

## Electronic supplementary information

### NEW PHOSPHORUS-CONTAINING AMINO ACIDS AND THEIR ANALOGS AS PROMISING BIOACTIVE SUBSTANCES

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#### Experimental section

##### General remarks

The  $^1\text{H}$ ,  $^{13}\text{C}\{^1\text{H}\}$  and  $^{31}\text{P}\{^1\text{H}\}$  NMR spectra were recorded on a Bruker Avance 400 spectrometer in  $\text{CDCl}_3$ ,  $\text{C}_6\text{D}_6$ , or  $\text{D}_2\text{O}$  at 400, 100, and 162 MHz, respectively. The chemical shifts are reported in ppm relative to TMS ( $^1\text{H}$ ,  $^{13}\text{C}$ ) or 85%  $\text{H}_3\text{PO}_4$  in  $\text{D}_2\text{O}$  ( $^{31}\text{P}$ ). The NMR spectra of compounds **1–12** contain characteristic signals of  $\text{PC}(1)\text{H}_2\text{NC}(2)\text{H}_2$  moieties, as well as the fragments of amino acid derivatives, the parameters of which are given below. Some of the compounds obtained contain amide units  $\text{NC}(\text{O})$  and are mixtures of two conformers that differ by the NMR signals, which is typical for the stereochemistry of *N*-substituted amides of carboxylic acids. The ratio of the conformers was determined by a complex superposition of the spatial and electronic properties of the substituents at the amide fragments. Thus, compounds **1e**, **4d**, **9a**, **9b**, **9d**, **10c**, **10d** consist of only one conformer. For some compounds, the proton signals of both conformers are multiplets that overlap in the  $^1\text{H}$  NMR spectra.

The melting points were determined in open capillaries and are uncorrected. The elemental analyses data were obtained on a PerkinElmer Series II CHNS/O 2400 Analyser. Analysis of compounds **1a–e**, which are easily oxidized or hydrolyzed, was carried out for their stable derivatives **2a–e**, and the structures of phosphonites **1a–e** were also confirmed by NMR spectroscopy. All reactions were carried out under a dry argon atmosphere in anhydrous solvents.

Compounds **1b**, **3b**, **3c**, **3d**, **4b**, **4c**, **4d**, **5**, **11**, **12** were synthesized and described by us earlier [1–5], but were not characterized by the complete set of spectral data.

#### Syntheses

**General procedure for the synthesis of phosphonites 1.** A solution of *N*-chloromethyl-*N*-ethoxycarbonylamino acid alkyl ester (65 mmol) in dichloromethane (35 mL) was added

dropwise to a stirred solution of bis(trimethylsiloxy)phosphine (90 mmol) in  $\text{CH}_2\text{Cl}_2$  (30 mL) at 10 °C. The reaction mixture was stirred at room temperature for 1 h. Then triethylamine (70 mmol) was added, and the resulting mixture was stirred for another 2 h. The solvent was removed under vacuum, and the residue obtained was treated with pentane (150 mL) and filtered. The filtrate was evaporated to dryness, and the resulting residue was distilled to give phosphonites **1**.

***N*-Ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethylphosphonous acid bis(trimethylsilyl) ester (**1a**).** Yield: 57%. Bp: 108 °C (0.5 Torr). First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.08 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.04 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.49 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 9.8$ ), 3.58 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.94 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ), 4.21 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.24 (s, 2  $\text{Me}_3\text{Si}$ ), 14.14 (s, Me), 50.58 (s,  $\text{C}(2)$ ), 51.74 (s, MeO), 58.72 (d,  $\text{C}(1)$ ,  $^1J_{\text{PC}} = 26.4$ ), 61.84 (s,  $\text{CH}_2\text{O}$ ), 156.47 (s,  $\text{NC}=\text{O}$ ), 169.89 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 148.34 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.11 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.04 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.42 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 10.0$ ), 3.54 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.94 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ), 4.16 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.29 (s, 2  $\text{Me}_3\text{Si}$ ), 14.14 (s, Me), 50.52 (s,  $\text{C}(2)$ ), 51.62 (s, MeO), 58.34 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 26.1$ ), 61.72 (s,  $\text{CH}_2\text{O}$ ), 156.26 (s,  $\text{NC}=\text{O}$ ), 169.42 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 149.34 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonous acid bis(trimethylsilyl) ester (**1b**).** Yield: 76%. Bp: 130 °C (2 Torr). First isomer (70%).  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.20 (s, 18H, 2  $\text{Me}_3\text{Si}$ ), 1.08–1.15 (m, 6H, 2  $\text{CH}_3$ ), 3.47 (d, 2H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 9.6$ ), 3.76–3.91 (m, 4H, 2  $\text{CH}_2\text{O}$ ), 4.15 (s, 2H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.33 (s, 2  $\text{Me}_3\text{Si}$ ), 14.52 (s, 2 Me), 50.58 (s,  $\text{C}(2)$ ), 58.66 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 26.1$ ), 62.03 (s, 2  $\text{CH}_2\text{O}$ ), 156.51 (s,  $\text{NC}=\text{O}$ ), 169.31 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm): 149.40 (s). Second isomer (30%).  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.20 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.08–1.15 (m, 6H, 2  $\text{CH}_3$ ), 3.38 (d, 2H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 10.1$ ), 3.76–3.91 (m, 4H, 2  $\text{CH}_2\text{O}$ ), 4.05 (s, 2H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.33 (s, 2  $\text{Me}_3\text{Si}$ ), 14.52 (s, 2 Me), 50.52 (s,  $\text{C}(2)$ ), 58.28 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 25.7$ ), 62.03 (s, 2  $\text{CH}_2\text{O}$ ), 156.15 (s,  $\text{NC}=\text{O}$ ), 169.31 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{C}_6\text{D}_6$ ,  $\delta$ , ppm): 148.47 (s).

***N*-Ethoxycarbonyl-*N*-(2-methoxycarbonylethyl)aminomethylphosphonous acid bis(trimethylsilyl) ester (**1c**).** Yield: 73%. Bp: 118 °C (1 Torr). First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.09 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.07 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.34–3.40 (m, 4 H,  $\text{C}(1)\text{H}_2$ ,  $\text{C}(2)\text{H}_2$ ), 3.52 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.94 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.25 (s, 2  $\text{Me}_3\text{Si}$ ), 14.62 (s, Me), 31.16 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 50.54 (s,  $\text{C}(2)$ ), 52.03 (s, MeO), 58.62 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 26.0$ ), 61.78 (s,  $\text{CH}_2\text{O}$ ), 156.59 (s,  $\text{NC}=\text{O}$ ), 170.23 (s,

