

Acetamido-TEMPO mediated electrochemical oxidation of alcohols to aldehydes and ketones

Chelsea M. Schroeder,^a Fabrizio Politano,^{a,b} Kristiane K. Ohlhorst,^a and Nicholas E. Leadbeater^{a,*}

^aDepartment of Chemistry, University of Connecticut, 55 North Eagleville Road, Storrs, Connecticut 06269, USA.

^bInstituto de Investigaciones en Físico Química de Córdoba (INFIQC)-CONICET, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, X5000HUA Córdoba, Argentina

* E-mail: nicholas.leadbeater@uconn.edu

SUPPORTING INFORMATION

General Considerations	3
Chemicals	3
Cyclic Voltammetry.....	3
General Procedure for the preparation of Ketones and Aldehydes.....	4
Product characterization	4
General Procedure for the preparation of Trifluoromethyl Ketones	8
Product characterization	8
References	9
¹H-, ¹³C-, and ¹⁹F-NMR spectra of synthesized compounds.....	11
¹ H-NMR (400MHz CDCl ₃) Acetophenone (3a)	11
¹ H-NMR (400 MHz CDCl ₃) 4-Methylacetophenone (3b).....	12
¹ H-NMR (400 MHz CDCl ₃) 1-(4-Methoxyphenyl)ethanone (3c).....	13
¹ H-NMR (400 MHz CDCl ₃) 1-(4-Fluorophenyl)ethanone (3d).....	14
¹ H-NMR (400 MHz CDCl ₃) 4-Chloroacetophenone (3e)	15
¹ H-NMR (400 MHz CDCl ₃) 4-Nitroacetophenone (3f)	16
¹ H-NMR (400 MHz CDCl ₃) 1-(4-Trifluoromethylphenyl)ethanone (3g).....	17
¹ H-NMR (400 MHz CDCl ₃) 3-Methylacetophenone (3h).....	18
¹ H-NMR (400 MHz CDCl ₃) 2-Bromoacetophenone (3i)	19
¹ H-NMR (400 MHz CDCl ₃) 2'-Fluoroacetophenone (3j).....	20
¹ H-NMR (400 MHz CDCl ₃) Benzoylacetyle (3k).....	21
¹ H-NMR (400 MHz CDCl ₃) Benzophenone (3l).....	22
¹ H-NMR (400 MHz CDCl ₃) 2-Acetonaphthone (3m)	23
¹ H-NMR (400 MHz CDCl ₃) 1-Phenylpropan-1-one (3n)	24
¹ H-NMR (400 MHz CDCl ₃) 4-Methylbenzaldehyde (3o)	25
¹ H-NMR (400 MHz CDCl ₃) 4-Nitrobenzaldehyde (3p)	26

¹ H-NMR (400 MHz CDCl ₃) 3-Methoxybenzaldehyde (3q)	27
¹ H-NMR (400 MHz CDCl ₃) 2-Bromobenzaldehyde (3r)	28
¹ H-NMR (300 MHz CDCl ₃) 3,4-Dimethoxybenzaldehyde (3s)	29
¹ H-NMR (400 MHz CDCl ₃) 3,4,5-Trimethoxybenzaldehyde (3t)	30
¹ H-NMR (400 MHz CDCl ₃) 6-Chloropicolinaldehyde (3u)	31
¹ H-NMR (400 MHz CDCl ₃) 2-Octanone (3v)	32
¹ H-NMR (400 MHz CDCl ₃) 4- <i>tert</i> -Butylcyclohexanone (3w)	33
¹ H-NMR (300 MHz CDCl ₃) 2-Adamantanone (3x)	34
¹ H-NMR (400 MHz CDCl ₃) Geranial (3y)	35
¹ H-NMR (400 MHz CDCl ₃) 1,1,1-Trifluoroacetophenone (3z)	36
¹³ C-NMR (101 MHz CDCl ₃) Acetophenone (3a)	37
¹³ C-NMR (101 MHz CDCl ₃) 4-Methylacetophenone (3b)	38
¹³ C-NMR (101 MHz CDCl ₃) 1-(4-Methoxyphenyl)ethanone (3c)	39
¹³ C-NMR (101 MHz CDCl ₃) 1-(4-Fluorophenyl)ethanone (3d)	40
¹³ C-NMR (101 MHz CDCl ₃) 4-Chloroacetophenone (3e)	41
¹³ C-NMR (101 MHz CDCl ₃) 4-Nitroacetophenone (3f)	42
¹³ C-NMR (101 MHz CDCl ₃) 1-(4-Trifluoromethylphenyl)ethanone (3g)	43
¹³ C-NMR (101 MHz CDCl ₃) 3-Methylacetophenone (3h)	44
¹³ C-NMR (101 MHz CDCl ₃) 2-Bromoacetophenone (3i)	45
¹³ C-NMR (101 MHz CDCl ₃) 2'-Fluoroacetophenone (3j)	46
¹³ C-NMR (101 MHz CDCl ₃) Benzoylacetylene (3k)	47
¹³ C-NMR (101 MHz CDCl ₃) Benzophenone (3l)	48
¹³ C-NMR (101 MHz CDCl ₃) 2-Acetonaphthone (3m)	49
¹³ C-NMR (101 MHz CDCl ₃) 1-Phenylpropan-1-one (3n)	50
¹³ C-NMR (101 MHz CDCl ₃) 4-Methylbenzaldehyde (3o)	51
¹³ C-NMR (101 MHz CDCl ₃) 4-Nitrobenzaldehyde (3p)	52
¹³ C-NMR (101 MHz CDCl ₃) 3-Methoxybenzaldehyde (3q)	53
¹³ C-NMR (101 MHz CDCl ₃) 2-Bromobenzaldehyde (3r)	54
¹³ C-NMR (101 MHz CDCl ₃) 3,4-Dimethoxybenzaldehyde (3s)	55
¹³ C-NMR (101 MHz CDCl ₃) 3,4,5-Trimethoxybenzaldehyde (3t)	56
¹³ C-NMR (101 MHz CDCl ₃) 6-Chloropicolinaldehyde (3u)	57
¹³ C-NMR (101 MHz CDCl ₃) 2-Octanone (3v)	58
¹³ C-NMR (101 MHz CDCl ₃) 4- <i>tert</i> -Butylcyclohexanone (3w)	59
¹³ C-NMR (75 MHz CDCl ₃) 2-Adamantanone (3x)	60
¹³ C-NMR (101 MHz CDCl ₃) Geranial (3y)	61
¹³ C-NMR (101 MHz CDCl ₃) 1,1,1-Trifluoroacetophenone (3z)	62
¹⁹ F-NMR (376 MHz CDCl ₃) 1-(4-Fluorophenyl)ethanone (3d)	63
¹⁹ F-NMR (376 MHz CDCl ₃) 1-(4-Trifluoromethylphenyl)ethanone (3g)	64
¹⁹ F-NMR (376 MHz CDCl ₃) 2'-Fluoroacetophenone (3j)	65
¹⁹ F-NMR (376 MHz CDCl ₃) 1,1,1-Trifluoroacetophenone (3z)	66

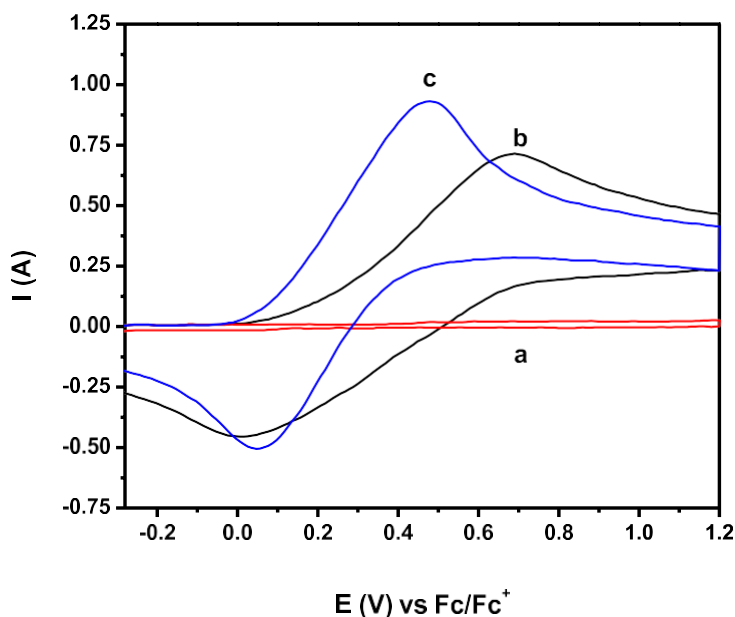
General Considerations

NMR spectra (^1H -, ^{13}C -, and ^{19}F -) were performed at 300 K using either a Bruker Avance Ultra Shield 300 MHz, or Bruker DRX-400 400 MHz spectrometer. ^1H -NMR spectra were referenced to residual CHCl_3 (7.26 ppm) in CDCl_3 . ^{13}C -NMR spectra were referenced to CDCl_3 (77.16 ppm). ^{19}F -NMR spectra were referenced to hexafluorobenzene (-161.64 ppm).¹ Reactions were monitored by ^1H , ^{19}F -NMR, and/or by TLC on silica gel plates (60 Å porosity, 250 μm thickness). TLC analysis was performed using UV light. Electrochemistry reactions were performed using an IKA ElectraSyn 2.0 unit equipped with either a single-vial holder or a carousel.

Chemicals

Deuterated chloroform (CDCl_3) was purchased from Cambridge Isotope Laboratories. Hexafluorobenzene was purchased from Oakwood Chemicals. 4-Acetamido-TEMPO (ACT, **1**) was prepared and recrystallized using a previously reported protocol.² All the alcohols used were purchased from Oakwood Chemicals, Sigma-Aldrich, or Alfa Aesar.

Cyclic Voltammetry

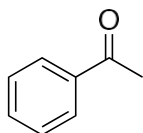


Cyclic voltammograms in 0.1 M LiClO_4 in MeCN solution of (a) 1-phenylethanol (2.0 mmol), (b) ACT (**1**, 0.4 mmol) and (c) 1-phenylethanol (2.0 mmol) + ACT (**1**, 0.4 mmol), at a scan rate of 200 mV s^{-1} . Working electrode: glassy carbon. Pseudo reference electrode: Ag/Ag^+ (ferrocene as internal reference). Counter electrode: Pt plated electrode.

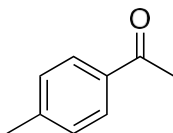
General Procedure for the preparation of Ketones and Aldehydes

Without precautions to exclude air or moisture; alcohol (2 mmol, 1 eq.), ACT (0.4 mmol, 0.2 eq.), lithium perchlorate in acetonitrile (4 mL, 0.1 M), and a stir bar were placed in an ElectraSyn 2.0 vial (5 mL capacity). The ElectraSyn vial cap was equipped with a graphite anode (working electrode) and a Ni cathode (counter electrode) and then secured onto the vial. The reaction mixture was electrolyzed at a constant current of 5 mA until the oxidation was deemed complete by ¹H-NMR spectroscopy monitoring (24 - 48 h). Upon completion, the product mixture was filtered through a pad of silica. The silica was washed with diethyl ether to elute the product. The solvent was then removed from the filtrate under vacuum, affording the pure product.

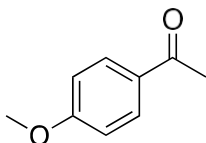
Product characterization



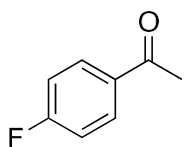
Acetophenone (3a). With a reaction time of 24 hours the product was obtained as a yellow oil (0.23 g, 90%). ¹H-NMR (400 MHz, Chloroform-*d*) δ 8.02 – 7.90 (m, 2H), 7.63 – 7.52 (m, 1H), 7.47 (ddt, *J* = 8.2, 6.7, 1.1 Hz, 2H), 2.61 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 198.17, 137.19, 133.15, 128.62, 128.35, 26.63.³



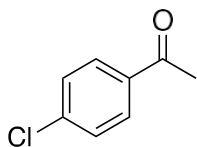
para-Methylacetophenone (3b). With a reaction time of 24 hours the product was obtained as a yellow oil (0.18 g, 66%). ¹H-NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.45 – 6.91 (m, 2H), 2.59 (s, 3H), 2.42 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 197.81, 143.86, 134.75, 129.24, 128.44, 26.51, 21.62.³



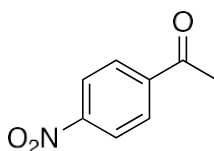
1-(4-Methoxyphenyl)ethanone (3c). With a reaction time of 24 hours the product was obtained as a yellow oil (0.21 g, 71%). ¹H-NMR (400 MHz, CDCl₃) δ 7.95 – 7.86 (m, 2H), 6.95 – 6.84 (m, 2H), 3.84 (s, 3H), 2.53 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 196.77, 163.55, 130.63, 130.41, 113.74, 55.50, 26.36.³



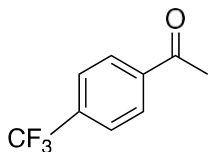
1-(4-Fluorophenyl)ethanone (3d). With a reaction time of 48 hours the product was obtained as a yellow oil (0.24 g, 88%). ¹H-NMR (400 MHz, CDCl₃) δ 8.02 – 7.92 (m, 2H), 7.17 – 7.06 (m, 2H), 2.58 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 196.44, 165.77 (d, *J* = 254.7 Hz), 133.62 (d, *J* = 3.2 Hz), 130.93 (d, *J* = 9.4 Hz), 115.64 (d, *J* = 22.0 Hz), 26.50. ¹⁹F-NMR (376 MHz, CDCl₃) δ -105.26 (ddd, *J* = 13.7, 8.7, 5.4 Hz).⁴



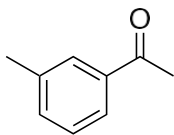
4-Chloroacetophenone (3e). With a reaction time of 24 hours the product was obtained as a yellow oil (0.29 g, 94%). ¹H-NMR (400 MHz, CDCl₃) δ 7.91 – 7.84 (m, 2H), 7.46 – 7.37 (m, 2H), 2.57 (q, *J* = 1.2 Hz, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 196.89, 139.67, 135.57, 129.83, 129.00, 26.64.³



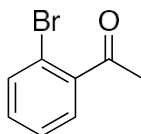
4-Nitroacetophenone (3f). With a reaction time of 48 hours the product was obtained as a yellow solid (0.26 g, 79%). ¹H-NMR (400 MHz, CDCl₃) δ 8.33 – 8.25 (m, 2H), 8.21 – 8.06 (m, 2H), 2.67 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 196.40, 150.46, 141.50, 129.40, 123.94, 27.06.⁵



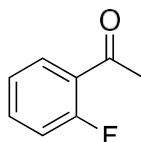
1-(4-Trifluoromethylphenyl)ethanone (3g). With a reaction time of 48 hours the product was obtained as a yellow solid (0.32 g, 84%). ¹H-NMR (400 MHz, CDCl₃) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H), 2.63 (s, 3H). ¹³C-NMR (101 MHz, Chloroform-d) δ 196.96, 139.78, 134.42 (q, *J* = 32.5 Hz), 128.67, 125.69 (q, *J* = 3.8 Hz), 123.69 (q, *J* = 272.5 Hz), 26.71. ¹⁹F-NMR (376 MHz, CDCl₃) δ -62.89. ⁴¹⁹F-NMR (376 MHz, CDCl₃) δ -105.26 (ddd, *J* = 13.7, 8.7, 5.4 Hz).⁴



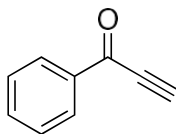
3-Methylacetophenone (3h). With a reaction time of 24 hours the product was obtained as a yellow oil (0.22 g, 84%). ¹H-NMR (400 MHz, CDCl₃) δ 7.80 – 7.69 (m, 2H), 7.41 – 7.30 (m, 2H), 2.59 (s, 3H), 2.41 (d, *J* = 0.8 Hz, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 198.37, 138.36, 137.20, 133.85, 128.79, 128.45, 125.59, 26.66, 21.33.³



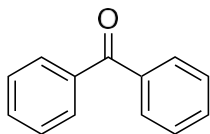
2-Bromoacetophenone (3i). With a reaction time of 24 hours the product was obtained as a yellow oil (0.32 g, 81%). ¹H-NMR (400 MHz, CDCl₃) δ 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.29 (ddd, *J* = 7.9, 7.4, 1.8 Hz, 1H), 2.63 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 201.38, 141.53, 133.86, 131.79, 128.92, 127.45, 118.93, 30.33.³



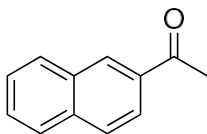
2'-Fluoroacetophenone (3j). With a reaction time of 48 hours the product was obtained as a yellow oil (0.21 g, 76%). ¹H-NMR (400 MHz, CDCl₃) δ 7.86 (td, *J* = 7.6, 1.9 Hz, 1H), 7.50 (dddd, *J* = 8.6, 7.1, 5.0, 1.9 Hz, 1H), 7.28 – 7.16 (m, 1H), 7.12 (ddd, *J* = 11.2, 8.3, 1.1 Hz, 1H), 2.63 (d, *J* = 5.0 Hz, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 195.99 (d, *J* = 3.5 Hz), 162.34 (d, *J* = 254.8 Hz), 134.76 (d, *J* = 9.1 Hz), 130.69 (d, *J* = 2.5 Hz), 125.84 (d, *J* = 12.8 Hz), 124.46 (d, *J* = 3.6 Hz), 116.75 (d, *J* = 23.8 Hz), 31.51 (d, *J* = 7.3 Hz). ¹⁹F-NMR (376 MHz, CDCl₃) δ -109.34 (ddq, *J* = 13.9, 9.8, 4.9 Hz).⁶



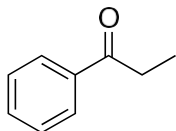
Benzoylacetylene (3k). With a reaction time of 36 hours the product was obtained as a yellow solid (0.18 g, 69%). ¹H NMR (400 MHz, CDCl₃) δ 8.20 – 8.13 (m, 2H), 7.68 – 7.59 (m, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 3.44 (s, 1H). ¹³C-NMR (101 MHz, CDCl₃) δ 177.50, 136.27, 134.63, 129.81, 128.80, 80.90, 80.39.⁷



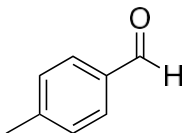
Benzophenone (3l). With a reaction time of 24 hours the product was obtained as a yellow solid (0.34 g, 92%). ¹H-NMR (400 MHz, CDCl₃) δ 7.85 – 7.78 (m, 4H), 7.64 – 7.53 (m, 2H), 7.49 (dd, *J* = 8.4, 7.0 Hz, 4H). ¹³C-NMR (101 MHz, CDCl₃) δ 196.86, 137.75, 132.53, 130.18, 128.40.³



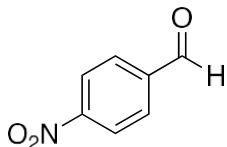
2-Acetonaphthone (3m). With a reaction time of 24 hours the product was obtained as a yellow solid (0.33 g, 97%). ¹H-NMR (400 MHz, CDCl₃) δ 8.44 (d, *J* = 1.8 Hz, 1H), 8.02 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 8.4, 4.4 Hz, 2H), 7.63 – 7.49 (m, 2H), 2.71 (s, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 198.09, 135.64, 134.55, 132.57, 130.23, 129.60, 128.51, 128.46, 127.83, 126.82, 123.94, 26.71.⁷



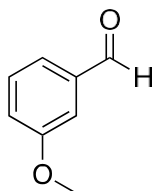
1-Phenylpropan-1-one (3n). With a reaction time of 24 hours the product was obtained as a yellow oil (0.20 g, 74%). ¹H-NMR (400 MHz, CDCl₃) δ 8.00 – 7.92 (m, 2H), 7.58 – 7.50 (m, 1H), 7.45 (dd, *J* = 8.3, 6.9 Hz, 2H), 2.99 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). ¹³C-NMR (101 MHz, CDCl₃) δ 200.88, 137.04, 132.95, 128.64, 128.06, 31.86, 8.33.⁴



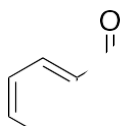
4-Methylbenzaldehyde (3o). With a reaction time of 36 hours the product was obtained as a yellow oil (0.14 g, 58%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 9.95 (s, 1H), 7.79 – 7.73 (m, 2H), 7.31 (d, J = 7.8 Hz, 2H), 2.42 (s, 3H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 192.03, 145.61, 134.30, 129.91, 129.78, 21.93.⁸



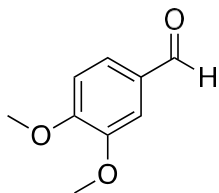
4-Nitrobenzaldehyde (3p). With a reaction time of 48 hours the product was obtained as a yellow solid (0.18 g, 60%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 10.14 (s, 1H), 8.40 – 8.33 (m, 2H), 8.10 – 8.02 (m, 2H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 190.42, 151.20, 140.16, 130.56, 124.37.⁸



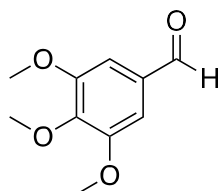
3-Methoxybenzaldehyde (3q). With a reaction time of 24 hours the product was obtained as a yellow oil (0.25 g, 92%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 9.95 (s, 1H), 7.47 – 7.39 (m, 2H), 7.37 (dd, J = 2.8, 1.1 Hz, 1H), 7.15 (dt, J = 6.4, 2.7 Hz, 1H), 3.84 (s, 3H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 192.17, 160.24, 137.91, 130.10, 123.56, 121.55, 112.18, 55.52.⁸



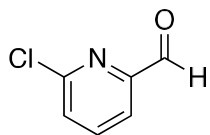
2-Bromobenzaldehyde (3r). With a reaction time of 48 hours the product was obtained as a yellow solid (0.28 g, 75%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 10.35 (s, 1H), 7.93 – 7.82 (m, 1H), 7.77 – 7.58 (m, 1H), 7.44 (tt, J = 6.1, 3.1 Hz, 2H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 191.94, 135.43, 134.00, 133.64, 129.97, 128.02, 127.21.⁸



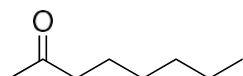
3,4-Dimethoxybenzaldehyde (3s). With a reaction time of 24 hours the product was obtained as a yellow oil (0.29 g, 87%). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 9.84 (s, 1H), 7.50 – 7.37 (m, 2H), 6.97 (d, J = 8.2 Hz, 1H), 3.95 (d, J = 7.6 Hz, 6H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 191.03, 154.58, 149.71, 130.23, 127.02, 110.47, 108.98, 56.30, 56.12.⁹



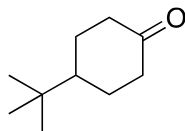
3,4,5-Trimethoxybenzaldehyde (3t). With a reaction time of 24 hours the product was obtained as a yellow solid (0.35 g, 88%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 9.83 (s, 1H), 7.10 (s, 2H), 3.91 (s, 3H), 3.90 (s, 7H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 191.08, 153.72, 143.70, 131.80, 106.80, 61.04, 56.34.¹⁰



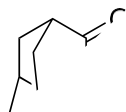
6-Chloropicolinaldehyde (3u). With a reaction time of 48 hours the product was obtained as a yellow solid (0.22 g, 77%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 9.96 (s, 1H), 7.90 – 7.80 (m, 2H), 7.55 (dd, J = 7.1, 1.8 Hz, 1H).¹¹ $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 191.77, 153.00, 152.16, 139.83, 129.05, 120.12. **HRMS (ESI)** m/z calculated for $\text{C}_6\text{H}_4\text{ClNO}$ $[\text{M}+\text{H}]^+$ 142.0060, found 142.0060; and 144.0030, found 144.0035.¹¹



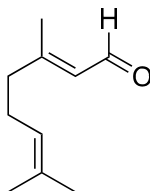
2-Octanone (3v). With a reaction time of 24 hours the product was obtained as a yellow oil (0.14 g, 55%). $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.40 (t, J = 7.4 Hz, 2H), 2.11 (s, 3H), 1.61 – 1.49 (m, 2H), 1.29 – 1.23 (m, 6H), 0.91 – 0.79 (m, 3H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 209.42, 43.92, 31.70, 29.92, 28.96, 23.95, 22.60, 14.11.¹²



4-*tert*-Butylcyclohexanone (3w). With a reaction time of 24 hours the product was obtained as a yellow solid (0.25 g, 79%). **¹H-NMR** (400 MHz, CDCl₃) δ 2.42 – 2.32 (m, 2H), 2.34 – 2.20 (m, 2H), 2.11 – 2.01 (m, 2H), 1.50 – 1.34 (m, 3H), 0.89 (s, 9H). **¹³C-NMR** (101 MHz, CDCl₃) δ 212.58, 46.81, 41.40, 32.56, 27.70.¹³



2-Adamantanone (3x). With a reaction time of 24 hours the product was obtained as a yellow solid (0.24 g, 80%). **¹H-NMR** (300 MHz, CDCl₃) δ 2.51 (s, 2H), 2.14 – 1.84 (m, 12H). **¹³C-NMR** (75 MHz, CDCl₃) δ 218.62, 47.05, 39.33, 36.37, 27.52.¹⁴

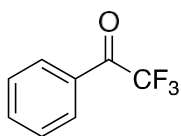


Geranial (3y). With a reaction time of 24 hours the product was obtained as a yellow oil (0.18 g, 59%). **¹H-NMR** (400 MHz, CDCl₃) δ 9.98 (d, *J* = 8.1 Hz, 1H), 5.90 – 5.82 (m, 1H), 5.06 (td, *J* = 6.1, 3.4 Hz, 1H), 2.26 – 2.17 (m, 4H), 2.16 (d, *J* = 1.3 Hz, 3H), 1.68 (s, 3H), 1.60 (s, 3H). **¹³C-NMR** (101 MHz, CDCl₃) δ 191.41, 163.92, 133.05, 127.55, 122.70, 40.73, 25.87, 25.76, 17.83, 17.70.¹⁵

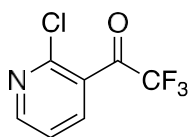
General Procedure for the preparation of Trifluoromethyl Ketones

Without precautions to exclude air or moisture; alcohol (2 mmol, 1 eq.), ACT (0.4 mmol, 0.2 eq.), lithium perchlorate in acetonitrile (4 mL, 0.1 M), and a stir bar were placed in an ElectraSyn vial (5 mL). The ElectraSyn vial cap was equipped with a graphite anode (working electrode) and a Ni cathode (counter electrode) and then secured onto the vial. The reaction mixture was electrolyzed at a constant current of 5 mA for 48 h. The product mixture was quenched with deionized water (50 mL), transferred to a separatory funnel, and extracted with Et₂O (3 x 30 mL). The combined organics were washed with 1 M HCl (30 mL) and brine (30 mL), then dried over sodium sulfate and the solvent removed in vacuo to afford the pure trifluoromethyl ketone.

Product characterization



1,1,1-Trifluoroacetophenone (3z). With a reaction time of 48 hours the product was obtained as a yellow oil (0.21 g, 61%). ¹H-NMR (400 MHz, CDCl₃) δ 8.12 (d, *J* = 7.6 Hz, 2H), 7.76 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 2H). ¹³C-NMR (101 MHz, CDCl₃) δ 179.73 (q, *J* = 35.0 Hz), 134.79, 129.34, 129.17, 128.37, 115.91 (q, *J* = 291.1 Hz). ¹⁹F-NMR (376 MHz, CDCl₃) δ -71.20.¹²



2-Chloro-3-trifluoroacetyl-pyridine (3aa). With a reaction time of 48 hours the product was obtained with a 83% conversion via ¹H NMR .

