Design and Synthesis of Organic Multi-Porphyrin Self-Assembled Supramolecules

by

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Abstract

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Chapter 1: Two aldehydes, 2,6-diacetamido-4-formylpyridine (7) and 1-butyl-6-formyluracil (11), are used to synthesize five pyridyl and four uracyl *meso*-subsituted porphyrins. With these complementary porphyrin building blocks, it is possible to build various types of multi-porphyrin supramolecules with different spatial relationships in predefined geometries. The formation and properties of self-complementary dimers and a closed tetrameric square are presented as a basis of comparison to the latter system in the solid state. An X-ray structure of 5,10-bis(4-*tert*-butylphenyl)-15,20-bis(3,5-diacetamido-4-pyridyl)porphyrin (IV) confirms its molecular structure and reveals a hydrogen-bonded supramolecular organization mediated by water molecules.

Chapter 2: Discrete squares and tapes of porphyrins are self-assembled by self-complementary hydrogen bonding between diacetamidopyridyl recognition groups rigidly linked to the chromophore.

Chapter 3: Discrete tapes, squares, nonomer, hexomer, and star pentamer of porphyrins may be self-assembled by hetro-complementary hydrogen bonding between diacetamidopyridyl and 1-butyluracyl recognition groups rigidly linked to the chromophores.

This work is dedicated to

my parents for their tremendous support and encouragement

Acknowledgments

I wish to express my gratitude to my parents for their love, encouragement, and patience and to my wife, Jingmin Lai, for her understanding, support, and help without which this work would have never been completed. I also wish to thank all graduate and undergraduate students who work in my laboratory. I thank Dr. Clifford E. Soll for the help with Mass spectra and Dr. Michael Blumenstein for the help with NMR spectra. I could also like to thank my committee members, Dr. Klaus Grohmann, Dr. Keith Ramig, and Dr. Xiangning Chen, for their helpful suggestions and discussions, which have improved this work significantly. Finally, I wish to express my appreciation to Dr. Charles M. Drain, my mentor, for his excellent guidance and assistance throughout in the preparation of this dissertation, and for his constant concern, encouragement, and patience during the extire period of my graduate study at the CUNY.

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Abbreviation

TFA: Trifluroacetic Acid

THF: Tetrahydrofuran

Ur: 1-Butyl-6-uracyl

Ac_2Py: 3,5-Diacetamido-4-pyridyl

Ar : 4-*tert*-Butylphenyl

PCC: Pyridium Chlorochromate

NBS: N-Bromosuccinimide

AIBN: *azo*-Bisisobutylronitrile

LAH: Lithium Aluminum Hydride

A: Hydrogen Bond Acceptor

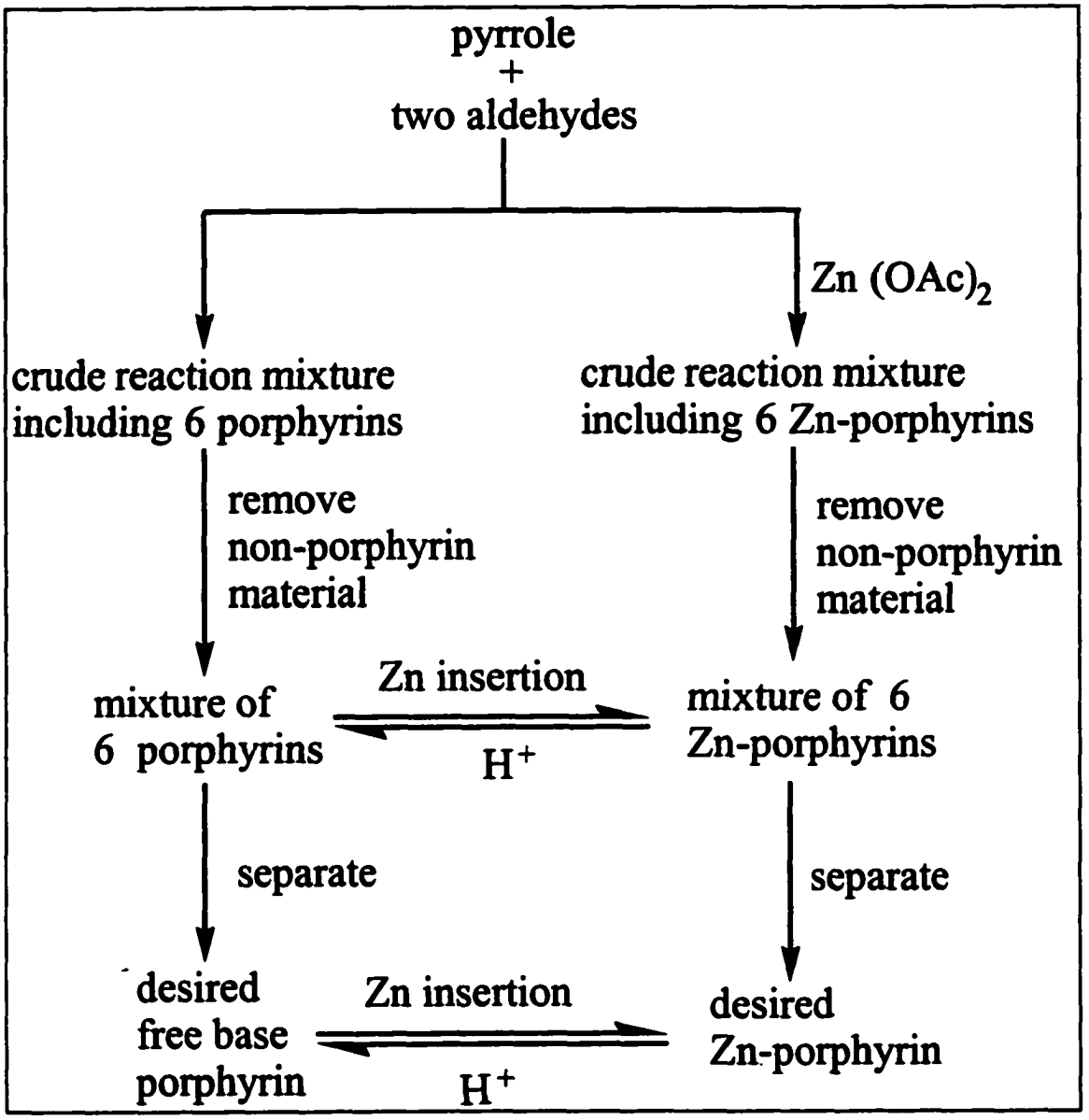
D: Hydrogen Bond Donator

Design and Synthetic Strategy

The 2,6-diacetamidopyridine has two possible positions (3-, or 4-) which could be grafted onto the *meso*-positions (5, 10, 15, 20) of porphyrins, but the 3,5-diacetamido-4-pyridyl group has higher molecular symmetry, which makes the self-assembly much easier and greatly simplifies the characterization of supramolecular structures. The 1-butyluracil also has two possible positions (5- or 6-) which could be grafted onto *meso*-positions of porphyrins, and the 1-butyl-6-uracyl group has higher molecular symmetry. The 2,4-diacetamido-3-pyridyl and 1-butyl-5-uracyl derivatives can be combined to form a supramolecular cage,[1] but the other can be used to make extended planar arrays and tapes. The 3,5-diacetamido-4-pyridyl or the 1-butyl-6-uracyl groups, when incorporated onto the *meso*-positions of the porphyrin's rigid framework, form two sets of complementary porphyrin building blocks for this project.

	Meso-Porphyrins			
	5	10	15	20
II	Ac_2Py	Ar	Ar	Ar
III	Ac_2Py	Ac_2Py	Ar	Ar
IV	Ac_2Py	Ar	Ac_2Py	Ar
V	Ac_2Py	Ac_2Py	Ac_2Py	Ar
VI	Ac_2Py	Ac_2Py	Ac_2Py	Ac_2Py
VIII	Ur	Ar	Ar	Ar
IX	Ur	Ur	Ar	Ar
X	Ur	Ar	Ur	Ar
XI	Ur	Ur	Ur	Ar
XII	Ur	Ur	Ur	Ur

Table 1-1. ***Identifies ten porphyrins and abbreviations used in this report, Ur = 1-butyl-6-uracyl, Ac_2Py = 3,5-diacetamido-4-pyridyl and Ar = 4-tert-butylphenyl.***



Scheme 1. *Scheme for preparing porphyrin building blocks: These mixtures of porphyrins can be separated by adsorption chromatography and the free-base and metalloporphyrin can be inter-converted at different steps.*

Since the four *meso*-positions are at 90° from each other, there are five possible porphyrins per hydrogen-bond moiety. The porphyrins prepared from the two complementary multiple hydrogen bonding pairs can be used to construct linear or 2-

dimensional porphyrin arrays and to keep the porphyrins almost co-planar in the supramolecular arrays.

The synthesis of these *meso*-substituted porphyrins can be accomplished by means of a mixed-aldehyde approach.[2] With equal moles of two aldehydes, a statistical mixture (1:4:6:4:1)[2c] of six porphyrins is expected. The proportions found are to some extent determined by the relative rates of reactivity of the starting aldehydes and the solubility of intermediates. The separation of the mixture is usually not too difficult. Since all five of the porphyrins can be obtained in one reaction and all of them are interesting and useful, this is an acceptable method.

References:

(1) Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1993**, 243-245.

(2) (a) Little, R. G.; Anton, J. A.; Loach, P. A.; Ibers, J. A. *J. Heterocycl. Chem.* **1975**, *12*, 343-349. (b) Walker, F. A.; Balke, V. L.; McDermott, G. A. *Inorg. Chem.* **1982**, *21*, 3342-3348. (c) Milgrom, L. R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1483-1487. (d) Johnstone, R. A. W.; Nunes, M. L. P. G.; Pereira, M. M.; Gonsalves, A. M. d'A. R.; Serra, A. C. *Heterocycles* **1996**, *43*, 1423-1436. (e) Drain, C. M.; Gong, X. *Chem. Commun.* **1997**, 2117-2118.

Chapter 1

Design and Synthesis of Porphyrins Bearing Rigid Hydrogen Bonding Motifs: Highly Versatile Building Blocks for Self-Assembly of Polymers and Discrete Arrays

Abstract: Two aldehydes, 2,6-diacetamido-4-formylpyridine (**7**) and 1-butyl-6-formyluracil (**11**), are used to synthesize five pyridyl and four uracyl *meso*-subsituted porphyrins. With these complementary porphyrin building blocks, it is possible to build various types of multi-porphyrin supramolecules with different spatial relationships in predefined geometries. The formation and properties of self-complementary dimers and a closed tetrameric square are presented as a basis of comparison to the latter system in the solid state. An X-ray structure of 5,10-bis(4-*tert*-butylphenyl)-15,20-bis(3,5-diacetamido-4-pyridyl)porphyrin (**IV**) confirms its molecular structure and reveals a hydrogen-bonded supramolecular organization mediated by water molecules.

Introduction

Self-assembly into specifically designed structures involves the spontaneous association of molecules through intermolecular interactions.[1] The ability to control the supramolecular organization of molecular entities by nonconvalent interactions remains a challenging goal in materials science,[1b] because of our still imperfect ability to predictably design supramolecular structures in solution and in the solid state. Due to their key role in many important biological systems, the self-assembly of porphyrin derivatives has attracted considerable attention because of their photoelectric properties, their potential use as

components of nanometer scale photonic devices, and as novel functional materials.[2] In addition to the free bases, the functionality (luminescence, redox, electronic, etc.) of these large, rigid aromatic macrocycles may be altered or fine-tuned by formation of various metal derivatives. For these reasons, porphyrins and metallo-porphyrins are particularly attractive molecular species to incorporate into supramolecular assemblies with special built-in properties or functions. Much effort has been applied to the design and synthesis of covalent porphyrinic arrays analogous to those found in nature for charge separation, electron transport,[3] and signal or energy transduction.[4] Formation of multiple hydrogen bonds between complementary molecular components is widely used in the fabrication of

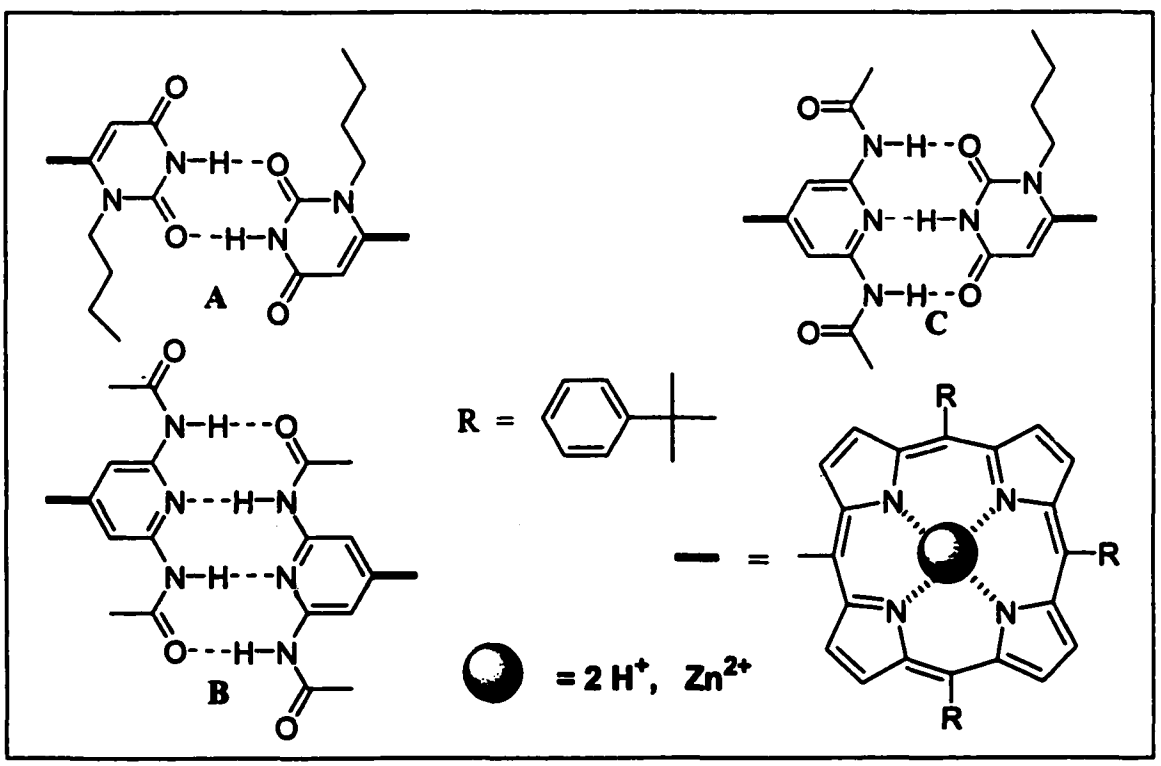


Figure 1. *Three kinds of interactions between two porphyrin building blocks: A, B self-complementary hydrogen bonding, and C hetero-complementary hydrogen bonding. Each has one or more isomeric forms.*

supramolecular assemblies because of their strength, directionality, specificity, and reversibility. Preparation of monomeric hydrogen bond recognition unit-bearing chromophores allows the self-assembly of both polymers and discrete arrays with various structures in high yields by appropriate combinations of the molecular building blocks.

Designed porphyrin arrays have been formed by hydrogen bonding,[5,6] axial metallo-porphyrin coordination,[7,8] and coordination of exocyclic ligands.[9] Several topologically complex structures such as catenanes and rotaxanes have utilized porphyrins.[10,11] Porphyrins have been incorporated into lipid membranes to form photo transistors,[12] and have been used in read-write devices, [13] and as receptors.[14] Several recent reviews on self-assembly of various molecules, including porphyrins, put the present work into context.[15] One conclusion that may be drawn from these numerous studies is that the nature of the chemical linker – covalent, coordination, or hydrogen bond – is just as important to the function of the array as the topology of the chromophores. Thus, porphyrinic squares formed by metal ion coordination have substantially different photo physical properties than porphyrin squares formed via hydrogen bonding.[9] For example, if fluorescence is a desired property of the material, say for a ns luminescent switch, then hydrogen bonding is preferred over metal ion coordination or acetylenic linkers, because these later reduce the quantum yield by heavy atom effects and energy or electron transfer, respectively. While there is an ever increasing number of discrete porphyrin arrays mediated by metal ion coordination, there are few discrete arrays mediated by hydrogen bonding.[5,6]

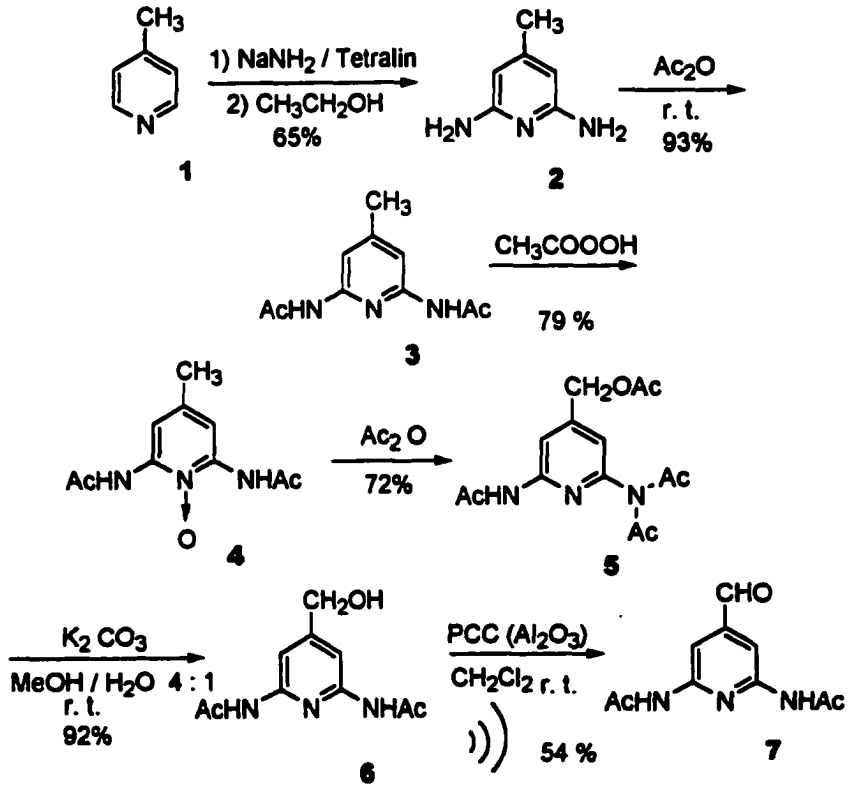
The primary objective of this work is to develop synthetic strategies for two sets of porphyrin building blocks bearing rigidly linked peripheral complementary triple hydrogen bonding moieties (see Figure 1C), and the heretofore unknown aldehydes. The

issue of a general synthesis of porphyrins bearing complex heterocyclic substituents is yet unresolved, *vide infra*. These can be joined into a variety of discrete nanostructures with remarkable control and precision.[1] By mixing these complementary synthons in organic solvents with accurately controlled stoichiometry, the directed triple hydrogen bonding moiety makes it possible to form various types of rigid multi-porphyrin arrays with different, designed spatial relationships. Low molecular weight polymers with somewhat tunable size, depending on the thermodynamics of binding, and molecular organization into higher order structures is also possible.[16] The use of free base or metalloporphyrin building blocks enables the fabrication of arrays with predetermined metallization states. These building blocks also provide hydrogen-bonded pathways through which energy or electron transfer might be facilitated.[17] In addition, an X-ray study of a 5,15-disubstituted pyridyl derivative reveals an unexpected new mode of hydrogen-bonded supramolecular aggregation mediated by adventitious water molecules.

Results and Discussion

The syntheses of two aldehydes **7**[17c] and **11** are shown in Scheme 2 & 3. The direct amination of 4-methylpyridine, **1**, with sodium amide in a tetralin solution affords 2,6-diamino-4-methylpyridine, **2**, in 65% yield. This factor of two increase in yield over previous methods[18] is largely due to milder reaction conditions (slowly heating by stages) and work-up (hydrolysis with ethanol). 2,6-Diacetamido-4-methylpyridine, **3**, is made through acylation of **2** with acetic anhydride. The oxidation of compound **3** with peracetic acid yields 2,6-diacetamido-4-methylpyridine-1-oxide, **4**. Refluxing **4** in acetic anhydride results in the oxidation of the methyl group by a transfer of the intermediate 1-acetoxy

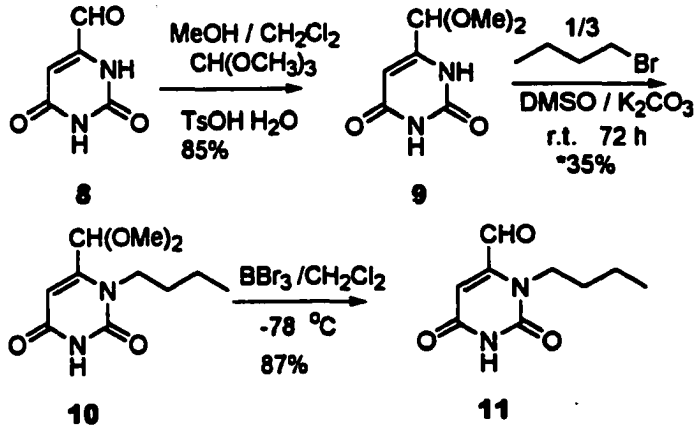
group[19] to yield 2-diacetimido-6-acetamido-4-acetoxymethylpyridine, **5**. Selective hydrolysis of one of the imide and the ester groups of **5** with K_2CO_3 in a methanol / water solution affords the 2,6-diacetamido-4-hydroxymethylpyridine, **6**. The alcohol **6** is oxidized with PCC (on alumina) under ultrasound conditions to yield 2,6-diacetamido-4-formylpyridine, **7**, where yields as high as 65% are observed in small-scale oxidation reactions. Starting from **2**, the 26-32% overall yield of this synthetic route (see Scheme 2) is reasonable because of the inexpensive starting materials and the easy scale-up.



Scheme 2. *Synthesis of the 2,6-diacetamido-4-formylpyridine from 4-methylpyridine*

Other routes to this aldehyde are not successful because of the substantial electronic effects at the 4 position. For example, the 2,6-diamino-3-formylpyridine isomer can be synthesized by the formylation of 2,6-diaminopyridine by a Vilsmeyer reaction.[20] Completely optimized structure calculations using Gaussean 98 (B3LYP/6-

311**) on the aldehyde 7 indicate that both the acetamido and aldehyde groups are co-planar with the pyridine ring, with the amide oxygen atoms pointing toward the ring. These calculations also suggest that there is some hydrogen bonding between the amide oxygen atoms and the pyridyl hydrogens, and one of the pyridyl hydrogens is near enough to hydrogen bond with the aldehyde oxygen. The difference in the chemical shifts for the two pyridyl protons is calculated (GIAO) to be 0.220 ppm in the gas phase, and that measured in chloroform-*d* is < 0.07 ppm. Interestingly, the pyridyl protons sense the formation of the self-complimentary hydrogen bond dimer of **II**, manifested as a small chemical shift of ~0.1 ppm, which is consistent with the expected inductive and geometric effects (see Appendix 1).



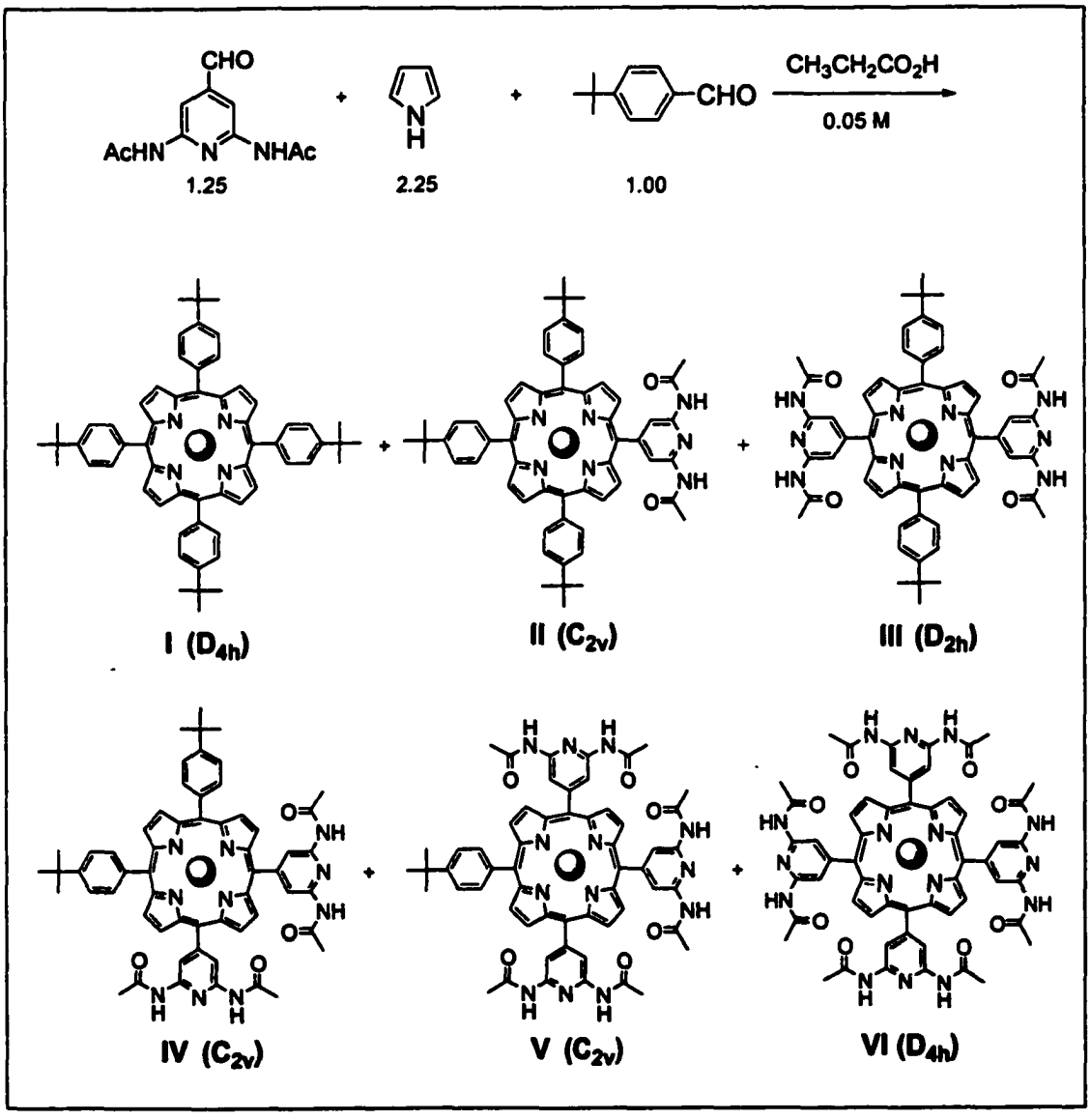
Scheme 3. *Synthesis of the 1-butyl-6-formyluracil from 6-formyluracil*

The synthesis of the complementary 1-butyl-6-formyluracil, **11**, from 6-formyluracil, **8**, is substantially different than that of the known 1-butyl-5-formyluracil[5a] (see Scheme 3). Unlike the 5-formyl derivative[21a], the 6-formyluracil[21b] does not alkylate preferentially at the 1-position so must be protected as the acetal, alkylated, and deprotected. Trimethyl orthoformate in methanol / methylene chloride and **8** were refluxed for 10h in the presence of the *p*-toluenesulfonic acid to form the 6-

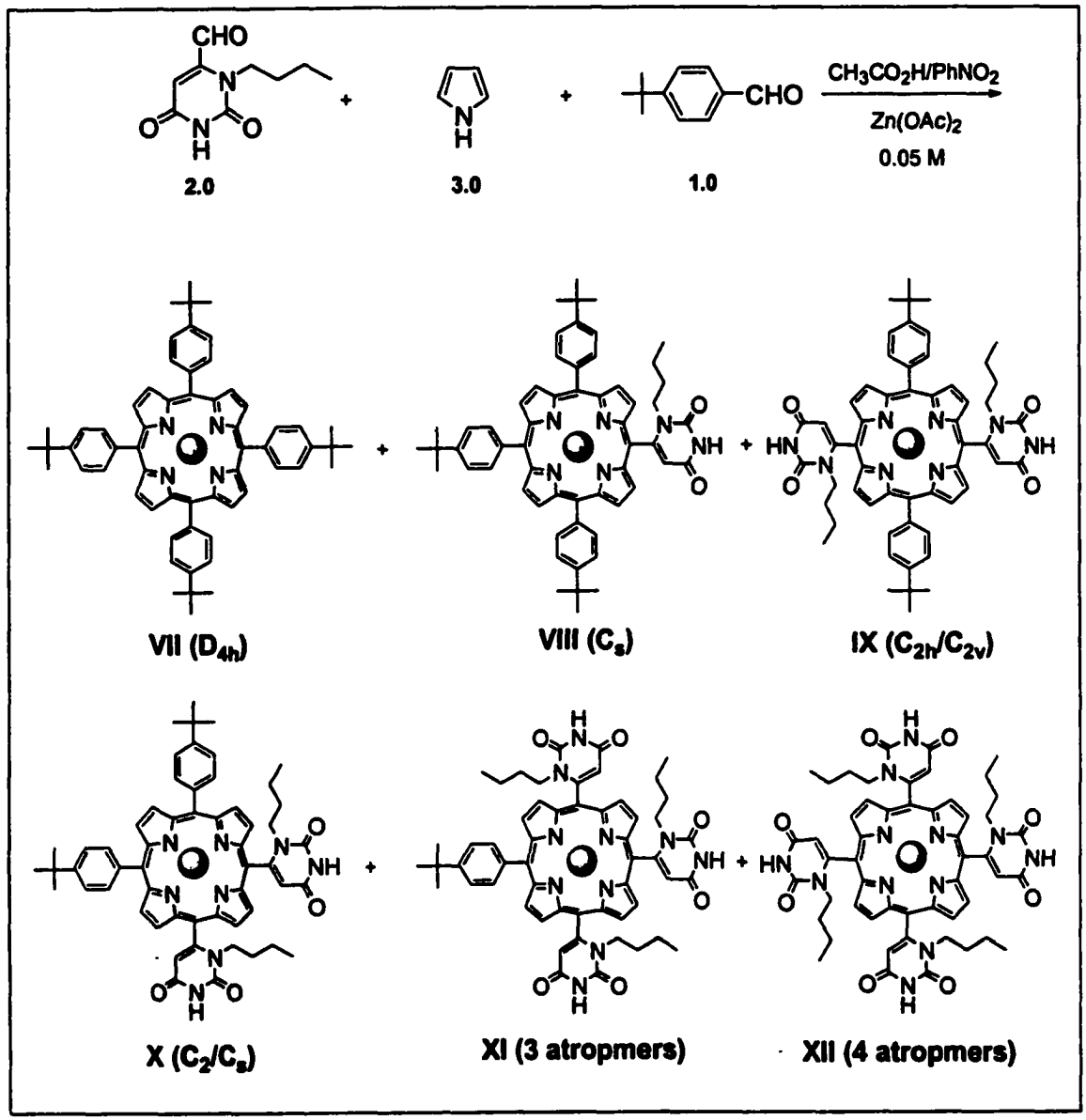
(dimethoxymethyl)uracil, **9**, in 86% yield.[22a] The dimethyl acetal **9** was alkylated with *n*-butylbromide catalyzed by K_2CO_3 in DMSO at room temperature for 72h to form the 1-butyl-6-(dimethoxymethyl)uracil (37% based on n-butylbromide)[23], **10**, and two by-products. The 1-butyl-6-(dimethoxymethyl)uracil **10** could not be converted to its corresponding aldehyde under a variety of aqueous acid conditions, so a Lewis acid, BBr_3, in CH_2Cl_2 was used to cleave the dimethyl acetal[22b] at -78°C in 87% yield. In dry solvents the uracil vinyl proton can be observed as two peaks, possibly as a consequence of self-complementary hydrogen bonding of **11**.

Both sets of porphyrin building blocks were prepared by the Adler[24] synthesis (see Schemes 4 and 5) and modifications thereof.[25] Using a mixture of two different aldehydes results in a mixture of six porphyrins in yields that are weighted by the reactivity, the solubility, and the relative amounts of the aldehydes.[8a,9a,25] All three of these can be exploited to obtain maximum yields of the desired porphyrins, *vide infra*. Since the polarities of the six porphyrins are very different, they are readily separated by column chromatography. The mixed aldehyde condensation[8a,25] was chosen for several reasons. (1) Heterocyclic aldehydes and/or those bearing Lewis bases are generally not tolerated or have poor yields using the Lindsey porphyrin syntheses[26] as well as most of the [n+(4-n)] coupling reactions. (2) The five compounds containing the heterocycles are all needed as building blocks for the self-assembled arrays. (3) The Adler[24] synthesis and its modifications[25] are quite amenable to large scale, multi gram reactions without significant sacrifice in yields or complications in purification. (4) All the porphyrins and isomers can be well characterized by the ^1H NMR spectra in the aromatic region, especially by the pyrrole β-H. Thus, with ample quantities of the two aldehydes in hand, a number of

porphyrin syntheses were explored: three different reaction solvents, acetic acid, propionic acid, and a mixture of nitrobenzene/acetic acid were tried each with and without zinc acetate as a possible template agent. All these conditions give good results with **7**, but **11** was more problematic.



Scheme 4. Synthesis of the pyridyl porphyrins by means of a mixed-aldehyde approach (see Scheme A5-3)



Scheme 5. *Synthesis of the uracyl porphyrins by means of a mixed-aldehyde approach (see Scheme A6-3)*

In order to increase the yield of the four porphyrin building blocks bearing both heterocyclic and alkylphenyl groups, we adopted three measures: (i) increasing the amount of the heterocyclic aldehydes, (ii) decreasing the concentration of the reaction mixture (0.05 M), (iii) for the uracyl porphyrin building blocks, changing the reactant addition order

whereby the 4-*tert*-butylbenzaldehyde was added 10 minutes after adding the pyrrole rather than adding two aldehydes together. During the course of this investigation only one method for the synthesis of the tetrauracylporphyrin was discovered, namely using acetic acid and nitrobenzene as reaction solvents[25d] with zinc acetate (see Scheme 5). The 5.1% yield of **XII** is consistent with previous Adler synthesis[25a] considering that it bears a non-aromatic heterocycle with a sterically hindering substituent next to the aldehyde.

The one striking aspect of the physical properties of both the di-heterocyclic porphyrin isomers is the abnormally low solubility of the 5,15-isomer compared to that of the 5,10-isomer. In non-polar organic solvents the solubility of the 5,10-porphyrins is usually expected to be less than that of the 5,15-isomers due to greater polarity; however, on the contrary, these 5,10-porphyrins are found to have much greater solubility than the 5,15-isomers. As discussed below, this anomalous solubility is explained by the self-complementary hydrogen-bond self-assembly of linear polymeric tapes *vs* closed tetrameric squares.

While the characterization of the 3,5-diacetamido-4-pyridylporphyrins is straightforward, the characterization of meso-1-butyl-6-uracylporphyrins merits comment. The four 1-butyl-6-uracyl groups are rigidly linked to the *meso*-positions of the porphyrin and rotation about the connecting bond is hindered by the butyl substituents. Thus the 1-butyl-6-uracyl group is oriented nearly normal to the porphyrin plane, projecting the butyl substituents above or below the macrocycle. The ^{1}H NMR spectra (see Appendix 1) of tetrauracyl compound **XII** reveals that: (1) all the chemical shifts of the butyl group are shifted up-field due to ring current effects; (2) the methylene group next to the 1-N atom showed four sets of multiplets rather than one triplet and the methyl group showed four sets

of triplets rather than one triplet. This proves that the butyl groups are on the 1-positions of the uracyl, and that there are four rotameric forms[27] in a ratio of 1:3:2:1 from low to high field. The statistical ratio for the αααα, ααaβ, ααββ, and αβαβ rotamers would be 1:4:2:1, respectively (α above and β below the porphyrin plane).[28] The integral areas of the terminal methyl group are consistent with the N-methylene, but may be in a different order. The observed deviations from the ideal ratios may be due to losses during the purification process. The rotameric forms of **VIII – XII** result in self-assembled supramolecular species with different isomeric forms, but the isomers are not observed. There are also no detectable consequences on the energetics and kinetics of the self-assembly process since the uracyl ADA (A = hydrogen bond acceptor, D = hydrogen bond donor) recognition function(s) are directed along the porphyrin plane.[29]

The ^{1}H NMR spectra of the various other uracyl porphyrin derivatives, **VIII – XI,** are similarly complex due to the presence of both 4-*tert*-butylphenyl and 1-butyl-6-uracyl groups and the resulting rotamers. Each porphyrin face is different in the monouracyl porphyrin, **VIII**. This results in an AB, A′B′ system, where A′, B′ represents the phenyl protons on the opposite side of the macrocycle relative to the butyl group on the uracil. Thus for **VIII**, the phenyl protons are observed as multiplets rather than a simple AB quartet. The spectrum of **VIII** shows the expected diagnostic pattern in the β-pyrrole region for this type of derivative, where there are four different chemical environments that should result in two AB quartets, but only the quartet from the pyrroles nearest the heterocycle is observed, while those on the opposite side of the heterocycle are observed as a singlet even on the 500 MHz instrument.

For analytical purposes both rotamers of **IX** and **X**, were isolated. Both the 5,15- and 5,10- compounds, can exist as αα or αβ rotamers, each with a different symmetry, with respect to the relative orientation of the two 1-butyl-6-uracyl groups. Thus, the chemical environments of the porphyrin faces are the same for the αβ rotamers and different for the αα rotamers for both **IX** and **X**. As in the mono substituted derivative, these rotameric forms are readily observed in the ^{1}H NMR in the region of the two 4-*tert*-butylphenyl groups. A simple doublet of doublets for the phenyl groups of the αβ rotamers of both compounds is observed, while multiplets for the same groups are observed for the αα rotamers. Because the pyrrole β-H are in the porphyrin plane, the rotameric forms of **IX** and **X** are not observed in this region, so there are the expected four different pyrrole resonances in **X**, and two for **IX**.

Structural Studies

As an additional, unexpected example of the intrinsic tendency of these compounds to aggregate by hydrogen bonding, we also present an X-ray study of **IV**. Atom names, displacements from planarity and an edge-on view of the macrocycle are given in Figure 2. The crystallographic determination provides unambiguous identification of **IV**. Complete experimental details, atomic coordinates and molecular geometry are included in Appendix 2. The C5-, C10-, and C20- meso substituents are completely ordered, but the *tert*-butylphenyl group at C15 exists in two discrete orientations with 75/25% occupancies. (Only the orientation of the major component is shown in Figure 2)

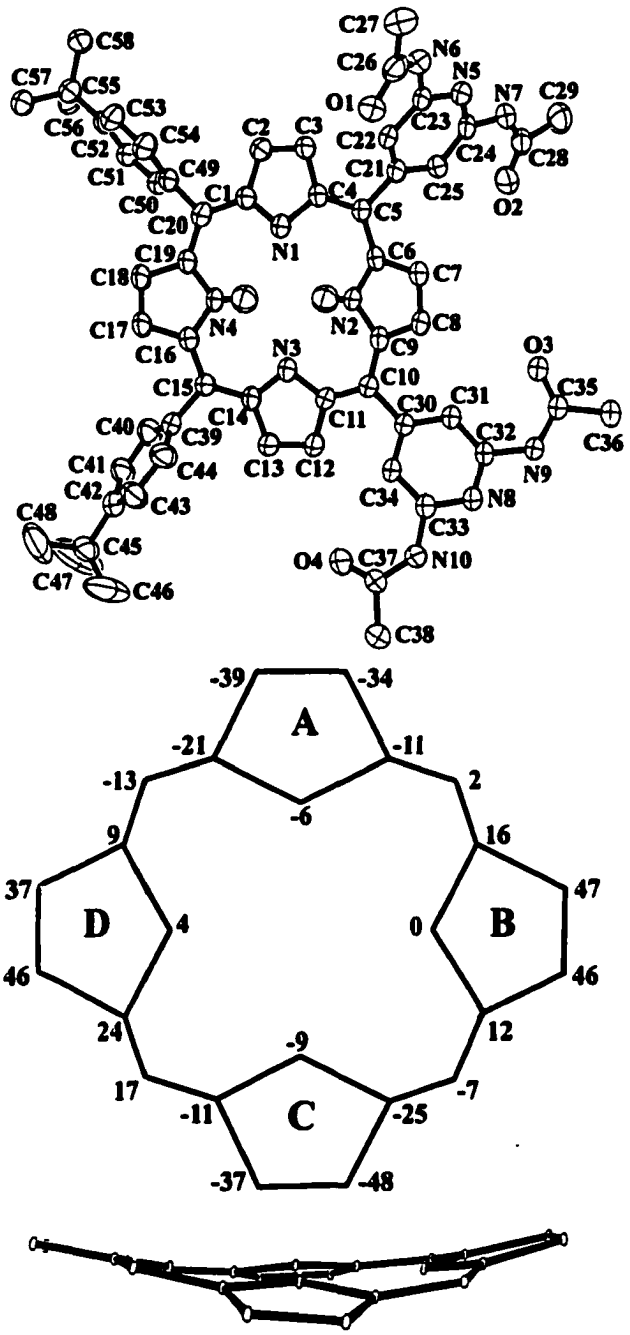


Figure 2. *Top) Molecular structure and atom names for IV. Thermal ellipsoids are drawn at the 50% probability level. Peripheral hydrogens are omitted for clarity. Middle) Displacements of the 24 atoms that comprise the macrocycle from the 24 atom mean porphyrin plane in units of 0.01 Å. Bottom) Edge-on view of the porphyrin core. Thermal ellipsoids enclose 1% probability for clarity.*

The skeleton of IV is mainly saddled with some degree of ruffling. The Cb atoms in each of the four pyrrole rings exhibit substantial unequal displacements from the mean porphyrin plane that range between 0.34-0.48Å (see Figure 2). The deviations of the meso carbons are also unequal; they are smaller at C5 and C10, 0.02Å and -0.07Å than at C15 and C20, 0.17Å and -0.13Å. The edge-on view in Figure 2 further illustrates the distorted conformation of the macrocycle, with rings B and D above the mean plane and rings A and C below it. Note that such out-of-plane distortions of the porphyrin macrocycle have been shown to have significant effects on the optical, redox and excited

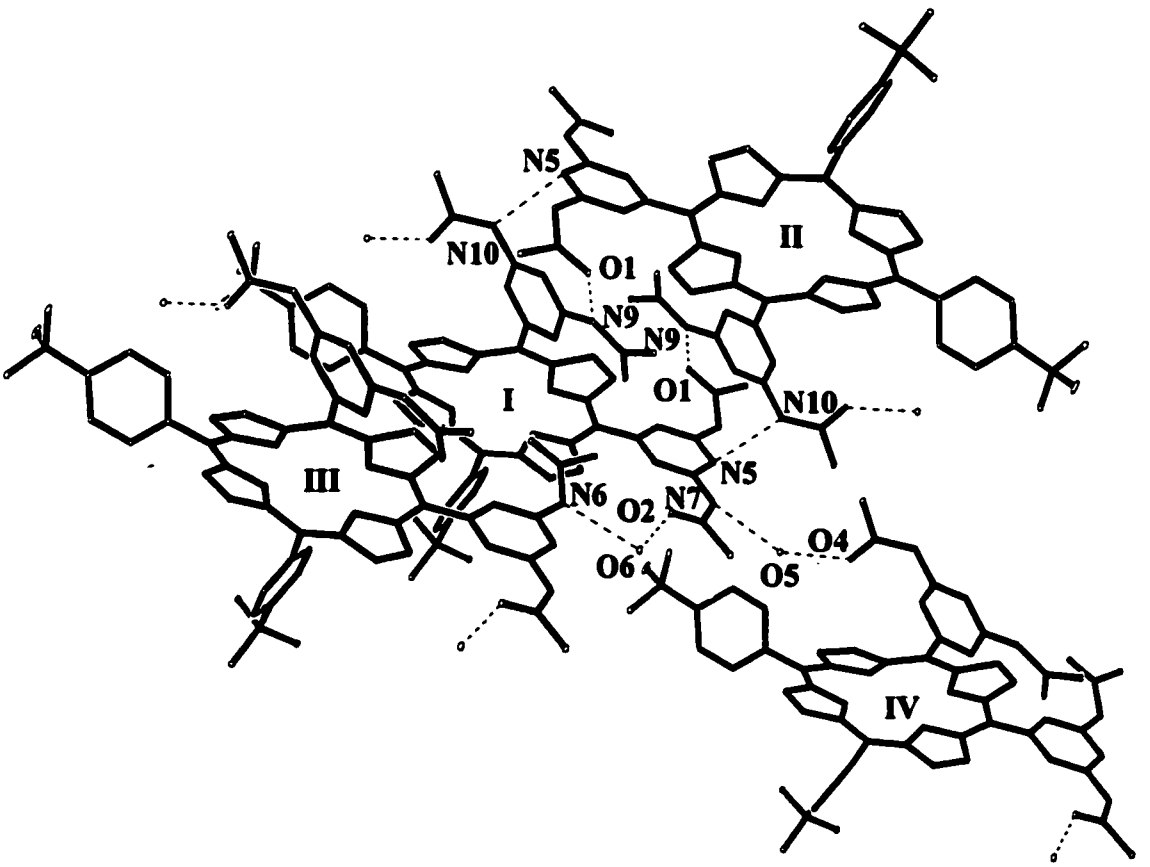


Figure 3. *Hydrogen-bonded supramolecular assembly of porphyrin IV mediated by water. (Hydrogen bonds are shown as dotted lines.)*

state properties of the chromophores.[30] Biological systems containing porphyrinic proteins such those used in photosynthesis and electron transport exploit these effects to fine-tune their reactivity and photo physical properties.[31]

As observed in other saddled porphyrins,[30,31] the dihedral angles between the meso-substituents and the porphyrin plane are unusually acute. They assume values of 62° at C5, 36° at C10, 60° and 72° at C15 and 62° at C20. The unusual dihedral angle of 36° of the C10 substitutent, compared to the nearly perpendicular angles of 80-90° normally observed in planar aryl-substituted porphyrins, is most likely related to its participation in hydrogen bonds (vide infra).

The sample was crystallized from a mixture of ethyl acetate and hexane, but the crystals do not incorporate either of these solvents. Instead, the lattice contains 2.5 molecules of adventitious water per porphyrin. The unexpected water molecules (O5 and O6) mediate a more extensive supramolecular array of IV via multiple hydrogen bonds (see Figure 3).

For simplicity, the basic porphyrin building blocks of this array are designated as 1, 2, 3, and 4. Only molecule I comprises the crystallographic asymmetric unit; the rest are generated by space group operators. Molecules 1 and 2 are joined by two reciprocal O1...N9 and two reciprocal N5...N10 hydrogen bonds at 3.02Å and 3.05Å. This dimeric unit is further incorporated into a complex multi-porphyrin array. O2 of molecule 1 associates with O6 (a water molecule of solvation) with an O2...O6 distance of 2.84Å. O6 then hydrogen bonds to N6 of molecule 3 which is 2.99Å from it. N7 of molecule 1 associates with O5 (another water molecule of solvation) with N7...O5 = 3.00Å. O5 sits 2.82Å away from O4 of molecule 4. (There are additional interactions involving O7, a

third water of crystallization that is present only 50% of the time.) The closest approach of ring centers is 3.87Å for the molecules 1 and 3, where the center of 3 is 6.42Å away from the edge of molecule 1, so if pi-pi interactions are present, they are weak. Since the center to center distance of 1 and 3 is 12.70Å, they interact only at the periphery.

All five possible hydrogen-bond donors and acceptors (O1, N6, N5, N7 and O2) of the C5-meso substituent participate in the network formation, whereas only N9, N10 and O4 of the C10-meso substituent participate, and may thus contribute to the differences in the orientations of the peripheral rings. The structure reveals that there are no substantial pi-pi interactions in this arrangement of macrocycles in the solid state. Therefore, the degree of porphyrin distortion caused solely by hydrogen bonding in this single-component system is unprecedented.[31] These results als indicate that the intentional addition of water to molecules designed to form networks or arrays mediated by hydrogen bonding may well lead to novel aggregates, as evidenced by this structure.

