Published in final edited form as:

Chemistry. 2013 November 25; 19(48): 16374–16381. doi:10.1002/chem.201302442.

Zwitterionic Moieties from the Huisgen Reaction-A Case Study with Amphiphilic Dendritic Assemblies

Rajasekhar R. Ramireddy^{[a],†}, Ayyagari V. Subrahmanyam^{[a],†}, and S. Thayumanavan^[a]

S. Thayumanavan: thai@chem.umass.edu

^[a]Department of Chemistry, University of Massachusetts, Amherst, MA 01003 (USA), Fax: (+1) 413 545 4490

Abstract

Supramolecular nano-assemblies that reduce non-specific interactions with biological macromolecules, such as proteins, are of great importance for various biological applications. Recently, zwitterionic materials have been shown to reduce non-specific interactions with biomolecules, owing both to their charge neutrality and their ability to form strong hydration layer around zwitterions via electrostatic interactions. In this article, we present new triazole-based zwitterionic moieties that are incorporated as the hydrophilic functionalities in facially amphiphilic dendrons. The amphiphilic zwitterionic dendrons spontaneously self-assemble in aqueous solutions forming micelle-type aggregates, which are confirmed by DLS, TEM, and fluorescence techniques. We also compare the structural and functional characteristics of the zwitterionic dendrons with the corresponding charge-neutral PEG-based dendrons and anionic carboxylate-based dendrons. Surface charge measurements, temperature sensitivity and evaluation of interactions of these assemblies with proteins form the bases for these comparisons.

Keywords

Zwitterionic dendrimers; Micelles; Triazole; Protein-dendrimer interactions

Introduction

There has been significant emphasis on the development of new anti-fouling materials, which reduce non-specific interactions with biological macromolecules.^{1–4} These types of materials can impact a variety of applications ranging from antifouling coatings in ships⁵ to biomedical applications such as drug delivery,^{6–8} implants,⁹ and sensors.¹⁰ Molecules that exhibit non-fouling features can be generally divided into two major classes: polyhydrophilics and polyzwitterionics. Popular polyhydrophilics include polyethylene glycol (PEG),^{11–14} polysaccharides,^{15, 16} and polyhydroxy materials.^{17–19} Besides being hydrophilic and hence the requisite water solubility, the key functional groups in these molecules are also charge neutral and present hydrogen bond donor/acceptor characteristics. PEG, the most extensively studied among the polyhydrophilics, has the advantage of being easily accessible and exhibiting good non-fouling characteristics. However, although the temperature sensitivity (often referred to as lower critical solution temperature (LCST) behavior) of the PEG moieties has been taken advantage of,^{20–23} the phase and hydrophilicity changes associated with this transition can be deleterious to other

Correspondence to: S. Thayumanavan, thai@chem.umass.edu.

[†]Authors contributed equally

Supporting information for this article is available on the WWW under <http://www.chemurj.org/> or from the author.

applications.^{24, 25} Also, it has been shown that PEG is susceptible to auto-oxidation at biologically relevant conditions, which converts them into reactive aldehyde moieties.^{26, 27} These features have resulted in search for alternate functional groups that can reliably endow non-fouling characteristics and a significant part of that focus has been on polyzwitterionics.

Zwitterionics, such as sulfobetaines,^{28, 29} carboxybetaines,^{30, 31} and phosphobetaines,^{32, 33} possess both positive and negative charges on the same monomer unit. These polybetaines are gaining attention as potential alternatives to PEG, due to their overall charge neutrality, high water solubility, and their ability to bind water *via* electrostatics. These features have been shown to decrease the rate of adsorption of proteins, cells, and bacteria to their surfaces.^{4, 34, 35} In general, the non-fouling nature of zwitterionics are studied by coating them on various surfaces and then measuring the extent of adsorption of proteins or cells upon exposure to biological milieu.³⁶ Considering the versatility of the 1,3-Huisgen cycloaddition reaction, the so-called click chemistry, we were interested in developing zwitterionic moieties that can be conveniently introduced with this reaction. In addition, the versatility of this reaction allows for high fidelity incorporation of the zwitterionic moieties on multiple surface sites on a molecular surface. Moreover, due to the continuing interest in amphiphilic supramolecular assemblies and their use in applications such as delivery and sensing, we were particularly interested in evaluating such a functional group on surfaces of assemblies in solution rather than on surfaces.

