DENDRITIC MATERIALS FOR OPTICAL APPLICATIONS:
A. SYNTHESIS AND STUDY OF NON-AGGREGATING OCTASUBSTITUTED
   DENDRITIC PHTHALOCYANINES FOR OPTICAL LIMITING
   APPLICATIONS
B. SYNTHESIS AND STUDY OF TWO-PHOTON DENDRITIC DYES FOR
   BIOMEDICAL IMAGING APPLICATIONS

by

Casey Alexander Kernag

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DEDICATION

I would like to dedicate this body of work to my beloved wife Jeannette, and wonderful daughter Brianna, as well as to all of my family and friends who believed in me throughout this last obstacle known only as graduate school.
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ABSTRACT

This dissertation investigates the synthesis and analysis of new dendritic compounds for their utility as nonlinear optical materials. Two-photon absorbing dendritic dyes and octasubstituted dendritic phthalocyanines utilize the dendrons along the periphery to shield the central, “active” core from the external environment.

An attempt to obtain phthalocyanine materials for use as optical limiters entailed the attachment of dendritic substituents through a hydroquinone spacer to phthalonitriles which were then cyclized to give the target phthalocyanines. Investigation of the aggregation properties of these compounds showed that as the generation of the dendritic substituent increased, the amount of aggregation decreased. This was seen both in thin films as well as in solution. However, as the dielectric constant of the solvent increased, aggregation of individual phthalocyanines in solution also increased. Substitution on the periphery of the dendron also had a role in how the phthalocyanine behaved in solution. The presence of t-butyl groups in the meta positions along the periphery of the dendrimer further decreased the amount of aggregation that occurred in solution. The addition of zinc to the core of the phthalocyanine led to further prevention of aggregation, again in both thin films and in solution. Fluorescence studies on these compounds had indicated the presence of an energy transfer mechanism between the dendron periphery and the phthalocyanine core. The dendritic zinc phthalocyanines also displayed small $K_{SV}$ values which suggest that the approach of quenching molecules to the core of the phthalocyanine is greatly hindered in solution by the dendritic periphery.
In the development of a material for biomedical imaging, a strong effect was exhibited by the change in polarity of the solvent on the two-photon absorption (TPA) of bis-styrylbenzene (BSB) dyes which resulted in a loss of the fluorescence quantum yield ($\Phi_f$) as the polarity increased. Covalent attachment of different generations of a 4-carboxy terminated dendron to the dye resulted in a smaller decrease in the $\Phi_f$ based upon the generation of the attached dendron. A study of the solvent effect on the dicyano-substituted BSB dendritic TPA dye indicated the presence of a possible hydrogen bonding interaction between the dendron and the dye at low pH. This interaction resulted in a strong decrease in the $\Phi_f$ of the dye, a loss that was partially remedied by raising the pH to 12.
CHAPTER 1

INTRODUCTION

1.1 Introduction to the synthesis of dendrimers

As technology progresses towards smaller and smaller devices, a need arises for materials which possess a wide range of properties including encapsulation of smaller molecules or switching a signal to either the on or off position within a system. Sometimes these applications are in environments that may be too harsh or incompatible with current target compounds. A relatively recent solution to some of these problems may be to use a dendritic material. Dendrimers can be defined as monodisperse macromolecules with a regular and highly branched three-dimensional architecture. There are three main regions located within the dendrimer: (i) a core or focal moiety, (ii) layers of branched repeat units emanating from this core, and (iii) end groups on the outer layer of the repeat units.

The field of dendrimer chemistry can be traced back to Vögtle’s groundbreaking paper published back in 1978 on the synthesis of low molecular weight branched amines. It is with this paper that the idea of a cascade synthesis was introduced, whereby “generational” compounds were prepared and characterized after each step of the construction process. Six years later, Tomalia published the synthesis of the first family of dendrimers. These poly(amidoamine), or PAMAM dendrimers, have been well-studied and are commercially available today. A few months later, Newkome reported preliminary results toward another family of polyamide dendrimers based upon an arborol core. It was not until four years later that a new way to synthesize
dendrimers was published with the work of Hawker and Fréchet in the synthesis of their polyaryl ether dendrimers.\textsuperscript{1,7,18} Since then, the growth of dendrimer chemistry has been exponential, spanning a wide range of applications from materials-based dendritic compounds to their use in biological systems.

1.1.1 Divergent approach to dendrimer synthesis

The divergent approach was the earliest method with which to construct dendritic compounds. The original work done by Vogtle was termed a “cascade synthesis” which is a reaction sequence that can be carried out repeatedly.\textsuperscript{1,3} Synthesis of the dendrimer begins at a focal point or the core of the dendritic structure. Growth continues outward through a series of coupling and deprotection steps (Scheme 1.1). Reaction of the peripheral functional groups on the core with a complimentary reactive group on the monomer leads to the introduction of a branching point and an increase of the number of peripheral functional groups on the molecule. Each of the new functional points are protected to prevent hyperbranched polymerization, and as such, need to be activated before further growth can be performed. Much of the work on PAMAM dendrimers done by Tomalia,\textsuperscript{1,5,19} and on Newkome’s “arborol” systems\textsuperscript{16} proceeded through this route.

The use of the divergent method is preferred for industrial scale synthesis as the molecular weight, and therefore the amount of sample basically doubles from generation
Scheme 1.1  Example of the divergent method for the synthesis of dendrimers
to generation and only large amounts of monomer are needed for growth. There are, however, several drawbacks for this method. The first is incomplete functionalization. Since the number of reactive groups grows exponentially from generation to generation, the likelihood that sections of periphery do not fully react with the monomer also increases. This is also a problem in the deprotection step as well, whereby certain areas are not activated, a problem that is compounded in the next coupling step. Then there comes the challenge of purifying the mixture of both the complete and incomplete dendritic structures. Due to these problems and the onset of spatial packing limitations, high generations of these compounds cannot be prepared having a single molecule, or monodisperse composition.

1.1.2 Convergent approach to dendrimer synthesis

The other method to synthesize dendritic structures was introduced in 1990 by Hawker and Fréchet. The convergent method begins at what will become the final periphery of the dendrimer and couples the end groups to the branching monomer. As with the divergent method, after each coupling has taken place, an activation is performed. Afterwards, the product is taken on to another coupling step with more monomer resulting in generational growth of the dendritic wedge. When the wedge has grown the desired generational size, attachment to a polyfunctional core through the focal point can occur. Scheme 1.2 illustrates the synthesis of a dendron by this method.
Scheme 1.2 Example of the convergent method for the synthesis of dendrimers
The main disadvantage to using the convergent method is loss of considerable amounts of sample in the synthesis of large generations. Large amounts of monomer are used because of the exponential decrease of its contribution to the mass of the final product, leading to considerable increases in cost. There is also significant sample loss from non-quantitative reaction yields and from sample purification.

However, there are many benefits in using the convergent approach. First, products are attained with much higher purity than with the divergent method because of the smaller number of components in the reaction mixture, which provides to the ability to purify products by chromatographic methods. Second, the use of this method enables synthetic versatility. By building the dendrons first, one has the ability to be able to vary the composition of the end groups. This creates possibilities, everything from attaching different dendritic wedges to a polyfunctional core,\textsuperscript{1,10} to having one specific functional group on the periphery of the dendrimer.\textsuperscript{1,11} Hence, the convergent method is more often used because it is much easier to modify for a wider diversity of applications while maintaining monodispersity in the final product compounds.

1.1.3 Synthesis of Fréchet polyarylether dendrons

Synthesis of the poly(benzyl ether) dendrons was pioneered by Hawker and Fréchet in 1990.\textsuperscript{1,8,12} The monomeric species in this synthesis is 3,5-dihydroxybenzyl alcohol (1). Coupling of 1 to benzyl bromide occurs in the presence of 18-crown-6 and potassium carbonate to form a first generation dendron 2. After purification, the benzylic alcohol is transformed into benzyl bromide 3 in the presence of triphenylphosphine and
carbon tetrabromide. A repetition of the first step is then performed with 1 to give the second generation dendron 4, and after conversion to the bromide 5, this process is again repeated until a dendron of the appropriate generational size is made (Scheme 1.3).

These materials are able to be obtained in high yields up to the sixth generation and exhibit chemical stability due to the ether linkages. This synthetic method leads to a high degree of versatility seen by the many groups who have varied the basic structure of the dendritic wedge to some degree. Some of the monomer variations have been the chiral protected diols 6-9 of McGrath and co-workers,\textsuperscript{1,13-1,17} the 4,4-bis(4'-hydroxyphenyl)pentanol monomer 10 published by Wooley et al.\textsuperscript{1,18} and the use of 3,4,5-trihydroxybenzyl alcohol 11 by Percec (Figure 1.1).\textsuperscript{1,19}

Changes can also be done to the periphery of the dendritic wedge. The groups along the outside of a dendrimer can affect something as simple as an enhancement of solubility in a specific solvent. Altering the periphery can result in the addition of a particular element that may tailor the dendrimer for a specific application. Hawker has placed ester groups in the 4-position of the peripheral phenyl groups 12 such that upon saponification a water-soluble dendrimer was created.\textsuperscript{1,20} Piotti et al. used 3,5-tetradecyloxy groups 13 to impart solubility in a non-polar environment for catalytic systems.\textsuperscript{1,21} Fréchet and co-workers have placed coumarin dyes 14 on the exterior of dendrimers in an attempt to show energy transfer properties between the periphery and the core.\textsuperscript{1,22} And, Li and McGrath placed azobenzene moieties (15) on the outside of
Scheme 1.3  Synthesis of unsubstituted Fréchet polyaryl ether dendrons

$$\text{HO}$$

$$\text{Br}$$

$$\text{K}_2\text{CO}_3, \text{18-crown-6, acetone, reflux}$$

$$\text{OH}$$

$$\text{Br}$$

$$\text{CBr}_4, \text{PPh}_3, \text{THF}$$

$$\text{HO}$$

$$\text{Br}$$

$$\text{CBr}_4, \text{PPh}_3, \text{THF}$$

$$\text{HO}$$

$$\text{Br}$$

$$\text{CBr}_4, \text{PPh}_3, \text{THF}$$
Figure 1.1 Modification of the branching unit in the polyaryl ether dendron
dendrimers to probe photoisomerization properties (Figure 1.2). These are but a few of the numerous examples which showcase the ease of the synthetic versatility of these polyaryl ether dendrimers.

1.2 Dendrimers used in biological applications

With the mapping of the human genome and the emergence of new diseases such as severe acute respiratory syndrome (SARS) and the West Nile Virus, the biotechnological field has grown exponentially. Because of this, the development of new means of drug delivery systems and early detection methods become important. Much has been done to inaugurate dendrimers into this developing field, and yet, it seems that there is much more work yet to be done. One can envision the use of a pro-drug as the monomeric pieces of the dendrimer, which after enzymatic degradation would act to time-release the medication to a specific area of the body. The medical field could also benefit by the modification of the periphery of the dendrimer to allow for the binding of either viruses or antibodies. Since there is an abundance of sites on the exterior of the dendrimer, one can expect a high degree of sensitivity for these systems. The groundwork of looking at the biocompatibility of dendrimers along with their uses as drug delivery systems and biosensors has been done. However, more research needs to be performed to bring this developing field to the forefront of biotechnology.
Figure 1.2  Examples of peripheral modifications to polyaryl ether dendrons
1.2.1 Biocompatibility of dendrimers

While there have been published reports of dendritic structures composed of both amino acids\textsuperscript{1,24} and carbohydrates,\textsuperscript{1,25} there have been no definitive studies performed on the biocompatibility of these structures. The only dendritic structures that have been looked at have been the PAMAM dendrimers. Work done by Roberts et al. looked at the \textit{in vitro} and \textit{in vivo} toxicity along with immunogenicity and biodistribution of PAMAM dendrimers in V79 Chinese hamster cells and Swiss-Webster mice.\textsuperscript{1,26} Of the generations that were looked at (G3, G5, and G7) only the G7 showed any degree of incompatibility. The biodistribution of the dendrimers in the mouse tissue showed the preferential localization of G3 in the kidneys while the G5 and G7 localized in the pancreas. It was concluded that the use of these dendrimers in biological systems should be allowed and that close attention should be paid to both the dose and the generation size, while further biodistribution studies be considered.

Another set of studies has also been performed on the biocompatibility of PAMAM dendrimers. Work done by Duncan and Malik has shown the cytotoxicity of G3 and G4 amine terminated dendrimers towards both the human cancerous CCRF and B16F10 cell lines.\textsuperscript{1,27} Modification of the periphery to carboxy terminated PAMAM dendrimers yielded materials which were non-toxic to those cell lines. Incorporation of the anticancer drugs doxorubicin and cisplatin as G3 dendritic complexes led to a high degree of \textit{in vitro} toxicity, opening the possibilities of using dendrimers as anti-cancer agents.
Many more studies have yet to be done to see how other types of dendrimers act in biological systems, and how the body processes such compounds. Further studies of the PAMAM systems, as well as amino acid-based, carbohydrate-based, and dendritic structures with polyethylene glycol (PEG) units on the periphery, need to be performed so that research in the drug delivery and treatment areas can move forward faster.

1.2.2 Use of dendrimers as hosts for drug delivery

One of the fastest growing areas within biotechnology is the research into using dendrimers as potential drug delivery agents. The use of a small spherical molecule which could be modified to target specific tissues, as well as remain hidden from the immune system would be ideal.

Liu et al. have looked at the selective modification of the dendritic periphery to result in water soluble PEG conjugates which could be used as potential drug carriers.\textsuperscript{1,28} PEG groups enable a shielding of the dendritic molecule from the immune system, a useful property that can save the targeted individual from anaphylactic shock, while imparting a high degree of water solubility. Attachment of cholesterol \textsuperscript{16}, phenylalanine \textsuperscript{17}, and tryptophan \textsuperscript{18} allowed for studies of this system with model drugs (Figure 1.3).

Fréchet and coworkers have synthesized a series of polyether dendrimers that contain peripheral folate residues to study tumor specificity.\textsuperscript{1,29} Since folate receptors have been known to be overexpressed on the surfaces of tumor cells, and such receptors mediate endocytosis, placement of these molecules on the surface of the dendrimer could result in a cell selective drug delivery system.\textsuperscript{1,30} Hydrazine
Figure 1.3  Liu's dendritic drug carrier system
derivatization of ester terminated dendrons followed by coupling with either folate 19 or methotrexate 20 resulted in the targeted dendrons (Figure 1.4). Currently, no results on tumor specificity have been published.

There have been a number of other studies that have been performed involving non-covalent attachment of drugs to dendrimers and attachment of other antitumor agents such as 5-fluorouracil and cis-platinum.

1.2.3 Use of dendrimers as biosensors

With growing terrorist threats, new methods for the early detection of bioterrorism agents have become a topic of growing interest. Early studies with dendrimers have shown their usefulness as both chemical and amperometric sensors for a number of different agents.

Wang et al. has developed biosensors for DNA. By using a system whereby the DNA sequences branch from core which is immobilized to a piezoelectric plate, they were able to adhere a G4 DNA dendritic system with sequences specific to Cryptosporidium parvum, a water-borne pathogen. The results were encouraging, as an eight-fold decrease in the detection limit was seen over the linear sensor. Also, the sensitivity was higher for the dendritic system by at least an order of magnitude. These effects were attributed to the higher hybridization capacity of the dendrimer system. However, such a low sensitivity gain indicates that not all of the arms are binding efficiently, which could be due to the arms bumping into one another or a flattening of the dendrimer on the surface of the plate after adsorption. This being the case, the system
Figure 1.4  Fréchet's cancer therapeutic dendritic groups
still gives hope to a new budding technology which could allow for early detection of pathogenic outbreaks.

Orentas and coworkers have looked at the detection of Epstein-Barr Virus (EBV) in a number of disease states such as HIV, Hodgkin’s lymphoma, and post-transplant immunocompromised patients. Any increase in EBV load can place the patient in a serious, life-threatening condition, making early detection extremely important. Use of a RNA dendrimer construct with eight different sequences and more than 100 arms gave results that approached the sensitivity of Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR). In two patients previously diagnosed with post-transplant lymphoproliferative disease (PTLD), the detection limit of EBV approached that of one infected mononuclear blood cell in 250,000. Further work needs to be done to optimize the effectiveness of the dendritic system so that it may surpass the RT-PCR method.

Losada et al. have utilized ferrocene containing dendrimers as a sensor for glucose. Incorporation of the dendrimer 21 with glucose oxidase on a carbon paste electrode led to detection of glucose at biological levels (Figure 1.5). These sensors were stable at low temperatures and in oxygen-free environments. In oxygen rich environments however, decomposition was relatively slow with a 15% loss of activity occurring over a period of 250 hours. Sensitivity was similar when compared to a polymeric ferrocenyl system, but the detection of the glucose in the dendritic system was performed at lower potentials. Higher potentials can result in the influence of interfering species in biological samples. Current work is focusing on the incorporation of a
Figure 1.5  Losada's ferrocenyl dendrimer for the detection of glucose
polymer coating to increase air stability and the linear range of the sensor as well as increasing the generational size of the ferrocenyl dendrimers.

With this pioneering work in the field of biosensors, it may not be long before the first field equipment containing dendrimers may be available for site research. Construction of such electronic sensors could lead to their use in the tracking of bacterial or viral infections through the population, allowing for early detection and treatment for potential life-threatening situations, or for the tracking of an individual’s glucose levels in the treatment of diabetes.

1.3 Dendrimers used in materials applications

The field of materials chemistry is growing almost as fast as its biological counterpart. The use of dendrimers as specific targets for materials design has been looked at for a wide variety of applications. The high degree of branching on the exterior of the dendrimer allows for a large amount of functionality at a high local concentration. The core could be a group such as a metal center for catalysis or a degradable moiety that could be applied to the field of lithography. Molecular switches can be attached in the branching regions which can be used for either a binary or recording function. This section will touch on a few of the more widely studied applications, namely: metallodendrimers used as catalysts, liquid crystalline dendrimers, light harvesting dendrimers, and dendrimers used as light emitting diodes (LEDs).
**Metallodendrimers used as catalysts**

Organometallic dendrimers have been designed to have advantages in both architecture and composition over the polymeric organometallic compounds. Individual metal centers have been incorporated as branching units, building block connectors, terminal groups, and as structural auxiliaries (incorporation of metal centers after dendritic construction) (Figure 1.6). Their use as catalysts involve placement of reactive metal centers in a different environment at the center of the dendrimer or in high concentrations along the periphery.

Moore et al. have investigated the use of a reactive manganese porphyrin as a catalyst for oxidation reactions. Attached to the porphyrin polyaryl ester dendrons terminated with 3,5-dimethylbenzoic acid of the 3rd 22 and 4th 4th generation were used, and the catalytic properties of the dendrimer were studied (Figure 1.7). Regioselective epoxidation of non-conjugated dienes and equimolar mixtures of various alkenes were looked at. Both of the dendrimers showed considerably high regioselectivity for less sterically hindered double bonds than did the core by itself.

Yamago and coworkers have looked at the placement of a titanium atom at the center of a dendrimer 24 (Figure 1.8). Ligated between two binaphthol groups which are substituted with polyaryl ether dendrons at 6,6' positions, this dendrimer was used as a catalyst in asymmetric allylation reactions. Yields were low (18-36%), but the corresponding enantiomer excesses (ee) were between 88-92%. The results were very similar to when (R)-binaphthol was used alone (yield 31%, ee 87%).
Figure 1.6  Positioning area of metals within dendritic structures
Figure 1.7  Third generation dendritic manganese epoxidation catalyst
Figure 1.8  Yamago’s titanium binaphthol dendrimer
van Koten has studied dendrimers as catalysts in the Kharasch addition of polyhaloalkanes to alkenes. Polysiloxane dendrimers terminated with aryl bromides were subjected to oxidative addition of a nickel species to give the active catalyst 24 (Figure 1.9). The catalytic activity of the dendrimers was found to be comparable to that of the monomeric species. However, the dendrimers were easily removed from the reaction mixture which allowed their use in subsequent reactions.

Hoveyda and coworkers examined the development of a catalyst to be used in ring closing metathesis reactions. The benzylidene ruthenium catalyst 25 was air-stable and produced conversions of greater than 87% in the metathesis reaction of bis(allyl)-N-tosylamide (Figure 1.10). The dendrimer had a high recovery after silica gel column chromatography (90%), with only a slight loss in ruthenium (8%) as confirmed by $^1$H NMR.

Many other dendritic systems have been synthesized and other catalytic reactions investigated. The chemistry in this area seems to be splitting into two subareas, the use of these systems as catalysts for synthetic applications and the investigation of biomimetic catalysts based on biological systems such as heme and cytochrome c. The ability to use the macromolecular architecture may bring scientists closer to understanding how complex systems work.
Figure 1.9  van Koten’s recyclable nickel catalyst for Kharasch additions
Figure 1.10 The Hoveyda metathesis catalyst
1.3.1 Liquid crystalline properties of dendrimers

A liquid crystalline phase is an intermediate state of matter whereby a liquid has some type of an ordering property reminiscent of the solid state. This ordering can be divided into three main types: nematic, smectic, and cholesteric. Nematic liquid crystals have ordering along the long axis of the molecule, much like cars on a freeway. Smectic liquid crystals are ordered along the long axis of the molecule as well as in one other direction, similar to soldiers marching in rows. Cholesteric liquid crystals maintain the highest degree of order where the molecules are arranged along their long axis with a layered helical effect suggestive of DNA.

Some of the seminal work done within the liquid crystal area involving dendrimers has involved that of the Percec group.\textsuperscript{1,44-1,48} What they found is that the generational size of the dendron can affect the self-assembly that results in the specific liquid crystalline phase. Smaller or less substituted dendrons form fan-like structures which assemble into washers that lead to the formation of 2-D hexagonal columns. The larger or more functionalized dendrons tend to adopt a conical shape that leads to a 3-D cubic thermotropic liquid crystalline phase (Figure 1.11). It was also found that a single spherical dendrimer could form a cubic phase. Utilizing Fréchet-type dendrons with dodecyl gallate groups at the periphery, dendrimers of generations G2-G5 took on a spherical cubic lattice. X-ray diffraction data was able to show that the G5 dendrimer was a single isolated spherical structure.
Figure I.11  Percec’s liquid crystalline dendrimers$^{1,44}$
Pesak and Moore have looked at the formation of liquid crystalline compounds by using phenylacetylene dendrimers. The use of the phenylacetylene units minimizes any globular formation within the dendritic structure by rigidifying the arms of the dendrimer. By placing [2-(2-(2-methoxyethoxy)ethoxy)ethyl] ester units along the periphery of the dendrimer, formation of columnar discotic liquid crystalline phases was seen in generations G1, G2 (26), and G3 (Figure 1.12).

Deschenaux et al. have looked dendritic compounds that contained cholesterol substituted ferrocene groups on the periphery. The 1st dendrimer 27 was based upon a 1,3,5-triacyl substituted core and exhibited a broad enantiotropic smectic phase along with good thermal stability (ca. 250°C). The 2nd dendrimer 28 contained a C60 substituted malonate core and also had exhibited a broad enantiotropic smectic A phase (Figure 1.13). The broad enantiotropic smectic A phase was determined from both the polarized optical microscopy and X-ray diffraction data in each molecule.

Future directions in this area will focus on the attachment of other mesogens to dendritic compounds to produce a wider diversity of compounds. Differentiation in the ordering stimuli, thermal stabilities, or transition temperatures can lead to a number of different applications. Liquid crystal dendrimers which can be oriented by light, heat, or electricity will be needed in this ever-expanding industry of portable computers, DVDs, and LCD televisions.
Figure 1.12  Pesak and Moore's phenylacetylene liquid crystalline dendrimers
Figure 1.13  Deschenaux's cholesterol substituted ferrocene dendrimers
1.3.2 Use of dendrimers as light harvesters

Nature uses peripheral chromophores to channel energy to a reactive center. Such energy drives natural processes such as photosynthesis from sunlight. Dendrimers have properties that can enable them to perform such actions. While this work is still in its infancy and the efficiency of this process leaves a lot to be desired, the results that have been obtained show the use of creative ways to transfer light to the core energy sink. Many applications are using this system as a model and include signal amplifiers, fluorescent sensors, and frequency converters.

Balzani and coworkers have synthesized dendrimers such as 29 containing two or more different metals (Figure 1.14). The absorption and electrochemical properties of these compounds are additive. The dendrimer then ends up being the sum of its individual parts. Couple this with the fact that the electronic interactions are strong enough to allow for fast energy transfer and this system becomes nearly ideal for utility in devices built upon the use of light-harvesters.

The work of Xu and Moore concentrated on using an arylacetylene dendrimer as a light harvester. With perylene attached at the focal point, energy was collected at the periphery of the dendrimer 30 and funneled to the fluorescent emitter (Figure 1.15). The photophysics of the molecule indicate that the excitation of the perylene at 312 nm, corresponding to the absorption maxima of the peripheral groups on the dendrimer, proceeded with an enhanced intensity when it was compared to that of 3-ethynylperylen. Spectroscopic evidence indicated a transfer efficiency of approximately 98% from the
Balzani’s light-harvesting metallocendrimers

Figure 1.14
Figure 1.15  Xu's dendrimer for energy collection and transmission
dendrimer to the perylene.\textsuperscript{1}\textsuperscript{54} Research has also been done that looked at the enhancement of extended versus compacted molecules.\textsuperscript{1}\textsuperscript{55}

Vögtle and Balzani have looked at the non-covalent encapsulation of an eosin dye within a PAMAM core having attached dansyl units and branching arylether dendrons terminated in naphthyl groups \textbf{31} (Figure 1.16).\textsuperscript{1}\textsuperscript{56} What was seen was that all 64 peripheral groups participated in energy transfer to the eosin molecule. This transfer process proceeded efficiently both through intra and intermolecular routes via a Förster-type mechanism due to the strong overlap between absorption and emission maxima of the individual units.

The use of attached dyes to the periphery of the dendrimer has also been attempted. Fréchet and coworkers have looked at the attachment of a coumarin-2 donor to the periphery and a coumarin-343 acceptor molecule to the focal point of arylether dendron \textbf{32} (Figure 1.17).\textsuperscript{1}\textsuperscript{57-1}\textsuperscript{59} Studies on the effects of the attachment of the coumarin molecules to the dendron in independent donor and acceptor models showed no loss of the spectral overlap between donor emission and acceptor excitation. With a family of the doubly labeled dendrons, there was a definite doubling of the donor absorption as a function of dendritic generation, while the acceptor absorption stayed constant. The only change that was noted was a shift in the absorbance of the acceptor with relation to generational growth that was due to the increasing polar environmental effects of the dendrons. As the donor groups were excited, only emission of the acceptor was seen. This indicates a high degree of energy transfer between the two groups. Work is still in progress as to explain the mechanism of the highly efficient transfer although it is
Figure 1.16  Vögtle and Balzani's non-covalent energy harvesting system\textsuperscript{1.56}
Figure 1.17 Fréchet's coumarin donor / acceptor dendritic system
believed to go through a Förster-type pathway. Other acceptors with significant overlap have also been studied such as oligothiophene units. The use of an oligothiophene pentamer linked through a terminal ring and a heptamer linked through the center ring, showed a quantitative amount of energy transfer up to the third generation.

While the above systems have been developed, the use of these systems as anything other than models will be both expensive as well as synthetically time consuming. However, this work will act to better develop systems for materials applications as well as try to reach a greater understanding of nature, such as the generation of molecules like ATP, through synthetic chemistry. Light harvesting dendrimers are just the first step to being able to convert the sun’s energy into an efficient, unlimited source of electricity.

1.3.3 Dendritic compounds used in light emitting displays (LEDs)

A direct benefit from the development of light harvesting dendritic systems is the direct application to LEDs. Organic LEDs (OLEDs) have advantages over their inorganic counterparts in that they are able to be manipulated so that they can span an energy gap between the ground and excited states that covers the visible spectrum. However, OLEDs tend to have low efficiencies and need to be doped with compounds that have a high electron affinity. This is usually only done with polymeric compounds and not with small molecule or oligomeric systems. The use of dendrimers helps to prevent aggregation of the emissive cores and functionalization of the wedges can lead to the incorporation of various charge transport moieties.
Fréchet et al. have utilized their light harvesting dendrimers as an initial OLED. By placing both the pentameric oligothiophene 33 and coumarin-343 dendritic species in a LED device, they were able to see simultaneous emission of both species (Figure 1.18). Devices made from blending the oligothiophene and coumarin-343 dyes resulted in the emission of the lower bandgap oligothiophene dye. Therefore, the encapsulation of the species within the dendrimer, along with the proximity of the excitation source (emission of the peripheral triarylamines) enables the observation of the coumarin-343 dendrimer emission.

Moore and coworkers have also reported the synthesis of a dendrimer LED. The dendrimer 35 was developed with phenylacetylenyl dendrons terminated with diarylamines for hole transport and an anthracene derivative at the core as the light emitter (Figure 1.19). Thin films of these molecules showed low electroluminescence intensities presumably caused by the solid state aggregation of the dendrons and the self-quenching of the cores.

The Burn group has looked at the incorporation of distyrylbenzene (DSB) units branching from a triarylamine core. This first generation dendrimer 36 was doped with 2-(4-biphenyl)-5-(4-tert-butylphenyl)-1,3,4-oxadiazole (PBD) (Figure 1.20). This blend was spin-coated onto a film of the neat dendrimer resulting in a blurred interface. This bilayer device was able to achieve some of the highest electroluminescence quantum efficiencies (0.17 %) yet seen in a dendrimer OLED system using an aluminum cathode.
Figure 1.18  Fréchet's dendrimer LED device$^{1,60}$
Figure 1.19  Moore's dendrimeric LED
Figure 1.20  Burn’s highly electroluminescent dendrimer
There is much more progress that needs to be made if dendrimers are to be utilized as OLEDs. An increase in the overall electroluminescence quantum efficiency along with more of a light harvesting approach that precludes the need for a polymeric blend may result in more mainstream uses for dendrimers. Materials applications for dendrimers are still in their infancy, but with the groundwork in place, it is only a matter of time before industries adapt these materials for new technologies.

1.4 Site isolation in dendritic materials

In nature, it seems that there are always integrated methods which act to shield or protect biologically important molecules. For example, the genetic code is nicely hidden away in the nucleus of the cell behind two membranes (cell and nuclear). Here it is tightly rolled into chromosomes which not only acts to conserve cellular space, but protects much of the DNA from external stimuli. It is only when cellular proteins are needed or cell replication is occurring that an unraveling of the chromosome occurs. In essence, our DNA is protected from its environment.

Much of understanding chemistry is the understanding of how and why molecules interact with one another. In some cases, such interactions can be beneficial, such as heme carrying oxygen through the vast areas of the body. However, there are times when these interactions are uncalled for, when a system loses its efficiency due to competing reactions with other molecules. Such problems can be caused by a lack of solubility, aggregation, or a lack of protection from the outside environment. When such problems
occur, it becomes important to try to fix things within the system without losing the desired activity.

Dendrimers can provide a method with which to shield particular molecules from the problems inflicted by their environment. By surrounding the active component within the dendrimer, external interactions are minimized, if not prevented all together. Yet the arms of the dendron are porous enough to allow for the passage of small, desired molecules to reach the interior or the active component to obtain a specific result. The following section looks at the influence of the dendrimer on the microscopic environment by increasing solubility or preventing aggregation in both organic and organometallic systems.

1.4.1 Influence of the dendrimer on the microscopic environment

An interesting aspect of dendrimers is their ability to act as insulators. By isolating a core from the external environment, one can decrease the effects of solvent or aggregation upon the active system. This is not a new idea, rather studies performed in the early 1990's by Fréchet and coworkers showed the influence of the dendritic environment upon the UV-Vis absorbance of a para-nitrophenoxy ether. A substantial increase in the overall absorbance was not seen with increasing generation size in relatively polar solvents such as acetone. When the solvent polarity shifted to more non-polar solvents, such as toluene and carbon tetrachloride, there was a noticeable shift of up to 20 nm in the UV-Vis spectra as a result of increasing from first to sixth generation dendrons. This shift in the absorbance was attributed to a shielding by the dendron,
resulting in a more thermodynamically stable polar environment surrounding the chromophore.

The dendrimer does not have to provide a polar environment; in fact it can do the opposite. Pan and Ford reported an increase in the solubility of pyrene in water in the presence of their dendrimer 37 (Figure 1.21).\textsuperscript{1,64,65} Their dendrimer, with its alternating amine and ether branches, acted as a non-polar environment that was able to encapsulate the pyrene molecules in an aqueous external environment. This work was similar to the work done by Wooley et al. which investigated the ability for dendrimers to solubilize pyrene and also act as unimolecular micelles, or compounds that maintain a micellar structure below a certain concentration threshold.\textsuperscript{1,20}

Dendrimers have also been used to block the external environmental influence on the activity of molecular wires. Diederich et al. have looked at the ability of dendritic wedges to insulate molecular wires from degenerative external stimuli.\textsuperscript{1,66} They were able to prepare poly(triacetylene) (PTA) oligomers with dendritic side chains 38 and then look at the effect of having the dendrons present on the overall electronic activity of the PTA (Figure 1.22). What was seen was that the dendrons did indeed protect and stabilize the conjugated backbone even though some distortion was seen in the PTA when higher dendritic generations were used.

With these examples, it is clear how dendrimers moderate the effects of the external environment upon a molecule by providing an alternate microenvironment. Whether this alteration occurs by increasing the solubility, changing the spectroscopic
Figure 1.21  Pan and Ford’s solubilizing dendrimer
Figure 1.22  Deiderich’s insulating PTA dendrimer
properties, or the insulation of a core to maintain a conjugated system, dendrimers provide a viable way to protect molecules from harsh environments.

1.4.2 Dendrimers used to isolate metal complexes

The isolation of a metal center can lead to beneficial applications. Whether one is trying to prevent self-quenching or to prevent aggregation, two processes that can decrease a material’s efficiency, the shielding properties of the dendritic bulk come in handy.

In work done by Kawa and Fréchet, lanthanide containing dendrimer 39 formed from the self assembly of the individual carboxylate dendrons, showed increases in the luminescence properties as the generation size grew from G1 to G4 (Figure 1.23). This increase was explained by a large antenna effect from the dendron as well as a shielding effect due to the site isolation of the lanthanide ions which prevents self-quenching. This enhancement of luminescence was not just seen in solution, but also in the solid state.

Balzani and Vögtle have utilized a tris(bipyridine)ruthenium core to study the effect that increasing dendritic size had on the photochemistry of the metal complex. Their results showed that the excited state lifetimes of the higher generations of dendrimer 40 were longer than that of their smaller counterparts in aerated acetonitrile (Figure 1.24). It was proposed that the increase in the luminescence was caused by a decrease in the quenching of the complex by oxygen and could be attributed
Figure 1.23  Kawa and Fréchet’s lanthanide dendrimer
Figure 1.24  Vögtle and Balzani's tris(bipyridine)ruthenium dendrimer
to one of three factors. Either there was a decrease in the diffusion rate of oxygen due to an increase in the molecular volume; a lower solubility of oxygen in the dendritic interior; or preferential solvation of the dendritic core by the dendritic branches.

There have also been reports of the isolation of redox centers. Gorman and coworkers prepared an iron-sulfur cluster dendrimer 41 (Figure 1.25). By increasing the generational size, the overall core reduction potential in dimethylformamide (DMF) became progressively more negative which was attributed to the shielding of the dendritic shell. Electrochemical reduction became less reversible at higher generations by cyclic voltammetry because of the increasing kinetic difficulty of transferring electrons from the electrode to the core. This property has been well established in natural systems with cytochrome c and other electron-transfer proteins.

The use of the dendritic shell to modulate both luminescence and redox properties is relatively new. In time this method could be used to tune the potential of electrophores for their use as redox mediators in electrocatalysis. But first, a more thorough investigation of the operating factors that control and shape the dendritic microenvironment must be performed. While the examples above showcased beneficial effects from the attachment of dendritic wedges, the use of other transition metals inside the dendritic core have shown no real increase in the electrochemical potentials and the only observable change was an increase in the irreversibility of the electron-transfer process at higher generations.
Figure 1.25  Gorman's iron-sulfur cluster dendrimer
1.4.3 Dendrimer isolation of porphyrins

Much of the work involving the site isolation of metal complexes has focused on the isolation of the macrocyclic porphyrins and phthalocyanines. Porphyrins consist of four interconnected pyrrole rings joined by a methine bridge. Phthalocyanines are analogous compounds which will be covered more in depth in Chapter 2. These compounds play an important role in nature as both oxygen carriers (hemoglobin) and redox centers (cytochrome c). In order to mimic these abilities in artificial systems, the surroundings must be duplicated, and to accomplish this, the porphyrin ring has to be isolated from the exterior environment.

Diederich and coworkers have reported the divergent synthesis of a series of aminotriester porphyrin dendrimers, like 42 for the purpose of modeling redox potentials through environmental polarity modification (Figure 1.26).\textsuperscript{178} The cyclic voltammetry values of the zinc porphyrin dendrimers in THF and methylene chloride with 0.1 M tetrabutylammonium hexafluorophosphine showed that the first oxidation potentials were up to 300 mV less positive than the unshielded zinc porphyrin core. These results suggest that modifications of the dendritic exterior can enable tailoring of the electrophoric environment.

Aida et al. have looked at the synthesis of the octasubstituted polyethereal dendrimer 43 (Figure 1.27).\textsuperscript{179, 180} These dendrimers maintained photochemical activity within the crowded core. For the larger dendrimers, the core was quenched by relatively small molecules such as vitamin K but larger quenchers such as G1 porphyrin dendrimer,
Figure 1.26  Diederich’s zinc porphyrin dendrimer
Figure 1.27  Aida’s polyethereal porphyrin dendrimer
were not able to gain access. Negatively charged fluorescence quenchers such as methyl viologen had no effect on the dendritic generations above G2.

The Fréchet group has also looked at the synthesis of zinc porphyrin dendrimers such as 44, using benzyl ether dendrons (Figure 1.28).\textsuperscript{1,81,1,82} What was seen was that the shell did not alter the physical properties of the porphyrin core. But, even with the lower generations, the rate of electron transfer was greatly reduced, mainly because of the separation of the porphyrin from the cyclic voltammetry electrode. The small molecule quenching experiments using this system resulted in data that mimics the work of Aida.

Other research groups have looked at placing palladium porphyrins to study phosphorescence\textsuperscript{1,83} and iron porphyrins to mimic cytochrome c.\textsuperscript{1,84} The results seen were similar to those above, that in which the dendritic shell protects the porphyrin from quenchers and enhances redox properties. While these examples have shown site isolation of the porphyrin in the core of the dendrimer, there have been examples where the porphyrin is placed throughout the dendrimer.\textsuperscript{1,85,1,86} However, it is the site isolation of the core which results in the promotion of desired properties in environments that would prevent these actions without the shielding of the dendrimer.

1.5 Introduction into nonlinear optics (NLO)

Much work has been done in the use of light as an information carrier. It is theorized that optical information technology will expand at a rate that roughly doubles transport, processing, and storage capacity every three years.\textsuperscript{1,87} The way that this will be
Figure 1.28  Fréchet’s zinc porphyrin dendrimer
done is through nonlinear optics. But to understand nonlinear optics, one must first understand linear optics.

