Synthesis and Applications of Polyester Dendrimers and Hyperbranched Polymers

by

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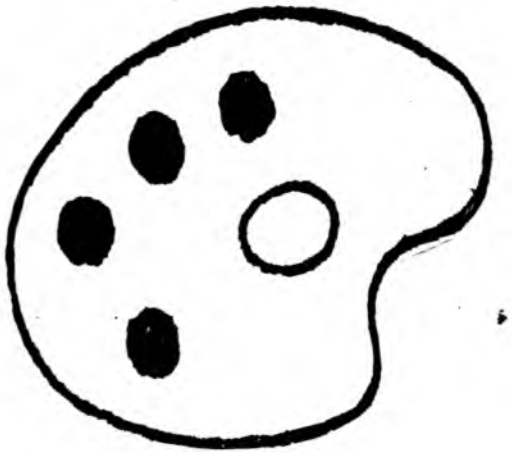
NUMEROUS ORIGINALS IN COLOUR



Dedicated to my parents

Contents

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Declaration

The work described in this thesis is the original of the author, except where acknowledgement has been made to results and ideas previously published. The work was carried out at the Department of Chemistry, University of Warwick, between October 1st 1993 and September 30th 1996 and has not been previously submitted for a degree at any institution.

Abstract

Dendrimers are an important new class of macromolecule which have many potential applications from drug delivery to metal extraction. A number of methods have been developed for the synthesis of dendrimers and related hyperbranched polymers. We chose the divergent initiator core method to synthesise three series of dendrimers with phloroglucinol, hydroquinone and naphthalene-2,6-diol as the core moieties, using DCC in the presence of DPTS as the esterification agent. The fluorescence of the naphthalene core was used to investigate the microenvironment of the core. Early investigations indicate there is a marked change in the core's environment between generations two and four.

MALDI-MS was tested as a method for the analysis of dendrimers and hyperbranched polymers. Molecular masses of dendrimers were obtained within 2 Da in every case, although low mass ions are sometimes observed. The origin of the low mass species is not yet entirely clear although there are indications that these arise from both the MALDI-MS process and during synthesis.

The synthesis of poly(3,5-dihydroxybenzoic acid), again using the DCC-DPTS esterification agent was investigated. This method was found to give hyperbranched polymers which were difficult to handle. Studies by MALDI-MS indicate the difficult handling properties are a result of DCC

being bound to the hyperbranched polymer. Thus, a modification of Fréchet's method was used to prepare poly(3,5-dihydroxybenzoic acid).

It was demonstrated that the hydroxyl terminated dendrimers and hyperbranched polymers could be functionalized at the branch termini with units such as acetyl, pent-4-enoyl, oleoyl and lineoyl. Epoxy terminated dendrimers and hyperbranched polymers were also prepared. The epoxy terminated dendrimers were analysed as potential crosslinking agents for polyester powder coatings. Initial results indicate that the epoxy groups prefer to react with one another rather than with the resin and thus little curing of the resin was observed.

Abbreviations

Ar	Aryl
Bn	Benzyl
bp	Boiling Point
br	Broad
CI	Chemical ionization
d	Doublet
DCC	N,N-Dicyclohexylcarbodiimide
ΔH	Heat of formation
DHB	2,5-Dihydroxybenzoic acid
DMAP	4-(Dimethylamino)pyridine
DMSO	Dimethyl sulfoxide
DPTS	4-(Dimethylamino)pyridinium toluene-*p*-sulfonate
E_a	Energy of Activation
EI	Electron Impact
equiv.	Equivalent
ESI-MS	Electrospray ionization mass spectrometry
Et	Ethyl
EtOH	Ethanol
F_n	Functionality N
FAB	Fast atom bombardment
GPC	Gel Permeation Chromatography
HMDS	1,1,1,3,3,3-hexamethyldisilazane
HA	Haemagglutinin

hr	Hour
hrs	Hours
Hz	Hertz
IR	Infra-red
J	Coupling constant
LD	Laser-desorption
m	Multiplet
MALDI-MS	Matrix assisted laser desorption-ionization mass spectrometry
Me	Methyl
MeOH	Methanol
mins	Minutes
M_n	Number average molecular weight
mol	Mole
mp	Melting point
MS	Mass spectrum
M_w	Weight average molecular weight
MW	Molecular weight
NMR	Nuclear Magnetic Resonance
Oxone	Potassium peroxymonosulfate
PAMAM	polyamidoamine
PCC	Pyridinium chlorochromate
PDi	Polydispersity
ppm	Parts per million

psi	Pounds per square inch
p-TSA	*p*-Toluenesulfonic acid
q	Quartet
R	Alkyl
s	Singlet
SEC	Size exclusion chromatography
t	Triplet
TEA	Triethylamine
TGA	Thermogravimetric analysis
TGIC	Triglycidyl isocyanurate
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
TMSCl	Chlorotrimethylsilane
TOF	Time of flight
wt %	Percent by weight

Chapter 1

Introduction

1.1 Introduction to Dendrimers

Starburst[†] dendrimers are cascade polymers which radiate from a central core moiety. The word 'dendrimer' is derived from Greek and means 'tree-like molecule'. Dendrimers possess highly ordered, three dimensional structures and may be prepared by a variety of methods, for example, the divergent initiator core method. Protecting group strategies are often essential for a successful synthesis.

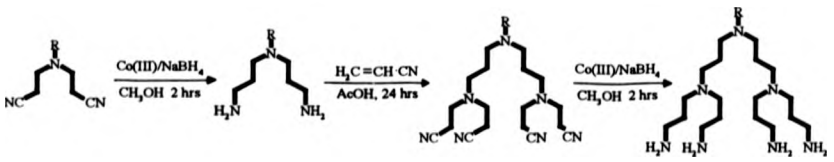
[†] Starburst is a registered trademark of The Dow Chemical Company.

1.1.1 Historical Background

Conventional polymer synthesis has involved the polymerization of monomer units in a relatively uncontrolled fashion to yield products with a distribution of molecular weights. Often the monomer units possess the ability to link with only two other monomers, hence 'linear' polymers are produced. In an attempt to produce polymers with specific topologies, to give, for example, unusual rheology, various methods have been employed. This may be achieved by the use of more than one type of monomer or by the blending of polymers. However, there is still a need for polymers with new properties which arise from novel shape/topology.

As long ago as the 1950's Flory suggested the possibility of the polymerization of an AB_n (n>1) type monomer unit, where A reacts with B, to produce highly branched structures.[1] However, it was not until 1978 that Vögtle *et al* reported an example of a protection-deprotection scheme using this very idea.[2] This consisted of a sequence of Michael addition reactions of an amine to acrylonitrile, followed by reduction of the nitrile to an amino group (**scheme 1.1**).

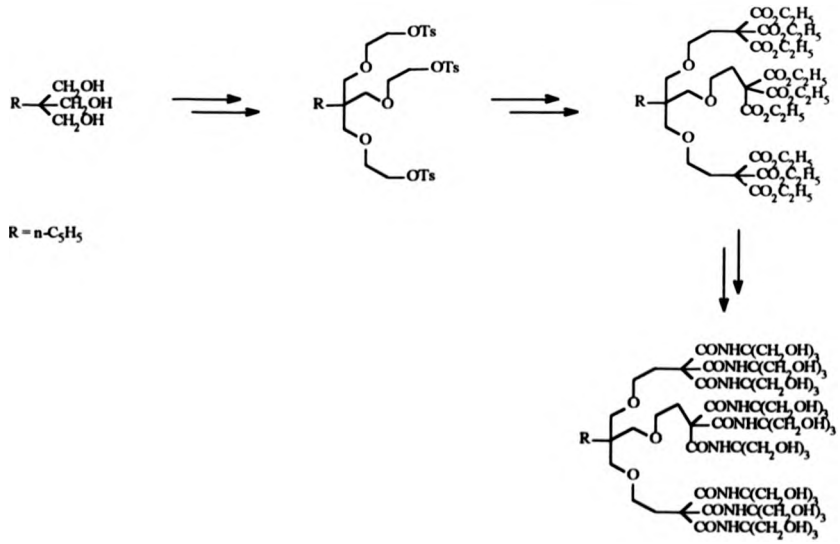
Scheme 1.1



No further results were published in this area until the early 1990's, due to the low yields and difficulties with the hydrogenation step.[3] However, the idea of 'cascade synthesis' had been introduced to the literature.

Tomalia's interest in controlled delivery systems and design of macromolecules led him to take an interest in this area. In the early 1980's, Tomalia began to publish work on poly(amidoamine) (PAMAM) Starburst dendrimers.[4] At approximately the same time, Newkome independently reported the synthesis of similar types of macromolecular structures, which he termed arborols[†] (**scheme 1.2**).[5]

Scheme 1.2



[†] The name arborol was coined by Newkome and is a composite term derived from 'arbor' (tree) and 'alcohol'.

Interest in the synthesis and characterization of dendritic molecules has grown since Tomalia's first publication in 1984.[6] Since then, there have been a number of reviews of dendrimer chemistry.[2, 7-10]

1.1.2 Structure

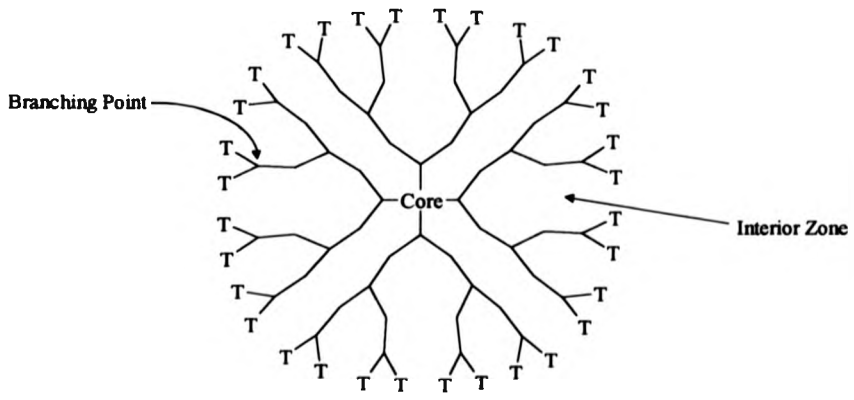
Dendrimers possess three key architectural features (**figure 1.1**):

(i) An initiator core - this is the innermost region of the dendrimer to which the dendrons (branches) are connected.

(ii) An interior zone - this region contains cascading tiers of branch units.

(iii) An exterior zone - this region contains the branch termini (T).

Figure 1.1 Structure of a Dendrimer



T = Terminal group

The initiator core may be as small as an atom, or as large as a molecule. It may or may not be homogenous with the rest of the dendrimer. This permits the 'building in' of any specialized function (*e.g.* metal atoms, chromophores) as long as it contains at least two reactive sites. The interior branch units need not be alike, and the use of differing branch units results in the formation of compounds with interesting physical properties.[11] The terminal groups also greatly affect the physical properties of the dendrimer, as they are thought to lie on or very near the surface of the dendrimer. Hence polar termini generally result in products with a greater affinity for polar solvents and *vice versa*.

1.1.3 Dendrimer Models

There are presently two dominant theoretical models of the structure of cascade dendrimers. The first and most popular of these is the de Gennes/Hervet model which has a density minimum at the core increasing to a maximum at the surface.[12] This model has the branch termini at the surface and, as a result, leaves internal cavities near the core. Similar results were also predicted by modelling carried out by Goddard *et al.*[13] This model predicts that as the dendrimers progress to higher generations, the density decreases at the core. This model does not take into account the possibility of back-folding termini which may be

an incorrect assumption, especially in the case of more flexible dendrimers.

The second model is that of Lescanec and Muthukumar and has the density maximum at the core.[14] This model is based on kinetically grown structures rather than equilibrium structures and predicts the inward folding of branch termini. The result is that branch termini are spread throughout the dendrimer. Although equilibrium structures were not calculated, this model does bring forward the idea of back-folding of termini as a method of releasing steric congestion at the surface.

The prediction of dendrimer properties such as size and intrinsic viscosity differ vastly for both the models. At present the de Gennes/Hervet model is the most widely accepted.

For the de Gennes model, the radial orientation of Starburst dendrimers would result in terminal groups being either on, or very close to the surface. Hence, they are very accessible to incoming reagents and media, at least in the earlier generations. As the dendrimers progress to higher generations, reaction kinetics would be expected to change dramatically as surface congestion increases. Mathematical calculations by de Gennes *et al* predicted that Starburst dendrimers should reach a point where branching could no longer occur in an ideal fashion - the Starburst limited generation.[12] At this point, the surface area per terminus approaches the

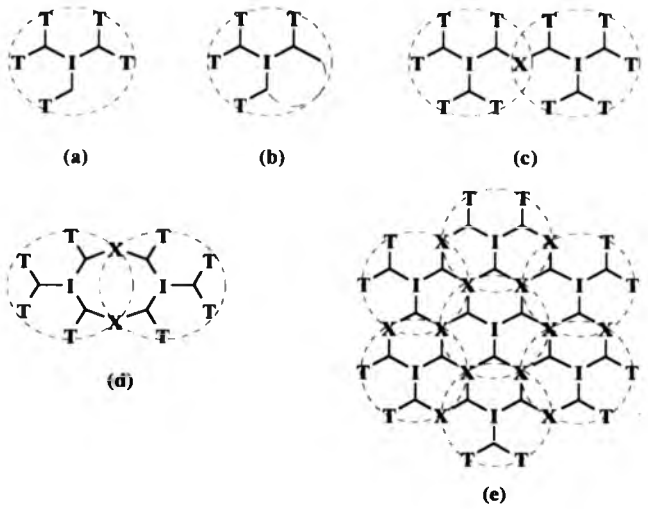
van der Waals diameter of the terminus and hence prevents complete functionalization to the next generation.

Studies of the hydrodynamic volume of PAMAM dendrimers by Tomalia *et al*, have shown that as the higher generations are approached, a new critical branching state occurs which is referred to as Starburst dense packing.[15] At this critically branched state, surface association occurs leading to solvent filled spheroids which are reminiscent of unimolecular micelles. The dendrimers appeared to expand three dimensionally in order to maintain a constant terminal group surface area as the number of termini increased per generation.

1.1.4 Defects

Dendrimer defects are mainly of two types, those due to intra-dendrimer or inter-dendrimer events.[7] Intra-dendrimer defects lead to deviation from branching ideality, whereas inter-dendrimer bridging or looping leads to more polydisperse systems.

Figure 1.2 Defects in Dendrimers



I = initiator core; T = terminal functions; X = inter-dendrimer bridging defect.

Defects such as **a** (incomplete branch unit growth) or **b** (intra-dendrimer cyclization) (**figure 1.2**) lead to a reduction in the number of terminal functions. This results in fewer points for branch growth and can immensely affect the size of later generations. Reduction in the number of branching points can also be due to:

(i) incomplete removal of terminal protecting groups;

(ii) fragmentation of branches;

(iii) abnormal branch unit formation;

(iv) steric prevention of branch growth.

Both these types of defects, as well as intramolecular cyclization, may lead to substantial changes in the symmetry properties of the dendrimer. Inter-dendrimer bridging or looping (**c**, **d**, **e** - **figure 1.2**) is the main cause of high mass polydispersities. Dendrimer fragmentation or incomplete removal of reagents (which may act as initiator cores), increases the low mass polydispersities.

1.1.5 Nomenclature

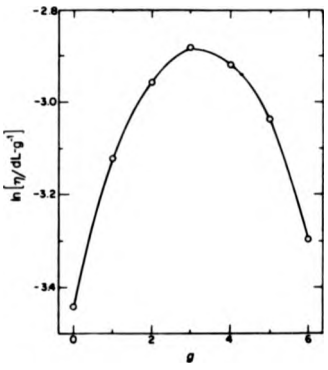
Attempting to use the normal nomenclature rules in naming dendrimers results in problems. Therefore a new method is required for naming these macromolecules. Basing the name on the core, branching unit and terminal functional group does not take into account dendrimers with differing branching unit. Nor would this take into account dendrimers with unsymmetrical branch units, for example, Denkewalter's polylysine dendrimers.[16] Newkome has devised a set of rules for naming dendrimers based on the core, branch units and terminal functional groups.[17] This method does not address the problems of differing branching units or unsymmetrical dendrimers and is little used today. The naming of dendrimers remains a complex task and in this work, dendrimers will be referred to by their commonly used descriptions, usually the author's name and the name of type of repeat unit (*e.g.* ester, ether).

1.1.6 Properties

There are many properties of dendrimers and hyperbranched polymers which may potentially be exploited. In general, compared to linear polymer analogues, it has been seen that dendrimers and hyperbranched polymers are much more soluble in common organic solvents.[7, 18] It has been found, particularly for higher generations, that the solubility characteristics of the dendrimer are those of the terminal functional groups.[9] This is true both for dendrimers and hyperbranched polymers. Thus, dendrimers with very hydrophobic interiors can be made water soluble by the use of an appropriate hydrophilic branch termini. Conversely, hydrophilic dendrimers or hyperbranched polymers can be made hydrophobic by simply modifying the branch termini.

Intrinsic viscosity studies by Fréchet *et al* have shown that the viscosity of the polyether dendrimers being studied does not follow a linear relationship with molecular weight, as would be expected for a linear polymer.[19] Fréchet found that polyether dendrimers go through a viscosity maximum and refractive index minimum as a function of generation, beyond which the viscosity decreases and the refractive index increases (**figure 1.3**).

Figure 1.3 Plot of Viscosity of Dendrimer versus Generation



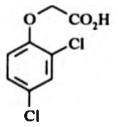
This phenomenon is attributed to the globular nature of dendrimers. Lower generations are thought to be disk-like, turning to oblate spheroids and finally to spheroids at higher generations. A point is reached where the dendrimers begin to take a more spheroidal form and the viscosity thus decreases. Similar results have been observed by Tomalia *et al.*[7]

1.1.6.1 Host-Guest Properties

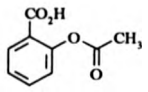
Dendrimers have been shown to behave as hosts for guest molecules. This idea was first suggested by Maciejewski in the early 1980's and has since been the focus of much attention.[7, 20] The de Gennes model predicts a density minimum at the core, indicating that there ought to be room for the inclusion of guest molecules. Several groups have reported instances of guest molecule inclusion in dendritic materials.[13, 21-23]

Tomalia *et al* reported the inclusion of 2,4-dichlorophenoxyacetic acid **1** and aspirin **2** (**figure 1.4**) in PAMAM dendrimers using NMR relaxation studies to detect their presence.[13] The addition of up to three or four equivalents of **1** or **2**, respectively, to a solution of PAMAM dendrimers in $CDCl_3$ resulted in lower T_1 relaxation times for the guest molecules, indicating a different environment for these molecules. Addition of greater quantities of these guests resulted in the appearance of a second relaxation time characteristic of the guest molecules in solvent free of dendrimer. Similarly, Fréchet *et al* reported the solubilization of pyrene in an aqueous medium by the use of a water soluble dendrimer.[24]

Figure 1.4 Structures of 1 and 2



1



2

However, both these examples are dynamic equilibrium processes and there is minimal control over the guest molecule which can easily diffuse in or out of the host molecule. Meijer *et al* have recently reported the inclusion of a guest molecule in a dendrimer which can be released from the dendrimer when required.[25] The guest was included in the dendrimer by having the molecule present when the dendrimer was synthesized. Molecules such as Bengal Rose and *p*-nitrobenzoic acid have been included in the 'dendritic box'. The molecules could be released by

partially destroying the dendritic container through acid catalyzed hydrolysis. Shape selectivity for the released molecules was observed. The smaller *p*-nitrobenzoic acid could be released through 'perforations' in the dendritic box made by the hydrolysis. However, the larger molecules of Bengal Rose could not be removed without further hydrolysis and dialysis of the dendrimer.

1.2 Synthesis

A wide variety of dendrimer families have been prepared, including polyesters,[26-28] polyamidoamines,[4, 15, 29, 30] polyethers,[31] polysiloxanes,[32-35] polythioethers,[36] polyamines,[37-41] polyalkanes,[42] polyorganometallics[43-46] and chiral dendrimers.[47-54]

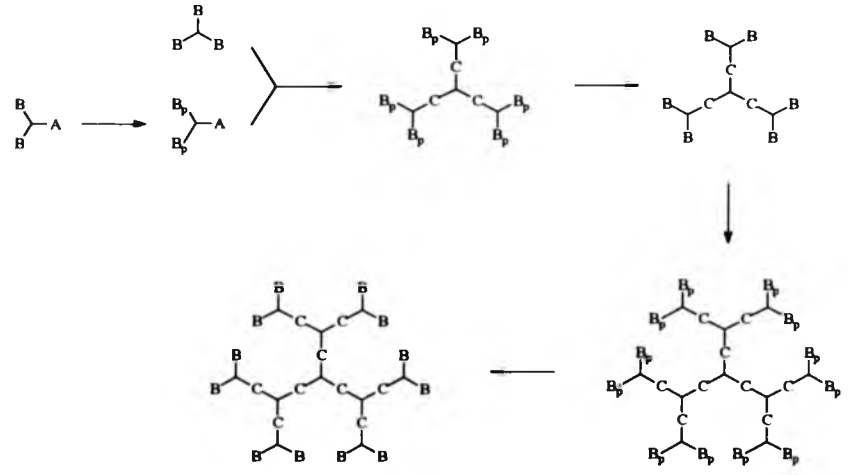
There has been much interest in recent years in new synthetic routes for dendrimer construction. This is mainly due to the large number of iterative steps required even for low generation dendrimers. The synthesis of dendrimers can be divided into two broad categories:

1. Divergent initiator core (or Starburst) method
2. Convergent method

1.2.1 Divergent Initiator Core Method

This is the original method for dendrimer synthesis. As the name suggests, dendrimer growth is from a polyfunctional initiator core molecule. By an iterative addition of protected branch units (with intermediate deprotection steps), a dendrimer is constructed radially from the initiator core. The overall synthetic strategy is outlined in **scheme 1.3**.

Scheme 1.3

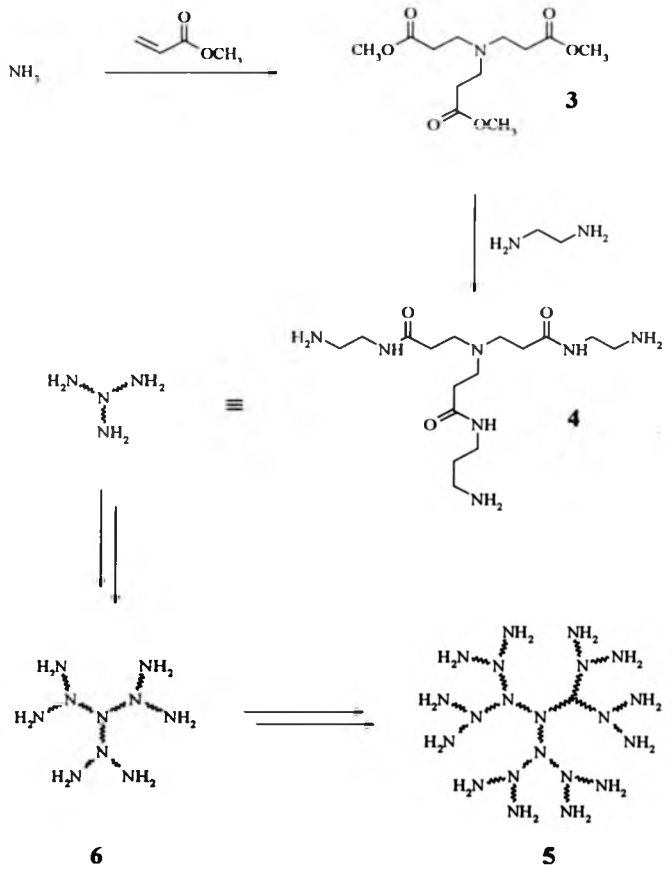


A, B = Functional Groups; A_p, B_p = Protected Functional Groups; C = A+B linkage

The divergent approach has been used to prepare perhaps the most well known of all dendrimers - Tomalia's Starburst PAMAM (polyamidoamine) dendrimers. Using a Michael addition of ammonia to three units of methyl acrylate, Tomalia first prepared **3** (referred to as a half generation)

(**scheme 1.4**). The second step of the synthesis converts the ester linkage to an amide by the addition of a large excess of ethylenediamine to produce the generation one dendrimer **4**. Repetition of these two steps yields the higher generation dendrimers **5** and **6** (**scheme 1.4**). Molecular modelling (using AMBER force field and POLYGRAF molecular simulation programs) indicated that the overall shape of the dendrimers changes with generation. The dendrimers start off as disk-like molecules (generations zero to two), evolving to oblate spheroids (generations three to four), then turning into nearly symmetrical spheroids at generations five and above.[13]

Scheme 1.4

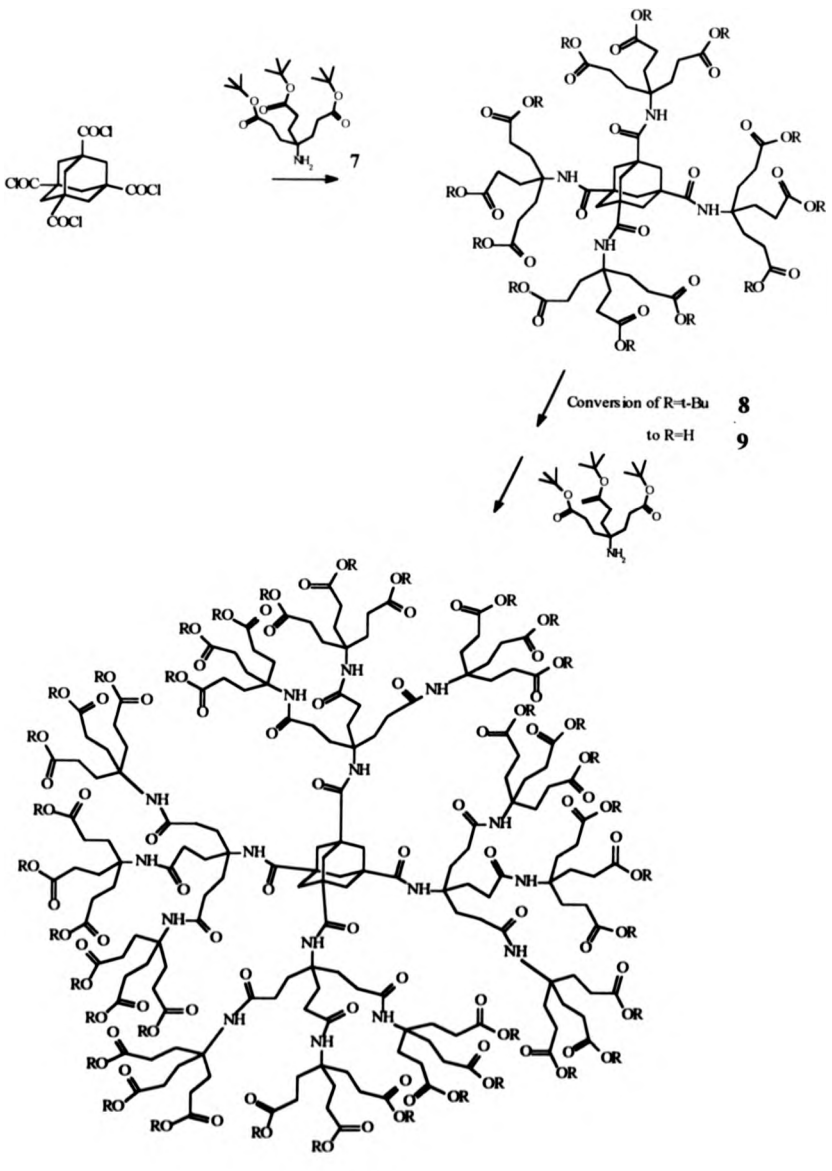


A number of dendritic systems containing polar functional groups at the termini, for example, hydroxyl or carboxylic acids, were designed by Newkome because of his interest in micellar mimics. Four-directional dendrimers based on an adamantane core substituted at the bridgehead positions (**scheme 1.5**), have been prepared successfully.[55] Using amine **7** containing three ester groups, Newkome first prepared the generation one dendrimer **8**. Acidic hydrolysis of **8** gave the first generation

deprotected dendrimer **9** containing twelve carboxylic acid groups. Repetition of these steps gave the second generation dendrimer **10**, with thirty-six carboxylic acid functional groups. This is one of the few examples in the literature of a dendritic system based upon a triply branched repeat unit, which leads to the rapid congestion at the branch termini.[56] Indeed, Newkome was unable to take the synthesis to the next generation.

One of the disadvantages of the divergent method is the large number of terminal functional groups. When higher generation dendrimers with a large number of terminal functional groups are used for synthesis, it is often difficult to determine whether all the termini have reacted or not. This can lead to characterization problems.

Scheme 1.5



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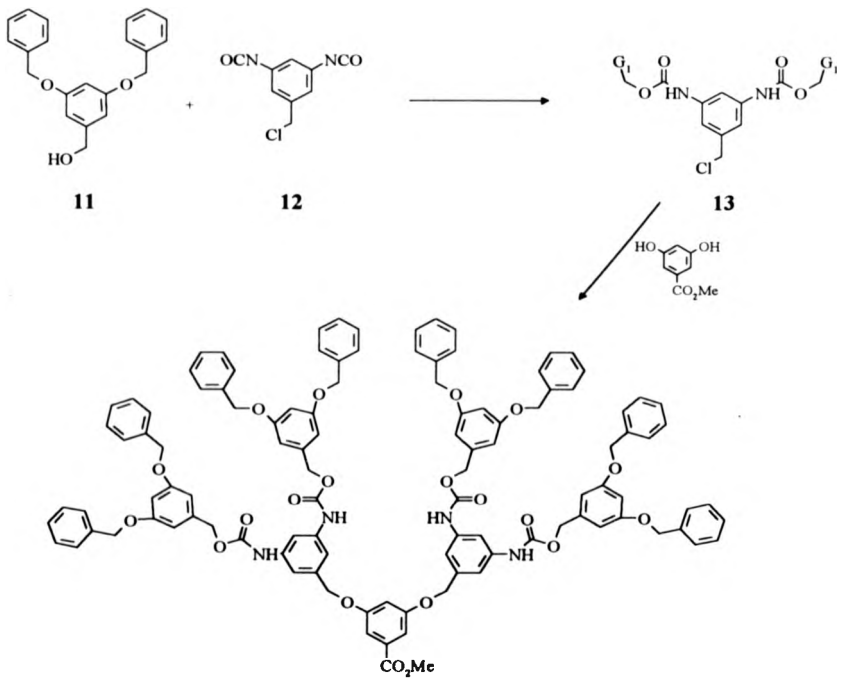
1.2.1.1 'Two Monomer' Approach

In an effort to minimize the number of steps required to synthesize dendrimers, and hence speed up synthesis for higher generations, a number of modified approaches have been published. The first of these is the so called 'two monomer' approach.[57] In this procedure, two AB_2 monomers which can react in a 'one pot' fashion are required. These are first reacted together to produce a generation two dendron. The generation two dendron can then be attached either directly to a core molecule or to a previously synthesized dendrimer, thus increasing the generation number by two. For example, Fréchet *et al* used 3,5-dihydroxybenzyl alcohol **11** and 3,5-diisocyanatobenzyl chloride **12** as the AB_2 monomers (**scheme 1.6**).[57] Direct coupling yielded the generation two dendron **13**. These dendrons were then reacted with methyl 3,5-dihydroxybenzoate to give the generation three dendrimer **14**. This method has the advantage that one intermediate deprotection and purification step is avoided.

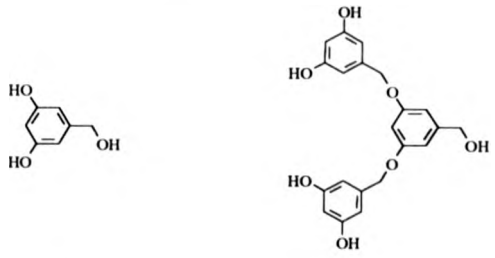
Scheme 1.6



1.2.1.2 'Branched Monomer' Approach

As an extension to this idea, Fréchet *et al* published their 'branched monomer' approach for the rapid synthesis of dendrimers.[58] A branch unit is constructed from three monomer units to give a large AB_4 type monomer as opposed to the normal AB_2 monomer, thus enabling generations to be increased two at a time. Hence, the monomer **15** would be the branched monomer for **16** (**figure 1.5**).

Figure 1.5 Structure of 15 and 16

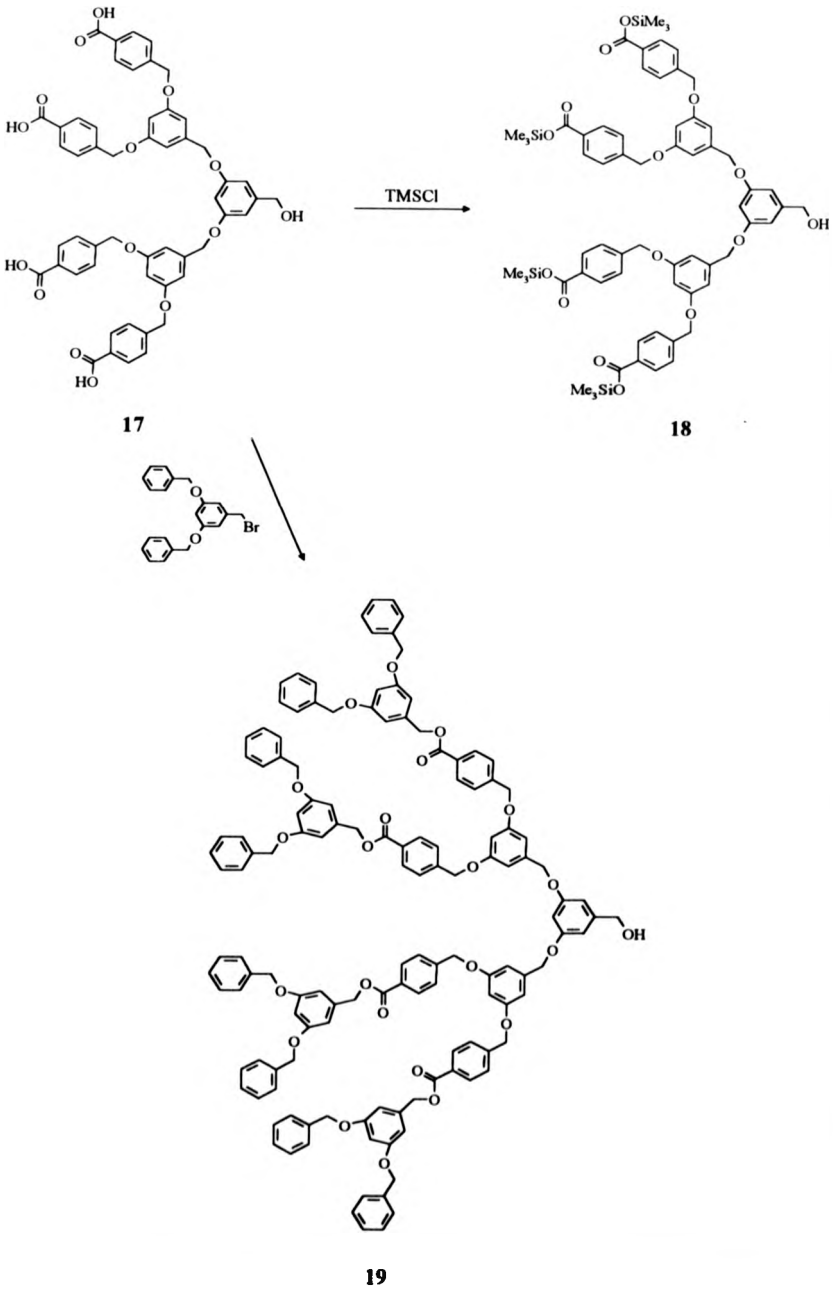


15 **16**

However, due to the difficulties encountered in the synthesis of **16**, Fréchet used the functionalized derivative **17** (**scheme 1.7**).

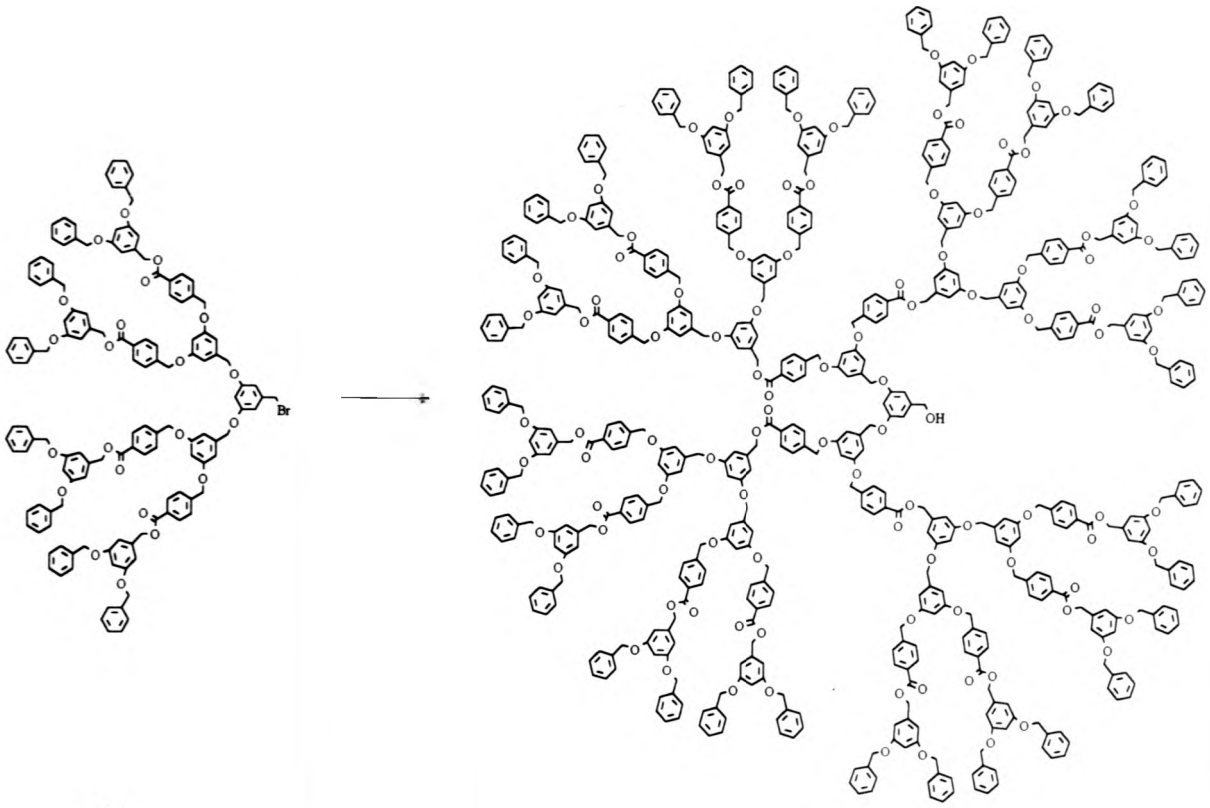
The AB_4 monomer **17** was converted to the silyl ester **18** and also to the ester **19**. The generation three dendron **19** was then converted to the bromide **20** (**scheme 1.7**). Four equivalents of **20** were then coupled with **18** to give the fifth generation dendrimer **21** in relatively few steps (**scheme 1.8**).

Scheme 1.7



17 18 19

Scheme 1.8



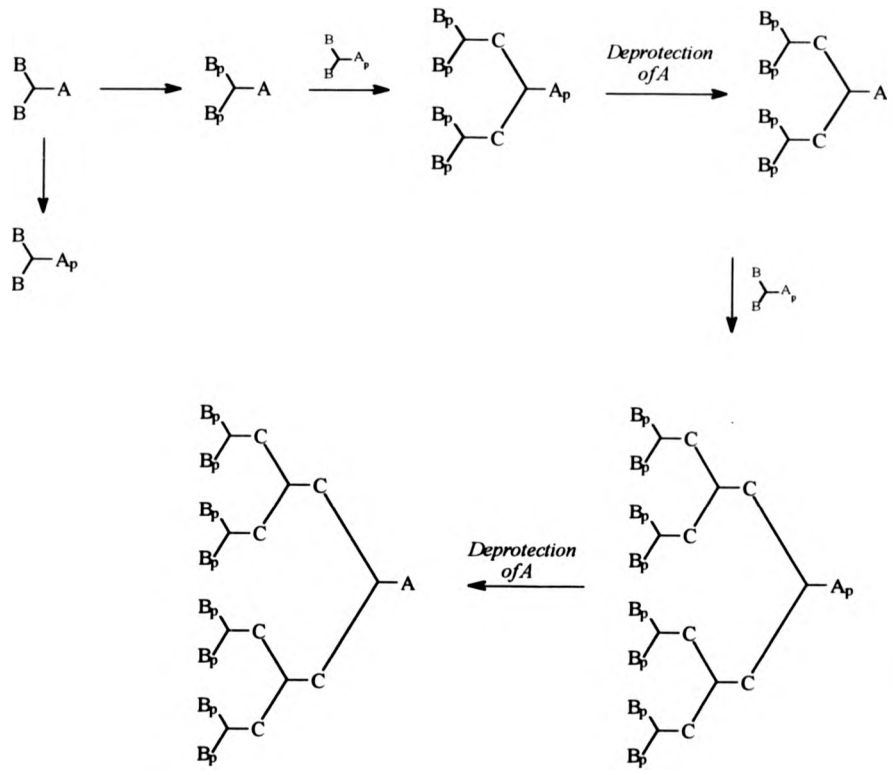
20 **21**

1.2.2 Convergent Method

Convergent dendron synthesis was reported simultaneously, but independently, by Fréchet *et al* [31, 59, 60] and by Neenan and Miller.[61] This method differs from the controlled divergent dendron synthesis in that in order to achieve exponential growth of the dendron, synthesis begins from what will eventually be the branch termini, to the focal point. The dendrons can then be tethered to a core molecule as a final step, to produce the dendrimer. An outline of dendron synthesis is shown in **scheme 1.9**.

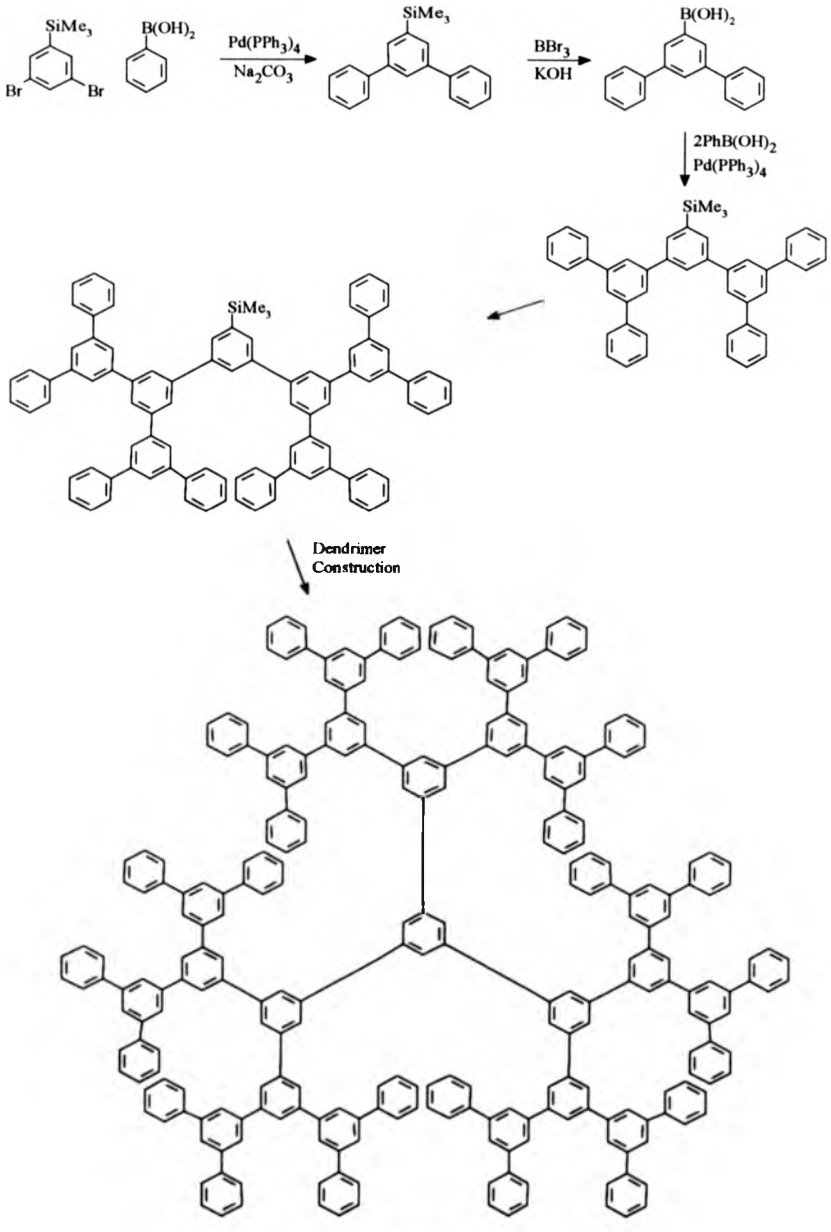
Examples of this type of synthesis abound in the literature and this has rapidly become the most commonly used type of synthesis for dendron/dendrimer construction. Neenan and Miller used this strategy to prepare all-aromatic dendrons consisting of tiers of aryl groups linked in 1,3,5-positions (**scheme 1.10**).[62] A Suzuki type coupling was employed to link the aromatic rings to ultimately produce the fourth generation dendrimer **22**.

Scheme 1.9



A, B = Functional Groups; A_p, B_p = Protected Functional Groups; C = A+B linkage.

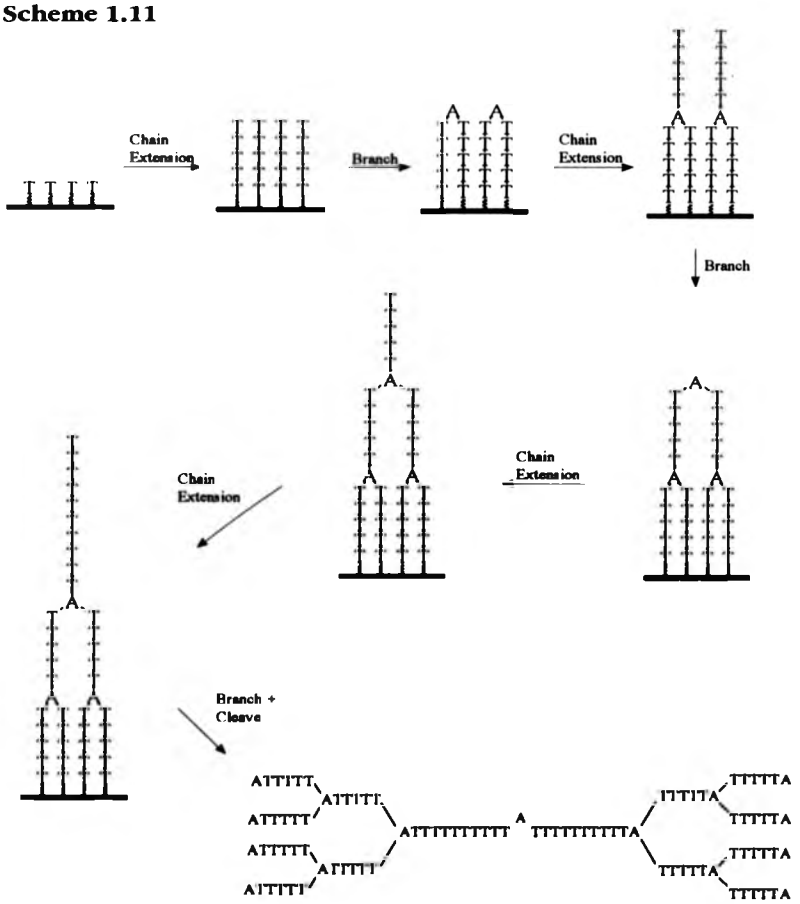
Scheme 1.10



22

Damha *et al* have used the convergent growth approach to prepare nucleic acid dendrimers.[63] These novel biopolymers were constructed using a solid support. It was found that high degrees of substitution on the support gave the best results as these ensured suitable distances between the growing branches. Dendrimers with up to eighty-seven units were prepared using this method (**scheme 1.11**).

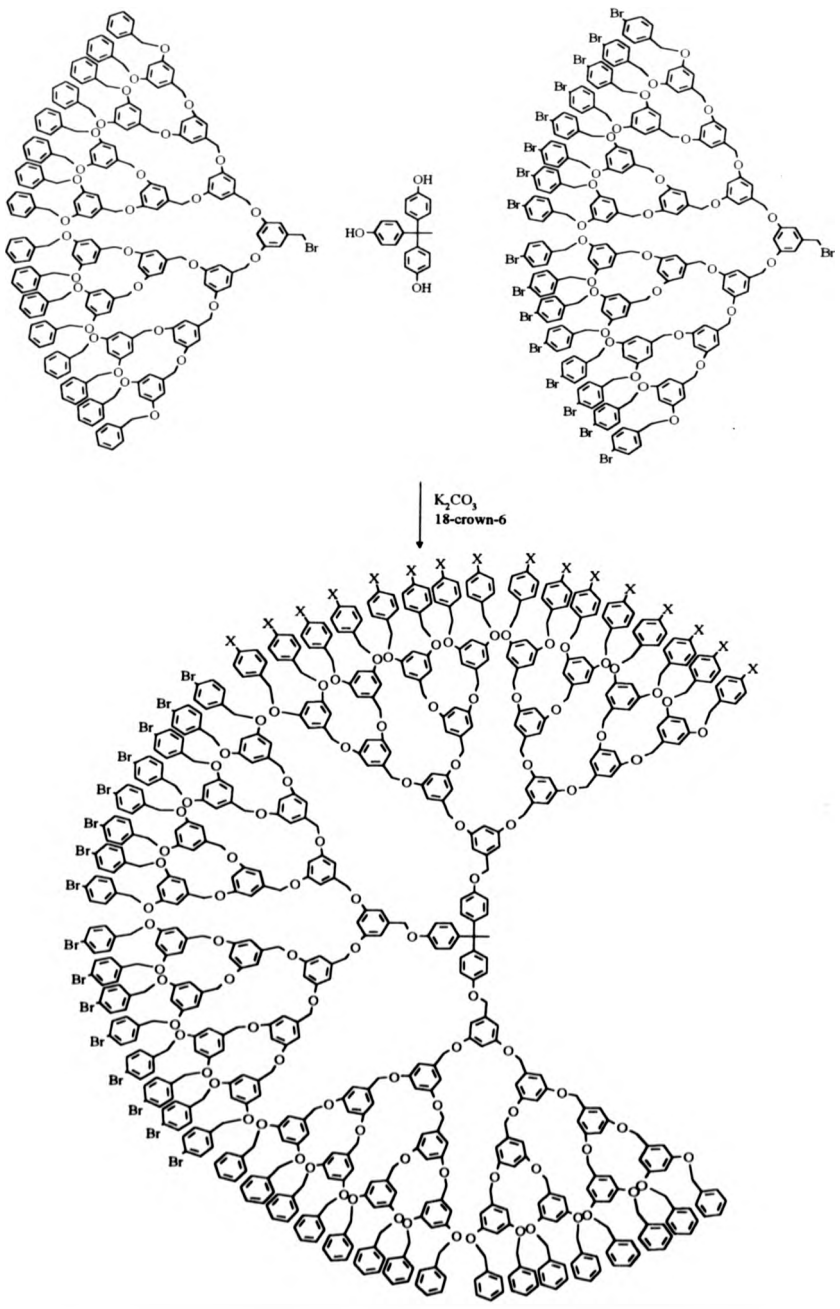
Scheme 1.11



1.2.2.1 Differing Dendrons

In the convergent growth approach, the dendrons do not have to be identical. Fréchet *et al* have synthesized polyether dendrimers with the same branch units but different branch termini.[64] **Scheme 1.12** shows a dendrimer with either sixteen or thirty-two bromine atoms at the periphery. This was prepared by the stepwise addition of appropriate dendrons to the core molecule. A single dendron is first attached to the core molecule. Secondly, the remaining two dendritic dendrons are attached to the core to give the dendrimer. Fréchet has also used this idea to prepare dendrimers with just one, two or three cyano groups at the periphery.[64] This level of surface functionality control is not available with the divergent approach.

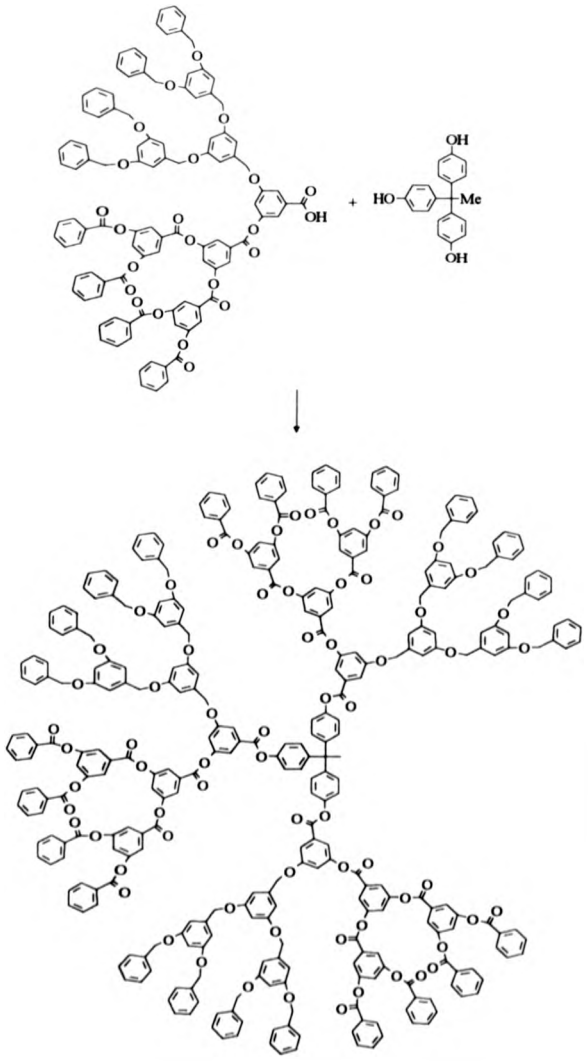
Scheme 1.12



X = H or Br

Fréchet has used an extension of this idea to prepare dendrimers which have differing branches in the dendrons.[11] **Scheme 1.13** shows the synthesis of a dendrimer using dendrons with ether and ester monomer units.

Scheme 1.13

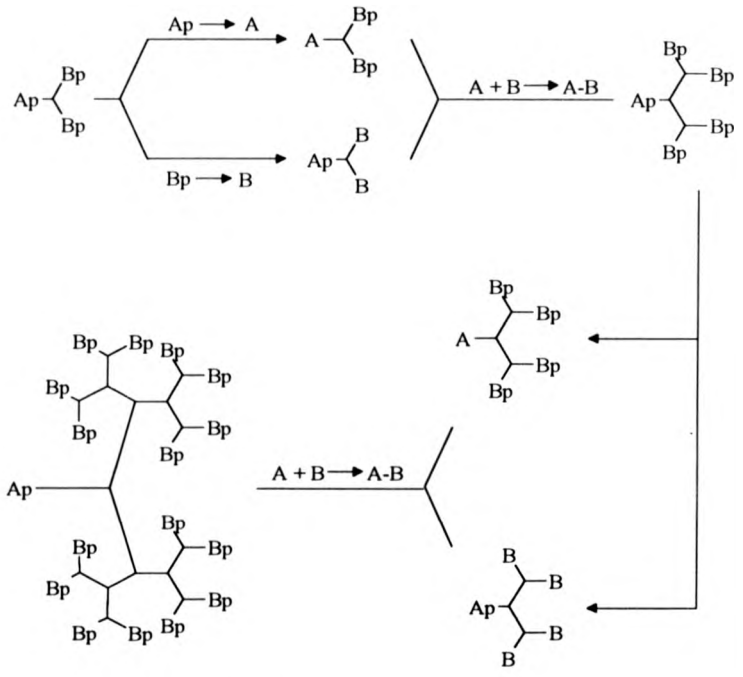


The convergent method has another advantage over the divergent method in that there is only one un-protected functional group at any one time. Hence it is easier to determine whether or not a coupling reaction has taken place. This means that perfect dendrimer growth is achieved with greater certainty. The disadvantage of this method is that the yields drop dramatically for higher generations, and it may be difficult to tether the large dendrons to relatively small core molecules.[65]

1.2.2.2 Double Exponential Growth

There have also been attempts to 'speed up' the convergent method. The double exponential growth method introduced by Moore *et al* [66, 67] is an extension of the 'branched monomer' approach.[58] This process involves selective removal of protecting groups on both the branch termini (A_p) and at the focal point of the dendron (B_p) (**scheme 1.14**). The two deprotected dendrons are then coupled together to produce a large dendron. Repeating this process on the larger dendron gives rise to exponentially larger dendrons.

