Synthesis of phospho-amino acid analogues as tissue adhesive cement additives

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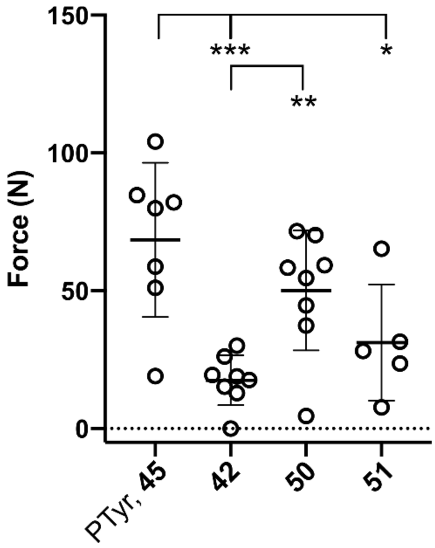


Figure S1: Comparison of cement adhesive strength when applied to bone cubes for representative compounds. Comparison between this graph and the data presented in Fig. 2b shows that trends match those observed for aluminium cube adhesion. Data are represented as scatter dot plots of each individual data point with the bars indicating the mean ± SD. * represents significant differences between groups (* $p < 0.05$, ** $p < 0.005$, *** $p < 0.001$). Details of the statistical analysis are provided on page S25.

Compound	CPC	Ser	Tyr	L-PSer, **1**	D/L-PSer, **1**	PTyr, **45**	PThr, **57**	**42**	**43**
Force (N)	0.2	9.4	3.9	211.6	237.2	142.5	150.6	43.4	19.1
Deviation	0.4	12.9	3.9	30.1	26.9	31.2	48.3	12.1	10.4

Compound	**47**	**48**	**50**	**51**	**52**	**53**	**54**	**55**	**56**
Force (N)	122.5	46.1	171.5	109.4	159.0	131.4	270.2	197.2	103.0
Deviation	32.4	9.8	38.6	28.1	50.1	14.9	26.8	41.8	33.2

Table S1: Tabulated mean adhesive strengths (aluminium-aluminium) and standard deviations for all compounds tested.

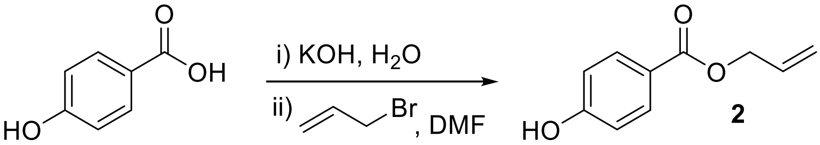
General considerations

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker AV-400 (400 MHz) spectrometer. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AV400 (100 MHz) spectrometer. NMR shifts were assigned using COSY, HSQC and HMBC spectra. All chemical shifts are quoted on the δ scale in ppm using residual solvent as the internal standard (^{1}H NMR: $CDCl_3$ = 7.26; MeOD

= 3.31; DMSO-d_6 = 2.50; D_2O = 4.79; and ^{13}C NMR: $CDCl_3$ = 77.16, MeOD = 49.00, DMSO-d_6 = 39.52). Coupling constants (*J*) are reported in Hz with the following splitting abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, app = apparent, br = broad. Melting points (m.p.) were recorded on a Zeiss Axio Imager: Z1M microscope equipped with a Linkam LTS 420 temperature controlled microscope stage and are uncorrected. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum 100 spectrophotometer with a Universal ATR Sampling Accessory. Absorption maxima (υ_{max}) are reported in wavenumbers (cm^{-1}). Low resolution mass spectra (LRMS) were recorded on an Agilent 6130 Quadrupole mass spectrometer using electrospray ionization (ESI), connected to an Agilent 1260 Infinity liquid chromatography set-up with a Phenomenex Gemini-NX-C16 column. High resolution mass spectra (HRMS) were recorded on a Waters LCT Premier (ES-ToF) spectrometer connected to an Aquity-iClass UPLC. Matrix-assisted laser desorption-ionization (MALDI) spectra were recorded on a Micromass MALDI-ToF spectrometer. Nominal and exact m/z values are reported in Daltons. Thin layer chromatography (TLC) was carried out using aluminium backed sheets coated with 60 F254 silica gel (Merck). Visualization of the silica plates was achieved using a UV lamp (λ_{max} = 254, 302, or 366 nm), and/or ammonium molybdate (5 % in 2M H_2SO_4), and/or potassium permanganate (5 % $KMnO_4$ in 1M NaOH with 5 % potassium carbonate). Flash column chromatography was carried out using Geduran Si 60 (40-63 μm) (Merck). Mobile phases are reported as % volume of more polar solvent in less polar solvent. Anhydrous solvents were purchased from Sigma-Aldrich and used as supplied. All other solvents were used as supplied (Analytical or HPLC grade), without prior purification. Reagents were purchased from Sigma-Aldrich and used as supplied, unless otherwise indicated. Brine refers to a saturated solution of sodium chloride. Anhydrous magnesium sulfate ($MgSO_4$) was used as the drying agent after reaction workup unless otherwise stated.

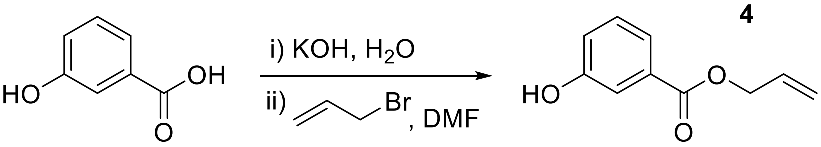
Cortical bovine cubes were created by cutting freshly harvested adult humerus into cubes 1 cm^3, with a water cooled, diamond coated, band saw blade (IMEB, California, USA). Each cube was cut in two to yield matching surfaces, and were stored frozen until use. Steel test cubes were made to a final dimension of 1 cm^3 +/- 0.1 mm. The surfaces were polished with 80 grit polishing paper.

Substrate synthesis



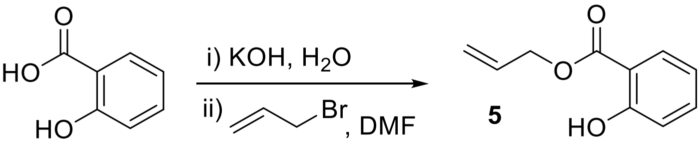
2

4-Hydroxybenzoic acid (2.76 g, 20 mmol) and potassium hydroxide (1.23 g, 22 mmol) were dissolved in water (20 mL) and stirred for 10 min. The mixture was then concentrated *in vacuo*. The residue was suspended in DMF (20 mL) and allyl bromide (1.9 mL, 22 mmol) was added. After stirring for 18 hrs, the mixture was diluted with EtOAc (150 mL) and the organics washed with brine (2 x 100 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a white solid. A yield of 2.8 g, 15.7 mmol (79 %) was obtained. Data were consistent with those previously reported.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (2H, d, *J* = 8.8 Hz, Ar$\underline{\mathrm{H}}$2), 6.89 (2H, d, *J* = 8.8 Hz, Ar$\underline{\mathrm{H}}$3), 5.88 (1H, ddt, *J* = 17.2, 10.4, 5.5 Hz, -C$\underline{\mathrm{H}}$=CH_2), 5.42 (1H, dd, *J* = 17.2, 1.6 Hz, -CH=C$\underline{\mathrm{H}}_2$), 5.30 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.6 Hz, -CH=C$\underline{\mathrm{H}}_2$), 4.82 (2H, dt, *J* = 5.5, 1.6 Hz, -C$\underline{\mathrm{H}}_2$CH=CH_2) ppm;



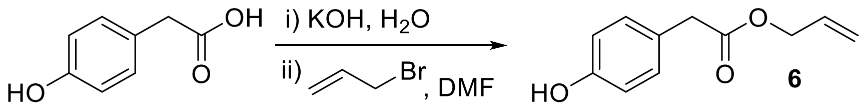
4

Run as described above on 3-hydroxybenzoic acid (2 g, 14.5 mmol). A yield of 2.3 g, 12.9 mmol (89 %) was obtained as a colourless oil. Data were consistent with those previously reported.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60-7.68 (2H, m, Ar$\underline{\mathrm{H}}$2 and Ar$\underline{\mathrm{H}}$6), 7.32 (1H, dd, J_1 = J_2 = 7.9 Hz, Ar$\underline{\mathrm{H}}$5), 7.10 (1H, d, *J* = 7.9 Hz, Ar$\underline{\mathrm{H}}$4), 6.02 (1H, ddt, *J* = 17.2, 10.4, 5.5 Hz, -C$\underline{\mathrm{H}}$=CH_2), 5.42 (1H, d, *J* = 17.2, -CH=C$\underline{\mathrm{H}}_2$), 5.30 (1H, d, *J* = 10.4 Hz, -CH=C$\underline{\mathrm{H}}_2$), 4.84 (2H, d, *J* = 5.5, -C$\underline{\mathrm{H}}_2$CH=CH_2) ppm;

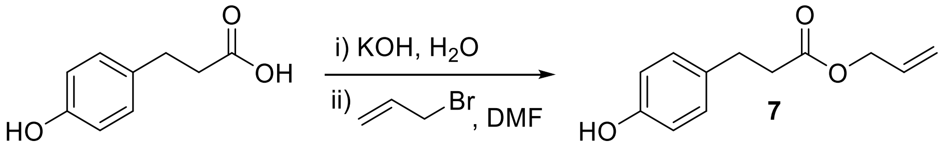


5

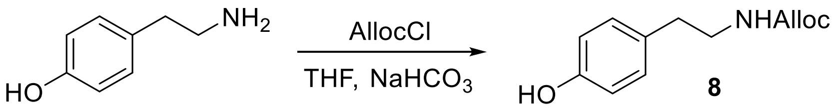
Run as described above on 2-hydroxybenzoic acid (2 g, 14.5 mmol). A yield of 2.2 g, 12.3 mmol (85 %) was obtained as a colourless oil. Data were consistent with those previously reported.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.78 (1H, s, -O$\underline{\mathrm{H}}$), 7.90 (1H, ddd, *J* = 7.6, 2.2, 0.4 Hz, Ar$\underline{\mathrm{H}}$6), 7.47 (1H, ddd, *J* = 7.1, 6.9, 1.4, 0.3 Hz, Ar$\underline{\mathrm{H}}$4), 7.00 (1H, ddd, *J* = 7.1, 0.8, 0.4 Hz, Ar$\underline{\mathrm{H}}$3), 6.9 (1H, ddd, *J* = 7.6, 7.1, 0.8 Hz, Ar$\underline{\mathrm{H}}$5), 6.05 (1H, ddt, *J* = 17.2, 10.4, 5.7 Hz, -C$\underline{\mathrm{H}}$=CH_2), 5.45 (1H, ddt, J = 17.2, 1.5, 1.4 Hz, $-CH{=}C\underline{H}_2$), 5.30 (1H, ddt, J = 10.4, 1.5, 1.4 Hz, $-CH{=}C\underline{H}_2$), 4.86 (2H, ddd, J_1 = 5.5 Hz, J_2 = J_3 = 1.5 Hz, $-C\underline{H}_2CH{=}CH_2$) ppm;



Run as described above on 4-hydroxyphenylacetic acid (2 g, 13.2 mmol). Purified by flash column chromatography eluting with 30 % EtOAc:Hexane. A yield of 2.3 g, 11.9 mmol (91 %) was obtained as a colourless oil. Data were consistent with those previously reported.[2] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (2H, d, J = 7.6 Hz, $Ar\underline{H}2$), 6.78 (2H, d, J = 7.6 Hz, $Ar\underline{H}3$), 5.92 (1H, ddd, J = 17.2, 10.4, 5.6 Hz, $-C\underline{H}{=}CH_2$), 5.29 (1H, d, J = 17.2 Hz, $-CH{=}C\underline{H}_2$), 5.24 (1H, d, J = 10.4 Hz, $-CH{=}C\underline{H}_2$), 4.62 (2H, d, J = 5.6 Hz, $-C\underline{H}_2CH{=}CH_2$), 3.59 (2H, s, $-C\underline{H}_2Ar$) ppm;

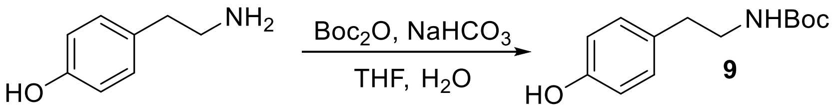


Run as described above on 3-(4-hydroxyphenyl)propionic acid (2 g, 12.0 mmol). Purified by flash column chromatography eluting with 30-40 % EtOAc:Hexane. A yield of 2.2 g, 10.6 mmol (88 %) was obtained as a colourless oil. Data were consistent with those previously reported.[3] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08 (2H, d, J = 8.6 Hz, $Ar\underline{H}2$), 6.77 (2H, d, J = 8.6 Hz, $Ar\underline{H}3$), 5.91 (1H, ddt, J = 17.2, 10.4, 5.7 Hz, $-C\underline{H}{=}CH_2$), 5.29 (1H, ddt, J_1 = 17.2 Hz, J_2 = J_3 = 1.3 Hz, $-CH{=}C\underline{H}_2$), 5.25 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.3 Hz, $-CH{=}C\underline{H}_2$), 4.59 (2H, dt, J = 5.7, 1.3 Hz, $-C\underline{H}_2CH{=}CH_2$), 2.91 (2H, t, J = 15.4 Hz, $-C\underline{H}_2Ar$), 2.65 (2H, t, J = 15.4 Hz, $-C\underline{H}_2CO_2All$) ppm;



Tyramine (0.5 g, 3.6 mmol) and sodium bicarbonate (919 mg, 10.9 mmol) were dissolved in a mixture of water (10 mL) and THF (10 mL). Allyl chloroformate (422 µL, 4.0 mmol) was added dropwise, and the reaction stirred for 2 hrs. The mixture was then diluted with hydrochloric acid (0.5 M, 50 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organics were washed with brine (50 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a brown oil. A yield of 620 mg, 2.8 mmol (78 %) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (2H, d, J = 8.4 Hz, $Ar\underline{H}3$), 6.80 (2H, d, J= 8.4 Hz, $Ar\underline{H}4$), 5.91 (1H, ddt, J = 17.2, 10.4, 5.5 Hz, $-C\underline{H}{=}CH_2$), 5.30 (1H, d, J = 17.2 Hz, $-CH{=}C\underline{H}_2$), 5.22 (1H, d, J = 10.4 Hz, $-CH{=}C\underline{H}_2$), 4.91 (1H, br s, $-N\underline{H}$), 4.58 (2H, d, J = 5.5 Hz, -

C$\underline{H}_2$CH=CH$_2$), 3.42 (2H, td, *J* = 7.0, 6.4 Hz, -C$\underline{H}_2$NHAlloc), 2.74 (2H, t, *J* = 7.0 Hz, -C$\underline{H}_2$Ar) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.62 (-$\underline{C}$O$_2$All), 154.82 (Ar$\underline{C}$4), 132.69 (-$\underline{C}$H=CH$_2$), 130.09 (Ar$\underline{C}$1), 129.82 (Ar$\underline{C}$2), 117.88 (-CH=$\underline{C}$H$_2$), 115.58 (Ar$\underline{C}$3), 65.75 (-$\underline{C}$H$_2$CH=CH$_2$), 42.46 (-$\underline{C}$H$_2$NHAlloc), 35.17 (-$\underline{C}$H$_2$Ar) ppm; IR (υ$_{max}$, film): 2939 (v br), 1695, 1614, 1596, 1509, 1441, 1365, 1219, 1170, 1134, 1106, 1053 cm^{-1}; HRMS m/z (ESI+): Found: 222.1124 (M+H), Calc.: 222.1130 (C$_{12}$H$_{16}$NO$_3$).



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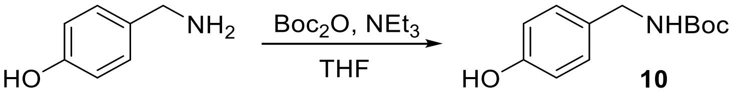
Tyramine (1 g, 7.2 mmol) and sodium bicarbonate (725 mg, 8.6 mmol) were dissolved in a mixture of water (20 mL) and THF (30 mL). A solution of di-*tert*-butyl dicarbonate (1.56 g, 7.2 mmol) in THF (20 mL) was then added dropwise, and the reaction stirred for 4 hrs. The mixture was then diluted with ethyl acetate (150 mL), and the organics washed with water (100 mL) and brine (100 mL), dried with MgSO$_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil. A yield of 1.60 g, 6.7 mmol (93 %) was obtained. Data were consistent with those previously reported.[4] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.05 (2H, d, *J* = 7.3 Hz, Ar$\underline{H}$2), 6.79 (2H, d, *J* = 7.3 Hz, Ar$\underline{H}$3), 5.49 (1H, br s, -O$\underline{H}$), 4.59 (1H, br s, -N$\underline{H}$), 3.30-3.40 (2H, m, -C$\underline{H}_2$NHBoc), 2.70-2.78 (2H, m, -C$\underline{H}_2$Ar), 1.46 (9H, s, Boc) ppm.



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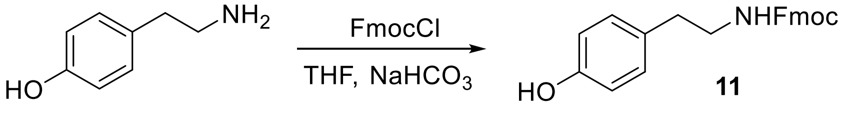
A solution of di-*tert*-butyl dicarbonate (2.1 g, 9.7 mmol) in THF (20 mL) was added dropwise to a mixture of 4-hydroxybenzylamine (1 g, 8.1 mmol) and trimethylamine (2.28 mL, 16.2 mmol) in THF (50 mL). After stirring for 18 hrs, the THF was removed *in vacuo* and the residue diluted with ethyl acetate (100 mL). The organics were washed with water (100 mL), hydrochloric acid (1 M, 100 mL), and brine (100 mL), dried with MgSO$_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil. A yield of 1.78 g, 7.9 mmol (98 %) was obtained. Data were consistent with those previously reported.[5] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.15 (2H, d, *J* = 8.1 Hz, Ar$\underline{H}$2), 6.80 (2H, d, *J* = 8.1 Hz, Ar$\underline{H}$3), 5.67 (1H, br s, -O$\underline{H}$), 4.82 (1H, br s, -N$\underline{H}$), 4.24 (2H, d, *J* = 5.4 Hz, -C$\underline{H}_2$NHBoc), 1.48 (9H, s, Boc) ppm;



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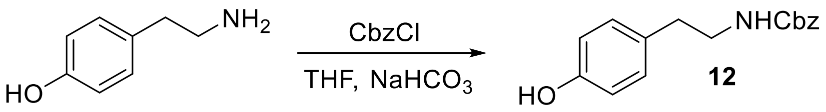
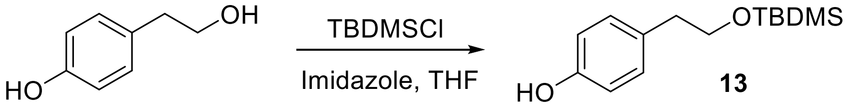
Tyramine (0.5 g, 3.6 mmol) and sodium bicarbonate (302 mg, 3.6 mmol) were dissolved in a mixture of water (20 mL) and THF (10 mL). A solution of fluorenylmethyloxycarbonyl chloride (1.03 g, 4.0 mmol) in THF (10 mL) was then added dropwise, and the reaction stirred for 4 hrs.

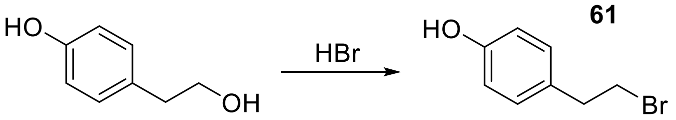
The mixture was then diluted with ethyl acetate (150 mL), and the organics washed with water (100 mL) and brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a white solid. A yield of 1.07 g, 3.0 mmol (83 %) was obtained. Data were consistent with those previously reported.[6] ^1H NMR (400 MHz, $CDCl_3$): δ = 7.75 (2H, d, *J* = 7.8 Hz, Fmoc), 7.52 (2H, d, *J* = 7.8 Hz, Fmoc), 7.38 (2H, dd, $J_1 = J_2$ = 7.8 Hz, Fmoc), 7.30 (2H, dd, $J_1 = J_2$ = 7.8 Hz, Fmoc), 7.02 (2H, d, *J* = 8.4 Hz, Ar$\underline{H}$3), 6.75 (2H, d, *J* = 8.4 Hz, Ar$\underline{H}$2), 4.71-4.79 (2H, m, -N$\underline{H}$ and -O$\underline{H}$), 4.39 (2H, d, *J* = 6.9 Hz, Fmoc), 4.19 (1H, t, *J* = 6.9 Hz, Fmoc), 3.39 (2H, dt, $J_1 = J_2$ = 6.9 Hz, -C$\underline{H}_2$NHFmoc), 2.72 (2H, t, *J* = 6.9 Hz, -C$\underline{H}_2$Ar) ppm.



Tyramine (0.5 g, 3.6 mmol) and sodium bicarbonate (302 mg, 3.6 mmol) were dissolved in a mixture of water (20 mL) and THF (10 mL). A solution of benzyl chloroformate (575 µL, 4.0 mmol) in THF (10 mL) was then added dropwise, and the reaction stirred for 4 hrs. The mixture was then diluted with ethyl acetate (150 mL), and the organics washed with water (100 mL) and brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil that solidified on standing. A yield of 861 mg, 3.2 mmol (88 %) was obtained. Data were consistent with those previously reported.[7] ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.41 (5H, m, Cbz), 7.03 (2H, d, *J* = 7.8 Hz, Ar$\underline{H}$3), 6.76 (2H, d, *J* = 7.8 Hz, Ar$\underline{H}$2), 5.09 (2H, s, Cbz), 4.76 (1H, br s, -N$\underline{H}$), 3.42 (2H, dt, $J_1 = J_2$ = 6.7 Hz, -C$\underline{H}_2$NHCbz), 2.74 (2H, t, *J* = 6.7 Hz, -C$\underline{H}_2$Ar) ppm.



A solution of 2-(4-hydroxyphenyl)ethanol (1.38 g, 10 mmol) and imidazole (748 mg, 11 mmol) in THF (20 mL) was cooled to 0 °C. A solution of TBDMSCl (1.65 g, 11 mmol) in THF (5 mL) was added dropwise, the mixture warmed to room temperature, and stirring continued for 18 hrs. The solvent was then removed *in vacuo* and the residue redissolved in ethyl acetate (100 mL). The organics were washed with aqueous citric acid (10 %, 50 mL) and brine (50 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil that solidified on standing. A yield of 1.92 g, 7.6 mmol (76 %) was obtained. Data were consistent with those previously reported.[8] ^1H NMR (400 MHz, $CDCl_3$): δ = 7.06 (2H, d, *J* = 8.2 Hz, Ar$\underline{H}$3), 6.74 (2H, d, *J* = 8.2 Hz, ArH2), 3.76 (2H, t, *J* = 7.1 Hz, -CH_2OR), 2.75 (2H, t, *J* = 7.1 Hz, -CH_2Ar), 0.88 (9H, s, TBDMS), 0.00 (6H, s, TBDMS) ppm.



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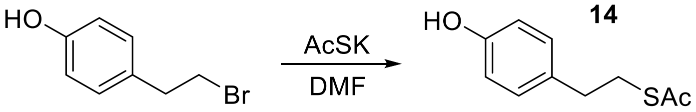
2-(4-hydroxyphenyl)ethanol (3 g, 21.7 mmol) was heated to 85 °C for 18 hrs in hydrobromic acid (48 %, 15 mL). After cooling to room temperature the mixture was diluted with water (75 mL) and extracted with DCM (3 x 100 mL). The combined organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a light brown solid. A yield of 4.2 g, 21.0 mmol (96 %) was obtained. Data were consistent with those previously reported.[9] ^{1}H NMR (400 MHz, $CDCl_3$): 7.08 (2H, d, *J* = 7.2 Hz, ArH3), 6.79 (2H, d, *J* = 7.2 Hz, ArH2), 4.75 (1H, br s, -OH), 3.52 (2H, t, *J* = 7.6 Hz, -CH_2Br), 3.09 (2H, t, *J* = 7.6 Hz, -CH_2Ar) ppm.



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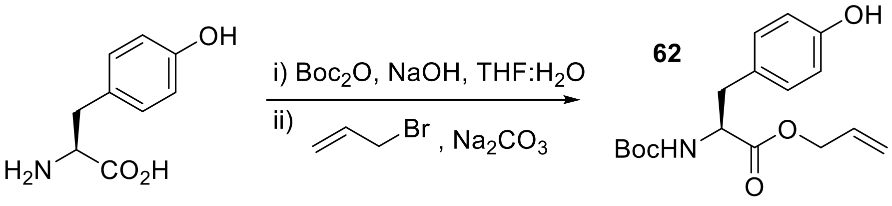
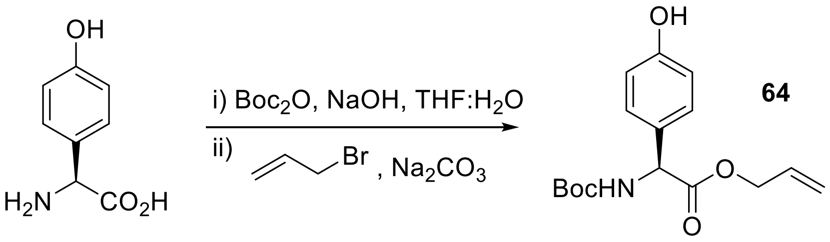
Potassium thioacetate (2.7 g, 24 mmol) was added to a solution of **61** (4 g, 20 mmol) in DMF (10 mL). After stirring for 18 hrs, the mixture was diluted with ethyl acetate (200 mL) and washed with brine (4 x 150 mL). The organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give the DP as a light brown oil. A yield of 3.6 g, 18.4 mmol (92 %) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$): 7.06 (2H, d, *J* = 7.3 Hz, ArH3), 6.77 (2H, d, *J* = 7.3 Hz, ArH2), 5.63 (1H, s, -OH), 3.07 (2H, t, *J* = 7.3 Hz, -CH_2Ar), 2.78 (2H, t, *J* = 7.3 Hz, -CH_2SAc) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.77 (-COMe), 154.32 (ArC4), 131.87 (ArC1), 129.67 (ArC2), 115.31 (ArC3), 34.81 (-CH_2Ar), 30.80 (-CH_2SAc), 30.67 (-COMe); IR (υ_{max}, film): 3375, 3023, 2928, 1687, 1660, 1613, 1596, 1514, 1444, 1354, 1262, 1219, 1172, 1130, 1100, 1016 cm^{-1}; HRMS m/z (ESI+): Found: 219.0454 (M+Na), Calc.: 219.0450 ($C_{10}H_{12}NaO_2S$).



62

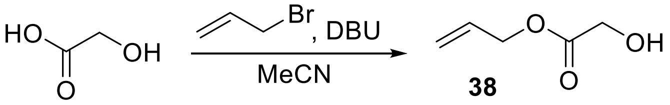
A solution of di-*tert*-butyl dicarbonate (3.97 g, 18.2 mmol) in THF (20 mL) was added dropwise to a mixture of L-tyrosine (3 g, 16.6 mmol) and sodium hydroxide (728 mg, 18.2 mmol) in water (20 mL) and THF (20 mL). After stirring for 4 hrs, the THF was removed *in vacuo* and the mixture washed with ethyl acetate (50 mL). The aqueous was then acidified with hydrochloric acid (2M, 50 mL), and extracted with ethyl acetate (3 x 100 mL). The combined were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was redissolved in DMF (30 mL), and potassium carbonate (2.4 g, 17.2 mmol) and allyl bromide (1.75 mL, 20.3 mmol) were sequentially added. After stirring for 18 hrs, the reaction was diluted with ethyl acetate (200 mL), and the organics washed with hydrochloric acid (1 M, 2 x 100 mL) and brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil which solidified on standing. A yield of 3.5 g, 10.9 mmol (70 %) was obtained. Data were consistent with those previously reported.[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (2H, d, *J* = 8.3 Hz, ArH2), 6.74 (2H, d, *J* = 8.3 Hz, ArH3), 5.89 (1H, ddt, *J* = 17.3, 10.4, 4.8 Hz, $-CH=CH_2$), 5.32 (1H, d, *J* = 17.3 Hz, $-CH=CH_2$), 5.26 (1H, d, *J* = 10.4 Hz, $-CH=CH_2$), 5.03 (1H, br d, *J* = 8.2 Hz, -NH), 4.62 (2H, d, *J* = 4.8 Hz, $-CH_2CH=CH_2$), 4.53-4.60 (1H, m, H_α), 3.06 (1H, dd, *J* = 13.9, 5.8 Hz, H_β), 3.00 (1H, dd, *J* = 13.9, 6.1 Hz, H_β), 1.43 (9H, s, Boc) ppm;

The use of D-tyrosine in the same procedure led to the production of enantiomer **63**.



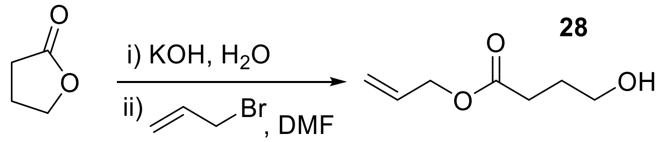
64

A solution of di-*tert*-butyl dicarbonate (2.4 g, 11 mmol) in THF (20 mL) was added dropwise to a mixture of L-phenylglycine (1.67 g, 10 mmol) and sodium hydroxide (440 mg, 11 mmol) in water (20 mL) and THF (20 mL). After stirring for 4 hrs, the THF was removed *in vacuo* and the mixture washed with ethyl acetate (50 mL). The aqueous was then acidified with hydrochloric acid (2M, 50 mL), and extracted with ethyl acetate (3 x 100 mL). The combined were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was redissolved in DMF (15 mL), and potassium carbonate (1.58 g, 11 mmol) and allyl bromide (1.03 mL, 12 mmol) were sequentially added. After stirring for 18 hrs, the reaction was diluted with ethyl acetate (200 mL), and the organics washed with hydrochloric acid (1 M, 2 x 100 mL) and brine (100 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil which solidified on standing. A yield of 2.3 g, 7.5 mmol (75 %) was obtained. Data were consistent with those previously reported.[10] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (1H, s, -OH), 7.07 (2H, d, *J* = 8.5 Hz, ArH2), 6.67 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$3), 5.60-5.76 (2H, m, -C$\underline{H}$=CH$_2$ & -N$\underline{H}$), 5.14 (1H, d, *J* = 7.1 Hz, -CH=C$\underline{H}_2$), 5.00-5.11 (2H, m, -CH=C$\underline{H}_2$ & $\underline{H}_\alpha$), 5.03 (1H, br d, *J* = 8.2 Hz, -N$\underline{H}$), 4.49 (2H, d, *J* = 5.1 Hz, -C$\underline{H}_2$CH=CH$_2$), 4.53-4.60 (1H, m, $\underline{H}_\alpha$), 1.34 (9H, s, $\underline{\text{Boc}}$) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.40 (-$\underline{C}$O$_2$All), 156.79 (Ar$\underline{C}$4), 155.09 (-$\underline{C}$O$_2{}^t$Bu), 131.29 (-$\underline{C}$H=CH$_2$), 128.47 (Ar$\underline{C}$2), 127.54 (Ar$\underline{C}$1), 118.52 (-CH=$\underline{C}$H$_2$), 115.91 (Ar$\underline{C}$3), 80.65 (-$\underline{C}$Me$_3$), 66.12 (d, *J* = 5.6 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 57.31 ($\underline{C}_\alpha$), 28.31 ($\underline{\text{Boc}}$) ppm; IR (υ_{max}, film): 3360, 2981, 1735, 1687, 1615, 1597, 1514, 1501, 1452, 1393, 1368, 1211, 1158, 1105, 1055, 1028 cm^{-1}; HRMS m/z (ESI+): Found: 330.1311 (M+Na), Calc.: 330.1312 ($C_{16}H_{21}NaNO_5$).



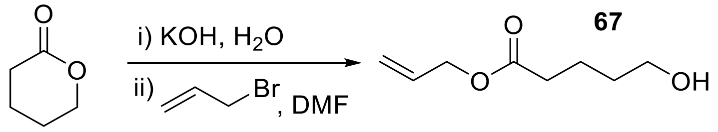
38

A mixture of glycolic acid (760 mg, 10 mmol), allyl bromide (951 µL, 11 mmol) and 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.65 mL, 11 mmol) was heated to 60 °C for 18 hrs, then concentrated *in vacuo*. The residue was purified by column chromatography, eluting with 30-40 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil. A yield of 980 mg, 8.4 mmol (84 %) was obtained. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.92 (1H, ddt, *J* = 17.2, 10.4, 5.8 Hz, -C$\underline{H}$=CH$_2$), 5.35 (1H, d, *J* = 17.2 Hz, -CH=C$\underline{H}_2$), 5.29 (1H, d, *J* = 10.4 Hz, -CH=C$\underline{H}_2$), 4.70 (2H, d, *J* = 5.8 Hz, -C$\underline{H}_2$CH=CH$_2$), 4.20 (2H, d, *J* = 5.5 Hz, -C$\underline{H}_2$OH), 2.70 (1H, t, *J* = 5.5 Hz, -O$\underline{H}$) ppm; IR (υ_{max}, film): 3439 (br), 2945, 1738, 1649, 1435, 1382, 1272, 1199, 1089 cm^{-1}; HRMS m/z (ESI+): Found: 117.0549 (M+H), Calc.: 117.0546 ($C_5H_9O_3$).



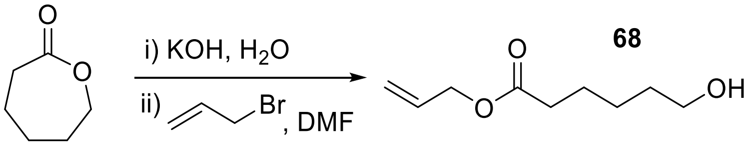
28

A mixture of γ-butyrolactone (2 mL, 26 mmol) and potassium hydroxide (1.6 g, 28.6 mmol) in water (30 mL) was stirred for 1 hr, then concentrated *in vacuo*. The residue was suspended in DMF (20 mL) and allyl bromide (2.5 mL, 28.6 mmol) was added. After stirring for 18 hrs, the mixture was diluted with EtOAc (150 mL) and the organics washed with hydrochloric acid (1 M, 100 mL) and brine (100 mL), dried with MgSO$_4$, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil. A yield of 3.5 g, 24.3 mmol (93 %) was obtained. Data were consistent with those previously reported.[11] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.89 (1H, ddt, *J* = 17.2, 10.4, 5.7 Hz, -C$\underline{H}$=CH$_2$), 5.29 (1H, ddt, J_1 = 17.2 Hz, J_2 = J_3 = 1.4 Hz, -CH=C$\underline{H}_2$), 5.22 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.4 Hz, -CH=C$\underline{H}_2$), 4.56 (2H, ddd, J_1 = 5.7 Hz, J_2 = J_3 = 1.4 Hz, -C$\underline{H}_2$CH=CH$_2$), 3.65 (2H, t, *J* = 5.8 Hz, -C$\underline{H}_2$OH), 2.45 (2H, t, *J* = 7.2 Hz, -C$\underline{H}_2$CO$_2$All), 1.87 (2H, tt, *J* = 7.2, 5.8 Hz, -C$\underline{H}_2$CH$_2$OH) ppm.



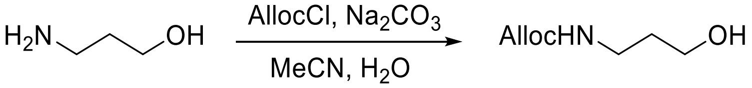
67

Run as described above on δ-valerolactone (2 g, 16.9 mmol). Purified by flash column chromatography eluting with 25-30 % EtOAc:Hexane. Pure fractions were dissolved in diethyl ether (100 mL), and the organics washed with brine (100 mL x 2), dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil. A yield of 2 g, 12.6 mmol (75 %) was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.89 (1H, ddt, *J* = 17.2, 10.4, 5.4 Hz, $-C\underline{H}=CH_2$), 5.30 (1H, d, *J* = 17.2, $-CH=C\underline{H_2}$), 5.23 (1H, d, *J* = 10.4 Hz, $-CH=C\underline{H_2}$), 4.56 (2H, d, *J* = 5.4 Hz, $-C\underline{H_2}CH=CH_2$), 3.59-3.67 (2H, m, $-C\underline{H_2}OH$), 2.37 (2H, t, *J* = 7.2 Hz, $-C\underline{H_2}CO_2All$), 2.16 (1H, br s, $-O\underline{H}$), 1.65-1.77 (2H, m, $-C\underline{H_2}CH_2CO_2All$) 1.54-1.64 (2H, m, $-C\underline{H_2}CH_2OH$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.43 ($-\underline{C}O_2All$), 132.16 ($-\underline{C}H=CH_2$), 118.21 ($-CH=\underline{C}H_2$), 65.06 ($-\underline{C}H_2CH=CH_2$), 62.08 ($-\underline{C}H_2OH$), 33.81 ($-\underline{C}H_2CO_2All$), 31.98 ($-\underline{C}H_2CH_2OH$), 21.07 ($-\underline{C}H_2CH_2CO_2All$) ppm; IR ($\upsilon_{max}$, film): 3395 (br), 2941, 2873, 1734, 1649, 1453, 1420, 1379, 1272, 1156, 1063 cm^{-1}; HRMS m/z (ESI+): Found: 159.1017 (M+H), Calc.: 159.1016 ($C_8H_{15}O_3$).



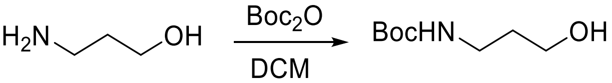
68

Run as described above on ε-caprolactone (2.21 mL, 21.5 mmol). Purified by flash column chromatography eluting with 50 % EtOAc:Hexane. Pure fractions were dissolved in diethyl ether (100 mL), and the organics washed with brine (100 mL x 2), dried with $MgSO_4$, filtered, and concentrated *in vacuo*, to give the DP as a light yellow oil. A yield of 2.5 g, 14.0 mmol (70 %) was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.91 (1H, ddt, *J* = 17.2, 10.4, 5.7 Hz, $-C\underline{H}=CH_2$), 5.31 (1H, ddt, J_1 = 17.2 Hz, $J_2 = J_3$ = 1.5 Hz, $-CH=C\underline{H_2}$), 5.23 (1H, ddt, J_1 = 10.4 Hz, $J_2 = J_3$ = 1.5 Hz, $-CH=C\underline{H_2}$), 4.57 (2H, ddd, J_1 = 5.7 Hz, $J_2 = J_3$ = 1.5 Hz, $-C\underline{H_2}CH=CH_2$), 3.63 (2H, t, *J* = 6.4 Hz, $-C\underline{H_2}OH$), 2.35 (2H, t, *J* = 7.4 Hz, $-C\underline{H_2}CO_2All$), 1.85 (1H, br s, $-O\underline{H}$), 1.62-1.71 (2H, m, $-C\underline{H_2}CH_2CO_2All$) 1.53-1.61 (2H, m, $-C\underline{H_2}CH_2OH$) 1.44-1.37 (2H, m, $-C\underline{H_2}CH_2CH_2OH$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.40 ($-\underline{C}O_2All$), 132.22 ($-\underline{C}H=CH_2$), 118.16 ($-CH=\underline{C}H_2$), 65.00 ($-\underline{C}H_2CH=CH_2$), 62.50 ($-\underline{C}H_2OH$), 34.13 ($-\underline{C}H_2CO_2All$), 32.26 ($-\underline{C}H_2CH_2OH$), 25.26 ($-\underline{C}H_2CH_2CH_2OH$), 24.60 ($-\underline{C}H_2CH_2CO_2All$) ppm; IR ($\upsilon_{max}$, film): 3373 (br), 2938, 2865, 1733, 1456, 1419, 1378,1272, 1173, 1073, 1053 cm^{-1}; HRMS m/z (ESI+): Found: 173.1174 (M+H), Calc.: 173.1172 ($C_9H_{17}O_3$).



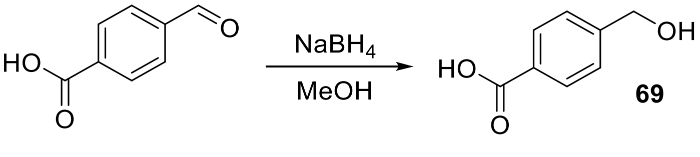
31

3-Amino-1-propanol (1.5 mL, 19.6 mmol) and sodium carbonate (2.3 g, 21.6 mmol) were dissolved in a mixture of acetonitrile (10 mL) and water (10 mL). Allyl chloroformate (2.3 mL, 21.6 mmol) was then added dropwise and the mixture stirred for 2 hrs. After removal of the acetonitrile *in vacuo*, the mixture was acidified slowly with 2 M hydrochloric acid and extracted with ethyl acetate (2 x 75 mL). The combined organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil. A yield of 1.9 g, 11.9 mmol (61 %) was obtained. Data were consistent with those previously reported.[12] ^1H NMR (400 MHz, $CDCl_3$): δ = 5.91 (1H, ddt, *J* = 17.2, 10.4, 5. Hz, $-C\underline{H}=CH_2$), 5.31 (1H, dd, *J* = 17.2, 1.5 Hz, $-CH=C\underline{H}_2$), 5.17-5.26 (2H, m, $-CH=C\underline{H}_2$ and $-N\underline{H}$), 4.56 (2H, d, *J* = 5.6 Hz, $-C\underline{H}_2CH=CH_2$), 3.68 (2H, t, *J* = 5.7 Hz, $-C\underline{H}_2OH$), 3.44 (2H, dt, $J_1 = J_2$ = 6.2 Hz, $-C\underline{H}_2$NHAlloc), 1.71 (2H, tt, *J* = 6.2, 5.7 Hz, $-C\underline{H}_2CH_2OH$) ppm.



30

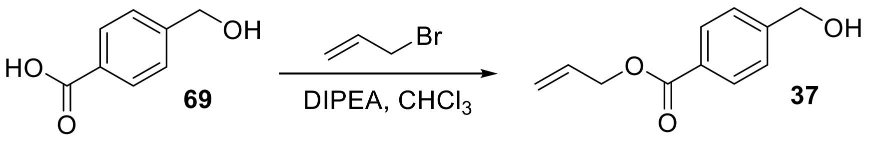
A solution of di-*tert*-butyl dicarbonate (2.4 g, 11 mmol) in DCM (5 mL) was added dropwise to a solution of 3-amino-1-propanol (740 mg, 10 mmol) in DCM (50 mL) and the mixture stirred for 4 hrs. The organics were then washed with water (2 x 50 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo* to give the DP as a colourless oil. A yield of 1.75 g, 10 mmol (98 %) was obtained. Data were consistent with those previously reported.[13] ^1H NMR (400 MHz, $CDCl_3$): δ = 4.78 (1H, br s, $-N\underline{H}$), 3.68 (2H, dt, *J* = 6.2, 5.9 Hz, $-C\underline{H}_2OH$), 3.30 (2H, dt, $J_1 = J_2$ = 6.0 Hz, $-C\underline{H}_2$NHBoc), 2.99 (1H, t, *J* = 6.2 Hz, $-O\underline{H}$), 1.67 (2H, tt, *J* = 6.0, 5.9 Hz, $-C\underline{H}_2CH_2OH$), 1.46 (9H, Boc) ppm.



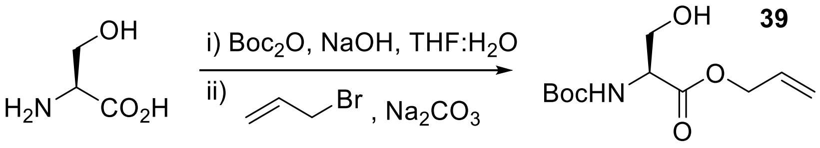
69

Sodium borohydride (1.26 g, 33.3 mmol) was added slowly over 10 min to a suspension of 4-carboxybenzaldehyde (2 g, 13.3 mmol) in methanol (50 mL) at 0 °C [CARE: GAS EVOLVED]. After stirring at room temperature for 1 hr, the mixture was acidified with hydrochloric acid (1 M, 150 mL) and extracted with ethyl acetate (150 mL). The organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was triturated in hexane (100 mL) for 1 hr, collected by filtration, and dried *in vacuo* to give the DP as a white solid. A yield of 1.7 g, 11.1 mmol (83 %) was obtained. Data were consistent with those previously reported.[14] ^1H NMR

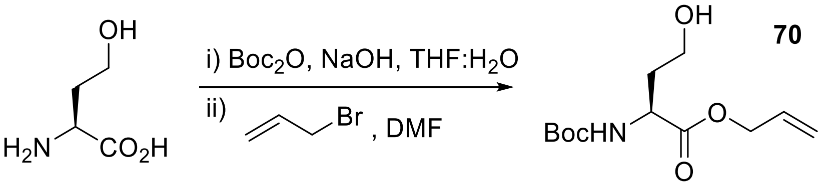
(400 MHz, DMSO-d_6): δ = 12.87 (1H, br s, -CO$_2$H), 7.91 (2H, d, *J* = 8.4 Hz, ArH2), 7.43 (2H, d, *J* = 8.4 Hz, ArH3), 4.58 (2H, s, -CH$_2$OH) ppm.



A mixture of **69** (1.6 g, 10.1 mmol), allyl bromide (1.3 mL, 15.1 mmol), and DIPEA (2.63 mmol, 15.1 mmol) in chloroform (50 mL) was refluxed for 2 hrs. After cooling to room temperature, the mixture was washed with water (50 mL), dried with MgSO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography eluting with 30-40 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil. A yield of 740 mg, 3.85 mmol (38 %) was obtained. Data were consistent with those previously reported.[15] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.07 (2H, d, *J* = 7.8 Hz, ArH2), 7.46 (2H, d, *J* = 7.8 Hz, ArH3), 6.06 (1H, ddt, *J* = 17.2, 10.4, 5.7 Hz, -CH=CH$_2$), 5.43 (1H, ddt, J_1 = 17.2 Hz, J_2 = J_3 = 1.5 Hz, -CH=CH$_2$), 5.31 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.5 Hz, -CH=CH$_2$), 4.84 (2H, ddd, J_1 = 5.7 Hz, J_2 = J_3 = 1.5 Hz, -CH$_2$CH=CH$_2$), 4.79 (2H, d, *J* = 5.8 Hz, -CH$_2$OH), 1.94 (1H, t, *J* = 5.8 Hz, -OH) ppm.



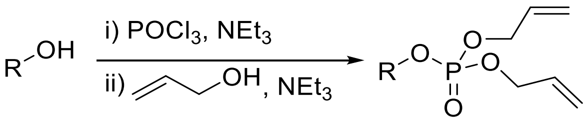
A solution of di-*tert*-butyl dicarbonate (6.85 g, 31.4 mmol) in THF (20 mL) was added dropwise to a solution of L-serine (3 g, 28.5 mmol) in THF (30 mL) and sodium hydroxide (1 M, 57 mL), and the mixture stirred for 4 hrs. After removing the THF *in vacuo* the mixture was acidified with 1 M hydrochloric acid and extracted with ethyl acetate (2 x 100 mL). The combined organics were dried with MgSO$_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in DMF (30 mL) and potassium carbonate (4.7 g, 34.2 mmol) and allyl bromide (2.7 mL, 31.4 mmol) were sequentially added. After stirring for 18 hrs, the mixture was diluted with ethyl acetate (250 mL) and the organics washed with water (100 mL), hydrochloric acid (1 M, 100 mL), and brine (100 mL), dried with MgSO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30-40 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil. A yield of 2.7 g, 11.0 mmol (39 %) was obtained. Data were consistent with those previously reported.[16] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.93 (1H, ddt, *J* = 17.1, 10.5, 5.7 Hz, -CH=CH$_2$), 5.47 (1H, br s, -NH), 5.36 (1H, ddt, J_1 = 17.1 Hz, J_2 = J_3 = 1.5 Hz, -CH=CH$_2$), 5.28 (1H, ddt, J_1 = 10.5 Hz, J_2 = J_3 = 1.5 Hz, -CH=CH$_2$), 4.69 (2H, ddd, J_1 = 5.7 Hz, J_2 = J_3 = 1.5 Hz, -CH$_2$CH=CH$_2$), 4.39-4.46 (1H, m, H$_\alpha$), 3.90-4.04 (2H, m, H$_\beta$), 1.47 (9H, s, Boc) ppm.



