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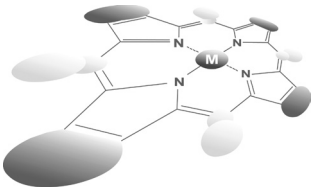

Amphiphilic zinc phthalocyanine dendrimers by the Click Chemistry approach

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Dedicated to Professor John A. Shelnutt on the occasion of his 65th birthday

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ABSTRACT: A series of new zinc phthalocyanine dendrimers with an increasing branched shell of oligoethylene glycol end groups has been synthesized. Owing to the presence of these hydrophilic termini at the dendrimer surface, all compounds are highly soluble in a wide range of solvents including water. The monodispersity of the amphiphilic dendrimers has been unambiguously evidenced by both NMR and MS techniques. UV-vis experiments point out that the tendency of the central phthalocyanine chromophore to aggregate in polar protic solvents is not significantly reduced regardless of the dendritic shell surrounding the macrocyclic chromophore.

KEYWORDS: phthalocyanines, dendrimers, Click Chemistry, hydrophilic systems.

INTRODUCTION

Phthalocyanines feature some remarkable properties originating not last from the exceptionally high absorption that lies typically in the visible region of the UV-vis spectrum between 630 to 750 nm [1, 2]. This so-called Q-band is the reason that makes such chromophores valuable in different fields of science and technology [3]. The particular interest in hydrophilic phthalocyanines arises from the prospective use in fields like biomedicine or photobiology for instance as photosensitizers in photodynamic therapy [2d, 4].

Similar to the synthesis of phthalocyanines in general, the preparation of hydrophilic phthalocyanine derivatives can be accomplished by two fundamental approaches, *i.e.* placing hydrophilic moieties in the peripheral or the axial positions, respectively. Whereas the former has been demonstrated to not suppress the phenomenon of aggregation, the latter is viable when aiming at non-aggregated water-soluble scaffolds. Phthalocyanines as functional units have also been in the centre of dendrimers [5]. Dendritic systems described in the literature dealing with an overall hydrophilic character for instance with charged exterior created by charged surfaces with *e.g.* carboxylate moieties of Fréchet- [6] or Newkome-type [7], or with neutral terminal oligoethylene chains [8]. A particular feature that is provided by neutral end groups is that they offer the incentive of conducting examination of the materials properties in both common organic solvents as well as aqueous media.

In line with aforementioned statements, placing dendritic wedges in either peripheral or axial positions confirms the general trend of aggregation and non-aggregated species, respectively. As part of the research on neutral hydrophilic dendritic topologies, we have recently reported on the in-depth study of either water-soluble free-base phthalocyanine- or perylene-derived dendrimers as potent electron-donor or -acceptor moieties [9]. Non-covalent immobilization onto single-wall carbon nanotubes led to the formation of nanostructures for which well-characterized radical ion pair states were evidenced. Likewise, coordination of dendritic oligoethylene-terminated

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pyridine based ligands in the axial positions of a ruthenium phthalocyanine centerpiece allowed for the investigation by photophysical means [10]. The results provided clear indication that these monodisperse and non-aggregated phthalocyanines are capable of efficiently generating singlet oxygen in organic media as reactive species for potential applications in photodynamic therapy.

Herein, we describe the high yield synthesis of a series of monodisperse zinc phthalocyanine-centered dendrimers encapsulated within an amphiphilic environment. The corresponding phthalonitrile precursors have been prepared with a triazole linking motif as introduced through the *Click Chemistry* approach. Owing to the presence of the hydrophilic triethylene glycol monomethyl ether