Scheme 1.14

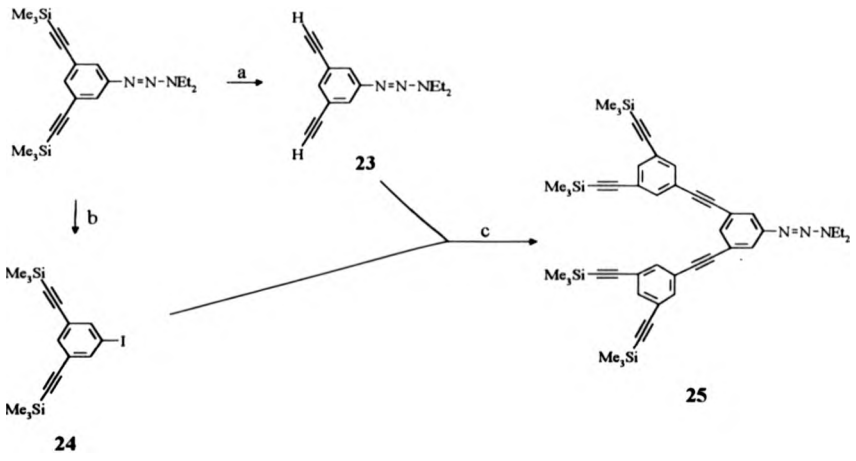


A, B = Functional Groups; A_p, B_p = Protected Functional Groups

To test the model experimentally, Moore repeated the preparation of his established phenylacetylene dendrimers.[67-69] Using chemistry previously employed, Moore demonstrated the double stage convergent growth approach and prepared the second generation dendron **25** from **23** and **24** (**scheme 1.15**). Repeating the process with the new monomer, Moore prepared the fourth generation dendron **26** in only six steps from the starting monomer (**scheme 1.16**). However, attempts to continue the synthesis to higher generations failed due to the production of complex

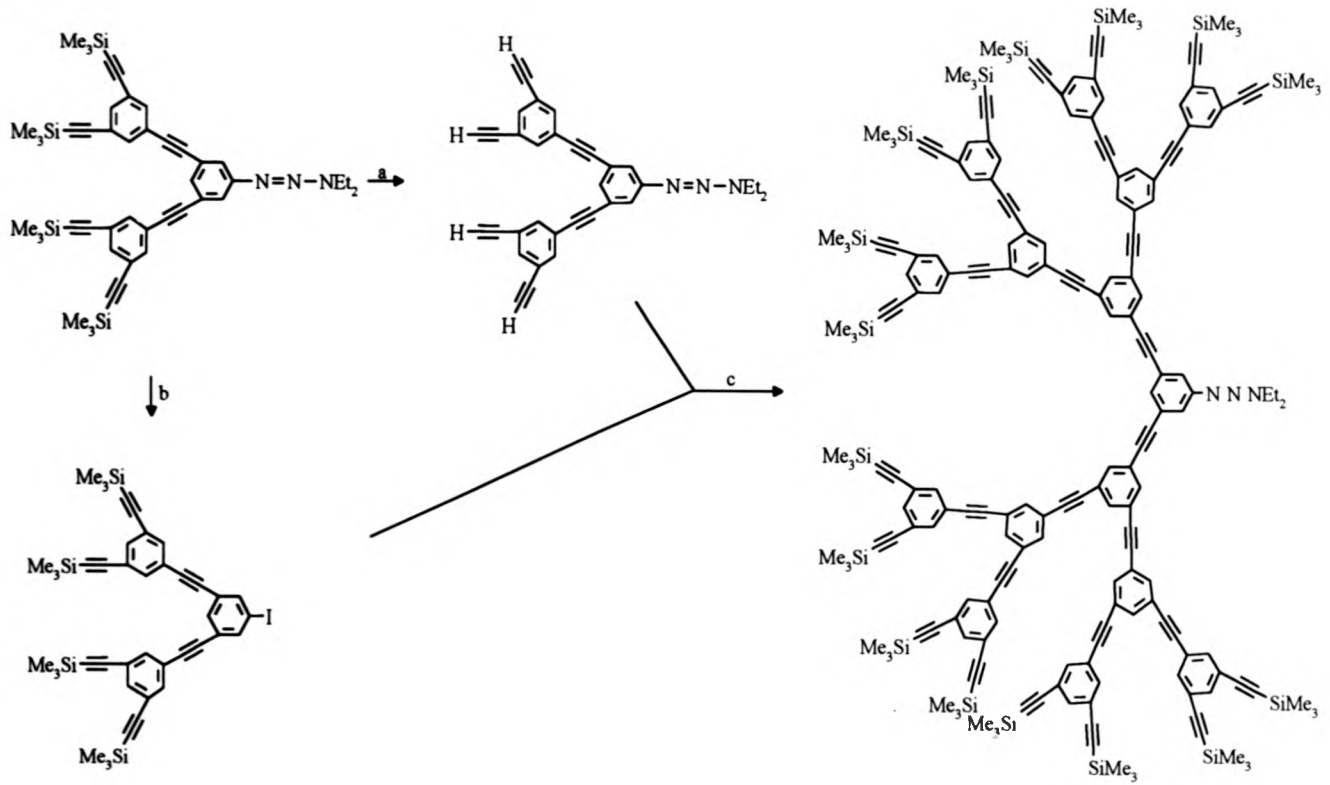
mixtures of broad molecular weight distribution, *i.e.* not perfect dendrimer formation.

Scheme 1.15



a = K_2CO_3 / MeOH; b = MeI, 90-110 °C; c = [$Pd(dba)_2$] /CuI /PPh_3 / TEA / 46-65 °C

Scheme 1.16



26

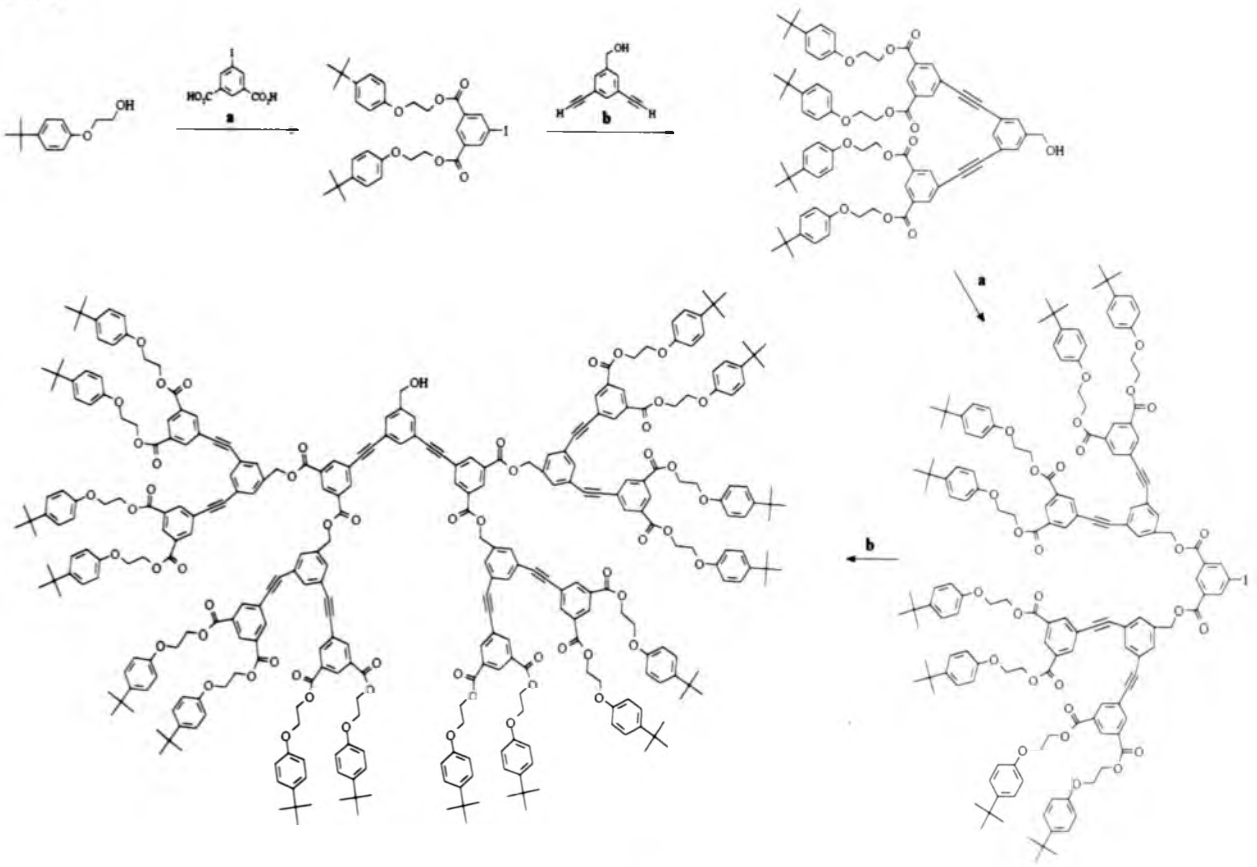
1.2.3 Orthogonal Coupling Strategies

All the routes for rapid dendrimer synthesis have so far relied upon protection-deprotection chemistry, albeit to a lesser extent than the classical methods of dendrimer synthesis. Zimmerman *et al* have recently prepared sixth generation dendrimers using an orthogonal coupling strategy without the use of protection chemistry.[70] The protection-deprotection steps are eliminated by the sequential use of two different branch units, each requiring different reaction conditions. It is essential that the individual coupling conditions do not affect the other functional groups.

Zimmerman achieved this by the use of the Mitsunobu esterification reaction and the Sonogashira reaction for the coupling of aryl iodides with terminal acetylenes (**scheme 1.17**).

The efficiency of the synthesis was increased further by merging this technique with Fréchet's branched monomer approach. Thus a second generation dendron was used as the branching unit. In comparison to the most efficient dendrimer synthesis, the orthogonal approach halves the number of steps by avoiding the protection-deprotection stages and is the most rapid route for dendrimer synthesis to date.

Scheme 1.17



1.3 Hyperbranched Polymers

1.3.1 Introduction to Hyperbranched Polymers

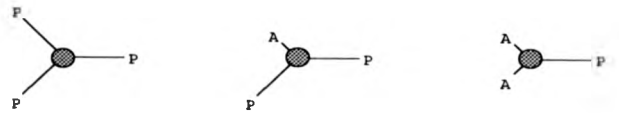
Most commonly available polymers are linear, for example, polystyrene and poly(methylmethacrylate). This means that the monomer used to prepare them has only two possible sites for polymer growth. This could be two functional groups or an unsaturated bond (*e.g.* alkenes, alkynes). Polymerization of monomers with more than two sites can result in the formation of highly branched polymers. The direct polymerization of an AB_n (n>1) type monomer unit results in the formation of highly branched polymers known as hyperbranched polymers. In comparison to dendrimers, hyperbranched polymers have an irregular structure consisting of branched and linear repeat units. However, they may have similar properties to dendrimers due to their branched structures without the need for long repetitive syntheses. Often only a single polymerization step is needed for the synthesis of hyperbranched polymers, hence they are more amenable to large scale preparation (and therefore more commercially viable) than dendrimers.

1.3.2 Degree of Branching

In principle it is possible to prepare both linear and fully branched polymers from an AB_2 type monomer unit. However, both these

outcomes are statistically unlikely. Consequently, hyperbranched polymers have three principal sub-units: fully branched, linear and terminal (**figure 1.6**).

Figure 1.6



branched linear terminal

A = branch terminus; P = polymer

The branching (and therefore the relative proportions of these three units) will have a profound influence on the physical properties of these materials. To quantify this, a 'degree of branching' (or branching factor) has been defined and is the sum of the branching (N_B) and terminal (N_T) units, divided by the total number of units (branching (N_B), terminal (N_T) and linear(N_L) - **equation 1**).

Equation 1

$$f_{br} = \frac{N_B + N_T}{N_B + N_T + N_L}$$

Hence

$$0 \leq f_{br} \leq 1$$

Thus, f_{br} = 0 for a completely linear polymer and f_{br} = 1 for a fully branched polymer (*i.e.* a dendrimer).

1.3.3 Molecular Weight Progression

One of the most notable physical characteristics of non-linear condensation polymerizations is the occurrence of a sharp gel-point.[71] The gel-point occurs at a well defined stage during the course of the polymerization where the mixture suddenly transforms from a viscous liquid to an elastic gel. Before the gel-point is reached, the mixture is soluble in the appropriate solvents. Beyond the gel point, the polymerization mixture is insoluble. The gelation effect is attributed to the near infinite size of the polymer, a feature which distinguishes non-linear polymerizations from linear polymerizations.

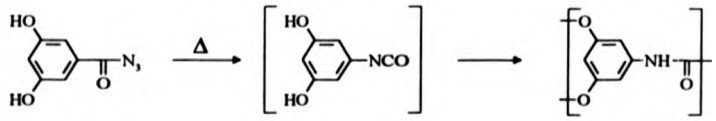
It is possible to limit gelation by limiting the extent of the reaction. This can be achieved by a stoichiometric imbalance of reactants. Hyperbranched polymers naturally have a stoichiometric imbalance due to the AB_n (n>1) type monomers used to prepare them and thus do not easily undergo gelation.

1.3.4 Synthesis

A wide variety of hyperbranched polymers have been prepared including polyamides,[72] polyethers[73, 74] polyphenylenes,[75] poly(siloxysilanes),[76] polyurethanes[18, 77, 78] and polyesters.[79-83] Some hyperbranched polymers have interesting physical properties with the formation of thermatropic[84] or lyotropic[72] liquid crystalline phases.

Hyperbranched polymers are generally prepared by direct polymerization of an AB_2 monomer. Pre-activation or *in situ* activation (*e.g.* by catalysts) may be required. Ramakrishnan *et al* have prepared hyperbranched polyurethanes by the thermal decomposition of 3,5-dihydroxybenzoyl azide **27** (**scheme 1.18**).[18] Upon heating **27** in DMSO with a catalytic amount of dibutyltin dilaurate, the isocyanate monomer **28** is prepared *in situ*. This polymerizes directly to give the polyurethane hyperbranched polymer **29** with M_n 1200 and polydispersity (PDi) 2.02 (**scheme 1.18**).

Scheme 1.18



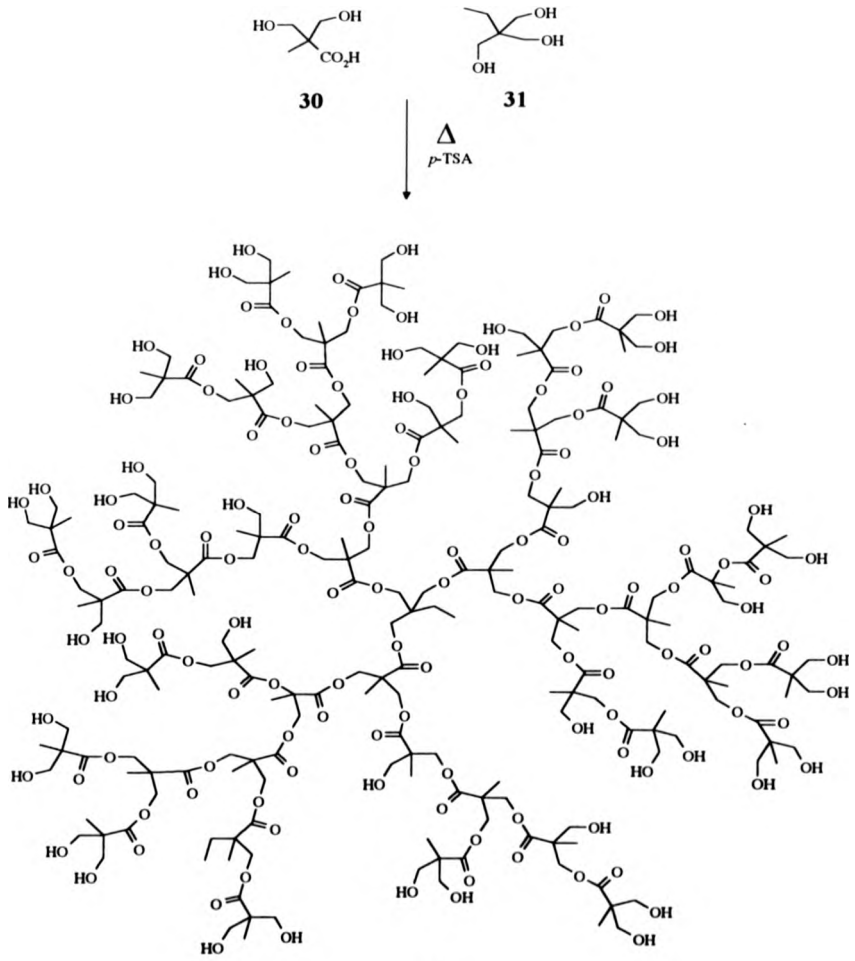
27 **28** **29**

The solvent was changed to refluxing toluene, in which both polymer and monomer are insoluble, and hence may be considered a dispersion

polymerization. This gave a polymer with higher PDi (3.23) and higher molecular weight (M_n 2800). The higher PDi may be attributed to the poorer mobility of the polymer in the solid state. The higher molecular weight was thought to be due to the higher purity and lower water content of toluene. The monomer **28** is also more likely to react with itself in the solid state than with impurities in the solvent, thus leading to higher molecular weight polymers. Ramakrishnan also found that the hyperbranched polymers were soluble in common organic solvents whereas the linear analogues derived from 4-hydroxybenzoyl azide are not.

Hult *et al* have recently prepared aliphatic polyester hyperbranched polymers based upon 2,2-bis(hydroxymethyl)propionic acid **30** and attempted to include a core molecule, 2-ethyl-2-(hydroxymethyl)-1,3-propanediol **31**, during the synthesis (**scheme 1.19**).[83] This was achieved by a pseudo one-step procedure using *p*-toluenesulfonic acid (*p*-TSA) as catalyst and gave polymer **32** with M_n ranging between 1400 and 5600 with PDi ranging between 1.36 and 1.92. In order to increase the probability of a core molecule reacting with a monomer molecule, the ratio of **30**:**31** was kept as low as possible by the addition of successive portions of **30** corresponding to the stoichiometric amounts for each generation.

Scheme 1.19



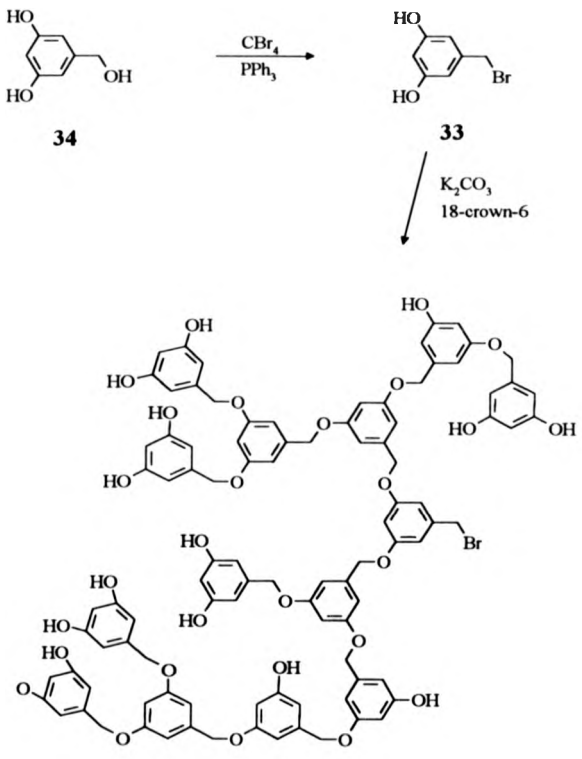
32

Hyperbranched polyesters **32** with a low glass transition temperatures (T_gs between 34-41 °C) were produced which were soluble in common organic solvents. The degree of branching was found to be approximately 80%, amongst the highest reported to date. When the same reaction was carried out without the inclusion of a core molecule, a

polymer with very low solubility resulted. It was found that the glass transition temperature was almost independent of the molecular mass of the polymer. This is not unexpected as a spherical shape is thought to be adopted at relatively low molecular mass.

Fréchet *et al* reported a one-pot synthesis of dendritic polyethers using 1,3-dihydroxybenzyl bromide **33** as the monomer unit (**scheme 1.20**).[7a] **33** was prepared *in situ* by the addition of carbon tetrabromide to a solution of 1,3-dihydroxybenzyl alcohol **34** in the presence of triphenylphosphine. **33** was polymerized by addition to an acetone suspension of potassium carbonate and a crown ether (18-crown-6) to produce a polymer **35** (M_n 38000, PDi 2.6). It was found that the rate of monomer addition did not greatly affect the polymer characteristics or molecular weight.

Scheme 1.20

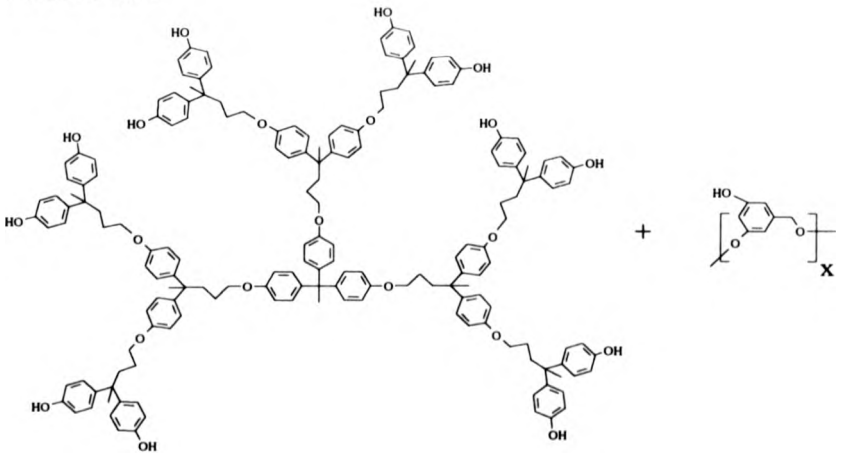


1.3.4.1 Double-Stage Convergent Growth

Fréchet *et al* have also reported a route for the synthesis of spherical hyperbranched polymers - the 'double stage' convergent growth approach.[85] In the first stage, a dendrimer ('hypercore') is prepared using either the divergent or convergent method. In the second stage, the dendrimer is utilized as an initiator core and a low PDi hyperbranched polymer is attached to the termini (**scheme 1.21**). This double-stage

convergent approach yields spherical hyperbranched molecules with near monodispersity but with greater ease and in less time than would be required to prepare a similar molecular weight perfect dendrimer. Fréchet thus prepared hyperbranched polymers with a flexible dendritic core derived from 4,4-bis(4'-hydroxyphenyl)pentanol and 1,1,1-tris(4'-hydroxyphenyl)ethane (the generation two dendrimer **36** is shown in **scheme 1.21**).[85] The hyperbranched dendrons were derived from **34**.

Scheme 1.21



36

Using this technique, Fréchet prepared hyperbranched polymers from generation zero to three dendrimers with molecular weights ranging from 20 kDa to 84 kDa. The molecular weight increased quite significantly on coupling the dendrimer and hyperbranched polymer. For example, the

generation three dendrimer of molecular weight 3351 gave a hyperbranched polymer of 84 kDa MW.

1.4 Characterization

A range of analytical methods is required for the complete characterization of dendrimers due to their unique structural aspects. The following techniques have been used to characterize both dendrimers and hyperbranched polymers.

1.4.1 Elemental Composition

The elemental composition of dendrimers has been determined using techniques such as elemental analysis and by studying the fragmentation patterns in mass spectra. However, problems arise when dendritic fragments (or dendrimers with defects) are the impurities as these may not adversely affect the content of any particular element, nor change the fragmentation ions seen in mass spectra.

1.4.2 Molar Mass

The molar mass may be determined in many ways. The two most common techniques for mass determination are mass spectrometry and analytical gel permeation chromatography (GPC). However, both have limitations. Mass spectrometry of high molecular weight materials is still a very young science and only recent developments have allowed molecular weights as high as one megadalton to be realized through techniques such as electrospray (ESI-MS)[86-88] and matrix assisted laser desorption-ionization mass spectrometry (MALDI-MS).[89, 90] This is mainly due to the difficulty of ionization of such large molecular weight molecules which tend to fragment using the more common, but softer, ionization techniques such as chemical ionization (CI) and fast atom bombardment (FAB).

Analytical GPC also has problems in determining molecular weights of dendrimers. It does not have the resolution of mass spectrometry and thus cannot give precise molecular weights. Problems arise because GPC determines relative molecular weights by comparing the elution time of the analyte with the elution time of a standard polymer. However, the standards are invariably linear polymers which do not possess the same physical characteristics as those of the dendrimer. GPC relies on viscosity as it separates by size and not mass. Dendrimers inherently have different sizes relative to their mass and thus discrepancies arise. Tomalia

has however, recently suggested the use of dendrimers themselves as calibrants for GPC, for greater accuracy molecular weight determination.[91] However, this does not entirely solve the problem as different dendrimers have different viscosity characteristics.

Other techniques which have been used include vapor pressure osmometry[92-94] and electrophoresis.[95] Both techniques rely on colligative properties for molecular weight determination.

1.4.3 Homogeneity

The homogeneity (polydispersity) of dendrimers can be determined by techniques such as GPC or GPC-LALLS (low angle laser light scattering). Theoretically, non destructive techniques such as MALDI-MS may be used to determine the homogeneity of a sample though this depends on the level of impurities. Low levels of impurities can often be invisible due to poor signal to noise ratio. NMR, particularly ^{13}C NMR, has been shown to be very useful for observing defects in dendrimers or the presence of fragmentation products.[9] ESI-MS has been shown by Tomalia to be useful for observing defects occurring in dendrimers, for example, intramolecular looping and bridging.[9]

1.4.4 Functional Groups

Functional groups on the dendrimer, whether on the branch termini or as part of the branching units of the dendrimer can be used to characterize dendrimers using techniques such as infra red spectroscopy, NMR and titration. Titration suffers from the possible inaccessibility of functional groups due to back-folding of branch termini or steric hindrance. Heteroatom NMR however, can be used as a non invasive technique for functional group determination.

1.4.5 Structures

Techniques such as ^{1}H, and ^{13}C NMR and a variety of more sophisticated NMR experiments such as COSY may be used for structure determination. Heteronuclear NMR in particular, can be very helpful. The inclusion of a fluorescent probe or computer assisted molecular modelling can also be used to aid structure determination.

1.5 Uses and Applications

The large number of functional groups, monodispersity (in the case of dendrimers), greater solubility, lower viscosity and the ability to include guest molecules all result in a molecule with very rich and exciting chemistry. However, to date only Tomalia's PAMAM dendrimers are commercially available.

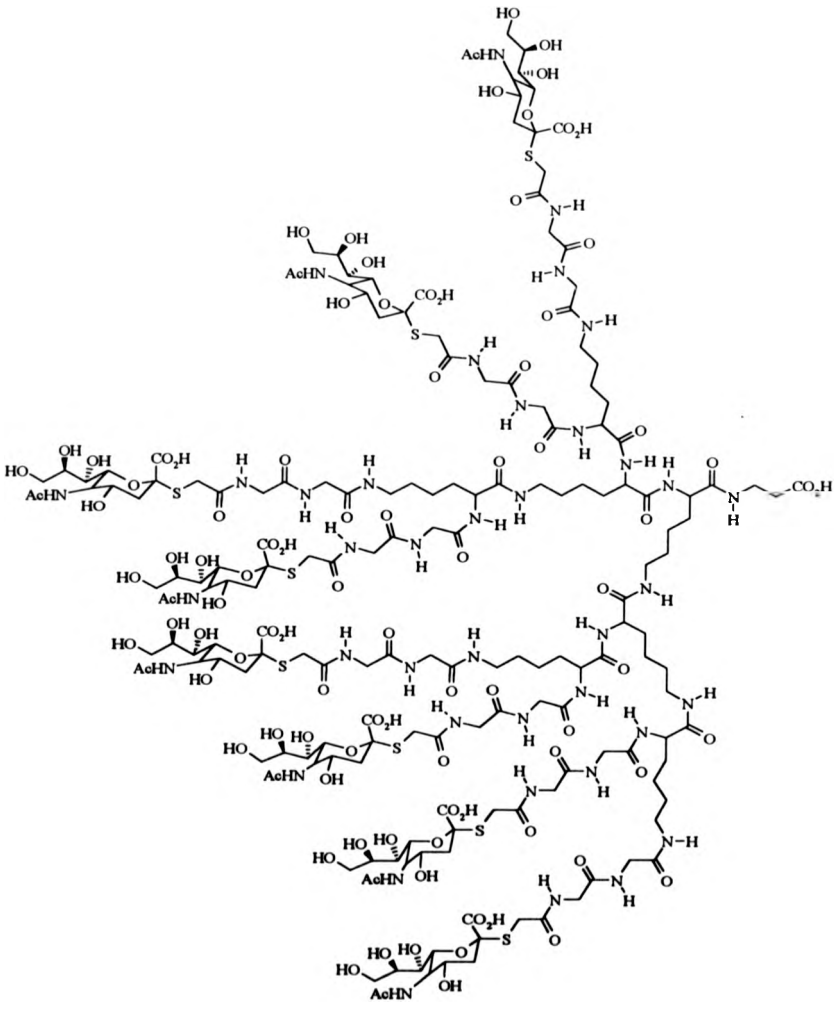
Tomalia has used PAMAM dendrimers as carriers in electrokinetic chromatography.[96] Hydrophobic compounds, for example naphthalene and fluorene, have been separated using negatively charged PAMAM dendrimers as carriers in water-methanol mixtures. These dendrimers have an advantage over previously used micellar systems, in that they do not decompose during separation. However, they do require the presence of a reasonably large percentage of organic solvent resulting in some loss of material through partition with the solvent.

Newkome has used carboxylic acid terminated dendrimers to carry out the separation of various substituted 4-hydroxybenzoate alkyl esters.[97] This was achieved with very low percentages of organic solvents present and consequently lower levels of material loss, an improvement on Tomalia's method.

Chujo *et al* have reported the use of PAMAM dendrimers to control the pore size of silica gel.[98] It was found that pyrolysis of polyoxazoline polymers failed to give adequate control over pore size on the silica gel. By using PAMAM dendrimers of differing generations, Chujo found that the pore size could be varied. Pyrolysis of the dendrimers yielded porous silica with pore sizes varying from 10 Å to 18 Å, using generations 0.5 to 5.5. Half generation PAMAM dendrimers are ester terminated dendrimers isolated after the addition of methyl acrylate to ammonia or the amine terminated dendrimer. These had to be used as it was found that amine terminated dendrimers caused phase separation.

Roy *et al* have prepared dendritic macromolecules containing α-sialoside molecules tethered to the branch termini (**figure 1.7**).[99] α-Sialosides are present on the cell wall and are the prime locations for an incoming influenza A virus haemagglutinin (HA) to bind. The presence of free monomeric α-sialoside has little effect on the virus as it has only a weak affinity for HA. However, it was found that clusters of α-sialoside showed up to a thousand times the inhibitory power of free α-sialoside.[100] Using a solid-phase support Roy synthesized dendritic macromolecules containing up to eighteen units of α-sialoside. Preliminary results have shown improvements of around 10^6 fold over free α-sialoside.

Figure 1.7 α-Sialoside Tethered to a Dendrimer



1.5.1 Surface Coatings

Surface coatings serve many functions. They may be decorative, protective, functional or any combination of these. For example, paints used on the hulls of ships reduce friction and protect against corrosion from the sea; coatings on metal food containers prevent contamination of the food by the metal.

Many coatings are supplied and applied in solution. On applying such films to a surface, the solvent is left to evaporate into the atmosphere. Often these solvents are organic and have effects (known and unknown) on the environment. Thus, there is an environmental drive to reduce or exclude the use of organic solvents entirely. This can be achieved by the use of aqueous based coatings which do not contain any volatile organic materials. However, many coatings are organic polymers which are not water-soluble and thus require different technology. Powder coatings provide one alternative. The use of solvent of any form is eliminated through direct application of the coating as a charged powder which is then cured by heating.

If organic solvents are necessary, the use of high solids coatings (coatings with minimal solvent) provides another solution. However, many linear polymers do not possess high solubility in common solvents and as a result a more dilute solution has to be used to keep the polymer in

solution. Linear polymers also have a near linear relationship of molecular weight and viscosity. Thus, more solvent is needed to make the solution of sufficiently low viscosity so that it can be applied easily in films of the desired thickness.

In an effort to reduce the amounts of solvent being emitted, new coatings and hence new polymers with improved solubility properties are being sought. Dendrimers and hyperbranched polymers may possess the required properties. It has been seen that dendrimers and hyperbranched polymers have reduced viscosity and greater solubility than their linear polymer analogues.[7, 19, 101] It may be possible that these dendritic systems could provide some of the answers to the problems faced by linear polymers. We are thus investigating the synthesis and uses of dendritic materials in surface coating applications.

Chapter 2

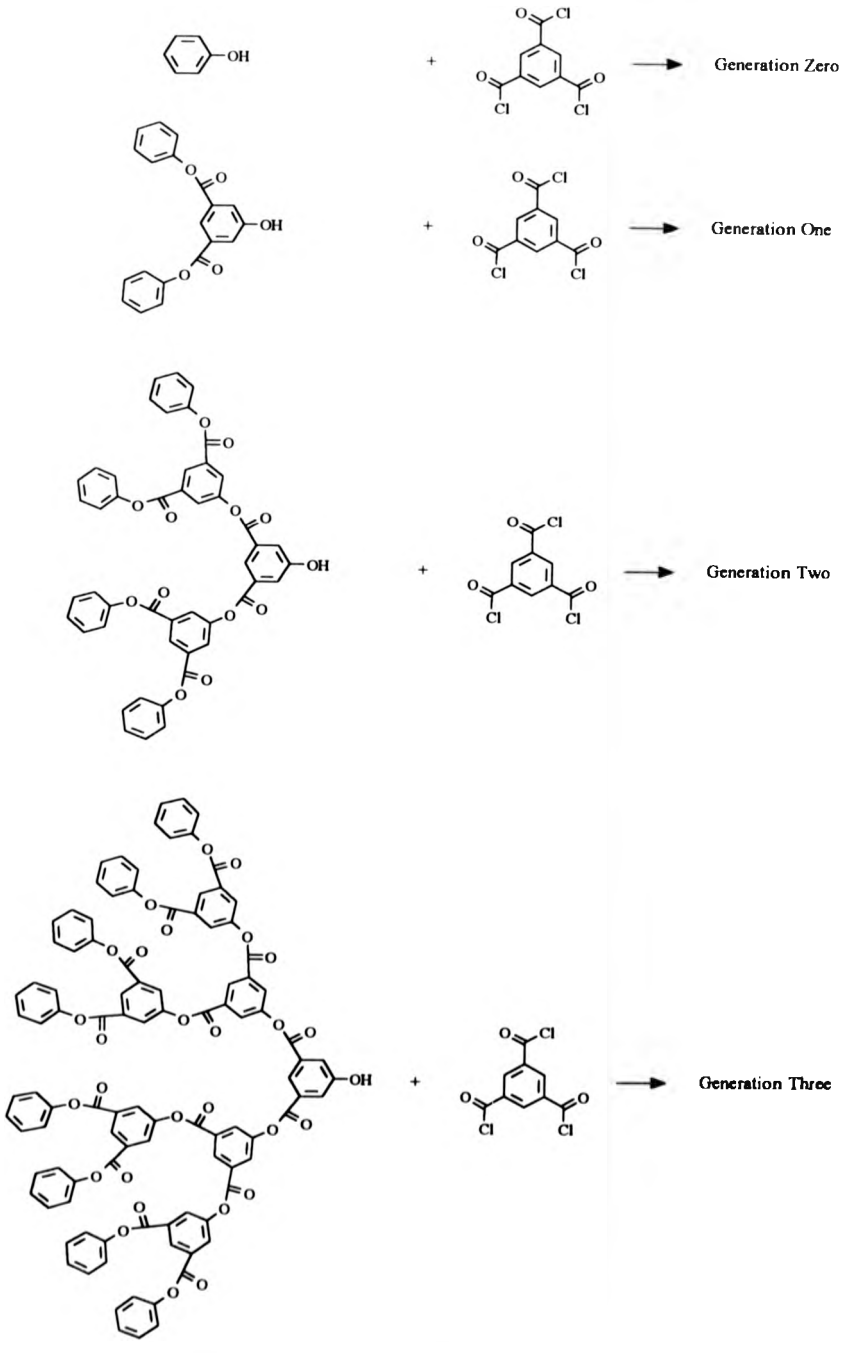
Synthesis of Dendrimers

2.1 Synthetic Strategy

We wished to prepare dendritic materials for use in polyester based surface coatings. To reduce the possibility of producing dendritic systems that were likely to be inhomogenous with currently used polymers, we decided to prepare wholly aromatic polyester dendrimers. The interesting viscosity properties exhibited by dendrimers is thought to occur at a stage when the dendrimer begins to take on a more spheroidal shape. For that reason, we decided to prepare dendrimers with a compact core unit and branching unit so that this stage could be reached at earlier generations avoiding unnecessarily long syntheses.

Neenan and Miller have prepared a series of aromatic polyester dendrimers using the convergent approach and have managed to synthesize up to a generation three dendrimer (**scheme 2.1**).[102] They have been unable to continue the synthesis to higher generations due to problems in attaching the dendron to the small core molecule. This problem is inherent in the convergent growth approach and has been observed by many groups.[9] The yields of the dendrimers also decreased as higher generations were prepared. The yields of generation zero, one, two and three dendrimers were 74%, 83%, 63% and 41% respectively.

Scheme 2.1


Generation Zero
Generation One
Generation Two
Generation Three

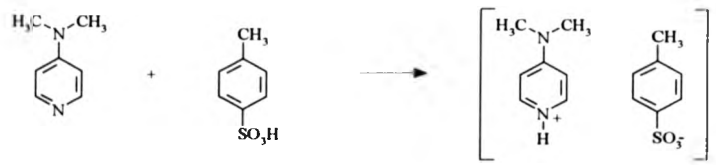
We wished to prepare dendrimers of all generations in high yields. Thus, the divergent method was chosen to prepare our dendrimers, in the expectation that the steric constraints of tethering dendrons to a small core molecule would be eliminated and yields for higher generation dendrimers would be improved.

The acid chloride method used by Neenan and Miller to prepare their dendrimers can lead to problems of transesterification. Indeed, Neenan and Miller found problems with the preparation of their generation three dendrimer. Species other than the pure dendrimer were found and discovered to be products resulting from transesterification. To avoid this problem we chose an esterification method which had previously been successfully used by Fréchet to prepare dendrimers.[11]

2.2 Synthesis of Trichloroethyl Terminated Dendrimers

As it was successfully employed in closely related reactions, we decided to use 1,3-dicyclohexylcarbodiimide (DCC) as the esterification agent, with 4-(dimethylamino)pyridinium *p*-toluenesulfonate (DPTS) as catalyst. DPTS **37** is a stable non-hygroscopic salt prepared from 4-dimethylaminopyridine **38** (DMAP) and *p*-toluenesulfonic acid **39** (*p*-TSA) (**scheme 2.2**).[103]

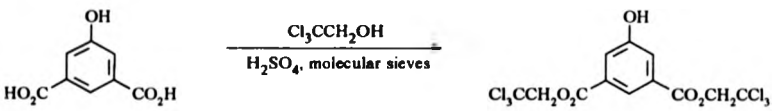
Scheme 2.2



38 **39** **37**

For the dendrimer core we chose the same as Neenan and Miller, *viz.* 1,3,5-benzenetricarboxylic acid **40**. The repeating monomer unit 5-hydroxyisophthalic acid **41** was chosen and protected as the trichloroethyl ester **42** using an adaptation of a literature method (**scheme 2.3**).[11]

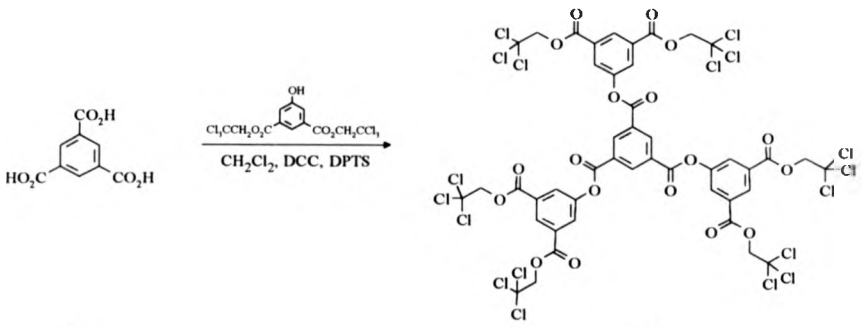
Scheme 2.3



41 **42**

Using slightly more than three equivalents of **42**, we prepared the generation one dendrimer **43**, in 89% yield (**scheme 2.4**). This was characterized by GPC (M_n 1600, PDi 1.006), elemental analysis, ^1H and ^{13}C NMR. The low polydispersity value obtained indicated the mono-molecularity of the dendrimer.

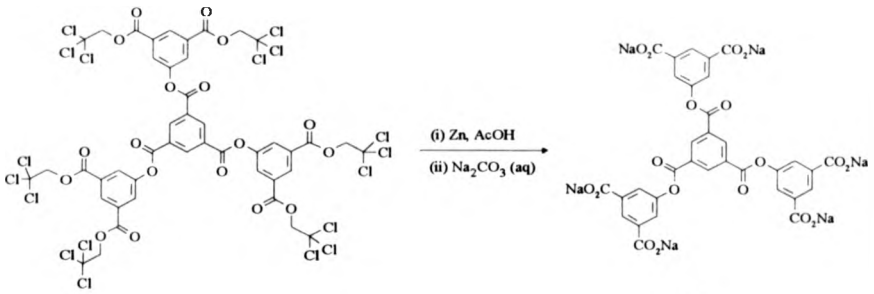
Scheme 2.4



40 **43**

Attempted removal of the trichloroethyl ester groups (deprotection), using zinc and acetic acid,[11] resulted in an almost insoluble material which could not be freed of residual acetic acid. This was thought to be due to strong hydrogen bonding between the carboxylic acid functions of the dendrimer and those of acetic acid. The near insolubility of the deprotected dendrimer may also be due to strong hydrogen bonding between dendrimers. Attempts at removing the acetic acid (*e.g.* freeze drying) failed. However, the dendrimer could be solubilized by the formation of the sodium salt **44** (**scheme 2.5**). This was prepared by stirring the solid with an excess of aqueous sodium carbonate solution. The salt was characterized by ^{1}H NMR only and was not pursued further.

Scheme 2.5



44

2.3 Synthesis of Benzyl Terminated Dendrimers

To eliminate the problems of low solubility and purification, it was decided to invert our dendrimer strategy and use a tri-hydroxyl core unit and the appropriate monomer unit. This enabled us to use the expertise gained from the preparation of the trichloroethyl terminated dendrimers.

2.3.1 Nomenclature

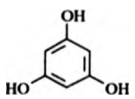
The dendrimers in the following chapters will be referred to by a four part code similar to that used by Fréchet. The first part refers to the generation number (*e.g.* G_1, G_2 for generations one and two). The second part defines the core moiety: P for phloroglucinol, H for hydroquinone and N for naphthalene-2,6-diol. The third part refers to the total number of functional groups of at the termini of the outermost

branch units (*e.g.* [6], [12]) and the fourth part refers to the nature of the chain termini (*e.g.* -OH, -OBn). For example, a second generation dendrimer with a phloroglucinol core and benzyl terminal groups would be referred to as G_2P-[12]-OBn.

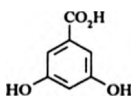
2.3.2 Phloroglucinol Core Dendrimers

Phloroglucinol **45** was chosen as the core molecule and 3,5-dihydroxybenzoic acid **46** as the repeating unit (**figure 2.1**).

Figure 2.1 Structures of 45 and 46



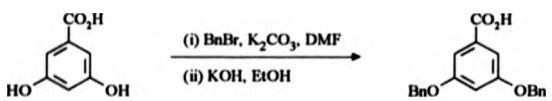
45



46

The hydroxyl functional groups of **46** were protected as benzyl (Bn) ethers to produce the monomer **47** using an adaptation of literature methods (**scheme 2.6**).[79, 104]

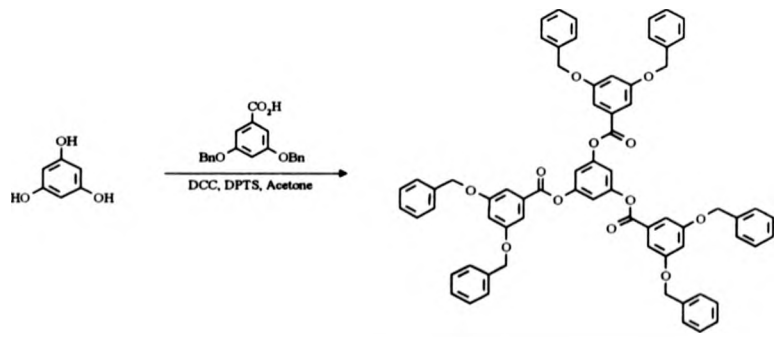
Scheme 2.6



46 **47**

Acetone was used as the solvent for dendrimer preparation instead of dichloromethane, as both the monomer unit **47** and phloroglucinol were poorly soluble in dichloromethane. Using the same esterification catalysts as previously, we prepared the generation one dendrimer G_1P-[6]-OBn **48** as a clear solid in 25% yield (**scheme 2.7**). The course of the reaction was monitored by GPC. The homogeneity of the dendrimer was determined by GPC and found to be good (M_n 1500, PDi 1.004). The molecular weight of the dendrimer was determined by matrix assisted laser desorption-ionization mass spectrometry (MALDI-MS) which gave good agreement with calculated values ([M+Na^+] at *m/z* 1097 - calculated 1098). The MALDI-MS of this and the following dendrimers will be discussed in more detail in chapter 5.

Scheme 2.7

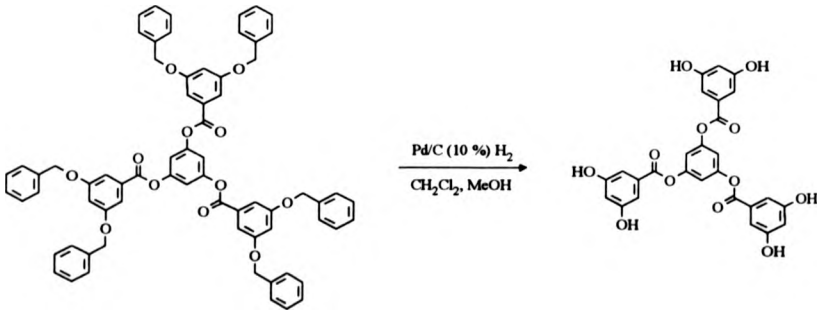


48

Deprotection was accomplished by catalytic hydrogenolysis using 10% palladium supported on carbon under an atmosphere of hydrogen, a

method known to give high yields with few impurities.[105] This yielded the generation one deprotected dendrimer G_1P-[6]-OH **49** as a colourless solid in 93% yield (**scheme 2.8**). The absence of a benzyl CH_2 signal at 5.1 ppm indicated removal of all benzyl groups which was verified by MALDI-MS. Analysis by GPC gave M_n 1200 and PDi 1.005, indicating good homogeneity. The molecular weight was determined by MALDI-MS analysis and gave good agreement with calculated values ([M+Na^+] at *m/z* 556 - calculated 557).

Scheme 2.8



48 **49**

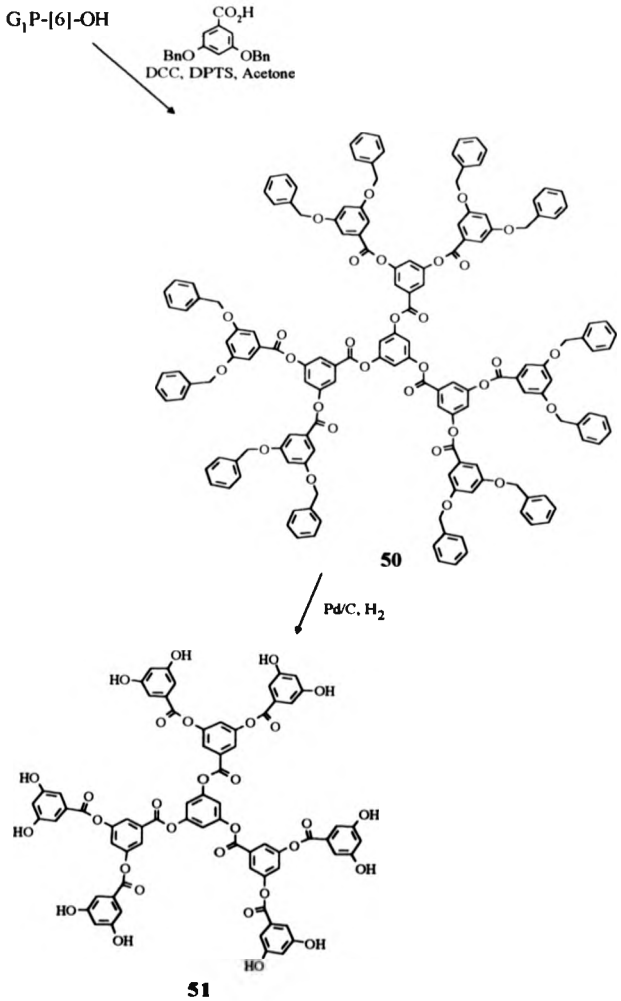
It was found that while the dendrimer was undergoing hydrogenolysis in dichloromethane, it started to precipitate out of solution. This was attributed to the change in polarity of the molecule during hydrogenolysis. The conversion of the relatively non-polar benzyl ethers to the polar hydroxyl groups, resulted in a molecule which was very insoluble in dichloromethane. This solubility dependence on the terminal functional groups has been noted by many other groups[106, 107] and was

overcome by the use of a mixed solvent system containing both dichloromethane and methanol. The methanol content was kept as high as possible, without precipitating the dendrimer, to ensure fast hydrogenolysis.

Using G_1P-[6]-OH, the second generation dendrimer G_2P-[12]-OBn **50** was prepared in 74% yield (**scheme 2.9**), a higher yield than for G_1P-[6]-OBn. GPC analysis of G_2P-[12]-OBn indicated that only a single species was present (M_n 3200, PDi 1.003), which was verified as G_2P-[12]-OBn by MALDI-MS (*m/z* calculated for $[M+Na^+]$ 2456, obtained 2455).

G_2P-[12]-OBn was deprotected using catalytic hydrogenolysis to give G_2P-[12]-OH **51** as a colourless solid in 92% yield (**scheme 2.9**). Analysis by GPC gave M_n 2600 and PDi 1.014, indicating good homogeneity. The molecular weight was determined by MALDI-MS analysis and gave good agreement with calculated values ($[M+Na^+]$ at *m/z* 1374 - calculated 1374)

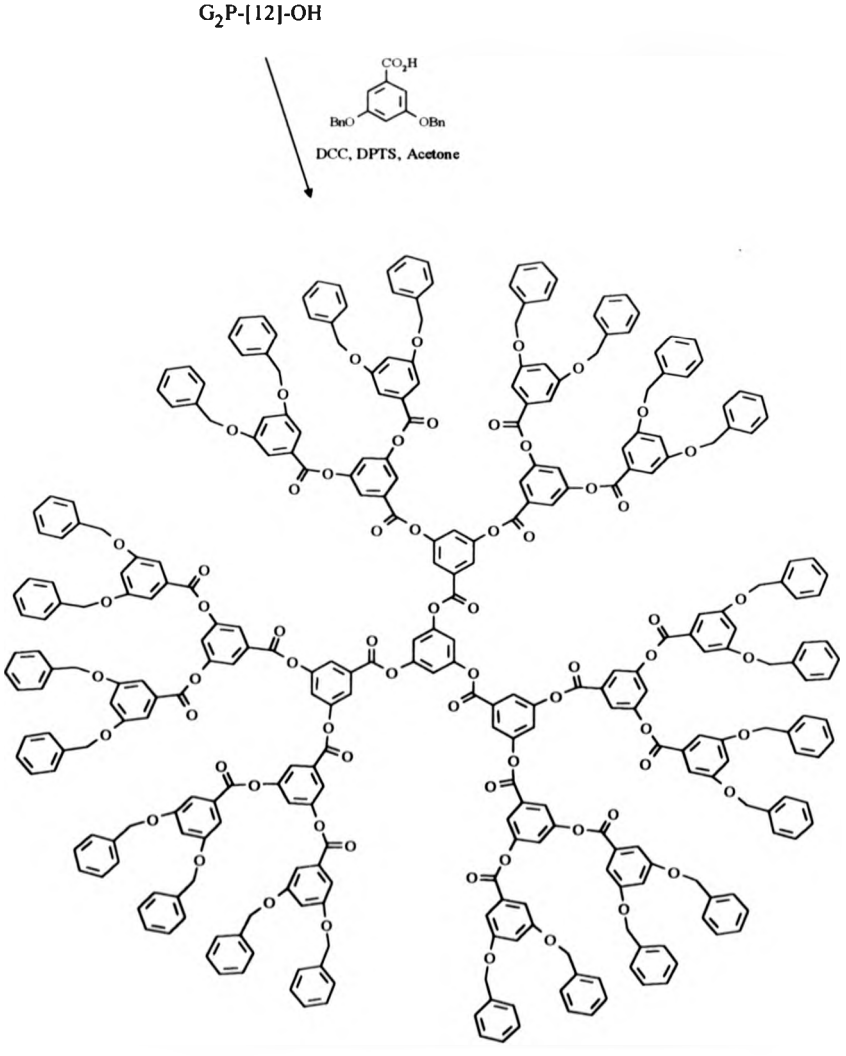
Scheme 2.9



Repetition of the esterification procedure with G_2P-[12]-OH yielded the third generation dendrimer G_3P-[24]-OBn **52** as a colourless solid in 94% yield (**scheme 2.10**). GPC analysis gave M_n 5800 and PDi 1.000 indicating good homogeneity. The product was verified as the desired

dendrimer by MALDI-MS (*m/z* calculated for $[M+Na^+]$ 5170, obtained 5168).

Scheme 2.10



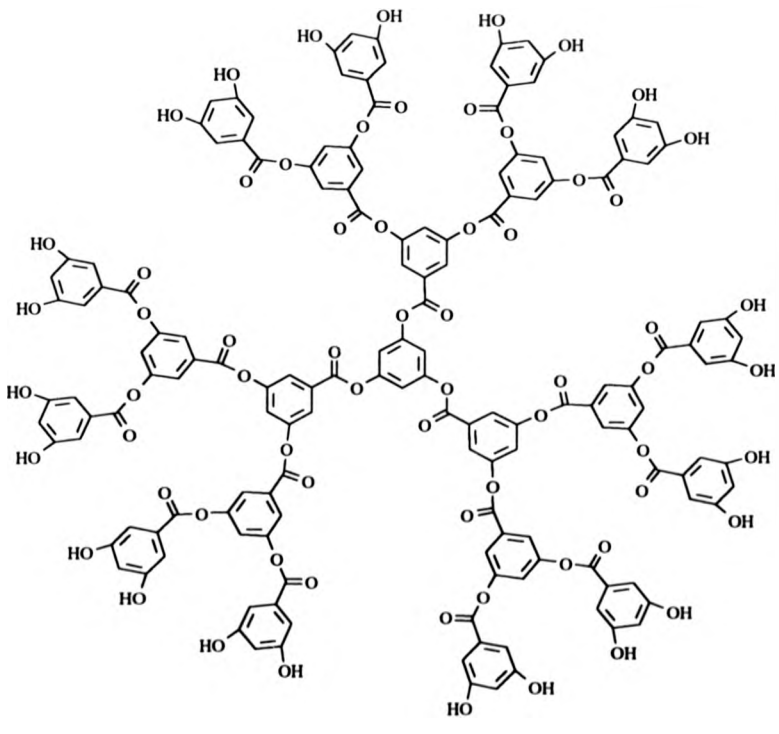
52

G_3P-[24]-OBn was deprotected using by catalytic hydrogenolysis to give G_3P-[24]-OH **53** as a tan solid in 92% yield (**scheme 2.11**). Analysis by GPC (M_n 4000, PDi 1.016) and MALDI-MS (*m/z* calculated for [M+Na^+] 3007, obtained 3007) indicated a successful synthesis.