C=O).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 149.36 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.09 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.07 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.34–3.40 (m, 4 H, C(1) $\text{H}_2$ , C(2) $\text{H}_2$ ), 3.48 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.94 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.25 (s, 2  $\text{Me}_3\text{Si}$ ), 14.62 (s, Me), 31.16 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 50.47 (s, C(2)), 52.03 (s, MeO), 58.51 (d, C(1),  $^1J_{\text{CP}} = 26.2$ ), 61.78 (s,  $\text{CH}_2\text{O}$ ), 156.46 (s,  $\text{NC}=\text{O}$ ), 170.12 (s, C=O).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 150.18 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonous acid bis(trimethylsilyl) ester (1d).** Yield: 78%. Bp: 121 °C (1 Torr). First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.05 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 0.95–1.06 (m, 6 H, 2  $\text{CH}_3$ ), 2.45–2.54 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.38–3.44 (m, 4 H, C(1) $\text{H}_2$ , C(2) $\text{H}_2$ ), 3.81–4.18 (m, 4 H, 2  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.22 (s, 2  $\text{Me}_3\text{Si}$ ), 14.07 (s, Me), 14.68 (s, Me), 31.21 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 50.58 (s, C(2)), 58.66 (d, C(1),  $^1J_{\text{CP}} = 25.9$ ), 60.74 (s,  $\text{CH}_2\text{O}$ ), 61.82 (s,  $\text{CH}_2\text{O}$ ), 156.26 (s,  $\text{NC}=\text{O}$ ), 171.09 (s, C=O).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 149.25 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.05 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 0.95–1.06 (m, 6 H, 2  $\text{CH}_3$ ), 2.45–2.54 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.38–3.44 (m, 4 H, C(1) $\text{H}_2$ , C(2) $\text{H}_2$ ), 3.81–4.18 (m, 4 H, 2  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.22 (s, 2  $\text{Me}_3\text{Si}$ ), 14.07 (s, Me), 14.68 (s, Me), 31.13 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 50.50 (s, C(2)), 58.26 (d, C(1),  $^1J_{\text{CP}} = 25.7$ ), 60.70 (s,  $\text{CH}_2\text{O}$ ), 61.64 (s,  $\text{CH}_2\text{O}$ ), 156.18 (s,  $\text{NC}=\text{O}$ ), 169.98 (s, C=O).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 150.12 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonous acid bis(trimethylsilyl) ester (1e).** Yield: 77%. Bp: 124 °C (1 Torr).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.12 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 0.97 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 1.62–1.78 (m, 2 H,  $\text{CH}_2$ ), 2.42–2.51 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.38 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.43–3.57 (m, 4 H, C(1) $\text{H}_2$ , C(2) $\text{H}_2$ ), 3.96 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.98 (s, 2  $\text{Me}_3\text{Si}$ ), 14.72 (s, Me), 23.10 (s,  $\text{CH}_2$ ), 31.04 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 50.46 (s, C(2)), 51.19 (s, MeO), 56.95 (d, C(1),  $^1J_{\text{CP}} = 26.4$ ), 55.10 (s, MeO), 61.49 (s,  $\text{CH}_2\text{O}$ ), 156.13 (s,  $\text{NC}=\text{O}$ ), 172.83 (s, C=O).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 149.78 (s).

**General procedure for the synthesis of sodium salts of amino acids and their analogs 2, 9.** A solution of phosphonite **1** (40 mmol) or phosphonates **4** (20 mmol) in diethyl ether (30 mL) was added to a stirred solution of sodium methylate (40 mmol) in methanol (70 mL) at 10 °C. The reaction mixture was heated to reflux, and the solvent was distilled off. The residue obtained was kept under vacuum (1 Torr) for 1 h to give compounds **2, 9** as white crystals.

***N*-Ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethylphosphonous acid sodium salt (2a).** Yield: 97%. Mp: 151 °C (dec.). Anal. Calcd for  $\text{C}_7\text{H}_{13}\text{NNaO}_6\text{P}$ : C, 32.19; H, 5.02. Found: C, 32.03; H, 4.96%.  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.07 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.0$ ), 3.42 (d, 2 H, C(1) $\text{H}_2$ ,  $^2J_{\text{HP}} = 9.2$ ), 3.55 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.96 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.0$ ), 4.23 (s, 2

H, C(2)H<sub>2</sub>), 6.84 (d, 1 H, PH,  $^1J_{\text{HP}} = 518.4$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.16 (s, Me), 50.64 (s, C(2)), 51.78 (s, MeO), 52.87 (d, C(1),  $^1J_{\text{CP}} = 89.5$ ), 61.96 (s, CH<sub>2</sub>O), 156.58 (s, NC=O), 169.98 (s, C=O).  $^{31}\text{P}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 22.74 (d, 1 P, PH,  $^1J_{\text{PH}} = 518.4$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 22.74 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonous acid sodium salt (2b).** Yield: 96%. Mp: 166 °C (dec.). Anal. Calcd for C<sub>8</sub>H<sub>15</sub>NNaO<sub>6</sub>P: C, 34.92; H, 5.49. Found: C, 34.78; H, 5.40%.  $^1\text{H}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.04–1.15 (m, 6 H, 2 CH<sub>3</sub>), 3.50 (d, 2 H, C(1)H<sub>2</sub>,  $^2J_{\text{HP}} = 8.3$ ), 3.75–3.91 (m, 4 H, 2 CH<sub>2</sub>O), 4.24 (s, 2 H, C(2)H<sub>2</sub>), 6.87 (d, PH, 1 H,  $^1J_{\text{HP}} = 516.3$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.20 (s, 2 Me), 50.54 (s, C(2)), 53.59 (d, C(1),  $^1J_{\text{CP}} = 88.9$ ), 62.15 (s, 2 CH<sub>2</sub>O), 156.60 (s, NC=O), 169.68 (s, C=O).  $^{31}\text{P}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 21.98 (d, 1 P, PH,  $^1J_{\text{PH}} = 516.3$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm): 21.98 (s).