Linear optics (LO) includes the phenomena of absorption, emission, reflection, refraction, and diffraction. The principle of LO states that electric polarization has a frequency which exactly corresponds to that of an electric field. The polarization is defined in terms of the incident electric field multiplied by the electric susceptibility which takes into consideration the refractive index of the material and any absorption or emission characteristics. Hence, at low intensities the relationship is linear where the polarization is proportional to the field applied, so the transmitted radiation through the medium has the same frequency as the incident radiation.

Nonlinear optics incorporates a more complex mathematical area. Here, the relationship between the polarization and the electric field is a power series, where the linear component is added to a squared component, plus a cubed component, and so on and so forth. Each term carries its own susceptibility factors ($\chi^n$) which are known as nth-order linearities. These terms greatly decrease as the value of n increases, meaning that under normal lighted conditions, one does not observe higher-order effects. However, these factors are extremely important, when high intensity fields (lasers) are used, since the values of the electric field terms compensate for the low values of the susceptibilities.

Second-order nonlinearities are generally used for frequency conversion experiments. Since lasers operate over a narrow band, there are some frequencies that are not accessible via LO methods. Frequency doubling uses a crystal to "alter" the
frequency of light. By using a high intensity laser beam, the close proximity of two photons entering the crystal enables the addition of their energies. What comes out the other side of the crystal is a photon that has roughly twice the energy of the incident beam. This process could also occur with two photons of different frequencies from separate sources which could again result in the release of a photon of higher energy. Finally, the opposite could be true, whereby the incident light is of higher energy and by passing through a material, is split into two component photons of the same energy, exactly one-half of the incident light.

Third-order nonlinearities are based upon the cube of the electric field and are especially important in applications such as fiber optics. These properties allow for self-focusing which is derived from the optical Kerr effect. Here, the higher the intensity of the light means the higher the refractive index. This can lead to high intensity light being focused down by media that has a high refractive index in the center and lower refractive indices on the outer edges. Another property derived from the optical Kerr effect is self-phase modulation or the alteration of the optical frequency. With high intensity light passing through a material of significant nonlinearity, it is possible to generate white light from a laser. One final third order NLO property is that of multiphoton absorption. Here, a material can absorb two or three photons of lower frequencies to promote an electron from the ground to an excited state. Chapter 3 will look at this area in more detail. This final area of Chapter 1 serves as an introduction to an area that underlies this body of work and will highlight NLO applications, techniques, and properties of organic and polymeric materials utilizing either second- or third-order nonlinear optical effects.
1.5.1 NLO applications

NLO applications tend to fall into two main categories: those that rely on multiphoton absorption, and those that utilize a nonlinear refractive index change. In the area of multiphoton absorption for second-order NLO materials, there exists an optical frequency conversion. This enables a single frequency laser to be transformed into a broadly tunable system. By placing a crystal of a nonlinear material within a resonator having two mirrors transparent to the incident frequency, one can obtain different frequencies by adjusting either the angle or the temperature. A number of organic materials have shown great promise in this area, including urea,$^{1,88}$ 3-methyl-4-nitropyridinium-$N$-oxide,$^{1,89}$ and $N$-4-nitrophenyl-$L$-prolinol.$^{1,90}$

Another application of second-order nonlinear materials is in electro-optic modulators which assay signals through a nonlinear change in the refractive index of the modulated material. These systems are needed in the telecommunications field to transmit information through optical cables at high bit rates. For rates to reach gigabits or terabits per second, modulators need to have a bandwidth greater than 100 GHz. Much of the initial work has used modulators based on Mach-Zehnder interferometers to assay the speed and efficiency of the transmission of light.$^{1,91-1,93}$ However, current work in NLO is pursuing the use of inline fiber modulators which can prevent the loss of information by not requiring light to pass through an electro-active medium (Figure 1.29).$^{1,94,1,95}$
Figure 1.29  Illustration of (a) Mach-Zender and (b) inline fiber modulators
Electro-optic sampling enables the noninvasive time domain measurements of high bandwidth electric circuits.\textsuperscript{1.96} Here, an electro-optic material is brought into close contact with the integrated circuit, and as the electric signal passes through the circuit, the leaking field will induce a refractive index change in the material which can be detected (Figure 1.30). The use of such sampling allows for the improvement of high frequency signal propagation on transmission lines. Organic materials are of great interest due to their large bandwidth and low dielectric constants, and some of the most promising work has been performed using 4-dimethylamino-N-methyl-4-stilbazolium tosylate (DAST).\textsuperscript{1.97}

Other applications have also utilized higher order nonlinear optical materials. There have been developments with both terahertz generation\textsuperscript{1.98} and thermo-optic switches using second-order NLO materials.\textsuperscript{1.99} As for third-order nonlinear optical materials, there has been much focus on their use as bulk media for both parallel\textsuperscript{1.100-1.102} and serial\textsuperscript{1.103-1.105} processing. Parallel processing deals with the bistability of NLO organic materials, materials which can lead to two possible output states at a given input power. These states lead to a binary response dependent upon the prior illumination of the device. Serial processing uses other optical devices for either further processing or transmission. The NLO materials are a part of directional couplers, distributed grating devices, Kerr gates, and soliton interconnects. However, many of the current materials studied in the area of third-order NLO applications rarely have the linear and two-photon absorption coefficients reported, making comparisons across the field nearly impossible. The utility of the higher-ordered NLO materials is still being researched, and a wider use of these compounds in our everyday life may not be that far behind.
Figure 1.30  Schematic of electro-optic sampling geometry
1.5.2 *NLO techniques*

There exists a wide variety of techniques used for the determination of NLO properties. These techniques employed for evaluation of the material not only involve different nonlinear interactions of the medium, but also different dispersion effects. However, organic materials offer many advantages because of their architectural flexibility to be tailored into desired molecular structures required for fabrication. Therefore, measurements are performed in the forms of powders, solutions, single crystals, thin films, and liquid crystals.

For the determination of the second order NLO properties, there are a number of different methods. To determine the second harmonic intensity, the wedge technique is performed. Here a sample, in the form of a wedge, is moved perpendicular to an incident laser beam, which leads to a change of the interference pattern resulting in an oscillation of the observed second harmonic signal. Another method to determine second harmonic intensity is the Maker-Fringe method. A plane-parallel sample is rotated perpendicular to the laser beam and an oscillation of the observed signal is detected. This is one of the most widely used methods and is especially suited to organic crystals which tend to grow plane-parallel faces.

In order to measure electro-optic coefficients, a Michelson interferometer is used. The sample is placed in the arm of the interferometer and an electric field is applied. The electro-optic effect changes the sample’s refractive index which then changes the optic path length. The resultant shifting of the intensity pattern at the output of the interferometer is then measured. It is mandatory that the values of the sample’s refractive
index, thickness, applied voltage, and the range of the interferometer's output be known.\textsuperscript{1,108}

To access the third harmonic generation, an intense optical field is incident on a transparent medium that results in a response which is partially dependent on the cube of the field strength giving rise to four-wave mixing, or giving rise to the second harmonic generation followed by two-wave mixing.\textsuperscript{1,109} Currently, it is possible to measure the third harmonic generation and obtain values for the third-order NLO susceptibilities for organic compounds in liquids,\textsuperscript{1,110} thin films,\textsuperscript{1,111} crystals,\textsuperscript{1,112} powders,\textsuperscript{1,113} and liquid crystals.\textsuperscript{1,114}

Another method to measure third-order NLO susceptibilities is through a four-wave mixing technique. Here, two incident laser beams of differing frequencies are focused on the sample to generate a third frequency. The output beam then passes through a slit that blocks the incident beams, and then through a double monochromator that blocks out any background noise. The intensity is then measured by a photomultiplier. Since the intensity and the third-order NLO susceptibility are proportional, a value can be obtained.\textsuperscript{1,115} A diagram of the instrument can be seen in Figure 1.31.

There exists a much wider variety of measurement techniques for both second and third-order NLO materials. In fact, there is enough done to dedicate an entire book on the topic. Techniques such as the optical Kerr gate, Z-scan absorption, saturation absorption, electric-field induced second harmonic (EFISH) generation, and reflection-type polarization spectroscopy can result in susceptibility values, but the theory and
Figure 1.31 Measurement of NLO susceptibility through four-wave mixing
mathematical understanding of these techniques goes beyond the scope of this dissertation. A good source for these techniques can be found in Bosshard et al. 1.108

1.5.3 NLO properties of organic materials

In order to better understand NLO effects in organic materials, it is necessary to understand from where these effects arise. Davydov and co-workers, while looking at NLO activity in substituted benzenes, were able to conclude that dipolar aromatic molecules possessing both an electron donor and acceptor group contribute to large second-order nonlinearity arising from the intramolecular charge transfer between the two groups of opposing nature.1116 However, π-conjugated systems with both a donor and an acceptor do not possess second-order NLO properties if there is a center of symmetry, a problem that is not seen for third-order materials. Another important consideration is the absorption properties of these materials which can be tailored based upon the conjugation length of the system and the type of donors and acceptors chosen. The relative ease in the chemical modification of organic molecules has made possible a wide number of compounds tailored for NLO devices. This section will deal with the properties that affect the second-order optical nonlinearity of organic compounds. This includes conjugation length, donor and acceptor strength, the nature of the π-bonding, and the peripheral substitution of the molecule. It is important to note that while this section deals with second-order NLO materials, the same ideas are also the starting point for looking at third-order NLO compounds.
The conjugation length of the molecule and its effect on the NLO properties has been studied by Huijits and Hesselink. By using a methoxy group as the donor and a nitro group as the acceptor, they were able to measure the hyperpolarizabilities ($\beta$) of a series of molecules. As shown in Table 1.1, the length of the $\pi$-conjugation has a very significant effect on the magnitude of the hyperpolarizability. It is important to remember that there is a direct relationship between the hyperpolarizability of a molecule and its second-order susceptibility. However, there is a trade-off associated with increasing the conjugation length that leads to a decrease in the materials’ optical transparency. One way in which to slightly increase the hyperpolarizability without placing the optical transparency at risk is to utilize triple-bonded end groups such as $\text{–CH=CN(CN)}_2$.

By looking at different conjugated groups such as benzene, stilbene, styrene, biphenyl, and fluorene; Chang et al. were able to conclude from the experimental results a number of observations. First, para-substituted benzenes show a strong increase in the hyperpolarizability over the sum of monosubstituted benzenes due to charge transfer. Next, the efficacies of acceptor groups increase in the following order: CN, CHO, COCF$_3$, NO, NO$_2$, CHC(CN)$_2$, and C$_2$(CN)$_3$. The effectiveness of donor groups are listed as: OH, Br, OPh, OCH$_3$, SCH$_3$, NH$_2$, and N(CH$_3$)$_2$. The best combination of donor-acceptor groups can provide about a 10x enhancement in the $\beta$ value (Table 1.2). Some of the effects in the aromatic systems showed that the charge-transfer in biphenyls promote coplanarity. Finally, it is important to note that the $\beta$ values of fluorenes are higher than biphenyls and that styrene $\beta$ values fell between benzenes and stilbenes.
Table 1.1  The effect of π-conjugation on hyperpolarizability

<table>
<thead>
<tr>
<th>Compound</th>
<th>N</th>
<th>Number of π-bonds</th>
<th>$\beta \times 10^{30}$ esu estimated</th>
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<tbody>
<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>N/A</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>N/A</td>
<td>3</td>
<td>12</td>
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<tr>
<td>H₃CO—/&gt;—NO₂</td>
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<td>1</td>
<td>81</td>
</tr>
<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>2</td>
<td>6</td>
<td>135</td>
</tr>
<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>3</td>
<td>7</td>
<td>274</td>
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<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>4</td>
<td>8</td>
<td>367</td>
</tr>
<tr>
<td>H₃CO—/&gt;—NO₂</td>
<td>5</td>
<td>9</td>
<td>623</td>
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Table 1.2  The effect of donor and acceptor strength on hyperpolarizability

<table>
<thead>
<tr>
<th>Acceptor (A)</th>
<th>Donor (D)</th>
<th>Solvent</th>
<th>$\lambda_{\text{max}}$ (nm)</th>
<th>$\beta$ ($10^{-30}$ esu)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN</td>
<td>N(CH$_3$)$_2$</td>
<td>dioxane</td>
<td>290</td>
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<tr>
<td>CHO</td>
<td>N(CH$_3$)$_2$</td>
<td>dioxane</td>
<td>326</td>
<td>6.3</td>
</tr>
<tr>
<td>COCF$_3$</td>
<td>N(CH$_3$)$_2$</td>
<td>dioxane</td>
<td>356</td>
<td>10</td>
</tr>
<tr>
<td>NO</td>
<td>N(CH$_3$)$_2$</td>
<td>dioxane</td>
<td>407</td>
<td>12</td>
</tr>
<tr>
<td>CHC(CN)$_2$</td>
<td>N(CH$_3$)$_2$</td>
<td>chloroform</td>
<td>420</td>
<td>32</td>
</tr>
<tr>
<td>C$_2$(CN)$_3$</td>
<td>N(CH$_3$)$_2$</td>
<td>CH$_2$Cl$_2$</td>
<td>516</td>
<td>50</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>N(CH$_3$)$_2$</td>
<td>acetone</td>
<td>376</td>
<td>12</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>NH$_2$</td>
<td>acetone</td>
<td>365</td>
<td>9.2</td>
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<td>dioxane</td>
<td>322</td>
<td>6.1</td>
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<td>OCH$_3$</td>
<td>dioxane</td>
<td>302</td>
<td>5.1</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>OPh</td>
<td>dioxane</td>
<td>294</td>
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<td>Br</td>
<td>dioxane</td>
<td>274</td>
<td>3.3</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>OH</td>
<td>dioxane</td>
<td>304</td>
<td>3.0</td>
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</table>
The nature of the bonds within the conjugation also has an effect on the hyperpolarizability of the molecule. By keeping the donor-acceptor groups constant, a series of experiments were done on compounds with acetylenic linkages versus compounds with ethylenic linkages.\(^{1,118,1,119}\) For all the compounds that were studied, it was apparent that there were larger increases in the $\beta$ values for the trans-stilbene derivatives, up to 50%. This is due to the fact that there is an energy mismatch between the electron-rich sp-hybridized orbitals of the acetylenic carbons and the sp\(^2\)-hybridized carbons of the phenyl group resulting in less effective delocalization. This is not the case in the stilbene compound where all of the carbons are sp\(^2\)-hybridized. These values are listed in Table 1.3.

Finally, it is important to see how the effect of substitution adjusts the optical nonlinearity of a compound. The use of aza and perfluoro groups on benzenes and azo and azomethine groups on stilbenes greatly reduced the $\beta$ values.\(^{1,120}\) However, substitution of carbons with nitrogens within the compound changed $\beta$ values significantly along with dipole moments and absorption properties based on the location of the nitrogen atom.\(^{1,121}\) Table 1.4 illustrates some of this data.

With this information, one may be able to have a starting point in the design of NLO materials. But there is sometimes a wide discrepancy between what should theoretically work, and what actually occurs inside a laboratory setting. However, there are other factors that may play a role in a compound's hyperpolarizability that were not already discussed. First, the locations of the donor and acceptor groups do not always have to be at the ends of the molecule. Likewise, a molecule may have just donor groups,
Table 1.3  Comparison of β values for acetylenic and ethylenic linkages

<table>
<thead>
<tr>
<th>Acceptor (A)</th>
<th>Donor (D)</th>
<th>$\lambda_{max}$ (nm)</th>
<th>$\beta \times 10^{30}$ esu</th>
<th>$\lambda_{max}$ (nm)</th>
<th>$\beta \times 10^{30}$ esu</th>
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<td>CN</td>
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<td>372</td>
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<tr>
<td>NO$_2$</td>
<td>Br</td>
<td>344</td>
<td>14</td>
<td>335</td>
<td>10</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>OCH$_3$</td>
<td>364</td>
<td>28</td>
<td>356</td>
<td>14</td>
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<td>N(CH$_3$)$_2$</td>
<td>427</td>
<td>73</td>
<td>415</td>
<td>46</td>
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### Table 1.4  Effect of atom substitution on hyperpolarizability

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<thead>
<tr>
<th>X</th>
<th>Substitution</th>
<th>$\lambda_{\text{max}}$ (nm)</th>
<th>$\beta \left(10^{-30} \text{ esu}\right)$</th>
</tr>
</thead>
<tbody>
<tr>
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<td>4-OCH$_3$</td>
<td>302</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>2-Aza; 4-OCH$_3$</td>
<td></td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>2-F; 4-OCH$_3$</td>
<td>304</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>2,5-F; 4-OCH$_3$</td>
<td>304</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>2,3,5,6-F; 4-OCH$_3$</td>
<td>270</td>
<td>1.7</td>
</tr>
<tr>
<td><img src="image.png" alt="Structural Diagram" /></td>
<td>OCH$_3$</td>
<td>N/A</td>
<td>376</td>
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<td></td>
<td>1-Aza</td>
<td></td>
<td>34</td>
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<tr>
<td><img src="image.png" alt="Structural Diagram" /></td>
<td>OCH$_3$</td>
<td>1'-Aza</td>
<td>349</td>
</tr>
<tr>
<td></td>
<td>1'-Aza</td>
<td></td>
<td>6.6</td>
</tr>
<tr>
<td><img src="image.png" alt="Structural Diagram" /></td>
<td>N(CH$_3$)$_2$</td>
<td>N/A</td>
<td>430</td>
</tr>
<tr>
<td></td>
<td>NH$_2$</td>
<td>1,1'-Azo</td>
<td>420</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>29</td>
</tr>
</tbody>
</table>
or the opposing group may be in the center of the molecule, an issue that will be expanded upon in Chapter 3. Secondly, the conjugated system can be in a ring structure, much like a porphyrin or phthalocyanine. The addition of a metal to the center of the compound could then have an effect upon the NLO properties of the molecule. This will be covered in greater depth in Chapter 2.

1.5.4 Dendritic NLO materials

Although there have been developments with dendrimers having electroactive, photoactive, and recognition elements, the application of these compounds to the area of photonics has rarely been explored. With dendrimers, NLO building blocks can be placed into the periphery, branch, or core to construct precise molecular architecture with predetermined chemical composition. Here the dendrimers can act to reduce active moieties from interacting through site isolation or lead to the promotion of interaction through the cooperative effect. This section points out a few of the examples of dendritic NLO materials that have been recently published.

The work of Jen et al. focused on the development of a crosslinkable NLO dendrimer 45 that exhibited a large optical nonlinearity with high thermal stability (Figure 1.32).<sup>1,122,1,123</sup> The use of a thiophene-stilbene based NLO core and crosslinkable trifluorovinylether containing dendrons resulted in a dendrimer that through spatial isolation of the individual chromophores enabled an enhancement of macroscopic optical nonlinearity. This compound was able to be easily spin-coated onto a surface and
Figure 1.32  Jen’s NLO dendrimer
possessed high alignment stability and mechanical properties derived from the sequential crosslinking reactions, a step that was necessary to increase thermal stability.

The use of polymeric materials in photorefractive applications is limited by their low charge-carrier mobility, which has an effect on the materials' overall response time. The mobility is again affected by the fact that there exists an inhomogeneity within the polymeric environment between the backbone and the chromophore. The development of the dendritic photorefractive material attempts to counteract these problems. By enabling the precise control of the architectural environment for these transport molecules and reducing inhomogeneity, a higher mobility and faster photorefractive response has been reported.

Azobenzene containing dendritic structures have been developed to study both their conformational and molecular NLO properties for second harmonic generation applications. Between 1-15 azobenzene branching units were used as the NLO chromophore which were connected via aliphatic chains. The $\beta$ value of the dendrimer containing 15 units similar to 46 was approximately 20 times greater than that of the individual azobenzene monomer (Figure 1.33). Structural information has indicated a non-centrosymmetric alignment of the chromophores leading to a large electronically dipolar macromolecular system, in which each azobenzene unit contributed to the second harmonic generation.

There have also been developments in the area of two-photon absorption, which will be covered in full in Chapter 3. This small gathering of papers is only the start of a connection between dendrimers and NLO optics. With the sudden growth of both of
Figure 1.33  Yokoyama’s azobenzene dendritic NLO material
these fields it remains a matter of time before more substantial results are obtained, and a stronger marriage is made between these two fields.
CHAPTER 2
SYNTHESIS AND STUDY OF NON-AGGREGATING OCTASUBSTITUTED
DENDRITIC PHTHALOCYANINES

2.1 Introduction

Phthalocyanines (Pcs) are a family of aromatic macrocycles which are structurally similar to porphyrins (Figure 2.1). The first Pc was synthesized in 1907 by Braun and Tcherniac after they heated o-cyanobenzamide at a high temperature. It was not until 25 years later that the structure was determined through the work of Linstead and Robertson. Since then, these compounds have been primarily used in inks, coloring for plastics, and as clothing dyes.

The optical properties of Pcs are related to their 18-π electron aromatic system. The additional π-orbital conjugation gained through the benzo moieties and the orbital perturbations caused by the nitrogen atoms at the four meso-positions have a significant affect on the UV-Vis spectrum. Therefore, the spectra of the central chromophore undergoes a red-shift of the Q-band and a strong enhancement of its intensity. Recent applications use Pcs as a photoconductor in Xerography, and in optical data storage as the laser absorption layer within recordable compact discs (CD-R). Research has also investigated Pcs for non-linear optics. The use of Pcs in molecular electronics, photodynamic cancer therapy, as solar energy converters, electrochromic and
Figure 2.1 The molecular structure of phthalocyanine
electroluminescent displays, gas sensors, and as optical limiting materials has been established.

One important physical property shown by PCs is their natural tendency to cofacially stack or aggregate. This property has been exploited in the creation of a set of materials which show conductivities in the semiconductor or metallic regimes when doped with weak oxidants. However, by modification of the Pc at the periphery, it is possible to decrease the cofacial interactions that lead to aggregation, the prevention of such can lead to high absorptivities of the monomer over a narrow spectral range.

This chapter will focus on peripheral modification of PCs with dendrons to achieve minimal aggregation. The dendritic compounds will then be tested and analyzed to understand the extent of Pc aggregation before looking at their development for use as optical limiting materials.

2.1.1 Optical limiting technology

With the increasing need for eye protection against laser emission in both the civilian and military arenas, the desire to develop materials to prevent injury has grown stronger. In 1999, the FAA investigated reports of external sources of laser light that had temporarily blinded pilots in the Los Angeles area and led to the landing of these passenger flights by the co-pilot. In 1998, two US helicopter pilots received minor corneal burns from a ground-based laser while on routine patrol in Bosnia. These examples only illustrate a growing need to develop coatings that add protection to an individual’s eyesight, blocking the transmission of high intensity light through a material.
Optical limiters are materials which attenuate light above a threshold intensity. Hence, the transmission is high at ambient intensities and is low at high intensities. This property is useful in not only protecting eyes, but also protecting optical detection elements and sensors. It is extremely important, however, to have rapid response times to minimize or prevent damage. This is accomplished by using materials that exhibit third order nonlinear absorption, where a material’s absorption of photons increases with the intensity of the incoming light.

The mechanism of optical limiting proceeds through sequential two-photon absorption or reverse saturable absorption (RSA) (Figure 2.2).\textsuperscript{228} As the light becomes more intense, the excited state population increases. If the material has an excited state cross section \( \sigma_{\text{ex}} \) that is higher than the ground state cross section \( \sigma_0 \), then the effective absorption coefficient of the material increases. Ideally, an effective optical limiter would have both a large excited state absorption cross section and a long excited state lifetime. A variety of both organic and organometallic compounds have fulfilled these requirements. Materials such as Pcs,\textsuperscript{229-232} porphyrins,\textsuperscript{233-236} organometallic cluster compounds,\textsuperscript{237-240} and other materials\textsuperscript{241-244} have shown great promise as optical limiting materials.

An ideal optical limiter should have a wide wavelength range over which to operate, as well as high linear transmission and a high threshold for damage. The nonlinear response should possess a low threshold and operate over a wide range of incident intensities before saturation of the nonlinear properties. This means that there should be a high local concentration of the material, either in solution or within a solid
Figure 2.2  Energy level diagrams for RSA and TPA chromophore behavior$^{2,48}$
film, prepared with good optical transparency. A prevalent problem is that many optical limiting dyes aggregate at high local concentrations, which shuts down optical limiting behavior.

2.1.2 Phthalocyanines as optical limiters

Phthalocyanines possess several structural variables that allow many of their physical and photophysical properties to make them ideal reverse saturable absorbers for optical limiting. These include the central metal atom, axial ligands, and peripheral ring substituents. The heavy atom effect is a common property of reverse saturable absorbers such as porphyrins and phthalocyanines, and has been illustrated by many groups including Perry et al. They have shown that Pc complexes of lead, indium and tin perform much better at optical limiting than those that have been substituted with silicon, aluminum or germanium.\[^{245-247}\] This effect results from the higher singlet (S\(_1\)) to triplet (T\(_1\)) intersystem crossing rate which increases proportionally with the atomic number of the central atom.\[^{248}\] Since the degree of RSA is dependent upon the triplet population, the heavier the atom within the core of the phthalocyanine, the more effective it is as an optical limiter. Currently, there are 70 separate elements, some of differing oxidation states, that find use as the central core of phthalocyanine-based optical limiting (OL) materials.\[^{249}\] Some of the most publicized OL materials are those containing lead, indium and titanium.

Lead Pcs have been investigated extensively by the Shirk group. The first major results incorporated a 5.9% by weight Pb Pc-urethane-butanediol copolymer. This
system gave a strong excited state absorption in the visible (430-610 nm) and the near-IR (1064 nm), areas where the excited state cross section values ($\sigma_{ex}$) surpassed that of the ground state ($\sigma_{g}$). The broad excited state absorption of this copolymer with its relatively slow decay and its large change in the refractive index make thin films of this material great candidates for OL measurements.

In their attempt to increase the amount of active OL Pc concentration, the Shirk group moved on to the study of ($\beta$-cumylphenoxy)phthalocyanine 2 since the bulk of this compound was thought to decrease aggregation (Figure 2.3). However, while the excited state cross section predominated throughout most of the visible spectrum, a lack of appreciable transparency limited this material from commercial application. This was only the first step leading to the alteration of the periphery to generate new materials with effective control over the spectral window. The use of poly(ethylene oxide) (PEO) to “cap” one face of the Pc 3 instead of the cumylphenoxy groups led to a visible decrease in the formation of higher Pc aggregates, limiting formation of dimers at high concentrations (Figure 2.3). This complex maintained the extended OL range within the visible region as well as the intense RSA that was seen in the other lead Pcs. Finally, this set of Pcs displayed photoinduced charge generation. This unique property was exhibited as both a photovoltaic response and a photoconductor, showing both optical breakdown and plasma formation at relatively low fluences.
Figure 2.3  Molecular structures of the Shirk lead Pcs
The use of indium as the central metal gives the added ability of axial substitution on one face of the Pc. The utilization of indium tetra(t-butyl)Pc chloride within a polymer matrix by Perry et al. formed an optical limiter that had a linear transmittance of 0.70 and could attenuate laser pulses by a factor of 540. The doping of a polymer matrix acted to dilute the concentration of the Pc so that aggregation was not a large problem. However, it was also established that a concentration range was necessary to give the optimum response. The optimal response resulted from the most concentrated area within the center of the focus and more diluted areas along the periphery of the polymer.

Hanack et al. demonstrated that axial substitution on indium Pcs can influence the degree to which a compound will act as an optical limiter. Using a tetra(t-butyl)-substituted Pc and altering the axial ligand on the indium atom from chloride (5) to perfluorophenyl (6) and (p-trifluoromethyl)phenyl (7), there was a definite shift in the optical limiting threshold to a lower value (Figure 2.4). This trend has been attributed to a disruption in the formation of aggregates.

The Hanack group was also involved in the study of titanium Pcs and the effect of axial substitution. It was found was that when the substitution on a ligating catechol was changed there was also an alteration in the nonlinear transmission of the compound. Overall, as the groups para to the catechol oxygens were made more electron-withdrawing the optical limiting performance improved, with the most effective optical
Figure 2.4 Molecular structures of Hanack’s ligated indium Pcs

5, L = Cl
6, L = C$_6$F$_5$
7, L = $p$-C$_6$H$_4$CF$_3$
limiting titanium Pc 8 being substituted with 4,5-dihydroxyphthalonitrile (Figure 2.5).\textsuperscript{2.58,2.59} This was the first report of a dipole moment being a direct factor related to the nonlinear optical properties of the Pc.

The utilization of Pcs for optical limiting applications is greatly hampered by the aggregation of these compounds in high concentrations. Since a large amount of Pc is required within a small area, it becomes necessary to find a method to resolve this problem. The use of a polymer matrix is only a temporary solution, and the lack of homogeneous dispersion of Pc makes this method non-reproducible. A method that covalently modifies the Pc so that aggregation does not occur at high concentrations is desired.

2.1.3 Current phthalocyanine dendrimers

Attaching dendrons to a Pc core to prevent aggregation has been previously attempted. McKeown placed four Fréchet-type dendritic substituents on the periphery of a Pc core (9-11) (Figure 2.6a). While the results showed definite trends related to generational size of the dendrimer minimizing prevention of aggregation in solution, there was no real difference between the G1 and the G3 Pcs in thin films.\textsuperscript{2.60} Advantage of the intermolecular interactions was taken by modifying the periphery of the dendrons with oligo(ethyleneoxy) groups to obtain discotic liquid crystalline materials.\textsuperscript{2.61,2.62} Substitution of the core with silicon led to materials that exhibited decreased aggregation. McKeown placed axial dendritic substituents on the silicon that prevented aggregation.\textsuperscript{2.63}
Figure 2.5  The molecular structure of Hanack’s Ti Pc OL
X-ray crystallography data show that the dendrons inhibited facial interactions between the Pc cores (Figure 2.6b). While this approach is successful, it does not leave any freedom to replace the central metal for different applications.

The Ng group attempted to prevent aggregation by modifying the periphery of the Pc with carboxylate substituted Fréchet-type dendrons (12-14) (Figure 2.7). These materials were water-soluble, and the carboxylate termini formed an ionic shield around the Pc, repelling the other charged Pc species and preventing aggregation. This was made more evident at higher dendritic generations, with the materials becoming less aggregated in solution.\(^{2,64}\) Although no solid state experiments were performed, the substitution of the core with zinc provided fluorescent materials. Intramolecular energy transfer was affected directly by the size of the attached dendrons. The blocking of aggregating species was enhanced by the introduction of both a cationic surfactant\(^{2,65}\) and poly(ethylene oxide)\(^{2,66}\) which further separated the molecules and acted much like a matrix that prevented the aggregation of the Pc molecules.

The work of the Kobayashi group developed the zinc phthalocyanine\(^{[8]}\)-arborol dendrimer 15 (Figure 2.8). Extent of aggregation decreased as dendrimer generation increased in both solution and solid states.\(^{2,67}\) The analogous Co Pc 16 (Figure 2.8) catalyzed the oxidation of mercaptoethanol in the presence of dioxygen with enhanced catalytic stability.\(^{2,68}\)
Figure 2.6  (a) Molecular structure of McKeown’s dendritic Pcs (b) X-ray crystal structure of McKeown’s dendritic silicon Pc
Figure 2.7 Molecular structure of Ng's water soluble zinc phthalocyanines
Figure 2.8  Molecular structures of Kobayashi’s dendritic Pcs

15 M = Zn
16 M = Co
The most current work that has been done at the Pc / dendrimer interface involved that of the Kasuga group. By changing the substitution pattern on the Pc from that of β-substitution (placement at the 3 or 4 position on the aryl ring of the Pc) to that of α-substitution (placement at the 2 or 5 positions), they were able to obtain results that showed increased activity in the photocatalysis of bilirubin over non-substituted Pcs. In the study of the absorption properties of compounds 17-19 substituted with zinc (Figure 2.9), it was noticed that there was a distortion in the spectra. This was attributed to the coordination of the zinc to the Fréchet-type dendritic oxygens, not seen in β-substitution due mainly to distance. This distortion was reversed by the addition of pyridine. By using the Pcs as catalysts in the photooxidation of bilirubin, it was shown that the rate of oxidation decreased as the generational size increased. This is thought to be due to the dendron in these compounds forming a tight cage around the Pc whereby large molecules, in this case the substrate, are not able to efficiently approach the core. The study of the aggregation properties of these compounds has not yet been reported.

While there has been some progress made in the development of Pc dendrimers, no work has been done investigating the aggregation properties in different solutions, or halting aggregation in the solid state. There has also been no report that looks at the use of these materials as optical limiters. Such compounds should be further developed to obtain the desired properties for direct applications such as OL and photodynamic therapy.
Figure 2.9  Molecular structure of Kasuga's α-substituted dendritic Zn Pcs
2.2 Goals

The main interest in this work came from looking at the progress being made in preventing aggregation using dendrons attached to Pcs, as well as understanding that the design of an effective optical limiter must incorporate a feature that limits these attractive forces at high concentrations. The initial goal was to synthesize a Pc molecule substituted in the 3 and 4 positions with Fréchet-type dendrons, resulting in an octasubstituted dendritic Pc. This would be followed by studies to see if aggregation was more effectively minimized than with the tetra-substituted Pcs previously reported in the literature. Further studies involved investigating the compounds in a number of different solvents as well as looking at their properties in thin films. Finally, zinc would be incorporated into the synthesized Pcs, leading to fluorescence aggregation experiments, Stern-Volmer quenching studies, further thin film work and initial optical limiting tests.

2.3 Synthesis of dendritic phthalocyanines

The initial strategy for the preparation of the octasubstituted dendritic Pcs was the cyclotetramerization of dendritic dialkoxyphthalonitriles. However, it was found that alkylation of 4,5-dihydroxy-phthalonitrile with poly(aryl ether) dendritic bromides \([\text{Gn}]\text{-Br} (n = 1, 2, 3)\), synthesized using the procedure developed by Fréchet and Hawker,\(^{2,71}\) did not proceed. Therefore, hydroquinone moieties were placed on the phthalonitrile using the procedure of Wöhrle et al.\(^{2,72}\) to act as spacers, which decrease the influence of the nitriles on the phenolic groups.
2.3.1 Synthesis of unsubstituted Fréchet-type dendritic phthalonitriles

Coupling of unsubstituted Fréchet-type dendrons to phthalonitrile 20 occurred in the presence of potassium carbonate (10 eq.) and 18-crown-6 (0.2 eq.). First through third generations were synthesized (Scheme 2.1) and purified to give the desired compounds 21-23 as colorless foams in yields ranging from 67-87%. Analysis by MS, $^{13}$C NMR and $^1$H NMR as well as gel permeation chromatography (GPC) showed the compounds as the desired, monodisperse materials.

2.3.2 Synthesis of 3,5-di-t-butyl Fréchet-type dendritic phthalonitriles

Synthesis of the dendritic precursor, 3,5-di-t-butylbenzyl bromide 27 was performed via a synthetic scheme developed by Adrian Ortiz of our laboratories. In the first step 3,5-di(t-butyl)toluene (24) is oxidized to the corresponding carboxylic acid 25 in the presence of potassium permanganate and pyridine in 65% yield.\textsuperscript{2,73} Subsequent reduction to alcohol 26 in the presence of lithium aluminum hydride followed by bromination with $N$-bromosuccinimide (NBS) (1.0 eq.) and triphenylphosphine (1.1 eq.) resulted in the isolation of the desired compound 27 in 92% yield (Scheme 2.2).

Coupling to obtain the dendrons was performed by the procedure of Zimmerman et al.\textsuperscript{2,74} Coupling of the 3,5-di-t-butyl dendrons (generations 0, 1, 2) to 20 was carried out in the presence of potassium carbonate (10 eq.) and 18-crown-6 (0.2 eq.) in acetone. The yields of the isolated material 28-30 ranged from 61-87% (Scheme 2.3).
Scheme 2.1  Synthesis of benzyl ether functional dendritic phthalonitriles
Scheme 2.2  Synthesis of 3,5-di-$t$-butyl benzyl bromide
Scheme 2.3  Synthesis of \( t \)-butyl dendritic phthalonitriles
2.3.3 Synthesis of diethyl isophthalic ester Fréchet-type dendritic phthalonitriles

Synthesis of the diethyl isophthalate dendrons was done following the procedure of Fréchet et al. The coupling of the dendrons to 20 had to be modified from previous methods (potassium carbonate (10 eq.), 18-crown-6 (0.2 eq.) in refluxing acetone). Where the G0 coupling proceeded without major problems (31 isolated in 56% yield), an increased amount of 18-crown-6 (0.8 eq.) had to be added to the G1 coupling along with a decrease in the reaction temperature to 40°C to prevent transesterification with the phenolic groups on 20. The product yield for 32 was 60%. For the G2 coupling, the solvent had to be switched to THF due to the starting dendritic bromide being insoluble in acetone. An increase in the reaction temperature to 45°C and decrease in the amount of 18-crown-6 (0.4 eq.) as compared to the G1 coupling resulted in the desired product 33 in good yield (84%) (Scheme 2.4).

2.3.4 Cyclization of dendritic phthalonitriles

Initial cyclization of the nitriles was performed using lithium bromide as the template salt and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) as the base in refluxing pentanol. The removal of the lithium ion in the acidic workup leaves an unmetallated phthalocyanine. These conditions worked well for the unsubstituted G1 (34) and G2 (35) dendritic phthalocyanines giving yields of 27% and 22% respectively. However, as the generation increased to G3 or the periphery was changed to the di-t-butyl dendrons or the diethyl phthalate dendrons, these conditions were shown to be unsuccessful at inducing any desired cyclizations of the nitriles. Conditions were then changed to lithium metal in
Scheme 2.4  Synthesis of isophthalate dendritic phthalonitriles
refluxing pentanol, which was effective in producing the desired phthalocyanines for the unsubstituted G3 phthalonitrile (36) as well as the di-\(t\)-butyl dendritic phthalonitriles (37-39) (Scheme 2.5).\(^{276}\) Problems were still encountered in the cyclization of the diethyl isophthalate phthalonitriles, and optimal conditions to give the desired phthalocyanines still need to be found.

2.3.5 Synthesis of a tetrasubstituted phthalocyanine analogue

In order to be able to compare the effectiveness in preventing phthalocyanine aggregation by having eight dendritic substituents versus four, a tetrasubstituted dendritic phthalocyanine needed to be made. Since the dendron is not directly attached to the phthalocyanine, as in the work published by McKeown,\(^{260,261}\) an analogue was synthesized incorporating the hydroquinone linker. This was accomplished by first reacting unsubstituted [G2] Fréchet dendritic bromide with an excess of hydroquinone (4 eq.) along with potassium carbonate (10 eq.) and 18-crown-6 (0.2 eq.) in refluxing acetone. The dendritic product 40 was isolated in 52% yield and coupled to 4-nitrophthalonitrile (41) in the presence of potassium carbonate and DMF at 60°C to give mono-substituted dendritic phthalonitrile 42 in a 62% yield. Cyclization in refluxing pentanol with lithium metal gave the desired \(meso\)-tetrasubstituted phthalocyanine 43 in 25% yield (Scheme 2.6).
Scheme 2.5  Cyclization of dendritic phthalonitriles
Scheme 2.6  Synthesis of a tetrasubstituted dendritic Pc
2.3.6 Synthesis of zinc phthalocyanines

There were two main methods by which zinc can be placed in the center of the phthalocyanine. The first uses the zinc atom as a template, and in refluxing pentanol with the appropriate phthalonitrile, the desired phthalocyanine could be isolated in moderately low yields (20-30%)\(^{2,64}\). However, purification of the product from the starting material is necessary and time consuming. Since there was unmetallated phthalocyanine available, a second method for inserting the zinc into the phthalocyanine center was pursued. Reacting the unmetallated phthalocyanine with zinc acetate in DMF at 40 °C gave the desired metallated phthalocyanines 44-50 without extensive purification and in yields ranging from 72-94% (Scheme 2.7).

