ISSN 1070-3632, Russian Journal of General Chemistry, 2010, Vol. 80, No. 3, pp. 543–544. © Pleiades Publishing, Ltd., 2010.
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LETTERS TO THE EDITOR

Carboxyalkylation of Ethylene Diamine with β-Chloropropionic Acid. A New Approach to Ethylene Diamine-*N,N*'-di- and Ethylene Diamine-*N,N,N′,N′*-tetrapropionic Acids

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Received August 13, 2009

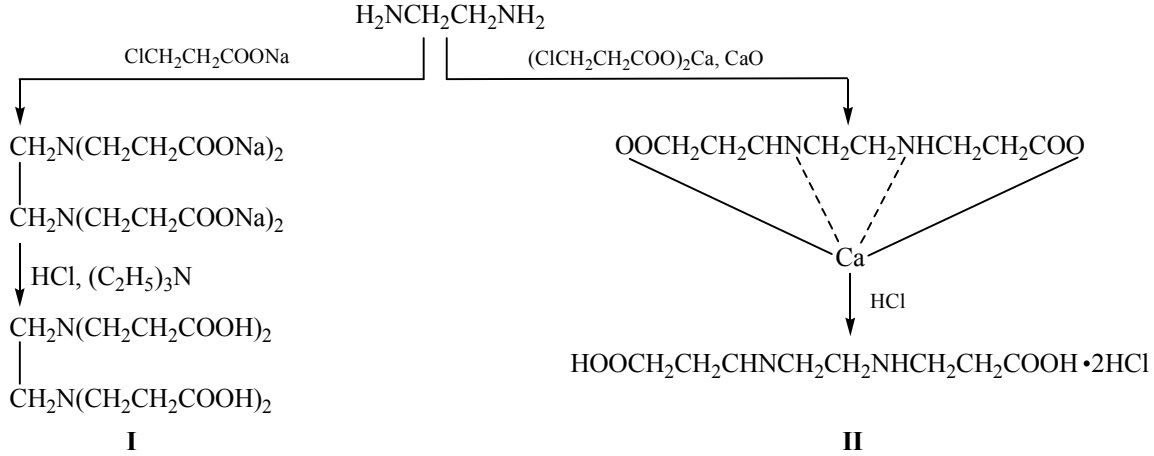
DOI: 10.1134/S107036321003031X

A purposeful synthesis of compounds with specified properties for solving special challenges of science and current industry is an actual problem of organic chemistry.

Unlike general-purpose ethylene diamine-*N,N,N′,N′*-tetraacetic acid, ethylene-*N,N,N′,N′*-tetrapropionic acid **I** is selective to copper(II) [1].

Reactive ethylene diamine-*N,N′*-dipropionic acid **II** is used as initial reagent for incorporating into chosen structures of organic compounds to obtain a number of reagents containing ethylene diamine propionate moieties. However, the most obvious way to obtain acid **II** by nucleophilic substitution of chlorine in β-chloropropionic acid by amino-group did not lead to desired results: By the reaction of β-chloropropionic acid with ethylene diamine in alkaline medium followed by acidifying of the reaction mixture and conversion of the forming dihydrochloride into the acid we for the first time synthesized tertiary amine derivative **I** in 48% yield [2] irrespective of the starting materials molar ratio.

Acid **I** was similarly obtained in [3] in 12% yield of using long and laborious way of isolation of the target product. In addition ethylene diamine tetrapropionitrile was used as starting reagent. The transformation of the latter into acid **I** requires energy-consuming distillation of acidic and ammonia aqueous solutions and four-fold recrystallization of technical acid **I**. Evidently, this synthesis method also is not optimal.



The hydrolysis of the corresponding nitriles is used to obtain acid **II** as well as other similar acids of the secondary amines series [3]. The main disadvantages of this process consist in the use of highly toxic acrylonitriles, poor processability and laboriousness (many stages, manifold use of energy-consuming procedures of distillation). The pure product **II** in this case was obtained in a low yield by multiple re-crystallization of technical acid **II**.

We found conditions for direct carboxyalkylation of ethylene diamine with calcium β-chloropropionate in the presence of calcium oxide to keep the pH of the reaction mixture at 9.0–11.0 at 75–85°C. Further decomposition of the formed calcium complex of the acid **II** by hydrochloric acid gives rise to acid **II** released as dihydrochloride [4].

Ethylene diamine-*N,N,N′,N′* -tetrapropionic acid (I). A four-neck flask equipped with mechanical stirrer, reflux condenser and dropping funnels was charged under stirring with 100 ml of water, 2.14 mol of β-chloropropionic acid and placed into a bath with heating and cooling. The acid was neutralized with 40% NaOH aqueous solution to pH 9.0–11.0. This mixture was heated to 40–45°C. Then 1 mol of ethylene diamine and 40% NaOH solution were slowly added dropwise for maintaining pH 9.0–11.0 with such rate that the temperature of the reaction mixture would not exceed 85°C. When all amine was charged and pH value became invariable in time, the reaction mixture was stirred at 80–85°C for 1.0–1.5 h, then it was cooled to room temperature and filtered from sodium chloride. The filtrate was cooled to 10–15°C and acidified with hydrochloric acid to pH 1.5–2.0. After 15–20 h dihydrochloride **I** was filtered off, dissolved in water and treated with triethylamine to pH 4.0–4.5 at cooling to 5–10°C. The precipitate of acid **I** was filtered off after 15–20 h and washed with distilled water to chloride ion disappearance. Yield 48%, mp 218–222°C with decomposition (mp 218–222°C with decomp. [3]). The product was identified by the ^{13}C NMR spectroscopy data.

Ethylene diamine-*N,N′*-dipropionic acid (II). Into a four-neck flask were charged under stirring 100 ml of water and 1.5 mol of β-chloropropionic acid, which was neutralized with calcium oxide to pH 9.0–11.0. To the obtained suspension was added dropwise 0.7 mol of ethylene diamine maintaining the temperature of the reaction mixture at 80–85°C and pH at 9.0–11.0 by adding calcium oxide. When all amine was added, the reaction mixture was kept for 1.0–1.5 h at the same temperature and pH, cooled to 50–55°C, and mixed with concentrated hydrochloric acid at 70–75°C to decompose the calcium complex. Then the obtained solution was cooled to 10–15°C, and after 20 h the acid **II** dihydrochloride precipitate was filtered off. The latter was washed with ethanol and dried. Yield 40%. The target product structure was confirmed with ^{13}C NMR spectra data.

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