70

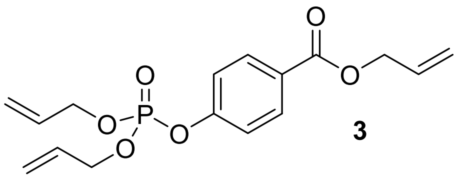
A solution of di-*tert*-butyl dicarbonate (4.8 g, 22 mmol) in THF (20 mL) was added dropwise to a solution of L-homoserine (2.38 g, 20 mmol) in THF (30 mL) and sodium hydroxide (1 M, 20 mL), and the mixture stirred for 4 hrs. After concentration *in vacuo*, the residue was dissolved in DMF (30 mL), allyl bromide (1.9 mL, 22 mmol) was added, and the mixture stirred for 18 hrs. Ethyl acetate (200 mL) was then added and the organics were washed with hydrochloric acid (1M, 2 x 150 mL) and brine (100 mL), dried with$MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography, eluting with 30-40 % EtOAc:Hexane. Pure fractions were concentrated *in vacuo* to give the DP as a colourless oil. A yield of 3.9 g, 15.0 mmol (75 %) was obtained. Data were consistent with those previously reported.[16] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91 (1H, ddt, J = 17.1, 10.4, 5.8 Hz, -C$\underline{H}$=CH$_2$), 5.43 (1H, br d, J = 7.3 Hz, -N$\underline{H}$), 5.35 (1H, ddt, J_1 = 17.1 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H_2}$), 5.27 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H_2}$), 4.65 (2H, ddd, J_1 = 5.8 Hz, J_2 = J_3 = 1.5 Hz, -C$\underline{H_2}$CH=CH$_2$), 4.47-4.55 (1H, m, $\underline{H_\alpha}$), 3.60-3.80 (2H, m, $\underline{H_\gamma}$), 3.24 (1H, t, J = 3.0 Hz, -O$\underline{H}$), 2.12-2.23 (1H, m, $\underline{H_\beta}$), 1.60-1.73 (1H, m, $\underline{H_\beta}$), 1.45 (9H, s, $\underline{\text{Boc}}$) ppm.

General phosphorylation procedure



A solution of the specified alcohol (1 mmol) in DCM (5 mL) was added dropwise to a solution of phosphorous (V) oxychloride (1.5 mmol) and triethylamine (1.5 mmol) in DCM (10 mL). After stirring for 4 hrs, allyl alcohol (4 mmol) and triethylamine (4 mmol) were added sequentially, and the mixture stirred for 18 hrs. The volatiles were then removed *in vacuo*, and the residue suspended in THF (10 mL). After stirring for 15 min, the precipitated triethylamine hydrochloride was removed by filtration and washed with THF (10 mL), and the combined organics concentrated *in vacuo*. The residue was purified by flash column chromatography and pure fractions combined to give the specified product. Phosphorous NMR is provided for representative compounds.

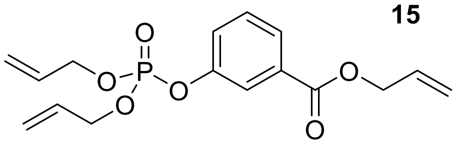
Phosphorylation – Tyrosine analogues



3

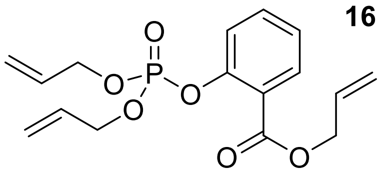
Run on **2** on a 5.6 mmol scale. Purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. A yield of 0.74 g, 2.2 mmol (40 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (2H, dd, *J* = 8.4, 0.6 Hz, Ar$\underline{H}$2), 7.29 (2H, dd, *J* = 8.4, 0.6 Hz, Ar$\underline{H}$3), 5.89-6.09 (3H, m, $-C\underline{H}=CH_2$), 5.35-5.44 (3H, m, $-CH=C\underline{H_2}$), 5.25-5.32 (3H, m, $-CH=C\underline{H_2}$), 4.81 (1H, ddd, J_1 = 5.6 Hz, J_2 = J_3 = 1.4 Hz, $-C\underline{H_2}CH=CH_2$), 4.63-4.68 (2H, m, $-C\underline{H_2}CH=CH_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.34 ($-\underline{C}O_2$All), 154.26 (d, *J* = 6.7 Hz, Ar$\underline{C}$4), 132.10 ($-\underline{C}H=CH_2$), 131.89 ($-\underline{C}H=CH_2$), 131.83 ($-\underline{C}H=CH_2$), 131.62 (Ar$\underline{C}$2), 127.02 (Ar$\underline{C}$1), 119.92 ($-CH=\underline{C}H_2$), 119.87 ($-CH=\underline{C}H_2$), 118.92 (Ar$\underline{C}$3), 118.34 ($-CH=\underline{C}H_2$), 69.06 ($-\underline{C}H_2CH=CH_2$), 69.00 ($-\underline{C}HCH=CH_2$), 65.64 ($-\underline{C}H_2CH=CH_2$) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = -6.12 ppm; IR (υ_{max}, film): 3084, 2022, 2948, 2887, 1718, 1649, 1603, 1505, 1458, 1424, 1414, 1362, 1266, 1220, 1163, 1095, 1013 cm^{-1}; HRMS m/z (ESI+): Found: 339.1002 (M+H), Calc.: 339.0998 ($C_{16}H_{20}O_6P$).

The reaction was amenable to synthesis on a 5 g scale (28 mmol), providing a yield of 4.5 g, 13.3 mmol (48 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (2H, dd, *J* = 8.5, 0.6 Hz, Ar$\underline{H}$2), 7.25 (2H, dd, *J* = 8.5, 0.6 Hz, Ar$\underline{H}$3), 5.84-6.06 (3H, m, $-C\underline{H}=CH_2$), 5.31-5.40 (3H, m, $-CH=C\underline{H_2}$), 5.22-5.29 (3H, m, $-CH=C\underline{H_2}$), 4.80 (1H, ddd, J_1 = 5.6 Hz, J_2 = J_3 = 1.4 Hz, $-C\underline{H_2}CH=CH_2$), 4.59-4.67 (2H, m, $-C\underline{H_2}CH=CH_2$) ppm;

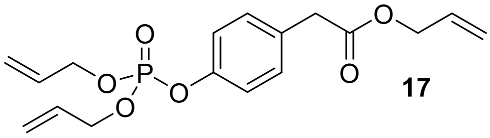


15

Run on **4** on a 10 mmol scale. Purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. A yield of 1.8 g, 5.3 mmol (53 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.91 (2H, m, *J* = 8.4 Hz, Ar$\underline{H}$2 and Ar$\underline{H}$6), 7.37-7.49 (2H, m, Ar$\underline{H}$4 and Ar$\underline{H}$5), 5.87-6.07 (3H, m, $-C\underline{H}=CH_2$), 5.33-5.43 (3H, m, $-CH=C\underline{H_2}$), 5.24-5.31 (3H, m, $-CH=C\underline{H_2}$), 4.82 (1H, ddd, J_1 = 5.6 Hz, J_2 = J_3 = 1.4 Hz, $-C\underline{H_2}CH=CH_2$), 4.62-4.67 (2H, m, $-C\underline{H_2}CH=CH_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.16 ($-\underline{C}O_2$All), 150.60 (d, *J* = 6.8 Hz, Ar$\underline{C}$3), 131.97 ($-\underline{C}H=CH_2$), 131.89 ($-\underline{C}H=CH_2$), 129.77 (Ar$\underline{C}$5), 126.36 (Ar$\underline{C}$1), 124.72 (d, *J* = 4.5 Hz, Ar$\underline{C}$4), 121.30 (Ar$\underline{C}$2/6), 121.24 (Ar$\underline{C}$2/6), 68.95 (d, *J* = 5.9 Hz, $-\underline{C}H_2CH=CH_2$), 65.81 ($-\underline{C}H_2CH=CH_2$) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = -5.66 ppm; IR (υ_{max}, film): 3084, 2947, 2890, 1721, 1649, 1587, 1486, 1443, 1362, 1292, 1266, 1202, 1097, 1021, 1006 cm^{-1}; HRMS m/z (ESI+): Found: 361.0829 (M+Na), Calc.: 361.0817($C_{16}H_{19}NaO_6P$).

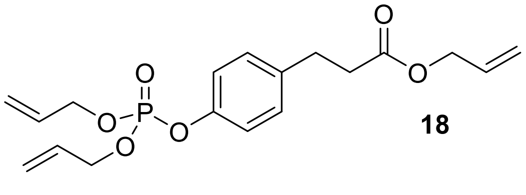


16 Run on **5** on a 1.1 mmol scale. Purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. A yield of 110 mg, 0.32 mmol (30 %) was obtained as a colourless oil. ^{1}H (400 MHz, CDCl$_3$): δ = 7.83 (1H, dd, J = 7.8, 2.5 Hz, Ar$\underline{H}$6), 7.36-7.46 (2H, m, Ar$\underline{H}$4 and Ar$\underline{H}$5), 7.16 (2H, dd, J = 7.0, 2.4 Hz, Ar$\underline{H}$3), 5.80-6.02 (3H, m, -C$\underline{H}$=CH$_2$), 5.25-5.37 (3H, m, -CH=C$\underline{H_2}$), 5.13-5.23 (3H, m, -CH=C$\underline{H_2}$), 4.73 (1H, ddd, J_1 = 5.6 Hz, J_2 = J_3 = 1.4 Hz, -C$\underline{H_2}$CH=CH$_2$), 4.57-4.63 (2H, m, -C$\underline{H_2}$CH=CH$_2$) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 164.46 (-$\underline{C}$O$_2$All), 149.65 (d, J = 6.6 Hz, Ar$\underline{C}$2), 133.60 (Ar$\underline{C}$4), 132.21 (-$\underline{C}$H=CH$_2$), 132.14 (-$\underline{C}$H=CH$_2$), 132.05 (-$\underline{C}$H=CH$_2$), 131.677 (Ar$\underline{C}$6), 124.95 (Ar$\underline{C}$3), 123.05 (d, J = 6.2 Hz Ar$\underline{C}$1), 121.61 (d, J = 2.6 Hz, Ar$\underline{C}$3), 118.47 (-CH=$\underline{C}$H$_2$), 69.01 (-$\underline{C}$H$_2$CH=CH$_2$), 68.95 (-$\underline{C}$H$_2$CH=CH$_2$), 65.83 (-$\underline{C}$HCH=CH$_2$) ppm; ^{31}P (160 MHz, CDCl$_3$): δ = -6.35 ppm; IR (υ_{max}, film): 3084, 3021, 2985, 2947, 2887, 1727, 1649, 1603, 1582, 1488, 1450, 1295, 1287, 1250, 1219, 1129, 1079, 1020 cm^{-1}; HRMS m/z (ESI+): Found: 339.1002 (M+H), Calc.: 339.0998 ($C_{16}H_{20}O_6P$).



17

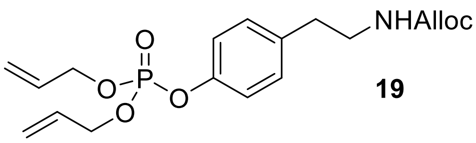
Run on **6** on a 11.9 mmol scale. Purified by flash column chromatography, eluting with 30-40 % EtOAc:Hexane. A yield of 1.8 g, 5.1 mmol (43 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.27 (2H, d, J = 9.0 Hz, Ar$\underline{H}$2), 7.29 (2H, dd, J = 9.0, 1.1 Hz, Ar$\underline{H}$3), 5.85-6.00 (3H, m, -C$\underline{H}$=CH$_2$), 5.34-5.41 (2H, m, -CH=C$\underline{H_2}$), 5.20-5.31 (4H, m, -CH=C$\underline{H_2}$), 4.54-4.67 (6H, m, -C$\underline{H_2}$CH=CH$_2$), 3.63 (2H, s, -C$\underline{H_2}$CO$_2$All) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.94 (-$\underline{C}$O$_2$All), 149.74 (d, J = 6.9 Hz, Ar$\underline{C}$4), 132.11 (-$\underline{C}$H=CH$_2$), 132.04 (-$\underline{C}$H=CH$_2$), 131.91 (-$\underline{C}$H=CH$_2$), 130.78 (Ar$\underline{C}$1), 130.60 (Ar$\underline{C}$2), 120.15 (-CH=$\underline{C}$H$_2$), 120.10 (-CH=$\underline{C}$H$_2$), 118.65 (Ar$\underline{C}$3), 118.37 (-CH=$\underline{C}$H$_2$), 68.14 (d, J = 5.4 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 65.54 (-$\underline{C}$H$_2$CH=CH$_2$), 40.51 (-$\underline{C}$H$_2$CO$_2$All) ppm; IR (υ_{max}, film): 3082, 2948, 2088, 1727, 1649, 1603, 1582, 1488, 1450, 1425, 1361, 1297, 1287, 1220, 1078, 1020 cm^{-1}; HRMS m/z (ESI+): Found: 375.0969 (M+Na), Calc.: 375.0968 ($C_{17}H_{21}NaO_6P$).



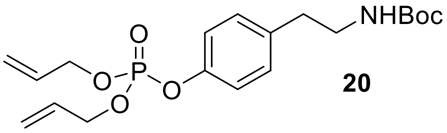
18

Run on **7** on a 8.7 mmol scale. Purified by flash column chromatography, eluting with 30 % EtOAc:Hexane. A yield of 1.7 g, 4.8 mmol (55 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.11-7.20 (4H, m, Ar$\underline{H}$2 & Ar$\underline{H}$3), 5.83-6.00 (3H, m, -C$\underline{H}$=CH$_2$), 5.30-5.41 (3H, m, -CH=C$\underline{H_2}$), 5.20-5.29 (3H, m, -CH=C$\underline{H_2}$), 4.61-4.67 (4H, m, -C$\underline{H_2}$CH=CH$_2$), 4.58 (2H, ddd, J_1 = 5.7 Hz, J_2 = J_3 = 1.4 Hz, -C$\underline{H_2}$CH=CH$_2$), 2.94 (2H, t, J = 7.7 Hz, -C$\underline{H_2}$Ar), 2.64 (2H, d, J = 7.7 Hz, -C$\underline{H_2}$CO$_2$All) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 172.31 (-$\underline{C}$O$_2$All), 149.06 (d, J = 6.9 Hz, Ar$\underline{C}$4), 137.32 (Ar$\underline{C}$1), 132.16 (-$\underline{C}$H=CH$_2$), 132.08 (-$\underline{C}$H=CH$_2$), 129.55 (Ar$\underline{C}$2), 120.06 (-CH=$\underline{C}$H$_2$), 120.02 (-CH=$\underline{C}$H$_2$), 118.59 (Ar$\underline{C}$3), 118.32 (-CH=$\underline{C}$H$_2$), 68.77 (d, J = 5.6 Hz, -

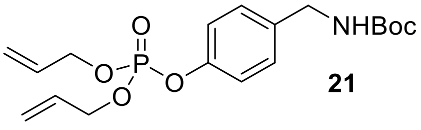
$\underline{C}H_2CH=CH_2$), 65.19 (-$\underline{C}H_2CH=CH_2$), 35.79 (-$\underline{C}H_2CO_2All$), 30.16 (-$\underline{C}H_2Ar$) ppm; IR (υ_{max}, film): 3080, 2984, 2943, 1733, 1649, 1608, 1507, 1454, 1424, 1377, 1277, 1214, 1165, 1099, 1016 cm^{-1}; HRMS m/z (ESI+): Found: 389.1145 (M+Na), Calc.: 389.1130 ($C_{18}H_{23}NaO_6P$).


19

Run on **8** on a 0.7 mmol scale. Purified by flash column chromatography, eluting with 30-50 % EtOAc:Hexane. A yield of 115 mg, 0.3 mmol (44 %) was obtained as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.13 (4H, app s, Ar$\underline{H}$2 & Ar$\underline{H}$3), 7.29 (2H, dd, *J* = 8.4, 0.6 Hz, Ar$\underline{H}$3), 5.83-5.98 (3H, m, -$C\underline{H}=CH_2$), 5.16-5.39 (6H, m, -$CH=C\underline{H}_2$), 4.98 (1H, br t, *J* = 6.7 Hz, -N$\underline{H}$), 4.59-4.66 (4H, m, -$C\underline{H}_2CH=CH_2$), 4.53 (2H, d, *J* = 5.6 Hz, -$C\underline{H}_2CH=CH_2$), 3.38 (2H, dt, $J_1 = J_2$ = 6.7 Hz, -$C\underline{H}_2$NHAlloc), 2.77 (2H, t, *J* = 6.7 Hz, -$C\underline{H}_2Ar$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.91 (-$NH\underline{C}O_2All$), 149.19 (d, *J* = 6.9 Hz, Ar$\underline{C}$4), 135.72 (Ar$\underline{C}$1), 132.92 (-$\underline{C}H=CH_2$), 132.10 (-$\underline{C}H=CH_2$), 132.03 (-$\underline{C}H=CH_2$), 129.99 (Ar$\underline{C}$2), 120.15 (-$CH=\underline{C}H_2$), 120.10 (-$CH=\underline{C}H_2$), 118.63 (Ar$\underline{C}$3), 117.57 (-$CH=\underline{C}H_2$), 68.79 (d, *J* = 5.8 Hz, -$\underline{C}H_2CH=CH_2$), 65.43 (-$\underline{C}H_2CH=CH_2$), 42.14 (-$\underline{C}H_2$NHAlloc), 35.36 (-$\underline{C}H_2Ar$) ppm; IR (υ_{max}, film): 3320, 3082, 2940, 2883, 1707, 1648, 1607, 1529, 1506, 1459, 1424, 1412, 1365, 1249, 1214, 1167, 1138, 1097, 1015 cm^{-1}; HRMS m/z (ESI+): Found: 382.1412 (M+H), Calc.: 382.1410 ($C_{18}H_{25}NO_6P$).

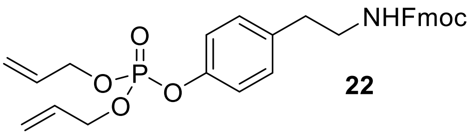

20

Run on **9** on a 5.4 mmol scale. Purified by flash column chromatography, eluting with 20-40 % EtOAc:Hexane. A yield of 1.2 g, 3.0 mmol (57 %) was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16 (4H, app s, Ar$\underline{H}$), 5.90-6.01 (2H, m, -$C\underline{H}=CH_2$), 5.38 (2H, ddt, J_1 = 17.1 Hz, $J_2 = J_3$ = 1.5 Hz, -$CH=C\underline{H}_2$), 5.24-5.30 (2H, m, -$CH=C\underline{H}_2$), 4.62-4.69 (4H, m, -$C\underline{H}_2CH=CH_2$), 4.52-4.60 (1H, m, -N$\underline{H}$), 3.35 (2H, td, *J* = 6.9, 6.4 Hz, -$C\underline{H}_2$NHBoc), 2.77 (2H, t, *J* = 6.9 Hz, -$C\underline{H}_2Ar$), 1.44 (9H, s, $\underline{Boc}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.82 (-$\underline{C}O_2R$), 149.19 (d, *J* = 7.1 Hz, Ar$\underline{C}$4), 135.91 (Ar$\underline{C}$1), 132.11 (d, *J* = 6.9 Hz, -$\underline{C}H=CH_2$), 130.00 (Ar$\underline{C}$2), 120.11 (d, *J* = 4.8 Hz, -$CH=\underline{C}H_2$), 118.61 (Ar$\underline{C}$3), 79.27 (-$\underline{C}Me_3$), 68.79 (d, *J* = 5.7 Hz, -$\underline{C}H_2CH=CH_2$), 47.73 (-$\underline{C}H_2$NHBoc), 35.46 (-$\underline{C}H_2Ar$), 28.39 (-$C\underline{Me}_3$) ppm; IR (υ_{max}, film): 3336, 2977, 2935, 1708, 1608, 1507, 1458, 1391, 1365, 1273, 1252, 1215, 1167, 1099, 1014 cm^{-1}; HRMS m/z (ESI+): Found: 415.1990 (M+H), Calc.: 415.1992 ($C_{19}H_{29}NO_6P$).


21

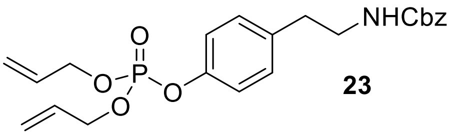
Run on **10** on a 4.5 mmol scale. Purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. A yield of 0.98 g, 2.6 mmol (57 %) was obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$2), 7.16-7.20 (2H, m, Ar$\underline{H}$3), 5.88-6.01 (2H, m, -$C\underline{H}=CH_2$), 5.34-5.41 (2H, m, -$CH=C\underline{H}_2$), 5.24-5.29 (2H, m, -$CH=C\underline{H}_2$), 4.91 (1H, br s, -N$\underline{H}$), 4.52-4.67 (4H, m, -$C\underline{H}_2CH=CH_2$), 4.28 (2H, br d, *J* = 5.7 Hz, -$C\underline{H}_2$NHBoc), 1.46 (9H, s, $\underline{Boc}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.84 (-$\underline{C}O_2R$), 149.79 (d, *J* = 6.4 Hz, Ar$\underline{C}$4), 135.94

(Ar$\underline{C}$1), 132.53 (d, J = 6.9 Hz, -$\underline{C}$H=CH$_2$), 128.81 (Ar$\underline{C}$2), 120.14 (d, J = 4.8 Hz, -CH=$\underline{C}$H$_2$), 118.65 (Ar$\underline{C}$3), 79.65 (-$\underline{C}$Me$_3$), 68.81 (d, J = 5.6 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 44.00 (-$\underline{C}$H$_2$NHBoc), 28.39 (-C$\underline{\text{Me}}_3$) ppm; IR (υ_{max}, film): 3328, 2978, 2934, 1708, 1607, 1506, 1458, 1425, 1391, 1365, 1268, 1252, 1214, 1162, 1098, 1014 cm^{-1}; HRMS m/z (ESI+): Found: 401.1839 (M+H), Calc.: 401.1836 ($C_{18}H_{27}NO_6P$).



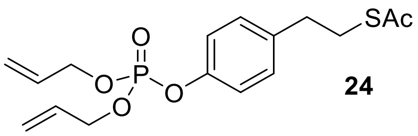
22

Run on **11** on a 180 μmol scale. Purified by flash column chromatography, eluting with 20-50 % EtOAc:Hexane. A yield of 72 mg, 138 μmol (77 %) was obtained. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.77 (2H, d, J = 7.3 Hz, $\underline{\text{Fmoc}}$), 7.57 (2H, d, J = 7.3 Hz, $\underline{\text{Fmoc}}$), 7.40 (2H, dd, J_1 = J_2 = 7.3 Hz, $\underline{\text{Fmoc}}$), 7.31 (2H, dd, J_1 = J_2 = 7.3 Hz, $\underline{\text{Fmoc}}$), 7.11-7.24 (4H, m, Ar$\underline{H}$), 5.89-6.01 (2H, m, -C$\underline{H}$=CH$_2$), 5.37 (2H, ddt, J_1 = 17.1 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H}_2$), 5.26 (2H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.5 Hz -CH=C$\underline{H}_2$), 4.78 (1H, br t, J = 7.1 Hz, -N$\underline{H}$), 4.50-4.69 (4H, m, -C$\underline{H}_2$CH=CH$_2$), 4.40 (2H, d, J = 6.9 Hz, $\underline{\text{Fmoc}}$), 4.20 (1H, t, J = 6.9 Hz, $\underline{\text{Fmoc}}$), 3.41 (2H, dt, J = 7.1, 6.9 Hz, -C$\underline{H}_2$NHFmoc), 2.77 (2H, t, J = 6.9 Hz, -C$\underline{H}_2$Ar) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.38 (-$\underline{C}$O$_2$R), 149.47 (Ar$\underline{C}$4), 144.02 ($\underline{\text{Fmoc}}$), 141.43 ($\underline{\text{Fmoc}}$), 132.19 (d, J = 6.9 Hz, -$\underline{C}$H=CH$_2$), 130.14 (Ar$\underline{C}$2), 127.78 ($\underline{\text{Fmoc}}$), 127.13 ($\underline{\text{Fmoc}}$), 125.11 ($\underline{\text{Fmoc}}$), 120.28 (d, J = 5.0 Hz, Ar$\underline{C}$3), 120.07 (-CH=$\underline{C}$H$_2$), 118.75 ($\underline{\text{Fmoc}}$), 118.38 (Ar$\underline{C}$1), 68.91 (d, J = 5.7 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 66.63 ($\underline{\text{Fmoc}}$), 47.38 ($\underline{\text{Fmoc}}$), 42.30 (-$\underline{C}$H$_2$NHFmoc), 35.52 (-$\underline{C}$H$_2$Ar) ppm; IR (υ_{max}, film): 3318, 3066, 2942, 1716, 1608, 1537, 1506, 1450, 1424, 1251, 1216, 1167, 1138, 1101, 1017 cm^{-1}; HRMS m/z (ESI+): Found: 542.1709 (M+Na), Calc.: 542.1703 ($C_{29}H_{30}NaNO_6P$).

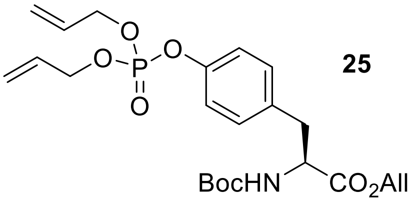


23

Run on **12** on a 180 μmol scale. Purified by flash column chromatography, eluting with 30-50 % EtOAc:Hexane. A yield of 38 mg, 88 μmol (49 %) was obtained. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.31 (5H, app s, $\underline{\text{Cbz}}$), 7.10 (4H, app s, Ar$\underline{H}$), 5.84-5.97 (2H, m, -C$\underline{H}$=CH$_2$), 5.33 (2H, ddt, J_1 = 17.1 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H}_2$), 5.22 (2H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.5 Hz -CH=C$\underline{H}_2$), 5.05 (2H, s, $\underline{\text{Cbz}}$), 4.92-4.99 (1H, br m, -N$\underline{H}$), 4.60 (4H, ddd, J_1 = 7.8 Hz, J_2 = J_3 = 1.5 Hz -C$\underline{H}_2$CH=CH$_2$), 3.33-3.41 (2H, m, -C$\underline{H}_2$NHCbz), 2.75 (2H, t, J = 6.9 Hz, -C$\underline{H}_2$Ar) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 156.79 (-$\underline{C}$O$_2$R), 149.65 (d, J = 7.2 Hz, Ar$\underline{C}$4), 136.99 (Ar$\underline{C}$1), 136.13 ($\underline{\text{Cbz}}$), 132.52 (d, J = 7.0 Hz, -$\underline{C}$H=CH$_2$), 130.46 (Ar$\underline{C}$2), 128.96 ($\underline{\text{Cbz}}$), 128.56 ($\underline{\text{Cbz}}$) 120.59 (d, J = 4.8 Hz, -CH=$\underline{C}$H$_2$), 119.10 (Ar$\underline{C}$3), 69.26 (d, J = 5.8 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 67.06 ($\underline{\text{Cbz}}$), 42.64 (-$\underline{C}$H$_2$NHR), 35.78 (-$\underline{C}$H$_2$Ar) ppm; IR (υ_{max}, film): 3315, 2940, 2885, 1713, 1607, 1528, 1506, 1455, 1425, 1366, 1249, 1214, 1167, 1135, 1098, 1015 cm^{-1}; HRMS m/z (ESI+): Found: 432.1569 (M+H), Calc.: 432.1571 ($C_{22}H_{27}NO_6P$).

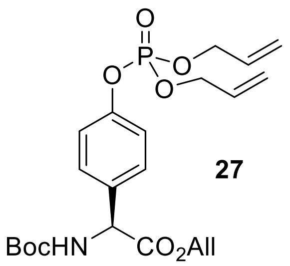

24

Run on **14** on a 1.5 mmol scale. The phosphorylation was quenched with 2.5 equiv allyl alcohol and triethylamine to minimise alcoholysis of the thioester. Purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. A yield of 287 mg, 0.85 μmol (57 %) was obtained. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.06-7.18 (4H, m, Ar$\underline{H}$), 5.82-5.96 (2H, m, -C$\underline{H}$=CH$_2$), 5.13-5.39 (4H, m, -CH=C$\underline{H}_2$), 4.43-4.67 (4H, m, -C$\underline{H}_2$CH=CH$_2$), 2.99-3.07 (2H, m, -C$\underline{H}_2$Ar), 2.80 (2H, t, *J* = 7.4 Hz, -C$\underline{H}_2$SAc), 2.30 (3H, s, -S$\underline{\text{Ac}}$); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 195.77 (-$\underline{C}$OMe), 149.23 (d, *J* = 6.6 Hz, Ar$\underline{C}$4), 136.91 (Ar$\underline{C}$1), 132.10 (d, *J* = 7.3 Hz, -$\underline{C}$H=CH$_2$), 129.89 (Ar$\underline{C}$2), 120.19 (d, *J* = 4.5 Hz, -CH=$\underline{C}$H$_2$), 118.67 (Ar$\underline{C}$3), 68.99 (d, *J* = 5.7 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 35.19 (-$\underline{C}$H$_2$Ar), 30.70 (-$\underline{C}$H$_2$SAc), 30.50 (-CO$\underline{\text{Me}}$) ppm; IR (υ_{max}, film): 2926, 1689, 1507, 1425, 1355, 1216, 1169, 1134, 1100, 1028, 1017 cm^{-1}; HRMS m/z (ESI+): Found: 357.0913 (M+H), Calc.: 357.0920 (C$_{16}$H$_{22}$O$_5$PS).


25

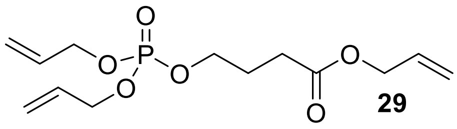
Run on **64** on a 3.5 mmol scale. Purified by flash column chromatography, eluting with 20-40 % EtOAc:Hexane. A yield of 570 mg, 1.2 mmol (35 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.99-7.11 (4H, m, Ar$\underline{H}$2 & Ar$\underline{H}$3), 5.72-5.92 (3H, m, -C$\underline{H}$=CH$_2$), 5.13-5.34 (6H, m, -CH=C$\underline{H}_2$), 4.93 (1H, br d, *J* = 6.8 Hz, -N$\underline{H}$), 4.43-4.60 (7H, m, -C$\underline{H}_2$CH=CH$_2$ & $\underline{H}_\alpha$), 2.91-3.08 (2H, m, $\underline{H}_\beta$), 1.34 (9H, s, $\underline{\text{Boc}}$) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.36 (-$\underline{C}$O$_2$All), 155.09 (-$\underline{C}$O$_2{}^t$Bu), 149.67 (d, *J* = 6.9 Hz, Ar$\underline{C}$4), 132.91 (Ar$\underline{C}$1), 132.07 (d, *J* = 6.9 Hz, -$\underline{C}$H=CH$_2$), 131.42 (-$\underline{C}$H=CH$_2$), 130.64 (Ar$\underline{C}$2), 120.05 (d, *J* = 4.6 Hz, -CH=$\underline{C}$H$_2$), 119.07 (-CH=$\underline{C}$H$_2$), 118.64 (Ar$\underline{C}$3), 79.98 (-$\underline{C}$Me$_3$), 68.80 (d, *J* = 5.6 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 65.98 (-$\underline{C}$H$_2$CH=CH$_2$), 54.39 ($\underline{C}_\alpha$), 37.52 ($\underline{C}_\beta$), 28.27 ($\underline{\text{Boc}}$) ppm; IR (υ_{max}, film): 3304, 3078, 2978, 2935, 2168, 1742, 1711, 1608, 1507, 1454, 1425, 1391, 1366, 1344, 1272, 1215, 1163, 1099, 1016 cm^{-1}; HRMS m/z (ESI+): Found: 504.1763 (M+Na), Calc.: 504.1758 (C$_{23}$H$_{32}$NaNO$_8$P).

The use of D-enantiomer **65** led to the production of **26**.


27

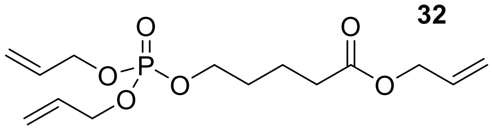
Run on **66** on a 5 mmol scale. Purified by flash column chromatography, eluting with 20-30 % EtOAc:Hexane. A yield of 1.7 g, 3.6 mmol (72 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ =7.36 (2H, d, *J* = 7.6 Hz, Ar$\underline{H}$2), 7.21 (2H, d, *J* = 7.6 Hz, Ar$\underline{H}$3) , 5.77-6.00 (3H, m, -C$\underline{H}$=CH$_2$), 5.59 (1H, br d, *J* = 7.0 Hz, -N$\underline{H}$), 5.17-5.43 (7H, m, -CH=C$\underline{H}_2$ & $\underline{H}_\alpha$), 4.53-4.68 (6H, m, -C$\underline{H}_2$CH=CH$_2$), 2.91-3.08 (2H, m, $\underline{H}_\beta$), 1.44 (9H, s, $\underline{\text{Boc}}$) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.55 (-$\underline{C}$O$_2$All), 154.70 (-$\underline{C}$O$_2{}^t$Bu), 150.55 (d, *J* = 6.7 Hz, Ar$\underline{C}$4), 133.90 (Ar$\underline{C}$1), 131.99 (d, *J* = 6.7 Hz, -$\underline{C}$H=CH$_2$), 131.22 (-$\underline{C}$H=CH$_2$), 128.58 (Ar$\underline{C}$2), 120.41 (d, *J* = 4.7 Hz, -CH=$\underline{C}$H$_2$), 118.75 (Ar$\underline{C}$3), 80.27 (-$\underline{C}Me_3$), 68.88 (d, *J* = 5.7 Hz, -$\underline{C}H_2CH=CH_2$), 66.24 (-$\underline{C}H_2CH=CH_2$), 56.98 ($\underline{C_\alpha}$), 28.29 ($\underline{Boc}$) ppm; IR (υ_{max}, film): 2980, 1744, 1711, 1608, 1505, 1457, 1367, 1275, 1218, 1161, 1098, 1016 cm^{-1}; HRMS m/z (ESI+): Found: 490.1606 (M+Na), Calc.: 490.1601 ($C_{22}H_{30}NaNO_8P$).

Phosphorylation – Serine analogues



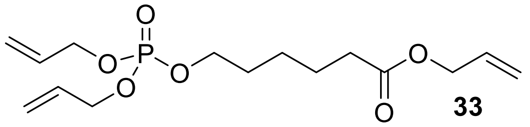
29

Run on **28** on a 13.8 mmol scale. Purified by flash column chromatography, eluting with 40 % EtOAc:Hexane. A yield of 1.7 g, 5.6 mmol (41 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.79-5.94 (3H, m, -$C\underline{H}=CH_2$), 5.26-5.36 (3H, m, -$CH=C\underline{H_2}$), 5.15-5.25 (3H, m, -$CH=C\underline{H_2}$), 4.44-4.45 (6H, m, -$C\underline{H_2}CH=CH_2$), 4.01-4.08 (2H, m, -$C\underline{H_2}OPO_3All_2$), 2.42 (2H, t, *J* = 7.3 Hz, -$C\underline{H_2}CO_2All$), 1.92-2.00 (2H, m, -$C\underline{H_2}CH_2CO_2All$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.26 (-$\underline{C}O_2All$), 132.41 (-$\underline{C}H=CH_2$), 132.34 (-$\underline{C}H=CH_2$), 132.03 (-$\underline{C}H=CH_2$), 118.21 (-$CH=\underline{C}H_2$), 118.19 (-$CH=\underline{C}H_2$), 118.04 (-$CH=\underline{C}H_2$), 68.06 (d, *J* = 5.5 Hz, -$\underline{C}H_2CH=CH_2$), 66.61 (d, *J* = 5.9 Hz, -$\underline{C}H_2$OPO3All_2), 65.11 (-$\underline{C}H_2CH=CH_2$), 30.00 (-$\underline{C}H_2CO_2All$), 25.48 (-$\underline{C}H_2CH_2CO_2All$) ppm; IR ($\upsilon_{max}$, film): 2877, 1727, 1607, 1508, 1438, 1206, 1158, 1104, 1053 cm^{-1}; HRMS m/z (ESI+): Found: 305.1152 (M+H), Calc.: 305.1154 ($C_{13}H_{22}O_6P$).



32

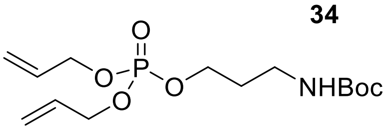
Run on **67** on a 1.2 mmol scale. Purified by flash column chromatography, eluting with 40 % EtOAc:Hexane. A yield of 180 mg, 0.52 mmol (44 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81-5.97 (3H, m, -$C\underline{H}=CH_2$), 5.28-5.38 (3H, m, -$CH=C\underline{H_2}$), 5.17-5.27 (3H, m, -$CH=C\underline{H_2}$), 4.47-4.54 (6H, m, -$C\underline{H_2}CH=CH_2$), 3.99-4.08 (2H, m, -$C\underline{H_2}OPO_3All_2$), 2.35 (2H, t, *J* = 6.9 Hz, -$C\underline{H_2}CO_2All$), 1.64-1.76 (4H, m, -$C\underline{H_2}C\underline{H_2}CH_2CO_2All$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.74 (-$\underline{C}O_2All$), 132.50 (-$\underline{C}H=CH_2$), 132.41 (-$\underline{C}H=CH_2$), 132.14 (-$\underline{C}H=CH_2$), 118.19 (-$CH=\underline{C}H_2$), 118.18 (-$CH=\underline{C}H_2$), 118.08 (-$CH=\underline{C}H_2$), 68.03 (d, *J* = 5.6 Hz, -$\underline{C}H_2CH=CH_2$), 67.21 (d, *J* = 6.0 Hz, -$\underline{C}H_2$OPO3All_2), 65.01 (-$\underline{C}H_2CH=CH_2$), 33.45 (-$\underline{C}H_2CO_2All$), 29.56 (d, *J* = 6.9 Hz, -$\underline{C}H_2CH_2OPO_3All_2$), 20.92 (-$\underline{C}H_2CH_2CO_2All$) ppm; IR ($\upsilon_{max}$, film): 3080, 2948, 1734, 1649, 1458, 1425, 1365, 1267, 1164, 1098, 1015 cm^{-1}; HRMS m/z (ESI+): Found: 319.1316 (M+H), Calc.: 319.1311 ($C_{14}H_{24}O_6P$).



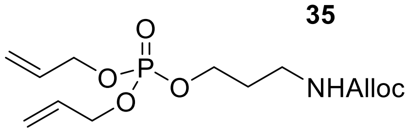
33

Run on **68** on a 10 mmol scale. Purified by flash column chromatography, eluting with 30-40 % EtOAc:Hexane. A yield of 1.5 g, 4.5 mmol (45 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.83-5.97 (3H, m, -$C\underline{H}=CH_2$), 5.29-5.38 (3H, m, -$CH=C\underline{H_2}$), 5.17-5.27 (3H, m, -$CH=C\underline{H_2}$), 4.47-4.56 (6H, m, -$C\underline{H_2}CH=CH_2$), 3.99-4.06 (2H, m, -$C\underline{H_2}OPO_3All_2$), 2.32 (2H, t, *J* = 7.4 Hz, -$C\underline{H_2}CO_2All$), 1.59-1.72 (4H, m, -

$C\underline{H}_2CH_2C\underline{H}_2CH_2CO_2All$), 1.35-1.45 (2H, m, $-C\underline{H}_2CH_2CH_2CO_2All$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.01 ($-\underline{C}O_2All$), 132.51 ($-\underline{C}H=CH_2$), 132.46 ($-\underline{C}H=CH_2$), 132.20 ($-\underline{C}H=CH_2$), 118.14 ($-CH=\underline{C}H_2$), 118.09 ($-CH=\underline{C}H_2$), 118.08 ($-CH=\underline{C}H_2$), 68.01 (d, *J* = 5.4 Hz, $-\underline{C}H_2CH=CH_2$), 67.52 (d, *J* = 6.0 Hz, $-\underline{C}H_2OPO3All_2$), 64.96 ($-\underline{C}H_2CH=CH_2$), 33.97 ($-\underline{C}H_2CO_2All$), 29.87 (d, *J* = 7.0 Hz, $-\underline{C}H_2CH_2OPO_3All_2$), 24.49 ($-\underline{C}H_2CH_2CO_2All$), 24.37 ($-\underline{C}H_2CH_2CH_2CO_2All$) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = -0.15 ppm; IR ($υ_{max}$, film): 3085, 2943, 1734, 1649, 1459, 1425, 1380, 1267, 1161, 1100,1024 cm^{-1}; HRMS m/z (ESI+): Found: 333.1478 (M+H), Calc.: 333.1467 ($C_{15}H_{26}NO_6P$).

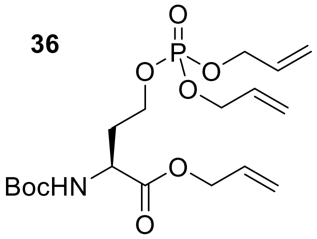


34 Run on **30** on a 5.7 mmol scale. Purified by flash column chromatography, eluting with 30-50 % EtOAc:Hexane. A yield of 470 mg, 1.4 mmol (25 %) was obtained as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.85-5.99 (2H, m, $-C\underline{H}=CH_2$), 5.20-5.42 (4H, m, $-CH=C\underline{H}_2$ and $-N\underline{H}$), 4.98 (1H, br s, $-N\underline{H}$), 4.46-4.56 (4H, m, $-C\underline{H}_2CH=CH_2$), 4.09 (2H, dt, *J* = 7.6, 6.0 Hz, $-C\underline{H}_2OPO_3All_2$), 3.18-3.26 (2H, m, $-C\underline{H}_2NHBoc$), 1.89-1.79 (2H, m, $-C\underline{H}_2CH_2OPO_3All_2$), 1.41 (9H, s, $\underline{Boc}$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.96 ($-\underline{C}O_2{}^tBu$), 132.34 (d, *J* = 6.8 Hz, $-\underline{C}H=CH_2$), 118.39 ($-CH=\underline{C}H_2$), 79.14 ($-\underline{C}Me_3$), 68.20 (d, *J* = 5.6 Hz, $-\underline{C}H_2CH=CH_2$), 65.35 (d, *J* = 5.8 Hz, $-\underline{C}H_2OPO3All_2$), 36.81 ($-\underline{C}H_2NHBoc$), 30.32 (d, *J* = 5.9 Hz, $-\underline{C}H_2CH_2OPO_3All_2$), 28.36 ($-C\underline{Me}_3$) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = 0.15 ppm; IR ($υ_{max}$, film): 3322, 2977, 2936, 1707, 1522, 1456, 1425, 1391, 1365, 1267, 1249, 1168, 1100, 1007cm^{-1}; HRMS m/z (ESI+): Found: 358.1387 (M+Na), Calc.: 358.1390 ($C_{14}H_{26}NaNO_6P$).



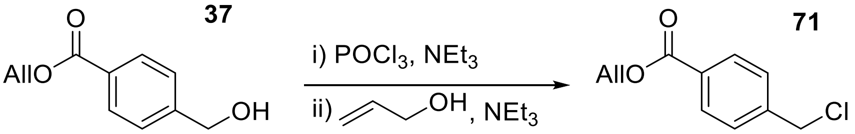
35 Run on **31** on a 1.25 mmol scale. Purified by flash column chromatography, eluting with 30-50 % EtOAc:Hexane. A yield of 140 mg, 0.44 mmol (35 %) was obtained as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.85-5.99 (3H, m, $-C\underline{H}=CH_2$), 5.17-5.42 (7H, m, $-CH=C\underline{H}_2$ and $-N\underline{H}$), 4.49-4.58 (6H, m, $-C\underline{H}_2CH=CH_2$), 4.13 (2H, dt, *J* = 7.6, 5.9 Hz, $-C\underline{H}_2OPO_3All_2$), 3.31 (2H, dt, $J_1 = J_2$ = 6.3 Hz, $-C\underline{H}_2NHAlloc$), 1.83-1.91 (2H, m, $-C\underline{H}_2CH_2OPO_3All_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.33 ($-\underline{C}O_2All$), 132.93 ($-\underline{C}H=CH_2$), 132.33 (d, *J* = 6.8 Hz, $-\underline{C}H=CH_2$), 118.46 ($-CH=\underline{C}H_2$), 117.54 ($-CH=\underline{C}H_2$), 68.29 (d, *J* = 5.5 Hz, $-\underline{C}H_2CH=CH_2$), 65.44 ($-\underline{C}H_2CH=CH_2$), 65.17 (d, *J* = 5.7 Hz, $-\underline{C}H_2OPO3All_2$), 37.20 ($-\underline{C}H_2NHAlloc$), 30.18 (d, *J* = 6.1 Hz, $-\underline{C}H_2CH_2OPO_3All_2$) ppm; IR ($υ_{max}$, film): 3309, 3084, 2947, 2897, 1702, 1648, 1533, 1460, 1425, 1245, 1145, 1094, 1067 cm^{-1}; HRMS m/z (ESI+): Found: 320.1267 (M+H), Calc.: 320.1263 ($C_{13}H_{23}NO_6P$).

36

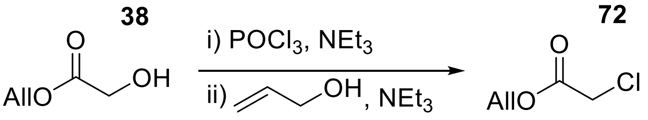


Run on **70** on a 3.8 mmol scale. Purified by flash column chromatography, eluting with 30-50 % EtOAc:Hexane. A yield of 430 mg, 1.1 mmol (27 %) was obtained as a colourless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.79-5.94 (3H, m, -C$\underline{H}$=CH$_2$), 5.14-5.39 (6H, m, -CH=C$\underline{H}_2$), 4.54-4.64 (3H, m, -C$\underline{H}_2$CH=CH$_2$ & -N$\underline{H}$), 4.41-4.52 (4H, m, -C$\underline{H}_2$CH=CH$_2$), 4.32-4.40 (1H, m, $\underline{H}_\alpha$), 4.03-4.15 (2H, m, $\underline{H}_\gamma$), 2.13-2.24 (1H, m, $\underline{H}_\beta$), 1.98-2.09 (1H, m, $\underline{H}_\beta$), 1.37 (9H, s, $\underline{\text{Boc}}$) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 171.38 (-$\underline{C}$O$_2$All), 155.30 (-$\underline{C}$O$_2{}^t$Bu), 132.37 (d, *J* = 6.9 Hz, -$\underline{C}$H=CH$_2$), 131.51 (-$\underline{C}$H=CH$_2$), 118.88 (-CH=$\underline{C}$H$_2$), 118.35 (-CH=$\underline{C}$H$_2$), 80.05 (-$\underline{C}$Me$_3$), 68.22 (d, *J* = 5.5 Hz, -$\underline{C}$H$_2$CH=CH$_2$), 66.11 (-$\underline{C}$H$_2$CH=CH$_2$), 63.88 (d, *J* = 5.5 Hz, $\underline{C}_\gamma$) 50.68 ($\underline{C}_\alpha$), 32.64 (d, *J* = 7.3 Hz, $\underline{C}_\beta$), 28.26 ($\underline{\text{Boc}}$) ppm; IR (υ_{max}, film): 3287, 2978, 1737, 1710, 1649, 1510, 1456, 1366, 1250, 1158, 1102, 1003 cm^{-1}; HRMS m/z (ESI+): Found: 442.1600 (M+H), Calc.: 442.1601 ($C_{18}H_{31}NO_8P$).

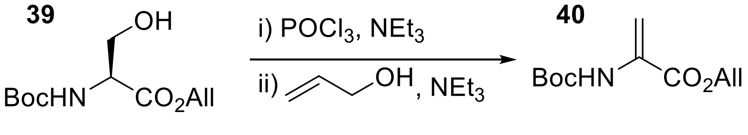
Unsuccessful phosphorylations



Run on **37** on a 3.8 mmol scale. The major product was purified by flash column chromatography, eluting with 10-20 % EtOAc:Hexane, and found to be the benzyl chloride product **71**. A yield of 705 mg, 3.33 mmol (87 %) was obtained as a colourless oil. Data were consistent with those previously reported.[17] ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.97 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$2), 7.38 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}$3), 5.95 (1H, ddt, *J* = 17.2, 10.4, 5.6 Hz, -C$\underline{H}$=CH$_2$), 5.33 (1H, ddt, J_1 = 17.2 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H}_2$), 5.21 (1H, ddt, J_1 = 10.4 Hz, J_2 = J_3 = 1.5 Hz, -CH=C$\underline{H}_2$), 4.74 (2H, ddd, J_1 = 5.6 Hz, J_2 = J_3 = 1.5 Hz, -C$\underline{H}_2$CH=CH$_2$), 4.53 (2H, s, -C$\underline{H}_2$Cl) ppm.

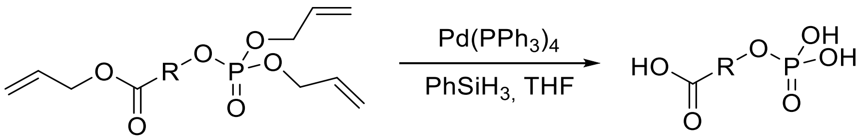


Run on **38** on a 1 mmol scale. NMR anaylsis of the crude mixture indicated formation of the alkyl chloride **72** as the major product. No further purification or characterisation was undertaken.



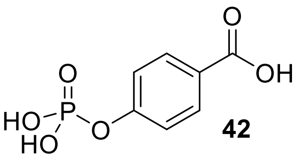
Run on **39** on a 1 mmol scale. The major product was purified by flash column chromatography, eluting with 20-40 % EtOAc:Hexane, and found to be the dehydroalanine derivative **40**, formed by dehydration. A yield of 193 mg, 0.86 mmol (86 %) was obtained as a colourless oil. Data were consistent with those previously reported.[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (1H, br s, -NH), 6.10 (1H, br s, H_β), 5.87 (1H, ddt, *J* = 17.2, 10.4, 5.7 Hz, -CH=CH_2), 5.70 (1H, d, *J* = 1.4 Hz, H_β), 5.17-5.34 (2H, m, -CH=CH_2), 5.61 (2H, dd, *J* = 5.6, 1.5 Hz, -CH_2CH=CH_2), 1.41 (9H, s, Boc) ppm.