***N*-Ethoxycarbonyl-*N*-(2-methoxycarbonylethyl)aminomethylphosphonous acid sodium salt (2c).** Yield: 95%. Mp: 142 °C (dec.). Anal. Calcd for C<sub>8</sub>H<sub>15</sub>NNaO<sub>6</sub>P: C, 34.92; H, 5.49. Found: C, 34.72; H, 5.43%.  $^1\text{H}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.05 (t, 3 H, CH<sub>3</sub>,  $^3J_{\text{HH}} = 7.1$ ), 3.38–3.45 (m, 6 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), CH<sub>2</sub>C(O)), 3.59 (s, 3 H, CH<sub>3</sub>O), 4.01 (q, 2 H, CH<sub>2</sub>O,  $^3J_{\text{HH}} = 7.1$ ), 6.88 (d, 1 H, PH,  $^1J_{\text{HP}} = 522.1$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.76 (s, Me), 31.88 (s, CH<sub>2</sub>C(O)), 50.89 (s, C(2)), 52.23 (s, MeO), 53.04 (d, C(1),  $^1J_{\text{CP}} = 90.1$ ), 61.82 (s, CH<sub>2</sub>O), 156.65 (s, NC=O), 170.46 (s, C=O).  $^{31}\text{P}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 22.94 (d, 1 P, PH,  $^1J_{\text{PH}} = 522.1$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm): 22.94 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonous acid sodium salt (2d).** Yield: 96%. Mp: 164 °C (dec.). Anal. Calcd for C<sub>9</sub>H<sub>17</sub>NNaO<sub>6</sub>P: C, 37.38; H, 5.93. Found: C, 37.29; H, 5.88%.  $^1\text{H}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.04–1.13 (m, 6 H, 2 CH<sub>3</sub>), 2.47–2.53 (m, 2 H, CH<sub>2</sub>C(O)), 3.45–3.53 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.83–4.15 (m, 4 H, 2 CH<sub>2</sub>O), 6.85 (d, 1 H, PH,  $^1J_{\text{HP}} = 519.0$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.11 (s, Me), 14.74 (s, Me), 31.26 (s, CH<sub>2</sub>C(O)), 50.62 (s, C(2)), 52.94 (d, C(1),  $^1J_{\text{CP}} = 89.8$ ), 60.79 (s, CH<sub>2</sub>O), 61.86 (s, CH<sub>2</sub>O), 156.48 (s, NC=O), 171.12 (s, C=O).  $^{31}\text{P}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 22.28 (d, 1 P, PH,  $^1J_{\text{PH}} = 519.0$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm): 22.28 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonous acid sodium salt (2e).** Yield: 95%. Mp: 168 °C (dec.). Anal. Calcd for C<sub>9</sub>H<sub>17</sub>NNaO<sub>6</sub>P: C, 37.38; H, 5.93. Found: C, 37.26; H, 5.86%.  $^1\text{H}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 1.04 (t, 3 H, CH<sub>3</sub>,  $^3J_{\text{HH}} = 7.2$ ), 1.67–1.81 (m, 2 H, CH<sub>2</sub>), 2.45–2.54 (m, 2 H, CH<sub>2</sub>C(O)), 3.42 (s, 3 H, CH<sub>3</sub>O), 3.49–3.63 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 4.02 (q, 2 H, CH<sub>2</sub>O,  $^3J_{\text{HH}} = 7.2$ ), 6.82 (d, 1 H, PH,  $^1J_{\text{HP}} = 520.1$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (D<sub>2</sub>O,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.78 (s, Me), 23.14 (s, CH<sub>2</sub>), 31.13 (s, CH<sub>2</sub>C(O)), 50.57 (s, C(2)), 51.22 (s, MeO), 52.68 (d, C(1),  $^1J_{\text{CP}} = 90.2$ ), 55.06 (s, MeO), 61.64 (s, CH<sub>2</sub>O), 156.28 (s, NC=O), 172.95

(s, C=O).  $^{31}\text{P}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 22.44 (d, 1 P, PH,  $^1J_{\text{PH}} = 520.1$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$ , ppm): 22.44 (s).

**General procedure for the synthesis of phosphonates 3–5 and phosphinates 6–8.** A solution of *N*-chloromethylamide (35 mmol) in dichloromethane (40 mL) was added dropwise to a stirred solution of tri-coordinate phosphorus acid ester (40 mmol) in  $\text{CH}_2\text{Cl}_2$  (35 mL) at 10 °C. The reaction mixture was stirred at room temperature for 1 h and then heated to reflux. The solvent was distilled off, and the residue obtained was distilled to give compounds 3–8.

***N*-Ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethylphosphonic acid diethyl ester (3a).** Yield: 87%. Bp: 165 °C (3 Torr). Anal. Calcd for  $\text{C}_{11}\text{H}_{22}\text{NO}_7\text{P}$ : C, 42.44; H, 7.12. Found: C, 42.26 H, 7.08%. First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.98–1.12 (m, 9 H, 3  $\text{CH}_3$ ), 3.48 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.58 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 11.4$ ), 3.84–3.92 (m, 6 H, 3  $\text{CH}_2\text{O}$ ), 4.30 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 13.95 (s, Me), 15.82 (d, Me,  $^3J_{\text{CP}} = 6.1$ ), 15.88 (d, Me,  $^3J_{\text{CP}} = 6.1$ ), 42.15 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 159.1$ ), 48.08 (s,  $\text{C}(2)$ ), 51.48 (s, MeO), 61.76 (s, Me), 61.89 (d, 2 Me,  $^2J_{\text{CP}} = 6.3$ ), 155.36 (s,  $\text{NC}=\text{O}$ ), 169.22 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.60 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.98–1.12 (m, 9 H, 3  $\text{CH}_3$ ), 3.48 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.55 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 11.4$ ), 3.84–3.92 (m, 6 H, 3  $\text{CH}_2\text{O}$ ), 4.34 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 13.95 (s, Me), 15.82 (d, Me,  $^3J_{\text{CP}} = 6.1$ ), 15.88 (d, Me,  $^3J_{\text{CP}} = 6.1$ ), 42.32 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 158.5$ ), 47.97 (s,  $\text{C}(2)$ ), 51.48 (s, MeO), 61.76 (s, Me), 61.89 (d, 2 Me,  $^2J_{\text{CP}} = 6.3$ ), 155.36 (s,  $\text{NC}=\text{O}$ ), 169.22 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.22 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonic acid diethyl ester (3b).** Yield: 85%. Bp: 153 °C (2 Torr). Anal. Calcd for  $\text{C}_{12}\text{H}_{24}\text{NO}_7\text{P}$ : C, 44.30; H, 7.44. Found: C, 44.40 H, 7.41%. First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.90 (t, 6 H, 2  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 1.02 (t, 6 H, 2  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 6.8$ ), 3.28–4.04 (m, 10 H,  $\text{C}(1)\text{H}_2$ , 4  $\text{CH}_2\text{O}$ ), 4.28 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.07 (s, 2 Me), 14.47 (s, Me), 16.40 (s, Me), 43.23 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 158.4$ ), 49.06 (s,  $\text{C}(2)$ ), 60.90 (s,  $\text{CH}_2\text{O}$ ), 62.02 (s,  $\text{CH}_2\text{O}$ ), 62.12 (d, 2  $\text{CH}_2\text{O}$ ,  $^2J_{\text{CP}} = 7.3$ ), 156.20 (d,  $\text{NC}=\text{O}$ ,  $^3J_{\text{CP}} = 4.6$ ), 169.35 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.39 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.90 (t, 6 H, 2  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 1.02 (t, 6 H, 2  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 6.8$ ), 3.28–4.04 (m, 10 H,  $\text{C}(1)\text{H}_2$ , 4  $\text{CH}_2\text{O}$ ), 4.41 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.02 (s, 2 Me), 14.47 (s, Me), 16.35 (s, Me), 43.28 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 158.1$ ), 48.98 (s,  $\text{C}(2)$ ), 60.90 (s,  $\text{CH}_2\text{O}$ ), 62.02 (s,  $\text{CH}_2\text{O}$ ), 62.12 (d, 2  $\text{CH}_2\text{O}$ ,  $^2J_{\text{CP}} = 7.3$ ), 156.49 (d,  $\text{NC}=\text{O}$ ,  $^3J_{\text{CP}} = 3.1$ ), 169.37 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.25 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonic acid diethyl ester (3c).** Yield: 90%. Bp: 185 °C (3 Torr). Anal. Calcd for  $\text{C}_{13}\text{H}_{26}\text{NO}_7\text{P}$ : C, 46.01; H, 7.72.

