Supplementary Information

Isopropenyl acetate, a remarkable, cheap and acylating agent of amines under solvent- and catalyst-free conditions: a systematic investigation.

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Table of Contents

General Information

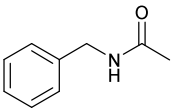
Chemical materials were purchased and used without further purifications, unless otherwise specified. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated. All reagents purchased from commercial sources were used as received. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light (254 nm and 365 nm) as the visualizing agent and an ethanolic solution of phosphomolybdic acid and heat as developing agents.
NMR spectra were recorded on Bruker AC 200 (200 and 50.3 MHz) instrument and calibrated using residual undeuterated solvent as an internal reference (peak at 7.26 ppm in ^{1}H NMR and peak at 77 ppm in ^{13}C NMR in the case of $CDCl_3$). The following abbreviations were used to designate multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, quin=quintuplet, sext=sextet, sep=septet, br=broad, dd=double-doublet, ddd=double-double-doublet. Chemical shifts were expressed in ppm and coupling constant (*J*) in Hz. The peak at 2.17 ppm in some of ^{1}H NMR spectra is acetone.[1]

Experimental procedures and characterization of acetamides

GP.1 General procedure for acetylation of amines

In a typical procedure, in a capped vessel the isopropenyl acetate (4 mmol) and a suitable amine (1 mmol) were mixed. The reaction mixture was stirred for 3h at 60°C and then was transferred in a round-bottomed flask and concentrated under reduced pressure in order to eliminate either the isopropenyl acetate in excess and acetone to obtain the crude product. This was analyzed by ^{1}H and ^{13}C NMR and their NMR spectral data were consistent with those available in the literature. Concerning optically active amines, it was measured the optical rotation by polarimeter and also these data were in full agreement with those reported in the literature. Starting materials and reagents used in this study were obtained commercially from Aldrich, Acros, Fluka and were used without purification.

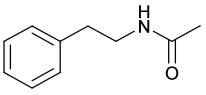
GP.2 Characterization of acetamides



3a

N-benzylacetamide[2]

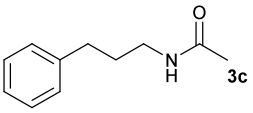
^{1}H NMR (200MHz, $CDCl_3$) δ 2.00 (s, 3H), 4.41 (d, *J* = 5.7 Hz, 2H), 6.01 (br s, 1H), 7.25-7.32 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.21, 138.17, 128.30, 127.41, 43.24, 22.69.



3b

***N*-phenethylacetamide**[3]

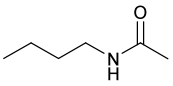
^{1}H NMR (200MHz, $CDCl_3$) δ 1.94 (s, 3H), 2.17 (s, 3H), 2.82 (t, *J* = 6.9 Hz, 2H), 3.51 (q, *J* = 6.9 Hz, 2H), 5.66 (br s, 1H), 7.10-7.40 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.37, 138.67, 128.40, 128.25, 126.12, 40.54, 35.28, 22.79.



3c

***N*-(3-phenyl-propyl)acetamide**[4]

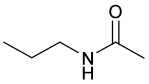
^{1}H NMR (200MHz, $CDCl_3$) δ 1.75-1.97 (m, 5H), 2.66 (t, *J* = 7.3 Hz, 2H), 3.29 (q, *J* = 7.1 Hz, 2H), 5.60 (br s, 1H), 7.05-7.40 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.40, 141.16, 128.06, 128.00, 125.59, 38.90, 32.90, 30.71, 22.72.



3d

***N*-butylethanamide**[5]

^{1}H NMR (200MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.20-1.55 (m, 4H), 1.97 (s, 3H), 2.17 (s, 2H), 3.23 (q, *J* = 6.8 Hz, 2H), 5.68 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.42, 38.97, 31.11, 22.54, 19.70, 13.33.



3e

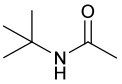
***N*-propylacetamide**[6]

^{1}H NMR (200MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.52 (sext, *J* = 7.2 Hz, 4H), 1.98 (s, 3H), 2.18 (s, 2H), 3.20 (q, *J* = 5.9 Hz, 2H), 5.62 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.41, 40.68, 22.11, 21.95, 10.72.

3f

***N*-methylacetamide**[7]

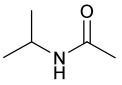
^{1}H NMR (200MHz, $CDCl_3$) δ 1.94 (s, 3H), 2.74 (d, *J* = 4.8 Hz, 3H), 5.65 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ171.28, 25.77, 22.27.



3g

***N*-*tert*-buthylethanamide**[8]

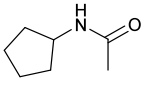
^{1}H NMR (200MHz, $CDCl_3$) δ 1.33 (s, 9H), 1.91 (s, 3H), 5.27 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.46, 51.01, 28.72, 24.37.



3h

***N*-isopropylethanamide**[9]

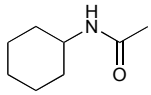
^{1}H NMR (200MHz, $CDCl_3$) δ 1.13 (d, *J* = 6.5 Hz, 6H), 1.93 (s, 3H), 4.07 (sep, *J* = 6.5 Hz, 1H), 5.45 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.46, 41.06, 23.01, 22.33.



3i

Cyclopentyl acetamide[10]

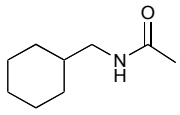
^{1}H NMR (200MHz, $CDCl_3$) δ 1.22-1.83 (m, 6H), 1.86-2.18 (m, 5H), 4.18 (sext, *J* = 7.3 Hz, 1H), 5.50 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.88, 50.91, 32.59, 23.45, 22.90.



3j

Cyclohexyl acetamide[11]

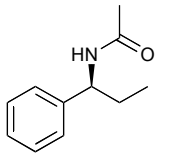
^{1}H NMR (200MHz, $CDCl_3$) δ 0.97-2.18 (m, 10H), 3.62-3.91 (m, 1H), 5.30-5.64 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.24, 48.01, 32.75, 25.22, 24.69, 23.06.



3k

Cyclohexanemethyl acetamide[12]

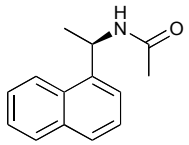
^{1}H NMR (200MHz, $CDCl_3$) δ 0.75-1.35 (m, 6H), 1.57-1.87 (m, 5H), 1.98 (s, 3H), 3.08 (t, *J* = 6.4 Hz, 2H), 5.67 (br s, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.34, 45.51, 37.43, 30.50, 26.01, 25.45, 22.64.



3l

***N*-(S)-phenylpropyl)acetamide**[13]

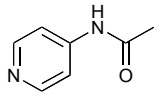
^{1}H NMR (200MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.3 Hz, 3H), 1.72-2.04 (m, 5H), 4.87 (q, *J* = 7.7 Hz, 1H), 5.91 (br d, 1H), 7.15-7.40 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.60, 142.27, 128.23, 126.88, 126.46, 54.81, 28.97, 22.91, 10.64.



3m

***N*-(R)1-naphthalen-2-yl)acetamide**[14]

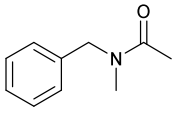
^{1}H NMR (200MHz, $CDCl_3$) δ 1.67 (d, *J* = 6.7 Hz, 3H), 1.97 (s, 3H), 5.62-5.78 (br s, 1H), 5.93 (dt, *J* = 6.7, 14.8 Hz, 1H), 7.44-7.62 (m, 4H), 7.75-7.91 (m, 2H), 8.05-8.15 (m, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.04, 138.43, 133.63, 130.80, 128.53, 127.87, 126.19, 125.54, 125.01, 123.15, 122.28, 44.35, 22.83, 20.64.



3n

***N*-(pyridin-4-yl)acetamide**[15]

^{1}H NMR (200MHz, $CDCl_3$) δ 2.21 (s, 3H), 7.54 (d, *J* = 5.2 Hz, 2H), 8.47 (d, *J* = 5.2 Hz, 2H), 8.9 (bs, 1H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.75, 150.20, 145.94, 113.81, 24.61.

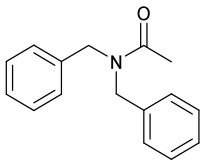


5a

***N*-benzyl-*N*-methylacetamide**[16]

Spectroscopic data of this amide were obtained as a mixture of two rotational isomers

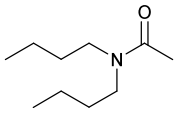
^{1}H NMR (200MHz, $CDCl_3$) δ 2.16 (s, 6H), 2.4 (minor isomer, s, 3H), 2.92 (major isomer, s, 3H), 4.53 (minor isomer, s, 2H), 4.59 (major isomer, s, 2H), 7.12-7.42 (m, 5); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.22, 169.94, 136.71, 135.95, 128.21, 127.85, 127.25, 126.87, 126.59, 125.63, 53.44, 49.78, 34.79, 32.92, 21.05, 20.69.



5c

***N,N*-dibenzylacetamide**[17]

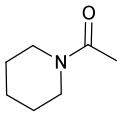
^{1}H NMR (200MHz, $CDCl_3$) δ 2.18 (s, 3H), 4.45 (s, 2H), 4.61 (s, 2H), 7.15-7.42 (m, 10H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.78, 139.73, 136.93, 136.01, 128.63, 128.27, 128.06, 127.93, 127.86, 127.30, 127.09, 126.65, 126.01, 52.65, 50.30, 47.54, 21.35.



5d

***N,N*-dibutylacetamide**[18]

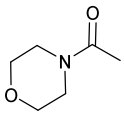
^{1}H NMR (200MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 6H), 1.26-1.59 (m, 8H), 2.17 (s, 3H), 2.59 (t, *J* = 7.3 Hz, 4H); ^{13}C NMR (75MHz, $CDCl_3$) δ 169.13, 48.85, 31.20, 19.82, 13.24.



5e

Piperidine acetamide[19]

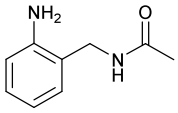
^{1}H NMR (200MHz, $CDCl_3$) δ 1.45-1.59 (m, 6H), 2.07 (s, 3H), 3.32-3.42 (m, 2H), 3.47-3.75 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 168.65, 47.24, 42.28, 26.19, 25.27, 24.23, 21.25.



5f

Morpholine acetamide[20]

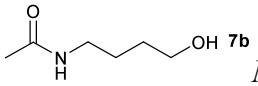
^{1}H NMR (200MHz, $CDCl_3$) δ 2.09 (s, 3H), 3.42-3.50 (m, 2H), 3.56-3.71 (m, 6H); ^{13}C NMR (75MHz, $CDCl_3$) δ 168.67, 66.16, 65.97, 46.05, 41.15, 20.54.



7a

2-aminobenzylacetamide[21]

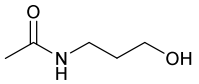
^{1}H NMR (200MHz, $CDCl_3$) δ 1.97 (s, 3H), 4.16 (br s, 2H), 4.34 (d, *J* = 6.2 Hz, 2H), 6.00 (br s, 1H), 6.60-6.72 (m, 2H), 6.95-7.15 (m, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.64, 145.33, 130.40, 128.99, 121.85, 117.56, 115.54, 40.57, 22.80.



7b

***N*-(4-hydroxybutyl)acetamide**[22]

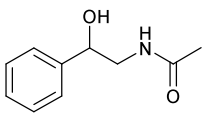
^{1}H NMR (200MHz, $CDCl_3$) δ 1.53-1.65 (m, 4H), 1.97 (s, 3H), 2.10 (br, s, 2H), 3.27 (q, *J* = 5.9 Hz, 2H), 3.67 (t, *J* = 5.9 Hz, 2H), 5.89 (br s, 1H); ^{13}C NMR (75MHz, CD_3COCD_3) δ 172.20, 62.72, 40.61, 31.51, 27.46, 23.68.



7c

***N*-(3-hydroxypropyl)acetamide**[23]

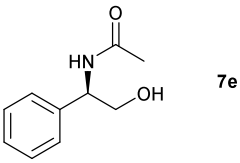
^{1}H NMR (200MHz, $CDCl_3$) δ 1.60-1.74 (m, 2H), 1.99 (s, 3H), 3.40 (q, *J* = 6.2 Hz, 2H), 3.63 (t, *J* = 5.7 Hz, 2H), 5.21 (br s, 1H), 6.11 (br s, 1H); ^{13}C NMR (75MHz, CD_3COCD_3) δ 172.76, 60.39, 37.71, 33.68, 23.59.



7d

***N*-(2-Hydroxy-2-phenylethyl)acetamide**[24]

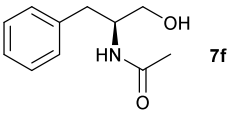
^{1}H NMR (200MHz, $CDCl_3$) δ 1.98 (s, 3H), 3.30 (ddd, *J* = 4.9, 8.0, 14.0 Hz, 2H), 3.67 (ddd, *J* = 3.3, 6.9, 14.0 Hz, 1H); 4.83 (dd, *J* = 3.3, 8.0 Hz, 1H), 6.12 (br s, 1H), 7.27-7.42 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 171.78, 141.62, 128.22, 127.70 125.64, 72.84, 47.28, 22.70.



7e

***N*-[(1*R*)-(2-Hydroxy-1-phenylethyl)]acetamide**[25]

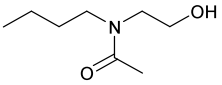
^{1}H NMR (200MHz, $CDCl_3$) δ 2.04 (s, 3H), 2.67 (br s, 1H), 3.86 (dd, *J* = 1.9, 4.9 Hz, 2H), 5.10-5.47 (m, 1H), 6.33 (br s, 1H), 7.25-7.41 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 171.78, 141.62, 128.22, 125.64, 72.84, 47.28, 22.70.



7f

2*S*-acetamido-3-phenylpropan-1-ol[26]

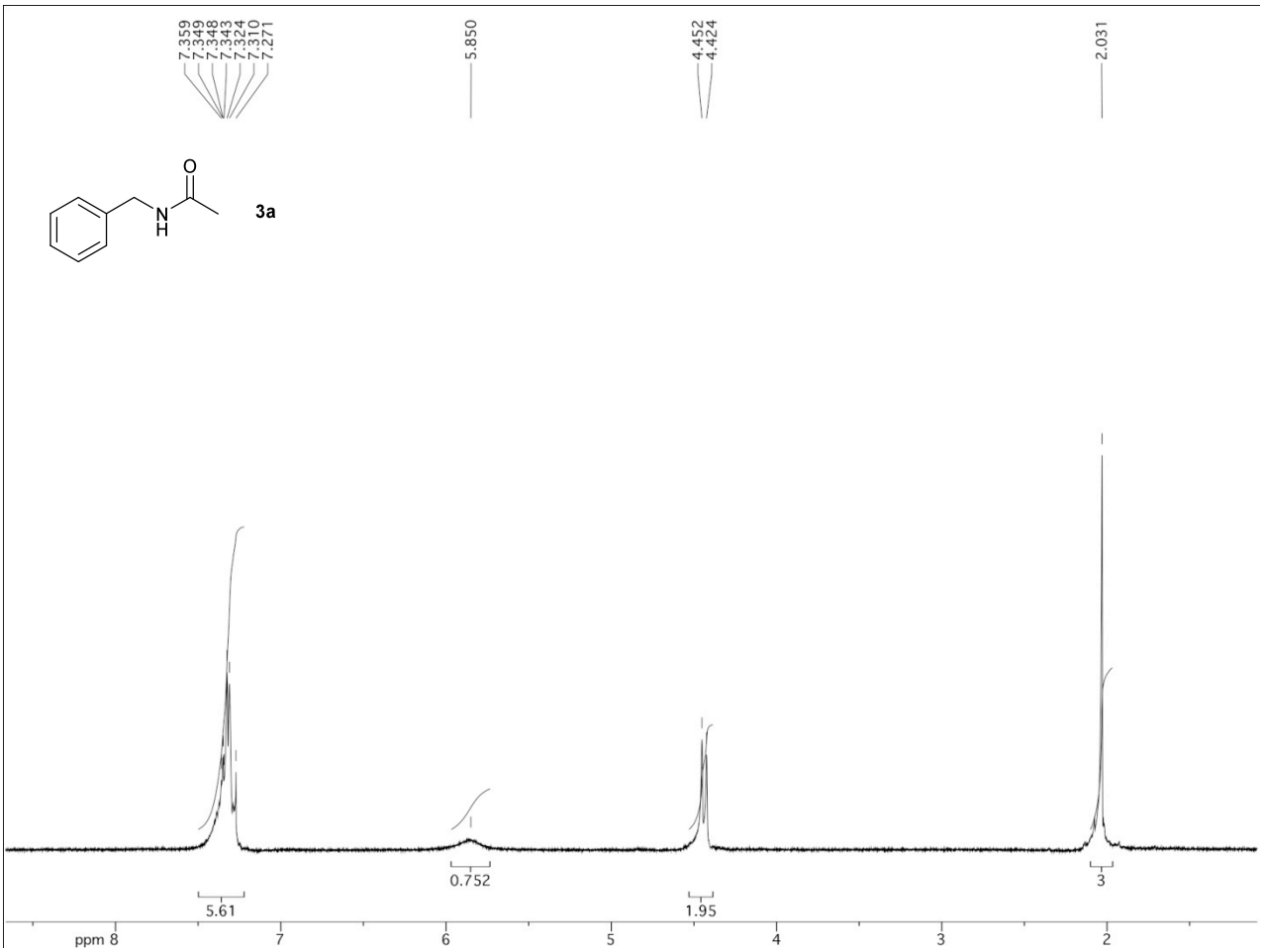
^{1}H NMR (200MHz, $CDCl_3$) δ 1.94 (s, 3H), 2.85 (d, *J* = 7.2 Hz, 2H), 3.18 (br s, 1H), 3.54 (dd, *J* = 5.1, 11.1 Hz, 1H), 3.66 (dd, *J* = 3.7, 11.1 Hz, 1H), 4.05-4.25 (m, 1H), 6.02 (br d, 1H), 7.15-7.35 (m, 5H); ^{13}C NMR (75MHz, $CDCl_3$) δ 170.77, 136.61, 129.15, 128.59, 126.62, 63.92, 52.83, 36.93, 23.33.

