

## Phosphonate-amidophosphate rearrangements in phosphorylated enamides and imines

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Dedicated to Professor Józef Drabowicz on the occasion of his 76th anniversary

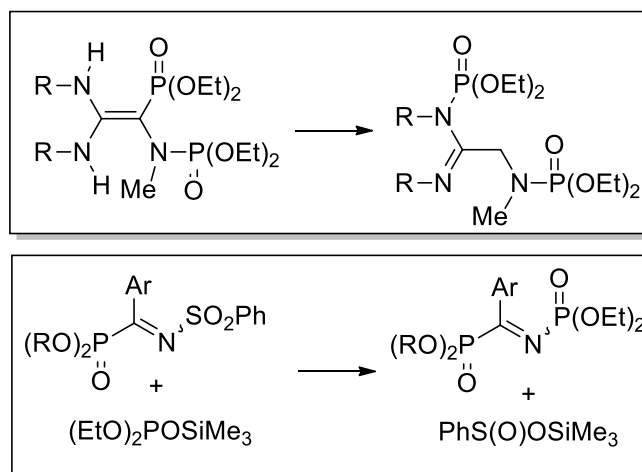
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### Abstract

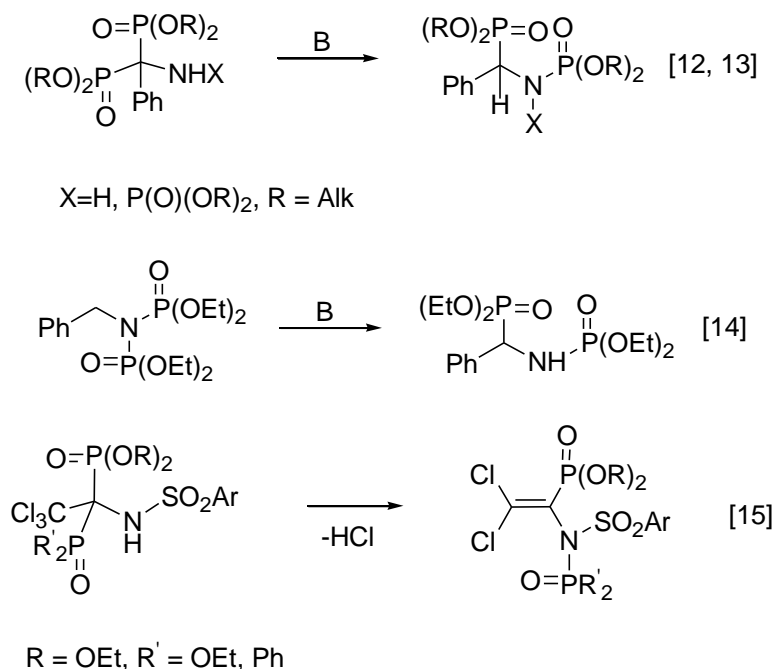
Reactions of C,N-diphosphorylated dichlorovinyl amides with primary amines lead to the respective 2,2-diaminovinylphosphonates. The latter undergo phosphoro- and prototropic rearrangements under heating to give diphosphorylated amidines. N-Sulfonyl iminophosphonates are converted into the corresponding N-phosphonyl iminophosphonates by reaction with diethyltrimethylsilylphosphite. The reaction of the latter with phosphonylimino trifluoropyruvate leads to the reduction of the C=N bond. Trimethylsilyl chloride mediated rearrangement of geminal amidobisphosphonates yields N-phosphonyl iminophosphonates.



**Keywords:** Phosphonates, amidophosphates, imines, amidines, enamides sulfonyl, rearrangements.

## Introduction

C,N-Diphosphonylated derivatives combine, in their structure, fragments of two important types of compounds, aminophosphonates and phosphoramidates. The first can serve as surrogates for amino acids and reveal a broad spectrum of biological activity.<sup>1-10</sup> Phosphoramidates, on the other hand, can be considered as analogues of the transition state of the hydrolysis of the peptide bond and are potent inhibitors of peptidases.<sup>11</sup> In addition, C,N-transfer of the phosphonyl group allows interconversions of aminophosphonates and phosphoramidates. Examples of phosphonate-amidophosphate rearrangements<sup>12,13,15</sup> in di- and triphosphorylated systems as well as reverse 1,2-N→C phosphonyl transfer (amidophosphate-phosphonate rearrangement)<sup>14</sup> are shown in Scheme 1.



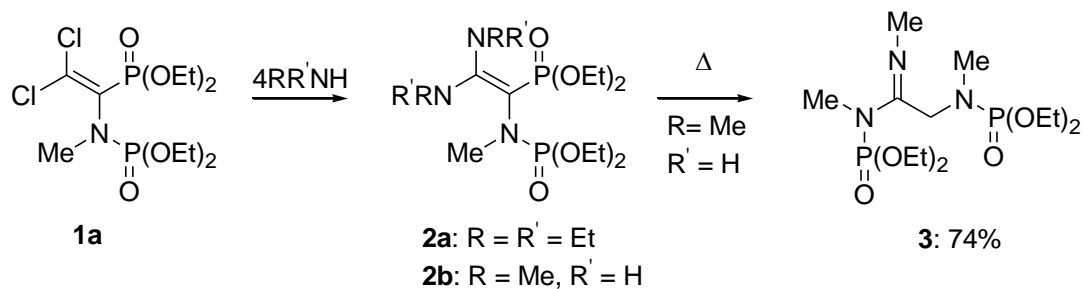
**Scheme 1.** Phosphonate-amidophosphate and amidophosphate-phosphonate rearrangements.

