

# One-pot Synthesis of Phosphinylphosphonate Derivatives and Their Anti-tumor Evaluations

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## *Supporting Information*

NMR DATA OF 1-HYDROXYMETHYLENE-1,1-(*H*-PHOSPHINYLPHOSPHONATES) 6A-P AND 14O-P ..... 2

# NMR data of 1-hydroxymethylene-1,1-(*H*-phosphinylphosphonates) 6a-p and 14o-p

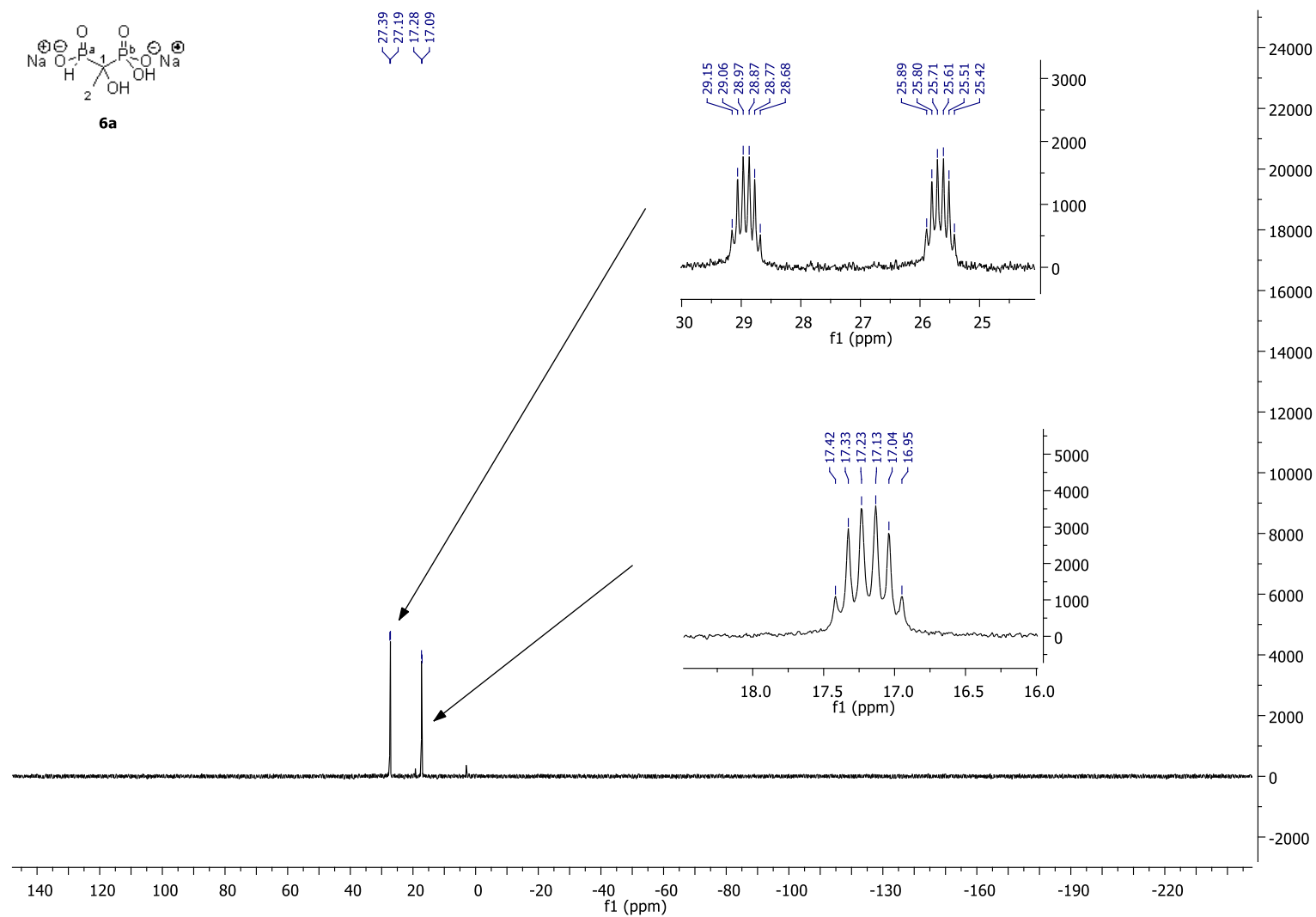


Figure S1: <sup>31</sup>P{<sup>1</sup>H} and <sup>31</sup>P NMR (162 MHz, D<sub>2</sub>O) spectra of 1-hydroxyethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt 6a

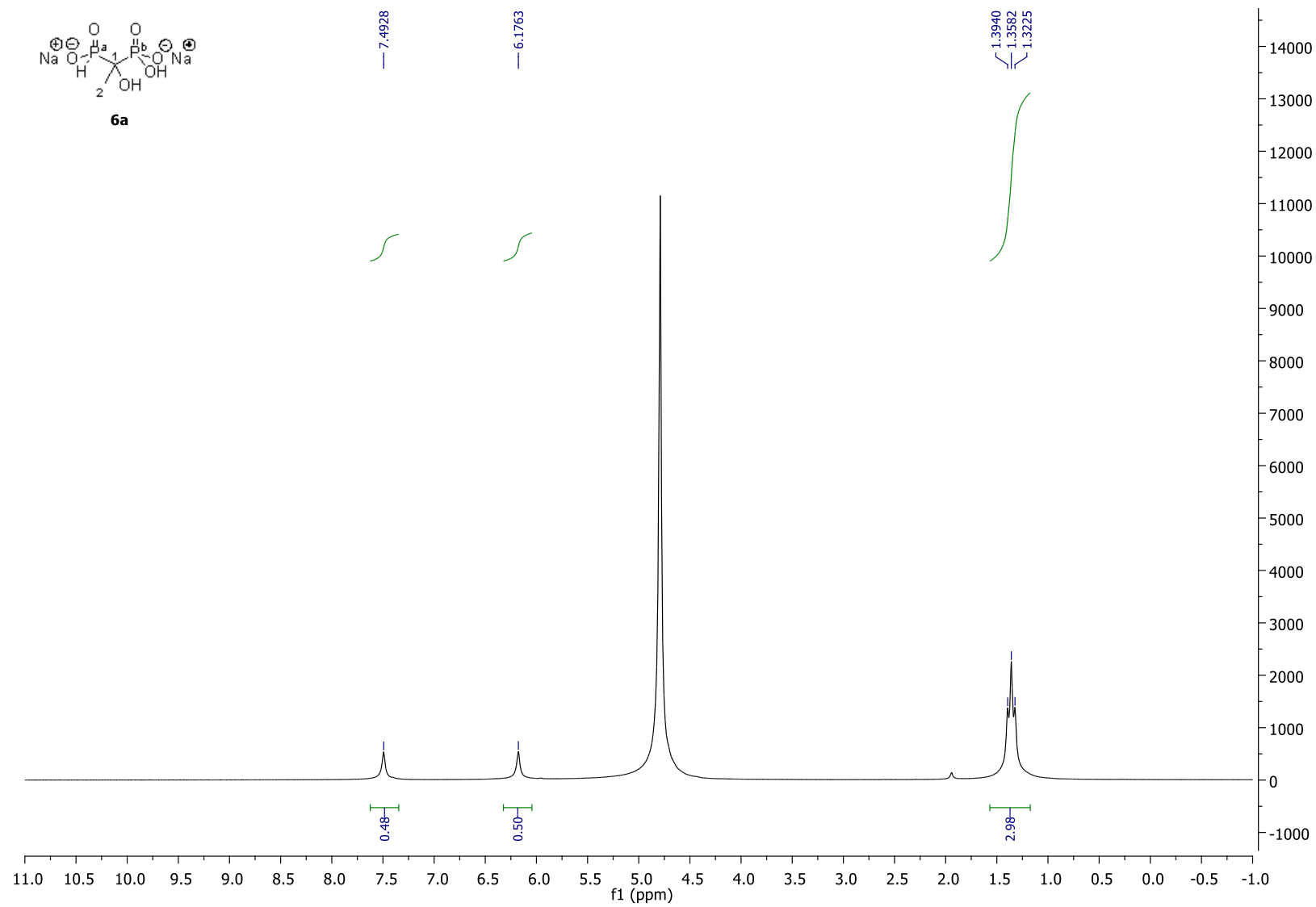


Figure S2:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxyethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6a**

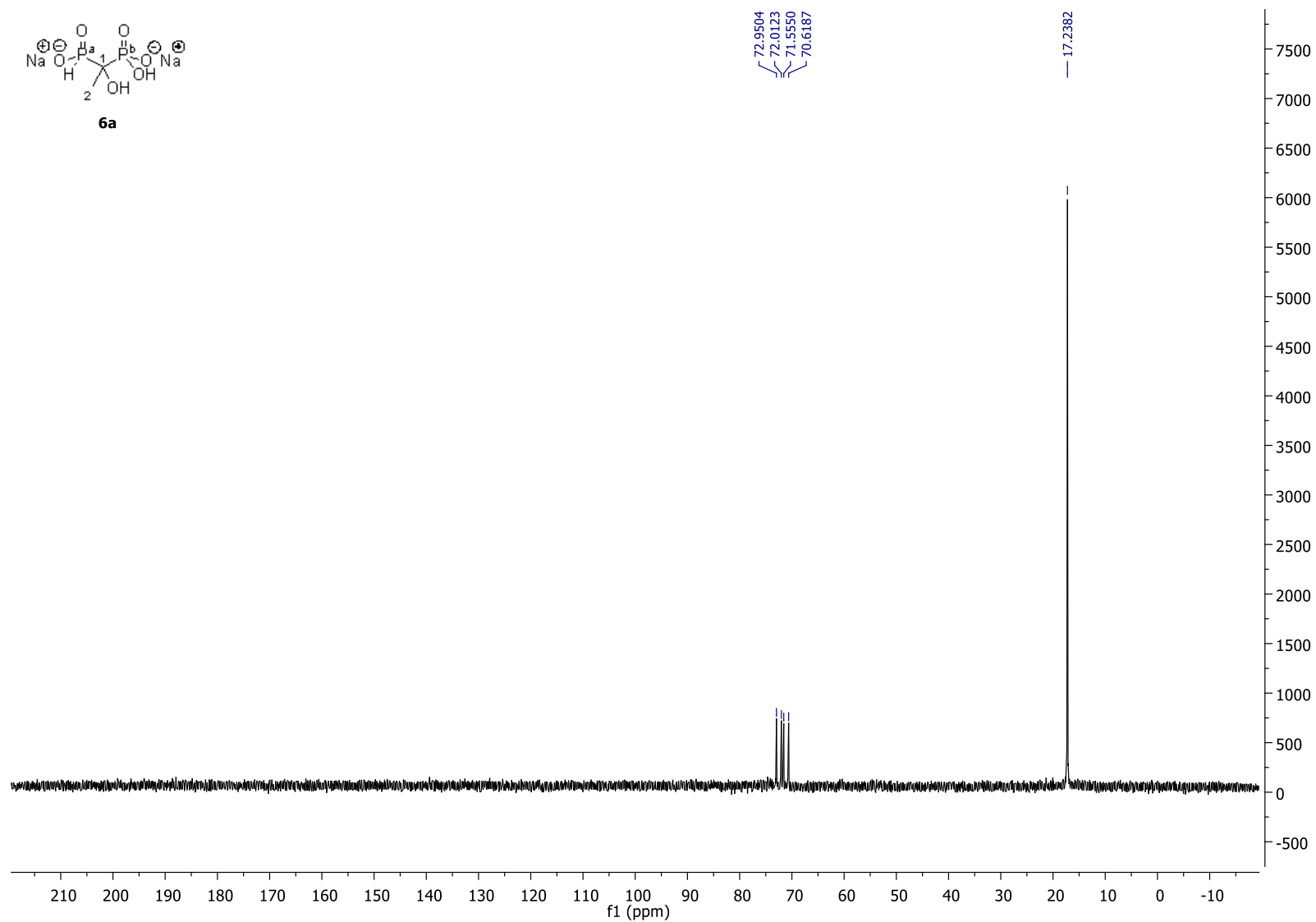


Figure S3:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxyethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6a**

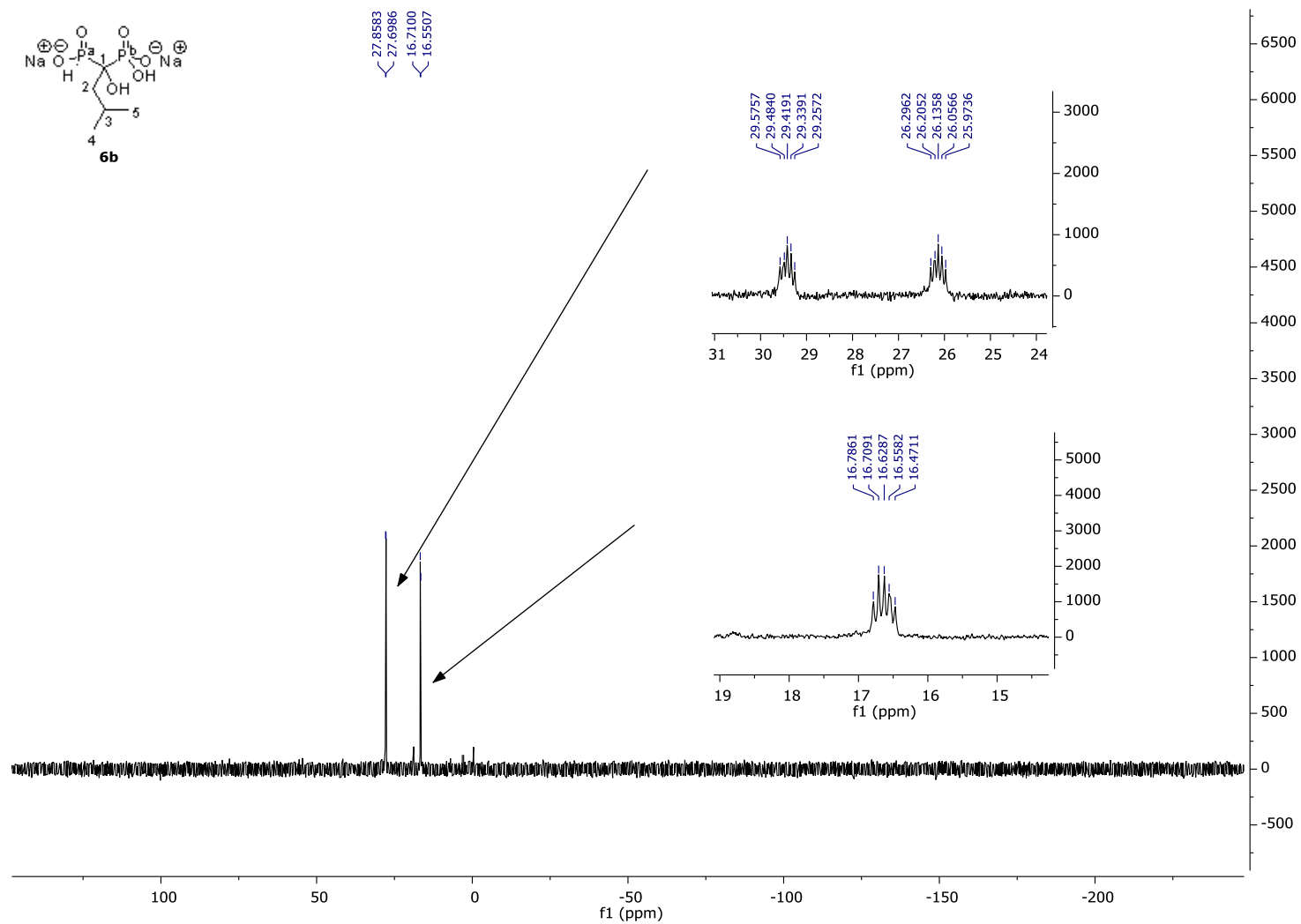


Figure S4:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-3-methylbutane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6b**

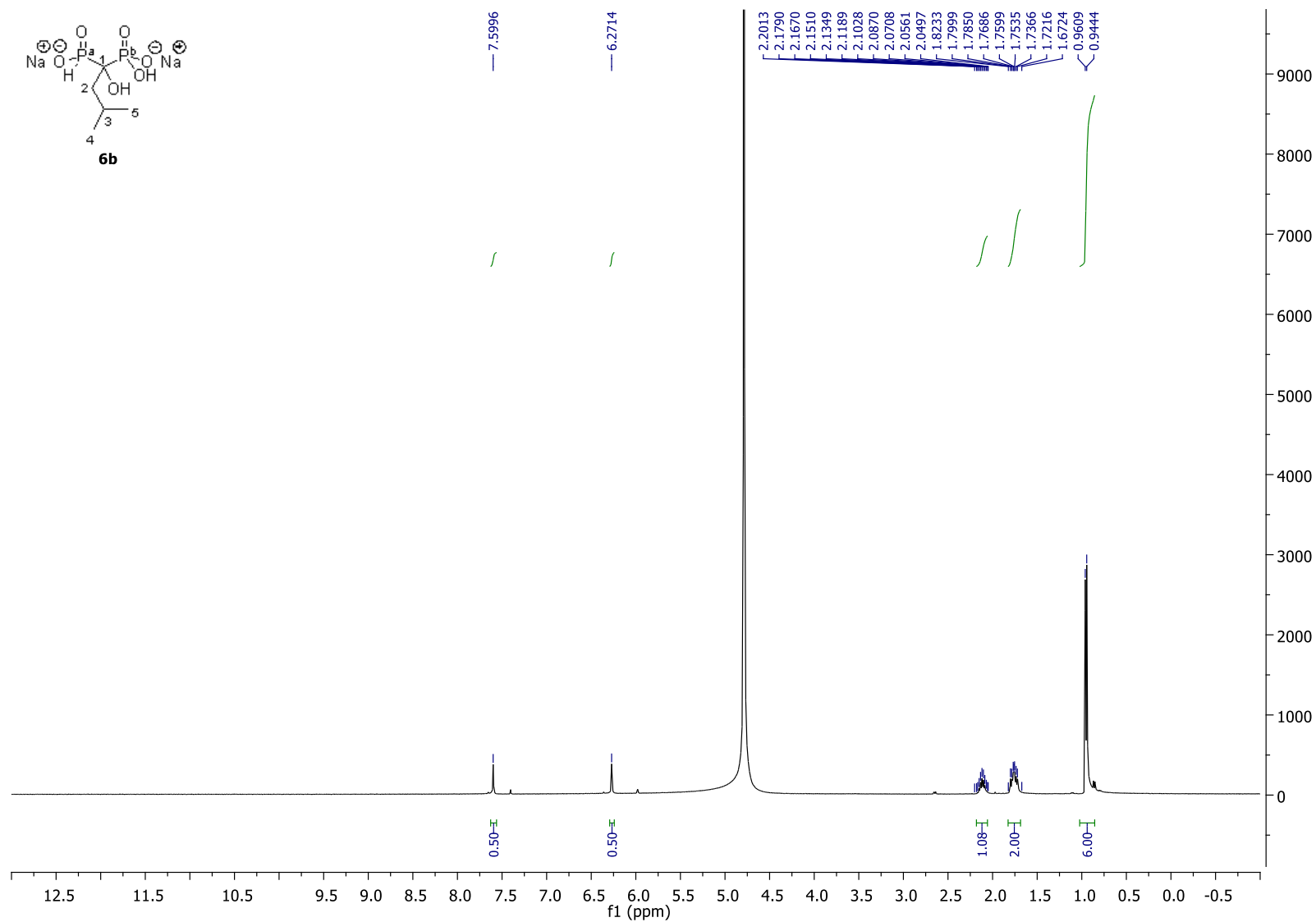


Figure S5:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-3-methylbutane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6b**

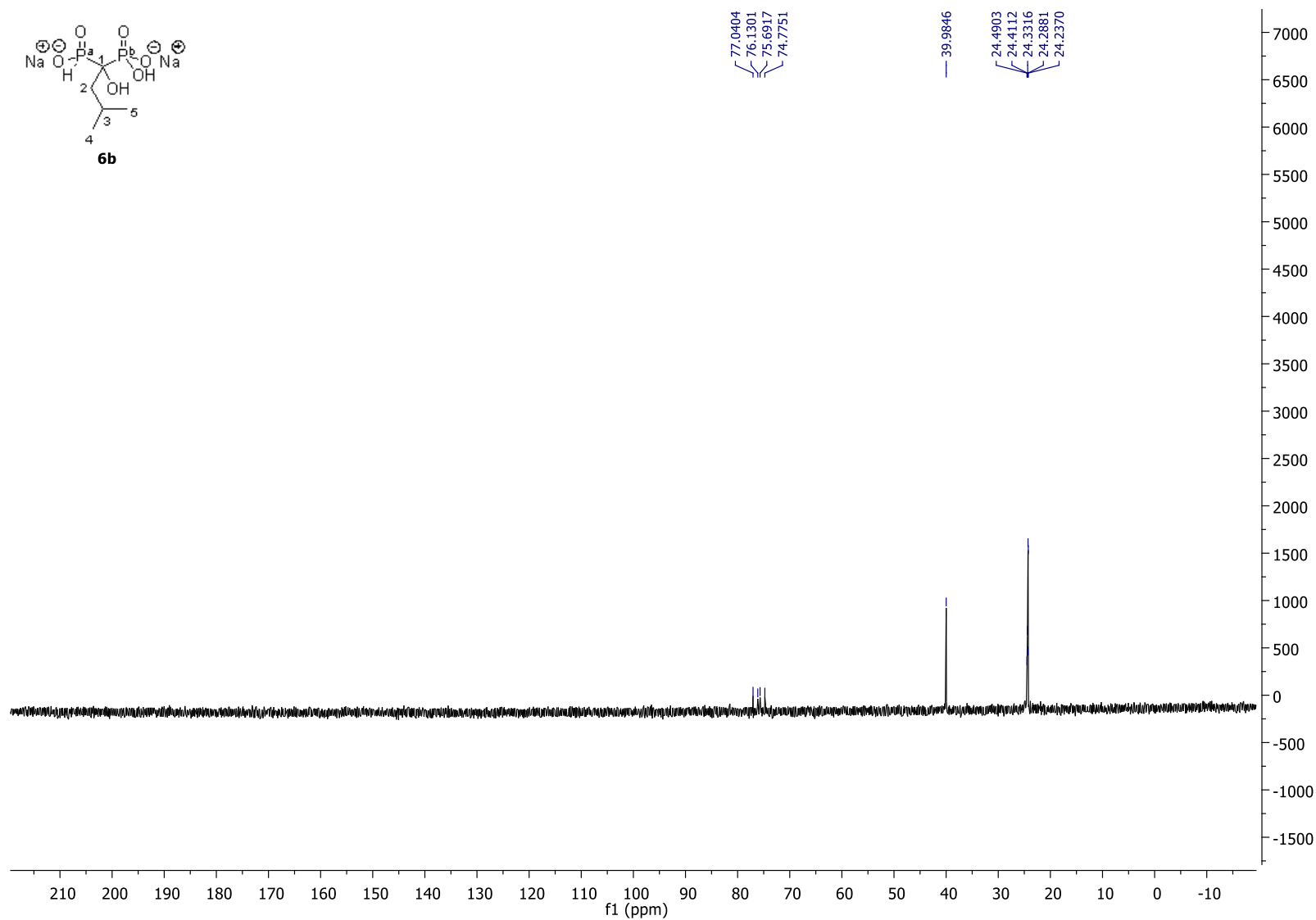


Figure S6:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-3-methylbutane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6b**

