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Retraction notice to 'Self-Assembly of Protoporphyrin IX-TEG Derivatives into Tunable Nanoscaled Spherical Structures' [Australian Journal of Chemistry 63(9) (2010), 1326–1329. doi:10.1071/CH10199]

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Refers to: RETRACTED: Self-Assembly of Protoporphyrin IX-TEG Derivatives into Tunable Nanoscaled Spherical Structures, published 9 September 2010, doi.org/10.1071/CH10199. Sheshanath V. Bhosale, Sidhanath V. Bhosale, Mohan B. Kalyankar, Steven J. Langford and Ceilica H. Lalander.

After due consideration of issues raised with respect to this paper by the co-author Cecilia Lalander, the Editors-in-Chief and the authors agree to retract the paper from *Australian Journal of Chemistry*.

Reason: The image in Fig. 3 is not consistent with the raw data and appears to have been altered to obtain the image that appears in the paper.

The Editors-in-Chief and Journal Publisher have determined these are grounds for retraction, according to the international guidelines established by the Committee on Publication Ethics. We regret the academic record was compromised and apologise for any inconvenience this may have caused.

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Self-Assembly of Protoporphyrin IX-TEG Derivatives into Tunable Nanoscaled Spherical Structures

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The results of a *solvo*-controlled self-assembly process involving a novel non-ionic protoporphy. X functionalized with triethylene glycol (**Proto-NTEG**) chains is discussed. In relatively non-polar aprotic solvents (cycerecane/CHCl₃), the protoporphyrin forms stable, uniformly-sized multilamellar micro-vesicles of approximately 66 nm diameter, while in more polar protic solvent mixes (CHCl₃/MeOH), the same protoporphyrin forms micro-vegices with dimensions of approximately 6 nm. The *solvo*-control operates based on the differing protecties of gravitationalized and methanol leading to inverse self-assembled structures.

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Introduction

Vesicles are important three-dimensional assemblies ely studied for their potential application in drug livery as 'nanoreactors' for chemical reaction enhancement and systems for biomembranes.^[1] Inspired by the latter, eral examples of amphiphilic polymers and survey nts that sp nan have been neously form vesicles of various sizes and fun developed.^[2] Recent examples incluse facially developed.^[2] Recent examples include facially uphiphilic segmented dendrimers and functionalized amphiphilic mole-cular building blocks based on encapede, ducurbituril, full-erene, cyclodextrin, cyclophene, an opphenylene vinylene derivatives.^[3] The formation on hese versus generally occurs through the self-assemble of synthes molecular building blocks of sr s that depend on the use of disinto supramolecular struc persive (van der Waals, $\pi - \pi$.) ring, etc) and electrostatic (e.g. H-bonding) interactions as well as inherent geometry to achieve the thermodynamic stability of the resultant spheres.^[1-3] In contrast, relatively few neutral synthetic porphyrin molecules are known to self-assemble into vesicles, [4] despite the significance of three-dimensional cyclic multiporphyrin arrays found in the light harvesting complexes of plants and purple bacteria.

Protoporphyrin IX is the iron-free form of heme, one of the most common natural forms of porphyrin. Amphiphiles based on protoporphyrin IX can be constructed through ester or amide linkages to the two propylenic carboxylic acid groups on the outer periphery.^[5] Glyconamide derivatives of protoporphyrin IX have been shown to form micellar fibres under aqueous conditions, although little other examples, particularly in competing organic media, are known.^[5b] As the limited number of examples grows, it remains an important objective to deepen the understanding of such processes and to tailor the self-assembly process for suitable applications in which the dye and/or

even memical properties of the porphyrin can be exploited. flerein, we report on the formation of two different nanosized pherical constructs based on protoporphyrin-triethylene glycol **1 (Proto-NTEG)** (Fig. 1) from organic solvent.

Results and Discussion

Proto-NTEG 1 consists of three important regions. The first region (coloured red in the schematic of Fig. 1) is the hydrophobic aromatic core of the porphyrin, which is utilized to optimize the dispersive interactions between the protoporphyrin cores within any three-dimensional construct. The second region incorporates amide bonds which are designed, based on our voctowell work,^[6] to participate in intermolecular hydrogen bonding, rigidifying the surface of any three-dimensional construct in a cooperative fashion. The third region (shaded blue in the schematic in Fig. 1) bears amphiphilic polyether groups capable of being influenced by solvophobic effects. For example, 2-methoxy(2-(2-(ethoxy(ethoxy(ethanol)))))) is miscible in methanol but immiscible in hexanes. Proto-NTEG 1 was prepared in one step from commercially available protoporphyrin IX and 2-methoxy(2-(2-(ethoxy(ethoxy(ethoxamine))))))^[7] under amide coupling conditions (EDCI and HOBt). Purification by column chromatography then re-precipitation in hexane resulted in a violet crystalline material in 94% yield.

