

## Supporting Information

for

# **A new method for the synthesis of $\alpha$ -aminoalkylidene-bisphosphonates and their asymmetric phosphonyl-phosphinyl and phosphonyl-phosphinoyl analogues**

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## **Experimental and analytical data**

### **Table of contents**

1. Spectroscopic properties of all synthesized compounds **6–8**..... S2–S5
2. <sup>1</sup>H NMR, <sup>13</sup>C NMR and <sup>31</sup>P NMR spectra of selected bisphosphoric acid esters **8**.. S6–S17

**Diethyl 1-(*N*-acetylamino)-1-methoxymethylphosphonate (6a).** Pale yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.63 (br d,  $J = 6.8$  Hz, 1H), 5.44 (dd,  $J_1 = 8.4$ ,  $J_2 = 10.4$  Hz, 1H), 4.25-4.12 (m, 4H)<sup>a</sup>, 3.43 (s, 3H), 2.10 (s, 3H), 1.35 (t,  $J = 7.2$  Hz, 3H)<sup>b</sup>, 1.32 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup> ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  170.8, 76.1 (d,  $J = 199.6$  Hz), 63.8 (d,  $J = 6.7$  Hz)<sup>c</sup> and 63.1 (d,  $J = 6.8$  Hz)<sup>c</sup>, 57.4 (d,  $J = 14.4$  Hz), 23.2, 16.44 (d,  $J = 5.3$  Hz)<sup>b</sup> and 16.39 (d,  $J = 5.3$  Hz)<sup>b</sup> ppm;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  16.8 ppm; IR (ATR) 3257, 1690, 1235, 1020  $\text{cm}^{-1}$ . HRMS (TOF-ESI) calcd for  $\text{C}_8\text{H}_{18}\text{NO}_5\text{PNa}$  [ $\text{M} + \text{Na}$ ]<sup>+</sup> 262.0820, found 262.0825. <sup>a</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>b</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ). <sup>c</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ).

**Diethyl 1-(*N*-acetylamino)-1-methoxyethylphosphonate (6b).** Pale yellow oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.14 (br s, 1H), 4.29-4.06 (m, 4H)<sup>a</sup>, 3.38 (s, 3H), 2.05 (s, 3H), 1.93 (d,  $J = 15.2$  Hz, 3H), 1.36 (t,  $J = 7.2$  Hz, 3H)<sup>b</sup>, 1.35 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup> ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  170.6, 85.0 (d,  $J = 195.0$  Hz), 63.9 (d,  $J = 6.9$  Hz)<sup>c</sup> and 63.1 (d,  $J = 6.9$  Hz)<sup>c</sup>, 50.4 (d,  $J = 9.8$  Hz), 24.8, 18.2, 16.32 (d,  $J = 5.3$  Hz)<sup>b</sup> and 16.30 (d,  $J = 6.1$  Hz)<sup>b</sup> ppm;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  19.3 ppm; IR (ATR) 3277, 1679, 1239, 1162, 1018  $\text{cm}^{-1}$ . HRMS (TOF-ESI) calcd for  $\text{C}_9\text{H}_{20}\text{NO}_5\text{PNa}$  [ $\text{M} + \text{Na}$ ]<sup>+</sup> 276.0977, found 276.0973. <sup>a</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>b</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ). <sup>c</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ).

**Diethyl 1-(*N*-acetylamino)-1-triphenylphosphoniummethylphosphonate tetrafluoroborate (7a).** Pale yellow resin.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 (br d,  $J = 9.2$  Hz, 1H), 7.87-7.49 (m, 15H), 6.41 (ddd,  $J_1 = 9.6$ ,  $J_2 = 16.0$ ,  $J_3 = 21.6$  Hz, 1H), 4.33-4.07 (m, 4H)<sup>a</sup>, 1.91 (s, 3H), 1.31 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup>, 1.15 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup>, ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6 (d,  $J = 2.3$  Hz), 135.3 (d,  $J = 3.1$  Hz), 133.0 (d,  $J = 10.5$  Hz), 130.1 (d,  $J = 13.0$  Hz), 116.5 (d,  $J = 85.1$  Hz), 65.0 (d,  $J = 7.8$  Hz)<sup>c</sup> and 64.9 (d,  $J = 6.7$  Hz)<sup>c</sup>, 44.9 (dd,  $J_1 = 49.3$ ,  $J_2 = 151.0$  Hz), 21.9, 16.2 (d,  $J = 5.3$  Hz)<sup>b</sup> and 15.9 (d,  $J = 4.6$  Hz)<sup>b</sup> ppm;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  28.5 (d,  $J = 34.5$  Hz), 11.7 ( $J = 33.2$  Hz) ppm; IR (ATR) 3359, 1667, 1270, 1015  $\text{cm}^{-1}$ . HRMS (TOF-ESI) calcd for  $\text{C}_{25}\text{H}_{30}\text{NO}_4\text{P}_2$  [ $\text{M}$ ]<sup>+</sup> 470.1650, found 470.1647. <sup>a</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>b</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ). <sup>c</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ).

**Diethyl 1-(*N*-acetylamino)-1-triphenylphosphoniummethylphosphonate tetrafluoroborate (7b).** Pale yellow resin.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15-8.12 (br dd,  $J_1 = 3.6$ ,  $J_2 = 8.0$  Hz, 1H), 7.92-7.49 (m, 15H), 4.23-4.09 (m, 4H)<sup>a</sup>, 1.93 (dd,  $J_1 = 15.8$ ,  $J_2 = 19.0$  Hz, 3H), 1.72 (s, 3H), 1.40-1.26 (m, 6H)<sup>b</sup> ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  171.2, 135.2 (d,  $J = 10.0$  Hz), 134.3 (d,  $J = 3.0$  Hz), 129.4 (d,  $J = 13.0$  Hz), 120.3 (d,  $J = 84.2$  Hz), 65.2 (d,  $J = 7.6$  Hz)<sup>c</sup> and 65.1 (d,  $J = 8.3$  Hz)<sup>c</sup>, 58.2 (dd,  $J_1 = 42.4$ ,  $J_2 = 160.1$  Hz), 21.6, 16.4, 16.4 (d,  $J = 5.3$  Hz)<sup>d</sup> and 16.2 (d,  $J = 5.3$  Hz)<sup>d</sup> ppm;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  37.0 (d,  $J = 48.1$  Hz), 16.5 (d,  $J = 48.1$  Hz) ppm; IR (ATR) 3325, 1679, 1248, 1163, 1017  $\text{cm}^{-1}$ . HRMS (TOF-ESI) calcd for  $\text{C}_{26}\text{H}_{32}\text{NO}_4\text{P}_2$  [ $\text{M}$ ]<sup>+</sup> 484.1807, found 484.1807. <sup>a</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>b</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>c</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ). <sup>d</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ).

**Tetraethyl 1-(*N*-acetylamino)methylidenebisphosphonate (8a).** White crystals, mp 25°C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.30 (br d,  $J = 10.4$  Hz, 1H), 5.04 (ddd,  $J_1 = 10.4$ ,  $J_2 = 21.6$ ,  $J_3 = 21.9$  Hz, 1H), 4.25-4.14 (m, 8H)<sup>a</sup>, 2.08 (d,  $J = 0.9$  Hz, 3H), 1.34 (t,  $J = 7.0$  Hz, 6H)<sup>b</sup>, 1.33 (t,  $J = 7.0$  Hz, 6H)<sup>b</sup> ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  169.0 (t,  $J = 4.2$  Hz), 63.67 (d,  $J = 3.1$  Hz)<sup>c</sup> and 63.64 (d,  $J = 3.0$  Hz)<sup>c</sup> and 63.49 (d,  $J = 3.8$  Hz)<sup>c</sup> and 63.46 (d,  $J = 3.0$  Hz)<sup>c</sup>, 43.6 (t,  $J = 146.5$  Hz), 22.8, 16.36 (d,  $J = 3.0$  Hz)<sup>d</sup> and 16.33 (d,  $J = 3.1$  Hz)<sup>d</sup> and 16.30

(d,  $J = 3.0$  Hz)<sup>d</sup>, 16.27 (d,  $J = 3.0$  Hz)<sup>d</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>)  $\delta$  17.0 ppm; IR (ATR) 3252, 1663, 1242, 1014 cm<sup>-1</sup>. HRMS (TOF-ESI) calcd for C<sub>11</sub>H<sub>25</sub>NO<sub>7</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 368.1004, found 368.1001. <sup>a</sup>Overlapping signals of four diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>b</sup>Two diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>c</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>). <sup>d</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>).