General deprotection procedure



Allyl-protected phosphate (1 mmol) and phenylsilane (6 mmol) were dissolved in dry THF (10 mL) under nitrogen. $Pd(PPh_3)_4$ (0.05 mmol) was then added and the mixture was stirred for 2 hrs. During this time, the reaction often solidified. The mixture was then diluted with water (20 mL), and the aqueous washed with diethyl ether (2 x 20 mL) and lyophilised to provide the specified product. Phosphorous NMR is provided for representative compounds.

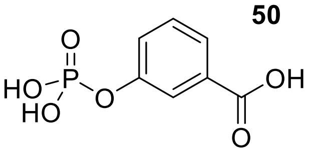
Deprotection - Tyrosine analogues



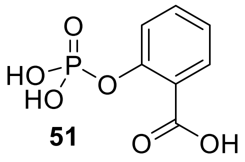
42

Run on **3** on a 1.5 mmol scale. A yield of 324 mg, 1.5 mmol (98 %) was obtained as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.96 (2H, d, *J* = 8.0 Hz, ArH2), 7.31 (2H, d, *J* = 8.0 Hz, ArH3) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 169.11 (-CO_2H), 156.65 (d, *J* = 6.3 Hz, ArC4), 132.64 (ArC2), 128.14 (ArC1), 121.15 (d, *J* = 5.0 Hz, ArC3) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = -4.15 ppm; m.p. = 187-191 ° C; IR ($υ_{max}$, solid): 2818 (v br), 2651, 2574, 2287 (br), 1683 (br), 1605, 1508, 1430, 1322, 1295, 1225, 1201, 1171, 1115, 1030 (br), 1016 cm^{-1}; HRMS m/z (ESI+): Found: 219.0053 (M+H), Calc.: 219.0053 ($C_7H_8O_6P$).

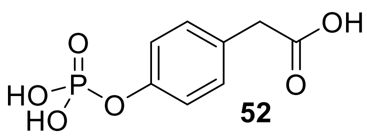
50



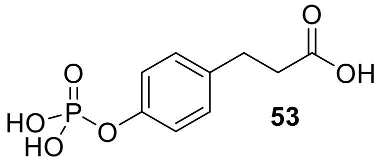
Run on **15** on a 0.34 mmol scale. A yield of 62 mg, 0.29 mmol (85 %) was obtained as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.93-7.90 (2H, m, ArH2 and ArH6), 7.43-7.51 (2H, m, ArH4 and ArH5) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 168.89 (-CO_2H), 152.93 (d, *J* = 6.5 Hz, ArH3), 133.67 (ArC1), 130.79 (ArC5), 126.90 (d, *J* = 0.8 Hz, ArC6), 126.05 (d, *J* = 4.7 Hz, ArC4), 122.55 (d, *J* = 4.7 Hz, ArC2) ppm; m.p. = 198-208 ° C; IR ($υ_{max}$, solid): 2658 (v br), 2554, 1682, 1585, 1486, 1451, 1416, 1295, 1271, 1215, 1156, 1105, 1046, 1012 cm^{-1}; HRMS m/z (ESI-): Found: 216.9897 (M-H), Calc.: 216.9902 ($C_7H_6O_6P$).


51

Run on **16** on a 0.35 mmol scale. A yield of 57 mg, 0.26 mmol (75 %) was obtained as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.75 (1H, dd, J = 7.8, 0.5 Hz, Ar$\underline{H}$6), 7.43 (1H, ddd, $J_1 = J_2$ = 7.4 Hz, J_3 = 1.8 Hz, Ar$\underline{H}$4), 7.31 (1H, ddd, J_1 = 8.3, $J_2 = J_3$ = 1.1 Hz, Ar$\underline{H}$3), 7.15 (1H, ddd, $J_1 = J_2$ = 7.6 Hz, J_3 = 1.0 Hz, Ar$\underline{H}$5) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 169.09 ($-\underline{C}O_2H$), 151.65 (d, J = 6.6 Hz, Ar$\underline{C}$2), 134.37 (d, J = 1.1 Hz, Ar$\underline{C}$4), 132.60 (Ar$\underline{C}$6), 125.62 (d, J = 0.9 Hz, Ar$\underline{C}$5), 125.53 (Ar$\underline{C}$6), 123.00 (d, J = 2.6 Hz, Ar$\underline{C}$3) ppm; m.p. = 183-186 ° C; IR ($υ_{max}$, solid): 2853 (v br), 2584, 2543, 2830 (br), 2171, 1687 (br), 1604, 1578, 1488, 1457, 1406, 1296, 1278, 1193 (br), 1159, 1096, 1087, 1020 cm^{-1}; HRMS m/z (ESI+): Found: 233.0210 (M+MeOH), Calc.: 233.0210 ($C_8H_{11}O_7P$).

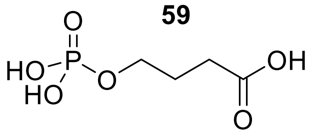

52

Run on **17** on a 4.2 mmol scale. A yield of 904 mg, 3.9 mmol (93 %) was obtained as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.25 (2H, d, J = 6.8 Hz, Ar$\underline{H}$3), 7.15 (2H, d, J = 6.8 Hz, Ar$\underline{H}$2), 3.62 (2H, s, $-C\underline{H}_2CO_2H$) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 173.91 ($-\underline{C}O_2H$), 151.90 (d, J = 6.6 Hz, Ar$\underline{C}$4), 132.06 (Ar$\underline{C}$1), 131.57 (Ar$\underline{C}$2), 121.40 (d, J = 4.5 Hz, Ar$\underline{C}$3), 40.89 ($-\underline{C}H_2CO_2H$) ppm; m.p. = 165-169 ° C; IR ($υ_{max}$, solid): 2955 (v br), 2919, 2737, 2655, 1694, 1609, 1509, 1408, 1343, 1291, 1214, 1196, 1133 cm^{-1}; HRMS m/z (ESI-): Found: 231.0070 (M-H), Calc.: 231.0059 ($C_8H_8O_6P$).

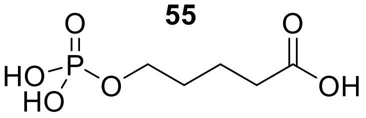

53

Run on **18** on a 1 mmol scale. A yield of 236 mg, 0.96 mmol (96 %) was obtained as a white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.23 (2H, d, J = 8.3 Hz, Ar$\underline{H}$3), 7.14 (2H, dd, J = 8.3, 1.2 Hz, Ar$\underline{H}$2), 2.90 (2H, t, J = 7.6 Hz, $-C\underline{H}_2Ar$), 2.60 (2H, t, J = 7.6 Hz, $-C\underline{H}_2CO_2H$) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 176.58 ($-\underline{C}O_2H$), 151.18 (d, J = 6.7 Hz, Ar$\underline{C}$4), 138.63 (Ar$\underline{C}$1), 130.49 (Ar$\underline{C}$2), 121.35 (d, J = 4.6 Hz, Ar$\underline{C}$3), 36.73 ($-\underline{C}H_2CO_2H$), 31.25 ($-\underline{C}H_2Ar$) ppm; ^{31}P (160 MHz, $CDCl_3$): δ = -3.38 ppm; m.p. = 148-152 ° C; IR ($υ_{max}$, solid): 2866 (v br), 2620, 2291, 1694, 1608, 1509, 1432, 1411, 1324, 1308, 1270, 1209, 1179, 1134, 1108 cm^{-1}; HRMS m/z (ESI-): Found: 245.0223 (M-H), Calc.: 245.0215 ($C_9H_{10}O_6P$).

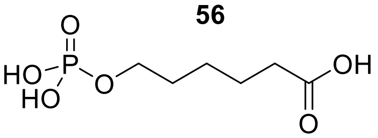
Deprotection - Serine analogues


59

Run on **29** on a 2 mmol scale. A yield of 225 mg, 1.22 mmol (61 %) was obtained as a highly hydroscopic white solid. ^{1}H NMR (400 MHz, MeOD): δ = 4.03 (2H, dt, $J_1 = J_2$ = 6.8 Hz, $-C\underline{H}_2OPO_3H_2$), 2.45 (2H, t, J = 7.4 Hz, $-C\underline{H}_2CO_2H$), 1.92-2.00 (4H, m, $-C\underline{H}_2C\underline{H}_2CH_2OPO_3H_2$) ppm; ^{13}C (100 MHz, MeOD): δ = 176.78 ($-\underline{C}O_2H$), 66.80 (d, J = 5.6 Hz, $-\underline{C}H_2OPO_3H_2$), 30.88 ($-\underline{C}H_2CO_2H$), 26.90 (d, J = 7.5 Hz, $-\underline{C}H_2CH_2OPO_3H_2$) ppm; m.p. = 98-104 ° C; IR ($υ_{max}$, solid): 2971, 2908 (v br), 2342 (br), 1690, 1508, 1483, 1430, 1421, 1401, 1209, 1131, 1099, 1077 cm^{-1}; HRMS m/z (ESI-): Found: 185.0214 (M-H), Calc.: 185.0215 ($C_4H_8O_6P$).

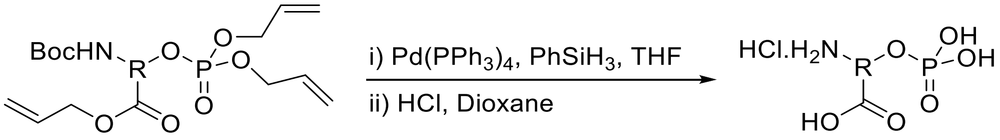

55

Run on **32** on a 1.1 mmol scale. A yield of 204 mg, 1.1 mmol (98 %) was obtained as a hydroscopic white solid. ^{1}H NMR (400 MHz, MeOD): δ = 3.97-4.03 (2H, m, $-C\underline{H}_2OPO_3H_2$), 2.34-2.39 ($-C\underline{H}_2CO_2H$), 1.69-1.77 (4H, m, $-C\underline{H}_2C\underline{H}_2CH_2OPO_3H_2$) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 177.29 ($-\underline{C}O_2H$), 67.32 (d, J = 5.9 Hz, $-\underline{C}H_2OPO_3H_2$), 34.33 ($-\underline{C}H_2CO_2H$), 30.83 (d, J = 7.3 Hz, $-\underline{C}H_2CH_2OPO_3H_2$), 22.69 ($-\underline{C}H_2CH_2CO_2H$) ppm; m.p. = 121-124 ° C; IR (υ_{max}, solid): 2945, 2909, 2870, 2695 (v br), 2287 (v br), 1692 (br), 1479, 1463, 1439, 1430, 1415, 1278, 1130, 1098, 996 (br) cm^{-1}; HRMS m/z (ESI+): Found: 199.0366 (M+H), Calc.: 199.0372 ($C_5H_{12}O_6P$).

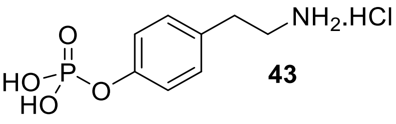

56

Run on **33** on a 0.37 mmol scale. A yield of 74 mg, 0.34 mmol (94 %) was obtained as a hydroscopic white solid. ^{1}H NMR (400 MHz, MeOD): δ = 3.87 (2H, dt, J_1 = J_2 = 6.6 Hz, $-C\underline{H}_2OPO_3H_2$), 2.21 (2H, t, J = 7.4 Hz, $-C\underline{H}_2CO_2H$), 1.49-1.64 (4H, m, $-C\underline{H}_2CH_2CO_2H$ and $-C\underline{H}_2CH_2OPO_3H_2$), 1.30-1.40 (2H, m, $-C\underline{H}_2CH_2CH_2OPO_3H_2$) ppm; ^{13}C NMR (100 MHz, MeOD): δ = 177.54 ($-\underline{C}O_2H$), 67.50 (d, J = 5.7 Hz, $-\underline{C}H_2OPO_3H_2$), 34.83 ($-\underline{C}H_2CO_2H$), 31.19 (d, J = 7.3 Hz, $-\underline{C}H_2CH_2OPO_3H_2$), 26.26 ($-\underline{C}H_2CH_2CH_2OPO_3H_2$), 25.66 ($-\underline{C}H_2CH_2CO_2H$) ppm; m.p. = 83-87 ° C; IR (υ_{max}, solid): 2945, 2876, 2652 (v br), 2279 (v br), 1698 (v br), 1476, 1464, 1431, 1411, 1317, 1258, 1242, 1209, 1160, 1133, 1103, 1045, 1009 (br) cm^{-1}; HRMS m/z (ESI+): Found: 213.0537 (M+H), Calc.: 213.0528 ($C_6H_{14}O_6P$).

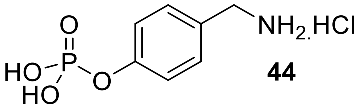
Allyl-Boc sequential deprotection



Allyl-protected phosphate (1 mmol) and phenylsilane (6 mmol) were dissolved in dry THF (10 mL) under nitrogen. $Pd(PPh_3)_4$ (0.05 mmol) was then added and the mixture was stirred for 3 hrs. The mixture typically stayed in solution during this time. The THF was then removed *in vacuo* and hydrochloric acid (4 M in dioxane, 15 mmol) was added. After stirring for 1 hr, the dioxane was removed *in vacuo*. The residue was diluted with water (20 mL), and the aqueous washed with diethyl ether (2 x 20 mL) and lyophilised to provide the specified product. Products were typically poorly soluble in a range of solvents, precluding analysis by ^{13}C NMR.


43

Run on **20** on a 2.77 mmol scale. A yield of 498 mg, 1.96 mmol (71 %) was obtained as an off white solid. ^{1}H NMR (400 MHz, D_2O): δ = 7.16 (2H, d, J = 8.4 Hz, Ar$\underline{H}$2), 7.06 (2H, dd, *J* = 8.4, Ar<u>H</u>3), 3.13 (2H, t, *J* = 7.1 Hz, -C<u>H</u>$_2$NH$_3$Cl), 2.84 (2H, t, *J* = 7.1 Hz, -C<u>H</u>$_2$Ar) ppm; ^{31}P (160 MHz, CDCl$_3$): δ = -3.38 ppm; m.p. = 240-245 ° C; IR (υ_{max}, solid): 2985, 2946, 2879, 2755, 1720, 1648, 1604, 1506, 1462, 1425, 1363, 1268, 1219, 1162, 1095, 1015 cm^{-1}; HRMS m/z (ESI+): Found: 218.0589 (M+H), Calc.: 218.0582 ($C_8H_{13}NO_6P$).


44

Run on **22** on a 1.56 mmol scale. A yield of 300 mg, 1.25 mmol (80 %) was obtained as an off white solid. ^{1}H NMR (400 MHz, D$_2$O): δ = 7.36 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>2), 7.17 (2H, dd, *J* = 8.6, 1.1 Hz, Ar<u>H</u>3), 4.08 (2H, s, -C<u>H</u>$_2$NH$_3$Cl) ppm; m.p. > 300 ° C; IR (υ_{max}, solid): 2990, 2877, 2754 (v br), 2302, 1715, 1608, 1507, 1380, 1217, 1154, 1072, 1017 cm^{-1}; HRMS m/z (ESI+): Found: 226.0232 (M+Na), Calc.: 226.0240 ($C_7H_{10}NaNO_6P$).

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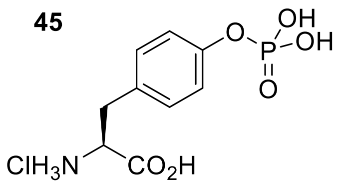
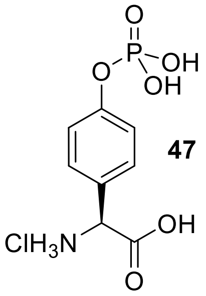


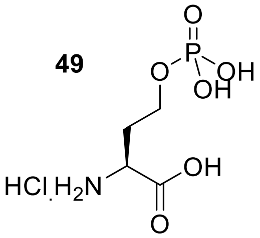
Run on **25** on a 1 mmol scale. A yield of 261 mg, 0.88 mmol (88 %) was obtained as an off white solid. Data were consistent with those previously reported.[19] ^{1}H NMR (400 MHz, MeOD): δ = 7.04-7.22 (4H, m, Ar<u>H</u>), 4.30-4.41 (1H, dd, *J* = 8.0, 5.2 Hz, <u>H</u>$_\alpha$), 3.02-3.29 (1H, m, <u>H</u>$_\beta$), 3.13 (14.6, 8.0 Hz) ppm.

The use of D-enantiomer **26** led to the production of **46**.


47

Run on **27** on a 0.5 mmol scale. A yield of 132 mg, 0.46 mmol (93 %) was obtained as an off white solid. ^{1}H NMR (400 MHz, MeOD): δ = 7.47 (2H, d, *J* = 8.7 Hz, Ar<u>H</u>2), 7.34 (2H, dt, *J* = 8.7, 1.1 Hz, Ar<u>H</u>3), 5.09 (1H, s, <u>H</u>$_\alpha$) ppm; m.p. = 208-214 ° C; IR (υ_{max}, solid): 3338, 2970, 2884, 1734, 1638, 1467, 1379, 1369, 1341, 1305, 1160, 1128, 1107 cm^{-1}; HRMS m/z (ESI-): Found: 246.0171 (M-H), Calc.: 246.0173 ($C_8H_9NO_6P$).

49



Run on **36** on a 0.71 mmol scale. A yield of 95 mg, 0.42 mmol (57 %) was obtained as an hydroscopic white solid. ^{1}H NMR (400 MHz, D$_2$O): δ = 4.10-4.27 (3H, m, <u>H</u>$_\alpha$ & <u>H</u>$_\gamma$), 2.34-2.45 (1H, m, <u>H</u>$_\beta$), 2.14-2.26 (1H, m, <u>H</u>$_\beta$) ppm; IR (υ_{max}, solid): 2870 (v br), 1726, 1606, 1507, 1438, 1204, 1155, 1106, 1051 cm^{-1}; HRMS m/z (ESI-): Found: 198.0172 (M-H), Calc.: 198.0173 ($C_4H_9NO_6P$); m.p. not determined due to hydroscopic nature of product.

Mechanical testing

Powdered α-TCP (50 mg), prepared as described previously,[19,20] was mixed with a solution of 25 % ethanol: 75 % ultrapure water containing the specified amino acid analogue to give a liquid to powder ratio (L/P) of 0.25 mL g^{-1}. Pre-dissolution of the amino acid was undertaken to avoid confounding effects related to solvation of the powder phase (e.g. dissolution rate, particle size, surface area). Amino acids were applied at a 1.13:1 molar ratio to α-TCP. After mixing for approximately 10 sec, the mixture was applied to a 1 cm^3 cube surface of aluminium or bone with a spatula and the opposing 1 cm^3 steel cube adjoined by hand. Universal grips (Cocraft spring clamps) were applied to hold the cubes together at 37 °C, in a 100 % humidity sealed container for 24 hrs. Shear testing was then performed on the construct at a rate of 1 mm min^{-1} with a 500 N load cell (Shimadzu) on an AGS-X Mechanical Testing System (Shimadzu). The peak force and shear modulus were recorded with Trapezium-Lite software (version 1.0.1) and the bond thickness and failure mode of each sample was recorded.

Statistical analyses

Aluminium adhesion tests were run with N = 4. For bone samples, where surface roughness is more varied N = 7/8 was used. Differences in adhesive strength between conditions were evaluated using a one-way ANOVA with Tukey's multiple comparison post-hoc test. Results with *p*-values lower than 0.05 were deemed significant.

Full statistical analysis of significance is provided below:

Fig. 1a

Tukey's multiple comparisons test	**Summary**	**Adjusted P Value**	
Blank vs. L-PSer, **1**	***	<0.0001	A-B
Blank vs. D/L-PSer, **1**	***	<0.0001	A-C
Blank vs. Ser	ns	0.9988	A-D
Blank vs. PTyr, **45**	***	<0.0001	A-E
Blank vs. Tyr	ns	>0.9999	A-F
Blank vs. PThr, **57**	***	<0.0001	A-G
L-PSer, **1** vs. D/L-PSer, **1**	ns	0.8264	B-C
L-PSer, **1** vs. Ser	***	<0.0001	B-D
L-PSer, **1** vs. PTyr, **45**	*	0.0231	B-E
L-PSer, **1** vs. Tyr	***	<0.0001	B-F
L-PSer, **1** vs. PThr, **57**	ns	0.0563	B-G
D/L-PSer, **1** vs. Ser	***	<0.0001	C-D
D/L-PSer, **1** vs. PTyr, **45**	**	0.0011	C-E
D/L-PSer, **1** vs. Tyr	***	<0.0001	C-F
D/L-PSer, **1** vs. PThr, **57**	**	0.0029	C-G
Ser vs. PTyr, **45**	***	<0.0001	D-E
Ser vs. Tyr	ns	>0.9999	D-F
Ser vs. PThr, **57**	***	<0.0001	D-G
PTyr, **45** vs. Tyr	***	<0.0001	E-F
PTyr, **45** vs. PThr, **57**	ns	0.9995	E-G
Tyr vs. PThr, **57**	***	<0.0001	F-G

Fig. 1b

Tukey's multiple comparisons test	**Summary**	**Adjusted P Value**	
PTyr, **45** vs. Tyr	***	<0.0001	A-B
PTyr, **45** vs. **43**	***	<0.0001	A-C
PTyr, **45** vs. **53**	ns	0.9922	A-D

PTyr, **45** vs. PSer, **1**	**	0.0012	A-E
PTyr, **45** vs. Ser	***	<0.0001	A-F
PTyr, **45** vs. **48**	***	<0.0001	A-G
PTyr, **45** vs. **54**	***	<0.0001	A-H
Tyr vs. **43**	ns	0.9576	B-C
Tyr vs. **53**	***	<0.0001	B-D
Tyr vs. PSer, **1**	***	<0.0001	B-E
Tyr vs. Ser	ns	>0.9999	B-F
Tyr vs. **48**	ns	0.099	B-G
Tyr vs. **54**	***	<0.0001	B-H
43 vs. **53**	***	<0.0001	C-D
43 vs. PSer, **1**	***	<0.0001	C-E
43 vs. Ser	ns	0.9968	C-F
43 vs. **48**	ns	0.5537	C-G
43 vs. **54**	***	<0.0001	C-H
53 vs. PSer, **1**	***	0.0002	D-E
53 vs. Ser	***	<0.0001	D-F
53 vs. **48**	***	<0.0001	D-G
53 vs. **54**	***	<0.0001	D-H
PSer, **1** vs. Ser	***	<0.0001	E-F
PSer, **1** vs. **48**	***	<0.0001	E-G
PSer, **1** vs. **54**	**	0.0075	E-H
Ser vs. **48**	ns	0.2053	F-G
Ser vs. **54**	***	<0.0001	F-H
48 vs. **54**	***	<0.0001	G-H

Fig. 2a

Tukey's multiple comparisons test	**Summary**	**Adjusted P Value**	
PSer, **1** vs. **54**	ns	0.0977	A-B
PSer, **1** vs. **55**	ns	0.9596	A-C
PSer, **1** vs. **56**	**	0.0012	A-D
PSer, **1** vs. Ser	***	<0.0001	A-E
54 vs. **55**	*	0.0282	B-C
54 vs. **56**	***	<0.0001	B-D
54 vs. Ser	***	<0.0001	B-E
55 vs. **56**	**	0.0042	C-D
55 vs. Ser	***	<0.0001	C-E
56 vs. Ser	**	0.0045	D-E

Fig. 2b

Tukey's multiple comparisons test	**Summary**	**Adjusted P Value**	
PTyr, **45** vs. **42**	**	0.0042	A-B
PTyr, **45** vs. **50**	ns	0.8536	A-C
PTyr, **45** vs. **51**	ns	0.7621	A-D
PTyr, **45** vs. **52**	ns	0.9892	A-E
PTyr, **45** vs. **53**	ns	0.9987	A-F
PTyr, **45** vs. **47**	ns	0.9707	A-G
42 vs. **50**	***	0.0002	B-C
42 vs. **51**	ns	0.0985	B-D
42 vs. **52**	***	0.0008	B-E
42 vs. **53**	*	0.0127	B-F

42 vs. **47**	*	0.0302	B-G
50 vs. **51**	ns	0.1359	C-D
50 vs. **52**	ns	0.9975	C-E
50 vs. **53**	ns	0.579	C-F
50 vs. **47**	ns	0.3535	C-G
51 vs. **52**	ns	0.341	D-E
51 vs. **53**	ns	0.955	D-F
51 vs. **47**	ns	0.9969	D-G
52 vs. **53**	ns	0.8785	E-F
52 vs. **47**	ns	0.6755	E-G
53 vs. **47**	ns	0.9996	F-G

Fig. S1

Tukey's multiple comparisons test	**Summary**	**Adjusted P Value**	
PTyr, **45** vs. **50**	ns	0.3245	A-B
PTyr, **45** vs. **51**	*	0.0251	A-C
PTyr, **45** vs. **42**	***	0.0004	A-D
50 vs. **51**	ns	0.4124	B-C
50 vs. **42**	*	0.0227	B-D
51 vs. **42**	ns	0.6566	C-D

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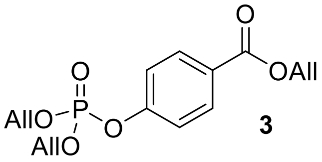

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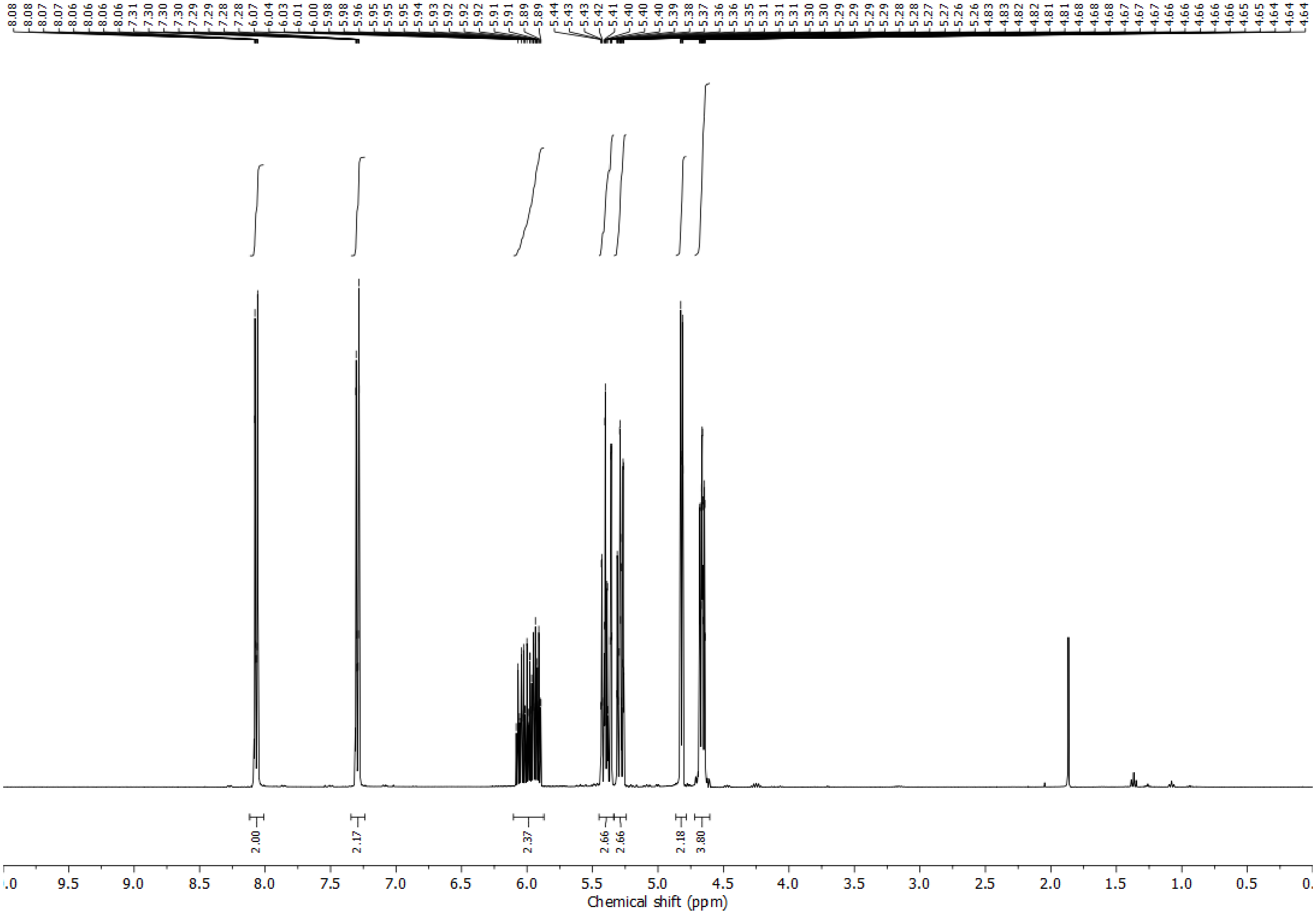

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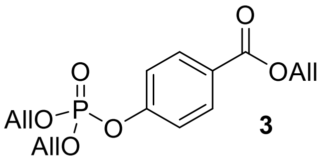

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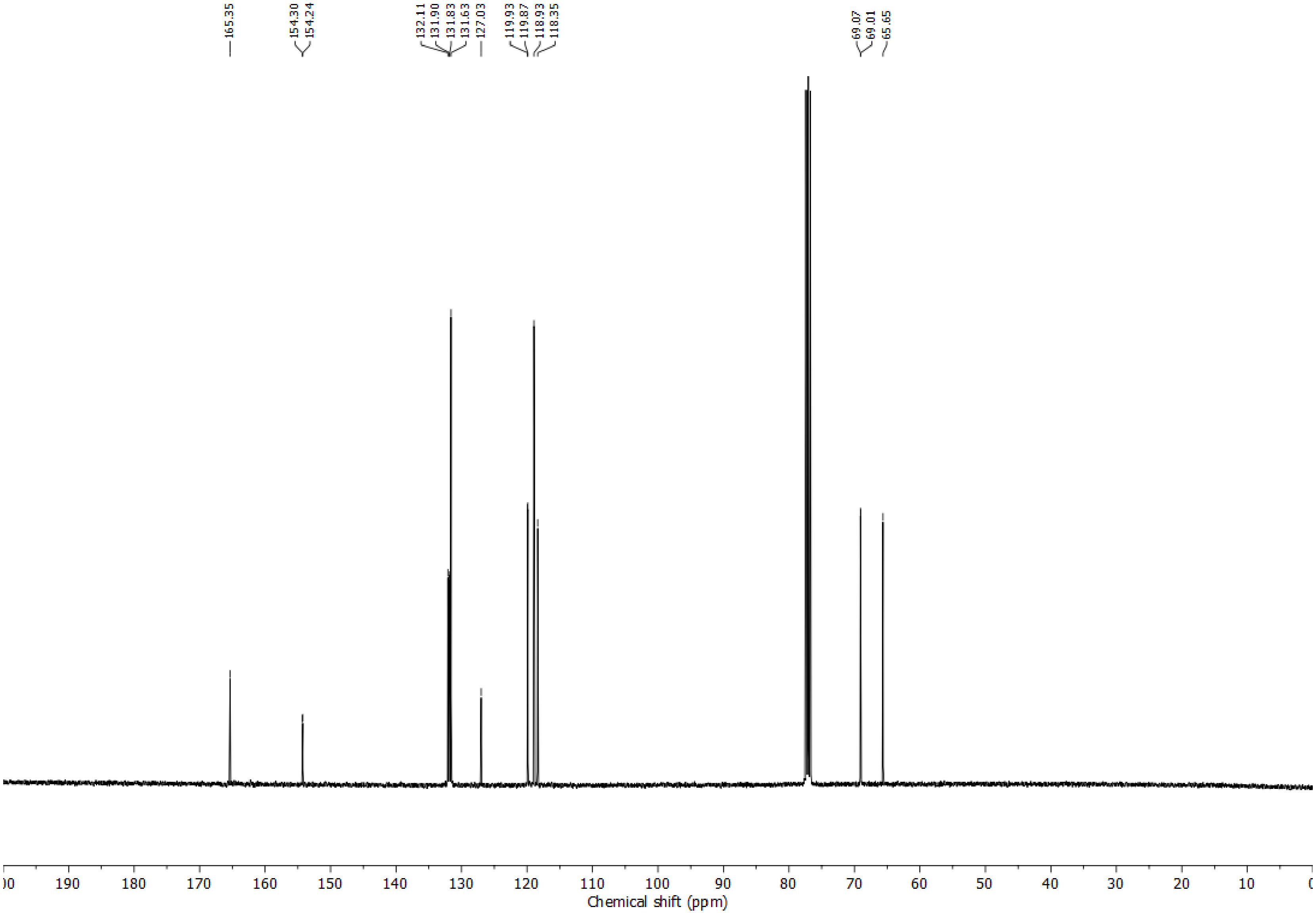

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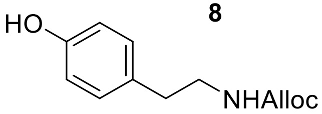

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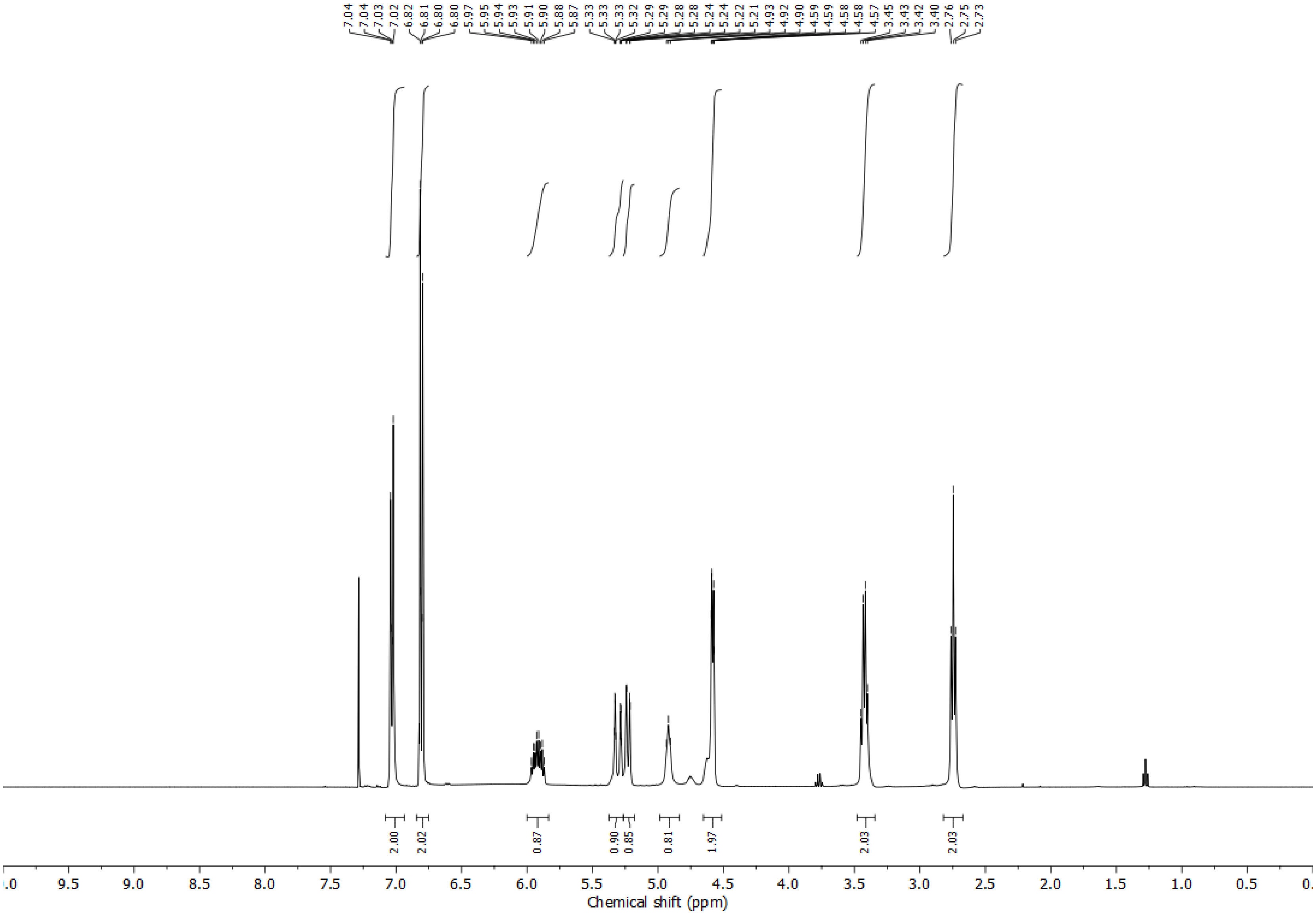

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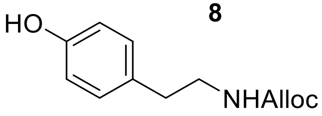

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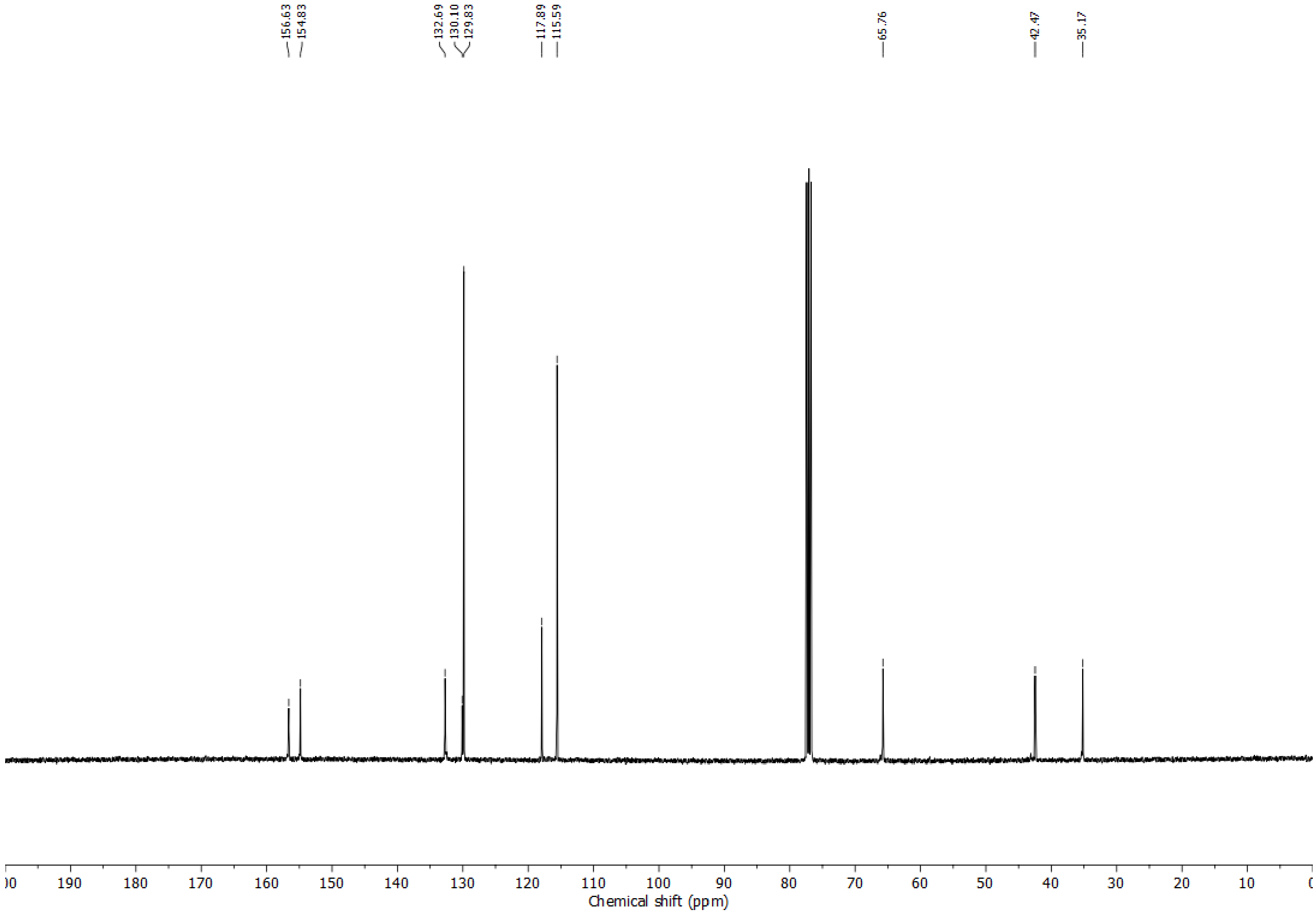

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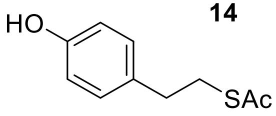

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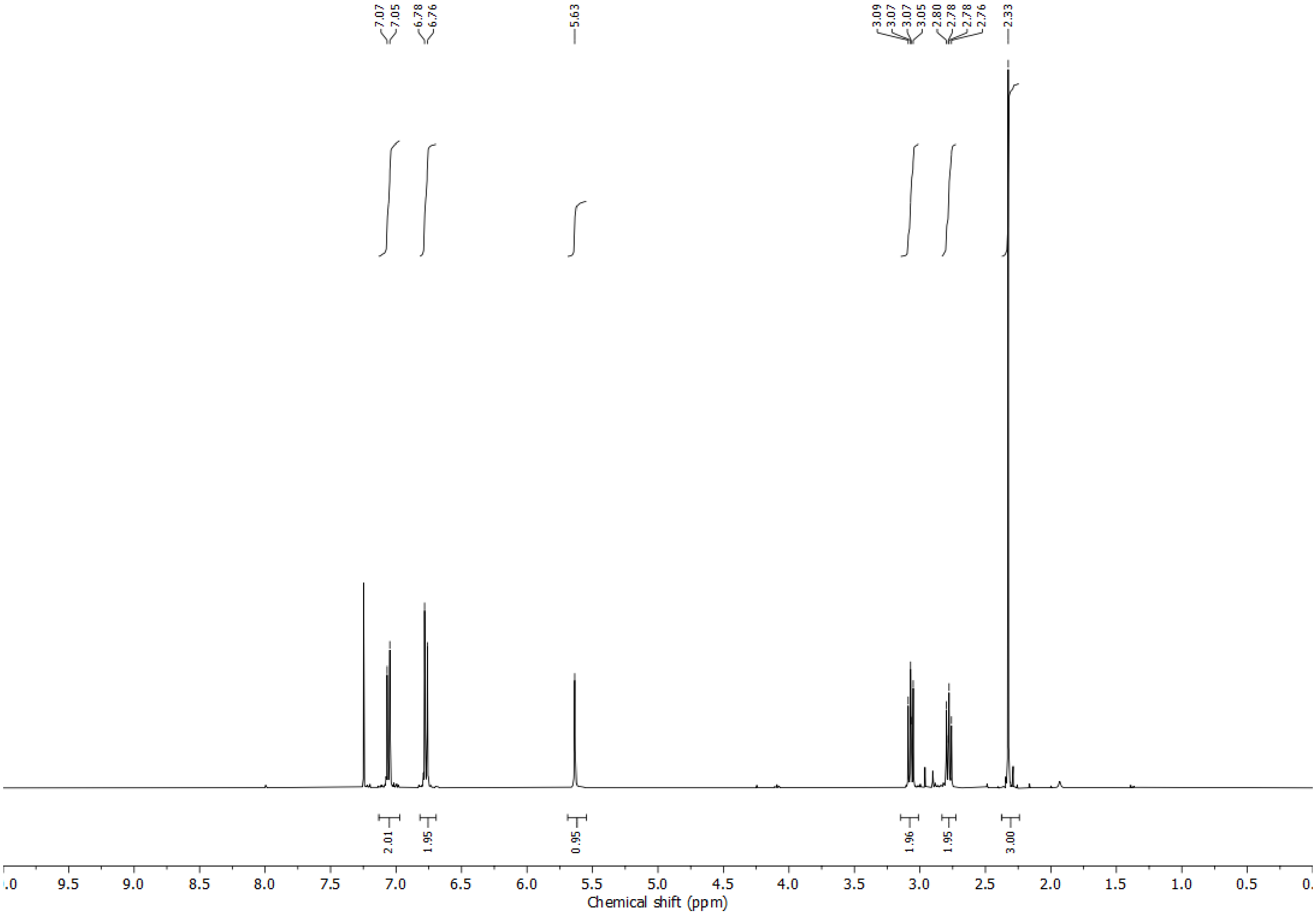

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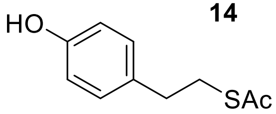

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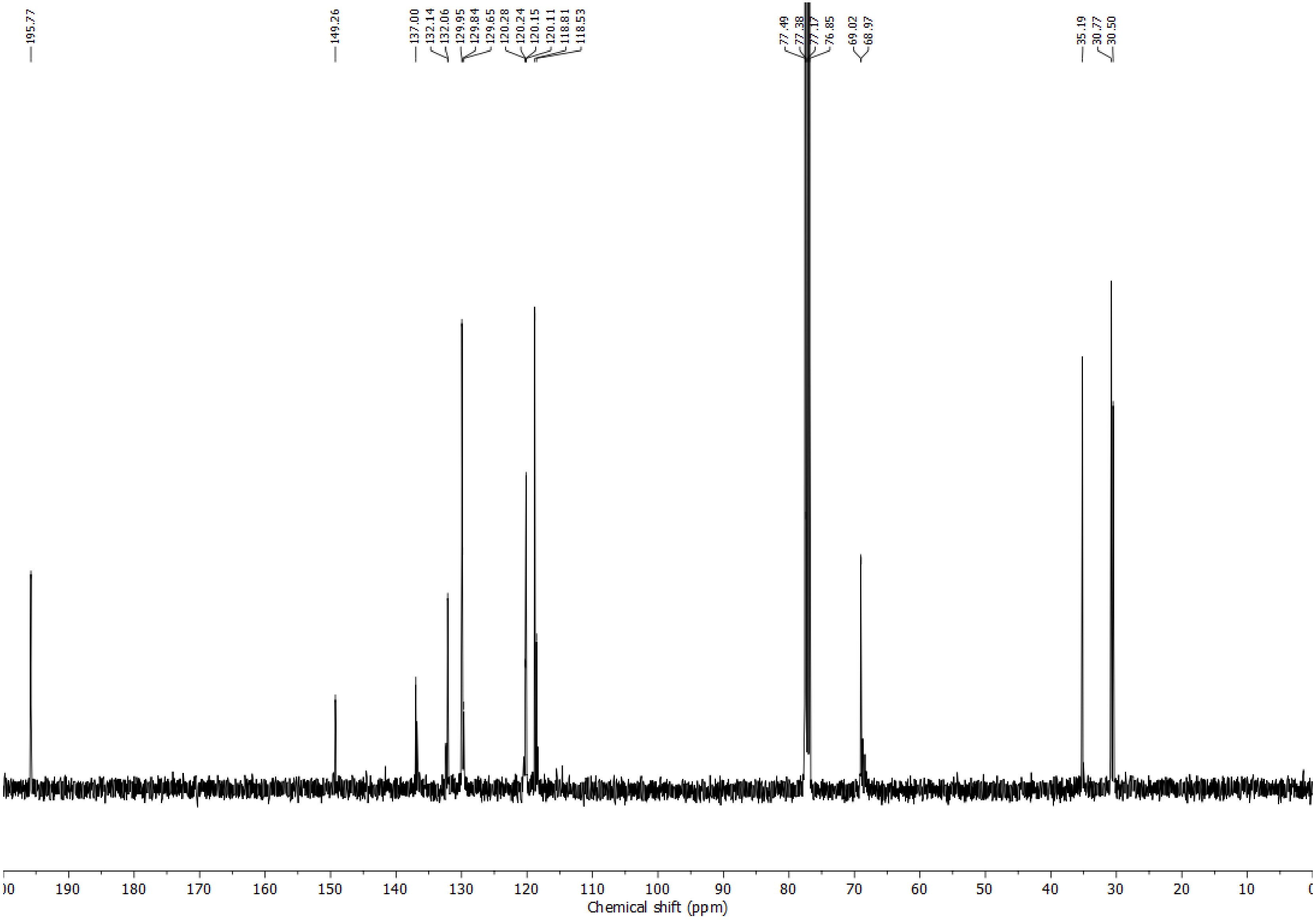

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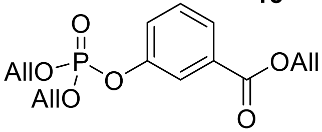

