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LETTERS TO THE EDITOR

New Method of the Synthesis of 1,3-Diamino-2-hydroxypropane-*N,N'*-bis(dihydroxyphosphorylmethyl)-*N,N'*-diacetic Acid

N. V. Tsirul'nikova, E. S. Dernovaya, Ya. V. Bolt, and T. S. Fetisova

Federal State Unitary Enterprise
"State Scientific Research Institute of Chemical Reagents and High Purity Chemical Substances,"
ul. Bogorodskii val 3, Moscow, 107076 Russia
e-mail: nv.tsir@mail.ru

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Complexones containing secondary amino groups are successfully used as synthons for the synthesis of practically valuable polyfunctional complexing agents [1, 2], in particular, for the design of biologically active substances [3] and contrasting agents for magnetic resonance tomography [4, 5].

Barsukov et al. [6] first used as a synthone 1,3-diamino-2-hydroxypropane-*N,N'*-diacetic acid **1**, whose firther methylphosphorylation afforded 1,3-diamino-2-hydroxypropane-*N,N'*-bis(dihydroxyphosphorylmethyl)-*N,N'*-diacetic acid **2**. Phosphorus-containing compounds to which acid **2** belongs are widely used as effective inhibitors of salt deposition and corrosion in household and industrial water–supply systems [7]. However, the presence in such phosphorus reagents, being a nutrient medium for phytoplankton, promotes its growth [8]. In order to decrease the phosphorus concentration, it was suggested to use inhibitors containing, along with methylphosphonous, also carboxylic groups. In view of this, compound **2** can be also of interest as a multipurpose inhibitor.

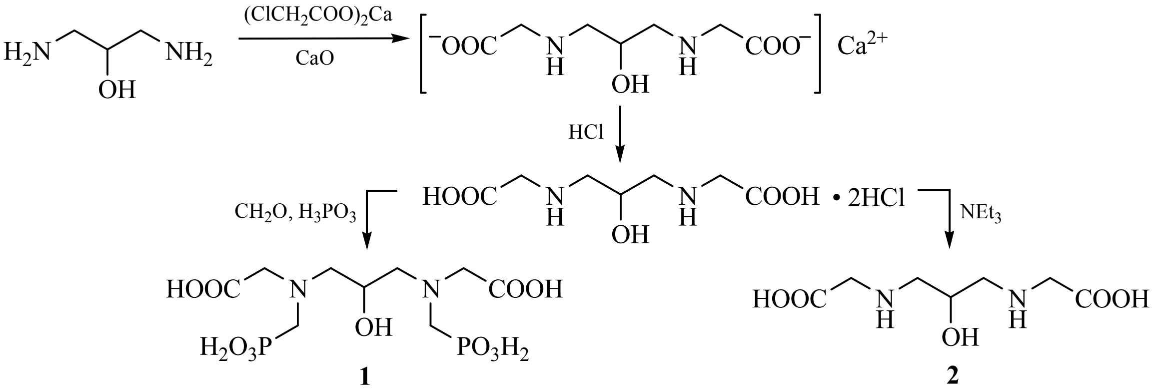
Acid **1** was synthesized without isolation from the reaction mixture by cyanomethylation of 1,3-diamino-2-propanol with formaldehyde and sodium cyanide with subsequent alkaline hydrolysis of the formed diacetonitrile [6]. Acid **1** was also prepared by nucleophilic substitution of chlorine in 1,3-dichloro-2-propanol by the amino group of glycine in alkaline medium and isolated as dihydrobromide in 33% yield after acidification of the reaction mass with hydrobromic acid to pH = 5 [2]. The statement of Kanamori et al. [2] on the nature of the obtained compound is in contrast to all known data: at pH = 4.5–5.0 compounds similar to acid **1** do not form salts with mineral acids.

The described methods for preparation of acid **1** [2, 6] are not optimal and the physicochemical characteristics of the product were not presented. The use of PCl_3 as a phosphorylating agent in methylphosphorylation of acid **1** by the Kabachnik–Fields reaction [6] results in the complication of the technological process and is followed by evolution of a substantial amount of hydrogen chloride, imparing the utilization of mother liquors after isolation of acid **2**.

We have first found the conditions for direct carboxyalkylation of 1,3-diamino-2-propanol with calcium salt of monochloroacetic acid in the presence of calcium oxide for maintaining the pH of the reaction mass equal to 9.0–11.0 at the temperature 65–70°C. Further decomposition of the formed calcium complex of acid **1** with hydrochloric acid leads to isolation of acid **1** in the form of dihydrochloride. The methylphosphorylation of acid **1** dihydrochloride by Kabachnik–Fields reaction gave acid **2** (Scheme 1).

1,3-Diamino-2-hydroxypropan-*N,N'*-diacetic acid (1) dihydrochloride. To the solution of 13.2 g (0.14 mol) of monochloroacetic acid in 6 mL of water 3.74 g (0.067 mol) of CaO was added at stirring to pH =

Scheme 1.