**Tetraethyl 1-(*N*-acetylamino)ethylidenebisphosphonate (8b).** Colourless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.02 (br t,  $J = 5.0$  Hz, 1H), 4.28-4.18 (m, 8H)<sup>a</sup>, 2.01 (s, 3H), 1.98 (t,  $J = 16.8$  Hz, 3H), 1.36 (t,  $J = 7.2$  Hz, 12H) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.5 (t,  $J = 5.3$  Hz), 63.76 (d,  $J = 3.1$  Hz)<sup>b</sup> and 63.73 (d,  $J = 3.7$  Hz)<sup>b</sup>, 56.8 (t,  $J = 146.0$  Hz), 24.6, 17.0 (t,  $J = 4.5$  Hz), 16.42 (d,  $J = 2.3$  Hz)<sup>c</sup> and 16.39 (d,  $J = 3.0$  Hz)<sup>c</sup> and 16.36 (d,  $J = 2.3$  Hz)<sup>c</sup> and 16.34 (d,  $J = 3.0$  Hz)<sup>c</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>)  $\delta$  20.5 ppm; IR (ATR) 3273, 1690, 1238, 1019 cm<sup>-1</sup>. HRMS (TOF-ESI) calcd for C<sub>12</sub>H<sub>27</sub>NO<sub>7</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 382.1160, found 382.1163. <sup>a</sup>Overlapping signals of four diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>b</sup>Diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>c</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>).

**Diethyl 1-(*N*-acetylamino)-1-[ethoxy(methylphosphinyl)methylphosphonate (8c)<sup>a</sup>.** Colourless oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  6.84 (br s, 1H)<sup>b</sup>, 6.50 (br d,  $J = 9.6$  Hz, 1H)<sup>b</sup>, 4.97 (ddd,  $J_1 = 10.2$ ,  $J_2 = 16.2$ ,  $J_3 = 26.4$  Hz, 1H)<sup>b</sup>, 4.95 (ddd,  $J_1 = 10.2$ ,  $J_2 = 14.4$ ,  $J_3 = 24.6$  Hz, 1H)<sup>b</sup>, 4.26-4.05 (m, 6H)<sup>c</sup>, 2.10 (s, 3H)<sup>b</sup> and 2.09 (s, 3H)<sup>b</sup>, 1.71 (d,  $J = 14.4$  Hz, 3H)<sup>b</sup>, 1.59 (d,  $J = 14.4$  Hz, 3H)<sup>b</sup>, 1.36-1.29 (m, 9H)<sup>d</sup> ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  169.5 (dd,  $J_1 = 3.0$ ,  $J_2 = 4.5$  Hz)<sup>b</sup>, 169.2 (dd,  $J_1 = 3.1$ ,  $J_2 = 3.8$  Hz)<sup>b</sup>, (63.71, 63.65, 63.62, 63.55, 63.48, 62.15, 62.08, 61.95, 61.88)<sup>e</sup>, 46.5 (dd,  $J_1 = 86.1$ ,  $J_2 = 143.4$  Hz)<sup>b</sup>, 46.0 (dd,  $J_1 = 85.2$ ,  $J_2 = 143.5$  Hz)<sup>b</sup>, 22.87<sup>b</sup>, 22.79<sup>b</sup>, (16.63, 16.58, 16.49, 16.43, 16.38, 16.37, 16.32, 16.28, 16.26, 16.22)<sup>f</sup>, 14.6 (d,  $J = 97.1$  Hz)<sup>b</sup>, 13.6 (dd,  $J_1 = 3.1$ ,  $J_2 = 100.1$  Hz)<sup>b</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>)  $\delta$  46.1 (d,  $J = 20.9$  Hz), 45.2 (d,  $J = 30.8$  Hz), 17.5 (d,  $J = 21.1$  Hz), 17.4 (d,  $J = 30.8$  Hz) ppm; IR (ATR) 3200, 1672, 1215, 1023 cm<sup>-1</sup>. HRMS (TOF-ESI) calcd for C<sub>10</sub>H<sub>23</sub>NO<sub>6</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 338.0898, found 338.0917. <sup>a</sup>The mixture of two diastereomers in the ratio of 1:1. <sup>b</sup>Separate signals of one diastereomer. <sup>c</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>d</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>e</sup>Partly overlapping doublets of two diastereotopic and one heterotopic Et groups of two diastereomers (OCH<sub>2</sub>CH<sub>3</sub>). <sup>f</sup>Partly overlapping signals of two diastereotopic and one heterotopic Et groups of two diastereomers (OCH<sub>2</sub>CH<sub>3</sub>).

**Diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)methylphosphonate (8d)<sup>a</sup>.** Colourless oil. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.87-7.81 (m, 2H)<sup>b</sup>, 7.60-7.56 (m, 1H)<sup>b</sup>, 7.51-7.46 (m, 2H)<sup>b</sup>, 6.32 (br d,  $J = 9.6$  Hz, 1H)<sup>c,d</sup>, 6.13 (br d,  $J = 10.2$  Hz, 1H)<sup>c,e</sup>, 5.144 (ddd,  $J_1 = 10.2$ ,  $J_2 = 18.0$ ,  $J_3 = 36.6$  Hz, 1H)<sup>c,e</sup>, 5.143 (ddd,  $J_1 = 5.7$ ,  $J_2 = 10.8$ ,  $J_3 = 17.4$  Hz, 1H)<sup>c,d</sup>, 4.28-4.01 (m, 6H)<sup>b,f</sup>, 2.02 (s, 3H)<sup>c,d</sup> and 1.81 (s, 3H)<sup>c,e</sup>, 1.37-1.31 (m, 6H)<sup>b,g</sup>, 1.24 (t,  $J = 7.1$  Hz, 3H)<sup>c,d,h</sup>, 1.22 (t,  $J = 7.0$  Hz, 3H)<sup>c,e,h</sup> ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  168.9 (dd,  $J_1 = 3.8$ ,  $J_2 = 3.8$  Hz)<sup>c,d</sup>, 168.6 (dd,  $J_1 = 3.8$ ,  $J_2 = 3.8$  Hz)<sup>c,e</sup>, [133.0 (d,  $J = 3.0$  Hz), 132.4 (d,  $J = 9.8$  Hz), 128.9 (dd,  $J_1 = 1.5$ ,  $J_2 = 132.8$  Hz), 128.44 (d,  $J = 16.0$  Hz)]<sup>d,i</sup> and [132.9 (d,  $J = 2.3$  Hz), 132.2 (d,  $J = 9.8$  Hz), 128.7 (dd,  $J_1 = 4.9$ ,  $J_2 = 134.7$  Hz), 128.44 (d,  $J = 11.4$  Hz)]<sup>e,i</sup>, (63.4, 63.35, 63.3, 63.2, 62.6, 62.5, 62.1, 62.0)<sup>j</sup>, 46.9 (dd,  $J_1 = 95.6$ ,  $J_2 = 146.5$  Hz)<sup>c,d</sup>, 46.0 (dd,  $J_1 = 100.9$ ,  $J_2 = 143.4$  Hz)<sup>c,e</sup>, 22.84<sup>c,d</sup>, 22.54<sup>c,e</sup>, (16.54, 16.48, 16.46, 16.40, 16.35, 16.30, 16.25, 16.21, 16.15)<sup>k</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>)  $\delta$  34.8 (d,  $J = 16.0$  Hz), 33.6 (d,  $J = 28.4$  Hz), 17.4 (d,  $J = 16.0$  Hz), 16.9 (d,  $J = 29.5$  Hz) ppm; IR (ATR) 3447, 2984, 1667, 1225, 1022 cm<sup>-1</sup>. HRMS (TOF-ESI) calcd for C<sub>15</sub>H<sub>25</sub>NO<sub>6</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 400.1055, found 400.1059. <sup>a</sup>The mixture of two diastereomers in the ratio of 1:1.4. <sup>b</sup>Overlapping signals of two diastereomers. <sup>c</sup>Separate signal of one diastereomer. <sup>d</sup>Minor