2.4 Properties of unmetallated dendritic phthalocyanines

After the octasubstituted dendritic Pcs were synthesized and purified, they were subjected to a series of studies to better understand what effect that the dendrons had upon the molecular structure of the Pc. The molecular size and degree of aggregation were examined using both gel permeation chromatography (GPC) and UV-Vis absorption. GPC studies were done relative to the other dendritic Pcs, while solvent and solid state aggregation studies were performed by UV-Vis absorption spectroscopy using either Beer's Law or by relative comparison of the Q-bands.
Scheme 2.7  Zinc insertion into octasubstituted dendritic Pcs
2.4.1.1 Size effects of phthalocyanines by gel permeation chromatography

The purpose of GPC measurements is to separate molecules based upon their size. Both unsubstituted Fréchet-type dendrimers (34-36) (Figure 2.10), and t-butyl substituted Fréchet-type dendrimers (37-39) exhibit an increase in molecular size with generation. The comparison of the approximate GPC molecular weights (Table 2.1), calculated using linear polyethylene standards based upon elution volume, indicate that as the molecules increase in generation, they also increase in molecular size. The GPC molecular weight of the smaller generations (unsubstituted G1 and G2, t-butyl G0 and G1) exceeded the theoretical MW, with compounds 35 and 38 being closer to the theoretical MW than 34 and 37. The GPC MW for the largest structures (36 and 39) was smaller than the actual value, indicating a globular structure. This trend indicates that as the dendritic exterior increases in size, the molecule behaves less like an extended conformation polymer and more like a globular conformation. One final observation is that the t-butyl groups add considerably to the overall MW of 37-39. However, when compared to 34-36, the GPC MW shows that the t-butyl Pcs behave as larger, more globular molecules than the unsubstituted Pcs at the same generation.

2.4.2 Aggregation properties of phthalocyanines in solution

It has been mentioned previously that a main property of interest in the Pc molecule is its ability to absorb light in the near-IR. Thus the UV-Vis spectrum of a Pc is very characteristic especially in the near-IR region. Changes within this area are directly correlated with the extent of aggregation of the molecules. Non-aggregated unmetallated
Figure 2.10  GPC comparisons of 34 (—), 35 (----), and 36 (-----) unmetallated dendritic Pcs
Figure 2.11  GPC comparisons of 37 (—), 38 (----), and 39 (-----) unmetallated t-butyl dendritic Pcs
### Table 2.1  Comparison of the MW of the unmetallated Pcs with the MW through GPC

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<th>Elution Volume (mL)</th>
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<td>2</td>
<td>10785</td>
<td>26.47</td>
<td>8761</td>
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</table>
Pcs exhibit a split Q-band in the 680-720 nm region with vibrational side bands appearing between 640-600 nm. As the aggregating species become more prominent, the Q-band broadens out and undergoes a large bathochromic shift. Here, there is no evidence of splitting, and the molar absorptivity greatly decreases in comparison with the non-aggregated species. Figure 2.12 illustrates these extremes seen in the UV-Vis spectra of both the non-aggregated and fully aggregated Pcs in solution.

Initial aggregation studies were performed by using CH₂Cl₂ (DCM) as the solvent and adding increasing amounts of ethanol (Figure 2.13). At 100% DCM, the presence of the split Q-band was seen in all of the unsubstituted Fréchet-type dendritic Pcs. However, there was a noticeable drop in the absorbance of the G1 Pc dendrimer when the solution contained 10% EtOH, a drop that continued until a broad peak indicative of full aggregation was seen at 50% EtOH. The tetrasubstituted G2 analogue exhibited the same trend as G1 with an immediate indication of aggregation after the introduction of EtOH. The G2 Pc dendrimer did not begin to greatly aggregate until the solution contained at least 20% EtOH, while the G3 Pc dendrimer held off aggregation until 30% EtOH was present.

When the t-butyl substituted Fréchet-type Pcs were subjected to the same experimental conditions, a much different result was observed (Figure 2.14). The ability of this family of compounds to remain monomeric in solution was much more pronounced than their unsubstituted counterparts. The G0 Pc dendrimer did not begin to show signs of aggregation until 20% EtOH was present in solution. The G1 Pc
Figure 2.12 UV-Vis spectra of non-aggregated 34 (2x10^{-5} M) in CH\textsubscript{2}Cl\textsubscript{2} (---) and fully aggregated 34 (2x10^{-5} M) in 1:1 CH\textsubscript{2}Cl\textsubscript{2}-EtOH (----) at 25 °C
Figure 2.13 Comparisons of the Q-band absorbance at 700 nm between 34 (♦), 35 (■), tetrasubstituted 43 (+), and 36 (▲) unmetallated dendritic Pcs (2x10⁻⁵ M) as a function of % ethanol present at 25 °C
dendrimer began to aggregate at 40% EtOH in solution and the G2 Pc dendrimer had no noticeable signs of aggregation up to 50% EtOH in solution. The amount of EtOH was limited to 50% based on solubility problems with the Pcs, so further tests to examine the limit of the G2 dendrimers were not possible. It seems that the t-butyl substituted dendrimers are better at resisting aggregation in solution than the unsubstituted dendrimers of equal size. This suggests that it is not merely the increased van der Waals size of the tert-butyl groups that is decreasing tendency of aggregation, but perhaps an entropic (solubility) effect as well.

Beer’s Law plots were constructed for compounds 34-39, and 43 to further investigate aggregation behavior in a wider variety of solvents. Ideally, the result should be a straight line with an intercept of zero and a slope equal to \( \varepsilon \). Deviation from linearity indicates either poor instrument sensitivity (low end of the curve), loss of effective solution transmittance (high end of the curve), or in the case of Pcs, aggregation.

\[
A = \varepsilon c \ell
\]

A typical deviation from linearity in a Beer’s Law plot is shown in Figure 2.15.

Second generation dendrimer 35 remained monomeric in 100% DCM over the concentration range studied \((10^{-7} - 10^{-5} \text{ M})\). Hence the Beer’s Law plot is linear. Additionally, the same dendrimer in 1:1 DCM-EtOH was aggregated at all concentrations studied, and the Beer’s Law plot is also linear, albeit with an alternated slope, indicative of the bathochromic shift the Q-band undergoes upon aggregation. In the case of
Figure 2.14  Comparisons of the Q-band molar absorptivities at 700 nm between 37 (♦), 38 (■), and 39 (▲) unmetallated t-butyl dendritic Pcs (2x10^{-5} M) as a function of % ethanol present at 25 °C
solutions that fell between both of these solvent extremes, there was a noticeable
deviation in the Beer’s Law plot. Note that as concentration of EtOH increases, the slope
decreases, reflecting the low absorptivity of the aggregated species at the wavelength
monitored.

2.4.3 Effect of solvent on the aggregation properties

We further studied the aggregation properties of the dendritic Pcs in a wide
variety of solvents. Solvents were chosen with the criteria that all of the Pcs must be
soluble, and the solvent was readily available. Along with the DCM-EtOH mixtures five
other solvents were chosen: acetone, ethyl acetate (EtOAc), dioxane, tetrahydrofuran
(THF), and toluene.

When the unsubstituted Fréchet-type dendritic Pcs (both tetra- and
octasubstituted) were looked at in each of these solvents, different characteristics became
apparent. The solvents were able to be divided by their ability to induce aggregation.
Dioxane and THF were similar to DCM in that the dendrimer remained non-aggregated
at all concentrations studied. Acetone and EtOAc acted very much like 1:1 DCM-EtOH
in that a large degree of aggregation was seen in all cases. Toluene seemed to allow for
moderate amounts of aggregation in each of the cases studied. Figure 2.16 illustrates the
effects of each of these solvents by focusing on the Beer’s Law plots of the Pc
absorbance at 700 nm of 34.
Figure 2.15  Beer's law plots of the Q-band absorbance at 700 nm for 35 in DCM (●), 7:3 DCM-EtOH (■), and 1:1 DCM-EtOH (▲) at 25 °C
Definite changes were once again seen with the tert-butyl substituted dendrimers. Here, the aggregation was not noticeable in THF, dioxane and toluene. Even EtOAc, known to strongly favor aggregation in the other set of dendrimers, only had a moderate effect on the G0 dendrimer which became almost nonexistent with the G2 Pc. However, an interesting observation was seen in the case of both the G0 and G1 Pcs when they were measured in acetone. In each case, the Q-band had seemed to collapse into a single strong peak, a characteristic that disappeared in the spectra of the G2 Pc (Figure 2.17). The solvent did not seem to induce aggregation, but rather prevent it. Since the Q-band is split because of the inherent symmetry of the Pc molecule (C2 axis), what may have happened is that the carbonyl oxygen of the acetone could have strongly hydrogen bonded to the hydrogens within the core of the Pc. If this was to occur, and the core was to take on the characteristic of ion-pairing with the acetone molecule, the core would change from C2 symmetry to C4 symmetry (commonly seen with metallated Pcs). This would then result in a single Q-band instead of the split Q-band seen in the other solvent cases. The reappearance of the split Q-band in the instance of the G2 Pc could be due to the fact that the strong non-polar character of the large number of tert-butyl groups does not allow for the approach of the carbonyl oxygen to the Pc core.

Both the effect of the addition of the EtOH to the solutions of Pc in DCM as well as the effects of the different solvents on the extent of aggregation will be examined in
Figure 2.16  Beer's law plots of the Q-band absorbance at 700 nm for 34 in dioxane (♦), THF (+), toluene (X), EtOAc (■), and acetone (▲) at 25 °C
Figure 2.17  (a) Beer's law plots of the Q-band absorbance at 700 nm for 37 in dioxane (♦), THF (+), toluene (X), EtOAc (■), and acetone (▲); (b) UV-Vis absorbance spectrum of t-Bu G1 Pc (1.79x10^{-5} M) in acetone
more detail in Section 2.6. There, the thermodynamic properties involved in the aggregation of the Pcs will be discussed.

2.4.4 Aggregation properties in thin films

For these compounds to be used for optical limiting applications, it is necessary to study their behavior in the solid state. Thin films of the dendritic Pcs were fabricated by spin-casting each compound onto a glass slide and then obtaining the absorbance spectra between 500 and 800 nm. When the unsubstituted Fréchet-type dendrimers 34-39 and 43 were cast onto the glass slides, a definite pattern was seen within their UV-Vis absorbance spectra (Figure 2.18). While the G1 dendrimer 34 showed full aggregation, the tetrasubstituted G2 43 and the octasubstituted G2 dendrimer 35 began to show signs of a split Q-band. This was in stark contrast to the results reported by McKeown et al. With the only major difference between the tetrasubstituted Pc (m-G2, 43) and McKeown’s Pc being that the m-G2 contained a hydroquinone linker, it is interesting to note that the presence of the linker seems to prevent full aggregation of the Pc. With those results aside, the G3 dendrimer showed no real signs of aggregation, giving a split Q-band in the solid state. This is the first case of an unmetallated dendritic Pc showing no signs of aggregation in the solid state.

The largest surprise came in the thin film absorption spectra of the t-butyl dendritic Pcs. Since the benzyl ether functional dendritic Pcs followed the same trend
Figure 2.18  UV-Vis spectra of the thin films for 34 (— —), 35 (—), 43 (— -), and 36 (—) Pcs
both in the solid state and in solution, it was thought that the \( t \)-butyl \( \text{Pc} \)s would follow suit and be much better candidates than their unsubstituted counterparts. However, the \( t \)-butyl \( \text{Pc} \)s exhibited very similar spectra in the solid state when compared to the unsubstituted \( \text{Pc} \)s (Figure 2.19). Again, the G0 \( \text{Pc} \) showed full aggregation while the G1 showed slight characteristics of the split Q-band. When the G2 was examined, there were no noticeable signs of aggregation present within the film. This means that between the two sets of \( \text{Pc} \)s, compounds of similar molecular weight had similar spectra in the solid state, regardless of how each performed in solution. This is further evidence that the lack of aggregation of the \( t \)-butyl materials in solution is not merely a van der Waals interaction.

2.5 Properties of dendritic zinc phthalocyanines

After investigating how the unmetallated \( \text{Pc} \)s would react to different solvent conditions, it was necessary to look at how their metallated counterparts would perform under similar circumstances. The most noticeable change between the absorbance spectra of the unmetallated and metallated \( \text{Pc} \)s is in the appearance of the Q-band. As mentioned before, the unmetallated species, with the two extra hydrogens, possess a C2 axis of symmetry. This results in the split absorbance peaks seen in the near-IR region. However, when the core of the \( \text{Pc} \) becomes metallated, it loses those two hydrogens and a C4 axis of symmetry is thus created. The absorbance band of the metallated \( \text{Pc} \) therefore
Figure 2.19  UV-Vis spectra of the thin films for 37 (--), 38 (---), and 39 (----) t-Bu Pcs
degenerates into a single peak in the near-IR region. The same trends can then be followed by concentrating on the single band which is sharp when no aggregation is present, and undergoes broadening as well as a bathochromic shift as aggregation becomes more evident (Figure 2.20). Here zinc was the metal of choice because it was inexpensive and readily available, imparted strong fluorescence properties to the molecule, and the Zn Pc was also an effective optical limiter.

2.5.1 Aggregation properties of zinc phthalocyanines in solution

The spectra for each of the Zn Pcs were measured under the same conditions as the unmetallated Pcs, namely the DCM-EtOH mixtures. Here, the change in the aggregation properties was monitored as a function of the solution polarity. While the concentrations were kept constant between measurements, it was observed that after the EtOH was added that the absorbance of the Pc began to increase. Work performed by Kasuga and coworkers,\textsuperscript{2,69} suggested that dendrons in the α-position of Pcs coordinate to the zinc. Hence, we surmised that the ethanol was coordinating to the zinc ion which contributed to the increase in the Pc absorbance. In order to obtain comparable data between the pure DCM solutions and those that contained EtOH it was necessary to add 0.1% pyridine in all cases. Here, the pyridine would bind more strongly to the zinc and occupy the open coordination sites. This would minimize the effect the ethanol may have on the absorbance and allow for comparisons to be made on the solutions studied (Figure 2.21).
Figure 2.20  UV-Vis spectra of 44 in DCM (——) in 2:3 DCM-EtOH (----) at $2 \times 10^{-5}$ M and at 25 °C
Figure 2.21  (a) UV-Vis spectra showing the increase in EtOH concentration for 45 (2x10^{-5} M, 25 °C); (b) The same experiment as above in the presence of 0.1% pyridine: 0% EtOH (—), 10% EtOH (----), 30% EtOH (---), 50% EtOH (——)
The substitution of the zinc into the core of the Pc helped to disfavor aggregation more than an unsubstituted core. This was most evident in the spectra obtained of the unsubstituted Fréchet-type dendritic Pcs, where the G1 compound 44 did not show any signs of strong aggregation until 40% of EtOH was present, and the tetrasubstituted G2 Pc 50 did not indicate any aggregation until 50% EtOH (Figure 2.22). This was in stark contrast to the unmetallated Pc which had begun to show strong signs of aggregation at 20% EtOH for both the octasubstituted G1 and tetrasubstituted G2. However, both the G2 and G3 Pcs showed no real difference between the metallated and unmetallated aggregation spectra, as both compounds had shown strong aggregation tendencies at 40% and 50% EtOH respectively. The reason as to why the G1 and tetrasubstituted G2 had such a strong difference between the unmetallated and metallated Pcs can be attributed to the lack of full coverage around the Pc core by the dendrons. The exposure of the metallated core leads to disfavorable intermolecular interactions (charge repulsion, steric caused by ligating pyridine) between Pcs in the absence of a strong polar solvent. When the polarity reached a certain value, these forces were overcome by the extra stability that is added by aggregation with the exclusion of a polar solvent from a predominantly non-polar environment. In the larger dendritic compounds (G2, G3), the dendrons through their sheer size gave a more complete coverage of the Pc core, which minimized the effect of having a charged core in relation to preventing aggregation. Figure 2.22 illustrates the change in the absorbance at 680 nm with respect to the increasing ethanol concentration.
Figure 2.22  Comparisons of the Q-band absorbance at 680 nm between 44 (●), 45 (■), 50 (+), and 46 (▲) as a function of % ethanol present in DCM at $2 \times 10^{-5}$ M and 25 °C
For the t-butyl substituted Fréchet-type dendrons, a similar trend, although not as drastic, was seen with the G0 and G1 Pcs (Figure 2.23). In both cases, there was no indication of aggregation present from pure DCM up to 50% EtOH added. In comparison, the unmetallated G0 and G1 Pc dendrimers had shown signs of aggregation at 20% and 40% EtOH respectively. The G2 dendritic Pc also showed no real signs of aggregation, although this was to be expected since the unmetallated G2 had no signs of strong self-association.

2.5.2 Aggregation properties of zinc phthalocyanines in thin films

Thin films were fabricated of the dendritic zinc Pcs by spin-casting from chloroform onto glass slides. Their absorbance between 500 and 800 nm was measured. The zinc Pcs exhibited much less aggregation when compared to the unmetallated Pcs in the solid state (Figure 2.24). For the unsubstituted Fréchet-type Pcs, the presence of the Q-band was observed in both the octasubstituted G1 Pc and the tetrasubstituted G2 Pc. In both of these cases, when the unmetallated compounds were studied in the solid state, only faint characteristics of a Q-band could be identified, if at all. In the second generation, only a small amount of aggregation was indicated in the zinc Pc versus the large amount seen in the unmetallated Pc. The only data that had shown agreement between the thin film spectra of the metallated and unmetallated Pcs was between the thin films of the G3 Pc where in either the zinc or the unmetallated Pc spectra, there was no sign of aggregation. The t-butyl Pc dendrimers followed the same trend that was seen with the unsubstituted Pc dendrimers (Figure 2.25), where again there
Figure 2.23 Comparisons of the Q-band molar absorptivities at 680 nm between 47 (♦), 48 (■), and 49 (▲) t-butyl dendritic zinc Pcs as a function of % ethanol present in DCM at 2x10^-5 M and 25 °C.
Figure 2.24  UV-Vis spectra of the thin films for 44 (—), 45 (---), 50 (—), and 46 (—)
Figure 2.25  UV-Vis spectra of the thin films for 47 (−→), 48 (−−−), and 49 (→) t-Bu Pcs
was the presence of a Q-band peak in the smallest generation (47). The two larger
dendritic Pcs showed considerably less aggregation with 49 appearing to contain only
monomeric species.

2.6 Determination of thermodynamic properties of aggregating phthalocyanines

In order to understand the extent of the aggregation within solutions of the
dendritic Pcs, it was necessary to utilize the expressions of Gibb’s free energy. By
manipulating the equations, values could be obtained that represent the equilibrium
constant for the first step of aggregation, or dimerization. It is with this information that
relationships between the size and type of dendritic peripheral substitution as well as the
solution dielectric constant and aggregation could be made. The variance in the
temperature of the solutions could then lead to relative enthalpies and entropies of
aggregation.

There are two main methods that have been used to obtain approximate values for
the dimerization constants ($K_D$). The first method, referred to here as the Tai-Hayashi
method, relies mainly on changes seen in the deviation from Beer’s law. The second
method, referred to as the monomer-dimer method, uses standard spectra that are either
pure monomer or pure dimer and measures the deviation of the sample from the ideal.
Both methods have their advantages and disadvantages, and there are particular times
when a specific method should be used. After the appropriate $K_D$ value is identified,
relationships can then be made between the dielectric constant and the extent of
aggregation; the solution entropic and enthalpic values and the extent of aggregation;
and finally, the size and peripheral dendritic substitution and the extent of aggregation.

2.6.1 Tai-Hayashi method of determining dimerization constants

The physical interactions between phthalocyanines has not been well studied. The complexity of multiple forms of aggregates (dimers, trimers, etc.) leads to a complex expression with multiple variables. However, with the assumption that in dilute solutions, high order aggregate formation (i.e. above dimer) is not favorable, the expression can be reduced into a workable form. Utilizing this theory, Tai and Hayashi set about to show the degree of aggregation that was occurring in naphthalocyanine solutions.²⁷⁷

By establishing that an equilibrium exists between the monomer and aggregate species \(nPc \rightleftharpoons Pc^n\), one can solve for the appropriate equilibrium constant, \(K_A\).

\[
K_A = \frac{[Pc^n]}{[Pc]^n}
\] (2)

Using the same method that was used by Osburn et al. to derivatize the expression to solve for two variables, the resulting equation is:

\[
K_A = \frac{x}{[n \ C_t^{n-1} (1 - x)^n]}
\] (3)

where \(x\) is the ratio of monomer concentration to total Pc concentration \(C_t\).²⁷⁸ By obtaining the extinction coefficients at the \(\lambda_{max}\) of both the monomer \((\epsilon_m,\ \text{dilute solution})\) and the aggregate \((\epsilon_n,\ \text{concentrated solution})\), a relationship can be made between these values and the observed extinction coefficient \((\epsilon)\) at a specific wavelength \((\lambda)\).

\[
\epsilon = x \ \epsilon_m / n + (1 - x) \ \epsilon_m
\] (4)
Assuming that $\varepsilon / \varepsilon_m \gg \varepsilon_n / (n \varepsilon_m)$ and $n \gg \varepsilon_n / \varepsilon_m$, equations 3 and 4 could be simplified to give:

$$\log [C_t (1 - \varepsilon / \varepsilon_m)] = \log (n K_A) + n \log [C_t (\varepsilon / \varepsilon_m)]$$

Plots of $\log [C_t (1 - \varepsilon / \varepsilon_m)]$ versus $\log [C_t (\varepsilon / \varepsilon_m)]$ would theoretically give a straight line of slope $n$, or average aggregation number, from which the $K_A$ could be derived with respect to the $y$-intercept $\log (n K_A)$ (Figure 2.26).

The main problem in using this method is the lack of a distinct monomeric peak for the Pcs in the aggregated solvents. This method assumes that UV-Vis spectra will fall between the ranges of monomer and aggregate spectra, and that discernable monomeric spectra can be obtained. It does not address the issues raised by a compound that will aggregate in even the most dilute conditions. Table 2.2 shows the Tai-Hayashi calculated $K_A$ and $n$ values for each of the Pcs in the different solutions. While the $K_A$ values were reasonable for Pcs in non-aggregating solvents, the problems with the method were greatly enhanced in the DCM-EtOH experiment. For the Pc in pure DCM, a $K_A$ value of 3.91 was obtained. After the addition of 10% EtOH to the solution, the value of the $K_A$ rose significantly to $4.37 \times 10^4$. It is here that the results begin to contradict the spectral information obtained. The highest $K_A$ value was at 10% EtOH in comparison to the value at 50% EtOH, where the $K_A$ dropped to a value of 9.09. This is almost a three and a half fold order of magnitude difference between a solution that showed signs of
Figure 2.26 Tai-Hayashi plot of 34 in DCM-EtOH solvent mixtures: DCM (◆); 9:1 DCM-EtOH (■); 4:1 DCM-EtOH (▲); 7:3 DCM-EtOH (X); 3:2 DCM-EtOH (−); 1:1 DCM-EtOH (+)
Table 2.2 Tai-Hayashi calculated values for G1 and G2 dendritic Pcs in various solvents

<table>
<thead>
<tr>
<th>Pc</th>
<th>Solvent</th>
<th>$K_A$ (M$^{-1}$)</th>
<th>$N$</th>
</tr>
</thead>
<tbody>
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<td>34</td>
<td>Acetone</td>
<td>2.86x10$^2$</td>
<td>1.22</td>
</tr>
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<td>Acetone</td>
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<td>Toluene</td>
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aggregation and a solution that was almost fully aggregated. With this glaring disparity in the data, it is important to note that this can be an effective method for determination of equilibrium values as long as the behavior of the species in solution are not linear according to Beer’s Law; however, these values are not useful for the synthesized octasubstituted dendritic Pcs.

2.6.2 The monomer-dimer method of determining equilibrium values

With the problems that were encountered in the previously mentioned method, it became necessary to obtain the equilibrium constant through another route. Using a nonlinear least-square fitting method, based upon the work of Ng and coworkers, became a feasible option. In order for this assumption to be valid, aggregates higher than a dimer can not be formed. Previous studies have shown that this is normally valid especially for dilute solutions.

Using the assumption that an equilibrium exists between the monomer and dimer species, the expression for the dimerization constant would be:

$$K_D = \frac{[D]}{[M]^2}$$  \hspace{1cm} (6)

with D representing the dimeric species and M being the monomeric species. The total concentration of Pc ($C_t$) in solution is:

$$[C_t] = [M] + 2[D]$$  \hspace{1cm} (7)

After solving for the dimer concentration and substituting back into the equilibrium expression, the following equation is obtained:

$$K_D = \frac{([C_t] - [M])}{(2[M]^2)}$$  \hspace{1cm} (8)
And the monomer concentration is expressed as:

$$[M] = -1 + \left(1 + 8K_D[C_t]\right)^{1/2} / 4K_D$$  \hspace{1cm} (9)

At this point, the monomer concentration is substituted into the Beer’s Law equation to give:

$$A_m = \frac{\varepsilon_m \left(1 + 8K_D[C_t] - 1\right)^{1/2}}{4K_D}$$  \hspace{1cm} (10)

where $A_m$ is the absorbance of the split Q-band, $\varepsilon_m$ is the molar absorptivity of a nonaggregated solution, and $l$ is the pathlength of the cell. Beer’s Law plots showing the line of best fit can be seen in Figure 2.27. The main problem with this equation is that it does not take into consideration the additive effect of the monomer absorbance along with the absorbance of the dimer. For reference, all $K_D$ approximations are taken in reference to the peak at 700 nm, and not 680 nm because the absorbance overlap between the two species is not as great (Figure 2.27). With solutions high in monomer concentration, this will not be an issue, and the approximations of the dimerization constant will be close to actual values. However, with solutions high in dimer content, these approximations will have a considerable amount of error.

The data that was collected and analyzed with this technique were found to be more in agreement with the observed results than the data collected through the Tai-Hayashi method. Comparative values between the two methods are listed in Table 2.3. The solutions that had no apparent concentration of dimer had a $K_D$ value of approximately 200 M$^{-1}$ for the unsubstituted Fréchet-type G2 Pc dendrimer 34 in DCM, higher than values collected via Tai-Hayashi (3.92 M$^{-1}$). The values with the
Figure 2.27  (a) Beer’s Law plot of 34 in DCM-EtOH solvent mixtures for determination of monomer / dimer ratios: DCM (○); 9:1 DCM-EtOH (■); 4:1 DCM-EtOH (▲); 7:3 DCM-EtOH (X); 3:2 DCM-EtOH (−); 1:1 DCM-EtOH (+); (b) Illustration of monomer (—) and dimer (---) overlap of 34 with respect to the Q-band absorbances at 670 and 700 nm
### Table 2.3  Comparison of aggregation values for G1 and G2 Pc in various solvents obtained via Tai-Hayashi and monomer-dimer methods

<table>
<thead>
<tr>
<th>Pc</th>
<th>Solvent</th>
<th>$K_D$ (M⁻¹) (M-D)</th>
<th>Monomer:Dimer</th>
<th>$K_A$ (M⁻¹) (T-H)</th>
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<td>60:40</td>
<td>2.53x10²</td>
</tr>
<tr>
<td>35</td>
<td>DCM-EtOH (4:1)</td>
<td>1.11x10⁴</td>
<td>80:20</td>
<td>1.50x10¹</td>
</tr>
<tr>
<td>34</td>
<td>DCM-EtOH (7:3)</td>
<td>3.04x10⁵</td>
<td>30:70</td>
<td>2.85x10⁴</td>
</tr>
<tr>
<td>35</td>
<td>DCM-EtOH (7:3)</td>
<td>9.64x10⁴</td>
<td>45:55</td>
<td>1.77x10²</td>
</tr>
<tr>
<td>34</td>
<td>DCM-EtOH (3:2)</td>
<td>1.28x10⁶</td>
<td>16:84</td>
<td>4.10x10³</td>
</tr>
<tr>
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<td>DCM-EtOH (3:2)</td>
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<td>3.47x10²</td>
</tr>
<tr>
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</tr>
<tr>
<td>35</td>
<td>DCM-EtOH (1:1)</td>
<td>1.56x10⁶</td>
<td>14:86</td>
<td>2.42x10¹</td>
</tr>
</tbody>
</table>
predominantly dimeric solutions were just the opposite. The same Pc dendrimer in 1:1 DCM-EtOH had a value of $1.6 \times 10^5 \text{ M}^{-1}$ by this method, with the value calculated by Tai-Hayashi was $24.2 \text{ M}^{-1}$. Overall, even though the values calculated are approximations, the observed trends fit this method better than they did when Tai-Hayashi was applied. It is because of this that all future reference to dimerization values will be ones that have been calculated using the monomer-dimer method.

2.6.3 Relationship between $K_D$ and dielectric constant for DCM-EtOH solutions

In an attempt to show the relationship between the extent of aggregation and the amount of ethanol present, we studied the effect of solvent dielectric constant on the dimerization constant. This was performed by first understanding that the Gibbs free energy is made up of both an electrostatic portion and a non-electrostatic portion. The Gibbs energies for the solvation of ions can be estimated using the Born equation:

$$
\Delta G_E = - \left( z^2 e^2 N_A / (8 \pi \varepsilon_o r_i) \right) \left( 1 - 1 / \varepsilon_r \right) = A / \varepsilon_r
$$

where $z$ is the charge number of the ion, $e$ is the elementary charge, $N_A$ is Avogadro's number, $\varepsilon_o$ is the vacuum permeativity, $r_i$ is the radius of the ion squared, and $\varepsilon_r$ is the dielectric constant of the solution. In order to solve for the solution dielectric, the composition of the solution must be taken into consideration:

$$
\varepsilon_r = \varepsilon_{mix} = \chi_{DCM} \varepsilon_{DCM} + \chi_{EtOH} \varepsilon_{EtOH}
$$
\( \chi \) represents the mole fraction with regard to the amount of each solvent present.

Dielectric values at 25°C are 9.08 for DCM and 24.3 for EtOH. Using the relationship between the dimerization constant and Gibbs free energy, substitution of the electrostatic and nonelectrostatic values give the following linear equation:

\[
\log (K_d) = - \frac{A}{2.3 R T} + C; \quad C = - \frac{\Delta G_{nE}}{2.3 R T}
\]

The slope represents the electrostatic interaction, while the intercept is the nonelectrostatic force.

The \( K_D \) values of the three dendritic Pcs which were the most affected by the change, 34, 35, and 43, in the dielectric were plotted, the slopes of which varies slightly (Figure 2.28). The slope of the tetrasubstituted dendrimer 43 was the lowest (67.54), followed by the first (70.81) and second (72.16) generation octasubstituted dendrimers 34 and 35, respectively. This shows that as the dendrimer increased in size, the influence of the electrostatic effect between both size and generation was negligible. The same could also be said about the nonelectrostatic function. Here the values had less variance between the tetrasubstituted 43 (10.18), first (10.55) and second (10.07) generation octasubstituted dendrimers 34 and 35, respectively, and it showed that the overall effect of these forces on the system was only a small piece of a bigger picture.

In order to be sure that the derivatization and theory were justified, an experiment was run to test the effect of temperature on the system. The solution of the G2 octasubstituted dendrimer 35 was cooled to 278 K and the experiment repeated. The overall result was drastic in comparison to the data between generations. The
Figure 2.28  Plot showing the determination of the effect of changing the dielectric constant on aggregation (all Pcs at 2x10^{-5} M): 34 (♦); 35 at 298K (■); 35 at 278K (▲); 43 (●)
electrostatic effect was 90.16 (278 K) versus 72.16 (298 K) and the nonelectrostatic effect was 12.62 (278 K) compared to 10.07 (298 K). The lowering of the temperature allowed for the smaller variables, such as the squared ionic radius in the Born equation, to have a stronger effect on aggregation. Overall while temperature seemed to have a moderate effect on how the electrostatic and nonelectrostatic forces acted at the different dielectric strengths, the differences attributed to these forces in relation to the generational size between the molecules were minimal. The effect on the $K_d$ by the dielectric however was much larger showing that there was a much greater relationship between the increase of the dielectric and the increase in aggregation.

2.6.4 Temperature effects on the aggregation of the dendritic Pcs

The effect of temperature on the $K_d$ can also be used to investigate the changes in the enthalpy and entropy of aggregation. This is extremely useful in the understanding of the effect that the peripheral substitution of the dendrons had on the different species in solution. The relationship between the dimerization constant and the values of entropy and enthalpy is derived from the free energy equations for both:

$$\Delta H - T\Delta S = -RT \ln K_d$$ (14)

By solving for the log $K_D$, the following expression is obtained:

$$\log K_D = - \Delta H / 2.3 R T + \Delta S / 2.3 R$$ (15)

The values of enthalpy and entropy are then obtained by plotting the log $K_D$ versus $1/T$ which gives a straight line (Figure 2.29). The enthalpic value is then derived from the slope, while the entropic value is gained from the intercept.
Figure 2.29  Thermodynamic plots to determine entropic and enthalpic values for 35 (■) and 38 (♦) at $2 \times 10^{-5}$ M.
The Pc dendrimers used were the first generation \textit{t}-butyl substituted Fréchet-type Pc 37, and the second generation unsubstituted Fréchet-type Pc 35. These dendrimers were chosen because both are approximately the same molecular weight and have similar molecular size. They also behave very similarly in thin films displaying a moderate degree of aggregation. The solvent toluene was used because it causes a moderate amount of aggregation in the unsubstituted Pcs, and was thus thought to be the best solvent to illustrate a range in the extent of aggregation over the temperatures studied. The enthalpic data gained from the experiments show that 38 has a slightly higher enthalpy of aggregation (-19.08 kJ / mol) than 35 (-15.63 kJ / mol). The difference in the values for the unsubstituted Pc 34 (77.8 J / mol K) and the \textit{t}-butyl Pc 38 (31.9 J / mol K) indicate that the aggregation of the dendritic Pcs is entropically driven.

Overall, the thermodynamic values on the aggregation of the Pcs fit the observations that the \textit{t}-butyl groups help to decrease the likeliness of self-association. As mentioned before, this could be because of the formation of a nonpolar shell around the Pc which interacts with the solvent in such a way that the aggregation of these species is disfavored.

\section*{2.6.5 Overall comparison of the Pc dendrimers based on size and substitution}

Each of the Pcs studied show trends with respect to the dimerization constants in various solvents and solvent mixtures (Tables 2.4 and 2.5). For studies in nonaggregating
Table 2.4  Dimerization constant values and monomer-dimer (m:d) ratios for the unsubstituted unmetallated dendritic Pes (34-36, 43) in different solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>34 $K_D$ (M⁻¹)</th>
<th>34 (m:d)</th>
<th>35 $K_D$ (M⁻¹)</th>
<th>35 (m:d)</th>
<th>36 $K_D$ (M⁻¹)</th>
<th>36 (m:d)</th>
<th>43 $K_D$ (M⁻¹)</th>
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<td>9.8</td>
<td>~100:0</td>
<td>8.2</td>
<td>~100:0</td>
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<td>~100:0</td>
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<tr>
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<td>2.40x10⁴</td>
<td>70:30</td>
<td>9.50x10³</td>
<td>82:18</td>
<td>1.34x10³</td>
<td>97:3</td>
<td>1.12x10⁴</td>
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</tr>
<tr>
<td>DCM-EtOH 4:1</td>
<td>3.65x10⁴</td>
<td>60:40</td>
<td>1.11x10⁴</td>
<td>80:20</td>
<td>3.97x10³</td>
<td>92:8</td>
<td>2.83x10⁴</td>
<td>67:33</td>
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<tr>
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<td>3.04x10⁵</td>
<td>30:70</td>
<td>9.64x10⁴</td>
<td>45:55</td>
<td>5.18x10³</td>
<td>90:10</td>
<td>1.77x10⁵</td>
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<td>8.98x10⁵</td>
<td>18:82</td>
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<td>8:92</td>
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<td>14:86</td>
<td>1.06x10⁶</td>
<td>18:82</td>
<td>2.36x10⁶</td>
<td>12:88</td>
</tr>
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<td>8.2</td>
<td>~100:0</td>
<td>7.4</td>
<td>~100:0</td>
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<tr>
<td>THF</td>
<td>7.9</td>
<td>~100:0</td>
<td>9.8</td>
<td>~100:0</td>
<td>8.2</td>
<td>~100:0</td>
<td>7.4</td>
<td>~100:0</td>
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<tr>
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<tr>
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<td>3.66x10⁶</td>
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<td>22:78</td>
<td>5.67x10⁶</td>
<td>9:91</td>
</tr>
<tr>
<td>EtOAc</td>
<td>2.39x10⁶</td>
<td>12:88</td>
<td>1.42x10⁶</td>
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<td>1.28x10⁵</td>
<td>28:72</td>
<td>9.25x10⁵</td>
<td>25:75</td>
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Table 2.5  Dimerization constant values and monomer-dimer (m:d) ratios for the t-butyl unmetallated dendritic PCs (37-39) in the different solvents

<table>
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<th>Solvent</th>
<th>37 $K_D$ (M$^{-1}$) (m:d)</th>
<th>37 $K_D$ (M$^{-1}$)</th>
<th>38 $K_D$ (M$^{-1}$) (m:d)</th>
<th>38 $K_D$ (M$^{-1}$)</th>
<th>39 $K_D$ (M$^{-1}$) (m:d)</th>
<th>39 $K_D$ (M$^{-1}$)</th>
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<tr>
<td>DCM-EtOH</td>
<td>8.3 ~100:0</td>
<td>8.3 ~100:0</td>
<td>8.2 ~100:0</td>
<td>8.2 ~100:0</td>
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<td></td>
</tr>
<tr>
<td>DCM-EtOH 4:1</td>
<td>8.3 ~100:0</td>
<td>8.3 ~100:0</td>
<td>8.2 ~100:0</td>
<td>8.2 ~100:0</td>
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<td></td>
</tr>
<tr>
<td>DCM-EtOH 7:3</td>
<td>9.34x10$^4$ 43:57</td>
<td>8.3 ~100:0</td>
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<tr>
<td>DCM-EtOH 3:2</td>
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<tr>
<td>DCM-EtOH 1:1</td>
<td>4.41x10$^5$ 23:77</td>
<td>4.02x10$^5$ 31:69</td>
<td>3.30x10$^4$ 70:30</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Dioxane</td>
<td>8.3 ~100:0</td>
<td>8.3 ~100:0</td>
<td>8.2 ~100:0</td>
<td>8.2 ~100:0</td>
<td></td>
<td></td>
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<tr>
<td>THF</td>
<td>8.3 ~100:0</td>
<td>8.3 ~100:0</td>
<td>8.2 ~100:0</td>
<td>8.2 ~100:0</td>
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<tr>
<td>Toluene</td>
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<td>8.3 ~100:0</td>
<td>8.2 ~100:0</td>
<td>8.2 ~100:0</td>
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<td></td>
</tr>
<tr>
<td>Acetone</td>
<td>8.32x10$^4$ 55:45</td>
<td>8.32x10$^4$ 55:45</td>
<td>8.02x10$^4$ 55:45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EtOAc</td>
<td>1.52x10$^5$ 45:55</td>
<td>3.02x10$^4$ 72:28</td>
<td>8.2 ~100:0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
solvents (DCM, dioxane, THF), each of the Pcs, whether substituted or unsubstituted, behaved very similarly. The calculated $K_D$ values were between $4.2 - 14.6 \ M^{-1}$ with a monomer / dimer (m:d) ratio of approximately 100:0.

