SOME ASPECTS OF DIPYRROMETHENE CHEMISTRY

by

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Abstract

Dipyrromethenes are a fascinating class of heterocyclic compounds. They were first brought to the forefront of chemistry research by Hans Fischer who employed them in his famous syntheses of porphyrins. Recently dipyrromethene research has undergone a renaissance and returned to the attention of academia and industry.

Following a brief overview of the history of dipyrromethene chemistry in the literature, this thesis includes accounts of the research into three aspects of dipyrromethene chemistry: their use as ligands in the synthesis of chiral helicates, their use as gemini metallosurfactants; and a survey of their ^{15}N NMR chemical shifts. Bis(dipyrromethene)s appended with homochiral point-chiral auxiliaries have been shown to form zinc(II) helicates with low diastereomeric excesses. Despite the disappointing stereoselectivity for the formation of these compounds, insight into their high structural integrity and studies of their circular dichroism spectra have proven interesting. Preliminary research into the development of a series of gemini metallosurfactants incorporating amphiphilic dipyrromethenes has led to the development of some promising compounds. The zinc(II) complex of a sodium sulfonate-appended dipyrromethene has displayed surfactant activity. Furthermore, using ^{15}N-^{1}H heteronuclear single quantum coherence (HSQC) NMR experiments, a survey of the ^{15}N NMR chemical shifts of dipyrromethenes and some related compounds has revealed a high regularity that can be used as a diagnostic indication of gross structure.

List of Abbreviations and Symbols Used

°C - degree Celsius

γ - magnetogyric ratio

δ - chemical shift

Δδ - change in chemical shift

ε - molar absorptivity

Δε - molar circular dichroism

[Θ] - molar ellipticity

APCI - atmospheric pressure chemical ionization

bipy - bipyridine

Bn - benzyl

br s - broad singlet

CD - circular dichroism

$CDCl_3$ - deuterated chloroform

COSY - correlation spectroscopy

CSP - chiral stationary phase

d - doublet

DCC - *N,N'*-dicyclohexylcarbodiimide

DCM - dichloromethane

DDQ - 2,3-dichloro-5,6-dicyano-*p*-benzoquinone

dec. - decomposition

deg - degree

DEPT - distortionless enhancement by polarization transfer

DMAP - 4-(*N*,*N*-dimethylamino)pyridine

DMSO - dimethylsulfoxide

EDC·HCl - *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride

EI-HRMS - electron impact high resolution mass spectrometry

ESI - electrospray ionization

g - gram

h - hour

HBTU - *O*-benzotriazol-1-yl-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate

HMBC - heteronuclear multiple-bond coherence

HOBT - 1-hydroxybenzotriazol hydrate

HPLC - high performance liquid chromatography

HSQC - heteronuclear single-quantum coherence

Hz - hertz

I - nuclear spin

Insol - insoluble

J - coupling constant

JMOD - *J*-modulated spin echo

K_t - Krafft temperature

L - liter

m - meter, or in context of NMR multiplicity - multiplet

MALDI - matrix-assisted LASER desorption ionization

min - minute

mol - mole

m.p. - melting point

n/a - not applicable

NMR - nuclear magnetic resonance

NOESY - nuclear Overhauser effect spectroscopy

OAc - acetate

Ph - phenyl

ppm - parts per million

R_f - retention factor

r.t. - room temperature

s - singlet

Sol - soluble

Sp Sol - sparingly soluble

t - triplet

TEG - triethyleneglycol

THF - tetrahydrofuran

V - volt

v/v - volume per volume

w/v - weight per volume

Acknowledgements

"It is good to have an end to journey toward,

but it is the journey that matters in the end."

-Ursula K. LeGuin, **The Left Hand of Darkness**

I am most thankful to my supervisor, Prof. Alison Thompson, who has provided thoughtful and supportive guidance through my graduate studies. I've learned so much from you and you've really helped me to develop skills in many aspects of chemistry research. I would also like to acknowledge the support and direction provided to me by my supervisory committee.

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Chapter 1. Introduction

1.1. Historical Aspects

Dipyrromethenes (dipyrrins) were originally reported by Piloty in 1914,[1] and shortly thereafter were given great attention by Hans Fischer, who implicated many dipyrromethenes in the synthesis of porphyrins. A large part of the first half of the second volume of Fischer and Orth's *Die Chemie des Pyrrols* is devoted to descriptions of the syntheses of an extensive list of dipyrromethenes.[2] Recommendations for dipyrromethene nomenclature were published by IUPAC in 1987, and the numbering scheme is seen in Figure 1.[3] Throughout the nearly one hundred years of published dipyrromethene research these compounds have been known by many names: dipyrrin, 4,6-dipyrrin, 4,6-dipyrromethene, dipyrrylmethene, pyrrylmethene, pyrromethene, 2,2'-dipyrrolylmethene, dipyrrolemethene, diaza-*s*-indacene, 2-pyrrol-2-ylmethylene-*2H*-pyrrolenine, and 2-(*2H*-pyrrol-2-ylidenemethyl)pyrrole.

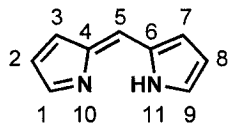


Figure 1. Numbering scheme for dipyrromethene nomenclature

1.2. Synthesis of Dipyrromethenes

Dipyrromethenes were originally developed as precursors in the synthesis of porphyrins and other tetrapyrroles. Brominated dipyrromethenes were used extensively in Hans Fischer's classical porphyrin syntheses including the synthesis of hemin in 1929,[4] as seen

in Figure 2, and a dipyrromethene was featured in R.B. Woodward's landmark synthesis of chlorophyll a,[5] as seen in Figure 3.

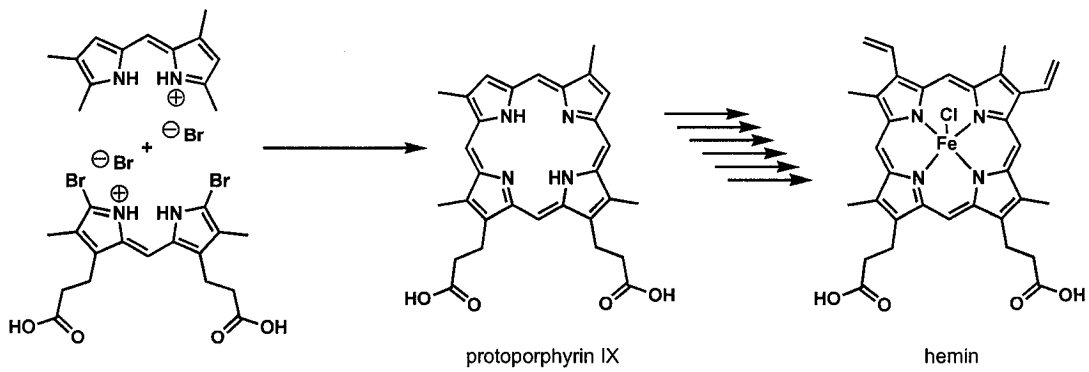


Figure 2. Dipyrromethene involvement in Fischer's total synthesis of hemin

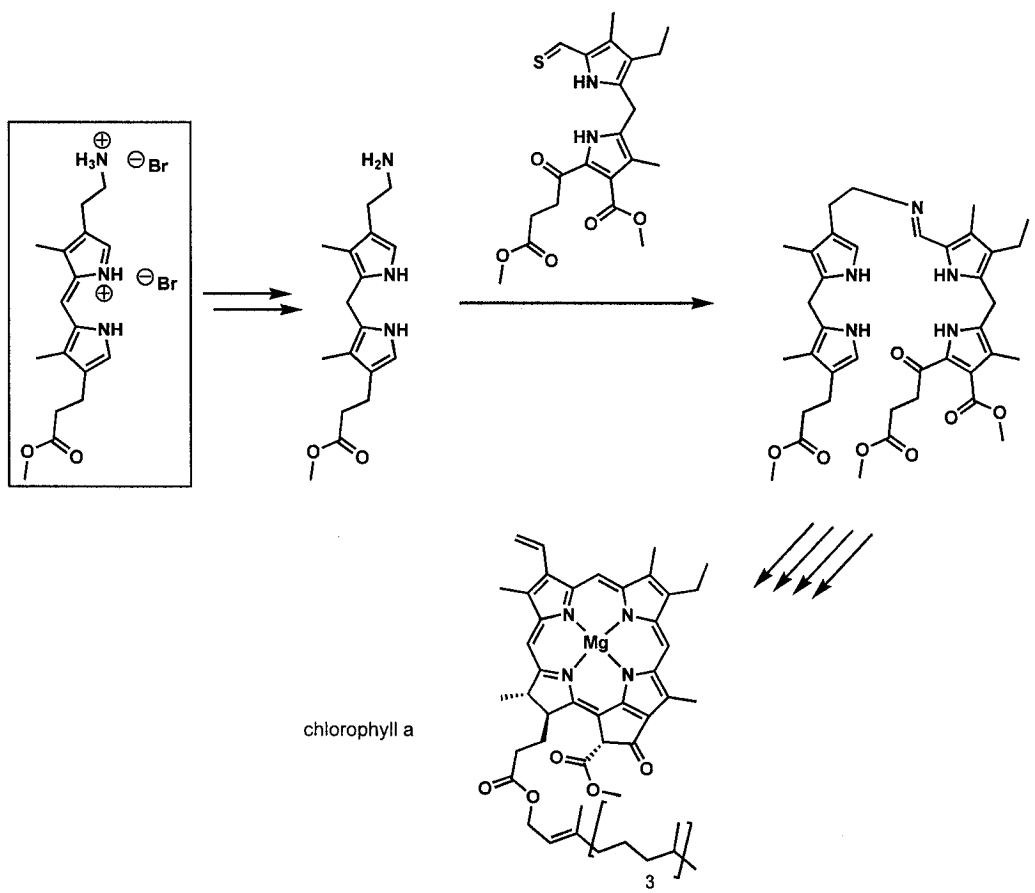
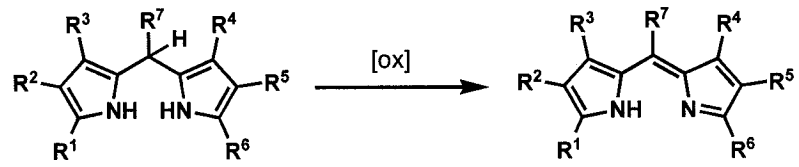


Figure 3. Dipyrromethene involvement in Woodward's synthesis of chlorophyll a

The two most significant methods that have been developed for the synthesis of dipyrromethenes consist of the oxidation of dipyrromethanes (Method A in Figure 4), or the condensation of equimolar 2-formylpyrrole with 2-unsubstituted pyrrole in the presence of a strong acid, typically hydrobromic acid (Method B in Figure 4). 5-Unsubstituted dipyrromethenes are known to be unstable, and so are commonly handled as their more stable hydrobromide salts.[6] As a result, the most common method for purification of 5-unsubstituted dipyrromethenes is crystallization.

Method A:



Method B:

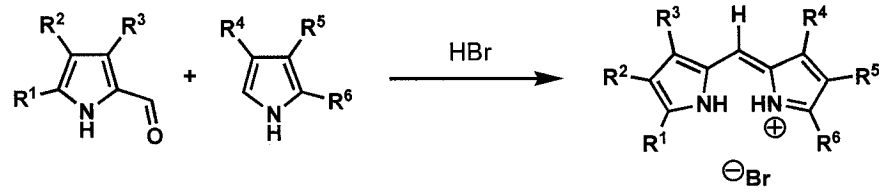


Figure 4. Synthesis of dipyrromethenes

With regards to substitution patterns about dipyrromethenes, symmetrical 5-substituted dipyrromethenes are best suited to synthesis by means of dipyrromethane oxidation (Method A). Recent advances in the preparation of dipyrromethanes by the condensation of aldehydes with pyrroles have greatly increased the versatility and usefulness of this approach.[7] Method B is best suited to the synthesis of either 5-unsubstituted or unsymmetrical dipyrromethenes.

As dipyrromethenes are universally prepared from pyrrolic precursors and there are very few examples of functional group manipulations of dipyrromethenes,[8] substitution patterns are generally limited to those available from the pyrrolic precursors. Alternatively, another commonly employed means of introducing different functionality into dipyrromethenes is through substitution at the 5-position. Fully unfunctionalized dipyrromethene (Figure 5) has been prepared, with the caveat that it readily decomposes at temperatures above -40 °C,[9] due to the susceptibility of the unsubstituted ring positions to nucleophilic and electrophilic attack.

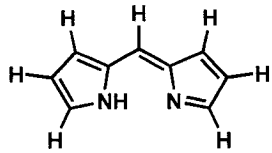


Figure 5. Unsubstituted dipyrromethene

1.3. Dipyrromethenes as Ligands

Dipyrromethenes have been reported to form complexes with a variety of metal cations. Known examples include complexes of magnesium(II),[10] calcium(II),[11,12] chromium(III),[13] manganese(II),[11,14,15] manganese(III),[14] iron(II),[16] iron(III),[16-20] cobalt(II),[21-23] cobalt(III),[17,20] nickel(II),[22,24,25] copper(II),[26-28] zinc(II),[29-31] rhodium(II),[32] palladium(II),[33,26,34] cadmium(II),[21,25] mercury(II),[21,25] thallium(I),[35] and thallium(III).[35] The first dipyrromethene complexes were prepared to serve as analogues of naturally occurring metalloporphyrins.[36] Dipyrromethene zinc(II) complexes have been isolated[37-41] from the syntheses of sterically-crowded porphyrins under Rothemund[42] condensation conditions, wherein the dipyrromethene complexes are seen as sideproducts

rather than intermediates.[41] Generally, dipyrromethenes bind metal cations in a κ^2 manner (Figure 6) with only a few known[43,44] exceptions.

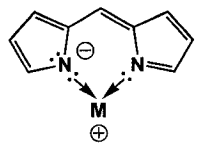


Figure 6. κ^2 binding in a dipyrromethene metal complex

The majority of known dipyrromethene complexes are homoleptic, and the coordination geometry of these complexes is almost exclusively tetrahedral, or distorted tetrahedral, with a few known examples of octahedral coordination for complexes of trivalent metal cations. The coordination geometry about the metal ion of dipyrromethene complexes is unable to assume a square planar formation due to the steric interaction of the 1,9-substituents, even if these substituents are hydrogen atoms.[21] For example, the dipyrromethene complexes of copper(II) and palladium(II) have been shown to assume distorted tetrahedral coordination geometries in the solid state, although both of these ions form square planar complexes almost exclusively with other ligands. For this reason dipyrromethene metal complexes became the focus of some research[21,34,45,46] during the early investigations of metal coordination geometries and ligand field theory.

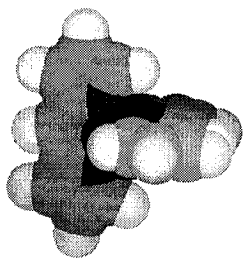


Figure 7. Tetrahedral coordination geometry in dipyrromethene metal complexes

In recent years, dipyrromethene complexes of borondifluoride, known as BODIPYs,[47] (Figure 8) have become recognized as commercially important products. They have found applications as laser dyes,[48] biological stains,[47] molecular sensors, and as components in light arrays because of their high fluorescence quantum yields, tunable emission maxima wavelengths, and their good photochemical stability.

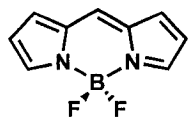


Figure 8. Dipyrromethene borondifluoride complex

Despite the decades of research into the chemistry of dipyrromethenes and their metal complexes, many unexplored areas remain. For example, there has been little reported mention of incorporating chirality into these molecules. The majority of dipyrromethenes described in the literature are symmetrical, although methods are known by which asymmetry can be introduced into these systems. Another facet of dipyrromethene research that has not yet reached its potential is the use of these compounds in practical applications. Dipyrromethenes are robust molecules that can be elaborated upon structurally in several ways, and their metal coordination properties create opportunities for interesting functions. Consequently, the research described herein details investigations into these ideas as well as advances in an underdeveloped method of characterizing dipyrromethenes and their derivatives.

Chapter 2. Chiral Zinc(II) Bis(dipyrromethene) Double Helicates

2.1. General Background

2.1.1. Supramolecular Self-Assembly

Chemistry has long been celebrated as the central science, an interdisciplinary field of research that overlaps many of the concepts from other physical sciences such as physics and biology. The point at which chemistry ends and chemical physics, computational chemistry, biochemistry, chemometrics, and quantum chemistry give way to non-chemistry is often highly subjective. The founders of supramolecular chemistry similarly find it difficult to classify their highly interdisciplinary research as strictly chemistry, and instead prefer the term "supramolecular science".[49] Supramolecular science involves the study of large multi-molecular systems that are held together by non-covalent, intermolecular bonds. Early research in this field involved the development of macrocyclic ligands, such as crown ethers[50] and cryptands[51] for selectively binding alkali metal cations.

As with all new disciplines that quickly gain wide interest, supramolecular scientists rapidly developed new terminology to describe the new ideas being presented. Supramolecular science was chosen as an inclusive term to describe the study of both supermolecules and supramolecules, terms that were originally coined by Jean-Marie Lehn, who received the Nobel Prize in 1987, jointly with Donald J. Cram and Charles J. Pedersen, for "their development and use of molecules with structure-specific interactions of high selectivity".[52]

A supermolecule is classified as a well-defined, discrete, oligomolecular species that arises through the association of just a few components.[49] An example of a supermolecule, or "Übermoleküle" as it was once known, is a compound that results from the binding of a receptor with its substrate. For example, cyclodextrins when bound to their guest molecules, such as naphthalene, are classified as supermolecules.[49] Another example is seen in Figure 9, a crown ether complex of a potassium ion, one of the first studied structures in supramolecular science.[50] Alternately, supramolecules are classified as polymolecular assemblies in less-defined structures, such as micelles, films or solid state assemblies.[49]

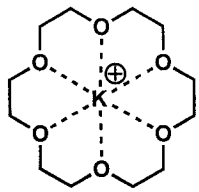


Figure 9. Supermolecular complex of [18]crown-6 with substrate, potassium ion

Self-assembly, another important term that arose through the studies of supramolecular scientists, is defined as the spontaneous construction of large molecular structures from a series of smaller molecules.[49] It is the process of recognition-directed, reversible, spontaneous association of a limited number of components under the intermolecular control of relatively labile noncovalent interactions, hydrogen bonds and dipolar interactions. The reversibility of supramolecular self-assembly is key to the resulting systems' abilities to sift through the available components to form the thermodynamically most favourable structure.[52]

2.1.2. Helicates

One class of supermolecules that has been of consistent interest is the helicates. This class includes molecules that involve the use of metal ions as an assembly pattern for the twisting of organic ligands into multiple-helical structures. The vast majority of ligands designed for the production of helicates, specifically known as helicands, involve pyridine-type nitrogen donors.[53]

Multiple ligands can be involved in the formation of one helicate by twisting around each other and coordinating to the same set of metal ions. Helicates of this type are referred to as double helicates when two ligands are twisted around each other or triple helicates when three ligands are involved. When the helicate involves two tetrahedral metal centers, the compound is classified as a [4+4] double helicate, which indicates the coordination number of the two metal centers, namely four and four.[53] An example of a [4+4] double helicate is shown in Figure 10.[54]

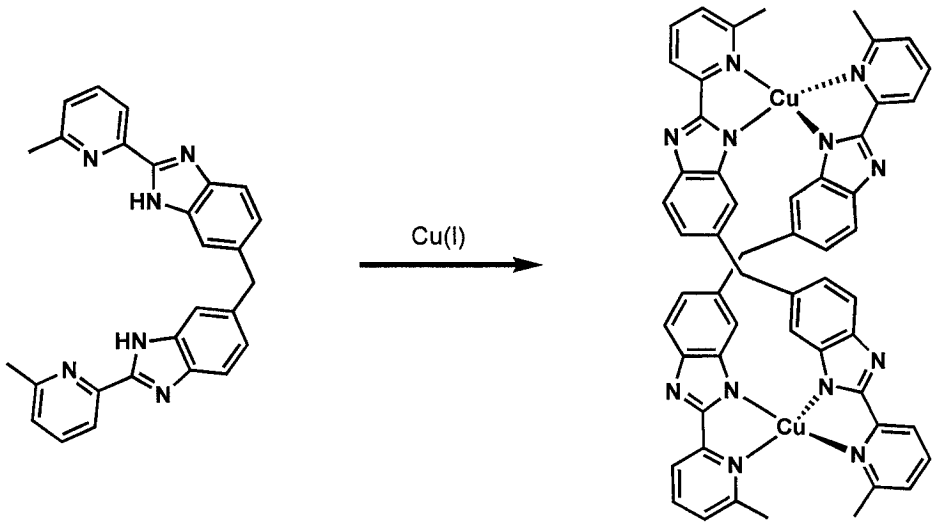


Figure 10. Formation of a [4+4] helicate

The majority of helicates are synthesized using self-assembly procedures and therefore most of the known examples of these molecules represent thermodynamic minimum structures. This suggests that the information for the formation of a helix lies "pre-programmed" into the components of the helicate, and that the structure of helicates can be controlled through ligand design and the choice of metal atom. This process is known as coding.[53] Ligands consist of a discrete number of metal-binding regions, linked by non-binding regions. Coding takes into account the number and type of donor atoms that are present in the ligand and how this is predicted to affect the geometric arrangement of the ligand in a helicate product. For example, although relatively unsubstituted bipyridyl (bipy) helicands are known to form triple helical complexes, a high degree of substitution on the ligand can preclude the formation of triple helices as a result of steric crowding around the metal center, resulting in the production of double helices only.[53]

As well, coding takes into account the optimum ligand-to-metal bond lengths, preferred coordination numbers, and coordination geometries of metal ions in predicting the helicate structure. An example of this type of coding can be seen in the preferential formation of triple helical bipy supermolecular compounds with nickel(II) ions, while double helical structures are observed for copper(I) and silver(I) ions (Figure 11).[55]

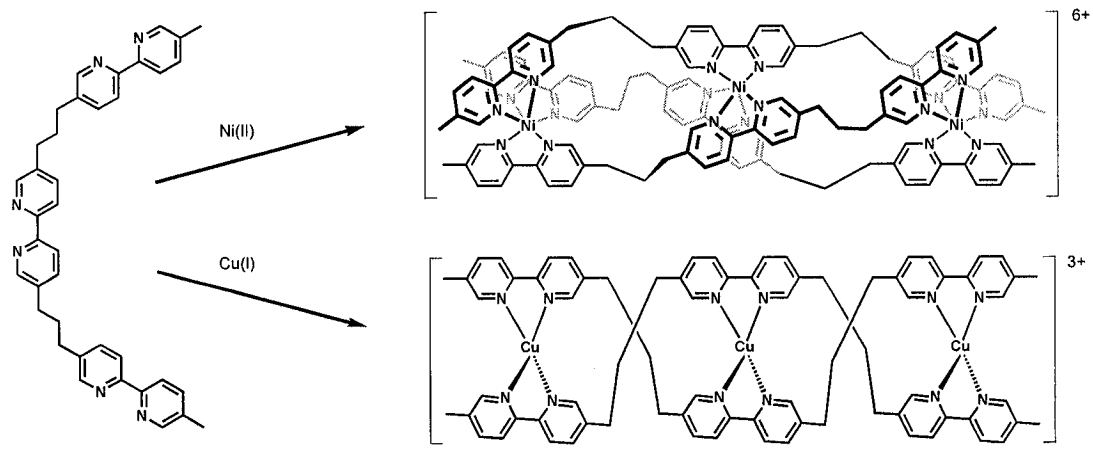


Figure 11. Metal ion coding: formation of bipy double- and triple-helicates

All helicates are subject to a phenomenon known as supramolecular chirality.[53] A helix is a chiral object, and the pair of helical enantiomers are identified as the *P* (for plus, clockwise) and the *M* (for minus, counterclockwise) helices, their enantiomeric relationship is shown in Figure 12.[49] Helices labelled *P* are also known as right-handed helices, and *M* helices are alternately known as left-handed helices.[49] Right-handed helices are most familiar to us in the form of deoxyribonucleic acid and the threads of standard wood screws.

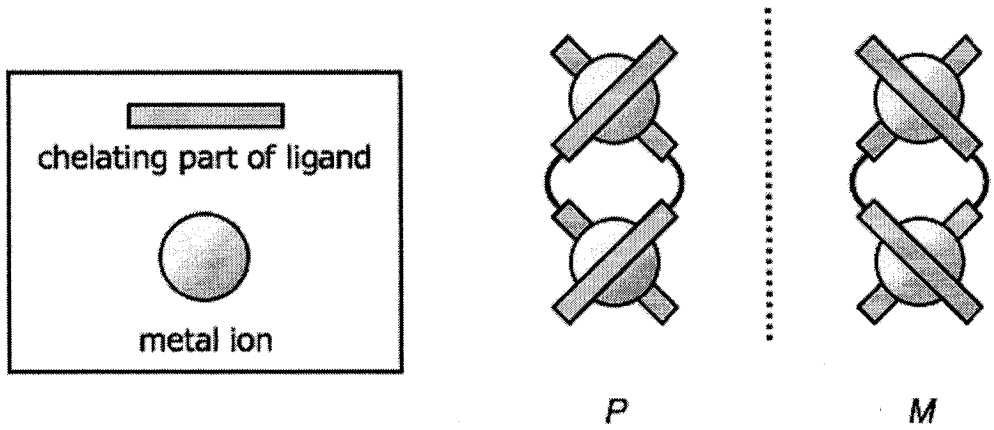


Figure 12. *P* and *M* enantiomers of dinuclear double helicates

2.1.3. Bis(dipyrromethene) Helicates

Bis(dipyrromethene)s consist of two dipyrromethene units linked together by a spacer. There are several possibilities for the connectivity of the two units, the two most common structures are shown in Figure 13. Upon deprotonation, bis(dipyrromethene)s form tetradentate ligands in analogy to dipyrromethenes.

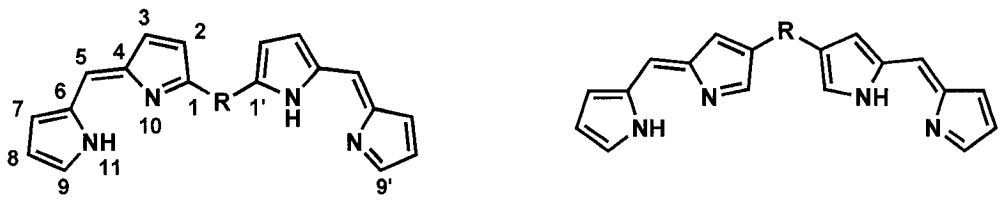


Figure 13. Bis(dipyrromethene) numbering scheme

The first examples of bis(dipyrromethene) metal complexes were reported by Fischer in 1939 during attempts to prepare macrocyclic tetrapyrroles from dipyrromethenes.[56] These complexes, both with ratios of metal-to-organic ligand of 1:1, were prepared by reacting 1,9-dibromodipyrromethenes with palladium hydroxide as shown in Figure 14. The report also demonstrated the ability to generate non-metallated 1,1'-bis(dipyrromethene)s from these complexes by reacting them with mineral acids.[56]

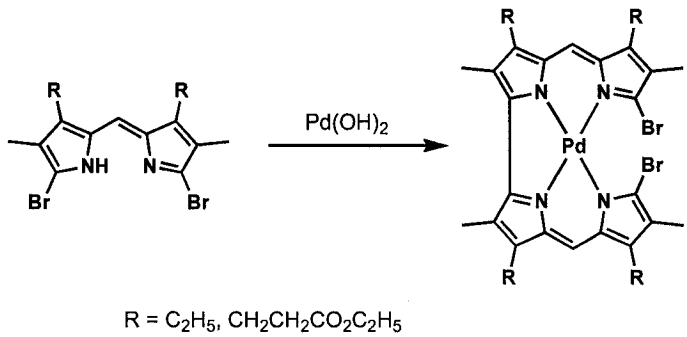


Figure 14. Preparation of 1,1'-bis(dipyrromethene) palladium(II) complexes from 1,9-dibromodipyrromethenes

Using a procedure that was similar to Fischer's previous work, Johnson and co-workers synthesized similar palladium(II) bis(dipyrromethene) complexes twenty years later.[57] This work also showed that a complex of this type could be cyclized using formaldehyde to produce a 10-oxacorrole palladium(II) complex, as seen in Figure 15a. Similarly, the oxidative cyclization of 9,9'-dimethyl-1,1'-bis(dipyrromethene) metal complexes was used for several decades as a method to synthesize porphyrins, as seen in Figure 15b.[58-64]

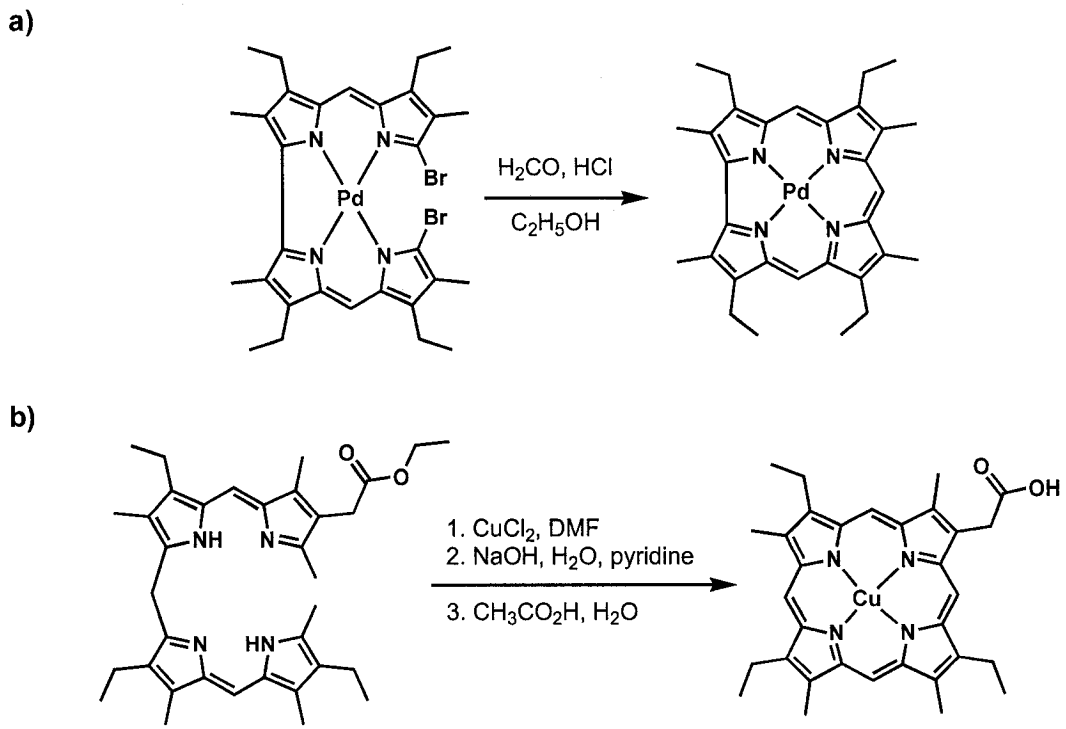


Figure 15. Oxidative cyclization of 1,1'-bis(dipyrromethene) complexes: a) preparation of 10-oxacorrole palladium(II) complex; b) preparation of porphyrin copper(II) complex

In the process of investigating their use in the synthesis of corroles[65] and tetrahydrocorrins,[66,67] it became apparent that several factors affect the formation of bis(dipyrromethene) metal complexes. It was observed that the use of ethanol as a solvent for the complexation reactions favoured the formation of products with a 1:1 metal-to-

bis(dipyrromethene) ratio while changing the solvent to methanol favoured the formation of 2:2 products.[68,69] Murakami and co-workers[70,71] demonstrated that for complexation reactions conducted in methanol, nickel(II) and copper(II) ions formed 1:1 bis(dipyrromethene) complexes while cobalt(II) and zinc(II) ions yielded 2:2 products. This difference in product compositions is most likely due to the preferred geometries of the involved metal ions since it has been observed that nickel(II) and copper(II) generally form distorted tetrahedral dipyrromethene complexes while those of cobalt(II) and zinc(II) deviate very little from perfect tetrahedral coordination. The monomeric structure would create significantly more strain in a tetrahedrally-coordinated bis(dipyrromethene), thus potentially explaining the preferences observed for the different metal ions.

The inability of dipyrromethene ligands to exist co-planar around a metal ion dictates that the complexation products of bis(dipyrromethene)s are helical. Although this theoretically applies to bis(dipyrromethene)s bound in an octahedral manner about a metal ion center, only examples of tetrahedrally-bound bis(dipyrromethene) complexes are known. Figure 16 depicts a schematic diagram that can be used for drawing bis(dipyrromethene) complexation products with 1:1 and 2:2 ratios of metal ion-to-ligand.

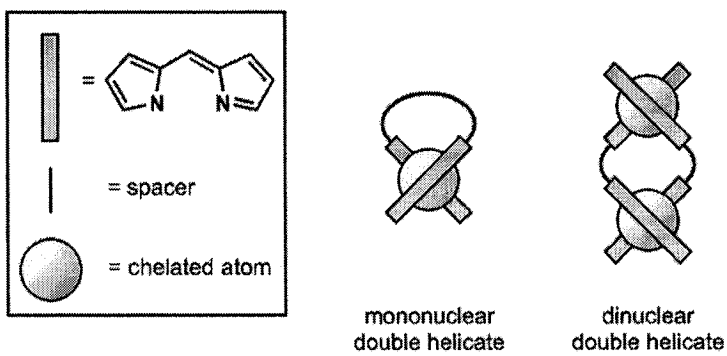


Figure 16. Schematic mononuclear and dinuclear bis(dipyrromethene) double helicates

Although researchers had proposed helical structures before,[72,71] the first solid state structure of a [4+4] double helicate bis(dipyrromethene) metal complex was not published until 1980.[73] The crystals of this compound, the structure of which is shown in Figure 17, were prepared during a survey of 1,1'-bis(dipyrromethene) cyclization reactivity.[73] The solid state structure[74] showed a dinuclear double helical conformation, and, although no mention is made of the handedness of the compound, the crystal was a racemate of right- and left-handed helices, an observation that has been made for the crystals of more recent analogues of this compound.[75] Mononuclear and dinuclear double helical structures had previously been reported for the zinc(II) complex of octaethylformylbiliverdin, a bile pigment analogue that is structurally related to bis(dipyrromethene)s.[76] As well, a nickel(II) complex of octaethylbilindione, another bile pigment analogue, had been shown to possess a mononuclear helical structure.[77]

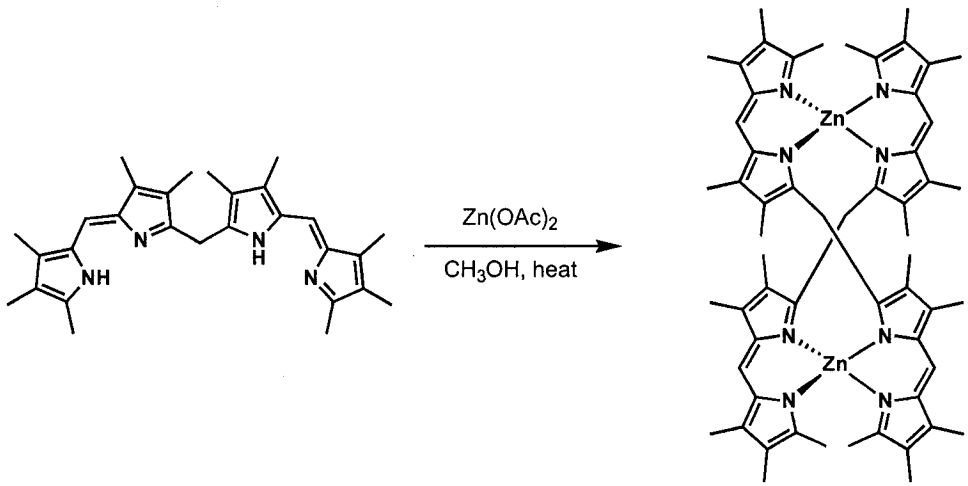


Figure 17. Structure of the first crystallographically characterized bis(dipyrromethene) metal complex

The effect of the nature of the spacers that link the dipyrromethene units upon the nature of the complexation products has also been investigated. Preliminary studies of

spacer length and steric bulk revealed the formation of products with ratios of 1:1 copper(II)-to-1,1'-bis(dipyrromethene).[69] More detailed studies[78-80] of the effect of connectivity and spacer length provided better insight. It was found that 2,2'-bis(dipyrromethene)s formed 3:3 complexes of zinc(II) for ligands bearing no spacer between the two dipyrromethene units. An example of these "molecular triangle" products was characterized crystallographically.[79] Compounds with a metal-to-bis(dipyrromethene) ratio of 2:2 are the exclusive product of complexations of 2,2'-bis(dipyrromethene)s with methylene, ethylene or propylene spacers.

Dinuclear double helical solid state structures have been characterized for cobalt(II)[78] and zinc(II)[78,73] complexes of methylene-linked 1,1'-bis(dipyrromethene)s and for cobalt(II),[80,81] nickel(II),[75] and zinc(II)[82,80] complexes of methylene-linked 2,2'-bis(dipyrromethene)s. The structures of the 1,1'-bis(dipyrromethene) complexes show a significantly shorter distance required for one full turn of the helix as measured along the helix axis, also known as the helical pitch, which results in shorter interatomic distances for the two metal centers.

For 2,2'-bis(dipyrromethene)s with spacers longer than a propylene unit, as the spacer length increases so does the proportion of monomeric complexation products.[80] This tendency towards the formation of monomeric products with increasing degrees of freedom in the bis(dipyrromethene) spacer can be attributed to a balance between two factors: the chelate effect, which describes the entropically favoured formation of monomeric products over dimeric complexes;[83] and the physical ability of the bis(dipyrromethene) ligand to bind both dipyrromethene units to one metal center. Modelling reveals that it is not possible for both units of 2,2'-bis(dipyrromethene)s with

short spacers to bind one metal center due to the large amount of strain incurred with such a structure, and hence the preferred formation of 3:3 and 2:2 complexation products for these ligands.

The demonstrated ability to change the macromolecular structure of bis(dipyrromethene) complexes by changing the connectivity and length of the spacers created an interest in using these ligands as supramolecular building blocks. Ma and co-workers reported the preparation and crystallographic characterization of a severely distorted dinuclear double helical zinc(II) complex of a 1,2'-bis(dipyrromethene) that resembled a "molecular rectangle".[84] Furthermore, the size of 9,9'-substituents on the bis(dipyrromethene) ligand has been found to have little effect upon the coordination geometry of complexes of these ligands.[85] In a study of nickel(II) 1,1'-bis(dipyrromethene) mononuclear helicates, Bröring and Brandt determined that altering the size of the 9,9'-substituents from hydrogen atoms to 1,4-butadiyl (as seen in Figure 18) resulted in very little structural variation. However, it was determined that the incorporation of *tert*-butyl groups at the 9,9'-positions of the bis(dipyrromethene) ligand precluded the formation of nickel(II) complexes.[85]

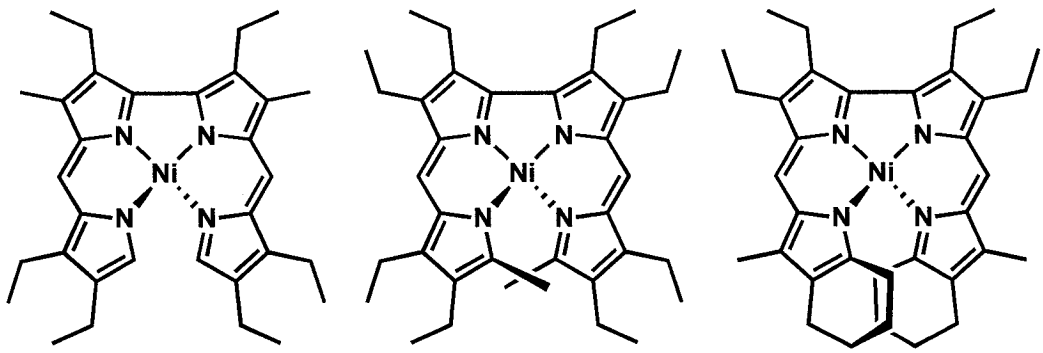


Figure 18. A series of nickel(II) complexes of 1,1'-bis(dipyrromethene)s with increasingly large 9,9'-substituents

2.1.4. Non-Racemic Bis(dipyrromethene) Helicates

In the absence of any chiral influence, helicates form as racemic mixtures of *P* and *M* helices; bis(dipyrromethene)s are not an exception to this rule.[86] The most common strategy to synthesize helicates stereoselectively is to use homochiral ligands such that the *P* and *M* products are related as diastereomers. The formation of diastereomeric products introduces the possibility of stereoselectivity in the complexation process. To better illustrate this strategy, consider an optically pure ligand that contains two symmetrically disposed homochiral centers (so as to eliminate the possible formation of head-to-head or head-to-tail isomeric complexes). The two homoleptic double helicate products of this ligand, shown as (*P*)-(*S*,*S*) and (*M*)-(*S*,*S*) in Figure 19, are related to each other as diastereomers and the difference between their chemical and physical properties dictates their relative ratios of formation, introducing the potential for stereoselectivity.

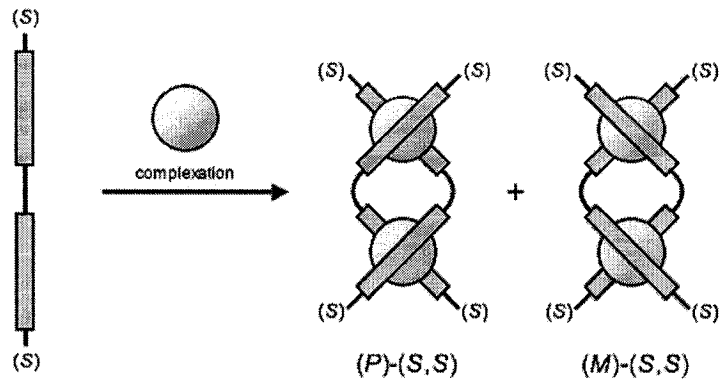


Figure 19. Illustration of stereoselective helicate synthesis from homochiral ligands

Two main strategies for the incorporation of chirality into helicands have been employed in the study of stereoselective helicate formation: placing point chiral groups at the termini of the ligand or incorporating a chiral template within the ligand. Examples of ligands based upon these two strategies are shown in Figure 20. Both types of helicands

have been successfully employed in highly diastereoselective complexation reactions (terminal[87-94] and internal[95-104]).

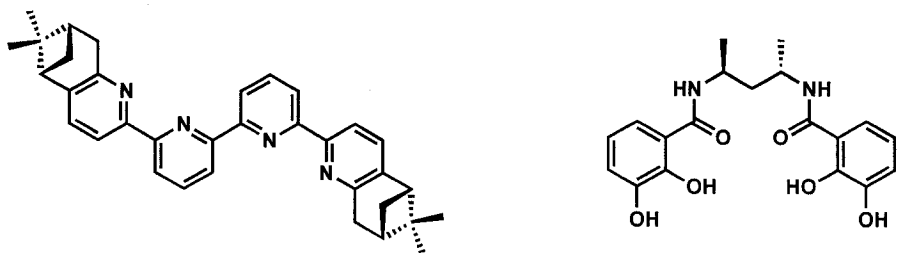
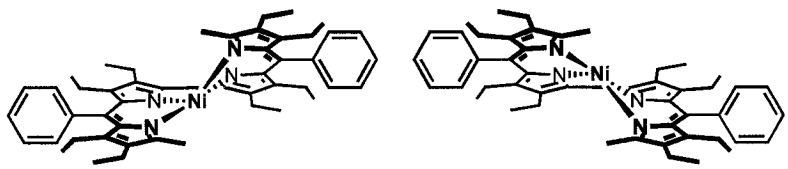


Figure 20. Examples of the two main strategies of chiral helicand design

Both internal and terminal chiral auxiliaries have been investigated for the induction of stereoselectivity in zinc(II) complexes of 19-alkoxybilin-1-ones. As alkylated derivatives of bilindiones, which demonstrate helicate formation,[77,105-110] 19-alkoxybilin-1-ones have also been reported to form helical metal complexes in a manner that is analogous to bis(dipyrromethene)s. A series of bilinone ligands was prepared with point chiral groups attached at the 19-position. Some of these 19-alkoxybilin-1-ones incorporated the point chiral group into the middle of the ligand[111] by joining two bilinone units together through the auxiliary while others were simply termininated by the point chiral group.[112,111,113] In another study, chiral amines and esters of chiral amino acids were added to racemic solutions of the zinc(II) 19-alkoxybilin-1-one helicates to act as ligands upon the zinc(II) center and induce helical stereoselectivity.[114-117]

The first report of optically pure bis(dipyrromethene) helicates was published in 2001.[118] In this study resolution of the *P* and *M* enantiomers from a racemic mixture of a mononuclear nickel(II) complex of 1,1'-bis(dipyrromethene) with no spacer was achieved by HPLC using a Pirkle column.[118] The separated enantiomers were analyzed by circular dichroism, and the stability of their helical chirality to heating in solution was evaluated.

The *M* enantiomer, in Figure 21, did not racemize after 14 hours in 218 °C molten naphthalene, which suggests the helicates possess a high barrier to racemization.[118] The stability of these complexes to racemization has been attributed[119] to strong nickel(II)-ligand bonds resulting from the dipyrromethene ligands acting as π-acceptors. This back bonding[83] is a property that has previously been ascribed to porphyrins in metal complexes.[120]



M *P*

Figure 21. *M* and *P* enantiomers of nickel(II) 1,1'-bis(dipyrromethene) complex

2.1.5. Circular Dichroism

The term "optically active" to describe a chiral molecule arises from the observation that pure samples of these compounds interact with polarized light to produce observable rotations of the incident light. The first studies into the idea of chirality began with the French researchers Jean-Baptiste Biot and Augustin Fresnel at the beginning of the nineteenth century.[121] Circular dichroism (CD) is a popular form of chiroptical absorption spectroscopy. Chiroptical spectroscopy is the study of molecular interactions with light that propagates in a right- or left-circularly polarized manner, in the absence of a magnetic field. Figure 22 shows the difference in propagation of right- and left-circularly polarized light. It is necessary that the molecule of interest be chiral in order for any

measurable interaction with the polarized light to occur. In this way, CD spectra can be used to study the conformations of chiral molecules.[121]

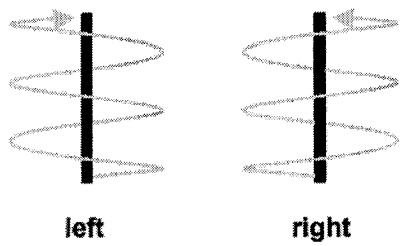


Figure 22. Propagation of left- and right-circularly polarized light

As observed in polarimetric studies, the angle of polarized light emerging from a solution of a homochiral molecule will be rotated a certain angle from the incident angle of polarization. This characteristic is known as optical rotation. The rotation of the angle of polarization arises from the circularly birefringent nature of optically active chromophores. Circular birefringence occurs when the refractive indices for left- and right-circularly polarized light are not equal in a medium. As the refractive index is a measure of the speed of light travelling through the medium, it can be seen that the two beams of circularly polarized light passing through a circularly birefringent medium are propagating with the same intensity, if they are absorbed equally, but at different speeds. Solutions of compounds that exhibit a circular dichroism not only display circular birefringence, but also absorb the two circularly polarized beams of light to a different degree.

Plane polarized light can be viewed as the vector sum of a beam of right-circularly polarized light and a beam of left-circularly polarized light. The effects of the combination of differential absorption and circular birefringence (that is to say, a circular dichroism) upon plane polarized light can be seen in Figure 23. Initially the two

circularly polarized beams are propagating at the same speed, ω_R or ω_L, and have the same intensity, E_R or E_L, resulting in a beam of plane polarized light, with intensity E (Figure 23A). The differential absorption aspect of circular dichroism causes the intensities of the two circularly polarized beams to be unequal and results in the oscillation of the resultant beam, E, in an elliptical manner (Figure 23B). The combination of differential absorption and circular birefringence, which causes the two circularly polarized beams to propagate at different speeds, ω_R and ω_L, and the resultant beam, E, to be rotated by an angle α (Figure 23C) results in elliptically polarized light that is the source of circular dichroism measurements (Figure 23D).

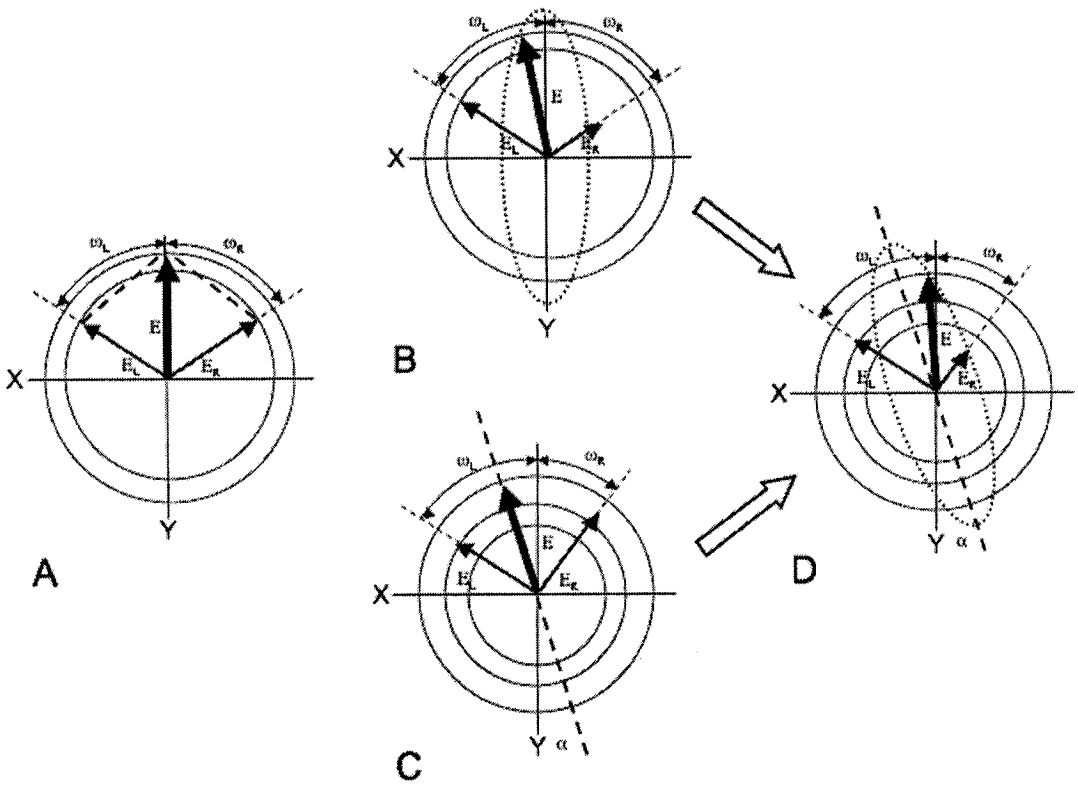


Figure 23. Aspects of circular dichroism: A) plane polarized light seen as the sum of left- and right-circularly polarized light; B) the effect of differential absorption upon plane polarized light; C) the effect of circular birefringence upon plane polarized light; D) the effects of circular dichroism upon plane polarized light

Depending upon the indices of refraction and whether a chiral chromophore preferentially absorbs the right- or the left-circularly polarized light determines the sign and magnitude of the observed circular dichroism effect. In the analysis of spectra these signals are referred to as Cotton effects, named in honour of A. Cotton, a pioneer in the optical rotatory dispersion analysis of copper and chromium tartrates.[122]

Consider the absorption spectrum for a simple, homochiral molecule such as (Δ)-tris(ethylenediamine) cobalt(III) chloride: electronic transitions within the molecule give rise to absorptions of light with wavelengths of maximum absorption around 429 nm and 493 nm. The CD spectrum of the same compound in solution shows a small negative Cotton effect at 429 nm and a large positive Cotton effect at 493 nm.[123] The analogous CD spectrum of homochiral (Λ)-tris(ethylenediamine) cobalt(III) chloride, the enantiomer of the (Δ)- derivative, shows a small positive Cotton effect at 429 nm and a large negative Cotton effect at 493 nm. This example illustrates the complementary nature of CD spectra for enantiomers. A racemic mixture of tris(ethylenediamine) cobalt(III) chloride shows no circular dichroism.[123]

Molecules that possess π-electron systems interact with the electromagnetic field of ultraviolet or visible light to absorb the resonance energy corresponding to the energy gap between the ground and excited states. Usually, electronic absorption and circular dichroic spectra are obtained of the molecule in solution, where intermolecular interactions are considered negligible. However, in molecules in which chromophores are held close to each other in fixed geometries, such as in dimers and polymers, the UV and CD spectra show considerable changes due to chromophore-chromophore intramolecular interactions.[124] This phenomenon is known as exciton coupling.

