The Rational Design of Diazenyl Amphiphiles for Self-Assembly into Nanotubes within Aqueous Systems

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Abstract

A combinatorial library of amphiphiles were synthesised with amino acid hydrophilic head groups (glutamic acid, serine or aspartic acid) linked by an amide bond to a hydrophobic tail having a diphenyldiazenyl (azo) group incorporated between the proximal alkoxy chain (6, 10, 11, or 12 methylene units long) and the distal alkyl chain (2, 4, 5, 6, 7, 8, 10, 12 or 14 methylene units long). All synthetic products were analysed by nuclear magnetic resonance (NMR) and Fourier transform infrared spectroscopic methods, while differential scanning calorimetry, elemental analysis, and isotope ratio mass spectrometry were used for selected compounds. These techniques affirmed the identity and purity of the compounds.

The synthesised amphiphiles were specifically designed to self-assemble into nanotubes based on the tight, helical winding of a bilayer ribbon. Transmission Electron Microscopy (TEM), Ultra Violet and Visible light spectroscopy (UV-Vis), scanning electron microscopy, atomic force microscopy and circular dichroism were used to analyse the self-assembled structures. TEM analysis of the entire library of amphiphile final products self-assembled from an aqueous methanolic solution (3:1 v/v) using a heated procedure showed that nanotubes, and chiral ribbon precursors to nanotubes, were commonly produced. The nanotubes observed were of two distinct varieties. The first variety of nanotubes were the result of helical assembly of a partially interdigitated bilayer ribbon driven by chiral symmetry breaking and also influenced by chiral molecular packing. Amphiphiles with a serine head group and an eleven methylene unit proximal chain assembled most efficiently into these helically based tubes, with the conversion to nanotubes increased with increasing distal chain length. There was no evidence that the second variety of nanotubes self-assembled from the synthesised amphiphiles had a helical basis, instead they were predicted to form from flat aggregates that rolled up to create the tubes.

TEM and UV-Vis spectroscopy were conducted on selected amphiphiles self-assembled with a room temperature method that used solvent mixtures that varied in ratios of methanol and water (100:0 – 10:90 v/v). TEM showed that for similar solvent ratios the heated and room temperature methods of self-assembly generated similar self-assembled morphologies, while solvent mixtures lower in water concentration using the room temperature method enabled more organised assembly for some amphiphiles. The UV-Vis spectroscopy results showed that the nanotubes observed in TEM were the result of H- and H*-aggregation azo groups.

The isomerisation of the azo group was investigated for both dissolved and aggregated amphiphiles. An amphiphile dissolved in deuterated dimethyl sulphoxide was isomerised to the *cis* form by UV radiation (λ_{max} 355 nm). The thermal reversion to the *trans* isomer was monitored by NMR spectroscopy and the activation energy for this transformation was 92.8 $kJ.mol^{-1}$. UV irradiation (λ_{max} 355 nm) of self-assembled nanotubes led to the destruction of the tubular structure upon isomerisation of the component amphiphiles from the *trans* to *cis* forms. Thermal and photo reversion to the *cis* form did not result in reconstruction of the nanotubes.

Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Thomas Geoffrey Barclay	Date

Acknowledgments

I would like to thank my supervisory team for their contribution to this research project. Prof. Janis Matisons, my principal supervisor, gave me the freedom to follow research directions of my own choosing, while still providing guidance to assist in steering the project. Nonetheless, occasionally I found that my chosen directions were blocked. In these instances Dr Kristina Constantopoulos provided the necessary advice to find new routes so I could continue my research. Kristina also gave valuable insight into the production of this thesis. I would also like to thank Dr Stephen Clarke and Assoc. Prof. Amanda Ellis, who filled supervisory gaps when Janis was unavailable.

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Without the financial and emotional support of my family and friends my education, which has culminated in this thesis, would not have been possible. I started university at 27, and my “significant other”, Jennifer Miron, has supported me in this from the first day of first year to the completion of this PhD. Perhaps now I will be home early enough to cook dinner more often.

Scope of Thesis

This thesis describes the work conducted in the design of amphiphiles capable of self-assembly into helically based nanotubes, the subsequent synthesis of the amphiphiles, and the analysis of their self-assembled structures. These long, straight, rigid nanotubes are formed by the tight, helical turning of a bilayer ribbon, driven by chiral organisation of the precursor amphiphiles.[1-4] To induce this chiral organisation molecular components of the amphiphile were selected rationally, and a combinatorial approach to construction provided a range of subtly modified molecular structures so that the optimal structures for self-assembly into nanotubes could be identified.

