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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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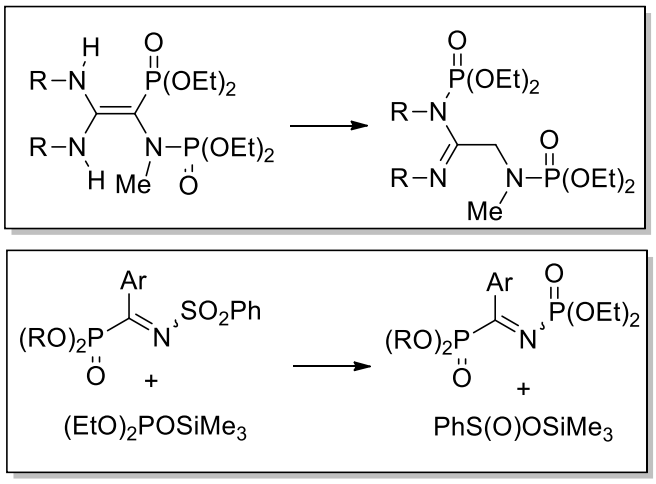
Abstract

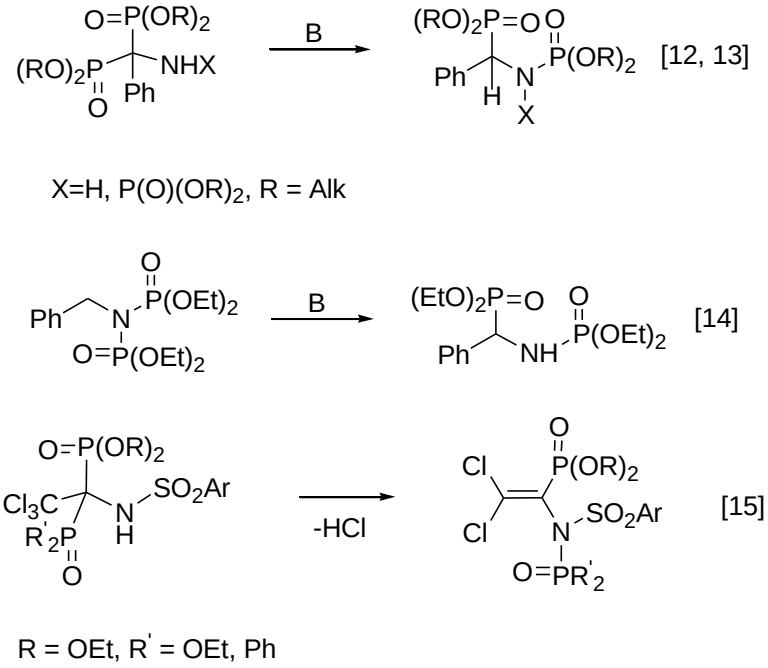
Reactions of C,N-diphosphorylated dichlorovinyl amides with primary amines lead to the respective 2,2-diaminovinylphosphonates. The latter undergo phosphoro- and prototropic rearrangements under heating to give diphosphorylated amidines. N-Sulfonyl iminophosphonates are converted into the corresponding 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 phosphonamides. The first can serve as surrogates for amino acids and reveal a broad spectrum of biological activity.[1-10] Phosphonamides, 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.[11] In addition, C,N-transfer of the phosphonyl group allows interconversions of aminophosphonates and phosphonamides. Examples of phosphonate-amidophosphate rearrangements[12,13,15] in di- and triphosphorylated systems as well as reverse 1,2-N→C phosphonyl transfer (amidophosphate-phosphonate rearrangement)[14] are shown in Scheme 1.



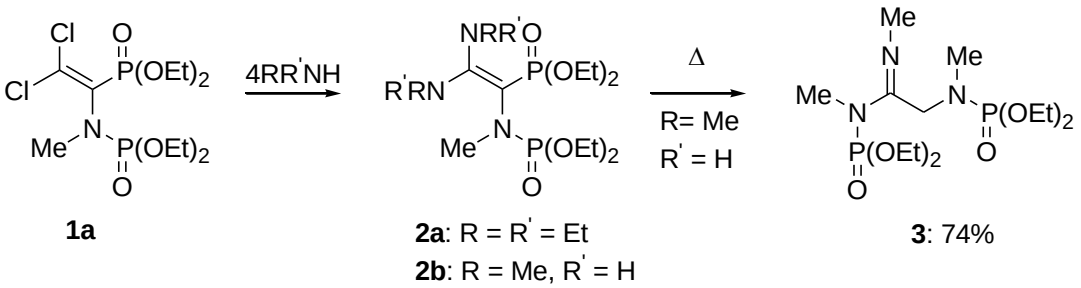
Scheme 1. Phosphonate-amidophosphate and amidophosphate-phosphonate rearrangements.