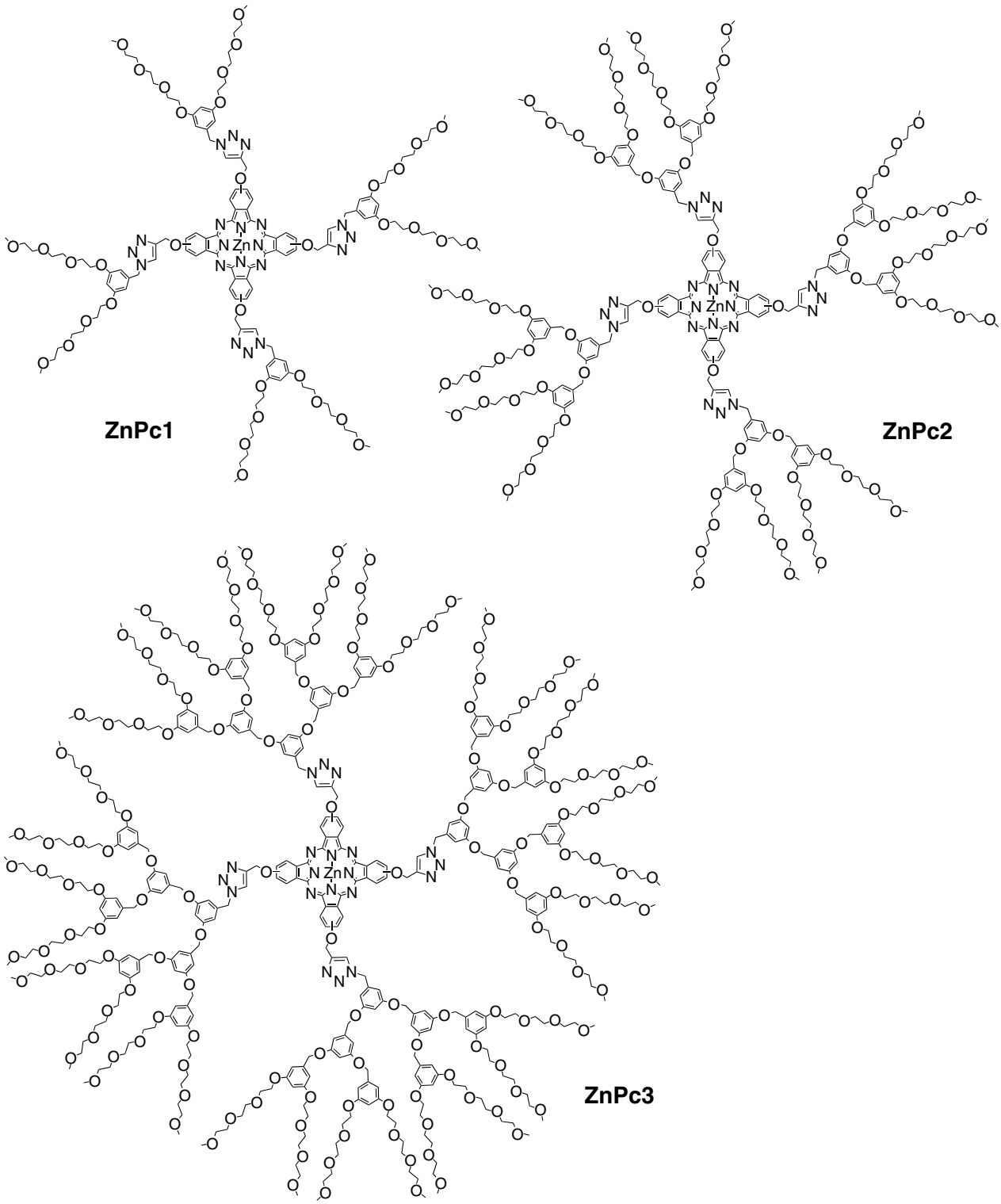


Chart 1. Chemical structures of amphiphilic zinc phthalocyanine dendrimers **ZnPc1–3**

peripheral groups, examination of the basic photophysical properties in both common organic solvents as well as aqueous media became attainable. The difference between this series of zinc phthalocyanines and structurally related free-base phthalocyanines will be discussed.

EXPERIMENTAL

General

All reagents used were purchased from commercial sources without further purification. Dendritic azides **4–6** were prepared according to a procedure as previously described in the literature [9, 11]. Solvents were dried using standard techniques prior to use. All reactions were performed in standard glassware under an inert argon atmosphere. Reactions were monitored by thin-layer chromatography using TLC plates precoated with silica gel $60F_{254}$ (Merck). Column chromatography was carried out on Merck silica gel 60, 40–63 μm (230–400 mesh). Gel permeation chromatography was performed using Biorad, Biobeads SX-1 and dichloromethane as eluent. ^{1}H and ^{13}C NMR spectra were recorded using Bruker Avance 300 MHz instruments; the solvent signal was used for internal calibration. Mass spectra were recorded using a MS-50 from A.E.I., Manchester, GB (EI), a Concept 1H from Kratos Analytical Ltd., Manchester, GB (FAB), and a MALDI-TofSpec-E from MICROMASS, GB (MALDI). UV-vis spectra were recorded on a Hewlett-Packard 8453 diode-array spectrophotometer instrument.

Synthesis

Compound 3. A solution of 4-nitrophthalonitrile (**1**, 300 mg, 1.73 mmol), 2-propyn-1-ol (**2**, 97 mg, 1.73 mmol) and K_2CO_3 (502 mg, 3.64 mmol) in *N*,*N*'-dimethylformamide (10 mL) was heated to reflux for 15 h. After cooling to rt, the mixture was poured onto ice water and extracted with CH_2Cl_2. The organic phase was washed several times with water, dried with Na_2SO_4 and the solvent removed under reduced pressure. Purification by flash column chromatography (SiO_2; CH_2Cl_2) gave **3** as colorless solid (298.9 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 2.61 (t, J = 2 Hz, 1 H, C≡CH), 4.81 (d, J = 2 Hz, 2 H, CH_2), 7.29 (dd, J = 9 Hz, J = 3 Hz, 1 H, H_{ar}), 7.36 (d, J = 3 Hz, 1 H, H_{ar}), 7.74 (d, J = 9 Hz, 1 H, H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 56.7, 76.3, 77.9, 108.4, 115.2, 115.6, 117.6, 120.0, 120.2, 135.3, 160.5. EI-MS: *m/z* (%) 181.0 ([M]$^+$, 100).

General procedure for the preparation of the dendronized phthalonitriles PN1–3. To a solution of the corresponding dendritic azide **4–6** (1 equiv.) and **3** (1 or 1.1 equiv.) in a mixture of water and THF (v/v 1:1) was added sodium ascorbate (0.1 equiv.) and then $CuSO_4$ (0.05 equiv.) dissolved in water (c = 0.1 mmol mL^{-1}). The resulting mixture was stirred at rt for 2 d. Water was added and the aqueous phase extracted several times with CH_2Cl_2. The organic phase was washed once with brine and water, dried with Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified as outlined in the following text.