Consider, for example, a molecule that consists of two identical chromophores, A and B, that are oriented in a certain position, and separated by a link composed of σ bonded atoms: the probability associated with the excited state for chromophore A is exactly equal to that associated with chromophore B, so mixing of the two states gives the excited state of the whole system. This can be viewed as delocalization of the exciton between the two chromophores.

Exciton coupling in a CD spectrum produces a characteristic bisignate Cotton effect that centers around the wavelength of maximum absorption in the UV-vis spectrum. A positive exciton chirality, that is to say a bisignate signal with a positive Cotton effect at long wavelengths and a negative Cotton effect at shorter wavelengths, can be assigned to one enantiomer of a helix by consideration of the directions of the electric dipole transition moments for a helical exciton. Consequently, a negative exciton chirality, that is to say a bisignate signal with a negative Cotton effect at long wavelengths and a positive Cotton effect at shorter wavelengths, can be assigned to the other enantiomer of the helix. Using this method the handedness of a helical enantiomer can be assigned based upon its CD spectrum.[125]

2.2. Project Goals

There is an interest in the preparation of enantiomerically pure helicates. Enantiomerically pure helicates have been successfully applied as catalysts for stereoselective organic transformations,[126-129] and the chirality of these helical catalysts has been shown to translate to high stereoselectivity in the products. Helicates also have proposed applications for use in enantiomeric separations.[114] For these reasons, and for the purpose of furthering understanding of helicate formation, the following research

describes the attempts to stereoselectively synthesize zinc(II) bis(dipyrromethene) dinuclear double helicates.

The majority of the research into this subject that has been conducted previously focused upon helical oligopyridyl complexes.[49] As was discussed previously in Chapter 2.1.4, optically pure bis(dipyrromethene) helicates represent a relatively unstudied area of chemical research. The reported stability of the helical chirality in complexes of this type[118] makes them suitable systems for the study of chiral induction. Bis(dipyrromethene)s offer the advantage over pyridine-type ligands that their complexation yields non-ionic neutral molecules that can be purified by common chromatographic techniques including flash column chromatography and standard HPLC methods. As well, the demonstrated ability to control the supramolecular structure of the bis(dipyrromethene) helicates, discussed in Chapter 2.1.3, provides an incentive to increase the understanding of these highly interesting molecules.

Three approaches to the stereoselective synthesis of bis(dipyrromethene) helicates that have been investigated are depicted in Figure 24. In one approach (Figure 24a) homochiral 1,1'-bi-2-naphthol and dimethyl tartrate were incorporated as chiral templates into 2,2'-bis(dipyrromethene) ligands.[130] In a different approach (Figure 24b), the 1,1'-bis(dipyrromethene) ligand was designed with 2,2,2-trifluoroethanol point chiral auxiliaries placed in the 2,2'-positions to influence the handedness of the dinuclear zinc(II) double helicates formed.[131] The chiral template design yielded >99% diastereoselectivity in the production of mononuclear helicates. The work described herein focuses upon a different approach (Figure 24c) to the stereoselective synthesis of

bis(dipyrromethene) helicates and a study of the configurational stability of zinc(II) 2,2'-bis(dipyrromethene) dinuclear double helicates.

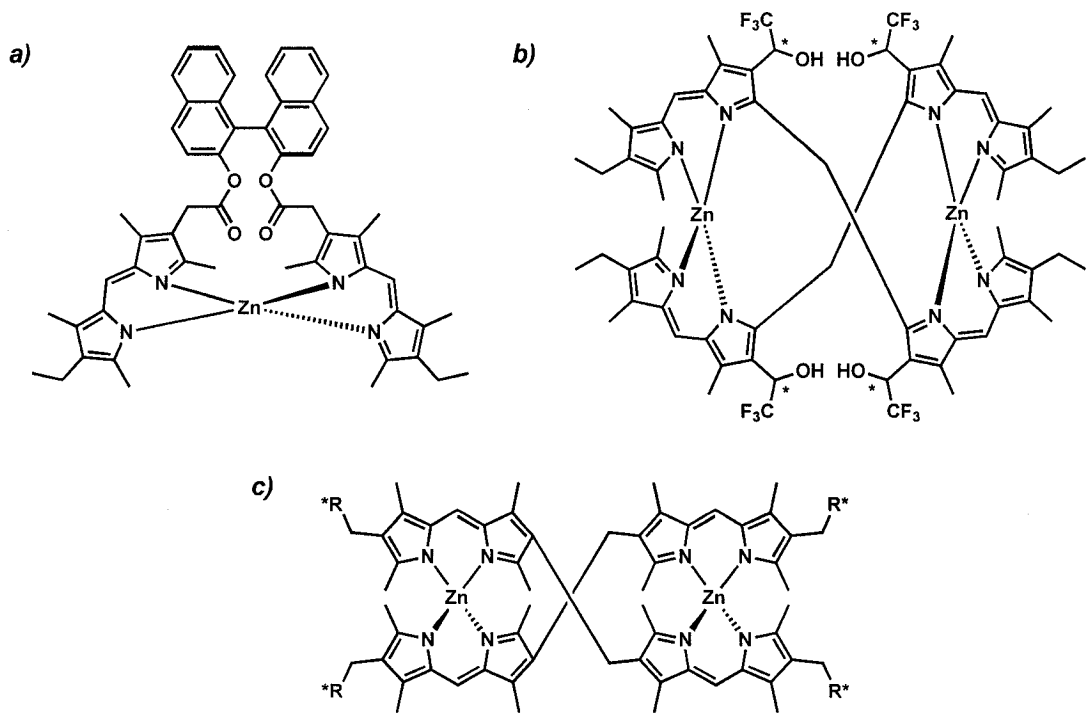


Figure 24. Three approaches to chiral induction in bis(dipyrromethene) helicates: a) internal point chiral auxiliaries; b) internal chiral template; c) terminal point chiral auxiliaries

2.3. Results and Discussion

2.3.1. Design and Synthesis of Chiral Bis(dipyrromethene) Helicates

The design of chiral zinc(II) bis(dipyrromethene)s, the generalized structure of which can be seen in Figure 25, can be rationalized in terms of ease of synthesis and anticipated simplification of spectroscopic data. A methylene-linked 2,2'-bis(dipyrromethene) structure was chosen because ligands of this type have been established to exclusively form dinuclear double helicates, as discussed in Chapter 2.1.3. The symmetry of the

bis(dipyrromethene) created by placing homochiral auxiliaries at both termini of the ligands reduces the number of potential complexation products that can be prepared by eliminating the possibility of head-to-head and head-to-tail isomers. This serves to simplify the results of the chiral induction study.

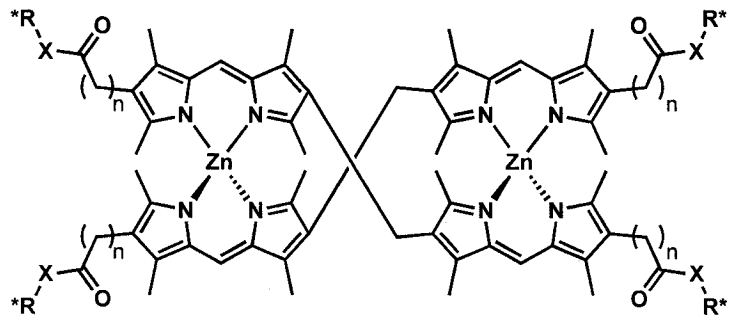


Figure 25. Generalized structure of the chiral zinc(II) bis(dipyrromethene) helicates that are the focus of this study

The synthesis of pyrroles bearing pendant carboxylate esters, for use in the synthesis of naturally occurring tetrapyrroles such as bilirubin and protoporphyrin IX, is well established.[132] With an eye towards easily creating diversity, point chiral auxiliaries were incorporated into the bis(dipyrromethene) ligands by amine and alcohol couplings to carboxylic acid functional groups. Alcohols and amines serve well as chiral auxiliaries because a wide variety of them are commercially available with high enantiopurity. Established pyrrole syntheses allow for the length of the spacer between the chiral auxiliary and the pyrrole ring to be modified, allowing the effects of the position of the auxiliary upon complex diastereoselectivity to be probed.

A disconnection strategy for the synthesis of zinc(II) bis(dipyrromethene) helicates is shown in Figure 26. The strategy uses the coupling of 2-formyl pyrroles and 2-unsubstituted pyrroles which, as discussed in Chapter 1.2, is the most suitable method for the formation of unsymmetrical dipyrromethenes. The appropriate 2-unsubstituted

pyrrole can be prepared *in situ* by decarboxylation of a 2-carboxylic acid pyrrole, itself prepared by hydrogenolysis of the corresponding benzyl ester derivative. Chemical manipulations of dipyrromethenes are relatively unknown and reportedly difficult,[133] and as a result the incorporation of the chiral auxiliary was performed at the pyrrole stage in the synthesis.

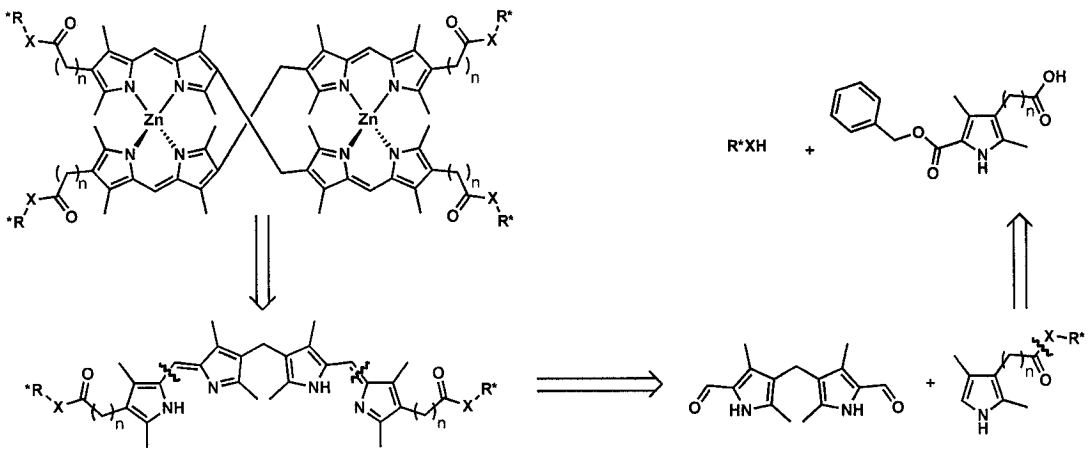


Figure 26. Retrosynthetic analysis of zinc(II) 2,2'-bis(dipyrromethene)s bearing terminal point chiral amides and esters

Synthesis of homochiral pyrrole amides and esters

A scheme for the synthesis of a series of homochiral pyrrole amides and esters is shown in Figure 27. The first molecules in the synthesis, benzyl 4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate (**1**)[134] and benzyl (4-methoxylcarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate (**2**),[130] can be synthesized on a large scale via Knorr-type reactions. The methyl ester functional groups of **1** and **2** were chemoselectively hydrolyzed using aqueous lithium hydroxide, giving carboxylic acids **3** and **4**, respectively, in excellent yield. It was found that repeated heating of solutions of **3** and **4** resulted in the formation of trace amounts of an unidentified red contaminant, the presence of which did not seem to impede the subsequent reactions.

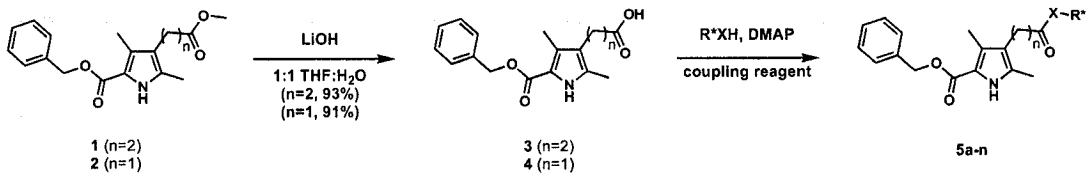


Figure 27. Synthesis of homochiral substituted pyrrole amides and esters

Several different coupling reagents were employed in the preparation of a series of pyrroles substituted with chiral amides and esters. In preliminary studies the historically well-established[135] carboxy group activating reagent *N,N'*-dicyclohexylcarbodiimide (DCC) was utilized in the synthesis of amides **5g-j**, and then other coupling reagents were also evaluated. The use of DCC detracted from the yield of the desired products in two ways: first, by the formation of an *N*-acylurea sideproduct,[135] **6** in Figure 28, and second by the formation of the byproduct *N,N'*-dicyclohexylurea, which proved difficult to separate from the desired products by flash chromatography. Consequently, *O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU), a coupling reagent originally developed as an alternative to DCC that would cause less racemization of amino acids during peptide synthesis was evaluated for the synthesis of **5a-n**.[135] The products of homochiral amine coupling of **3** and **4** with HBTU proved much easier to purify from the reaction mixture than they had been when using DCC. Coupling with HBTU provided high yields for the coupling of α-methylbenzylamine, but lower yields for 1-(1-naphthyl)-α-ethylamine. A mixture of *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC·HCl) and 1-hydroxybenzotriazol hydrate (HOBT) proved to be a more suitable coupling reagent for the coupling of **4** with homochiral alcohols for the synthesis of **5k-n**. EDC was developed as a water-soluble alternative to DCC so that the urea byproducts could be removed by

washing the product.[135] Unfortunately, the couplings using alcohols were plagued by poor yields resulting from the consistent failure of these reactions to proceed to completion despite increasing the reaction times and increasing the temperature at which the reaction was conducted.

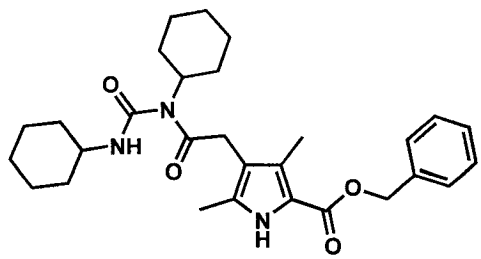


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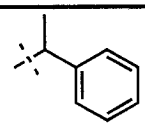
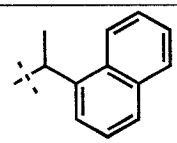
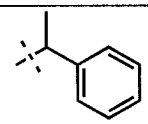
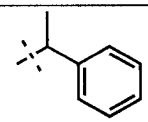
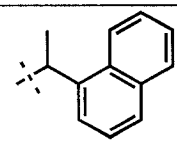
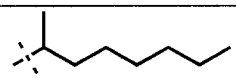
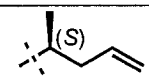
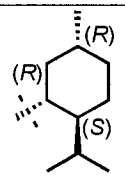
Figure 28. *N*-Acylurea sideproduct obtained when using DCC for amide couplings

The use of dichloromethane (DCM) as a solvent for the coupling reactions, especially at lowered temperatures, is reported to suppress the formation of *N*-acylureas, a common sideproduct of such couplings.[135] Therefore, the optimized procedure for the coupling reactions involved dissolving 4-(*N*,*N*-dimethylamino)pyridine (DMAP) and the appropriate pyrrole carboxylic acid derivative in DCM (or a mixture of DCM and tetrahydrofuran (THF) in the case of **4**, which was sparingly soluble in DCM) followed by chilling the reaction mixture in an ice bath. At this lowered temperature, the appropriate chiral amine or alcohol and suitable coupling reagents were added to the reaction mixture. The addition of chiral amines typically caused the pyrrole carboxylic acid reactant to precipitate from solution as its carboxylate salt with a chiral ammonium counterion, and in these instances more solvent was added. As the reaction proceeded over two days a white precipitate formed. The precipitate was identified as HOBT and urea byproducts based upon thin-layer chromatography (TLC) analysis, and this was

filtered from the reaction mixture followed by washing the concentrated filtrate with a dilute aqueous acid solution to remove DMAP and any water-soluble by-products from the coupling reaction. Silica flash column chromatography using a mixture of ethyl acetate and hexanes as eluent was successful for purifying the homochiral substituted pyrroles. The isolated yields of compounds **5a-n** are listed in Table 1.

Table 1. Isolated yields for the synthesis of pyrrole derivatives **5a-n**

5[a]	n	X	R*	Yield (%)
a,b	2	NH		99[b]
c,d	2	NH		72[b]
e,f	2	NBn		95[b]
g,h	1	NH		89[b]
i,j	1	NH		68[b]
k,l	1	O		39[b]
m	1	O		44

n	1	O		54

[a] **5a,c,e,g,i,k** have (*S*) absolute stereochemistry. [b] averaged yields for the two enantiomers.

The ^{1}H NMR spectra of the enantiomeric pair **5e,f** warrant further comment. It is apparent in the spectra that the amide exists as two conformational isomers with a ratio of approximately 3:1, calculated by integration of ^{1}H NMR signals. The conformers were further characterized by two-dimensional correlation with ^{13}C signals using an HSQC experiment. The spectra of the two conformers are most apparently different in the signals representing the diastereotopic methylene protons of the benzyl group bound to the amide nitrogen, labelled H_a and H_b in Figure 29, for **5e**. These diastereotopic protons appear as two AB quartets, one corresponding to the major conformer and one to the minor. The diastereotopic relationship of the corresponding protons is apparent in the spectrum of the precursor amine, seen in Figure 30. However, the conformational differences are not apparent until the spectrum of the amide is analyzed, therefore suggesting that the conformational differences involve orientation about the amide bond. The observation of conformers is not unusual in spectra of peptides.[136]

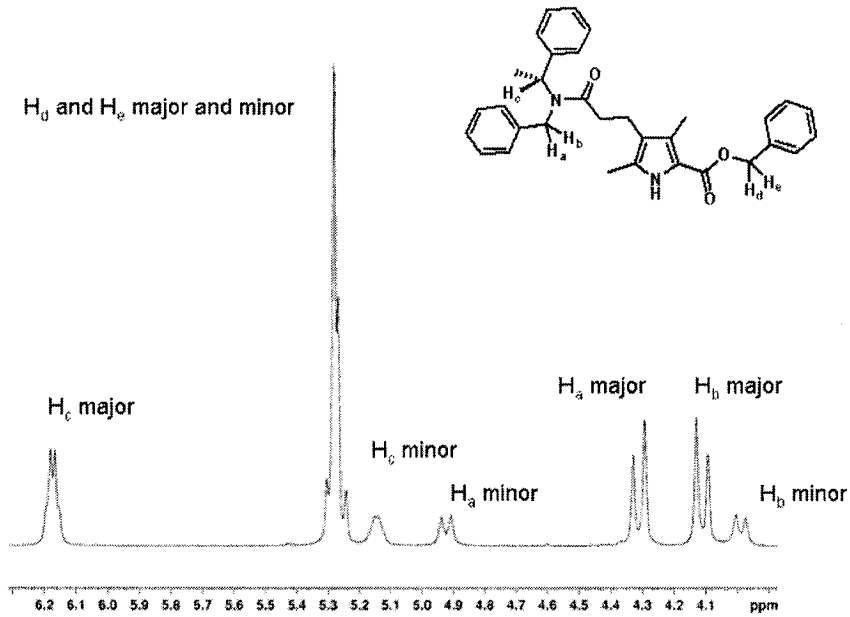


Figure 29. ^{1}H NMR spectrum of benzyl 4-[(*S*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate **5e**

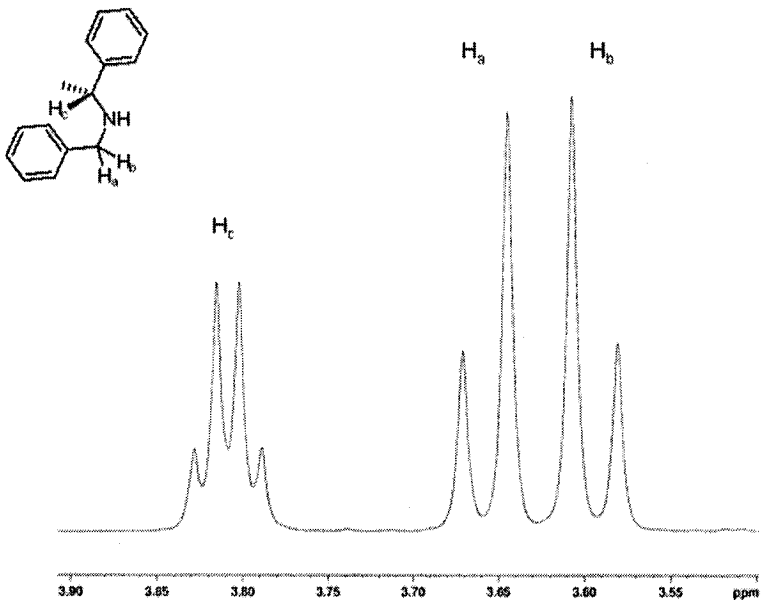


Figure 30. ^{1}H NMR spectrum of (*S*)-(-)-*N*-benzyl-α-methylbenzylamine

Synthesis of homochiral bis(dipyrromethene) hydrobromides

With the requisite pyrroles bearing homochiral auxiliaries in hand, the preparation of the chiral bis(dipyrromethene) ligands **8a-n** was achieved as shown Figure 31. The benzyl ester functional groups were transformed into carboxylic acids by atmospheric pressure hydrogenolysis using palladium on activated carbon as a catalyst and THF as a solvent. The hydrogenolysis reactions were completed in 16 hours by using 0.04 molar equivalents of palladium with respect to the pyrrole dervatives. The reactions were monitored by TLC so as to avoid sidereactions such as hydrogenolysis of the benzylic amides in compounds **5a**,**b**,**e**,**f**,**g**,**h**. Although the hydrogenation of the pentene substituent in compound **5m** occurred concurrently with the hydrogenolysis of the benzyl ester this was not seen as a detrimental sidereaction. After filtration through Celite® to remove the catalyst, the prepared 2-carboxylic acid derivatives of pyrroles **5a-n** were decarboxylated *in situ* using hydrobromic acid, and subsequently coupled with 2,2',4,4'-tetramethyl-5,5'-diformyl-3,3'-dipyrromethane[137] (**7**) to yield the homochirally substituted bis(dipyrromethene)s **8a-n** as their hydrobromide salts. Dipyrromethane **7**, which is a key component to the synthesis of methylene linked 2,2'-bis(dipyrromethene)s, was prepared following a literature procedure.[137] Repeated attempts to crystallize the bis(dipyrromethene) hydrobromide salts proved unfruitful, and so the method used for isolating these products instead involved concentrating the reaction mixture followed by the addition of diethyl ether to precipitate the product, which could then be isolated by filtration. The yields for the preparation of the hydrobromide salts **8a-n**, which are quite consistent, are presented in Table 2.

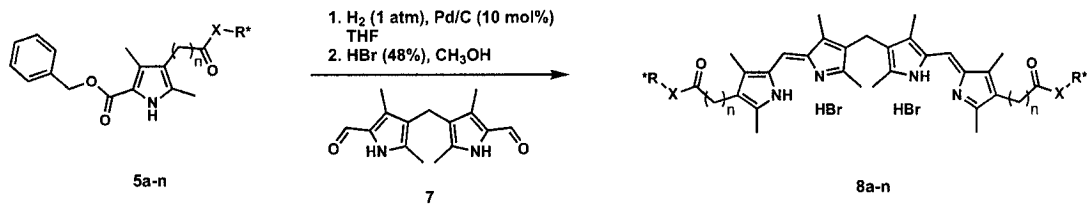
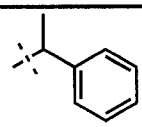
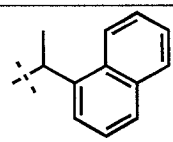
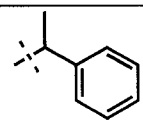
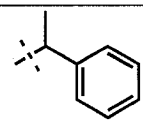
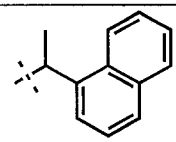
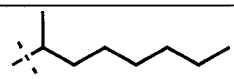
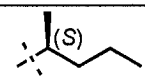
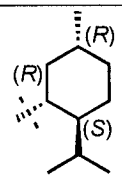


Figure 31. Synthesis of bis(dipyrromethene) hydrobromide salts bearing homochiral amide and ester substituents

Table 2. Isolated yields for the synthesis of bis(dipyrromethene) derivatives **8a-n**

8[a]	n	X	R*	Yield (%)
a,b	2	NH		67[b]
c,d	2	NH		71[b]
e,f	2	NBn		72[b]
g,h	1	NH		86[b]
i,j	1	NH		64[b]
k,l	1	O		58[b]
m	1	O		61

n	1	O		72

[a] **8a,c,e,g,i,k** have (*S*) absolute stereochemistry. [b] averaged yields for the two enantiomers.

Synthesis of homochiral zinc(II) di(bis[dipyrromethene]) helicates

Complexation of the homochiral bis(dipyrromethene) ligands was performed using zinc acetate dihydrate as the metal ion source. In a general reaction procedure, zinc acetate dihydrate and sodium acetate trihydrate were dissolved in methanol and added to a mixture of the ligand dissolved in chloroform, or a suspension in the case of ligands **8c,d,i,j** which were sparingly soluble in chloroform. Although the theoretical stoichiometry of the complexation is 1:1 zinc(II) ions-to-bis(dipyrromethene) ligands, five molar equivalents of zinc(II) were used, in keeping with literature precedent.[80] The progress of the reaction can be monitored by analyzing the absorption spectrum of the reaction mixture; the wavelength of maximum absorption (λ_{max}) undergoes an approximately 20 nm bathochromic shift from bis(dipyrromethene) hydrobromide salt to the corresponding dinuclear zinc(II) double helicate. The rapid change in colour of the reaction mixture from orange to red is visible to the naked eye. Although it can be seen from TLC analysis of the complexation reactions as they progress that the reactions are nearly quantitative, the highly variable and sometimes low yields of the zinc(II) bis(dipyrromethene) complexes **9a-n**, seen in Table 3, are a result of the difficulties in isolating the products in the form of a solid.

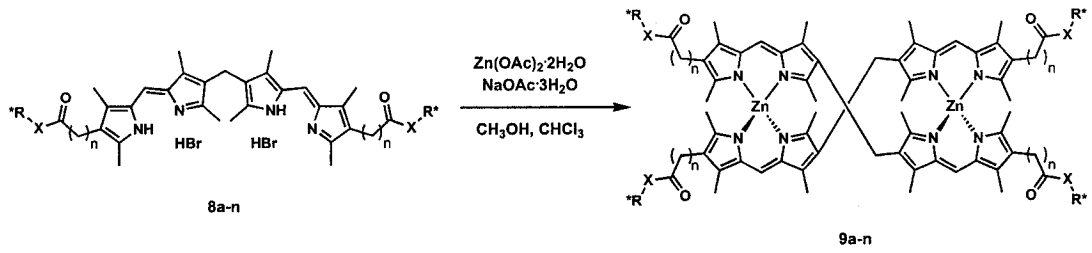
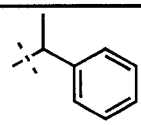
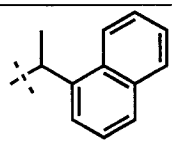
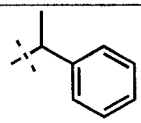
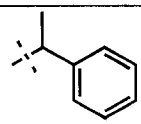
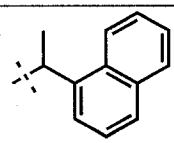
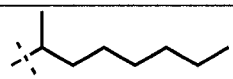
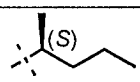
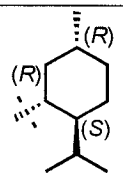


Figure 32. Synthesis of zinc(II) bis(dipyrromethene) complexes bearing homochiral amide and ester substituents

Table 3. Isolated yields for the synthesis of zinc(II) bis(dipyrromethene) complexes **9a-n**

9[a]	n	X	R*	Yield (%)
a,b	2	NH		29[b]
c,d	2	NH		48[b]
e,f	2	NBn		45[b]
g,h	1	NH		71[b]
i,j	1	NH		61[b]
k,l	1	O		99[b]
m	1	O		99

n	1	O		99

[a] **9a,c,e,g,i,k** have (*S*) absolute stereochemistry. [b] averaged yields for the four diastereomers.

Analysis of the helicate products by mass spectrometry to confirm the 2:2 zinc(II) to ligand ratio required the use of soft ionization methods in order to observe the molecular ion. Hard ionization techniques, such as electron impact (EI), can cause the decomplexation of dipyrromethene ligands, resulting in failure to observe the complexed molecular ion in the generated mass spectra. Atmospheric pressure chemical ionization (APCI) proved to be a suitable ionization technique for observing the molecular ion of compounds **9a-d,g-n** and matrix-assisted laser desorption ionization (MALDI) was appropriate for the highest mass compounds **9e,f**.

2.3.2. Assessment of the Diastereoselectivity of Zinc(II) Bis(dipyrromethene) Helicate Synthesis

Characterization by routine NMR experiments provided the first indications of the degree of stereoselectivity in the homochiral bis(dipyrromethene) complexation reactions. The NMR spectra of the zinc(II) bis(dipyrromethene) helicates reported herein were acquired from mixtures of *P* and *M* diastereomers as prepared from the complexation reactions. As a result the spectra are quite complicated, and they suggested that the two diastereomers were present in nearly equal amounts. The ^{13}C NMR spectrum of **9n** most clearly demonstrates the two sets of peaks, which correspond to the presence of the two diastereomers. Figure 33 provides a section of the ^{13}C NMR spectrum of **9n** that shows the two peaks for the carbonyl carbon atom in the *P* and *M* diastereomers.

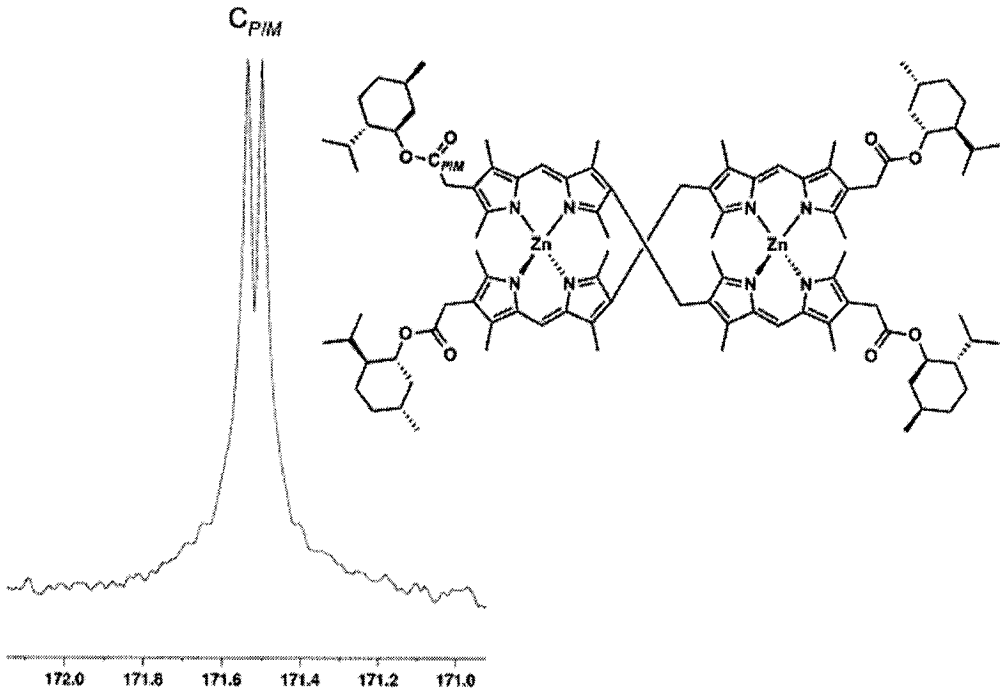


Figure 33. Section of the ^{13}C NMR spectrum of zinc(II) helicate **9n** showing peaks for both *P* and *M* diastereomers

Some of the complexity seen in the NMR spectra of the zinc(II) bis(dipyrromethene) helicates can be attributed to conformational isomerism caused by the generally high barrier to rotation about amide N-C(carbonyl) bonds, as discussed previously for compounds **9e,f** in Chapter 2.3.1. However, the NMR spectra of the ester derivatives, for which the energy barrier to rotation is low enough to preclude the observation of conformers in the NMR spectra, are also quite complicated and can be used to illustrate the presence of a mixture of diastereomers. Consider the differences between the ^{1}H NMR spectra of **8k**, the bis(dipyrromethene) hydrobromide ligand in which the point chiral center was installed by esterification with 2-octanol versus its zinc(II) complex, **9k**, seen in Figure 34. As can be seen in the spectra, the signal for the

proton that is attached to the point chiral center in the molecule matches the theoretical sextet multiplicity in the case of the hydrobromide ligand **8k** but is complicated by the presence of two diastereomers in the spectrum of the zinc(II) helicate.

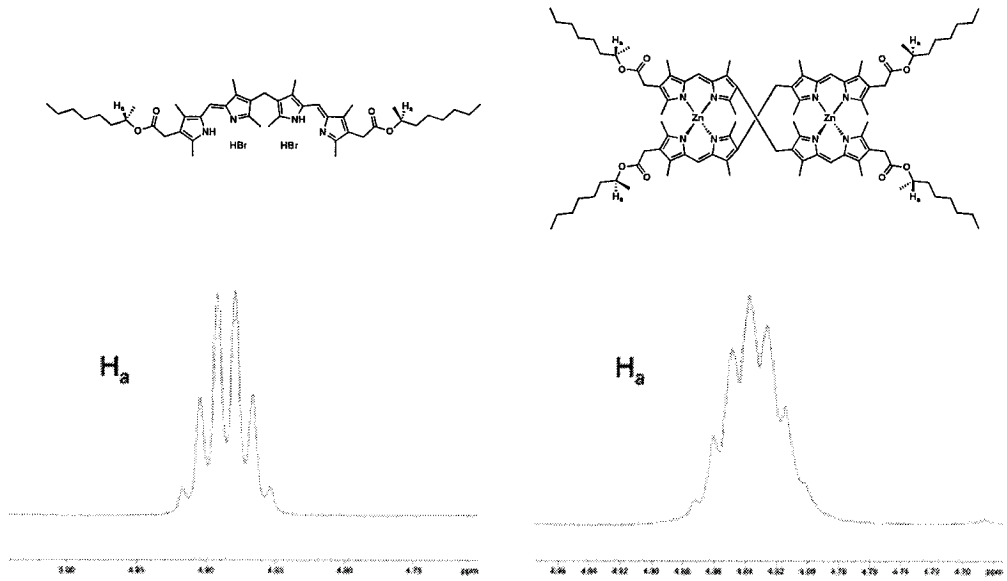


Figure 34. Sections of the ^{1}H NMR spectra of **8k** and **9k**

Circular dichroism provided a more sensitive measurement of the diastereomeric excess present in the product mixtures. CD spectra were recorded for the complexation products of each of the homochiral bis(dipyrromethene) ligands. Each CD spectrum showed optical activity, indicating that the diastereomeric excesses of the complexation reactions were not zero. The CD spectra of several of the ligand hydrobromide salts were also recorded. Although the ligands did show some optical activity, it was much less than that of the *P*/*M* helicate mixtures. Without optically pure standards with which to compare the CD measurements for the complexes, the diastereomeric excess of complexation could not be determined.

Although in theory the diastereomeric *P* and *M* helicates could be resolved using conventional chromatographic methods, in practice flash chromatography using silica gel failed to provide pure samples. Instead, chiral high performance liquid chromatography (HPLC) using derivatized cellulose columns[138] was used to resolve the *P* and *M* diastereomers. Compounds **9a-f** were analyzed in this manner. Fractions from the HPLC resolution were used to measure the CD and absorption spectra of pure *P* and *M* zinc(II) bis(dipyrromethene) dinuclear double helicates. An example of the equal and opposite relationship between CD spectra of *P* and *M* diastereomers for **9a** and **b** is shown in Figure 35. An interesting feature of the CD spectra of the zinc(II) helicates is the observation of the phenomenon known as exciton coupling. Exciton coupling, as discussed in Chapter 2.1.5, results from the proximity of two identical, non-conjugated chromophores, such as the two identical dipyrromethene units that are coordinated to a single zinc(II) center in the helicates in question. Exciton coupling is seen in CD spectra as a bisignate Cotton effect, and based upon the sign of this bisignate CD the handedness of helicates can be assigned.[124] It has been established that a signal that is negative at higher wavelengths is characteristic of *P* helicates. This has been corroborated by CD analysis and the partially solved crystal structure of a highly analogous zinc(II) 2,2'-bis(dipyrromethene) helicate.[130]

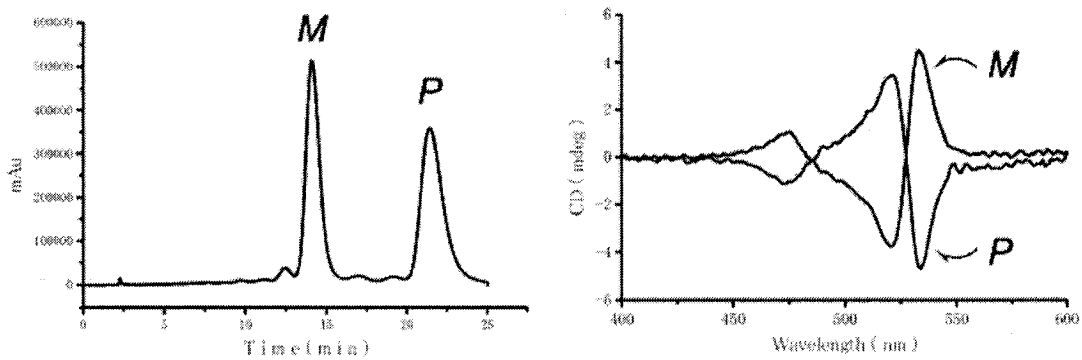


Figure 35. HPLC trace and CD spectra of resolved **9a** *P* and *M* helicates

The concentration of the helicates in the HPLC fractions were calculated from UV-vis spectra using the Beer-Lambert equation and making the reasonable assumption that the molar absorptivity of the dinuclear helicates, as measured from absorption spectra of the *P*/*M* mixture, were the same for the two diastereomers. The nearly 1:1 diastereomeric ratios were thus calculated for the synthesis of compounds **9a-f**.

At this point an assumption was made to simplify the analysis of the remaining zinc(II) bis(dipyrromethene) helicate mixtures: the molar circular dichroisms, $\Delta\varepsilon$, of optically pure dinuclear zinc(II) 2,2'-bis(dipyrromethene) double helicates are approximately the same. Operating under this reasonable assumption, the diastereoselectivity for the formation of *P* and *M* helicates from homochiral bis(dipyrromethene) ligands could be assessed from the circular dichroism spectra of product mixtures, without having to resolve the diastereomers.

It is difficult to make comparisons between the CD data measured for this study and that which has been reported in the literature for related bis(dipyrromethene) complexes. The structures and molar circular dichroism values for the CD maxima or minima at highest wavelength for reported optically pure bis(dipyrromethene) metal

complexes are shown in Figure 36. Although Δε values for the *P* and *M* helicates of **9a-f** are within an order of magnitude of the Δε values reported for the *P* and *M* nickel(II) bis(dipyrromethene) helicates shown in Figure 36,[118] it is difficult to draw any quantitative comparisons. One very significant difference between the spectra of the nickel(II) and zinc(II) bis(dipyrromethene) complexes is that the former do not exhibit exciton coupling because the two dipyrromethene units of the ligand are in conjugation. As well, the spectra were recorded from solutions in different solvents, which can have a profound effect upon the magnitude and shape of the CD spectrum.[139] The Δε values reported for the zinc(II) complex of the BINOL-templated bis(dipyrromethene) shown in Figure 36 recorded in a similar methanol-chloroform solvent mixture displayed the expected exciton coupling, but was found to have a lower value for Δε than **9a**. This may be the result of a different number of chromophores as well as different dihedral angles between the two chromophores in the mononuclear versus dinuclear helicates, a factor that has also been shown to have an effect upon the magnitude of CD spectra.[121] As crystallographic quality crystals have never been obtained for any of the zinc(II) helicates **9a-n**, it is difficult to substantiate this hypothesis.

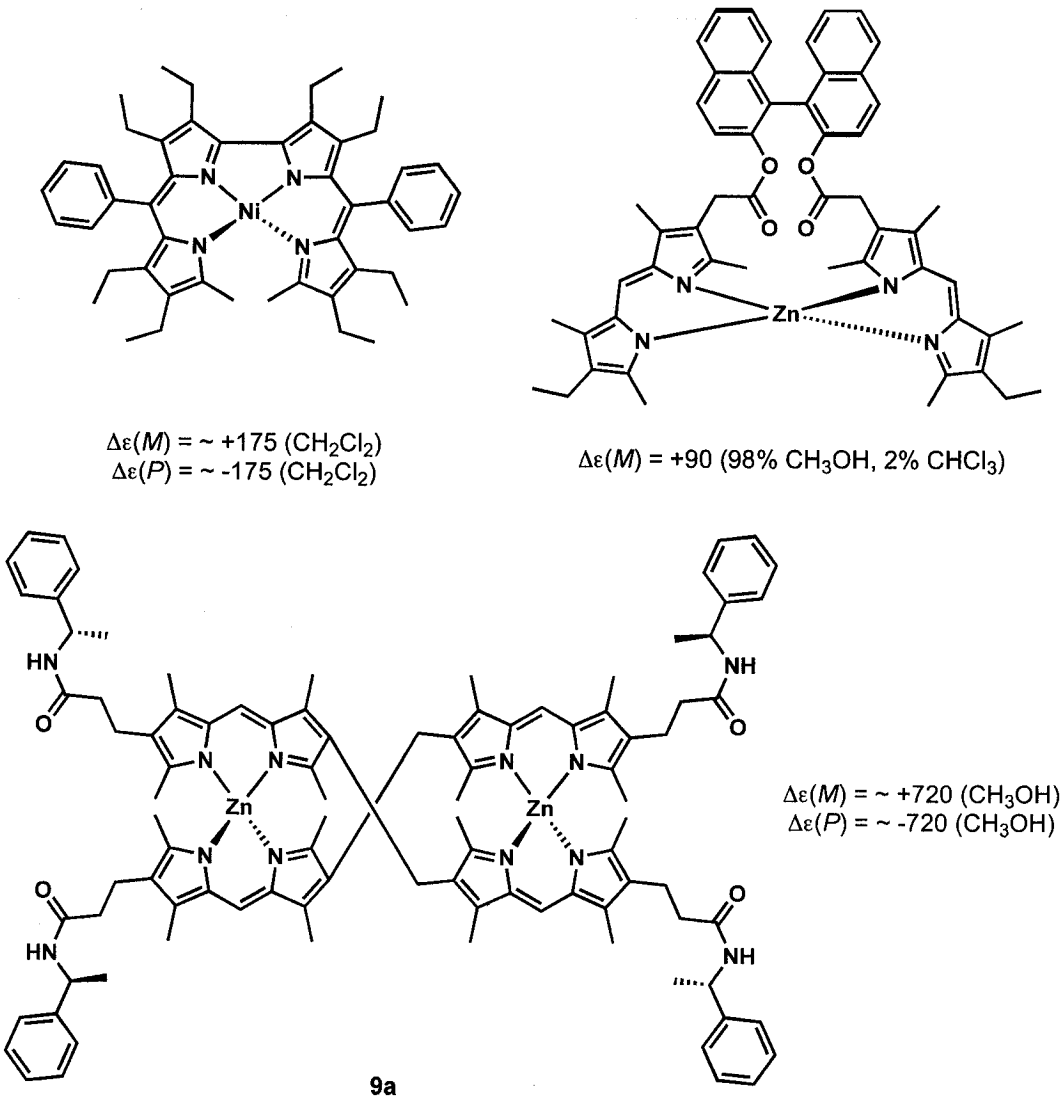
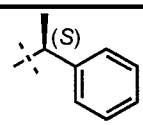
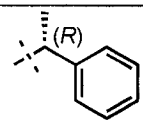
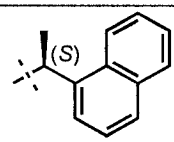
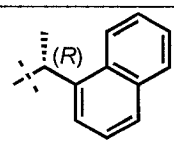
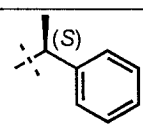


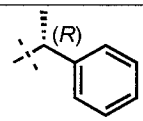
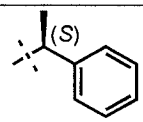
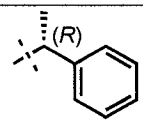
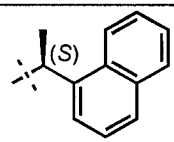
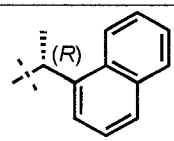
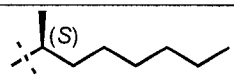
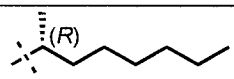
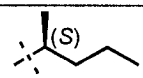
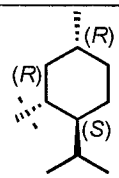
Figure 36. Reported Δε values for optically pure bis(dipyrromethene) helicates, molar CD values are reported for the highest wavelength CD maxima or minima

The Δε values measured for each of the *P*/*M* zinc(II) bis(dipyrromethene) helicates mixtures are shown in Table 4. Comparison of Δε for the product mixtures of **9a-n** does not reveal any trends. The size of the substituents in the point chiral functional group, as seen by comparing **9a** and **9c**, does not seem to affect the degree of diastereoselectivity. The length of the chain between the point chiral group and the

dipyrromethene ligand, as seen by comparing **9a** and **9g**, does not affect the magnitude of the molar CD nor does the difference between amide and ester chiral auxiliaries, as evidenced by the similar Δε for **9a** and **9k**. Regardless of the structure of the homochiral bis(dipyrromethene) ligand, no significant stereoselectivity was achieved. Molecular modelling was employed in an attempt to calculate the heat of formation energies of the diastereomers, for the purposes of predicting the observed diastereoselectivities, but these calculations failed to provide satisfactory results.

Table 4. Values of Δε at the extrema of highest wavelength for diastereomeric mixtures of *P* and *M* zinc(II) bis(dipyrromethene) helicates **9a-n**

9	**n**	**X**	**R***	**Δε (cm^2 $mmol^{-1}$)**
a	2	NH		-60.94
b	2	NH		+47.69
c	2	NH		-40.75
d	2	NH		+17.98
e	2	NBn		-69.50

f	2	NBn		+176.02
g	1	NH		-41.86
h	1	NH		+21.35
i	1	NH		-64.75
j	1	NH		+28.43
k	1	O		+105.83
l	1	O		-103.01
m	1	O		+37.62
n	1	O		-2.15

A dinuclear zinc(II) double helicate, **10** in Figure 37, was prepared according to a literature procedure[82] by complexation of an achiral 2,2'-bis(dipyrromethene) ligand possessing a structure analogous to the homochiral bis(dipyrromethene)s **8a-n**. The

racemic mixture of helicate products were shown to display no optical activity by CD analysis, as anticipated. The *P* and *M* helicates were successfully resolved by chiral HPLC, Figure 37, and CD analysis of the two enantiomers showed equal and opposite spectra, as was seen for the zinc(II) complexes of the homochiral bis(dipyrromethene)s. These similarities in the CD spectra between the *P* and *M* helices of **9a-n** and **10** eliminated the possibility that the circular dichroism that was being observed for the diastereomers of **9a-h** was induced by the aromatic substituents of the point chiral auxiliaries, and thus supported the proposed helical structure of the complexes and the small diastereomeric excesses for complexation.

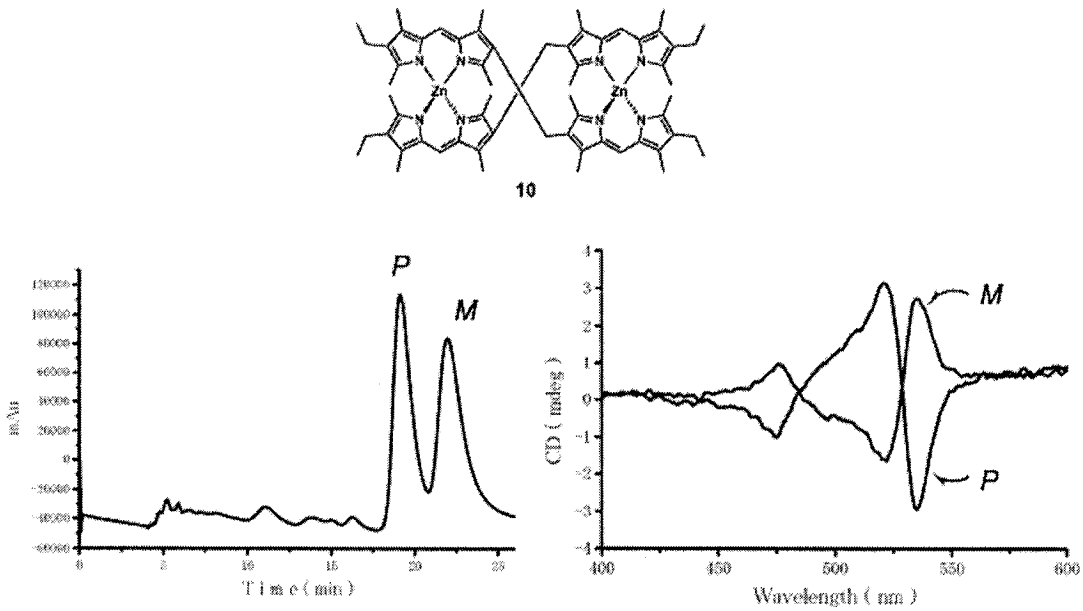


Figure 37. HPLC trace and CD spectra of resolved **10** *P* and *M* helicates

Literature precedent shows that helically-chiral mononuclear nickel(II) bis(dipyrromethene) helicates are stable to racemization under neutral conditions, even at very high temperatures.[118] There are two major mechanisms[49] for the racemization of

helical chirality in helicates: inversion at the metal center; and scrambling of the ligands. In order to assess the tendency of the zinc(II) bis(dipyrromethene) helicates **9a-n** to undergo ligand scrambling, mixtures of **9a** and **9e** were dissolved in either DCM or toluene and stirred for twenty-four hours, with the toluene solution simultaneously heated to reflux. The reaction mixtures were analyzed by mass spectrometry, revealing the absence of any mixed-ligand species. These results suggest that the helical chirality established during the complexation process to form zinc(II) bis(dipyrromethene) helicates is not racemized by ligand scrambling.