With respect to the difference in substitution, as previously mentioned, the $t$-butyl substituted Fréchet-type dendrimers did not aggregate as much as the unsubstituted dendrons. As a reference, consider 35 and 38. Both have the same approximate size, but both behave differently in solution. The G1 $t$-butyl Pc 38 maintained the nonaggregated state up to 40% EtOH, while the G2 35 began showing signs of aggregation almost immediately after ethanol was introduced ($K_D = 9.5 \times 10^3 \ M^{-1}$ at 10% EtOH (m:d = 82:18)). The behavior of the different substitution types in various solvents followed the same trend. In toluene, 38 did not show any signs of aggregation while 35 was found to have a majority of dimer present ($K_D = 2.3 \times 10^5 \ M^{-1}$ m:d = 42:58). Both in acetone ($K_D = 8.3 \times 10^4 \ M^{-1}$ m:d = 55:45) and ethyl acetate ($K_D = 3.0 \times 10^4 \ M^{-1}$ m:d = 72:28), 38 still showed a predominance of nonaggregated Pc, while 35 exhibited a large dimer concentration in both of these solvents ($K_D = 1.4 \times 10^6 \ M^{-1}$ m:d = 20:80 (EtOAc); $K_D = 3.6 \times 10^6 \ M^{-1}$ m:d = 13:87 (acetone)) illustrating again that the $t$-butyl dendrons are better at preventing aggregation in solution.

Within the $t$-butyl series, there was a trend that showed that as the size of the dendritic periphery increased, so too did its ability to prevent aggregation. Not only was this shown in the amount of ethanol that had to be added to see changes to the absorbance spectra, but also when the Pcs were compared in solvents that induced aggregation eg. EtOAc, 1:1 DCM-EtOH. While the G0 dendrimer (37) showed signs of self-association
at 30% EtOH, the G1 (38) and G2 (39) compounds remained non-aggregated until 50% EtOH was added. Here 37 had a large $K_D$ value ($4.4 \times 10^5$ M$^{-1}$ m:d = 23:47), with the values for 38 ($K_D = 4.0 \times 10^5$ M$^{-1}$ m:d = 31:69) and 39 ($K_D = 3.0 \times 10^4$ M$^{-1}$ m:d = 70:30) being somewhat smaller. This trend was the most striking in EtOAc where 37 was predominantly dimer ($K_D = 1.5 \times 10^5$ M$^{-1}$ m:d = 45:55), 38 was predominantly monomer ($K_D = 3.0 \times 10^4$ M$^{-1}$ m:d = 72:28) and 39 showed no signs of aggregation at all.

Trends were much more evident among the unsubstituted Pes. With the exception of the nonaggregating solvents, the tendency to prevent aggregation followed the trend: 36 > 35 > 43 > 34. Some of the representative values that illustrate this behavior are those that are in 7:3 DCM-EtOH and acetone. In the DCM-EtOH mixture, 34 showed a large presence of dimer ($K_D = 3.0 \times 10^5$ M$^{-1}$ m:d = 30:70), as did 43 ($K_D = 1.7 \times 10^5$ M$^{-1}$ m:d = 37:63) and 35 ($K_D = 9.6 \times 10^4$ M$^{-1}$ m:d = 45:55). Only 36 had shown any significant amount of monomer ($K_D = 5.1 \times 10^4$ M$^{-1}$ m:d = 90:10). While all four Pes showed a considerable amount of dimer in acetone, the proof of a trend was clear. The values of the dimerization constants were all very close, which was evident by the increase in the monomer concentration (10% (34); 11% (43); 13% (35); 18% (36)).

The data acquired throughout these experiments had indicated that the presence of a bulky periphery helps to decrease the amount of Pc aggregation. It was found that the dielectric constant of the solvent proves to be a significant factor in the aggregation of these Pes. Also, the $t$-butyl periphery was shown to be better at halting aggregation than were the unsubstituted dendrons, lending some insight into the observed trend. Finally, by using the monomer-dimer method, values were assigned to the spectral observations,
and more thorough comparisons were able to be made showing trends among the size and peripheral substitution of the Pc dendrimers.

2.7 Probing molecular structure of dendritic zinc Pcs using fluorescence

Zinc Pcs are fluorescent, hence, another set of experiments were performed to see if the fluorescent data mimicked the absorbance information, and to investigate trends through another analytical method. In addition, quenching studies would probe the molecular structure of the dendrimers in solution and provide a better understanding of how the dendrons are preventing aggregation.

2.7.1 Aggregation of dendritic zinc Pcs in DCM-EtOH solutions

The measurement of the dimerization constants for the zinc Pcs was performed following the same procedure as the unmetallated compounds with DCM-EtOH mixtures as solvent. However, a small amount of pyridine was added to the solutions of zinc Pcs to prevent the coordination of ethanol to the zinc atom.\(^{2.69}\) In all cases, no significant aggregation was present in solutions containing up to 30% ethanol (Table 2.6). The presence of the \(t\)-butyl groups on the periphery prevented self-association up to 40% ethanol, after which only 47 \((K_D = 4.5 \times 10^3 \text{ M}^{-1}; \text{m:d} = 93:7)\) showed any indication of aggregated species (Table 2.7).
Table 2.6  Dimerization constant values and monomer-dimer (m:d) ratios for the unsubstituted zinc dendritic Pcs (44-46, 50) in DCM-EtOH solutions at 25 °C and 2x10⁻⁵ M

<table>
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<tr>
<th>Solvent</th>
<th>44 K_D (M⁻¹)</th>
<th>44 (m:d)</th>
<th>45 K_D (M⁻¹)</th>
<th>45 (m:d)</th>
<th>46 K_D (M⁻¹)</th>
<th>46 (m:d)</th>
<th>50 K_D (M⁻¹)</th>
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<td>~100:0</td>
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<tr>
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<td>7.40</td>
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<td>4:1 DCM-EtOH</td>
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<td>~100:0</td>
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<td>~100:0</td>
</tr>
<tr>
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<td>77:23</td>
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</table>
Table 2.7  Dimerization constant values and monomer-dimer (m:d) ratios for the t-butyl zinc dendritic Pcs (47-49) in DCM-EtOH solutions at 25 °C and 2x10⁻⁵ M

<table>
<thead>
<tr>
<th>Solvent</th>
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<th>47 (m:d)</th>
<th>48 K_D (M⁻¹)</th>
<th>48 (m:d)</th>
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<td>~100:0</td>
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<tr>
<td>9:1</td>
<td>6.19</td>
<td>~100:0</td>
<td>5.77</td>
<td>~100:0</td>
<td>5.53</td>
<td>~100:0</td>
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<tr>
<td>DCM-EtOH</td>
<td>6.19</td>
<td>~100:0</td>
<td>5.77</td>
<td>~100:0</td>
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</tr>
<tr>
<td>7:3</td>
<td>6.19</td>
<td>~100:0</td>
<td>5.77</td>
<td>~100:0</td>
<td>5.53</td>
<td>~100:0</td>
</tr>
<tr>
<td>DCM-EtOH</td>
<td>6.19</td>
<td>~100:0</td>
<td>5.77</td>
<td>~100:0</td>
<td>5.53</td>
<td>~100:0</td>
</tr>
<tr>
<td>3:2</td>
<td>6.19</td>
<td>~100:0</td>
<td>5.77</td>
<td>~100:0</td>
<td>5.53</td>
<td>~100:0</td>
</tr>
<tr>
<td>DCM-EtOH</td>
<td>3.43x10³</td>
<td>95:5</td>
<td>4.58x10³</td>
<td>93:7</td>
<td>1.73x10³</td>
<td>97:3</td>
</tr>
</tbody>
</table>
Similar to what was seen with the unmetallated Pcs, 45 had shown the largest amount of dimer in solution. The results indicated that 45 contained 75% dimer at 50% ethanol ($K_D = 8.7 \times 10^5 \text{ M}^{-1} \text{ m:d = 25:75}$). The third generation dendrimer (46) was still predominantly dimer at 50% ethanol ($K_D = 4.3 \times 10^5 \text{ M}^{-1} \text{ m:d = 33:67}$). The two smallest Pcs, 50 ($K_D = 3.0 \times 10^4 \text{ M}^{-1} \text{ m:d = 77:23}$) and 44 ($K_D = 3.4 \times 10^4 \text{ M}^{-1} \text{ m:d = 75:25}$) had shown the least amount of aggregation at 50% ethanol. A plausible theory is that as the concentration of ethanol increases, the dendritic arms become more extended allowing for favorable interactions with the solvent. When the dendritic arms are smaller, there is enough steric bulk in proximity to the Pc core that aggregation is prevented. As the generation size increases, the interactions between dendrons cause them to "flatten" out and enable the core of the Pc to become exposed, hence aggregation becomes more likely. The difference between the 45 and 46 is again sterically related and the amount of bulk seen with the third generation dendrons limits the ability of the arms to fully "flatten" out.

2.7.2 Relationship between fluorescence data and absorbance data

A comparison between fluorescence and absorbance data of both 45 and 44 was done (Figure 2.30). It is important to note that this experiment was done in the absence of pyridine. Hence, this data shows an initial rise in the UV-Vis absorbance or
fluorescence intensity followed by a slow decline with increasing EtOH content. For the fluorescence measurement, the solution was excited at 616 nm for samples containing 0-50% EtOH and at 630 nm for samples containing 60-70% EtOH. The plot of the fluorescence intensity at 690 nm was similar to the absorbance at 680 nm graph (Figures 2.22 and 2.23) with a few minor differences. First, the initial fluorescence intensity of 44 was lower than that of 45 while the opposite was true for the absorbance measurement. Second, at 50% ethanol the 44 absorbance was greater than the 45 absorbance although the fluorescence intensities were similar. Third, at 60% ethanol, the fluorescence intensity of 44 was greater than 45 while both compounds had similar absorbances. Except for these few minor instances, the fluorescence measurements reproduced the trends seen in the UV-Vis absorbance data.

A second experiment was run using the fluorescence of the Pcs and was also related to the absorbance spectra. Ng had previously reported the energy transfer from the dendron (280 nm) and the Soret band of the Pc (350 nm). His results showed that when a tetrasubstituted water soluble dendritic Pc was compared against a non-dendritic Pc, the dendritic Pc exhibited a large emission at 690 nm while the normal Pc showed a weak emission upon excitation at 310 nm.\textsuperscript{264} In a similar experiment, we excited 35 at 281 nm, 335 nm (Soret band), 668 and 702 nm (Q band) (Figure 2.31). While the excitation at the Q-band produced the strongest emission (690 nm), there was evidence of
Figure 2.30  Comparison of the (a) UV-Vis absorbance and (b) fluorescence ($\lambda_{\text{ex}} = 616$ nm, $\lambda_{\text{em}} = 690$ nm) of 44 (●) and 45 (■) with respect to increasing amounts of EtOH in DCM at 680 nm (25 °C, $2 \times 10^{-5}$ M)
energy transfer from the dendrons to the core — significant emission at 690 nm upon excitation at 281 nm.

2.7.3 Stern-Volmer quenching experiments

By removing energy from a fluorescent species, the emission intensity of the target species is quenched. One way to do this is through the addition of a second compound that either competes in the absorbance of the incoming photon, or causes a non-radiative decay of the excited state species. For the second statement to be true, the quenching species must be in close proximity to the excited compound. It is by these means that the structure of a compound in solution can be probed using fluorescence.

A Stern-Volmer plot is a measure of the effect of a quencher on the overall change in the fluorescence intensity. The linear equation illustrates this relationship where \( I_0 \) and \( I \) are the intensities before and after addition of quencher, \([Q]\) is the concentration of the quencher and \(K_{sv}\) is the Stern-Volmer quenching constant which is the product of the bimolecular quenching rate constant and the fluorescent lifetime of the species in the absence of quencher:

\[
\frac{I_0}{I} = 1 + K_{sv} [Q] 
\]  

Overall, the larger the value for \( K_{sv} \), the less hindered the approach to the core of the Pc.
Figure 2.31  Fluorescence emission spectra of $35$ ($25^\circ$C, $2\times10^{-7}$ M) with excitation at: $281$ nm (—), $335$ nm (---), $702$ nm (—), and $668$ nm (——)
In work with the water-soluble carboxylate Fréchet-type dendritic PCs, Ng used Stern-Volmer plots to probe the structure of his compounds. The quenchers used were anthraquinone, a small aromatic molecule which acts as an electron acceptor; sodium picrate, a negatively charged quenching species; and 5,10,15,20-tetrakis(1-methyl-4-pyridyl)porphyrin tetraiodide \((\text{TMePyP})_4\) a cationic quencher. There was a trend associated with anthraquinone in that the smaller generation PCs was quenched more rapidly than the larger ones. In the case of the ionic quenchers, sodium picrate was repelled by the negatively charged dendritic periphery and quenching was ineffective. The \((\text{TMePyP})_4\) salt, a large molecule which was attracted to the target through electrostatic interactions, effectively quenched the G0 and G1 dendrimers. The G2 dendrimer was not affected apparently due to the separation imparted by the dendrons. Since our octasubstituted PCs are, except for the cationic zinc core, uncharged, the electrostatic effect and quenching should be negligible. Hence, we used a small molecule quencher (anthraquinone), and a larger uncharged quencher (tetraphenylporphyrin (TPP)) to help understand the dendritic environment in nonpolar THF solutions.

2.7.4 Stern-Volmer data using anthraquinone as the quencher

Anthraquinone, a small planar molecule which is a good electron acceptor was added to solutions of the dendritic PCs in THF. Aliquots of an anthraquinone solution \((9.99 \times 10^{-3} \text{ M})\) were added to a solution of the Pc, and the fluorescence intensity was measured at 684 nm. The ratio of the original intensity versus the intensity after the addition of the anthraquinone was plotted against the concentration of the quencher to
give a straight line with an intercept of 1 and a slope corresponding to the $K_{sv}$ (Figure 2.32).

For a reference, the values obtained by Ng in his use of a tetrasubstituted, carboxy-terminated dendritic Pc were 4310 mol$^{-1}$ L (G0), 1860 mol$^{-1}$ L (G1), and 787 mol$^{-1}$ L.$^{264}$ In contrast, the values for the octasubstituted dendritic Pcs ranged from 22.3 mol$^{-1}$ L to 33.7 mol$^{-1}$ L, at least an order of magnitude difference (Table 2.8). First, because of the relative small size of the $K_{sv}$ values, the approach of the anthraquinone to the Pc core is greatly hindered in both cases. This is due to either the steric bulk of the dendrons or stable van der Waals interactions between the anthraquinone and the individual rings of the dendrimer. The large difference between the values of Ng and those obtained for the octasubstituted Pcs may be attributed to a greater shielding of the Pc core in solution or a solvent effect. The use of an aqueous system may have acted to force the quencher to seek out the dendrimer, a more thermodynamically favorable environment. The utilization of THF as the solvent decreased the unfavorable interactions between the quencher and the solvent and may have resulted in the smaller Stern-Volmer constant values.

2.7.5 Stern-Volmer data using tetraphenylporphyrin as the quencher

With the previous results showing that when using anthraquinone as the quencher there was minimal interaction with the Pc core, another experiment was necessary to see
Figure 2.32  Stern-Volmer plot of $2.59 \times 10^{-6}$ M 44 (♦) and $3.32 \times 10^{-6}$ M 47 (■) using anthraquinone ($9.99 \times 10^{-3}$ M stock) as a quencher
Table 2.8  Values for synthesized Pcs obtained from Stern-Volmer plots using anthraquinone (9.99x10^{-3} M stock) as a quencher

<table>
<thead>
<tr>
<th>Zinc Pc</th>
<th>Pc concentration (M)</th>
<th>$K_{sv}$ (M^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>2.59x10^{-6}</td>
<td>22.7</td>
</tr>
<tr>
<td>45</td>
<td>2.76x10^{-6}</td>
<td>22.4</td>
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<tr>
<td>46</td>
<td>2.14x10^{-6}</td>
<td>27.6</td>
</tr>
<tr>
<td>50</td>
<td>2.55x10^{-6}</td>
<td>35.1</td>
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<tr>
<td>47</td>
<td>3.23x10^{-6}</td>
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<td>48</td>
<td>3.54x10^{-6}</td>
<td>28.9</td>
</tr>
<tr>
<td>49</td>
<td>2.77x10^{-6}</td>
<td>33.7</td>
</tr>
</tbody>
</table>
if access to the core was really hindered or if the anthraquinone was being held up within the arms of the dendrons. Therefore, the next experiment involved the use of tetraphenylporphyrin (TPP) as the quencher. TPP is a macrocyclic compound which acts as a potent Pc quencher, and is modeled after the (TMePyP)4 quencher used by Ng.64 A stock solution of TPP was made in THF (1x10^-3 M) and again small aliquots were added to a set concentration of the Pc (2.70x10^-6 M) after which the fluorescence intensity was measured at 684 nm (Figure 2.33).

The use of the cationic quencher (TMePyP)4 by Ng resulted in quenching of both the G0 and G1 tetrasubstituted carboxy-terminated dendrimers, while the G2 showed a smaller quenching giving a Ksv value of 261000 mol^-1 L. The use of TPP with the octasubstituted dendritic Pcs gave Ksv values that ranged from 354 to 690 mol^-1 L, three orders of magnitude lower than the data reported by Ng (Table 2.9). While much of that difference can be attributed to the presence of attractive forces between the Pc and the quencher in the work of Ng, there may be other forces preventing the quencher from interacting with the octasubstituted Pc. Within the results obtained from the octasubstituted Pcs, TPP acted to quench the octasubstituted Pcs more effectively than did the anthraquinone (by an order of magnitude) presumably due to fewer interactions with the dendrons. Still, in both cases, the quenching was slight and only began to
Figure 2.33  Stern-Volmer plot of $2.59 \times 10^{-6} \text{ M} \text{ 44 (•)}$ and $3.32 \times 10^{-6} \text{ M} \text{ 47 (■)}$ using TPP (1$\times$10$^{-3}$ M stock) as a quencher
Table 2.9  Values for synthesized Pcs obtained from Stern-Volmer plots using TPP (1x10^-3 M stock) as a quencher

<table>
<thead>
<tr>
<th>Zinc Pc</th>
<th>Pc concentration (M)</th>
<th>$K_{sv}$ (M^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>2.59x10^-6</td>
<td>673</td>
</tr>
<tr>
<td>45</td>
<td>2.76x10^-6</td>
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</tr>
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<td>47</td>
<td>3.23x10^-6</td>
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<td>48</td>
<td>3.54x10^-6</td>
<td>573</td>
</tr>
<tr>
<td>49</td>
<td>2.77x10^-6</td>
<td>354</td>
</tr>
</tbody>
</table>
occur at high concentrations of quencher. What this indicates is that there is a definite shield that is formed around the core of the Pc which not only minimizes interactions with other Pcs, but also minimizes interactions with other molecules.

The comparison between the individual octasubstituted Pcs showed no clear trends in the data (Table 2.9). Rather, the largest difference in the values was between 44 (22.7 mol⁻¹ L) and 50 (35.1 mol⁻¹ L) for the anthraquinone and between 49 (354 mol⁻¹ L) and 45 (690 mol⁻¹ L) for the TPP. Because the differences between the values are so small, any comparisons between the Pcs become difficult to make. While no real conclusions can be drawn from how the Pcs interacted with anthraquinone, there are the beginnings of a trend based on size with the TPP, showing that while the smaller generations in each of the series are close in value (673 mol⁻¹ L (44), 690 mol⁻¹ L (45), 582 mol⁻¹ L (47), 573 mol⁻¹ L (48)), the difference in regard to the largest dendrimers in each series is significant (553 mol⁻¹ L (46); 354 mol⁻¹ L (49)) suggesting that the t-butyl groups may be adding to the prevention of the approach of the quencher.

The insertion of zinc into the Pc gave results that followed the same general trend that was seen in the unmetallated dendrimers. This trend indicated that the presence of zinc helped to further prevent aggregation and that the larger dendrimers performed better than the small ones, with t-butyl substitution being better than no peripheral substitution. The utilization of fluorescence was successful in further understanding the properties of aggregation for the octasubstituted Pcs. There was definite agreement in the data obtained with the same zinc Pcs using both UV-Vis absorption and fluorescence, and there was certain indication that the presence of the dendrons in unmetallated Pcs acted to
transfer energy to the Pc core. Finally, the use of Stern-Volmer plots helped to show that the environment surrounding the Pc core acts as a shield, preventing the approach of the different fluorescence quenchers that were used.

2.8 Summary of results

A series of octasubstituted Pcs was synthesized using a hydroquinone linker to attach the dendron to the Pc. Different substituents on the periphery of the dendrimer gave two groups of Pcs, the unsubstituted and the \( t \)-butyl Fréchet-type octasubstituted dendritic Pcs. The introduction of a metal ion into the core of the Pc was also successful, resulting in the zinc derivatives of each of the octasubstituted Pcs.

Studies involving the unmetallated Pcs were performed to look at the effect of the dendrons on the overall size of the Pc, as well as the presence of the eight dendritic arms in preventing aggregation of the cores. GPC data indicated that there was a significant change in size between the lower generations that decreased with respect to the two largest generations. Aggregation studies were performed in DCM with increasing amounts of ethanol, as well as a few other solvents which showed that there were some solvents that tended to induce aggregation and some that helped to prevent it. Clear trends with respect to dendritic size and substitution were also seen. Thin films studies indicated that the presence of the dendrons prevented aggregation in the largest generations studied in the solid state.

When zinc Pcs were investigated, many of the same studies that were performed on the unmetallated Pcs were used. Similar trends were seen in the experiments
performed with DCM-EtOH mixtures; however the presence of the zinc ion helped to further prevent aggregation. The coordination of ethanol to zinc further minimized aggregation, resulting in the absorbances of some of the ethanolic solutions being greater than in 100% DCM. Therefore, it was necessary to alter the protocol for this experiment with the addition of a small amount of pyridine. The most pertinent data though was the aggregation activity of the zinc Pcs in the solid state. Much like the unmetallated Pcs, thin film studies showed that the largest generation again showed no signs of the presence of aggregates.

Further work was done to study the effect that the presence of dendrons had on the thermodynamic properties of the Pcs. While two methods were introduced to determine of the equilibrium constant involved in aggregation, it became clear that one method was better suited to use with these particular Pcs. The use of the monomer-dimer method was chosen over the Tai-Hayashi method because the values obtained within aggregating solvents agreed more with the observed trends. The change in the dielectric constant was then investigated to try to see if there were any strong electrostatic forces which influenced the self-associations of the Pc cores. While both the electrostatic and nonelectrostatic energy did not alter greatly between the generations studied, the influence of the dielectric constant on the ability of the Pc to favor aggregation was clear. Further studies examined the difference between an aggregating Pc (35) and a nonaggregating Pc (38) with respect to the values of entropy and enthalpy. The results found that difference in aggregation between the two dendritic compounds was an entropically driven process. Finally, comparisons were drawn between the aggregation
activity with respect to both size and substitution. The trends in the $K_D$ values showed that the ability to prevent aggregation increased with respect to size, and that the presence of the $t$-butyl groups was better at halting self-association of the Pc cores.

The last set of experiments involved the zinc Pcs. Much like their unmetallated counterparts, there were trends in the ability to hinder aggregation based on both size and peripheral substitution. While the onset of aggregation happened at higher concentrations of ethanol, the trends illustrated by the comparison of dimerization constants were somewhat similar. The $t$-butyl Pcs once again were better at halting aggregation; however the mid-generation Pc showed the greatest amount of aggregation when compounds with similar substitution were compared. The comparison between the data obtained from fluorescence and UV-Vis absorption showed no real differences between the trends of data. Another observation was that with the excitation of the dendrons, moderate emission was seen in the Pc indicating energy transfer between the periphery and the core. The final experiment looked at the use of Stern-Volmer plots to probe the Pc structure in solution. The results indicated that for both of the quenchers used, anthraquinone and TPP, the approach to the Pc core was hindered resulting in rather low $K_{sv}$ values and showing that the dendrons act like a shield while in solution.

2.9 Future directions

Further investigation into the use of eight dendritic arms is necessary to see if aggregation can be prevented in both solution and the solid state. The introduction of charged water-soluble groups may be effective, since Ng has shown that a degree of
aggregation can be prevented with the use of four dendritic arms. These types of PCs may also be used to construct charged multilayers for device applications in a fashion similar to that reported by Rubner and Hammond. Also, the introduction of rigid aryl-alkynyl dendritic arms using procedures introduced by Leznoff and Moore should be performed and their effect on both the overall molecular size and prevention of aggregation be thoroughly investigated.

Another modification that would be useful in drawing closer comparisons with the tetrasubstituted dendritic PCs would be the replacement of the hydroquinone linker with a phloroglucinol one. Using this trihydroxyl linker, the branching of the dendrons would be situated closer to the core. This would enable comparisons to be drawn and the effect of the linker could be elucidated. Substitution in the α-position (2,5) of the Pc should also be examined at to see if the effect in preventing aggregation is as drastic as the effect reported by Shirk and coworkers.

Expanding the use of these compounds towards other applications could be performed by using other metal ions. Magnesium could be used to investigate applications involving artificial photosynthetic centers. Indium and rare earth metals could be examined for comparison in optical limiting applications. Iron could be used to study electron transport in a synthetic environment. And another use of the zinc PCs would be for applications where their utility would provide a means of photodynamic therapy for the treatment of cancer.

Finally, the investigation of the ability for each of the PCs to act as optical limiters needs to be pursued. Measurements of the transient absorption data and quantum yields
in solution need to be done and compared to values obtained from the solid state. Laser measurements would also need to be performed in both solution and the solid state. These values should then be compared to published results to determine the effectiveness of the Pcs as optical limiters.
2.10 Experimental section

NMR spectra were recorded on either a Bruker 250 MHz or 500 MHz NMR spectrometer. Chemical shifts are reported in ppm (δ) referenced to internal residual solvent protons (1H). 13C NMR spectra were recorded as proton-decoupled spectra. Electro spray ionization (ESI), fast atom bombardment (FAB), and matrix assisted laser desorption ionization (MALDI) mass spectra were performed at the University of Arizona Mass Spectrometry Facilities. All chemicals were purchased from commercial suppliers and used as received. THF was distilled from benzophenone and potassium metal. Toluene was distilled from calcium hydride. Flash chromatography using silica (Natland International Corp., silica gel 200-400 Mesh) was performed by the method of Still et al. Gel permeation chromatography (GPC) was done using a Shimadzu HPLC system (LS-10AT pump, RID-6A refractive index detector) with DCM as the eluent at ambient temperature (21°C). The flow rate was 1 ml/min through three 250x10 mm Jordi DVB columns of 10^4, 10^3, and 500 Angstrom pore size. Preparatory GPC was done on a 500x30mm Jordi gel DVB mixed bed column at a flow rate of 10 ml/min. Analytical thin-layer chromatography (TLC) was performed on precoated TLC plates (Merck precoated 0.25 mm silica gel 60 F254 plates). The synthesis of the [Gn]-Br dendrons, 4,5-bis-(4-hydroxy-phenoxy)-phthalonitrile (20), 3,5-di-tert-butylbenzoic acid (25), 3,5-di-tert-butylbenzyl alcohol (26), 3,5-di-tert-butyl [Gn]-Br dendrons, 4-nitrophthalonitrile (41), and 3,5-ethyl isophthalate [Gn]-Br dendrons were performed according to published procedures.
Spectroscopic Measurements. All spectroscopic measurements were performed on spectrophotometric grade solvents (Aldrich). UV-Visible spectra were recorded on a Shimadzu UV-2401Pc spectrophotometer and temperature measurements were done with the attached Shimadzu CPS-Controller. Corrected fluorescence spectra were collected on a Spex Fluorolog-2 spectrophotometer.

1-Bromomethyl-3,5-di-tert-butyl-benzene (27). Compound 27 was prepared as follows: to a solution of 26 (3.80 g, 17.3 mmol) in a minimum amount of dry THF was added triphenylphosphine (5.45 g, 20.8 mmol) and carbon tetrabromide (8.61 g, 26.0 mmol). Additional portions of CBr₄ and PPh₃ were added as necessary until the reaction mixture turned a dark yellow. The reaction was poured into water immediately after the color change and extracted with CH₂Cl₂ (3 x 50 mL). The combined extracts were dried (MgSO₄), filtered, and evaporated to dryness to give a colorless, powdery residue. Purification by flash chromatography (SiO₂, 1:1 hexanes/EtOAc) gave the product as a fluffy, colorless powder (2.98 g, 61%): ¹H NMR (250 MHz, CDCl₃) δ 7.24-7.26 (m, 3 H), 4.53 (s, 2 H), 1.32 (s, 18 H).

General procedure for the preparation of dinitriles
Potassium carbonate (10 equiv.), 20 (1 equiv.), 18-crown-6 (0.2 equiv.) and the dendritic bromide (2 equiv.) were stirred at an elevated temperature for 2 d. The reaction mixture was cooled, and the solvent removed in vacuo. The residue was partitioned between a mixture of DCM and water (1:1, 50 mL) and the aqueous layer was extracted with DCM
(3 x 25 mL). The combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness. The crude product was purified by flash column chromatography (SiO₂, CH₂Cl₂) to give a colorless foam.

4,5-Bis(4-[G1]-phenoxy)phthalonitrile (21). According to the general procedure, [G1]-Br (0.12 g, 0.3 mmol), 20 (50 mg, 0.15 mmol), potassium carbonate (0.21 g, 1.5 mmol), and 18-crown-6 (4 mg, 0.02 mmol) in acetone (10 mL) at reflux gave 21. Yield: 121 mg (87%): ¹H NMR (250 MHz, CDCl₃) δ 7.47-7.25 (m, 20 H), 7.05 (s, 2 H), 7.01 (s, 8 H), 6.69-6.68 (d, J = 2.3 Hz, 4 H), 6.59-6.57 (t, J = 2.2 Hz, 2 H), 5.03 (s, 8 H), 5.00 (s, 4 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 160.25, 156.65, 152.40, 147.33, 138.96, 136.70, 128.61, 128.06, 127.55, 121.45, 120.64, 116.60, 115.56, 106.42, 104.32, 101.63, 70.49, 70.16; MS (FAB) m/z 949.35 (M⁺).

4,5-Bis(4-[G2]-phenoxy)phthalonitrile (22). By using the general procedure, [G2]-Br (0.12 g, 0.15 mmol), 20 (25 mg, 0.07 mmol), potassium carbonate (0.1 g, 0.75 mmol), and 18-crown-6 (2 mg, 0.01 mmol) in acetone (10 mL) at reflux gave 22. Yield: 97 mg (74%): ¹H NMR (250 MHz, CDCl₃) δ 7.48-7.19 (m, 40 H), 7.03 (s, 2 H), 7.00 (s, 8 H), 6.68-6.63 (m, 12 H), 6.58-6.54 (m, 6 H), 5.01 (s, 16 H), 4.99 (s, 4 H), 4.97 (s, 8 H); ¹³C NMR (125.7 MHz, CDCl₃) δ 160.17, 160.11, 156.63, 152.36, 147.30, 139.14, 138.94, 136.72, 128.60, 128.02, 127.55, 121.44, 120.60, 116.59, 115.12, 109.74, 106.45, 106.41, 101.67, 101.56, 70.47, 70.12, 70.02; MS (FAB) m/z 1798.69 (M⁺).
4,5-Bis(4-[G3]-phenoxy)phthalonitrile (23). According to the general procedure, [G3]-Br (0.25 g, 0.15 mmol), 20 (25 mg, 0.07 mmol), potassium carbonate (0.1 g, 0.75 mmol), and 18-crown-6 (2 mg, 0.01 mmol) in acetone (10 mL) at reflux gave 23. Yield: 171 mg (67%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 7.52-7.13 (m, 80 H), 7.01 (s, 2 H), 6.97 (s, 8 H), 6.68-6.61 (m, 28 H), 6.59-6.51 (m, 14 H), 4.99 (s, 32 H), 4.95 (s, 12 H), 4.93 (s, 16 H); $^{13}$C NMR (125.7 MHz, CDCl$_3$) $\delta$ 160.15, 160.13, 160.06, 156.61, 152.32, 147.25, 139.17, 139.13, 138.82, 136.74, 128.56, 127.98, 127.53, 121.44, 120.34, 116.54, 115.22, 109.71, 106.44, 106.38, 106.36, 102.12, 101.59, 101.57, 70.42, 70.08, 70.02, 69.98; MS (MALDI) m/z 3534.32 (M + K$^+$$)$.

4,5-Bis(4-((m-r-Bu)$_2$-[G0])-phenoxy)phthalonitrile (28). According to the general procedure, (m-r-Bu)$_2$-[G0]-Br (0.5 g, 1.8 mmol), 20 (0.3 g, 0.85 mmol), potassium carbonate (0.52 g, 3.8 mmol), and 18-crown-6 (45 mg, 0.17 mmol) in acetone (25 mL) at reflux gave 28. Yield: 551 mg (87%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 7.42-7.41 (m, 2 H), 7.28-7.27 (m, 4 H), 7.06 (s, 8 H), 7.04 (s, 2 H), 5.04 (s, 4 H), 1.33 (s, 36 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 157.05, 152.49, 151.19, 147.11, 135.34, 122.42, 122.23, 121.52, 120.41, 116.53, 115.16, 109.67, 71.45, 34.88, 31.44; MS (MALDI) m/z 748.40 (M$^+$).

4,5-Bis(4-((m-r-Bu)$_4$-[G1])-phenoxy)phthalonitrile (29). According to the general procedure, (m-r-Bu)$_4$-[G1]-Br (1.8 g, 1.1 mmol), 20 (0.3 g, 0.85 mmol), potassium carbonate (0.69 g, 5.0 mmol), and 18-crown-6 (45 mg, 0.17 mmol) in acetone (25 mL) at
reflux gave 29. Yield: 721 mg (59%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 7.41-7.40 (m, 4 H), 7.28-7.27 (m, 8 H), 7.07 (s, 2 H), 7.04 (s, 8 H), 6.74-6.73 (m, 4 H), 6.67-6.65 (m, 2 H), 5.03 (s, 4 H), 5.01 (s, 8 H), 1.33 (s, 72 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 160.50, 156.75, 152.42, 151.08, 147.28, 138.80, 135.59, 122.32, 122.27, 121.48, 120.55, 116.60, 115.41, 109.74, 106.45, 101.57, 71.06, 70.62, 34.86, 31.45; MS (ESI) $m/z$ 1419.52 (M + Na$^+$).

$4,5$-Bis(4-((m- Bu)$_8$-[G2])-phenoxy)phthalonitrile (30). According to the general procedure, (m- Bu)$_8$-[G2]-Br (2.3 g, 1.8 mmol), 20 (0.31 g, 0.87 mmol), potassium carbonate (0.69 g, 5.0 mmol), and 18-crown-6 (45 mg, 0.17 mmol) in acetone (25 mL) at reflux gave 30. Yield: 1.73 g (74%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.40 (bs, 8 H), 7.28 (bs, 16 H), 7.05 (s, 2 H), 7.03 (s, 8 H), 6.74 (bs, 8 H), 6.72 (bs, 4 H), 6.65 (bs, 4 H), 6.62 (bs, 2 H), 5.02 (bs, 12 H), 5.01 (s, 16 H), 1.33 (s, 144 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 160.46, 160.27, 156.75, 152.43, 151.06, 147.22, 138.97, 138.92, 135.67, 122.31, 122.30, 121.59, 120.35, 116.59, 115.16, 109.70, 106.49, 106.48, 101.69, 101.55, 71.06, 70.52, 70.19, 34.87, 31.48; MS (ESI) $m/z$ 2716.44 (M + Na$^+$).

$4,5$-Bis(4-((m-CO$_2$Et)$_2$-[G0])-phenoxy)phthalonitrile (31). According to the general procedure, (m-CO$_2$Et)$_2$-[G0]-Br (0.63 g, 2.0 mmol), 20 (0.33 g, 1.0 mmol), potassium carbonate (0.55 g, 4.0 mmol), and 18-crown-6 (53 mg, 0.2 mmol) in acetone (25 mL) at reflux gave 31. Yield: 431 mg (56%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.65-8.64 (m, 2 H), 8.31-8.30 (m, 4 H), 7.06 (s, 2 H), 7.05 (s, 8 H), 5.15 (s, 4 H), 4.54-4.37 (q, $J = 7.1$ Hz,
8 H), 1.44-1.38 (t, J = 7.3 Hz, 12 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) δ 165.57, 156.32, 147.62, 137.49, 132.60, 131.45, 130.35, 121.54, 121.49, 120.73, 117.10, 116.61, 115.08, 69.58, 61.53, 14.32; MS (FAB) m/z 813.08 (M$^+$).

4,5-Bis(4-((m-CO$_2$Et)$_4$-[G1])-phenoxy)phthalonitrile (32). According to the general procedure, (m-CO$_2$Et)$_4$-[G1]-Br (0.6 g, 0.91 mmol), 20 (0.16 g, 0.45 mmol), potassium carbonate (0.28 g, 2.0 mmol), and 18-crown-6 (0.1 g, 0.41 mmol) in acetone (10 mL), reacted at 40°C gave 32. Yield: 423 mg (62%): $^1$H NMR (500 MHz, CDCl$_3$) δ 8.64-8.63 (m, 4 H), 8.29-8.28 (m, 8 H), 7.06-7.02 (m, 10 H), 6.72-6.72 (m, 4 H), 6.61-6.60 (m, 2 H), 5.13 (s, 8 H), 5.02 (s, 4 H), 4.42-4.38 (q, J = 7.2 Hz, 16 H), 1.42-1.39 (t, J = 7.2 Hz, 24 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) δ 165.59, 159.88, 156.62, 152.31, 147.43, 139.30, 137.62, 132.57, 131.37, 130.26, 121.52, 120.37, 116.59, 115.12, 109.76, 106.64, 101.70, 70.35, 69.16, 61.48, 14.32; MS (ESI) m/z 1525.50 (M$^+$).

