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Supporting Information

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Dynamic Kinetic Resolution of α-Substituted β-Ketoesters Catalyzed by Baeyer–Villiger Monooxygenases: Access to Enantiopure α-Hydroxy Esters**

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Supporting Information

Contents:

1. General

Recombinant histidine-tagged phenylacetone mononoxygenase (PAMO), its M446G mutant (M446G-PAMO) and recombinant 4-hydroxyacetophenone monooxygenase (HAPMO) were overexpressed and purified as previously described.[1] 1.0 Unit of BVMO will oxidise 1.0 μmol of phenylacetone to benzyl acetate per minute at pH 9.0 and room temperature in the presence of NADPH. Glucose 6-phosphate dehydrogenase from *Leuconostoc mesenteroides* was obtained from Fluka-Biochemika. Starting racemic α-alkyl-β-ketoesters *rac*-**2a**, *rac*-**6a** and enantiopure hydroxyesters (*S*)-**1**-**3c** and (*S*)-**10c** were obtained from Sigma-Aldrich-Fluka, whereas *rac*-**5a** was purchased from Alfa Aesar. All other reagents and solvents were of the highest quality grade available and were acquired from Sigma-Aldrich-Fluka and Acros Organics. Chemical reactions were monitored by analytical TLC, performed on Merck silica gel 60 F_{254} plates and visualised by UV irradiation. Flash chromatography was carried out with silica gel 60 (230-240 mesh, Merck). IR spectra were recorded on a Perkin-Elmer 1720-X infrared Fourier transform spectrophotometer using KBr pellets. ^{1}H-NMR, ^{13}C-NMR and DEPT spectra were recorded with tetramethylsilane (TMS) as the internal standard with a Bruker AC-300 DPX (^{1}H: 300.13 MHz; ^{13}C: 75.5 MHz) spectrometer. The chemical shift values (δ) are given in ppm. Optical rotations were measured using a Perkin-Elmer 241 polarimeter and are quoted in units of 10^{-1} deg cm^2 g^{-1}. APCI$^+$ and ESI$^+$ using a Hewlett Packard 1100 chromatograph mass detector or EI$^+$ with a Hewlett Packard 5973 mass spectrometer were used to record mass spectra (MS). High-resolution mass spectra were obtained with a Bruker Microtof-Q-spectrometer. Kinetic determinations were performed with a Varian Cary50Bio UV/Vis spectrophotometer.

2. Experimental procedures

2.1. Enzymatic Baeyer-Villiger oxidation of racemic α-alkyl-β-ketoesters.

Racemic compounds *rac*-**1-10a** (10 mM) were dissolved in a Tris-HCl buffer (50 mM, pH 8.0 or 9.0, 1.0 mL) containing 1% *v* v^{-1} DMSO. Then, NADPH (0.2 mM), glucose-6-phosphate (20 mM), glucose-6-phosphate dehydrogenase (5 U) and the BVMO (1 U) were added. The mixture was shaken at 250 rpm at the selected temperature. Reactions were stopped by extraction with ethyl acetate (2 × 0.5 mL) and the organic layer was dried over Na_2SO_4. Conversions and enantiomeric excesses of compounds (*S*)-**1-10b** were determined by GC or HPLC analysis (Table S1).

Table S1. BVMO-catalysed Baeyer-Villiger oxidation of racemic α-alkyl-β-ketoesters.

Entry	Substrate	BVMO	T (ºC)	*c* [%][a]	*ee* [%][b]
1[c]	*rac*-**1a**	PAMO	30	28	≥99(*S*)
2	*rac*-**1a**	M446G	30	15	≥99(*S*)
3	*rac*-**2a**	HAPMO	20	28	≥99(*S*)
4	*rac*-**2a**	M446G	30	25	≥99(*S*)
5	*rac*-**3a**	HAPMO	20	5	≥99(*S*)
6	*rac*-**3a**	M446G	30	36	≥99(*S*)
7	*rac*-**4a**	HAPMO	20	30	82(*S*)
8	*rac*-**4a**	M446G	30	7	≥99(*S*)
9	*rac*-**8a**	M446G	30	59	≥99(*S*)
10	*rac*-**10a**	M446G	30	22	≥99(*S*)

[a] Determined by GC.[b] Determined by GC or HPLC. [c] Reaction carried out at pH 8.0.

2.2. Study of the substrate concentration in the PAMO-catalysed oxidation of rac-***7a*** *employing two different reaction media.*

Racemic isopropyl 2-ethyl-3-oxobutanoate (1.7-13.8 g L^{-1}) was dissolved in two different reaction media: a) Tris-HCl buffer (50 mM, pH 9.0, 1.0 mL) containing 1% *v* v^{-1} DMSO or b) Tris-HCl buffer (50 mM, pH 9.0, 0.95 mL) containing 5% *v* v^{-1} TBME (50 μL) and 1% *v* v^{-1} DMSO. Then, NADPH (0.2 mM), glucose-6-phosphate (20 mM), glucose-6-phosphate dehydrogenase (5 U) and PAMO (1 U) were added. The mixture was shaken at 250 rpm at 30ºC during 48 hours. Reactions were then stopped by extraction with EtOAc (2 × 0.5 mL) and the organic layer was dried over Na_2SO_4. Conversions and enantiomeric excesses of compounds (*S*)-**7b** were determined by GC or HPLC analysis. The space time yields (expressed as mg of **7a** consumed per L of solution per h) are indicated in Figure S1.

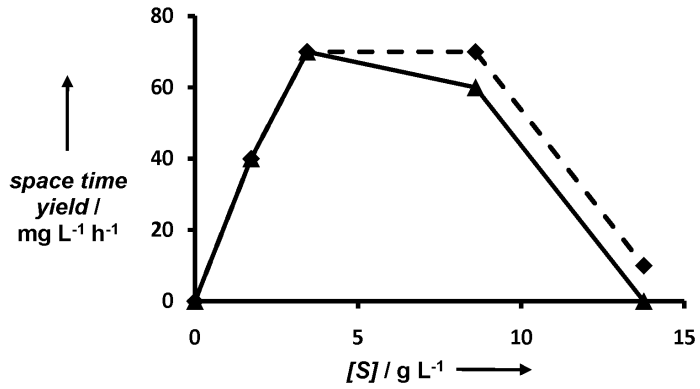

Figure S1. Effect of *rac*-**7a** concentration in the space time yield while using as reaction medium: Tris-HCl 50 mM pH 9.0 (▲, solid line) and Tris-HCl 50 mM pH 9.0 containing 5% *v* v^{-1} TBME (♦, dashed line).

2.3. Baeyer-Villiger oxidation of rac-***1-10a*** *at multimilligram scale catalysed by PAMO.*

α-Alkyl-β-ketoesters *rac*-**1-10a** (50 mg, 1 equiv.) were dissolved in a Tris-HCl buffer (50 mM, pH 9.0, 13.0 mL) containing 1% *v* v^{-1} DMSO. Then, NADPH (0.2 mM), glucose-6-phosphate (40 mM), glucose-6-phosphate dehydrogenase (150 units) and PAMO (30 units) were added. The reactions were stirred at 250 rpm and 30ºC and stopped after 24 hours by extraction with ethyl acetate (3 × 10 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated. No further purification was required, except for substrates *rac*-**4b** and *rac*-**5b**, which were purified by *flash* chromatography on silica gel using hexane/ethyl acetate 9:1 as eluent. All the final products (*S*)-**1-10b** were achieved enantiopure except (*S*)-**9b**, which was isolated with *ee*=50%: (*S*)-**1b** (70% yield, 39.3 mg), (*S*)-**2b** (62% yield, 35.1 mg), (*S*)-**3b** (59% yield, 32.8 mg), (*S*)-**4b** (68% yield, 38.3 mg), (*S*)-**5b** (65% yield, 36.0 mg), (*S*)-**6b** (61% yield, 33.4 mg), (*S*)-**7b** (63% yield, 34.4 mg), (*S*)-**8b** with (65% yield, 35.6 mg), (*S*)-**9b** (74% yield, 39.6 mg), and (*S*)-**10b** with (76% yield, 41.0 mg).

Compounds **1a**,[2a] and **2b**[2b] exhibit physical and spectral properties in accord with those reported.

(*S*)-Methyl 2-acetoxypropanoate, (*S*)-1b. R_f (8:2 hexane-EtOAc): 0.28. Colourless liquid. IR (KBr): υ 2998, 1741, 1643, 1454, and 1237 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.46 (d, $^3J_{H,H}$ 7.2 Hz, 3H), 2.11 (s, 3H), 3.73 (s, 3H), 5.07 (q, $^3J_{H,H}$ 7.2 Hz, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 16.8 (CH_3), 20.6 (CH_3), 52.2 (CH_3), 68.4 (CH), 170.3 (CO), 171.2 (CO). MS (ESI^+, *m/z*): 169 [$(M+Na)^+$, 24%].

(*S*)-Ethyl 2-acetoxypropanoate, (*S*)-2b. R_f (8:2 hexane-EtOAc): 0.32. Colourless liquid. IR (KBr): υ 2997, 1743, 1640, 1441, and 1370 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.26 (t,

$^{3}J_{H,H}$ 7.2 Hz, 3H), 1.47 (d, $^{3}J_{H,H}$ 7.0 Hz, 3H), 2.12 (s, 3H), 4.19 (q, $^{3}J_{H,H}$ 7.2 Hz, 2H), 5.10 (q, $^{3}J_{H,H}$ 7.0 Hz, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 14.0 (CH_3), 16.8 (CH_3), 20.6 (CH_3), 61.3 (CH_2), 68.6 (CH), 170.3 (CO), 171.2 (CO). MS (ESI^+, *m/z*): 183 [$(M+Na)^+$, 100%].

(*S*)-Isopropyl 2-acetoxypropanoate, (*S*)-3b. R_f (8:2 hexane-EtOAc): 0.34. Colourless liquid. IR (KBr): υ 2986, 1745, 1455, 1386, and 1200 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.23 (d, $^{3}J_{H,H}$ 6.4 Hz, 3H), 1.24 (d, $^{3}J_{H,H}$ 6.4 Hz, 3H), 1.45 (d, $^{3}J_{H,H}$ 7.0 Hz, 3H), 2.11 (s, 3H), 4.97-5.08 (m, 2H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 16.8 ($2CH_3$), 20.6 (CH_3), 21.5 (CH_3), 68.7 (CH), 68.9 (CH), 166.3 (CO), 170.3 (CO). MS (ESI^+, *m/z*): 197 [$(M+Na)^+$, 92%]. HRMS (ESI^+) calcd. for $C_8H_{14}NaO_4$ $(M+Na)^+$: 197.0784; found: 197.0776. $[\alpha]_D^{25}$= -37.9 (*c* 1.00, $CHCl_3$), *ee* = 99%.

(*S*)-Methyl 2-propionyloxypropanoate, (*S*)-4b. R_f (8:2 hexane-EtOAc): 0.34. Colourless liquid. IR (KBr): υ 2991, 1746, 1461, 1305, and 1277 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.15 (t, $^{3}J_{H,H}$ 7.5 Hz, 3H), 1.47 (d, $^{3}J_{H,H}$ 7.0 Hz, 3H), 2.36-2.47 (m, 2H), 3.73 (s, 3H), 5.08 (q, $^{3}J_{H,H}$ 7.0 Hz, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 8.8 (CH_3), 16.9 (CH_3), 27.2 (CH_2), 52.2 (CH_3), 68.3 (CH), 171.3 (CO), 173.8 (CO). MS (ESI^+, *m/z*): 183 [$(M+Na)^+$, 50%]. HRMS (ESI^+) calcd. for $C_7H_{12}NaO_4$ $(M+Na)^+$: 183.0628; found: 183.0619. $[\alpha]_D^{25}$= -34.6 (*c* 1.00 $CHCl_3$), *ee* = 99%.

(*S*)-Methyl 2-acetoxybutanoate, (*S*)-5b. R_f (8:2 hexane-EtOAc): 0.34. Colourless liquid. IR (KBr): υ 2957, 1746, 1440, 1376, and 1235 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.96 (t, $^{3}J_{H,H}$ 7.4 Hz, 3H), 1.79-1.90 (m, 2H), 2.11 (s, 3H), 3.72 (s, 3H), 4.91-4.95 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 9.4 (CH_3), 20.5 (CH_3), 24.4 (CH_2), 52.0 (CH_3), 73.2 (CH), 170.5 (CO), 170.6 (CO). MS (ESI^+, *m/z*): 183 [$(M+Na)^+$, 34%]. HRMS (ESI^+) calcd. for $C_7H_{12}NaO_4$ $(M+Na)^+$: 183.0628; found: 183.0637. $[\alpha]_D^{25}$= -25.0 (*c* 0.90, $CHCl_3$), *ee* = 99%.

(*S*)-Ethyl 2-acetoxybutanoate, (*S*)-6b. R_f (8:2 hexane-EtOAc): 0.36. Colourless liquid. IR (KBr): υ 2980, 1744, 1464, 1375, and 1234 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.96 (t, $^{3}J_{H,H}$ 7.4 Hz, 3H), 1.25 (t, $^{3}J_{H,H}$ 7.2 Hz, 3H), 1.79-1.90 (m, 2H), 2.10 (s, 3H), 4.17 (q, $^{3}J_{H,H}$ 7.2 Hz, 2H), 4.88-4.92 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 9.4 (CH_3), 14.0 (CH_3), 20.5 (CH_3), 24.4 (CH_2), 61.1 (CH_2), 73.3 (CH), 170.1 (CO), 170.5 (CO). MS (ESI^+, *m/z*): 197 [$(M+Na)^+$, 70%]. HRMS (ESI^+) calcd. for $C_8H_{14}NaO_4$ $(M+Na)^+$: 197.0782; found: 197.0784. $[\alpha]_D^{25}$= -28.7. (*c* 1.00, $CHCl_3$), *ee* = 99%.

(*S*)-Isopropyl 2-acetoxybutanoate, (*S*)-7b. R_f (8:2 hexane-EtOAc): 0.41. Colourless liquid. IR (KBr): υ 2989, 1745, 1464, 1426, 1375, 1234, and 1207 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.96 (t, $^{3}J_{H,H}$ 7.4 Hz, 3H), 1.22 (d, $^{3}J_{H,H}$ 6.3 Hz, 3H), 1.23 (d, $^{3}J_{H,H}$ 6.8 Hz, 3H), 1.77-1.88 (m, 2H), 2.10 (s, 3H), 4.84-4.88 (m, 1H), 4.99-5.08 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC):

δ 9.3 (CH_3), 20.5 (CH_3), 21.5 (CH_3), 21.6 (CH_3), 24.3 (CH_2), 68.8 (CH), 73.4 (CH), 169.6 (CO), 170.5 (CO). MS (ESI^+, *m/z*): 211 [$(M+Na)^+$, 52%]. HRMS (ESI^+) calcd. for $C_9H_{16}NaO_4$ $(M+Na)^+$: 211.0946; found: 211.0948. $[\alpha]_D^{25}$= -38.7 (*c* 0.98, $CHCl_3$), *ee* = 99%.

(*S*)-Ethyl 2-acetoxypent-4-enoate, **(*S*)-8b.** R_f (8:2 hexane-EtOAc): 0.44. Colourless liquid. IR (KBr): υ 3080, 2983, 1800, 1643, 1469, and 1431 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.25 (t, $^3J_{H,H}$ 7.0 Hz, 3H), 2.20 (s, 3H), 2.54-2.60 (m, 2H), 4.18 (q, $^3J_{H,H}$ 7.0 Hz, 2H), 5.01-5.06 (m, 1H), 5.08-5.28 (m, 2H), 5.72-5.79 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 14.0 (CH_3), 20.5 (CH_3), 35.4 (CH_2), 61.3 (CH_2), 71.6 (CH), 118.6 (CH_2), 131.9 (CH), 169.5 (CO), 170.3 (CO). MS (ESI^+, *m/z*): 209 [$(M+Na)^+$, 30%]. HRMS (ESI^+) calcd. for $C_9H_{14}NaO_4$ $(M+Na)^+$: 209.0784; found: 209.0767. $[\alpha]_D^{25}$= -17.3 (*c* 1.12, $CHCl_3$), *ee* = 99%.

(*S*)-Isopropyl 2-acetoxy-3-phenylpropanoate, (*S*)-9b. R_f (8:2 hexane-EtOAc): 0.29. Pale yellow liquid. IR (KBr): υ 3030, 2934, 1731, 1496, 1455, and 1375 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.17 (d, $^3J_{H,H}$ 6.4 Hz, 3H), 1.23 (d, $^3J_{H,H}$ 6.4 Hz, 3H), 2.09 (s, 3H), 3.10 (dd, $^2J_{H,H}$ 11.6 Hz, $^3J_{H,H}$ 8.6 Hz, 1H), 3.16 (dd, $^2J_{H,H}$ 11.6 Hz, $^3J_{H,H}$ 5.0 Hz, 1H), 4.98-5.07 (m, $^3J_{H,H}$ 6.4 Hz, 1H), 5.16 (dd, $^3J_{H,H}$ 8.6 Hz, $^3J_{H,H}$ 5.0 Hz, 1H), 7.23-7.31 (m, 5H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 20.5 (CH_3), 21.5 (CH_3), 21.6 (CH_3), 37.2 (CH_2), 69.1 (CH), 73.1 (CH), 126.9 (CH_{ar}), 128.3 ($2CH_{ar}$), 129.3 ($2CH_{ar}$), 135.9 (C_{ar}), 169.1 (CO), 170.3 (CO). MS (ESI^+, *m/z*): 273 [$(M+Na)^+$, 100%]. HRMS (ESI^+) calcd. for $C_{14}H_{18}NaO_4$ $(M+Na)^+$: 273.1097; found: 273.1105. $[\alpha]_D^{25}$= -5.7 (*c* 1.05, $CHCl_3$), *ee* = 54%.

(*S*)-Benzyl 2-acetoxypropanoate, **(*S*)-10b.** R_f (8:2 hexane-EtOAc): 0.31. Pale yellow liquid. IR (KBr): υ 3035, 2994, 1744, 1455, 1305, 1257, and 1196 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.49 (d, $^3J_{H,H}$ 7.0 Hz, 3H), 2.12 (s, 3H), 5.09-5.16 (m, 1H), 5.17 (s, 2H), 7.33-7.36 (m, 5H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 16.8 (CH_3), 20.6 (CH_3), 66.9 (CH_2), 68.5 (CH), 128.0 ($2CH_{ar}$), 128.3 ($2CH_{ar}$), 135.3 (CH_{ar}), 166.3 (C_{ar}), 170.3 (CO), 170.6 (CO). MS (ESI^+, *m/z*): 245 [$(M+Na)^+$, 55%]. HRMS (ESI^+) calcd. for $C_{12}H_{14}NaO_4$ $(M+Na)^+$: 245.0784; found: 245.0795. $[\alpha]_D^{25}$= -91.4 (*c* 1.00, $CHCl_3$), *ee* = 99%.

2.4. General procedure for the enzymatic hydrolysis of rac-*isopropyl 2-acetoxybutanoate,* rac-***7b.***

In a typical experiment, to a solution of compound *rac*-**7b** (9.4 mg, 1.0 equiv) in a Tris-HCl buffer (50 mM, pH 9.0, 500 μL), 9.4 mg of commercially available hydrolase (CAL-A, CRL, PPL, SD, PLE, subtilisin, CAL-B, AK, IM) was added. The reaction was shaken at 30°C and 250 rpm in a rotator shaker for the times established (3.5 hours or 7 hours), stopped by extraction with EtOAc

containing 1 mg mL^{-1} mesitylene (2 x 400 μL) and dried over Na_2SO_4. Conversions and enantiomeric excesses of the reactions were measured by GC and HPLC analysis.

For CRL, PLE, subtilisin and CAL-B, it was observed the disappearance of *rac*-**7b**, but expected product *rac*-**7c** was not obtained. PPL led to *rac*-**7c** with very low conversions. Lipases AK and IM were not able to hydrolyse the *S* enantiomer of *rac*-**7b** while lipases CAL-A and SD were not regioselectivity in the process, being achieved other hydrolysis products.

*2.5. Procedure for the chemical hydrolysis of diesters (S)-**3-9b.***

To a solution of the corresponding diester (25 mg, 1.0 equiv.) in 5.0 mL of MeOH, EtOH or ^{i}PrOH, traces of HCl were added. The reaction was refluxed and followed by TLC using CH_2Cl_2 as eluent. After disappearance of the starting product, the reaction was stopped and the solvent was evaporated under reduced pressure. (*S*)-α-hydroxyesters were obtained without any further purification. All the products were achieved enantiopure except for (*S*)-**9c**, isolated with *ee*=54%. (*S*)-**3c** (60% yield, 11.3 mg), (*S*)-**4c** (60% yield, 9.8 mg), (*S*)-**5c** was obtained with 64% yield (11.8 mg), (*S*)-**6c** with 70% yield (13.2 mg), (*S*)-**7c** with 65% yield (12.6 mg), (*S*)-**8c** with 70% yield (13.5 mg), and (*S*)-**9c** with 85% yield (17.6 mg).

Compounds **5c**,[3a] and **6c**[3b] exhibit physical and spectral properties in accordance with those reported.