Found: C, 45.86; H, 7.64%. First isomer (60%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.84–1.04 (m, 12 H, 4  $\text{CH}_3$ ), 2.18–2.29 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.16–3.28 (m, 2 H,  $\text{C}(2)\text{H}_2$ ), 3.34–3.43 (m, 2 H,  $\text{C}(1)\text{H}_2$ ), 3.66–3.82 (m, 8 H, 4  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 13.27 (s, 2 Me), 13.72 (s, Me), 15.51 (s, Me), 32.47 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 42.11 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 158.5$ ), 42.90 (s,  $\text{C}(2)$ ), 59.54 (s,  $\text{CH}_2\text{O}$ ), 59.54 (s,  $\text{CH}_2\text{O}$ ), 60.99 (s,  $\text{CH}_2\text{O}$ ), 61.27 (s, 2  $\text{CH}_2\text{O}$ ), 155.01 (s,  $\text{NC}=\text{O}$ ), 170.57 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 20.12 (s). Second isomer (40%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.84–1.04 (m, 12 H, 4  $\text{CH}_3$ ), 2.18–2.29 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.16–3.28 (m, 2 H,  $\text{C}(2)\text{H}_2$ ), 3.34–3.43 (m, 2 H,  $\text{C}(1)\text{H}_2$ ), 3.66–3.82 (m, 8 H, 4  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 13.27 (s, 2 Me), 13.72 (s, Me), 15.51 (s, Me), 31.81 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 42.50 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 155.9$ ), 43.48 (s,  $\text{C}(2)$ ), 59.54 (s,  $\text{CH}_2\text{O}$ ), 60.84 (s,  $\text{CH}_2\text{O}$ ), 61.27 (s, 2  $\text{CH}_2\text{O}$ ), 154.49 (s,  $\text{NC}=\text{O}$ ), 170.85 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.71 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonic acid diethyl ester (3d).** Yield: 92%. Bp: 175 °C (2 Torr). Anal. Calcd for  $\text{C}_{13}\text{H}_{26}\text{NO}_7\text{P}$ : C, 46.01; H, 7.72. Found: C, 45.81; H, 7.68%. First isomer (70%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.98–1.02 (m, 9 H, 3  $\text{CH}_3$ ), 1.57–1.61 (m, 2 H,  $\text{CH}_2$ ), 2.02–2.54 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.37 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.45–3.70 (m, 4 H,  $\text{C}(1)\text{H}_2$ ,  $\text{C}(2)\text{H}_2$ ), 3.86–4.04 (m, 6 H, 3  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.60 (s, Me), 16.43 (d, Me,  $^3J_{\text{CP}} = 5.4$ ), 23.24 (s,  $\text{CH}_2$ ), 31.00 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 42.59 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 156.0$ ), 46.92 (s,  $\text{C}(2)$ ), 51.11 (s, MeO), 61.59 (s,  $\text{CH}_2\text{O}$ ), 61.90 (d, 2  $\text{CH}_2\text{O}$ ,  $^2J_{\text{CP}} = 6.1$ ), 156.11 (s,  $\text{NC}=\text{O}$ ), 172.96 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 20.27 (s). Second isomer (30%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.98–1.02 (m, 9 H, 3  $\text{CH}_3$ ), 1.57–1.61 (m, 2 H,  $\text{CH}_2$ ), 2.02–2.54 (m, 2 H,  $\text{CH}_2\text{C}(\text{O})$ ), 3.37 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.45–3.70 (m, 4 H,  $\text{C}(1)\text{H}_2$ ,  $\text{C}(2)\text{H}_2$ ), 3.86–4.04 (m, 6 H, 3  $\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 14.60 (s, Me), 16.43 (d, Me,  $^3J_{\text{CP}} = 5.4$ ), 22.91 (s,  $\text{CH}_2$ ), 31.00 (s,  $\text{CH}_2\text{C}(\text{O})$ ), 42.59 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 156.0$ ), 47.30 (s,  $\text{C}(2)$ ), 51.11 (s, MeO), 61.59 (s,  $\text{CH}_2\text{O}$ ), 61.90 (d, 2  $\text{CH}_2\text{O}$ ,  $^2J_{\text{CP}} = 6.1$ ), 155.72 (s,  $\text{NC}=\text{O}$ ), 172.96 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 19.94 (s).

***N*-Ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethylphosphonic acid bis(trimethylsilyl) ester (4a).** Yield: 82%. Bp: 168 °C (2 Torr). Anal. Calcd for  $\text{C}_{13}\text{H}_{30}\text{NO}_7\text{PSi}_2$ : C, 39.08; H, 7.57. Found: C, 38.89; H, 7.52%. First isomer (65%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.10 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.09 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.61 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.83 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 10.0$ ), 3.98 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ), 4.33 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.82 (s, 2  $\text{Me}_3\text{Si}$ ), 14.14 (s, Me), 45.37 (d,  $\text{C}(1)$ ,  $^1J_{\text{CP}} = 167.0$ ), 48.60 (s,  $\text{C}(2)$ ), 51.52 (s, MeO), 61.99 (s,  $\text{CH}_2\text{O}$ ), 156.06 (s,  $\text{NC}=\text{O}$ ), 169.84 (s,  $\text{C}=\text{O}$ ).  $^{31}\text{P}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm): 1.32 (s). Second isomer (35%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ): 0.10 (s, 18 H, 2  $\text{Me}_3\text{Si}$ ), 1.09 (t, 3 H,  $\text{CH}_3$ ,  $^3J_{\text{HH}} = 7.2$ ), 3.61 (s, 3 H,  $\text{CH}_3\text{O}$ ), 3.77 (d, 2 H,  $\text{C}(1)\text{H}_2$ ,  $^2J_{\text{HP}} = 10.0$ ), 3.98 (q, 2 H,  $\text{CH}_2\text{O}$ ,  $^3J_{\text{HH}} = 7.2$ ), 4.46 (s, 2 H,  $\text{C}(2)\text{H}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ,  $\delta$ , ppm,  $J/\text{Hz}$ ):

