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Click chemistry to fluorescent hyperbranched polymers. 1 – Synthesis, characterization and spectroscopic properties

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ABSTRACT

The synthesis of two new fluorescent hyperbranched polymers with low molecular weight macromolecular skeleton is presented. An experimental approach to obtain fluorescent dansyl derivatives of commercial hydroxyl-terminated hyperbranched polymers (HBPs) have been obtained through click chemistry reactions. Photophysical characterization of the HBP probes compared with their low molecular weight reference compounds shows that the fluorophore in the polymer skeleton behaves as an individual molecule, showing similar emission properties in terms of absorption extinction coefficient, fluorescence quantum yields and position of the fluorescent band. Solvatochromic study of the HBPs in several solvents using E_T30, π^* and SPP scales demonstrates that there is not a loss of sensitivity towards polarity when the sensor moiety is included in the HBP structure. The absence of quenching deactivation processes in these multifunctional sensors has been attributed to their irregular hyperbranched skeleton, in contrast to what occurs in highly regular dendrimeric analogues. The advantage of the oligomeric probes versus the monomeric ones has been checked preparing transparent and sensitive films using the fluorophores as dopants. The swelling kinetics of the films has been monitored by fluorescence and the diffusion coefficient estimated. Negligible extraction of the hyperbranched probes was found for long time immersions of the films in acetonitrile, whereas low molecular weight derivatives showed continuous extraction.

1. Introduction

The fluorescent labeling of molecules is a powerful method for investigating events at a molecular level. It is a well-developed field in the area of biomolecules [1], whereas in the field of materials science it is increasing in importance [2]. The use of specific labels for proteins and biological molecules is very well developed, but in general, the reactive labels are commercialized as expensive kits optimized for biological tests [3].

The preparation of fluorescent dendritic polymers has been the subject of deep research for the last 20 years. After the commercialization of amine-terminated dendrimers, fluorescent dendrimers have been used for many different purposes such as: gene carriers [4], nanoclusters [5], guest encapsulation [6], functionalization of surfaces [7], chemosensors [8], molecular recognition [9] and many others.

However, the development of these molecules for a practical use has not been extended very much given the high price of the dendrimer starting material, the low availability of different chemical structures of the dendrimer

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branches or the difficulty and time consuming synthetic steps. In addition, a strong quenching of the fluorescence emission is found with increasing generation for highly modified dendrimers [10].

In materials science, and looking for a practical use of the sensors, the large-scale preparation of the sensors should be possible.

For most cases, hyperbranched polymers may be able to replace dendrimers in utility, because they can be prepared much more rapidly and economically [11]. Their structure gives them excellent flow and processing properties, and they are characterized by lower viscosity than those linear polymers of comparable molecular weight. The highly branched structures gives further access to a larger number of reactive end groups and thus, HBPs have found commercial applications, such as in coatings and nanotechnology [12].

The functionalization of hyperbranched structures with fluorescent groups has not attracted the same interest. A very few specific architectures have been described [13,14], but little effort has been devoted to develop a general methodology to obtain fluorescent hyperbranched polymers. Recently, the synthesis of different fluorescent HBPs have been described for different applications such as biological imaging [15], detection of explosives [16] or detection of chemicals (ascorbic acid [17], glucose [18]). In general, all of them involve *de novo* multi-step synthetic procedures.

The azide–alkyne click reaction has been used as an efficient functionalization tool since the pioneering work of Sharpless et al. [19]. Its advantages of efficiency, mild reaction conditions, and function tolerance, etc. [20,21], make it an attractive and efficient strategy. It has been recently used to graft hyperbranched polymers to different substrates, such as surfaces [22], carbon nanotubes [23] or membranes [24], for the preparation of functional hyperbranched polymers [25–28] and for the functionalization of their peripheral groups [29]. Furthermore, the 1,2,3-triazole ring formed is resistant to hydrolysis, oxidation, reduction and other modes of cleavage.

