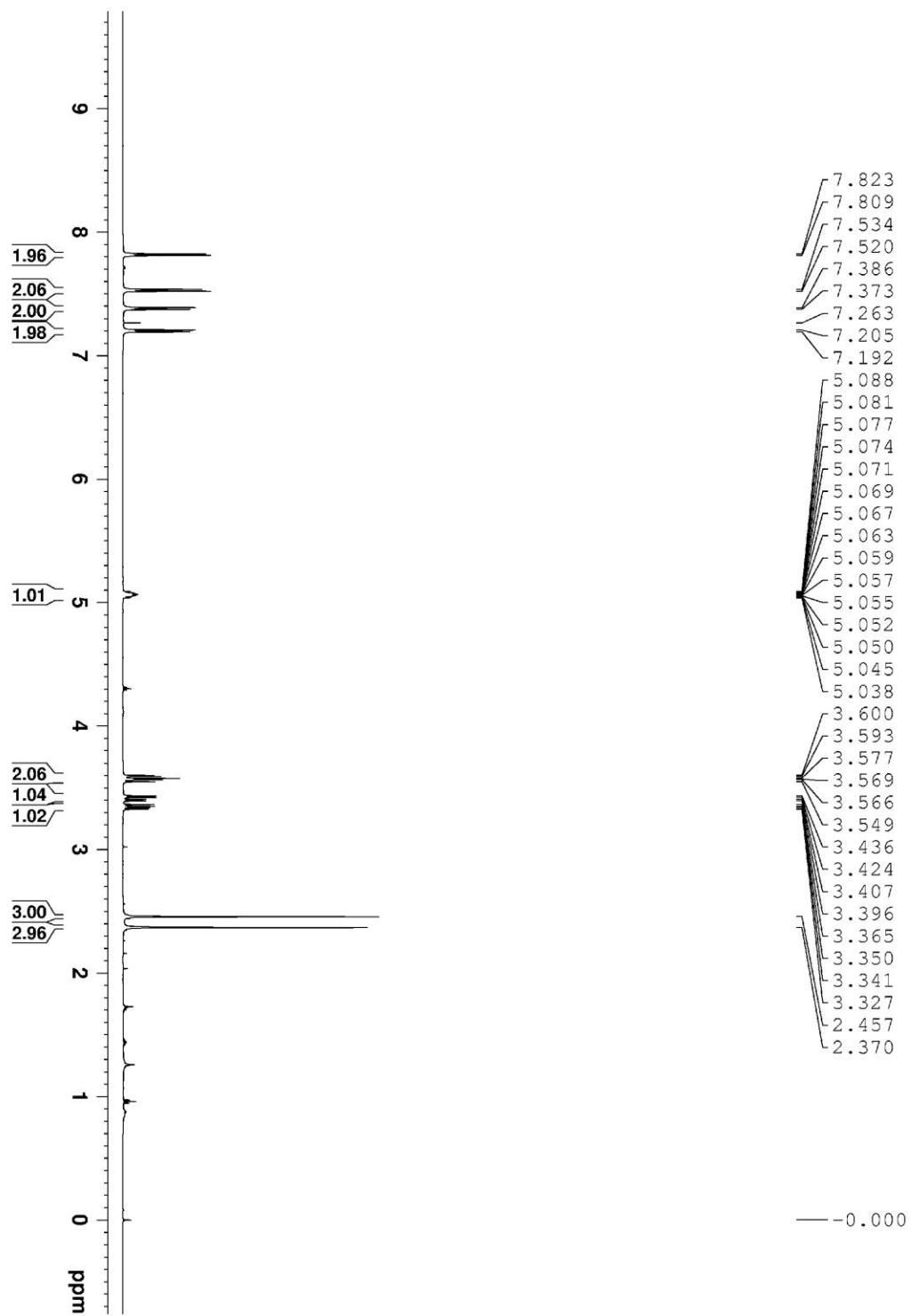
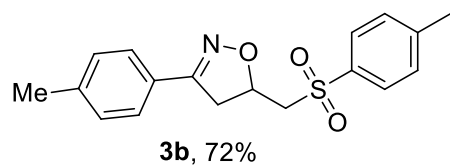
3a, 80%

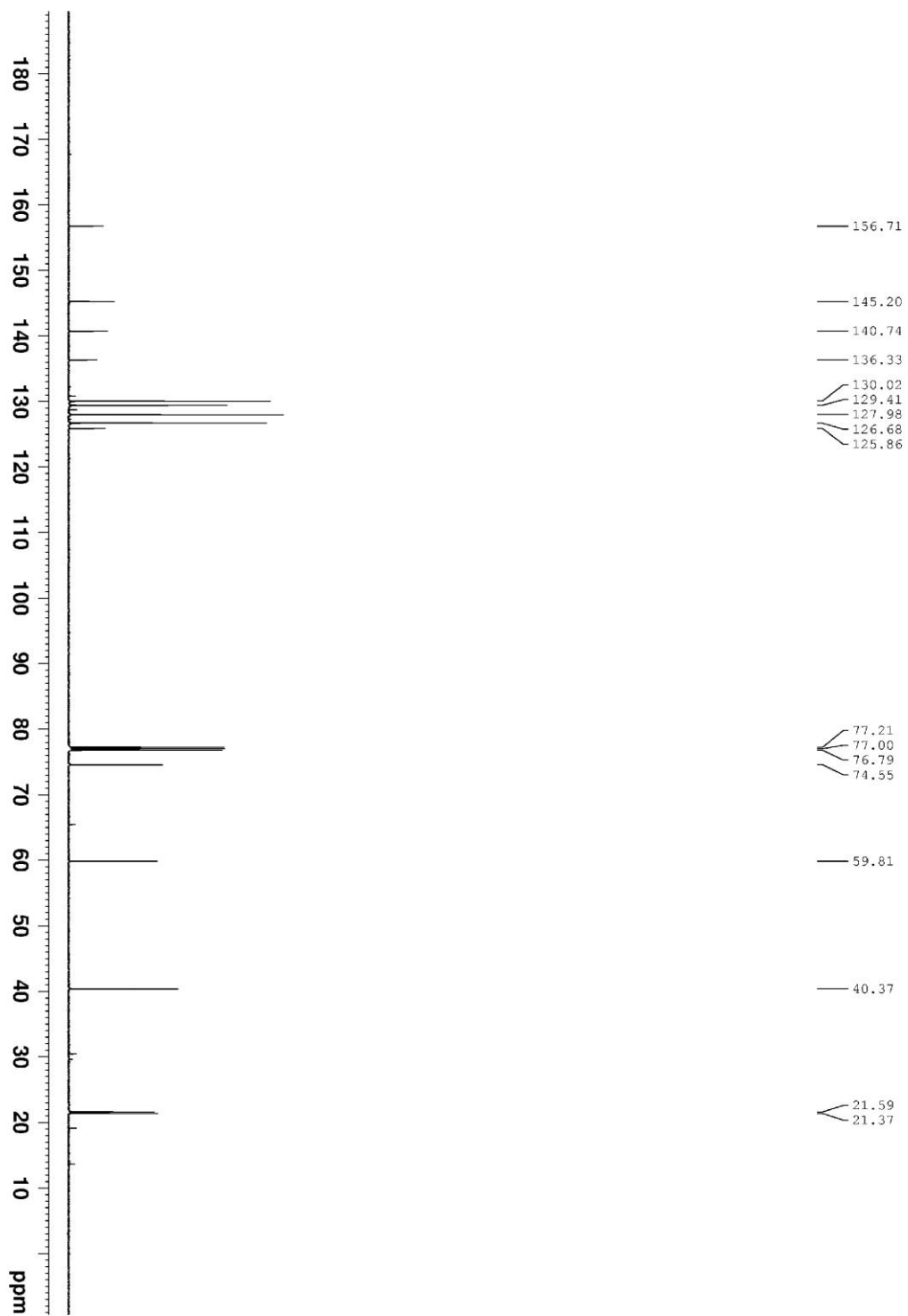
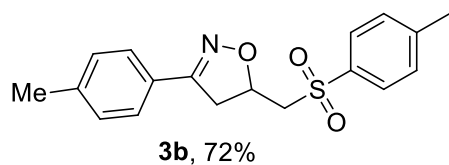


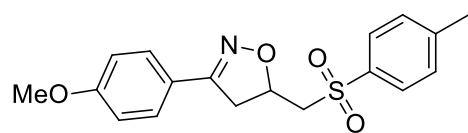


3a, 80%

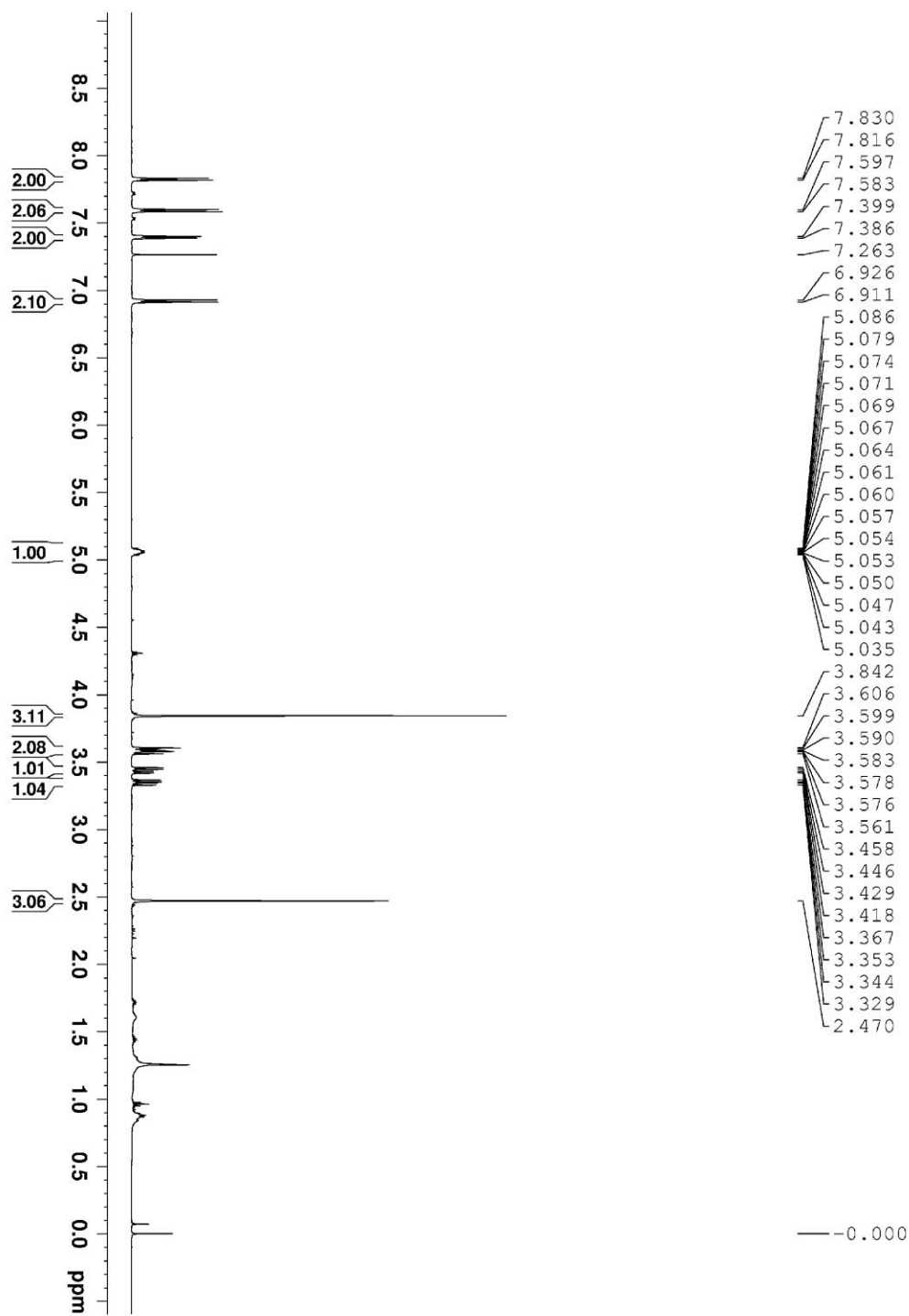


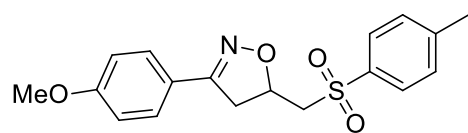




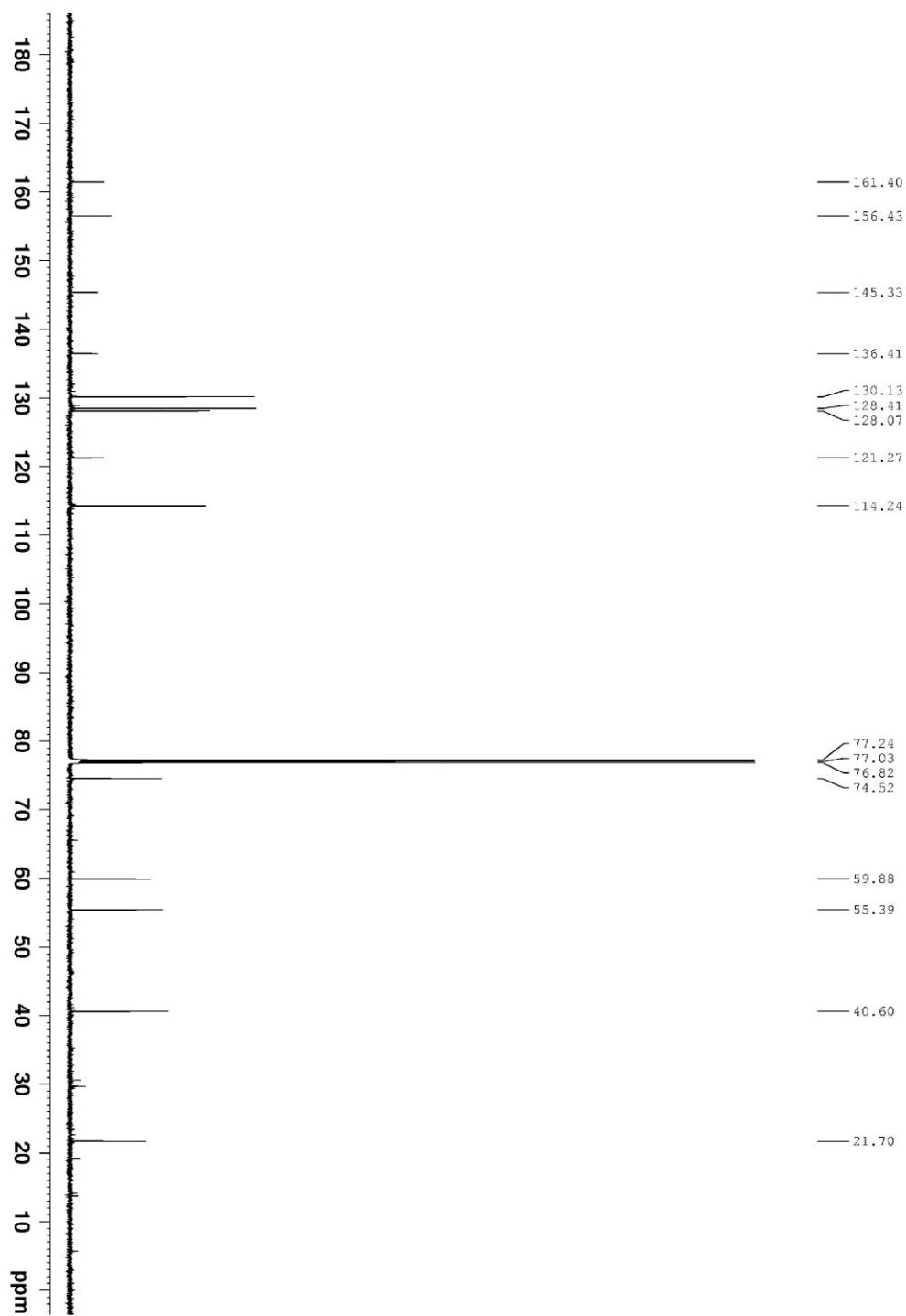


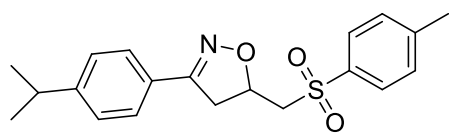
3c, 25%



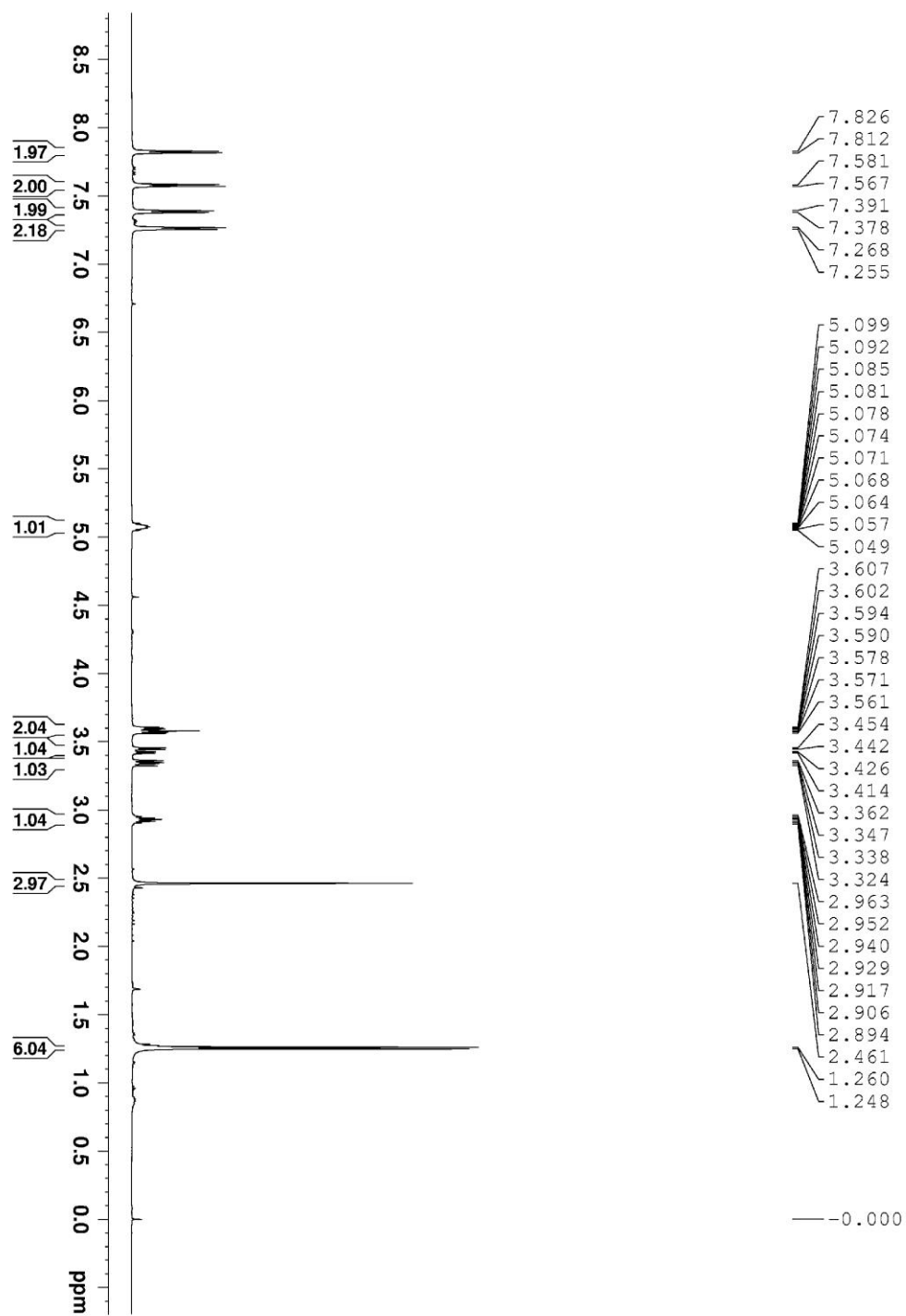


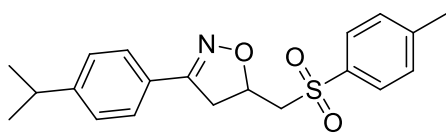
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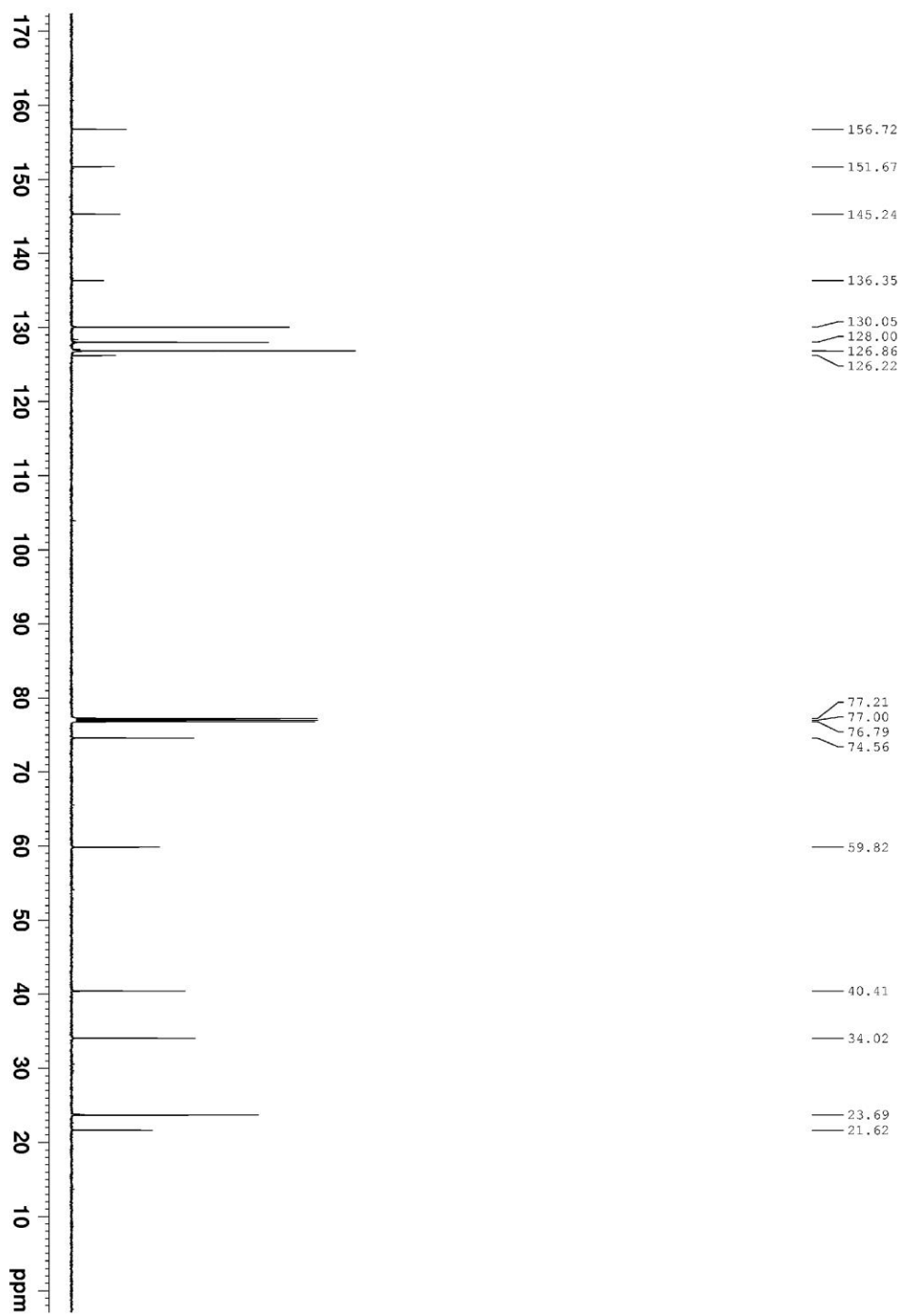