Scheme 2.11

G_3P-[24]-OH

Pd/C, H_2



53

Attempts to continue the synthesis and prepare the fourth generation dendrimer from G_3P-[24]-OH, resulted in a material with broad molecular weight distribution (PDi > 1.1) by GPC. Analysis by ^{1}H and ^{13}C NMR also indicated that the attempted preparation of generation four had failed.

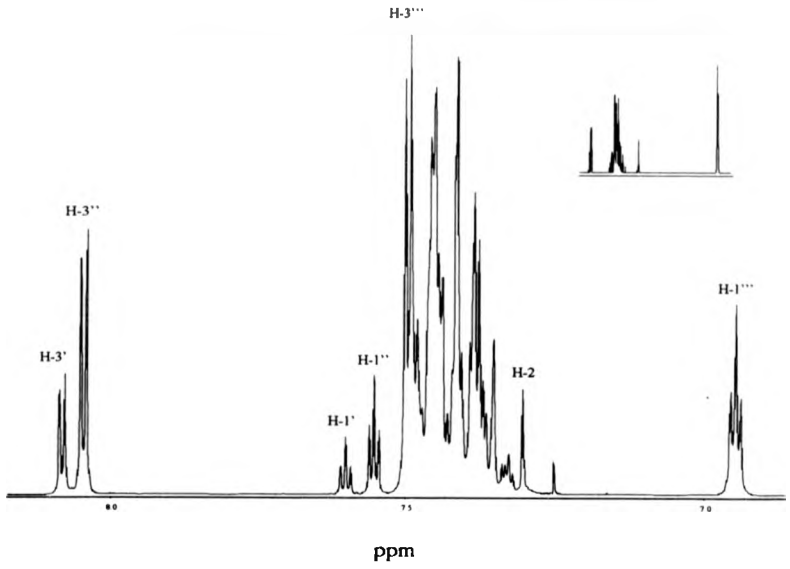
The synthesis was repeated in a range of solvents (dichloromethane, tetrahydrofuran (THF), chloroform, ethyl acetate) and mixed solvent systems (acetone-dichloromethane (1:1), THF-dichloromethane (1:1)) all of which gave similar results. Heating of the reaction mixture resulted in products with an even greater PDi and more complex NMR spectra.

2.3.3 Characterization of Dendrimers

2.3.3.1 ^{1}H and ^{13}C NMR

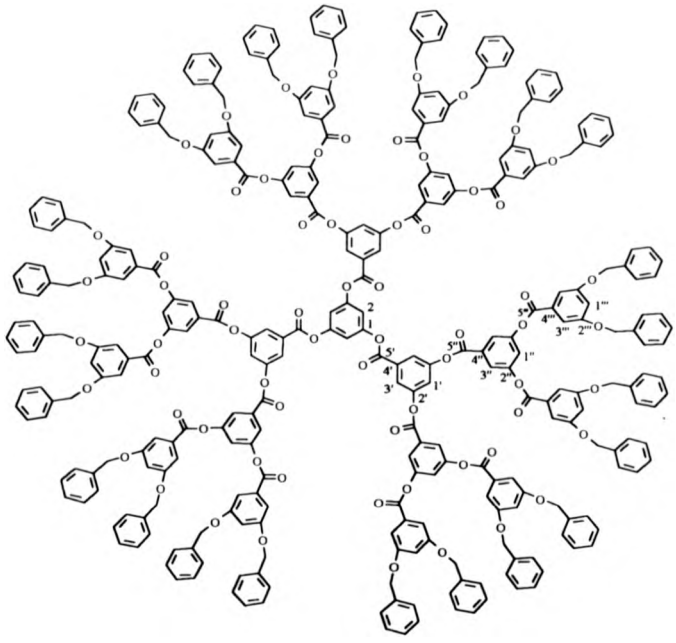
Both ^{1}H and ^{13}C were found to be invaluable tools for the characterization of these dendrimers. The symmetrical nature of these products resulted in discrete resonances being observed for each generation in both the ^{1}H and ^{12}C NMR spectra. **Figure 2.2** shows the aromatic region of the ^{1}H NMR spectrum of G_3P-[24]-OBn.

Figure 2.2 ^{1}H NMR Spectrum of G_3P-[24]-OBn



The three generations of branch unit can clearly be seen in the ^{1}H NMR spectrum. The most useful signals are the three sets of doublets due to H-3', H-3" and H-3"' (8.1, 8.05 and 7.5 ppm; 6, 12 and 24 H) and the three sets of triplets due to H-1', H-1" and H-1"' (7.6, 7.55 and 6.9 ppm; 3, 6 and 12 H). The initiator core H-2, can also be seen as a sharp singlet (7.3 ppm, 3 H).

Figure 2.3 Labelled Structure of G_3P-[24]-OBn



The ^{13}C NMR spectrum of G_3P-[24]-OBn is shown in **figure 2.4**. Once again the symmetrical nature of the molecule has resulted in the carbonyl resonances of C-5"', C-5" and C-5' (164, 162.7 and 162.3 ppm) occurring as three peaks with an approximate integral ratio of 4:2:1 for the three generations of branch unit. Similar patterns occur elsewhere in the ^{13}C NMR spectrum. The appearance of only one type of benzyl resonance at 70 ppm, confirmed the purity of the dendrimer.

Figure 2.4 ^{13}**C NMR Spectrum of** G_3**P-[24]-OBn**

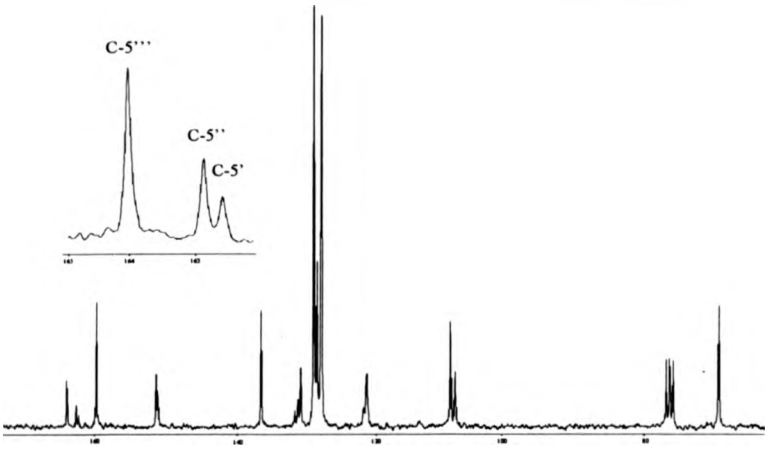
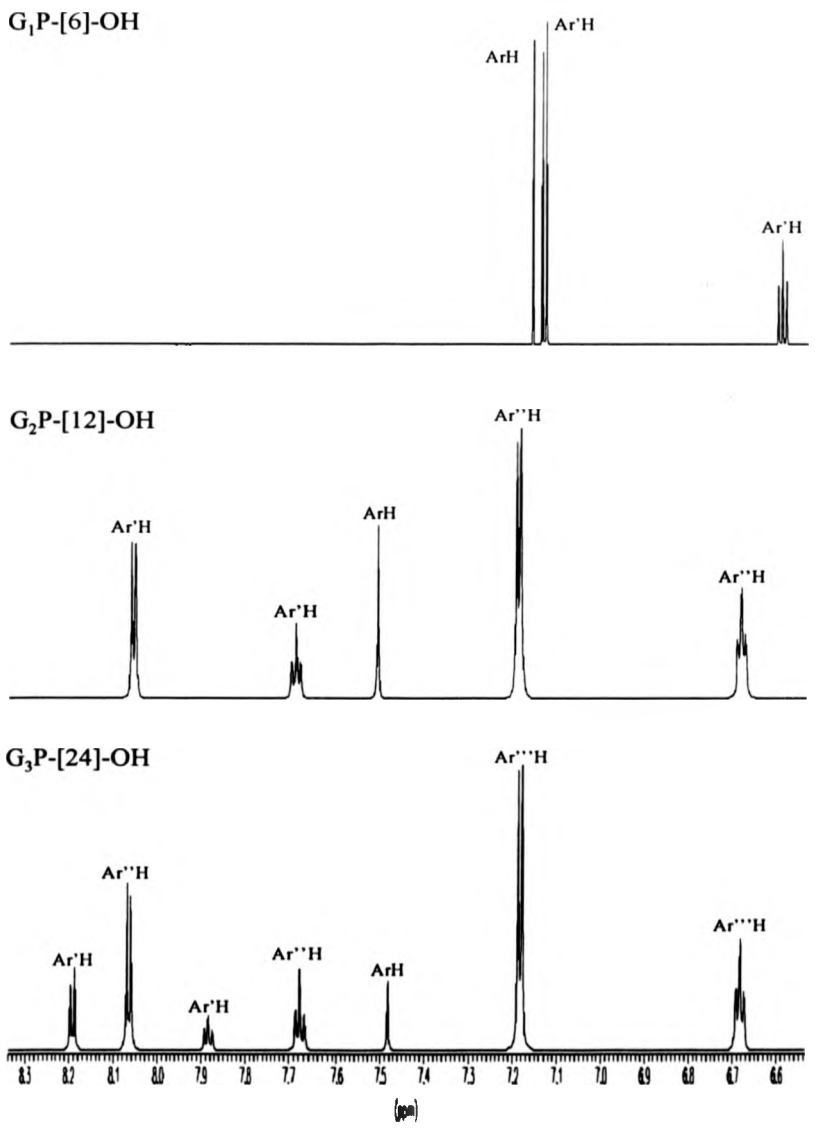


Figure 2.5 shows the ^{1}H NMR stack-plot of the three deprotected dendrimers G_1P-[6]-OH, G_2P-[12]-OH and G_3P-[24]-OH. ArH refers to the core, Ar'H refers to generation one branch units, Ar"H refers to generation two branch units and Ar'"H refers to generation three branch units. It is interesting to note that the second and third generation dendrimers give significantly broader signals. The second and third generation dendrimers also show similar shift signals for the external branch cells, for example, both give a doublet from the external branch cells at 7.18 ppm.

Figure 2.5 Stack Plot of G_1P-[6]-OH, G_2P-[12]-OH and G_3P-[24]-OH



The presence of repeating units in these dendrimers results in resonances which are either very near or overlapping. To assign rigorously all ^{13}C resonances, HETEROCOSY (heteronuclear correlated spectroscopy) NMR experiments were carried out when necessary.

2.3.3.2 Elemental Analysis

Satisfactory elemental analysis data was obtained for all the dendrimers. However, the data initially obtained for hydroxyl terminated dendrimers was not within acceptable limits. This was found to be due to the hygroscopic nature of these dendrimers which readily absorb moisture from the air. This problem was rectified by drying these dendrimers over phosphorus pentoxide *in vacuo*. The dendrimers were then found to give satisfactory results. Moisture absorbance was not found to be a problem with the benzyl terminated dendrimers.

2.3.3.3 GPC

GPC has been used extensively by many groups to characterize dendrimers and hyperbranched polymers. However, GPC has limited use as a means of determining the molecular weight of these macromolecules. This is because GPC is calibrated by linear standards and is suitable for

materials which have similar properties. Dendrimers are globular molecules and thus have different dimensions in solution to those of a linear polymer of similar molecular weight. Errors as great as 30% can occur, even with the application of the universal calibration principle or the use of low-angle laser light scattering (LALLS) detection method.[19, 89]

All of our dendrimers were analyzed by GPC. The M_n and PDi values found by GPC are summarized in **table 2.1**. The M_ns obtained by GPC for benzyl terminated dendrimers are all within 32% of the calculated molecular weights. However, the M_ns obtained by GPC for hydroxyl terminated dendrimers are significantly dissimilar from the calculated values. For example, the M_n obtained by GPC is more than twice the calculated value for the generation one dendrimer G_1P-[6]-OH and, at best, within 35% of the calculated value, for G_3P-[24]-OH.

Table 2.1 GPC Data of Phloroglucinol Core Dendrimers

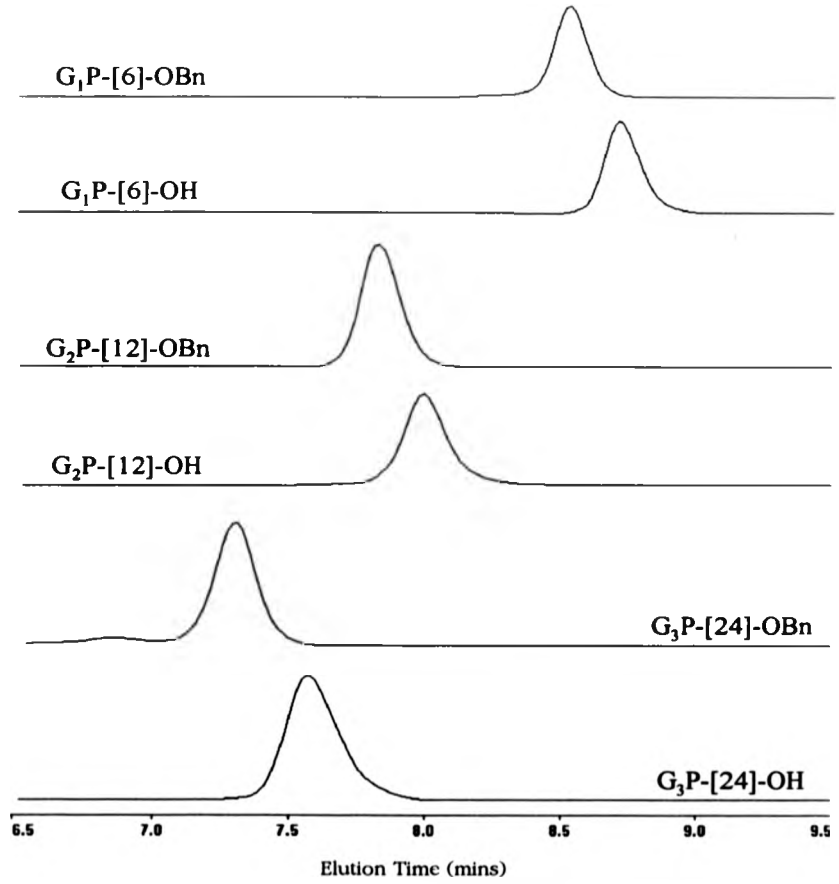
Dendrimer	M_n	PDi	Calculated MW
G_1P-[6]-OBn	1500	1.004	1075
G_1P-[6]-OH	1200	1.005	534
G_2P-[12]-OBn	3200	1.003	2433
G_2P-[12]-OH	2600	1.014	1351
G_3P-[24]-OBn	5800	1.000	5147
G_3P-[24]-OH	4000	1.016	2984

The low PDi values for all dendrimers indicates that they are monodisperse products. The slightly higher values of PDi for the hydroxyl terminated dendrimers could be as a result of interactions of the polar hydroxyl groups with the polystyrene packing material of the column, the effect being more noticeable with higher generation dendrimers which have larger numbers of hydroxyl groups. A similar observation was also noted by Turner *et al*, who reported incomplete elution and poor reproducibility of his phenol terminated hyperbranched polymers.[80]

A small percentage of unidentified higher molecular weight material was seen in some GPC traces, particularly for the higher generation dendrimers. Estimations by GPC (using integrals) indicated that they constituted no more than 5% of the dendrimer. These could not be isolated nor removed even after repeated purification steps (including precipitation, re-crystallization and flash chromatography). Estimations of the molecular weight using GPC put the mass of the impurities at twice the molecular weight of the dendrimer. We thus consider that this material may be an association product of two dendrimers, perhaps due to the entanglement of branches. The satisfactory elemental analyses obtained for these dendrimers, indicates that these higher molecular weight materials are dendritic as they do not adversely affect the element content. **Figure 2.6** shows an overlay of the GPC traces of G_1P-[6]-OBn, G_1P-[6]-OH, G_2P-[12]-OBn, G_2P-[12]-OH, G_3P-[24]-OBn and G_3P-[24]-OH.

The small percentage of high molecular weight material is seen for the third generation dendrimer G_3P-[24]-OBn.

Figure 2.6 GPC Traces of Phloroglucinol Core Dendrimers



2.4 Failed Synthesis of Generation Four

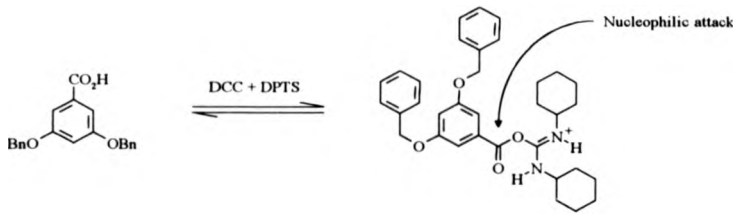
Our inability to prepare the fourth generation dendrimer indicated one of the following:

(i) the alcohol branch termini are buried within the dendrimer and hence unreachable to reagents;
(ii) our esterification procedure is not suitable;
(iii) we have reached the theoretical de Gennes limit.

The first of these possible reasons was tackled by the use of differing solvent systems in an attempt to 'open up' the dendrimer by solvation to release buried hydroxyl groups to reagents. This was, as mentioned earlier, found to be unsuccessful.

The second possible cause was attacked by using a different esterification procedure. The DCC-DPTS esterification agents pass through an activated state where the acid is bound to the DCC (**scheme 2.12**).[108] The alcohol then attacks nucleophilically at the carbonyl carbon with the loss of dicyclohexylurea (DCU). However the DCC-acid intermediate **54** is rather large, and access to the dendritic alcohols may be limited due to steric reasons, particular if the dendrimer is very near the de Gennes limit.

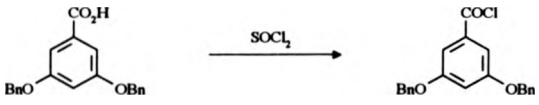
Scheme 2.12



54

To circumvent this problem, we prepared the acid chloride derivative **55** from **47** (**scheme 2.13**) and repeated the syntheses.

Scheme 2.13



55

Reaction at room temperature and at reflux in dichloromethane failed to produce the fourth generation dendrimer using either pyridine or the stronger base DMAP. However, we were able to successfully prepare the generation one dendrimer G_1P-[6]-OBn in excellent (100%) yield using this procedure. Preparation of second and third generation dendrimers G_2P-[6]-OBn and G_3P-[12]-OBn, also failed using this method. It is not yet clear why the acid chloride method is superior to the DCC-DPTS method for generation one, but inferior for higher generations.

2.4.1 Molecular Modelling

Molecular modelling of the dendrimers was carried out using HyperChem Lite™. Energy minimizations were carried out using the MM+ molecular mechanics algorithm.

Figures 2.7, **2.8**, **2.9** and **2.10** show the dendrimers G_1P-[6]-OBn, G_2P-[12]-OBn, G_3P-[24]-OBn and the unsynthesized G_4P-[48]-OBn, respectively. **Figure 2.7** indicates that the generation one dendrimer has limited scope for back-folding of dendrons. **Figure 2.8** shows that by generation two, branch termini are able to fold back onto the core unit. The back-folding of dendrons was put forward by the Lescanec model, perhaps to relieve steric congestion.

The third and fourth generation dendrimers, whilst able to fold back onto the core to relieve steric congestion, give considerably different models from that of the second generation dendrimer. The second generation dendrimer shows significant back-folding, whereas the third and fourth generation dendrimers do not. Unfortunately, HyperChem Lite™ is unable to determine accurately the lowest energy molecular conformation, and thus few conclusions can be drawn about the shape of the dendrimer. However, it is rather unexpected that conformations calculated for generations three and four should be so different from those of generation two.

Figure 2.7 HyperChem Model of G_1P-[6]-OBn

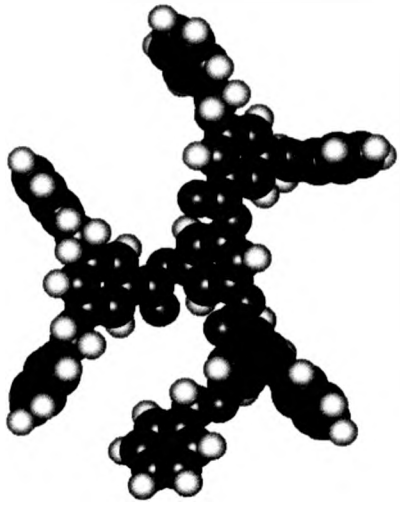
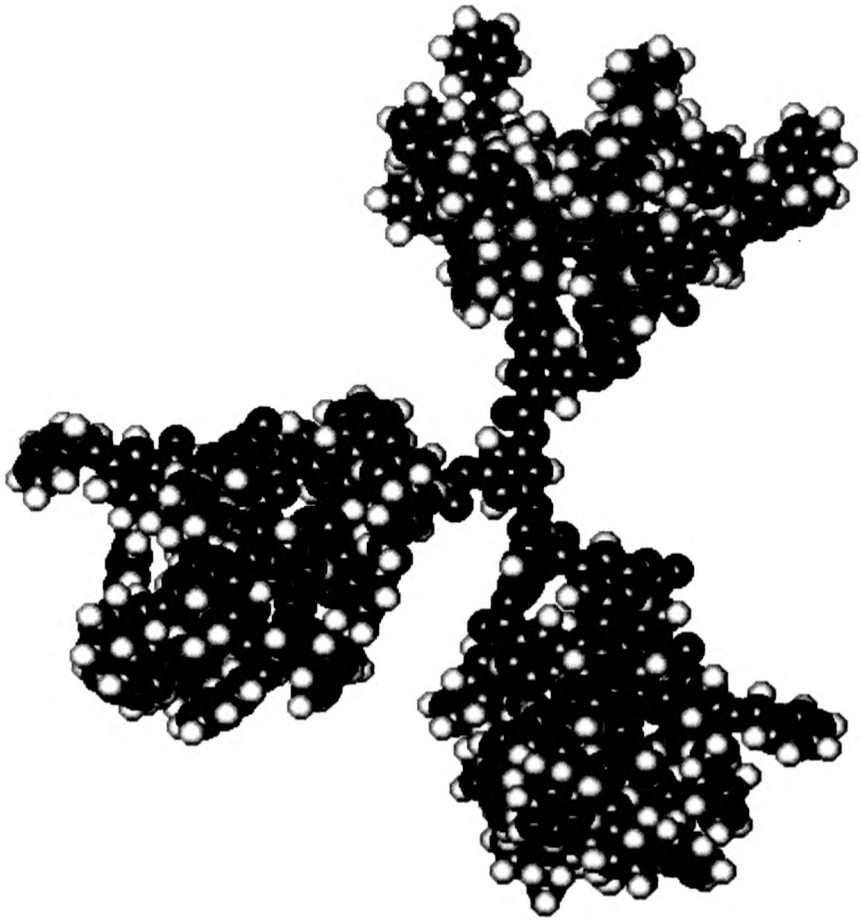


Figure 2.8 HyperChem Model of G_2P-[12]-OBn

Figures 2.9 and **2.10** show that the third and fourth generation dendrimers are very congested at the branch termini. Here, the three main branches of the dendrimers have begun to cluster together, giving dendrimers which have three very congested branches and relatively accessible cores. The high accessibility of the core molecule as indicated by these models, imply that the de Gennes limit is not reached at the third generation or even the fourth for the whole dendrimer. However, these models suggest that perfect dendrimer growth may have been prevented due to having reached the de Gennes limit for the individual dendrons. It must be noted that using a bi-functional core (chapter 2.5) we were able to prepare dendrimers beyond generation three. These conflicting results may be due to a limitation of the modelling which minimizes the energy of the molecule in a vacuum. In solution, the molecules will be solvated which may result in the dendrons being much more open.

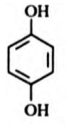
Figure 2.9 HyperChem Model of G_3P-[24]-OBn



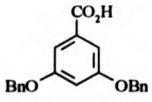
2.5 Hydroquinone Core Dendrimers

To test whether we had indeed reached the de Gennes limit, we decided to prepare dendrimers with bi-functional cores instead of the tri-functional unit previously used. By having only two branching units, we expected to reduce steric congestion at the branch termini. If steric reasons were to blame for our inability to prepare fourth generation dendrimers, the use of a two-branched core would allow us to prepare higher generation dendrimers. Thus, we chose hydroquinone **56** as the core unit (**figure 2.11**).

Figure 2.11 Structures of 56 and 47



56



47

Using the same branch unit **47** as for the phloroglucinol core dendrimers and the same reaction conditions (DCC, DPTS, acetone), we prepared the generation one dendrimer G_1H-[4]-OBn **57** in poor yield (8%). Having achieved high yields previously for the preparation of the generation one phloroglucinol dendrimer using the acid chloride **55**, we decided to employ this chemistry for the preparation of G_1H-[4]-OBn **57**. Once again we achieved a very high yield (100%) (**scheme 2.14**). Analysis by GPC indicated the presence of a single species (M_n 1000, PDi 1.005) and

Figure 2.9 HyperChem Model of G_3P-[24]-OBn

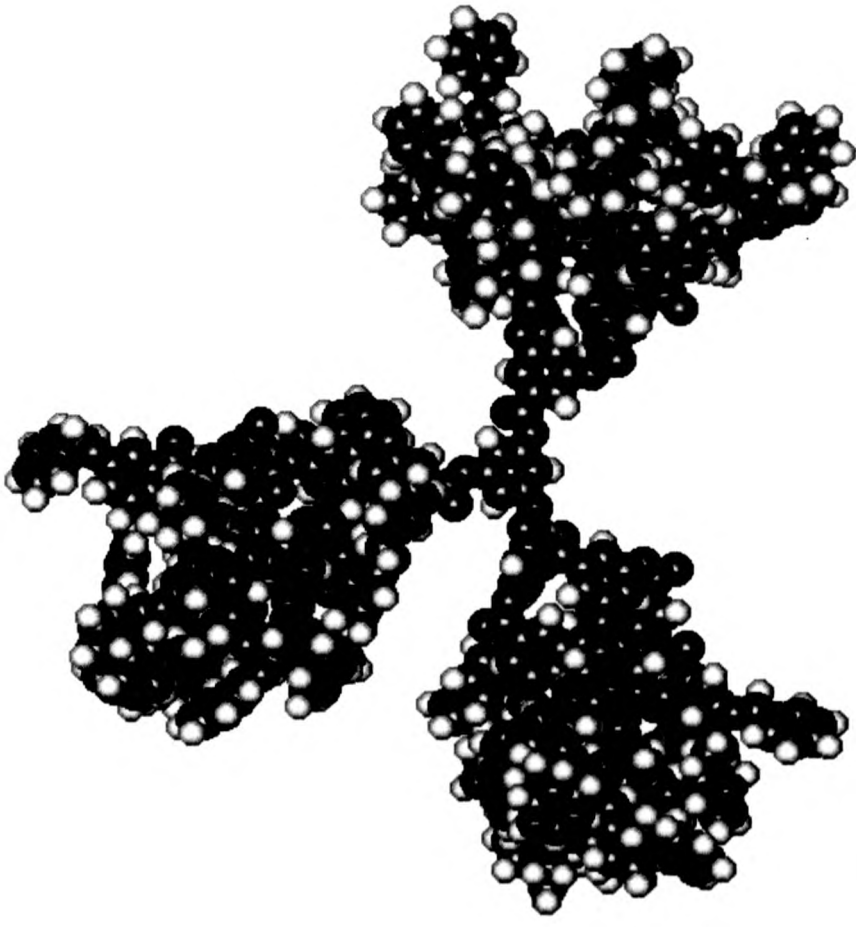
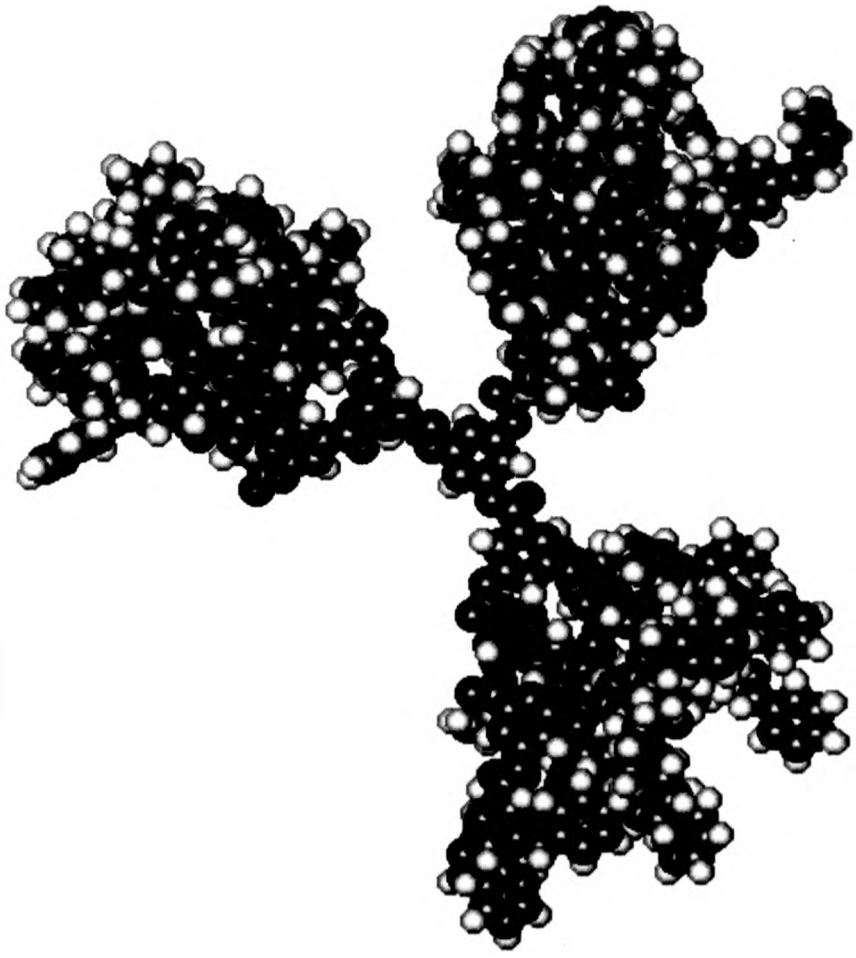


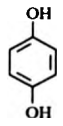
Figure 2.10 HyperChem Model of G_4P-[48]-OBn



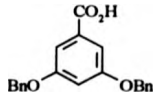
2.5 Hydroquinone Core Dendrimers

To test whether we had indeed reached the de Gennes limit, we decided to prepare dendrimers with bi-functional cores instead of the tri-functional unit previously used. By having only two branching units, we expected to reduce steric congestion at the branch termini. If steric reasons were to blame for our inability to prepare fourth generation dendrimers, the use of a two-branched core would allow us to prepare higher generation dendrimers. Thus, we chose hydroquinone **56** as the core unit (**figure 2.11**).

Figure 2.11 Structures of 56 and 47



56



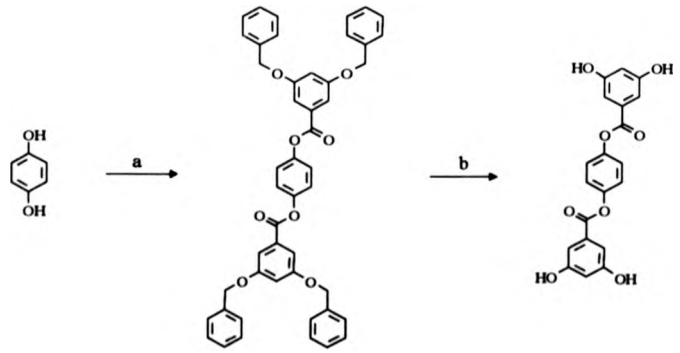
47

Using the same branch unit **47** as for the phloroglucinol core dendrimers and the same reaction conditions (DCC, DPTS, acetone), we prepared the generation one dendrimer G_1H-[4]-OBn **57** in poor yield (8%). Having achieved high yields previously for the preparation of the generation one phloroglucinol dendrimer using the acid chloride **55**, we decided to employ this chemistry for the preparation of G_1H-[4]-OBn **57**. Once again we achieved a very high yield (100%) (**scheme 2.14**). Analysis by GPC indicated the presence of a single species (M_n 1000, PDi 1.005) and

MALDI-MS verified this as the dendrimer G_1H-[4]-OBn (*m/z* calculated for [M+Na^+] 765, obtained 765).

The low solubility of G_1H-[4]-OBn in dichloromethane meant that we had to use chloroform-methanol as our solvent mixture for hydrogenolysis. Hydrogenolysis of G_1H-[4]-OBn overnight using 10% Pd/C and H_2 gave the deprotected dendrimer G_1H-[4]-OH **58** in 95% yield (**scheme 2.14**). Analysis by GPC indicated that only a single species was present (M_n 900, PDi 1.005).

Scheme 2.14

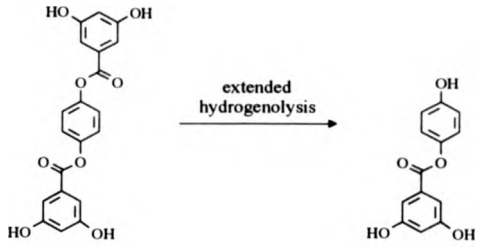


57 **58**

a = **47**, DCC, DPTS and acetone or **55**, DMAP and CH_2Cl_2; b = 10% Pd/C, H_2

It was found that extended hydrogenolysis over a period of several days resulted in the formation of breakdown products **59** resulting from hydrolysis of the esters under the reaction conditions (**scheme 2.15**). Fragmentation of this sort was not observed for any other dendrimer.

Scheme 2.15

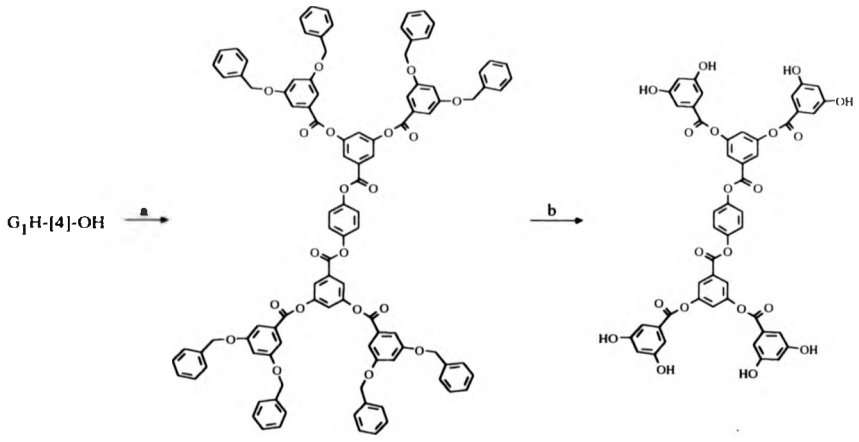


59

The second generation dendrimer G_2H-[8]-OBn **60** was prepared using both the DCC-DPTS method and the acid chloride method (**scheme 2.16**). Both methods were successful, giving yields of 85% and 86% respectively. GPC analysis gave M_n 2400 and PDi 1.008 indicating good homogeneity of the product which was verified as the desired dendrimer by MALDI-MS (*m/z* calculated for [M+Na^+] 1670, obtained 1670)

Catalytic hydrogenolysis of G_2H-[8]-OBn gave G_2H-[8]-OH **61** as a colourless solid in 89% yield (**scheme 2.16**). GPC analysis gave M_n 2100 and PDi 1.006 indicating good homogeneity. MALDI-MS analysis gave *m/z* of [M+Na^+] 949 (calculated 949).

Scheme 2.16



60 **61**

a = **47**, DCC, DPTS and acetone or **55**, DMAP and CH_2Cl_2; b = 10% Pd/C, H_2

Repetition of the DCC-DPTS esterification procedure yielded the generation three dendrimer G_3H-[16]-OBn **62** in 88% yield. However, attempts with the acid chloride **55** failed (**scheme 2.17**). The homogeneity of the dendrimer was determined by GPC and found to be good (M_n 4700, PDi 1.000). MALDI-MS analysis gave the molecular ion at *m/z* 3478 (calculated 3478) indicating successful synthesis.

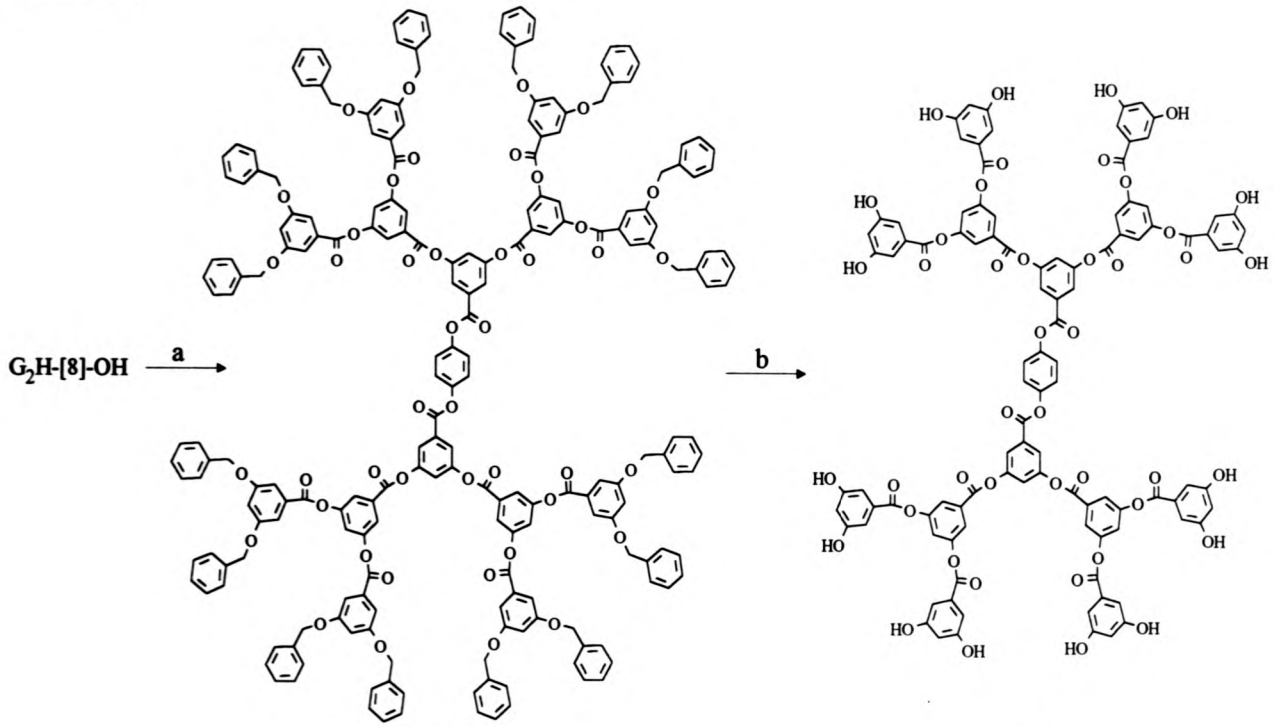
G_3H-[16]-OBn was deprotected to give G_3H-[16]-OH **63** in 89% yield as a tan coloured solid (**scheme 2.17**). Analysis by GPC gave M_n 3500 and PDi 1.020, indicating good homogeneity. The molecular weight was determined by MALDI-MS analysis and gave good agreement with calculated values ([M+Na^+] at *m/z* 2037 - calculated 2037).

Using the DCC-DPTS method, the generation four dendrimer G_4H-[32]-OBn **64** was prepared in 86% yield as a colourless solid (**scheme 2.18**). Once again, the acid chloride method failed to give the desired product. Analysis by GPC (M_n 7800, PDi 1.000) indicated that a single species was present.

Deprotection of G_4H-[32]-OBn gave the fourth generation dendrimer G_4H-[32]-OH **65** as a tan coloured solid in 92% yield (**scheme 2.18**). GPC analysis (M_n 2600, PDi 1.011) indicated good homogeneity.

Attempts to continue the synthesis to the fifth generation failed using both the DCC-DPTS method and the acid chloride method. In both cases, a material with broad molecular weight distribution (PDi > 1.1) and complex ^1H and ^{13}C NMR spectra resulted. A variety of solvents (dichloromethane, THF) and mixed solvent systems (dichloromethane-acetone (1:1), dichloromethane-THF (1:1)) were also tried, but all failed to yield the desired product.

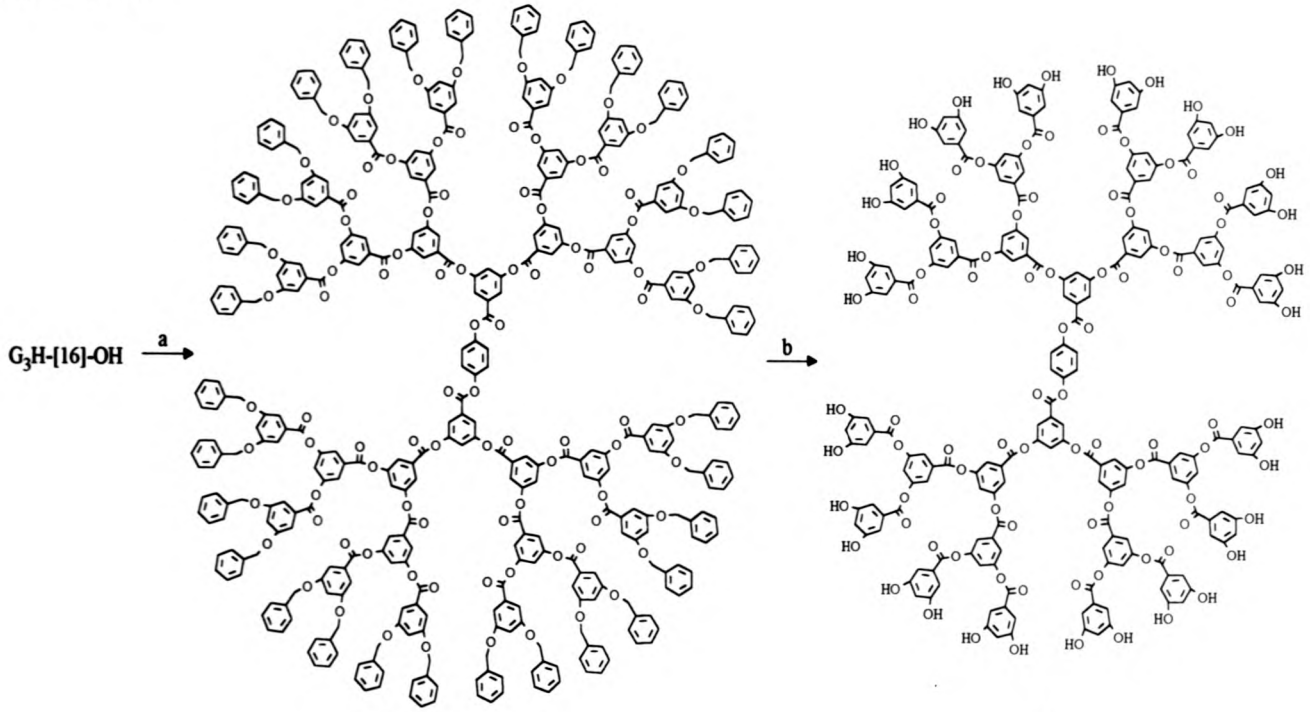
Scheme 2.17



62 **63**

a = 47, DCC, DPTS and acetone; b = 10% Pd/C, H_2

Scheme 2.18

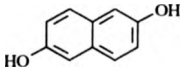


a = **47**, DCC, DPTS and acetone; b = 10% Pd/C, H_2

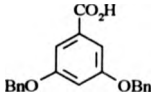
2.6 Naphthalene-2,6-diol Core Dendrimers

To enable us to carry out studies on the accessibility of the core moiety (see chapter 6), we decided to prepare dendrimers containing the fluorescent naphthalene-2,6-diol unit **66** (**figure 2.12**). This was used as the core unit with the branching unit **47**.

Figure 2.12 Structure of 66 and 47



66

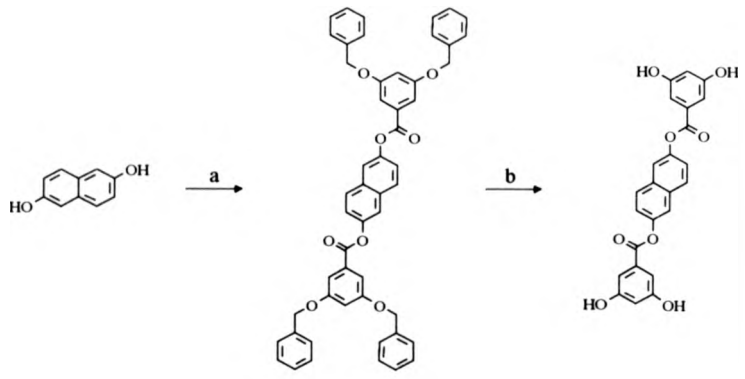


47

The generation one dendrimer G_1N-[4]-OBn **67** was prepared easily from naphthalene-2,6-diol using both the DCC-DPTS method and the acid chloride method (**scheme 2.19**). As with both the phloroglucinol and hydroquinone core dendrimers, the generation one dendrimer was isolated in greater yield with the acid chloride method (100%) than with the DCC-DPTS method (30%). GPC analysis gave M_n 1200 and PDi 1.006 indicating good homogeneity of the product which was verified as the desired dendrimer by MALDI-MS (*m/z* calculated for [M+Na^+] 815, obtained 816).

Deprotection using Pd/C and H_2, gave the generation one dendrimer G_1N-[4]-OH **68** in 95% yield (**scheme 2.19**). The homogeneity was found to be good by GPC (M_n 900, PDi 1.005).

Scheme 2.19



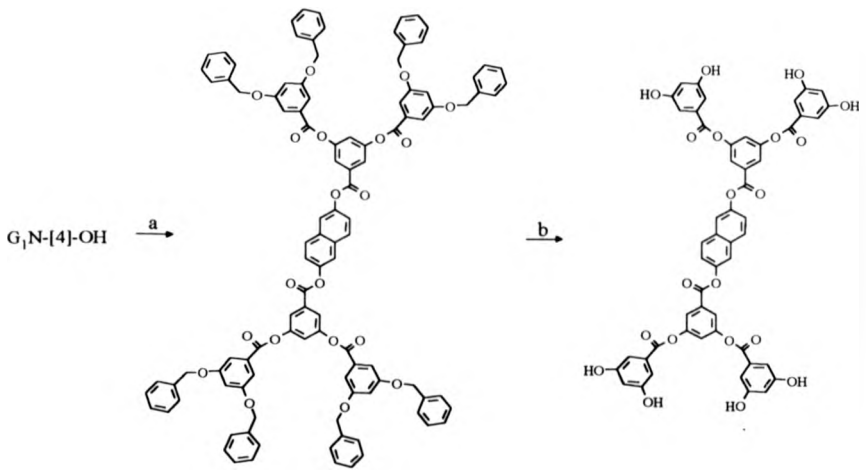
67 **68**

a = **47**, DCC, DPTS and acetone or **55**, DMAP and CH_2Cl_2; b = 10% Pd/C, H_2

The second generation dendrimer G_2N-[8]-OBn **69** was prepared using both the DCC-DPTS method and the acid chloride method (**scheme 2.20**). Both methods were successful, giving yields of 92% and 80% respectively. Analysis by GPC (M_n 2600, PDi 1.003) and MALDI-MS (*m/z* calculated for [M+Na^+] 1720, obtained 1720) indicated a successful synthesis.

Catalytic hydrogenolysis of G_2N-[8]-OBn gave G_2N-[8]-OH **70** as a colourless solid in 89% yield (**scheme 2.20**). GPC analysis gave M_n 1900 and PDi 1.003 indicating that only a single species is present which was verified as the desired product by MALDI-MS (*m/z* calculated for [M+Na^+] 999, obtained 999).

Scheme 2.20



69 **70**

a = **47**, DCC, DPTS and acetone or **55**, DMAP and CH_2Cl_2; b = 10% Pd/C, H_2

The third generation dendrimer G_3N-[16]-OBn **71** was prepared in 96% yield using the DCC-DPTS method (**scheme 2.21**). The acid chloride method failed to give the pure dendrimer; a broad molecular weight distribution was seen by GPC. Analysis by GPC (M_n 4300, PDi 1.003) and MALDI-MS (*m/z* calculated for [M+Na^+] 3529, obtained 3529) indicated a successful synthesis.

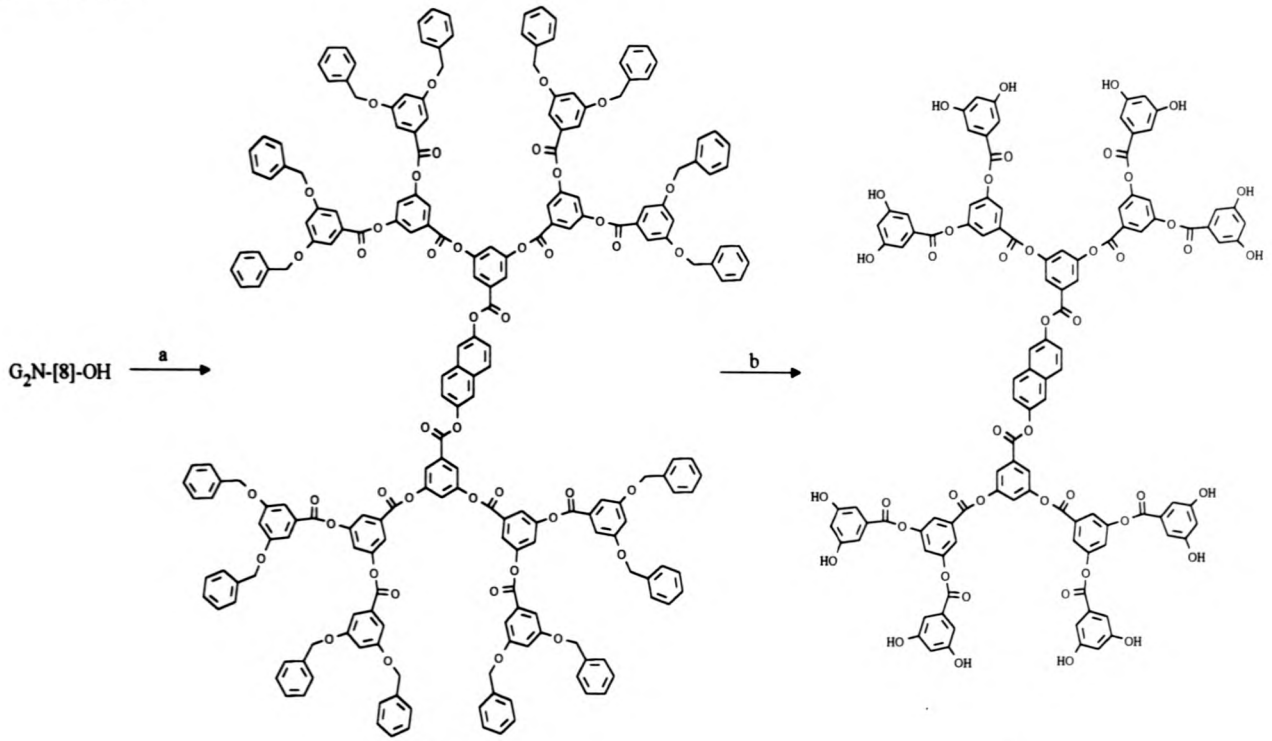
G_3N-[16]-OBn was deprotected to give the third generation dendrimer G_3N-[16]-OH **72** as a colourless solid in 96% yield (**scheme 2.21**). Analysis by GPC (M_n 3200, PDi 1.009) and MALDI-MS (*m/z* calculated for [M+Na^+] 2087, obtained 2086) indicated a successful synthesis.

Using the DCC-DPTS method, the fourth generation dendrimer G_4N-[32]-OBn **73** was prepared in 95% yield (**scheme 2.22**). The acid chloride method failed to produce the desired product. Analysis by GPC gave M_n 7800 and PDi 1.000 indicating the presence of a single species.

G_4N-[32]-OBn was deprotected to give the fourth generation dendrimer G_4N-[32]-OH **74** in 87% yield (**scheme 2.22**). GPC gave M_n 2600 and PDi 1.088. Although this dendrimer gave a broader molecular weight distribution than the previous dendrimers, satisfactory elemental analysis was obtained and the dendrimer was fully characterized by ^1H and ^{13}C NMR.

The attempted preparation of the fifth generation dendrimer resulted in a material with a broad molecular weight distribution (PDi > 1.1) and complex NMR. This material was isolated for use in luminescence studies.

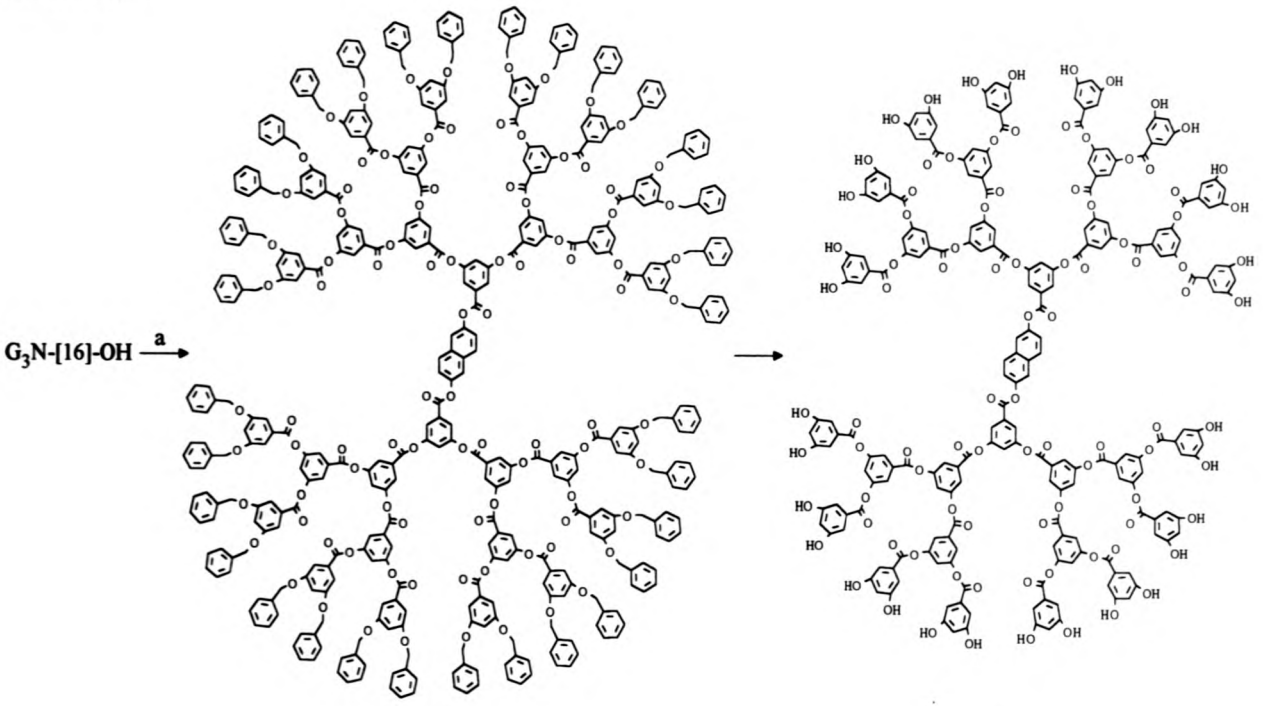
Scheme 2.21



71 **72**

a = **47**, DCC, DPTS and acetone; b = 10% Pd/C, H_2

Scheme 2.22



73 **74**

a = 47, DCC, DPTS and acetone; b = 10% Pd/C, H_2

2.7 Characterization of Hydroquinone and Naphthalene-2,6-diol Dendrimers

All hydroquinone and naphthalene-2,6-diol core dendrimers were characterized by GPC, elemental analysis and ^{1}H and ^{13}C NMR. It was found that the ^{1}H NMR spectra of all fourth generation dendrimers showed a broadening of the resonances of the outermost branch cells. This is probably due to the small variations in the micro-environments of the branch termini.