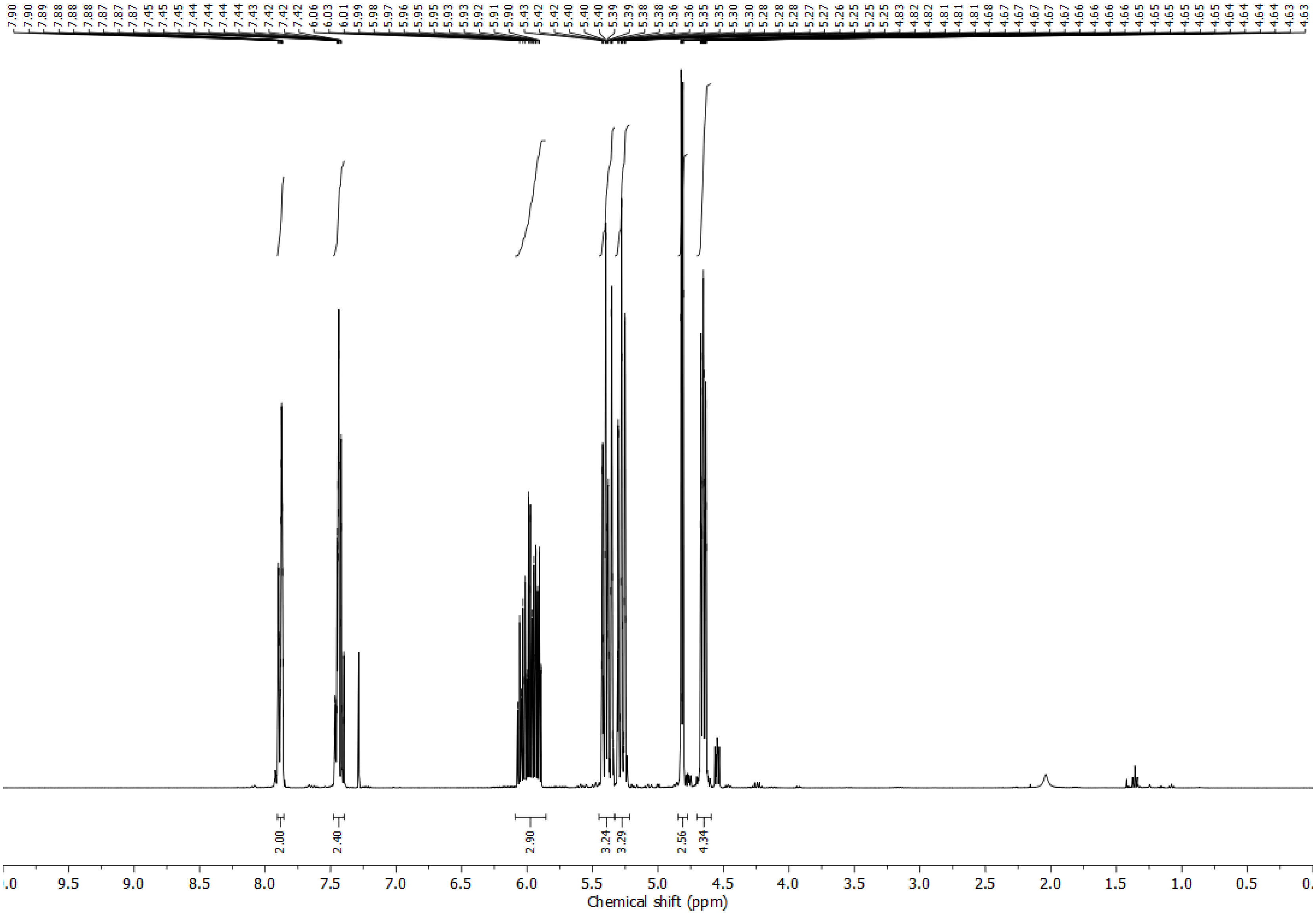

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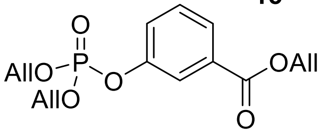

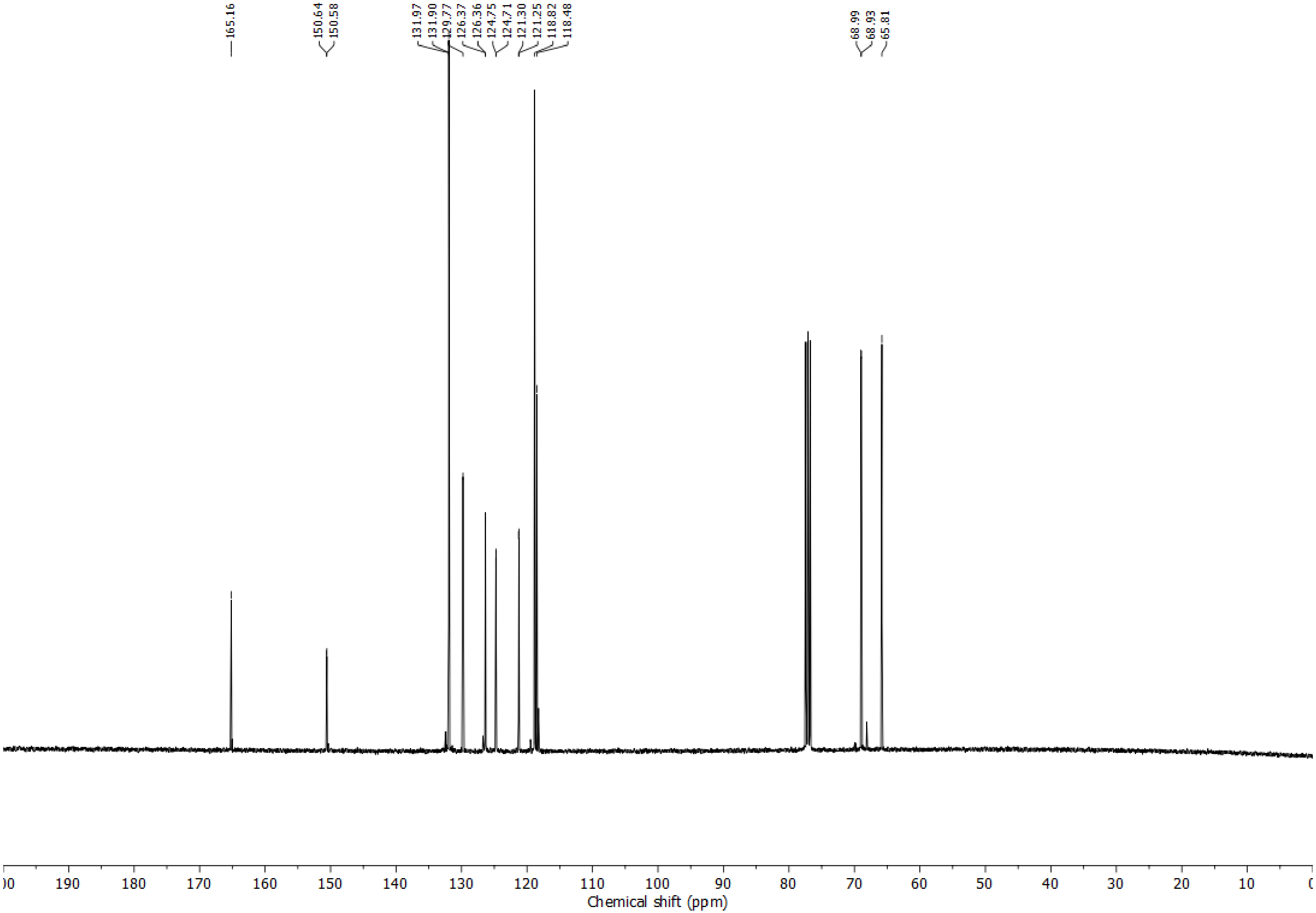

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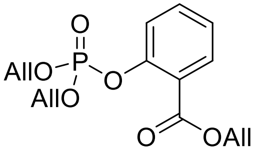

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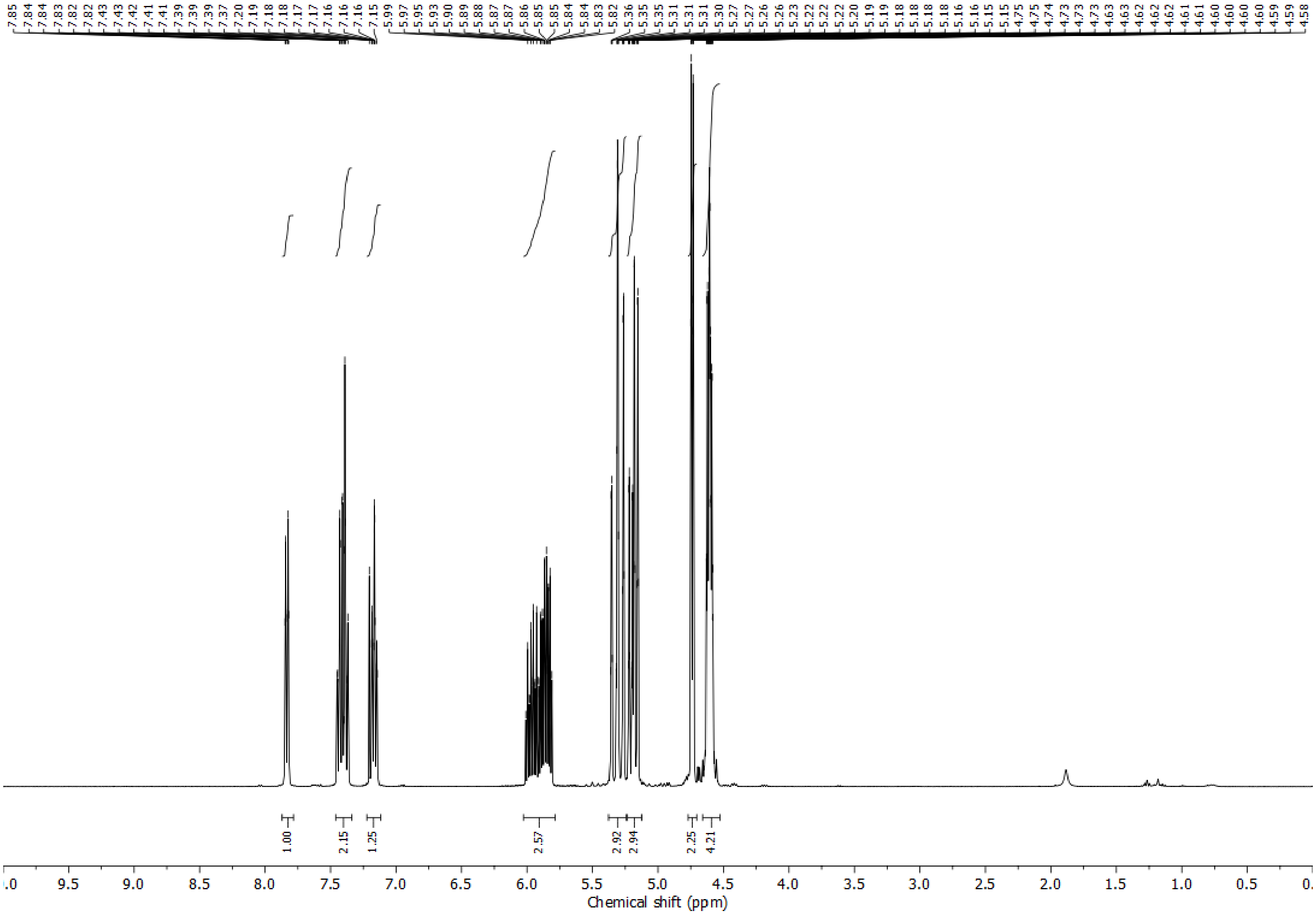

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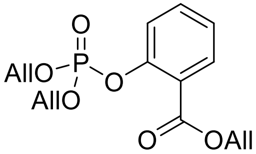

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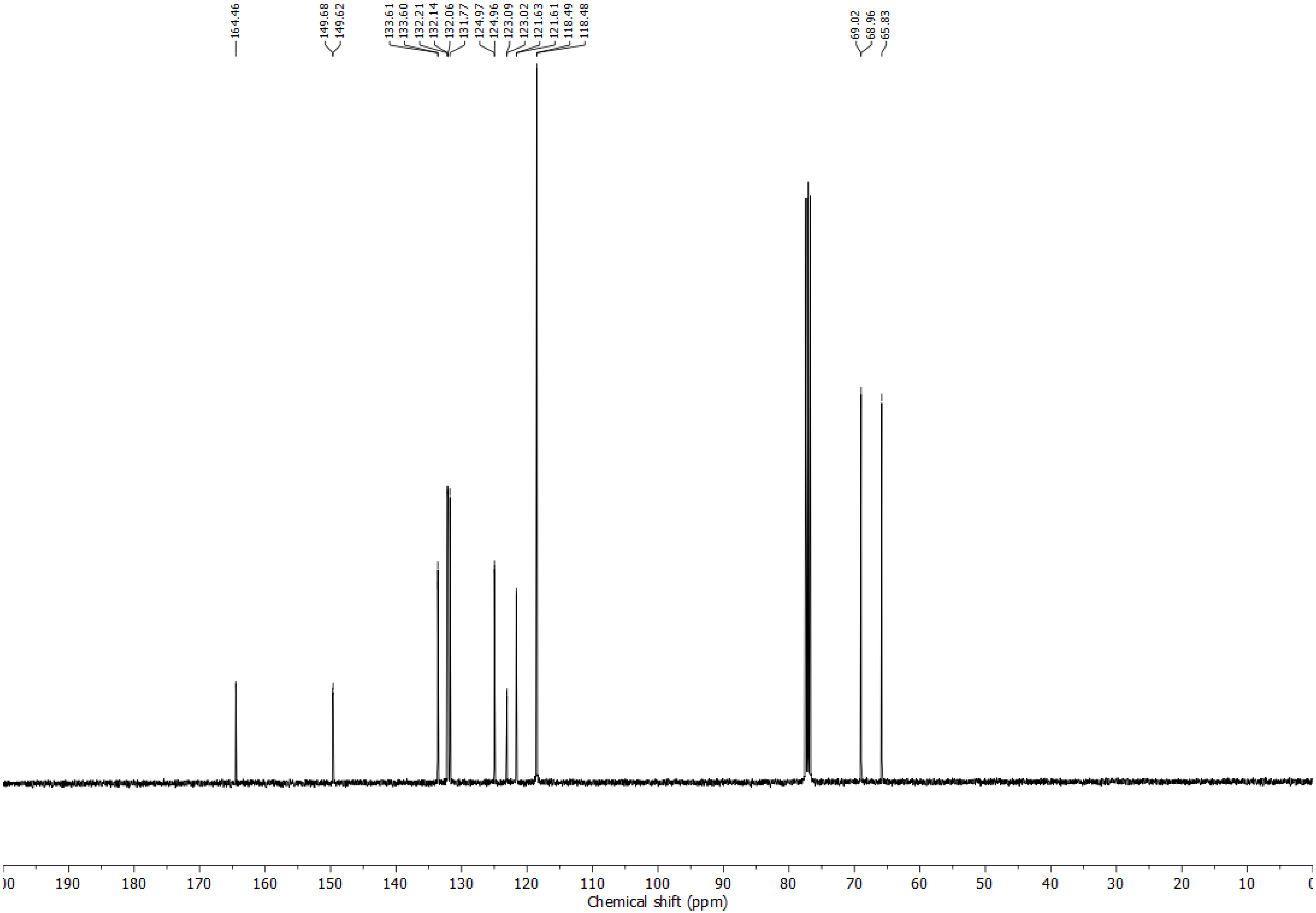

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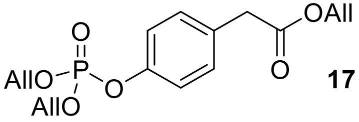

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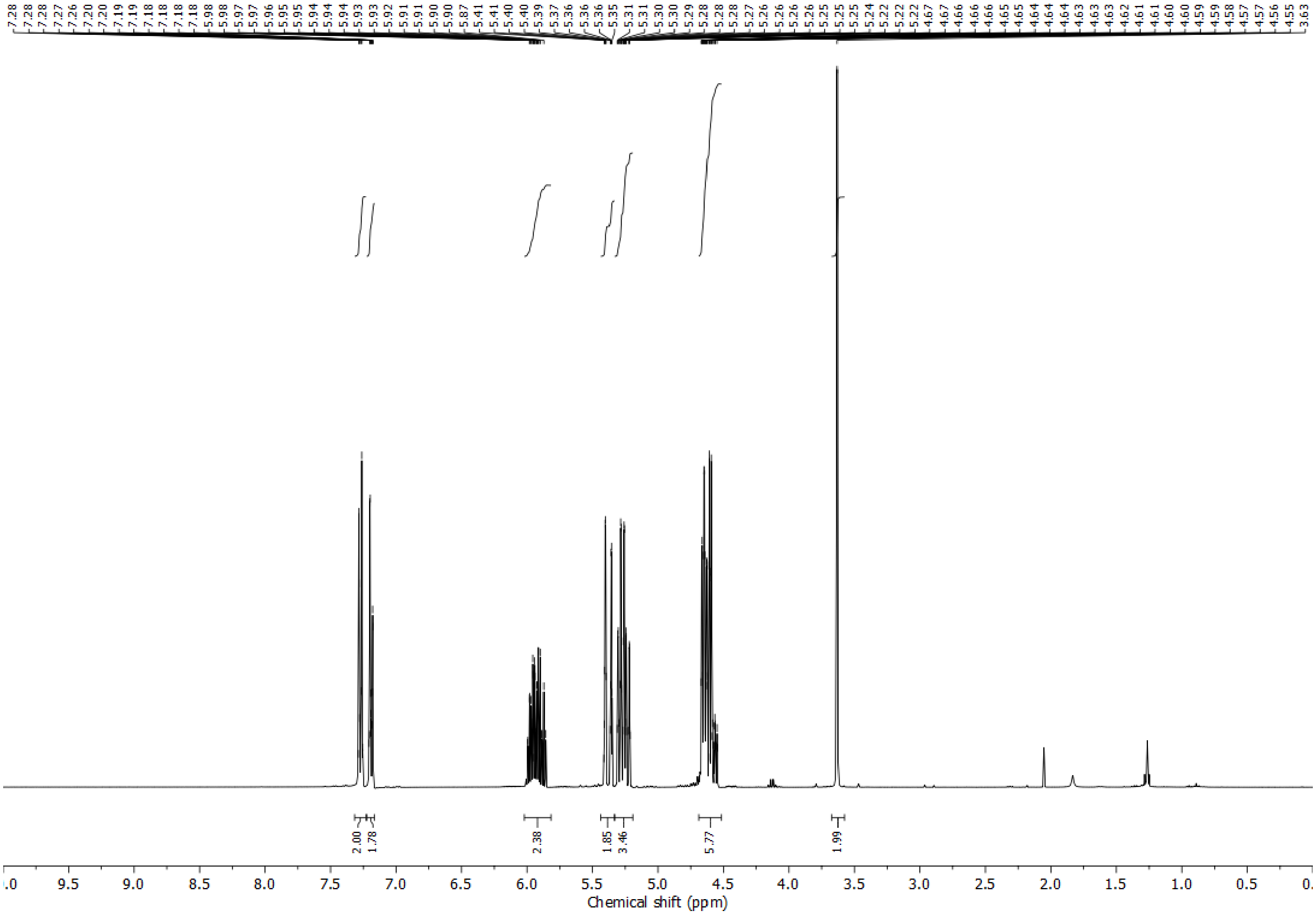

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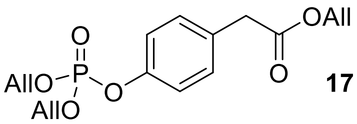

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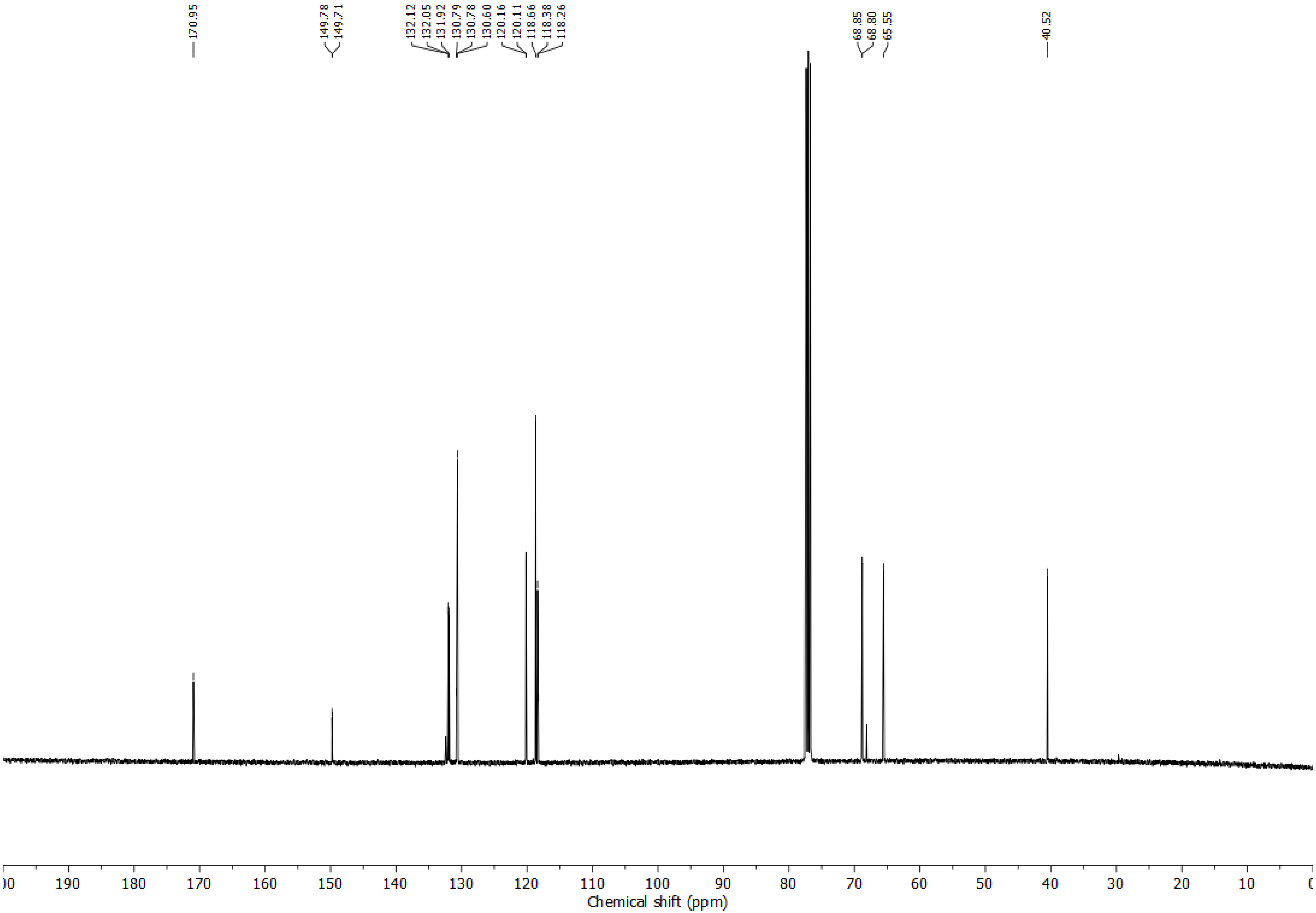

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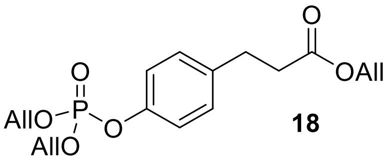

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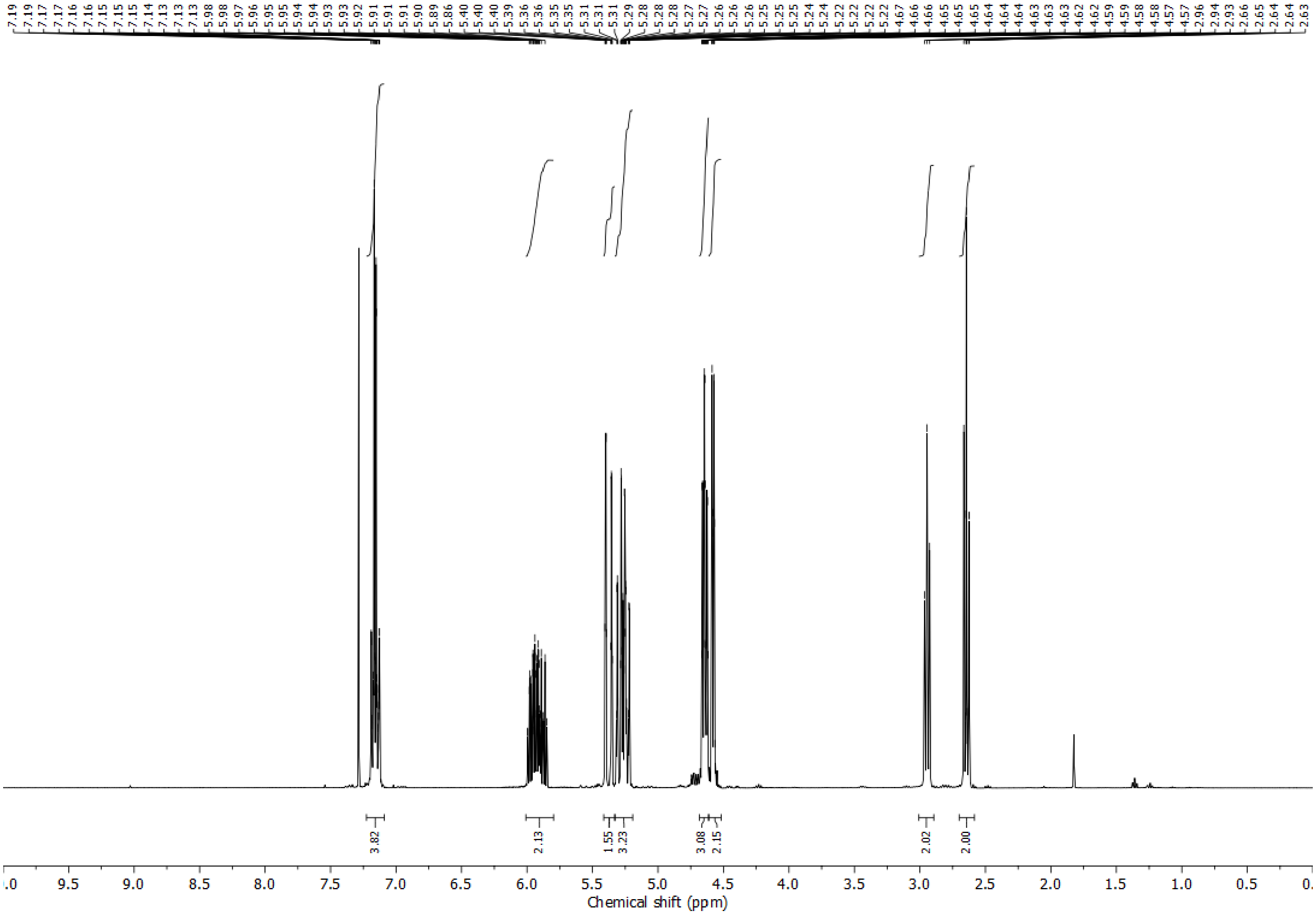

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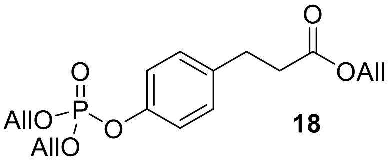

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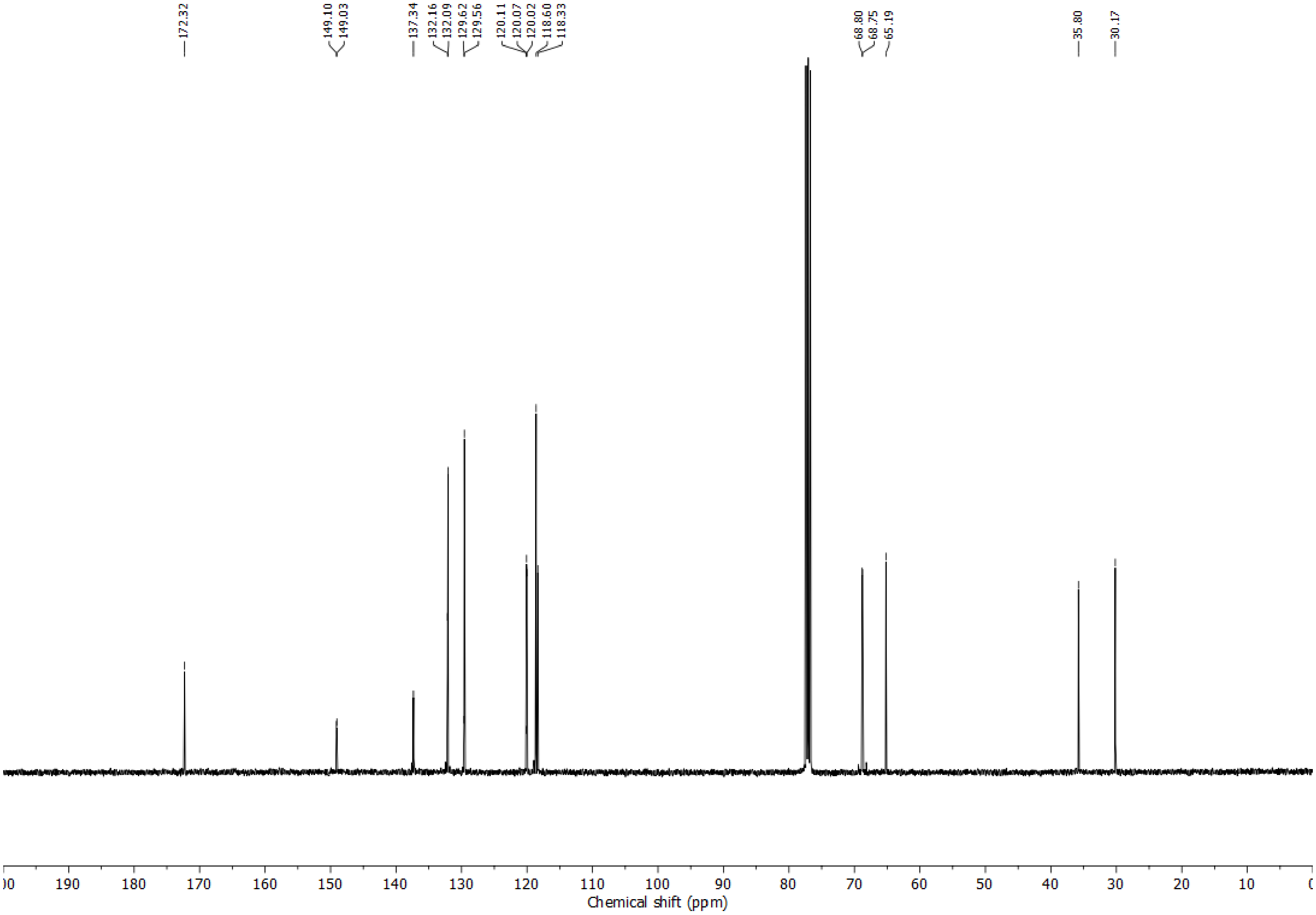

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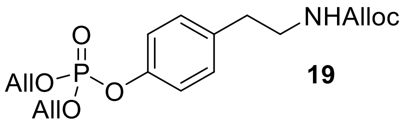

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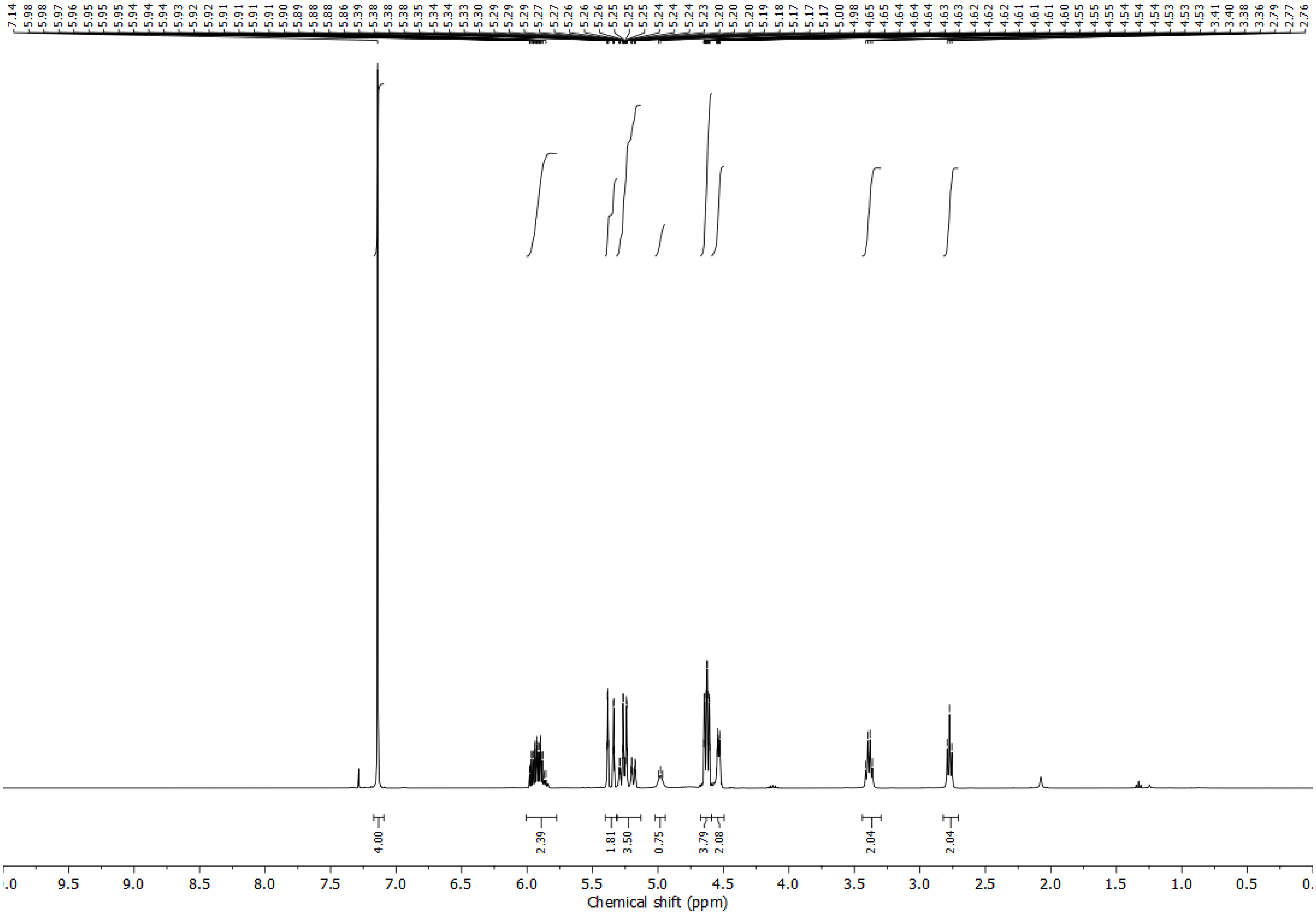

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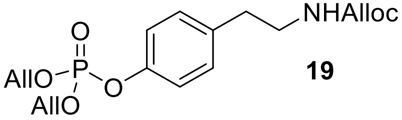

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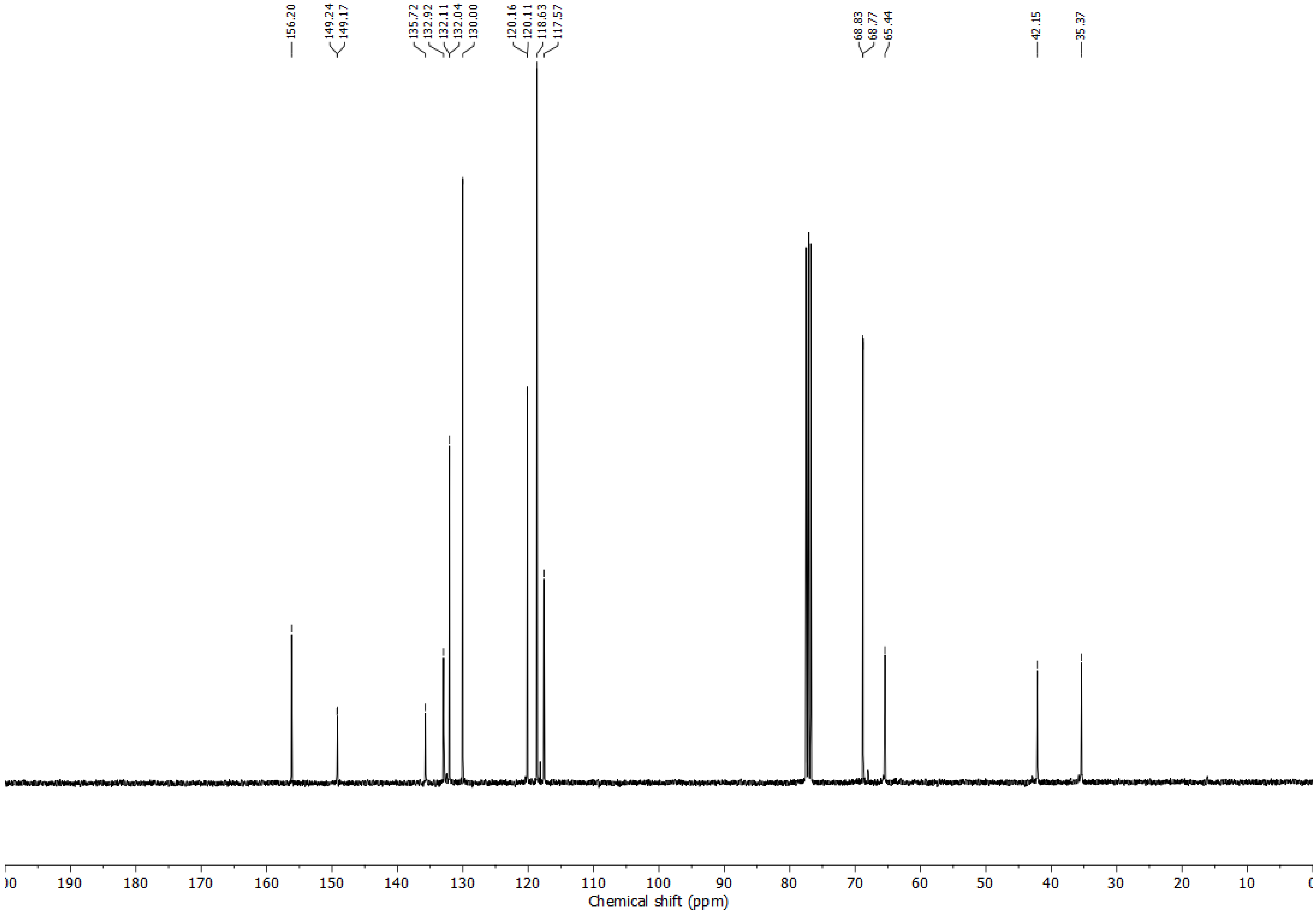

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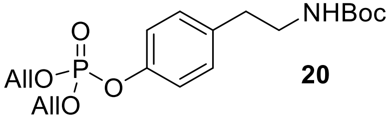

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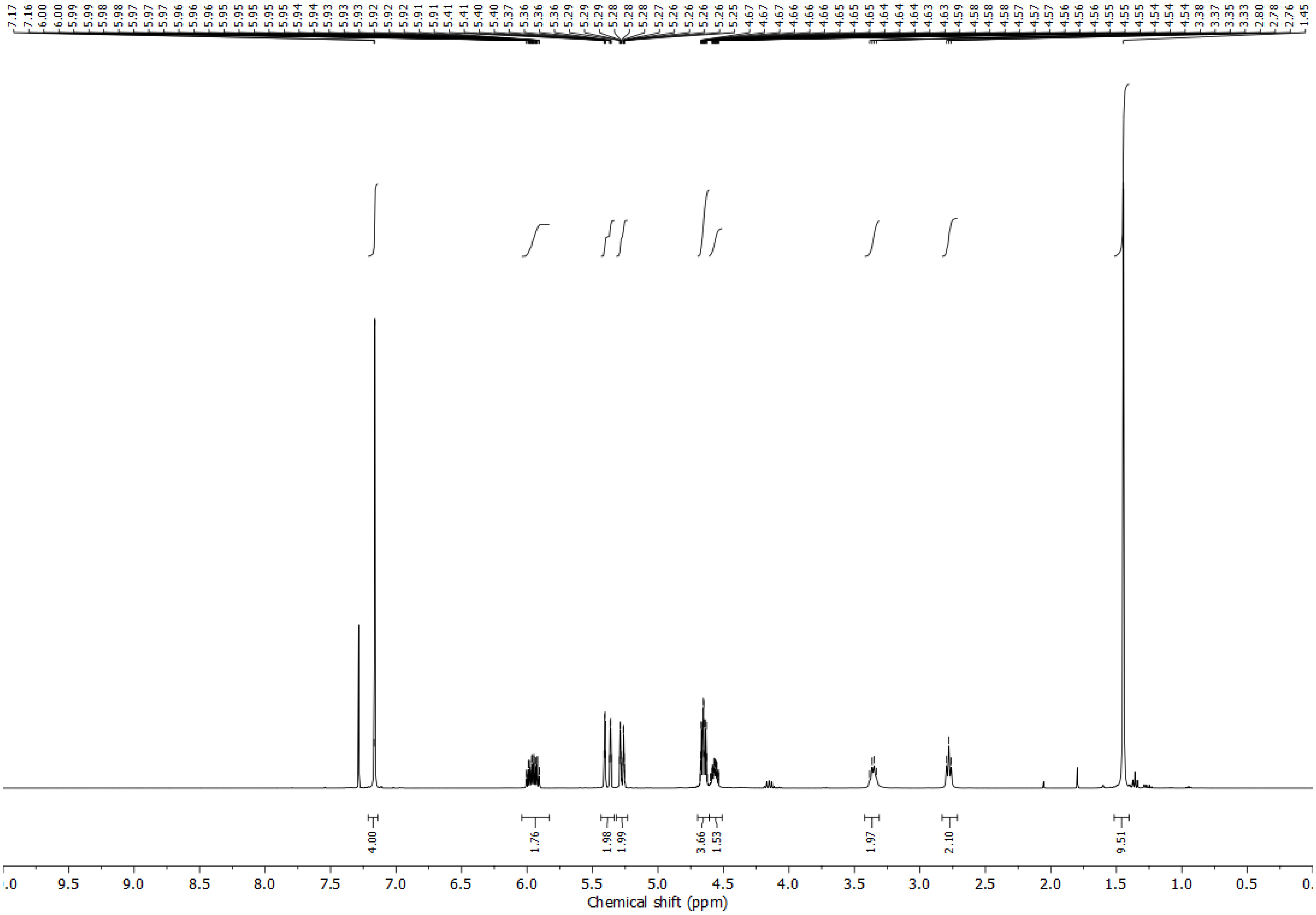

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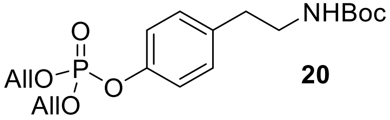

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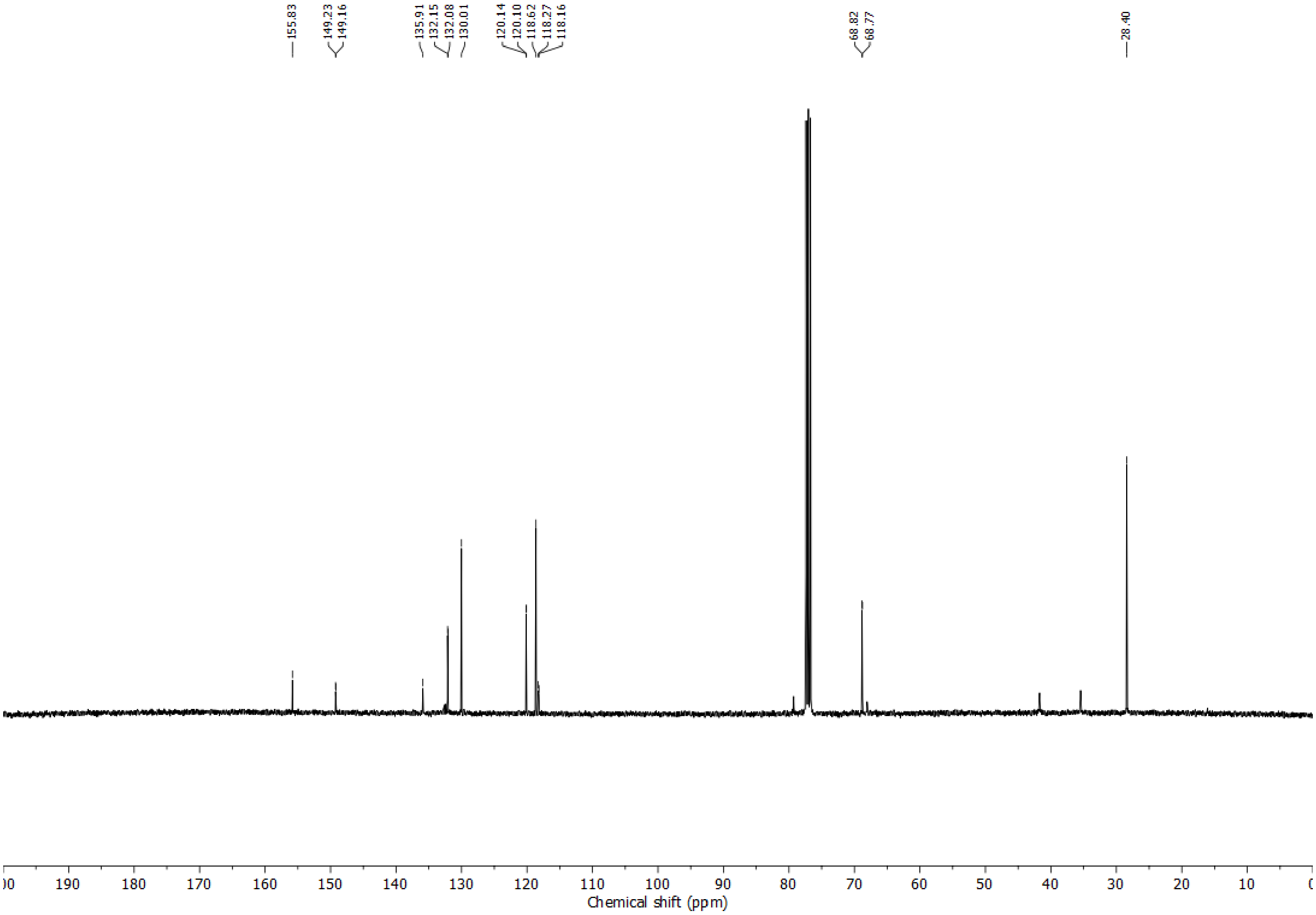

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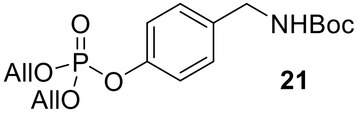

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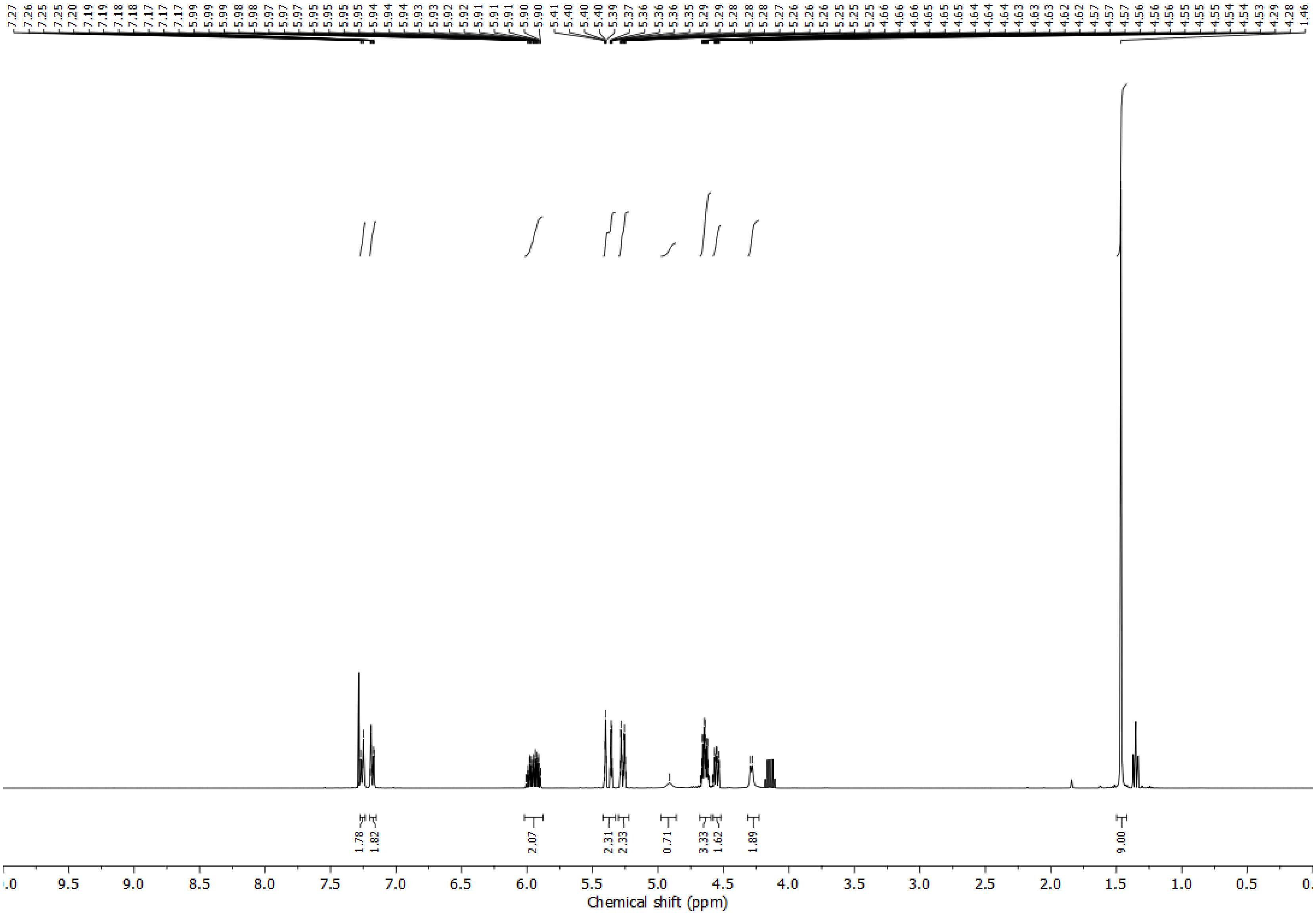