The study of such processes is important both from theoretical and synthetic points of view. The present paper reports on phosphonate-amidophosphate rearrangements accompanying reactions of diphosphorylated dichlorovinyl amides with amines and iminophosphonates with diethyltrimethylsilyl phosphite.

## Results and Discussion

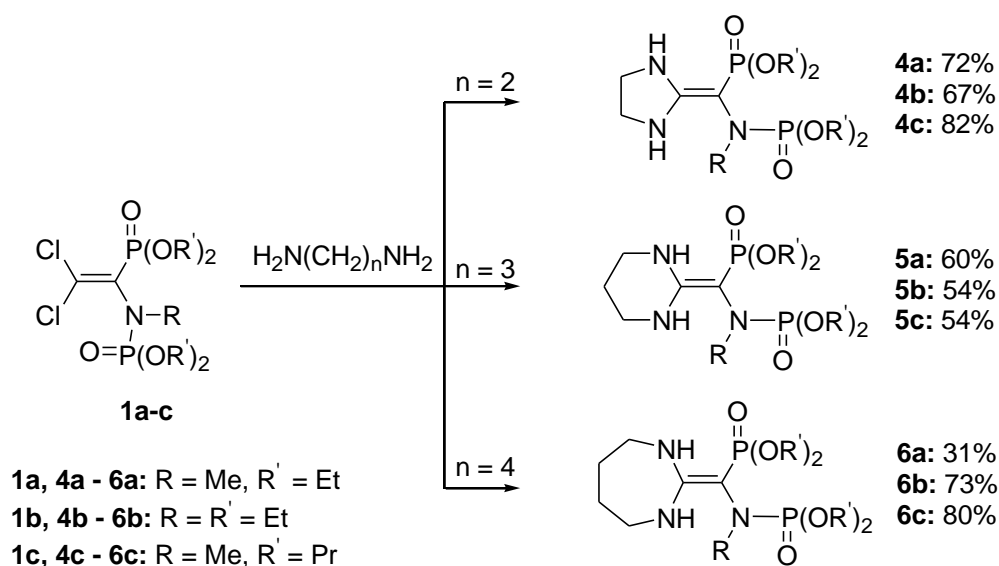
### Reactions of C,N-diphosphorylated dichlorovinyl amides with primary amines.

Activated chlorine atoms in C,N-diphosphorylated enamide **1a** are readily substituted with nucleophiles.<sup>16</sup> Thus, the reaction with amines proceeds under mild conditions (ether, r.t.) and leads to 2,2-diaminovinylphosphonates **2a,b**. The compound **2a** with diethylamino groups is thermally stable. At the same time, 2,2-bis(methylamino)vinylphosphonate **2b**, bearing an N-hydrogen, undergoes an unusual 1,3-C→N transfer of a phosphonyl group during distillation, accompanied by 1,3-N→C transfer of two protons to form N-phosphorylated amidine **3** (Scheme 1).



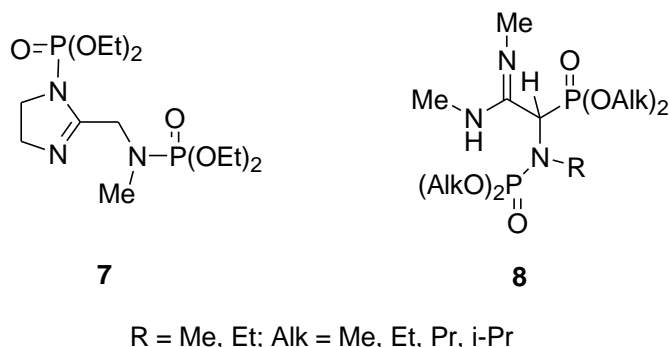
**Scheme 2.** Reactions of **1a** with primary and secondary amines.

Reactions of C,N-diphosphorylated dichlorovinyl amides **1a-c** with primary diamines proceed similarly with formation of vinylphosphonates, incorporating imidazolidine (**4a-c**), hexahydropyrimidine (**5a-c**), or 1,3-diazepane (**6a-c**) heterocyclic residues.



**Scheme 3.** Reactions of enamides **1a-c** with primary diamines.

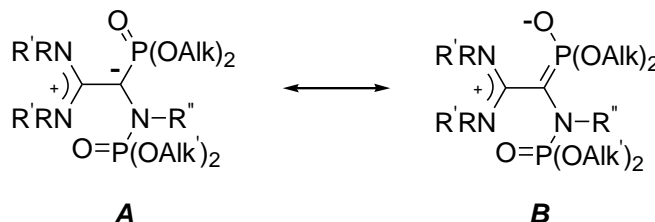
Imidazolidine **4a** upon heating (175 °C, 25 min) also undergoes combined phosphorotropic and prototropic isomerizations, leading to N-phosphorylated imidazoline **7** with a conversion of 70% according to <sup>31</sup>P NMR.



**Scheme 4.** Spectrally detected cyclic amidine **7** and the literature claimed<sup>16,17</sup> structure **8** of the reaction products of dichlorides such as **1** with primary amines.