(*S*)-Isopropyl 2-hydroxypropanoate, **(*S*)-3c.** R_f (8:2 hexane-EtOAc): 0.20. Colourless liquid. IR (KBr): υ 3480, 2984, 1651, 1463, 1376, and 1271 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.24 (d, $^3J_{H,H}$ 6.1 Hz, 3H), 1.25 (d, $^3J_{H,H}$ 6.4 Hz, 3H), 1.37 (d, $^3J_{H,H}$ 6.4 Hz, 3H), 2.94 (s, 1H), 4.15-4.23 (m, 1H), 5.02-5.10 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 20.3 (CH_3), 21.6 ($2CH_3$), 66.7 (CH), 69.3 (CH), 175.2 (CO). MS (ESI^+, *m/z*): 155 [$(M+Na)^+$, 73%]. HRMS (ESI^+) calcd. for $C_6H_{12}NaO_3$ $(M+Na)^+$: 155.0684; found: 155.0687. $[\alpha]_D^{25}$= -5.20 (*c* 1.00, $CHCl_3$), *ee* = 99%.[4a]

(*S*)-Methyl 2-hydroxybutanoate, **(*S*)-5c.** R_f (8:2 hexane-EtOAc): 0.20. Colourless liquid. IR (KBr): υ 3433, 2969, 1738, 1645, 1420, 1296, and 1135 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.95 (t, $^3J_{H,H}$ 7.4 Hz, 3H), 1.60-1.89 (m, 2H), 2.77 (d, $^3J_{H,H}$ 5.9 Hz, 1H), 3.78 (s, 3H), 4.15 (q, $^3J_{H,H}$ 5.9 Hz, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 8.8 (CH_3), 27.4 (CH_2), 52.4 (CH_3), 71.4 (CH), 175.6 (CO). MS (ESI^+, *m/z*): 141 [$(M+Na)^+$, 40%]. $[\alpha]_D^{25}$= -6.4 (*c* 1.15, $CHCl_3$), *ee* = 99%.[4b]

(*S*)-Ethyl 2-hydroxybutanoate, **(*S*)-6c.** R_f (8:2 hexane-EtOAc): 0.21. Colourless liquid. IR (KBr): υ 3429, 2980, 1733, 1600, 1464, and 1212 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.96 (t, $^3J_{H,H}$ 7.3 Hz, 3H), 1.29 (t, $^3J_{H,H}$ 7.1 Hz, 3H), 1.63-1.88 (m, 2H), 2.77 (d, $^3J_{H,H}$ 5.7 Hz, 1H),

4.10-4.16 (m, 1H), 4.24 (q, $^{3}J_{H,H}$ 7.1 Hz, 2H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 8.7 (CH_3), 14.1 (CH_3), 27.4 (CH_2), 61.6 (CH_2), 71.3 (CH), 175.2 (CO). MS (ESI^+, *m/z*): 155 [$(M+Na)^+$, 36%]. $[\alpha]_D^{25}$= -5.95 (*c* 1.20, CH_3CH_2OH), *ee* = 99%.[3b]

(*S*)-Isopropyl 2-hydroxybutanoate, **(*S*)-7c.** R_f (8:2 hexane-EtOAc): 0.31. Colourless liquid. IR (KBr): υ 3413, 2982, 1731, 1463, 1376, and 1107 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.94 (t, $^{3}J_{H,H}$ 7.4 Hz, 3H), 1.25 (d, $^{3}J_{H,H}$ 6.3 Hz, 3H), 1.27 (d, $^{3}J_{H,H}$ 6.3 Hz, 3H), 1.64-1.71 (m, 1H), 1.77-1.81 (m, 1H), 2.80 (d, $^{3}J_{H,H}$ 5.7 Hz, 1H), 4.09-4.10 (m, 1H), 5.09 (m, $^{3}J_{H,H}$ 6.3 Hz, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 8.7 (CH_3), 21.7 ($2CH_3$), 27.4 (CH_2), 69.3 (CH), 71.3 (CH), 174.7 (CO). MS (ESI^+, *m/z*): 169 [$(M+Na)^+$, 61%]. HRMS (ESI^+) calcd for $C_7H_{14}NaO_3$ $(M+Na)^+$: 169.0835; found: 169.0838. $[\alpha]_D^{25}$= -6.1 (*c* 0.85, $CHCl_3$), *ee* = 99%.

(*S*)-Ethyl 2-hydroxypent-4-enoate, (*S*)-8c. R_f (8:2 hexane-EtOAc): 0.23. Colourless liquid. IR (KBr): υ 3409, 2984, 1747, 1376, and 1243 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.29 (t, $^{3}J_{H,H}$ 7.2 Hz, 3H), 2.38-2.48 (m, 1H), 2.52-2.61 (m, 1H), 2.81 (d, 1H), 4.20-4.28 (m, 3H), 5.11-5.18 (m, 2H), 5.73-5.87 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 14.0 (CH_3), 38.5 (CH_2), 61.4 (CH_2), 69.8 (CH), 118.4 (CH_2), 132.4 (CH), 174.2 (CO). MS (ESI^+, *m/z*): 167 [$(M+Na)^+$, 67%]. $[\alpha]_D^{25}$= -4.2 (*c* 0.95, $CHCl_3$), *ee* = 99%.

(*S*)-Isopropyl 2-hydroxy-3-phenylpropanoate, (*S*)-9c. R_f (8:2 hexane-EtOAc): 0.23. Colourless liquid. IR (KBr): υ 3359, 3088, 2982, 1731, 1496, 1375, and 1273 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.26 (d, $^{3}J_{H,H}$ 6.1 Hz, 3H), 1.28 (d, $^{3}J_{H,H}$ 6.1 Hz, 3H), 2.99 (dd, $^{2}J_{H,H}$ 13.8 Hz, $^{3}J_{H,H}$ 6.8 Hz, 1H), 3.15 (dd, $^{2}J_{H,H}$ 13.8 Hz, $^{3}J_{H,H}$ 4.8 Hz, 1H), 4.43 (m, 1H), 5.08 (m, $^{3}J_{H,H}$ 6.1 Hz, 1H), 7.20-7.36 (m, 5H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 21.6 ($2CH_3$), 40.3 (CH_2), 69.4 (CH), 71.1 (CH), 126.7 (CH_{ar}), 128.1 ($2CH_{ar}$), 129.4 ($2CH_{ar}$), 136.3 (C_{ar}), 173.6 (CO). MS (ESI^+, *m/z*): 231 [$(M+Na)^+$, 100%]. HRMS (ESI^+) calcd. for $C_{12}H_{16}NaO_3$ $(M+Na)^+$: 231.0992; found: 231.0995. $[\alpha]_D^{25}$= -9.7 (*c* 0.78, $CHCl_3$), *ee* = 99%.

2.6. General procedure for the synthesis of racemic α-alkyl-β-ketoesters rac-***1a***, rac-***3-4a***, rac-***7-10a***.[5]

A mixture of the corresponding alkyl acetoacetate or methyl-3-oxo-pentanoate (2.0 g, 1.0 equiv) and anhydrous powdered K_2CO_3 (1.3 equiv) in 20.0 mL of dry acetone was stirred under nitrogen atmosphere for five minutes. Then, methyl iodide, ethyl iodide, allyl bromide or benzyl bromide (1.3 equiv) was added carefully. The reaction was refluxed for 18 hours. The crude mixture was then filtered and the solvent evaporated under reduced pressure. The residues were purified by *flash* chromatography on silica gel with hexane/ethyl acetate 9:1 to afford methyl 2-methyl-3-

oxobutanoate *rac*-**1a** (67% yield, 1.54 g), isopropyl 2-methyl-3-oxobutanoate *rac*-**3a** (81% yield, 1.80 g), methyl 2-methyl-3-oxopentanoate *rac*-**4a** (29% yield, 0.64 g), isopropyl 2-ethyl-3-oxobutanoate *rac*-**7a** (42% yield, 0.91 g), ethyl 2-acetylpent-4-enoate *rac*-**8a** (84% yield, 1.84 g), isopropyl 2-benzyl-3-oxobutanoate *rac*-**9a** (53% yield, 1.13 g), and benzyl 2-methyl-3-oxobutanoate *rac*-**10a** (47% yield, 1.01 g).

Compounds *rac*-**1a**,[6a] *rac*-**3a**,[6b], *rac*-**8a**,[6c] and *rac*-**10a**,[6d] exhibit physical and spectral properties in accord with those reported.

***rac*-Methyl 2-methyl-3-oxobutanoate, *rac*-1a**. R_f (8:2 hexane-EtOAc): 0.27. Colourless liquid. IR (KBr): υ 2999, 1750, 1720, 1380, and 1359 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.35 (d, $^3J_{H,H}$ 7.2 Hz, 3H), 2.23 (s, 3H), 3.51 (q, $^3J_{H,H}$ 7.2 Hz, 1H), 3.79 (s, 3H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 12.7 (CH_3), 28.3 (CH_3), 52.2 (CH_3), 53.3 (CH), 170.8 (CO), 203.5 (CO). MS (ESI^+, *m/z*): 153 [$(M+Na)^+$, 56%].

***rac*-Isopropyl 2-methyl-3-oxobutanoate, *rac*-3a.** R_f (8:2 hexane-EtOAc): 0.41. Colourless liquid. IR (KBr): υ 2942, 1738, 1715, 1455, 1376, and 1359 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.24 (d, $^3J_{H,H}$ 6.1 Hz, 6H), 1.28 (d, $^3J_{H,H}$ 7.0 Hz, 3H), 2.20 (s, 3H), 3.44 (q, $^3J_{H,H}$ 7.0 Hz, 1H), 4.27-5.29 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 12.6 (CH_3), 21.4 ($2CH_3$), 28.3 (CH_3), 53.8 (CH), 68.8 (CH), 170.0 (CO), 203.6 (CO). MS (ESI^+, *m/z*): 181 [$(M+Na)^+$, 53%].

***rac*-Methyl 2-methyl-3-oxopentanoate, *rac*-4a.** R_f (8:2 hexane-EtOAc): 0.37. Colourless liquid. IR (KBr): υ 2984, 2940, 1747, 1594, 1455, and 1435 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.06 (t, $^3J_{H,H}$ 7.2 Hz, 3H), 1.34 (d, $^3J_{H,H}$ 7.0 Hz, 3H), 2.52-2.59 (m, 2H), 3.52 (q, $^3J_{H,H}$ 7.2 Hz, 1H), 3.71 (s, 3H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 7.6 (CH_3), 12.8 (CH_3), 34.6 (CH_2), 52.3 (CH), 52.4 (CH_3), 171.1 (CO), 206.3 (CO). MS (ESI^+, *m/z*): 167 [$(M+Na)^+$, 76%]. HRMS (ESI^+) calcd for $C_7H_{12}NaO_3$ $(M+Na)^+$: 167.0679; found: 167.0671.

***rac*-Isopropyl 2-ethyl-3-oxobutanoate, *rac*-7a.** R_f (8:2 hexane-EtOAc): 0.46. Colourless liquid. IR (KBr): υ 2980, 1736, 1714, 1463, 1375, and 1359 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 0.82 (t, $^3J_{H,H}$ 7.5 Hz, 3H), 1.14 (d, $^3J_{H,H}$ 6.4 Hz, 3H), 1.15 (d, $^3J_{H,H}$ 6.2 Hz, 3H), 1.71-1.82 (m, 2H), 2.10 (s, 3H), 3.18-3.22 (t, $^3J_{H,H}$ 7.2 Hz, 1H), 4.94-5.22 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 11.5 (CH_3), 21.2 (CH_3), 21.3 (CH_3), 21.4 (CH_2), 28.4 (CH_3), 61.3 (CH), 68.4 (CH), 169.0 (CO), 203.6 (CO). MS (ESI^+, *m/z*): 195 [$(M+Na)^+$, 28%]. HRMS (ESI^+) calcd. for $C_9H_{16}NaO_3$ $(M+Na)^+$: 195.0992; found: 195.0993.

***rac*-Ethyl 2-acetylpent-4-enoate**, ***rac*-8a.** R_f (8:2 hexane-EtOAc): 0.28. Colourless liquid. IR (KBr): υ 3081, 2983, 1743, 1715, 1643, 1441, and 1367 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.25 (t, $^3J_{H,H}$ 7.0 Hz, 3H), 2.21 (s, 3H), 2.54-2.59 (m, 2H), 3.50 (t, $^3J_{H,H}$ 7.5 Hz, 1H), 4.18

(q, $^3J_{H,H}$ 7.0 Hz, 2H), 5.01-5.28 (m, 2H), 5.65-5.79 (m, 1H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 14.0 (CH_3), 28.9 (CH_3), 32.1 (CH_2), 59.1 (CH), 61.3 (CH_2), 117.3 (CH_2), 132.1 (CH), 169.1 (CO), 202.4 (CO). MS (ESI$^+$, *m/z*): 193 [(M+Na)$^+$, 100%].

***rac*-Isopropyl 2-benzyl-3-oxobutanoate, *rac*-9a.** R_f (8:2 hexane-EtOAc): 0.43. Colourless liquid. IR (KBr): υ 3056, 2982, 1738, 1715, 1496, and 1455 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.14-1.29 (m, 6H), 2.20 (s, 3H), 3.14 (d, $^3J_{H,H}$ 7.2 Hz, 2H), 3.76 (t, $^3J_{H,H}$ 7.2 Hz, 1H), 4.98-5.12 (m, 1H), 7.18-7.31 (m, 5H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 21.4 (CH_3), 21.5 (CH_3), 29.3 (CH_3), 33.7 (CH_2), 61.4 (CH), 69.0 (CH), 128.0 ($2CH_{ar}$), 128.5 ($2CH_{ar}$), 128.7 (CH_{ar}), 138.1 (C_{ar}), 168.6 (CO), 202.3 (CO). MS (ESI$^+$, *m/z*): 257 [(M+Na)$^+$, 100%]. HRMS (ESI$^+$) calcd. for $C_{14}H_{18}NaO_3$ (M+Na)$^+$: 257.1148; found: 257.1169.

***rac*-Benzyl 2-methyl-3-oxobutanoate**, ***rac*-10a.** R_f (8:2 hexane-EtOAc): 0.35. Colourless liquid. IR (KBr): υ 3050, 2990, 1744, 1715, 1498, 1455, and 1359 cm^{-1}. ^{1}H-NMR (300.13 MHz, $CDCl_3$, 25ºC): δ 1.36 (d, $^3J_{H,H}$ 7.1 Hz, 3H), 2.19 (s, 3H), 3.55 (q, $^3J_{H,H}$ 7.1 Hz, 1H), 5.17 (s, 2H), 7.32-7.37 (m, 5H). ^{13}C-NMR (75.5 MHz, $CDCl_3$, 25ºC): δ 12.6 (CH_3), 28.3 (CH_3), 53.5 (CH), 70.0 (CH_2), 128.2 (CH_{ar}), 128.4 ($2CH_{ar}$), 128.5 ($2CH_{ar}$), 134.0 (C_{ar}), 170.3 (CO), 203.3 (CO). MS (ESI$^+$, *m/z*): 229 [(M+Na)$^+$, 100%].

2.7. General procedure for the synthesis of racemic diesters rac-***1-7b*** *and* rac-***9-10b*.**

For the preparation of the diesters *rac*-**2-3b**, *rac*-**5-7b** and *rac*-**9b**, a two-step procedure starting from commercially available *rac*-lactic acid, *rac*-2-hydroxybutanoic acid or *rac*-phenyllactic acid was carried out.

Step 1: Synthesis of α-hydroxy esters rac-***2-3c***, rac-***5-7c***, *and* rac-***9c***.

To a solution of the corresponding acid (1.0 g, 1.0 equiv) in 40.0 mL of MeOH, EtOH, ^{i}PrOH or benzyl alcohol, traces of HCl were added. The reaction was refluxed and followed by TLC CH_2Cl_2/MeOH 95:5. After 24 hours, the reaction was stopped; the solvent was evaporated under reduced pressure. The crude mixture was then solved in 20 mL CH_2Cl_2, washed with a saturated solution of $NaHCO_3$ (2 × 15 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent evaporated under reduced pressure. Racemic α-hydroxy esters were obtained without any further purification: *rac*-**2c** (29% yield, 328.4 mg), *rac*-**3c** (27% yield, 395.6 mg), *rac*-**5c** (52% yield, 589.0 mg), *rac*-**6c** (66% yield, 836.3 mg), *rac*-**7c** (76% yield, 1.06 g), and *rac*-**9c** (72% yield, 893 mg).

For the preparation of *rac*-**1b** and *rac*-**10b**, this step was not necessary since *rac*-methyl lactate and *rac*-benzyl 2-hydroxypropanoate were commercially available.

Step 2: Synthesis of diesters rac-***1-7b*** *and* rac-***9-10b.***

α-Hydroxy esters *rac*-**1-3c**, *rac*-**5-7c**, and *rac*-**9-10c** (300 mg, 1.0 equiv) were acylated with acetic anhydride (2.0 equiv) or propionic anhydride (in case of **4b**) and a catalytic amount of *N*,*N*-dimethylaminopyridine in dry CH_2Cl_2 (6.0 mL). Racemic diesters were achieved without any further purification: *rac*-**1b** (75% yield, 315.9 mg), *rac*-**2b** (21% yield, 85.4 mg), *rac*-**3b** (46% yield, 181.9 mg), *rac*-**4b** (22% yield, 101.5 mg), *rac*-**5b** (74% yield, 301.0 mg), *rac*-**6b** (61% yield, 241.2 mg), *rac*-**7b** (69% yield, 266.5 mg), *rac*-**9b** (35% yield, 126.2 mg), and *rac*-**10b** (45% yield, 166.5 mg).

2.8. Experimental procedure for obtaining rac-*ethyl 2-acetoxypent-4-enoate,* rac-***8b.***

For the preparation of the diester *rac*-**8b**, a two-step procedure starting from commercially avaliable ethyl glyoxilate was employed.

Step 1: Synthesis of rac-*ethyl 2-hydroxypent-4-enoate*, rac-***8c.***[7]

To a solution of ethyl glyoxylate (500 mg, 1.0 equiv) and allyltrimethylsilane (2.0 equiv) in dry CH_2Cl_2 (25 mL) at 0ºC, boron trifluoride diethyl etherate (2.0 equiv) was added dropwise. The solution was allowed to warm up to room temperature and then stirred for 1.5 h. The reaction was then quenched with a saturated aqueous solution of NH_4Cl and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 and concentrated by reduced pressure to yield a crude mixture that was purified by *flash* chromatography on silica gel with hexane/ethyl acetate 7:3 as eluent to afford ethyl 2-hydroxypent-4-enoate, *rac*-**8c** (59% yield, 300 mg) as a colourless liquid.
Compound **8c**[7] exhibits physical and spectral properties in accordance with those reported.

Step 2: Acylation of rac-*ethyl 2-hydroxypent-4-enoate* rac-***8c***.

Racemic 2-hydroxypent-4-enoate *rac*-**8c** (300 mg, 1.0 equiv) was acylated with acetic anhydride (2 equiv) and catalytic *N*,*N*-dimethylaminopyridine in dry CH_2Cl_2 (6.0 mL) in order to obtain pure *rac*-ethyl 2-acetoxypent-4-enoate *rac*-**8b** in quantitative yield (373.1 mg) and without further purification.

3. GC and HPLC analyses

The following columns were used for the determination of conversions and enantiomeric excesses (Table S2) of some α-alkyl-β-keto esters, their corresponding oxidation and hydrolysis products: A: Restek RT-BetaDEXse (30 m x 0.25 mm x 0.25 μm, 12 psi N_2) and B: Hewlett Packard HP-1 (30 m x 0.32 mm x 0.25μm, 12.2 psi N_2).

Table S2. Determination of conversions and enantiomeric excesses by employing GC.

Substrate	Program[a]	Column	t_R [min] **a**	t_R [min] **b**	t_R [min] **c**
1	50/20/3/110/0	A	35.9, 36.1	32.8 (*S*), 33.5 (*R*)	27.1 (*S*), 29.0 (*R*)
2	50/20/3/110/0	A	37.9	35.7 (*S*), 36.2 (*R*)	26.6 (*S*), 28.5 (*R*)
3	50/20/1/90/0	A	52.2, 52.6	49.3 (*S*), 50.2 (*R*)	34.8 (*S*), 39.7 (*R*)
4	50/20/1/110/0	A	54.2, 57.9	51.0 (*S*), 52.1(*R*)	21.4 (*S*), 27.5 (*R*)
5	50 Isotherm	B	6.0	7.5	2.4
6	50 Isotherm	B	10.2	12.8	3.5
7	50 Isotherm	B	13.3	16.3	5.7
8	50/25/20/200/0	B	22.7	26.6	6.6
9	70/5/1/120/0	B	44.3	46.0	25.5
10	70/5/1/123/0	B	35.7	37.7	33.1

[a] Program: initial T (ºC)/ time (min)/ slope (ºC/min)/ T (ºC)/ time (min)/

For the determination of the enantiomeric excesses of compounds **5-10b** (Table S3), the following columns were employed: column A: Chiralcel OB-H (0.46 cm x 25 cm) and column B: Chiralcel OD (0.46 cm x 25 cm), both from Daicel.

Table S3. Determination of enantiomeric excesses by HPLC.

Substrate	Column	Flow rate [mL min^{-1}]	T [ºC]	Eluent[a]	Retention time [min]
5b	A	0.7	25	*n*-hexane-IPA 99:1	12.9 (*R*); 17.7 (*S*)
6b	A	0.5	25	*n*-hexane-IPA 99:1	17.8 (*R*); 21.1 (*S*)
7b	A	0.5	20	*n*-hexane-IPA 99:1	12.7 (*R*); 14.3 (*S*)
8b	A	0.5	20	*n*-hexane-IPA 99:1	22.6 (*R*); 26.3 (*S*)
9b	B	1.0	25	*n*-hexane-IPA 99:1	25.8 (*R*); 34.8 (*S*)
10b	A	0.8	20	*n*-hexane-IPA 95:5	23.8 (*R*); 26.3 (*S*)

[a] All the experiments were performed with isocratic eluent.

4. Determination of absolute configurations

Absolute configurations of acylated 2-hydroxy esters **1-7b** and **9-10b** were established by comparison of their HPLC or GC retention times with the ones obtained after the esterification and/or acetylation of the corresponding commercial chiral α-hydroxy esters/acids.

Absolute configuration of ethyl 2-acetoxypent-4-enoate **8b** was obtained comparing the retention times on HPLC with the product achieved after hydrolysis of the racemic compound **8b** employing lipase AK from *Pseudomonas fluorescens*.[8]

Absolute configurations of α-hydroxy esters were achieved by its previous derivatisation into the corresponding acetate or propionate derivatives.