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.[16] 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).



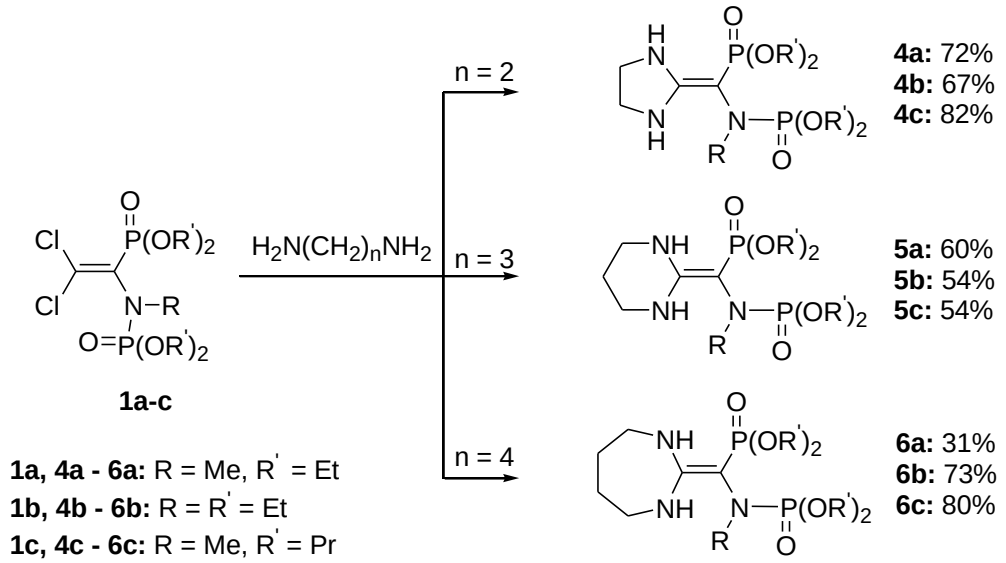
1a

2a: R = R' = Et
2b: R = Me, R' = H

3: 74%

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.

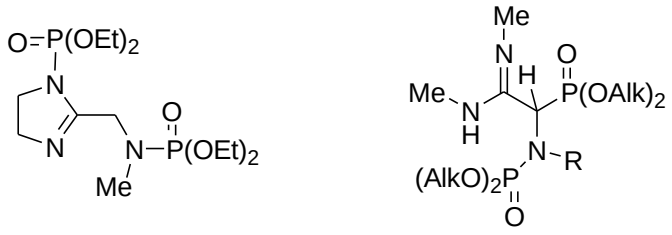


1a-c

1a, 4a - 6a: R = Me, R' = Et
1b, 4b - 6b: R = R' = Et
1c, 4c - 6c: R = Me, R' = Pr

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 ^{31}P NMR.



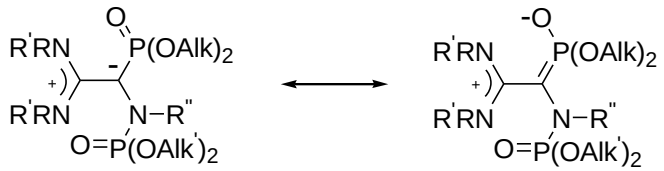
7 **8**

R = Me, Et; Alk = Me, Et, Pr, i-Pr

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

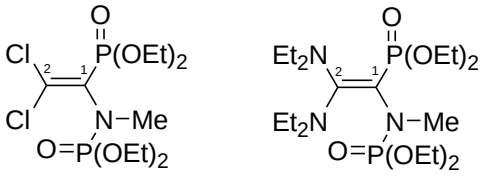
Unfortunately, further heating leads to the degradation of the molecule with the formation of a number of unidentified products. Compounds **5a** and **6a**, when heated to 175 °C, also undergo degradation with the formation of a complex mixture in which isomerization products similar to **7** were identified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

The unusual isomerization of **2b** to **3** is due to the electronic influence of electron-releasing RR'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}C, ^{31}P NMR spectra for compounds **1a** and **2a** (Scheme 6):