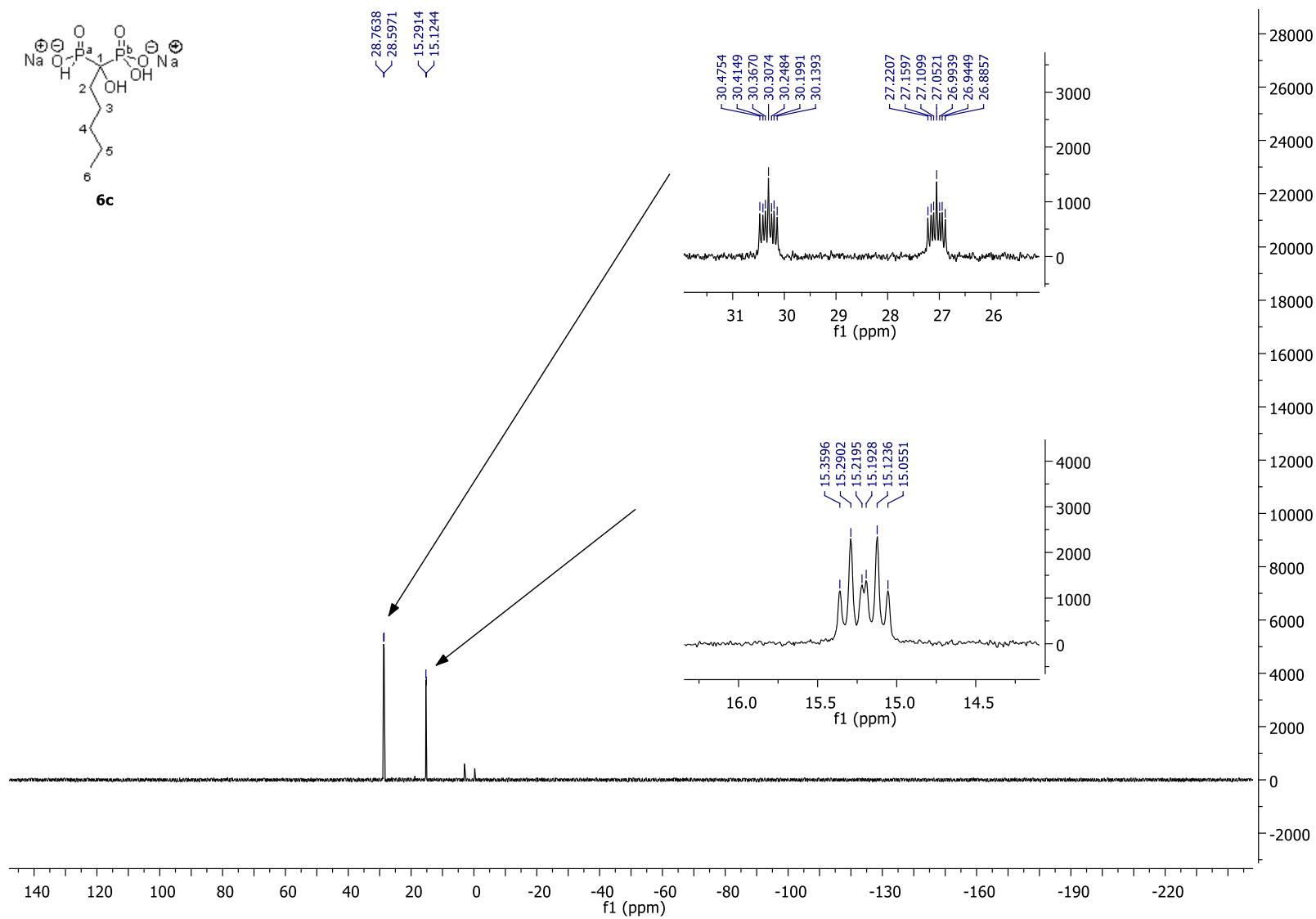


Figure S7:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxyhexane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6c**



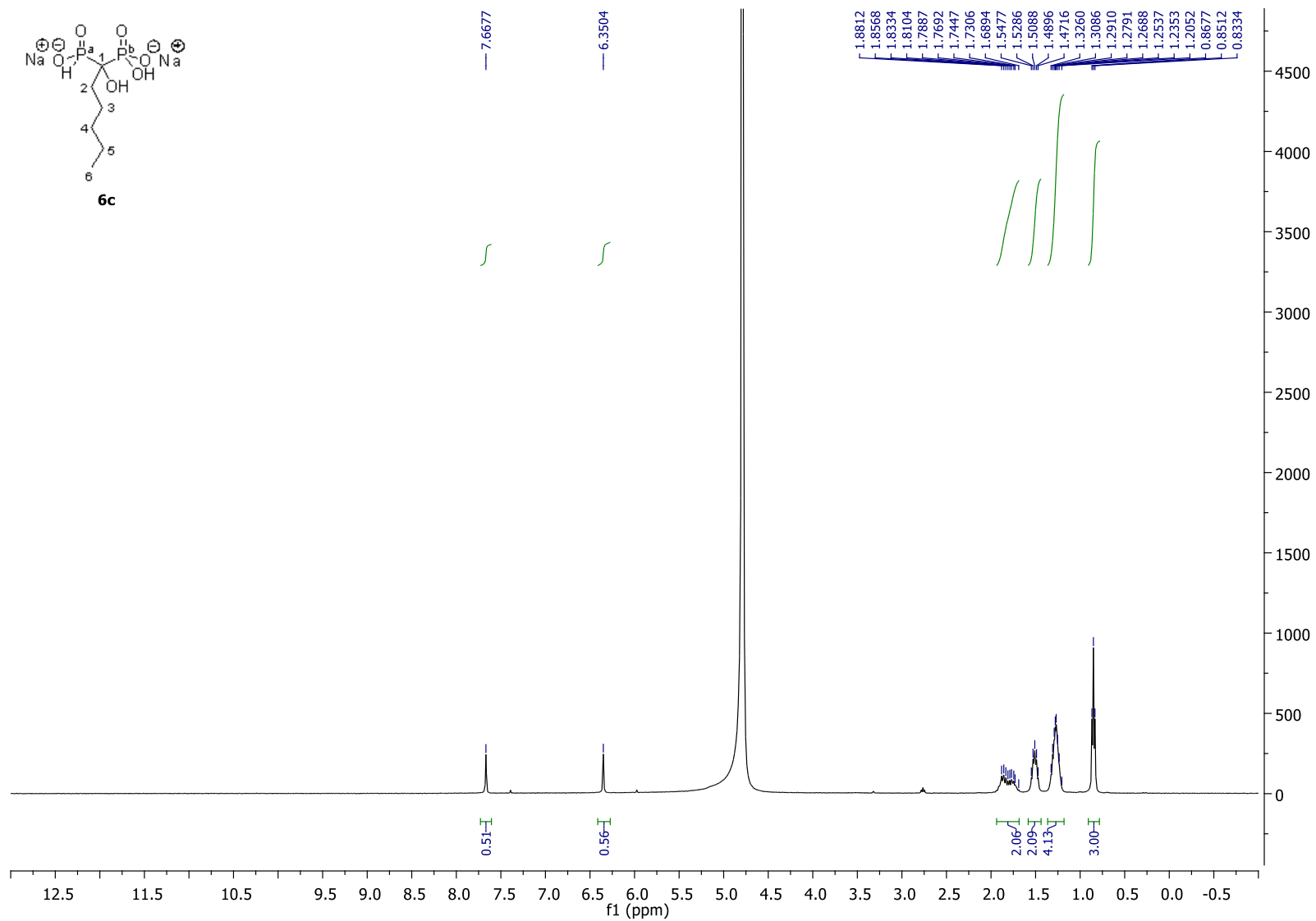


Figure S8: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxyhexane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6c**

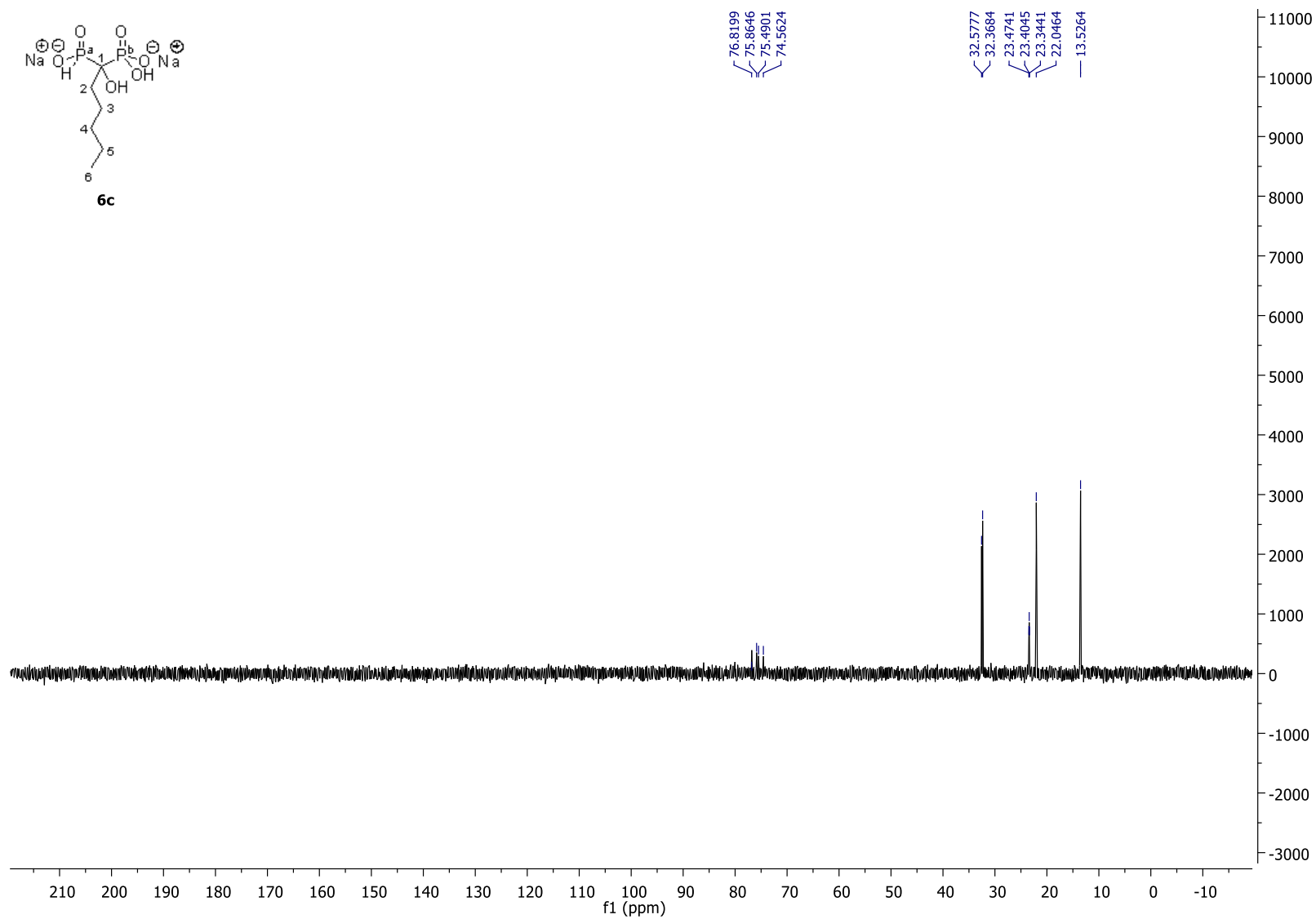


Figure S9:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxyhexane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6c**

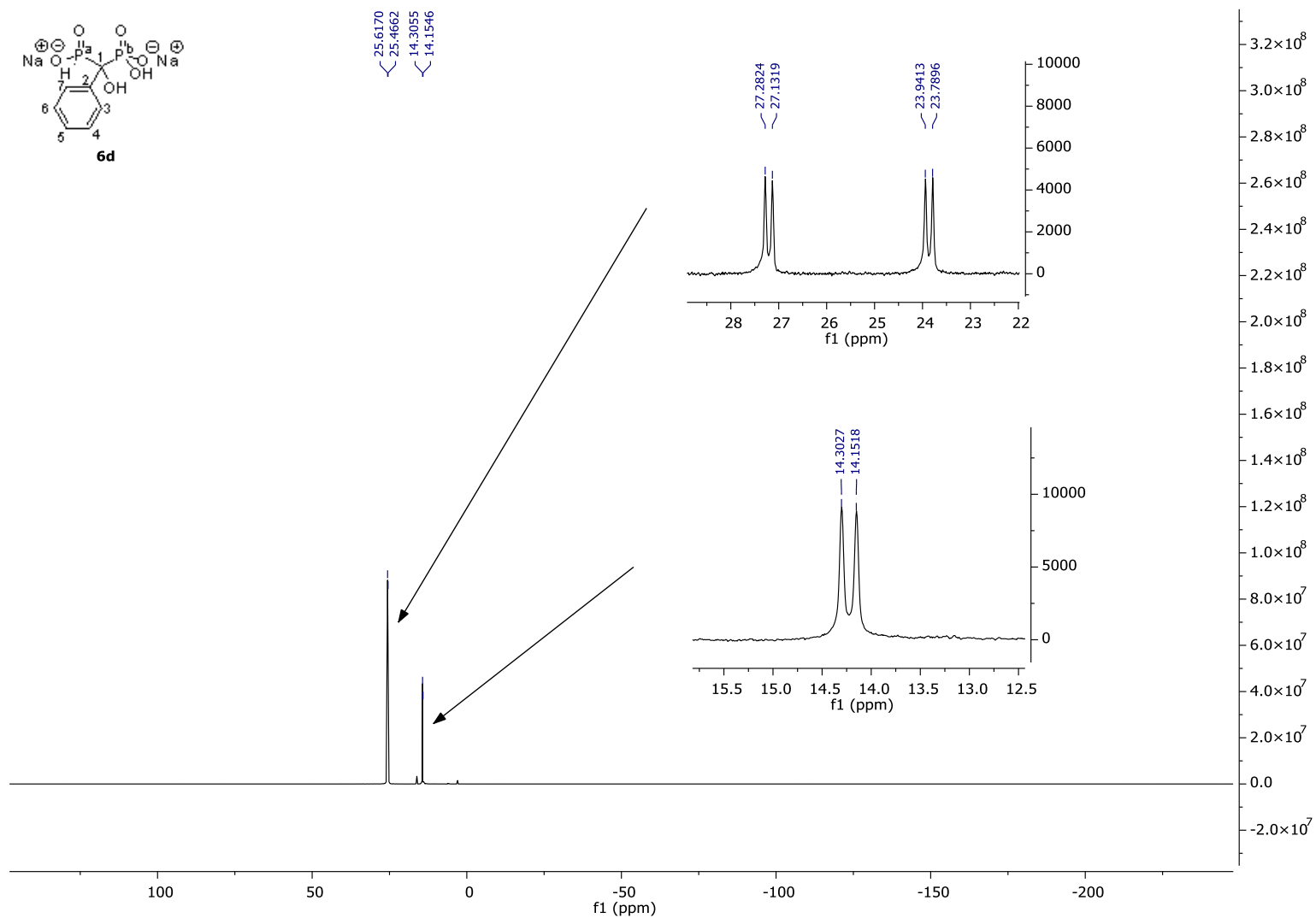


Figure S10:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-phenylmethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6d**

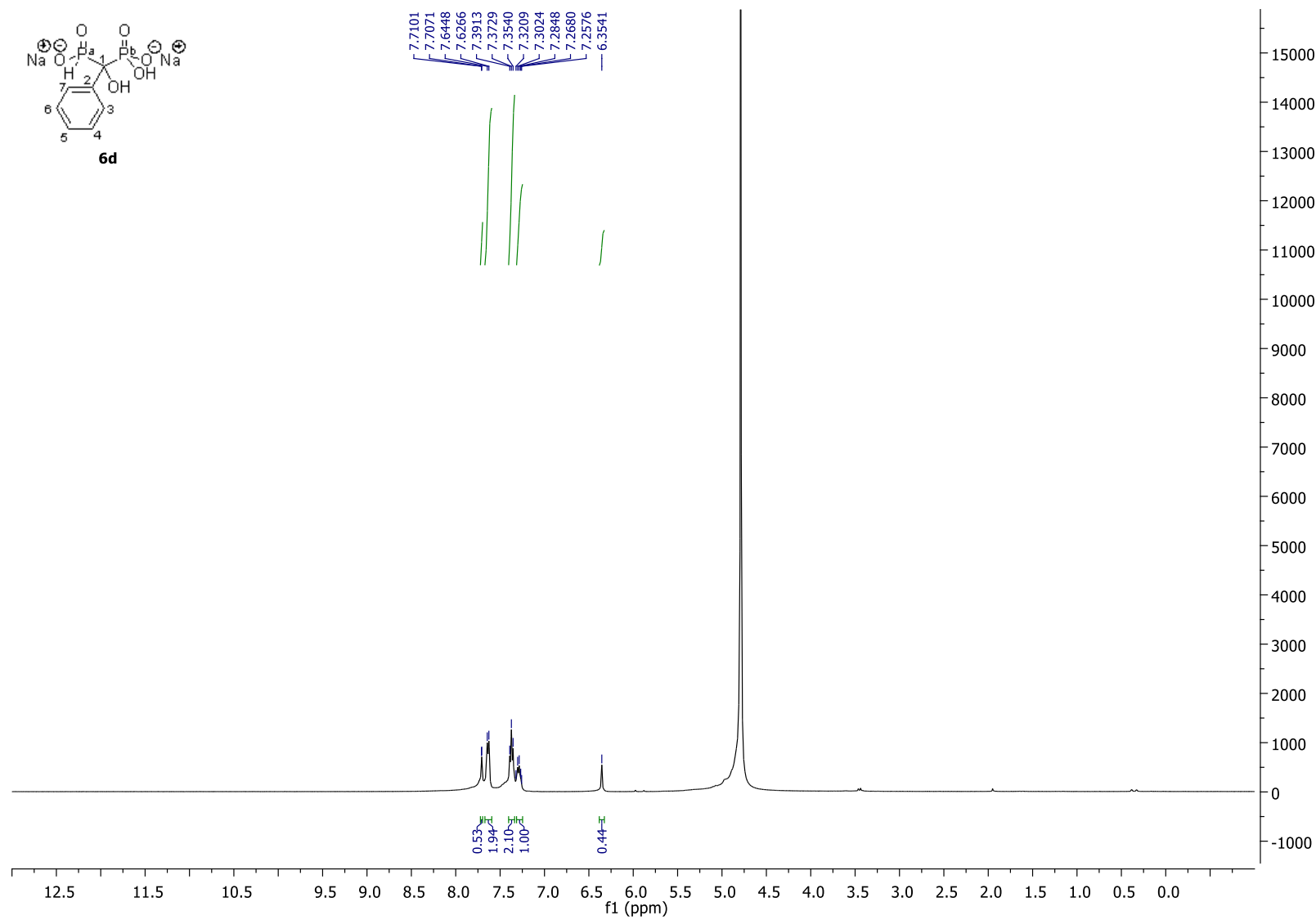


Figure S11: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-phenylmethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6d**

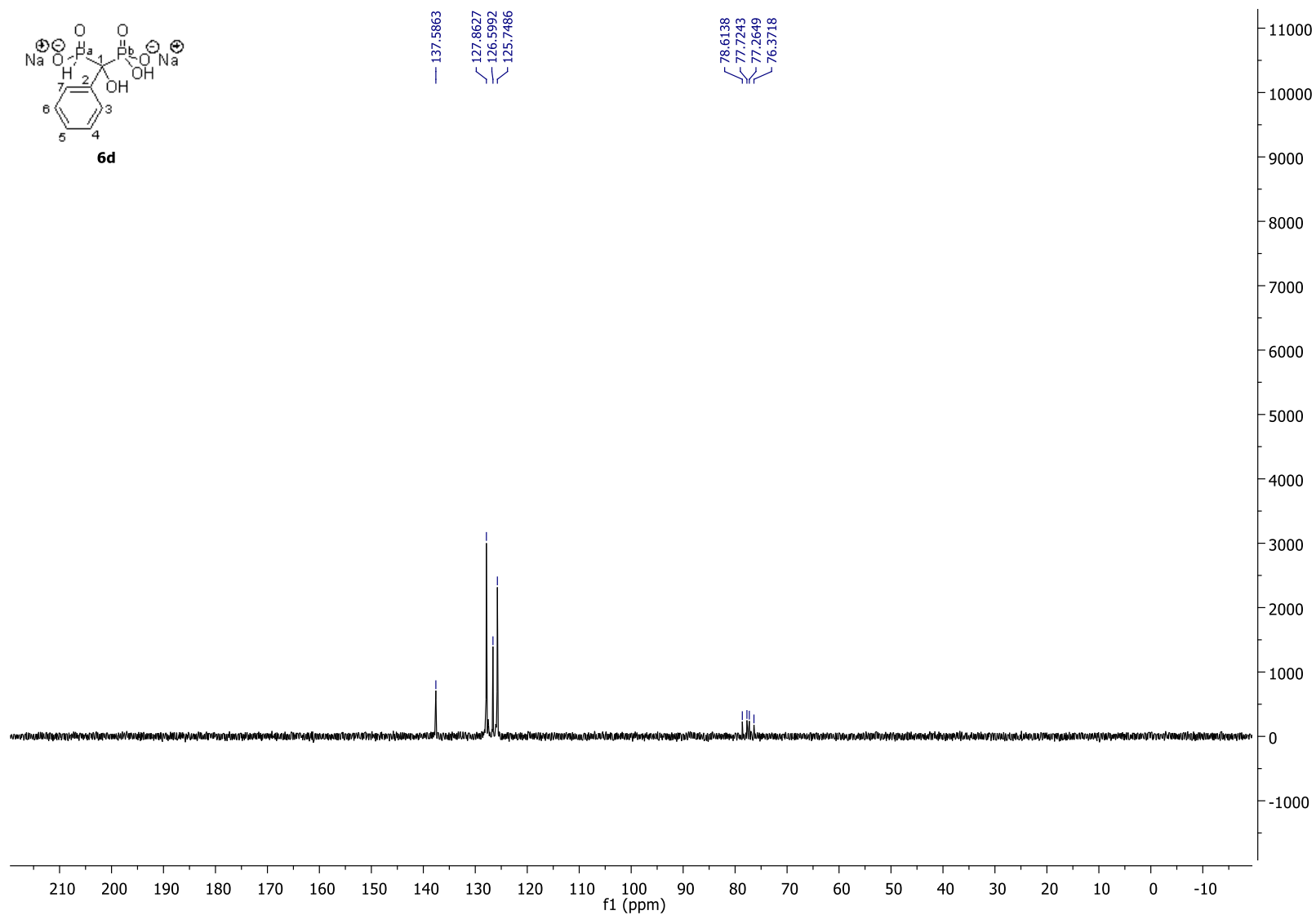


Figure S12:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-phenylmethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6d**

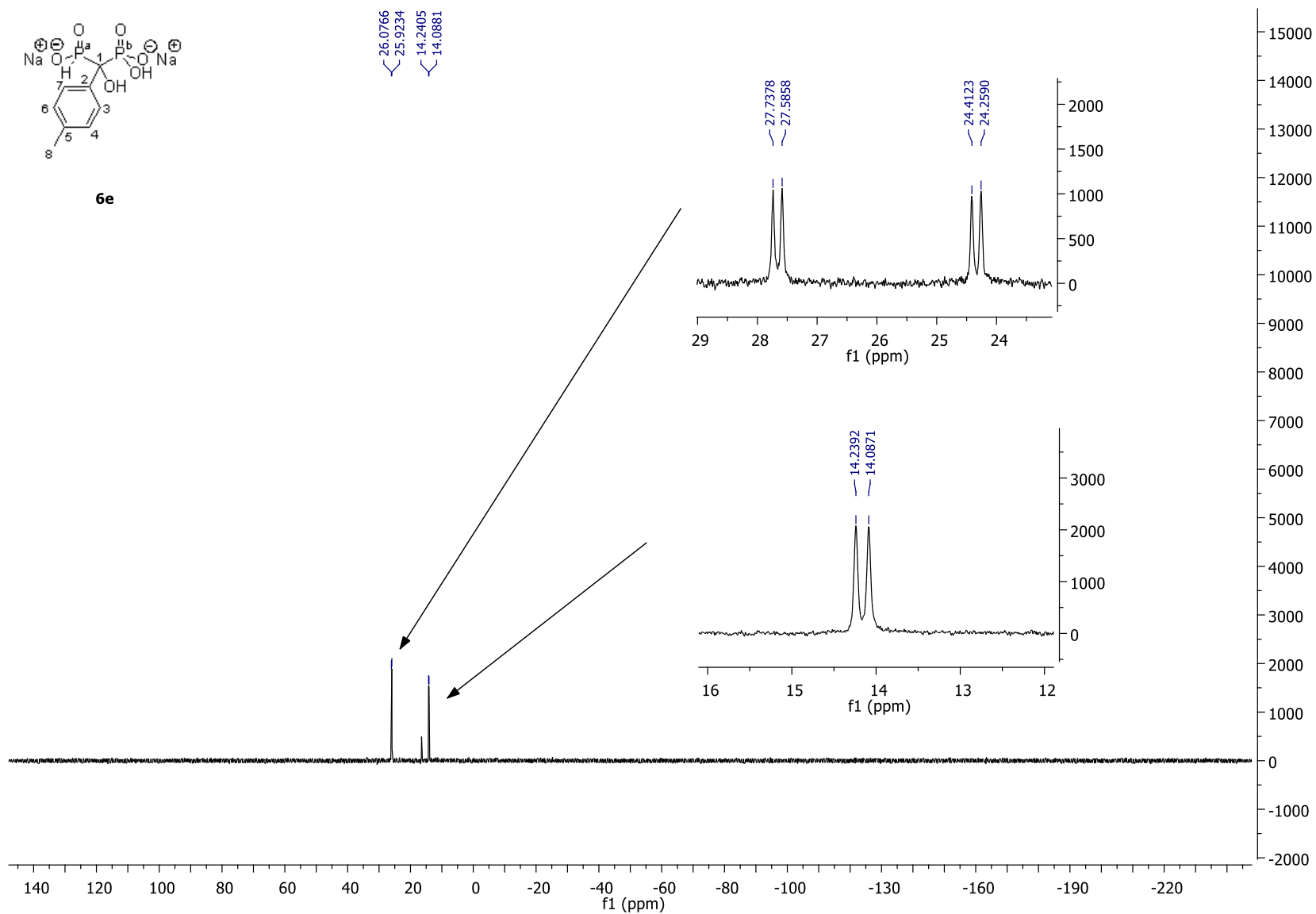


Figure S13:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(4-tolyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6e**