UV-vis Absorption, Fluorescence, and Dynamic Light Scattering Measurements

Proto-NTEG 1 does not dissolve in either water or cyclohexane, but easily dissolves in chloroform, yielding a transparent reddish solution. The UV-visible absorption spectrum of 1 in CHCl₃ (Fig. 2) shows the distinctive porphyrin Soret band at



Fig. 1. Schematic representation of the self-assembly chocess of Proparious solvent mixtures: (a) micellar formation in chloroform/methanol (6:4 v/v, (b) vesicles are formed with **Proto-NTEG** in cyclohexane/chloroform (10:1 v/v).



Fig. 2. (a) UV-vis absorption spectra of **Proto-NTEG 1** $(1 \times 10^{-4} \text{ M})$: broken lines = CHCl₃, solid line = cyclohexane/CHCl₃ (10:1 v/v) at 25°C, (b) apparent hydrodynamic radius distributions of spherical vesicles of 1 in cyclohexane/CHCl₃ (10:1 v/v) $(1 \times 10^{-4} \text{ M})$ at $\theta = 30^{\circ}$.

403 nm ($\varepsilon = 3.41 \times 10^5 \text{ L mol}^{-1} \text{ cm}^{-1}$) accompanied by four less intense Q-bands at 503, 538, 573, and 627 nm. The addition of a solution of **1** in chloroform to cyclohexane (10 volume equivalents) leads to significant changes in the absorption spectrum as illustrated by broadening of the Soret band and loss in fine structure of the Q bands (Fig. 2). The broadness and asymmetry of the absorption bands of **1**, upon the addition of cyclohexane supports its aggregation.^[8] Dynamic light scattering experiments on **1** (1×10^{-4} M) in cyclohexane/CHCl₃ (10:1 v/v) supports the presence of nanosized aggregates from solution. These aggregates give a narrow distribution range for the apparent hydrodynamic radii. It appears that the hydrodynamic radius ($R_{\rm H}$) of the aggregates derived from the characteristic line width have little angular dependence, suggesting the

presence of spherical aggregates. The average $R_{\rm H}$ values of the aggregates were found to be ~90 ± 12 nm.^[9] No aggregates of **Proto-NTEG 1** were observed in CHCl₃ solution by this technique.

Atomic Force Microscopy and Transmission Electron Microscopy Measurements

In order to gain more structural information, the aggregates formed in cyclohexane were examined by both atomic force microscopy (AFM) and transmission electron microscopy (TEM) techniques. For AFM imaging, samples were spincoated onto silica wafers and analyzed in the tapping mode. Fig. 3 shows images of the results obtained. The mean dimensions of the near symmetrical aggregates can be estimated at



Fig. 3. An AFM height image of **1** upon spin-cast on silica wafer shows spherical aggregates: (a) height image; (b) cross-section analysis of a magnified region from image (a).

 \sim 75 nm in diameter with a height of \sim 65 nm. The average diameter of these particles is therefore significantly larger than the molecular dimension of **Proto-NTEG 1** (\sim 2 nm) consistent with the supramolecular vesicular aggregation proposed in Fig. 1. The smaller particle size determined by AFM as compared to DLS is most likely due to the fact that the AFM tip distorts the particles on the surface.^[4]

Compound 1 produces well defined and regular spheres by TEM (Fig. 4) with a mean diameter of 60-70 nm for larger spheres and an estimated membrane thickness of $\sim 2.5-3$ nm. The membrane thickness is commensurate with the structure shown in Fig. 1, in which the solvophobic polyether chains form the main body of a vesicle bilayer leaving the porphyrin to solvate. In addition, the TEM images indicate that the vesicles are completely dispersed and do not tend to associate with each other. The fact that both AFM and TEM measurements vire an assembly-substrate interaction suggests that the esicle are very stable as opposed to convention in which vest faces surfactants in non-aqueous solution collapse in solid upon evaporation of the solvent.

Mixing of 1 in a more polar solvent sesten HCl₃/MeOH; 6:4 v/v) also leads to a commensurate 1 ss of fine cture (see Accessory Publication). AFM imaging of sample, from this solution mix spin-coated onto afers also show well defined and regulation (Fig. 5). The height of the regg defined and regular aggregates, but much smaller diameter ates fo. by 1 was estimated is approximately an order of aggregates formed from magnitude smaller than 01 cyclohexane solution. These regates appear relatively monodispersed in their size and ten not to aggregate appreciably. While the structure is unknown, the results obtained are consistent with a more micellar structure (Fig. 1a) and also consistent with a self-assembly process recently reported by us for a naphthalene diimide derivative in a similar solvent mix.^[8]

Conclusion

We have demonstrated a novel solvent-controlled approach in the self-assembly a novel non-ionic porphyrin amphiphile into uniformly-sized, multilamellar micro-vesicles in more non-polar solvent mixes and micellar aggregates in more polar solvent mixes. We believe the *solvo*-control operates as a result of the differing properties of glycol units in cyclohexane and methanol solution. Further investigations on the photochemical communication between the interior and exterior spaces of the vesicles will be of great interest for examining their potential application in molecular photonics and artificial photosynthesis and are underway.