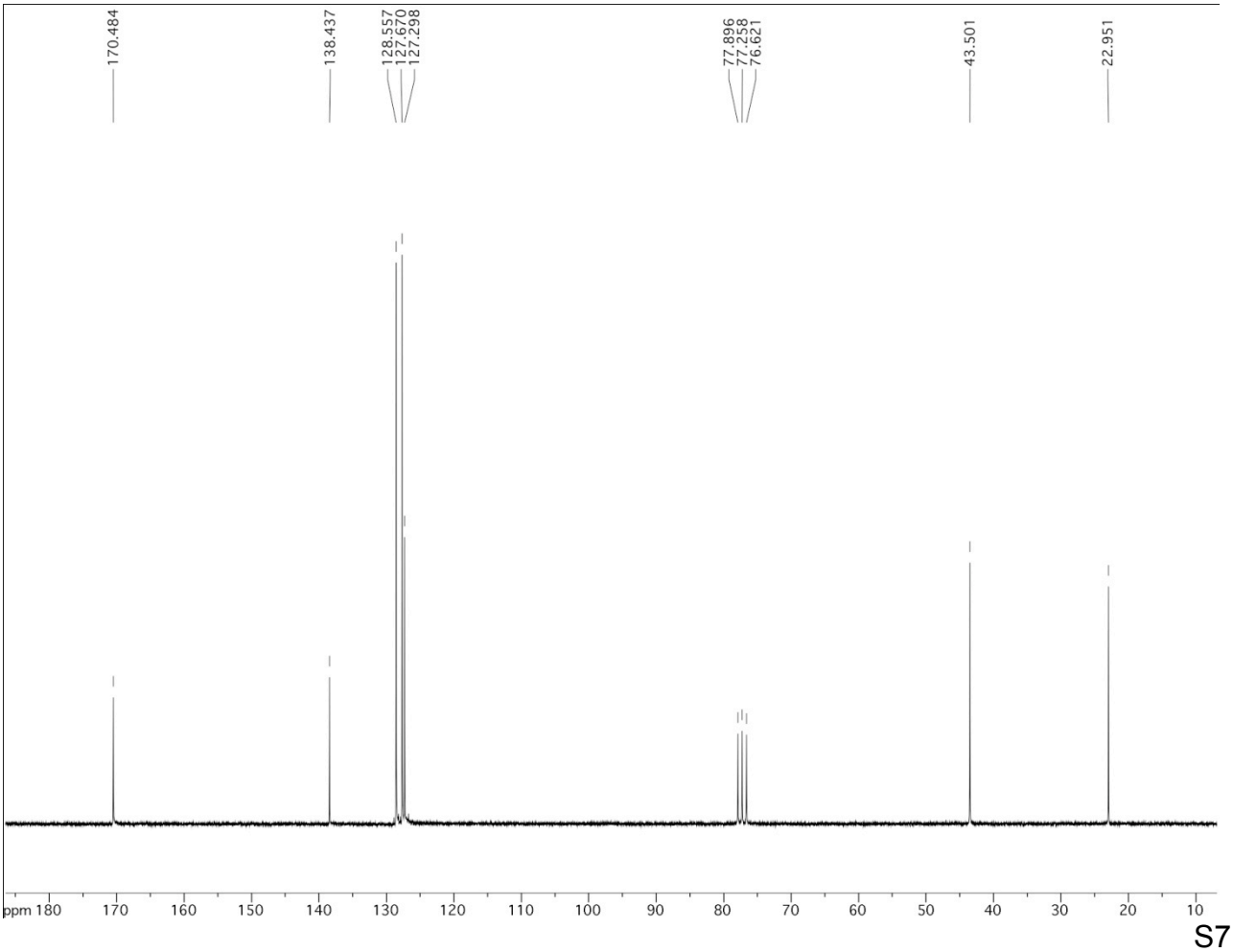


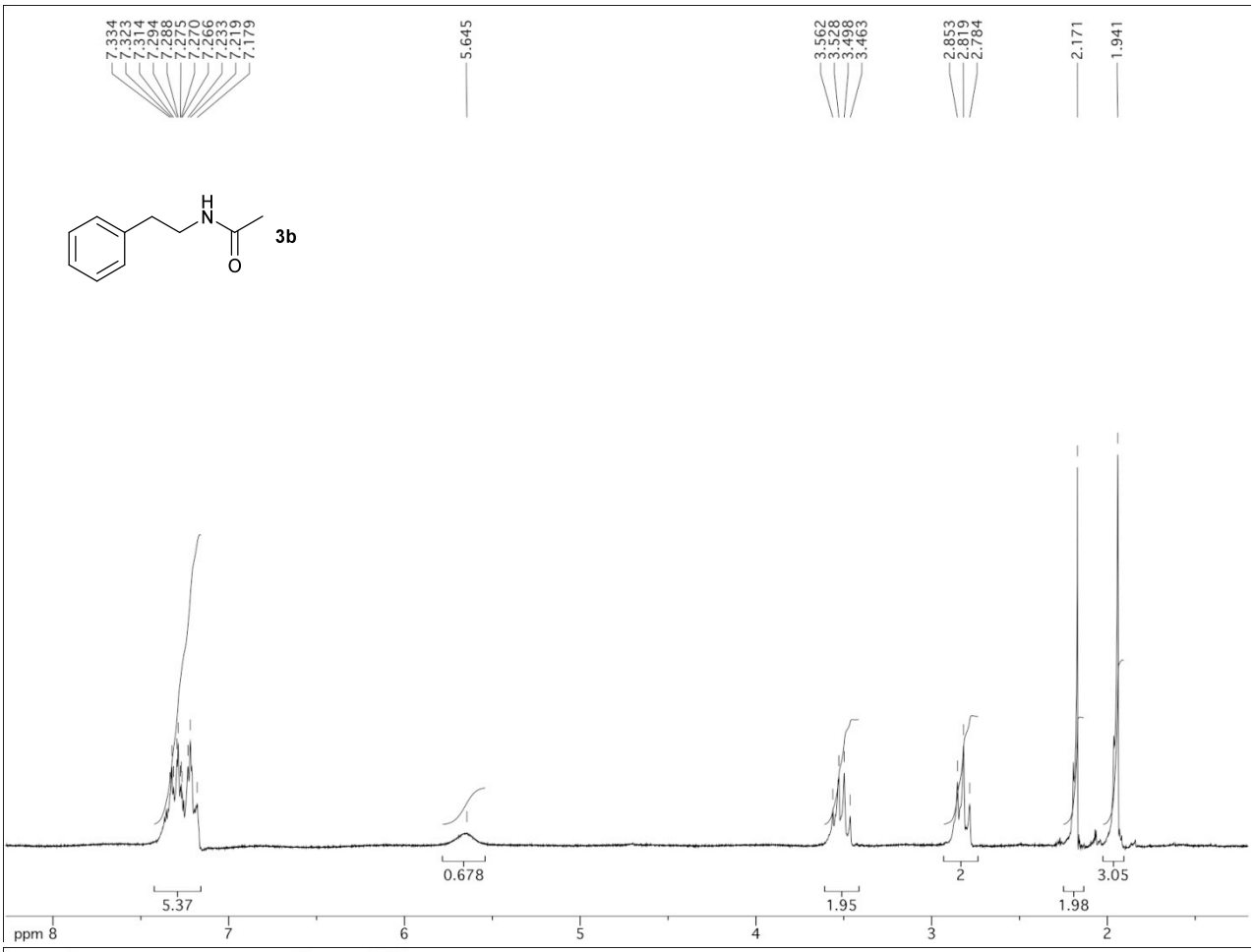
7g

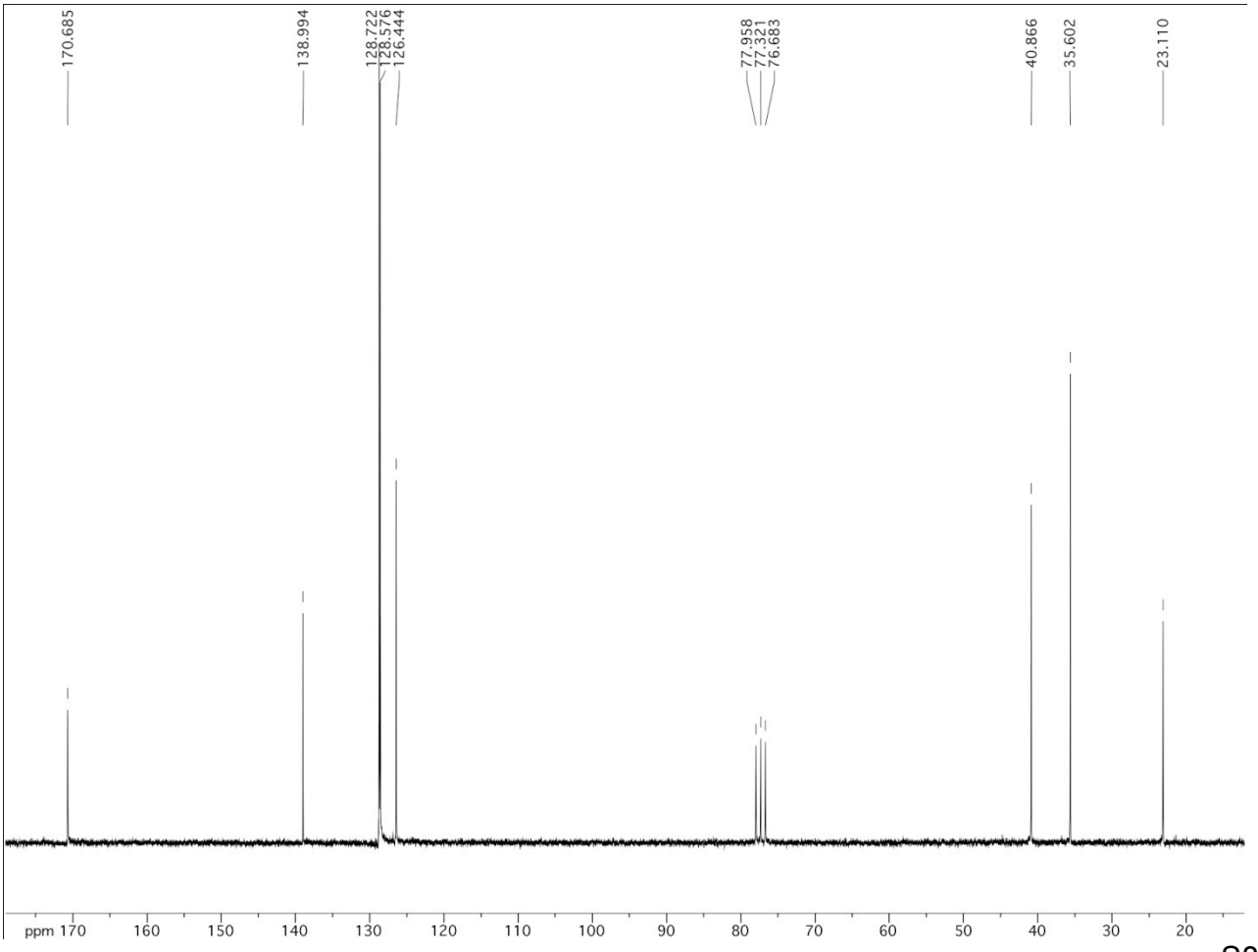
***N*-butyl-2-hydroxyethylacetamide**[27]

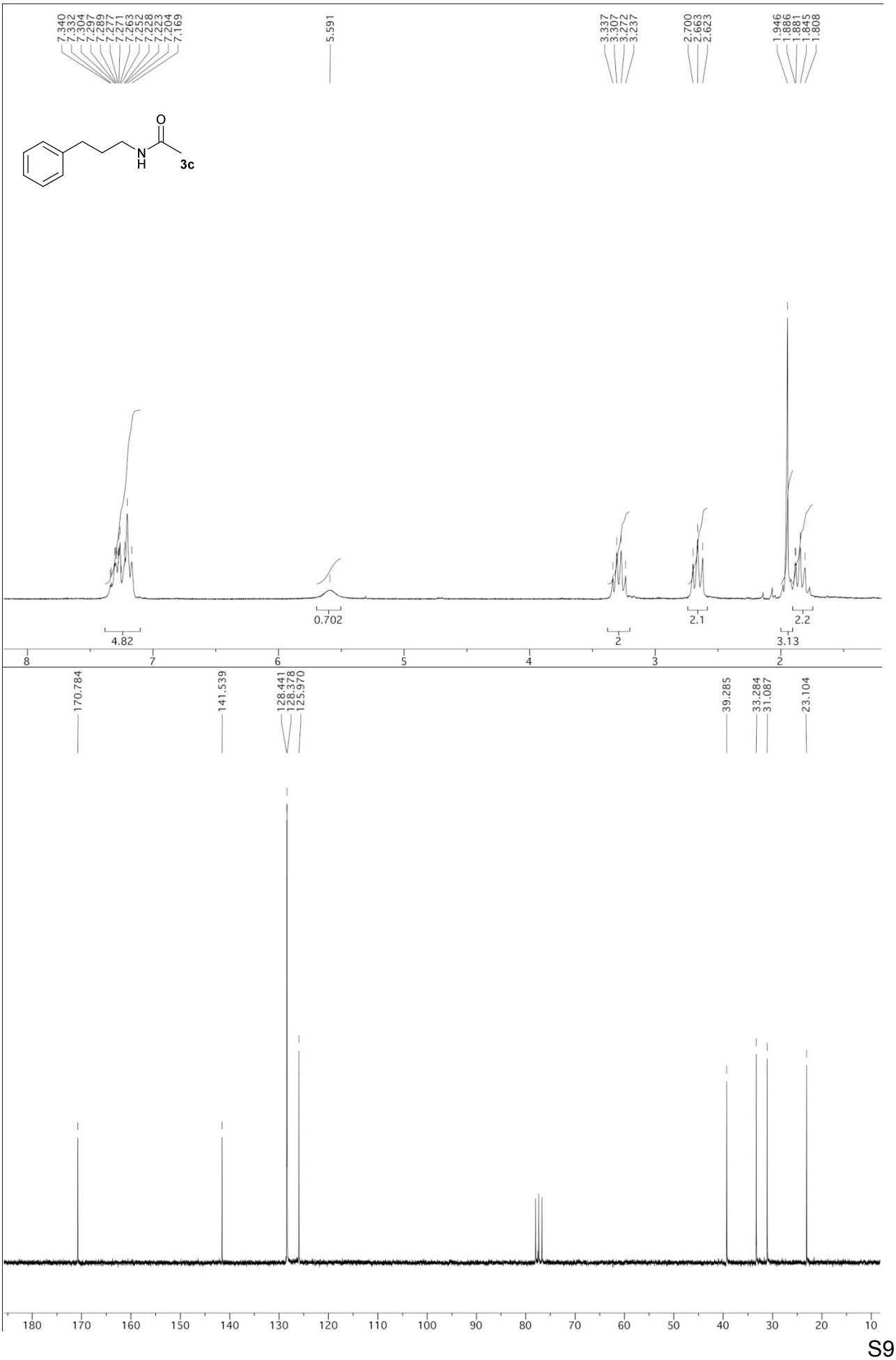
^{1}H NMR (200MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.1 Hz, 3H), 1.20-1.64 (m, 4H), 1.97 (s, 3H), 2.10 (s, 3H), 3.00-3.35 (m, 3H), 3.49 (t, *J* = 5.3 Hz, 2H), 3.73 (t, *J* = 4.9 Hz, 2H); ^{13}C NMR (75MHz, $CDCl_3$) δ 172.15, 61.50, 50.05, 49.23, 30.71, 21.14, 19.77, 13.58.

