Organic Materials For Nonlinear Optics

A thesis submitted for the degree of

Doctor of Philosophy

by

Peter D. Turner B.Sc. (Hons)

The Department of Chemistry

The University of Adelaide

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Contents

Abstract

The preparation of a series of conjugated cyclophanes is described. The cyclophanes were constructed by the coupling of various monomeric or dimeric systems to a series of anthracene templates to produce a range of 'bis-coupled' systems which were then manipulated to effect cyclophane formation. The monomers and dimers were derivatives of benzene and phenylethynylene respectively, and contained 'linker-arm' precursor groups along with groups amenable to palladium catalysed coupling reactions. The anthracene template systems were functionalised in the 1,8-positions for palladium catalysed coupling reactions, and several possessed functionality in the 10-position to aid in solubility. The monomeric and dimeric systems were coupled to the templates using palladium catalysis to produce a series of bis-coupled systems. Subsequent functional group manipulations of the linker-arm precursors afforded a number of bis-, tetrakis- and tetra-bromomethyl bis-coupled derivatives. Nucleophilic displacement reactions with these systems led to the formation of the cyclophanes.

Molecular modelling studies were performed on the bis-coupled systems and the cyclophanes to investigate steric interactions between the unconstrained and constrained aromatic systems.

Ultraviolet-visible and fluorescence spectra were recorded for many of the bis-coupled and cyclophane systems, and an x-ray crystal structure was obtained for one of the cyclophanes.

A new catalytic protocol was discovered and developed for the palladium catalysed coupling of terminal alkynes to aryl-halides using zinc co-catalysts.

Statement

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Peter D. Turner.

Acknowledgments

Many people must be acknowledged in the preparation of this thesis. First and foremost I would like to thank my supervisor Dr Geoff Crisp for providing me with an interesting and challenging project, and for all the guidance he has given me over many years.

I would like to thank all the Staff of the Department of Chemistry for their help, especially: Tom Blumenthal (Mass Spec.), Jeff Borkent (Computing), John Cameron (Store), Phil Clements (NMR), Barry Hyde-Parker (Workshop) and Dr Edward Tiekink (X-Ray). Acknowledgment must also go to the Australian Research Council for providing me with an Australian Postgraduate Award.

Many thanks to all my friends and colleagues in the Department, whose names are too numerous to list here, I thank you all for your help, encouragement and for sharing a beer or two with me. Thanks also to the past and present members of lab 1, you were all great people to work alongside.

Finally, I would like to thank my family for all their support over the years.

List of Abbreviations

Ac	Acetyl
BTMA.ICl_2	Benzyltrimethylammonium dichloroiodate
conc	Concentration
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DIBAL-H	Diisobutylaluminium hydride
DMAP	Dimethylaminopyridine
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
EI	Electron Impact
eq	Equivalents
FAB	Fast Atom Bombardment
IR	Infrared Spectrum
LSIMS	Liquid Secondary Ionisation Mass Spectrometry
mp	Melting Point
NBS	N-Bromosuccinimide
NLO	Nonlinear Optics
NMR	Nuclear Magnetic Resonance
ppm	Parts Per Million
py	Pyridine
TBDMS	*tert*-Butyldimethylsilyl
t-Bu	*tert*-Butyl
TDS	Thexyldimethylsilyl
THF	Tetrahydrofuran
tlc	Thin Layer Chromatography
TsOH	*p*-Toluenesulphonic acid
UV-Vis	Ultraviolet-Visible

1. Introduction

Nonlinear optics (NLO) is a relatively new field of research providing many opportunities for advances in Physics, Chemistry and Engineering. New compounds are constantly being sought as researchers the world over look to understand more about the processes involved in NLO. This thesis aims to present new methodologies towards the design and synthesis of new materials for possible nonlinear optical applications. The very novelty of these new materials infers that they should possess interesting physical and chemical properties, and they may find applications in areas other than NLO, such as in the field of conducting polymers.[1]

Since the mid-1980's a significant research effort has been directed towards the study of NLO. This is reflected in the wealth of articles being published on nonlinear optics each year.[2,3,4] The reason for this is the potential for nonlinear optical materials to have applications in the technology of optical processing of information. For all optical processing, which involves the control of light by light, 'third-order' materials provide the necessary functions of optical logic, optical switching and optical memory storage for ultrafast light operated computers.[5,6,7] Other properties arising from these materials include optical phase conjugation, new frequency generation and eye/sensor protection.[8,9]

Initially, NLO studies were focused on inorganic materials, such as GaAs and InSb crystals. Both materials possessed reasonable nonlinear optical properties, but they had drawbacks with their response times, magnitude of nonlinearity, processibility and production costs. The inorganics also absorb strongly in the visible region of the electromagnetic spectrum and can have poor optical quality, limiting their potential applications.[9]

Organic systems, on the other hand, tend to be of low cost, have fast response times ($<10^{-9}$ s), large nonlinear properties, are active over a broad frequency range, are inherently synthetically flexible and often have high damage thresholds (especially for solutions).[2]

1.1. The Basic Principles of Nonlinear Optics

Nonlinear optics is the study of the interaction of an electromagnetic field of a high intensity laser beam with a nonlinear optical material. The applied electromagnetic field interacts with the molecules within the material, causing changes to the original laser beam's phase, frequency, amplitude and polarisation, thereby producing new electromagnetic fields.[9,10] From a theoretical and mathematical viewpoint, nonlinear optical properties arise from the nonlinear induced polarisability of the material. This can be described by Equation (1).[11,12,13]

$$P = \chi^{(1)}E + \chi^{(2)}E \,.\, E + \chi^{(3)}E \,.\, E \,.\, E + \ldots \qquad (1)$$

Where P is the induced polarisation and the susceptibilities $\chi^{(n)}$ are tensor quantities. The linear susceptibility of the material, $\chi^{(1)}$, is usually adequate for describing optical responses with a weak optical field. The linear susceptibility relates to the dielectric constant and refractive index of a material. If a material is subjected to a laser beam, which has a correspondingly high intensity electric field E, the induced polarisation can be driven beyond the linear region. This gives rise to second- and third-order nonlinear optical susceptibilities, $\chi^{(2)}$ and $\chi^{(3)}$, with $\chi^{(3)}$ values being studied more intensely at the moment. Higher orders of susceptibility are possible, however, these phenomena have yet to be pursued experimentally in any depth.

1.1.1 Second-Order Materials

Briefly, second-order organic materials had been studied much more than their third-order counterparts and there are several rules that are generally accepted for designing second-order materials. The basic rules are that the materials should be dipolar, highly polarisable, extensively π-conjugated and show charge transfers between electron-donor (e.g. NH_2) and electron-acceptor groups (e.g. NO_2).[9] An example of this type of material is shown below in Figure 1 for the compound known as DANS (N,N-dimethylamino-nitrostilbene).[14]

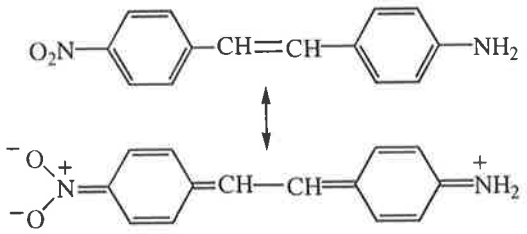


Figure 1. A second-order material (DANS).

Second-order nonlinearities are also highly symmetry dependent.[15] The material must crystallise in a non-centrosymmetric manner to produce a significant nonlinear response. Non-centrosymmetry is where all the dipoles are aligned with one-another in the same direction, and centrosymmetry is where the dipoles oppose each other to cancel the charges. When this happens, the second-order properties are lost, and this is a major problem as most achiral molecules crystallise into centrosymmetric space groups. To overcome this, a whole range of techniques have been developed, including synthetic designs incorporating chiral molecules or groups with hydrogen bonds, or physical techniques such as 'poling'.[9] Poling requires the heating of the sample (~90-130°) to near the glass transition temperature (T_g) of the material, and applying a d.c. field. The field is kept on while the temperature is then reduced to room temperature, and this 'freezes in' the dipolar alignment in the field direction.[16]

1.1.2. Third-Order Materials

Unlike the second-order materials there are, as yet, no 'hard and fast' rules for designing third-order materials. The only generalisations that can be made though, are that incorporation of a high degree of conjugation into the molecule is most important,[9] and that the incorporation of electron-donor/electron-acceptor groups into the molecular structure has only a moderate effect on nonlinearity.[14,17] Third-order materials also have no symmetry requirements unlike second-order materials, due to the spatial symmetry of the tensor $\chi^{(3)}$.[13] The mechanisms involved in actually producing the optical nonlinearities fall into three main areas. Firstly, thermo-optic nonlinearities (thermal effects). These are observed for pulse times of nanoseconds or greater and generally produce large $\chi^{(3)}$ values, especially in polydiacetylenes.[10] For device fabrication, however, they are not useful, due to slow (microsecond) response times. Since these thermal effects are time dependent, the shorter the pulse width the smaller the net index

change and so thermal effects can be separated from the more important nuclear and electronic nonlinearities by reducing the pulse width of the laser to the sub-nanosecond region.[18,19]

Nuclear and electronic contributions to nonlinearities are the most significant processes in terms of response times and magnitude. Nuclear contributions arise from optical field induced changes in the motions of the nuclei. After the sudden impression of the field, this contribution can only be observed after a time of approximately 10^{-12} s. This is because the nucleus has to undergo a vibrational or rotational decay cycle.[20] Electronic contributions are those arising from the nonlinear distortion of the electronic orbits around the average positions of the nuclei (e.g. exciton formation). These processes occur on a very short timescale (~10^{-16} s), and are considered to be virtually instantaneous.[20] Both of these contributions can be resolved from one another by Raman Scattering techniques.[20]

Electronic contributions can be enhanced by designing molecules and polymers with high degrees of conjugation. It is the π-electron delocalisation which promotes induced polarisation within the material when subjected to high intensity laser beams. In general, for small molecules the trend is that the higher the degree of conjugation, the larger the nonlinearity observed. However, this is not the case when considering larger oligomeric systems. Conjugation effects are known to be limiting in oligomeric and polymeric systems, in the sense that after a discrete number of repeat units, the respective increase in nonlinearity becomes less and less. This is illustrated in Figure 2.