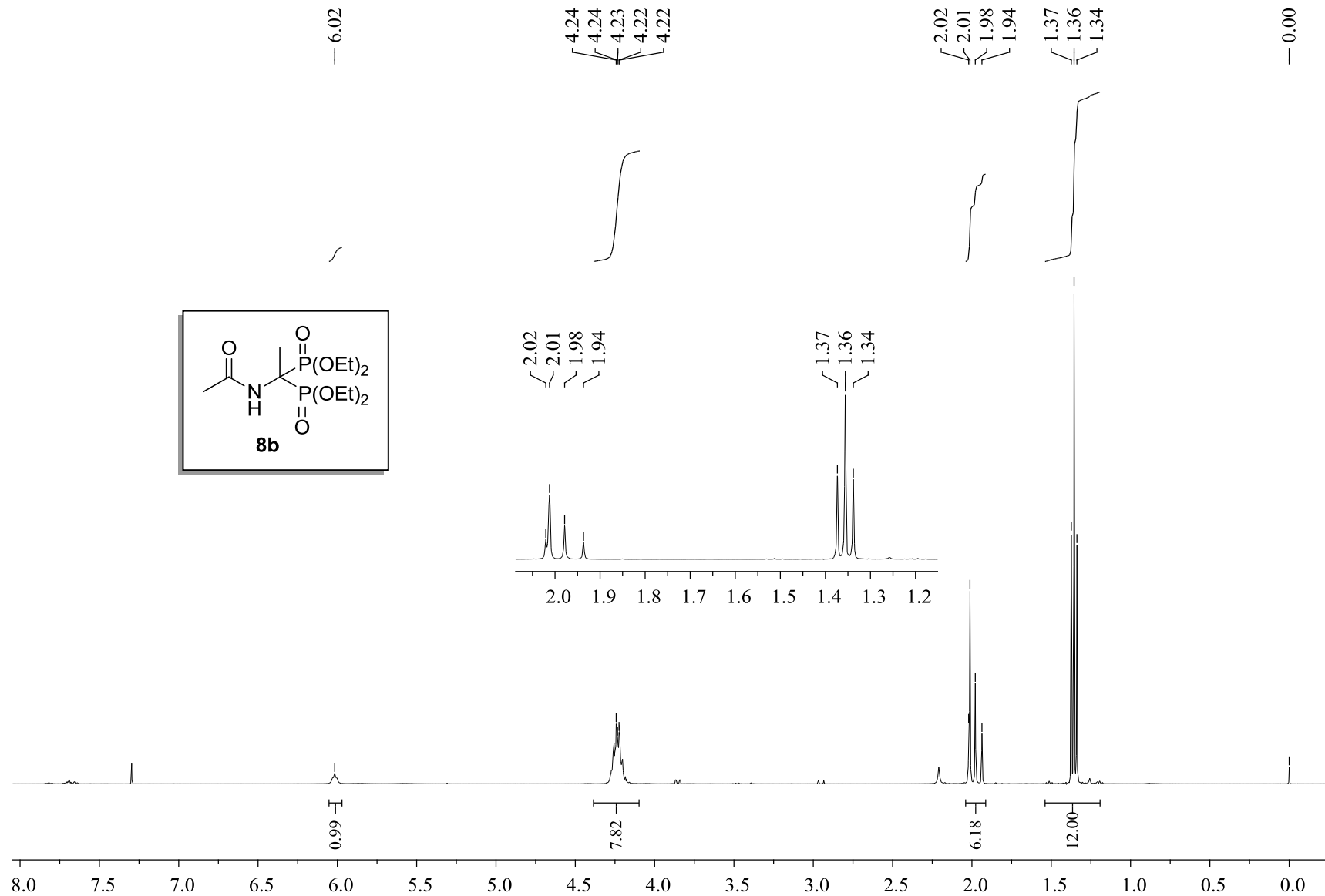
diastereomer. <sup>e</sup>Major diastereomer. <sup>f</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>g</sup>Overlapping signals of two diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>h</sup>Heterotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>). <sup>i</sup>Separate signal of PhP=O group of one diastereomer. <sup>j</sup>Partly overlapping doublets of two diastereotopic and one heterotopic Et groups of two diastereomers (OCH<sub>2</sub>CH<sub>3</sub>). <sup>k</sup>Partly overlapping signals of two diastereotopic and one heterotopic Et groups of two diastereomers (OCH<sub>2</sub>CH<sub>3</sub>).

**Diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (8e).** Major diastereomer. Colourless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.87-7.81 (m, 2H), 7.60-7.46 (m, 3H), 6.19 (br s, 1H), 4.31-4.10 (m, 6H)<sup>a</sup>, 1.91 (s, 3H), 1.89 (dd, *J*<sub>1</sub> = 16.4, *J*<sub>2</sub> = 16.8 Hz, 3H), 1.40-1.30 (m, 9H)<sup>b</sup> ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.6 (dd, *J*<sub>1</sub> = 4.5, *J*<sub>2</sub> = 5.3 Hz), 133.3 (d, *J* = 9.1 Hz), 132.9 (d, *J* = 3.1 Hz), 128.2 (d, *J* = 12.1 Hz), 128.0 (dd, *J*<sub>1</sub> = 3.4, *J*<sub>2</sub> = 131.7 Hz), [63.7 (d, *J* = 7.6 Hz), 63.5 (d, *J* = 7.6 Hz) and 62.7 (d, *J* = 6.8 Hz)]<sup>c</sup>, 58.5 (dd, *J*<sub>1</sub> = 97.6, *J*<sub>2</sub> = 144.6 Hz), 24.6, (17.15, 17.13, 17.10, 17.09)<sup>d</sup>, 16.45 (d, *J* = 6.0 Hz)<sup>e</sup> and 16.37 (d, *J* = 5.3 Hz)<sup>e</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 39.4 (d, *J* = 16.0 Hz), 20.8 (d, *J* = 15.9 Hz) ppm; IR (ATR) 3277, 1558, 1184, 1023 cm<sup>-1</sup>. HRMS (TOF-ESI)<sup>f</sup> calcd for C<sub>16</sub>H<sub>27</sub>NO<sub>6</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 414.1211, found 414.1208. <sup>a</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>b</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>c</sup>Signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>d</sup>Overlapping signals of the Me group at C<sub>α</sub> position and heterotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>). <sup>e</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>). <sup>f</sup>MS spectrum was performed for the mixture of diastereomers.

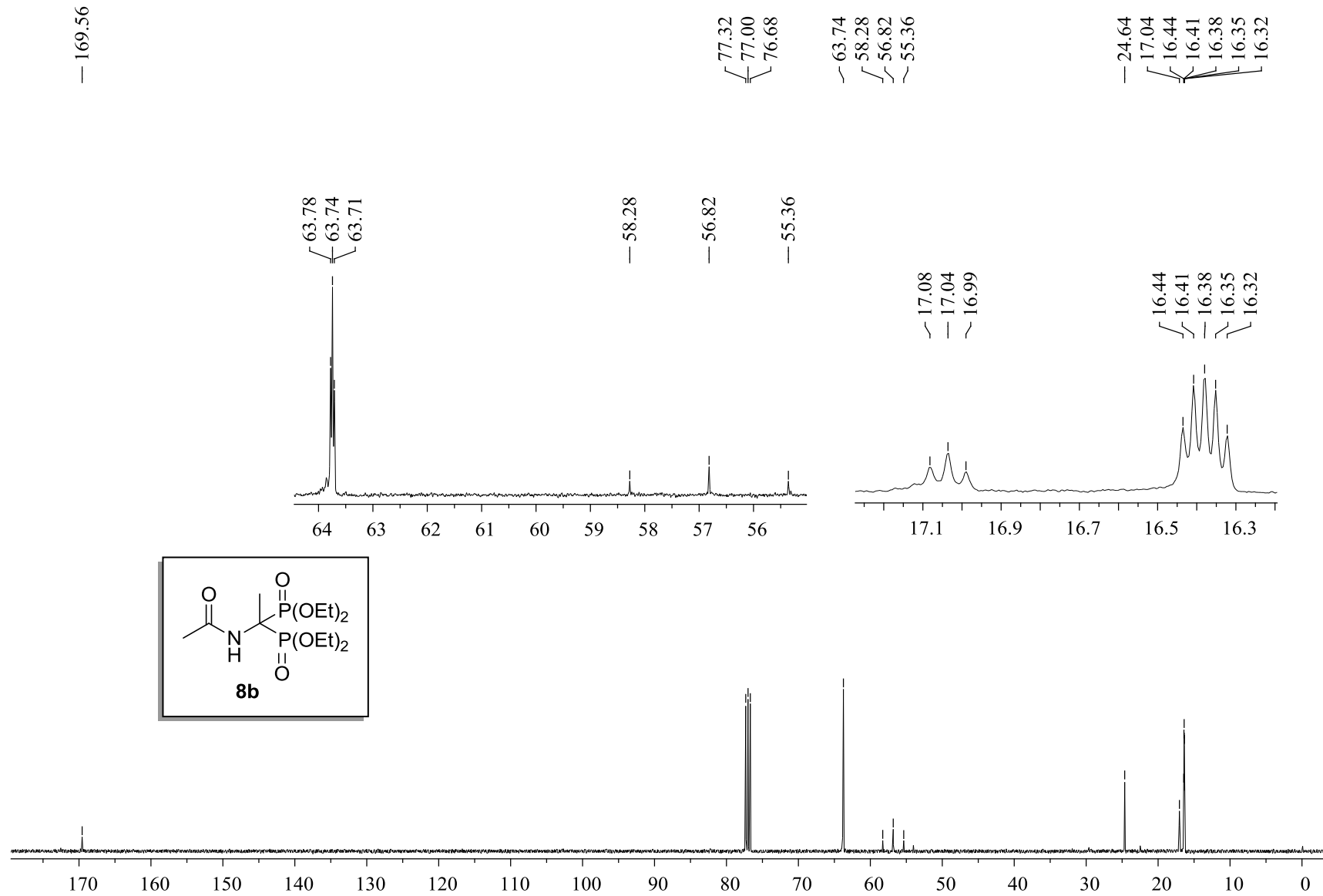
**Diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (8e).** Minor diastereomer. Colourless oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.88-7.83 (m, 2H), 7.62-7.48 (m, 3H), 6.36 (br s, 1H), 4.29-4.05 (m, 6H)<sup>a</sup>, 2.02 (s, 3H), 1.93 (dd, *J*<sub>1</sub> = 16.8, *J*<sub>2</sub> = 17.2 Hz, 3H), [1.37 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) and 1.23 (t, *J* = 7.0 Hz, 3H)]<sup>b</sup> ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.0, 133.5 (d, *J* = 9.1 Hz), 133.0 (d, *J* = 2.2 Hz), 128.2 (d, *J* = 12.9 Hz), 127.7 (d, *J* = 131.3 Hz), [63.8 (d, *J* = 7.5 Hz), 63.5 (d, *J* = 7.6 Hz) and 62.6 (d, *J* = 6.8 Hz)]<sup>c</sup>, 58.7 (dd, *J*<sub>1</sub> = 94.1, *J*<sub>2</sub> = 146.4 Hz), 24.8, 16.9 (d, *J* = 3.2 Hz), [16.49 (d, *J* = 6.0 Hz), 16.43 (d, *J* = 6.1 Hz) and 16.22 (d, *J* = 6.1 Hz)]<sup>b</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 38.2 (d, *J* = 27.5 Hz), 20.1 (d, *J* = 27.5 Hz) ppm; IR (ATR) 3268, 1689, 1227, 1019 cm<sup>-1</sup>. <sup>a</sup>Overlapping signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>b</sup>Signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>c</sup>Signals of two diastereotopic and one heterotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>).