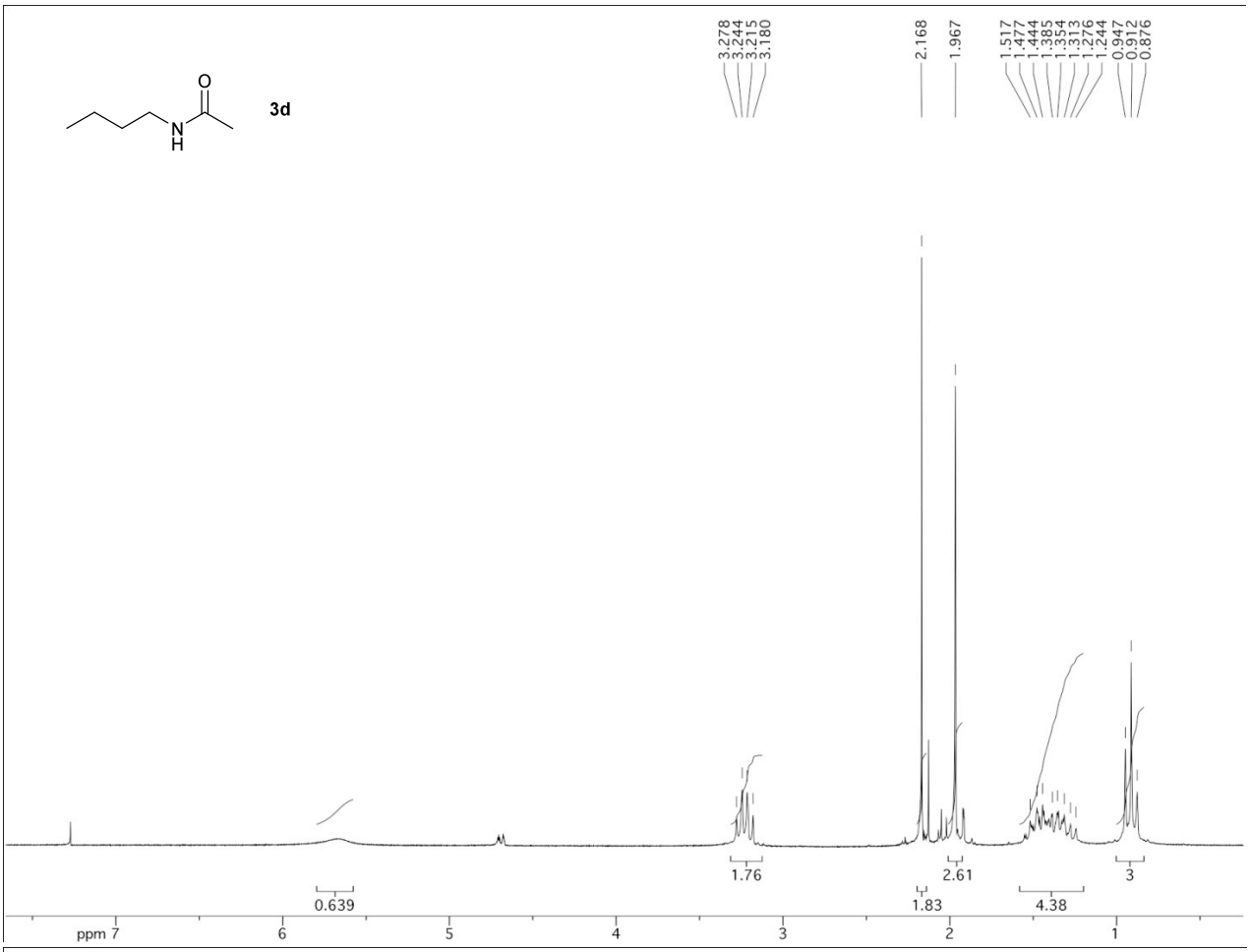


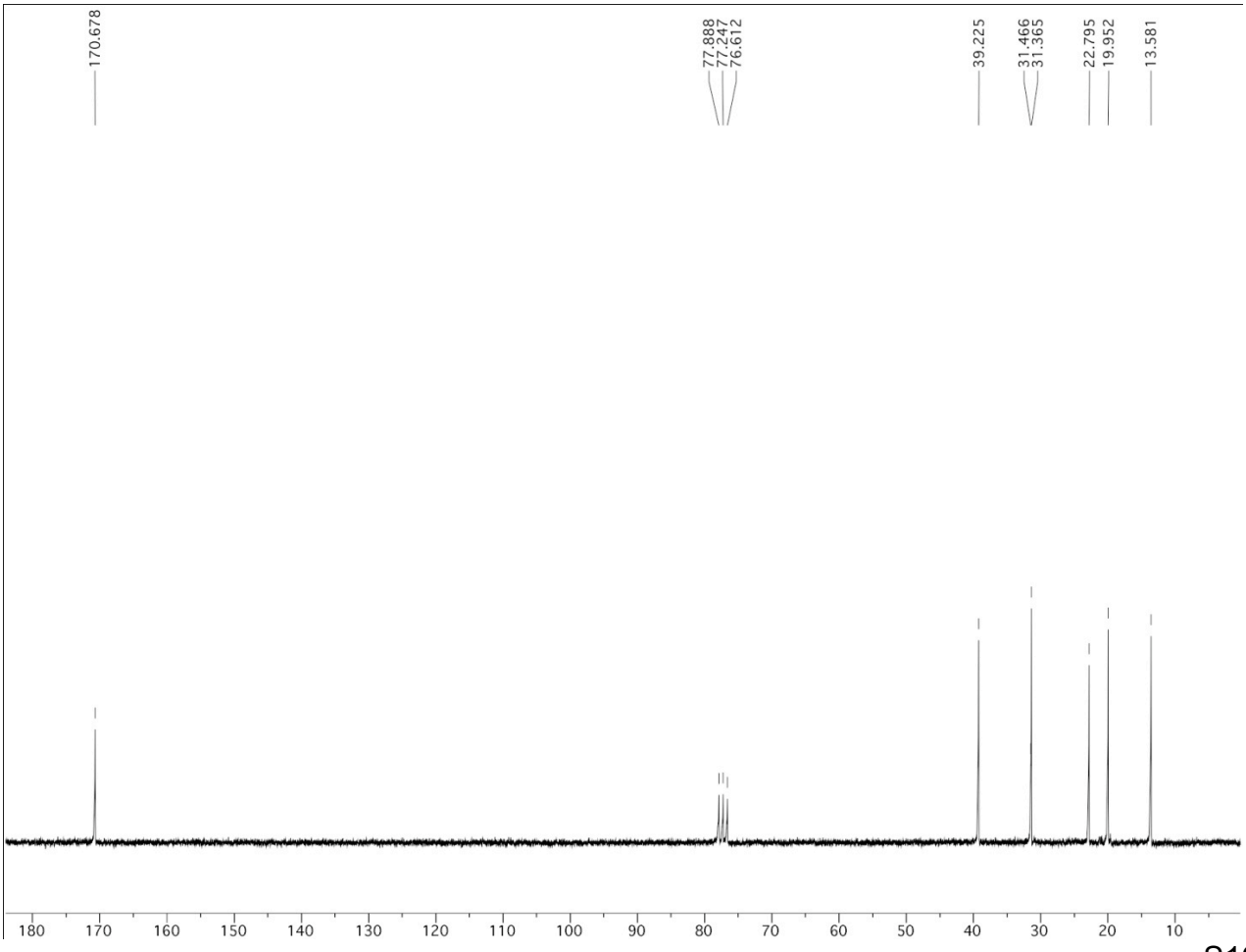


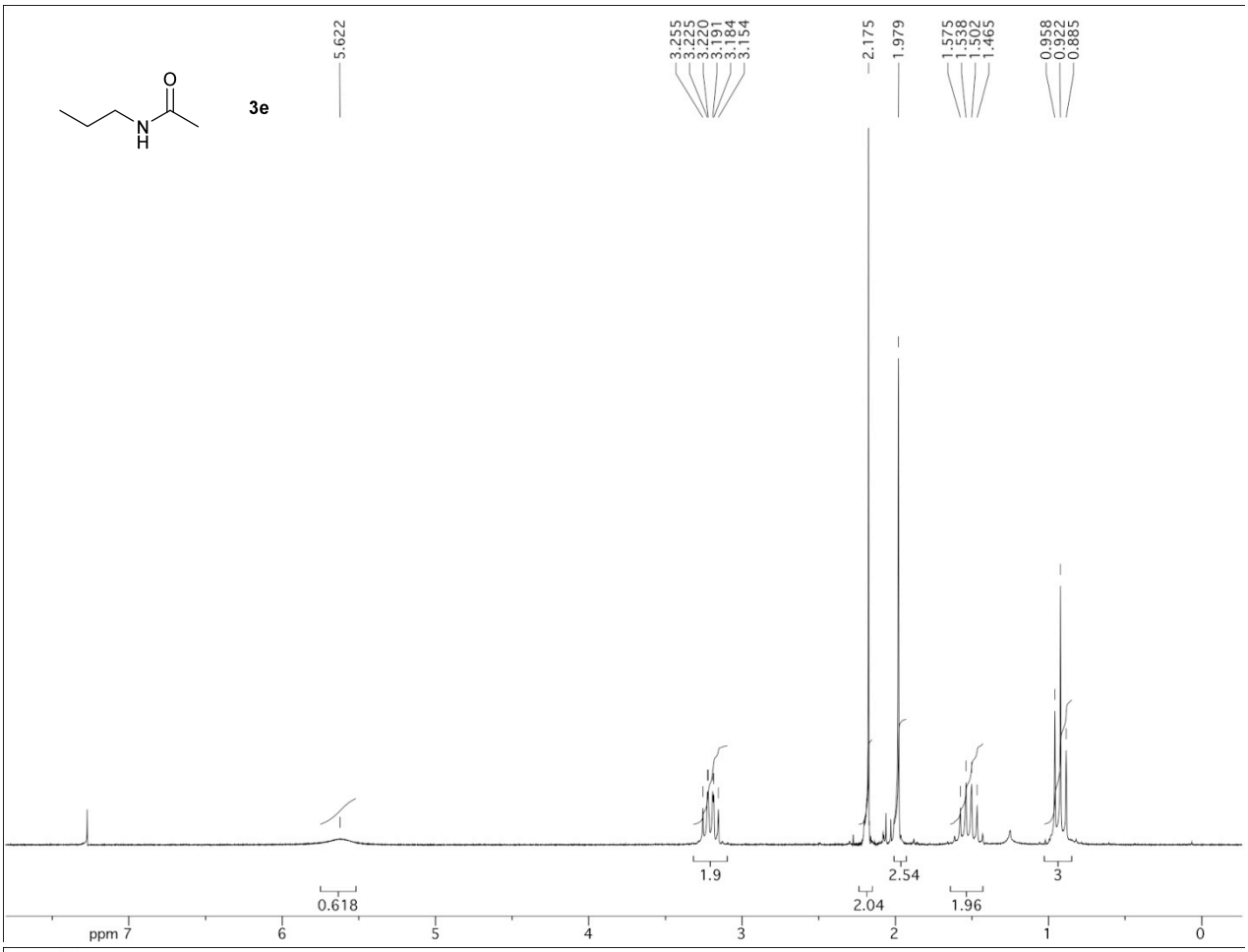


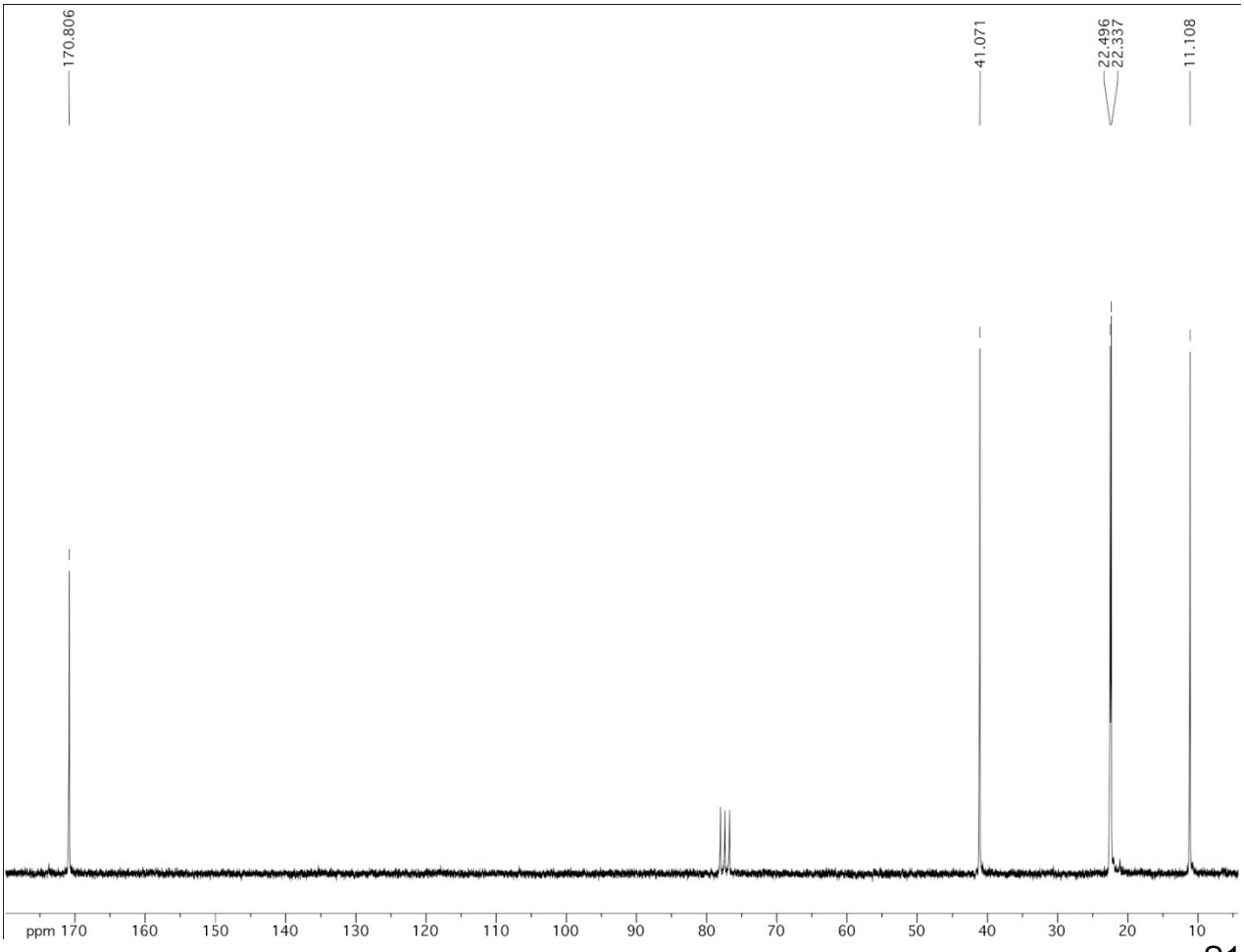


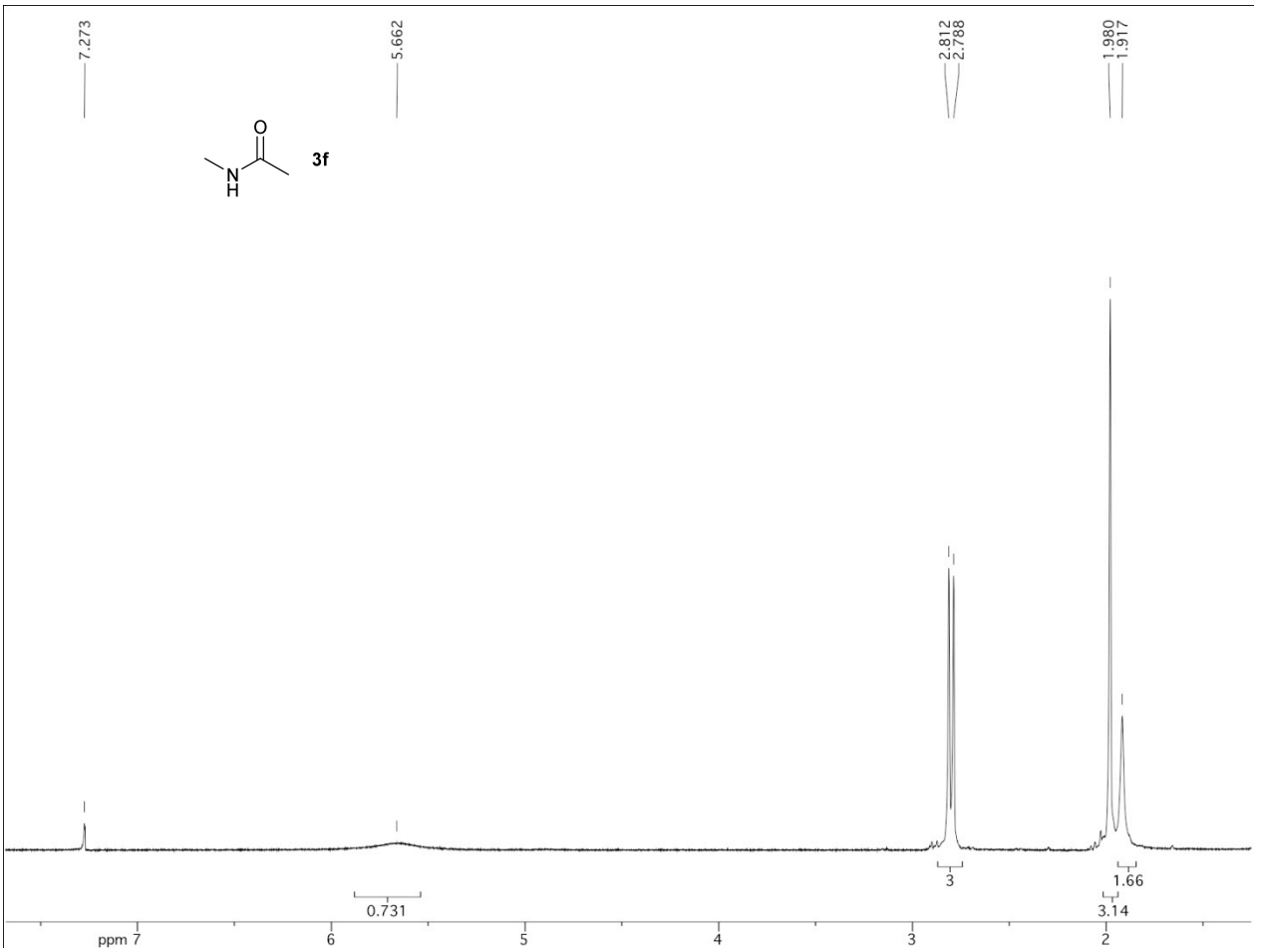


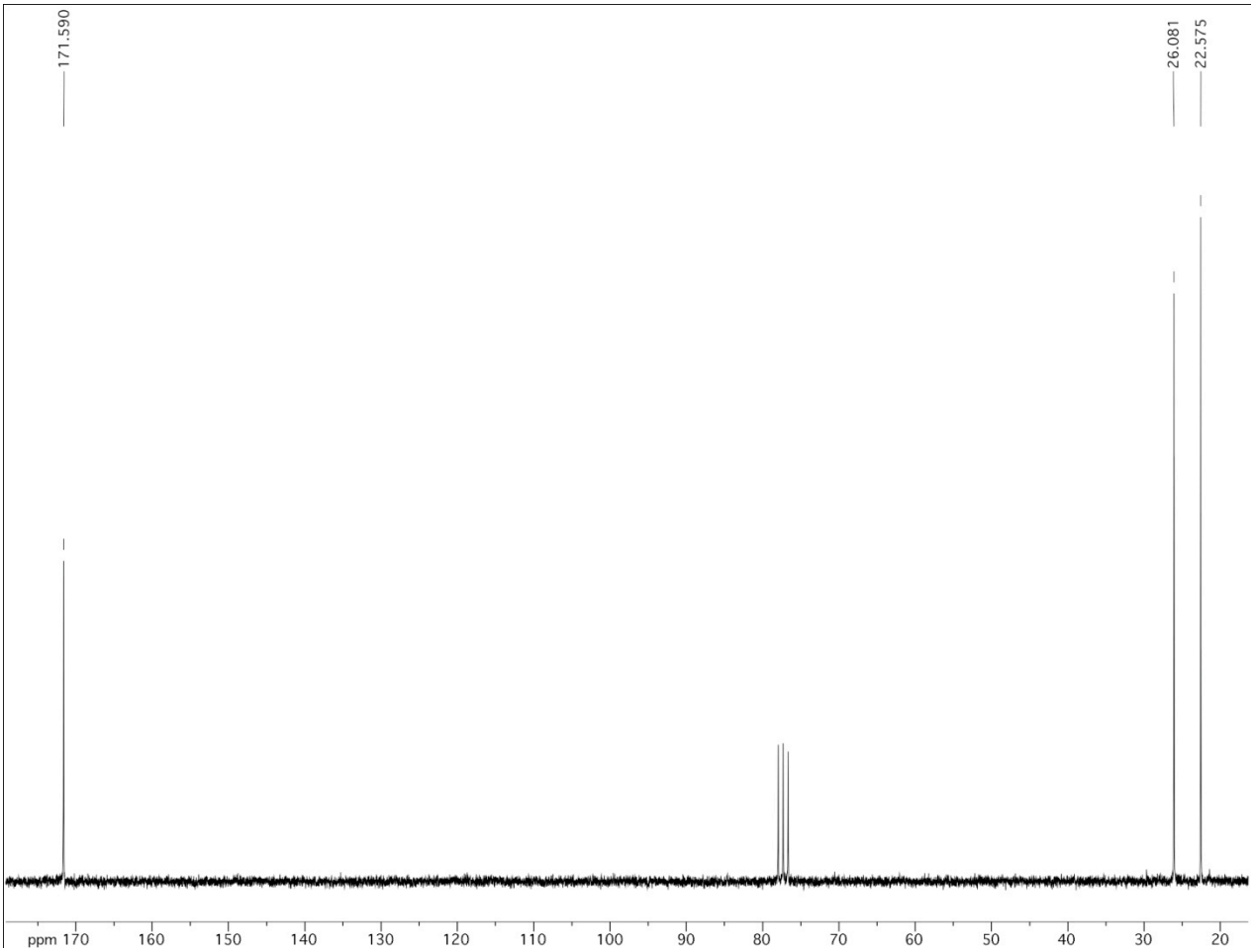


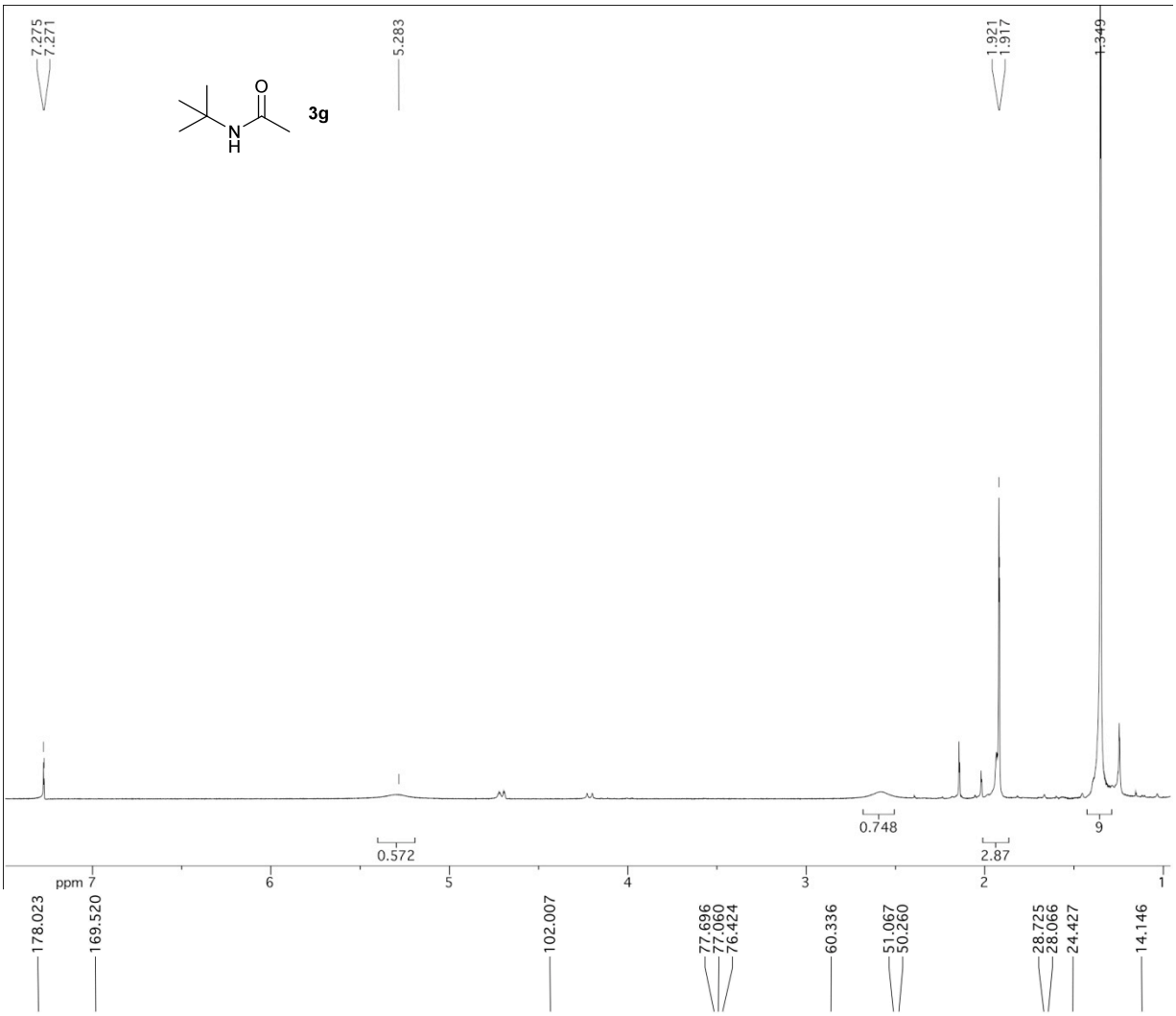


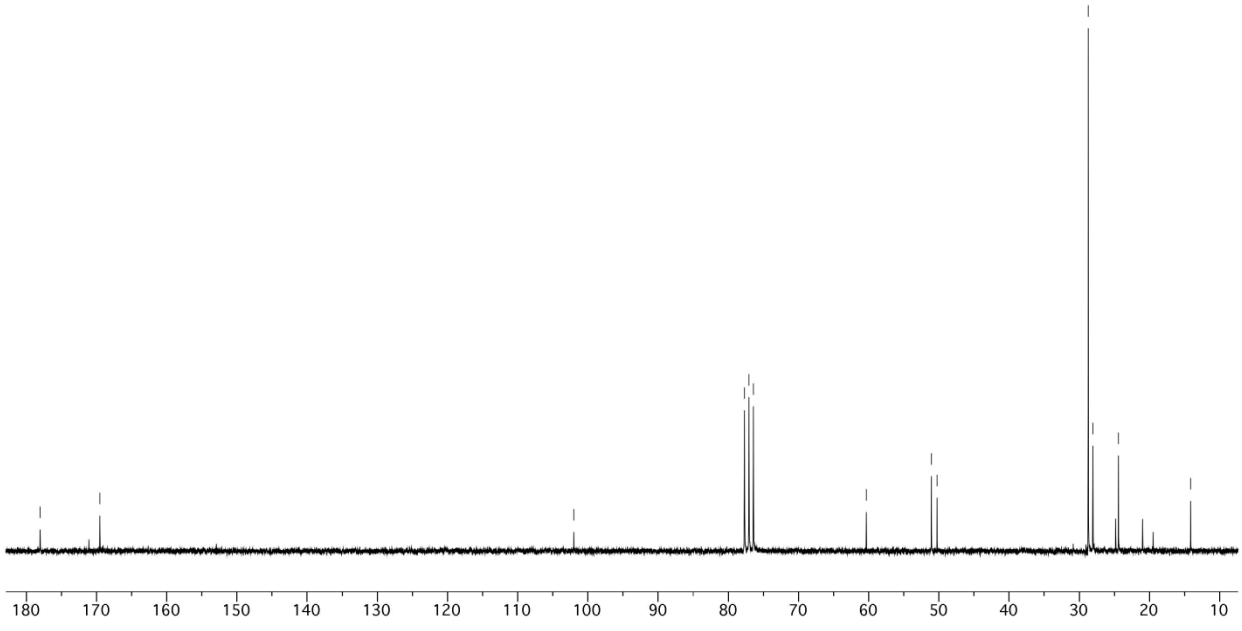


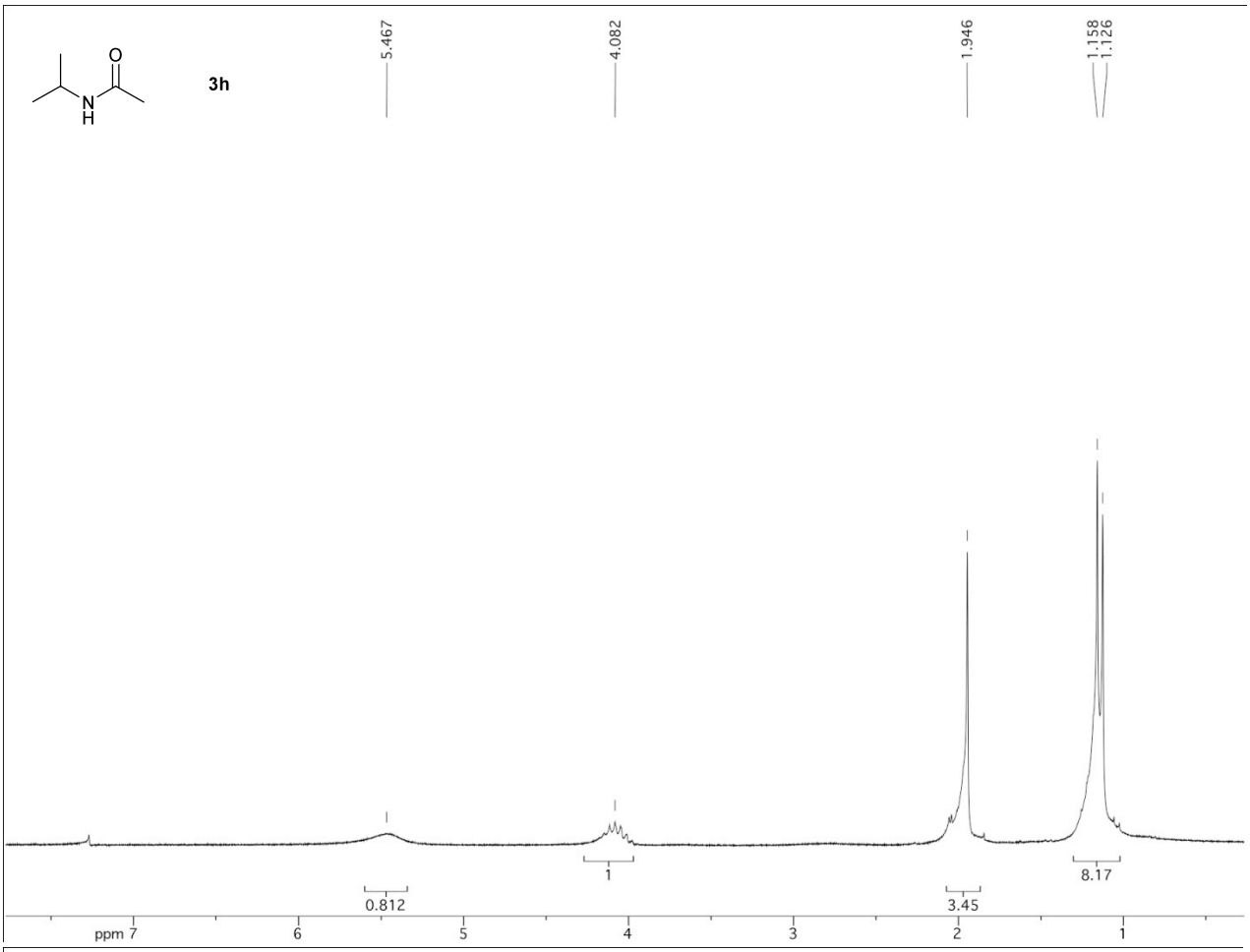


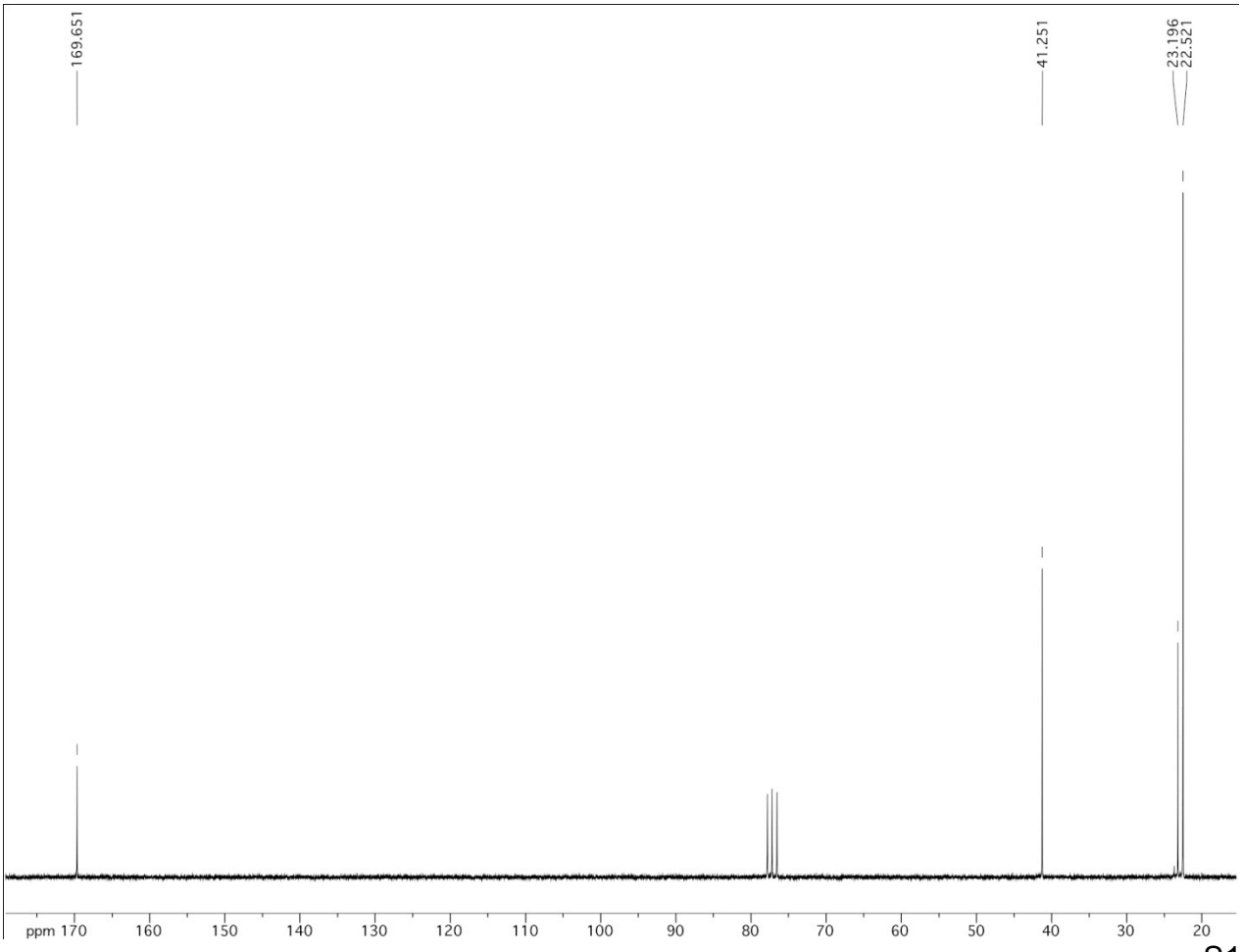


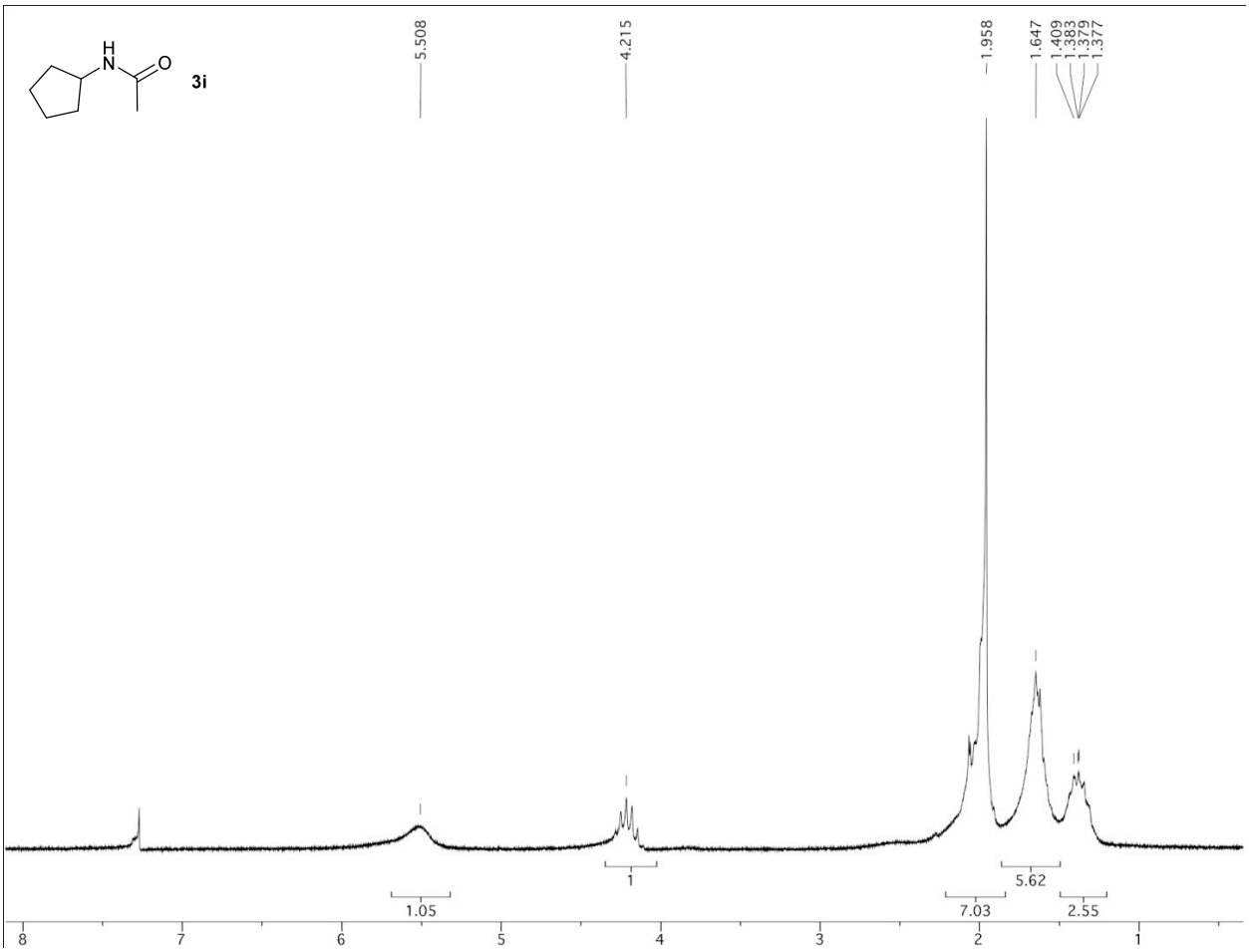


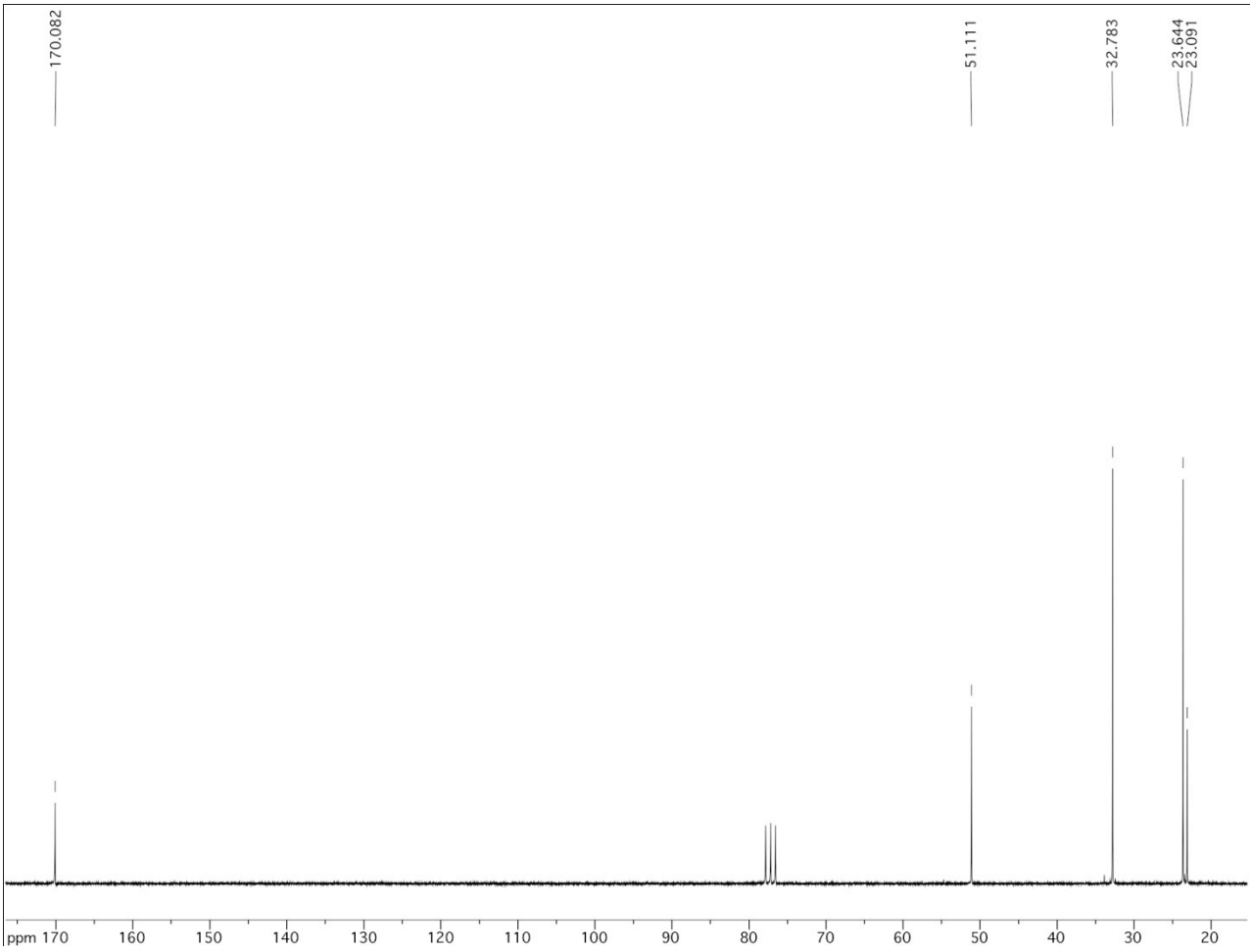


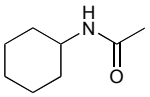












