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ISSN 1070-3632, Russian Journal of General Chemistry, 2018, Vol. 88, No. 9, pp. 1874–1879. © Pleiades Publishing, Ltd., 2018.
Original Russian Text © A.R. Gataulina, E.M. Khasanova, N.A. Ulakhovich, G.A. Kutyrev, M.P. Kutyreva, 2018, published in Zhurnal Obshchei Khimii, 2018, Vol. 88, No. 9, pp. 1532–1537.

Dedicated to the 110th anniversary of M.I. Kabachnik's birth

Synthesis and Properties of Water-Soluble Branched Polyester Poly{3-[3-(morpholin-4-yl)propyl]amino}propionate and Its Copper(II) Complex

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Received June 29, 2018

Abstract—A new water-soluble multidentate ligand based on a second-generation hyperbranched polyester containing 3-(morpholin-4-yl)propionate fragments in the terminal position has been synthesized, and its complex with copper(II) has been obtained. The degree of polyester functionalization with aminopropylmorpholine is 56%.

Keywords: hyperbranched polyester poly{3-[3-(morpholin-4-yl)propyl]amino}propionate, copper(II) complex, ionization, pH potentiometry

DOI: 10.1134/S1070363218090189

Heterocyclic compounds such as morpholine, thiomorpholine, piperazine, and their derivatives are chelating ligands containing different donor groups and are among the most important pharmacophores in medicinal chemistry [1–6]. Therefore, these compounds are significant subunits of biologically active macromolecules and structures [7–9] that are used in the design of new antidepressants [10] or antifungal agents [11, 12]. Another equally important application of chelating heterocyclic ligands is synthesis of new coordination compounds of endogenous *d*-metals, which exhibit cytotoxicity against cancer cells [13–15]. Proper selection of base organic macromolecular structures in combination with their surface modification with pharmacophoric heterocycles and metal ions makes it possible to obtain new biodegradable amphiphilic derivatives for biotechnology and medicine. In this respect, nontoxic hyperbranched polyester polyols [16] can be successfully used as precursors with a persistent structure of the internal polyester moiety and widely variable peripheral hydroxo groups accessible for modification.

The present work continues the series of our studies aimed at synthesizing multidentate macromolecular ligands and polynuclear metal complexes on the basis of hyperbranched polyesters. Using hyperbranched polyester polyols as base structures we previously synthesized polyamines [17–20], polyester polycarboxylic acids [21–23], and polyester poly(phenylcarbamate) [24] that are capable of self-organizing [25], coordinating *d*-metal ions and binding to medicinal agents [19–21, 23, 26], and stabilizing metal nanoparticles [27, 28]. Study of their physicochemical properties has shown that not all hyperbranched polyester derivatives are amphiphilic. Therefore, the synthesis of new water-soluble derivatives and metal complexes based thereon is an independent and important problem of biomedical chemistry. In view of the aforesaid we have synthesized a second-generation hyperbranched polyester, poly(3-{[3-(morpholin-4-yl)propyl]amino}propionate).

The synthesis of hyperbranched polyester with terminal 4-(3-aminopropyl)morpholine fragmens included two stages. In the first stage, polyol **1** was modified via substitution of the terminal hydroxy groups by acrylate to obtain polyacrylate **2**. The subsequent addition of 4-(3-aminopropyl)morpholine to polyacrylate **2** (aza-Michael reaction) afforded morpholine derivative **3** (Scheme 1).