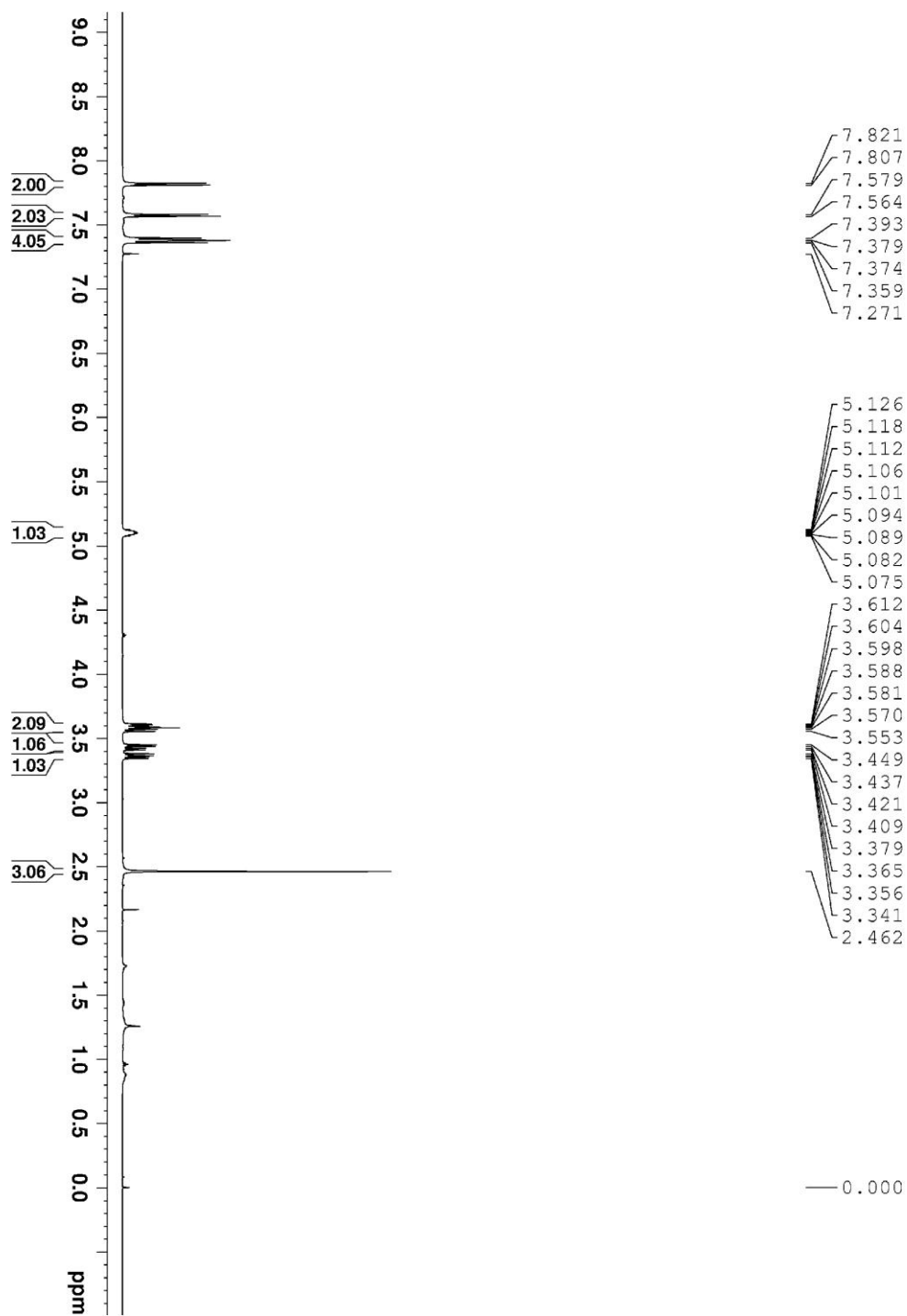
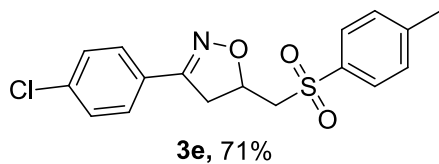
3d, 73%

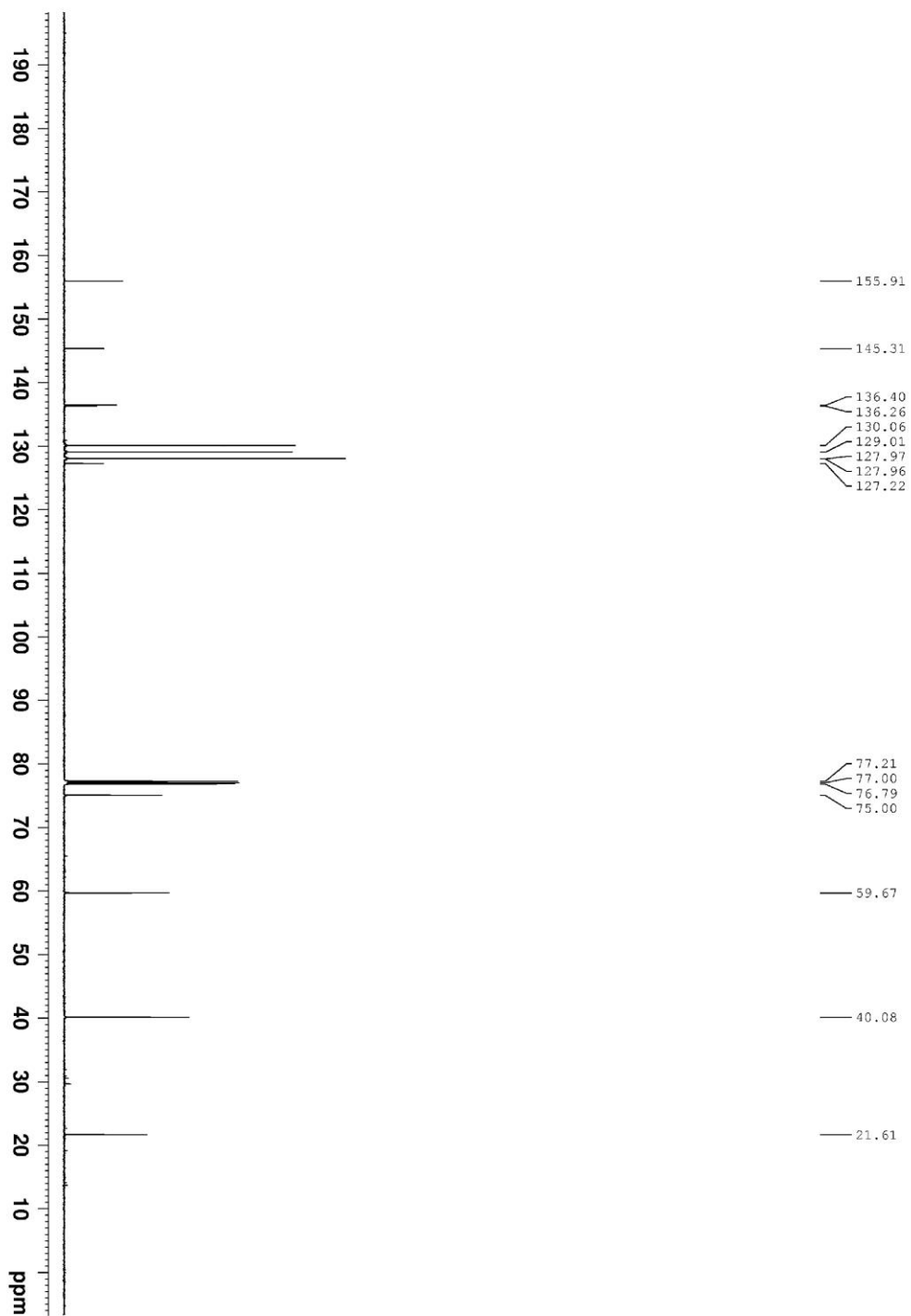
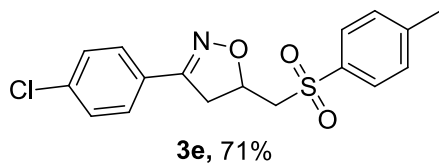


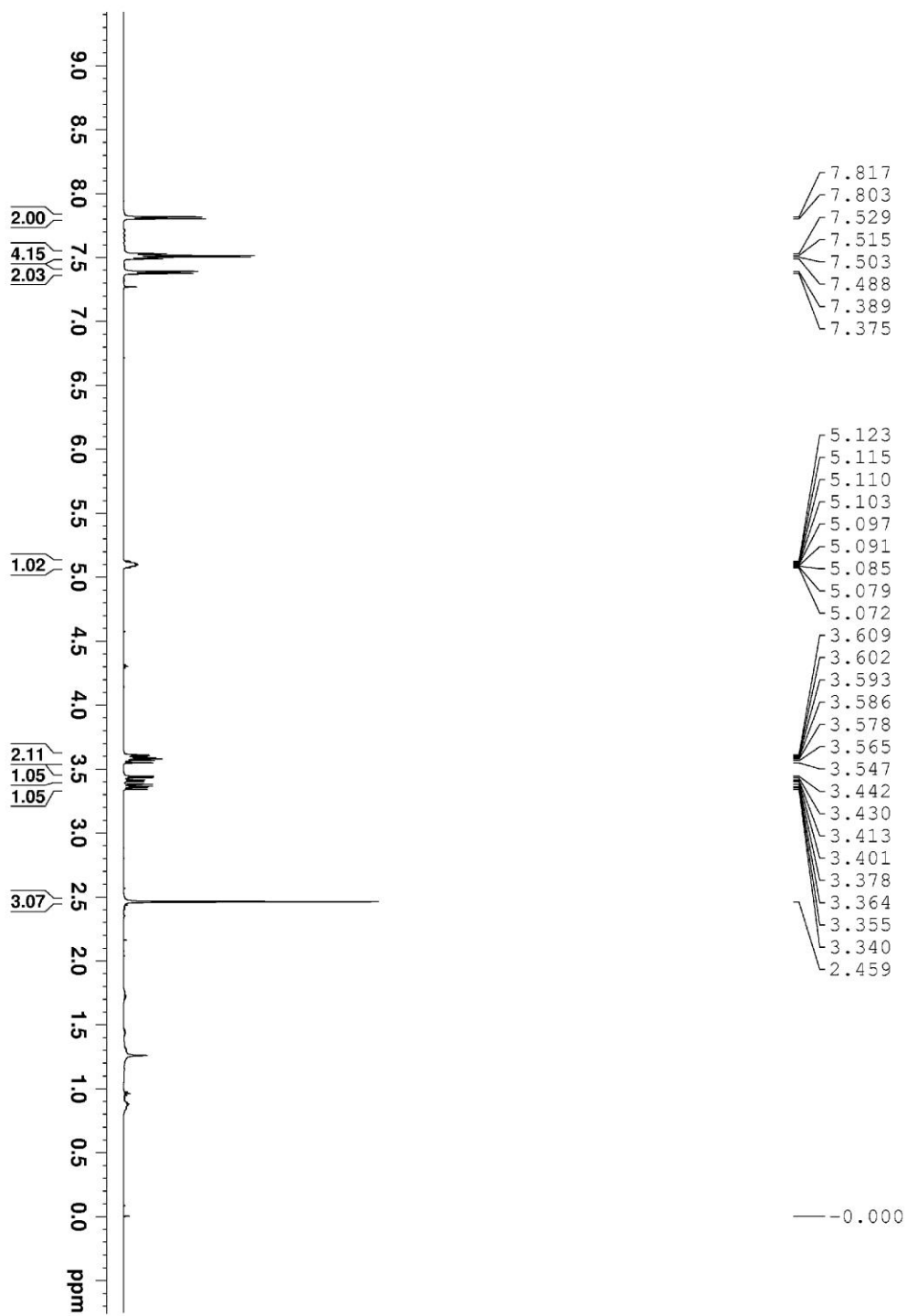
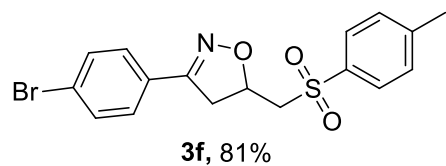


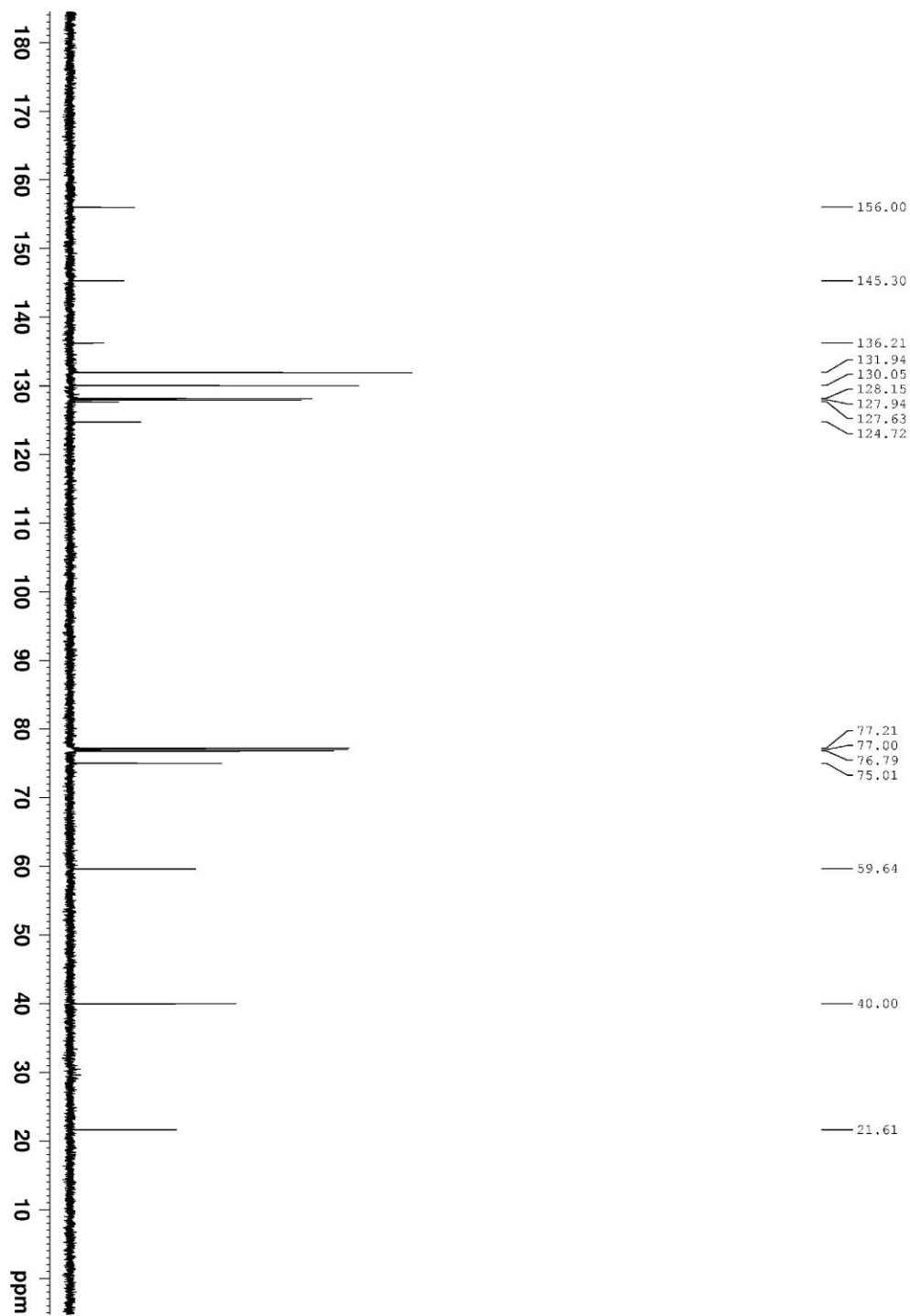
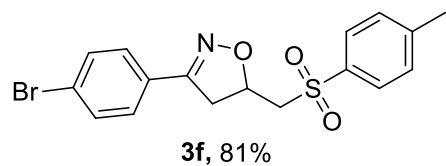
3d, 73%

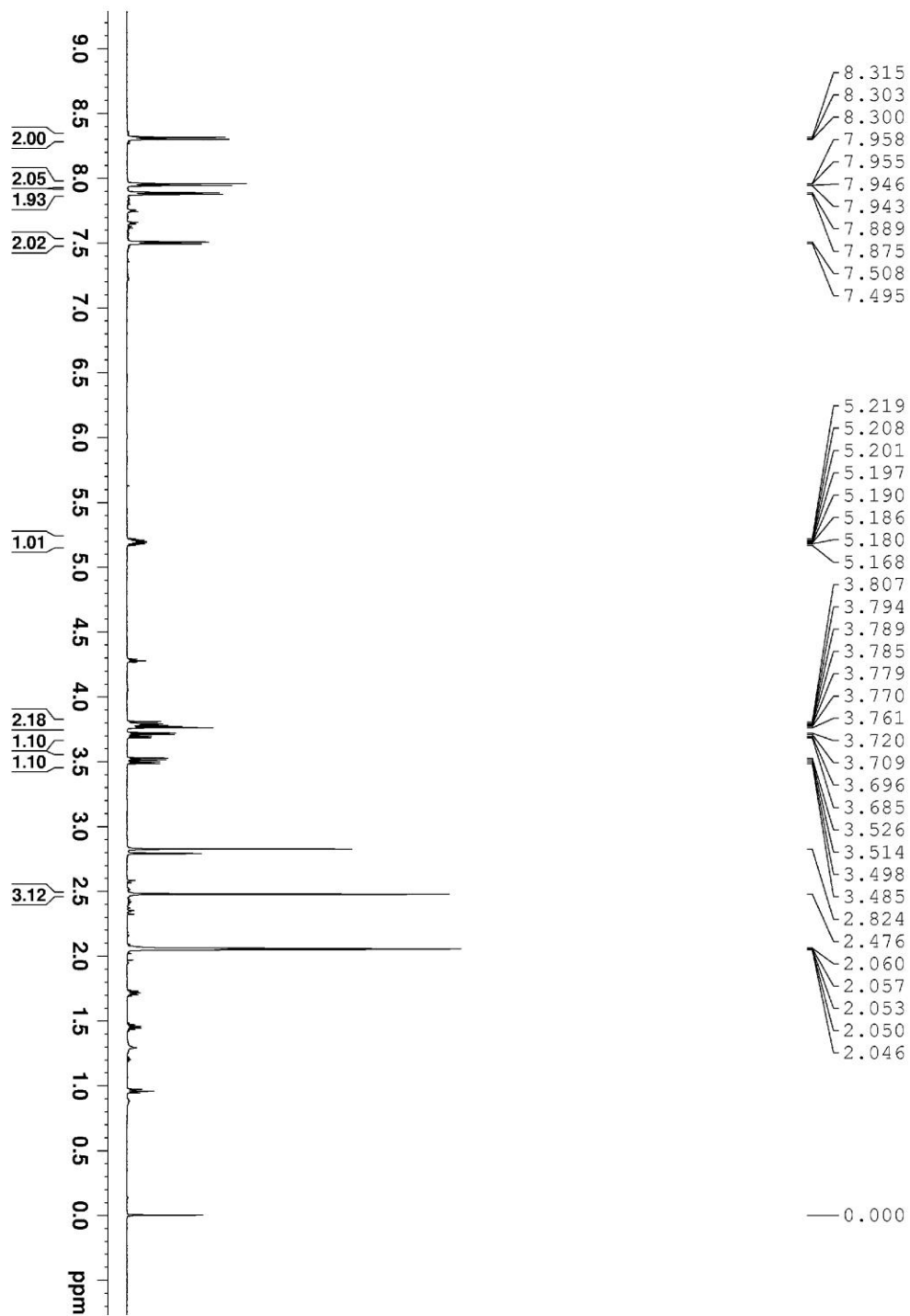
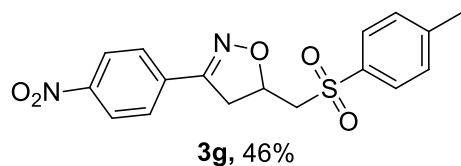


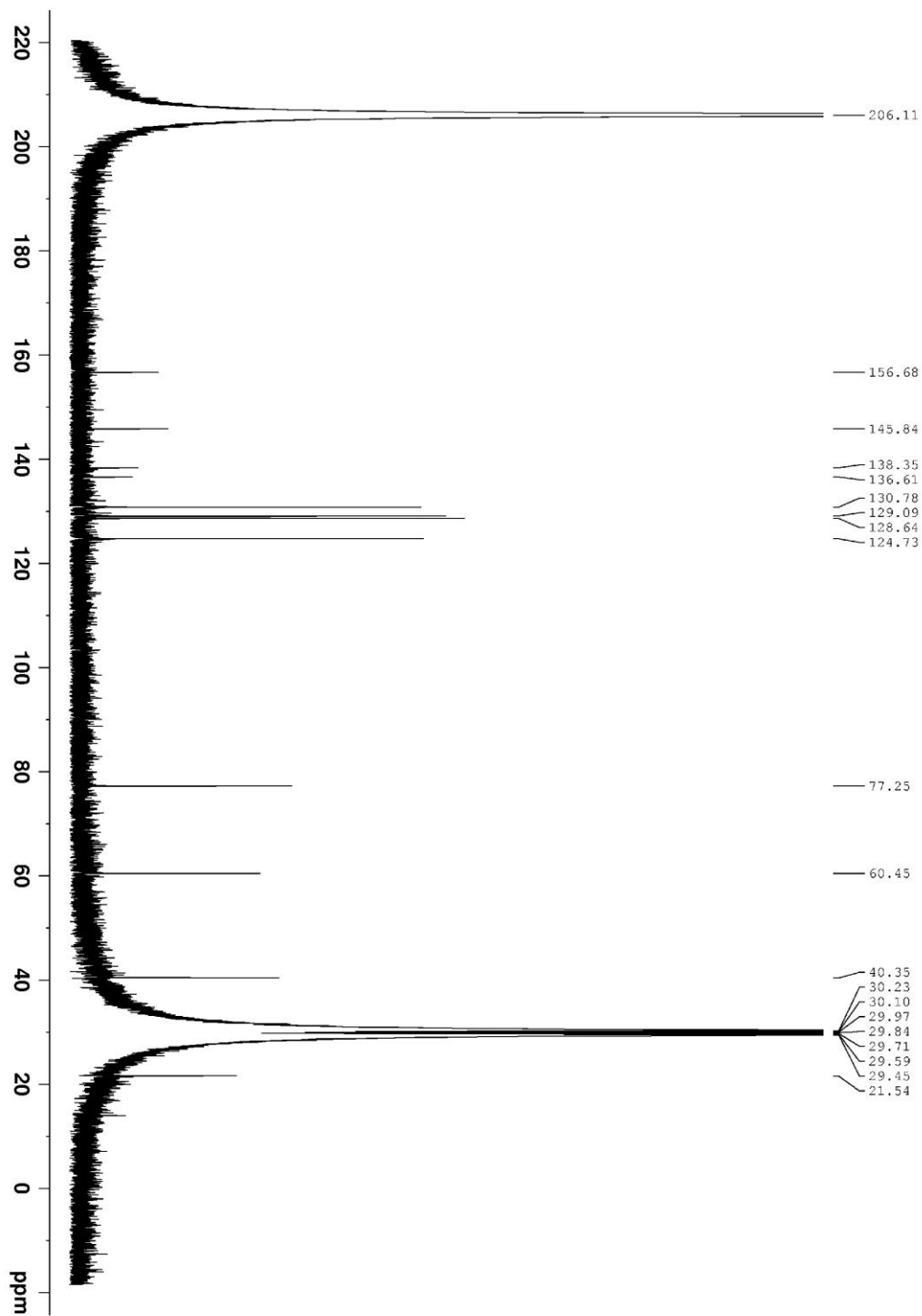
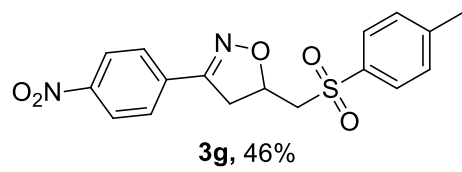


