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LETTERS TO THE EDITOR

Synthesis of Lactam-containing Amido(ethoxy)methylphosphonates

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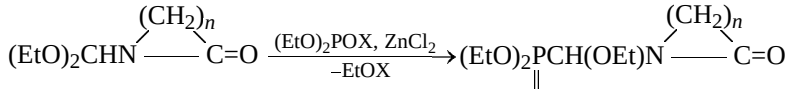
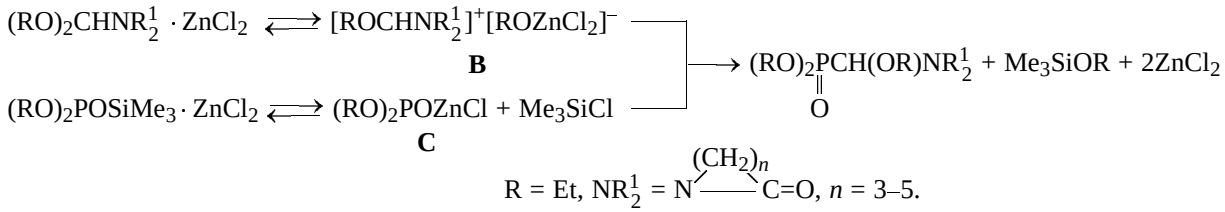
Organophosphorus derivatives of lactams attract attention as promising ligands and biologically active compounds [1]. In the present work we propose a convenient synthesis of amido(ethoxy)methylphosphonates **I** containing pyrrolidone and valero- and caprolactams fragments. Hence *N*-diethoxymethyllactams **A** react with diethyl trimethylsilyl and diethyl hydrogen phosphites at 130–150°C in the presence of zinc chloride to form phosphonates **I**. Using diethyl trimethylsilyl phosphite is optimal and provides high yields of phosphonates **I**, whereas with diethyl hydrogen phosphite, the yield is much lower.



A **Ia–Ic**

X = Me_3Si, H; *n* = 3 (**a**), 4 (**b**), 5 (**c**).

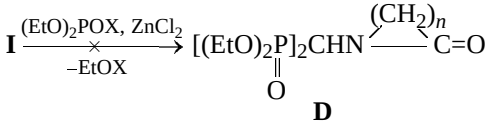
Evidently, the catalytic effect of zinc chloride is connected with its ability to generate electrophilic carbonioimmonium ions **B**, as well as nucleophilic zinc-containing salts **C** in the course of the process (cf. [2]).



B **C**

R = Et, NR^1_2 = N(CH$_2$)$_n$C=O, *n* = 3–5.

Using an excess of phosphite in this reaction did not lead to formation of diphosphorylation products, amidomethylenebisphosphonates **D**.



D

X = Me_3Si, *n* = 3–5.

This is connected with the fact that phosphonates **I** are much weaker amidomethylating agents compared with substituted amino(alkoxy)methylphosphonates [2] because of the electronic and steric effects of the lactam-containing fragments. Starting *N*-(diethoxymethyl)lactams **A** were obtained by the procedure in [3].

The NMR spectra of compounds **I** contain cha-

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racteristic signals of the $P^1C^1H(OC^4H_2)N(C^2H_2)C^3O$ fragments.

Diethyl ethoxy[*N*-(2-oxopyrrolidino)]methylphosphonate (Ia). *a*. A mixture of 5.3 g of *N*-(diethoxymethyl)pyrrolidone, 15 g of diethyl trimethylsilyl phosphite, and 0.2 g of zinc chloride was heated at 130–150°C for 1 h and then distilled to give 6.6 g of phosphonate **Ia**, yield 78%, bp 142°C (1 mm Hg), n_D^{20} 1.4615. ^{1}H NMR spectrum, δ, ppm: 5.14 d (C^1H, $^2J_{PH}$ 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 76.11 d (C^1, $^1J_{PC}$ 202 Hz), 42.37 s (C^2), 175.19 d (C^3, $^3J_{PC}$ 6.0 Hz), 64.40 d (C^4, $^3J_{PC}$ 14.6 Hz). ^{31}P NMR spectrum, δ_P 15.91 ppm. Found, %: C 47.03; H 7.81; P 10.89. $C_{11}H_{22}NO_5P$. Calculated, %: C 47.31; H 7.94; P 11.09.

Compounds **Ib** and 26)Ic were obtained analogously.

b. A mixture of 7 g of *N*-(diethoxymethyl)pyrrolidone, 14 g of diethyl hydrogen phosphite, and 0.2 g of zinc chloride was heated for 1 h at 130–140°C and then distilled to give 6.6 g (59%) of phosphonate **Ia**.

Phosphonates **Ib** and **Ic** were obtained analogously, yields 42 and 10%, respectively.

Diethyl ethoxy[*N*-(2-oxopiperidino)]methylphosphonate (Ib). Yield 74%, bp 148°C (1 mm Hg), n_D^{20} 1.4660. ^{1}H NMR spectrum, δ, ppm: 5.76 d (C^1H, $^2J_{PH}$ 9.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 76.83 d (C^1, $^1J_{PC}$ 200.3 Hz), 41.63 s (C^2), 169.89 d (C^3, $^3J_{PC}$ 5.9 Hz), 64.49 d (C^4, $^3J_{PC}$ 15.2 Hz). ^{31}P NMR spectrum, δ_P, ppm: 16.55 s. Found, %: C 48.87; H 8.03; P 10.26. $C_{12}H_{24}NO_5P$. Calculated, %: C 49.14; H 8.25; P 10.56.

Diethyl ethoxy[*N*-(2-oxoperhydroazepino)]methylphosphonate (Ic). Yield 64%, bp 157°C (1 mm Hg), n_D^{20} 1.4687. ^{1}H NMR spectrum, δ, ppm: 5.68 d (C^1H, $^2J_{PH}$ 9.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 77.42 d (C^1, $^1J_{PC}$ 202.6 Hz), 42.97 s (C^2), 176.13 d (C^3, $^3J_{PC}$ 5.1 Hz), 64.73 d (C^4, $^3J_{PC}$ 15.2 Hz). ^{31}P NMR spectrum, δ_P, ppm: 16.77 s. Found, %: C 50.64; H 8.42; P 9.97. $C_{13}H_{26}NO_5P$. Calculated, %: C 50.81; H 8.53; P 10.08.

The NMR spectra were measured on a Varian VXR-400 spectrometer in $CDCl_3$ against TMS (^{1}H, ^{13}C) and 85% H_3PO_4 in D_2O (^{31}P).

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