Self-Assembled Squares in Solution

The preponderance of evidence from ^{1}H NMR, UV-Visible, ESI-MS, light scattering, and osmometry suggests that **IV** self-assembles into tetrameric squares in solvents with low hydrogen-bonding potential by self-complementary hydrogen bonds.[32] This is well demonstrated by fits of the chemical shift of the amide proton versus concentration to yield an apparent equilibrium constant, K, and the number of molecules in the final assembly, n (see Figure 4A). If there are several products or dynamic processes, such as the breaking apart of one or more sets of hydrogen bonds occurring on

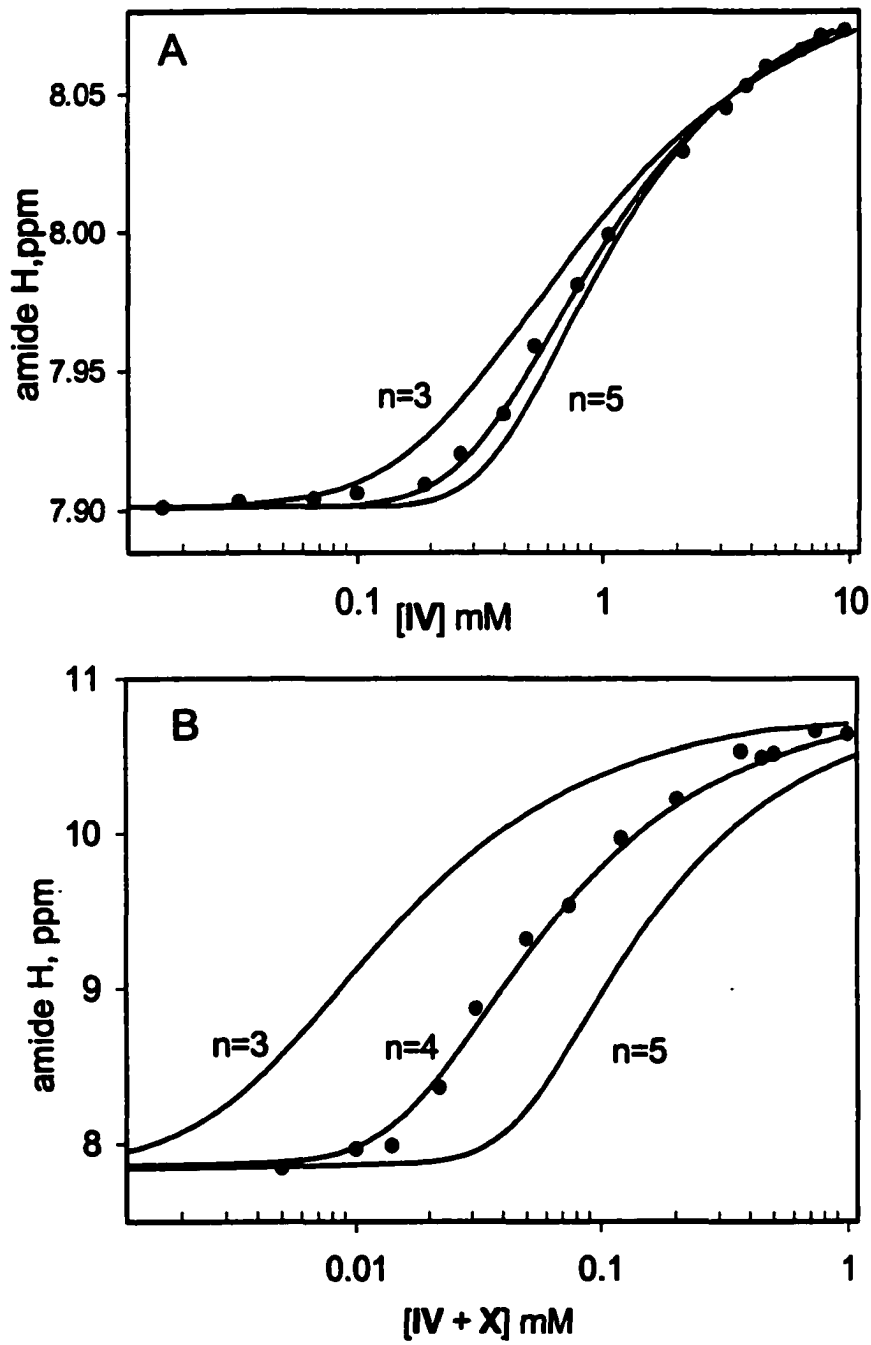
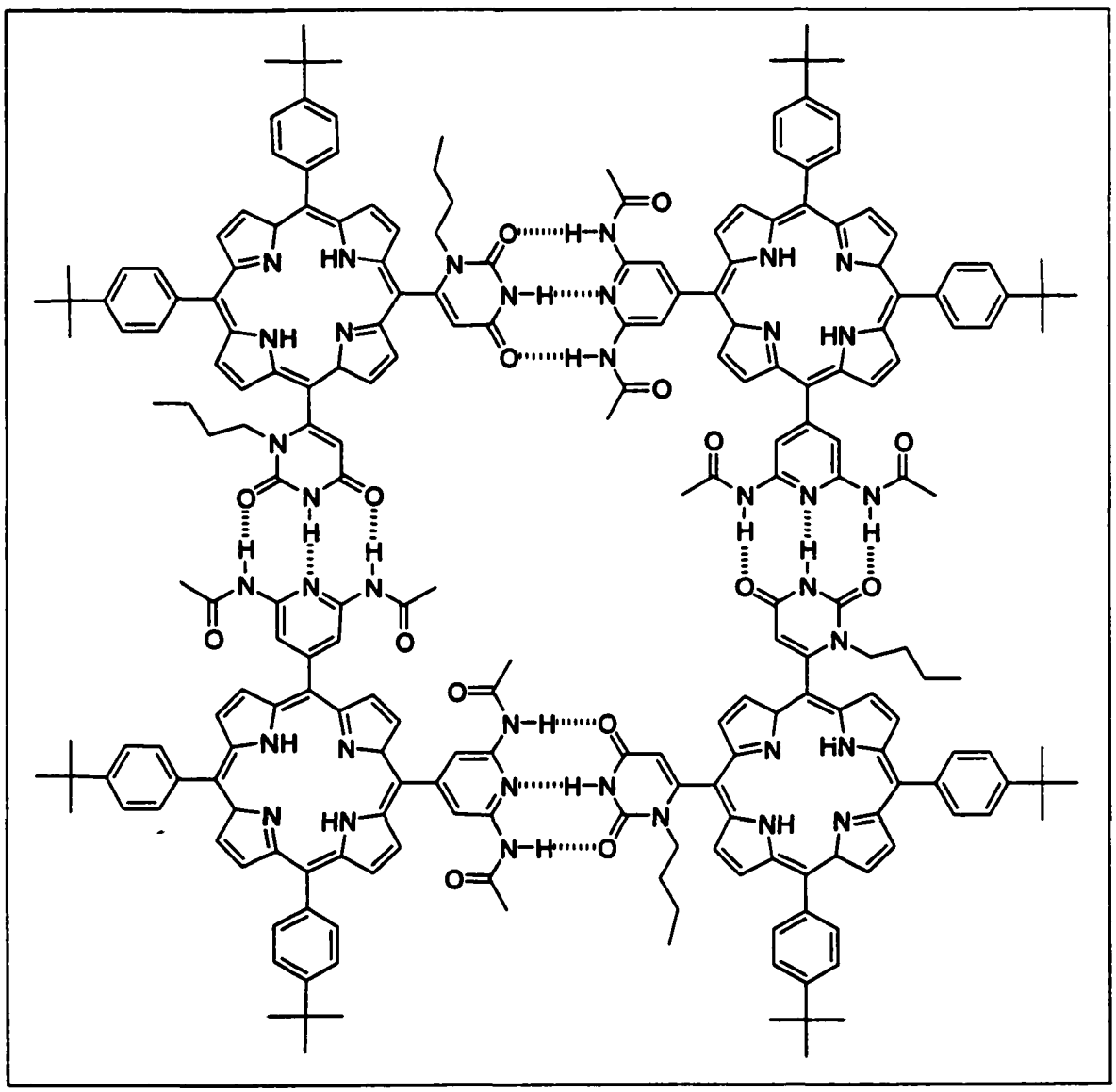


Figure 4. ***Formation of closed tetrameric squares. A) The self-complimentary association of IV in $CDCl_3$, is compared to B) the complementary association of a 1:1 mixture of IV and X in $THFd_8$.***

the NMR time scale, these result will only give rough estimates of K, but this serves as a basis of comparison for the square formed by complimentary H-bonds, below. Analysis of the NMR data[32] for the self-complimentary self-assembly of the square tetramer of IV yields $K = 2.1 \pm 1 \times 10^9\ M^{-3}$, and $n = 3.9 \pm 0.3$ in chloroform. In toluene the equilibrium constants are greater, as expected, where K is $\sim 2 \pm 1 \times 10^{10}\ M^{-3}$). ESI-MS and vapor phase osmometry data also indicate a tetrameric species.

The thermodynamics of these self-complementary systems in solution are discussed herein. The association for the diacetamidopyridyl moiety is usually considered weak,[29] ΔG_{dimer} ranges from 4 to 13 kJ mol^{-1}, and the double hydrogen bond considered the dominant interaction. However, the strengths of these recognition units are substantially altered by the presence of the directly linked porphyrin. Thus there is likely an equilibrium between the various self-complimentary interactions of the diacetamidopyridyl groups – double, triple, quadruple hydrogen bonds. Van't Hoff plots of the ^1H NMR data for the self-complementary dimerization of II indicate ΔH_f of the dimer is $\sim 21 \pm 5$ kJ mol^{-1} in toluene versus the expected ~13 kJ mol^{-1} for the alkyl substituted derivative in the same solvent.[29] AM1 calculations indicate that the presence of a phenyl group on the 4 position of the 2,6-diacetamidopyridyl moiety increases the self-complementary H-bond enthalpy by ~4 kJ mol^{-1}. Typically, the electronic effects of the porphyrin are greater than the phenyl group, so a further increase in the ΔH of the self-complementary interaction(s) is expected and calculated to be ~6 kJ mol^{-1} greater than the parent recognition unit. Thus the experimental and calculated results are qualitatively consistent. The 90° geometry of the rigidly linked recognition groups on the porphyrins, and the thermodynamic stability of the self-assembled H-bond squares

compared to others structures,[29d] assure that the squares are formed in ~ 75% in chloroform, and ~90% in toluene.[32,33] Both experimental and computational results show



Scheme 6. ***The closed tetrameric square: the 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-tert-butylphenyl)porphyrin (X) and 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-tert-butylphenyl)porphyrin (IV) are mixed in THF-d8 can form a square tetramer by spontaneous self-assembly.***

that the presence of the phenyl has little effect on the self-complementary 1-butyl-6-uracyl system. Calculations indicated there should be a modest increase of ~ 3 kJ mol^{-1} for hetero-complementary 2,6-diacetamido-4-phenylpyridine and 1-butyl-6-phenyluracil. The H-bond strengths between the complementary porphyrins **II**, and **VIII**, are calculated to be 45 kJ mol^{-1}, ~7 kJ mol^{-1} greater than for the isolated recognition units bearing neither porphyrin nor phenyl substituent.[29,33] Thus the porphyrin ring is expected and observed to enhance the basicity of the pyridyl nitrogen and therefore the H-bond strength. This is a well-documented phenomenon in the coordination chemistry of pyridylporphyrins.[9]

The formation of a tetrameric square from two equivalents each of **IV** and **X** (see Scheme 6) in THF, used because of the limited solubility of **X**, is indicated by similar experiments as described above. The overall shape of the NMR concentration vs amide chemical shift (see Figure 4B) clearly indicate a tetrameric species with n = 4 and an apparent equilibrium constant, see caveats vide supra, of $6 \pm 3 \times 10^{12}$ M^{-3} which is somewhat greater than that estimated by solely by equilibrium considerations from the $C_{1/2}$ data.[29e] Note that the $C_{1/2}$ for the complementary square is about two-fold less than that of the self-complementary species, and the Δppm for the amide protons is a factor of 5 greater. These are all indicative that the complementary interactions between the uracyl and diacetamidopyridyl moieties, calculated by various means to be ~45 kJ mol^{-1}, are much stronger than either self-complementary interaction even in a solvent known to be less favorable to H-bonding than chloroform. Dynamic light scattering detects only species with ~ 4 nm hydrodymic radius between 0.04 and 0.1 mM. Vapor phase osmometry experiments using concentrations between 0.1 and 1 mM yields an average molecular

weight of 3500 ± 300 da. ESI-MS using a mixture of **IV**, Co(III)**IV**, and **X** (1:1:2) shows the doubly charged tetramer as well as other multimers and the monomers. Taken together, these data indicate that the complementary tetrameric square forms in solution. Experimental and computational work on these latter assemblies is in progress.

Conclusion

These two sets of complementary porphyrin building blocks, can be used for constructing diverse multi-porphyrin arrays in defined geometry through self-complementary or hetero-complementary assembly. The enthalpy of the latter is stronger by more than two-fold, and this insures that the self-complementary products are not complicating factors in the hetero self-assembly process. The 1-butyl-6-uracyl and 3,5-diacetamido-4-pyridyl groups can be used to form linear, square, and junction structures in a predefined metallation state. The ability to self-assemble nanoscaled building blocks with precisely controlled size and composition, and to incorporate them into larger electronics components – which may entail secondary self-assembly steps to form hierarchical structures – with unique properties and functions may have significant implications for the incorporation of these types of molecules into photonic devices. These studies are also demonstrate that water can mediate the self-aggregation of H-bonding species and dictate the supramolecular arrangement of subunits, as it does in many protein structures.

Experimental Section

Materials and Methods. Melting points were determined on a Thomas-Hoover UniMelt capillary apparatus and are uncorrected. Flash column chromatography was performed using 230-400 mesh ASTM Merck silica gel-60. ^{1}H and ^{13}C NMR spectra were recorded on Jeol 400 MHz, a Varian VXR-300 MHz, or a Varian 500 MHz instruments. Chemical shifts are reported in ppm relative to TMS for ^{1}H and ^{13}C spectra, and coupling constants in Hz. NMR assignments are consistent with those published previously. Agilent Technologies HP 1100 LC/MSD, and a Cary Bio-3 were used. Typical Electrospray Ionization Mass Spectroscopy (ESI-MS) method: ~0.05mM solutions in acetonitrile : water (50:50) containing 1% trifluoroacetic acid, positive ion mode, and the fragmentor voltage between 100-350 V. Elemental analysis by Schwarzkopf Microanalytical Laboratory, Inc.

2,6-Diamino-4-methylpyridine (2). A solution of 4-methylpyridine 1 (9.31 g, 9.73mL, 0.10 mole) in 50 mL tetralin was added to a solution of sodium amide (9.33 g, 0.24 mole) in 100 mL tetralin at 130~140°C over 6h, afterwards heated to 195°C and kept at this temperature for 10h.[18d] After cooling, the reaction mixture was filtered, and the remaining black solid material worked up by the dropwise addition of 150 mL ethanol. 10 g of silica gel was added, and the ethanol was removed under reduced pressure. The resultant dark solid was added to the top of a 45 g column of silica gel and eluted with ethyl acetate to afford 8.02 g (65%) of **2** as a white powder. Recrystallized from chloroform, mp 85-86°C (lit.[18a] 87-88°C, sublimed crystal, 109-111°C). ^{1}H NMR ($CDCl_3$) δ 5.74 (s, 2H), 4.06 (br, s, 4H), 2.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 158.3, 151.3, 99.5, 21.8; MS (ESI) m/z (MH^+, 124).

2,6-Diacetamido-4-methylpyridine (3). 16.0 ml of acetic anhydride was added to 1.5 g (12.2 mmol) of the diamine **2**. The resultant solution was stirred for 1h and 2.35 g (93%) of a white crystalline solid **3** was collected by filtration, mp 199-201°C. ^{1}H NMR ($CDCl_3$) δ 7.72 (s, 2H), 7.64 (br, m, 2H), 2.35 (s, 3H), 2.17 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 168.9, 153.4, 149.9, 110.9, 25.5, 22.5; MS (ESI) m/z (MH^+, 208). Anal. Calcd for $C_{10}H_{13}N_3O_2$: C, 57.97; H, 6.32; N, 20.27. Found: C, 57.84; H, 6.50; N 20.10.

2,6-Diacetamido-4-methylpyridine-1-oxide (4). To a solution of the diamide **3** (2.07g, 10.0 mmol) in 10 mL acetic acid, 3.0 mL of 32% peracetic acid was added carefully at room temperature. The resulting solution was heated for 3h at 50-60°C and 4h at 65-70°C. After cooling to r.t., adding $FeSO_4$ solid to destroy residual oxidant, and removing the acetic acid under reduced pressure, the residue was recrystallized from water to yield 1.76 g (79%) of the oxide **4** as a white powder: mp 210-211°C. ^{1}H NMR ($CDCl_3$) δ 9.83 (s, 2H), 7.92 (s, 2H), 2.35 (s, 3H), 2.27 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 164.4, 137.4, 137.0, 104.1, 21.0, 17.8; MS (ESI) m/z (MH^+, 224). Anal. Calcd for $C_{10}H_{13}N_3O_3$: C, 53.80; H, 5.87; N, 18.82. Found: C, 53.94; H, 5.96; N, 18.90.

2-Diacetimido-6-acetamido-4-acetoxymethylpyridine (5). A solution of the oxide **4** (1.50 g, 6.73 mmol) in acetic acid (3.0 ml) was added to stirred, refluxing acetic anhydride (20 mL) over a 30-min. period. The reaction mixture was stirred at reflux temperature for 30h, cooled, 5.0 g silica-gel was added to the reaction mixture, and the solvent removed under reduced pressure. The resultant dark material was added to the top of a 20 g column of silica gel and eluted with ethyl acetate/petroleum ether (1:1) to afford 1.49 g (72%) of **5** as a white powder, mp 177-178°C. ^{1}H NMR ($CDCl_3$) δ 8.24 (s, 1H), 7.89 (br, s, 1H), 6.93 (s, 1H), 5.17 (s, 2H), 2.29 (s, 6H), 2.21 (s, 3H), 2.20 (s, 3H); ^{13}C

NMR ($CDCl_3$) δ172.9, 170.9, 169.2, 152.3, 151.7, 151.6, 118.0, 112.3, 64.7, 27.3, 25.5, 21.5; MS (ESI) m/z (MH^+, 308). Anal. Calcd for $C_{14}H_{17}N_3O_5$ C, 54.72; H, 5.57; N, 13.67. Found: C, 54.66; H, 5.64; N, 13.71.

2,6-Diacetamido-4-hydroxymethylpyridine (6). A solution of the acetate **5** (1.20 g, 3.9 mmol) and K_2CO_3 (0.59 g) in methanol/water (10 mL, 4:1) was stirred at room temperature for 8 h. The reaction mixture was loaded on 3.0 g silica-gel. The resultant yellow material was added to the top of a 25 g column of silica gel and eluted with ethyl acetate/ethanol (9:1) to afford 0.80 g (92%) of the alcohol **6** as a white powder. mp 194-195°C; ^1H NMR (DMSO-d_6) δ 9.93 (s, 2H), 7.65 (s, 2H), 5.34 (t, 1H), 4.43 (d, 2H), 2.05 (s, 6H); ^{13}C NMR (DMSO-d_6) δ 170.1, 156.8, 151.2, 107.5, 63.4, 25.2; MS (ESI) m/z (MH^+, 224). Anal. Calcd for $C_{10}H_{13}N_3O_3$: C, 53.80; H, 5.87; N, 18.82. Found: C, 53.72; H, 6.04; N 18.86.

2,6-Diacetamido-4-formylpyridine (7). A solution of the alcohol **6** (0.80 g, 3.58 mmol) in CH_2Cl_2 (15 mL) was treated with NaOAc (2.85 g, 14.32 mmol) followed by portionwise addition of pyridinium chlorochromate (PCC/Alumina, 1.15 g, 5.38 mmol). The reaction mixture was placed in a sonication bath[22c] at room temperature for 1h, at which time additional PCC/Alumina (0.43 g, 2.01 mmol) was added. After being sonicated an additional 3h, the reaction mixture was loaded on 3.0 g silica-gel, added to the top of a 25 g column of silica gel, and eluted with ethyl acetate/ethanol (9:1) to afford 0.43 g (54 %) of the aldehyde **7**, mp 223-224°C. ^1H NMR (DMSO-d_6) δ 10.33 (s, 2H), 9.96 (s, 1H), 8.11 (s, 2H), 2.10 (s, 6H); ^{13}C NMR (DMSO-d_6) δ 194.1, 170.7, 152.6, 146.5, 108.9, 25.3; MS (ESI) m/z (MH^+, 222). Anal. Calcd for $[C_{10}H_{12}N_3O_3]^+$: C, 54.05; H, 5.44; N, 18.91. Found: C, 53.63; H, 5.27; N, 18.26.

6-(Dimethoxymethyl)uracil (9). A solution of orotaldehyde (**8**) (3.0 g, 21.42 mmol) and trimethyl orthoformate (9.08 g, 9.4 mL, 85.68 mmol) in MeOH (50 mL) and CH_2Cl_2 (100 mL) was refluxed for 10h in the presence of *p*-toluenesulfonic acid (0.3 g, 1.58 mmol). After the reaction mixture cooled to room temperature, triethylamine was added to the reaction mixture until it turned weakly basic. 5.0 g silica-gel was added to the reaction mixture and the solvent removed under reduced pressure. The resultant yellow material was added to the top of a 25 g column of silica gel and eluted with ethyl acetate/ethanol (9:1) to afford 3.46 g (87%) of the acetal **9** as a white powder. mp 185-186°C, (lit.[22a]: 185-186°C). ^{1}H NMR ($CDCl_3$) δ 11.02 (br, s, 1H), 10.83 (br, s, 1H), 5.45 (s, 1H), 4.99 (s, 1H), 3.25, (s, 6H); ^{13}C NMR ($CDCl_3$) δ 164.9, 152.4, 151.8, 99.5, 99.1, 54.8; MS (ESI) m/z ($M\text{-}H^+$, 185).

1-butyl-6-(dimethoxymethyl)uracil (10). To a solution of the acetal (**9**) (3.20 g, 17.20 mmol) in DMSO (200 mL) were added 1-bromobutane (0.7850 g, 0.62 mL, 5.73 mmol) and anhydrous K_2CO_3 (2.61 g, 18.92 mmol). The suspension was stirred for 72h at room temperature after which it was filtered and the DMSO was removed in vacuo. The solid was absorbed on 5 g silica gel, loaded on the top of a 25 g column of silica gel, and eluted with hexane to afford 0.140 g (8.2%) of 1,3-dibutyl-6-(dimethoxymethyl)uracil as an oil. Further elution with ethyl acetate / hexane (1:9) afforded 0.222 g (16%) 3-butyl-6-(dimethoxymethyl)uracil and 0.513 g (37%) of **10**. Yields reported for this compound are based on 1-bromobutane. mp 91-92°C. ^{1}H NMR ($CDCl_3$) δ 9.28 (br, s, 1H), 5.95 (s, 1H), 5.05 (s, 1H), 3.87 (t, 2H, J = 7.7 Hz), 1.67-1.57, (m, 2H), 1.42-1.30, (m, 2H), 0.95, (t, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 163.4, 152.2, 151.3, 102.7, 99.9, 54.5, 45.1, 31.7, 20.8, 14.5; MS (ESI) m/z (MH^+, 243).

1-Butyl-6-formyluracil (11). A solution of the butylacetal **10** (0.50 g, 2.07 mmol) in 20 mL of CH_2Cl_2 was cooled to -78°C and treated with 1.6 mL of BBr_3 and stirred for 2h at that temperature. The cold bath was removed and the solution was allowed to reach room temperature. Saturated $NaHCO_3$ (15 mL) was added until the pH reached 7-7.5. The organic layer was removed and the aqueous layer was extracted with CH_2Cl_2. The extracts were combined, dried (with Na_2SO_4), and the solvent was removed to afford 0.315 g of the aldehyde **11** as a white solid (87%) mp 146-147°C. ^1H NMR ($CDCl_3$), δ 9.57 (s, 1H), 9.18 (br, s, 1H), 6.25 (s, 1H), 4.19 (t, 2H, J = 7.3 Hz), 1.63-1.53, (m, 2H), 1.43-1.33, (m, 2H), 0.95, (t, 3H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 186.0, 162.6, 151.5, 147.6, 115.0, 44.5, 32.3, 20.5, 14.4; MS (ESI) m/z ($M\text{-}H^+$, 195). Anal. Calcd for $C_{11}H_{18}N_2O_4$: C, 55.09; H, 6.16; N, 14.28. Found: C, 55.49; H, 6.13; N, 14.25.

5,10,15,20-Tetrakis(3,5-diacetamido-4-pyridyl)porphyrin (VI). Pyrrole (69.5 μL, 1.0 mmol) and 2,6-diacetamido-4-formylpyridine **7** (221 mg, 1.0 mmol) were added to boiling propionic acid (10.0 mL). The reaction mixture was refluxed for 2h and then taken to dryness under vacuum. The resulting solid was purified by chromatography on silica gel eluting with ethanol / ethyl acetate (1:1) to yield 77.1 mg (29%) of **VI**. ^1H NMR (DMSO-d_6) δ 10.52 (s, 8H), 8.99 (s, 8H), 8.60 (s, 8H), 2.16 (s, 24H), -3.10, (s, 2H); ^{13}C NMR (DMSO-d_6) δ170.7, 153.2, 150.1, 132.7, 119.4, 116.5, 25.4; MS (ESI) m/z (MH^+, 1075). Anal. Calcd for [$C_{56}H_{50}N_{16}O_8$ plus 2 H_2O] C, 60.45; H, 4.89; N, 20.16. Found: C, 60.92; H, 4.95; N, 20.01.

Diacetamidopyridyl / *tert*-butylphenyl porphyrins. 2,6-diacetamido-4-formylpyridine **7** (2.763 g, 12.5 mmol) and 4-*tert*-butylbenzaldehyde (1.63 g, 1.68 mL, 10.0 mmol) were added to 450 mL of boiling propionic acid and then 1.56 mL (22.6 mmol) of

pyrrole was added. The reaction mixture was refluxed for 2h at which time a 23.8% yield of the mixture of porphyrins was detected spectroscopically. The solvent was removed under vacuum, and the resulting solid was purified by chromatography eluting with hexane (I), to chloroform (II), chloroform / ethyl acetate (1:1) (III, IV), and ethyl acetate (V, VI) to get the four porphyrins with two different motifs at the *meso* positions. A second column using 10% v/v dioxane in chloroform is used to purify the fractions containing both III and IV, and typically the tetra-substituted derivatives are not isolated as they can be made directly. Based on starting pyrrole, the isolated yield is 20.6%, and the isolated amounts are I, 0.153 g (3.5%); II, 0.261 g (5.14%); III, 0.222 g (4.11%); IV, 0.290 g (5.36%); V, 0.149 g (2.60%); VI, 0.052 g (0.86%). The relative amounts are II (24%), III (20%), IV (26%), and V (11%), and the two homo-substituted porphyrins I (14.5%) and VI (4.5%).

5-(3,5-Diacetamido-4-pyridyl)-10,15,20-tris(4-*tert*-butylphenyl)porphyrin (II). ^{1}H NMR ($CDCl_3$) [500 MHz NMR, 50°C] δ 9.11, 9.05 (d, 2H, J = 5.0 Hz), 8.92 (s, 4H), 8.81 (s, 2H), 8.89 (s, 2H), 8.175, 7.785 (d, 12H, J = 7.5 Hz), 2.298 (s, 6H), 1.637 (s, 27H), -2.761 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 169.0, 156.1, 151.1, 148.4, 139.7, 135.1, 131.7-131.9, 124.2, 121.6, 121.2, 117.0, 35.7, 32.5, 25.6; MS (ESI) m/z (MH^+, 898).

5,15-Bis(3,5-diacetamido-4-pyridyl)-10,20-bis(4-*tert*-butylphenyl)porphyrin (III). ^{1}H NMR ($CDCl_3$) δ 9.27, 9.23 (dd, 8H, J = 4.4), 9.15 (s, 4H), 8.49, 8.10 (d, 8H, J = 8.1), 8.35 (s, 4H), 2.62 (s, 12H), 1.95 (s, 18H), -2.49 (s, 2H) ; MS (ESI) m/z (MH^+, 957).

5,10-Bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (IV). ^{1}H NMR ($CDCl_3$) [500 MHz NMR, 50°C] δ 8.98 (s, 2H), 8,95, 8.91 (dd, 4H, J = 5.0 Hz), 8.89 (s, 2H), 8.77 (s, 2H), 7.90 (s, 2H), 8.17, 7.79 (d, 8H, J = 7.5 Hz), 2.29 (s, 6H), 1.64 (s, 27H), -2.72 (s, 2H); ^{13}C NMR (DMSO-d_6) δ 170.3, 150.9, 149.6, 138.6,

134.7,131.2~132.6, 124.3, 121.5, 117.9, 115.8, 35.1, 31.9, 24.7; MS (ESI) m/z (MH^+, 957).

5,10,15-Tris(3,5-diacetamido-4-pyridyl)-20-(4-*tert*-butylphenyl)porphyrin (V). ^1H NMR (DMSO-d_6) δ 10.51 (s, 6H), 8.81~8.97 (m, 8H), 8.59 (s, 6H), 8.12, 7.77 (dd, 4H, J = 8.1), 2.16 (s, 18H), 1.51 (s, 18H), -3.10, (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 170.8, 153.5, 151.4, 150.1, 138.9, 135.2, 132.4~132.5, 129.9, 129.2, 126.3, 124.7, 122.3, 119.2, 116.4, 35.7, 32.5, 25.4; MS (ESI) m/z (MH^+, 1016).

5,10,15,20-Tetrakis(1'-butyl-6'-uracyl)porphyrinatto(Zn)(II) (XII). Pyrrole (69.5μL, 1.0 mmol), 1-butyl-6-formyluracil (196 mg, 1.0 mmol) and zinc acetate (109.8 mg, 0.50 mmol) were added to a boiling mixture of acetic acid (7.5 mL) and nitrobenzene (5.0 mL). The reaction mixture was refluxed for 10h while monitoring the yields spectroscopically, and then taken to dryness under vacuum. The resulting solid was purified by chromatography, eluting with ethyl acetate to afford ~5.1% **12**. ^1H NMR (DMSO-d_6) δ 11.83 (br, s, 4H), 9.50 (m, 8H), 6.26 (s, 4H), 3.56~3.08 (m, 8H), 1.10~0.91 (m, 8H), 0.30~0.08 (m, 8H), 0.00~-0.60 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 185.0, 163.4, 150.6, 142.3, 110.4, 41.9, 30.3, 20.9, 14.5; MS (ESI) m/z (MH^+, 1037 for ZnXII). Anal. Calcd for $C_{52}H_{52}N_{12}O_8Zn$: C, 60.15; H, 5.05; N, 16.18, for $C_{52}H_{52}N_{12}O_8Zn$ with 1 H_2O: C, 59.12; H, 5.16; N, 15.90. Found: C, 60.04; H, 5.24; N 15.92.

1-Butyluracyl / *tert*-butylphenyl porphyrins. Pyrrole (0.83 mL, 12.0 mmol), 1-butyl-6-formyluracil (1.568 g, 8.0 mmol) and zinc acetate (2.90 g, 13.2 mmol) were added to a boiling mixture of acetic acid (90.0 mL) and nitrobenzene (60.0 mL). After 10 min. 4-*tert*-butylbenzaldehyde (0.652 g, 0.67 mL, 4.0 mmol) was added to the reaction mixture and reflux continued for 10h. A 22.4% overall yield of the mixture of porphyrins was detected

spectroscopically in the reaction mixture. The solvent was removed under vacuum. The resulting solid was purified by chromatography using a solvent gradient (isolated yield, % yield based on starting pyrrole): starting with hexane **I** (0.075 g, 2.37%), then chloroform **VIII** (0.225 g, 6.44%), then chloroform / ethyl acetate (1:1) **IX** (0.08 g, 2.21%), and **X** (0.10 g, 2.76%), and ethyl acetate **XI** (0.02 g, 0.51%), and **XII** (5 mg, 0.12%) to get the four uracyl / phenyl porphyrins. A second column using a 15% v/v dioxane / chloroform solution as eluent can be used to separate **IX, X,** and their rotameric forms. An ~18 %, 0.5 g, isolated yield is obtained for the collection of porphyrins with relative yields of **I** 15%, **VIII** 45%, **IX** 15%, **X** 20%, **XI** 4%, **XII** 1%. Typically the tetra-substituted derivatives are not isolated as they can be made directly.

5-(1'-Butyl-6'-uracyl)-10,15,20-tris(4-*tert*-butylphenyl)porphyrin (VIII). ^{1}H NMR ($CDCl_3$) [500 MHz NMR] δ 9.11, 9.05 (dd, 4H, J = 4.5 Hz), 8.92 (s, 4H), 8.81 (s, 1H), 8.12~8.22, 7.81~7.84 (m, 12H), 6.60 (s, 1H), 3.47 (t, 2H, J = 8.0 Hz), 1.20 (m, 2H), 0.41(m, 2H), 0.08(t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 162.5, 156.9, 151.6, 151.7, 139.4, 135.1, 129.2~132.6, 124.5, 124.3, 123.56, 122.16, 110.31, 106.81, 47.62, 35.74, 32.48, 31.82, 19.94, 13.65; MS (ESI) m/z (MH^+, 873).

5,15-Bis(1'-butyl-6'-uracyl)-10,20-bis(4-*tert*-butylphenyl)porphyrinatto(Zn)(II) (IX). ^{1}H NMR (DMSO-d_6): **(IXa)** αβ rotamer ($CDCl_3$) 11.84 (s, 4H), 9.32, 8.83 (dd, 8H, J = 4.8 Hz), 8.08, 7.81 (2d, 8H, J = 8.2 Hz), 6.21 (s, 2H), 3.20~3.32 (m, 4H), 1.56 (s, 18H), 1.05~1.10 (m, 4H) 0.21~0.23 (m, 4H), -0.20 (t, 6H, J = 7.33 Hz); MS (ESI) m/z (MH^+, 907).

(IXb) αα rotamer ($CDCl_3$) 11.84(s, 4H), 9.32, 8.82 (dd, 8H, J = 4.76), 8.09, 7.77 (2d, 8H, J = 7.3 Hz), 6.23 (s, 2H), 3.21~3.34 (m, 4H), 1.54 (s, 18H), 1.03~1.08 (m, 4H) 0.31~0.35 (m, 4H), -0.11 (t, 6H, J = 7.32); MS (ESI) m/z (MH^+, 907).

5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-*tert*-butylphenyl)porphyrinatto(Zn)(II) (X). ^1H NMR (DMSO-d_6) 11.81 (s, 1H), 9.26, 8.79 (d, 4H, J = 4.8 Hz), 8.75 (s, 4H), 8.12~7.77 (m, 12H), 6.27 (s, 2H), 3.22~3.34 (m, 2H), 1.55 (s, 27H), 1.01~1.08 (m, 2H), 0.19~0.26 (m, 2H), -0.18 (t, 3H, J = 7.32 Hz); ^{13}C NMR ($CDCl_3$) δ 162.00, 156.10, 151.13, 148.42, 139.75, 135.14, 131.70~131.88, 124.21, 121.64, 121.15, 116.97, 35.68, 32.48, 25.58; MS (ESI) m/z (MH^+, 907).

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Supporting Information Available: ESI-MS, ^1H and ^{13}C NMR for key intermediates and porphyrins, table of UV-visible data for the porphyrins are presented. Experimental crystallographic details, atomic coordinates, bond lengths and angles, anisotropic thermal parameters, and schemes for unsuccessful synthetic routes. This material is available free of charge via the Internet at http://pubs.acs.org.

References 1

(1) (a) Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1304-1319. (b) Dagani, R. *Chem. & Eng. News*, **1998**, *76*, 35-46.

(2) Lindsey, J. S. *New J. Chem.* **1991**, *15*, 153-180.

(3) For reviews on reaction center models see: (a) Wasielewski, M. R. In *The Photosynthetic Reaction Center*; Deisenhofer, J.; Norris, J., Eds.; Academic Press, New York, NY, **1993**; Vol. 2, pp 465-511. (b) Gust, D.; Moore, T. A. In *The Porphyrin Handbook;* Kadish, K.; Smith, K.; Guilard, R., Eds.; Academic Press, New York, NY, **2000**; Vol. 8, pp 153-190.

(4) For examples of various types of discrete multiporphyrinic covalent arrays: (a) Lin, V. S.-Y.; DiMagno, S. G.; Therien, M. J. *Science* **1994**, *264*, 1105-1111. (b) Wagner, R. W.; Seth, J.; Yang, S. I.; Kim, D.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Org. Chem.* **1998**, *63*, 5042-5049. (c) Lindsey, J. S.; Gust, D.; Moore, T. A.; Moore, A. L.; Weghorn, S. J.; Johnson, T.E.; Lin, S.; Liddell, P. A.; Kuciauskas, D. *J. Am. Chem. Soc.* **1999**, *121*, 8604-8614. (d) Aratani, N.; Osuka, A.; Kim, Y. H.; Jeong, D. H.; Kim, D. *Angew. Chem., Int. Ed. Engl. 2000, 39*, 1458-1462. (e) Khoury, R.; Jaquinod, L.; Nurco, D. J.; Pandey, R. K.; Senge, M. O.; Smith, K. M. *Angew. Chem, Int. Ed. Engl.* **1996**, *35*, 2496-2499. (f) Burrell, A. K.; Officer, D. L. *Synlett.* **1998**, 1297-1307. (g) Osuka, A.; Yamazaki, I.; Nakano, A.; Yamazaki, T.; Nishimura, Y. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3023-3027. (h) Li, J.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 9101-9108. (i) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *J. Chem Soc. Perkin I* **1995**, 2247-2254 references therein.

(5) For examples of discrete multiporphyrinic arrays formed by hydrogen bonding: (a) Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1993**, 243-245. (b) Drain, C. M.; Russell, K. C.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1996**, 337-338 (c) Ikeda, C.; Nagahara, N.; Motegi, E.; Yoshioka, N.; Inoue, H. *Chem. Commun.* **1999**, 1759-1760. (d) Balaban, T.S.; Eichhoffer, A.; Lehn, J.-M.. *Eur. J. Org. Chem.* **2000**, 4047-4057.

(6) For examples of porphyrin hydrogen bonding in solid state networks: (a) Dahal, S.; Goldberg, I. *J. Phys. Org. Chem.* **2000**, *13*, 1-6. (b) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *J. Am. Chem. Soc.* **1997**, *119*, 8492-8502. (c) Diskin-Posner, Y.; Dahal, S.; Goldberg, I. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 1288-1291.

(7) For examples of discrete axial coordination arrays: (a) Stibrany, R. T.; Vasudevan, J.; Knapp, S.; Potenza, J. A.; Emge, T.; Schugar, H. J. *J. Am. Chem. Soc.* **1996**, *118*, 3980-3981. (b) Knapp, S.; Vasudevan, J.; Emge, T.; Arison, B. H.; Potenza, J. A.; Schugar, H. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2368-2370. (c) Sanders, J. K. M.; Bampos, N.; Mak, C. C. *Chem. Commun.* **1999**, 1086-1086. (d) Chi, X.; Guerin, A. J.; Haycock, R. A.; Hunter, C. A.; Sarson, L. D. *Chem. Commun.* **1995**, 2563-2565.

(8) For examples of axial coordination polymers or networks: (a) Fleischer, E. B.; Shachter, A. M. *Inorg. Chem.* **1991**, *30*, 3763-3769. (b) Abrahams, B. F.; Hoskins, B. F.; Robson, R. *J. Am. Chem. Soc.* **1991**, *113*, 3606-3607. (c) Kumar, R. K.; Balasubramanian, S.; Goldberg, I. *Mol. Cryst. Liq. Cryst.* **1998**, *313*, 105-114. (d) Goldberg, I. *Chem. Eur. J.* **2000**, *6*, 3863-3870.

(9) For examples of discrete arrays formed by exocyclic ligand coordination: (a) Drain, C. M.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 2313-2315. (b) Drain, C.M.;

Nifiatis, F.; Vasenko, A.; Batteas, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2344-2347. (c) Yuan, H.; Thomas, L.; Woo, L. K. *Inorg. Chem.* **1995**, *36*, 2808-2817. (d) Slone, R. V.; Hupp, J. T. *Inorg. Chem.* **1997**, *36*, 5422-5423. (e) Stang, P. J.; Fan, J.; Olenyuk, B. *Chem. Commun.* **1997**, 1453-1454. (f) Fan, J.; Whiteford, J. A.; Olenyuk, B.; Levin, M. D.; Stang, P. J.; Fleischer, E B. *J. Am. Chem. Soc.* **1999**, *121*, 2741-2752.

(10) For examples of hybrid arrays: (a) Burrell, A. K.; Jones, B. M.; Hall, S. B.; Officer, D. L.; Reid, D. C. W.; Wild, K. Y. *J. Incl. Phenom. Macrocycl. Chem.* **1999**, *35*, 185-190. (b) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469-475. (c) Anderson, S.; Anderson, H. L.; Bashall, A.; McPartin, M.; Sanders, J. K. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1096-1099. (d) Funatsu, K.; Kimura, A.; Imamura, T.; Ichimura, A.; Sasaki, Y. *Inorg. Chem.* **1997**, *36*, 1626-1653.

(11) For example: (a) Hungerford, G.; Auweraer, M. V.; Chambron, J.-C.; Heitz, V.; Sauvage, J.-P.; Pierre, J.-L.; Zurita, D. *Chem. Eur. J.* **1999**, 5(7), 2089-2100. (b) Feiters, M. C.; Fyfe, M. C. T.; Martinez-Diaz, M.-V.; Menzer, S.; Nolte, R. J. M.; Stoddart, J. F.; van Kan, P. J. M.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 8119-8120.

(12) (a) Drain, C. M.; Mauzerall, D. *Bioelectrochem. Bioenerg.* **1990**, *24*, 263-268. (b) Drain, C. M.; Mauzerall, D. *Biophys. J.* **1992**, *63*, 1544-1555. (c) Drain, C.M.; Christensen, B.; Mauzerall, D. *Proc. Natl. Acad. Sci., USA* **1989**, *86*, 6959-6962.

(13) (a) Fox, M. A.; Jones, W. E.; Watkins, D. M. *Chem. & Eng. News* **1993**, 38-48. (b) Liu, C.; Pan, H.; Fox, M. A.; Bard, A. J. *Science* **1993**, *261*, 897-899.

(14) Hayashi, T.; Miyahara, T.; Koide, N.; Kato, Y.; Masuda, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1995**, 119, 7281-7290.

(15) (a) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502-518. (b) Burrell, A. K.; Wasielewski, M. R. *J. Porph. Phthal.* **2000**, *4*, 401-406. (c) Suslick, K. S.; Rakow, N. A.; Kosal, M. E.; Chou, J.-H. *J. Porph. Phthal.* **2000**, *4*, 407-413. (d) Philp, D.; Stoddart, J. F. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1154-1196. (e) Linton, B.; Hamilton, A. D. *Chem. Rev.* **1997**, *97*, 1669-1680.

(16) (a) Lehn, J.-M. *Chem. Eur. J.* **2000**, *6*, 2097-2102. (b) Berl, V.; Krische, M. J.; Huc, I.; Lehn, J.-M.; Schmutz, M. *Chem. Eur. J.* **2000**, *6*, 1938-1946.

(17) For example: (a) Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1995**, 117, 704-714. (b) Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1993**, 115, 10418-10419. (c) The synthesis of aldehyde similar to 7 from 2,6-dihydroxyisonicotinic acid in lesser yields, and a deca substituted porphyrin with one diacetamidopyridyl group was heuristically described in: Osuka, A.; Yoneshima, R.; Shiratroi, H.; Okada, T.; Taniguchi, S.; Mataga, N. *J. Chem. Soc., Chem. Commun.* **1998**, 1567-1568. (d) Vollmer, M. S.; Wurthner, F.; Effenberger, F.; Emele, P.; Meyer, D. U.; Stumpfig, T.; Port, H.; Wolf, H. C. *Chem. Eur. J.* **1998**, 4(2), 260-269. (e) de Rege, P. J. F.; Williams, S.A.; Therien, M. J. *Science* **1995**, *269*, 1409-1413. (f) Smeets, S.; Asokan, C.V.; Motmans, F.; Dehaen, W. *J. Org. Chem.* **2000**, *65*, 5882-5885.

(18) (a) There are two different melting points reported in this reference: one for the recrystallized material and one for sublimed material, which reverted to the lower melting point on standing. Bernstein, J.; Stearns, B.; Shaw, E.; Lott, W. A. *J. Am. Chem. Soc.* **1947**, 69, 1151-1158. (b) Leffer, M. T. In *Organic Reactions*; Adams, R.; Bachmann, W. E.; Fieser, L. E.; Johnson, J. R. Snyder, H. R., Eds.; John Wiley and Sons, Inc.: New York, NY, 1941; Vol. 1, pp 91-104. (c) Shreve, R. N.; Riechers, E. H.; Rubenkoenig, H.;

Goodman, A. H. *Ind. Eng. Chem.* **1940**, *32*, 173-178. (d) 2,6-diamino-4-isoropylpyridine is made in 53% using 4-isopropylpyridine and sodium amide in tetralin K. K. Kogyo, Japanese Patent: Kokai. Tokyo Koho 80 76, 861, 10, Jun. 1980. (CA 93-204,467n).

(19) Adams, R.; Miyano, S. *J. Am. Chem. Soc.* **1954**, *76*, 2785-2786.

(20) Fenlon, E. E.; Murray, T. J.; Baloga, M. H.; Zimmerman, S. C. *J. Org. Chem.* **1993**, *58*, 6625-6628.

(21) (a) Brossmer, R.; Ziegler, D. *Tetrahedron Lett.* **1966**, 5253-5256. (b) Zee-Cheng, K.-Y.; Cheng, C. C. *J. Heterocycl. Chem.* **1967**, 4(1) 163-165. (c) Demuynck, M.; DeClercq, P.; Vandewalle, M. *J. Org. Chem.* **1979**, *26*, 4863-4866.

(22) (a) Botta, M.; DeAngelis, F.; Corelli, F.; Menichincheri, M.; Nicoletti, R.; Marongiu, M. E.; Pani, A.; Colla, P. L. *Arch. Pharm.* (Weinheim), **1991**, 324, 203-207. (b) Demuynck, m; DeClercq, P.; Van de Walle, M. *J. Org. Chem.* **1979**, 44, 4683-4866. (c) Adams, L. L.; Luzzio,F. A. *J. Org. Chem.* **1989**, *54*, 5387-5390.

(23) Brown, D. T.; Eisinger, J.; Leonard, N. J. *J. Am. Chem. Soc.* **1968**, 90, 7302-7306.

(24) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476-480.

(25) (a) Little, R. G.; Anton, J. A.; Loach, P. A.; Ibers, J. A. *J. Heterocycl. Chem.* **1975**, *12*, 343-349. (b) Walker, F. A.; Balke, V. L.; McDermott, G. A. *Inorg. Chem.* **1982**, *21*, 3342-3348. (c) Milgrom, L. R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1483-1487. (d) Johnstone, R. A. W.; Nunes, M. L. P. G.; Pereira, M. M.; Gonsalves, A. M. d'A. R.; Serra, A. C. *Heterocycles* **1996**, *43*, 1423-1436. (e) Drain, C. M.; Gong, X. *Chem. Commun.* **1997**, 2117-2118.

(26) (a) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827-836. (b) Gryko, D.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 2249-2252.

(c) Rao, P. D.; Dhanalekshmi, S.; Littler, B. J.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 7323-7344.

(27) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1982**, *104*, 4500-4502.

(28) Lindsey, J. S. In *The Porphyrin Handbook*; Kadish, K.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 1, pp 45-118 and references therein.