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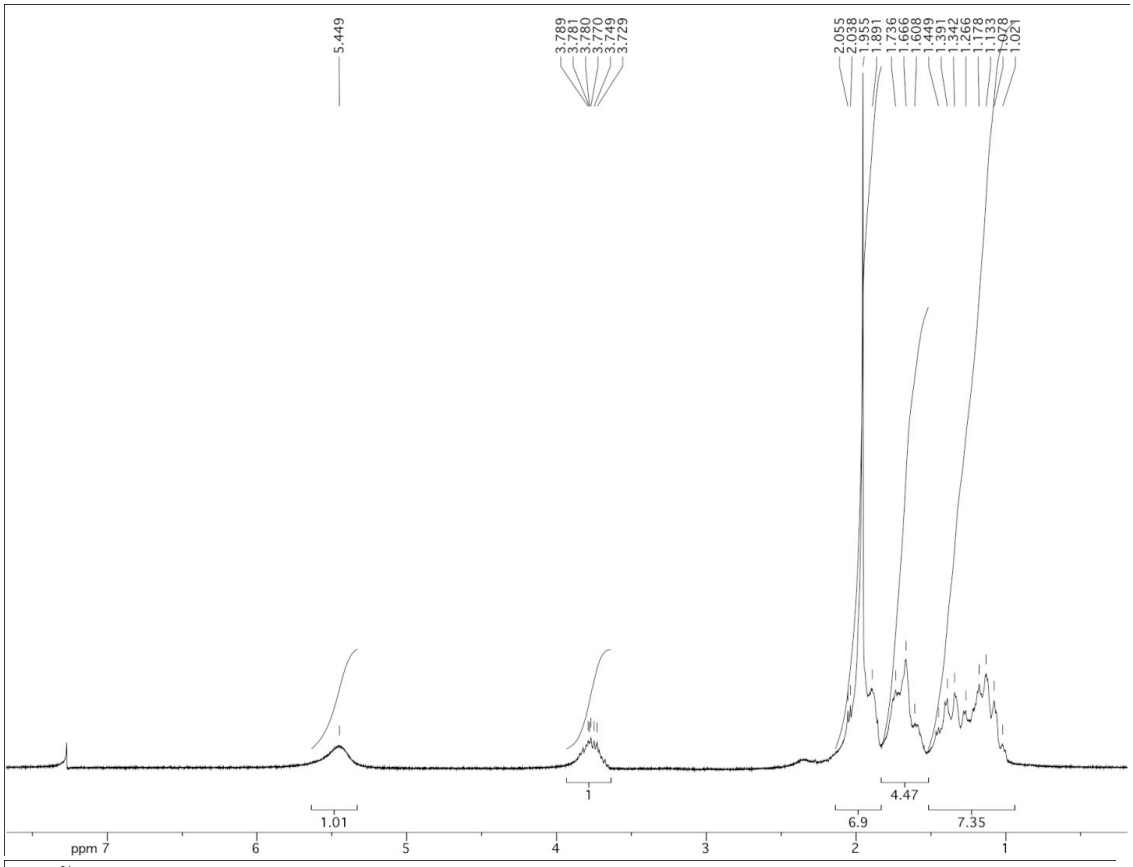

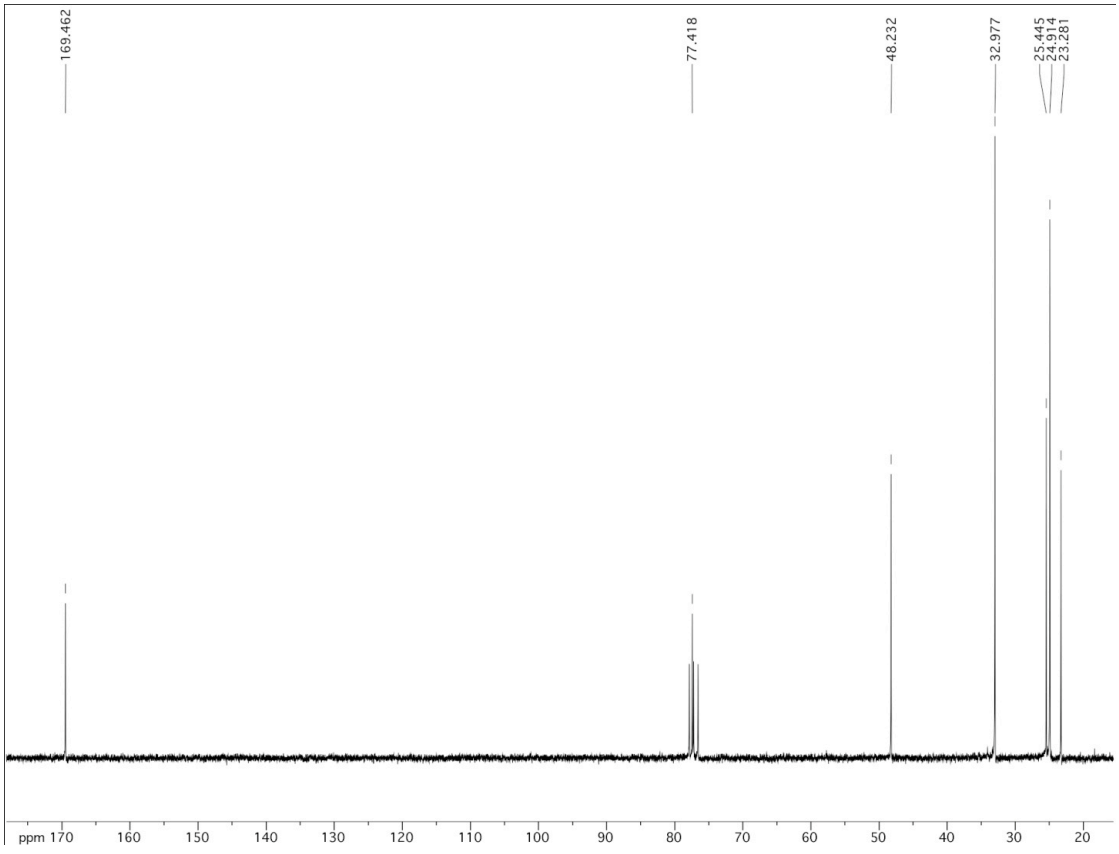

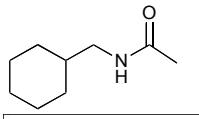

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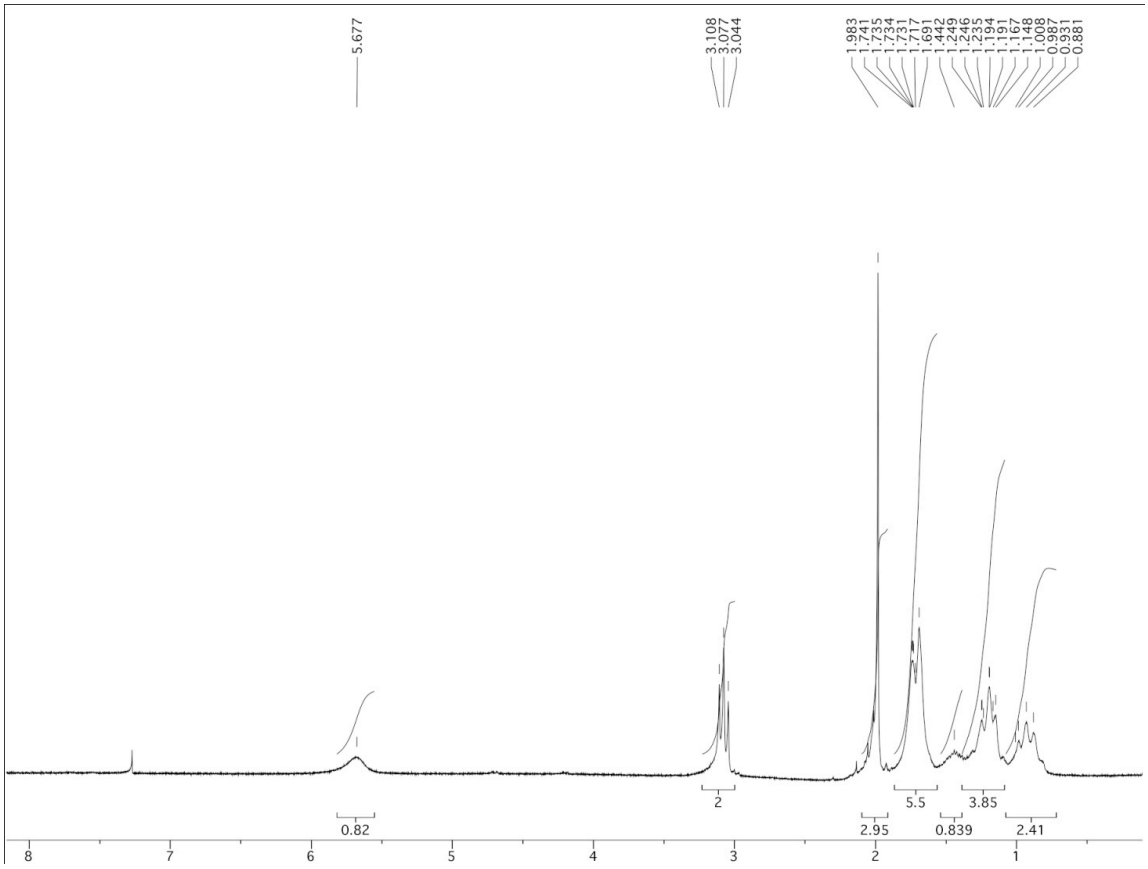

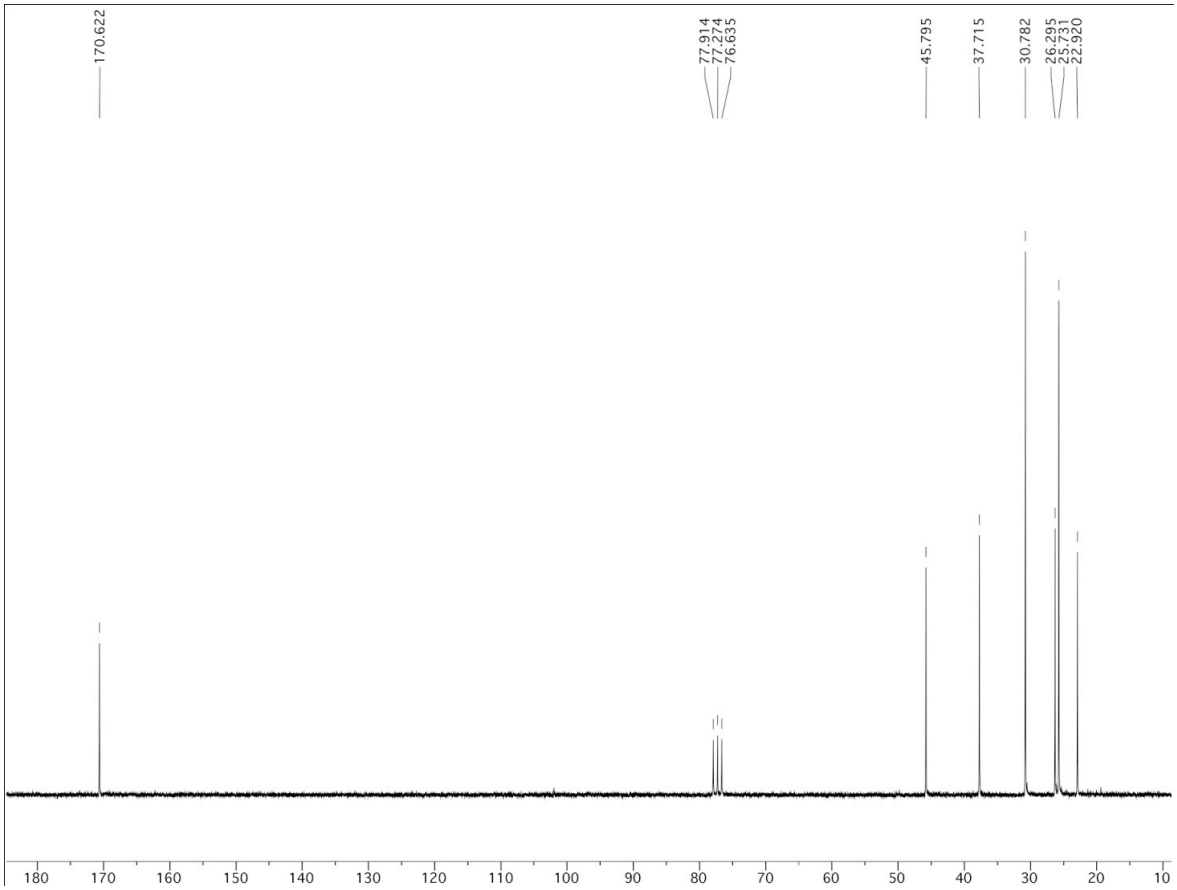

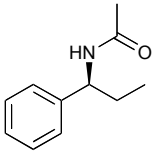

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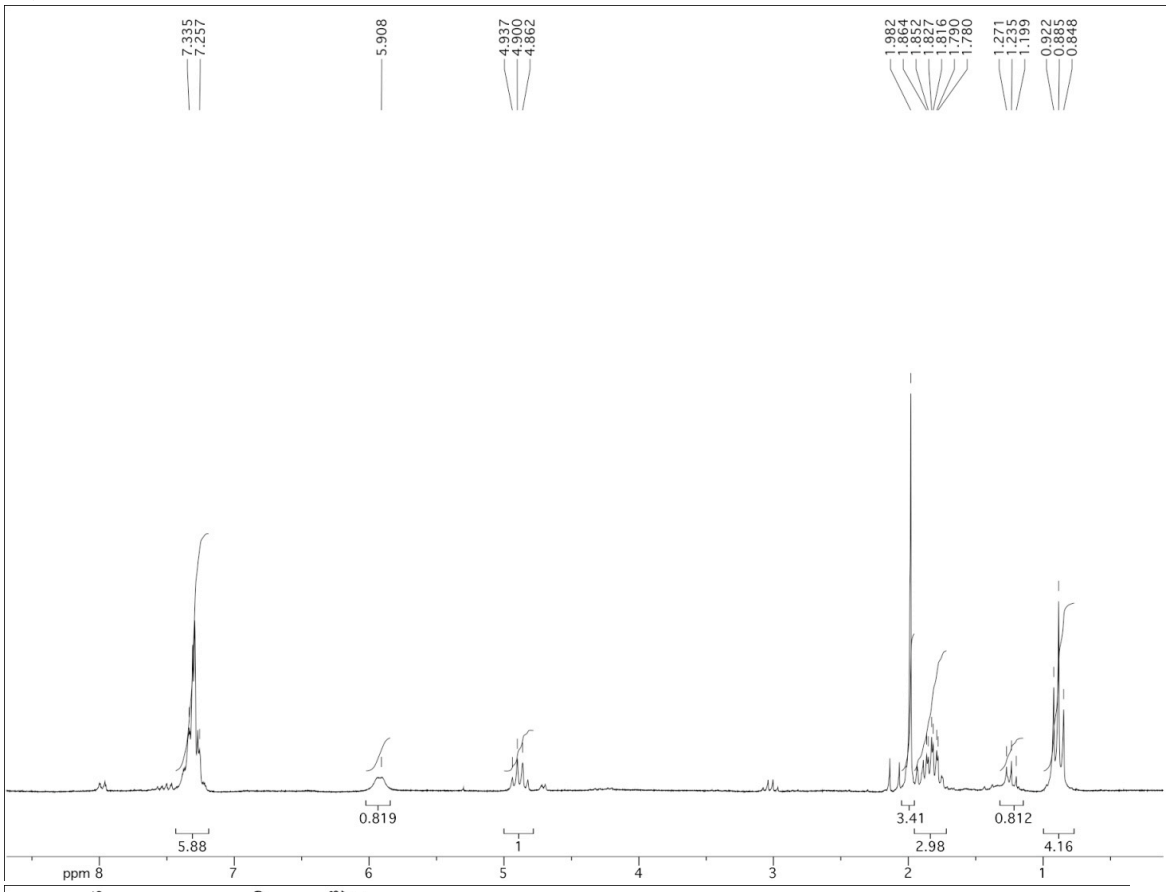

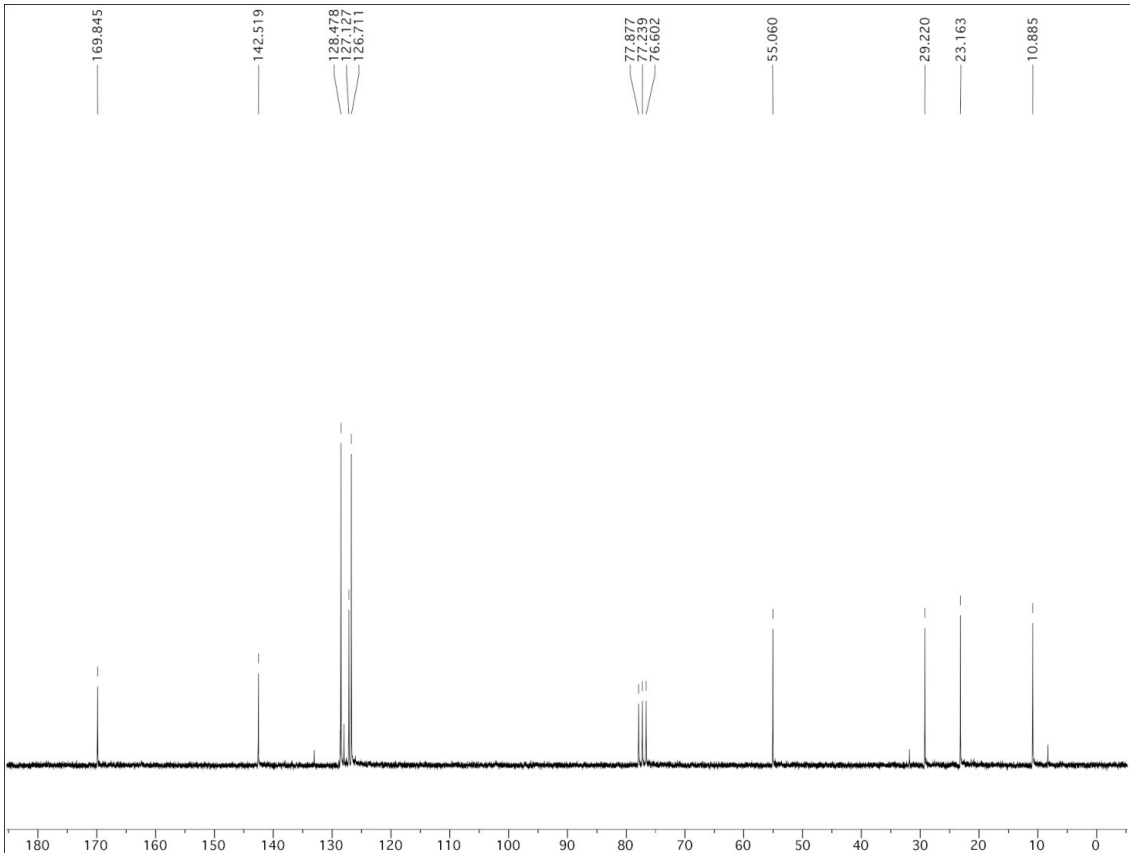

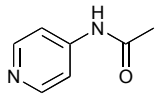

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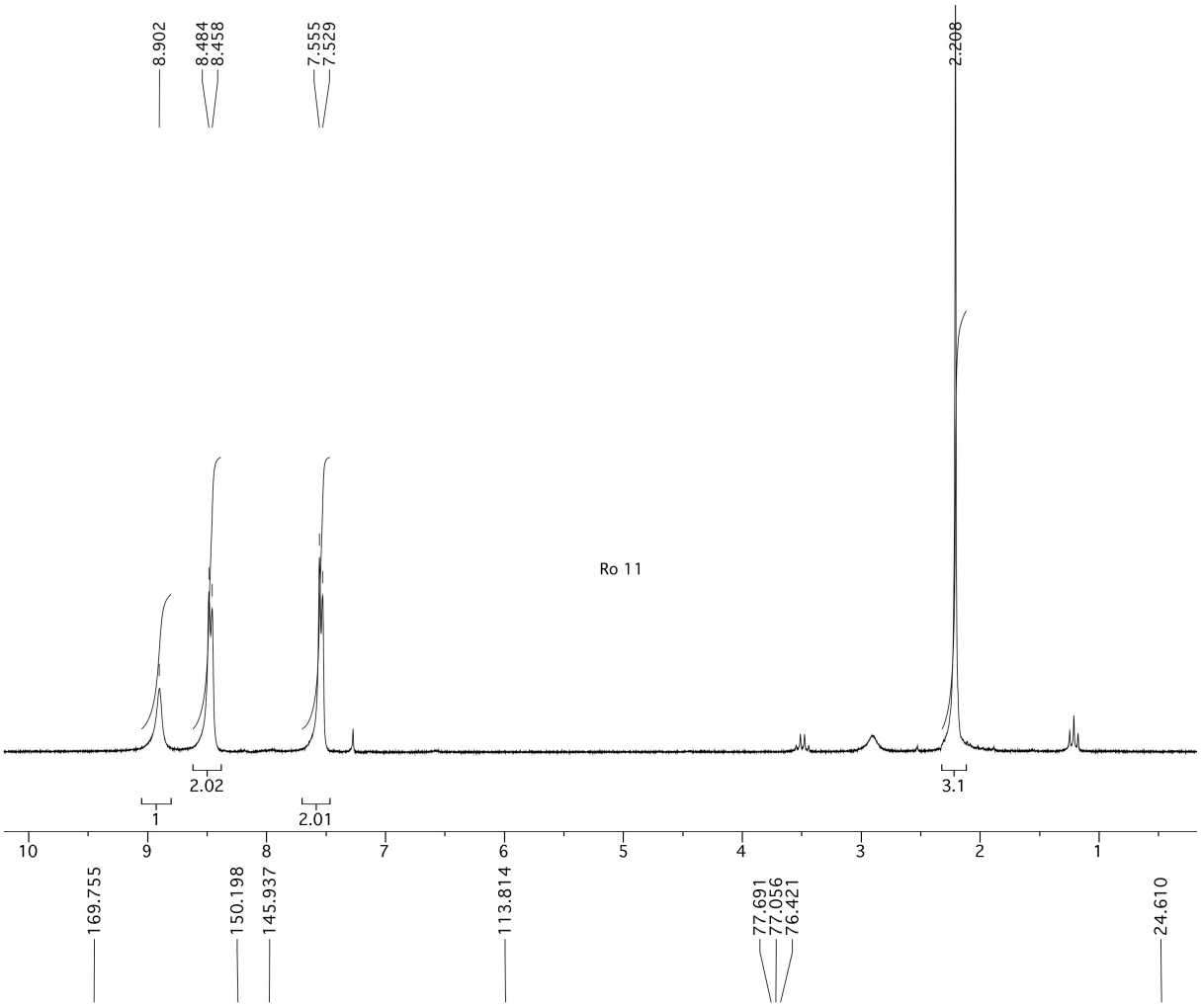

