Intramolecular cyclization of 1,3-diamino-2-hydroxypropan-*N,N,N′,N′*-tetrakis(methylphosphonic acid) upon phosphonomethylation of 1,3-diaminopropan-2-ol

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Phosphonomethylation of 1,3-diaminopropan-2-ol affords the mixture of 1,3-diamino-2-hydroxypropan-*N,N,N′,N′*-tetrakis(methylphosphonic acid) (**1**) with its cyclic ether, *viz.*, [(6-{[bis(phosphonomethyl)amino]methyl}-2-hydroxy-2-oxido-1,4,2-oxazaphosphinan-4-yl)-methyl]phosphonic acid (**2**), but not **1**, as assumed earlier.

Key words: 1,3-diaminopropan-2-ol, phosphonomethylation, NMR spectroscopy, 1,3-diamino-2-hydroxypropan-*N,N,N′,N′*-tetrakis(methylphosphonic acid), cyclic ester.

The chelating agent synthesized for the first time by Soviet scientists in the beginning of 1980s, *viz.*, methylphosphorylated 1,3-diaminopropan-2-ol derivative,[1,2] was found to be an efficient inhibitor of mineral salt deposition for water stabilization treatment in water utilization systems, which is superior to the same-purpose reagents in consumer properties.[3,4] The authors of Ref. 2 characterized the obtained product as 1,3-diamino-2-hydroxypropan-*N,N,N′,N′*-tetrakis(methylphosphonic acid) (**1**) based on the data from IR spectroscopy.

Based on the $^{13}C\{^1H\}$ and ^{31}P NMR$\{^1H\}$ spectral study of phosphonomethylated 1,3-diaminopropan-2-ol derivative obtained by the Kabachnik—Fields reaction, we found for the first time that the product is a mixture of phosphorus-containing 1,3-diaminopropan-2-ol derivatives, which are difficult to separate.

We have assumed that the resulted mixture along with acid **1** contains its intramolecular cyclic ester, *viz.*, [(6-{[bis-(phosphonomethyl)amino]methyl}-2-hydroxy-2-oxido-1,4,2-oxazaphosphinan-4-yl)methyl]phosphonic acid (**2**) (Scheme 1) by the analogy with the mixture formed during phosphonomethylation of 2-aminoethanol,[5—7] from which 2-hydroxyethylamino-*N,N*-bis(methylphosphonic acid) (**3**) and its intramolecular ester, [(2-hydroxy-2-oxido-1,4,2-oxazaphosphinan-4-yl)methyl]phosphonic acid (**4**), were isolated (Scheme 2).

To determine the composition of the mixture under study, we performed the comparative analysis of the $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR spectra of this mixture and model compounds **3** and **4**, which confirmed the assumption of that, along with acid **1**, the phosphonomethylation product of 1,3-diaminopropan-2-ol contains its intramolecular cyclic ester **2**: the $^{13}C\{^1H\}$ NMR spectra of the mixture display identical-intensity signals for two methylene and one methyne group of the 1,4,2-oxazaphosphinane heterocycle whose fine structures correspond to the positions and multiplicities of the signals for the ring carbon atoms observed in the $^{13}C\{^1H\}$ NMR spectra of the model compound **4** (Table 1) which proves the presence of compound **2** in the mixture under study

The contents of acids **1** and **2** in the mixture according to the $^{31}P\{^1H\}$ spectral data were 56% and 44%, respectively.

Scheme 1

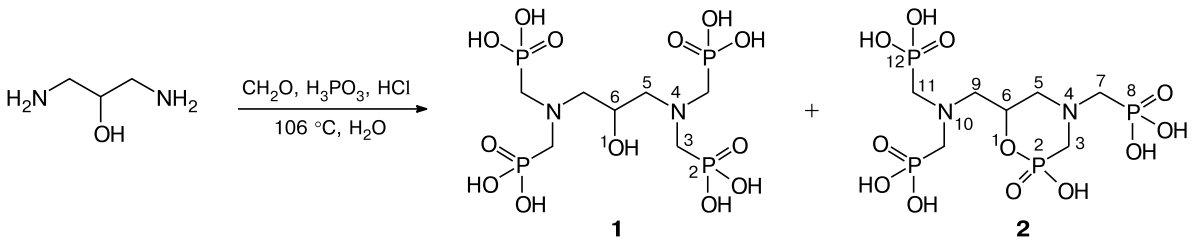

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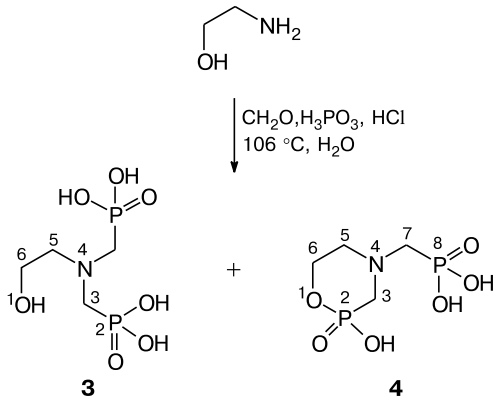
Table 1. $^{13}C\{^1H\}$ NMR spectra (D_2O) of the mixture of compounds **1** and **2** and model compounds **3** and **4**