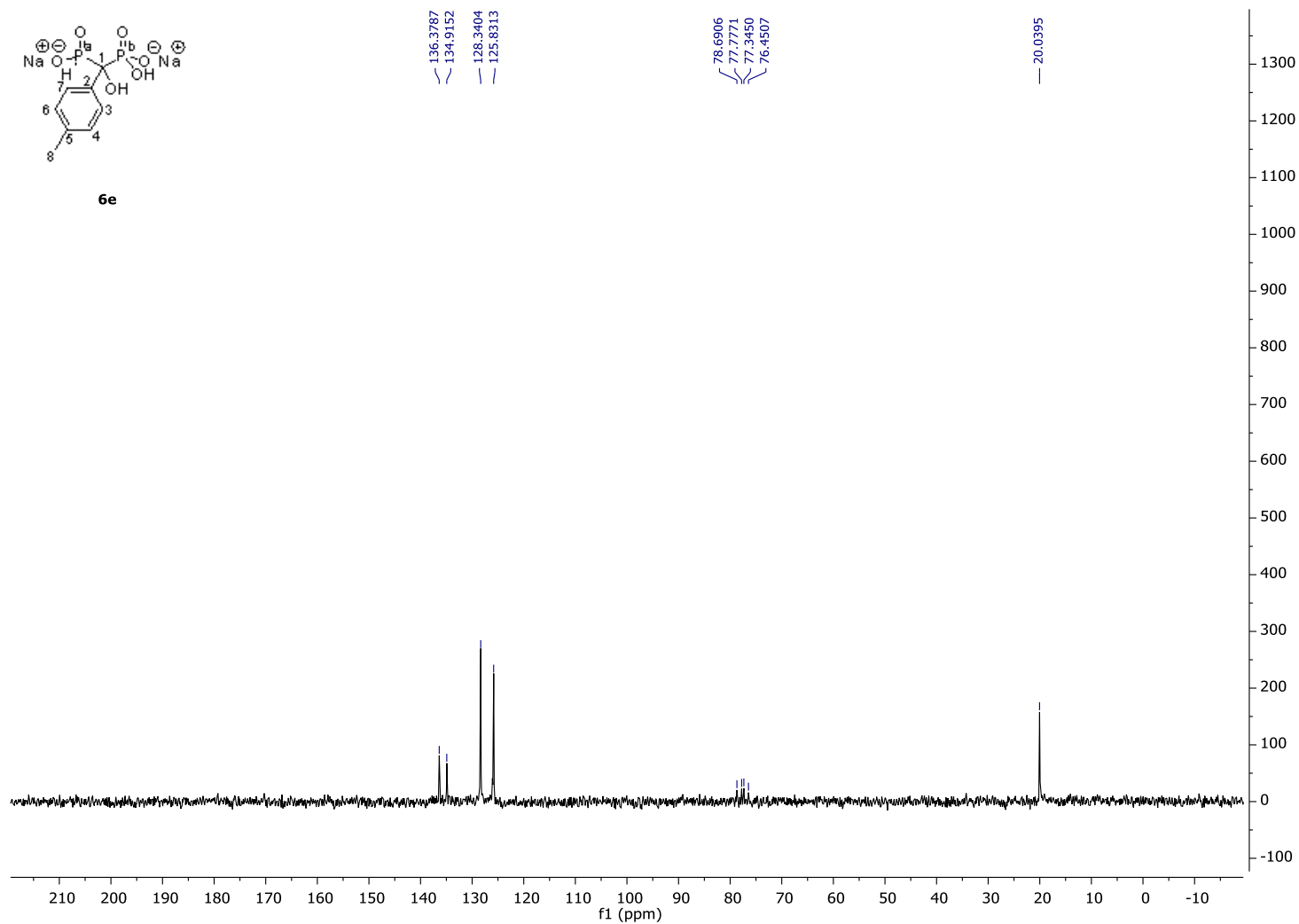


Figure S15: <sup>13</sup>C NMR (101 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(4-tolyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6e**



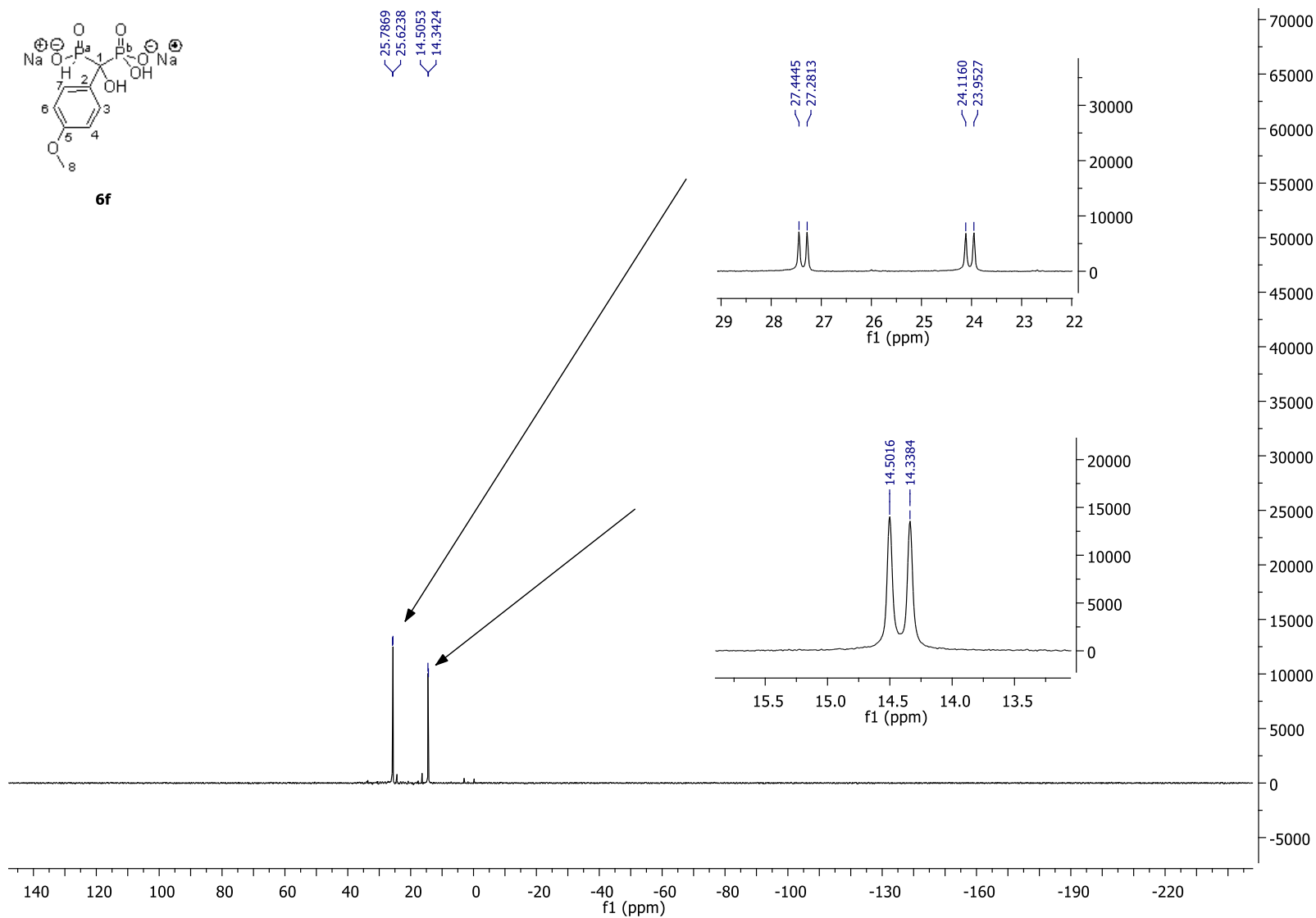


Figure S16:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of hydroxy-1-(4-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6f**

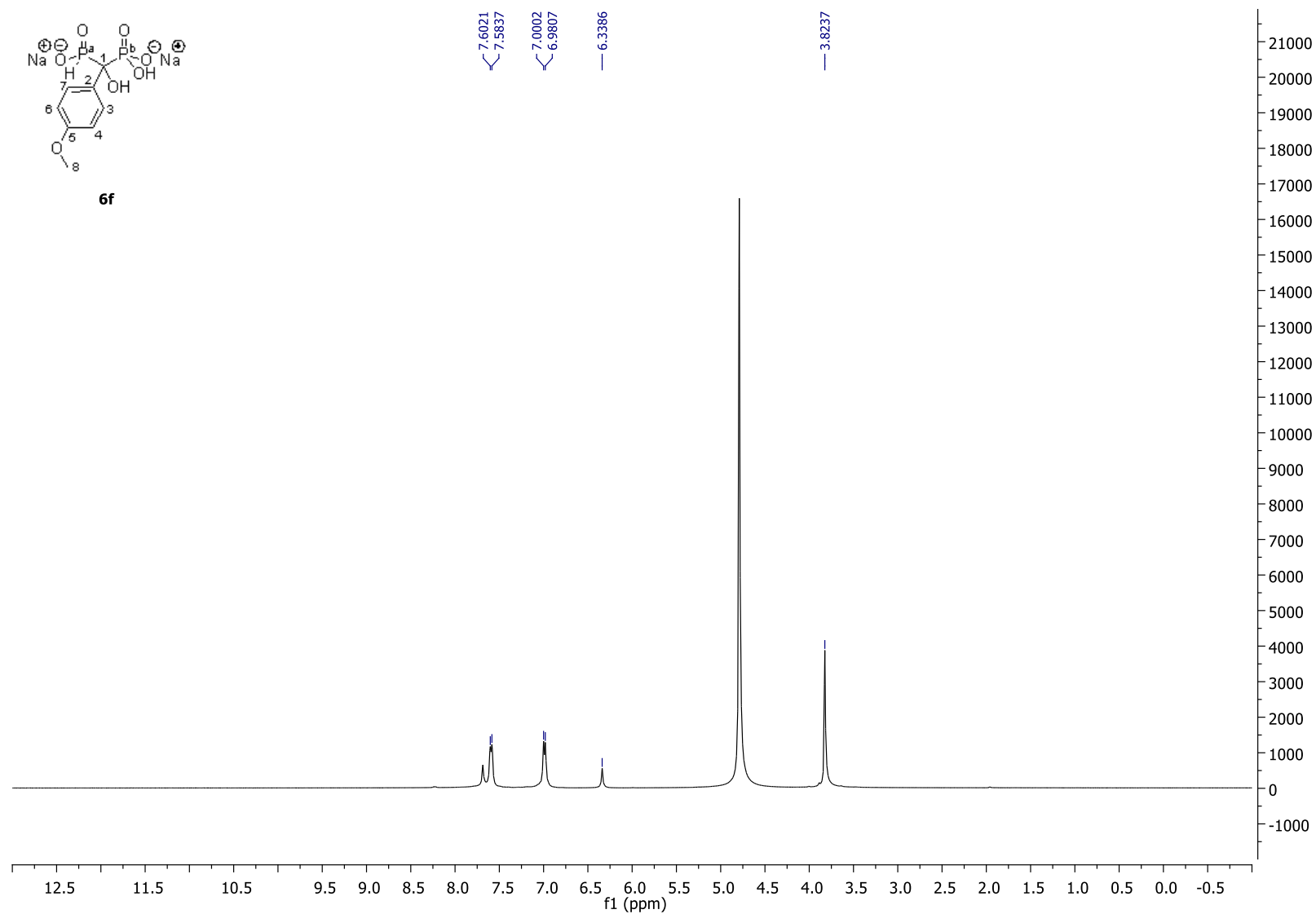


Figure S17:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of hydroxy-1-(4-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6f**

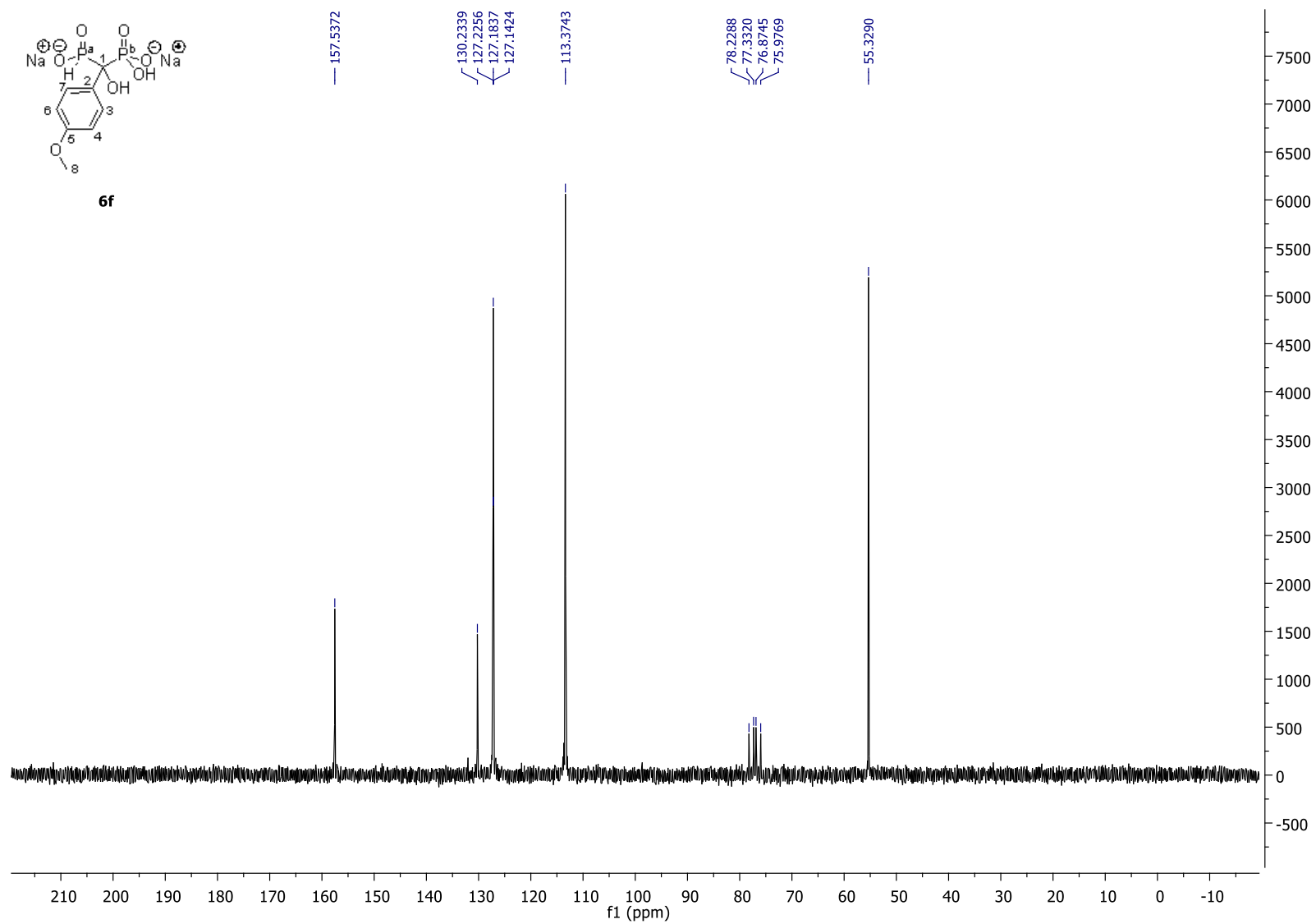


Figure S18:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of hydroxy-1-(4-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6f**

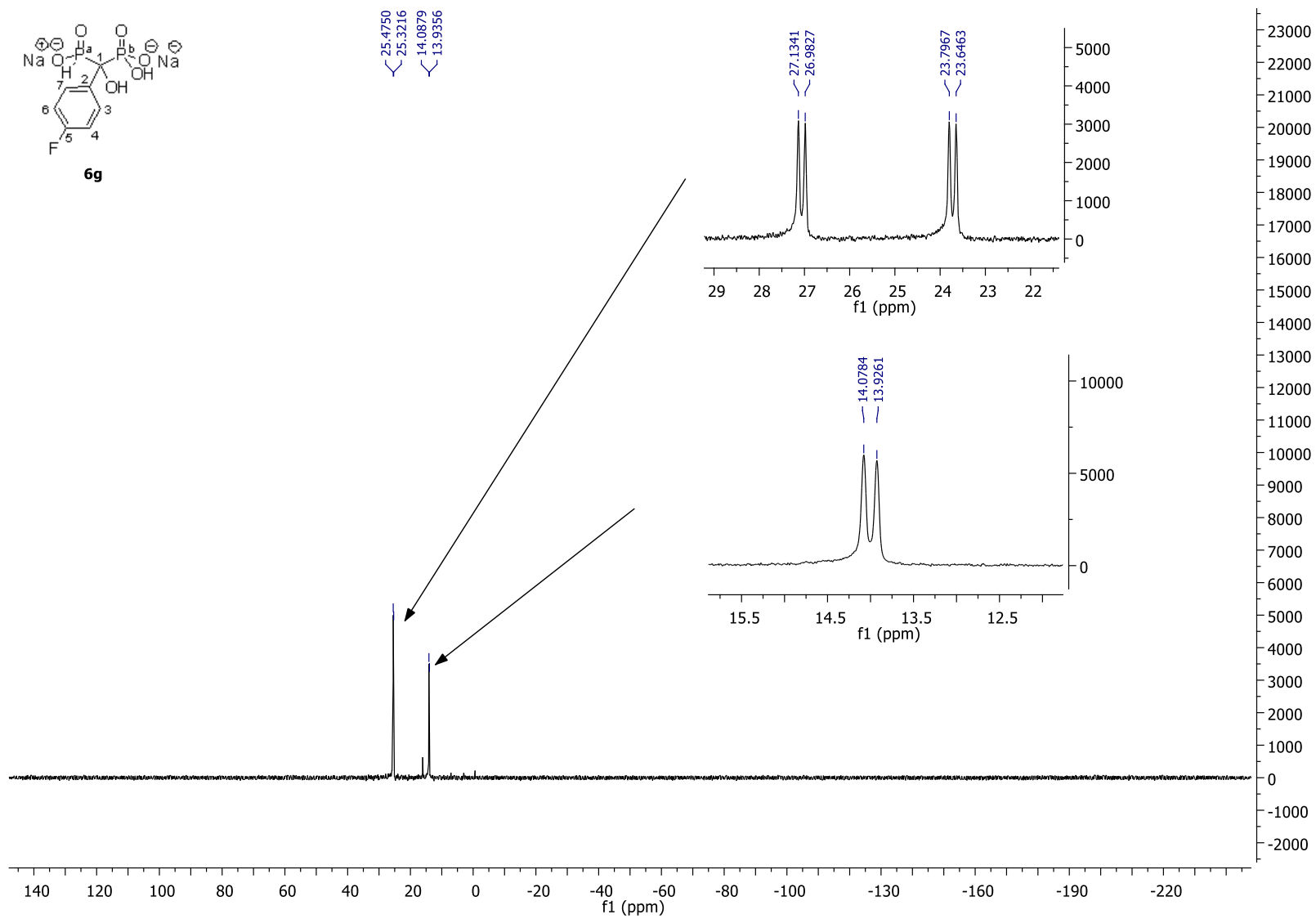


Figure S19:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(4-fluorophenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6g**

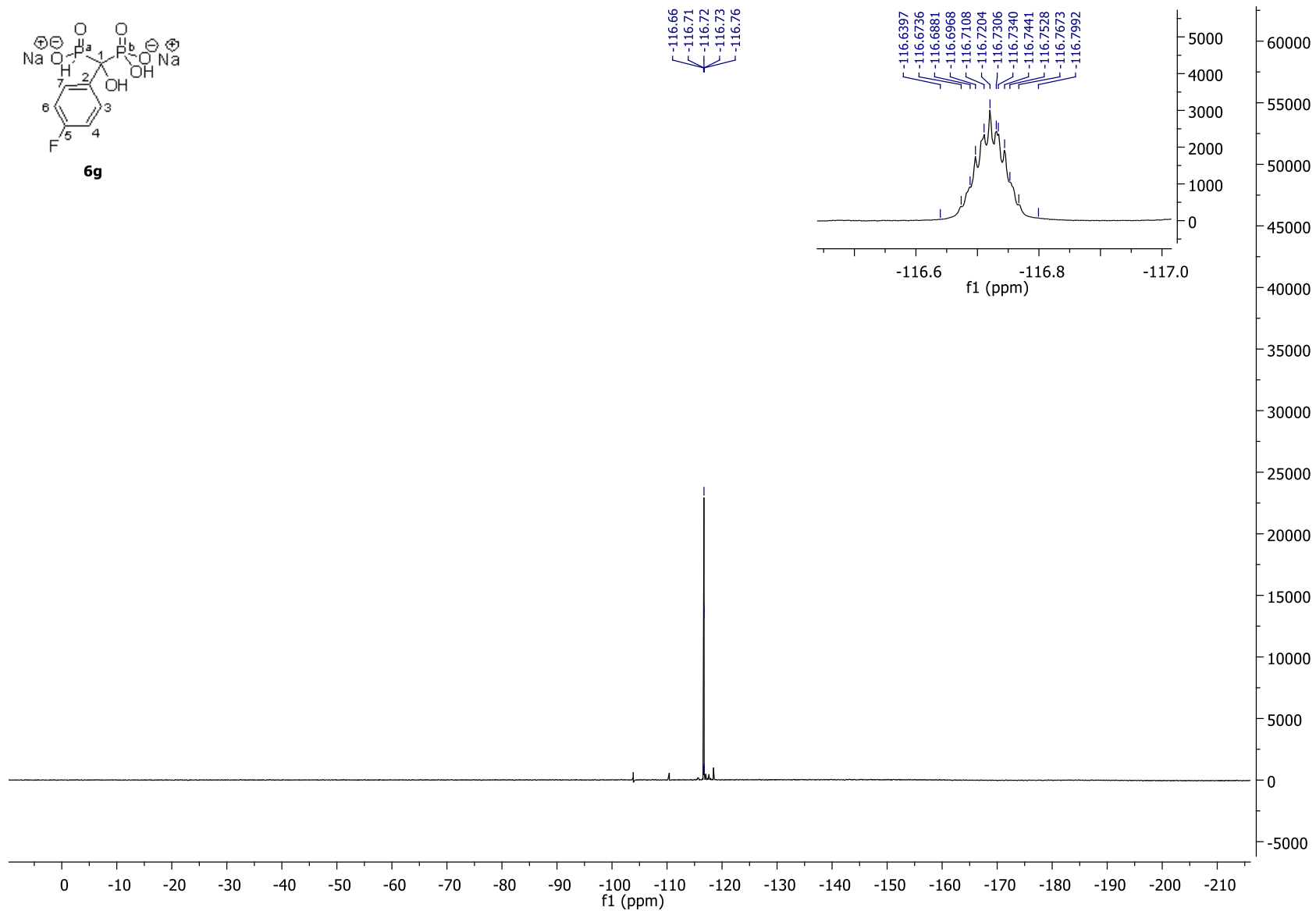


Figure S20:  $^1\text{H}$  and  $^{19}\text{F}$  (377 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(4-fluorophenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6g**