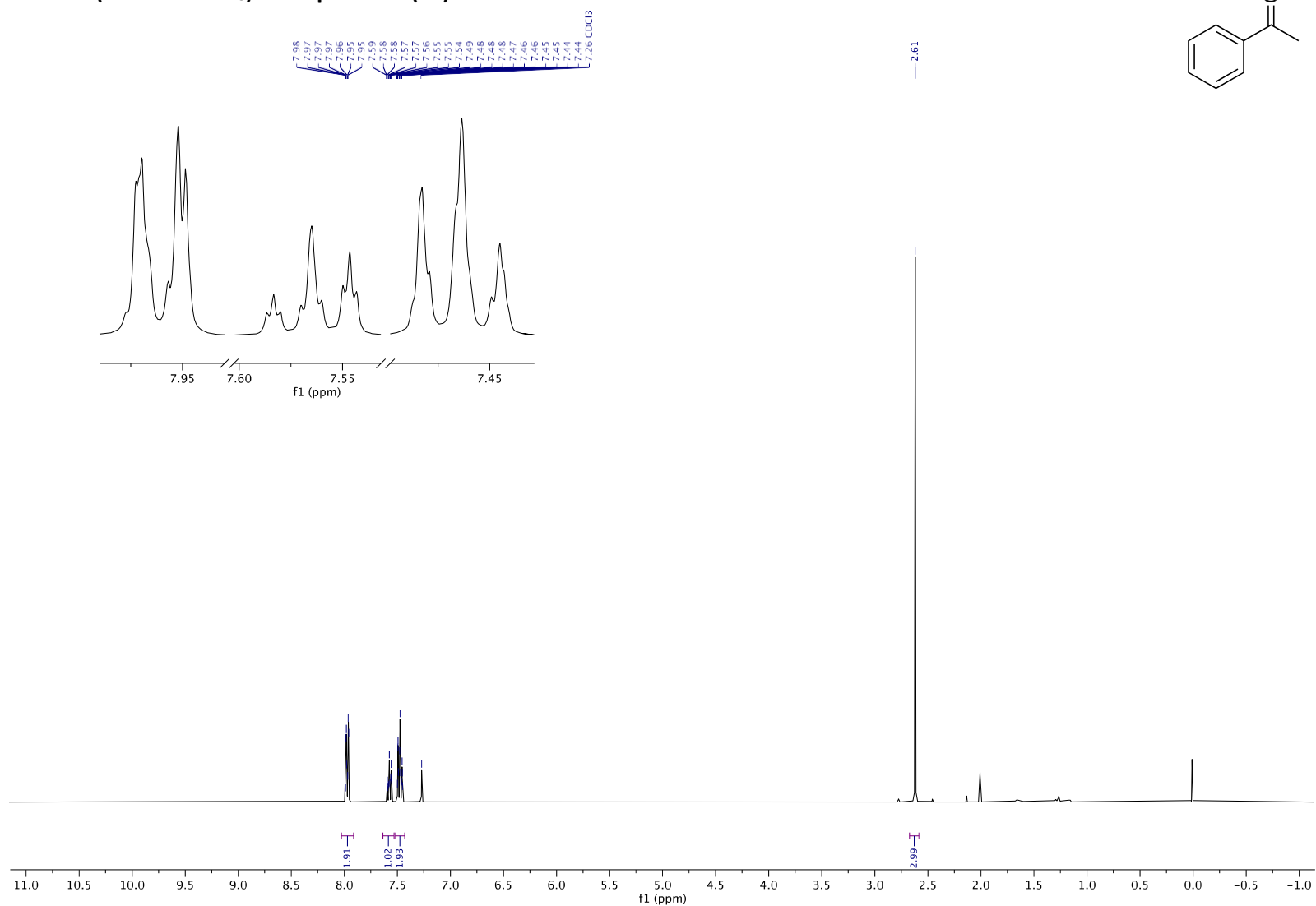
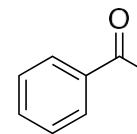
References

- (1) Rosenau, C. P.; Jelier, B. J.; Gossert, A. D.; Togni, A. Exposing the Origins of Irreproducibility in Fluorine NMR Spectroscopy. *Angew. Chem. Int. Ed.* **2018**, *57* (30), 9528–9533. <https://doi.org/10.1002/anie.201802620>.
- (2) Mercadante, M. A.; Kelly, C. B.; Bobbitt, J. M.; Tilley, L. J.; Leadbeater, N. E. Synthesis of 4-Acetamido-2,2,6,6-Tetramethylpiperidine-1-Oxoammonium Tetrafluoroborate and 4-Acetamido-(2,2,6,6-Tetramethyl-Piperidin-1-Yl)Oxyl and Their Use in Oxidative Reactions. *Nat. Protoc.* **2013**, *8* (4), 666–676. <https://doi.org/10.1038/nprot.2013.028>.
- (3) Zhong, J.; Zhou, W.; Yan, X.; Xia, Y.; Xiang, H.; Zhou, X. Selective Activation of Unstrained C(O)–C Bond in Ketone Suzuki–Miyaura Coupling Reaction Enabled by Hydride-Transfer Strategy. *Org. Lett.* **2022**, *24* (6), 1372–1377. <https://doi.org/10.1021/acs.orglett.2c00110>.
- (4) Gu, J.; Wan, Y.; Ma, H.; Zhu, H.; Bu, H.; Zhou, Y.; Zhang, W.; Wu, Z.-G.; Li, Y. Ferric Ion Concentration-Controlled Aerobic Photo-Oxidation of Benzylic C–H Bond with High Selectivity and Conversion. *Tetrahedron* **2021**, *93*, 132298. <https://doi.org/10.1016/j.tet.2021.132298>.
- (5) Yang, Y.-M.; Yan, W.; Hu, H.-W.; Luo, Y.; Tang, Z.-Y.; Luo, Z. Photoinduced Acetylation of Anilines under Aqueous and Catalyst-Free Conditions. *J. Org. Chem.* **2021**, *86* (17), 12344–12353. <https://doi.org/10.1021/acs.joc.1c01290>.
- (6) Wu, Q.; Mao, Y.-J.; Zhou, K.; Wang, S.; Chen, L.; Xu, Z.-Y.; Lou, S.-J.; Xu, D.-Q. Pd-Catalysed Direct C(Sp²)–H Fluorination of Aromatic Ketones: Concise Access to Anacetrapib. *Chem. Commun.* **2021**, *57* (37), 4544–4547. <https://doi.org/10.1039/D1CC01047F>.
- (7) Zhao, Y.; Li, Y.; Shen, Z.; Hu, X.; Hu, B.; Jin, L.; Sun, N.; Li, M. 3-BocNH-ABNO-Catalyzed Aerobic Oxidation of Alcohol at Room Temperature and Atmospheric Pressure. *Tetrahedron Lett.* **2019**, *60* (35), 150994. <https://doi.org/10.1016/j.tetlet.2019.150994>.
- (8) You, S.; Zhang, R.; Cai, M. A Magnetically Recyclable Palladium-Catalyzed Formylation of Aryl Iodides with Formic Acid as CO Source: A Practical Access to Aromatic Aldehydes. *Synthesis* **2021**, *53* (11), 1962–1970. <https://doi.org/10.1055/s-0040-1706621>.
- (9) Guan, R.; L. Bennett, E.; Huang, Z.; Xiao, J. Decarboxylative Oxygenation of Carboxylic Acids with O₂ via a Non-Heme Manganese Catalyst. *Green Chem.* **2022**, *24* (7), 2946–2952. <https://doi.org/10.1039/D1GC04603A>.
- (10) Azeez, S.; Sureshbabu, P.; Sabiah, S.; Kandasamy, J. Controlled Reduction of Activated Primary and Secondary Amides into Aldehydes with Diisobutylaluminum Hydride. *Org. Biomol. Chem.* **2022**, *20* (10), 2048–2053. <https://doi.org/10.1039/D1OB02414K>.
- (11) Ashimori, A.; Ono, T.; Uchida, T.; Ohtaki, Y.; Fukaya, C.; Watanabe, M.; Yokoyama, K. Novel 1, 4-Dihydropyridine Calcium Antagonists. I. : Synthesis and Hypotensive Activity of 4-(Substituted Pyridyl)-1, 4-Dihydropyridine Derivatives. *Chem. Pharm. Bull. (Tokyo)* **1990**, *38* (9), 2446–2458. <https://doi.org/10.1248/cpb.38.2446>.
- (12) Miller, S. A.; Bisset, K. A.; Leadbeater, N. E.; Eddy, N. A. Catalytic Oxidation of Alcohols Using a 2,2,6,6-Tetramethylpiperidine-N-Hydroxyammonium Cation. *Eur. J. Org. Chem.* **2019**, *2019* (6), 1413–1417. <https://doi.org/10.1002/ejoc.201801718>.
- (13) Huang, Z.; Guan, R.; Shanmugam, M.; Bennett, E. L.; Robertson, C. M.; Brookfield, A.; McInnes, E. J. L.; Xiao, J. Oxidative Cleavage of Alkenes by O₂ with a Non-Heme Manganese Catalyst. *J. Am. Chem. Soc.* **2021**, *143* (26), 10005–10013. <https://doi.org/10.1021/jacs.1c05757>.
- (14) Miller, S. A.; León Sandoval, A.; Leadbeater, N. E. N. E. Oxidation of Alcohols Using an Oxoammonium Salt Bearing the Nitrate Anion. *Tetrahedron Lett.* **2019**, *61* (6), 151464. <https://doi.org/10.1016/j.tetlet.2019.151464>.
- (15) *Oxidation of Alcohols to Carbonyl Compounds with Diisopropyl Azodicarboxylate Catalyzed by Nitroxyl Radicals | The Journal of Organic Chemistry.* <https://pubs.acs.org/doi/full/10.1021/jo300088b> (accessed 2022-06-29).

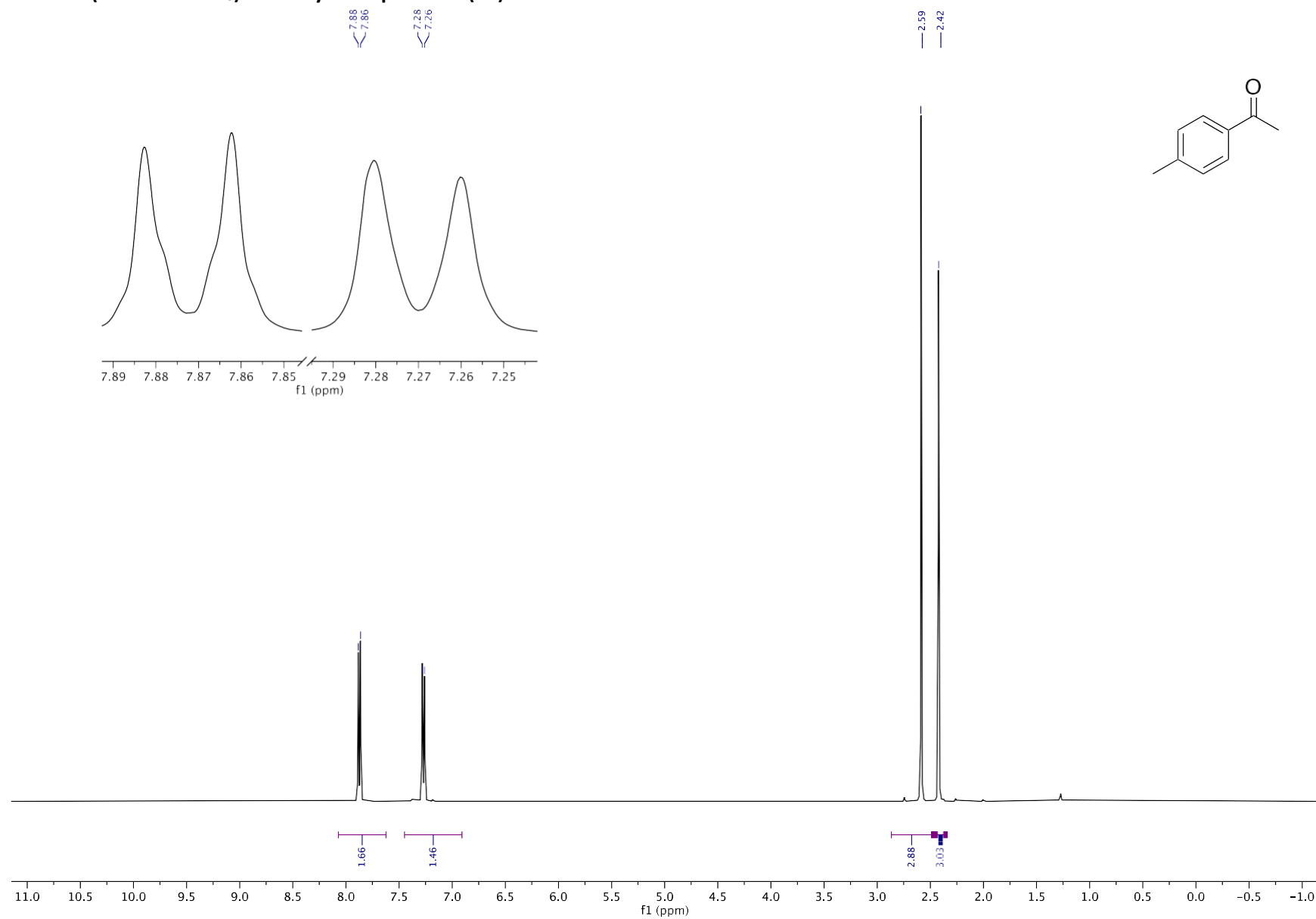
- (16) Pistritto, V. A.; Paolillo, J. M.; Bisset, K. A.; Leadbeater, N. E. Oxidation of α -Trifluoromethyl and Non-Fluorinated Alcohols *via* the Merger of Oxoammonium Cations and Photoredox Catalysis. *Org. Biomol. Chem.* **2018**, *16* (25), 4715–4719. <https://doi.org/10.1039/C8OB01063C>.

^1H -, ^{13}C -, and ^{19}F -NMR spectra of synthesized compounds

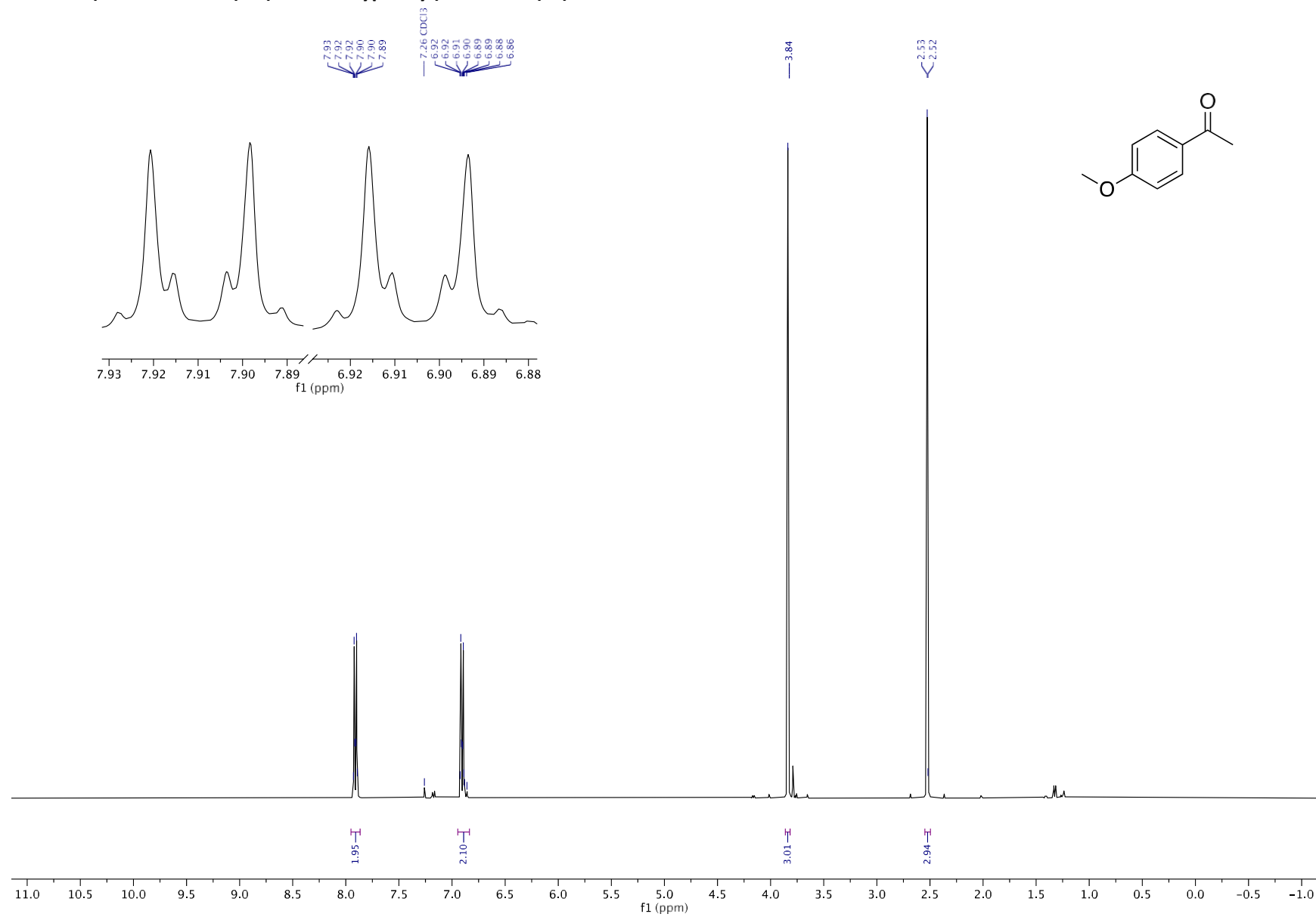
^1H -NMR (400MHz CDCl_3) Acetophenone (3a)



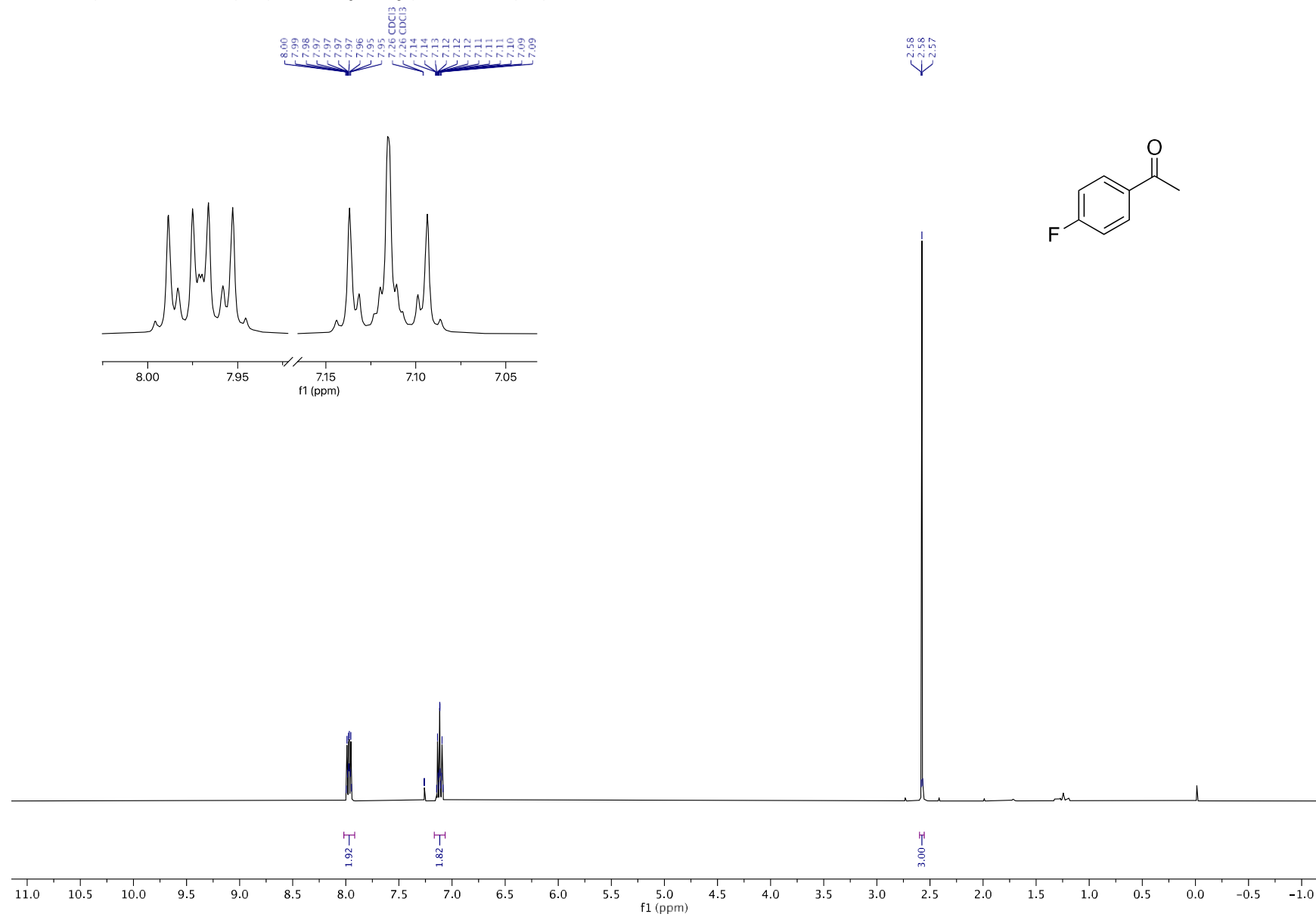
¹H-NMR (400 MHz CDCl₃) 4-Methylacetophenone (3b)



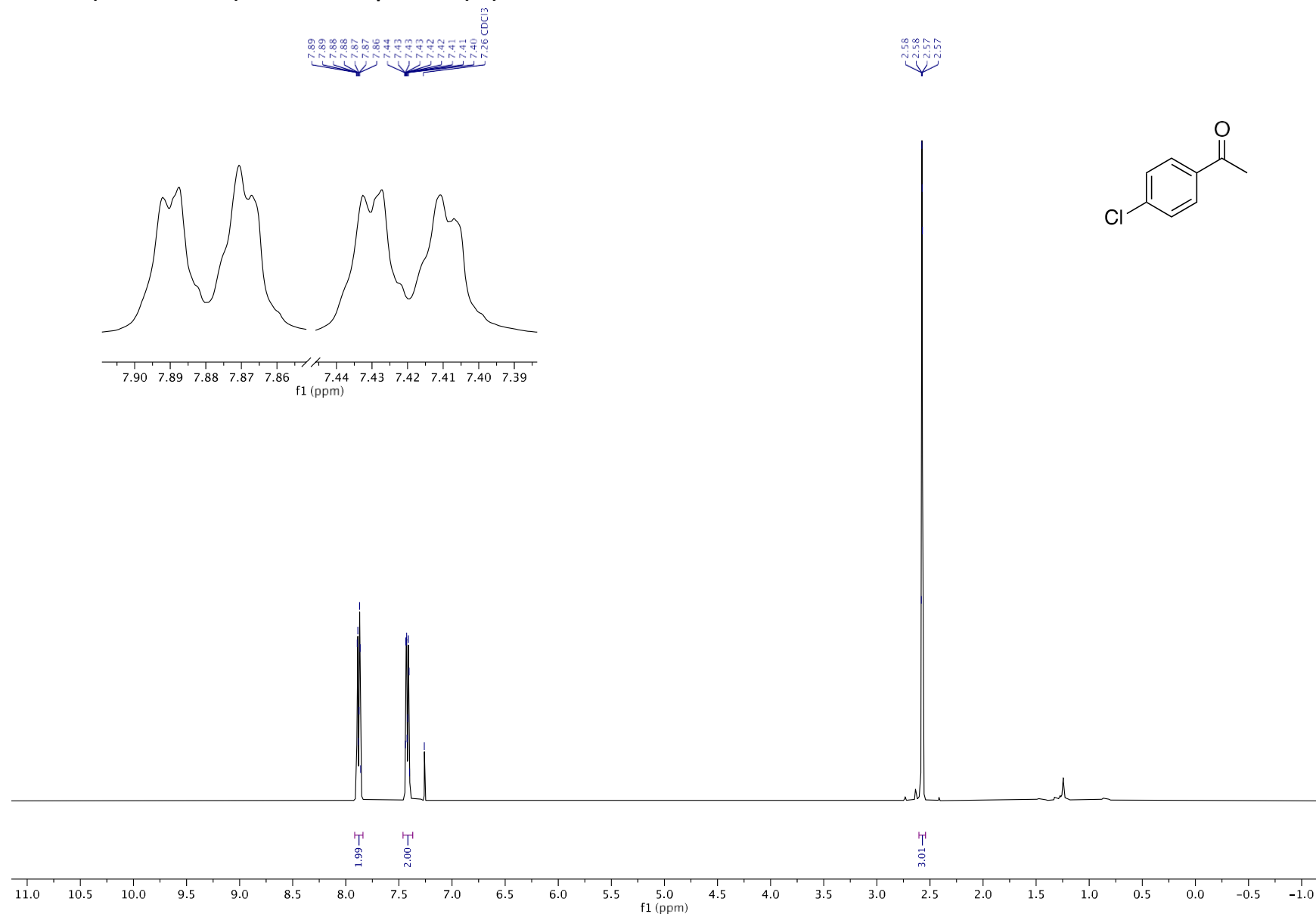
¹H-NMR (400 MHz CDCl₃) 1-(4-Methoxyphenyl)ethanone (3c)



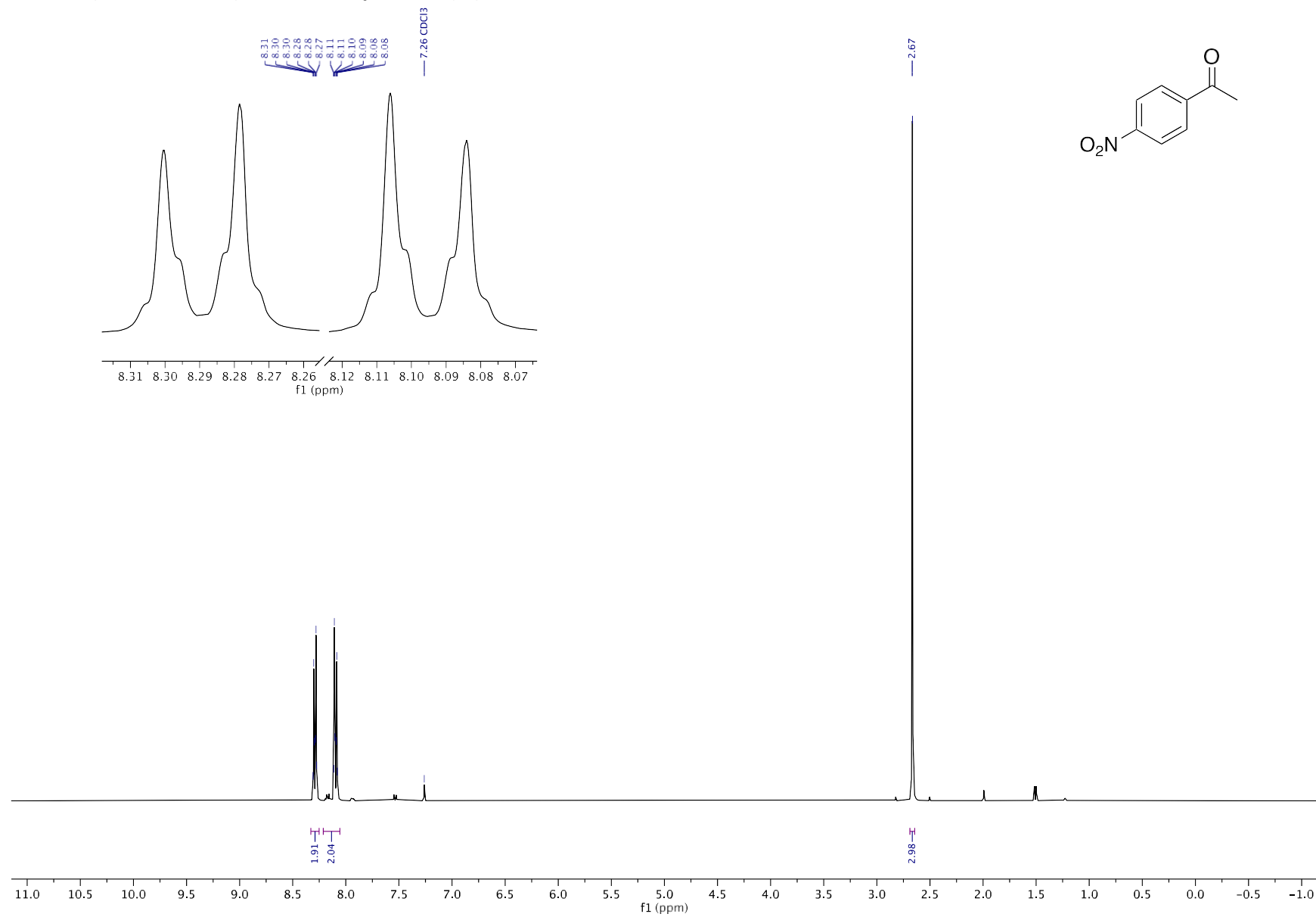
¹H-NMR (400 MHz CDCl₃) 1-(4-Fluorophenyl)ethanone (3d)



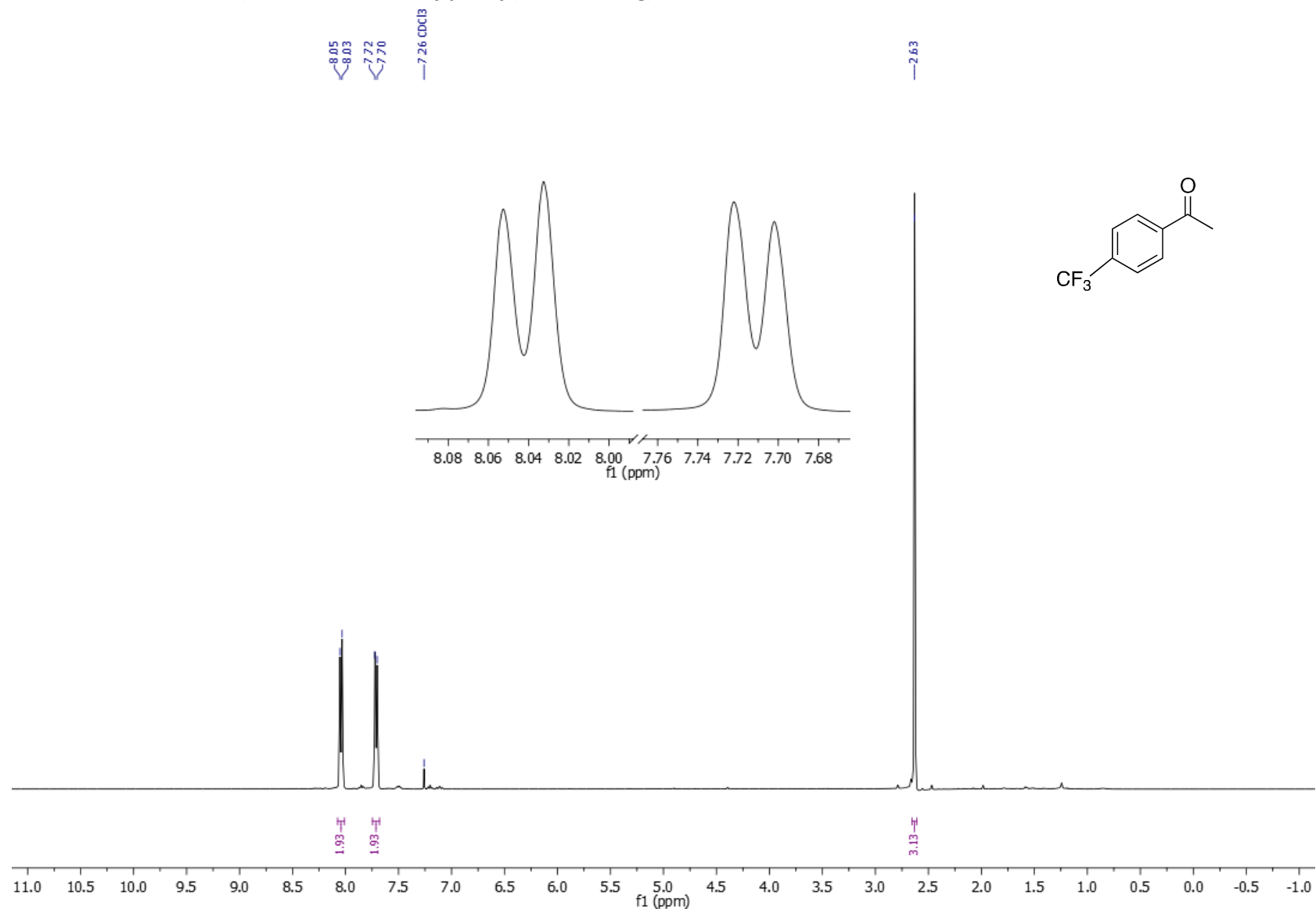
¹H-NMR (400 MHz CDCl₃) 4-Chloroacetophenone (3e)