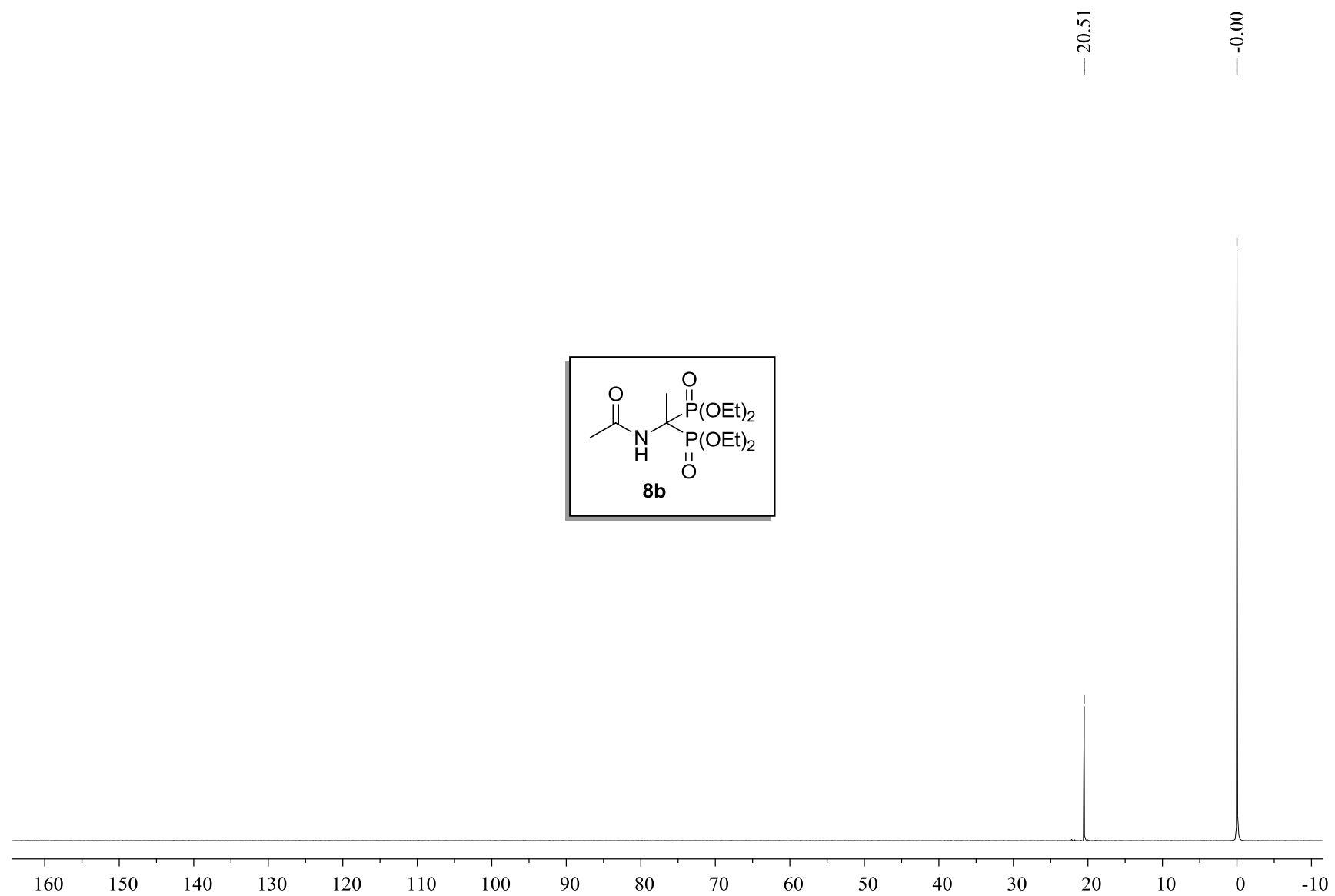
**Diethyl 1-(*N*-acetylamino)-1-(diphenylphosphinoyl)methylphosphonate (8f).** White resin. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 7.92-7.88 (m, 2H), 7.84-7.81 (m, 2H), 7.55-7.43 (m, 6H), 6.71 (br d, *J* = 9.6 Hz, 1H), 5.62 (ddd, *J*<sub>1</sub> = 9.6, *J*<sub>2</sub> = 10.2, *J*<sub>3</sub> = 21.6 Hz, 1H), 4.13-3.93 (m, 4H)<sup>a</sup>, 1.85 (s, 3H), 1.23 (dt, *J*<sub>1</sub> = 0.6, *J*<sub>2</sub> = 7.5 Hz, 3H)<sup>b</sup> and 1.12 (t, *J* = 7.2 Hz, 3H)<sup>b</sup> ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 169.4 (dd, *J*<sub>1</sub> = 3.1, *J*<sub>2</sub> = 3.8 Hz), [132.2 (d, *J* = 3.0 Hz), 132.1 (d, *J* = 3.0 Hz), 131.4 (d, *J* = 9.8 Hz), 131.0 (d, *J* = 9.9 Hz), 130.71 (dd, *J*<sub>1</sub> = 7.6, *J*<sub>2</sub> = 133.9 Hz), 130.68 (d, *J* = 100.2 Hz), 128.5 (d, *J* = 12.2 Hz) and 128.4 (d, *J* = 12.2 Hz)]<sup>c</sup>, 63.3 (d, *J* = 6.8 Hz)<sup>d</sup>, 62.9 (d, *J* = 6.1 Hz)<sup>d</sup>, 46.4 (dd, *J*<sub>1</sub> = 66.4, *J*<sub>2</sub> = 146.1 Hz), 22.4, 16.2 (d, *J* = 6.0 Hz)<sup>b</sup> and 15.9 (d, *J* = 6.1 Hz)<sup>b</sup> ppm; <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>) δ 30.6 (d, *J* = 16.0 Hz), 17.3 (d, *J* = 16.0 Hz) ppm; IR (ATR) 3229, 2988, 1668, 1258, 1187, 1019 cm<sup>-1</sup>. HRMS (TOF-ESI) calcd for C<sub>19</sub>H<sub>25</sub>NO<sub>5</sub>P<sub>2</sub>Na [M + Na]<sup>+</sup> 410.1286, found 410.1285. <sup>a</sup>Overlapping signals of two diastereotopic Et groups (OCH<sub>2</sub>CH<sub>3</sub>). <sup>b</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>). <sup>c</sup>Signals of two diastereotopic Ph groups. <sup>d</sup>Diastereotopic Et group (OCH<sub>2</sub>CH<sub>3</sub>).

**Diethyl 1-(*N*-acetylamino)-1-(diphenylphosphinoyl)ethylphosphonate (8g).** Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.10-7.97 (m, 4H) and 7.58-7.48 (m, 6H), 6.80 (br s, 1H), 4.18-3.96 (m, 4H)<sup>a</sup>, 1.98 (dd,  $J_1 = 16.4$ ,  $J_2 = 16.8$  Hz, 3H), 1.96 (s, 3H), 1.21 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup> and 1.18 (t,  $J = 7.0$  Hz, 3H)<sup>b</sup> ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  170.0, [132.9 (d,  $J = 9.2$  Hz), 132.7 (d,  $J = 9.2$  Hz), 132.41 (d,  $J = 3.0$  Hz), 132.39 (d,  $J = 1.5$  Hz), 129.1 (d,  $J = 97.9$  Hz), 128.6 (d,  $J = 81.2$  Hz), 128.4 (d,  $J = 12.3$  Hz), 128.2 (d,  $J = 12.2$  Hz)]<sup>c</sup>, 63.5 (d,  $J = 6.8$  Hz), 59.4 (dd,  $J_1 = 63.3$ ,  $J_2 = 147.6$  Hz), 24.7, 18.2 (d,  $J = 1.5$  Hz), 16.3 (d,  $J = 5.5$  Hz)<sup>b</sup> and 16.2 (d,  $J = 6.0$  Hz)<sup>b</sup> ppm;  $^{31}\text{P}$  NMR (162 MHz,  $\text{CDCl}_3$ )  $\delta$  35.3 (d,  $J = 18.5$  Hz), 20.8 (d,  $J = 18.5$  Hz) ppm; IR (ATR) 3429, 1690, 1237, 1181, 1020  $\text{cm}^{-1}$ . HRMS (TOF-ESI) calcd for  $\text{C}_{20}\text{H}_{27}\text{NO}_5\text{P}_2\text{Na}$   $[\text{M} + \text{Na}]^+$  446.1262, found 446.1254. <sup>a</sup>Overlapping signals of two diastereotopic Et groups ( $\text{OCH}_2\text{CH}_3$ ). <sup>b</sup>Diastereotopic Et group ( $\text{OCH}_2\text{CH}_3$ ). <sup>c</sup>Signals of two diastereotopic Ph groups.