(29) (a) Beijer, F. H.; Sijbesma, R. P.; Vekemans, J. A. J. M.; Meijer, E. W.; Kooijman, H.; Spek, A. L. *J. Org. Chem.* **1996**, *61*, 6371 – 6380. (b) Beijer, F.H.; Sijbesma, R.P.; Kooijman, H.; Spek, A.L.; Meijer, E.W. *J. Am. Chem. Soc.* **2000**, *120*, 6761-6769. (c) Beijer, F.H.; Kooijman, H.; Spek, A. H.; Sijbesma, R.P.; Meijer, E.W. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 75-78. (d) Ercolani, G. *J. Phys. Chem.*. **1998**, *91*, 5699-5703. (e) Ercolani, G. *Chem. Commun.* **2001**, June advanced web addition. Note that a ΔG of – 7 to -12 kJ mol^{-1} corresponds to 2.8 to 4.9 k_BT, thus dynamic processes are expected at room temperature. Though common practice, equilibrium constants for weakly H-bonding systems determined by NMR data are probably internally comparable, but should be treated with caution unless the dynamics of the system(s) are specifically addressed. Theoretical treatments of equilibrium constants based on simple dimer interactions to predict product distributions in larger systems that neglect cooperativity[29d,29e] –especially in aromatic systems such as these – should also be used with caution.

(30) (a) Drain, C. M.; Gentemann, S.; Roberts, J. A.; Nelson, N. Y.; Medforth, C. J.; Jia, S.; Simpson, M. C.; Smith, K. M.; Fajer, J.; Shelnutt, J. A.; Holten, D. *J. Am. Chem. Soc.* 1998, *120*, 3781-3791. (b) Drain, C. M.; Kirmaier, C.; Medforth, C. J.; Nurco, D. J.; Smith, K. M.; Holten, D. *J. Phys. Chem.* 1996, *100*, 11984-11993.

(31) Shelnutt, J. A.; Song, X.-Z.; Ma, J. G.; Jia, S.-L.; Jentzen, W.; Medforth, C. J. *Chem. Soc. Rev.* **1998**, *27*, 31-41.

(32) Drain, C.M.; Shi, X.; Milic, T; Nifiatis, F. *Chem. Commun.* **2001**, 287-288.

(33) (a) DeGrado, W. F.; Lear, J. D. *J. Am. Chem. Soc.* **1985**, *107*, 7684 – 7689. (b) Deranleau, D. A.; *J. Am. Chem. Soc.* **1969**, *91*, 4044 – 4054. (c) Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 3910 - 3915.

Appendix 1

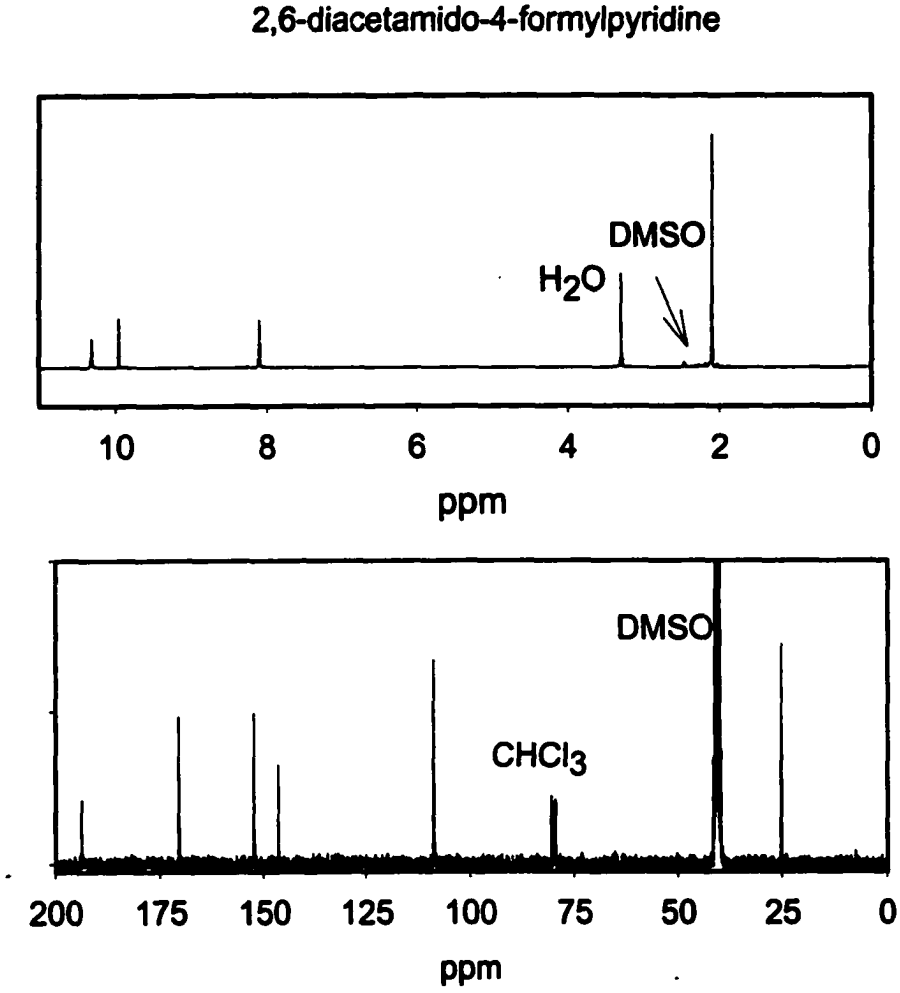

Figure A1-1 Compound 7 NMR

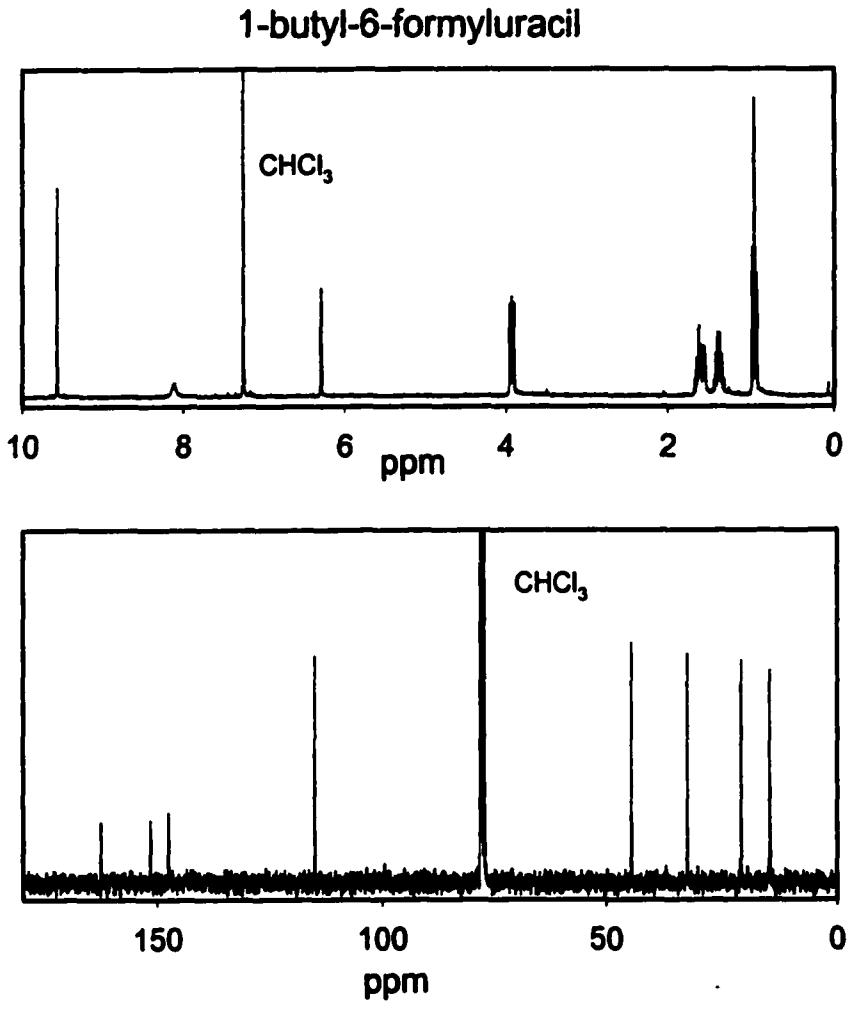

Figure A1-2 Compound 11 NMR

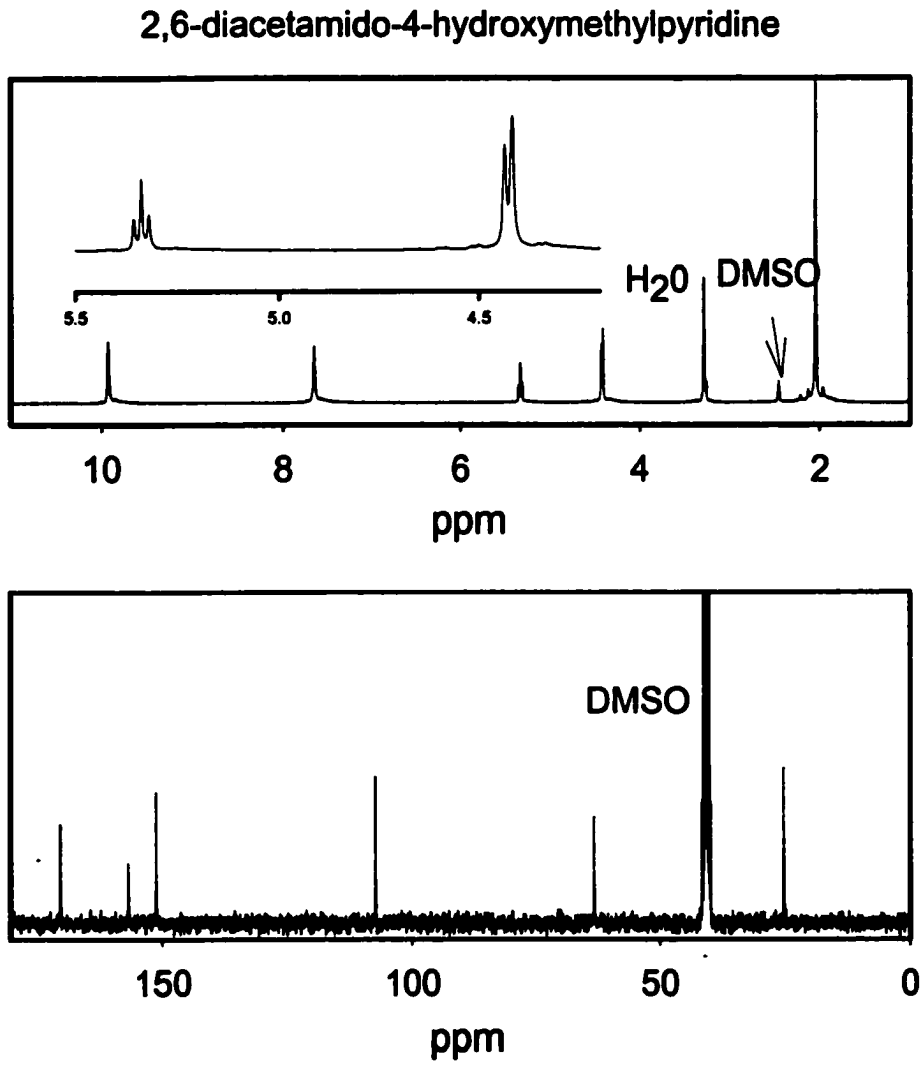

Figure A1-3 Compound 6 NMR

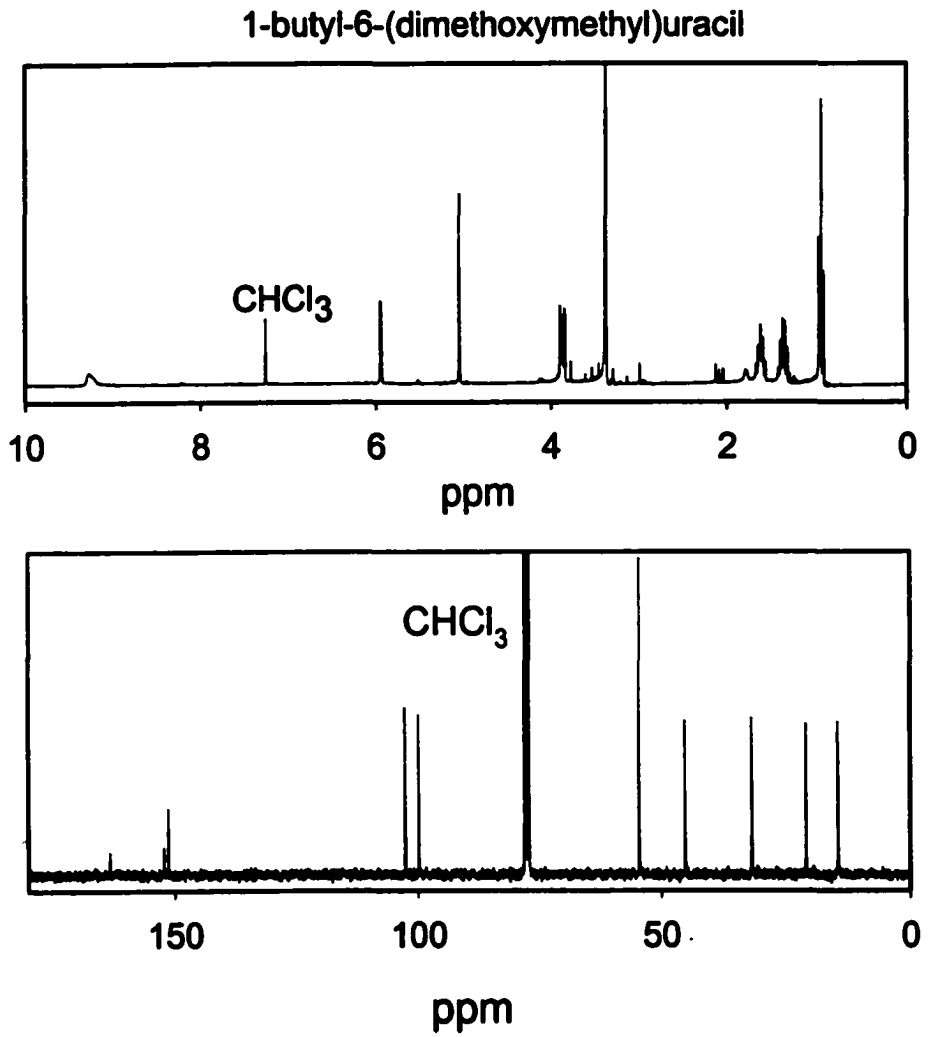

Figure A1-4 Compound 10 NMR

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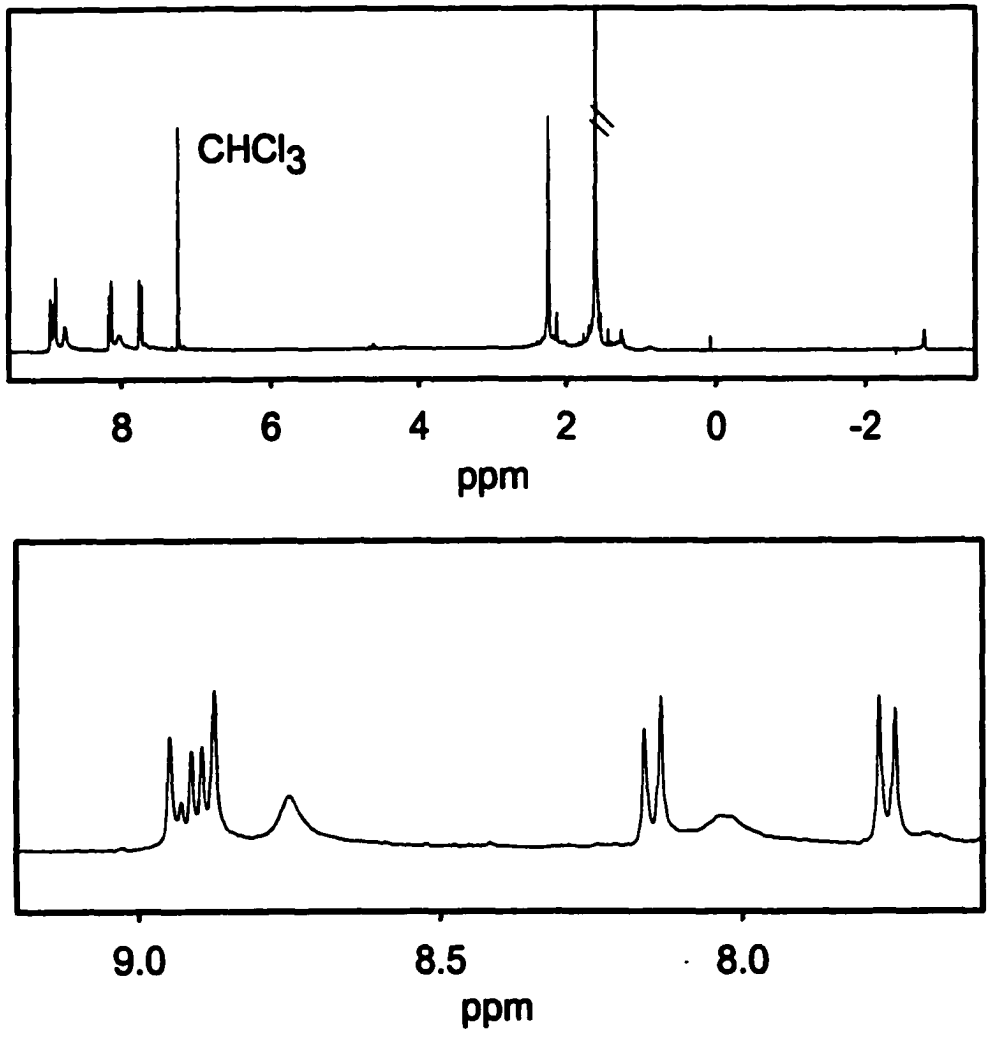


Figure A1-5 Compound IV NMR

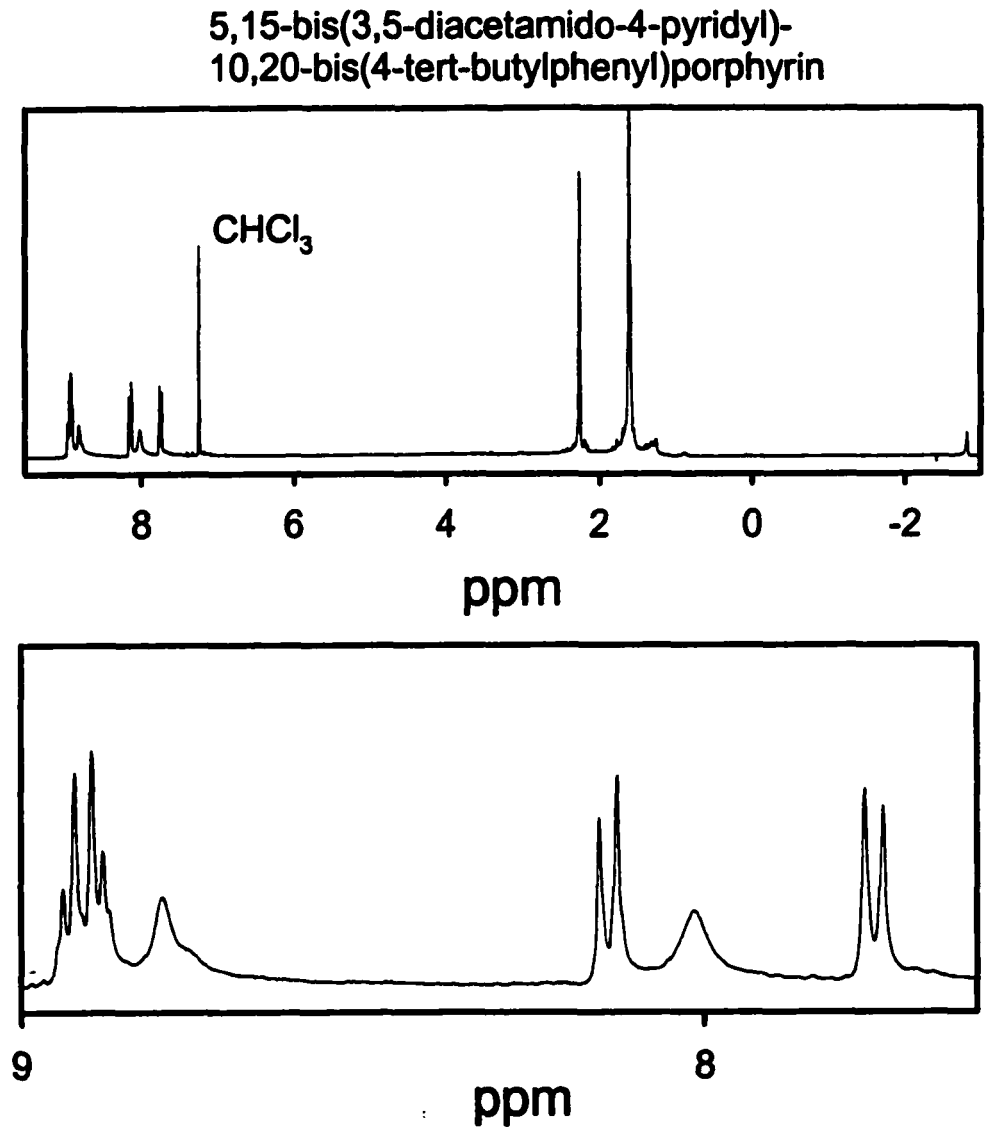


Figure A1-6 Compound III NMR

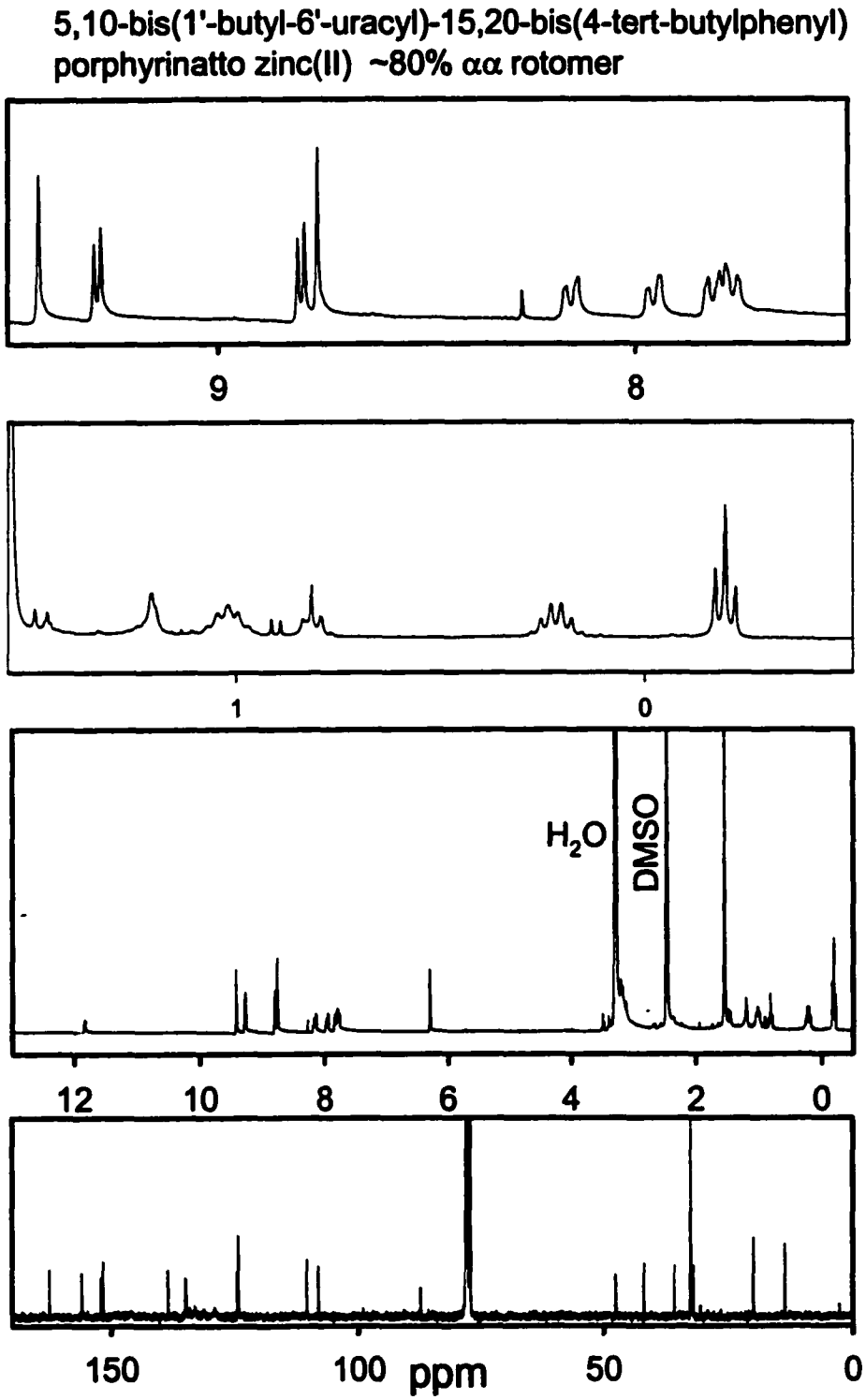


Figure A1-7 Compound X NMR

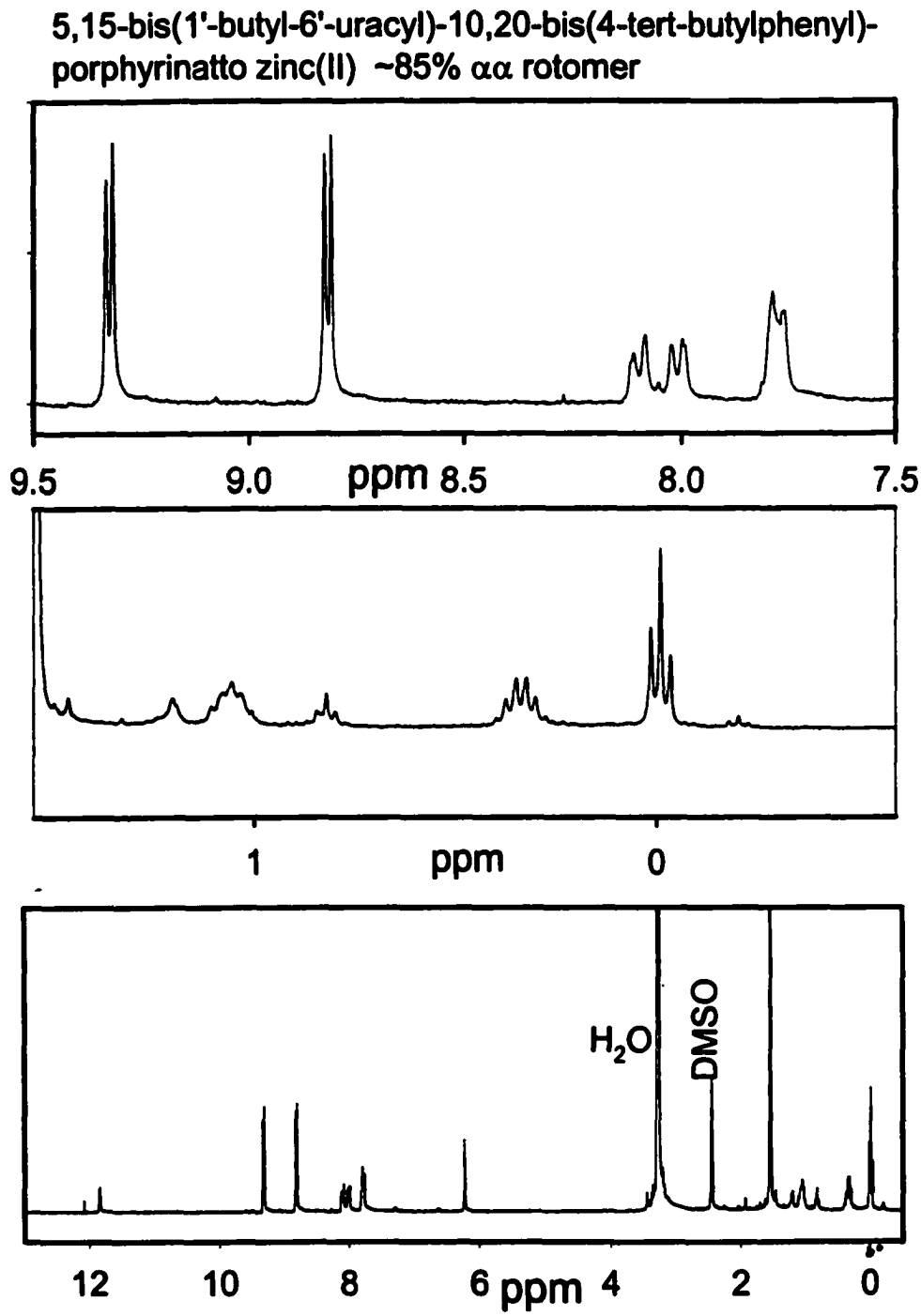


Figure A1-8 Compound IX NMR

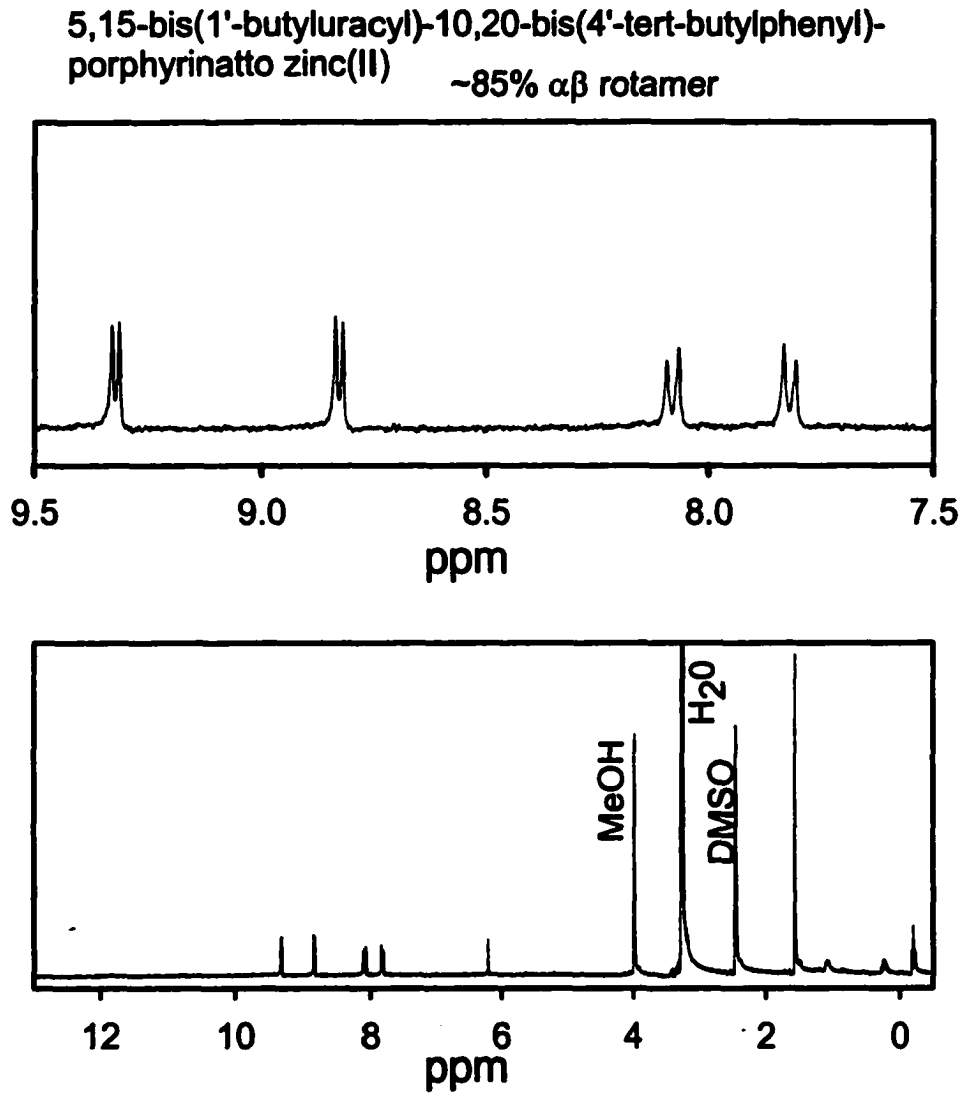


Figure A1-9 Compound IX NMR

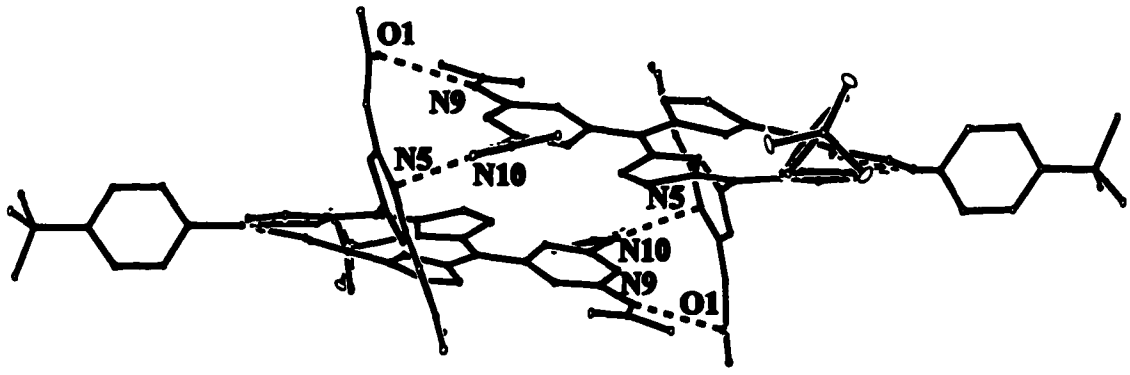


Figure A1-10 *The basic building block, edge-on.*

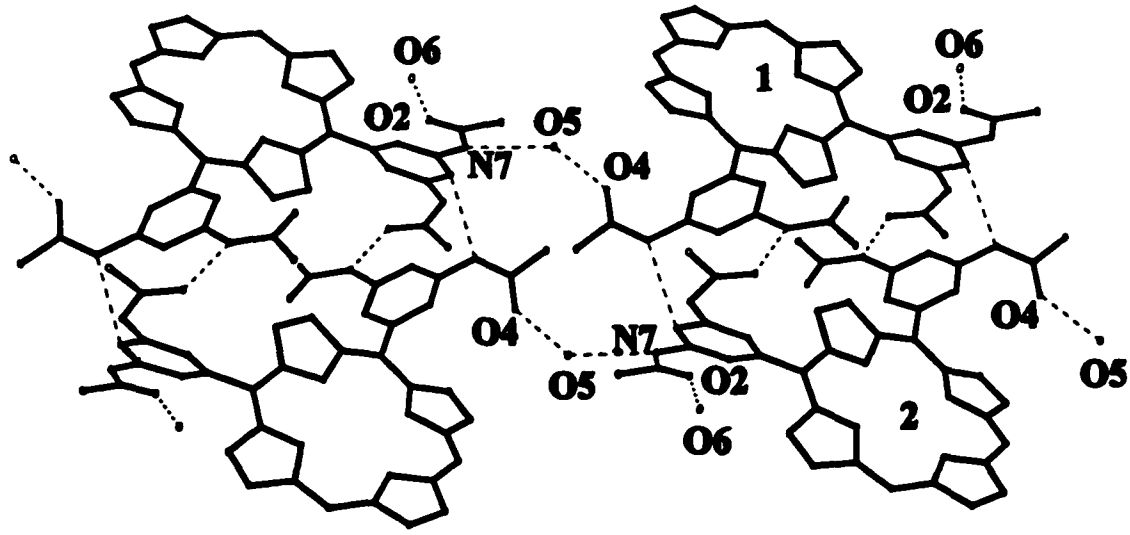


Figure A1-11 *Now consider the water molecules of crystallization, O5 and O6. O5 hydrogen bonds to O4 and N7, cross-linking the basic building block to another set of dimers.*

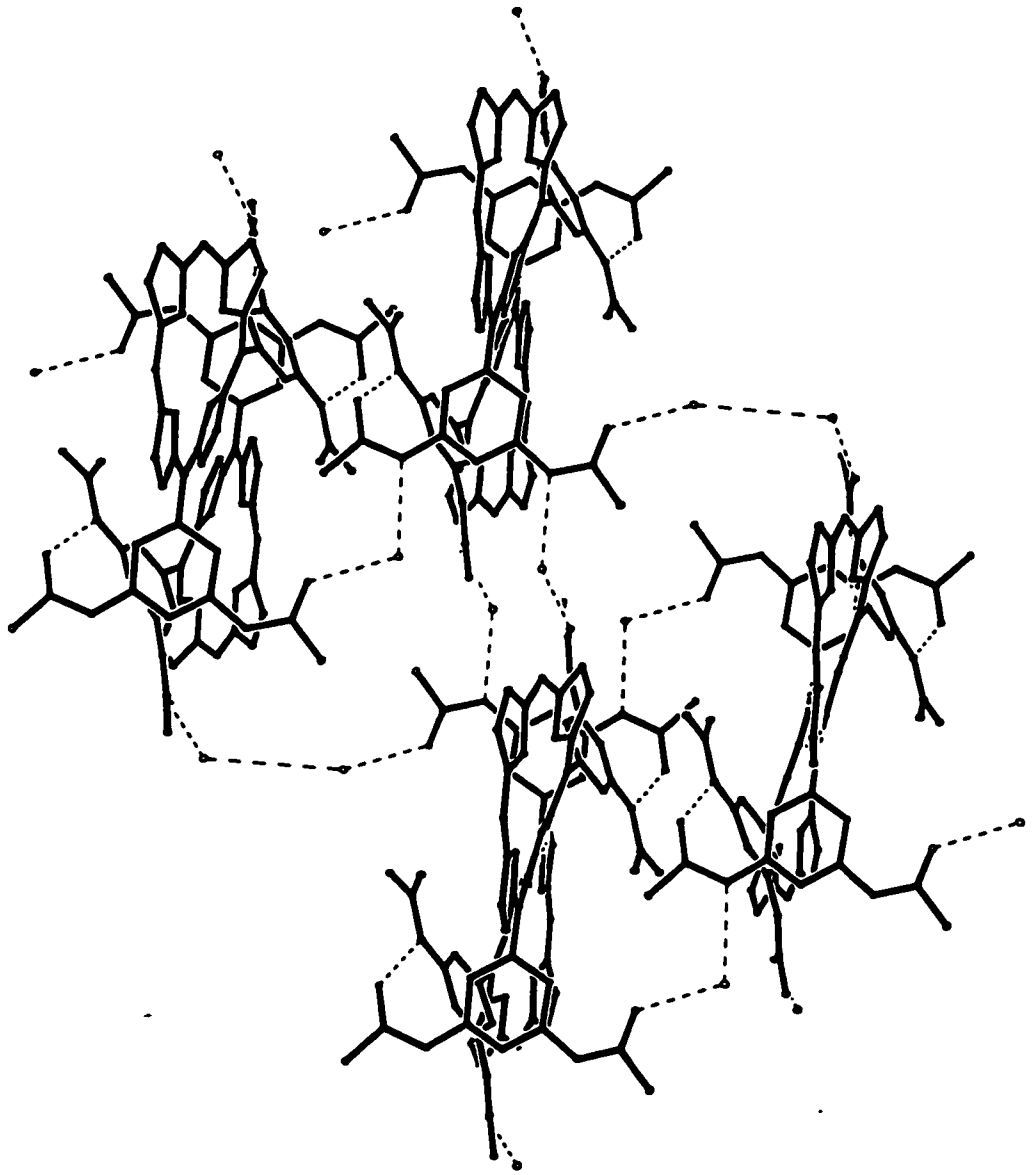


Figure A1-12 *In addition, O6 hydrogen bonds to O2 and N6 for another cross link.*