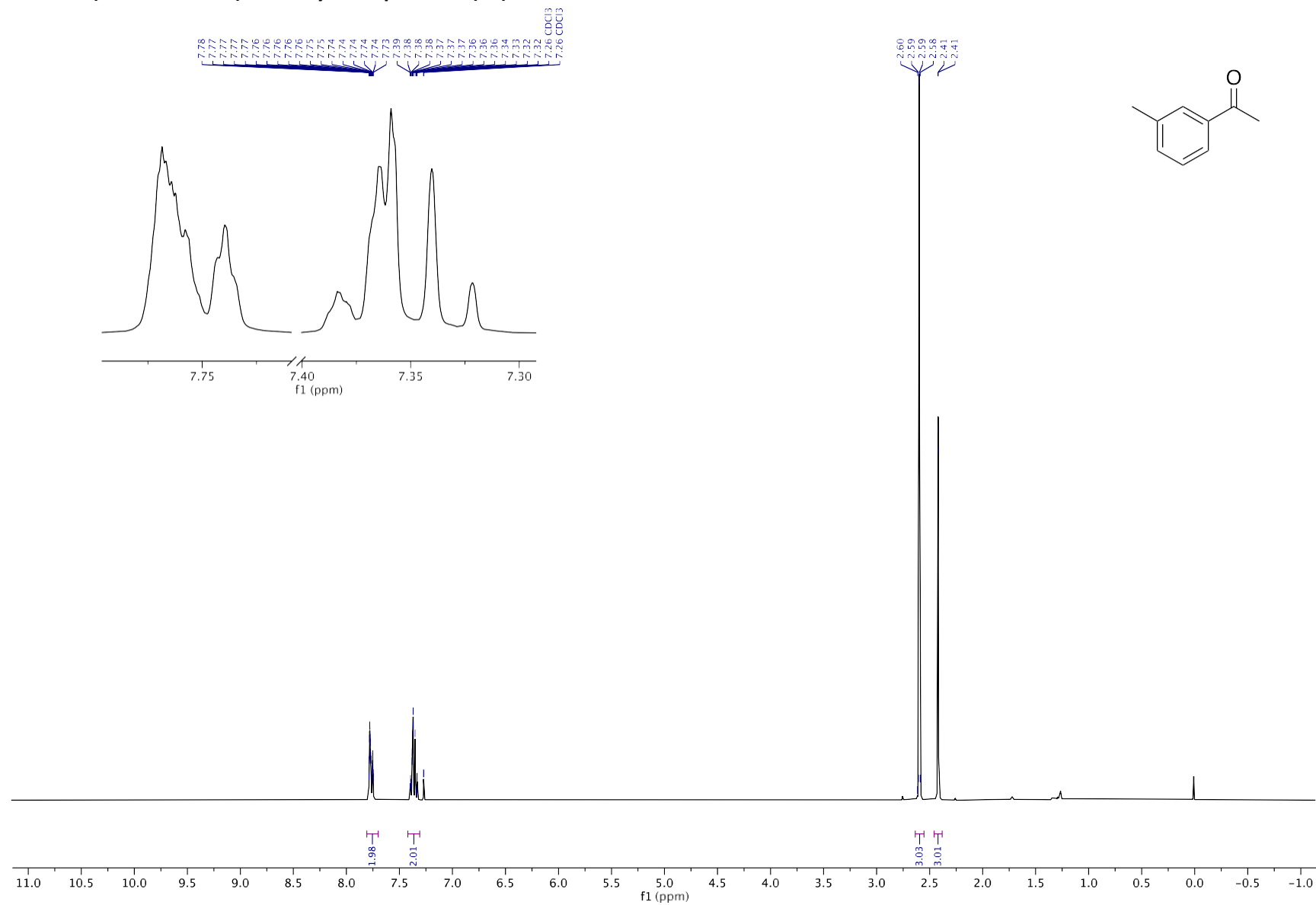
¹H-NMR (400 MHz CDCl₃) 4-Nitroacetophenone (3f)



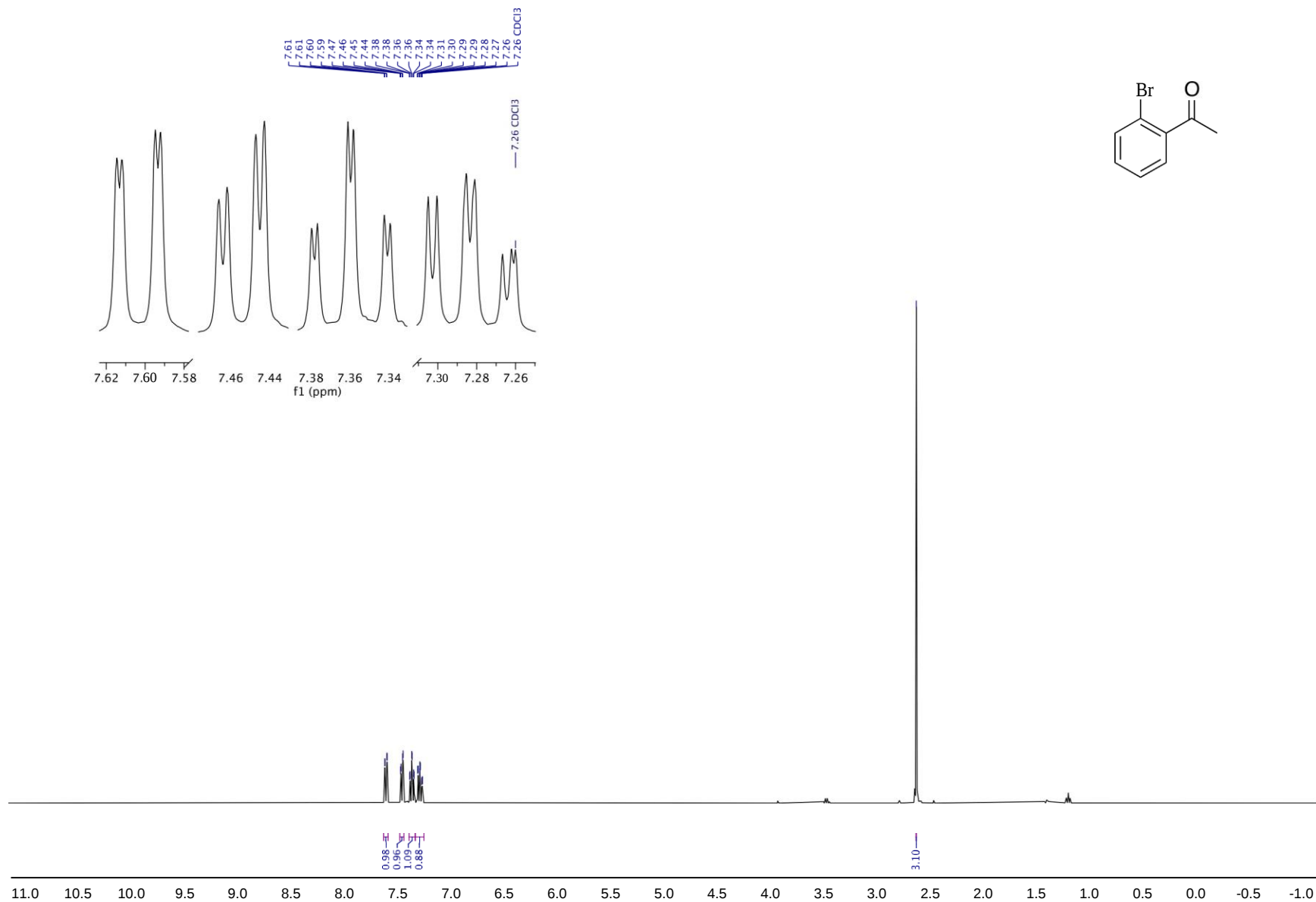
¹H-NMR (400 MHz CDCl₃) 1-(4-Trifluoromethylphenyl)ethanone (3g)



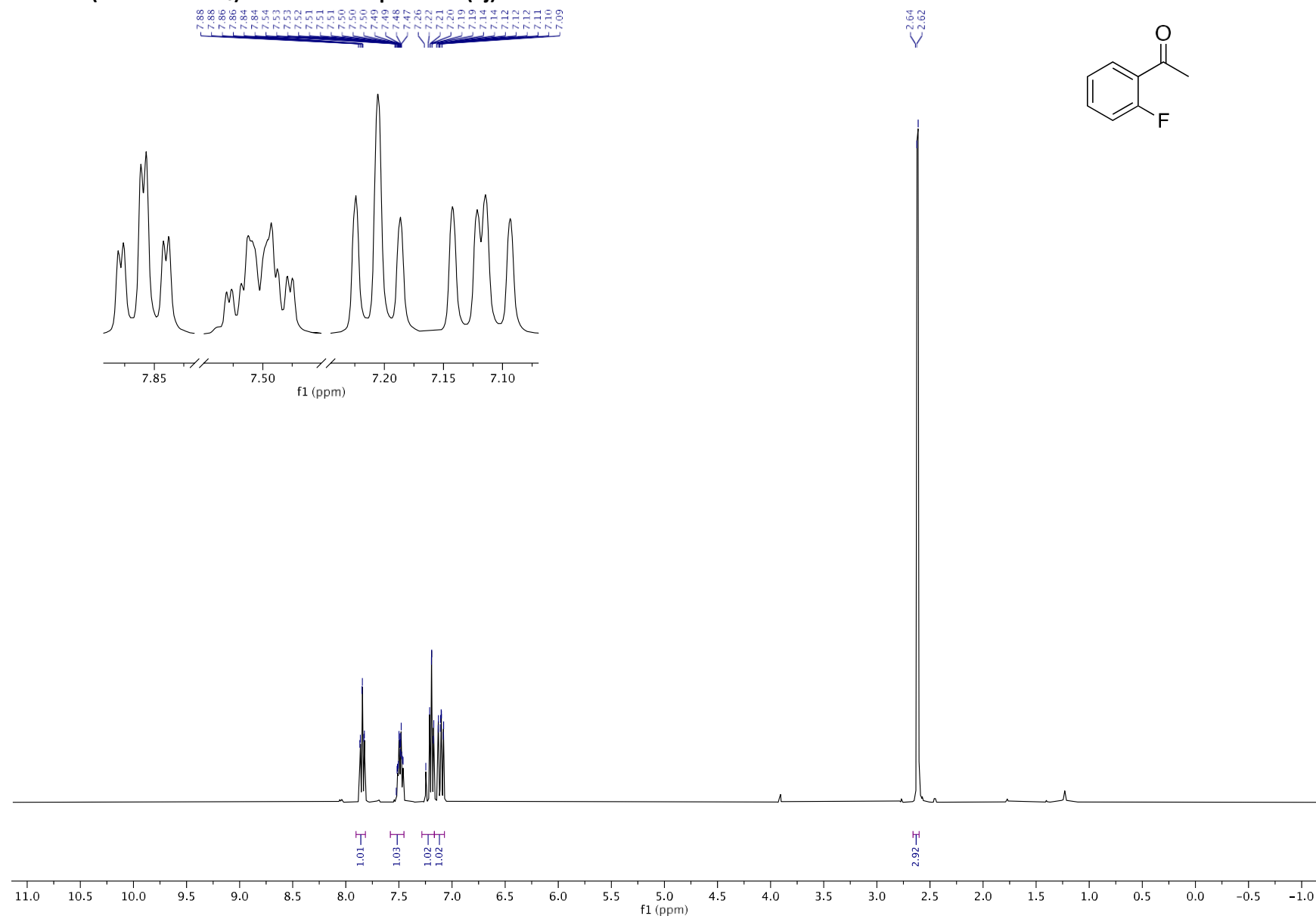
¹H-NMR (400 MHz CDCl₃) 3-Methylacetophenone (3h)



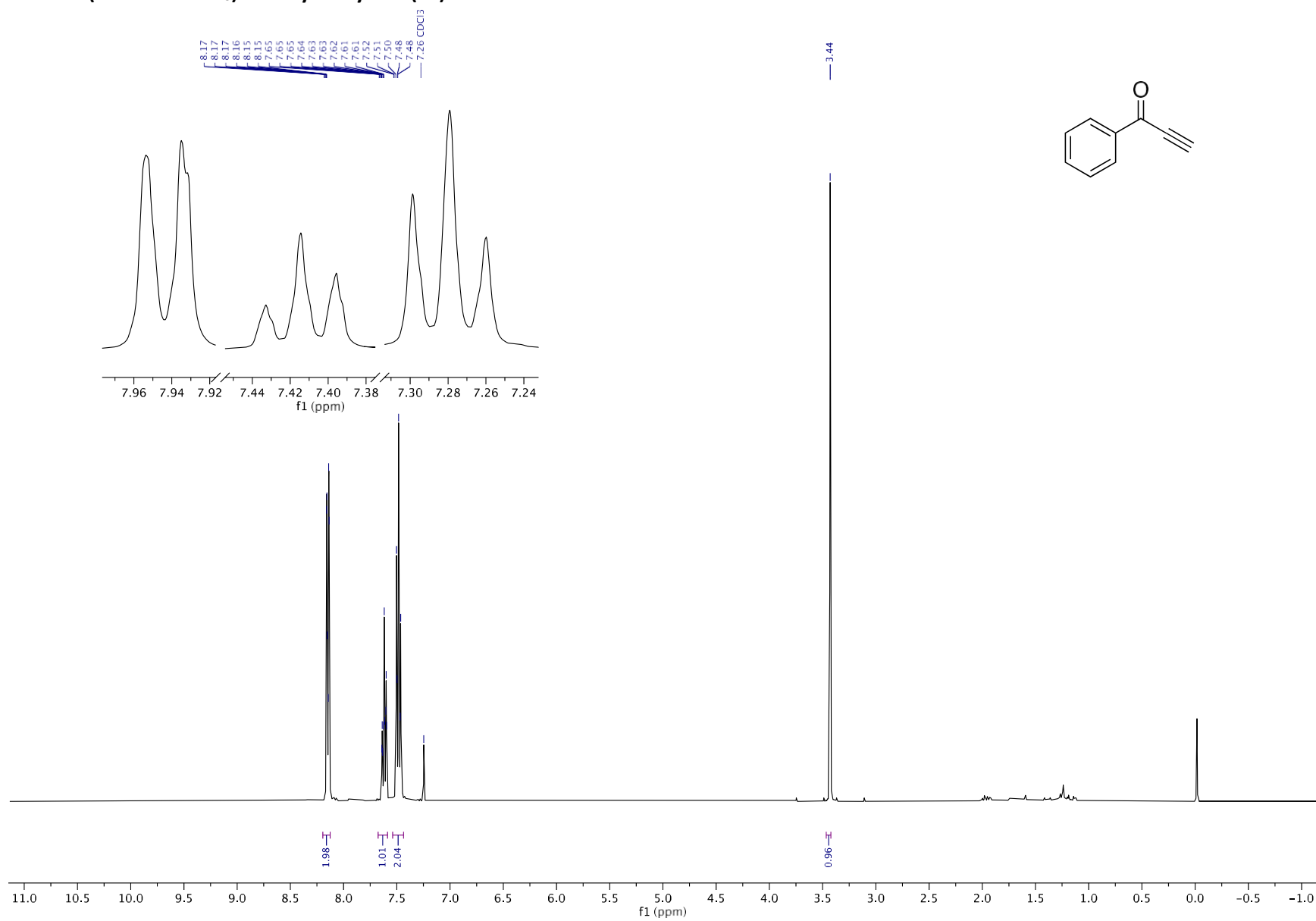
^1H -NMR (400 MHz CDCl_3) 2-Bromoacetophenone (3i)



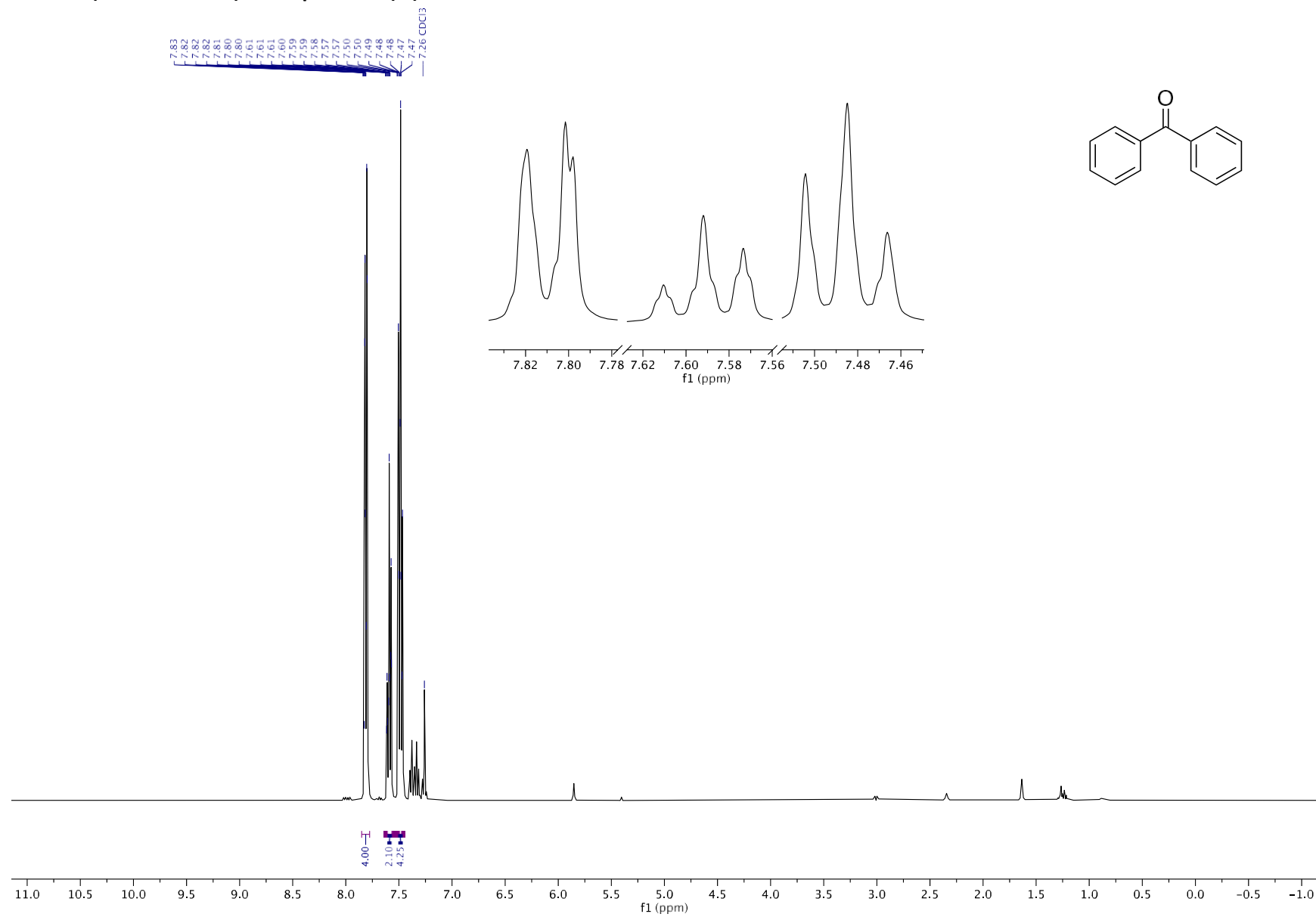
¹H-NMR (400 MHz CDCl₃) 2'-Fluoroacetophenone (3j)



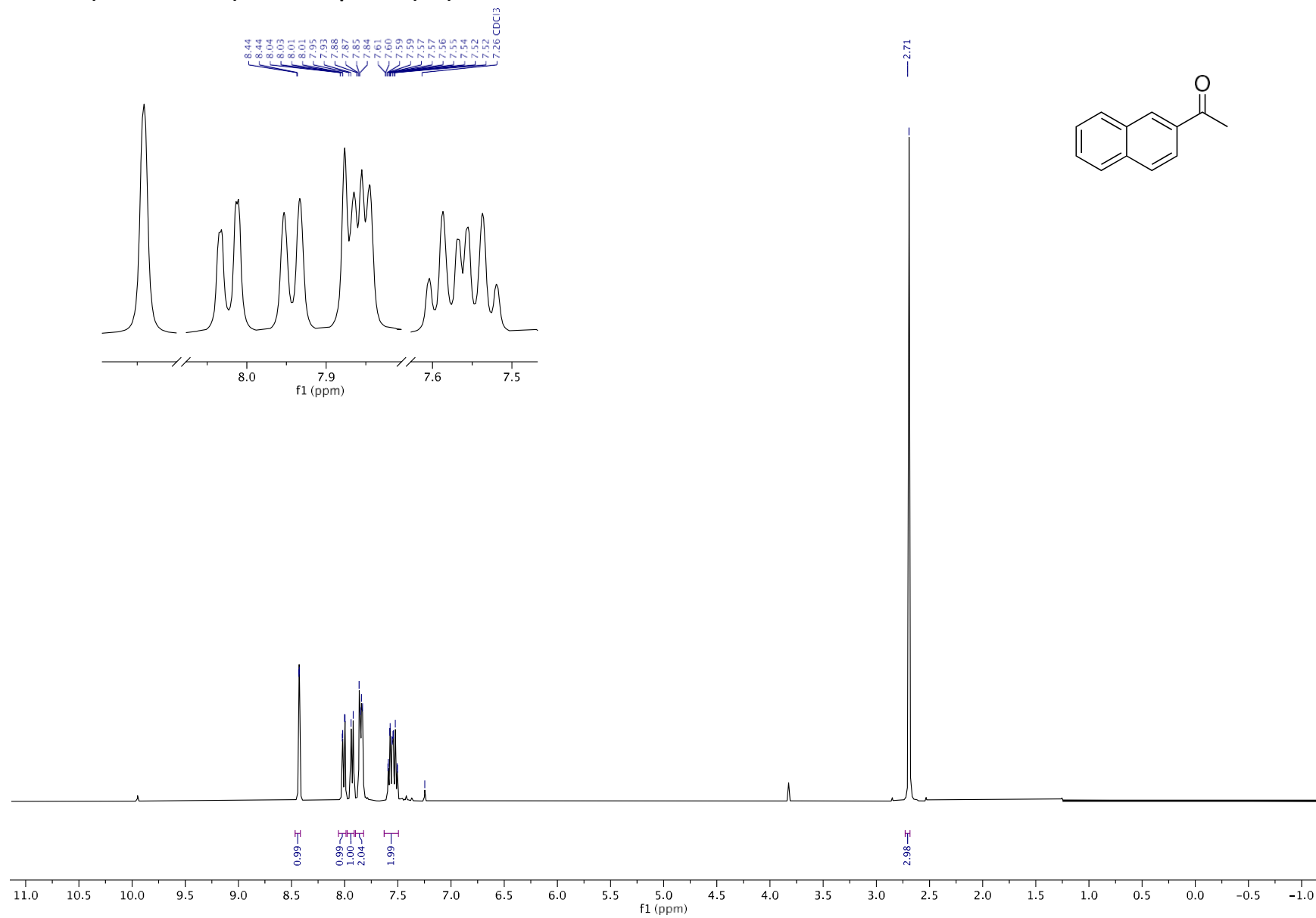
¹H-NMR (400 MHz CDCl₃) Benzoylacetylene (3k)



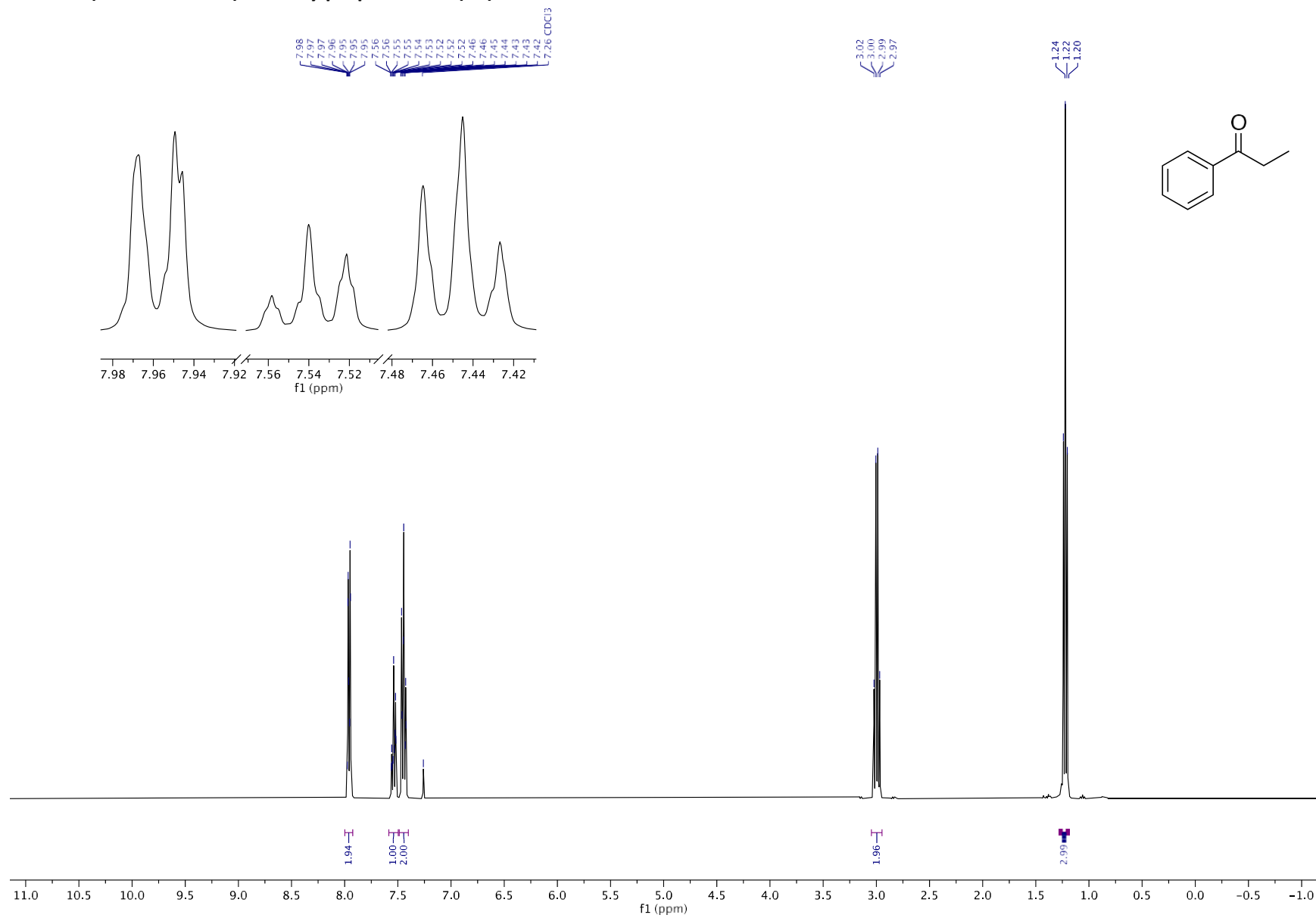
¹H-NMR (400 MHz CDCl₃) Benzophenone (3l)



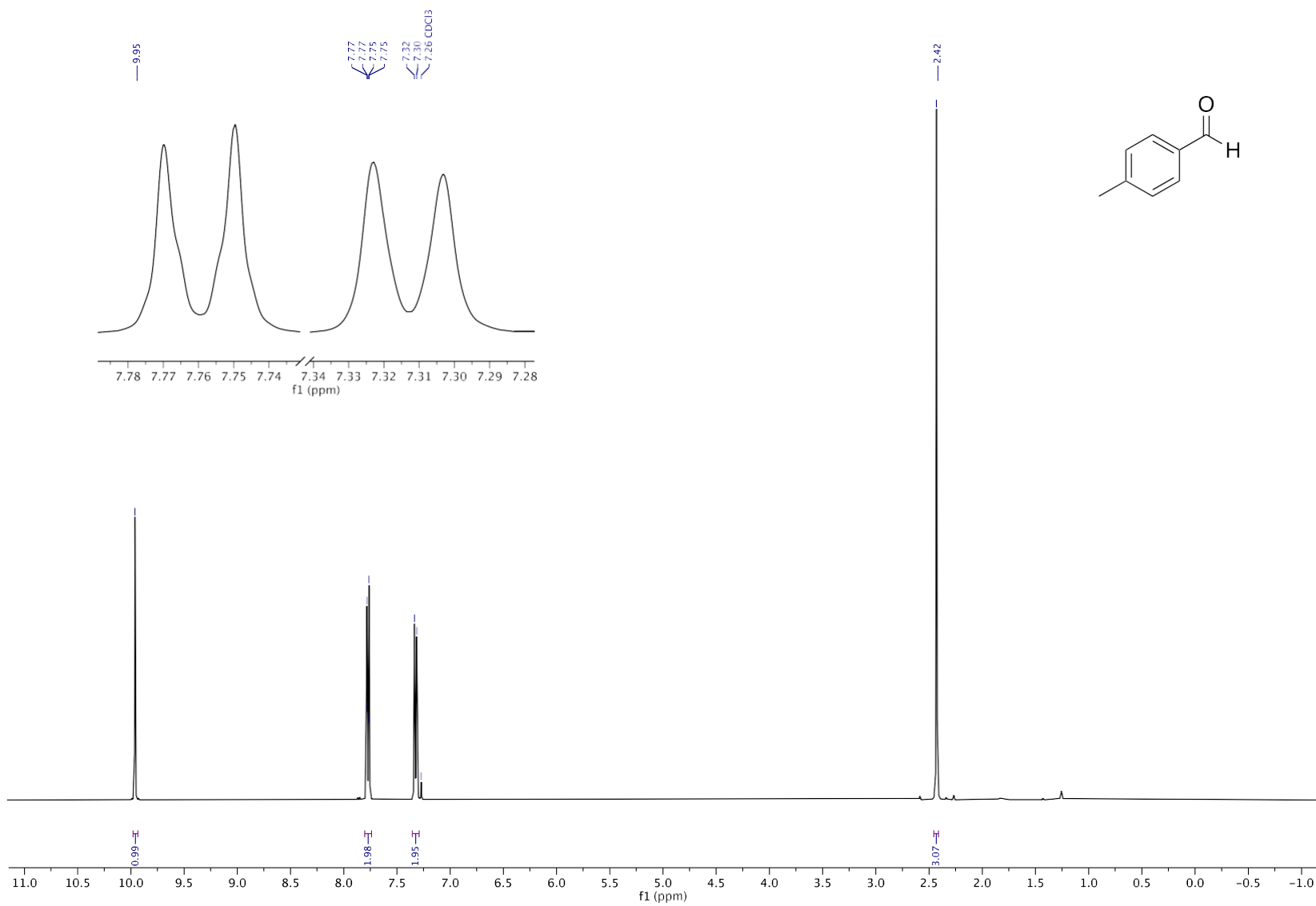
¹H-NMR (400 MHz CDCl₃) 2-Acetonaphthone (3m)