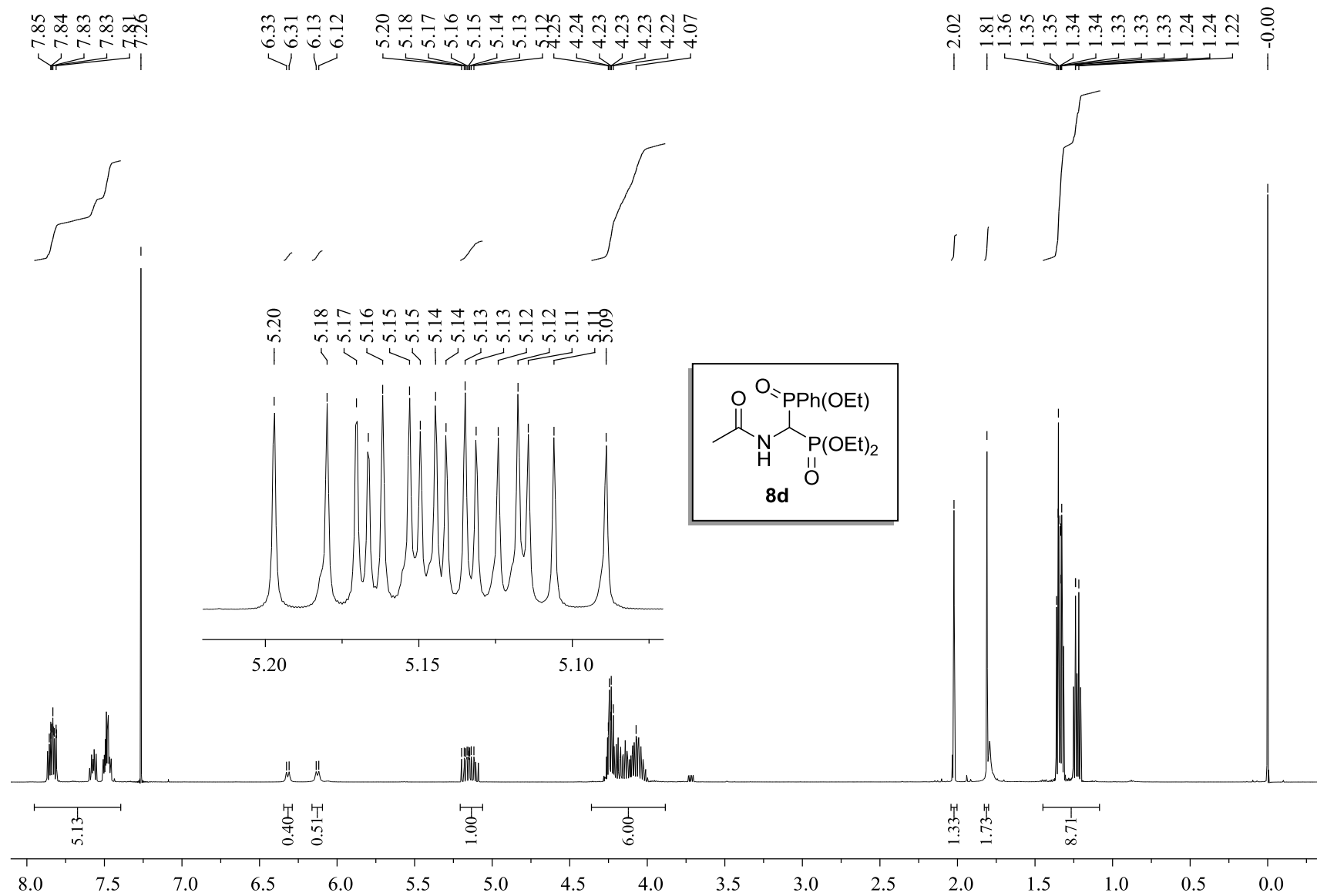
$^1\text{H}$  NMR spectrum of tetraethyl 1-(*N*-acetylamino)ethylidenebisphosphonate (**8b**); 400 MHz/ $\text{CDCl}_3$ /TMS;  $\delta$  (ppm).



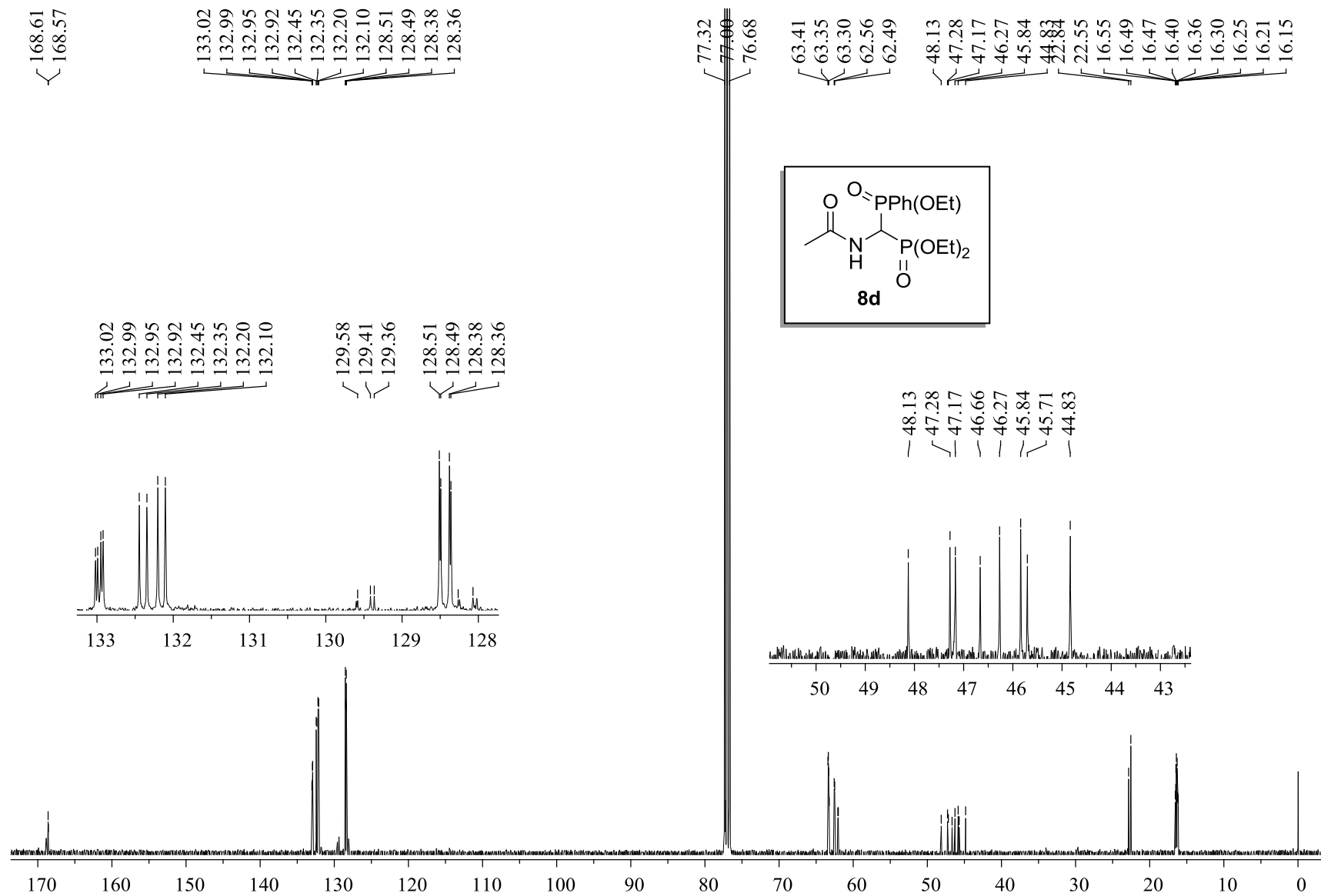


$^{31}\text{P}$  NMR spectrum of tetraethyl 1-(*N*-acetylamino)ethylidenebisphosphonate (**8b**); 162 MHz/ $\text{CDCl}_3/\text{H}_3\text{PO}_4$  (80%);  $\delta$  (ppm).