Unfortunately, further heating leads to the degradation of the molecule with the formation of a number of unidentified products. Compounds **5a** and **6a**, when heated to 175 °C, also undergo degradation with the formation of a complex mixture in which isomerization products similar to **7** were identified by  $^{31}\text{P}$  NMR.

The unusual isomerization of **2b** to **3** is due to the electronic influence of electron-releasing  $\text{RR}'\text{N}$  groups, giving compounds **2** an ylide-like character (Scheme 5).



**Scheme 5.** Electronic structure of phosphorylated 2,2-diaminovinylphosphonates.

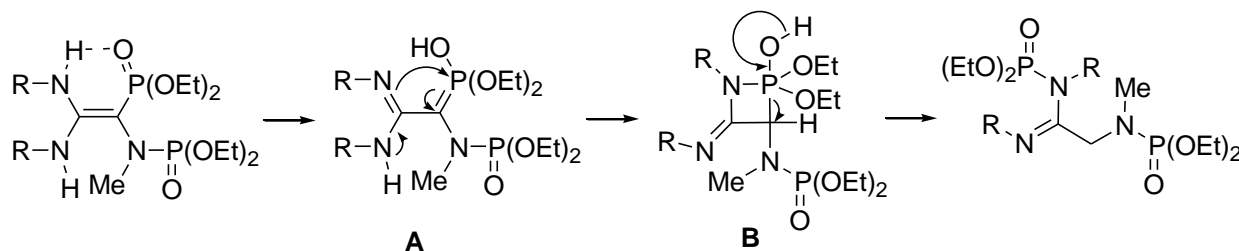
Spectral data are consistent with the contribution of resonance forms *A* and *B* to the electronic structure of aminals **2**. Given below are chemical shifts of olefinic carbons and phosphonate phosphorus atoms in the  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR spectra for compounds **1a** and **2a** (Scheme 6):

	$\Delta\delta = \delta(2a) - \delta(1)$ , ppm	
C-1	$\delta_{\text{C}}$ 132.6 ppm $^1J_{\text{CP}}$ 206 Hz	$\delta_{\text{C}}$ 86 ppm $^1J_{\text{CP}}$ 245 Hz - 49
C-2	$\delta_{\text{C}}$ 139 ppm $^1J_{\text{CP}}$ 42 Hz	$\delta_{\text{C}}$ 167 ppm $^1J_{\text{CP}}$ 40.3 Hz 28.7
$\delta_{\text{CP}}^{\text{P}}$	10.0	25.4 15.4

**Scheme 6.** Selected spectral data of compounds **1a** and **2a**.

It is very interesting to note that the signal of the C-1 carbon atom of compound **2a** is substantially shifted upfield (49 ppm) and that of the C-2 atom to a lower field (28.7 ppm), relative to compound **1a**, indicating a significant contribution of the bipolar resonance form *A*. The position of the phosphorus atom signal in compound **2a** and the large value of P-C coupling constant ( $\delta_{\text{P}}$  29.7 ppm,  $^1J_{\text{CP}}$  245 Hz) are consistent with the contribution of ylide-like structure *B*. The spectral distinctions indicate significant differences in the electronic nature of the C=C bond in compounds **1a** and **2a**.

A possible isomerization mechanism is shown in the Scheme 7. Protonation of the nucleophilic oxygen atom of the phosphonyl group, followed by proton transfer from nitrogen to carbon (arrows on **A**) and subsequent migration of the phosphonium-like group from carbon to nitrogen, possibly via the four centered cyclic intermediate **B**, results in the highly functionalized amidine **3**.

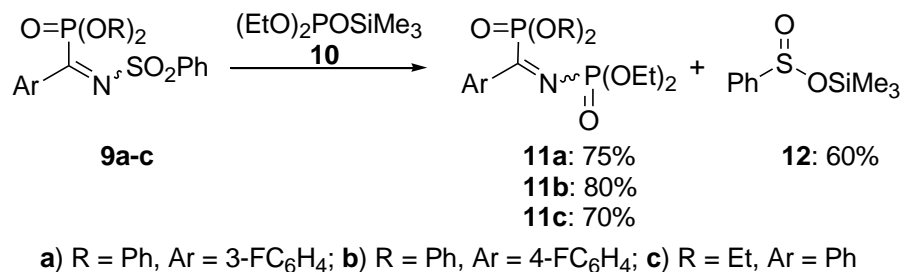


**Scheme 7.** Proposed mechanism for formation of compound **3**.

It should be noted that for compounds **2b**, **4a-c**, **5a-c**, **6a-c**, a possible isomeric structure of type **8** was not detected. Spectral data of these compounds are consistent with an enamide rather than an amidine structure. Previously described compounds **8** (R = Me, Et; R' = Me, Et, Pr),<sup>16,17</sup> claimed to be imine tautomers of enamides analogous to **2b**, most likely have the structure of N,N-diphosphorylated rather than C,N-diphosphorylated amidines. The NMR spectra of compounds **2-6** are in accordance with their structure. The most indicative of the amidine structure **3** are signals of CH<sub>2</sub>N and C=N carbon atoms in the <sup>13</sup>C NMR spectra (44.8-53 ppm and 154.2-153.7 ppm, respectively) and the absence of a carbon atom signal with a high value of C-P coupling constant, characteristic of phosphonates. The signals of amidophosphate phosphorus atoms of amidine **3** (2.7-10.3 ppm) differ significantly from those of compounds **2**, **4-6** with an isomeric phosphonate structure (27-29 ppm). Doubling of signals in the <sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P NMR spectra of compound **3** is associated with restricted rotation around the C-N bond and/or *E-Z* isomerism of the C=N bond, which is characteristic of amidines.<sup>18,19</sup>