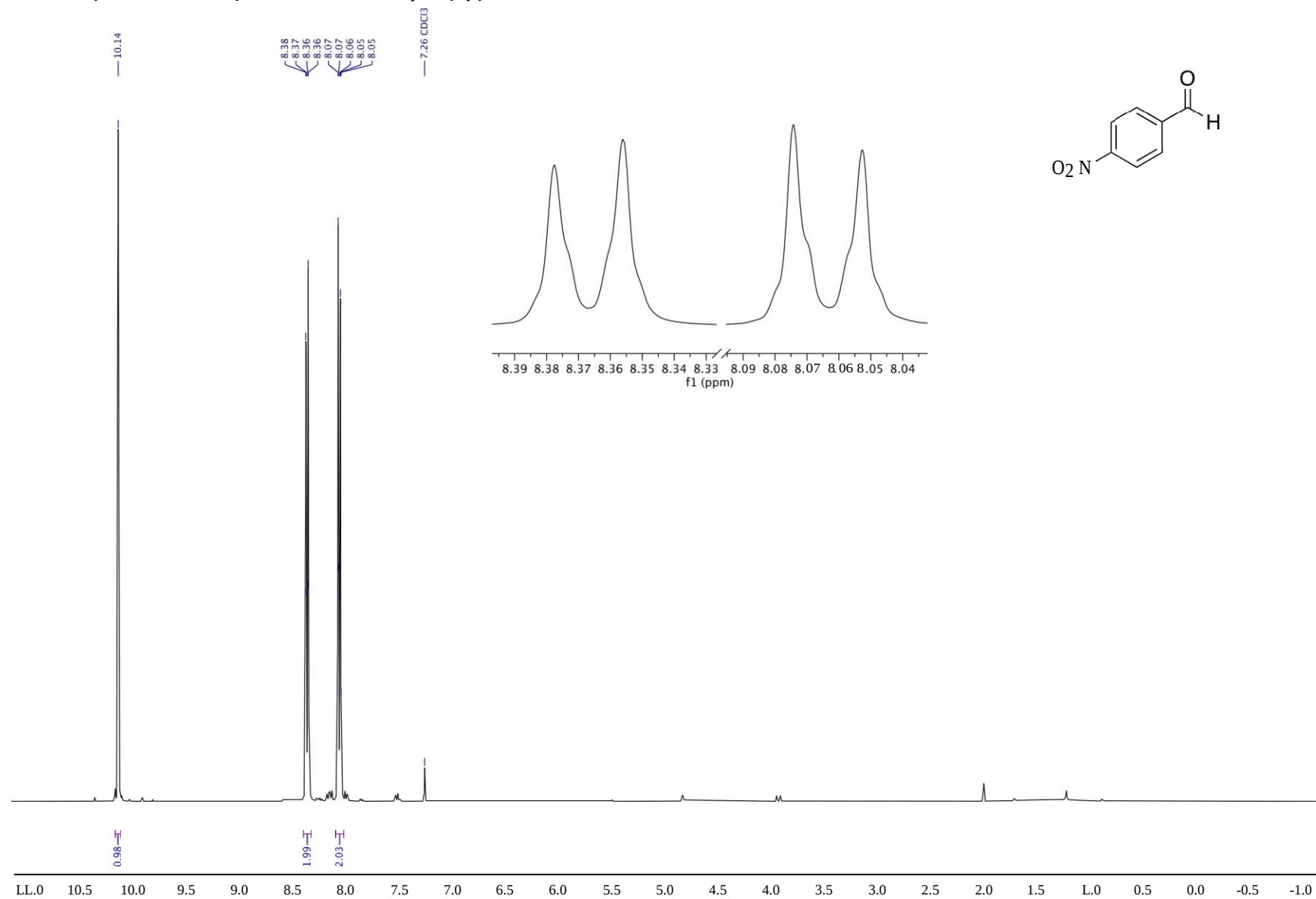
¹H-NMR (400 MHz CDCl₃) 1-Phenylpropan-1-one (3n)



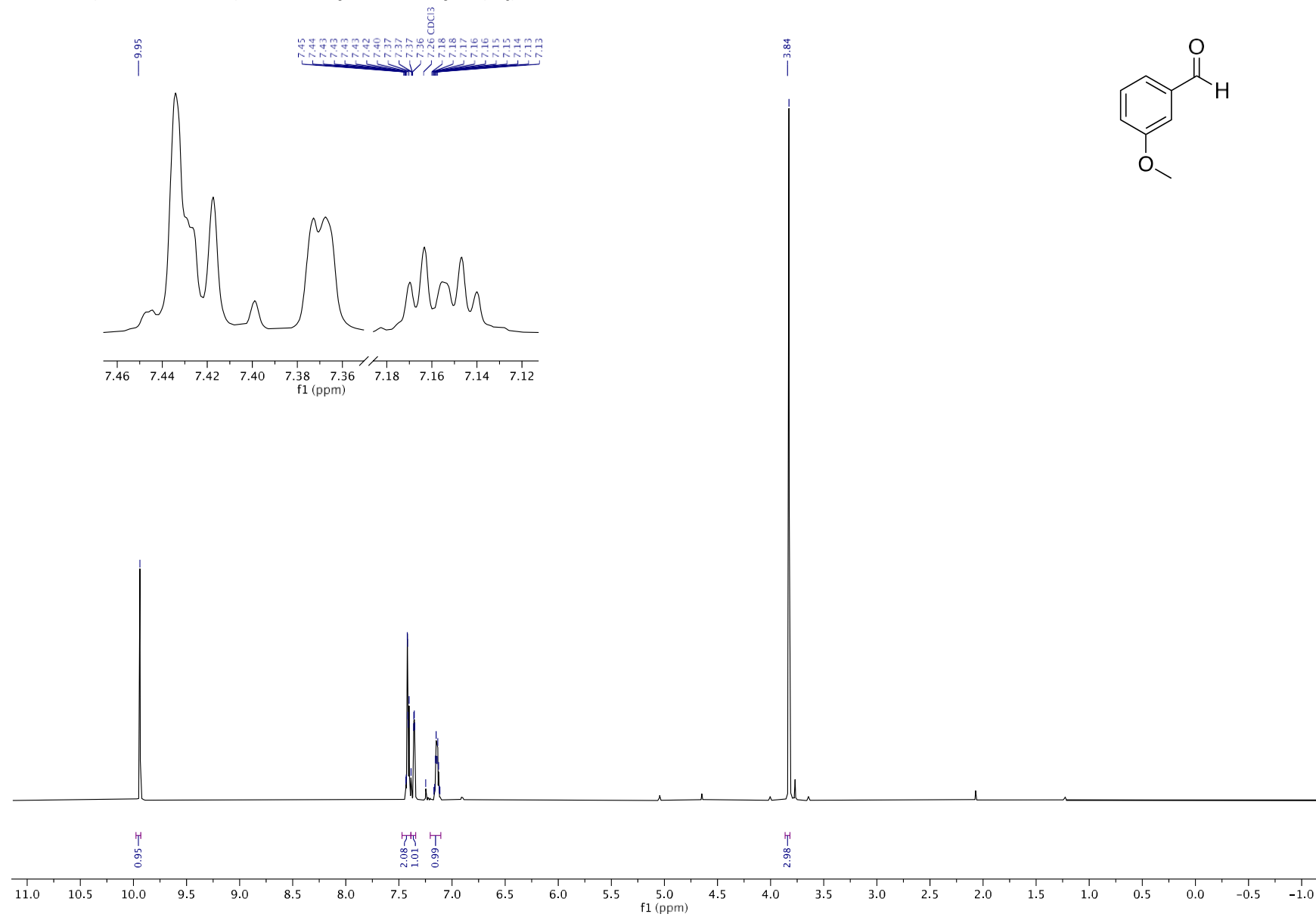
¹H-NMR (400 MHz CDCl₃) 4-Methylbenzaldehyde (3o)



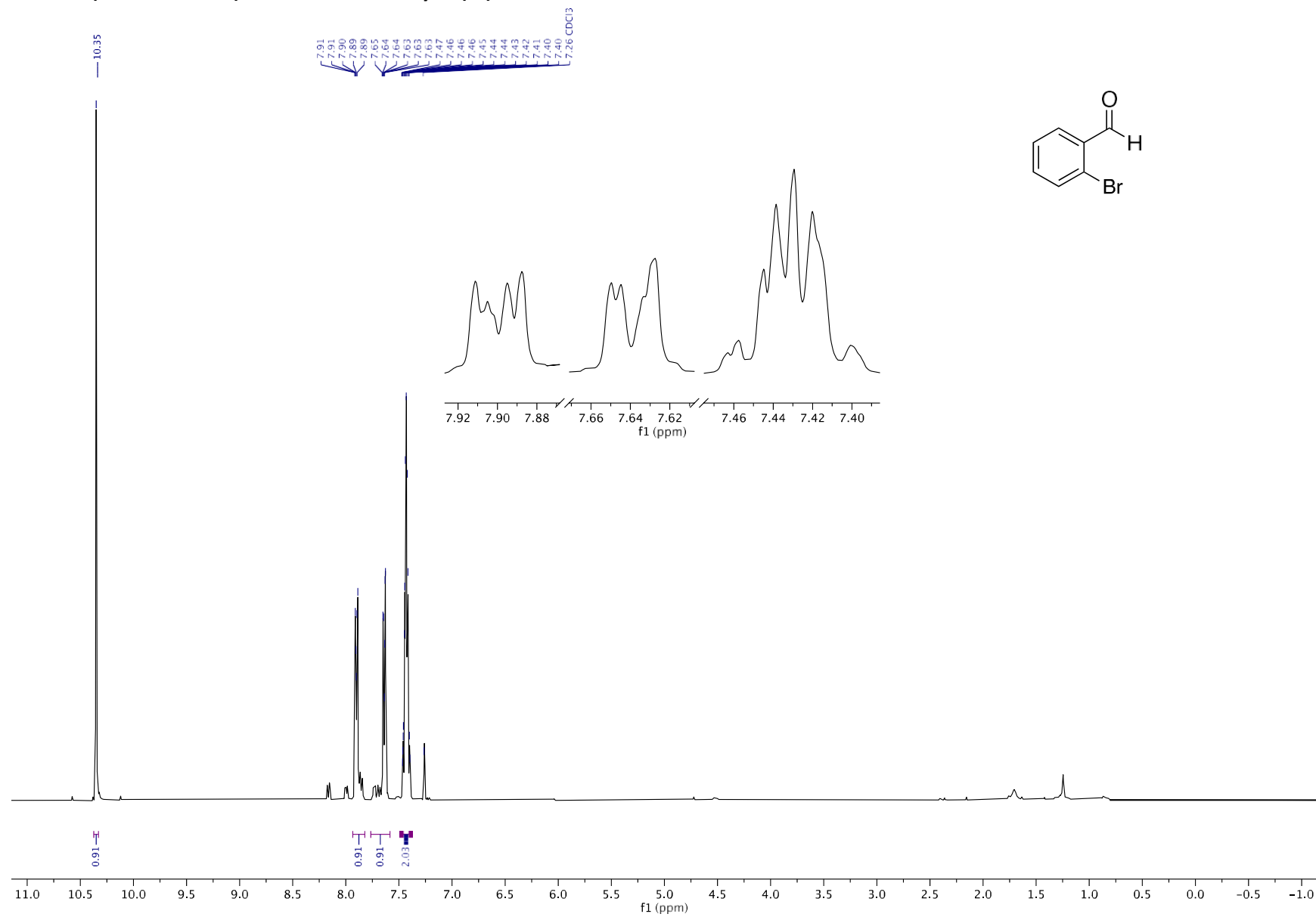
¹H-NMR (400 MHz CDCl₃) 4-Nitrobenzaldehyde (3p)



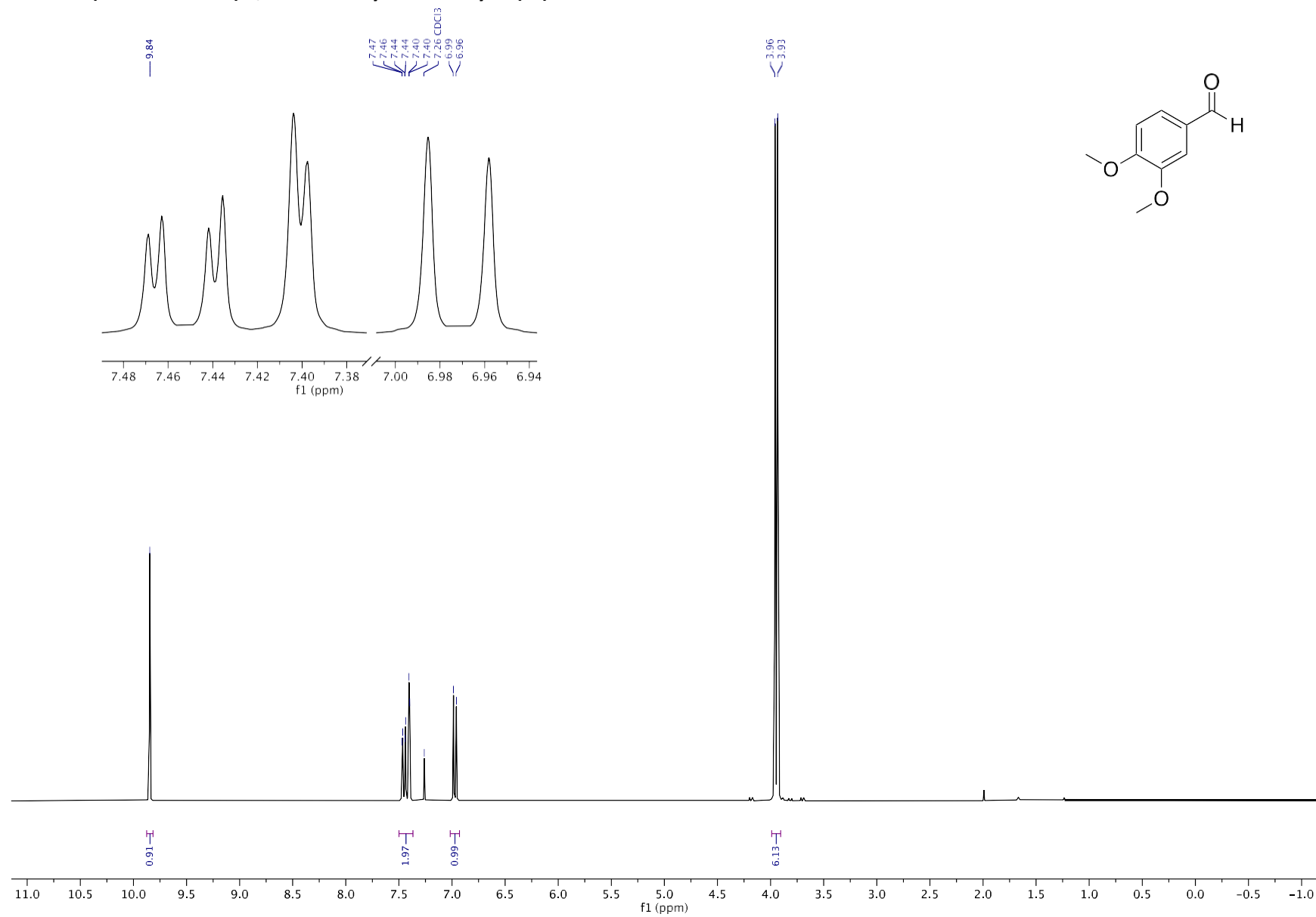
¹H-NMR (400 MHz CDCl₃) 3-Methoxybenzaldehyde (3q)



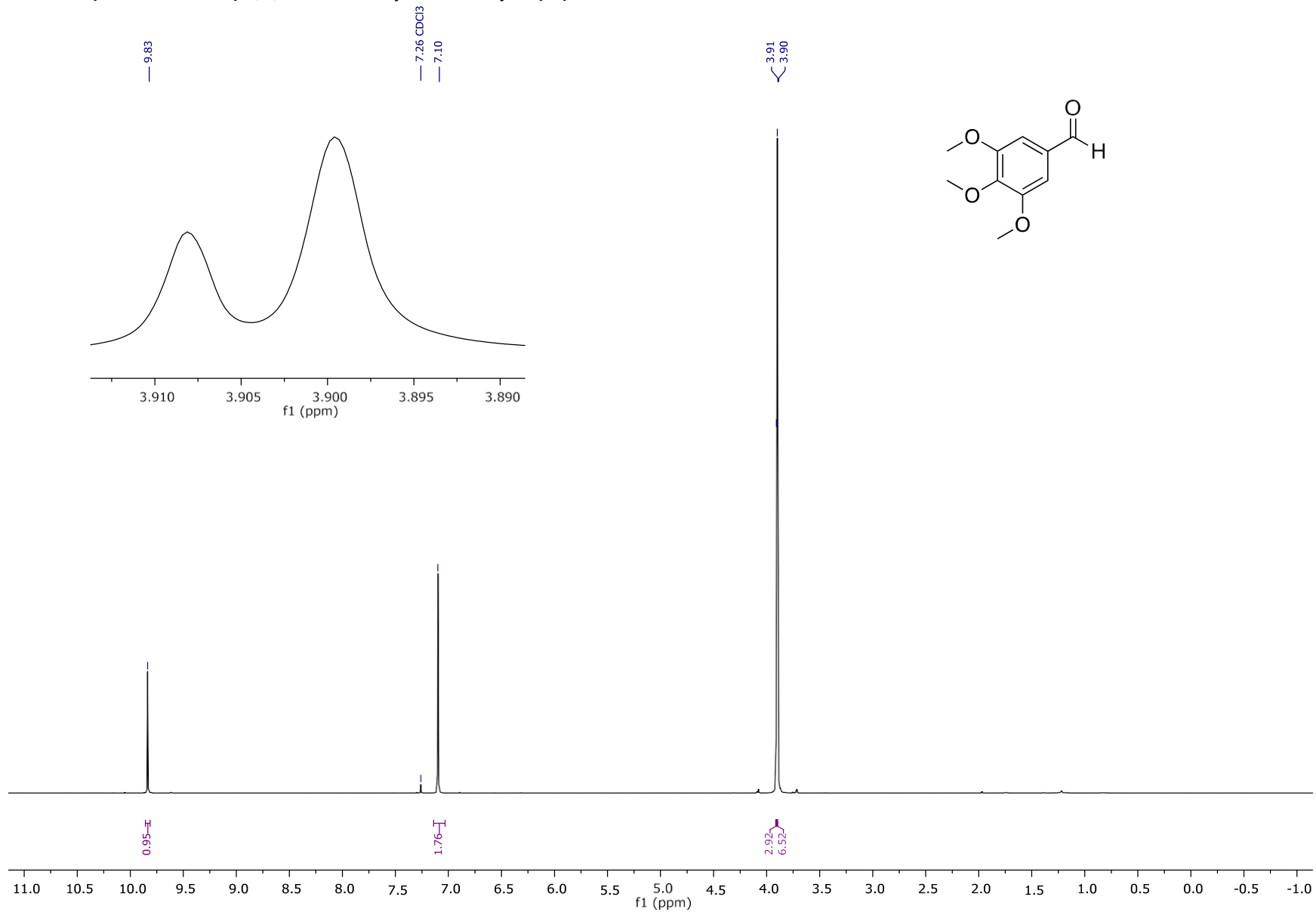
¹H-NMR (400 MHz CDCl₃) 2-Bromobenzaldehyde (3r)



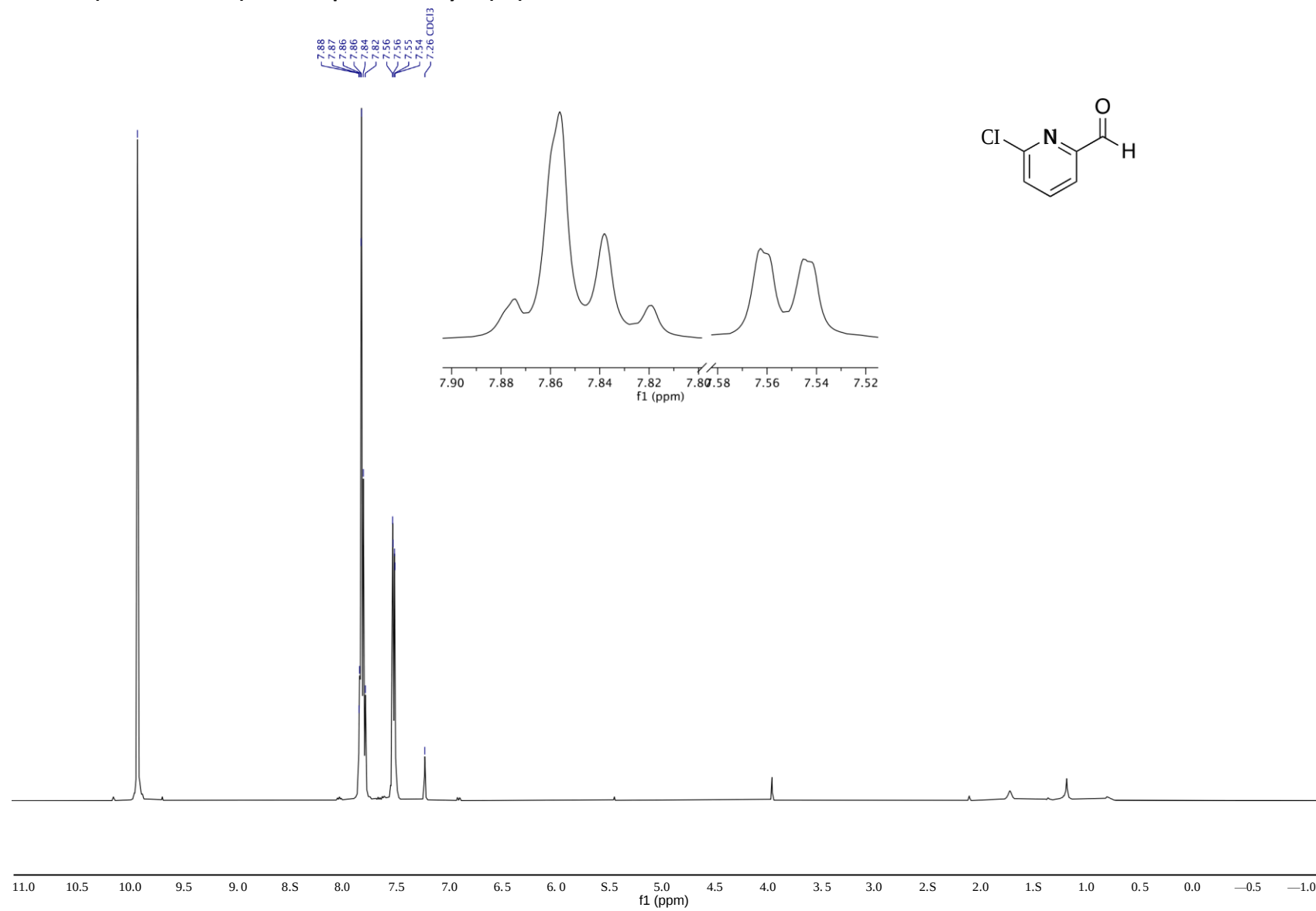
¹H-NMR (300 MHz CDCl₃) 3,4-Dimethoxybenzaldehyde (3s)



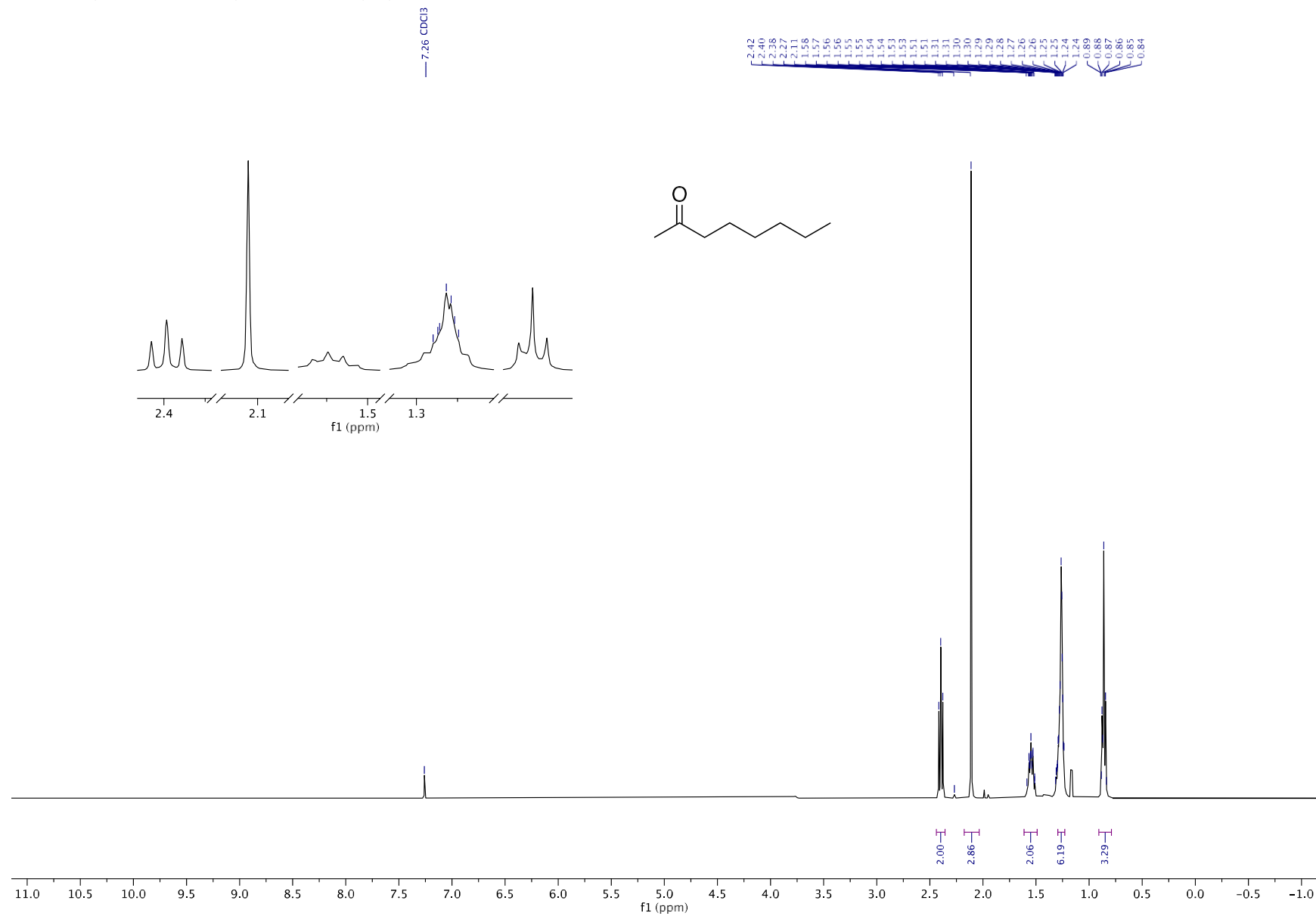
¹H-NMR (400 MHz CDCl₃) 3,4,5-Trimethoxybenzaldehyde (3t)



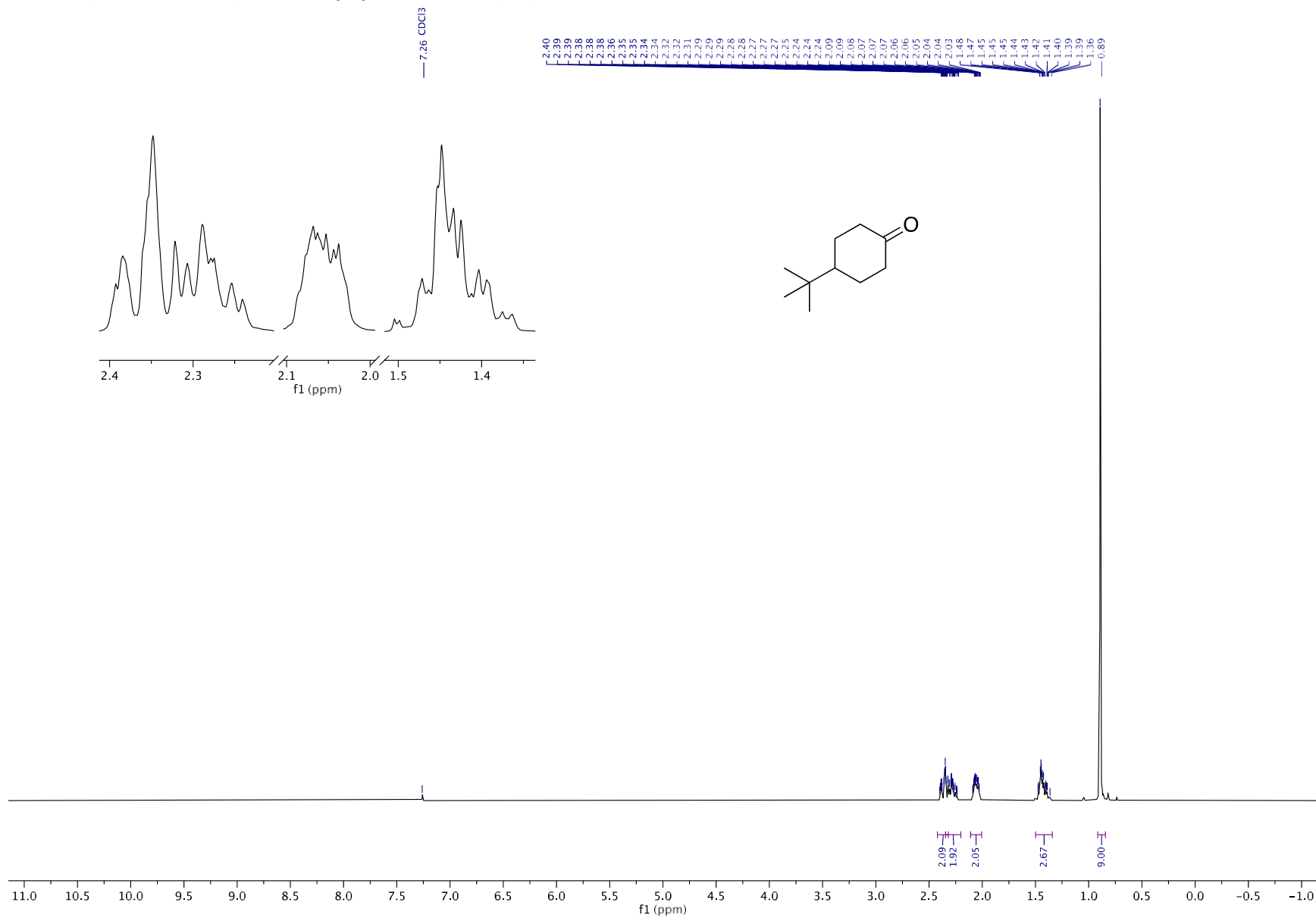
¹H-NMR (400 MHz CDCl₃) 6-Chloropicolinaldehyde (3u)