2.4. Conclusions

A method has been established for the formation of 2,2'-bis(dipyrromethene)s bearing homochiral amide and ester substituents at the termini of the molecules. These bis(dipyrromethene) ligands have been shown to form dinuclear zinc(II) double helicates with a very small degree of diastereoselectivity. NMR spectra of the product mixtures show 1:1 ratios for *P* and *M* helicates although CD spectra show some diastereomeric excess has been produced. The inability to enhance diastereoselectivity with changing the length of the tether between the point chiral auxiliary and the bis(dipyrromethene) ligand, or changing the connecting functional group from amide to ester, or changing the size of the substituents at the point chiral center suggests that the use of terminal point chiral groups is a poor means for inducing stereoselectivity during the formation of bis(dipyrromethene) helicates of this type.

This work[140,141] represents the first diastereoselective synthesis of dipyrromethene helicates. The triumphs of this study are in establishing that the helical chirality of bis(dipyrromethene) complexes is stable to resolution using HPLC, and that it is not

susceptible to racemization by ligand scrambling. As well, the experiments described here have helped to eliminate the possibility of induced circular dichroism from the aromatic substituents of the chiral auxiliaries as the source of the observed optical activity in zinc(II) bis(dipyrromethene) helicates.

Future work in the area of the stereoselective bis(dipyrromethene) helicates will focus upon the use of chiral auxiliaries and templates to induce stereoselectivity that are closer to the bis(dipyrromethene) core. The occurrence of inversion at the metal centers, a possible mechanism for helix racemization, can be assessed by measuring the effects of time upon the circular dichroism spectra of the zinc(II) helicates.

Chapter 3. Zinc(II) Dipyrromethene Gemini Metallosurfactants

3.1. General Background

3.1.1. Surface Activity

Surface activity is a characteristic that only some molecules possess. A compound is said to be surface active if it congregates at interfaces, and thus affects the behaviour of that interface.[142] Usually, these molecules are strongly adsorbed at interfaces or surfaces in the form of a monomolecular layer (monolayer). The properties of these surface active agents (surfactants) arise from their amphiphilic nature, usually expressed as a balance between hydrophilicity and lipophilicity (or hydrophobicity).[143] The structure of a surfactant molecule can be generalized as an apolar region, commonly called the tail, which is attached to an ionic or polar functional group, known as the head. Very common examples of surfactants are soaps and detergents. Hydrophilic functional groups that have proven successful in the production of surfactants include sulfates, carboxylates, phosphates, and tetrasubstituted ammonium groups. Anionic surfactants are the most widely used class of surfactant because of their relatively low cost and excellent performance.[143] Compared to the variety of sources for hydrophilicity in surfactants, there are relatively few successful sources of hydrophobicity; these are limited mostly to long alkyl chains or other large hydrocarbon substituents. A huge variety of natural and synthetic surfactants are known today. Natural surfactants include the biological membrane-forming phospholipids and the fatty acid-emulsifying bile salts, a few examples of which can be seen in Figure 38. The first recognized synthetic surfactant was prepared in 1834 by the sulfation of castor oil for use in the textile industry.[144] Sodium

lauryl stearate is commonly used as an emulsifier in cosmetics and sodium dodecylsulfate is a very common detergent used in biological experiments.

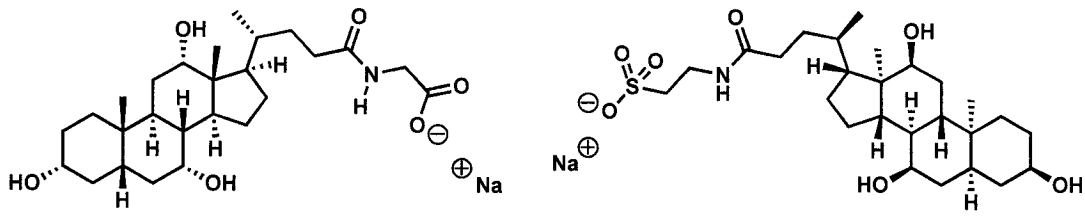


Figure 38. Representative structures of some sterol bile salts sodium glycocholate (*right*) and sodium taurocholate (*left*)

Surfactants are amongst the most widely used chemical additives in industry, both for manufacturing and in consumer products. Their applications include use as detergents to remove foreign materials from solid surfaces, as wetting agents to decrease the surface tension between water and some solid surface, as emulsifiers to decrease the tension between two liquids, and as dispersants for solubilizing insoluble compounds.[145] Each of these applications exploits the ability of surfactants to solubilize compounds that would not otherwise be soluble in a given medium (usually water).

The property of surface activity arises from the special physical properties of surfactant molecules.[145] Oil can be emulsified in water by soap because the long hydrocarbon tails of the soap molecules penetrate the oil, whereas the carboxylate heads surround the surface, forming hydrogen bonds with the water interface. The chemical interactions between the water and the carboxylate groups make the entire oil-soap structure soluble. In this particular example, the carboxylate heads also serve to create a charged shell that electrostatically repels the other similarly-charged oil-fat congregations and allows the oil to become dispersed, or emulsified in the water, rather than forming a large oil mass. These clusters of surfactants are known as micelles, and are typically <500

nm in diameter.[146] This act of aggregation, illustrated in Figure 39, is a form of self-assembly, where a micelle is considered a supramolecular structure. In a polar medium, such as water, their hydrophobic tails tend to congregate, while their hydrophilic heads are arranged around the surface of the micelle, providing protection for any solubilized otherwise insoluble solute from the surrounding solvent. In such a situation the micelle is termed a 'normal' micelle, while in an apolar medium 'reverse' micelles are formed in which the hydrophilic heads are buried within the center of a cluster of surfactant molecules with the hydrophobic tails providing solubility for the large structure. Analogous to normal micelles, reverse micelles serve to solubilize non-soluble solutes in apolar solvents.

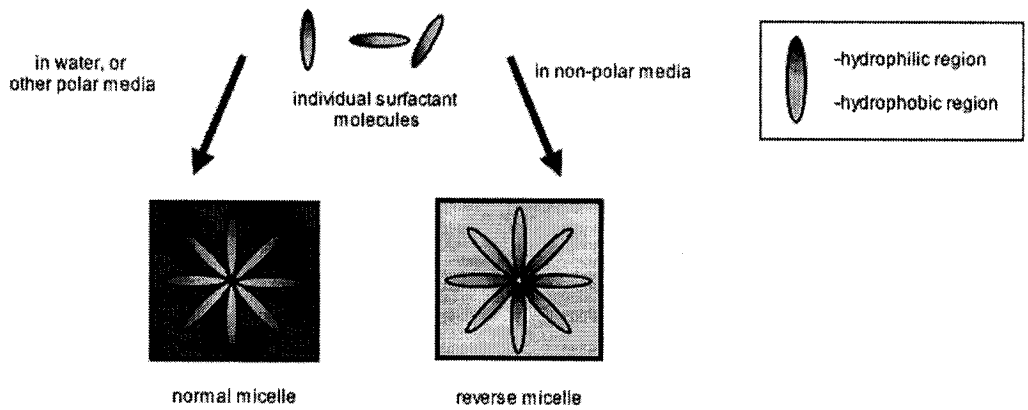


Figure 39. Illustration of the formation of normal and reverse micelles

Micelles form only above the Krafft temperature (K_t) and above the critical micelle concentration (cmc). The general relationship between the solubility of surfactant molecules with changing temperature can be seen in Figure 40. Below K_t the surfactants exist mostly as a monolayer, and with increasing temperature the concentration of individual molecules free in solution also increases. The monomer-monolayer-micelle equilibrium illustrated in Figure 41 exists for surfactant molecules in solution between

being a monolayer, a free molecule in solution or becoming involved in a micelle. As the concentration of free surfactant molecules in solution increases, this equilibrium for the act of micellization is pushed further towards the formation of micelles, until the solution reaches its cmc and micelles begin to form.

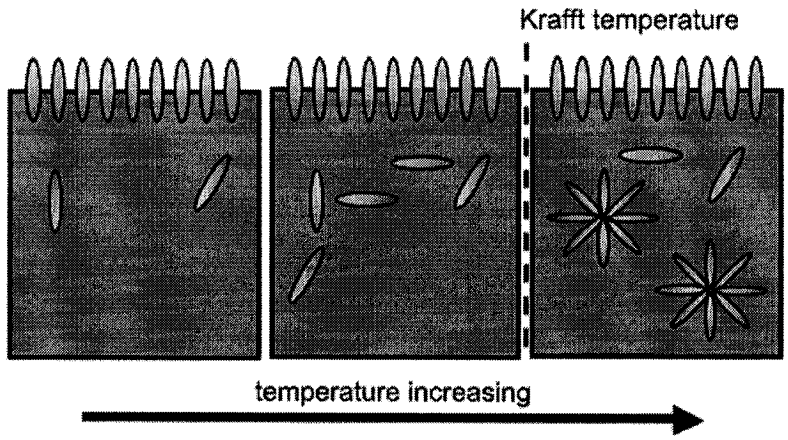


Figure 40. Micelle formation begins above the Krafft temperature

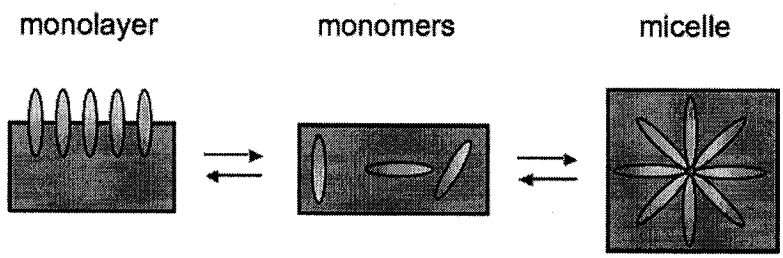


Figure 41. The equilibria that exist for surfactant molecules in solution

The cmc for a particular surfactant can be determined by measuring several physical properties of a solution of the compound and looking for the appropriate concentration at which there is a pronounced discontinuity in the values of the physical properties (Figure 42). At dilute concentrations, surfactants display the properties of normal solutes.[143] At concentrations above the cmc, however, properties such as thermal

conductivity and surface tension undergo abrupt changes. Surface tension is the property most commonly observed in order to determine cmc values.[147] The cmc is often used as a measure of the quality of a surfactant because a molecule that begins to form micelles at a relative low concentration does not need to be present in a large amount in order to be effective.

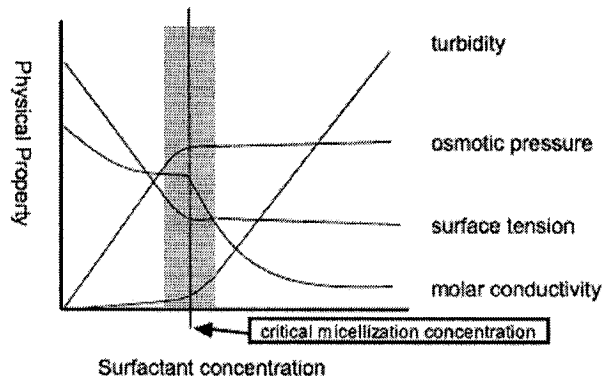


Figure 42. Typical pronounced discontinuity of several physical properties of a solution of surfactant around the critical micellization concentration

The number of molecules that may cluster together to form a micelle is varied even in a solution of only one surfactant and is highly dependent upon the nature of the surfactant molecule. For example, 1000 or more molecules of a non-ionic surfactant may form one micelle, while ionic species tend to cluster in groups of less than 100 molecules because the electrostatic repulsions between the polar head groups repel each other.[143] The shapes of micelles depend upon the concentration and nature of the surfactant. Spherical micelles are common, although these spheres tend to appear slightly flattened. Some micelles, above the cmc, form extended bilayers known as lamellar micelles, others form long cylinders that stack together in a hexagonal close-packed pattern.[143]

The formation of micelles is commonly endothermic and therefore must be entropically favourable even though the molecules are forming ordered structures. This positive change in entropy upon micellization is commonly interpreted as being due to a significant contribution from the solvent molecules that are now able to move about more freely after the solute molecules have been sequestered into the micelles.[143]

3.1.2. Gemini Surfactants

Surfactants have been synthesized with a variety of architectures.[148] Some of these can be seen in Figure 43, which shows the conventional 1:1 polar head group-to-apolar group ratio, and other more exotic ratios such as the bolaform 2:1 surfactants, 2:2 dimeric (gemini) surfactants, and the relatively new n:n polymeric surfactants.[148]

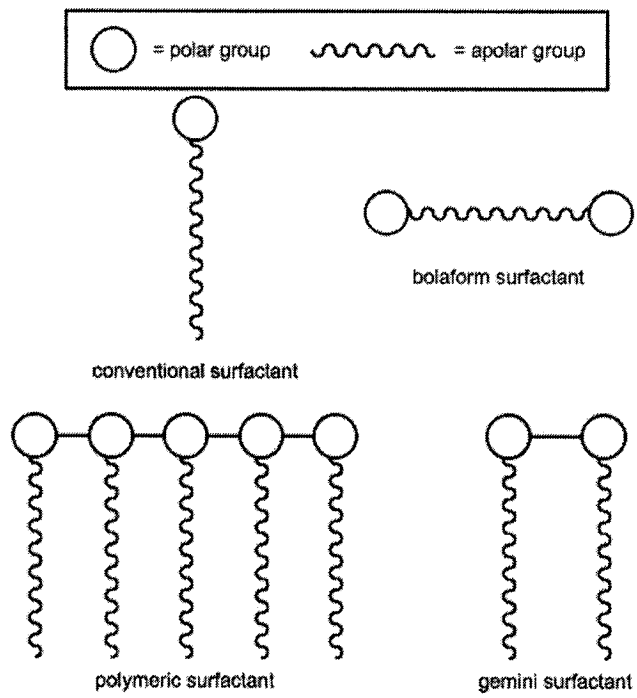


Figure 43. Representative surfactant architectures

The term "gemini" surfactant was coined by Frederic Menger in 1991 to describe a relatively new class of dimeric surfactant molecules that possesses two ionic, or polar, head groups that were linked to two hydrophobic tails all in one molecule.[149] Since the functional groups that provide amphiphilicity to the molecules remain the same as those of conventional surfactants, the great diversity in structures for gemini surfactants arises from the many different spacer groups that have been used to attach the two head groups together. For example, flexible alkyl spacers consisting of two to twelve methylene units, rigid stilbene spacers, and polar polyethers have all been used in the design of gemini surfactants.[147]

Gemini surfactants display some remarkable properties. Compared with a corresponding conventional surfactant with the same type of head group and the same tail length the cmc of a gemini surfactant is generally at least an order of magnitude lower. The two comparisons shown in Figure 44 illustrate this property dramatically.[147,150,151] The low cmc values for gemini surfactants in comparison to conventional surfactants have been attributed largely to the thermodynamically-favourable transfer of two hydrophobic tails, rather than one, at one time between the water and the micelle pseudophase during the process of micellization.[152]

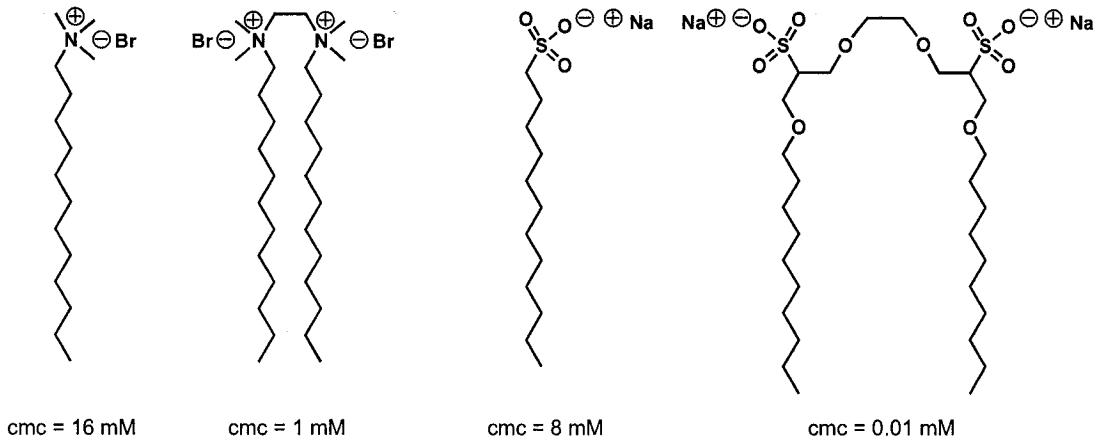


Figure 44. Comparison of cmc values for gemini surfactants relative to conventional surfactants with comparable structures

At the cmc of a gemini surfactant the surface tension of water generally decreases from the pure water value of 72 mNm^{-1} to about 30-40 mNm^{-1}.[147] The ability of a surfactant to decrease the surface tension of water is usually expressed as the concentration of surfactant that is required to decrease the surface tension by 20 mNm^{-1}.[147] This value is known as the c_{20} of the surfactant. Consequently, the c_{20} of gemini surfactants is usually remarkably lower than those of analogous conventional surfactants. This is shown by the two examples seen in Figure 45.[147,153] As many of the applications of surfactants involve the ability of the molecules to decrease the surface tension of water, this is another property that makes gemini surfactants such an attractive commercial target.

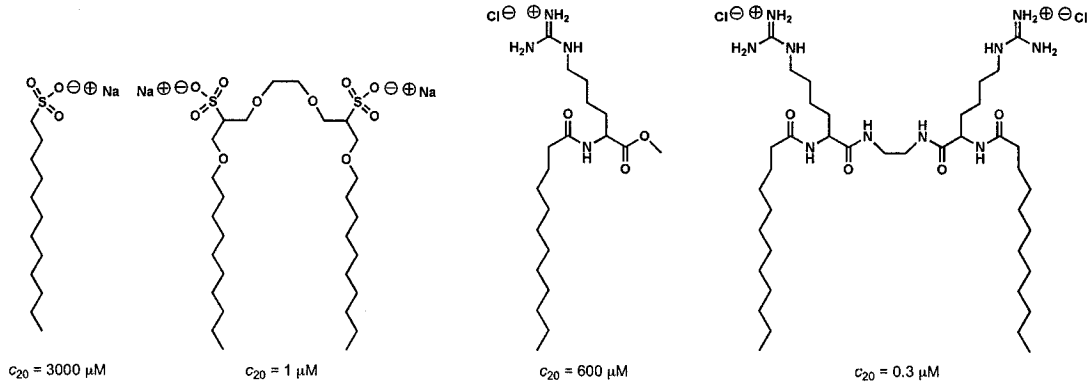


Figure 45. Comparison of c_{20} values for gemini surfactants relative to conventional surfactants with comparable structures

3.1.3. Cleavable Surfactants

The surfactant properties of cleavable surfactants[154,155] can be reduced or eliminated by cleaving the surfactant into parts. The applications of this behaviour are in situations where the persistence of aggregated surfactants, after the stages in the reaction or process where the surfactants are beneficial, can lead to complications such as foaming or the formation of unwanted, stable, persistent emulsions. Reducing or removing the ability of the compound to act as a surfactant allows for the removal of these complications.

In what are known as "first generation cleavable surfactants"[154] the surface activity is destroyed by cleaving the hydrophobic portion from the hydrophilic portion of the molecule. Figure 46 shows several examples of this strategy including the cleavage of surfactants in which a quaternary ammonium functional group is connected to a hydrophobic portion through an ester linkage[156] (by alkaline hydrolysis) (Figure 46A) or through a ketal linkage[157] (by acidic hydrolysis) (Figure 46B). Other examples include hydrolysis of siloxy bonds[158] (Figure 46C) that connect hydrophobic and hydrophilic portions of a surfactant or the cleavage of β-aryloxysulfone surfactants (Figure 46D).[159]

Another report describes the use of photolysis to decrease the surface activity of a class of diazosulfonate surfactants (Figure 46E).[160]

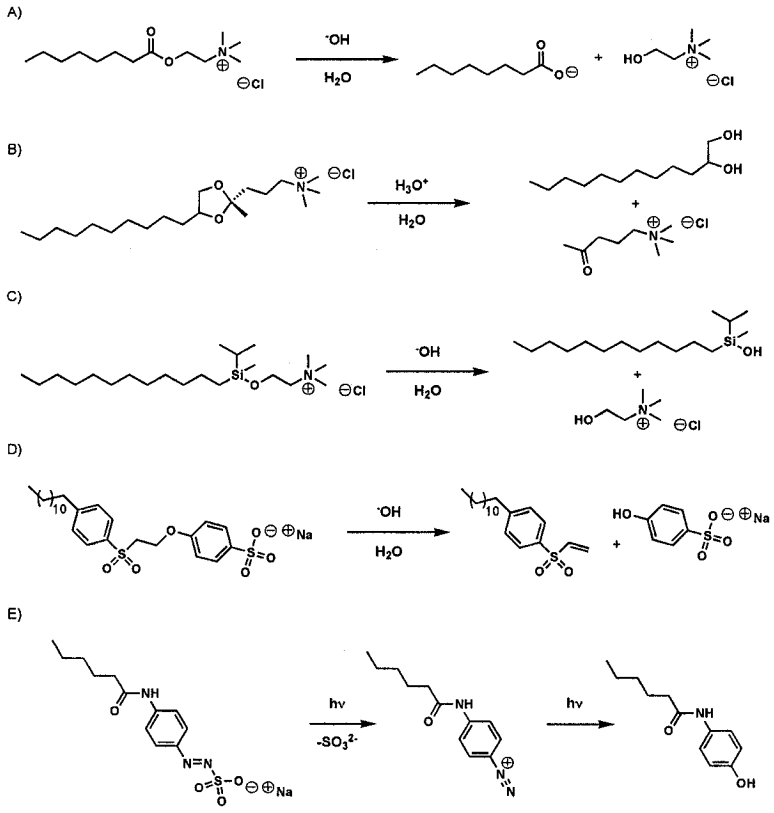


Figure 46. Examples of first generation cleavable surfactants

For the class of molecules known as "second generation cleavable surfactants" the surface activity is reduced by the cleavage of the surfactant into less effective "daughter surfactants".[154] Some examples of second generation cleavable surfactants can be seen in Figure 47. In the first example (Figure 47A),[161] the ketal functional group in the surfactant is hydrolyzed to produce a less effective surfactant. Gemini surfactants in which the two surfactants are connected by a disulfide bond[162,163] (Figure 47B) are readily cleaved in reducing conditions. These disulfide bond-containing surfactants show the enhanced gemini surfactant properties, as demonstrated by comparing the cmc value

to the reduced monomeric surfactant thiol. In the third a metal complex that exhibits surfactant properties can be cleaved by reduction of the cobalt(III) ions to cobalt(II)[164] (Figure 47C). This cobalt complex belongs to a class of surfactants known as metallosurfactants.

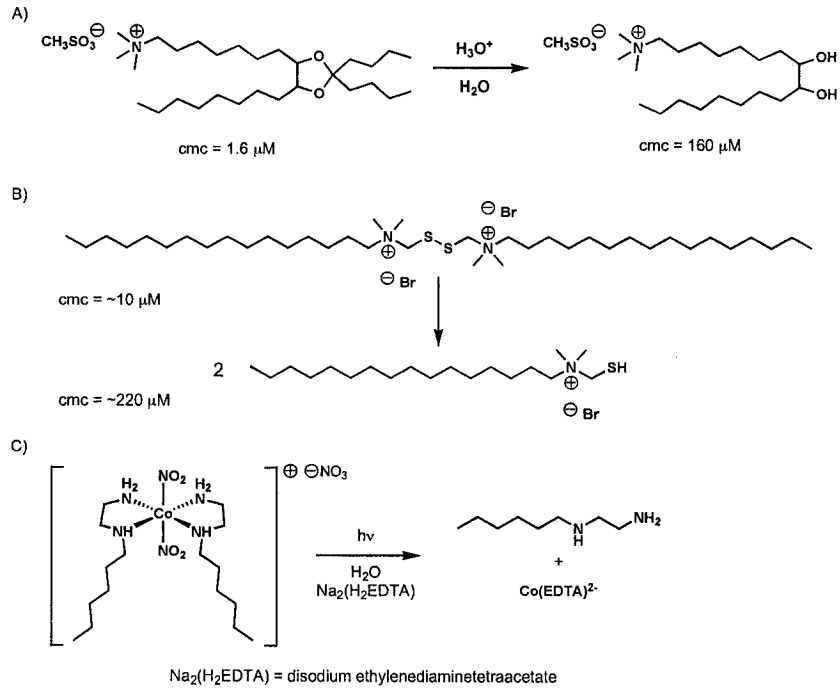


Figure 47. Examples of second generation cleavable surfactants

3.1.4. Metallosurfactants

Surfactant researchers have been keen to embrace the incorporation of transition metals into the design of new surfactant molecules.[148] These compounds, known as metallosurfactants, have appeared only recently in research accounts, but already many examples are known. Metallosurfactants can be defined exclusively as surfactants in which the polar head group of the molecule contains a metal center as an integral structural component,[165] or more generally as any surfactant that contains a metal center

in its structure.[166] An example of a metallosurfactant is the complex formed by an amphiphilic ligand and sodium hexanitrocobalt(III), shown in Figure 48.[167] The incorporation of metal ions into surfactant introduces new properties such as expanded coordination geometries, different catalytic abilities, and magnetism.

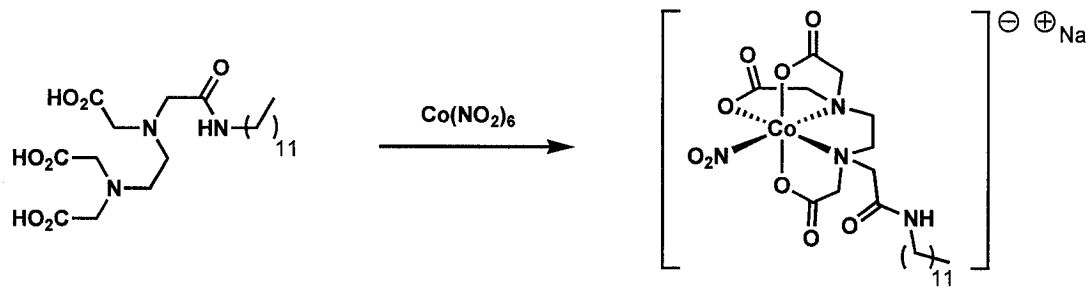


Figure 48. Metallosurfactant cobalt complex

There are some reports in the literature of metallosurfactants acting as catalysts in two-phase systems.[168,169] Figure 49 shows an example of a water-soluble diphosphine rhodium complex that has been shown to hydroformylate alkenes in water with high regioselectivity.[168] Other applications of metallosurfactants are as models of metalloenzymes[170,171] and as metal-containing liquid crystals.[172]

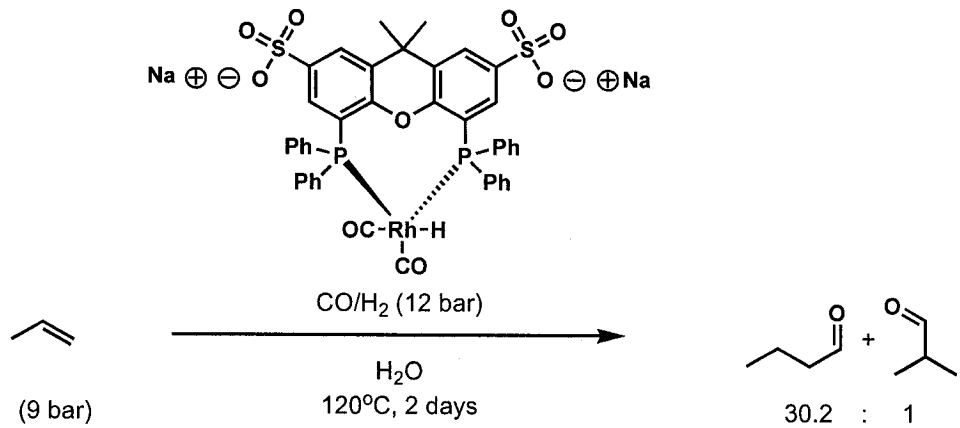


Figure 49. Metallosurfactant rhodium catalyst

A remarkably interesting new class of molecules is the gemini metallosurfactants. These compounds are, as their name suggests, surfactants in which the link between the two polar head groups is a metal ion. Gemini metallosurfactants form through the complexation of two amphiphilic ligands by a single metal ion. For example, the phosphine ligand shown in Figure 50 was designed to possess an amphiphilic nature by inclusion of both a nonpolar iso-octyl substituent as well as a polar hydrophilic region that includes both a repeating ethyleneglycol region and a sulfonate head group.[166] The phosphine exhibited surfactant properties, with a cmc of 49 μM. Upon complexation to palladium(II) chloride the gemini metallosurfactant product exhibited a superior cmc of 5.4 μM. This leap in surfactant effectiveness, as measured by cmc, is similar to that observed for gemini surfactants; sometimes these metallosurfactants are referred to as pseudo-geminis.[166]

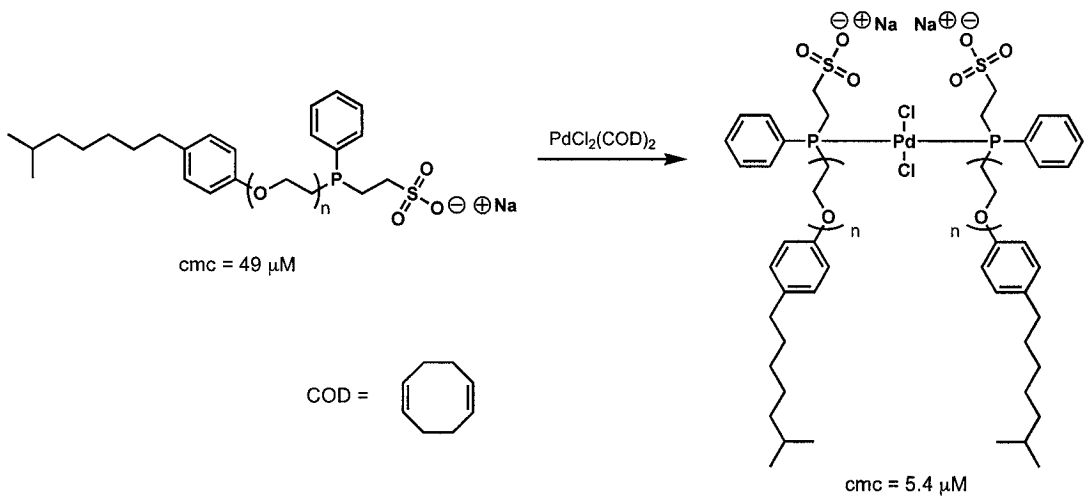


Figure 50. Palladium phosphine gemini metallosurfactant

3.2. Project Goals

Surfactants based upon the dipyrromethene structure respresent an unexplored area of chemical study. There are several properties of dipyrromethenes that could contribute to the design of a very interesting surfactant with valuable attributes. The ability of dipyrromethenes to reversibly form homoleptic complexes of metal cations led to the proposal of a reversible, pH-cleavable, pseudo-gemini metallosurfactant (Figure 51). Although the dipyrromethene ligand would possess surfactant properties, the dimeric dipyrromethene metal complex should exhibit enhanced surfactant properties as a pseudo-gemini surfactant. The complexation of metal ions by dipyrromethenes has been shown to be switchable by changing the pH of the solution and so the proposed dipyrromethene surfactants represent a novel system in which the properties of a gemini surfactant are able to be reversibly decreased by changing the pH of the solution.

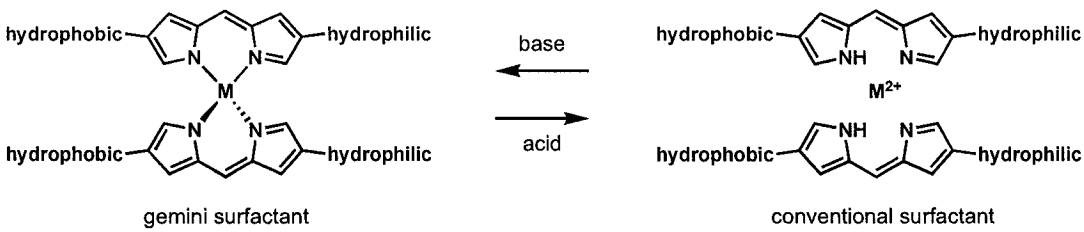


Figure 51. Proposed reversible, cleavable, pseudo-gemini dipyrromethene metallosurfactant

The proposed surfactant has the potential for several possible applications. These include temporary emulsification in textile/paper processing, oil recovery, DNA condensation, and on/off surfactants for electrospray/MALDI mass spectrometry.

3.3. Results and Discussion

3.3.1. Design of Zinc(II) Dipyrromethene Gemini Metallosurfactants

Based upon the traditional methods of dipyrromethene synthesis, as discussed in Chapter 1, several dipyrromethene surfactant designs are feasible, as shown in Figure 52. Dipyrromethene surfactants based upon the 5-unsubstituted unsymmetrical design in Figure 52 are the focus of the research described here.

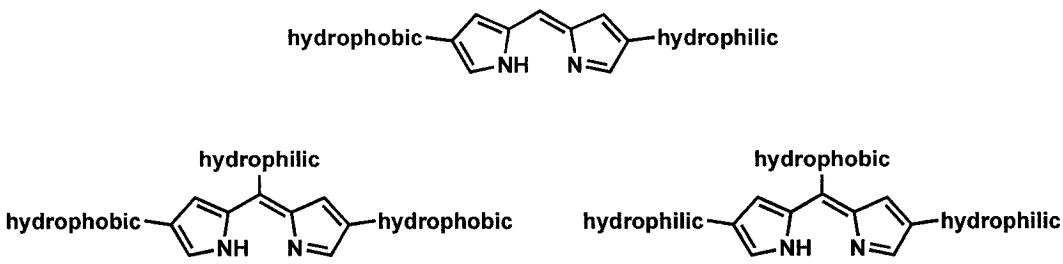


Figure 52. Three general dipyrromethene-based surfactant designs

Generally, dipyrromethene complexes have good solubility in organic media and low solubility in water. Therefore, in the design of a dipyrromethene surfactant, emphasis was placed upon incorporating an appropriate polar head group into the dipyrromethene structure. Three different polar head groups were proposed to yield three fundamentally different surfactant series, as seen in Figure 53. The incorporation of a tetraalkylammonium functional group would yield a cationic surfactant (A in Figure 53), a triethyleneglycol (TEG) ester functionality would yield a neutral surfactant (B), and a sulfonate functional group would yield an anionic surfactant (C). The installation of varying degrees of hydrophobicity was seen as a relatively straightforward procedure, since the preparation of pyrroles with alkyl groups of varying lengths has been reported in the literature.

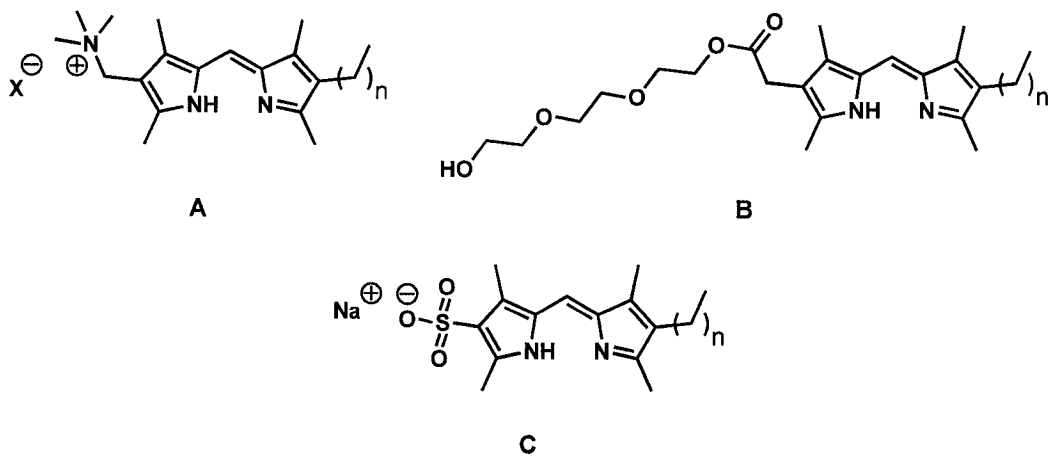


Figure 53. Three proposed dipyrromethene surfactant series

Upon considering the synthetic method used to prepare 5-unsubstituted unsymmetrical dipyrromethenes, there are two routes that could be followed to prepare the proposed surfactants. The difference between the two proposed routes, both of which are shown in Figure 54, is the identity of the pyrrole precursor that bears the formyl functional group. The Vilsmeier-Haack formylation reaction is used to introduce formyl fuctional groups at the 2-position of pyrroles,[173] such as in the pyrrole reagents involved in the proposed syntheses. The Vilsmeier-Haack formylation of pyrroles is notoriously low-yielding, involving several pH and temperature changes, and requiring the isolation of several intermediates during the course of the multi-step procedure. As purification difficulties were anticipated for the pyrroles bearing polar-head groups, Route A was seen as advantageous over Route B and so the formylation reaction would be performed upon the hydrophobic pyrroles for which manipulations of this type are well established.

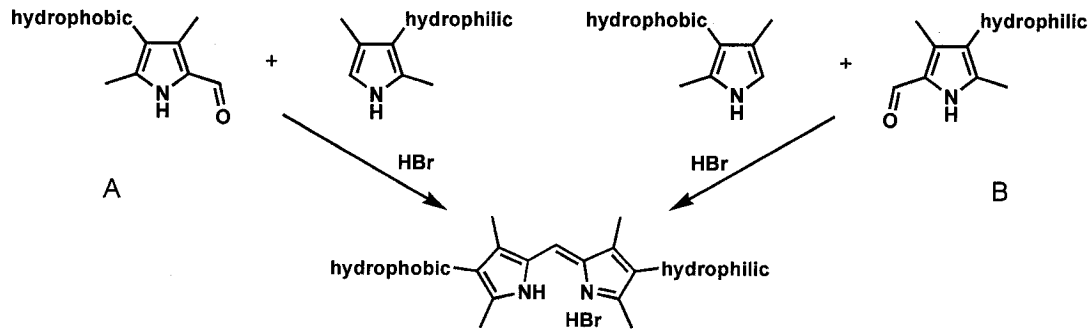


Figure 54. Two routes to 5-unsubstituted unsymmetrical dipyrromethene surfactants

Zinc(II) was selected as the metal ion used in the formation of the dipyrromethene metal complex surfactants. As was outlined in Chapter 2, a great deal of research has already been collected regarding the synthesis, structure, and behaviour of zinc(II) dipyrromethene complexes. Knowledge of these compounds simplifies the analysis of the results from this surfactant study.

3.3.2. Synthesis of Zinc(II) Dipyrromethene Gemini Metallosurfactants

Synthesis of hydrophobic pyrrole series

Varying the length of one of the alkyl substituents can alter the hydrophobicity of the proposed dipyrromethene surfactants. For this purpose, a series of 2-formyl pyrroles bearing alkyl chains of different lengths in the 4-position, compounds **11a,b** in Figure 55, were prepared following a modified literature procedure[174] while compound **11c** was prepared according to a literature procedure.[60]

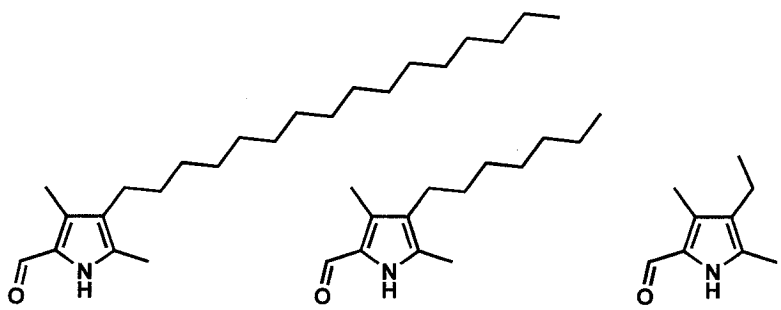


Figure 55. Series of 4-alkyl substituted pyrroles

A scheme for the synthesis of precursors to **11a** and **b** is depicted in Figure 56. Both the ethyl and benzyl 2-carboxy ester derivatives were prepared as precursors to **11a** and **b**, so that the different synthetic routes could be compared to each other. Pyrroles **12a**[175] and **12b**[176] were acylated using palmitoyl chloride and heptanoyl chloride following a Friedel-Crafts acylation procedure using a stoichiometric amount of tin(IV) chloride as a Lewis acid. Dichloromethane is the solvent of choice for Friedel-Crafts acylation of pyrroles and tin(IV) chloride has previously been established as an effective catalyst.[173] These reactions are amenable to being conducted on a multigram scale and the yields were good. The progress of the acylation reactions was monitored frequently because the pyrrole-2-carboxylate esters **13c** and **d** were observed to undergo debenzylation during prolonged exposure to tin(IV) chloride. Compound **13a**[177-179] has been prepared previously by different methods and comparison of characterization data showed good correlation.

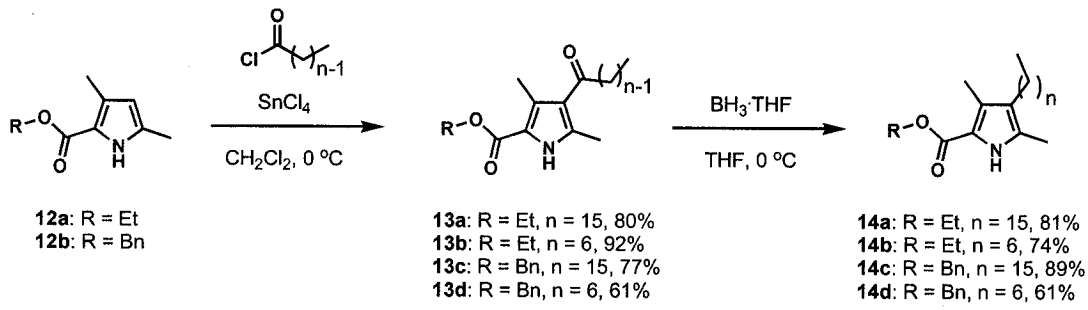


Figure 56. Synthesis of 4-alkyl pyrroles

The acyl groups of pyrroles **14a-d** were reduced to alkyl groups in good yields using borane (Figure 56). This is another procedure that is well established for pyrroles.[132] Early in the course of this reaction the alcohol intermediate can be observed by TLC analysis, so care must be taken to run the reaction for an appropriate amount of time to obtain the desired product in good yield. Compounds **14a**[177] and **b**[180,181] have been reported in the literature, prepared by different methods, and show good correlation for the characterization data.

Using another reaction that has been proven very successful for use in pyrrole chemical manipulations, the formyl groups of compounds **11a** and **b** were installed using the Vilsmeier-Haack formylation procedure (Figure 57). This reaction involves the nucleophilic attack of a 2-unsubstituted pyrrole upon an iminium electrophile prepared *in situ* from phosphorous(V) oxychloride and *N*,*N*-dimethylformamide (DMF). The iminium functional group is then hydrolyzed, producing the 2-formyl pyrrole. The precursor 2-unsubstituted pyrroles were prepared by decarboxylation of the corresponding 2-carboxylic acid pyrrole derivatives (**15a,b**). These carboxylic acids were in turn prepared by the ester cleavage of ethyl esters **14a** and **b** by saponification in aqueous alkaline solution or hydrogenolysis of the benzyl esters **14c** and **d** using 10 mol% palladium on

activated carbon as a catalyst. Although the final yields of the formylation reactions were not found to be significantly different between procedures that began with the ethyl ester derivatives in comparison to those that began with the benzyl ester derivatives, the benzyl esters were found to be the better starting material. This decision was made based upon the relative ease of isolating the pyrrole carboxylic acids from the hydrogenolysis reactions of **14c** and **d** versus the aqueous saponifications of **14a** and **b**.

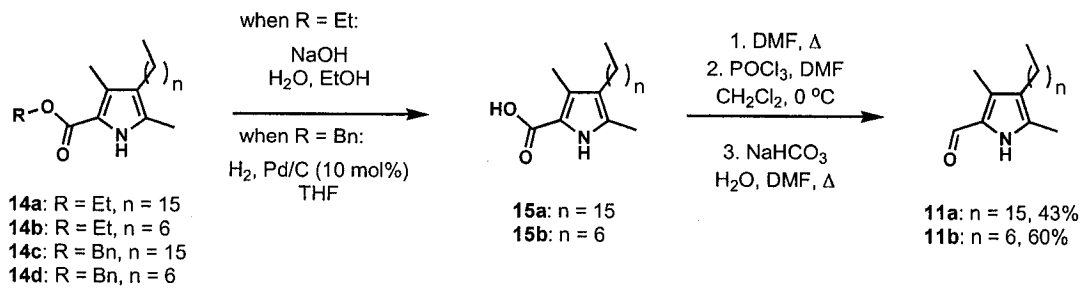
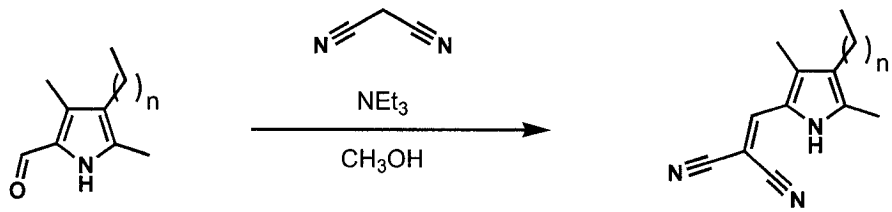


Figure 57. Synthesis of 2-formylpyrroles

The use of cyanovinyl protecting groups for pyrrole formyl groups was developed for porphyrin synthesis.[182] These protecting groups are introduced by a Knoevenagel reaction and can be removed in high yield by alkaline hydrolysis.[182] A benefit of protecting groups of this type is that by masking the formyl group they decrease the retention time of the compound on silica during chromatographic purification. As well the protected products are bright yellow in colour, making them very easy to monitor during their elution. Consequently, an attempt was made to prepare dicyanovinyl derivatives **16a,b** from crude product mixtures from the synthesis of formyl pyrroles **11a** and **b** by heating the crude mixtures with malononitrile and a catalytic amount of triethylamine in methanol (Figure 58). The yields obtained for the synthesis and isolation of **16a** and **b** were lower than those obtained for the isolation of **11a** and **b** directly from

the formylation crude product mixtures, so this method of protecting the formyl functional groups for the purpose of purification was not pursued further.



11a: n = 15
11b: n = 6

16a: n = 15, 27%
16b: n = 6, 20%

Figure 58. Protection of 2-formyl pyrroles with dicyanovinyl functional groups

Synthesis of tetra-alkyl ammonium pyrrole

The polar head group in the majority of cationic surfactants consists of a tetra-alkyl ammonium functionality. Compound **17** (Figure 59) was prepared using the Mannich reaction with the ultimate goal of synthesizing a cationic dipyrromethene surfactant. Using Mannich conditions adopted from a literature procedure[183] diethylamino-substituted pyrrole **17** was prepared in high yield. In this reaction an iminium intermediate, prepared *in situ* from diethylamine and formaldehyde, undergoes nucleophilic attack from the 4-position of pyrrole **12b**. Alkylation with iodomethane was proposed as the means of quaternizing the amine nitrogen. However initial studies of the hydrogenolysis of the tertiary amine derivative **17** halted further investigation of this route as a means of synthesizing cationic dipyrromethenes.

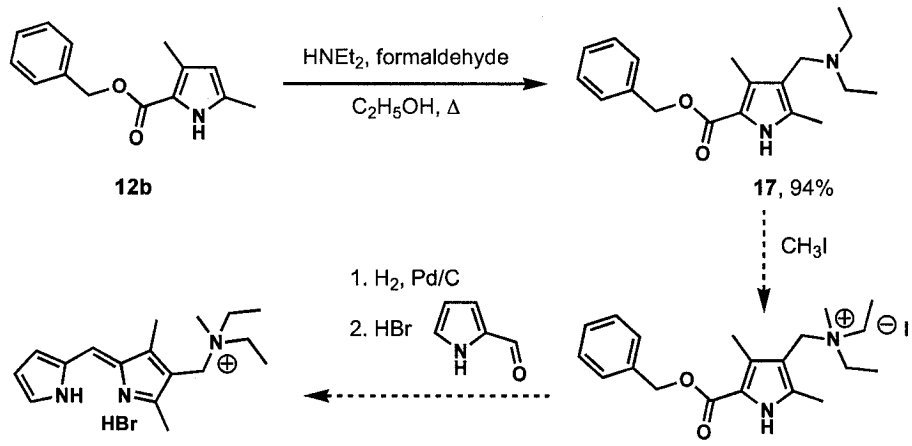


Figure 59. Proposed synthesis of cationic dipyrromethene surfactant

As seen in Figure 60 the diethylamino functional group of compound **17** was found to be susceptible to hydrogenolysis during the reaction with hydrogen and palladium on activated carbon to cleave the benzyl ester for subsequent dipyrromethene condensation. The transformation of this easily-installed diethylaminomethylene substituent into a methyl group may prove to be a synthetically useful reaction in other applications, but was an obstacle in the synthesis of cationic dipyrromethene surfactants by this route, and so focus was placed upon developing other polar head groups.

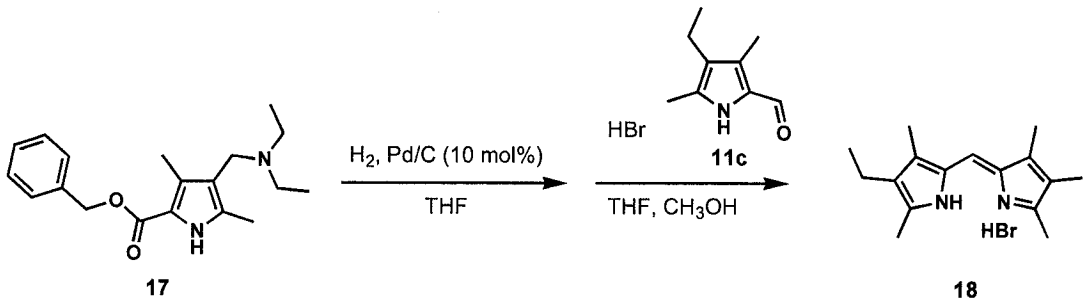


Figure 60. Hydrogenolysis of diethylamino pyrrole

Synthesis of triethyleneglycol-derivatized dipyrromethene

Triethyleneglycol (TEG) moieties are frequently incorporated into molecules as non-ionic water-solubilizing groups. The alcohol coupling methodology developed for the preparation of homochiral pyrrole esters described in Chapter 2.3.1 was applied to the goal of preparing a dipyrromethene substituted with TEG. The synthesis of pyrrole esters of TEG is shown in Figure 61. Coupling TEG with benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate (**3**) using a combination of EDC·HCl and HOBT resulted in the production of ester products that were the result of mono- and disubstitution of the diol, compounds **19** and **20**, respectively. These two esters were easy to resolve by flash chromatography due to the enormous difference in retention factors. Combined high yields of the pyrrole esters were consistently achieved, and the ratio of the products could be controlled by varying the number of equivalents of TEG, with respect to the pyrrole reagent, used in the reaction. The yields of mono- and di-substituted products for ester coupling reactions conducted using different equivalents of TEG are shown in Table 5. The findings are in keeping with predictions that an excess of TEG promotes mono-substitution.