- In **Chapter 1** the thesis begins with a review of the relevant literature for helically based, self-assembled nanotubes. This review has been accepted for consideration by Chemical Reviews on the basis of a topic outline submitted recently, explaining the structure and length of the review. After the discussion of the literature on nanotubes, the literature review chapter briefly discusses the approach to the design of the amphiphiles used in this research. A major molecular component incorporated into the amphiphile design was an azo group. As this chemistry has rarely been used in helically based, self-assembled nanotubes, literature on azo chemistry and azo aggregation is also reviewed.
- **Chapter 2** provides the experimental details for all the work conducted in this research.
- **Chapter 3** details the design of the amphiphiles, examining how each component of the molecules contributes to the formation of helically based nanotubes and how the design was tuned by the synthesis of a combinatorial library of compounds based on three molecular variables. Discussion of the synthetic routes follows before moving to the analysis of the synthesised molecules in terms of molecular identity and purity.
- In **Chapter 4** the isomerisation of the azo component of both dissolved and aggregated amphiphiles is investigated.
- **Chapter 5** is the first of three chapters describing the self-assembly of the synthesised amphiphiles. The focus of the fifth chapter is on evaluating the self-assembly behaviour observed using TEM of the full combinatorial library of amphiphiles self-assembled from methanolic aqueous solution (1:3 v/v) using a heated method. The influence of each of three molecular variables is evaluated to identify the optimal molecular form for the production of helically based nanotubes, and also to provide further understanding of how this type of self-assembly occurs.
- In **Chapter 6** further investigation is conducted on selected amphiphiles from the combinatorial library self-assembled from methanolic aqueous solutions varying in solvent ratio at room temperature. UV-Vis spectroscopy is used to probe the environment of the azo

group in self-assembled structures. This analysis is combined with TEM observation of the aggregated structures to provide a better understanding of the forces driving helical self-assembly.

- **Chapter 7** investigates the self-assembly of synthesised amphiphiles that vary from those azo based amphiphiles with amino acid head groups that make up the main combinatorial library of compounds. The major component of this chapter is extracted from an article published previously in the Journal of Material Research.[5]
- **Chapter 8** concludes the thesis and provides suggestions for future work.

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Abbreviations

AFM	Atomic Force Microscopy
ANS	1-Anilino-8-Naphthalene Sulphonate
APTES	Aminopropyltriethoxy Silane
BOP	(Benzotriazol-1-yloxy)-tris-(dimethylamino)phosphonium hexafluorophosphate
CD	Circular Dichroism
CDCl$_3$	Deuterated Chloroform
CdS	Cadmium Sulphide
COSY	Correlation Spectroscopy
DAP	2,6 diaminopyridine
DC$_{8,9}$PC	1,2-bis(10,12-tricosadiynoyl)-*sn*-glycero-3-phosphocholine
DC$_{8,9}$PE	1,2-bis(10,12-tricosadiynoyl)-*sn*-glycero-3-phosphoethanolamine
DC$_{8,9}$PEOH	1,2-bis(10,12- tricosadiynoyl)-*sn*-glycero-3-phosphohydroxyethanol
DIEA	Diisopropylethylamine
DMSO-d$_6$	Deuterated Dimethyl Sulphoxide
DRIFT	Diffuse Reflectance Infrared Fourier Transform
DSC	Differential Scanning Calorimetry
FTIR	Fourier Transform Infrared
FWHM	Full-Width Half-Maximum
HATU	O-(7-Azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate
HBC	Hexa-*peri*-hexabenzocoronene
HBTU	*N*-(Benzotriazol-1-yl)-1,1,3,3-tetramethylguanidinium hexafluorophosphate

HMBC	Heteronuclear Multiple Bond Coherence
HMQC	Heteronuclear Multiple Quantum Coherence
HOAt	1-hydroxy-7-azabenzotriazole
HOBt	1-Hydroxybenzotriazole
IRMS	Isotope Ratio Mass Spectrometry
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
PyBOP	(Benzotriazol-1-yloxy)-tris-(pyrrolidino)phosphonium hexafluorophosphate
SANS	Small Angle Neutron Scattering
SAXS	Small Angle X-Ray Scattering
SDS	Sodium Dodecyl Sulfate
SEM	Scanning Electron Microscopy
TEM	Transmission Electron Microscopy
TEOG	Germanium Tetraethoxide
TEOS	Tetraethyl Orthosilicate
TGA	Thermal Gravimetric Analysis
UV	Ultraviolet light
UV-Vis	Ultraviolet and Visible light
WAXS	Wide Angle X-Ray Scattering
XRD	X-Ray Diffraction

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