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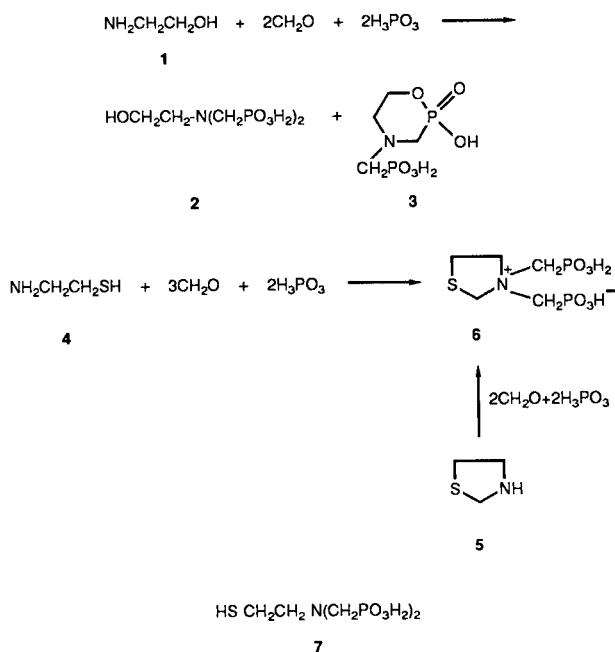
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Phosphonomethylation of 2-aminoethanethiol and thiazolidine gives the unexpected dimethylene diphosphonic acid **6**.

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Phosphonomethylation of ethanolamine **1** is reported [1] to give a mixture of [(2-hydroxyethyl)imino]dimethylene diphosphonic acid **2** and 4-(phosphonomethyl)-2-hydroxy-2-oxo-1,4,2-oxazaphosphorinane **3** from which **3** can be readily isolated. We report here that the phosphonomethylation of 2-aminoethanethiol **4** and thiazolidine **5** gives the unexpected product **6**.



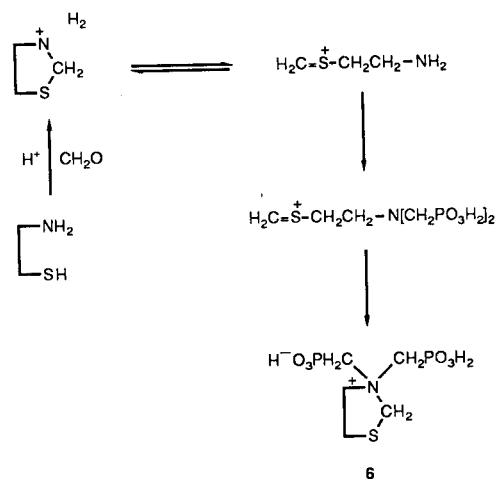
Treatment of **4** with 2 equivalents of phosphorous acid and 4 equivalents of formaldehyde in presence of concentrated hydrochloric acid gave a white crystalline solid which exhibited following spectral properties [2]; ^{31}P nmr (deuterium oxide/phosphoric acid Cap): +6.1; ^1H nmr: 3.35 (t, $J_{\text{HH}} = 7$ Hz, 2H, S-CH₂), 4.06 (d, $J_{\text{PH}} = 13$ Hz, 4H, CH₂-P), 4.12 (t, 2H, N-CH₂), 4.87 (s, 2H, S-CH₂-N); ^1H nmr (pH 12.90): 3.36 (t, $J_{\text{H-H}} = 7$ Hz, 2H, SCH₂), 3.85 (d, $J_{\text{PH}} = 12$ Hz, 4H, CH₂-P), 4.30 (t, $J_{\text{H-H}} = 7$ Hz, 2H, N-CH₂), 5.05 (s, 2H, S-CH₂-N).

The ^{31}P nmr rules out the cyclic ester type structure which is expected to exhibit two phosphorus signals. The ^1H nmr shows the presence of dimethylene diphosphonic

acid group but contains one additional CH₂ group not expected from the open chain structure **7**. The elemental analysis confirms this and is in agreement with the molecular formula C₅H₁₃NO₆P₂S.

These data are consistent with the structure **6**. Phosphonomethylation of thiazolidine **5** with 2 equivalents of phosphorous acid and excess of formaldehyde also yielded **6**, providing further support for the assigned structure. To our knowledge, the formation of dimethylene diphosphonic acid **6** from **4** or **5** constitutes the first example of a quaternary nitrogen product from the formaldehyde/phosphorous acid (Mannich) reaction.

A possible mechanism [3] for the formation of **6** from 2-aminoethanethiol or thiazolidine is:



EXPERIMENTAL

Phosphonomethylation of 2-Aminoethanethiol (**4**).

A mixture of 2-aminoethanethiol hydrochloride (5.68 g, 0.05 mole), water (29.0 g), phosphorous acid (8.2 g, 0.1 mole) and concentrated hydrochloric acid (21.0 ml) was heated to reflux. Formaldehyde (16.65 ml of 36% aqueous solution, 0.2 mole) was added over a period of 45 minutes. The reaction mixture was refluxed for an additional 3 hours and then evaporated to dryness on rotary evaporator. Water (70 ml x 2) was added and the solution was reevaporated. The crude product (syrup) was dissolved in water (40 ml) and allowed to stand. There was obtained 2.5 g of **6** as a white crystalline solid, mp 218° dec.

Anal. Calcd. for $C_8H_{13}NO_6P_2S$: C, 21.66; H, 4.67; N, 5.05, P, 22.38; S, 11.55. Found: C, 21.66; H, 4.69; N, 5.00; P, 22.39; S, 11.55.

Phosphonomethylation of Thiazolidine (5).

A mixture of thiazolidine (2.22 g, 0.025 mole), water (14.5 ml), phosphorous acid (4.1 g, 0.05 mole), and concentrated hydrochloric acid (14.5 ml) was heated to reflux. Formaldehyde (7.91 g, 37.9%, 0.1 mole) was added over a period of 30 minutes. The reaction mixture was refluxed for 4 hours and then evaporated to dryness. The crude product was stirred with 15 ml water. There was obtained 1.5 g of **6** as a white crystalline

solid, mp 218° dec.

REFERENCES AND NOTES

- [1] K. H. Worms and K. Wollman, *Z. Anorg. Allg. Chem.*, **381**, 260 (1971).
- [2] The 1H nmr spectra were obtained in deuterium oxide with 3-(trimethylsilyl)propionic acid, sodium salt as the internal standard. The pH was adjusted by adding sodium hydroxide.
- [3] J. J. Peseck and J. H. Frost, *Tetrahedron*, **31**, 907 (1975).