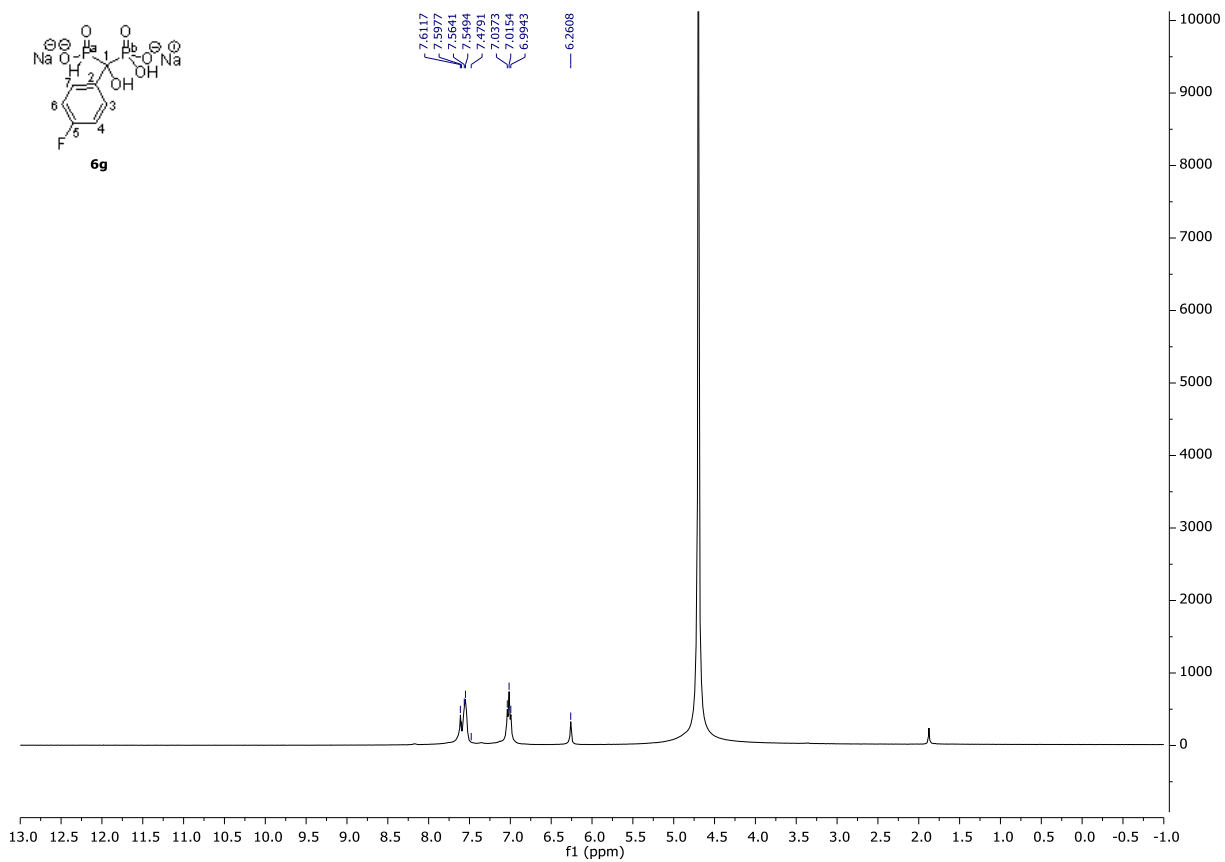


Figure S21: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(4-fluorophenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6g**

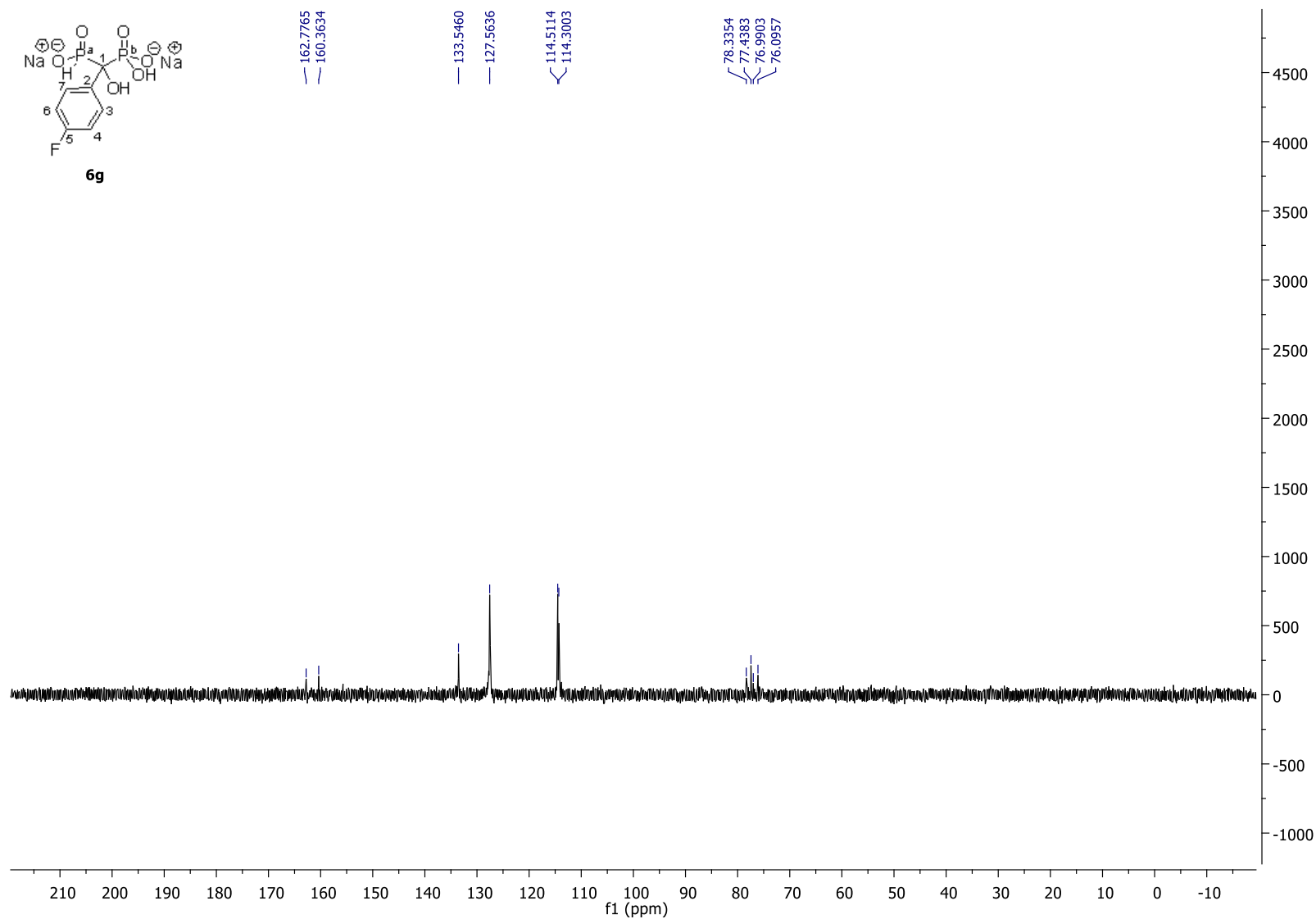


Figure S22: <sup>13</sup>C NMR spectrum of 1-hydroxy-1-(4-fluorophenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt 6g

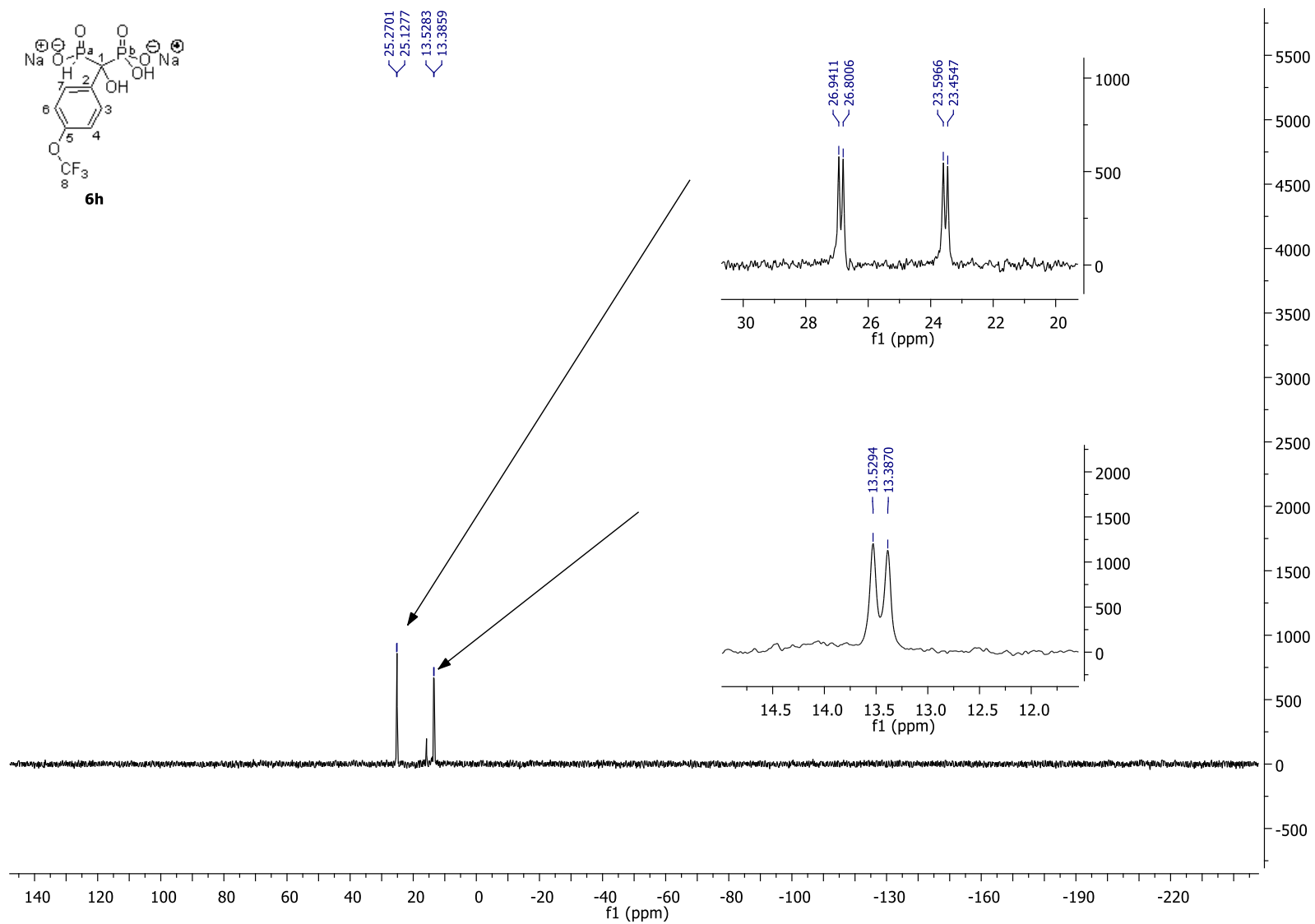


Figure S23:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(4-trifluoromethoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6h**



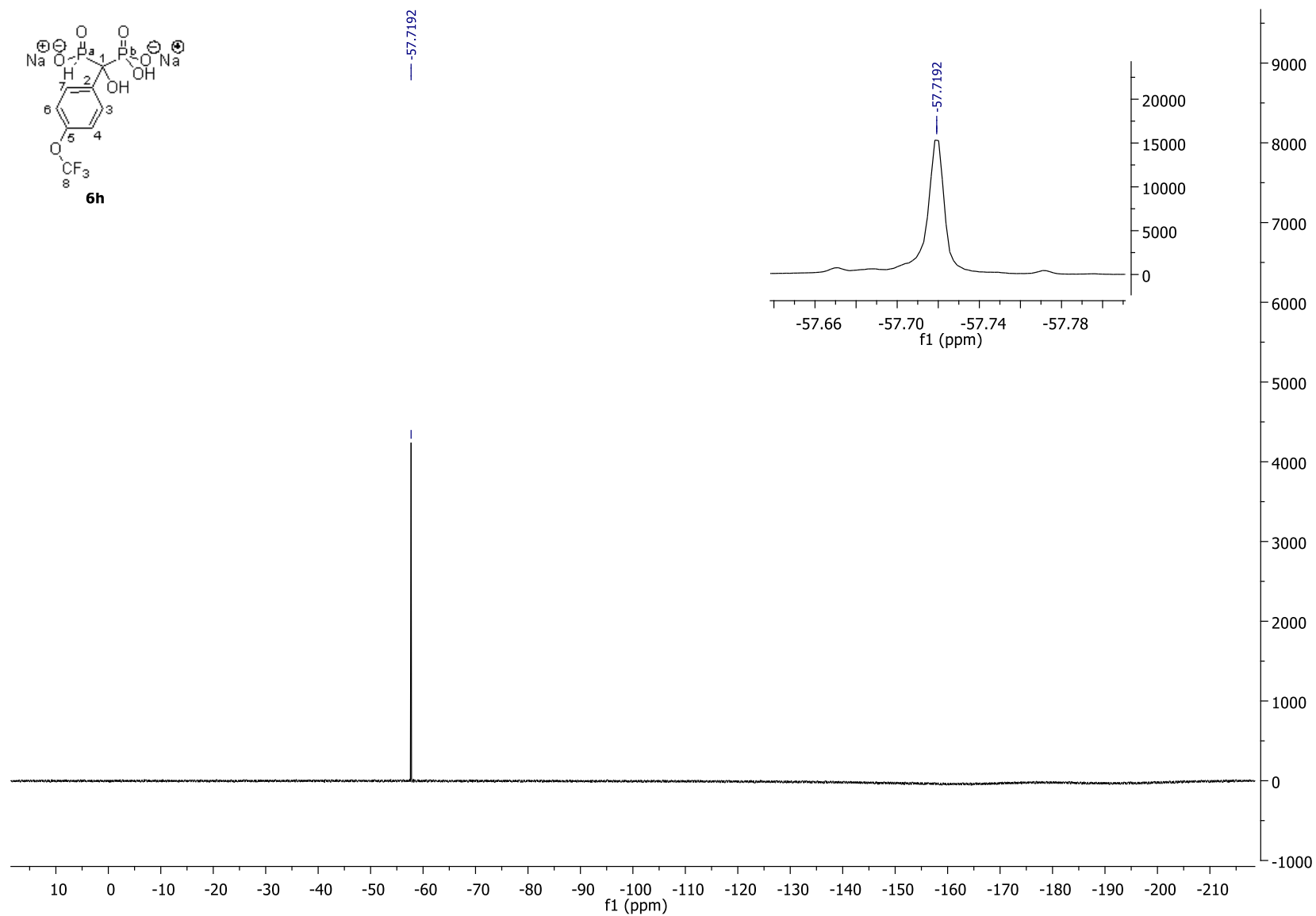


Figure S24:  $^{19}\text{F}$   $\{^1\text{H}\}$  and  $^{19}\text{F}$  (377 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(4-trifluoromethoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6h**

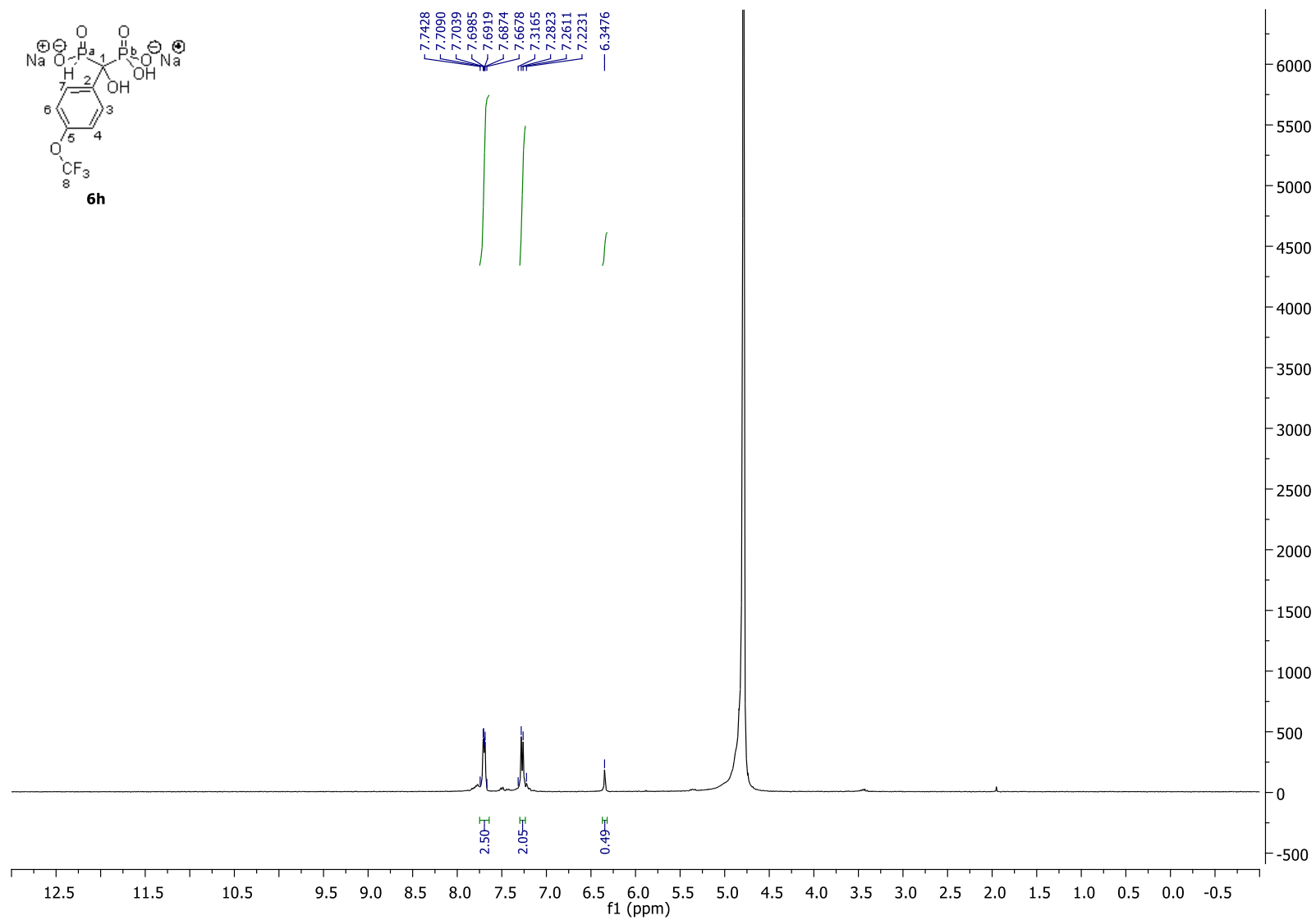


Figure S25: <sup>1</sup>H NMR spectrum (400 MHz, D<sub>2</sub>O) of 1-hydroxy-1-(4-trifluoromethoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6h**

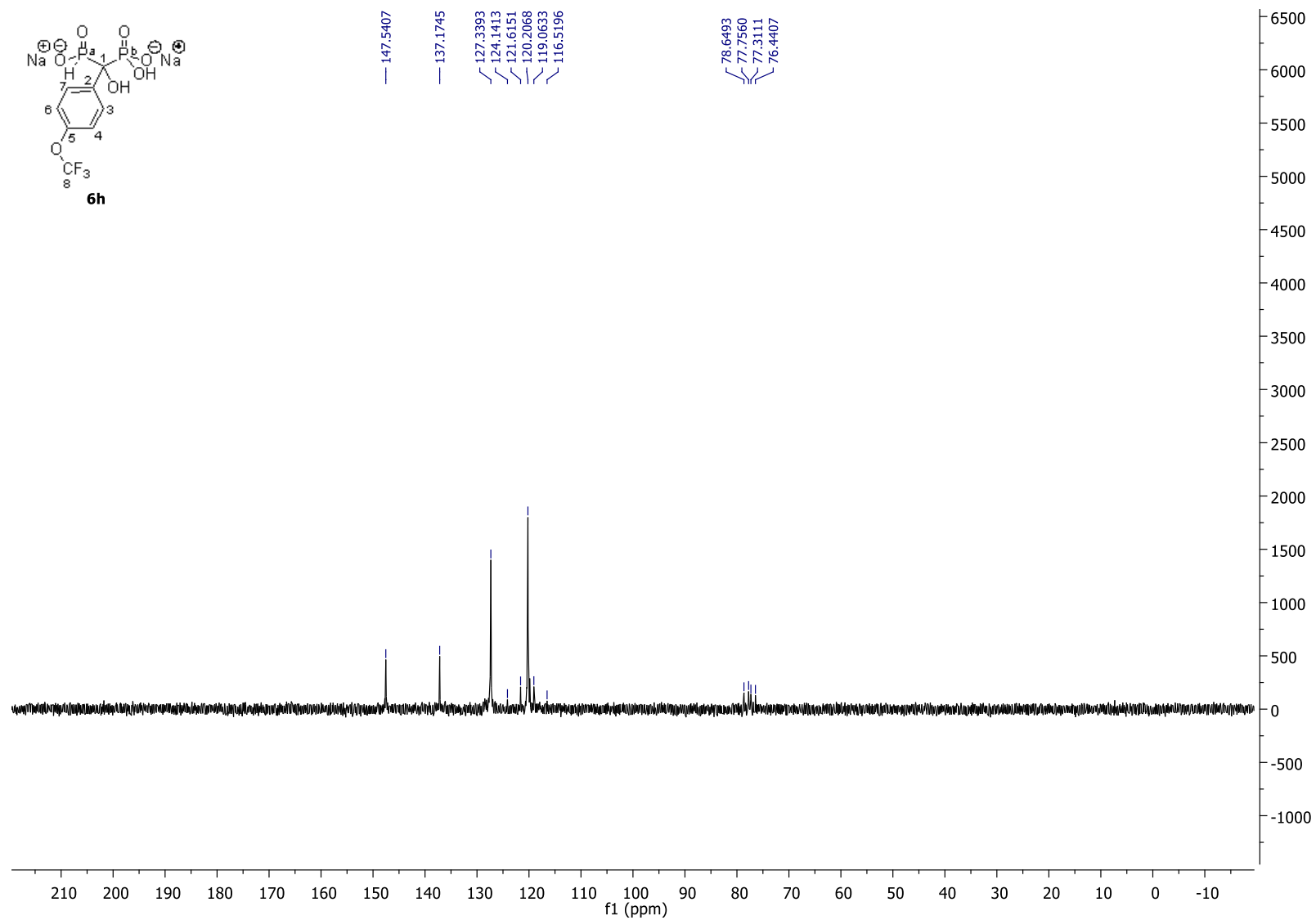
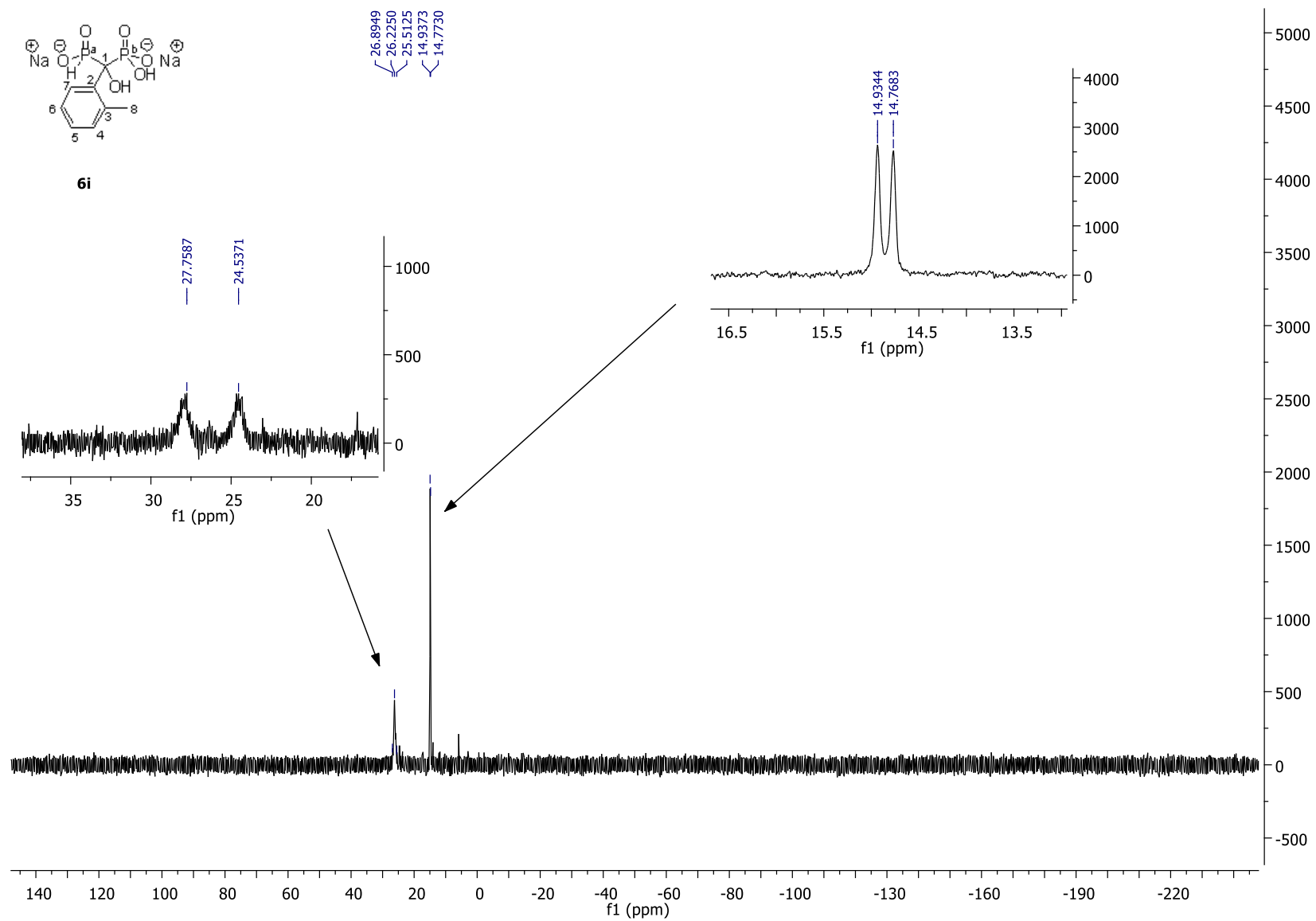