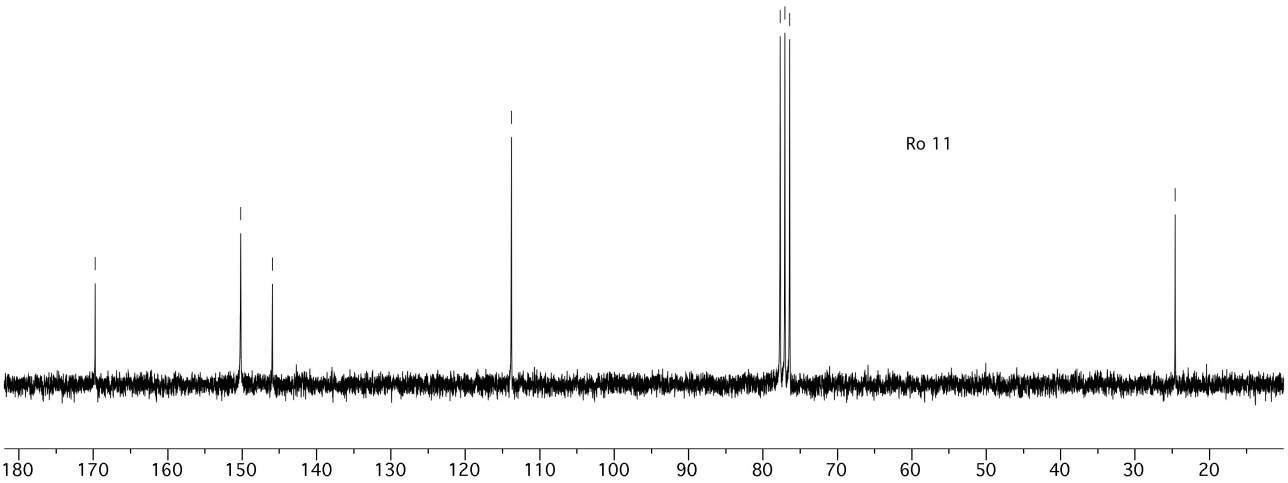

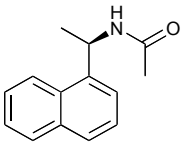

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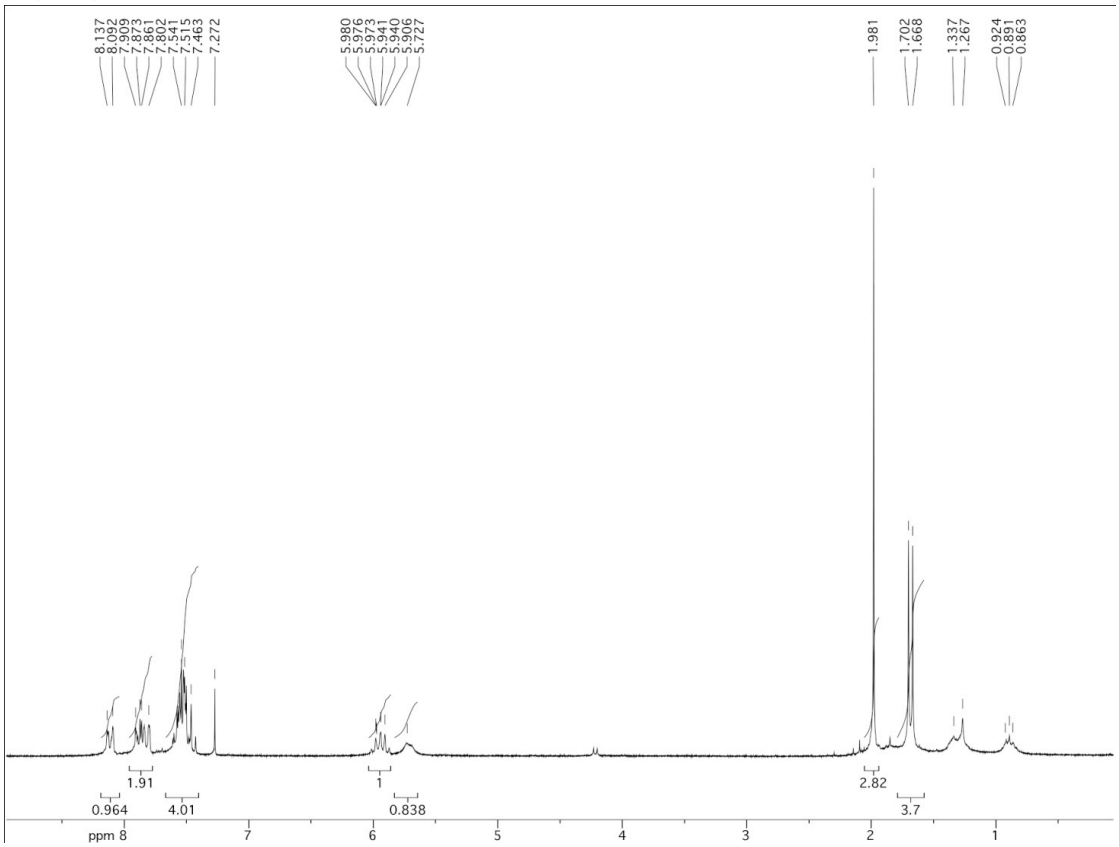