5. Supporting references

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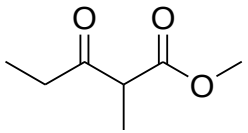
6. NMR Spectra



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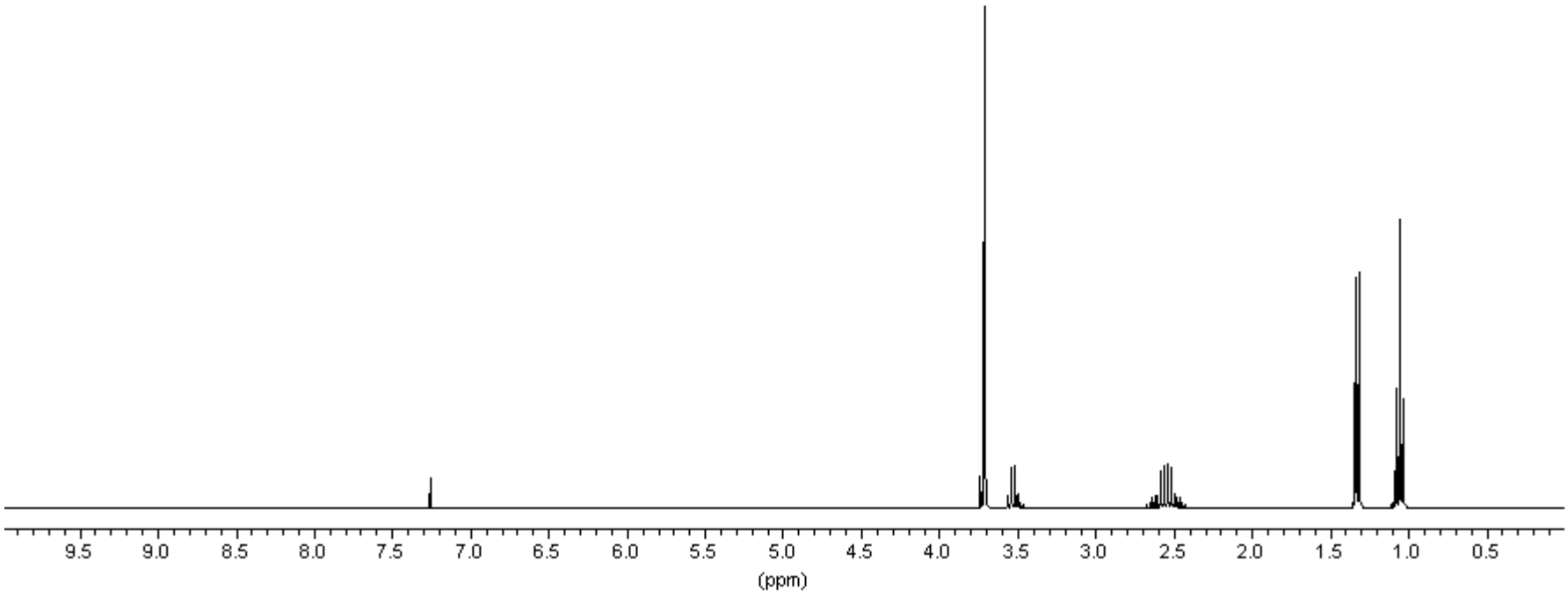

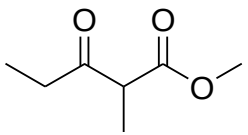

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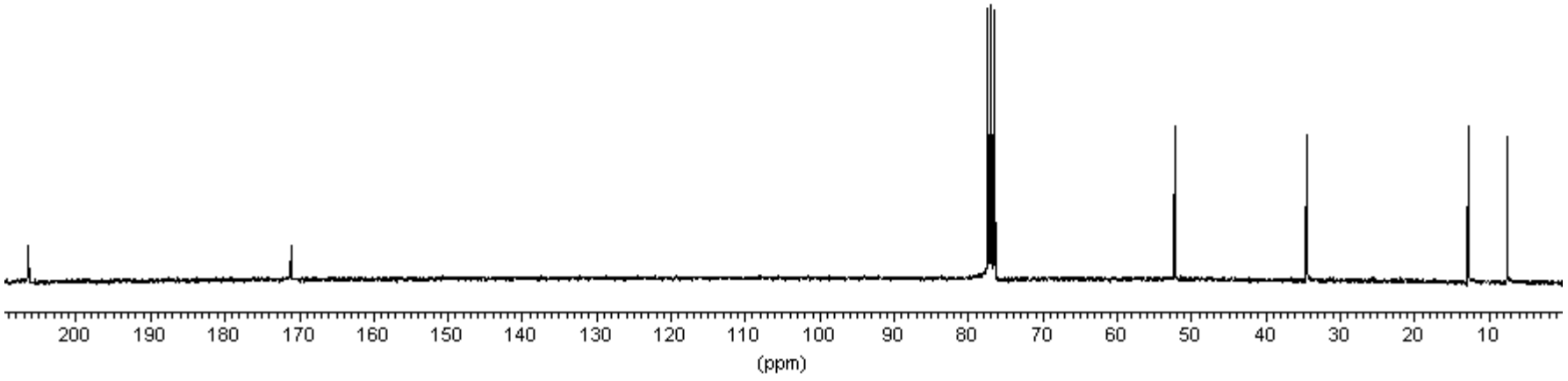
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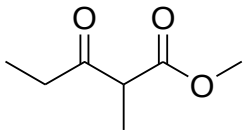

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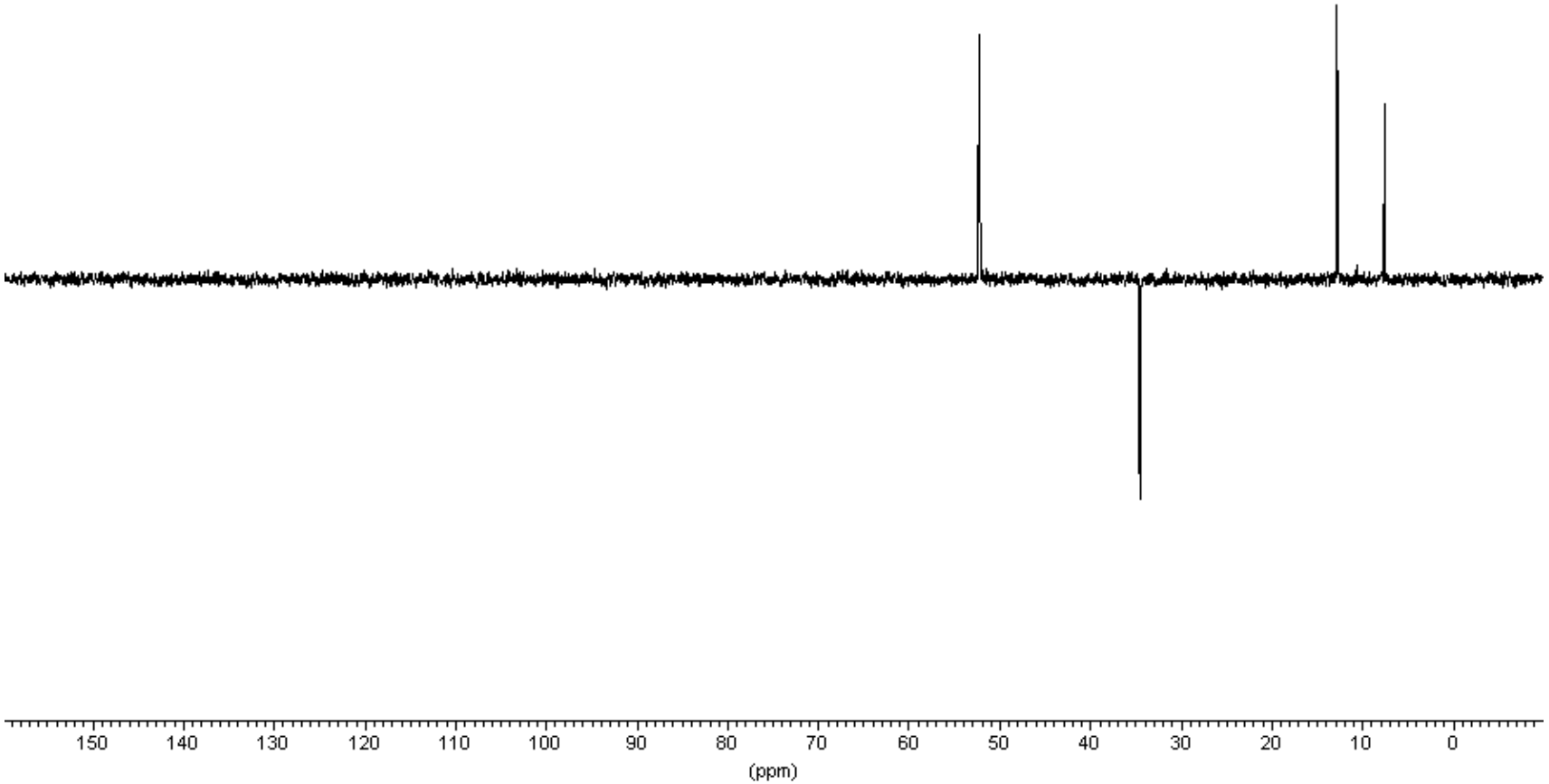

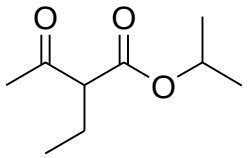

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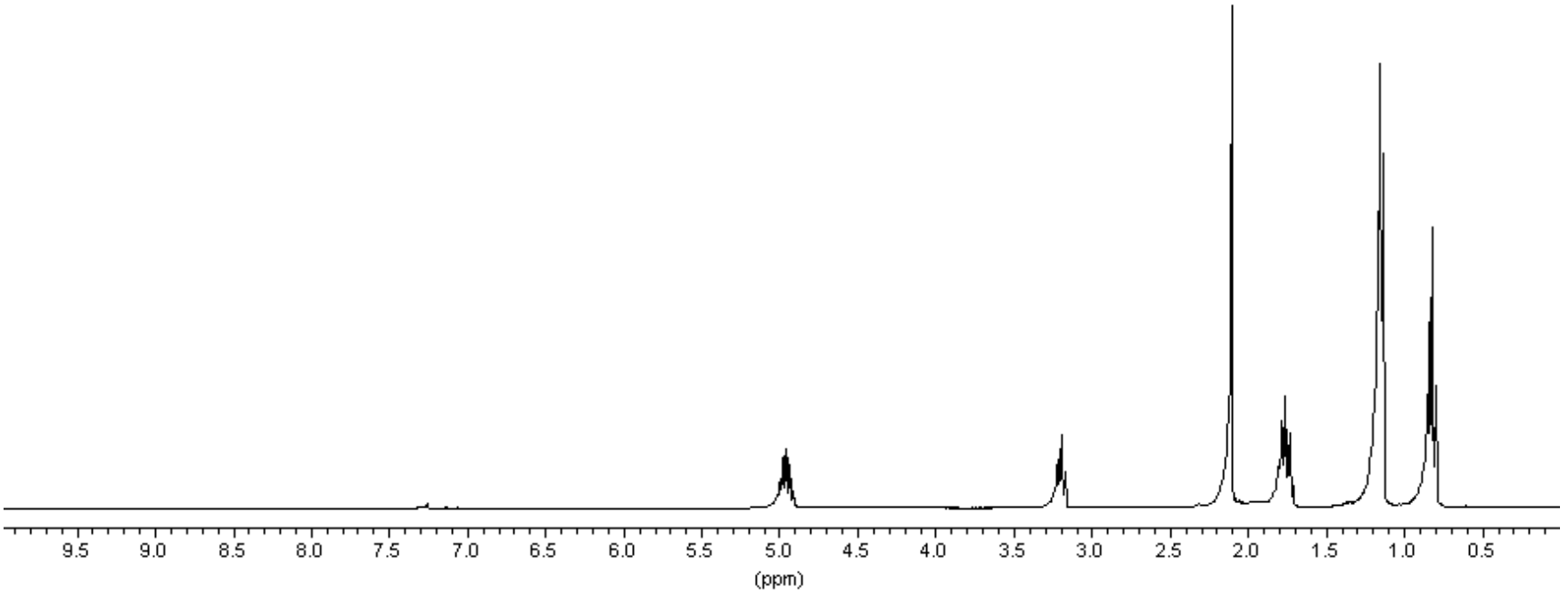

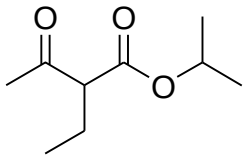

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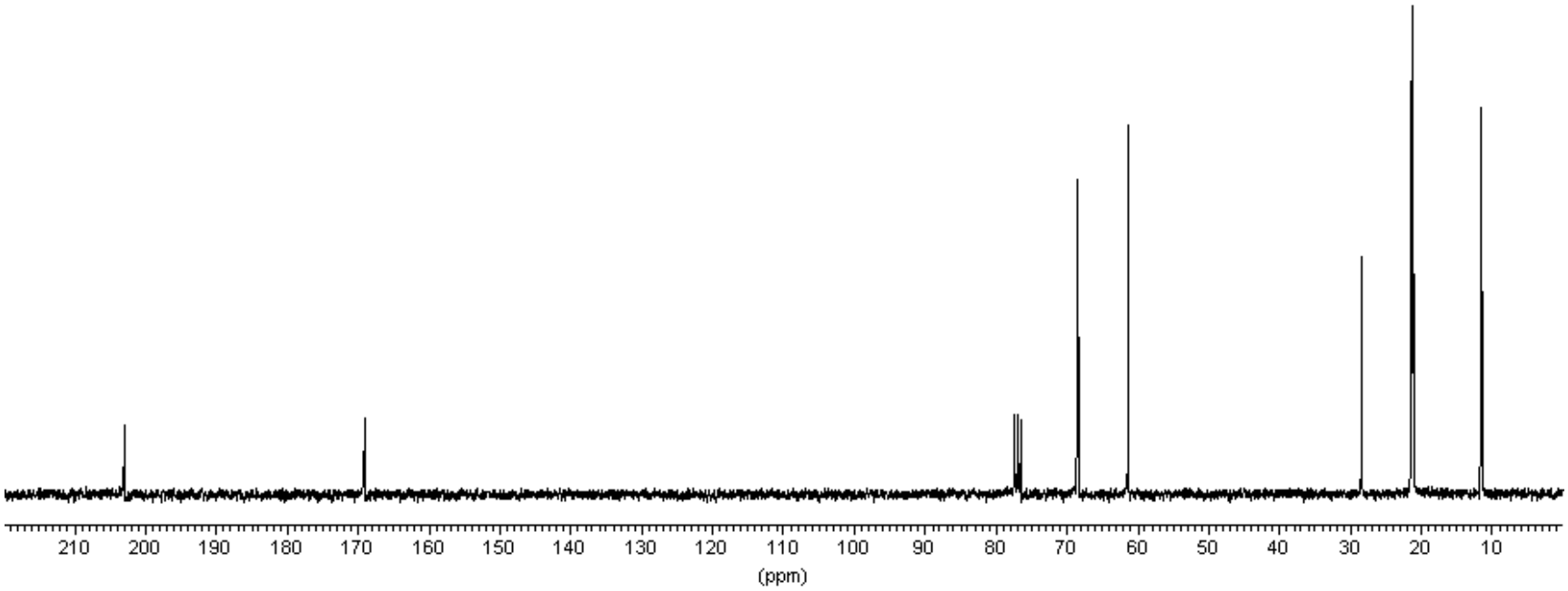
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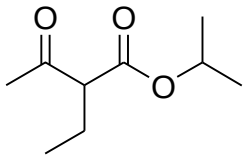

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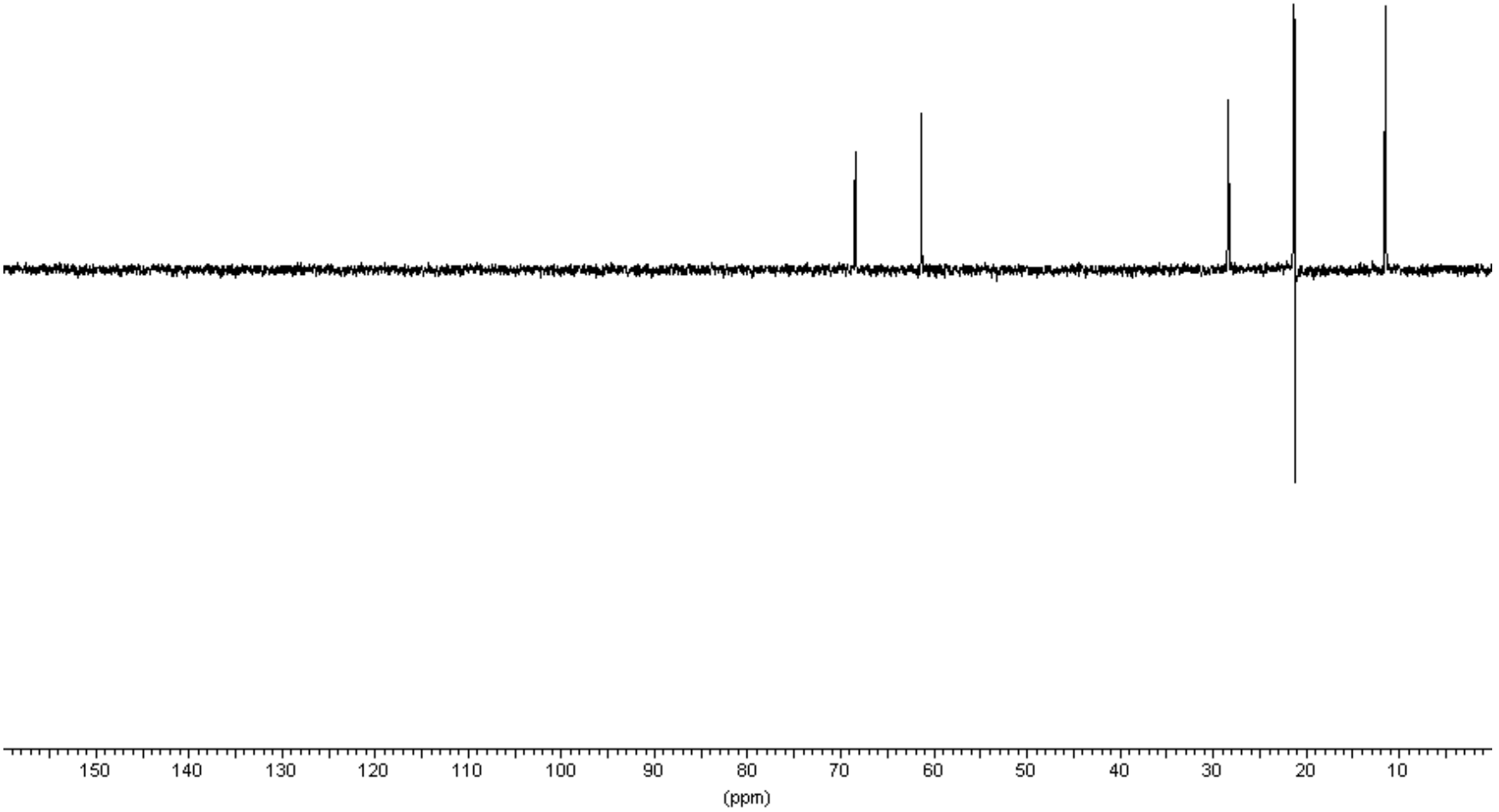

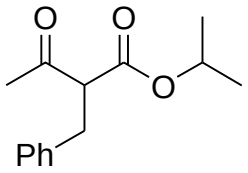

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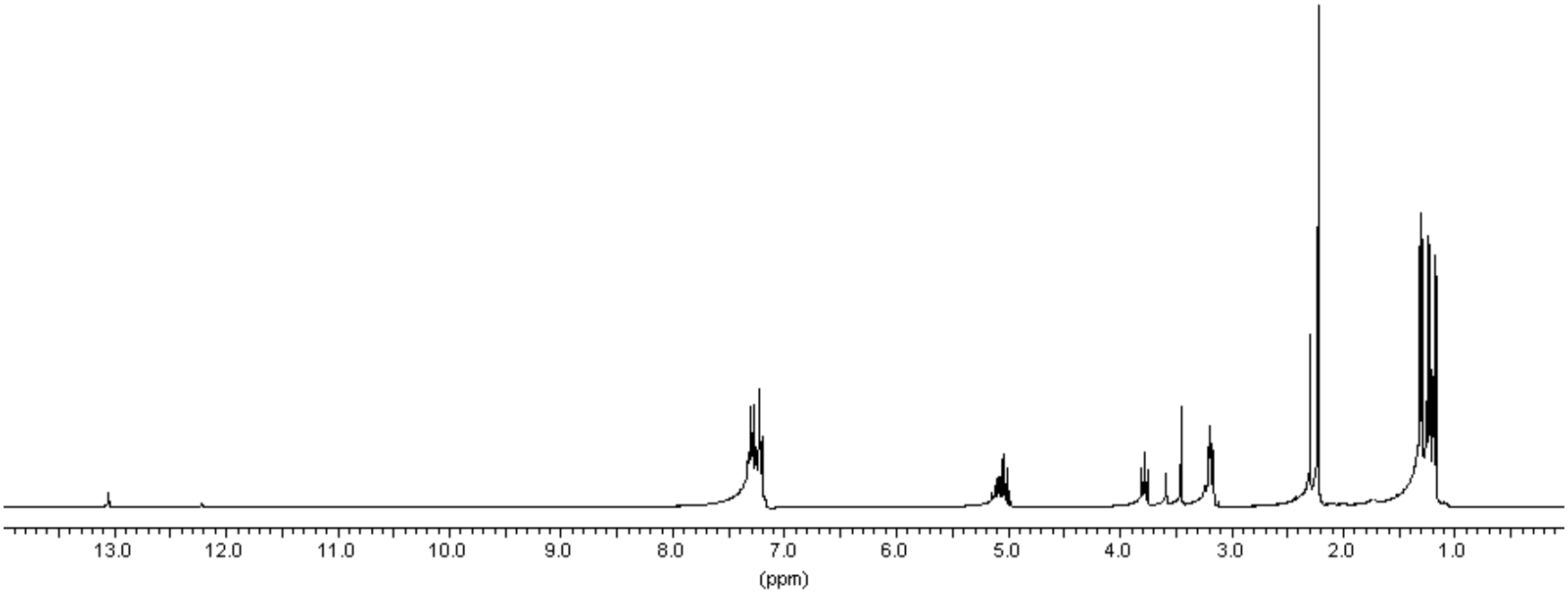