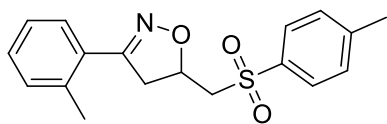




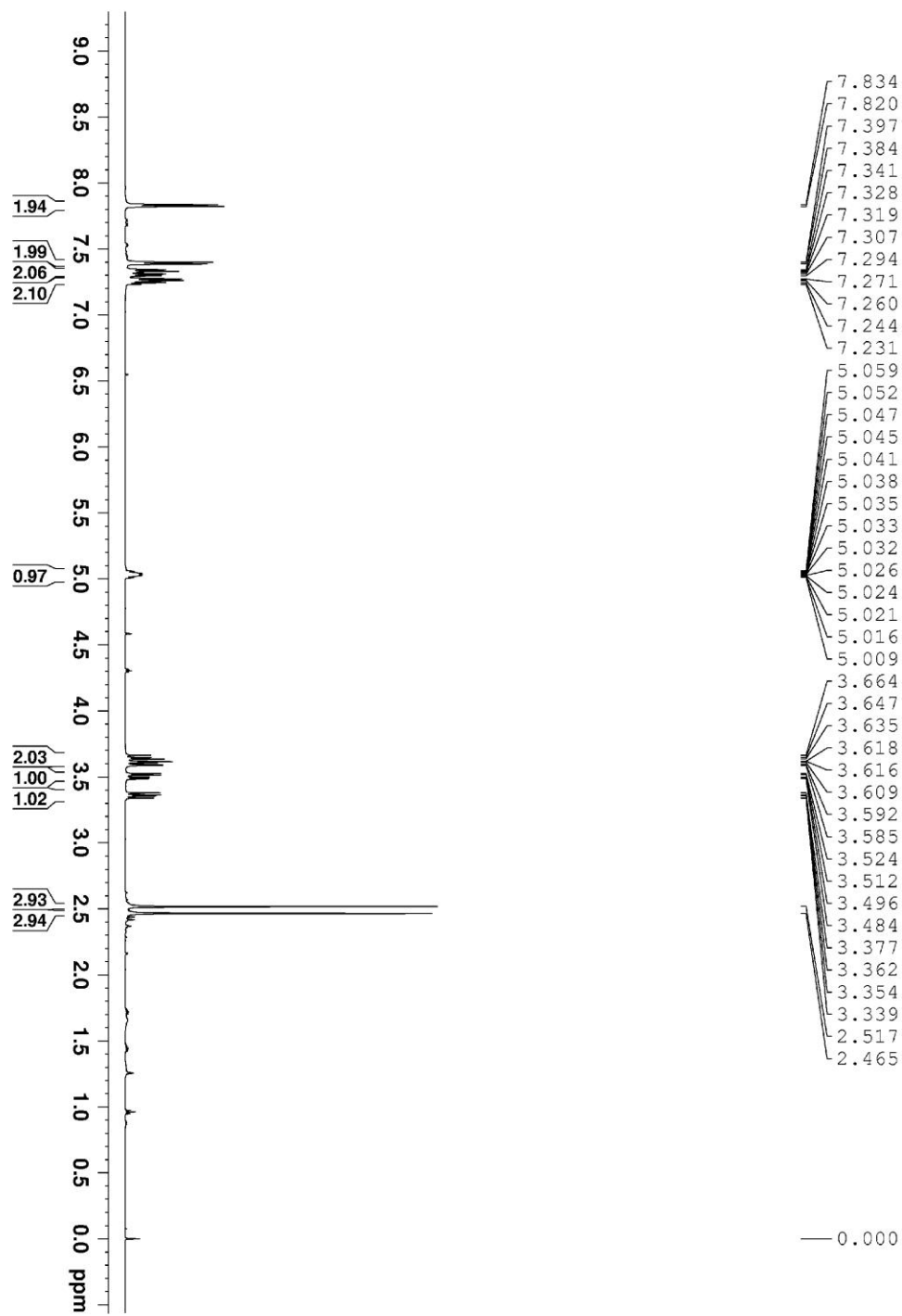


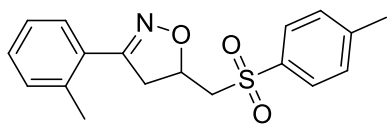




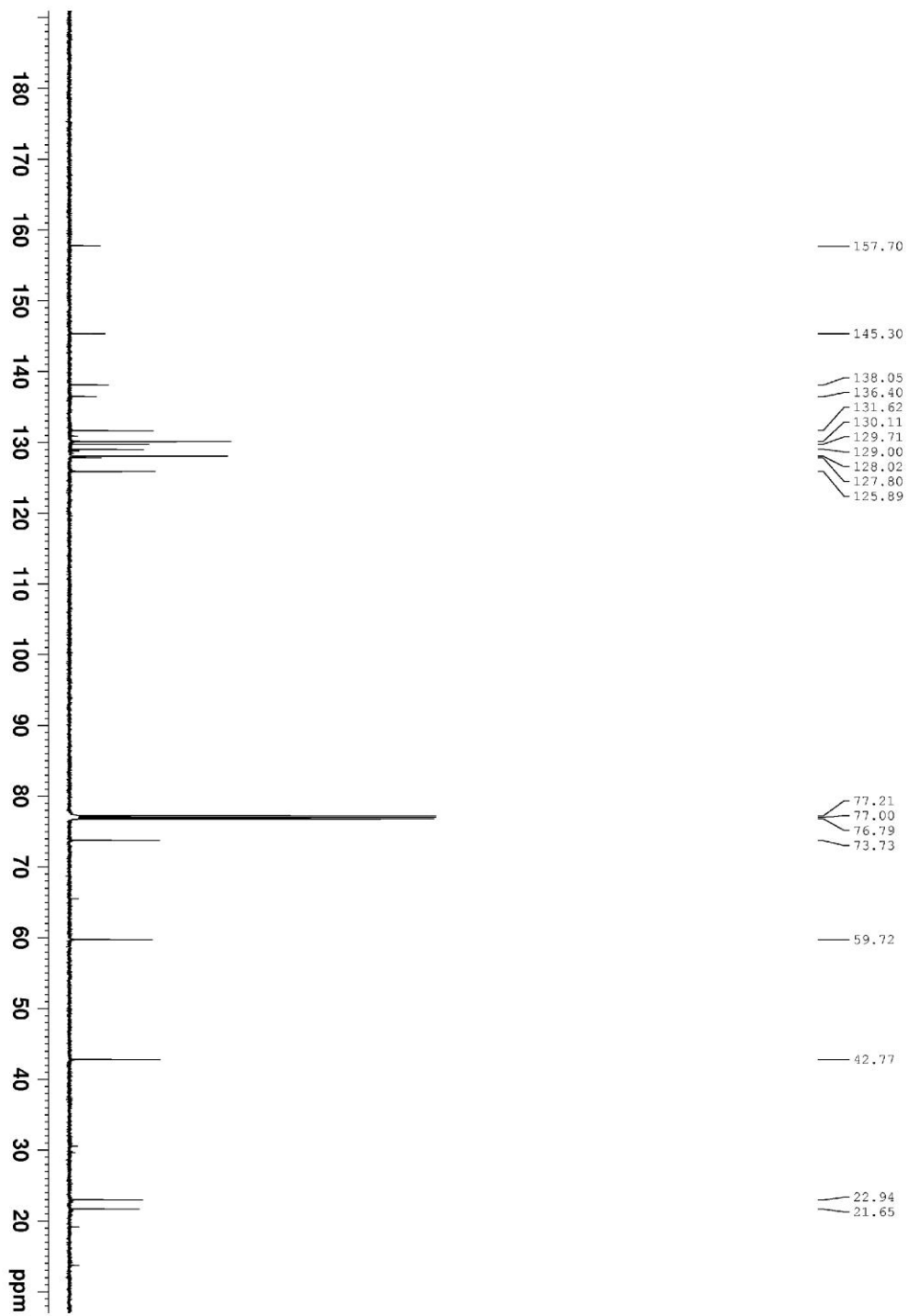


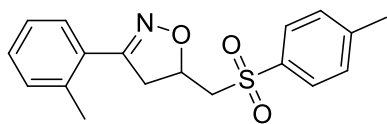
3h, 37%



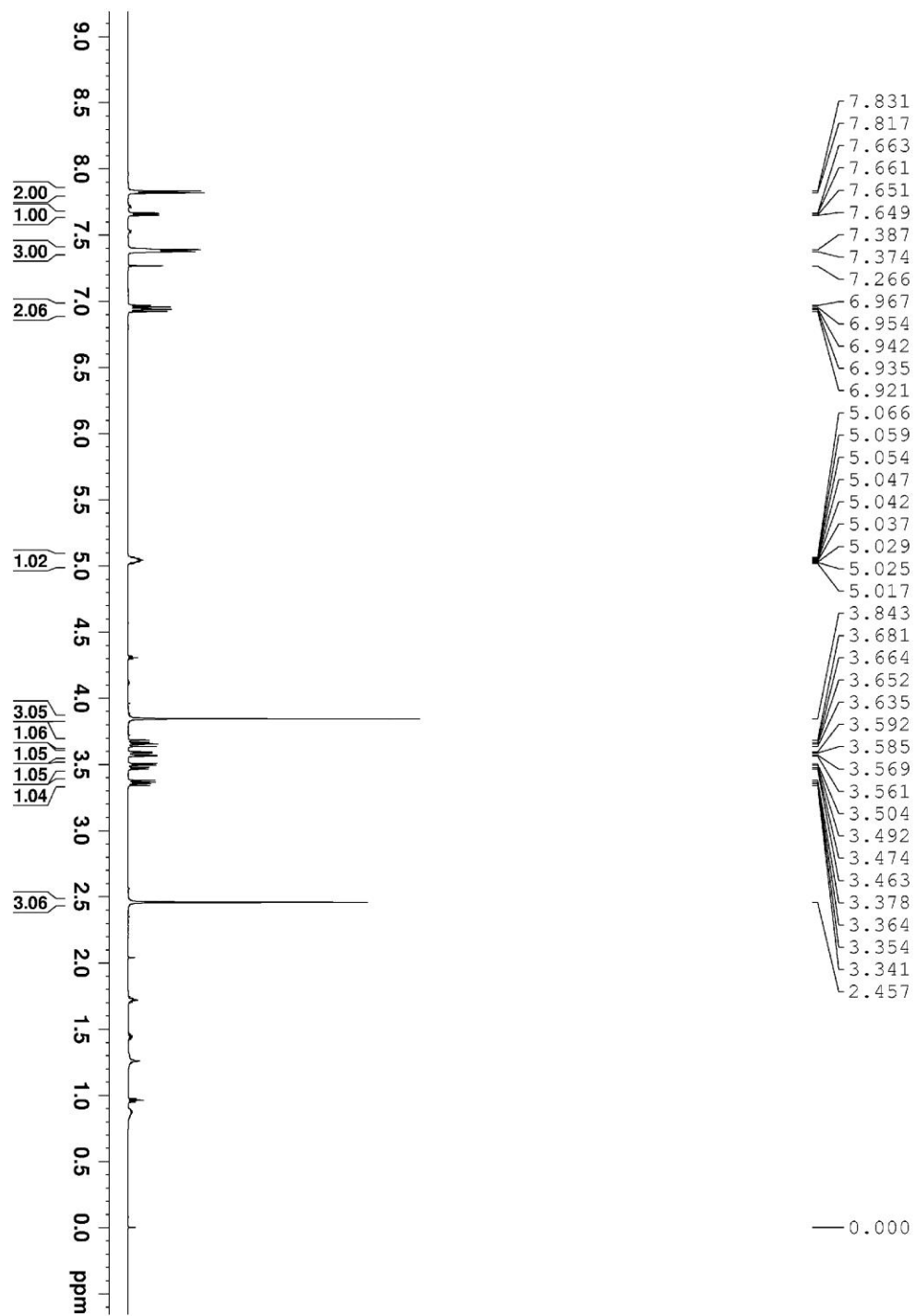


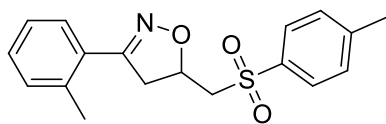
3h, 37%



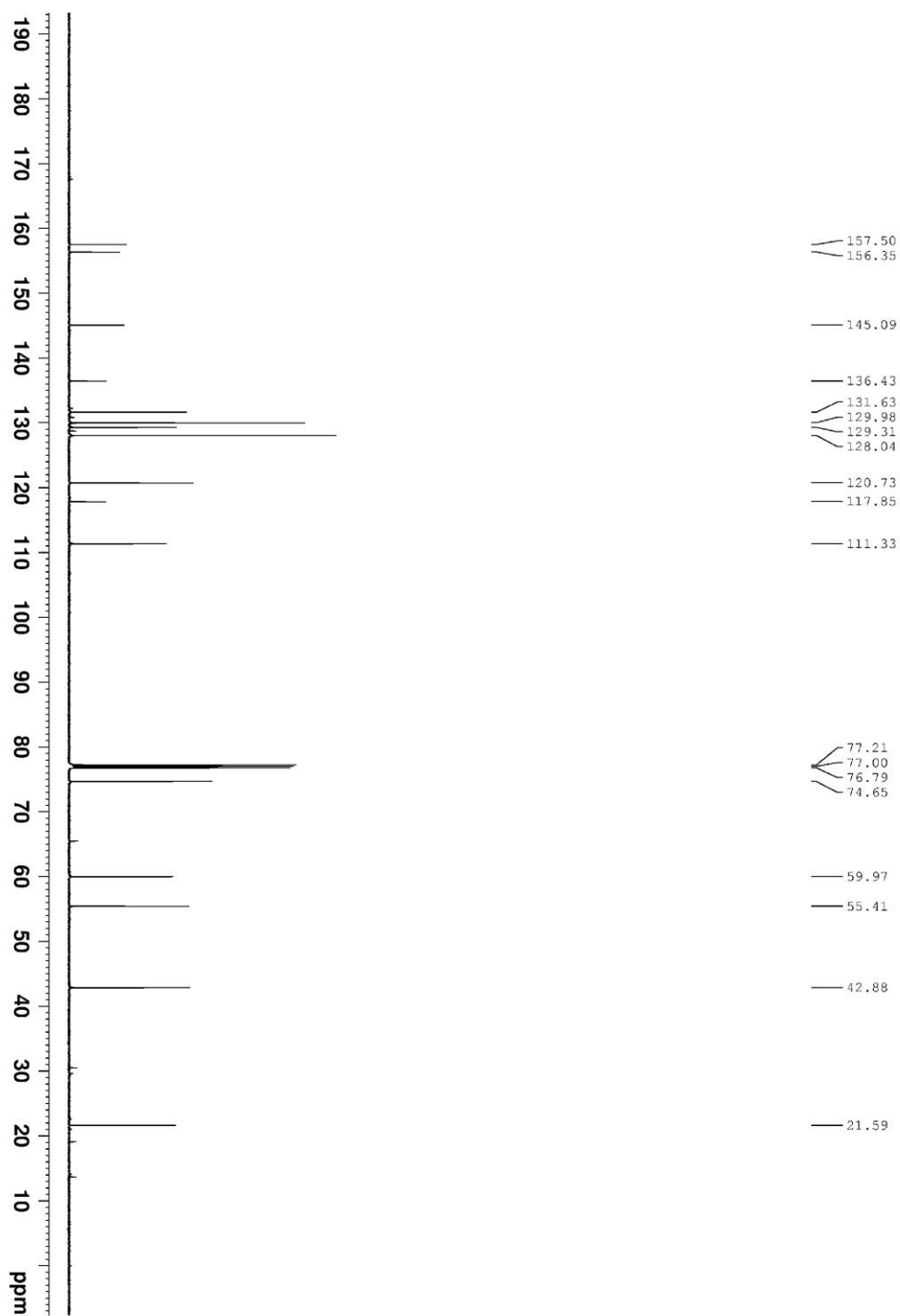


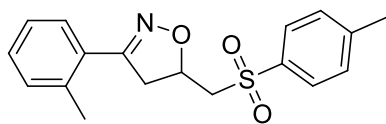
3i, 69%



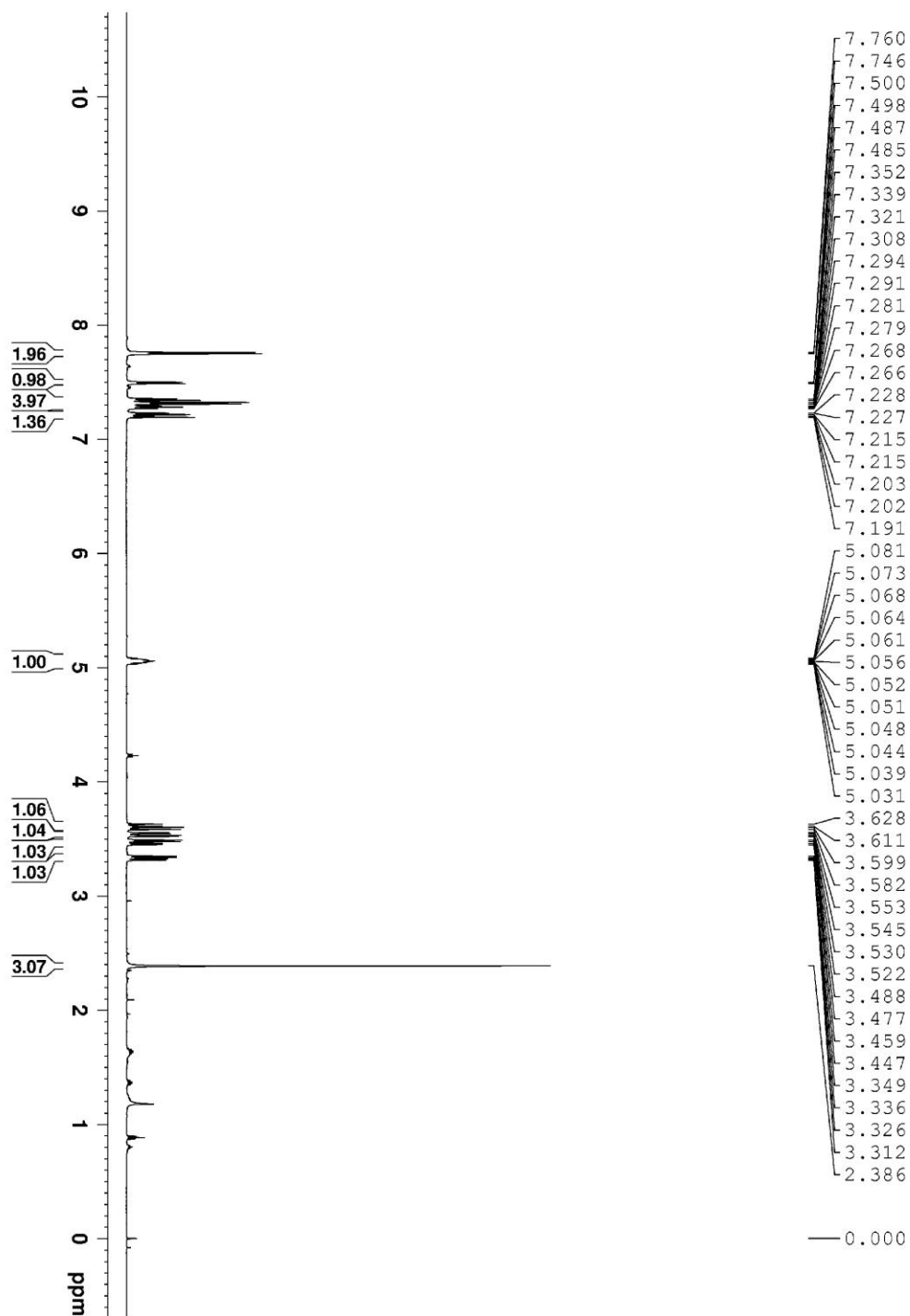


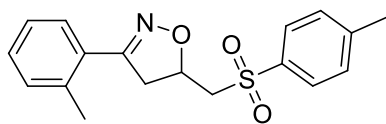