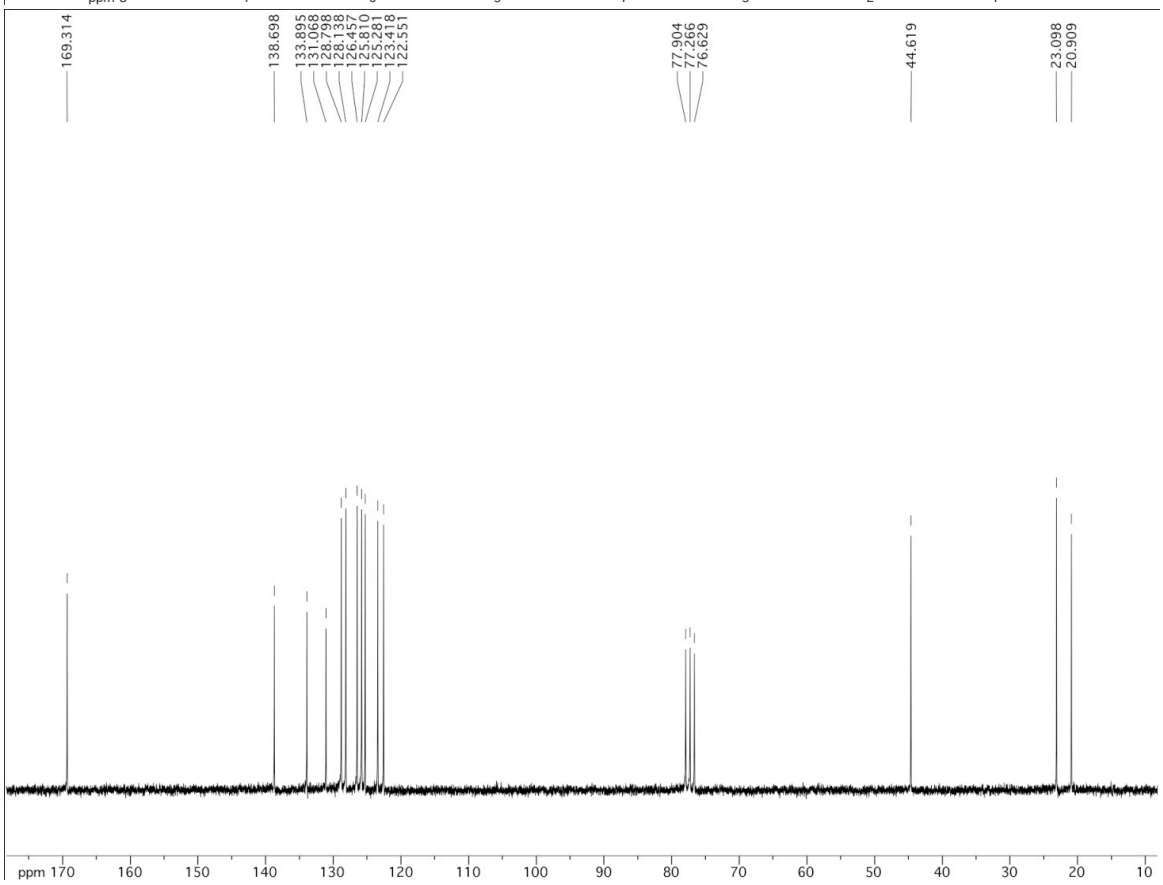

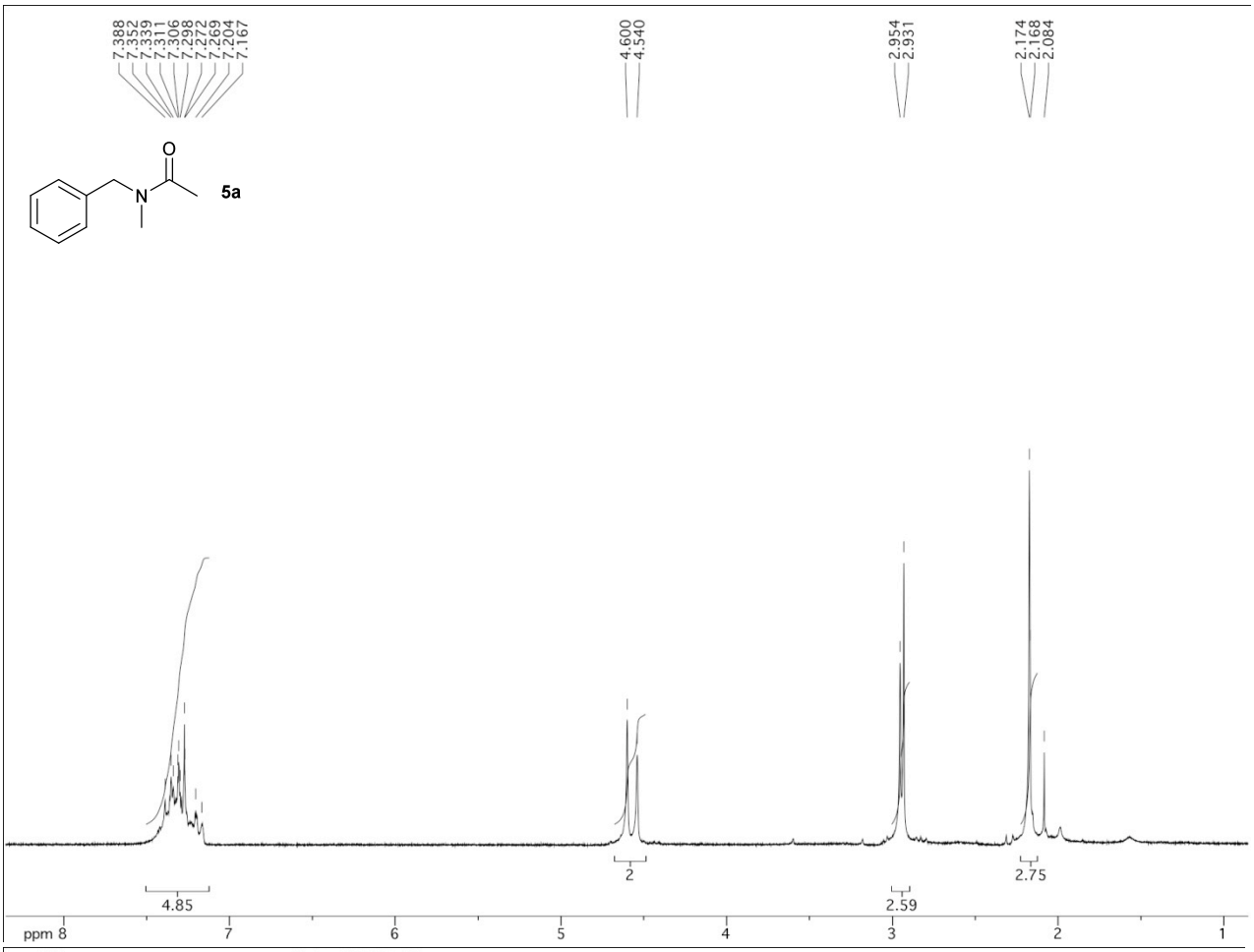

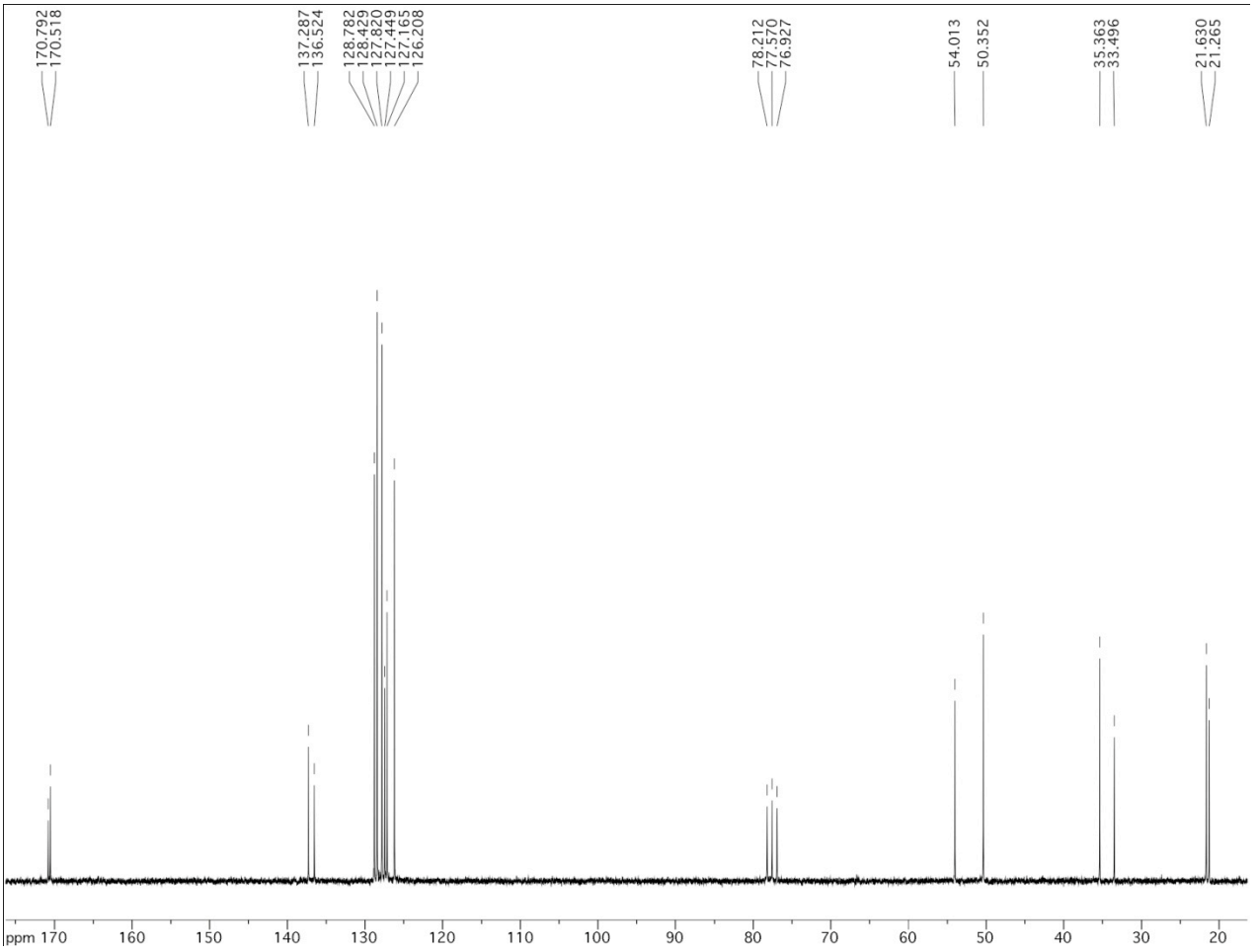

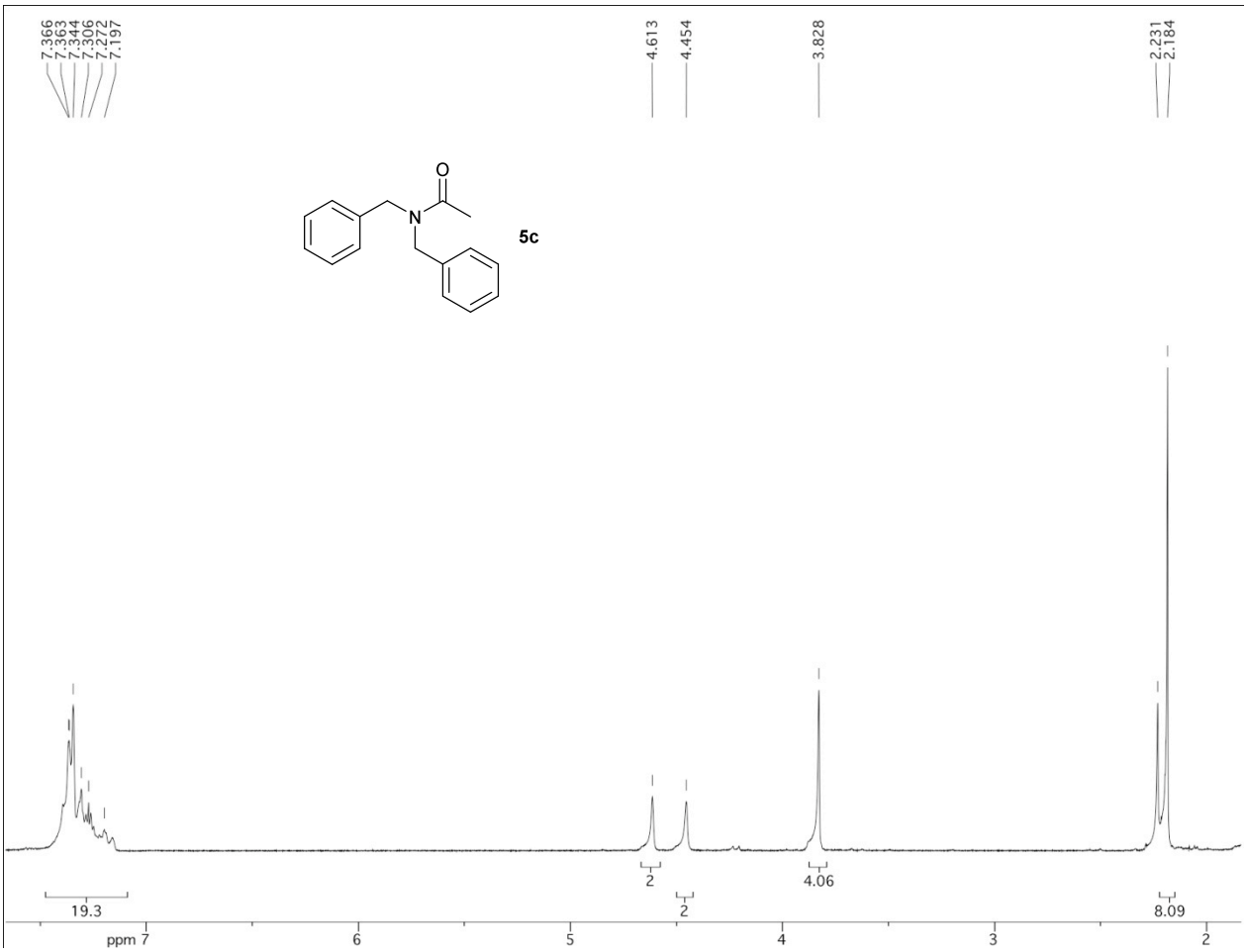

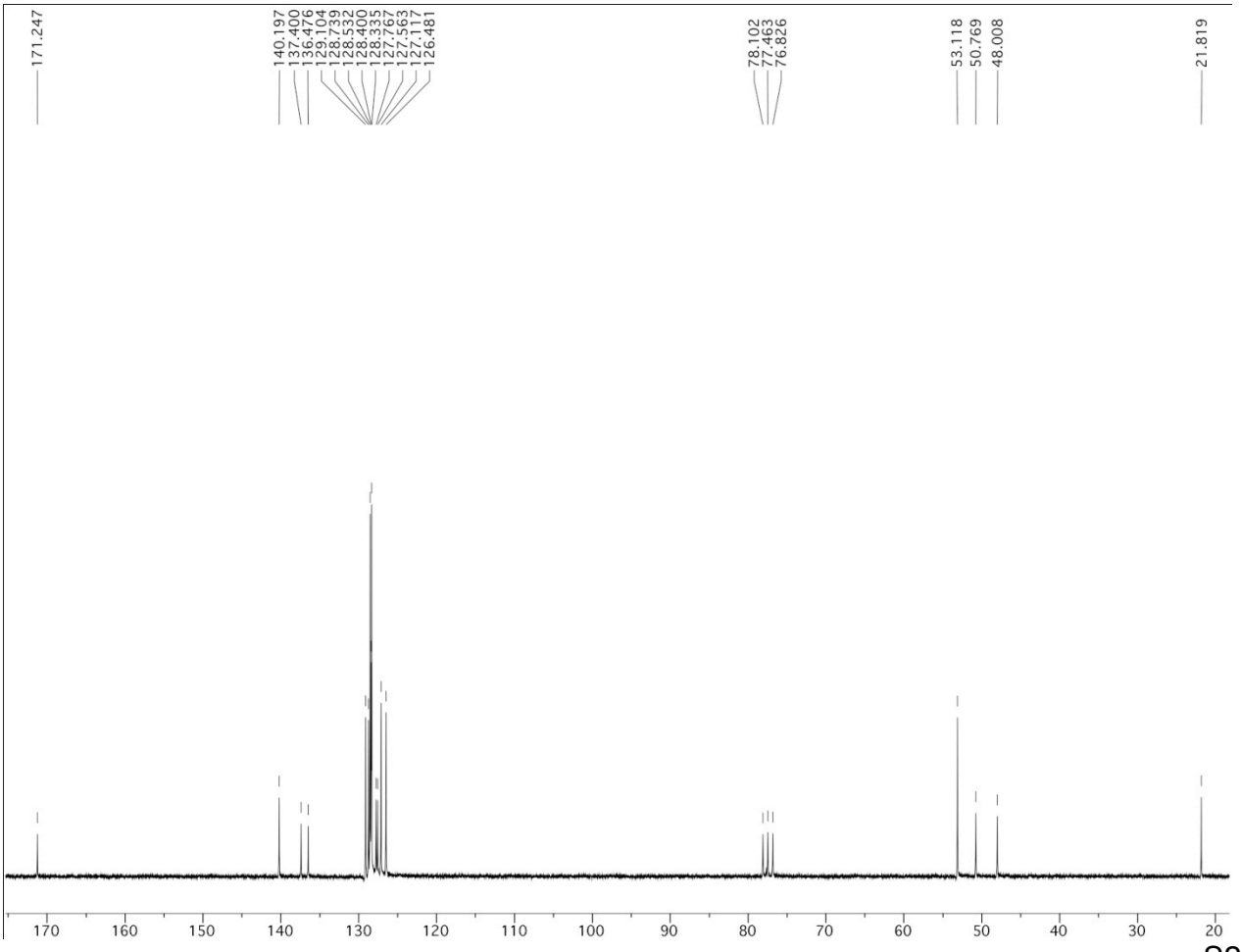

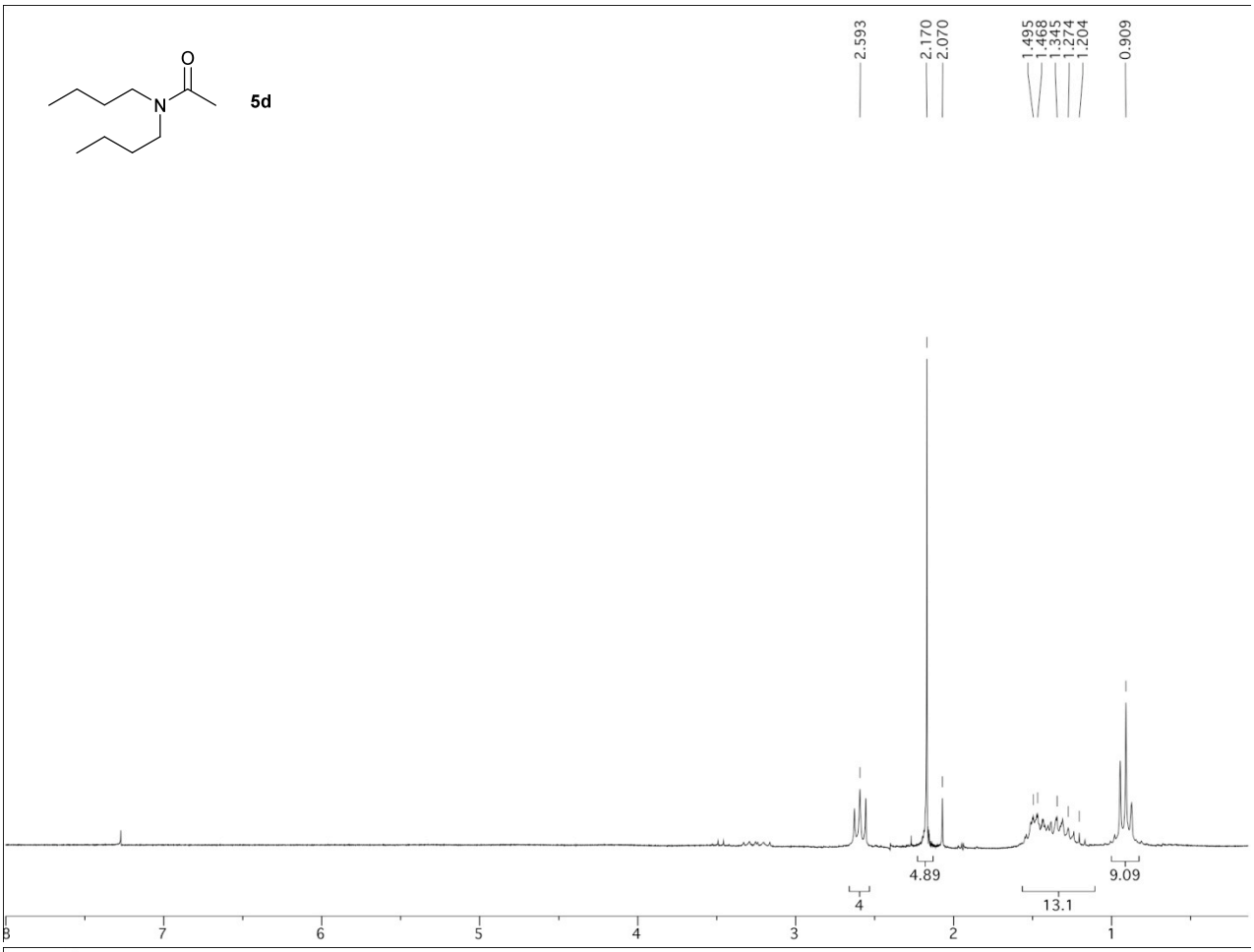

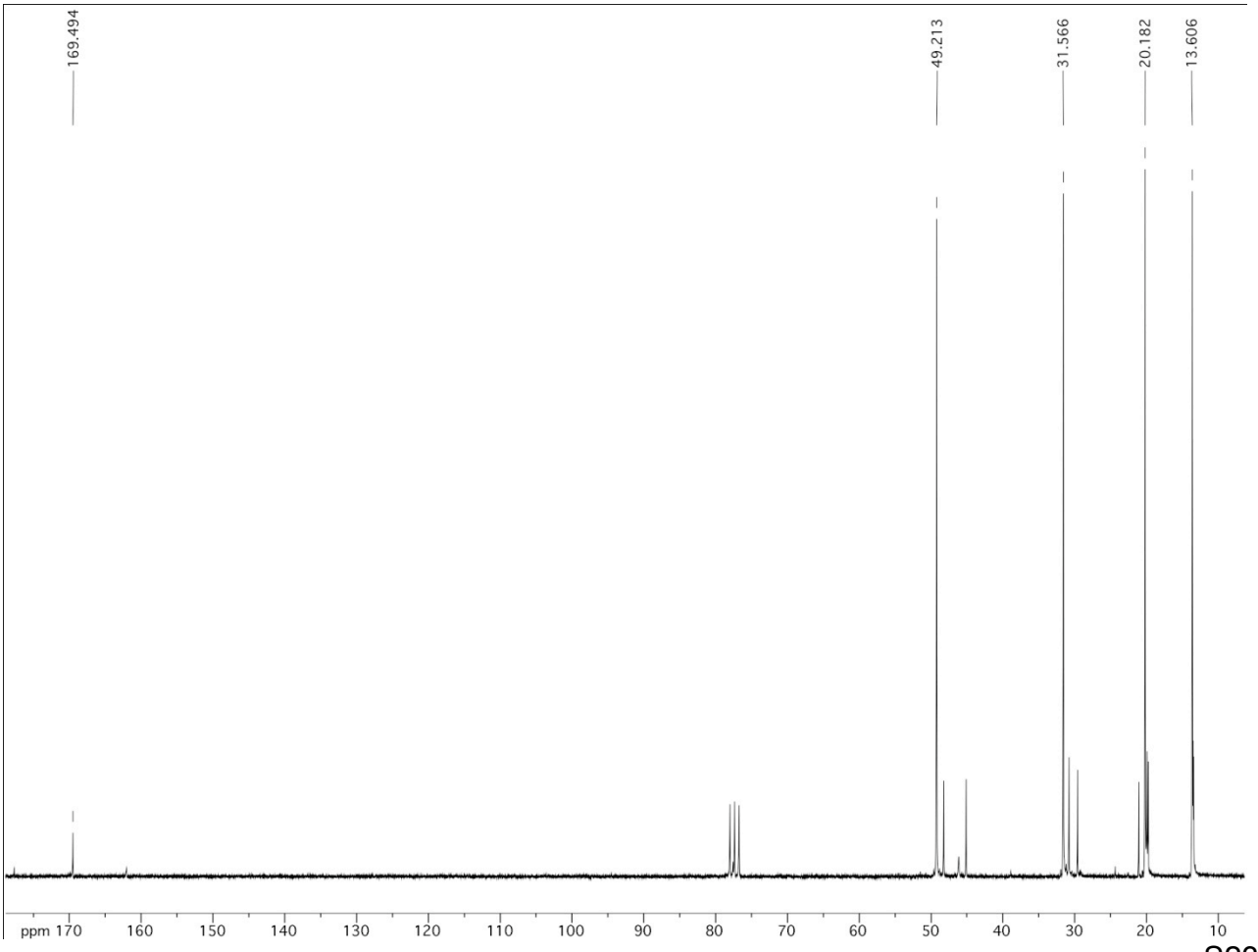

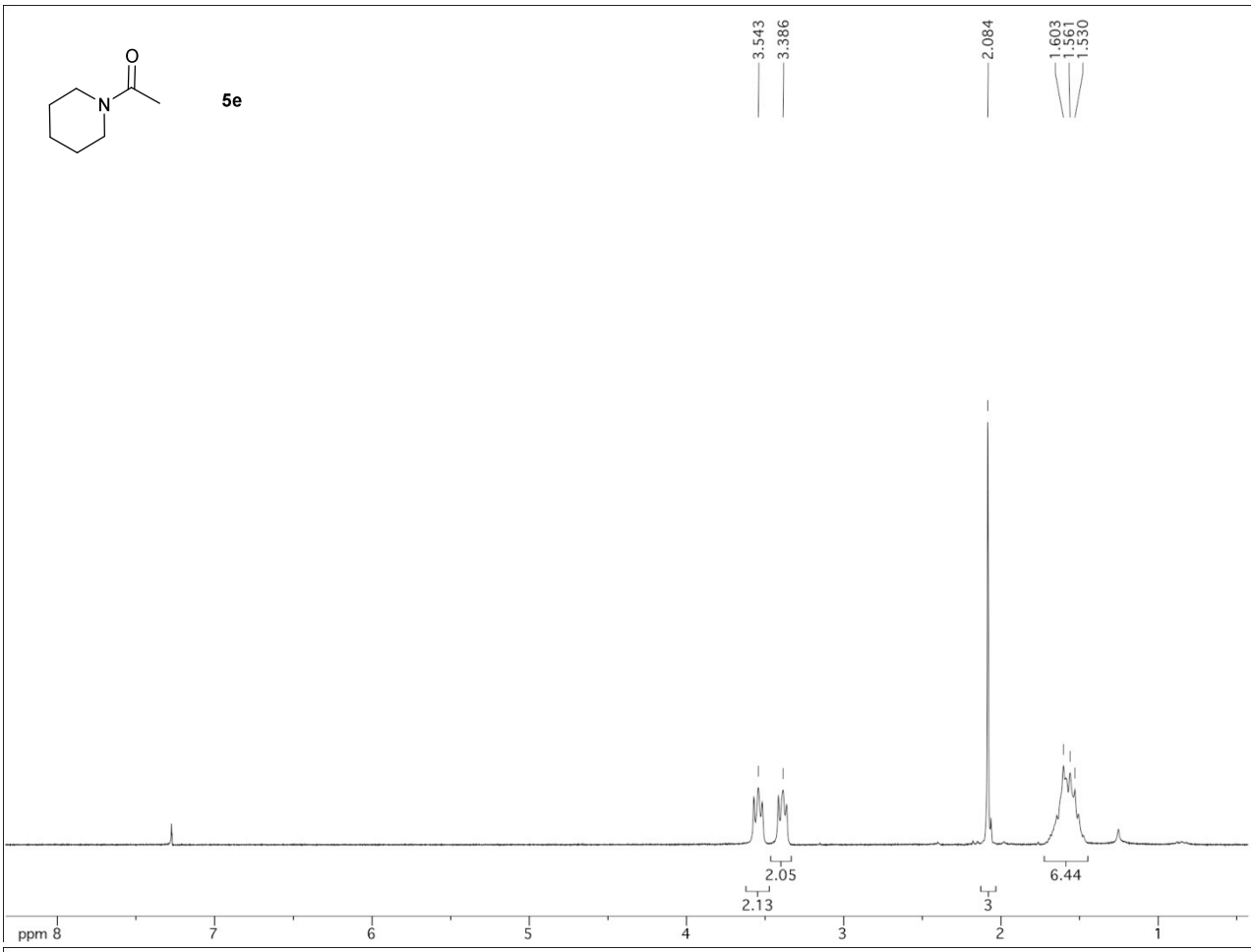