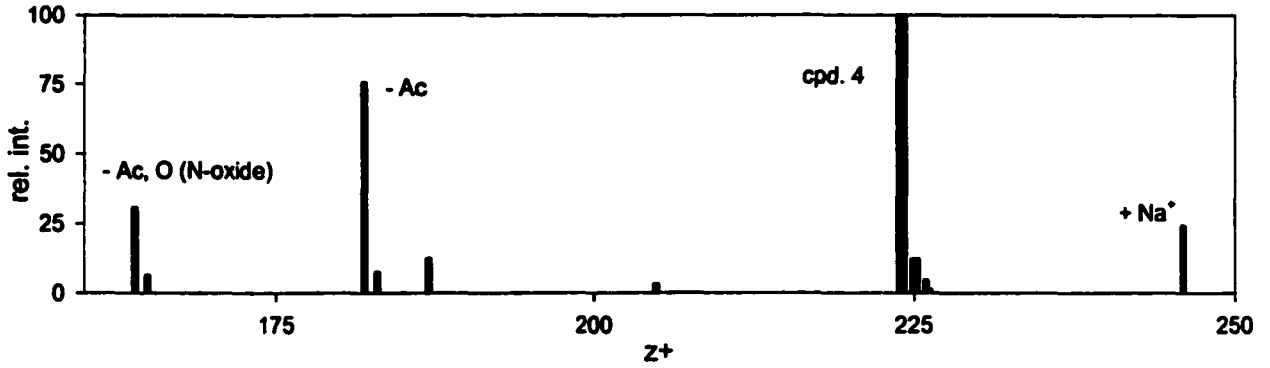


Figure A1-13 Compound 4 ESI-MS

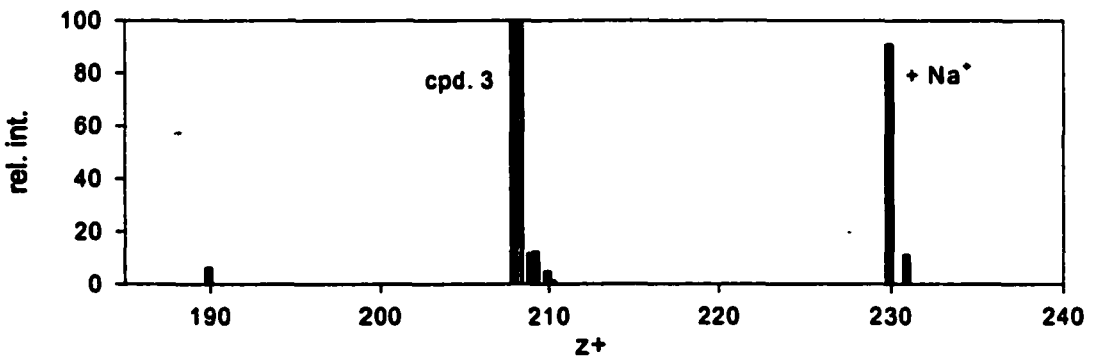


Figure A1-14 Compound 3 ESI-MS

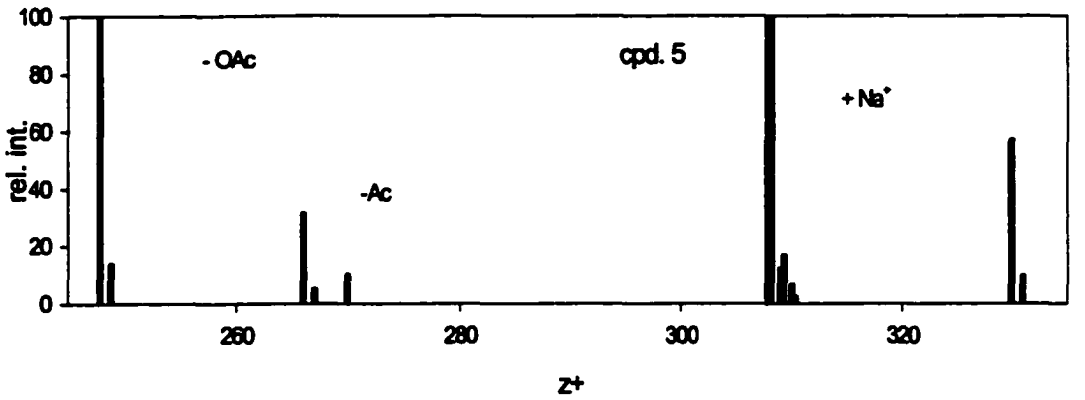


Figure A1-15 Compound 5 ESI-MS

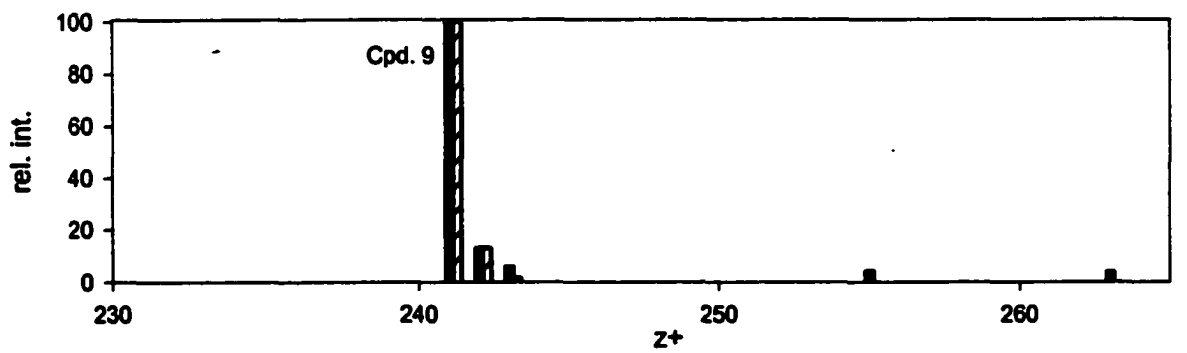


Figure A1-16 Compound 9 ESI-MS

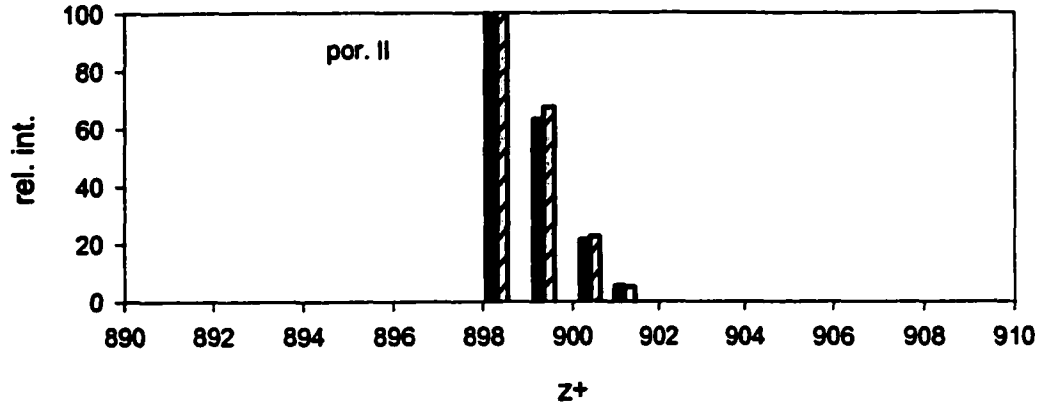


Figure A1-17 Compound II ESI-MS

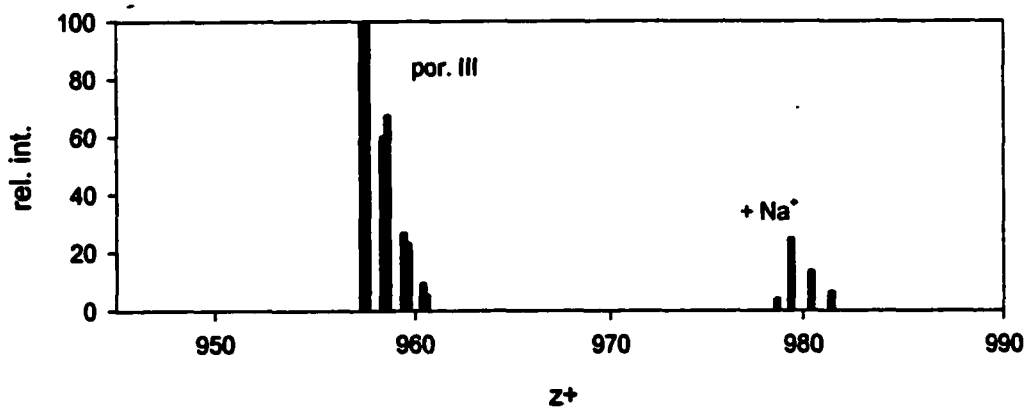


Figure A1-18 Compound III ESI-MS

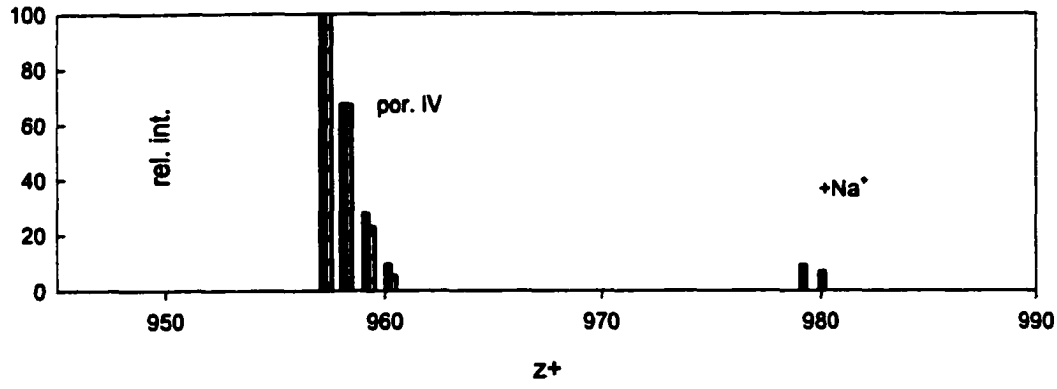


Figure A1-19 Compound IV ESI-MS

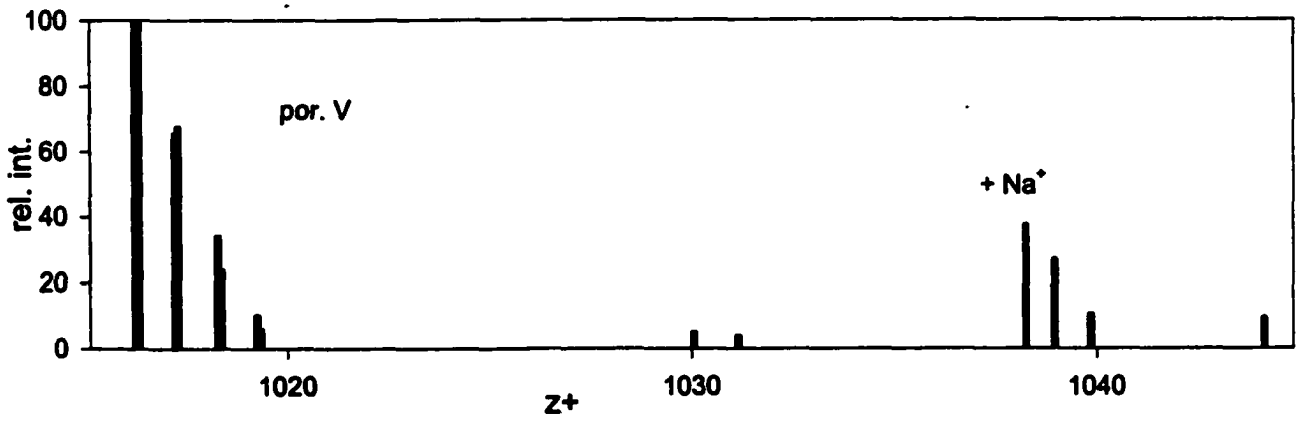


Figure A1-20 Compound V ESI-MS

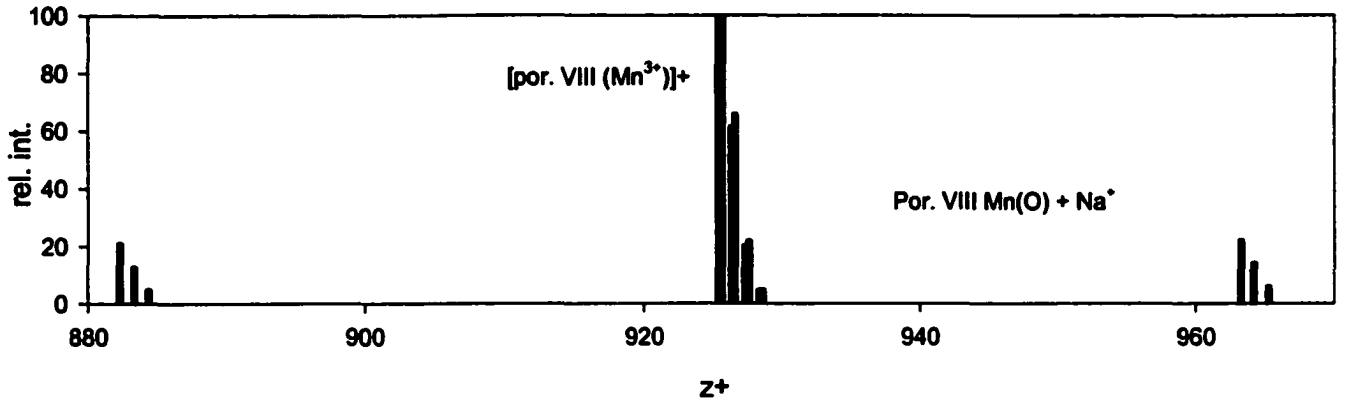


Figure A1-21 Compound VIII ESI-MS

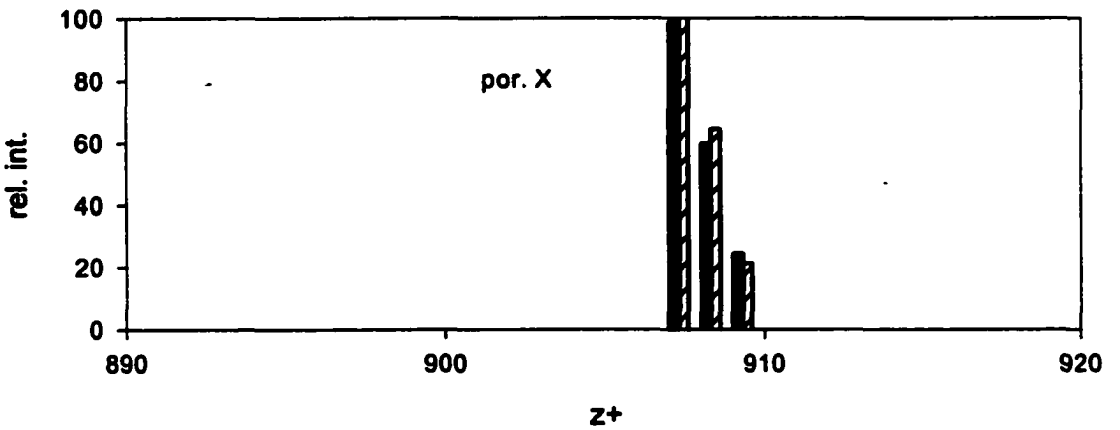


Figure A1-22 Compound X ESI-MS

Low resolution ESI-MS for selected compounds. The gray bars represent the calculated spectra using the SIS exact mass calculator at: http://www.sisweb.com/cgi-bin/mass11.pl

Appendix 2

Table A2-1 Experimental Crystallographic Details

formula	$C_{58}H_{61}N_{10}O_4 \cdot 2.5(H_2O)$
crystallized from	ethyl acetate/hexane
fw	1002.17
space group	P -1 (S.G. #2)
Z	2
T (K)	107
a (Å)	10.373(1)
b (Å)	16.090(3)
c (Å)	17.225(3)
α (deg)	67.23(2)
β (deg)	76.38(1)
γ (deg)	79.99(1)
V (Å^3)	2565.3(7)
crystal color	Red
crystal shape	very thin plate
density calcd (g/cm^3)	1.297
dimensions (mm)	0.175x0.150x0.006
μ (mm^{-1})	0.584
λ (Å)	0.9385
instrument	MAR345 imaging plate detector[1]
no of reflns measd	26597
no of reflns unique	4554
no of reflns with I>2σ(I)	3875
2θ range (deg)	2.90-31.02
data measd	±h±k±l
data reduction	DENZO/SCALEPACK[2]
absorption correction	None
structure solution/refinement	SHELXS-86/SHELXL93[3]
number of parameters refined	713

R1; wR2 (I>2σ(I))	0.070;0.190
R1; wR2 (all data)	0.081;0.201
GOF	1.041

[1]Rotation method with MAR345 imaging plate detector; 90 rotations of 2° in phi for 300 seconds with the detector at 90 millimeters from the sample; 36 rotations of 5° for 30 seconds with the detector at 120 millimeters from the sample (for scaling and better estimation of overloaded reflections).

[2]Data were indexed with DENZO and merged with SCALEPACK. (Otwinowski, Z., Minor, W. "Processing of X-ray Diffraction Data Collected in Oscillation Mode", Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, p. 307-326, C. W. Carter, Jr. & R. M. Sweet, Eds, Academic Press).

3Sheldrick, G.M., SHELXTL. Version 5.0. Siemens Analytical X-ray Instruments Inc. Madison, WI, USA, 1995.

Table A2-2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for $C_{58}H_{61}N_{10}O_4 \cdot 2.5(H_2O)$. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.*

	x	y	z	U(eq)
N1	5373(5)	6350(3)	-9404(2)	49(1)
N2	6227(5)	5554(3)	-7735(2)	48(1)
N3	8250(5)	4428(3)	-8412(2)	51(1)
N4	7305(5)	5123(3)	-10036(2)	51(1)
C1	5190(6)	6697(4)	-10244(3)	53(2)
C2	4230(7)	7479(4)	-10363(3)	59(2)
C3	3829(7)	7585(4)	-9600(3)	59(2)
C4	4528(6)	6879(3)	-8999(3)	49(2)
C5	4381(6)	6744(3)	-8128(3)	48(2)
C6	5118(6)	6091(3)	-7543(3)	46(2)
C7	4850(6)	5874(3)	-6631(3)	50(2)

	C8	5807(6)	5235(4)	-6301(3)	
50(2)					
	C9	6713(6)	5041(3)	-6998(3)	47(2)
	C10	7894(6)	4452(3)	-6956(3)	46(2)
	C11	8651(6)	4217(3)	-7646(3)	46(2)
	C12	9875(6)	3634(4)	-7631(3)	55(2)
	C13	10169(6)	3452(4)	-8358(3)	54(2)
	C14	9151(6)	3932(3)	-8841(3)	51(2)
	C15	9034(6)	3872(3)	-9616(3)	49(2)
	C16	8176(6)	4424(4)	-10155(3)	50(2)
	C17	8086(7)	4395(4)	-10962(3)	58(2)
	C18	7191(7)	5082(4)	-11310(3)	57(2)
	C19	6707(6)	5548(4)	-10729(3)	50(2)
	C20	5802(6)	6324(4)	-10869(3)	49(2)
	C21	3336(7)	7348(3)	-7793(3)	47(2)
	C22	2012(7)	7312(3)	-7753(3)	47(2)
	C23	1077(7)	7901(4)	-7446(3)	48(2)
	C24	2720(8)	8591(3)	-7308(3)	49(2)
	C25	3731(6)	7996(3)	-7544(3)	45(2)
	N5	1418(6)	8545(3)	-7241(2)	49(1)
	N6	-291(6)	7882(3)	-7335(3)	53(1)
	C26	-927(7)	7123(4)	-7154(3)	55(2)
	C27	-2428(7)	7256(4)	-6975(4)	68(2)
	O1	-302(4)	6387(3)	-7138(2)	59(1)
	N7	2973(6)	9334(3)	-7131(3)	52(1)
	C28	4160(9)	9558(4)	-7108(3)	59(2)
	C29	4110(8)	10443(4)	-6978(4)	77(2)
	O2	5223(5)	9092(3)	-7176(3)	69(1)
	C30	8346(6)	4039(3)	-6117(3)	49(2)
	C31	8368(6)	4548(4)	-5633(3)	50(2)
	C32	8738(6)	4122(3)	-4841(3)	49(2)
	C33	9178(6)	2765(4)	-5019(3)	52(2)
	C34	8735(6)	3110(4)	-5786(3)	50(2)
	N8	9155(5)	3234(3)	-4524(2)	48(1)
	N9	8712(5)	4559(3)	-4277(2)	51(1)
	C35	8135(7)	5404(4)	-4329(3)	56(2)
	C36	8170(7)	5653(4)	-3586(3)	65(2)
	O3	7630(5)	5922(3)	-4933(2)	72(1)
	N10	9685(5)	1844(3)	-4658(3)	53(1)
	C37	10389(6)	1328(4)	-5099(4)	55(2)
	C38	10933(7)	413(4)	-4533(4)	68(2)
	O4	10588(4)	1579(3)	-5879(2)	66(1)
	C39	9886(7)	3111(4)	-9832(3)	51(2)
	C44A	10916(12)	3220(6)	-10484(6)	61(3)
	C44B	11353(29)	3095(16)	-10045(17)	47(7)
	C43A	11742(11)	2479(6)	-10600(6)	66(3)
	C43B	12148(33)	2348(21)	-10177(17)	60(9)
	C42	11519(8)	1604(4)	-10086(4)	57(2)
	C41A	10370(10)	1485(5)	-9402(5)	65(3)
	C41B	10213(35)	1696(15)	-10100(13)	63(8)
	C40A	9584(9)	2218(5)	-9281(5)	63(3)
	C40B	9399(24)	2450(15)	-9952(14)	47(6)
	C45	12394(8)	763(4)	-10161(4)	68(2)
	C46	12561(13)	116(6)	-9322(5)	183(7)
	C47	13666(11)	994(6)	-10744(7)	167(6)
	C48	11813(13)	328(8)	-10606(10)	204(7)
	C49	5498(7)	6779(4)	-11748(3)	49(2)
	C50	6486(7)	7200(4)	-12415(3)	54(2)
	C51	6293(7)	7595(4)	-13256(3)	55(2)

C52	5104(7)	7578(4)	-13469(3)	53(2)
C53	4114(7)	7170(4)	-12809(4)	64(2)
C54	4305(7)	6772(4)	-11956(3)	63(2)
C55	4864(7)	7994(4)	-14399(3)	60(2)
C56	6068(7)	8488(4)	-15012(3)	71(2)
C57	4692(7)	7231(4)	-14676(3)	66(2)
C58	3639(7)	8674(4)	-14458(4)	75(2)
O5	10988(5)	957(3)	-7245(3)	89(2)
O6	7811(5)	9467(3)	-7197(3)	91(2)
O7	8439(24)	1267(13)	-7838(14)	235(11)

*One of the t-butyl substituted phenyl rings is disordered over 2 positions. The 75% component consists of C39, C40A, C41A, C42, C43A, C44A and the associated hydrogens. The 25% component consists of C39, C40B, C41B, C42, C43B, C44B and the associated hydrogens.

Table A2-3 Complete bond lengths (Å) and angles (°) for $C_{58}H_{61}N_{10}O_4 \cdot 2.5(H_2O)$.

N1-C4	1.376(6)
N1-C1	1.382(6)
N2-C6	1.371(6)
N2-C9	1.376(6)
N3-C11	1.375(6)
N3-C14	1.389(6)
N4-C19	1.359(6)
N4-C16	1.364(6)
C1-C20	1.403(7)
C1-C2	1.441(7)
C2-C3	1.349(7)
C3-C4	1.430(7)
C4-C5	1.404(6)
C5-C6	1.402(7)
C5-C21	1.492(7)
C6-C7	1.439(6)
C7-C8	1.350(7)
C8-C9	1.441(7)
C9-C10	1.410(7)
C10-C11	1.407(7)
C10-C30	1.490(7)
C11-C12	1.440(7)
C12-C13	1.348(7)
C13-C14	1.428(7)
C14-C15	1.408(7)
C15-C16	1.386(7)
C15-C39	1.497(7)
C16-C17	1.434(7)
C17-C18	1.355(8)
C18-C19	1.424(7)

C19-C20	1.402(7)
C20-C49	1.488(7)
C21-C22	1.370(8)
C21-C25	1.419(8)
C22-C23	1.394(7)
C23-N5	1.340(7)
C23-N6	1.390(8)
C24-N5	1.341(7)
C24-C25	1.390(8)
C24-N7	1.421(7)
N6-C26	1.383(8)
C26-O1	1.241(7)
C26-C27	1.508(9)
N7-C28	1.356(8)
C28-O2	1.229(7)
C28-C29	1.515(8)
C30-C31	1.381(7)
C30-C34	1.401(7)
C31-C32	1.382(7)
C32-N8	1.348(6)
C32-N9	1.395(6)
C33-N8	1.334(6)
C33-C34	1.376(7)
C33-N10	1.424(6)
N9-C35	1.366(6)
C35-O3	1.219(6)
C35-C36	1.492(7)
N10-C37	1.347(6)
C37-O4	1.220(6)
C37-C38	1.515(7)
C39-C44A	1.334(11)
C39-C40B	1.35(2)
C39-C40A	1.423(10)
C39-C44B	1.48(3)
C44A-C43A	1.395(12)
C44B-C43B	1.40(3)
C43A-C42	1.367(11)
C43B-C42	1.40(3)
C42-C41B	1.34(3)
C42-C41A	1.445(11)
C42-C45	1.525(8)
C41A-C40A	1.369(10)
C41B-C40B	1.43(3)
C45-C46	1.447(9)
C45-C47	1.464(12)
C45-C48	1.490(11)
C49-C54	1.369(9)
C49-C50	1.383(8)
C50-C51	1.388(7)
C51-C52	1.374(8)
C52-C53	1.373(9)
C52-C55	1.541(7)
C53-C54	1.406(8)
C55-C58	1.520(8)
C55-C57	1.528(8)
C55-C56	1.543(9)

C4-N1-C1	106.5(4)
C6-N2-C9	109.1(4)

C11-N3-C14	105.9(4)
C19-N4-C16	109.3(4)
N1-C1-C20	125.2(4)
N1-C1-C2	109.1(4)
C20-C1-C2	125.6(4)
C3-C2-C1	107.3(4)
C2-C3-C4	107.6(5)
N1-C4-C5	124.9(4)
N1-C4-C3	109.6(4)
C5-C4-C3	125.5(5)
C6-C5-C4	126.2(5)
C6-C5-C21	117.0(4)
C4-C5-C21	116.8(4)
N2-C6-C5	126.3(4)
N2-C6-C7	107.7(4)
C5-C6-C7	126.0(5)
C8-C7-C6	107.8(5)
C7-C8-C9	108.1(4)
N2-C9-C10	125.2(4)
N2-C9-C8	107.2(5)
C10-C9-C8	127.6(4)
C11-C10-C9	124.4(4)
C11-C10-C30	118.2(5)
C9-C10-C30	117.4(4)
N3-C11-C10	124.5(5)
N3-C11-C12	109.3(4)
C10-C11-C12	125.8(4)
C13-C12-C11	107.8(5)
C12-C13-C14	107.0(5)
N3-C14-C15	124.9(5)
N3-C14-C13	110.0(4)
C15-C14-C13	125.0(5)
C16-C15-C14	125.7(5)
C16-C15-C39	119.0(4)
C14-C15-C39	115.2(4)
N4-C16-C15	126.3(4)
N4-C16-C17	107.3(4)
C15-C16-C17	126.3(5)
C18-C17-C16	107.6(4)
C17-C18-C19	107.7(4)
N4-C19-C20	126.6(4)
N4-C19-C18	108.0(4)
C20-C19-C18	125.4(5)
C19-C20-C1	124.4(4)
C19-C20-C49	116.8(4)
C1-C20-C49	118.8(5)
C22-C21-C25	119.6(5)
C22-C21-C5	121.2(5)
C25-C21-C5	119.1(6)
C21-C22-C23	118.9(6)
N5-C23-N6	113.8(5)
N5-C23-C22	122.9(7)
N6-C23-C22	123.3(6)
N5-C24-C25	124.4(5)
N5-C24-N7	112.7(5)
C25-C24-N7	122.8(7)
C24-C25-C21	116.4(6)
C23-N5-C24	117.5(5)
C26-N6-C23	125.2(5)

O1-C26-N6	122.1(6)
O1-C26-C27	122.8(6)
N6-C26-C27	115.1(6)
C28-N7-C24	128.2(5)
O2-C28-N7	124.3(6)
O2-C28-C29	120.4(7)
N7-C28-C29	115.3(6)
C31-C30-C34	118.0(4)
C31-C30-C10	121.6(4)
C34-C30-C10	120.4(4)
C30-C31-C32	119.2(5)
N8-C32-C31	123.6(4)
N8-C32-N9	112.4(4)
C31-C32-N9	123.9(4)
N8-C33-C34	124.7(5)
N8-C33-N10	112.7(4)
C34-C33-N10	122.5(4)
C33-C34-C30	118.2(4)
C33-N8-C32	116.0(4)
C35-N9-C32	127.4(4)
O3-C35-N9	123.2(4)
O3-C35-C36	122.0(5)
N9-C35-C36	114.8(5)
C37-N10-C33	126.0(4)
O4-C37-N10	123.3(5)
O4-C37-C38	123.2(5)
N10-C37-C38	113.5(5)
C44A-C39-C40A	118.9(6)
C40B-C39-C44B	114.2(14)
C44A-C39-C15	124.3(6)
C40B-C39-C15	123.8(11)
C40A-C39-C15	116.7(6)
C44B-C39-C15	121.5(10)
C39-C44A-C43A	121.2(8)
C43B-C44B-C39	121(2)
C42-C43A-C44A	122.7(9)
C44B-C43B-C42	118(3)
C41B-C42-C43B	120(2)
C43A-C42-C41A	116.1(6)
C41B-C42-C45	120.6(11)
C43A-C42-C45	125.6(7)
C43B-C42-C45	118.1(14)
C41A-C42-C45	118.3(6)
C40A-C41A-C42	120.7(8)
C42-C41B-C40B	119(2)
C41A-C40A-C39	120.3(8)
C39-C40B-C41B	123(2)
C46-C45-C47	112.7(8)
C46-C45-C48	109.3(9)
C47-C45-C48	101.0(9)
C46-C45-C42	110.5(5)
C47-C45-C42	111.7(6)
C48-C45-C42	111.3(6)
C54-C49-C50	116.8(5)
C54-C49-C20	124.0(6)
C50-C49-C20	119.1(6)
C49-C50-C51	122.2(6)
C52-C51-C50	121.2(6)
C53-C52-C51	116.9(5)

C53-C52-C55	120.4(7)
C51-C52-C55	122.6(6)
C52-C53-C54	121.9(7)
C49-C54-C53	121.0(7)
C58-C55-C57	111.1(5)
C58-C55-C52	109.9(5)
C57-C55-C52	108.6(5)
C58-C55-C56	108.4(5)
C57-C55-C56	107.9(5)
C52-C55-C56	110.9(6)

Table A2-4 Anisotropic thermal parameters (A^2x10^3) for $C_{58}H_{61}N_{10}O_4 \cdot 2.5(H_2O)$.

	U11	U22	U33	U23	U13	U12
N1	61(4)	58(3)	35(2)	-26(2)	-16(2)	12(2)
N2	61(4)	58(3)	32(2)	-26(2)	-17(2)	14(2)
N3	71(4)	54(3)	35(2)	-25(2)	-17(2)	10(2)
N4	70(4)	57(3)	34(2)	-29(2)	-19(2)	15(3)
C1	68(5)	56(3)	39(3)	-26(3)	-18(3)	18(3)
C2	76(5)	60(4)	41(3)	-23(3)	-23(3)	20(3)
C3	77(5)	61(4)	43(3)	-30(3)	-24(3)	25(3)
C4	62(5)	52(3)	39(3)	-27(3)	-17(3)	14(3)
C5	59(5)	53(3)	36(3)	-26(3)	-17(3)	15(3)
C6	57(5)	54(3)	34(3)	-28(3)	-9(3)	9(3)
C7	61(5)	56(3)	36(3)	-25(3)	-12(3)	10(3)
C8	68(5)	55(3)	31(3)	-22(2)	-14(3)	9(3)
C9	64(5)	48(3)	35(3)	-24(2)	-13(3)	4(3)
C10	53(5)	51(3)	38(3)	-23(2)	-16(3)	9(3)
C11	58(5)	51(3)	37(3)	-23(2)	-20(3)	10(3)
C12	62(5)	69(4)	44(3)	-34(3)	-22(3)	17(3)
C13	64(5)	60(4)	44(3)	-28(3)	-20(3)	17(3)
C14	71(5)	51(3)	34(3)	-23(3)	-14(3)	

9(3)					
C15	61(5)	52(3)	37(3)	-24(3)	-17(3)
14(3)					
C16	60(5)	54(3)	40(3)	-27(3)	-13(3)
10(3)					
C17	87(5)	54(3)	41(3)	-29(3)	-22(3)
15(3)					
C18	82(5)	60(4)	37(3)	-29(3)	-18(3)
11(3)					
C19	66(5)	55(3)	36(3)	-26(3)	-15(3)
9(3)					
C20	57(5)	59(3)	37(3)	-24(3)	-15(3)
4(3)					
C21	65(6)	48(3)	32(3)	-19(2)	-16(3)
11(3)					
C22	59(5)	54(3)	36(3)	-24(3)	-20(3)
10(3)					
C23	65(6)	51(3)	31(3)	-21(3)	-18(3)
13(3)					
C24	69(6)	52(3)	34(3)	-25(3)	-18(3)
8(3)					
C25	47(4)	54(3)	37(3)	-25(3)	-10(3)
10(3)					
N5	59(4)	54(3)	36(2)	-22(2)	-16(2)
11(2)					
N6	55(5)	59(3)	48(3)	-24(2)	-19(3)
10(3)					
C26	57(5)	67(4)	38(3)	-14(3)	-16(3)
0(4)					
C27	61(6)	68(4)	72(4)	-19(3)	-26(4)
5(3)					
O1	67(3)	52(2)	63(2)	-27(2)	-27(2)
13(2)					
N7	62(4)	56(3)	48(3)	-32(2)	-15(3)
8(3)					
C28	88(6)	53(4)	45(3)	-27(3)	-22(4)
11(4)					
C29	109(7)	62(4)	76(4)	-37(3)	-31(4)
2(4)					
O2	72(4)	76(3)	77(3)	-49(2)	-25(2)
9(3)					
C30	63(5)	53(3)	37(3)	-24(3)	-19(3)
16(3)					
C31	66(5)	52(3)	38(3)	-25(3)	-18(3)
13(3)					
C32	65(5)	52(3)	37(3)	-26(3)	-17(3)
12(3)					
C33	68(5)	52(3)	39(3)	-23(3)	-16(3)
13(3)					
C34	66(5)	54(3)	40(3)	-27(3)	-20(3)
13(3)					
N8	56(4)	55(3)	38(2)	-26(2)	-16(2)
13(2)					
N9	70(4)	54(3)	34(2)	-25(2)	-20(2)
16(2)					
C35	69(5)	64(4)	42(3)	-30(3)	-20(3)
16(3)					
C36	89(6)	68(4)	47(3)	-34(3)	-22(3)
16(4)					

O3	105(4)	71(3)	50(2)	-38(2)	-37(2)
34(3)					
N10	65(4)	52(3)	40(2)	-22(2)	-16(2)
18(2)					
C37	71(5)	51(3)	51(4)	-28(3)	-24(3)
19(3)					
C38	83(6)	62(4)	69(4)	-37(3)	-34(4)
26(4)					
O4	84(4)	67(3)	48(2)	-32(2)	-17(2)
21(2)					
C39	66(6)	54(4)	41(3)	-26(3)	-24(3)
12(3)					
C44A	85(9)	54(5)	38(5)	-18(4)	-2(6)
1(5)					
C44B	50(24)	54(15)	45(15)	-33(13)	-5(13)
4(12)					
C43A	89(9)	58(6)	42(5)	-23(5)	-1(5)
12(5)					
C43B	68(24)	77(21)	38(16)	-28(15)	-16(15)
13(17)					
C42	65(6)	60(4)	51(4)	-28(3)	-18(4)
10(4)					
C41A	81(8)	48(5)	62(6)	-23(4)	-12(5)
10(5)					
C41B	113(31)	61(16)	27(13)	-26(11)	-18(14)
-4(16)					
C40A	73(7)	60(6)	48(5)	-21(4)	-9(5)
17(5)					
C40B	41(18)	59(14)	44(14)	-27(12)	-13(11)
14(12)					
C45	75(6)	66(4)	57(4)	-30(3)	-9(4)
22(4)					
C46	278(15)	122(7)	62(5)	-11(5)	-15(7)
131(9)					
C47	148(11)	91(7)	188(11)	-36(7)	48(9)
41(7)					
C48	204(14)	207(12)	333(17)	-234(13)	-159(13)
122(11)					
C49	64(5)	54(3)	34(3)	-24(3)	-16(3)
13(3)					
C50	62(5)	59(4)	46(3)	-28(3)	-19(3)
11(3)					
C51	65(5)	61(4)	44(3)	-27(3)	-18(3)
14(3)					
C52	71(5)	52(3)	35(3)	-20(3)	-13(3)
13(3)					
C53	69(6)	78(4)	51(4)	-28(3)	-24(4)
7(4)					
C54	74(6)	75(4)	42(3)	-25(3)	-18(3)
6(4)					
C55	77(6)	62(4)	44(3)	-21(3)	-23(3)
12(4)					
C56	97(6)	75(4)	39(3)	-15(3)	-22(4)
-3(4)					
C57	90(6)	68(4)	47(3)	-31(3)	-29(3)
19(4)					
C58	103(6)	65(4)	59(4)	-25(3)	-42(4)
30(4)					
O5	115(5)	82(3)	75(3)	-44(3)	-11(3)

9(3)					
O6	89(4)	101(4)	97(3)	-61(3)	-25(3)
20(3)					
O7	308(28)	205(17)	287(23)	-161(18)	-169(21)
68(17)					

The form of the anisotropic displacement parameter is:

$\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$.

Table A2-5 Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for $C_{58}H_{61}N_{10}O_4 \cdot 2.5(H_2O)$.

	x	y	z	U(eq)
H2	6573(5)	5539(3)	-8248(2)	58
H4	7154(5)	5275(3)	-9581(2)	61
H2A	3933(7)	7850(4)	-10882(3)	71
H3A	3198(7)	8046(4)	-9484(3)	71
H7A	4128(6)	6133(3)	-6316(3)	60
H8A	5871(6)	4961(4)	-5713(3)	60
H12A	10384(6)	3416(4)	-7188(3)	66
H13A	10912(6)	3077(4)	-8518(3)	65
H17A	8568(7)	3971(4)	-11209(3)	69
H18A	6932(7)	5227(4)	-11844(3)	69
H22A	1734(7)	6892(3)	-7931(3)	56
H25A	4637(6)	8022(3)	-7540(3)	54
H6A	-792(6)	8394(3)	-7383(3)	64
H27A	-2715(7)	7884(4)	-7021(4)	102
H27B	-2768(7)	6847(4)	-6395(4)	102
H27C	-2777(7)	7125(4)	-7392(4)	102
H7	2270(6)	9693(3)	-7021(3)	62
H29A	3192(8)	10724(4)	-6937(4)	116
H29B	4682(8)	10852(4)	-7464(4)	116
H29C	4425(8)	10326(4)	-6448(4)	116
H31A	8131(6)	5183(4)	-5842(3)	60
H34A	8695(6)	2728(4)	-6082(3)	61
H9A	9113(5)	4255(3)	-3839(2)	61
H36A	8616(7)	5148(4)	-3171(3)	97
H36B	7258(7)	5786(4)	-3312(3)	97
H36C	8660(7)	6189(4)	-3786(3)	97
H10A	9523(5)	1588(3)	-4096(3)	63
H38A	10653(7)	354(4)	-3931(4)	102
H38B	11909(7)	359(4)	-4680(4)	102
H38C	10591(7)	-67(4)	-4623(4)	102
H44A	11089(12)	3813(6)	-10876(6)	73
H44B	11763(29)	3601(16)	-10093(17)	56
H43A	12491(11)	2586(6)	-11055(6)	79
H43B	13090(33)	2346(21)	-10324(17)	72
H41A	10157(10)	892(5)	-9033(5)	78

H41B	9836(35)	1263(15)	-10208(13)	76
H40A	8834(9)	2130(5)	-8828(5)	75
H40B	8469(24)	2492(15)	-9937(14)	57
H46A	11685(13)	-16(6)	-8958(5)	275
H46B	13064(13)	368(6)	-9063(5)	275
H46C	13047(13)	-444(6)	-9377(5)	275
H47A	13499(11)	1433(6)	-11301(7)	251
H47B	14167(11)	445(6)	-10817(7)	251
H47C	14183(11)	1258(6)	-10503(7)	251
H48A	11700(13)	766(8)	-11175(10)	307
H48B	10946(13)	127(8)	-10270(10)	307
H48C	12413(13)	-195(8)	-10667(10)	307
H50A	7324(7)	7219(4)	-12292(3)	65
H51A	6996(7)	7883(4)	-13694(3)	66
H53A	3275(7)	7155(4)	-12934(4)	77
H54A	3597(7)	6494(4)	-11517(3)	75
H56A	6867(7)	8059(4)	-14982(3)	107
H56B	6202(7)	8979(4)	-14845(3)	107
H56C	5898(7)	8740(4)	-15599(3)	107
H57A	5493(7)	6803(4)	-14632(3)	99
H57B	4555(7)	7486(4)	-15270(3)	99
H57C	3919(7)	6915(4)	-14304(3)	99
H58A	3774(7)	9155(4)	-14277(4)	112
H58B	2859(7)	8367(4)	-14085(4)	112
H58C	3495(7)	8937(4)	-15051(4)	112

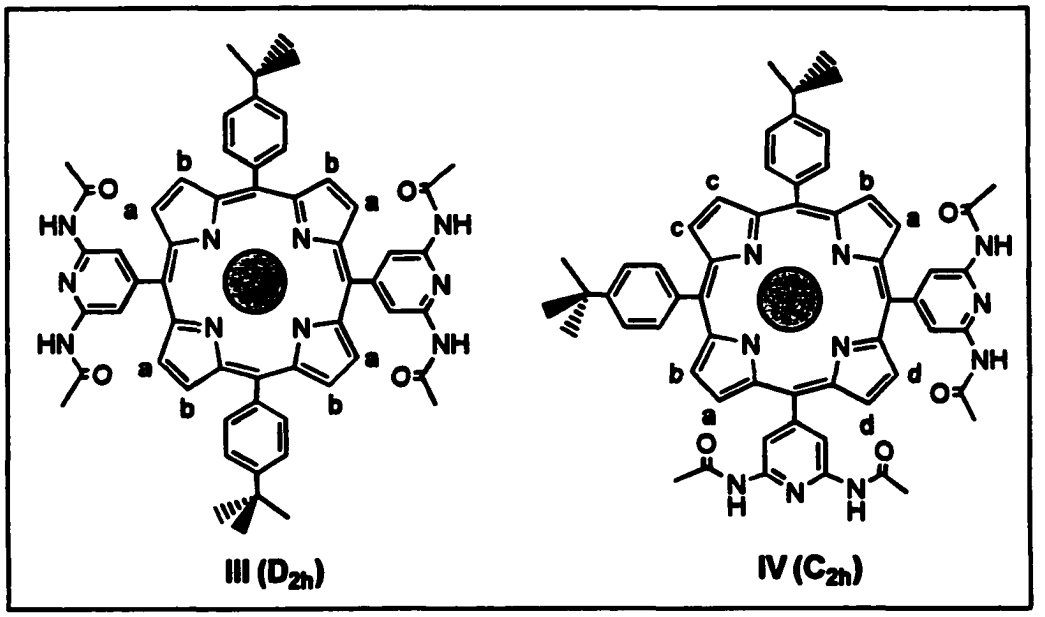


Figure A2-1. *Disubstituted pyridyl porphyrins: 5,15-isomer III and 5,10-isomer IV*

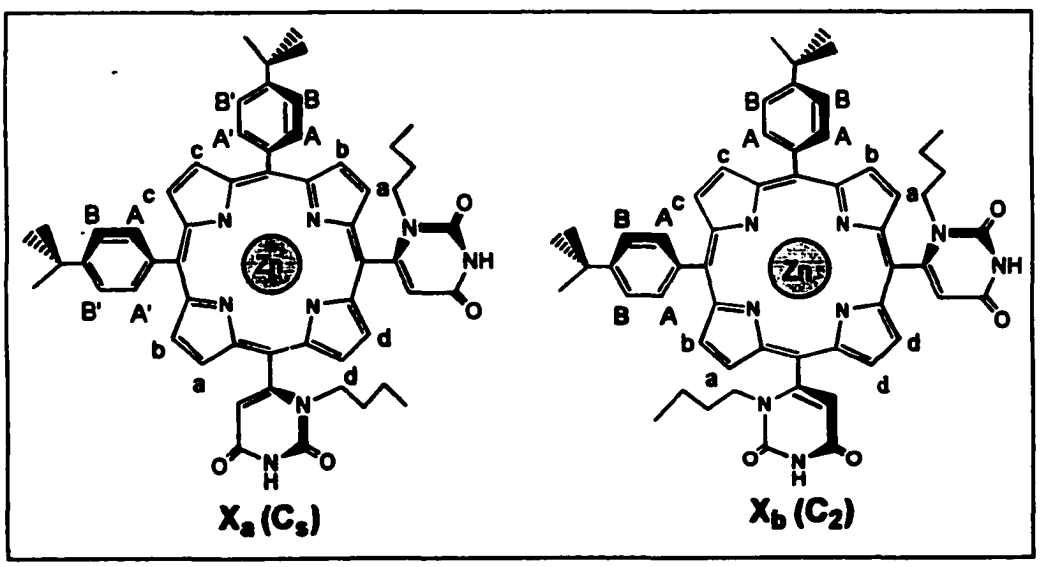


Figure A2-2. *Two rotomers of the 5,10-diuracylporphyrin(Zn) (X): αα (Xa) and αβ (Xb). Symmetry labels a, b, c, d for types of pyrrole H and A, B, A', B' for types of phenyl H are discussed in the text. In this illustration α is above and β is below the plane of the porphyrin.*

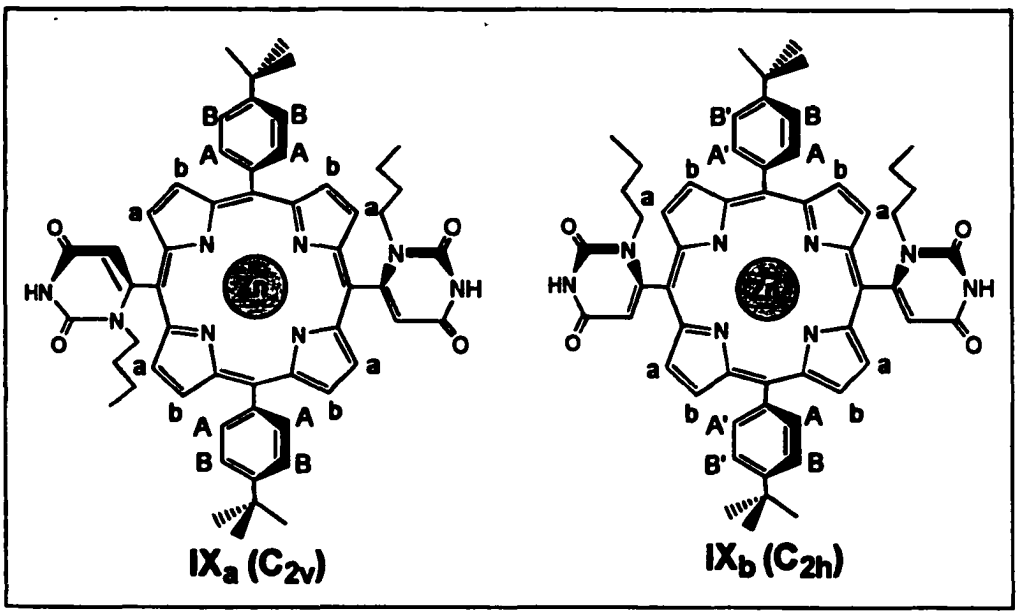


Figure A2-3. *Two rotomers of the 5,15-diuracyl porphyrin(Zn) (IX): αβ (IX$_a$) and αα (IX$_b$) with point groups. Labels a, b for types of β-pyrrole H and A, B, A',B' for types of phenyl H are discussed in the text. In this illustration α is above and β is below the plane of the porphyrin.*

There are four different kinds of pyrrole β-H in IV. The chemical shift of H_c and H_d are unique and give two unsplit signals, H_b and H_a have their proton resonances split into an AB quartet. There are two different kinds of pyrrole β-H in 5,15-isomer which appear as an AB quartet. Consistent with several reports on these types of porphyrin isomer, the R_f of 5,15-isomer is greater than that of 5,10-isomer (see Experimental Section).

For X, the NMR resonances of H_c and H_d are observed as two singlets, and H_b and H_a have their proton resonances split into an AB quartet. Again, due to the two 1-butyl-6-uracyl groups the two 5,10-diuracylporphyrin rotomers have different splitting patterns.

The two butyl groups in the αα-rotomer, **Xa**, face the same side of the porphyrin plane so the faces of the macrocycle are different, and the 4-*tert*-butylphenyl groups have AB, A'B' spin-systems that are observed as two AB quartets. The porphyrin faces are the same for the αβ rotamer, **Xb**, so the phenyl proton resonances are split into one AB quartet.

The 5,15-bis(1-butyl-6-uracyl)porphyrin(Zn) (**IXa**) also has two rotomeric forms αβ (**IXa**) and αα (**IXb**) with respect to the relative orientation of the two 1-butyl-6-uracyl groups. There are two different kinds of β-pyrrole protons (H_a and H_b) in the both rotomers, which is observed as an AB-type quartet. The two 4-*tert*-butylphenyl groups of the 5,15-rotomers have different splitting patterns. The two 1-butyl-6-uracyl groups in the αα-rotomer (**IXb**) face the same side of the porphyrin plane so the molecule has a plane of symmetry that bisects the porphyrin plane, but not one containing the porphyrin plane, so the two 4-*tert*-butylphenyl groups have two different AB-types spin-systems. Since the two butyl groups in the αβ-rotomer face opposite sides of the porphyrin plane and the porphyrin faces are the same and the two 4-*tert*-butylphenyl groups have only one AB quartet.

Each porphyrin face is different in the 5-uracyl porphyrin, **VIII**. This results in an AB, A'B' system where A', B' represents the phenyl protons on the opposite sites of the macrocycle. Thus for **VIII**, the phenyl protons are observed as multiplets rather than an AB quartet. On the basis of their observed chemical shift, one group (7.77-7.80 ppm) for H_B and $H_{B'}$ are the *meta* protons and another group (7.98-8.11, three doublets) for H_A and $H_{A'}$ are the *ortho* protons. The 5-uracylporphyrin shows the expected pattern in the β-

pyrrole region: there is an AB quartet, and the H_cH_d system is observed as a singlet rather than an AB quartet even on the 500 MHz instrument.

Table A2-6. ^{1}H NMR Peaks for Mono, Bis, and Tetrakis(1′-butyl-6′-uracyl)porphyrins

Description	VIII	X		IX		XIII
	ArArArα	ArAr$\alpha\alpha$	ArAr$\alpha\beta$	ArαArα	ArαArβ	$\alpha\alpha\alpha\alpha$, $\alpha\alpha\alpha\beta$ $\alpha\alpha\beta\beta$, $\alpha\beta\alpha\beta$
N-H	11.81(s)	11.79(s)		11.84(s)	11.84(s)	11.83(s)
Ha Hb Hc, c'/Hd, d' β-H of pyrrol	9.26((4.76) 8.79(4.76) 8.75(s)	9.355(4.76) 8.806(4.76) 9.42(s), 8.77(s)		9.324 (4.76) 8.815 (4.76)	9.32(4.76) 8.83(4.76)	9.45(s)
2,3,5,6-H of p-BuPh	8.12~7.77(m)	8.16, 7.82(8.79) 7.96, 7.78(6.59)		8.09, 7.77(8.1) 8.01, 7.77(7.3)	8.08(8.03) 7.81(8.42)	
=CH	6.27(s)	6.30(s)		6.23(s)	6.21(s)	6.26(s)
-CH_2	3.34~3.22(m)	3.35~3.22(m)		3.34~3.21(m)	3.32~3.20(m)	3.08~3.56(m)
-$C(CH_3)_3$	1.55(s)	1.55(s)		1.54(s)	1.56(s)	
-CH_2	1.08~1.01(m)	1.05~0.99(m)		1.08~1.03(m)	1.10~1.05(m)	0.91~1.10(m)
-CH_2	0.26~0.19(m)	0.26~0.18(m)		0.35~0.31(m)	0.23~0.21(m)	0.08~0.30(m)
-CH_3	-0.18(t)	-0.19(t)		-0.11(t)	-0.20(t)	-0.14(t), -0.19(t) -0.31(t), -0.55(t)

Table A2-7 Uv-Visible Spectra of Eight Porphyrins

In Chloroform	Soret	Q1	Q2	Q3	Q4
II	25.3 421.4	1.0 517.7	0.52 553.3	0.31 591.4	0.24 647.3
IV	22.0 421.8	1.0 517.2	0.46 552.3	0.33 591.4	0.21 647.2
III	18.4 421.7	1.0 517.8	0.54 553.3	0.38 592.8	0.21 650.6
VI	22.6 421.9	1.0 517.3	0.46 552.4	0.33 591.3	0.20 647.7
VIII	23.8 421.5	1.0 517.4	0.49 553.3	0.34 590.8	0.18 646.8
X	21.3 422.2	1.0 517.4	0.34 552.3	0.35 589.5	0.11 648.9
IX	20.2 420.5	1.0 515.8	0.40 550.0	0.32 591.4	0.22 647.4
XII	14.0 419.7	1.0 512.0	0.19 543.9	0.35 587.9	0.09 641.3

Appendix 3

During the syntheses of the two complementary functionalized heterocycloaldelydes, 2,6-diacetamino-4-formylpyridine and 1-butyl-6-formyluracil, we have tried a lot of interesting heterocyclic chemistry.

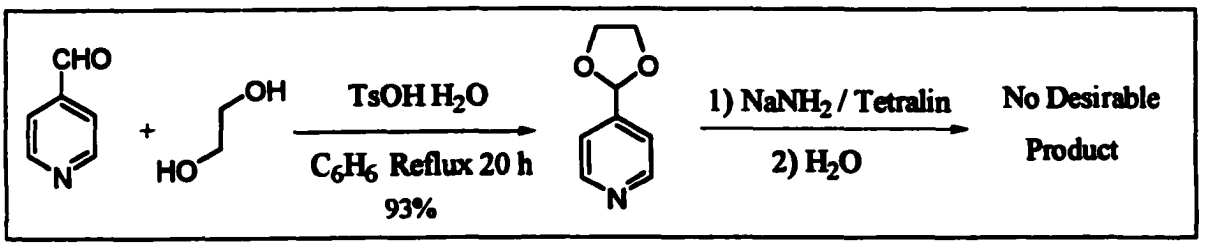
A. Synthesis of 2,6-diacetamido-4-formylpyridine

The reactivity of the pyridine ring or of its substituents has to be exploited in order to complete the preparation of the desired pyridine derivatives. An aldehyde group or groups which can be converted to an aldehyde group should be at 4-position before amino or amido groups are introduced onto the pyridine ring, because the amino or amido groups have a stronger directing effect (*ortho-/para*-directing) than that of the nitrogen atom (*meta*-directing) in pyridine ring. The influence of the nitrogen atom is to distort the electron distribution in both the π-bonding system and in the α-bonds (by the inductive affect). This conjugated imine system is susceptibility to attack by nucleophiles at the α- and γ-carbon atoms. The isomer, 2,6-diamino-3-formylpyridine, has been synthesized by Reimer-Tiemann's methods from the 2,6-diaminopyridine.[1]

We first used the 4-formylpyridine as starting materials to prepare this aldehyde by protecting the aldehyde group as an acetal with ethylene glycol and then aminating with sodium amide in tetralin. But this did not yield the desired product (see Scheme A3-1). A possible reason may be that the sodium amide is so strong a base and destroys the acetal.