9–11, and to the obtained suspension 6.0 g (0.067 mol) of 1,3-diamino-2-propanol was added, keeping the temperature at 65–70°C and pH = 9–11 by addition of CaO. After charging 1,3-diamino-2-propanol the reaction mixture was stirred for 2 h at the same temperature and pH, then the formed calcium complex of acid **1** was decomposed by the treatment with conc. HCl to pH = 1.5–2.0. The obtained solution was cooled to 10–15°C, after 12 h the formed precipitate was filtered off, washed with methanol, and dried. 5.58 g of dihydrochloride **1** was obtained, yield 30%. ^1H NMR spectrum, δ, ppm: 3.22 d.d (CH_2, $^2J_{HH}$ 13.10 Hz, $^3J_{HH}$ 9.61 Hz, 2H), 3.37 d.d (CH_2, $^2J_{HH}$ 13.10 Hz, $^3J_{HH}$ 3.11 Hz, 2H), 4.03 s (CH_2CO, 4H), 4.41 t.t (CH, $^3J_{HH}$ 9.60 Hz, $^3J_{HH}$ 3.09 Hz, 1H). ^{13}C NMR spectrum, δ, ppm: 47.52 (CH_2), 49.73 ($\underline{C}H_2CO$), 62.77 (CH), 168.75 (CO). Found, %: C 29.9; H 5.98; N 9.87; Cl 25.5. $C_7H_{16}N_2O_5Cl_2$. Calculated, %: C 30.12; H 5.78; N 10.03; Cl 25.4.

1,3-Diamino-2-hydroxypropane-*N,N'*-bis(dihydroxyphosphorylmethyl)-*N,N'*-diacetic acid (2). To 5.58 g (0.020 mol) of dihydrochloride of 1,3-diamino-2-hydroxypropane-*N,N'*-diacetic acid 3.4 mL (0.042 mol) of 61.8% aqueous solution of phosphorous acid was added and the obtained mixture was heated at reflux. Then in the reaction mixture 3.1 mL (0.042 mol) of 37% formaldehydr water solution was introduced, and the reaction mixture was stirred for 3 h. When the reaction was completed, the solution was evaporated to 1/3 of volume, the residue was added dropwise at stirring to methanol taken in seven-fold volume. The formed precipitate was filtered, washed with methanol and dried in vacuum. 5.43 g of acid **2** was obtained, yield 68%. ^1H NMR spectrum, δ, ppm: 3.42–3.64 m (CH_2, CH_2P, 8H), 4.25 s (CH_2CO, 4H), 4.60 t.t (CH, $^3J_{HH}$ 9.81 Hz, $^3J_{HH}$ 2.38 Hz, 1H). ^{13}C NMR spectrum, δ, ppm: 50.91 d (CH_2P, $^1J_{CP}$ 135.90 Hz), 56.06 d ($\underline{C}H_2CO$, $^3J_{CP}$ 2.75 Hz), 57.93 d ($\underline{C}H_2CH$, $^3J_{CP}$ 3.30 Hz), 168.32 (CO). ^{31}P NMR spectrum, δ, ppm: 6.72 t ($^2J_{PH}$ 12.16 Hz). Found, %: C 27.34; H 5.19; N 7.03. $C_9H_{20}N_2O_{11}P_2$. Calculated, %: C 27.42; H 5.11; N 7.11.

^1H, ^{13}C and ^{31}P NMR spectra were registered on a Bruker AVANCE III NanoBay instrument (300.23, 75.51, and 121.56 MHz respectively) in D_2O at 25°C.

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REFERENCES

1. Kuznik, N., Szafraniec-Gorol, G., Oczek, L., Grucela, A., Jewula, P., Kuznik, A., Zassowski, P., and Domagala, W., *J. Organomet. Chem.*, 2014, vol. 769, p. 100. DOI: 10.1016@j.jorganchem.2014.07.011.
2. Kanamori, K., Jamomoto, K., Okayasu, T., Matsui, N., Okamoto, K., and Mori, W., *Bull. Chem. Soc.*, 1997, vol. 70, p. 3031.
3. Pitt, C., Bao, Y., Thompson, J., Wani, M., Rosenkrantz, H., and Metterville, J., *J. Med. Chem.*, 1986, vol. 29, no. 7, p. 1231. DOI: 10.1021/jm00157a020.
4. Chatterton, N., Gateau, C., Mazzanti, M., Pecaut, J., Borel, A., Helm, L., and Merbach, A., *Dalton Trans.*, 2005, no. 6, p. 1129. DOI: 10.1039/B416150E.
5. Song, K. and Liu, O., *Can. J. Chem.*, 2001, vol. 79, nos. 5–6, p. 1058. DOI: 10.1139/v00-179.
6. Barsukov, A.V., Yaroshenko, G.F., Dyatlova, N.M., Zhadanov, B.V., Polyakova, I.A., and Matkovskaya, T.A., *Zh. Obshch. Khim.*, 1984, vol. 54, no. 4, p. 763.
7. Tsirul'nikova, N.V., Driker, B.N., Fetisova, T.S., and Tarantaev, A.G., *Korroziya: Materialy i Zashchita*, 2007, no. 7, p. 42.
8. Ahmed, S., Alansari, M., and Kannari, T., *Desalination*, 1989, vol. 74, p. 69. DOI: 10.1016/0011-9164(89)85043-X.