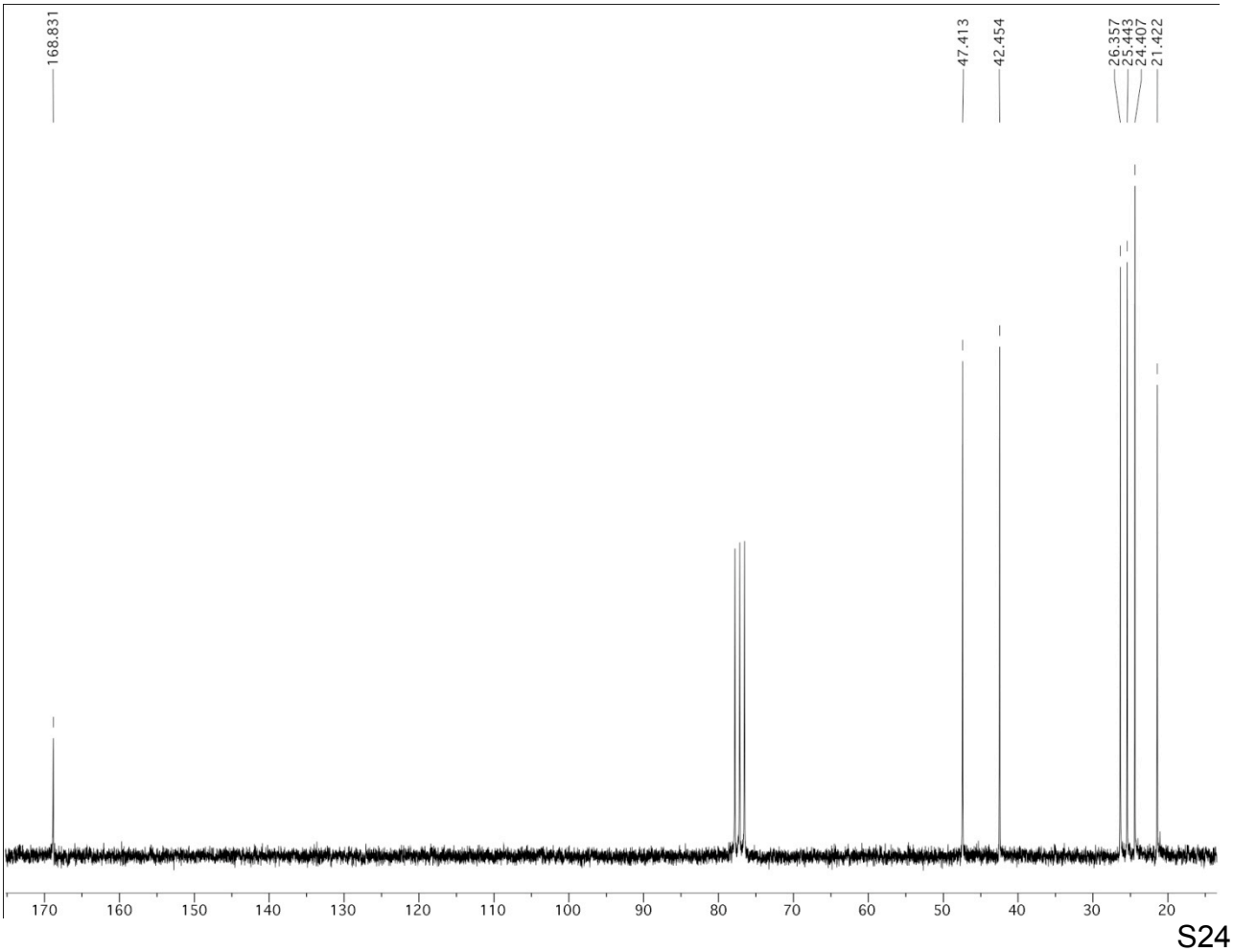

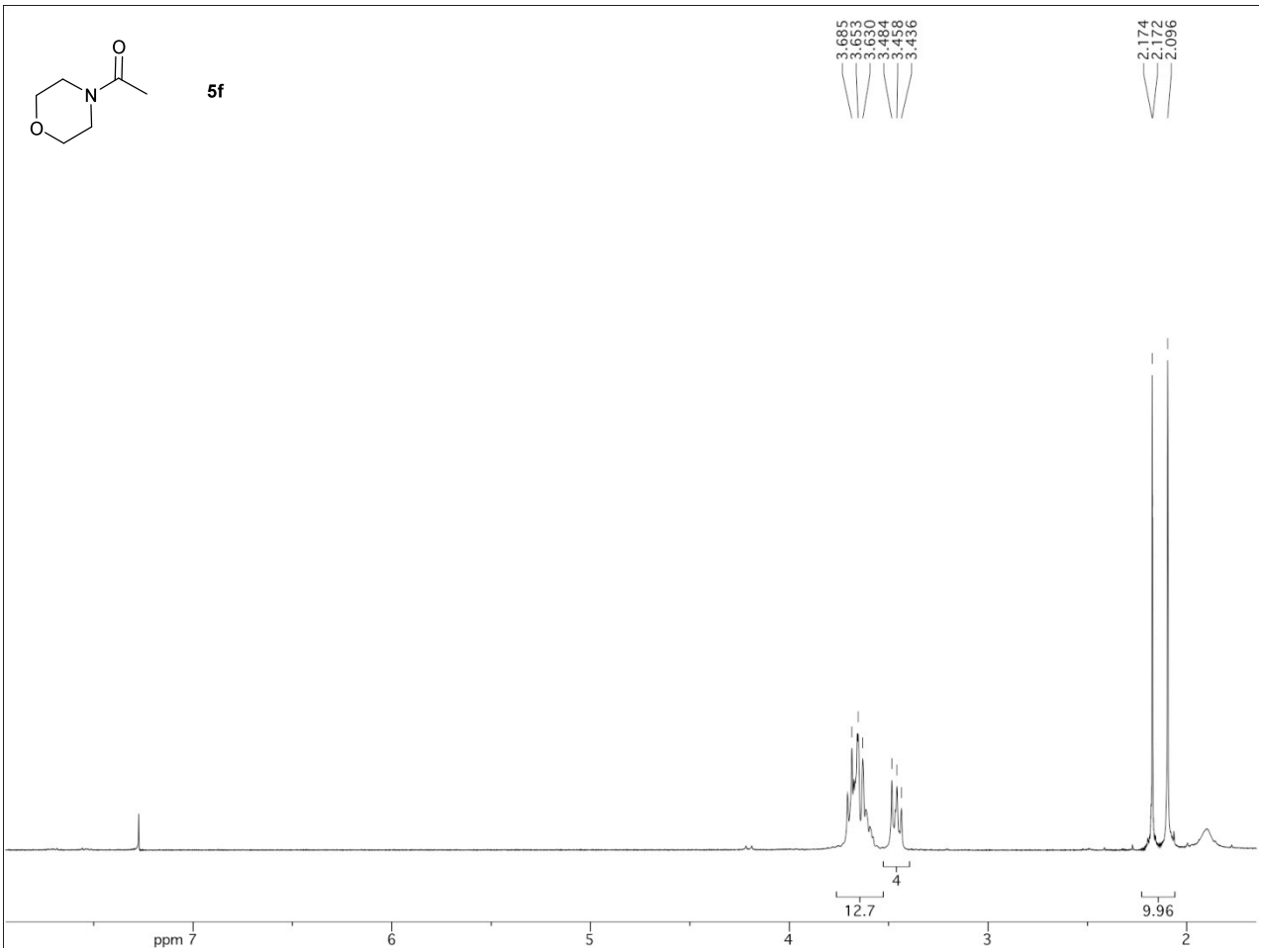

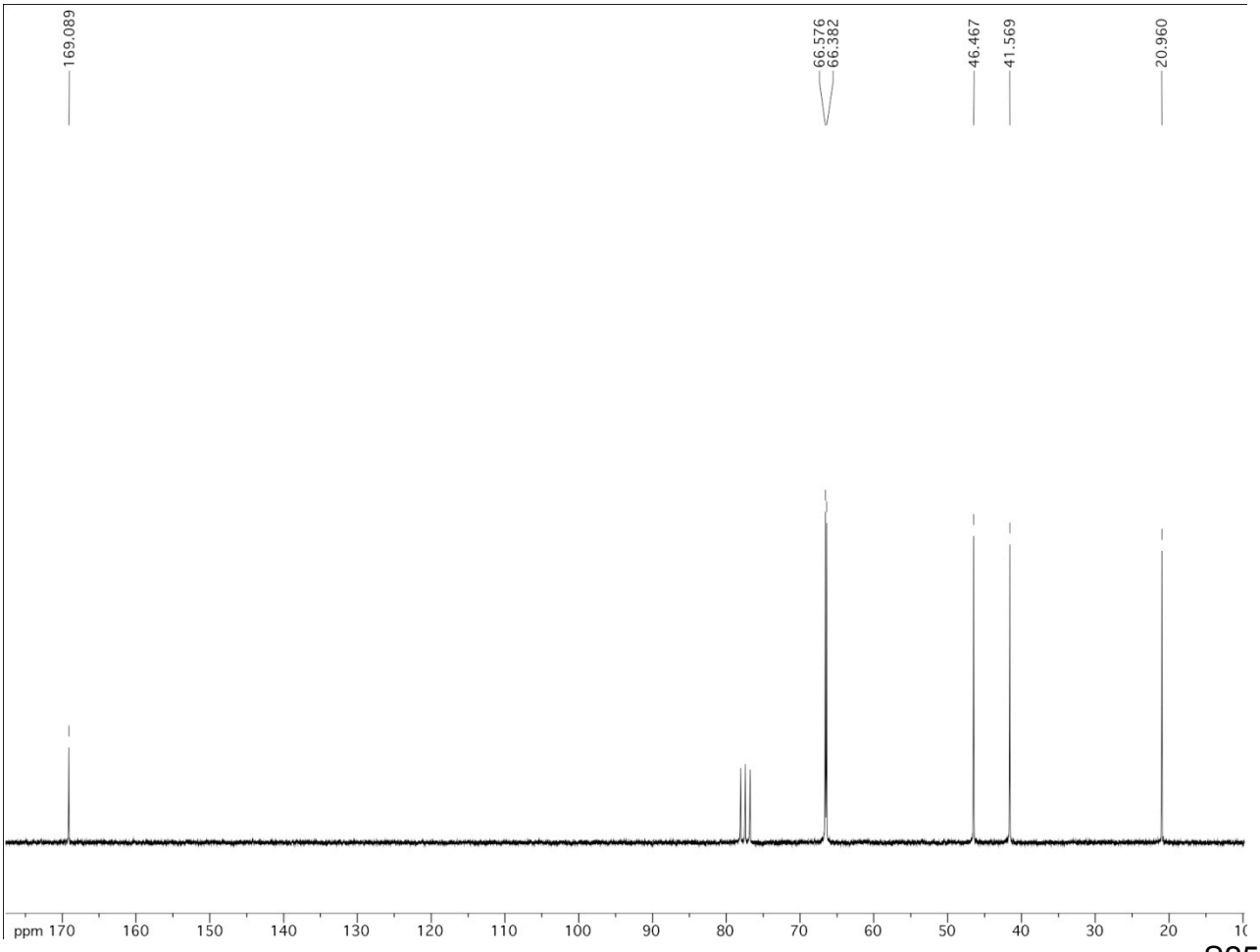

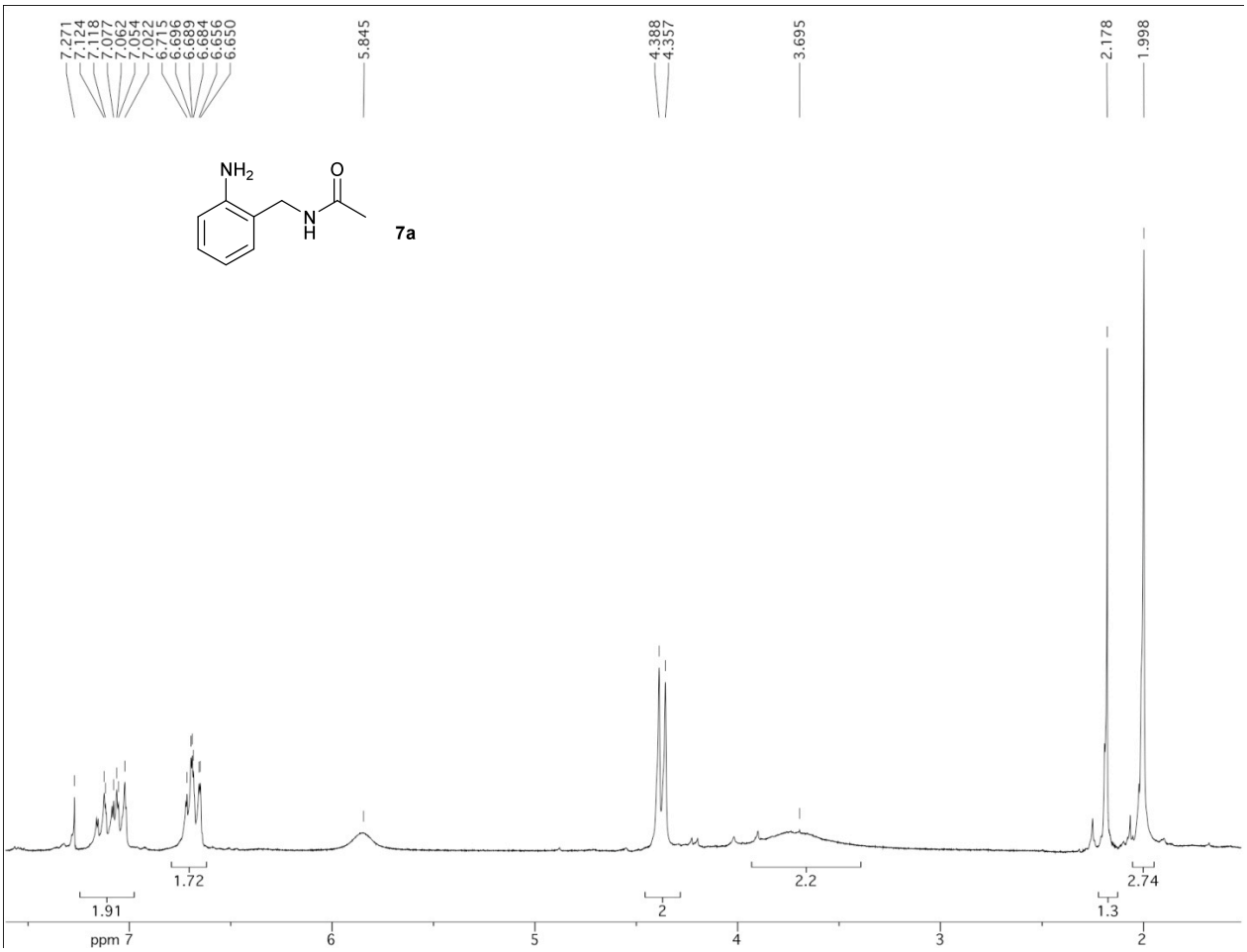

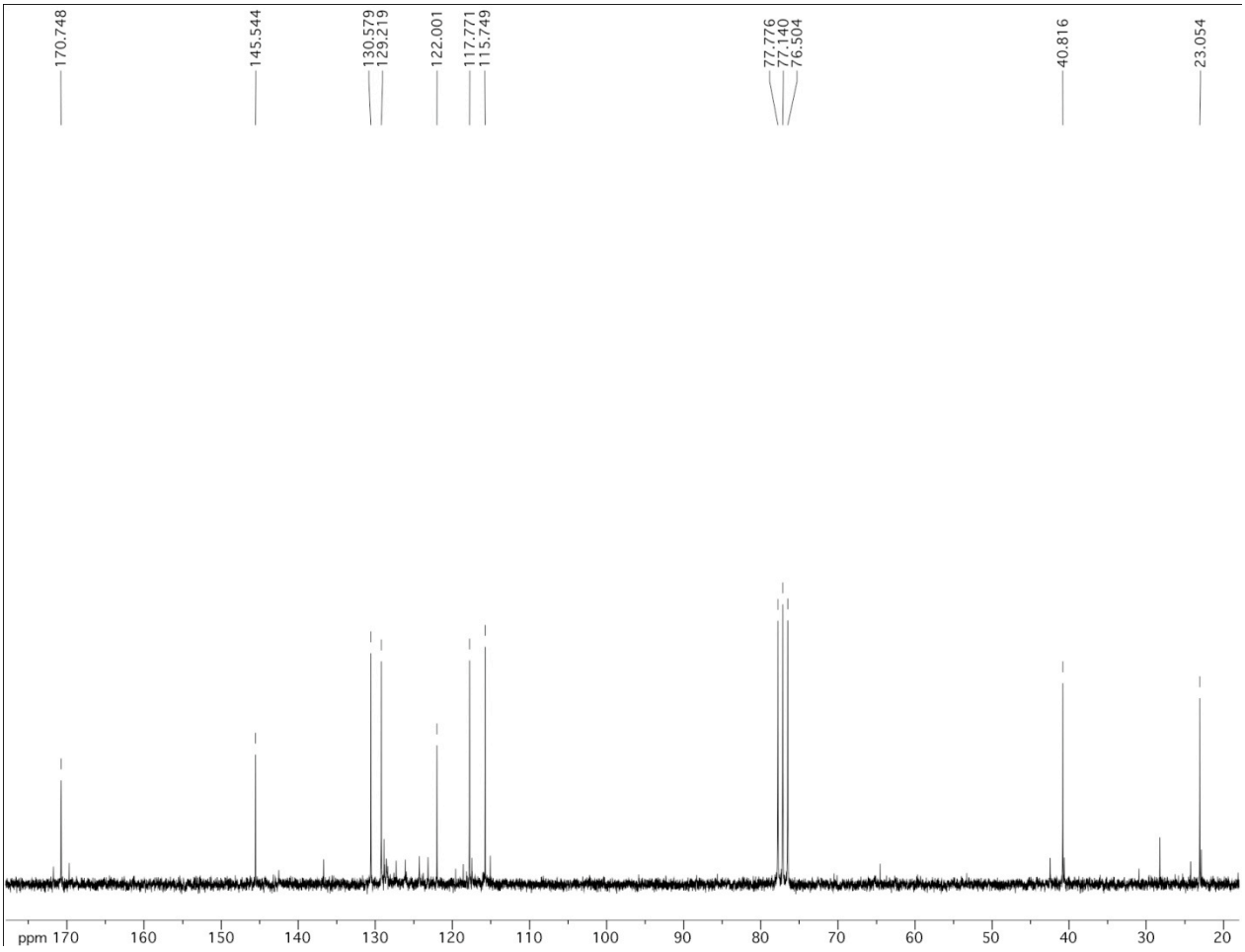

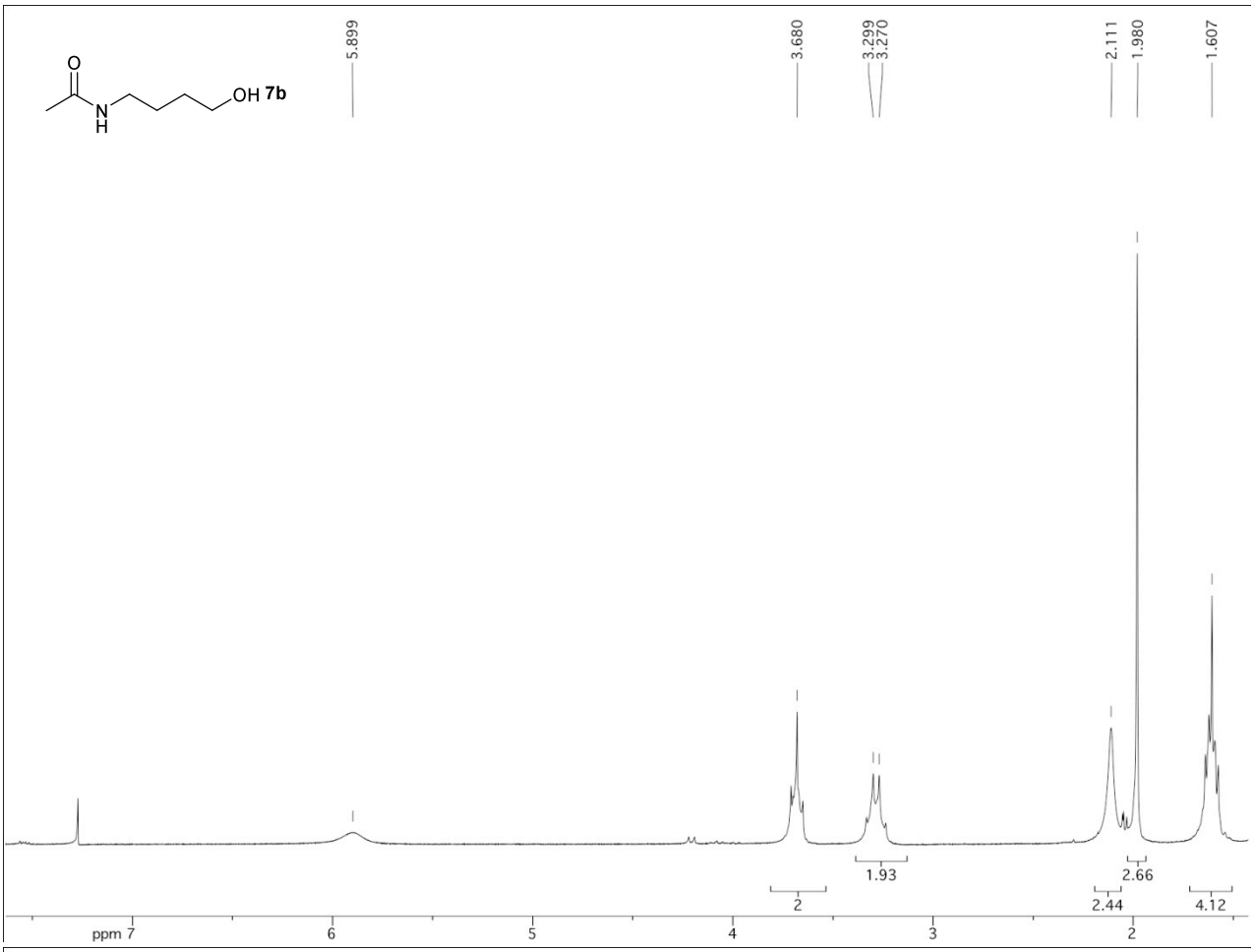

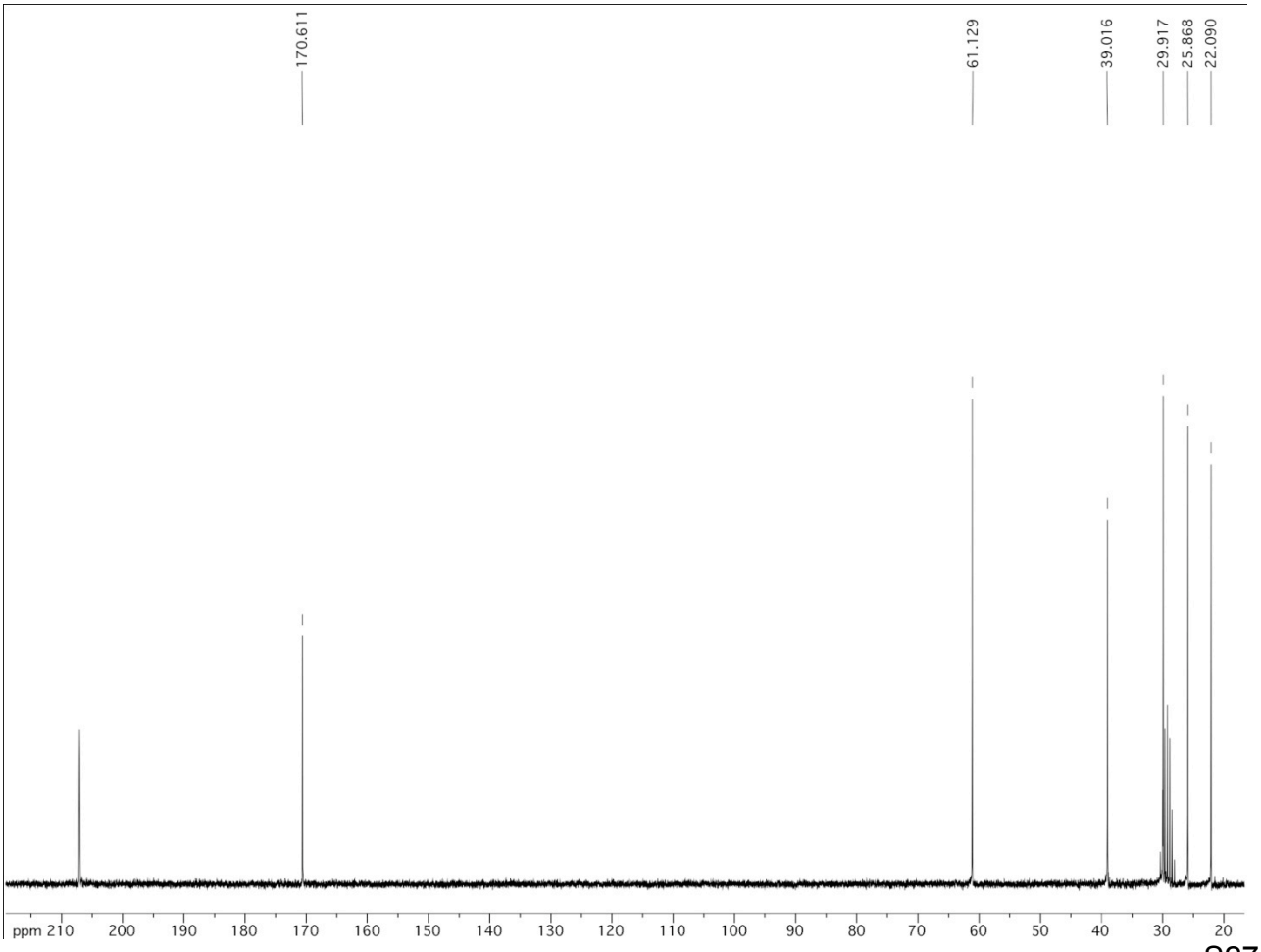

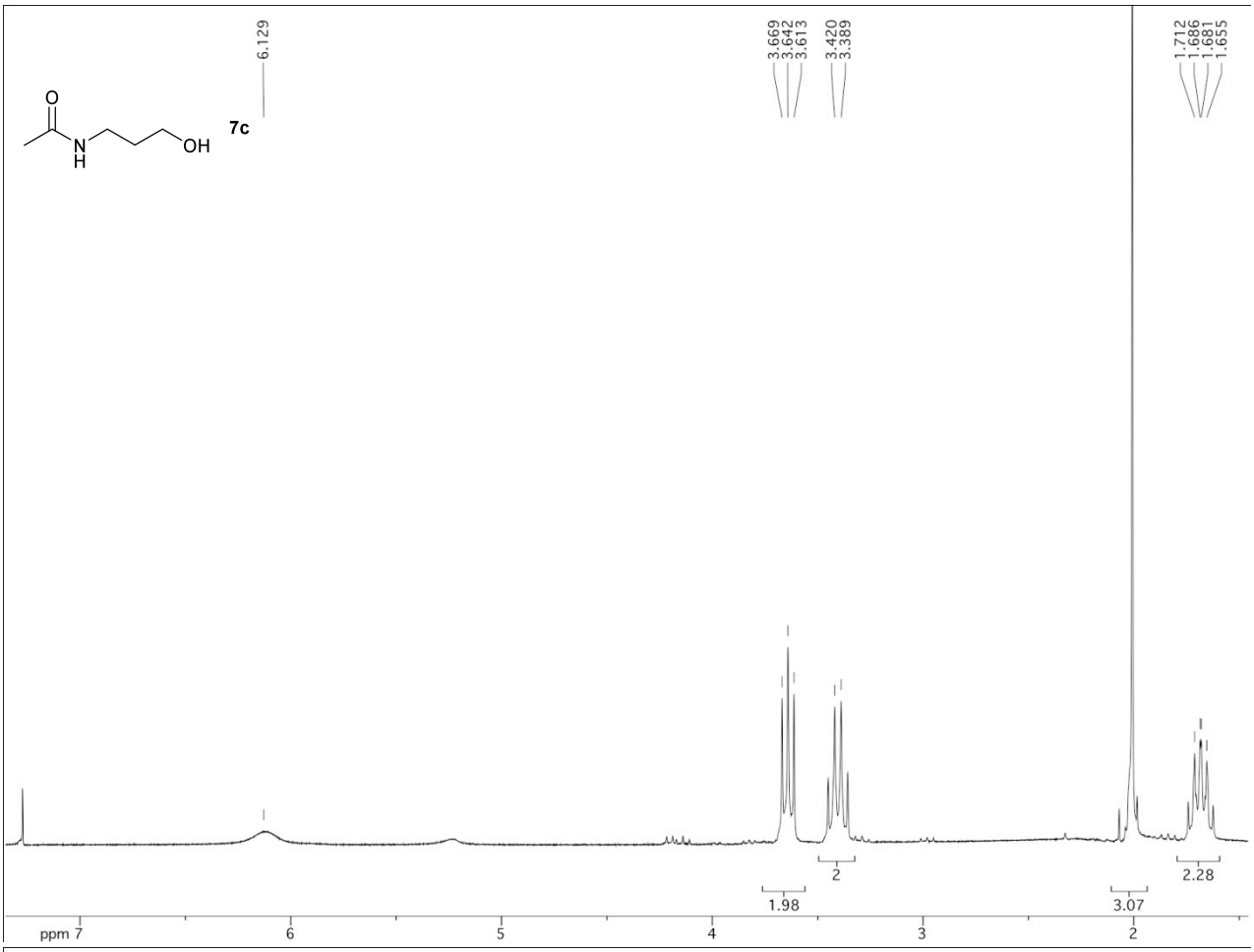

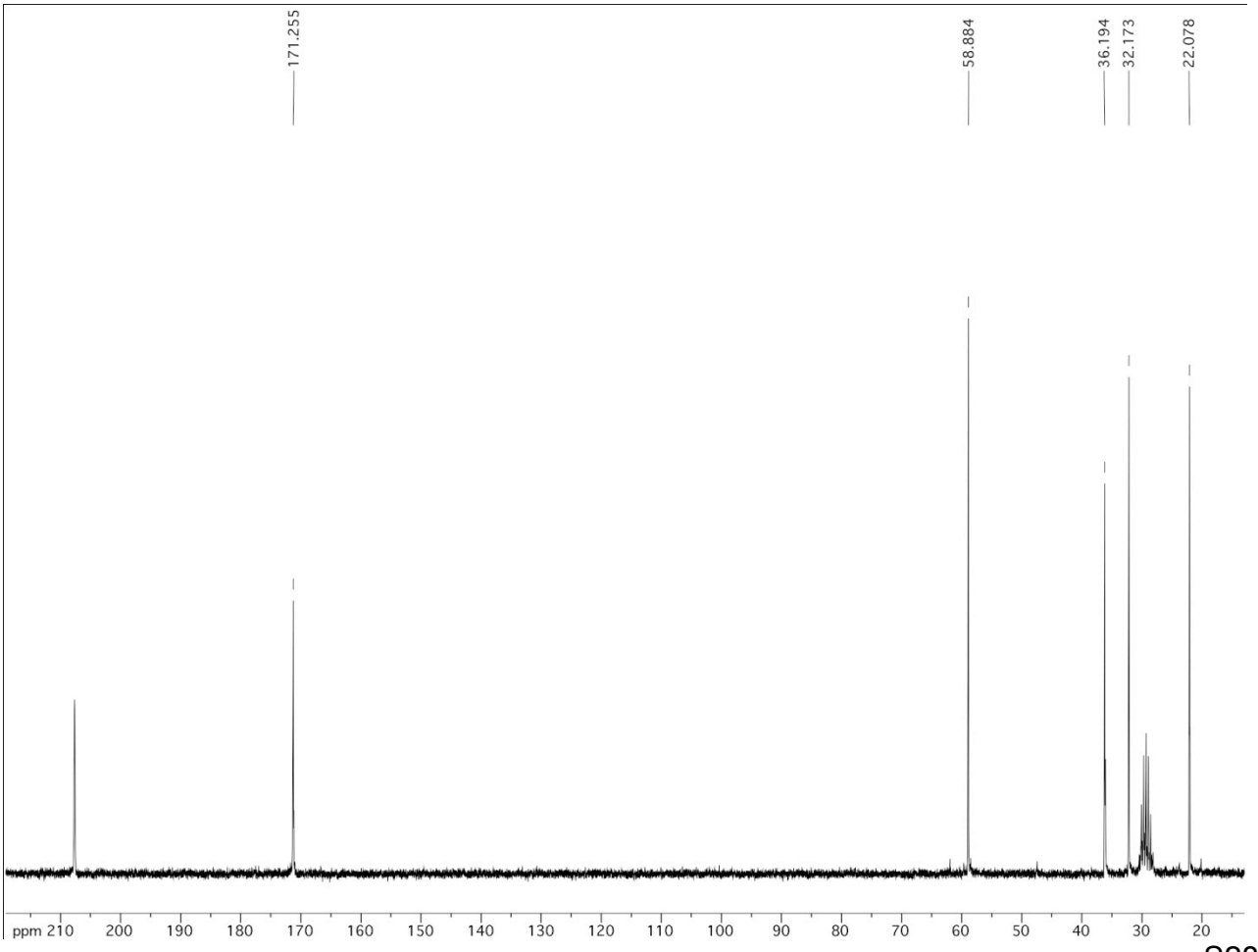