3i, 69%



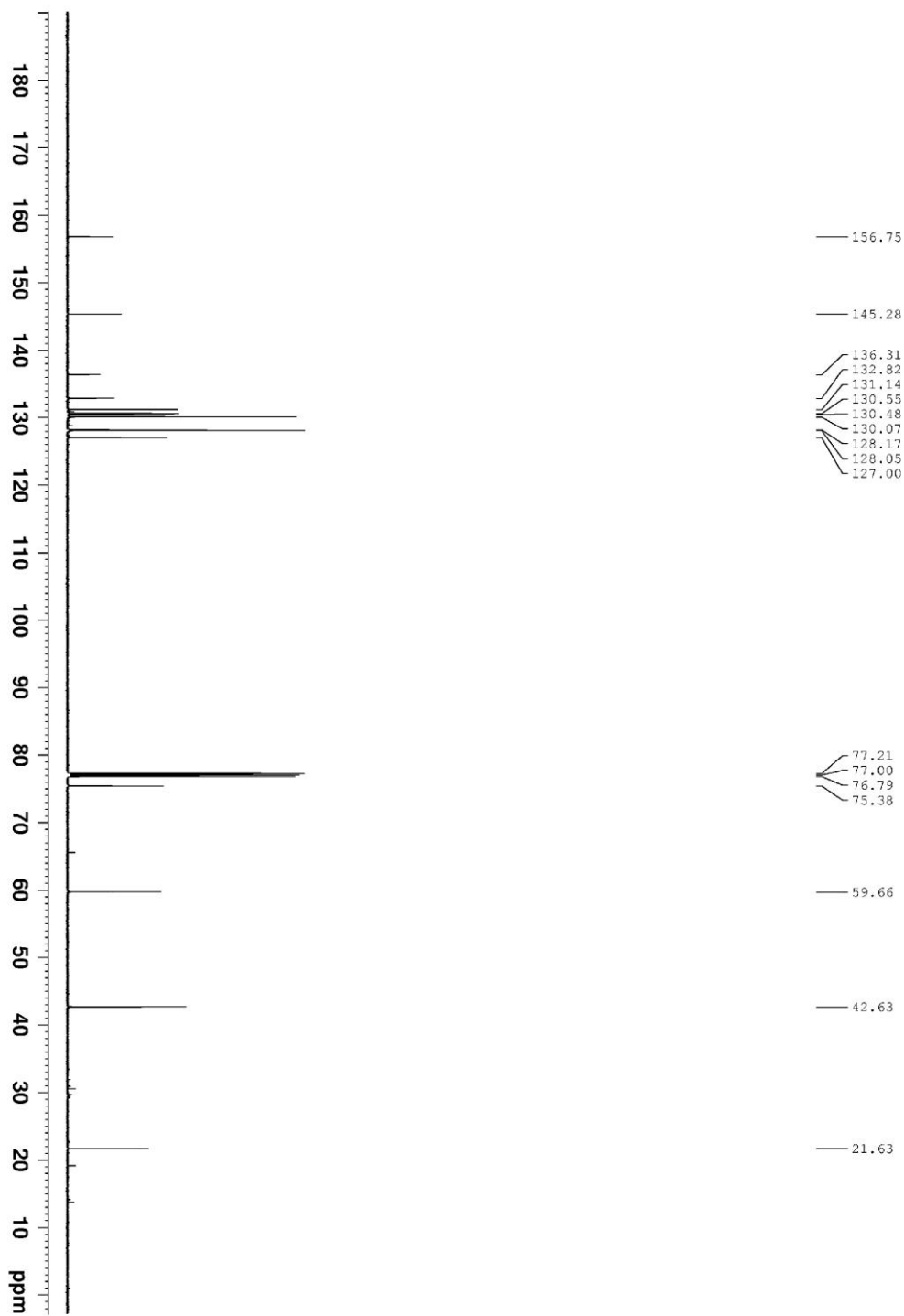


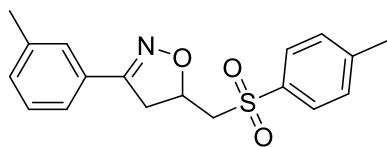
3j, 34%



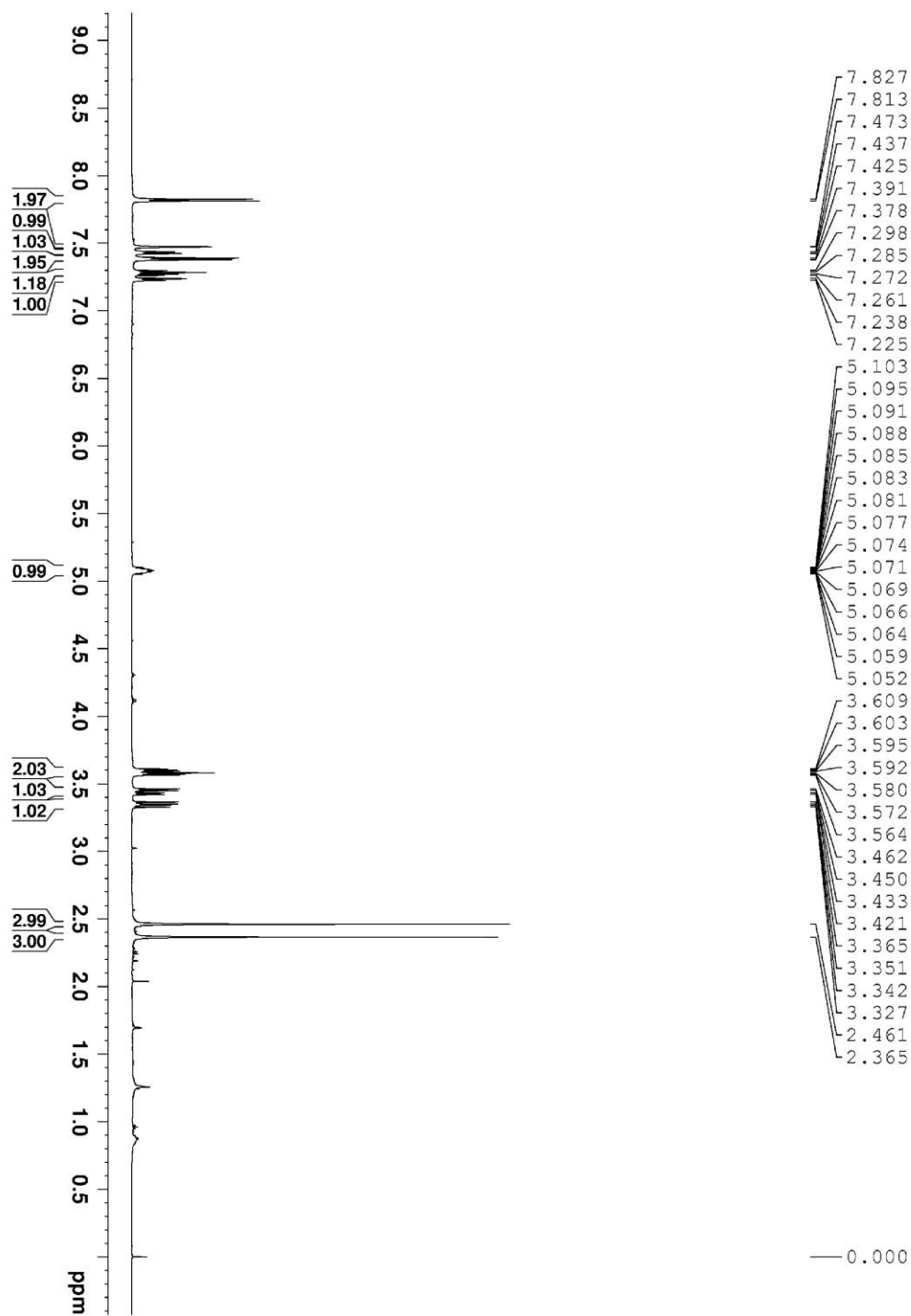


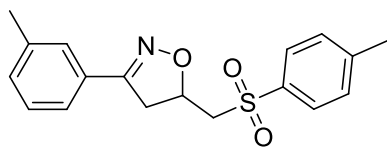
3j, 34%



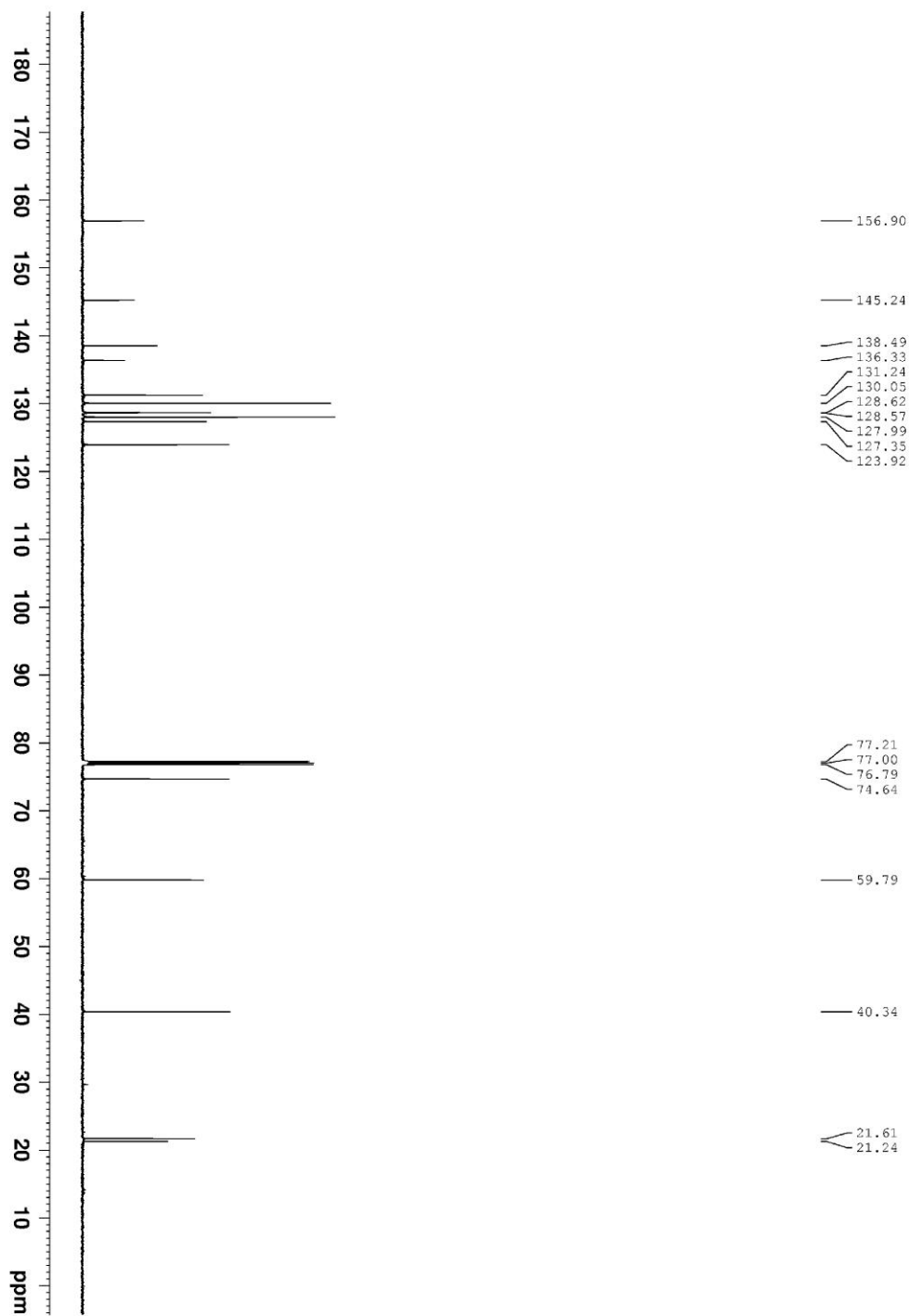


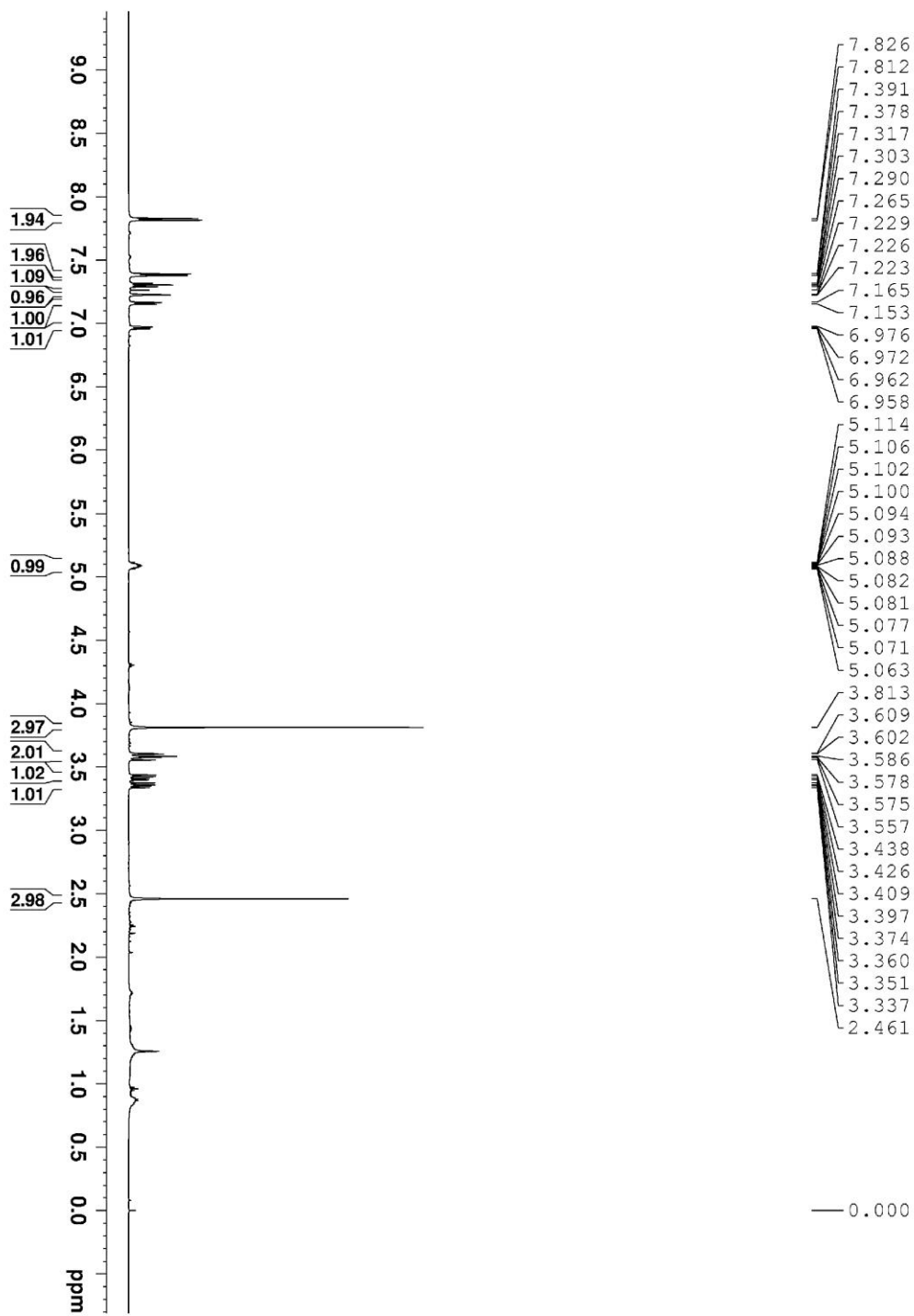
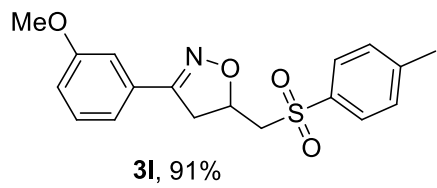
3k, 75%

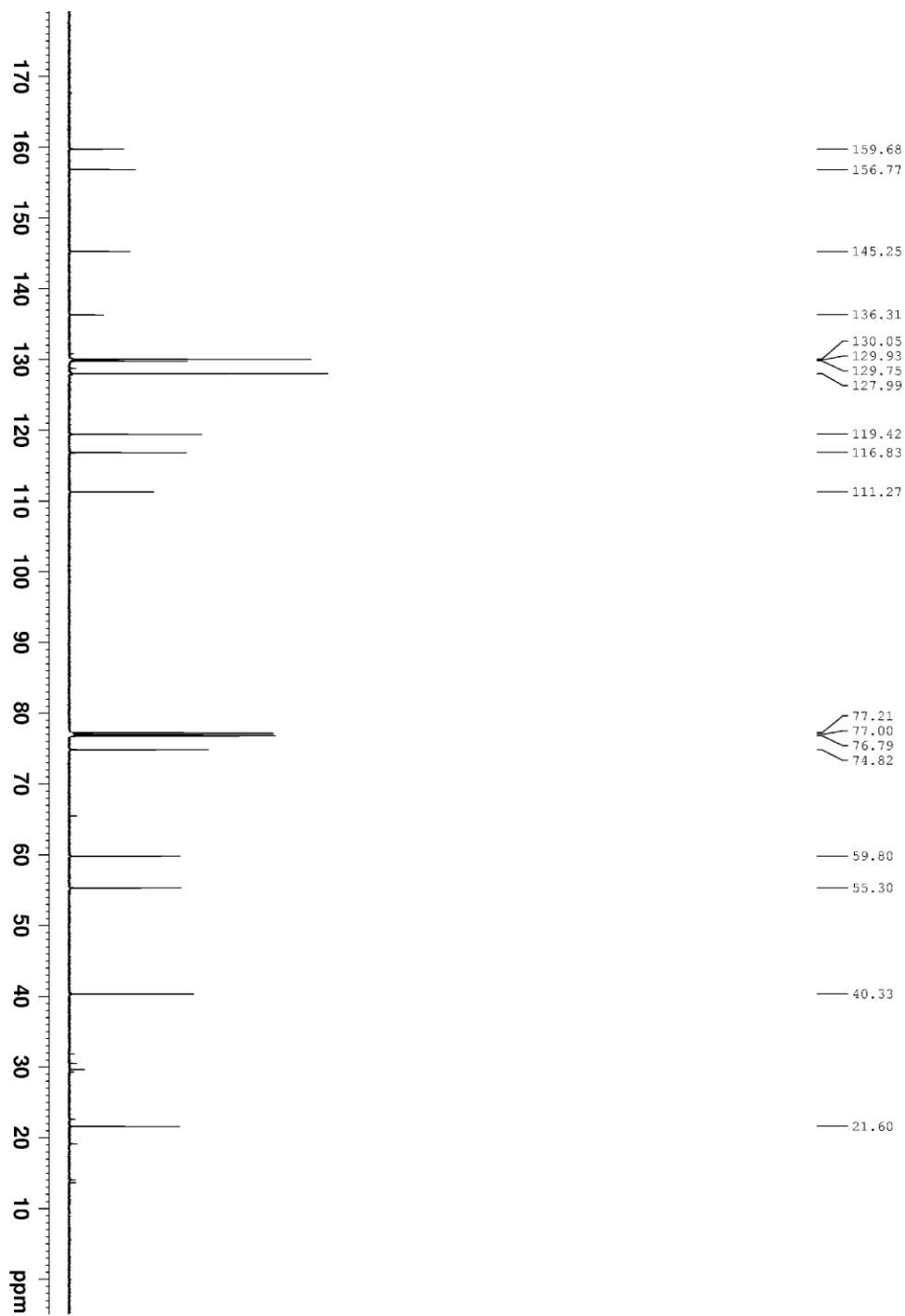
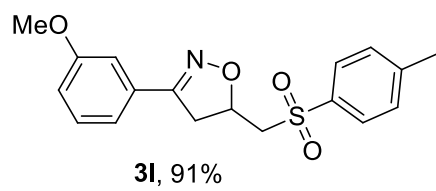


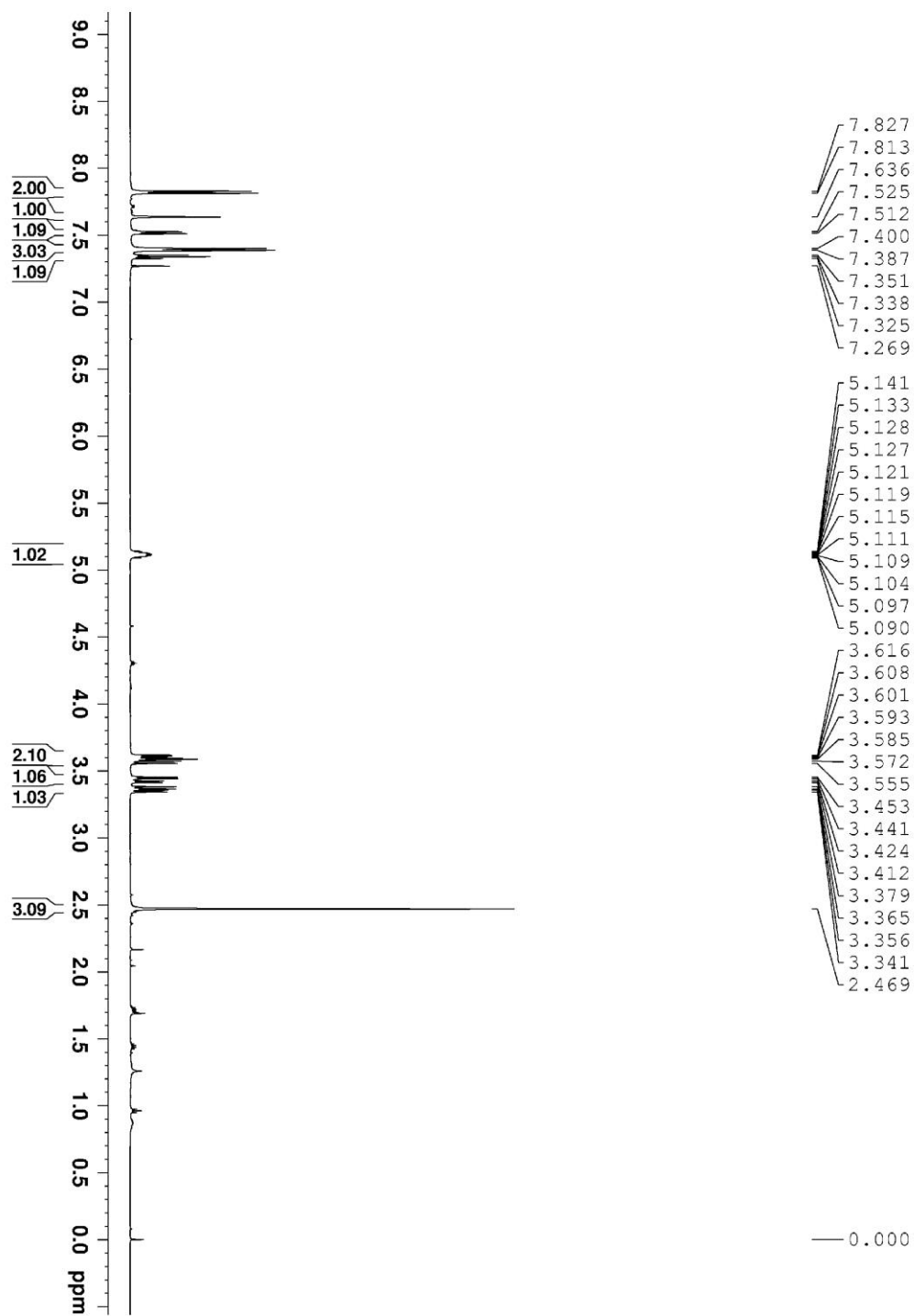
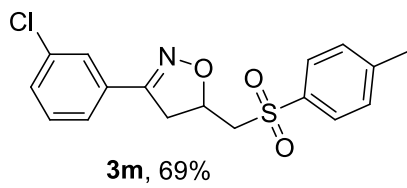