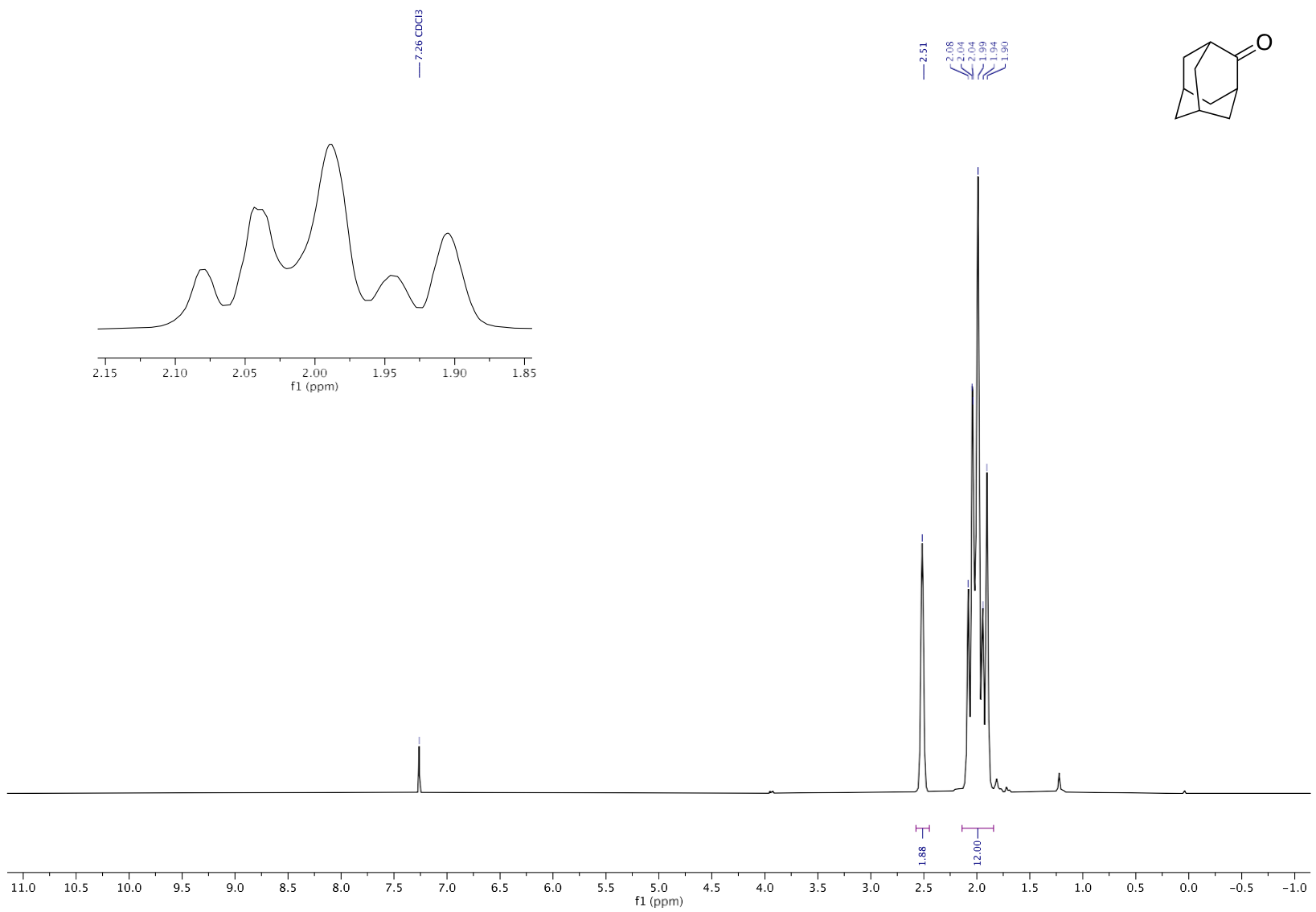
¹H-NMR (400 MHz CDCl₃) 2-Octanone (3v)



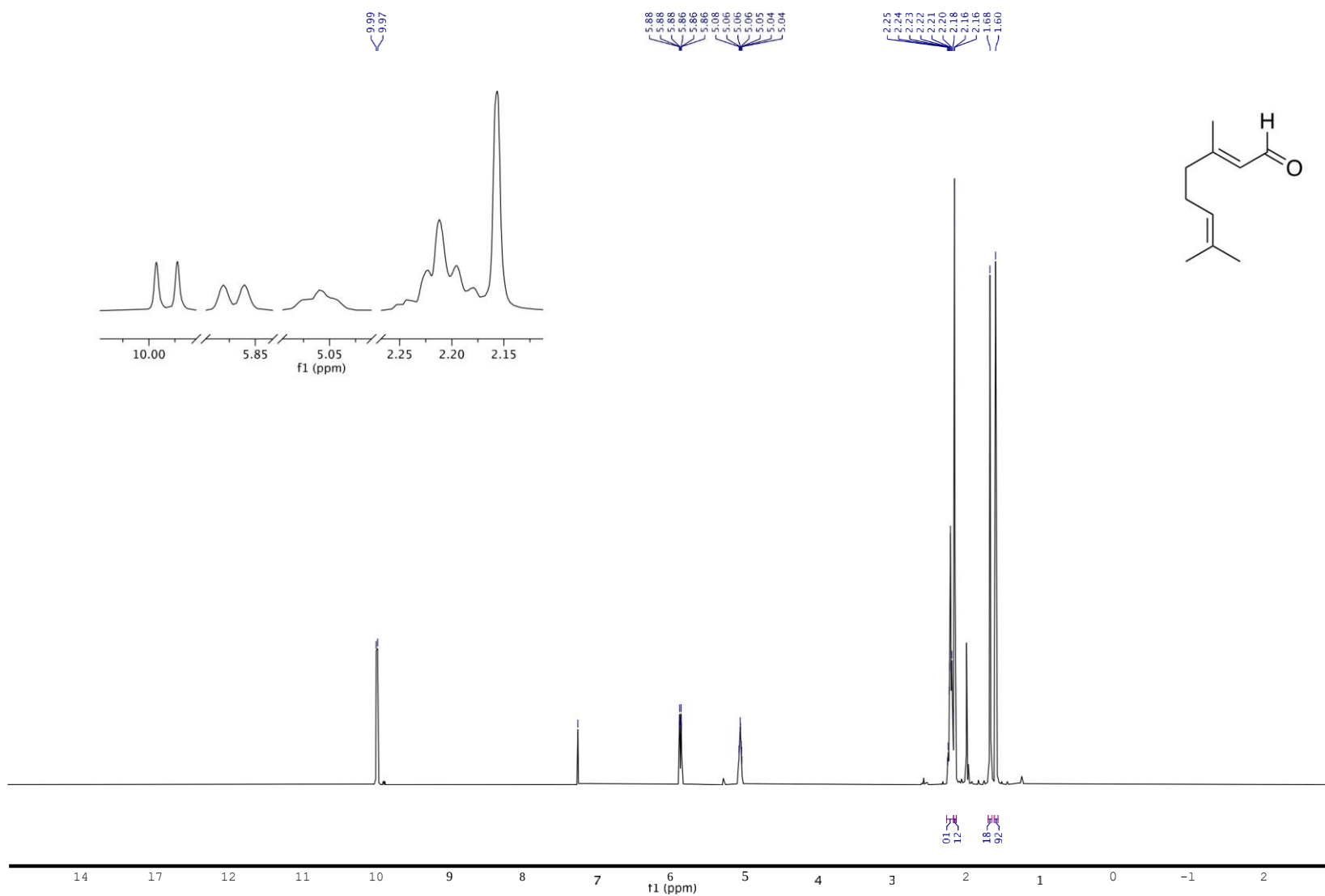
¹H-NMR (400 MHz CDCl₃) 4-*tert*-Butylcyclohexanone (3w)



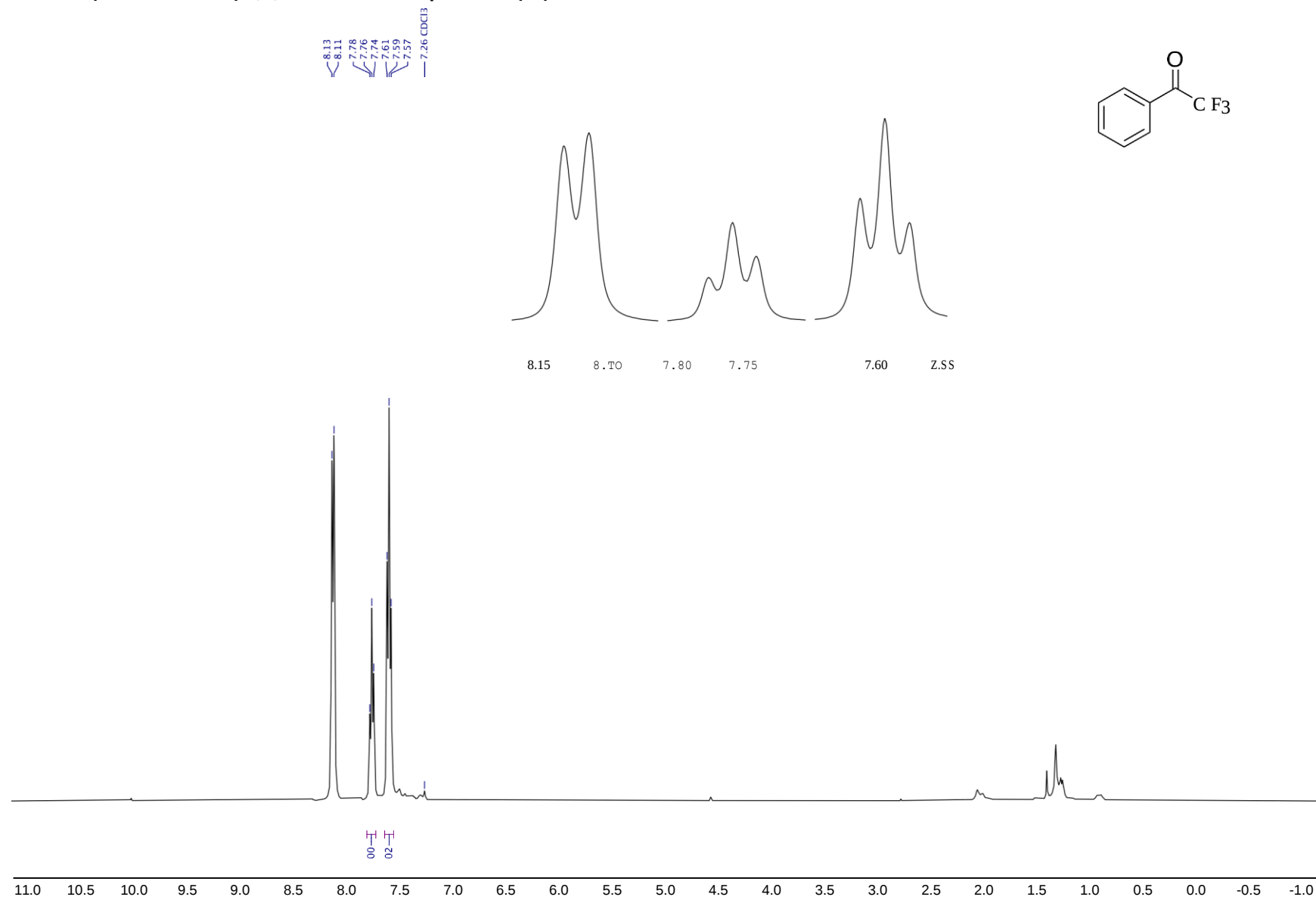
¹H-NMR (300 MHz CDCl₃) 2-Adamantanone (3x)



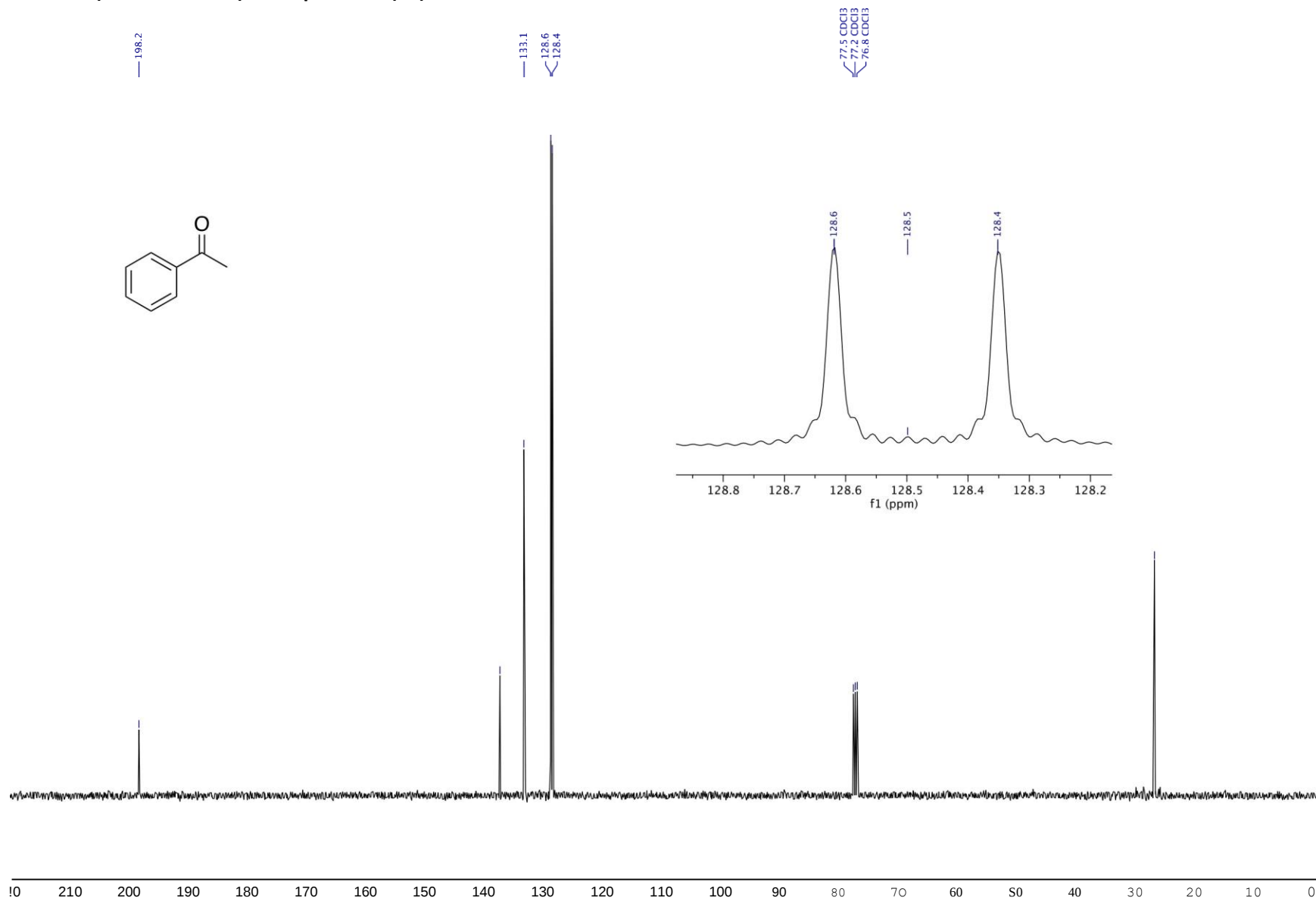
¹H-NMR (400 MHz CDCl₃) Geranial (3y)



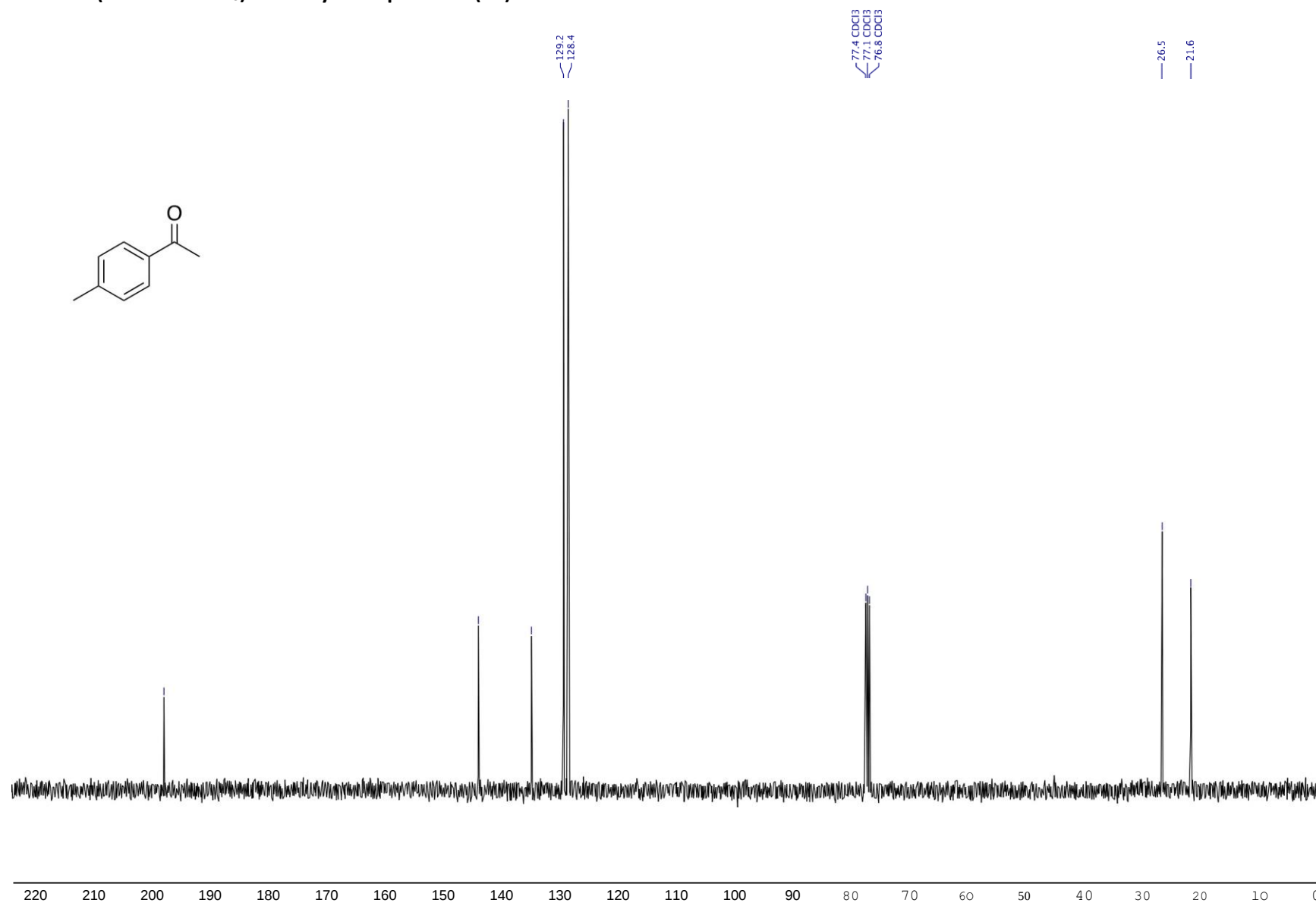
¹H-NMR (400 MHz CDCl₃) 1,1,1-Trifluoroacetophenone (3z)



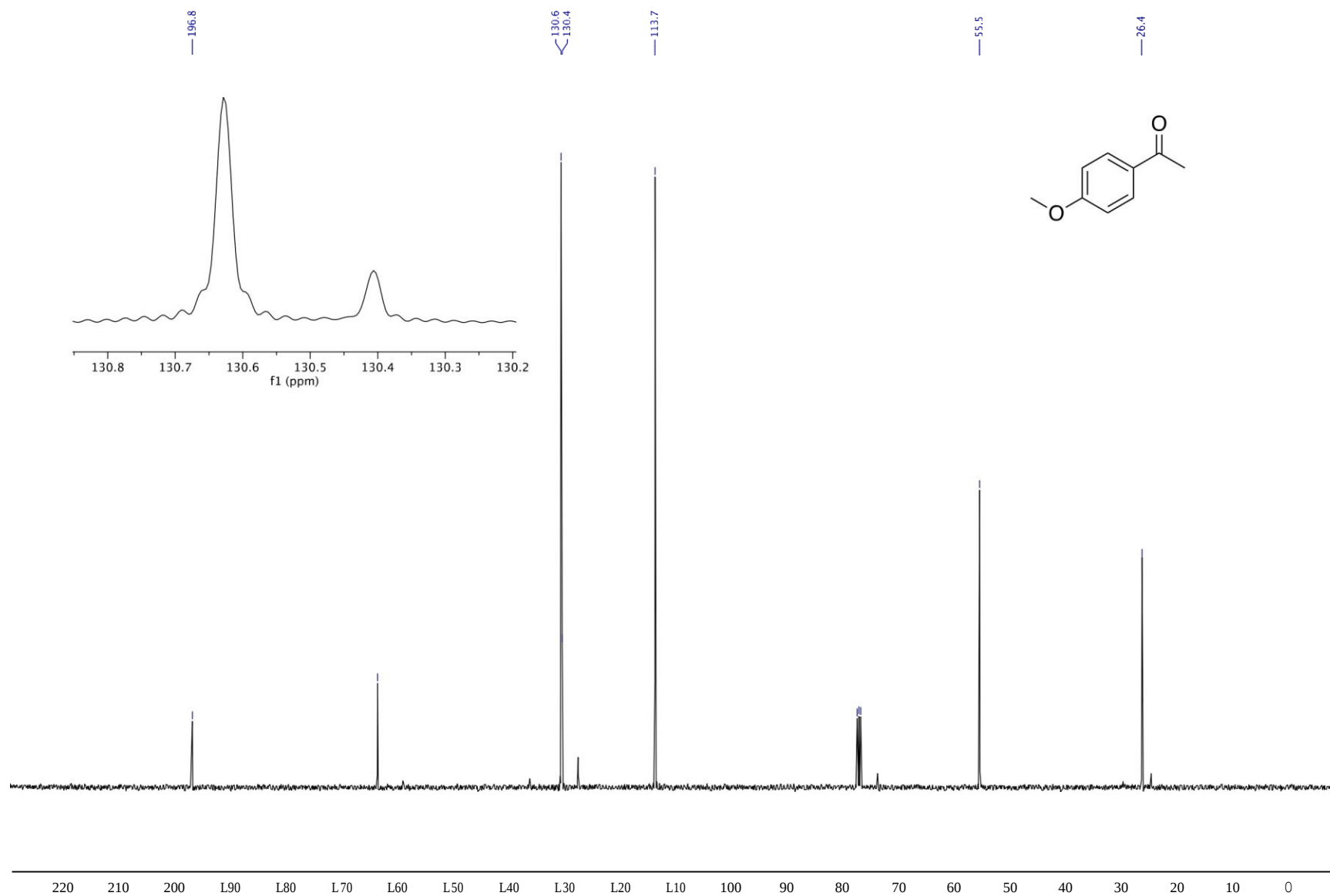
^{13}C -NMR (101 MHz CDCl_3) Acetophenone (3a)



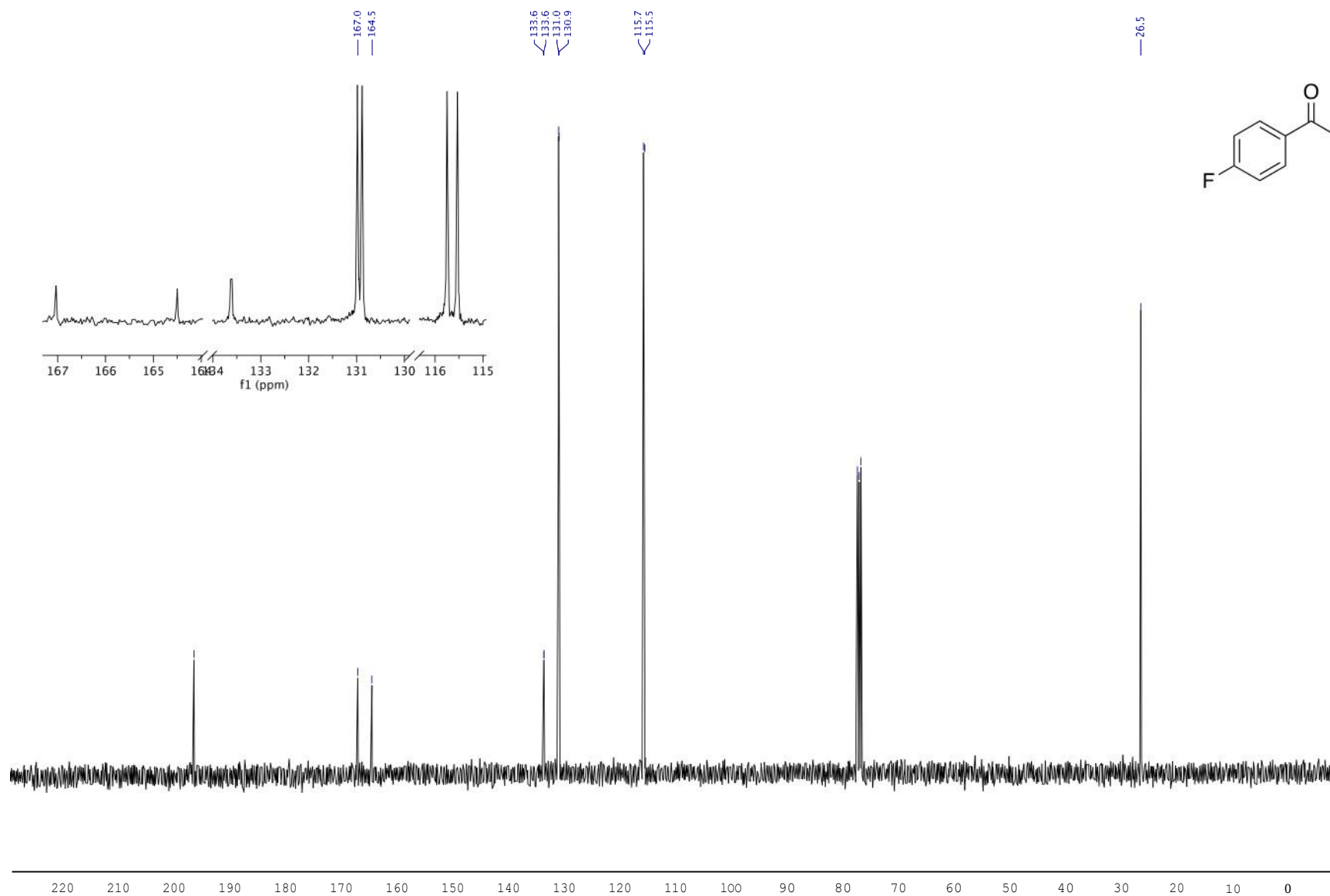
^{13}C -NMR (101 MHz CDCl_3) 4-Methylacetophenone (3b)



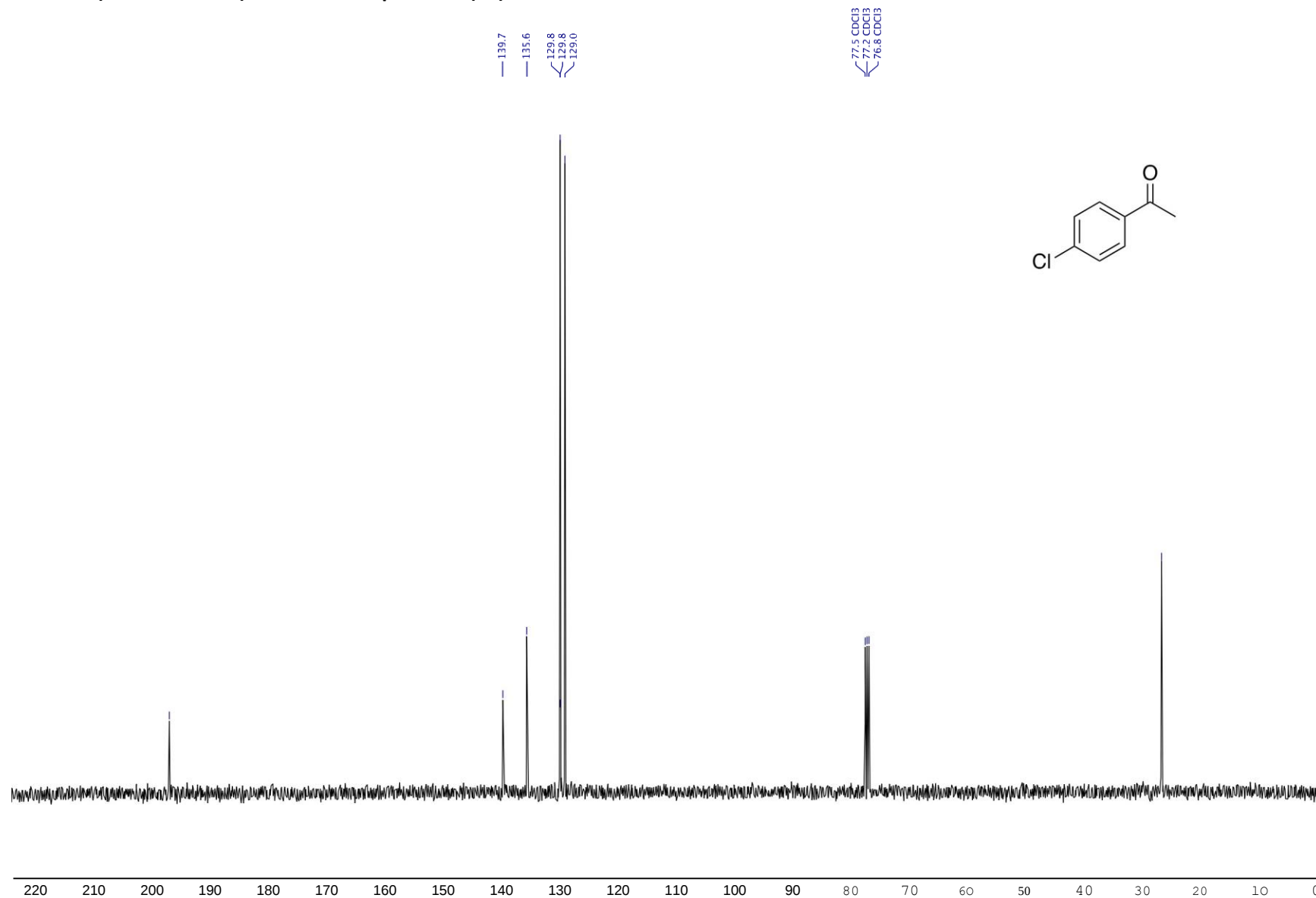
^{13}C -NMR (101 MHz CDCl_3) 1-(4-Methoxyphenyl)ethanone (3c)



^{13}C -NMR (101 MHz CDCl_3) 1-(4-Fluorophenyl)ethanone (3d)