Figure S26:  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(4-trifluoromethoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6h**



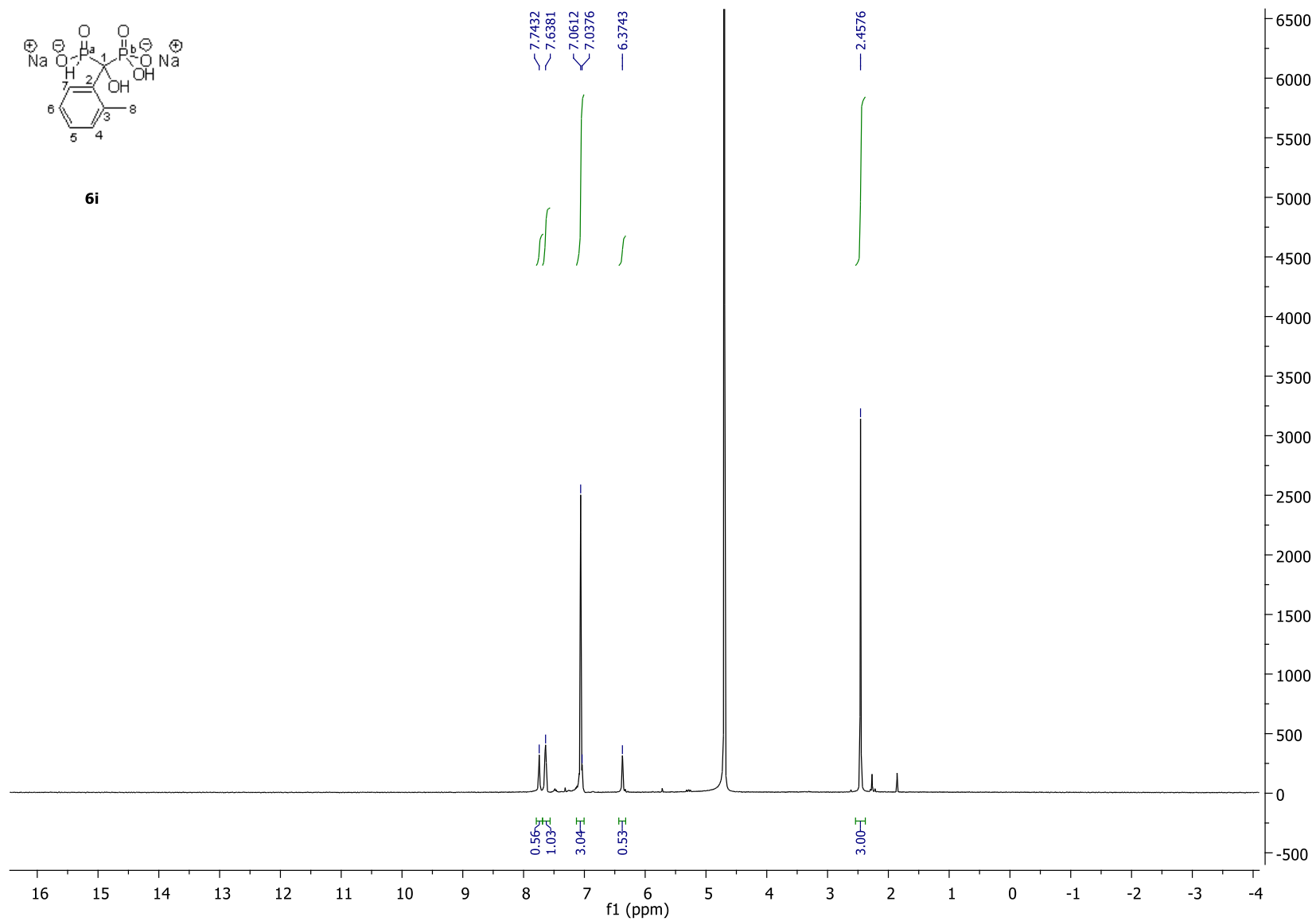


Figure S28:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(2-tolyl)methane-1,1-bis(*H*-phosphonate) disodium salt **6i**

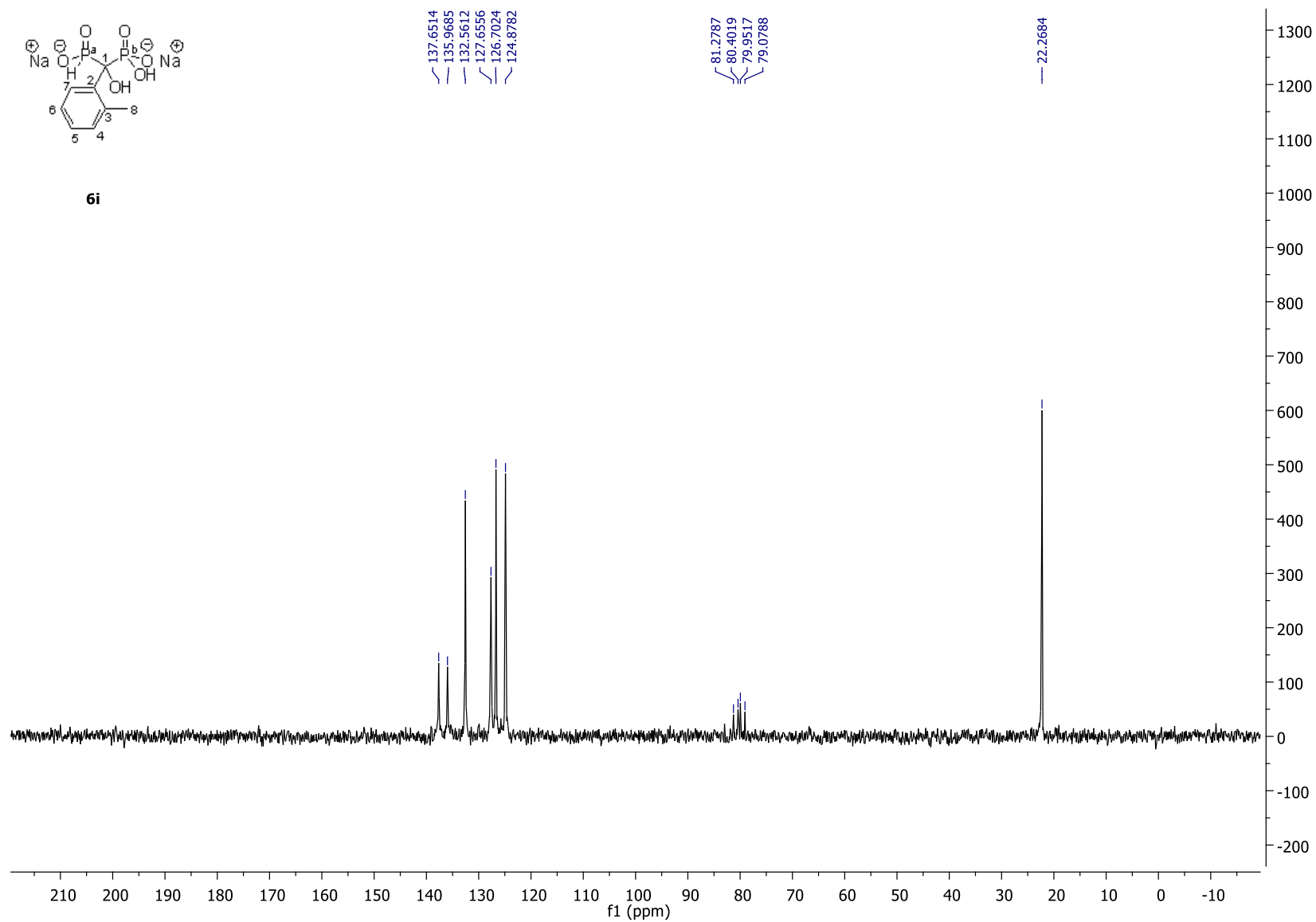


Figure S29: <sup>13</sup>C NMR (101 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(2-tolyl)methane-1,1-bis(*H*-phosphonate) disodium salt **6i**

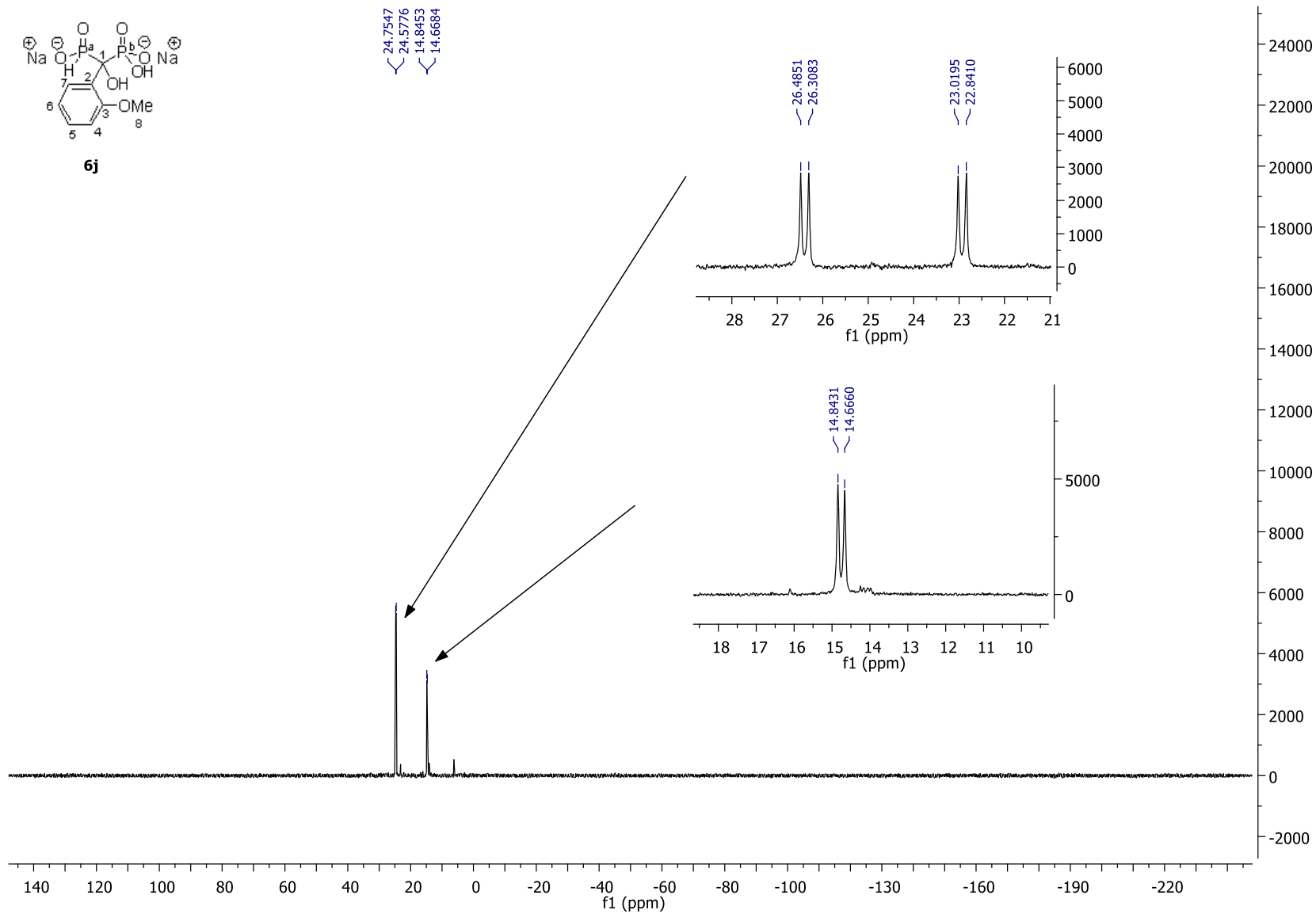


Figure S30: <sup>31</sup>P{<sup>1</sup>H} and <sup>31</sup>P NMR (162 MHz, D<sub>2</sub>O) spectra of 1-hydroxy-1-(2-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6j**

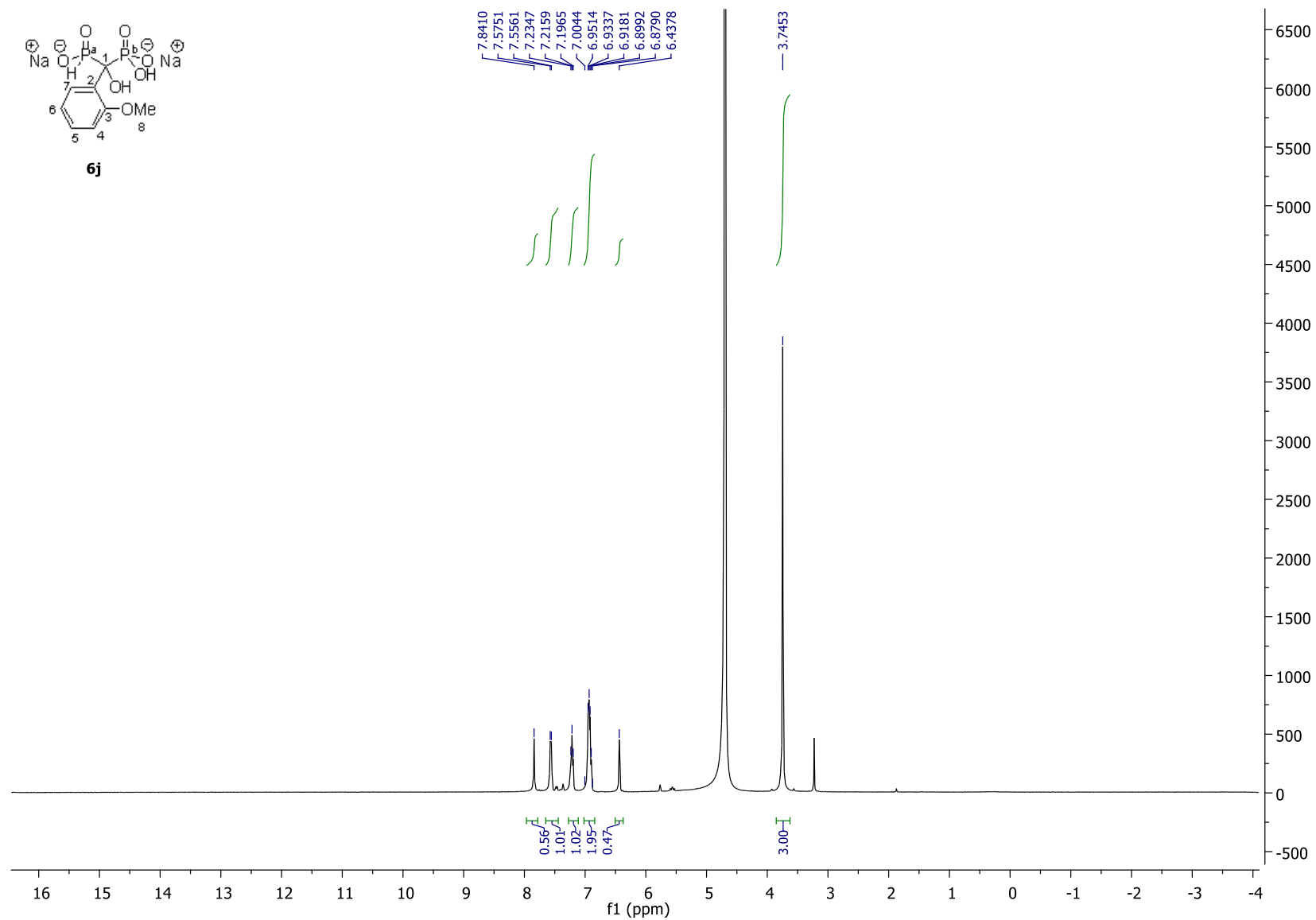


Figure S31: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(2-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6j**



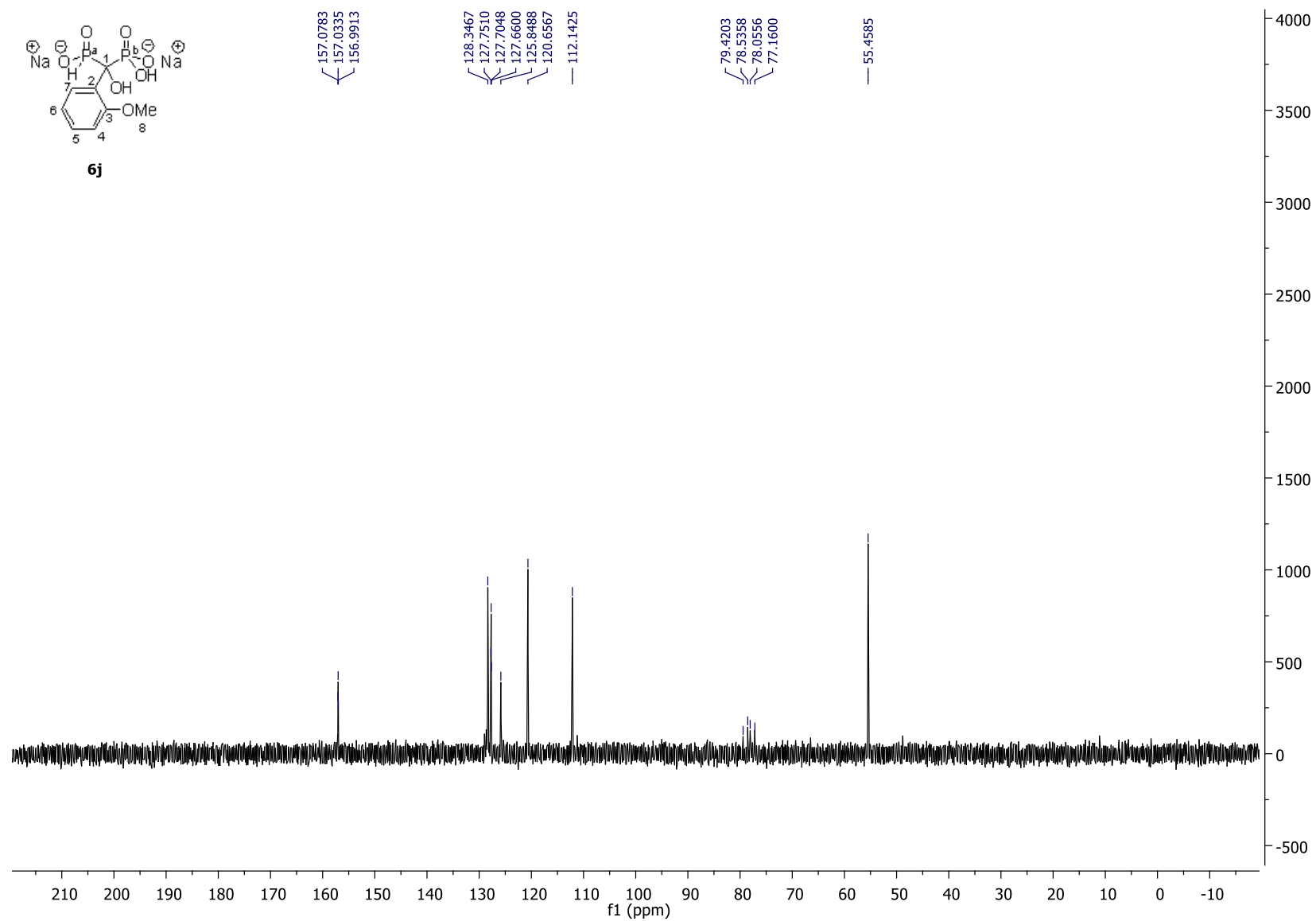


Figure S32: <sup>13</sup>C NMR spectrum (101 MHz, D<sub>2</sub>O) of 1-hydroxy-1-(2-methoxyphenyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6j**

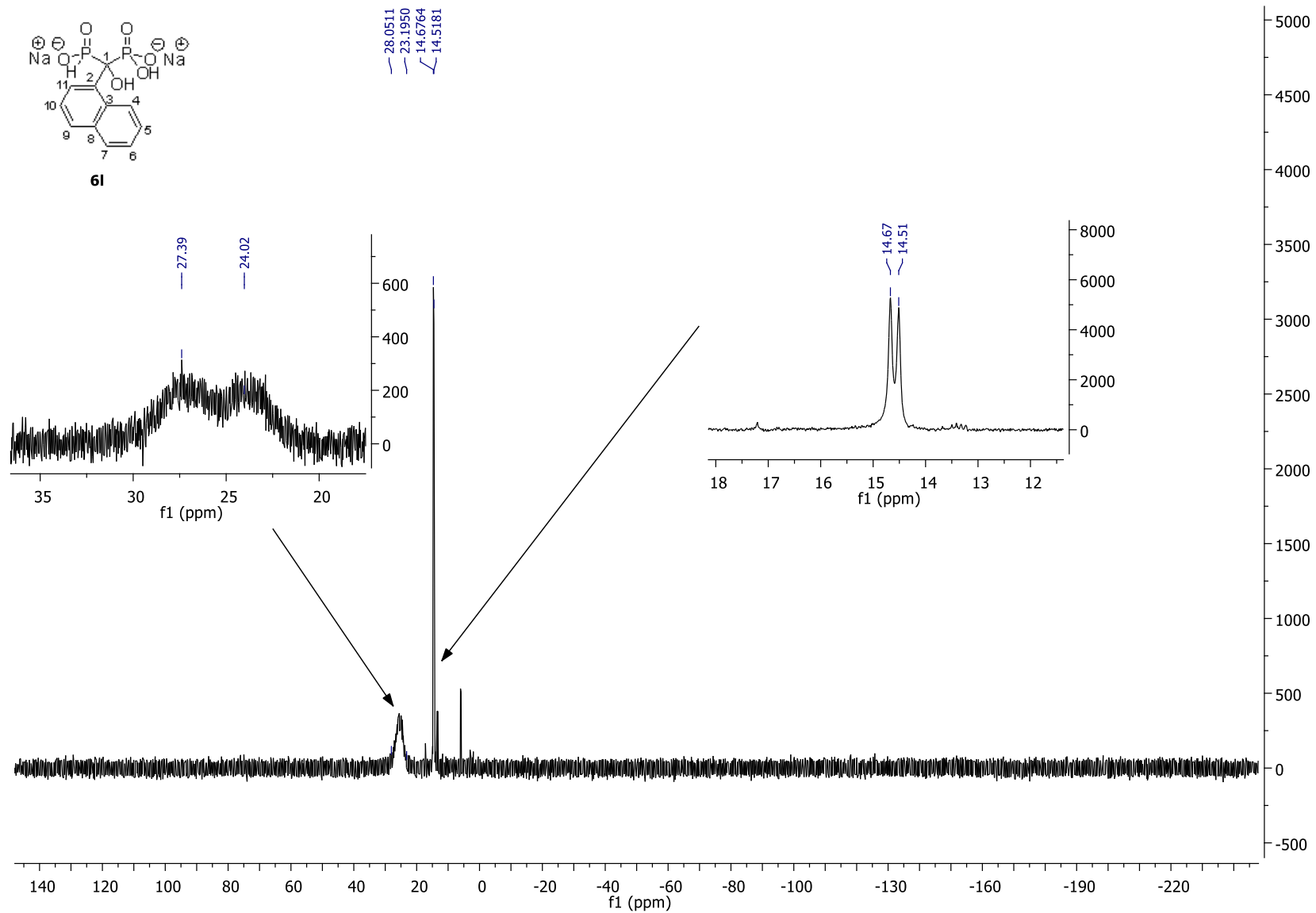


Figure S33:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(1-naphthyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6I**