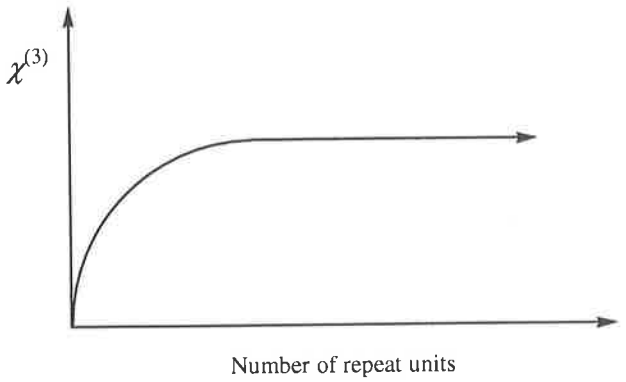


Figure 2. Conjugation effects in polymers.

Polymers with heteroaromatics in their structure such as pyrrole, furan and thiophene derivatives are all known to have nonlinear optical effects. Polythiophene has the largest $\chi^{(3)}$ value in this series. This is probably due to the higher density of

electrons near to the sulphur atom.[21] In mathematical terms, the effects of the heteroatom in the ring can be explained using Frontier Molecular Orbital Theory to determine the charge transfer mechanisms between orbitals.[22]

The extent of conjugation throughout a molecule is a major factor influencing $\chi^{(3)}$ and so planarity of a conjugate system becomes an important issue. In a study of systematically derivatised heteroaromatic polymers, it has been observed that poly-furan, -pyrrole and -thiophene polymers can easily adopt a planar conformation.[22] This maximises the p-orbital overlap and thus conjugation, between the monomer units as there are no H^{β} and $H^{\beta'}$ interactions. Figure 3 shows this conformation, where X=S, N or O.

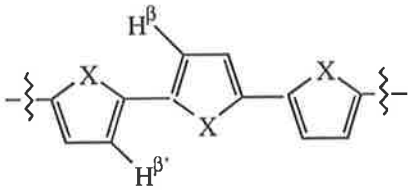


Figure 3. Heteroaromatic polymers.

Whereas with polyparabenzene, shown in Figure 4 (a), the benzene rings twist out of a coplanar arrangement, due to H^2 and $H^{2'}$ interactions.[22] Consequently the $\chi^{(3)}$ value for these systems are lower than for the heteroaromatic polymers.

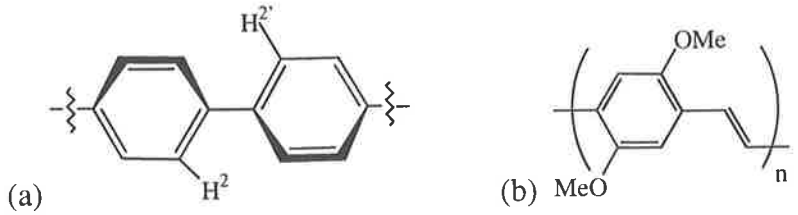


Figure 4(a). Polyparabenzene, (b) 2,5-dimethoxy-PPV.

Structural design and manipulation of organic systems has been employed with these polymers and various PPV (polyparaphenylvinylene) polymers have been synthesised and studied.[6,23,24,25] A dimethoxy substituted PPV, Figure 4(b), has one of the largest $\chi^{(3)}$ values known, 4×10^{-9} esu.[25]

1.1.3. Measuring $\chi^{(3)}$ Values

Experiments to determine $\chi^{(3)}$ values are usually performed using a technique called Degenerate Four Wave Mixing (DFWM). Degenerate four wave mixing involves the use of two counter propagating, high intensity (GigaWatt) pump laser beams to establish a transient diffraction grating within the sample solution cell. This is shown schematically in Figure 5. A lower intensity probe beam (~5% of the pump beam intensity) is then directed onto the sample cell at ~5^0 from the pump beams. This produces a fourth beam, counterpropagating to the probe beam which returns from the grating containing information about the nonlinear material being probed.

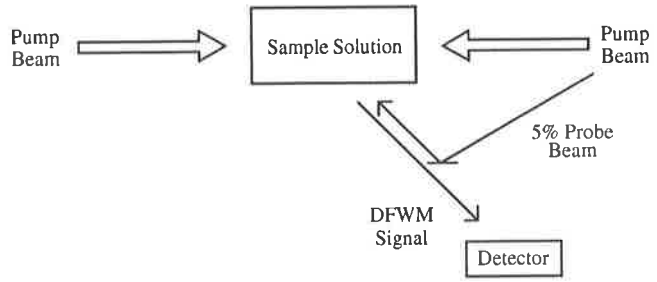


Figure 5. Schematic DFWM setup.

A typical DFWM experiment would produce a graph similar to the one shown in Figure 6.

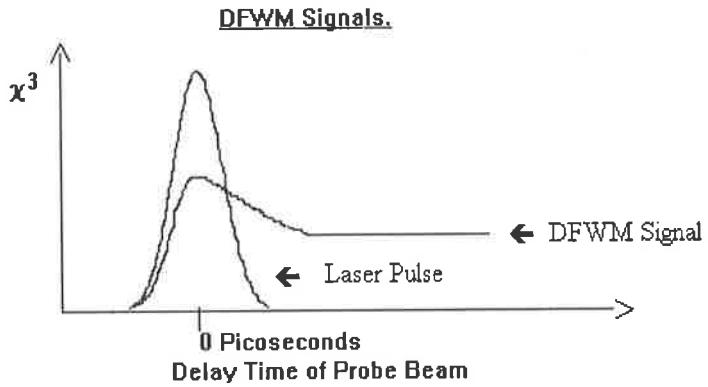


Figure 6. Typical DFWM signals.

Delay time is the time interval separating the pump beams (which are synchronous) and the probe beam. This allows the decay characteristics and mechanisms of the nonlinear process to be studied from the shape of the graph produced.

One of the most important features of these graphs is the excellent correlation between the rise time of the nonlinear response and the rise of the actual laser pulse.[6]

This implies that some nonlinear responses are virtually instantaneous. Decay of the DFWM signal is determined by various quantum electronic processes, such as exciton and bipolaron decay.[26] The main goal at the moment in this field is to minimise the decay of the signal after impression of the laser pulse and to extend the life of the transient grating (extend the tail-end of the signal).

Other common methods of measuring $\chi^{(3)}$ include the optical Kerr gate,[26] third harmonic generation[9] and the Z-scan technique.[27]

1.2. The Project

We have seen earlier that enhancement of conjugation throughout a molecular structure increases the magnitude of the nonlinearity and minimises the fall off in the nonlinearity as the number of repeat units increases. From work done previously in our group it was found that the extent of conjugation throughout several tolane oligomers could be increased by restricting the intraannular rotations.[28,29] Examples of these oligomers are shown below in Figure 7. These restrictions led to the narrowing of the absorption bands of the ultraviolet-visible spectra and an increase in the extinction coefficient (ε_{max}) as compared to similar unconstrained oligomers.[29]

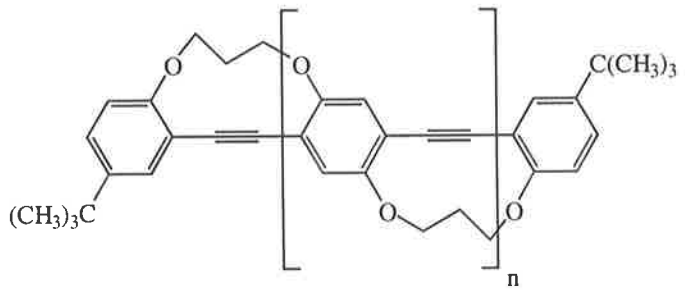


Figure 7. Sterically constrained arylalkyne oligomers (n=1,2 or 3).