0.82 (s, 2 Me<sub>3</sub>Si), 14.14 (s, Me), 45.08 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 165.7), 48.40 (s, C(2)), 51.47 (s, MeO), 62.13 (s, CH<sub>2</sub>O), 156.10 (s, NC=O), 169.88 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 1.51 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonic acid bis(trimethylsilyl) ester (4b).** Yield: 81%. Bp: 132 °C (0.5 Torr). Anal. Calcd for C<sub>14</sub>H<sub>32</sub>NO<sub>7</sub>PSi<sub>2</sub>: C, 40.66; H, 7.80. Found: C, 40.53; H, 7.68%. First isomer (60%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.18 (s, 18 H, 2 Me<sub>3</sub>Si), 0.84–0.99 (m, 6 H, 2 CH<sub>3</sub>), 3.85 (d, 2 H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.0), 3.90–4.02 (m, 4 H, 2 CH<sub>2</sub>O), 4.34 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 1.16 (s, 2 Me<sub>3</sub>Si), 14.20 (s, Me), 14.63 (s, 2 Me), 45.46 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 167.0), 48.77 (s, C(2)), 60.62 (s, CH<sub>2</sub>O), 61.08 (s, CH<sub>2</sub>O), 156.15 (d, NC=O, <sup>3</sup>J<sub>CP</sub> = 4.5), 169.40 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 1.36 (s). Second isomer (40%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.15 (s, 18 H, 2 Me<sub>3</sub>Si), 0.84–0.99 (m, 6 H, 2 CH<sub>3</sub>), 3.79 (d, 2 H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.0), 3.90–4.02 (m, 4 H, 2 CH<sub>2</sub>O), 4.48 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 1.16 (s, 2 Me<sub>3</sub>Si), 14.05 (s, Me), 14.63 (s, 2 Me), 45.13 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 166.6), 48.53 (s, C(2)), 60.62 (s, CH<sub>2</sub>O), 62.12 (s, CH<sub>2</sub>O), 156.11 (d, NC=O, <sup>3</sup>J<sub>CP</sub> = 3.1), 169.44 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 1.56 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonic acid bis(trimethylsilyl) ester (4c).** Yield: 85%. Bp: 171 °C (2 Torr). Anal. Calcd for C<sub>15</sub>H<sub>34</sub>NO<sub>7</sub>PSi<sub>2</sub>: C, 42.14; H, 8.01. Found: C, 41.94; H, 7.92%. First isomer (70%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): –0.01 (s, 18 H, 2 Me<sub>3</sub>Si), 0.90–1.02 (m, 6 H, 2 CH<sub>3</sub>), 2.32–2.38 (m, 2 H, CH<sub>2</sub>C(O)), 3.34–3.42 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.76–4.02 (m, 4 H, 2 CH<sub>2</sub>O). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.29 (s, 2 Me<sub>3</sub>Si), 13.56 (s, 2 Me), 32.63 (s, CH<sub>2</sub>C(O)), 42.94 (s, C(2)), 44.49 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 165.6), 61.08 (s, CH<sub>2</sub>O), 155.16 (s, NC=O), 170.78 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 1.47 (s). Second isomer (30%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.01 (s, 18 H, 2 Me<sub>3</sub>Si), 0.90–1.02 (m, 6 H, 2 CH<sub>3</sub>), 2.32–2.38 (m, 2 H, CH<sub>2</sub>C(O)), 3.34–3.42 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.76–4.02 (m, 4 H, 2 CH<sub>2</sub>O). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.29 (s, 2 Me<sub>3</sub>Si), 14.08 (s, 2 Me), 31.94 (s, CH<sub>2</sub>C(O)), 43.44 (s, C(2)), 44.49 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 165.6), 59.79 (s, CH<sub>2</sub>O), 154.80 (s, NC=O), 171.05 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 1.54 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonic acid bis(trimethylsilyl) ester (4d).** Yield: 82%. Bp: 155 °C (1 Torr). Anal. Calcd for C<sub>15</sub>H<sub>34</sub>NO<sub>7</sub>PSi<sub>2</sub>: C, 42.14; H, 8.01. Found: C, 41.88; H, 7.96%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.20 (s, 18 H, 2 Me<sub>3</sub>Si), 1.00 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.2), 1.65–1.80 (m, 2 H, CH<sub>2</sub>), 1.95–2.12 (m, 2 H, CH<sub>2</sub>C(O)), 3.35 (s, 3 H, CH<sub>3</sub>O), 3.38–3.65 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.97 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.2). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.94 (s, 2 Me<sub>3</sub>Si), 14.74 (s, Me), 23.14 (s, CH<sub>2</sub>), 31.02 (s, CH<sub>2</sub>C(O)), 44.67 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 160.4), 46.61 (s, C(2)), 51.09 (s, MeO), 61.47 (s, CH<sub>2</sub>O), 155.97 (s, NC=O), 172.75 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 2.14 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonic acid diisopropyl ester (5).** Yield: 74%. Bp: 141 °C (1 Torr). Anal. Calcd for C<sub>14</sub>H<sub>28</sub>NO<sub>7</sub>P: C, 47.59; H, 7.99. Found: C, 47.73; H, 8.02%. First isomer (60%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.89–1.04 (m, 6 H, 2 CH<sub>3</sub>), 1.08–1.21 (m, 12 H, 4 CH<sub>3</sub>), 3.78–4.03 (m, 6 H, C(1)H<sub>2</sub>, 2 CH<sub>2</sub>O), 4.34 (s, 2 H, C(2)H<sub>2</sub>), 4.56–4.73 (m, 2 H, 2 CH). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 14.53 (s, 2 Me), 23.87 (d, 4 Me, <sup>3</sup>*J*<sub>CP</sub> = 4.8), 43.52 (d, C(1), <sup>1</sup>*J*<sub>CP</sub> = 160.7), 48.32 (s, C(2)), 60.87 (s, CH<sub>2</sub>O), 62.94 (d, CH<sub>2</sub>O, <sup>2</sup>*J*<sub>CP</sub> = 4.5), 70.78 (s, 2 CHO), 155.61 (d, NC=O, <sup>3</sup>*J*<sub>CP</sub> = 5.4), 168.79 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} (CDCl<sub>3</sub>, δ, ppm): 17.71 (s). Second isomer (40%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.89–1.04 (m, 6 H, 2 CH<sub>3</sub>), 1.08–1.21 (m, 12 H, 4 CH<sub>3</sub>), 3.78–4.03 (m, 6 H, C(1)H<sub>2</sub>, 2 CH<sub>2</sub>O), 4.48 (s, 2 H, C(2)H<sub>2</sub>), 4.56–4.73 (m, 2 H, 2 CH). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 14.03 (s, 2 Me), 23.74 (d, 4 Me, <sup>3</sup>*J*<sub>CP</sub> = 5.7), 43.52 (d, C(1), <sup>1</sup>*J*<sub>CP</sub> = 160.7), 48.21 (s, C(2)), 60.87 (s, CH<sub>2</sub>O), 62.94 (d, CH<sub>2</sub>O, <sup>2</sup>*J*<sub>CP</sub> = 4.5), 70.78 (s, 2 CHO), 155.52 (d, NC=O, <sup>3</sup>*J*<sub>CP</sub> = 3.4), 168.79 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 17.47 (s).

**Methyl[*N*-ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethyl]phosphinic acid isopropyl ester (6).** Yield: 87%. Bp: 157 °C (2 Torr). Anal. Calcd for C<sub>11</sub>H<sub>22</sub>NO<sub>6</sub>P: C, 44.74; H, 7.51. Found: C, 44.59; H, 7.45%. First isomer (65%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.92 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>*J*<sub>HH</sub> = 7.0), 1.07 (d, 6 H, 2 CH<sub>3</sub>, <sup>3</sup>*J*<sub>HP</sub> = 6.4), 1.35 (d, 3 H, PCH<sub>3</sub>, <sup>2</sup>*J*<sub>HP</sub> = 14.0), 3.36 (s, 3 H, CH<sub>3</sub>O), 3.49–3.72 (m, 2 H, C(1)H<sub>2</sub>), 3.82–4.04 (m, 2 H, CH<sub>2</sub>O), 4.23 (s, 2 H, C(2)H<sub>2</sub>), 4.46–4.52 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 13.59 (d, PMe, <sup>1</sup>*J*<sub>CP</sub> = 90.2), 14.49 (s, Me), 24.24 (s, 2 Me), 47.61 (d, C(1), <sup>1</sup>*J*<sub>CP</sub> = 106.1), 49.41 (s, C(2)), 51.60 (s, MeO), 62.16 (s, CH<sub>2</sub>O), 69.46 (d, CHO, <sup>2</sup>*J*<sub>CP</sub> = 5.4), 156.27 (s, NC=O), 169.94 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} (CDCl<sub>3</sub>, δ, ppm): 44.82 (s). Second isomer (35%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.92 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>*J*<sub>HH</sub> = 7.0), 1.05 (d, 6 H, 2 CH<sub>3</sub>, <sup>3</sup>*J*<sub>HP</sub> = 6.0), 1.26 (d, 3 H, PCH<sub>3</sub>, <sup>2</sup>*J*<sub>HP</sub> = 14.0), 3.33 (s, 3 H, CH<sub>3</sub>O), 3.49–3.72 (m, 2 H, C(1)H<sub>2</sub>), 3.82–4.04 (m, 2 H, CH<sub>2</sub>O), 4.33 (s, 2 H, C(2)H<sub>2</sub>), 4.46–4.52 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 13.39 (d, PMe, <sup>1</sup>*J*<sub>CP</sub> = 90.0), 14.49 (s, Me), 24.24 (s, 2 Me), 47.48 (d, C(1), <sup>1</sup>*J*<sub>CP</sub> = 105.0), 49.41 (s, C(2)), 51.55 (s, MeO), 62.16 (s, CH<sub>2</sub>O), 69.46 (d, CHO, <sup>2</sup>*J*<sub>CP</sub> = 5.4), 156.76 (s, NC=O), 169.87 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 44.23 (s).