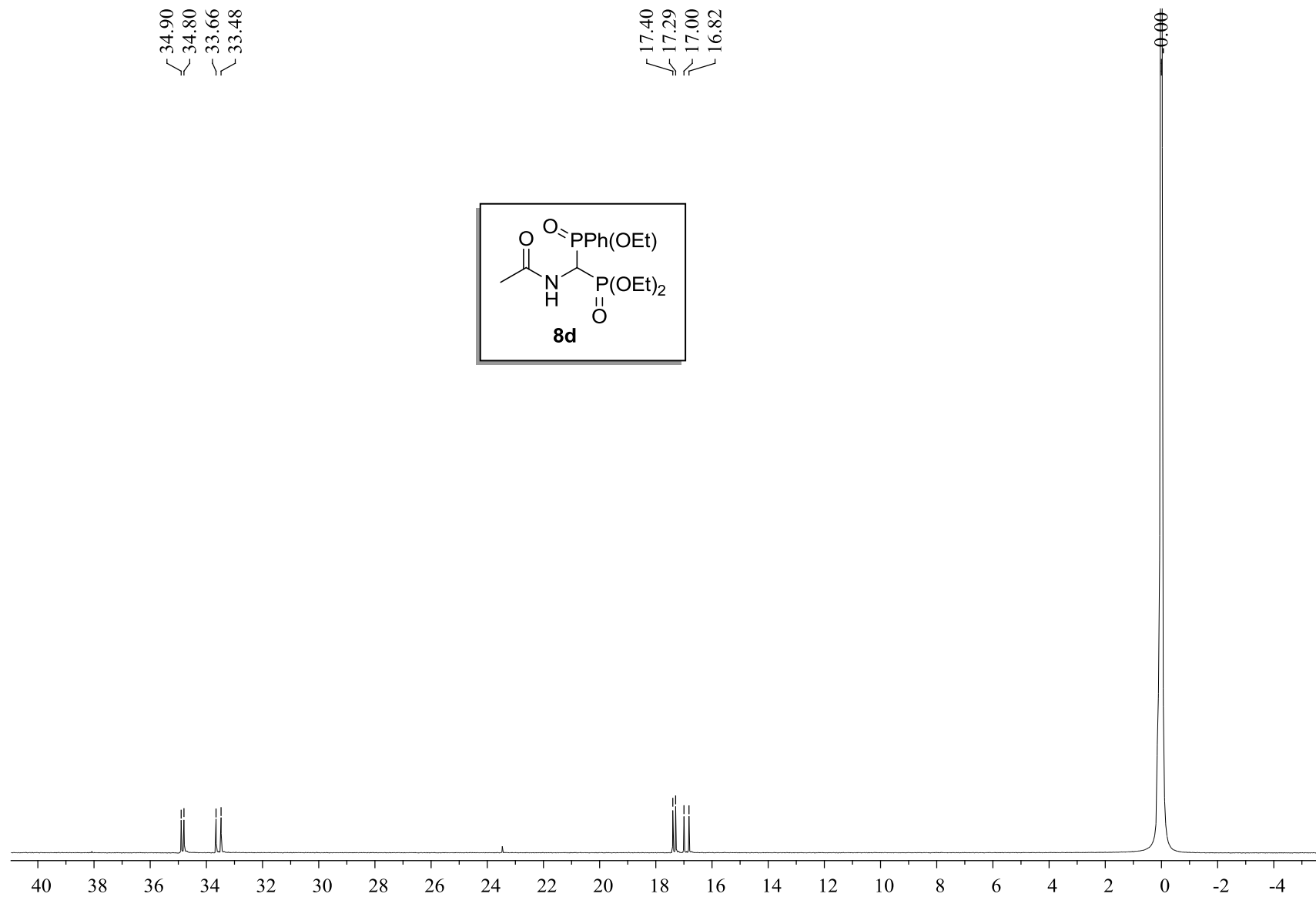




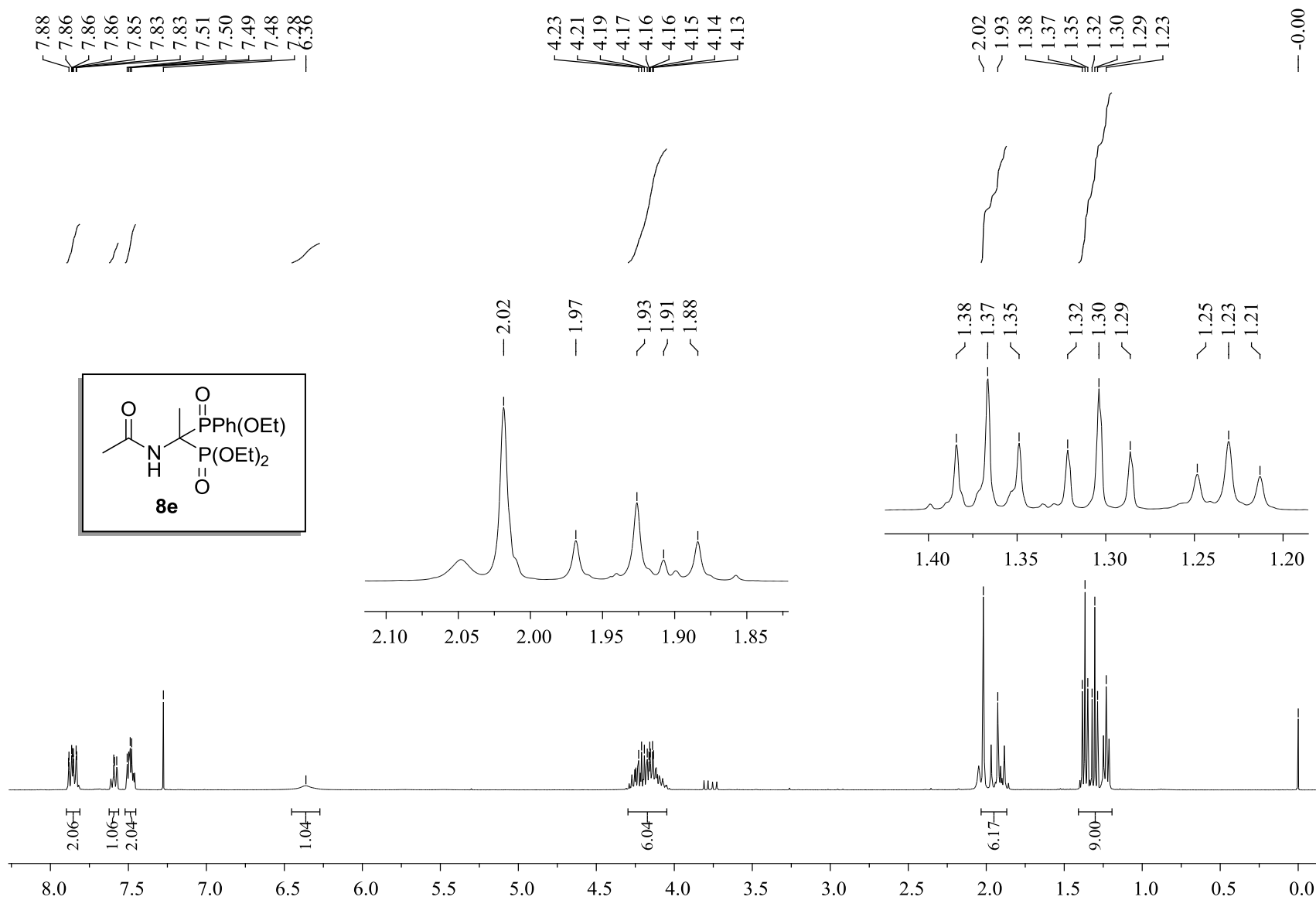
<sup>1</sup>H NMR spectrum of the mixture of diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphiny)]methylphosphonate (**8d**); 600 MHz/CDCl<sub>3</sub>/TMS; δ (ppm).



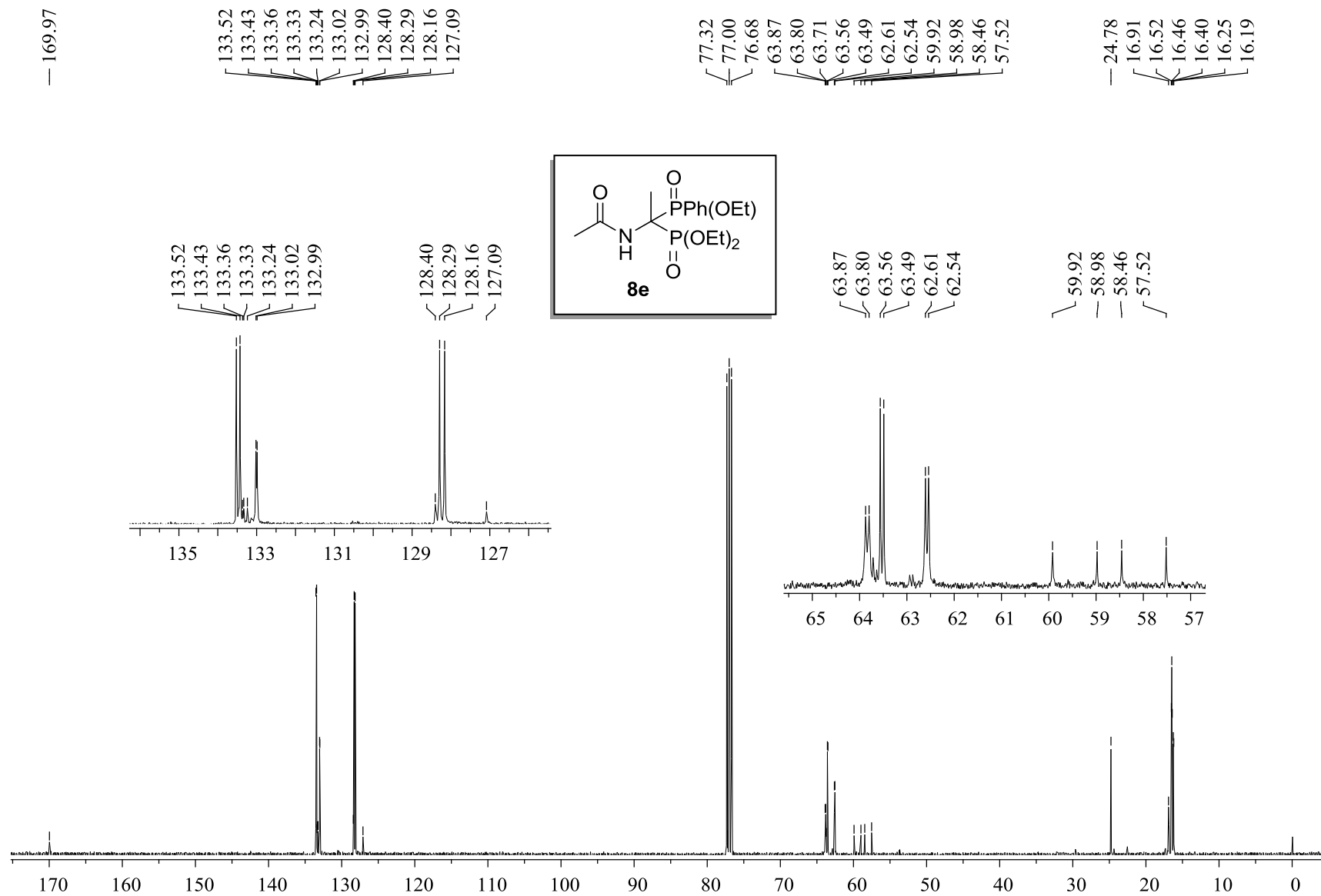
<sup>13</sup>C NMR spectrum of the mixture of diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]methylphosphonate (**8d**); 100 MHz/<sup>13</sup>CDCl<sub>3</sub>/TMS; δ (ppm).