The previous investigations into constrained arylalkyne systems led us to consider developing a series of rigid cyclophane oligomers, also containing the tolane motif. To elaborate this idea, a series of 'two-arm' cyclophane monomers are to be synthesised and coupled with acetylene linkages to form a system of rigid derivatised oligomers, shown in Figure 8a, where L=O, S or N and is a bridging unit between the two aromatic systems. Similarly, a series of 'one-arm' cyclophane oligomers, shown in Figure 8b, will be synthesised using the same chemistry as for the two-arm cyclophane systems. Templates are to be employed to aid in construction of the cyclophane

structures. Coupling of the monomers to the templates will be achieved using palladium catalysed coupling reactions.[30]

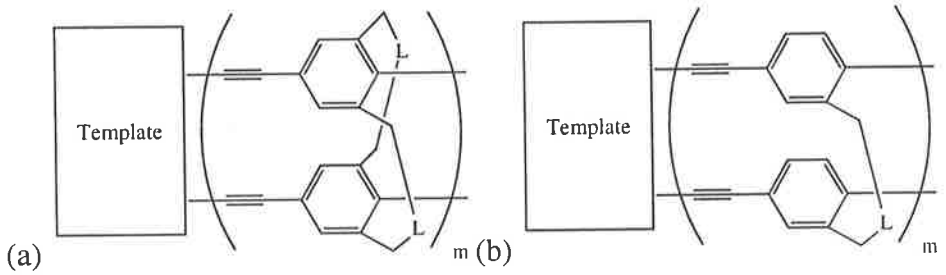


Figure 8. The target systems: (a) the 'two-arm' cyclophane oligomers, (b) the 'one-arm' cyclophane oligomers.

1.2.1. Cyclophane Systems

The general structure of cyclophanes has been known since the late 1940's. The first cyclophane made being [2.2]paracyclophane, Figure 9(a), by C.J. Brown and A.C. Farthing.[31] In general, cyclophanes are classed as compounds containing at least one aromatic ring and being bridged by at least one aliphatic n-membered bridge. Early interest in cyclophanes was due to the discovery of transannular interactions between the aromatic rings, arising from the deformations of the normally planar benzene ring.[32] This led to interesting UV-Vis spectra, influenced by various electronic processes such as excimer emission.[32,33] X-ray crystallography studies have been performed to determine the angles of deformation for cyclophanes.[32] This is illustrated below in Figure 9(b) for [2.2]paracyclophane.

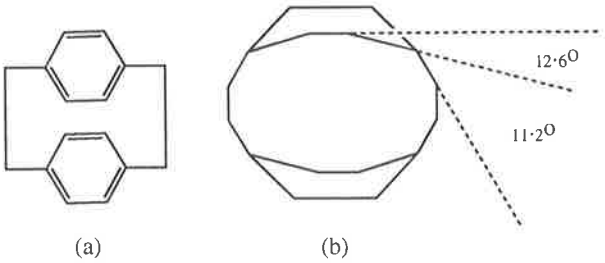


Figure 9(a) [2.2]paracyclophane, (b) x-ray crystallographic measurements.

Cyclophanes have also been used for modelling the interactions and reactions present in biological systems. For example, porphyrin-cyclophanes (porphyrinophanes), are used to model oxygen transport and storage proteins, such as haemoglobin and myoglobin.[34] Inclusion complexation studies have also been performed on many types

of cyclophanes, since various molecules can form stable complexes if the cyclophane cavity is sufficiently large.[35] An interesting aspect of these complexes is the inclusion of an apolar substrate within a cyclophane host in both aqueous solutions and solid state.[35] The most recent research at the moment is with regards to chiral molecular recognition, using cyclophanes containing one or more chiral centres. This allows enantioselectivity of substrates to form inclusion complexes.[36]

1.2.2. Cyclophane Nomenclature

The nomenclature for cyclophanes has only recently been published.[37] Previously there were no 'hard and fast' rules, and only partial I.U.P.A.C. guidelines[38] along with various naming methodologies by authors of cyclophane-related papers were available.[33,39] Now a new form of nomenclature called 'Phane Nomenclature' has been developed for naming cyclophanes and other complex structures. It is based on the idea of simplifying a complex structure to a 'simplified skeleton' consisting of a 'simplified phane parent graph' with 'superatoms' and 'skeletal locants'. An example of a 'simplified skeleton' is given below in Figure 10. The 'simplified phane parent graph' is generally a ring structure for cyclophanes, but can be an acyclic chain as in Figure 11. In the example below (Figure 10), the simplified phane parent graph is a cycloheptane structure, and consequently the simplified skeletal name is cycloheptaphane. The superatoms represent ring structures and skeletal locants refer to the substitution positions on the rings, with respect to the simplified skeleton. In the example below, the superatom at position one (**1**) of the simplified skeleton is a naphthalene ring and is connected to the simplified skeleton in the two and seven positions. Similarly, the superatom in position four (**4**) of the simplified skeleton is a benzene ring which is connected to the simplified skeleton in the one and three positions. There are various rules governing the priority and location of the superatoms in the simplified skeleton, and with the numbering of the locants.[37] After the complex structure has been reduced down to the various simplified components, the cyclophane name is built-up in a process called amplification. The first part of the name refers to the superatom number, followed by the skeletal locants in parentheses and then the ring name. This is repeated till all the superatoms have been incorporated. Finally, the simplified skeletal name is

added on the end. For example, the structure in Figure 10 has the full name 1(2,7)-naphthalena-4(1,3)-benzenacycloheptaphane.

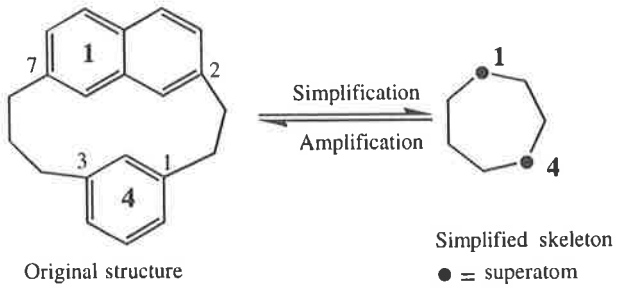


Figure 10. An example of phane nomenclature.

Phane nomenclature can be applied to structures other than cyclophanes. An example of which is shown below in Figure 11. The full name for this compound is 1(4)-pyrimidina-3,6(5,2),9(3)-tripyridinanonaphane.

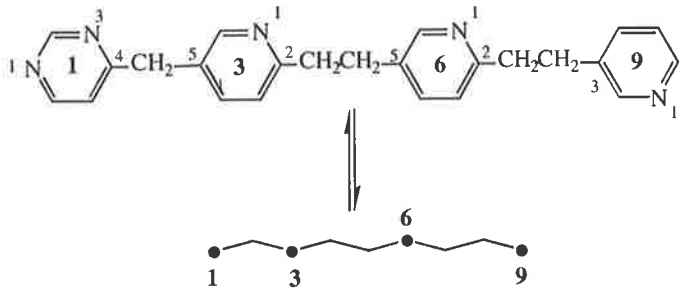


Figure 11. A non-cyclic example of phane nomenclature.

An example of naming a cyclophane described in this thesis is given below in Figure 12. Information about substitution of the superatom is incorporated into the beginning of the name. In the example below, the 1^{10} refers to the first superatom, which is the anthracene ring and the number ten refers to the substitution position of the methoxy group in the ring. Heteroatoms are incorporated into the simplified skeleton as superatoms. By using the phane naming rules the complete name for the compound in Figure 12 is 1^{10}-methoxy-6-thia-1(1,8)-anthacena-4,8(1,3)-dibenzacyclodeca-2,9-diynaphane.

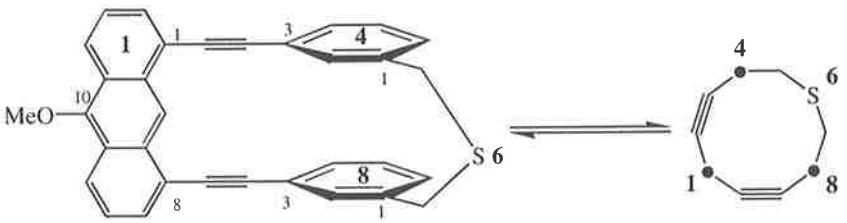


Figure 12. An example of a thiacyclophane.

1.2.3. Cyclophanes for Nonlinear Optics

In terms of using the cyclophanes for nonlinear optics, we propose that their structure will serve to restrict the rotations between the aromatic rings and the acetylenic linkages, effectively locking the π-conjugated systems into two discrete parallel planes. This clamping effect will serve to maximise conjugation throughout the molecular backbone of the oligomer and hence maximise any nonlinear response. These restrictions should produce a lowering of the band gap (E_g), as compared to unrestricted poly-paraphenylacetylene and a narrowing of the UV-visible absorption spectrum with a red-shifting of λ_{max}. These ideas are consistent with restricted rotations of π-conjugated systems.[40,41,42] There also exists the possibility that any transannular interactions involving charge transfer mechanisms may promote photorefractive properties in these materials.[43]

Briefly, photorefractive materials are at the 'crossroads' between second-order and third-order materials.[43] They have contributions from both types of nonlinearities. These materials generally have slow response times (~100 ms) due to second-order processes. Nevertheless, these materials have many applications in optical computing, real-time holography and the optical storage of information.[44,45]

1.2.4. Cyclophane Formation Methodology

The formation of both the two-arm cyclophanes and the one-arm cyclophanes is to be developed using a new methodology. The main aspects of which are outlined schematically in Figure 13 for the two-arm cyclophanes. Exactly the same methodology will be used for the one-arm cyclophanes.