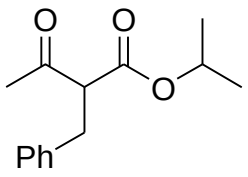
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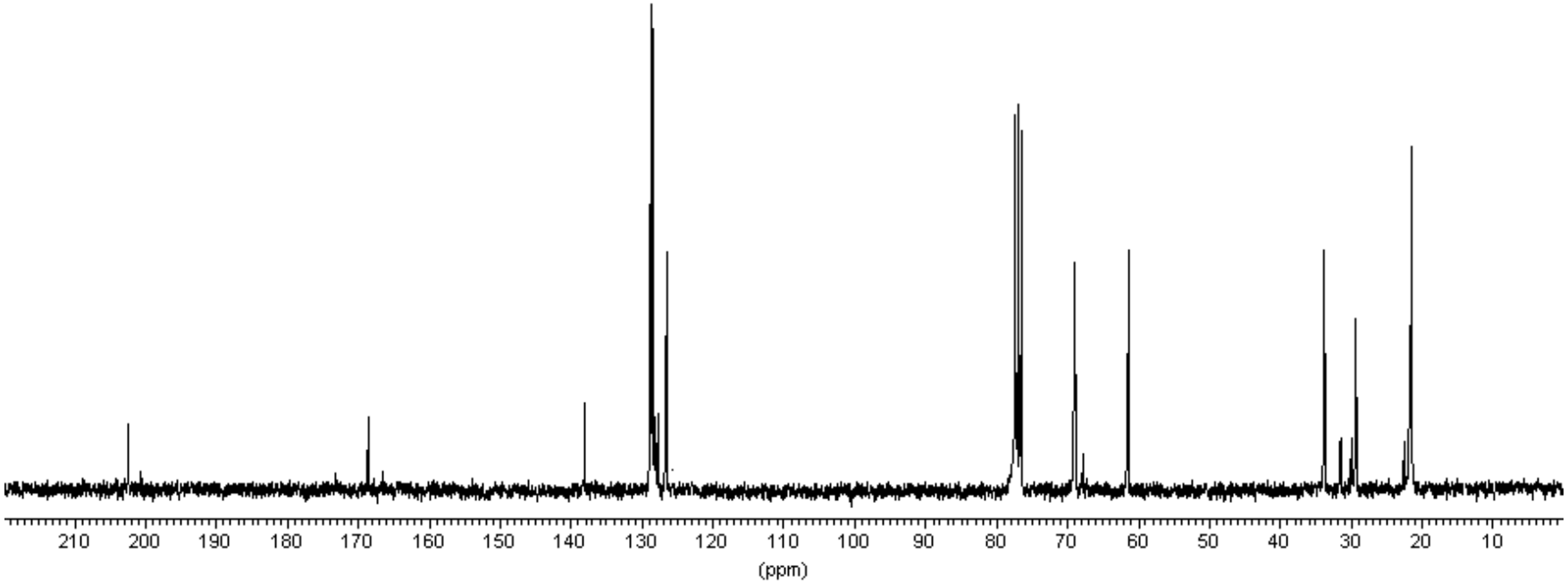
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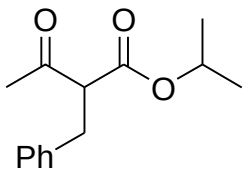

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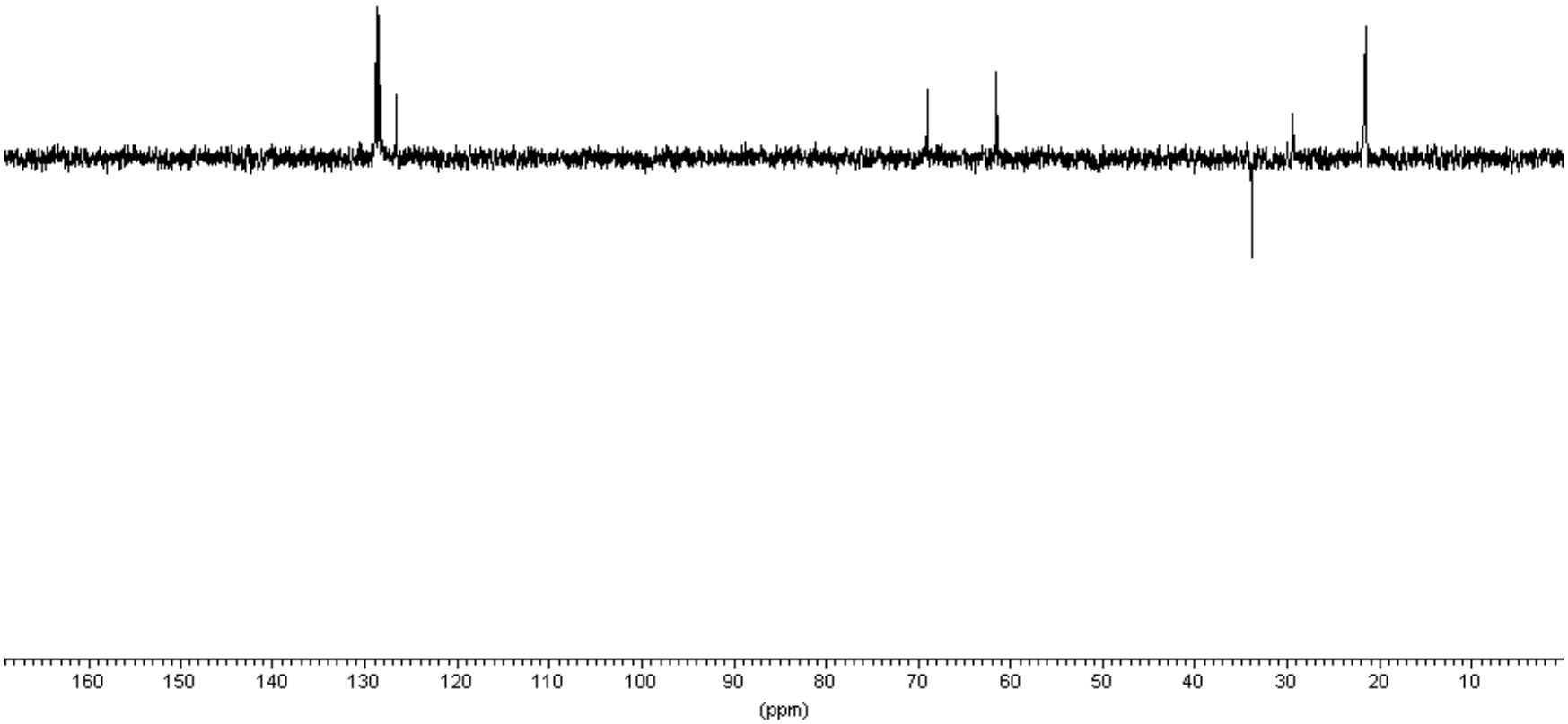

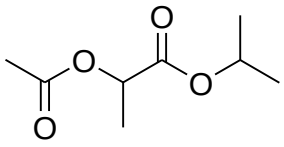

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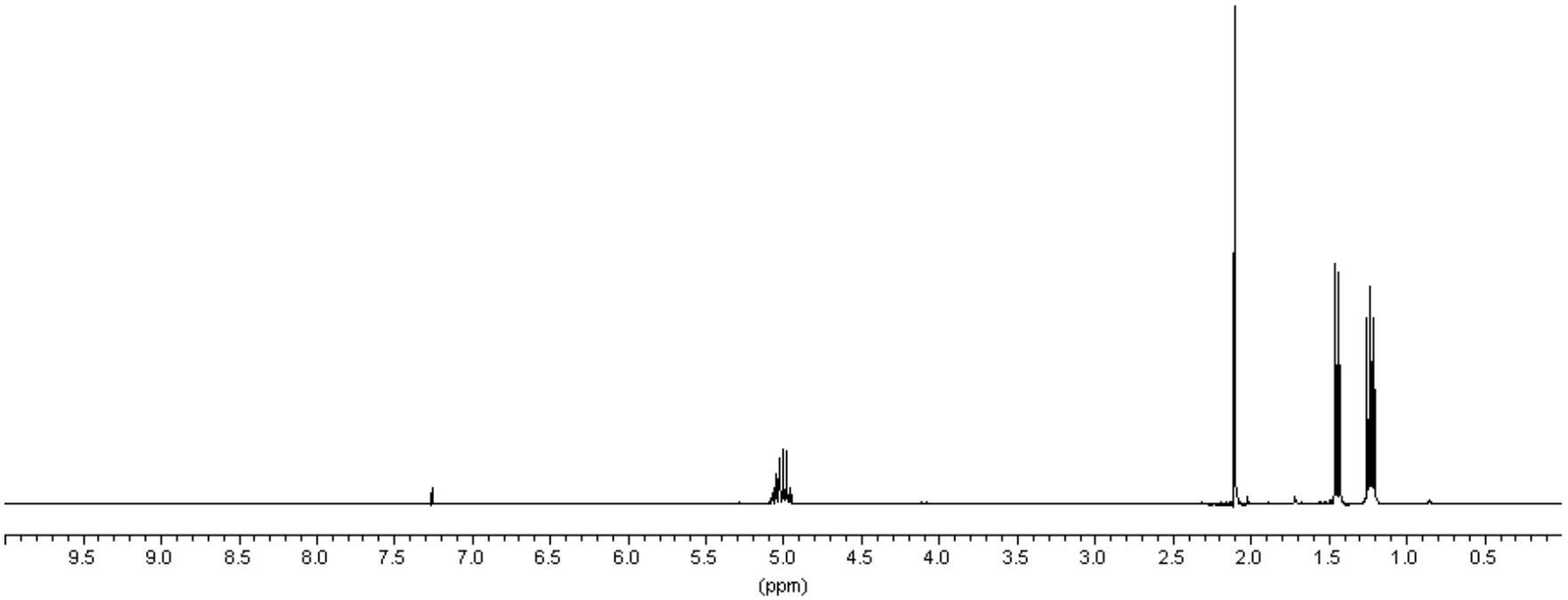

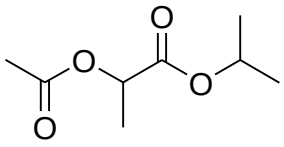

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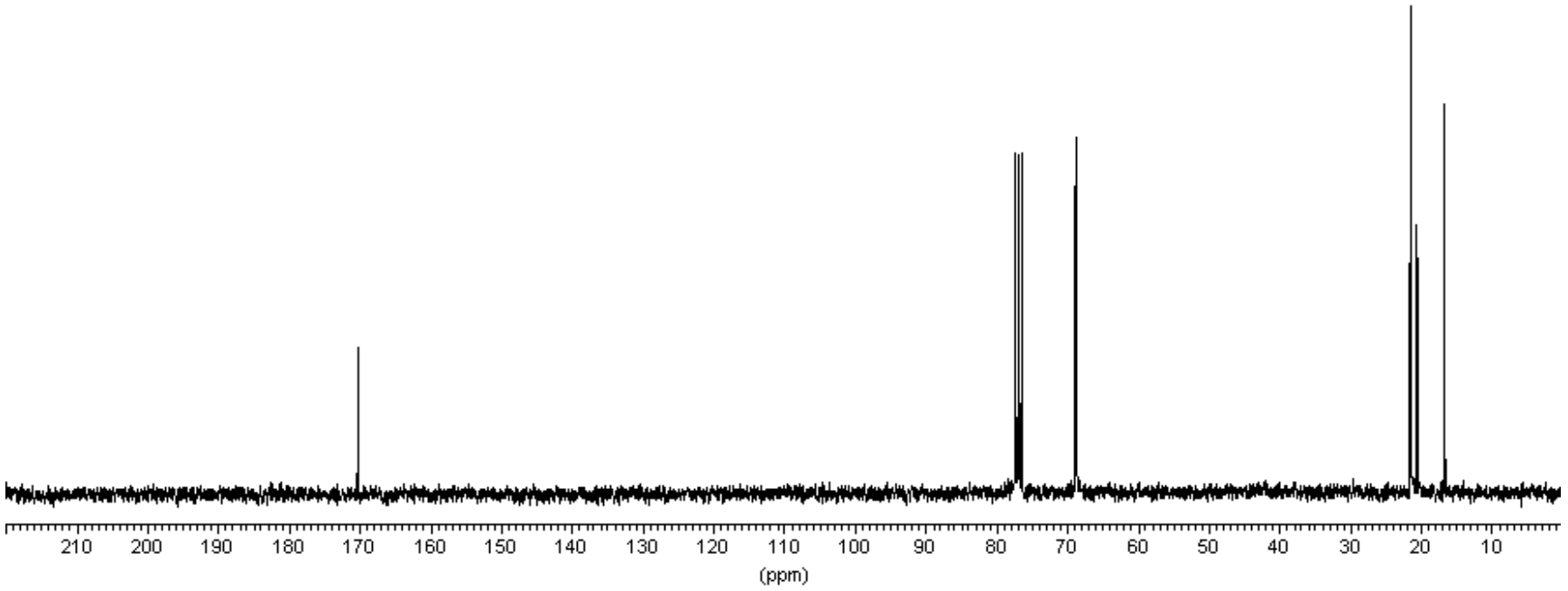
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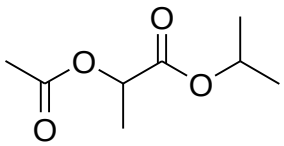

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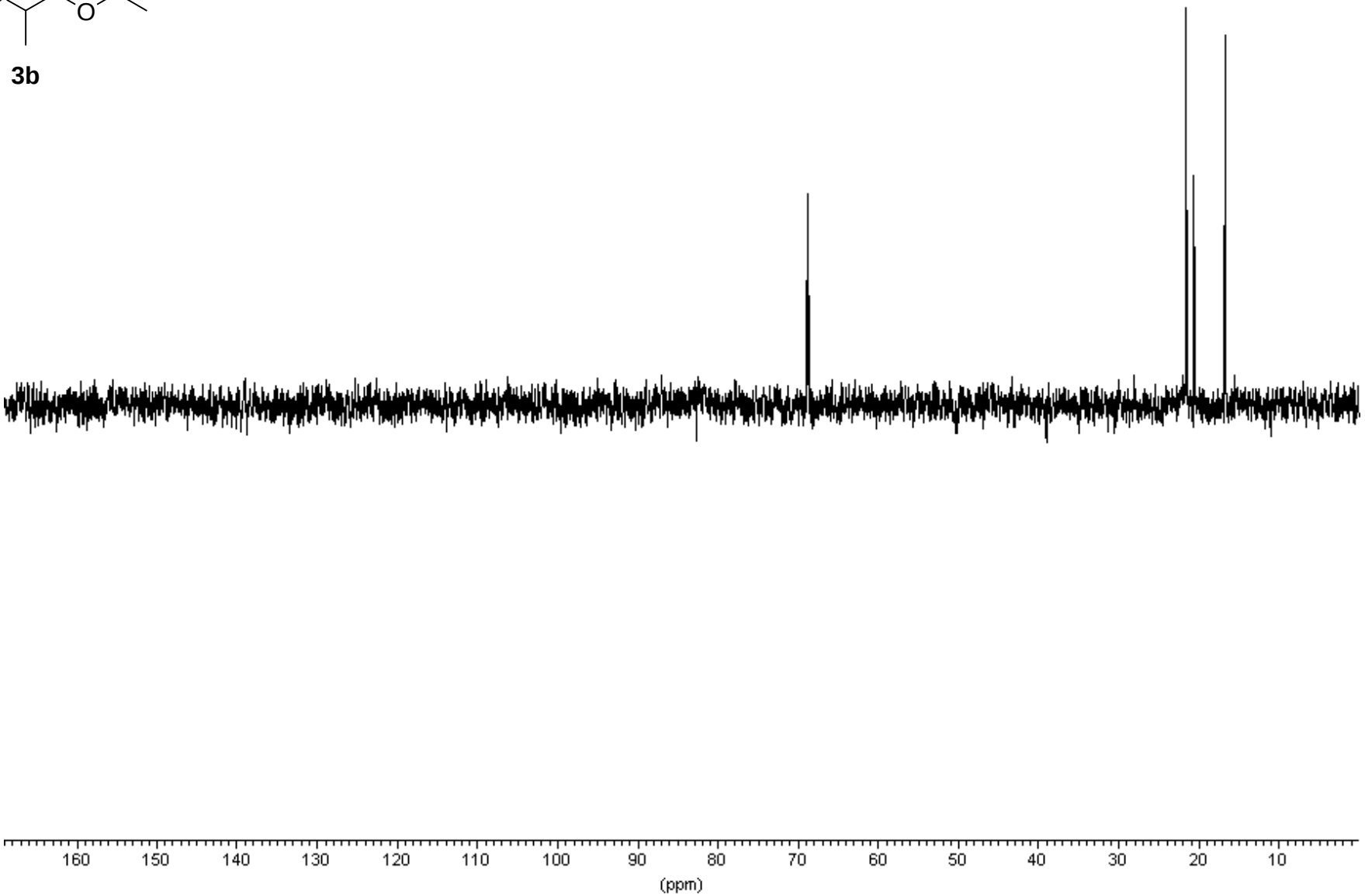

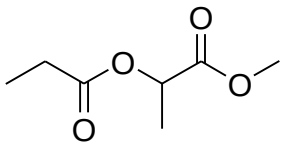

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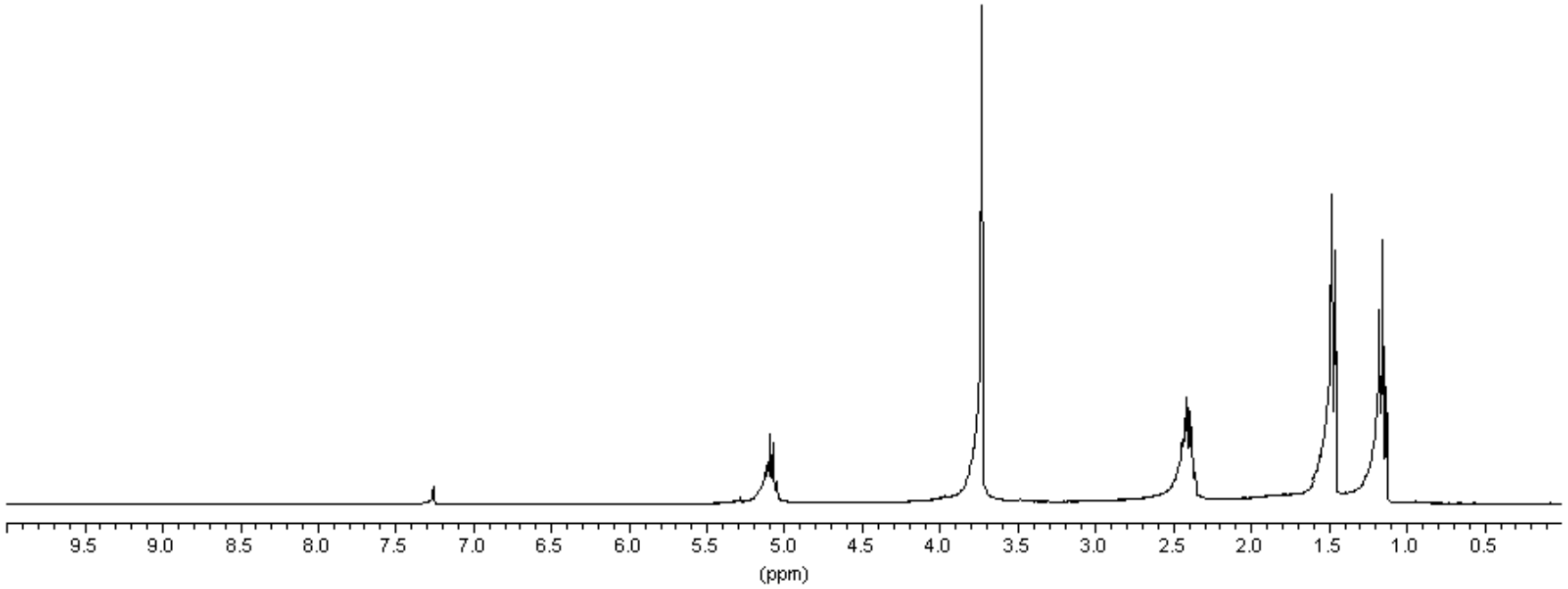

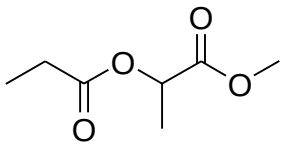

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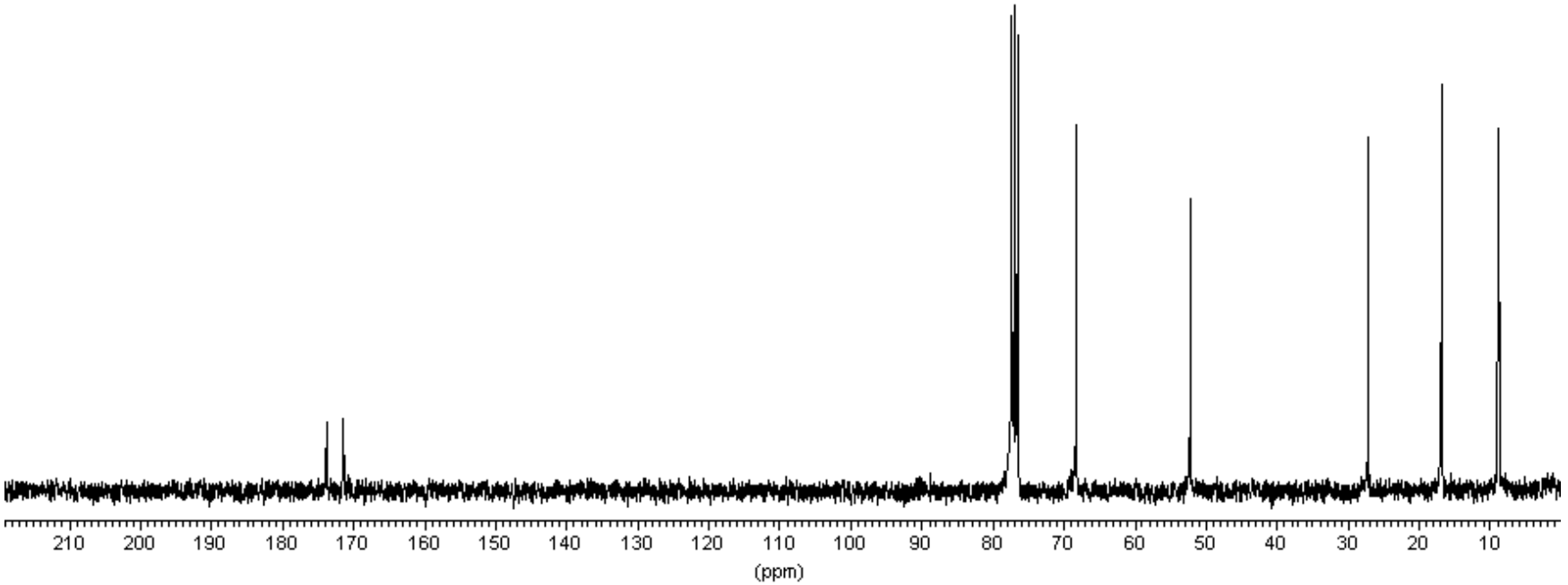
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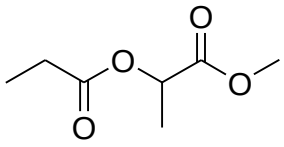