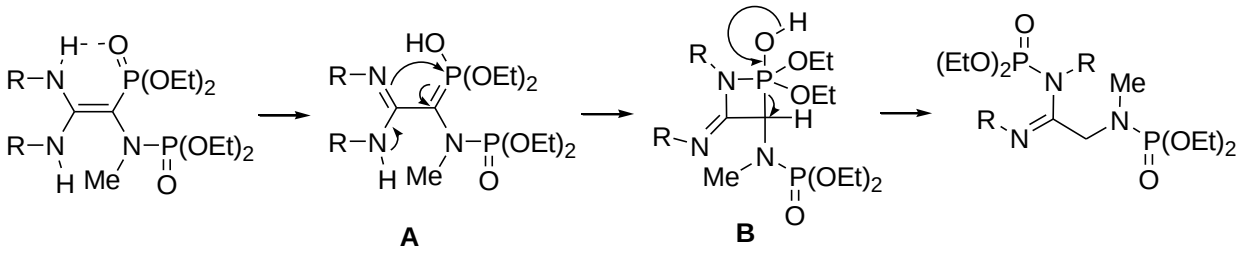


			$\Delta\delta = \delta(2a) - \delta(1)$, ppm
C-1	δ_c 132.6 ppm $^1J_{cp}$ 206 Hz	δ_c 86 ppm $^1J_{cp}$ 245 Hz	- 49
C-2	δ_c 139 ppm $^1J_{cp}$ 42 Hz	δ_c 167 ppm $^1J_{cp}$ 40.3 Hz	28.7
δ_{cp}^{p}	10.0	25.4	15.4

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 (δ_P 29.7 ppm, $^1J_{CP}$ 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**.

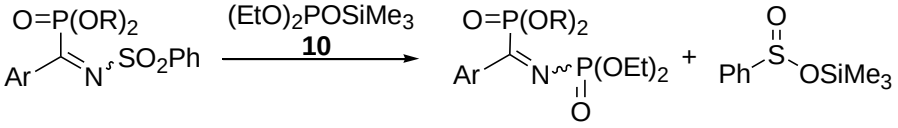
A possible isomerization mechanism is shown in the Scheme 7. Protonation of the nucleophilic oxygen atom of the phosphonyl group, followed by proton transfer from nitrogen to carbon (arrows on **A**) and subsequent migration of the phosphonium-like group from carbon to nitrogen, possibly via the four 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),[16, 17] 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_2N and C=N carbon atoms in the ^{13}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 ^{1}H,^{13}C,^{31}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.[18, 19]

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).