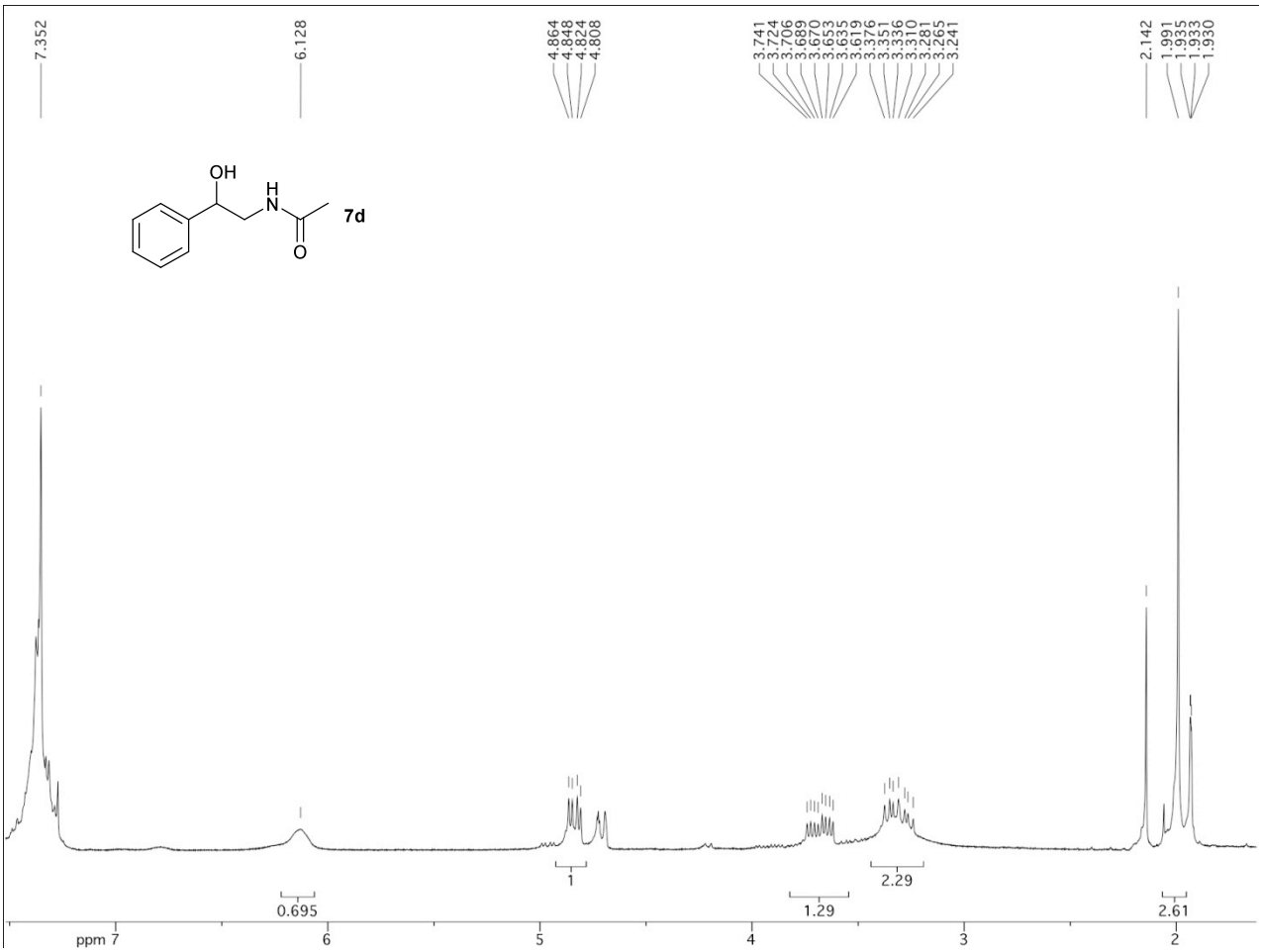

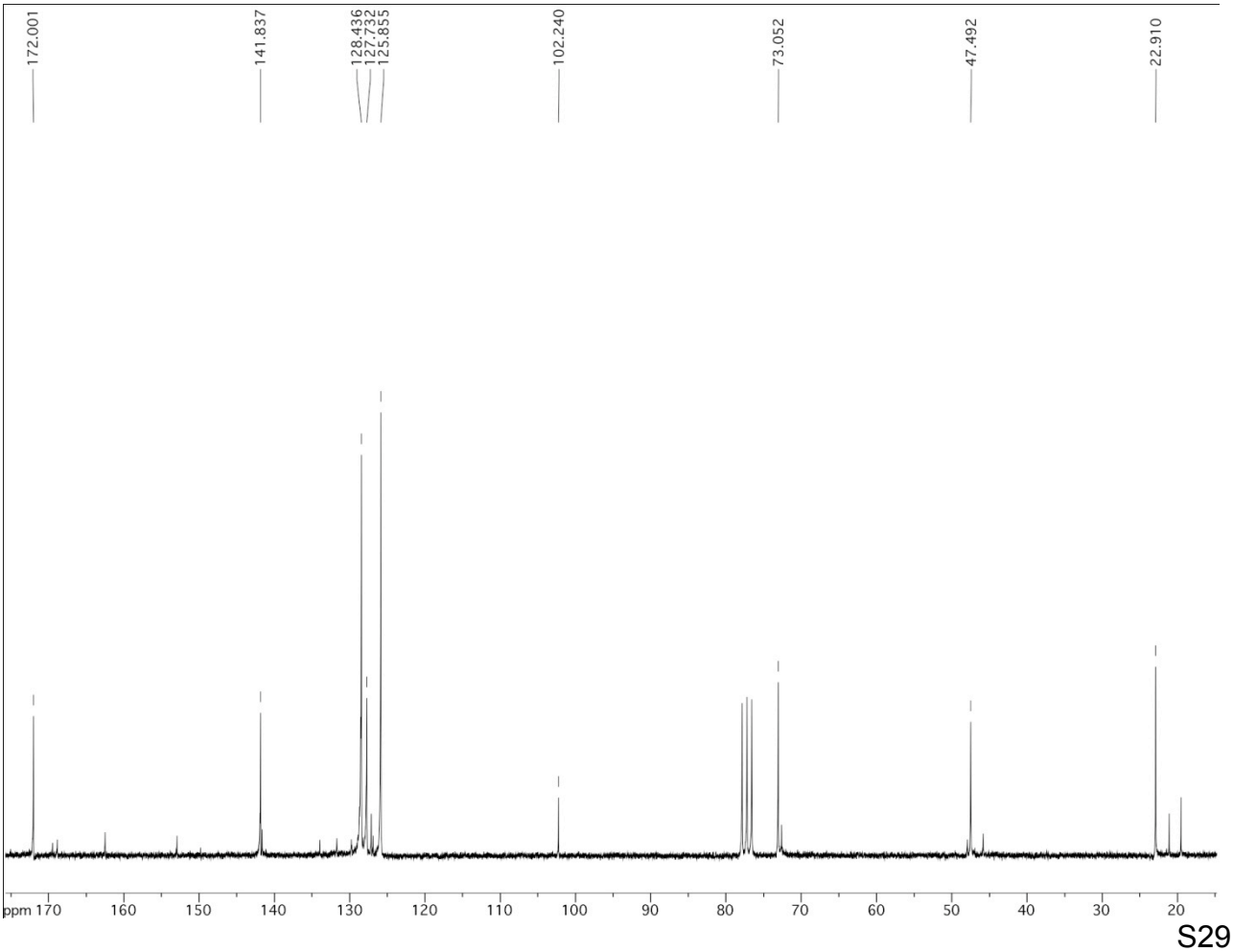

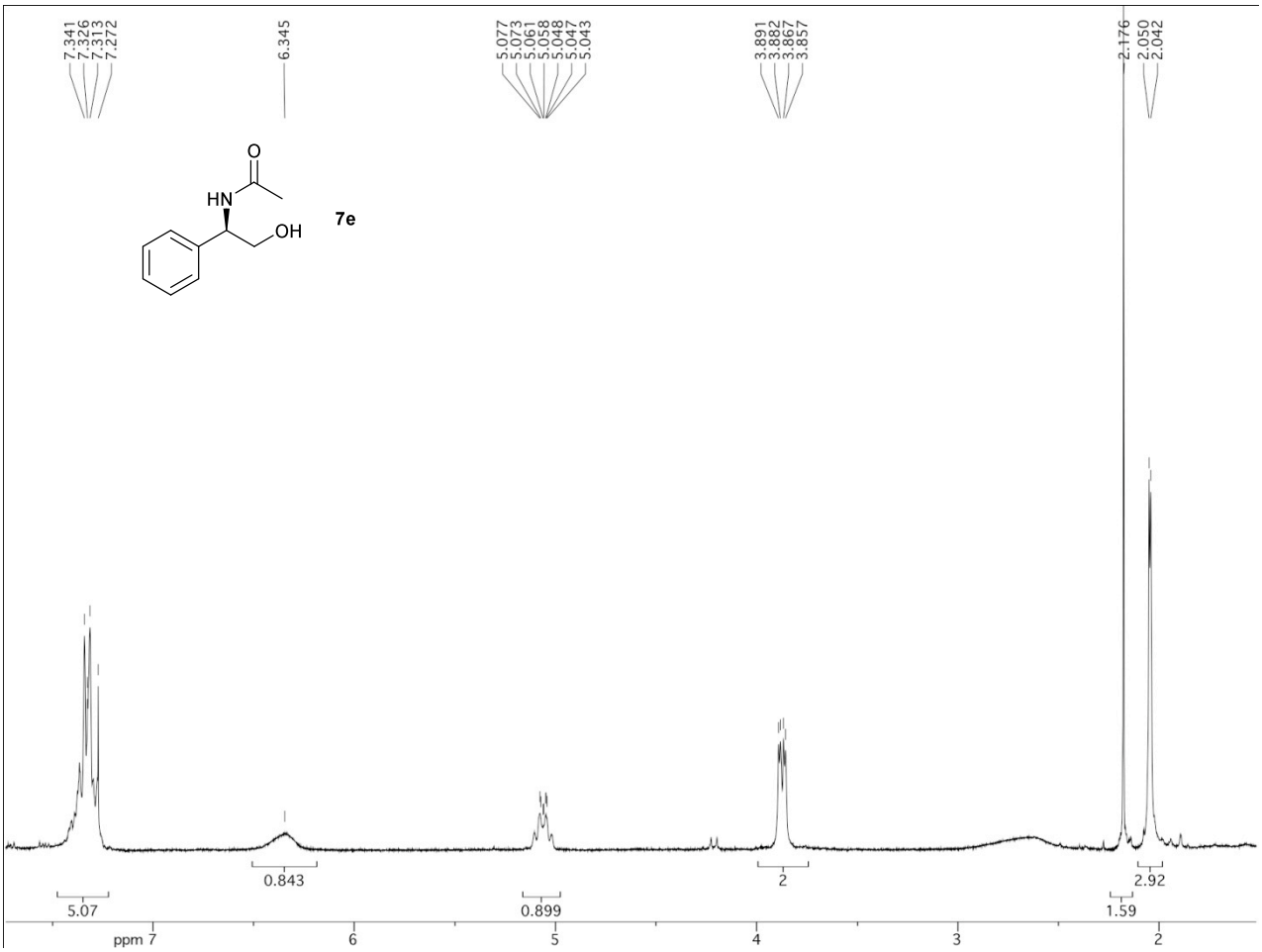

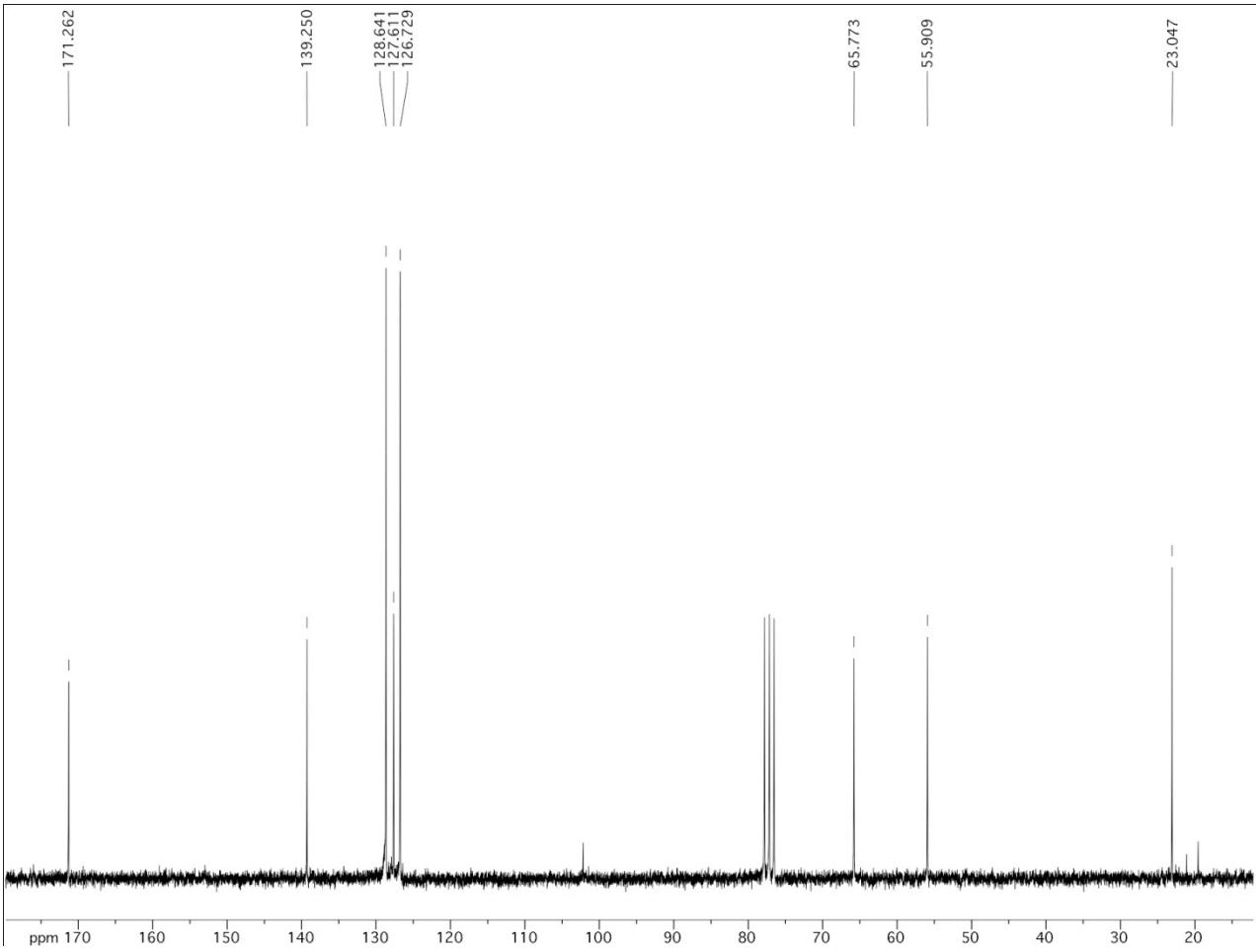

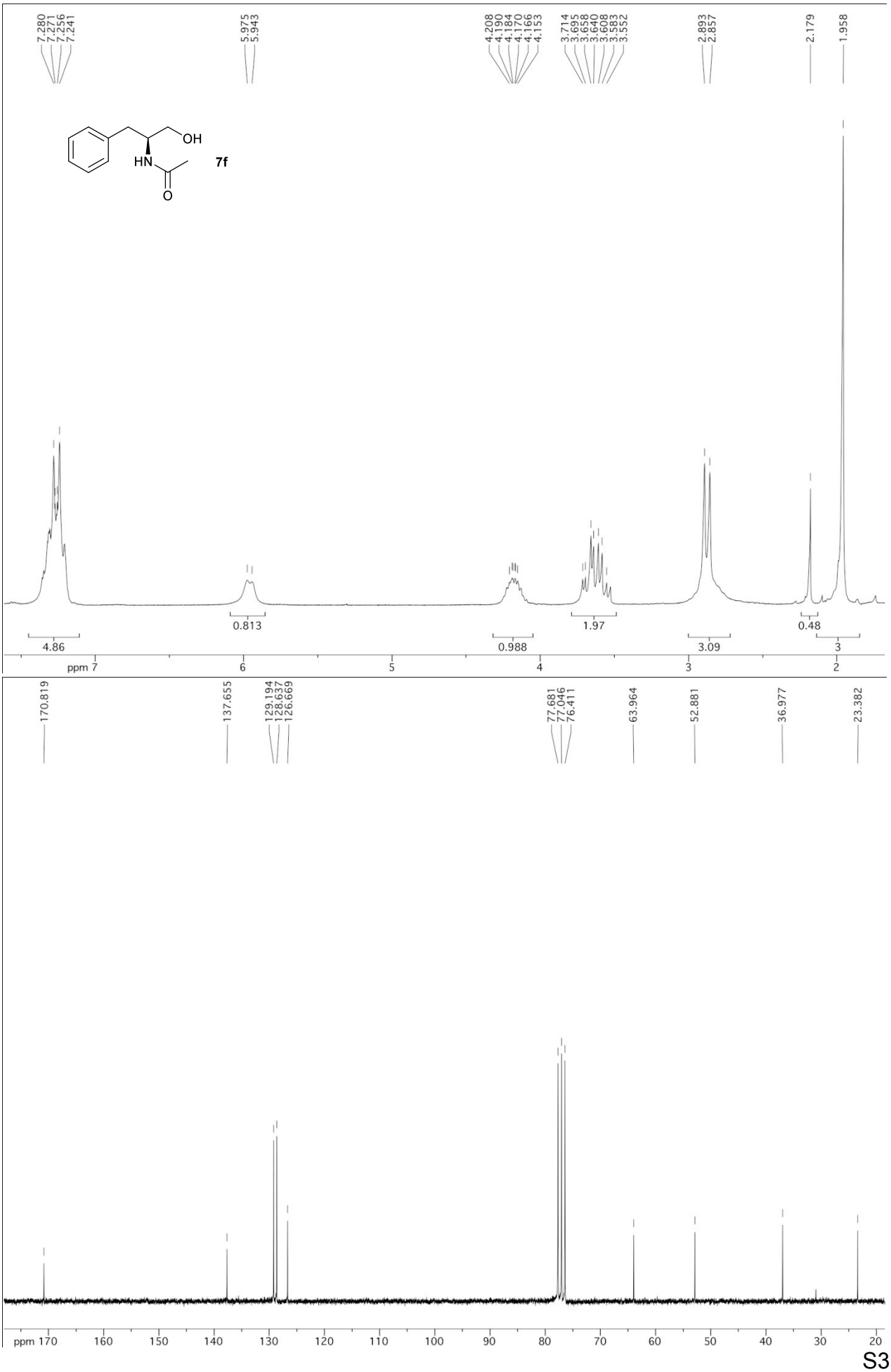

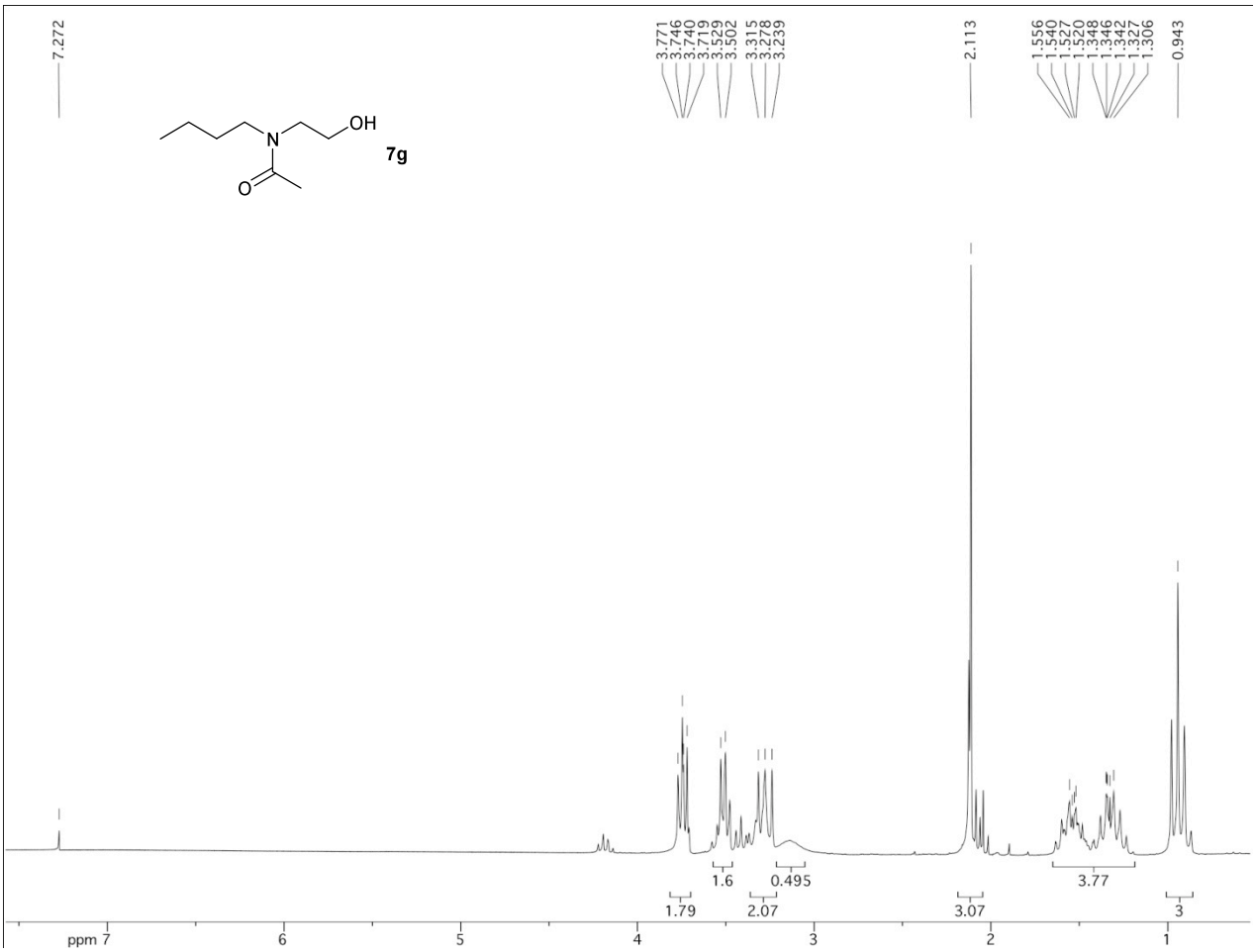

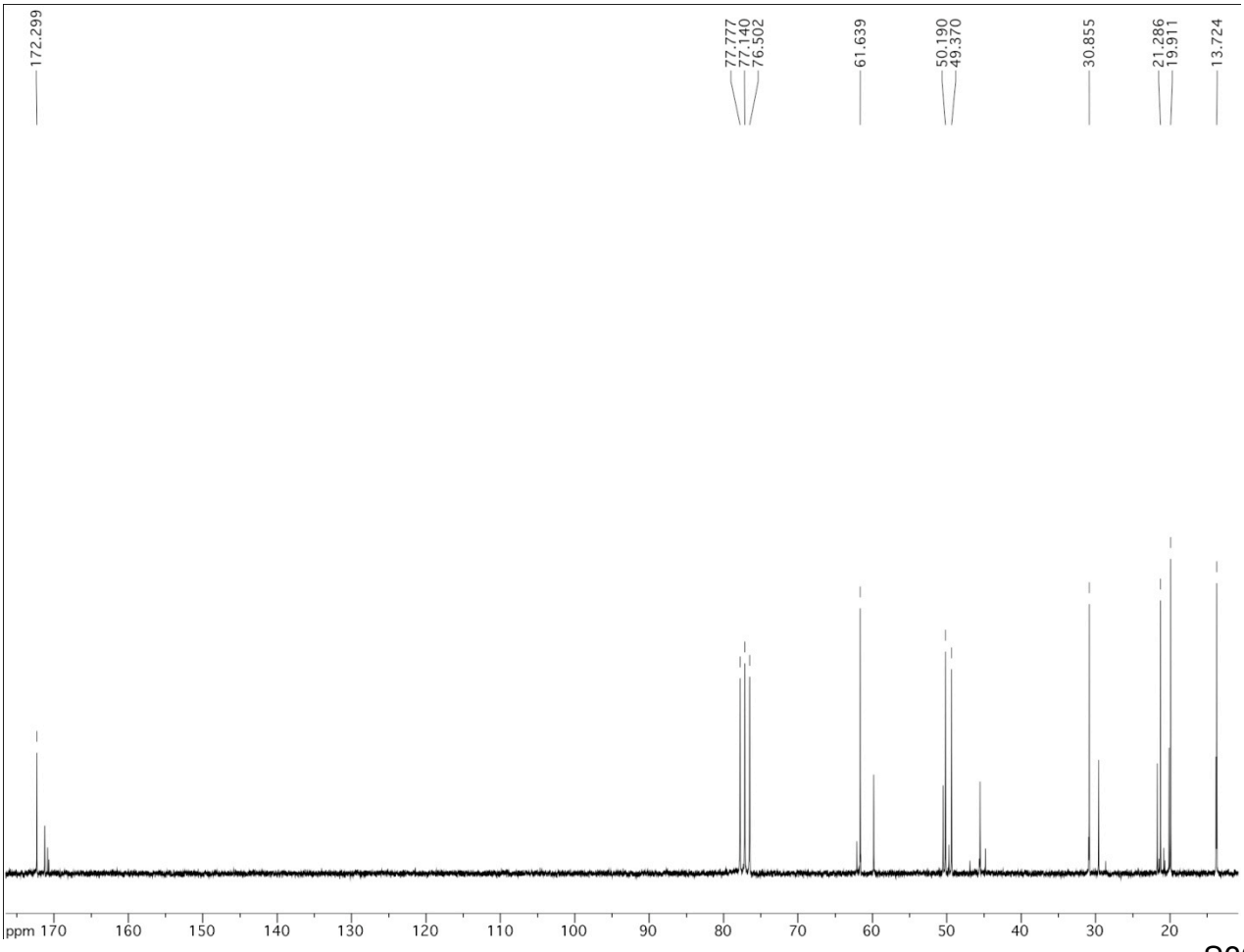

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