Towards this goal, we envisaged the possibility of triazole based zwitterionic functionalities and introduce them as hydrophilic groups on the surfaces of assemblies based on facially amphiphilic dendrons (Figure 1). These dendrons are known to form micelle-like assemblies in the aqueous phase, where the hydrophilic functional groups are presented on the surface of the spherical assembly.³⁷ Most importantly, since both polyelectrolyte and PEG-based facially amphiphilic dendrons have been shown to provide similar assemblies, this architecture provides the foundation for direct evaluation of the targeted zwitterionic assemblies through comparisons.

Results and Discussion

Molecular Design and Synthesis

Since the key objective here is to incorporate a zwitterionic moiety through the Huisgen cycloaddition chemistry,^{38–43} we targeted a triazolium-based zwitterionic moiety. With the cationic part of the zwitterion in the triazolium group, we envisaged a simple introduction of the anionic moiety through the click chemistry. Accordingly, we use a functional equivalent of azidoacetic acid to react with the alkyne-containing dendrons. The targeted facially amphiphilic dendrimers are based on a biaryl repeat unit (Scheme 1).^{14, 44} In most other amphiphilic dendrimers,^{45, 46} the amphiphilicity arises from the difference in hydrophilicity between the functional groups at the periphery and the dendrimer backbone. In these facially amphiphilic dendrimers, both hydrophobic and hydrophilic units are placed in every repeat unit. The zwitterionic triazolium unit will be introduced on the hydrophilic face of the dendron.

Synthesis of the zwitterionic dendron **G1** began by first preparing the biaryl monomer **1** in five steps using a previously reported procedure (Scheme 2).⁴⁷ Alkylation of phenolic groups with 1-bromodecane and isolation of the mono-substituted product (43% yield) resulted in incorporation of the hydrophobic decyl moiety on one of the face of the monomer unit. The resultant mono-phenol was then treated with propargyl bromide to introduce the acetylenic moiety for the click chemistry in 83% yield. The methoxymethyl ether (MOM) protecting group was then removed by treatment with a Dowex resin to afford the biaryl monomer **2** in 64% yield. This biaryl molecule is the repeating unit for the dendron. The

monomer incorporated at the periphery of these dendrons does not contain the biaryl units; these are based on the simple benzyl ether dendron monomers. Reaction between the bromomethyl version of the peripheral monomer **3** and the biaryl molecule **2** yielded the G1 dendron **4** in 74% yield. The G2 dendron was prepared similarly by reacting the bromomethyl version of **4** with the repeat monomer unit **2** (see Supporting Information for details).

These acetylene-containing dendrons were then used for the Huisgen cycloaddition reaction (click chemistry) with α -azido-*t*-butylacetate **5** (synthesized from α -bromo-*t*-butylacetate and sodium azide). This reaction afforded the G1-triazole ester **6** in 71% yield. Methylation of the triazole groups, using iodomethane in acetonitrile at 80 °C for 12 h, afforded the cationic dendron containing the *N*-methyl-triazolium esters. The *tert*-butyl ester moieties were then hydrolysed using trifluoroacetic acid (TFA) to provide the targeted zwitterionic dendron **G1** (Scheme 2). The conversion of the propargyl moiety to the triazole ester and the subsequent conversion to the zwitterionic moiety were monitored by both IR and NMR spectroscopy (Figure 2). The acetylenic proton in the precursor and the triazole proton in the clicked products were used as the key diagnostic peaks in NMR. Similarly, the disappearance of the acetylenic peaks and the change in the C=O stretching frequencies were used as the diagnostic peaks in IR. A similar approach was used for the syntheses of G0 and G2 zwitterionic dendrons, the details of which are outlined in the Supporting Information.