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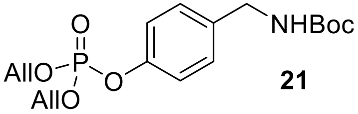

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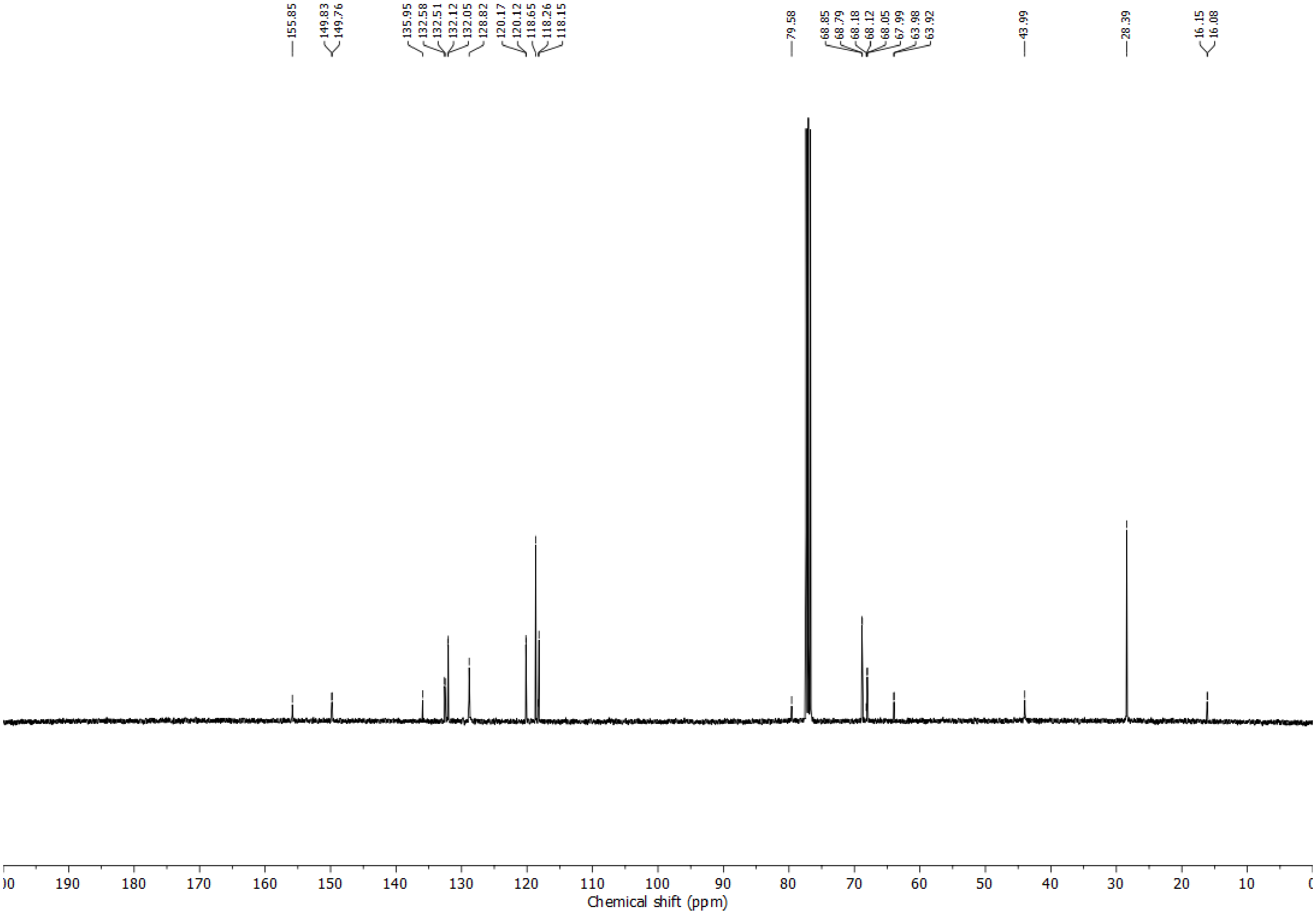
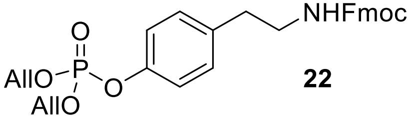


^{1}H NMR (400 MHz, $CDCl_3$)



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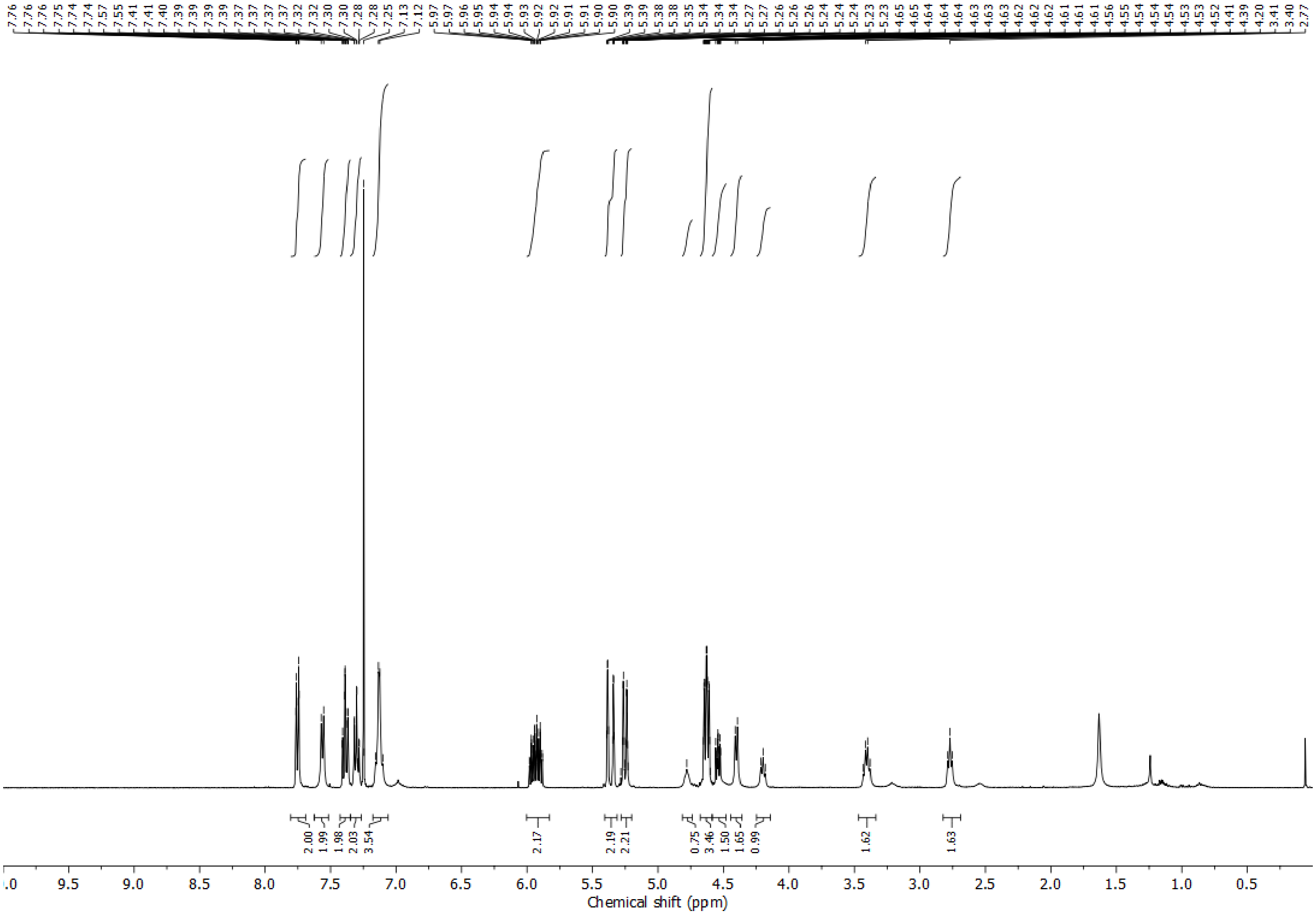

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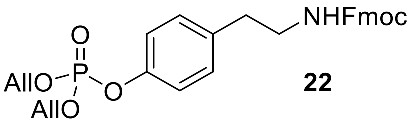

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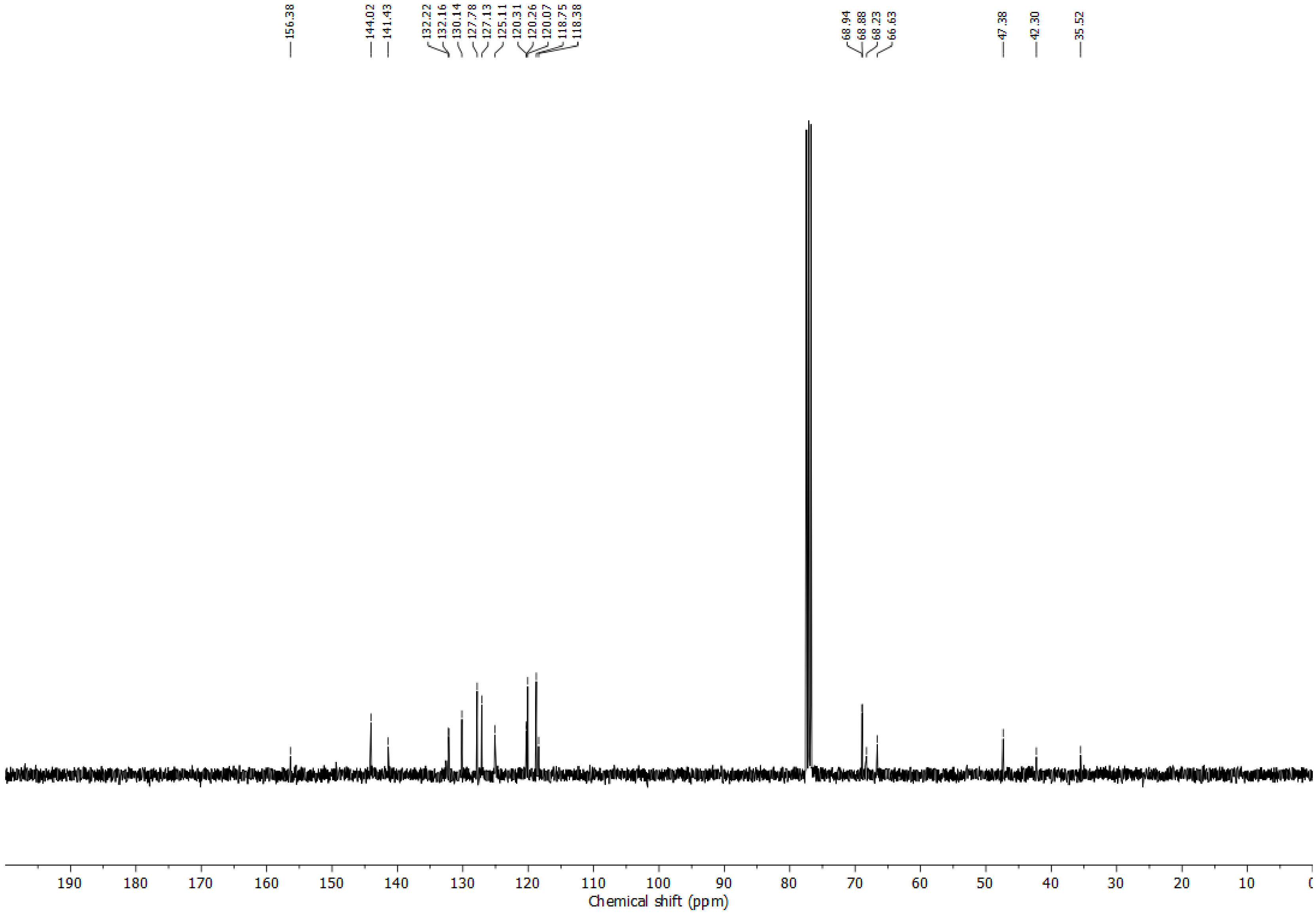

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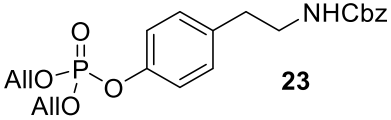

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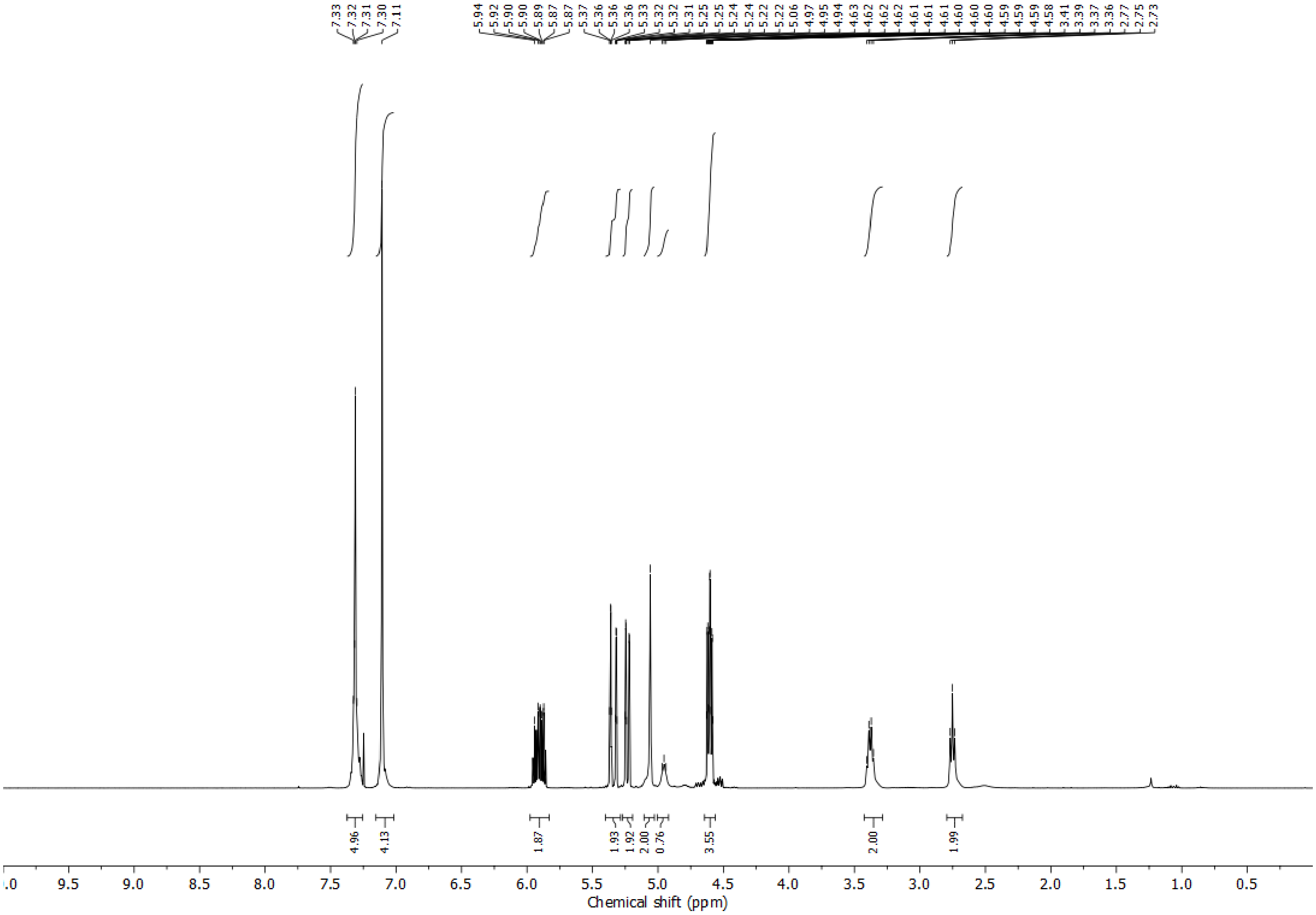

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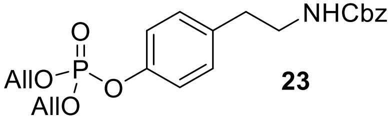

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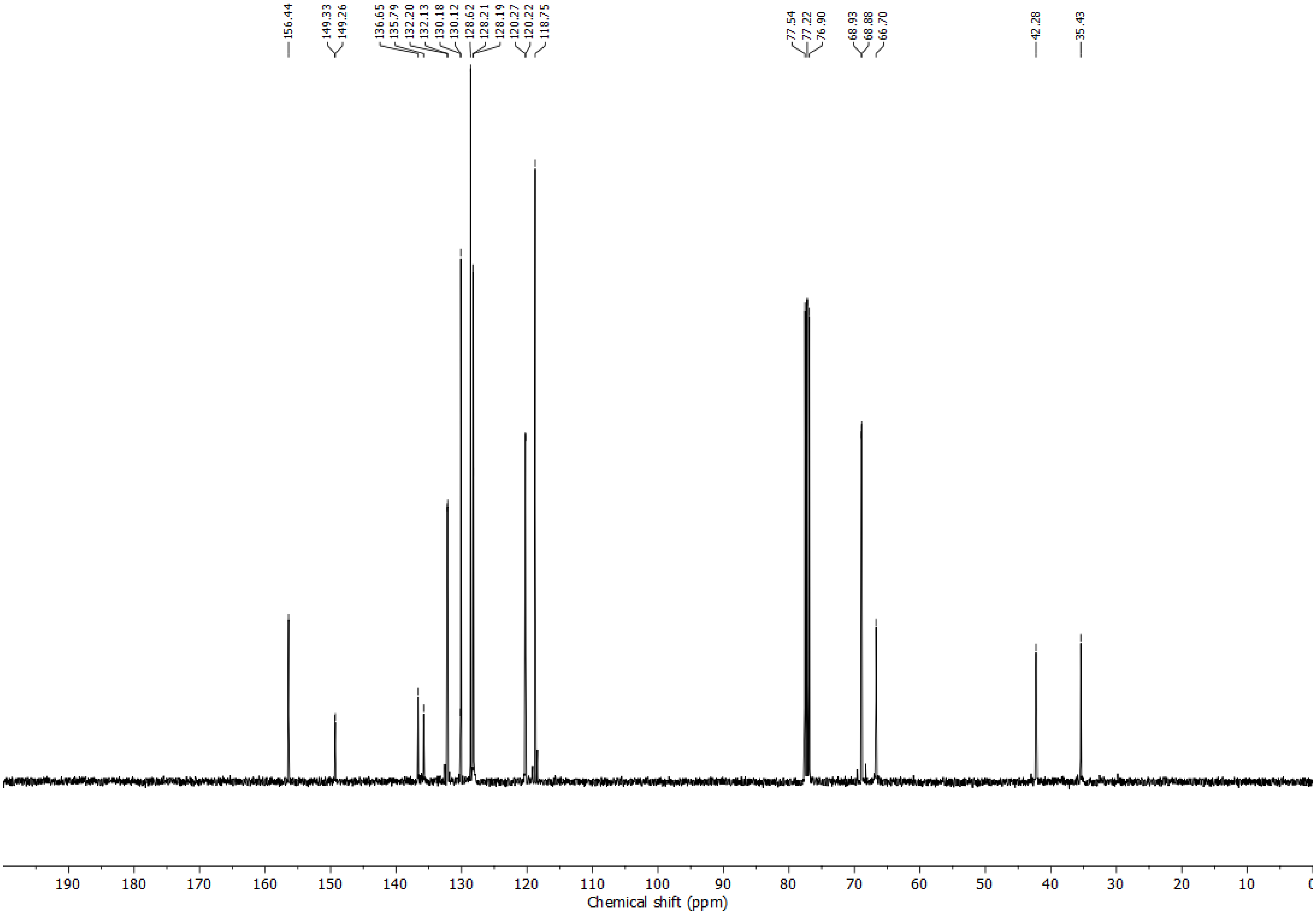

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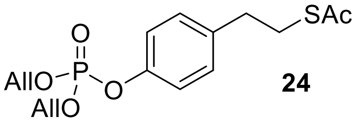

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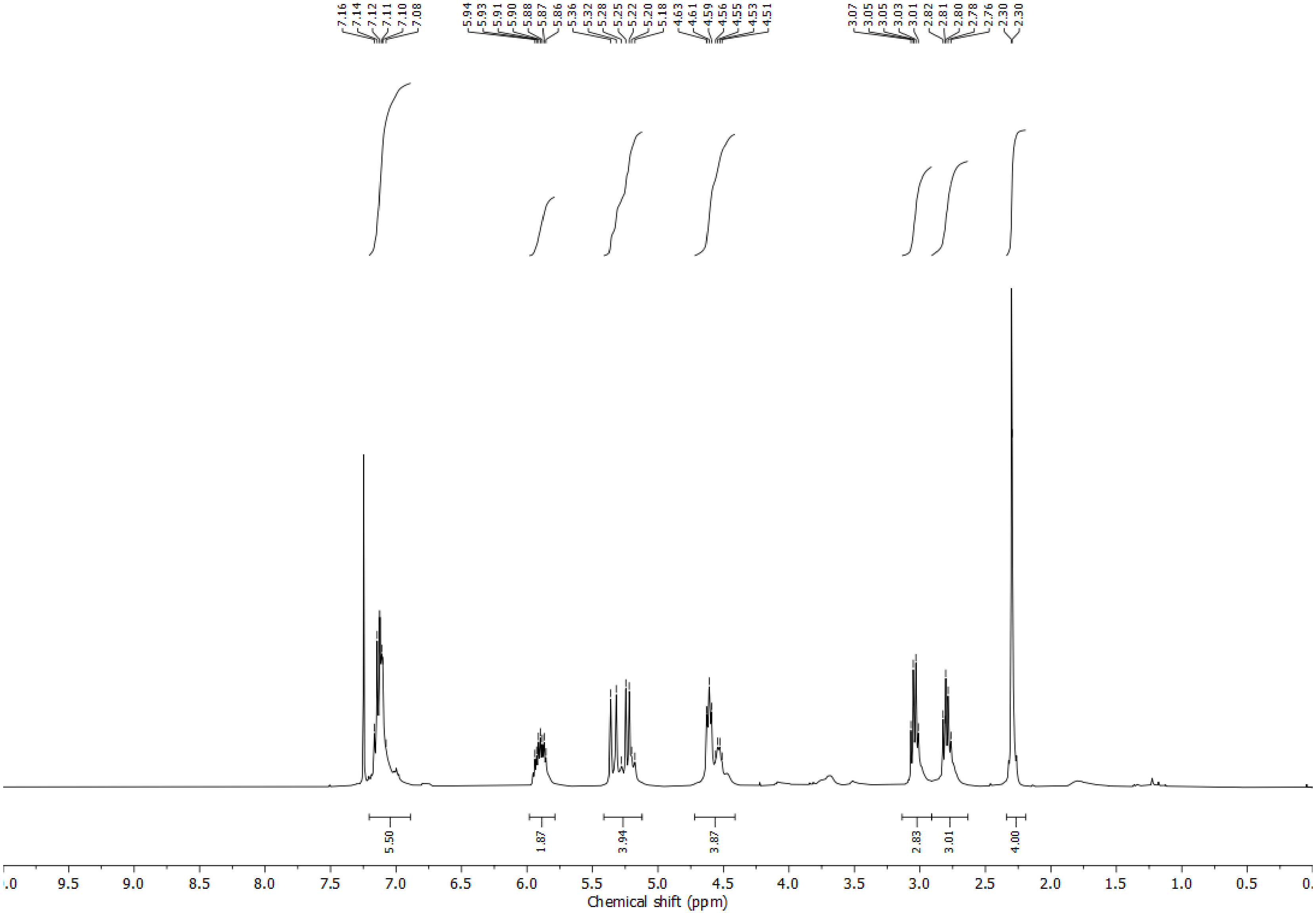
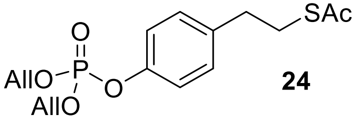


^{13}C NMR (100 MHz, $CDCl_3$)



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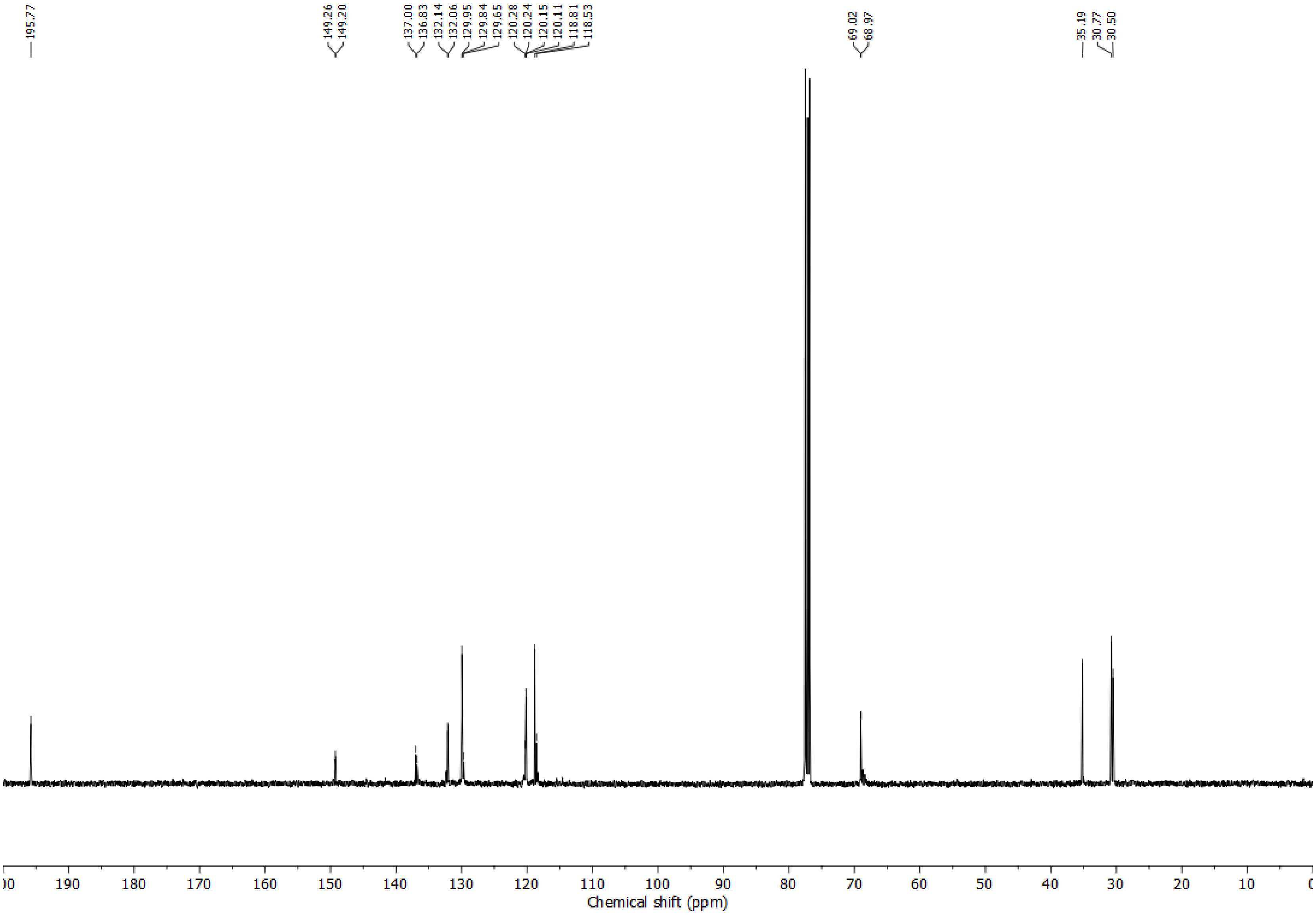

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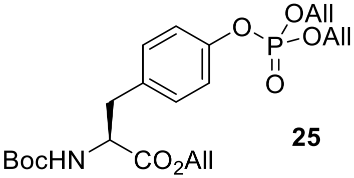

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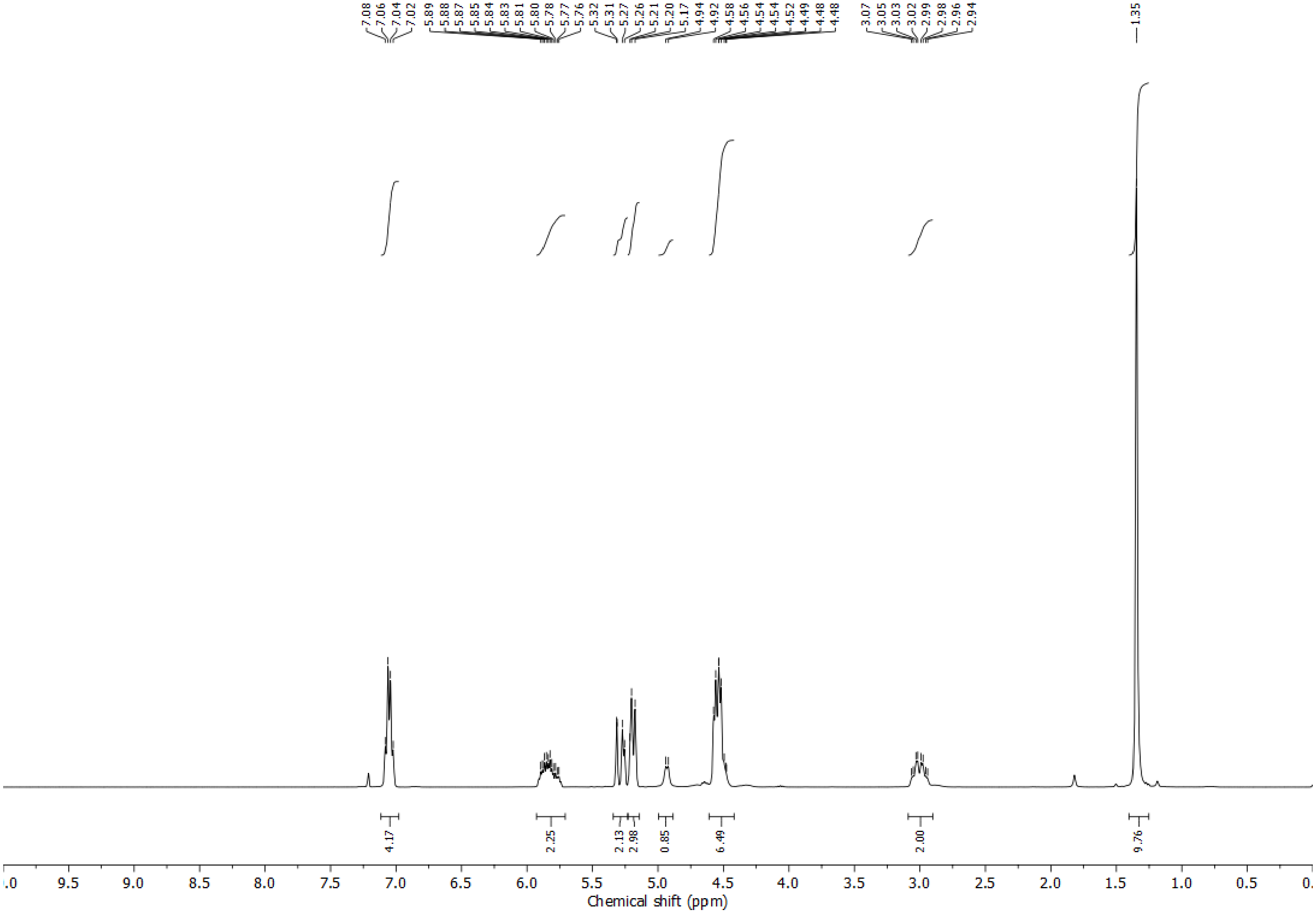

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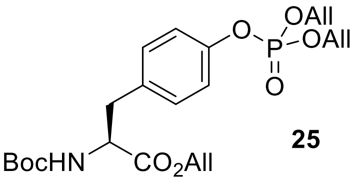

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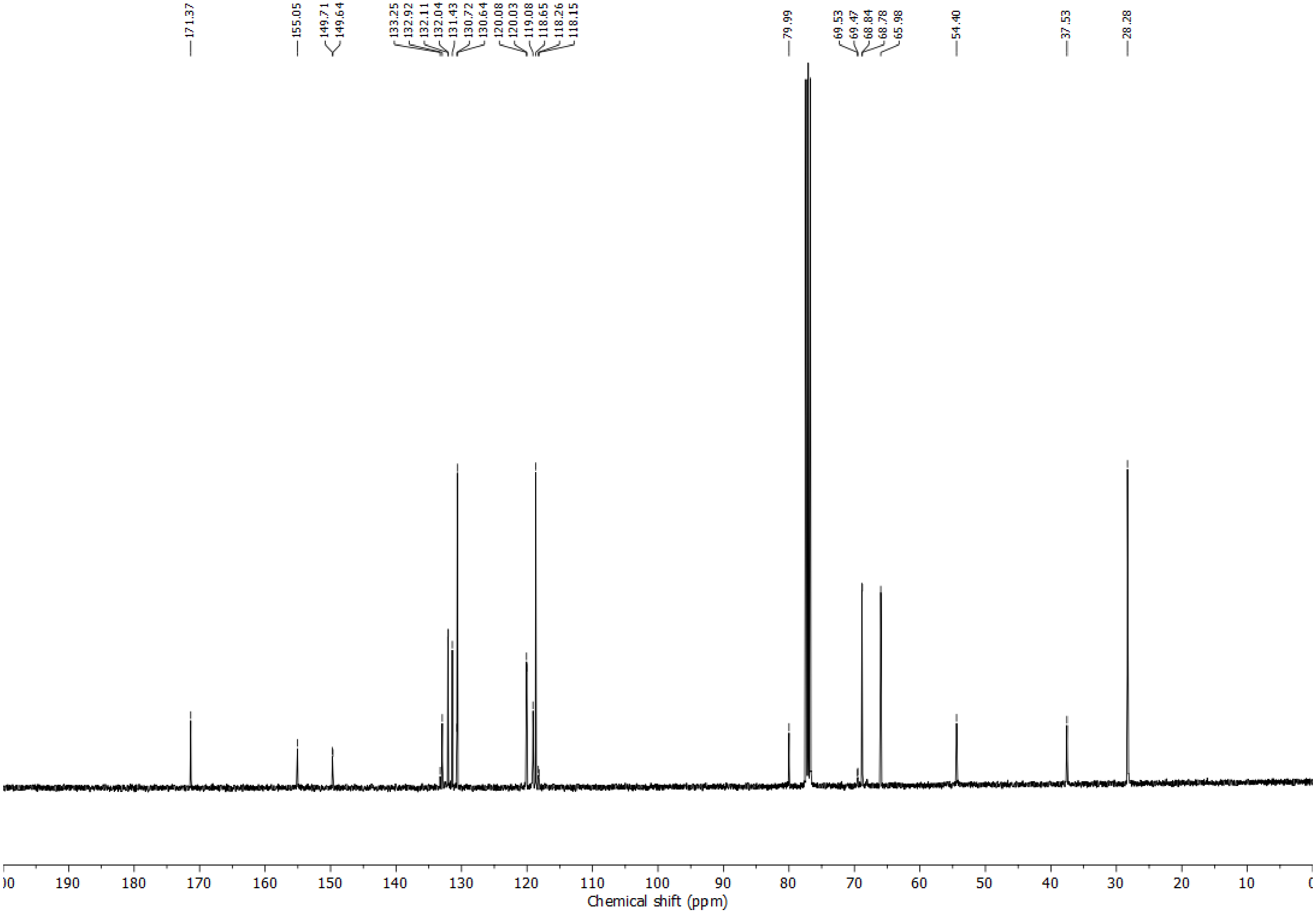

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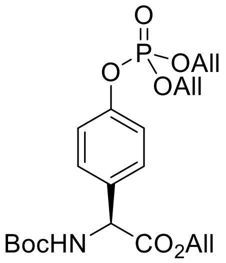

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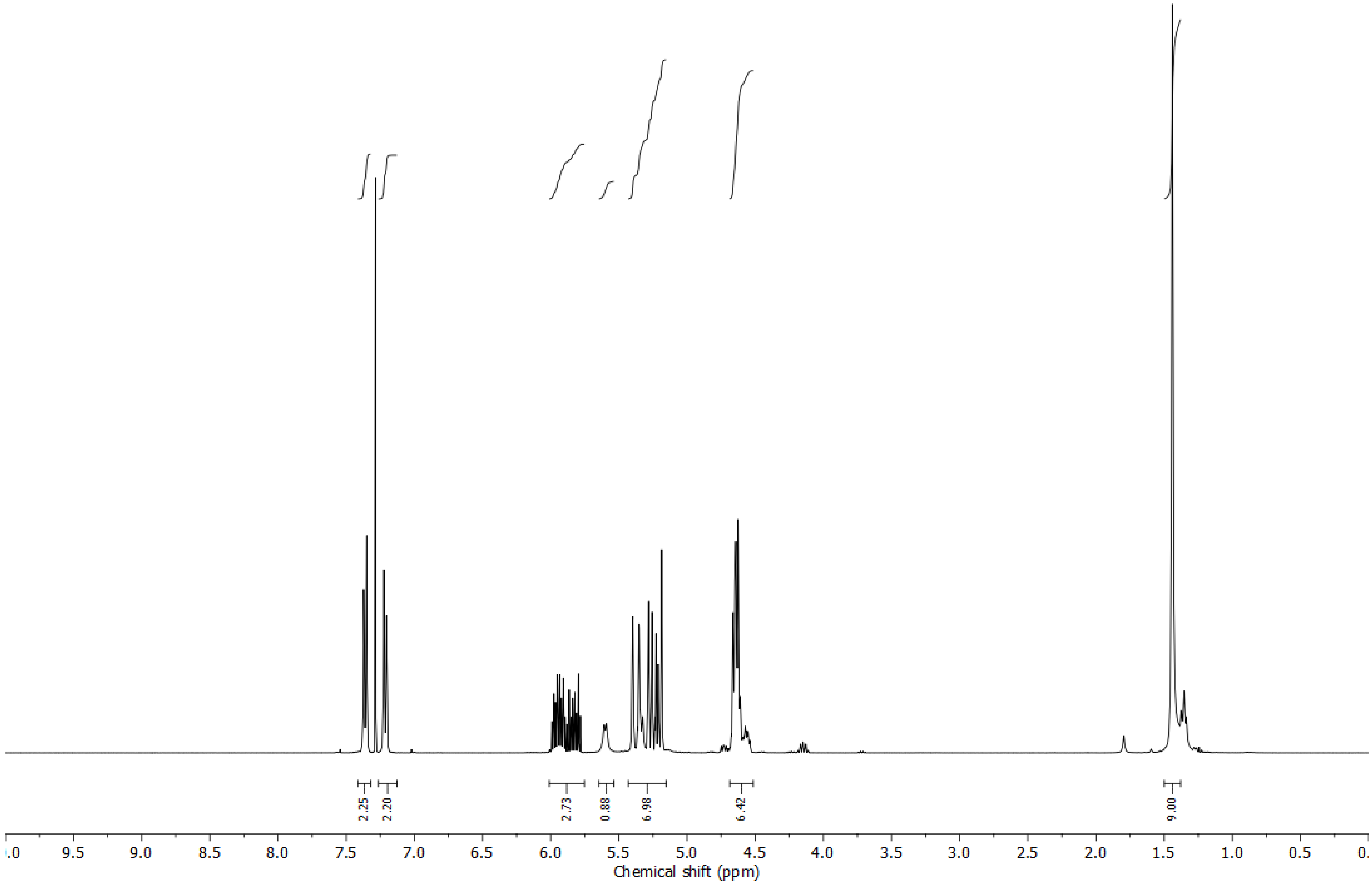

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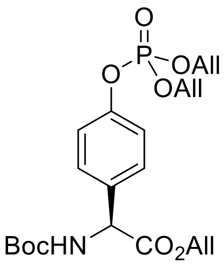

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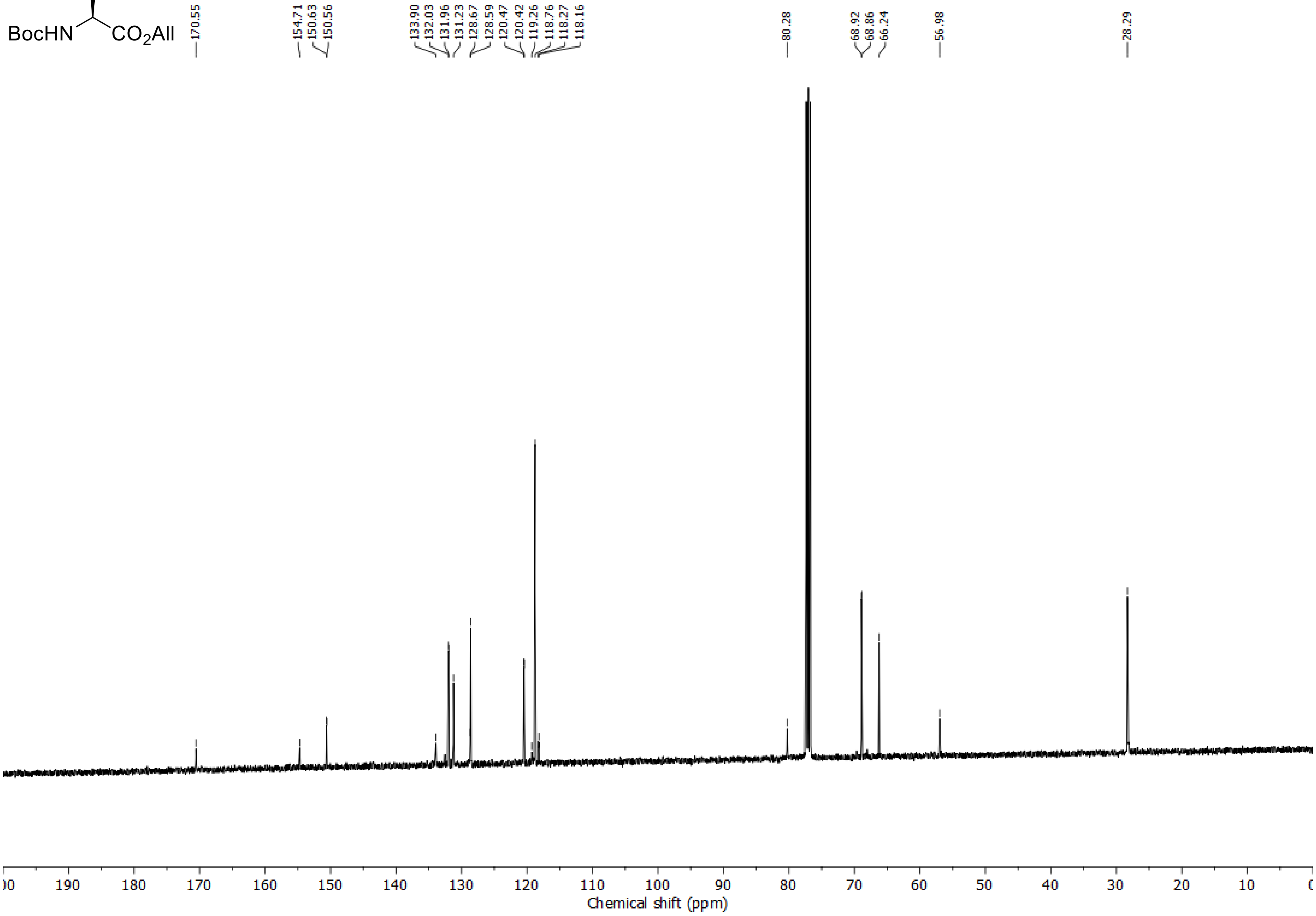

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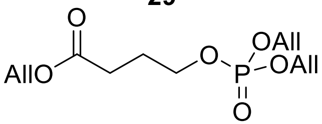

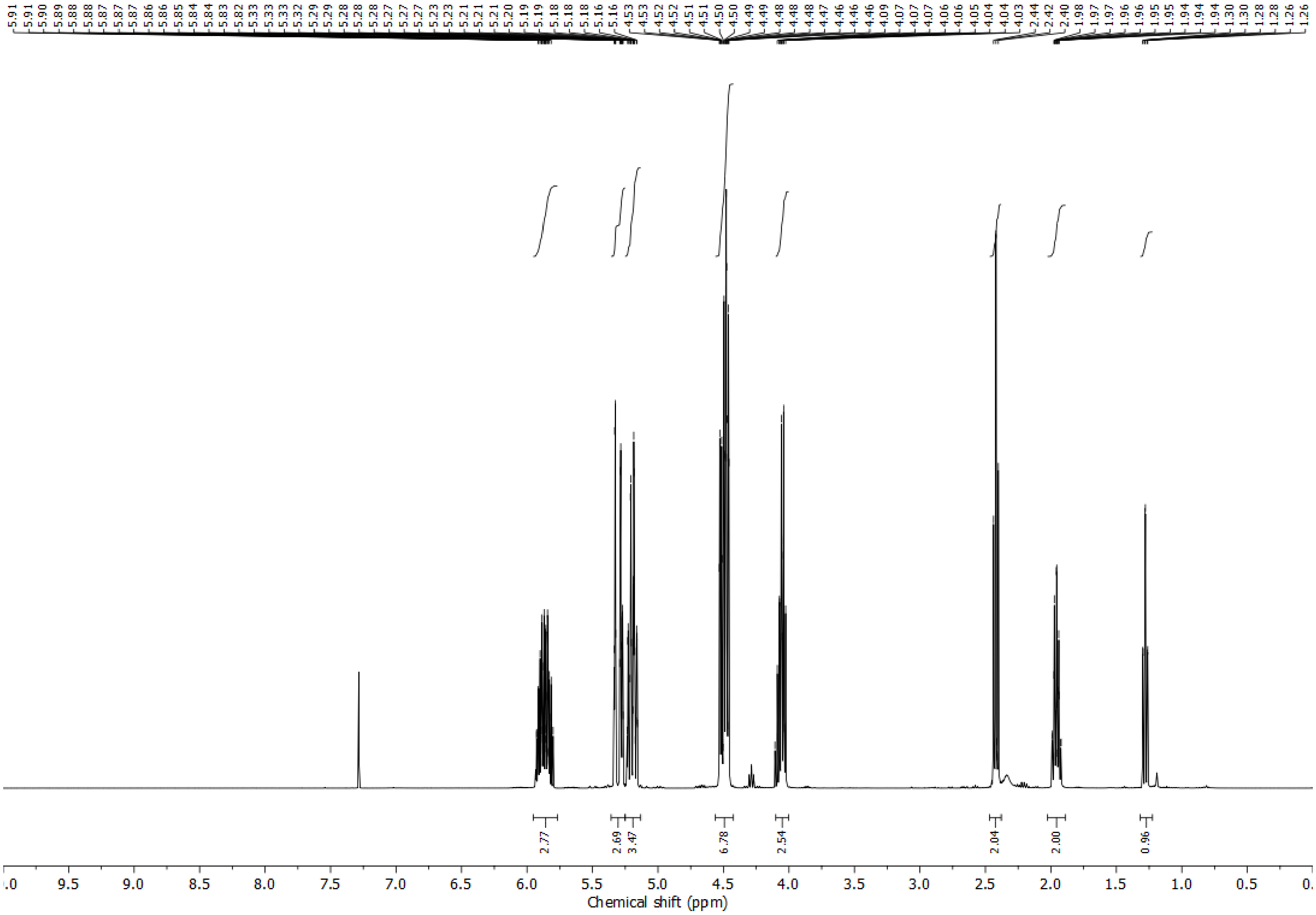

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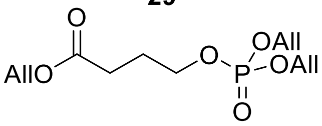