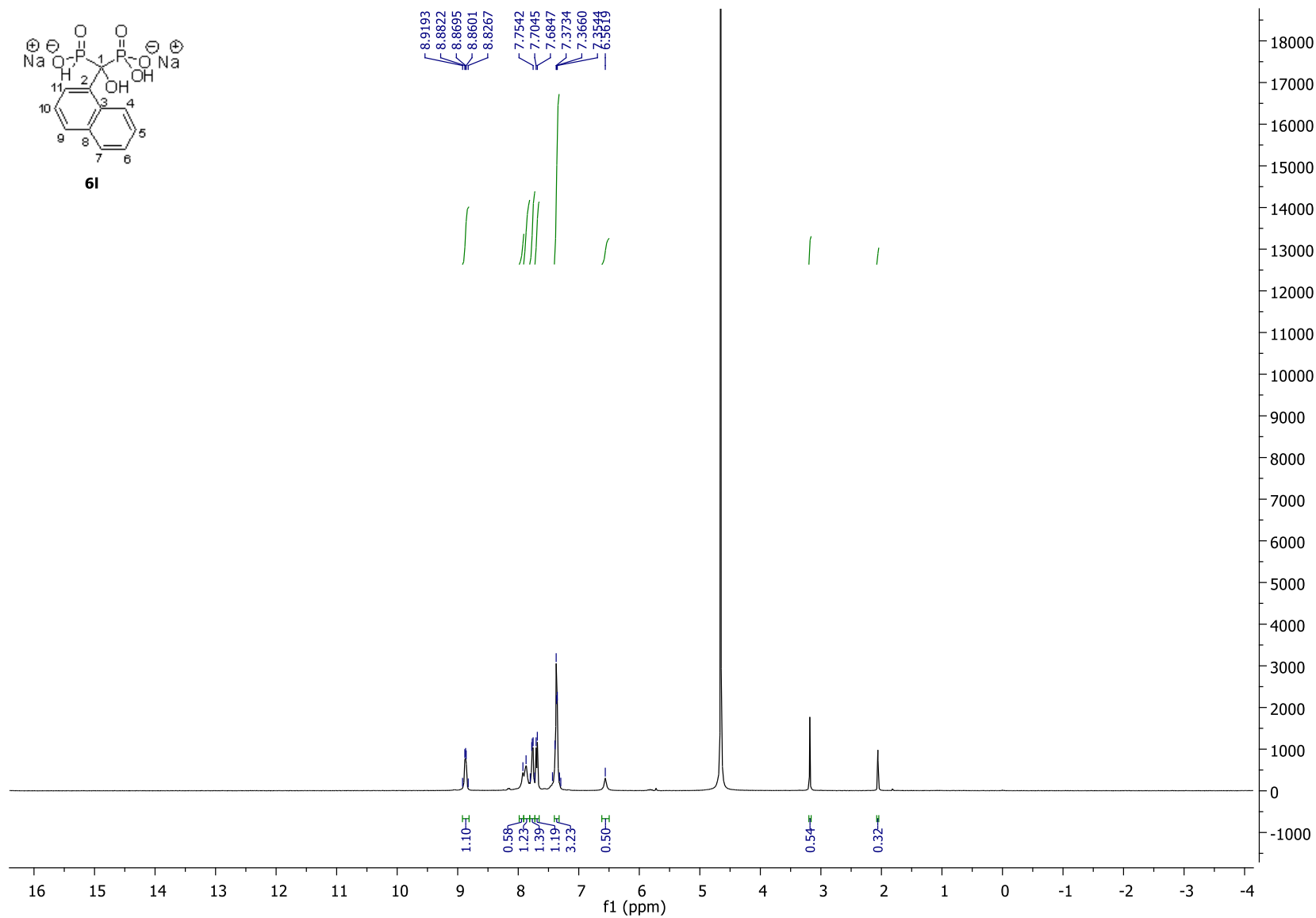


Figure S34:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(1-naphthyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6I**

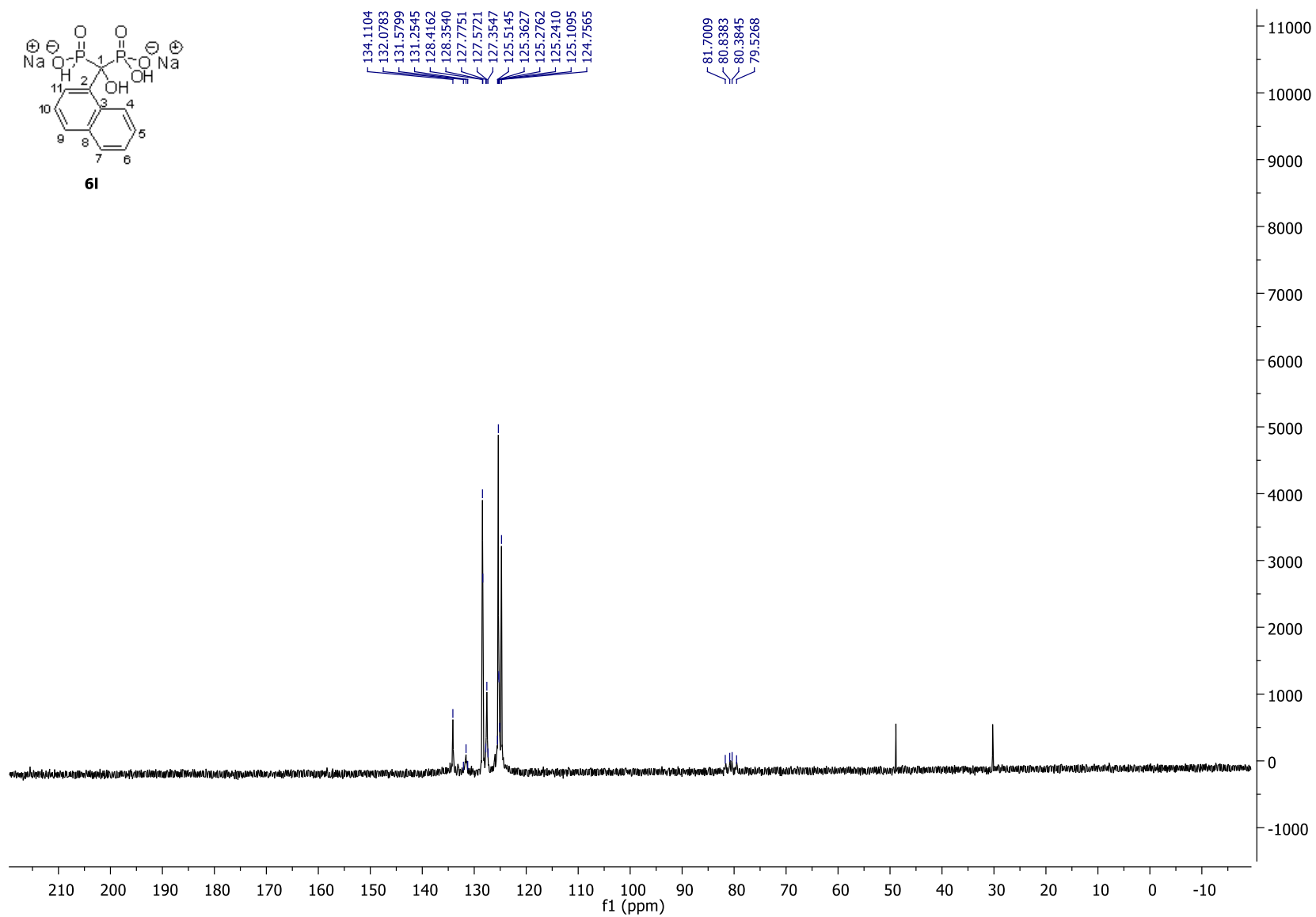


Figure S35:  $^{13}\text{C}$  NMR spectrum (101 MHz,  $\text{D}_2\text{O}$ ) of 1-hydroxy-1-(1-naphthyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6l**

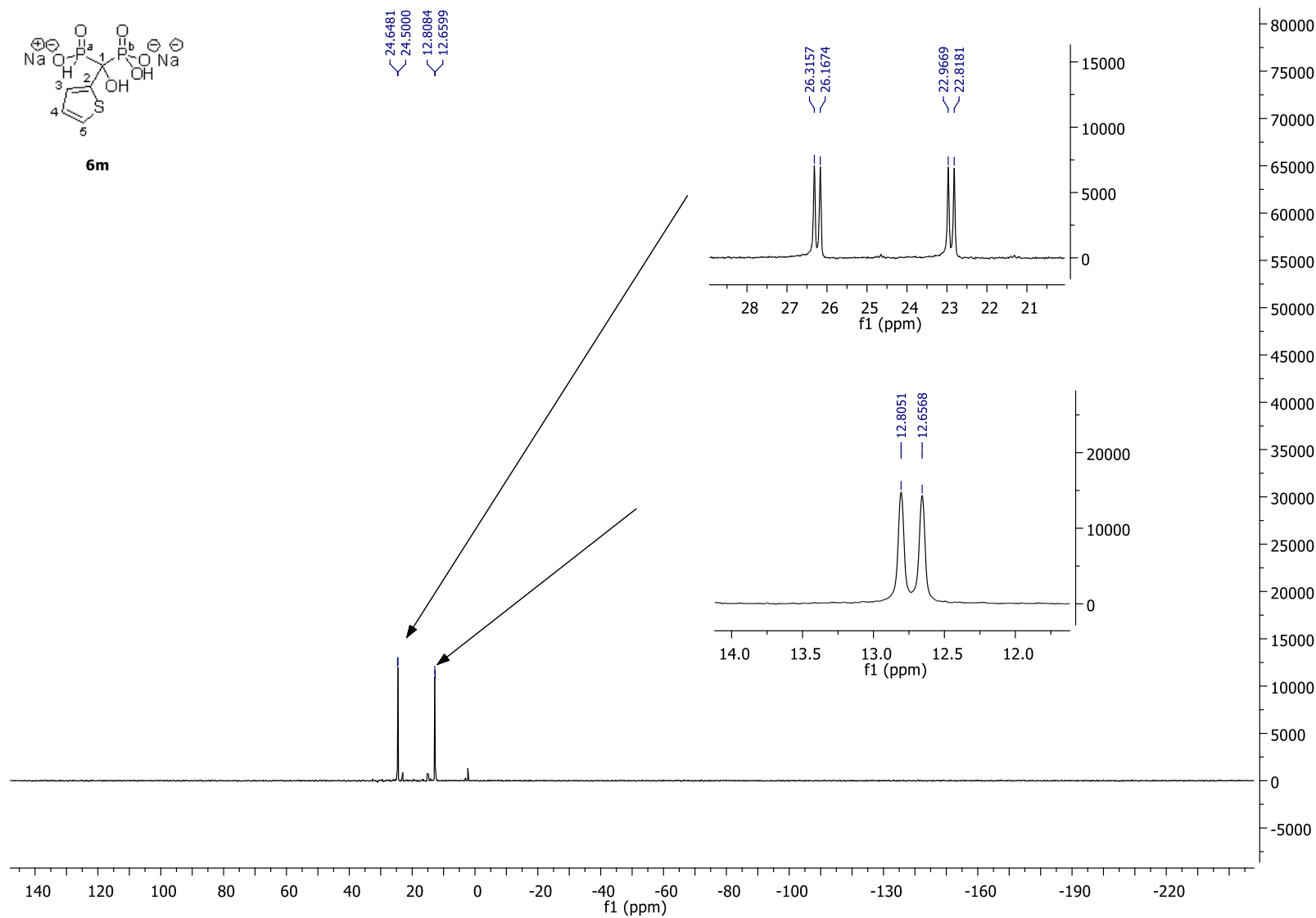


Figure S36:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(2-thienyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6m**

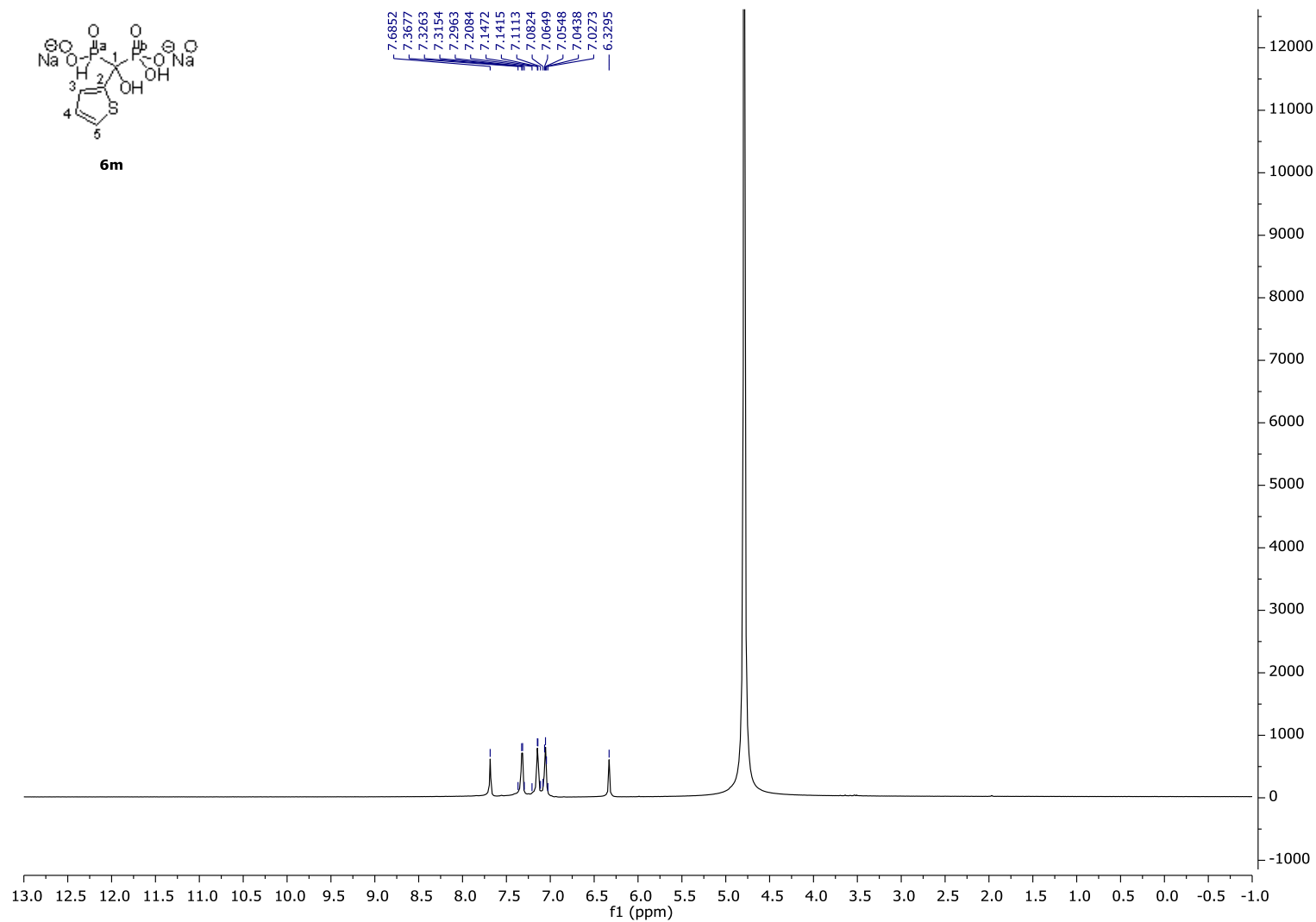


Figure S37:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(2-thienyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6m**

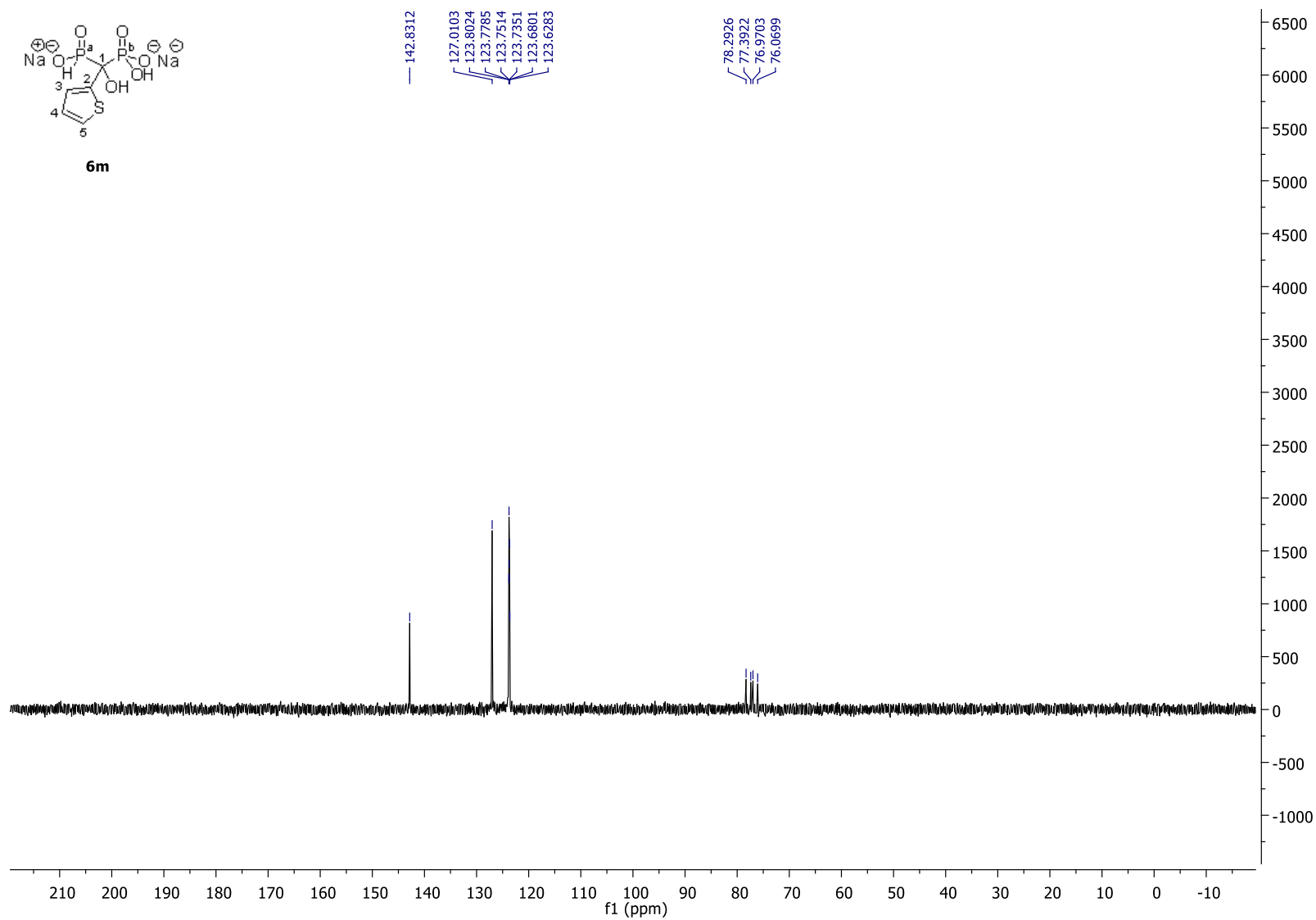
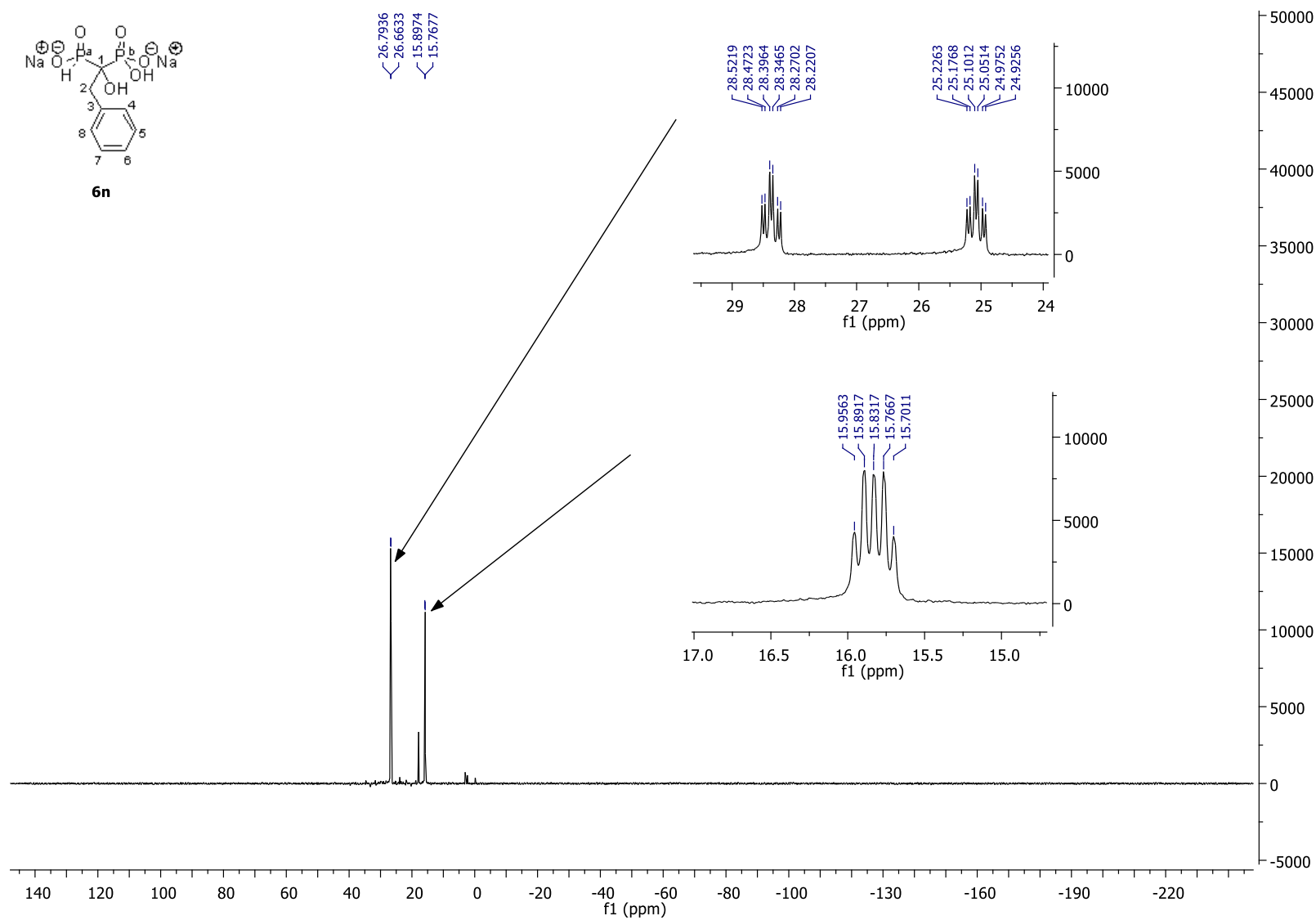


Figure S38: <sup>13</sup>C NMR (101 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(2-thienyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6m**