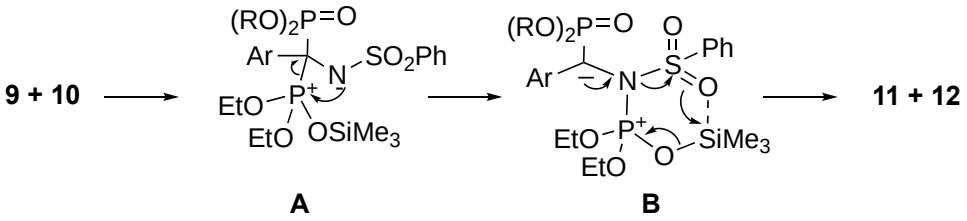


9a-c **11a**: 75% **12**: 60%
11b: 80%
11c: 70%

a) R = Ph, Ar = 3-FC_6H_4; **b**) R = Ph, Ar = 4-FC_6H_4; **c**) R = Et, Ar = Ph

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

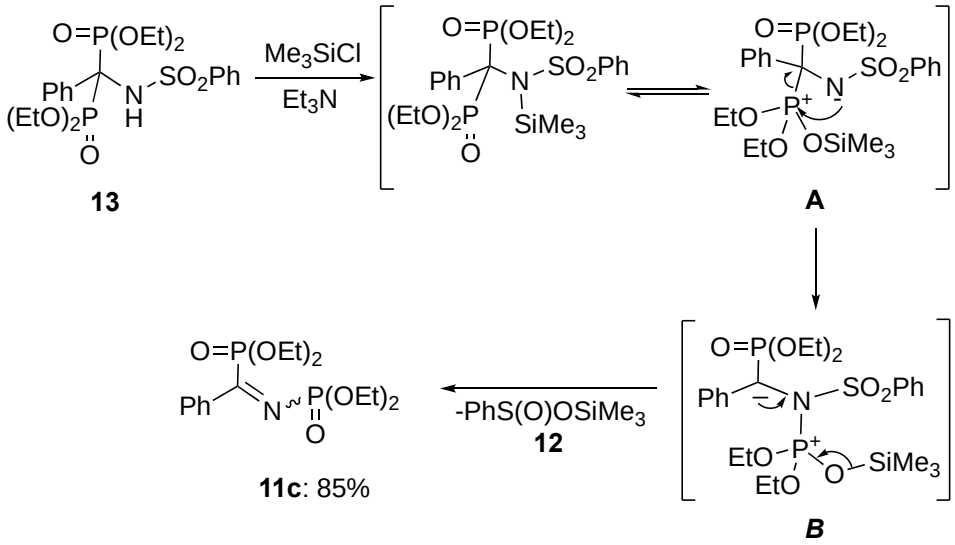
Such an unexpected result can be explained as shown in the Scheme 9. Nucleophilic attack of phosphite on the most electrophilic center, the imine carbon atom, followed by C-N transfer of the phosphorus group in 1,1-diphosphonated product **A** leads to C,N-diphosphorylated dipolar intermediate **B** 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 phenylsulfinic 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.[20,21]

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.

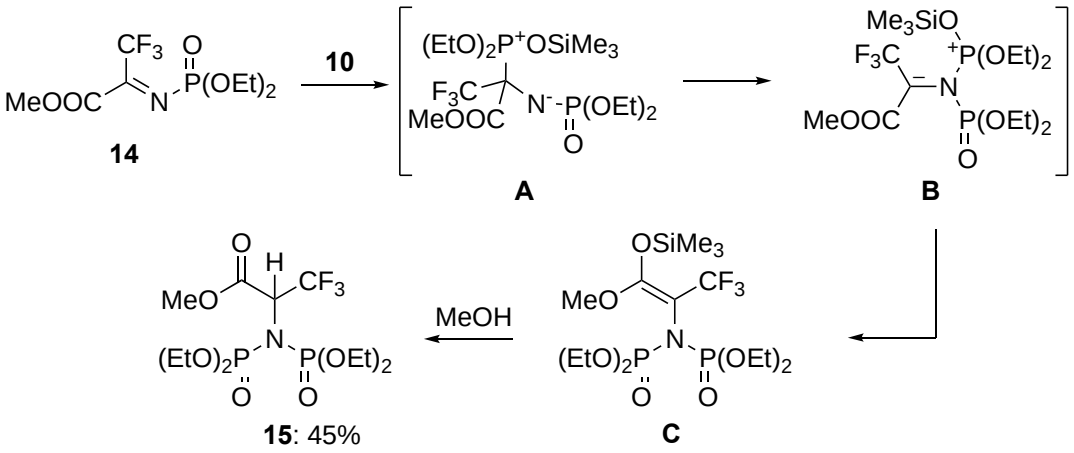


Scheme 10. Proposed mechanism for conversion of bisphosphonate **13** to iminophosphonates **11.**