Compound PN1. Prepared from dendritic azide **4** (250.0 mg, 0.546 mmol), **3** (99.5 mg, 0.546 mmol), sodium ascorbate (10.8 mg, 55 μmol) and $CuSO_4$ (6.8 mg, 27.3 μmol) in water and THF (v/v 1:1, 10 mL). Gradient flash column chromatography (SiO_2, CH_2Cl_2/MeOH 100:1 to 20:1) gave **PN1** as a highly viscous liquid (341.1 mg, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 3.38 (s, 6 H, CH_3), 3.52 (m, 4 H, CH_2), 3.60–3.75 (m, 12 H, CH_2), 3.82 (t, J = 5 Hz, 4 H, CH_2), 4.06 (t, J = 5 Hz, 4 H, CH_2), 5.24 (s, 2 H, CH_2), 5.40 (s, 2 H, CH_2), 6.01 (d, J = 2 Hz, 2 H, H_{ar}), 6.47 (t, J = 2 Hz, 1 H, H_{ar}), 7.32 (m, 2 H; H_{ar}), 7.54 (s, 1 H; $H_{triazole}$), 7.71 (dd, J = 3 Hz, J = 1 Hz, 1 H; H_{ar}). ^{1}H NMR (300 MHz, DMSO-d_6): δ, ppm 3.30 (s, 6 H, CH_3), 3.41 (m, 4 H, CH_2), 3.44–3.60 (m, 12 H, CH_2), 3.70 (t, J = 5 Hz, 4 H, CH_2), 4.03 (t, J = 5 Hz, 4 H, CH_2), 5.33 (s, 2 H, CH_2), 5.51 (s, 2 H, CH_2), 6.45 (d, J = 2 Hz, 2 H, H_{ar}), 6.47 (t, J = 2 Hz, 1 H, H_{ar}), 7.56 (m, 2 H; H_{ar}), 7.88 (s, 1 H; $H_{triazole}$), 8.06 (dd, J = 3 Hz, J = 1 Hz, 1 H; H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 54.1, 58.7, 62.3, 67.4, 69.3, 70.3, 70.4, 70.5, 71.7, 101.3, 106.9, 107.4, 115.0, 115.4, 117.1, 119.4, 120.1, 123.3, 135.1, 136.0, 142.0, 160.2, 161.1. MALDI-TOF-MS: *m/z* (%) 640.3 ([M + H]$^+$, 100).

Compound PN2. Prepared from dendritic azide **5** (470.0 mg, 0.473 mmol), **3** (86.1 mg, 0.473 mmol), sodium ascorbate (9.4 mg, 47 μmol) and $CuSO_4$ (5.9 mg, 24 μmol) in water and THF (v/v 1:1, 10 mL). Gradient flash column chromatography (SiO_2, CH_2Cl_2/MeOH 100:1 to 20:1) gave **PN2** as a highly viscous liquid (513.7 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 3.32 (s, 12 H, CH_3), 3.52 (m, 8 H, CH_2), 3.60–3.75 (m, 24 H, CH_2), 3.79 (t, J = 5 Hz, 8 H, CH_2), 4.05 (t, J = 5 Hz, 8 H, CH_2), 4.88 (s, 4 H, CH_2), 5.22 (s, 2 H, CH_2), 5.40 (s, 2 H, CH_2), 6.38 (t, J = 2 Hz, 2 H, H_{ar}), 6.40 (d, J = 2 Hz, 2 H, H_{ar}), 6.48–6.52 (m, 5 H, H_{ar}), 7.28–7.37 (m, 2 H; H_{ar}), 7.58 (s, 1 H; $H_{triazole}$), 7.66 (dd, J = 3 Hz, J = 1 Hz, 1 H; H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 54.1, 58.8, 62.4, 67.4, 69.5, 69.8, 70.3, 70.4, 70.6, 71.7, 101.0, 102.0, 105.9, 107.1, 107.4, 115.1, 115.5, 117.1, 119.6, 120.1, 123.5, 135.2, 136.3, 138.6, 142.1, 160.0, 160.2, 161.2. MALDI-TOF-MS: *m/z* (%) 1198.5 ([M + Na]$^+$, 32), 1176.5 ([M + H]$^+$, 100).

Compound PN3. Prepared from dendritic azide **6** (330.0 mg, 160 μmol), **3** (32.0 mg, 176 μmol), sodium ascorbate (3.2 mg, 16 μmol) and $CuSO_4$ (2.0 mg, 8 μmol) in water and THF (v/v 1:1, 10 mL). Gradient flash column chromatography (SiO_2, CH_2Cl_2/MeOH 100:1 to 15:1) gave **PN3** as a highly viscous liquid (338.0 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 3.37 (s, 24 H, CH_3), 3.55 (m, 16 H, CH_2), 3.58–3.76 (m, 48 H, CH_2), 3.86 (t, J = 5 Hz, 16 H, CH_2), 4.10 (t, J = 5 Hz, 16 H, CH_2), 4.96 (s, 12 H, CH_2), 5.19 (s, 2 H, CH_2), 5.46 (s, 2 H, CH_2), 6.44

(t, J = 2 Hz, 6 H, H_{ar}), 6.55 (t, J = 2 Hz, 2 H, H_{ar}), 6.58–6.64 (m, 13 H, H_{ar}), 7.27–7.37 (m, 2 H; H_{ar}), 7.56 (s, 1 H; $H_{triazole}$), 7.68 (dd, J = 3 Hz, J = 1 Hz, 1 H; H_{ar}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 54.1, 58.9, 62.4, 67.4, 69.6, 69.9, 70.5, 70.6, 70.7, 71.8, 101.0, 101.6, 102.2, 106.0, 106.2, 107.1, 107.5, 115.1, 115.6, 117.2, 119.5, 120.1, 123.5, 135.2, 136.4, 138.8, 138.9, 142.1, 160.0, 160.2, 161.2. MALDI-TOF-MS: *m/z* (%) 2272.0 ($[M + H]^+$, 100).

General procedure for the preparation of the dendritic zinc phthalocyanines ZnPc1–3. A mixture of dendritic phthalonitrile **PN1–3** (4 equiv.) and zinc acetate (1.1 equiv.) in dimethylaminoethanol (DMAE) was heated to reflux for 18 h. After this time, the intense green colored solution was cooled to rt and the solvent evaporated to dryness. The residue was dissolved in a small quantity of CH_2Cl_2, filtered and purified by size exclusion chromatography on Biobeads, BioRad S-X1 (eluent: CH_2Cl_2).