4,5-Bis(4-((m-CO$_2$Et)$_8$-[G2])-phenoxy)phthalonitrile (33). According to the general procedure, (m-CO$_2$Et)$_8$-[G2]-Br (0.5 g, 1.8 mmol), 20 (0.3 g, 0.85 mmol), potassium carbonate (0.52 g, 3.8 mmol), and 18-crown-6 (45 mg, 0.17 mmol) in THF (25 mL) at reflux gave 33. Yield: 551 mg (87%): $^1$H NMR (250 MHz, CDCl$_3$) δ 8.62-8.60 (m, 8 H), 8.28-8.27 (m, 16 H), 7.03-7.01 (m, 10 H), 6.71-6.68 (m, 12 H), 6.59-6.55 (m, 6 H), 5.11 (s, 16 H), 5.00 (s, 12 H), 4.43-4.34 (q, J = 7.1 Hz, 32 H), 1.42-1.36 (t, J = 7.1 Hz, 48 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) δ 165.56, 160.09, 159.82, 156.71, 152.37, 147.21, 139.47, 139.02, 137.67, 132.55, 131.34, 130.21, 121.59, 120.32, 116.56, 115.13, 109.66,
106.59, 106.46, 101.61, 70.44, 69.88, 69.12, 61.45, 14.31; MS (MALDI) m/z 2990.71 (M + Na⁺).

**4-[G2]-Phenol (40).** Hydroquinone (0.66 g, 6 mmol), [G2]-Br (1.0 g, 1.2 mmol), potassium carbonate (2.1 g, 15 mmol), and 18-crown-6 (63 mg, 0.24 mmol) were stirred in acetone (40 mL) at reflux for 2 d. The reaction mixture was cooled, and the solvent removed *in vacuo*. The residue was partitioned between a mixture of DCM and water (1:1, 50 mL) and the aqueous layer was extracted with DCM (3 x 25 mL). The combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness. The crude product was purified by flash column chromatography (SiO₂, CH₂Cl₂) to give 40 as a colorless foam. Yield: 500 mg (48%): ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.30 (m, 20 H), 6.81-6.79 (d, J = 9.0 Hz, 2 H), 6.70-6.68 (d, J = 8.9 Hz, 2 H), 6.66-6.65 (d, J = 2.2 Hz, 4 H), 6.63-6.62 (d, J = 2.1 Hz, 2 H), 6.56-6.55 (t, J = 2.2 Hz, 2 H), 6.52-6.51 (t, J = 2.1 Hz, 1 H), 5.01 (s, 8 H), 4.95 (s, 4 H), 4.91 (s, 2 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 160.15, 160.00, 149.62, 146.51, 139.77, 139.24, 136.75, 128.58, 127.99, 127.55, 116.05, 116.02, 106.36, 106.33, 101.58, 101.53, 70.63, 70.10, 69.96; MS (FAB) m/z 837.16 (M⁺).

**4-(4-[G2]-Phenoxy)phthalonitrile (42).** 4-Nitrophthalonitrile (0.12 g, 0.7 mmol), 40 (0.45 g, 0.54 mmol), and potassium carbonate (0.1 g, 0.7 mmol) were stirred in dry DMF (10 mL) under Ar and at 60°C for 2 d. The reaction mixture was cooled and poured into 100 mL cold water. The resulting cloudy solution was extracted with DCM (3 x 30 mL). The combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness.
The crude product was purified by flash column chromatography (SiO₂, CH₂Cl₂) to give 42 as an off-white foam. Yield: 319 mg (62%): ¹H NMR (500 MHz, CDCl₃) δ 7.66-7.64 (d, J = 8.7 Hz, 1 H), 7.39-7.25 (m, 20 H), 7.21-7.20 (d, J = 2.5 Hz, 1 H), 7.16-7.14 (dd, J = 2.5 Hz, 8.7 Hz, 1 H), 6.99-6.93 (m, 4 H), 6.66-6.65 (d, J = 2.2 Hz, 2 H), 6.65-6.64 (d, J = 2.1 Hz, 2 H), 6.56-6.55 (t, J = 2.2 Hz, 2 H), 6.54-6.53 (t, J = 2.1 Hz, 1 H), 5.01 (s, 8 H), 4.99 (s, 2 H), 4.97 (s, 4 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 160.18, 160.12, 156.72, 147.12, 139.12, 139.04, 136.69, 135.30, 133.61, 128.58, 128.02, 127.52, 121.77, 121.05, 120.85, 116.63, 116.05, 106.38, 106.36, 101.51, 101.50, 70.41, 70.11, 70.00; MS (ESI) m/z 985.43 (M + Na⁺).

General procedure for the cyclization of dinitriles

To the dinitrile (4 equiv.), was added 1-pentanol and the mixture was heated to reflux under Ar. Lithium bromide (2 equiv.), and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) (10 equiv.) for 34 and 35, or lithium metal (20 equiv.) for 36-39 and 43 was added and the reaction was allowed to proceed for 24 h. The mixture was cooled to 0°C and the solvent decanted. The crude product was precipitated from DCM by addition of hexanes and purified by flash column chromatography (SiO₂, CH₂Cl₂) giving a dark green solid.

[2,3,9,10,16,17,23,24-Octakis(4-[G1]-phenoxy)phthalocyanine (34). By using the general procedure, dinitrile 21 (0.5 g, 0.53 mmol), lithium bromide (0.02 mg, 0.26 mmol), and DBU (0.20 mg, 1.3 mmol) in 1-pentanol (25 mL) gave 34. Yield: 140 mg (27%): ¹H NMR (500 MHz, CDCl₃) δ 8.91 (s, 2 H), 7.42-7.21 (br m, 104 H), 6.98-6.96
(d, J = 8.5 Hz, 16 H), 6.66 (s, 16 H), 6.52 (s, 8 H), 4.93 (s, 32 H), 4.90 (s, 16 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) δ 160.25, 156.65, 147.30, 139.14, 138.94, 136.71, 128.61, 128.06, 127.55, 127.52, 121.45, 120.64, 118.24, 116.60, 108.21, 106.42, 101.63, 70.49, 70.16, 70.02; MS (MALDI) m/z 3798.39 (M$^+$).

**[2,3,9,10,16,17,23,24-Octakis(4-[G2]-phenoxy)phthalocyanine (35).** According to the general procedure, dinitrile 22 (0.35 g, 0.19 mmol), lithium bromide (0.01 mg, 0.10 mmol), and DBU (0.08 mg, 0.50 mmol) in 1-pentanol (10 mL) gave 35. Yield: 77 mg (22%): $^1$H NMR (500 MHz, CDCl$_3$) δ 8.89 (s, 2 H), 7.31-7.18 (m, 168 H), 7.17-7.15 (d, J = 9 Hz, 16 H), 7.00-6.99 (d, J = 9 Hz, 16 H), 6.68-6.65 (m, 16 H), 6.60-6.57 (m, 32 H), 6.52-6.48 (m, 8 H), 6.47-6.44 (m, 16 H), 4.95 (s, 16 H), 4.88 (s, 64 H), 4.86 (s, 32 H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 160.26, 160.15, 156.65, 152.17, 147.32, 139.14, 138.94, 136.72, 128.61, 128.06, 127.55, 127.52, 121.45, 120.64, 118.21, 116.60, 109.74, 108.21, 106.42, 101.63, 101.59, 70.49, 70.17; MS (MALDI) m/z 7194.74 (M$^+$).

**[2,3,9,10,16,17,23,24-Octakis(4-[G3]-phenoxy)phthalocyanine (36).** By using the general procedure, dinitrile 23 (0.2 g, 0.05 mmol) and lithium metal (7 mg, 1 mmol) in 1-pentanol (5 mL) gave 36, which was further purified by preparatory gel permeation chromatography using DCM as the eluent. Yield: 32 mg (16%): $^1$H NMR (500 MHz, CDCl$_3$) δ 8.85 (s, 2 H), 7.40-7.12 (m, 344 H), 6.95-6.93 (d, J = 9 Hz, 16 H), 6.68-6.62 (m, 24 H), 6.59-6.52 (m, 96 H), 6.44-6.39 (m, 48 H), 4.89 (s, 16 H), 4.82 (s, 128 H), 4.79 (s, 32 H), 4.75 (s, 64 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) δ 160.26, 160.14, 160.06, 156.61,
152.21, 147.25, 139.17, 139.13, 138.82, 136.74, 128.56, 127.57, 127.53, 121.44, 120.34,
118.24, 116.57, 109.71, 108.25, 106.38, 106.36, 101.65, 101.59, 101.57, 70.42, 70.08,
70.02, 69.98; MS (MALDI) m/z 13983.21 (M+).

[2,3,9,10,16,17,23,24-Octakis(4-((m-t-Bu)4-[G0])-phenoxy)phthalocyanine (37).] By
using the general procedure, dinitrile 28 (0.25 g, 0.33 mmol) and lithium metal (46 mg,
6.6 mmol) in 1-pentanol (10 mL) gave 37, which was further purified by preparatory gel
permeation chromatography using DCM as the eluent. Yield: 64 mg (26%): ¹H NMR
(500 MHz, CDCl₃) δ 8.79 (s, 2 H), 7.42-7.41 (m, 8 H), 7.28-7.27 (m, 24 H), 6.62 (s, 32
H), 4.92 (s, 16 H), 1.28 (s, 144 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 154.03, 151.49,
149.19, 147.11, 137.34, 121.52, 120.41, 118.42, 116.53, 115.16, 114.23, 109.67, 70.43,
34.76, 31.41; MS (MALDI) m/z 2998.52 (M+).

[2,3,9,10,16,17,23,24-Octakis(4-((m-t-Bu)4-[G1])-phenoxy)phthalocyanine (38).] By
using the general procedure, dinitrile 29 (0.25 g, 0.18 mmol) and lithium metal (25 mg,
3.6 mmol) in 1-pentanol (10 mL) gave 38, which was further purified by preparatory gel
permeation chromatography using DCM as the eluent. Yield: 58 mg (23%): ¹H NMR
(500 MHz, CDCl₃) δ 8.85 (s, 2 H), 7.41-7.40 (m, 16 H), 7.28-7.27 (m, 32 H), 6.74-6.73
(m, 16 H), 6.67-6.60 (m, 48 H), 4.93 (s, 16 H), 4.91 (s, 32 H), 1.28 (s, 288 H); ¹³C NMR
(62.9 MHz, CDCl₃) δ 160.49, 154.05, 151.42, 149.18, 147.11, 137.34, 135.59, 121.52,
120.41, 118.42, 116.58, 115.16, 114.27, 109.74, 106.45, 101.57, 71.06, 70.52, 34.76,
31.45; MS (MALDI) m/z 5594.92 (M+).
[2,3,9,10,16,17,23,24-Octakis(4-((m-t-Bu)_8-[G2])-phenoxy)phthalocyanine (39). By using the general procedure, dinitrile 30 (0.5 g, 0.19 mmol) and lithium metal (26 mg, 3.8 mmol) in 1-pentanol (10 mL) gave 39, which was further purified by preparatory gel permeation chromatography using DCM as the eluent. Yield: 90 mg (18%): ^1^H NMR (500 MHz, CDCl₃) δ 8.87 (s, 2 H), 7.40 (bs, 32 H), 7.28 (bs, 64 H), 6.74-6.62 (br m, 112 H), 4.92 (s, 48 H), 4.91 (s, 64 H), 1.28 (s, 576 H); ^1^3^C NMR (62.9 MHz, CDCl₃) δ 160.46, 160.27, 154.05, 151.43, 149.16, 147.12, 138.97, 137.32, 135.57, 121.59, 120.35, 118.45, 116.59, 115.16, 114.23, 109.70, 106.49, 106.48, 101.69, 101.55, 71.06, 70.52, 70.19, 34.77, 31.48; MS (MALDI) m/z 10785.31 (M⁺).

[2,9(10),16(17),23(24)-Tetrakis(4-[G2]-phenoxy)phthalocyanine (43). By using the general procedure, dinitrile 42 (0.17 g, 0.17 mmol) and lithium metal (24 mg, 3.4 mmol) in 1-pentanol (5 mL) gave 43, which was further purified by preparatory gel permeation chromatography using DCM as the eluent. Yield: 43 mg (25%): ^1^H NMR (500 MHz, CDCl₃) δ 8.91 (s, 2 H), 7.39-7.14 (br m, 92 H), 6.66-6.53 (br m, 36 H), 4.91 (s, 32 H), 4.89 (s, 8 H), 4.87 (s, 8 H); ^1^3^C NMR (62.9 MHz, CDCl₃) δ 160.18, 160.12, 154.02, 147.12, 139.12, 139.04, 136.69, 135.30, 133.61, 128.58, 128.02, 127.52, 121.05, 120.85, 118.37, 116.63, 116.05, 106.38, 106.36, 101.51, 101.50, 70.41, 70.11, 70.00; MS (MALDI) m/z 3854.24 (M⁺).
**General procedure for the synthesis of zinc phthalocyanines**

Zinc acetate (1.1 equiv.) and the dendritic phthalocyanine (1 equiv.) were added to dry DMF and heated at 60°C overnight under argon. The reaction was cooled and poured into cold water and the desired compound was obtained by filtration, taken up in DCM, dried (MgSO₄), concentrated and evaporated to dryness.

[2,3,9,10,16,17,23,24-Octakis(4-[G1]-phenoxy)zinc phthalocyanine (44).]  By following the generalized procedure, zinc acetate (7.0 mg, 0.03 mmol) and 34 (0.1 g, 0.03 mmol) in dry DMF (10 mL) gave 44, as a dark green solid. Yield: 5.5 mg (78%): ¹H NMR (500 MHz, CDCl₃) 8: 8.56 (s, 8 H), 7.45-7.27 (br m, 96 H), 6.98-6.96 (d, J = 8.5 Hz, 16 H), 6.64 (s, 16 H), 6.57 (s, 8 H), 4.91 (s, 32 H), 4.89 (s, 16 H); ¹³C NMR (62.9 MHz, CDCl₃) δ: 160.25, 156.65, 149.37, 142.34, 138.94, 136.74, 128.51, 128.26, 127.55, 127.52, 121.45, 120.44, 118.24, 116.66, 108.21, 106.42, 101.63, 79.49, 70.16, 70.02; MS (ESI) m/z 3861.76 (M⁺).

[2,3,9,10,16,17,23,24-Octakis(4-[G2]-phenoxy)zinc phthalocyanine (45).]  By following the generalized procedure, zinc acetate (7.0 mg, 0.03 mmol) and 34 (0.1 g, 0.03 mmol) in dry DMF (10 mL) gave 45, as a dark green solid. Yield: 2.4 mg (72%): ¹H NMR (500 MHz, CDCl₃) 8: 8.54 (s, 8 H), 7.45-7.24 (br m, 96 H), 6.98-6.96 (d, J = 9 Hz, 16 H), 7.00-6.98 (d, J = 9 Hz, 16 H), 6.69-6.65 (m, 16 H), 6.60-6.56 (m, 32 H), 6.52-6.47 (m, 8 H), 6.45-6.43 (m, 16 H), 4.93 (s, 16 H), 4.87 (s, 64 H), 4.85 (s, 32 H); ¹³C NMR (62.9 MHz, CDCl₃) δ: 160.26, 160.15, 156.65, 152.17, 149.32, 142.33, 138.94,
136.72, 128.61, 128.06, 127.56, 127.51, 121.45, 120.64, 118.21, 116.64, 109.74, 108.21, 106.52, 101.63, 101.57, 70.49, 70.17; MS (MALDI) m/z 7258.90 (M⁺).

[2,3,9,10,16,17,23,24-Octakis(4-[G3]-phenoxy)zinc phthalocyanine (46). By following the generalized procedure, zinc acetate (3.3 mg, 0.02 mmol) and 36 (0.11 g, 0.02 mmol) in dry DMF (10 mL) gave 46, as a dark green solid. Yield: 2.7 mg (83%): ¹H NMR (500 MHz, CDCl₃) δ 8.52 (s, 8 H), 7.42-7.14 (m, 336 H), 6.97-6.94 (d, J = 9 Hz, 16 H), 6.65-6.59 (m, 24 H), 6.57-6.51 (m, 96 H), 6.42-6.36 (m, 48 H), 4.91 (s, 16 H), 4.85 (s, 128 H), 4.81 (s, 32 H), 4.79 (s, 64 H); ¹³C NMR (125 MHz, CDCl₃) δ 160.26, 160.14, 160.06, 156.61, 152.21, 149.25, 142.17, 139.18, 138.82, 136.79, 128.66, 127.59, 127.53, 121.44, 120.34, 118.24, 116.57, 109.71, 108.45, 106.38, 106.36, 101.63, 101.59, 101.57, 70.42, 70.28, 70.02, 69.98; MS (MALDI) m/z 14050.32 (M⁺).

[2,3,9,10,16,17,23,24-Octakis(4-((m-r-Bu)₂-[G0])-phenoxy)zinc phthalocyanine (47). By following the generalized procedure, zinc acetate (3.3 mg, 0.02 mmol) and 37 (0.11 g, 0.02 mmol) in dry DMF (10 mL) gave 47, as a dark green solid. Yield: 3.1 mg (94%): ¹H NMR (500 MHz, CDCl₃) δ 8.51 (s, 8 H), 7.41-7.40 (m, 8 H), 7.41-7.35 (m, 16 H), 6.59 (s, 32 H), 4.97 (s, 16 H), 1.29 (s, 144 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 154.03, 151.49, 149.19, 149.11, 142.34, 121.56, 120.37, 118.22, 116.53, 115.16, 114.29, 109.61, 101.59, 70.43, 34.76, 31.41; MS (MALDI) m/z 3060.39 (M⁺).
[2,3,9,10,16,17,23,24-Octakis(4-((m-t-Bu)₈-[G1])-phenoxy)zinc phthalocyanine (48).]

By following the generalized procedure, zinc acetate (3.3 mg, 0.02 mmol) and 38 (0.11 g, 0.02 mmol) in dry DMF (10 mL) gave 48, as a dark green solid. Yield: 2.9 mg (87%):

$^1$H NMR (500 MHz, CDCl₃) δ 8.55 (s, 8 H), 7.41-7.38 (m, 16 H), 7.28-7.25 (m, 24 H), 6.77-6.73 (m, 16 H), 6.67-6.58 (m, 48 H), 4.95 (s, 16 H), 4.93 (s, 32 H), 1.29 (s, 288 H);

$^{13}$C NMR (62.9 MHz, CDCl₃) δ 160.49, 154.05, 151.42, 149.18, 149.12, 142.37, 135.51, 121.52, 120.41, 118.41, 116.38, 115.11, 114.27, 109.74, 106.42, 101.58, 71.01, 70.32, 34.71, 31.55; MS (MALDI) m/z 5656.10 (M+).

[2,3,9,10,16,17,23,24-Octakis(4-((m-t-Bu)₈-[G2])-phenoxy)zinc phthalocyanine (49).]

By following the generalized procedure, zinc acetate (3.3 mg, 0.02 mmol) and 39 (0.11 g, 0.02 mmol) in dry DMF (10 mL) gave 49, as a dark green solid. Yield: 2.7 mg (81%):

$^1$H NMR (500 MHz, CDCl₃) δ 8.57 (s, 2 H), 7.42 (bs, 32 H), 7.21 (bs, 56 H), 6.71-6.60 (br m, 112 H), 4.97 (s, 48 H), 4.92 (s, 64 H), 1.29 (s, 576 H);

$^{13}$C NMR (62.9 MHz, CDCl₃) δ 160.46, 160.27, 154.07, 151.43, 149.16, 149.10, 142.31, 138.97, 135.57, 121.59, 120.30, 118.45, 116.57, 115.26, 114.27, 109.70, 106.44, 106.41, 101.69, 101.57, 71.16, 70.72, 70.49, 34.78, 31.58; MS (MALDI) m/z 10848.67 (M+).

[2,9(10),16(17),23(24)-Tetrakis(4-[G2]-phenoxy)zinc phthalocyanine (50). By

following the generalized procedure, zinc acetate (3.3 mg, 0.02 mmol) and 43 (0.11 g, 0.02 mmol) in dry DMF (10 mL) gave 50, as a dark green solid. Yield: 2.9 mg (89%):

$^1$H NMR (500 MHz, CDCl₃) δ 8.51 (s, 8 H), 7.38-7.17 (br m, 84 H), 6.67-6.56 (br m, 36
H), 4.95 (s, 32 H), 4.93 (s, 8 H), 4.90 (s, 8 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 160.18, 160.14, 154.22, 149.12, 142.12, 139.14, 136.71, 135.38, 133.61, 128.51, 128.02, 127.56, 121.15, 120.83, 118.37, 116.61, 116.25, 106.38, 106.36, 101.57, 101.50, 70.42, 70.21, 70.09; MS (MALDI) $m/z$ 3917.40 (M$^+$).
CHAPTER 3
SYNTHESIS AND STUDY OF WATER SOLUBLE BIS-STYRYL BENZENE
TWO PHOTON DYES

3.1 Introduction

Two-photon absorption (TPA) is a higher order nonlinear optical process whereby a material absorbs two low energy photons via virtual states (virtual energy levels located between the ground and excited states), to promote an electron from the ground state to the excited state. Relaxation from that excited state results in the emission of one photon which is approximately twice the energy of the incident photons (Figure 3.1). This process requires high peak power that is only available through pulsed lasers. Applications that utilize TPA have been limited because of both the high power needed and the lack of developed materials with high TPA cross sections. TPA cross sections ($\delta$) are defined as the product of two one-photon cross sections ($\sigma_i$, $\sigma_f$) and a term that is defined as the intermediate-state lifetime ($\tau_i$). The development of dyes with large cross sections is extremely important for new advancements in optics and photonics.

The advantages of TPA materials include the ability to achieve 3D spatial resolution. The rate of absorption of two photons depends quadratically on the intensity of the incoming laser light. When a tightly focused beam is used, the intensity is highest at the focus and decreases exponentially with distance from the focal plane. The rate of excitation then decreases by a factor of $(z^{-4})$ with distance from the focus and therefore, the excitation is confined in a small volume around the focus. Since the linear absorption
Figure 3.1  Illustration of the methods of TPA
of certain materials do not absorb in the wavelength range where TPA occurs, it becomes possible to excite compounds at greater depths that would prove possible with one-photon techniques. Additionally, since the wavelength used for two-photon excitation is roughly twice that for one-photon excitation, the influence of scattering on the beam intensity is reduced by a factor of 16 ($\lambda^4$).

These properties enable the use of TPA molecules in a number of different applications from optical limiting, to 3D fluorescence microscopy, to 3D microfabrication and optical data storage. This section will look at the use of TPA molecules in biomedical imaging; the properties of some of the materials with highest TPA cross section (bis-styrylbenzene TPA dyes); and a few of the published examples whereby the field of dendrimers have interfaced with the field of TPA dyes.

### 3.1.1 Two photon biomedical imaging

Conventional microscopy is limited in that the area imaged is only seen from the surface. The development of three dimensional techniques such as confocal and two-photon excitation fluorescence microscopy has helped open doors to seeing inside the body from all perspectives non-invasively.

Confocal fluorescence microscopy utilizes a laser excitation in the range of 360-650 nm which scans a fluorescently labeled sample. Both the reflected light and fluorescence emission is collected through the objective lens and passed to the detector. A confocal aperture, or pinhole, is placed in front of the detector to limit the amount of reflected light reaching the focal plane. The pinhole also prevents much of the unfocused
emitted light from reaching the detector, increasing the resolution of the instrument. In order to obtain three dimensional images, a series of optical scans are collected and stacked on top of one another digitally. The layout of the instrument is illustrated in Figure 3.2.

Two-photon excitation (TPE) microscopy uses a longer wavelength laser source which is focused upon the sample. The emitted light then passes back through the objective lens and is detected by a photomultiplier tube (Figure 3.3). Since there is no overlap between the excitation wavelength and the emission wavelength, an aperture is not needed to screen out reflected light. The lack of an aperture increases the fluorescence detection efficiency, increases the overall sensitivity, and allows for deeper penetration of light by enabling the detection of the emitted light that would be out-of-focus in a confocal system. Also, because there is a large wavelength difference between the excitation and emission, and the excitation volume is small any damage due to photobleaching is limited. Finally, seeing as biological tissues are being measured, the use of less harmful, lower energy light reduces photodamage to cells and is not as readily absorbed by tissue allowing for deeper penetration.

While both of these instruments have similar contrast mechanisms and give high signal to noise ratios, the only area where confocal microscopy surpasses TPE microscopy is in spatial resolution. Figure 3.4 shows a side by side comparison of pollen granules obtained by both confocal and TPE microscopy. It is clear that while the resolution on the confocal picture is better, the detail and depth of the TPE image is
Figure 3.2  Schematic representation of the confocal microscope\textsuperscript{3,5}
Figure 3.3  Schematic representation of a TPE microscope.\textsuperscript{3,6}
Figure 3.4  (a) Image of a pollen granule obtained by confocal laser scanning microscopy; (b) Same granule imaged by TPE microscopy\textsuperscript{3,7}
greater. Currently, medicine utilizes the confocal technique much more often because it is less expensive and more methods have been developed for its use. The cost of maintenance for a picosecond laser and the lack of dyes with high two-photon cross sections have prevented the TPE microscope from becoming the preferred instrument. It is the improvement in either of these areas that may lead to TPE becoming the instrument of choice in the future.

3.1.2 Utility of bis-styrylbenzene two-photon dyes

The dye that is most commonly used in the imaging of biomolecules, through both confocal and TPE microscopy is rhodamine B, 1 (Figure 3.5). This dye possesses a high solubility in water, is biocompatible, has a high two-photon cross section, and a high fluorescence quantum yield. However, if another dye could also have these properties as well as a higher two-photon cross section, better resolution or lower biological concentrations could be obtained.

In the pioneering work done by Albota et al. a new class of compounds was discovered to have large two-photon cross sections. These bis-styrylbenzene (BSB) derivatives 2-6 possessed motifs of different functional groups either on the periphery or attached to the central ring. These motifs can be classified by the type of functional groups involved. Placing donor groups such as Ph₂N and Et₂N at the para positions of the outside rings yields a D-π-D pattern (2). A group of acceptors such as CN para to one another on the center ring gives a D-A-D motif (3). The converse motif (A-D-A)
Figure 3.5  Structure of rhodamine B
has the acceptor (C_2(CN)₂) on the outer rings and the donor (OMe) in the center (4). Finally, a D-D-D pattern has N(n-Bu)₂ groups along the outside and OMe in the center (5). Figure 3.6 shows examples from each of these groups along with the fluorescence quantum yield in toluene (Φ) and the two-photon cross sections (δ). For reference, rhodamine B has a fluorescence quantum yield of 0.68 in 94% ethanol, ³⁹ and a two-photon cross section of 200x10⁻⁵⁰ cm⁴/s/photon-molecule.³¹⁰

There is an apparent connection between motif and an increase in the two-photon cross section.³¹¹ The bis-donor system itself increases the δ values. An increase in the conjugation length of the linker in molecules having the D-π-D motif leads to a linear increase in δ with phenylene-vinylene bridges having larger overall values than diphenylpolyene bridges. This growth in the cross-section value is thought to occur because the bis-donor system lowers the overall energy of the excited state.

The placement of the acceptor group on D-A-D molecules has also been looked at closely. Pond et al. found that the placement of a cyano group on either the vinylene bridge or the central phenyl ring greatly affected the overall one and two-photon properties of the molecule.³¹¹ They found that the molecules with a large distorted ground state undergo a fast nonradiative decay resulting in low fluorescence quantum yields. For BSB with terminal amino groups and cyano substitution on the central phenylene ring 6, the two-photon cross section was two times higher than when the cyano substitution was on the vinylene bridge 7 (Figure 3.7). This increase was attributed to both a change in the distance between the donor and acceptor which results in a change in
Donor-π-Donor (D-π-D) Dye
\[ \Phi_f = 0.88 \]
\[ \delta = 995 \]

Donor-Acceptor-Donor (D-A-D) Dye
\[ \Phi_f = 0.86 \]
\[ \delta = 3670 \]

Acceptor-Donor-Acceptor (A-D-A) Dye
\[ \Phi_f = 0.82 \]
\[ \delta = 650 \]

Donor-Donor-Donor (D-D-D) Dye
\[ \Phi_f = 0.88 \]
\[ \delta = 900 \]

\[ \delta = \text{Two photon cross section} \ (GM = 10^{-50} \text{ cm}^4 \text{ s/photon-molecule}) \]

**Figure 3.6**  Illustration of the different motifs investigated in BSB dyes
Figure 3.7  Effect of cyano substitution on two-photon properties

6
\[ \Phi_t = 0.87 \]
\[ \delta = 1640 \text{ GM} \]

7
\[ \Phi_t = 0.015 \]
\[ \delta = 730 \text{ GM} \]
the intramolecular charge transfer and the degree of distortion from planarity in the ground state.

From this data, it is clear that the BSB dyes have both high fluorescence quantum yields and two photon cross sections. Modification to make these dyes more soluble in an aqueous environment and compatible in biological systems without the loss in fluorescence quantum yield could make their use in TPE imaging a reality.

3.1.3 Current dendritic two-photon dyes

A popular method for increasing the two-photon cross sections is to join together individual dyes. Dendrimers composed of oxadiazole TPA dyes, such as 8, exhibited increases in the overall two-photon cross section as the generational size of the dendrimer increased (Figure 3.8). A linear correlation between cross-section and number of dyes showed that there were neither additive nor deleterious effects from joining together the dyes or having them in environments with a high local dye concentration.

The Prasad group reported an example of a branched dye which shows cooperative effects. The measured two-photon cross section of the dye (Figure 3.9) was six times greater than that of the monomeric dye. This increase is thought to be caused by the interaction of the individual dye units and the extension of the delocalization of charge throughout the individual arms.

Work done by Drobizhev et al. also focused on dendritic two-photon dyes (Figure 3.10). By maintaining the π-conjugation throughout the molecule’s constituent branches, a strong cooperative effect was observed. It was found that there was a linear
Figure 3.8  Dendron constructed of TPA units
Figure 3.9  Prasad’s tri-branched dye
Figure 3.10  Drobizhev's cooperative TPA dendrimer
correlation between the number of chromophore units within the dendrimer and the magnitude of the two-photon cross section. For a dendrimer composed of 30 individual chromophores a value of 11000 GM was obtained for the cross section which reduces to an approximate value of 370 GM per chromophore. If this is compared to a dendritic compound of two chromophores, the cross section per chromophore is doubled.

One final example of a TPA dendrimer involves the work of Kwok and Wong. By functionalizing a BSB with dendrons on the \textit{para} positions of the peripheral rings, two main types of dyes were synthesized as either the zero or first generation dendrimer. The first was a tetrasubstituted or symmetric dye, such as 11 (G0 dendrimer), while the second type was disubstituted or asymmetric, with both dendrons branching from the same outside ring (Figure 3.11). The periphery of the dendron was functionalized with either propoxy or oxadiazole (11) groups. While the degree of energy transfer was higher with the asymmetric dendrimers, the solution fluorescence lifetimes and photoluminescence quantum efficiencies were smaller due to the inefficient shielding of the dye. In the practical aspect of this work, LEDs were made with both the symmetric and asymmetric oxadiazole dendrons. The asymmetric version outperformed the symmetric analogue with high external quantum efficiencies and better charge balance properties. This observation can possibly be explained because of the high local concentration of oxadiazole which can act as an electron trap, thus preventing efficient electron transfer.

While there have been many other reports of TPA dendrimers, not one has dealt with looking at improving upon the work of Albota et al. as far as the generation of
Figure 3.11  Kwok and Wong’s symmetric oxadiazole dendrimer
dyes for bioimaging are concerned. One may, in fact, be able to combine both TPE bioimaging dyes and dendrimers to make a compound which would have all four desired properties of a bioimaging dye: biocompatibility, high solubility in water, high two-photon cross section and a high fluorescence quantum yield in water.

3.2 Goals

The main problem with the use of BSB TPA dyes as bioimaging agents is that the dyes are known to be environmentally sensitive. For example, in unpublished results by Halik, a decrease in the fluorescence quantum yield ($\Phi_f$) of donor-acceptor-donor (D-A-D) BSB TPA dyes as the solvent polarity increased was observed. For dyes that have excited states whereby the charge is redistributed, polar environments can lead to non-fluorescent twisted charge transfer states.

As was mentioned in Chapter 1, dendrimers with hydrophilic exteriors and hydrophobic interiors represent “unimolecular micelles,” which have been shown to be capable, much like traditional micelles, of encapsulating organic guest molecules within their interior voids. Second, specific groups can be structurally incorporated into the interior of the dendrimer without the danger of disrupting the overall micellar nature of the structure. Third, they can provide a constant, tailorable microenvironment to covalently encapsulated residues.

In order to control the first solvent sphere of the TPA dyes while simultaneously imparting water solubility, the synthesis of a dye encapsulated within the core of a
dendrimer was undertaken. Attempts were made to synthesize a tetrasubstituted dendritic TPA dye, as well as the alteration of two dyes previously made in the Marder group. Fluorescence and absorbance properties of the altered dyes were acquired, focusing on the change in fluorescence quantum yields with respect to a change in the solvent polarity.

3.3 Synthesis of a tetrasubstituted dendritic bis-styrylbenzene two photon dye

Our first approach to obtain an encapsulated dendritic two photon dye was to place four carboxy terminated dendrons on unsubstituted bis-styrylbenzene (BSB) two photon dye. Figure 3.12 illustrates the retrosynthetic approach employed in the synthesis of the dendritic dye. Two paths were investigated in the generation of the target dye which included: (1) synthesizing the core of the dye and later attaching dendrons; and (2) attachment of dendrons to a triarylamine followed by the synthesis of the dye core.

3.3.1 Approach from core to dendrimer

The syntheses of the water-soluble dendron precursors proceeded using the methods published by Fréchet.\textsuperscript{3,24} Dendron generations were synthesized up to G3 with the easily saponified \textit{p}-methylbenzoate functionality on the periphery.

Synthesis of the triarylamine 12 was carried out by using the methodology of Buchwald where aryl bromides are allowed to react with aryl amines in the presence of Pd\textsubscript{2}(dba)\textsubscript{3}, DPPF, and sodium tert-butoxide.\textsuperscript{3,27} Although methods for a one-pot
Figure 3.12  Retrosynthetic analysis of tetrasubstituted bis-styrylbenzene two photon dye
procedure have been developed, the reaction was performed in a stepwise fashion. The first step involved the reaction of \( p \)-methoxyaniline (13) with \( p \)-bromoanisole (14) in the presence of the catalyst to give the diarylamine 15 in a 54% yield. Conversion to the triarylamine occurred by reacting 2-(4-bromo-phenyl)-1,3-dioxolane (16) with previously isolated 15 in the presence of the catalyst system to give 12 in 31% yield (Scheme 3.1).

Deprotection of 12 in the presence of catalytic \( p \)-TsOH and acetone to give the aldehyde 17 in 60% yield. The aldehyde (17) was then coupled with 1,4-bis(diethoxyphosphorylmethyl) benzene (18) in the presence of potassium tert-butoxide in THF to give the protected two photon dye 19 in 35% yield (Scheme 3.2). The removal of the methoxy groups on the dye was performed using \( \text{BBR}_3 \) and the generation of the tetraphenolic compound (20) was monitored by TLC (Scheme 3.3). Reaction of 20 with the appropriate dendritic bromide resulted in a mixture of products favoring di- and tri-substituted dendritic dyes over the desired tetrasubstituted product as determined via FAB-MS.

Investigation into the stability of 20 was then necessary. The electron-rich tetraphenol could be oxidized into a possible unreactive radical species which could be the reason as to why dendritic substitution did not proceed fully. In order to more fully understand this phenomenon, a study was done where the UV-Vis spectra of 19 and 20 (in the presence and absence of the reducing agent \( \text{NaHSO}_3 \)) were taken in acetone-water (4:1). Figure 3.13 shows the results of this study where there is a definite decrease in the absorbance from 19 to 20 but some of this is regained when the reducing agent is added. A new approach was needed to get to the target dendritic dye.
Scheme 3.1  Synthesis of the acetal protected triarylamine
Scheme 3.2  Synthesis of the protected BSB TPA dye
Scheme 3.3  Deprotection protocol for the core BSB TPA dye
Figure 3.13  UV-Vis spectra of 20 (—), 19 (---), and 20 with NaHSO₃ added (-----) in 4:1 acetone-water
3.3.2 Approach from dendrimer to core

By deprotecting the methyl ethers on the triarylamine at an earlier stage, it becomes possible to attach the dendrons before the Horner-Emmons coupling. To do this, 17 was treated with BBr₃ in CH₂Cl₂ to give the diphenolic triarylamine aldehyde 21 in an 80% yield. Coupling of 21 with ester terminated zeroth through second generation dendrons in the presence of potassium carbonate and 18-crown-6 in refluxing acetone resulted in the dendritic triarylamine aldehydes 22-24 in yields ranging from 67-82% (Scheme 3.4).

Subjecting aldehydes 22-24 to the Horner-Emmons conditions used in the first approach (18, potassium tert-butoxide, THF) gave low yields of the desired material which were not easily separated from the starting material. Changing the temperature of the reaction did not greatly increase the amount of product being produced. Changing the base to NaH or n-butyl lithium also gave low yields of the target dye. Another path needs to be pursued to obtain the desired set of dendritic tetrasubstituted BSB dyes.

3.3.3 Optical properties of the tetramethoxy-BSB TPA dye

An initial study was performed on the tetramethoxybis-styrylbenzene two photon dye, 19 which would serve as a comparison for any later studies done on a dendritic series of these dyes. The focus of this study included looking at the change in the fluorescence intensity of the dye as the polarity of the solvent was increased. Figure 3.14 shows the fluorescence emission spectra of 19 in toluene, acetone and 3:1 acetone/water. The main trend seen is that there is a definite decrease in the fluorescence intensity as the
Scheme 3.4  Dendritic derivatization of the triarylamine aldehyde
Figure 3.14  Fluorescence emission spectra of 19 at 0.36 μM in toluene (λ<sub>ex</sub> = 422 nm) (—), acetone (λ<sub>ex</sub> = 416 nm) (—●—), and 3:1 acetone-water (λ<sub>ex</sub> = 416 nm) (— —)
polarity of the solvent increases as well as a red-shifting and broadening of the $\lambda_{em}$. This was expected for an unprotected dye under conditions whereby the polarity of the solvent was increased.