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 (δ_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.[22] 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. ^{1}H, ^{19}F, ^{31}P and ^{13}C NMR spectra were recorded using Bruker Avance NMR spectrometers operating at 300 and 400 MHz ^{1}H frequencies; 75.8 and 125.7 MHz for ^{13}C experiments; 188 MHz for ^{19}F; 81 and 202.3 MHz for ^{31}P. Chemical shifts are reported relative to internal TMS (^{1}H, ^{13}C), $CFCl_3$ (^{19}F) and external 85%-H_3PO_4 (^{31}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 $MeNH_2$. An excess of dry methylamine was passed through a solution of **1a** (2.98 g, 7.5 mmol) in dry Et_2O (15 mL) at 0 °C. The precipitate was filtered off and the filtrate was concentrated. The crude product contained mainly compound **2b**. ^{31}P-NMR ($CDCl_3$, 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}H-NMR ($CDCl_3$, 300 MHz) δ 1.3 m (12H, MeCH_2), 2.61 and 2.68, doublets, $^3J_{HP}$ 9.9 and 9.6 Hz (3H, MeN), 2.80 and 2.96, doublets, $^3J_{HP}$ 9 and 7.2 Hz (3H, MeN), 3.22 and 3.28 (3H, MeN=), 3.9-4.3 m (10H, NCH_2, OCH_2). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 15.8-15.9 (C<u>Me</u>), 36.8 and 37.3 (MeN=), 32.8 and 33.2, doublets, J_{CP} 3.2 and 2 Hz (MeN), 33.6 and 33.9, doublets, $^2J_{CP}$ 2.9 and 1.6 Hz (MeN) 44.8 and 53.0 (CH_2N), 61.8, 62.0, 62.6, and 62.7, doublets, $^2J_{CP}$ 5.1, 5.9, 4,7, and 5 Hz (OCH_2), 154.2 dd (C=N, J_{CP} 3 and 5 Hz), 157.3 t (C=N, J_{CP} 5 Hz). ^{31}P-NMR ($CDCl_3$, 202 MHz) δ 10.3 (1P), 5.5 and 2.7 (1P). Anal. calcd for $C_{13}H_{31}N_3O_6P_2$, %: 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 $NH_2(CH_2)_nNH_2$, n=2, 3, 4. A solution of appropriate diamine (8 mmol) in Et_2O (40 mL) was added at 0 °C to a stirred solution of enamide (**1a-c**) (2.5 mmol) in Et_2O (30 mL). After completion of reaction (7-10 days, ^{31}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}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 m (12H, OCH_2<u>CH_3</u>), 2.77 d (3H, NMe, *J* = 7.5 Hz), 3.49 m (4H, NCH_2CH_2N), 4.07 m (8H, OCH_2), 5.31 s (1H, NH), 6.62 s (1H, NH). ^{13}C-NMR ($CDCl_3$, 75.43 MHz) δ 15.9-16.4 (C<u>Me</u>), 37.1 d (MeN, $^2J_{CP}$ 11.9 Hz), 43.1 and 44.1 (CH_2N), 60.5 d (OCH_2, $^2J_{CP}$ 5 Hz), 60.7 d (OCH_2, $^2J_{CP}$ 3.2 Hz), 62.3 d (OCH_2, $^2J_{CP}$ 6.4 Hz), 62.5 d (OCH_2, $^2J_{CP}$ 6 Hz), 70.6 d (=CP, $^1J_{CP}$ 251 Hz), 165.8 d (=CN, $^2J_{CP}$ 45.4 Hz). ^{31}P -NMR ($CDCl_3$, 121.42 MHz) δ 10.4 (NP), 27.5 (CP). Anal. calcd for $C_{13}H_{29}N_3O_6P_2$, %: 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}P-NMR ($CDCl_3$, 121.42 MHz) δ 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}H-NMR ($CDCl_3$, 300 MHz) δ 1.11 t (3H, NCH_2<u>CH_3</u>), 1.30 m (12H, OCH_2<u>CH_3</u>), 3.20 m (2H, N<u>CH_2</u>Me), 3.47 m (4H, NCH_2CH_2N), 4.07 m (8H, OCH_2), 5.27 s (1H, NH), 6.72 s (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.6 (NP), 27.5 (CP). Anal. calcd for $C_{14}H_{31}N_3O_6P_2$, %: 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)phosphoro-amidate (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}H-NMR ($CDCl_3$, 300 MHz) δ 0.96 m (12H, OCH_2CH_2<u>CH_3</u>), 1.69 m (8H, OCH_2<u>CH_2</u>CH_3), 2.77 d (3H, NMe, *J* = 7.8 Hz), 3.49 m (4H, NCH_2CH_2N), 3.96 m (8H, OCH_2), 5.27 s (1H, NH), 6.59 s (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.6 (NP), 27.5 (CP). Anal. calcd for $C_{17}H_{37}N_3O_6P_2$, %: C 46.25; H 8.45; P 14.03. Found, %: C 45.92; H 8.64; P 13.87.

Diethyl ((diethoxyphosphoryl)(tetrahydropyriimidin-2(1*H*)-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}H-NMR ($CDCl_3$, 300 MHz) δ 1.30 t (12H, OCH_2<u>CH_3</u>), 1.88 m (2H, NCH_2<u>CH_2</u>), 2.72 d (3H, NMe, *J* 7 Hz), 3.22-3.30 m (4H, N<u>CH_2</u>CH_2), 4.05 m (8H, OCH_2), 5.38 s (1H, NH), 7.58 s (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.9 (NP), 29.0 (CP). Anal. calcd for $C_{14}H_{31}N_3O_6P_2$, %: C 42.10; H 7.82; P 15.51. Found, %: C 41.89; H 7.96; P 15.65.