Lott et al. brominated 2,6-dihydroxy-4-methylpyridine with phosphorus tribromide, got 2,6-dibromo-4-methylpyridine as the intermediate, then reacted with concentrated ammonia at high pressure to afford the diamine.[2] The over-all yield was less than 26% and

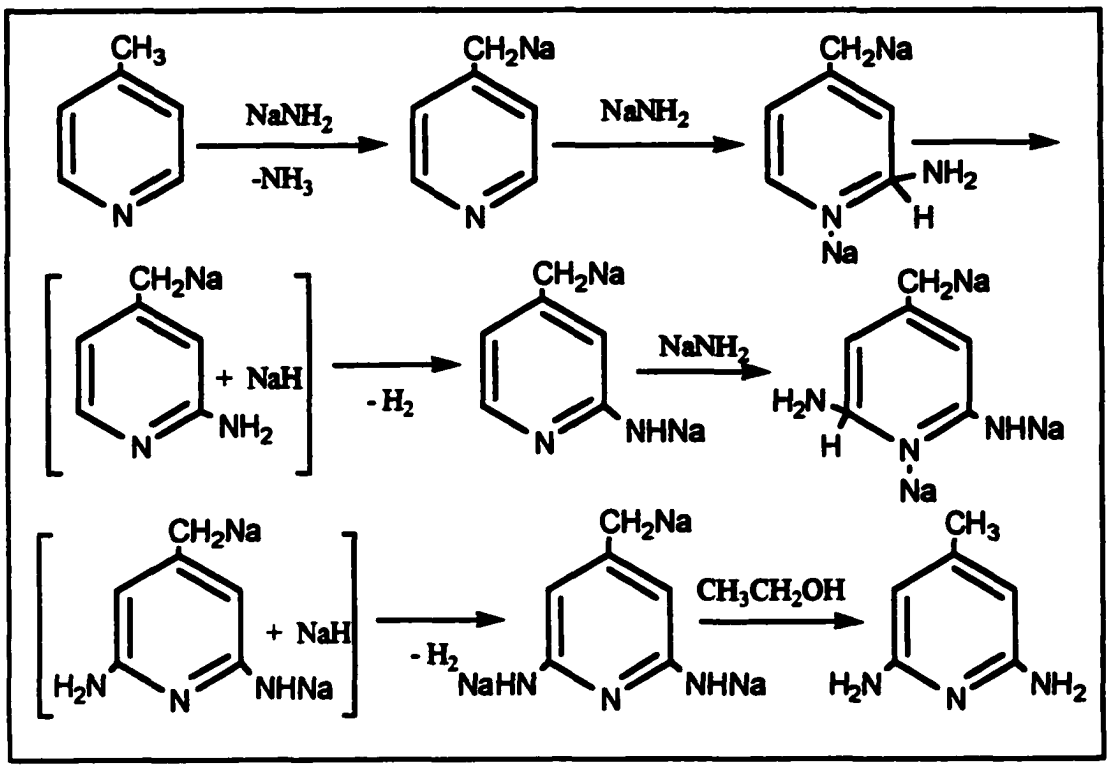
moreover the starting material was not commercially available. This procedure is also long and tedious.



Scheme A3-1 *Protecting the aldehyde group with ethylene glycol followed by amination*

We developed a new method to prepare the 2,6-diamino-4-methylpyridine directly introducing two amino groups onto the pyridine ring in one step. 4-Methylpyridine reacted with sodium amide in tetralin. First, an intermediate metal salt derivative was formed which was then hydrolyzed to 2,6-diamino-4-methylpyridine (65%).

This procedure has several features compared with previous methods.[3] i) When the 4-methylpyridine is added to the sodium amide solution, the temperature of reaction mixture must be kept below 140°C. This avoids evaporation of the 4-methylpyridine (b.p.145°C) and allows the 4-methylpyridine to react with sodium amide under milder conditions to form the monoamine intermediate. After the 4-methylpyridine addition, the temperature of reaction mixture was raised slowly to 195°C to complete the reaction. ii) Tetralin was removed from the reaction mixture by filtration. iii) The remaining solid was hydrolyzed with ethanol rather than water, and was directly loaded on silica gel. All of these features make this procedure operable and contribute to the higher yield. This direct aminating method started from simple and commercially available starting materials and one pot yields the desired product in 65% yield. This direct amination method is a convenient and economical way and has proved to be a more straightforward route.

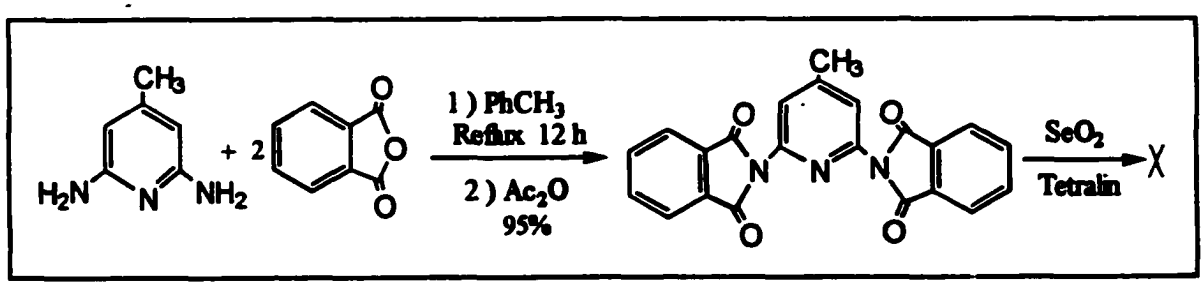


Scheme A3-2 *Suggested mechanism of amination of 4-methylpyridine*[3b]

The presence of the nitrogen atom in pyridine ring has an important influence on the activation of methyl group. The 4-methylpyridine has the strongest acidity in the three isomers (pKa values are: 4-methylpyridine, 26; 2-methylpyridine, 29.5; 3-methylpyridine, 33.5; toluene (estimated), ca. 42).[4] It has been suggested that the initial step in the reaction is the addition of the sodium amide to the –CH=N– group; the resulting product is then transformed to the soldium derivative of the monoamine, either through intramolecular rearrangement or through decomposition to the monoamino compound and sodium hydride which interact to give the sodium derivative. The second amino group is introduced in similar way (see Scheme A3-2).

Due to the reactivity of the amino groups, the 2,6-diamino-4-methylpyridine was converted to a diamide or diimide by reaction with acetic anhydride or phthalic anhydride. We tried to directly oxidize the methyl group to the aldehyde group with selenium dioxide or manganese dioxide in different solvents but this did not work

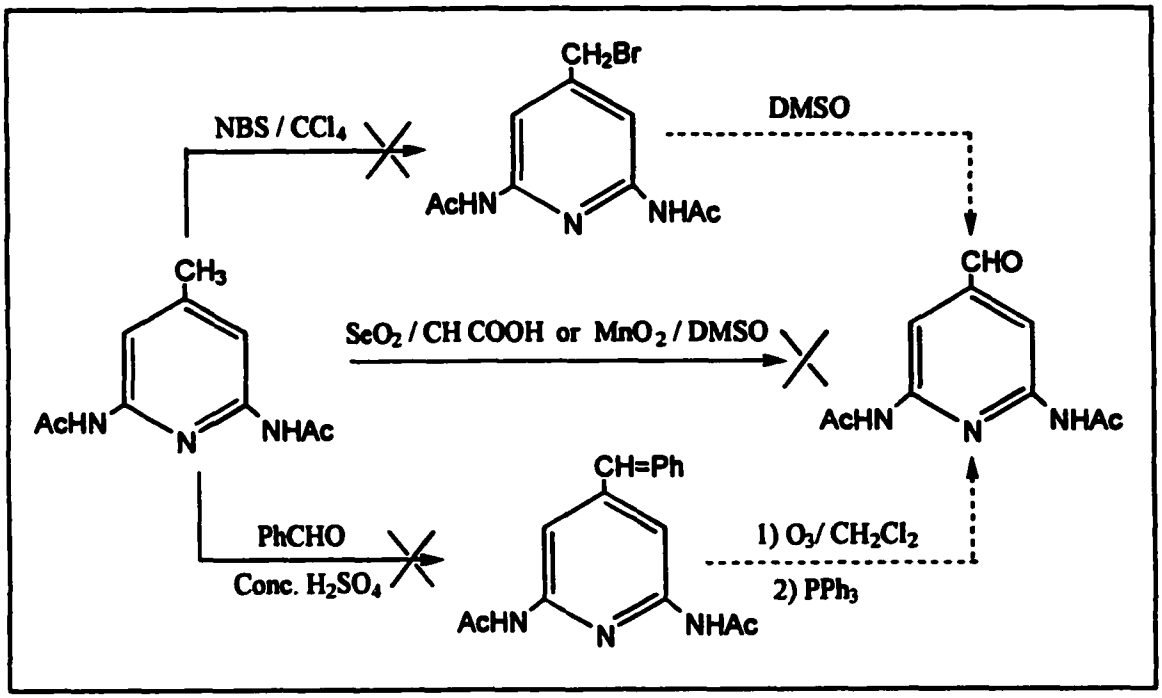
There are a lot of examples where the methyl group connected to a pyridine ring may be oxidized directly to an aldehyde with selenium dioxide or other oxidants. In our case, the problem may be due to the hydrogens of the amido groups. Amido substituents have two different effects on the reactivity of pyridine, donating electrons to pyridine ring through mesomeric interactions and withdrawing electrons through inductive effects. Inductive and mesomeric interactions of acetamido groups on the pyridine ring result in withdrawal of electronic density from the aromatic ring. So we protected the amino groups of the 2,6-diamino-4-methylpyridine with phthalic anhydride in refluxing toluene,[5] and attempted to oxidize it with selenium dioxide in acetic acid, propoinic acid, toluene, and tetralin, but the oxidizing step did not work (see Scheme A3-3).



Scheme A3-3 *Protecting the amino groups by phthalic anhydride then oxidized by different oxidants.*

Therefore, we turned to indirect ways. Considering the structure of 2,6-diacetamido-4-methylpyridine, we tried to brominate the methyl group with N-bromosuccinimide (NBS) in

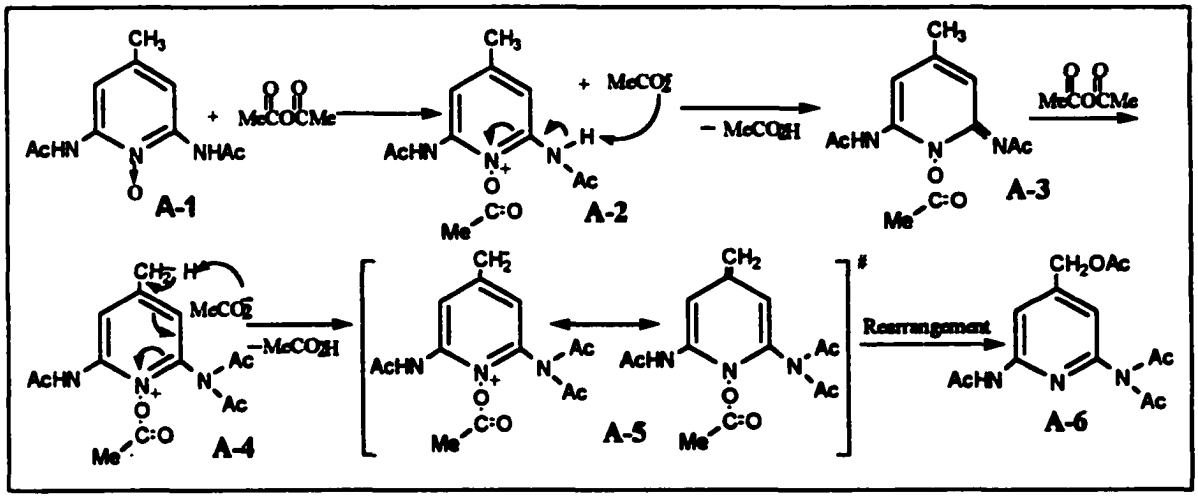
CCl_4 catalyzed by *uv*, but it did not work. The 2,6-diacetamido-4-methylpyridine was condensed with benzene aldehyde in conc. H_2SO_4 in 150°C, but it did not work either (see Scheme A3-4).



Scheme A3-4 *Attempted to convert the methyl group to the aldehyde group*

Considering that the N-oxide of methylpyridines can significantly modify the reactivity of the methyl group, we converted the 2,6-diacetamido-4-methylpyridine to 2,6-diacetamido-4-methylpyridine-1-oxide by N-oxidation with peracetic acid in acetic acid. Of considerable interest was the remarkable action of acetic anhydride on 2,6-diacetamido-4-methylpyridine-1-oxide at 140°C, which yields mainly 2-diacetimido-6-acetamido-4-acetoxymethylpyridine (see Scheme A3-5).

The mechanism is generally believed to involve acetylation of the N-oxide function resulting in 2,6-diacetamido-1-acetoxypyridinium ion (A-2).[6] The removal of a proton from the acetamido group of A-2 yields an imide intermediate (A-3), which reacts with acetic anhydride to result a 2-diacetimido-6-acetamido-1-acetoxypyridinium ion(A-4) and followed by the removal of a proton from the ring methyl group of A-4 to yield an anhydrobase intermediate (A-5). An external acetate ion then attacks the anhydrobase A-5 with simultaneous expulsion of the acetate group to form 2-diacetimido-6-acetamido-4-acetoxy methylpyridine (A-6).



Scheme A3-5 *The suggested mechanism of 2,6-diacetamido-4-mythylpyridine-1-oxide with acetic anhydride*

We obtained the expected 2-diacetimido-6-acetamido-4-acetoxymethylpyridine, but also obtained another product---2,6-diacetamido-4-acetoxymethylpyridine. Carefully checking the reaction conditions, we found that 2,6-diacetamido-4-acetoxymethylpyridine came from the hydrolysis of 2-diacetimido-6-acetamido-4-acetoxymethylpyridine in the isolation step. To reduce the hydrolysis product we added silica gel to the reaction mixture and removed the

acetic anhydride under reduced pressure. In this way only 2,6-diacetamido-4-acetoxymethylpyridine was isolated.

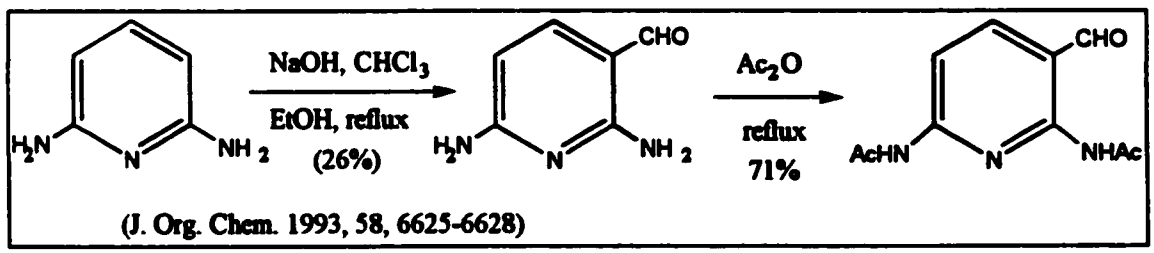
Amides differ from esters only in the nature of the leaving group, $-NR_2$, which is more difficult to displace than -OR. Under basic conditions; therefore, amides hydrolyze considerably more slowly than do esters. In the diacetimido group, one acetyl group is more active than the other and even more active than -OR. So it is possible to selectively hydrolyze one of two acetyl groups to get 2,6-diacetamido-4-hydroxymethylpyridine. For hydrolysis using K_2CO_3 in CH_3OH: H_2O (4:1), the reproducibility is good and the alcohol is easy to separate from reaction mixture.

The 2,6-diacetamido-4-hydroxymethylpyridine was oxidized with PCC/alumina under ultrasound conditions to give 2,6-diacetamido-4-formylpyridine. This procedure has two notable features. i) PCC was loaded on alumina (PCC/alumina), the alumina absorbs the reduced chromium tars that may otherwise entrain the desired product and reduce yields. ii) The ultrasound was introduced into the alumina reagent system for several reasons.[7] Since PCC has limited solubility in dichloromethane, and a typical PCC/alumina oxidation is a heterogeneous process, we can expect that ultrasound would activate both the alumina and the PCC. We found that PCC/alumina/ultrasound oxidation of 2,6-diacetamido-4-hydroxypyridine required a greatly decreased reaction time (4h). Without ultrasound this reaction takes about 20h and is more difficult to work up.

In conclusion, the ~16 % overall yield of this six-step synthetic route is not optimized, but is not bad because of the inexpensive starting material and reactions. This synthetic route is suitable for small- and large-scale preparations.

B. Synthesis of 2,6-diacetamido-3-formylpyridine

After 2,6-diacetamido-4-formylpyridine was prepared, we tried to prepare its isomer---2,6-diacetamido-3-formylpyridine. Reaction of commercially available 2,6-diaminopyridine under Reimer-Tiemann conditions afforded 2,6-diamino-3-formylpyridine in a single step in 26% yield according to literature procedure.[1] 2,6-diamino-3-formylpyridine after refluxing 2h in acetic anhydride, resulted in 2,6-diacetamido-3-formylpyridine in 71% yield (see Scheme A3-6). Acetylation of the 2,6-diamino-3-formylpyridine was much more difficult than that of the 2,6-diamino-4-methylpyridine. 2,6-Diamino-4-methylpyridine was acetylated with acetic anhydride at room temperature releasing large amount of heat, but 2,6-diamino-3-formylpyridine was acetylated with same condition only giving 2-amino-6-acetamido-3-formylpyridine. The difference in acetylations of the two compounds may be due to their substitutent effects. The aldehyde group of 2,6-diamino-3-formylpyridine is electron withdrawing (decreasing the basicity of the amino groups) and located on *ortho*-position of one amino group. Both electronic and steric effects of the aldehyde group disfavor the acetylation of 2,6-diamino-3-formylpyridine.



Scheme A3-6 *Synthesis of 2,6-diacetamido-3-formylpyridine from2,6-diaminopyridine*

References:

(1) Fenlon, E. E.; Murray, T. J.; Baloga, M. H.; Zimmerman, S. C. *J. Org. Chem.* **1993**, *58*, 6625-6628.

(2) Bernstein, J.; Stearns, B.; Shaw, E.; Lott, W. A. *J. Am. Chem. Soc.* **1947**, *69*, 1151-1158.

(3) (a) Leffer, M. T. In *Organic Reactions*; Adams, R.; Bachmann, W. E.; Fieser, L. E.; Johnson, J. R. Snyder, H. R., Eds.; John Wiley and Sons, Inc.: New York, NY, **1941**; *Vol. 1*, pp 91-104. (b) Shreve, R. N.; Riechers, E. H.; Rubenkoenig, H.; Goodman, A. H. *Ind. Eng. Chem.* **1940**, *32*, 173-178. (c) 2,6-diamino-4-isoropylpyridine is made in 53% using 4-isopropylpyridine and sodium amide in tetralin K. K. Kogyo, Japanese Patent: *Kokai. Tokyo Koho* 80 76, 861, 10, Jun. **1980**. (CA 93-204,467n).

(4) Seconi, G.; Eaborn, C. ; Fischer, A.; *J. Organometal. Chem.*, **1979**. *177*, 129

(5) Sasaki, T.; Minamoto, K.; Itoh, H.; *J. Org. Chem.* **1978**, *43*, 2320.

(6) Boekelheide, V.; Linn, W. J; *J. Am. Chem. Soc.*, **1954**, *76*, 1286-1291

(7) (a) Abdulla, R. F.; *Aldrichimica Acta* **1988**, *21*, 31. (b) Adams, L. L.; Luzzio, F. A.; *J. Org. Chem.* **1989**, *54*, 5387-5390.

Appendix 4

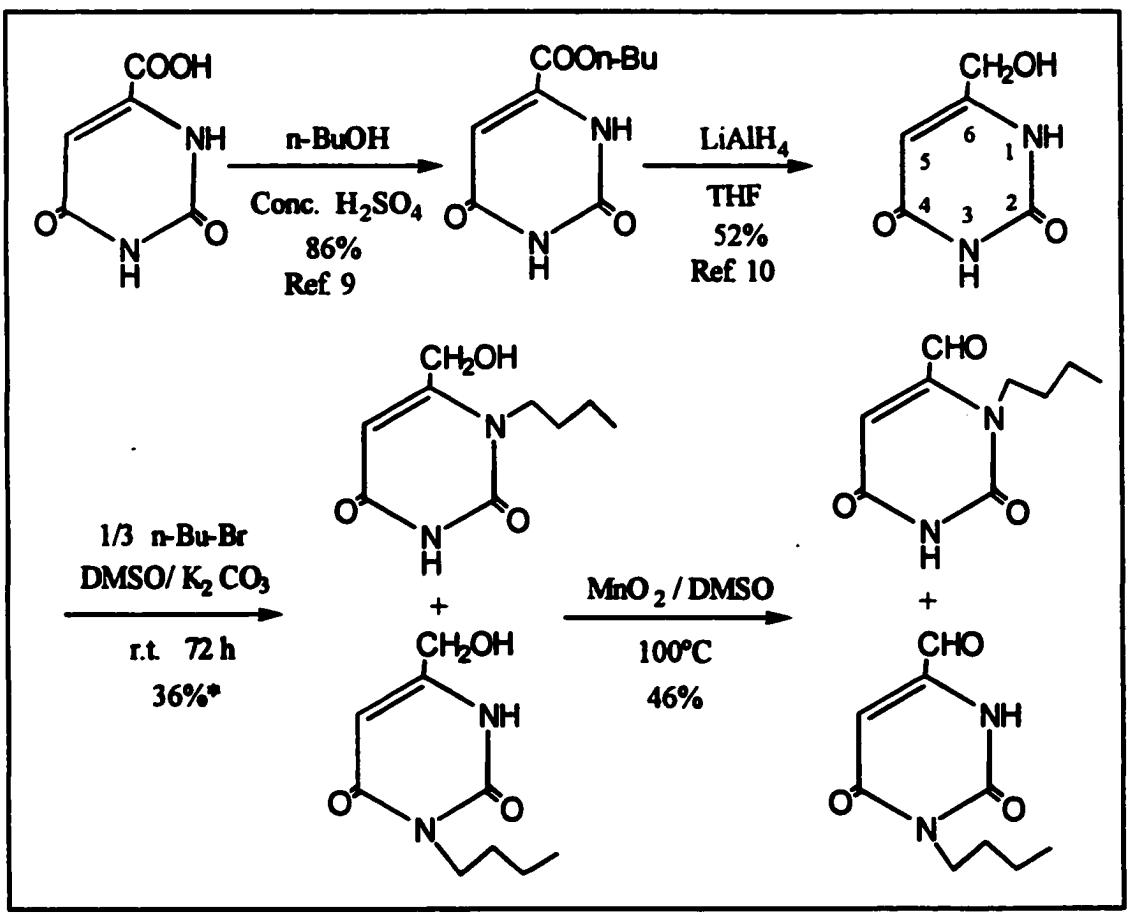
Synthesis of 1-butyl-6-formyluracil

The 6-formyluracil was prepared from the commercially available 6-methyluracil according to slight modifications of literature procedure.[1] We first tried to alkylate directly 6-formyluracil with butyl bromide catalyzed by potassium carbonate in DMSO at room temperature for 72h.[2] No desired product was found. The aldehyde group may be too sensitive under this basic condition. So we thought of alkylating first the 6-methyluracil to introduce a butyl group at 1-position of uracil ring then oxidizing the methyl group to an aldehyde. This alkylation step worked very well and afforded the desired product---1-butyl-6-methyluracil (no 3-butyl isomer formed), but the methyl group of 1-butyl-6-methyluracil can not be oxidized by selenium dioxide in acetic acid or propionic acid.

We tried to use indirect ways to transform the methyl group to an aldehyde. Considering the structure of 1-butyl-6-methyluracil (the methyl group attached a C=C double bond), we tried to brominate it with N-bromosuccinimide (NBS) in CCl_4 catalyzed by AIBN (*azo*-bis isobutylronitrile) and *uv*, but no desired product formed.

We tried other synthetic routes starting from orotic acid. The hydroxymethyl group of 1-butyl-6-hydroxymethyluracil can be oxidized more easily than the methyl group of 1-butyl-6-methyluracil. The orotic acid was esterified with *n*-butyl alcohol catalyzed by concentrated sulfuric acid to afford *n*-butyl orotate.[3] In the original procedure, there is some unreacted orotic acid left in the reaction mixture after finishing the reaction. The unreacted orotic acid has to be removed from the reaction mixture. This may cause the loss of certain amount of product, because of the low solubility of *n*-butyl orotate in *n*-

butyl alcohol at low temperature. In the original procedure a large amount of concentrated sulfuric acid was added. The concentrated sulfuric acid acts as a catalyst and dehydrating agent. But the second function was not good enough to remove water which produced during the reaction. If the water can be removed more efficiently, it would favor forming the ester. Considering the low solubility of *n*-butyl alcohol in water, it was possible to remove the water using a Dean-Stark water trap. The Dean-Stark water trap works very well. There is no unreacted orotic acid left in the reaction mixture after finishing the reaction, and we can also reduce



Scheme A4-1 ***Synthesis of 1-butyl-6-formyluracil from orotate***

the amount of concentrated sulfuric acid. The improved procedure makes it easier to synthesize the *n*-butyl orotate. This modification avoided the filtration step and improved the yield from 78% (based on reacted orotic acid) to 86% (based on all orotic acid). The *n*-butyl orotate was reduced by LAH (Lithium Aluminum Hydride) in dry THF to obtain the 6-hydroxymethyluracil (52%) according to the literature procedure (see Scheme A4-1).[4]

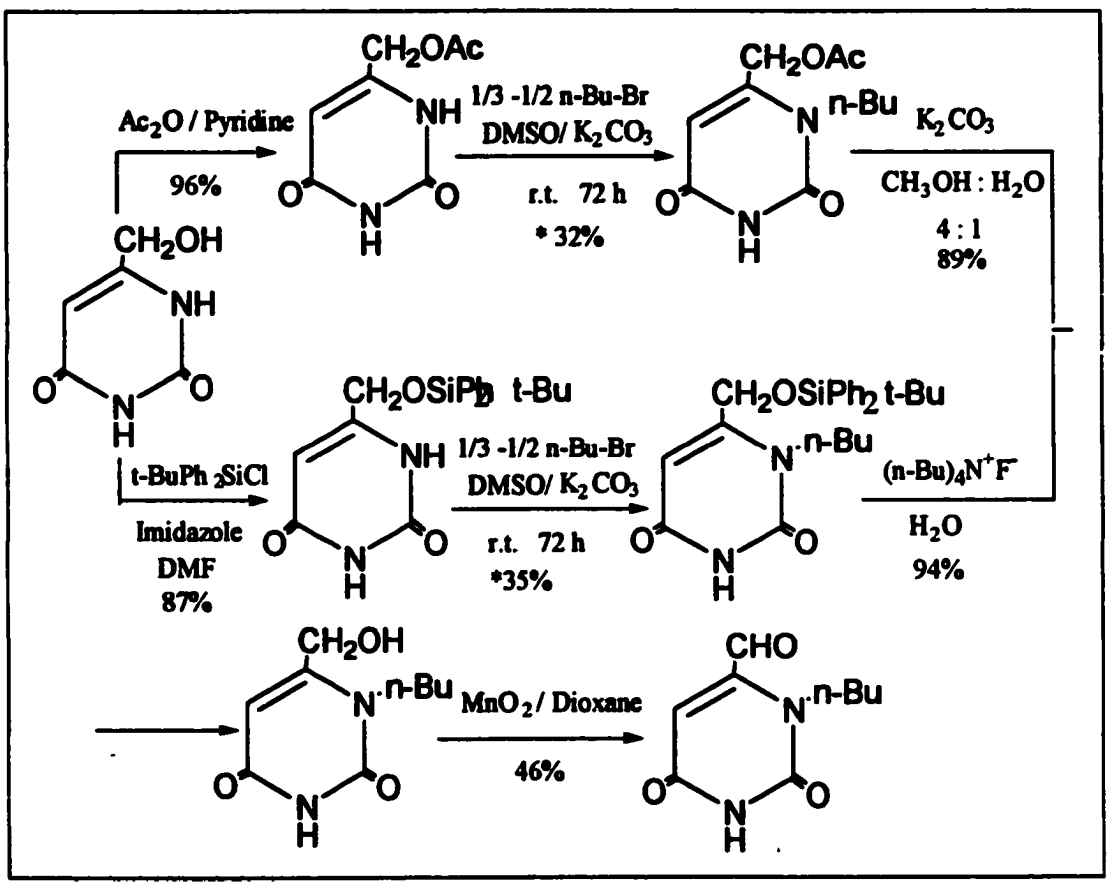
The LAH is very strong reducing agent and using it needs special caution (anhydrous and anaerobic). Another inconvenience of this procedure is that it has to use large amounts of dry THF (one gram of product needs about 200 mL dry THF). We tried another synthetic route. The 6-formyluracil was reduced with sodium borohydride in absolute ethanol, but the yield of this reducing step is very low.

The 6-hydroxymethyluracil was alkylated with *n*-butyl bromide catalyzed by potassium carbonate in DMSO at room temperature 72h to afford a mixture of 1-butyl-6-hydroxymethyluracil and 3-butyl-6-hydroxymethyluracil.[2] The two isomers had almost same Rf value (silica gel / ethyl aectate, only one spot on TLC). It was difficult to separate them through column chromatography. ^{1}H NMR spectra show the relative amount of each isomer. The ratio of the two alcohol isomers depended on the ratio of the starting material (see Table A4-1).

Table A4-1 *The relative amount of 1-butyl-6-hydroxymethyluracil and 3-butyl-6-hydroxymethyluracil*

Starting material ratio		Product ratio	
n-butyl bromide	6-hydroxymethyluracil	1-butyl-6-hydroxymethyluracil	3-butyl-6-hydroxymethyluracil
1	2	1	1
1	3	2	1

The mixture of 1-butyl-6-hydroxymethyluracil and 3-butyl-6-hydroxymethyluracil can be oxidized to the mixture of their corresponding aldehydes by activated manganese dioxide in DMSO at 100°C.[2] The two aldehyde isomers can be separated by column chromatography (see Table A4-2).

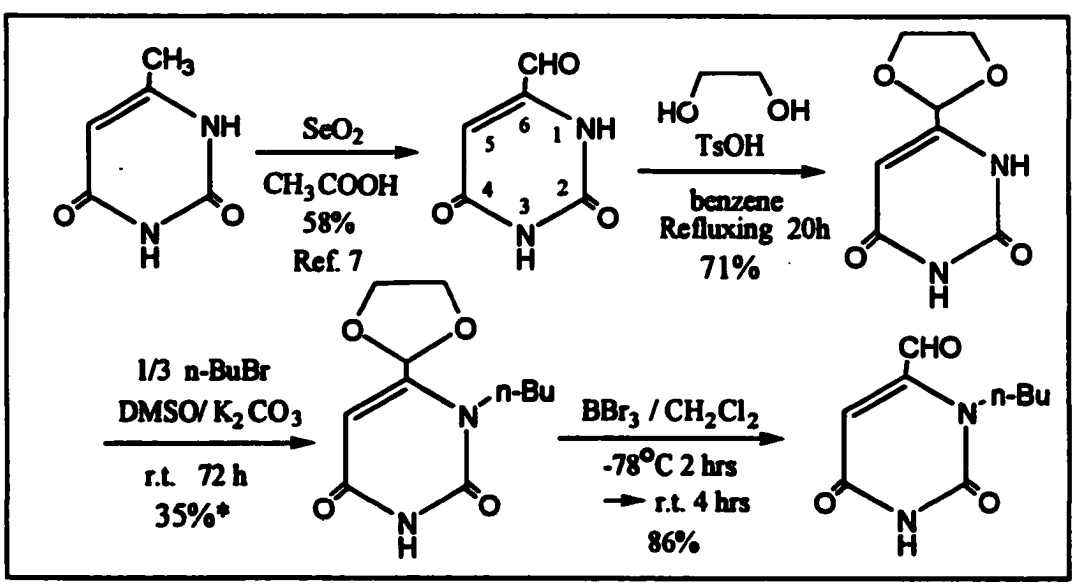


Scheme A4-2 *Synthesis of 1-butyl-6-formyluracil through protecting the hydroxymethyl group by acetic anhydride or tert-butyldiphenylsilyl chloride then alkyating results in similar yields. * based on n-butyl bromide.*

We tried to protect the 6-hydroxymethyluracil with three fold excess *tert*-butyldiphenylsilyl chloride, to form 6-[(*tert*-butyldiphenylsilyl)oxy]methyluracil in 87% yield, but not to form 2,4-bis[(*tert*-butyldiphenylsilyl)oxy]-6-[[(*tert*-butyldiphenylsilyl)

oxy]methyl]pyrimidine.[4] The former was alkylated with *n*-butyl bromide catalyzed by potassium carbonate in DMSO at room temperature for 72h to afford 1-butyl-6-[[(*tert*-butyldiphenylsilyl)oxy] methyl]uracil in 35% based on n-butyl bromide.[2] The protecting group was removed with $(n\text{-Bu})_4NF$ to afford the 1-butyl-6-hydroxmethyluracil in 94%. Treatment of the alcohol with activated manganese dioxide afforded 1-butyl-6-formyluracil in 46% (see Scheme A4-2). This second method produces the desired aldehyde in 19% overall yield.

A third route was explored. The 6-hydroxymethyluracil reacted with acetic anhydride in pyridine to form 6-acetoxymethyluracil in 96% yield, which was alkylated with *n*-butyl bromide catalyzed by potassium carbonate in DMSO at room temperature for 72h to afford 1-butyl-6-acetoxymethyluracil in 32% based on *n*-butyl bromide (see Scheme A4-2).[2]

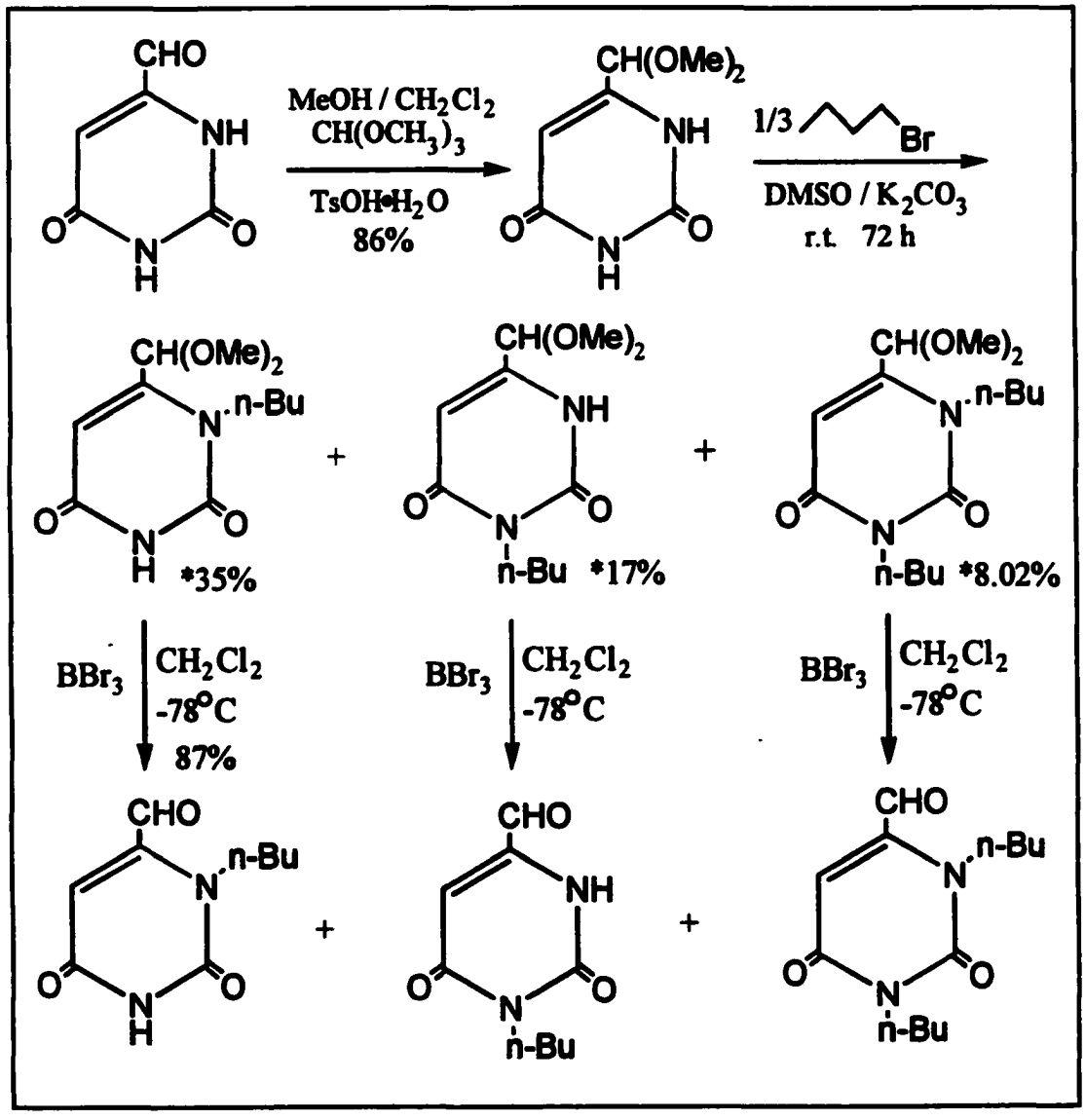


Scheme A4-3 ***Synthesis of 1-butyl-6-formyluracil by protecting the aldehyde with ethylene glycol***

We thought about the synthesis starting with 6-formyluracil. The failure of direct alkylation of the 6-formyluracil may be due to sensitivity of the aldehyde group to basic conditions. Thus the aldehyde group was protected before alkylation. The 6-formyluracil reacted with ethylene glycol catalyzed by the *p*-toluenesulfonic acid in benzene using a Dean-Stark water trap to remove water azeotropically to form 6-(1,3-dioxolan-2-yl)uracil in 71% yield.[6] The 6-(1,3-dioxolan-2-yl)uracil was alkylated with *n*-butyl bromide (3:1) catalyzed by potassium carbonate in DMSO at room temperature 72h in 35 % based on *n*-butyl bromide.[2] The 1-butyl-6-(1,3-dioxolan-2-yl)uracil surprisingly could not be transferred to the corresponding aldehyde under a variety of aqueous acid conditions (1~6 N $HClO_4$, HCl, TsOH, TFA in THF, AcOH in EtOH solutions). The recovery of the starting material in most case was unexpected in view of the extensive literature on dioxolane cleavage (see Scheme A4-3).

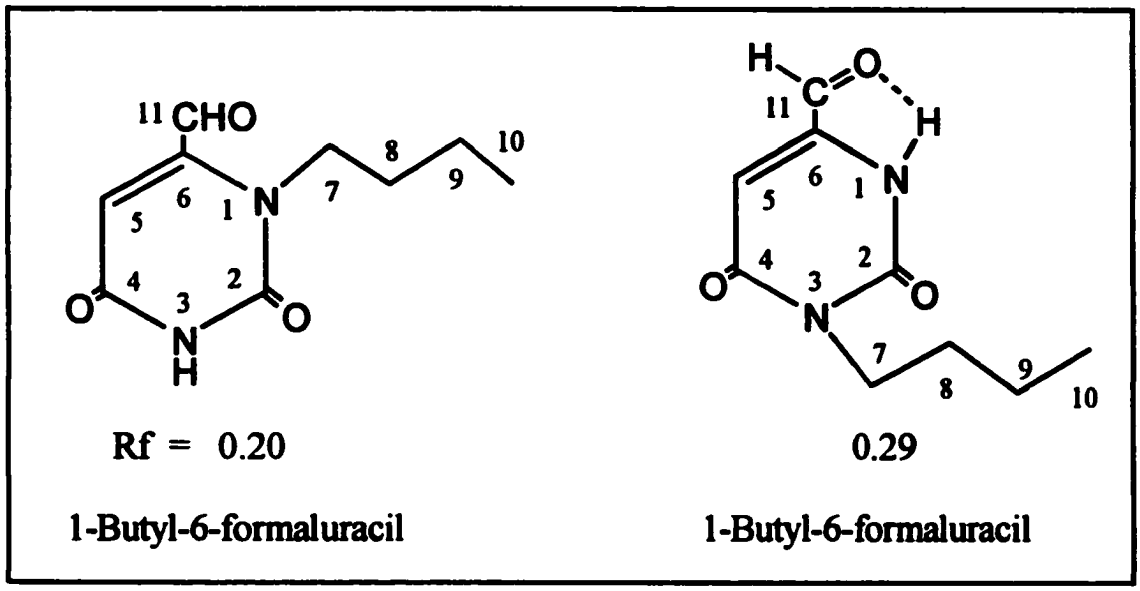
In general, the deprotection of a dimethyl acetal was easier than that of a dioxolane. So we tried to protect the aldehyde group as dimethyl acetal. The 6-formyluracil with trimethyl orthoformate in MeOH and CH_2Cl_2 was refluxed for 10 hours in the presence of the *p*-toluenesulfonic acid to form the 6-(dimethoxymethyl)uracil in 86% yield. The dimethyl acetal was alkylated with *n*-butyl bromide catalyzed by potassium carbonate in DMSO at room temperature 72h to form three products: 1,3-dibutyl-6-(dimethoxymethyl)uracil (*8.2%), 3-butyl-6-(dimethoxymethyl)uracil (*16%) and 1-butyl-6-(dimethoxymethyl)uracil (*37%).[2] The 1-butyl-6-(dimethoxymethyl)uracil could not be transferred to its corresponding aldehyde under a variety of aqueous acid conditions (1~6 N $HClO_4$, HCl, TsOH,TFA in THF, AcOH in EtOH solutions), either. The recovery of the dimethyl acetal in most cases was unexpected in view of the

extensive literature on dimethyl acetal cleavage. But its isomer, 3-butyl-6-(dimethoxymethyl)uracil, can easily be cleaved under normal conditions. So we tried to use the Lewis Acid in organic solution to cleave the dimethyl acetal. A solution of the dimethyl acetal was dissolved in the minimum volume of CH_2Cl_2 and treated with BBr_3 for two hours at -78°C and the solution was allowed to slowly reach room temperature.



Scheme A4-4. ***Synthesis of 1-butyl-6-formyluracil by protecting the aldehyde with dimethyl acetal***

After standing the mixture was cooled to 0°C and excess of water added slowly to hydrolyize the unreacted BBr_3. The mixture afforded 1-butyl-6-formyluracil in 87% yield (see Scheme A4-4).



Scheme A4-5 *1-Butyl-6-formylurcail and 3-butyl-6-formylurcail*

The structural assignments of the 1-butyl-6-formylurcail and 3-butyl-6-formylurcail can be given according to their Rf values. The 3-butyl-6-formylurcail (Rf = 0.29, ethyl acetate:hexane / 1 : 1) can form intramolecular hydrogen bonding so it would be expected to have a smaller dipole moment relative to 1-butyl-6-formylurcail (R_f = 0.20, ethyl acetate : hexane / 1 : 1). The NH and C=O groups are on one side of the 1-butyl isomer and the enol forms may paly a role. The less polar compound would be expected to have a greater Rf value, hence the Rf values can help make the assignments. The NMR data is helpful in distinguishing between the two isomers. The only structural difference of the 1-butyl-6-formylurcail and 3-butyl-6-formylurcail is the positions of *n*-butyl groups. The 1-N of uracil ring (next to one carbonyl group) has a higher electron density than that of 3-

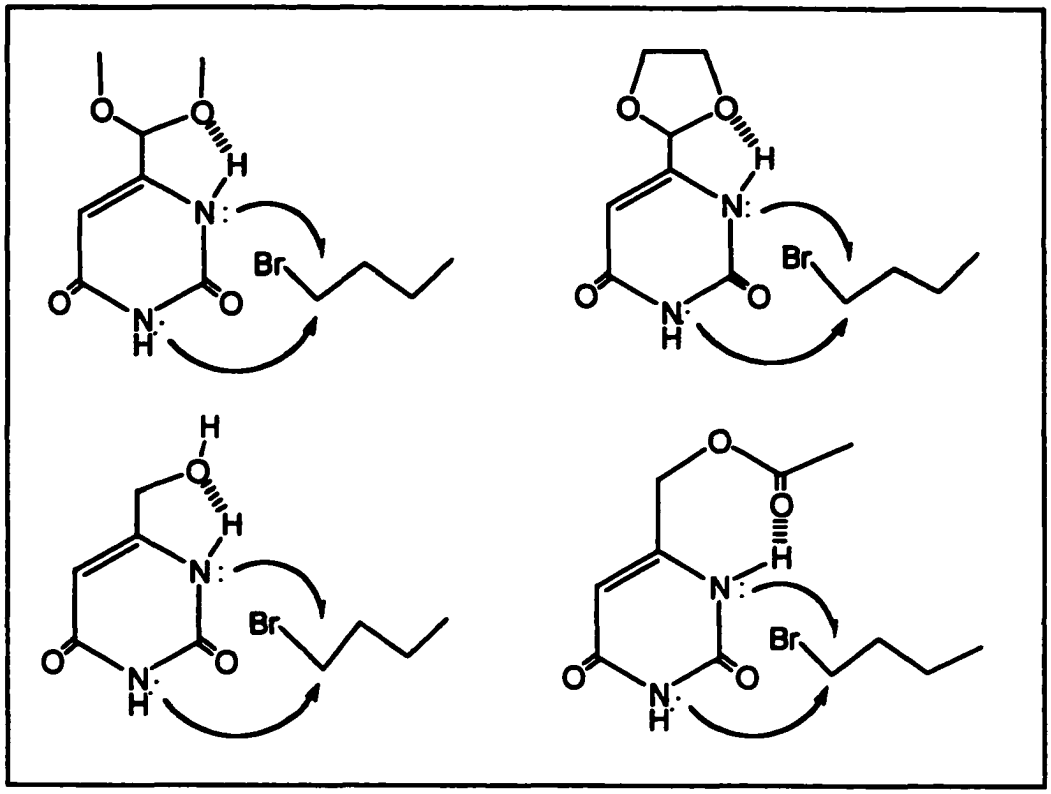
N (next to two carbonyl groups), so the chemical shifts of hydrogens and carbons attached to 1-N should be located at a little higher upfield.

Table A4-2 ^{13}C NMR Peaks of 1-butyl-6-formyluracil and 3-butyl-6-formyluracil

	1-Butyl-6-formyluraci	3-Butyl-6-formyluracil	Description
11	186.0	185.0	-CHO
4	162.6	163.4	4-carbonyl C of uracyl groups
6	151.5	150.6	6-C of uracyl groups
2	147.6	142.3	2-carbonyl C of uracyl groups
5	115.0	110.4	5-C of uracyl groups
7	44.5	41.9	1-C of n-butyl groups
8	32.3	30.3	2-C of n-butyl groups
9	20.5	20.9	3-C of n-butyl groups
10	14.4	14.5	Methyl C of n-butyl groups

Table A4-3 ^{1}H NMR Peaks of 1-butyl-6-formyluracil and 3-butyl-6-formyluracil

	1-Butyl-6-formyluracil	3-Butyl-6-formyluracil	Description
11	9.57	9.57	Singlet, 1H, CHO
	9.18 (3-NH)	8.47 (1-NH)	(br. Singlet, 1H, NH)
5	6.25	6.30	(Singlet, 1H, =CH)
7	4.19	3.93	(triplet, 2H, CH_2)
8	1.53~1.63	1.57~1.67	(Multiplet, 8H, $4CH_2$)
9	1.33~1.43	1.34~1.44	(Multiplet, 8H, $4CH_2$)
10	0.95	0.94	(triplet, 2H, CH_2)
10	0.95	0.94	(triplet, 2H, CH_3)



Scheme A4-6 *The steric hindrance of C-6 substituents and the hydrogen bonding between the oxygens and 1-N-H*

The alkylation of 6-hydroxymethyluracil, 6-acetoxymethyluracil, 6-(1,3-dioxolan-2-yl)uracil, and 6-(dimethoxymethyl)uracil afforded 1-N substituted products and considerable amount of 3-substituted by-products. One reason is due to the steric hindrance of C-6 substituents but this is not the main reason because the 6-[[(*tert*-butyldiphenylsilyl)oxy]methyl]uracil with even a huge substituent next to it was alkylated mainly at the 1-N position. The main reason may be the hydrogen bonding between the oxygens of C-6 substituents and 1-N-H. The hydrogen bonding makes the 1-N-H group less reactive by any method. It is impossible to selectively alkylate 1-N-H group. We have synthesized the 1-butyl-6-formyluracil by several methods. The protected aldehyde

approach is a more practical method. The chemical agents used in this method are cheap and the reaction conditions are mild and easy to operate. Although the alkylation of the protected aldehyde produced the desired product and two by-products, it is not difficult to separate them. It is a convenient and economical way to synthesize the 1-butyl-6-formyluracil in large scale. Since 6-formyluracil is capable of hydrogen-bonding as well, selective alkylation of this molecule at the 1-position was not successful.