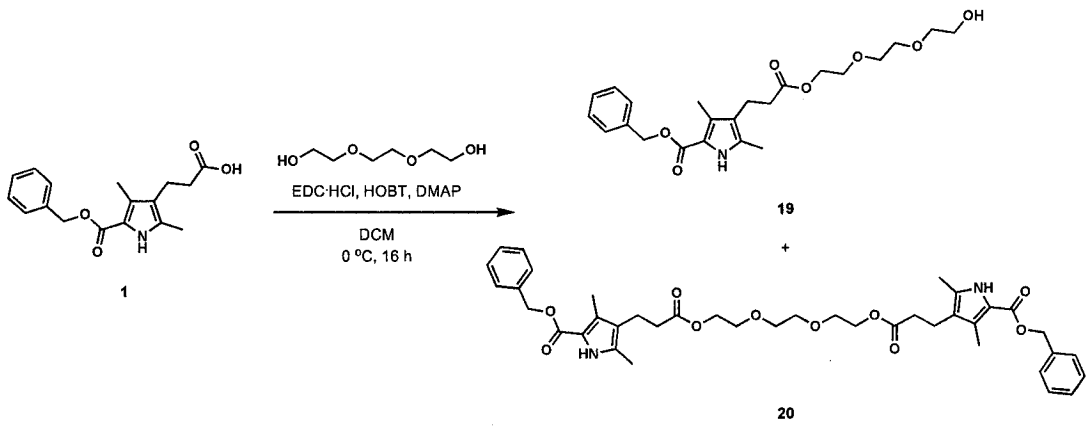


Figure 61. Synthesis of triethyleneglycol pyrrole esters

Table 5. Isolated yields of triethyleneglycol esters **19** and **20** related to the number of equivalents of triethyleneglycol, with respect to **3**, used in the synthesis

equivalents of TEG	Yield 19 (%)	Yield 20 (%)
5	89	6
2	69	20
1.2	55	31
0.5	27	60

The proposed TEG-substituted dipyrromethene **21** could be prepared from the mono-substitution product **19** using the general procedure employed for the synthesis of unsymmetrical dipyrromethenes as outlined in Chapter 1.2, seen in Figure 62. However, the methanol that is usually added as a solvent during the acid-catalyzed synthesis of dipyrromethenes was not used in the synthesis of **21** and the reaction was conducted using THF as the only solvent for this step. The reason for this modification was to prevent the production of methyl ester **22** by trans-esterification of the TEG esters by methanol in the presence of a strong acid as seen in Figure 63. This trans-esterification

resulted in complications in the isolation of the desired product, and low yields, when the dipyrromethene synthesis reaction was conducted in the presence of methanol. It is worthy of mention that the dipyrromethene **21** was isolated as an oil, which is very unusual for dipyrromethene hydrobromide salts. Since precipitation or crystallization is the usually method employed in the isolation of dipyrromethene hydrobromides, an alternate procedure involving extraction was developed for dipyrromethene **21**. The technique of salting-out was used to minimize the solubility of the TEG-substituted dipyrromethene in the aqueous phase during the extraction.

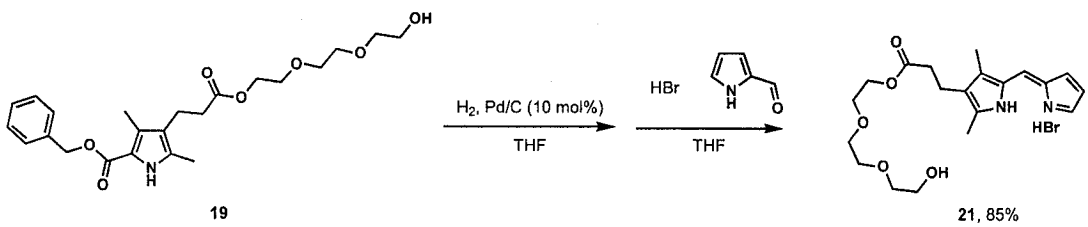


Figure 62. Synthesis of triethyleneglycol-substituted dipyrromethene

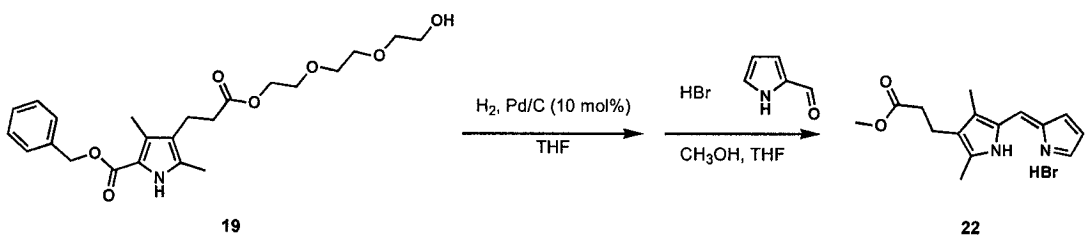


Figure 63. Trans-esterification of triethyleneglycol esters by methanol

The zinc(II) complex of the TEG-substituted dipyrromethene **21** was prepared according to the procedure shown in Figure 64. Following a standard procedure,[80] a solution of five molar equivalents of zinc(II) acetate dihydrate and sodium acetate trihydrate was added to a solution of dipyrromethene **21** in chloroform resulting in an observable colour change indicating the formation of zinc(II) dipyrromethene complex.

The complex was isolated in good yield and was purified by filtering a solution of the crude product mixture through silica.

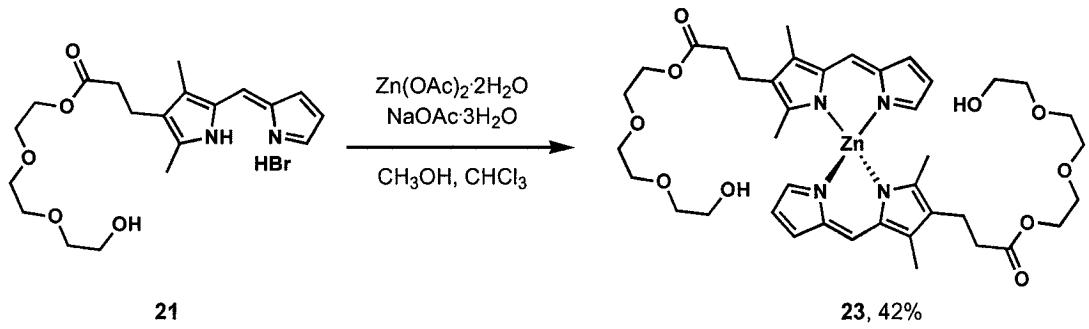


Figure 64. Synthesis of zinc(II) complex of triethyleneglycol-substituted dipyrromethene

To further investigate the use of hydroxy functional groups to enhance water solubility of dipyrromethenes, an ethyl alcohol substituted dipyrromethene and the corresponding zinc(II) complex were prepared according to the scheme seen in Figure 65. Benzyl 4-(2-hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate (**24**), prepared according to a literature procedure,[184] was used to prepare the dipyrromethene **25**, which precipitated from the reaction mixture as a microcrystalline powder in excellent yield. The product obtained from complexation of **25** with zinc(II) was prepared in low yield, much the same as the yield obtained for **23**, the zinc(II) complex of the TEG-substituted dipyrromethene.

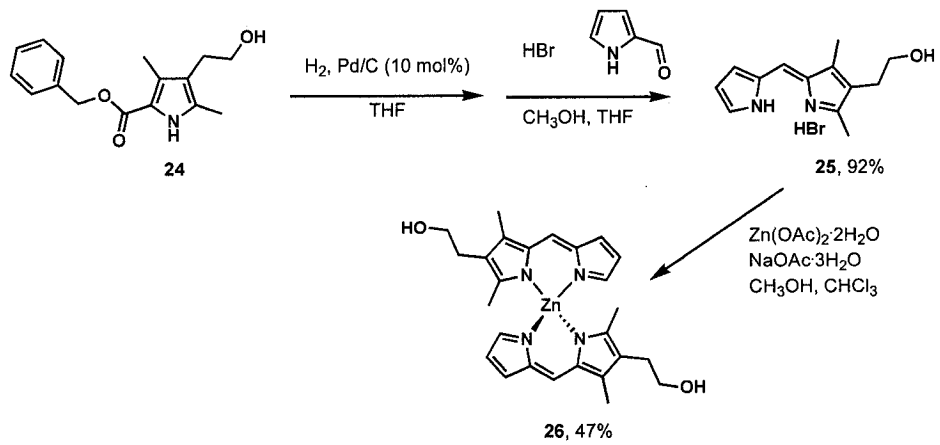


Figure 65. Synthesis of zinc(II) complex of ethyl alcohol-substituted dipyrromethene

Synthesis of sulfonate dipyrromethene

Sulfonate and sulfate functional groups are very effective at increasing the water solubility of organic compounds.[143] The incorporation of sulfonate groups has been employed as a strategy for preparing water-soluble porphyrins[185] and linear oligopyrroles.[186,187] Two particularly relevant reports describe the synthesis of sulfonated BODIPYs,[188,189] and a modified procedure based upon this example from literature was used to prepare sulfonated zinc(II) dipyrromethene complexes.

The synthesis of sulfonated zinc(II) complexes began with the synthesis of 8-unsubstituted dipyrromethene hydrobromide salts **27a-c** as shown in Figure 66. Using the standard procedure for the synthesis of unsymmetrical dipyrromethenes hydrophobic 2-formyl pyrroles **11a-c** were coupled with the 2-unsubstituted pyrrole derived from benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) to produce a series of 8-unsubstituted dipyrromethenes bearing alkyl substituents of varying length in the 2-position, **27a-c**. Compounds **27a** and **b** were obtained in moderate yield (**27a** was particularly difficult to handle as it was a waxy solid) while compound **27c** was easily obtained in excellent yield

as a crystalline solid. The yields of the zinc(II) complexes **28a-c** prepared from these dipyrromethenes decreased with increased length of the 8-alkyl substituents. For these reasons, in addition to the relative simplicity of the NMR spectra of **28c**, subsequent research into the sulfonation of zinc(II) dipyrromethene complexes were conducted using **28c**.

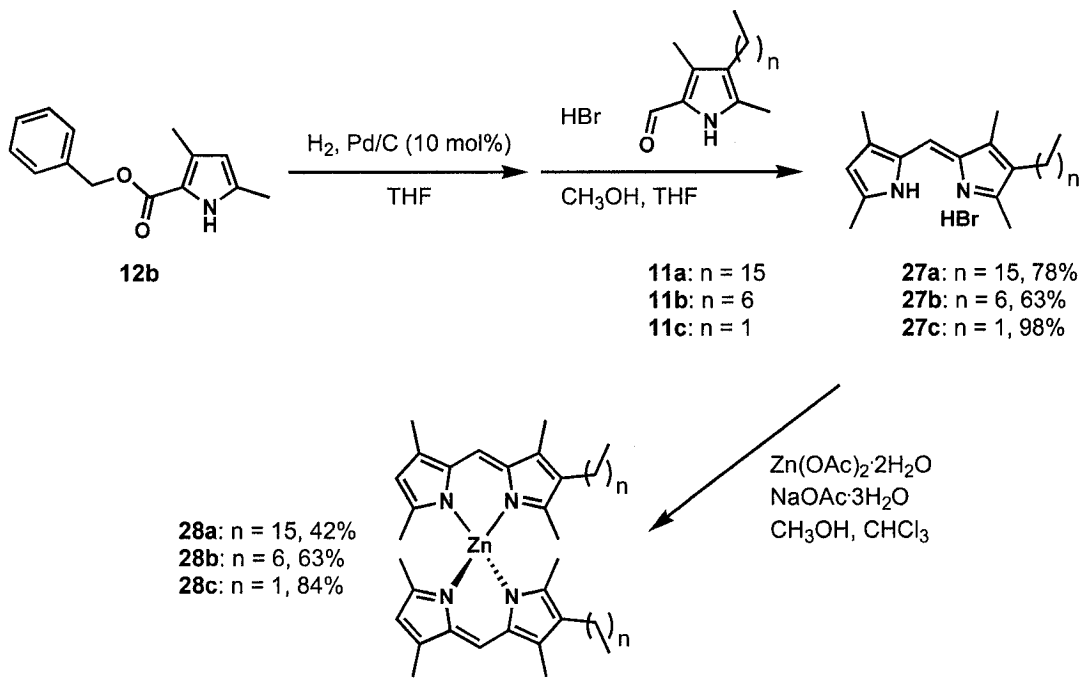


Figure 66. Synthesis of zinc(II) 8-alkyl dipyrromethene complexes

The reaction conditions for the sulfonation of **28c** to produce disodium salt **30** have been optimized in regards to the number of equivalents of chlorosulfonic acid, the temperature of the reaction, and the method of neutralization. The sulfonation reaction has been performed at five temperatures: -80, -7, 0, 25, and 40 °C. The nature of the product mixture did not change significantly with changes in reaction temperature. However, performing the reaction at 0 °C was very convenient and resulted in the formation of the intermediate sulfonic acid derivative, **29**, of the zinc(II) dipyrromethene

complex as a powdery precipitate. The solvent containing unreacted **28c** and chlorosulfonic acid in solution could easily be decanted from the powder before the neutralization step.

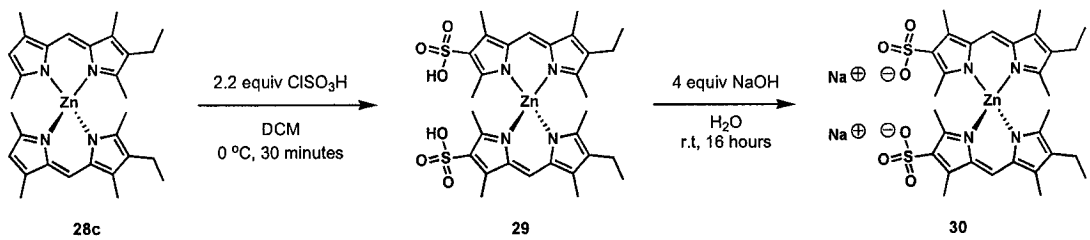


Figure 67. Synthesis of sulfonated zinc(II) dipyrromethene complex

Varying the number of equivalents of chlorosulfonic acid, with respect to **28c**, used in the reaction resulted in very different products. Using 1.5 equivalents of chlorosulfonic acid resulted in a very complicated mixture of possibly six different products, as estimated from the ^{1}H NMR spectrum of the reaction mixture after neutralization. These unexpected products could not be isolated and identified, however it is expected that one of them may be the mono-sulfonated derivative of **28c**. The use of exactly 2 equivalents, as predicted by the stoichiometry of the reaction, resulted in the same mixture of several products, however the desired product now dominated the mixture. A small excess of chlorosulfonic acid, using 2.2 equivalents, reduced the number of products to three and the major product was **30**. Using a larger excess of chlorosulfonic acid, 3 equivalents, produced the same results as the use of a small excess.

Using the optimized conditions of 2.2 equivalents of chlorosulfonic acid and conducting the reaction at 0 °C, the conditions of the neutralization step were examined next. Neutralization with aqueous solutions of sodium bicarbonate or sodium hydroxide proved effective. It was found that 4 equivalents of sodium base was the minimum

number of equivalents required to completely neutralize the sulfonic acid intermediate in 16 hours. A larger excess of base could be used to neutralize the reaction in less time, but created the problem of unreacted base as a contaminant in the final product. The drawback to the use of water as a solvent is the subsequent removal of the water, which required freeze-drying because aqueous solutions of the product **30** foam significantly when evacuated using a rotary evaporator. Consequently, methanol was chosen as an alternative solvent for the neutralization reaction. Sodium bicarbonate has low solubility in methanol, so only solutions of sodium hydroxide in methanol were used. Solutions of **30** in methanol do not foam as much as aqueous solutions of **30**, so the solvent could be removed using a rotary evaporator, which greatly simplified the isolation of product. However, a new obstacle appeared in the form of an unidentifiable sideproduct when methanol was used as the solvent for the neutralization step.

The ^{1}H NMR spectrum of the compound isolated from the neutralization reaction conducted using a solution of sodium hydroxide in methanol contains an unidentifiable signal, a singlet at $\delta = 3.70$ ppm in methanol-d_4 which correlates to a ^{13}C signal at 55.1 ppm. The NMR chemical shifts for the unidentified signal do not correspond to those of sodium methoxide. These signals are speculatively assigned to a sideproduct in which an oxygen in one or both of the sulfonate groups has been methylated. Assumedly, the other signals for this compound are coincident with the signals for **30**. When the neutralization reaction is performed using a solution of sodium hydroxide in 95% ethanol a corresponding unidentifiable signal appears as a quartet at 4.04 ppm which shows coupling with a triplet signal in the ^{1}H spectrum at 1.28 ppm. Attempted purification using reverse phase liquid chromatography, ion-exchange chromatography, and dialysis

yielded unsatisfactory results. Unfortunately, the sodium sulfonate salt **30** has not yet been isolated in pure form. Repeated attempts to crystallize the product have failed. As an alternative to the sodium sulfonate salt, synthesis of the corresponding ammonium sulfonate salt was attempted by neutralization of the sulfonic acid intermediate using aqueous ammonia. This reaction yielded a mixture of at least three products, as estimated by the ^{1}H NMR spectra of the reaction mixtures. The best optimized conditions for the neutralization reaction are therefore 4 equivalents of sodium hydroxide as an aqueous solution stirred at room temperature for 16 hours.

3.3.3. Assessment of the Surfactant Properties of Zinc(II) Dipyrromethene Gemini Metallosurfactants

Preliminary indications of the potential surfactant properties of the dipyrromethenes are limited to their relative water solubility. The TEG dipyrromethene **21** was found to be more soluble in water than its corresponding zinc(II) complex **23**. Similarly, ethyl alcohol dipyrromethene **25** was found to be more water soluble than zinc(II) complex **26**. This may indicate that the Krafft temperature for the zinc(II) complexes is higher than for the dipyrromethene hydrobromide salts. The zinc(II) dipyrromethene sodium sulfonate salt **30** has demonstrated surface activity in preliminary studies, and this compound is presently undergoing analysis to determine a cmc value.

3.4. Conclusions

The study of dipyrromethene surfactants presented herein is very preliminary. There remains a great deal of work to be done, for both the compounds that have been synthesized and for the many potential future targets. Values that reflect the surfactant properties of the dipyrromethenes that are reported herein will be measured. These

include Kt, especially for those dipyrromethenes that exhibited low solubility in water, as well as c20 values and cmc values. Once obtained, comparison of the values for the dipyrromethene ligand versus their corresponding zinc(II) complexes will reveal whether these compounds indeed act as gemini metallosurfactants. Since the solubility of the dipyrromethenes that have been synthesized, which bear relatively short alkyl substituents, is not very high, it is unlikely that dipyrromethenes prepared from the pyrroles 11a and b, with the longer alkyl substituents will have adequate water-solubility. Therefore the emphasis of future research should be towards the improved preparation of the dipyrromethenes described herein, as well as those with different water-solubilizing groups, for example phosphates, sugars, and *N*-alkylated pyridinium functional groups are reportedly effective[144] and should be explored for use in this project. Alternatively, gemini metallosurfactants based on ligands other than dipyrromethenes could be investigated.

Future directions for this work include assessment of different tetra-alkyl ammonium pyrroles designed so that the amine functional group will not be cleaved during the hydrogenolysis of the benzyl ester. Some possible syntheses for these compounds are shown in Figure 68. By placing the nitrogen of the amine functional group closer or further away from the aromatic pyrrole ring, hydrogenolysis will no longer be means of removing this group. The preparation of amino pyrroles from proline derivatives has been reported in the literature.[190] Alternatively pyrroles in which the amino group is attached to the pyrrole ring by an ethylene moiety would make suitable targets.

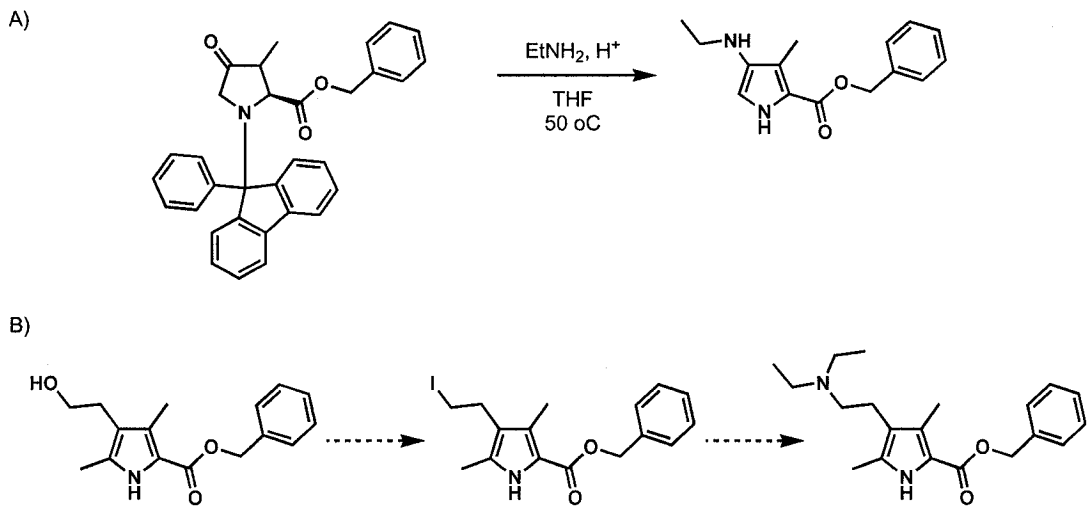


Figure 68. Potential syntheses of alternative amino pyrroles

Since the dipyrromethene ligands are hydrobromide salts, which may improve their solubility in water, monomeric complexes of the dipyrromethenes could be prepared for comparison purposes to measure the gemini surfactant effect of forming dimeric metallosurfactants. An excellent example of a monomeric dipyrromethene complex is a BODIPY. Very preliminary results from the attempted preparation of BODIPY complexes of dipyrromethene **27c**, used in the synthesis of the sodium sulfonate zinc(II) dipyrromethene complex **31**, has revealed some unexpected results. Reported only once in literature,[191] the conditions used in standard BODIPY preparations result in scrambling of unsymmetrical dipyrromethenes by disproportionation. Consequently, the attempted synthesis of borondifluoride complex **31** resulted in a mixture of three products, as seen in Figure 69.

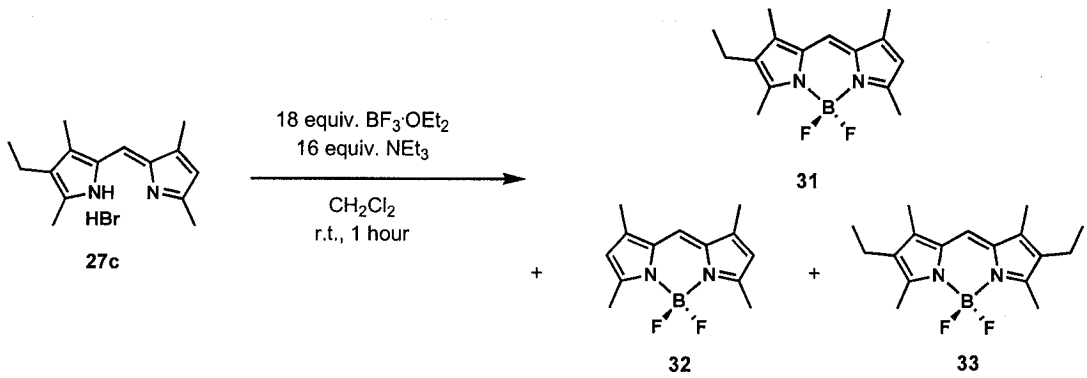


Figure 69. Mixture of products obtained from synthesis of unsymmetrical borondifluoride dipyrromethene complex

A systematic analysis of the borondifluoride complexation reaction is required in order to determine the appropriate conditions for synthesizing unsymmetrical BODIPY **31** without producing the disproportionation products **32** and **33**. This is an opportunity to enhance understanding of this interesting phenomenon while in the process of advancing research about dipyrromethene surfactants.

Chapter 4. ^{15}N NMR Chemical Shifts of Dipyrrolic Compounds

4.1. General Background

4.1.1. ^{15}N Nuclear Magnetic Resonance Spectroscopy

The element nitrogen is nearly ubiquitous in biologically relevant molecules and is a popular component of many organometallic compounds. Although the nitrogen chemical shift was the first to be reported in NMR spectroscopy,[192] it is not routinely reported as part of standard characterization data. Difficulties are encountered measuring and interpreting nitrogen NMR data as a result of the technical problems related to the unfavourable physical properties of the nitrogen nucleus. Although ^{14}N possesses a high natural abundance (99.63%), it has a nuclear spin (I) = 1 and gives broad signals which are of little use for structural determinations. Alternatively, ^{15}N has $I = ½$ but it suffers from low natural abundance (0.37%) and a low magnetogyric ratio (γ), resulting in low sensitivity.[193] In early nitrogen NMR studies the samples were frequently isotopically enriched with ^{15}N to overcome the inherently low sensitivity and increase the signal-to-noise ratio in the spectra. Advances in NMR spectrometer stability, probe design, electronics, and in inverse detection techniques such as heteronuclear single quantum coherence (HSQC) and heteronuclear multiple bond correlation (HMBC) spectroscopy have made the use of natural abundance ^{15}N NMR experiments routine.

4.1.2. ^{15}N NMR Chemical Shifts of Pyrroles and Tetrapyrrolic Compounds

Reports of the ^{14}N and ^{15}N chemical shifts of pyrroles show a wide range in values related to the structure of the molecules. For example, coordination of the nitrogen atom

to a metal center causes a change in ^{15}N chemical shift, $\delta^{15}N$, and the difference between the coordinated and the uncoordinated nitrogen is called a coordination shift ($\Delta\delta$).[193] Some trends can be seen based upon the nature of the substituents on the pyrrole,[194] and these have been compared to the predictable trends seen for ^{13}C chemical shifts based upon the substituents on the carbon atom.[193] However, a survey of $\delta^{15}N$ for a series of *N*-substituted pyrroles showed, through computational modelling, that, although $\delta^{13}C$ is largely predictable based upon the electron-withdrawing nature of the substituents on the carbon atom, the systematic interpretation of substituent effects upon $\delta^{15}N$ is not straightforward.[195]

There have been several reports of the $\delta^{15}N$ for a series of porphyrins and metalloporphyrins.[196-203] These compounds exhibit coordination shifts that are different for different metal complexes of the same porphyrin and, similarly, changes in $\delta^{15}N$ occur upon protonation, called protonation shifts. Tautomerization rates of free-base porphyrins have been measured using the ^{15}N chemical shifts at variable temperatures.[197] There have been two reports of studies into the ^{15}N NMR chemical shifts for bilirubin, a linear tetrapyrrolic dipyrrinone.[204,205] However there has only been one report of $\delta^{15}N$ for a dipyrromethene[206] and previous to the present work no reports for dipyrromethanes or metal complexes of dipyrromethenes.

4.2. Project Goals

The aim of this project was to provide a survey of ^{15}N NMR chemical shifts and one-bond ^{15}N-^{1}H coupling constants for dipyrrolic compounds. These values were measured using two-dimensional ^{15}N-^{1}H correlation experiments and examined for trends for use in developing a tool for assessing the nitrogen environment and gross chemical structure of

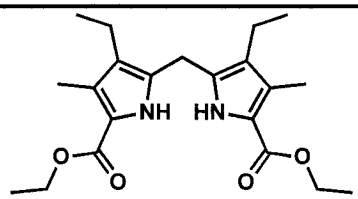
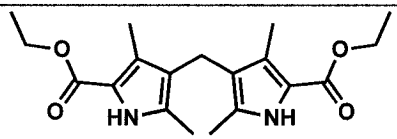
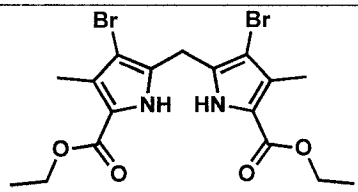
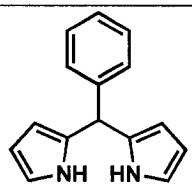
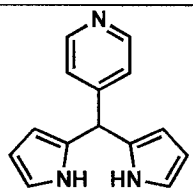
dipyrrolic compounds. The effects of protonation, complexation, and substitution patterns were examined for series of dipyrromethanes and dipyrromethenes.

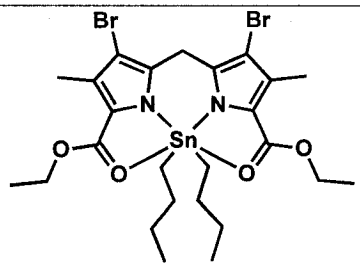
4.3. Results and Discussion

4.3.1. Assessment of ^{15}N NMR Chemical Shifts of Dipyrrolic Compounds

A variety of dipyrrolic compounds including dipyrromethanes, dipyrromethenes, and dipyrromethene complexes were prepared for the measurement of ^{15}N chemical shifts. Some of the compounds used in this study were prepared following reported procedures, as detailed in Chapter 5.3. The tin(IV) dipyrromethane complex **39** was prepared following a procedure modified from literature[207] in which complexes of this type were used for the preparation of 5,5'-diacyldipyrromethanes.[207] Table 6 shows the structures, ^{15}N NMR chemical shifts and one-bond ^{1}H-^{15}N coupling constants for a series of dipyrromethanes **34-39** obtained from samples of the compounds as solutions in deuterated chloroform. The $\delta^{15}N$ values were indirectly measured using ^{15}N-^{1}H HSQC NMR experiments that correlated the ^{15}N signals with ^{1}H NMR signals for the hydrogen atoms bonded to the nitrogen atoms in compounds **34-38** and with the meso-hydrogen atoms for compound **39**. For compound **38** the $\delta^{15}N$ for the pyridine nitrogen was also measured. The $\delta^{15}N$ for compounds **34-38** are very consistent and are nearly the same as for pyrrole, which exhibits a resonance at -231.4 ppm.[194] As well, the $^{1}J(^{15}N^{1}H)$ for compounds **34-38** are all around -96 Hz, which is again not unlike pyrrole with a $^{1}J(^{15}N^{1}H)$ of -96.5 Hz.[194] The chemical shift of the nitrogen atom in the pyridine ring of compound **38** is typical of those observed for pyridine derivatives.[194]

Table 6. Data for ^{15}N chemical shifts and $^{1}J_{NH}$ for dipyrromethane compounds **34-39**

Structure	$\delta^{15}N$ (ppm)	$^{1}J(^{15}N^{1}H)$ (Hz)
 **34**	-231.8	-96
 **35**	-231.4	-97
 **36**	-226.8	-97
 **37**	-232.1	-94
 **38**	-232.2 -73.3	-96 n/a

 **39**	-194.1	n/a

Comparison of compounds **34**[137] and **35**[137] shows that the difference in $\delta^{15}N$ between 2,2'- and 3,3'-dipyrromethanes is very little. Comparison of compounds **34** and **36**[208] shows that altering the substituents from ethyl groups to bromine atoms results in a small change in $\delta^{15}N$. The inclusion of aryl substituents at the meso-position of dipyrromethanes, such as the phenyl and pyridyl rings in compounds **37**[7] and **38**,[209] produces uniform results in a similar value for the chemical shift of the nitrogen nuclei as for the meso-unsubstituted dipyrromethanes **34** and **35**.

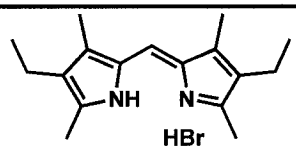
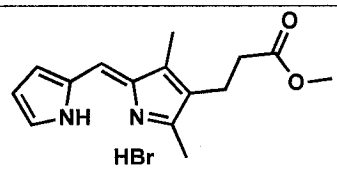
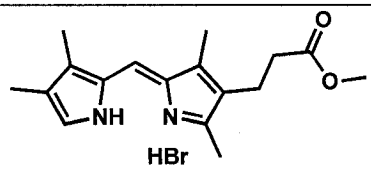
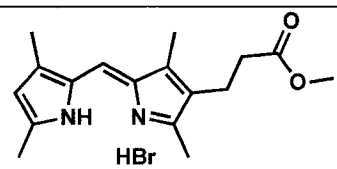
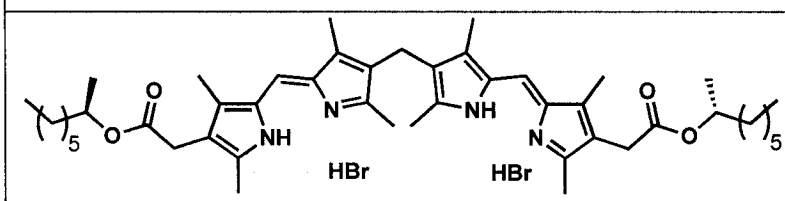
By comparison of the $\delta^{15}N$ for compounds **36** and **39** a tin(IV) complexation shift of +32.7 ppm (more deshielded) can be calculated using the equation $\Delta\delta = \delta^{15}N(\mathbf{39}) - \delta^{15}N(\mathbf{36})$. In keeping with this observation, complexation shifts for $\delta^{15}N$ of pyrrole with tin(IV) have been reported as deshielding, although the magnitude of the shift was significantly different.[210] As well, complexation shifts for the pyrrolic nitrogen atom in a *N,N'*-(dipyrrolyl-α-methyl)-*N*-methylamine have been reported as deshielding for the formation of complexes with titanium(IV), zirconium(IV), and halfnium(IV).[211]

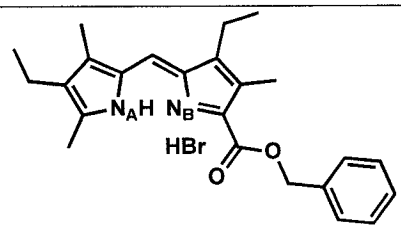
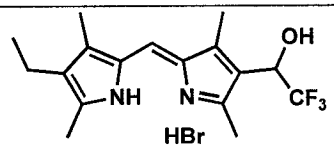
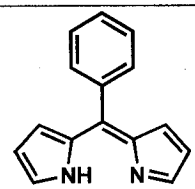
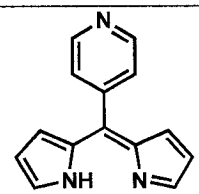
Several different techniques were employed to synthesize the dipyrromethenes investigated in this study. Dipyrromethene **40** was synthesized following a procedure used for the preparation of symmetrical 5-unsubstituted dipyrromethenes from pyrrole-2-

carboxylate esters,[212] and compounds **22**, **41**, **42**, **8l**, **43**,[213] and **44**[131] were synthesized using the acid-catalyzed condensation of appropriately-substituted 2-formylpyrroles and 2-unsubstituted pyrroles. Compound **40** has been reported in the literature, prepared by different methods, and the characterization data matched with the data obtained for this investigation.[214,215] Free-base dipyrromethenes **45**[209] and **46**, which are substituted in the 5-position with aryl substituents, were prepared by oxidation of the corresponding dipyrromethanes **37** and **38** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ).

Table 7 shows structures and NMR data, measured by correlation of the nitrogen atoms to directly-bonded hydrogen atoms, for the dipyrromethene compounds studied. The ^{15}N chemical shifts for the dipyrromethene hydrobromide salts are consistently around $\delta^{15}N = -210$ ppm, which matches the only previously reported value, $\delta^{15}N = -209.2$ ppm for the protonated form of 1,2,3,7,8,9-hexamethydipyrromethene.[206] The ^{15}N NMR spectrum of symmetrical dipyrromethene hydrobromide salt **40** exhibits only one signal, which can be explained by the equivalence of the two nitrogen atoms in the molecule by resonance. Other spectroscopic indications of this equivalence include the observation of only one signal corresponding to the hydrogens bonded to nitrogen in the ^1H NMR spectrum of protonated symmetrical dipyrromethenes and the symmetry seen in X-ray photoelectron spectra.[216]

Table 7. Data for ^{15}N chemical shifts and $^{1}J_{NH}$ for dipyrromethene compounds **8k**, **22**, and **40-46**

Structure	$\delta^{15}N$ (ppm)	$^{1}J(^{15}N^{1}H)$ (Hz)
 **40**	-213.7	-95
 **22**	-207.8 -210.0	-95 -95
 **41**	-210.7 -213.6	-96 -95
 **42**	-211.5 -212.3	-96 -95
 **8l**	-211.6 -212.0	-95 -95

 **43**	-202.7 (A) -224.6 (B)	-94 -97
 **44**	-210.9 -212.3	-96 -95
 **45**	-156.2	-
 **46**	-156.1 -68.0	- n/a

Upon consideration of the $\delta^{15}N$ values measured for the series of dipyrromethenes **22**, **41**, and **42** it can be seen that the chemical shift of the nitrogen atoms depends not only upon the nature of the substituents attached to the ring of the pyrrolic unit in which the nitrogen is located in the dipyrromethene, but also upon the substituents on the other pyrrolic unit. Although each of the dipyrromethenes contains a 1,3-dimethyl-2-(methoxycarbonylethyl)-substituted ring, the ^{15}N chemical shift does not remain constant

between their recorded values. Therefore, the different substituents on the varying ring in the dipyrromethenes **22**, **41**, and **42** affect the chemical shift of both nitrogen atoms in the molecule. The values of $\delta^{15}N$ measured for bis(dipyrromethene) hydrobromide **8l** correlated well with the chemical shifts of the monomeric dipyrromethenes.

The presence of strong electron-withdrawing substituents on the dipyrromethene hydrobromide salts is seen to have an effect upon the ^{15}N chemical shifts. Nuclear Overhauser effect spectroscopy (NOESY) NMR experiments in conjunction with the ^{15}N-^{1}H HSQC data were used to assign the $\delta^{15}N$ for compound **43**, and showed that the benzyl 1-carboxylate substituent produced a more shielded chemical shift (relative to the average $\delta^{15}N$ of the previously mentioned protonated dipyrromethenes) for the nearest nitrogen atom to $\delta^{15}N$ = -224.6 ppm while that of the furthest nitrogen atom was more deshielded, at -202.7 ppm. The presence of the electron-withdrawing trifluoroethanol substituent in the 2-position of compound **44** has a less pronounced effect upon the ^{15}N chemical shifts of this compound. As well, the values of $^{1}J(^{15}N\text{-}^{1}H)$, measured as -94 and -97 Hz, for dipyrromethene **43** deviate from the unvarying -96 or -95 Hz observed for the other dipyrromethene hydrobromide salts.

The $\delta^{15}N$ of free-base 1,2,3,7,8,9-hexamethyldipyrromethene has been reported to be -162.0 ppm, indicating a protonation $\Delta\delta^{15}N$ of +47.2 ppm.[206] This is significantly different from the chemical shift values measured for free-base 5-aryl dipyrromethenes **45** and **46**. This suggests that unlike dipyrromethanes, the presence of an aryl substituent in the meso-position of dipyrromethenes has an effect upon the ^{15}N chemical shifts of the molecule in comparison to those without meso-substituents, for example 1,2,3,7,8,9-hexamethyldipyrromethene.[206] However, the protonation $\Delta\delta^{15}N$ for tetraphenylporphyrin,

which can be viewed as structurally related to dipyrromethene **45**, has been measured as +55 ppm.[196] Without having conducted further studies of the protonation shifts for $\delta^{15}N$ of 5-unsubstituted dipyrromethenes and 5-aryl dipyrromethenes, no further conclusions can be drawn on this matter. The $\delta^{15}N$ of the pyridyl substituent of dipyrromethene **46** was found to be -68.0 ppm, which is 5.3 ppm more deshielded than the corresponding nitrogen in the precursor dipyrromethane **38**. Unlike the equivalence of the nitrogens in the protonated symmetrical dipyrromethene **40**, the nitrogen atoms in the free-base dipyrromethenes **45** and **46** exhibit equivalence due to rapid tautomerization involving the exchange of a hydrogen atom. Below the coalescence temperature for tautomerization of the free-base dipyrromethenes, which has been measured as 288K for tetraphenylporphyrin in chloroform at 18.25 MHz,[196] the two nitrogen atoms would presumably correspond to two resolvable signals.

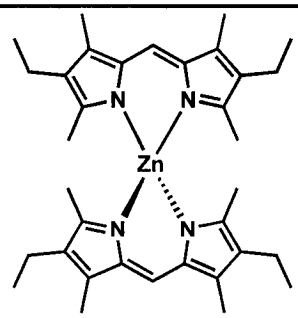
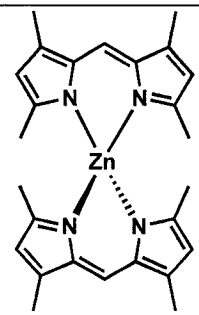
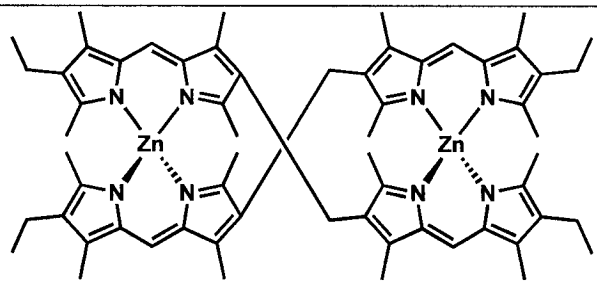
Zinc(II) dipyrromethene complexes **9l**, **10**,[137] **47**, **48**, **49**,[130] **50**, and **51**[131] were synthesized using the standard procedure of reacting the corresponding dipyrromethene hydrobromide salt with 5 equivalents of both zinc(II) actetate dihydrate and sodium acetate trihydrate.[80] Characterization data reported in the literature for compound **47** agree with the data collected for this study.[217] A procedure involving the in-situ preparation of the dipyrromethene followed by subsequent complexation by zinc(II) was used for the synthesis of zinc(II) 5-aryl dipyrromethene complexes **52**[26] and **53**. The isolation of the zinc(II) di[5-(4-pyridyl)dipyrromethene] (**53**) was complicated by decomplexation of the dipyrromethene complex during purification by silica flash chromatography. Consequently, the product was obtained as a mixture with dipyrromethene **46**. The use of basic alumina as a stationary phase also resulted in

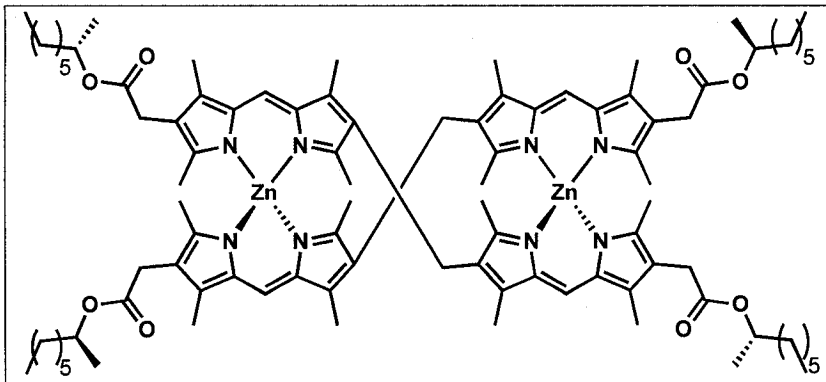
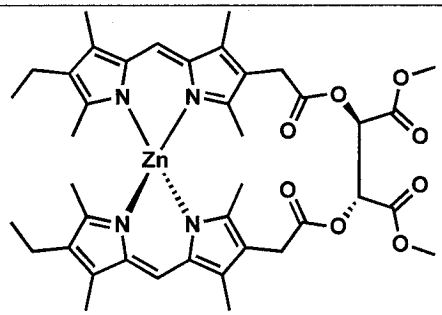
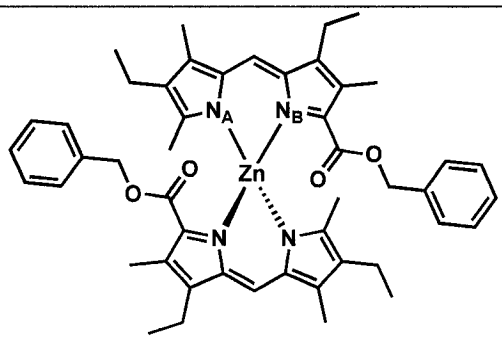
decomplexation of the product and the inclusion of 0.5% (v/v) triethyamine in the eluent failed to prevent this reaction.

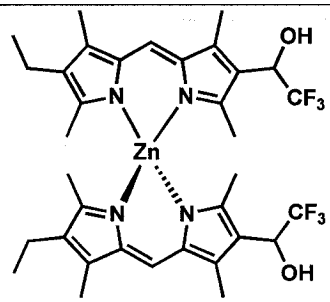
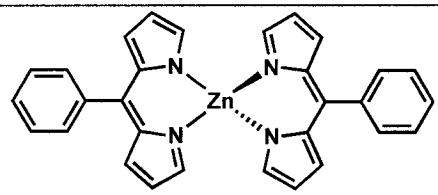
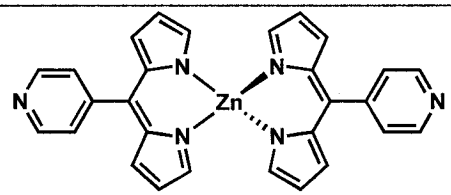
The measurement of ^{15}N chemical shifts for the series of zinc(II) dipyrromethene complexes was conducted by correlating the ^{1}H NMR signal of the hydrogen atoms three bonds away from the nitrogen centers. A similar HMBC NMR experiment was tried for obtaining the $\delta^{15}N$ data for compound **9l**, however there was no improvement in signal-to-noise ratio in the same amount of experiment time obtained using the HSQC experiment, and so the HSQC experiment was employed for the zinc(II) complexes herein.

The structures and $\delta^{15}N$ data for zinc(II) dipyrromethene complexes are shown in Table 8. The ^{15}N chemical shift values show some variation, although an average value of approximately -167 ppm represents the data for the zinc(II) complexes of the 5-unsubstituted dipyrromethenes. Symmetrical zinc(II) complexes **47**, **48**, **52**, and **53** exhibit only one signal corresponding to the two nitrogen atoms located in the dipyrromethene portion of each molecule, and this equivalence by resonance is supported by X-ray photoelectron studies.[216] Analysis of ^{15}N NMR spectra for diastereomeric mixtures of the *P* and *M* helicates of zinc(II) bis(dipyrromethene) complexes **9l** and **49**[130] failed to resolve separate chemical shifts for the two diastereomers.

Table 8. Data for ^{15}N chemical shifts and complexation shifts of zinc(II) dipyrromethene complexes **9k**, **51**, and **47-53**

Structure	$\delta^{15}N$ (ppm)	$\Delta\delta^{15}N$ (ppm)
 **47**	-169.5	+44.2[a]
 **48**	-167.5	-
 **10**	-166.3 -171.1	-

 **91**	-165 -172	+49.8 [a]
 **49**	-167.5 -170.5	-
 **50**	-152.8 (A) -174.9 (B)	+49.9 [a] +49.7 [a]

 **51**	-166.6 -170.2	+43.2 [a]
 **52**	-162.2	-6.0 [b]
 **53**	-162.5 -69.0	-6.4 [b] n/a

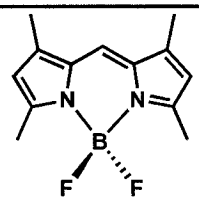
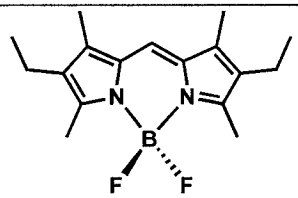
[a]average, measured from corresponding dipyrromethene hydrobromide salt. [b]measured from corresponding free-base dipyrromethene

The ^{15}N zinc(II) complexation shifts were calculated for compounds **47**, **9l**, **50**, and **51** from their corresponding dipyrromethene hydrobromide salts. The majority of this shift, which averages +45 ppm, likely constitutes a deprotonation shift, as discussed previously, with a small contribution from zinc(II) complexation. The $\Delta\delta^{15}N$ shown for compound **50** were assigned using NOESY NMR experiments. The complexation shift for compounds **52** and **53** were calculated from the free-base dipyrromethenes and therefore represent $\Delta\delta^{15}N$ calculated by its true definition.[193] The calculated value for $\Delta\delta^{15}N$ of approximately -6 ppm for the formation of zinc(II) complexes from free-base

dipyrromethenes is much lower and in the opposite direction of those measured for the formation of zinc(II) complexes from protonated dipyrromethenes. This value is also opposite in direction, although similar in magnitude, relative to the zinc(II) complexation shift reported for free-base tetraphenylporphyrin.[196] The ^{15}N chemical shift of the pyridyl nitrogen in compound **53** did not change significantly from that of the corresponding dipyrromethene **46** which supports the discrete 2:1 dipyrromethene:zinc(II) structure proposed for this compound rather than the coordination polymer structure that has been reported for similar 5-(pyridyl)dipyrromethene metal complexes.[218,219]

The structures and values for $\delta^{15}N$ of borondifluoride complexes **32**[220] and **33**,[217] prepared according to literature procedures, are shown in Table 10. In analogy to their corresponding zinc(II) complexes, **48** and **47** respectively, the BODIPY compounds exhibit equivalence by resonance of the two nitrogen atoms in their structures. The ^{15}N complexation shift for compound **33**, as measured from the dipyrromethene hydrobromide salt **40**, is +19.1 ppm. This value, which should encompass a deprotonation shift as well as a borondifluoride complexation shift, is less than the reported value of +47.2 ppm for 1,2,3,7,8,9-tetramethyldipyrromethene, a highly structurally-related compound.[206] Therefore it can be predicted that the borondifluoride complexation shift is ~-28 ppm when calculated from the corresponding free-base dipyrromethene. ^{15}N NMR analysis of a borondifluoride 5-aryl dipyrromethene complex would clarify this matter.

Table 9. Data for ^{15}N chemical shifts of borondifluoride dipyrromethene complexes **32** and **33**

Structure	$\delta^{15}N$ (ppm)	$\Delta\delta^{15}N$ (ppm)
 **32**	-192.1	-
 **33**	-194.6	+19.1 (from **40**)

4.4. Conclusions

The use of ^{15}N NMR chemical shifts measured using ^{15}N-^{1}H correlation experiments such as HSQC and HMBC is feasible as a means of routine characterization of dipyrrolic compounds such as dipyrromethanes, dipyrromethenes and dipyrromethene complexes. Although the $\delta^{15}N$ values are not yet suitable for predicting fine structural differences due to the unpredictable effect of substituents, they are suitable for predicting gross structural features of unknown dipyrrolic compounds. A chart showing patterns in $\delta^{15}N$ collected for this study as related to structure is presented in Figure 70. The outlying values for the 5-unsubstituted dipyrromethene hydrobromide salts and the zinc(II) 5-unsubstituted dipyrromethene complexes arise from compound **43** and its corresponding zinc(II)

complex **50**, respectively. It can be seen from the diagram that $\delta^{15}N$ values are diagnostic for the structure of the dipyrrolic compound.[221]

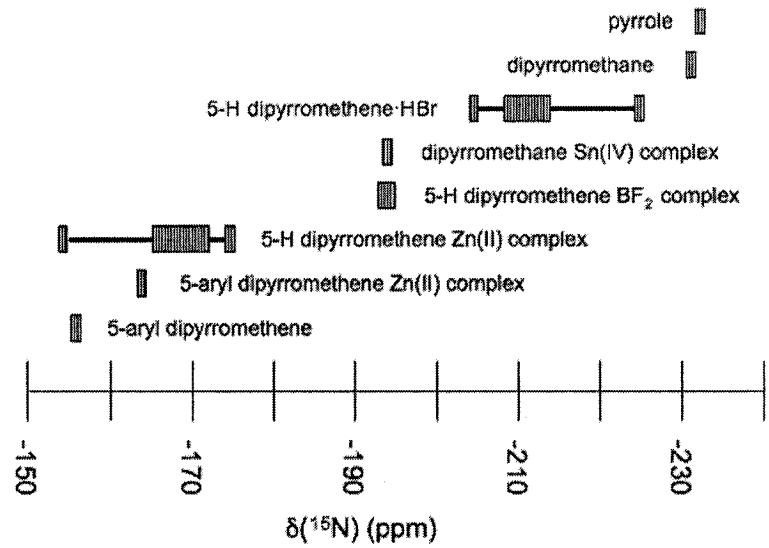


Figure 70. Summary of ^{15}N chemical shifts for a variety of dipyrrolic structures in comparison to pyrrole

Future work in this area will involve the measurement of complexation shifts for 5-aryl and 5-unsubstituted dipyrromethene complexes of a variety of metal ions, including nickel(II) and palladium(II). Making the HSQC and HMBC experiments more generalized is another future goal for this project, because there have been some unexplained instances when signals were not obtained for samples analyzed using these experiments.