Self-assembly characteristics of dendrimers

We were first interested in identifying whether these (otherwise quite hydrophobic) dendrons can be solubilized (or dispersed) in the aqueous phase. We were gratified to find that these dendrons were indeed quite soluble in water. Next, we were interested in investigating whether these dendrons do form the amphiphilic assemblies that we have previously observed. To probe the assembly characteristics, we first utilized the possibility of hydrophobic guest encapsulation by these assemblies. We used Nile red as a fluorescent hydrophobic guest for this purpose. Nile red is not soluble in aqueous solutions. However, in the presence of the dendrons, significant amounts of Nile red is solubilized in the aqueous phase, indicating that these molecules are accommodated in the hydrophobic pockets of self-assembled aggregates (Figure 3a). This feature was then used to calculate the critical aggregation concentrations (CAC) of **G1** and **G2** dendrons (Figure 3b). The CACs of the **G1** and **G2** dendrons were calculated to be $\sim 6 \mu\text{M}$ and $8 \mu\text{M}$ respectively. We observed that, the solubility of **G0** is very low; hence, we did not perform any further studies with this molecule. The size and shape of these assemblies were then investigated by dynamic light scattering (DLS) and transmission electron microscopy (TEM). The sizes of the assemblies were found to be about 20 nm and 26 nm for the **G1** and **G2** dendrons respectively (Figure 3c). Finally, TEM experiments verified the micelle-like assembly formation of these dendritic aggregates above their CAC and that the shapes of these assemblies are spherical (Figure 3d). Overall, the combination of experiments unambiguously suggests that the zwitterionic dendrimers form self-assembled aggregates in aqueous solutions.

Surface charge studies

Surface charge plays an important role in an assembly's non-specific interactions with proteins. The reason then for targeting the zwitterionic moieties is that these species would result in a neutral overall surface charge. For this reason, we evaluated the zeta potential of zwitterionic dendrimer assemblies at $25 \mu\text{M}$ concentration, well above their CAC. The zeta potential of the **G1** and **G2** dendrons were found to be -3 mV and -2 mV respectively (Figure 4). This clearly demonstrates the near charge neutral nature of the zwitterionic dendritic aggregates. To get a better perspective on the magnitude of these numbers, we

compared the zeta potentials of structurally similar dendritic assemblies as controls. The anionic carboxylate G1 and G2 dendrons (**7** and **8**, Scheme 3) exhibited much higher negative zeta potentials of -24 mV and -40 mV. On the other hand, the charge neutral PEG-based G1 and G2 dendrons (**9** and **10**, Scheme 3) exhibited the zeta potentials of -2 mV and -10 mV respectively. PEG-based assemblies exhibit slightly negative surface charges the reason for which is not clear.^{48, 49} These comparisons further support the charge neutral features of the zwitterionic dendritic aggregates.

Temperature sensitivity

One among the reasons for our interest in zwitterionic functionalities as hydrophilic moieties arises from their lack of temperature sensitivity and thus the stability of the assemblies in a broader range of temperatures. To test this, we investigated whether the turbidity of the solution increases with temperatures. It is known that the PEG-based assemblies do exhibit the so-called LCST behaviour.¹⁴ Turbidity generation in solution can be conveniently measured by measuring the anomalous scattering that arises in solution. We used the high-tension voltage, arising due to the turbidity induced scattering, in a circular dichroism spectrometer to probe the LCST behaviour of these molecules. As seen in Figure 5, while the PEG-based dendrons **9** and **10** exhibits significant temperature dependent turbidity, the **G1** and **G2** zwitterionic dendrons remained clear in solution in the entire temperature range (25 – 50 °C) or even at higher temperatures (Fig S3).

Dendrimer-protein interactions

Finally, to assess the non-specific interactions of the zwitterionic dendritic assemblies, we used binding-induced disassembly as the probe. We have previously shown that non-specific interaction between amphiphilic assemblies and proteins can result in binding induced disassembly that can be read by changes in the emission properties of an encapsulated fluorophore.^{50, 51} Accordingly, we exposed 20 μ M concentration of dendritic assemblies, containing encapsulated Nile red, with equimolar concentrations of several proteins at pH 7.4. The emission changes were monitored over a 12 hour time period (Figure 6). We chose three different proteins, pepsin ($pI = 2.8$, $M_n = 30$ kDa), thrombin ($pI = 7.2$, $M_n = 36$ kDa), and chymotrypsin ($pI = 9.2$, $M_n = 25$ kDa), for this study. These proteins were chosen for their divergence in surface charge; these are anionic, neutral, and cationic respectively at the experimental pH 7.4. Interestingly, the zwitterionic moieties did not show any significant release of the dye molecules ($<20\%$ change in emission). However, when these were compared with the corresponding carboxylate and PEG-based dendrons, we found that these dendrons also did not exhibit any significant changes in emission intensity with time. Considering that we have shown that anionic assemblies do interact very well with chymotrypsin and modify its enzymatic properties,⁵² we ascribed this result to the possibility that these interactions do not result in binding-induced disassembly and thus the dye molecules are not released. To test this possibility, we used metalloproteins instead of the non-metalloproteins above.

