Synthesis of Novel Aromatic Core Zero Generation Dendrimers

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Abstract. Bromomethyl arenes used as polyfunctional core of dendrimers were derivatized with diethanolamine branches. The obtained compounds containing 4 or 6 hydroxyl terminal surface groups are highly water-soluble.

Keywords: dendrimer, bromomethyl arenes, diethanolamine

INTRODUCTION

The first dendrimer-like structure was presented in 1978 by Fritz Vögtle as a highly-branched macromolecule.1 Dendrimers are typically symmetric around the core, mono-dispersed molecules, having a very well defined size and delimited shape, respectively. The core is derivatized with branching molecules, containing functional groups, organized in generations. A subunit of the dendrimer is called a dendron. Dendrimers can be obtained by divergent (construction of the molecule is progressing from the core to the surface) or by convergent (starting from the end-groups and stepwise progressing inwards and lately attaching the dendron to the core) routes.2 The control over size, shape, and surface functionality makes dendrimers one of the “smartest” or customizable commercially nanotechnology products.3

Herein we report the synthesis of zero generation dendrimers using 1,4-bis(bromomethyl)benzene, 1,3,5-tris(bromomethyl)benzene and 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene as the core. Derivatization was made with diethanolamine and led to highly polar compounds.

Diethanolamine (DEA) is known for its application in several fields: as surface-active agent in cosmetics, agricultural products or pharmaceuticals.4 Biological testing proved that DEA derivatives show antibacterial, antifungal, anticancer and antioxidant properties.5

In the synthesis of some metallodendrimers 1,4-bis(bromomethyl)benzene has been used as a linking agent.6 Dendrimers constructed from 1,3,5-tris(bromomethyl)benzene core and derivatized with sodium tris(ethoxycarbonyl)methanide, 4-formylnbenzoic acid, triethyl phospine, 2-(2-pyridyl)benzimidazole, tosylate or N-tosylated aminoisophtalate diester7–11 had been reported. Literature data regarding the use of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene as central unit is related mainly to metallodendrimer synthesis.12

Since diethanolamine possesses the properties of secondary amines and alcohols due to the presence of both amino and hydroxyl functional groups, it undergoes different reactions. DEA reacts with acyl chlorides, cellulose derivatives or acids. It is also a suitable precursor for the morpholine synthesis.12 Morpholine was first obtained by the dehydration of diethanolamine in the presence of sulfuric acid. Several methods have been tested in order to obtain the heterocyclic compound in higher yield.13 Morpholine derivatives have a large scale of applications: as sulfur dioxide absorbent,14 as catalyst,15,16 in biochemical applications,17,18 in different hydrogels preparation,19,20 in morpholine-based chemotherapeutic agent synthesis.21–23

EXPERIMENTAL

Materials and Methods

The starting chemicals: 1,4-bis(bromomethyl)benzene, 1,3,5-tris-(bromomethyl)benzene, 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene, anhydrous potassium carbonate and diethanolamine were purchased from Sigma-Aldrich. Acetonitrile, ethanol, diethyl ether and 48 % aqueous hydrobromic acid were supplied from Merck. All chemicals and reagents were used as received.
Thin layer chromatography (TLC) monitoring was carried out using Merck Kieselgel 60 F 254 sheets. Spots were visualized by the use of UV light at 254 nm and colored via treatment with 5% ethanolic phosphomolybdic acid solution followed by heating. UV-Visible absorbance spectra were obtained us...
purpose. Reactions were carried out also using triethylamine instead of potassium carbonate to remove the formed hydrogen bromide from the reaction mixture; unfortunately, we encountered difficulties in separation of the formed triethylammonium bromide, it being soluble in acetonitrile. For the purification of compounds 3a–c column chromatography was first used but the separation of unreacted DEA from the dendrimer was not successful; vacuum distillation made this possible.

Mass Spectrometry

The ESI technique,\textsuperscript{25} being useful in both low mass molecules and macromolecules characterization, was involved as characterization method. Methanolic solutions of the synthesized compounds containing 0.5 mg mL\textsuperscript{-1} substrate per sample were analyzed. Figure 1 illustrates the recorded mass spectrum of compound 3b. The peak at \( m / z = 430 \) corresponds to [M+H]\textsuperscript{+}. Also the peak for [M+Na]\textsuperscript{+} is detectable at \( m / z = 452 \).

In the mass spectrum of compound 3c (Figure 2) the peak for [M+H]\textsuperscript{+} appears at 472 \( m / z \) value.

NMR Spectroscopy

All compounds were structurally characterized by nuclear magnetic resonance spectroscopy. In Figure 3 the \(^1\)H-NMR spectrum for compound 3b recorded in CD\textsubscript{3}CN is depicted. Comparing the signals with the ones appearing on the spectrum recorded in D\textsubscript{2}O, a new signal is present at 3.14 ppm assigned to the terminal –OH protons. Based on these findings in order to differentiate the methylene protons from the diethanolamine chains, the corresponding quaternary ammonium salt of the product was formed by adding HCl to compound 3b.

The spectrum recorded in DMSO-\textit{d}\textsubscript{6} (Figure 4) shows a broad multiplet of four peaks at 3.28 ppm, 3.26 ppm, 3.22 ppm and 3.20 ppm assigned to the H-a, H-a' noted protons while another multiplet is detected, with four peaks at 3.79 ppm, 3.79 ppm, 3.78 ppm and 3.77 ppm assigned to protons noted by H-b, H-b'. This unexpected splitting of the signals suggests that the geminal H-a, H-a' and H-b, H-b' pairs are diastereotopic. In the aromatic zone, the splitting of the signal is also observed. A multiplet appears between 7.82-8.05 ppm, corresponding to the benzenic protons (1-H, 3-H, 5-H).

Forasmuch the diethanolamine branch methylene protons are differenced and the aromatic protons are not
The aqueous solution of the considered compounds shows no UV absorption changes in the range of 200–400 nm.

In order to grow the dendrimer by one generation, a new derivatization step with diethanolamine is required. For this purpose, the terminal hydroxyl groups must be halogenated first to allow the coupling of secondary amine branches, by adding concentrated HBr and heating at 160 °C. It is known that diethanolamine undergoes dehydration with sulfuric acid to form morpholine. In the presence of hydrobromic acid the compound 4a was formed when 2,2',2'',2'''-[1,4-phenylenebis(methylene)]tetra-ethanol was used.

CONCLUSION

In this paper we reported the synthesis of two new dendrimers, having as the core 1,3,5-tris(bromo-methyl)-benzene and 1,3,5-tris(bromomethyl)-2,4,6-trimethyl-benzene, by derivatization with diethanolamine branches. The obtained compounds, with 4 or 6 hydroxyl terminal surface groups, show an increased water-solubility, in comparison with the parent molecules. 2,2',2'',2'''-[1,4-phenylenebis(methylene)nitriilo)]tetra-ethanol in presence of aqueous hydrogen bromide led to the formation of 4,4''-[1,4-phenylene-bis-(methylene)]-dimorpholine.

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