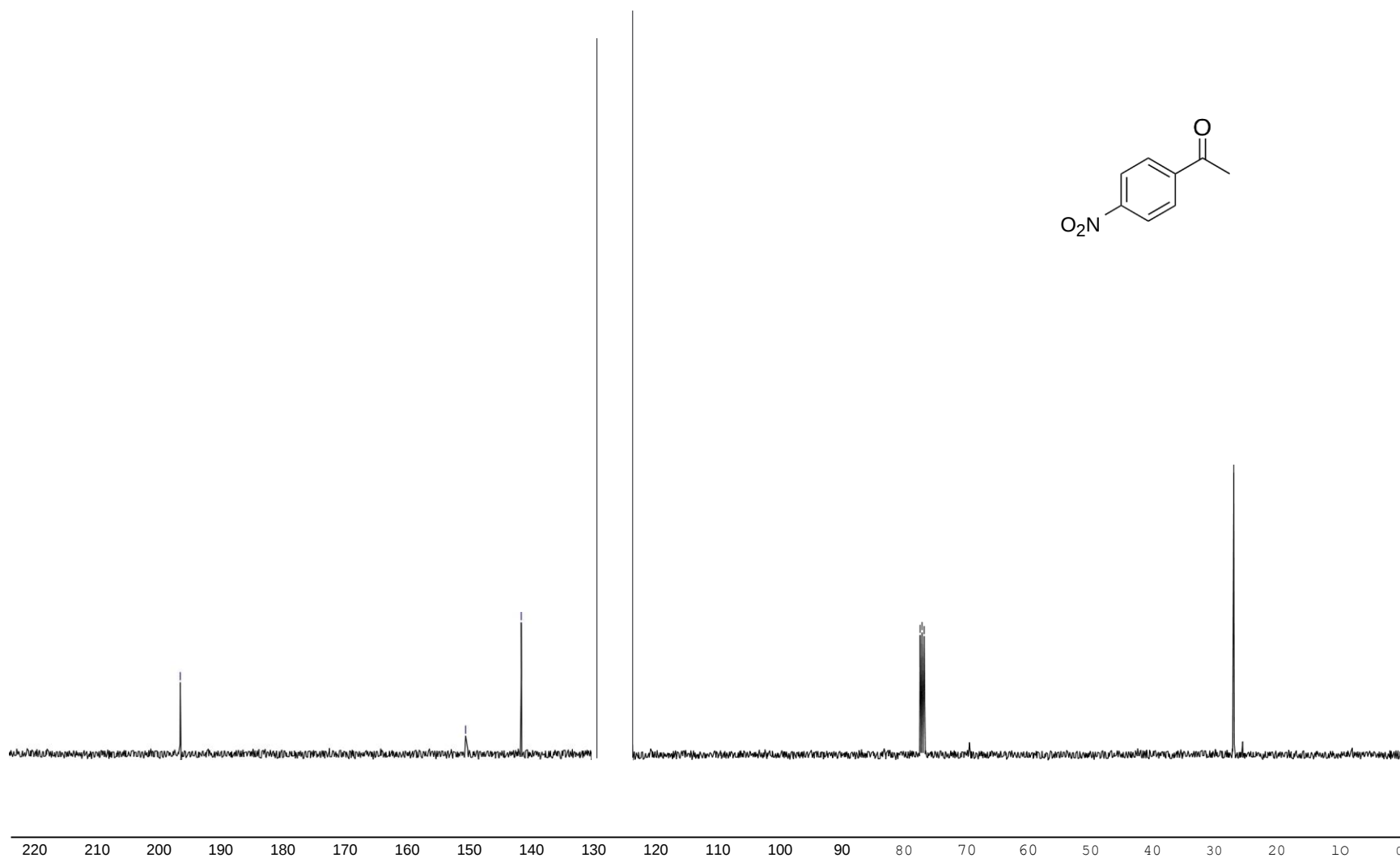
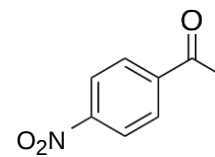


^{13}C -NMR (101 MHz CDCl_3) 4-Chloroacetophenone (3e)

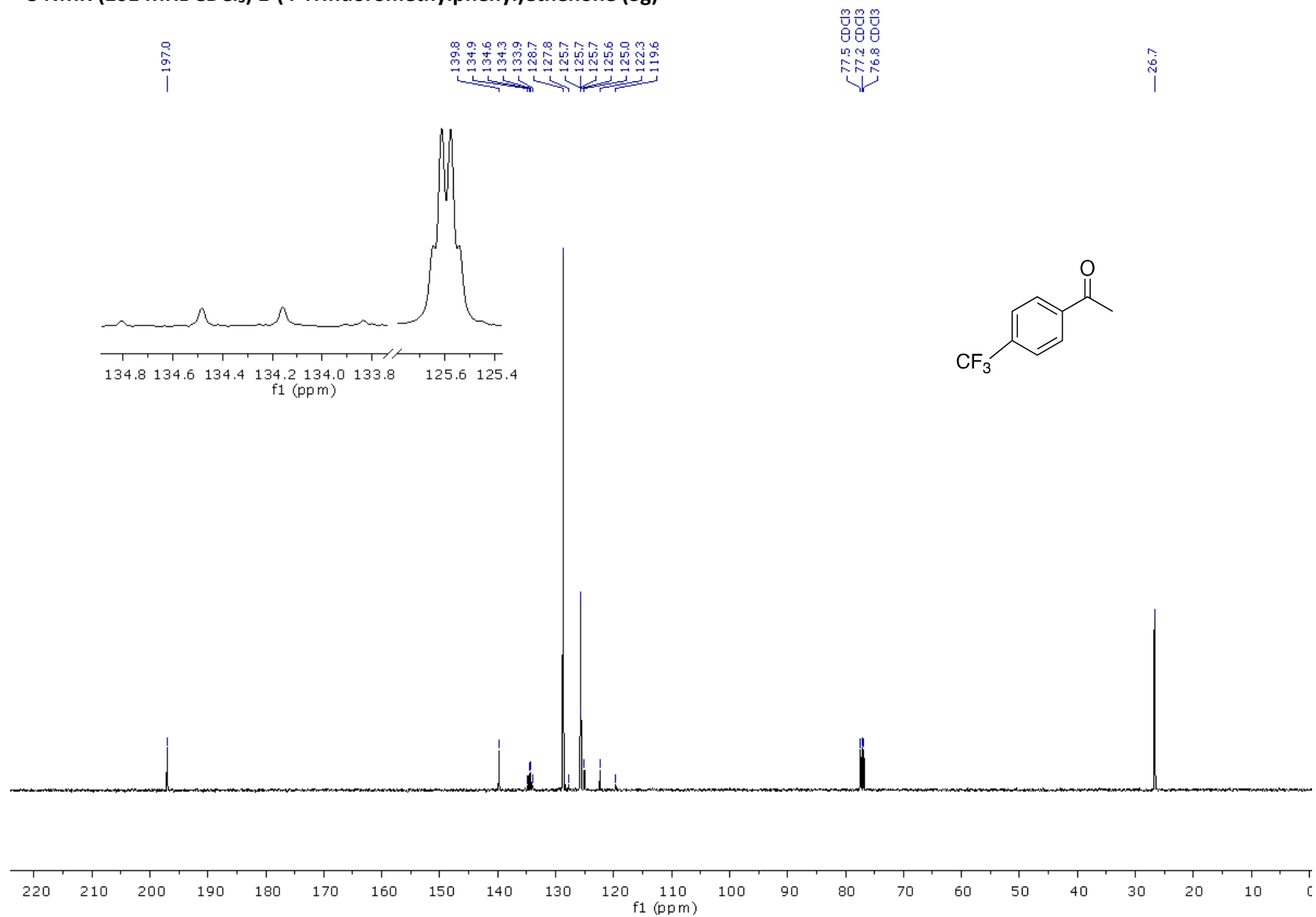


^{13}C -NMR (101 MHz CDCl_3) 4-Nitroacetophenone (3f)

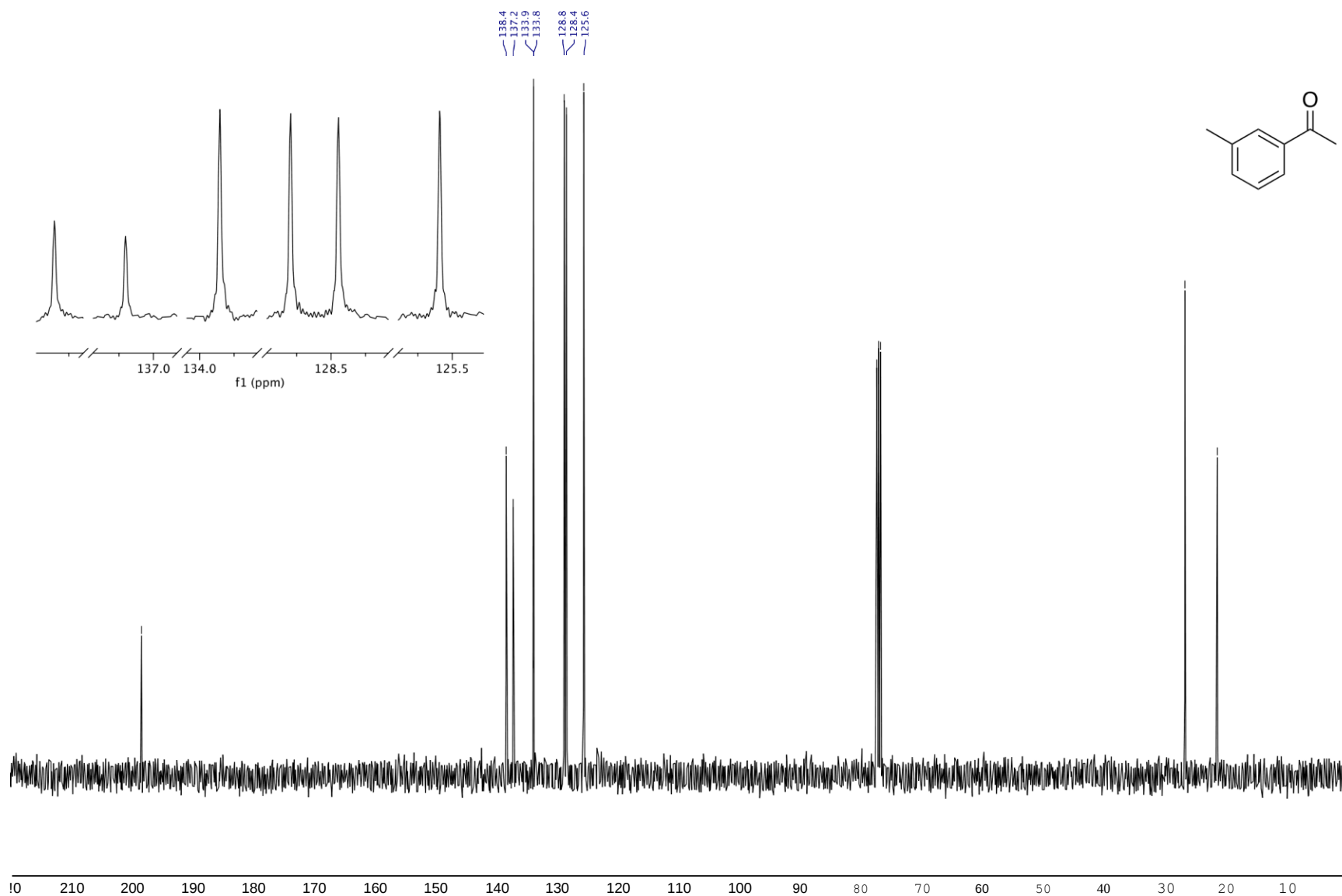
77.5 CDCl_3
77.2 CDCl_3
76.8 CDCl_3



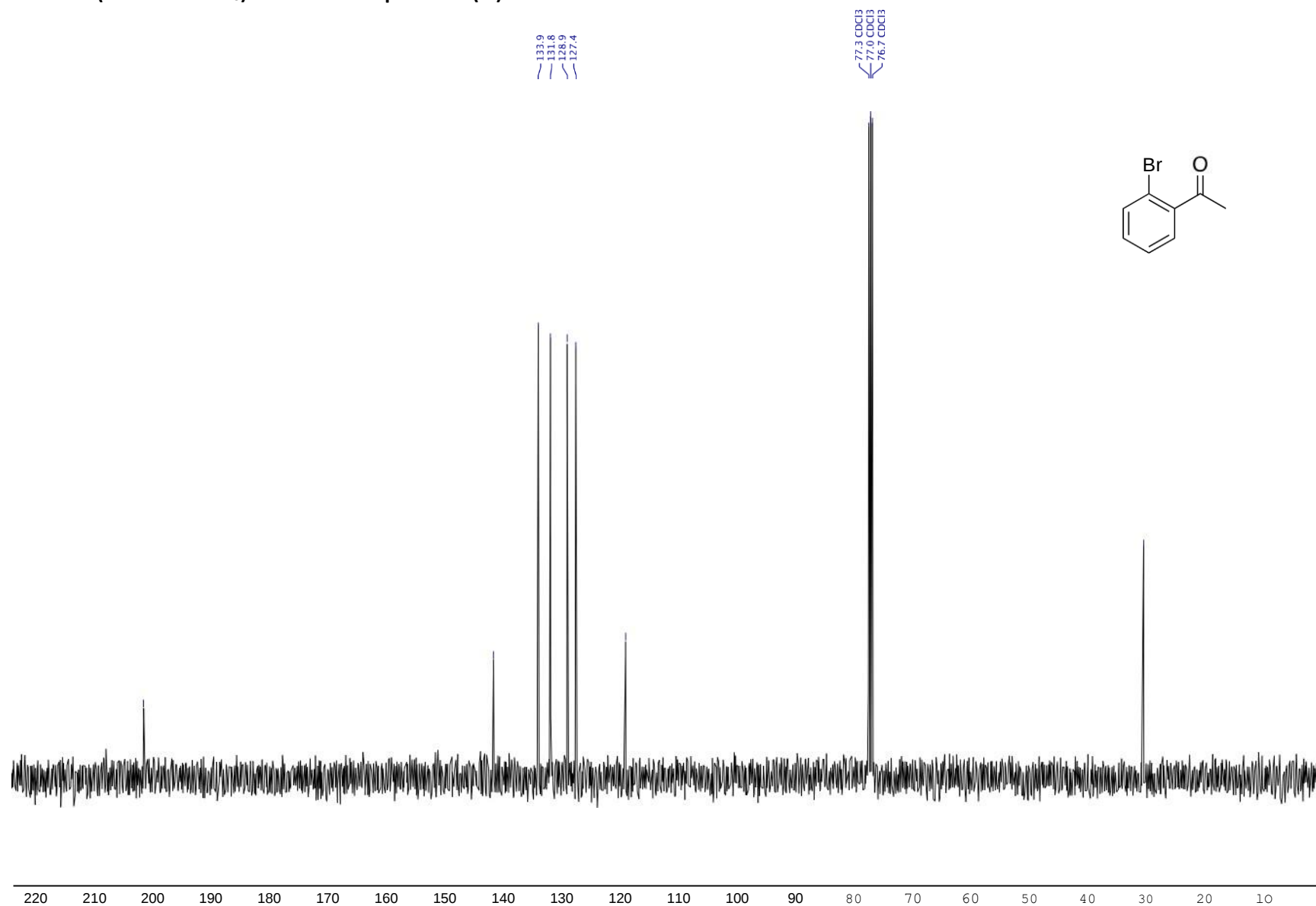
^{13}C -NMR (101 MHz CDCl_3) 1-(4-Trifluoromethylphenyl)ethenone (3g)



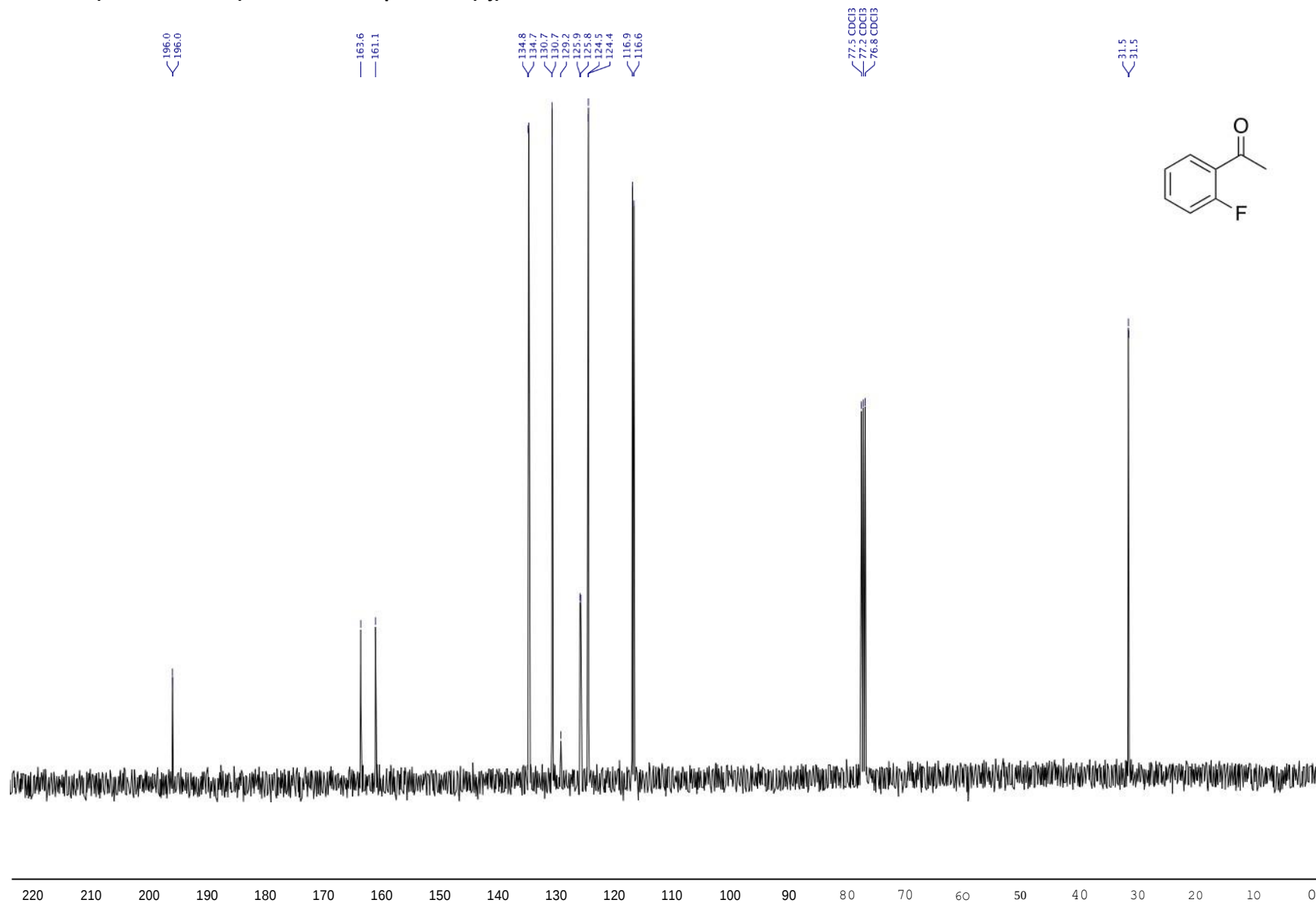
^{13}C -NMR (101 MHz CDCl_3) 3-Methylacetophenone (3h)



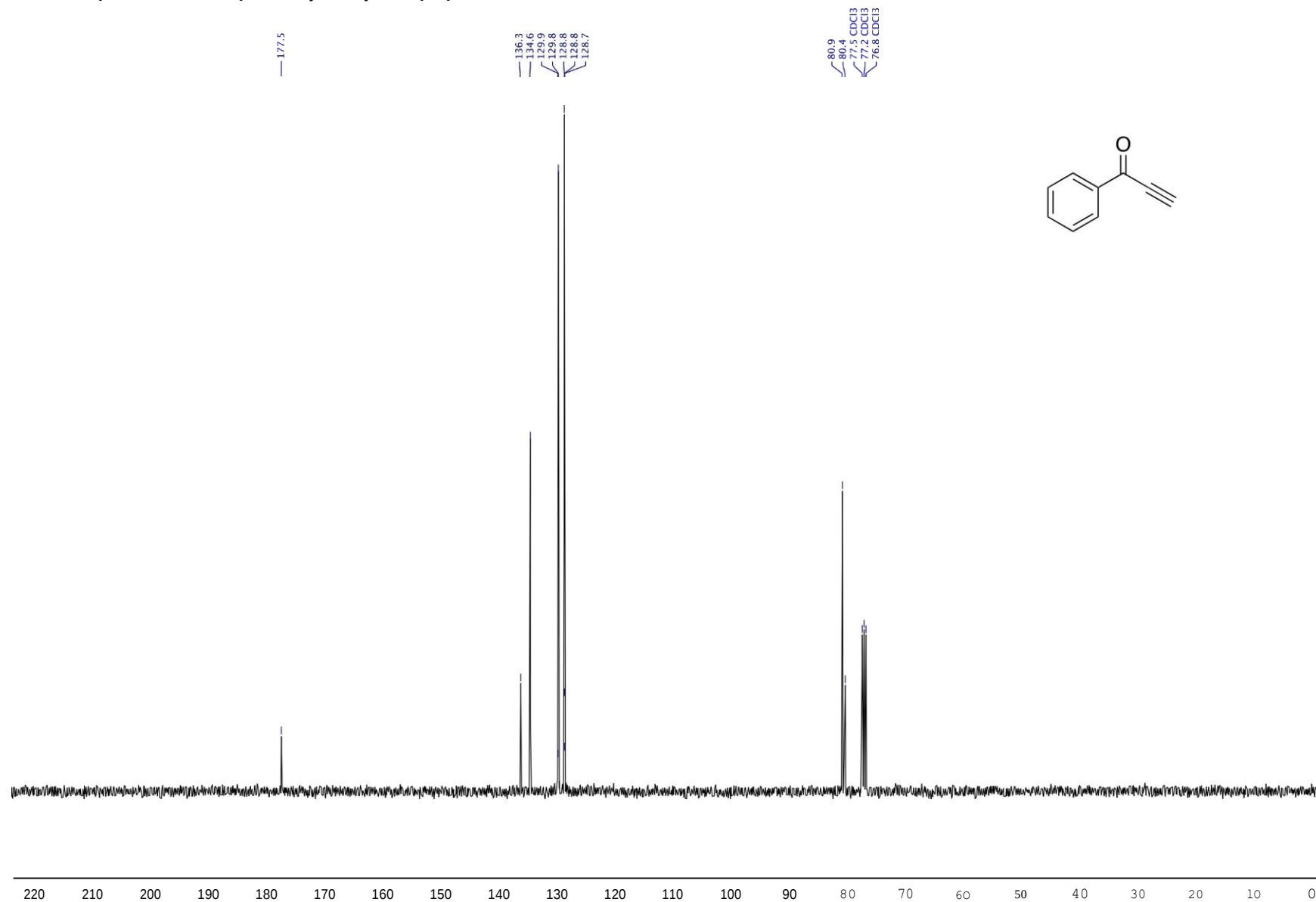
^{13}C -NMR (101 MHz CDCl_3) 2-Bromoacetophenone (3i)



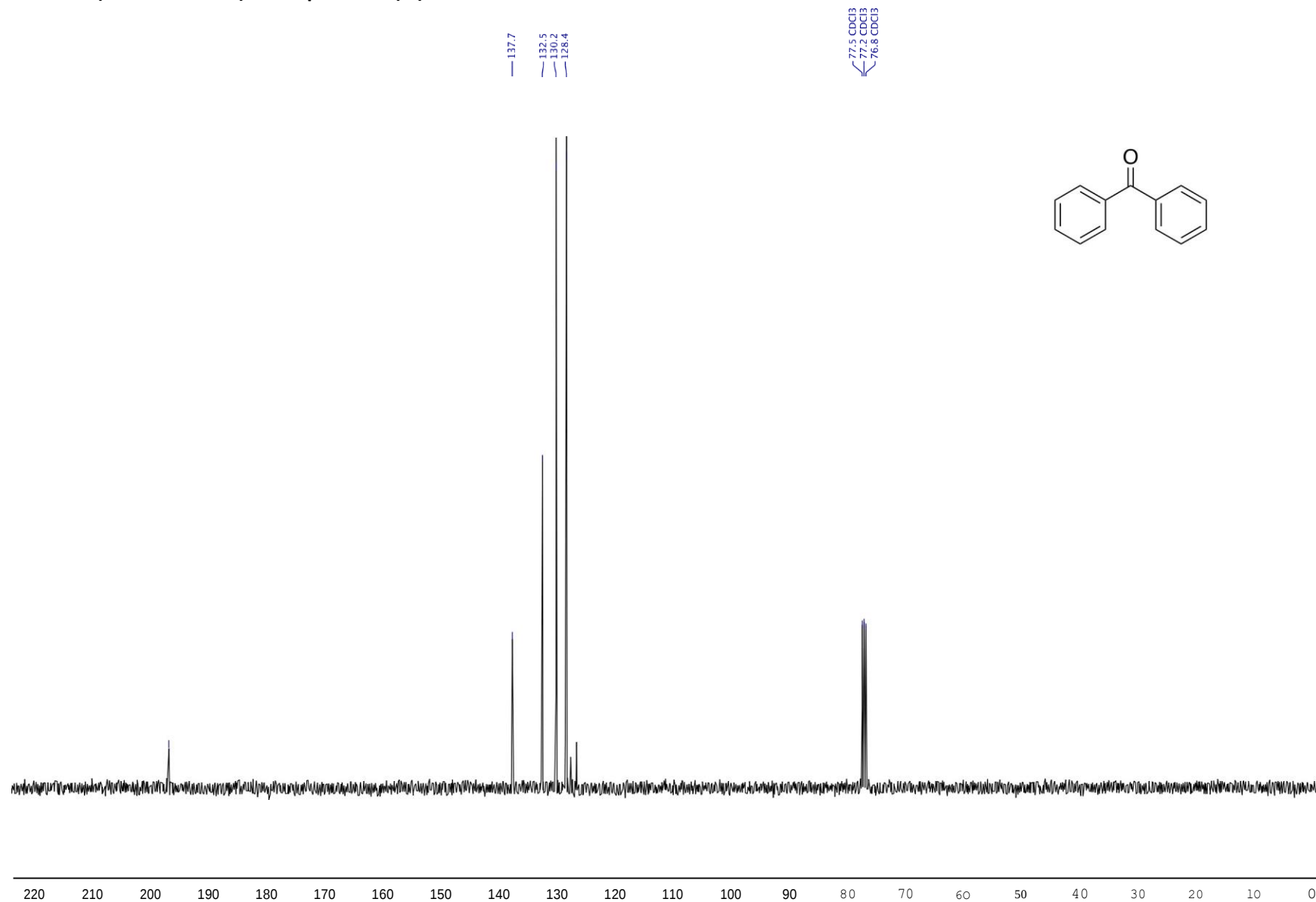
^{13}C -NMR (101 MHz CDCl_3) 2'-Fluoroacetophenone (3j)



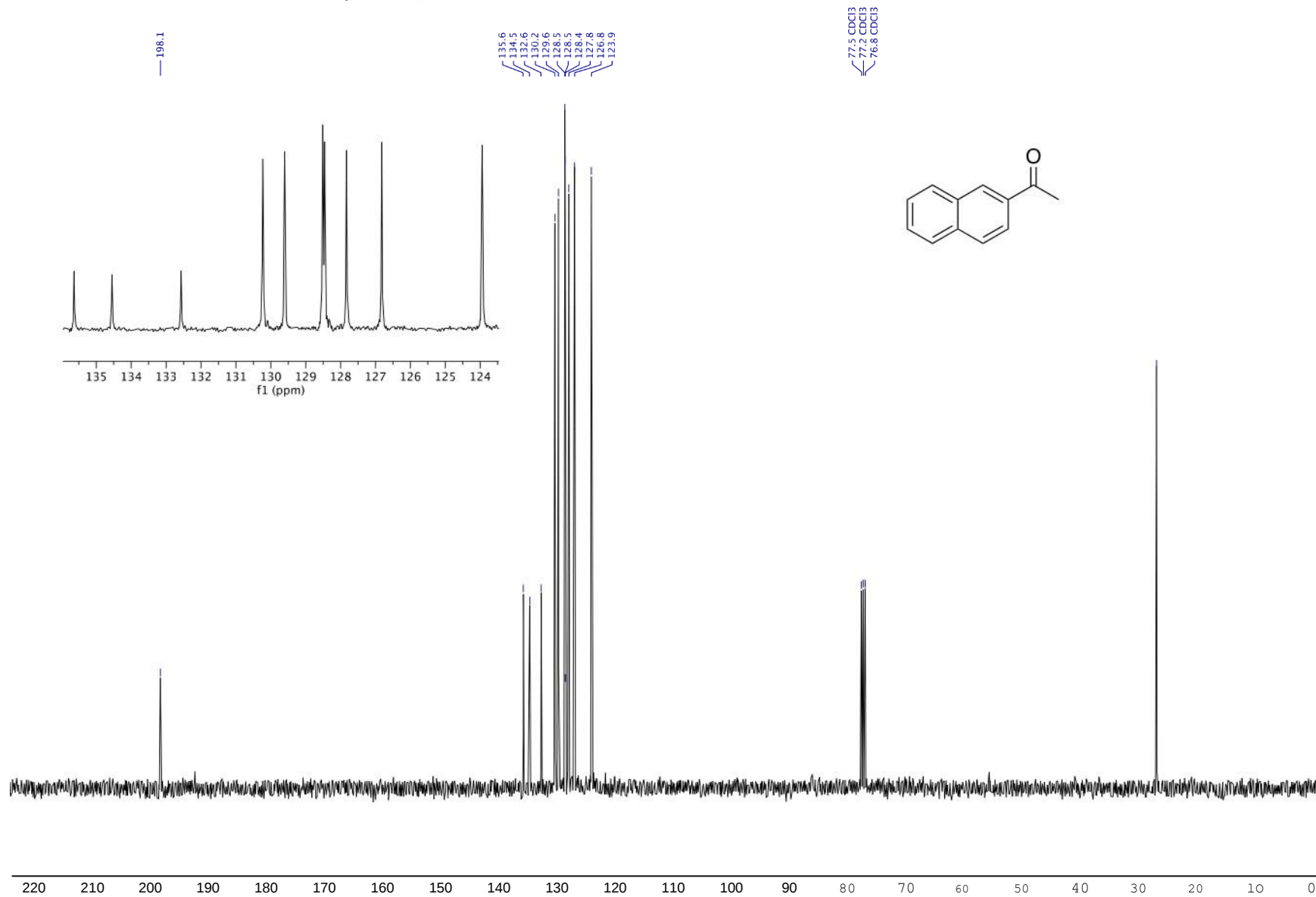
^{13}C -NMR (101 MHz CDCl_3) Benzoylacetylene (3k)