We have previously shown that the proximity resulting from the binding interaction between metalloproteins and polyelectrolyte assemblies is sufficient to quench the emission of an encapsulated fluorophore.⁵³ In this case, the binding-induced disassembly process is not required. The emission quenching should directly report the binding interaction between the proteins and the amphiphilic assemblies. The fluorescence quenching here would be due to the energy or electron transfer to the cofactor functional groups in the proteins. We chose three metalloproteins, cytochrome C (Cyt C, $pI = 10.2$, $M_n = 12$ kDa), myoglobin (Myo, $pI = 6.8$, $M_n = 18$ kDa), and hemoglobin (Hb, $pI = 7.2$, $M_n = 68$ kDa). We were gratified to find that indeed the zwitterionic dendrons did not exhibit any appreciable fluorescence quenching with Cyt C and Myo (Figure 7). However, emission quenching was observed

with Hb. The value of these results were further tested by comparing them with the charge neutral PEG and the anionic carboxylate dendritic assemblies using these three metalloproteins. Interestingly, the fluorophore in the PEG-based dendrons were also not quenched by both Cyt C and Myo, but these also exhibited quenching with Hb. However, in the case of assemblies based on the anionic dendrons, all three metalloproteins strongly quenched the emission of the encapsulated fluorophore. This is attributed to the anticipated non-specific interactions between the polyelectrolyte assemblies and proteins. The reasons for the non-specific quenching with hemoglobin in the zwitterionic and the PEG based assemblies are not clear to us at this time. Overall, the triazolium carboxylate based zwitterionic dendritic assemblies behave very similar to that of the popular PEG-based assemblies in their interactions with proteins.

Conclusions

In summary, we have designed and developed a clickable zwitterionic functional group, which has been tested for its synthetic and functional utility using the facially amphiphilic dendritic scaffold. We have shown that: (i) these dendrons based on the triazolium carboxylate zwitterionic moieties can indeed be solubilized in the aqueous phase; (ii) these dendrons form self-assembled aggregates in aqueous solutions with guest encapsulation capabilities; (iii) these assemblies are charge neutral, as confirmed by zeta potential measurements; (iv) these assemblies are stable aggregates over a wide temperature range and do not exhibit any LCST behaviour, providing a promising alternative to PEG-based systems; (iv) the non-specific interactions of these zwitterionic assemblies are comparable to those from PEG-based assemblies. Although our initial demonstration has been with triazolium carboxylate, the design can be easily extended to a variety of other zwitterionic combinations and for a variety of polymeric scaffolds. Since biofouling is a major hurdle in multiple areas, the findings here will not only be useful in applications such as drug delivery and surface coatings, but also in areas such as controlled multivalent presentation of ligands for interactions with biological macromolecules.^{54, 55}

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Support from NIGMS of the NIH (GM-065255) is gratefully acknowledged.

Notes and References

1. Ratner BD, Bryant SJ. *Ann Rev Biomed Eng.* 2004; 6:41–75. [PubMed: 15255762]
2. Dalsin JL, Messersmith PB. *Mater Today.* 2005; 8:38–46.
3. Chen S, Jiang S. *Adv Mater.* 2008; 20:335–338.
4. Chen S, Li L, Zhao C, Zheng J. *Polymer.* 2010; 51:5283–5293.
5. Grozea CM, Walker GC. *Soft Matter.* 2009; 5:4088–4100.
6. Duncan R. *Nat Rev Drug Discovery.* 2003; 2:347–360.
7. Torchilin VP. *J Controlled Release.* 2001; 73:137–172.
8. Salmaso S, Caliceti P. *J Drug Deliv.* 2013; 2013:19.
9. Banerjee I, Pangule RC, Kane RS. *Adv Mater.* 2011; 23:690–718. [PubMed: 20886559]
10. Lin PC, Weinrich D, Waldmann H. *Macromol Chem Phys.* 2010; 211:136–144.
11. Harris, JM. *Poly (ethylene glycol) chemistry: biotechnical and biomedical applications.* Plenum Publishing Corporation; 1992.