**Methyl[*N*-ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethyl]phosphinic acid isopropyl ester (7).** Yield: 87%. Bp: 177 °C (1.5 Torr). Anal. Calcd for C<sub>13</sub>H<sub>26</sub>NO<sub>6</sub>P: C, 48.29; H, 8.11. Found: C, 48.07; H, 8.06%. First isomer (70%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 0.67–0.68 (m, 6 H, 2 CH<sub>3</sub>), 0.75–0.78 (m, 6 H, 2 CH<sub>3</sub>), 0.91 (d, 3 H, CH<sub>3</sub>P, <sup>2</sup>*J*<sub>HP</sub> = 14.0), 2.04–2.12 (m, 2 H, CH<sub>2</sub>C(O)), 3.01–3.28 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.52–3.64 (m, 4 H, 2 CH<sub>2</sub>O), 4.10–4.22 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, *J*/Hz): 13.01 (s, Me), 13.46 (s, Me), 13.24 (d, MeP, <sup>1</sup>*J*<sub>CP</sub> = 88.7), 23.15 (s, 2 Me), 32.14 (s, CH<sub>2</sub>C(O)), 43.11 (s, C(2)), 46.26 (d, C(1), <sup>1</sup>*J*<sub>CP</sub> =



104.7), 59.16 (s, CH<sub>2</sub>O), 60.67 (s, CH<sub>2</sub>O), 68.26 (s, CHO), 154.80 (s, NC=O), 170.16 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 45.58 (s). Second isomer (30%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 0.67–0.68 (m, 6 H, 2 CH<sub>3</sub>), 0.75–0.78 (m, 6 H, 2 CH<sub>3</sub>), 0.91 (d, 3 H, CH<sub>3</sub>P, <sup>2</sup>J<sub>HP</sub> = 14.0), 2.04–2.12 (m, 2 H, CH<sub>2</sub>C(O)), 3.01–3.28 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.52–3.64 (m, 4 H, 2 CH<sub>2</sub>O), 4.10–4.22 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 13.01 (s, Me), 13.46 (s, Me), 13.24 (d, MeP, <sup>1</sup>J<sub>CP</sub> = 88.7), 23.15 (s, 2 Me), 31.45 (s, CH<sub>2</sub>C(O)), 43.57 (s, C(2)), 46.26 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 104.7), 59.16 (s, CH<sub>2</sub>O), 60.54 (s, CH<sub>2</sub>O), 68.26 (s, CHO), 153.98 (s, NC=O), 170.37 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 44.93 (s).

**Methyl[N-ethoxycarbonyl-N-(3-methoxycarbonylpropyl)aminomethyl]phosphinic acid isopropyl ester (8).** Yield: 84%. Bp: 150 °C (1 Torr). Anal. Calcd for C<sub>13</sub>H<sub>26</sub>NO<sub>6</sub>P: C, 48.29; H, 8.11. Found: C, 48.12; H, 8.03%. First isomer (70%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 0.97 (t, 3 H, CH<sub>3</sub>, <sup>2</sup>J<sub>HH</sub> = 7.2), 1.08 (d, 6 H, 2 CH<sub>3</sub>, <sup>2</sup>J<sub>HH</sub> = 6.0), 1.28 (d, 3 H, CH<sub>3</sub>P, <sup>2</sup>J<sub>HP</sub> = 14.2), 1.62–1.76 (m, 2 H, CH<sub>2</sub>), 1.93–2.08 (m, 2 H, CH<sub>2</sub>C(O)), 3.37 (s, 3 H, CH<sub>3</sub>O), 3.43–3.66 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.94 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.2), 4.50–4.62 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 14.62 (s, Me), 14.95 (d, MeP, <sup>1</sup>J<sub>CP</sub> = 89.8), 24.33 (d, 2 Me, <sup>3</sup>J<sub>CP</sub> = 3.1), 31.00 (s, CH<sub>2</sub>C(O)), 46.83 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 103.5), 47.34 (s, C(2)), 51.12 (s, MeO), 61.58 (s, CH<sub>2</sub>O), 68.92 (d, CHO, <sup>2</sup>J<sub>CP</sub> = 6.2), 156.24 (s, NC=O), 172.93 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 44.09 (s). Second isomer (30%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 0.97 (t, 3 H, CH<sub>3</sub>, <sup>2</sup>J<sub>HH</sub> = 7.2), 1.11 (d, 6 H, 2 CH<sub>3</sub>, <sup>2</sup>J<sub>HH</sub> = 6.0), 1.18 (d, 3 H, CH<sub>3</sub>P, <sup>2</sup>J<sub>HP</sub> = 14.2), 1.62–1.76 (m, 2 H, CH<sub>2</sub>), 1.93–2.08 (m, 2 H, CH<sub>2</sub>C(O)), 3.37 (s, 3 H, CH<sub>3</sub>O), 3.43–3.66 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.94 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.2), 4.50–4.62 (m, 1 H, CHO). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 14.62 (s, Me), 14.95 (d, MeP, <sup>1</sup>J<sub>CP</sub> = 89.8), 24.33 (d, 2 Me, <sup>3</sup>J<sub>CP</sub> = 3.1), 31.00 (s, CH<sub>2</sub>C(O)), 46.83 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 103.5), 47.34 (s, C(2)), 51.12 (s, MeO), 61.58 (s, CH<sub>2</sub>O), 68.92 (d, CHO, <sup>2</sup>J<sub>CP</sub> = 6.2), 155.54 (s, NC=O), 172.93 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): 43.56 (s).

**N-Ethoxycarbonyl-N-(methoxycarbonylmethyl)aminomethylphosphonic acid disodium salt (9a).** Yield: 95%. Mp: 204 °C (dec.). Anal. Calcd for C<sub>7</sub>H<sub>12</sub>NNa<sub>2</sub>O<sub>7</sub>P: C, 28.11; H, 4.04. Found: C, 27.96; H, 3.98%. <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 1.02 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.0), 3.60 (s, 3 H, CH<sub>3</sub>O), 3.86 (d, 2 H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.0), 4.03 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.0), 4.35 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 14.08 (s, Me), 44.91 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 152.4), 48.84 (s, C(2)), 51.55 (s, MeO), 62.12 (s, CH<sub>2</sub>O), 63.38 (s, CH<sub>2</sub>O), 156.86 (s, NC=O), 170.16 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 16.89 (s).