Chapter 5. Experimental

5.1. General Experimental

Melting points were measured using a Fisher-Johns apparatus, and are reported uncorrected. Nuclear magnetic resonance experiments for ^{1}H, ^{13}C, ^{15}N, ^{119}Sn nuclei were conducted using a Bruker Avance 500 MHz spectrometer using a BBO probe equipped with *z*-axis gradients, except for those ^{1}H spectra, as indicated, that were conducted using a Bruker/Tecmag AC-250 spectrometer equipped with a 5 mm QNP probe. The shift scales were referenced as outlined in the IUPAC Recommendations of 2001.[222] High-resolution EI mass spectrometry measurements were obtained using a DuPont CEC 21-110B double-focusing magnetic sector instrument, with an ionization voltage of 70 V. ESI Mass spectrometry measurements were obtainted using a Thermo Finnigan LCQ Duo ion trap, operating in flow-injection mode using a flow rate of 1.5 mL h^{-1} (methanol), and using a spray voltage of 4 kV. APCI Mass spectrometry measurements were obtainted using a Thermo Finnigan LCQ Duo ion trap, using a vapourizing temperature of 350 °C. MALDI Mass spectrometry measurements were obtained using a Bruker Biflex IV instrument using dithranol as the matrix. UV-Visible spectral data were obtained using a Varian-Cary 100-BIO UV-visible spectrometer. Circular dichroism spectra were recorded using a Jasco J-810 spectropolarimeter. Chiral HPLC resolutions were performed using a Jasco MD-910 instrument, with columns as indicated in the experimental data. Chromatography was performed using 230-400 mesh ultra pure silica. With the exclusion of solvents, chemicals used in the preparations were received from suppliers and used without further purification. Dry DCM and THF were obtained from an Innovative Technology solvent purification system by filtration through alumina.

5.2. ^{15}N NMR Experiment Parameters

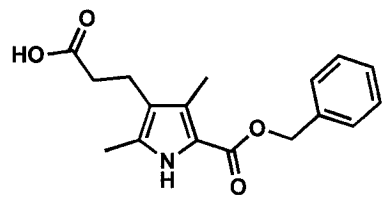
^{15}N-^{1}H HSQC experiments were used to measure ^{15}N NMR chemical shifts as described in Chapter 4.3.1. The ^{15}N chemical shift scale was referenced as outlined in the IUPAC Recommendations of 2001 by which nitromethane exhibits $\delta^{15}N = 0$ ppm.[222] Non-decoupled experiments were used to determine the one-bond ^{15}N-^{1}H coupling constants. Each experiment had an acquisition time of about 1 hour for samples that had a concentration of approximately 0.2 M. All samples were prepared as solutions in $CDCl_3$. *J*-values of -95 Hz were used to correlate one-bond ^{15}N-^{1}H couplings while -5 Hz was used for three-bond ^{15}N-^{1}H couplings.

5.3. Synthesis of Compounds

The following compounds were prepared by established procedures: benzyl 4-(methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate[134] (**1**), benzyl 4-(methoxycarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate[175] (**2**), 2,2',4,4'-tetramethyl-5,5'-diformyl-3,3'-dipyrromethane[137] (**7**), zinc(II) di[2,2'-bis(8-ethyl-1,3,7,9-tetramethyldipyrromethene)][137] (**10**), 4-ethyl-3,5-dimethylpyrrole-2-carboxaldehyde[60] (**11c**), ethyl 3,5-dimethylpyrrole-2-carboxylate[175] (**12a**), benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**), benzyl 4-(2-hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate[184] (**24**), *N,N'*-difluoroboryl-1,3,7,9-tetramethyldipyrromethene[220,191] (**32**), *N,N'*-difluoroboryl-2,8-diethyl-1,3,7,9-tetramethyldipyrromethene[217] (**33**), diethyl 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate[223] (**34**), diethyl 2,2',4,4'-tetramethyl-3,3'-dipyrromethane-5,5'-dicarboxylate[137] (**35**), diethyl 3,3'-dibromo-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate[208] (**36**), *meso*-phenyldipyrromethane[7] (**37**), 5-(4-pyridyl)dipyrromethene[209] (**38**), benzyl 3,8-diethyl-2,7,9-

trimethyldipyrromethene-1-carboxylate hydrobromide[213] (**43**), 8-ethyl-1,3,7,9-tetramethyl-2-(2,2,2-trifluoro-1-hydroxyethyl)dipyrromethene hydrobromide[131] (**44**), 5-phenyldipyrromethene[224] (**45**), zinc(II) dimethyl-(L)-tartrate-*O,O'*-(8-ethyl-1,3,7,9-tetramethyldipyrromethene-2-propanoate)[130] (**49**), zinc(II) di[8-ethyl-1,3,7,9-tetramethyl-2-(2,2,2-trifluoro-1-hydroxyethyl)dipyrromethene][131] (**51**), zinc(II) di(5-phenyldipyrromethene)[26] (**52**) ethyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate,[225] 3,4-dimethylpyrrole-2-carboxaldehyde,[226] 3,5-dimethylpyrrole-2-carboxaldehyde,[227] and 1,3,7,9-tetramethyldipyrromethene hydrobromide.[228]

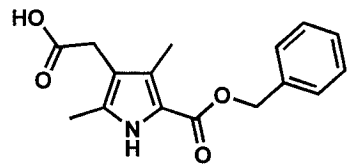
Benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate[140] (**3**)



A solution of lithium hydroxide monohydrate (2.0 g, 47 mmol) in a 1:1 (v/v) tetrahydrofuran (THF):water solution (190 mL) was added, with stirring, to a solution of benzyl 3,5-dimethyl-4-(methoxycarbonylethyl)pyrrole-2-carboxylate[134] (**1**) (15 g, 48 mmol) dissolved in a 1:1 (v/v) THF:water solution (60 mL) contained in a 500 mL round-bottom flask. This mixture was stirred at room temperature for 24 hours. The reaction mixture was washed with dichloromethane (DCM) (2 x 30 mL), and then the aqueous phase was acidified with 5% (w/v) aqueous solution of hydrochloric acid, resulting in the precipitation of a white solid. The mixture was filtered to give the product as a white powder. (Yield: 13 g, 93%)

Sol: acetone, chloroform, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: DCM, ethanol; Insol: water, diethyl ether, hexanes; R_f 0.11 (silica, 30% ethyl acetate 70% hexanes); m.p. 126-127 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 2.15 (3H, s, ArCH_3), 2.29 (3H, s, ArCH_3), 2.47 (2H, t, J = 7.5 Hz, $CH_2CH_2C(O)$), 2.72 (2H, t, J = 7.5 Hz, ArCH_2CH_2), 5.29 (2H, s, CH_2Ph), 7.32-7.42 (5H, m, Ar*H*), 8.86 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, acetone-d_6): 10.9 (ArCH_3), 11.3 (ArCH_3), 20.3 (ArCH_2CH_2), 35.4 ($CH_2CH_2C(O)$), 65.5 (CH_2Ph), 117.3 (4° Ar), 121.0 (4° Ar), 127.9 (4° Ar), 128.7 (ArH), 128.9 (ArH), 129.3 (ArH), 131.7 (4° Ar), 138.3 (4° Ar), 161.6 (*C*(O)OBn), 174.7 (*C*(O)OH) (assignment by JMOD and ^{13}C-^1H HSQC experiments); calcd 301.1314 for $C_{17}H_{19}NO_4$; EI(+ve)-HRMS found *m/z* 301.1312 $(M)^+$.

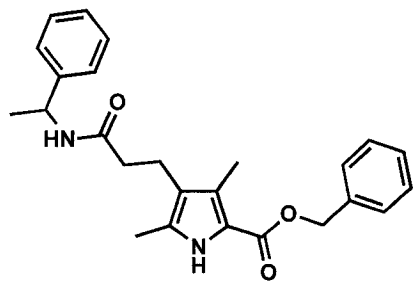
Benzyl 4-(ethanoic acid)-3,5-dimethylpyrrole-2-carboxylate[130] (**4**)



A solution of lithium hydroxide monohydrate (2.0 g, 47 mmol) in a 1:1 (v/v) THF:water solution (40 mL) was added, with stirring, to a solution of benzyl 4-(methoxycarbonylmethyl)-3,5-dimethylpyrrole-2-carboxylate[175] (**2**) (14 g, 47 mmol) dissolved in a 1:1 (v/v) THF:water solution (100 mL) contained in a 500 mL round-bottom flask. The mixture was stirred at room temperature for 24 hours. The reaction mixture was washed with ethyl acetate (2 x 30 mL), and then the aqueous phase was acidified with 5% (w/v) aqueous solution of citric acid, resulting in the precipitation of a white solid. The mixture was filtered to give the product as a white powder. (Yield: 12.2 g, 91%)

Sol: acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: chloroform, DCM, ethanol; Insol: water, diethyl ether, hexanes; m.p. 193-194 °C; ^{1}H: δ(500 MHz, acetone-d_6): 2.24 (3H, s, ArCH_3), 2.29 (3H, s, ArCH_3), 3.38 (2H, s, ArCH_2C(O)), 5.26 (2H, s, CH_2Ph), 7.30-7.44 (5H, m, ArH), 10.37 (1H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, acetone-d_6): 10.9 (ArCH$_3$), 11.3 (ArCH$_3$), 30.2 (ArCH$_2$C(O)), 65.5(CH$_2$Ph), 115.9 (4° Ar), 117.4 (4° Ar), 128.6 (4° Ar), 128.7 (ArH), 128.9 (ArH), 129.3 (ArH), 132.5 (4° Ar), 138.3 (4° Ar), 161.6 (C(O)OBn), 173.1 (C(O)OH) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 287.1157 for $C_{16}H_{17}NO_4$; EI(+ve)-HRMS found *m/z* 287.1160 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*S* or *R*)-2-(1-phenylethylcarbamoyl)ethyl]pyrrole-2-carboxylate[140] (**5a,b**)

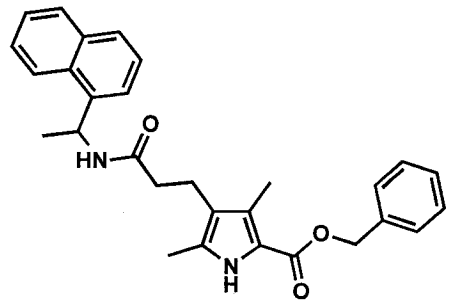


Under dry conditions and using nitrogen gas as an inert atmosphere benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate (**3**) (2.0 g, 6.6 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (0.81g, 6.6 mmol) were dissolved, with stirring, in dry DCM (50 mL) in a dry two-neck 250 mL round-bottom flask. The resulting solution was cooled to 0 °C by suspension in an ice bath. At this lowered temperature (*S*)-(-)-α-methylbenzylamine (to prepare **5a**) or (*R*)-(+)-α-methylbenzylamine (to prepare **5b**) (0.86 mL, 6.7 mmol) was added by syringe. The resulting solution was stirred for 30

seconds until a light pink solid began to form. At this time additional dry DCM (20 mL) was added, followed by *O*-benzotriazol-1-yl-*N,N,N′,N′*-tetramethyluronium hexafluorophosphate (HBTU) (2.5 g, 6.6 mmol). The reaction warmed to room temperature and was stirred for two days. The mixture was then filtered, concentrated, washed with 5% (w/v) aqueous hydrochloric acid solution (2 x 50 mL), washed with brine (20 mL) and concentrated using a rotary evaporator. Chromatographic separation on silica using 30% (v/v) ethyl acetate/hexanes as the eluent gave the product as a white solid. (Yield: 2.6 g, 99%)

Sol: chloroform, methanol, dimethylsulfoxide; Sp. Sol: DCM, acetone, ethyl acetate, ethanol; Insol: water, diethyl ether, hexanes; R_f 0.21 (silica, 40% ethyl acetate 60% hexanes); m.p. 200-203 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.41 (3H, d, J = 6.7 Hz, $CHCH_3$), 2.09 (3H, s, $ArCH_3$), 2.23-2.29 (5H, m, $ArCH_3$ + $CH_2CH_2C(O)$), 2.72 (2H, t, J = 6.9 Hz, $ArCH_2CH_2$), 5.04-5.09 (1H, m, $CHCH_3$), 5.30 (2H, s, CH_2Ph), 5.42 (1H, br d, J = 7.6 Hz, amide N*H*), 7.14-7.41 (10H, m, Ar*H*), 8.44 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.9 ($ArCH_3$), 11.6 ($ArCH_3$), 20.4 ($ArCH_2CH_2$), 22.0 ($CHCH_3$), 37.8 ($CH_2CH_2C(O)$), 48.8 ($CHCH_3$), 65.7 (CH_2Ph)), 116.9 (4° Ar), 120.6 (4° Ar), 126.3 (ArH), 127.5 (ArH), 127.6 (4° Ar), 128.3 (ArH), 128.4 (ArH), 128.8 (ArH), 128.8 (ArH), 130.6 (4° Ar), 136.8 (4° Ar), 143.9 (4° Ar), 156.9 (*C*=O), 171.2 (*C*=O) (assignment by ^{13}C-^1H HSQC experiments); calcd 404.2100 for $C_{25}H_{28}N_2O_3$; EI(+ve)-HRMS found *m/z* 404.2093 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)ethyl]pyrrole-2-carboxylate[141] (**5c,d**)

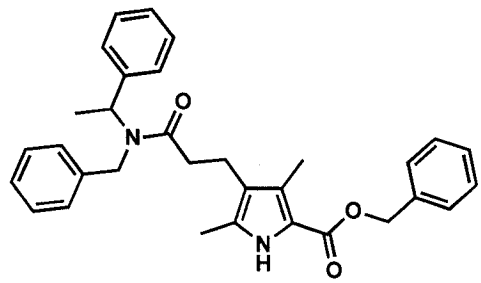


Following the procedure used for the preparation of **5a**, **3** (2.0 g, 6.6 mmol) and DMAP (0.81 g, 6.6 mmol) were dissolved in dry DCM (50 mL). (*S*)-(-)-1-(1-Naphthyl)-α-ethylamine (to prepare **5c**) or (*R*)-(+)-1-(1-naphthyl)-α-ethylamine (to prepare **5d**) (1.1 mL, 6.7 mol) and HBTU (2.5 g, 6.6 mmol) were added to this solution. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white solid. (Yield: 2.2 g, 72%)

Sol: chloroform, methanol, dimethylsulfoxide; Sp. Sol: DCM, acetone, ethyl acetate, ethanol; Insol: water, diethyl ether, hexanes; R_f 0.28 (silica, 40% ethyl acetate 60% hexanes); m.p. 189-190 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.58 (3H, d, J = 7.0 Hz, $CHCH_3$), 2.06 (3H, s, $ArCH_3$), 2.25 (3H, s, $ArCH_3$), 2.27 (2H, t, J = 7.3 Hz, $CH_2CH_2C(O)$), 2.72 (2H, t, J = 7.0 Hz, $ArCH_2CH_2$), 5.29 (2H, s, CH_2Ph), 5.50 (1H, d, J = 7.6 Hz, amide NH), 5.82-5.93 (1H, m, $CHCH_3$), 7.29-7.51 (9H, m, ArH), 7.75 (1H, d, J = 7.9 Hz, ArH), 7.83 (1H, d, J = 8.1 Hz, ArH), 8.03 (1H, d, J = 7.3 Hz, ArH), 8.43 (1H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.9 ($ArCH_3$), 11.6 ($ArCH_3$), 20.4 ($ArCH_2CH_2$), 21.1 ($CHCH_3$), 37.7 ($CH_2CH_2C(O)$), 44.9 ($CHCH_3$), 65.7 (CH_2Ph), 116.9 (4° Ar), 120.6 (4° Ar), 122.7 (ArH), 123.6 (ArH), 125.4 (ArH), 126.0 (ArH), 126.7 (ArH), 128.3 (ArH), 128.5 (ArH), 128.8 (ArH), 129.0 (ArH), 130.5 (4° Ar), 131.2 (4°

Ar), 134.1 (4° Ar), 136.8 (4° Ar), 138.6 (4° Ar), 162.0 (*C*=O), 171.4 (*C*=O) (one ArH and one 4° Ar signal not resolved, assignment by ^{13}C-^{1}H HSQC experiment); calcd 454.2256 for $C_{29}H_{30}N_2O_3$; EI(+ve)-HRMS found *m/z* 454.2266 $(M)^+$.

Benzyl 4-[(*S* or *R*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate[141] (**5e,f**)

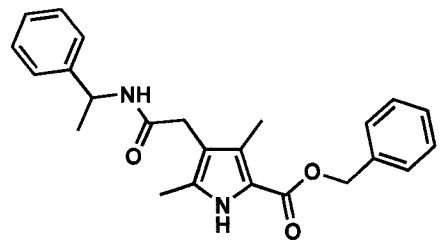


Following the procedure used for the preparation of **5a**, **3** (2.0 g, 6.6 mmol) and DMAP (0.81 g, 6.6 mmol) were dissolved in dry DCM (50 mL). (*S*)-(-)-*N*-Benzyl-α-methylbenzylamine (to prepare **5e**) or (*R*)-(+)-*N*-benzyl-α-methylbenzylamine (to prepare **5f**) (1.4 mL, 6.7 mol) and HBTU (2.5 g, 6.6 mmol) were added to this solution. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a yellow oil. (Yield: 3.1 g, 95%)

Sol: chloroform, DCM, acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: ethanol; Insol: water, diethyl ether, hexanes; R_f 0.26 (silica, 30% ethyl acetate 70% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.42 (3H, d, J = 7.0 Hz, $CHCH_3$), 2.08 (3H, s, $ArCH_3$), 2.11 (3H, s, $ArCH_3$), 2.25-2.39 (2H, m, $CH_2CH_2C(O)$), 2.68-2.88 (2H, m, $ArCH_2CH_2$), 3.99 (¼ x 1H, d, J = 15.5 Hz, $CH_AH_{A'}Ph$), 4.11 (¾ x 1H, d, J = 18.0 Hz, $CH_AH_{A'}Ph$), 4.31 (¾ x 1H, d, J = 18.0 Hz, $CH_AH_{A'}Ph$), 4.92 (¼ x 1H, d, J = 15.5 Hz, $CH_AH_{A'}Ph$), 5.13-5.14 (¼ x 1H, m, $CHCH_3$), 5.28 (2H, s, CH_2Ph), 6.17-6.18 (¾ x 1H, m,

C*H*CH_3), 6.99-7.39 (15H, m, Ar*H*), 8.48 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.7, 11.4, 17.1, 20.2, 34.6, 47.2, 51.6, 56.0, 65.5, 77.0, 77.2, 77.5, 116.6, 120.7, 125.7, 126.6, 127.1, 127.5, 127.6, 128.0, 128.3, 128.5, 128.6, 128.7, 128.8, 130.9, 136.8, 138.6, 139.4, 140.9, 141.2, 161.5, 173.9; calcd 494.2569 for $C_{32}H_{34}N_2O_3$; EI(+ve)-HRMS found *m/z* 494.2567 $(M)^+$.

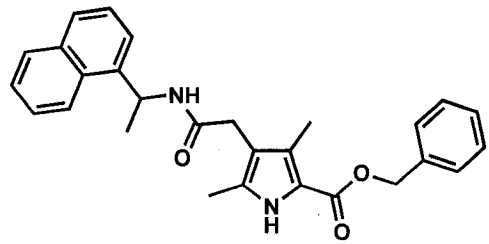
Benzyl 3,5-dimethyl-4-[(*S* or *R*)-2-(1-phenylethylcarbamoyl)methyl]pyrrole-2-carboxylate[141] (**5g,h**)



Following the procedure used for the preparation of **5a**, benzyl 4-(ethanoic acid)-3,5-dimethylpyrrole-2-carboxylate (**4**) (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). (*S*)-(-)-α-Methylbenzylamine (to prepare **5g**) or (*R*)-(+)-α-methylbenzylamine (to prepare **5h**) (0.27 mL, 2.1 mol) and HBTU (0.87 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white solid. (Yield: 0.76 g, 95%)
Sol: chloroform, DCM, acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: ethanol; Insol: water, diethyl ether, hexanes; R_f 0.52 (silica, 60% ethyl acetate 40% hexanes); m.p. 182-184 °C; ^1H NMR: δ(250 MHz, $CDCl_3$): 1.39 (3H, d, J = 7.0 Hz, CHC*H*$_3$), 2.16 (3H, s, ArC*H*$_3$), 2.24 (3H, s, ArC*H*$_3$), 3.35 (2H, s, ArC*H*$_2$C(O)), 5.08-5.19 (1H, m, C*H*CH_3), 5.30 (2H, s, C*H*$_2$Ph), 5.73 (1H, br d, *J* = 8.3 Hz, amide N*H*), 7.16-7.45 (10H, m, Ar*H*), 8.88 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.9, 11.6,

21.9, 32.4, 48.6, 65.9, 115.2, 117.7, 126.1, 127.4, 128.0, 128.3, 128.4, 128.8, 131.7, 136.5, 143.3, 161.5, 170.2 (one signal not resolved); calcd 390.1943 for $C_{24}H_{26}N_2O_3$; EI(+ve)-HRMS found *m/z* 390.1949 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)methyl]pyrrole-2-carboxylate[141] (**5i,j**)

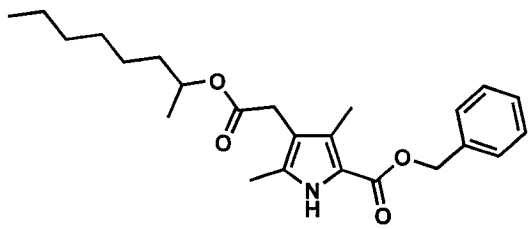


Following the procedure used for the preparation of **5g**, **4** (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). (*S*)-(-)-1-(1-Naphthyl)-α-ethylamine (to prepare **5i**) or (*R*)-(+)-1-(1-naphthyl)-α-ethylamine (to prepare **5j**) (0.33 mL, 2.1 mol) and HBTU (0.87 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white solid. (Yield: 0.62 g, 68%)

Sol: methanol, dimethylsulfoxide; Sp. Sol: chloroform, DCM, acetone, ethyl acetate, ethanol; Insol: water, diethyl ether, hexanes; R_f 0.60 (silica, 60% ethyl acetate 40% hexanes); m.p. 174-177 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.58 (3H, d, J = 7.3 Hz, CHC*H*$_3$), 2.03 (3H, s, ArC*H*$_3$), 2.15 (3H, s, ArC*H*$_3$), 3.35 (2H, s, ArC*H*$_2$C(O)), 5.26 (2H, s, C*H*$_2$Ph), 5.73 (1H, br d, J = 8.3 Hz, amide N*H*), 5.85-5.96 (1H, m, C*H*CH$_3$), 7.31-7.53 (9H, m, Ar*H*), 7.74-7.86 (2H, m, Ar*H*), 8.01-8.04 (1H, m, Ar*H*), 8.64 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.8 (Ar*C*H$_3$), 11.6 (Ar*C*H$_3$), 21.0 (CH*C*H$_3$), 32.4 (Ar*C*H$_2$C(O)), 44.9 (*C*HCH$_3$), 65.9 (*C*H$_2$Ph), 115.2 (4° Ar), 117.6 (4° Ar), 122.7 (ArH),

123.6 (ArH), 125.3 (ArH), 126.0 (ArH), 126.6 (ArH), 128.4 (ArH), 128.6 (ArH), 128.8 (ArH), 129.0 (ArH), 131.2 (4° Ar), 131.4 (4° Ar), 134.1 (4° Ar), 136.5 (4° Ar), 138.3 (4° Ar), 161.2 (*C*=O), 170.0 (*C*=O) (two 4° Ar signals not resolved, assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 440.2100 for $C_{28}H_{28}N_2O_3$; EI(+ve)-HRMS found *m/z* 440.2101 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*S* or *R*)-1-(methylheptyloxycarbonyl)methyl]pyrrole-2-carboxylate[141] (**5k,l**)

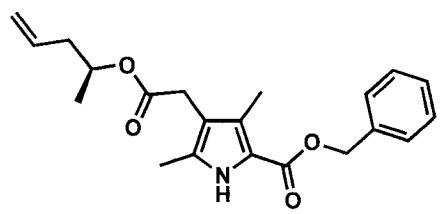


Following the procedure used for the preparation of **5g**, **4** (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). (*S*)-(+)-2-Octanol (to prepare **5k**) or (*R*)-(-)-2-octanol (to prepare **5l**) (0.27 mL, 2.1 mol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC·HCl) (0.44 g, 2.3 mmol) and 1-hydroxybenzotriazol hydrate (HOBT) (0.31 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white waxy solid. (Yield: 0.32 g, 39%)

Sol: chloroform, DCM, acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: ethanol; Insol: water, diethyl ether, hexanes; R_f 0.77 (silica, 50% ethyl acetate 50% hexanes); m.p. 39-41 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 0.86 (3H, t, J = 6.6 Hz, CH_2CH_3), 1.16-1.25 (11H, m, $CHCH_3$ + $CH_2(CH_2)_4CH_3$), 1.43-1.59 (2H, m, $CHCH_2CH_2$), 2.23 (3H, s, $ArCH_3$), 2.30 (3H, s, $ArCH_3$), 3.34 (2H, s, $ArCH_2C(O)$), 4.86

(1H, sextet, J = 6.4 Hz, C*H*CH_3), 5.30 (2H, s, CH_2Ph), 7.32-7.43 (5H, m, Ar*H*), 8.58 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.9 (Ar*C*H_3), 11.6 (Ar*C*H_3), 14.2 (CH_2*C*H_3), 20.1 (CH*C*H_3), 22.6 (CH_2*C*H_2CH_2), 25.3 (CH_2*C*H_2CH_2), 29.2 (CH_2*C*H_2CH_2), 30.7 (Ar*C*H_2C(O)), 31.8 (CHCH_2*C*H_2), 36.0 (CH*C*H_2CH_2), 65.6 (*C*H_2Ph), 71.4 (*C*HCH_3), 115.1 (4° Ar), 116.8 (4° Ar), 128.0 (4° Ar), 128.1 (ArH), 128.2 (ArH), 128.6 (ArH), 131.7 (4° Ar), 136.7 (4° Ar), 161.7 (*C*=O), 171.6 (*C*=O) (assignment by DEPT and ^{13}C-^1H HSQC experiments); calcd 399.2409 for $C_{24}H_{33}NO_4$; EI(+ve)-HRMS found *m/z* 399.2403 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*S*)-1-(methylbut-3-enyloxycarbonyl)methyl]pyrrole-2-carboxylate[141] (**5m**)

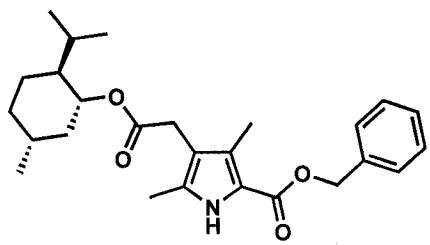


Following the procedure used for the preparation of **5g**, **4** (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). (*S*)-4-Penten-2-ol (0.21 mL, 2.1 mol), EDC·HCl (0.44 g, 2.3 mmol), and HOBT (0.31 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a colourless oil. (Yield: 0.36 g, 44%)

Sol: chloroform, DCM, acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: ethanol; Insol: water, diethyl ether, hexanes; R_f 0.68 (silica, 60% ethyl acetate 40% hexanes); ^1H NMR: δ(500 MHz, $CDCl_3$): 1.19 (3H, d, J = 6.5 Hz, CHC*H*$_3$), 2.20 (3H, s, ArC*H*$_3$), 2.22-2.32 (5H, m, CHC*H*$_2$ + ArC*H*$_3$), 3.33 (2H, s, ArC*H*$_2$C(O)), 4.93 (1H,

sextet, J = 6.5 Hz, C*H*CH$_3$), 5.04 (2H, d, J = 7.0 Hz, HC=C*H*$_2$), 5.29 (2H, s, C*H*$_2$Ph), 5.65-5.73 (1H, m, *H*C=CH$_2$), 7.29-7.41 (5H, m, Ar*H*), 8.99 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, CDCl$_3$): 11.0 (ArCH$_3$), 11.7 (ArCH$_3$), 19.6 (CHCH$_3$), 30.6 (ArCH$_2$C(O)), 40.4 (CHCH$_2$), 65.7 (CH$_2$Ph), 70.5 (CHCH$_3$), 115.0 (4° Ar), 116.9 (4° Ar), 117.8 (HC=CH$_2$), 128.2(ArH), 128.3 (4° Ar), 128.7 (ArH), 131.5 (4° Ar), 133.8 (HC=CH$_2$), 136.8 (4° Ar), 161.6 (C=O), 171.4 (C=O) (one ArH signal not resolved, assignment by ^{13}C-^{1}H HSQC experiment); calcd 355.1783 for $C_{21}H_{25}NO_4$; EI(+ve)-HRMS found *m/z* 355.1777 $(M)^+$.

Benzyl 3,5-dimethyl-4-[(*R*)-1-(5-(*R*)-isopropyl-2-(*S*)-methylcyclohexyloxycarbonyl)methyl]pyrrole-2-carboxylate[141] (**5n**)

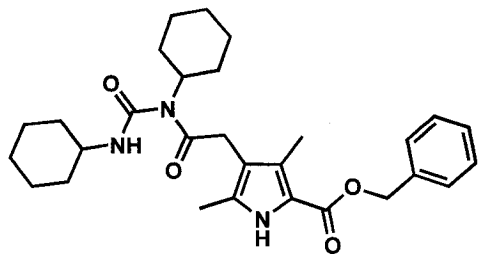


Following the procedure used for the preparation of **5g**, **4** (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). (1*R*,2*S*,5*R*)-Menthol (0.32 g, 2.1 mol), EDC·HCl (0.44 g, 2.3 mmol), and HOBT (0.31 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white solid. (Yield: 0.47 g, 54%)

Sol: chloroform, DCM, acetone, ethyl acetate, methanol, dimethylsulfoxide; Sp. Sol: ethanol; Insol: water, diethyl ether, hexanes; R_f 0.52 (silica, 20% ethyl acetate 80% hexanes); m.p. 99-101 °C; ^{1}H NMR: δ(250 MHz, CDCl$_3$): 0.70 (3H, d, J = 7.0 Hz, CHC*H*$_3$), 0.84-1.04 (9H, m, CH(C*H*$_3$)$_2$ + C*H*$_a$H$_b$ + C*H*$_c$H$_d$ + C*H*$_e$H$_f$), 1.31-1.35 (1H, m,

C*H*CH(CH_3)$_2$), 1.44-1.46 (1H, m, C*H*CH_3), 1.62-1.75 (3H, m, CH_aH_b + CH_eH_f + C*H*(CH_3)$_2$), 1.92-1.95 (1H, m, CH_cH_d), 2.21 (3H, s, ArCH_3), 2.29 (3H, s, ArCH_3), 3.34 (2H, s, ArCH_2C(O)), 4.61-4.67 (1H, m, C*H*O), 5.29 (2H, s, CH_2Ph), 7.30-7.40 (5H, m, Ar*H*), 8.78 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.9 (ArCH_3), 11.8 (ArCH_3), 16.5 (CHCH_3), 20.9 (CH(CH_3)$_a$(CH_3)$_b$), 22.2 (CH(CH_3)$_a$(CH_3)$_b$), 23.7 (CH_2CH_2 $CH(CH_3)$), 26.5 (*C*H(CH_3)$_2$), 30.7 (ArCH_2C(O)), 31.6 (*C*HCH_3), 34.5 (CH_2CH_2 $CH(CH_3)$), 41.0 (*C*H_2CHO), 47.4 (*C*HCH(CH_3)$_2$), 65.7 (*C*H_2Ph), 74.7 (*C*HO), 115.3 (4° Ar), 116.9 (4° Ar), 128.2 (ArH), 128.4 (4° Ar), 128.7 (ArH), 131.3 (4° Ar), 136.8 (4° Ar), 161.5 (*C*=O), 171.5 (*C*=O) (one ArH signal not resolved, assignment by JMOD and ^{13}C-^1H HSQC experiments); calcd 425.2566 for $C_{26}H_{35}NO_4$; EI(+ve)-HRMS found *m/z* 425.2572 $(M)^+$.

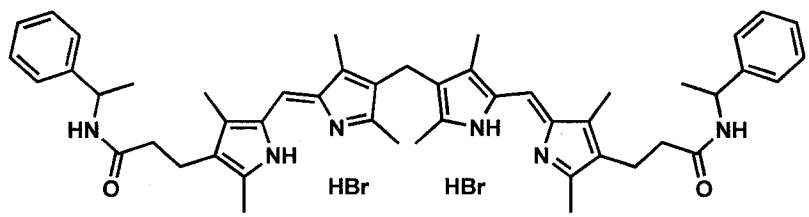
Benzyl 3,5-dimethyl-4-[2-(1,3-dicyclohexylureido)-2-oxoethyl]pyrrole-2-carboxylate[141] (**6**)



Obtained as a sideproduct during the preparation of **5g-j** using *N,N'*-dicyclohexylcarbodiimide (DCC) as the coupling reagent instead of HBTU. Procedure: **4** (0.59 g, 2.1 mmol) and DMAP (0.27 g, 2.3 mmol) were dissolved in dry THF (20 mL). The appropriate chiral amine (2.1 mol) and DCC (0.47 g, 2.3 mmol) were added. The mixture was stirred for two days. The work-up and purification were the same as for **5a**. The product is a white solid. (Yield varied between ~15-30%)

Sol: chloroform, methanol; Sp. Sol: DCM, acetone; Insol: water, diethyl ether, hexanes; R_f 0.79 (silica, 60% ethyl acetate 40% hexanes); m.p. 156-159 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.12-1.37 (12H, m, CH_2 + CH_2 + CH_aH$_b$ + CH_cH$_d$ + CH_eH$_f$ + CH_gH$_h$) 1.58-1.81 (4H, m, CH$_c$$H_d$ + CH$_e$$H_f$), 1.92-1.95 (4H, m, CH$_a$$H_b$ + CH$_g$$H_h$), 2.16 (3H, s, ArC$H_3$), 2.25 (3H, s, ArC$H_3$), 3.53 (2H, s, ArC$H_2$C(O)), 3.65-3.67 (1H, m, HNC*H*), 3.93-3.97 (1H, m, C(O)NC*H*), 5.28 (2H, s, CH_2Ph), 7.18 (1H, br s, C(O)N*H*), 7.31-7.40 (5H, m, Ar*H*), 9.06 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 11.1 (ArCH_3), 11.8(ArCH_3), 24.9 (CH_2), 25.5 (CH_2), 25.6 (CH_2), 26.5 (CH_2), 31.1 (CH_2), 32.1 (ArCH_2C(O)), 32.9 (CH_2), 49.9 (NC*H*), 56.7 (NC*H*), 65.6 (CH_2Ph), 115.1 (4° Ar), 117.0 (4° Ar), 128.1 (ArH), 128.2 (ArH), 128.7 (ArH), 131.7 (4° Ar), 136.7 (4° Ar), 154.2 (*C*=O), 161.6 (*C*=O), 172.5 (*C*=O) (one 4° Ar signal not resolved, assignment by ^{13}C-^{1}H HSQC experiment); calcd 493.3 for $C_{29}H_{39}N_3O_4$; ESI(+ve) found *m/z* 516.3 $(M+Na)^+$.

2,2'-Bis{8-[(*S* or *R*)-2-(1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[140] (**8a,b**)



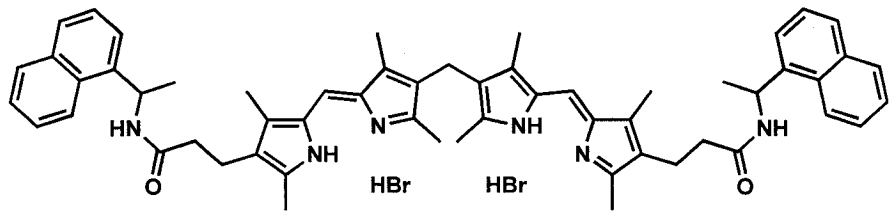
Hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-phenylethylcarbamoyl)ethyl]pyrrole-2-carboxylate (**5a**) (to prepare **8a**) or benzyl 3,5-dimethyl-4-[(*R*)-2-(1-phenylethylcarbamoyl)ethyl]pyrrole-2-carboxylate (**5b**) (to prepare **8b**) (0.50 g, 1.2 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0055 g) in THF (25 mL) contained in a 100 mL round-bottom flask. The

reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (5 mL), 2,2′,4,4′-tetramethyl-5,5′-diformyl-3,3′-dipyrromethane[137] (7) (0.16 g, 0.62 mmol), and 48% (w/v) aqueous hydrobromic acid (0.53 mL, 3.1 mmol) were added to the filtrate contained in a 100 mL round-bottom flask. The reaction immediately turned from a light brown suspension to a very dark red homogenous solution. The reaction mixture was stirred for 30 minutes and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The mixture was filtered and the residue rinsed with cold methanol to give the product as a dark orange solid. (Yield: 0.36 g, 63%)

Sol: methanol, dimethylsulfoxide; Sp. Sol: chloroform, DCM, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, DMSO-d_6): 1.28 (6H, d, J = 7.2 Hz, CHCH_3), 2.11 (6H, s, ArCH_3), 2.27 (6H, s, ArCH_3), 2.31-2.35 (10H, m, ArCH_3 + CH_2CH_2C(O)), 2.44 (6H, s, ArCH_3), 2.50 (6H, s, ArCH_3), 2.63-2.74 (4H, m, ArCH_2CH_2), 3.73 (2H, s, ArCH_2Ar), 4.83-4.89 (2H, m, CHCH$_3$), 7.14-7.25 (10H, m, ArH), 7.37 (2H, s, meso H), 8.28 (2H, br d, J = 7.5 Hz, amide NH), 12.29 (2H, br s, NH), 12.31 (2H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, DMSO-d_6): 10.3 (ArCH$_3$), 10.5 (ArCH$_3$), 13.2 (ArCH$_3$), 13.3 (ArCH$_3$), 19.2 (ArCH$_2$Ar), 20.2 (ArCH$_2$CH$_2$), 22.9 (CHCH$_3$), 35.4 (CH_2CH_2C(O)), 48.2 (CHCH$_3$), 121.0 (meso C), 125.5 (ArH), 126.3 (4° Ar), 126.8 (ArH), 127.1 (4° Ar), 128.5 (ArH), 142.7 (4° Ar), 144.5 (4° Ar), 145.1 (4° Ar), 152.5 (4° Ar), 155.5 (4° Ar), 170.7 (C=O) (two 4° Ar signals not resolved, assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 922.3 for

$C_{49}H_{60}N_6O_2Br_2$; ESI(+ve) found *m/z* 763.2 $(M+1-2HBr)^+$; λ_{max}(DCM): 506 nm, 462 nm; ε_{506}(DCM): $1.72x10^6$ $Lmol^{-1}dm^{-1}$.

2,2'-Bis{8-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8c,d**)

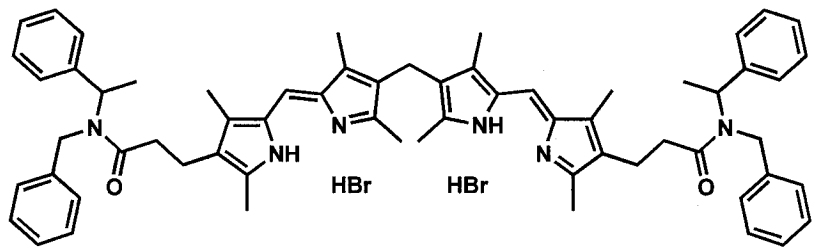


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-naphthylethylcarbamoyl)ethyl]pyrrole-2-carboxylate (**5c**) (to prepare **8c**), or benzyl 3,5-dimethyl-4-[(*R*)-2-(1-naphthylethylcarbamoyl)ethyl]pyrrole-2-carboxylate (**5d**) (to prepare **8d**) (0.56 g, 1.2 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0055 g) in THF (25 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 100 mL round-bottom flask and diluted with methanol (5 mL). Reaction with **7**[137] (0.16 g, 0.62 mmol) and 48% (w/v) aqueous hydrobromic acid (0.53 mL, 3.1 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.45 g, 71%)

Sol: methanol, dimethylsulfoxide; Sp. Sol: chloroform, DCM, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, DMSO-d_6): 1.42 (6H, d, J = 7.2 Hz, $CHCH_3$), 2.23 (6H, s, $ArCH_3$), 2.30 (6H, s, $ArCH_3$), 2.34-2.36 (4H, t, J = 6.9 Hz, $CH_2CH_2C(O)$), 2.43 (6H, s, $ArCH_3$), 2.46 (6H, s, $ArCH_3$), 2.62-2.72 (4H, m, $ArCH_2CH_2$), 3.73 (2H, s, $ArCH_2Ar$), 5.62-5.68 (2H, m, $CHCH_3$), 7.32-

7.38 (4H, m, meso *H* + Ar*H*), 7.35 (2H, d, J = 7.7 Hz, Ar*H*), 7.46 (2H, t, J = 7.5 Hz, Ar*H*), 7.52 (2H, t, J = 7.2 Hz, Ar*H*), 7.75 (2H, d, J = 8.2 Hz, Ar*H*), 7.89 (2H, d, J = 7.7 Hz, Ar*H*), 8.05 (2H, d, J = 8.2 Hz, Ar*H*), 8.41 (2H, d, J = 7.7 Hz, amide N*H*), 12.16 (2H, br s, N*H*), 12.20 (2H, br s, N*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, DMSO-d_6): 10.4 (Ar*C*H_3), 10.4 (Ar*C*H_3), 13.4 (Ar*C*H_3), 13.4 (Ar*C*H_3), 19.3 (Ar*C*H_2Ar), 20.1 (Ar*C*H_2CH_2), 22.1 (CH*C*H_3), 35.3 (CH_2*C*H_2C(O)), 44.4 (*C*HCH$_3$), 121.4 (ArH), 122.6 (4° Ar), 122.7 (ArH), 123.6 (ArH), 125.8 (ArH), 126.6 (ArH), 127.6 (ArH), 128.6 (4° Ar), 129.1 (ArH), 130.7 (4° Ar), 140.8 (4° Ar), 142.9 (4° Ar), 144.5 (4° Ar), 152.4 (4° Ar), 152.7 (4° Ar), 155.2 (meso *C*), 155.3 (4° Ar), 170.6 (*C*=O) (two 4° Ar signals not resolved, due to low sensitivity the ^{13}C NMR data was obtained from calculated projections of ^{13}C-^{1}H HSQC and ^{13}C-^{1}H HMBC experiments); calcd 1022.3 for $C_{57}H_{64}N_6O_2Br_2$; ESI(+ve) found *m/z* 863.5 $(M+1-2HBr)^+$; λ_{max}(DCM): 505 nm, 462 nm; ε_{505}(DCM): $2.37x10^7$ $Lmol^{-1}dm^{-1}$.

2,2'-Bis{8-[(*S* or *R*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8e,f**)

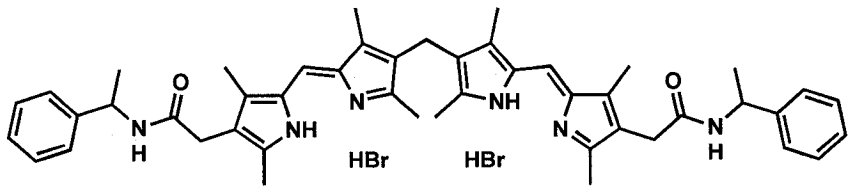


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 4-[(*S*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate (**5e**) (to prepare **8e**) or benzyl 4-[(*R*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-3,5-dimethylpyrrole-2-carboxylate (**5f**) (to prepare **8f**) (0.61 g, 1.2 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0055 g) in THF

(25 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 100 mL round-bottom flask and diluted with methanol (5 mL). Reaction with **7**[137] (0.16 g, 0.62 mmol) and 48% (w/v) aqueous hydrobromic acid (0.53 mL, 3.1 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.49 g, 72%)

Sol: chloroform, DCM, methanol, dimethylsulfoxide; Sp. Sol: ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.47 (6H, d, J = 7.0 Hz, CHCH_3), 2.12 (6H, s, ArCH_3), 2.14 (6H, s, ArCH_3), 2.30-2.34 (4H, m, $CH_2CH_2C(O)$), 2.45 (6H, s, ArCH_3), 2.58 (6H, s, ArCH_3), 2.74-2.80 (4H, m, ArCH_2CH_2), 3.57 (2H, s, ArCH_2Ar), 4.14 (¼ x 2H, d, J = 16.0 Hz, CH_AH$_A$'Ph), 4.21 (¾ x 2H, d, J = 18.0 Hz, CH_AH$_A$'Ph), 4.32 (¾ x 2H, d, J = 18.0 Hz, CH$_A$H$_A$'Ph), 4.98 (¼ x 2H, d, J = 16.0 Hz, CH$_A$H$_A$'Ph), 6.16-5.14 (¼ x 2H, m, CHCH$_3$), 6.16-6.20 (¾ x 2H, m, CHCH$_3$), 6.98-7.33 (22H, m, meso H + ArH), 13.07 (2H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.2, 10.6, 13.0, 13.2, 17.1, 19.7, 19.9 (ArCH_3), 33.7, 47.2, 52.0, 119.2, 124.7, 125.6, 125.8, 126.8, 127.6, 127.7, 128.5, 128.8, 129.0, 138.3, 141.2, 141.3, 143.5, 152.6, 156.4, 172.8 (one peak not resolved); calcd 1102.4 for $C_{63}H_{72}N_6O_2Br_2$; ESI(+ve) found *m/z* 943.5 $(M+1-2HBr)^+$; λ_{max}(DCM): 506 nm, 462 nm; ε_{506}(DCM): $2.35x10^7$ $Lmol^{-1}dm^{-1}$.

2,2'-Bis{8-[(*S* or *R*)-2-(1-phenylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8g,h**)

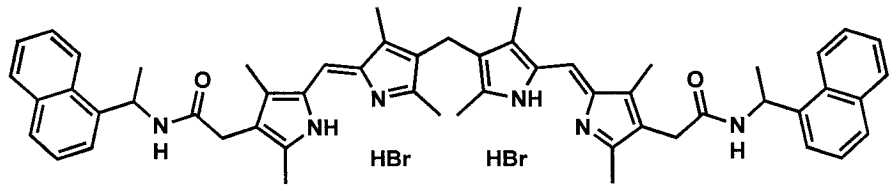


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-phenylethylcarbamoyl)methyl]pyrrole-2-carboxylate (**5g**) (to prepare **8g**) or benzyl 3,5-dimethyl-4-[(*R*)-2-(1-phenylethylcarbamoyl)methyl]pyrrole-2-carboxylate (**5h**) (to prepare **8h**) (0.31 g, 0.80 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0036 g) in THF (20 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 50 mL round-bottom flask and diluted with methanol (10 mL). Reaction with **7**[137] (0.10 g, 0.40 mmol) and 48% (w/v) aqueous hydrobromic acid (0.34 mL, 2.0 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.31 g, 86%)

Sol: dimethylsulfoxide; Sp. Sol: chloroform, DCM, methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, DMSO-d_6): 1.37 (6H, d, J = 5.8 Hz, CHCH_3), 2.28 (6H, s, ArCH_3), 2.30 (6H, s, ArCH_3), 2.39 (6H, s, ArCH_3), 2.50 (6H, s, ArCH_3), 3.40 (4H, s, ArCH_2C(O)), 3.69 (2H, s, ArCH_2Ar), 4.89 (2H, m, CHCH$_3$), 7.19 (2H, s, meso H), 7.31-7.43 (8H, m, ArH), 8.60 (2H, d, J = 8.0 Hz, ArH), 12.2 (4H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, DMSO-d_6): 10.0, 12.9, 13.0, 18.1, 22.4, 30.6, 48.1, 121.3, 124.2, 125.2, 125.9, 126.4, 126.6, 126.9, 128.2, 142.6, 143.6, 144.2, 144.5, 152.5, 154.7, 168.0; calcd 894.3 for $C_{47}H_{56}N_6O_2Br_2$;

ESI(+ve) *m/z* found 735.4 $(M+1-2HBr)^+$; λ_{max}(95% methanol, 5%Chloroform): 492 nm; ε_{492}(95% methanol, 5% chloroform): 7.79 x10^5 $Lmol^{-1}dm^{-1}$.

2,2'-Bis{8-[(*S* or *R*)-2-(1-naphthylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8i,j**)

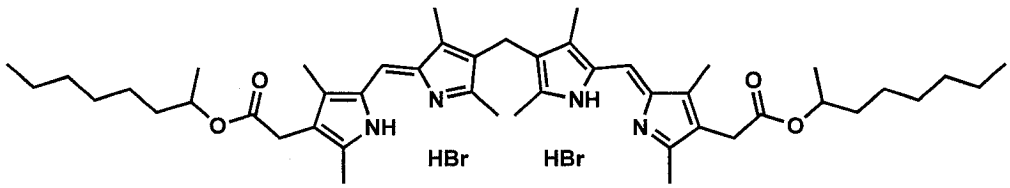


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-2-(1-naphthylethylcarbamoyl)methyl]pyrrole-2-carboxylate (**5i**) (to prepare **8i**) or benzyl 3,5-dimethyl-4-[(*R*)-2-(1-naphthylethylcarbamoyl)methyl]pyrrole-2-carboxylate (**5j**) (to prepare **8j**) (0.38 g, 0.80 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0036 g) in THF (20 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 50 mL round-bottom flask and diluted with methanol (10 mL). Reaction with **7**[137] (0.10 g, 0.40 mmol) and 48% (w/v) aqueous hydrobromic acid (0.34 mL, 2.0 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.28 g, 64%)

Sol: dimethylsulfoxide; Sp. Sol: chloroform, DCM, methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, DMSO-d_6): 1.53 (6H, d, J = 7.0 Hz, CHCH_3), 2.27 (6H, s, ArCH_3), 2.29 (6H, s, ArCH_3), 2.38 (6H, s, ArCH_3), 2.46 (6H, s, ArCH_3), 3.39-3.42 (4H, m, ArCH_2C(O)), 3.69 (2H, s, ArCH_2Ar), 5.67-5.69 (2H, m, C*H*CH_3), 7.43-7.59 (10H, m, meso *H* + Ar*H*), 7.84 (2H, d, J = 8.0 Hz, Ar*H*), 7.94 (2H, d, J = 4.0 Hz, Ar*H*), 8.06 (2H, d, J = 4.0 Hz, Ar*H*), 8.73 (2H,

d, J = 7.5 Hz, amide N*H*), 12.13 (2H, br s, N*H*), 12.14 (2H, br s, N*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, DMSO-d_6): 10.6 (two Ar*C*H$_3$), 13.5 (two Ar*C*H$_3$), 19.3 (Ar*C*H$_2$Ar), 21.9 (CH*C*H$_3$), 31.0 (Ar*C*H$_2$C(O)), 44.7 (*C*HCH$_3$), 121.8 (meso *C*), 122.9 (ArH), 123.5 (ArH), 124.6 (4° Ar), 125.7 (4° Ar), 126.1 (ArH), 127.3 (4° Ar), 127.9 (ArH), 129.1 (ArH), 131.1 (4° Ar), 140.3 (4° Ar), 142.8 (4° Ar), 144.8 (4° Ar), 153.1 (4° Ar), 155.3 (4° Ar), 168.6 (*C*=O) (two ArH signals and two 4° Ar signal not resolved, due to low sensitivity the ^{13}C NMR data was obtained from calculated projections ^{13}C-^{1}H HSQC and ^{13}C-^{1}H HMBC experiments); calcd 994.3 for $C_{55}H_{60}N_6O_2Br_2$; ESI(+ve) found *m/z* 835.5 $(M+1-2HBr)^+$; λ_{max}(95% methanol, 5% chloroform): 489 nm; ε_{489}(95% methanol, 5% chloroform): 8.82 x10^5 Lmol^{-1}dm^{-1}.