2.8 Conclusion

The preparation of all dendrimers was attempted with both the DCC-DPTS method (method A) and the acid chloride method (method B). The yields for the esterification steps are shown in **table 2.2**. The deprotection of the benzyl terminated dendrimers gave consistently high yields (89-97%).

It can be seen from **table 2.2** that the acid chloride method can be useful for the synthesis of a few of the lower generation dendrimers. However, the most important observation is that the two methods of activation are entirely complementary. That is, the acid chloride method (A) is much higher yielding in preparation of low generation dendrimers, whereas the

DCC method (B) is clearly superior for higher generations. We currently have no explanation for this.

Table 2.2

Initiator core	Method	% Yield G_1-OBn	% Yield G_2-OBn	% Yield G_3-OBn	% Yield G_4-OBn
Phloroglucinol	A	25	74	94	-
	B	100	0	0	-
Hydroquinone	A	8	85	88	86
	B	100	86	0	0
Naphthalene-2,6-diol	A	30	92	96	95
	B	100	80	0	0

It was found that the yield of the synthesis of G_1P-[6]-OBn dendrimer using method A, could be increased by the addition of an equal volume of dichloromethane to the reaction mixture after it had been allowed to stir overnight. The yield increased dramatically from 25% to 89%. Using this method, the yields of G_1H-[4]-OBn and G_1N-[4]-OBn were increased to 72% and 76% respectively.

Preparation of these dendrimers in multi-gram quantities presented problems. The original work had been carried out under Schlenk conditions. The scale-ups, requiring greater volumes of solvent, were carried out in suitably sized round bottomed flasks. The reduced stirring resulting from the spherical shape of the flask resulted in low yields. The

reactions could all be successfully scaled up using specially prepared very large Schlenk tubes and vigorous stirring.

Chapter 3

Synthesis of Hyperbranched Polymers

3.1 Introduction

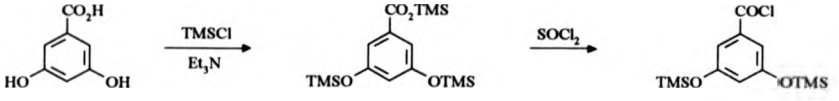
Hyperbranched polymers are polydisperse materials which may have similar physical properties to dendrimers. Their properties differ from linear and crosslinked polymers. For example, they tend to have lower melt viscosities and increased solubility compared to similar molecular weight linear polymers.

To compare the properties of dendrimers and hyperbranched polymers, we wished to prepare hyperbranched polymers constructed from the same branch unit as previously used in the preparation of dendrimers. Dendrimers are prepared by a repetitive multi-step procedure which often requires chromatographic purification at each stage. Hyperbranched polymers on the other hand, may be prepared in a one-step fashion. They are thus far more amenable to large scale preparation than dendrimers and consequently more attractive for industrial applications.

At the outset of our work, there were very few publications on the preparation of hyperbranched polyesters. There were no examples of the use of 5-hydroxyisophthalic acid as a monomer for the synthesis of hyperbranched polyesters but there were two examples of hyperbranched polyesters derived from 3,5-dihydroxybenzoic acid **46**.[79, 80]

Fréchet *et al* reported the one-step synthesis of hyperbranched polymers by first converting **46** to the silyl ether-ester **75** using trimethylsilyl chloride (TMSCl) and triethylamine (**scheme 3.1**).[79] The silyl ester was then converted to the acid chloride **76** using thionyl chloride.

Scheme 3.1

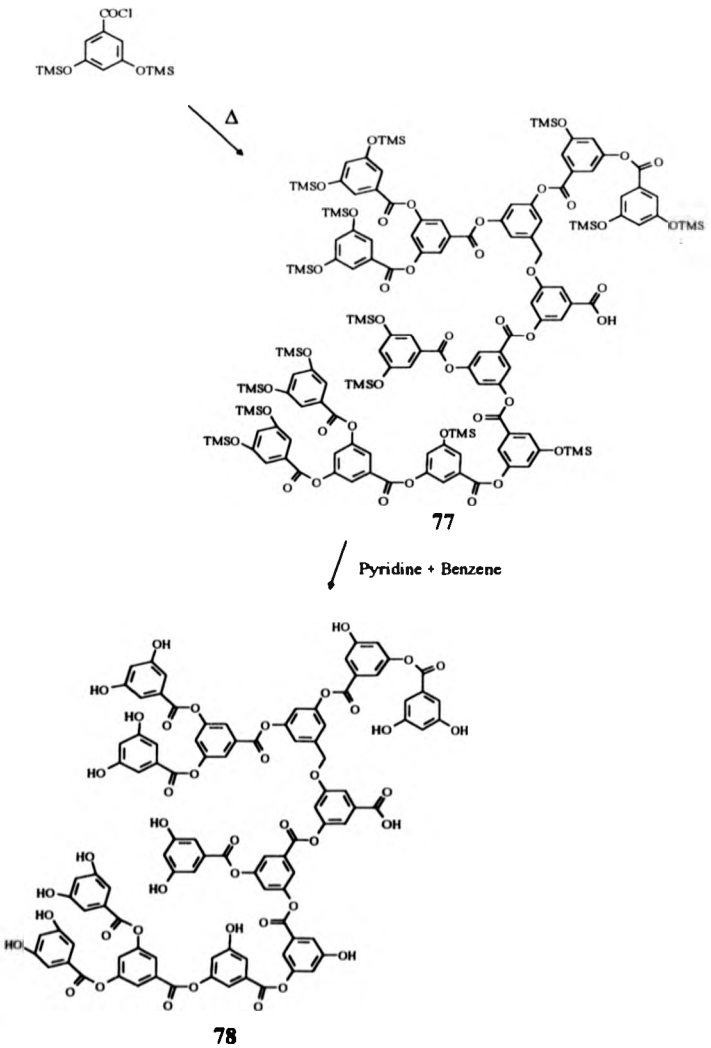


46 **75** **76**

Thermal polymerization of **76** at a variety of temperatures gave the silyl terminated hyperbranched polyester **77** (**scheme 3.2**). The silyl groups were removed by stirring in pyridine-benzene to give products with M_n ranging between 16000 and 55000 and polydispersities ranging from 1.9 to 3.8 (**78**, **scheme 3.2**). The highest polydispersities occurred when longer reaction times were employed at lower (~200 °C) temperatures. Conversely, the lowest polydispersities were observed at higher reaction temperatures (~260 °C) and short reaction times. The molecular weights of the polymers were inversely proportional to the temperature of polymerization, thus the highest molecular weights were obtained at 190 °C and the lowest at 260 °C. The degree of branching was determined by NMR and found to be between 55-60%. In a subsequent publication, Fréchet *et al* reported the improved chloride free preparation of **76** using hexamethyldisilazane (HMDS) instead of TMSCl.[109] The absence of

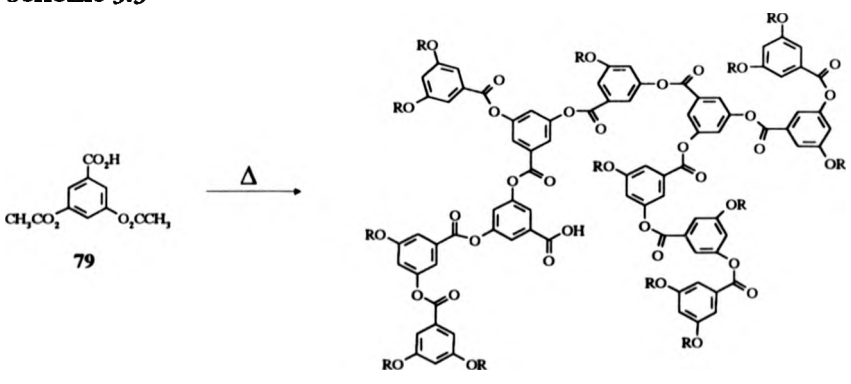
chloride improved the stability of **76**, allowing greater reproducibility in the preparation of hyperbranched polymers.

Scheme 3.2



Turner *et al* prepared all aromatic hyperbranched polyesters by modifying **46**.[80] The hydroxyl functional groups were converted to acetate esters **79** with acetic anhydride. Polymerization of **79** in the melt (**scheme 3.3**) gave a brittle material, which upon purification, gave the polymer as a white solid (M_n 33000, PDi 3.9). The acetate groups were removed by partial hydrolysis using hydrochloric acid (M_n 29000, PDi 3.3). It was estimated by NMR that the hydrolysis removed approximately 85-89% of the acetate groups. More vigorous conditions were not employed as Turner feared this would lead to degradation of the polymer backbone.

Scheme 3.3



79

R = CH_3CO or H

3.2 Poly(5-hydroxyisophthalic acid)

We decided to investigate the synthesis of hyperbranched polymers using 5-hydroxyisophthalic acid **41** and the same esterification method as used

to synthesize dendrimers (DCC-DPTS). This method would, if successful, have the advantage of being carried out at room temperature and using a commercially available monomer instead of a silyl or acetyl derivative.

Esterification of **41** in dichloromethane or acetone resulted in the formation of a solid which was insoluble in acetone, methanol and THF. The insolubility of this material in THF meant that no GPC data was obtained. Attempted dissolution in THF overnight also failed. The insolubility may have been due to anhydride formation caused by the dehydrating agent DCC. Turner remarked that anhydride formation in his hyperbranched polyesters resulted in insoluble crosslinked networks.[81]

It was at this time that we were also experiencing solubility problems with our 5-hydroxyisophthalic acid dendrimers and it was thus decided to investigate a system which was known to be soluble.

3.3 Poly(3,5-dihydroxybenzoic acid)

3.3.1 Method 1

We decided to investigate the synthesis of hyperbranched polymers based upon **46**, using the DCC-DPTS esterification agents. These were known to be soluble in solvents such as THF and thus were less likely to present problems of solubility.[79, 80]

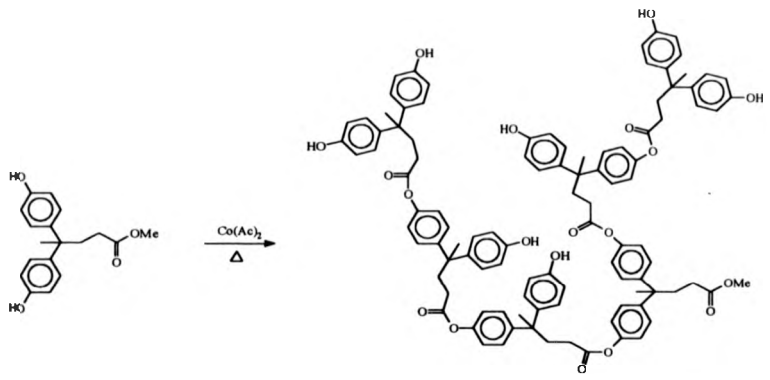
GPC analysis of the crude product of the polymerization of **46** (in the presence of DCC and DPTS) indicated the formation of poly(3,5-dihydroxybenzoic acid) **80**. Samples were taken 10 mins, 30 mins, 1 hr, 2 hrs, 4 hrs and 24 hrs after the reaction had started and analyzed by GPC. After 30 mins, no further change was observed by GPC, indicating reaction completion. However, the thick white dicyclohexylurea (DCU) precipitate normally seen for DCC-DPTS reactions, was not observed until 1 hr after the reaction had started. Filtration of the crude mixture removed the DCU by-product and precipitation by dichloromethane gave **80** as an off white solid (M_n = 1800, PDi = 1.09). Analysis by ^1H and ^{13}C NMR indicated the presence of a high proportion of DCC. All attempts to remove traces of DCC by precipitation from a variety of solvents (dichloromethane, ethyl acetate and water) failed. Heating **80** also failed to sublime the excess DCC.

3.3.2 Degree of Branching

We attempted to assess the degree of branching of **80** using Hawker's termini functionalization technique.[110] This method utilizes a mild, non-basic procedure to methylate terminal hydroxyl functions. Hawker used thermal condensation to produce a hyperbranched polymer **81** with M_n of 22000 derived from 4,4-bis(4'-hydroxyphenyl)pentanoic acid (**scheme 3.4**). Complete methylation, using silver oxide and methyl iodide

(**scheme 3.5**), was verified by a range of techniques (including ^{1}H and ^{13}C NMR) which also showed no evidence of side reactions or degradation.

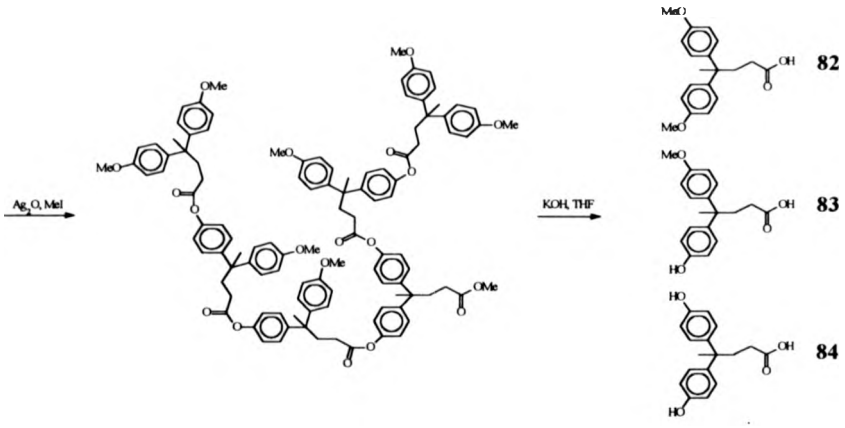
Scheme 3.4



81

The resultant methylated chain ends were stable to base and treatment of the hyperbranched polyester with potassium hydroxide resulted in cleavage of the monomer units from one another to produce only three products: di-methylated, mono-methylated and diphenolic derivatives (**scheme 3.5**). The relative percentages of **82**, **83** and **84** were found to be 24, 51 and 25% respectively by capillary gas chromatography. Using **equation 1** (chapter 1.3.2), the degree of branching was calculated and found to be 49% (f_{br} = 0.49).

Scheme 3.5



We attempted to methylate **80** using methyl iodide and silver oxide. Functionalization was monitored by observing the hydroxyl resonance at 8.85 ppm in the ^1H NMR (the position of the hydroxyl was verified by a D_2O shake). Reaction over several days revealed insignificant changes in the relative intensity of the hydroxyl signal, indicating very little methylation. The failure to methylate the hydroxyl groups may have been as a result of impurities present in our polymer system poisoning the silver oxide catalyst.

3.3.3 Poly(3,5-dihydroxybenzoic acid) and Phloroglucinol

The inclusion of a core molecule in **80** may result in a polymer with a more spheroidal shape. This idea was used by Fréchet who prepared hypercores (generation one dendrimers) and attached hyperbranched

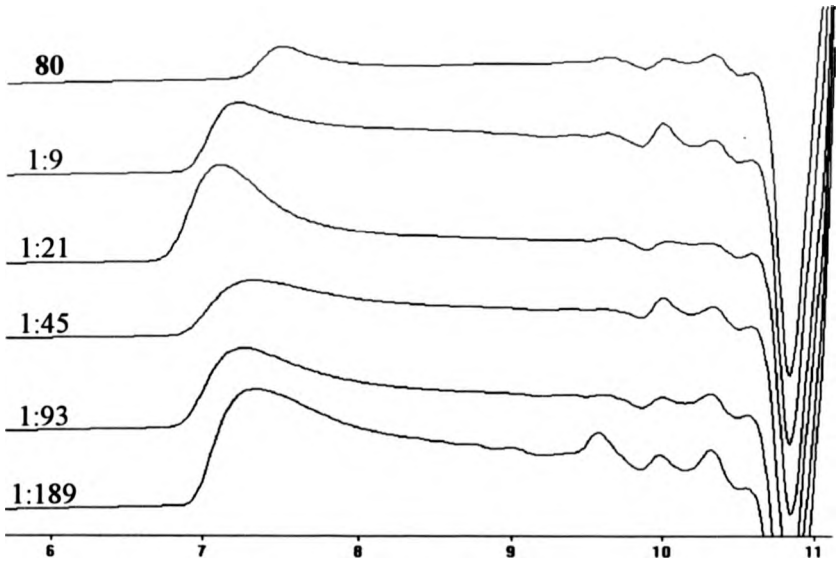
polymers to these.[85] The importance of a core moiety to improve handling properties was demonstrated by Hult *et al* who prepared hyperbranched polyesters with and without a core unit.[83] The polymer containing a core molecule was found to have greater solubility and easier purification than the polymer with no core molecule.

We decided to attempt the inclusion of a core moiety in our hyperbranched polyester in a one-pot fashion, in the hope that this would also lead to easier handling properties and perhaps eliminate problems of DCC removal. Having successfully prepared dendrimers with phloroglucinol **45**, we attempted to directly polymerize **46** with **45** in the presence of the esterification agents DCC and DPTS. Ratios of **45**:**46** were chosen of 1:9, 1:21, 1:45, 1:93, 1:189 corresponding to the dendrimer generations two to six. The polymers were isolated but no significant differences could be seen either by GPC (M_n 800-1000, PDi 2.1-3.0) or NMR from **80** derived from **46** alone. The difficult handling properties also remained.

The slow stepwise addition of monomer to a solution of the core molecule was also attempted, but no significant change was observed by GPC or ^{1}H NMR. Slow addition of the monomer to a flask containing the core molecule and esterification agents using a syringe pump over a period of 9 hrs was also attempted. Once again, no obvious change in either handling properties or GPC was observed from that of **80**

constructed entirely from **46**. **Figure 3.1** shows the GPC overlay of **80** prepared by method 1 using ratios of **45**:**46** of 1:9, 1:21, 1:45, 1:93, 1:189 corresponding to dendrimer generations two to six.

Figure 3.1 GPC Overlay of 80 Containing Differing Quantities of 45 During Polymerization



Attempting to scale-up the synthesis of the hyperbranched polyester led to several problems. Yields dropped dramatically even when vigorous stirring was employed. For example, a preparation using 1.5 g of **46** typically gave 0.25 g of **80** upon purification. Scaling up the synthesis to 8.0 g of **46** gave less than 0.4 g of **80** after purification. A brown insoluble product was isolated which was found to be insoluble in

acetone, methanol and THF. The insolubility of the solid in THF meant we were unable to carry out GPC analysis. The brown solid was thought to be a crosslinked by-product. The hyperbranched polymer which remained in solution, was isolated and purified by precipitation. However, this also became an insoluble brown solid on standing, particularly if traces of solvent were present. It was considered that the insoluble by-products were perhaps resulting from impurities in **46**. The monomer was purified by flash chromatography using acetone-dichloromethane (40:60) prior to polymerization, but this did not prevent the formation of the side products upon polymerization.

3.3.4 Methods 2 and 3

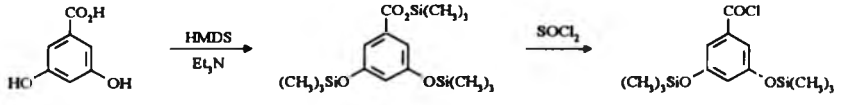
Our inability to prepare and purify large quantities of **80** led us to seek an alternative method for its synthesis. We decided to use Fréchet's acid chloride method for the preparation of hyperbranched polyesters as this resulted in a polymer with functionalizable chain ends. Turner's method was not used as this led to extra hydrolysis steps which did not lead to entirely un-functionalized hyperbranched polyesters.

To enable us to compare hyperbranched polymers with dendrimers, we needed to prepare materials with similar molecular weights. However, the method used by Fréchet gave polymers with a minimum M_n of 16000,

and this was only obtainable at temperatures of 260 °C. The yield of polymer was reported as 86% at this temperature. However, subsequent studies by Turner *et al* indicated that polymerizations of **76** at temperatures greater than 180 °C resulted in very dark solids which were only partially soluble.[80] Turner reported that the yields reported by Fréchet could not be reproduced. Turner also noticed that the greatest effect on the molecular weight was not temperature, as Fréchet had indicated, but the quality and duration of the vacuum. This effect was also noticed by Turner for his own hyperbranched system, but he was unable to use this to control molecular weight in any of these systems.

Using HMDS, we prepared the silyl ether-ester **75** from **46** (**scheme 3.6**). This was converted to the acid chloride **75** using thionyl chloride.

Scheme 3.6



46 **75** **76**

However, attempted distillation of the acid chloride, as reported by Fréchet *et al*, led to large amounts of polymer and very little monomer was isolated. Interestingly, the distillation temperature reported by Fréchet is actually higher than the polymerization temperatures Fréchet used. We thus polymerized **76** without prior distillation. Volatile by-

products and excess thionyl chloride were removed under vacuum (method 2).

Attempted removal of the TMS groups using a mixed pyridine-benzene (1:1) solvent system followed by precipitation from methanol, as reported by Fréchet, led to the formation of a brown residue which was difficult to filter. To combat this problem, we removed the TMS groups by heating the polymer in dimethyl sulfoxide. Precipitation from dichloromethane gave **80** in good yield with M_n of 800 and PDi of 1.82. This method was found to be suitable for scale-up, and we were thus able to prepare multi-gram quantities of **80**.

To try to control the dispersity of the polymerization, solution polymerization of **76** was attempted in nitrobenzene (method 3). We found that the M_n remained the same at 800 but the PDi decreased to 1.49.

3.3.5 Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) was used to analyse **80**. Samples were heated from ambient temperature to 300 °C. For polymerization method 1, a single transition was seen in all cases regardless of whether a core unit had been included or not (**figure 3.2**). The transition was

observed from 40 °C to 155 °C, with a maximum at 100 °C and is thought to be due to water, present because of the known hygroscopic nature of the polyhydroxy compounds. The transition disappeared, as expected, when the sample was cooled and reheated. Allowing **80** to stand in air over a period of approximately 1 hr did not result in the re-emergence of the transition.

80 prepared by method 2 were also analyzed by DSC. A single transition was observed between 60 °C and 120 °C (**figure 3.3**). This transition did not reappear when the sample was cooled and reheated, nor did it re-appear on standing the sample in air for approximately 1 hr.

Poly(3,5-dihydroxybenzoic acid) prepared by Fréchet *et al*[109] with M_n of 20000 showed a T_g at 197 °C. We did not see any transition other than those shown in **figure 3.2** and **3.3** for poly(3,5-dihydroxybenzoic acid) prepared by methods 1, 2 or 3. This may have been due to the low molecular weight polymers obtained - M_n of 1800, 800 and 800 from methods 1, 2 and 3 respectively.

Figure 3.2 DSC Trace of Poly(3,5-dihydroxybenzoic acid) Prepared by Method 1

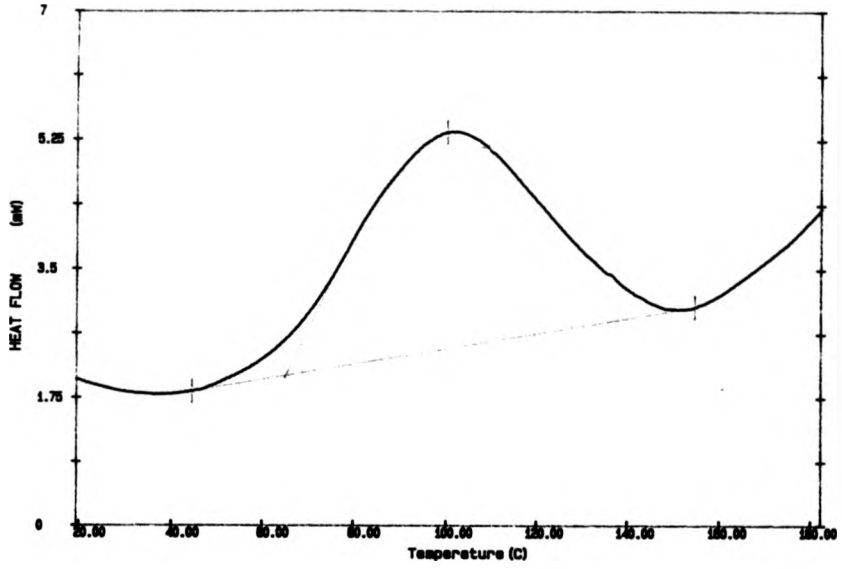
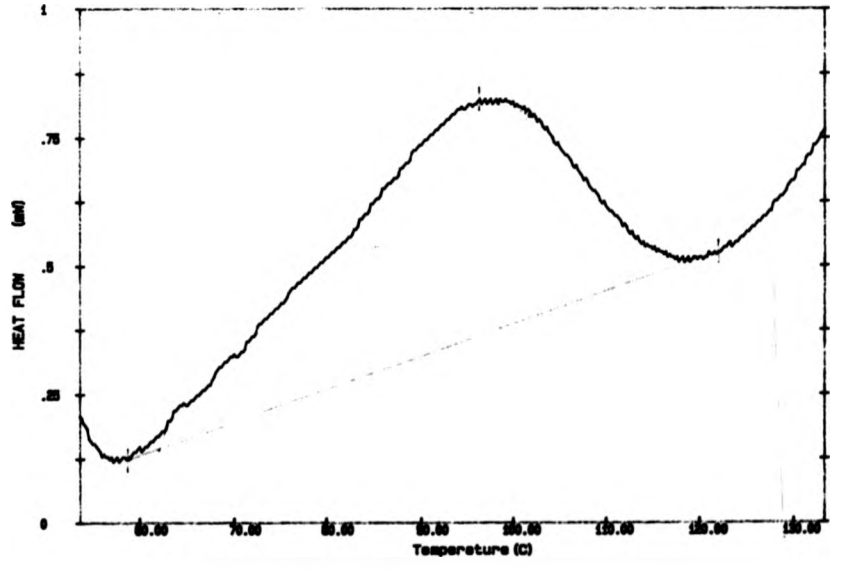


Figure 3.3 DSC Trace of Poly(3,5-dihydroxybenzoic acid) Prepared by Method 2



3.4 Conclusion

We have prepared hyperbranched polyesters from 3,5-dihydroxybenzoic acid using both the DCC-DPTS esterification agents and by an adaptation of Fréchet's acid chloride method. The DCC-DPTS method proved troublesome with poor reproducibility. Fréchet's literature procedure was not successful in our hands. However, modification of Fréchet's method gave polymers, with a higher degree of reproducibility, which were considerably easier to purify. We were able to use this method to prepare multi-gram quantities of poly(3,5-dihydroxybenzoic acid).

Chapter 4

Functionalization of Dendrimers and Hyperbranched Polymers

4.1 Introduction

Both dendrimers and hyperbranched polymers possess large numbers of terminal functional groups. It has been observed that the nature of these groups greatly influences the physical properties, such as solubility and melting points, of these dendritic materials.[106, 107]

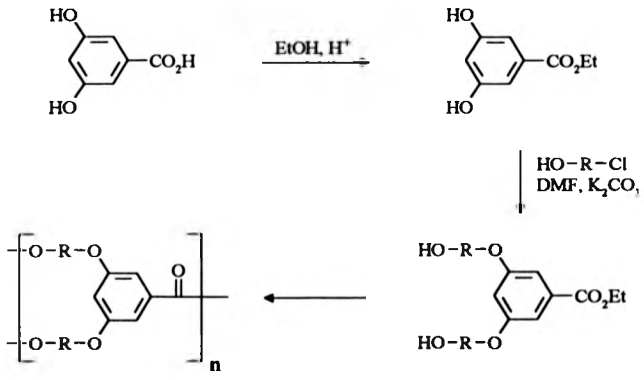
There are few literature reports of dendrimer functionalization carried out with the express purposes of modifying physical properties to preparing functionally useful dendrimers. Shi *et al* have prepared dendrimers with terminal methacrylate groups. These were then photopolymerized at room temperature (chapter 7).[111] The large number of functional groups were utilized by Roy *et al* to prepare dendrimers acting as a support for α-sialoside, the inhibitor of the influenza A virus haemagglutinin (chapter 1).[99]

Similarly, there have been few literature reports of the functionalization of hyperbranched polymers. Fréchet *et al* have prepared hyperbranched polyesters with methyl, acetyl, trimethylsilyl and benzyl terminal functional groups by the direct modification of a hydroxyl terminated hyperbranched polyester.[109] Interestingly, it was found that the benzyl

groups could not be removed under a variety of hydrogenolysis conditions in contrast with the facile removal of benzyl groups from analogous dendrimers.[106, 112]

Kumar *et al* have modified the physical properties of aromatic hyperbranched polyesters, not by chain end modification, but by modification of the monomer unit.[113] 3,5-Dihydroxybenzoic acid was first converted to its ethyl ester and differing length aliphatic chains were attached to the hydroxyl functions to create an extended monomer (**scheme 4.1**).

Scheme 4.1



R = $(CH_2)_2$, $(CH_2)_2O(CH_2)_2$ or $(CH_2)_2O(CH_2)_2O(CH_2)_2$

Polymerization using a trans-esterification catalyst gave hyperbranched polymers with spacers of differing chain lengths incorporated into the polymer. It was found that the differences in the T_gs of hyperbranched polymers with longer R groups and linear polymer analogues were as

small as 3 K. This was attributed to the lower branch density of these hyperbranched polymers.

In order to study further the effect of terminal groups on the physical properties of these materials, we decided to prepare a number of functionally modified dendrimers and hyperbranched polymers. At the same time we also wished to prepare dendrimers with synthetically useful functional groups at the branch termini.

4.2 Alkene Terminated Dendrimers

Alkenes have a great deal of synthetic utility in conventional organic synthesis and polymer chemistry. In organic synthesis, alkenes are regularly used as a means of introducing new chemical functionality into a molecule. Their facile conversion into alcohols, epoxides, halides and various carbonyl moieties, has resulted in their use as masked functional groups.

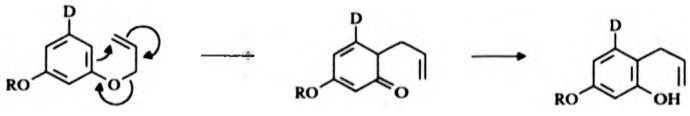
In polymer chemistry, alkenes are regularly used as the polymerization group. Many polymers are prepared this way, for example, polystyrene, poly(vinyl chloride), poly(methylmethacrylate).

We thus decided to attempt to modify our dendrimers such that they contained terminal alkene functions.

4.2.1 Allyl Bromide Functionalization

Alcohols readily undergo condensation reactions with alkyl halides to produce ethers. With a view to using this type of chemistry to introduce alkene groups to our hydroxyl terminated dendrimers, allyl bromide was chosen. Reaction of both G_1P-[6]-OH **49** and G_2P-[12]-OH **51** with sodium hydride in THF followed by allyl bromide gave a complex mixture of products, none of which appeared to be the desired dendrimer. This may have been due to unwanted side reactions such as that shown in **scheme 4.2**.

Scheme 4.2

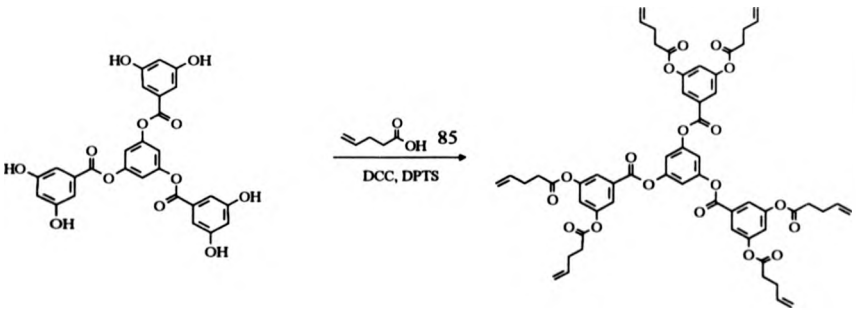


4.2.2 Pent-4-enoyl Terminated Dendrimers

We then turned our attention to using esterification to introduce the alkene function and so pent-4-enoic acid **85** was chosen. Using the DCC-

DPTS esterification agents, we prepared the pent-4-enoyl ester G_1P-[6]-O-pent-4-enoyl **86** from G_1P-[6]-OH (**scheme 4.3**) in 89% yield. G_1P-[6]-O-pent-4-enoyl was collected as a colourless solid which showed good homogeneity by GPC (M_n 1600, PDi 1.019). Complete functionalization was determined by comparing the alkene:aromatic signal ratio in the ^{1}H NMR spectrum. MALDI-MS analysis verified complete functionalization of G_1P-[6]-OH, showing essentially a single signal at *m/z* 1050 (calculated $M+Na^+$ = 1050).

Scheme 4.3



86

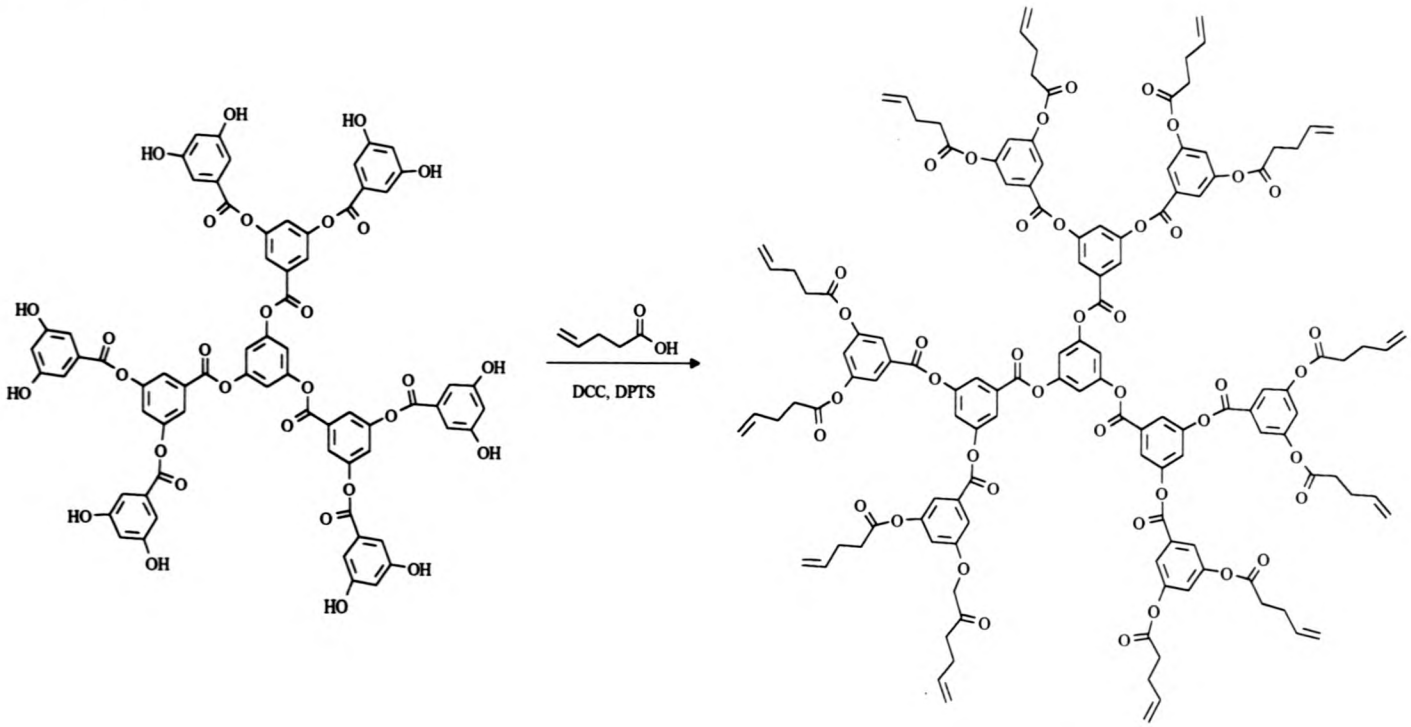
Using similar esterification conditions, the second generation dendrimer G_2P-[12]-OH was functionalized with pent-4-enoic acid to give G_2P-[12]-O-pent-4-enoyl **87** as a colourless solid in 79% yield (**scheme 4.4**). As with G_1P-[6]-O-pent-4-enoyl, complete functionalization was determined by comparing the alkene:aromatic signal ratio in the ^{1}H NMR and verified by MALDI-MS (calculated *m/z* for $[M+Na^+]$ = 2359, *m/z* obtained = 2360).

Homogeneity of the sample was determined by GPC (M_n 3200, PDi 1.018) which indicated the presence of a single species.

4.3 Epoxide Terminated Dendrimers

Epoxides are employed a great deal in organic synthesis. Their reactive nature is primarily due to strain in the three-membered ring. As a result, most reactions of epoxides involve a ring opening. This may be by nucleophilic attack of water to produce a diol, attack by amine to produce an amino-alcohol or attack by a Grignard reagent to produce an alcohol. The usefulness of epoxides is not limited to organic synthesis alone. Epoxides are regularly used to prepare polymers such as poly(ethylene oxide) and poly(propylene oxide)glycol. They are also employed in the area of crosslinking agents and as epoxy resins which have good adhesive properties and outstanding toughness.

Scheme 4.4



87

4.3.1 Crosslinking Agents

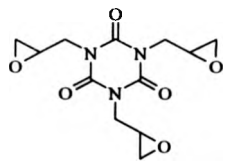
Improvements in the formulation and application of powder coatings has established their use as a reliable coatings medium. Powder coatings have been used on many metal and glass surfaces, for example, refrigerators, radiators, bottles and vehicle parts. Powder coatings are applied to the desired surface as a solid by electrostatic deposition (a method similar to that currently used to deposit ink on paper in photocopiers and laser printers). This is then cured by converting the powder to a liquid by the action of heat which then polymerizes to a solid film. The absence of solvent means that this is, in principle, an environmentally friendly coatings technology as no harmful organic vapours are released into the atmosphere.

Materials are added to powder coatings which act as crosslinkers. During the curing process, the powder is first converted to a liquid by heating. At this point the polymer is still of relatively low molecular weight which is slowly increasing. Curing of the polymer with the aid of a crosslinker leads to a higher molecular weight polymer which solidifies. The melt viscosity of the polymer usually increases in 2 - 5 mins after the beginning of the baking process, although this is a temperature variable event and faster or slower curing is possible. Thus, it is essential that the crosslinking agents begin to act after the coating has had a chance to level in order to obtain a smooth, defect free film.

Crosslinkers not only affect the curing process (curing time, temperature, flow behaviour *etc.*), they also exert an influence on the production, storage and application of the coating. The right choice of crosslinker is one which is resistant to moisture and UV light, particularly for outdoor coatings.

One of the most commonly used crosslinking agents for polyester powder coatings is triglycidyl isocyanurate **88** (TGIC) - **figure 4.1**.

Figure 4.1 Structure of TGIC



88

The theoretical epoxy equivalent weight of TGIC is 99 (MW of TGIC = 297, three epoxy groups per molecule, therefore epoxy equiv. = 99), but due to factors such as partial condensation and hydrolysis, this figure is nearer to 105-110 (higher values mean a larger amount is needed to produce the same effect). The low molecular weight of TGIC means that it lowers the T_g of the powder coating by approximately 2 °C per weight percent. The percentage of TGIC in powder formulations is usually no more than 10% (commonly 7%), which does not lower the T_g of the composition by an unacceptable amount.

An obvious disadvantage of TGIC is its inhomogeneity with polyester systems. Polyester-TGIC blends suffer from flow and levelling problems during the melt. TGIC is also a potent respiratory and mucous membrane irritant, which has resulted in these type of polyester systems being less utilized, despite their good performance abilities. The toxicity problems have led to the use of TGIC containing coatings being prohibited in some countries and so alternate systems are being sought.

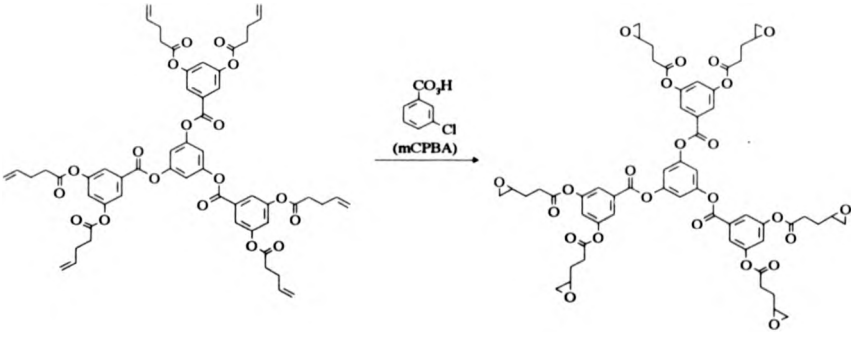
Crosslinking agents require a minimum of three positions for a growing polymer chain to react in order to achieve crosslinking. Dendrimers and hyperbranched polymers contain many more than three functional sites and thus may provide an alternative system for crosslinking.

4.3.2 Synthesis of Epoxide Terminated Dendrimers

Epoxides may be prepared by a number of different methods.[114] A well known and commonly used route is through the epoxidation of an alkene. The alkene functional groups of the dendrimer G_1P-[6]-O-pent-4-enoyl were epoxidised using *m*-chloroperoxybenzoic acid (mCPBA). The reaction was monitored by the disappearance of the alkene signal at 5.9 ppm and the emergence of the epoxide signal at 3.0 ppm in the ^{1}H NMR spectrum. Complete epoxidation was verified by MALDI-MS which showed essentially a single signal at *m/z* 1146 (calculated = 1146). The

reaction proceeded with 61% yield to give G_1P-[6]-O-pent-4-enoyl hexaoxide **89** as a colourless solid (**scheme 4.5**). Good homogeneity of G_1P-[6]-O-pent-4-enoyl hexaoxide was indicated by GPC analysis (M_n 1500, PDi 1.023).

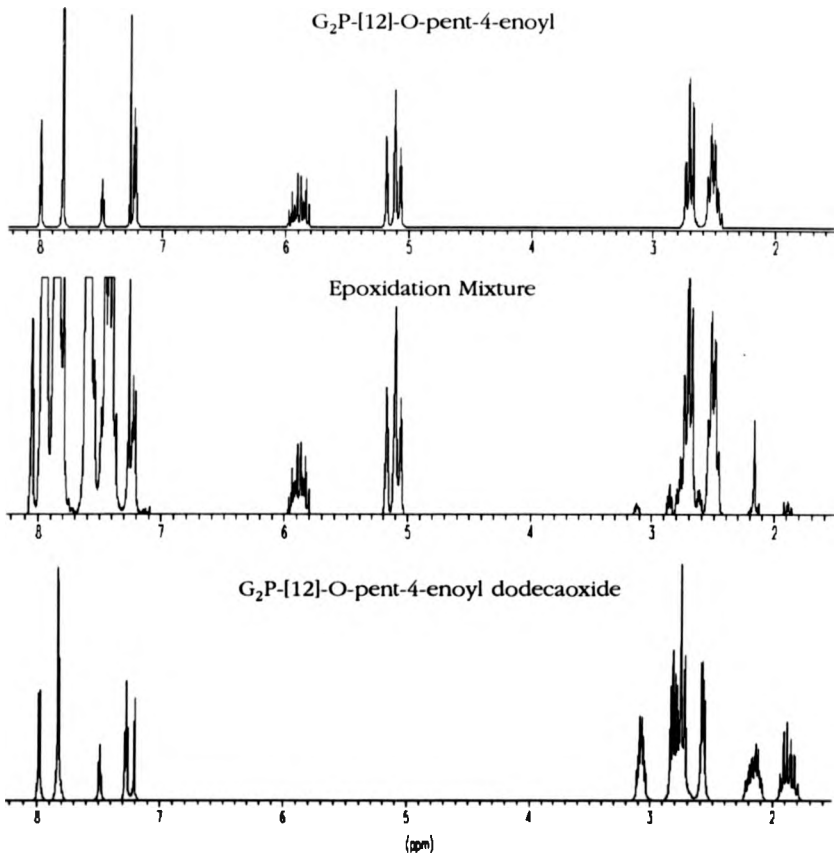
Scheme 4.5



89

Similarly, the second generation dendrimer G_2P-[12]-O-pent-4-enoyl was epoxidised using mCPBA to give G_2P-[12]-O-pent-4-enoyl dodecaoxide **90** as a colourless solid in 73% yield (**scheme 4.6**). The epoxidation was followed by monitoring the disappearance of the alkene signal at 5.9 ppm and the emergence of the epoxide signal at 3.0 ppm in the ^{1}H NMR spectrum. **Figure 4.2** shows the stack plot of the ^{1}H NMR of G_2P-[12]-O-pent-4-enoyl, G_2P-[12]-O-pent-4-enoyl at the early stages of epoxidation and G_2P-[12]-O-pent-4-enoyl dodecaoxide. The emergence of the epoxide signal at approximately 3.0 ppm can be clearly seen in the reaction mixture.

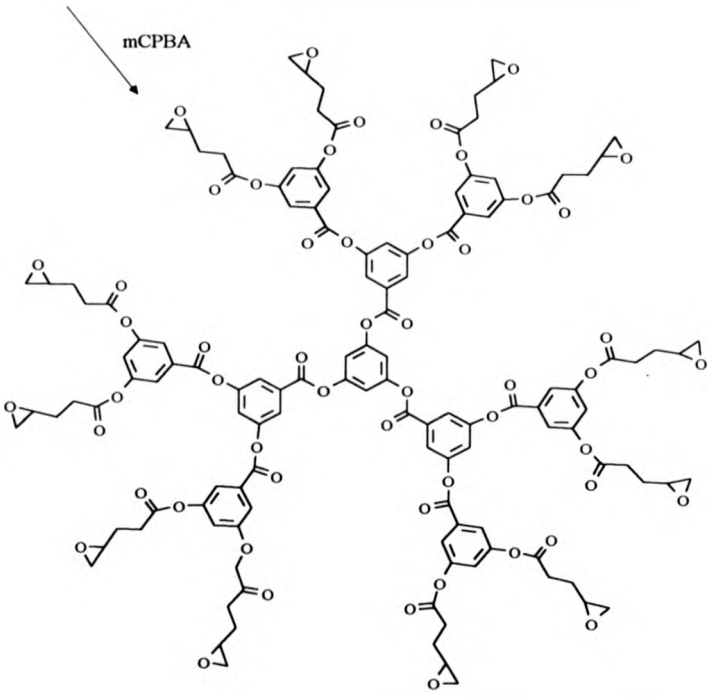
Figure 4.2 Stack Plot Showing Epoxidation of G_2P-[12]-O-pent-4-enoyl



Complete epoxidation was verified by MALDI-MS (calculated *m/z* for $[M+Na^+]$ = 2551, *m/z* obtained = 2552) and good homogeneity indicated by **90** by GPC (M_n = 3400, PDi 1.020).

Scheme 4.6

G_2P-[12]-O-pent-4-enoyl



90

4.4 Hydrosilylation of Alkene Terminated Dendrimers

Alkoxylsilanes are useful intermediates in organic synthesis and polymer chemistry. A commonly used method to introduce silicon to a molecule is through the hydrosilylation of an alkene. The Si-H bond adds across the double bond to form the saturated alkylsilane and is a high yielding reaction.

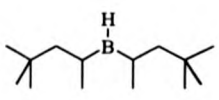
Using an adaptation of a literature method, we attempted to hydrosilylate the generation one dendrimer G_1P-[6]-O-pent-4-enoyl using a model alkylsilane (triethylsilane) in chloroform at room temperature. No catalyst was used at first and there were no signs of any reaction taking place by ^{1}H NMR. Thus, 1% chloroplatinic acid catalyst was introduced. Despite reaction over several days, even with heating, there was no sign of the alkene function changing. If hydrosilylation were taking place, the alkene protons signal at 5.9 ppm would slowly decrease in intensity in the ^{1}H NMR. Thus, the reactions were monitored by observing the integral ratio of the alkene signals and the aromatic signals in the ^{1}H NMR. The failure to react was thought to be due to the low solubility of chloroplatinic acid in chloroform and thus the solvent system was changed to chloroform-methanol (50:50). Pure methanol, which is often used for hydrosilylations, could not be used due to the insolubility of G_1P-[6]-O-pent-4-enoyl in methanol. Analysis by ^{1}H and ^{13}C NMR indicated a reaction was taking place, but of the ester functionality, not the alkene.

After a thorough survey of the literature, we were able to find numerous examples of the hydrosilylation of unconjugated alkenes. We were also able to find several examples of the hydrosilylation of an alkene in the presence of an ester, provided that the two groups were conjugated, *viz.* α,β-unsaturated esters. However, we were unable to find any literature examples of the hydrosilylation of alkenes in the presence of an unconjugated ester.

4.5 Hydroboration of Alkene Terminated Dendrimers

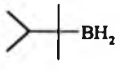
Organoboranes are generally prepared by the addition of diborane to an alkene or alkyne. This proceeds by the addition of the B-H bond across the multiple bond. Reactions nearly always occur rapidly at room temperature and only a limited number of the most hindered alkenes do not react. Mono- and di-substituted alkenes normally give a trialkylborane, but the more hindered tri- and tetra-substituted alkenes generally give the di- or mono-alkylboranes. These mono- and di-alkylboranes still have reactive B-H bonds intact which can be utilized for the preparation of unsymmetrical boranes. Amongst the most important boranes of this class are disiamylborane **91**, 9-borabicyclo[3,3,1]nonane (**92**, commonly known as 9-BBN) and thexylborane **93** - **figure 4.3**.

Figure 4.3 Structures of 91, 92 and 93



91

92



93

These boranes are milder and more selective than diborane or the commonly used BH_3:THF solutions. Their hindered nature results in a strong preference for the least substituted end of an alkene or alkyne, for example, disiamylborane hydroborates hex-1-ene with 99% attack at the C-1 position; BH_3:THF gave 94% at C-1.[115]

To achieve high selectivity in the hydroboration, we chose to try 9-BBN with the generation one dendrimer G_1P-[6]-O-pent-4-enoyl. This was stirred in dry THF under a nitrogen atmosphere with 9-BBN at 0 °C, at room temperature and at reflux. No reaction was observed under any of these conditions, perhaps for steric reasons.

Hydroboration can be catalyzed by a number of transition-metal catalysts; rhodium (I) and iridium (I) based materials have been proved to be the most effective.[116] The use of these types of catalyst often results in greater regioselectivity than for uncatalyzed reactions. We thus chose Wilkinson's catalyst (tris(triphenylphosphine)rhodium(I) chloride) which has been shown to effectively catalyze the reaction between an alkylborane and an alkene.[117]

The attempted reaction of G_1P-[6]-O-pent-4-enoyl with 9-BBN in the presence of Wilkinson's catalyst also failed to hydroborate the alkene functional groups. It was thus decided to use a less hindered borane to reduce steric effects. Catechol borane **94** has approximately the same reactivity as 9-BBN but is less hindered. Attempted reactions of G_1P-[6]-O-pent-4-enoyl with **94** at room temperature and at reflux, both in the presence and absence of Wilkinson's catalyst, failed to yield any hydroborated dendrimer.

It was at this point decided to design a model compound to see if the failure to hydroborate the dendrimers was as a result of some aspect of the dendrimer or simply due to low reactivity of the alkene functions. We thus prepared the ester **95** from pent-4-enoic acid and phenol using the DCC-DPTS esterification agent (**scheme 4.7**).

Scheme 4.7

95

We repeated the reactions of 9-BBN and catechol borane on the model compound, both with and without Wilkinson's catalyst. We found that in all these cases, the reaction either did not occur or led to unexpected products. However, the reaction between **95** and BH_3:THF occurred rapidly at 0 °C and the alkene resonances in the ^1H NMR spectrum disappeared completely within 1 hr. This led us to try the reaction between G_1P-[6]-O-pent-4-enoyl and BH_3:THF, which we found to entirely consume all alkene functions rapidly at 0 °C.

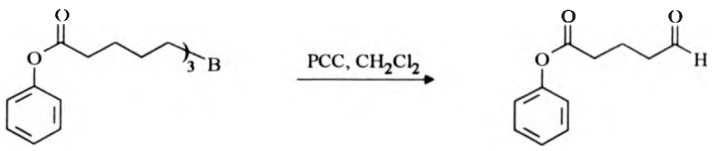
One of the most well known applications of boranes in organic synthesis, is their use in the conversion of alkenes to alcohols. The alkene is hydroborated by the borane reagent and oxidation of the product using

hydrogen peroxide in the presence of a base, typically sodium hydroxide, gives the alcohol.

We attempted to apply this common technique to the hydroborated model compound. Using aqueous hydrogen peroxide (30%) and sodium hydroxide solutions (3 M), we found that the model compound underwent hydrolysis of the ester groups, possibly due to the basic conditions of the reaction.[118] We therefore searched for milder conditions for the conversion of the alkylborane to the alcohol. A review by McKillop on the uses of sodium percarbonate and sodium perborate as mild, near neutral, replacements to H_2O_2-NaOH led us to try these reagents.[119] Both sodium percarbonate and sodium perborate were found to hydrolyze the ester groups, yielding phenol and other by-products.

Alkylboranes can be converted to functional groups other than alcohols. Oxidation of primary alkylboranes using pyridinium chlorochromate (PCC) is known to yield aldehydes.[120] We thus attempted to oxidize the alkylborane of the model compound using PCC and isolated the aldehyde **96** in 16% yield (**scheme 4.8**).

Scheme 4.8



96

We attempted to extend this reaction to the dendrimer alkylborane (the product of G_1P-[6]-O-pent-4-enoyl and BH_3:THF), but the reaction yielded an intractable brown residue.

4.6 Fatty Acid Dendrimers

Drying oils form solid, dry films when a liquid film is exposed to the air. The use of drying oils as surface coatings dates back to Roman times where linseed oil was used in making paints. By the nineteenth century, drying oils and materials derived from them, were used for many applications including paints, artists colours, printing inks and putty.[121] The use of drying oils in the USA peaked around 1950 and though this has declined through more use of synthetic polymers, significant amounts are still used today.

Most drying oils are of natural origin and derived mainly from plant seeds. Linseed oil, which is the most commonly used of the natural

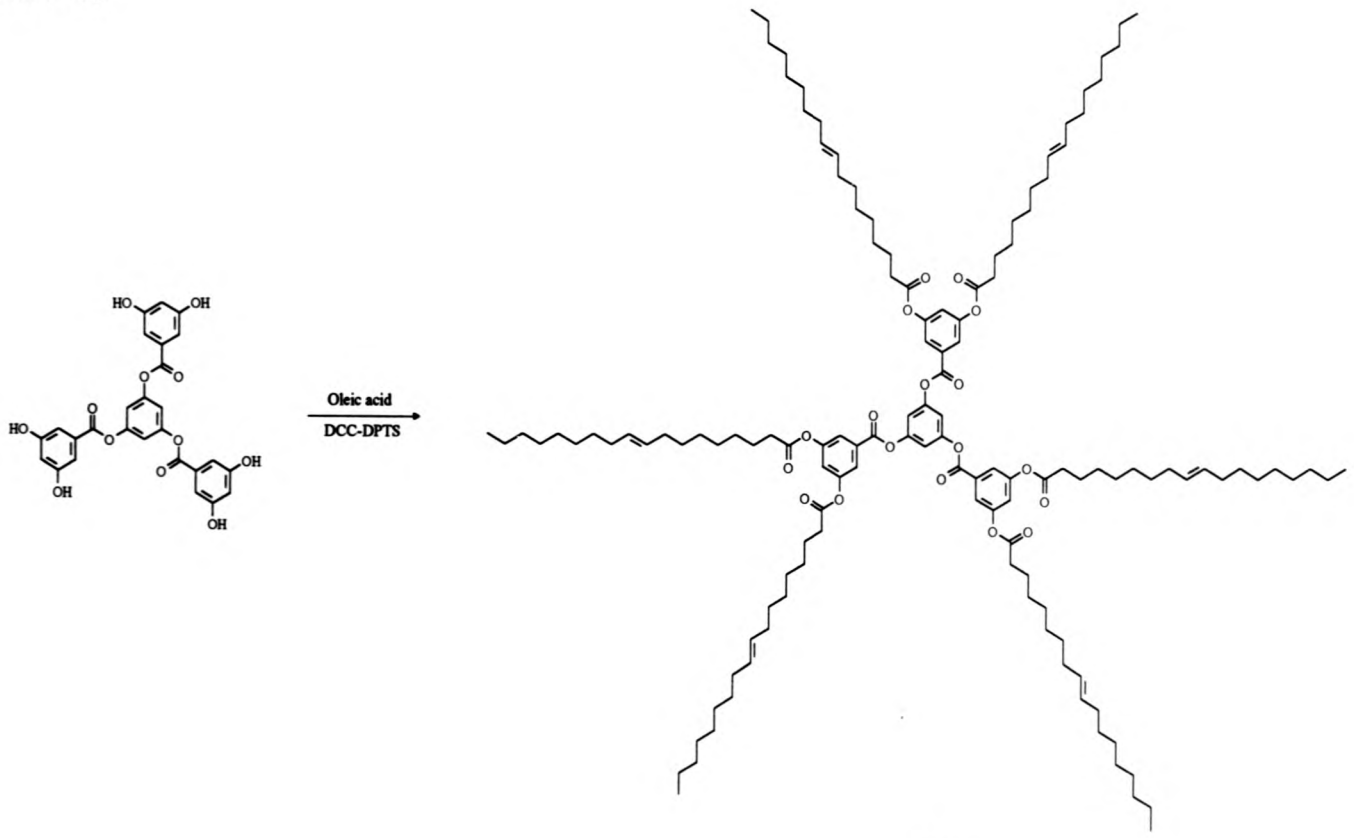
drying oils, is obtained from flaxseed. The oil is extracted from the seed by a continuous pressing process followed by solvent extraction.