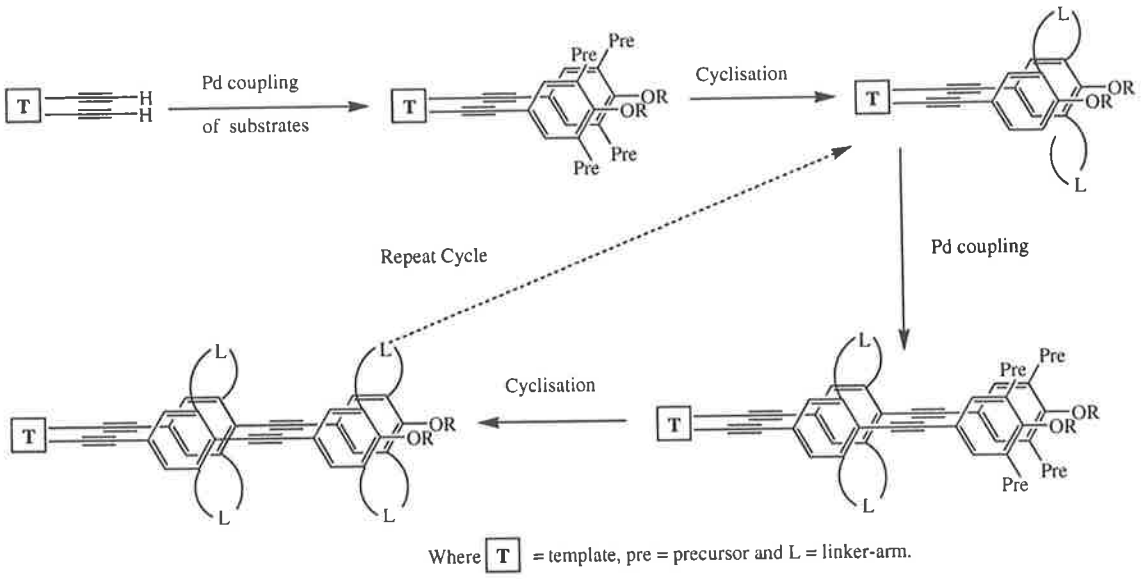


Figure 13. Reaction scheme employing templates.

Initially, functionalised monomer units containing 'linker-arm' precursors will be coupled to the 'template' system using palladium catalysed coupling reactions. The monomer units may be equivalent or inequivalent. The inequivalent ones being coupled to the template separately. The monomers are to be designed to possess the following structural characteristics, Figure 14a and Figure 14b, where R=H, Tf, Y=precursor group and X=Br, I.

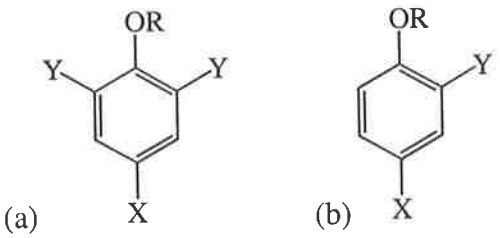


Figure 14. The general form of the monomers: (a) two-armed or, (b) one-armed.

The monomers are to be functionalised in the 1,4-positions in a manner suitable for palladium catalysed coupling reactions. This will be achieved by basing the monomeric system around phenol derivatives since halogens can easily be introduced to the 4-position. The phenolic group can be readily converted to the corresponding triflate at a later stage for further palladium catalysed coupling chemistry.

The choice of linker-arm precursor groups in the 2,6-positions will be done in such a manner that once the monomer substrate is coupled to the template system, a minimal number of synthetic steps will be required to manipulate these linker-arm precursors to achieve cyclophane formation. Suitable linker-arm precursors will be the

esters, acetoxymethyl and hydroxymethyl groups which will ultimately lead to [3.3]-cyclophanes. The linker-arms in these [3.3]-cyclophanes will contain one of a range of different heteroatoms, namely O, N and S. In doing so, a determination of the influence of heteroatoms on nonlinearity can be performed through a comparative study.

The function of the template is to dramatically aid the cyclisation step, by holding the linker-arm precursors in close proximity thereby pre-organising the system. Previous methods of cyclophane formation involved the use of high dilution techniques which are in general tedious and can produce low yields due to entropy factors.[46] Even though these entropy factors have been reduced in some cases through the use of the caesium effect,[46] the utilisation of these template systems should give cyclophanes in much higher yields. Apart from the clamping and rigidifying nature of the cyclophanes on the molecular structure the templates themselves will serve to add a degree of rigidity to the oligomeric system. The introduction of a high degree of rigidity to the oligomers may have adverse effects on solubility.[29] It may become necessary to incorporate alkyl groups into the template structures to increase solubility.

After cyclophane formation, further monomeric groups will be coupled to the oligomer where each aromatic ring is separated by an acetylene unit. This is followed by linker-arm manipulation and cyclisation to form the second repeat unit. The oligomer length is then built up by simple repetition of this cycle.

Another route to forming the cyclophanes is to firstly build up the basic oligomer length using the monomer substrates, off the template, as shown schematically for the two-arm cyclophanes in Figure 15. Once the correct functional groups have been introduced to form the functionalised oligomer, they will be then coupled to the template. Finally, with a minimum number of steps, the linker-arm precursors will then be manipulated to effect cyclophane formation.

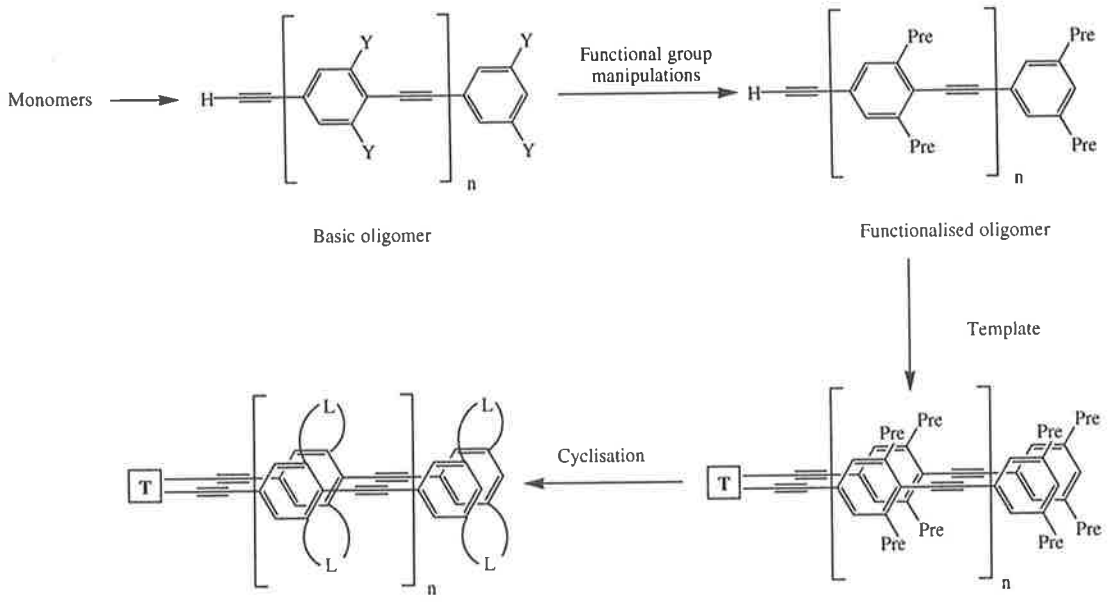


Figure 15. The alternative route to the cyclophanes.

1.2.5. Structural Isomers of Cyclophanes

The reason for investigating the two-arm cyclophanes possessing a meta relationship between the linker-arms, 'metacyclophanes,' rather than the isomeric two-arm 'paracyclophanes,' lies in the problem of structural isomers. For example, forming the paracyclophanes with two repeats units and higher, inequivalent rotamers will arise from rotations of the un-linked precursor substrates, before the linker-arms are formed. This is illustrated for the two unit case schematically in Figure 16. The number of possible isomers increases dramatically as the number of repeat units increases.