2,2'-Bis{8-[(*S* or *R*)-1-(methylheptyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8k,l**)

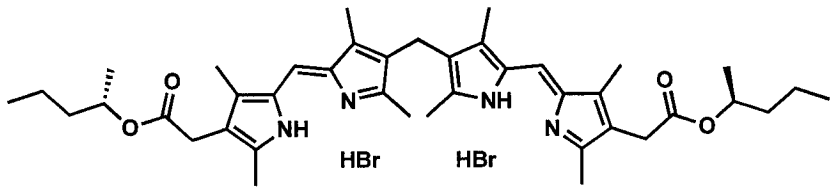


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-1-(methylheptyloxycarbonyl)methyl]pyrrole-2-carboxylate (**5k**) (to prepare **8k**) or benzyl 3,5-dimethyl-4-[(*R*)-1-(methylheptyloxycarbonyl)methyl]pyrrole-2-carboxylate (**5l**) (to prepare **8l**) (0.32 g, 0.80 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0036 g) in THF (20 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 50 mL round-bottom flask and diluted with methanol (10 mL). Reaction with **7**[137] (0.10 g, 0.40 mmol) and 48% (w/v) aqueous

hydrobromic acid (0.34 mL, 2.0 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.21 g, 58%)

Sol: chloroform, DCM, methanol, dimethylsulfoxide; Sp. Sol: ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.86 (6H, t, J = 6.5 Hz, CH_2CH_3), 1.18-1.29 (22H, m, $CHCH_3$ + $CH_2(CH_2)_4CH_3$), 1.46-1.48 (2H, m, $CHCH_aH_bCH_2$), 1.53-1.56 (2H, m, $CHCH_aH_bCH_2$), 2.16 (6H, s, $ArCH_3$), 2.32 (6H, s, $ArCH_3$), 2.61 (6H, s, $ArCH_3$), 2.71 (6H, s, $ArCH_3$), 3.41 (4H, s, $ArCH_2C(O)$), 3.59 (2H, s, $ArCH_2Ar$), 4.89 (2H, sextet, J = 6.5 Hz, $CHCH_3$), 7.09 (2H, s, meso *H*), 13.22 (br s, 2H, N*H*), 13.26 (br s, 2H, N*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.6 ($ArCH_3$), 10.6 ($ArCH_3$), 13.1 ($ArCH_3$), 13.2 ($ArCH_3$), 14.2 (CH_2CH_3), 19.7 ($ArCH_2Ar$), 20.0 ($CHCH_3$), 22.7 ($CH_2CH_2CH_3$), 25.4 ($CH_2CH_2CH_2$), 29.2 ($CH_2CH_2CH_2$), 30.6 ($ArCH_2C(O)$), 31.9 ($CH_2CH_2CH_2$), 36.0 ($CHCH_2CH_2$), 72.4 ($CHCH_3$), 119.8 (meso *C*), 122.3 (4° Ar), 125.0 (4° Ar), 126.1 (4° Ar), 126.5 (4° Ar), 142.0 (4° Ar), 143.9 (4° Ar), 153.7 (4° Ar), 155.7 (4° Ar), 169.7 (C=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); ^{15}N NMR: δ(51 MHz, $CDCl_3$): -211.6 (d, J = -95 Hz), -212.0 (d, J = -95 Hz); calcd 912.4 for $C_{47}H_{70}N_4O_4Br_2$; ESI(+ve) found *m/z* 753.5 $(M+1-2HBr)^+$.

2,2'-Bis{8-[(*S*)-1-(methylbutyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8m**)

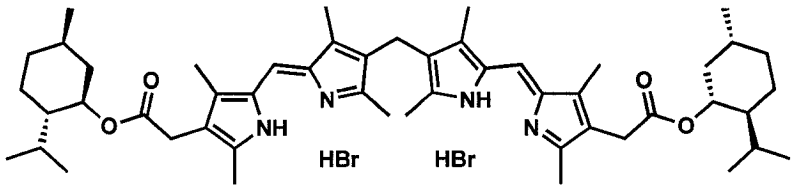


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*S*)-1-(methylbut-3-enyloxycarbonyl)methyl]pyrrole-2-carboxylate (**5m**) (0.28 g, 0.80 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0036 g) in THF (20 mL). The mixture was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 50 mL round-bottom flask and diluted with methanol (10 mL). Reaction with **7**[137] (0.10 g, 0.40 mmol) and 48% (w/v) aqueous hydrobromic acid (0.34 mL, 2.0 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.20 g, 61%)

Sol: chloroform, DCM, methanol, dimethylsulfoxide; Sp. Sol: ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.89 (6H, t, J = 7.5 Hz, CH_2CH_3), 1.19 (6H, d, J = 6.5 Hz, $CHCH_3$), 1.25-1.32 (4H, m, CH_2CH_3), 1.42-1.47 (2H, m, $CH_2CH_aH_b$), 1.52-1.57 (2H, m, $CH_2CH_aH_b$), 2.16 (6H, s, $ArCH_3$), 2.31 (6H, s, $ArCH_3$), 2.61 (6H, s, $ArCH_3$), 2.71 (6H, s, $ArCH_3$), 3.40 (4H, s, $ArCH_2C(O)$), 3.59 (2H, s, $ArCH_2Ar$), 4.90 (2H, sextet, J = 6.5 Hz, $CHCH_3$), 7.09 (2H, s, meso *H*), 13.22 (br s, 2H, N*H*), 13.26 (br s, 2H, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.6 ($ArCH_3$), 10.6 ($ArCH_3$), 13.2 ($ArCH_3$), 13.3 ($ArCH_3$), 14.0 (CH_2CH_3), 18.8 ($CH_2CH_2CH_3$), 19.7 ($ArCH_2Ar$), 20.1 ($CHCH_3$), 30.6 ($ArCH_2C(O)$), 38.1 ($CH_2CH_2CH_3$), 72.2 ($CHCH_3$), 119.8 (meso *C*), 122.3 (4° Ar), 125.0 (4° Ar), 126.2 (4° Ar), 126.6 (4° Ar),

142.0 (4° Ar), 143.9 (4° Ar), 153.8 (4° Ar), 155.7 (4° Ar), 169.8 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 828.3 for $C_{41}H_{58}N_4O_4Br_2$; ESI(+ve) found *m/z* 669.4 $(M+1-2HBr)^+$.

2,2'-Bis{8-[(*R*)-1-(5-(*R*)-isopropyl-2-(*S*)-methylcyclohexyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide[141] (**8n**)

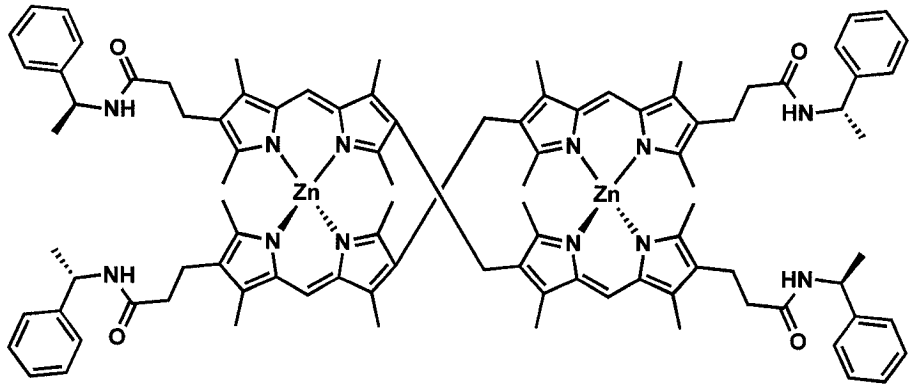


Following the procedure used for the preparation of **8a**, hydrogenolysis of benzyl 3,5-dimethyl-4-[(*R*)-1-(5-(*R*)-isopropyl-2-(*S*)-methylcyclohexyloxycarbonyl)methyl]pyrrole-2-carboxylate (**5n**) (0.34 g, 0.80 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0036 g) in THF (20 mL). The mixtured was stirred for 16 hours and was then filtered through a plug of Celite® to remove the catalyst. The filtrate was collected in a 50 mL round-bottom flask and diluted with methanol (10 mL). Reaction with **7**[137] (0.10 g, 0.40 mmol) and 48% (w/v) aqueous hydrobromic acid (0.34 mL, 2.0 mmol), followed by a similar work-up to **8a**, yielded the product as a dark orange powder. (Yield: 0.20 g, 72%)

Sol: chloroform, DCM, methanol, dimethylsulfoxide; Sp. Sol: ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.72 (6H, d, J = 7.0 Hz, $CHCH_3$), 0.84-1.05 (18H, m, $CH(CH_3)_2$ + CH_aCH_b + CH_cCH_d + CH_eCH_f), 1.32-1.37 (2H, m, $CHCH(CH_3)_2$), 1.44-1.48 (2H, m, $CHCH_3$), 1.65-1.75 (6H, m, CH_aCH_b + CH_cCH_d + $CH(CH_3)_2$), 1.91-1.93 (2H, m, CH_eCH_f), 2.17 (6H, s, $ArCH_3$), 2.31 (6H, s, $ArCH_3$), 2.60 (6H, s, $ArCH_3$), 2.70 (6H, s, $ArCH_3$), 3.42 (4H, s,

ArCH_2C(O)), 3.59 (2H, s, ArCH_2Ar), 4.68 (2H, td, J = 11.0 Hz, 4.5 Hz, CH(CH_3) O), 7.10 (2H, s, meso H), 13.21 (br s, 2H, NH), 13.26 (br s, 2H, NH); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.6 (ArCH_3), 10.6 (ArCH_3), 13.1 (ArCH_3), 13.2 (ArCH_3), 16.5 (CHCH_3), 19.7 (ArCH_2Ar), 20.8 (CH(CH_3)$_a$(CH_3)$_b$), 22.1 (CH(CH_3)$_a$(CH_3)$_b$), 23.6 (CH(CH_3)CH_2), 26.6 (CH(CH_3)$_2$), 30.5 (ArCH_2C(O)), 31.5 ($CHCH_3$), 34.2 (CH(CH_3)CH_2CH_2), 40.9 (CH_2CHO), 47.2 ($CHCH$(CH_3)$_2$), 75.4 (CHO), 119.7 (meso C), 122.2 (4° Ar), 125.0 (4° Ar), 126.1 (4° Ar), 126.5 (4° Ar), 142.1 (4° Ar), 143.9 (4° Ar), 153.7 (4° Ar), 155.5 (4° Ar), 169.6 (C=O) (assignment by JMOD and ^{13}C-^1H HSQC experiments); calcd 964.4 for $C_{51}H_{74}N_4O_4Br_2$; ESI(+ve) found m/z 805.5 $(M+1-2HBr)^+$.

Zinc(II) di(2,2'-bis{8-[(*S*)-2-(1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[140] (**9a**)

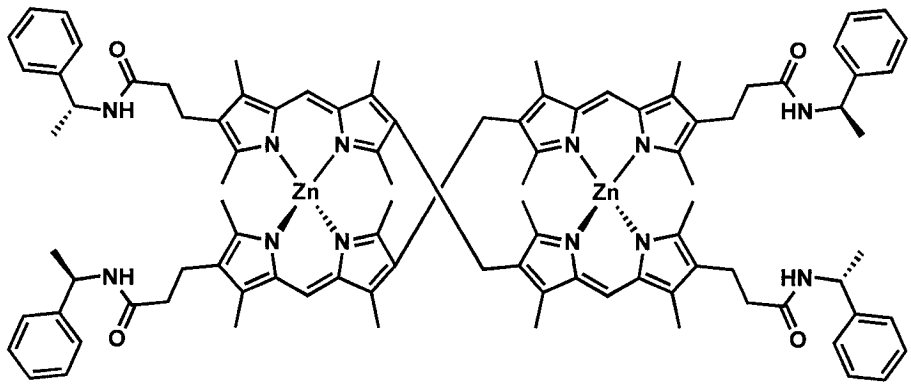


A solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added, with stirring, to a solution of 2,2'-bis{8-[(*S*)-2-(1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8a**) (0.10 g, 0.11 mmol) in chloroform (5 mL) contained in a 50 mL round-bottom flask. The mixture was stirred for 20 minutes. The resulting dark purple solution was washed with distilled water (2 x 30 mL), dried with anhydrous sodium

sulfate, filtered and the solvent was removed using a rotary evaporator. A minimal amount of DCM was added, followed by hexanes to precipitate the product as a fuscia-coloured powder that was collected by suction filtration. (Yield: 0.023 g, 25%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.37-1.39 (24H, m , $CHCH_3$ + $ArCH_3$), 1.93 (12H, d, J = 5.5 Hz, $ArCH_3$), 2.13 (12H, d, J = 3.3 Hz, $ArCH_3$), 2.20 (12H, s, $ArCH_3$), 2.26-2.32 (8H, m, $CH_2CH_2C(O)$), 2.65-2.71 (8H, m, $ArCH_2CH_2$), 3.41 (4H, br s, $ArCH_2Ar$), 5.00-5.11 (4H, m, $CHCH_3$), 5.55-5.66 (4H, m, amide N*H*), 6.87 (4H, d, J = 2.3 Hz, meso *H*), 7.16-7.28 (20H, m, Ar*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.1, 10.2, 15.2, 15.3, 21.1,* 21.9, 22.2, 37.6,* 37.7,* 48.8, 48.9, 121.0, 126.3,* 126.4,* 127.4, 128.8, 135.4,* 135.8,* 137.1,* 137.4,* 143.4,* 155.1,* 158.3,* 171.7* (* denotes negative phase peak in JMOD experiment); calcd 1652.8 for $C_{98}H_{112}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1653.5 $(M+1)^+$; λ_{max}(DCM): 478 nm, 526 nm; λ_{max}(90% methanol, 10% chloroform): 475 nm, 525 nm; ε_{527}(DCM): 1.96×10^7 $Lmol^{-1}dm^{-1}$; ε_{525}(90% methanol, 10% chloroform): 2.50×10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{476}$(90% methanol, 10% chloroform) = -29.75 cm^2mmol^{-1}, $\Delta\varepsilon_{521}$ = +82.28 cm^2mmol^{-1}, $\Delta\varepsilon_{537}$ = -60.94 cm^2mmol^{-1}; HPLC: eluent: methanol; flow rate 1 mL/min; column: CHIRALCEL OD (25 cm x 0.46 cm); retention time: 14.1 min (*M*), 21.6 min (*P*).

Zinc(II) di(2,2'-bis{8-[(*R*)-2-(1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[140] (**9b**)

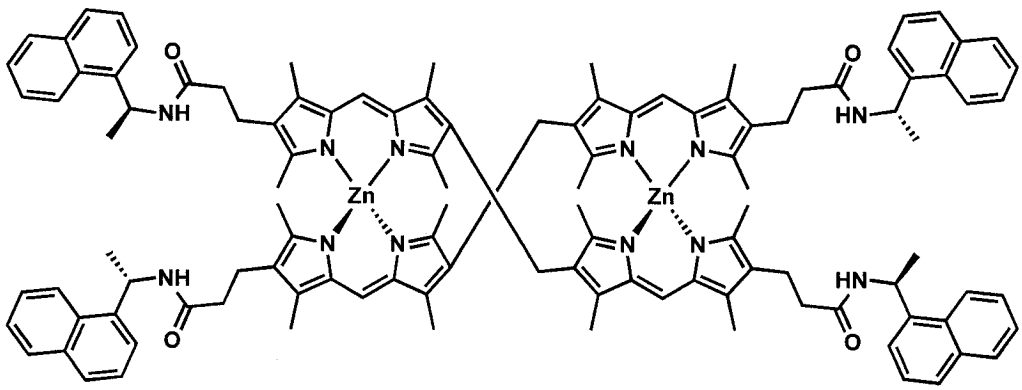


Following the procedure used for the preparation of (**9a**), a solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-2-(1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8b**) (0.10 g, 0.11 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.029 g, 32%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.37-1.39 (24H, m , $CHCH_3$ + $ArCH_3$), 1.93 (12H, d, J = 5.3 Hz, $ArCH_3$), 2.13 (12H, d, J = 3.0 Hz, $ArCH_3$), 2.20 (12H, s, $ArCH_3$), 2.26-2.31 (8H, m, $CH_2CH_2C(O)$), 2.65-2.71 (8H, m, $ArCH_2CH_2$), 3.41 (4H, br s, $ArCH_2Ar$), 5.00-5.11 (4H, m, $CHCH_3$), 5.54-5.65 (4H, m, amide N*H*), 6.87 (4H, d, J = 2.3 Hz, meso *H*), 7.19-7.29 (20H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.1 ($ArCH_3$), 10.2 ($ArCH_3$), 15.3 ($ArCH_3$), 15.3 ($ArCH_3$), 21.1 ($ArCH_2Ar$ and $ArCH_2CH_2$), 21.9 (CHC_aH_3), 22.2 (CHC_bH_3), 37.5 ($CH_2C_aH_2C(O)$), 37.7 ($CH_2C_bH_2C(O)$), 48.8 (C_aHCH_3), 48.9 (C_bHCH_3), 121.0 (meso *C*), 125.5 (4° Ar), 126.3 (ArH), 126.4 (ArH), 127.4 (ArH), 128.8 (ArH), 135.8 (4° Ar), 137.1 (4° Ar), 137.4 (4°

Ar), 143.4 (4° Ar), 155.1 (4° Ar), 158.3 (4° Ar), 171.8 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 1652.8 for $C_{98}H_{112}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1652.4 $(M)^+$; λ_{max}(DCM): 478 nm, 527 nm; λ_{max}(90% methanol, 10% chloroform): 476 nm, 524 nm; ε_{527}(DCM): 1.96×10^7 $Lmol^{-1}dm^{-1}$; ε_{524}(90% methanol, 10% chloroform): 2.19×10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{474}$(90% methanol, 10% chloroform) = +21.83 cm^2mmol^{-1}, $\Delta\varepsilon_{524}$ = -65.36 cm^2mmol^{-1}, $\Delta\varepsilon_{538}$ = +47.69 cm^2mmol^{-1}; HPLC: eluent: methanol; flow rate 1 mL/min; column: CHIRALCEL OD (25 cm x 0.46 cm); retention time: 8.9 min (*P*), 12.7 min (*M*).

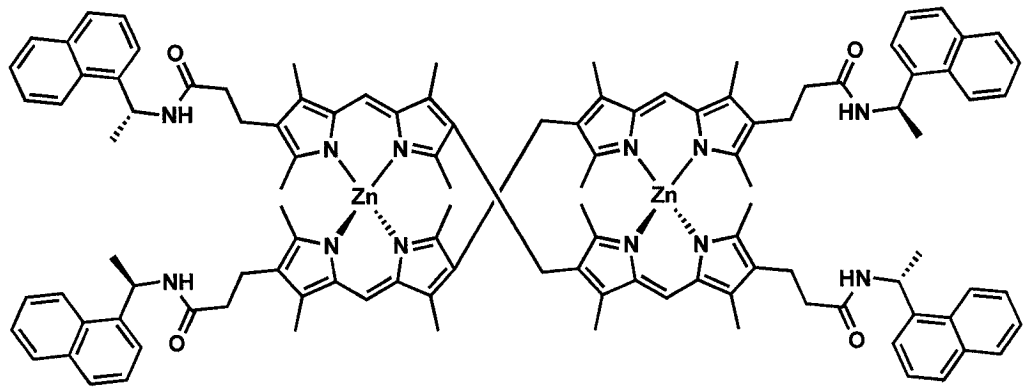
Zinc(II) 2,2'-di(bis{8-[(*S*)-2-(1-naphthylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9c**)



Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-2-(1-naphthylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8c**) (0.11 g, 0.11 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.076 g, 75%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.38 (12H, d, J = 4.5 Hz, CHCH_3), 1.48-1.55 (12H, m, ArCH_3), 1.89 (12H, d, J = 7.0 Hz, ArCH_3), 2.10 (12H, d, J = 2.0 Hz, ArCH_3), 2.13-2.28 (20H, m, ArCH_3 + $CH_2CH_2C(O)$), 2.60-2.69 (8H, m, ArCH_2CH_2), 3.41 (4H, br s, ArCH_2Ar), 5.63-5.72 (4H, m, amide N*H*), 5.77-5.90 (4H, m, C*H*CH_3), 6.86 (4H, d, J = 3.3 Hz, meso *H*), 7.31-7.54 (20H, m, Ar*H*), 7.71-7.85 (4H, m, Ar*H*), 7.97-8.08 (4H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.1, 10.2, 15.2, 15.3, 20.9, 21.0, 21.3, 37.4, 44.7, 44.8, 121.0, 122.6, 122.6, 123.6, 125.4, 125.5, 126.0, 126.3, 126.7, 128.4, 129.0, 131.2, 134.1, 135.4, 135.7, 137.3, 138.7, 155.5, 171.6; calcd 1848.8 for $C_{114}H_{120}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1857.6 $(M+6)^+$; λ_{max}(90% methanol, 10% chloroform): 525 nm, 478 nm; ε_{525}(90% methanol, 10% DCM): 2.30×10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{475}$(90% methanol, 10% DCM) = -46.46 cm^2mmol^{-1}, $\Delta\varepsilon_{528}$ = +117.31 cm^2mmol^{-1}, $\Delta\varepsilon_{539}$ = -40.75 cm^2mmol^{-1}; HPLC: eluent: 90% methanol, 10% chloroform; flow rate 0.3 mL/min; column: silica-based CSP immobilizing with cellulose 3,5-dimethylphenylcarbamate (25 cm x 0.20 cm); retention time: 8.0 min (*M*), 15.1 min (*P*).

Zinc(II) di(2,2'-bis{8-[(*R*)-2-(1-naphthylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9d**)

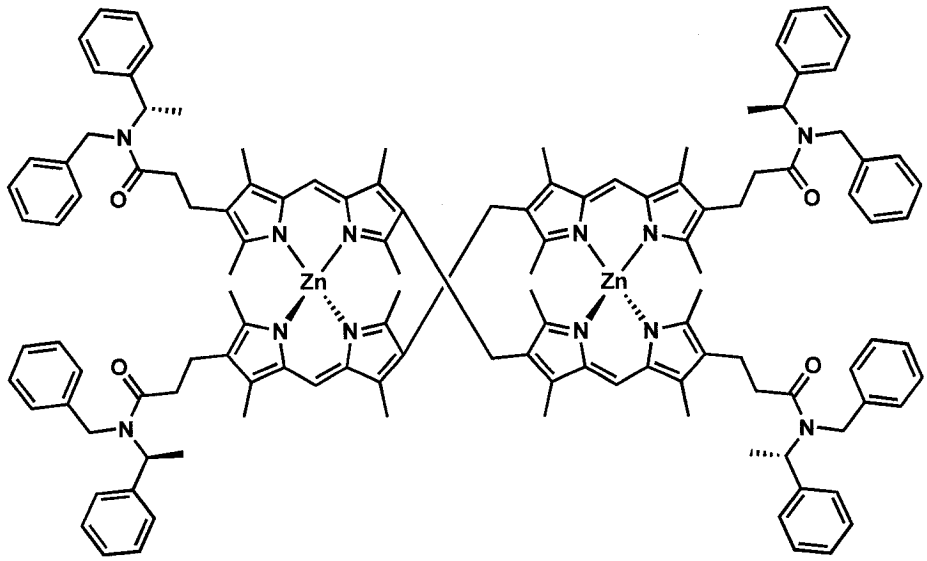


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-2-(1-naphthylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8d**) (0.11 g, 0.11 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.021 g, 21%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.38 (12H, d, J = 4.5 Hz, CHC*H*$_3$), 1.48-1.56 (12H, m, ArC*H*$_3$), 1.89 (12H, d, J = 6.8 Hz, ArC*H*$_3$), 2.10 (12H, d, J = 1.8 Hz, ArC*H*$_3$), 2.15-2.28 (20H, m, ArC*H*$_3$ + $CH_2CH_2C(O)$), 2.55-2.73 (8H, m, ArC*H*$_2$CH$_2$), 3.41 (4H, br s, ArC*H*$_2$Ar), 5.62-5.72 (4H, m, amide N*H*), 5.75-5.89 (4H, m, C*H*CH$_3$), 6.86 (4H, d, J = 3.3 Hz, meso *H*), 7.31-7.53 (20H, m, Ar*H*), 7.71-7.85 (4H, m, Ar*H*), 7.97-8.07 (4H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.2, 15.2, 15.4, 20.9, 21.1, 21.3, 22.9, 37.3, 37.4, 44.7, 44.8, 121.0, 122.6, 122.6, 123.6, 125.4, 125.4, 125.6, 126.0, 126.7, 128.4, 129.0, 131.3, 134.1, 135.4, 137.3, 138.5, 138.7, 155.5, 171.6; calcd 1848.8 for $C_{114}H_{120}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1857.5 $(M+6)^+$; λ_{max}(90%

methanol, 10% chloroform): 523 nm, 478 nm; ε_{525}(90% methanol, 10% chloroform): 2.30×10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{474}$(90% methanol, 10% chloroform) = +42.35 cm^2mmol^{-1}, $\Delta\varepsilon_{529}$ = -112.87 cm^2mmol^{-1}, $\Delta\varepsilon_{541}$ = +17.98 cm^2mmol^{-1}; HPLC: eluent: 95% methanol, 5% chloroform; flow rate 0.2 mL/min; column: silica-based CSP immobilizing with cellulose 3,5-dimethylphenylcarbamate (25 cm x 0.20 cm); retention time: 12.8 min (*P*), 15.6 min (*M*).

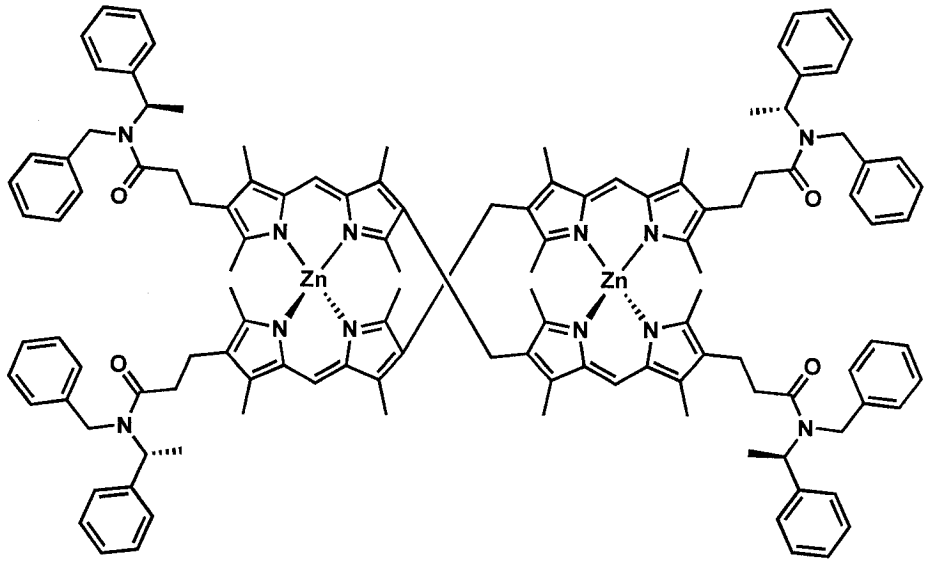
Zinc(II) di(2,2'-bis{8-[(*S*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9e**)



Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8e**) (0.12 g, 0.11 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.054 g, 49%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.22-1.40 (24H, m, CHC*H*$_3$ + ArC*H*$_3$), 1.81-2.21 (36H, m, 3 x ArC*H*$_3$), 2.30-2.83 (16H, m, C*H*$_2$C*H*$_2$C(O)), 3.38-3.58 (4H, s, ArC*H*$_2$Ar), 3.90-4.30 (¼ x 4H + ¾ x 8H, C*H*$_A$H$_A$Ph(minor) + C*H*$_A$H$_A$Ph(major) + CH$_A$*H*$_A$Ph(major)), 4.91-4.94 (¼ x 4H, m, CH$_A$*H*$_A$Ph(minor)), 5.15 (¼ x 4H, br s, C*H*CH$_3$(minor)), 6.13-6.15 (¾ x 4H, m, C*H*CH$_3$(major)), 6.83-7.24 (44H, m, meso *H* + Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.0, 15.0, 15.2, 17.2, 19.5, 20.7, 21.2, 21.3, 34.5, 34.7, 46.6, 47.3, 51.7, 56.0, 120.7, 125.8, 126.2, 126.7, 127.1, 127.4, 127.6, 127.7, 128.4, 128.6, 128.8, 128.9, 135.4, 135.6, 136.8, 137.4, 138.6, 138.7, 139.5, 140.9, 141.2, 141.3, 155.5, 158.1, 174.2; calcd 2008.9 for $C_{126}H_{136}N_{12}O_4Zn_2$; MALDI(+ve) found *m/z* 2012.7 $(M+1)^+$; λ_{max}(90% methanol, 10% chloroform): 523 nm, 478 nm; ε_{523}(90% methanol, 10% chloroform): 2.70x10^6 Lmol^{-1}dm^{-1}; $\Delta\varepsilon_{470}$(90% methanol, 10% chloroform) = +26.72 cm^{2}mmol^{-1}, $\Delta\varepsilon_{519}$ = +29.78 cm^{2}mmol^{-1}, $\Delta\varepsilon_{534}$ = -69.50 cm^{2}mmol^{-1}; HPLC: eluent: 80% methanol, 20% THF; flow rate 0.2 mL/min; column: silica-based CSP immobilizing with cellulose 3,5-dimethylphenylcarbamate (25 cm x 0.20 cm); retention time: 11.3 min (*M*), 15.0 min (*P*).

Zinc(II) di(2,2'-bis{8-[(*R*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9f**)

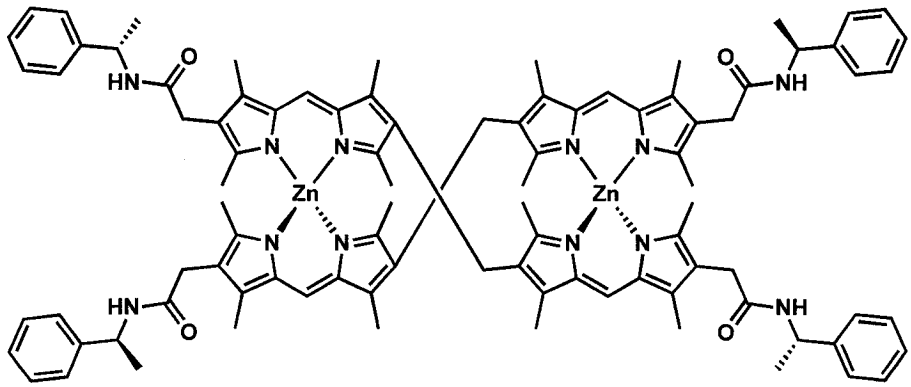


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.12 g, 0.55 mmol) and sodium acetate trihydrate (0.075 g, 0.55 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-2-(benzyl-1-phenylethylcarbamoyl)ethyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8f**) (0.12 g, 0.11 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.045 g, 41%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.28-1.39 (24H, m, $CHCH_3$ + $ArCH_3$), 1.82-2.18 (36H, m, 3 x $ArCH_3$), 2.33-2.81 (16H, m, $CH_2CH_2C(O)$), 3.39 (4H, s, $ArCH_2Ar$), 3.93-4.31 (¼ x 4H + ¾ x 8H, CH_AH_APh(minor) + CH_AH_APh(major) + CH_AH_APh(major)), 4.92-4.94 (¼ x 4H, m, CH_AH_APh(minor)), 5.15 (¼ x 4H, br s, $CHCH_3$(minor)), 6.14-6.15 (¾ x 4H, m, $CHCH_3$(major)), 6.85-7.28 (44H, m, meso *H* + Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.0 ($ArCH_3$), 10.1 ($ArCH_3$),

15.0 (ArCH_3), 15.1 (ArCH_3), 17.2 (CHC_aH_3), 19.4 (CHC_bH_3), 20.6 (ArCH_2Ar), 21.1 (Ar$C_aH_2CH_2$), 21.2 (Ar$C_bH_2CH_2$), 34.4 ($CH_2C_aH_2$C(O)), 34.7 ($CH_2C_bH_2$C(O)), 46.4 (C_aH_2Ph), 47.2 (C_bH_2Ph), 51.7 (C_aHCH_3), 55.9 (C_bHCH_3), 120.7 (meso *C*), 125.8 (ArH), 125.8 (4° Ar), 126.1 (4° Ar), 126.7 (ArH), 127.1 (ArH), 127.4 (ArH), 127.5 (ArH), 127.6 (ArH), 128.3 (ArH), 128.5 (ArH), 128.7 (ArH), 128.8 (ArH), 135.3 (4° Ar), 135.5 (4° Ar), 136.7 (4° Ar), 137.4 (4° Ar), 138.6 (4° Ar), 138.6 (4° Ar), 139.4 (4° Ar), 140.9 (4° Ar), 141.1 (4° Ar), 141.2 (4° Ar), 155.4 (4° Ar), 157.8 (4° Ar), 158.0 (4° Ar), 174.1 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 2008.9 for $C_{126}H_{136}N_{12}O_4Zn_2$; MALDI(+ve) found *m/z* 2012.3 $(M+4)^+$; λ_{max}(90% methanol, 10% chloroform): 523 nm, 478 nm; ε_{523}(90% methanol, 10% chloroform): 2.70 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{480}$(90% methanol, 10% chloroform) = +13.17 cm^2mmol^{-1}, $\Delta\varepsilon_{519}$ = -144.10 cm^2mmol^{-1}, $\Delta\varepsilon_{533}$ = +176.02 cm^2mmol^{-1}; HPLC: eluent: 75% methanol, 25% THF; flow rate 0.1 mL/min; column: silica-based CSP immobilizing with cellulose 3,5-dichlorophenylcarbamate (25 cm x 0.20 cm); retention time: 19.6 min (*M*), 22.8 min (*P*).

Zinc(II) di(2,2'-bis{8-[(*S*)-2-(1-phenylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9g**)

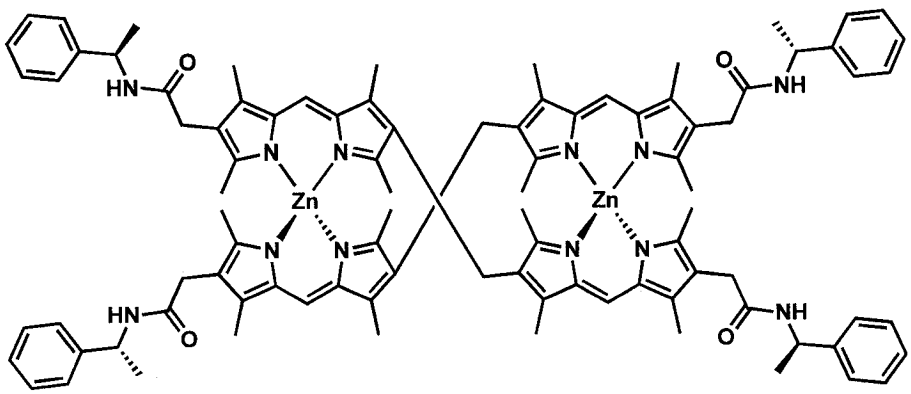


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-2-(1-phenylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8g**) (0.090 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.036 g, 42%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.32-1.39 (24H, m, CHC*H*$_3$ + ArC*H*$_3$), 1.79 (12H, s, ArC*H*$_3$), 1.92 (12H, s, ArC*H*$_3$), 2.19-2.21 (12H, m, ArC*H*$_3$), 3.31-3.36 (8H, m, ArC*H*$_2$C(O)), 3.41 (4H, s, ArC*H*$_2$Ar), 5.06-5.11 (4H, m, C*H*CH$_3$), 5.69-5.73 (4H, m, amide N*H*), 6.93-6.94 (4H, m, meso *H*), 7.08-7.09 (8H, m, Ar*H*), 7.17-7.22 (12H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.2, 14.6, 14.8, 15.4, 20.7, 22.1, 33.2, 48.3, 119.6, 121.6, 125.8, 127.2, 127.4, 128.8, 135.0, 136.6, 137.7, 138.4, 143.2, 154.1, 160.2, 170.5; calcd 1592.7 for $C_{94}H_{104}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1595.5 $(M+3)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 473 nm; ε_{522}(90%

methanol, 10% chloroform): 2.22 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{469}$(90% methanol, 10% chloroform) = -8.18 cm^2mmol^{-1}, $\Delta\varepsilon_{520}$ = +54.46 cm^2mmol^{-1}, $\Delta\varepsilon_{531}$ = -41.86 cm^2mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*R*)-2-(1-phenylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9h**)

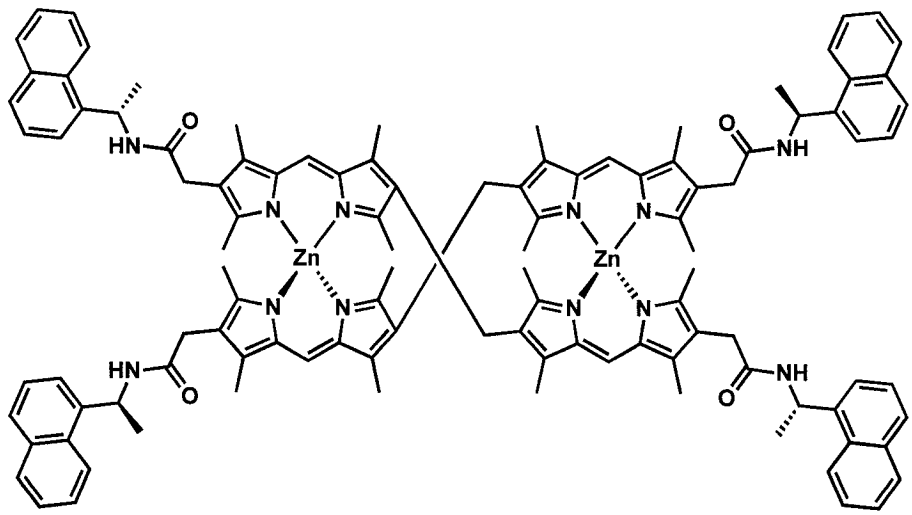


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-2-(1-phenylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8h**) (0.090 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.080 g, 99%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.32-1.39 (24H, m, CHC*H*$_3$ + ArC*H*$_3$), 1.79 (12H, s, ArC*H*$_3$), 1.92 (12H, s, ArC*H*$_3$), 2.19-2.21 (12H, m, ArC*H*$_3$), 3.31-3.36 (8H, m, ArC*H*$_2$C(O)), 3.41 (4H, s, ArC*H*$_2$Ar), 5.06-5.11 (4H, m, C*H*CH_3), 5.69-5.73 (4H, m, amide N*H*), 6.93-6.94 (4H, m, meso *H*), 7.08-7.09 (8H, m, Ar*H*), 7.20-7.23 (12H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.2 (ArCH_3), 10.3 (ArCH_3), 14.6 (ArCH_3), 14.8 (ArCH_3), 15.3 (ArCH_3), 20.7 (ArCH_2Ar), 22.1 (C_aHCH_3),

22.4 (C_aHCH$_3$), 33.2 (ArCH$_2$C(O)), 48.3 (C_aHCH$_3$), 48.6 (C_bHCH$_3$), 119.6 (4° Ar), 119.7 (4° Ar), 121.6 (meso *C*), 125.8 (ArH), 126.0 (ArH), 127.1 (4° Ar), 127.2 (4° Ar), 127.4 (ArH), 127.6 (ArH), 128.8 (ArH), 128.9 (ArH), 135.0 (4° Ar), 136.5 (4° Ar), 136.6 (4° Ar), 137.7 (4° Ar), 137.8 (4° Ar), 138.4 (4° Ar), 138.5 (4° Ar), 143.2 (4° Ar), 143.4 (4° Ar), 154.1 (4° Ar), 154.2 (4° Ar), 160.1 (4° Ar), 160.2 (4° Ar), 170.4 (C_a=O), 170.5 (C_b=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 1592.7 for $C_{94}H_{104}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1597.4 $(M+5)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 473 nm; ε_{522}(90% methanol, 10% chloroform): 2.22 x10^6 Lmol^{-1}dm^{-1}; $\Delta\varepsilon_{466}$(90% methanol, 10% chloroform) = +5.51 cm^{2}mmol^{-1}, $\Delta\varepsilon_{519}$ = -26.77 cm^{2}mmol^{-1}, $\Delta\varepsilon_{531}$ = +21.35 cm^{2}mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*S*)-2-(1-naphthylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9i**)

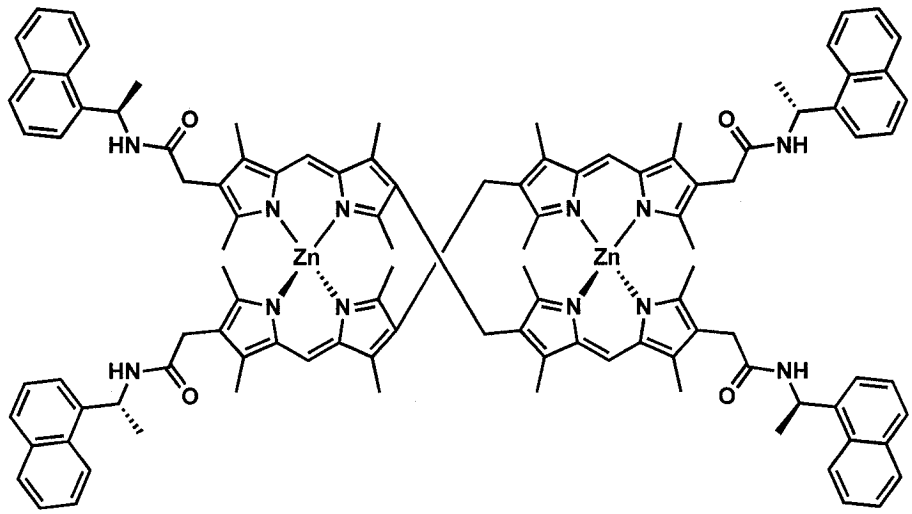


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-2-(1-

naphthylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8i**) (0.10 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.057 g, 63%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.28 (12H, s, ArC*H*$_3$), 1.49-1.53 (12H, m, CHC*H*$_3$), 1.57 (12H, s, ArC*H*$_3$), 2.09 (12H, s, ArC*H*$_3$), 2.18 (12H, s, ArC*H*$_3$), 3.31-3.40 (12H, m, ArC*H*$_2$C(O) + ArC*H*$_2$Ar), 5.77-5.86 (8H, m, C*H*CH$_3$ + amide N*H*), 6.86 (4H, s, meso *H*), 7.15-7.30 (8H, m, Ar*H*), 7.40-7.46 (8H, m, Ar*H*), 7.71-7.81 (8H, m, Ar*H*), 7.99-8.02 (4H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.1, 10.2, 14.3, 14.7, 15.2, 20.6, 21.4, 21.7, 33.1, 44.8, 44.9, 119.5, 121.5, 122.0, 122.2, 123.5, 125.2, 126.0, 126.1, 126.6, 127.1, 128.3, 128.4, 128.9, 128.9, 131.0, 131.1, 134.1, 134.9, 136.4, 136.5, 137.7, 138.2, 138.3, 138.5, 138.8, 154.0, 154.2, 160.0, 160.1, 170.3; calcd 1792.8 for $C_{110}H_{112}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1799.7 $(M+7)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 474 nm; ε_{522}(90% methanol, 10% chloroform): 1.77 x10^6 Lmol^{-1}dm^{-1}; $\Delta\varepsilon_{469}$(90% methanol, 10% chloroform) = -11.73 cm^{2}mmol^{-1}, $\Delta\varepsilon_{518}$ = +54.92 cm^{2}mmol^{-1}, $\Delta\varepsilon_{531}$ = -64.75 cm^{2}mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*R*)-2-(1-naphthylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9j**)

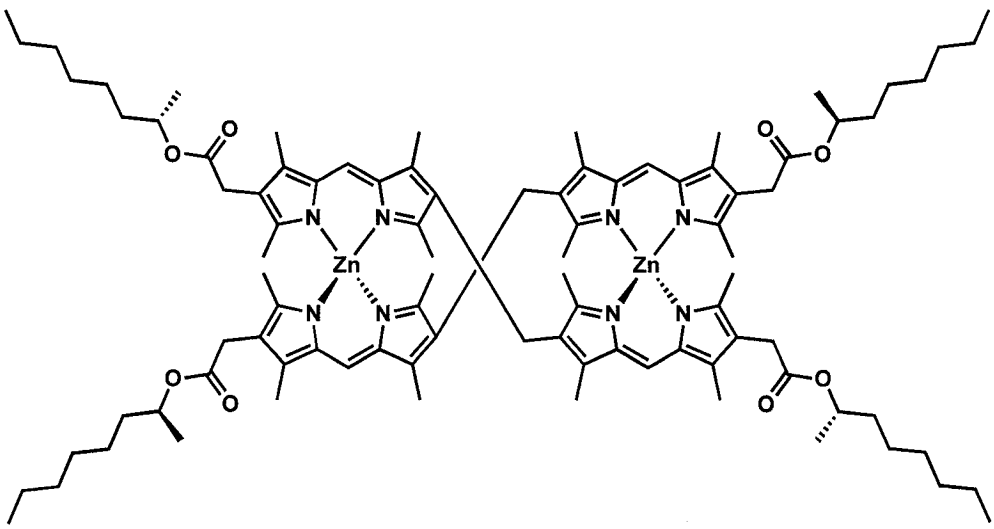


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-2-(1-naphthylethylcarbamoyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8j**) (0.10 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9a**, the product was obtained as a fuscia-coloured powder. (Yield: 0.053 g, 59%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.28 (12H, s, ArC*H*$_3$), 1.49-1.52 (12H, m, CHC*H*$_3$), 1.56 (12H, s, ArC*H*$_3$), 2.09 (12H, s, ArC*H*$_3$), 2.18 (12H, s, ArC*H*$_3$), 3.30-3.41 (12H, m, ArC*H*$_2$C(O) + ArC*H*$_2$Ar), 5.77-5.85 (8H, m, C*H*CH$_3$ + amide N*H*), 6.86 (4H, s, meso *H*), 7.16-7.30 (8H, m, Ar*H*), 7.40-7.46 (8H, m, Ar*H*), 7.71-7.82 (8H, m, Ar*H*), 7.99-8.01 (4H, m, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.1 (ArCH$_3$), 10.2 (ArCH$_3$), 14.4 (ArC_aH$_3$), 14.8 (ArC_bH$_3$), 15.2 (ArCH$_3$), 20.7 (ArCH$_2$Ar), 21.4 (CHC_aH$_3$), 21.7 (CHC_bH$_3$), 33.2 (ArCH$_2$C(O)), 44.9 (*C*HCH$_3$), 119.5

(4° Ar), 121.5 (meso *C*), 122.0 (ArH), 122.2 (ArH), 123.5 (ArH), 125.2 (ArH), 126.0 (ArH), 126.1 (ArH), 126.6 (ArH), 126.7 (ArH), 127.1 (4° Ar), 128.3 (ArH), 128.5 (ArH), 128.9 (ArH), 129.0 (ArH), 131.0 (4° Ar), 131.1 (4° Ar), 134.1 (4° Ar), 135.0 (4° Ar), 136.4 (4° Ar), 136.5 (4° Ar), 137.7 (4° Ar), 137.8 (4° Ar), 138.2 (4° Ar), 138.4 (4° Ar), 138.5 (4° Ar), 138.8 (4° Ar), 154.1 (4° Ar), 154.2 (4° Ar), 160.0 (4° Ar), 160.1 (4° Ar), 170.3 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 1792.8 for $C_{110}H_{112}N_{12}O_4Zn_2$; APCI(+ve) found *m/z* 1798.5 $(M+6)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 474 nm; ε_{522}(90% methanol, 10% chloroform): 1.77 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{469}$(90% methanol, 10% chloroform) = +6.94 cm^2mmol^{-1}, $\Delta\varepsilon_{518}$ = -18.92 cm^2mmol^{-1}, $\Delta\varepsilon_{530}$ = +28.43 cm^2mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*S*)-1-(methylheptyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9k**)

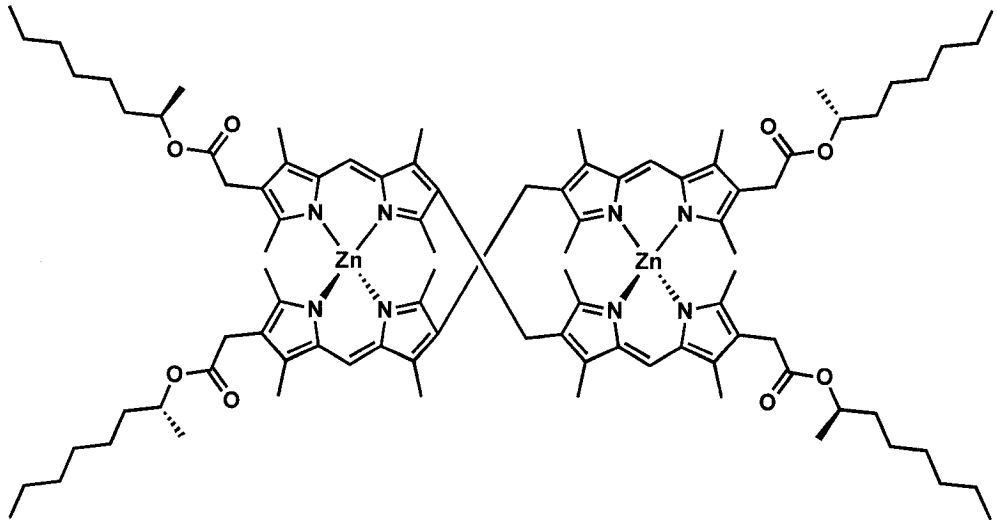


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-1-

(methylheptyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8k**) (0.091 g, 0.10 mmol) in chloroform (5 mL). The mixture was stirred for 20 minutes. The resulting dark purple solution was washed with distilled water, dried with anhydrous sodium sulfate, filtered and the solvent was partially removed using a rotary evaporator. The concentrated solution was filtered through a short plug of silica, rinsed with DCM and the solvent was removed using a rotary evaporator, yielding the product as a fuscia-coloured film. (Yield: 0.081 g, 99%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.82-0.85 (12H, m, CH_2CH_3), 1.12 (12H, d, J = 6.5 Hz, $CHCH_3$), 1.15-1.26 (32H, m, $CH_2(CH_2)_4CH_3$), 1.38-1.50 (20H, m, $CHCH_2CH_2$ + $ArCH_3$), 2.01 (12H, s, $ArCH_3$), 2.20 (12H, s, $ArCH_3$), 2.23 (12H, s, $ArCH_3$), 3.32 (8H, s, $ArCH_2C(O)$), 3.40 (4H, s, $ArCH_2Ar$), 4.81-4.85 (4H, m, $CHCH_3$), 6.91 (4H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.1 ($ArCH_3$), 10.3 ($ArCH_3$), 14.2 (CH_2CH_3), 15.1 ($ArCH_3$), 15.1 ($ArCH_3$), 20.1 ($CHCH_3$), 20.6 ($ArCH_2Ar$), 22.9 ($CH_2CH_2CH_3$), 25.2 ($CH_2CH_2CH_2$), 29.5 ($CH_2CH_2CH_2$), 30.3 ($ArCH_2C(O)$), 31.7 ($CH_2CH_2CH_2$), 36.1 ($CHCH_2$), 71.2 ($CHCH_3$), 119.7 (4° Ar), 121.2 (meso *C*), 126.5 (4° Ar), 135.1 (4° Ar), 135.1 (4° Ar), 135.9 (4° Ar), 137.2 (4° Ar), 138.0 (4° Ar), 138.1 (4° Ar), 155.3 (4° Ar), 155.3 (4° Ar), 158.8 (4° Ar), 158.8 (4° Ar), 171.6 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 1628.9 for $C_{94}H_{132}N_8O_8Zn_2$; APCI(+ve) found *m/z* 1632.7 $(M+5)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 473 nm; ε_{522}(90% methanol, 10% chloroform): 2.71 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{466}$(90% methanol, 10% chloroform) = -21.25 cm^2mmol^{-1}, $\Delta\varepsilon_{513}$ = -47.92 cm^2mmol^{-1}, $\Delta\varepsilon_{529}$ = +105.83 cm^2mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*R*)-1-(methylheptyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9l**)



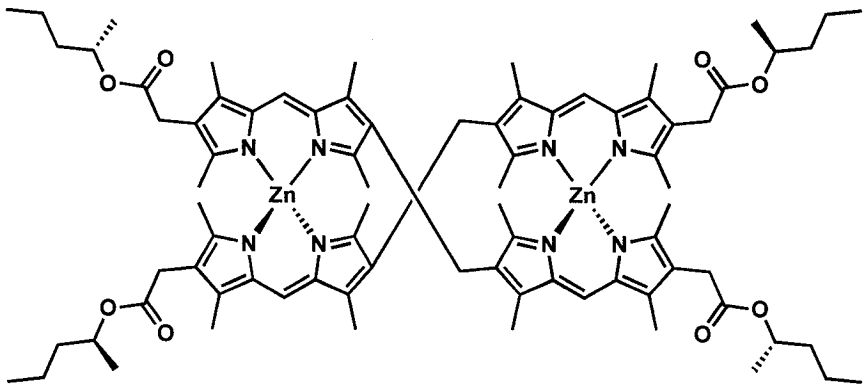
Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a soution of 2,2'-bis{8-[(*R*)-1-(methylheptyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8l**) (0.091 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9k**, the product was obtained as a fuscia-coloured film. (Yield: 0.081 g, 99%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.82-0.85 (12H, m, CH_2CH_3), 1.13 (12H, d, J = 6.0 Hz, $CHCH_3$), 1.20-1.26 (32H, m, $CH_2(CH_2)_4CH_3$), 1.37-1.51 (8H, m, $CHCH_2CH_2$), 1.54 (12H, s, $ArCH_3$), 2.00 (12H, s, $ArCH_3$), 2.20 (12H, s, $ArCH_3$), 2.22 (12H, s, $ArCH_3$), 3.32 (8H, s, $ArCH_2C(O)$), 3.39 (4H, s, $ArCH_2Ar$), 4.82-4.84 (4H, m, $CHCH_3$), 6.91 (4H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.0 ($ArCH_3$), 10.3 ($ArCH_3$), 14.2 (CH_2CH_3), 15.1 ($ArCH_3$), 15.1 ($ArCH_3$), 20.1 ($CHCH_3$), 20.6 ($ArCH_2Ar$), 22.8 ($CH_2CH_2CH_3$), 25.4 ($CH_2CH_2CH_2$), 29.3 ($CH_2CH_2CH_2$), 31.7

($CH_2CH_2CH_2$), 31.9 ($ArCH_2C(O)$), 36.1 ($CHCH_2CH_2$), 71.1 (C_aHCH_3), 71.2 (C_bHCH_3), 119.7 (4° Ar), 121.2 (meso *C*), 126.5 (4° Ar), 135.1 (4° Ar), 135.9 (4° Ar), 137.2 (4° Ar), 138.0 (4° Ar), 138.1 (4° Ar), 155.3 (4° Ar), 155.3 (4° Ar), 158.9 (4° Ar), 171.6 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments);

^{15}N NMR: δ(51 MHz, $CDCl_3$): -165, -172; calcd 1628.9 for $C_{94}H_{132}N_8O_8Zn_2$; APCI(+ve) found *m/z* 1633.7 $(M+5)^+$; λ_{max}(90% methanol, 10% chloroform): 523 nm, 473 nm; ε_{523}(90% methanol, 10% chloroform): 2.71 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{469}$(90% methanol, 10% chloroform) = +22.15 cm^2mmol^{-1}, $\Delta\varepsilon_{516}$ = +48.60 cm^2mmol^{-1}, $\Delta\varepsilon_{531}$ = -103.01 cm^2mmol^{-1}.