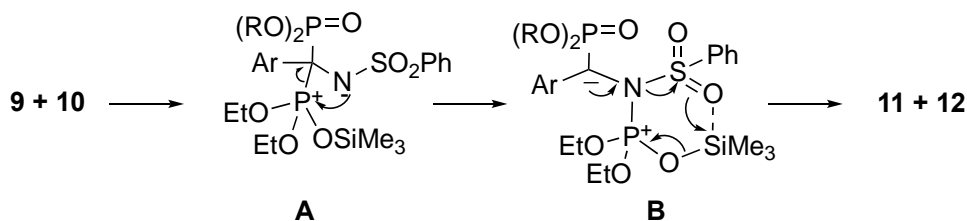
#### Rearrangements in reactions of N-sulfonylimino phosphonates with diethyltrimethylsilyl phosphite **10**.

It was found that the reactions of iminophosphonates **9** with the silyl phosphite **10** occur rather unusually and lead to N-phosphonylimino phosphonates **11** in high yields (Scheme 8).



**Scheme 8.** Silyl phosphite mediated conversion of N-sulfonylimino phosphonates **9** into N-phosphonylimino phosphonates **11**.

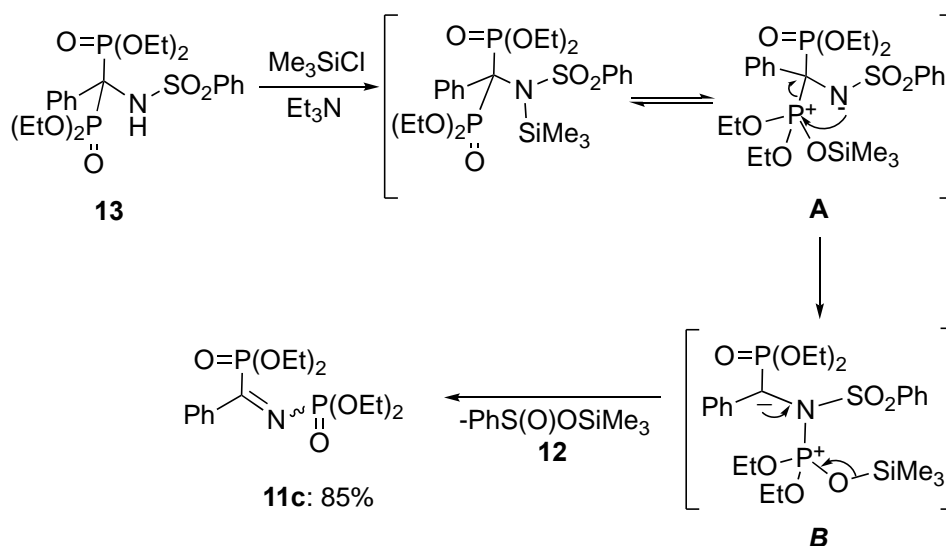
Such an unexpected result can be explained as shown in the Scheme 9. Nucleophilic attack of phosphite on the most electrophilic center, the imine carbon atom, followed by C-N transfer of the phosphorus group in 1,1-diphosphonated product **A** leads to C,N-diphosphorylated dipolar intermediate **B** stabilized by elimination of silyl sulfinate **12**. It should be noted that despite the complex multi-step nature of the interaction, iminophosphonates **11** are formed almost quantitatively, which indicates the high chemoselectivity of the process. By distillation, silyl phenylsulfinate **13** was also isolated and fully characterized. When exposed in air, it is converted to free phenylsulfonic acid.



**Scheme 9.** Proposed mechanism of conversion of **9** into **11**.

Scheme 9 represents a novel simple method for converting sulfonylimino phosphonates into corresponding phosphonylimino phosphonates, important precursors of biorelevant aminophosphonic derivatives.<sup>20,21</sup>

The individual steps of the process in Scheme 9 were simulated in reaction of diphosphonate **13** with chlorotrimethylsilane in the presence of base. Silylation was found to be accompanied by C→N phosphonyl transfer leading to N-phosphonylimino phosphonates **11**. It is most likely that the initially formed N-silylsulfonylamide is unstable and even at room temperature undergoes reversible N→O migration of the trimethylsilyl group, followed by C→N transfer of the phosphonium group and stabilization of bipolar intermediate **B** by elimination of trimethylsilyl sulfinate **12** (Scheme 10). The reaction in Scheme 10 represents a novel method of synthesizing phosphonylimino phosphonates from geminal amidobisphosphonates.