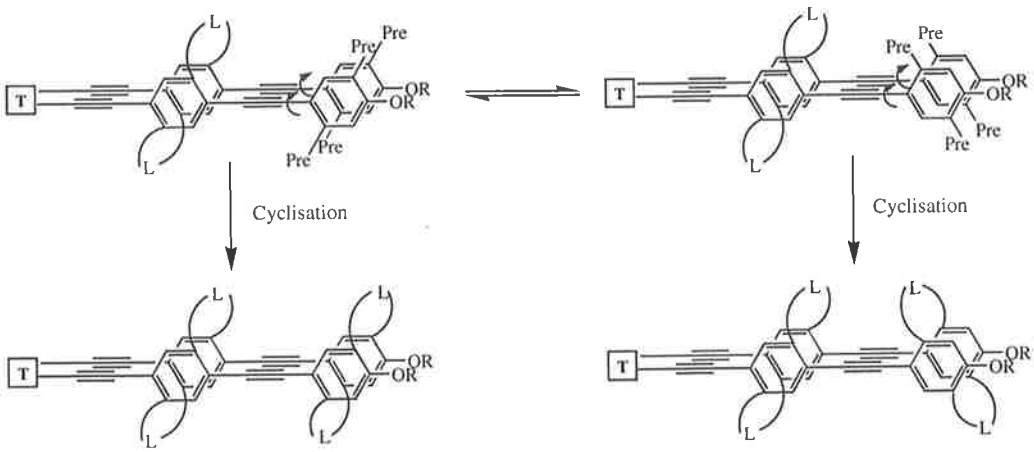


Figure 16. The structural isomers possible.

By using metacyclophanes we effectively remove the problem of regiospecificity completely. The use of monomers with linker-arm precursors in the 2,6-positions will

produce coupled systems where the rotamers are equivalent. This methodology, shown in Figure 17, will lead to only one type of cyclophane structure.

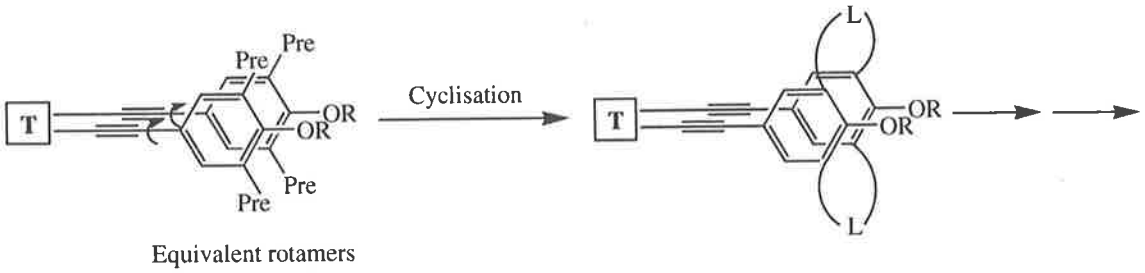


Figure 17. Formation of the 'metacyclophanes'.

The cyclophane systems incorporating only one linker-arm are anticipated to contain similar regiospecificity problems as with the paracyclophane systems. This is shown schematically for a two-unit oligomer in Figure 18. Nevertheless, these one-arm cyclophanes will be synthesised to compare the degrees of planarity and conjugation between the two types of oligomers.

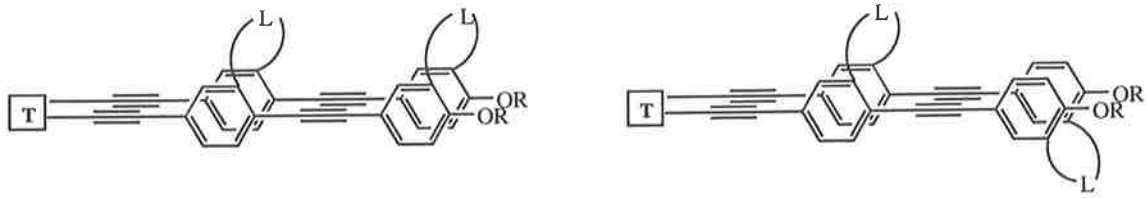


Figure 18. The regiospecificity problems with one-arm cyclophanes.

1.2.6. Templates In Cyclophane Synthesis

A survey of the literature on the use templates for the synthesis of cyclophanes produced few results. Apart from the use of caesium cations in conjunction with high dilution techniques[46] the only other use of templates was by the group of Stoddart *et al.*[47,48,49] In this case, the templates employed are derivatives of hydroquinone,[47] naphthaquinone[49] or ferrocene[48] (Figure 19(a-c)).

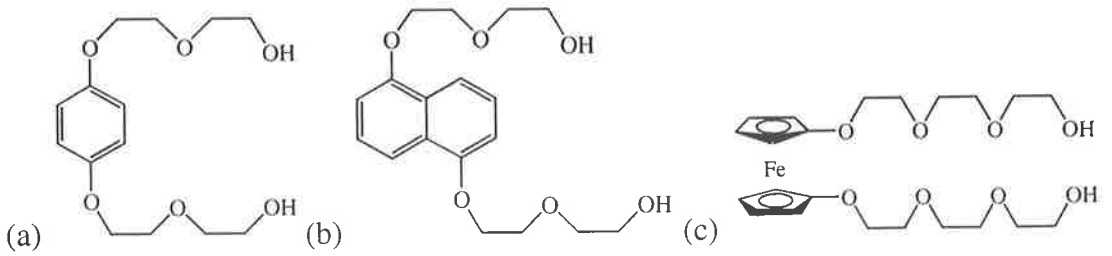


Figure 19. The templates: (a) hydroquinone, (b) naphthaquinone and (c) ferrocene derivatives.

These templates were used to form various cyclophanes based around bipyridium units of the type shown in Figure 20(a-c). Cyclophanes of this type could be produced using these templates in reasonable yields (~30-50%) without the use of high dilution.

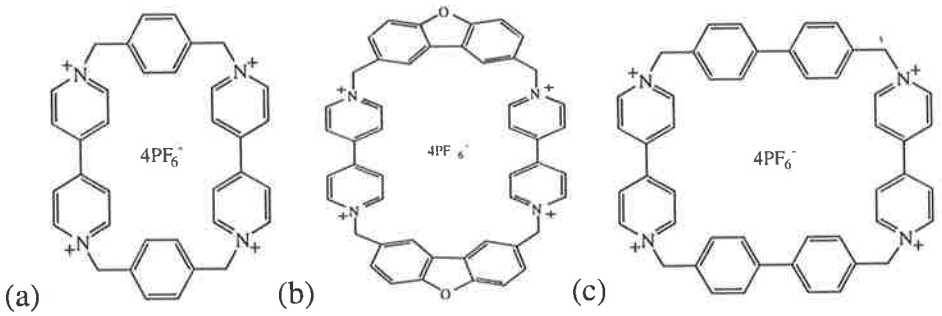


Figure 20. The bis-bipyridium cyclophanes of the Stoddart group (a), (b) and (c).

The templates work by self-assembling the two precursor molecules in solution. This is shown for the hydroquinone template in Figure 21. Two main factors influence this self-assembly, namely i) π–π stacking interactions between the π-electron deficient bipyridium units and the π–electron rich template rings, ii) hydrogen-bonding interactions between the primary hydroxyl groups of the template and the two acidic protons *alpha* to the nitrogen atoms.

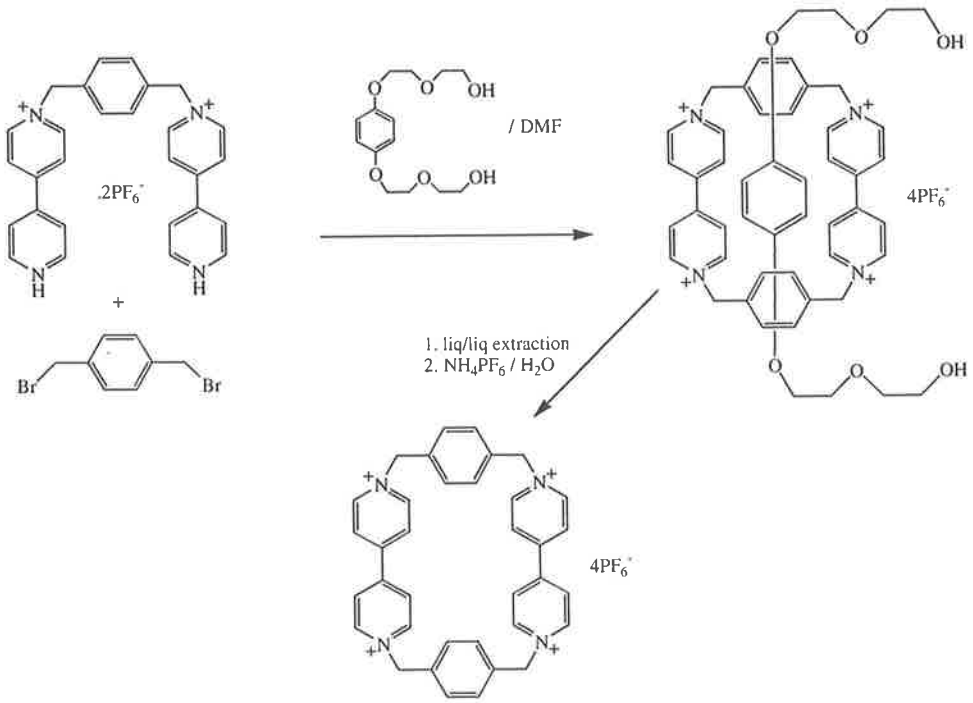


Figure 21. The self-assembly of the templates and substrates in solution.