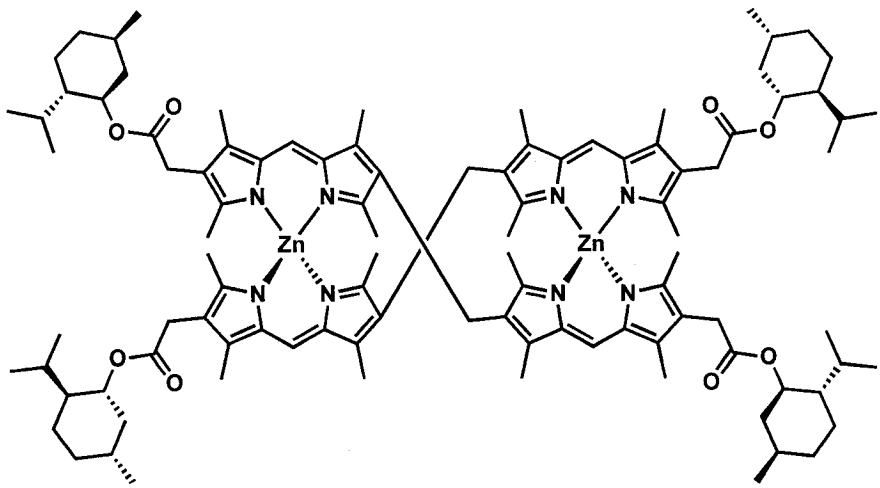
Zinc(II) di(2,2'-bis{8-[(*S*)-1-(methylbutyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9m**)



Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*S*)-1-(methylbutyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8m**) (0.083 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9k**, the product was obtained as a fuscia-coloured film. (Yield: 0.072 g, 99%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.84 (12H, td, J = 1.5 Hz, J = 7.3 Hz, CH_2CH_3), 1.13 (12H, dd, J = 1.0 Hz, J = 5.5 Hz, $CHCH_3$), 1.19-1.28 (8H, m, CH_2CH_3), 1.35-1.42 (16H, m, $CH_2CH_aH_b$ + $ArCH_3$), 1.47-1.52 (4H, m, $CH_2CH_aH_b$), 2.01 (12H, s, $ArCH_3$), 2.20 (12H, s, $ArCH_3$), 2.23 (12H, s, $ArCH_3$), 3.32 (8H, s, $ArCH_2C(O)$), 3.40 (8H, s, $ArCH_2Ar$), 4.83-4.87 (4H, m, $CHCH_3$), 6.91 (4H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.0 ($ArCH_3$), 10.3 ($ArCH_3$), 14.1 (CH_2CH_3), 15.1 ($ArCH_3$), 15.1 ($ArCH_3$), 18.7 (CH_2CH_3), 20.1 ($CHCH_3$), 20.6 ($ArCH_2Ar$), 31.7 ($ArCH_2C(O)$), 38.2 ($CHCH_2$), 71.0 ($CHCH_3$), 119.7 (4° Ar), 121.2 (meso *C*), 126.5 (4° Ar), 135.1 (4° Ar), 135.9 (4° Ar), 137.2 (4° Ar), 138.1 (4° Ar), 138.1 (4° Ar), 155.3 (4° Ar), 158.8 (4° Ar), 171.6 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 1460.7 for $C_{82}H_{108}N_8O_8Zn_2$; APCI(+ve) found *m/z* 1465.5 $(M+5)^+$; λ_{max}(90% methanol, 10% chloroform): 522 nm, 472 nm; ε_{522}(90% methanol, 10% chloroform): 3.03 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{477}$(90% methanol, 10% chloroform) = +4.23 cm^2mmol^{-1}, $\Delta\varepsilon_{518}$ = -21.81 cm^2mmol^{-1}, $\Delta\varepsilon_{532}$ = +37.62 cm^2mmol^{-1}.

Zinc(II) di(2,2'-bis{8-[(*R*)-1-(5-(*R*)-isopropyl-2-(*S*)-methylcyclohexyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene})[141] (**9n**)

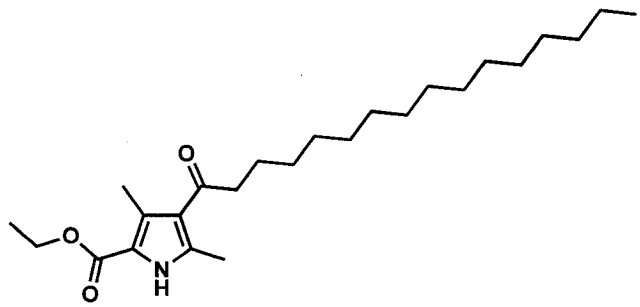


Following the procedure used for the preparation of **9a**, a solution of zinc acetate dihydrate (0.11 g, 0.50 mmol) and sodium acetate trihydrate (0.068 g, 0.50 mmol) in methanol (5 mL) was added to a solution of 2,2'-bis{8-[(*R*)-1-(5-(*R*)-isopropyl-2-(*S*)-methylcyclohexyloxycarbonyl)methyl]-1,3,7,9-tetramethyldipyrromethene} hydrobromide (**8n**) (0.096 g, 0.10 mmol) in chloroform (5 mL). Following a similar work-up as for **9k**, the product was obtained as a fuscia-coloured film. (Yield: 0.086 g, 99%)

Sol: chloroform, DCM; Sp. Sol: methanol, ethanol, acetone, ethyl acetate; Insol: water, diethyl ether, hexanes; m.p. >250 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.68 (12H, t, J = 6.3 Hz, CHCH_3), 0.80-0.91 (32H, m, CH(CH_3)$_2$ + CH_aCH$_b$ + CH_cCH$_d$) 0.97-1.05 (4H, m, CH_eCH$_f$), 1.26-1.32 (4H, m, CHCH(CH$_3$)$_2$), 1.38-1.45 (16H, m, ArCH_3 + CHCH$_3$), 1.62-1.75 (8H, m, CH$_a$CH_b + CH$_e$CH_f) 1.72-1.77 (4H, m, CH(CH$_3$)$_2$), 1.88-1.90 (4H, m, CH$_c$CH_d), 2.01 (12H, s, ArCH_3), 2.20 (12H, s, ArCH_3), 2.23 (12H, s, ArCH_3), 3.33 (8H, s, ArCH_2C(O)), 3.39 (4H, s, ArCH_2Ar), 4.58-4.64 (4H, m, CH(CH$_3$)O), 6.91 (4H, s, meso

H); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.0 (Ar*C*H_3), 10.3 (Ar*C*H_3), 15.1 (Ar*C*H_3), 15.1 (Ar*C*H_3), 16.5 (CH*C*$_a$$H_3$), 16.6 (CH*C*$_b$$H_3$), 20.6 (Ar*C*$H_2$Ar), 20.9 (CH(*C*$H_3$)$_a$($CH_3$)$_b$), 20.9 (CH($CH_3$)$_a$(*C*$H_3$)$_b$), 22.2 (*C*$H_2$CH($CH_3$)), 26.5 (*C*H($CH_3$)$_2$), 31.5 (*C*H), 31.7 (Ar*C*H_2C(O)), 34.3 (*C*H_2), 41.0 (*C*H_2), 47.3 (*C*HCH(CH_3)$_2$), 74.3 (*C*$_a$HO), 74.4 (*C*$_b$HO), 119.6 (4° Ar), 119.6 (4° Ar), 121.1 (meso *C*), 126.5 (4° Ar), 126.5 (4° Ar), 135.1 (4° Ar), 135.9 (4° Ar), 135.9 (4° Ar), 137.2 (4° Ar), 138.1 (4° Ar), 138.1 (4° Ar), 155.3 (4° Ar), 155.3 (4° Ar), 158.8 (4° Ar), 158.8 (4° Ar), 171.5 (*C*$_a$=O), 171.5 (*C*$_b$=O) (assignment by JMOD and ^{13}C-^1H HSQC experiments); calcd 1732.9 for $C_{102}H_{140}N_8O_8Zn_2$; APCI(+ve) found *m/z* 1737.5 $(M+5)^+$; λ_{max}(90% methanol, 10% chloroform): 523 nm, 473 nm; ε_{523}(90% methanol, 10% chloroform): 2.48 x10^6 $Lmol^{-1}dm^{-1}$; $\Delta\varepsilon_{471}$(90% methanol, 10% chloroform) = -11.66 cm^2mmol^{-1}, $\Delta\varepsilon_{520}$ = +23.57 cm^2mmol^{-1}, $\Delta\varepsilon_{530}$ = -2.15 cm^2mmol^{-1}.

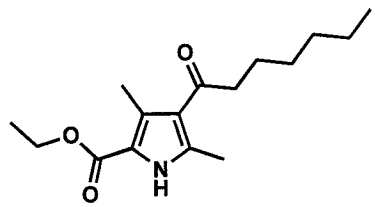
Ethyl 4-hexadecanoyl-3,5-dimethylpyrrole-2-carboxylate (**13a**)



Under dry conditions and using nitrogen gas as an inert atmosphere ethyl 3,5-dimethylpyrrole-2-carboxylate[175] (**12a**) (8.4 g, 50 mmol) was dissolved, with stirring, in dry DCM (100 mL) in a dry two-neck 250 mL round-bottom flask. Palmitoyl chloride (15.9 mL, 14.4 g, 53 mmol) was added and the resulting solution was cooled to 0 °C by suspension in an ice bath. At this lowered temperature tin(IV) chloride (5.9 mL,

13.0 g, 50 mmol) was added slowly dropwise by syringe. The reaction was warmed to room temperature and was stirred for 2 hours. The reaction mixture was then poured into 2% (w/v) aqueous hydrochloric acid solution (400 mL) contained in a 800 mL beaker and was stirred for 15 minutes. Two phases were separated using a separatory funnel and the aqueous phase was extracted with DCM (2 x 80 mL). The combined organic phase was washed with 5% (w/v) aqueous sodium hydrogencarbonate solution (3 x 60 mL) and brine (20 mL), dried with anhydrous sodium sulfate, filtered and the solvent was removed using a rotary evaporator. Chromatographic separation on silica using 1% (v/v) methanol/DCM as the eluent gave the product as a white solid. (Yield: 16.2 g, 80%) m.p. 87-89 °C (literature:[177,179] 90-91 °C, 93-94 °C); R_f 0.66 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_{14}CH_3$), 1.25-1.39 (27H, m, $(CH_2)_{12}CH_3$ + OCH_2CH_3), 1.68 (2H, p, J = 7.3 Hz, $C(O)CH_2CH_2$), 2.53 (3H, s, $ArCH_3$), 2.59 (3H, s, $ArCH_3$), 2.72 (2H, t, J = 7.3 Hz, $C(O)CH_2$), 4.34 (2H, q, J = 7.1 Hz, OCH_2CH_3), 9.62 (1H, br s, NH); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 12.9 ($ArCH_3$), 14.3 ($(CH_2)_{14}CH_3$), 14.6 (OCH_2CH_3), 15.2 ($ArCH_3$), 22.9 (CH_2CH_2), 24.5 ($C(O)CH_2CH_2$), 29.5 (CH_2CH_2), 29.7 (CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 32.1 (CH_2CH_2), 43.1 ($C(O)CH_2$), 60.6 (OCH_2CH_3), 118.1 (4° Ar), 123.8 (4° Ar), 129.2 (4° Ar), 138.1 (4° Ar), 162.1 ($C(O)OEt$), 198.7 ($C(O)CH_2$) (five CH_2CH_2 signals not resolved, assignment by COSY, JMOD, and ^{13}C-^1H HSQC experiments); calcd 405.3243 for $C_{25}H_{43}NO_3$; EI(+ve)-HRMS found m/z 405.3256 $(M)^+$.

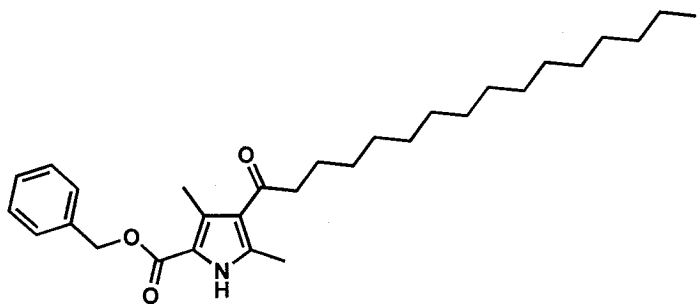
Ethyl 4-heptanoyl-3,5-dimethylpyrrole-2-carboxylate (**13b**)



Following the procedure used for the preparation of **13a**, **12a**[175] (8.4 g, 50 mmol), dissolved in dry DCM (100 mL), was reacted with heptanoyl chloride (8.1 mL, 7.8 g, 53 mmol) and tin(IV) chloride (5.9 mL, 13.0 g, 50 mmol). The mixture was stirred for 2 hours. The work-up was the same as for **13a**. Chromatographic separation on silica using DCM as the eluent gave the product as a white solid. (Yield: 12.9 g, 92%)

m.p. 87-88 °C; R_f 0.55 (silica, 30% ethyl acetate 70% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_5CH_3$), 1.31-1.39 (6H, m, $(CH_2)_3CH_3$), 1.69 (2H, p, J = 7.4 Hz, $C(O)CH_2CH_2$), 2.55 (3H, s, $ArCH_3$), 2.59 (3H, s, $ArCH_3$), 2.73 (2H, t, J = 7.5 Hz, $C(O)CH_2$), 4.34 (2H, q, J = 7.0 Hz, OCH_2CH_3), 10.22 (1H, br s, NH); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 12.8 ($ArCH_3$), 14.1 ($(CH_2)_3CH_3$), 14.4 (OCH_2CH_3), 14.9 ($ArCH_3$), 22.6 (CH_2CH_2), 24.4 ($C(O)CH_2CH_2$), 29.2 (CH_2CH_2), 31.8 (CH_2CH_2), 42.9 ($C(O)CH_2$), 60.5 (OCH_2CH_3), 118.1 (4° Ar), 123.5 (4° Ar), 129.2 (4° Ar), 138.5 (4° Ar), 162.4 (C(O)OEt), 198.6 ($C(O)CH_2$) (assignment by COSY, JMOD, and ^{13}C-^1H HSQC experiments); calcd 279.1834 for $C_{16}H_{25}NO_3$; EI(+ve)-HRMS found *m/z* 279.1827 $(M)^+$.

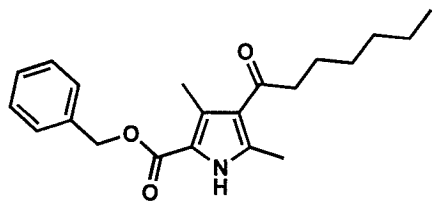
Benzyl 4-hexadecanoyl-3,5-dimethylpyrrole-2-carboxylate (**13c**)



Following the procedure used for the preparation of **13a**, benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) (11.5 g, 50 mmol), dissolved in dry DCM (100 mL), was reacted with palmitoyl chloride (15.9 mL, 14.4 g, 53 mmol) and tin(IV) chloride (5.9 mL, 13.0 g, 50 mmol). The mixture was stirred for 2 hours. The work-up was the same as for **13a**. Chromatographic separation on silica using 1% (v/v) methanol/DCM as the eluent gave the product as a white solid. (Yield: 18.0 g, 77%)

m.p. 104-105 °C; R_f 0.59 (silica, 30% ethyl acetate 70% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_{14}CH_3$), 1.25-1.31 (24H, m, $(CH_2)_{12}CH_3$), 1.67 (2H, p, J = 7.0 Hz, $C(O)CH_2CH_2$), 2.48 (3H, s, $ArCH_3$), 2.59 (3H, s, $ArCH_3$), 2.70 (2H, t, J = 7.5 Hz, $C(O)CH_2$), 5.31 (2H, s, CH_2Ph), 7.31-7.0 (5H, m, Ar*H*), 9.50 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 13.0 ($ArCH_3$), 14.3 ($(CH_2)_{14}CH_3$), 15.2 ($ArCH_3$), 22.9 (CH_2CH_2), 24.5 ($C(O)CH_2CH_2$), 29.5 (CH_2CH_2), 29.6 (CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 32.1 (CH_2CH_2), 43.1 ($C(O)CH_2$), 66.3 (CH_2Ph), 117.7 (4° Ar), 123.8 (4° Ar), 128.3 (ArH), 128.5 (ArH), 128.8 (ArH), 129.9 (4° Ar), 136.2 (4° Ar), 138.4 (4° Ar), 161.7 ($C(O)OEt$), 198.7 ($C(O)CH_2$) (five CH_2CH_2 signals not resolved, assignment by COSY, JMOD, and ^{13}C-^1H HSQC experiments); calcd 467.3399 for $C_{30}H_{45}NO_3$; EI(+ve)-HRMS found *m/z* 467.3394 $(M)^+$.

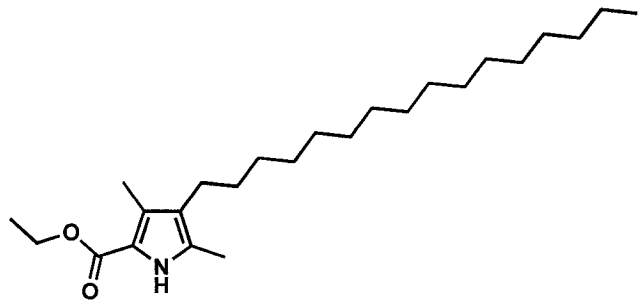
Benzyl 4-heptanoyl-3,5-dimethylpyrrole-2-carboxylate (**13d**)



Following the procedure used for the preparation of **13a**, **12b**[176] (11.5 g, 50 mmol), dissolved in dry DCM (100 mL), was reacted with heptanoyl chloride (8.1 mL, 7.8 g, 53 mmol) and tin(IV) chloride (5.9 mL, 13.0 g, 50 mmol). The mixture was stirred for 2 hours. The work-up was the same as for **13a**. Chromatographic separation on silica using DCM as the eluent gave the product as a white solid. (Yield: 10.4 g, 61%)

m.p. 101-102 °C; R_f 0.69 (30% ethyl acetate 70% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.8 Hz, $(CH_2)_4CH_3$), 1.28-1.36 (6H, m, $(CH_2)_3CH_3$), 1.67 (2H, p, J = 7.5 Hz, $C(O)CH_2CH_2$), 2.48 (3H, s, $ArCH_3$), 2.60 (3H, s, $ArCH_3$), 2.71 (2H, t, J = 7.5 Hz, $C(O)CH_2$), 5.32 (2H, s, OCH_2Ph), 7.33-7.41 (5H, m, Ar*H*), 9.23 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 13.0 ($ArCH_3$), 14.2 ($(CH_2)_4CH_3$), 15.3 ($ArCH_3$), 22.8 (CH_2CH_2), 24.5 ($C(O)CH_2CH_2$), 29.3 (CH_2CH_2), 32.0 (CH_2CH_2), 43.1 ($C(O)CH_2$), 66.3 (CH_2Ph), 117.7 (4° Ar), 123.9 (4° Ar), 128.4 (ArH), 128.5 (ArH), 128.8 (ArH), 129.9 (4° Ar), 136.2 (4° Ar), 138.3 (4° Ar), 161.5 ($C(O)OEt$), 198.7 ($C(O)CH_2$) (assignment by COSY, JMOD, and ^{13}C-^1H HSQC experiments); calcd 341.1991 for $C_{21}H_{27}NO_3$; EI(+ve)-HRMS found *m/z* 341.1992 $(M)^+$.

Ethyl 4-hexadecyl-3,5-dimethylpyrrole-2-carboxylate (**14a**)

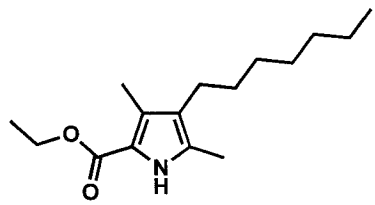


Under dry conditions and using nitrogen gas as an inert atmosphere ethyl 4-hexadecanoyl-3,5-dimethylpyrrole-2-carboxylate (**13a**) (12.2 g, 30 mmol) was dissolved, with stirring, in dry THF (50 mL) in a dry two-neck 250 mL round-bottom flask. The resulting solution was cooled to 0 °C by suspension in an ice bath. At this lowered temperature 1.0 M borane-tetrahydrofuran complex (60.0 mL, 60 mmol) in THF was added slowly dropwise by syringe. The mixture was warmed to room temperature and was stirred for 16 hours. The reaction mixture was then cooled to 0 °C by suspension in an ice bath. Distilled water (50 mL) (CAUTION: effervescence) and 5% (w/v) aqueous hydrochloric acid solution (50 mL) were added to the reaction mixture, and the solution was stirred for 30 minutes. The reaction mixture was concentrated using a rotary evaporator, resulting in the formation of a precipitate that was collected by suction filtration. The solid was dissolved in DCM (200 mL) and washed with 5% (w/v) aqueous hydrochloric acid solution (3 x 60 mL) and brine (20 mL), dried with anhydrous sodium sulfate, filtered and the solvent was removed using a rotary evaporator. Chromatographic separation on silica using DCM as the eluent gave the product as a white solid. (Yield: 9.5 g, 81%)

m.p. 74-75 °C (literature:[177] 68-69 °C); R_f 0.72 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.8 Hz, $(CH_2)_{15}CH_3$), 1.26-1.42 (31H, m,

(CH_2)$_{14}$$CH_3$ + OCH_2CH_3), 2.19 (3H, s, ArCH_3), 2.26 (3H, s, ArCH_3), 2.33 (2H, t, J = 7.5 Hz, ArCH_2), 4.29 (2H, q, J = 7.2 Hz, O$CH_2$$CH_3$), 9.07 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.8 (ArCH_3), 11.6 (ArCH_3), 14.3 ((CH_2)$_{15}$$CH_3$), 14.8 ($OCH_2CH_3$), 22.9 ($CH_2CH_2$), 24.2 (Ar$CH_2$), 29.6 ($CH_2CH_2$), 29.7 ($CH_2CH_2$), 29.8 ($CH_2CH_2$), 29.9 ($CH_2CH_2$), 31.1 (Ar$CH_2CH_2$), 32.1 ($CH_2CH_2$), 59.7 (O$CH_2CH_3$), 116.9 (4° Ar), 122.5 (4° Ar), 127.1 (4° Ar), 129.9 (4° Ar), 162.2 (*C*=O) (seven CH_2CH_2 signals not resolved, assignment by COSY, JMOD, and ^{13}C-^{1}H HSQC experiments); calcd 391.3450 for $C_{25}H_{45}NO_2$; EI(+ve)-HRMS found *m/z* 391.3447 $(M)^+$.

Ethyl 4-heptyl-3,5-dimethylpyrrole-2-carboxylate (**14b**)

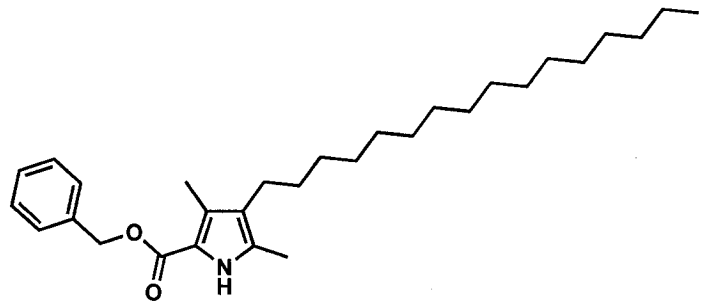


Following the procedure used for the preparation of **14a**, ethyl 4-heptanoyl-3,5-dimethylpyrrole-2-carboxylate (**13b**) (8.4 g, 30 mmol) was dissolved in dry THF (50 mL). 1.0 M Borane-tetrahydrofuran complex (60.0 mL, 60 mmol) in THF was added to this solution. The mixture was stirred for 16 hours. The work-up was the same as for **14a**. Chromatographic separation on silica using 50% (v/v) hexanes/DCM as the eluent gave the product as a white solid. (Yield: 5.9 g, 74%)

m.p. 50-51 °C (literature[181,180] 47-49 °C, 54-55 °C); R_f 0.67 (30% ethyl acetate 70% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.8 Hz, (CH_2)$_6$$CH_3$), 1.24-1.44 (13H, m, CH_2(CH_2)$_5$$CH_3$ + OCH_2CH_3), 2.19 (3H, s, ArCH_3), 2.26 (3H, s, ArCH_3), 2.34 (2H, t, J = 7.8 Hz, ArCH_2), 4.29 (2H, q, J = 7.2 Hz, O$CH_2$$CH_3$), 9.00 (1H, br s, N*H*);

$^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.8 (Ar*C*H_3), 11.5 (Ar*C*H_3), 14.2 ((*C*H_2)$_6$*C*H_3), 14.7 (O*C*H_2*C*H_3), 22.8 (*C*H_2*C*H_2), 24.2 (Ar*C*H_2), 29.4 (*C*H_2*C*H_2), 29.6 (*C*H_2*C*H_2), 31.1 (ArCH$_2$*C*H_2), 32.1 (*C*H_2*C*H_2), 59.7 (O*C*H_2CH$_3$), 116.9 (4° Ar), 122.5 (4° Ar), 127.1 (4° Ar), 130.1 (4° Ar), 162.3 (*C*=O) (assignment by COSY and ^{13}C-^1H HSQC experiments); calcd 265.2042 for $C_{16}H_{27}NO_2$; EI(+ve)-HRMS found *m/z* 265.2032 $(M)^+$.

Benzyl 4-hexadecyl-3,5-dimethylpyrrole-2-carboxylate (**14c**)

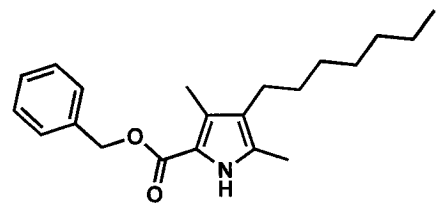


Following the procedure used for the preparation of **14a**, benzyl 4-hexadecanoyl-3,5-dimethylpyrrole-2-carboxylate (**13c**) (14.0 g, 30 mmol) was dissolved in dry THF (50 mL). 1.0 M Borane-tetrahydrofuran complex (60.0 mL, 60 mmol) in THF was added to this solution. The mixture was stirred for 16 hours. The work-up was the same as for **14a**. Chromatographic separation on silica using a gradient of 0→0.5% (v/v) methanol/DCM as the eluent gave the product as a white solid. (Yield: 12.1 g, 89%)

m.p. 66-67 °C; R_f 0.73 (40% ethyl acetate 60% hexanes); ^1H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, *J* = 7.0 Hz, (CH$_2$)$_{15}$C*H*$_3$), 1.25-1.41 (28H, m, (C*H*$_2$)$_{14}$CH$_3$), 2.16 (3H, s, ArC*H*$_3$), 2.28 (3H, s, ArC*H*$_3$), 2.33 (2H, t, *J* = 7.5 Hz, ArC*H*$_2$), 5.29 (2H, s, OC*H*$_2$Ph), 7.29-7.41 (5H, m, Ar*H*), 8.88 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 11.0 (Ar*C*H$_3$), 11.7 (Ar*C*H$_3$), 14.3 ((CH$_2$)$_{15}$*C*H$_3$), 22.9 (*C*H$_2$*C*H$_2$), 24.2 (Ar*C*H$_2$), 29.6

(CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 31.1 ($ArCH_2CH_2$), 32.1 (CH_2CH_2), 65.5 (CH_2Ph), 116.5 (4° Ar), 122.8 (4° Ar), 127.8 (4° Ar), 128.1 (ArH), 128.2 (ArH), 128.7 (ArH), 130.2 (4° Ar), 137.0 (4° Ar), 161.7 (C=O) (seven CH_2CH_2 signals not resolved, assignment by COSY and ^{13}C-^1H HSQC experiments); calcd 453.3607 for $C_{30}H_{47}NO_2$; EI(+ve)-HRMS found *m/z* 453.3588 $(M)^+$.

Benzyl 4-heptyl-3,5-dimethylpyrrole-2-carboxylate (**14d**)

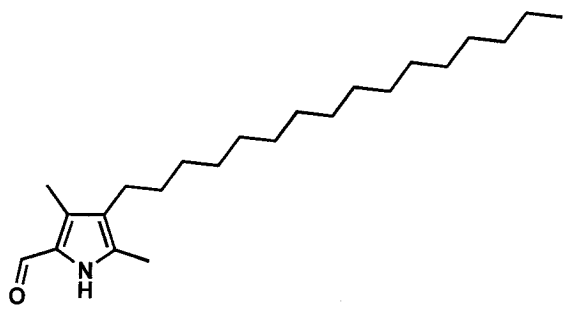


Following the procedure used for the preparation of **14a**, benzyl 4-heptanoyl-3,5-dimethylpyrrole-2-carboxylate (**14d**) (10.2 g, 30 mmol) was dissolved in dry THF (50 mL). 1.0 M Borane-tetrahydrofuran complex (60.0 mL, 60 mmol) in THF was added to this solution. The mixture was stirred for 16 hours. The work-up was the same as for **14a**. Chromatographic separation on silica using a gradient of 0→35% (v/v) DCM/hexanes as the eluent gave the product as a white solid. (Yield: 6.0 g, 61%)

m.p. 65-67 °C; R_f 0.64 (silica, 30% ethyl acetate 70% hexanes); ^1H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_6CH_3$), 1.22-1.33 (8H, m, $CH_2(CH_2)_4CH_3$), 1.37-1.43 (2H, m, $ArCH_2CH_2$), 2.17 (3H, s, $ArCH_3$), 2.28 (3H, s, $ArCH_3$), 2.33 (2H, t, J = 7.5 Hz, $ArCH_2$), 5.29 (2H, s, OCH_2Ph), 7.29-7.41 (5H, m, ArH), 8.72 (1H, br s, NH); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.9 ($ArCH_3$), 11.7 ($ArCH_3$), 14.3 ($(CH_2)_6CH_3$), 22.9 (CH_2CH_2), 24.2 ($ArCH_2$), 29.4 (CH_2CH_2), 29.6 (CH_2CH_2), 31.1 ($ArCH_2CH_2$), 32.1 (CH_2CH_2), 65.6 (CH_2Ph), 116.5 (4° Ar), 112.8 (4° Ar), 127.9 (4° Ar), 128.1 (ArH), 128.2

(ArH), 128.7 (ArH), 130.1 (4° Ar), 136.9 (4° Ar), 161.6 (*C*=O) (assignment by COSY and ^{13}C-^{1}H HSQC experiments); calcd 327.2198 for $C_{21}H_{29}NO_2$; EI(+ve)-HRMS found *m/z* 327.2190 $(M)^+$.

4-Hexadecyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11a**)



Isolation of **15a**:

Method A (starting from **14a**):

A solution of sodium hydroxide (2.0 g, 50 mmol) in water (10 mL) was added, with stirring, to a solution of ethyl 4-hexadecyl-3,5-dimethylpyrrole-2-carboxylate (**14a**) (7.8 g, 20 mmol) dissolved in 95% ethanol (40 mL) contained in a 100 mL round-bottom flask equipped with a condenser. This mixture was heated to reflux, with stirring, for 16 hours. The reaction mixture was then cooled to room temperature and acidified with 5% (w/v) aqueous solution of hydrochloric acid, resulting in the precipitation of a white solid. The product was collected by suction filtration and used immediately in the formylation reaction.

Method B (starting from **14c**):

Hydrogenolysis of benzyl 4-hexadecyl-3,5-dimethylpyrrole-2-carboxylate (**14c**) (9.1 g, 20 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.018 g) in THF (100 mL) contained in a 250 mL round-bottom flask. The

reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. The solvent from the filtrate was removed using a rotary evaporator, producing a white solid that was used immediately in the formylation reaction.

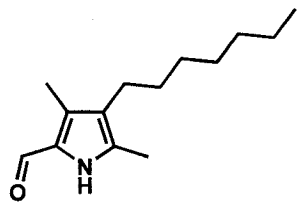
Formylation:

Under dry conditions and using nitrogen gas as an inert atmosphere a solution of 4-hexadecyl-3,5-dimethylpyrrole-2-carboxylic acid (**15a**) in *N*,*N*-dimethylformamide (30 mL) contained in a 100 mL two-neck round-bottom flask equipped with a condenser was heated to reflux for 2 hours with stirring. The reaction mixture was cooled to 0 °C by suspension in an ice bath. At this lowered temperature the Vilsmeier-Haack reagent, prepared by mixing phosphorus(V) oxychloride (11.5 mL, 123 mmol) and *N*,*N*-dimethylformamide (11.5 mL, 149 mmol) in DCM (40 mL), was added slowly dropwise by syringe. The reaction was heated to reflux, with stirring, for 1 hour and then poured into distilled water (400 mL) contained in a 1000 mL beaker. Sodium carbonate was added slowly (CAUTION: effervescence) with stirring until the pH of the solution was 8, as indicated by pH paper. The reaction mixture was transferred to a 1000 mL round-bottom flask equipped with a condenser and heated to reflux with stirring for 2 hours. The reaction mixture was then cooled to room temperature and was stirred for 16 hours resulting in the formation of a precipitate that was collected by suction filtration. Chromatographic separation on silica using 1% (v/v) methanol/DCM as the eluent gave the product as a beige solid. (Yield: 3.0 g, 43%)

m.p. 98-99 °C; R_f 0.58 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.879 (3H, t, J = 6.8 Hz, $(CH_2)_{15}CH_3$), 1.26-1.29 (26H, m, $CH_2(CH_2)_{13}CH_3$), 1.41-1.42

(2H, m, $CH_2(CH_2)_{13}CH_3$), 2.23 (3H, s, $ArCH_3$), 2.25 (3H, s, $ArCH_3$), 2.34 (2H, t, J = 7.5 Hz, $ArCH_2$), 9.45 (1H, br s, NH), 9.46 (1H, s, C(O)H); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 9.1 ($ArCH_3$), 11.9 ($ArCH_3$), 14.3 ($(CH_2)_{15}CH_3$), 22.9 (CH_2CH_2), 24.0 ($ArCH_2$), 29.6 (CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 30.8 ($ArCH_2CH_2$), 32.1 (CH_2CH_2), 123.7 (4° Ar), 128.1 (4° Ar), 132.3 (4° Ar), 135.6 (4° Ar), 175.9 (C=O) (seven CH_2CH_2 signals not resolved, assignment by COSY and ^{13}C-^1H HSQC experiments); calcd 347.3188 for $C_{23}H_{41}NO$; EI(+ve)-HRMS found *m/z* 347.3194 $(M)^+$.

4-Heptyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11b**)



Isolation of **15b**:

Method A (starting from **14b**):

A solution of sodium hydroxide (2.0 g, 50 mmol) in water (10 mL) was added, with strring, to a solution of ethyl 4-heptyl-3,5-dimethylpyrrole-2-carboxylate (**14b**) (5.3 g, 20 mmol) dissolved in 95% ethanol (40 mL) contained in a 100 mL round-bottom flask equipped with a condenser. This mixture was heated to reflux, with stirring, for 16 hours. The reaction mixture was then cooled to room temperature and acidified with 5% (w/v) aqueous solution of hydrochloric acid, resulting in the precipitation of a white solid. The product was collected by suction filtration and used immediately in the formylation reaction.

Method B (starting from **14d**):

Hydrogenolysis of benzyl 4-heptyl-3,5-dimethylpyrrole-2-carboxylate (**14d**) (6.5 g, 20 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.018 g) in THF (100 mL) contained in a 250 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. The solvent from the filtrate was removed using a rotary evaporator, producing a white solid that was used immediately in the formylation reaction.

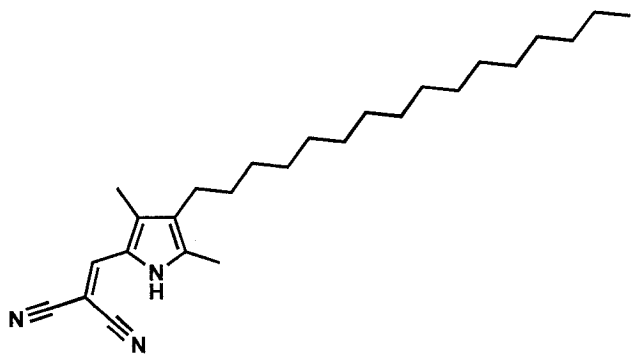
Formylation:

Following the procedure used for the preparation of **11a**, **15b** was decarboxylated in *N*,*N*-dimethylformamide (30 mL) and reacted with Vilsmeier-Haack reagent, prepared by mixing phosphorus(V) oxychloride (11.5 mL, 123 mmol) and *N*,*N*-dimethylformamide (11.5 mL, 149 mmol) in DCM (40 mL). The work-up procedure was the same as for **11a**. Chromatographic separation on silica using a gradient of 0→2% (v/v) methanol/DCM as the eluent gave the product as a beige solid. (Yield: 2.7 g, 60%)

m.p. 81-82 °C; R_f 0.76 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_6CH_3$), 1.24-1.33 (8H, m, $(CH_2)_4CH_3$), 1.39-1.45 (2H, m, $CH_2CH_2(CH_2)_4$), 2.25 (3H, s, $ArCH_3$), 2.26 (3H, s, $ArCH_3$), 2.34 (2H, t, J = 7.5 Hz, $ArCH_2(CH_2)_5$), 9.44 (1H, s, C(O)*H*), 9.88 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 9.0 ($ArCH_3$), 11.9 ($ArCH_3$), 14.3 ($(CH_2)_6CH_3$), 22.9 (CH_2CH_2), 24.0 ($ArCH_2$), 29.4 (CH_2CH_2), 29.6 (CH_2CH_2), 30.8 ($ArCH_2CH_2$), 32.1 (CH_2CH_2), 123.7 (4° Ar), 128.1 (4° Ar), 132.6 (4° Ar), 136.1 (4° Ar), 175.8 (*C*=O) (assignment by COSY and ^{13}C-^1H

HSQC experiments); calcd 221.1780 for $C_{14}H_{23}NO$; EI(+ve)-HRMS found *m/z* 221.1780 $(M)^+$.

2-(2,2-Dicyanovinyl)-4-hexadecyl-3,5-dimethylpyrrole (**16a**)

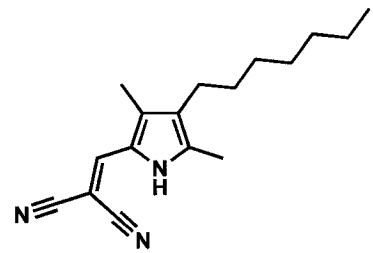


Malononitrile (1.6 g, 24 mmol) was added, with stirring, to a solution of a crude mixture of 4-hexadecyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11a**) (~20 mmol) and a catalytic amount of triethylamine (0.72 mL, 5.2 mmol) in methanol (50 mL) contained in a 100 mL round-bottom flask equipped with a condenser. The reaction mixture was heated to reflux, with stirring, for 5 hours and then cooled to room temperature, resulting in the formation of a precipitate that was collected by suction filtration. Chromatographic separation on silica using a gradient of 0→35% (v/v) DCM/hexanes as the eluent gave the product as a yellow solid. (Yield: 2.1 g, 27 %)

m.p. 114-116 °C; R_f 0.88 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_{15}CH_3$), 1.26-1.42 (28H, m, $(CH_2)_{14}CH_3$), 2.13 (3H, s, $ArCH_3$), 2.32 (3H, s, $ArCH_3$), 2.36 (2H, t, J = 7.5 Hz, $ArCH_2$), 7.31 (1H, s, C(NCCCN)*H*), 9.31 (1H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 9.8 ($ArCH_3$), 12.8 ($ArCH_3$), 14.3 ($(CH_2)_{15}CH_3$), 22.9 (CH_2CH_2), 24.1 ($ArCH_2$), 29.5 (CH_2CH_2), 29.6 (CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 29.9 (CH_2CH_2), 30.5

($ArCH_2CH_2$), 32.1 (CH_2CH_2), 62.8 ($C(CN)_2$), 116.4 ($C{\equiv}N$), 117.9 ($C{\equiv}N$), 124.3 (4° Ar), 126.0 (4° Ar), 136.6 (4° Ar), 140.7 (*C*(NCCCN)H), 141.3 (4° Ar) (five CH_2CH_2 signals not resolved, assignment by COSY, JMOD, and ^{13}C-^{1}H HSQC experiments); calcd 395.3300 for $C_{26}H_{41}N_3$; EI(+ve)-HRMS found *m/z* 395.3320 $(M)^+$.

2-(2,2-Dicyanovinyl)-4-heptyl-3,5-dimethylpyrrole (**16b**)

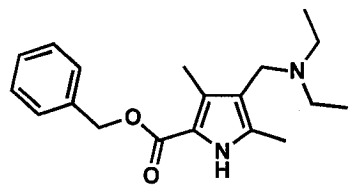


Following the procedure used for the preparation of **16a**, a crude mixture of 4-heptyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11b**) (~20 mmol) was reacted with malononitrile (1.6 g, 24 mmol) and triethylamine (0.72 mL, 5.2 mmol) in methanol (50 mL). Chromatographic separation on silica using 40% (v/v) DCM/hexanes as the eluent gave the product as a yellow solid. (Yield: 1.1 g, 20%)

m.p. 119-120 °C; R_f 0.62 (40% ethyl acetate 60% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, $(CH_2)_6CH_3$), 1.27-1.30 (6H, m, $(CH_2)_3CH_3$), 1.39-1.43 (2H, m, $ArCH_2CH_2$), 2.14 (3H, s, $ArCH_3$), 2.33-2.39 (5H, m, $ArCH_3$ + $ArCH_2$), 7.31 (1H, s, C(NCCCN)*H*), 9.41 (1H, br s, N*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 9.7 ($ArCH_3$), 12.6 ($ArCH_3$), 14.1 ($(CH_2)_6CH_3$), 22.7 (CH_2CH_2), 23.9 ($ArCH_2$), 29.2 (CH_2CH_2), 29.4 (CH_2CH_2), 30.3 ($ArCH_2CH_2$), 31.9 (CH_2CH_2), 62.2 ($C(CN)_2$), 116.4 ($C{\equiv}N$), 117.6 ($C{\equiv}N$), 124.2 (4° Ar), 126.0 (4° Ar), 136.6 (4° Ar), 140.5 (*C*(NCCCN)H), 141.7 (4° Ar)

(assignment by COSY, JMOD, and ^{13}C-^{1}H HSQC experiments); calcd 269.1892 for $C_{17}H_{23}N_3$; EI(+ve)-HRMS found *m/z* 269.1886 $(M)^+$.

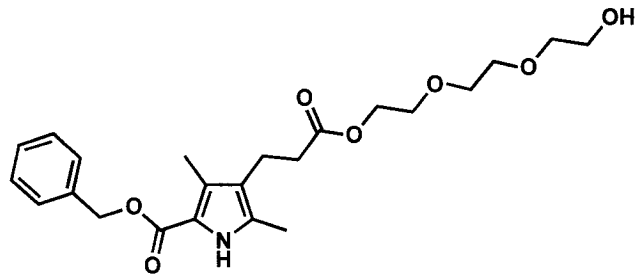
Benzyl 4-(diethylamino)methyl-3,5-dimethylpyrrole-2-carboxylate (**17**)



37% (w/v) Aqueous formaldehyde (1 mL, 13.4 mmol) was added, with stirring, to a solution of benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) (1.62 g, 7.06 mmol) and diethylamine (2.3 mL, 21.9 mmol) in 95% ethanol (3 mL) contained in a 10 mL round-bottom flask equipped with a condenser. The reaction mixture was heated, with stirring, to reflux for 4 hours, then cooled to room temperature and was stirred for 16 hours. The reaction mixture was poured into 5% (w/v) aqueous sodium hydroxide solution (75 mL) and was stirred for 30 minutes resulting in the formation of a precipitate. The product was isolated by suction filtration as a beige powder. (Yield: 2.09 g, 94%)

^{1}H NMR: δ(250 MHz, $CDCl_3$): 1.01 (6H, t, J = 7.5 Hz, $N(CH_2CH_3)_2$), 2.23 (3H, s, $ArCH_3$), 2.33 (3H, s, $ArCH_3$), 2.43 (4H, q, J = 7.5 Hz, $N(CH_2CH_3)_2$), 3.28 (2H, s, $ArCH_2$), 5.29 (2H, s, CH_2Ph), 7.29-7.44 (5H, m, ArH), 8.60 (1H, br s, NH).