12. Zalipsky S. *Adv Drug Delivery Rev.* 1995; 16:157–182.
13. Cheng J, Teply BA, Sherifi I, Sung J, Luther G, Gu FX, Levy-Nissenbaum E, Radovic-Moreno AF, Langer R, Farokhzad OC. *Biomaterials.* 2007; 28:869–876. [PubMed: 17055572]
14. Aathimanikandan SV, Savariar EN, Thayumanavan S. *J Am Chem Soc.* 2005; 127:14922–14929. [PubMed: 16231948]
15. Holland NB, Qiu Y, Ruegsegger M, Marchant RE. *Nature.* 1998; 392:799–801. [PubMed: 9572137]
16. Dwek RA. *Chem Rev.* 1996; 96:683–720. [PubMed: 11848770]
17. Zhao C, Li L, Wang Q, Yu Q, Zheng J. *Langmuir.* 2011; 27:4906–4913. [PubMed: 21405141]
18. Gam-Derouich S, Gosecka M, Lepinay S, Turmine M, Carbonnier B, Basinska T, Slomkowski S, Millot MC, Othmane A, Ben Hassen-Chehimi D, Chehimi MM. *Langmuir.* 2011; 27:9285–9294. [PubMed: 21678957]
19. Martwiset S, Koh AE, Chen W. *Langmuir.* 2006; 22:8192–8196. [PubMed: 16952261]
20. Chua GBH, Roth PJ, Duong HTT, Davis TP, Lowe AB. *Macromolecules.* 2012; 45:1362–1374.
21. Qin S, Geng Y, Discher DE, Yang S. *Adv Mater.* 2006; 18:2905–2909.
22. Lutz JF, Akdemir O, Hoth A. *J Am Chem Soc.* 2006; 128:13046–13047. [PubMed: 17017772]
23. Lutz JF. *Adv Mater.* 2011; 23:2237–2243.
24. Knop K, Hoogenboom R, Fischer D, Schubert US. *Angew Chem-Int Edit.* 2010; 49:6288–6308.
25. Keefe AJ, Jiang S. *Nat Chem.* 2011; 4:59–63. [PubMed: 22169873]
26. Herold DA, Keil K, Bruns DE. *Biochem Pharmacol.* 1989; 38:73–76. [PubMed: 2642704]
27. Li L, Chen S, Jiang S. *J Biomater Sci, Polym Ed.* 2007; 18:1415–1427. [PubMed: 17961324]
28. Terayama Y, Kikuchi M, Kobayashi M, Takahara A. *Macromolecules.* 2010; 44:104–111.
29. Lee WF, Chen YM. *J Appl Polym Sci.* 2003; 89:1884–1889.
30. Cao ZQ, Zhang L, Jiang SY. *Langmuir.* 2012; 28:11625–11632. [PubMed: 22783927]
31. Zhang Z, Chen S, Jiang S. *Biomacromolecules.* 2006; 7:3311–3315. [PubMed: 17154457]
32. Santonicola MG, Memesa M, Meszynska A, Ma YJ, Vancso GJ. *Soft Mater.* 2012; 8:1556–1562.
33. Trippett S, Walker DM. *J Chem Soc (Resumed).* 1961; 0:1266–1272.
34. Chen H, Yuan L, Song W, Wu Z, Li D. *Prog Polym Sci.* 2008; 33:1059–1087.
35. Chen S, Zheng J, Li L, Jiang S. *J Amer Chem Soc.* 2005; 127:14473–14478. [PubMed: 16218643]
36. Ladd J, Zhang Z, Chen S, Hower JC, Jiang S. *Biomacromolecules.* 2008; 9:1357–1361. [PubMed: 18376858]
37. Ramireddy RR, Raghupathi KR, Torres DA, Thayumanavan S. *New J Chem.* 2012; 36:340–349.
38. Nulwala H, Takizawa K, Odukale A, Khan A, Thibault RJ, Taft BR, Lipshutz BH, Hawker CJ. *Macromolecules.* 2009; 42:6068–6074.
39. Rostovtsev VV, Green LG, Fokin VV, Sharpless KB. *Angew Chem-Int Edit.* 2002; 41:2596–2599.
40. Wu P, Feldman AK, Nugent AK, Hawker CJ, Scheel A, Voit B, Pyun J, Fréchet MJM, Sharpless KB, Fokin VV. *Angew Chem-Int Edit.* 2004; 43:3928–3932.
41. Takizawa K, Nulwala H, Thibault RJ, Lowenhielm P, Yoshinaga K, Wooley KL, Hawker CJ. *J Polym Sci, Part A: Polym Chem.* 2008; 46:2897–2912.
42. Nulwala HB, Tang CN, Kail BW, Damodaran K, Kaur P, Wickramanayake S, Shi W, Luebke DR. *Green Chem.* 2011; 13:3345–3349.
43. Perroni DV, Mahanthappa MK. *Soft Matter.* 2013; 9:7919–7922.
44. Vutukuri DR, Basu S, Thayumanavan S. *J Am Chem Soc.* 2004; 126:15636–15637. [PubMed: 15571373]
45. Newkome GR, Moorefield CN, Baker GR, Saunders MJ, Grossman SH. *Angew Chem-Int Edit.* 1991; 30:1178–1180.
46. Hawker CJ, Wooley KL, Frechet MJM. *J Chem Soc, Perkin Trans 1.* 1993:1287–1297.
47. Azagarsamy MA, Sokkalingam P, Thayumanavan S. *J Am Chem Soc.* 2009; 131:14184–14185. [PubMed: 19757790]
48. Zhang S, Zou J, Zhang F, Elsabahy M, Felder SE, Zhu J, Pochan DJ, Wooley KL. *J Am Chem Soc.* 2012; 134:18467–18474. [PubMed: 23092249]