**N-Ethoxycarbonyl-N-(ethoxycarbonylmethyl)aminomethylphosphonic acid disodium salt (9b).** Yield: 95%. Mp: 197 °C (dec.). Anal. Calcd for C<sub>8</sub>H<sub>14</sub>NNa<sub>2</sub>O<sub>7</sub>P: C, 30.68; H, 4.51. Found: C, 30.42; H, 4.47%. <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 0.95–1.06 (m, 6 H, 2 CH<sub>3</sub>), 3.74 (d, 2

H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.2), 3.92–4.04 (m, 4 H, 2 CH<sub>2</sub>O), 4.36 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 14.22 (s, Me), 14.66 (s, 2 Me), 45.01 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 151.8), 48.89 (s, C(2)), 60.66 (s, CH<sub>2</sub>O), 61.12 (s, CH<sub>2</sub>O), 156.22 (s, NC=O), 167.31 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 17.04 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonic acid disodium salt (9c).** Yield: 96%. Mp: 192 °C (dec.). Anal. Calcd for C<sub>9</sub>H<sub>16</sub>NNa<sub>2</sub>O<sub>7</sub>P: C, 33.04; H, 4.93. Found: C, 32.86; H, 4.89%. <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 1.05–1.15 (m, 6 H, 2 CH<sub>3</sub>), 2.34–2.39 (m, 2 H, CH<sub>2</sub>C(O)), 3.37–3.44 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 3.82–4.07 (m, 4 H, 2 CH<sub>2</sub>O). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 13.72 (s, Me), 32.09 (s, CH<sub>2</sub>C(O)), 42.53 (s, C(2)), 44.91 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 151.4), 61.10 (s, CH<sub>2</sub>O), 155.29 (s, NC=O), 170.95 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 17.09 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonic acid disodium salt (9d).** Yield: 95%. Mp: 193 °C (dec.). Anal. Calcd for C<sub>9</sub>H<sub>16</sub>NNa<sub>2</sub>O<sub>7</sub>P: C, 33.04; H, 4.93. Found: C, 32.83; H, 4.85%. <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 1.08 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.0), 1.60–1.77 (m, 2 H, CH<sub>2</sub>), 1.98–2.10 (m, 2 H, CH<sub>2</sub>C(O)), 3.89 (s, 3 H, CH<sub>3</sub>O), 3.42–3.69 (m, 4 H, C(1)H<sub>2</sub>, C(2)H<sub>2</sub>), 4.01 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.0). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 14.78 (s, Me), 23.19 (s, CH<sub>2</sub>), 31.12 (s, CH<sub>2</sub>C(O)), 44.49 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 152.2), 46.92 (s, C(2)), 51.12 (s, MeO), 61.58 (s, CH<sub>2</sub>O), 156.13 (s, NC=O), 172.97 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 17.34 (s).

**General procedure for the synthesis of functionalized acids 10.** A solution of phosphonate **4** or phosphinate **15–24** (40 mmol) in diethyl ether (30 mL) was added upon stirring to methanol (50 mL) at 10 °C. The reaction mixture was heated to reflux, the solvent was distilled off, and the residue obtained was kept under vacuum (1 Torr) for 1 h to give acids **10** as viscous oils or crystals.

***N*-Ethoxycarbonyl-*N*-(methoxycarbonylmethyl)aminomethylphosphonic acid (10a).** Yield: 95%. Viscous oil. Anal. Calcd for C<sub>7</sub>H<sub>14</sub>NO<sub>7</sub>P: C, 32.95; H, 5.53. Found: C, 32.78; H, 5.48%. First isomer (65%). <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 1.12 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.1), 3.94 (s, 3 H, CH<sub>3</sub>O), 3.94 (d, 2 H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.1), 4.07 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.1), 4.35 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 14.16 (s, Me), 45.39 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 152.3), 48.68 (s, C(2)), 51.57 (s, MeO), 62.04 (s, CH<sub>2</sub>O), 156.69 (s, NC=O), 171.24 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 16.32 (s). Second isomer (35%). <sup>1</sup>H NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 1.12 (t, 3 H, CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.1), 3.63 (s, 3 H, CH<sub>3</sub>O), 3.86 (d, 2 H, C(1)H<sub>2</sub>, <sup>2</sup>J<sub>HP</sub> = 10.1), 4.07 (q, 2 H, CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.1), 4.48 (s, 2 H, C(2)H<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm, J/Hz): 14.14 (s, Me), 45.39 (d, C(1), <sup>1</sup>J<sub>CP</sub> = 152.3), 48.40 (s, C(2)), 51.67 (s, MeO), 62.04 (s, CH<sub>2</sub>O), 156.95 (s, NC=O), 171.18 (s, C=O). <sup>31</sup>P{<sup>1</sup>H} NMR (D<sub>2</sub>O, δ, ppm): 17.21 (s).

***N*-Ethoxycarbonyl-*N*-(ethoxycarbonylmethyl)aminomethylphosphonic acid (10b).**

Yield: 97%. Viscous oil. Anal. Calcd for  $C_8H_{16}NO_7P$ : C, 35.69; H, 5.99. Found: C, 35.49; H, 5.94%. First isomer (55%).  $^1H$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 1.15–1.28 (m, 6 H, 2  $CH_3$ ), 3.75–3.81 (m, 2 H,  $C(1)H_2$ ), 4.03–4.22 (m, 6 H, 2  $CH_2O$ ,  $C(2)H_2$ ).  $^{13}C\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 13.49 (s, Me), 13.89 (s, Me), 44.62 (d,  $C(1)$ ,  $^1J_{CP} = 151.6$ ), 49.72 (s,  $C(2)$ ), 62.49 (s,  $CH_2O$ ), 63.23 (s,  $CH_2O$ ), 157.58 (s,  $NC=O$ ), 171.46 (s,  $C=O$ ).  $^{31}P\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm): 16.79 (s). Second isomer (45%).  $^1H$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 1.15–1.28 (m, 6 H, 2  $CH_3$ ), 3.75–3.81 (m, 2 H,  $C(1)H_2$ ), 4.03–4.22 (m, 6 H, 2  $CH_2O$ ,  $C(2)H_2$ ).  $^{13}C\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 13.49 (s, Me), 13.89 (s, Me), 44.62 (d,  $C(1)$ ,  $^1J_{CP} = 151.6$ ), 49.72 (s,  $C(2)$ ), 62.49 (s,  $CH_2O$ ), 63.23 (s,  $CH_2O$ ), 157.39 (s,  $NC=O$ ), 171.24 (s,  $C=O$ ).  $^{31}P\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm): 17.14 (s).