1.2.7. The Project Templates

The synthesis of the cyclophanes in the previous section relied on non-covalent interactions between the substrates and the templates in solution. Our aim, however, is to employ templates which are covalently bonded to the substrates. This method should produced high yields in the cyclisation step since it doesn't rely on weak dispersive forces or hydrogen bonding.

Various anthracene template systems will be developed and their synthetic utility evaluated. The main structural motif of the templates to be studied is shown below in Figure 22. Where R=H or a non-polar (alkyl containing) group. The introduction of non-polar groups into the template structure may be required with the expectation of solubility problems with the cyclophanes.

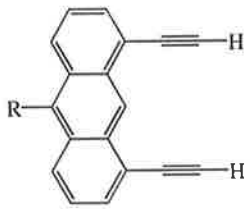


Figure 22. The 1,8-diethynylanthracene with substitution in the 10 position.

Molecular modelling studies will be done to examine the geometries and relative energies of the oligomeric systems, and to make comparisons between the two-arm and one-arm oligomers with regards planarity of the aromatic rings. Similarly, the nature of the linker-arm and its effect on the cyclophane geometries will also be investigated.

1.3. Summary

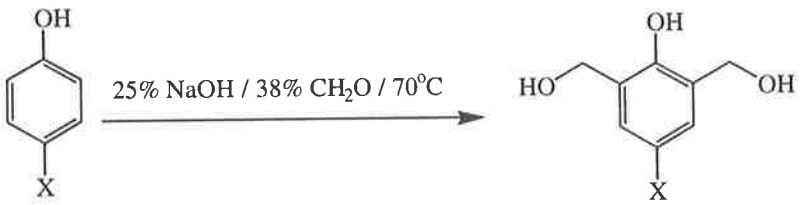
In summary, from the basic theory of third-order NLO, oligomers containing cyclophanes present the possibility of possessing significant nonlinear optical properties including large $\chi^{(3)}$ values. Synthesis of these oligomers will be investigated through the use of specifically engineered templates to increase cyclisation yields through system pre-organisation. The development and utilisation of such templates will ultimately lead to a new methodology for cyclophane formation. Lastly, optical studies performed on the series of oligomers will determine the effects of the restricted rotation between π-systems, the change in oligomer length and the nature of the linker-arm on nonlinearity.

2. The Monomers

The organic chemist is often faced with a multitude of possible pathways for any synthetic goal. The choice of the 'right' pathway is often difficult and can only be made after much experimentation. This reasoning lead to the development of a wide range of monomeric synthons which could, potentially, be used to prepare the desired cyclophane oligomers.

2.1. Introducing Functionality to Phenol Derivatives

Initially, the bis-hydroxymethylation of both *p*-bromo-[50] and *p*-iodophenol was investigated (**Scheme 1**). While the *p*-bromophenol could be bis-hydroxymethylated to give the desired compound (**1**) in a low yield of 14%, the reaction involving *p*-iodophenol produced no isolable material. It was thought that both these phenols underwent extensive polymerisation resulting in low yields of the required product. In the *p*-iodophenol case decomposition of the aryl iodide bond was also a contributing factor.



X=Br, I

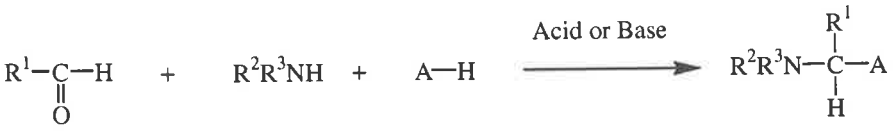
1, X=Br, 14%
2, X=I, 0%

Scheme 1

Clearly, a more practical method for introducing 2,6-functionality had to be found. This was investigated with the formation of bis(morpholinomethyl) compounds, and their subsequent conversion to acetoxymethyl groups.

2.2.1. The Mannich Reaction

Over the years quite a lot of work has been directed towards investigating the scope of the Mannich reaction in both aromatic and aliphatic systems.[51,52] The reaction can be expressed in the following general form (**Scheme 2**), where A-H is a substrate containing an active or substitutable hydrogen.



Scheme 2

Examples of this type of reaction are shown below in Figure 23 with the active hydrogens underlined.[52] The products of these reactions are known as Mannich bases.

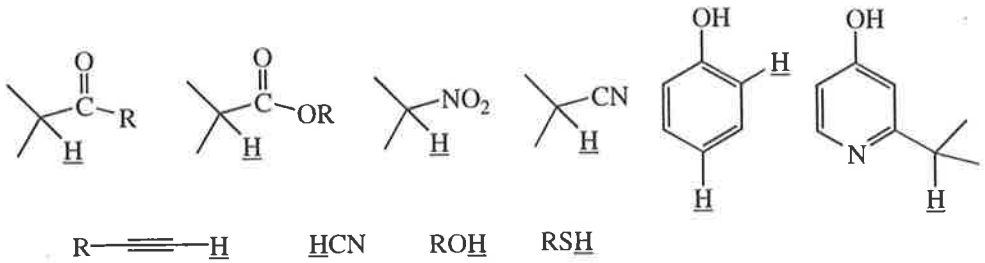
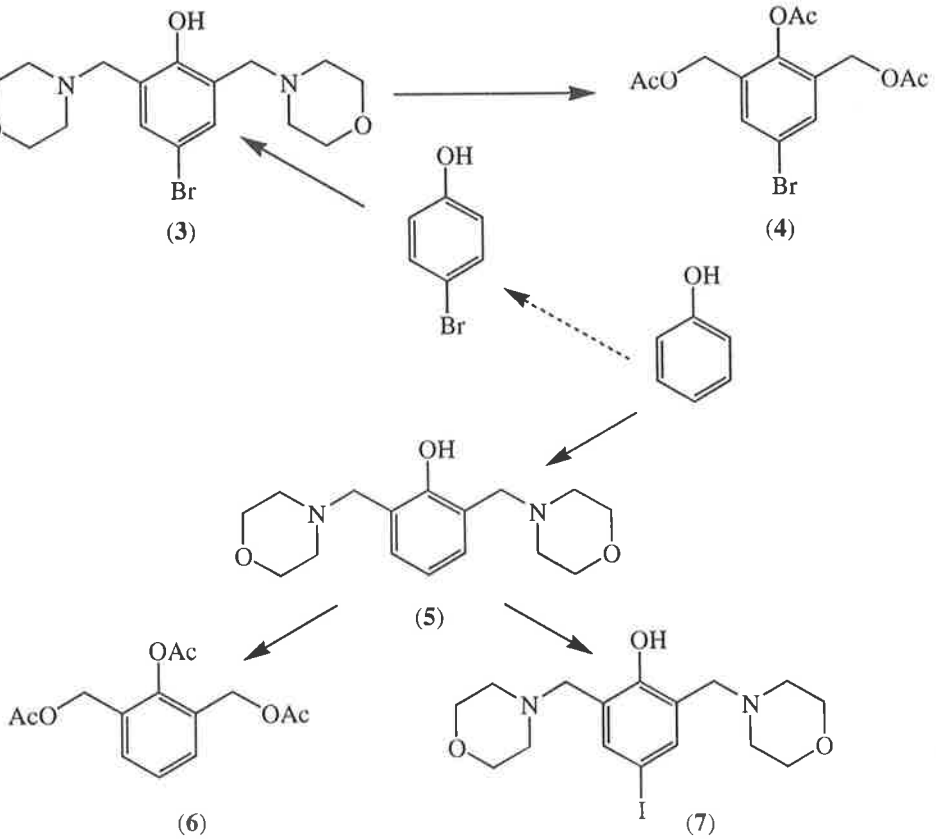


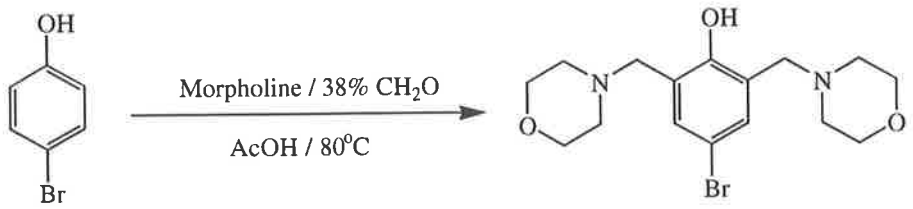
Figure 23. Examples of Substrates for the Mannich Reaction.

The Mannich reaction was then applied to phenol and phenol derivatives in an effort to introduce 2,6-functionality to the aromatic systems. The scope of these Mannich-type reactions is outlined below in **Scheme 3**.