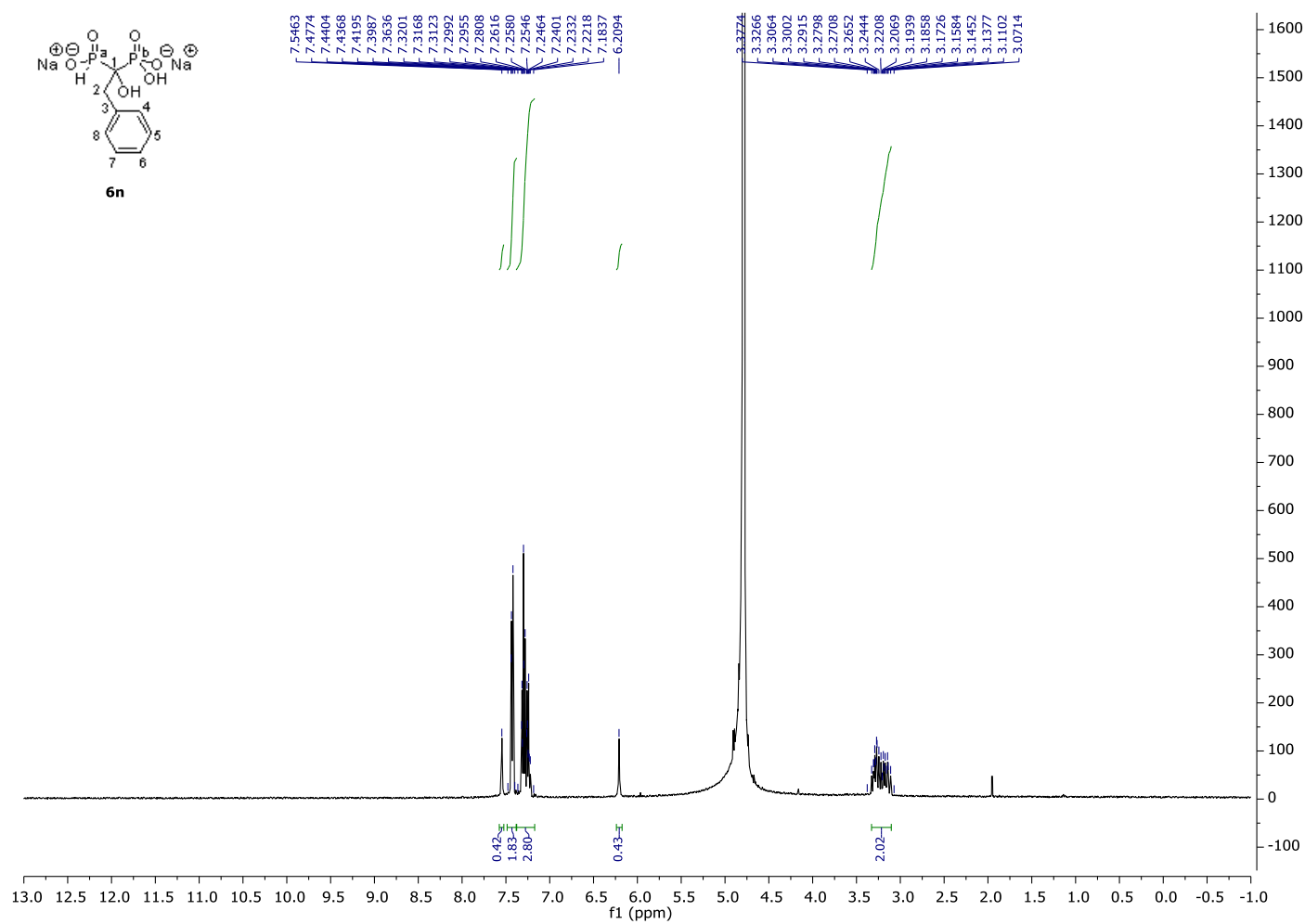


Figure S40: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-2-phenylethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6n**

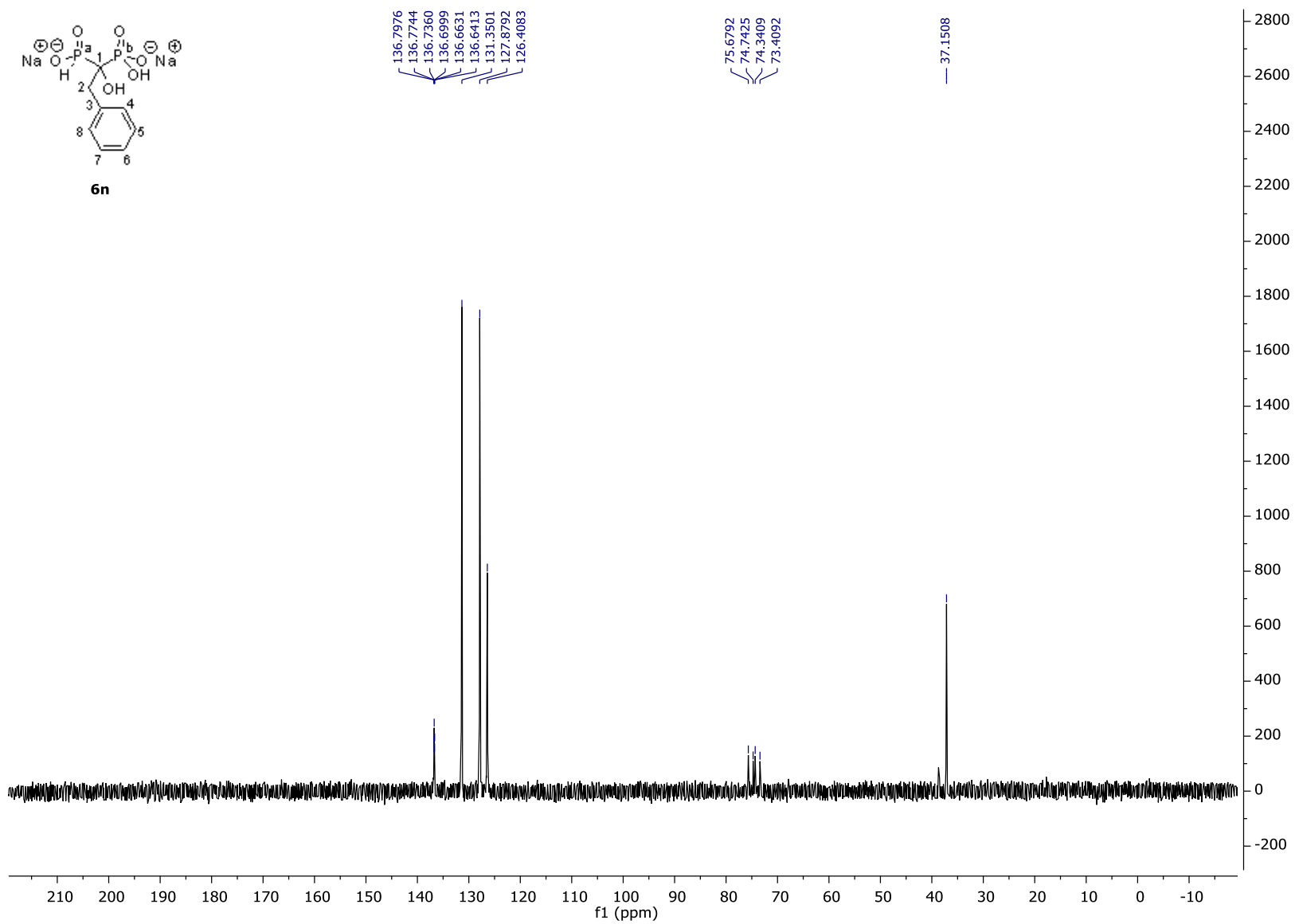


Figure S41: <sup>13</sup>C NMR (101 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-2-phenylethane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6n**

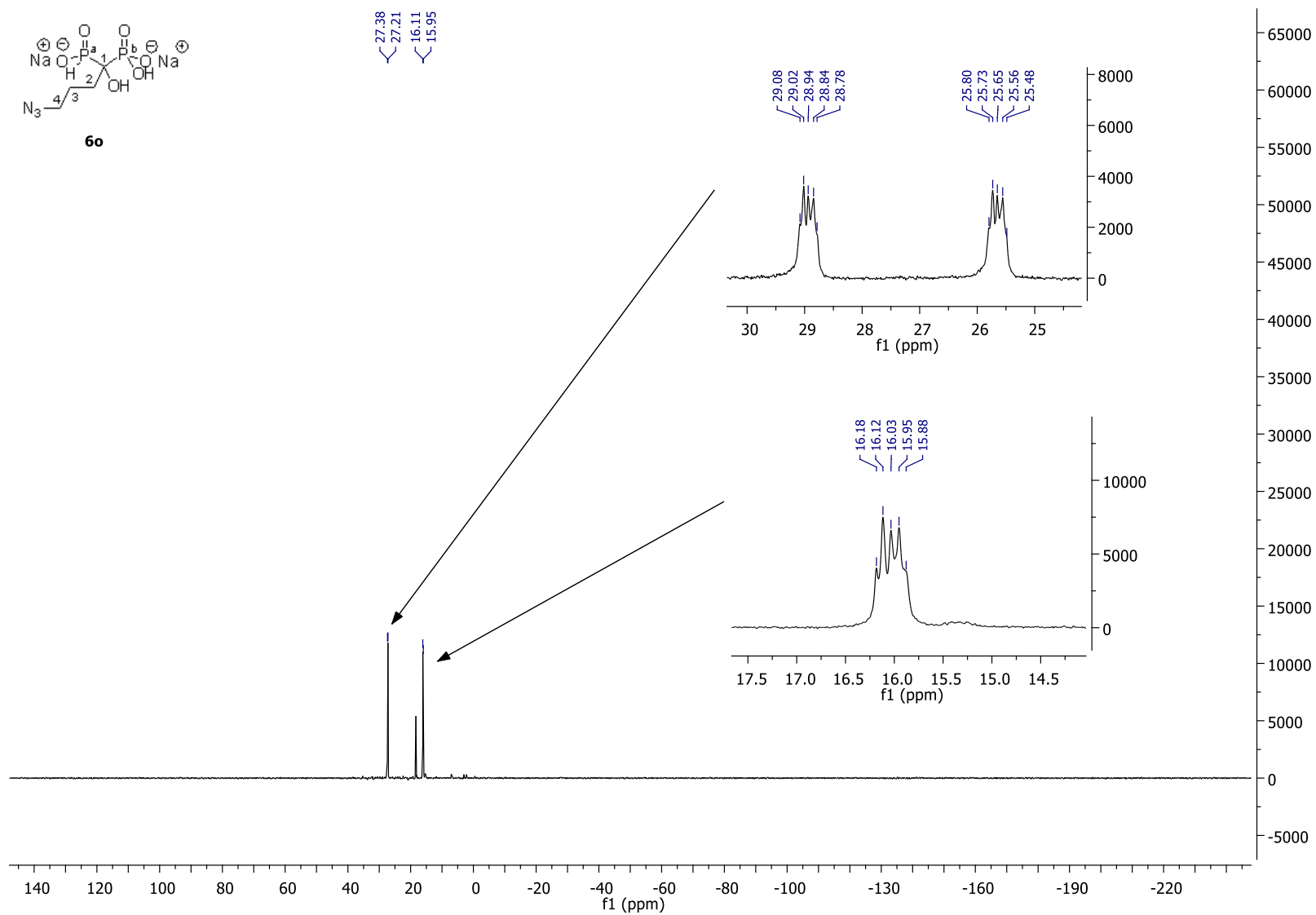


Figure S42:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(3-azidopropyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6o**

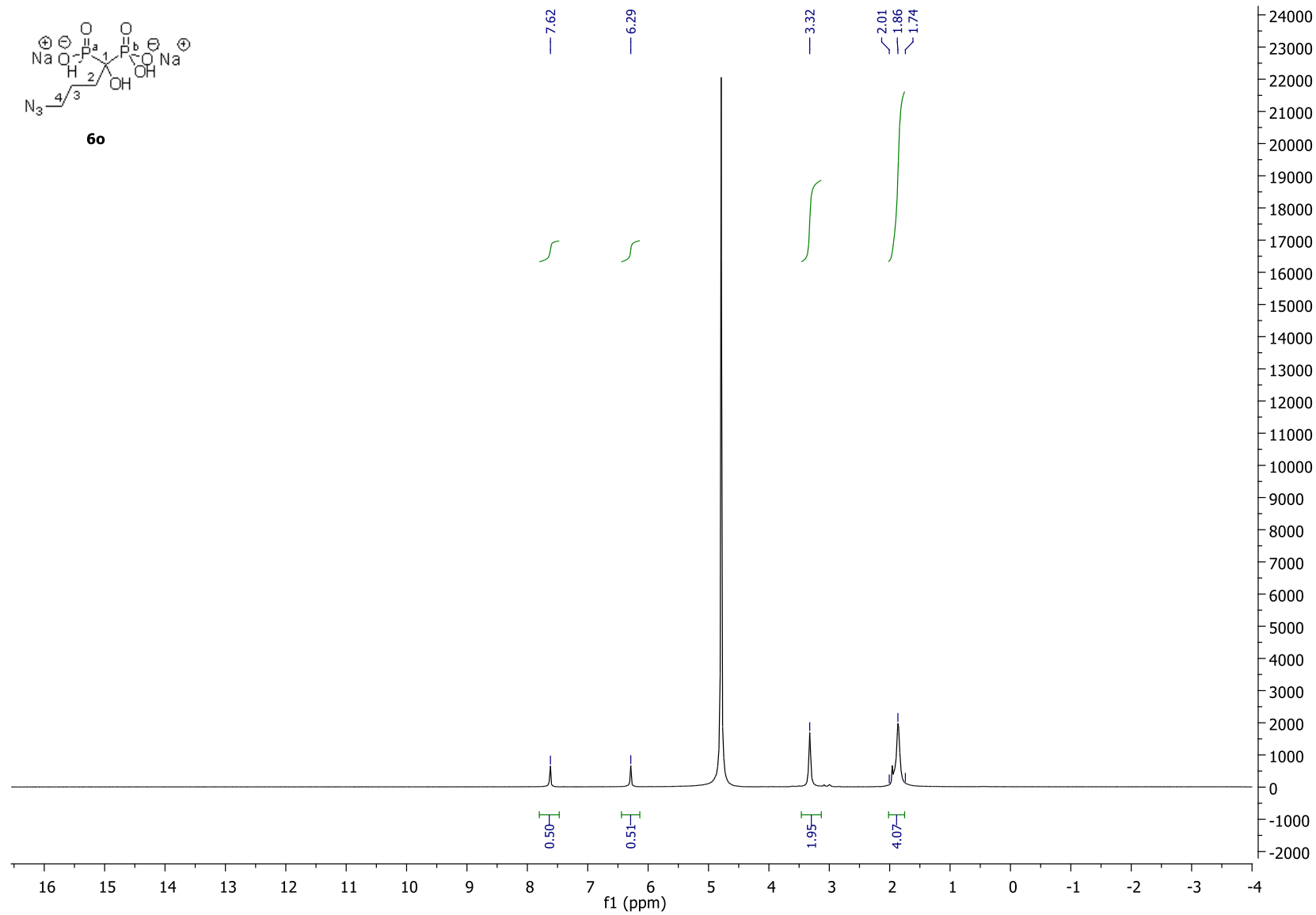


Figure S43: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(3-azidopropyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **60**

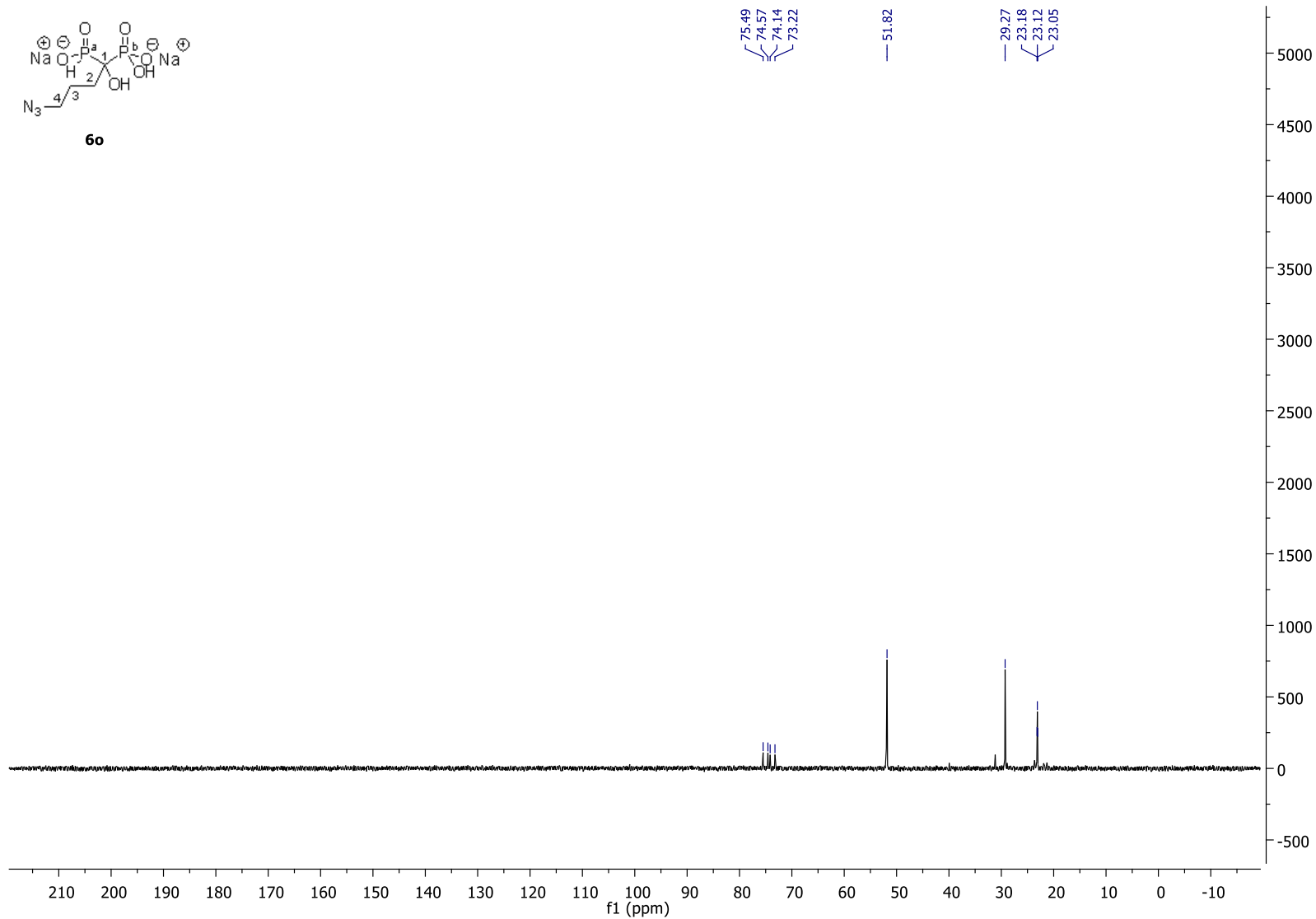


Figure S44: <sup>13</sup>C NMR (101 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(3-azidopropyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **60**

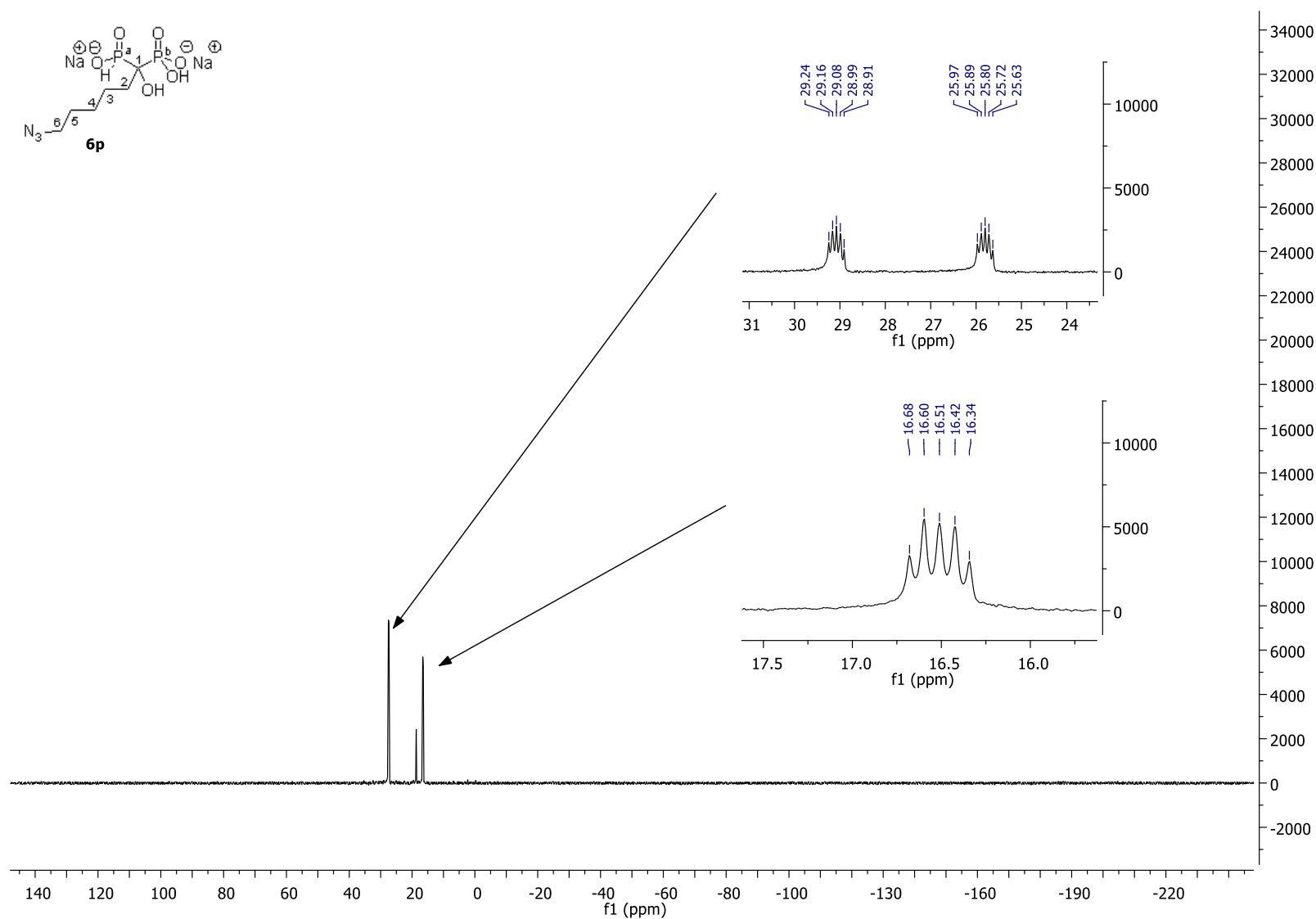


Figure S45: <sup>31</sup>P{<sup>1</sup>H} and <sup>31</sup>P NMR (162 MHz, D<sub>2</sub>O) spectra of 1-hydroxy-1-(5-azidopentyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6p**

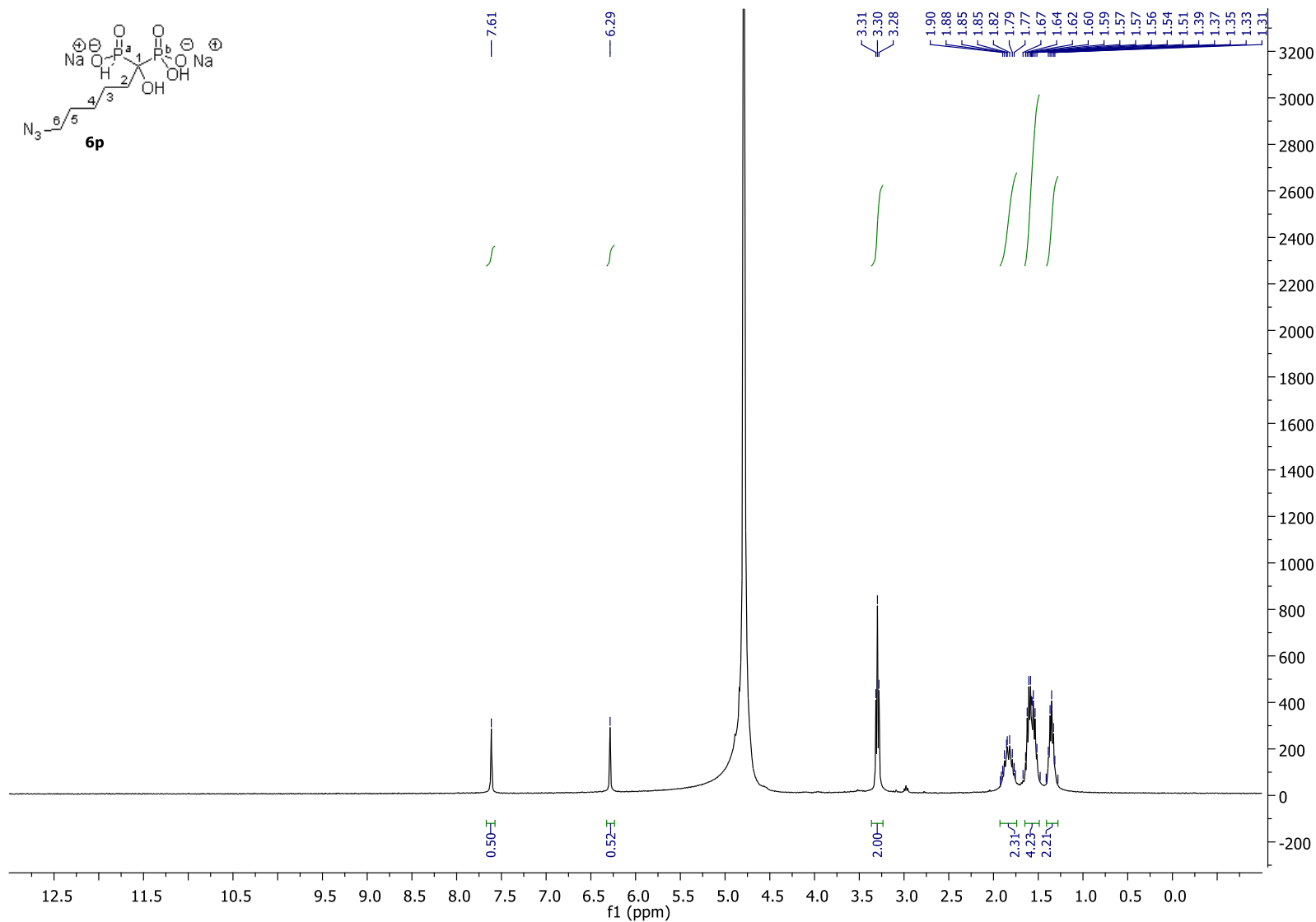


Figure S46: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(5-azidopentyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6p**