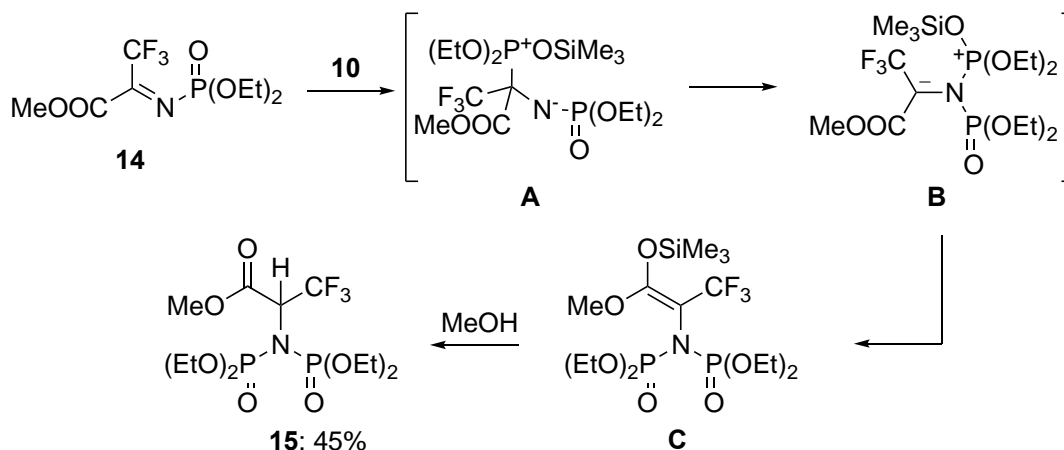


**Scheme 10.** Proposed mechanism for conversion of bisphosphonate **13** to iminophosphonates **11**.

Spectral data of phosphonylimino phosphonates **11** confirm their structure. Phosphorus nuclei signals resonate in the typical imidoyl phosphonates region (3.6-4.0 ppm and -5.2 to -6.4 ppm) for ethyl and phenyl esters, respectively. The most characteristic feature of N-phosphonylimino phosphonates **11** is the high spin-spin coupling constant of non-equivalent phosphorus nuclei ( $^3J_{PC=NP}$  118–126 Hz). In the IR spectra, an intense band of C=N bond valence vibrations (1610-1650  $cm^{-1}$ ) appears. The presence of the P-C=N fragment is unambiguously confirmed by NMR  $^{13}C$  spectra, in which the signal of C=N carbon atom with a high value of direct C-P coupling constant is manifested ( $\delta_C$  174.6-181.1 ppm,  $^1J_{CP}$  181-204 Hz).

Propensity of phosphorylated imines to isomerizations, promoted by the organylsilyl group, clearly reveals itself in reactions of trifluoropyruvate N-phosphonylimine **14** with phosphites. Dialkyl phosphites,  $(RO)_2P(O)H$ ,

readily add across C=N bond of **14** with the formation of stable adducts with P-C bond.<sup>22</sup> At the same time, trimethylsilyl phosphite **10**, which is often considered to be the synthetic equivalent of diethyl phosphite, reacts with **14** to give N,N-diphosphorylated derivative of trifluoroalanine **15**, resulting from transformations of the primary addition product **A** (Scheme 11). This unexpected result can be explained by C-N transfer of phosphorus group in quasi-phosphonium intermediate **A** followed by silyl migration in bipolar ion **B** and deprotection of acetal **C** with methanol.



**Scheme 11.** Reaction of iminopyruvate **14** with silylphosphite **10**.

## Conclusions

We have demonstrated that 1,2- and 1,3-C-N transfers of phosphorus groups are typical of phosphorylated imines and enamides and should be considered in the development of synthetic strategies. Unexpected thermal conversion of phosphorylated 2,2-diaminovinylphosphonates to N-phosphorylated amidines has been found. A new method has been developed for the conversion of N-sulfonyliminophosphonates and geminal N-sulfonylamidobisphosphonate to N-phosphonylimino phosphonates, important precursors of biorelevant aminophosphonates.

## Experimental Section

**General.** <sup>1</sup>H, <sup>19</sup>F, <sup>31</sup>P and <sup>13</sup>C NMR spectra were recorded using Bruker Avance NMR spectrometers operating at 300 and 400 MHz <sup>1</sup>H frequencies; 75.8 and 125.7 MHz for <sup>13</sup>C experiments; 188 MHz for <sup>19</sup>F; 81 and 202.3 MHz for <sup>31</sup>P. Chemical shifts are reported relative to internal TMS (<sup>1</sup>H, <sup>13</sup>C), CFCl<sub>3</sub> (<sup>19</sup>F) and external 85%-H<sub>3</sub>PO<sub>4</sub> (<sup>31</sup>P) standards. Melting points are uncorrected. Solvents were dried before use according to standard methods. Elemental analysis was carried out in the analytical laboratory of Institute of Organic Chemistry, NAS of Ukraine.

**Reaction of 1a with MeNH<sub>2</sub>.** An excess of dry methylamine was passed through a solution of **1a** (2.98 g, 7.5 mmol) in dry Et<sub>2</sub>O (15 mL) at 0 °C. The precipitate was filtered off and the filtrate was concentrated. The crude product contained mainly compound **2b**. <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 202 MHz) δ 10.2 (NP), 27.6 (CP).