Scheme 3

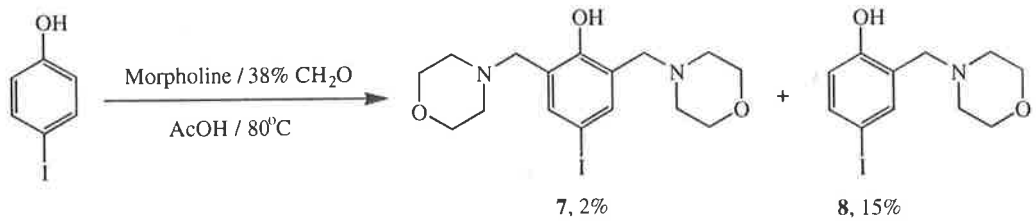
The first route to be investigated was that of *p*-bromophenol (**Scheme 4**). Initially, reaction conditions that had been previously described in the literature were trialed but met with little success.[53] This involved adding morpholine and 38% formaldehyde to an ethanolic solution of *p*-bromophenol. After being allowed to stir overnight, the reaction mixture was heated at reflux with a small amount of concentrated sulphuric acid in an attempt to catalyse the reaction. After five days only starting materials were present by tlc.



3, 82%

Scheme 4

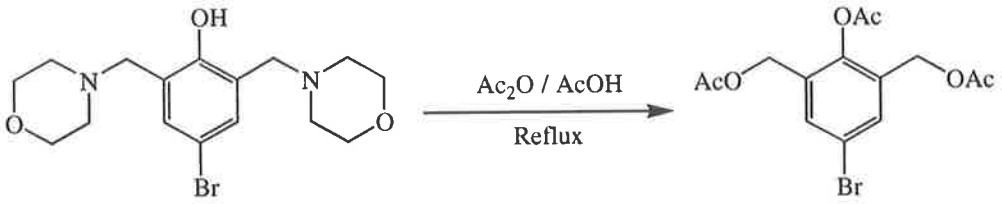
A successful reaction took place when acetic acid was used as both solvent and activator. In this case the desired material (**3**) was isolated in 82% yield in only 6 hours. Unfortunately, application of this procedure to *p*-iodophenol met with little success. The bis-substituted compound (**7**) could only be isolated in 2% yield with the majority of the isolable reaction product being the mono-morpholinomethyl compound (**8**) (**Scheme 5**). The mono-morpholinomethyl compound was isolated in a low 15% yield. This was thought to be due to the decomposition of the starting material since apart from the appearance of baseline material by tlc, the reaction mixture turned from colourless to dark red which may have indicated the formation of iodine. This colour was discharged during the extractive workup when the reaction mixture was washed with a 5% sodium thiosulphate solution. The formation of (**7**) was achieved *via* a different approach, as discussed later.



7, 2% **8**, 15%

Scheme 5

The 2,6-bis(morpholinomethyl)-4-bromophenol (**3**) was then converted through to the corresponding triacetate (**4**) using a modified literature procedure.[53] This conversion could be carried out in a reasonable yield of 64% (**Scheme 6**).

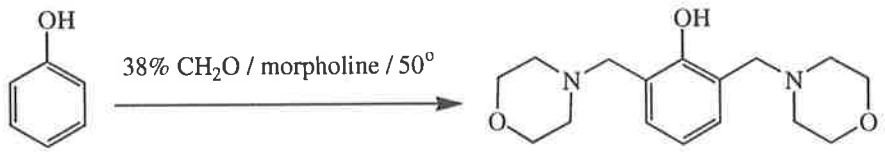


(**3**) **4**, 64%

Scheme 6

2.1.2. Ortho Selectivity with the Mannich Reaction

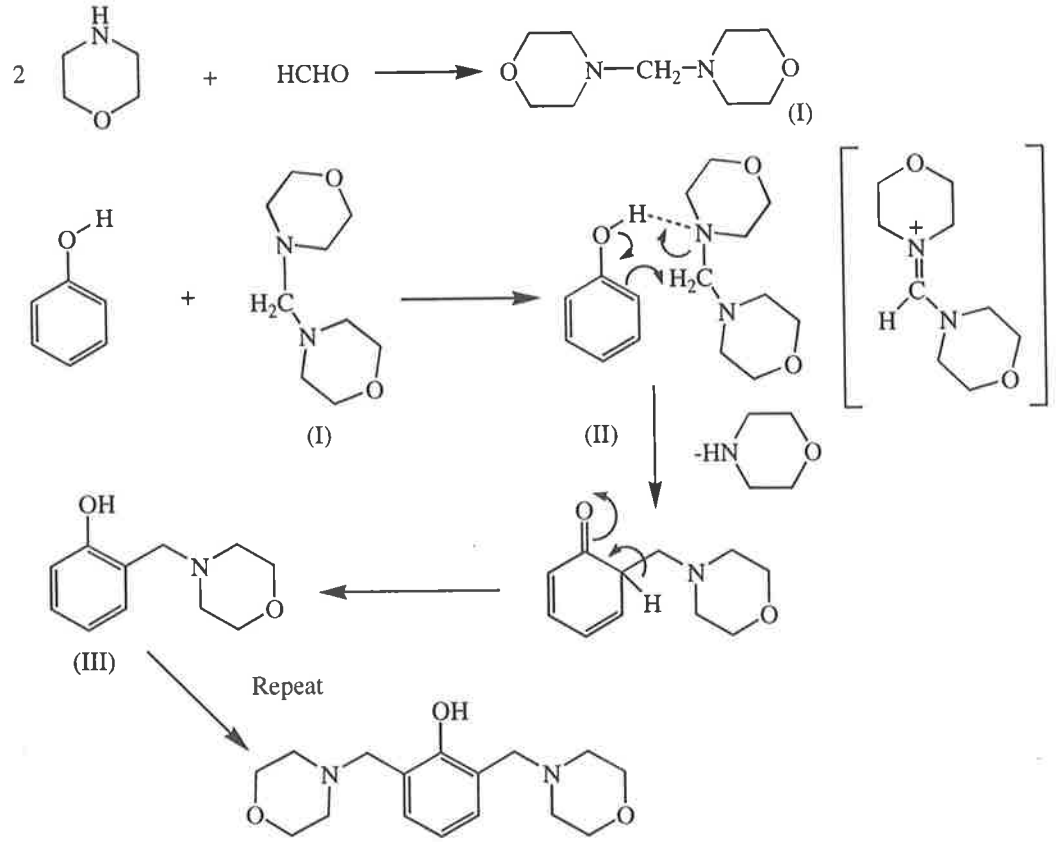
In considering phenolic systems, the first substitutions are known to proceed in the 2 and 6 positions.[51,54] A mechanism to rationalise this preference for ortho substitution, at high pH, has been established in the literature.[55] This led us to investigate the formation of 2,6-bis(morpholinomethyl)phenol (**5**). The purified yields for the production of the phenol (**5**) were between 20-30% and although low, they were repeatable with the lower yields being observed for the larger scale (~60g) preparations (**Scheme 7**).



5, 20-30%

Scheme 7

The mechanism for the above reaction, incorporating the established mechanistic results, is outlined below in **Scheme 8**.[55]



Scheme 8

This reaction proceeds *via* the initial formation of a methylenebisamine (I, **Scheme 8**) which has been shown to be the rate determining intermediate.[55] The methylenebisamine can then hydrogen bond to the phenol and the reaction then proceeds *via* a quasi six-membered transition state (II, **Scheme 8**) to ultimately give the ortho substituted system (III, **Scheme 8**). For the second substitution to produce 2,6-bis(morpholinomethyl)phenol (**5**), this mechanism is simply repeated.

It has been noted in the literature that these types of Mannich bases can possess reverse solubility, i.e. they are more soluble in cold water than hot.[56] This has been observed for the tri-substituted phenol (**9**), shown in Figure 24.[56] The low yields associated with the formation of the bis-substituted phenol (**5**) can be explained by this phenomenon as the phenol was precipitated from a cold solution.

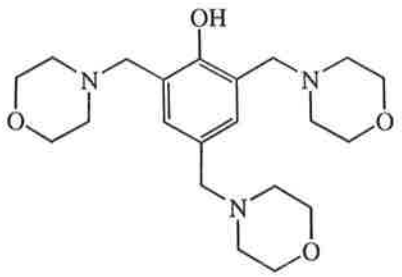
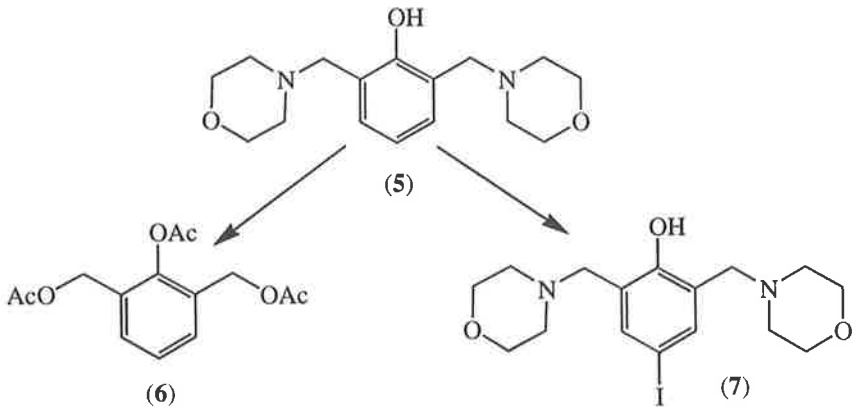


Figure 24. The tri-substituted phenol (**9**).