The noticeable change in the properties of this dye was also seen in the calculation of the fluorescence quantum yield of the compound. The quantum yield is basically a ratio of the number of photons absorbed to the number of photons emitted. The maximum value is 1, where the number of photons emitted equals the number of photons absorbed. The property is obtained experimentally by using the quantum yield of a standard compound ($\Phi_{ST}$) along with the integrated area of its fluorescence spectra ($A_{ST}$) and the refractive index of the solvent ($\eta_{ST}$). Combine this with the area of the fluorescence spectra for the sample ($A_X$) and the refractive index of the sample’s solvent ($\eta_X$), and simple substitution of terms in Equation 2.2 gives the sample’s fluorescence quantum yield ($\Phi_X$).

$$\Phi_X = \Phi_{ST} \left( \frac{A_X}{A_{ST}} \right) \left( \frac{(\eta_X)^2}{(\eta_{ST})^2} \right)$$  \hspace{1cm} (1)

The values obtained for 19 were compared to the fluorescence quantum yields of two known dyes: 9,10-bis(phenylethynyl)anthracene (BPEA) in cyclohexane ($\lambda_{ex} = 420$ nm; $\Phi_f = 1$)\textsuperscript{329} and coumarin 6 in ethanol ($\lambda_{ex} = 420$ nm; $\Phi_f = 0.85$).\textsuperscript{330} A $\Phi_f$ value of 0.83 for 19 in toluene was comparable to the value of the dicyano BSB dye 6 (0.87), which was measured in the same solvent. When acetone was used as the solvent, which increased the polarity of the external environment, the quantum yield of 19 was decreased by more than half to a value of 0.41.
A reasonable explanation as to why the dye loses its normally intense fluorescence properties in a polar medium is that after the molecule is promoted to an excited state, a charged state is generated within the molecule. In non-polar media, the excited state is not stabilized by the external environment. This makes the excited state much less stable than the ground state, and so the molecule quickly fluoresces. In polar media, the excited state is stabilized due to its charged nature and the nature of the external environment. Relaxation back to the ground state can happen slowly through non-radiative decay. So, since initial attempts to make a tetrasubstituted dendritic TPA dye failed, it was hoped that the derivatization of previously synthesized dyes could exhibit a trend that would make the pursuit of a multisubstituted dendritic system necessary.

3.4 Synthesis of a dendritic thiourea bis-styrylbenzene two photon dye

Having no success in attaching dendrons to bis-styrylbenzene dyes through ether linkages, we next attempted to utilize the high reactivity of isothiocyanates toward amines to attach the dendron to the dye. Treatment of a TPA dye that contained an aliphatic amine with a dendritic isothiocyanate would result in thiourea linkage. These dyes could then be studied to see if the size of the dendritic exterior had any significant effect on preventing the non-radiative decay of the dyes in polar environments.
3.4.1 Synthesis of the bis-styrylbenzene two photon dye core

Two bis-styrylbenzene two photon dyes (TP-II-275, 25 and TP-III-9, 26) were obtained from Dr. Seth Marder at the University of Arizona. Whereas 25 was already present in the free base form, 26 needed to be deprotected. Removal of the butoxycarbamate (BOC) group was accomplished by treatment of 26 with 3 M hydrochloric acid in THF to give the free base 27 after alkaline workup in 90% yield (Scheme 3.5).

3.4.2 Attachment of the dendron wedge

It was necessary to modify [G0-G2] dendritic bromides 28-30 to have isothiocyanate moieties which could be used to attach to the free primary amines on the bis-styrylbenzene two photon dyes. Accordingly, treatment of the bromides 28-30 with sodium azide and DMF at 100 °C gave the azides 31-33 in yields ranging from 91-99%. Using the procedure of Taber and Hoermer, reduction of the azides with triphenylphosphine and water in THF gave the free primary benzyl amines 34-36 in 72-96% yield.\textsuperscript{31} Reaction of the amine with thiophosgene and triethylamine, similar to the work of Wrigglesworth et al.\textsuperscript{32} in ethyl acetate provided the isothiocyanates 37-39 in yields of 52-65% (Scheme 3.6).

Attachment of the isothiocyanate to the two photon dye core was accomplished in THF. Yields of the dendritic two photon dye esters 40-42 ranged from 62-72%. The
Scheme 3.5  Preparation of BSB TPA dyes for dendritic derivitization
Scheme 3.6  Synthesis of the isothiocyanate dendrons G0-G2
dicyanosubstituted dendritic two photon dye esters 43-45 were obtained in slightly lower yields (59-68%) (Scheme 3.7).

3.4.3 Saponification of the dendritic esters

In order to have viable water soluble dyes for aqueous studies, deprotection of the ester functionalities was necessary. Caution had to be employed due to the sensitivity of the thiourea functionality to either very acidic or very alkaline conditions. A number of methods were attempted, but it was the use of a 1 M solution of potassium tert-butoxide in DMSO that proved to be the most effective. Here, it is the presence of the tert-butoxide anion that acts to remove the methyl group from the ester, resulting in the generation of the potassium carboxylate and tert-butyl methyl ether. Treatment of esters 40-42 with the above solution gave the acids 46-48 in yields ranging from 87-95%. The saponification of the dicyanosubstituted two photon dye dendritic esters 33 and 34 resulted in the acids 49 and 50 in 75 and 67% yields, respectively (Scheme 3.8).

The saponification product of 45 was not isolated. The product likely decomposed upon treatment with the basic solution. Not only was there a definite loss of the fluorescent red color of the dye, but also the characterization of the isolated material by NMR showed no common peaks with either the starting material or the expected product.
Scheme 3.7  Attachment of the dendrons to the TPA dyes
Scheme 3.8  Saponification of dendritic TPA dyes
3.5 Absorbance properties of the thiourea dyes

A study of the absorbance properties of 40-45 and 46-50 was necessary to get pertinent information that would enable a later critical assessment of the fluorescence properties.

3.5.1 Comparison of the UV-Vis properties of ester dyes to the acid dyes

There were two main issues that needed to be investigated through the use of UV-Vis spectroscopy. First, it was necessary to see if the saponification of the peripheral ester has an effect on either set of dyes. Next, the increase in the dendritic size from a G0 to a G2 dendron needed to be closely examined to see if the larger dendrons acted to better insulate the dye from the external environment. This section presents a comparison between the ester and acid forms of the dyes and the original non-dendritic substituted precursor dye.

The UV-Vis spectra were obtained in THF and water-dioxane (9:1) at a $2\times10^{-5}$ M concentration. Figures 3.15a, b, and c show the spectra for the non-dicyano substituted dyes illustrating the different effects of environment and peripheral substitution. The dicyano comparisons can be seen in Figures 3.16a and b.

There was not much to note in the comparisons between the unsubstituted, or non-dicyano, dyes. The changes in the environmental conditions led to the ester periphery having the highest absorbance in the G0 terminated dendrons, while for the G1 and G2 it turned out that the highest absorbance was that of the carboxylic acid periphery within the most polar solvent. The changes between the peaks were greatest in the first
Figure 3.15 The effects of the alteration of the dendritic periphery and solvent on the UV-Vis absorbance spectra for TPA dyes at 25 °C and 2×10⁻⁵ M: (a) 40 in THF (—), 46 in THF (— —), and 46 in water-dioxane (9:1) (— — —); (b) 41 in THF (— —), 47 in THF (— — —), and 47 in water-dioxane (9:1) (— — —); (c) 42 in THF (— —), 48 in THF (— — —), and 48 in water-dioxane (9:1) (— — —)
Figure 3.16  The effects of the alteration of the dendritic periphery and solvent on the UV-Vis absorbance spectra for dicyano TPA dyes at 25 °C and 2x10^{-3} M: (a) 43 in THF (-----), 49 in THF (---), and 49 in water-dioxane (9:1) (-----); (b) 44 in THF (-----), 50 in THF (---), and 50 in water-dioxane (9:1) (-----)
generation system, but were hardly noticeable in the G2 substituted dye, suggesting that the addition of the dendron helps to protect the dye from outside influences as generation increases. In essence, the hypothesis of the dendron protecting the dye is viable.

Within the dicyano substituted dyes, there is a definite change between the ester and acid periphery, namely with the change in the $\lambda_{\text{max}}$. The $\lambda_{\text{max}}$ migrated from a value of 490 nm in the dendritic ester BSB dyes (43, 44) to that of about 430 nm for the G0 carboxylic acid (49), and to 410 nm for the G1 acid terminated dendrimer (50). The change in wavelength along with the drop in absorbance intensity may be due to an intramolecular binding between the dye and the carboxylic acid group, an effect that will be covered in greater detail later. The disparity between the absorbance of the acid in the different solvents is greatest in the G0 dendritic dye with the intensity actually being greater in the more polar water-dioxane (9:1). This change is lessened when the dendron is increased by one generation, which shows that the environmental effect is not as strong. It is interesting to note that while the absorbance maximum had shifted between the compounds, the original hypothesis still holds, which is that as the generation size of the dendron increases, the environmental effects decrease.

3.5.2 Comparison of the properties of the dyes with respect to generation size

While looking at the correlation of the effect of the changing environment and peripheral substitution with respect to the dendritic size, it was also necessary to compare the dyes according to differences in generational growth. The idea was to keep the external environment and the peripheral substitution constant, and to look at the change
in spectral shape as well as absorbance intensity with respect to the dendritic generation. Figure 3.17 shows the comparisons between each of the different generations of the dendritic esters and the dendritic carboxylic acids in the two separate solvents at the same concentration and compares them to the underivatized TPA dye, 25. The effects on the dicyano dyes are illustrated in Figure 3.18, where they are compared to the underivatized dicyano TPA dye, 27.

The spectra of the non-dicyano substituted dyes behave as theorized, that is the absorbance increases as the generational size increases. While the absorbances appear similar for the ester and acid peripheral dyes in THF, there was a definite change in the overall spectra when the dyes were analyzed using water-dioxane (9:1) as the solvent. There was a large disparity between the absorbance of the G0 and G1/G2 dyes; which, along with the previous data involving the alteration of the periphery and the solvent, indicates that the larger dendrons are quite possibly acting to protect the absorbance properties of the dye.

These differences are much more evident in the dicyano substituted TPA dyes. In the case of the ester terminated dendrons, the spectral profiles are very similar. The only difference is in the G2 dendritic dye, which not only shows a change in the absorbance intensity, but also a red shift in the wavelength maxima. When the acid peripheral dendrons were investigated, there was a significant drop off in the absorbance as well as a blue shift in the \( \lambda_{\text{max}} \). Once again, this effect can be attributed to an intramolecular binding which will be looked at in the next section. The absorbance spectra of the acidic
Figure 3.17  Comparison of absorption spectra for TPA dendritic dyes of different generational size with similar peripheral substitution and external environment at 25 °C and 2.0x10^{-5} M: (a) 40 (--), 41 (-- - -), 42 (-- -), and 25 (-- -) in THF; (b) 46 (--), 47 (-- - -), 48 (-- -), and 25 (-- -) in THF; (c) 46 (--), 47 (-- - -), 48 (-- -), and 25 (-- -) in water-dioxane (9:1)
Figure 3.18  Comparison of absorption spectra for TPA dicyano dendritic dyes of different generational size with similar peripheral substitution and external environment at 25 °C and 2x10⁻⁵ M: (a) 43 (—), 44 (- - -), 45 (- - -), and 27 (- - -) in THF; (b) 49 (---), 50 (---), and 27 (---) in THF; (c) 49 (---), 50 (---), and 27 (---) in water-dioxane (9:1)
dyes in THF indicated that there was an increase, however slight, in the absorbance with respect to an increase in generational size. When these dyes were placed into the aqueous environment, the intensity of the G1 dye decreased while the G0 dye nearly doubled its absorbance. Therefore, whatever had caused the lower absorbance in THF for the G1 dye remained the same in the water-dioxane solution while the G0 dye showed an enhancement upon changing solvents. Here, the introduction of a great polar, hydrogen-binding solvent may actually have helped to stabilize the dye, which is the opposite of what was originally intended.

3.5.3 Aggregation properties of the dyes

When two or more separate molecules come together through non-covalent interactions to form a larger structure, the molecules are said to have aggregated. This process is commonly observed in solutions of high concentration. It is necessary to understand whether or not this is happening within the solutions of the TPA dyes. If aggregation occurs at the concentrations critical for fluorescence then the molecules may self-quench, and the values for the quantum yields may not reach a value that could be used for comparison and the determination of trends.

In order to ascertain whether or not a molecule is undergoing aggregation, a Beer’s Law analysis was carried out. Equation 2.2 is Beer’s Law where \( A = \text{absorbance} \), \( c = \text{concentration (M)} \), \( l = \text{path length (cm)} \), and \( \varepsilon = \text{molar absorptivity (M}^{-1}\text{cm}^{-1}) \).

\[
A = \varepsilon \cdot c \cdot l
\]  
(2)
A plot of absorbance versus concentration should be a straight line passing through the origin. The molar absorptivity is the slope. A deviation from Beer’s Law can indicate aggregation of the dyes.

Beer’s Law analyses were performed on dyes 40-50. The graphs of dyes 40-42 and 46-48 are illustrated in Figure 3.19, while the graphs of the dicyano-substituted dyes 43-45 and 49-50 are shown in Figure 3.20. Data listing the corresponding molar absorptivity and $\lambda_{\text{max}}$ can be seen in Table 3.1.

A trend in the non-dicyano dyes can be seen whereby the molar absorptivity increases with respect to the increase in the dendritic generation, independent of the functional group at the dendron periphery or the solvent used. However, a change was seen in the molar absorptivity when comparing the same carboxylate terminated dye in both THF and a water-dioxane (9:1) mixture. In fact, for dyes with the G1 and G2 dendrons attached, the molar absorptivity was higher in the water-dioxane solution than it was in THF. This could be due to van der Waals forces causing the collapse of the dendron around the dye in these cases, protecting the dye from interacting with the much more polar external environment.

There were definite differences with the dicyano dyes when comparing them to the non-dicyano dyes. First of all, these dyes were obviously more sensitive to the environmental conditions. It is also interesting to note that in the two dyes that were saponified (49 and 50), the molar absorptivity values were almost half those of the esterified dyes (43 and 44) within the same solvent (THF). There were slight changes as
Figure 3.19  Beer's Law plots of the dendritic TPA dyes: (a) 40 in THF (*), 46 in THF (▲), 46 in water-dioxane (9:1) (■); (b) 41 in THF (*), 47 in THF (▲), 47 in water-dioxane (9:1) (■); (c) 42 in THF (*), 48 in THF (▲), 48 in water-dioxane (9:1) (■)
Figure 3.20  Beer's Law plots of the dendritic TPA dyes: (a) 43 in THF (*), 49 in THF (▲), 49 in water-dioxane (9:1) (■); (b) 44 in THF (*), 50 in THF (▲), 50 in water-dioxane (9:1) (■); (c) 45 in THF (*)
Table 3.1 Molar absorptivities, \( \lambda_{\text{max}} \) values, and linear correlation values for the TPA dendritic dyes in organic and aqueous solutions

<table>
<thead>
<tr>
<th>Dye</th>
<th>Solvent</th>
<th>( \varepsilon ) (M(^{-1})cm(^{-1}))</th>
<th>( \lambda ) (nm)</th>
<th>( R^2 ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 (NH(_2) dye)</td>
<td>THF</td>
<td>6.98x10(^5)</td>
<td>410</td>
<td>N/A</td>
</tr>
<tr>
<td>27 (NH(_2) dc dye)</td>
<td>THF</td>
<td>4.88x10(^5)</td>
<td>485</td>
<td>N/A</td>
</tr>
<tr>
<td>40 (G0 ester)</td>
<td>THF</td>
<td>5.18x10(^5)</td>
<td>415</td>
<td>0.995</td>
</tr>
<tr>
<td>41 (G1 ester)</td>
<td>THF</td>
<td>5.88x10(^5)</td>
<td>410</td>
<td>0.995</td>
</tr>
<tr>
<td>42 (G2 ester)</td>
<td>THF</td>
<td>6.40x10(^5)</td>
<td>410</td>
<td>1.00</td>
</tr>
<tr>
<td>43 (G0 dc ester)</td>
<td>THF</td>
<td>5.10x10(^5)</td>
<td>490</td>
<td>1.00</td>
</tr>
<tr>
<td>44 (G1 dc ester)</td>
<td>THF</td>
<td>4.35x10(^5)</td>
<td>490</td>
<td>1.00</td>
</tr>
<tr>
<td>45 (G2 dc ester)</td>
<td>THF</td>
<td>4.76x10(^5)</td>
<td>500</td>
<td>1.00</td>
</tr>
<tr>
<td>46 (G0 acid)</td>
<td>THF</td>
<td>5.15x10(^5)</td>
<td>415</td>
<td>0.999</td>
</tr>
<tr>
<td>46 (G0 acid)</td>
<td>water/dioxane (9:1)</td>
<td>5.03x10(^5)</td>
<td>415</td>
<td>0.999</td>
</tr>
<tr>
<td>47 (G1 acid)</td>
<td>THF</td>
<td>5.77x10(^5)</td>
<td>415</td>
<td>0.998</td>
</tr>
<tr>
<td>47 (G1 acid)</td>
<td>water/dioxane (9:1)</td>
<td>6.46x10(^5)</td>
<td>415</td>
<td>0.998</td>
</tr>
<tr>
<td>48 (G2 acid)</td>
<td>THF</td>
<td>6.05x10(^5)</td>
<td>410</td>
<td>0.996</td>
</tr>
<tr>
<td>48 (G2 acid)</td>
<td>water/dioxane (9:1)</td>
<td>6.21x10(^5)</td>
<td>415</td>
<td>0.996</td>
</tr>
<tr>
<td>49 (G0 dc acid)</td>
<td>THF</td>
<td>1.84x10(^5)</td>
<td>425</td>
<td>0.999</td>
</tr>
<tr>
<td>49 (G0 dc acid)</td>
<td>water/dioxane (9:1)</td>
<td>2.62x10(^5)</td>
<td>435</td>
<td>0.998</td>
</tr>
<tr>
<td>50 (G1 dc acid)</td>
<td>THF</td>
<td>2.20x10(^5)</td>
<td>405</td>
<td>0.997</td>
</tr>
<tr>
<td>50 (G1 dc acid)</td>
<td>water/dioxane (9:1)</td>
<td>1.97x10(^5)</td>
<td>405</td>
<td>0.999</td>
</tr>
</tbody>
</table>
the solution was changed to water-dioxane. The G0 dye actually had a higher value than in THF while the G1 dye stayed about the same. A reasonable explanation can be the interaction between the cyano groups through the lone pair on the nitrogen and the proton on the peripheral carboxylic acid functionalities, a possibility since the effective pH of the measured solutions were approximately 5.5. With the larger dendritic structure this interaction is more stable due to less strain placed on the molecule in the formation of the macrocycle. When the compound is subjected to light, the absorption range is broader due to the twisting of the structure due to these interactions. In the smaller G0 molecule, the cyano / carboxylic acid interaction is less stable for two reasons. First, there is half the number of carboxylic acid groups present. Secondly, the amount of strain placed on the molecule for this interaction is increased because of the smaller dendritic size. Therefore, this macrocycle is broken up more readily by hydrogen bonding interactions with the water molecules leading to a slightly sharper peak in the absorbance spectrum and a higher molar absorptivity. The effect on the second generation dendritic structure would even be greater, yielding really low molar absorptivities and a $\lambda_{\text{max}}$ at a wavelength less than 400 nm. This hypothesis will be investigated further in the next section with the measurement of the fluorescence quantum yields.

3.6 **Fluorescence properties of the thiourea dyes**

The way to best understand the effects of the environment on the activity of TPA dyes is to study their fluorescence spectra. Measuring the quantitative changes in the fluorescence quantum yield values can give a better picture of how sensitive the dyes are
to the solvent. The hope is that as the dendritic environment is increased in size that the any decrease in the values of the quantum yields with increasing solvent polarity would lessen.

3.6.1 Fluorescence quantum yields of the synthesized dyes

Using the same set of equations that resulted in the fluorescence quantum yield values for the tetramethoxy-substituted TPA dye 19, calculations were performed on 25, 27, and 40-50. Table 3.2 shows the quantum yield values for these dyes under different sets of conditions, along with a set of values that were derived from an experiment that was designed to see if the presence of the acidic protons along the periphery of the dicyano dyes led to much lower absorbance values and a blue-shift in the wavelength maxima. The fluorescence quantum yields were measured in THF, water-dioxane (9:1), as well as in a dilute basic solution (water-dioxane, 9:1) that contained sodium hydroxide (0.01 M) at a pH of 12.

With the non-dicyano TPA dyes, there was not much of a change in the fluorescence quantum yields between the higher generation dendritic dyes (G1, G2) when compared to the underivatized dye, 25. However, in the case of the G0 dye, there was a rather large change in values. With the underivatized dye having a quantum yield of 0.74, there was a noticeable drop with the addition of the benzyl ester. After the saponification of the G0 ester to 46, the quantum yield rose to surpass the value of 25. At this time, it is not fully understood why this disparity was present, especially since there
Table 3.2  Fluorescence data and $\Phi_f$ values for the TPA dendritic dyes in organic and aqueous solutions

<table>
<thead>
<tr>
<th>Dye</th>
<th>Solvent</th>
<th>$\Phi_f$</th>
<th>$\lambda_{ex}$ (nm)</th>
<th>$\lambda_{em}$ (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 (NH$_2$ dye)</td>
<td>THF</td>
<td>0.74</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>27 (NH$_2$ dc dye)</td>
<td>THF</td>
<td>0.50</td>
<td>490</td>
<td>570</td>
</tr>
<tr>
<td>40 (G0 ester)</td>
<td>THF</td>
<td>0.50</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>41 (G1 ester)</td>
<td>THF</td>
<td>0.79</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>42 (G2 ester)</td>
<td>THF</td>
<td>0.75</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>43 (G0 dc ester)</td>
<td>THF</td>
<td>0.49</td>
<td>490</td>
<td>570</td>
</tr>
<tr>
<td>44 (G1 dc ester)</td>
<td>THF</td>
<td>0.52</td>
<td>490</td>
<td>570</td>
</tr>
<tr>
<td>45 (G2 dc ester)</td>
<td>THF</td>
<td>0.28</td>
<td>490</td>
<td>570</td>
</tr>
<tr>
<td>46 (G0 acid)</td>
<td>THF</td>
<td>0.84</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>46 (G0 acid)</td>
<td>water/dioxane (9:1)</td>
<td>0.58</td>
<td>415</td>
<td>505</td>
</tr>
<tr>
<td>47 (G1 acid)</td>
<td>THF</td>
<td>0.70</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>47 (G1 acid)</td>
<td>water/dioxane (9:1)</td>
<td>0.55</td>
<td>415</td>
<td>505</td>
</tr>
<tr>
<td>47 (G1 acid)</td>
<td>water/dioxane/NaOH</td>
<td>0.52</td>
<td>415</td>
<td>505</td>
</tr>
<tr>
<td>48 (G2 acid)</td>
<td>THF</td>
<td>0.39</td>
<td>415</td>
<td>475</td>
</tr>
<tr>
<td>48 (G2 acid)</td>
<td>water/dioxane (9:1)</td>
<td>0.65</td>
<td>415</td>
<td>505</td>
</tr>
<tr>
<td>49 (G0 dc acid)</td>
<td>THF</td>
<td>0.21</td>
<td>415</td>
<td>605</td>
</tr>
<tr>
<td>49 (G0 dc acid)</td>
<td>water/dioxane (9:1)</td>
<td>0.06</td>
<td>415</td>
<td>530</td>
</tr>
<tr>
<td>49 (G0 dc acid)</td>
<td>water/dioxane/NaOH</td>
<td>0.21</td>
<td>415</td>
<td>530</td>
</tr>
<tr>
<td>50 (G1 dc acid)</td>
<td>THF</td>
<td>0.08</td>
<td>415</td>
<td>580</td>
</tr>
<tr>
<td>50 (G1 dc acid)</td>
<td>water/dioxane (9:1)</td>
<td>0.05</td>
<td>415</td>
<td>555</td>
</tr>
<tr>
<td>50 (G1 dc acid)</td>
<td>water/dioxane/NaOH</td>
<td>0.13</td>
<td>415</td>
<td>555</td>
</tr>
</tbody>
</table>
was no real change in the case of the G1 dendritic dye. The saponification of the G2 dendritic dye to 48 resulted in the reduction of the quantum yield value by almost a factor of two in THF. Here, the carboxylic acid functionalities may be affecting the charged transfer state of the dye in the non-polar environment. This is supported by the data in the water-dioxane system, in which the quantum yield increases with generation (47 → 48 → 49). Apparently, when given a opportunity to interact strongly with the solvent, the dendron acts as a shield. With the smaller dendritic dyes (G0, G1), there is a slight decrease in quantum yield values within the polar solvent system, an observation that could be due to a lack of sufficient protection because of size.

The effects upon the fluorescence quantum yields of the dicyano dyes were more drastic. While the ester terminated dendritic dyes had values comparable to the underivatized dicyano dye, there was a large decrease in both the G0 (two-fold) and G1 (six-fold) case for the saponified dyes. When the saponified dyes were placed in the polar environment, there was another drop in the quantum yield values, showcasing the sensitivity of this type of dye to the external environment.

In order to determine whether or not the protonated state of the peripheral carboxylic acids participated in the large decrease in the fluorescence quantum yield values, measurements were performed under basic conditions (0.1 M NaOH, pH = 12). Using the normal dendritic G1 TPA dye as a standard case, both of the dicyano dendritic dyes were analyzed. The results showed that while the values for the dicyano dyes did not approach the same values as the dendrimers with the esterified periphery, there was a definite improvement over their protonated counterparts. This study does lead credence
to the hypothesis that the protonated state of the periphery affects the spectroscopic properties of the dyes. It also shows that along with being sensitive to the polarity of the solvent, that the dyes are also sensitive to the pH of the solution.

3.6.2 *Comparison of the fluorescence properties as a function of solvent*

The calculation of the fluorescence quantum yield values take into consideration the concentration of the compound in solution and the intensity of the fluorescence of that compound. What was not focused on was the effect of the solvent on the excitation and emission wavelengths. The non-dicyano dyes were not affected by the change in the periphery functionality from ester to acid. In fact, the excitation (determined from the UV-Vis $\lambda_{\text{max}}$) and emission wavelengths remained the same from the underivatized dye to the second generation dendritic dye, so long as the measurements were taken in THF. When the solvent was changed to the water-dioxane (9:1) mixture, the emission maxima shifted equally in all three dendritic dyes remaining the same even under basic conditions.

However, when the measurements were taken for the dicyano-substituted dyes, there was a noticeable shift in both the excitation wavelengths and emission maxima dependent upon the external periphery and the solvent. Even though more energy was needed to excite the acidic dyes, their emission was of lower energy than the esterified dyes. This can be caused by a non-emissive relaxation to a lower energy state before the compound returns to the ground state. The change in solvent from THF to water-dioxane decreases this effect, possibly by pulling the dendritic periphery away from the dye by
increasing the compound / solvent interaction, and thus from the resultant charge transfer state which allows for a higher energy emission of light. The same emission maxima was obtained when the basic conditions were used, conditions that would favor the stronger interaction between the solvent and the dendritic periphery.

3.6.3 Comparison of the fluorescence properties as a function of generation size

As was stated previously, the non-dicyano dendritic dyes did not show high sensitivity to changes in the environment and thus excitation wavelengths and emission maxima were not affected as the generation of the dendrons was altered.

In the case of the dicyano-substituted dyes, there was a strong generational effect with the G0 and G1 carboxylic acid peripheral dendrons. The large change in the emission max for the G0 dye between THF and the water-dioxane (9:1) (a change of 75 nm) can be related to the lack of shielding of the dye from the solvent by the dendron. As the dendron increased in size, the overall change in the emission maxima lessened as the dye was better shielded from the solvent by the dendron. The expectation is that the G2 dendritic dicyano-dye would be even less affected by changes in the external environment.

3.7 Summary of results

Initial study of a tetramethoxy-TPA BSB dye indicated that there was a strong environmental effect upon the spectroscopic properties of these types of dyes. By
changing the solvent from toluene to an acetone-water (3:1) mixture, the fluorescence quantum yield decreased by a factor of two.

The synthesis of a tetrasubstituted dendritic TPA dye has been attempted through two routes, and as of yet, been unsuccessful. The initial steps toward the placement of a single dendron on a TPA dye have been accomplished through the derivatization of the dendritic focal point to give an isothiocyanate. Attachment occurred through the formation of a thiourea linkage with the primary amine present on a set of dyes supplied by the Marder group. While relatively stable, the linkage is fairly facile to strongly basic conditions (pH > 13) leading to problems with the saponification of the esters on the dendritic periphery. Saponification was accomplished, however by the use of a polar aprotic system (KOTBu / DMSO) which acted to cleave the methyl esters on dyes 40-44 and give the target carboxylate dendritic dyes 46-50.

Spectroscopic studies of the synthesized dendritic thiourea dyes were carried out using three sets of conditions: (1) dendritic esters in THF; (2) dendritic acids in THF; and (3) dendritic acids in water-dioxane (9:1). UV-Vis data showed that for the normal, unsubstituted TPA dendritic dyes, the addition of dendrons helped to shield the dye from the environment. Although there were variations in the molar absorptivity values, the evident trend indicated that as the size of the dendron increased so did the absorbance properties of the dye. The use of the dicyano-substitued dyes led to compounds which proved to be much more sensitive to environmental conditions. The shifting of absorbance maxima, the decrease in the molar absorptivity indicated that there were many more problems with this system than was previously thought. Carboxylic acid
groups on the periphery of the dendritic groups ended up being a rather poor choice for solubilizing the dye in an aqueous environment. Interactions between the cyano group and the protonated carboxylic acid allowed for a favoring of the charged transfer state. This was indicated by decreases in the molar absorptivity values for the larger acidic G1 dendritic dye as well as the decrease in the absorbance intensity for the same compound when compared to the smaller G0 dye.

Investigation of the fluorescence spectra of the dyes illustrated the differences associated with the changing of the periphery or the solvent. Variations in the fluorescence quantum yields indicated that the dyes were definitely sensitive to the environment with the dicyano-substituted dyes being remarkably affected. It was found that in part, this sensitivity is due to the pH of the solution, and that basic conditions actually lead to increases in the values of the quantum yields. The interactions between the dendritic periphery and the cyano groups of these dyes also led to changes in the excitation wavelength and emission maxima. The interaction derived from this interface led to blue-shifted excitation and red-shifted emission. When the external environment was altered to one that encouraged contact between the dendron periphery and the solvent, the emission energy increased. This indicates that the dye / dendron interaction may retard the efficient fluorescence emission of the compound.

The non-dicyano dyes did not seem to be as easily influenced by the environment, but definite trends were able to be seen allowing the illustration of the theorized dendritic protection of the dye from the external environment. The effect of the environment on the dendritic dyes altered the emission wavelength by 30 nm largely due to the change in
the solvent polarity, but the peripheral substitution did not affect the excitation wavelength.

Overall, this study should provide the groundwork for a further investigation into the utility of dendritic TPA BSB dyes. The fact that the non-dicyano dyes were not as sensitive to the external environment and were positively influenced by the addition of the dendron shows that the possibility of using more wedges or larger dendrons to increase the spectroscopic properties even more. Also, the discovery of the pH sensitivity of the dicyano-substituted dyes shows that there needs to be an alteration to the dendritic design so that this variable can be minimized and further work can be attempted that would increase the spectroscopic properties, such as fluorescence quantum yields, and absorbance intensities, of this type of dye in more polar environments.

3.8 Future directions

A more thorough look at the effect of dendritic size on the properties of the TPA dye is absolutely necessary. In order to do this, the initial failures in the synthesis of the tetrasubstituted dendritic dye must be overcome. The use of a Heck reaction to attach the triarylamine arms to the core of the dye may prove to be the answer. Once this is done, work on the attachment of a dicyano substituted core should be done as well, since this dye is more sensitive to the aqueous environment, and more extensive work can be performed using a dicyano dye in the presence of multiple carboxylic acid functionalities.

Another possibility is to investigate disubstituted dendritic TPA dyes. This can be accomplished by using a designed dye with two functional points of attachment. The use
of a robust attachment point is desired because subsequent processes after attachment, such as saponification, may degrade particular functional groups like thioureas.

The carboxylic acid periphery is not the best choice in the design of a bioimaging dye. Since biological systems are sensitive to changes in pH levels, the use of basic solutions may end up destroying the targets before imaging has occurred. The most common way around this is to use sulfonated dendrons which would have a high water-solubility at biological pHs. Another way would be to use dendrons terminated with high molecular weight polyethylene glycol or PEG groups. The use of PEG substitution would be two-fold: first, the dyes would have a high water solubility at biological pHs; and the PEG groups would act to mask the dye from the patient’s immune system enabling a higher concentration around the target tissue and increasing the half-life of the dye within the body.

Finally, the development of a place of attachment for a bioactive linker or cell targeting molecule is necessary. The functional group involved should contain a reactive, nucleophilic center and maintain stability through a large number of chemical steps in the synthesis of the dye. A nitro group could serve this purpose by providing a masked amine functionality. Initial development of the nitro-functionalized dendrons was accomplished; however, no attachment of biomolecules has yet been performed.

The dendrons were formed by first taking methyl 4-(bromomethyl)benzoate (28) and coupling it to a four fold excess of 3,5-dihydroxybenzyl alcohol (51). Isolation of the mono-substituted dendron 52, and subsequent coupling to m-nitro benzyl bromide 53 led to the formation of first generation m-nitro dendron 54 (Scheme 3.9). A similar protocol
Scheme 3.9 Synthesis of $m$-nitro-substituted [G1]-OH
was used to furnish 57 (Scheme 3.10). The yields of mono substituted dendrons 52 and 55 were 57% and 59%, respectively. Conversion to the \( m \)-nitro dendrons went in yields of 94% (54) and 77% (57). Reduction of the nitro functionality on 57 to give amine 58 occurred in the presence of zinc and a substoichiometric amount of calcium chloride to give an 80% yield (Scheme 3.11).

The attachment of a bioactive linker such as biotin or folate to the amine functionality would be the next step. Since these groups would allow for cell targeting, initial data could then be obtained for the use of BSB TPA dyes as bioimaging agents. This work could result in the mainstreaming of two-photon microscopy through the use of these dyes; since they would be the first to have both high two-photon cross sections and large fluorescence quantum yields in water.
Scheme 3.10  Synthesis of m-nitro-substituted [G2]-OH
Scheme 3.11  Deprotection of $m$-nitro-substituted [G1]-OH
3.9 Experimental

Materials and Methods

NMR spectra were recorded on either a Bruker 250 MHz or 500 MHz NMR spectrometer. Chemical shifts are reported in ppm (δ) referenced to internal residual solvent protons (1H). 13C NMR spectra were recorded as proton-decoupled spectra. Electrospray ionization (ESI), fast atom bombardment (FAB), and matrix assisted laser desorption ionization (MALDI) mass spectra were performed at the University of Arizona Mass Spectrometry Facilities. Compounds 25 and 26 were obtained from the labs of Dr. Seth Marder and were synthesized by Dr. Tim Parker. The synthesis of the (CO2Me)-[Gn]-Br dendrons (28-30), 2-(4-bromophenyl)-[1,3]-dioxolane (16), and 1,4-bis-(diethylphosphorylmethyl)-benzene(18) were performed according to published procedures. All other chemicals were purchased from commercial suppliers and used as received. THF was distilled from benzophenone and potassium metal. Toluene was distilled from calcium hydride. Flash chromatography using silica (Natland International Corp., silica gel 200-400 Mesh) was performed by the method of Still et al. Analytical thin-layer chromatography (TLC) was performed on precoated TLC plates (Merck precoated 0.25 mm silica gel 60 F254 plates).

Spectroscopic Measurements. All spectroscopic measurements were performed with spectrophotometric grade solvents (Aldrich). UV-Visible spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. Corrected fluorescence spectra were collected on a Spex Fluorolog-2 spectrophotometer. Quantum yields, Φ, of dilute solutions were
determined using 9,10-bis-(phenylethynyl)anthracene in cyclohexane ($\Phi = 1.00$) as the reference compound.\textsuperscript{337}

**Bis(4-methoxyphenyl)amine (15).** Compound 15\textsuperscript{338} was prepared as follows: a solution of 13 (7.1 g, 38 mmol) and 14 (4.68 g, 38 mmol) in dry toluene was degassed for 15 min. To this was added Pd$_2$(dba)$_3$ (0.6 g, 0.7 mmol) and DPPF (0.6 g, 1.1 mmol) and the reaction was stirred for an additional 10 min. Sodium tert-butoxide (4.8 g, 50 mmol) was then added and the resulting slurry was stirred for an additional 10 min before heating to 100°C for 24 h. After cooling, water was added to quench, and the mixture was passed through SiO$_2$. Extraction with EtOAc followed by subsequent concentration gave the crude product as a dark oil. Purification by chromatography (SiO$_2$, 1:4 Hexanes/EtOAc) yielded the product as an orange solid (4.7 g, 54%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 6.94-6.91 (d, $J$ = 9.1 Hz, 4 H), 6.82-6.78 (d, $J$ = 9.0 Hz, 4 H), 5.3 (bs, 1 H), 3.76 (s, 6 H).

**4-[1,3]Dioxolan-2-yl-phenyl)bis(4-methoxyphenyl)amine (12).** Following the procedure for 15, toluene (50 mL), 15 (3.05 g, 13.3 mmol), 16 (3.04 g, 13.3 mmol), Pd$_2$(dba)$_3$ (0.24 g, 0.3 mmol), DPPF (0.22 g, 0.4 mmol), and sodium tert-butoxide (1.68 g, 17.3 mmol), gave after flash chromatography (SiO$_2$, 9:1 Hexanes/EtOAc), 12 as a yellow oil (1.6 g, 31%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 7.31-7.28 (d, $J$ = 8.6 Hz, 2 H), 7.08-7.05 (d, $J$ = 6.7 Hz, 4 H), 6.97-6.93 (d, $J$ = 8.5 Hz, 2 H), 6.85-6.82 (d, $J$ = 6.6 Hz, 4
H), 6.72 (s, 1 H), 4.17-3.98 (m, 4 H), 3.79 (s, 6 H); \(^1^3^C\) NMR (125 MHz, CDCl\(_3\)) \(\delta\) 156.62, 141.24, 133.67, 132.11, 128.28, 122.03, 121.14, 115.89, 114.63, 72.52, 58.14.

**4-[Bis(4-methoxyphenyl)amino]benzaldehyde (17).** Compound 17\(^3^\)\(^3^9\) was prepared as follows: to a solution of 12 (9.8 g, 26 mmol) in acetone (100 mL) was added \(p\)-toluenesulfonic acid (0.5 g, 3 mmol) and the resulting solution was stirred at room temperature for 12 h. Saturated potassium carbonate (25 mL) was added, and the mixture was stirred for 30 min to quench the reaction. The solvent was removed in vacuo and the residue was taken up with equal portions of water and CH\(_2\)Cl\(_2\) (150 mL), and the organic layer was removed. After washing the organic portion with 1 M NaOH (35 mL), the organic layer was dried (MgSO\(_4\)), filtered, and evaporated to dryness to give the crude product as a dark oil. Purification by flash chromatography (SiO\(_2\), 7:3 hexanes/EtOAc) gave the product as a red, fragrant oil (5.1 g, 60%): \(^1^H\) NMR (250 MHz, CDCl\(_3\)) \(\delta\) 9.75 (s, 1 H), 7.62-7.59 (d, \(J=8.8\) Hz, 2 H), 7.13-7.09 (d, \(J=9\) Hz, 4 H), 6.89-6.81 (m, 6 H), 3.79 (s, 6 H).