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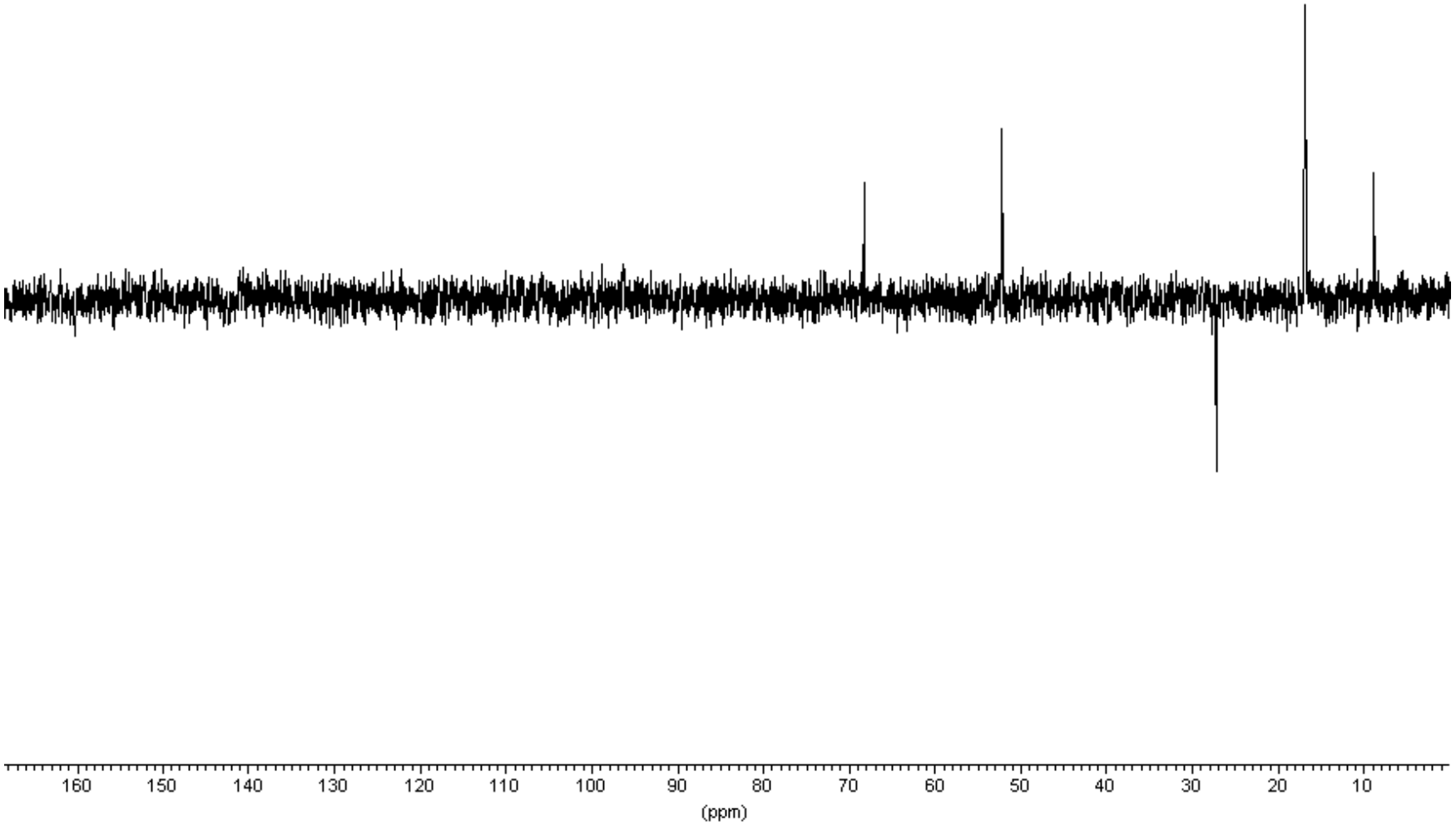

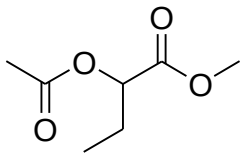

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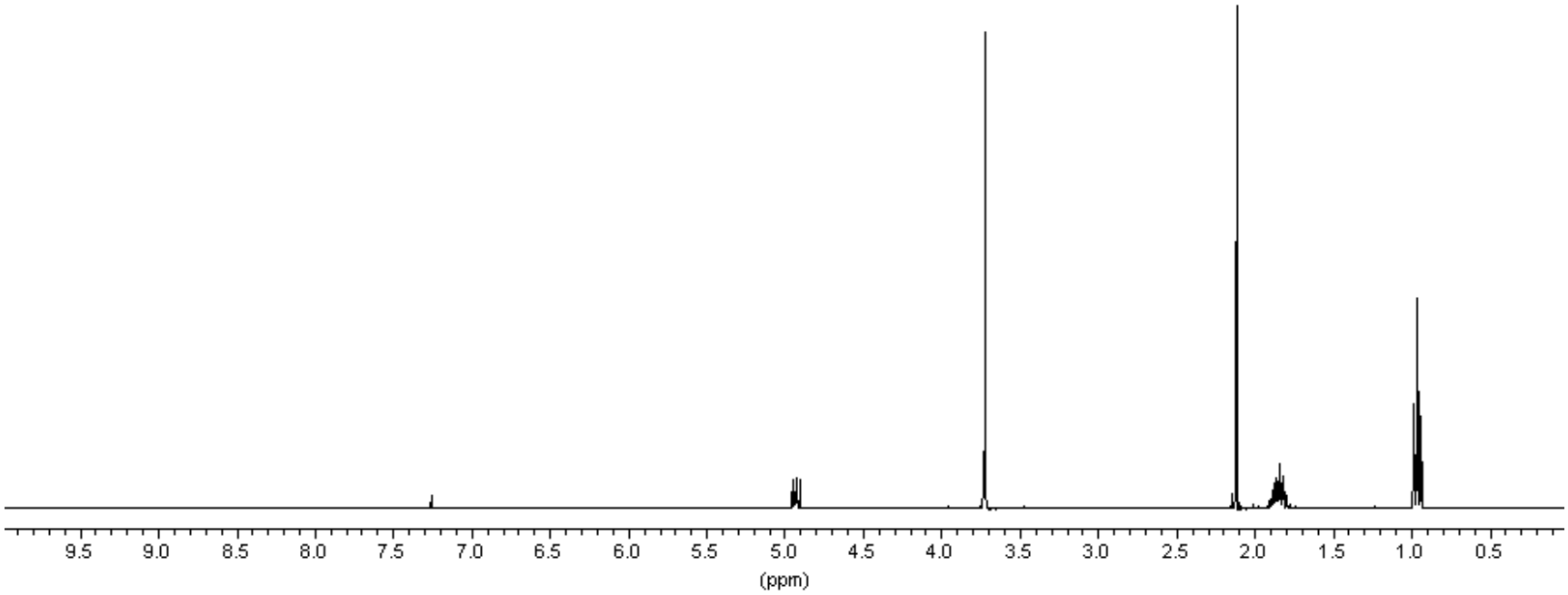

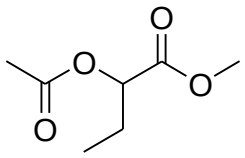

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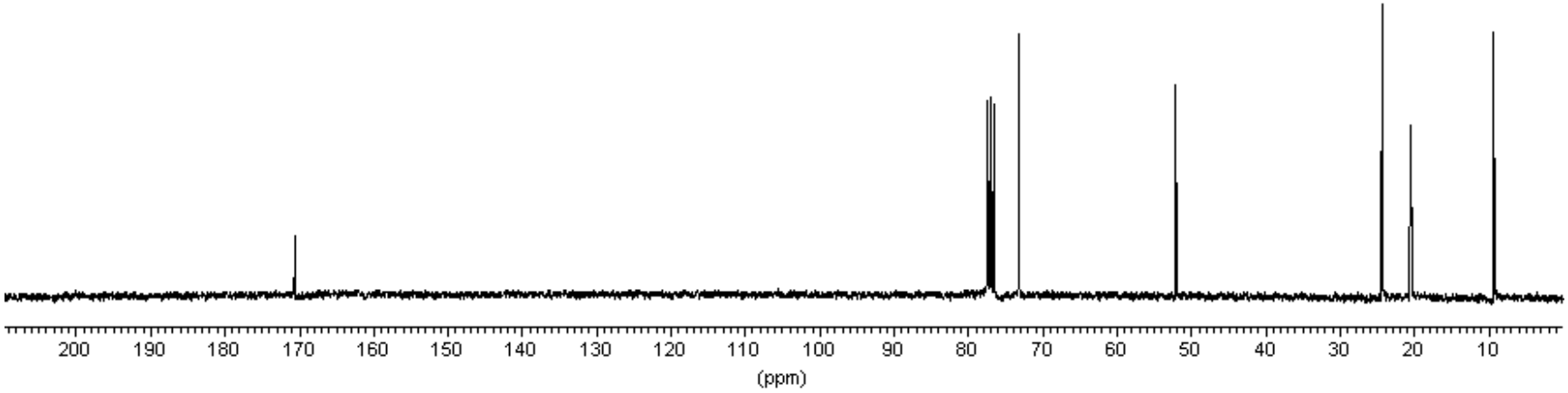
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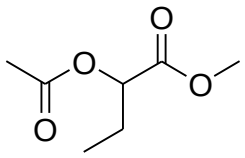

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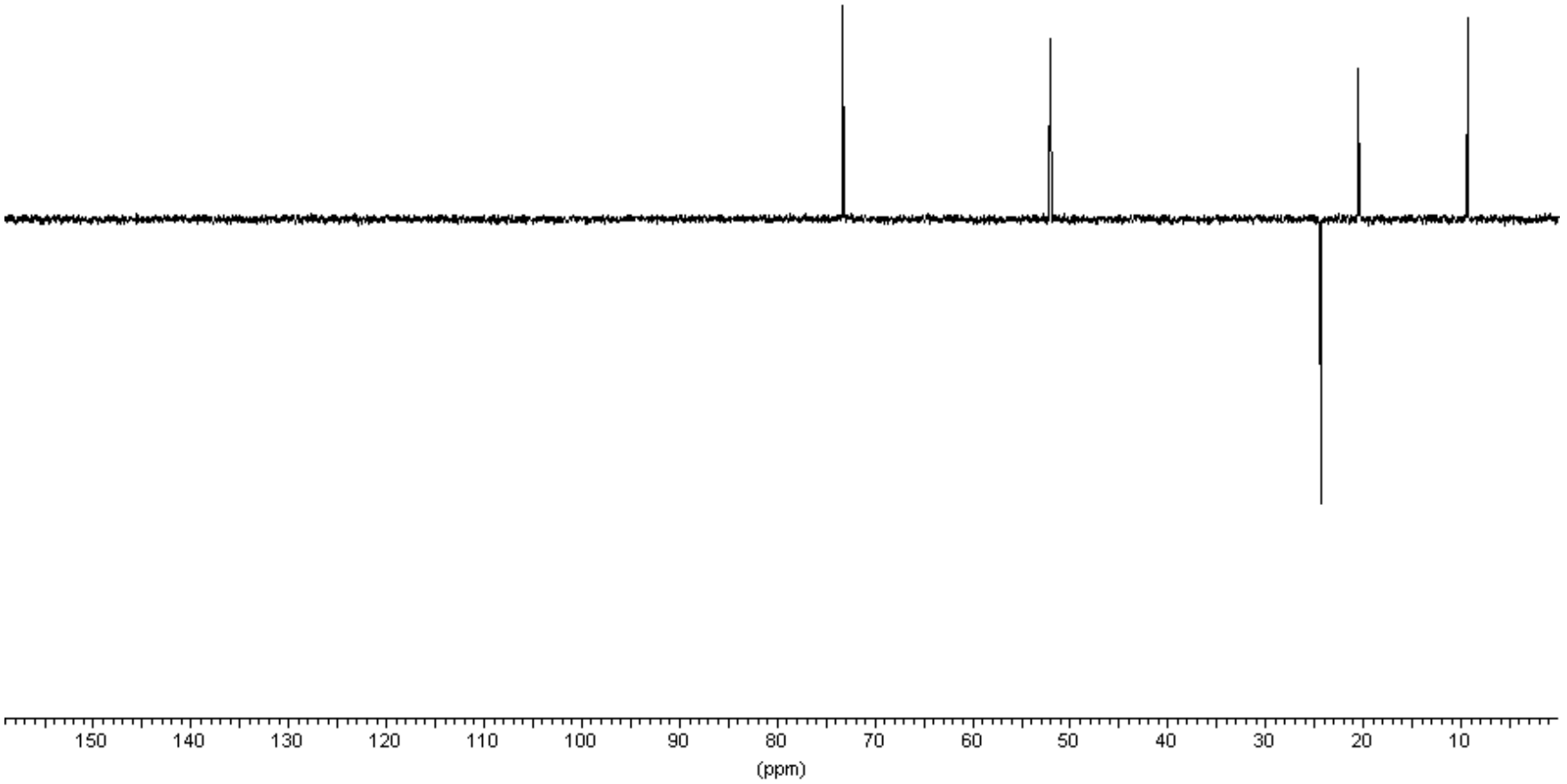

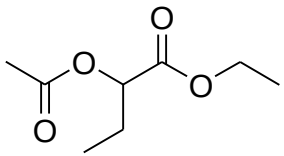

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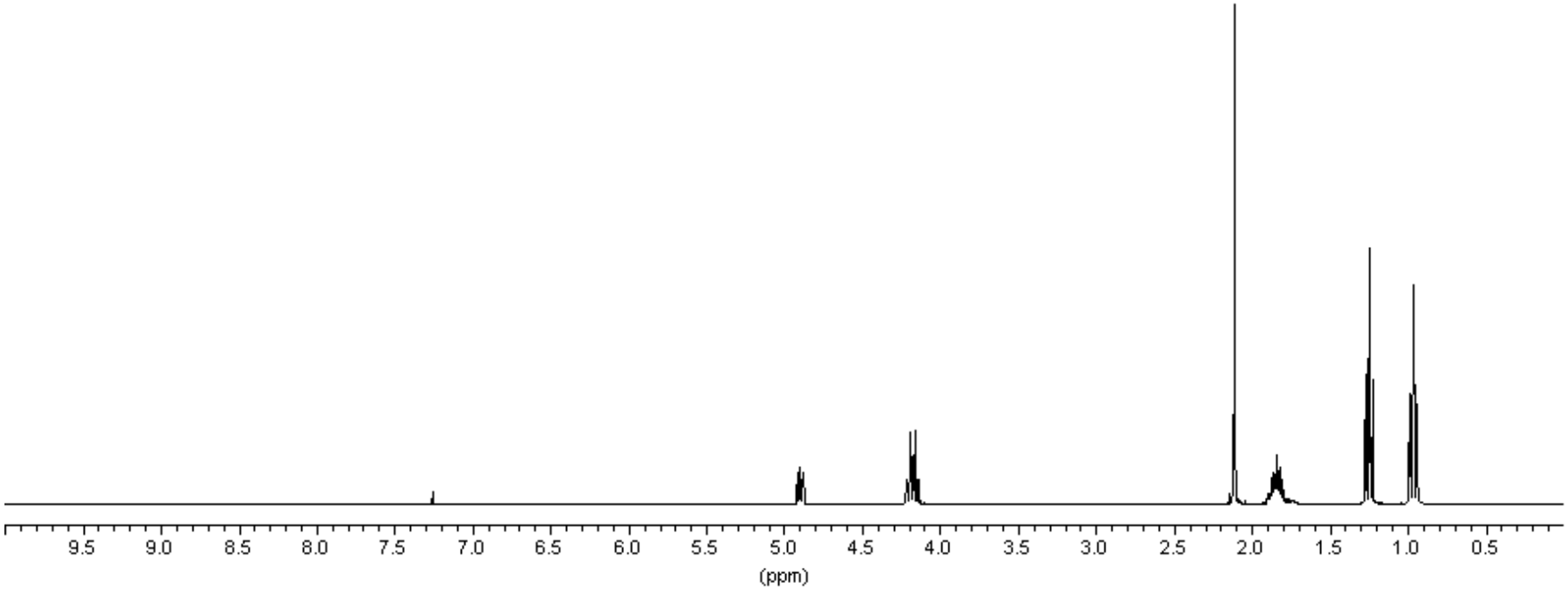

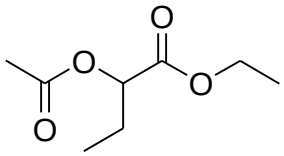

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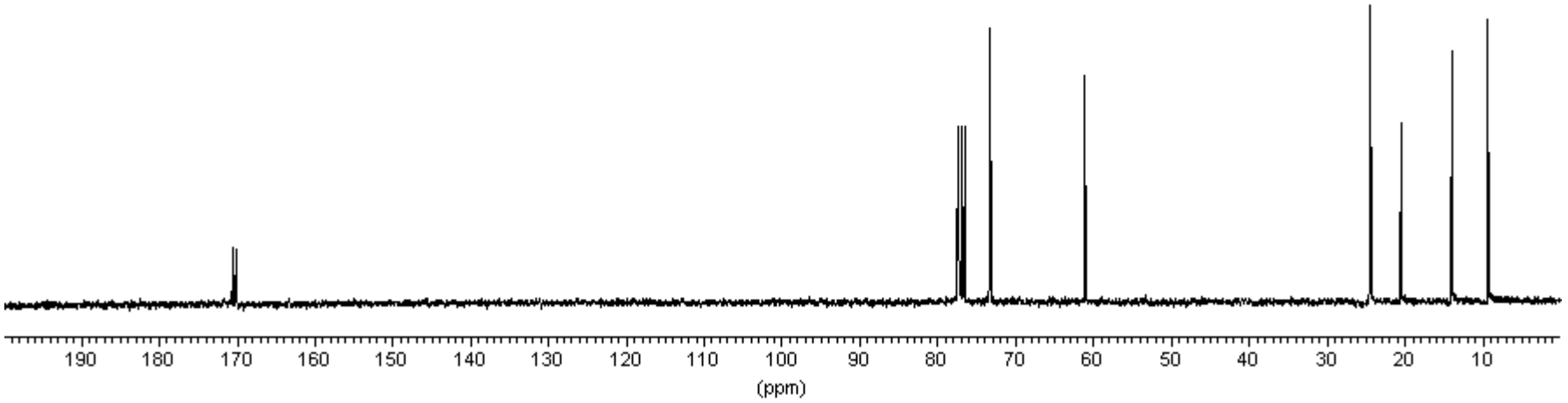
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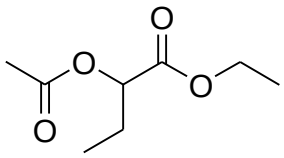

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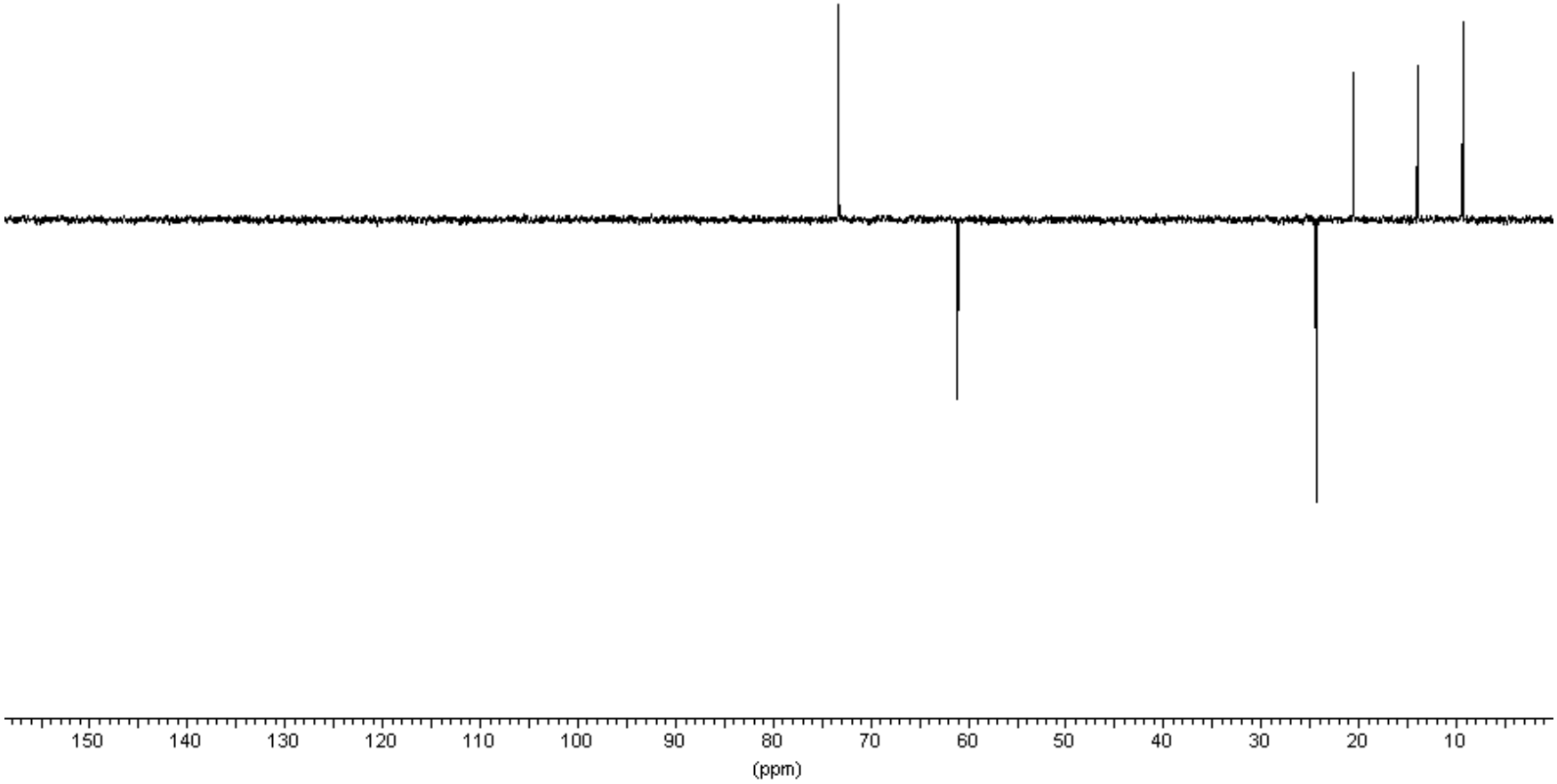