Compound ZnPc1. Prepared from dendritic phthalonitrile **PN1** (54.2 mg, 84.7 μmol) and zinc acetate (5.1 mg, 23.3 μmol) in DMAE (1.5 mL). **ZnPc1** was obtained as intense green solid (22.4 mg, 37%). ^{1}H NMR (300 MHz, DMSO-d_6): δ, ppm 3.33 (s, 24 H, CH_3), 3.39 (m, 16 H, CH_2), 3.44–3.56 (m, 48 H, CH_2), 3.68 (t, J = 5 Hz, 16 H, CH_2), 4.05 (t, J = 5 Hz, 16 H, CH_2), 5.63 (s, 8 H, CH_2), 5.72 (s, 8 H, CH_2), 6.49 (t, J = 2 Hz, 4 H, H_{ar}), 6.59 (t, J = 2 Hz, 8 H, H_{ar}), 7.70 (m, 4 H, H_{Pc}), 8.56 (s, 4H, $H_{triazole}$), 8.73 (m, 4 H, H_{Pc}), 8.99 (m, 4 H, H_{Pc}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 53.0, 58.0, 62.0, 67.2, 68.8, 69.6, 69.7, 69.9, 71.2, 100.5, 106 (br, C_{Pc}), 106.7, 106.8, 117 (br, C_{Pc}), 123 (br, C_{Pc}), 125.0, 131 (br, C_{Pc}), 131.2, 138.1, 140 (br, C_{Pc}), 143.2, 151–153 (br, C_{Pc}), 159.9. MALDI-TOF-MS: *m/z* (%) 2621.1 ($[M + H]^+$, 44).

Compound ZnPc2. Prepared from dendritic phthalonitrile **PN2** (183.0 mg, 155.6 μmol) and zinc acetate (9.4 mg, 42.8 μmol) in DMAE (1.0 mL). **ZnPc2** was obtained as intense green highly viscous liquid (78.5 mg, 42%). ^{1}H NMR (300 MHz, DMSO-d_6): δ, ppm 3.34 (s, 48 H, CH_3), 3.39 (m, 32 H, CH_2), 3.45–3.57 (m, 96 H, CH_2), 3.70 (br s, 32 H, CH_2), 4.05 (br s, 32 H, CH_2), 5.00 (m, 16 H, CH_2), 5.67 (s, 8 H, CH_2), 5.78 (s, 8 H, CH_2), 6.44 (m, 8 H, H_{ar}), 6.55 (m, 16 H, H_{ar}), 6.65 (s, 4 H, H_{ar}), 6.69 (m, 8 H, H_{ar}), 7.88 (br s, 4 H, H_{Pc}), 8.58 (s, 4 H, $H_{triazole}$), 9.04 (br s, 4 H, H_{Pc}), 9.28 (br s, 4 H, H_{Pc}). ^{13}C NMR (100 MHz, $CDCl_3$): δ, ppm 53.0, 58.0, 62.2, 67.1, 68.8, 69.2, 69.5, 69.7, 69.9, 71.2, 100.3, 101.4, 105.9, 106.0, 106 (br, C_{Pc}), 107.1, 118 (br, C_{Pc}), 123 (br, C_{Pc}), 125.0, 131 (br, C_{Pc}), 131.3, 138.1, 138.9, 139.0, 140 (br, C_{Pc}), 143.1, 151–153 (br, C_{Pc}), 159.5, 159.6, 159.7. MALDI-TOF-MS: *m/z* (%) 4766.1 ($[M + H]^+$, 100).

Compound ZnPc3. Prepared from dendritic phthalonitrile **PN3** (130.0 mg, 60.0 μmol) and zinc acetate (3.8 mg, 17.3 μmol) in DMAE (1.0 mL). **ZnPc3** was obtained as intense green highly viscous liquid (51.3 mg, 39%). ^{1}H NMR (300 MHz, DMSO-d_6): δ, ppm 3.16 (br s, 96 H, CH_3), 3.22–3.74 (br m, 320 H, CH_2), 4.01 (br s, 64 H, CH_2), 4.97 (br s, 48 H, CH_2), 5.58 (br m, 16 H, CH_2), 6.42 (br m, 24 H, H_{ar}), 6.43–6.73 (m, 60 H, H_{ar}), 7.80 (br m, 4 H, H_{Pc}), 8.50 (br s, 4 H, $H_{triazole}$), 9.04 (br m, 4 H, H_{Pc}), 9.28 (br m, 4 H, H_{Pc}). MALDI-TOF-MS: *m/z* (%) 9061 ($[M + H]^+$, 100).

RESULTS AND DISCUSSION

Synthesis

Dendrimers are synthetic macromolecules with a tree-like well-defined branched structure [12, 13]. The modification of these peculiar and most often flexible architectures has been an active area of research throughout the last two decades [12, 13]. By far the most often used method for the construction of dendritic phthalocyanines is the approach *via* pre-functionalization of the corresponding phthalontrile by a fractal species which is subsequently subjected to cyclotetramerization [5–8]. This way, the synthesis of peripherally substituted phthalocyanine dendrimers can be achieved as has been demonstrated by numerous examples. As mentioned before, the rational design of dendritic ligands bearing a single functional unit in the focal point can be used for the orthogonal assembly onto *e.g.* ruthenium or silicon phthalocyanines. However, also the postmodification of a previously synthesized phthalocyanine precursor by dendritic units could be envisaged. Nonetheless, this approach has been considered to a lesser degree presumably as a result of the problem of steric hindrance that might be encountered upon functionalization with the first dendrons. This might ultimately hamper the access of the residual functional units and will in most cases lead to ill-defined dendrimers rather than monodisperse nanoarchitectures.