In this work we present a convenient general route for the functionalization of hydroxyl terminated commercial hyperbranched polymers with fluorescent groups, particularly centered on the preparation of two dansyl-functionalized hyperbranched polymers, Boltorn H20 and Hybrane P1000, and their study as fluorescent sensors for polarity changes in their microenvironment. Taking into account the versatility and the high yields obtained through click chemistry, the approach for the synthesis has been the synthesis of azide-modified hyperbranched polymers and subsequent reaction with a dansyl moiety functionalized with a triple bond. The advantages of the hyperbranched probes versus the monomeric ones are presented.

The dansyl chromophoric group, 5-(dimethylamino)-1-naphthalenesulfonamide, has been selected for labeling the hyperbranched polymers because it shows intense absorption bands in the near UV and a strong fluorescence in the visible region. These properties made this fluorophore to be extensively used for sensing or labeling purposes [30].

2. Experimental

2.1. Materials

Propargylamine (98%), mesyl chloride (>99.7%), sodium bicarbonate (99.7%), anhydrous magnesium sulfate (>99.5%), dansyl chloride (>99%), triethylamine (>99%), hydrochloric acid (37%), sodium hydroxide (>98%), sodium chloride (>99%), sodium azide (>99%), (+)-sodium-L-ascorbate (>98%), copper(II) sulfate pentahydrate (>98%), ethylenediaminetetraacetic acid (>98.5%), ammonium hydroxide sol. (28.0–30.0% NH_3 basis), anhydrous sodium sulfate (>99%), *p*-toluenesulfonic acid monohydrate (>98.5%), methyl 4-chlorobutyrate (>98%) were obtained from Aldrich and used without further purification. 2-Hydroxyethyl methacrylate (HEMA) and 1,6-hexanediol dimethacrylate (HDDMA), both form Aldrich, were used as received. Phenyl bis(2,4,6-trimethyl benzoyl) phosphine oxide (Irgacure 819) from Ciba Specialty Chemicals was used without purification. Solvents used for the synthesis were: anhydrous dichloromethane (99.5%, Aldrich, dried over molecular sieves), pyridine (anhydrous, 99.8%, Aldrich), diethyl ether (Carlo Erba), chloroform (Scharlau), benzene (>99%, Aldrich), ethyl acetate (99.5%, Aldrich) and dimethylformamide (99%, Aldrich), all reagent grade and used as received. MilliQ water was obtained from water purification facility (Millipore Milli-U10). Hybrane P1000 (Mw_{theor} = 1186 g/mol, —OH_{theor} = 7) and Boltorn H20 (Mw_{theor} = 1706 g/mol, —OH_{theor} = 16), both from Polymer Factory, were used as received.

Flash column chromatography was performed by using silica gel (60 Å pore size, 230–400 mesh particle size, Merck). Reactions were monitored using thin layer chromatography (TLC) on silica gel-coated plates (Merck 60 F254). Detection was performed with UV light and/or by insertion in an iodine chamber.

Solvents for spectroscopic analysis (acetonitrile, methanol, ethyl acetate, chloroform, tetrahydrofuran, diethyl ether, cyclohexane and toluene, from Sigma–Aldrich) and ethanol (from Scharlau) were of spectroscopic grade and used as received.

2.2. Synthesis

2.2.1. Synthesis of 5-(dimethylamino)-N-(2-propynyl)-1-naphthalenesulfonamide (DANSyne)

According to previously published methods [31–33] propargylamine (360 μL, 5.55 mmol, 3 equiv.) was added to a solution of dansyl chloride (500 mg, 1.85 mmol, 1 equiv.) and triethylamine (260 μL, 1.85 mmol, 1 equiv.) in anhydrous dichloromethane (15 mL) at 0 °C under nitrogen. After stirring for 1 h, the reaction mixture was warmed to room temperature and stirred for an additional hour (TLC monitoring). The volatiles were removed under vacuum and the crude product was purified by column chromatography on silica gel (CH_2Cl_2:Et_2O, 1:1 v/v) giving DANSyne (460 mg, 86%) as a pure yellow powder.

ESI-MS (*m*/*z*) Calcd for $C_{15}H_{16}N_2O_2S$ $[M]^+$ 288; found $[M+H]^+$ 289.