49. Zhuang J, Jiwanich S, Deepak VD, Thayumanavan S. ACS Macro Lett. 2011; 1:175–179.
50. Savariar EN, Ghosh S, Gonzalez DC, Thayumanavan S. J Am Chem Soc. 2008; 130:5416–5417. [PubMed: 18384200]
51. Gonzalez DC, Savariar EN, Thayumanavan S. J Am Chem Soc. 2009; 131:7708–7716. [PubMed: 19435315]
52. Klaikherd A, Sandanaraj BS, Vutukuri DR, Thayumanavan S. J Am Chem Soc. 2006; 128:9231–9237. [PubMed: 16834397]
53. Sandanaraj BS, Demont R, Thayumanavan S. J Am Chem Soc. 2007; 129:3506–3507. [PubMed: 17341087]
54. Sashiwa H, Shigemasa Y, Roy R. Macromolecules. 2001; 34:3905–3909.
55. Wolfenden ML, Cloninger MJ. J Am Chem Soc. 2005; 127:12168–12169. [PubMed: 16131163]

Figure 1.
Cartoon representation of zwitterionic dendrimer aggregation formation and its protein-resistant characteristics

Figure 2.
Spectral data indicating the conversion of the propargyl/decyl dendron to the zwitterionic dendron

Figure 3. Self-assembly characteristics of the zwitterionic dendrons: a) Emission spectrum of an aqueous solution of Nile red in the presence and absence of G1 and G2 dendrons ($\lambda_{\text{ex}} = 550$ nm); (b) CAC calculation for G1 by plotting fluorescence intensity of Nile red vs concentration of G1 dendron ($\lambda_{\text{ex}} = 550$ nm; $\lambda_{\text{em}} = 618$ nm). (c) Size of the aggregates determined by DLS at 25- μM concentrations of G1 and G2. (d) TEM images of G1 and G2 dendrons confirming the formation of micelle assemblies.

Figure 4.
Zeta potential of G1 and G2 dendritic assemblies

Figure 5. HT voltage measurements for a) PEG dendrimers, b) Zwitterionic dendrimers. c) LCST behavior of PEG G1 dendrimer at 40 °C, compared to zwitterionic dendrimers.

a) G1 Dendrimers + Non-metalloprotein interactions

b) G2 Dendrimers + Non-metalloprotein interactions

Figure 6.

Interactions of G1 and G2 dendrons with non-metalloproteins (at equal concentrations) monitored by fluorescence intensity decrease attributed to precipitation of released dyes over time.

a) G1 Dendrimers + Metalloprotein interactions

b) G2 Dendrimers + Metalloprotein interactions

Figure 7.

Interactions of G1 and G2 dendrons with metalloproteins (at equal concentrations) monitored by fluorescence intensity decrease attributed to quenching by metalloproteins over time.

Scheme 1.
Chemical structures of the zwitterionic dendrons

Scheme 2.
Synthetic scheme for the clickable zwitterionic G1 dendron.

Scheme 3.
Chemical structures of G1 and G2 control dendrons