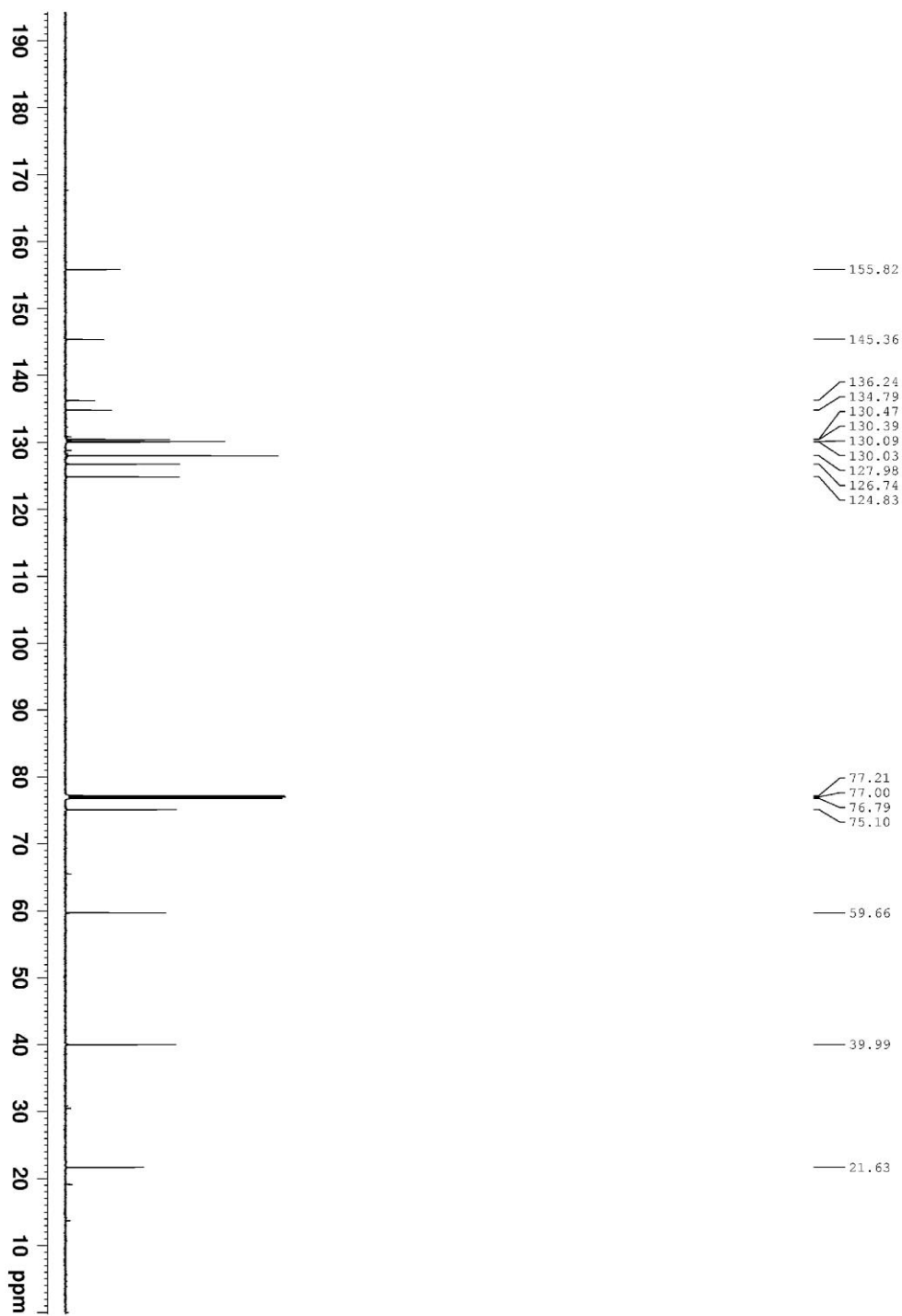
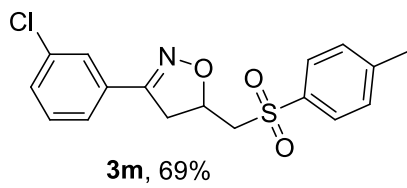
3k, 75%

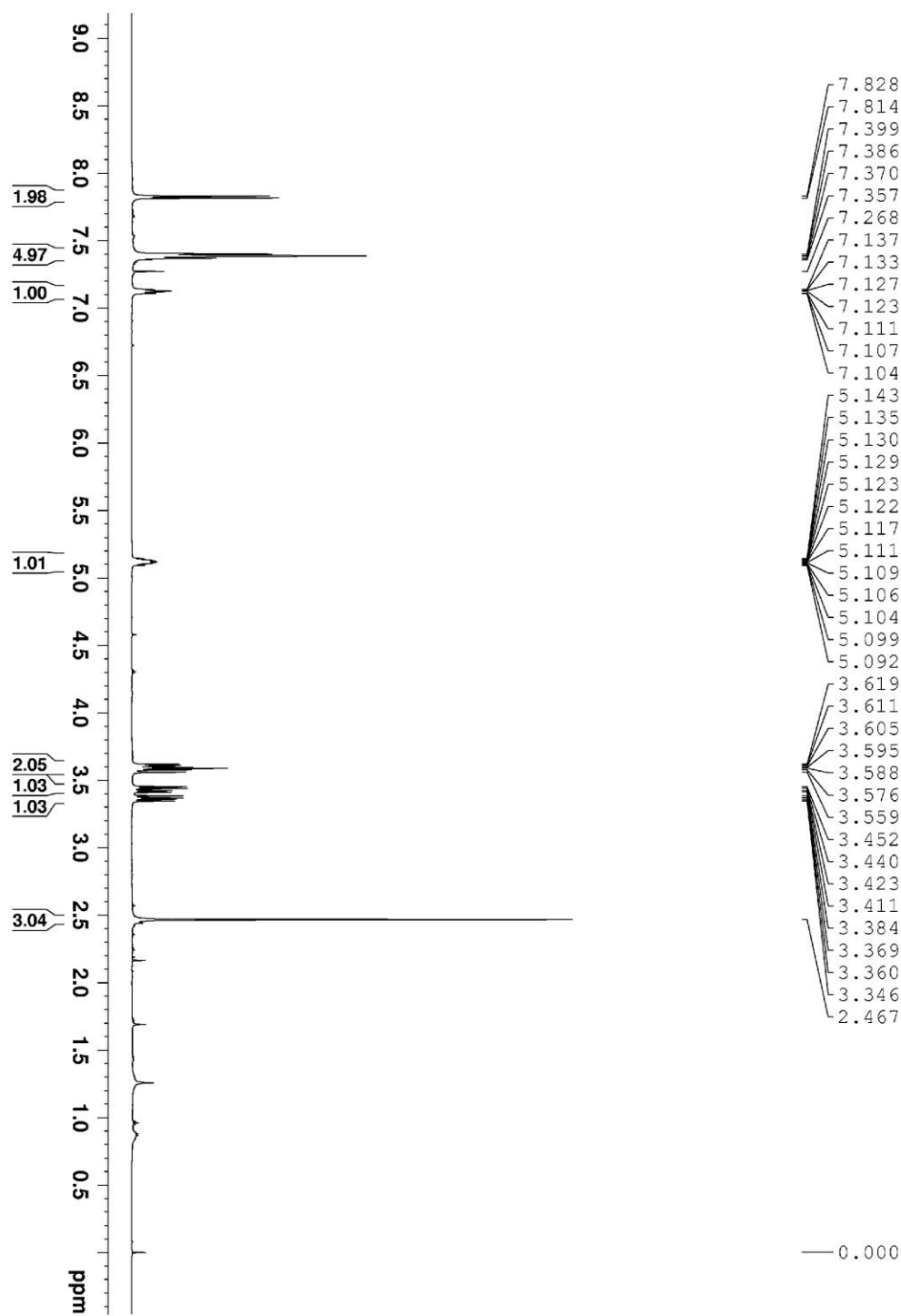
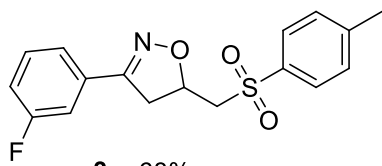