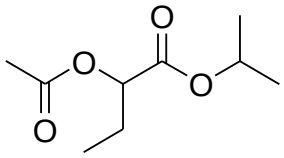

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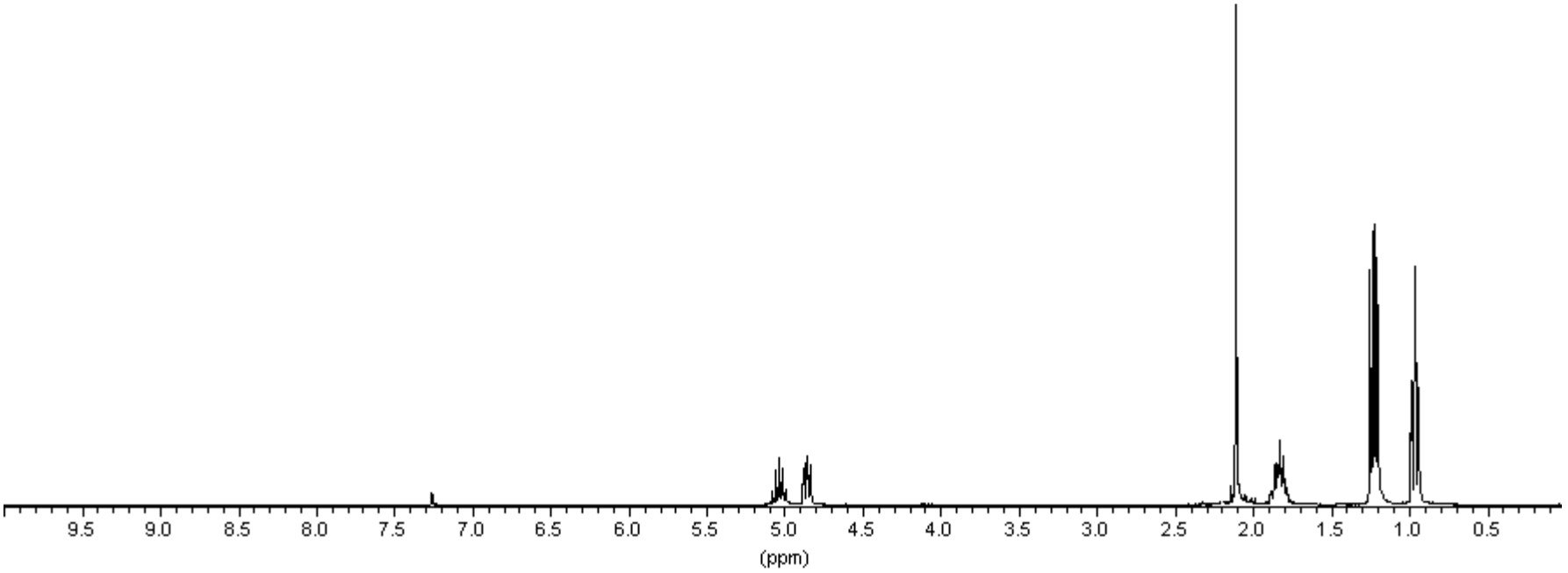

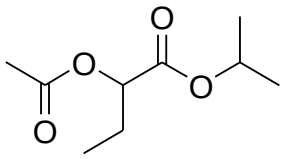

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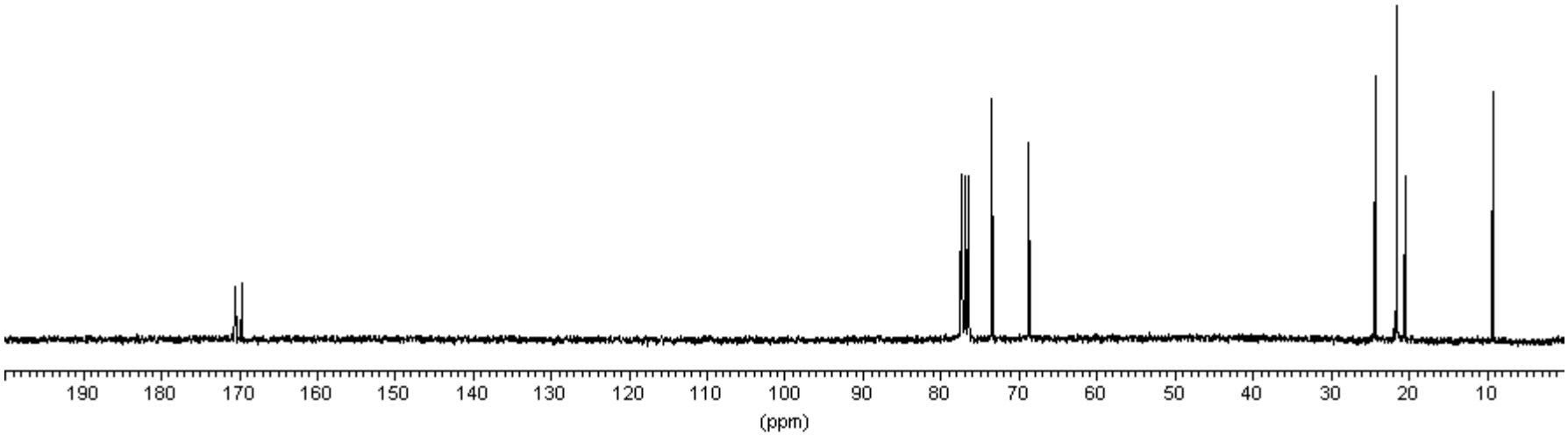
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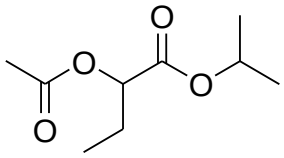

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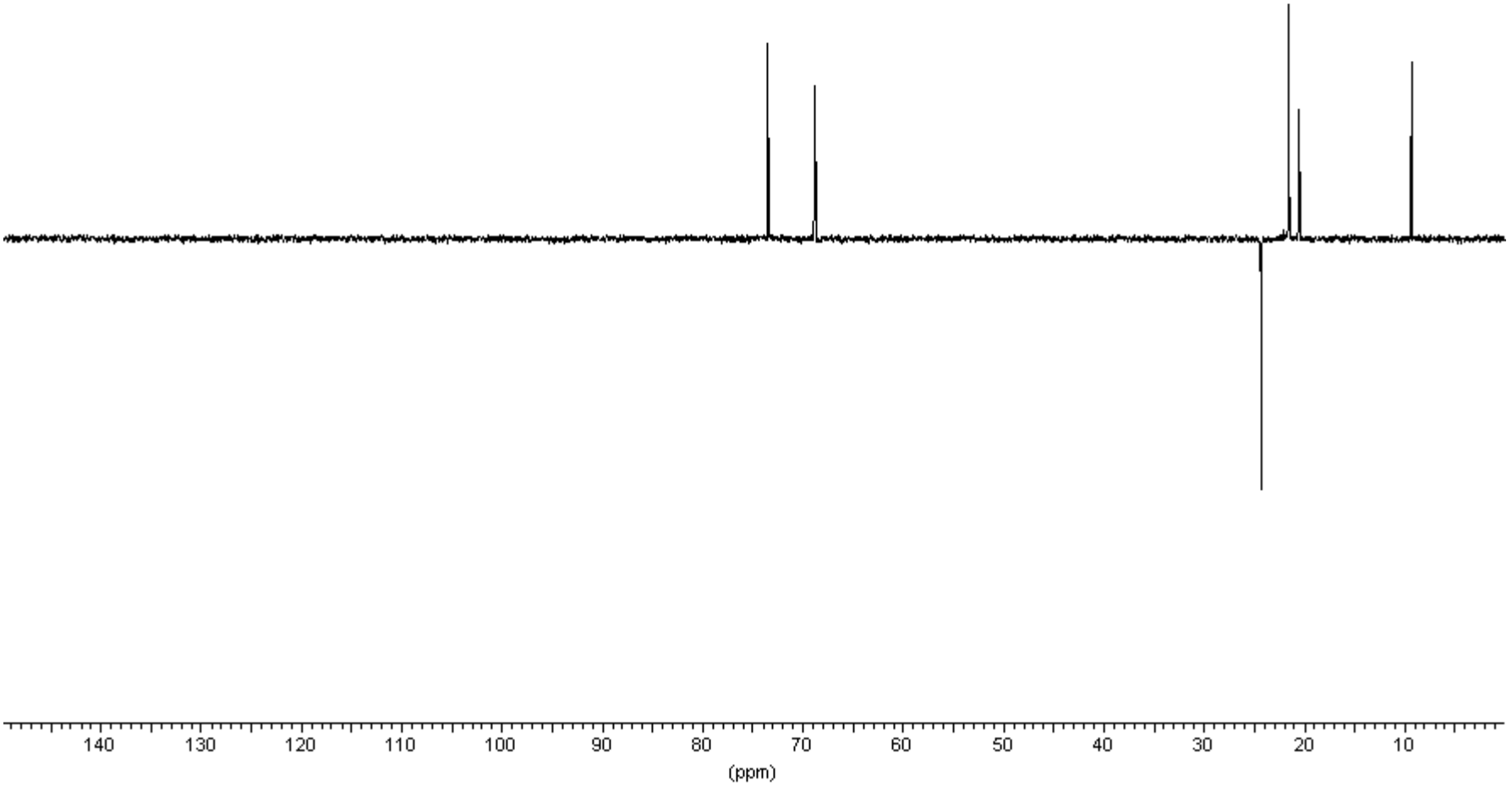

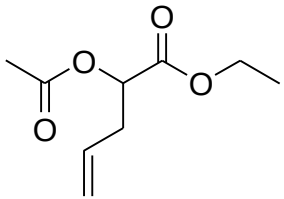

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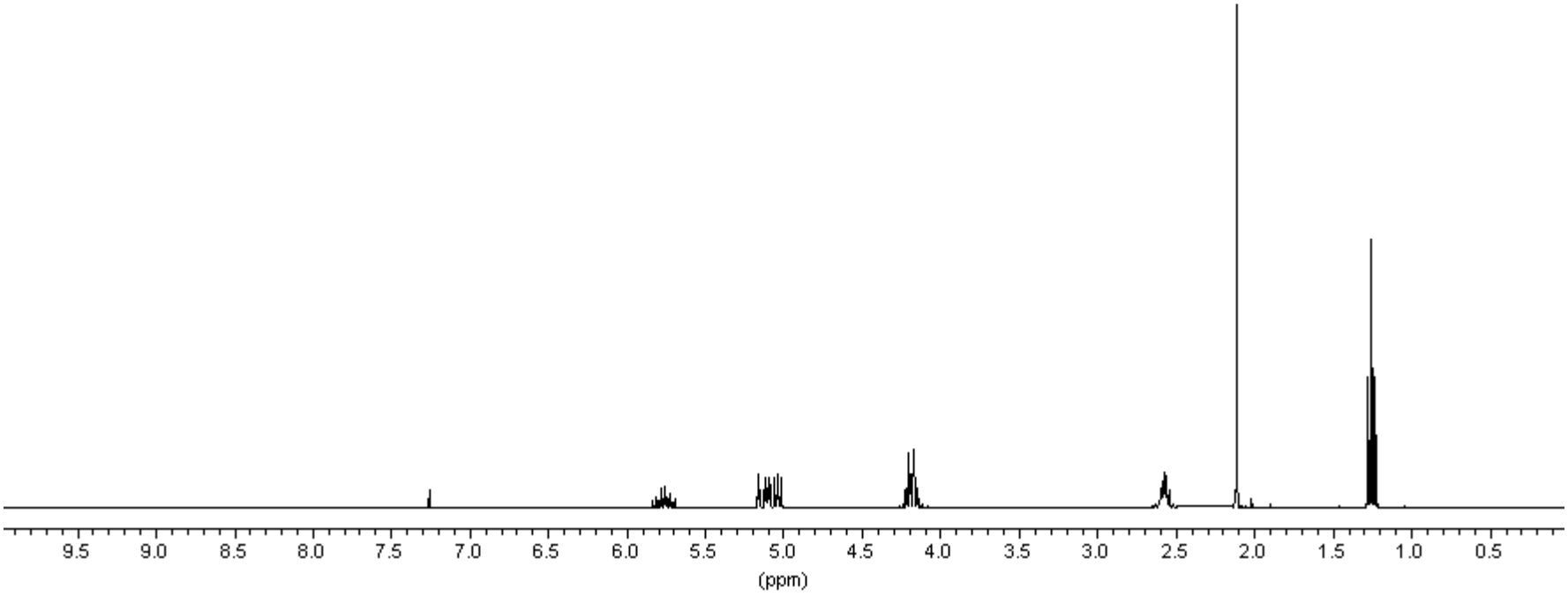

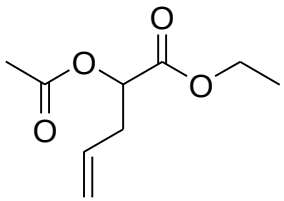

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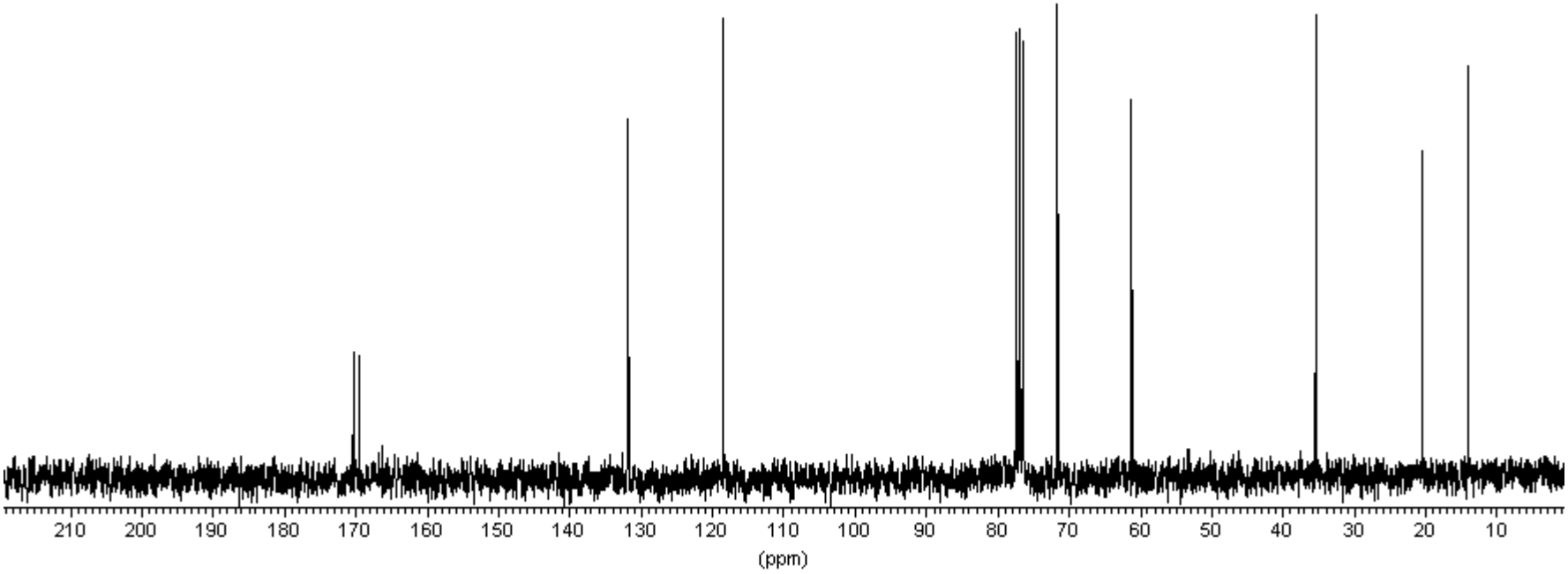
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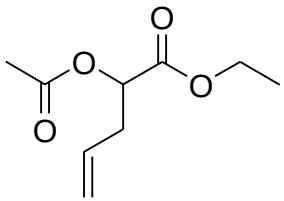

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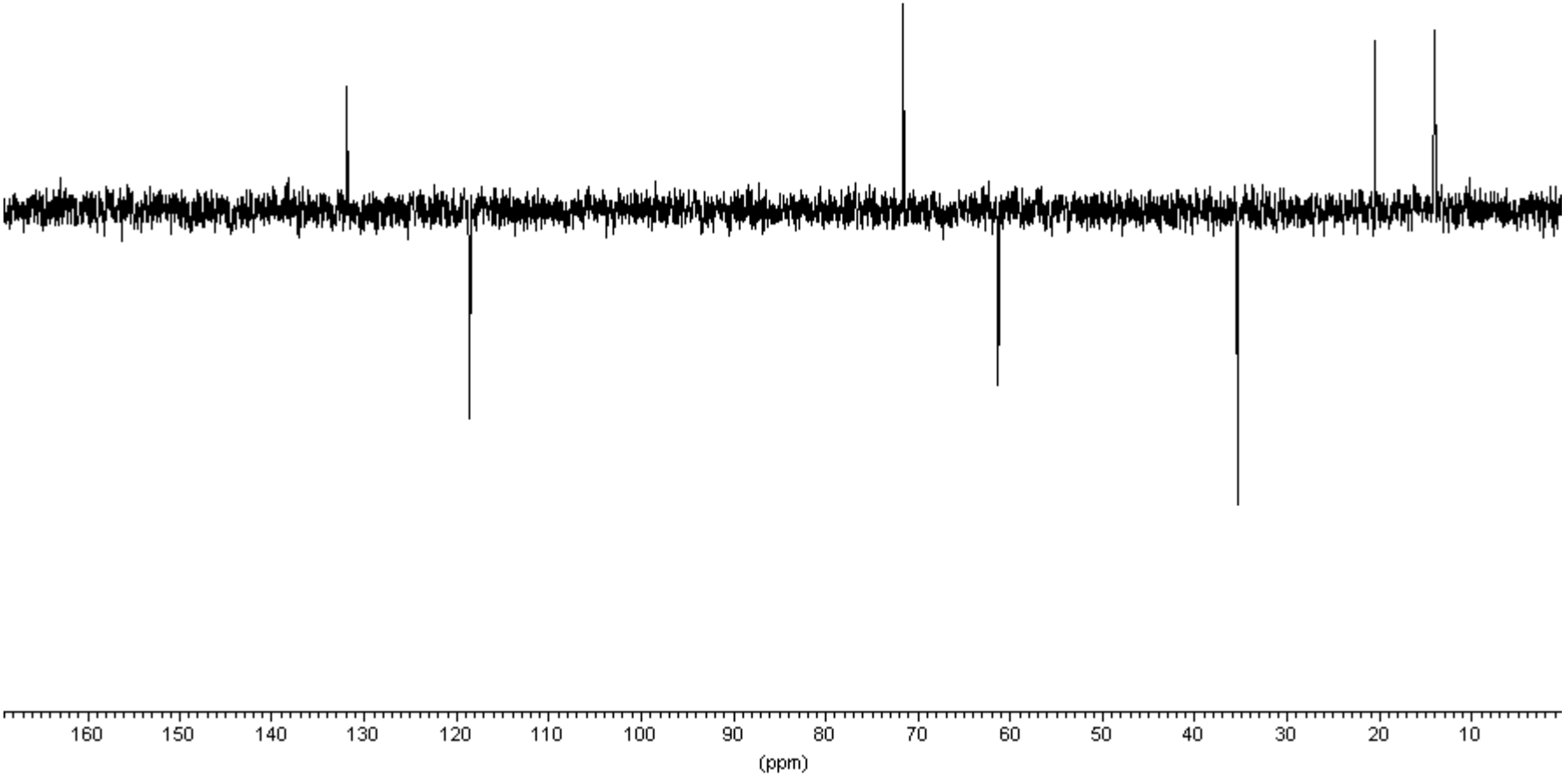

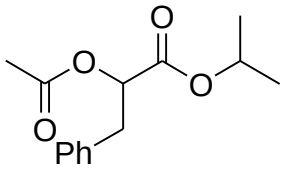

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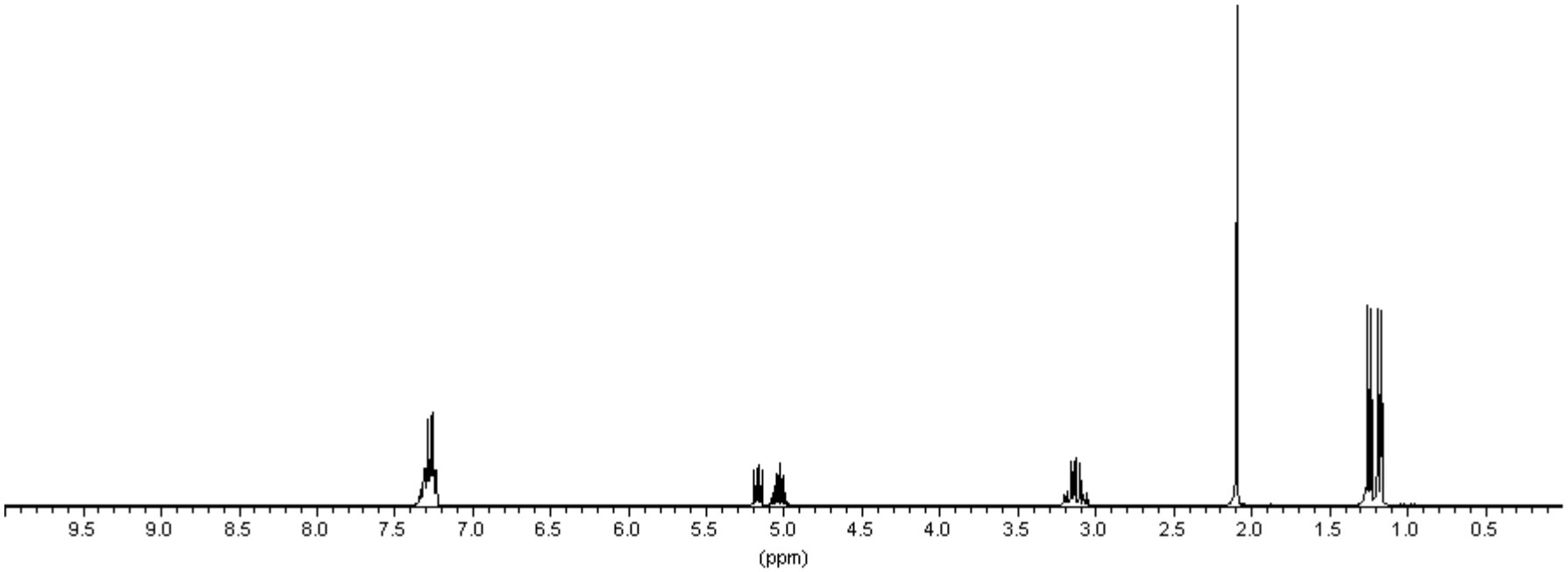