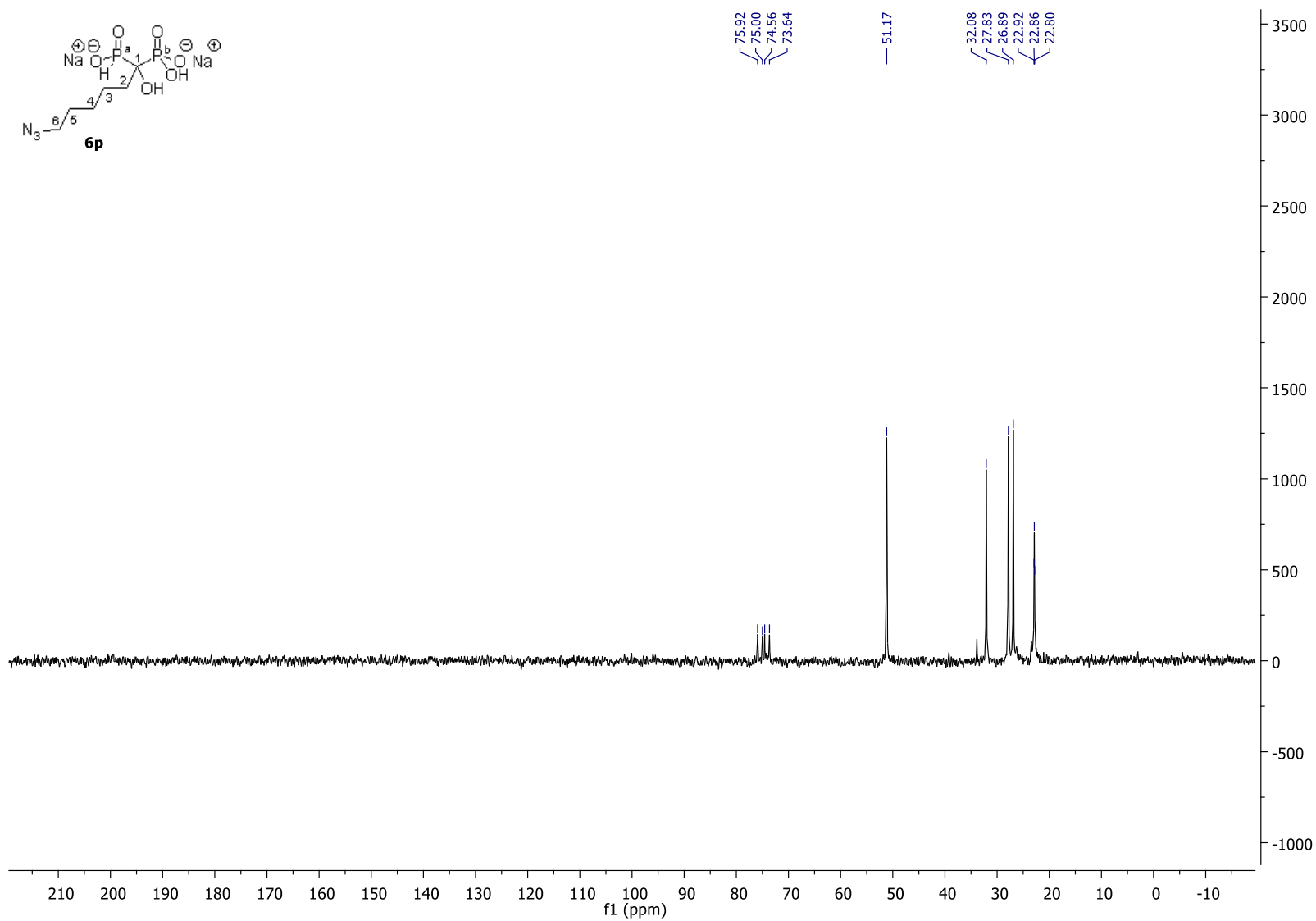


Figure S47 :  $^{13}\text{C}$  NMR (101 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(5-azidopentyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **6p**



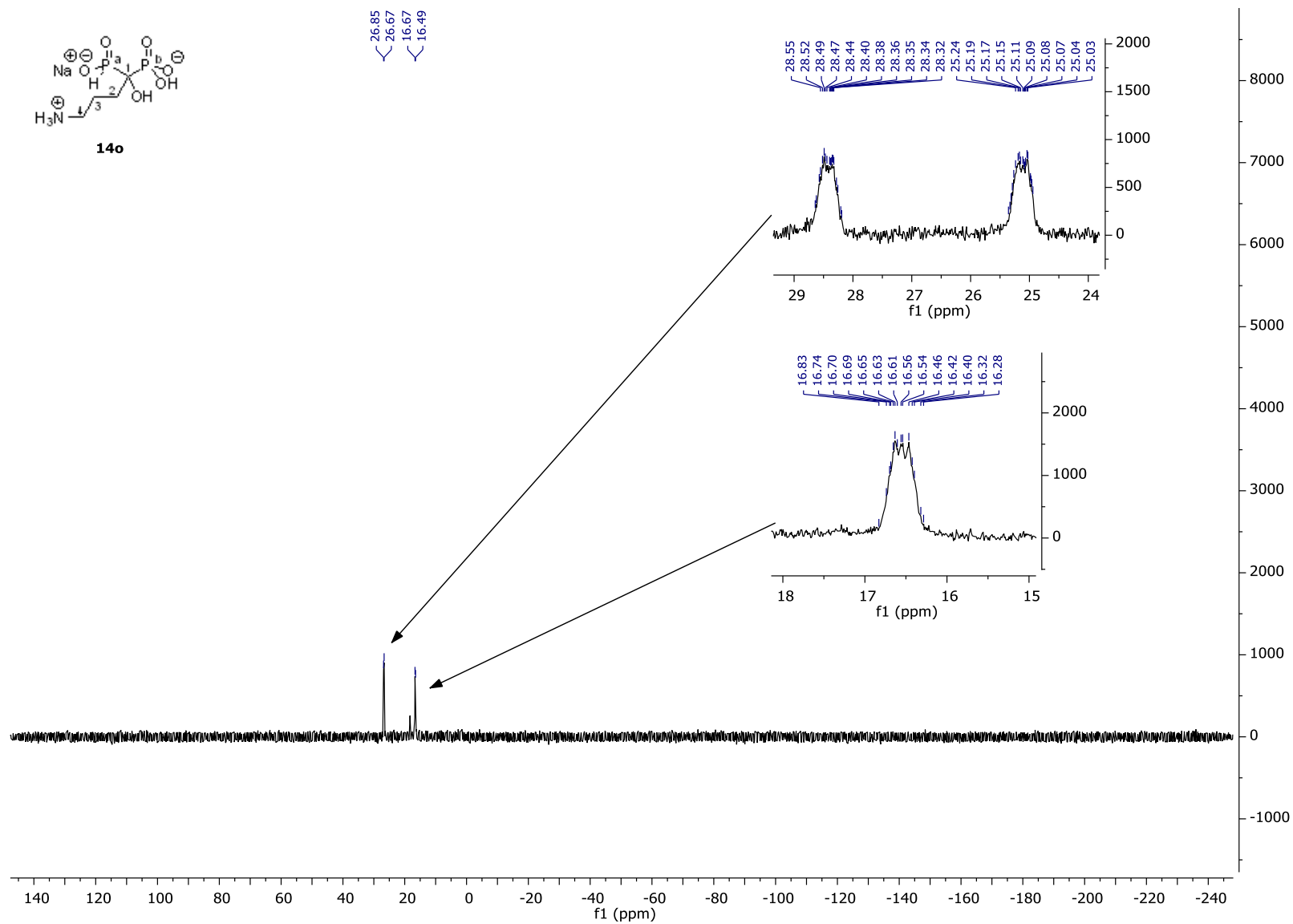


Figure S48: <sup>31</sup>P{<sup>1</sup>H} and <sup>31</sup>P NMR (162 MHz, D<sub>2</sub>O) spectra of 1-hydroxy-1-(3-aminopropyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **14o**

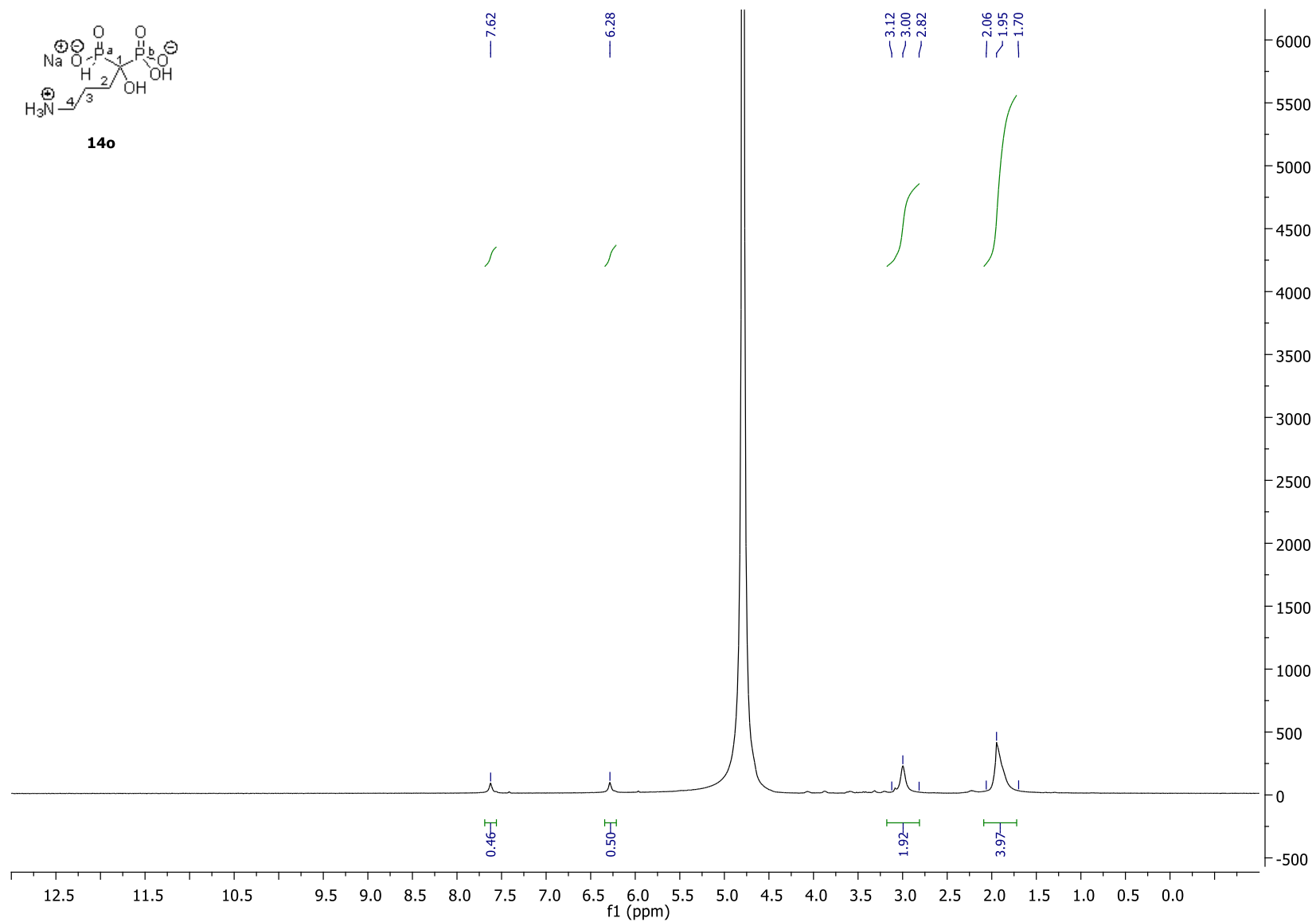
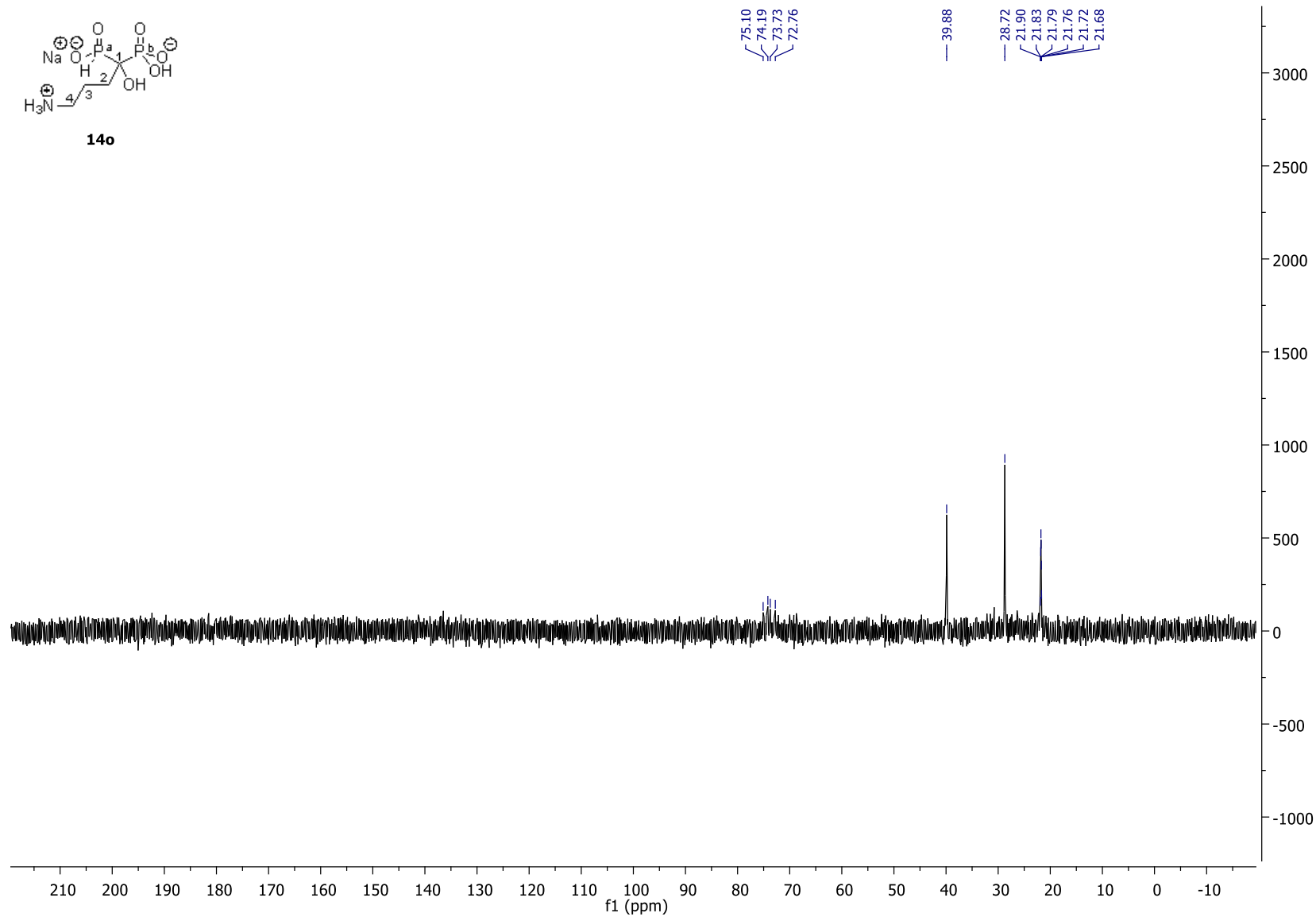


Figure S49: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O) spectrum of 1-hydroxy-1-(3-aminopropyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **14o**



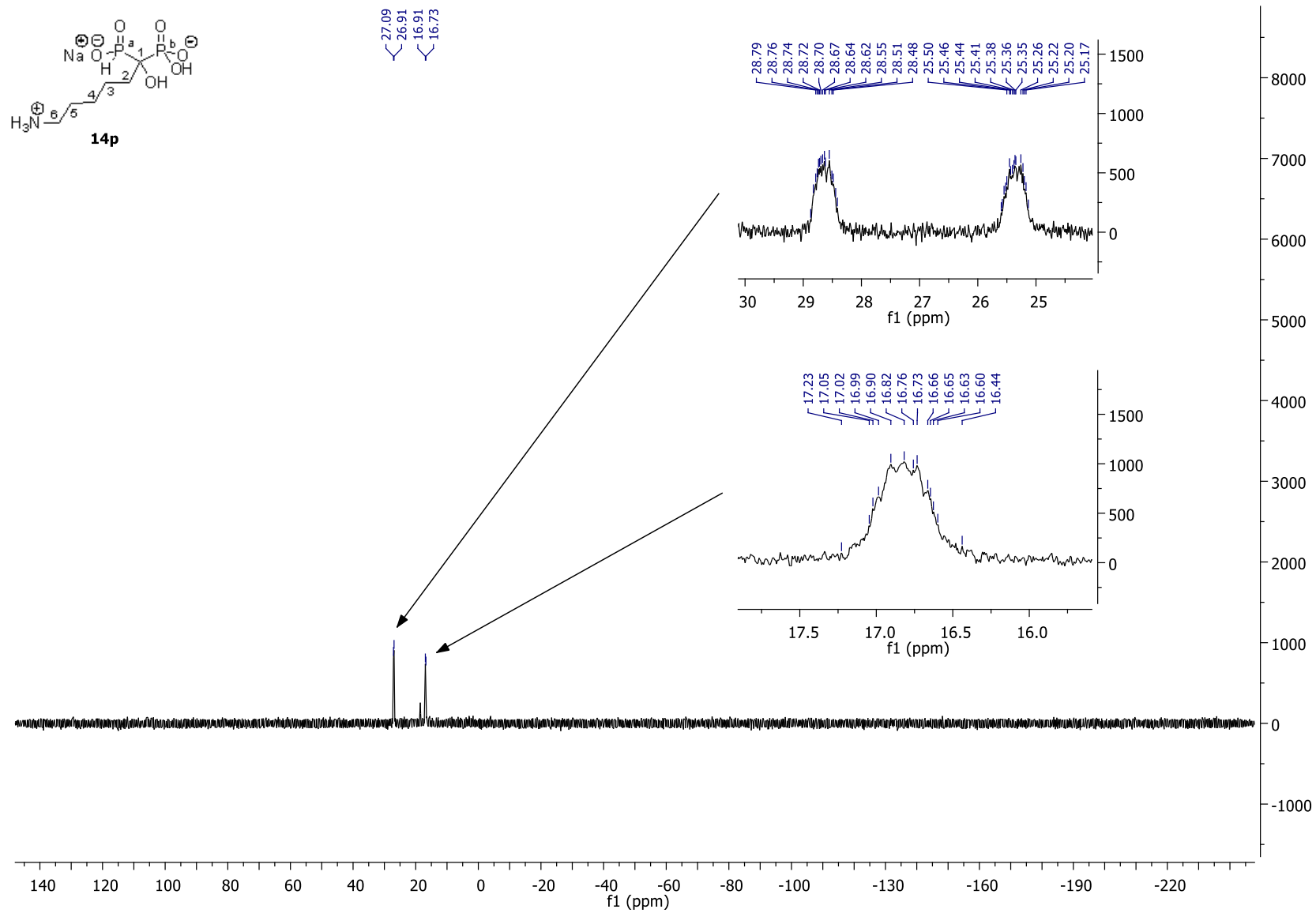


Figure S51:  $^{31}\text{P}\{^1\text{H}\}$  and  $^{31}\text{P}$  NMR (162 MHz,  $\text{D}_2\text{O}$ ) spectra of 1-hydroxy-1-(5-aminopentyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **14p**

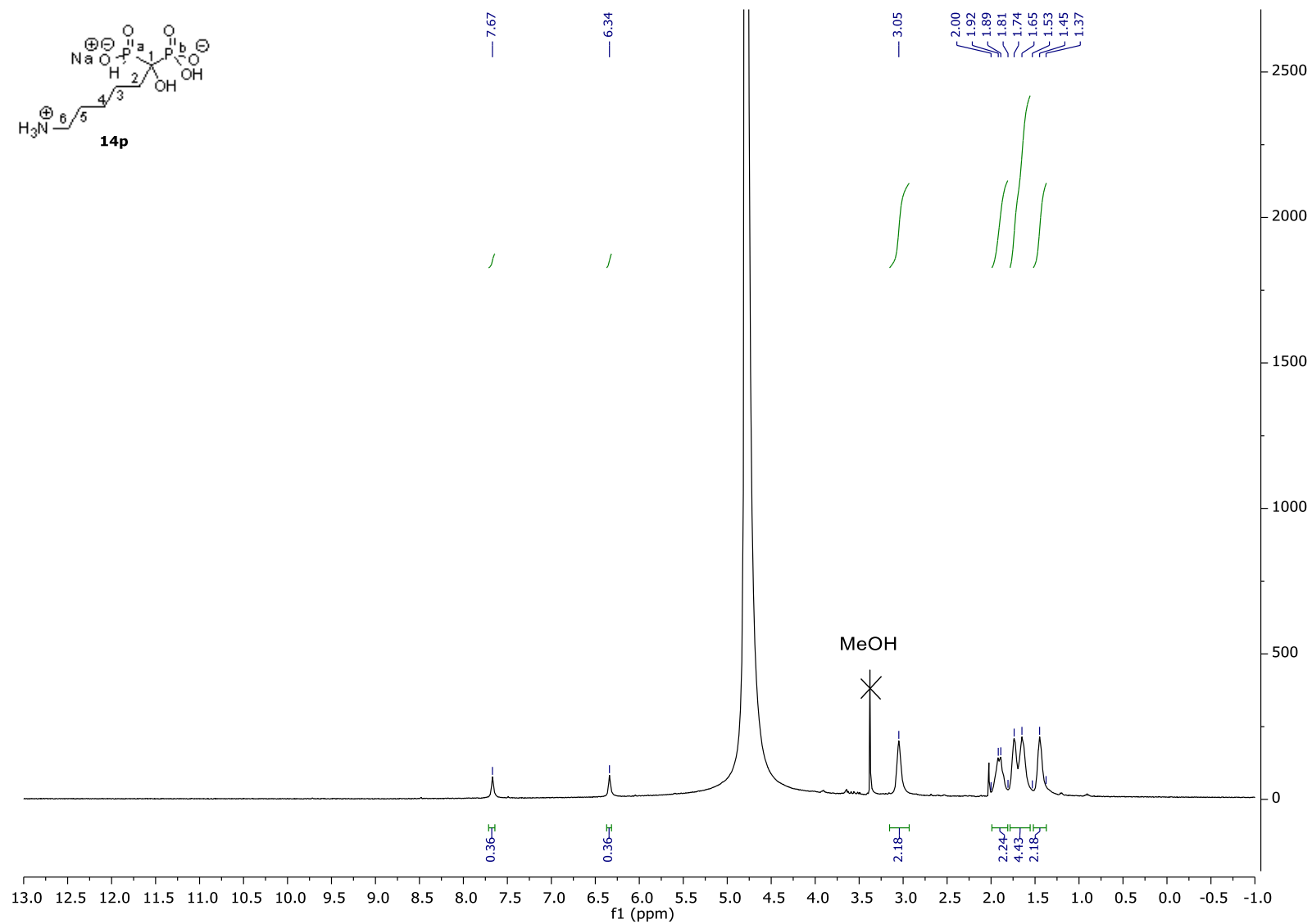


Figure S52:  $^1\text{H}$  NMR (400 MHz,  $\text{D}_2\text{O}$ ) spectrum of 1-hydroxy-1-(5-aminopentyl)methane-1,1-bis(*H*-phosphinylphosphonate) disodium salt **14p**