References:

(1) Kwang-Yuen, Z.C.; Cheng, C. C.; *J. Heterocycl. Chem.* **1967**, *4*, 163-165.

(2) Brown, D. T.; Eisinger, J.; Leonard, N. J. *J. Am. Chem. Soc.* **1968**, *90*, 7302-7306.

(3) Ross, L. O.; Goodman, L.; Baker, B. R.; *J. Org. Chem.*, **1960**. *25*, 1950-1953.

(4) Nagpal, K. L.; *J. Med. Chem.*, **1972**. *15* , 121-122

(5) Botta, M.; Angelis, F. D.; Corelli, Menichincheri, M.; Nicoletti, R.; Marongiu, M. E.; Pani, A.; Colla, P. L.; *Arch. Pharm. Bull*, **1991**, *324 (4)*, 203-207

(6) Sulzbacher, M.; Bergmann, E.; Pariser, E. R.; *J. Am. Chem. Soc.*, **1948**, *70*, 2827

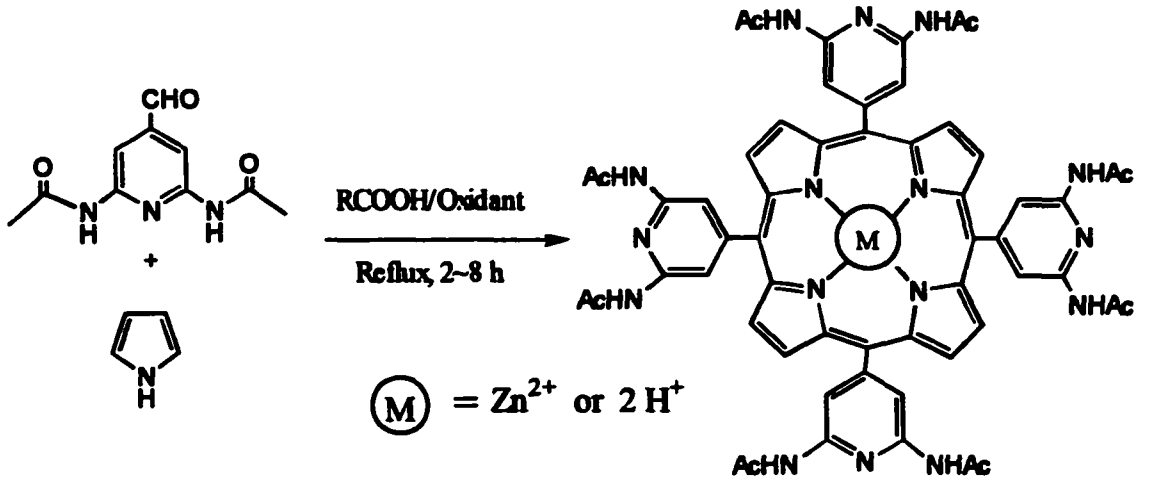
Appendix 5

Synthesis of pyridyl porphyrins

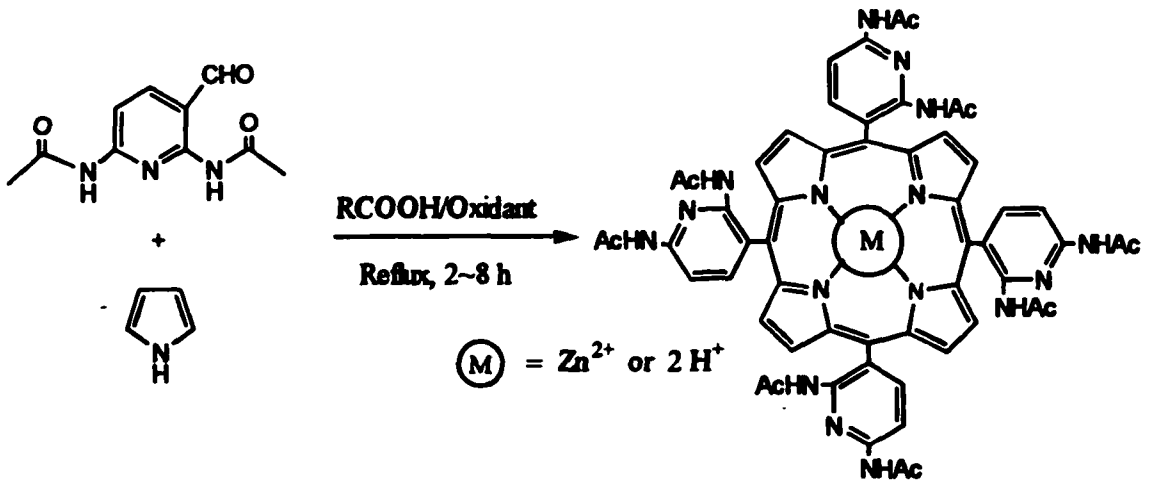
With ample quantities of the two isomeric pyridine aldehydes in hand, a number of porphyrins syntheses were explored. The gentle conditions of Lindsey's method[1] are compatible with diverse array of sensitive, highly functionalized aldehydes. There are two amido groups on their pyridine ring of the two functional aldehydes, so we first tried the Lindsey's two-step one-flask method.[1] Very little porphyrin is obtained and it is not suitable for these porphyrins.

We turned to Adler's one-pot method.[2] Aldehyde and pyrrole (0.1M each) are combined in refluxing acetic acid, propionic acid, or a mixture of acetic acid and nitrobenzene with zinc acetate or without zinc acetate. For the 2,6-diacetamido-4-formylpyridine, all these conditions give pretty good results. But for its isomer, it was necessary to add zinc acetate to form the porphyrin. If the zinc acetate was not added, there was almost no porphyrin formed. Both nitrobenzene and zinc acetate were needed for obtaining best yields (13%).

The effect of zinc acetate is very different in the syntheses of the two isomeric porphyrins. The zinc ions have several favorable functions during forming porphyrins. First, it is generally taken for granted that the zinc ion has a template effect acting during the cyclization process. Second, in the presence of zinc salt, the porphyrinogen can be efficiently oxidized by oxygen to the zinc porphyrinogenate, because the porphyrin zinc complex is more stable to the reaction conditions than the free porphyrin.[3] Moreover, the zinc acetate could increase the reactivity of 2,6-diacetamido-3-formylpyridine by binding



Reaction conditions	Acetic acid		Acetic acid / Nitrobenzene		Propionic acid	
	Zn Salt	No Zn Salt	Zn Salt	No Zn Salt	Zn Salt	No Zn Salt
Yields	27.6%	19.0%	17.6%	22.2%	23.0%	26.7%
Reaction Time	8h	8h	2h	2h	2h	2h



Reaction Conditions	Acetic acid		Acetic acid / Nitrobenzene		Propionic acid	
	Zn Salt	No Zn Salt	Zn Salt	No Zn Salt	Zn Salt	No Zn Salt
Yields	3.2%	<0.5%	13.0%	<0.5%	4.9%	<0.5%
Reaction Time	8 h	8 h	2 h	2 h	2 h	2 h

Scheme A5-1 ***Research on the synthesis of the 5,10,15,20-tetrakis(3,5-diacetamido-4-pyridyl)porphyrin (top) and 5,10,15,20-tetrakis(2,4-diacetamido-3-pyridyl)porphyrin (bottom) by Adler's method in different reaction conditions. Yields were determined spectroscopically form the reaction mixture.***

to the nitrogen of pyridine. The 'complex' results in an electron withdrawing effect, increasing the reactivity of aldehyde group.

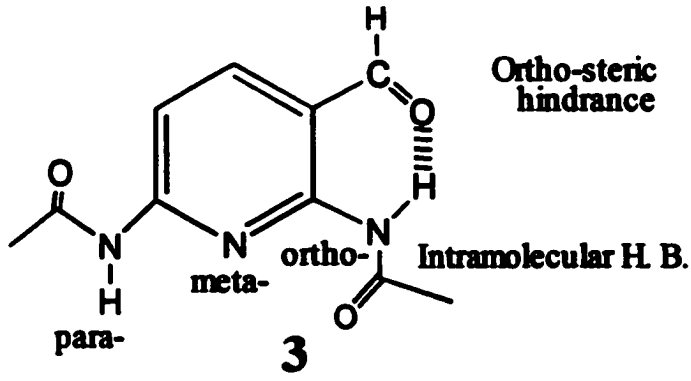
The nitrobenzene is a joint oxidant with oxygen, it enhances the oxidation ability of oxygen to oxidize the intermediate porphyrinogen to the porphyrin.[3] The porphyrinogens are very efficiently oxidized to porphyrins by nitrobenzene in acetic acid. The mixture of acetic acid and nitrobenzene has proved to be a substantial improvement in the synthesis of tetrakis(2,4-diacetamido-3-pyridyl)porphyrin (13%).

For the tetrakis(2,4-diacetamido-3-pyridyl)porphyrin, the TLC and UV-*vis* spectra of the solution after column chromatography showed that there were several different porphyrins formed. The 2,4-diacetamido-3-pyridyl groups were rigidly linked to the porphyrin macrocycle and rotation about the connecting bond is hindered by the *ortho*-acetamido groups on the pyridines. Thus, tetrakis(2,4-diacetamido-3-pyridyl)porphyrin has four rotameric forms---αααα, ααaβ ααββ, and αβαβ---with respect to the relative orientation of the four 2,4-diacetamido-3-pyridyl groups.

Discussion of substituent effect:

From the above experimental results, the two isomeric aldehydes have very different reactivity. These can be explained from the steric and electronic effects of their substituents (see Scheme A5-1). First considering the steric effects, the two amido groups of 2,6-diacetamido-4-formylpyridine (4) are located at *meta*-positions, so there are little or no steric effects. In its isomer 2,6-diacetamido-3-formylpyridine (3), one amido group is on the *ortho*-position, so there should be a definite steric hindrance to the attack at the carbonyl carbon during the addition, condensation, and ring-closure steps. Steric hindrance

by substituents on the aldehyde moiety can subvert the reaction at the steps where structural changes occur.



2,6-diacetamido-3-(or –4-)formylpyridine	
Isomer (3)	Isomer (4)
Steric Effects	
Ortho-steric hindrance	No steric hindrance
Electronic Effects	
N of pyridine ring (electron withdrawing) favors the initial condensation step	
on *meta*-position	on *para*-position
only inductive effect	inductive and resonance effect
The acetamido groups (electron donating) disfavor the initial condensation steps	
ortho- and *para*-positions	on *meta*-positions
inductive and resonance effect	only inductive effect

Scheme A5-2 *Substituent electronic effects and steric effects of 2,6-diacetamido-4-formylpyridine (4) and 2,6-diacetamido-3-formylpyridine (3)*

Considering electronic effects, the functional groups of the two aldehydes are exactly same only their positions are different. (i) The nitrogen atom of pyridine ring has similar electronic effects as the nitro group in nitrobenzene (electron withdrawing) and favors the initial condensation steps by making the carbonyl carbon more susceptible to nucleophilic attack by the α carbon of the pyrrole. But the effectiveness of the property is different for the aldehydes because the position of the pyridine nitrogen relative to the aldehyde group. The pyridyl nitrogen of the 2,6-diacetamido-4-formylpyridine is located at the *para*-

position relative to the aldehyde group, so it has both inductive and resonance effects. However the pyridyl nitrogen of the 2,6-diacetamido-3-formylpyridine is located at the *meta*-position relative to the aldehyde group, so only has inductive effects. (ii) The amido groups (electron donating) disfavor the initial condensation steps. But the extent of this effect for the two aldehydes is different because of the position of the amide groups relative to the aldehyde group. Both amide groups of the 2,6-diacetamido-4-formylpyridine are located at *meta*-positions relative to the aldehyde group, they only have inductive effects on the aldehyde group. However the two amide groups of the 2,6-diacetamido-3-formylpyridine are located at on the *para*- and *ortho*-positions relative to the aldehyde group, so they have both inductive and resonance effects.

Moreover one amido group of the 2,6-diacetamido-3-formylpyridine is located at an *ortho*-position relative to the aldehyde group and the two groups are suitable for forming intramolecular hydrogen bonding. The formation of intramolecular hydrogen bonding would increase the reactivity of the aldehyde, somewhat compensating for the unfavourable electronic and steric effects.

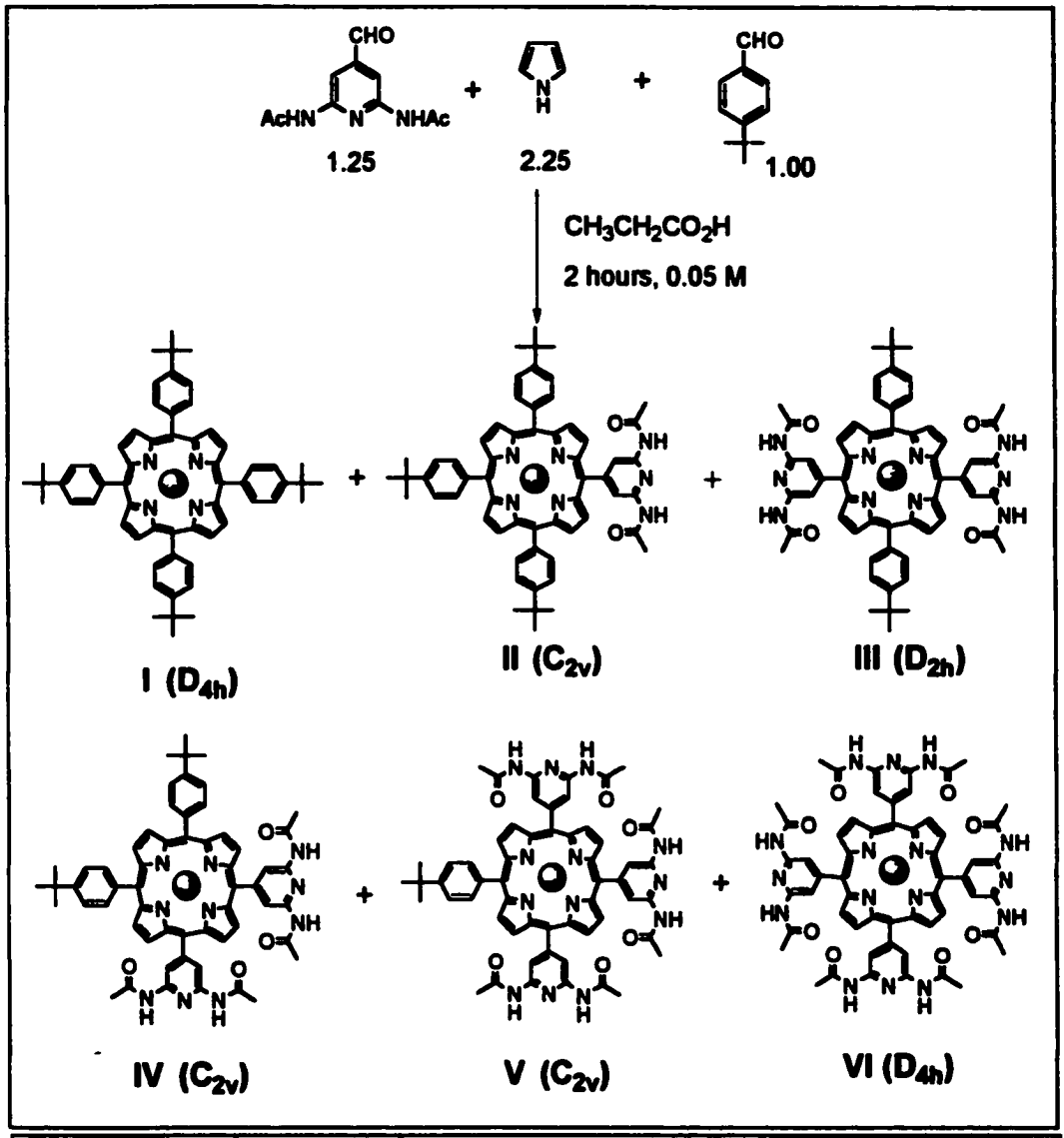
In summary, **from both electronic and steric effects** we can conclude that the 2,6-diacetamido-4-formylpyridine (**4**) reacts with pyrrole to form porphyrins much easier than its isomer (**3**).

Synthesis of the 3,5-diacetamido-4-pyridyl/*tert*-butylphenyl porphyrins

Since the four *meso*-positions of porphyrins are at 90° from each other, there are five possible porphyrin building blocks per hydrogen-bond moiety. The synthesis of these substituted porphyrins may be accomplished by means of a mixed-aldehyde approach.[4]

This mixed-aldehyde method gives a statistical mixture six porphyrins. With equal moles of two aldehydes, a statistical mixture of six porphyrins (A_4:A_3B:(A_2B_2+ABAB):AB_3:B_4 = 1:4:6:4:1) is expected,[4c] but these proportions are to some extent determined by the relative rates of reactivity of the starting aldehydes and the solubility of the various intermediates. The separation of this mixture is usually not too difficult. Since all five functional porphyrins can be obtained in one reaction, and all of them are interesting and useful, this is an acceptable method. We can separate the porphyrin mixtures by 'flash' chromatography.

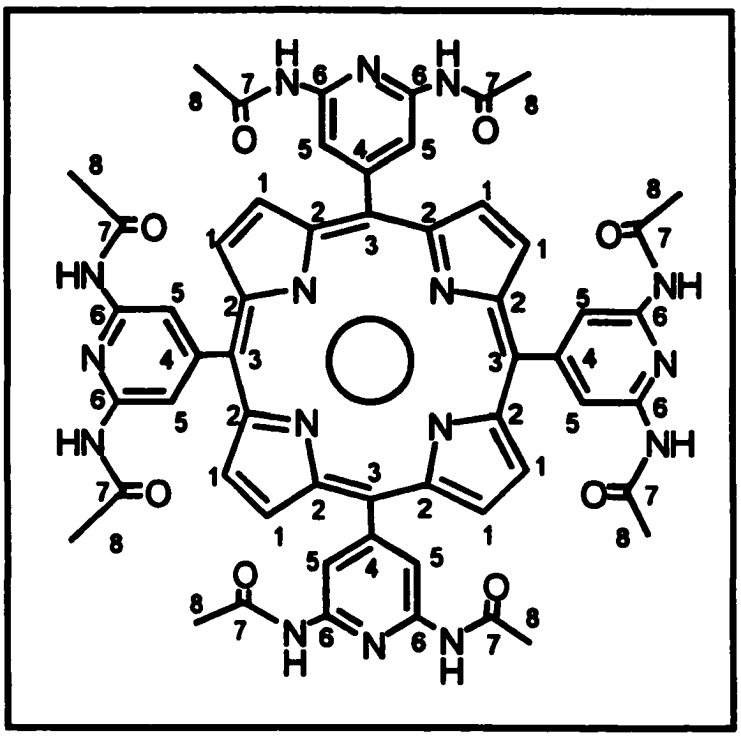
The pyridyl porphyrins were prepared by means of a mixed-aldehyde approach (see Scheme A5-3.). The symmetrical porphyrins (I) and (VI) can be obtained from the mixture of pyrrole and one aldehyde so we did not take care to isolate the small quantities of these compounds from the mixed aldehyde reaction mixture. The other four asymmetrical pyridyl porphyrins were more important in our project and could not be obtained easily from other methods. In order to increase the yield of the four asymmetrical pyridyl porphyrins we adopted two measures: (i) increasing the amount of the 2,6-diacetamido-4-formylpyridine (1.25 times large than the 4-*tert*-butylbenaldehyde), (ii) decreasing the concentration of the reaction mixture (0.05 M) (normal concentration in the Adlar method is 0.1 M). These measures worked very well and made an ideal distribution. The relative amounts of the four asymmetrical porphyrins are high [II(25%), III(20%), IV(25%), and V(15%)] and the relative amounts of the two symmetrical porphyrins are small [I(10%), and VI(5%)]. Since the polarities of the two *meso*-substituted groups are very different, six porphyrins were separated easily by column chromatography.



Compound	Rf	Developing Sovlents	Rel. Amount
I	0.89	EtOAc:EtOH(9:1)	15%
II	0.69	EtOAc:EtOH(9:1)	25%
III	0.50	EtOAc:EtOH(9:1)	20%
IV	0.16	EtOAc:EtOH(9:1)	25%
V	0.43	EtOAc:EtOH(1:1)	10%
VI	0.26	EtOAc:EtOH(1:1)	~5%

Scheme A5-3 ***A combinatorial porphyrin synthesis: Six porphyrins are obtained from the mixture of pyrrole and 2,6-diacetamido-4-formylpyridine and 4-tert-butylbenzaldehyde. The 4-tert-butylphenyl group makes it easier to separate the porphyrins and improves their solubility in organic solvents.***

The Rf values and approximate relative amounts (estimated from TLC and column separation) of each porphyrin are given in Scheme A5-3 for the six porphyrins. As expected, the more polar compounds had lower Rf values.



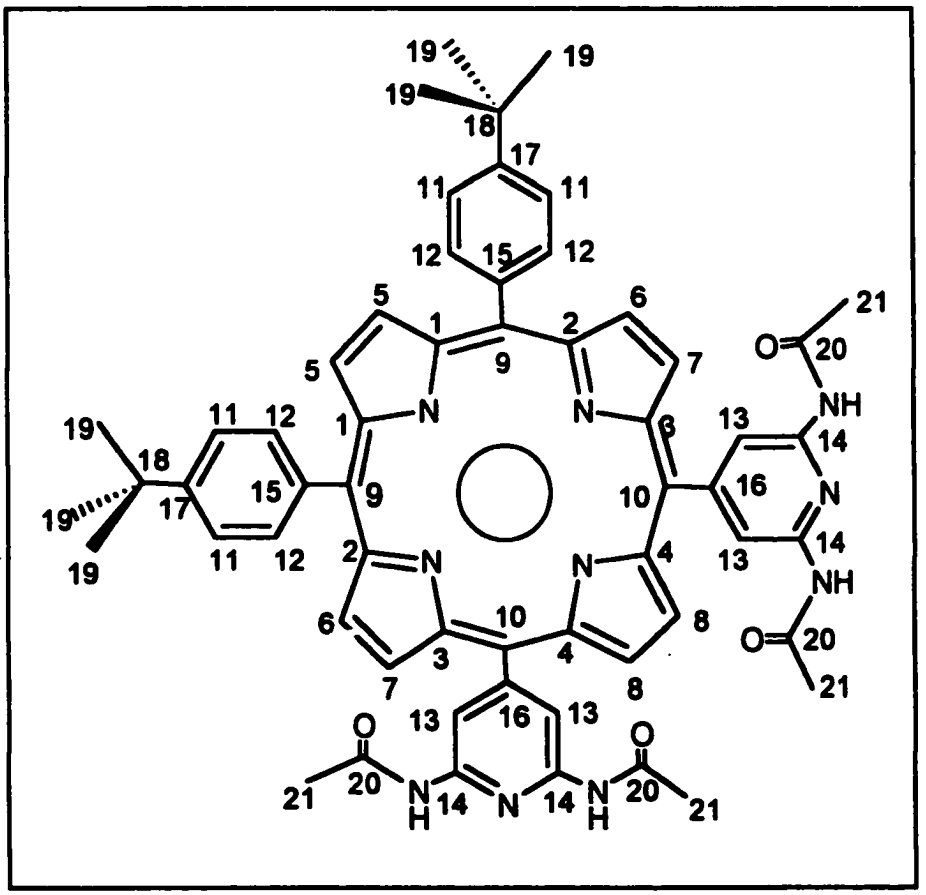
Scheme A5-4 *Structure of the tetrakis(3,5-diacetamido-4-pyridyl)porphyrin(VI)*

Table A5-1 ^{1}H NMR peaks of the tetrakis(3,5-diacetamido-4-pyridyl)porphyrin(VI)

hydrogen	ppm	description	^{1}H of the aldehyde
	10.52	s, 8 H, 8 amide NH	10.33
1	8.99	s, 8 H, β-H of pyrrole	
5	8.60	s, 8 H, 3-H of pyridine	8.11
8	2.16	s, 18 H, methyl-H of amide	2.10
	-3.10	s, 2 H, 2 N-H	

Table A5-2 ^{13}C **NMR peaks of the tetrakis(3,5-diacetamido-4-pyridyl)porphyrin(VI)**

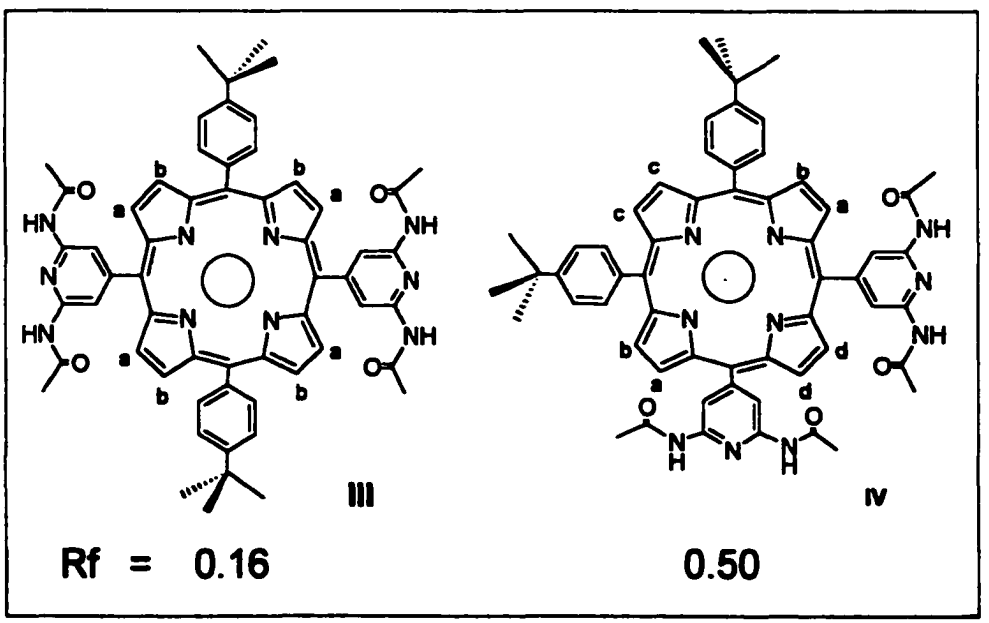
carbon	ppm	description	^{13}C of the aldehyde
7	170.3	carbonyl C of amido groups	170.7
4	152.8	4-C of diacetamidopyridyl groups	152.6
5	149.6	3-C of diacetamidopyridyl groups	146.5
2	131.5~132.6	α-C of pyrrole	
6	123.8	2-C of diacetamidopyridyl groups	108.9
3	118.9	*meso*-C of porphyrin	194.1(-CHO)
	115.9	β-C of pyrrole	
8	24.7	methyl C of amido groups	25.3



Scheme A5-5 *Structure of the 5,10-bis(3,5-diacetamido-4-pyridyl) 15, 20-bis(4-tert-phenyl)porphyrin(VI)*

Table A5-3 ^{13}C **NMR peaks of the 5,10-bis(3,5-diacetamido-4-pyridyl) 15, 20-bis(4-*tert*-butylphenyl)porphyrin(VI)**

	Carbon	Ppm	Description
A	20	170.3	carbonyl C of amido groups
B	16	153.1	4-C of diacetamidopyridyl groups
C	15	150.9	4-C of *t*-butylphenyl groups
D	13	149.6	3-C of diacetamidopyridyl groups
E	17	138.6	1-C of *t*-butylphenyl groups
F	11, 12	134.7	2, 3-C of *t*-butylphenyl groups
G	1, 2, 3, 4	131.2~132.6	α-C of pyrrole
H	5, 6, 7, 8	124.3	β-C of pyrrole
I	10	121.5	*meso*-C attached to Py
J	9	117.9	*meso*-C attached to Ph
K	14	115.8	2-C of diacetamidopyridyl groups
L	18	35.1	*tert*-C of *t*-butyl groups
M	19	31.9	methyl C of *t*-butyl groups
N	22	24.7	methyl C of amido groups



Scheme A5-6 *Two meso-disubstituted pyridyl porphyrins: trans isomer (III) and cis isomer (IV).*

The disubstituted pyridyl/phenyl porphyrins have two isomers: *trans* (III) and *cis* (IV). The confirmation of the *trans* and *cis* configurations can be provided by the ^{1}H NMR spectrum. There are four different kinds of pyrrole β-Hs in *cis*-isomer, based upon the identity of their nearest and next nearest *meso* neighbors (see Scheme A5-6). H_a nearest to Ac_2Py and next-nearest to *t*-BuPh, while H_b the reverse, H_c nearest and next-nearest to *t*-BuPh, and H_d nearest and next-nearest to Ac_2Py. The chemical shift of H_c and H_d are identical and give two unsplit signals, H_b and H_a have their proton resonances split into an AB quartet. There are two different kinds of pyrrole β-Hs in *trans*-isomer. This showed an AB-type spin-system in the region of the porphyrin β-hydrogen. This is indicative of two different β-hydrogen environments, only possible with a '*trans*' configuration of the *meso*-substituted porphyrin. The nmr data was helpful in distinguishing between the disubstituted isomers. The structural assignments given to the two isomers were also made on the basis of their Rf values. The *trans*-isomer (III)(Rf = 0.50) would be expected to have a small dipole moment relative to the *cis*-isomer (IV) (Rf = 0.16). The less polar compound would be expected to have a larger Rf value, hence the assignments.

References:

(1) (a) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827-836. (b) Gryko, D.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 2249-2252.

(2) (a) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476-480. (b) Johnstone, R. A. W.; Nunes, M. L. P. G.; Pereira, M. M.; Gonsalves, A. M. d'A. R.; Serra, A. C. *Heterocycles* **1996**, *43*, 1423-1436.

(3) Gonsalves, A. M. d'A. R.; Varejao, J. M. T. B.; Pereira, M. M. *J. Heterocycl. Chem.* **1991**, *28*, 635-640.

(4) (a) Little, R. G.; Anton, J. A.; Loach, P. A.; Ibers, J. A. *J. Heterocycl. Chem.* **1975**, *12*, 343-349. (b) Walker, F. A.; Balke, V. L.; McDermott, G. A. *Inorg. Chem.* **1982**, *21*, 3342-3348. (c) Milgrom, L. R. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 1483-1487.

Appendix 6

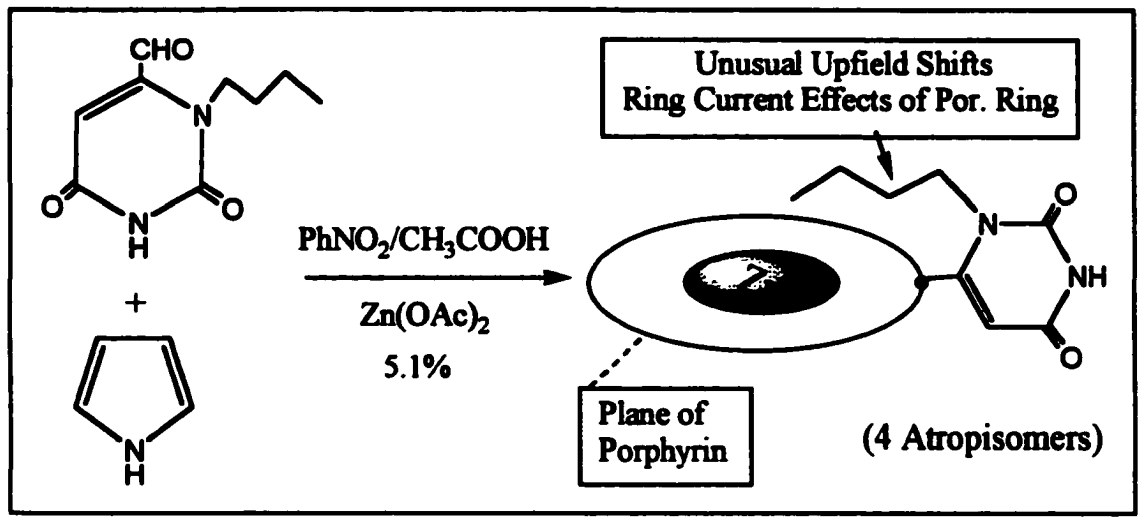
Synthesis of the Uracyl Porphyrins

With ample quantities of the 1-butyl-6-formyluracil in hand a number of porphyrin syntheses were explored. We first tried the Lindsey's two-step one-flask method,[1] but no porphyrin was detected in the reaction mixture by spectroscopic methods. We turned to the Adler one-pot method,[2] in which aldehyde and pyrrole are combined in refluxing propionic or acetic acid in air. No porphyrin was detected in this reaction mixture either. Considering our modified Adler procedure using 2,4-diacetamido-3-formylpyridine to prepare porphyrin in pretty good yeild, we tried modification in the Adler procedure.

Equivalents of pyrrole and 1-butyl-6-formyluracil and half equivalent of zinc acetate were added to a boiling mixture of acetic acid and nitrobenzene (3:2). The reaction mixture was refluxed for 10h. 5.1% of the desired porphyrin was detected in the reaction mixture. During the course of the investigation, several cases were found that required a modified Adler procedure (such as the addition of zinc acetate and nitrobenzene). Although the 5.1% yield is low, this may still allow for the production of gram-scale quantities of the porphyrin. There are at least two reasons that can account for the lower yield: a) The 1-butyl-6-formyluracil is non-aromatic aldehyde; b) There is a large butyl group next to the aldehyde group.

The 1-butyl-6-formyluracil is the first non-aromatic sterically hindered hertocyclic aldehyde used to prepare porphyrins. The experimental results showed that it was necessary to add zinc acetate and nitrobenzene for the synthesis of tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn). If neither the zinc acetate nor nitrobenzene were added, there was no

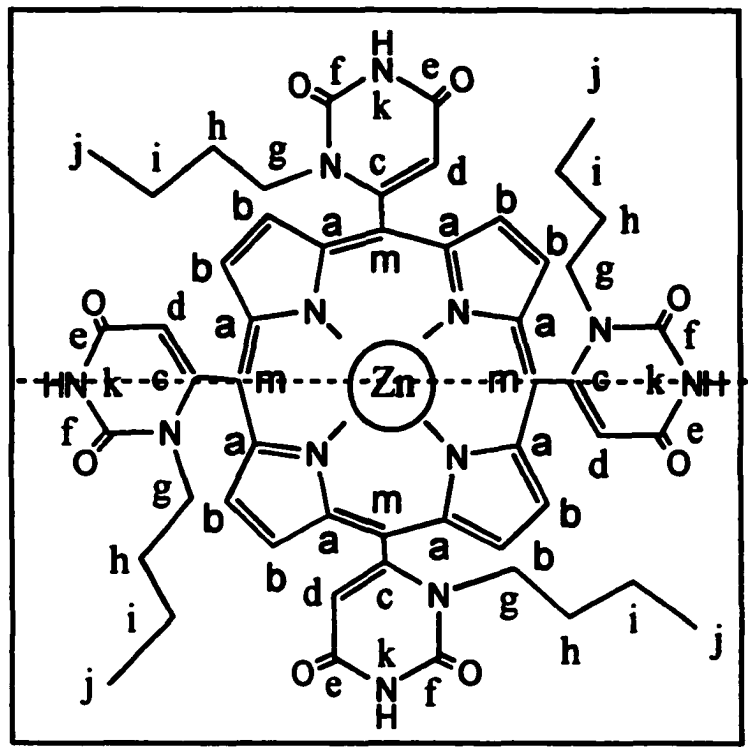
porphyrin formed. This results in the formation of the porphyrin(Zn), which is easily transformed to free-base porphyrin by 6M HCl.



Scheme A6-1 *Synthesis of tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn) by a modified Adler's method. There are four atropisomers of the porphyrins —αααα, ααaβ ααββ, and αβαβ-- -with respect to the relative orientation of the four 1-butyl-6-uracyl groups. The peaks corresponding to the butyl groups are shifted upfield due to ring current effects.*

The zinc ions have several favorable functions during the forming porphyrins. First, it is generally taken for granted that the zinc ion has a template effect during the cyclization process. Second, in the presence of zinc salt, the porphyrinogen can be efficiently oxidized by air to the zinc porphyrinogenate, because the porphyrin(Zn) is more stable to the reaction conditions than the free base porphyrin.[3] The mixture of acetic acid and nitrobenzene is more efficient in promoting the oxidation of the intermediate porphyrinogens to the porphyrins. The nitrobenzene and air use as joint oxidants, and the presence of both nitrobenzene and air are necessary for obtaining best yields.

^{1}H NMR results showed that there were several isomeric porphyrins formed, and that the butyl groups are positioned over the macrocycle. There is only one long spot on their TLC plate, and it is difficult to separate these rotamers on a normal column.



Scheme A6-2 *Structure of the tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn)*

Table A6-1 ^{13}C NMR peaks of the tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn)

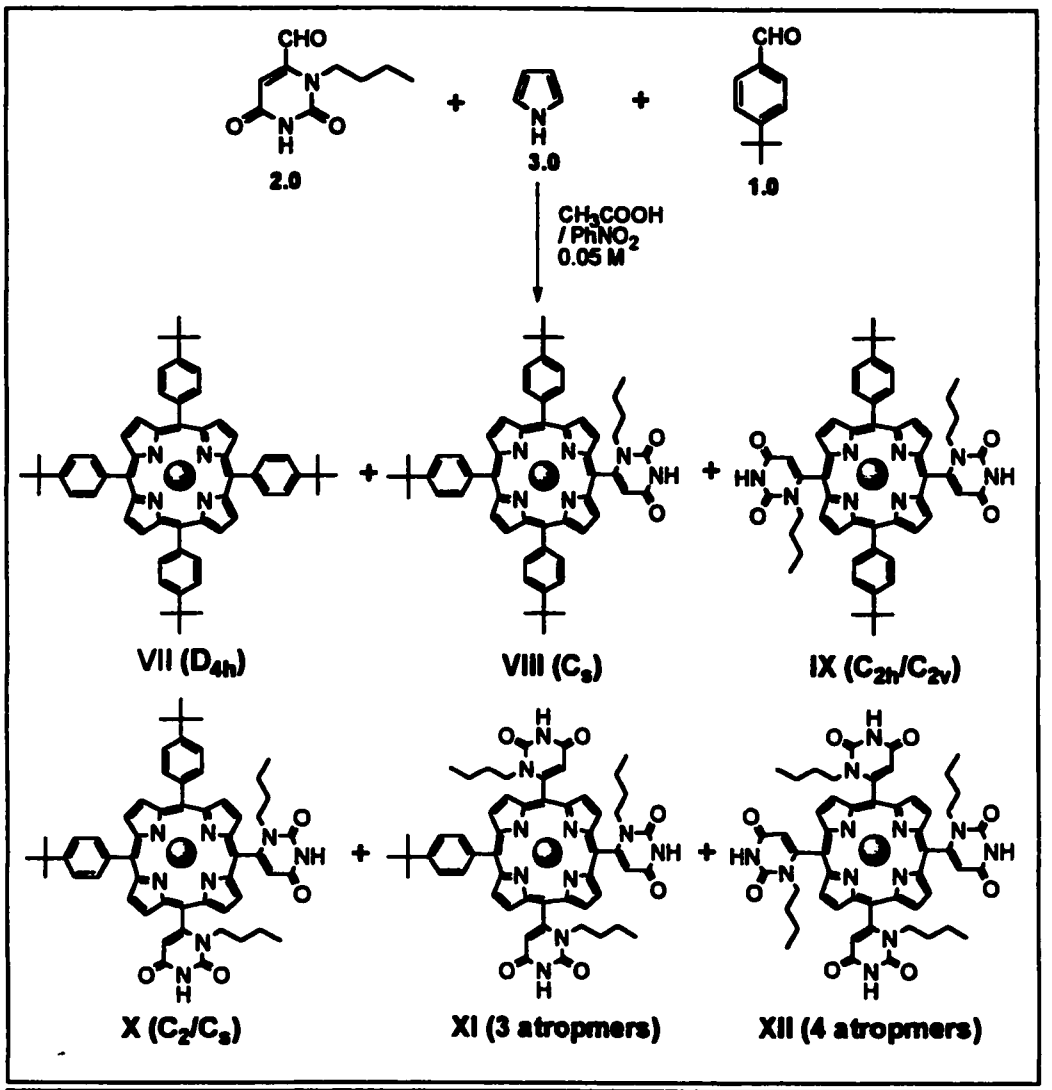
Carbon	ppm	Description	^{13}C of the Aldehyde
e	162.9	4-carbonyl C of uracyl groups	162.6
c	155.2	6-C of uracyl groups	147.6
f	152.3	2-carbonyl C of uracyl groups	151.5
b	149.8	β-C of pyrrol	
a	133.6, 133.7	α-C of pyrrol	
m	112.0, 111.9	*meso*-C	186.0 (-*CHO)
d	110.4, 110.7	5-C of uracyl groups	115.0
g	41.9	1-C of *n*-butyl groups	44.5
h	30.3	2-C of *n*-butyl groups	32.3
i	20.9	3-C of *n*-butyl groups	20.5
j	14.9	methyl C of *n*-butyl groups	14.4

Table A6-2 ^{1}H NMR peaks of the tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn)

Hydrogen	Ppm	Description (DMSO-d_6)	^{1}H of the Aldehyde ($CDCl_3$)
K	11.83	Br. s, 4 H, 4 NH, imide	9.18 ($CDCl_3$, br. s, 1H, NH)
B	9.45	s, 8 H, 8 CH, β-H pyrrole	
D	6.26	s, 4 H, 4 =CH, vinyl	6.25 (s, 1H, =CH)
G	3.08~3.56	m, 8 H, 4 CH_2, butyl	4.19 (t, 2H, CH_2)
H	0.91~1.10	m, 8 H, 4 CH_2, butyl	1.53~1.63 (m, 8H, 4 CH_2)
I	0.08~0.30	m, 8 H, 4 CH_2, butyl	1.33 ~1.43 (m, 8H, 4 CH_2)
J	-0.14, -0.19, -0.31, -0.55	Approximate ratio of 4 sets of triplet peaks is 2:1:2:1, 12 H, 4 CH_3, butyl	0.95 (t, 2H, CH_3)

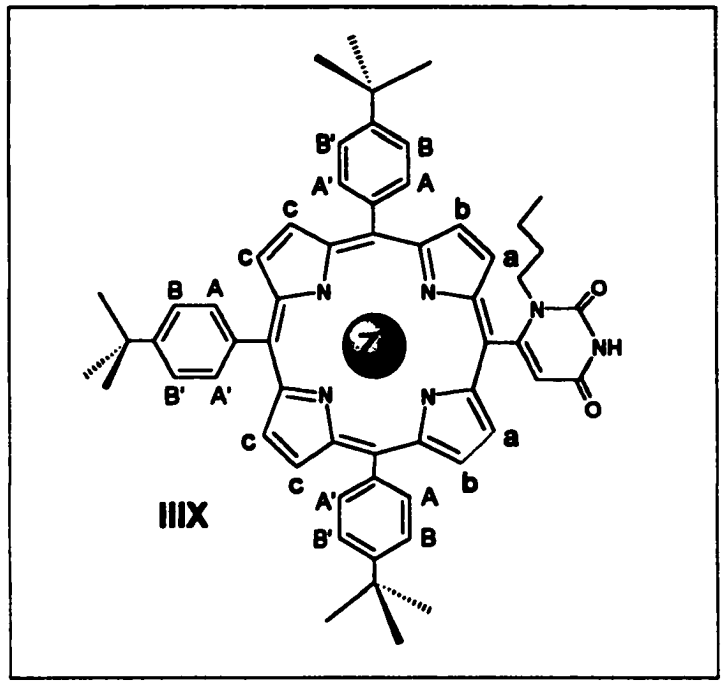
Synthesis of 1-butyl-6-uracyl /4-*tert*-butylphenyl porphyrins

The other uracyl porphyrins were also prepared by this modified Adler method: 1-butyl-6-formyluracil and zinc acetate were added to a boiling mixture of acetic acid and nitrobenzene, pyrrole was added immediately. After 10 min. 4-*tert*-butylbenzaldehyde was added to the reaction mixture and then refluxed for ten hours. 22.4% yield of the mixture of porphyrins was detected spectroscopically in the reaction mixture. The Rf values and approximate relative amounts of each porphyrin (estimated by TLC and column separation) are given in the scheme A6-3 for the six porphyrins. As expected, the more polar compounds had lower Rf values.



Compound	Rf	Developing Sovlents	Rel. Amount
VII	0.76	EtOAc:PE(1:1)	15%
VIII	0.63	EtOAc:PE(1:1)	45%
IX	0.37	EtOAc:PE(1:1)	15%
X	0.14	EtOAc:PE(1:1)	20%
XI	0.67	EtOH:EtOAc(1:9)	~4%
XII	0.32	EtOH:EtOAc(1:9)	~1%

Scheme A6-3 *A combinatorial porphyrin synthesis: Six porphyrins are obtained from the mixture of pyrrole, 1-butyl-6-formyluracil, and 4-tert-butylbenzaldehyde. The 4-tert-butylphenyl groups make the porphyrin mixtures make easier to separate on the column, and improve their solubility in organic solvents.*



Scheme A6-4 *Structure of tri(4-tert-butylphenyl)(1'-butyl-6'-uracyl)porphyrin(Zn) Symmetry labels a, b, c, and A, B, A', B' are discussed in the text*

The reaction mixture was purified by removing the acetic acid on a rotating evaporator, loading the resultant dark material on silica gel column, and eluting with petroleum ether, petroleum ether-ethyl acetate (1:1), ethyl acetate, ethyl acetate-ethanol (4:1) respectively. We have separated and characterized three of the five uracyl porphyrins ---5-, 5,10-, 5,15-bis(1'-butyl-6'-uracyl)porphyrin from the mixed-aldehyde reaction mixture. The 5- (45%), 5,15- (15%), 5,10- (20%) 1-butyl-6-uracyl porphyrins were formed in rather high ratios (see Scheme A6-3). The tetrakis(1'-butyl-6'-uracyl)porphyrin(Zn) has been separated and characterized, vide supra. The amount of tri(1'-butyl-6'-uracyl)porphyrin(Zn) is relatively small, and it is difficult to separate from the reaction mixture. In order to prepare the tri(1'-butyl-6'-uracyl)porphyrin(Zn), we can increase the

relative amount of the 1-butyl-6-formyluracil (4 or 5 times large than the 4-*tert*-butylbenzaldehyde).

References:

(1) (a) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827-836. (b) Gryko, D.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 2249-2252.

(2) (a) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476-480. (b) Johnstone, R. A. W.; Nunes, M. L. P. G.; Pereira, M. M.; Gonsalves, A. M. d'A. R.; Serra, A. C. *Heterocycles* **1996**, *43*, 1423-1436.

(3) Gonsalves, A. M. d'A. R.; Varejao, J. M. T. B.; Pereira, M. M. *J. Heterocycl. Chem.* **1991**, *28*, 635-640.

Chapter 2

Self-Assembled Multi-Porphyrin Arrays Mediated by Self-Complementary Quadruple Hydrogen Bond Motifs

Abstract: Discrete squares and tapes of porphyrins are self-assembled by self-complementary hydrogen bonding between diacetamidopyridyl recognition groups rigidly linked to the chromophore.