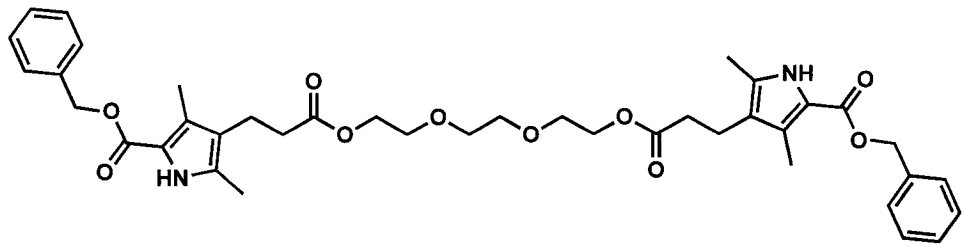
Benzyl 4-[3-(2-[2-(2-hydroxyethoxy)ethoxy]ethoxy)]-3-oxopropyl-3,5-dimethylpyrrole-2-carboxylate (**19**)



Under dry conditions and using nitrogen gas as an inert atmosphere benzyl 3,5-dimethyl-4-(propanoic acid)pyrrole-2-carboxylate (**3**) (2.0 g, 6.6 mmol) and DMAP (0.89 g, 7.3 mmol) were dissolved, with stirring, in dry DCM (150 mL) in a dry two-neck 250 mL round-bottom flask. The resulting solution was cooled to 0 °C by suspension in an ice bath. At this lowered temperature triethyleneglycol (4.4 mL, 33 mmol) was added, followed by HOBT (0.99 g, 7.3 mmol) and EDC·HCl (1.4 g, 7.3 mmol). The reaction mixture warmed to room temperature and was stirred for 16 hours. The solvent was removed from the reaction mixture using a rotary evaporator. Chromatographic separation on silica using a gradient of 40→80% ethyl acetate/hexanes as the eluent gave the product as a colourless oil. (Yield: 2.6 g, 89%)

R_f 0.12 (70% ethyl acetate 30% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 2.20 (3H, s, ArCH_3), 2.28 (3H, s, ArCH_3), 2.42-2.47 (4H, m, CH_2OH + CH_2CH_2C(O)), 2.70 (2H, t, J = 7.5 Hz, CH_2CH_2C(O)), 3.58-3.73 (8H, m, $CH_2CH_2OCH_2CH_2OCH_2CH_2$OH), 4.21 (2H, t, J = 4.8 Hz, CH_2OC(O)), 5.28 (2H, s, OCH_2Ph), 7.30-7.42 (5H, m, ArH), 8.75 (1H, br s, NH); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.9, 11.7, 19.7, 35.1, 62.0, 63.7, 65.7, 69.4, 70.6, 70.8, 72.7, 116.8, 120.3, 127.8, 128.2, 128.3, 128.7, 130.5, 136.8, 161.5, 173.3; calcd 433.2101 for $C_{23}H_{31}NO_7$; EI(+ve)-HRMS found m/z 433.2096 $(M)^+$.

Benzyl 4-(3-(2-(2-(2-(3-(5-(benzyloxycarbonyl)-2,4-dimethylpyrrol-3-yl)propanoyloxy)ethoxy)ethoxy)ethoxy)-3-oxopropyl)-3,5-dimethylpyrrole-2-carboxylate (**20**)

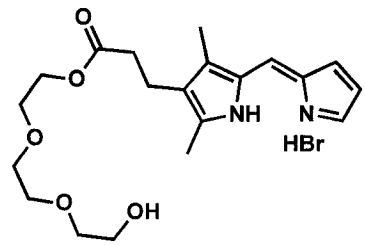


Obtained as a sideproduct of the preparation of **19**. The product is a faintly yellow oil.

(Yield: 0.29 g, 6.0%)

R_f 0.68 (70% ethyl acetate 30% hexanes); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 2.18 (6H, s, ArCH_3), 2.27 (6H, s, ArCH_3), 2.44 (4H, t, J = 7.8 Hz, $CH_2CH_2C(O)$), 2.69 (4H, t, J = 7.5 Hz, $CH_2CH_2C(O)$), 3.57 (4H, s, $CH_2CH_2OCH_2$), 3.63 (4H, t, J = 4.8 Hz, CH_2CH_2O), 4.19 (4H, t, J = 4.8 Hz, $CH_2OC(O)$), 5.28 (4H, s, OCH_2Ph), 7.31-7.41 (10H, m, Ar*H*), 8.69 (2H, br s, N*H*); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.8 (CH_3), 11.7 (CH_3), 19.7 (CH_2), 35.1 (CH_2), 63.7 (CH_2), 65.6 (CH_2), 69.4 (CH_2), 70.7 (CH_2), 116.8 (C), 120.3 (C), 127.8 (C), 128.2 (CH), 128.3 (CH), 128.7 (CH), 130.5 (C), 136.8 (C), 161.4 (C), 173.3 (C) (assignment by DEPT experiment); calcd 716.3 for $C_{40}H_{48}N_2O_{10}$; ESI(+ve) found *m/z* 739.3 $(M+Na)^+$.

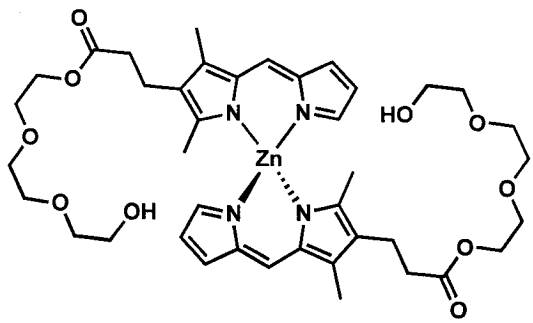
2-[3-(2-[2-(2-hydroxyethoxy)ethoxy]ethoxy)]-3-oxopropyl-1,3-dimethyldipyrromethene hydrobromide (**21**)



Hydrogenolysis of benzyl 4-[3-(2-[2-(2-hydroxyethoxy)ethoxy]ethoxy)]-3-oxopropyl-3,5-dimethylpyrrole-2-carboxylate (**19**) (0.87 g, 2.0 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0089 g) in THF (40 mL) contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas and then was filtered through a plug of Celite® to remove the palladium catalyst. Pyrrole-2-carboxaldehyde (0.19 g, 2.0 mmol) and 48% (w/v) aqueous hydrobromic acid (0.85 mL, 5.0 mmol) were added to the filtrate contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was concentrated by partial removal of solvent using a rotary evaporator. DCM (50 mL) and brine (50 mL) were added to the product mixture. The aqueous phase was separated and extracted with DCM (2 x 20 mL). The combined organic phase was dried with anhydrous sodium sulfate, filtered and the solvent was removed using a rotary evaporator to give the product as a red oil. (Yield: 0.78 g, 85%)

^{1}H NMR: δ(250 MHz, $CDCl_3$): 2.34 (3H, s, ArCH_3), 2.55 (2H, t, J = 6.3 Hz, ArCH_2CH_2), 2.72-2.81 (5H, m, ArCH_3 + ArCH_2CH_2), 3.58-3.77 (10H, m, $CH_2CH_2OCH_2CH_2OCH_2CH_2OH$), 4.22-4.25 (2H, m, CH_2CH_2OH), 6.50-6.52 (1H, m, Ar*H*), 7.11-7.13 (1H, m, Ar*H*), 7.23 (1H, s, meso *H*), 7.72 (1H, s, Ar*H*), 13.83 (1H, br s, N*H*), 14.15 (1H, br s, N*H*).

Zinc(II) bis(2-[3-(2-[2-(2-hydroxyethoxy)ethoxy]ethoxy)]-3-oxopropyl-1,3-dimethyldipyrromethene) (**23**)

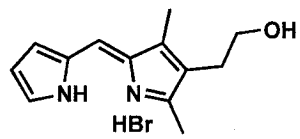


A solution of zinc acetate dihydrate (5.0 g, 23 mmol) and sodium acetate trihydrate (3.1 g, 23 mmol) in methanol (40 mL) was added, with stirring, to a solution of 2-[3-(2-[2-(2-hydroxyethoxy)ethoxy]ethoxy)]-3-oxopropyl-1,3-dimethyldipyrromethene hydrobromide (**21**) (2.1 g, 4.6 mmol) in chloroform (40 mL) contained in a 250 mL round-bottom flask. The reaction mixture was stirred 30 minutes and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as an iridescent red film. (Yield: 1.9 g, 42%)

m.p. 96-102 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.85 (6H, s, ArCH_3), 2.23 (6H, s, ArCH_3), 2.42 (4H, t, J = 7.8 Hz, $CH_2CH_2C(O)$), 2.50 (2H, br s, O*H*), 2.66 (4H, t, J = 7.5 Hz, ArCH_2CH_2), 3.56-3.70 (20H, m, $CH_2CH_2OCH_2CH_2OCH_2CH_2OH$), 4.20 (4H, t, J = 4.8 Hz, $CH_2OC(O)$), 6.38 (2H, d, J = 3.5 Hz, Ar*H*), 7.00 (2H, d, J = 3.5 Hz, Ar*H*), 7.11 (2H, s, C*H*), 7.29 (2H, s, Ar*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.1 (ArCH_3), 14.9 (ArCH_3), 20.2 (ArCH_3), 34.5 ($ArCH_2CH_2C(O)$), 61.9 (CH_2CH_2O), 63.7 (CH_2CH_2OH), 69.3 (CH_2CH_2O), 70.5 (CH_2CH_2O), 70.7 (CH_2CH_2O), 72.6 (CH_2CH_2O), 114.7 (ArH), 126.7 (meso *C*), 127.8 (ArH), 129.1 (4° Ar), 137.7 (4° Ar), 138.9 (4° Ar), 141.7 (4° Ar), 144.6 (ArH), 163.0 (4° Ar), 173.0 (*C*=O) (assignment by ^{13}C-^{1}H HSQC experiment);

calcd 814.3 for $C_{40}H_{54}N_4O_{10}Zn$; ESI(+ve) found *m/z* 674.5 (M-$HO(CH_2)_2O(CH_2)_2O(CH_2)_2OC + Na)^+$.

2-(2-Hydroxyethyl)-1,3-dimethyldipyrromethene hydrobromide (**25**)

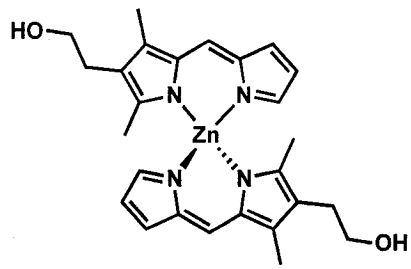


Hydrogenolysis of benzyl 4-(2-hydroxyethyl)-3,5-dimethylpyrrole-2-carboxylate (**24**)[184] (0.93 g, 3.4 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.015 g) in THF (25 mL) contained in a 50 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (5 mL), pyrrole-2-carboxaldehyde (0.32 g, 3.4 mmol), and 48% (w/v) aqueous hydrobromic acid (1.4 mL, 8.5 mmol) were added to the filtrate contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 1 hour the mixture and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The solution was filtered and the residue rinsed with cold methanol to give the product as a red solid. (Yield: 0.93 g, 92%)

m.p. 189-195°C (dec.); ^{1}H NMR: δ(500 MHz, CD_3OD): 2.39 (3H, s, ArCH_3), 2.61 (3H, s, ArCH_3), 2.74 (2H, t, J = 6.3 Hz, ArCH_2CH_2), 3.69 (2H, t, J = 6.5 Hz, $ArCH_2CH_2OH$), 6.70-6.71 (1H, m, Ar*H*), 7.67 (1H, d, J = 1.8 Hz, Ar*H*), 7.71 (1H, s, Ar*H*), 7.73 (1H, s, meso *H*); ^{13}C{^{1}H} NMR: δ(125 MHz, CD_3OD): 10.4 ($ArCH_3$), 13.7 ($ArCH_3$), 28.3 ($ArCH_2CH_2$), 62.0 ($ArCH_2CH_2OH$), 117.9 (ArH), 127.6 (ArH + meso *C*), 129.9 (4° Ar), 131.2 (4° Ar), 132.6 (4° Ar), 136.4 (ArH), 149.9 (4° Ar), 164.5 (ArH) (assignment by

COSY, JMOD, and ^{13}C-^{1}H HSQC experiments); calcd 296.0524 for $C_{13}H_{17}N_2OBr$; EI(+ve)-HRMS found *m/z* 216.1259 $(M\text{-}HBr)^+$.

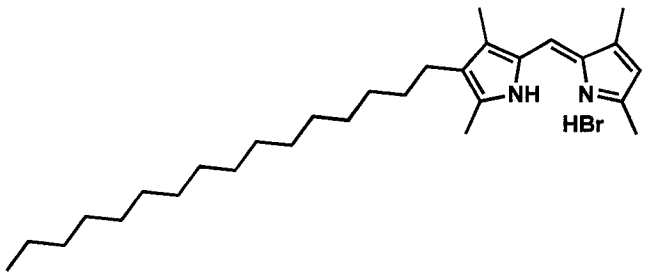
Zinc(II) bis[2-(2-hydroxyethyl)-1,3-dimethyldipyrromethene] (**26**)



A solution of zinc acetate dihydrate (0.51 g, 1.7 mmol) and sodium acetate trihydrate (0.23 g, 1.7 mmol) in methanol (10 mL) was added, with stirring, to a solution of 2-(2-hydroxyethyl)-1,3-dimethyldipyrromethene hydrobromide (**25**) (0.10 g, 0.34 mmol) in chloroform (10 mL) contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 30 minutes and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.040 g, 47%)

^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.86 (6H, s, $ArCH_3$), 2.25 (6H, s, $ArCH_3$), 2.61 (4H, t, J = 6.8 Hz, $ArCH_2CH_2$), 3.64 (4H, t, J = 6.8 Hz, $ArCH_2CH_2OH$), 6.39-6.40 (2H, m, Ar*H*), 7.02 (2H, d, J = 3.7 Hz, Ar*H*), 7.13 (2H, s, meso *H*), 7.31 (2H, s, Ar*H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.3 ($ArCH_3$), 15.1 ($ArCH_3$), 28.4 ($ArCH_2CH_2$), 62.5 ($ArCH_2CH_2OH$), 114.9 (meso *C*), 126.8 (ArH), 126.9 (4° Ar), 128.0 (ArH), 137.8 (4° Ar), 138.9 (4° Ar), 142.6 (4° Ar), 144.9 (ArH), 163.4 (4° Ar) (assignment by COSY and DEPT experiments).

2-Hexadecyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**27c**)

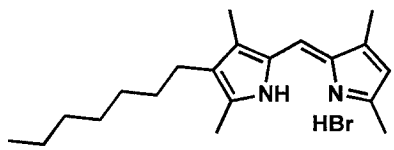


Hydrogenolysis of benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) (0.39 g, 1.7 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0076 g) in THF (20 mL) contained in a 50 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (5 mL), 4-hexadecyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11a**) (0.59 g, 1.7 mmol), and 48% (w/v) aqueous hydrobromic acid (0.72 mL, 4.3 mmol) were added to the filtrate contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The mixture was filtered to give the product as a bronze-coloured waxy solid. (Yield: 0.67 g, 78%)

m.p. 118-124 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.8 Hz, CH_2CH_3), 1.26-1.29 (26H, m, $CH_2(CH_2)_{14}CH_3$), 1.41-1.44 (2H, m, $CH_2CH_2CH_2$), 2.27 (3H, s, $ArCH_3$), 2.34 (3H, s, $ArCH_3$), 2.39 (2H, t, J = 7.8 Hz, $ArCH_2$), 2.66-2.67 (6H, m, $ArCH_3$ + $ArCH_3$), 6.12 (1H, s, Ar*H*), 7.05 (2H, s, meso *H*), 12.9 (1H, br s, N*H*), 13.0 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.4, 12.3, 13.2, 14.3, 14.6, 22.8,* 24.1,* 29.5,* 29.6,* 29.6,* 29.7,* 29.8,* 29.8,* 29.9,* 30.1,* 32.1,* 117.1, 119.4, 126.5,* 126.6,* 130.0,* 142.6,* 145.0,* 154.1,* 155.9* (five CH_2 signals not resolved, * denotes

negative phase peak in JMOD experiment); calcd 504.3 for $C_{29}H_{49}N_2Br$; ESI(+ve) found *m/z* 425.5 $(M+1\text{-}HBr)^+$.

2-Heptyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**27b**)

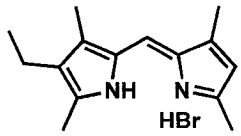


Hydrogenolysis of benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) (1.2 g, 5.4 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.024 g) in THF (25 mL) contained in a 50 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (10 mL), 4-heptyl-3,5-dimethylpyrrole-2-carboxaldehyde (**11b**) (1.2 g, 5.4 mmol), and 48% (w/v) aqueous hydrobromic acid (2.4 mL, 14 mmol) were added to the filtrate contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 1 hour, and then the solvent was removed using a rotary evaporator. The product mixture was dissolved in a minimal amount of methanol, and distilled water was added to form a precipitate. The mixture was filtered to give the product as an orange solid. (Yield: 1.3 g, 63%)

m.p. 137-140 °C (dec.); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (3H, t, J = 7.0 Hz, CH_2CH_3), 1.24-1.33 (8H, m, $CH_2(CH_2)_4CH_3$), 1.40-1.45 (2H, m, $CH_2CH_2CH_2$), 2.28 (3H, s, $ArCH_3$), 2.35 (3H, s, $ArCH_3$), 2.39 (2H, t, J = 7.5 Hz, $ArCH_2$), 2.66-2.67 (6H, m, $ArCH_3$ + $ArCH_3$), 6.11 (1H, s, Ar*H*), 7.06 (1H, s, meso *H*), 12.91 (1H, br s, N*H*), 13.02 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.4 ($ArCH_3$), 12.3 ($ArCH_3$), 13.2 ($ArCH_3$), 14.2 ($(CH_2)_6CH_3$), 14.5 ($ArCH_3$), 22.7 (CH_2CH_2), 24.1 ($ArCH_2$), 29.2 (CH_2CH_2), 29.5

(CH_2CH_2), 30.0 ($ArCH_2CH_2$), 31.9 (CH_2CH_2), 117.0 (ArH), 119.4 (meso *C*), 126.5 (4° Ar), 126.6 (4° Ar), 129.9 (4° Ar), 142.6 (4° Ar), 145.0 (4° Ar), 154.0 (4° Ar), 155.7 (4° Ar); calcd 378.2 for $C_{20}H_{31}N_2Br$; ESI(+ve) found *m/z* 299.2 $(M+1-HBr)^+$.

2-Ethyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**27c**)

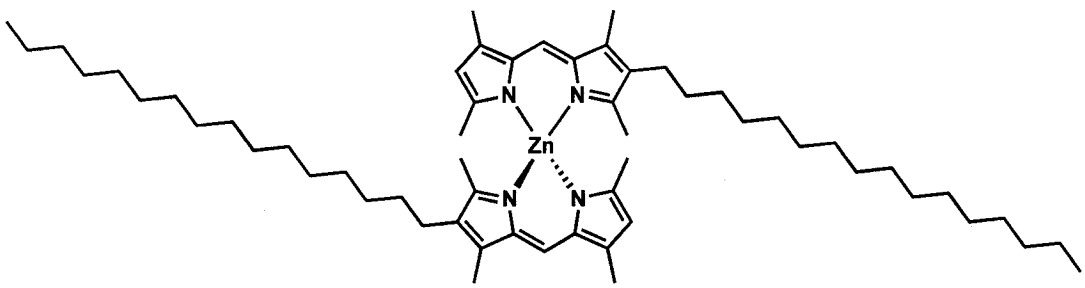


Hydrogenolysis of benzyl 3,5-dimethylpyrrole-2-carboxylate[176] (**12b**) (5.0 g, 22 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.098 g) in THF (100 mL) contained in a 250 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (20 mL), 4-ethyl-3,5-dimethylpyrrole-2-carboxaldehyde[60] (**11c**) (3.3 g, 22 mmol), and 48% (w/v) aqueous hydrobromic acid (9.3 mL, 55 mmol) were added to the filtrate contained in a 250 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was cooled to 4 °C, resulting in crystallization of the prouct. The mixture was filtered to give the product as a red solid. (Yield: 6.6 g, 98%)

m.p. 176-182 °C (dec.) (literature:[2] 215 °C); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.07 (3H, t, *J* = 7.5 Hz, CH_2CH_3), 2.29 (3H, s, $ArCH_3$), 2.35 (3H, s, $ArCH_3$), 2.42 (2H, q, *J* = 7.7 Hz, CH_2CH_3), 2.65 (3H, s, $ArCH_3$), 2.66 (3H, s, $ArCH_3$), 6.11 (1H, s, ArH), 7.07 (1H, s, meso H), 12.88 (1H, br s, NH), 12.97 (1H, br s, NH); $^{13}C\{^1H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.1 ($ArCH_3$), 12.2 ($ArCH_3$), 12.9 ($ArCH_3$), 14.4 ($ArCH_3$ + CH_2CH_3), 17.3 (CH_2CH_3), 116.9 (ArH), 119.4 (meso *C*), 126.4 (4° Ar), 126.5 (4° Ar), 131.1 (4° Ar), 142.3 (4° Ar),

145.1 (4° Ar), 153.9 (4° Ar), 155.3 (4° Ar) (assignment by JMOD, ^{13}C-^{1}H HSQC, and ^{13}C-^{1}H HMBC experiments); calcd 308.1 for $C_{15}H_{21}N_2Br$; ESI(+ve) found *m/z* 229.2 $(M+1-HBr)^+$.

Zinc(II) bis(2-hexadecyl-1,3,7,9-tetramethyldipyrromethene) (**28a**)

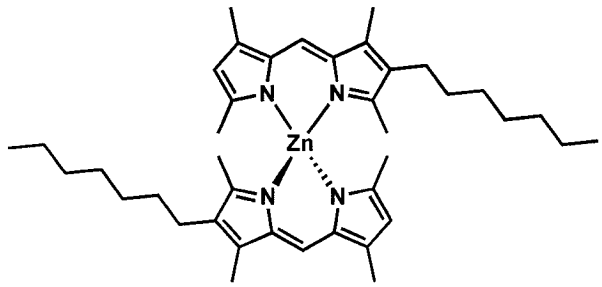


A solution of zinc acetate dihydrate (1.2 g, 5.5 mmol) and sodium acetate trihydrate (0.75 g, 5.5 mmol) in methanol (20 mL) was added, with stirring, to a solution of 2-hexadecyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**27a**) (0.54 g, 1.1 mmol) in chloroform (20 mL) contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 30 minutes, and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.21 g, 42%)

m.p. 83-87 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.88 (6H, t, J = 7.0 Hz, CH_2CH_3), 1.25-1.38 (56H, m, $CH_2(CH_2)_{15}CH_3$), 1.90 (6H, s, $ArCH_3$), 1.92 (6H, s, $ArCH_3$), 2.21 (6H, s, $ArCH_3$), 2.30-2.33 (10H, m, $ArCH_2$ + $ArCH_3$), 5.95 (2H, s, Ar*H*), 6.98 (2H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.2 ($ArCH_3$), 11.9 ($ArCH_3$), 14.3 ($(CH_2)_{15}CH_3$), 15.0 ($ArCH_3$), 16.5 ($ArCH_3$), 22.9 (CH_2CH_2), 25.0 ($ArCH_2$), 29.6 (CH_2CH_2), 29.7 (CH_2CH_2), 29.8 (CH_2CH_2), 29.9 (CH_2CH_2), 30.7 ($ArCH_2CH_2$), 32.2 (CH_2CH_2), 116.0

(ArH), 121.3 (meso *C*), 129.2 (4° Ar), 136.2 (4° Ar), 136.3 (4° Ar), 138.1 (4° Ar), 140.5 (4° Ar), 156.1 (4° Ar), 158.6 (4° Ar) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 910.7 for $C_{58}H_{94}N_4Zn$; ESI(+ve) found *m/z* 927.5 $(M+H_2O)^+$.

Zinc(II) bis(2-heptyl-1,3,7,9-tetramethyldipyrromethene) (**28b**)

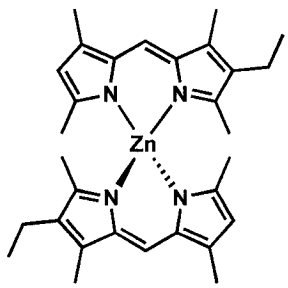


A solution of zinc acetate dihydrate (4.4 g, 20 mmol) and sodium acetate trihydrate (2.7 g, 20 mmol) in methanol (20 mL) was added, with stirring, to a solution of 2-heptyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**27b**) (1.5 g, 4.0 mmol) in chloroform (20 mL) contained in a 100 mL round-bottom flask. The reaction mixture was stirred for 30 minutes, and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.83 g, 63%)

m.p. 118-123 °C; ^{1}H NMR: δ(500 MHz, $CDCl_3$): 0.86 (6H, t, J = 7.0 Hz, CH_2CH_3), 1.21-1.29 (16H, m, $CH_2(CH_2)_4CH_3$), 1.36-1.39 (4H, m, $CH_2CH_2CH_2$), 1.90 (6H, s, $ArCH_3$), 1.92 (6H, s, $ArCH_3$), 2.21 (6H, s, $ArCH_3$), 2.30-2.33 (10H, m, $ArCH_2$ + $ArCH_3$), 5.95 (2H, s, Ar*H*), 6.98 (2H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ(125 MHz, $CDCl_3$): 10.2, 11.9, 14.3, 15.0, 16.5, 22.9,* 25.0,* 29.5,* 29.6,* 30.7,* 32.1,* 115.9, 121.3, 129.2,* 136.2,*

136.3,* 138.1,* 140.5,* 156.1,* 158.6* (* denotes negative phase peak in JMOD experiment); calcd 658.4 for $C_{40}H_{58}N_4Zn$; ESI(+ve) found *m/z* 675.3 $(M+H_2O)^+$.

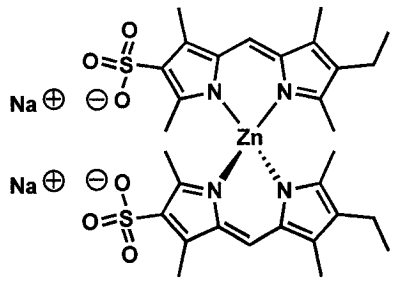
Zinc(II) bis(2-ethyl-1,3,7,9-tetramethyldipyrromethene) (**28c**)



A solution of zinc acetate dihydrate (25 g, 115 mmol) and sodium acetate trihydrate (16 g, 115 mmol) in methanol (80 mL) was added, with stirring, to a solution of 2-ethyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**11c**) (7.1 g, 23 mmol) in chloroform (80 mL) contained in a 250 mL round-bottom flask. The reaction mixture was stirred for 30 minutes, and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 5.0 g, 84%)

m.p. 160-165 °C (dec.); ^{1}H NMR: δ(500 MHz, $CDCl_3$): 1.00 (6H, t, J = 7.5 Hz, CH_2CH_3), 1.92 (6H, s, ArCH_3), 1.93 (6H, s, ArCH_3), 2.22 (6H, s, ArCH_3), 2.30 (6H, s, ArCH_3), 2.34 (4H, q, CH_2CH_3), 5.95 (2H, s, Ar*H*), 6.99 (2H, s, meso *H*); ^{13}C{^{1}H} NMR: δ(125 MHz, $CDCl_3$): 10.0, 11.9, 14.8, 15.2, 16.5, 18.2,* 116.0, 121.3, 130.6,* 136.2,* 136.3,* 137.7,* 140.5,* 156.2,* 158.2* (* denotes negative phase peak in JMOD experiment); calcd 518.2 for $C_{30}H_{38}N_4Zn$; ESI(+ve) found *m/z* 535.1 $(M+H_2O)^+$.

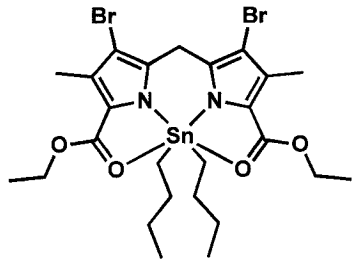
Disodium zinc(II) bis(8-ethyl-1,3,7,9-tetramethyldipyrromethene-2-sulfonate) (**30**)



Under dry conditions and using nitrogen gas as an inert atmosphere zinc(II) bis(2-ethyl-1,3,7,9-tetramethyldipyrromethene) (**28c**) (0.10 g, 0.19 mmol) was dissolved in dry DCM (5 mL) in a 25 mL two-neck round-bottom flask. The solution was cooled to 0 °C by suspension in an ice bath. A solution of chlorosulfonic acid (0.028 mL, 0.42 mmol) in dry DCM (2 mL) was added slowly dropwise, with stirring, resulting in the formation of a precipitate. The reaction mixture was stirred for 30 minutes, and then the supernatant was decanted from the precipitate. A solution of sodium hydroxide (0.030 g, 0.76 mmol) in water (5 mL) was added to the precipitate. The reaction mixture was stirred for 16 hours at room temperature, and then the water was removed by freeze-drying. The product has not yet been obtained in pure form.

^{1}H NMR: δ(500 MHz, CD_3OD): 1.03 (6H, t, J = 7.5 Hz, CH_2CH_3), 1.91 (6H, s, $ArCH_3$), 2.15 (6H, s, $ArCH_3$), 2.25 (6H, s, $ArCH_3$), 2.38 (4H, q, J = 7.5 Hz, CH_2CH_3), 2.52 (6H, s, $ArCH_3$), 7.19 (2H, s, meso *H*); ^{13}C{^{1}H} NMR: δ(125 MHz, CD_3OD): 8.4 ($ArCH_3$), 9.8 ($ArCH_3$), 13.5 ($ArCH_3$),13.6 (CH_2CH_3), 14.9 ($ArCH_3$), 17.2 (CH_2CH_3), 121.7 (meso *C*), 128.3 (4° Ar), 132.3 (4° Ar), 132.3 (4° Ar), 133.2 (4° Ar), 137.3 (4° Ar), 138.2 (4° Ar), 140.0 (4° Ar), 151.7 (4° Ar), 161.8 (4° Ar) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); calcd 722.1 for $C_{30}H_{36}N_4ZnS_2O_6Na_2$; ESI(-ve) found *m/z* 699.3 $(M\text{-}Na)^-$.

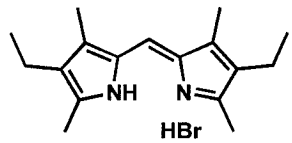
Diethyl *N,N'*-(dibutyl)tin(IV)-3,3'-dibromo-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate[221] (**39**)



This compound was prepared by Dr. Cory S. Beshara. Triethylamine (0.58 mL, 0.42 mmol) was added to a solution of diethyl 3,3'-dibromo-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate[208] (**36**) (0.10 g, 0.22 mmol) and dibutyltin dichloride (0.061 g, 0.20 mmol) in DCM (2 mL). The reaction mixture was stirred at room temperature for 6 hours, and then methanol (5 mL) was added. The solvent reaction mixture was concentrated using a rotary evaporator (without heating), which caused the product to crystallize. The mixture was filtered, and the residue was rinsed with methanol to give the product as a colourless crystalline solid. (Yield: 0.083 g, 53%)

m.p. 110-111 °C; ^{1}H NMR: δ (500 MHz, $CDCl_3$): 0.75 (6H, t, J = 7.5 Hz, $(CH_2)_3CH_3$), 1.16-1.22 (4H, m, $(CH_2)_2CH_2CH_3$), 1.32-1.37 (14H, m, $Sn(CH_2)_2$ + OCH_2CH_3), 2.32 (6H, s, $ArCH_3$), 4.02 (2H, s, $ArCH_2Ar$), 4.35 (1H, q, J = 7.0 Hz, OCH_2CH_3); $^{13}C\{^{1}H\}$ NMR: δ (125 MHz, $CDCl_3$): 12.1, 13.5, 14.5, 24.6, 26.1, 27.1, 61.3, 101.8, 121.4, 128.1, 138.6, 166.8; ^{15}N NMR: δ(51 MHz, $CDCl_3$): -194.1; ^{119}Sn NMR: δ (186 MHz, $CDCl_3$): -247.1; calcd 706.0 for $C_{25}H_{36}N_2O_4Br_2Sn$; ESI(-ve) found *m/z* 704.9 $(M-1)^-$.

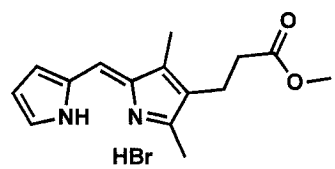
2,8-Diethyl-1,3,7,9-tetramethyldipyrromethene hydrobromide[221] (**40**)



48% (w/v) Aqueous hydrobromic acid (0.7 mL, 4.2 mmol) was added to a solution of ethyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate[225] (1.0 g, 5.2 mmol) in 96% (w/v) aqueous formic acid (2.7 mL). The reaction mixture was heated to reflux, with stirring, for 1 hour and then cooled to 4 °C, causing the product to crystallize. The mixture was filtered and the residue rinsed with cold methanol to give the product as a red solid. (Yield: 0.51 g, 58%)

m.p. 214-218 °C (dec.); ^{1}H NMR: δ (500 MHz, $CDCl_3$): 1.07 (6H, t, J = 7.5 Hz, CH_2CH_3), 2.27 (6H, s, $ArCH_3$), 2.42 (4H, q, J = 7.5 Hz, CH_2CH_3), 2.65 (6H, s, $ArCH_3$), 7.04 (1H, s, meso *H*), 12.87 (2H, br s, N*H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 10.1, 12.8, 14.5, 17.3,* 118.7, 126.1,* 130.5,* 141.4,* 153.7* (* denotes negative phase peak in JMOD experiment); ^{15}N NMR: δ(51 MHz, $CDCl_3$): -213.7 (d, J = -95 Hz); calcd 336.1 for $C_{17}H_{25}N_2Br$; ESI(+ve) found *m/z* 257.2 $(M+1-HBr)^+$.

1,3-Dimethyl-2-(methoxycarbonylethyl)dipyrromethene hydrobromide[221] (**22**)

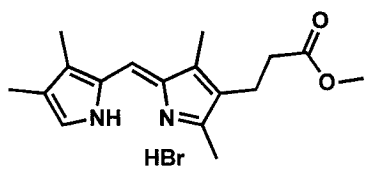


Hydrogenolysis of benzyl 3,5-dimethyl-4-(methoxycarbonylethyl)pyrrole-2-carboxylate[134] (**1**) (0.103 g, 0.33 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0015 g) in THF (8 mL) and triethylamine (1

drop) contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (1 mL), pyrrole-2-carboxaldehyde (0.031 g, 0.33 mmol), and 48% (w/v) aqueous hydrobromic acid (0.14 mL, 0.83 mmol) were added to the filtrate contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The mixture was filtered and the residue rinsed with cold methanol to give the product as a red-brown solid. (Yield: 0.098 g, 90%)

m.p. 148-151°C (dec.); ^{1}H NMR: δ (500 MHz, $CDCl_3$): 2.33 (3H, s, ArC*H*$_3$), 2.50 (2H, t, J = 7.5 Hz, $CH_2CH_2C(O)$), 2.73 (3H, s, ArC*H*$_3$), 2.78 (2H, t, J = 7.5 Hz, $ArCH_2CH_2$), 3.67 (3H, s, OC*H*$_3$), 6.52-6.53 (1H, m Ar*H*), 7.11 (1H, s, Ar*H*), 7.21 (1H, s, meso *H*), 7.72 (1H, s, Ar*H*), 14.00 (1H, br s, N*H*), 14.34 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 10.5, 13.6, 19.4, 33.6, 52.1, 115.0, 125.3, 127.9, 129.4, 129.6, 132.6, 138.5, 146.1, 161.4, 172.6; ^{15}N NMR: δ(51 MHz, $CDCl_3$): -207.8 (d, J = -95 Hz), -210.0 (d, J = -95 Hz); calcd 338.1 for $C_{15}H_{19}N_2O_2Br$; ESI(+ve) found *m/z* 259.3 $(M+1-HBr)^+$.

1,3,7,9-Tetramethyl-2-(methoxycarbonylethyl)dipyrromethene hydrobromide[221] (**41**)

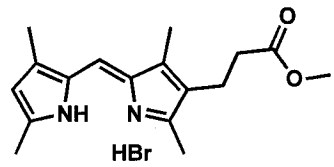


Hydrogenolysis of benzyl 3,5-dimethyl-4-(methoxycarbonylethyl)pyrrole-2-carboxylate[134] (**1**) (0.100 g, 0.32 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0014 g) in THF (8 mL) and triethylamine (1

drop) contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas, and then filtered through a plug of Celite® to remove the palladium catalyst. Methanol (1 mL), 3,4-dimethylpyrrole-2-carboxaldehyde[226] (0.040 g, 0.32 mmol), and 48% (w/v) aqueous hydrobromic acid (0.14 mL, 0.80 mmol) were added to the filtrate contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The mixture was filtered and the residue rinsed with cold methanol to give the product as a brown solid. (Yield: 0.086 g, 73%)

m.p. 195-198°C (dec.); ^{1}H NMR: δ (500 MHz, $CDCl_3$): 2.06 (3H, s, ArC*H*$_3$), 2.27 (3H, s, ArC*H*$_3$), 2.33 (3H, s, ArC*H*$_3$), 2.48 (2H, t, J = 7.5 Hz, $CH_2CH_2C(O)$), 2.78-2.73 (5H, m, $ArCH_2CH_2$ + ArC*H*$_3$), 3.67 (3H, s, OC*H*$_3$), 7.16 (1H, s, meso *H*), 7.52-7.53 (1H, m, Ar*H*), 13.10 (1H, br s, N*H*), 13.21 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 10.2 (Ar*C*H$_3$), 10.3 (Ar*C*H$_3$), 10.5 (Ar*C*H$_3$), 13.4 (Ar*C*H$_3$), 19.5 (Ar*C*H$_2$CH$_2$), 33.8 ($CH_2CH_2C(O)$), 52.1 (O*C*H$_3$), 121.2 (meso *C*), 124.9 (4° Ar), 127.1 (4° Ar), 127.6 (4° Ar), 128.2 (4° Ar), 139.8 (ArH), 141.7 (4° Ar), 144.3 (4° Ar), 157.5 (4° Ar), 172.8 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); ^{15}N NMR: δ(51 MHz, $CDCl_3$): -210.7 (d, J = -96 Hz), -213.6 (d, J = -95 Hz); calcd 366.1 for $C_{17}H_{23}N_2O_2Br$; ESI(+ve) found *m/z* 287.3 $(M+1-HBr)^+$.

1,3,7,9-Tetramethyl-2-(methoxycarbonylethyl)dipyrromethene hydrobromide[221] (**42**)

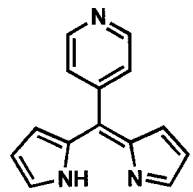


Hydrogenolysis of benzyl 3,5-dimethyl-4-(methoxycarbonylethyl)pyrrole-2-carboxylate[134] (**1**) (0.102 g, 0.32 mmol) was performed using a catalytic amount of 10 mol% palladium on activated carbon (0.0014 g) in THF (8 mL) and triethylamine (1 drop) contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 16 hours under 1 atm of hydrogen gas and then was filtered through a plug of Celite® to remove the palladium catalyst. Methanol (1 mL), 3,5-dimethylpyrrole-2-carboxaldehyde[227] (0.040 g, 0.32 mmol), and 48% (w/v) aqueous hydrobromic acid (0.14 mL, 0.8 mmol) were added, with stirring, to the filtrate contained in a 25 mL round-bottom flask. The reaction mixture was stirred for 1 hour and then was concentrated by partial removal of solvent using a rotary evaporator. The product was precipitated by the addition of diethyl ether. The mixture was filtered and the residue rinsed with cold methanol to give the product as a red solid. (Yield: 0.067 g, 56%)

m.p. 164-168°C (dec.); ^{1}H NMR: δ (500 MHz, $CDCl_3$): 2.31 (3H, s, ArC*H*$_3$), 2.36 (3H, s, ArC*H*$_3$), 2.47 (2H, t, J = 7.5 Hz, $CH_2CH_2C(O)$), 2.67 (3H, s, ArC*H*$_3$), 2.69 (3H, s, ArC*H*$_3$), 2.75 (2H, t, J = 7.5 Hz, $ArCH_2CH_2$), 3.67 (3H, s, OCH_3), 6.15 (1H, s, Ar*H*), 7.07 (1H, s, meso *H*), 13.03 (1H, br s, N*H*), 13.08 (1H, br s, N*H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 10.4 ($ArCH_3$), 12.3 ($ArCH_3$), 13.0 ($ArCH_3$), 14.6 ($ArCH_3$), 19.5 ($ArCH_2CH_2$), 33.9 ($CH_2CH_2C(O)$), 51.9 (OCH_3), 117.5 (ArH), 119.8 (meso *C*), 126.3 (4°

Ar), 126.9 (4° Ar), 127.2 (4° Ar), 142.9 (4° Ar), 145.8 (4° Ar), 154.9 (4° Ar), 155.2 (4° Ar), 172.8 (*C*=O) (assignment by JMOD and ^{13}C-^{1}H HSQC experiments); ^{15}N NMR: δ(51 MHz, $CDCl_3$): -211.5 (d, J = -96 Hz), -212.3 (d, J = -95 Hz); calcd 366.1 for $C_{17}H_{23}N_2O_2Br$; ESI(+ve) found *m/z* 287.2 $(M+1-HBr)^+$.

5-(4-Pyridyl)dipyrromethene[221] (**46**)

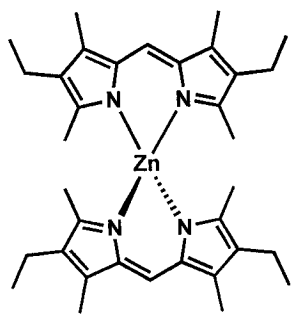


A solution of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) (0.169 g, 0.73 mmol) in toluene (50 mL) was added dropwise, with stirring, to a solution of 5-(4-pyridyl)dipyrromethane[209] (**38**) (0.163 g, 0.73 mmol) in chloroform (80 mL) contained in a 250 mL round-bottom flask at 0 °C. After the addition was complete the reaction mixture was stirred for 10 minutes and then the solution was filtered through a plug of Celite® and the solvent was removed using a rotary evaporator. Chromatographic separation on silica using a gradient of 10→20% ethyl acetate/DCM as the eluent gave the product as a product as a yellow film. (Yield: 0.025 g, 16%)

^{1}H NMR: δ (500 MHz, $CDCl_3$): 6.41 (2H, dd, J = 4.5 Hz, J = 1.0 Hz, pyrrolic Ar*H*), 6.52 (2H, dd, J = 4.5 Hz, J = 1.0 Hz, pyrrolic Ar*H*), 7.42 (2H, dd, J = 4.5 Hz, J = 1.5 Hz, pyridyl Ar*H*), 7.67 (2H, s, pyrrolic Ar*H*), 8.72 (2H, dd, J = 4.5 Hz, J = 1.5 Hz, pyridyl Ar*H*); $^{13}C\{^{1}H\}$ NMR: δ (125 MHz, $CDCl_3$): 118.5 (pyrrolic ArH), 125.3 (pyridyl ArH), 128.4 (pyrrolic ArH), 138.4 (4° Ar), 140.3 (4° Ar), 144.7 (pyrrolic ArH), 145.4 (4° Ar), 149.5 (pyridyl ArH) (assignment by COSY, JMOD, and ^{13}C-^{1}H HSQC experiments);

$^{15}N\{^{1}H\}$ NMR: δ(51 MHz, $CDCl_3$): -156.1 (dipyrromethene), -68.0 (pyridyl); calcd 221.1 for $C_{14}H_{11}N_3$; ESI(+ve) found *m/z* 222.3 $(M+1)^+$.

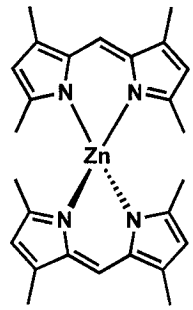
Zinc(II) bis(2,8-diethyl-1,3,7,9-tetramethyldipyrromethene)[221] (**47**)



A solution of zinc acetate dihydrate (0.088 g, 0.4 mmol) and sodium acetate trihydrate (0.054 g, 0.4 mmol) in methanol (10 mL) was added, with stirring, to a solution of 2,8-diethyl-1,3,7,9-tetramethyldipyrromethene hydrobromide (**40**) (0.027 g, 0.08 mmol) in chloroform (10 mL) contained in a 50 mL round-bottom flask. The reaction mixture was stirred for 30 minutes and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.20 g, 83%)

m.p. 145-149°C; ^{1}H NMR: δ (500 MHz, $CDCl_3$): 1.01 (12H, t, J = 7.5 Hz, CH_2CH_3), 1.89 (12H, s, $ArCH_3$), 2.22 (12H, s, $ArCH_3$), 2.34 (8H, q, J = 7.5 Hz, CH_2CH_3), 6.96 (2H, s, meso *H*); $^{13}C\{^{1}H\}$ NMR: δ (125 MHz, $CDCl_3$): 10.1, 14.7, 15.3, 18.2, 120.7, 129.6, 135.7, 136.5, 156.4; $^{15}N\{^{1}H\}$ NMR: δ(51 MHz, $CDCl_3$): -169.5; calcd 574.3 for $C_{34}H_{46}N_4Zn$; ESI(+ve) found *m/z* 574.4 $(M)^+$.

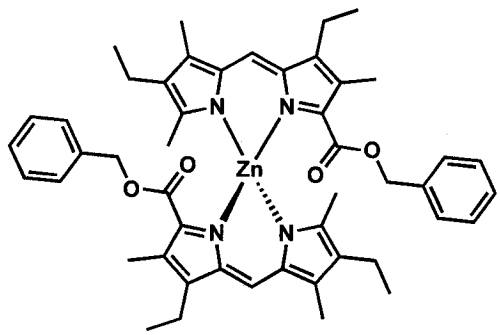
Zinc(II) bis(1,3,7,9-tetramethyldipyrromethene)[221] (**48**)



A solution of zinc acetate dihydrate (1.8 g, 8.0 mmol) and sodium acetate trihydrate (1.1 g, 8.0 mmol) in methanol (60 mL) was added, with stirring, to a solution of 1,3,7,9-tetramethyldipyrromethene hydrobromide[228] (0.44 g, 1.6 mmol) in chloroform (60 mL) contained in a 250 mL round-bottom flask. The reaction mixture was stirred for 30 minutes, and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.33 g, 44%)

m.p. >250°C; ^{1}H NMR: δ (500 MHz, $CDCl_3$): 1.95 (12H, s, ArC*H*$_3$), 2.31 (12H, s, ArC*H*$_3$), 5.98 (4H, s, Ar*H*), 7.02 (2H, s, meso *H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 12.0, 16.6, 116.9, 122.0, 136.7,* 142.1,* 157.9* (* denotes negative phase peak in JMOD experiment); ^{15}N{^{1}H} NMR: δ(51 MHz, $CDCl_3$): -167.5; calcd 462.2 for $C_{26}H_{30}N_4Zn$; ESI(+ve) found *m/z* 462.1 $(M)^+$.

Zinc(II) bis(benzyl 3,8-diethyl-2,7,9-trimethyldipyrromethene-1-carboxylate)[221] (**50**)

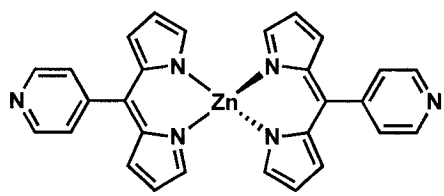


A solution of zinc acetate dihydrate (0.70 g, 3.2 mmol) and sodium acetate trihydrate (0.44 g, 3.2 mmol) in methanol (8 mL) was added, with stirring, to a solution of benzyl 3,8-diethyl-2,7,9-trimethyldipyrromethene-1-carboxylate hydrobromide[213] (**43**) (0.29 g, 0.63 mmol) in chloroform (10 mL) contained in a 50 mL round-bottom flask. The reaction mixture was stirred for 30 minutes, and then the solvent was removed using a rotary evaporator. The crude product mixture was dissolved in DCM and filtered through a plug of silica. The solvent was removed using a rotary evaporator to give the product as a fuscia solid. (Yield: 0.25 g, 48%)

m.p. 162-163°C; ^{1}H NMR: δ (500 MHz, $CDCl_3$): 1.00 (6H, t, J = 7.5 Hz, 8-CH_2CH_3), 1.09 (6H, t, J = 7.5 Hz, 3-CH_2CH_3), 1.74 (6H, s, 9-CH_3), 2.10 (6H, s, 7-CH_3), 2.29-2.27 (10H, m, 8-CH_2CH_3 + 2-CH_3), 2.63-2.61 (4H, m, 3-CH_2CH_3), 4.55 (2H, d, J = 12.5 Hz, CH_aH_bPh), 4.77 (2H, d, J = 12.5 Hz, CH_aH_bPh), 6.76-6.75 (4H, m, *o*-Ar*H*), 6.89 (2H, s, meso *H*), 7.07-7.00 (6H, m, *m*-Ar*H* + *p*-Ar*H*); ^{13}C{^{1}H} NMR: δ (125 MHz, $CDCl_3$): 9.9 (7-CH_3), 10.9 (2-CH_3), 14.5 (9-CH_3), 14.6 (8-CH_2CH_3), 17.2 (3-CH_2CH_3), 18.0 (8-CH_2CH_3), 18.1 (3-CH_2CH_3), 64.6 (CH_2Ph), 121.5 (meso *C*), 127.0 (*p*-ArH), 127.3 (*o*-ArH), 127.6 (4° Ar), 127.9 (*m*-ArH), 135.2 (4° Ar), 135.3 (4° Ar), 136.1 (4° Ar), 137.4 (4° Ar), 139.8 (4° Ar), 140.9 (4° Ar), 142.5 (4° Ar), 162.8 (4° Ar), 168.3 (*C*=O) (assignment

by COSY, NOESY, and ^{13}C-^{1}H HSQC experiments); $^{15}N\{^{1}H\}$ NMR: δ(51 MHz, $CDCl_3$): -152.8, -174.9; calcd 814.3 for $C_{48}H_{54}N_4O_4Zn$; ESI(+ve) found *m/z* 837.4 $(M+Na)^+$.

Zinc(II) bis[5-(4-pyridyl)dipyrromethene][221] (**53**)



A solution of DDQ (0.13 g, 0.57 mmol) in benzene (40 mL) was added slowly dropwise, with stirring, to a solution of 5-(4-pyridyl)dipyrromethane[209] (**38**) (0.13 g, 0.57 mmol) in chloroform (60 mL) at 0°C contained in a 250 mL round-bottom flask. After the addition was complete the reaction mixture was stirred for 10 minutes and then the solvent was removed using a rotary evaporator. Triethylamine (0.4 mL) and a solution of zinc chloride (0.040 g, 0.29 mmol) in methanol (1 mL) were added to a solution of the crude mixture in methanol (20 mL) and chloroform (20 mL). This mixture was heated to reflux for 16 hours under a nitrogen atmosphere and then the solvent was removed using a rotary evaporator. The product was obtained as a mixture with (**46**) as an iridescent red solid.

m.p. >250°C; ^{1}H NMR: δ (500 MHz, $CDCl_3$): 6.41 (4H, dd, J = 4.0 Hz, J = 1.0 Hz), 6.64 (4H, dd, J = 4.0 Hz, J = 1.0 Hz), 7.50 (4H, dd, J = 4.5 Hz, J = 1.5 Hz), 7.57 (4H, s), 8.74 (4H, dd, J = 4.5 Hz, J = 1.5 Hz); $^{13}C\{^{1}H\}$ NMR: δ (125 MHz, $CDCl_3$): 118.1, 125.4, 132.8, 139.7, 145.1, 147.1, 149.2, 150.9; $^{15}N\{^{1}H\}$ NMR: δ(51 MHz, $CDCl_3$): -162.2; calcd 504.1 for $C_{28}H_{20}N_6Zn$; ESI(+ve) found *m/z* 505.2 $(M+1)^+$.

Chapter 6. Conclusions

Several advances in the research of dipyrromethene chemistry have been described in this work. The formation of zinc(II) dinuclear double helicates of bis(dipyrromethene)s bearing terminal homochiral substituents was shown to proceed with modest diastereoselectivity. An analysis of the helical chirality of these compounds showed that the helicates were stable to racemization by ligand exchange under the conditions tested. With the aim of developing practical applications for dipyrromethene complexes, some preliminary results regarding the development of dipyrromethene gemini metallosurfactants have been described. The methods for characterization of dipyrromethenes and related compounds have been expanded through an investigation into the use of ^{15}N NMR chemical shifts as a routine characterization tool. A survey of the ^{15}N NMR chemical shifts of a variety of dipyrrolic molecules has shown a correlation with the gross structure of the compound. Further investigation into aspects of these three projects will continue to produce insight into the chemistry of dipyrromethenes in the future.

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