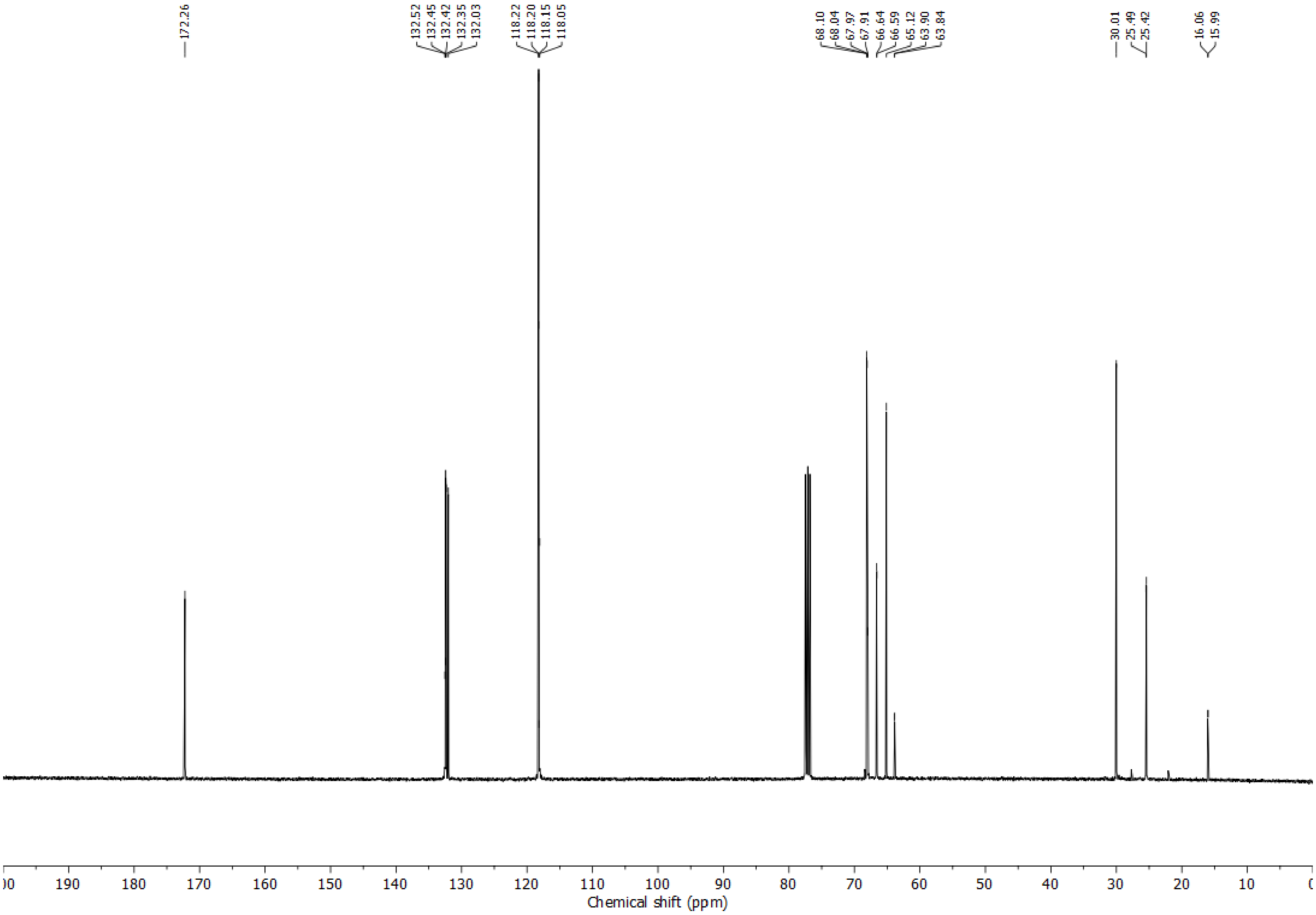

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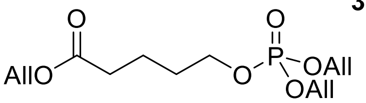

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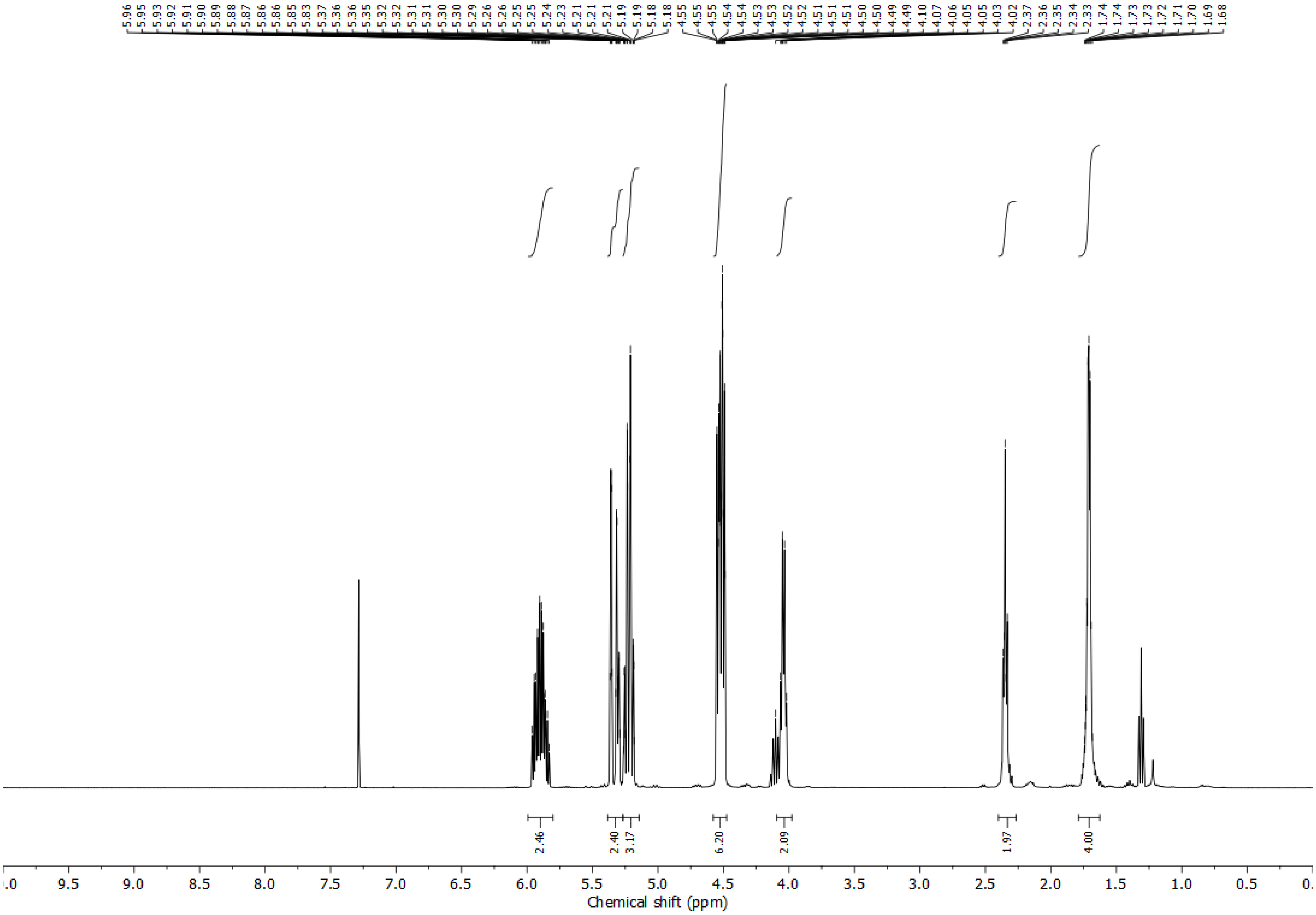

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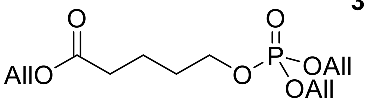

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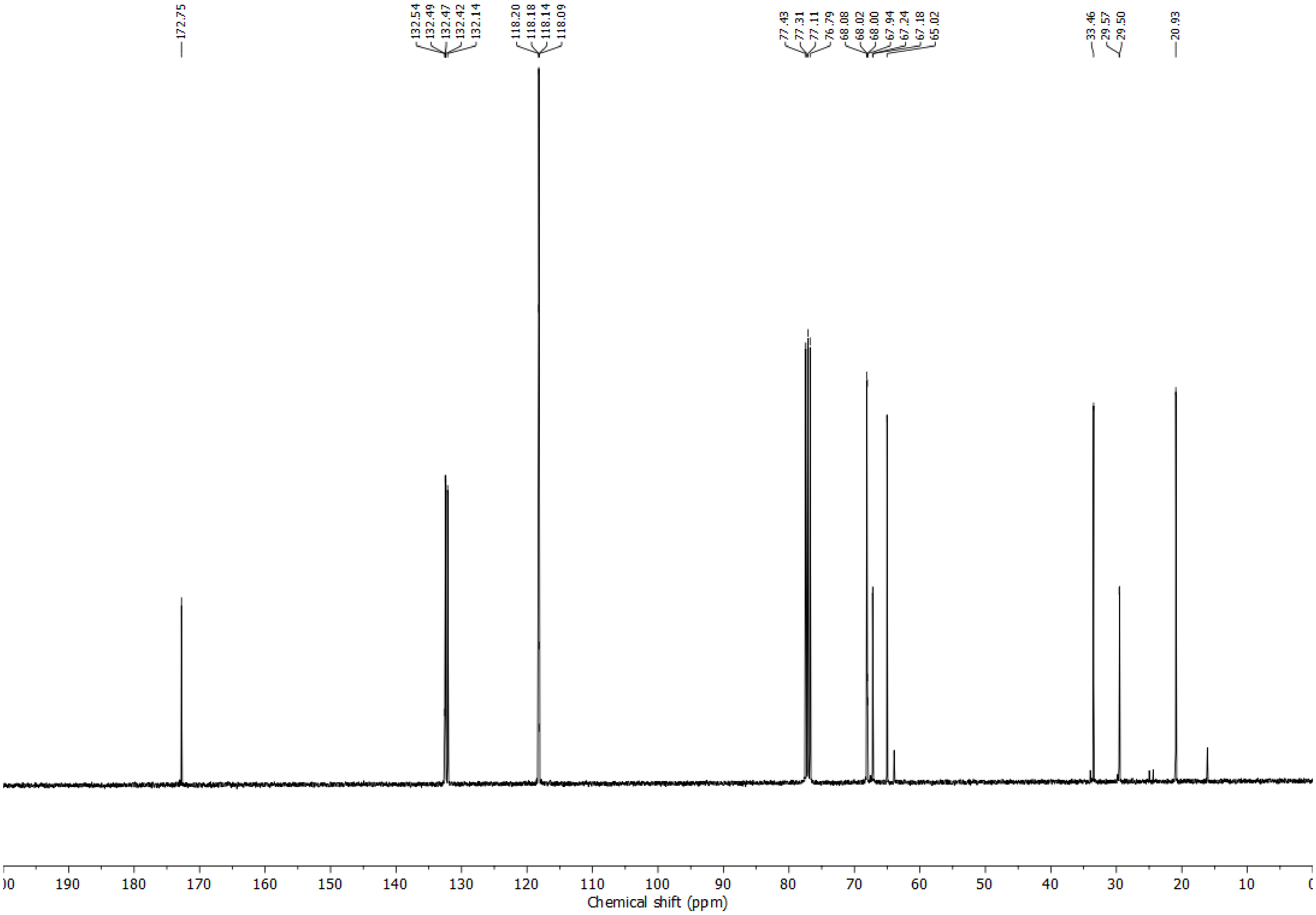

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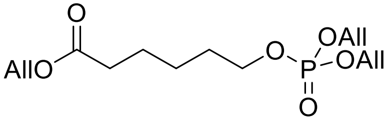

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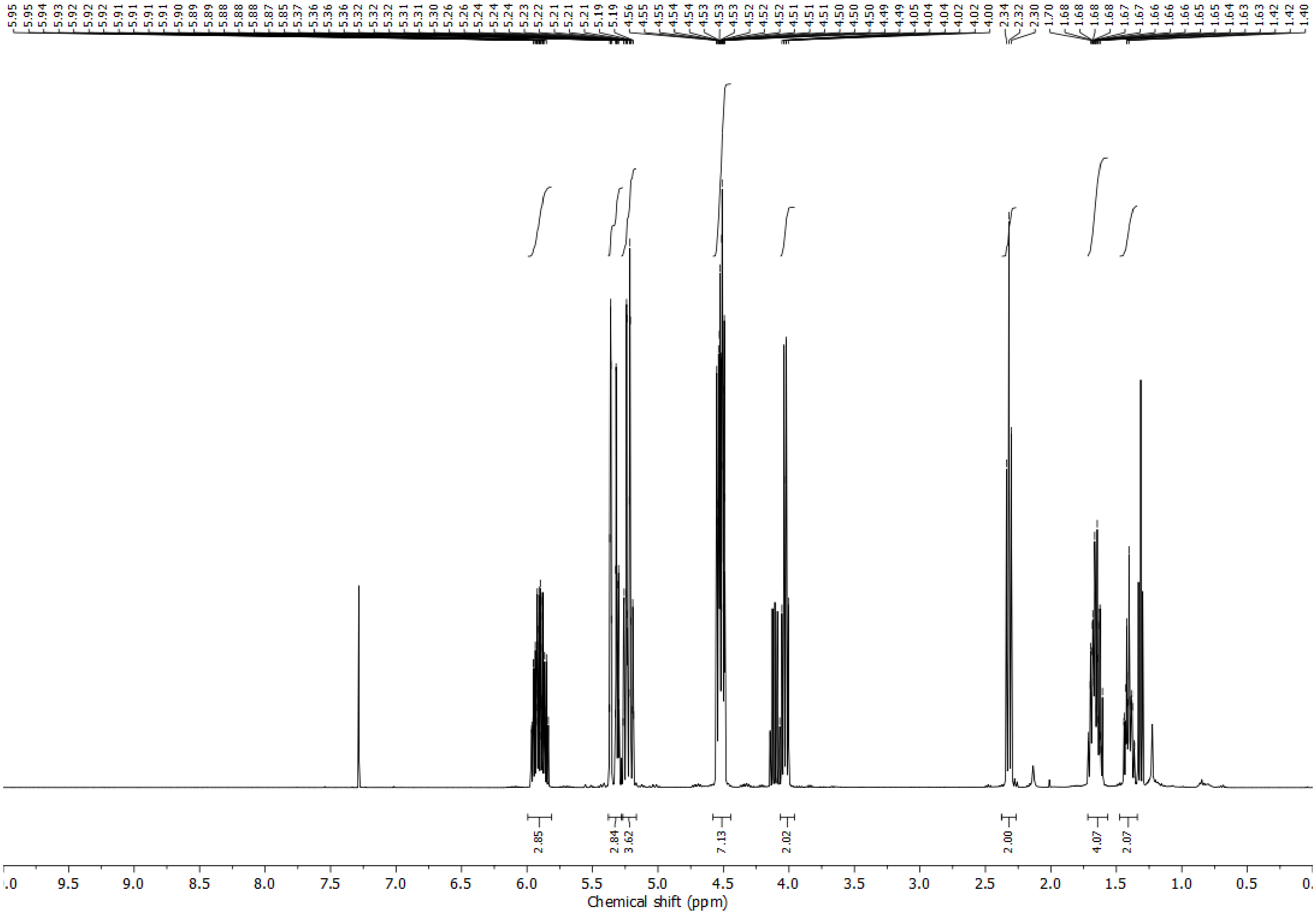

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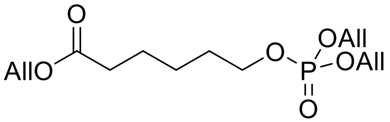

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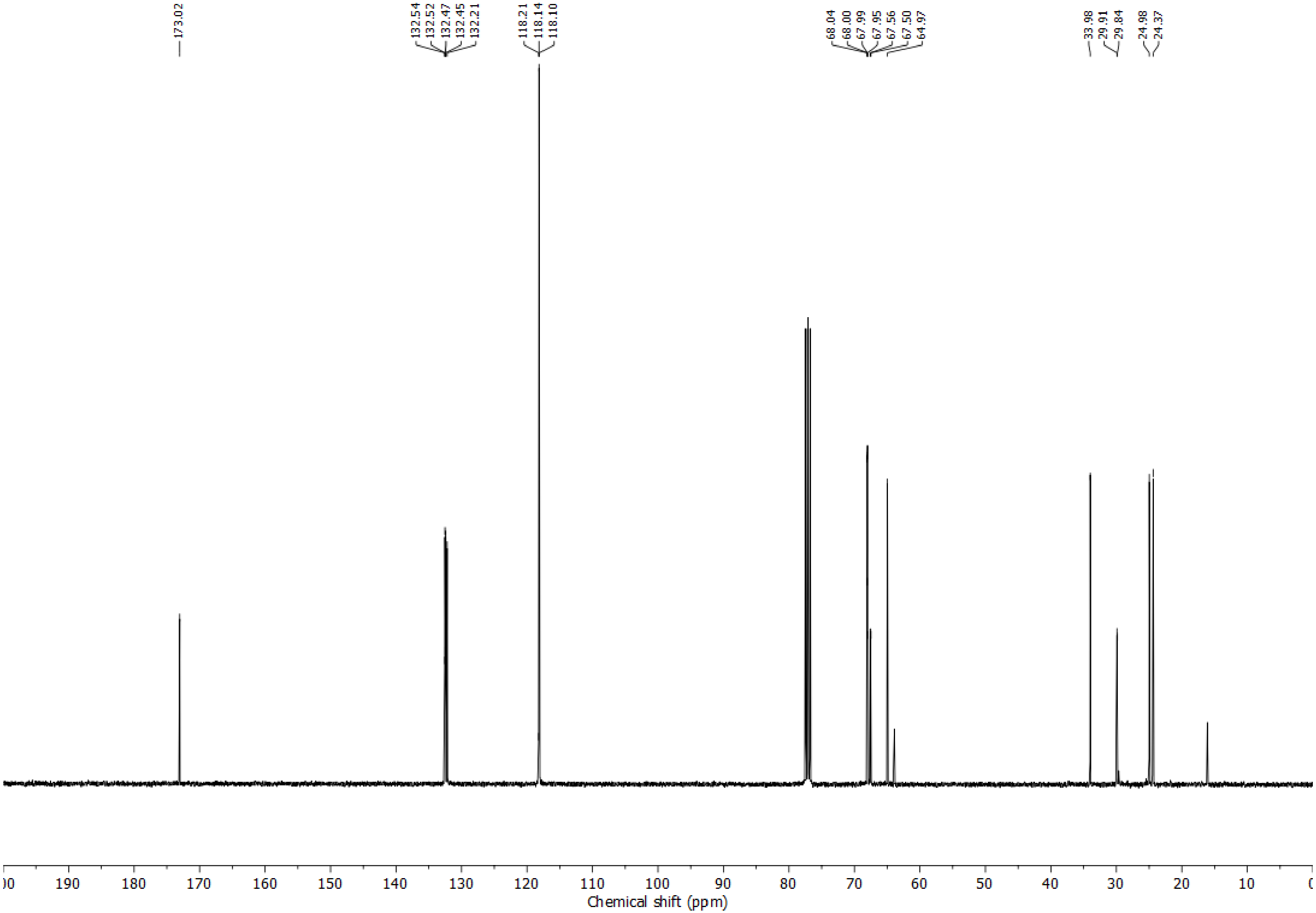

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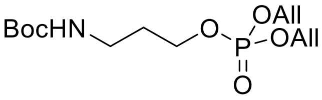

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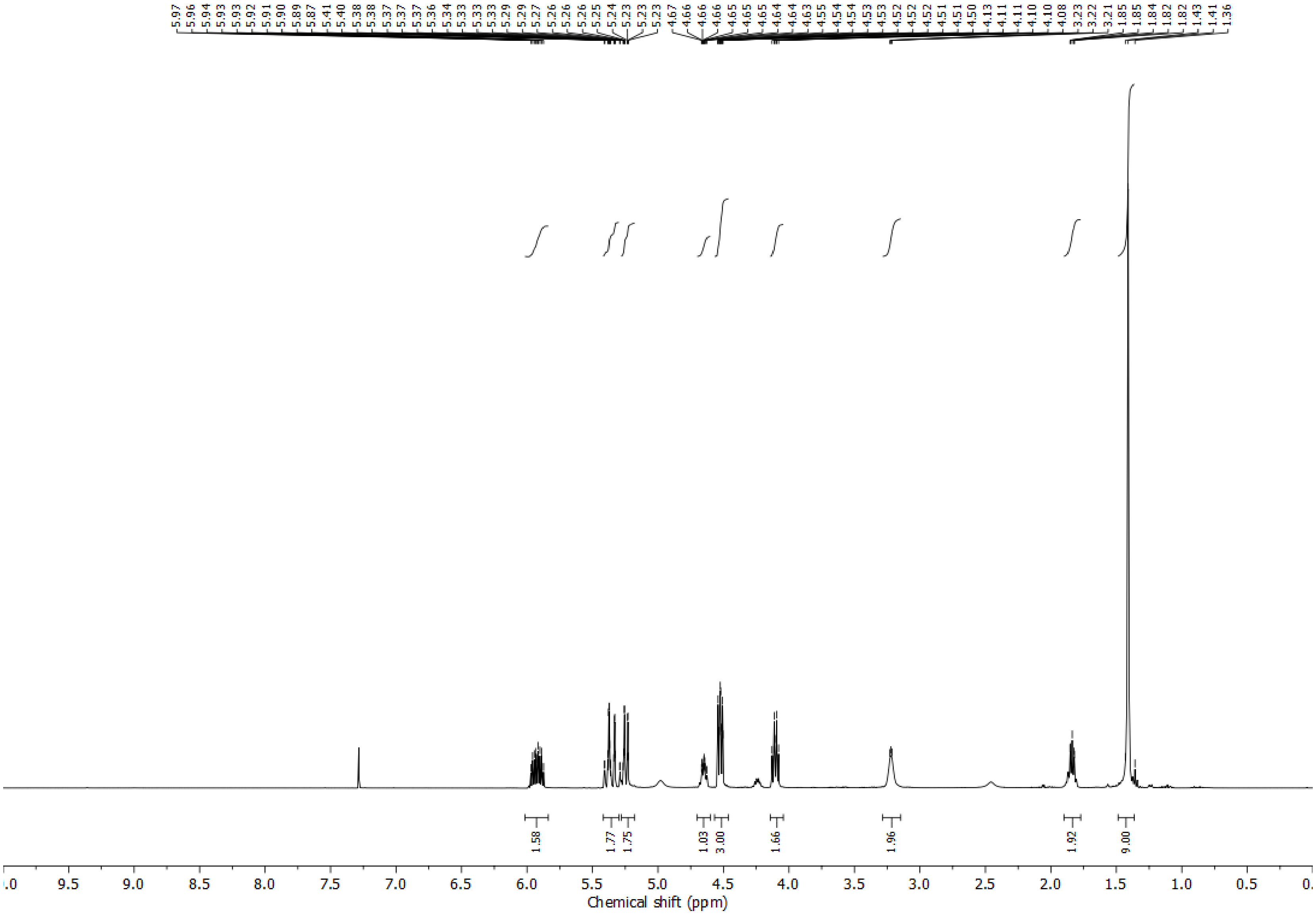

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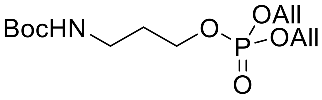

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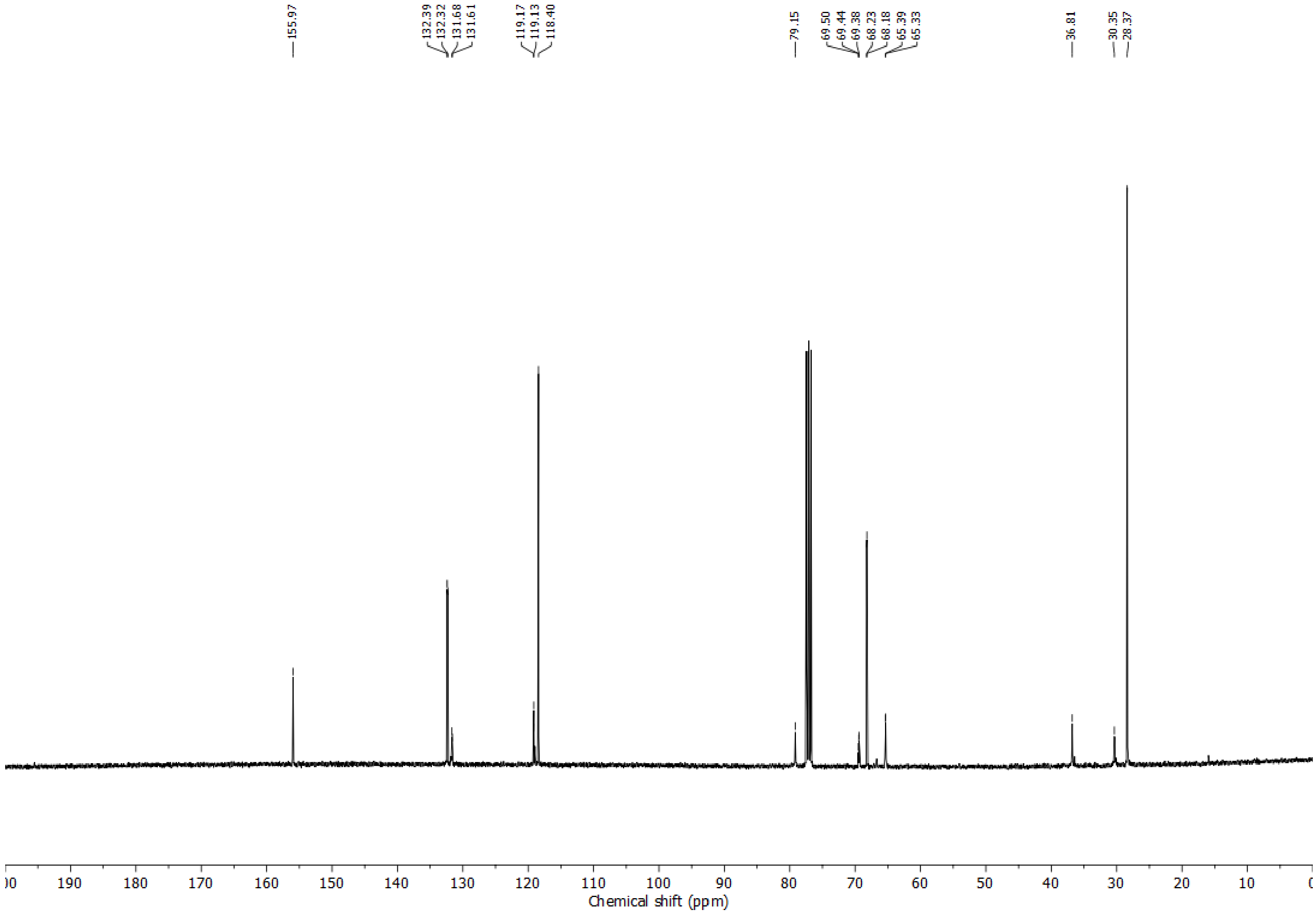

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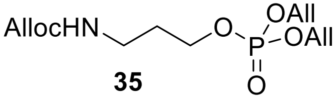

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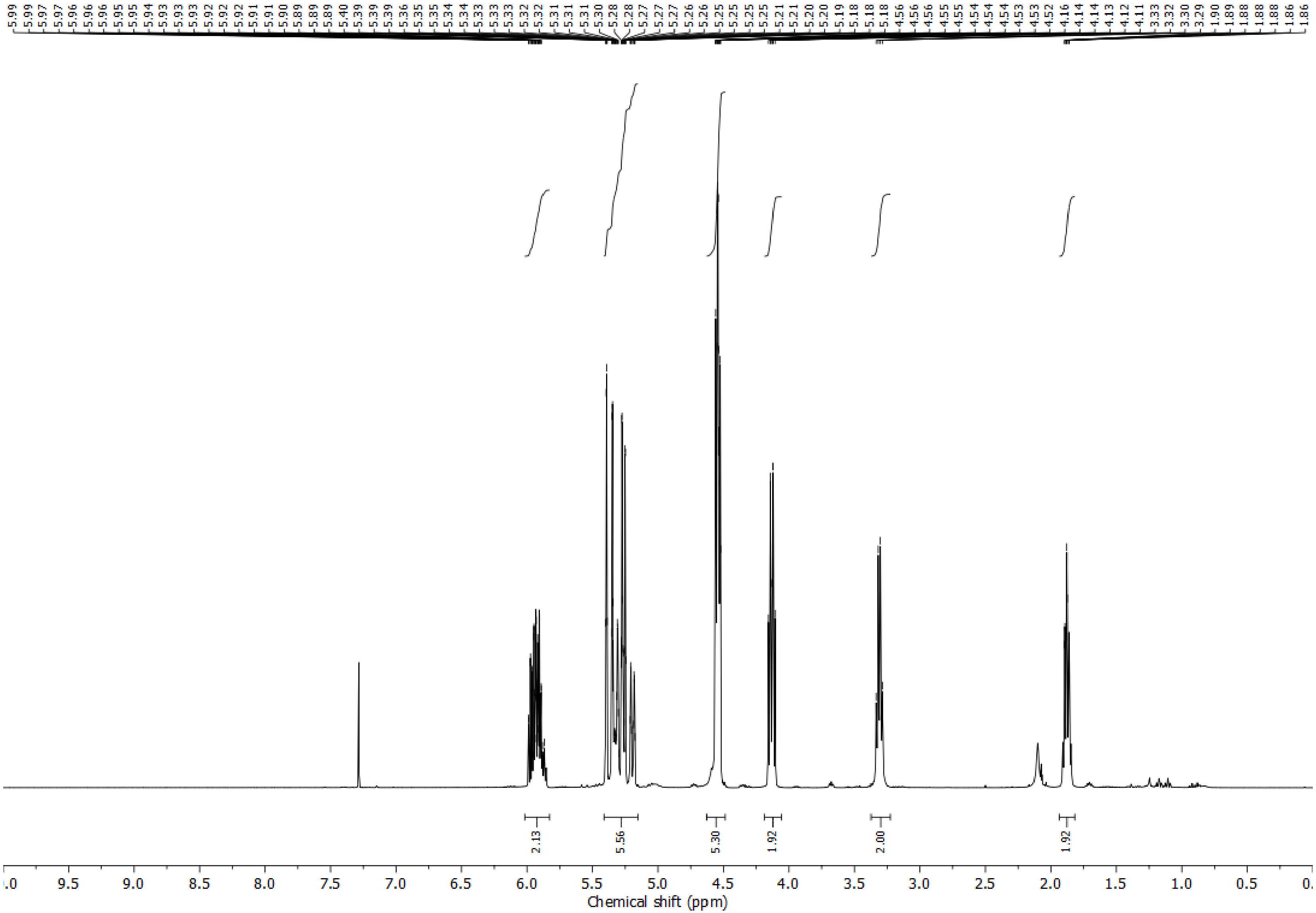

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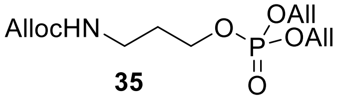

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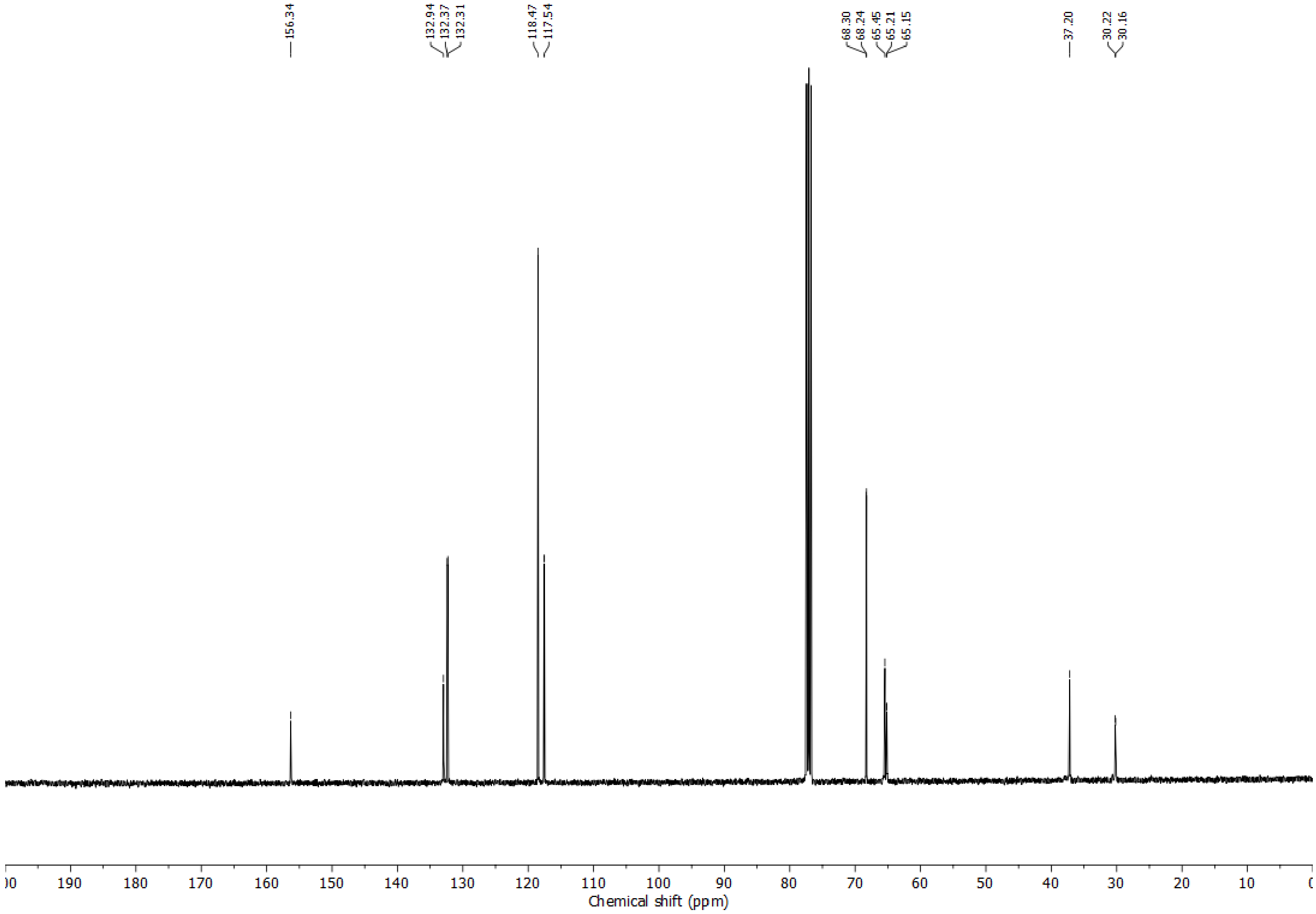

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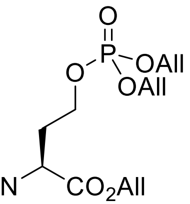

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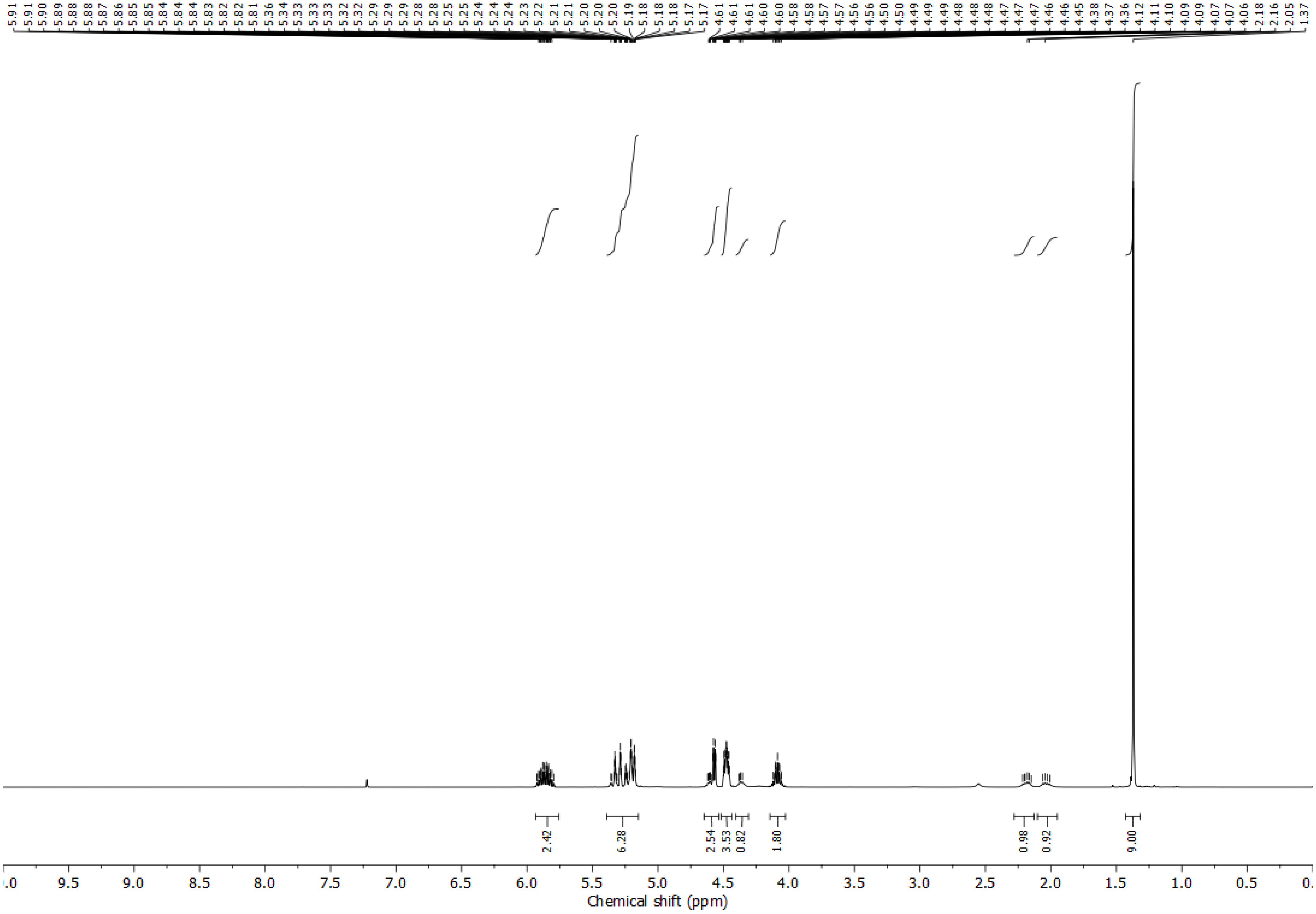

^{13}C NMR (100 MHz, CDCl$_3$)

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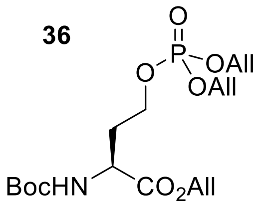

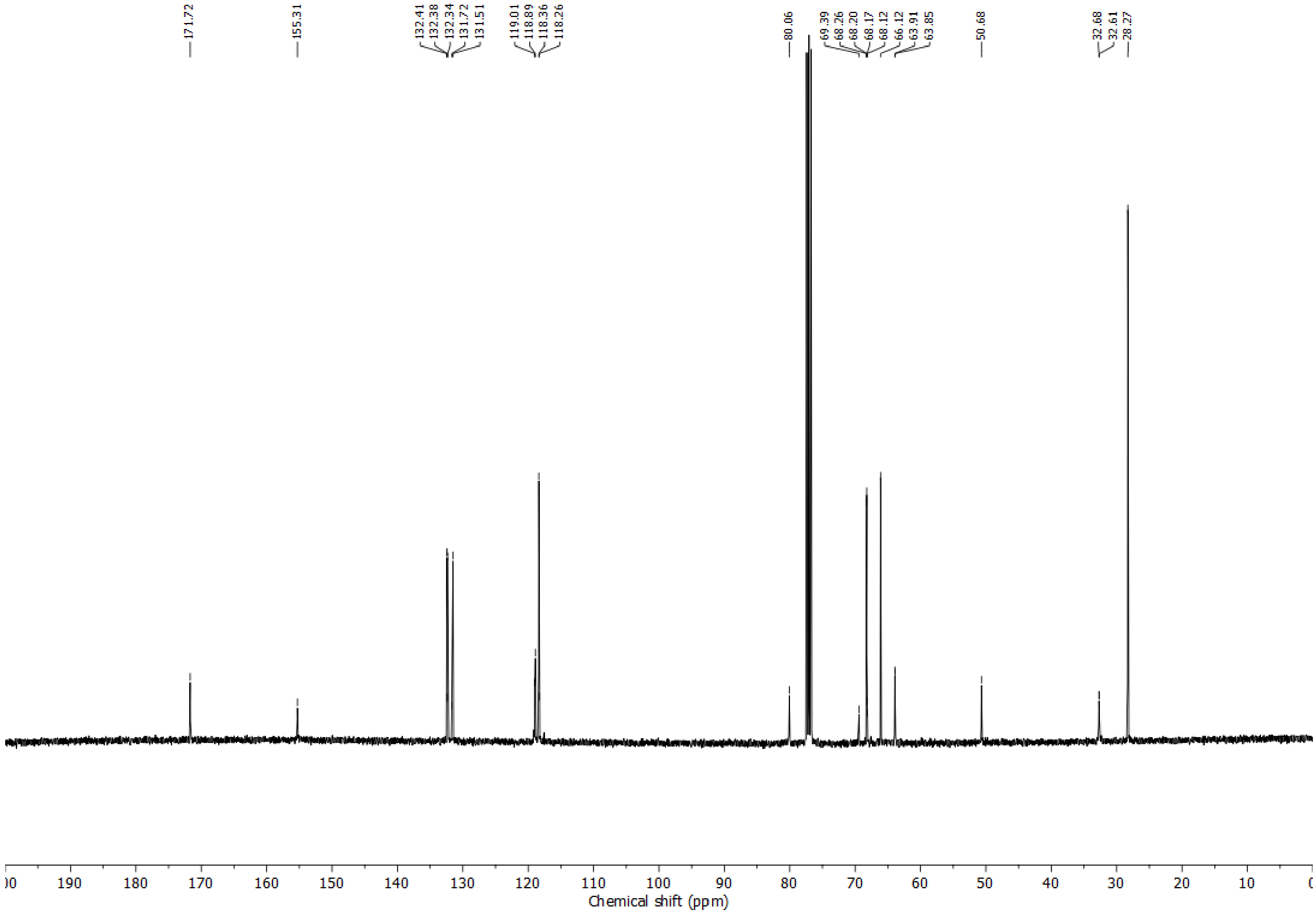

^{1}H NMR (400 MHz, $CDCl_3$)

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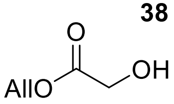
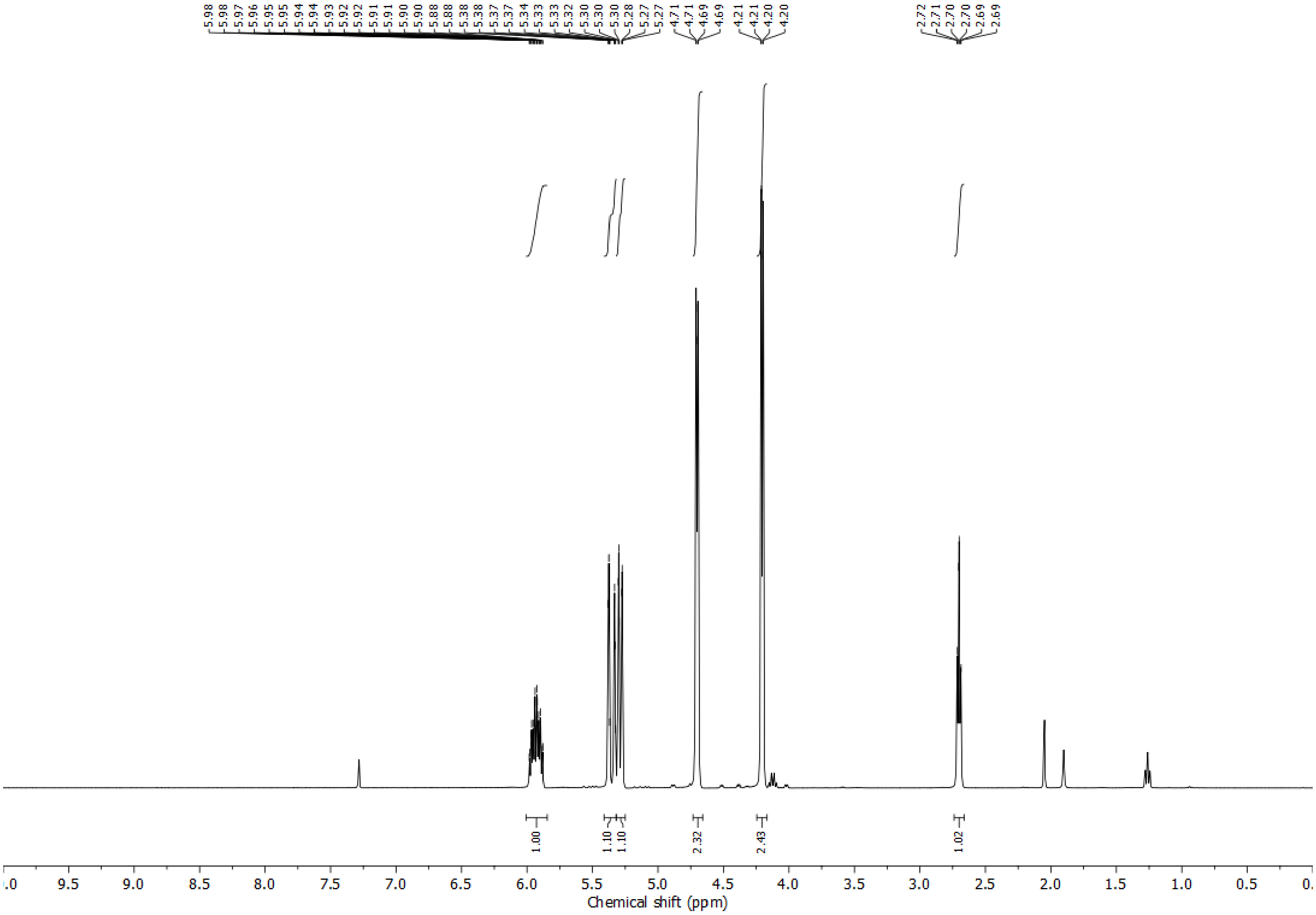
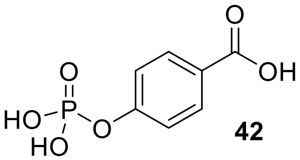




^{1}H NMR (400 MHz, MeOD)



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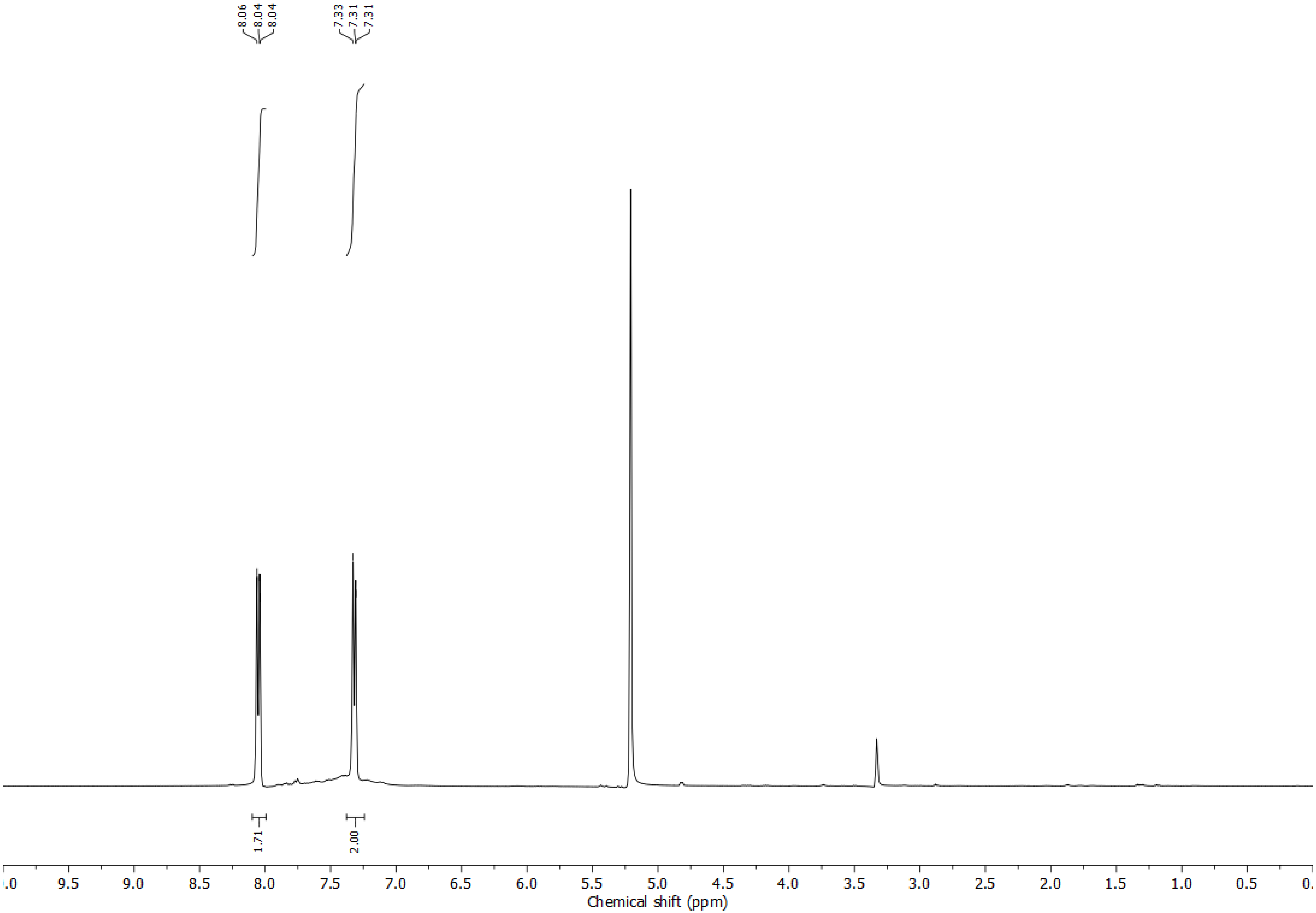