Experimental

Synthesis Proto-NTEG 1

Protoporphyrin IX (100 mg, 0.17 mmol) and HOBt (71 mg, 0.53 mmol) were combined in DMF (10 mL) under an argon atmosphere. The solution was cooled to 0°C, stirred for 40 min, then EDCI (100 mg, 0.53 mmol) was added and the solution was stirred for a further 60 min at 0°C. 2-(2-(2-Methoxyethoxy) ethoxy)ethanamine^[6] (87 mg, 0.53 mmol) was added in DMF (2 mL) at once and the resulting solution was stirred for additional 4 h at 0°C, then warmed to room temperature and left to stir for a further 24 h. After this time, the reaction solvent was removed by rotary evaporation under reduced pressure. The gummy reaction mixture was taken up in dichloromethane (100 mL) and washed with 10% NaHCO₃ solution (3×20 mL), 0.1 M HCl $(1 \times 20 \text{ mL})$, followed by water (20 mL), and brine (20 mL). The organic solvent was dried over sodium sulfate, filtered, and concentrated using a rotary evaporator. Purification of the crude material was carried out on a flash silica gel chromatography (SiO₂) column eluting first with chloroform, followed by 2% methanol in chloroform to give a dark violet crystalline material of the title compound 1 (80 mg, 94%), mp >300°C. $\delta_{\rm H}$ (CDCl₃, 400 MHz) -4.07 (br s, 2H), 2.21 (s, 12H), 2.4-2.6 (m, 8H), 3.03-3.52 (m, 20H), 3.56 (s, 6H), 4.23 (t, J 7.7, 4H), 6.14 (d, J 7.6, 2H), 6.89 (d, J 7.8, 2H), 8.17 (m, 2H), 9.97 (m, 1H), 10.00 (m, 3H). $\delta_{\rm C}$ (CDCl₃, 125 MHz) 173.3, 142.1, 137.5, 137.4, 135.9, 129.8, 120.0, 97.7, 95.4, 96.7, 71.6, 71.5, 69.8, 69.7, 69.6, 69.5, 69.3, 69.2, 58.8, 36.8, 21.7, 12.8,



Fig. 5. (a) AFM image of **1** upon spin-cast on silica wafer shows spherical micellar aggregates in $CHCl_3/MeOH$ (6:4 v/v), (b) cross-section analysis of a magnified region from image (a), provides a height of 5–6 nm.

12.7, 11.8, 11.7. λ_{max} (CHCl₃)/nm (log ε) 403 (5.16), 503 (4.03), 538 (3.94), 6573 (3.61), 627 (3.36). *m/z* (LD) 853.3 (M+H)⁺, 875.2 (M+Na)⁺. *m/z* (HRMS-ESI-TOF) Anal. Calc. for C₄₈H₆₄N₆O₈ (M)⁺ 852.4786. Found 852.4785.

UV-vis Absorption Spectroscopy

Stock solutions (concentration 1×10^{-3} M) of **proto-TEG1** were prepared in spectroscopic grade chloroform. For spectral measurements, a sample of this solution (0.2 mL) was delivered to 2 mL of CHCl₃, cyclohexane, or CHCl₃/MeOH (6:4 v/v) in a cuvette by micropipette. The solutions were allowed to equilibrate for 2 h before the spectroscopic measurements. UV-vis absorption spectra were recorded on a Perkin–Elmer Lambda 40p spectrophotometer.

TEM

Measurements were performed on an electron icros py Igo 1200EX TEM, operating at an accelerating yolt. volume of 5 µL of a freshly prepared solution of Prot TEG 1 in cyclohexane $(1 \times 10^{-4} \text{ M})$ was dropped o a TEM d (400mesh copper grid coated with carbon) and the lvent was allowed to evaporate before introduction in the vacuum tem. Negative stain was performed by addition of a drop of urany, acetate onto the carbon grid, and after a few h te, the emaining solvent was removed by blotting with filter pa and mages were collected.

AFM

AFM images of **1** in appropriate solvent mix were made using an AFM from tilent Technologies (5500 AFM). Micromach Ultrasharp probes with silica wafer coating for enhanced reflectivity (NSC15/AIBS), with a typical resonance frequency of 325 kHz and a force constant of 40 Nm^{-1} , were used for imaging. A sample of **Proto-NTEG 1** was prepared by spin-coating the freshly prepared solution (1×10^{-4} M in cyclohexane) onto silica coating at 2000 rpm. The vesicle diameter and height was performed by measuring the mean horizontal distance and height of particles.

Accessory Publication

Further characterization of **1** and aggregates are available on the Journal's website.

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