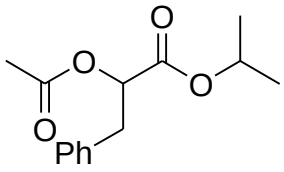
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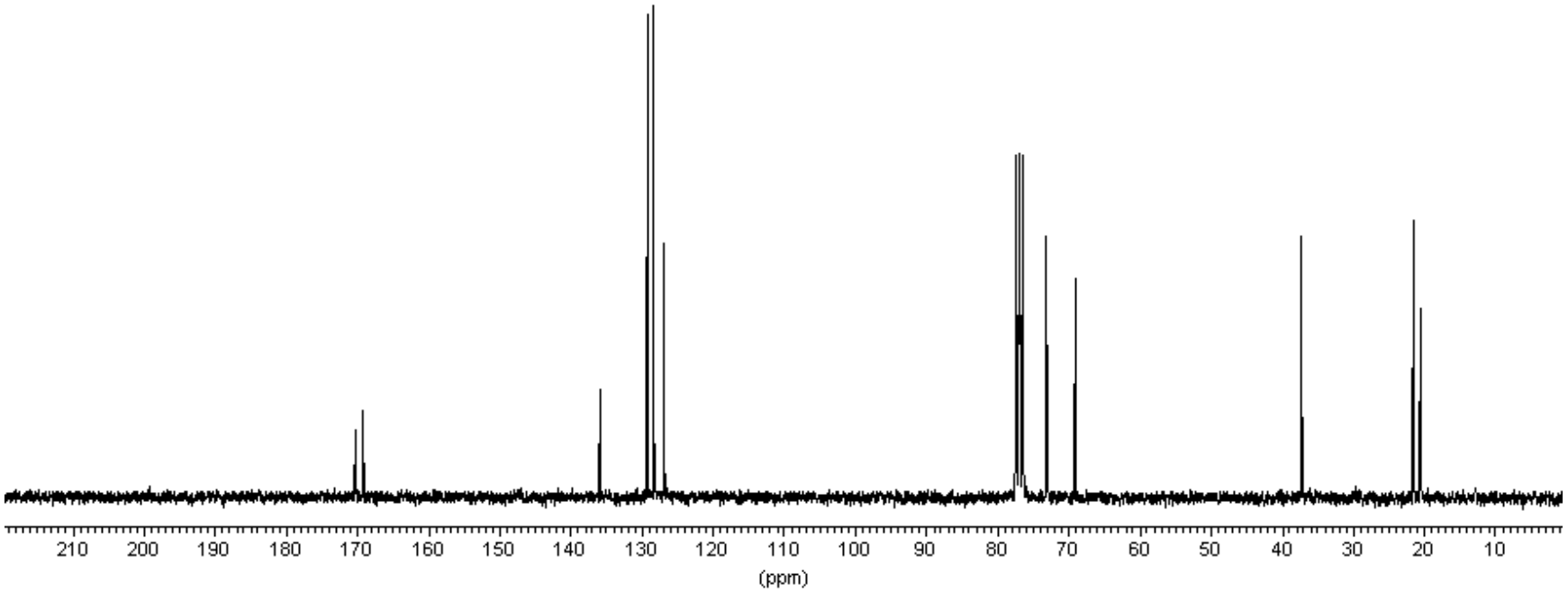
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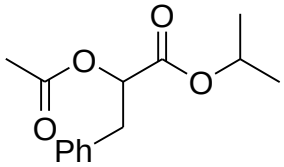
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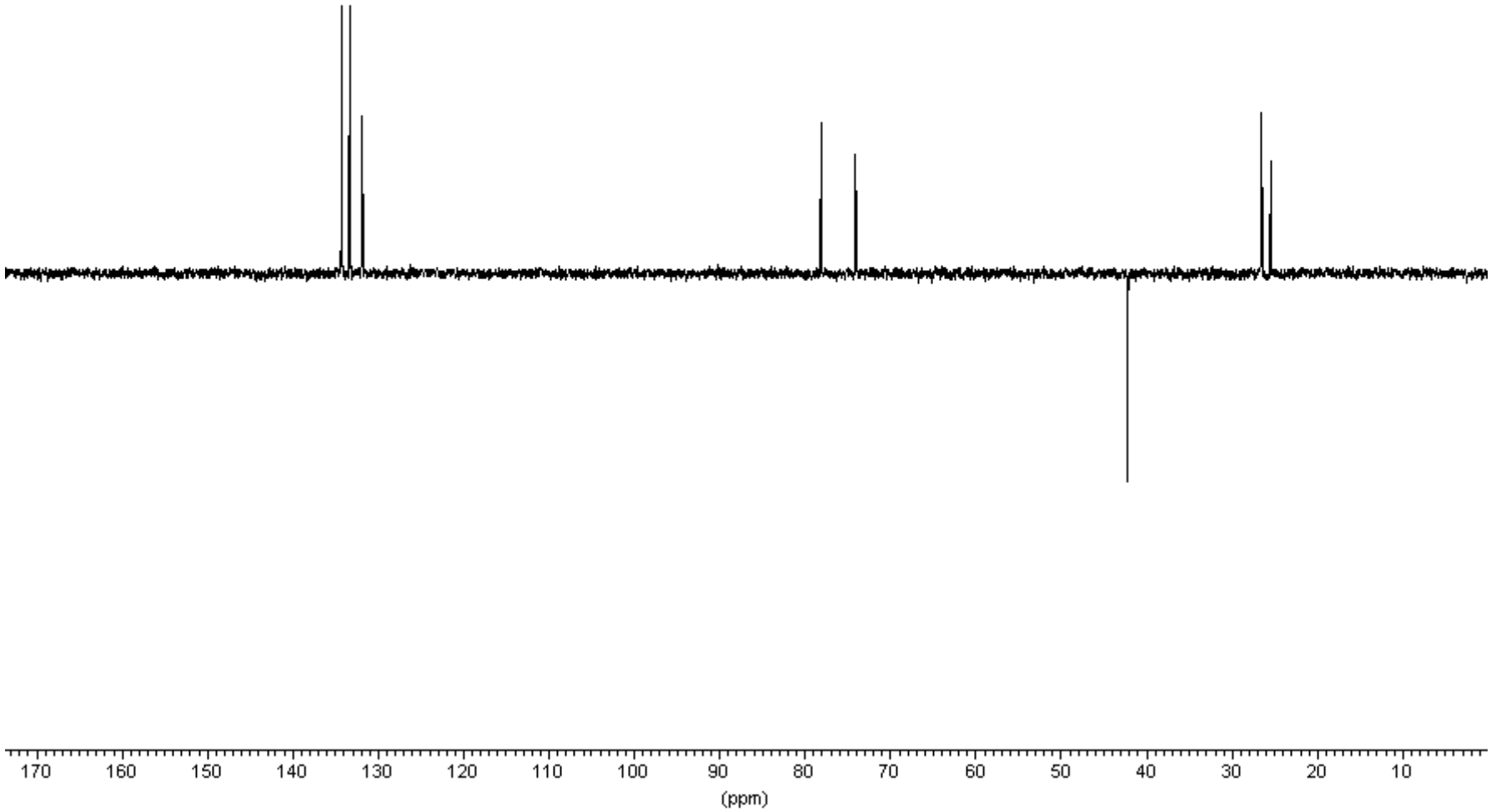
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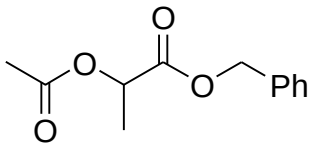

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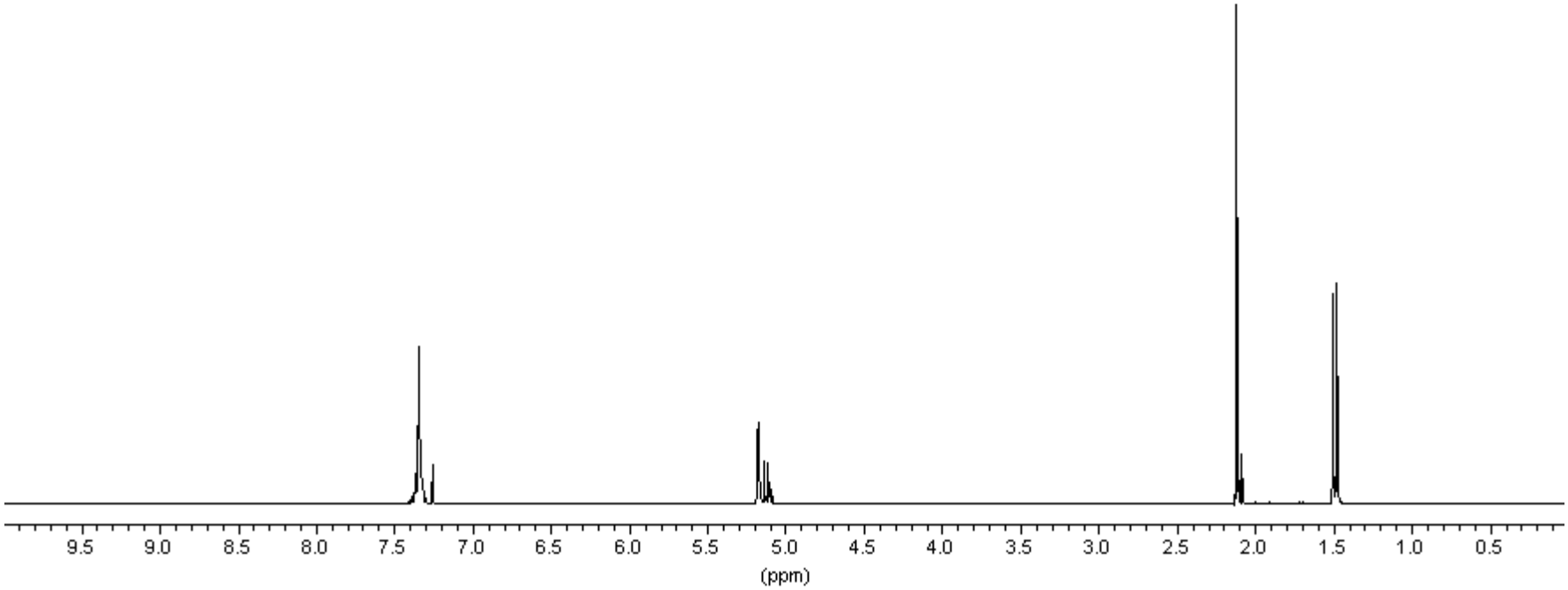

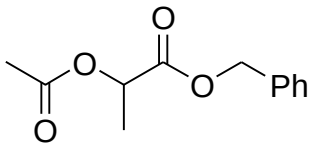
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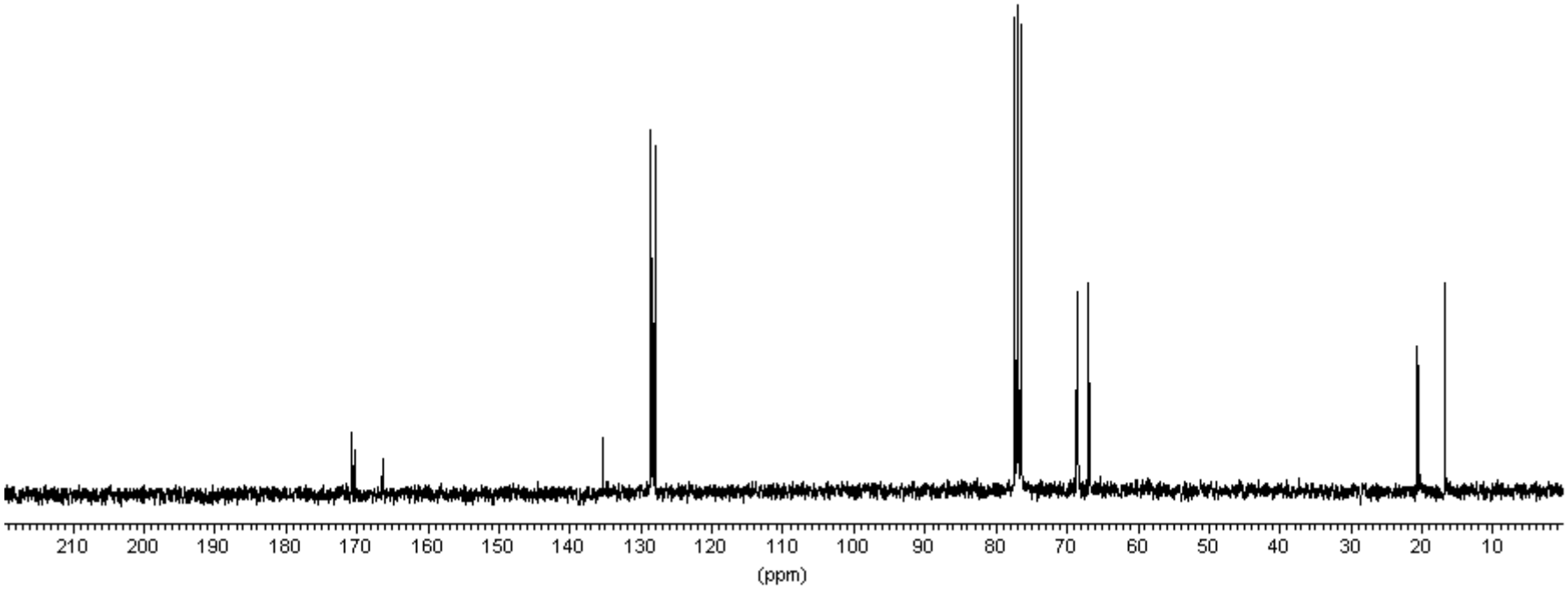
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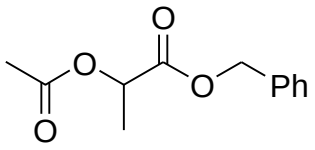

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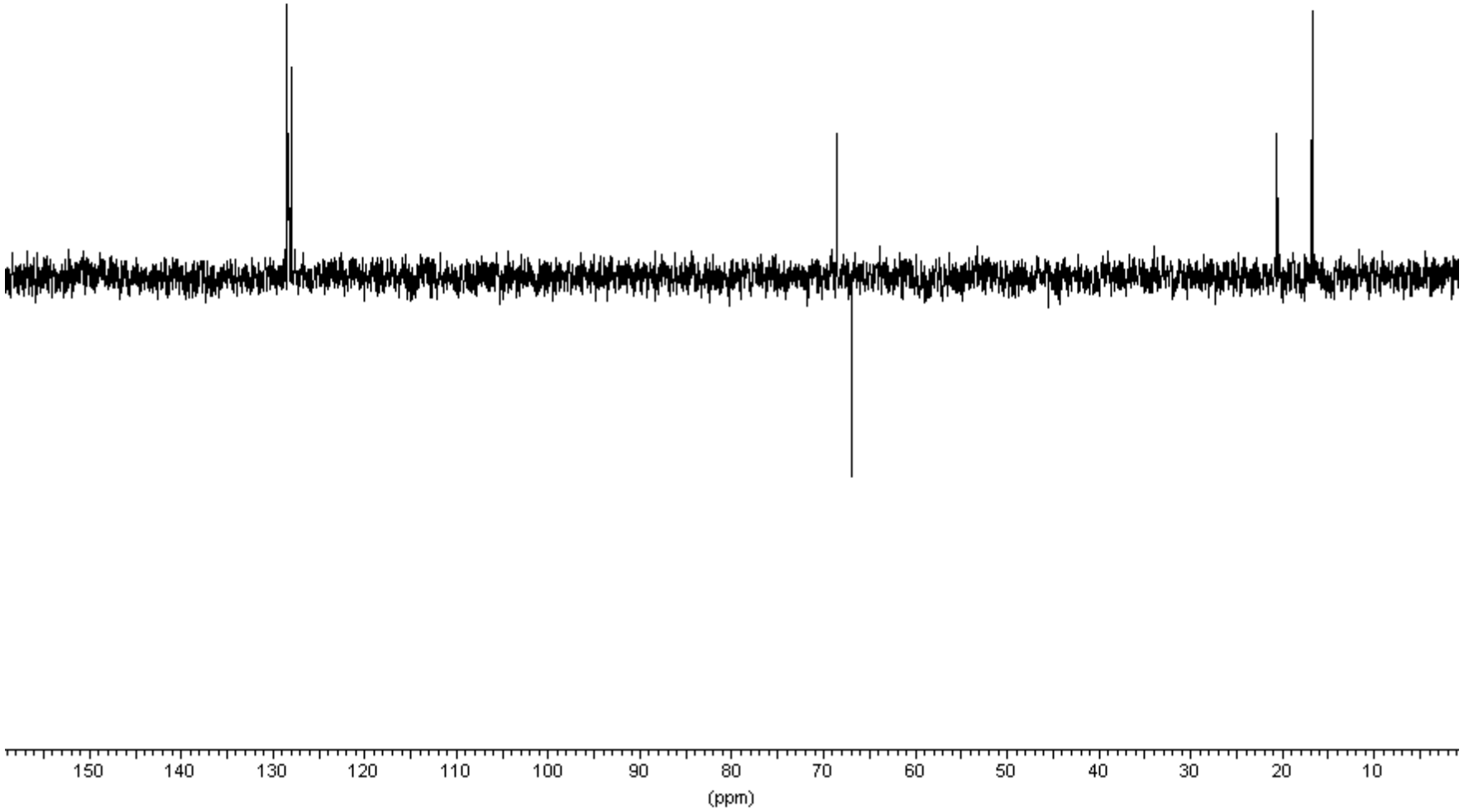

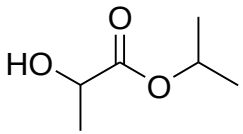

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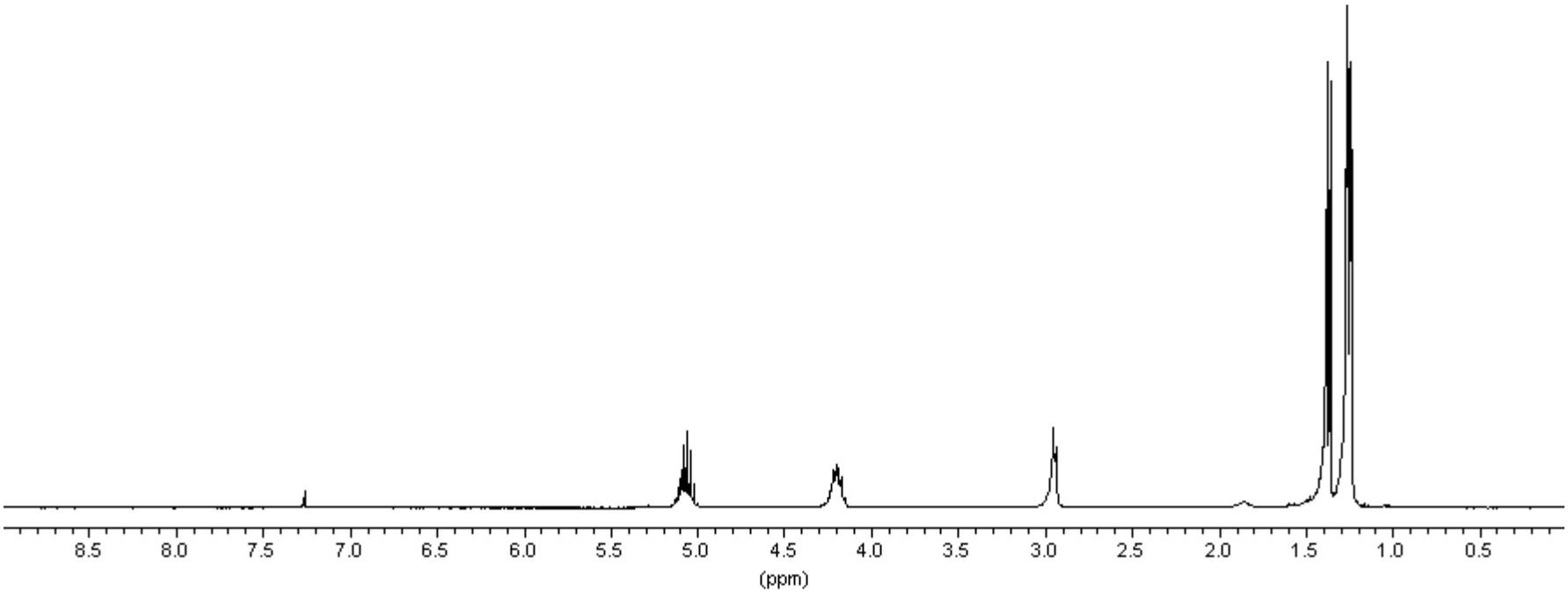