The strategy pursued herein relies on pre-functionalizing the phthalonitrile with the corresponding branched moiety. The covalent linker chosen to covalently connect the two precursors is the triazole ring structure. This approach is well-known as *Click Chemistry* and originates from the reaction of an alkyne and an azide catalyzed by copper(II) ions and has first been introduced and exploited in the 1970s by Huisgen [14]. This particular motif has experienced a dramatic revival during recent years not last due to the fact that target structures can be produced in a vast number of cases in up to quantitative yields. It is not surprising that the "click" methodology has also been used for the construction of regularly shaped dendritic nanoarchitectures [15]. Likewise, this approach has also been employed in the modification of phthalocyanines [16].

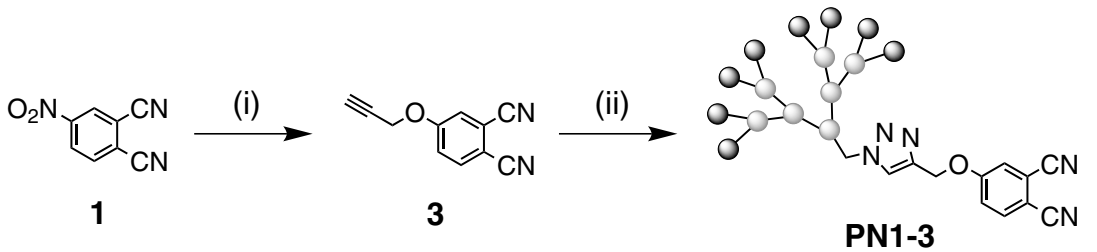
By implementing the triazole moiety as linker between the dendrimer part and the central macrocycle, a considerable expansion of the dendrimer structures has been obtained. However, the triazole unit itself has no significant impact on the materials properties of the target molecules as will be shown below. Such hollow cavities might be especially interesting for hosting small guest

molecules within the interior of the flexible dendrimer structure which have demonstrated their value when aiming at for instance drug delivery [17]. In particular lipophilic guest molecules could penetrate through the uncharged dendrimer shell to be accommodated close to the hydrophobic centre of the overall amphiphilic structure.

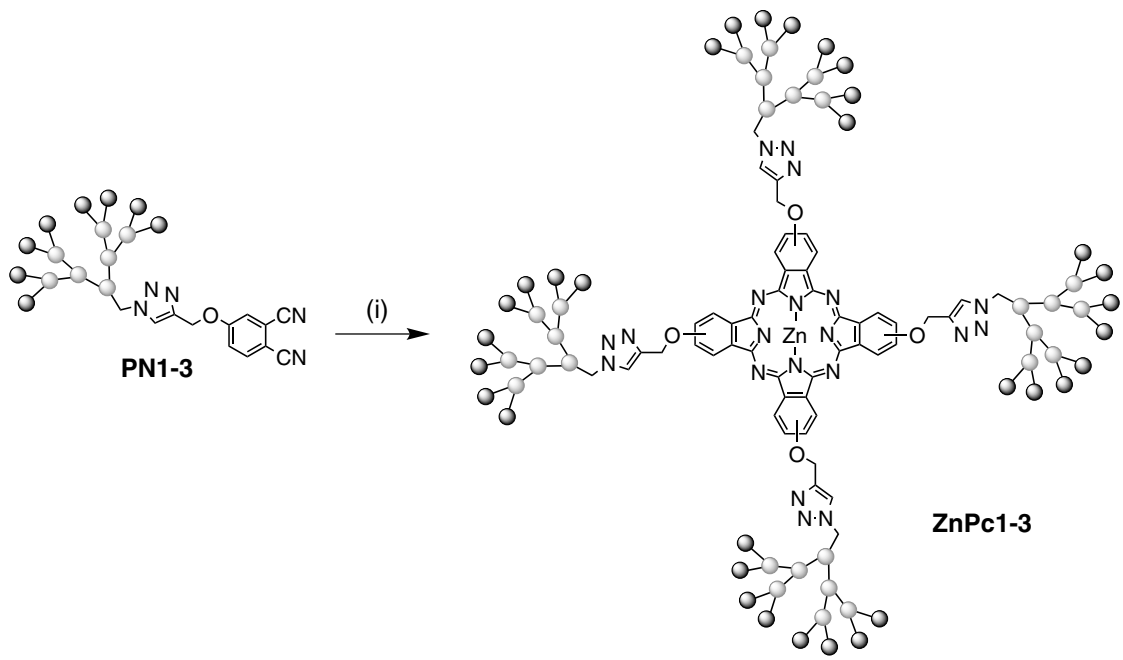
The first precursor **PN1** bearing the terminal alkyne moiety has been obtained in 95% yield through *ipso*-substitution of 4-nitrophthalonitrile (**1**) with propargyl alcohol (**2**) in the presence of K_2CO_3 as base. On the other hand, dendrons carrying triethylene glycol monomethyl ether end groups and a benzylic bromide function at the centre were obtained following a literature procedure [8–11]. Subjection to a reaction with sodium azide then readily formed the corresponding azide derivatives **4–6** in quantitative yields [9]. The aforementioned highly reliable and high yielding *Click Chemistry* reaction under formation of a triazole ring structure was then performed for all azides of different generations. Indeed, it was found that this copper ion-catalyzed reaction led to the very high yielding or virtually quantitative formation of the dendritic phthalonitriles **PN1–3** irrespective of the dendron size. With the dendritically modified phthalonitriles **PN1–3** of first to third generation in hands, the corresponding cyclotetramerizations have been conducted in the presence of zinc acetate as metal template. The target dendrimers **ZnPc1–3** have hence been obtained as intense green products in reasonably good yields of 37 to 42% for the preparation of phthalocyanines after purification by size exclusion chromatography.