***N*-Ethoxycarbonyl-*N*-(2-ethoxycarbonylethyl)aminomethylphosphonic acid (10c).**

Yield: 96%. Viscous oil. Anal. Calcd for  $C_9H_{18}NO_7P$ : C, 38.17; H, 6.41. Found: C, 37.98; H, 6.38%.  $^1H$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 1.07–1.15 (m, 6 H, 2  $CH_3$ ), 2.27–2.43 (m, 2 H,  $CH_2C(O)$ ), 3.48–3.59 (m, 4 H,  $C(1)H_2$ ,  $C(2)H_2$ ), 3.85–4.04 (m, 4 H, 2  $CH_2O$ ).  $^{13}C\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 13.76 (s, 2 Me), 32.68 (s,  $CH_2C(O)$ ), 42.98 (s,  $C(2)$ ), 46.15 (d,  $C(1)$ ,  $^1J_{CP} = 152.8$ ), 61.12 (s,  $CH_2O$ ), 155.43 (s,  $NC=O$ ), 172.18 (s,  $C=O$ ).  $^{31}P\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm): 17.92 (s).

***N*-Ethoxycarbonyl-*N*-(3-methoxycarbonylpropyl)aminomethylphosphonic acid (10d).**

Yield: 97%. Viscous oil. Anal. Calcd for  $C_9H_{18}NO_7P$ : C, 38.17; H, 6.41. Found: C, 37.95; H, 6.37%.  $^1H$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 1.08 (t, 3 H,  $CH_3$ ,  $^3J_{HH} = 7.0$ ), 1.69–1.82 (m, 2 H,  $CH_2$ ), 1.98–2.14 (m, 2 H,  $CH_2C(O)$ ), 3.40 (s, 3 H,  $CH_3O$ ), 3.43–3.76 (m, 4 H,  $C(1)H_2$ ,  $C(2)H_2$ ), 4.04 (q, 2 H,  $CH_2O$ ,  $^3J_{HH} = 7.0$ ).  $^{13}C\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm,  $J/Hz$ ): 14.78 (s, Me), 23.23 (s,  $CH_2$ ), 31.11 (s,  $CH_2C(O)$ ), 44.04 (d,  $C(1)$ ,  $^1J_{CP} = 152.4$ ), 47.97 (s,  $C(2)$ ), 51.15 (s,  $MeO$ ), 61.64 (s,  $CH_2O$ ), 155.92 (s,  $NC=O$ ), 172.85 (s,  $C=O$ ).  $^{31}P\{^1H\}$  NMR ( $D_2O$ ,  $\delta$ , ppm): 17.72 (s).

**Synthesis of methyl esters of *N*-(spiroposphoranylmethyl)sarcosine 11 or proline 12.**

A mixture of spiroposphorane **D** (100 mmol) and bis[*N*-methyl-*N*-(methoxycarbonylmethyl)amino]methane or *N*-ethoxymethylproline methyl ester (110 mmol) was heated at 100 °C for 2 h. The resulting mixture was distilled under vacuum to give phosphoranes **11**, **12**.

**5-[*N*-Methyl-*N*-(methoxycarbonylmethyl)aminomethyl]-1,4,6,9-tetraoxa-5-phosphaspiro[4.4]nonane (11).** Yield: 83%. Bp: 130 °C (1.5 Torr). Anal. Calcd for  $C_9H_{18}NO_6P$ : C, 40.45; H, 6.79. Found: C, 40.31; H, 6.58%.  $^1H$  NMR ( $CDCl_3$ ,  $\delta$ , ppm,  $J/Hz$ ): 2.43 (s, 3 H,  $CH_3N$ ), 3.28 (d, 2 H,  $PCH_2N$ ,  $^3J_{HP} = 7.5$ ), 3.41 (d, 2 H,  $NCH_2C(O)$ ,  $^4J_{HP} = 2.2$ ), 3.46 (s, 3 H,  $CH_3O$ ), 3.91–3.98 (m, 8H, 2  $OCH_2CH_2O$ ).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ ,  $\delta$ , ppm,  $J/Hz$ ): 43.51 (d,  $MeN$ ,  $^3J_{CP} = 8.6$ ), 51.15 (s,  $MeO$ ), 57.89 (d,  $PCH_2N$ ,  $^1J_{CP} = 180.8$ ), 58.29 (d,  $NCH_2C(O)$ ,  $^3J_{CP} =$

7.5), 61.08 (d, OCH<sub>2</sub>CH<sub>2</sub>O, <sup>3</sup>J<sub>CP</sub> = 2.8), 171.36 (d, C=O, <sup>4</sup>J<sub>CP</sub> = 2.6). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): –9.63 (s).

**5-(2-Methoxycarbonylpyrrolidin-1-ylmethyl)-1,4,6,9-tetraoxa-5-phosphaspiro[4.4]nonane (12).** Yield: 74%. Bp: 168 °C (21.5 Torr). Anal. Calcd for C<sub>11</sub>H<sub>20</sub>NO<sub>6</sub>P: C, 45.05; H, 6.87. Found: C, 44.91; H, 6.72%. <sup>1</sup>H NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 1.36–1.52 (m, 2H, CH<sub>2</sub>). 1.71–2.57 (m, 2H, CH<sub>2</sub>). 3.40 (ABX m, 2 H, PCH<sub>2</sub>N, <sup>2</sup>J<sub>HP</sub> = 7.5, <sup>2</sup>J<sub>HP</sub> = 15.5, <sup>2</sup>J<sub>HH</sub> = 15.8), 3.30–3.44 (m, 3H, CH<sub>2</sub>N, CHN), 3.49 (s, 3 H, CH<sub>3</sub>O), 3.89–4.02 (m, 8H, 2 OCH<sub>2</sub>CH<sub>2</sub>O). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm, J/Hz): 17.78 (s, CH<sub>2</sub>), 22.24 (s, CH<sub>2</sub>), 51.23 (s, MeO), 54.40 (d, PCH<sub>2</sub>N, <sup>1</sup>J<sub>CP</sub> = 179.2), 54.46 (d, CH<sub>2</sub>N, <sup>3</sup>J<sub>CP</sub> = 2.9), 61.04 (d, OCH<sub>2</sub>CH<sub>2</sub>O, <sup>3</sup>J<sub>CP</sub> = 2.6), 65.13 (d, CHN, <sup>3</sup>J<sub>CP</sub> = 10.4), 174.31 (d, C=O, <sup>4</sup>J<sub>CP</sub> = 2.9). <sup>31</sup>P{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, δ, ppm): –9.37 (s).

## References

1. A. A. Prishchenko, M. V. Livantsov, D. N. Kustrya, E. V. Grigoriev, *Zh. Obshch. Khim.*, **1995**, 65, 1211–1213.
2. A. A. Prishchenko, M. V. Livantsov, O. P. Novikova, L. I. Livantsova, *Russ. J. Gen. Chem.*, **2006**, 76, 1960–1962. DOI: 10.1134/S1070363206120243
3. A. A. Prishchenko, M. V. Livantsov, O. P. Novikova, L. I. Livantsova, V. S. Petrosyan, *Heteroat. Chem.*, **2010**, 21, 361–367. DOI: 10.1002/hc.20620
4. A. A. Prishchenko, M. V. Livantsov, O. P. Novikova, L. I. Livantsova, V. S. Petrosyan, *Heteroat. Chem.*, **2010**, 21, 515–520. DOI: 10.1002/hc.20642
5. A. A. Prishchenko, R. S. Alekseyev, M. V. Livantsov, O. P. Novikova, L. I. Livantsova, V. I. Terenin, V. S. Petrosyan, *Heteroat. Chem.*, **2017**, 28, e21353. DOI: 10.1002/hc.21353