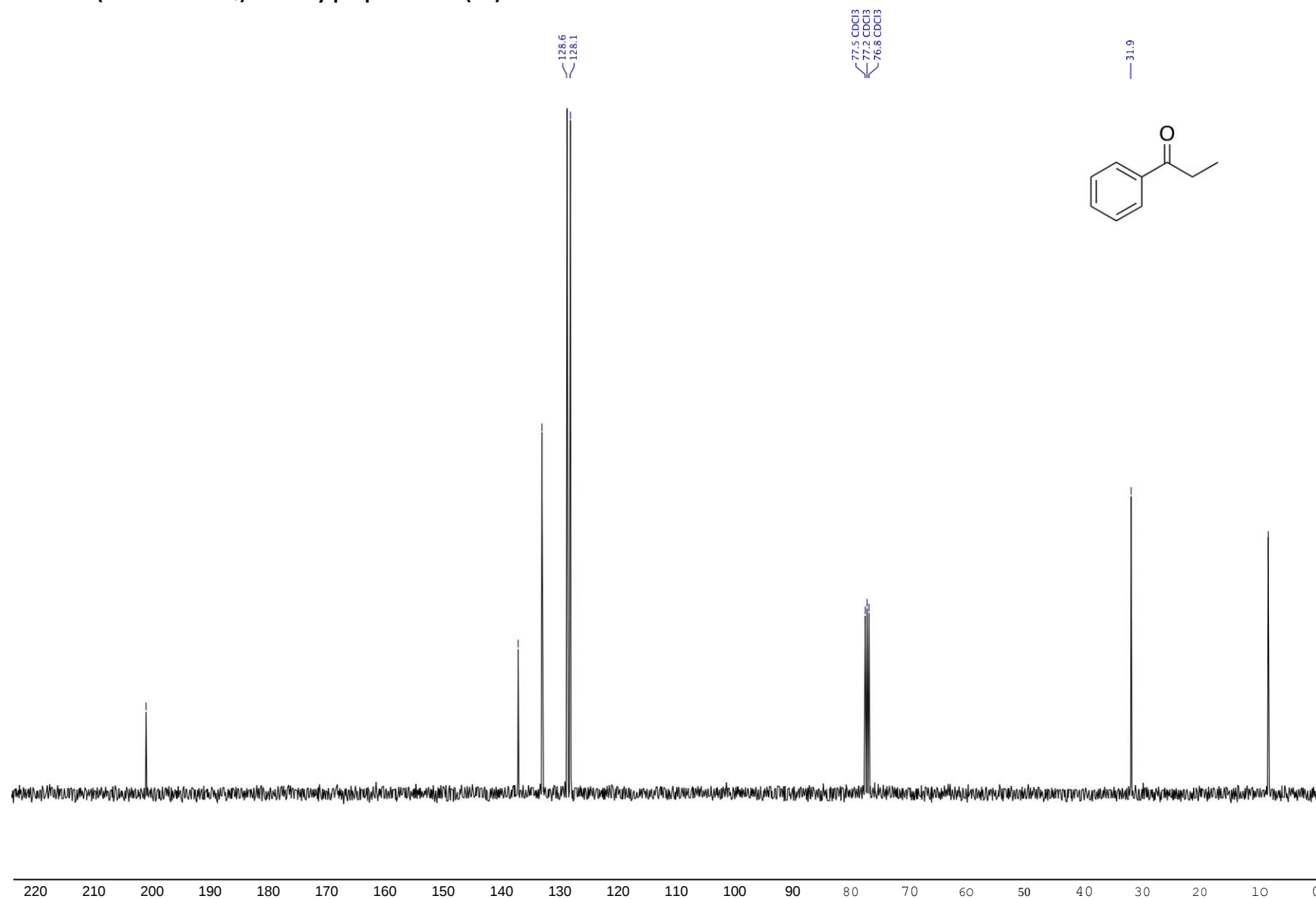
^{13}C -NMR (101 MHz CDCl_3) Benzophenone (3I)



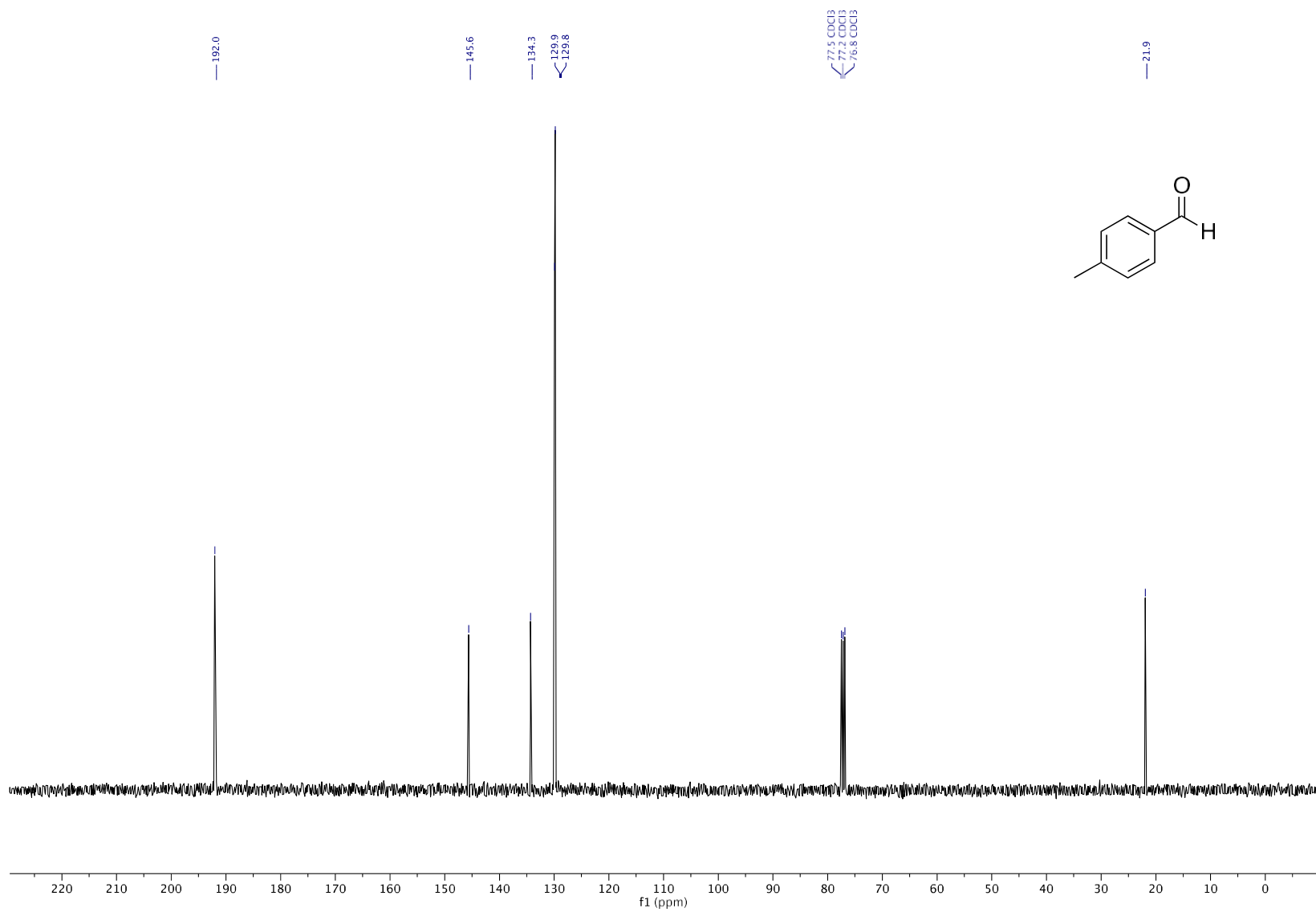
^{13}C -NMR (101 MHz CDCl_3) 2-Acetonaphthone (3m)



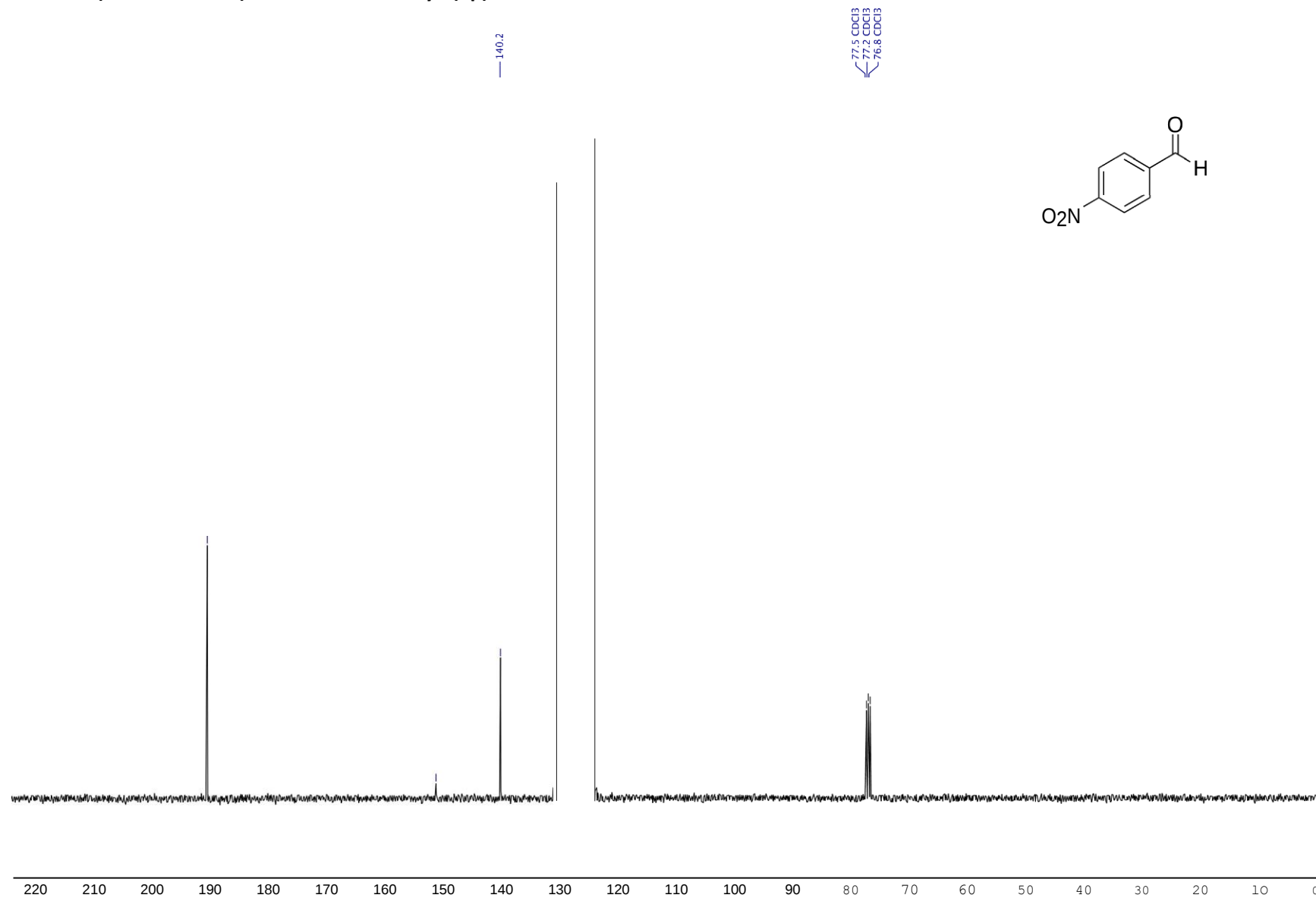
^{13}C -NMR (101 MHz CDCl_3) 1-Phenylpropan-1-one (3n)



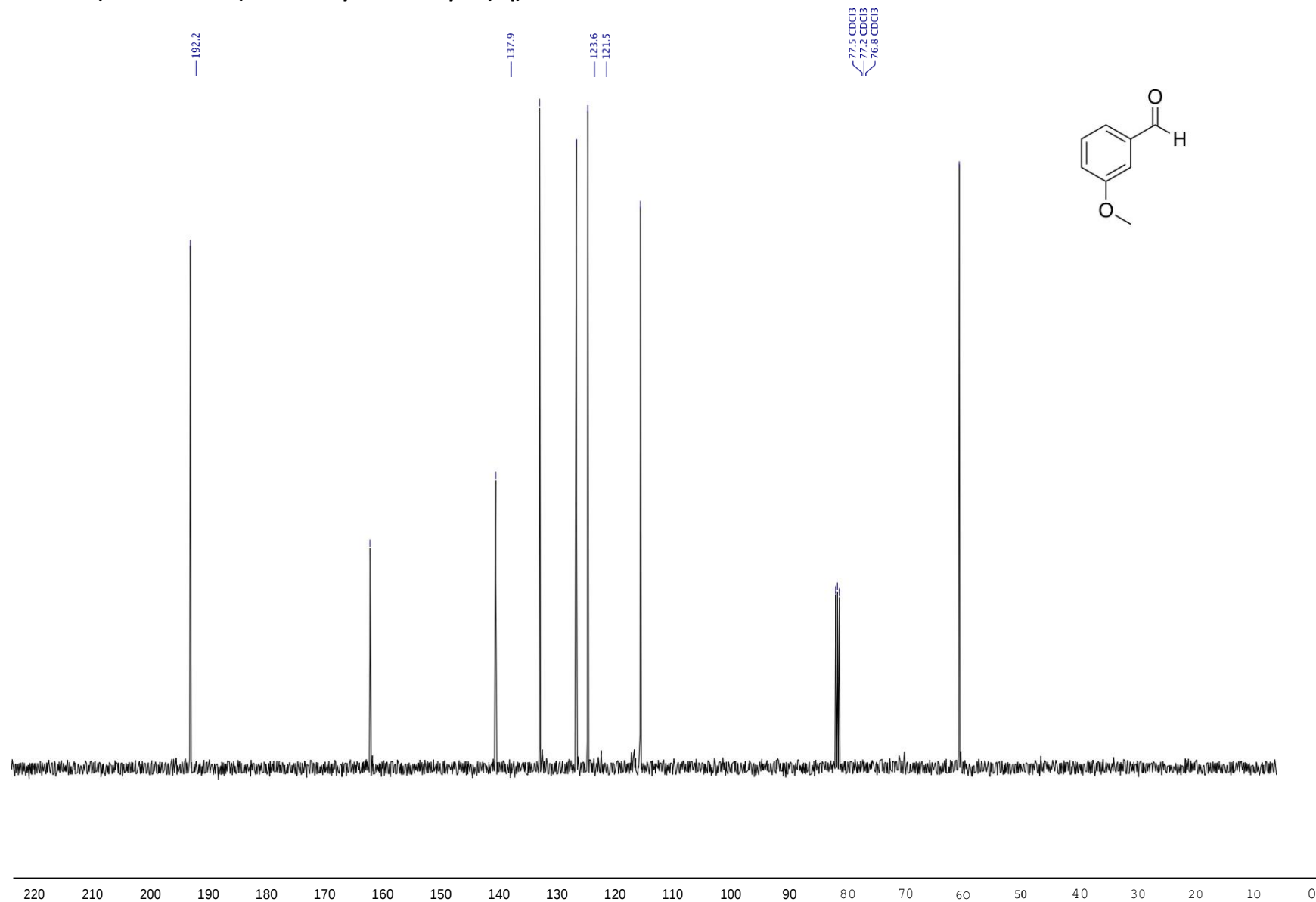
^{13}C -NMR (101 MHz CDCl_3) 4-Methylbenzaldehyde (3o)



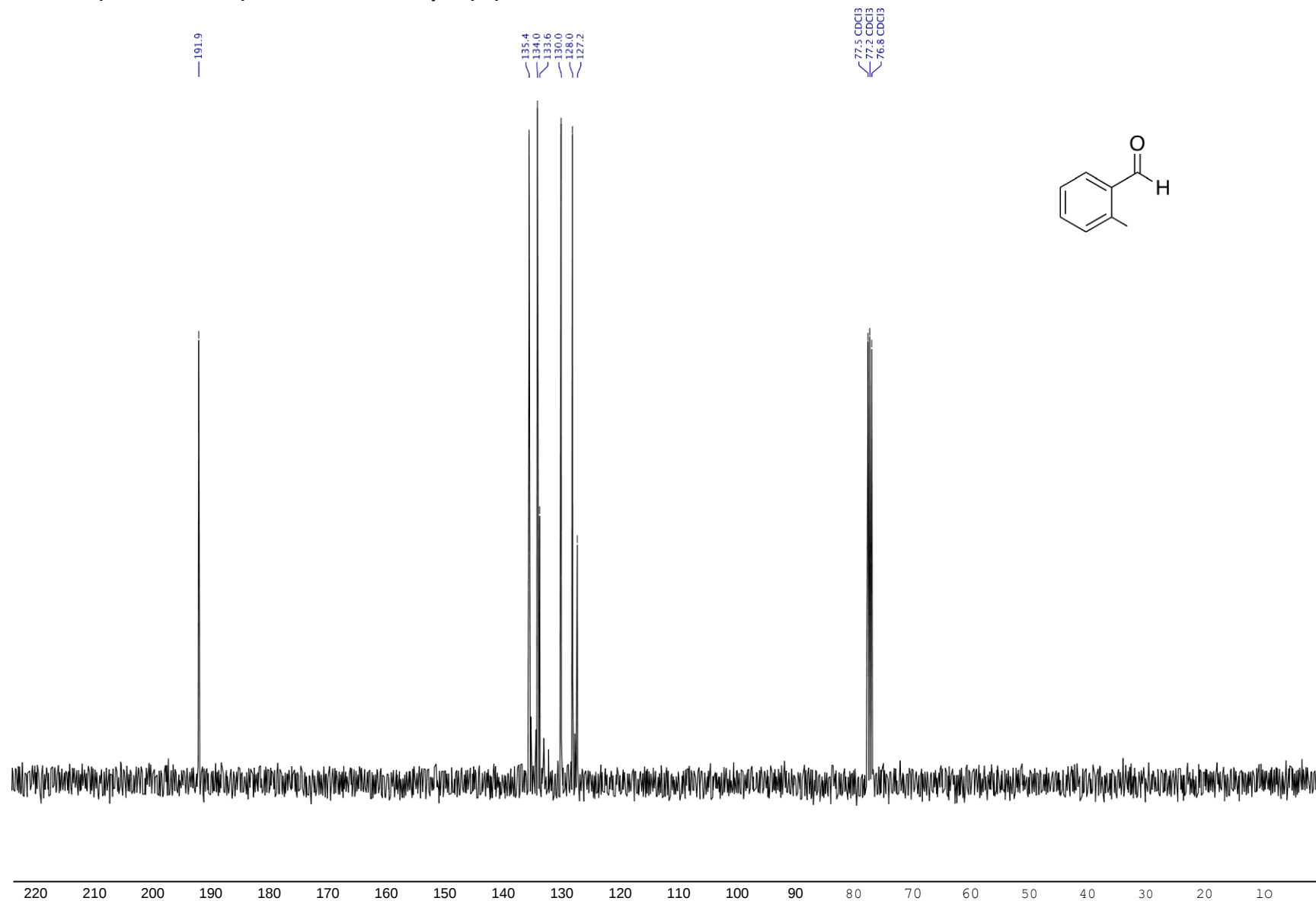
^{13}C -NMR (101 MHz CDCl_3) 4-Nitrobenzaldehyde (3p)



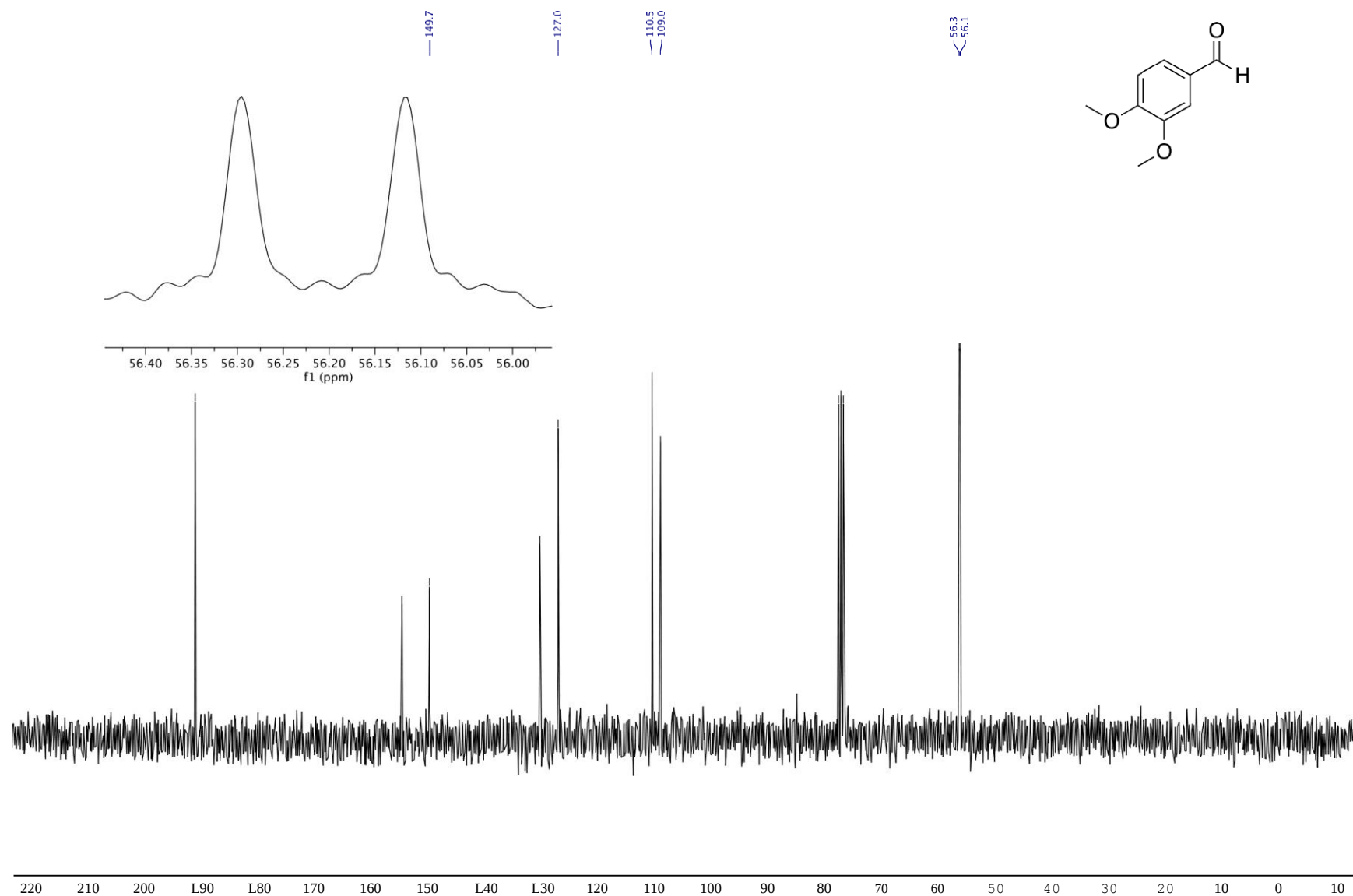
^{13}C -NMR (101 MHz CDCl_3) 3-Methoxybenzaldehyde (3q)



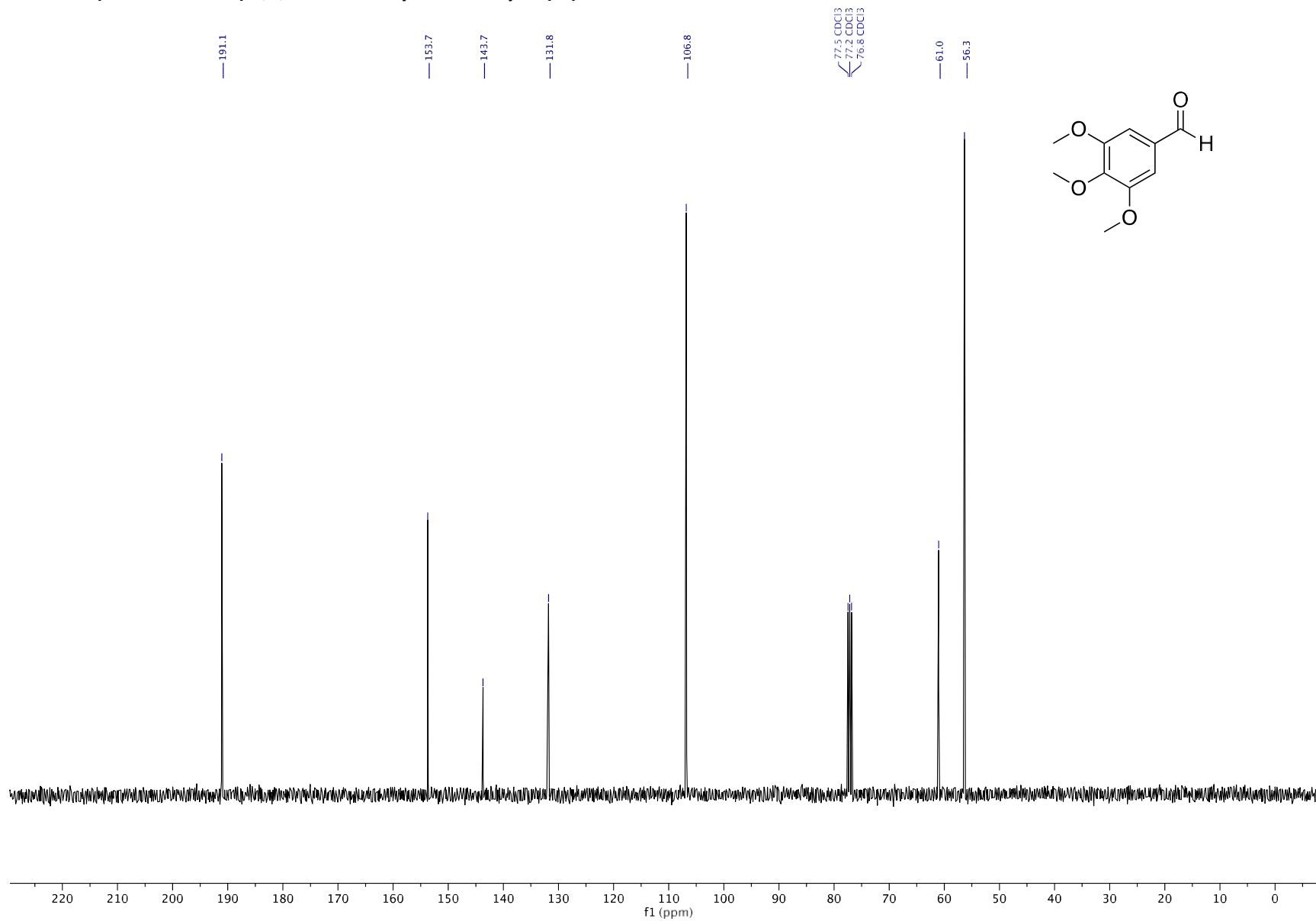
^{13}C -NMR (101 MHz CDCl_3) 2-Bromobenzaldehyde (3r)



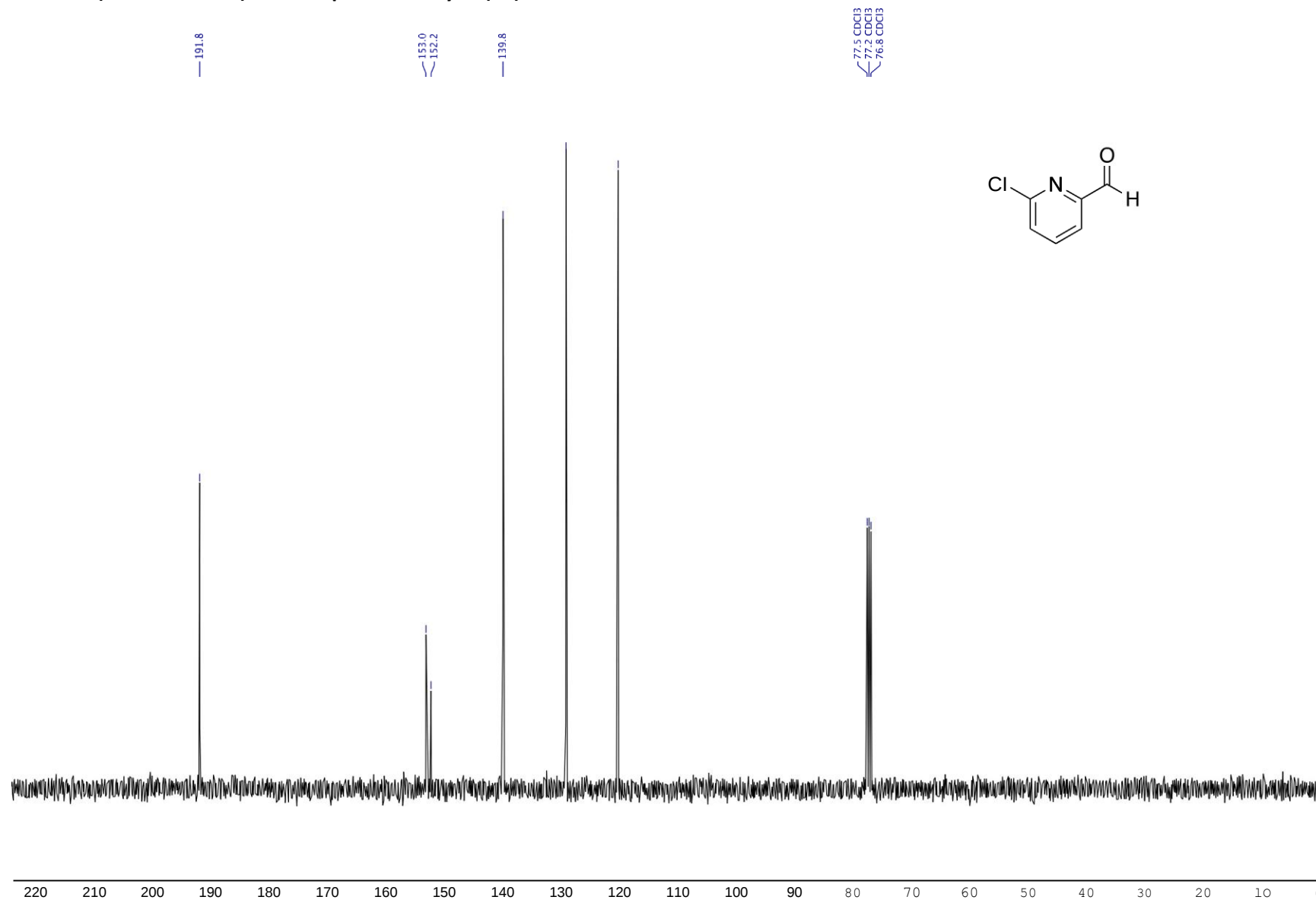
^{13}C -NMR (101 MHz CDCl_3) 3,4-Dimethoxybenzaldehyde (3s)