Structural characterization

Owing to the appended oligoethylene glycol peripheral moieties present in all fractal structures studied herein, it turned out that the entire series showed good solubility in common organic solvents such as CH_2Cl_2, $CHCl_3$ or THF, thus facilitating spectroscopic characterization by NMR, UV-vis, and MS techniques. Furthermore, all



Scheme 1. Preparation of dendritic phthalonitriles **PN1–3** with terminal oligoethylene glycol chains (light spheres represent polyarylether branching units, dark spheres represent triethylene glycol monoethyl ether end groups). Reagents and conditions: (i) 2-propyn-1-ol (**2**), K_2CO_3, DMF, reflux, 15 h (95%); (ii) dendritic azide **4–6**, sodium ascorbate (10 mol.%), $CuSO_4$ (5 mol.%), THF - H_2O (v/v 1:1), rt, 2d (**PN1**: 98%, **PN2**: 92%, **PN3**: 94%)



Scheme 2. Preparation of zinc phthalocyanine dendrimers **ZnPc1–3** with terminal oligoethylene glycol chains (light spheres represent polyarylether branching units, dark spheres represent triethylene glycol monoethyl ether end groups). Reagents and conditions: (i) zinc acetate, DMAE, reflux, 18 h (**ZnPc1**: 37%, **ZnPc2**: 42%, **ZnPc3**: 39%)

dendrimers **ZnPc1–3** could be readily dissolved in water. The increasing amount of hydrophilic surface moieties leads to the creation of an amphiphilic environment in which the hydrophobic core is embedded in the interior, thus generating a shielding effect. However, it is important to note that solubilisation of **ZnPc1** in aqueous media only proceeds slowly and no high concentrations can be reached. Elucidation of both series of phthalonitrile and phthalocyanine structures was easily possible as all signals of the various parts of the dendrimers appeared in specific regions and did thus assist the assignment of sets of signals. Figure 1 displays the proton spectra of **PN1** and **ZnPc1** as recorded in DMSO-d_6 thus allowing direct comparison of the corresponding shifts. Accordingly, apart from the multiplets at 7.70, 8.73, and 8.99 ppm that can be recognized as fingerprints for the various inseparable phthalocyanine isomers as formed during the cyclotetramerization reaction, the single signals obtained for the triazole protons are indicative of the structural integrity. Upon metal-assisted phthalocyanine formation, these protons are shifted by approx. 0.2 ppm as a result of the strong influence as exerted by the macrocycle. Also the two sets of methylene protons adjacent to the triazole motif encounter similar shifts of 0.2 or 0.3 ppm shifts. Furthermore, the aromatic signals of the inner shell of the dendritic branches are inverted in appearance. All the other protons that are not in close proximity to the phthalocyanine core do not experience a strong shift rather than showing minor changes in chemical shifts with respect to the corresponding phthalonitrile. Similar effects have been found for the respective larger second and third generation dendrimers. It could be added that a significant broadening has been observed on passing from **ZnPc1** to **ZnPc3** in the ^{1}H NMR spectra. This observation could be ascribed to significant changes in the relaxation time T2 as a result of the large increase in molecular weight. This is a typical phenomenon frequently observed for large dendritic assemblies. The respective ^{13}C NMR spectra confirmed the general trend and showed analogous shifts for the corresponding carbon atoms.

Structural elucidation of both series **PN1–3** and **ZnPc1–3** has also been conducted under the use of mass spectrometry. The dendritic phthalonitriles gave clean spectra as obtained by the MALDI-TOF-MS technique with the target mass as base peak in all cases. Likewise, also the structures of the branched zinc phthalocyanines were unequivocally determined by their corresponding MALDI-TOF-MS spectra. The spectra gave clear evidence with the observed signals that could be explicitly ascribed to the ion mass peaks of **ZnPc1–3**. This is in strong contrast with findings reported in the literature for structurally related free-base phthalocyanines [8b]. In these cases, the MS spectra as obtained under similar conditions as for **ZnPc1–3** gave rise to clusters and aggregates. Moreover, the significant cleavage of remote benzylic sites as mentioned by McKeown *et al.* does not coincide with the results as observed for **ZnPc1–3**.