**Di[bis(4-methoxyphenyl)-4-bis(styryl)phenyl]amine (19).** Compound 19\(^3^\)\(^4^0\) was prepared as follows: to a solution of [4-(diethoxyphosphorylmethyl)benzyl]phosphonic acid diethyl ester (18) (2.84 g, 7.5 mmol) in dry THF (150 mL) was added potassium \(t\)-butoxide (3.60 g, 32 mmol) at \(-10^\circ\)C and the resulting slurry was stirred for 5 min. A solution of 17 (5.05 g, 15.1 mmol) in THF was slowly added to the mixture, keeping the temperature below \(0^\circ\)C. After addition, the reaction was slowly warmed to room
temperature, and stirred under nitrogen for 10 h. The reaction was quenched by the slow addition of water (10 mL), followed by the removal of the solvent in vacuo. The emulsion was taken up in a 1:1 mixture of brine and CH$_2$Cl$_2$ (200 mL), and the organic portion was removed. The aqueous layer was then extracted twice with CH$_2$Cl$_2$ (200 mL), and the combined organic fractions were dried (MgSO$_4$), filtered, and concentrated to give the crude product as a dark oil. Purification by flash chromatography (SiO$_2$, CH$_2$Cl$_2$) gave the product as a bright, yellow powder (1.7 g, 35%): $^1$H NMR (500 MHz, CDCl$_3$) δ 7.44 (s, 4 H), 7.33-7.31 (d, J = 9 Hz, 4 H), 7.07-7.05 (d, J = 9 Hz, 8 H), 7.00 (s, 2 H), 6.93 (s, 2 H), 6.91-6.89 (d, J = 8.5 Hz, 4 H), 6.84-6.82 (d, J = 9 Hz, 8 H), 3.80 (s, 12 H); MS (FAB) m/z 736 (M$^+$).

4-[Bis(4-hydroxyphenyl)amino]benzaldehyde (21). To a solution of boron tribromide (8.51 mL, 90.0 mmol) in 100 mL CH$_2$Cl$_2$ at 0°C under an inert atmosphere was slowly added a solution of 17 (5.82 g, 17.5 mmol) in 20 mL CH$_2$Cl$_2$. After addition, the progress of the reaction was monitored by TLC (1:1 hexanes/ethyl acetate) until the disappearance of the starting material. The reaction was then warmed to room temperature and quenched with the addition of distilled water (50 mL). The product was extracted with ethyl acetate (3 x 50 mL) and the combined extracts were washed with saturated sodium bisulfite (50 mL). After drying (MgSO$_4$), the organic portion was concentrated and purified using flash chromatography (SiO$_2$, 1:1 hexanes/ethyl acetate) to give 21 as an red-orange solid (4.26 g, 80%): $^1$H NMR (250 MHz, CDCl$_3$) δ 9.72 (s, 1 H), 8.51 (s, 2 H), 7.64-7.60 (d, J = 8.8 Hz, 2 H), 7.13-7.09 (d, J = 6.6 Hz, 4 H), 6.90-6.87
(d, J = 6.6 Hz, 4 H), 6.75-6.72 (d, J = 8.8 Hz, 2 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 206.28, 190.26, 156.36, 138.56, 131.87, 129.43, 128.34, 117.25, 116.30; MS (MALDI) m/z 305.08 (M$^+$).

**General procedure for the synthesis of dendritic triarylamines**

Potassium carbonate (10 equiv.), 21 (1 equiv.), 18-crown-6 (0.2 equiv.) and the dendritic bromide (2 equiv.) were stirred at an elevated temperature for 12 h. The reaction mixture was cooled and the solvent removed in vacuo. The residue was partitioned between a mixture of CH$_2$Cl$_2$ and water (1:1, 50 mL) and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 30 mL). The combined organic extracts were dried (MgSO$_4$), filtered, and evaporated to dryness. The crude product was purified by flash column chromatography (SiO$_2$, 9:1 CH$_2$Cl$_2$ / Et$_2$O) to give a yellow foam.

4-[Bis((CO$_2$Me)-[G0])amino] benzaldehyde (22). According to the general procedure, 28 (0.76 g, 3.3 mmol), 21 (0.5 g, 1.6 mmol), potassium carbonate (2.2 g, 16 mmol) and 18-crown-6 (0.09 g, 0.33 mmol) in acetone (50 mL) at reflux gave 22. Yield: 0.81 g (82%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.76 (s, 1 H), 8.06-8.04 (d, $J$ = 8.2 Hz, 4 H), 7.62-7.60 (d, $J$ = 8.8 Hz, 2 H), 7.50-7.48 (d, $J$ = 8.2 Hz, 4 H), 7.11-7.09 (d, $J$ = 8.9 Hz, 4 H), 6.95-6.93 (d, $J$ = 8.9 Hz, 4 H), 6.85-6.83 (d, $J$ = 8.8, 2 H), 5.10 (s, 4 H), 3.91 (s, 6 H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 190.28, 166.78, 156.16, 153.86, 141.94, 139.33, 131.40, 129.95, 129.83, 128.02, 126.98, 117.12, 116.00, 69.64, 52.17; MS (MALDI) m/z 601.09 (M$^+$).
4-[Bis((CO$_2$Me)$_2$-[G1])amino] benzaldehyde (23). Following to the general procedure, 29 (1.3 g, 2.6 mmol), 21 (0.4 g, 1.3 mmol), potassium carbonate (1.8 g, 13 mmol) and 18-crown-6 (0.07 g, 0.26 mmol) in acetone (50 mL) at reflux gave 23. Yield: 1.1 g (73%):

$^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 9.74 (s, 1 H), 8.05-8.01 (d, $J$ = 8.2 Hz, 8 H), 7.63-7.59 (d, $J$ = 8.8 Hz, 2 H), 7.48-7.45 (d, $J$ = 8.2 Hz, 8 H), 7.11-7.08 (d, $J$ = 8.9 Hz, 4 H), 6.93-6.89 (d, $J$ = 8.9 Hz, 4 H), 6.85-6.81 (d, $J$ = 8.8, 2 H), 6.67-6.65 (m, 4 H), 6.54-6.52 (m, 2 H), 5.09 (s, 8 H), 4.96, (s, 4 H), 3.90 (s, 12 H); $^1$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 190.26, 166.75, 156.32, 153.90, 141.84, 139.46, 139.15, 131.39, 129.89, 129.77, 128.02, 127.93, 126.96, 116.96, 115.98, 106.56, 101.59, 70.07, 69.44, 52.14; MS (MALDI) m/z 1141.42 (M$^+$).

4-[Bis((CO$_2$Me)$_4$-[G2])amino] benzaldehyde (24). According to the general procedure, 30 (0.5 g, 0.5 mmol), 21 (0.08 g, 0.25 mmol), potassium carbonate (0.35 g, 2.5 mmol) and 18-crown-6 (0.01 g, 0.05 mmol) in acetone (25 mL) at reflux gave 24. Yield: 0.38 g (67%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.74 (s, 1 H), 8.01-8.00 (d, $J$ = 8.2 Hz, 16 H), 7.60-7.58 (d, $J$ = 8.8 Hz, 2 H), 7.44-7.43 (d, $J$ = 8.2 Hz, 16 H), 7.08-7.07 (d, $J$ = 8.9 Hz, 4 H), 6.92-6.90 (d, $J$ = 8.9 Hz, 4 H), 6.83-6.81 (d, $J$ = 8.8, 2 H), 6.65-6.63 (m, 12 H), 6.51-6.49 (m, 6 H), 5.06 (s, 16 H), 4.94, (s, 12 H), 3.88 (s, 24 H); $^1$C NMR (125 MHz, CDCl$_3$) $\delta$ 190.26, 166.74, 159.88, 156.39, 153.90, 141.85, 139.41, 139.25, 139.15, 131.37, 129.90, 129.85, 129.73, 128.01, 127.97, 126.96, 117.01, 115.99, 106.52, 101.61, 70.18, 69.86, 69.43, 52.14; MS (MALDI) m/z 2221.68 (M$^+$).
2-[2-(2-(3-Aminopropoxy)-4-diethylaminophenyl)-vinyl]-5-[2-(4-diethy lamino-2-(2-methoxyethoxy)phenyl)vinyl]terephthalonitrile (27). HCl (3 M, 10 mL) was added to a solution of 26 (0.5 g, 0.71 mmol) in THF (25 mL) and stirred at ambient temperature for 12 h. Sodium hydroxide (5 M, 50 mL) was added and the aqueous layer extracted with CH₂Cl₂ (3 x 25 mL). The combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness. The crude product was purified by flash column chromatography (SiO₂, 95:5 CH₂Cl₂ / triethylamine) to give 27 as a red solid. Yield: 0.40 g (90%): ¹H NMR (500 MHz, CDCl₃) δ 7.93-7.91 (m, 2 H), 7.51-7.32 (m, 4 H), 6.32-6.27 (m, 3 H), 6.19-6.15 (m, 3 H), 4.14-4.11 (t, J = 6.5 Hz, 2 H), 3.89-3.85 (t, J = 6.9 Hz, 4 H), 3.50 (s, 3 H), 3.39-3.35 (q, J = 7.2 Hz, 8 H), 3.00-2.98 (m, 2 H), 2.09-2.07 (m, 2 H), 1.78 (br s, 2 H), 1.24-1.22 (t, J = 7.2 Hz, 12 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 158.76, 149.74, 139.24, 139.12, 130.36, 130.13, 129.84, 129.59, 129.26, 128.77, 128.51, 126.95, 117.45, 117.11, 113.80, 105.18, 104.50, 96.20, 95.06, 71.13, 68.39, 66.02, 59.31, 52.96, 44.56, 39.36, 32.98, 12.70, 12.67; MS (FAB) m/z 622.19 (M⁺).

**General procedure for the synthesis of dendritic azides**

Sodium azide (1.03 equiv.) and the dendritic bromide (1.0 equiv.) were stirred in DMF at 100°C for 12 h. The reaction mixture was cooled and the solvent was removed in vacuo, and the residue partitioned between a mixture of CH₂Cl₂ and water (1:1, 50 mL). The aqueous layer was extracted with CH₂Cl₂ (3 x 25 mL), and the combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness to give the final product.
(CO$_2$Me)$_2$-[G0]-N$_3$ (31). Compound 31$^{3,41}$ was prepared as follows: according to the general procedure, sodium azide (0.59 g, 9.0 mmol) and 28 (2.0 g, 8.7 mmol) in DMF (30 mL) at elevated temperature gave 31 as a colorless oil. Yield: 1.52 g (91%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.05-8.02 (d, $J$ = 8.3 Hz, 2 H), 7.48-7.44 (d, $J$ = 8.3 Hz, 2 H), 5.08 (s, 2 H), 4.24 (s, 2 H), 3.90 (s, 3 H).

(CO$_2$Me)$_2$-[G1]-N$_3$ (32). By following the general procedure, sodium azide (0.18 g, 2.7 mmol) and 29 (1.3 g, 2.6 mmol) in DMF (30 mL) at elevated temperature gave 32 as a colorless solid. Yield: 1.15 g (96%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.05-8.02 (d, $J$ = 8.3 Hz, 4 H), 7.48-7.44 (d, $J$ = 8.3 Hz, 4 H), 6.53 (s, 3 H), 5.08 (s, 4 H), 4.24 (s, 2 H), 3.90 (s, 6 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 166.75, 159.95, 141.74, 137.92, 129.79, 128.37, 126.95, 107.32, 101.86, 69.45, 54.70, 52.12; MS (FAB) m/z 462.02 (M$^+$).

(CO$_2$Me)$_4$-[G2]-N$_3$ (33). According to the general procedure, sodium azide (0.04 g, 0.6 mmol) and 30 (0.5 g, 0.5 mmol) in DMF (30 mL) at elevated temperature gave 33 as a colorless solid. Yield: 0.47 g (99%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.02-8.00 (d, $J$ = 8.3 Hz, 8 H), 7.45-7.44 (d, $J$ = 8.3 Hz, 8 H), 6.64-6.63 (m, 4 H), 6.51-6.48 (m, 5 H), 5.07 (s, 8 H), 4.95 (s, 4 H), 4.22 (s, 2 H), 3.89 (s, 12 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 166.76, 160.03, 159.87, 141.86, 139.30, 129.86, 129.71, 126.95, 107.20, 106.44, 101.80, 101.66, 69.84, 69.41, 54.74, 52.12; MS (MALDI) m/z 1004.45 (M$^+$).
General procedure for the reduction of dendritic azides

The dendritic azide (1 equiv.) and triphenylphosphine (2 equiv.) were dissolved in THF which was followed by the slow addition of water (10 equiv.) and stirring at 45°C for 12 h. The reaction mixture was cooled and the solvent removed in vacuo. The residue was partitioned between a mixture of CH₂Cl₂ and water (1:1, 50 mL) and the aqueous layer extracted with CH₂Cl₂ (3 x 25 mL). The combined organic extracts were dried (MgSO₄), filtered, and evaporated to dryness. The crude product was purified by gradient flash column chromatography (SiO₂, CH₂Cl₂ - 95:5 CH₂Cl₂ / triethylamine) to give the final product.

(CO₂Me)-[G0]-NH₂ (34). Compound 34 was prepared as follows: according to the general procedure, triphenylphosphine (4.1 g, 15.6 mmol), 31 (1.5 g, 7.8 mmol), and water (1.4 g, 78 mmol) in THF (30 mL) at elevated temperature gave 34 as an orange oil. Yield: 1.09 g (84%): ¹H NMR (250 MHz, CDCl₃) δ 8.04-8.01 (d, J = 8.3 Hz, 2 H), 7.47-7.44 (d, J = 8.3 Hz, 2 H), 5.08 (s, 2 H), 3.90 (s, 3 H), 3.79 (s, 2 H), 1.37 (br s, 2 H).

(CO₂Me)₂-[G1]-NH₂ (35). By following the general procedure, triphenylphosphine (1.1 g, 4.0 mmol), 32 (0.9 g, 2 mmol), and water (0.4 g, 20 mmol) in THF (30 mL) at elevated temperature gave 35 as a yellow oil. Yield: 0.61 g (72%): ¹H NMR (250 MHz, CDCl₃) δ 8.04-8.01 (d, J = 8.3 Hz, 4 H), 7.47-7.44 (d, J = 8.3 Hz, 4 H), 6.56-6.55 (m, 2 H), 6.46-6.44 (m, 1 H), 5.08 (s, 4 H), 3.90 (s, 6 H), 3.79 (s, 2 H), 1.37 (br s, 2 H); ¹³C NMR (62.9
MHz, CDCl₃) δ 166.78, 159.82, 146.16, 142.06, 129.86, 129.68, 126.95, 106.25, 100.44, 69.34, 52.11, 46.52; MS (FAB) m/z 436.03 (M⁺).

(CO₂Me)₄-[G₂]-NH₂ (36). According to the general procedure, triphenylphosphine (0.26 g, 1.0 mmol), 33 (0.48 g, 0.5 mmol), and water (0.09 g, 5.0 mmol) in THF (30 mL) at elevated temperature gave 36 as a colorless solid. Yield: 0.45 g (96%); ¹H NMR (500 MHz, CDCl₃) δ 8.02-8.00 (d, J = 8.3 Hz, 8 H), 7.45-7.44 (d, J = 8.3 Hz, 8 H), 6.64-6.63 (m, 4 H), 6.52-6.51 (m, 4 H), 6.42-6.41 (m, 1 H), 5.07 (s, 8 H), 4.94 (s, 4 H), 3.89 (s, 12 H), 3.77 (s, 2 H), 1.82 (br s, 2 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 166.76, 157.36, 159.84, 159.83, 141.89, 139.59, 131.95, 129.86, 128.58, 126.96, 106.45, 106.11, 101.58, 100.39, 69.75, 69.40, 52.11, 46.46; MS (MALDI) m/z 976.29 (M⁺).

General procedure for the synthesis of dendritic isothiocyanates

A solution of thiophosgene (1 equiv.) in ethyl acetate was cooled to 0°C to which a solution of the dendritic amine (1 equiv.) and triethylamine (2 equiv.) in ethyl acetate was slowly added. The mixture slowly warmed to ambient temperature and was stirred for 12 h under an inert atmosphere. The reaction mixture was then washed with water (2 x 25 mL) and brine (25 mL) and the organic fraction was dried (MgSO₄), filtered, and evaporated to dryness to give the final product.

(CO₂Me)₄-[G₀]-NCS (37). Compound 37 was prepared as follows: according to the general procedure, triethylamine (0.84 mL, 6.0 mmol) and 34 (0.5 g, 3.0 mmol) in ethyl...
acetate (10 mL) was added to thiophosgene (0.23 mL, 3.0 mmol) in ethyl acetate (25 mL) at 0°C and gave 37 as a red oil. Yield: 0.40 g (65%): \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.03-7.99 (d, \(J = 8.2\) Hz, 2 H), 7.36-7.33 (d, \(J = 8.2\) Hz, 2 H), 4.74 (s, 2 H), 3.88 (s, 3 H).

\((\text{CO}_2\text{Me})_2-\text{[G1]}\)-NCS (38). By following the general procedure, triethylamine (0.23 mL, 2.0 mmol) and 35 (0.4 g, 1 mmol) in ethyl acetate (10 mL) was added to thiophosgene (0.07 mL, 1 mmol) in ethyl acetate (25 mL) at 0°C and gave 38 as a red solid. Yield: 0.26 g (58%): \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.05-8.02 (d, \(J = 8.3\) Hz, 4 H), 7.48-7.45 (d, \(J = 8.3\) Hz, 4 H), 6.52 (s, 3 H), 5.08 (s, 4 H), 4.62 (s, 2 H), 3.91 (s, 6 H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)) \(\delta\) 166.75, 160.04, 141.61, 136.77, 129.93, 129.86, 126.99, 106.08, 101.88, 69.52, 52.15, 48.59; MS (FAB) \(m/z\) 477.99 (M\(^+\)).

\((\text{CO}_2\text{Me})_4-\text{[G2]}\)-NCS (39). According to the general procedure, triethylamine (0.13 mL, 0.9 mmol) and 36 (0.42 g, 0.45 mmol) in ethyl acetate (10 mL) was added to thiophosgene (0.03 mL, 0.45 mmol) in ethyl acetate (25 mL) at 0°C and gave 39 as a red solid. Yield: 0.23 g (52%): \(^1\)H NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.03-8.00 (d, \(J = 8.2\) Hz, 8 H), 7.46-7.43 (d, \(J = 8.2\) Hz, 8 H), 6.64-6.63 (m, 4 H), 6.53-6.52 (m, 2 H), 6.47-6.45 (m, 3 H), 5.08 (s, 8 H), 4.95 (s, 4 H), 4.59 (s, 2 H), 3.90 (s, 12 H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)) \(\delta\) 166.76, 160.13, 159.91, 141.86, 139.23, 136.56, 129.87, 129.74, 126.96, 106.42, 105.91, 101.80, 101.72, 69.90, 69.43, 52.14, 48.60; MS (MALDI) \(m/z\) 1058.45 (M+K\(^+\)).
General procedure for the coupling of the dendritic isothiocyanates to the TPA dyes

The dendritic isothiocyanate (1 equiv.) and TPA dye (1 equiv.) in THF were stirred under an inert atmosphere and at ambient temperature for 12 h. The progress of the reaction was monitored until no isothiocyanate was seen by TLC (1:1 hexanes / ethyl acetate). The solvent was removed *in vacuo*, and the crude material was purified by flash column chromatography (SiO₂, 1:1 hexanes / ethyl acetate) to give the desired product.

(CO₂Me)-[G0]-bis-styryl benzene TPA dye (40). Following the general procedure, 25 (0.21 g, 0.36 mmol) and 37 (0.08 g, 0.36 mmol) in THF (10 mL) at ambient temperature gave 40 as a yellow solid. Yield: 203 mg (72%): ¹H NMR (250 MHz, CDCl₃) δ 7.82-7.78 (d, J = 8.3 Hz, 2 H), 7.45-7.25 (m, 10 H), 7.06-7.02 (d, J = 8.3 Hz, 2 H), 6.92-6.78 (m, 2 H), 6.34-6.27 (m, 2 H), 6.21 (s, 1 H), 6.09 (s, 1 H), 4.39 (br s, 2 H), 4.19-4.11 (m, 4 H), 3.89-3.72 (m, 5 H), 3.49 (s, 3 H), 3.37-3.31 (m, 8 H), 2.14-2.12 (m, 2 H), 1.20-1.14 (t, J = 6.9 Hz, 12 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 182.16, 157.74, 156.78, 148.61, 137.85, 135.93, 129.70, 128.96, 128.18, 127.56, 127.11, 126.36, 125.96, 125.26, 123.76, 123.57, 122.58, 114.80, 105.36, 97.06, 95.70, 71.27, 68.43, 59.31, 51.95, 47.76, 44.52, 28.49, 12.69; MS (MALDI) m/z 778.07 (M⁺).

(CO₂Me)₂-[G1]-bis-styryl benzene TPA dye (41). According to the general procedure, 25 (0.06 g, 0.10 mmol) and 38 (0.05 g, 0.10 mmol) in THF (10 mL) at ambient temperature gave 41 as a yellow solid. Yield: 70.4 mg (67%): ¹H NMR (250 MHz, CDCl₃) δ 8.00-7.97 (d, J = 8.3 Hz, 4 H), 7.40-7.24 (m, 12 H), 6.87-6.77 (m, 2 H), 6.37-
6.36 (m, 1 H), 6.31 (s, 1 H), 6.29-6.25 (m, 5 H), 6.18 (s, 1 H), 6.12 (s, 1 H), 5.98 (br s, 2 H), 4.89 (s, 4 H), 4.35-4.32 (m, 2 H), 4.12-4.10 (m, 4 H), 3.88 (s, 6 H), 3.79-3.75 (m, 4 H), 3.45 (s, 3 H), 3.36-3.28 (m, 8 H), 1.19-1.12 (m, 12 H); \(^1^3\)C NMR (62.9 MHz, CDCl\(_3\)) \(\delta\) 182.37, 166.81, 159.71, 157.68, 156.96, 148.66, 142.00, 137.65, 136.04, 129.74, 129.51, 128.02, 126.95, 126.26, 125.95, 125.02, 123.72, 123.44, 122.52, 114.67, 114.15, 106.36, 105.32, 101.34, 96.92, 96.03, 71.21, 69.17, 68.31, 59.27, 53.39, 52.05, 44.47, 30.88, 28.48, 12.68; MS (MALDI) m/z 1048.50 (M\(^+\)).

(CO\(_2\)Me)\(_4\)[G2]-bis-styryl benzene TPA dye (42). Following the general procedure, 25 (0.05 g, 0.09 mmol) and 39 (0.09 g, 0.09 mmol) in THF (10 mL) at ambient temperature gave 42 as a yellow solid. Yield: 86.2 mg (62%). \(^1^H\) NMR (250 MHz, CDCl\(_3\)) \(\delta\) 8.01-7.98 (d, \(J = 8.3\) Hz, 8 H), 7.40-7.24 (m, 16 H), 6.87-6.77 (m, 2 H), 6.37-6.36 (m, 4 H), 6.31 (s, 1 H), 6.29-6.25 (m, 6 H), 6.18-6.13 (m, 5 H), 5.98 (br s, 2 H), 4.95 (s, 4 H), 4.89 (s, 8 H), 4.36-4.33 (m, 2 H), 4.13-4.10 (m, 4 H), 3.88 (s, 12 H), 3.79-3.76 (m, 4 H), 3.44 (s, 3 H), 3.35-3.28 (m, 8 H), 1.18-1.11 (m, 12 H); \(^1^3\)C NMR (62.9 MHz, CDCl\(_3\)) \(\delta\) 183.23, 166.82, 159.71, 157.68, 156.95, 148.66, 143.27, 142.03, 137.65, 136.04, 129.71, 129.51, 128.02, 126.95, 126.26, 125.95, 125.43, 125.02, 123.72, 123.44, 122.52, 114.67, 114.15, 106.36, 105.32, 104.72, 101.34, 96.92, 96.03, 95.73, 71.21, 69.17, 68.31, 67.57, 59.27, 53.39, 52.05, 44.47, 42.12, 30.88, 28.48, 12.68; MS (MALDI) m/z 1589.56 (M\(^+\)).

(CO\(_2\)Me)-[G0]-bis-styryl benzene dicyano-TPA dye (43). Following the general procedure, 27 (0.10 g, 0.16 mmol) and 37 (0.03 g, 0.16 mmol) in THF (10 mL) at
ambient temperature gave 43 as a red solid. Yield: 88.4 mg (68%): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.08-7.85 (m, 5 H), 7.44-7.19 (m, 8 H), 6.32-6.26 (m, 2 H), 6.19 (s, 1 H), 6.12 (s, 1 H), 4.94 (br s, 2 H), 4.20-4.14 (m, 4 H), 3.90-3.84 (m, 8 H), 3.73 (s, 3 H), 3.48-3.36 (m, 8 H), 2.26-2.24 (m, 2 H), 1.20-1.14 (t, $J$ = 6.9 Hz, 12 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 182.11, 158.85, 149.81, 137.81, 132.96, 129.93, 129.51, 128.85, 127.40, 126.96, 125.42, 124.26, 118.21, 118.01, 117.43, 117.04, 105.19, 103.97, 96.19, 71.13, 68.37, 67.96, 59.24, 52.09, 44.64, 44.59, 28.91, 12.69; MS (MALDI) m/z 829.48 (M$^+$).

(CO$_2$Me)$_2$-[G1]-bis-styryl benzene dicyano-TPA dye (44). According to the general procedure, 27 (0.06 g, 0.10 mmol) and 38 (0.05 g, 0.10 mmol) in THF (10 mL) at ambient temperature gave 44 as a red solid. Yield: 66.8 mg (63%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.00-7.96 (d, $J$ = 8.2 Hz, 4 H), 7.80-7.78 (m, 2 H), 7.43-7.33 (m, 7 H), 7.23-7.15 (m, 3 H), 6.62-6.61 (m, 1 H), 6.52-6.51 (m, 2 H), 6.43 (s, 1 H), 6.29-6.23 (m, 3 H), 6.16-6.12 (m, 2 H), 5.00 (s, 4 H), 4.51-4.49 (m, 2 H), 4.17-4.13 (m, 4 H), 3.89-3.80 (m, 10 H), 3.41-3.32 (m, 11 H), 2.24 (br s, 2 H), 1.21-1.15 (t, $J$ = 6.9 Hz, 12 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 182.20, 166.73, 159.84, 158.81, 149.75, 141.84, 139.16, 131.38, 129.84, 129.59, 128.71, 128.45, 126.90, 118.11, 117.84, 117.42, 116.97, 113.94, 112.93, 112.07, 106.76, 105.10, 104.47, 101.28, 96.08, 94.95, 71.08, 69.38, 68.25, 59.18, 52.10, 46.18, 44.55, 29.91, 28.90, 12.68; MS (MALDI) m/z 1098.44 (M$^+$).

(CO$_2$Me)$_4$-[G2]-bis-styryl benzene dicyano-TPA dye (45). Following the general procedure, 27 (0.05 g, 0.08 mmol) and 39 (0.08 g, 0.08 mmol) in THF (10 mL) at
ambient temperature gave 45 as a red solid. Yield: 77.9 mg (59%): \[^1\text{H NMR}\] (250 MHz, CDCl\textsubscript{3}) δ 8.01-7.97 (d, \(J=8.2\) Hz, 8 H), 7.81-7.77 (m, 2 H), 7.42-7.34 (m, 11 H), 7.21-7.11 (m, 3 H), 6.63-6.62 (m, 1 H), 6.51-6.49 (m, 4 H), 6.41 (s, 1 H), 6.29-6.25 (m, 5 H), 6.18-6.11 (m, 5 H), 5.62 (br s, 2 H), 4.97 (s, 4 H), 4.92 (s, 8 H), 4.50-4.48 (m, 2 H), 4.15-4.10 (m, 4 H), 3.88-3.78 (m, 16 H), 3.44-3.28 (m, 11 H), 1.20-1.14 (m, 12 H); \[^13\text{C NMR}\] (62.9 MHz, CDCl\textsubscript{3}) δ 181.31, 166.71, 159.82, 158.61, 149.86, 142.57, 141.89, 139.35, 131.27, 129.81, 129.51, 128.72, 128.38, 126.99, 126.26, 118.23, 117.92, 117.39, 116.84, 114.03, 113.52, 112.97, 112.09, 106.76, 105.12, 104.52, 101.34, 96.71, 96.03, 94.73, 71.11, 69.39, 68.31, 67.59, 59.24, 52.31, 46.07, 44.48, 42.15, 30.02, 28.98, 12.68; MS (MALDI) \(m/z\) 1639.71 (M\(^+\)).

**General procedure for the saponification of dendritic esters**

The dendritic ester (1 equiv.) was added to a solution of KOTBu in DMSO (1 M, 10 equiv./ester) and stirred at ambient temperature for 12 h. The reaction mixture was poured over ice and acidified with 0.1 M HCl until pH = 2.0. The product was extracted with ethyl acetate (3 x 10 mL), and the combined organic fractions were dried (Na\textsubscript{2}SO\textsubscript{4}), filtered, and evaporated to dryness.

(CO\textsubscript{2}H)-[G0]-bis-styryl benzene TPA dye (46). Following the general procedure, 40 (0.1 g, 0.13 mmol) and 1 M KOTBu in DMSO (1.3 mL, 1.3 mmol) at ambient temperature gave 46 as a yellow solid. Yield: 94.4 mg (95%): \[^1\text{H NMR}\] (250 MHz, CDCl\textsubscript{3}) δ 7.84-7.79 (d, \(J=8.3\) Hz, 2 H), 7.46-7.25 (m, 10 H), 7.08-7.04 (d, \(J=8.3\) Hz, 2 H), 6.91-6.75
(CO₂H)₂-[G1]-bis-styryl benzene TPA dye (47). According to the general procedure, 41 (0.05 g, 0.05 mmol) and 1 M KOTBu in DMSO (0.5 mL, 0.5 mmol) at ambient temperature gave 47 as a yellow solid. Yield: 46.4 mg (91%); ¹H NMR (250 MHz, CDCl₃) δ 8.02-7.99 (d, J = 8.3 Hz, 4 H), 7.43-7.27 (m, 12 H), 6.85-6.75 (m, 2 H), 6.37-6.35 (m, 1 H), 6.30 (s, 1 H), 6.27-6.23 (m, 5 H), 6.16 (s, 1 H), 6.10 (s, 1 H), 5.12 (br s, 2 H), 4.81 (s, 4 H), 4.36-4.31 (m, 2 H), 4.16-4.12 (m, 4 H), 3.75-3.71 (m, 4 H), 3.41 (s, 3 H), 3.32-3.24 (m, 8 H), 1.22-1.16 (m, 12 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 182.37, 174.61, 159.75, 157.62, 156.12, 148.34, 142.13, 137.85, 136.01, 129.64, 129.57, 128.12, 126.99, 126.36, 125.85, 125.22, 123.72, 123.44, 122.52, 114.77, 114.15, 106.31, 105.32, 101.31, 96.95, 95.91, 71.22, 69.15, 68.43, 59.27, 47.95, 44.27, 30.81, 28.48, 12.69; MS (MALDI) m/z 1020.46 (M⁺).

(CO₂H)₄-[G2]-bis-styryl benzene TPA dye (48). Following the general procedure, 42 (0.05 g, 0.03 mmol) and 1 M KOTBu in DMSO (0.3 mL, 0.3 mmol) at ambient temperature gave 48 as a yellow solid. Yield: 42.0 mg (87%); ¹H NMR (250 MHz,
CDCl₃ δ 8.03-7.99 (d, J = 8.3 Hz, 8 H), 7.42-7.26 (m, 16 H), 6.89-6.79 (m, 2 H), 6.38-6.36 (m, 4 H), 6.32 (s, 1 H), 6.28-6.24 (m, 6 H), 6.19-6.12 (m, 5 H), 5.28 (br s, 2 H), 4.91 (s, 4 H), 4.87 (s, 8 H), 4.37-4.33 (m, 2 H), 4.15-4.12 (m, 4 H), 3.77-3.72 (m, 4 H), 3.41 (s, 3 H), 3.33-3.27 (m, 8 H), 1.21-1.15 (t, J = 6.9 Hz, 12 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 183.23, 174.62, 159.72, 157.64, 156.15, 148.36, 143.23, 142.12, 137.81, 136.03, 129.61, 129.55, 128.11, 126.97, 126.32, 125.84, 125.23, 125.00, 123.72, 123.41, 122.50, 114.72, 114.12, 106.34, 105.31, 104.70, 101.32, 96.92, 96.03, 95.93, 71.21, 69.16, 68.41, 67.55, 59.25, 47.99, 44.21, 42.10, 30.82, 28.48, 12.69; MS (MALDI) m/z 1555.91 (M + Na⁺).

(CO₂H)₂-[G0]-bis-styryl benzene dicyano-TPA dye (49). Following the general procedure, 43 (0.05 g, 0.06 mmol) and 1 M KOTBu in DMSO (0.6 mL, 0.6 mmol) at ambient temperature gave 49 as a red solid. Yield: 36.9 mg (75%): ¹H NMR (500 MHz, CDCl₃) δ 8.09-7.82 (m, 5 H), 7.45-7.18 (m, 8 H), 6.31-6.24 (m, 2 H), 6.17 (s, 1 H), 6.11 (s, 1 H), 5.24 (br s, 2 H), 4.22-4.15 (m, 4 H), 3.91-3.86 (m, 5 H), 3.71 (s, 3 H), 3.45-3.32 (m, 8 H), 2.21-2.18 (m, 2 H), 1.21-1.15 (t, J = 6.9 Hz, 12 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 182.11, 174.65, 148.71, 137.80, 133.26, 129.63, 129.50, 128.55, 127.10, 126.96, 125.22, 124.23, 118.24, 118.02, 117.41, 117.07, 105.09, 104.27, 96.59, 71.23, 68.39, 67.66, 59.24, 44.64, 44.29, 28.41, 12.69; MS (MALDI) m/z 814.43 (M⁺).

(CO₂H)₂-[G1]-bis-styryl benzene dicyano-TPA dye (50). According to the general procedure, 44 (0.05 g, 0.05 mmol) and 1 M KOTBu in DMSO (0.5 mL, 0.5 mmol) at ambient temperature gave 50 as a red solid. Yield: 32.6 mg (67%): ¹H NMR (250 MHz,
CDCl\textsubscript{3} \( \delta \) 8.04-7.99 (d, \( J = 8.2 \) Hz, 4 H), 7.87-7.82 (m, 2 H), 7.44-7.31 (m, 7 H), 7.22-7.14 (m, 3 H), 6.63-6.61 (m, 1 H), 6.52-6.50 (m, 2 H), 6.42 (s, 1 H), 6.27-6.21 (m, 3 H), 6.15-6.10 (m, 2 H), 5.02 (s, 4 H), 4.53-4.49 (m, 2 H), 4.21-4.17 (m, 4 H), 3.88-3.81 (m, 4 H), 3.43-3.35 (m, 11 H), 3.24 (br s, 2 H), 1.21-1.16 (t, \( J = 6.9 \) Hz, 12 H); \(^{13}\)C NMR (62.9 MHz, CDCl\textsubscript{3}) \( \delta \) 182.20, 174.63, 159.82, 158.85, 148.75, 141.81, 138.16, 132.38, 129.84, 129.61, 128.72, 128.55, 126.94, 118.21, 117.94, 117.42, 116.99, 113.97, 112.91, 112.17, 106.71, 105.11, 104.21, 101.23, 96.58, 94.91, 71.28, 69.31, 68.35, 59.28, 44.63, 44.25, 29.92, 28.40, 12.69; MS (MALDI) \( m/z \) 1071.47 (M\(^+\)).

**(CO\textsubscript{2}Me)-[M]-[G1]-OH (52).** A slurry of acetone (125 mL), 28 (5.0 g, 21.8 mmol), 51 (12.2 g, 87.1 mmol), potassium carbonate (3.46 g, 25 mmol), and 18-crown-6 (0.58 g, 2.2 mmol) was then maintained at reflux for 12 h. After cooling the reaction to RT, the solvent was removed \textit{in vacuo}, and the residue was taken up in a mixture of H\textsubscript{2}O/CH\textsubscript{2}Cl\textsubscript{2} (1:1), and the organic layer was removed. The aqueous portion was extracted with CH\textsubscript{2}Cl\textsubscript{2} (3 x 75 mL). The organic layers were combined, dried (MgSO\textsubscript{4}), filtered, and concentrated to a thick, yellow oil. Flash chromatography of the crude product (SiO\textsubscript{2}, 4:1 CH\textsubscript{2}Cl\textsubscript{2} / Et\textsubscript{2}O) gave 52 as a colorless solid (3.67 g, 58%): \(^1\)H NMR (250 MHz, CDCl\textsubscript{3}) \( \delta \) 7.99-7.95 (d, \( J = 8.3 \) Hz, 2 H), 7.42-7.38 (d, \( J = 8.3 \) Hz, 2 H), 6.57-6.56 (m, 2 H), 6.44 (m, 1 H), 4.99 (s, 2 H), 4.56 (s, 2 H), 3.85 (s, 3 H); \(^{13}\)C NMR (62.9 MHz, CDCl\textsubscript{3}) \( \delta \) 167.42, 163.13, 159.27, 144.34, 143.18, 129.92, 128.75, 126.41, 106.89, 104.94, 101.52, 79.26, 68.57, 52.88.
(p-CO₂Me)-(m-NO₂)-(G1)-OH (54). Following the procedure for 52, acetone (50 mL), 52 (3.55 g, 12.3 mmol), 53 (2.7 g, 12.5 mmol), potassium carbonate (2.59 g, 18.8 mmol), and 18-crown-6 (0.26 g, 0.98 mmol) gave, after flash chromatography (SiO₂, 1:1 Hexane / EtOAc), dendron 54 as a colorless powder (4.89 g, 94%): ¹H NMR (250 MHz, CDCl₃) δ 8.26 (m, 1 H), 8.16-8.13 (d, J = 8.1 Hz, 1 H), 8.03-8.00 (d, J = 6.6 Hz, 2 H), 7.73-7.70 (d, J = 7.7 Hz, 1 H), 7.56-7.50 (m, 1 H), 7.47-7.43 (d, J = 6.7 Hz, 2 H), 6.62-6.61 (m, 2 H), 6.50-6.48 (m, 1 H), 5.09-5.08 (m, 4 H), 4.62 (s, 2 H), 3.89 (s, 3 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 168.13, 162.46, 148.67, 144.22, 143.79, 140.53, 132.11, 129.78, 129.42, 126.98, 122.76, 122.47, 105.72, 100.34, 76.91, 75.27, 68.52, 52.81.

(CO₂Me)₃-[M]-[G2]-OH (55). Following the procedure for 52, acetone (100 mL), 29 (2.3 g, 4.6 mmol), 51 (2.58 g, 18.4 mmol), potassium carbonate (0.83 g, 6 mmol), and 18-crown-6 (0.11 g, 0.37 mmol) gave, after flash chromatography (SiO₂, 7:3 CH₂Cl₂/Et₂O), 55 as a colorless powder (1.51 g, 59%): ¹H NMR (250 MHz, CDCl₃) δ 8.03-7.99 (d, J = 8.1 Hz, 4 H), 7.46-7.43 (d, J = 8.1 Hz, 4 H), 6.58 (m, 2 H), 6.46-6.37 (m, 4 H), 6.23-6.21 (m, 1 H), 5.08 (s, 4 H), 4.93 (s, 2 H), 3.90 (s, 6 H); ¹³C NMR (62.9 MHz, CDCl₃) δ 167.42, 163.76, 163.13, 159.28, 144.30, 143.19, 142.93, 129.95, 128.77, 126.41, 106.83, 105.78, 105.49, 101.51, 98.56, 79.22, 78.30, 68.54, 52.87.