Introduction

Porphyrins and their cousins the phthalocyanins have attracted considerable attention recently because of their potential use as components of nanometer scale photonic devices and materials.[1] The functionality of many, if not most, photonic devices,[1] including those found in nature,[2] strongly depends on the relative order of the chromophores throughout the entire material and on the mode of assembly. Supramolecular chemistry has been used as a stratagem to achieve the desired geometric order of porphyrin and other entities in both the solids and in solution.[3] Crystallization of porphyrins bearing groups capable of hydrogen bonding has yielded fascinating networks,[3,4] and co- crystallization with other compounds has yielded interesting host-guest[3,5] and magnetic[5] materials. Yet consistently predicting long range three-dimensional order in crystals remains elusive. Several discrete hydrogen bond[6] and metal ion[7] assembled porphyrin systems in solution also have been reported. In order to better understand the role of non-covalent bonds in mediating electron and energy transfer in biological systems such as photosynthetic antenna complexes,[2] several non-coplanar or

non-rigid hydrogen bonding supramolecular porphyrin – electron acceptor species have been synthesized and characterized.[8,9] One of the primary goals of work reported herein is to understand the process of self-assembly and to reliably predict the structure of self-assembled porphyrin arrays in solution, as opposed to the solid state where packing and other forces may determine the structure of the lattice. We report the self-assembly of several rigid, co-planar multiporphyrin arrays and tapes by self-complementary hydrogen bond motifs that exploit both the directionality of the recognition groups and the square planar geometry of the porphyrin macrocycle to design predictable arrays in high yields. Though topologically similar to the square porphyrin arrays formed by coordination chemistry,[3,7] it is well understood that the nature of the self-assembly linker has profound effects on the properties of the resultant array. For example, if porphyrin fluorescence is a desired property of the array, metal ion assembly is generally deleterious. Thus this, and hetero-complimentary modes of hydrogen bonding further expands the repertoire of porphyrinic building blocks, and their potential applications.

Experimental Section

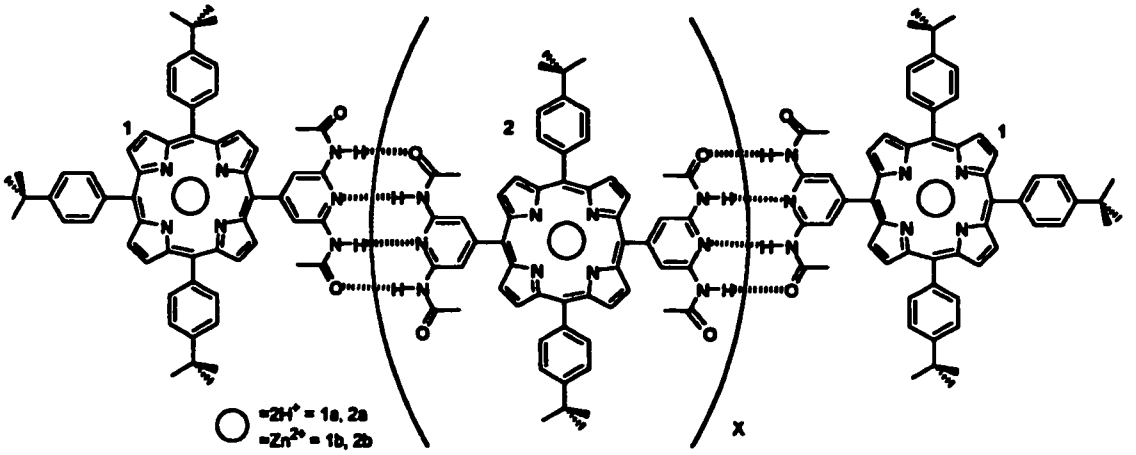
Instrumentation: Steady state and fluorescence life time measurements (phase modulated) were made on a Spex Tau-3 instrument. Varian 400 MHz and Joel 300 MHz NMR, Hewlett-Packard HP 1100 LC/MSD, and a Carey Bio-3 were used in characterization of the compounds and assemblies.

The complete synthesis and characterization of the porphyrin building blocks, as well as the starting aldehydes will be described elsewhere, but were made via modifications of the Adler[15a] or in lower yields by the solventless[15b] synthesis using a mixed aldehyde

approach.[7] All compounds had satisfactory ^{1}H and ^{13}C NMR, electrospray ionization mass, and uv-visible spectra, as did all the squares and tapes. The electronic spectra were taken in toluene or chloroform and the NMR in chloroform-d and toluene-d_8 unless noted otherwise. Since these are self-complementary species, self-assembly is accomplished by adding **1a** or **1b** for the dimer, and **3a** or **3b** for the square to an aprotic solvent – usually toluene, chloroform, or 2-methyltetrahydrofuran. The amount of the self-assembled species depends on the resultant thermodynamic equilibrium, thus on solvent, temperature and concentration.

Result and Discussion

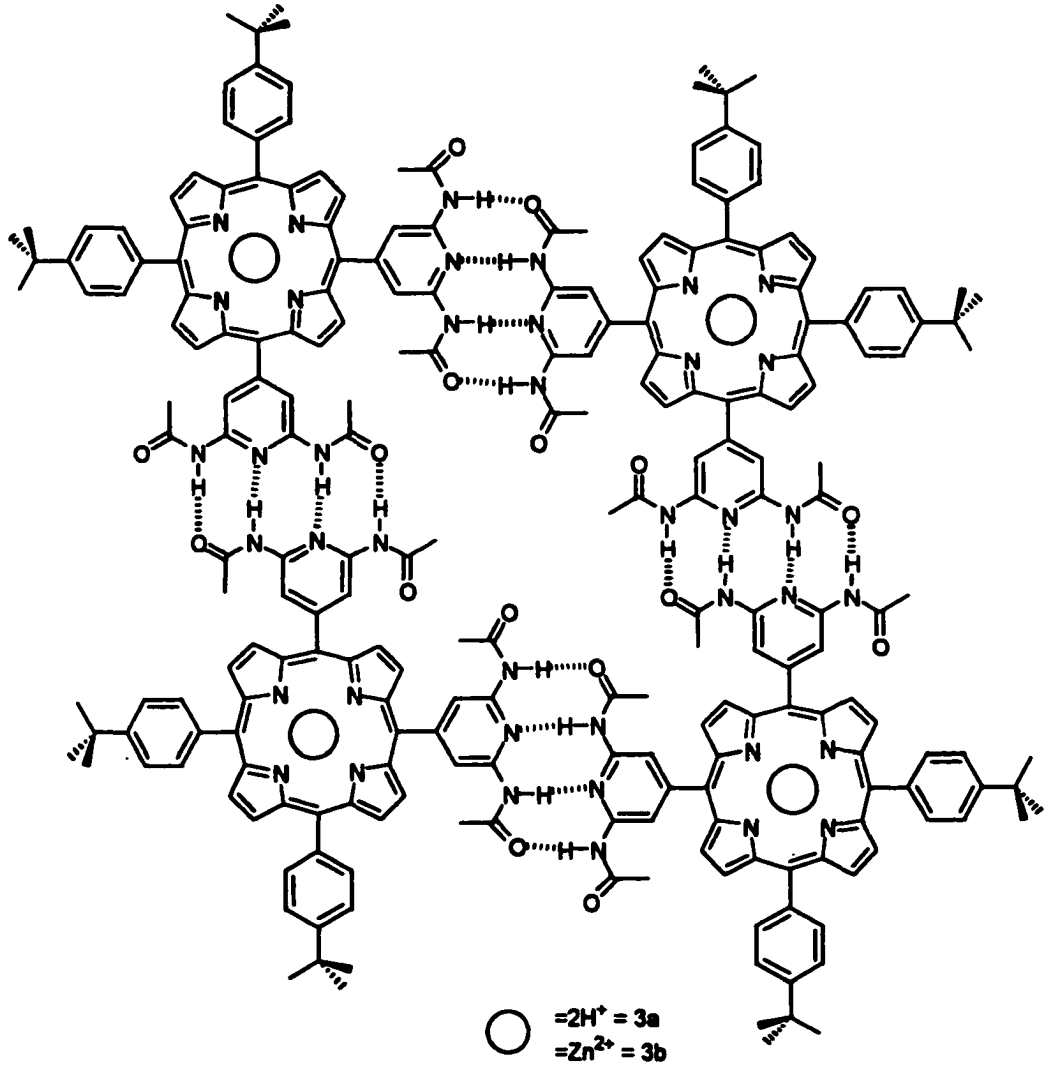
There are several ways in which 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-tertbutylphenyl)porphyrin, [10,11] **1a**, may form a dimer by self-complementary hydrogen-bonds.[12] With two hydrogen-bonds the dimer would be bent with respect to the porphyrin planes, yet with rotation about the amide bonds, a linear, quadruple hydrogen bonded system forms (see Scheme 1). The directionality and the increased stability of the quadruple hydrogen bond system may be exploited to form a variety of one and two-dimensional porphyrin structures. In the present case we demonstrate this by the formation of linear dimers with the 5-substituted compound, linear trimers using a 2:1 stoichiometry of the 5 and the 5,15-substituted compounds, **1a**, **2a**, respectively, and a linear tetramer using a 2:2 ratio of **1a** to **2a**. Additionally, a square tetramer is formed cooperatively from only the 5,10-diacetamidopyridyl substituted porphyrin, **3a** (see Scheme 2).



Scheme 1 *The 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-tertbutylphenyl)porphyrin, 1a, and 5,15-bis(3,5-diacetamido-4-pyridyl)-10, 20-bis(4-tertbutylphenyl)porphyrin, 2a, may form a dimer, trimer, tetramer, or polymers by self-complementary hydrogen-bonds.*

If there are no dynamic processes occurring on the NMR[13] time scale, both the number of species self-assembling into the final structure, n, and the equilibrium constants, K, may be determined by ^{1}H-NMR experiments that monitor the chemical shift of suitable protons versus the concentration of the self-complementary porphyrin.[14,6] Noting the usual caveats and that these experiments do not yield structural information *per se*, fits of these curves for solutions of **1a** [11] indicate that the ultimate self-assembled product contains ~2 units – consistent with the dimeric structure shown in scheme 1, where x = 0. For the linear systems these experiments and their fits show that ~3.2 units are in the final assembly when a 2:1 mixture of **1a** and **2a** is used to form the trimer, and ~4.1 subunits are present in the 2:2 mixture of the same subunits (Scheme 1, where x =1, and x =2 respectively). In the case of the linear tapes, there is no *a priori* reason that all of the self-assembled structures in the chloroform solution are the 2:1 trimers, and 2:2 tetramers, thus the NMR results are likely indicative of a mixture of dimers, trimers, tetramers, etc. substantially weighted toward the tape resulting from the starting

stoichiometries. However, the 180° geometry of the recognition groups on the central porphyrin(s), and the thermodynamic stability of the quadruple hydrogen bond compared to other conformations with fewer hydrogen bonds, assures that the linear tapes are predominantly present at appropriate stoichiometries and at equilibrium.[11]



Scheme 2 *The 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-tertbutylphenyl) porphyrin, 3a, may form a square tetramer by self-complementary hydrogen-bonds.*

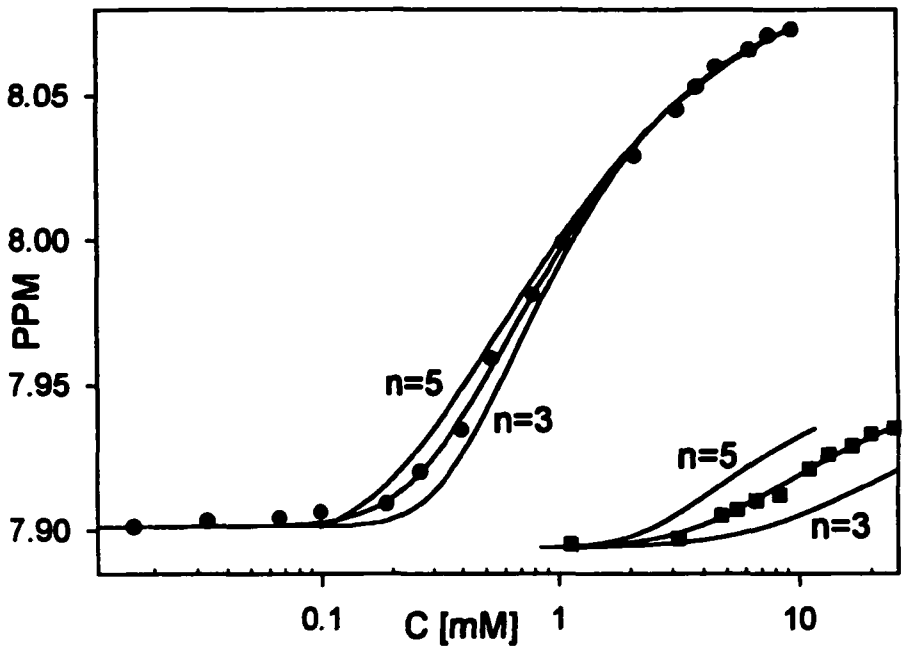


Figure 1 *Chemical shift of the amide NH versus concentration of the self-complementary porphyrins in $CDCl_3$. For* ***3a*** *forming the square (•) the fit yields an n = 3.9; and for a 2:2 ratio of* ***1a*** *to* ***1b****, forming the linear tape (-) n = 4.1.*

The self-assembly of a square tetramer (see Scheme 2) from only **3a** is also indicated by similar plots of concentration versus amide NH chemical shifts. The dramatic differences in these plots for the linear tetramer and closed square tetramer are seen in Figure 1 (the 3'H of the pyridyl moiety yield similar results for n). The rapid increase in the chemical shift with concentration for the square, compared to the linear tetramer, is indicative of the cooperative formation of a closed system with a more favorable ΔG.

Fits of this ^{1}H-NMR data clearly show that ~3.9 units of **3a** self-assemble by these self-complementary hydrogen bonding motifs.

Although fits of the titration data can also yield information on the equilibrium constants for the four structures, because of the different power of the concentration units it is difficult to directly compare the values of K for all but the linear and square tetramers. Additionally, the Ks found by this data are about 4-fold weaker then those found by fluorescence quenching experiments – indicating that dynamic processes are occurring during the NMR acquisition. To contrast the NMR data from all four systems, it may be more informative to compare the $C_{1/2}$ values, where this represents the concentration at the half maximum increase in the chemical shift. The $C_{1/2}$ value from the above NMR data for the closed tetrameric square, 0.8 mM, is a factor of ~10 less than the comparable open tetrameric tape (therefore a greater "K," from fits of the data: K= 2400 M^{-3} versus 70 M^{-3}, respectively). Note that the linear systems have somewhat similar $C_{1/2}$ values: 8 mM, 5 mM, and 9 mM for the dimer, trimer, and tetramer, respectively.[11,12] The cooperativity in forming closed systems is exploited here to form the squares. In toluene, where the hydrogen bonds are expected to be stronger, similar results for n are obtained for all systems, but the $C_{1/2}$ values are ~4 fold lower for the linear assemblies and ~2 fold lower for the square.

As the concentration in chloroform, toluene, 2-methylTHF, and ethanol increases from 1 μM to ~250 μM there is little change in the observed UV-visible spectra, with <1nm shifts in the Q bands for both the free bases and the zinc complexes, **1b** and **3b**. Thus the UV-visible spectra indicate very little electronic communication between the macrocycles in the self-assembled tapes and squares in the ground state. However, the

emission is substantially diminished with increasing concentrations of **1a** and **3a** in chloroform, or 2-methylTHF, compared to ethanol.[11] This indicates that there is aggregation, which decreases the emission intensity by organization of the chromophores, and quenching of the excited state by energy transfer to neighboring subunits. Significant energy transfer among subunits is well demonstrated by the excitation and emission (see Figure 1) spectra of squares formed from a 1:1 mixture of the free base, **3a** and the zinc complex **3b** in 2-methylTHF. In solvents favoring hydrogen bonding, excitation in the zinc porphyrin Q-band region where **3b** absorbs >2.5 that of the free base, the self-complementary square emits predominantly from the free base, with concomitant quenching of **3b**. This direct observation of energy transfer is not observed in dilute solutions (<10μM) or in ethanol where the emission is essentially similar to the mathematical addition of the two individual spectra.

The emission from **3b** (see Figure 2, inset) is substantially quenched as the concentration of the 1:1 mixture in 2-methylTHF increases, and to a much lesser extent in ethanol. The fluorescence lifetime, determined by phase modulation, of **3a** is 10 ns and that of **3b** is 2 ns at 1 μM concentrations in air in chloroform. At 0.100 mM, **3a** exhibits two time constants 10 ns (80%) and 0.8 ns (20%). A 0.100 mM mixture of 1:1 **3a** and **3b** shows decays of 10 ns (50 %), 1 ns (40%), and <0.2 ns (10%). This is consistent with the notion of energy transfer from the singlet manifold, rather than the triplet manifold for the metallo self-assembled squares; making optical switching possible on the ns rather than μs time scale.

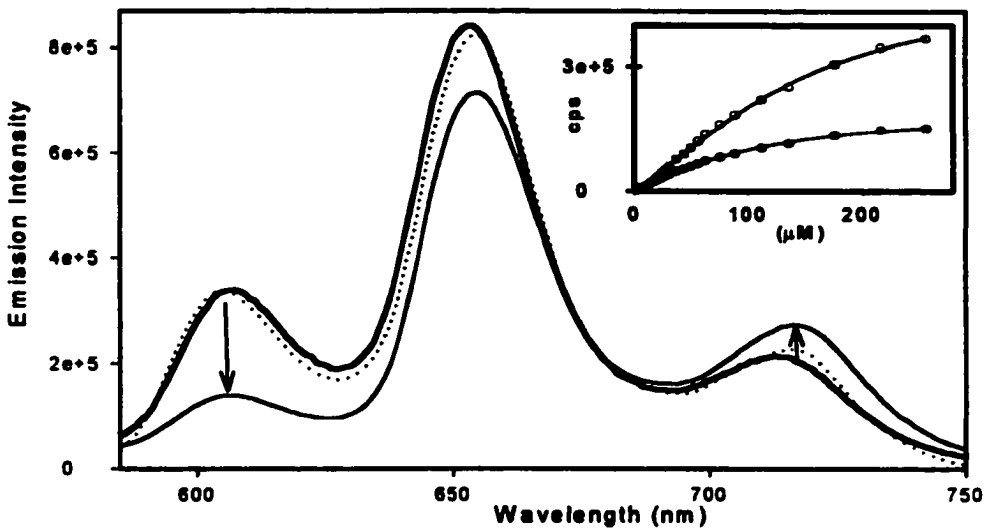


Figure 2 *Fluorescence emission spectra of a solution that is 140 μM in 3a and 140 μM in 3b in 2-methylTHF (—) and in ethanol (—) under identical experimental conditions. The zinc compound absorbs >3 times that of the free base at the excitation wavelength of 557 nm where the O.D. is <0.5 in a 3x3 mm cell. Note that in ethanol where the hydrogen bonding between the diaceamidopyridyl groups is minimal, the emission spectra is nearly identical to the sum of the two components (---). Whereas in 2-methylTHF where hydrogen bonding is significant, there is a substantial quenching of 3b, and enhanced emission from 3a. The inset plots the emission intensity of 3b at 610 nm versus concentration in ethanol (o) and 2-methylTHF (•).*

There is no indication of substantial pi-stacking or axial ligation of the zinc complexes, by UV-visible, fluorescence emission, resonance and dynamic light scattering, and NMR shifts and line widths. [11] Electrospray ionization mass spectra (ESI-MS) has been shown to be a powerful tool in examining the relative concentrations of self-assembled species. To avoid using acids to protonate the free bases, the Mn(III) or

Co(III) complexes of these porphyrins (acetate counter ions) are added at a ratio to impart one or more positive charges to the self-assembled arrays.

In solvents with low hydrogen bonding potential, the added thermodynamic stability of the closed, square tetramer, as opposed to a open chain polymer with an average length of four units with enthalpically unfavorable 'unbonded' ends or entropically unfavorable higher order polymers, strongly argues in favor of the square structure when **3a** is the self-assembling species. Note that the ^{1}H-NMR data and fits also indicate the relative amounts of the monomers and self-assembled species at each concentration. This information is then used to interpret the results of other spectroscopic techniques, and to estimate the formation enthalpy of the quadruple hydrogen bond. Estimations of ΔG for these systems from the NMR concentration and temperature data[8] show that the square tetramer is favored over the linear tapes by ~8 kJ mol^{-1}. Van't Hoff plots[11] of the chemical shift versus temperature for the free base dimer of **1a**, in the same solvent using several concentrations, indicate that the formation enthalpy, ΔH_f, of the quadruple hydrogen bond is -31 ± 5 kJ mol^{-1} and the entropy is about -80 ± 80 Jmol^{-1}, yielding a ΔG of -7 kJ mol^{-1}, which is in qualitative agreement with the NMR equilibrium studies above. Factoring in the four sets of hydrogen bonding pairs, the formation enthalpy is –96 kJ mol^{-1} for the square tetramer, or about -24 kJ mol^{-1} per set. This lower value may reflect some strain on a system that is unlikely to be exactly planar because of the small offset required for the quadruple hydrogen bond links.

The characterization of these supramolecular systems will serve as the basis for the characterization of future complex two- and three-dimensional arrays using various combinations of both hydrogen bonding and metal ion coordinating porphyrins. For

example, arrays and tapes may be formed by using complementary uracyl-diacetamidopyridyl motifs.[9] The above data show that the self-complementary hydrogen bonds afforded by the 3,5-diacetamido-4-pyridyl group is surprisingly effective in mediating the self-assembly of these photo and electro active species in solution. The solution phase chemistry, in turn, is vitally important for the understanding of how to direct the formation of solid state structures, and will help understanding of the resulting properties of the materials.

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References 2

1 A. Aviram, M. Ratner, Eds. *Molecular Electronics: Science and Technology*, Ann. NY Acad. Sci. **1998**, *852*, and references therein; C.M. Drain, D. Mauzerall *Biophys. J.* **1992**, 1556-1563, and references therein.

2 T. Pullerits, V. Sundstrom, *Acc. Chem. Res.* **1996**, *29*, 381 – 389; V. Novoderezhkin, R. Monshouwer, R. van Grondelle, *Biophys. J.* **1999**, *77*, 666 - 681.

3 For reviews: A.K. Burrell, M. R. Wasielewski, *J. Porph. Phthal.* **2000**, *4*, 401-406; B. Maiya, *J. Porph. Phthal.* **2000**, *4*, 393-397; K. S. Suslick, N. Rakow, M. E. Kosal, J.-H. Chou, *J. Porph. Phthal.* **2000**, *4*, 407-413; R. Dagani, *Chem. Eng. News*, **1998**, (76)23, 35-46.

4 For example: P. Bhyrappa, S. R. Wilson, K. S. Suslick, *J. Am. Chem. Soc.* **1997**, *119*, 8492 – 8502; S. Dahal, I. Goldberg, *J. Phys. Org. Chem.* **2000**, *13*, 1-6. Y. Diskin-Posner, S. Dahal, I. Goldberg *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 1288-1292.

5 For example: T. Hayashi, T. Miyahara, N. Koide, Y. Kato, H. Masuda, H. Ogoshi, *J. Am. Chem. Soc.* **1997**, *119*, 7281 – 7290; A. J. Epstein, C.M. Wynn, M. A. Girtu, W. B. Brinckerhoff, K.-I. Sugiura, J. S. Miller, *Mol. Cryst. Liq. Cryst.* **1997**, *305*, 321-322.

6 C.M. Drain, R. Fischer, E.G. Nolen, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.*, **1993**, 243-245; C.M. Drain, K.C. Russel, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1996**, 337-338; C. Ikeda, N. Nagahara, E. Motegi, N. Yoshioka, H. Inoue, *Chem. Commun.* **1999**, 1759 – 1760.

7 C. M. Drain, F. Nifiatis, A. Vasenko, J. D. Batteas, *Angew. Chem.* **1998**, *37*, 2344-2347; C. M. Drain, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1994**, 2313-2315; J.-C. Chambron, V. Heitz, J.-P. Sauvage in *The Porphyrin Handbook, Vol 6* (eds.: K.M. Kadish, K.M. Smith, R. Guilard), Academic Press, San Diego, **2000**, 1-41, and references therein; A. Prodi, M. T. Indelli, C. J. Kleverlaan, F. Scandola, E. Alessio, T. Gianferrara, L. G. Marzilli, *Chem. Eur. J.* **1999**, *5*, 2668-2679.

8 J. L. Sessler, B. Wang, A. Harriman, *J. Am. Chem. Soc.* **1995**, *117*, 704 – 714; J. L. Sessler, C. T. Brown, D. O'Connor, S. L. Springs, R. Wang, M. Sathiosatham, T. Hirose, *J. Org. Chem.* **1998**, *63*, 7370 – 7374; T. Arimura, S. Ide, H. Sugihara, S. Murata, J. L. Sessler, *New J. Chem.* **1999**, *23*, 977 - 979.

9 A. Osuka, R. Yoneshima, H. Shiratori, T. Okada, S. Taniguchi, N. Mataga, *Chem. Commun.* **1998**, 1567-1568; P. J. F. de Rege, S.A. Williams, M. J. Therien *Science*, **1995**, *269*, 1409-1413.

10 A distorted porphyrin bearing a single 3,5-diamidopyridyl group was reported.[8c]

11 Supporting information include the parameters from the NMR fits, the results of the van't Hoff plots, uv-vis and fluorescence data for the monomeric and square tetrameric species, and ESI-MS spectrum for the self-assembled square species.

12 F. H. Beijer, R. P. Sijbesma, J. A. J. M. Vekemans, E. W. Meijer, H. Kooijman, A. L. Spek, *J. Org. Chem.* **1996**, *61*, 6371 – 6380.

13 Though common practice, equilibrium constants for weakly H-bonding systems determined by NMR[12] data are probably internally consistent, but should be

treated with caution unless of the dynamics of the system(s) are specifically addressed.

14 W. F. DeGrado, J. D. Lear, *J. Am. Chem. Soc.* **1985**, *107*, 7684 – 7689; D. A. Deranleau, *J. Am. Chem. Soc.* **1969**, *91*, 4044 – 4054; B. J. Whitlock, H. W. Whitlock, *J. Am. Chem. Soc.* **1990**, *112*, 3910 - 3915.

15 A. D. Adler, F. R. Longo, W. Shergalis, *J. Am. Chem. Soc.* **1964**, *86*, 3145 - 3148; C. M. Drain, X. Gong, *Chem. Commun.* **1997**, 2117 –2118.

Appendix 7

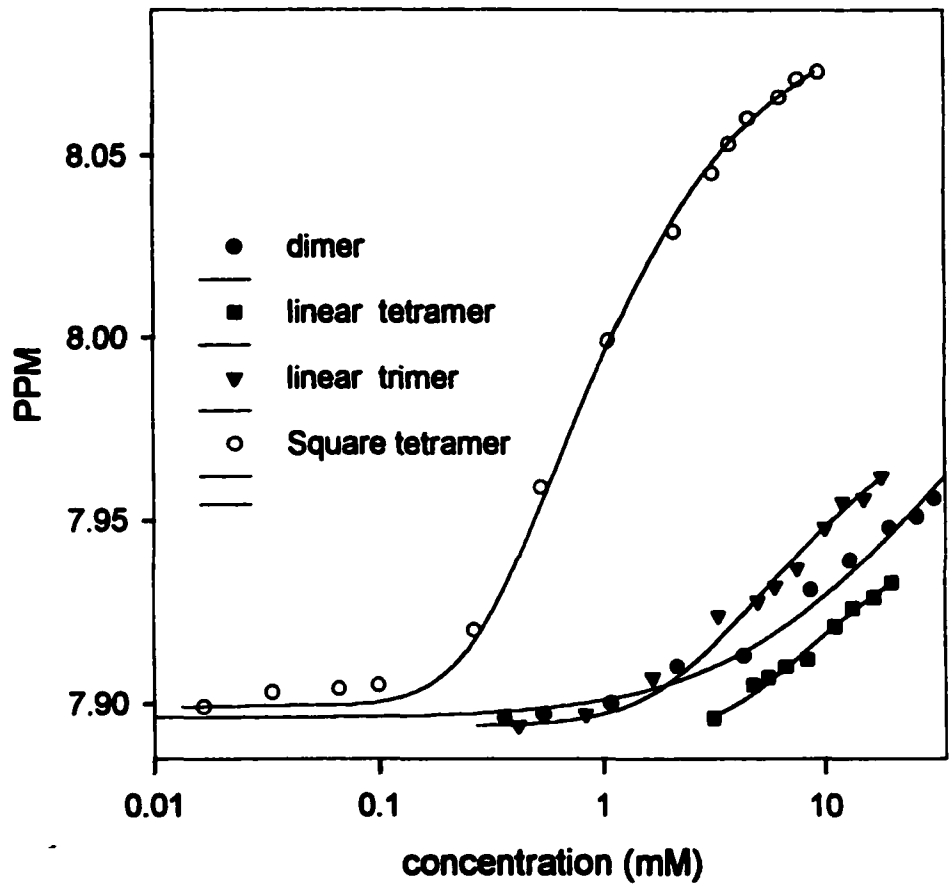


Figure A7-1 *Chemical shift vs. concentration plots for the self-complementary porphyrins. Fits of the data are summarized in table A7-1. At any concentration or temperature, only one amide proton is observed; thus supporting the quadruple and dynamic nature of the intermolecular interactions.*

If there are several products or dynamic processes, such as the breaking apart of one or more sets of hydrogen bonds occurring on the NMR time scale, these result will only give rough estimates of especially K, and to a lesser extent n. Note that a ΔG of 7-12 kJ

mol^{-1} corresponds to 2.8 – 4.9 k_BT, thus dynamic process would be expected at room temperature. Though common practice, equilibrium constants for weakly H-bonding systems determined by NMR[12] data are probably internally consistent, but should be treated with caution unless of the dynamics of the system(s) are specifically addressed.

Species	n	K	r^2	$C_{1/2}$ M^{-1}	ΔG ($kJmol^{-1}$)
1a dimer	2 ± 0.5	160 ± 80 M^{-1}	0.9943	125 (~600)	-12.6 (-12.0)b
1a-2a-1a trimer	3.2 ± 1.2	110 ± 60 M^{-2}	0.9952	200	-11.6 (-13.1)
1a-2a-2a-1a tetramer	4.1 ± 1.8	70 ± 40 M^{-3}	0.9925	111	-10.5 (-10.5)
3a square	3.9 ± 1.1	2400 ± 220 M^{-3}	0.9977	1250 (~3000)	-19.3 (-17.7)

Table A7-1 *Fits of the ^{1}H-NMR data at 298K in $CDCl_3$ for the self-complementary arrays. n = number of particles, K = equilibrium constant from the fit of the data, r^2=correlation coefficient of the fit, $C_{1/2}$=[Por] at ½ rise to maximum, ( ) = in tolunene. [a]in toluene d_8. ΔG=-RTln(K) and [b](using $C_{1/2}$ values to estimate ΔG).*

A K of 160 M^{-1} for the dimer of **1a** is a factor of 100 greater than the value obtained for parent unsubstituted derivative of this recognition group.[12] This greater K is explained by the known electronic coupling of the porphyrin to the recognition group, making the pyridyl nitrogen more basic.[7a]

Assembly	$-\Delta H$ (kJmol^{-1}) (kcal)	ΔS (Jmol^{-1}K^{-1})	ΔG (kJmol^{-1})
1a dimer	31 ± 5 (7)	-80 ± 30	-7
3a square	96 ± 32 (23)	-240 ± 150	-24.5

Table A7-2 *Estimations of ΔH and ΔS (298K) from van't Hoff plots of the ^{1}H-NMR data in $CDCl_3$ at temperatures between 270 and 328 K in $CDCl_3$. $\Delta G=\Delta H-T\Delta S$*

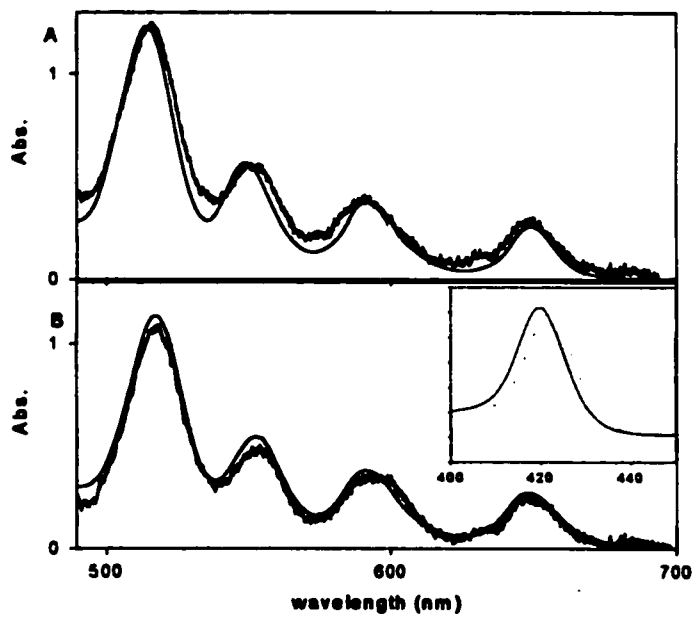


Figure A7-1 *The Uv-visible spectra of 3a in ethanol (A) and chloroform (B). The smooth lines are at ~250 μM, and the jagged lines are at 2 μM multiplied by a factor of 110. Inset: the Soret band in chloroform (—) is ~ 3nm to the red of that in ethanol (___).*

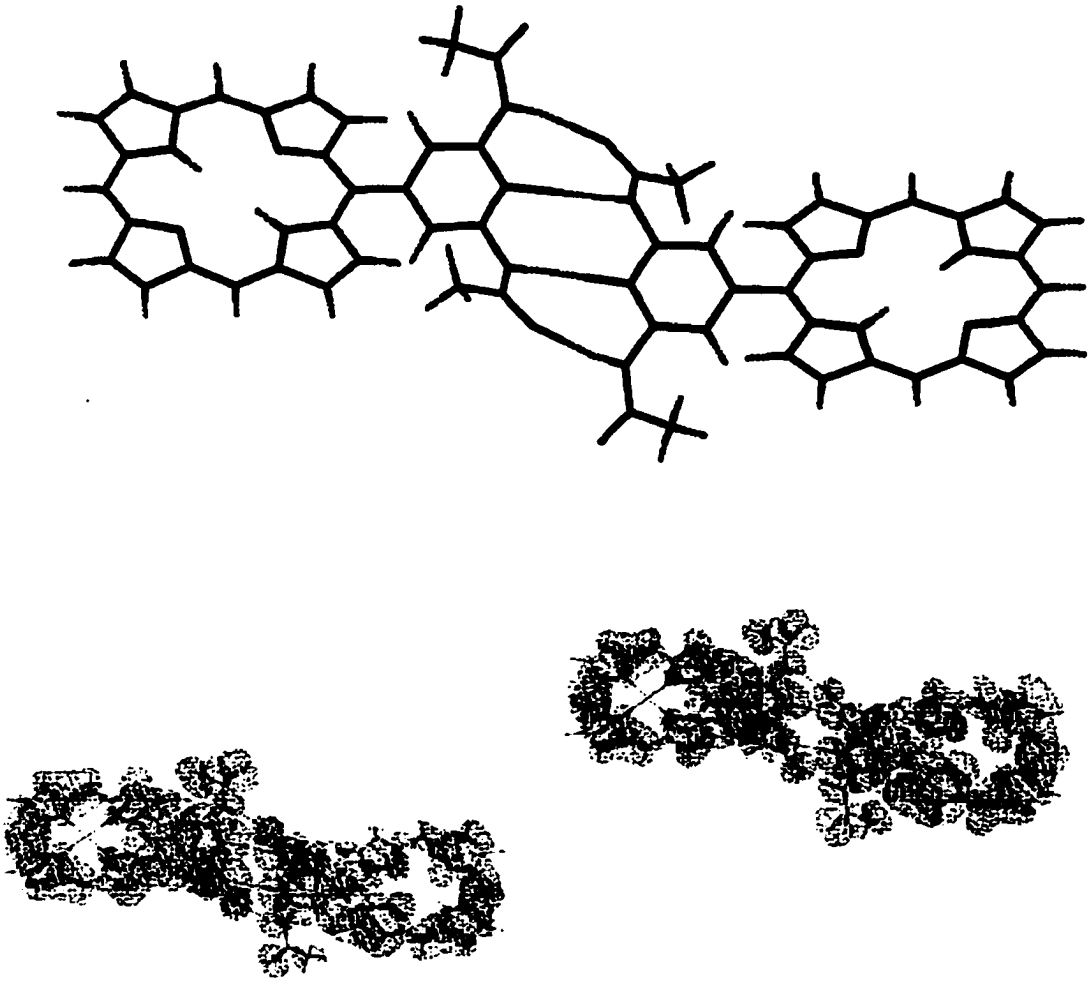


Figure A7-2 *AM1 calculations of the molecular orbital densities for the free base dimers indicate two nearly degenerate orbitals with substantial electron density spanning from one porphyrin, across the diacetamidopyridy groups to the other porphyrin. These orbitals persist with somewhat different densities in the case of the 3a –3b dimer.*

Vapor Phase Osmometry (VPO) of **3a** on a Jupiter 833 instrument at 50°C in toluene using a 5KD polystyrene standard, shows two lines – one for low concentrations and one for concentration over ~ 0.1mM. The first yield a molar mass of 893 ± 10% consistent with the monomer (957 D), and the second 3.6 KD which is consistent with the square (3.828 KD). Thus, no larger aggregates are indicated.

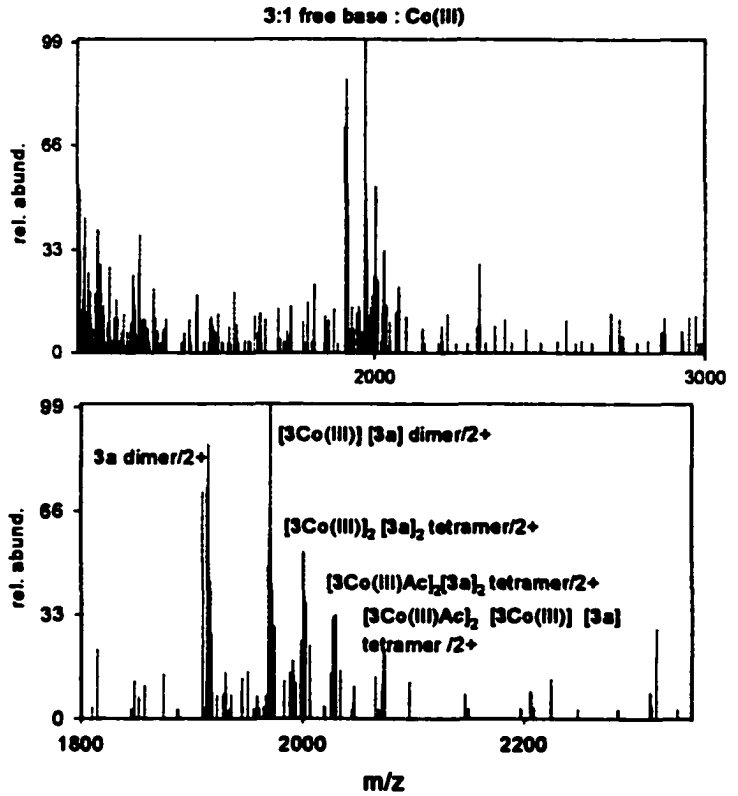


Figure A7-3 ***ESI-MS of the self-complementary hydrogen bond assembled square using a 3:1 ratio of 3a to the Co(III) acetate porphyrin, 3Co(III)Ac. Positive ion mode, in chloroform, voltage was ramped from 50 to 300V.***

Thus, at 0.1 mM ~10% of the dimer is observed in chloroform (1 equivalent of 1Mn(III) Ac). The greater equilibrium constant of the square, allows for lower concentrations to be used, and a more thorough ESI-MS study. As the concentration of **3a** (with a 1:3 ratio of the Co(III) acetate complex to **3a**) increases so does the formation of the square. At very low concentrations, only the monomers are observed. As the concentrations increase, the amount of the self-assembled species increases up to the concentration limit of the experiment. In the present case, the parent ions of the dimers, trimers, and square tetramers are readily observed with relative abundances consistent with those predicted the NMR data.

Several observations mitigate against simple aggregation by pi-stacking or large open chain polymers: (i) the ground state spectra of 1 μM and 280 μM solutions of these compounds are quantitatively similar in ethanol, chloroform and 2-methylTHF, (ii)the lower symmetry of the porphyrin, (iii)the bulky *meta* acetamido substituents, (iv)Stern-Volmer plots show a linear relation with a small slope for the ethanol data, and a substantially curved spectra for the 2-methyl-THF data, (v)NMR data shows neither axial coordination of the zinc nor the characteristic shifts due to ring the currents of the macrocycle even at the highest concentrations possible. At 0.480 mM concentrations of **3a**, few if any (< 2%) large aggregates (mean radius 4.2 nm) are detected by Dynamic light scattering, and at lower concentrations, no aggregates are detected and a weak signal that may be the square (hydrodynamic radius of ~3) is observed. Resonance light scattering only detects aggregates of undetermined size at saturated concentrations.

Chapter 3

Self-assembled multiporphyrin arrays mediated by hetero-complementary triple hydrogen bond motifs

Abstract: Discrete tapes, squares, nonomer, hexomer, and star pentamer of porphyrins may be self-assembled by hetro-complementary hydrogen bonding between diacetamidopyridyl and 1-butyluracyl recognition groups rigidly linked to the chromophore.

Introduction

The donor-acceptor-donor (DAD) arrangement of hydrogen bonding sites in a 2,6-diacetamidopyridyl group allows it to pair with the acceptor-donor-acceptor (ADA) arrangement in a uracil to form triple hydrogen-bonded hetero-complementary pairs (DAD-ADA).

Now that the porphyrins are made, we have two sets of porphyrin building blocks suitable for the systematic build-up of desired structures of increasing complexity. This modular building-block approach is designed with the goal of constructing arrays composed of large numbers of porphyrins in defined geometries. For example, when the 5,15-bis(1'-butyl-6'-uracyl)-10,20-bis(4-*tert*-butylphenyl)porphyrin (IX), 5,15-bis(3,5-diacetamido-4-pyridyl)-10,20-bis(4-*tert*-butylphenyl)porphyrin (III), the 5-(1'-butyl-6'-uracyl)-10,15,20-tris(4-*tert*-butylphenyl)porphyrin (VIII) and , 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-*tert*-butylphenyl)porphyrin (II) put together in organic solvents, they can self-assemble into the linear tapes (see Figure 1). The simple dimer can be used to develop the physical methods to characterize the large arrays. When the 5,10-bis(1'-butyl-

6'-uracyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (X) and 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (IV) are mixed in organic solvents, they can form a square tetramer by spontaneous self-assembly (see Figure 2.). A light-harvesting system may be made from four peripheral 5-(1'-butyl-6'-uracyl)-10,15,20-tris(4-*tert*-butylphenyl)porphyrin (Zn) (VIII) or 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-*tert*-butylphenyl) porphyrin(Zn) (II) units and a central free-base 5,10,15,20-Tetrakis(3,5-diacetamido-4-pyridyl)porphyrin (VI) or 5,10,15,20-Tetrakis(1'-butyl-6'-uracyl)porphyrin (XII) by spontaneous self-assembly (see Figure 3). In these Zn/free-base systems, the antenna effect may be obtained by efficient energy transfer which conveys the excitation energy from the peripheral metallated chromophores to the central one. Four 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (IX), four 5,10,15-tris(3,5-diacetamido-4-pyridyl)-20-(4-*tert*-butylphenyl)porphyrins (V), and one 5,10,15,20-tetrakis(1'-butyl-6'-uracyl)porphyrin (XII) put together in organic solvents, may form a

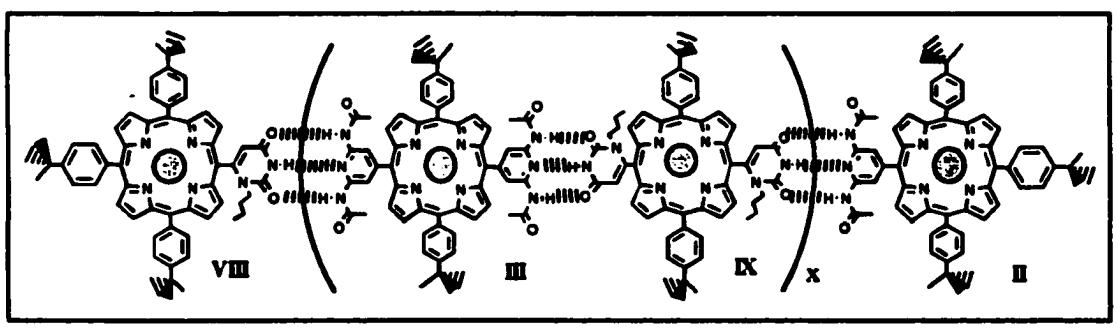


***Figure 1** Linear Tapes: the 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-tert-butylphenyl) porphyrin (IX), 5,15-bis(3,5-diacetamido-4-pyridyl)-10,20-bis(4-tert-butylphenyl) porphyrin (III), the 5-(1'-butyl-6'-uracyl)-10,15,20-tris(4-tert-butylphenyl)porphyrin (VIII), and 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-tert-butylphenyl)porphyrin (II) can self-assemble into linear tapes. X = 0, dimer; x = 1, linear tetramer.*

nonomer by spontaneous self-assembly (see Figure 4). Four 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-*tert*-butylphenyl) porphyrins (IV), two 5,10,15-tris(3,5-diacetamido-4-pyridyl)-20-(4-*tert*-butylphenyl) porphyrins (V) and six diimides put together in organic solvents, can form a hexamer by spontaneous self-assembly (see Figure 5).

With multiple hydrogen bond linkers photonic subunits can be placed at designated positions and at fixed distances, making this strategy amenable to formation of arrays capable of energy or electron transfer. These supermolecules may be studied as functional models of biological systems capable of inducing directional motion of electrons or excitation energy through hydrogen bonds. Gaining a deeper understanding of the design of electron and energy transfer systems through hydrogen bonding is a central aspect of this work.