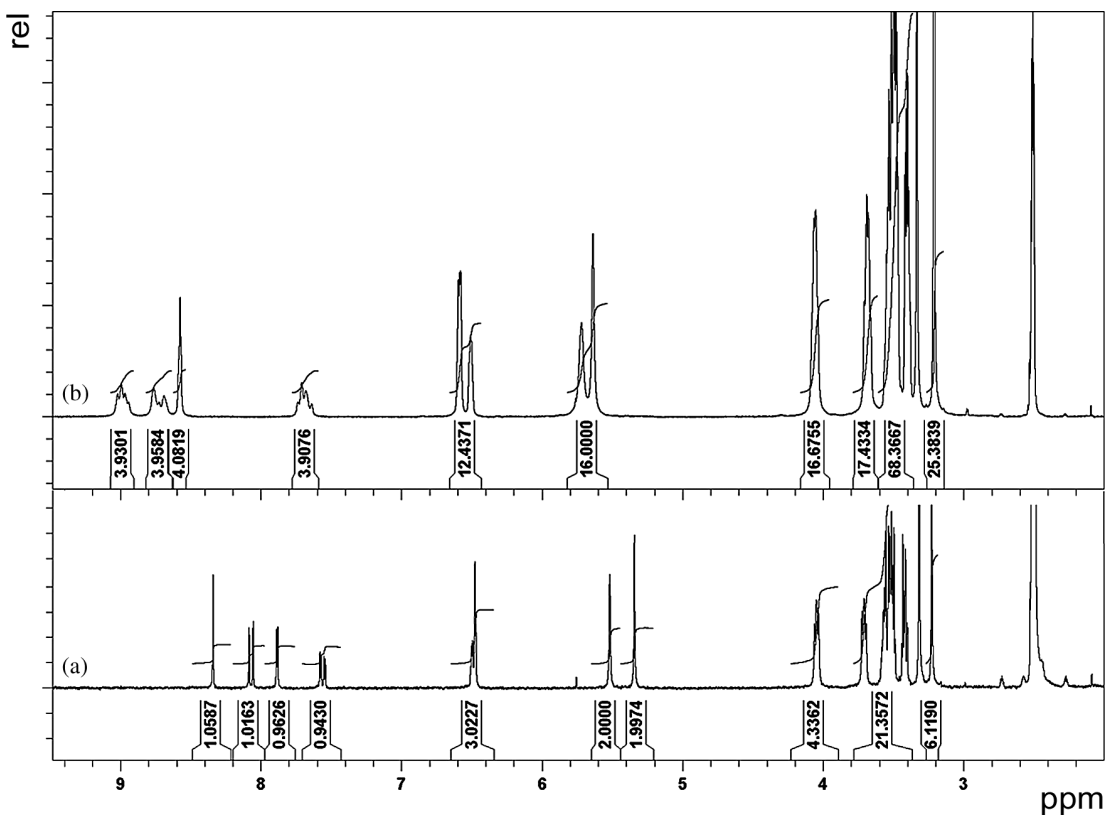


Fig. 1. ^{1}H NMR spectra of (a) **PN1** and (b) **ZnPc1** recorded in DMSO-d_6

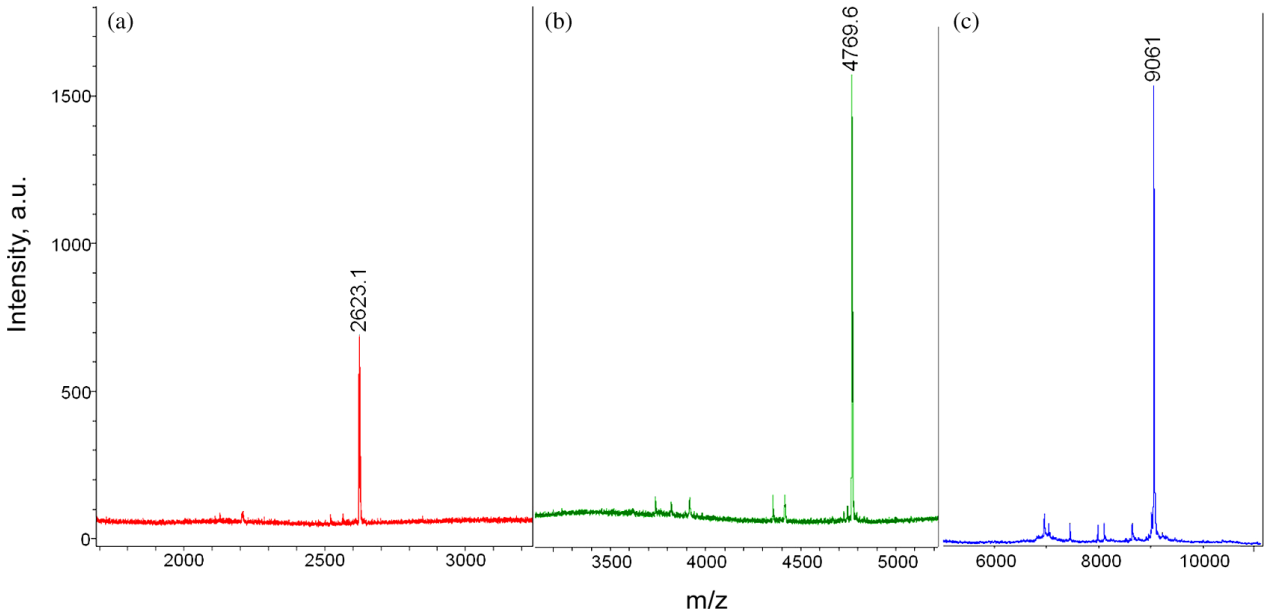


Fig. 2. MALDI-TOF-MS spectra of (a) **ZnPc1**, (b) **ZnPc2** and (c) **ZnPc3**

UV-visible absorption spectroscopy

The absorption spectra of the series of **ZnPc1–3** dendrimers have been recorded using three categories of solvents, *i.e.* in chloroform (Fig. 3a) as moderately polar solvent, in THF (Fig. 3b) as polar aprotic solvent and in water (Fig. 3c) as polar protic environment. For the former two, the spectral features are almost identical for the respective dendritic generation and are dominated by well-defined Q-bands centred at λ_{max} = 682 nm in chloroform and λ_{max} = 678 nm in THF, respectively. However, it is important to note two trends: (i) lower Q-band absorption coefficients in chloroform when compared to THF and (ii) decreasing absorption upon going to larger generation species in a given solvent. These effects presumably result from a certain degree of intra- or intermolecular aggregation that is noticeable between **ZnPc1** and **ZnPc2** and more pronounced when switching to **ZnPc3**. The two additional maxima located at around λ_{max} = 682 nm and 280 nm can be assigned to the B-band and the dimethoxybenzene moieties of the dendrimer skeleton. Whereas the former remains at constant intensity the latter increases in intensity on passing to the larger generation species. Another feature that indicates intra- or intermolecular aggregation is the appearance of the rather broad absorption in the region between B- and Q-band that again ascends with increasing dendrimer generation.