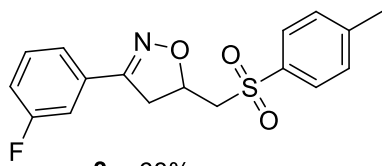




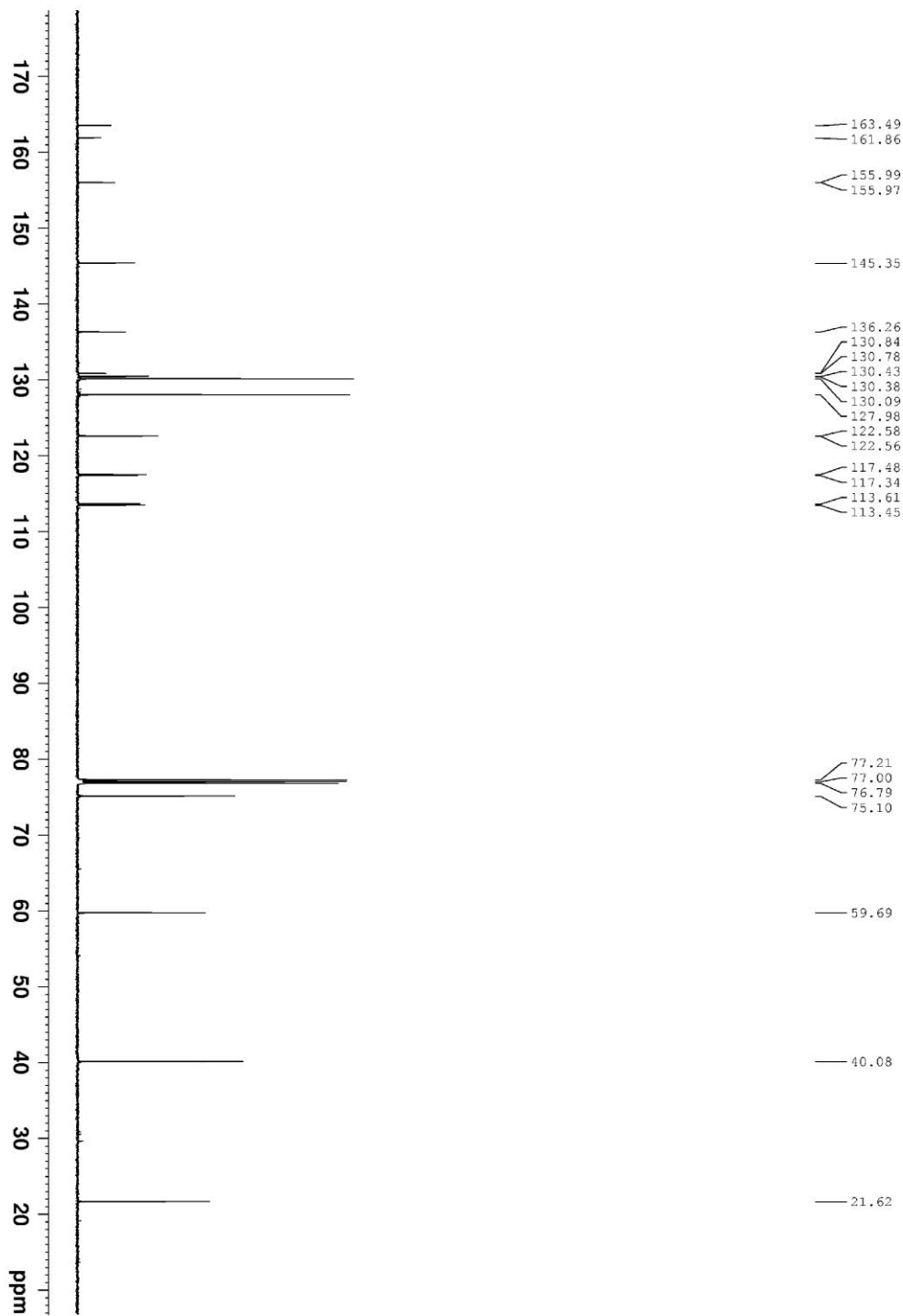


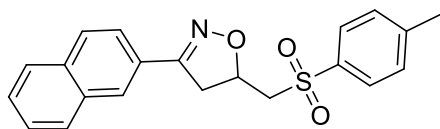




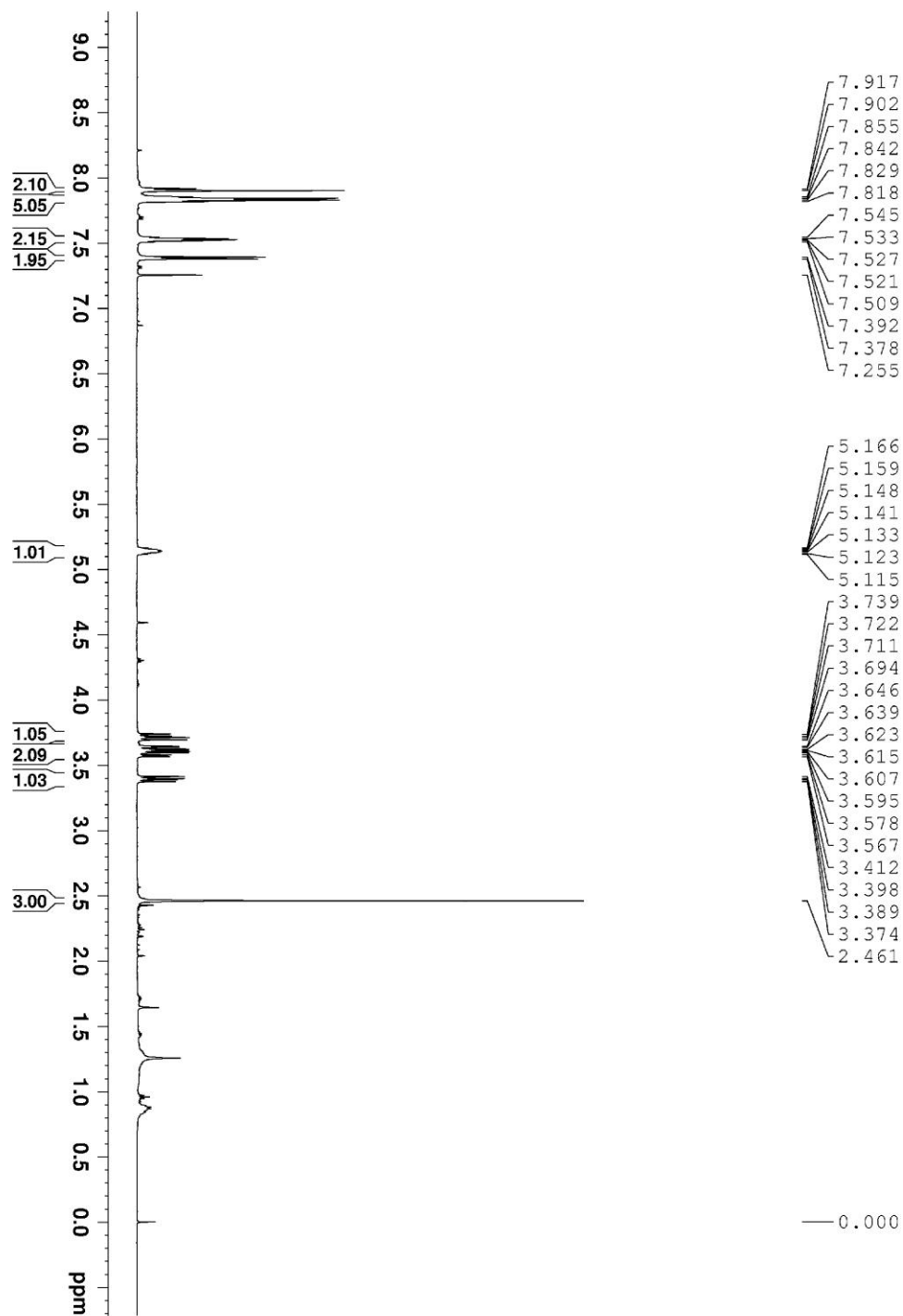


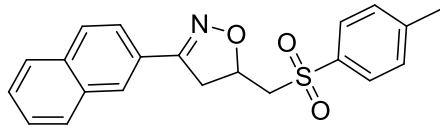
3n, 68%



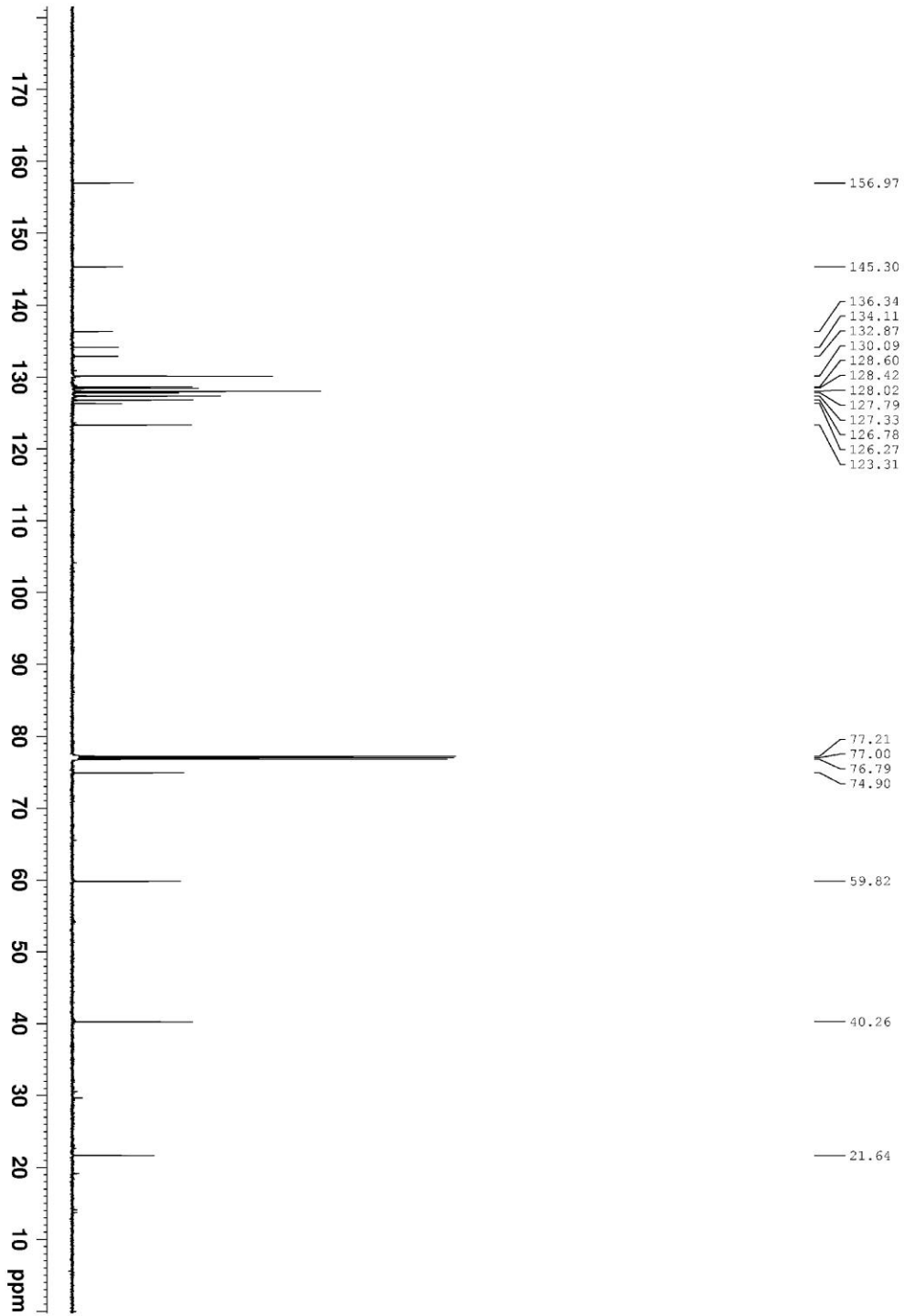


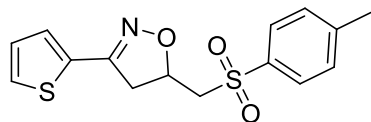
3o, 75%



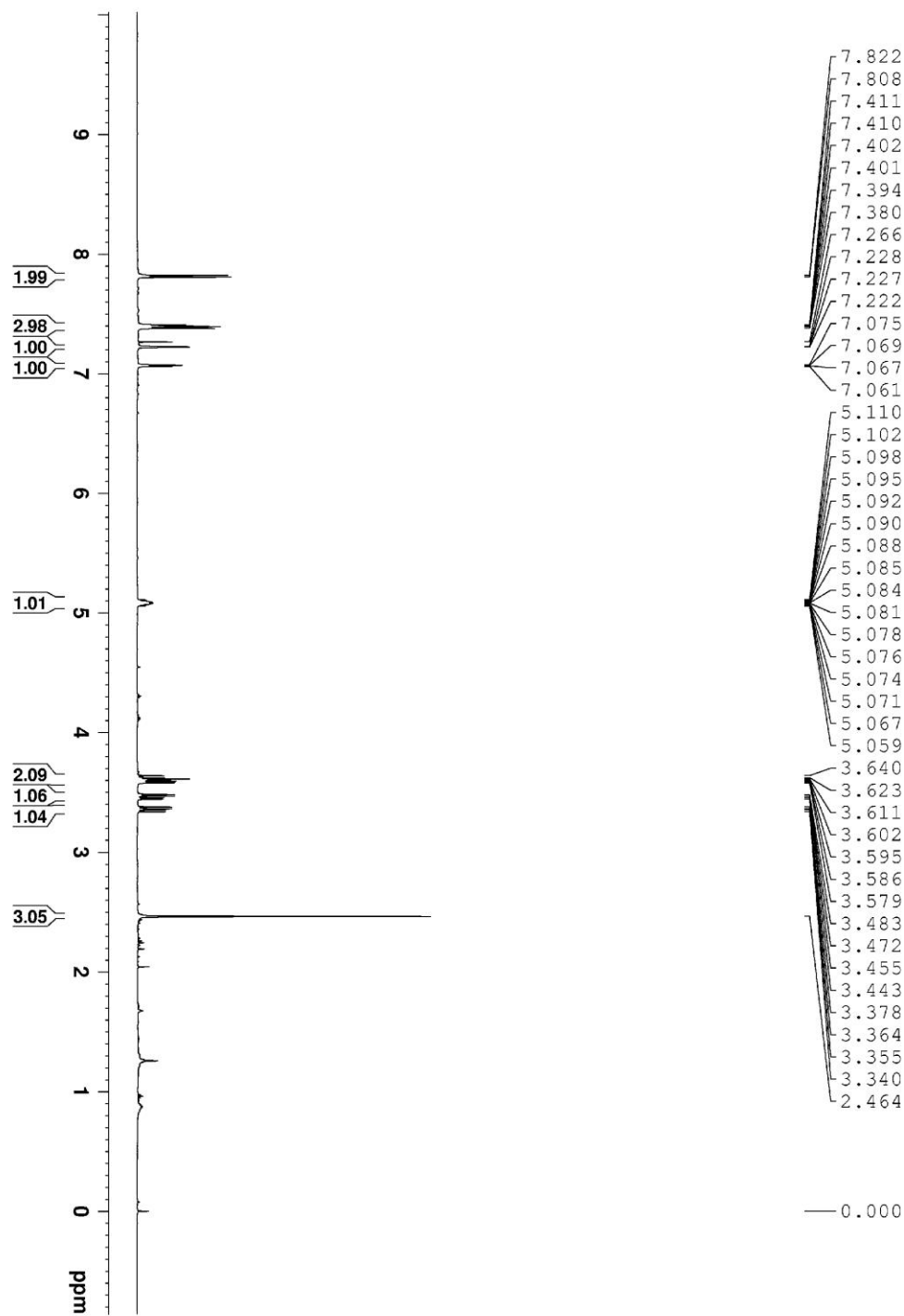


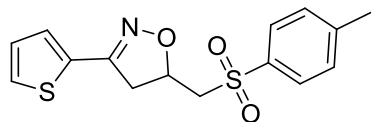
3o, 75%



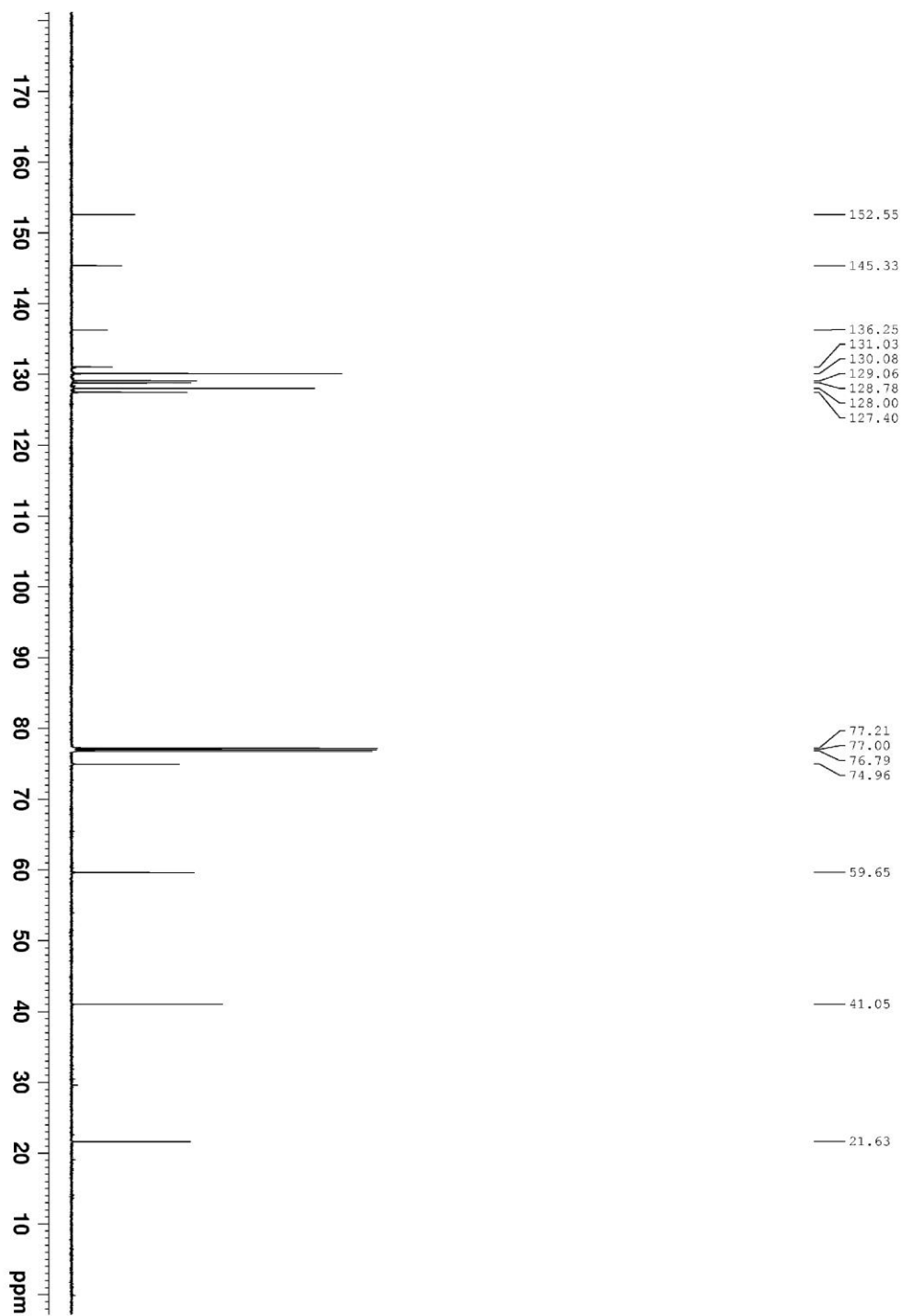


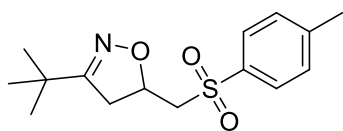
3p, 68%



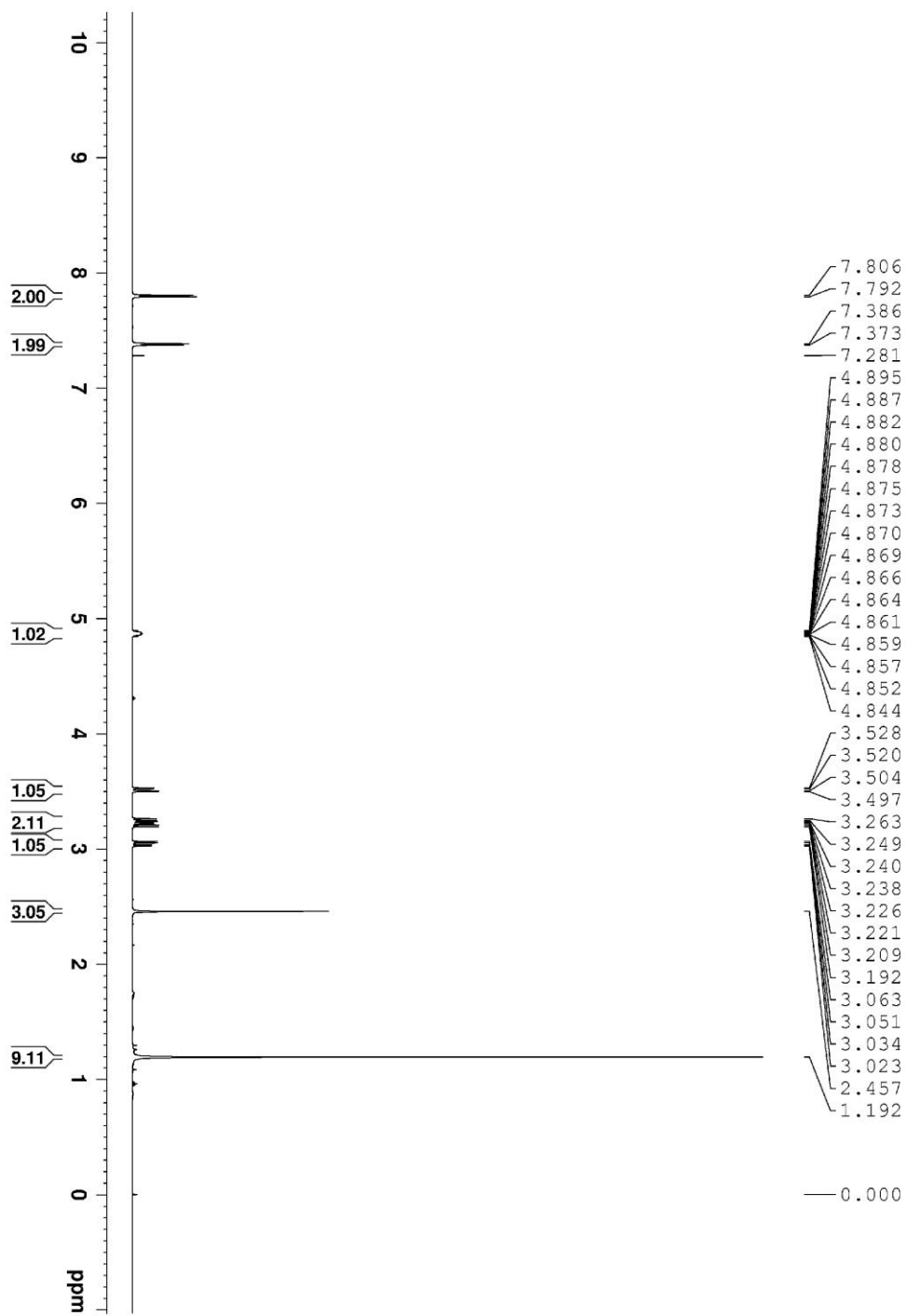


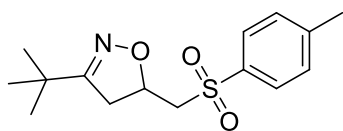
3p, 68%



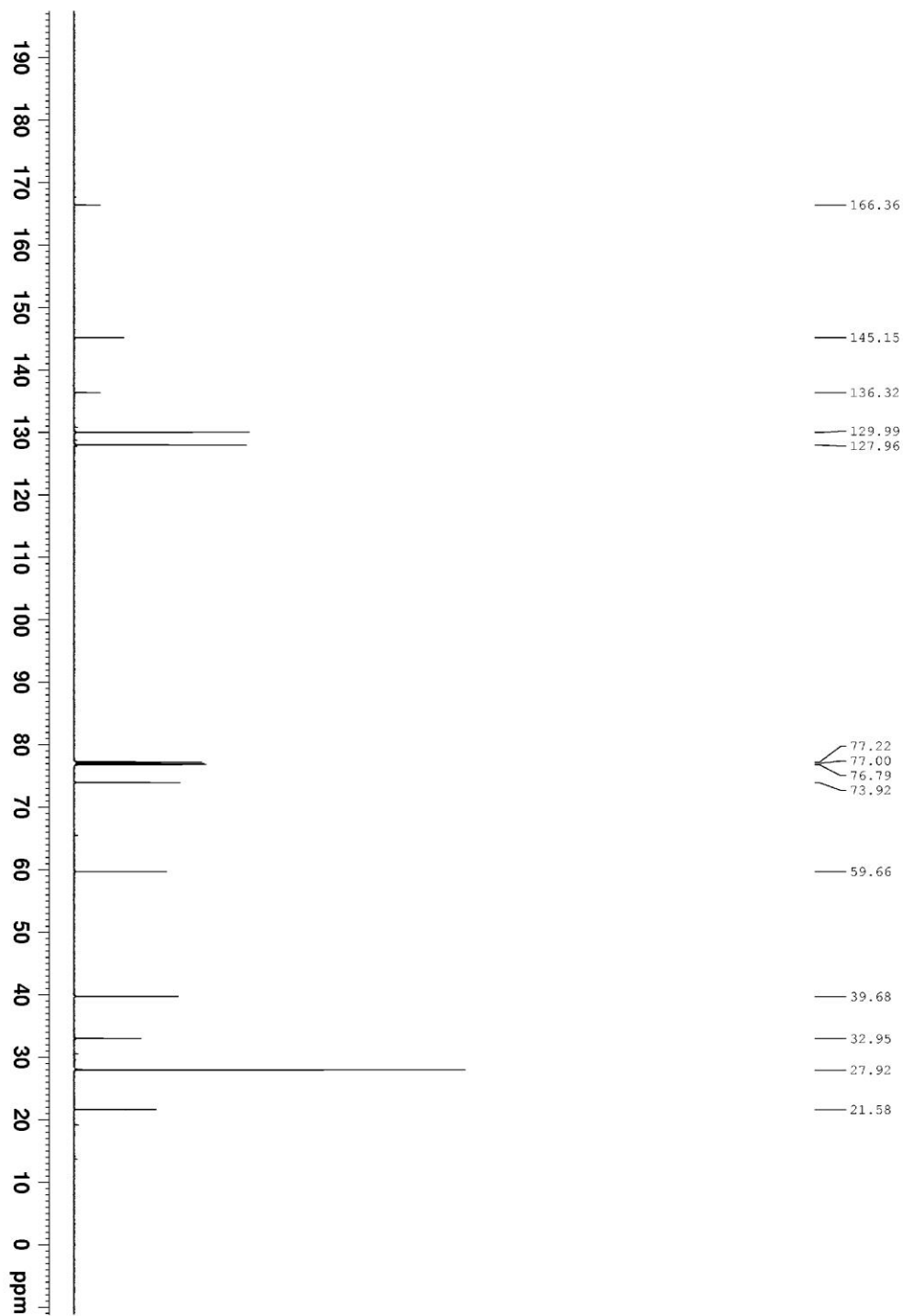


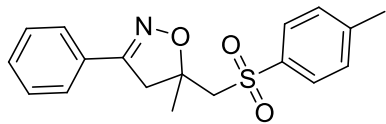
3q, 73%