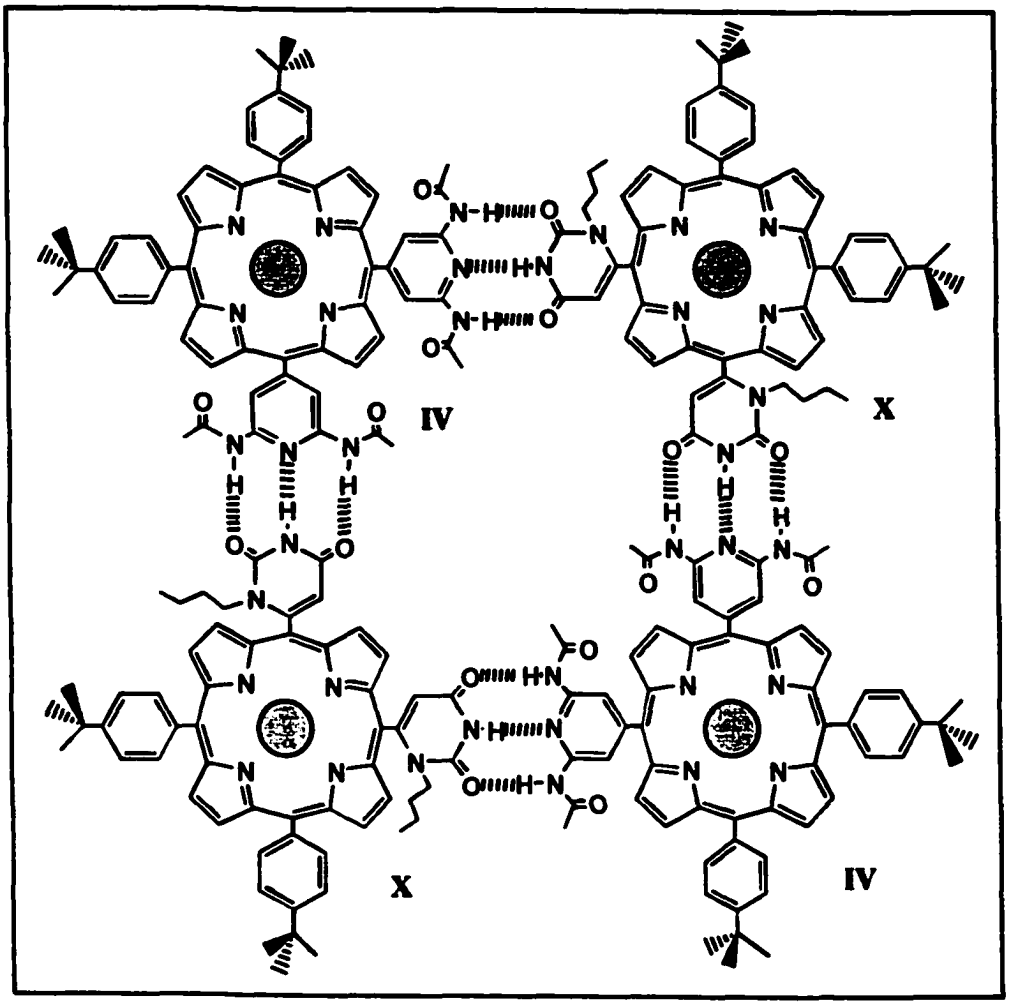


***Figure 2** Square tetramer: the 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-tert-butylphenyl)porphyrin (X) and 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-tert-butylphenyl)porphyrin (IV) are mixed in organic solvents can form a square tetramer by spontaneous self-assembly.*

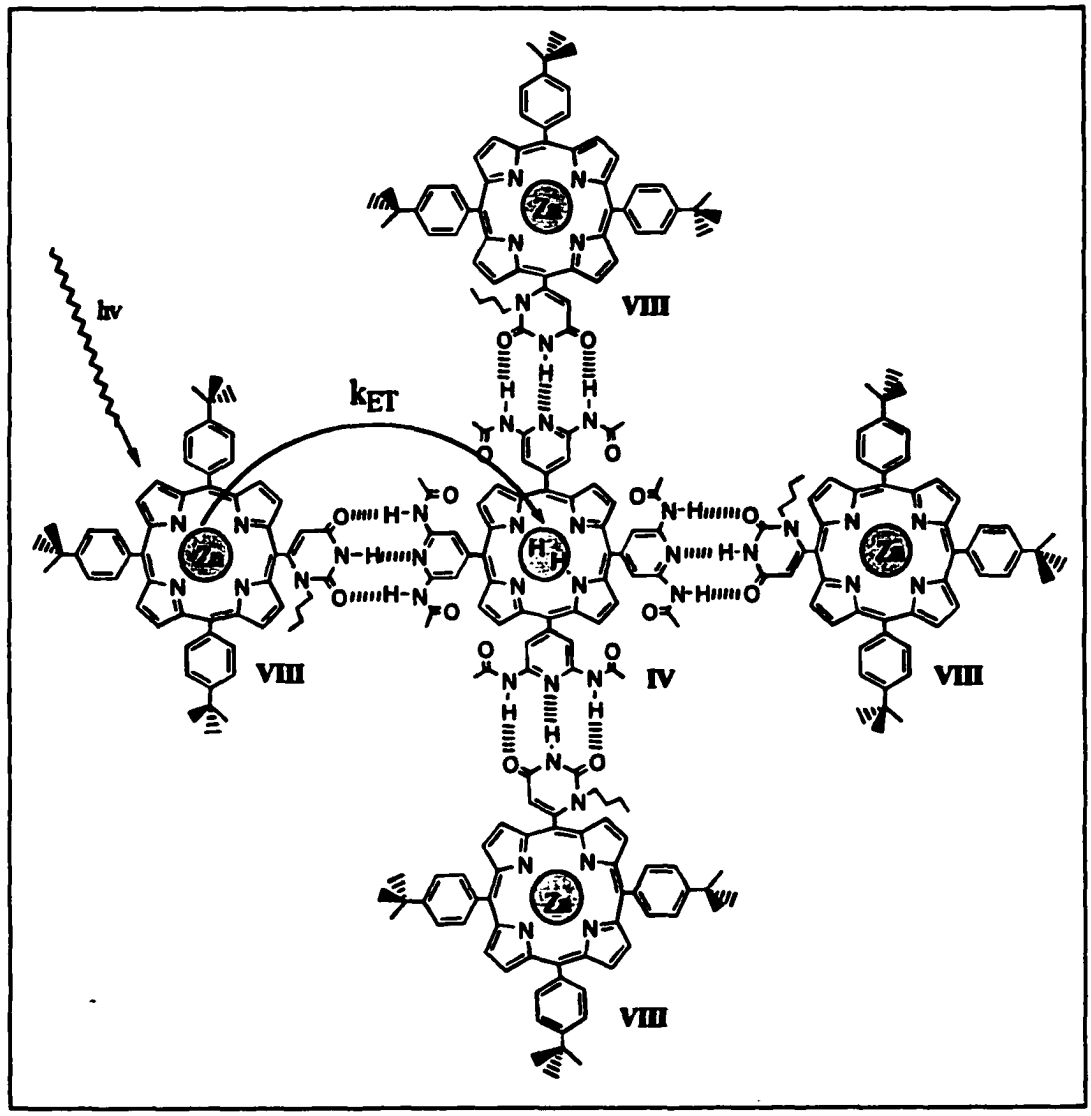


Figure 3 Star pentamer: *the light-harvesting system may be made from photodonors, four peripheral 5-(1'-butyl-6'-uracyl)-10,15,20-tris(4-tert-butylphenyl)porphyrin (Zn) (VIII) or 5-(3,5-diacetamido-4-pyridyl)-10,15,20-tris(4-tert-butylphenyl) porphyrin(Zn) (II) units and a photoacceptor, a central free-base 5,10,15,20-tetrakis(3,5-diacetamido-4-pyridyl)porphyrin (VI) or 5,10,15,20-Tetrakis(1'-butyl-6'-uracyl)porphyrin (XII) by spontaneous self-assembly. Since porphyrin(Zn) is about 100 mV higher in potential energy, electrons can transfer from the metalloporphyrins to the free base porphyrin in the center.*

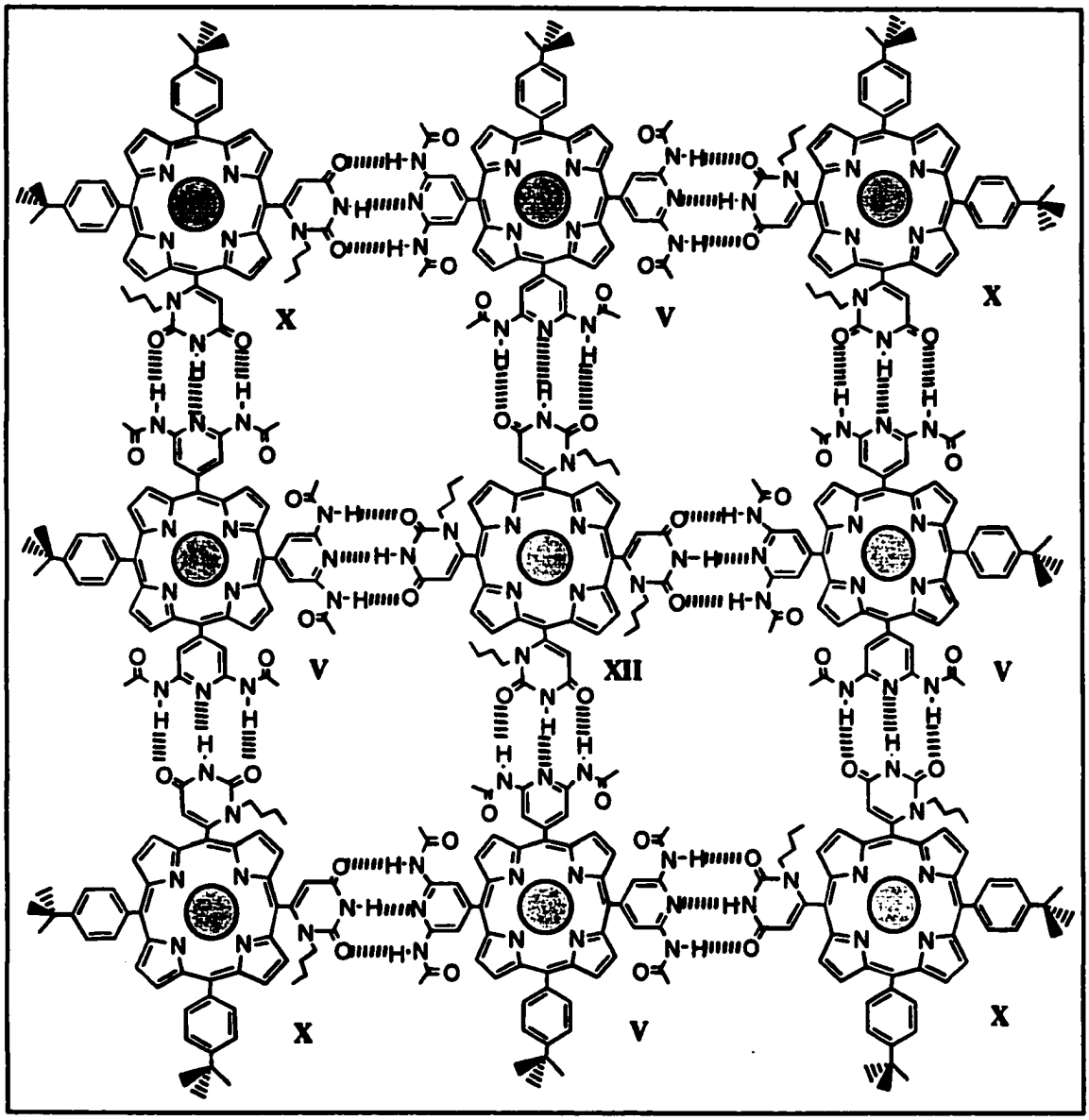


Figure 4 *The nonomer: four 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-tert-butylphenyl)porphyrin (IX), four 5,10,15-tris(3,5-diacetamido-4-pyridyl)-20-(4-tert-butylphenyl)porphyrins (V), and one 5,10,15,20-tetrakis(1'-butyl-6'-uracyl)porphyrin (XII) put together in organic solvents, may form a nonomer by spontaneous self-assembly.*

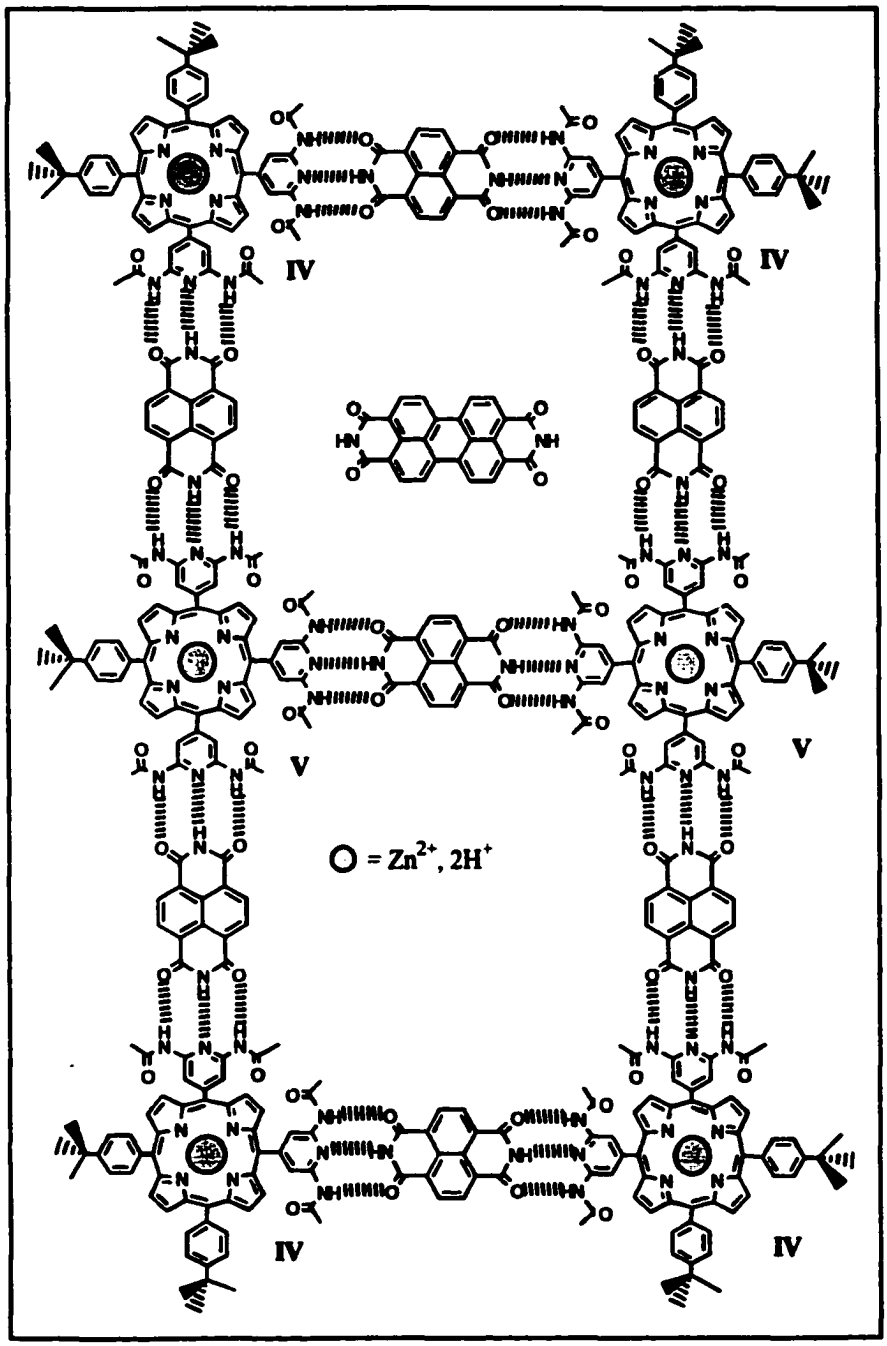


Figure 5 *The hexomer: four 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-tert-butylphenyl)porphyrins (IV), two 5,10,15-tris(3,5-diacetamido-4-pyridyl)-20-(4-tert-butylphenyl)porphyrins (V) and six 1,4,5,8-naphthalenetetracarboxylic diimides(NTDI) or 3,4,9,10-perylenetetracarboxlic diimides (PTDI) are mixed in organic solvents, may form a hexamer by spontaneous self-assembly.*

The AM1 molecular calculation of triple hydrogen-bonding

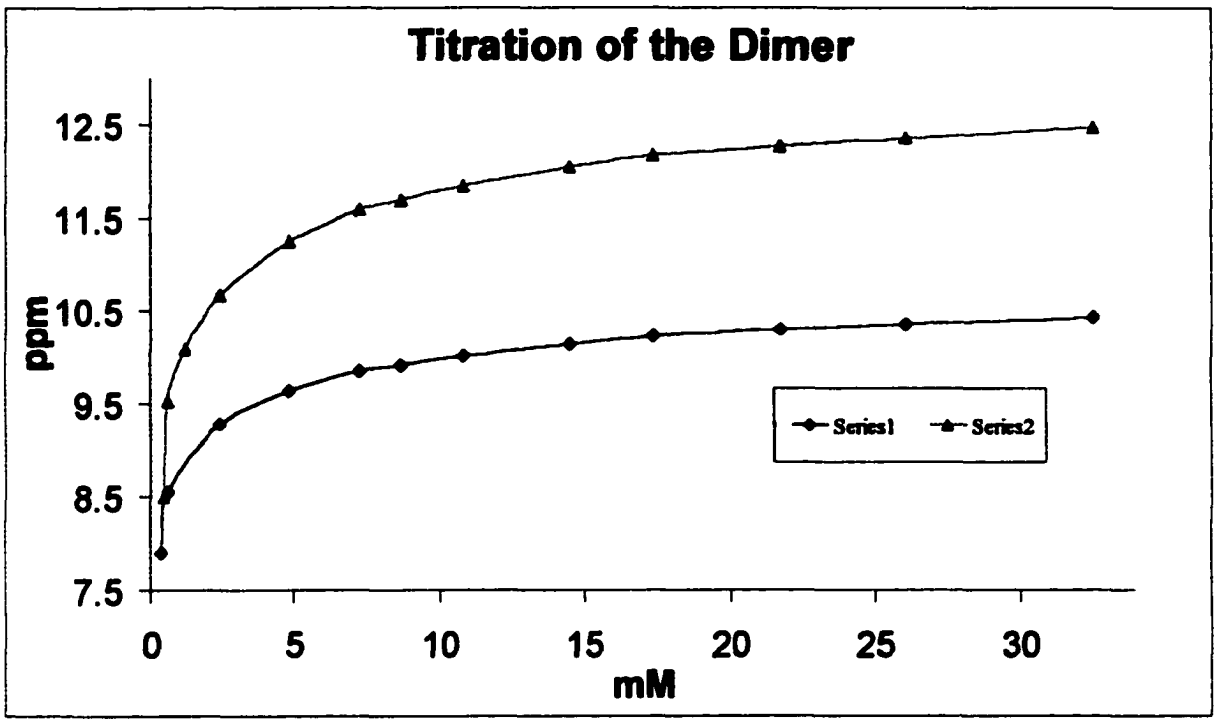
Because the supramolecule, including porphyrin rings, is too large to carry out quantum mechanical calculations, we choose the 2,6-diacetamido-4-formylpyridine and 4-formyluracil as substrates to form a dimer with a triple hydrogen bonding system(DAD--ADA). Because of the structural simplicity of this model system, it provides an opportunity to evaluate the accuracy with which computational methods reproduce the balance of non-covalent forces that control intermolecular hydrogen bond formation. The AM1 molecular orbital method is an effective, general method for the calculation of hydrogen bonding. It has been used with success in several hydrogen-bonding studies[8].

Heats of Formation

4-Formyluracil	78.957412 Kcal / mol
2,6-Diacetamido-4-formylpyridine	63.370679 Kcal / mol
Dimer (through triple hydrogen bonding)	151.126817 Kcal / mol
Interaction Energy	-8.798726 Kcal / mol

The interaction energy of the triple hydrogen-bond is 8.8 Kcal / mol. The average energy of each hydrogen bond has less than 3.0 Kcal / mol. This result showed that the strength of the hydrogen bonds is not very strong. It is probable due to the smaller electronegativity of nitrogen atoms which are the major atoms of the hydrogen bonding system. There are insignificant changes in the geometry of the two monomers in the hydrogen-bonding dimer. The bond angles near the hydrogen bonding system vary no more than 0.5°. All atoms that form hydrogen bond lie in almost the same plane. This fact tell us that 2,6-diacetamido-4-

formylpyridine is suitable to pair with 4-formyluracil (ADA) to form a triple hydrogen bonding system.



▲ = imide; ♦ = amide.

Table 3-1 The concentration dependencies of the chemical shift of mono[3, 5-diacetamido-4-pyridyl]porphyrin and mono(1'-butyl-6'-uracyl)porphyrin in $CDCl_3$

No.	1	2	3	4	5	6	
Rel. [ ]	1	0.8	0.6667	0.5333	0.4444	0.3333	
[ ] mM	32.53	26.02	21.69	17.35	14.46	10.84	
Ppm (imide)	12.470	12.380	12.258	12.156	12.030	11.828	
Ppm (amide)	10.427	10.360	10.292	10.223	10.138	10.007	
No.	7	8	9	10	11	12	
Rel. [ ]	0.2667	0.2222	0.1481	0.0741	0.0370	0.0185	
[ ]	8.675	7.229	4.819	2.410	1.205	0.603	
Ppm (imide)	11.683	11.579	11.240	10.670	10.084	9.529	*8.500
Ppm (amide)	9.913	9.850	9.636	9.274		8.553	**7.897

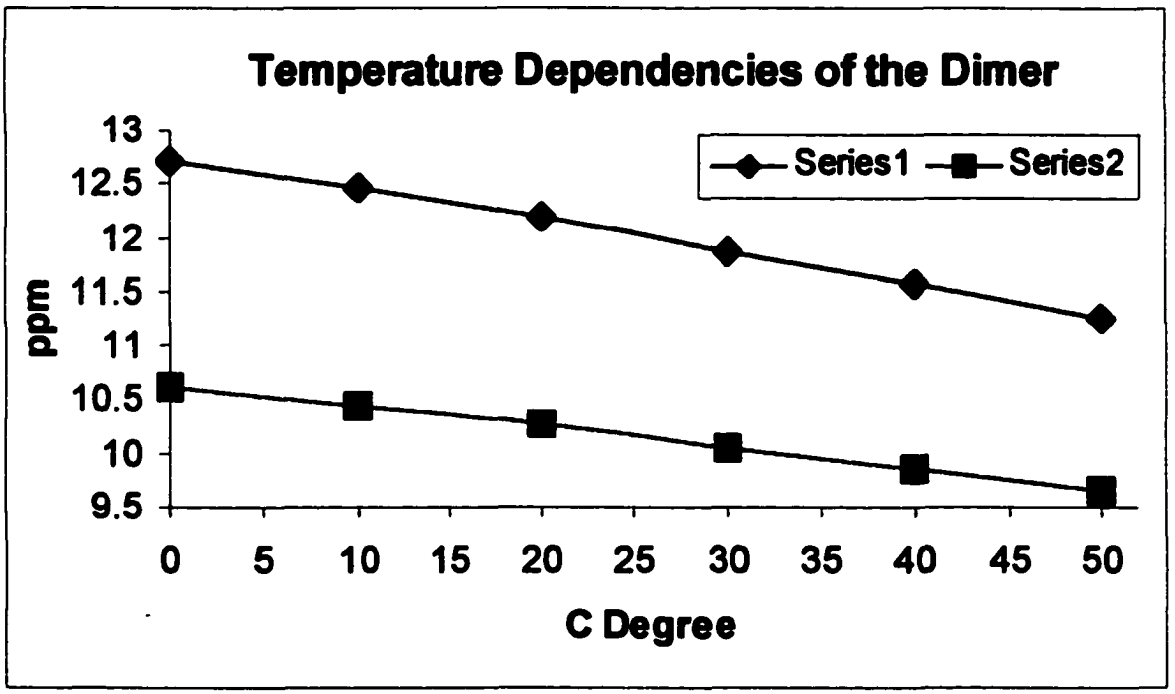
* From *mono*(1-butyl-6-uracyl)porphyrin data at 2.48 mM

**From mono(3, 5-diacetamido-4-pyridyl)porphyrin data at 0.361 mM

Table 3-2 The temperature dependencies of the chemical shift of 5-(3, 5-diacetamido-4-pyridyl)porphyrin and 5-(1-butyl-6-uracyl)porphyrin in $CDCl_3$

No.	1	2	3	4	5	6
T (°C)	0.0 °C	10.0 °C	20.0 °C	30.0 °C	40.0 °C	50.0 °C
δ (ppm) (imide)	12.698	12.454	12.179	11.870	11.579	11.260
δ (ppm) (amide)	10.599	10.439	10.256	10.046	9.851	9.638

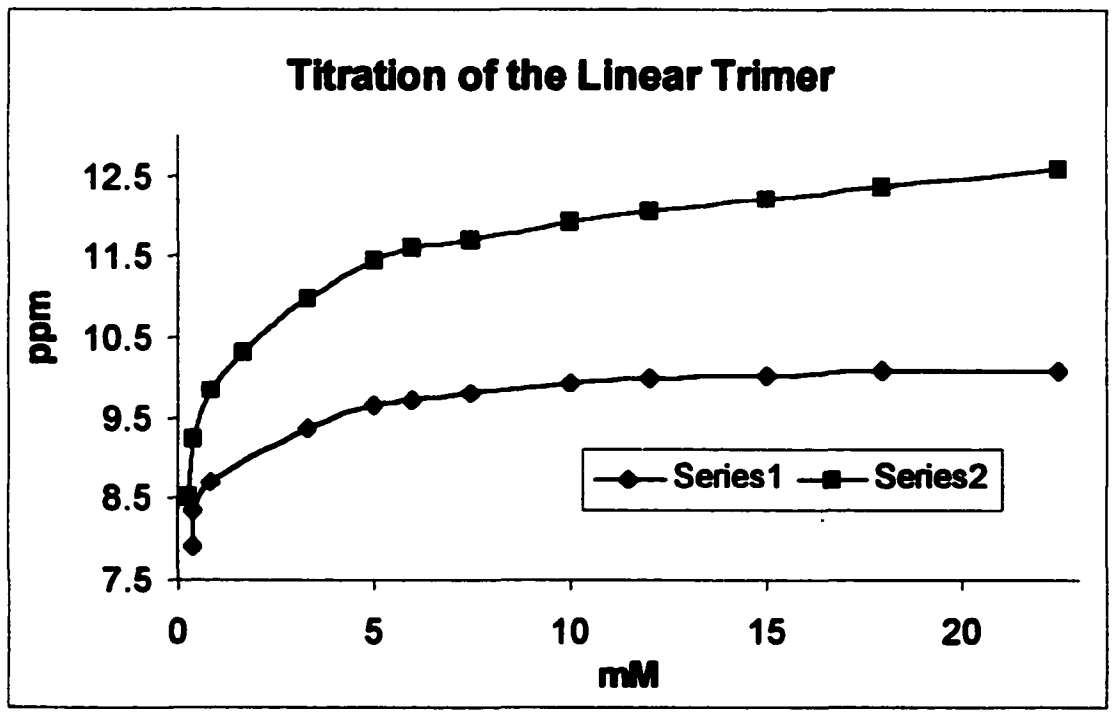
[C] ≈ 1.5 mM



♦ = imide; ■ = amide

Table 3-3 The concentration dependencies of the chemical shift of two mono(3, 5-diacetamido-4-pyridyl)porphyrins and *trans*-di(1-butyl-6-uracyl)porphyrin in $CDCl_3$

No.	1	2	3	4	5	6	
Rel. [ ]	1	0.8	0.6667	0.5333	0.4444	0.3333	
[ ] mM	22.50	18.00	15.00	12.00	10.00	7.500	
Ppm (imide)	12.593	12.364	12.218	12.062	11.934	11.715	
Ppm (amide)	10.103	10.080	10.033	9.998	9.923	9.792	
No.	7	8	9	10	11	12	
Rel. [ ]	0.2667	0.2222	0.1481	0.0741	0.0370	0.0185	
[ ]	6.000	5.000	3.333	1.667	0.8333	0.4167	
Ppm (imide)	11.601	11.445	11.988	10.306	9.835	9.251	*8.500
Ppm (amide)	9.725	9.634	9.366		8.695	8.367	**7.897



■ = imide; ♦ = amide.

* From *mono*(1-butyl-6-uracyl)porphyrin data at 2.48 mM

**From mono(3, 5-diacetamido-4-pyridyl)porphyrin data at 0.361 mM

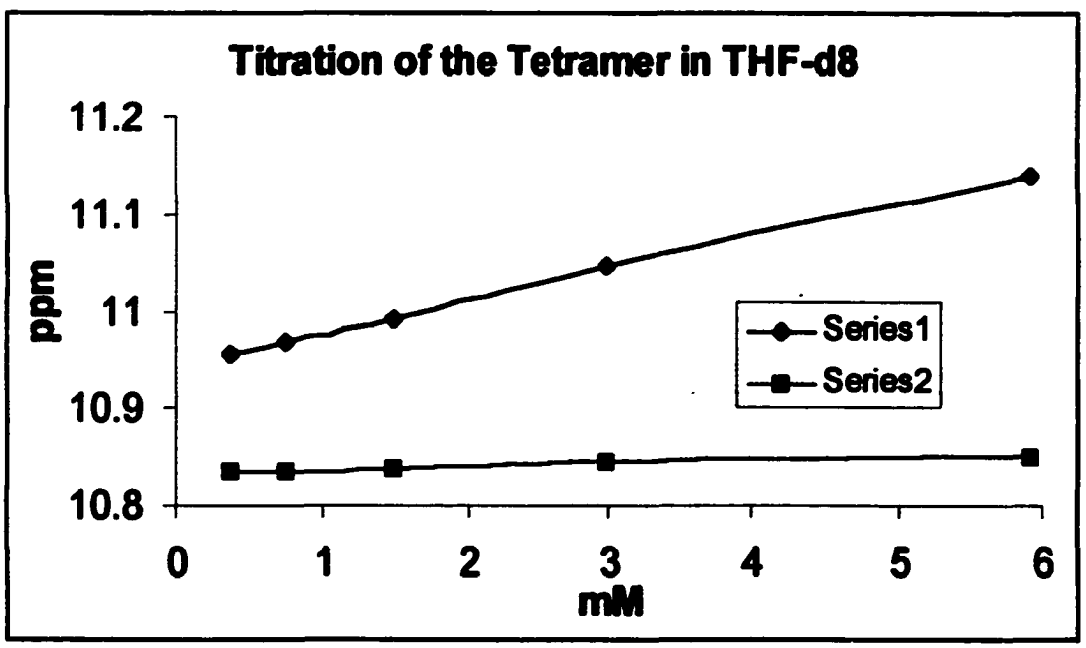
Square tetramer:

Table 3-4 The concentration dependencies of the chemical shift Of *Cis*-diUrP + *Cis*-diPyP in THF-d8

No.	1	2	3	4	5	
Rel. [ ]	1.000	0.5000	0.2500	0.1250	0.0625	
[ ]	5.917	2.9891	1.4794	0.7397	0.3699	
ppm(imide)	11.14	11.047	10.991	10.968	10.955	**8.53
ppm(amide)	10.85	10.845	10.838	10.834	10.834	*7.881

* From 5,10-bis(3,5-diacetamido-4-pyridyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (IV) data at 0.132 mM in $CDCl_3$

** From 5,10-bis(1'-butyl-6'-uracyl)-15,20-bis(4-*tert*-butylphenyl)porphyrin (X) data at 0.193 mM in $CDCl_3$



◆= imide; ■= amide.

Bibliography

Chapter 1

(1) (a) Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* 1990, *29*, 1304-1319. (b) Dagani, R. *Chem. & Eng. News*, 1998, *76*, 35-46.

(2) Lindsey, J. S. *New J. Chem.* 1991, *15*, 153-180.

(3) For reviews on reaction center models see: (a) Wasielewski, M. R. In *The Photosynthetic Reaction Center*; Deisenhofer, J.; Norris, J., Eds.; Academic Press, New York, NY, 1993; Vol. 2, pp 465-511. (b) Gust, D.; Moore, T. A. In *The Porphyrin Handbook;* Kadish, K.; Smith, K.; Guilard, R., Eds.; Academic Press, New York, NY, 2000; Vol. 8, pp 153-190.

(4) For examples of various types of discrete multiporphyrinic covalent arrays: (a) Lin, V. S.-Y.; DiMagno, S. G.; Therien, M. J. *Science* **1994**, *264*, 1105-1111. (b) Wagner, R. W.; Seth, J.; Yang, S. I.; Kim, D.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Org. Chem.* **1998**, *63*, 5042-5049. (c) Lindsey, J. S.; Gust, D.; Moore, T. A.; Moore, A. L.; Weghorn, S. J.; Johnson, T.E.; Lin, S.; Liddell, P. A.; Kuciauskas, D. *J. Am. Chem. Soc.* **1999**, *121*, 8604-8614. (d) Aratani, N.; Osuka, A.; Kim, Y. H.; Jeong, D. H.; Kim, D. *Angew. Chem., Int. Ed. Engl. 2000, 39*, 1458-1462. (e) Khoury, R.; Jaquinod, L.; Nurco, D. J.; Pandey, R. K.; Senge, M. O.; Smith, K. M. *Angew. Chem, Int. Ed. Engl.* **1996**, *35*, 2496-2499. (f) Burrell, A. K.; Officer, D. L. *Synlett.* **1998**, 1297-1307. (g) Osuka, A.; Yamazaki, I.; Nakano, A.; Yamazaki, T.; Nishimura, Y. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3023-3027. (h) Li, J.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 9101-9108. (i) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *J. Chem Soc. Perkin I* **1995**, 2247-2254 references therein.

(5) For examples of discrete multiporphyrinic arrays formed by hydrogen bonding: (a) Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1993**, 243-245. (b) Drain, C. M.; Russell, K. C.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1996**, 337-338 (c) Ikeda, C.; Nagahara, N.; Motegi, E.; Yoshioka, N.; Inoue, H. *Chem. Commun.* **1999**, 1759-1760.

(6) For examples of porphyrin hydrogen bonding in solid state networks: (a) Dahal, S.; Goldberg, I. *J. Phys. Org. Chem.* **2000**, *13*, 1-6. (b) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *J. Am. Chem. Soc.* **1997**, *119*, 8492-8502. (c) Diskin-Posner, Y.; Dahal, S.; Goldberg, I. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 1288-1291.

(7) For examples of discrete axial coordination arrays: (a) Stibrany, R. T.; Vasudevan, J.; Knapp, S.; Potenza, J. A.; Emge, T.; Schugar, H. J. *J. Am. Chem. Soc.* **1996**, *118*, 3980-3981. (b) Knapp, S.; Vasudevan, J.; Emge, T.; Arison, B. H.; Potenza, J. A.; Schugar, H. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2368-2370. (c) Sanders, J. K. M.; Bampos, N.; Mak, C. C. *Chem. Commun.* **1999**, 1086-1086. (d) Chi, X.; Guerin, A. J.; Haycock, R. A.; Hunter, C. A.; Sarson, L. D. *Chem. Commun.* **1995**, 2563-2565.

(8) For examples of axial coordination polymers or networks: (a) Fleischer, E. B.; Shachter, A. M. *Inorg. Chem.* **1991**, *30*, 3763-3769. (b) Abrahams, B. F.; Hoskins, B. F.; Robson, R. *J. Am. Chem. Soc.* **1991**, *113*, 3606-3607. (c) Kumar, R. K.; Balasubramanian, S.; Goldberg, I. *Mol. Cryst. Liq. Cryst.* **1998**, *313*, 105-114.

(9) For examples of discrete arrays formed by exocyclic ligand coordination: (a) Drain, C. M.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 2313-2315. (b) Drain, C. M.; Nifiatis, F.; Vasenko, A.; Batteas, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2344-2347. (c) Yuan, H.; Thomas, L.; Woo, L. K. *Inorg. Chem.* **1995**, *36*, 2808-2817. (d) Slone, R. V.;

Hupp, J. T. *Inorg. Chem.* **1997**, *36*, 5422-5423. (e) Stang, P. J.; Fan, J.; Olenyuk, B. *Chem. Commun.* **1997**, 1453-1454. (f) Fan, J.; Whiteford, J. A.; Olenyuk, B.; Levin, M. D.; Stang, P. J.; Fleischer, E B. *J. Am. Chem. Soc.* **1999**, *121*, 2741-2752.

(10) For examples of hybrid arrays: (a) Burrell, A. K.; Jones, B. M.; Hall, S. B.; Officer, D. L.; Reid, D. C. W.; Wild, K. Y. *J. Incl. Phenom. Macrocycl. Chem.* **1999**, *35*, 185-190. (b) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469-475. (c) Anderson, S.; Anderson, H. L.; Bashall, A.; McPartin, M.; Sanders, J. K. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1096-1099. (d) Funatsu, K.; Kimura, A.; Imamura, T.; Ichimura, A.; Sasaki, Y. *Inorg. Chem.* **1997**, *36*, 1626-1653.

(11) For example: (a) Hungerford, G.; Auweraer, M. V.; Chambron, J.-C.; Heitz, V.; Sauvage, J.-P.; Pierre, J.-L.; Zurita, D. *Chem. Eur. J.* **1999**, 5(7), 2089-2100. (b) Feiters, M. C.; Fyfe, M. C. T.; Martinez-Diaz, M.-V.; Menzer, S.; Nolte, R. J. M.; Stoddart, J. F.; van Kan, P. J. M.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 8119-8120.

(12) (a) Drain, C. M.; Mauzerall, D. *Bioelectrochem. Bioenerg.* **1990**, *24*, 263-268. (b) Drain, C. M.; Mauzerall, D. *Biophys. J.* **1992**, *63*, 1544-1555. (c) Drain, C.M.; Christensen, B.; Mauzerall, D. *Proc. Natl. Acad. Sci., USA* **1989**, *86*, 6959-6962.

(13) (a) Fox, M. A.; Jones, W. E.; Watkins, D. M. *Chem. & Eng. News* **1993**, 38-48. (b) Liu, C.; Pan, H.; Fox, M. A.; Bard, A. J. *Science* **1993**, *261*, 897-899.

(14) Hayashi, T.; Miyahara, T.; Koide, N.; Kato, Y.; Masuda, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1995**, 119, 7281-7290.

(15) (a) Stang, P. J.; Olenyuk, B. *Acc. Chem. Res.* **1997**, *30*, 502-518. (b) Burrell, A. K.; Wasielewski, M. R. *J. Porph. Phthal.* **2000**, *4*, 401-406. (c) Suslick, K. S.; Rakow, N. A.; Kosal, M. E.; Chou, J.-H. *J. Porph. Phthal.* **2000**, *4*, 407-413. (c) Philp, D.; Stoddart, J. F.

Angew. Chem. Int. Ed. Engl. **1996**, *35*, 1154-1196. (d) Linton, B.; Hamilton, A. D. *Chem. Rev.* **1997**, *97*, 1669-1680.

(16) (a) Lehn, J.-M. *Chem. Eur. J.* **2000**, *6*, 2097-2102. (b) Berl, V.; Krische, M. J.; Huc, I.; Lehn, J.-M.; Schmutz, M. *Chem. Eur. J.* **2000**, *6*, 1938-1946.

(17) For example: (a) Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1995**, 117, 704-714. (b) Sessler, J. L.; Wang, B.; Harriman, A. *J. Am. Chem. Soc.* **1993**, 115, 10418-10419. (c) The synthesis of aldehyde 7 from 2,6-dihydroxyisonicotinic acid in lesser yields, and a deca substituted porphyrin with one diacetamidopyridyl group was heuristically described in: Osuka, A.; Yoneshima, R.; Shiratroi, H.; Okada, T.; Taniguchi, S.; Mataga, N. *J. Chem. Soc., Chem. Commun.* **1998**, 1567-1568. (d) Vollmer, M. S.; Wurthner, F.; Effenberger, F.; Emele, P.; Meyer, D. U.; Stumpfig, T.; Port, H.; Wolf, H. C. *Chem. Eur. J.* **1998**, 4(2), 260-269. (e) de Rege, P. J. F.; Williams, S.A.; Therien, M. J. *Science* **1995**, *269*, 1409-1413.

(18) (a) There are two different melting points reported in this reference: one for the recrystallized material and one for sublimed material, which reverted to the lower melting point on standing. Bernstein, J.; Stearns, B.; Shaw, E.; Lott, W. A. *J. Am. Chem. Soc.* **1947**, 69, 1151-1158. (b) Leffer, M. T. In *Organic Reactions*; Adams, R.; Bachmann, W. E.; Fieser, L. E.; Johnson, J. R. Snyder, H. R., Eds.; John Wiley and Sons, Inc.: New York, NY, 1941; Vol. 1, pp 91-104. (c) Shreve, R. N.; Riechers, E. H.; Rubenkoenig, H.; Goodman, A. H. *Ind. Eng. Chem.* **1940**, *32*, 173-178. (d) 2,6-diamino-4-isoropylpyridine is made in 53% using 4-isopropylpyridine and sodium amide in tetralin K. K. Kogyo, Japanese Patent: Kokai. Tokyo Koho 80 76, 861, 10, Jun. 1980. (CA 93-204,467n).

(19)Adams, R.; Miyano, S. *J. Am. Chem. Soc.* **1954**, *76*, 2785-2786.

(20) Fenlon, E. E.; Murray, T. J.; Baloga, M. H.; Zimmerman, S. C. *J. Org. Chem.* **1993**, *58*, 6625-6628.

(21) (a) Brossmer, R.; Ziegler, D. *Tetrahedron Lett.* **1966**, 5253-5256. (b) Zee-Cheng, K.-Y.; Cheng, C. C. *J. Heterocycl. Chem.* **1967**, 4(1) 163-165. (b) Demuynck, M.; DeClercq, P.; Vandewalle, M. *J. Org. Chem.* **1979**, *26*, 4863-4866.

(22) (a) Botta, M.; DeAngelis, F.; Corelli, F.; Menichincheri, M.; Nicoletti, R.; Marongiu, M. E.; Pani, A.; Colla, P. L. *Arch. Pharm.* (Weinheim), **1991**, 324, 203-207.

(23)Brown, D. T.; Eisinger, J.; Leonard, N. J. *J. Am. Chem. Soc.* **1968**, 90, 7302-7306.

(24) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476-480.

(25) (a) Little, R. G.; Anton, J. A.; Loach, P. A.; Ibers, J. A. *J. Heterocycl. Chem.* **1975**, *12*, 343-349. (b) Walker, F. A.; Balke, V. L.; McDermott, G. A. *Inorg. Chem.* **1982**, *21*, 3342-3348. (c) Milgrom, L. R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1483-1487. (d) Johnstone, R. A. W.; Nunes, M. L. P. G.; Pereira, M. M.; Gonsalves, A. M. d'A. R.; Serra, A. C. *Heterocycles* **1996**, *43*, 1423-1436. (e) Drain, C. M.; Gong, X. *Chem. Commun.* **1997**, 2117-2118.

(26) (a) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827-836. (b) Gryko, D.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 2249-2252.

(27) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1982**, *104*, 4500-4502.

(28) Lindsey, J. S. In *The Porphyrin Handbook*; Kadish, K.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, CA, **2000**; Vol. 1, pp 45-118 and references therein.

(29) Beijer, F. H.; Sijbesma, R. P.; Vekemans, J. A. J. M.; Meijer, E. W.; Kooijman, H.; Spek, A. L. *J. Org. Chem.* **1996**, *61*, 6371 – 6380. Note that a ΔG of – 7 to -12 kJ mol^{-1} corresponds to 2.8 to 4.9 k_BT, thus dynamic processes would be expected at room temperature. Though common practice, equilibrium constants for weakly H-bonding systems determined by NMR data are probably internally consistent, but should be treated with caution unless of the dynamics of the system(s) are specifically addressed.

(30) (a) Drain, C. M.; Gentemann, S.; Roberts, J. A.; Nelson, N. Y.; Medforth, C. J.; Jia, S.; Simpson, M. C.; Smith, K. M.; Fajer, J.; Shelnutt, J. A.; Holten, D. *J. Am. Chem. Soc.* 1998, *120*, 3781-3791. (b) Drain, C. M.; Kirmaier, C.; Medforth, C. J.; Nurco, D. J.; Smith, K. M.; Holten, D. *J. Phys. Chem.* 1996, *100*, 11984-11993.

(31) Shelnutt, J. A.; Song, X.-Z.; Ma, J. G.; Jia, S.-L.; Jentzen, W.; Medforth, C. J. *Chem. Soc. Rev.* **1998**, *27*, 31-41.

(32) Drain, C.M.; Shi, X.; Milic, T; Nifiatis, F. *Chem. Commun.* **2001**, 287-288.

(33)(a) DeGrado, W. F.; Lear, J. D. *J. Am. Chem. Soc.* **1985**, *107*, 7684 – 7689. (b)Deranleau, D. A.; *J. Am. Chem. Soc.* **1969**, *91*, 4044 – 4054. (c) Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 3910 - 3915.

Chapter 2

1 A. Aviram, M. Ratner, Eds. *Molecular Electronics: Science and Technology*, Ann. NY Acad. Sci. **1998**, *852*, and references therein; C.M. Drain, D. Mauzerall *Biophys. J.* **1992**, 1556-1563, and references therein.

2 T. Pullerits, V. Sundstrom, *Acc. Chem. Res.* **1996**, *29*, 381 – 389; V. Novoderezhkin, R. Monshouwer, R. van Grondelle, *Biophys. J.* **1999**, *77*, 666 - 681.

3 For reviews: A.K. Burrell, M. R. Wasielewski, *J. Porph. Phthal.* **2000**, *4*, 401-406; B. Maiya, *J. Porph. Phthal.* **2000**, *4*, 393-397; K. S. Suslick, N. Rakow, M. E. Kosal, J.-H. Chou, *J. Porph. Phthal.* **2000**, *4*, 407-413; R. Dagani, *Chem. Eng. News*, **1998**, (76)23, 35-46.

4 For example: P. Bhyrappa, S. R. Wilson, K. S. Suslick, *J. Am. Chem. Soc.* **1997**, *119*, 8492 – 8502; S. Dahal, I. Goldberg, *J. Phys. Org. Chem.* **2000**, *13*, 1-6. Y. Diskin-Posner, S. Dahal, I. Goldberg *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 1288-1292.

5 For example: T. Hayashi, T. Miyahara, N. Koide, Y. Kato, H. Masuda, H. Ogoshi, *J. Am. Chem. Soc.* **1997**, *119*, 7281 – 7290; A. J. Epstein, C.M. Wynn, M. A. Girtu, W. B. Brinckerhoff, K.-I. Sugiura, J. S. Miller, *Mol. Cryst. Liq. Cryst.* **1997**, *305*, 321-322.

6 C.M. Drain, R. Fischer, E.G. Nolen, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.*, **1993**, 243-245; C.M. Drain, K.C. Russel, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1996**, 337-338; C. Ikeda, N. Nagahara, E. Motegi, N. Yoshioka, H. Inoue, *Chem. Commun.* **1999**, 1759 – 1760.

7 C. M. Drain, F. Nifiatis, A. Vasenko, J. D. Batteas, *Angew. Chem.* **1998**, *37*, 2344-2347; C. M. Drain, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1994**, 2313-2315; J.-C. Chambron, V. Heitz, J.-P. Sauvage in *The Porphyrin Handbook, Vol 6* (eds.: K.M. Kadish, K.M. Smith, R. Guilard), Academic Press, San Diego, **2000**, 1-41, and references therein; A. Prodi, M. T. Indelli, C. J. Kleverlaan, F. Scandola, E. Alessio, T. Gianferrara, L. G. Marzilli, *Chem. Eur. J.* **1999**, *5*, 2668-2679.

8 J. L. Sessler, B. Wang, A. Harriman, *J. Am. Chem. Soc.* **1995**, *117*, 704 – 714; J. L. Sessler, C. T. Brown, D. O'Connor, S. L. Springs, R. Wang, M. Sathiosatham, T. Hirose, *J. Org. Chem.* **1998**, *63*, 7370 – 7374; T. Arimura, S. Ide, H. Sugihara, S. Murata, J. L. Sessler, *New J. Chem.* **1999**, *23*, 977 - 979.

9 A. Osuka, R. Yoneshima, H. Shiratori, T. Okada, S. Taniguchi, N. Mataga, *Chem. Commun.* **1998**, 1567-1568; P. J. F. de Rege, S.A. Williams, M. J. Therien *Science*, **1995**, *269*, 1409-1413.

10 A distorted porphyrin bearing a single 3,5-diamidopyridyl group was reported.[8c]

11 Supporting information include the parameters from the NMR fits, the results of the van't Hoff plots, uv-vis and fluorescence data for the monomeric and square tetrameric species, and ESI-MS spectrum for the self-assembled square species.

12 F. H. Beijer, R. P. Sijbesma, J. A. J. M. Vekemans, E. W. Meijer, H. Kooijman, A. L. Spek, *J. Org. Chem.* **1996**, *61*, 6371 – 6380.

13 Though common practice, equilibrium constants for weakly H-bonding systems determined by NMR[12] data are probably internally consistent, but should be

treated with caution unless of the dynamics of the system(s) are specifically addressed.

14 W. F. DeGrado, J. D. Lear, *J. Am. Chem. Soc.* **1985**, *107*, 7684 – 7689; D. A. Deranleau, *J. Am. Chem. Soc.* **1969**, *91*, 4044 – 4054; B. J. Whitlock, H. W. Whitlock, *J. Am. Chem. Soc.* **1990**, *112*, 3910 - 3915.

A. D. Adler, F. R. Longo, W. Shergalis, *J. Am. Chem. Soc.* **1964**, *86*, 3145 - 3148; C. M. Drain, X. Gong, *Chem. Commun.* **1997**, 2117 –2118.