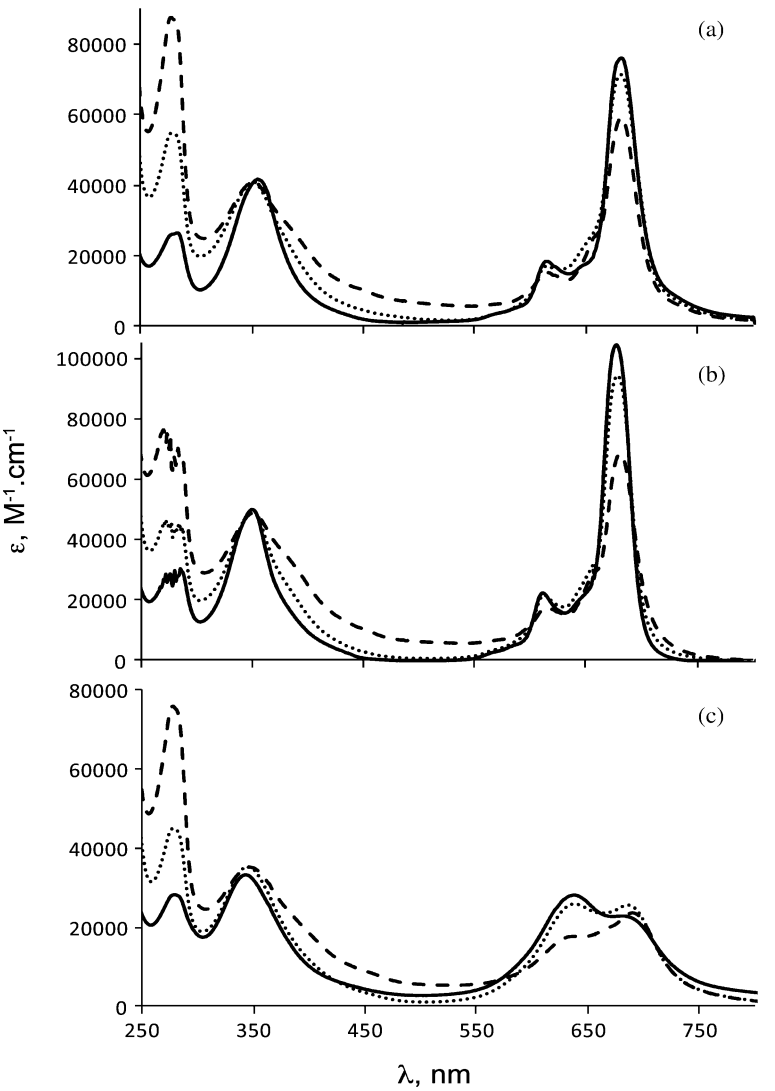


Fig. 3. UV-vis spectra of **ZnPc1–3** in (a) $CHCl_3$, (b) THF and (c) H_2O

As expected, the behavior drastically changes upon switching to polar protic medium. The spectra in water show many facets archetypical of aggregation phenomena in this kind of dyes, *i.e.* broad Q-bands with lower absorption coefficients than the typical monomer phthalocyanines. This phenomenon results from the coplanar association under formation of dimers, trimers, and higher oligomers, respectively [24]. Also imparting bulky substituents in the peripheral positions can help to reduce the formation of such aggregates, but still aggregation has to be considered. Accordingly, a broadening of the Q-band with maxima at λ_{max} = 641 and 684 nm, respectively, has been obtained with significant decrease in intensity as a result of the aggregation phenomenon. The B-band for the whole series experiences a slight hypsochromical shift to be centred at λ_{max} = 345 nm. As observed for the measurements conducted in organic solutions, also in water an additional broad band in the region between B- and Q-band appears thus giving further proof for a pronounced aggregation behavior in the case of the higher generation dendrimer derivatives. It can be added that for the three dendritic species presented herein aggregation is an effect that apperas to be generation-independent, *i.e.* the Q-band has basically same intensities along the whole series. On the contrary, the absorption coefficients of the dendritic branches remain virtually unaffected and increase in intensity within **ZnPc1–3**.

CONCLUSION

A new series of monodisperse zinc phthalocyanine-centered dendrimers **ZnPc1–3** encapsulated within an amphiphilic environment has been presented. Dendritic modification of the phthalonitrile precursor was accomplished through the *Click Chemistry* approach under formation of the triazole ring structure motif. These dendritic benzodinitriles as obtained in excellent yields for all steps of the synthetic protocol were then involved in cyclotetramerization reactions to furnish the three monodisperse **ZnPc1–3** dendrimers in good yields for such macrocyclic compounds. All structures have been unequivocally identified by both NMR and MS techniques. Owing to the presence of the hydrophilic triethylene glycol monomethyl ether peripheral groups, the whole series of dendrimers is soluble in both common organic solvents and aqueous media. UV-vis absorption spectra in different types of solvents evidenced in organic solvents the typical features as usually obtained for independent phthalocyanines. However, along the series the Q-band absorption coefficients decreased thus indicating a certain degree of intra- or intermolecular aggregation. Experiments conducted in aqueous medium confirm the general trend that steric isolation of the macrocycle by bulky peripheral substituents is not effective in polar protic solvents as shown by broad Q-bands with significant lower absorption coefficients.

The considerable expansion of the dendrimer interior as obtained by the triazole spacer moieties may lead to the formation of hollow cavities that might be exploited in *e.g.* drug delivery applications. The overall amphiphilic structure as generated by the outer water-soluble groups and the internal lipophilic phthalocyanine core could assist the accommodation of lipophilic guest molecules. Likewise, the preparation of asymmetric dendrimers carrying a specific function in a predetermined position is currently underway. With this implemented functional moiety the use in specific bioorganic or medicinal applications can be envisaged thereby *e.g.* addressing specific target positions in cells.

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