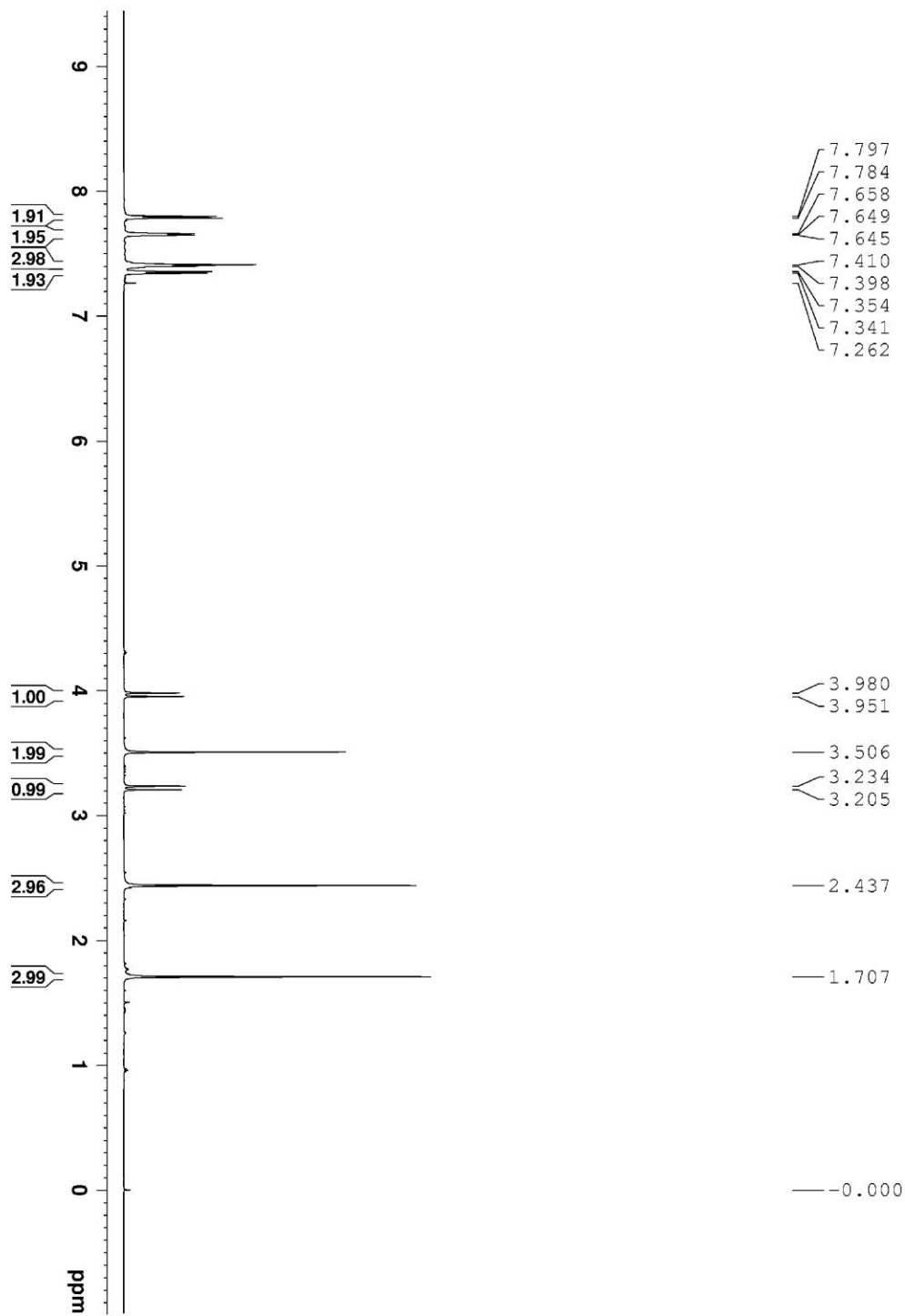


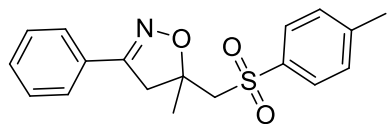
3q, 73%



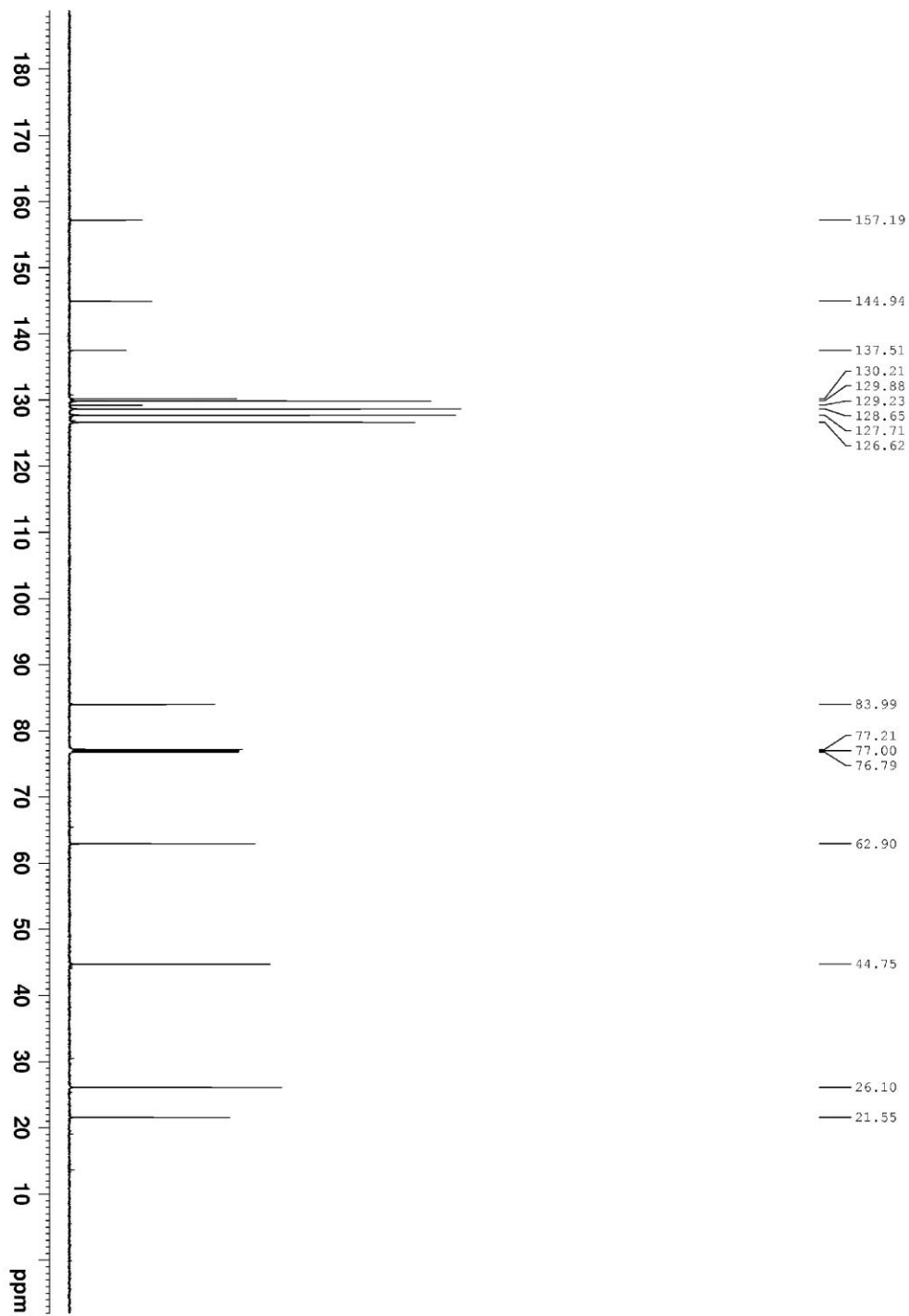


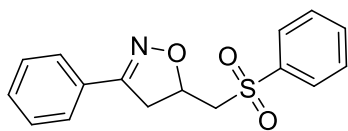
3r, 54%



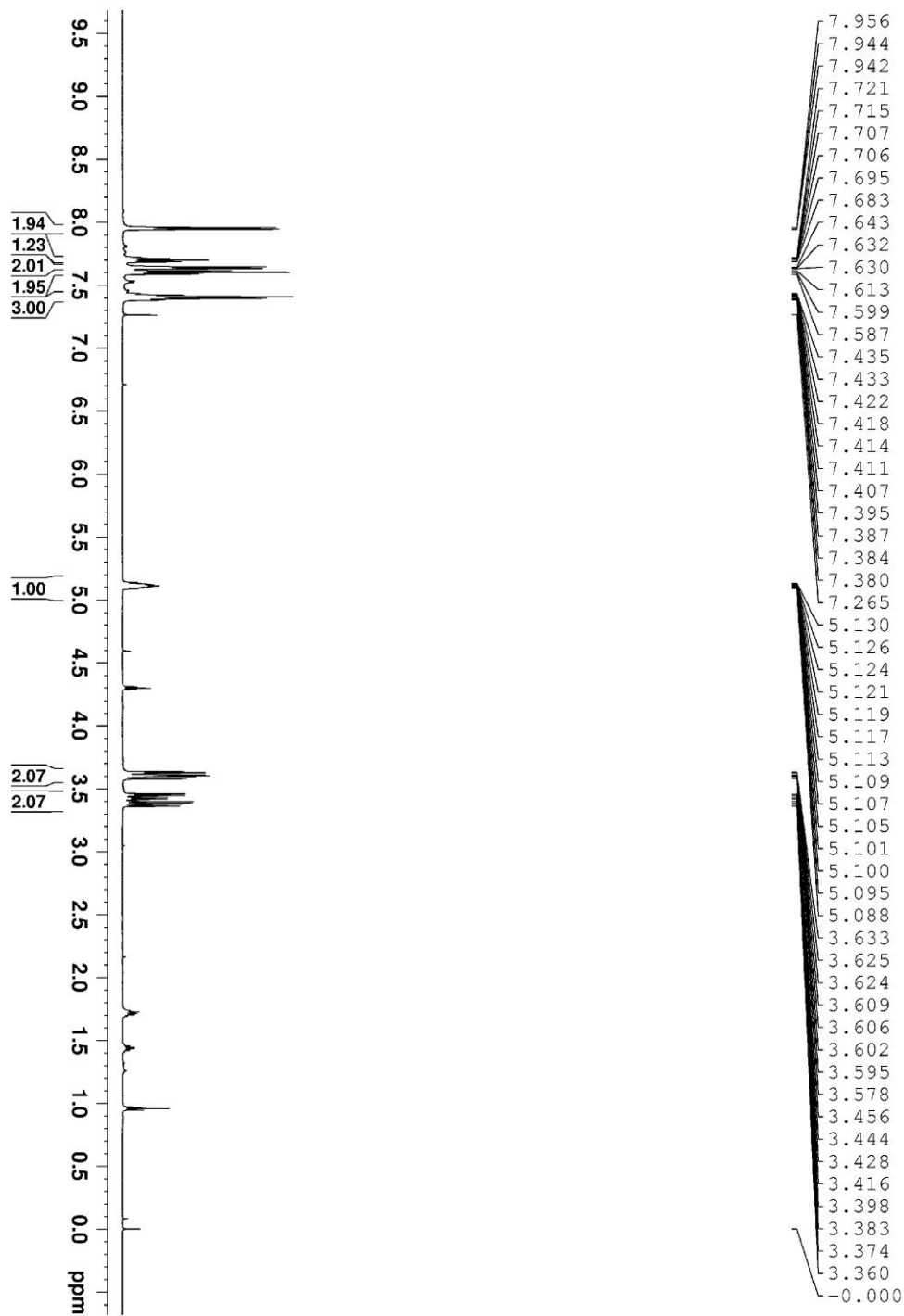


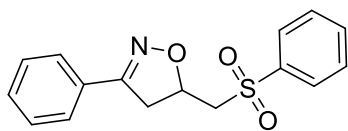
3r, 54%



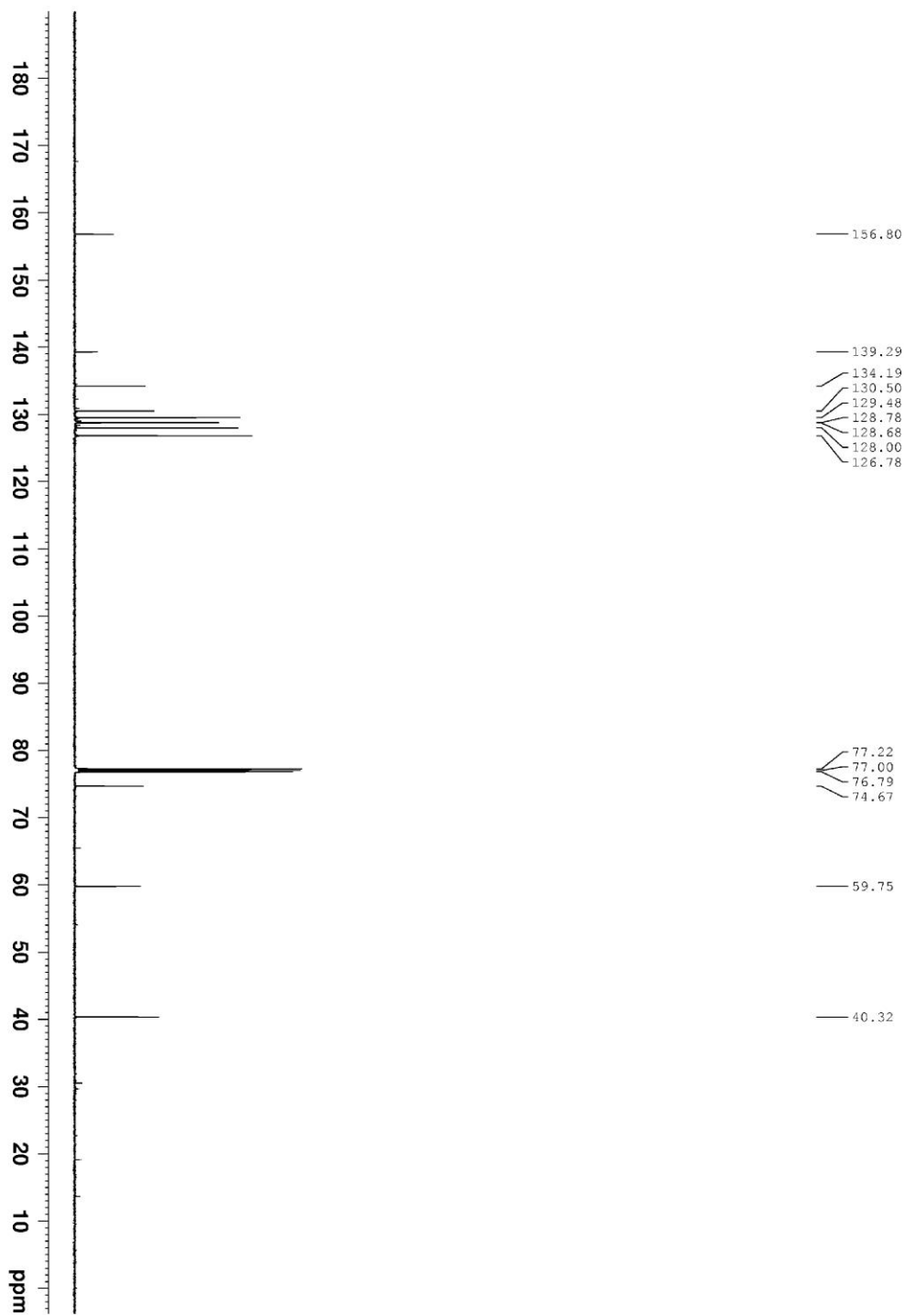


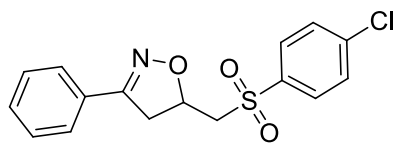
3ab, 80%



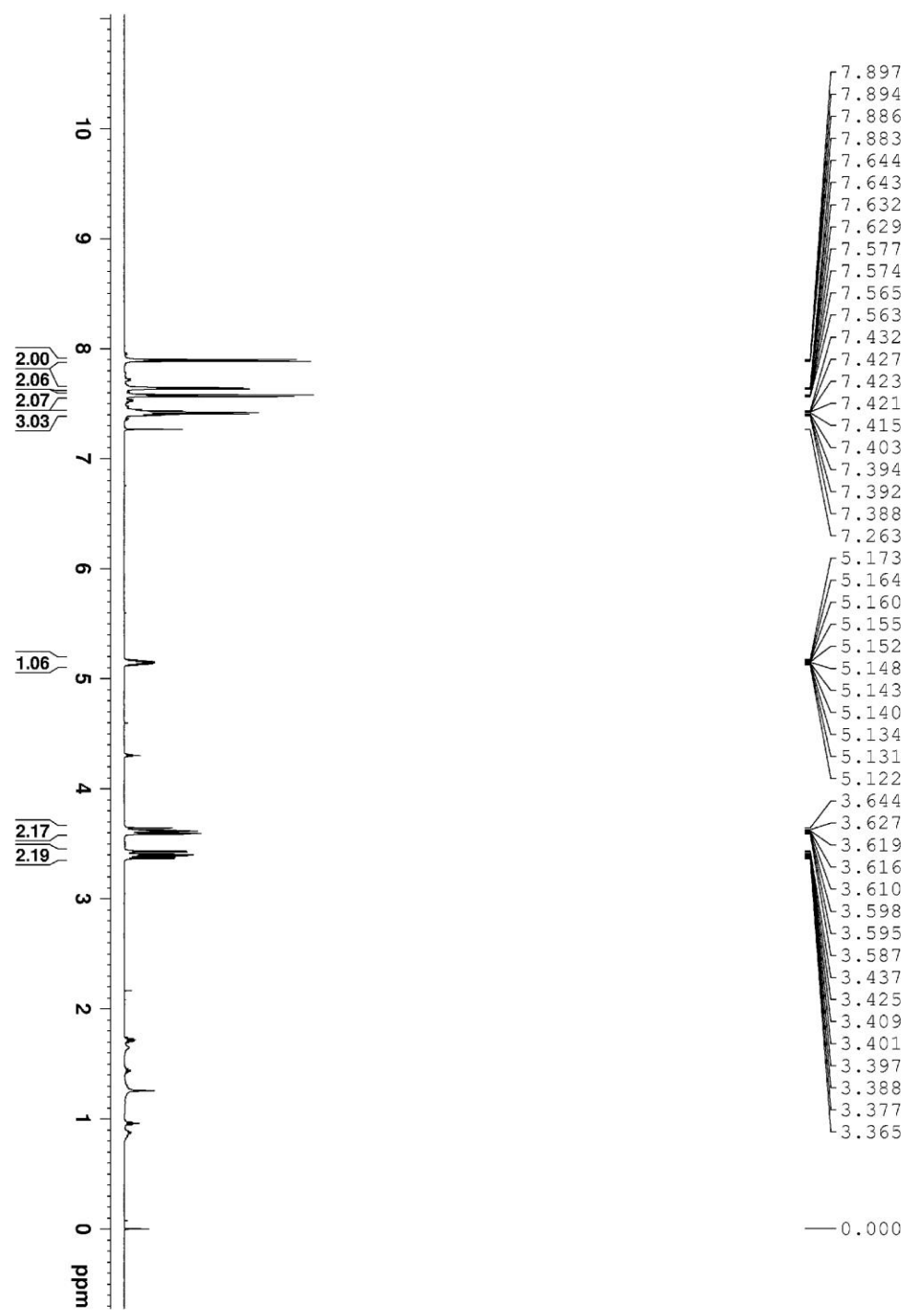


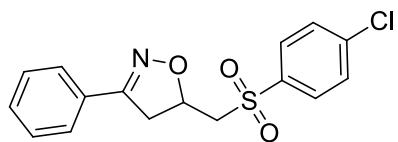
3ab, 80%



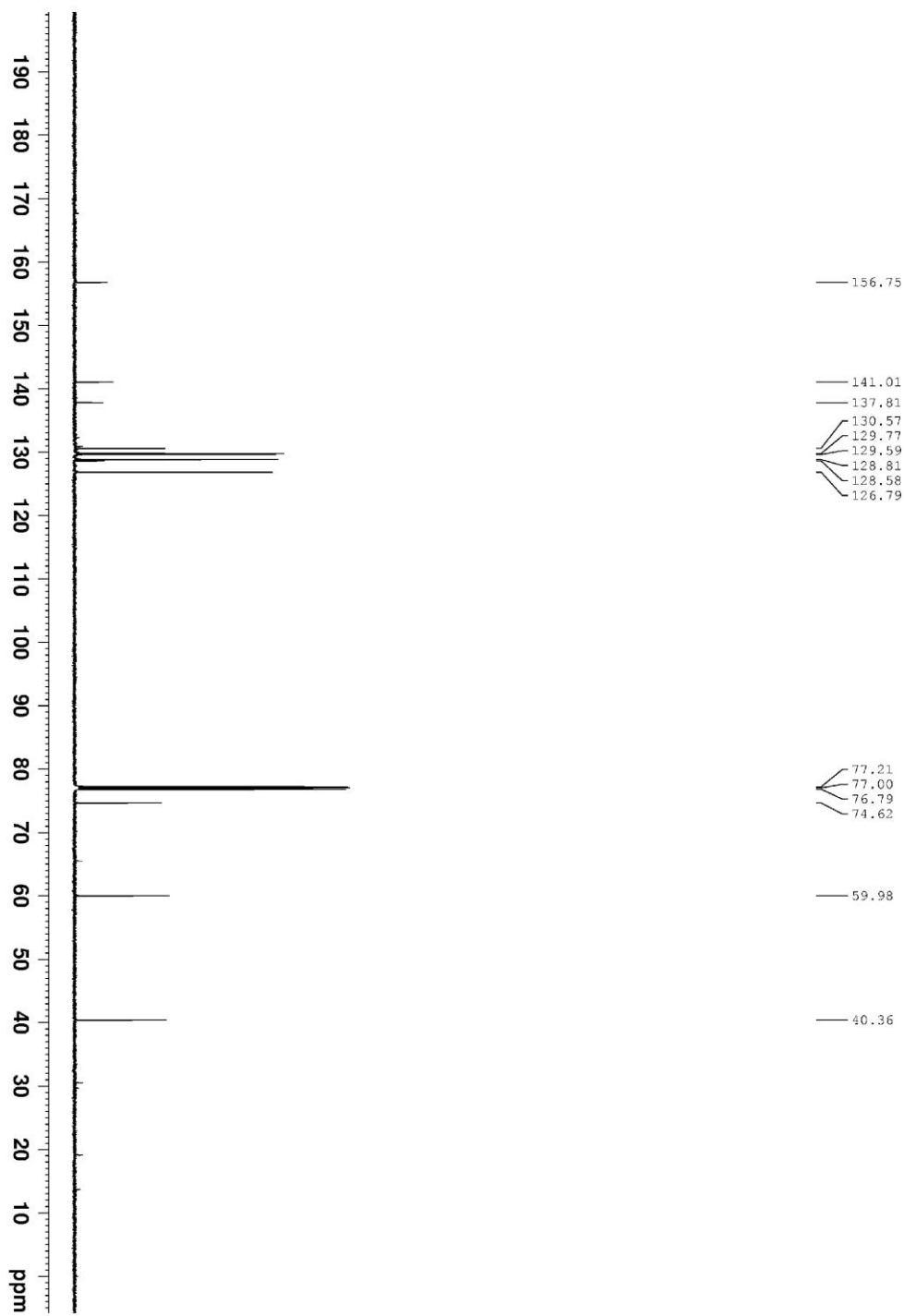


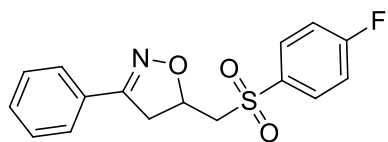
3ac, 49%



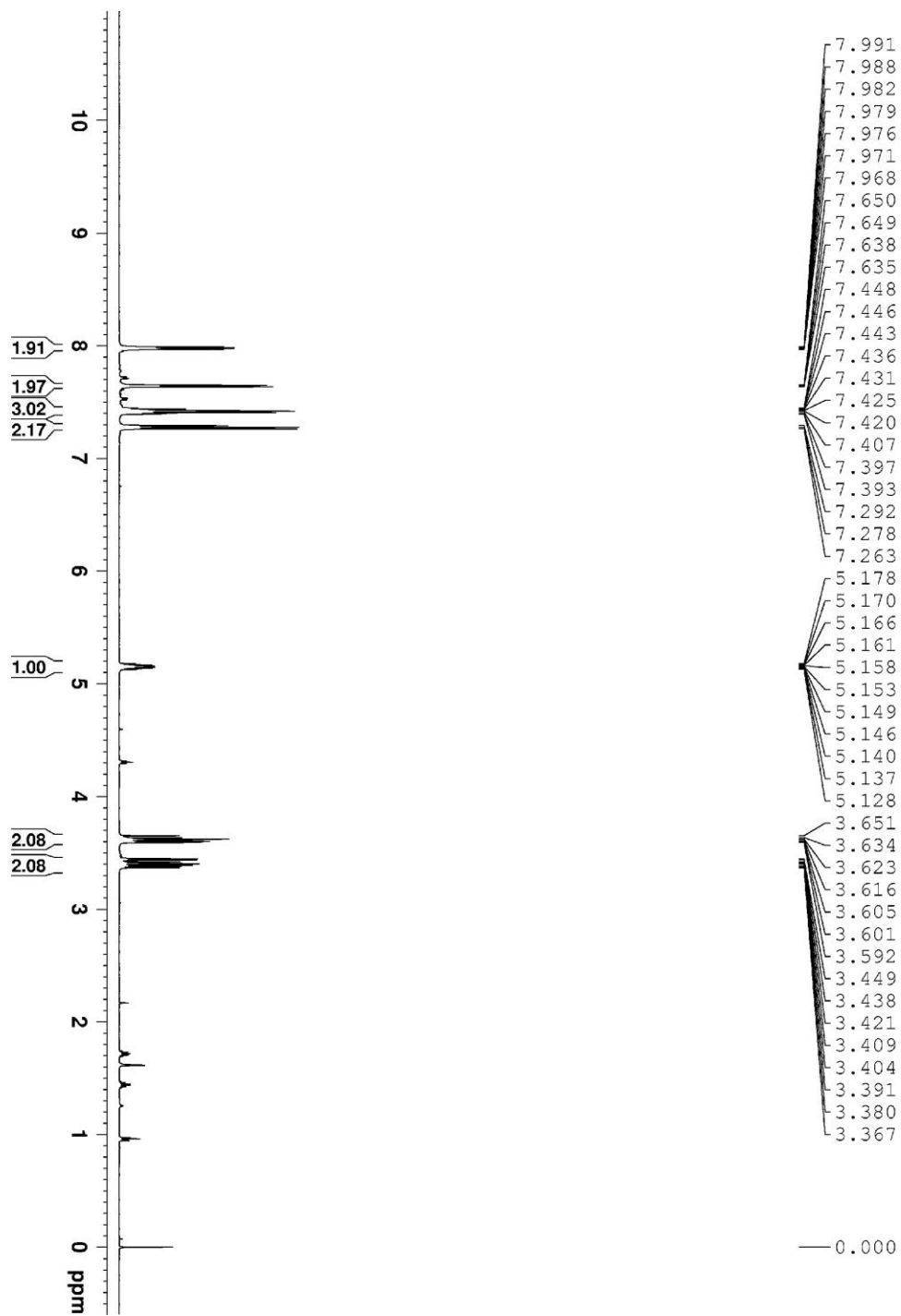


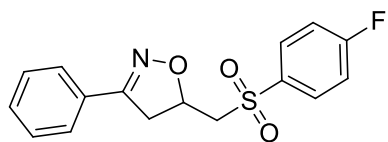
3ac, 49%



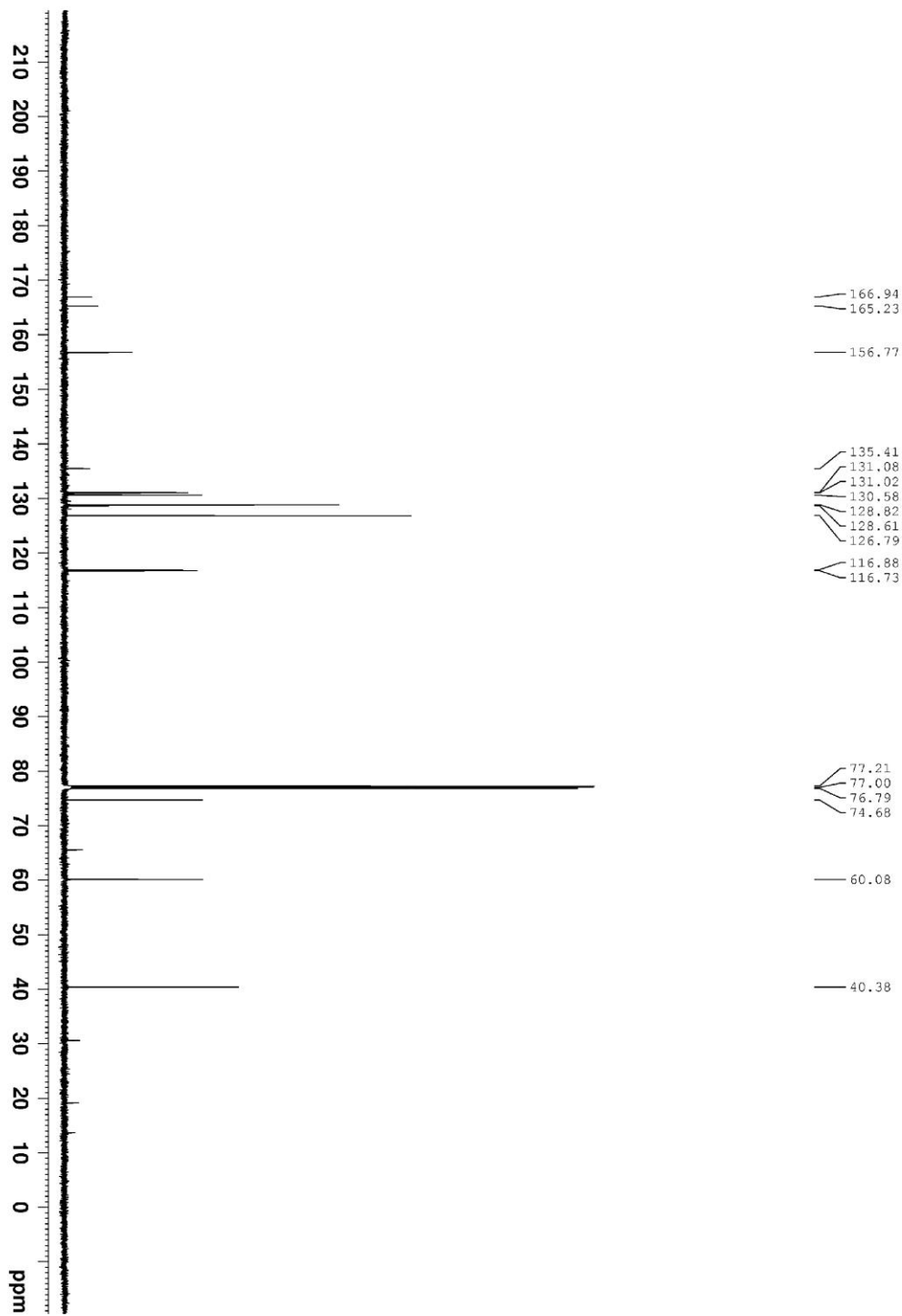


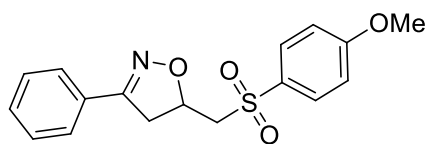