Atom	δ (*J*/Hz)			
	1	**2**	**3**	**4**
C(3)	52.47 (dd, $J_{C,P}$ = 135.9, $^3J_{C,P}$ = 3.3)	50.18 (dd, $J_{C,P}$ = 131.5, $^3J_{C,P}$ = 3.9)	51.52 (dd, $J_{C,P}$ = 136.7, $^3J_{C,P}$ = 4.1)	51.05 (dd, $J_{C,P}$ = 128.4, $^3J_{C,P}$ = 4.4)
C(5)	58.59 (t, $^3J_{C,P}$ = 2.7)	54.84 (t, $^3J_{C,P}$ = 3.3)	57.82 (t, $^3J_{C,P}$ = 3.1)	54.25 (t, $^3J_{C,P}$ = 5.0)
C(6)	60.71 (s)	67.32 (d, $^2J_{C,P}$ = 4.5)	55.13 (s)	61.83 (d, $^2J_{C,P}$ = 5.0)
C(7)		55.13 (dd, $J_{C,P}$ = 135.9, $^3J_{C,P}$ = 8.3)		54.73 (dd, $J_{C,P}$ = 136.5, $^3J_{C,P}$ = 7.7)
C(9)		56.02 (t, $^3J_{C,P}$ = 2.8)		
C(11)		52.14 (dd, $J_{C,P}$ = 135.9, $^3J_{C,P}$ = 4.4)		

Scheme 2



3 **4**

Experimental

$^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR spectra were recorded on a Bruker AVANCE III NanoBay (75.51 and 121.56 MHz, respectively) instrument in D_2O in standard tubes with an external diameter of 5 mm at 25 °C. Melting points were determined on a Stuart SMP30 Melting Point Apparatus.

Phosphonomethylation of 1,3-diaminopropan-2-ol. To 36% HCl (28.2 mL, 0.33 mol), 1,3-diaminopropan-2-ol (13.5 g, 0.15 mol) was added portionwise at 0 °C and, then, 61.8% aqueous solution of H_3PO_3 (57.6 mL, 0.60 mol) was added. 37% formalin (18.9 mL, 0.63 mol) was added dropwise to the resulted mixture at 106 °C and the solution was heated for 3 h at 106 °C and evaporated to 1/3 of the starting volume. The residue was added dropwise to methanol taken in the seven-fold volume. The crystalline precipitated product was filtered off, washed with methanol (2×50 mL), and dried *in vacuo* to yield a hygroscopic product (45.4 g). $^{31}P\{^1H\}$ NMR (D_2O), δ: 4.0 (s, 1 P, P(2) (**2**)); 6.2 (s, 1 P, P(8) (**2**)); 7.0 (s, 2 P, P(12) (**2**)); 7.2 (s, 4 P (**1**)).

[(2-Hydroxy-2-oxido-1,4,2-oxazaphosphinan-4-yl)methyl]-phosphonic acid (4) was prepared by the procedure described in Ref. 6. M.p. 258—261 °C (decomp.) (data of Ref. 6: 258—260 °C (decomp.)). $^{31}P\{^1H\}$ NMR (D_2O), δ: 4.8 (s, 1 P, P(2)); 7.6 (s, 1 P, P(8)).

2-Hydroxyethylamino-*N,N*-bis(methylphosphonic acid) (3) was prepared under the conditions of the earlier described synthesis[6] as tetrasodium salt, which was transformed into the acid by acidification of a cooled to 0 °C solution of the salt with 36% HCl until pH 1.5. The precipitate that formed was filtered off, the filtrate was evaporated to 1/3 of the starting volume, and the residue was added dropwise with stirring to DMF (150 mL). The crystalline precipitated product was filtered off, washed with DMF (2×20 mL), and dried *in vacuo* to yield acid **2** (76.0 g, 71%), m.p. 264—266 °C (decomp.). $^{31}P\{^1H\}$ NMR (D_2O), δ: 8.4 (s).

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