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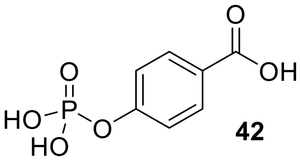

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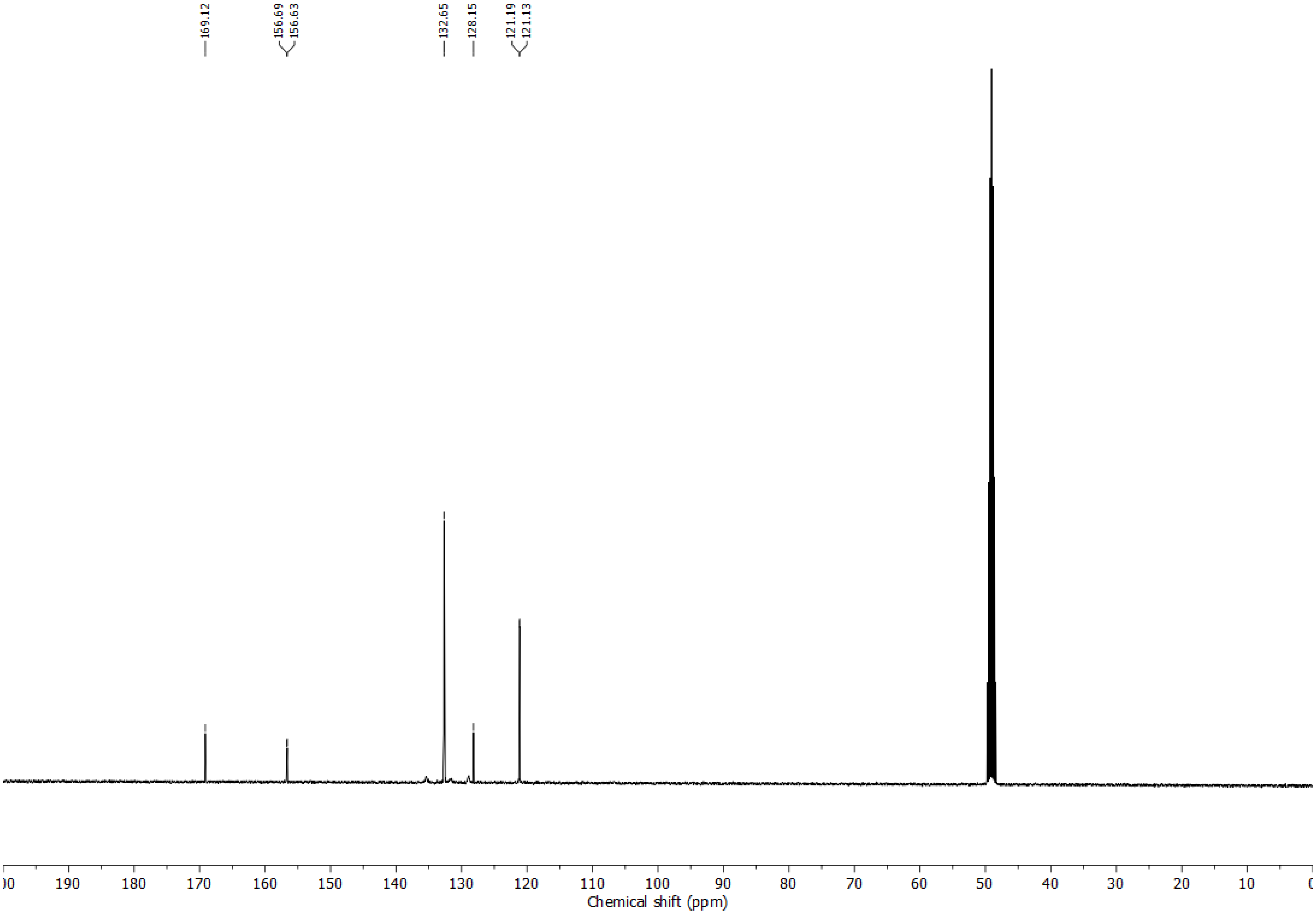
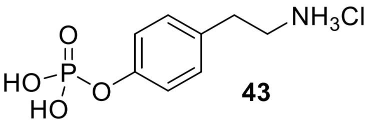


^{1}H NMR (400 MHz, D_2O)



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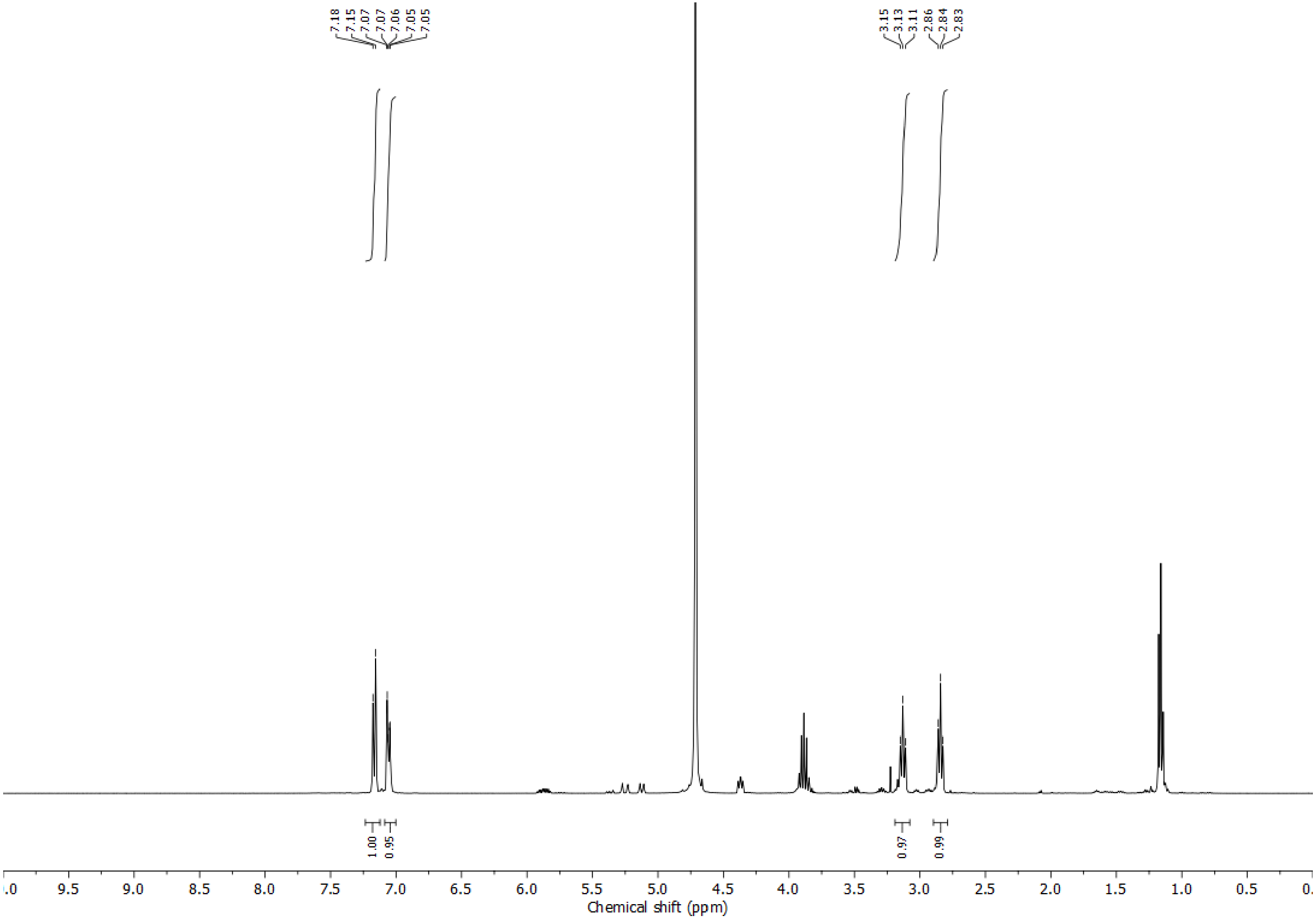
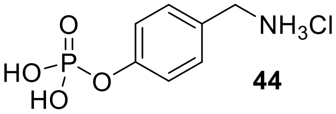


^{1}H NMR (400 MHz, D_2O)



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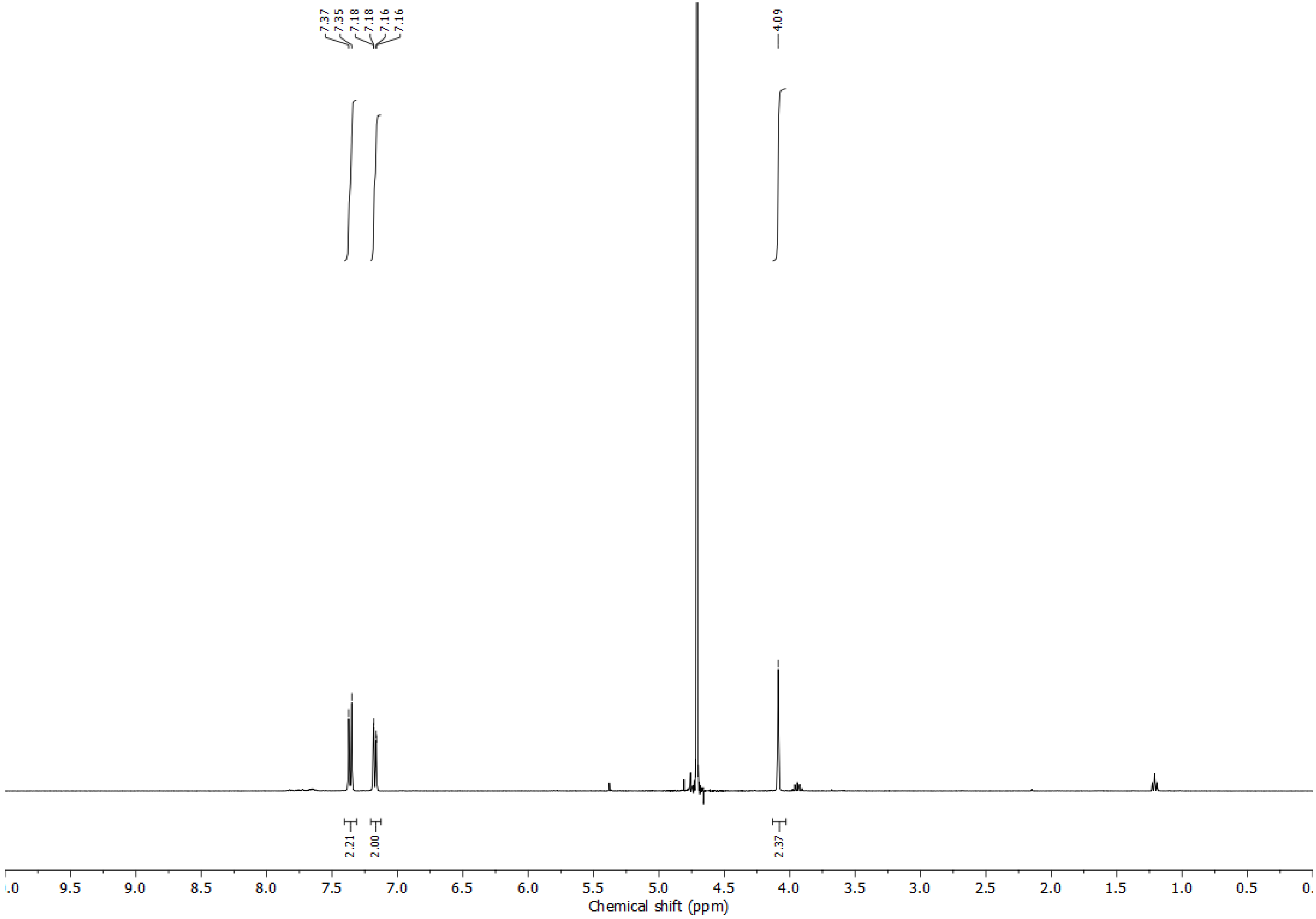
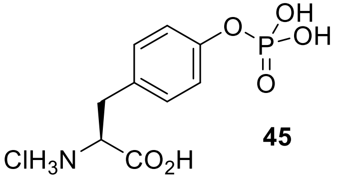


^{1}H NMR (400 MHz, MeOD)



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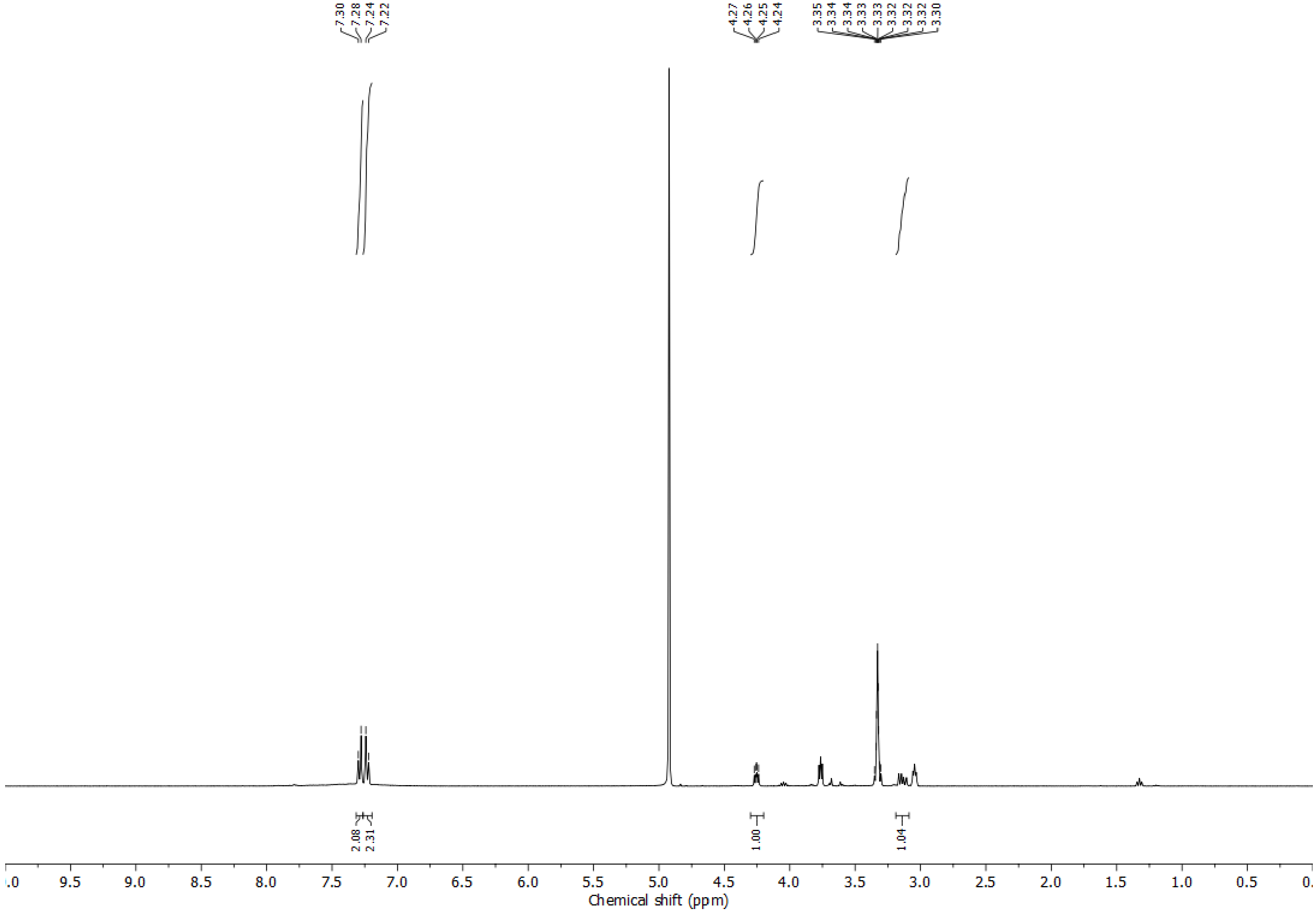

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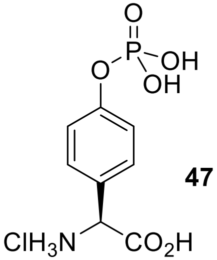

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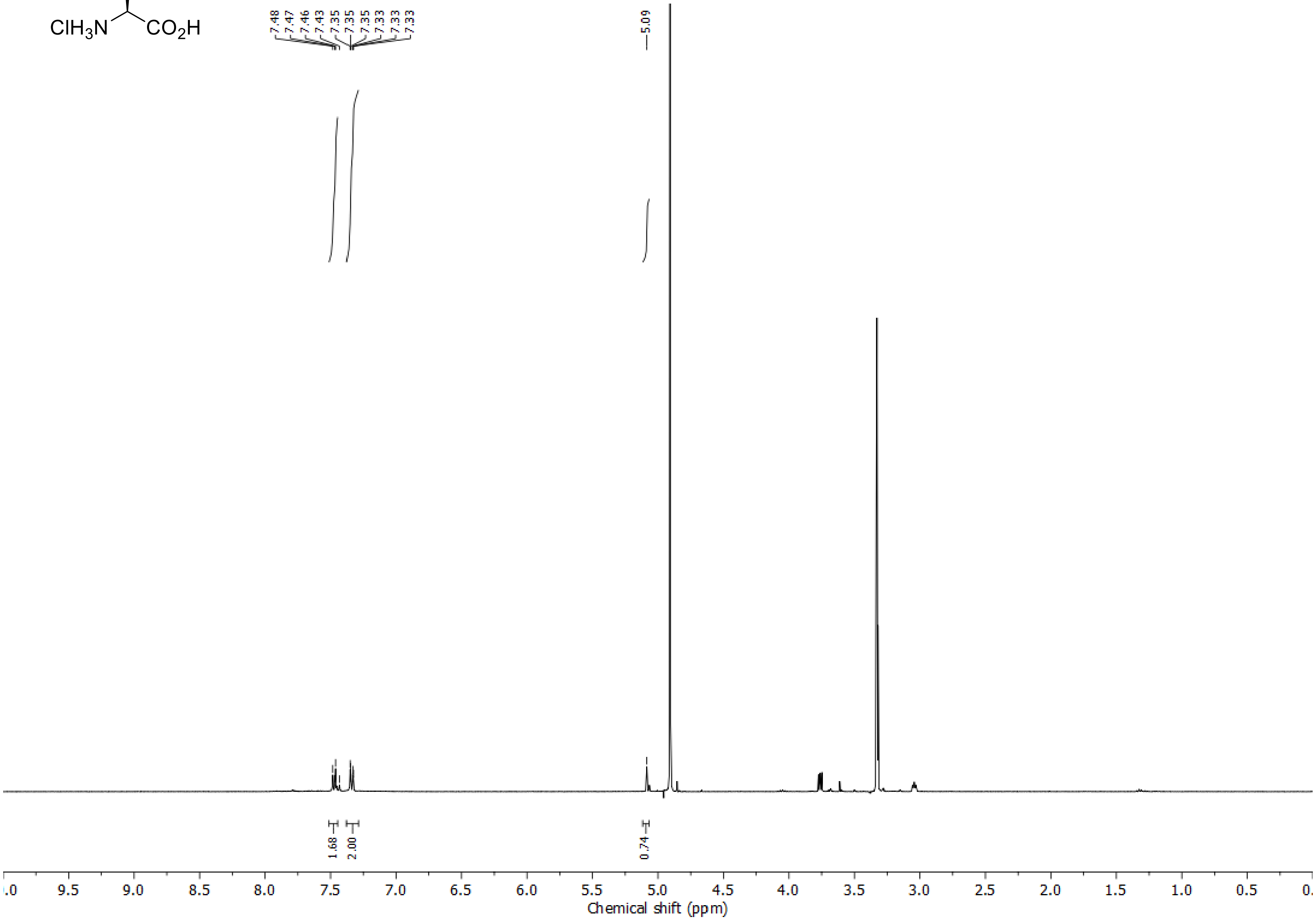

^{1}H NMR (400 MHz, D_2O)

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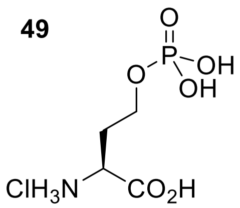

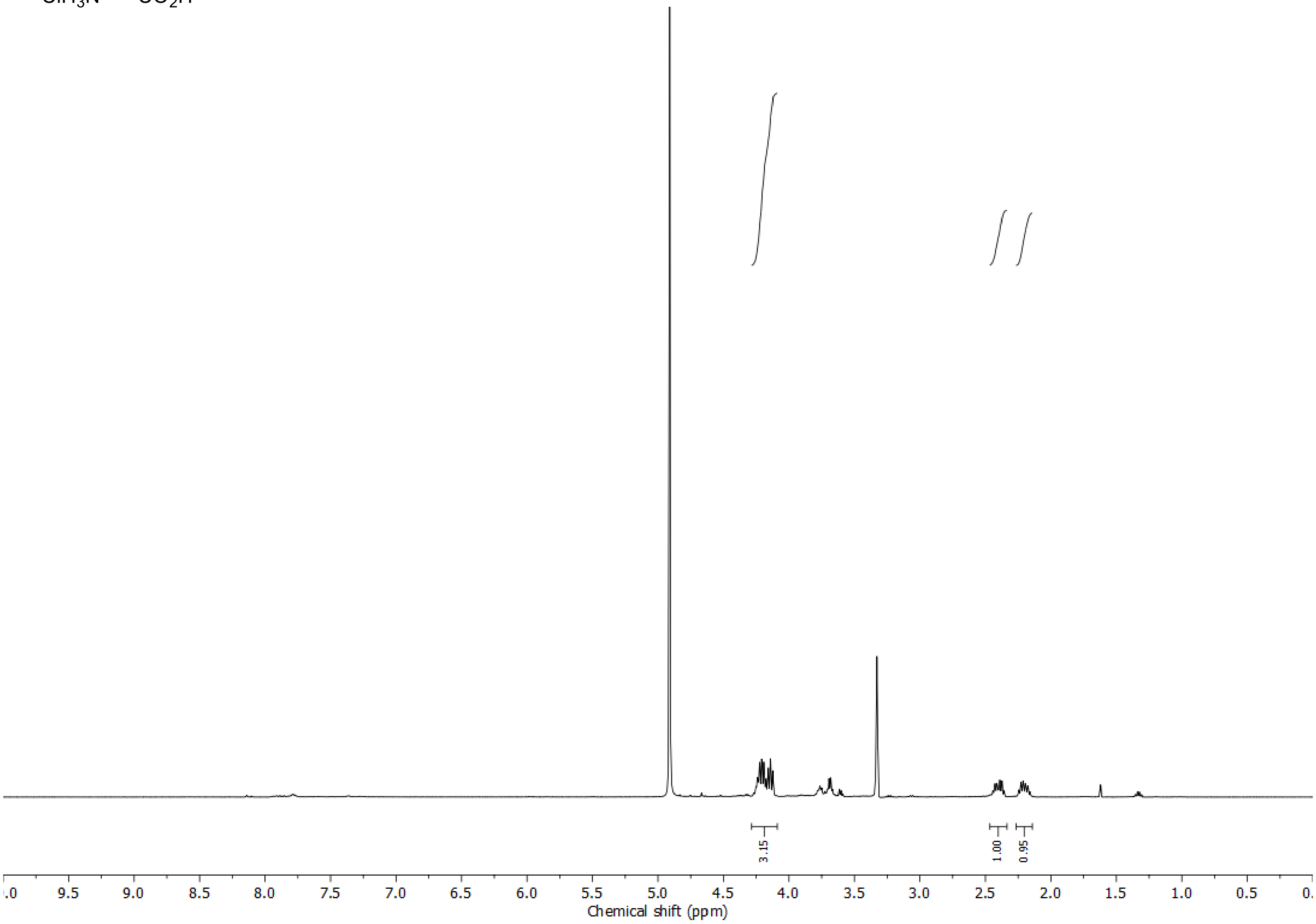

^{1}H NMR (400 MHz, MeOD)

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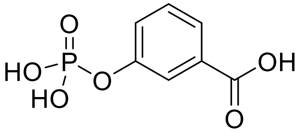

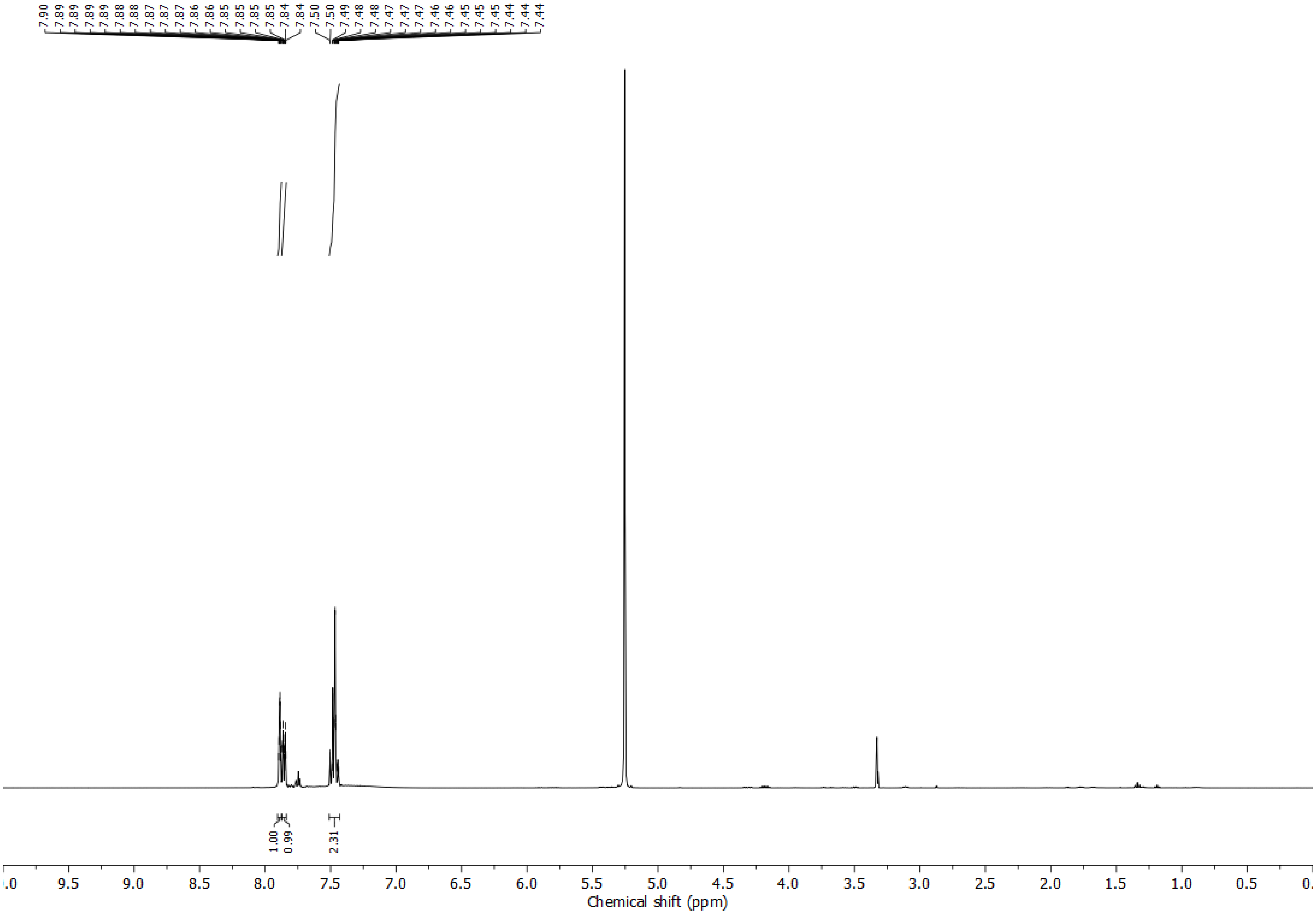

^{13}C NMR (100 MHz, MeOD)

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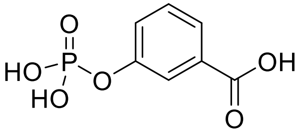

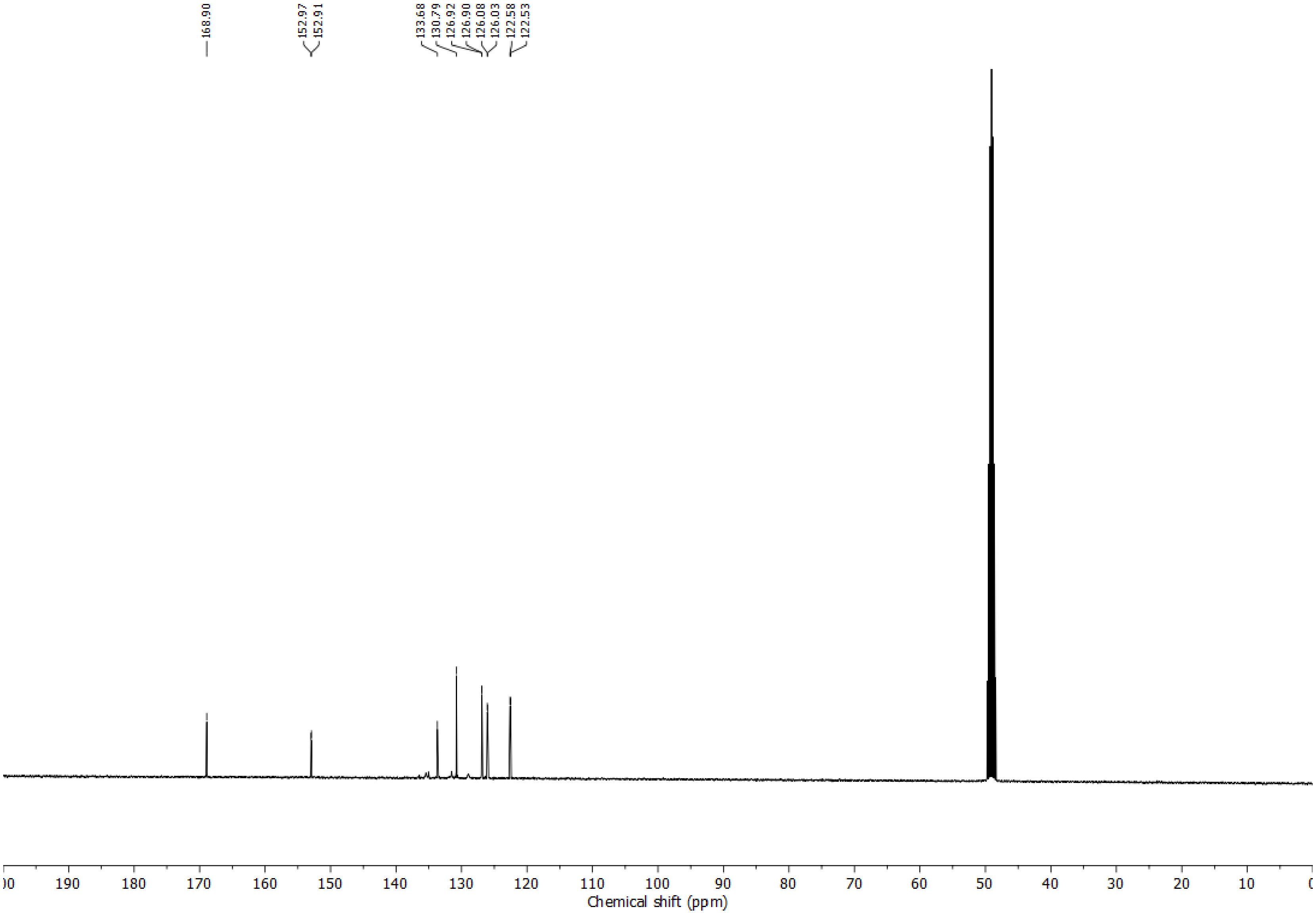

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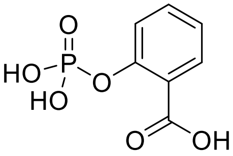

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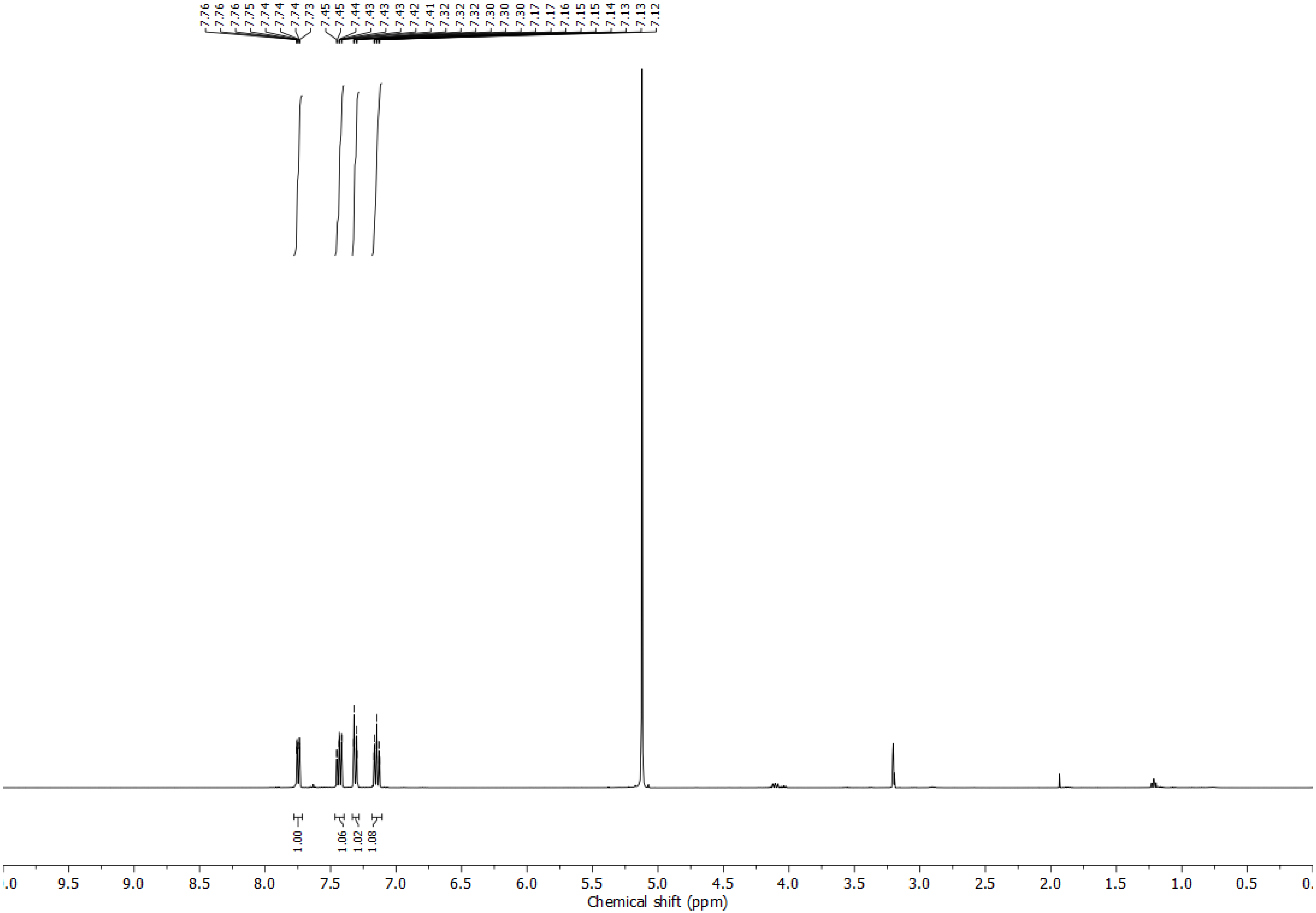

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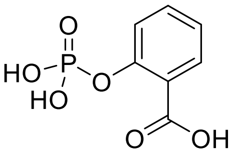

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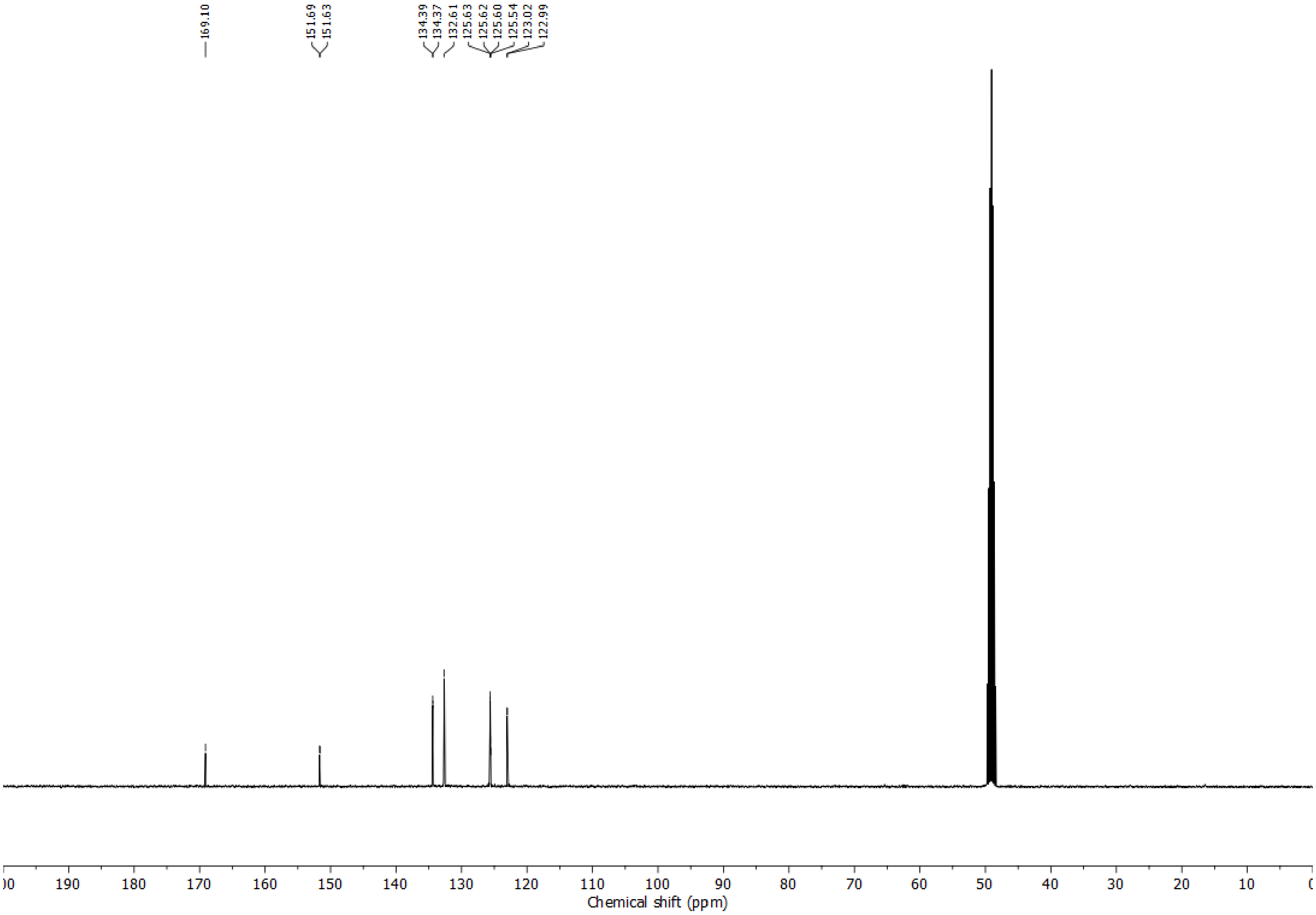

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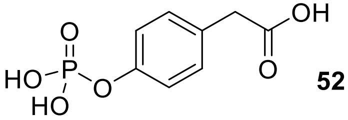

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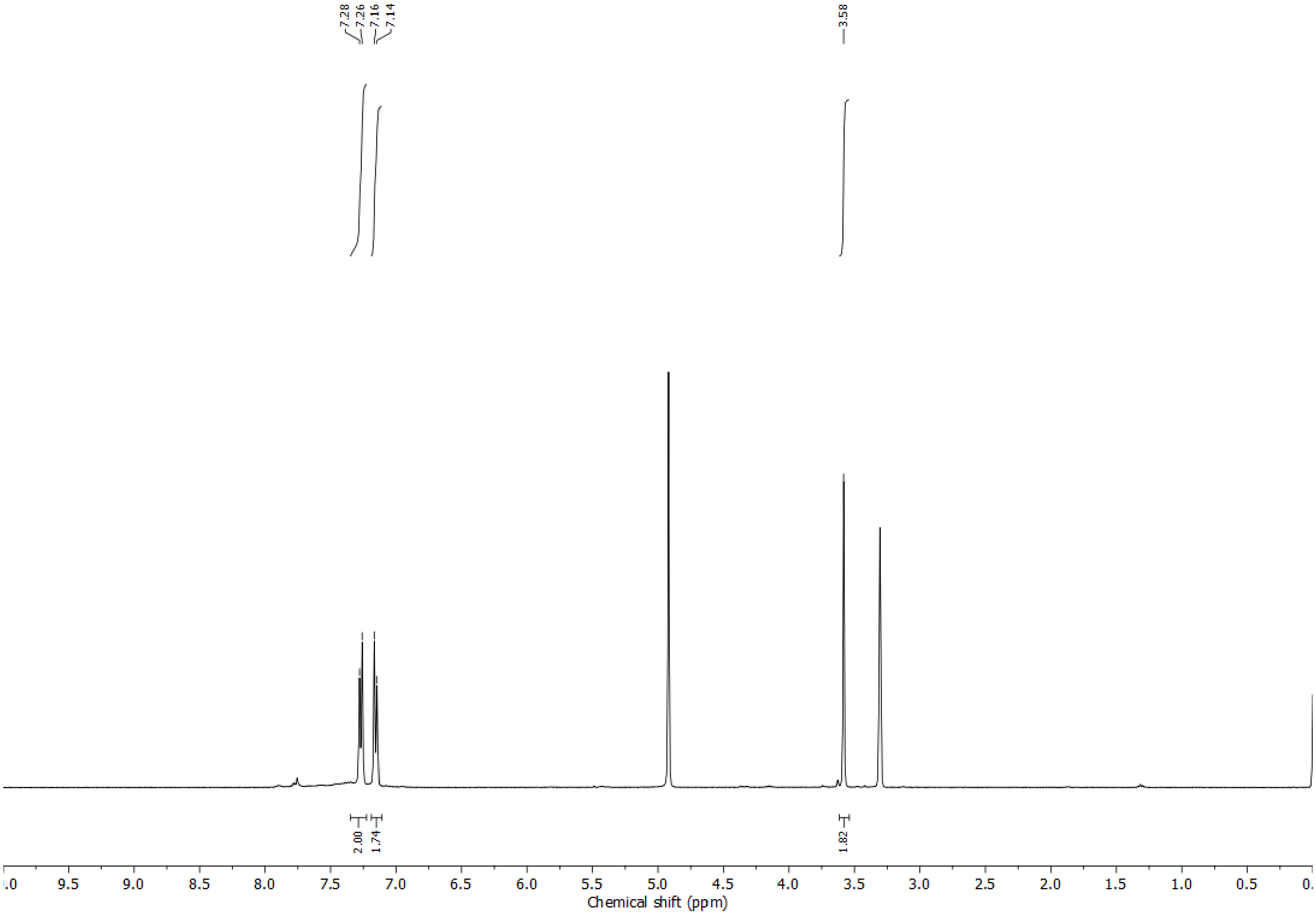
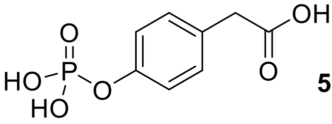


^{13}C NMR (100 MHz, MeOD)



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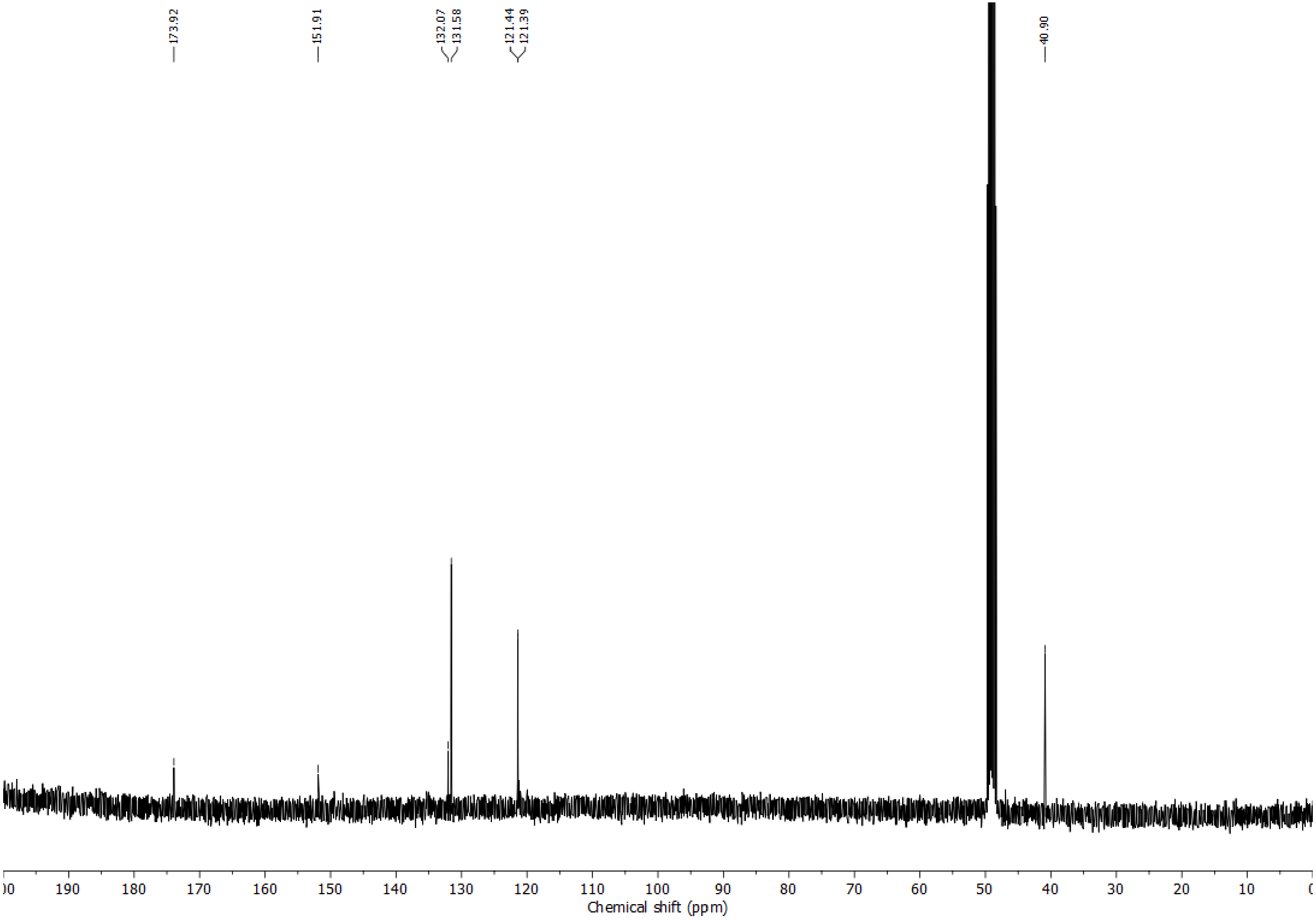
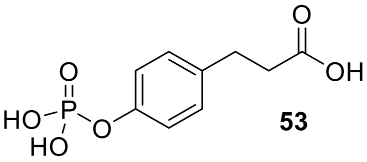


^{1}H NMR (400 MHz, MeOD)