3ad, 58%



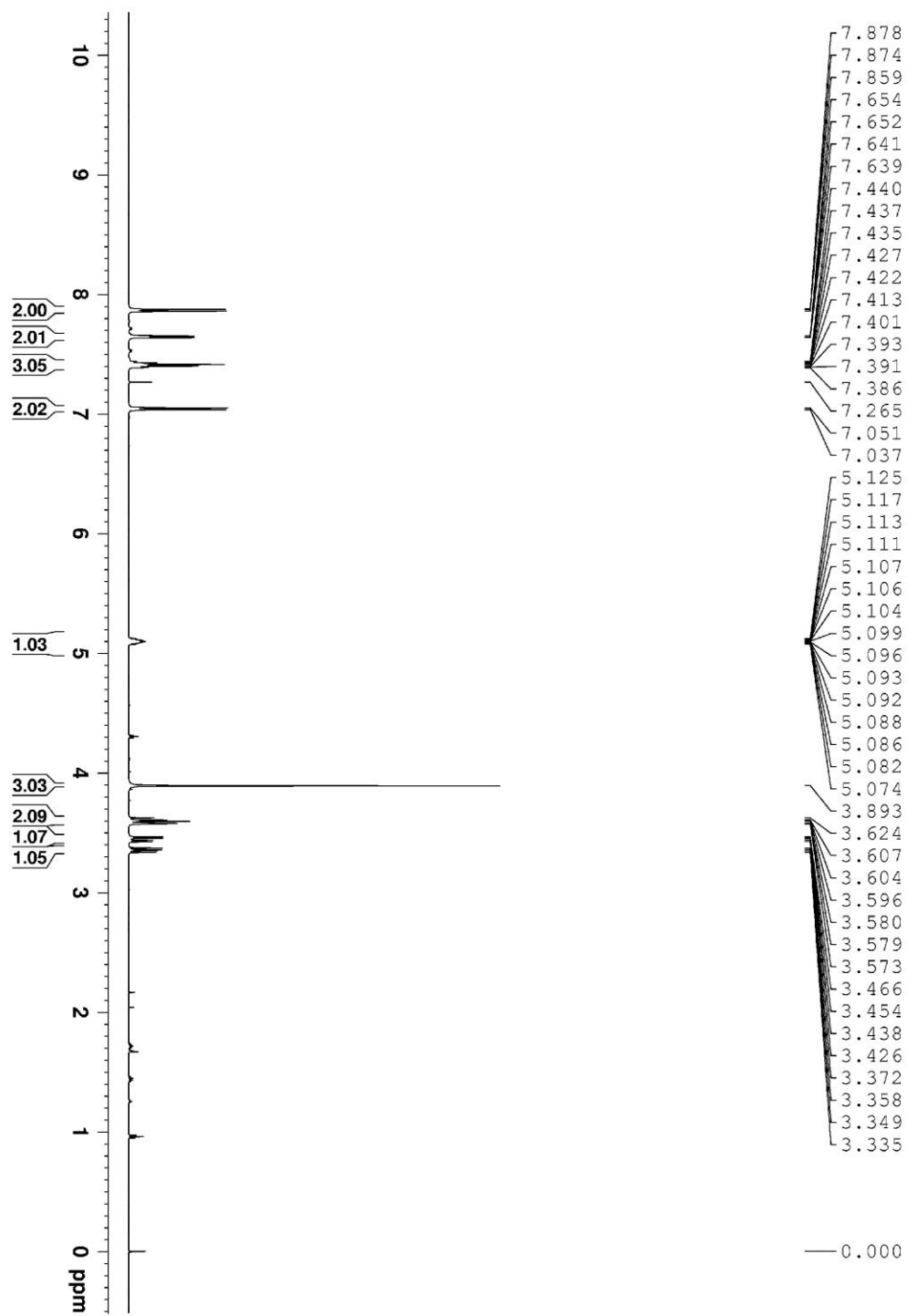


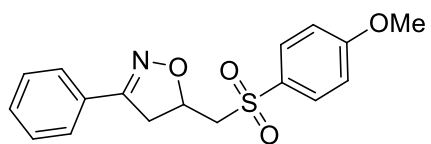
3ad, 58%



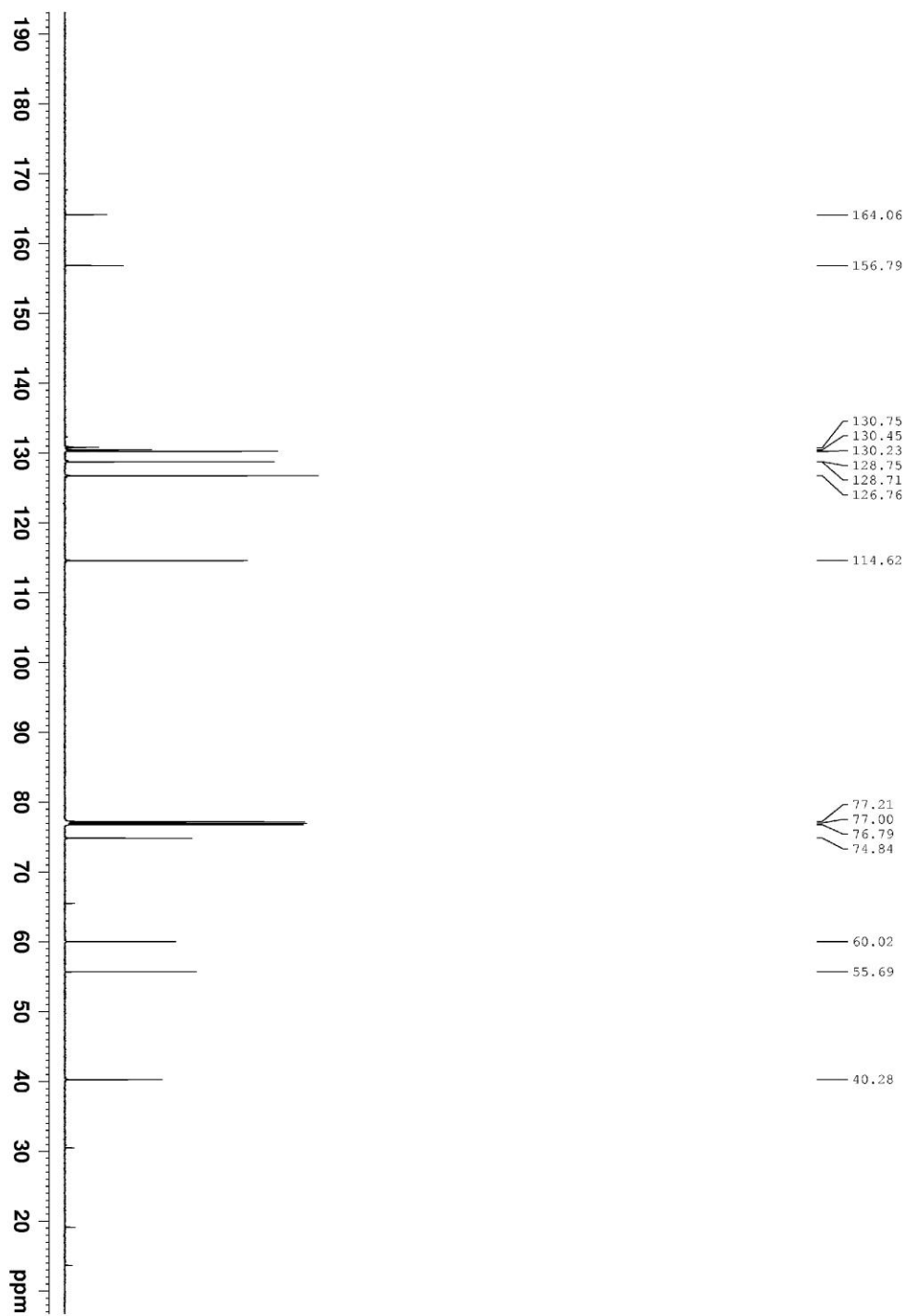


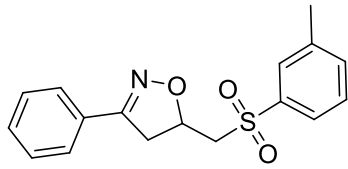
3ae, 88%



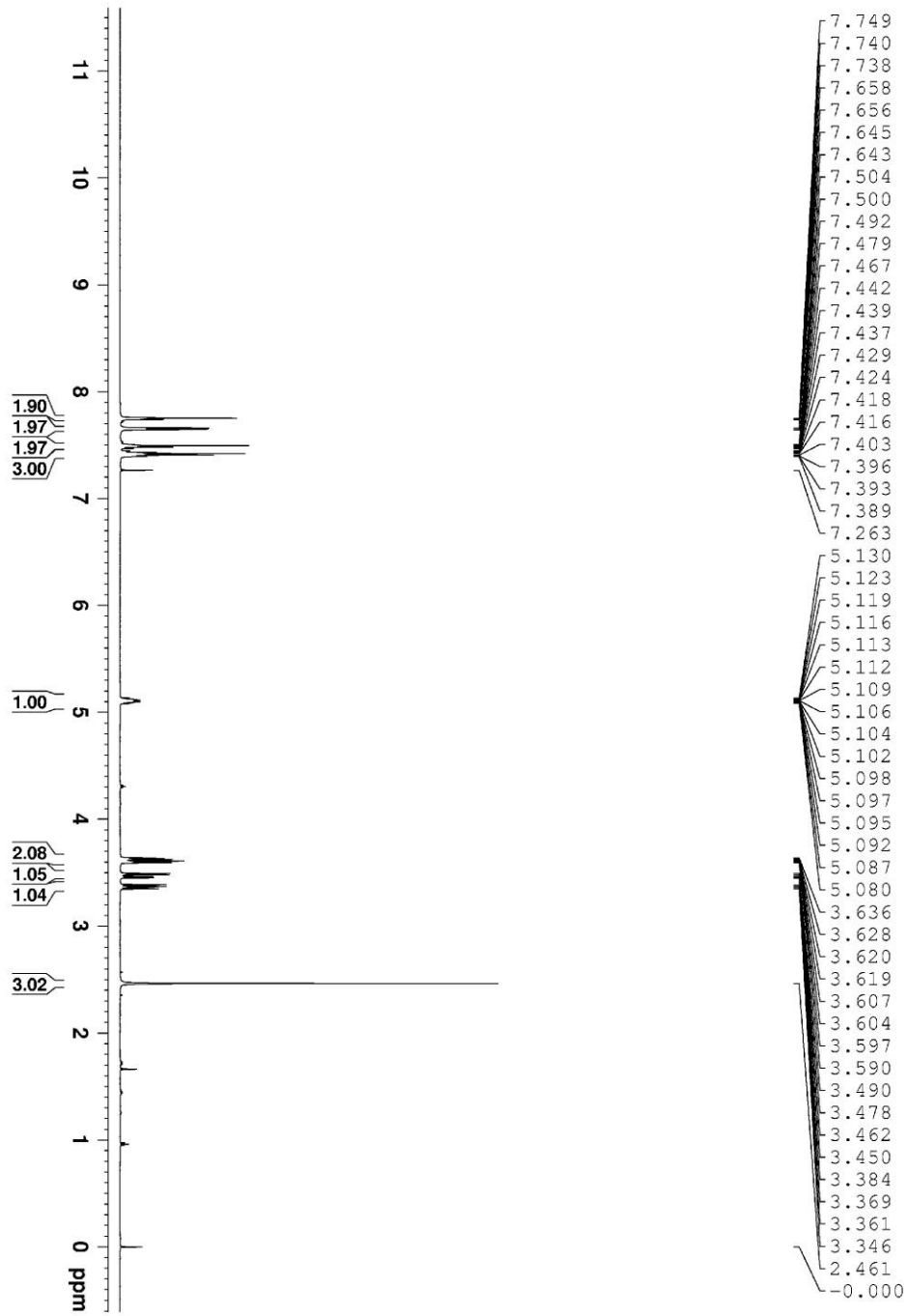


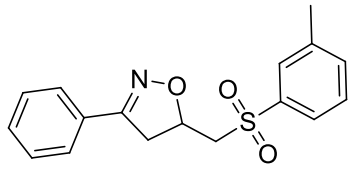
3ae, 88%



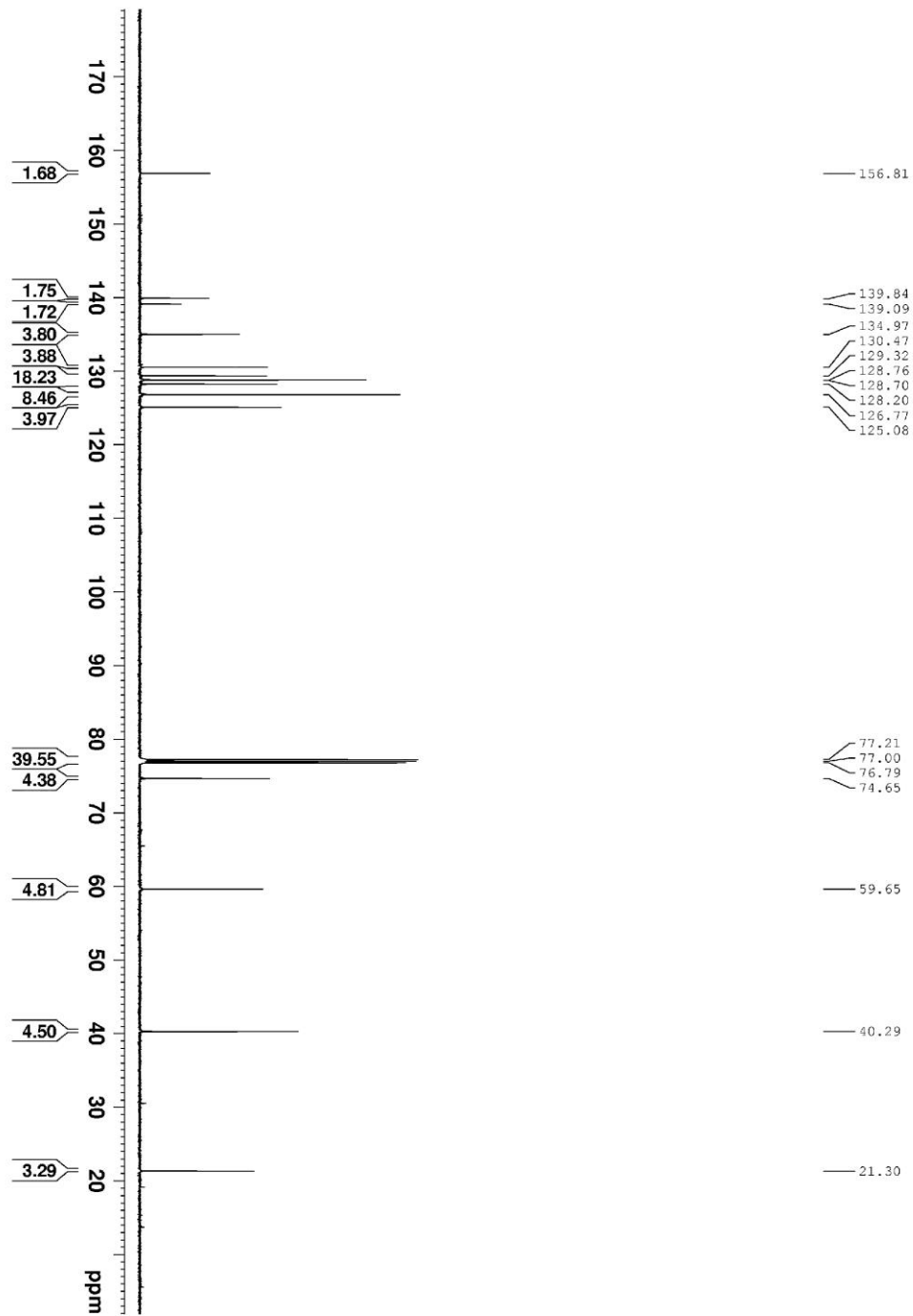


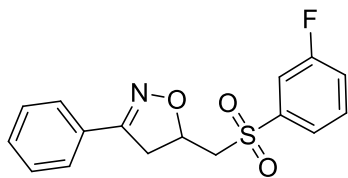
3ag, 82%



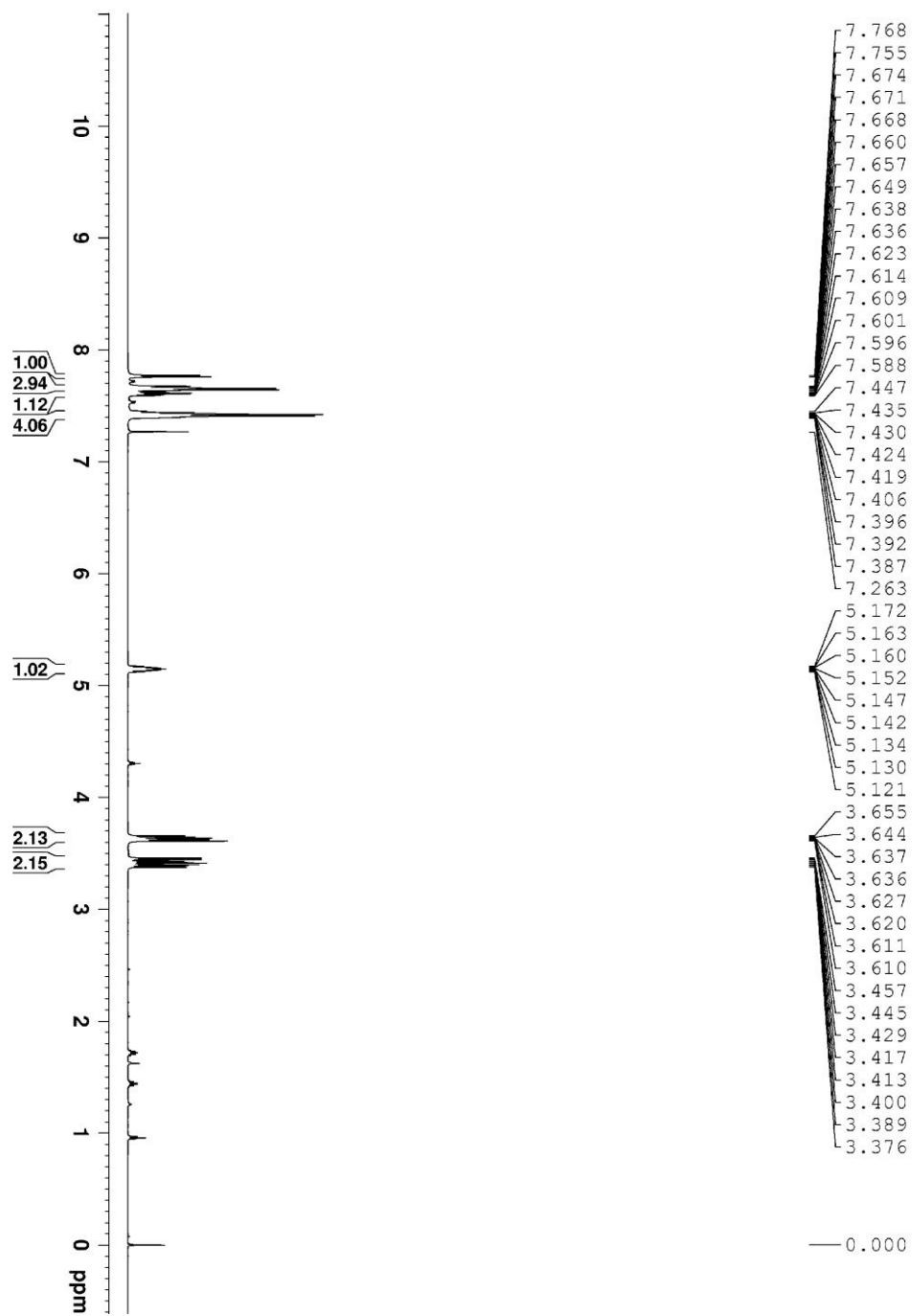


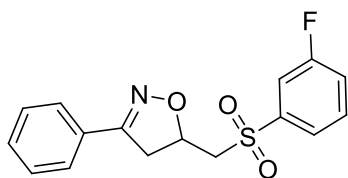
3ag, 82%



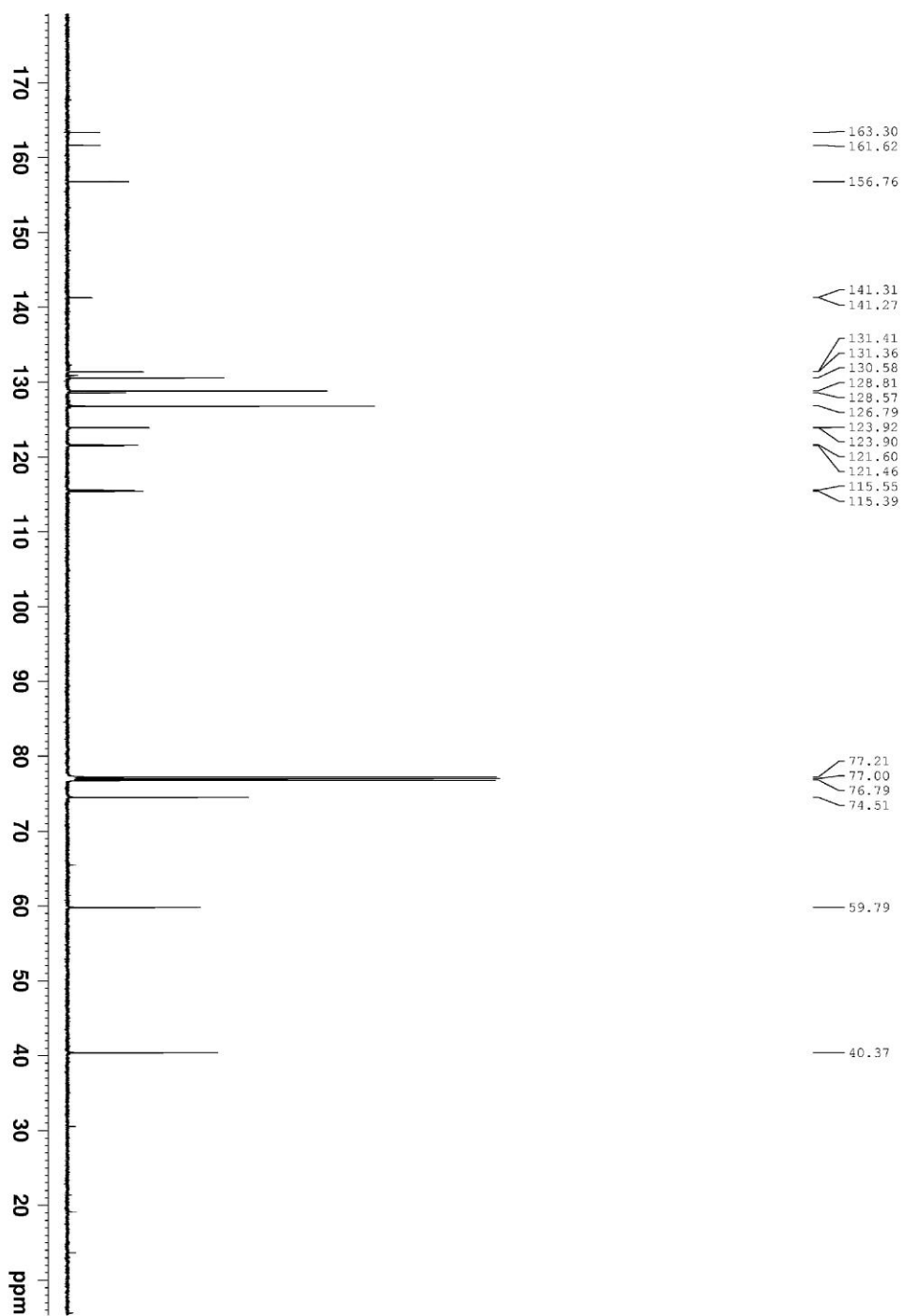


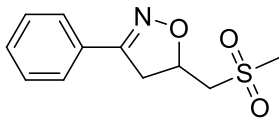
3ah, 60%



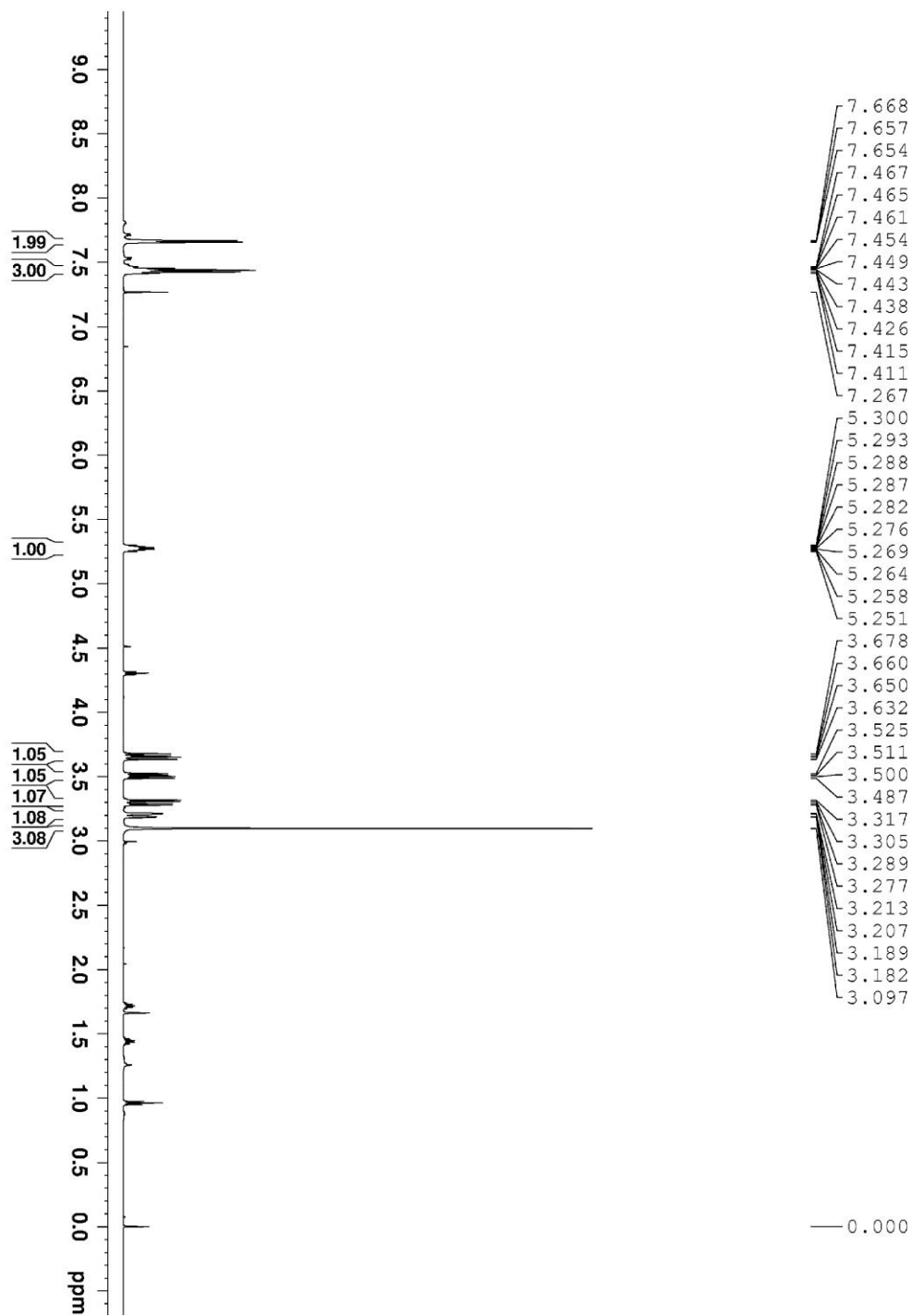


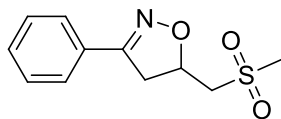
3ah, 60%





3ai, 84%





3ai, 84%