Distillation of the crude product afforded **3**. Yield 2.14 g (74%), bp 118-120 °C (0.09 Torr),  $n_D^{20}$  1.4586.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.3 m (12H,  $\text{MeCH}_2$ ), 2.61 and 2.68, doublets,  $^3J_{\text{HP}}$  9.9 and 9.6 Hz (3H, MeN), 2.80 and 2.96, doublets,  $^3J_{\text{HP}}$  9 and 7.2 Hz (3H, MeN), 3.22 and 3.28 (3H, MeN=), 3.9-4.3 m (10H,  $\text{NCH}_2$ ,  $\text{OCH}_2$ ).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  15.8-15.9 (CMe), 36.8 and 37.3 (MeN=), 32.8 and 33.2, doublets,  $J_{\text{CP}}$  3.2 and 2 Hz (MeN), 33.6 and 33.9, doublets,  $^2J_{\text{CP}}$  2.9 and 1.6 Hz (MeN) 44.8 and 53.0 ( $\text{CH}_2\text{N}$ ), 61.8, 62.0, 62.6, and 62.7, doublets,  $^2J_{\text{CP}}$  5.1, 5.9, 4.7, and 5 Hz ( $\text{OCH}_2$ ), 154.2 dd (C=N,  $J_{\text{CP}}$  3 and 5 Hz), 157.3 t (C=N,  $J_{\text{CP}}$  5 Hz).  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 202 MHz)  $\delta$  10.3 (1P), 5.5 and 2.7 (1P). Anal. calcd for  $\text{C}_{13}\text{H}_{31}\text{N}_3\text{O}_6\text{P}_2$ , %: C 40.31; H 8.07; N 10.85; P 15.99. Found, %: C 40.01; H 7.96; N 10.62; P 16.18.

**General procedure for the reactions of 1a-c with  $\text{NH}_2(\text{CH}_2)_n\text{NH}_2$ , n=2, 3, 4.** A solution of appropriate diamine (8 mmol) in  $\text{Et}_2\text{O}$  (40 mL) was added at 0 °C to a stirred solution of enamide (**1a-c**) (2.5 mmol) in  $\text{Et}_2\text{O}$  (30 mL). After completion of reaction (7-10 days,  $^{31}\text{P}$  NMR control), the precipitate was filtered off. The organic layer was concentrated, the residue was crystallized from petroleum ether or purified by column chromatography.

**Diethyl ((diethoxyphosphoryl)(imidazolidin-2-ylidene)methyl)(methyl)phosphoroamidate (4a).** Obtained from **1a** (1 g, 2.5 mmol) and ethylenediamine (0.48 g, 8 mmol). Yield 0.69 g (72%), colorless solid, mp 116-117 °C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.31 m (12H,  $\text{OCH}_2\text{CH}_3$ ), 2.77 d (3H, NMe,  $J = 7.5$  Hz), 3.49 m (4H,  $\text{NCH}_2\text{CH}_2\text{N}$ ), 4.07 m (8H,  $\text{OCH}_2$ ), 5.31 s (1H, NH), 6.62 s (1H, NH).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 75.43 MHz)  $\delta$  15.9-16.4 (CMe), 37.1 d (MeN,  $^2J_{\text{CP}}$  11.9 Hz), 43.1 and 44.1 ( $\text{CH}_2\text{N}$ ), 60.5 d ( $\text{OCH}_2$ ,  $^2J_{\text{CP}}$  5 Hz), 60.7 d ( $\text{OCH}_2$ ,  $^2J_{\text{CP}}$  3.2 Hz), 62.3 d ( $\text{OCH}_2$ ,  $^2J_{\text{CP}}$  6.4 Hz), 62.5 d ( $\text{OCH}_2$ ,  $^2J_{\text{CP}}$  6 Hz), 70.6 d (=CP,  $^1J_{\text{CP}}$  251 Hz), 165.8 d (=CN,  $^2J_{\text{CP}}$  45.4 Hz).  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 121.42 MHz)  $\delta$  10.4 (NP), 27.5 (CP). Anal. calcd for  $\text{C}_{13}\text{H}_{29}\text{N}_3\text{O}_6\text{P}_2$ , %: C 40.52; H 7.59; P 16.08. Found, %: C 40.39; H 7.46; P 16.08. Heating the compound **4a** for 3 hours at 170 °C results in isomerization to **7** with 70% conversion:  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 121.42 MHz)  $\delta$  7.6 (NP), 9.9 (NP). Longer heating is accompanied by the appearance of decomposition products.

**Diethyl ((diethoxyphosphoryl)(imidazolidin-2-ylidene)methyl)(ethyl)phosphoroamidate (4b).** Obtained from **1b** (1.03 g, 2.5 mmol) and ethylenediamine (0.48 g, 8 mmol). Yield 0.67 g (67%), colorless solid, mp 72-73 °C (petroleum ether).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.11 t (3H,  $\text{NCH}_2\text{CH}_3$ ), 1.30 m (12H,  $\text{OCH}_2\text{CH}_3$ ), 3.20 m (2H,  $\text{NCH}_2\text{Me}$ ), 3.47 m (4H,  $\text{NCH}_2\text{CH}_2\text{N}$ ), 4.07 m (8H,  $\text{OCH}_2$ ), 5.27 s (1H, NH), 6.72 s (1H, NH).  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 121.42 MHz)  $\delta$  10.6 (NP), 27.5 (CP). Anal. calcd for  $\text{C}_{14}\text{H}_{31}\text{N}_3\text{O}_6\text{P}_2$ , %: C 42.10; H 7.82; P 15.51. Found, %: C 41.93; H 7.75; P 15.46.