Natural drying oils are triglycerides (triesters of propan-1,2,3-triol) with mixtures of fatty acids. The triglycerides contain two or more non-conjugated double bonds (separated by a methylene group). It is these double bonds that undergo aerial oxidation, followed by polymerization to form solid films. Linseed oil contains 22% oleic acid, 16% linoleic acid and 52% linolenic acid. These acids possess one, two and three double bonds respectively. Films prepared from drying oils which contain significant amounts of triesters of fatty acids with three or more double bonds, are particularly prone to discolouration.

4.6.1 Synthesis of Fatty Acid Terminated Dendrimers

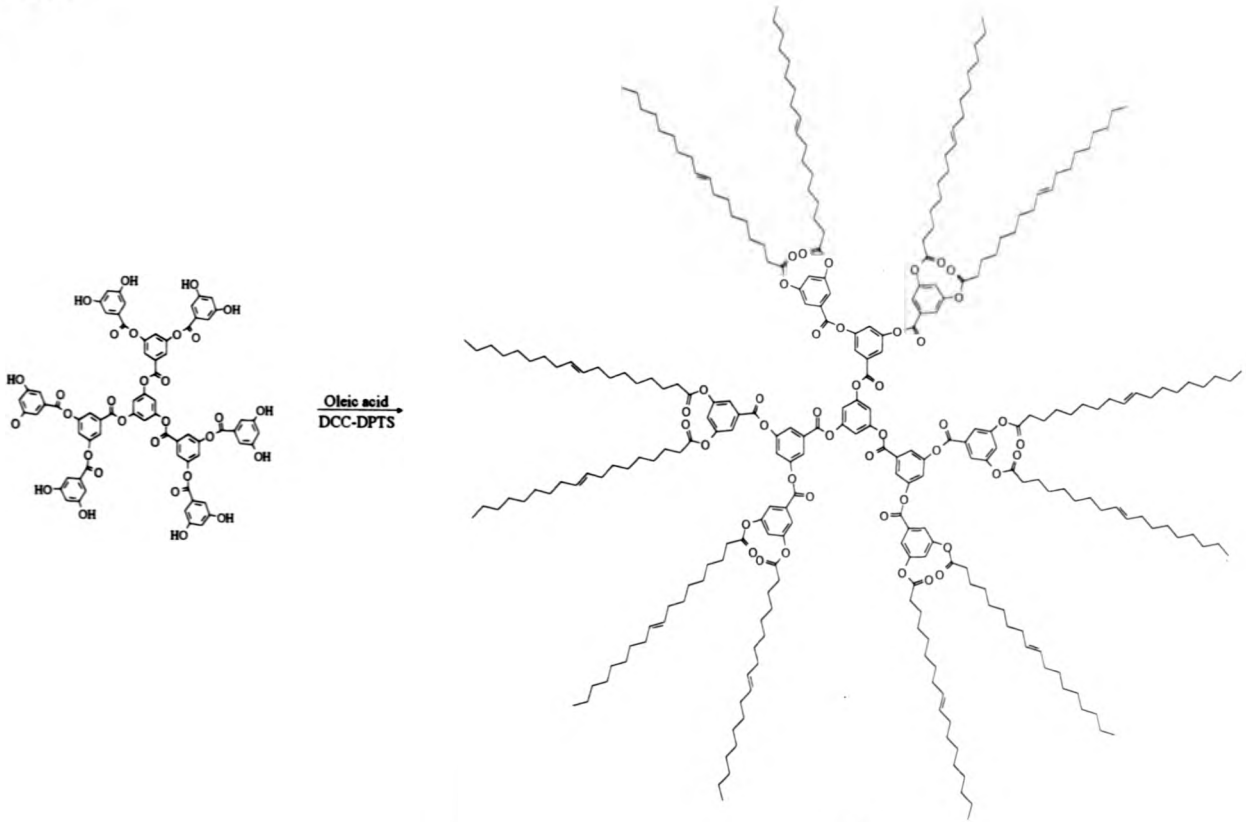
We thus decided to prepare dendrimers functionalized with fatty acids. Using the DCC-DPTS method of ester formation we prepared G_1P-[6]-O-oleoyl **97** from G_1P-[6]-OH and oleic acid in 71% yield (**scheme 4.9**). The dendrimer G_1P-[6]-O-oleoyl, was isolated as a clear viscous oil. Analysis by GPC indicated good homogeneity (M_n 3400, PDi 1.020) and the dendrimer was fully characterized by ^1H and ^{13}C NMR.

Scheme 4.9



97

Scheme 4.10



98

The second generation dendrimer G_2P-[12]-OH, was functionalized with oleic acid to produce the dendrimer G_2P-[12]-O-oleoyl **98**, using DCC-DPTS esterification agents, as a clear viscous oil in 88% yield (**scheme 4.10**). Complete functionalization was verified by ^1H NMR and good homogeneity was indicated GPC (M_n 6300, PDi 1.021). We were unable to obtain MALDI-MS data for G_1P-[6]-O-oleoyl nor for G_2P-[12]-O-oleoyl.

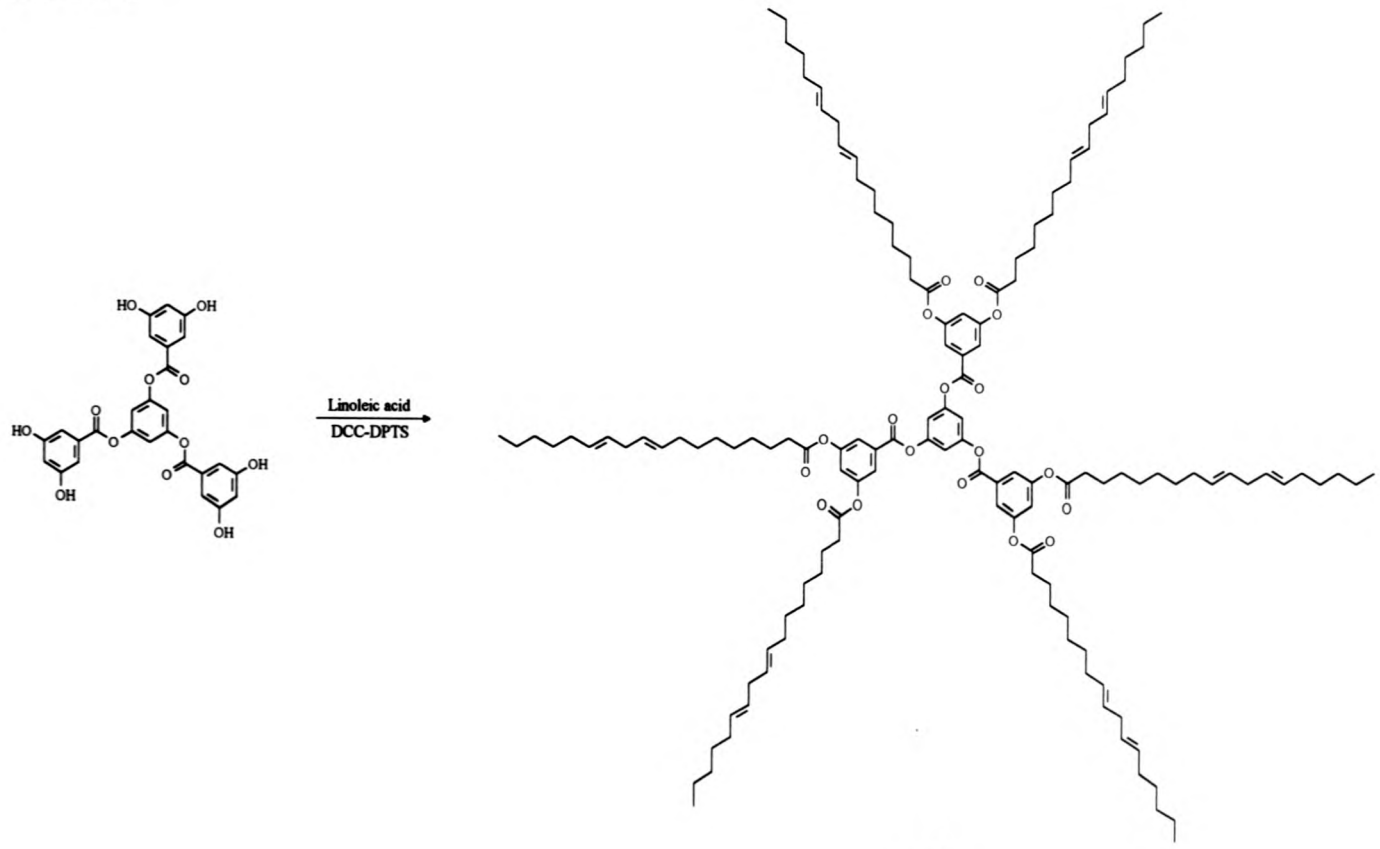
The linoleic acid derivative of G_1P-[6]-OH was prepared using the same esterification procedure to give G_1P-[6]-O-lineoyl **99** as a colourless viscous oil in almost quantitative yield (98%, **scheme 4.11**). Good homogeneity of the dendrimer was indicated by GPC (M_n 3400, PDi 1.019).

The second generation dendrimer, G_2P-[12]-OH, was also functionalized with linoleic acid to give G_2P-[12]-O-lineoyl **100** in 90% yield (**scheme 4.12**). Good homogeneity of the dendrimer was indicated by GPC (M_n 6300, PDi 1.019). Both G_1P-[6]-O-lineoyl and G_2P-[12]-O-lineoyl were fully characterized using ^1H and ^{13}C NMR. However, no MALDI-MS data was obtained for either dendrimer.

The fatty acid dendrimers were purified by column chromatography using a solvent gradient. Interestingly, the R_f values were found to change dramatically over the range of solvent polarities used. For example, G_2P-[12]-O-lineoyl was initially eluted with dichloromethane-hexane (40:60) in

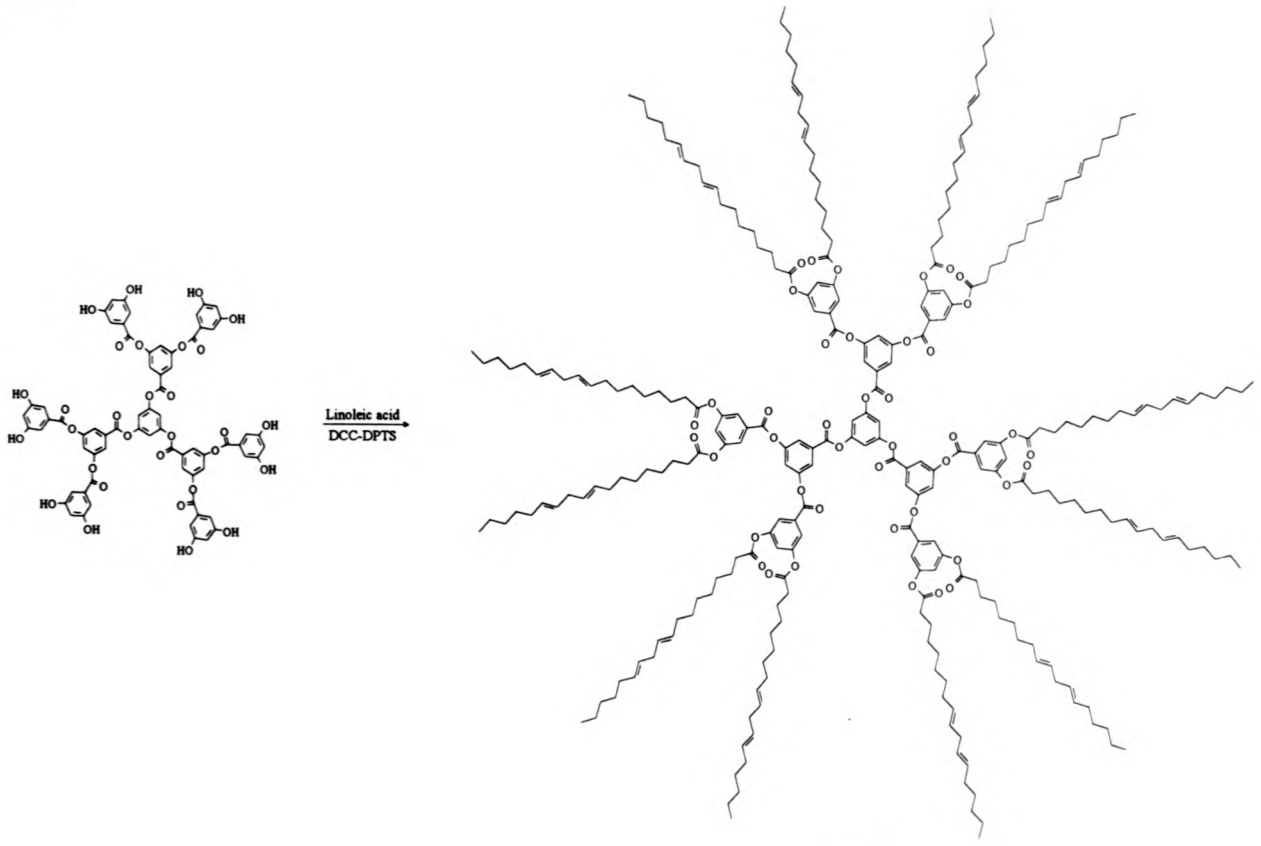
which the dendrimer ran very close to the baseline and excess DCC ran at approximately R_f 0.3. TLC of the dendrimer in pure dichloromethane gave an R_f of approximately 0.7 whereas DCC now ran at R_f 0.6. This strange elution phenomenon was noted for all the oleoyl and lineoyl dendrimers.

Scheme 4.11



99

Scheme 4.12



100

4.7 Functionalized Hyperbranched Polyesters

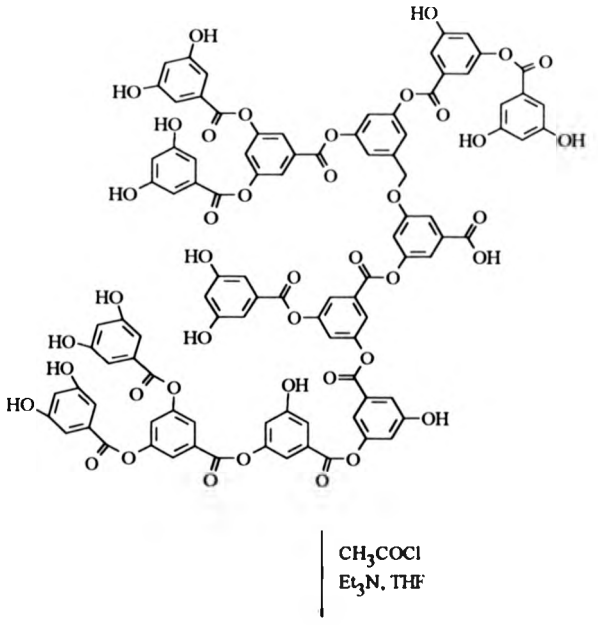
As mentioned earlier, hyperbranched polymers provide a faster and more economically feasible route to dendritic materials than the preparation of dendrimers. In particular, dendrimers are not well suited for bulk applications due to the long syntheses required to prepare these materials. Hyperbranched polymers have potentially similar properties to dendrimers and thus an examination of their uses as alternatives to dendrimers is essential.

To enable us to compare dendrimers and hyperbranched polymers, we attempted to prepare functionally modified hyperbranched analogues of the dendrimers synthesized earlier in this chapter.

Fréchet *et al* prepared chain end modified hyperbranched polyesters by the use of acid chloride chemistry.[109] Poly(3,5-dihydroxybenzoic acid) **80** with M_n 800 and PDi 1.8, prepared by method 2, was used for the following syntheses. We prepared polyacetylpoly(3,5-dihydroxybenzoic acid) **101**, as reported by Fréchet, by the addition of acetyl chloride and triethylamine to a THF solution of **80** (**scheme 4.13**). In agreement with Fréchet's findings, we found that the polydispersity of our acetylated polymer decreased to 1.2, due to the loss of low molecular weight material on precipitation by methanol. The M_n increased, as expected, to 3300. The hydroxyl signal of **80** in the ^{1}H NMR spectra was verified by a

D_2O shake and found to be at 8.85 ppm. For **101**, the absence of this signal verified complete functionalization of the isolated polymer.

Scheme 4.13



101

4.7.1 Fatty Acid Terminated Hyperbranched Polymers

Adapting this technique, we prepared hyperbranched polyesters with oleoyl terminal functional groups using oleoyl chloride. Polyoleoylpoly(3,5-dihydroxybenzoic acid) **102** was isolated as a pale viscous oil of M_n 1700, after precipitation by methanol. The reaction yielded **102** in 320 mg from 116 mg of **80**. However, the PDi increased to 7.4 from 1.8 indicating considerable broadening of the molecular weight distribution.

For the synthesis of polylineoylpoly(3,5-dihydroxybenzoic acid), we prepared lineoyl chloride **103** from linoleic acid and oxalyl chloride. Polylineoylpoly(3,5-dihydroxybenzoic acid) **104** was isolated as a viscous pale brown oil of M_n of 2500 with PDi of 8.3 after precipitation by methanol. 480 mg of **104** was yielded by 210 mg of **80**. Both **102** and **104** gave fully functionalized polymers after precipitation by methanol (verified by ^{1}H NMR).

4.7.2 Pent-4-enoic and Pent-4-enoic Oxide Terminated Hyperbranched Polymers

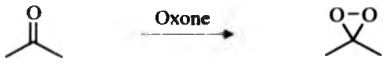
Pent-4-enoic acid was converted to pent-4-enoyl chloride **105** using oxalyl chloride.[122] Using the same conditions as previously used for the

acetyl terminated polyesters, we prepared poly(pent-4-enoyl)poly(3,5-dihydroxybenzoic acid) **106** as a viscous brown oil with M_n 3400 and PDi 2.9 from **80**. 4.2 g of **106** was isolated after purification from 3.2 g of **80**.

We wished to epoxidise the alkene groups of the pent-4-enoyl group to prepare hyperbranched analogues of the dendritic epoxides G_1P-[6]-O-pent-4-enoyl hexaoxide and G_2P-[12]-O-pent-4-enoyl dodecaoxide. The per-acid mCPBA was used in the epoxidation of the dendrimers G_1P-[6]-O-pent-4-enoyl and G_2P-[12]-O-pent-4-enoyl. We therefore attempted to epoxidise **106** with mCPBA in chloroform. ^{1}H NMR analysis showed no change in the intensity of the alkene signal at 5.7 ppm indicating little or no epoxidation was taking place.

We therefore turned our attention to dioxiranes, a powerful new class of epoxidising agents.[123] The instability of dioxiranes at room temperature and resulting storage problems, means that they have to be either prepared *in situ* or used shortly after preparation. We prepared a solution of dimethyldioxirane **107** in acetone using Oxone (potassium peroxymonosulfate) and used this to epoxidise **106** (**scheme 4.14**).[124]

Scheme 4.14



107

The reaction was monitored by observing the relative intensity of the alkene signal at 5.7 ppm in the ^{1}H NMR spectrum. Very little reaction was observed by ^{1}H NMR, possibly due to the low yields of the synthesis **107**.

The *in situ* preparation and reaction of **107** with **106** was attempted and found to be successful.[125] Precipitation in hexane gave poly(pent-4-enoyl)poly(3,5-dihydroxybenzoic acid) polyoxide **108** as a viscous brown oil in 0.18 g yield from 0.3 g of **106**. The molecular weight increased from M_n 3400 of **106** to 4300 for **108** and the polydispersity also increased from 2.9 to 3.8. The absence of the alkene resonance at approximately 5.7 ppm in the ^{1}H NMR spectrum and the emergence of the epoxide resonance at approximately 3.0 ppm indicated that all the pent-4-enoyl groups had been epoxidised.

4.8 Conclusion

We have successfully prepared pent-4-enoyl, oleoyl and lineoyl functionalized dendrimers. We have had some success in the modification of these groups once attached to the dendrimer. In particular, epoxidation of the pent-4-enoyl terminated dendrimers proceeded in good yield. We were also able to hydroborate the pent-4-enoyl terminated dendrimers, but due to the labile nature of the ester

functions, subsequent transformations could not be carried out. Hydrosilylation of the pent-4-enoyl terminated dendrimers was found to be problematic as the ester groups appear to be more reactive than the alkene groups under the conditions used.

The hyperbranched polymers were also successfully functionalized with a range of groups. These included acetyl, pent-4-enoyl, oleoyl and lineoyl. Epoxidation of the pent-4-enoyl terminated hyperbranched polyesters was once again successful, though dimethyldioxirane, prepared *in situ*, was required in this case.

Chapter 5

MALDI Mass Spectrometry of Dendrimers and Hyperbranched Polymers

5.1 Introduction

Mass spectrometry (MS) is the method of choice for determining the molecular mass of molecules. Of the common techniques used in the analysis of organic compounds (NMR, MS, IR and elemental analysis), MS requires the least material and thus, when limited amounts of material are available, it is often the only available method for analysis.

The first stage inside a mass spectrometer is the formation of gaseous ions of the analyte. Well established techniques include chemical ionization (CI) and electron impact (EI). However, these may only be used for molecules which are already in the gaseous state and are therefore restricted to volatile materials. The ionization of thermally labile molecules has required other methods to be developed. These include fast atom bombardment (FAB), laser desorption (LD) and electrospray ionization (ESI-MS).

All of the ionization methods mentioned above can lead to fragmentation of the analyte, resulting in a multi-lined spectrum. Indeed, fragmentation patterns are often used for characterization. Fragmentation is more pronounced for higher molecular mass materials due to the difficulty of

ionization and thus techniques such as FAB have an upper usable limit beyond which useful information is not obtained. ESI-MS is frequently used for the mass determination of high molecular mass proteins. A multi-lined spectrum is usually produced, not because of fragmentation, but due to the formation of multiply charged ions. LD of is of limited use for analyzing high molecular mass thermally labile materials because of the heating effect of the laser. LD has an upper working limit of approximately 9000 Da, which is decreased to approximately 1000 Da for biopolymers.[126] Beyond these limits, fragmentation of the molecular ion is observed due to heating caused by the laser.

In the late 1980's a new laser desorption technique was reported independently by both Karas[127] and Tanaka.[128] The new technique involved the use of a matrix to aid desorption and ionization of the analyte and was named matrix-assisted laser desorption-ionization mass spectrometry (MALDI-MS). MALDI-MS has been used to analyse a variety of large molecules such as biomolecules and more recently, polymers.[129] MALDI-MS is well suited to the analysis of polymers as it is generally believed to be a non-fragmenting technique.[130]

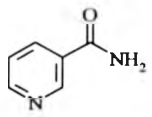
5.2 How MALDI-MS Works

LD works by supplying the analyte with enough laser energy to allow desorption to occur. The higher the molecular mass, the more laser energy (power per unit area) is required to effect desorption. To prevent thermal decomposition of the analyte, only very short laser pulse widths (often nanosecond lengths) are used. However, the higher laser powers required by larger molecules result in decomposition of the analyte, thus limiting the molecular mass of materials which can be analyzed by this technique.

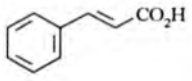
To circumvent this problem, Karas and Tanaka independently showed that a matrix which absorbed the laser energy could be mixed with the analyte. Typically, the matrix is in three orders of magnitude greater concentration than the analyte, although molar ratios ranging from 100:1 to 50000:1 have been used.[126] When the matrix-analyte mixture is irradiated by a laser, the energy is absorbed, predominantly by the matrix, and both matrix and analyte are ejected into the gas phase. The actual mechanism of ion formation is not fully understood. However, the presence of the matrix is known to be crucial for the desorption-ionization process to occur. In particular, the matrix must strongly absorb at the irradiation frequency of the laser. Often, carbon dioxide or nitrogen lasers (337 nm), which emit in the near UV, are used for the desorption process. Nicotinic acid **109**, cinnamic acid **110**, 2,5-

dihydroxybenzoic acid **111** (DHB),[131] 9-nitroanthracene **112**, α-cyano-4-hydroxycinnamic acid **113** and sinapinic acid **114** (**figure 5.1**) have been developed as very efficient matrices.

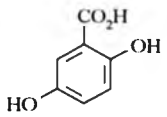
Figure 5.1 Structures of Matrices



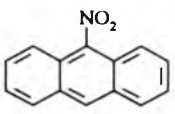
109



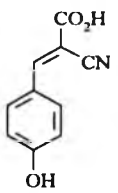
110



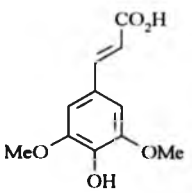
111



112



113



114

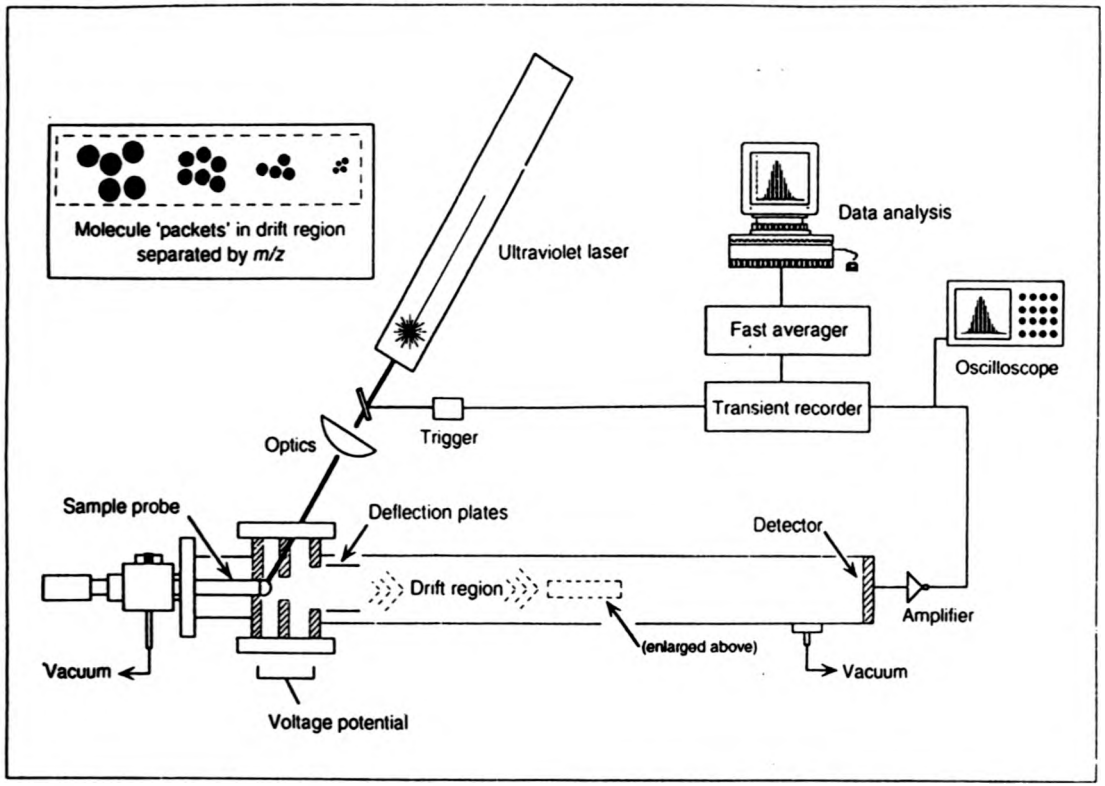
The use of a matrix in the laser desorption technique has allowed biopolymers with molecular masses as high as 150000 Da to be analyzed successfully.[132]

After desorption-ionization has occurred, the ion packets are analyzed to determine their molecular masses. Time of flight (TOF) is the analytical method of choice with MALDI-MS. TOF analyzers work by accelerating all of the ions produced by the application of an acceleration voltage, to gives ions all with equal kinetic energy. The ions pass through a drift tube where they separate according to velocity. Lower molecular mass

ions have higher velocity, for a given amount of energy, than higher molecular mass ions. An electron multiplier detector at the end of the drift tube detects the ion packets. The time of flight of a particular ion is proportional to $(m_i/z_i)^{+½}$, where m_i is the mass of the ion and z_i is the charge.[126] Thus, the time taken for an ion to traverse the drift tube is used to determine its molecular mass. Accurate calibration of the drift tube over the range of molecular masses used is essential. TOF is, in principal, an ideal detection method for MALDI-MS as the short laser pulse widths result in the ions being produced from a point source at essentially the same instance in time.[126] However, in practice, a small range of energies are produced for any particular ion resulting in a degree of peak broadening.

Figure 5.2 shows a schematic representation of a MALDI-TOF MS instrument.[133] There are two principal modes of operation of a MALDI-TOF MS instrument; linear and reflectron. The linear mode can give resolution up to 500 Da whereas in reflectron mode resolutions up to 6000 Da can be achieved. Linear mode is the simplest arrangement. The ions travel down the drift tube to the detector in a straight line (as shown in **figure 5.2**). The reflectron mode increases the path length by using an ion-mirror to reflect the ions down a second tube. The ion mirror also decelerates the ions, so that ions with higher kinetic energy spend a

Figure 5.2 Schematic of MALDI-TOF Mass Spectrometer



H. S. Creel, *Trends in Polymer Science*, 1993, **1** (11), 336

longer time in the mirror. This also has the effect of bringing ions of different energy, but of the same mass, back together. The overall effect is an ion focus, increasing mass resolution but lowering sensitivity.

One of the limiting factors in MALDI-MS is the poor shot to shot reproducibility. This effect could be due to a number of different phenomena, one of which is inhomogeneity of the sample spot. The sample spot is the region on the analysis slide were the analyte and matrix are deposited in solution and allowed to dry to form a thin film. The matrix is usually laid either prior to the analyte or a combined solution of analyte and matrix is prepared and both are deposited at the same time. This poor shot to shot reproducibility has resulted in the search for matrices which give better results, including liquid matrices.[134]

5.3 Analysis of Dendrimers

The soft nature of the desorption-ionization process means that MALDI-MS is well suited for the analysis of dendrimers. As dendrimers are monomolecular and defect-free, MALDI-MS analysis should give rise to a single signal in the spectrum. Defects in the dendrimer, or fragmentation of the dendrimer would result in a multi-lined spectrum. The first use of MALDI-MS for dendrimer analysis was reported simultaneously reported by Walker *et al* [135] and ourselves.[89] Walker analyzed Moore's

phenylacetylene dendrimers[68, 69] and found good agreement with calculated empirical formulae for dendrimers with molecular masses as high as 14776 Da. Since this work, MALDI-MS has become a more routine method for dendrimer analysis.[90, 112, 136, 137]

Using a Kratos Kompact III MALDI-TOF MS equipped with a nitrogen laser irradiating at 337 nm, we analyzed the dendrimers and hyperbranched polymers reported in chapters 2, 3 and 4. The instrument was used in reflectron mode. 2,5-Dihydroxybenzoic acid (DHB) was chosen as the matrix, as this had been found to perform well under a variety of conditions.[131] Earlier analysis of these dendrimers by GPC indicated that they consisted essentially of a single species with the presence of a small percentage of high molecular mass material in some cases. These high molecular mass species are approximately twice the molecular mass of the dendrimer by GPC analysis. However, due to the limitations of GPC in determining molecular masses of dendrimers, we were unable to determine if the main trace observed is the defect-free dendrimer or not.

5.3.1 Phloroglucinol Core Dendrimers

Samples of phloroglucinol core dendrimers were prepared at 1×10^{-4} M concentration in either water-acetone (50:50) or THF for the hydroxyl

terminated and benzyl terminated dendrimers respectively. The matrix, DHB, was prepared at 0.1 M concentration in a solution of water-acetone (50:50).

Cationated species are generally observed in the MALDI-MS technique. For example, analysis of the second generation dendrimer G_2P-[12]-OBn using DHB gave a spectrum with two signals, both of which were of higher mass than the calculated molecular mass of the dendrimer (2432 Da). The first signal was [dendrimer + Na]$^+$ at 2455 Da (+23 Da) and the second signal was [dendrimer + K]$^+$ at 2471 Da (+39 Da - **figure 5.3**). The spectra were thus simplified by the addition of either a sodium or potassium salt to the matrix which resulted in essentially a single signal being observed at either (M + 23) or (M + 39). The single signal of the correct molecular mass indicated that the synthesis had indeed been successful. Mass spectra were also recorded for the other phloroglucinol core dendrimers and are shown in **table 5.1**.

Figure 5.3 MALDI-MS Spectrum of G_2P-[12]-OBn

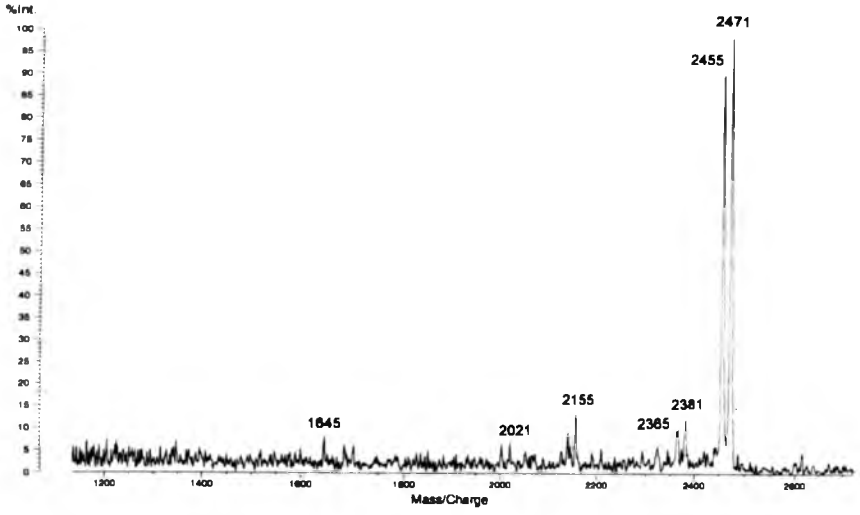
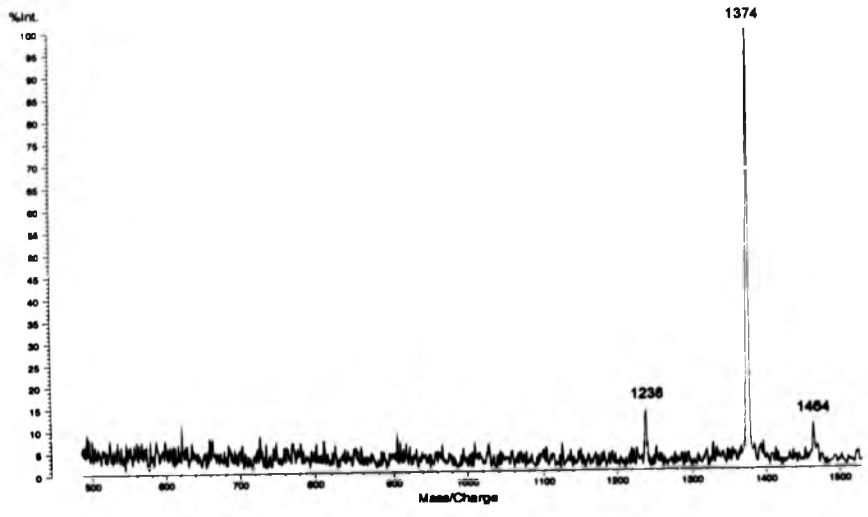


Table 5.1 MALDI-MS Data for Phloroglucinol Core Dendrimers

Dendrimer	Calculated MW + Na^+	MW determined by MALDI-MS + Na^+
G_1P-[6]-OBn	1098	1097
G_1P-[6]-OH	557	556
G_2P-[12]-OBn	2456	2455
G_2P-[12]-OH	1374	1374
G_3P-[24]-OBn	5170	5168
G_3P-[24]-OH	3007	3007

MALDI-MS analysis was found to be particularly useful for following hydrogenolyses of the benzyl terminated dendrimers. If any benzyl groups remain attached to the dendrimer molecule, then higher molecular mass species are observed at multiples of 90 Da (benzyl) above the deprotected dendrimer signal. **Figure 5.4** shows the MALDI-MS spectrum of incompletely deprotected G_2P-[12]-OBn. The signal at 1374 is G_2P-[12]-OH and the signal at 1464 is G_2P-[12]-OH with one benzyl group still attached. Thus, this sample needs further hydrogenolysis to remove remaining benzyl groups to give monodisperse G_2P-[12]-OH.

Figure 5.4 MALDI-MS Spectrum of Incomplete Hydrogenolysis of G_2P-[12]-OBn



5.3.2 Lower Molecular Mass Species

It was noticed that some lower molecular mass species could be seen for several dendrimers when the laser power was increased. **Figure 5.5** shows the MALDI-MS spectrum of G_3P-[24]-OH. The separation of the species at 3007, 2871, 2725, 2599, 2463 is multiples of 136 Da, corresponding to the mass of a branch unit **115** (**figure 5.6**).

Figure 5.5 MALDI-MS Spectrum of G_3P-[24]-OH (at Power = 94)

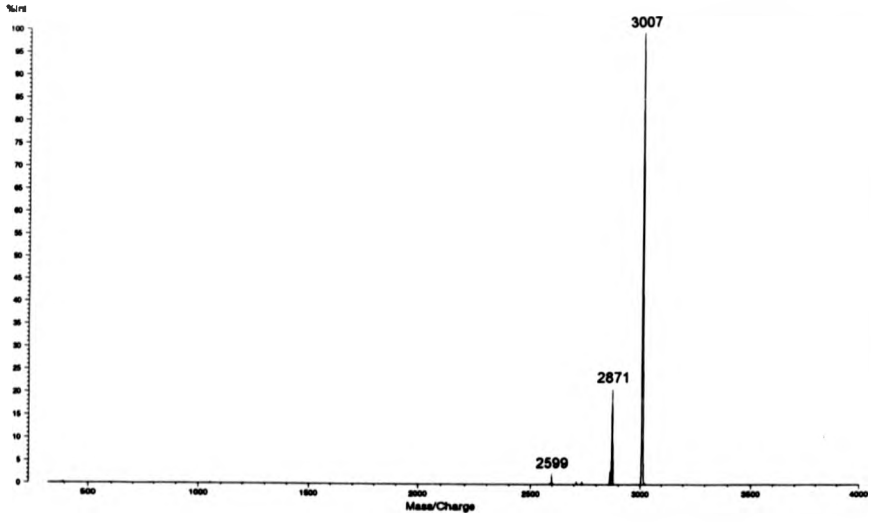
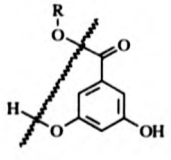


Figure 5.6



= $C_7H_4O_3$

115

The species at lower molecular mass could be due to a number of different reasons:

(i) defects arising during synthesis;

(ii) fragmentation due to the MALDI-MS technique;

(iii) differing thresholds and desorption characteristics for individual species.

5.3.2.1 Defects Arising Due to the Synthesis

There is no evidence for defects in either the ^{1}H or the ^{13}C NMR spectra of G_3P-[24]-OH, although it must be remembered that small amounts of defects may not be seen by NMR due to overlap of signals. GPC does show a broadening of the trace for this dendrimer. This broadening could be due to the large number of hydroxyl groups interacting with the column (see chapter 2)[80] or due to species other than the perfect dendrimer being present.

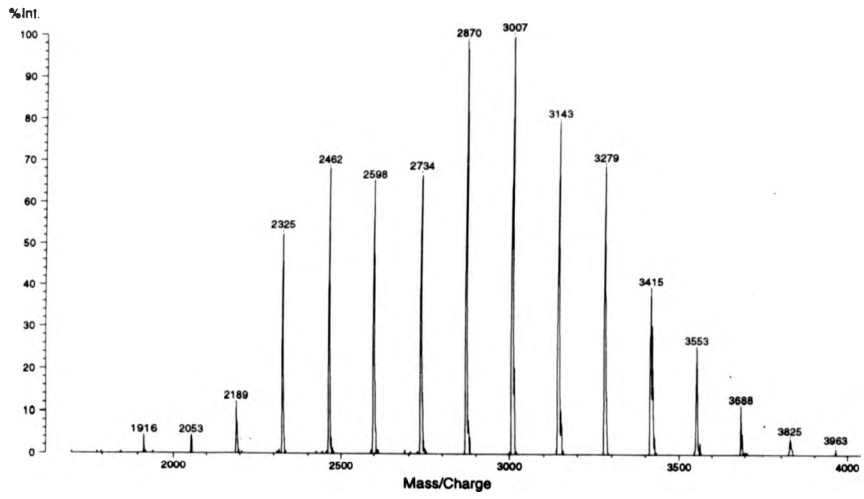
5.3.2.2 Fragmentation Due to MALDI-MS Technique

If fragmentation is occurring due to the MALDI-MS technique, there are two areas where decomposition is likely to occur. The first of these is the

sample preparation. The deprotected dendrimers, in particular, are cast onto the sample slide in aqueous acetone solution. Hydrolysis and transesterification of the ester linkages can be envisaged to create low molecular mass impurities.

To test this, a sample of G_3P-[24]-OH in water-acetone (1:1) solution was prepared and a MALDI-MS spectrum obtained within 10 mins of the solution preparation (**figure 5.5**). The sample was allowed to stand for a few days in aqueous acetone solution to accentuate the hydrolysis conditions and a MALDI-MS spectrum once again obtained (**figure 5.7**). As can be seen from the two spectra, there are considerable differences. The appearance of several signals at both higher and lower molecular mass at a separation of 136 Da, indicates that substantial hydrolysis and/or transesterification has taken place resulting in a polydisperse material. The hydrolysis and transesterification may have been catalyzed by the acidic hydroxyl functional groups of the dendrimer. This highlights the importance of rapid analysis of the dendrimer solutions to obtain a true representation of which species are present.

Figure 5.7 MALDI-MS Spectrum of G_3P-[24]-OH on Standing in Water-Acetone (50:50) Solution for a Five Days



The second area where fragmentation could be occurring is at the irradiation stage, when the sample is subjected to high power laser energy. To test this idea, a sample of G_3P-[24]-OH was irradiated at laser powers from 95 to 135 (on a scale of 0 - 180) and the spectra were averaged over 200 shots. **Figures 5.8**, **5.9**, **5.10** and **5.11** show that as the laser power is increased, the relative intensities of the lower molecular mass signals increase. A plot of the area under the peaks as a function of the laser power is shown in **figure 5.12**. The dendrimer signal at 3007 was taken as 100% signal intensity in each case.

Figure 5.8 MALDI-MS Spectrum of G_3P-[24]-OH (at Power = 105)

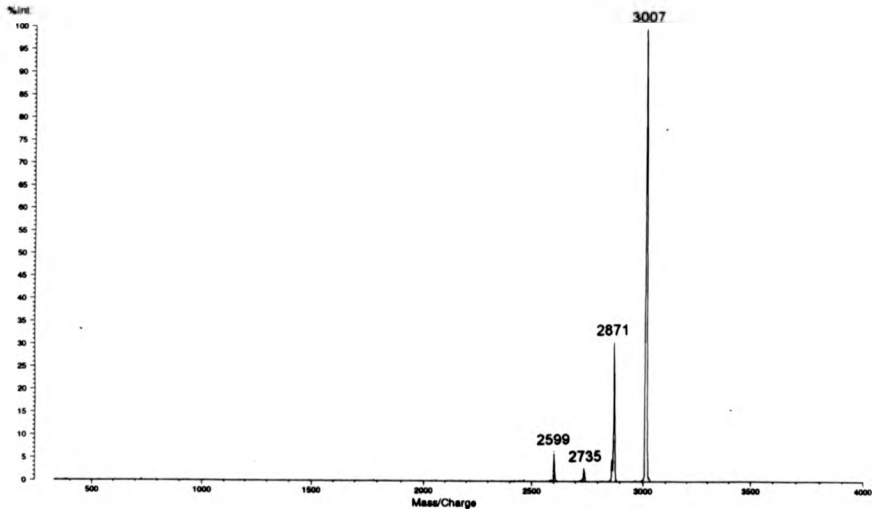


Figure 5.9 MALDI-MS Spectrum of G_3P-[24]-OH (at Power = 115)

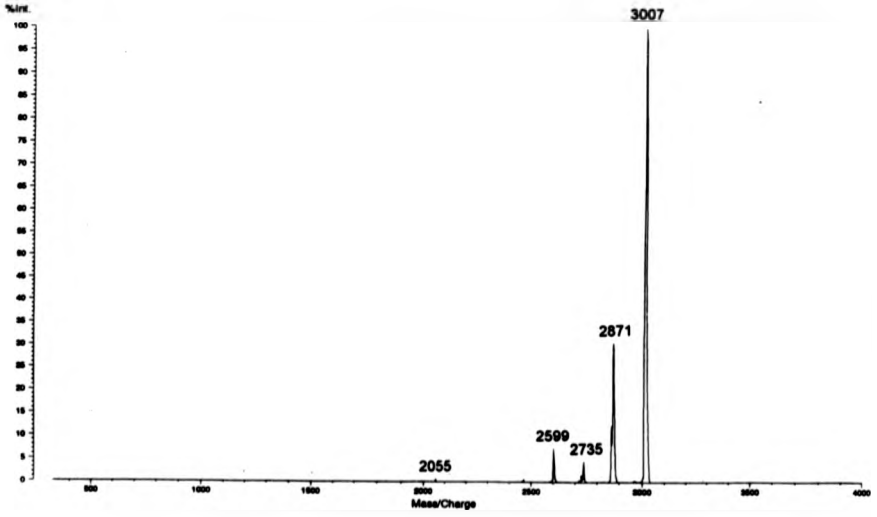


Figure 5.10 MALDI-MS Spectrum of G_3P-[24]-OH (at Power = 125)

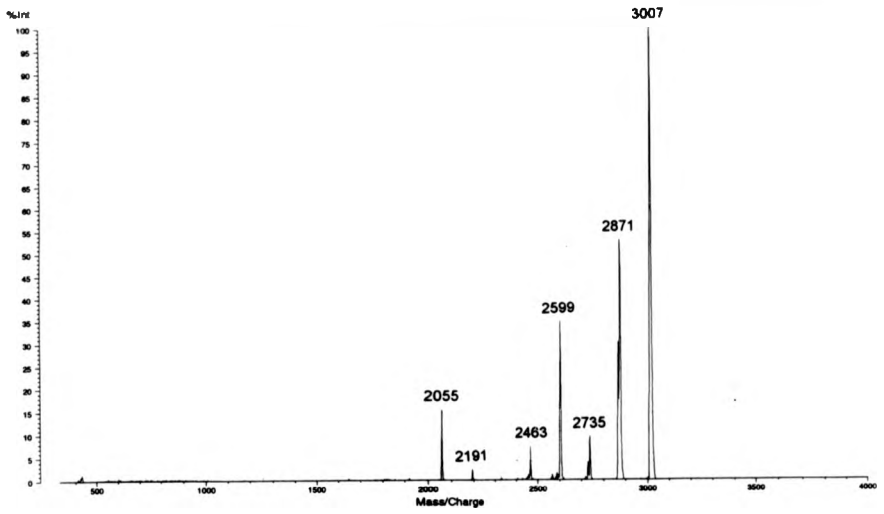


Figure 5.11 MALDI-MS Spectrum of G_3P-[24]-OH (at Power = 135)

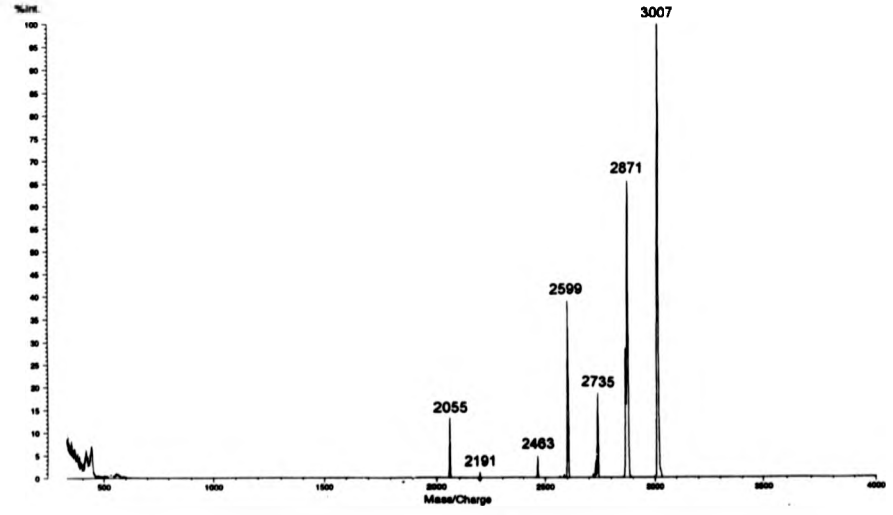
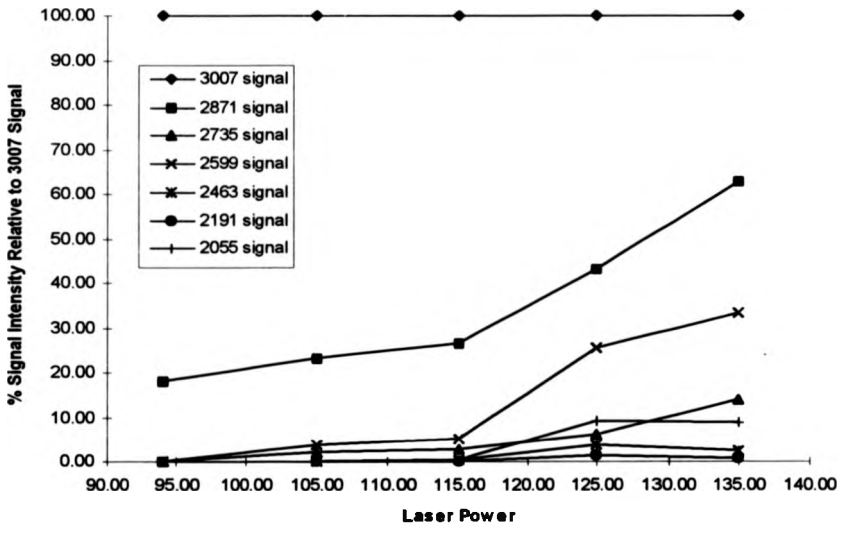


Figure 5.12 Graph of Laser Power versus Signal Intensity for G_3P-[24]-OH



It is noteworthy that all our dendrimers show strong UV absorption at the laser wavelength of 337 nm. Thus it is likely that the dendrimers absorb some of the laser energy, resulting in an increased probability of laser induced fragmentation. Note the similarity between the structure of the dendrimer and that of the matrix.

Lower molecular mass species were also observed for dendrimers G_2P-[12]-OH, G_2P-[12]-OBn and G_3P-[24]-OBn. For G_2P-[12]-OH, species 136 Da below the molecular ion were seen. Once again, this may be ascribed either to problems in the synthesis or to fragmentation as a result of the MALDI-MS process.

However, the spectra obtained from both G_2P-[12]-OBn and G_3P-[24]-OBn showed signals 90 Da and 316 Da below the molecular ion. Whereas the species 316 Da below the molecular ion of G_2P-[12]-OBn (**figure 5.3**) could be explained by a defect in the synthesis as well as an artifact of the MALDI-MS process, the signal at 2381 Da (90 Da below the dendrimer signal) cannot be easily explained in this way as benzyl ethers are stable until below pH 1.[138] These conditions were not present during synthesis but the higher pHs created as the acidic matrix solution dries may be sufficient for cleavage of the benzyl ethers. Signals are also seen at 2021 Da and 1645 Da corresponding to species with 5 and 9 benzyl groups, respectively, fewer than G_2P-[12]-OBn. The loss of benzyl groups in the presence of an acidic matrix was later noticed by Fréchet *et al* when investigating polyether dendrimers using MALDI-MS.[90]

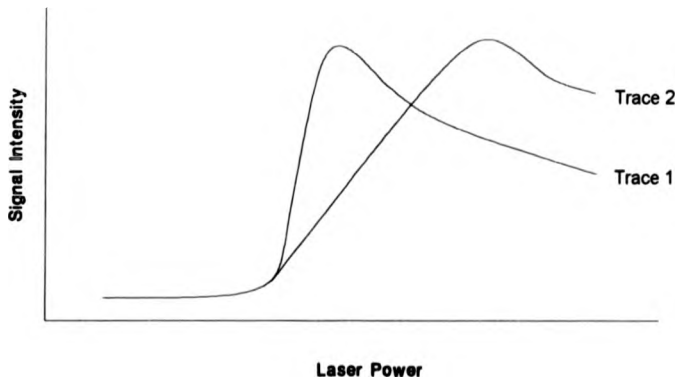
We should note that the signals at 2381, 2021 and 1645 Da could alternatively be due to photolytic fission of the O-benzyl linkage due to laser irradiation.

5.3.2.3 Differing Characteristics of Individual Species

The threshold power is the minimum laser power required for the desorption-ionization process to occur. Signal intensity is known to vary with laser power, first increasing rapidly just above the threshold, then

falling off as laser power is increased (**figure 5.13**, trace 1). The individual desorption characteristics of different species vary. Thus, the increase in intensity of the lower molecular mass species with laser power could be a result of the variation of the different desorption characteristics. If the lower molecular mass species had desorption characteristics of trace 2 (**figure 5.13**), their relative intensity would indeed increase with higher laser powers.

Figure 5.13



5.3.3 Hydroquinone and Naphthalene-2,6-diol Core Dendrimers

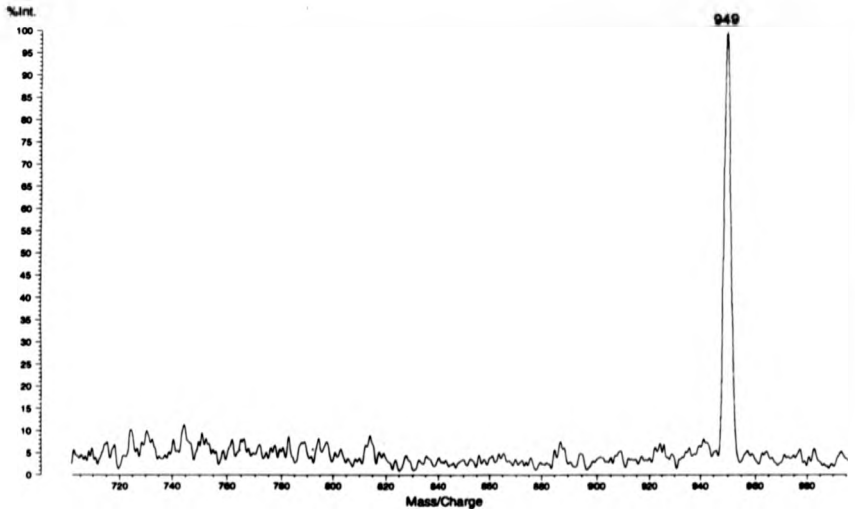
Using DHB as matrix we were able to characterize all second and third generation hydroquinone core dendrimers (**table 5.2**). For example,

G_2H-[8]-OH has a calculated mass of 949 Da, the molecular mass obtained was 949 Da, indicating a successful synthesis (**figure 5.14**).