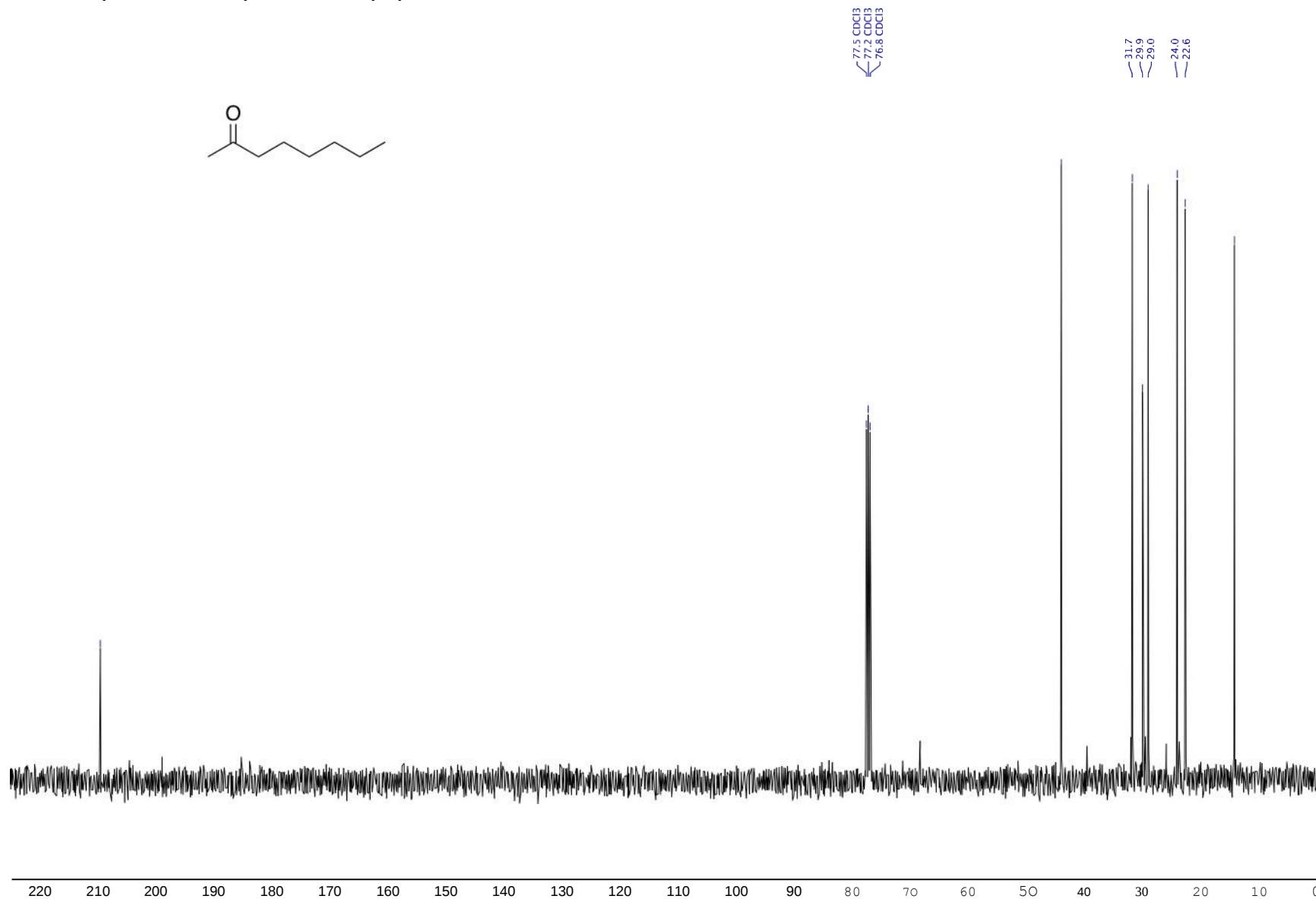
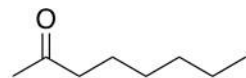
^{13}C -NMR (101 MHz CDCl_3) 3,4,5-Trimethoxybenzaldehyde (3t)



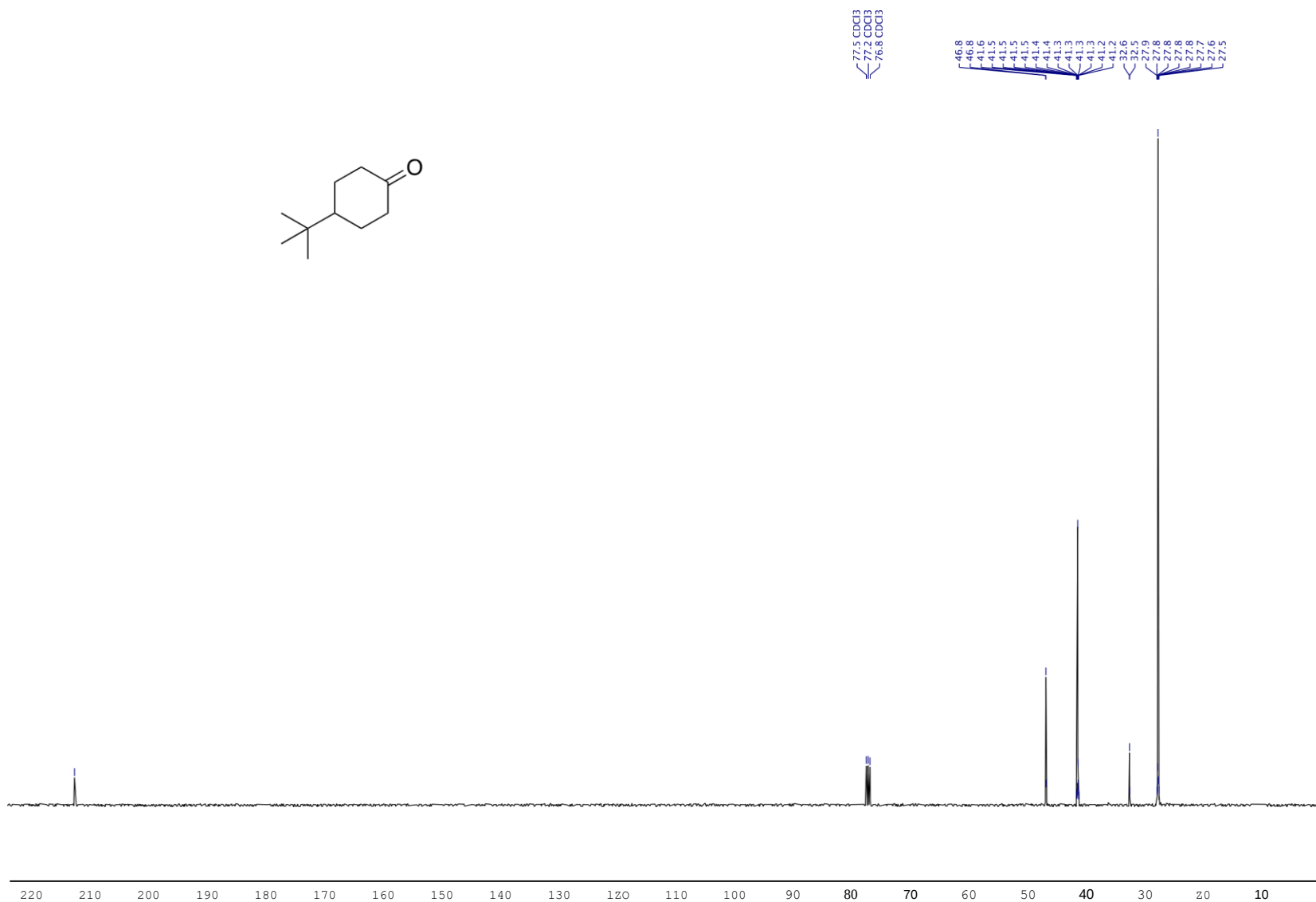
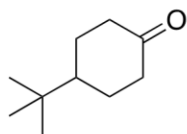
^{13}C -NMR (101 MHz CDCl_3) 6-Chloropicolinaldehyde (3u)



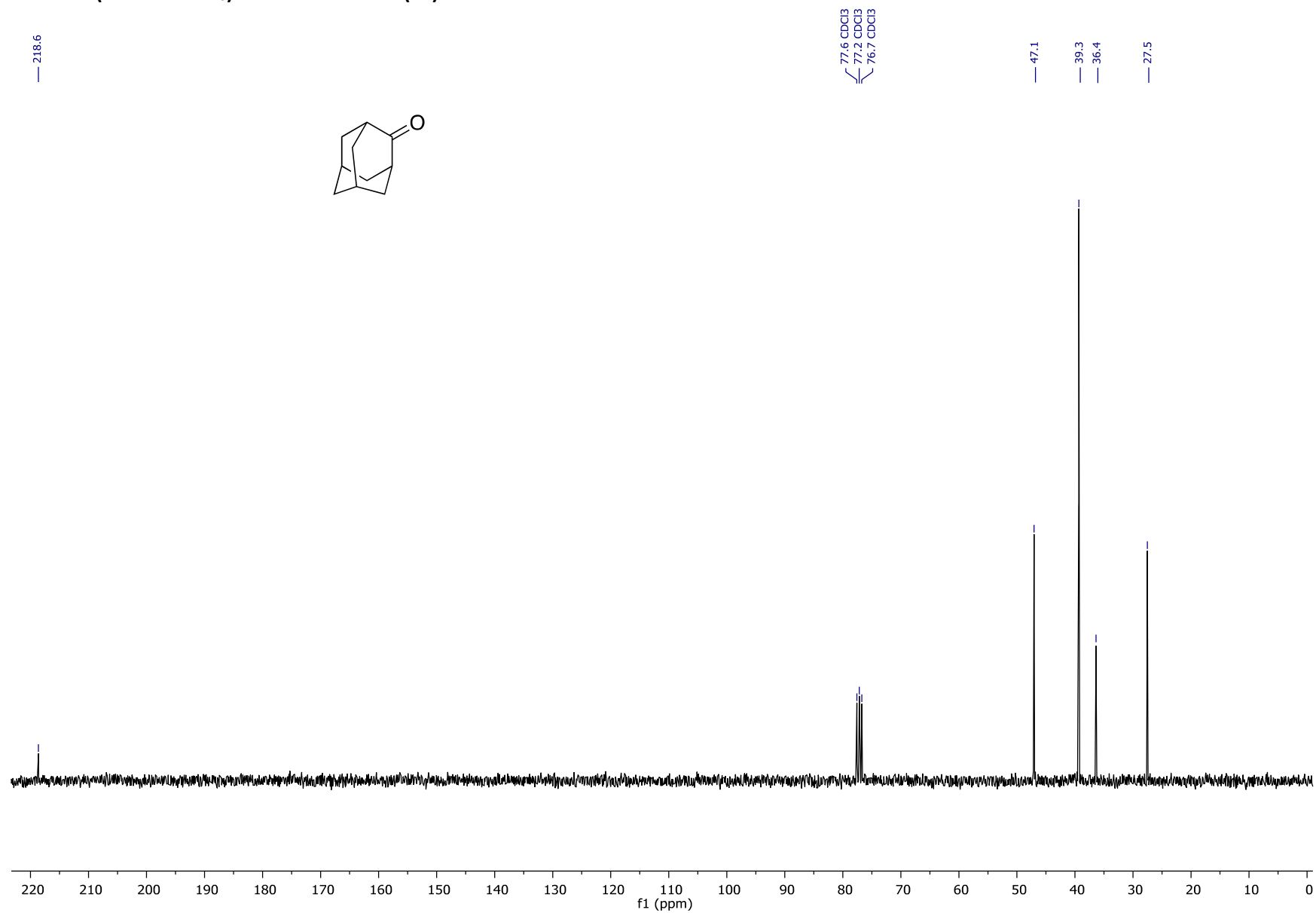
^{13}C -NMR (101 MHz CDCl_3) 2-Octanone (3v)



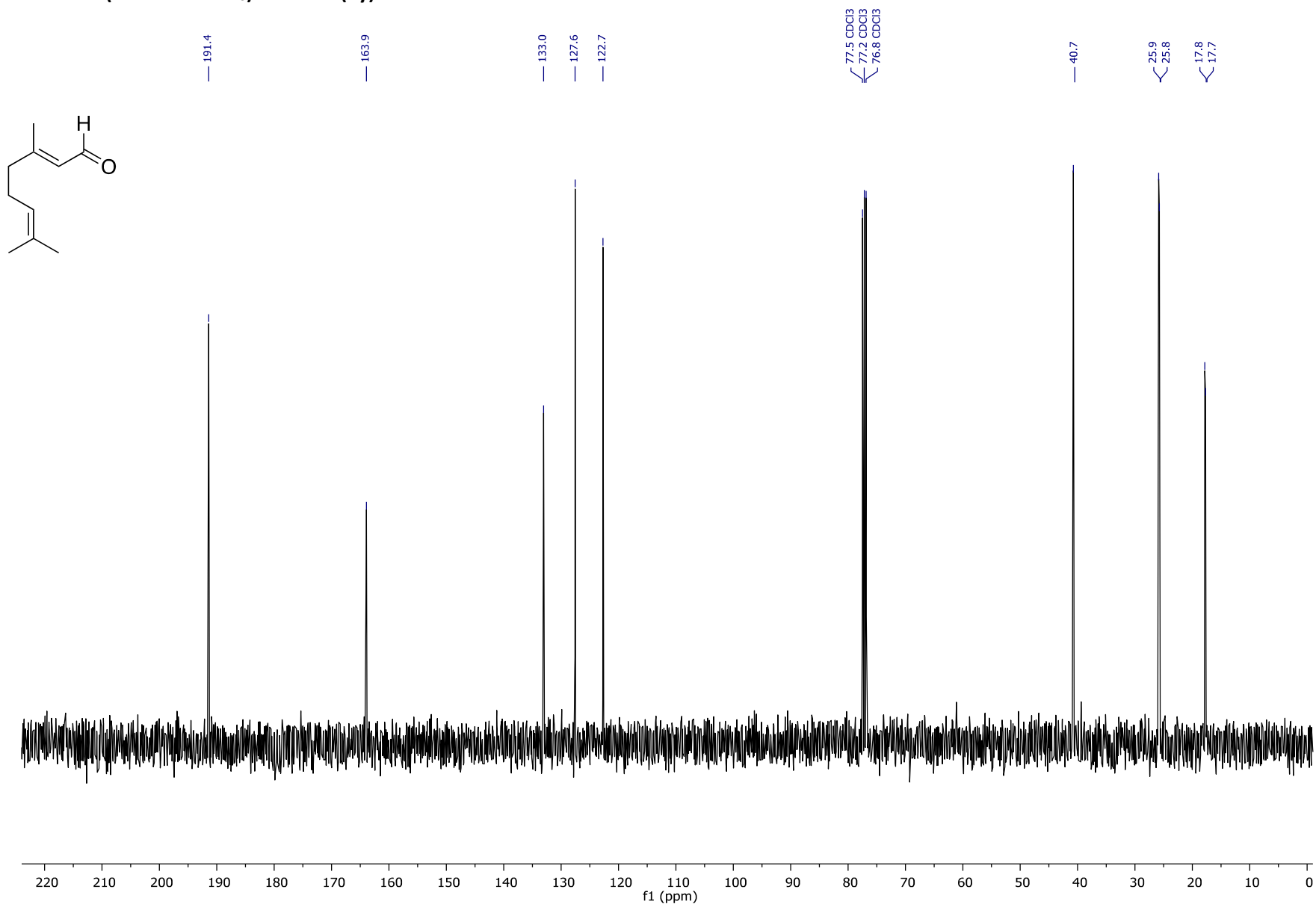
^{13}C -NMR (101 MHz CDCl_3) 4-*tert*-Butylcyclohexanone (3w)



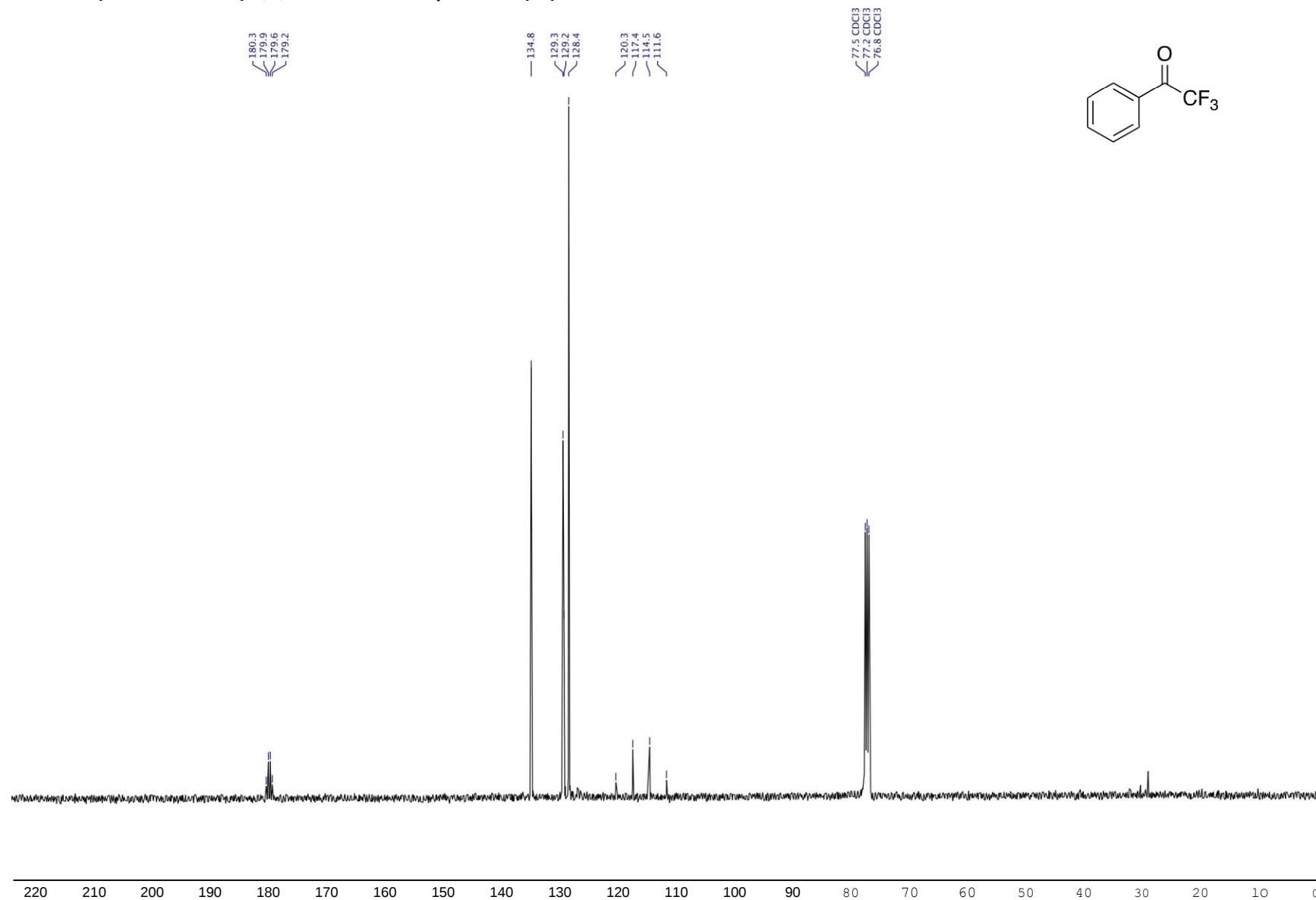
^{13}C -NMR (75 MHz CDCl_3) 2-Adamantanone (3x)



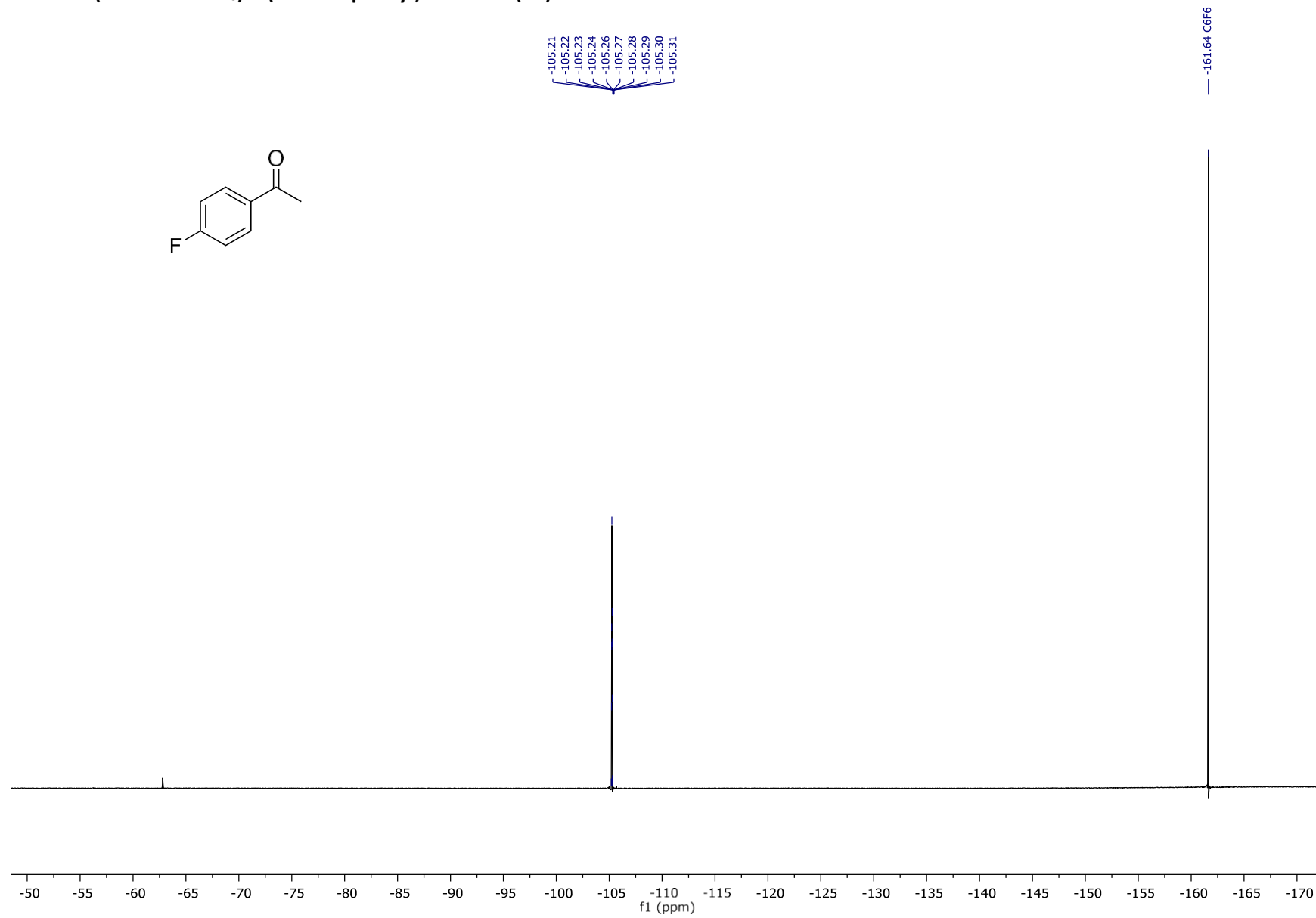
^{13}C -NMR (101 MHz CDCl_3) Geranial (3y)



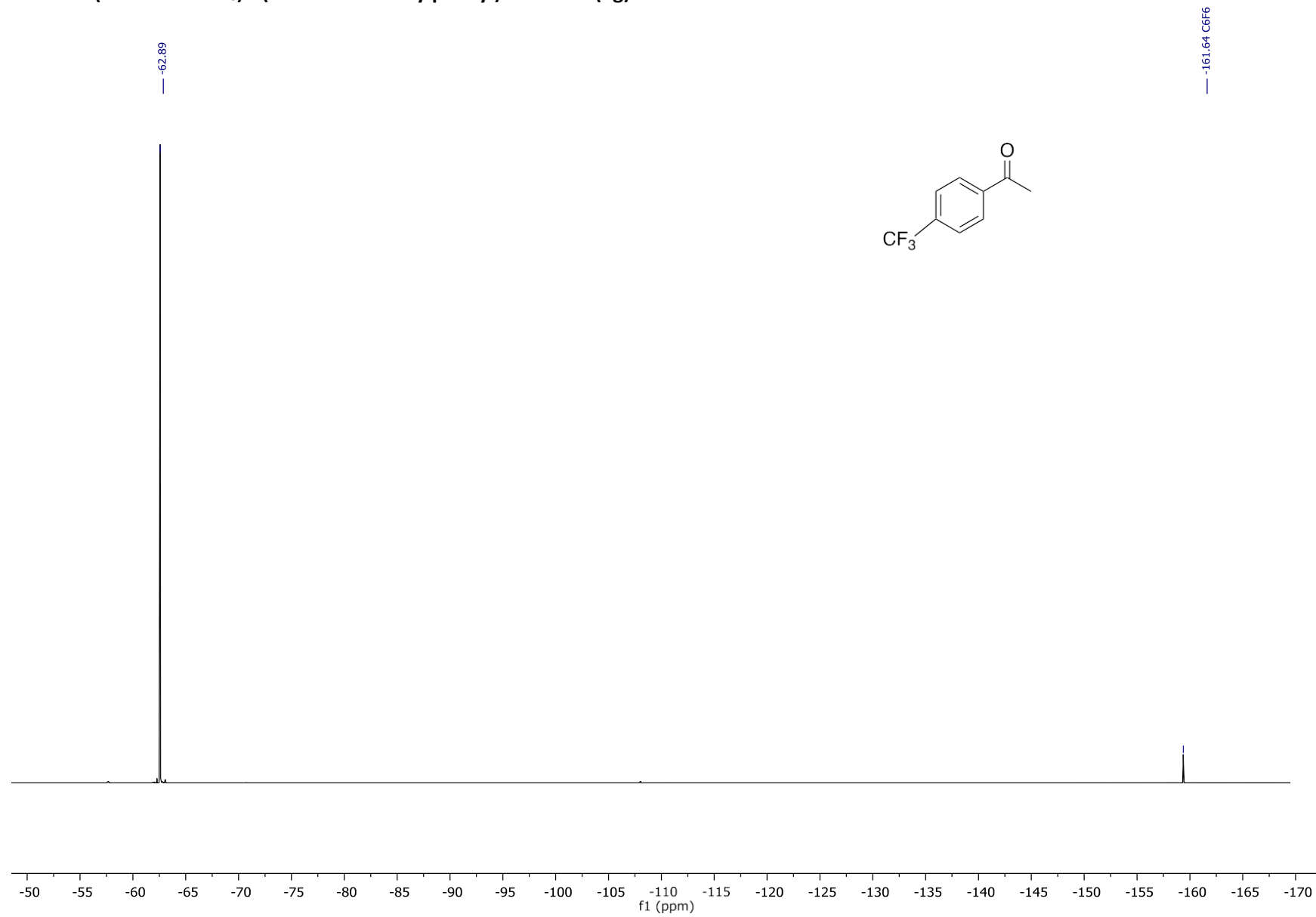
^{13}C -NMR (101 MHz CDCl_3) 1,1,1-Trifluoroacetophenone (3z)



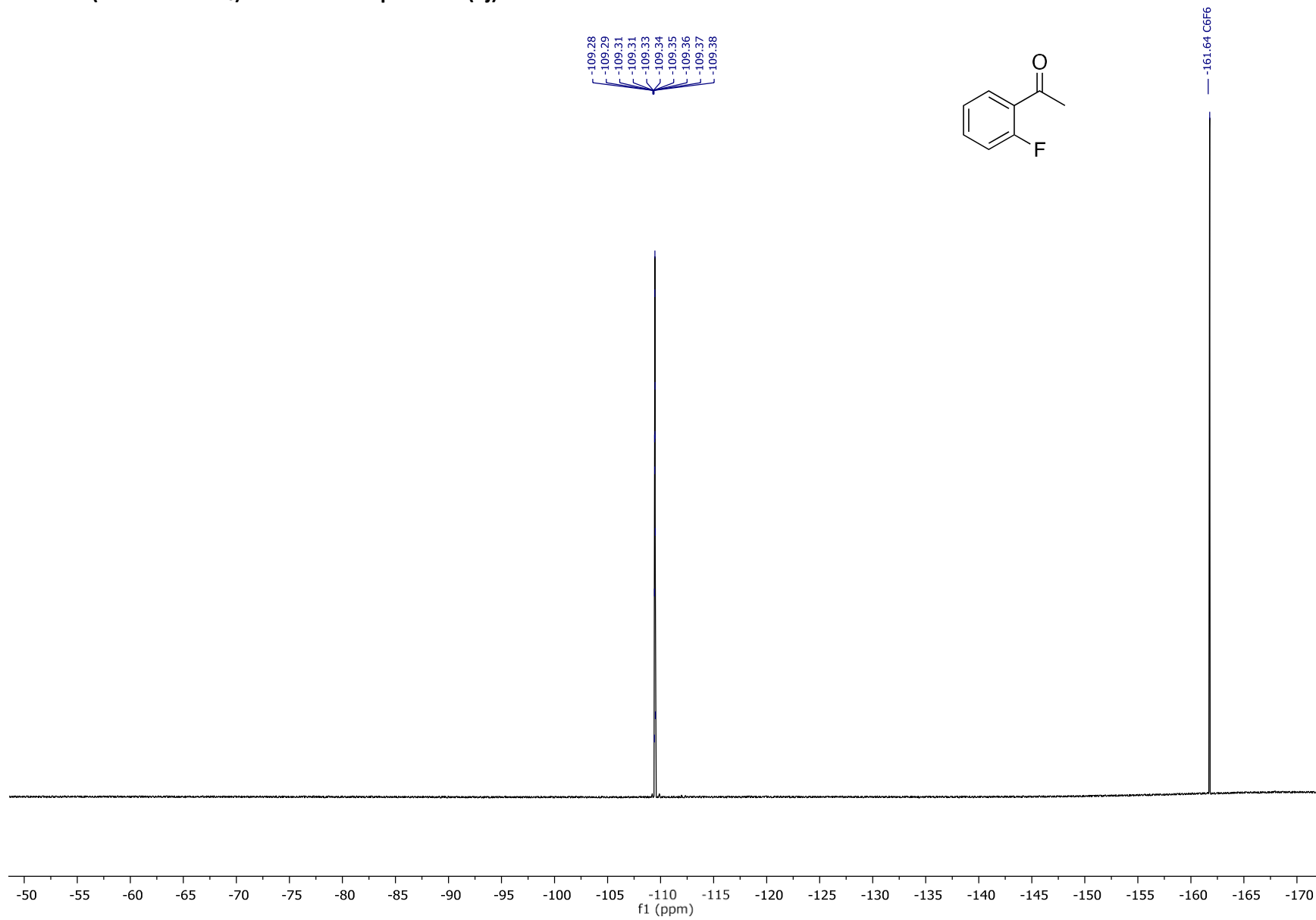
^{19}F -NMR (376 MHz CDCl_3) 1-(4-Fluorophenyl)ethenone (3d)



^{19}F -NMR (376 MHz CDCl_3) 1-(4-Trifluoromethylphenyl)ethanone (3g)



^{19}F -NMR (376 MHz CDCl_3) 2'-Fluoroacetophenone (3j)



^{19}F -NMR (376 MHz CDCl_3) 1,1,1-Trifluoroacetophenone (3z)