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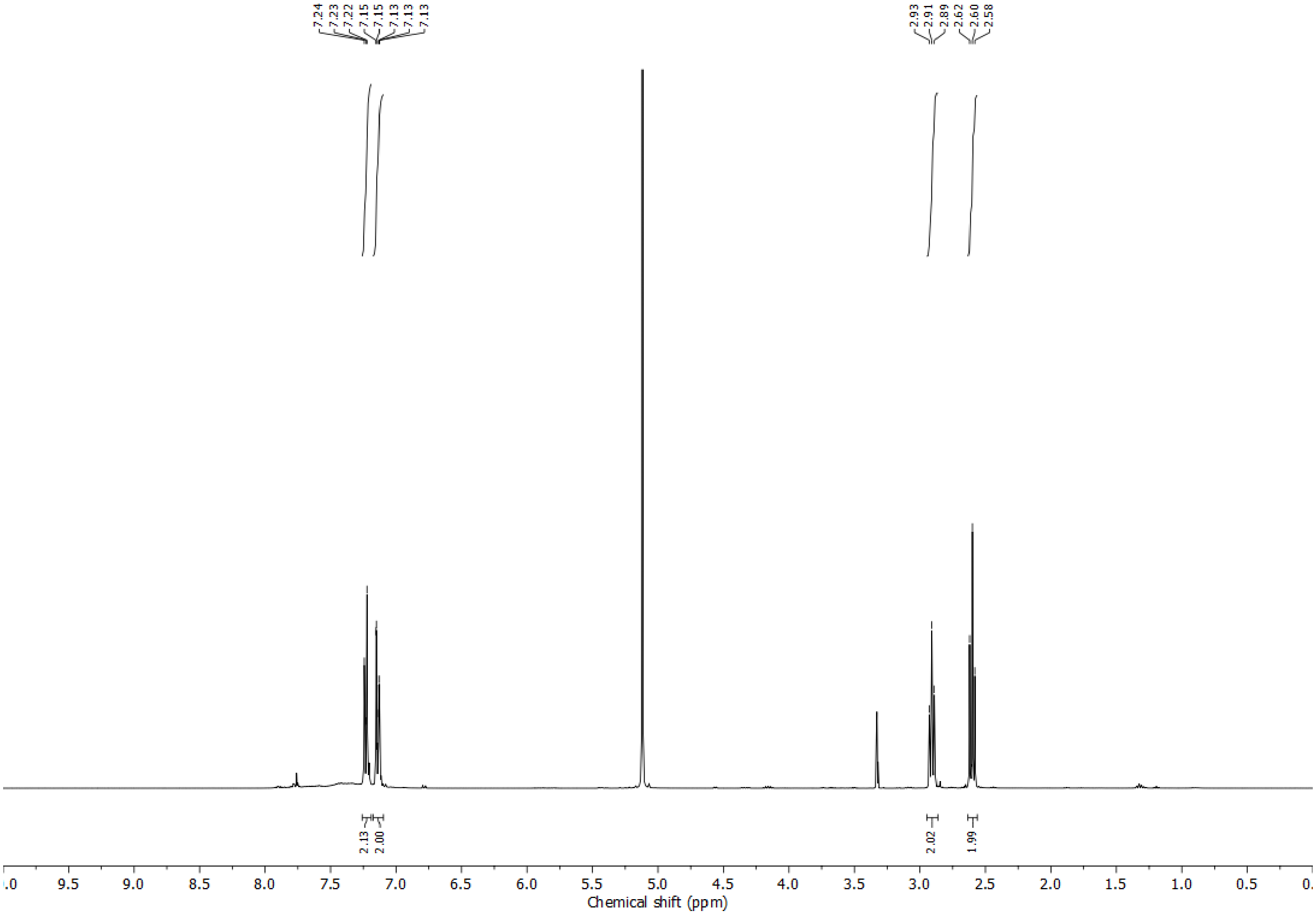
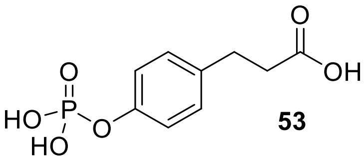


^{13}C NMR (100 MHz, MeOD)



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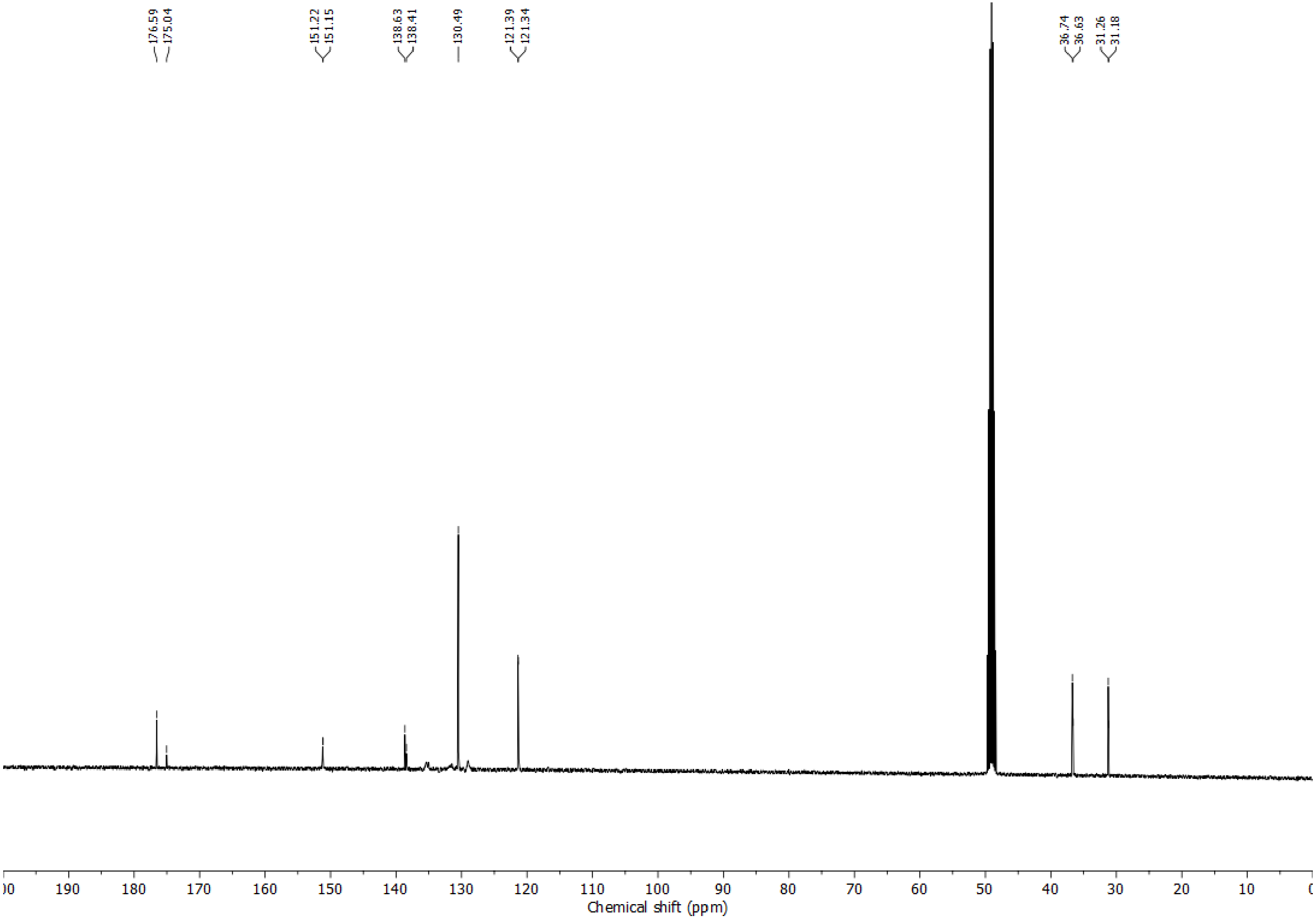
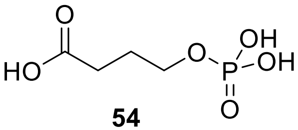


^{1}H NMR (400 MHz, MeOD)



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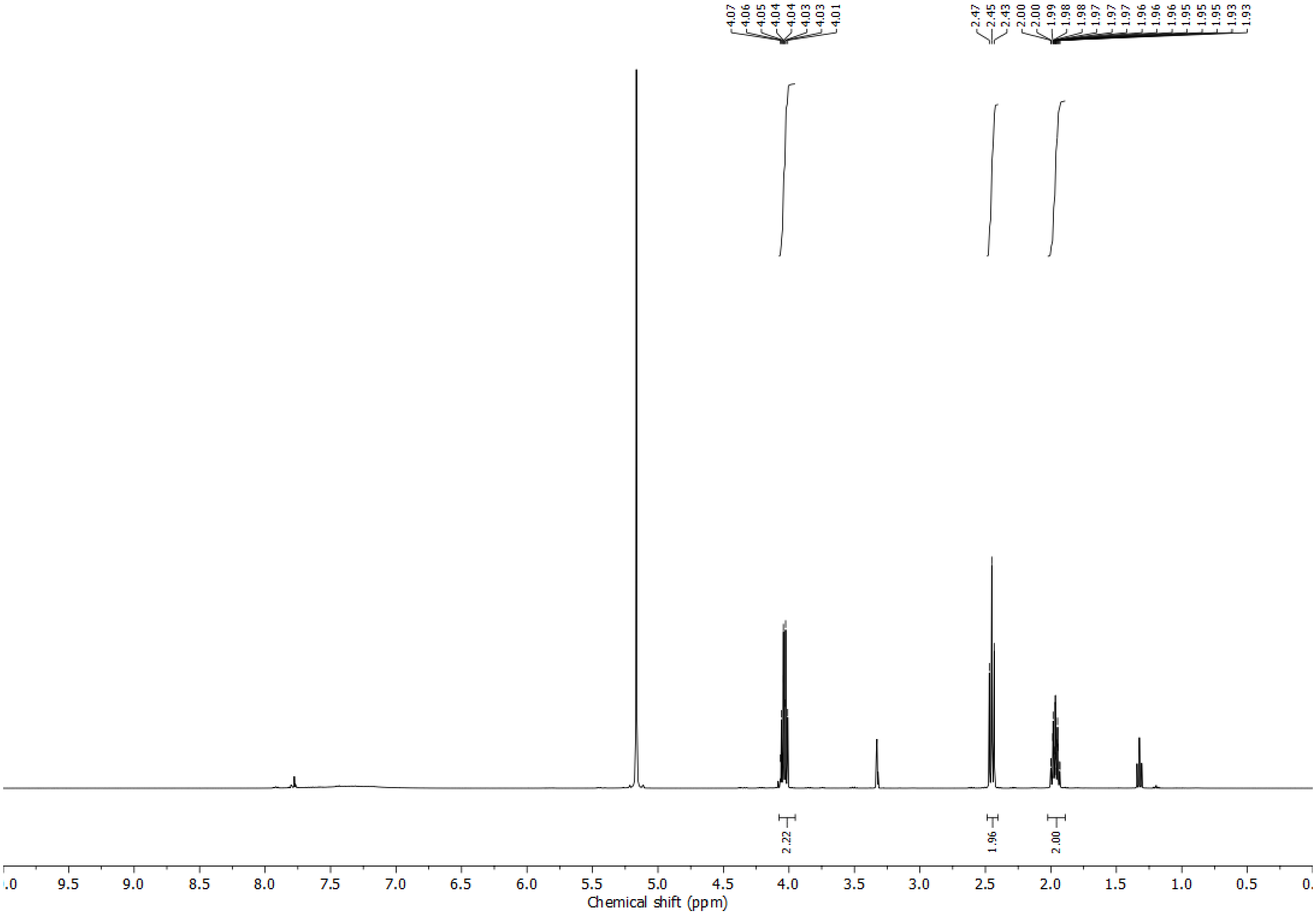
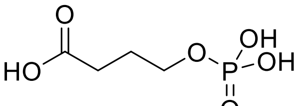


^{13}C NMR (100 MHz, MeOD)



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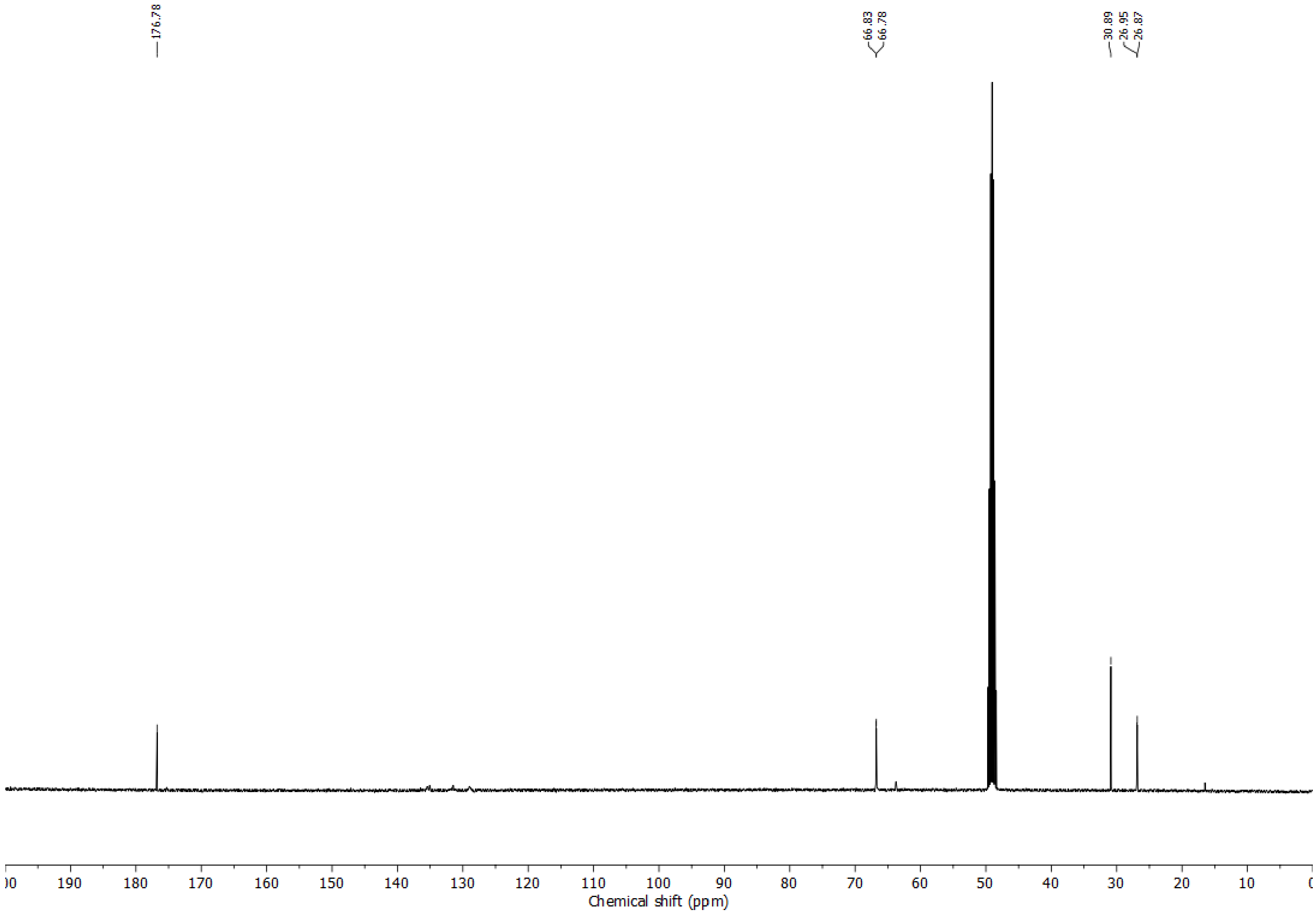

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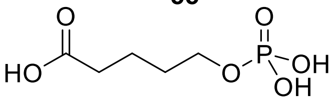

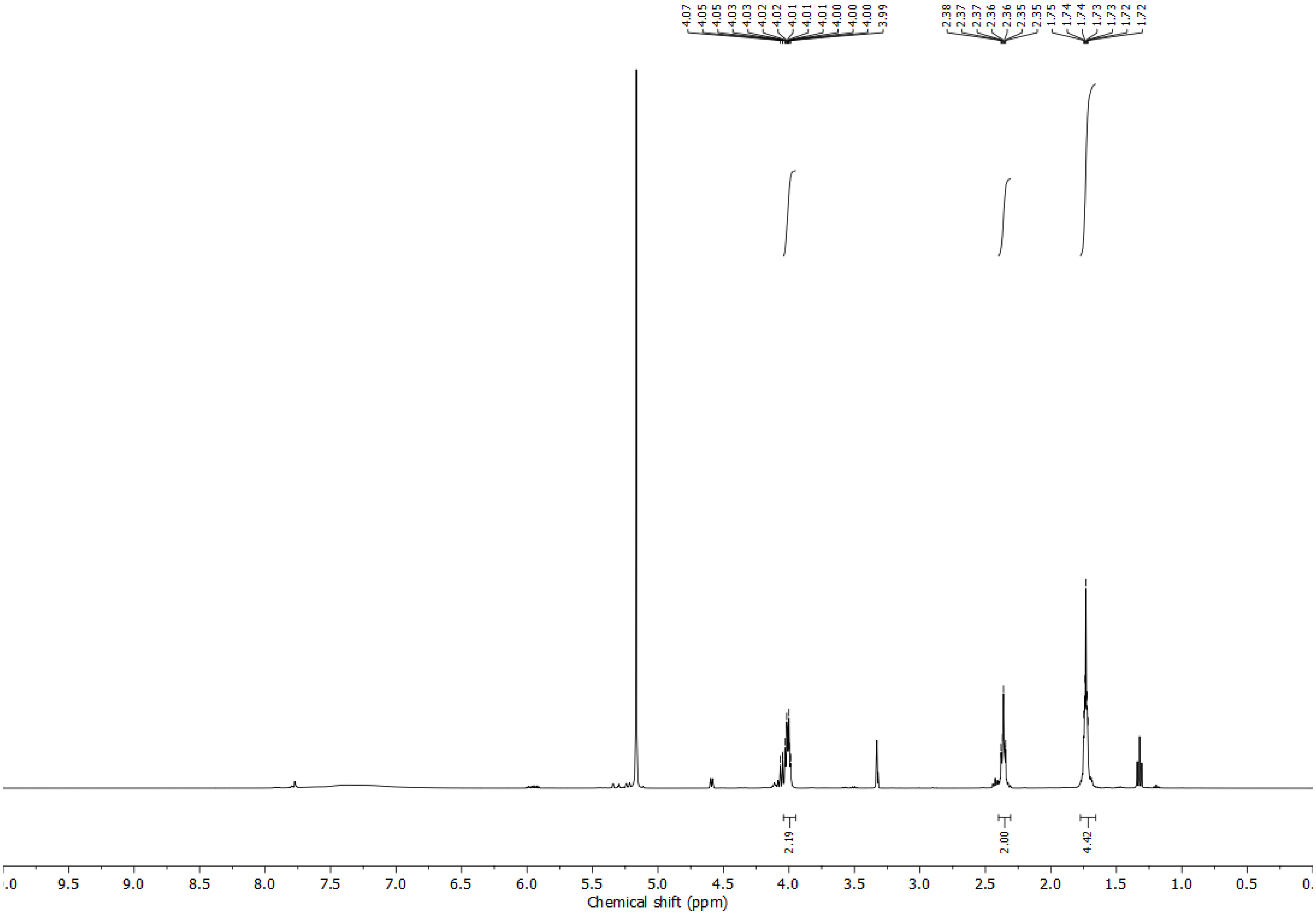

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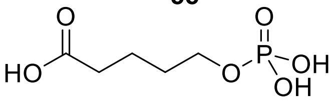

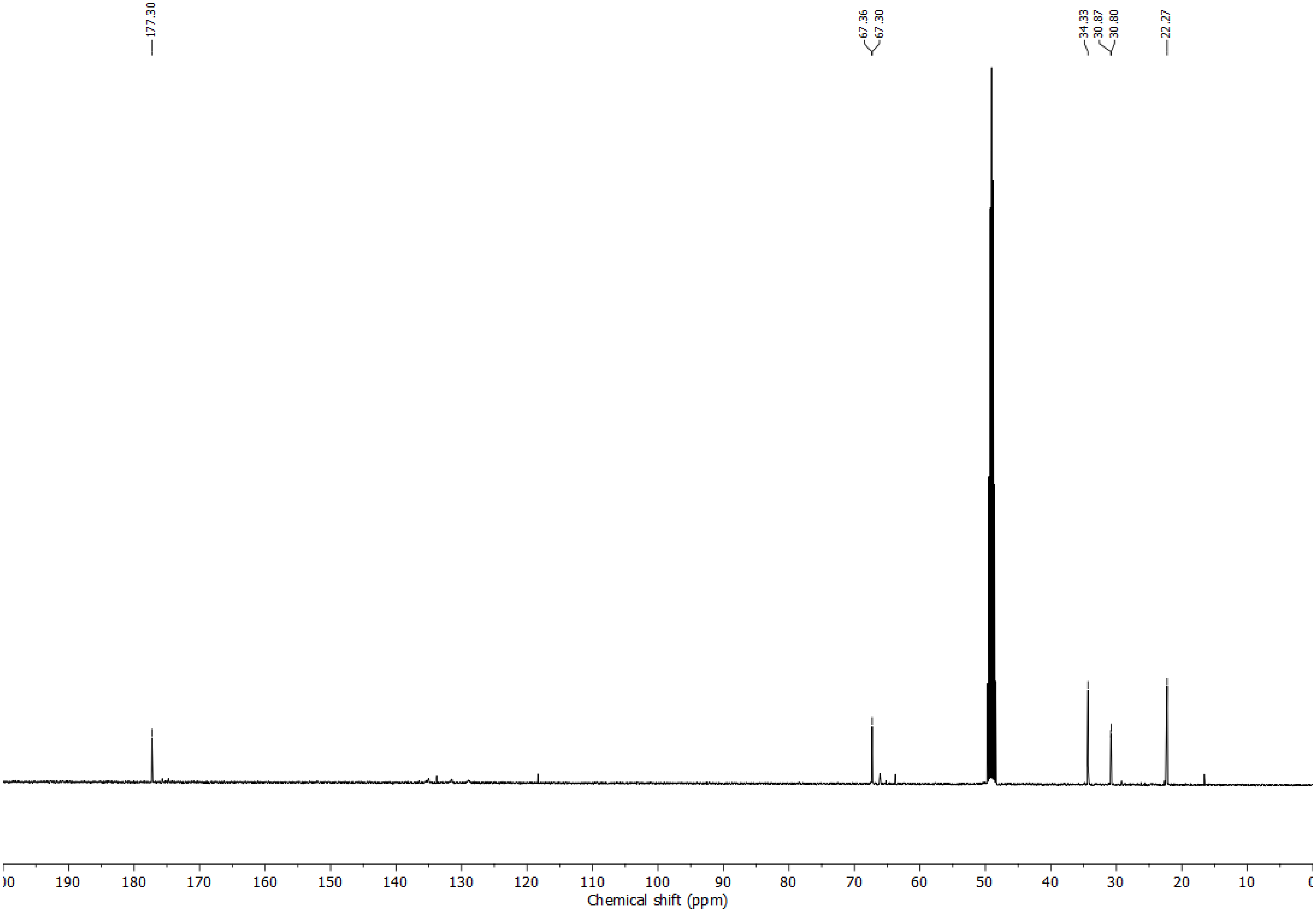

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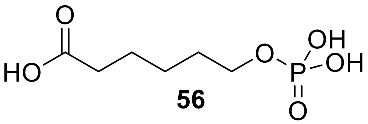

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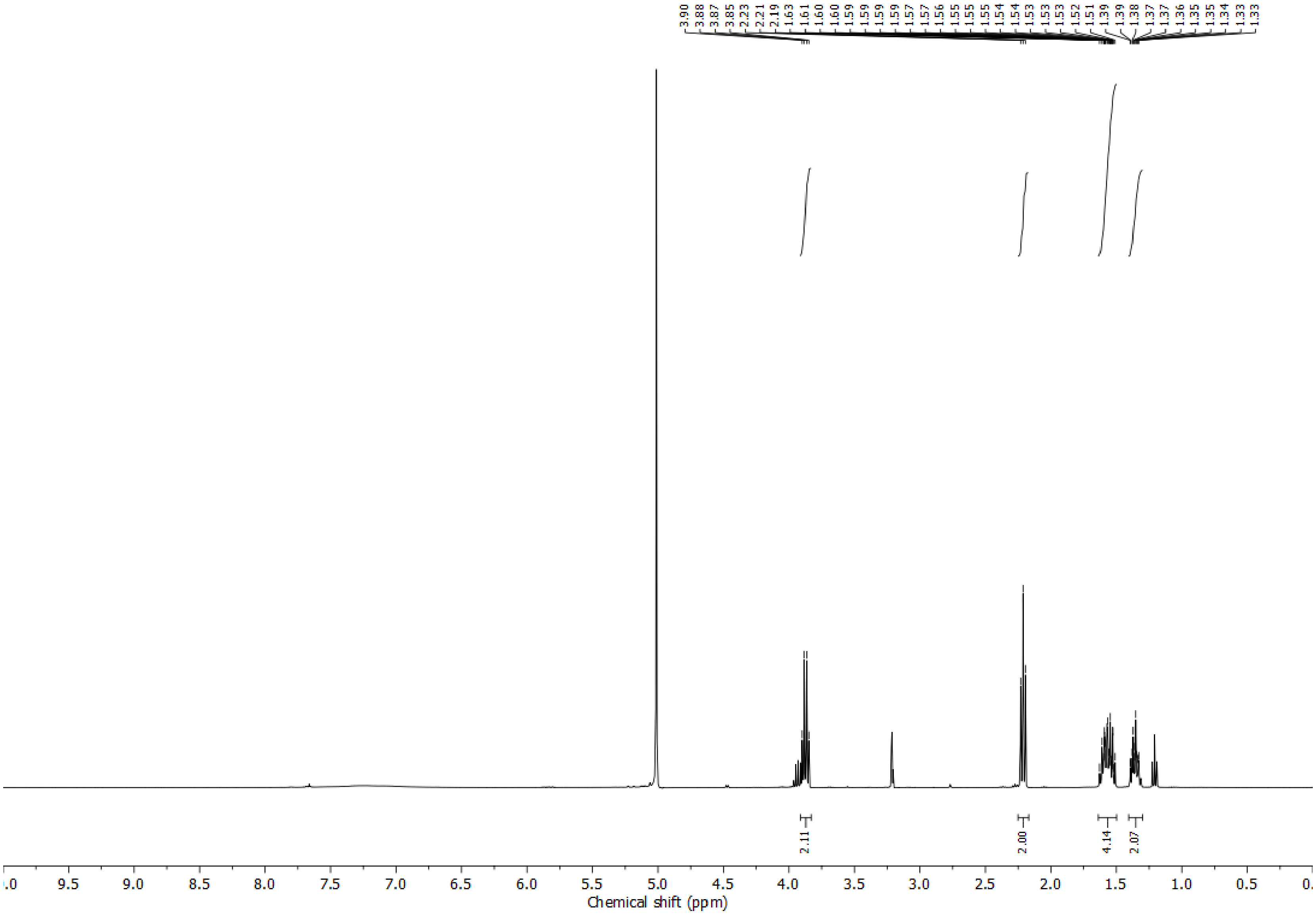
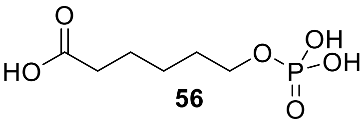


^{13}C NMR (100 MHz, MeOD)



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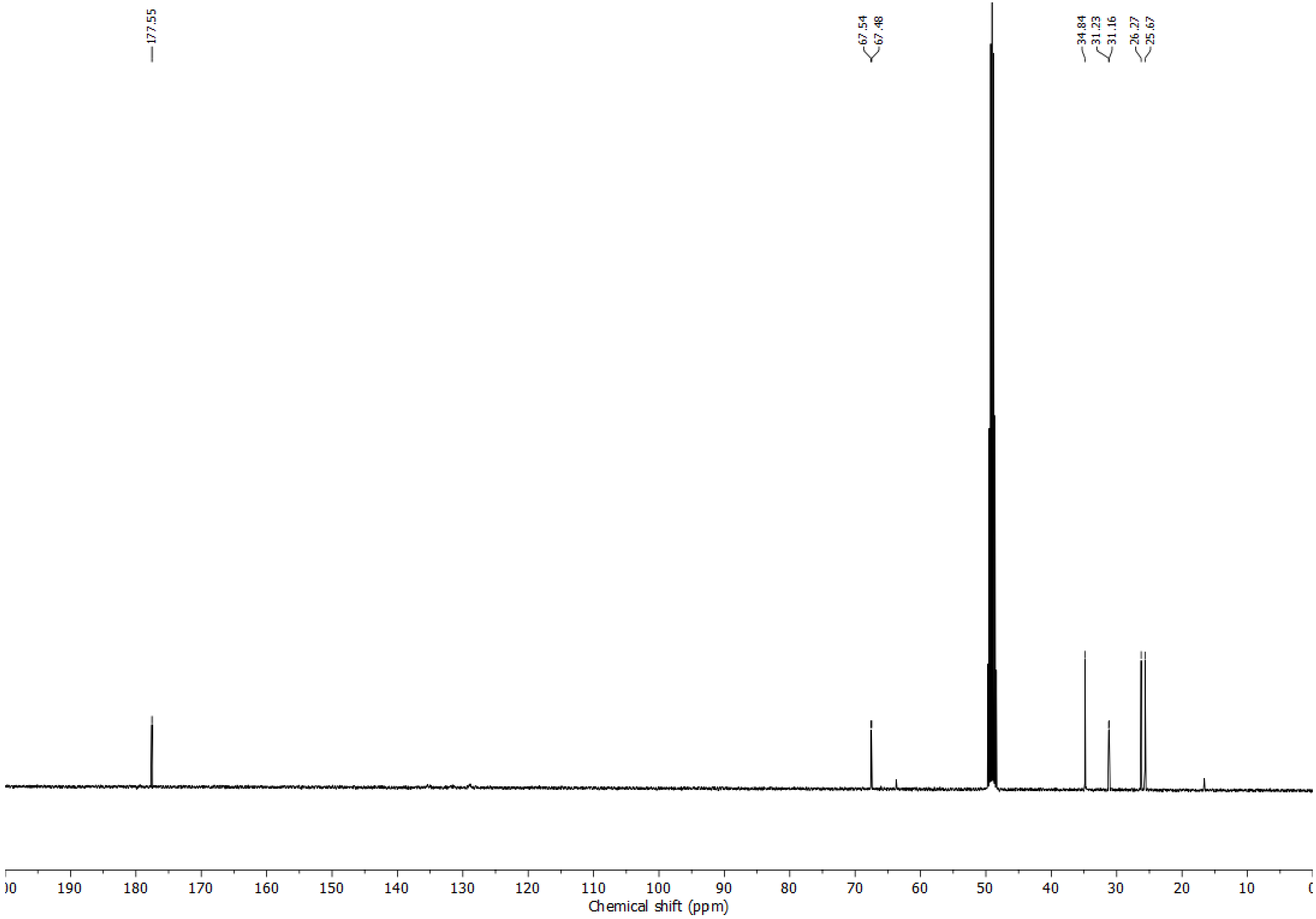
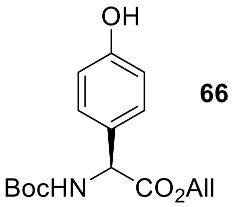


^{1}H NMR (400 MHz, CDCl$_3$)



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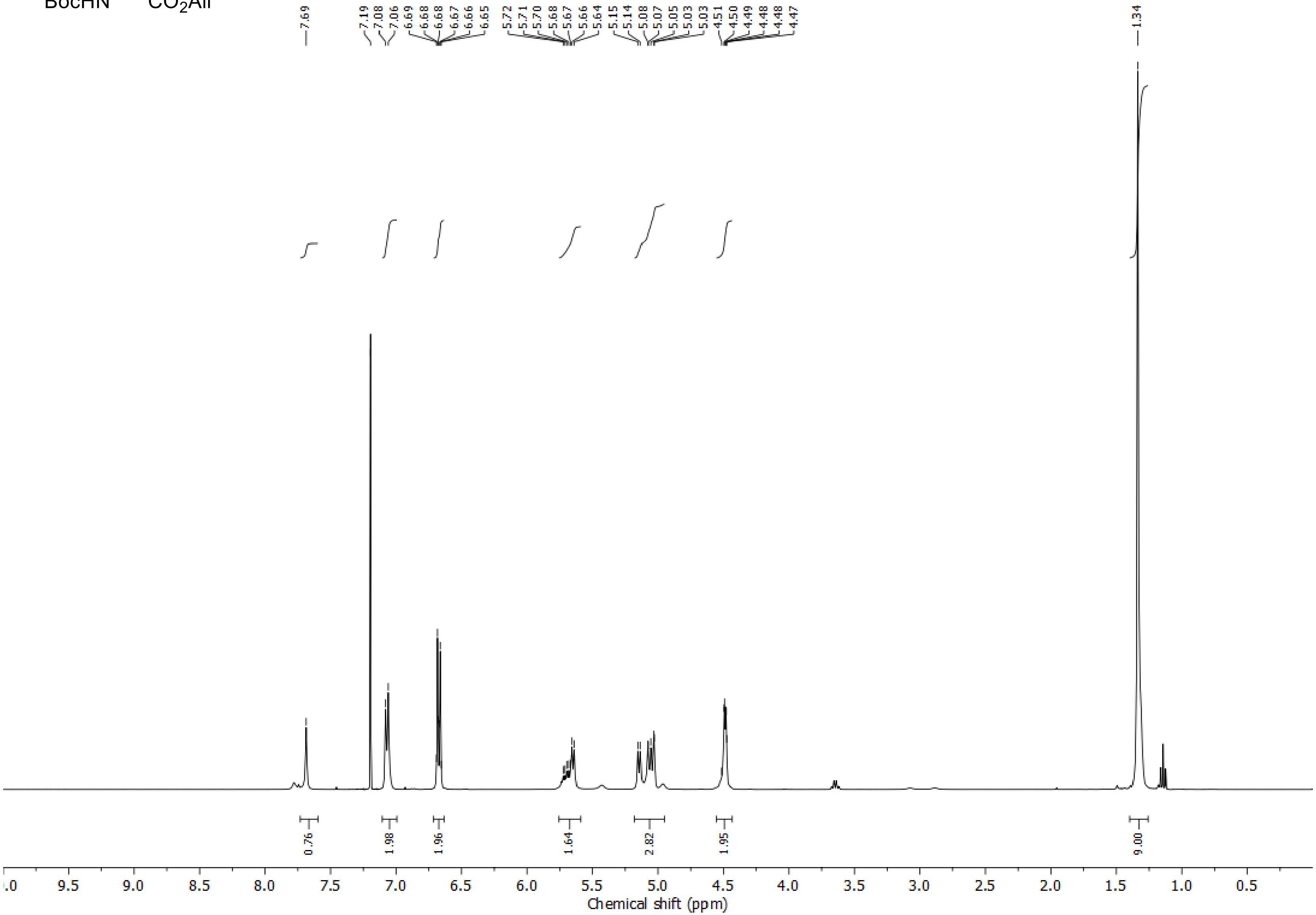
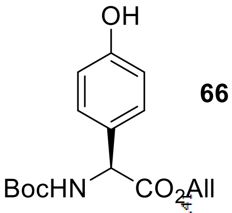


^{13}C NMR (100 MHz, $CDCl_3$)



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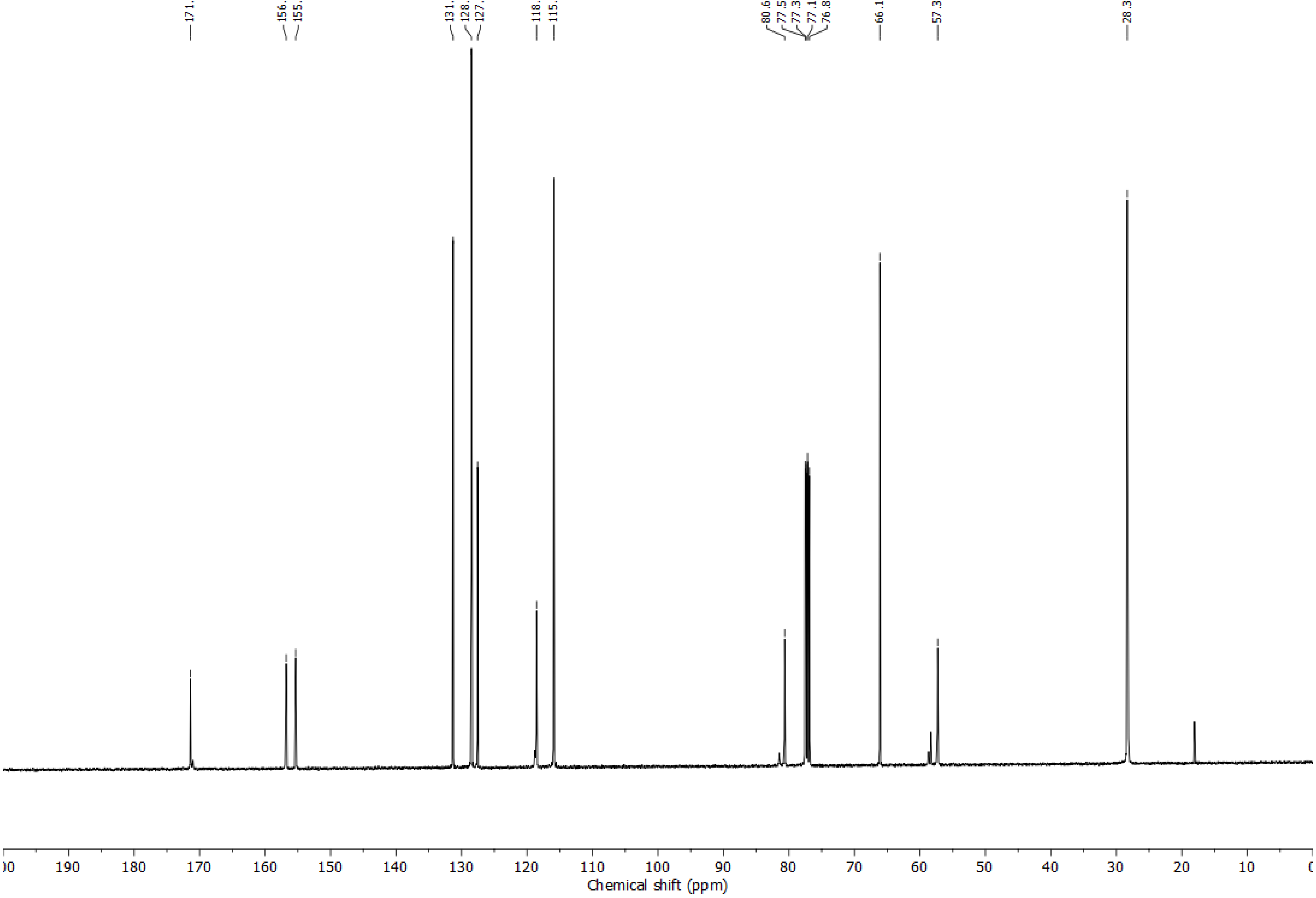

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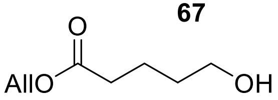

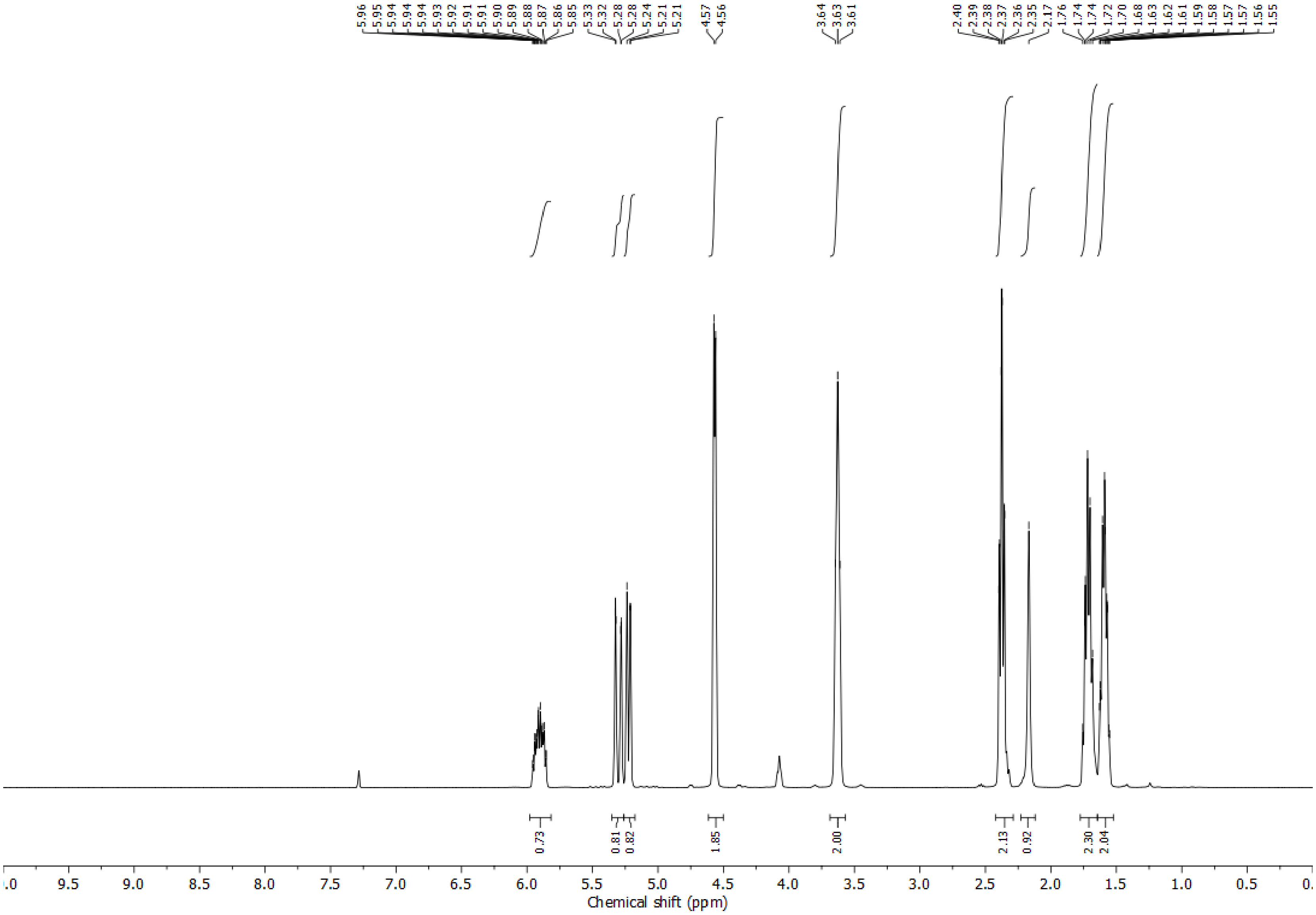

^{13}C NMR (100 MHz, CDCl$_3$)

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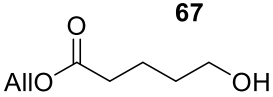

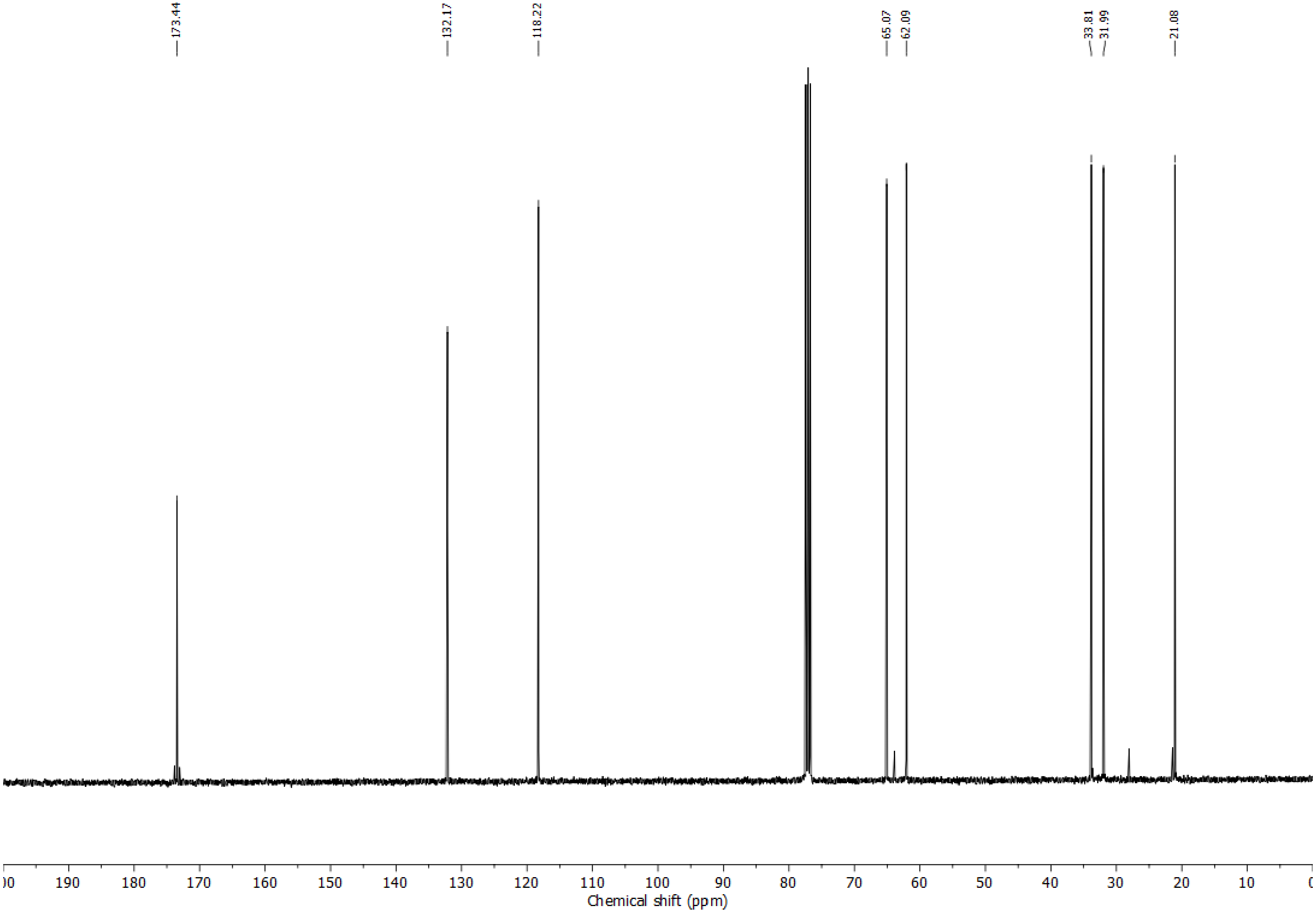

^{1}H NMR (400 MHz, $CDCl_3$)

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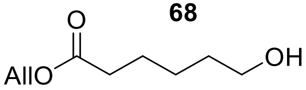
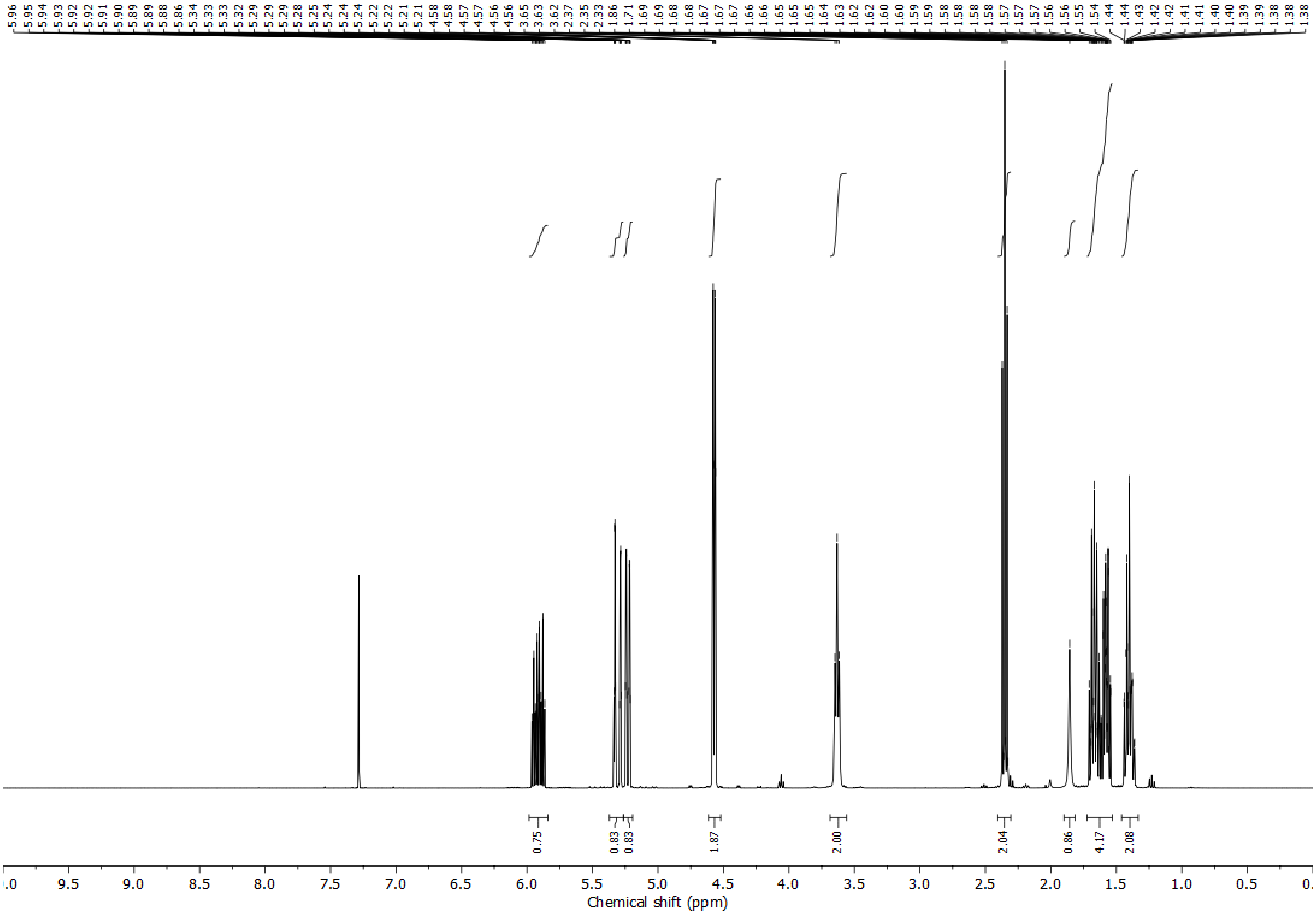
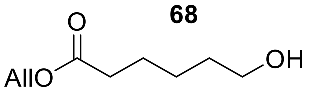




^{13}C NMR (100 MHz, CDCl$_3$)



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