Table 5.2 MALDI-MS Data for Hydroquinone Core Dendrimers

Dendrimer	Calculated MW + Na^+	MW determined by MALDI-MS + Na^+
G_1H-[4]-OBn	765	765
G_2H-[8]-OBn	1670	1670
G_2H-[8]-OH	949	949
G_3H-[16]-OBn	3478	3478
G_3H-[16]-OH	2037	2037

Figure 5.14 MALDI-MS Spectrum of G_2H-[8]-OH



However, we were unable to characterize G_1H-[4]-OH due to its low molecular mass. The low molecular mass region (<450 Da) suffers from the presence of many lines due to the matrix. Other exceptions were the highest molecular mass dendrimers G_4H-[32]-OBn and G_4H-[32]-OH for which we were unable to obtain any MALDI-MS data. Various molar ratios of matrix-analyte from 100:1 to 20000:1 were attempted without success. A variety of matrices were attempted including sinapinic acid, 9-nitroanthracene and α-cyano-4-hydroxycinnamic acid but all failed to give any MS data.

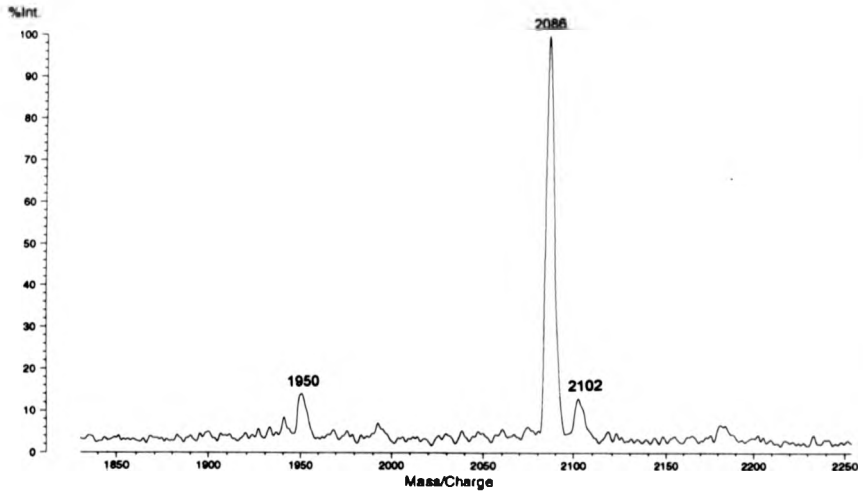
We were similarly able to obtain MALDI-MS data for all second and third generation dendrimers with naphthalene-2,6-diol cores (**table 5.3**). As with the hydroquinone core dendrimers, we were unable to obtain data for G_1N-[4]-OH, G_4N-[32]-OH or G_4N-[32]-OBn.

Table 5.3 MALDI-MS Data for Naphthalene-2,6-diol Core Dendrimers

Dendrimer	Calculated MW + Na^+	MW determined by MALDI-MS + Na^+
G_1N-[4]-OBn	815	816
G_2N-[8]-OBn	1720	1720
G_2N-[8]-OH	999	999
G_3N-[16]-OBn	3529	3529
G_3N-[16]-OH	2087	2086

Figure 5.15 shows the MALDI-MS spectrum of G_3N-[16]-OH. As with the phloroglucinol core dendrimers, species were observed at 136 Da below the molecular ion.

Figure 5.15 MALDI-MS Spectrum of G_3N-[16]-OH



Our inability to obtain molecular mass data for the generation four dendrimers may have been due to signal intensity problems. Signal intensities as high as 1000 mV were obtained for the generation one dendrimer G_1P-[6]-OBn, but dropped to just 10 mV for the generation three dendrimer G_3P-[24]-OBn (averaged over 100 shots). This decreasing signal intensity indicates that the generation four dendrimers may give very low intensity signals.

The difficulty in obtaining MALDI-MS spectra for higher generation benzyl terminated dendrimers was experienced with all three series of dendrimers. This was thought to be due to the different solubility properties of benzyl terminated dendrimers and matrix, and perhaps due to the developing three-dimensional structure of the dendrimer. For the matrix to be effective, incorporation of the dendrimer into the crystallizing matrix is essential.[139] The differing solubility properties may lead to phase separation of benzyl terminated dendrimer and matrix compared to the hydroxyl terminated dendrimers.

5.3.4 Analysis of Functionalized Dendrimers

All functionalized dendrimers were analyzed by MALDI-MS. We were able to record MALDI-MS spectra for all pent-4-enoyl and pent-4-enoyl oxide functionalized dendrimers. These all gave the appropriate [M+Na^+] signal to within 1 Da indicating successful syntheses. For example, G_2P-[12]-O-pent-4-enoyl dodecaoxide gave a signal at *m/z* 2552 and had an expected *m/z* of 2551. **Figure 5.16** shows the MALDI-MS spectrum of G_1P-[6]-O-pent-4-enoyl. The absence of species 16 Da below the calculated masses for the pent-4-enoyl oxide functionalized dendrimers confirmed that the pent-4-enoyl dendrimers, from which these were derived, had been fully epoxidised (**figure 5.17** and **5.18**). This was also confirmed by ^{1}H NMR spectroscopy (chapter 4). It was found that these

dendrimers also showed species at lower molecular mass (corresponding to multiples of the appropriate chain termini molecule) than the fully functionalized dendrimer. The relative intensity of the lower molecular mass signals was found to increase when the laser power was increased. **Figure 5.18** and **5.19** show the spectra obtained from G_2P-[12]-O-pent-4-enoyl dodecaoxide at laser powers of 90 and 125 respectively. The signal at 2454 Da corresponds to a dendritic material with one less pent-4-enoyl oxide unit less than the perfect dendrimer. Once again, this may be due either to defects arising during synthesis, or to fragmentation as a result of the MALDI-MS process.

Figure 5.16 MALDI-MS Spectrum of G_1P-[6]-O-pent-4-enoyl

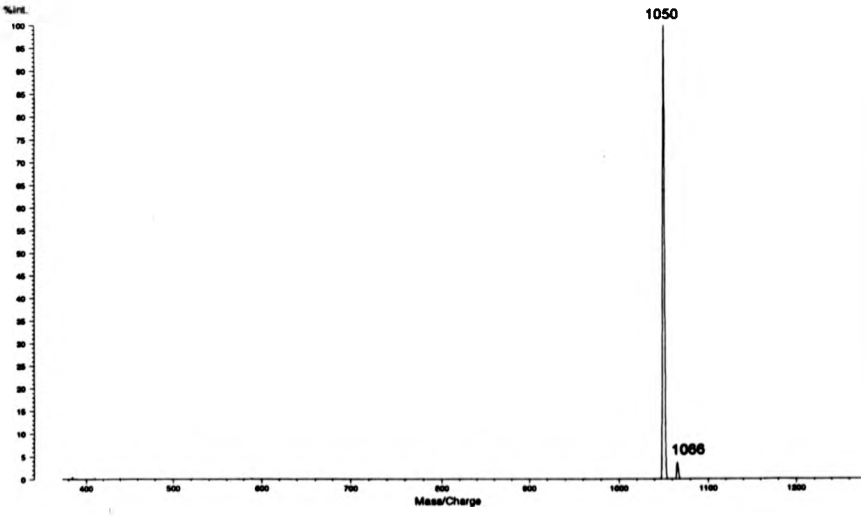


Figure 5.17 MALDI-MS Spectrum of G_1P-[6]-O-pent-4-enoyl hexaoxide

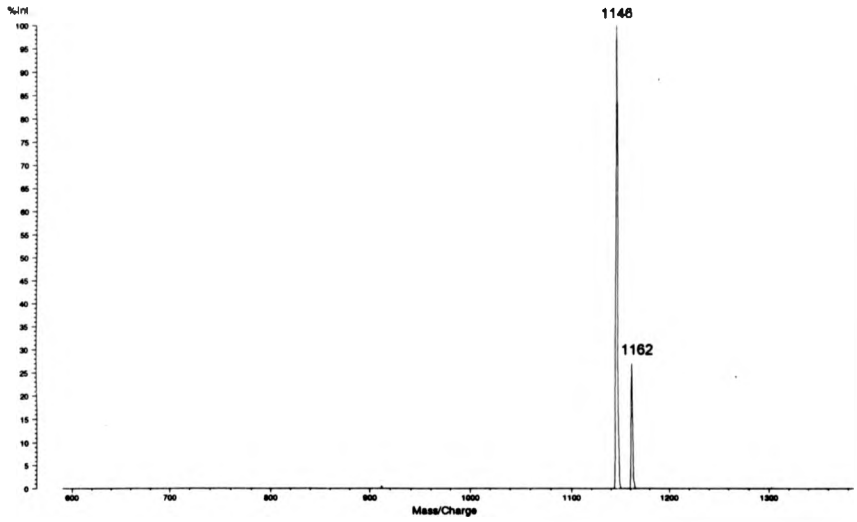


Figure 5.18 MALDI-MS Spectrum of G_2P-[12]-O-pent-4-enoyl dodecaoxide (Power = 90)

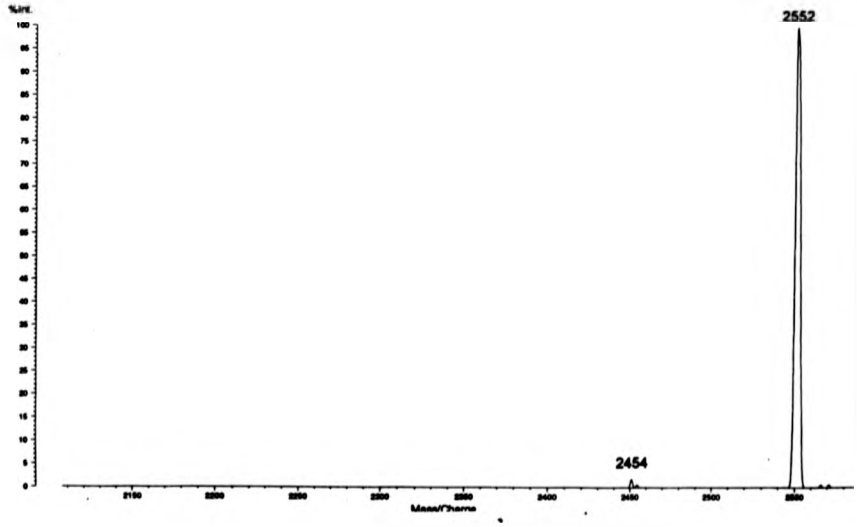
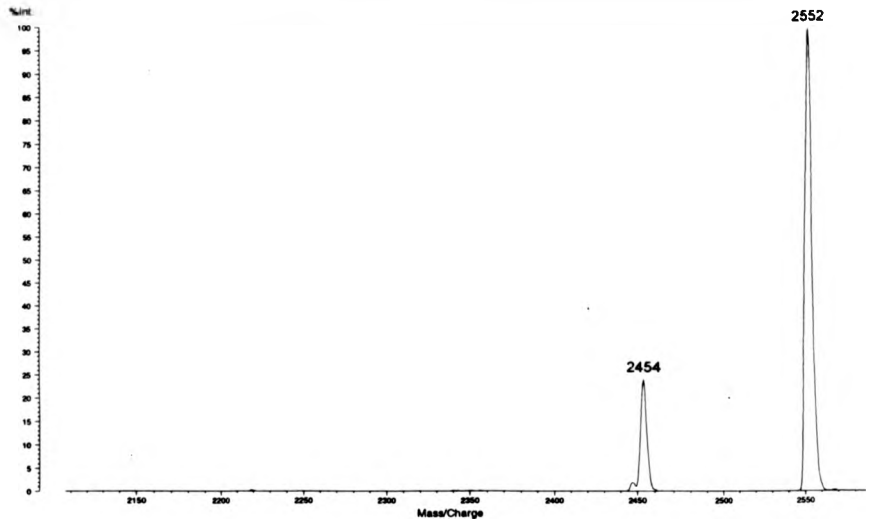


Figure 5.19 MALDI-MS Spectrum of G_2P-[12]-O-pent-4-enoyl dodecaoxide (Power = 125)



We were unable to record MALDI-MS spectra for any of the lineoyl or oleoyl terminated dendrimers. Various molar ratios of matrix-analyte were attempted without success, probably due to the non-polar nature of the terminal groups preventing incorporation of the dendrimer into the polar DHB crystals. Similar analysis problems are also observed for non-polar polymers such as poly(isobutene) and poly(ethene). Further experiments using non-polar matrices, for example, 9-nitroanthracene, may yield mass spectral data.

5.4 Analysis of Hyperbranched Polymers

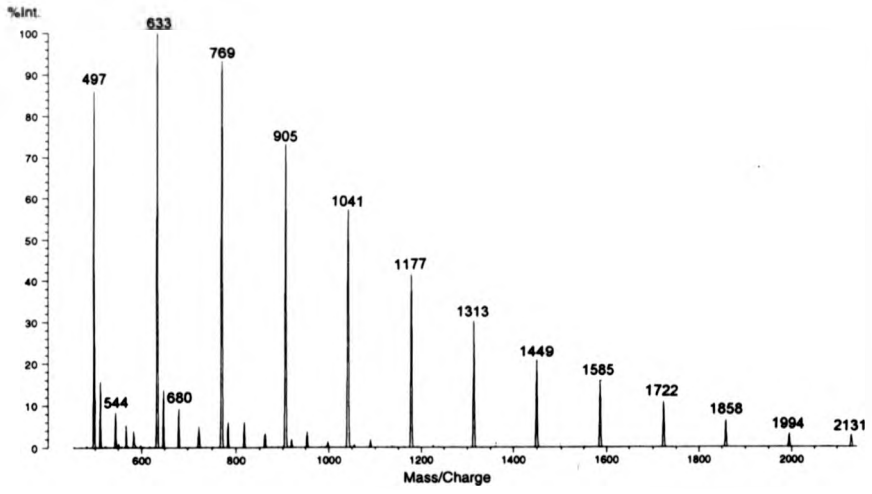
MALDI-MS is well suited as an analytical tool for the analysis of polymers. The soft ionization of intact polymers means that end group determination is possible.[130] MALDI-MS has been used to calculate M_n and M_w of polymers using peak areas and compared to values obtained by GPC.[130, 140] However, there is a question about the mass sensitivity of the MALDI-MS technique over large ranges of molecular mass.[129, 141] To date, there have been no literature reports of the use of MALDI-MS for analyzing hyperbranched polymers.

5.4.1 Polymerization Method 1

The spectrum of poly(3,5-dihydroxybenzoic acid), obtained by polymerization method 1 using DHB as matrix, showed a series of signals separated by 136 Da as expected (**figure 5.20**). However, the molecular masses of the strongest signals (at 497, 633 and 769 Da) do not correspond to either that of the polymer or that of polymer plus cation (*e.g.* proton, sodium, potassium). Calculations of the various combinations of all species present in the reaction mixture, indicate that the species observed were [poly(3,5-dihydroxybenzoic acid) + DCC + H^+]. The presence of DCC was also observed by ^1H NMR analysis. Lower intensity signals can be seen at the lower molecular mass end of the

spectrum. However, these could not be correlated to any combination of the materials present in the reaction mixture (poly(3,5-dihydroxybenzoic acid), DCC, dicyclohexylurea (byproduct of DCC), DPTS and acetone).

Figure 5.20 MALDI-MS Spectrum of Poly(3,5-dihydroxybenzoic acid) Prepared Using Method 1

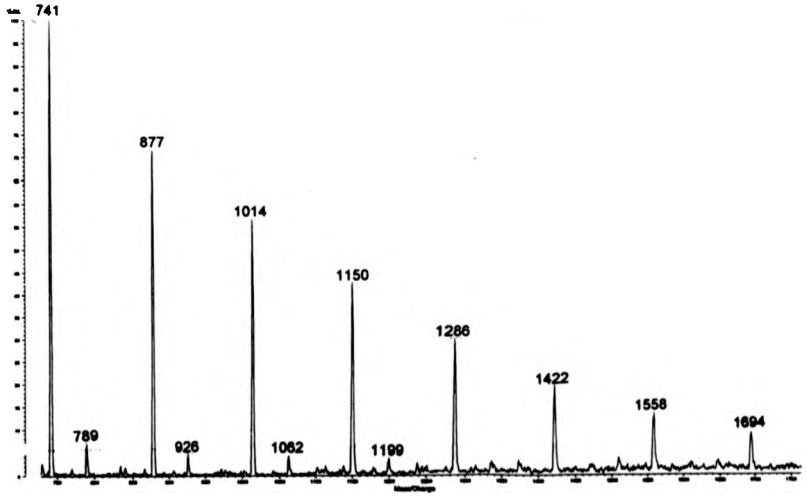


5.4.2 Polymerization Method 1 Containing Phloroglucinol

Poly(3,5-dihydroxybenzoic acid) polymers prepared using method 1, but including a core unit were analyzed next. Once again a spectrum was obtained with species separated by 136 Da and the strongest signals were those corresponding to [poly(3,5-dihydroxybenzoic acid) + phloroglucinol + DCC + H^+] at 741, 878 and 1014 Da (**figure 5.21**). The spectra also showed signals of [poly(3,5-dihydroxybenzoic acid) + phloroglucinol +

Na^+] at much lower intensity (1102, 1238 and 1373 Da). Polymerization of 3,5-dihydroxybenzoic acid using method 1 without a core results in the formation of a polymer with a single carboxylic acid function at the core. Thus, at the end of the reaction there will be a number of acid-DCC adducts remaining (**scheme 2.12**). However, the addition of a core molecule reduces the number of these groups. Signals were also observed in the MALDI-MS which could not be explained.

Figure 5.21 MALDI-MS Spectrum of Poly(3,5-dihydroxybenzoic acid) Prepared Using Method 1 Including Phloroglucinol

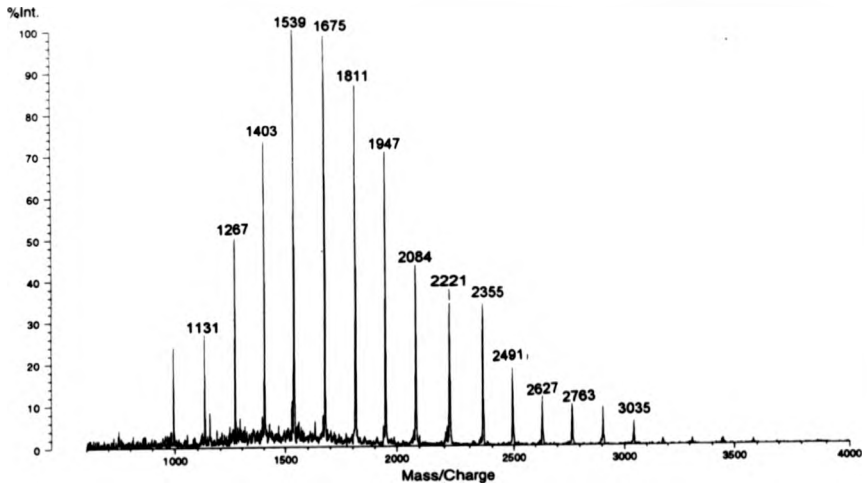


5.4.3 Polymerization Methods 2 and 3

Polymers prepared by an adaptation of Fréchet's method (methods 2 and 3) were also analyzed by MALDI-MS. These gave spectra with signals

separated by 136 Da as expected (**figure 5.22**). The molecular masses of the signals indicated that the species observed are [poly(3,5-dihydroxybenzoic acid) + Na^+]. From the molecular mass, it could also be deduced that all the trimethylsilyl ether and acid chloride groups have been hydrolysed.

Figure 5.22 MALDI-MS Spectrum of Poly(3,5-dihydroxybenzoic acid) Prepared Using Method 2



5.5 Conclusion

Mass spectrometry is the method of choice for the analysis of dendrimers and hyperbranched polymers. MALDI-MS is a relatively new technique of which our understanding is steadily increasing.

MALDI-MS has been tested to see if it fulfils the requirements (*e.g.* mild ionization) for the analysis of dendrimers. We have shown that MALDI-MS is an excellent tool for the characterization of aromatic polyester dendrimers. The molecular masses of these dendrimers were measured to within 2 Da, with the exception of the very high and very low molecular mass dendrimers. However, we observed additional signals in the mass spectra which may be a result either of the synthesis or of the MALDI-MS process. A more detailed analysis, for example by the use of different matrices, is required to fully understand the origin these signals. MALDI-MS analysis has allowed us to follow the extent of hydrogenolysis of benzyl terminated dendrimers and ensure complete deprotection.

We have shown that the conditions used for MALDI-MS sample preparation led, in some cases, to hydrolysis and/or transesterification reactions of the dendrimers. This is an important consideration when using MALDI-MS in characterizing dendrimers or indeed any other materials which may be hydrolytically labile or sensitive to acidic conditions.

MALDI-MS is been an invaluable tool for the analysis of hyperbranched polymers. The inability of other techniques (*e.g.* GPC) to accurately determine molecular weights has meant that mass spectrometry and, in particular, MALDI-MS, is the only technique available for precise mass characterization. Incorporation of core molecules and DCC in the polymer structure would have been very difficult to observe by any other method.

Chapter 6

Fluorescence Investigation of Dendrimers with a Naphthalene Core

6.1 Introduction

Fluorescence has been little used to study dendrimers. Shinkai *et al* have used fluorescence spectroscopy to follow the binding of small amounts of D-galactose and D-fructose to PAMAM Starburst dendrimers (PSBDs) functionalized with anthracene moieties.[142] The binding events were monitored by changes in the fluorescence of the anthracene unit as a function of saccharide concentration. A variety of partially protected derivatives of the sugars were analyzed and it was found that these had lower binding constants than the unprotected saccharides.

Turro *et al* have investigated the interactions of half generation (carboxyl-terminated) PSBDs with anionic and cationic surfactants using fluorescence spectroscopy.[143] Using pyrene as the luminescence probe, they found that lower generations (0.5 to 3.5) behaved as relatively open structures with surfactant molecules randomly condensed on the dendrimer structure. Higher generation PSBDs (4.5 to 9.5) were found to behave as increasingly compact surfaces, similar to micellar systems, due to the close-packed nature of the charged groups. The lower generations thus act as weak electrolytes. However, the higher generation dendrimers appeared to be able to form self-organizing supramolecular structures.

Subsequent studies by Turro *et al* using methylene blue as the adsorbate, have found similar generation dependent results.[144]

Turro *et al* have investigated the binding constant of $Ru(Phen)_3^{2+}$ to PSBDs, utilizing changes in the probe's excited state lifetime as a function of PSBD concentration.[145] The increase of the probe's lifetime in the presence of PSBDs was attributed to a lower concentration of O_2 (which acts as a quencher) at the dendrimer's surface than in water. The experiments were performed at high PSBD concentrations, relative to those of the probe and quencher. At this concentration range, the quenching of $^*Ru(Phen)_3^{2+}$ by $Co(Phen)_3^{3+}$ was found to be independent of quencher concentration. This indicates that the quenching is intra-dendrimer in nature by $Co(Phen)_3^{3+}$ bound to the PSBDs.

6.2 Naphthalene Core Dendrimers

None of the fluorescence studies described above has investigated the microenvironment of the dendrimer core molecule, of which little is known. We therefore prepared a series of dendrimers incorporating a fluorescent naphthalene core.[112]

Using solutions with a common concentration of naphthalene (10^{-5} M) we investigated the fluorescence excitation and emission of these

dendrimers.[146, 147] **Figure 6.1** shows the excitation and emission spectra of G_1N-[4]-OBn, G_2N-[8]-OBn, G_3N-[16]-OBn and G_4N-[32]-OBn in dichloromethane. This shows that the fluorescence intensity increases with higher generation dendrimers. As the dendrimers progress to higher generations, there is also a change in the shape and wavelength of the maximum emission in both excitation and emission spectra. The effect is most noticeable in the excitation spectra (**figure 6.1**) and the greatest changes in spectral shape occur between generations one and two. **Figure 6.2** shows the changes in the spectral profile of G_1N-[4]-OBn and G_4N-[32]-OBn normalised to a common maximum intensity.

The spectral shifts may be due to changes in the chromophore's local (solvating) environment as the dendritic layers develop. It may be that the benzoate dendrons of generations two, three and four fold back around the core to varying extents resulting in an 'inner filtering'. This inner filtering effect may be more pronounced with higher generations as the concentration of the benzoate units increases if the core concentration is kept constant.

The excitation and emission spectra of the hydroxyl terminated dendrimers G_1N-[4]-OH, G_2N-[8]-OH and G_4N-[32]-OH in acetone-water (1:1) are shown in **figure 6.3** (G_3N-[16]-OH was not available at the time of study). As with the benzyl terminated dendrimers, the spectral profiles

Figure 6.1 Excitation and Emission Spectra of G_1N-[4]-OBn, G_2N-[8]-OBn, G_3N-[16]-OBn and G_4N-[32]-OBn

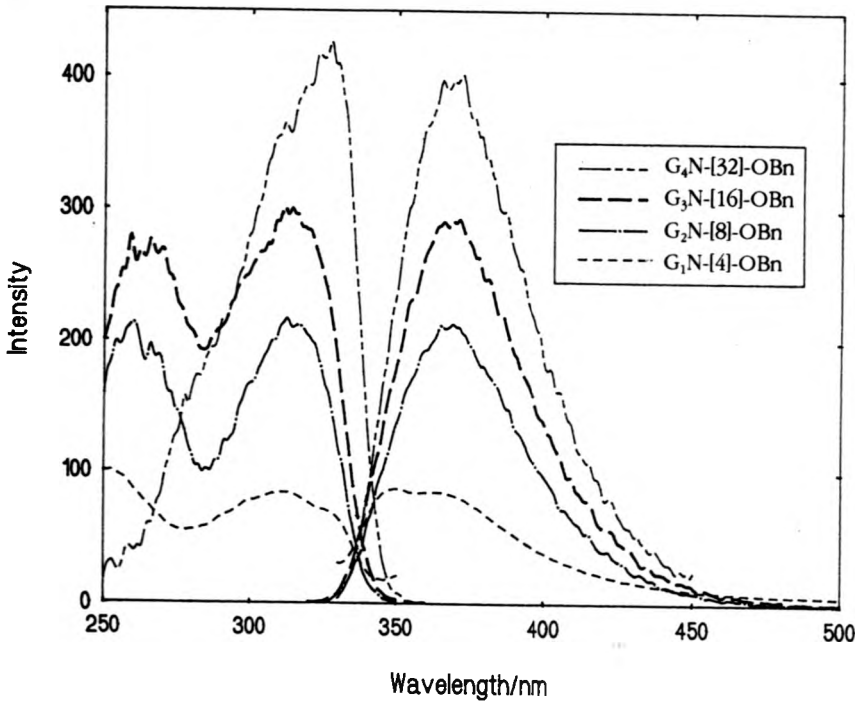
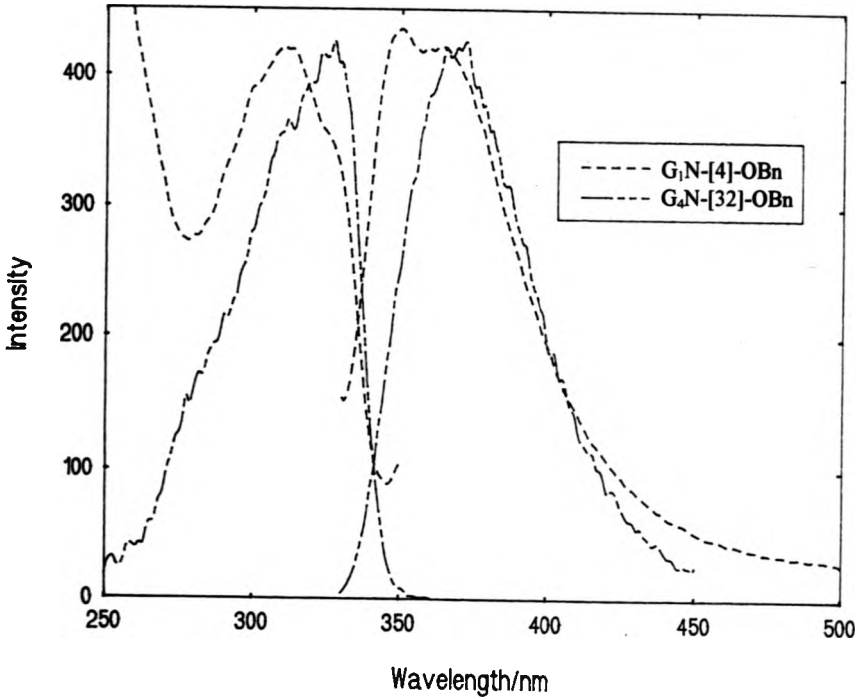


Figure 6.2 Excitation and Emission Spectra of G_1N-[4]-OBn and G_4N-[32]-OBn Normalised to a Common Maximum Intensity



and wavelengths of maximum emission were found to change with higher generation dendrimers. The fluorescence intensity was also found to increase, the greatest changes occurring between generations two and four. **Figure 6.4** emphasizes the effects of spectral changes by normalizing the intensities of the fluorescence. Note that the spectra of generations one and two are badly distorted by inner filtering by acetone and perhaps also by the benzoate units of the dendrimer.

and wavelengths of maximum emission were found to change with higher generation dendrimers. The fluorescence intensity was also found to increase, the greatest changes occurring between generations two and four. **Figure 6.4** emphasizes the effects of spectral changes by normalizing the intensities of the fluorescence. Note that the spectra of generations one and two are badly distorted by inner filtering by acetone and perhaps also by the benzoate units of the dendrimer.

Figure 6.3 Excitation and Emission Spectra of G_1N-[4]-OH, G_2N-[8]-OH and G_4N-[32]-OH

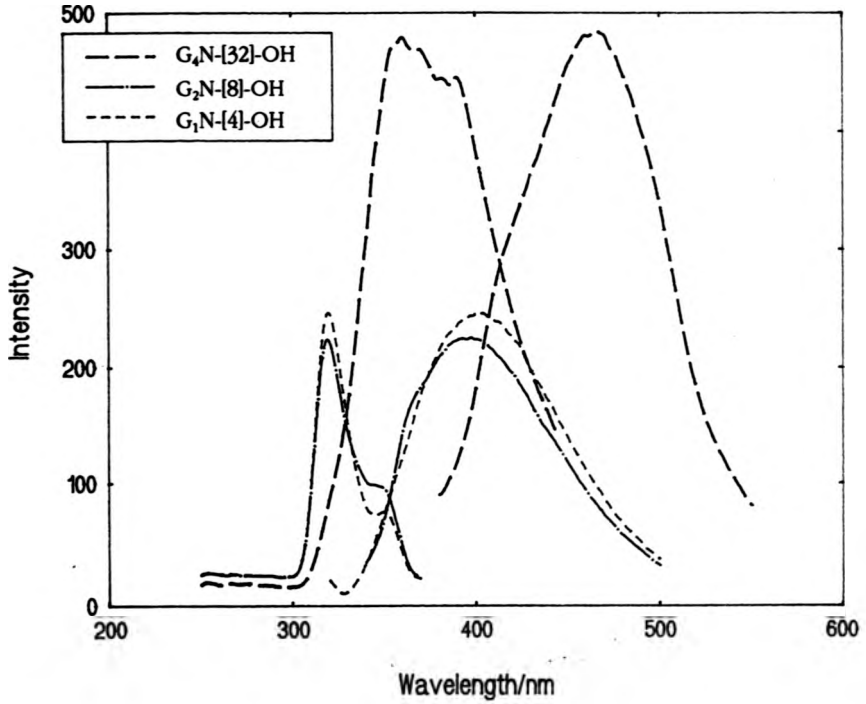
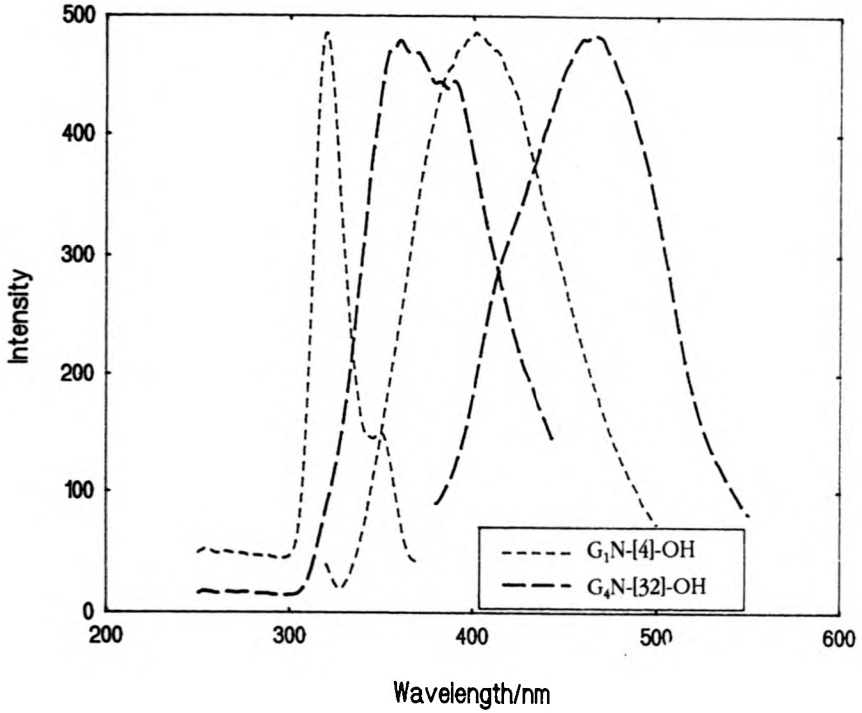


Figure 6.4 Excitation and Emission Spectra of G_1N-[4]-OH and G_4N-[32]-OH Normalised to a Common Maximum Intensity



6.2.1 Excited State Lifetimes

Table 6.1 lists the lifetime values resultant upon fitting a single exponential model function to the time-resolved fluorescences of the cores of G_1N-[4]-OBn, G_2N-[8]-OBn, G_3N-[16]-OBn and G_4N-[32]-OBn.

Table 6.1 Fluorescence Lifetime Data (Single Exponential Analyses) for Benzyl Terminated Dendrimers in Dichloromethane.

Dendrimer	τ_f (ns)	χ^2
G_1N-[4]-OBn	2.9	16.7
G_2N-[8]-OBn	0.9	8.7
G_3N-[16]-OBn	1.0	16.1
G_4N-[32]-OBn	0.8	15.6

It can be seen that the fluorescence lifetime, τ_f, decreases from that of generation one in the higher generation dendrimers. Clearly, the environment of the excited state is changing as the dendrimer size increases. This observation is in broad agreement with those made upon spectroscopic evidence. However, the quenching effect observed here might appear unexpected. If the dendrimer folds around the core and, to an extent, excludes the dichloromethane solvent, it might have been predicted that τ_f would increase as chlorinated species tend to act as fluorescence quenchers. On the other hand, the benzoate units of the dendrimer might well act as quenchers of the excited state. In the latter

instance, the current data would provide good evidence for back-folding of dendrons in higher generations.

The fluorescence decays are poorly described by single exponential model functions indicated by the high values of χ^2 (a 'fitting' coefficient) obtained. For a good fit, χ^2 should be less than 1.3. Dual exponential modelling improved the fitting but did not yield a trend in lifetimes which seemed meaningful.

The lifetime data for the hydroxyl terminated dendrimers in acetone-water are listed in **tables 6.2** and **6.3**. **Table 6.2** shows that the fluorescent lifetime of the naphthalene core is invariant between generations one and two, and that the fluorescence decays exponentially ($\chi^2 < 1.3$). However, the generation four dendrimer G_4N-[32]-OH has a fluorescence which is markedly non-exponential in character. The average excited state lifetime is longer and depends upon the wavelength chosen for excitation. Even triple exponential fitting is less than adequate ($\chi^2 > 1.3$) in describing the fluorescence characteristics of G_4N-[32]-OH. Some of this 'inadequacy' is due to radiofrequency interference in the synchrotron-generated decay data.

The lifetime data confirms the implications of the spectral data that the core's microenvironment changes markedly between generations two and four.

Table 6.2 Fluorescence Lifetime Data (Single Exponential Analyses) for Hydroxyl Terminated Dendrimers in Acetone-Water.

Dendrimer	τ_f (ns)	χ^2
G_1N-[4]-OH	1.8	1.2
G_2N-[8]-OH	1.8	1.1
G_4N-[32]-OH†	4.0	306
G_4N-[32]-OH‡	2.9	150

† Excited at 350 nm
‡ Excited at 390 nm

Table 6.3 Fluorescence Lifetime Data (Triple Exponential Analyses) for G_4N-[32]-OH in Acetone-Water.

Excitation Wavelength (nm)	τ_1 (ns)	τ_2 (ns)	τ_3 (ns)	χ^2
350	0.3	2.8	7.5	3.2
390	0.3	2.2	8.1	2.5

6.2.2 Time Resolved Anisotropy Measurements (TRAMS)

The use of polarized radiation for excitation introduces, during the absorption process, an anisotropic distribution for excited state species which is reflected in the polarization characteristics of the observed

fluorescence. The fluorescence anisotropy, r, decays as a function of time (**equation 2**) according to a first order rate law (to an approximation).

Equation 2

$$r(t) = r_0 \exp(-k_c t)$$

The rate constant k_c, or its reciprocal, the correlation time, τ_c, characterizes the rate of molecular tumbling of the chromophore (in this case, of the dendrimer) in solution; the larger the value of τ_c, the slower the molecular reorientation.

Table 6.4 lists the values of τ_c obtained for the benzyl terminated dendrimers in dichloromethane and the hydroxyl terminated dendrimers in water-acetone (1:1) . The generation one dendrimer G_1H-[4]-OBn seems to have a finite, measurable correlation time but the generation two to four dendrimers have sub-nanosecond values on the limits of resolution of the apparatus. For generations two to four, the emissions seem to contain very little anisotropy (consistent with the results).

In the case of the hydroxyl terminated dendrimers, generations one and two gave sub-nanosecond correlation times. However, the generation four dendrimer G_4N-[32]-OH, showed a complex anisotropy decay characterized, in dual exponential fitting, by a sub-nanosecond

Table 6.4 Rotational Correlation Times, τ_c, for Naphthalene Core Dendrimers.

Dendrimer	τ_1 (ns)	τ_2 (ns)
G_1N-[4]-OBn	1.2	-
G_2N-[8]-OBn	0.1	-
G_3N-[16]-OBn	0.1	-
G_4N-[32]-OBn	0.04	-
G_1N-[4]-OH	0.4	-
G_2N-[8]-OH	0.03	-
G_4N-[32]-OH[‡]	0.3	5.8

component and a longer (5.8 ns) component. Clearly, the bulk of this dendrimer (and associated solvent sheath) is sufficient to slow its rotational motion into the nanosecond domain. Again, as was apparent in the spectroscopic and lifetime experiments on these systems, there is a dramatic change in character between generations two and four.

6.3 Conclusions

Only tentative conclusions may be drawn at present with the initial results presented here. Preliminary investigations indicate that there is a significant change in the microenvironment of the dendrimer above generation two.

The fluorescence intensity of the naphthalene core increases with increasing generation which is accompanied by a change in the shape and wavelength of emission and excitation. The reason for this phenomenon is unknown and further work using, for example, different solvents, is required to help clarify these points.

Analysis of these dendrimers in differing solvent systems is also required to help understand the trends in the excited state lifetimes. Analysis in solvents such as methanol, which are 'transparent', may yield more meaningful results.

Chapter 7

Physical Properties of Dendrimers and Hyperbranched Polymers

7.1 Thermogravimetric Analysis

Thermogravimetric analysis (TGA) is used to determine the thermal stabilities of materials. The phloroglucinol, hydroquinone and naphthalene-2,6-diol core dendrimers were analyzed by thermogravimetric analysis (TGA) to determine their thermal stabilities.

7.1.1 Experimental Conditions

The samples were analyzed by TGA under a nitrogen atmosphere at a heating rate of 10 °C min^{-1}. Samples of approximately 20 mg were used in each case.

7.1.2 Phloroglucinol Core Dendrimers

Table 7.1 summarizes the TGA results for the phloroglucinol core dendrimers when heated to 300 °C.

Table 7.1 TGA Analysis of Phloroglucinol Core Dendrimers

Dendrimer	% Weight Loss 1 (Range - °C)	% Weight Loss 2 (Range - °C)	% Weight Loss 3 (Range - °C)
G_1P-[6]-OBn	0.6% (220-300 °C)	-	-
G_2P-[6]-OBn	0.3% (216-300 °C)	-	-
G_2P-[6]-OH	3.7% (40-133 °C)	2.9% (133-246 °C)	1.0% (246-300 °C)
G_3P-[6]-OH	3.2% (40-119 °C)	7.7% (119-300 °C)	-

From **table 7.1** it can be seen that benzyl terminated dendrimers show less decomposition upon heating than hydroxyl terminated dendrimers, losing less than 1% of the sample mass when heated to 300 °C. The mass lost when the hydroxyl terminated dendrimers are heated does not correspond to the loss of any particular fragment of the dendrimer. The initial mass lost for the hydroxyl terminated dendrimers may be water, as these dendrimers were found to be very hygroscopic.

7.1.3 Hydroquinone Core Dendrimers

Table 7.2 summarizes the TGA results for the hydroquinone core dendrimers. As with the phloroglucinol core dendrimers, the benzyl terminated dendrimers were found to show virtually no thermal degradation when heated to 300 °C. The hydroxyl terminated dendrimers all showed significant decomposition. The mass lost cannot be correlated in any of the examples to any dendritic fragments, with exception of G_3H-[16]-OH. The mass loss of 6.7% corresponds to the loss of a single branching unit ($C_7H_5O_3$) of molecular weight 135 Da (calculated 137 Da). If it is assumed that the initial loss of 4.7% is moisture or solvents, then adjusting for this, the mass loss is 142 Da which is still within experimental limits.

Table 7.2 TGA Analysis of Hydroquinone Core Dendrimers

Dendrimer	% Weight Loss 1 (Range - °C)	% Weight Loss 2 (Range - °C)
G_1H-[4]-OBn	0.5% (165-300 °C)	-
G_2H-[8]-OBn	0.9% (103-300 °C)	-
G_2H-[8]-OH	4.3% (40-93 °C)	4.3% (93-300 °C)
G_3H-[16]-OBn	0.8% (165-300)	-
G_3H-[16]-OH	4.7% (40-158 °C)	6.7% (158-300 °C)
G_4H-[32]-OH	2.7% (40-113 °C)	7.9% (113-300 °C)

7.1.4 Naphthalene-2,6-diol Core Dendrimers

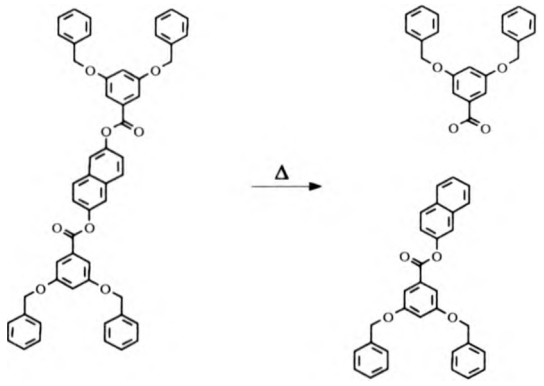
The naphthalene-2,6-diol core dendrimers were analyzed by TGA to higher temperatures (500 °C) than either the hydroquinone or phloroglucinol core dendrimers. **Table 7.3** summarizes the results.

Table 7.3 TGA Analysis of Naphthalene-2,6-diol Core Dendrimers

Dendrimer	% Weight Loss 1 (Range - °C)	% Weight Loss 2 (Range - °C)
G_1N-[4]-OBn	59.0% (255-500 °C)	-
G_1N-[4]-OH	25.1% (176-270 °C)	34.6% (270-500 °C)
G_2N-[8]-OBn	54.3% (277-500 °C)	-
G_2N-[8]-OH	5.9% (40-192 °C)	40.2% (192-500 °C)
G_3N-[16]-OBn	1.9% (40-185 °C)	40.2% (185-500 °C)

The mass losses which occurred upon heating G_1N-[4]-OBn, G_2N-[8]-OBn, G_2N-[8]-OH and G_3N-[16]-OBn, could be correlated to dendritic fragments, though not for G_1N-[4]-OH. G_1N-[4]-OBn shows a mass loss of 59% which corresponds to thermal fragmentation occurring at the core, with loss of **116 (scheme 7.1)**. The calculated mass loss for this fragment is 58%.

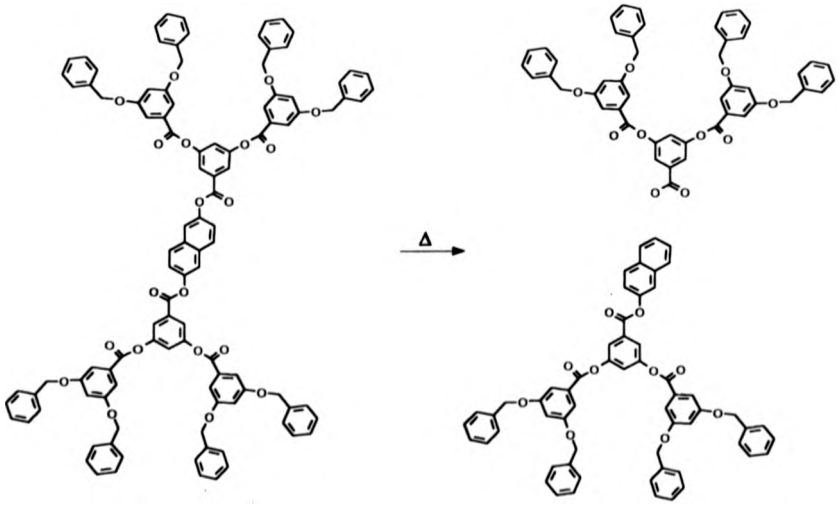
Scheme 7.1



116

G_2N-[8]-OBn also shows thermal fragmentation at the core. The loss of 54% mass corresponds to **117**. The calculated loss for this fragment is 54% (**scheme 7.2**).

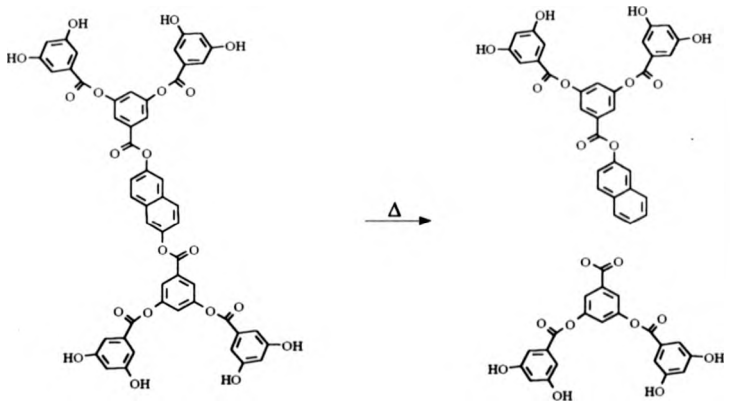
Scheme 7.2



117

G_2N-[8]-OH shows thermal fragmentation at the core with the loss of **118** (**scheme 7.3**). Assuming that the initial mass loss is water (or solvent), the corrected mass loss is 43% which corresponds to fragmentation at the core. The calculated mass loss for fragment **118** is 44%.

Scheme 7.3



118

7.2 Conclusions

Hydroxyl terminated dendrimers are more thermally labile than the benzyl terminated dendrimers. This is perhaps as a result of the acidic phenolic groups. It should be noted that MALDI-MS analysis also led to more low mass ions with hydroxyl terminated dendrimers than with benzyl terminated dendrimers. When heated to higher temperatures (500 °C) it

appears that the phenolic bond at the core is generally broken indicating that this is the weakest bond.

7.3 Applications of Dendrimers

There have been few reports of the investigation of the properties or uses of dendrimers and hyperbranched polymers. In particular, there have been no reports of the use of dendritic materials as crosslinking agents.

Hult *et al* have prepared allyl ether functional hyperbranched polyesters and investigated their curing and film formation properties.[148] Allyl ether monomers are generally used for low temperature applications when oxygen inhibition may be a problem, for example, the radical curing of coatings. The monomer 2,2-di(hydroxymethyl)propionic acid (DMPA) was used to construct the hyperbranched polymer. Hult reported that the extent of the functionalization with allyl ethers could be controlled by limiting the amount of allyl-ether added. Initial results indicate that the nature of the terminal functional groups affects the viscosity of the resin to a much greater extent than the molecular weight. With increasing hydroxyl functionality, they found the viscosity also increased. The cured resins showed increasing hardness with increasing allyl ether functionality. Similar functionality dependence of viscosity of the resin and final film hardness were also observed for acrylate functionalized hyperbranched polyesters prepared by Hult *et al.*[149]

Rånby *et al* have controlled the extent of branch termini functionalization of polyester dendrimers by limiting the reagents added to functionalise

the dendrimer. Thus, non-stoichiometric amounts of glycidyl methacrylate were added to methacrylate the chain termini of the dendrimer.[150] Photopolymerization of the methacrylate groups resulted in highly crosslinked polymers with some residual unreacted double bonds remaining (determined by FT-IR spectroscopy).[111] The rate of polymerization was found to increase with increasing functionality of the dendrimer.

7.3.1 Polyester Powder Coatings

TGIC is the crosslinker most commonly used in Europe for polyester powder coatings.[151] However, due the toxicity of TGIC, alternatives are being sought. There is also a general trend towards crosslinkers which have lower cure temperatures and can therefore be used to coat temperature sensitive materials such as paper and wood.

The dendrimers G_1P-[6]-O-pent-4-enoyl hexaoxide **89** and G_2P-[12]-O-pent-4-enoyl dodecaoxide **90** (chapter 4) were analyzed for crosslinking ability in polyester powder coatings. These dendrimers may be potential replacements for TGIC as they have large numbers of reactive epoxy groups. TGIC also contains nitrogen, an element not present in many polyester resins, thus the dendrimers **89** and **90** are more homogenous with the commonly used polyester resins. These epoxy dendrimers are

also of much higher molecular weight than TGIC and are therefore likely to have lower diffusion rates through human cell membranes, thus decreasing possible health hazards due to the reactive epoxy groups.[151]

7.3.2 Mechanism of Crosslinking

The reaction between acid and epoxy functional groups is the most important curing reaction for crosslinking thermosetting powder coatings.[151] The mechanism of the reaction between the acid and epoxy groups has been widely investigated.[152, 153]

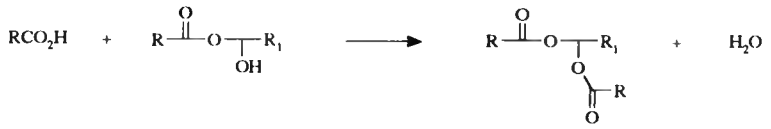
There are thought to be four main pathways for the curing of acid-epoxy blends:[151]

1. Ring opening addition of the epoxy group by the carboxylic acid groups resulting in the formation of the corresponding hydroxyl ester (**scheme 7.4**).

Scheme 7.4

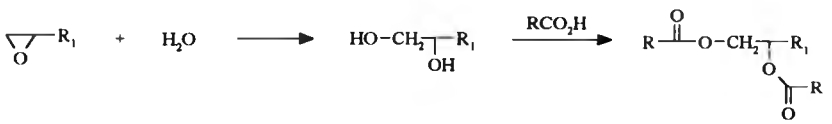
2. Esterification between the acid and the hydroxyl group formed in **scheme 7.4** (**scheme 7.5**).

Scheme 7.5



3. Hydrolysis of the epoxy ring by water followed by reaction with the carboxylic acid (**scheme 7.6**).

Scheme 7.6



4. Ring opening addition of the epoxy group to the hydroxyl groups formed in **scheme 7.4** or **7.6** (**scheme 7.7**). This type of reaction occurs only when strong acid catalysts are used.[151]

Scheme 7.7

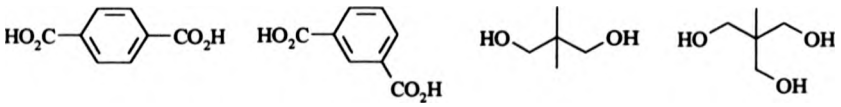
The curing reaction is often catalyzed by a basic salt (*e.g.* tetrabutylammonium bromide), which de-protonates the appropriate acid or alcohol. Thus, only pathways 1-3 are important for base catalyzed crosslinking. A reaction not mentioned by Misev is that between

epoxides, as he assumed the epoxide would be both highly dispersed within the resin and in low concentration. The structural nature of dendritic epoxides means that there is a high probability of epoxy groups being in close proximity.

7.3.3 Analysis of Epoxide Terminated Dendrimers

We chose to investigate the crosslinking ability of **89** and **90** with the resin Neocrest P660, a commercially available polyester resin used for powder coatings. Neocrest P660 is derived from terephthalic acid **119**, isophthalic acid **120**, 2,2-di(hydroxymethyl)propane **121** and 1,1,1-tris(hydroxymethyl)ethane **122** in a 552:117:28:436 ratio respectively (**figure 7.1**).

Figure 7.1 Structures of 118, 119, 120 and 121



119 **120** **121** **122**

7.3.3.1 Experimental Conditions

Samples were analyzed by DSC under a nitrogen atmosphere at heating rates of 20 °C min^{-1} unless specified. Samples of between 5-15 mg were used in each case. Blends of **89**-P660 were prepared in ratios of 18:82 and 90.1:9.9 denoted by F_3 and F_6 respectively. Blends of **90**-P660 were prepared in ratios of 33.8:66.2, 20.3:79.7 and 11.3:88.7 denoted by F_3, F_6 and F_{12} respectively.

To see if the dendrimers **89** and **90** cured (crosslinked), the pure solids were heated to 300 °C and the reaction monitored by DSC. Both dendrimers were found to cure; **figure 7.2** shows the DSC trace of **89** which shows curing at 280-335 °C. Interestingly, **90** showed an exotherm between 90-170 °C as well as curing between 210-335 °C (**figure 7.3**). The reason for the low temperature exotherm is not understood, but it may be due to alignment or crystallization phenomena. The exotherm was found to disappear when the sample was heated to 170 °C, cooled to 90 °C (both rapidly - 200 °C min^{-1} and more slowly - 5 °C min^{-1}), and then re-heated to 170 °C. A more detailed analysis is required to enable us to understand this phenomenon.

Figure 7.2 DSC Trace of 89 Without Catalyst

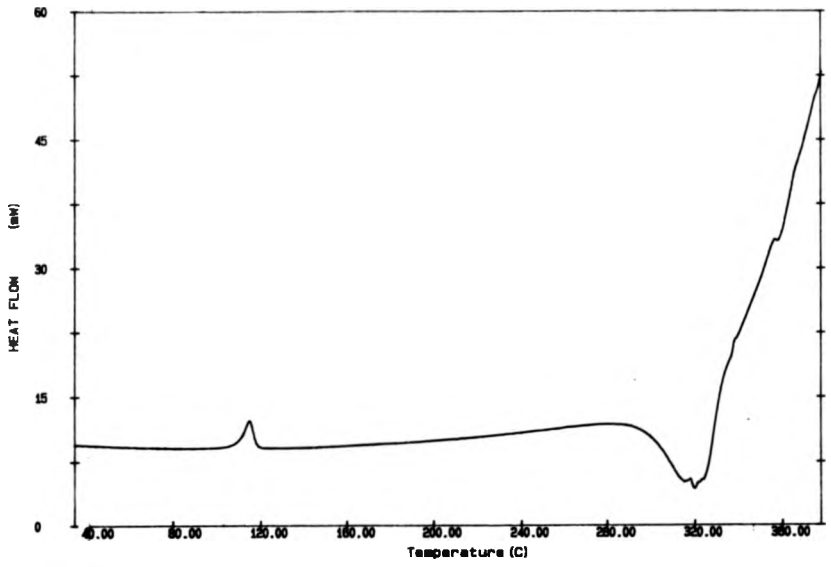
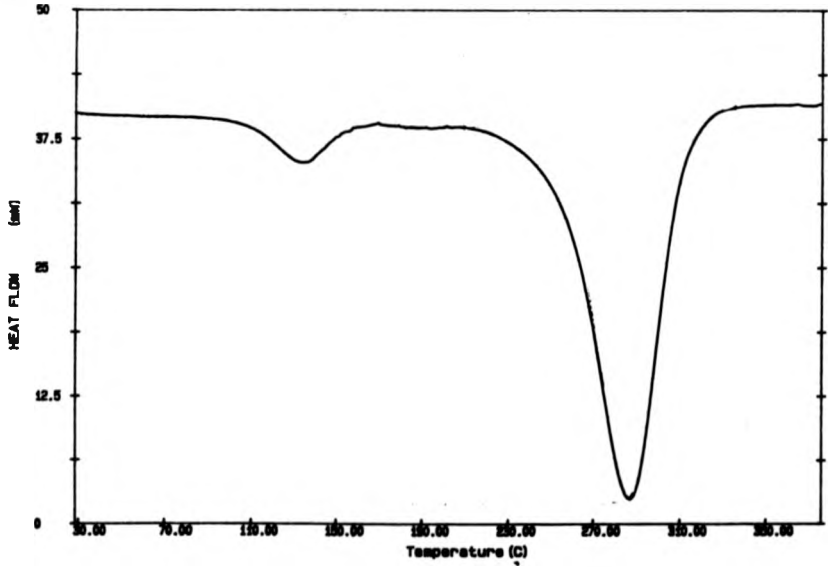


Figure 7.3 DSC Trace of 90 Without Catalyst



Basic catalysts (1%) were added to both dendrimers and the analysis repeated. The two catalysts chosen were tetrabutylammonium bromide (TBAB) and ethyltriphenylphosphonium bromide (TRAP), both of which are used commercially to catalyze TGIC/carboxyl polyester crosslinking. Both dendrimers showed curing by DSC, however, the cure temperature range was considerably lowered, for example, from 280-335 °C to 115-235 °C for **89** (**figure 7.4**). The bi-modal trace observed without catalyst for **90** (**figure 7.3**), was not observed when **90** was cured in the presence of catalyst, perhaps due to overlap with the cure range (**figure 7.5**).