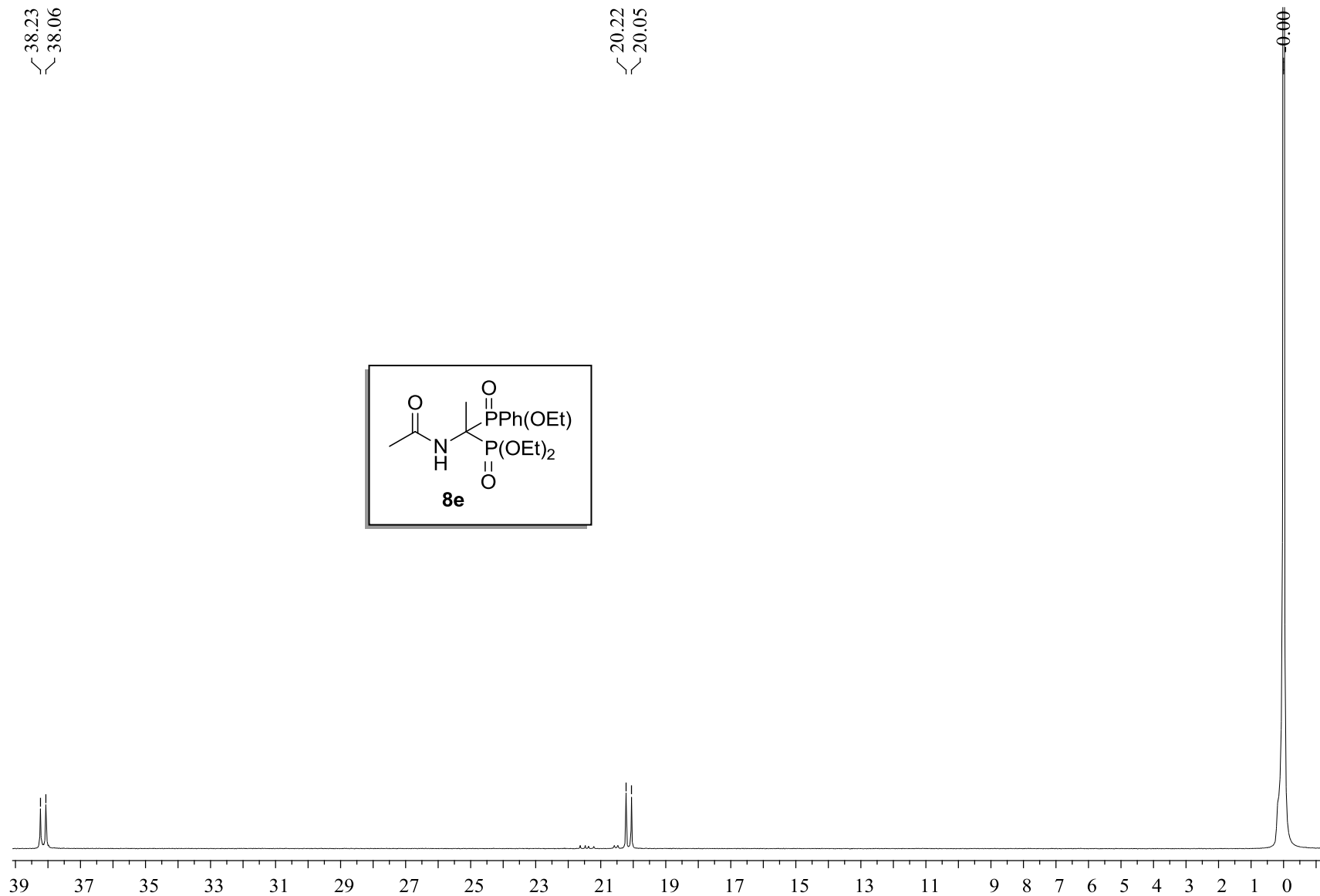
$^{31}\text{P}$  NMR spectrum of the mixture of diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]methylphosphonate (**8d**); 162 MHz/ $\text{CDCl}_3$ ;  $\delta$  (ppm).



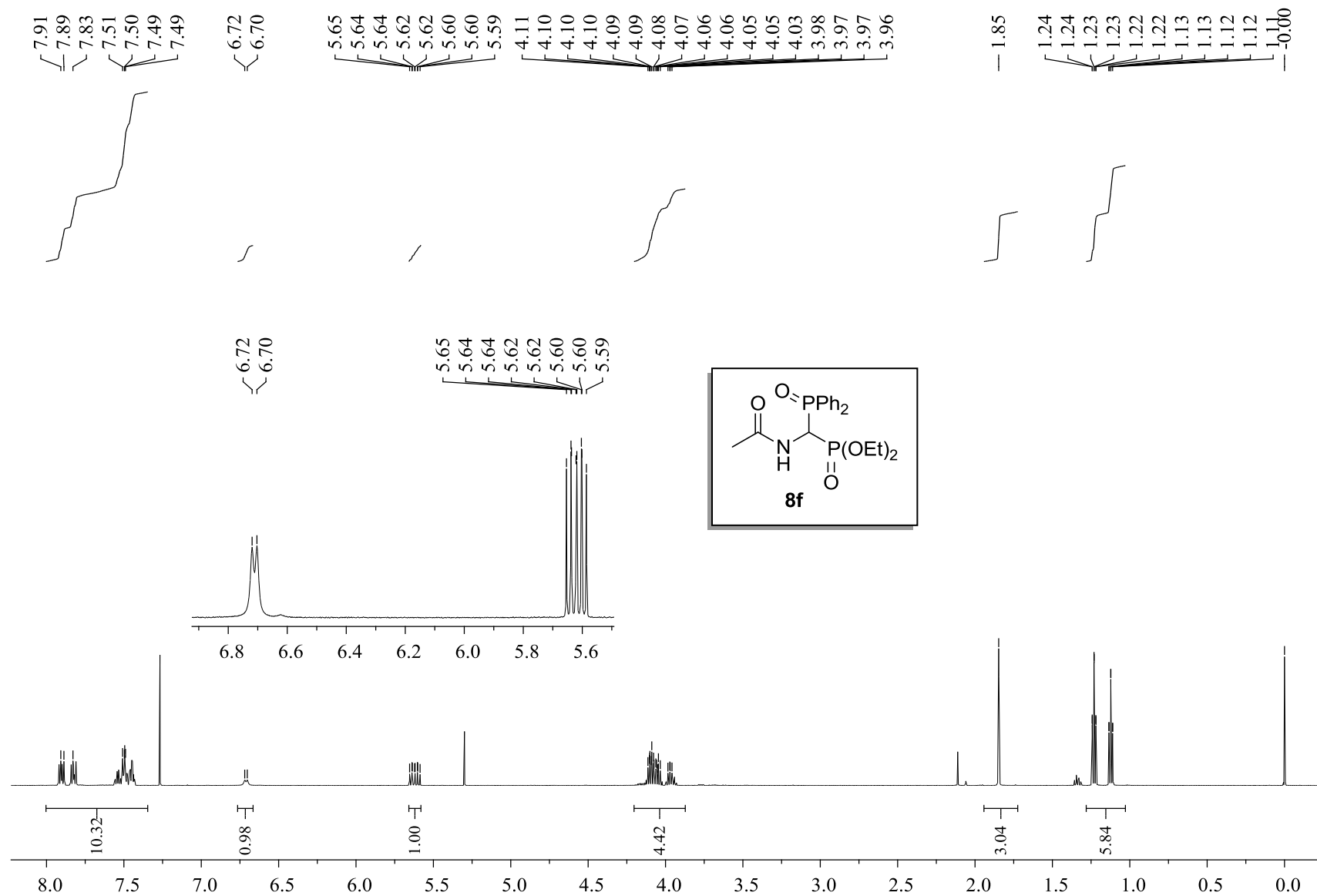
<sup>1</sup>H NMR spectrum of one of the diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (**8e**); 400 MHz/CDCl<sub>3</sub>/TMS; δ (ppm).