**Dipropyl ((dipropoxyphosphoryl)(imidazolidin-2-ylidene)methyl)(methyl)phosphoroamidate (4c).** Obtained from **1a** (1.14 g, 2.5 mmol) and ethylenediamine (0.48 g, 8 mmol). Yield 0.90 g (82%), colorless solid, mp 38-41 °C (petroleum ether).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  0.96 m (12H,  $\text{OCH}_2\text{CH}_2\text{CH}_3$ ), 1.69 m (8H,  $\text{OCH}_2\text{CH}_2\text{CH}_3$ ), 2.77 d (3H, NMe,  $J = 7.8$  Hz), 3.49 m (4H,  $\text{NCH}_2\text{CH}_2\text{N}$ ), 3.96 m (8H,  $\text{OCH}_2$ ), 5.27 s (1H, NH), 6.59 s (1H, NH).  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 121.42 MHz)  $\delta$  10.6 (NP), 27.5 (CP). Anal. calcd for  $\text{C}_{17}\text{H}_{37}\text{N}_3\text{O}_6\text{P}_2$ , %: C 46.25; H 8.45; P 14.03. Found, %: C 45.92; H 8.64; P 13.87.

**Diethyl ((diethoxyphosphoryl)(tetrahydropyrimidin-2(1H)-ylidene)methyl)(methyl)phosphoroamidate (5a).** Obtained from **1a** (1 g, 2.5 mmol) and 1,3-diaminopropane (0.59 g, 8 mmol). Yield 0.60 g (60%), colorless solid, mp 87-88 °C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.30 t (12H,  $\text{OCH}_2\text{CH}_3$ ), 1.88 m (2H,  $\text{NCH}_2\text{CH}_2$ ), 2.72 d (3H, NMe,  $J$  7 Hz), 3.22-3.30 m (4H,  $\text{NCH}_2\text{CH}_2$ ), 4.05 m (8H,  $\text{OCH}_2$ ), 5.38 s (1H, NH), 7.58 s (1H, NH).  $^{31}\text{P-NMR}$  ( $\text{CDCl}_3$ , 121.42 MHz)  $\delta$  10.9 (NP), 29.0 (CP). Anal. calcd for  $\text{C}_{14}\text{H}_{31}\text{N}_3\text{O}_6\text{P}_2$ , %: C 42.10; H 7.82; P 15.51. Found, %: C 41.89; H 7.96; P 15.65.

**Diethyl ((diethoxyphosphoryl)(tetrahydropyrimidin-2(1H)-ylidene)methyl)(ethyl)phosphoroamidate (5b).** Obtained from **1b** (1.03 g, 2.5 mmol) and 1,3-diaminopropane (0.59 g, 8 mmol). Yield 0.56 g (54%), colorless solid, mp 48-51 °C.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.09 t (3H,  $\text{NCH}_2\text{CH}_3$ ), 1.29 t (12H,  $\text{OCH}_2\text{CH}_3$ ), 1.86 m (2H,  $\text{NCH}_2\text{CH}_2$ ), 3.0-3.2 m (6H,  $\text{NCH}_2\text{CH}_2$  and  $\text{NCH}_2\text{CH}_3$ ), 4.05 m (8H,  $\text{OCH}_2$ ), 5.40 s (1H, NH), 7.66 s (1H, NH).  $^{31}\text{P-NMR}$



(CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  10.7 (NP), 28.9 (CP). Anal. calcd for C<sub>15</sub>H<sub>33</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 43.58; H 8.05; P 14.99. Found, %: C 43.19; H 8.34; P 15.31.

**Dipropyl ((dipropoxyphosphoryl)(tetrahydropyrimidin-2(1H)-ylidene)methyl)(methyl)phosphoroamidate (5c).** Obtained from **1c** (1.14 g, 2.5 mmol) and 1,3-diaminopropane (0.59 g, 8 mmol). The crude product was purified by column chromatography (SiO<sub>2</sub>, MeOH). Yield 0.61 g (54%),  $n_D^{20}$  1.4852. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  0.96 m (12H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.68 m (8H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.88 m (2H, NCH<sub>2</sub>CH<sub>2</sub>), 2.72 d (3H, NMe), 3.21-3.29 m (4H, NCH<sub>2</sub>CH<sub>2</sub>), 3.93 m (8H, OCH<sub>2</sub>), 5.34 s (1H, NH), 7.58 s (1H, NH). <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  11.1 (NP), 29.0 (CP). Anal. calcd for C<sub>18</sub>H<sub>39</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 47.47; H 8.63; %: P 13.60. Found, %: C 47.31; H 8.78; P 13.62.

**Diethyl ((diethoxyphosphoryl)(1,3-diazepene-2-ylidene)methyl)(methyl)phosphoroamidate (6a).** Obtained from **1a** (1 g, 2.5 mmol) and 1,4-diaminobutane (0.70 g, 8 mmol). The crude product was purified by column chromatography (SiO<sub>2</sub>, MeOH). Yield 0.32 g (31%),  $n_D^{20}$  1.4883. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  1.30 t (12H, OCH<sub>2</sub>CH<sub>3</sub>), 1.57 m (4H, C-CH<sub>2</sub>-C), 2.74 d (3H, NMe, *J* 7.5 Hz), 3.05-3.20 m (4H, NCH<sub>2</sub>CH<sub>2</sub>), 4.06 m (8H, OCH<sub>2</sub>), 5.41 br (1H, NH), 7.89 br (1H, NH). <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  10.1 (NP), 27.3 (CP). Anal. calcd for C<sub>15</sub>H<sub>33</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 43.58; H 8.05; P 14.99. Found, %: C 43.86; H 8.23; P 14.85.