Figure 7.4 DSC Trace of 89 With 1% TRAP Catalyst

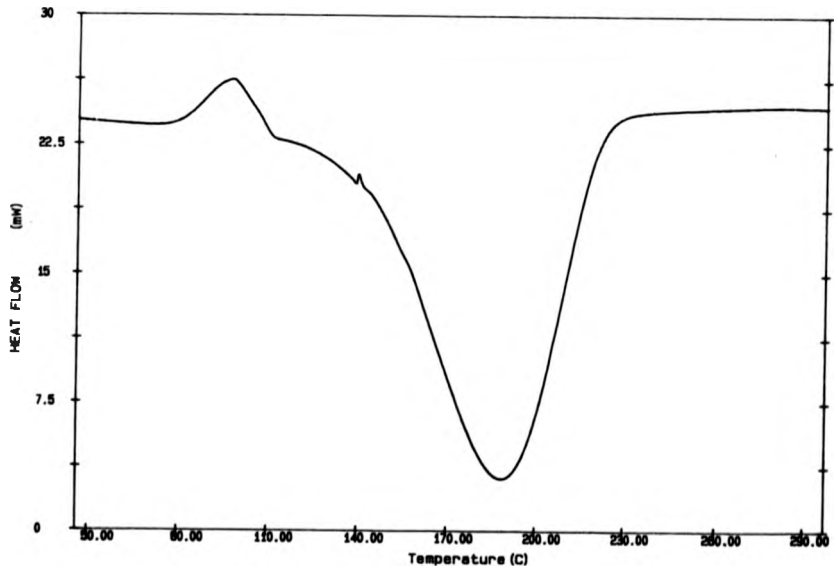
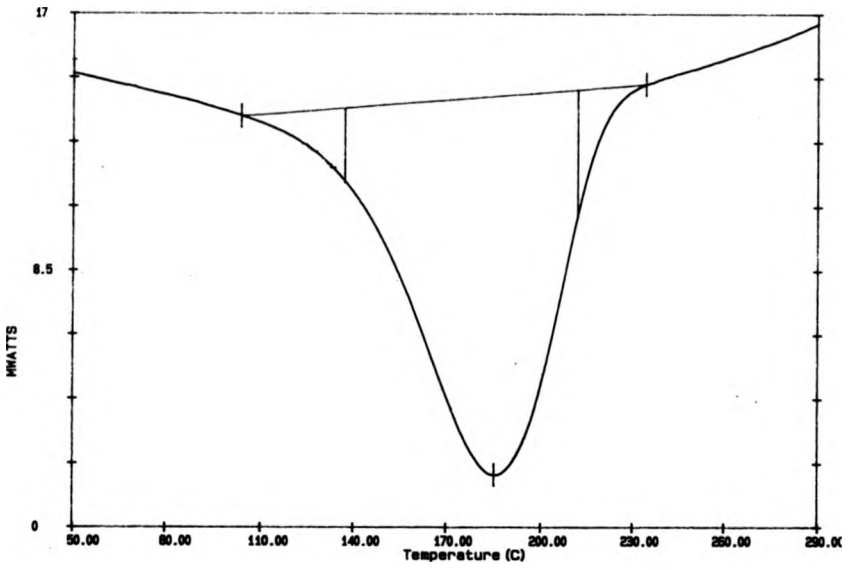
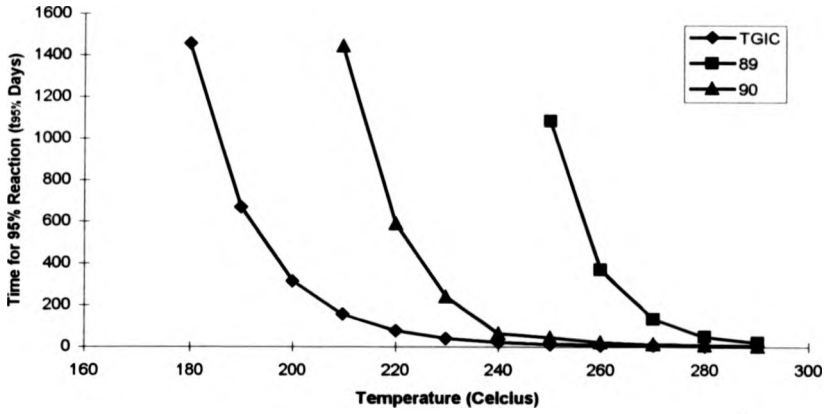


Figure 7.5 DSC Trace of 90 With 1% TRAP Catalyst



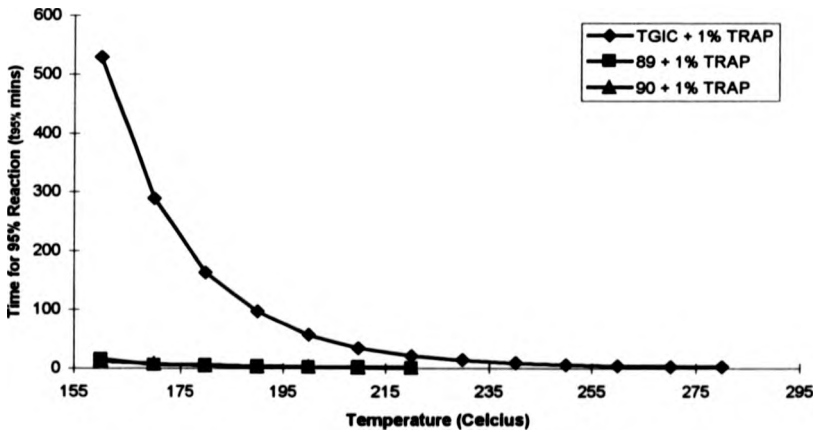
To enable us to compare TGIC with out dendrimers, TGIC reactions was also analyzed by DSC with and without catalysts. Once again, the catalysts decreased the cure temperature range, from 195-315 °C to 170-315 °C. Comparing TGIC with the dendrimers, it was found that TGIC cured at lower temperatures in the absence of catalyst than either **89** or **90**. **Figure 7.6** shows a plot of time for 95% reaction at temperature T ($t_{95\%}$) of TGIC, **89** and **90** versus temperature (T).

Figure 7.6 $t_{95\%}$ versus Temperature for 89 and 90



When catalysts were added, the dendrimers were found to cure at lower temperatures than TGIC. **Figure 7.7** shows a plot of $t_{95\%}$ of TGIC, **89** and **90** with 1% TRAP catalyst versus temperature (**89** and **90** are overlapped).

Figure 7.7 $t_{95\%}$ versus Temperature for 89 and 90 with 1% TRAP



The results are summarized in **table 7.4**.

Table 7.4 Summary of Curing Analysis of 89 and 90 by DSC

Crosslinker	Catalyst (wt-%)	Catalyst Type	DSC data: 20 °C min^{-1}		
			E_a ($kJmol^{-1}$)	ΔH_{reac} ($J\ g^{-1}$)	Peak (°C)
TGIC	0	0	137	-895	195-315 °C
	1	TBAB	100	-968	170-320 °C
	1	TRAP	95	-895	170-315 °C
89	0	0	250	-563	280-335 °C
	1	TBAB	91	-494	115-230 °C
	1	TRAP	87	-532	115-235 °C
90	0	0	183	-440	210-355 °C
	1	TBAB	80	-398	135-250 °C
	1	TRAP	80	-440	105-235 °C

7.3.3.2 Epoxy Dendrimers With P660

The dendrimers **89** and **90** were tested to see if they crosslinked P660. P660 is a carboxylic acid terminated polyester resin with M_n of 3300 and a functionality of 2.3 ($F_{2.3}$) - the average number of carboxylic acid functional groups per molecule. The value of F_n is greater than 2 for this polymer, indicating that P660 is partially branched.

To allow for potentially non-reacting epoxy groups, two blends of **89** were prepared with P660 assuming half (3) or all (6) epoxy groups would react (denoted by F_3 and F_6 respectively). No catalyst was used at this stage. Analysis of the blends by DSC showed an exotherm indicating that reactions were taking place. **Figure 7.8** shows the DSC trace of **89** with P660. A plot of $t_{95\%}$ versus temperature is shown in **figure 7.9**.

Figure 7.8 DSC trace of 89 with P660

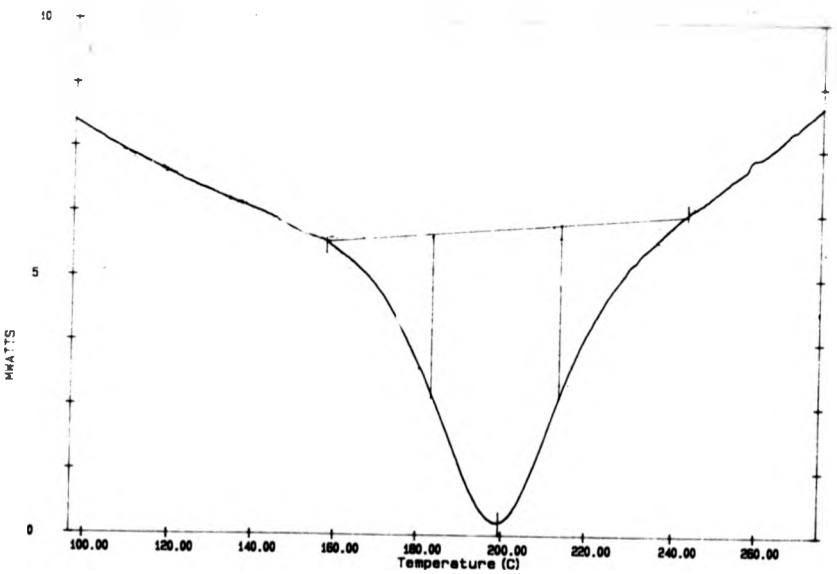
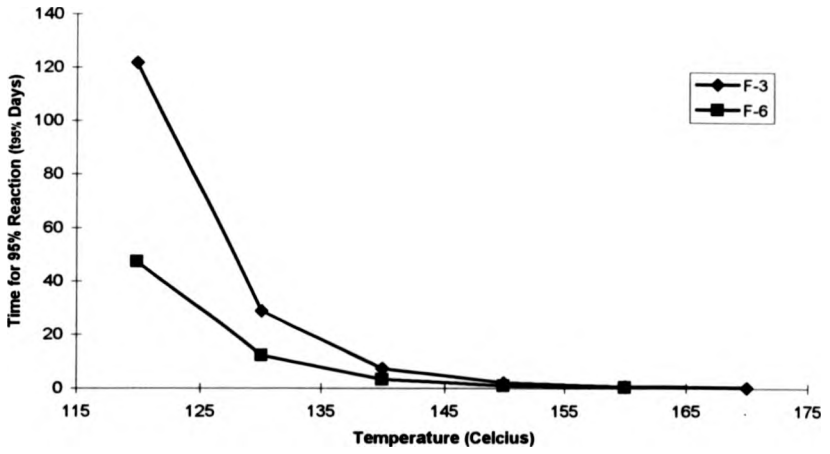


Figure 7.9 Plot of $t_{95\%}$ versus Temperature for 89 + P660



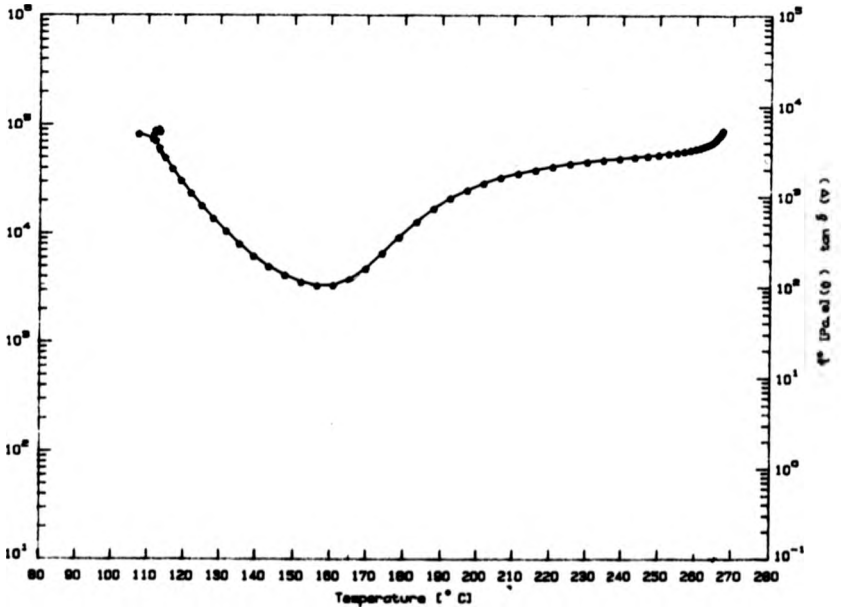
From **figure 7.9** it can be seen that when F_3 was assumed, curing took longer than when F_6 was assumed. This may be explained by the relative stoichiometries of acid and epoxy groups. The blend where F_6 is cured has an acid-epoxy stoichiometry of 1:1. When this blend is cured, a fast reaction (or set of reactions) occurs which we will call reaction 1. When blends of F_3 are heated (acid-epoxy ratio of 1:2), reaction 1 occurs, but due to the larger number of epoxides, a second reaction (or set of reactions) occurs which we will call reaction 2.

With the limited data we presently have, we can only speculate as to the nature of reaction 1 and reaction 2. The two most probable reactions are acid-epoxy or epoxy-epoxy. However, reactions 1 and 2 may be the same reaction proceeding to a greater extent when F_3 is assumed. This is evidenced by the greater ΔH_{reac} of the blends when F_3 is assumed. The

ΔH_{reac} for F_3 was found experimentally to be 92 J g^{-1}, for F_6, ΔH_{reac} was 50 J g^{-1}. This indicates that there are more reactions taking place in the blends of F_3. This may be due to incomplete reactions in the blends where F_6 is assumed, or due to reactions other than acid-epoxy taking place in blends of F_3.

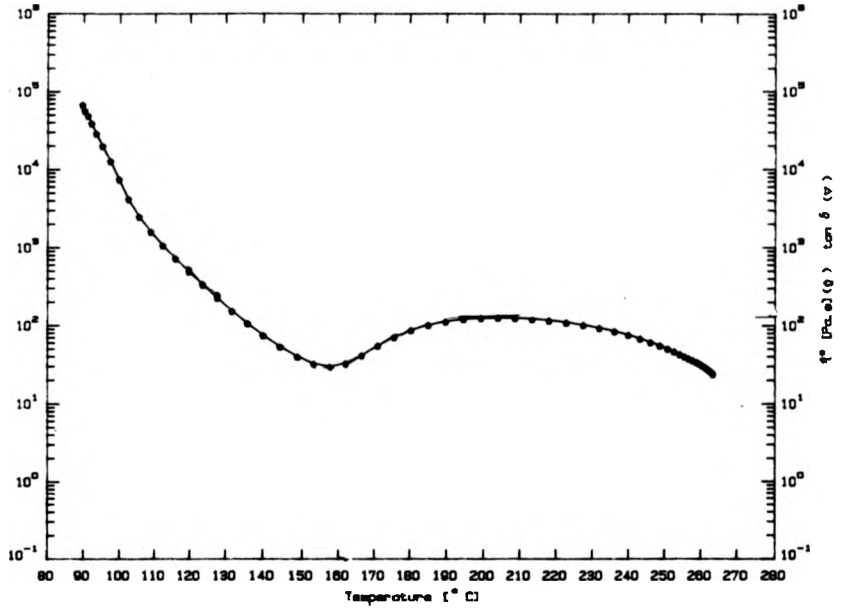
Further evidence may be obtained from rheology measurements. **Figure 7.10** shows rheology measurements of a TGIC-P660 blend. This shows the expected trace if curing of the resin is taking place. An initial drop in viscosity, due to melting, is followed by an increase in viscosity due to crosslinking.

Figure 7.10 Rheometrics Trace of TGIC + P660



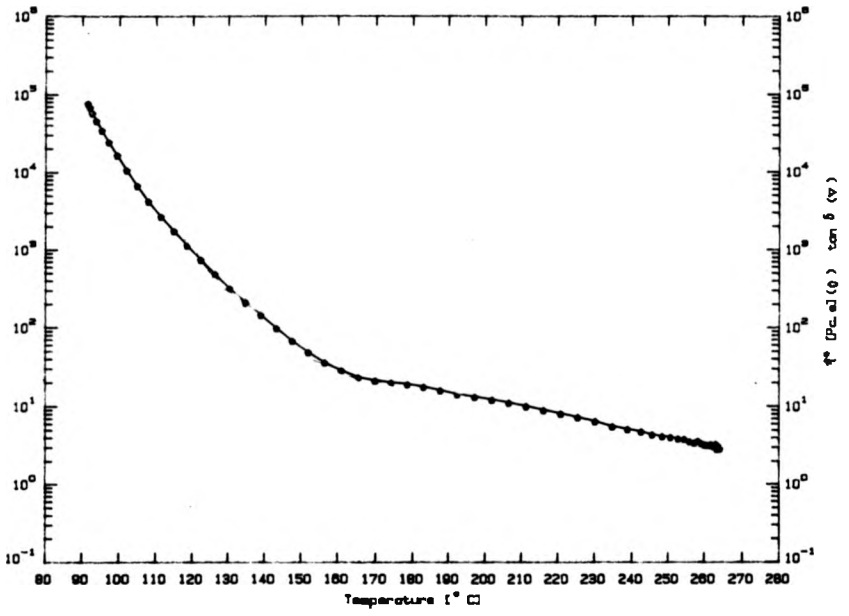
Blends of **89** and **90** with P660 were analyzed by rheology measurements. **Figures 7.11** and **7.12** show the rheometrics traces of blends of **89** at F_3 and F_6 respectively with P660. As the temperature increases, there is a decrease in the viscosity of the sample due to melting. Further heating results in an increase in viscosity for F_3 blends, but a decrease for F_6 blends. This indicates that when F_3 is assumed, where the acid-epoxide ratio is 1:2, there is crosslinking of the resin to some extent, resulting in a small increase in viscosity. However, the blends of F_6 where the acid-epoxide ratios are equal do not show significant crosslinking of the resin. This suggests that curing seen by DSC is predominantly chain extension when F_6 is assumed, and a situation somewhere between crosslinking and chain extension occurring when F_3 is assumed.

Figure 7.11 Rheometrics Trace of 89 + P660 at F_3



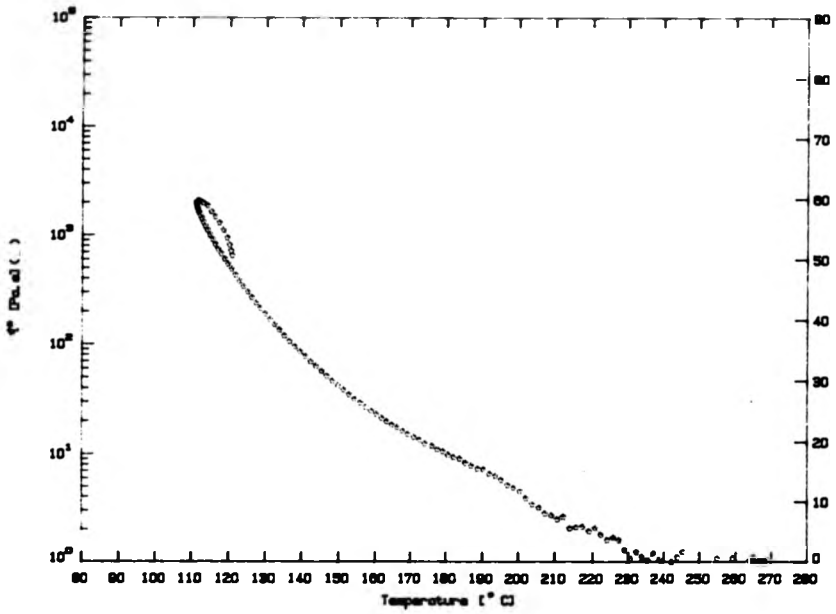
Addition of 0.25% TRAP catalyst to the blends resulted in a lowering of the activation energy (E_a) of the reaction. For example, the blends where F_3 is assumed, have E_a of 190 kJ mol^{-1} in the absence of catalyst. The addition of TRAP catalyst lowered the E_a to 60 kJ mol^{-1}. Addition of catalyst also resulted in small increases in the ΔH_{reac}. For example, the blends where F_6 is assumed, have ΔH_{reac} of 50 J g^{-1}. This was increased to 80 J g^{-1} by the addition of 0.25% TRAP. A catalyst cannot change ΔH_{reac}, thus the extra energy given by the reaction must be either as a

Figure 7.12 Rheometrics Trace of 89 + P660 at F_6



result of more acid-epoxy reactions taking place, or due to an increase in the number of side reactions. Rheology measurements of blends of **89** with catalyst showed no inflexion points whatsoever, indicating that the addition of catalyst has resulted in the catalysis of non-crosslinking events *i.e.* epoxy-epoxy (**figure 7.13**).

Figure 7.13 Rheometrics Trace of 89 + P660 at F_3 With 0.25% TRAP



Blends of **90** were prepared assuming F_3, F_6 and F_{12} with P660 in the absence of catalyst. Analysis by DSC indicated reactions were taking place. However, a bi-modal DSC trace was observed. This may be related to the bi-modal traces seen when pure **90** is cured (**figure 7.3**). **Figures 7.14**, **7.15** and **7.16** show curing at F_3, F_6 and F_{12}. It can be seen that as the assumed F_n is increased, the exotherm at lower temperature increases relative to the exotherm at higher temperature.

Figure 7.14 DSC Trace of 90 + P660 Without Catalyst at F_3

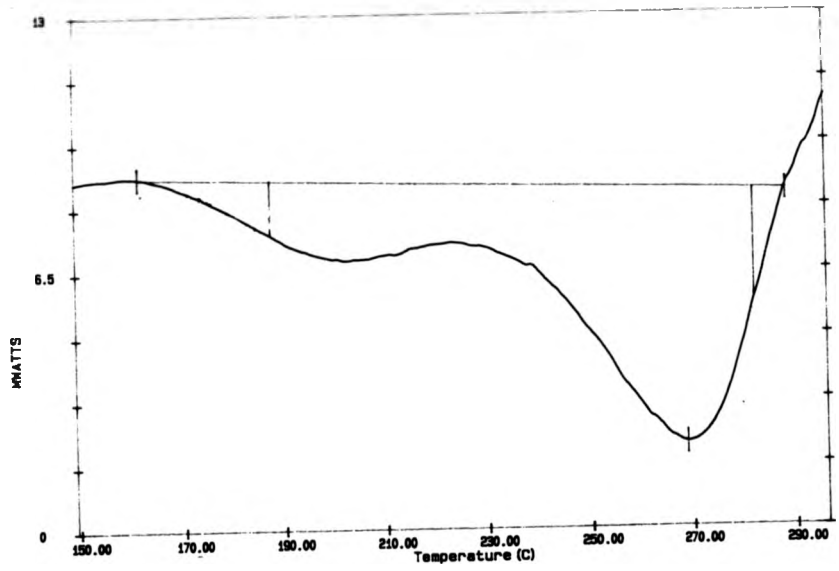


Figure 7.15 DSC Trace of 90 + P660 Without Catalyst at F_6

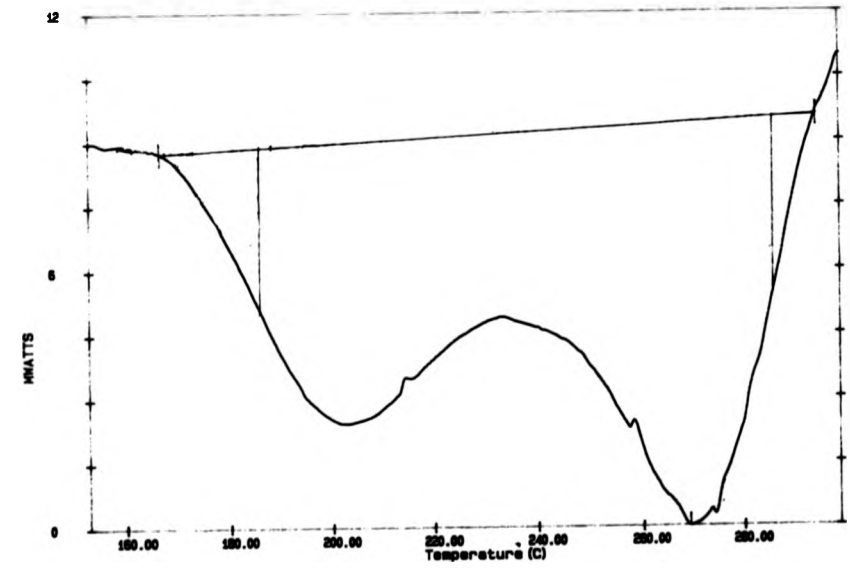
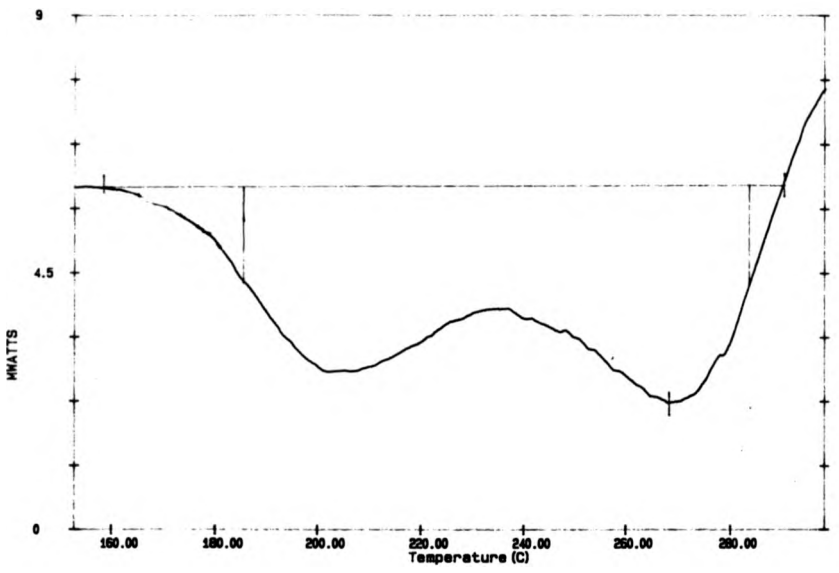


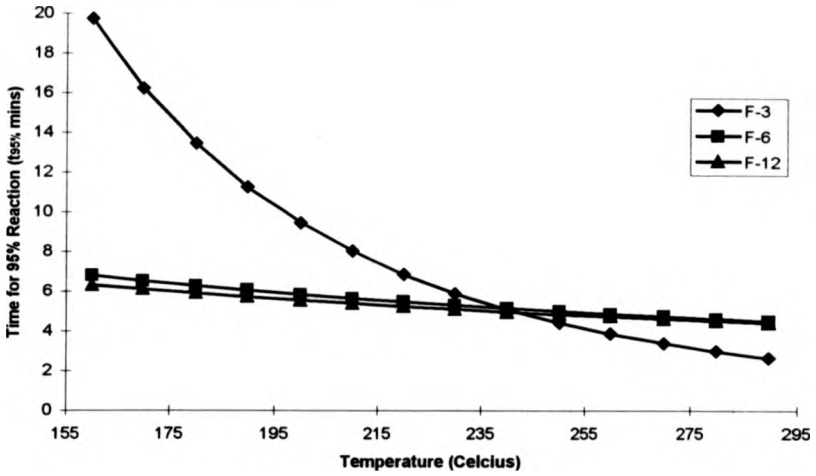
Figure 7.16 DSC Trace of 90 + P660 Without Catalyst at F_{12}



As with **89**, $t_{95\%}$ was found to be faster for F_{12} than F_6, which in turn is initially faster than F_3 (**figure 7.17**). However, at higher temperatures (>240 °C) the curing of F_3 is faster than both F_6 and F_{12}. This phenomenon may be as a result of the bi-modal curing trace.

Rheological studies on these blends showed no crosslinking of the resin to any extent and gave similar rheometrics traces to **figure 7.13**. Thus, either chain extension is occurring or non acid-epoxy events (*i.e.* epoxy-epoxy) are dominant.

Figure 7.17 Plot of $t_{95\%}$ versus Temperature at F_3, F_6 and F_{12} for 90

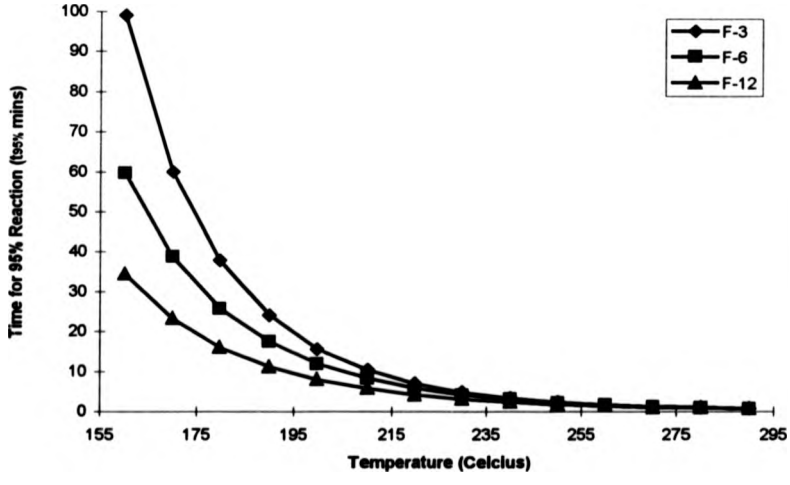


Addition of 0.25% TRAP catalyst resulted in a decrease in the reaction rate in each case (**figure 7.18**). This may be explained by the solubility of **90** in P660 in the melt. If **90** is insoluble in molten P660 and has phase separated, then it would be expected that any reactions taking place are predominantly epoxy-epoxy. If **90** is soluble in molten P660 and has dissolved, then acid-epoxy and/or epoxy-epoxy reactions would be taking place. By curing **90** without resin, ΔH_{reac} of epoxy-epoxy reactions was determined experimentally and found to be 440 J g^{-1}. Using this figure, it is possible to compare curing of **90** in the presence of a resin. For example, when F_3 is assumed, if all reactions were epoxy-epoxy exclusively, then the ΔH_{reac} of the reaction would be 149 J g^{-1} (as 33.8% **90** present). The actual ΔH_{reac} obtained for this reaction was found to be 147 J g^{-1}. Similarly, the ΔH_{reac} was calculated for the blends of F_6 and F_{12}

and found to be 90 and 50 J g^{-1} respectively. Experimentally, the ΔH_{reac} was 100 and 70 J g^{-1} respectively. This suggests that reactions seen in blends of **90** with P660 in the presence of catalyst are predominantly epoxy-epoxy.

Rheological studies on these blends showed no crosslinking of the resin to any extent and gave similar rheometrics traces to **figure 7.13**. This reinforces the idea that non acid-epoxy events (*i.e.* epoxy-epoxy) are dominant.

Figure 7.18 Plot of $t_{95\%}$ versus Temperature at F_3, F_6 and F_{12} for 90 With 0.25% TRAP



The results for the crosslinking of P660 are summarized in **table 7.5**.

Table 7.5 Summary of Curing Analysis of 89 and 90 by DSC With P660

Crosslinker	Epoxy Equivalent Weight	F_n	Resin:cross -linker (w/w)	Catalyst (wt-%)	Catalyst Type	DSC data: 20 °C min^{-1}		
						E_a ($kJmol^{-1}$)	ΔH_{reac} ($J\ g^{-1}$)	Peak (°C)
TGIC	110	2.7	93/7	0	0	105	-29	140-210 °C
	110	2.7	93/7	0.25	TRAP	70	-10	120-205 °C
89	362	3	82/18	0	0	189	-92	140-245 °C
	362	3	82/18	0.25	TRAP	61	-79	135-250 °C
89	181	6	90.1/9.9	0	0	178	-50	155-240 °C
	181	6	90.1/9.9	0.25	TRAP	125	-80	145-205 °C
90	843	3	66.2/33.8	0	0	31	-89	160-290 °C
	421	6	79.7/20.3	0	0	6.4	-72	165-295 °C
	211	12	88.7/11.3	0	0	5.6	-42	160-290 °C
90	843	3	66.2/33.8	0.25	TRAP	69	-147	135-280 °C
	421	6	79.7/20.3	0.25	TRAP	79	-99	160-285 °C
	211	12	88.7/11.3	0.25	TRAP	63	-69	140-270 °C

7.4 Conclusion

Only tentative conclusions can be drawn at this early stage of the analysis of **89** and **90**. Both **89** and **90** are unsatisfactory crosslinking agents of P660 either with or without TRAP catalyst. The epoxy groups of **89** and **90** appear to be too reactive, reacting with one another faster than reacting with the resin. The addition of catalyst results in considerable acceleration of the epoxy-epoxy reaction resulting in little reaction with the resin. Without catalyst present, only **89** at high concentrations shows any significant crosslinking of P660. Perhaps analysis at higher concentration of **89** may show significantly more crosslinking of the resin. However, this would require large amounts of the relatively expensive dendrimer and very little of the cheap resin making the process economically un-viable.

Chapter 8

Experimental

8.1 General Experimental

Melting points and glass transition points were determined on a Stuart Scientific SMP1 melting point apparatus (uncorrected), a Netzsch High Temperature Differential Scanning Calorimeter DSC 404 or a Perkin Elmer DSC7, indicated by SS, Net and PE respectively. Melting points and glass transition points determined on the Netzsch and Perkin Elmer instruments are quoted at the onset. Microanalyses were performed at the University of Warwick. Infra red spectra were recorded neat or as a KBr disc on a Perkin-Elmer 1720X Fourier transform infra red spectrophotometer using sodium chloride plates. Selected absorbances (υ_{max}) are reported. ^{1}H NMR spectra were recorded in $CDCl_3$, CD_3OD or [$^{2}H_6$]-acetone solution either at 250 MHz or 400 MHz on a Bruker ACF250 or a Bruker ACP400 instrument respectively. Chemical shifts (δ) are quoted in parts per million (ppm) using solvent deuterium signal as internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$, CD_3OD or [$^{2}H_6$]-acetone solution either at 62.9 MHz or 100.6 MHz on a Bruker ACF250 or a Bruker ACP400 instrument respectively. Chemical shifts (δ) are quoted in ppm using solvent deuterium signal as internal standard. UV spectra were recorded on a Phillips PU8700 Series UV/VIS spectrophotometer in a quartz cell. Chemicals were purchased from Aldrich, Fluka or Avocado at the highest possible grade. All solvents were purchased from Fisons Scientific

Equipment at SLR grade and purified, when required, by literature methods. Anhydrous solvents were obtained as follows: dichloromethane, distilled from calcium hydride under nitrogen; THF, distilled from sodium benzophenone ketal under nitrogen; DMF, distilled from calcium hydride under nitrogen and acetone, distilled from calcium sulfate under nitrogen. Analytical TLC was performed on aluminium backed commercial plates pre-coated with silica gel 60 F_{254} (0.2 mm thick) which were developed using one or more of the following agents: UV fluorescence (254 nm), iodine vapour, ammonium molybdate (2.5% *w/v*), *p*-anisaldehyde (2.5% *w/v*) or sulfuric acid in methanol (5% *w/v*). Merck Kieselgel 60 (230-400 mesh) was used for flash chromatography. Hydrogenolyses were carried out on a Parr hydrogenation apparatus at pressures of 30-55 pounds per square inch (psi). GPC analysis was carried out on a Polymer Laboratories™ modular system using a 3 μm, 15 cm mixed-E column with PL Caliber™ GPC software (version 5.1) with THF eluent at 1 ml min^{-1} and DRI detection. Calibration was with Polymer Labs polystyrene narrow molecular weight standards. All accurate mass spectra and electron ionization mass spectra were recorded on Kratos MS 90 spectrometer with (M^{+}) and major peaks being reported. All mass spectra of dendrimers were measured by matrix assisted laser desorption-ionization mass spectrometry (MALDI-MS) carried out on a Kratos KOMPACT. Irradiation was at 337 nm from a nitrogen laser source. 2,5-Dihydroxybenzoic acid was used as the matrix laid down in solution with the sample. Deprotected dendrimers were deposited from a

water-acetone mixture and protected dendrimers were cast from THF. Rheology studies were carried out on a Rheometrics RDSII instrument. The following abbreviations are used for dendrimers: Ar refers to the core aromatic ring, Ar' refers to first generation aromatic rings, Ar'' refers to second generation aromatic rings *etc*., $PhCH_2$ refers to benzyl groups.

8.2 Experimental for Chapter 2

8.2.1 4-(Dimethylamino)pyridinium *p*-toluenesulfonate 37 (DPTS).[103]

Mono-hydrated *p*-toluenesulfonic acid (2.0 g, 10.5 mmol) was dried by azeotropic distillation in benzene (70 ml) using a Dean-Stark trap. An equimolar solution of 4-(dimethylamino)pyridine (1.3 g, 10.5 mmol) in warm benzene (60 ml) was added with stirring to the anhydrous solution of the acid. The mixture was allowed to cool and the resulting precipitate was collected by filtration. The crude product was recrystallised from dry 1,2-dichloroethane yielding white needle-like crystals (2.56 g, 82%) mp 164-165 °C (SS, lit. 165 °C), $\delta_H(CDCl_3, 250)$ 2.36 (3 H, s, $ArCH_3$), 2.53 (1 H, br m, PyNH), 3.15 (6 H, s, $PyN(CH_3)_2$), 6.73 (2 H, d, *J* 7.4, PyH), 7.13 (2 H, d, *J* 8.0, PhH), 7.78 (2 H, d, *J* 8.0, PhH) and 8.15 (2 H, dd, *J* 5.8 and 7.4, PyH); $\delta_C(CDCl_3, 250)$ 21.2, 40.0, 106.7, 125.8, 128.6, 139.4, 139.7, 142.6 and 157.2.

8.2.2 5-Hydroxyisophthalic acid 2,2,2-trichloroethyl ester 42.

This compound was prepared using an adaptation of a literature method.[11] Concentrated sulfuric acid (1 ml) was added to a slurry of 5-hydroxyisophthalic acid (5.3 g, 29 mmol) in 2,2,2-trichloroethanol (50 ml) and the mixture was heated at 80 °C under nitrogen for 2 days. Dried 3A molecular sieves were added and the mixture allowed to stir for another 8 days at 80 °C. Excess 2,2,2-trichloroethanol was removed *in vacuo*. The

residue was purified by flash chromatography eluting first with dichloromethane, then with dichloromethane-methanol (9:1) to give the product as a white solid (8.2 g, 63%), mp 111-112 °C (SS) (Found: C, 32.4; H, 1.7. Calc. for $C_{12}H_8Cl_6O_5$: C, 32.4; H, 1.8%); υ_{max} /cm^{-1} 2920-2860 (CH), 1740 (C=O) and 1375 (C-Cl); δ_H($CDCl_3$, 250) 4.98 (4 H, s, CH_2), 7.87 (1 H, d, *J* 1.5, ArH) and 8.43 (2 H, t, *J* 1.5, ArH); δ_C($CDCl_3$, 250) 74.6, 94.6, 121.8, 123.9, 130.7, 156.2 and 183.8 (carbonyl).

8.2.3 G_1P-[6]-$CO_2CH_2CCl_3$ 43.

To a slurry of 1,3,5-benzenetricarboxylic acid (144 mg, 0.69 mmol) in dry dichloromethane (8 ml), were added **42** (1.0 g, 2.25 mmol), DCC (464 mg, 2.25 mmol) and DPTS (72 mg, 2.4 mmol). The mixture was stirred vigorously at room temperature under nitrogen for 3 days during which time a heavy white precipitate formed. The reaction was monitored by GPC. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by flash chromatography eluting with dichloromethane to yield the product as a white solid (89%), mp 181-183 °C (SS) (Found: C, 36.3; H, 1.8. Calc. for $C_{45}H_{24}Cl_{18}O_{18}$: C, 36.2; H, 1.6%); υ_{max} /cm^{-1} 2920-2860 (CH), 1740 (C=O) and 1370 (C-Cl); δ_H($CDCl_3$, 250) 5.03 (12 H, s, CH_2), 8.28 (3 H, d, *J* 1.5, Ar'H), 8.85 (6 H, t, *J* 1.5, Ar'H) and 9.33 (3 H, s, ArH); δ_C($CDCl_3$, 250) 74.7, 94.5, 128.2, 129.4, 130.6, 131.1, 136.7, 150.6, 162.5 (carbonyl) and 162.7 (carbonyl); GPC: M_n 1600, PDi 1.006.

8.2.4 G_1P-[6]-CO_2Na 44.

To a stirred solution of **43** (0.9 g, 0.6 mmol) in glacial acetic acid (2 ml) and THF (15 ml) was added zinc dust (1.5 g). The mixture was stirred for three hrs then filtered through a pad of celite. The mixture was evaporated to dryness and freeze-dried to remove traces of acetic acid. Sodium carbonate solution (2 ml, 1 M) was added to the residue and the solution stirred for 1 hr. The solution was evaporated to dryness and freeze-dried to remove traces of water to give a white solid, $\delta_H(D_2O, 250)$ 7.54 (3 H, s, ArH), 7.92 (6 H, d, *J* 1.5, Ar'H) and 8.33 (3 H, t, *J* 1.5, Ar'H).

8.2.5 3,5-Bis(benzyloxy)benzoic acid 47.

This compound was prepared by an adaptation of two literature methods.[79, 104] A slurry of anhydrous potassium carbonate (17 g), 3,5-dihydroxybenzoic acid (10 g, 65 mmol) and benzyl bromide (24 ml, 200 mmol) in DMF (35 ml) was stirred using an overhead stirrer at 60 °C for 14 hrs. The mixture was allowed to cool, then evaporated to dryness under reduced pressure. Water (200 ml) was added to the resulting oil and the slurry extracted with dichloromethane (4 × 100 ml). The combined extracts were evaporated under reduced pressure and the resulting oil was dissolved in ethanol (50 ml) and refluxed with 40% aqueous potassium hydroxide (100 ml) for 14 hrs. The solution was allowed to cool and poured into water (300 ml) and the resulting mixture was adjusted to pH 5 with hydrochloric acid. The resulting precipitate was collected by filtration and dried *in vacuo*. The off-white solid was

recrystallised from acetone to give white crystals (67% yield), mp 210-211 °C (SS) (Found: C, 75.4; H, 5.5. Calc. for $C_{21}H_{18}O_4$: C, 75.4; H, 5.4%); υ_{max} /cm^{-1} 3300-2400, 1695, 1600 and 1500; δ_H([$^2H_6$]-acetone, 250) 5.18 (4 H, s, CH_2), 6.92 (1 H, t, *J* 2.3, ArH), 7.28 (2 H, d, *J* 2.3, ArH) and 7.31-7.53 (10 H, m, $PhCH_2$); δ_C([$^2H_6$]-acetone, 250) 70.7, 107.4, 109.2, 128.4, 128.7, 129.3, 133.5, 137.9, 160.8 and 167.2 (carbonyl).

8.2.6 3,5-Bis(benzyloxy)benzoyl chloride 55.

47 (10 g, 30 mmol) was heated at 80 °C in freshly distilled thionyl chloride (30 ml) for 2 hrs. The excess thionyl chloride was removed by distillation under reduced pressure and the resulting solid was recrystallised from diethyl ether-hexane (1:1). It was found that the crude solid could be used without purification; mp 81-83 °C (SS) (Found: M^+, 352.0869. M^+ requires 352.0866); υ_{max} /cm^{-1} 3100-2700 (CH), 1760 (C=O) and 1500 (C=C ring); δ_H($CDCl_3$, 250) 5.10 (4 H, s, CH_2), 6.99 (1 H, t, *J* 2.3, ArH), 7.37 (2 H, d, *J* 2.3, ArH) and 7.31-7.53 (10 H, m, $PhCH_2$); δ_C($CDCl_3$, 250) 70.4, 109.6, 109.9, 127.6, 127.7, 128.3, 128.7, 135.9, 151.2 and 160.1 (carbonyl).

8.2.7 General procedure for the synthesis of benzyl terminated dendritic esters.[11]

Method A. Reactions were carried out on a 0.01-30 g scale. To a solution of phloroglucinol, hydroquinone, naphthalene-2,6-diol or dendritic ester (1.0 equiv.) in dry acetone (5-400 ml), were added **47** (1.2

equiv. per hydroxyl group), DCC (1.2 equiv. per hydroxyl group) and DPTS (0.2 equiv. per hydroxyl group). The mixture was stirred vigorously at room temperature under nitrogen for 2-7 days during which time a heavy white precipitate formed. The reaction was monitored by GPC. The crude product was filtered and purified as indicated below.

Method B

Reactions were carried out on a 0.5-20 g scale using an adaptation of a literature procedure.[102] To a solution of phloroglucinol, hydroquinone, naphthalene-2,6-diol or dendritic ester (1.0 equiv.) in dry dichloromethane (5-400 ml), were added **55** (1.2 equiv. per hydroxyl group) and 4-(dimethylamino)-pyridine (1 equiv. per hydroxyl group). The mixture was stirred at room temperature under nitrogen for 5 days during which time the reaction was monitored by GPC. The mixture was evaporated to dryness under reduced pressure and purified by flash chromatography.

8.2.8 General procedure for the deprotection of dendritic benzyl terminated polyesters

Hydrogenolyses were carried out in batches of up to 3 g.[105] The dendritic ester was dissolved in dichloromethane (chloroform for hydroquinone core dendrimers) (150 ml) and methanol was added until slight precipitation was seen. The precipitate was redissolved by addition of a small amount of dichloromethane (chloroform). 10% Pd/C (100 mg g^{-1} of

dendrimer) and a few drops of acetic acid were added to the solution which was then shaken under an atmosphere of hydrogen at 30-55 psi for 4-5 hrs. An equivalent volume of methanol was added to the solution which was then shaken under hydrogen (30-55 psi) overnight. Hydrogenolyses were monitored by a combination of GPC and TLC.

8.2.9 G_1P-[6]-OBn 48.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane and precipitated from diethyl ether to yield a white solid. The solid was collected by filtration and washed with diethyl ether (25%).

Method B. The crude product was purified by flash chromatography eluting with dichloromethane and collected as a white solid (100%), mp 200 °C (Net) (Found: C, 77.1; H, 5.1. Calc. for $C_{69}H_{54}O_{12}$: C, 77.1; H, 5.1%); υ_{max}/cm^{-1} 3090-2930 (CH), 1740 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)/nm$ 229, 260, 311 and 323; $\delta_H(CDCl_3, 400)$ 5.10 (12 H, s, CH_2), 6.88 (3 H, t, *J* 2.3, Ar'H), 7.13 (3 H, s, ArH), 7.3-7.4 (30 H, m, $PhCH_2$), 7.43 (6 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3, 400)$ 70.3, 108.1, 108.9, 113.2, 127.5, 128.1, 128.6, 130.7, 136.2, 151.4, 159.8 and 164.0; GPC: M_n 1500, PDi 1.004; ***m/z*** 1097 ($M+Na^+$ requires 1098).

8.2.10 G_1P-[6]-OH 49.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (45:55) and collected as a white solid (93%), mp 250 °C (Net) (Found: C, 60.8; H, 3.4. Calc. for $C_{27}H_{18}O_{12}$: C, 60.7; H, 3.4%); υ_{max}/cm^{-1} 3355br (OH) and 1720 (C=O); λ_{max} (MeOH)/nm 210, 260 and 317; $\delta_H([^2H_6]$-acetone, 400) 6.68 (3 H, t, *J* 2.3, Ar'H), 7.18 (6 H, d, *J* 2.3, Ar'H), 7.26 (3 H, s, ArH) and 8.80 (6 H, br s, OH); $\delta_C([^2H_6]$-acetone, 400) 108.9, 109.2, 114.6, 131.8, 152.7, 159.7 and 164.9 (carbonyl); GPC: M_n 1200, PDi 1.005; *m/z* 556 ($M+Na^+$ requires 557).

8.2.11 G_2P-[12]-OBn 50.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane (74%), mp 55 °C (Net) (Found: C, 75.4; H, 4.7. Calc. for $C_{153}H_{114}O_{30}$: C, 75.5; H, 4.7%); υ_{max}/cm^{-1} 3070-2930 (CH), 1740 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)$/nm 231, 257 and 313; $\delta_H(CDCl_3$, 400) 5.12 (24 H, s, CH_2), 6.91 (6 H, t, *J* 2.3, Ar"H), 7.24 (3 H, s, ArH), 7.3-7.45 (60 H, m, $PhCH_2$), 7.48 (12 H, d, *J* 2.3, Ar"H), 7.53 (3 H, t, *J* 2.3, Ar'H), 8.01 (6 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3$, 400) 70.2, 108.2, 108.9, 113.2, 121.0, 121.4, 127.5, 128.0, 128.5, 130.4, 131.0, 136.1, 151.1, 151.3, 159.8, 162.5

(carbonyl) and 164.1 (carbonyl); GPC: M_n 3200, PDi 1.003; *m/z* 2455 ($M+Na^+$ requires 2456).

8.2.12 G_2P-[12]-OH 51.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (30:70) and collected as a white solid (92%), mp 206 °C (Net) (Found: C, 61.1; H, 3.0. Calc. for $C_{69}H_{42}O_{30}$: C, 61.3; H, 3.1%); υ_{max}/cm^{-1} 3370br (OH) and 1740 (C=O); λ_{max}(MeOH)/nm 208, 254 and 317; $\delta_H([^2H_6]$-acetone, 400) 6.69 (6 H, t, *J* 2.3, Ar"H), 7.20 (12 H, d, *J* 2.3, Ar"H), 7.51 (3 H, s, ArH), 7.69 (3 H, t, *J* 2.3, Ar'H), 8.06 (6 H, d, *J* 2.3, Ar'H) and 8.78 (12 H, br s, OH); $\delta_C([^2H_6]$-acetone, 400) 108.9, 109.3, 114.9, 121.9, 122.7, 131.6, 132.1, 152.5, 152.7, 159.6, 163.7 (carbonyl) and 165.1 (carbonyl); GPC: M_n 2600, PDi 1.014; *m/z* 1374 ($M+Na^+$ requires 1374).

8.2.13 G_3P-[24]-OBn 52.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane (94%), mp 66 °C (Net) (Found: C, 74.7; H, 4.6. Calc. for $C_{321}H_{234}O_{66}$: C, 74.9; H, 4.6%); υ_{max}/cm^{-1} 3090-2870 (CH), 1740 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)$/nm 235, 254infl, and 312; $\delta_H(CDCl_3$, 400)

5.12 (48 H, s, CH_2), 6.92 (12 H, t, *J* 2.3, Ar'''H), 7.29 (3 H, s, ArH), 7.3-7.5 (120 H, m, $PhCH_2$), 7.49 (24 H, d, *J* 2.3, Ar'''H), 7.55 (6 H, t, *J* 2.3, Ar''H), 7.60 (3 H, t, *J* 2.3, Ar'H), 8.06 (12 H, d, *J* 2.3, Ar''H) and 8.09 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 70.2, 108.2, 108.8, 113.3, 121.0, 121.1, 121.3, 121.4, 127.4, 128.0, 128.5, 130.4, 130.8, 131.2, 136.1, 151.05, 151.1, 151.3, 159.8, 162.3 (carbonyl), 162.7 (carbonyl) and 164.0 (carbonyl); GPC: M_n 5800, PDi 1.000; *m/z* 5168 ($M+Na^+$ requires 5170).

8.2.14 G_3P-[24]-OH 53.

The crude product was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The solid was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone 30:70 and collected as a tan solid (92%) which decomposed when heated (Found: C, 61.5; H, 3.0. Calc. for $C_{153}H_{90}O_{66}$: C, 61.6; H, 3.0%); λ_{max} (MeOH)/nm 207, 213infl, 250infl and 315; υ_{max} /cm^{-1} 3600-2900br (OH), 1740 (C=O) and 1500 (C=C ring); δ_H([$^2H_6$]-acetone, 400) 6.70 (12 H, t, *J* 2.3, Ar'''H), 7.21 (24 H, d, *J* 2.3, Ar'''H), 7.40 (3 H, s, ArH), 7.70 (6 H, t, *J* 2.3, Ar''H), 7.90 (3 H, t, *J* 2.3, Ar'H), 8.09 (12 H, d, *J* 2.3, Ar''H), 8.21 (6 H, d, *J* 2.3, Ar'H) and 8.90 (24 H, br s, OH); δ_C([$^2H_6$]-acetone, 400) 109.0, 109.2, 121.9, 122.1, 122.5, 122.6, 131.5, 132.0, 132.2, 152.4 (2 C), 152.7, 159.6, 163.5 (carbonyl), 163.8 (carbonyl) and 165.1 (carbonyl); GPC: M_n 4000, PDi 1.016; *m/z* 3007 ($M+Na^+$ requires 3007).

8.2.15 G_1H-[4]-OBn 57.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane as eluent. Addition of diethyl ether to the filtrate yielded transparent needle-like crystals on standing. The crystals were collected by filtration and washed with diethyl ether (8%).

Method B. The crude product was purified by flash chromatography eluting with chloroform to give the product as a white solid (100%), mp 113 °C (Net) (Found: C, 77.3; H, 5.2. Calc. for $C_{48}H_{38}O_8$: C, 77.6; H, 5.2%); υ_{max}/cm^{-1} 3040-2870 (CH), 1740 (C=O) and 1505 (C=C ring); $\lambda_{max}(CH_2Cl_2)/nm$ 229, 260, 311 and 323; $\delta_H(CDCl_3, 400)$ 5.12 (8 H, s, CH_2), 6.89 (2 H, t, *J* 2.3, Ar'H), 7.27 (4 H, s, ArH), 7.3-7.4 (20 H, m, $PhCH_2$) and 7.46 (4 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3, 400)$ 70.4, 108.0, 109.1, 122.5, 127.5, 128.0, 128.5, 131.3, 136.4, 148.4, 159.9 and 164.6 (carbonyl); GPC: M_n 1000, PDi 1.005; *m/z* 765 ($M+Na^+$ requires 765).

8.2.16 G_1H-[4]-OH 58.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (60:40) and collected as a white solid (95%), mp 278 °C (Net) (Found: C, 66.6; H, 3.7. Calc. for $C_{20}H_{14}O_8$: C, 66.8; H, 3.7%); υ_{max}/cm^{-1} 3415br (OH), 1720 (C=O) and 1505 (C=C); λ_{max}

(MeOH)/nm 208, 260 and 317; $\delta_H(CD_3OD, 400)$ 6.60 (2 H, t, *J* 2.3, Ar'H), 7.13 (4 H, d, *J* 2.3, Ar'H) and 7.32 (4 H, s, ArH); $\delta_C(CD_3OD, 400)$ 109.0, 109.2, 123.8, 132.2, 149.9, 160.0 and 166.6 (carbonyl); GPC: M_n 900, PDi 1.005.