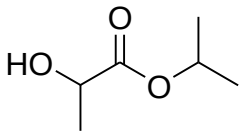
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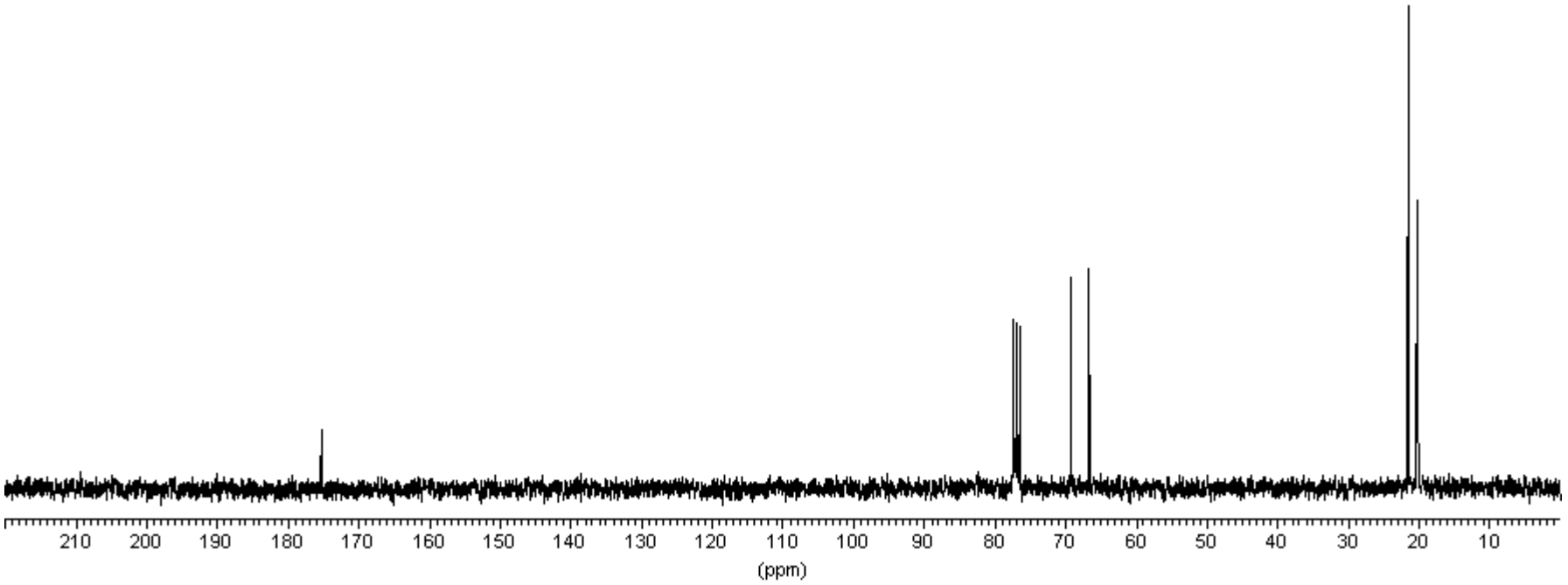
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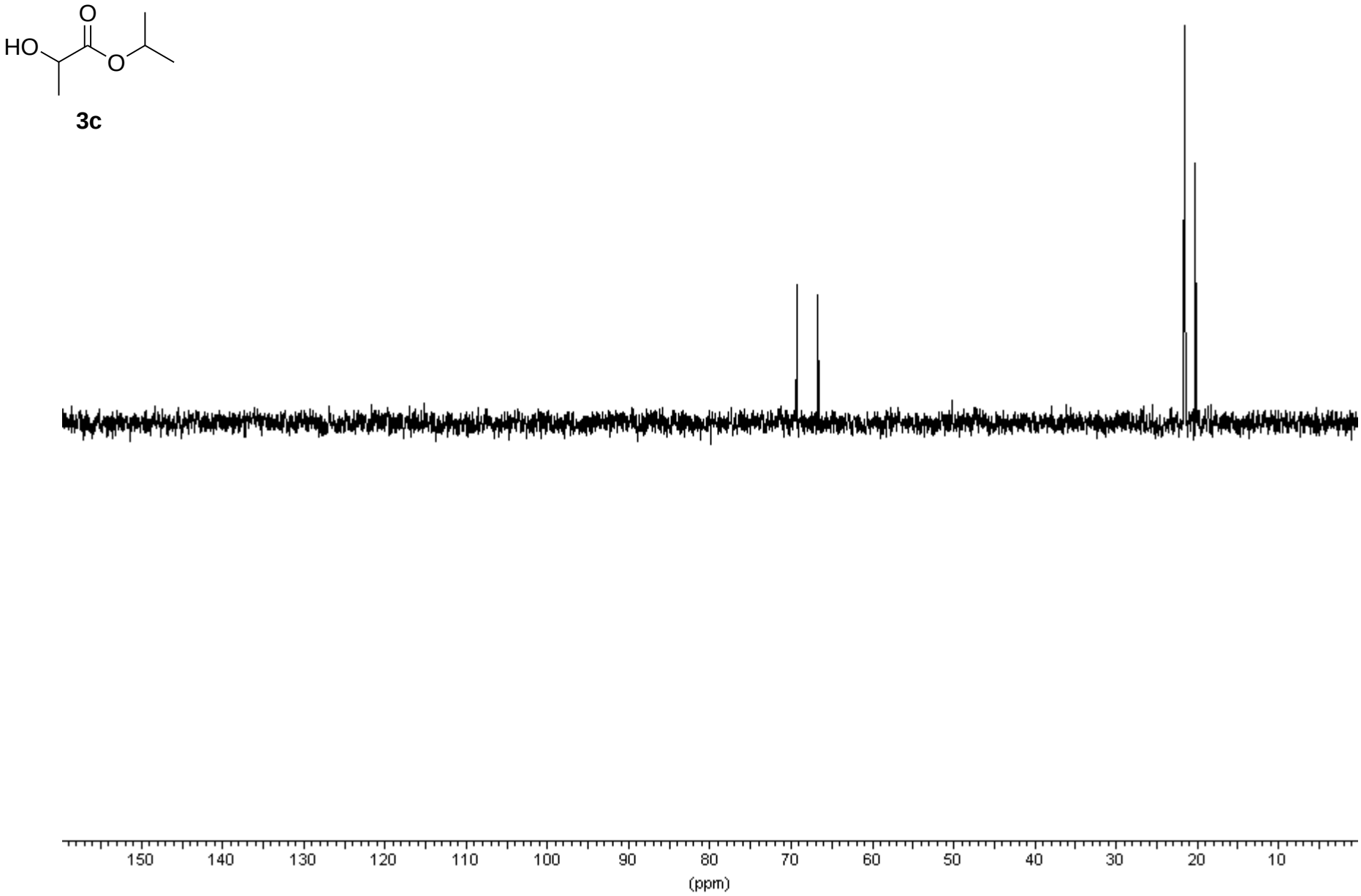
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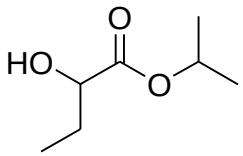

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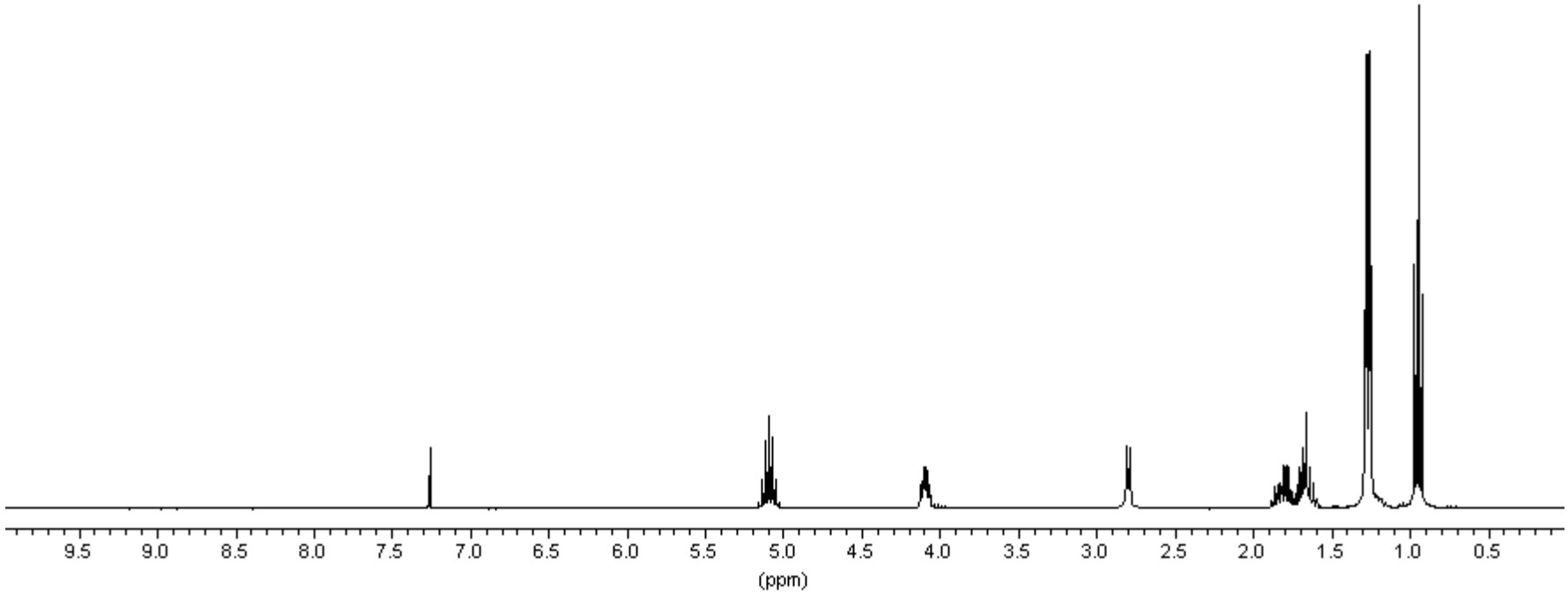

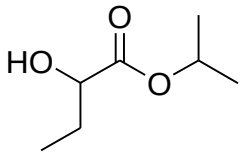
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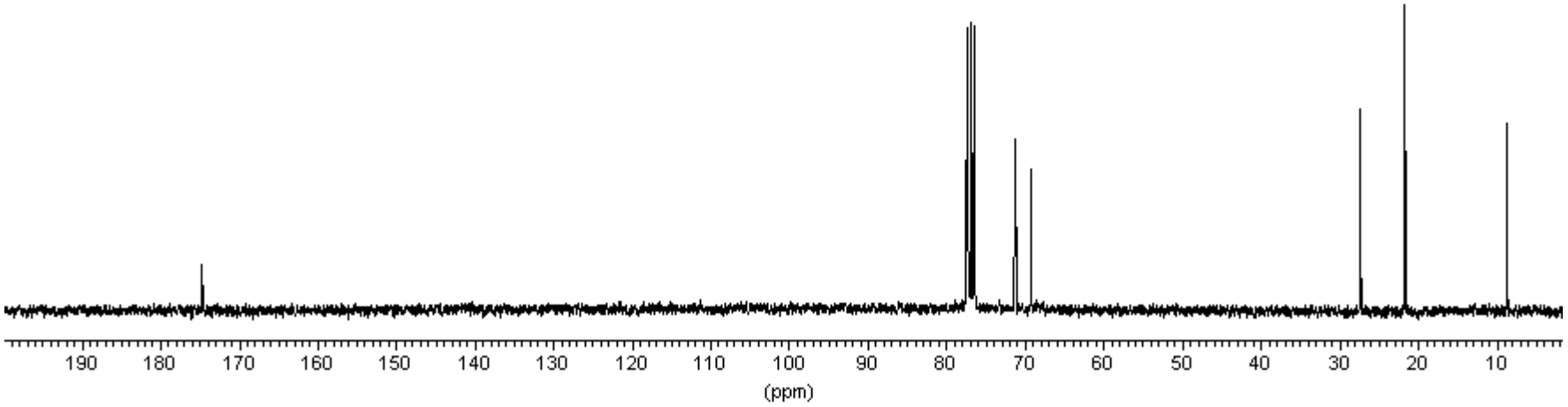
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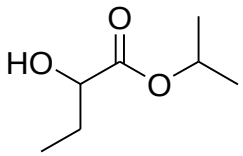

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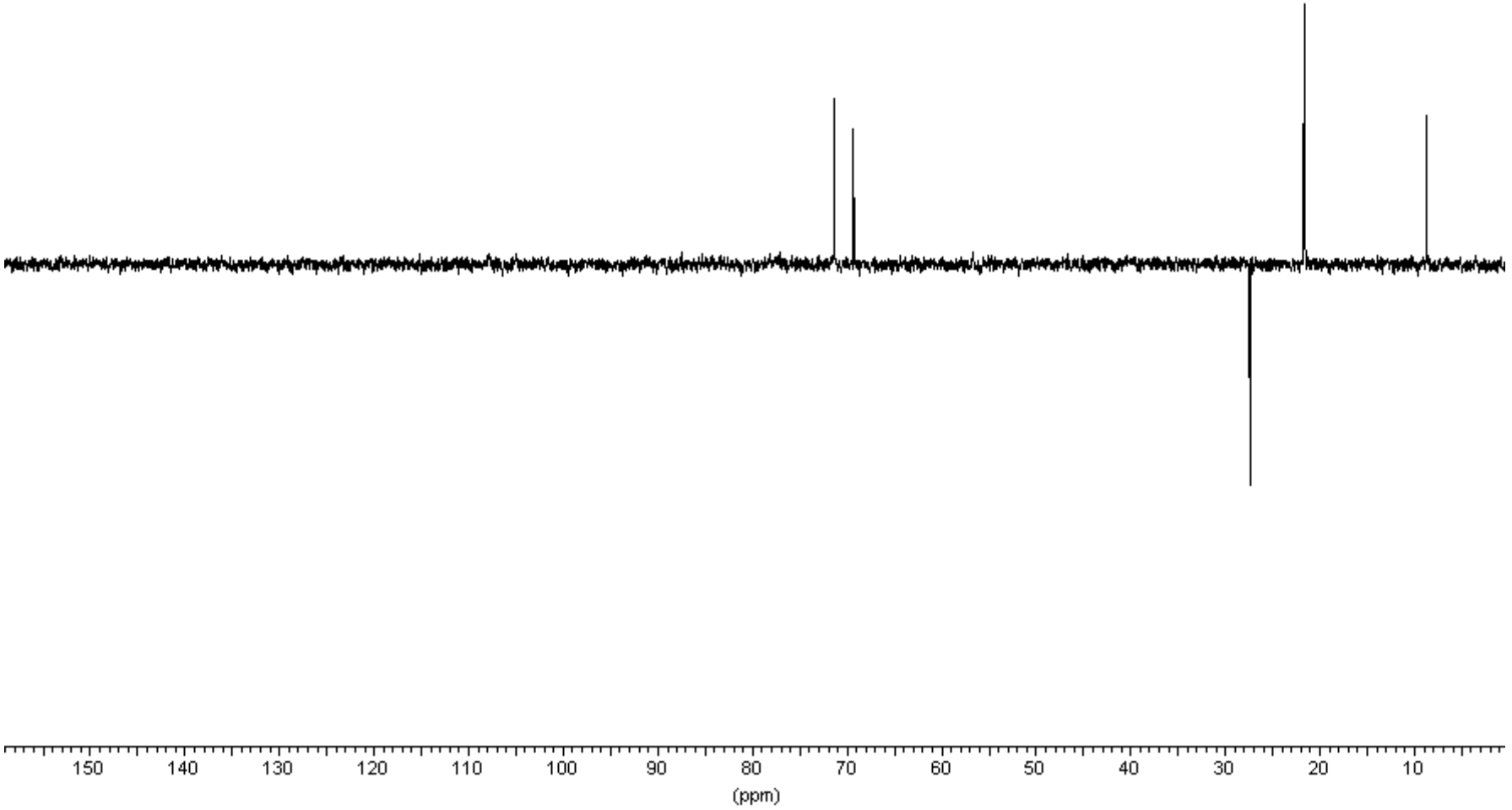

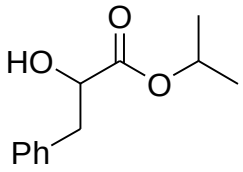

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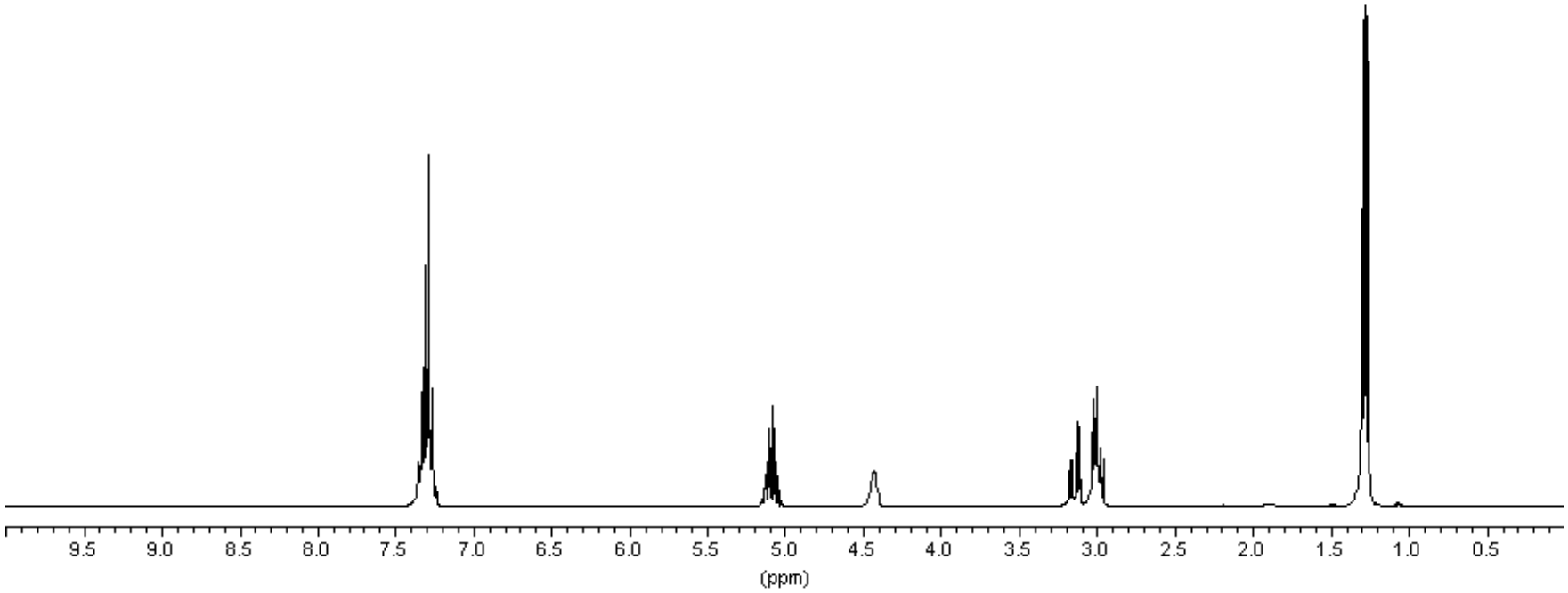

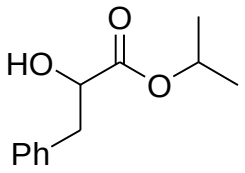
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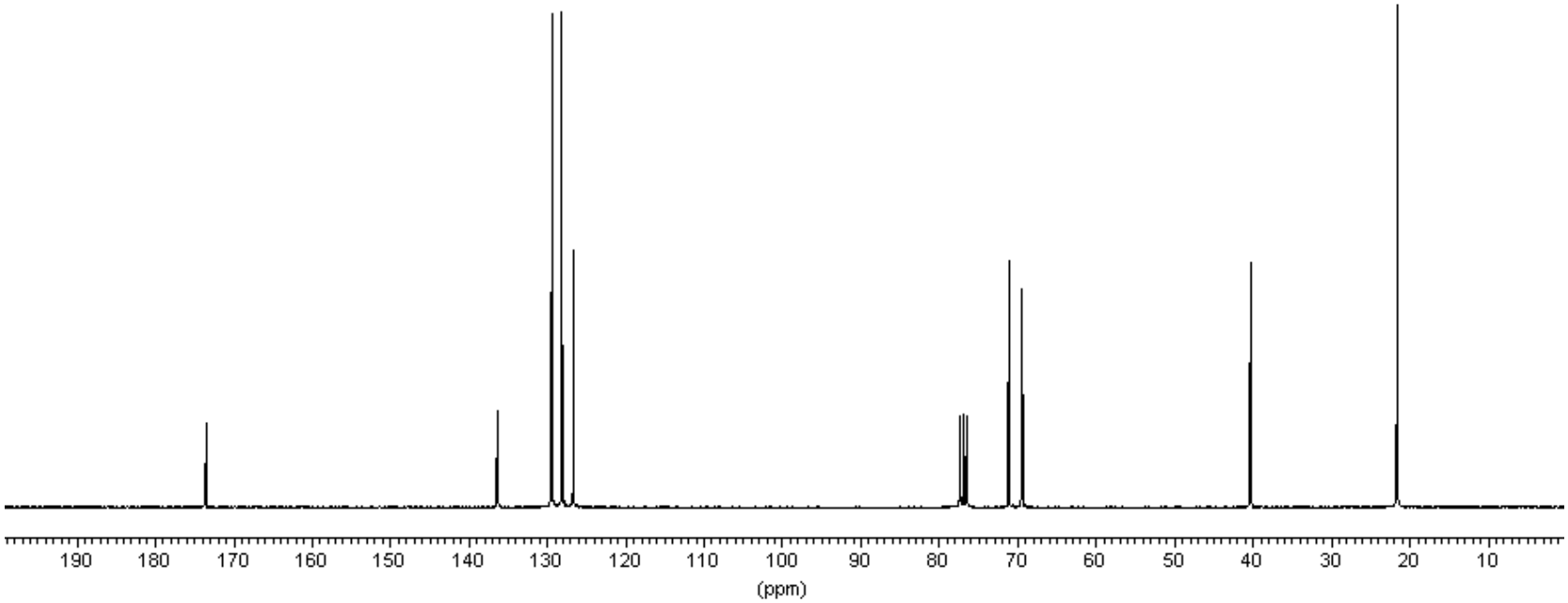
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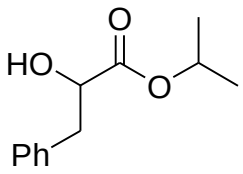

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