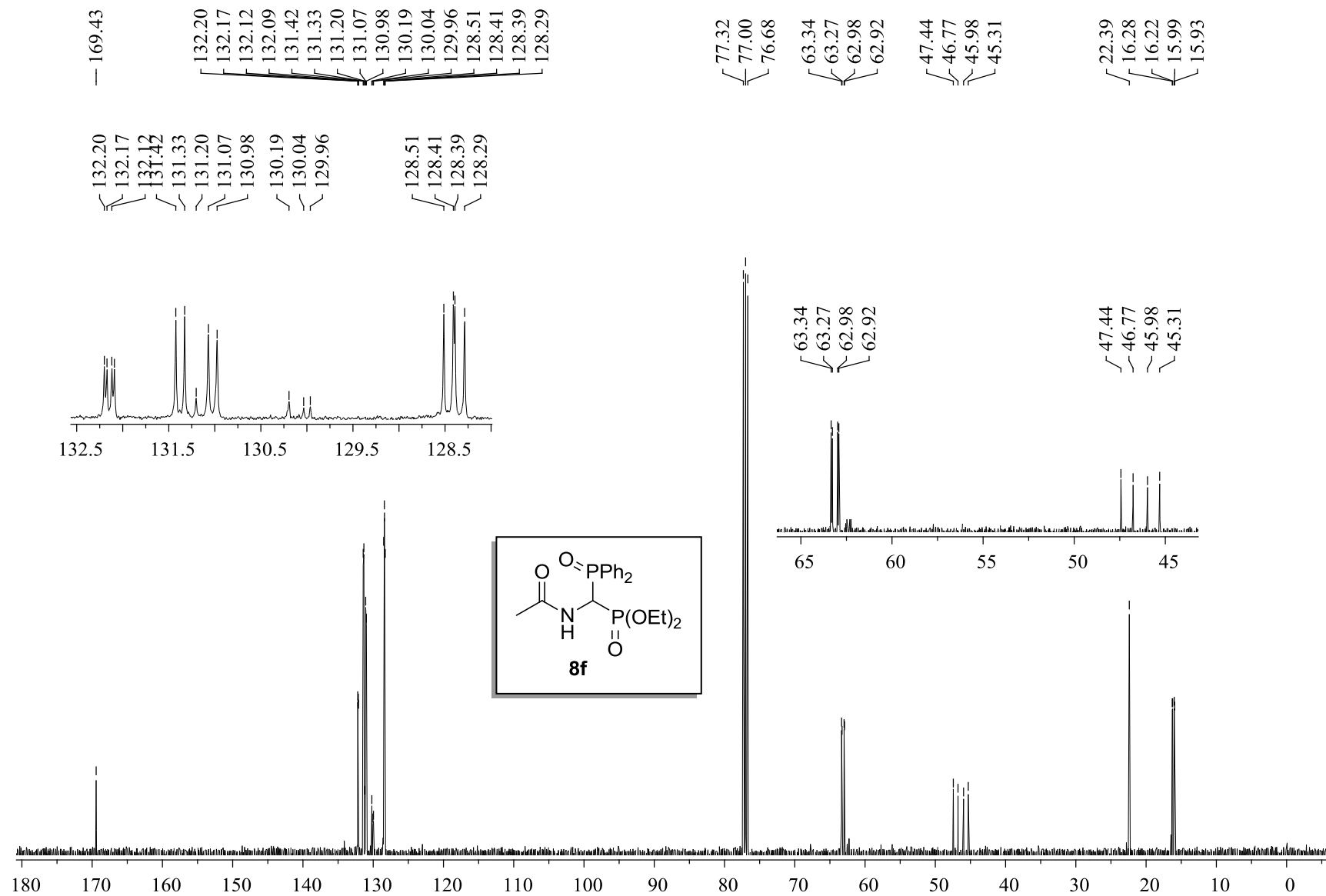
<sup>13</sup>C NMR spectrum of one of the diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (**8e**); 100 MHz/CDCl<sub>3</sub>/TMS; δ (ppm).



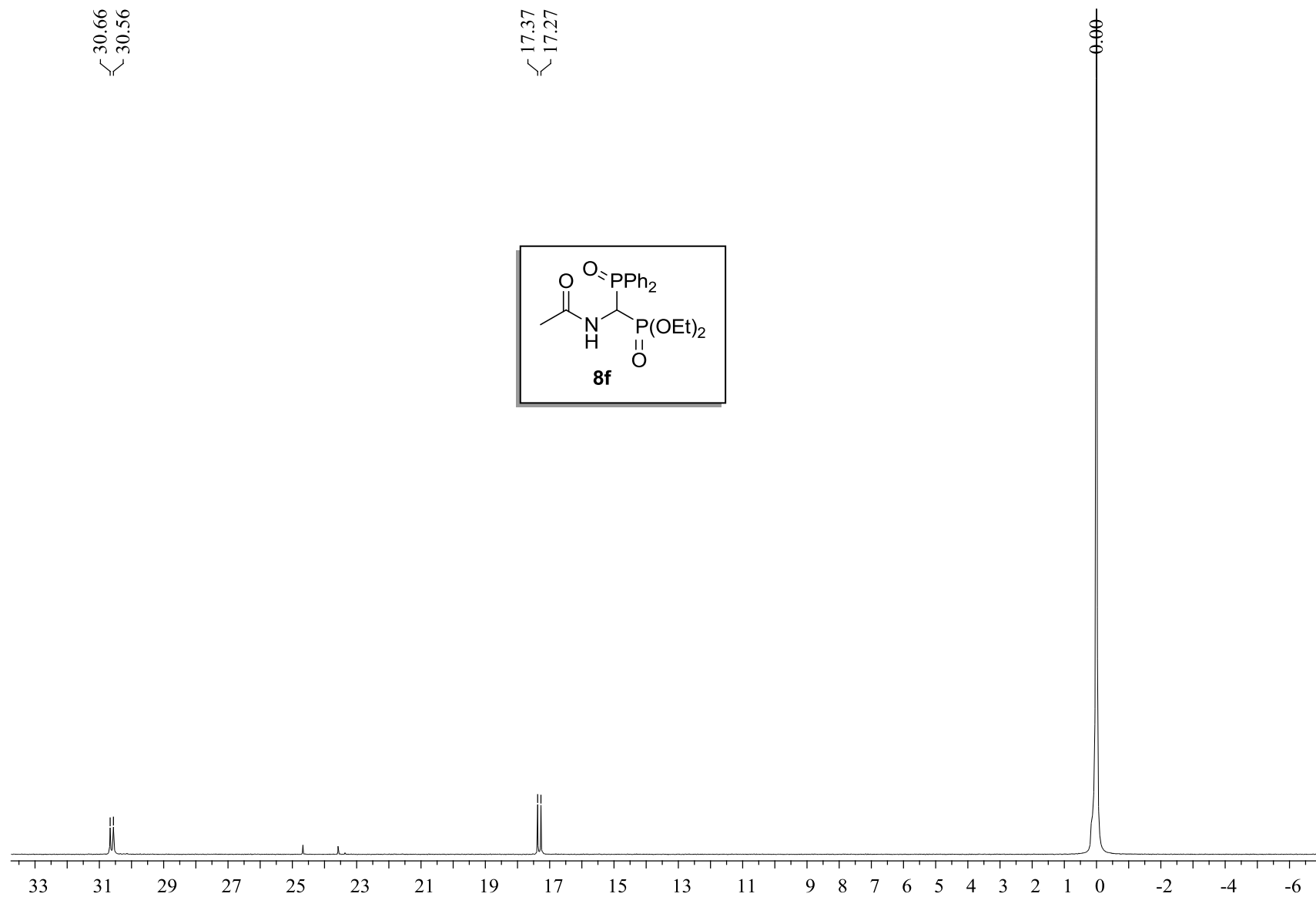
$^{31}\text{P}$  NMR spectrum of one of the diastereomers of diethyl 1-(*N*-acetylamino)-1-[ethoxy(phenylphosphinyl)]ethylphosphonate (**8e**); 162 MHz/ $\text{CDCl}_3$ ;  $\delta$  (ppm).



<sup>1</sup>H NMR spectrum of diethyl 1-(N-acetylamino)-1-(diphenylphosphinoyl)methylphosphonate (**8f**); 600 MHz/CDCl<sub>3</sub>/TMS; δ (ppm).







$^{31}\text{P}$  NMR spectrum of diethyl 1-(*N*-acetylamino)-1-(diphenylphosphinoyl)methylphosphonate (**8f**); 162 MHz/ $\text{CDCl}_3$ ;  $\delta$  (ppm).