8.2.17 Fragmented G_1H-[4]-OH 59.

This material was isolated as a by-product from the extended hydrogenolysis of G_1H-[4]-OBn, υ_{max} /cm^{-1} 3800-2700br (OH), 1700 (C=O) and 1490 (C=C ring); $\delta_H([^2H_6]$-acetone, 250) 6.65 (1 H, t, *J* 2.1, Ar'H), 6.88 (2 H, m, ArH), 7.07 (2 H, m, ArH), 7.14 (2 H, d, *J* 2.1, Ar'H), 8.43 (1 H, s, ArOH) and 8.68 (2 H, s, Ar'OH); $\delta_C([^2H_6]$-acetone, 250) 108.4, 109.0, 116.4, 123.4, 132.6, 144.7, 156.0, 159.6 and 165.7 (carbonyl).

8.2.18 G_2H-[8]-OBn 60.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane as eluent; addition of diethyl ether to the filtrate yielded a white solid which was collected by filtration and washed with diethyl ether (85%).

Method B. The crude product was purified by eluting through a short pad of silica using dichloromethane as eluent. Precipitation from diethyl ether yielded a white solid (86%), mp 181 °C (Net) (Found: C, 75.8; H, 4.8. Calc. for $C_{104}H_{78}O_{20}$: C, 75.8; H, 4.8%); υ_{max}/cm^{-1} 3040-2870 (CH), 1745

(C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)$/nm 230, 258 and 312; $\delta_H(CDCl_3, 400)$ 5.12 (16 H, s, CH_2), 6.90 (4 H, t, *J* 2.3, Ar''H), 7.31 (4 H, s, ArH), 7.30-7.45 (40 H, m, $PhCH_2$), 7.46 (8 H, d, *J* 2.3, Ar''H), 7.49 (2 H, t, *J* 2.3, Ar'H) and 8.00 (4 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3, 400)$ 70.3, 108.2, 108.9, 121.0, 121.1, 122.5, 127.5, 128.1, 128.5, 130.5, 131.5, 136.2, 148.2, 151.3, 159.9, 163.2 (carbonyl) and 164.2 (carbonyl); GPC: M_n 2400, PDi 1.008; *m/z* 1670 ($M+Na^+$ requires 1670).

8.2.19 G_2H-[8]-OH 61.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (50:50) and collected as a white solid (89%), mp 210 °C (Net) (Found: C, 62.3; H, 3.4. Calc. for $C_{48}H_{30}O_{20}$: C, 62.2; H, 3.3%); υ_{max}/cm^{-1} 3405br (OH), 1720 (C=O) and 1500 (C=C ring); λ_{max}(MeOH)/nm 205, 258 and 317; $\delta_H([^2H_6]$-acetone, 400) 6.70 (4 H, t, *J* 2.3, Ar''H), 7.20 (8 H, d, *J* 2.3, Ar''H), 7.50 (4 H, s, ArH), 7.68 (2 H, t, *J* 2.3, Ar'H), 8.04 (4 H, d, *J* 2.3, Ar'H) and 8.88 (8 H, s, OH); $\delta_C([^2H_6]$-acetone, 400) 109.0, 109.2, 121.8, 122.5, 123.7, 131.6, 132.5, 149.5, 152.7, 159.7, 164.1 (carbonyl) and 165.1 (carbonyl); GPC: M_n 2100, PDi 1.006; *m/z* 949 ($M+Na^+$ requires 949).

8.2.20 G_3H-[16]-OBn 62.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane as eluent and precipitated from diethyl ether to yield a white solid. The solid was collected by filtration and washed with diethyl ether (88%), T_g 71 °C (Net) (Found: C, 75.1;H, 4.6. Calc. for $C_{216}H_{158}O_{44}$: C, 75.0; H, 4.6); υ_{max}/cm^{-1} 3030-2930 (CH), 1740 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)/nm$ 235, 254infl and 312; $\delta_H(CDCl_3, 400)$ 5.12 (32 H, s, CH_2), 6.91 (8 H, t, *J* 2.3, Ar'''H), 7.3-7.45 (84 H, m, $PhCH_2$ + ArH), 7.47 (16 H, d, *J* 2.3, Ar'''H), 7.53 (4 H, t, *J* 2.3, Ar''H), 7.56 (2 H, t, *J* 2.3, Ar'H), 8.03 (8 H, d, *J* 2.3, Ar''H) and 8.05 (4 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3, 400)$ 70.3, 108.2, 108.9, 121.1, 121.5, 122.5, 127.5, 128.1, 128.5, 130.8, 130.4, 131.7, 136.1, 148.1, 151.1, 151.4, 159.8, 162.8 (carbonyl), 163.0 (carbonyl) and 164.1 (carbonyl); GPC: M_n 4700, PDi 1.000; *m/z* 3478 ($M+Na^+$ requires 3478).

8.2.21 G_3H-[16]-OH 63.

The crude product was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The solid was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone 30:70 and collected as a tan solid (89%), mp 206 °C (Net) (Found: C, 62.1; H, 3.1. Calc. for $C_{104}H_{62}O_{44}$: C, 62.0; H, 3.1); υ_{max} $/cm^{-1}$ 3700-2700br (OH), 1730 (C=O) and 1505 (C=C ring); λ_{max}

(MeOH)/nm 206, 214infl, 254 and 316; δ_H([$^2H_6$]-acetone, 400) 6.70 (8 H, t, *J* 2.3, Ar'''H), 7.21 (16 H, d, *J* 2.3, Ar'''H), 7.49 (4 H, s, ArH), 7.70 (4 H, t, *J* 2.3, Ar''H), 7.89 (2 H, t, *J* 2.3, Ar'H), 8.09 (8 H, d, *J* 2.3, Ar''H), 8.19 (4 H, d, *J* 2.3, Ar'H) and 8.79 (16 H, br s, OH); δ_C([$^2H_6$]-acetone, 400) 109.0, 109.3, 121.9, 122.1, 122.4, 122.7, 123.7, 131.6, 132.0, 132.6, 149.5, 152.5, 152.7, 159.6, 163.8 (carbonyl), 164.0 (carbonyl) and 165.1 (carbonyl); GPC: M_n 3500, PDi 1.020; *m/z* 2037 ($M+Na^+$ requires 2037).

8.2.22 G_4H-[32]-OBn 64.

Method A. The crude product was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane (86%), mp 70 °C (Net) (Found: C, 74.7; H, 4.5. Calc. for $C_{440}H_{318}O_{92}$: C, 74.7; H, 4.5%); υ_{max} /cm^{-1} 3200-2700 (CH), 1745 (C=O) and 1500 (C=C ring); λ_{max} (CH_2Cl_2)/nm 231, 256infl and 312; δ_H($CDCl_3$, 400) 5.14 (64 H, s, CH_2), 6.95 (16 H, t, *J* 2.3, Ar''''H), 7.3-7.5 (164 H, m, $PhCH_2$ + ArH), 7.52 (32 H, d, *J* 2.3, Ar''''H), 7.59 (8 H, t, *J* 2.3, Ar'''H), 7.64 (2 H, t, *J* 2.3, Ar'H), 7.66 (4 H, t, *J* 2.3, Ar''H), 8.09 (16 H, d, *J* 2.3, Ar'''H), 8.13 (4 H, d, *J* 2.3, Ar'H) and 8.15 (8 H, d, *J* 2.3, Ar''H); δ_C($CDCl_3$, 400) 70.1, 108.1, 108.8, 121.0 (3 C), 121.4 (3 C), 122.4, 127.4, 128.0, 128.4, 130.3, 130.7, 131.0, 131.6, 136.1, 148.1, 151.0, 151.1, 151.3, 159.8, 162.6 (carbonyl), 162.6 (carbonyl), 162.9 (carbonyl) and 164.0 (carbonyl); GPC: M_n 7800, PDi 1.000.

8.2.23 G_4H-[32]-OH 65.

The crude product was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The solid was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (30:70) and collected as a tan solid (92%), T_g 168 °C (Net) (Found: C, 62.0; H, 2.9. Calc. for $C_{216}H_{126}O_{92}$: C, 61.9; H, 3.0%); υ_{max} /cm^{-1} 3700-2900br (OH), 1730 (C=O) and 1505 (C=C ring); λ_{max} (MeOH)/nm 209, 250infl and 314; δ_H([$^2H_6$]-acetone, 400) 6.70 (16 H, t, *J* 2.3, Ar''''H), 7.21 (32 H, d, *J* 2.3, Ar''''H), 7.47 (4 H, s, ArH), 7.70 (8 H, t, *J* 2.3, Ar'''H), 7.89 (2 H, t, *J* 2.3, Ar'H), 7.90 (4 H, t, *J* 2.3, Ar''H), 8.09 (16 H, d, *J* 2.3, Ar'''H), 8.20 (4 H, d, *J* 2.3, Ar'H), 8.24 (8 H, d, *J* 2.3, Ar''H) and 8.86 (32 H, br s, OH); δ_C([$^2H_6$]-acetone, 400) 109.0, 109.2, 121.8 (2 C), 122.1, 122.6 (3 C), 123.6, 131.5, 131.9, 132.1, 132.5, 149.4, 152.4 (2 C), 152.6, 159.5, 163.7 (carbonyl), 163.7 (carbonyl), 163.9 (carbonyl) and 165.0 (carbonyl); GPC: M_n 2600, PDi 1.011.

8.2.24 G_1N-[4]-OBn 67.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane. The residue was precipitated with diethyl ether to give a white solid which was collected by filtration and washed with diethyl ether (30%).

Method B. The crude product was purified by flash chromatography eluting with chloroform to give the product as a clear solid (100%), mp 168 °C (Net) (Found: C, 78.6; H, 5.2. Calc. for $C_{52}H_{40}O_8$: C, 78.8; H, 5.1%); υ_{max}/cm^{-1} 3030-2920 (CH), 1730 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)/nm$ 230, 259, 303 and 324; $\delta_H(CDCl_3, 400)$ 5.13 (8 H, s, CH_2), 6.90 (2 H, t, *J* 2.3, Ar'H), 7.3-7.5 (22 H, m, $PhCH_2$ + ArH), 7.51 (4 H, d, *J* 2.3, Ar'H), 7.72 (2 H, d, *J* 2.3, ArH) and 7.89 (2 H, d, *J* 8.8, ArH); $\delta_C(CDCl_3, 400)$ 70.3, 107.8, 108.9, 118.6, 121.9, 127.5, 128.1, 128.5, 129.1, 131.2, 131.7, 136.2, 148.5, 159.8 and 164.9 (carbonyl); GPC: M_n 1200, PDi 1.006; *m/z* 816 ($M+Na^+$ requires 815).

8.2.25 G_1N-[4]-OH 68.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (60:40) and collected as a white solid (95%), mp 264 °C (Net) (Found: C, 66.6; H, 3.7. Calc. for $C_{24}H_{16}O_8$: C, 66.7; H, 3.7%); υ_{max}/cm^{-1} 3365br (OH), 1720 (C=O) and 1500 (C=C ring); λ_{max}(MeOH)/nm 223, 260 and 312; $\delta_H([^2H_6]$-acetone, 400) 6.70 (2 H, t, *J* 2.3, Ar'H), 7.22 (4 H, d, *J* 2.3, Ar'H), 7.50 (2 H, dd, *J* 2.3 and 8.8, ArH), 7.85 (2 H, d, *J* 2.3, ArH), 8.04 (2 H, d, *J* 8.8, ArH) and 8.90 (4 H, br s, OH); $\delta_C([^2H_6]$-acetone, 400) 108.7, 109.2, 119.6, 123.2, 129.8, 132.2, 132.7, 149.7, 159.7 and 165.6 (carbonyl); GPC: M_n 900, PDi 1.005.

8.2.26 G_2N-[8]-OBn 69.

Method A. The reaction mixture was evaporated to dryness under reduced pressure and the residue was dissolved in a small quantity of dichloromethane. The solution was eluted through a short pad of silica using dichloromethane as eluent and precipitated from diethyl ether to yield a white solid. The solid was collected by filtration and washed with diethyl ether (92%).

Method B. The crude product was purified by elution through a short pad of silica using dichloromethane as eluent and subsequent precipitation from diethyl ether to yield a white solid (80%), mp 128 °C (Net) (Found: C, 76.4; H, 4.8. Calc. for $C_{108}H_{80}O_{20}$: C, 76.4; H, 4.8%); υ_{max}/cm^{-1} 3090-2870 (CH), 1740 (C=O) and 1500 (C=C ring); $\lambda_{max}(CH_2Cl_2)/nm$ 229, 259, 309 and 323; $\delta_H(CDCl_3, 400)$ 5.13 (16 H, s, CH_2), 6.93 (4 H, t, *J* 2.3, Ar''H), 7.3-7.5 (42 H, m, $PhCH_2$ + ArH), 7.50 (8 H, d, *J* 2.3, Ar''H), 7.54 (2 H, t, *J* 2.3, Ar'H), 7.77 (2 H, d, *J* 2.3, ArH), 7.93 (2 H, d, *J* 8.8, ArH) and 8.08 (4 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3, 400)$ 70.2, 108.2, 108.9, 118.6, 121.0, 121.1, 121.8, 127.4, 128.0, 128.5, 129.2, 130.5, 131.6, 131.8, 136.1, 148.3, 151.3, 159.8, 163.5 (carbonyl) and 164.1 (carbonyl); GPC: M_n 2600, PDi 1.003; *m/z* 1720 ($M+Na^+$ requires 1720).

8.2.27 G_2N-[8]-OH 70.

The reaction mixture was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The residue was purified by flash chromatography (pre-loading recommended) eluting with

dichloromethane-acetone (30:70) and collected as a white solid (89%), mp 230 °C (Net) (Found: C, 63.8; H, 3.2. Calc. for $C_{52}H_{32}O_{20}$: C, 63.9; H, 3.3%); υ_{max}/cm^{-1} 3380br (OH) and 1720 (C=O); λ_{max}(MeOH)/nm 220, 257 and 315; $\delta_H([^2H_6]$-acetone, 400) 6.70 (4 H, t, *J* 2.3, Ar"H), 7.21 (8 H, s, Ar"H), 7.62 (2 H, dd, *J* 2.3 and 8.8, ArH), 7.70 (2 H, t, Ar'H), 7.97 (2 H, d, *J* 2.3, ArH), 8.09 (2 H, d, *J* 8.8, ArH), 8.09 (4 H, d, *J* 2.3, Ar'H) and 8.83 (8 H, br s, OH); $\delta_C([^2H_6]$-acetone, 400) 109.0, 109.3, 119.3, 121.8, 122.5, 123.2, 130.0, 131.7, 132.6, 132.8, 149.6, 152.8, 159.7, 164.3 (carbonyl) and 165.1 (carbonyl); GPC: M_n 1900, PDi 1.003; *m/z* 999 ($M+Na^+$ requires 999).

8.2.28 G_3N-[16]-OBn 71.

Method A. The crude product was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane (96%), mp 122 °C (Net) (Found: C, 75.4; H, 4.6. Calc. for $C_{220}H_{160}O_{44}$: C, 75.3; H, 4.6%); λ_{max} (CH_2Cl_2)/nm 235, 255infl and 310; υ_{max} /cm^{-1} 3090-2870 (CH), 1740 (C=O) and 1500 (C=C ring); $\delta_H(CDCl_3$, 400) 5.13 (32 H, s, CH_2), 6.93 (8 H, t, *J* 2.3, Ar'"H), 7.3-7.5 (82 H, m, $PhCH_2$ + ArH), 7.49 (16 H, d, *J* 2.3, Ar'"H), 7.55 (4 H, t, *J* 2.3, Ar"H), 7.60 (2 H, t, *J* 2.3, Ar'H), 7.79 (2 H, d, *J* 2.3, ArH), 7.93 (2 H, d, *J* 8.8, ArH), 8.06 (8 H, d, *J* 2.3, Ar"H) and 8.12 (4 H, d, *J* 2.3, Ar'H); $\delta_C(CDCl_3$, 400) 70.2, 108.2, 108.9, 118.6, 121.0 (2 C), 121.4 (2 C), 121.7, 127.4, 128.0, 128.5, 129.2 (2 C), 130.4, 130.8, 131.8, 136.1, 148.2, 151.1, 151.4, 159.8, 162.8

(carbonyl), 163.2 (carbonyl) and 164.1 (carbonyl); GPC: M_n 4300, PDi 1.003; *m/z* 3529 ($M+Na^+$ requires 3529).

8.2.29 G_3N-[16]-OH 72.

The crude product was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The solid was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone (30:70) and collected as a clear solid (96%), mp 184 °C (Net) (Found: C, 62.8;H, 3.2. Calc. for $C_{108}H_{64}O_{44}$: C, 62.8; H, 3.1%); υ_{max} /cm^{-1} 3000-3700br (OH), 1740 (C=O) and 1505 (C=C ring); λ_{max} (MeOH)/nm 210, 217, 250infl and 310; δ_H([$^2H_6$]-acetone, 400) 6.70 (8 H, t, *J* 2.3, Ar'''H), 7.21 (16 H, d, *J* 2.3, Ar'''H), 7.61 (2 H, dd, *J* 2.3 and 8.8, ArH), 7.70 (4 H, t, *J* 2.3, Ar''H), 7.91 (2 H, t, *J* 2.3, Ar'H), 7.96 (2 H, d, *J* 2.3, ArH), 8.07 (2 H, d, *J* 8.8, ArH), 8.10 (8 H, d, *J* 2.3, Ar''H), 8.23 (4 H, d, *J* 2.3, Ar'H) and 8.81 (16 H, br s, OH); δ_C([$^2H_6$]-acetone, 400) 109.0, 109.2, 109.3, 119.6, 121.9, 122.1, 122.7, 123.1, 130.0, 132.0, 131.6, 132.7, 132.8, 149.6, 152.5, 152.7, 159.6, 163.8 (carbonyl), 164.1 (carbonyl) and 165.0 (carbonyl); GPC: M_n 3200, PDi 1.009; *m/z* 2086 ($M+Na^+$ requires 2087).

8.2.30 G_4N-[32]-OBn 73.

Method A. The crude product was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane (95%), mp 53 °C (Net) (Found: C, 74.9; H, 4.5. Calc. for

$C_{444}H_{320}O_{92}$: C, 74.8; H 4.5%); υ_{max} /cm^{-1} 3010-2880 (CH), 1740 (C=O) and 1500 (C=C ring); λ_{max} (CH_2Cl_2)/nm 230, 256infl and 309; δ_H($CDCl_3$, 400) 5.13 (64 H, s, CH_2), 6.93 (16 H, t, *J* 2.3, Ar''''H), 7.3-7.5 (162 H, m, $PhCH_2$ + ArH), 7.51 (32 H, d, *J* 2.3, Ar'''H), 7.57 (8 H, t, *J* 2.3, Ar'''H), 7.64 (6 H, t, *J* 2.3, Ar'H + Ar''H), 7.79 (2 H, br m, ArH), 7.93 (2 H, d, *J* 8.8, ArH), 8.08 (16 H, d, *J* 2.3, Ar'''H), 8.14 (8 H, d, *J* 2.3, Ar''H) and 8.15 (4 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 70.2, 108.2, 108.9, 118.5, 121.0 (2 C), 121.1 (2 C), 121.4 (2 C), 121.7, 127.4, 128.0, 128.5, 129.2, 130.4, 130.7, 131.0, 136.1, 131.7, 131.8, 148.2, 151.0, 151.1, 151.3, 159.8, 162.6 (carbonyl), 162.7 (carbonyl), 163.2 (carbonyl) and 164.0 (carbonyl); GPC: M_n 7800, PDi 1.000.

8.2.31 G_4N-[32]-OH 74.

The crude product was evaporated to dryness under reduced pressure and freeze-dried to remove traces of acetic acid. The solid was purified by flash chromatography (pre-loading recommended) eluting with dichloromethane-acetone 20:80 and collected as a clear solid (87%) which decomposed when heated (Found: C, 62.2; H, 3.1. Calc. for $C_{220}H_{128}O_{92}$: C, 62.3; H, 3.0%); υ_{max} /cm^{-1} 3700-2900br (OH), 1740 (C=O) and 1510 (C=C ring); λ_{max} (MeOH)/nm 206, 252infl and 313; δ_H([$^2H_6$]-acetone, 400) 6.69 (16 H, t, *J* 2.3, Ar''''H), 7.20 (32 H, d, *J* 2.3, Ar''''H), 7.60 (2 H, dd, *J* 2.3 and 8.8, ArH), 7.69 (8 H, t, *J* 2.3, Ar'''H), 7.91 (6 H, t, *J* 2.3, Ar'H and Ar''H), 7.95 (2 H, br m, ArH), 8.05 (2 H, d, *J* 8.8, ArH), 8.08 (16 H, d, *J* 2.3, Ar'''H), 8.22 (4 H, d, *J* 2.3, Ar'H), 8.24 (8 H, d, *J* 2.3, Ar''H) and 8.80 (32 H,

br s, OH); δ_C([$^2H_6$]-acetone, 400) 109.0, 109.3, 119.6, 121.7, 121.9, 122.2 (2 C), 122.7, 123.1, 130.0, 131.6, 132.0, 132.2, 132.7, 132.8, 149.6, 152.5, 152.6, 152.7, 159.6, 163.7 (carbonyl), 163.8 (carbonyl), 164.1 (carbonyl) and 165.0 (carbonyl); GPC: M_n 2600, PDi 1.088.

8.2.32 Incomplete G_5N-[64]-OBn.

Method A. The crude product was evaporated to dryness under reduced pressure and purified by flash chromatography (pre-loading recommended) eluting with diethyl ether changing slowly to dichloromethane to give a clear solid, δ_C($CDCl_3$, 250) 4.90-5.15 (br m, CH_2), 6.80-6.90 (br m), 7.20-7.60 (br m), 7.85-8.10 (br m); GPC: M_n 11200, PDi 1.164.

8.3 Experimental for Chapter 3

8.3.1 Poly(3,5-dihydroxybenzoic acid) 80 method 1.

To a solution of 3,5-dihydroxybenzoic acid (1.5 g, 9.7 mmol) and DPTS (0.54 g, 1.9 mmol) in dry acetone (4 ml), was added DCC (2.41 g, 13.6 mmol). The solution was allowed to stir at room temperature under nitrogen overnight, during which time a heavy white precipitate formed. The mixture was filtered and concentrated *in vacuo*. The polymer was precipitated from dichloromethane, collected by filtration and dried in a vacuum desiccator to give an off-white solid (0.25 g), $\delta_H([^2H_6]$-acetone, 250) 0.82-2.38 (m, CyH), 6.65-6.78 (m, ArH), 6.70-7.00 (m, ArH), 7.08-7.20 (m, ArH), 7.51-7.65 (m, ArH), 7.95-8.23 (m, ArH) and 8.75-8.95 (m, ArOH); $\delta_C(CD_3OD$, 250) 19.6, 24.3, 32.9, 38.3, 51.5, 67.9, 106.5, 107.1, 107.4, 107.6, 112.8-114.5, 121.1-123.0, 125.1, 128.1, 130.3, 130.6, 131.2, 131.5, 138.0-141.5, 150.2-151.8, 156.6-158.4, 163.5-165.3, 166.0 and 167.0; GPC: M_n 1800, M_w 1900, PDi 1.093.

8.3.2 Poly(3,5-dihydroxybenzoic acid) 80 method 2 with stepwise addition of monomer.

A solution of DCC (1.6 g, 7.8 mmol), phloroglucinol (91 mg, 39 mg, 18 mg, 8.8 mg, 4.3 mg and 0 mg (equiv. proportion to G_2P-[12]-OH, G_3P-[24]-OH, G_4P-[48]-OH, G_5P-[96]-OH, G_6P-[192]-OH dendrimers and pure hyperbranched respectively) and DPTS (40 mg, 140 μmol) were stirred in dry acetone (3 ml) under nitrogen. A solution of 3,5-dihydroxybenzoic

acid (1.0 g, 6.5 mmol) in dry acetone (4 ml) was prepared and 0.25 ml of this solution added every 15 mins. The solution was then allowed to stir overnight during which time a heavy white precipitate formed. The mixture was filtered and concentrated *in vacuo*. The polymer was precipitated from dichloromethane, collected by filtration and dried in a vacuum desiccator to give an off-white solid (0.15 - 0.40 g).

8.3.3 Poly(3,5-dihydroxybenzoic acid) 80 method 1 with syringe pump addition of monomer.

A solution of DCC (1.6 g, 7.8 mmol), phloroglucinol (91 mg, 39 mg, 18 mg, 8.8 mg, 4.3 mg and 0 mg (equiv. proportion to G_2P-[12]-OH, G_3P-[24]-OH, G_4P-[48]-OH, G_5P-[96]-OH, G_6P-[192]-OH dendrimers and pure hyperbranched respectively) and DPTS (40 mg, 140 μmol) were stirred in dry acetone (3 ml) under nitrogen. A solution of 3,5-dihydroxybenzoic acid (1.0 g, 6.5 mmol) in dry acetone (4 ml) was added slowly, using a syringe pump, over a period of 9 hrs. The solution was then allowed to stir overnight during which time a heavy white precipitate formed. The mixture was filtered and concentrated *in vacuo*. The polymer was precipitated from dichloromethane, collected by filtration and dried in a vacuum desiccator to give an off-white solid (0.15 - 0.40 g).

8.3.4 Trimethylsilyl-3,5-bis(trimethylsiloxy)benzoate 75.[79]

To a slurry of 3,5-dihydroxybenzoic acid (2.30 g, 14.9 mmol) in dichloromethane (6 ml) was added 1,1,1,3,3,3-hexamethyldisilazane (4.81

g, 29.8 mmol). The mixture was stirred at 45 °C under nitrogen for 24 hrs during which the slurry turned into a light brown solution. The volatile by-products were removed *in vacuo* and the residue distilled (140 °C, 0.1 mmHg) to give a pale yellow oil (4.87 g, 88%) $\delta_H(CDCl_3)$ 0.24 (18 H, s, $ArOSi(CH_3)_3$), 0.34 (9 H, s, $CO_2Si(CH_3)_3$), 6.51 (1 H, t, *J* 2.3, ArH) and 7.12 (2 H, d, *J* 2.3, ArH); $\delta_C(CDCl_3)$ -0.5, -0.1, 114.8, 116.5, 133.1, 155.8 and 165.9 (carbonyl).

8.3.5 3,5-Bis(trimethylsiloxy)benzoyl chloride 76.[79]

To a solution of **75** (10.5 g, 28.3 mmol) and triethylamine hydrochloride (72 mg, 0.53 mmol) in dichloromethane (15 ml) was added thionyl chloride (2.48 ml, 34.0 mmol). The mixture was stirred at room temperature for a few mins and then refluxed for 3 hrs. The solution was then concentrated *in vacuo* to give a brown oil (9.0 g) $\delta_H(CDCl_3)$ 0.27 (18 H, s, $ArOSi(CH_3)_3$), 6.64 (1 H, t, *J* 2.3, ArH) and 7.19 (2 H, d, *J* 2.3, ArH); $\delta_C(CDCl_3)$ -0.1, 116.0, 118.9, 134.7, 156.3 and 167.2 (carbonyl).

8.3.6 Poly(3,5-dihydroxybenzoic acid) 80 method 2.

76 (17.2 g, 65.8 mmol) was heated to 140 °C with stirring for 1 hr during which the polymer set to a hard mass. The flask was allowed to cool, DMSO (100 ml) was added and the mixture heated to 100 °C for a further 30 mins during which time the solid dissolved. The mixture was allowed to cool to room temperature and added dropwise to a water (2 l) to give the polymer as a brown precipitate. The polymer was recovered as a

brown gum which could be scooped out with a spatula. The brown gum was dissolved in acetone and dried over anhydrous magnesium sulfate. The solution was concentrated *in vacuo* to give a brown solid. Slight traces of dimethylsulfide were removed by grinding the polymer in dichloromethane (4.4 g), $\delta_H([^2H_6]$-acetone, 250) 6.50-6.60 (m, ArH), 6.90-7.28 (m, ArH), 7.40-7.63 (m, ArH), 7.70-8.24 (m, ArH) and 8.75-8.95 (m, ArOH); $\delta_C(CD_3OD$, 250) 109.0-110.0, 114.0-117.0, 119.5-123.5, 124.4, 130.3-134.7, 150.0-153.7, 156.9, 158.0-160.2, 164.0-167.0, 167.7 and 168.7; GPC: M_n 800, M_w 1500, PDi 1.82.

8.3.7 Poly(3,5-dihydroxybenzoic acid) 80 method 3.

A nitrobenzene (50 ml) solution of **76** (17.2 g, 65.8 mmol) was heated to 160 °C for 1 hr during which time the polymer set to a hard mass. The flask was allowed to cool, DMSO (100 ml) was added and the mixture heated to 100 °C for a further 30 mins. The solution was allowed to cool and the mixture poured with stirring into a beaker containing dichloromethane (200 ml) and water (200 ml). The polymer was recovered as a brown gum which could be scooped out with a spatula. The brown gum was dissolved in acetone and dried over anhydrous magnesium sulfate. The solution was concentrated *in vacuo* to give a brown solid (4.1 g) GPC: M_n 800, M_w 1100, PDi 1.487.

8.4 Experimental for Chapter 4

8.4.1 G_1P-[6]-O-pent-4-enoyl 86.

To a solution of **49** (3.30 g, 6.2 mmol) in dry acetone (35 ml), were added pent-4-enoic acid (4.45 g, 44 mmol), DCC (9.18 g, 44 mmol) and DPTS (2.06 g, 7.4 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in dichloromethane and washed with saturated sodium carbonate solution (2 × 100 ml), then water (100 ml). The organic fraction was dried over sodium sulfate, concentrated *in vacuo* and purified by flash chromatography eluting with dichloromethane to give a clear solid (5.63 g, 89%), mp 98 °C (PE); υ_{max} /cm^{-1} 3100-2900 (CH) and 1770 (C=O); δ_H($CDCl_3$, 250) 2.47 (12 H, m, $CH_2CH{=}CH_2$), 2.68 (12 H, m, $COCH_2$), 5.04-5.19 (12 H, m, $CH_2CH{=}CH_2$), 5.88 (6 H, ddt, *J* 6.4, 10.2 and 16.6, $CH_2CH{=}CH_2$), 7.16 (3 H, s, ArH), 7.21 (3 H, t, *J* 2.3, Ar'H) and 7.78 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 250) 28.6, 33.3, 113.2, 116.1, 120.7, 121.2, 130.8, 135.9, 151.08, 151.14, 162.6 (carbonyl) and 170.7 (carbonyl); GPC: M_n 1600, PDi 1.019; *m/z* 1050 ($M+Na^+$ requires 1050).

8.4.2 G_2P-[12]-O-pent-4-enoyl 87.

To a solution of **51** (1.93 g, 17 mmol), in dry acetone (25 ml), were added pent-4-enoic acid (2.06 g, 21 mmol), DCC (4.24 g, 21 mmol) and

DPTS (0.95 g, 3.4 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was dissolved in dichloromethane and washed with saturated sodium carbonate solution (2 × 100 ml), then water (100 ml). The organic fraction was dried over sodium sulfate, concentrated *in vacuo* and purified by flash chromatography eluting with dichloromethane to give a colourless solid (2.64 g, 79%), mp 106 °C (PE); υ_{max} /cm^{-1} 3100-2900 (CH) and 1765 (C=O); δ_H($CDCl_3$, 250) 2.46 (24 H, m, $CH_2CH{=}CH_2$), 2.69 (24 H, m, $COCH_2$), 5.04-5.19 (24 H, m, $CH_2CH{=}CH_2$), 5.88 (12 H, ddt, *J* 6.4, 10.2 and 16.6, $CH_2CH{=}CH_2$), 7.23 (6 H, t, *J* 2.3, Ar''H), 7.25 (3 H, s, ArH), 7.52 (3 H, t, *J* 2.3, Ar'H), 7.82 (12 H, d, *J* 2.3, Ar''H) and 8.01 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 250) 28.6, 33.4, 113.2, 116.1, 120.8, 121.1 (2 C), 121.2, 130.6, 131.2, 135.9, 151.1 (3 C), 162.4 (carbonyl), 162.7 (carbonyl) and 170.7 (carbonyl); GPC: M_n 3200, PDi 1.018; *m/z* 2360 ($M+Na^+$ requires 2359).

8.4.3 G_1P-[6]-O-pent-4-enoyl hexaoxide 89.

A solution of mCPBA (25 mg, 0.14 mmol) in dichloromethane (3 ml) was washed with aqueous sodium phosphate (0.2 M, 5 ml) and dried over anhydrous magnesium sulfate. This was added dropwise to a stirred solution of **86** (9.4 mg, 9.2 µmol) in dichloromethane (3 ml) at 0 °C. The solution was stirred for 2 hrs then allowed to warm to room temperature overnight. The ^{1}H NMR spectrum of the crude product indicated that the

reaction had gone to completion. The mixture was filtered, washed with aqueous sodium hydroxide (1 M, 2 × 5 ml), filtered if necessary, washed with water (5 ml) and dried over anhydrous magnesium sulfate. The solution was concentrated *in vacuo* and the product was precipitated from diethyl ether (40 ml) (6.3 mg, 61%), mp 94 °C (PE); υ_{max} /cm^{-1} 3100-2900 (CH) and 1760 (C=O); δ_H($CDCl_3$, 250) 1.83 (6 H, m, RC*H*$_2$CH(O)CH$_2$), 2.12 (6 H, m, RC*H*$_2$CH(O)CH$_2$), 2.54 (6 H, dd, *J* 2.6 and 4.9, RCH$_2$CH(O)C*H*$_2$), 2.71 (12 H, apparent t, *J* 7.0, COC*H*$_2$), 2.77 (6 H, dd, *J* 3.9 and 4.9, RCH$_2$CH(O)C*H*$_2$), 3.03 (6 H, ddt, *J* 2.6, 3.9 and 5.6, RCH$_2$C*H*(O)CH$_2$), 7.12 (3 H, s, ArH), 7.23 (3 H, t, *J* 2.3, Ar'H) and 7.78 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 250) 27.3, 30.3, 46.9, 50.9, 113.2, 120.8, 121.1, 130.8, 151.0, 151.1, 162.5 (carbonyl) and 170.7 (carbonyl); GPC: M_n 1500, PDi 1.023; *m/z* 1146 (M+Na$^+$ requires 1146).

8.4.4 G_2P-[12]-O-pent-4-enoyl dodecaoxide 90.

A solution of mCPBA (152 mg, 0.88 mmol) in dichloromethane (18 ml) was washed with aqueous sodium phosphate (0.2 M, 30 ml) and dried over anhydrous magnesium sulfate. This was added dropwise to a stirred solution of **87** (107 mg, 46 μmol) in dichloromethane (18 ml) at 0 °C. The solution was stirred for 2 hrs and then allowed to warm to room temperature overnight. The ^{1}H NMR spectrum of the crude product indicated that the reaction had gone to completion. The solution was filtered, washed with aqueous sodium hydroxide (1 M, 2 × 5 ml), filtered if necessary, washed with water (5 ml) and dried over magnesium sulfate.

The solution was concentrated *in vacuo* and the product was precipitated from diethyl ether (40 ml) to give a very fine suspension. The product was collected by filtration through a grade 4 sinter (85 mg, 73%), υ_{max} /cm^{-1} 3100-2900 (CH), 1750 (C=O) and 1600 (C=C ring); δ_H($CDCl_3$, 400) 1.82 (12 H, m, $RCH_2CH(O)CH_2$), 2.10 (12 H, m, $RCH_2CH(O)CH_2$), 2.53 (12 H, dd, *J* 2.6 and 4.9, $RCH_2CH(O)CH_2$), 2.70 (24 H, apparent t, *J* 7.0, $COCH_2$), 2.76 (12 H, dd, *J* 3.9 and 4.9, $RCH_2CH(O)CH_2$), 3.02 (12 H, ddt, *J* 2.6, 3.9 and 5.6, $RCH_2CH(O)CH_2$), 7.19 (3 H, s, ArH), 7.24 (6 H, t, *J* 2.3, Ar"H), 7.48 (3 H, t, *J* 2.3, Ar'H), 7.80 (12 H, d, *J* 2.3, Ar"H) and 7.95 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 27.2, 30.3, 46.9, 50.9, 113.2, 120.8, 121.0 (2 C), 121.1, 130.6, 131.2, 151.0 (3 C), 162.4 (carbonyl), 162.7 (carbonyl) and 170.6 (carbonyl); GPC: M_n 3200, PDi 1.020; *m/z* 2552 ($M+Na^+$ requires 2551).

8.4.5 Phenol pent-4-enoate 95.

To a solution of phenol (2.80 g, 30 mmol), DPTS (1.65 g, 6 mmol) and pent-4-enoic acid (2.00 g, 20 mmol) in dry dichloromethane (10 ml), was added DCC (6.20 g, 30 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. Methanol (3 ml) and acetic acid (3 ml) were added and the mixture was allowed to stir for 1 hr. The mixture was filtered and washed with aqueous sodium bicarbonate (3 × 20 ml, 1 M) and water (20 ml). The aqueous washings were combined and extracted with dichloromethane (2 × 20 ml). The organic fractions were combined,

dried over magnesium sulfate and concentrated *in vacuo*. Purification by flash chromatography eluting with dichloromethane yielded a clear oil (3.24 g, 92%), (Found: M^+, 176.0841. M^+ requires 176.0927); υ_{max} /cm^{-1} 3100-2900 (CH), 1760 (C=O) and 1495 (C=C ring); δ_H($CDCl_3$, 250) 2.53 (2 H, m, CH_2), 2.67 (2 H, m, CH_2), 5.11 (1 H, m, RCH=CH_2), 5.19 (1 H, m, RCH=CH_2), 5.95 (1 H, ddt, *J* 6.4, 10.2 and 16.9, RC*H*=CH_2), 7.12 (2 H, m, PhH), 7.24 (1 H, m, PhH) and 7.39 (2 H, m, PhH); δ_C($CDCl_3$, 250) 28.8, 33.5, 115.8, 121.5, 125.7, 129.3, 136.3, 150.7 and 171.3 (carbonyl).

8.4.6 Phenyl 5-oxopentanoate 96.

To a solution **95** (197 mg, 1.12 mmol) in THF (2 ml), was added borane:THF complex (1 M, 1.3 ml) and the mixture was stirred at room temperature under nitrogen for 1 hr. The solution was concentrated *in vacuo* and redissolved in dry dichloromethane (2 ml). The dichloromethane solution was added dropwise to a well-stirred slurry of pyridinium chlorochromate (723 mg, 3.35 mmol) in dichloromethane (5 ml) and refluxed for 90 mins. The green/brown slurry was allowed to cool and an equal volume of diethyl ether was added. The slurry was filtered through a pad of Florosil (100-200 mesh) and purified by flash chromatography eluting with dichloromethane increasing to acetone-dichloromethane (1:99) to give the product as a clear oil (34 mg, 16%), υ_{max} /cm^{-1} 3100-2750 (CH), 1760 (C=O), 1733 (C=O), 1600, 1500 and 1455 (C=C ring); δ_H($CDCl_3$, 250) 2.07 (2 H, m, $CH_2CH_2CH_2$), 2.62 (2 H, dt, *J* 1.2 and 7.0, CH_2CHO), 2.64 (2 H, t, *J* 7.3, $PhOCOCH_2$), 7.0-7.5 (5 H, m, PhH)

and 9.80 (1 H, t, *J* 1.3, CHO); δ_C($CDCl_3$, 250) 17.1, 33.1, 42.7, 121.4, 125.8, 129.4, 150.4, 171.6 (carbonyl) and 201.6 (carbonyl).

8.4.7 G_1P-[6]-O-oleoyl 97.

To a solution of **49** (47 mg, 88 μmol) in dry dichloromethane (7 ml), were added oleic acid (180 mg, 0.64 mmol), DCC (130 mg, 0.63 mmol) and DPTS (29 mg, 0.1 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by flash chromatography eluting with dichloromethane-hexane (40:60), then dichloromethane-hexane (80:20) to yield the product as a clear viscous oil (132 mg, 71%), υ_{max} /cm^{-1} 3100-2800 (CH), 1770 (C=O) and 1750 (C=O); δ_H($CDCl_3$, 250) 0.88 (18 H, apparent t, *J* 6.8, CH_3), 1.2-1.6 (120 H, m, CH_2), 1.77 (12 H, m, CH_2), 2.03 (24 H, m, CH_2), 2.58 (12 H, apparent t, *J* 7.5, CH_2), 5.35 (12 H, m, CH_2CH=$CHCH_2$), 7.15 (3 H, s, ArH), 7.24 (3 H, t, *J* 2.3, Ar'H) and 7.79 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 250) 14.0, 22.6, 24.7, 27.06, 27.12, 28.97 (2 C), 29.05, 29.2 (2 C), 29.4, 29.6, 29.7, 31.8, 34.2, 113.2, 120.7, 121.2, 129.6, 129.9, 130.8, 151.1 (2 C), 162.6 (carbonyl) and 171.4 (carbonyl); GPC: M_n 3400, PDi 1.020.

8.4.8 G_2P-[12]-O-oleoyl 98.

To a solution of **51** (57 mg, 42 μmol) in dry dichloromethane (7 ml), were added oleic acid (172 mg, 0.61 mmol), DCC (126 mg, 0.61 mmol)

and DPTS (28 mg, 0.1 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by flash chromatography eluting with dichloromethane-hexane (60:40) increasing to dichloromethane-hexane (80:20) to yield the product as a clear viscous oil (168, 88%), υ_{max} /cm^{-1} 3100-2800 (CH), 1770 (C=O) and 1750 (C=O); δ_H($CDCl_3$, 400) 0.87 (36 H, apparent t, *J* 6.8, CH_3), 1.2-1.5 (240 H, m, CH_2), 1.76 (24 H, m, CH_2), 2.01 (48 H, m, CH_2), 2.58 (24 H, apparent t, *J* 7.5, CH_2) 5.34 (24 H, m, CH_2CH=$CHCH_2$), 7.20 (3 H, s, ArH), 7.24 (6 H, t, *J* 2.3, Ar"H), 7.48 (3 H, t, *J* 2.3, Ar'H), 7.81 (12 H, d, *J* 2.3, Ar"H) and 7.99 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 14.0, 22.6, 24.7, 27.0, 27.1, 28.96 (2 C), 29.02, 29.2 (2 C), 29.4, 29.57, 29.65, 31.8, 34.1, 113.3, 120.7 (3 C), 121.1, 121.2, 129.6, 129.9, 130.6, 151.10, 151.15 (2 C), 162.4 (carbonyl), 162.8 (carbonyl) and 171.4 (carbonyl); GPC: M_n 6300, PDi 1.021.

8.4.9 G_1P-[6]-O-lineoyl 99.

To a solution of **49** (100 mg, 0.19 mmol) in dry dichloromethane (10 ml), were added linoleic acid (380 mg, 1.4 mmol), DCC (280 mg, 1.4 mmol) and DPTS (63 mg, 0.23 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by flash chromatography eluting with dichloromethane-hexane (40:60), then

dichloromethane to yield the product as a clear viscous oil (390 mg, 98%), υ_{max} /cm^{-1} 3000-2800 (CH), 1770 (C=O) and 1750 (C=O); δ_H($CDCl_3$, 400) 0.89 (18 H, apparent t, *J* 6.7, CH_3), 1.2-1.5 (84 H, m, CH_2), 1.65-1.85 (12 H, m, CH_2), 2.0-2.1 (24 H, m, CH_2), 2.57 (12 H, apparent t, *J* 5.8, CH_2), 2.77 (12 H, apparent t, *J* 7.3, CH_2), 5.3-5.4 (24 H, m, CH_2CH=$CHCH_2$), 7.14 (3 H, s, ArH), 7.23 (3 H, t, *J* 2.3, Ar'H) and 7.79 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 13.9, 22.4, 24.5, 24.5, 25.3, 25.4, 27.0, 27.0, 28.9, 28.9, 29.4, 31.3, 34.0, 113.1, 120.5, 121.0, 127.7, 127.9, 129.7, 129.9, 130.7, 151.1 (2 C), 162.5 (carbonyl) and 171.3 (carbonyl); GPC: M_n 3400, PDi 1.019.

8.4.10 G_2P-[12]-O-lineoyl 100.

To a solution of **51** (100 mg, 74 μmol) in dry dichloromethane (10 ml), were added linoleic acid (300 mg, 1.1 mmol), DCC (220 mg, 1.1 mmol) and DPTS (49 mg, 0.18 mmol). The mixture was stirred vigorously at room temperature under nitrogen overnight during which time a heavy white precipitate formed. The mixture was filtered and the filtrate was evaporated to dryness. The residue was purified by flash chromatography eluting with dichloromethane-hexane (40:60) increasing to dichloromethane to yield the product as a clear viscous oil (300 mg, 90%), υ_{max} /cm^{-1} 3000-2800 (CH), 1770 (C=O) and 1750 (C=O); δ_H($CDCl_3$, 400) 0.89 (36 H, apparent t, *J* 6.7, CH_3), 1.2-1.5 (168 H, m, CH_2), 1.65-1.85 (24 H, m, CH_2), 2.0-2.1 (48 H, m, CH_2), 2.58 (24 H, apparent t, *J* 5.8, CH_2), 2.77 (24 H, apparent t, *J* 7.3, CH_2), 5.3-5.4 (48 H, m, CH_2CH=$CHCH_2$), 7.21 (3 H, s, ArH), 7.24 (6 H, t, *J* 2.3, Ar''H), 7.49 (3 H, t, *J* 2.3, Ar'H), 7.82 (12

H, d, *J* 2.3, Ar"H) and 8.00 (6 H, d, *J* 2.3, Ar'H); δ_C($CDCl_3$, 400) 13.9, 22.4, 24.5, 24.6, 25.3, 25.4, 27.0, 27.0, 28.9, 28.9, 29.4, 31.3, 34.0, 120.6 (3 C), 121.0, 121.1. 127.7, 127.9, 129.8, 130.0, 130.5, 131.2, 151.0, 151.1, 151.1, 162.3 (carbonyl), 162.7 (carbonyl) and 171.3 (carbonyl); GPC: M_n 6300, PDi 1.019.

8.4.11 Polyacetylpoly(3,5-dihydroxybenzoic acid) 101.[109]

To a stirred solution of **80** (50 mg, M_n 800, M_w 1500, PDi 1.82) in dry THF (50 ml), was added acetyl chloride (0.14 ml, 2.0 mmol) followed by triethylamine (17 ml, 2.0 mmol). A white precipitate formed immediately and the resulting white slurry was allowed to stir overnight under nitrogen. The crude mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in dichloromethane (5 ml) and washed with dilute hydrochloric acid (2 × 5 ml), water (2 × 5 ml) then dried over sodium sulfate. The polymer was precipitated from methanol and collected by filtration. The polymer was dried in a vacuum desiccator to give an off-white solid (49 mg), δ_H($CDCl_3$, 250) 2.32 (br s, $COCH_3$), 2.34 (br s, $COCH_3$), 7.25 (m, ArH), 7.35-7.42 (m, ArH), 7.48-7.56 (m, ArH), 7.80-7.85 (m, ArH), 7.85-7.92 (m, ArH), 7.93-7.98 (m, ArH) and 7.98-8.05 (m, ArH); GPC: M_n 3300, M_w 3400, PDi 1.22.

8.4.12 Polyoleoylpoly(3,5-dihydroxybenzoic acid) 102.

To a stirred solution of **80** (116 mg, M_w 1500, M_n 800, PDi 1.82) in dry THF (3 ml), was added oleoyl chloride (460 mg, 1.5 mmol) followed by

triethylamine (213 μl, 1.53 μmol). A white precipitate formed immediately and the resulting white slurry was allowed to stir overnight under nitrogen. The crude mixture was filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane (5 ml) and washed with dilute hydrochloric acid (2 × 5 ml) and water (2 × 5 ml), then dried over sodium sulfate. The polymer was precipitated from methanol as a pale yellow oil. The oil was allowed to settle and the methanol removed by decanting. Re-precipitation from methanol gave the product as a pale yellow oil (320 mg), δ_H($CDCl_3$, 250) 0.80-0.95 (m, CH_3), 1.2-1.6 (m, CH_2), 1.7-1.9 (m, CH_2), 1.9-2.1 (m, CH_2), 2.5-2.7 (m, CH_2), 5.3-5.4 (m, CH_2CH=$CHCH_2$), 7.2-7.25 (m, ArH), 7.3-7.4 (m, ArH), 7.40-7.60 (m, ArH), 7.75-7.83 (m, ArH), 7.83-7.93 (ArH), 7.93-7.99 (m, ArH) and 7.99-8.08 (m, ArH); δ_C($CDCl_3$, 250) 14.0, 22.6, 24.7, 27.05, 27.11, 28.97, 29.05, 29.2, 29.4, 29.6, 29.7, 31.8, 34.2, 120.7, 121.2, 129-131, 151.0-151.2, 162.6 and 171.4; GPC: M_n 1700, M_w 12600, PDi 7.345.

8.4.13 Lineoyl chloride 103.

Lineoyl chloride was prepared by an adaptation of a literature method.[122] Oxalyl chloride (3.0 ml, 34 mmol) was added dropwise with stirring to neat linoleic acid (5.0 g, 18 mmol) under nitrogen. Once the effervescence had subsided, the mixture was refluxed for 2 hrs. The solution was allowed to cool and evaporated to dryness to give a pale yellow oil (5.3 g), (Found: M^+, 298.2060. M^+ requires 298.2063); υ_{max} /cm^{-1} 3000-2800 (CH), 1800 (C=O), 1655 (C=C) and 955 (C=C); δ_H($CDCl_3$,

250) 0.89 (3 H, apparent t, *J* 6.7, CH_3), 1.2-1.5 (14 H, m, CH_2), 1.6-1.8 (2 H, m, CH_2), 2.0-2.1 (4 H, m, CH_2), 2.76 (2 H, apparent t, *J* 5.8, CH_2), 2.87 (2 H, apparent t, *J* 7.3, CH_2) and 5.25-5.45 (4 H, m, CH_2CH=$CH$$CH_2$); δ_C($CDCl_3$, 250) 14.0, 22.5, 24.9, 25.5, 27.0, 27.1, 28.3, 28.9 (2 C), 29.3, 29.4, 31.4, 47.0, 127.8, 128.0, 129.7, 130.1 and 173.5 (carbonyl).

8.4.14 Polylineoylpoly(3,5-dihydroxybenzoic acid) 104.

To a stirred solution of **80** (210 mg, M_w 1500, M_n 800, PDi 1.82) in dry THF (6 ml), was added lineoyl chloride (850 mg, 2.8 mmol) followed by triethylamine (380 µl, 2.8 µmol). A white precipitate formed immediately and the resulting white slurry was allowed to stir overnight under nitrogen. The crude mixture was filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane (10 ml) and washed with dilute hydrochloric acid (2 × 10 ml) and water (2 × 10 ml), then dried over sodium sulfate. The polymer was precipitated from methanol as a brown oil which solidified in the refrigerator overnight. The methanol was removed by decanting. Re-precipitation from methanol gave the product as a pale brown oil (480 mg), δ_H($CDCl_3$, 250) 0.80-0.95 (m, CH_3), 1.10-1.85 (m, CH_2), 1.90-2.15 (m, CH_2), 2.45-2.83 (m, CH_2), 5.20-5.45 (m, CH_2CH=$CH$$CH_2$), 7.10-7.40 (m, ArH), 7.45-7.55 (m, ArH) and 7.70-8.08 (m, ArH); δ_C($CDCl_3$, 250) 14.0, 22.4, 24.5, 24.7, 25.5, 26.2, 27.1, 27.4, 28.8, 29.0, 29.2, 29.4, 29.5, 31.4, 33.5-34.2, 120.2-122.0, 127.5-128.4, 129.4-130.4, 145.5, 150.0-151.5, 162.3-163.0 and 169.0-171.8; GPC: M_n 2500, M_w 20900, PDi 8.295.

8.4.15 Pent-4-enoyl chloride 105.[122]

Oxalyl chloride (3 ml, 34 mmol) was added dropwise with stirring to neat pent-4-enoic acid (2.05 g, 20.5 mmol) under nitrogen. Once the effervescence had subsided, the mixture was refluxed for 2 hrs. The crude product was distilled (85 °C) under nitrogen to give a clear liquid (2.01 g, 83%), $\delta_H(CDCl_3, 250)$ 2.43 (2 H, apparent q, *J* 7.0, $CH_2CH=CH_2$), 2.98 (2 H, apparent t, *J* 7.0, $COCH_2$), 5.06 (1 H, dd, *J* 1.3 and 10.2, $CH_2CH=CH_2$), 5.09 (1 H, dd, *J* 1.3, 17.0, $CH_2CH=CH_2$) and 5.77 (1 H, ddt, *J* 6.7, 10.2 and 17.0, $RCH=CH_2$); $\delta_C(CDCl_3, 250)$ 28.8, 46.1, 116.7, 134.5 and 173.0 (carbonyl).

8.4.16 Poly(pent-4-enoyl)poly(3,5-dihydroxybenzoic acid) 106.

To a stirred solution of **80** (3.21 g, M_n 800, M_w 1500, PDi 1.82) in dry THF (50 ml), was added pent-4-enoyl chloride (13.3 ml, 0.12 mol) followed by triethylamine (17 ml, 0.12 mol). A white precipitate formed immediately and the resulting white slurry was allowed to stir overnight under nitrogen. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was dissolved in dichloromethane (30 ml) and washed with dilute hydrochloric acid (2 × 30 ml), saturated sodium carbonate solution (2 × 30 ml) and water (2 × 30 ml), then dried over sodium sulfate. Precipitation from methanol yielded a viscous brown oil (4.2 g), t_g 159 °C (PE); $\delta_H(CDCl_3, 250)$ 2.05-2.64 (br m, $CH_2CH=CH_2$), 2.73 (br m, $COCH_2$), 4.72-5.21 (br m, $CH_2CH=CH_2$), 5.53-5.93 (br m, $CH_2CH=CH_2$), 7.00-7.14 (m, ArH), 7.17-7.33 (m, ArH), 7.40-7.55 (m, ArH),

7.60-8.05 (m, ArH); $\delta_C(CDCl_3, 250)$ 27-29, 32.1, 33.1, 114-117, 120-122, 130-133, 136-138, 145.5, 151.1, 162.4 and 168-171; GPC: M_n 3400, M_w 10000, PDi 2.943.

8.4.17 Poly(pent-4-enoyl)poly(3,5-dihydroxybenzoic acid) polyoxide 108.

To a solution of **105** (0.3 g, M_n 3400, M_w 10000, PDi 2.943) and 18-crown-6 (0.15 g, 0.57 mmol) in acetone (2 ml), was added aqueous sodium phosphate buffer (10 ml, 0.05 M). The mixture was stirred vigorously and cooled to <5 °C. A solution of aqueous Oxone (15 ml, 0.4 M) was added dropwise over 30 mins ensuring the temperature did not exceed 5 °C. The solution was maintained at pH 7.5 throughout the addition of Oxone by addition of aqueous potassium hydroxide (0.5 N) and this pH maintained for a further 3 hrs. The mixture was allowed to warm to room temperature and left to stir overnight, then extracted with dichloromethane (3 × 30 ml). The extracts were combined and dried over sodium sulfate, filtered and concentrated *in vacuo*. Precipitation in hexane gave a viscous brown oil (0.18 g), $\delta_H(CDCl_3, 250)$ 1.70-2.00 (br m $RCH_2CH(O)CH_2$), 2.00-2.25 (br m, $RCH_2CH(O)CH_2$), 2.40-2.60 (br m, $RCH_2CH(O)CH_2$), 2.60-2.85 (br m, $COCH_2$ and $RCH_2CH(O)CH_2$), 2.90-3.10 (br m, $RCH_2CH(O)CH_2$), 7.05-7.15 (m, ArH), 7.30-7.42 (m, ArH), 7.45-7.60 (m, ArH), 7.75-7.85 (m, ArH), 7.85-7.97 (m, ArH) and 7.97-8.05 (m, ArH); GPC: M_n 4300, M_w 17000, PDi 3.82.

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