Diethyl ((diethoxyphosphoryl)(tetrahydropyrimidin-2(1*H*)-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}H-NMR ($CDCl_3$, 300 MHz) δ 1.09 t (3H, NCH_2<u>CH_3</u>), 1.29 t (12H, OCH_2<u>CH_3</u>), 1.86 m (2H, NCH_2<u>CH_2</u>), 3.0-3.2 m (6H, N<u>CH_2</u>CH_2 and N<u>CH_2</u>CH_3), 4.05 m (8H, OCH_2), 5.40 s (1H, NH), 7.66 s (1H, NH). ^{31}P-NMR

($CDCl_3$, 121.42 MHz) δ 10.7 (NP), 28.9 (CP). Anal. calcd for $C_{15}H_{33}N_3O_6P_2$, %: C 43.58; H 8.05; P 14.99. Found, %: C 43.19; H 8.34; P 15.31.

Dipropyl ((dipropoxyphosphoryl)(tetrahydropyrimidin-2(1*H*)-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_2, MeOH). Yield 0.61 g (54%), n_D^{20} 1.4852. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.96 m (12H, $OCH_2CH_2\underline{CH_3}$), 1.68 m (8H, $OCH_2\underline{CH_2}CH_3$), 1.88 m (2H, $NCH_2\underline{CH_2}$), 2.72 d (3H, NMe), 3.21-3.29 m (4H, $N\underline{CH_2}CH_2$), 3.93 m (8H, OCH_2), 5.34 s (1H, NH), 7.58 s (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 11.1 (NP), 29.0 (CP). Anal. calcd for $C_{18}H_{39}N_3O_6P_2$, 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_2, MeOH). Yield 0.32 g (31%), n_D^{20} 1.4883. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.30 t (12H, $OCH_2\underline{CH_3}$), 1.57 m (4H, C-CH_2-C), 2.74 d (3H, NMe, *J* 7.5 Hz), 3.05-3.20 m (4H, $N\underline{CH_2}CH_2$), 4.06 m (8H, OCH_2), 5.41 br (1H, NH), 7.89 br (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.1 (NP), 27.3 (CP). Anal. calcd for $C_{15}H_{33}N_3O_6P_2$, %: 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_2, MeOH). Yield 0.78 g (73%), n_D^{20} 1.4882. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.05 t (3H, $NCH_2\underline{CH_3}$), 1.30 t (12H, $OCH_2\underline{CH_3}$), 1.4-1.7 m (4H, C-CH_2-C), 2.9-3.3 m (6H, NCH_2), 4.07 m (8H, OCH_2), 5.48 br (1H, NH), 7.1 br (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.1 (NP), 27.5 (CP). Anal. calcd for $C_{16}H_{35}N_3O_6P_2$, %: 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_2, MeOH). Yield 0.94 g (80%), n_D^{20} 1.4838. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.96 m (12H, $OCH_2CH_2\underline{CH_3}$), 1.57 m (4H, C-$CH_2$-C), 1.68 m (8H, $OCH_2\underline{CH_2}CH_3$), 2.74 d (3H, NMe, J 6.3 Hz), 3.0-3.1 m (4H, NCH_2), 3.94 m (8H, OCH_2), 5.41 s (1H, NH), 7.33 s (1H, NH). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 10.1 (NP), 27.3 (CP). Anal. calcd for $C_{19}H_{41}N_3O_6P_2$, %: 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_2O (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.[23] 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 ^{1}H, ^{19}F, ^{31}P NMR spectra with literature data.[13]

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_2O (10 mL). After 24 h, the formed precipitate was filtered off, and the filtrate was evaporated to afford (**11c**)[13] 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_2O (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_4), ν 1080 (POC), 1280 (P=O), 1740 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.33–1.39 m (12 H, $C\underline{H_3}CH_2$), 3.85 s (3H, CH_3O), 4.05-4.28 m (8H, CH_2O), 5.15 dq (1 H, CH, $^3J_{HP}$ 19.5 Hz, $^3J_{HF}$ 8 Hz). ^{19}F-NMR ($CDCl_3$, 282.2 MHz) δ – 68.3 d ($^3J_{FH}$ 8 Hz). ^{31}P-NMR ($CDCl_3$, 121.42 MHz) δ 2.9 br. Anal. calcd for $C_{14}H_{31}N_3O_6P_2$, %: 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}H, ^{31}P NMR data for previously[11, 12] described compounds **1a-c, 2a** are presented in the Supplementary Material file associated with this article.

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