**Diethyl ((diethoxyphosphoryl)(1,3-diazepene-2-ylidene)methyl)(ethyl)phosphoroamidate (6b).** Obtained from **1b** (1.03 g, 2.5 mmol) and 1,4-diaminobutane (0.70 g, 8 mmol). The crude product was purified by column chromatography (SiO<sub>2</sub>, MeOH). Yield 0.78 g (73%),  $n_D^{20}$  1.4882. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  1.05 t (3H, NCH<sub>2</sub>CH<sub>3</sub>), 1.30 t (12H, OCH<sub>2</sub>CH<sub>3</sub>), 1.4-1.7 m (4H, C-CH<sub>2</sub>-C), 2.9-3.3 m (6H, NCH<sub>2</sub>), 4.07 m (8H, OCH<sub>2</sub>), 5.48 br (1H, NH), 7.1 br (1H, NH). <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  10.1 (NP), 27.5 (CP). Anal. calcd for C<sub>16</sub>H<sub>35</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 43.58; H 8.05; P 14.49. Found, %: C 43.39; H 8.16; P 14.58.

**Dipropyl ((dipropoxyphosphoryl)(1,3-diazepene-2-ylidene)methyl)(methyl) phosphoroamidate (6c).** Obtained from **1c** (1.14 g, 2.5 mmol) and 1,4-diaminobutane (0.70 g, 8 mmol). The crude product was purified by column chromatography (SiO<sub>2</sub>, MeOH). Yield 0.94 g (80%),  $n_D^{20}$  1.4838. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  0.96 m (12H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.57 m (4H, C-CH<sub>2</sub>-C), 1.68 m (8H, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.74 d (3H, NMe, *J* 6.3 Hz), 3.0-3.1 m (4H, NCH<sub>2</sub>), 3.94 m (8H, OCH<sub>2</sub>), 5.41 s (1H, NH), 7.33 s (1H, NH). <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  10.1 (NP), 27.3 (CP). Anal. calcd for C<sub>19</sub>H<sub>41</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 48.61; H 8.80; P 13.19. Found, %: C 48.27; H 8.97; P 13.38.

**General procedure for reactions of iminophosphonates 9a-c with phosphite 10.** Trimethylsilylphosphite (**10**) (1.4 g, 6.6 mmol) was added at 0 °C to a stirred solution of iminophosphonate (**9a, b**) (3.27 g, 6.6 mmol) or (**9c**) (2.51 g, 6.6 mmol) in Et<sub>2</sub>O (10 mL). After 24 h, solvent was evaporated at rt, trimethylsilylsulphinate (**12**) was distilled off [yield 0.85 g (60%), bp 60 °C (0.3 (0.3 Torr) [lit.<sup>23</sup> bp 55-60 °C (0.3 Torr)] to give pure compound (**11a-c**) in 2.43 g, (75%), 2.59 g (80%), and 1.74 g, (70%) yields, which were identified by comparison of <sup>1</sup>H, <sup>19</sup>F, <sup>31</sup>P NMR spectra with literature data.<sup>13</sup>

**Reaction of 13 with chlorotrimethylsilane.** Triethylamine (0.78 g 7.7 mmol) and trimethylchlorosilane (0.91 g, 8.3 mmol) was added to a solution of bisphosphonate (**13**) (3.32 g, 6.4 mmol) in dry Et<sub>2</sub>O (10 mL). After 24 h, the formed precipitate was filtered off, and the filtrate was evaporated to afford (**11c**)<sup>13</sup> in 85% yield.

**Methyl 2-[bis(diethoxyphosphoryl)amino]-3,3,3-trifluoropropionate (15).** Trimethylsilylphosphite (**10**) (0.18 g, 1 mmol) was added to a stirred solution of imine (**14**) (0.29 g, 1 mmol) in Et<sub>2</sub>O (10 mL). After 1 h, MeOH (1 mL) was added to the reaction mixture, the solvent was evaporated, the residue was washed with petroleum ether to afford **15**. Yield 0.19 g (45%). IR (CCl<sub>4</sub>),  $\nu$  1080 (POC), 1280 (P=O), 1740 (C=O) cm<sup>-1</sup>. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  1.33–1.39 m (12 H, CH<sub>3</sub>CH<sub>2</sub>), 3.85 s (3H, CH<sub>3</sub>O), 4.05-4.28 m (8H, CH<sub>2</sub>O), 5.15 dq (1 H, CH, <sup>3</sup>J<sub>HP</sub> 19.5 Hz, <sup>3</sup>J<sub>HF</sub> 8 Hz). <sup>19</sup>F-NMR (CDCl<sub>3</sub>, 282.2 MHz)  $\delta$  –68.3 d (<sup>3</sup>J<sub>FF</sub> 8 Hz). <sup>31</sup>P-NMR (CDCl<sub>3</sub>, 121.42 MHz)  $\delta$  2.9 br. Anal. calcd for C<sub>14</sub>H<sub>31</sub>N<sub>3</sub>O<sub>6</sub>P<sub>2</sub>, %: C 33.57; H 5.63; P 14.43. Found, %: C 33.48; H 5.71; P 14.29.

## Supplementary Material

Slightly modified procedures and  $^1\text{H}$ ,  $^{31}\text{P}$  NMR data for previously<sup>11, 12</sup> described compounds **1a-c**, **2a** are presented in the Supplementary Material file associated with this article.

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