(p-CO₂Me)-(m-NO₂)-(G1)-Br (56). To a solution of 54 (1.48 g, 3.5 mmol) in a minimum amount of dry THF was added triphenylphosphine (1.1 g, 4.2 mmol) and carbon tetrabromide (1.74 g, 5.25 mmol). Additional portions of CBr₄ and PPh₃ were
added as necessary until the reaction mixture turned a dark yellow. The reaction was poured into water immediately after the color change and extracted with CH₂Cl₂ (3 x 25 mL). The combined extracts were dried (MgSO₄), filtered, and evaporated to dryness to give a colorless, powdery residue. Purification by flash chromatography (SiO₂, 8:2 hexanes/EtOAc) gave the product as a fluffy, colorless powder (1.65 g, 97%): 

\[ ^1H \text{ NMR (250 MHz, CDCl}_3 \] \( \delta \) 8.29 (m, 1 H), 8.18-8.15 (d, \( J = 8.1 \) Hz, 1 H), 8.05-8.02 (d, \( J = 8.3 \) Hz, 2 H), 7.75-7.72 (d, \( J = 8.0 \) Hz, 1 H), 7.58-7.53 (m, 1 H), 7.48-7.45 (d, \( J = 8.2 \) Hz, 2 H), 6.64-6.63 (m, 2 H), 6.51-6.49 (m, 1 H), 5.11-5.08 (m, 4 H), 4.40 (s, 2 H), 3.90 (s, 3 H); 

\[ ^{13}C \text{ NMR (62.9 MHz, CDCl}_3 \] \( \delta \) 167.49, 162.44, 148.67, 144.23, 143.77, 140.26, 132.19, 129.74, 129.42, 126.98, 122.73, 122.45, 106.31, 100.36, 80.43, 76.96, 52.80, 38.73.

\((p-CO_2Me)_3-(m-NO_2)-[G2]-OH (57)\). Following the procedure for 52, acetone (75 mL), 55 (2.23 g, 4.0 mmol), 56 (2.04 g, 4.2 mmol), potassium carbonate (1.11 g, 8 mmol), and 18-crown-6 (0.09 g, 0.34 mmol) gave, after flash chromatography (SiO₂, 9:1 CH₂Cl₂/Et₂O), 57 as a pale yellow powder (2.97 g, 77%): 

\[ ^1H \text{ NMR (250 MHz, CDCl}_3 \] \( \delta \) 8.26 (m, 1 H), 8.26 (m, 1 H), 8.16-8.13 (d, \( J = 8.1 \) Hz, 1 H), 8.02-7.99 (d, \( J = 6.6 \) Hz, 6 H), 7.73-7.70 (d, \( J = 7.7 \) Hz, 1 H), 7.56-7.50 (m, 1 H), 7.47-7.43 (d, \( J = 6.7 \) Hz, 6 H), 6.63 (m, 4 H), 6.54-6.51 (m, 4 H), 6.42 (m, 1 H), 5.07 (m, 8 H), 4.94 (s, 4 H), 4.58 (s, 2 H), 3.89 (s, 9 H); 

\[ ^{13}C \text{ NMR (62.9 MHz, CDCl}_3 \] \( \delta \) 167.41, 162.43, 148.65, 144.24, 143.77, 140.51, 132.12, 129.78, 129.54, 129.37, 126.95, 122.78, 122.40, 105.73, 100.31, 77.56, 76.92, 75.27, 69.14, 52.88.
(p-CO$_2$Me)-(m-NH$_2$)-[G1]-OH (58). A slurry of 78% EtOH (25 mL), 54 (1.0 g, 2.4 mmol), zinc dust (5 g), and calcium chloride (0.2 g) was maintained at reflux for 2 h. After cooling the reaction to RT, the zinc was filtered off, and washed with EtOAc. The filtrate was extracted with EtOAc (3 x 20 mL), and the combined organic extracts were dried (MgSO$_4$), filtered, and concentrated to give the desired product as a red-orange solid (0.74 g, 80%): $^1$H NMR (250 MHz, CDCl$_3$) $\delta$ 8.02-7.98 (d, $J$ = 8.2 Hz, 2 H), 7.45-7.41 (d, $J$ = 8.2 Hz, 2 H), 7.14-7.08 (m, 1 H), 6.75-6.72 (d, $J$ = 7.7 Hz, 1 H), 6.68 (m, 1 H), 6.61-6.55 (m, 3 H), 6.47-6.46 (m, 1 H), 5.03 (s, 2 H), 4.89 (s, 2 H), 4.56 (s, 2 H), 3.88 (s, 3 H); $^{13}$C NMR (62.9 MHz, CDCl$_3$) $\delta$ 167.41, 162.45, 146.92, 144.27, 143.72, 140.96, 129.72, 129.47, 129.24, 126.95, 118.18, 115.79, 114.11, 105.70, 101.54, 76.92, 69.18, 52.82.
APPENDIX A

$^1$H AND $^{13}$C SPECTRA FOR NOVEL COMPOUNDS SYNTHESIZED IN CHAPTER 2
AU PROG: CARBON, AU
DATE 25-7-2
SF 62.896
SY 93.0
V1 2500000
S1 32768
TO 32768
SW 15151.515
HZ/PT .925
PW 4.2
PO 400
AG 1.081
AE 200
NS 4444
TE 297
FW 19000
GB 40000.000
DP 20H CPD
LB 0.0
GB 0.0
CK 25.00
CY 5.00
F1 220.004P
F2 -4.995P
HZ/CM 555.036
PPM/CW 9.000
SR -4043.65
F2 - Acquisition Parameters
Date: 20020723
Time: 5.09

PROBUD: 5 mm Nikon 1
PUL/PROG: T
TD: 16384
SOLVENT: CDCl3
NS: 16
DS: 2
SWH: 6348.750 Hz
FIDRES: 0.381393 Hz
AQ: 1.3110322 sec
RG: 181
DW: 80.016 usec
DE: 6.00 usec
TE: 300.0 K
D1: 2000000000 usec

********* CHANNEL f1 ***********
NUCL: 1H
PI: 7.00 usec
PL1: 0.00 dB
SFO1: 499.9328112 MHz

F2 - Processing parameters
SI: 32768
SF: 499.930046 MHz
WDW: 0
SSI: 0
LR: 0.00 Hz
CR: 0
PC: 1.00

[Diagram of chemical structure]
F2 - Acquisition Parameters
Date: 20020725
Time: 2:40
INSTRUM: spec
PROBAND: 5 mm盅Cl)
PROG: prog10
TO: 65536
SOLVENT: CDCl3
VS: 10085
DS: 4
SW1: 31446.541 Hz
FIDRES: 0.79838 Hz
AQ: 1.042072 sec
RG: 3250
DW: 15.900 us
DEF: 6.0 us
TF: 0.0 K
DI: 0.00000 sec
DII: 0.00000 sec
DII: 0.00000 sec

********** CHANNEL F1 **********
NUC1: 13C
P1: 5.20 usec
PL1: 0.000 dB
SF01: 125.7219073 MHz

********** CHANNEL F2 **********
CPWPROC: walt16
NUC2: 1H
P2/P21: 22.60 usec
PL2: 120.00 dB
PLC2: 19.00 dB
PLC3: 23.00 dB
SF02: 499.981500 MHz

F2 - Processing parameters
SI: 65536
SF: 125.7075033 MHz
WD: 0
SSB: 0
EB: 0.00 Hz
GB: 0
PC 100
AU PROD: CARBON.AU
DATE 25-7-2
SF 62.896
SV 93.0
CI 2500.000
TD 32768
SW 31515.115
HZ/FT 2.925
PW 4.2
AQ 1.081
RS 300
NS 4666
TE 257
FW 12900
G2 4000.000
JP 20M CPG
LB 0.0
GB 0.0
CX 25.00
CY 0.0
FI 220.004P
F2 -4.985P
HZ/CM 566.036
PPM/CM 9.000
SR -4042.73

(3,5)-t-Bu-[G0]O

(3,5)-t-Bu-[G0]O
F2 - Acquisition Parameters
Date: 20020723
Time: 4:51
INSTRUM: spect
PROBHD: 5 mm Naierac
PULPROG: IF
TD: 16384
SOLVENT: CDC13
NS: 16
ITS: 2
SW1: 6254.750 Hz
FIDRES: 0.3841393 Hz
AQ: 311022 sec
Q: 101.6
DW: 80.016 usec
DE: 6.00 usec
TE: 300.0 K
D1: 2.0000000000 usec

= CHANNEL 1 =
NUCl: 1H
F1: 7.00 usec
PL1: 0.00 dB
SFO1: 499.932752 MHz

F2 - Processing parameters
a1: 12568
SF: 499.9300246 MHz
W/DW: no
SSB: 0
LB: 0.00 Hz
GB: 0
PC: 1.00
F2 - Acquisition Parameters

Date: 20020723
Time: 4:40
INSTRUM: spect
PROBNO: 5 mm Nalorac
PULPRG: zg
TD: 16384
SOLVENT: CDC13
NS: 16
DS: 2
SOLV: 6288.750 Hz
FIDRES: 0.381393 Hz
AQ: 1.321022 sec
RG: 64
DW: 80.016 usec
DE: 6.00 usec
TE: 300.0 K
DI: 2.00000000 sec

F2 - Processing parameters

SI: 32768
SF: 499.930425 MHz
WDW: no
SSB: 0
LB: 0.00 Hz
UB: 0
PC: 1.00
### F2 - Acquisition Parameters

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<tr>
<th>Parameter</th>
<th>Value</th>
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<td>Date</td>
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<tr>
<td>Time</td>
<td>20</td>
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<tr>
<td>INSTRUM spec</td>
<td>Prodigy</td>
</tr>
<tr>
<td>PROBHD</td>
<td>5 mm Dual 13</td>
</tr>
<tr>
<td>T1D</td>
<td>65536</td>
</tr>
<tr>
<td>SOLVENT</td>
<td>CDCl3</td>
</tr>
<tr>
<td>NS</td>
<td>10588</td>
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<tr>
<td>DS</td>
<td>4</td>
</tr>
<tr>
<td>SWH</td>
<td>31466.51 Hz</td>
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<tr>
<td>FIDRES</td>
<td>0.479336 Hz</td>
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<tr>
<td>RG</td>
<td>3251</td>
</tr>
<tr>
<td>DW</td>
<td>15000 usc</td>
</tr>
<tr>
<td>DF</td>
<td>6.00 usc</td>
</tr>
<tr>
<td>TE</td>
<td>0.0 K</td>
</tr>
<tr>
<td>Q1</td>
<td>0.00000000 sec</td>
</tr>
<tr>
<td>Q11</td>
<td>0.00000000 sec</td>
</tr>
<tr>
<td>Q2</td>
<td>0.00000000 sec</td>
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**--- CHANNEL 1 ---**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>NUC1</td>
<td>13C</td>
</tr>
<tr>
<td>FL1</td>
<td>5.20 usc</td>
</tr>
<tr>
<td>PLL1</td>
<td>0.00 db</td>
</tr>
<tr>
<td>SFQ1</td>
<td>125.72 MHz</td>
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</table>

**--- CHANNEL 2 ---**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>NUC2</td>
<td>1H</td>
</tr>
<tr>
<td>NM1</td>
<td>72.60 usc</td>
</tr>
<tr>
<td>PLL2</td>
<td>120.00 db</td>
</tr>
<tr>
<td>PLL1</td>
<td>19.00 db</td>
</tr>
<tr>
<td>PLL3</td>
<td>23.00 db</td>
</tr>
<tr>
<td>SFQ2</td>
<td>499.91500 MHz</td>
</tr>
</tbody>
</table>

### F2 - Processing parameters

<table>
<thead>
<tr>
<th>Value</th>
<th>65536</th>
</tr>
</thead>
</table>

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![Chemical Structure](image1.png)

---

![Chemical Structure](image2.png)

---

![Chemical Structure](image3.png)
<table>
<thead>
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<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Date</td>
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<tr>
<td>Time</td>
<td>2:42</td>
</tr>
<tr>
<td>Instrument</td>
<td>spect</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>5 mm Dual 13</td>
</tr>
<tr>
<td>Pulprog</td>
<td>2ppm</td>
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<tr>
<td>Solvent</td>
<td>CDC13</td>
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<tr>
<td>NS</td>
<td>2238</td>
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<td>DSS</td>
<td>4</td>
</tr>
<tr>
<td>SWH</td>
<td>31466.5 Hz</td>
</tr>
<tr>
<td>PDMR</td>
<td>0.479836 Hz</td>
</tr>
<tr>
<td>AQ</td>
<td>1.042072 sec</td>
</tr>
<tr>
<td>RC</td>
<td>6500</td>
</tr>
<tr>
<td>DW</td>
<td>15468.76 sec</td>
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<tr>
<td>TE</td>
<td>0.000020 sec</td>
</tr>
<tr>
<td>DD1</td>
<td>0.0999999 sec</td>
</tr>
<tr>
<td>DD2</td>
<td>0.03000000 sec</td>
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<td>CHANNEL n</td>
<td></td>
</tr>
<tr>
<td>nuC1</td>
<td>13C</td>
</tr>
<tr>
<td>F1</td>
<td>5.20 usec</td>
</tr>
<tr>
<td>PL1</td>
<td>0.00 dB</td>
</tr>
<tr>
<td>SFQ1</td>
<td>125.7219073 MHz</td>
</tr>
<tr>
<td>CHANNEL n</td>
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</tr>
<tr>
<td>nuC2</td>
<td>1H</td>
</tr>
<tr>
<td>PCPD1</td>
<td>72.60 usec</td>
</tr>
<tr>
<td>PL2</td>
<td>120.00 dB</td>
</tr>
<tr>
<td>PL2</td>
<td>15.00 dB</td>
</tr>
<tr>
<td>PL1</td>
<td>23.00 dB</td>
</tr>
<tr>
<td>SFQ2</td>
<td>499.9315001 MHz</td>
</tr>
<tr>
<td>F2 - Processing parameters</td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>65536</td>
</tr>
<tr>
<td>SF</td>
<td>125.707533 MHz</td>
</tr>
<tr>
<td>W1W</td>
<td>100</td>
</tr>
<tr>
<td>SS</td>
<td>0</td>
</tr>
<tr>
<td>LR</td>
<td>0.00 Hz</td>
</tr>
<tr>
<td>GL</td>
<td>0</td>
</tr>
<tr>
<td>TC</td>
<td>0</td>
</tr>
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</table>

![Chemical Structure](image)
F2 - Acquisition Parameters
Date 20020724
Time 5.44
INSTRUM spect
PROBHD 5 mm NaIcor
PULPROG zg
TD 16384 zg
SOLVENT CDCl3
NS 16
DS 2
SWH 6248.750 Hz
FIORES 0.343393 Hz
AQ 1.310327 sec
RG 101.6
IQ 80.016 usec
DE 6.00 usec
TE 500.0 Hz
DJ 2.00000000 sec

============= CHANNEL 1 ==============
N(C) 1H
F1 7.00 usec
PL1 0.00 dB
SFO1 999.9328752 MHz

F2 - Processing parameters
SI 32768
SF 999.9300246 MHz
WOW mu
SSB 0 Hz
LR 0.00 Hz
GB 0
PC 1.00
F2 - Acquisition Parameters

- Time: 3.45
- INSTRUM: spec
- PREDNFQ: 5 mm Nucleic
- PULPROG: XG
- TD: 163.4°
- SOLVENT: CDCl3

NS = 16
DS = 2
S/NH = 6248,750 Hz
FIDRES = 0.381393 Hz
AQ = 1.311032 sec
RG = 64
DQ = 80.016 usec
DF = 6.00 usec
TE = 80.0 K
DT = 1,00000000 sec

---------------- CHANNEL f1 -----------------
NUC1 = IH
P1 = 0.00 usec
PL1 = 0.00 dB
SP01 = 499,9328732 MHz

F2 - Processing parameters
SI = 32768
SF = 499,9330266 MHz
WDW = no
SSB = 0
L3 = 0.00 Hz
GB = 0
PC = 1.00
Acquisition Parameters

Date: 20020723
Time: 5:55

INSTRUM: spect
PROBH: 5 mm Natural
PULPROG: zg
TD: 16384
SOLVENT: CDCl3
NS: 16
DS: 2
SOL: 6244.750 Hz
FORES: 1.761139 Hz
AQ: 1.310322 sec
RG: 128
DW: 80.016 usec
DE: 6.00 usec
TE: 300.0 K
D1: 2.00000000 sec

Processing parameters
SD: 32768
SF: 499.9328752 MHz
WDW: no

Channel 1
NUC1: 1H
P1: 7.00 usec
PL1: 0.00 dB
SFQ: 499.9328752 MHz

Channel 2
SD: 32768
SF: 499.9300240 MHz
WDW: no

LB: 0.00 Hz
GB: 0
PC: 1.00
**F2 - Acquisition Parameters**

- **Date**: 20020723
- **Time**: 3.33
- **INSTRUM**: spec
- **F negot**: 5 mm Natorac
- **PHILPROG**: 22
- **TD**: 16384
- **SOLVENT**: CDCl3
- **NS**: 32
- **DS**: 2
- **SWH**: 6248.750 Hz
- **FIDRES**: 0.381393 Hz
- **AQ**: 1.31103272 sec
- **RG**: 256
- **JW**: 85.016 usec
- **DE**: 6.00 usec
- **TE**: 300.0 K
- **DI**: 2.00000000 sec

**CHANNEL II**

- **NUCI**: 1H
- **P1**: 7.00 usec
- **P1I**: 0.00 dB
- **SFO1**: 499.9328752 MHz

**F3 - Processing parameters**

- **SI**: 32768
- **SF**: 499.9300246 MHz
- **WDW**: no
- **SSB**: 0
- **LR**: 0.00 Hz
- **GR**: 0
- **PC**: 1.00

---

![Chemical Structure Image]
F2 - Acquisition Parameters

Date: 20020823
Time: 2.31

INSTRUM: spect
PROBND: 5 mm Nucleus
PHILPROG: zg
TD: 16384
SOLVENT: CDC13
NS: 32
DS: 2
SWH: 62.48750 Hz
PDOMES: 0.381393 Hz
AQ: 1.3110352 sec
RU: 256
JW: 50,010 uscc
DE: 6.00 uscc
TE: 300.0 K
DT: 2000000000 sec

********** CHANNEL (1) **********
NUC1: 1H
P1: 7.00 uscc
PL1: 0.00 dB
SPO1: 499.9321752 MHz

F2 - Processing parameters
SL: 32768
SF: 499.9300246 MHz
WDW: no
SSB: 0
LB: 0.00 Hz
GB: 0
PC: 1.00

---

[Image of a chemical structure with labels [G2] and 43]
F2 - Acquisition Parameters
Date  20/03/828
Time  3:31
INSTRUM spec
PRISMID  5 mm Nalorac
PULPROG zg
TD  16384
SOLVENT CDC13
NS  32
DS  2
SWH  624.750 Hz
PIDRES  0.381593 Hz
AQ  1.311022 sec
RG  256
DW  80.016 usec
OE  6.00 usec
TE  300.0 K
D1  2.00000000 sec

---------- CHANNEL 1 ----------
NUCI  1H
PL1  7.00 usec
PL1  0.00 dB
SDO1  499.932872 MHz

F2 - Processing parameters
SI  32768
SF  499.9300246 MHz
WDW  0
SSB  0
LB  0.00 Hz
GB  0
FC  1.00
H2 - Acquisition Parameters

Date: 2002-10-28
Time: 4:38

INSTRUM: spect
PROBHD: 5 mm Nalorac
PULPROG: zg
TD: 16364
SOLVENT: CDCl3
NS: 32
DS: 1
SW: 52488750 Hz
FIDRES: 0.381393 Hz
AQ: 1311022 sec
BG: 2.56
G1W: 80.016 usec
DE: 0.00 usec
TE: 300.0 K
DI: 2000000000 sec

========== CHANNEL (f) ===========

NUC1: 1H
PI: 7.00 usec
PL1: 0.00 dB
SFO1: 499.9928752 MHz

F3 - Processing parameters
SI: 32768
SF: 499.9900246 MHz
WDW: no
SSB: 0
LB: 0.00 Hz
GR: 0
PC: 1.00

---

[Chemical Structure]

---

1.0 0.9 0.8 0.7 0.6 0.5 0.4 0.3 0.2 0.1 0.0 ppm
**F2 - Acquisition Parameters**

- **Date:** 20200407
- **Time:** 1:28
- **INSTRUMENT:** spec
- **PRO/SHD:** 5 mm Dual 13
- **PULPROG:** zgpp30
- **TD:** 65536
- **SOLVENT:** CDCl3
- **NS:** 10314
- **DS:** 4
- **SW11:** 31446.54 Hz
- **FIDRES:** 0.078336 Hz
- **AQ:** 1.0420724 sec
- **RG:** 3251
- **DW:** 15400 usec
- **DE:** 6.00 usec
- **TF:** 0.0 K
- **DI:** 0.699999 sec
- **U1:** 0.000000 sec
- **d1:** 0.000020000 sec

---

**CHANNEL 1**

- **NUC1:** 13C
- **PL1:** 5.20 usec
- **SFO1:** 12572.9073 MHz

---

**CHANNEL 2**

- **NUC2:** 1H
- **PCV2:** 72.60 usec
- **PL2:** 12.00 dB
- **PL3:** 18.00 dB
- **PL4:** 23.00 dB
- **SFO2:** 499915300 MHz

---

**F2 - Processing Parameters**

- **SI:** 65536
F3 - Acquisition Parameters
Date: 2002.10.18
Time: 11:11
INSTRUM: spect
PROBHD: 5 mm NaIO
PULPROG: "2G"
TO: 16384
SOLVENT: CDCl3
NS: 32
DS: 2
SWHF: 6248.750 Hz
FIORES: 0.361393 Hz
AQ: 1.3110222 sec
RG: 256
DW: 80.0016 usec
DE: 6.00 usec
TE: 100.0 K
D1: 2.00000000 usec

*************** CHANNEL (f) ***************
NUCl: 1H
P1: 7.00 usec
PL1: 0.00 dB
SF01: 499.9328752 MHz

F3 - Processing parameters
SI: 32768
SF: 499.9302246 MHz
WDW: 40
SSB: 0
LB: 0.00 Hz
GB: 0
FC: 1.00
F1 - Acquisition Parameters
Date: 2002/09/24
Time: 4:27
INSTRUM: spect
PNMRHDT: 5 mm Dual 13
LLPRPG: zgpg10
TD: 65536
SOLVENT: CDCl3
NS: 3655
DS: 4
SWH: 31446.54 Hz
PIDORES: 0.479836 Hz
AQ: 1.0420724 sec
RG: 602
DW: 15.400 usec
DE: 6.000 usec
TF: 0.0 Hz
d1: 0.0000000 sec
d2: 0.0000000 sec

======== CHANNEL (1) ========
NUC1: 13C
PI: 5.200 usec
PL1: 0.00 dB
SF01: 125.7212073 MHz

======== CHANNEL (2) ========
CPDPRG: wait11
NIT2: 1H
PCPD2: 72.600 usec
PL2: 125.000 dB
PL1: 19.000 dB
PL13: 3.000 dB
SF02: 499.5315001 MHz

F2 - Processing Parameters
SI: 65536
SF: 125.7212073 MHz
W/DW: nm
SSB: on
JR: 0.00 Hz
GO: 0
PC: 1.00

[Diagram of molecule with labels (G1), (G2), (G3), and (G4)]

337
INSTRUM: 5 mm Nadorac

PROBDH: 100 KHz

PULPROG: 2G

TD: 10634

SOLVENT: CDCl3

NS: 16

DS: 2

SW1: 6248.750 Hz

FIDRES: 0.031393 Hz

AQ: 1.3110522 sec

RG: 101 H

DM: 80.016 usec

UI: 6.00 usec

TR: 300.0 K

L1: 2000000000 usec

N(C1): 1H

PL: 0.00 usec

SFO1: 499.9328752 MHz

F2 - Processing parameters:

SI: 12768

SF: 499.9300246 MHz

WTTW: 80

SSS: 0

LB: 1.000 Hz

C0: 0

PC: 1.00
**F2 - Acquisition Parameters**

Date: 2002/10/30

Time: 2:58

**INSTRUM**: spec

**PROBUSD**: 5 mm Naorac

**PULPROG**: 16.34

**TD**: 16.34

**SOLVENT**: CDCl3

**NS**: 16

**DS**: 2

**SWH**: 6248.750 Hz

**FIDRES**: 0.361393 Hz

**AQ**: 1.31/1032 sec

**RG**: 64

**DW**: 80.016 usec

**DE**: 6.00 usec

**TE**: 300.0 K

**DI**: 2.00000000 sec

---

**--------------- CHANNEL 1 ---------------**

**N(C)1**: 1H

**PL1**: 7.00 usec

**PL1**: 0.00 dB

**SF01**: 499.9328752 MHz

---

**F2 - Processing parameters**

**SI**: 32768

**SF**: 499.930246 MHz

**WDW**: no

**SSB**: 0

**LB**: 0.00 Hz

**GB**: 0

**PC**: 1.00
**F2 - Acquisition Parameters**

- **Date:** 20021023
- **Time:** 1:11
- **INSTRUM:** Xpcc
- **PROBHD:** 5 mm Nafion
- **PL/JPOG:** 65
- **TD:** 16384
- **SOLVENT:** CDC13
- **NS:** 32
- **DS:** 2
- **SW1:** 124.750 Hz
- **FIDRES:** 0.381393 Hz
- **AQ:** 1.31 (0.722 sec)
- **RG:** 22
- **HFW:** 80.016 usec
- **DE:** 6.00 usec
- **TE:** 300.0 K
- **DI:** 2.00000000 usec

**== CHANNEL f1 ==**

- **NUC:** 1H
- **P1:** 7.00 usec
- **PL1:** 0.00 dB
- **SFQ:** 499.9328752 MHz

**F2 - Processing parameters**

- **SI:** 32768
- **SF:** 499.300246 MHz
- **WDW:** no
- **SSB:** 0
- **LB:** 0.00 Hz
- **GB:** 0
- **PC:** 1.00
APPENDIX B

$^1$H AND $^{13}$C SPECTRA FOR NOVEL COMPOUNDS SYNTHESIZED IN CHAPTER 3
**F2 - Acquisition Parameters**

**Date:** 20020224  
**Time:** 20.42  
**INSTRUM:** spect  
**PROBHO:** 5 mm Dual 13  
**PL/PROG:**  
**TD:** 65536  
**SOLVENT:** CDC13  
**NS:** 3586  
**DS:** 4  
**SWH:** 37444.64 Hz  
**FLUKES:** 0.479036 Hz  
**AQ:** 1.8420724 sec  
**NG:** 1024  
**UW:** 15 900 usec  
**DE:** 6.00 usec  
**TE:** 0.0 K  
**P1:** 0.000000000000000000 sec  
**d11:** 0.0300000000 sec  
**d12:** 0.0000000000 sec

----------- CHANNEL 1 -----------

**NUC1:** 13C  
**P1:** 5.20 usec  
**PL1:** 0.0000000000 dB  
**SFQ1:** 125.719077 MHz

----------- CHANNEL 2 -----------

**NUC2:** 1H  
**PCPD1:** 72.60 usec  
**PL2:** 120.000000 dB  
**PL12:** 19.00 dB  
**PL13:** 23.00 dB  
**SFQ2:** 499.931501 MHz

**F2 - Processing parameters**

**SI:** 65536  
**SF:** 135 707019 MHz  
**WTW:** 0  
**33B:** 0  
**LB:** 0.00 Hz  
**GIB:** 0  
**PC:** 1.00
F2 - Acquisition Parameters
Date  20020723
Time  3.41
INSTRUM spec
PROBHD  5 mm NaJorat
PULPROG zg
TD  16384
SOLVENT CDC13
NS  16
DS  2
SWH  6248.750 Hz
FIDRES  0.381193 Hz
AQ  13110322 sec
RG  225
DW  80.016 usec
DE  6.000 usec
TE  300.1 K
DI  2000000000 usec

============= CHANNEL 1 ===============
NUC  1H
PT  500 usec
PE  0.000 usec
SFO  499.9328752 MHz

F2 - Processing parameters
SI  12768
SF  499.930046 MHz
WTW no
SSB  0
LR  0.00 Hz
CH  0
FC  1.00
Acquisition Parameters
Date  20020724
Time  20.02

INSTRUM
PROBHD  5 mm Dual 13
PULPROG  zgpg30
TD  65536
SOLVENT  CDCl3
NS  3586
DS  4
SNV  31446.541 Hz
FIDRES  0.479836 Hz
AQ  1.0420724 sec
KG  1024
DW  15.900 usec
DE  6.00 usec
TE  0.0 K
DI  0.69999999 sec
d11  0.00000000 sec
d12  0.00002000 sec

******* CHANNEL f1 ***********
NUCl  13C
P1  5.20 usec
PL1  1.00 dB
SF01  125.7219073 MHz

******* CHANNEL f2 ***********
CUPROG  w-0318
NUC2  1H
PCP1  72.60 usec
PL2  120.00 dB
PL12  19.00 dB
PL13  19.00 dB
SF02  399.999999 MHz

F2 - Processing parameters
SI  65536
SF  125.7075019 MHz
WTW  0
SSB  0
LB  0.00 Hz
GJ  0
PC  100

4 -(CO2Me)-[GO]O

4 -(CO2Me)-[GO]O

22
F2 - Acquisition Parameters
Date: 20020713
Time: 246
INSTRUM: nmr
PROBHD: 5 mm Nalorac
PULPROG: zg
TD: 16384
SOLVENT: CDCl3
NS: 32
DS: 2
SWH: 6248.750 Hz
FIDRES: 0.381393 Hz
AQ: 1.3113022 sec
RG: 128
DW: 80.016 us
DE: 6.00 us
TE: 300.0 K
D1: 0.00000000 sec

=============== CHANNEL f1 ================
NUCI: 1H
FI: 7.00 us
PL: 0.00 dB
SF01: 496.322752 MHz

F2 - Processing parameters
SI: 32768
SF: 496.930246 MHz
WDW: 60 us
SSB: 0
LB: 0.00 Hz
GB: 0
PC: 1.00
**Acquisition Parameters**

- **Date:** 20020724
- **Time:** 23:03
- **Instrument:** NMR
- **Probe:** 5 mm Dual 13
- **Pulse Program:**anggan30
- **TD:** 8536
- **Solvent:** CD2Cl2
- **NS:** 2795
- **SN:** 31.446 54 Hz
- **FID RES:** 15376436 Hz
- **AQ:** 1024 59000000 sec
- **DW:** 6.900000000 sec
- **TE:** 0.000000000 sec
- **d11:** 0.000000000 sec
- **d12:** 0.000000000 sec

---

**Channel 1**

- **Nuc1:** 13C
- **F1:** 5.300000000 sec
- **PL1:** 0.000000000 dB
- **SF1:** 125.7219073 MHz

---

**Channel 2**

- **Nuc2:** 1H
- **PCP02:** 72.600000000 sec
- **PL2:** 120.0000000 dB
- **PL12:** 19.0000000 dB
- **PL13:** 23.0000000 dB
- **SF2:** 494.9315001 MHz

---

**Processing parameters**

- **SI:** 65536
- **SF:** 125.7075019 MHz
- **W1:** 0
- **SSB:** 0
- **LB:** 0.000000000 Hz
- **GB:** 0
- **NC:** 1.00

---

**Structures:**

- **4-(CO2Me)-[G2]O
- **4-(CO2Me)-[G2]O
- **24**
**F2 - Acquisition Parameters**

- **Date**: 20000723
- **Time**: 3.50
- **INSTRUM**: spect
- **PROT/HD**: 5 mm Nalorsc
- **PULPROG**: zg
- **TD**: 16.364
- **SOLVENT**: CDC13
- **NS**: 16
- **DS**: 2
- **SWH**: 62.48720 Hz
- **FIDRES**: 0.381393 Hz
- **AQ**: 1.3110322 sec
- **RG**: 128
- **DW**: 80.016 usec
- **DE**: 6.00 usec
- **TE**: 200.0 K
- **D1**: 2.00000000000 usec

**--------------- CHANNEL 11 -------------**
- **N1/C1**: 14
- **PL1**: 7.00 usec
- **PL2**: 0.00 dB
- **SFO1**: 499.9328752 MHz

**F2 - Processing parameters**
- **XI**: 32768
- **SF**: 499.9300246 MHz
- **W/DW**: on
- **SSB**: 0
- **LB**: 0.00 Hz
- **GB**: 0
- **P**: 1.00
AU: PROG:
CARBON AU
DATE 26-7-2
SF 62.986
SY 93.0
CI 2500.000
SI 39768
TO 39768
SW 15151.515
HZ/DF 4.925
Pm 4.2
RD 0.500
AQ 1.081
RD 200
NS 6235
TE 297
FM 19000
GP 4000.000
DP 20H CPD
LB 0.0
GB 0.0
CX 25.00
CY 0.0
F1 220.004P
F3 -4.971P
HZ/CM 565.999
PPM/CM 8.999
SR -4042.73

Bruker

H2/PT 925
PW 4.2
RO 500
AQ 1.081
RD 200
NS 6235
TE 297
FM 19000
GP 4000.000
DP 20H CPD
LB 0.0
GB 0.0
CX 25.00
CY 0.0
F1 220.004P
F3 -4.971P
HZ/CM 565.999
PPM/CM 8.999
SR -4042.73
**Acquisition Parameters**
- **Date:** 20020723
- **Time:** 4:28
- **INSTRUMENT:** spect
- **PROBND:** 5 mm Nalorac
- **PULPROG:** 2g
- **SOLVENT:** CDC13
- **TS:** 16
- **DS:** 2
- **SWH:** 6248.750 Hz
- **FIDRES:** 0.381393 Hz
- **AQ:** 1.314032 sec
- **RG:** 64
- **DW:** 80.014 sec
- **DE:** 6.00 sec
- **TR:** 300.0 K
- **DT:** 20000.000 sec

**CHANNEL 11**
- **NUC1:** HH
- **PL1:** 7.00 sec
- **PL1:** 0.00 dB
- **SF01:** 499.932752 MHz

**Processing parameters**
- **SI:** 32768
- **SF:** 499.930050 MHz
- **DTW:** no
- **SSB:** 0
- **LB:** 00.00 Hz
- **GI:** 0
- **PC:** 1.00
AU PROG:
CARBON AU
DATE 2-B-2

SF 62.896
SY 93.0
D1 2500.000
SI 32768
TC 32768
Sw 15151.515
H2/PT .925
PW 4.2
AQ 500
AG 1.081
NG 200
NS 4298
TE 297
FW 49000
DQ 4000.000
DP 20H CPD
LB 0.0
GR 0.0
CX 25.00
SY 0.0
F1 220.004
FE -4.8889
Hz/CM 566.036
PPM/CM 9.000
SR -4043.85

[Graph of a chemical structure]

Buishk

[Chemical structure image]
**F2 - Acquisition Parameters**

**Date:** 2002/07/23  
**Time:** 6.22  
**INSTRUM:** spect  
**PROBNO:** 5 mm Nalorac  
**PULPROG:** 2g  
**TD:** 163  
**SOLVENT:** CDCl3  
**NS:** 16  
**DE:** 2  
**SWH:** 6248.750 Hz  
**FIDRES:** 0.381393 Hz  
**AQ:** 1.3110322 sec  
**RG:** 128  
**DW:** 0.016 usec  
**DE:** 6.00 usec  
**TE:** 300.0 K  
**T1:** 2.0000000 sec

**CHANNEL f1**

**NUC1:** 1H  
**PI1:** 7.00 usec  
**SI1:** 0.00 dB  
**SFO1:** 499.938752 MHz

**F2 - Processing parameters**

**SI:** 32768  
**SF:** 300  
**SSB:** 0  
**LB:** 0.00 Hz  
**GB:** 0  
**PC:** 1.00
AU PROG: CARBON AU
DATE 16-8-2
SF 62.896
SV 93.0
SI 2500.000
SD 32768
SM 15151.515
HF/Pt 925
PW 4.2
RD 500
AG 1.081
NS 15579
TE 257
FW 18000
DG 4000.000
DP 20H CPD
LB 0.0
GB 0.0
CX 25.00
CY 0.0
F1 220.004P
FS 4.9885P
HZ/CM 566.036
PPM/CM 9.000
SR -4041.80

4-((CO2Me)-(G2)-N)

382
AU PGG:
CARBON AU
DATE 23-B-2
SF 82.696
SY 93.0
D1 3500.000
TO 32768
SM 5151.515
HZ/PT .955
PW 4.2
RD .500
AD 1.081
RG 200
NS 5906
TE 287
FW 190000
Q2 4000.000
DP 20H CPD
LE 0.0
GB 0.0
CX 25.00
CY 0.9
F1 220.004P
F2 -4.998P
HZ/CM 566.036
PPM/CM 9.000
SR -4041.80

Et2N
\[\text{47}\]

\[4-\text{CO}_2\text{H}\text{-G1}-\text{N}^+\text{N}^+\text{S}\]

\[\text{O} \quad \text{O} \quad \text{O}\]

\[\text{Et}_2\text{N}\]

\[\text{NEt}_2\]

200 160 120 180 140 120 PPM 100 60 40 20 0
F2 - Acquisition Parameters
Date: 20020727
Time: 7:22
INSTRUM spect
PROBMD 5 mm Nalorac
PULPROG zg
TD 16384
SOLVENT CDC13
NS 16
DS 2
SWM 62.48750 Hz
FIDRES 0.381393 Hz
AQ 1.3110322 Hz
RG 128
DW 80.016 usec
DE 6.00 usec
TE 300.0 K
D1 0.00000000 usec

======== CHANNEL f1 ========
NUC 1H
FL 7.00 usec
PL 0.00 db
SFO 6.999328375 MHz
F2 - Processing parameters
SL 32768
SF 69999300246 MHz
WOW on
SSB 0
LB 0.00 Hz
GB 0
PC 1.000

---

4-(CO2H)-[G0]NH

---

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
DATE 17-8-0
SF 250,133
SY 83.0
D1 4100.780
ST 16384
TD 16384
SW 2994.012
HZ/PT .385
PW 6.0
RD 0.0
AG 2.736
AG 160
NS 64
TE 297
FW 3800
O2 3900.000
DP 20H P0
LB 0.0
GB 0.0
EX 25.00
EV 0.0
F1 10.500P
F2 .500P
HZ/CM 110.053
PPM/CM .440
SR 2858.75

O3N
\[\text{structure image}\]
CO\textsubscript{2}Me
REFERENCES

Chapter 1


REFERENCES – Continued


REFERENCES – Continued


REFERENCES – Continued


REFERENCES – Continued


REFERENCES – Continued


REFERENCES – Continued


REFERENCES – Continued


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Chapter 2


REFERENCES – Continued


REFERENCES - Continued


REFERENCES - Continued


REFERENCES - Continued


REFERENCES - Continued


REFERENCES - Continued

Chapter 3


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