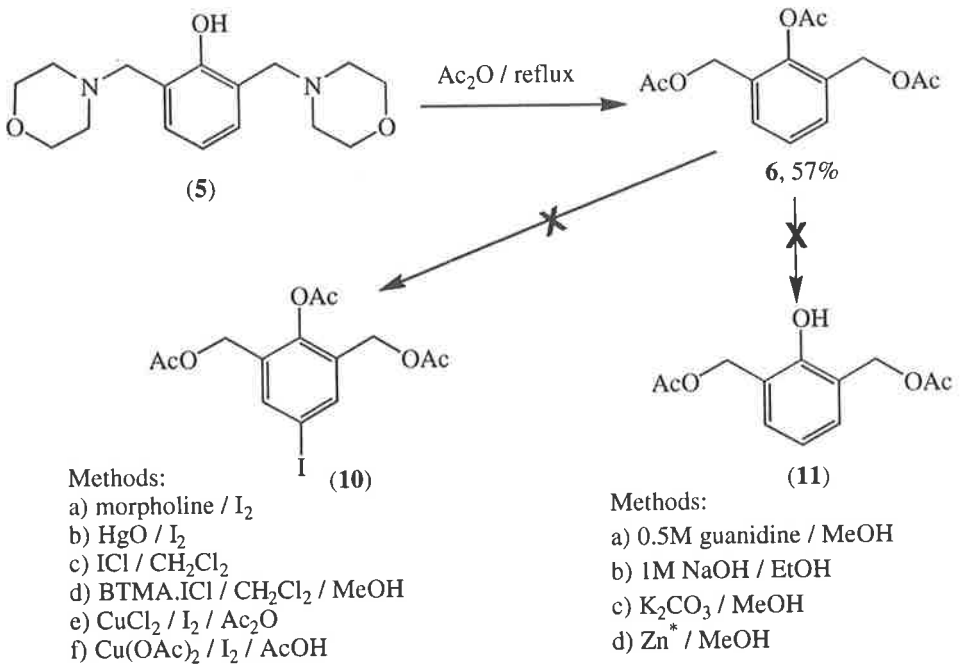
2.1.3. Derivatives of the Mannich Bases

The formation of the bis-substituted phenol (**5**), in multi-gram quantities, made a variety of synthetic routes accessible. The two main routes that were investigated are shown in **Scheme 9**.



Scheme 9

Firstly, the phenol (**5**) was converted through to the triacetate (**6**).[57] This was achieved by refluxing the phenol (**5**) in acetic anhydride to give the triacetate in 57% yield. At this stage experiments were performed to iodinate the triacetate (**6**). Various reagent combinations were tried that had previously worked on phenols and aromatic ethers in the literature.[58,59,60,61,62] All methods were totally unsuccessful in converting the triacetate (**6**) into the aryl-iodide (**10**), the triacetate remaining unchanged under the conditions used (**Scheme 10**).



Scheme 10

Attempts were then made to deacylate (**6**) to the corresponding phenol (**11**) (**Scheme 10**). The greater electron donating ability of the phenol as compared to that of the acetylated phenol, would have significantly assisted the electrophilic substitution reaction. Unfortunately, the triacetate (**6**) either polymerised under strongly basic conditions, 0.5M guanidine in methanol and 1M NaOH, or no selectivity could be achieved in using the milder K_2CO_3/methanol and activated zinc/methanol techniques. Polymerisation for these type of systems under basic conditions has been encountered before, with the tetra-acetate (**12**), Figure 25, forming a resin.[56] A rationale of how this occurs has yet to be established. However, consultation of the literature showed that this phenomenon has been used commercially with the tri-acetate (**6**), in forming resins under strongly basic conditions.[57]

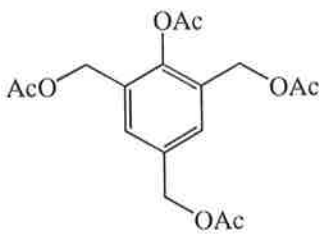
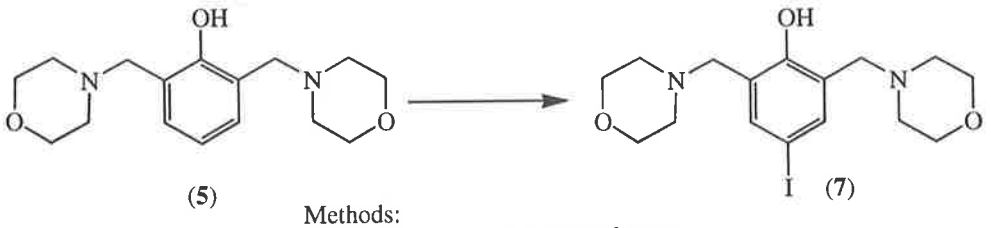


Figure 25. The tetra-acetate (**12**).

Pursuit of this pathway has been suspended at this stage, although hydrolysis in acidic media has yet to be investigated.

The other route investigated with the 2,6-bis-substituted system (**5**) was the direct iodination to form 2,6-bis(morpholinomethyl)-4-iodophenol (**7**). This could be achieved by using either a combination of NaI/*t*-BuOCl in acetonitrile[63] or NaI/Chloramine-T in dimethylsulphoxide.[64] Both of these methods gave the desired compound (**7**) in yields of 33% and 68% respectively (**Scheme 11**).



(**5**) (**7**)

Methods:
a) NaI / t-BuOCl / CH_3CN / 0°, 33%
b) NaI / Chloramine-T / DMSO / 50°, 68%

Scheme 11

Recrystallisation of compound (**7**) from hexane gave crystals of sufficient quality for x-ray analysis (Figure 26), and showed strong hydrogen bonding between the phenolic proton and one of the nitrogens of a morpholine ring.[65]

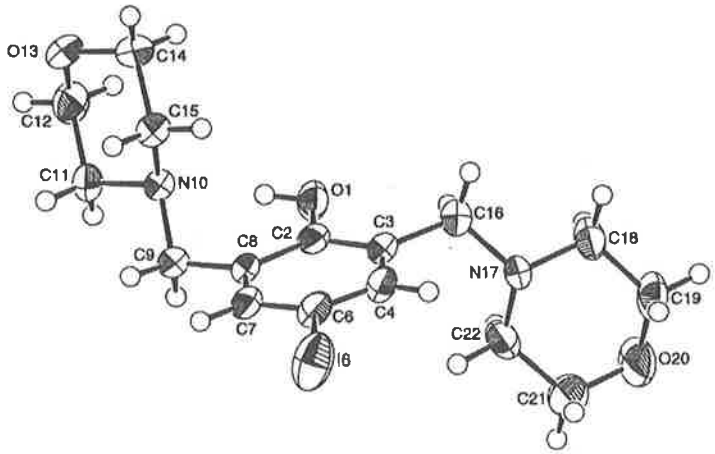
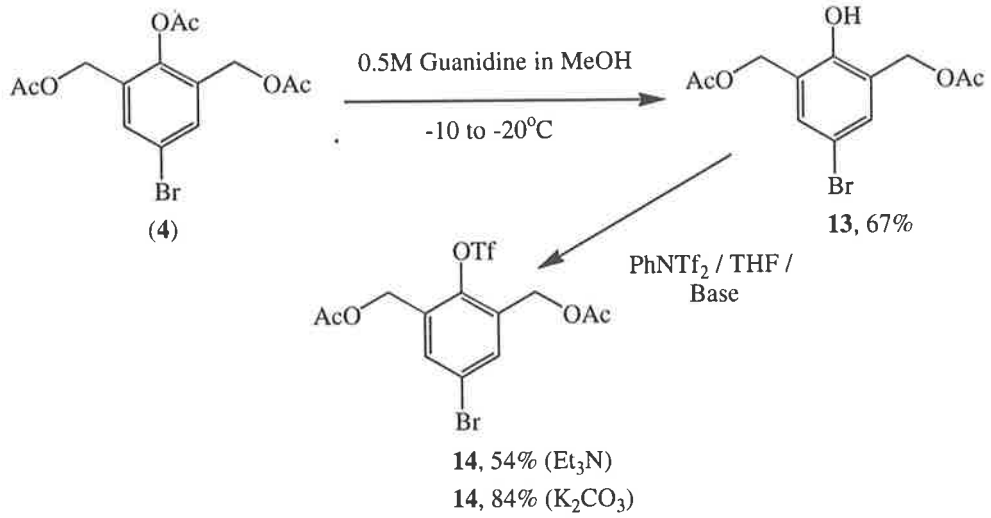


Figure 26. The x-ray structure of compound (**7**).

Conversion of the phenol (**5**) to the corresponding triacetate was not attempted since cleavage of the aryl-iodide bond was expected with heating. Nevertheless, this substrate proved to be synthetically useful since it could be coupled directly to a template system and the functionality manipulated to a large extent. These results are discussed in detail in Sections 4.2 and 6.1 respectively.

2.1.4. Triflation Studies

The triacetate (**4**) at this stage may be suitable for coupling to the templates but additional work was done to convert the masked phenol into the corresponding triflate (**14**). This process was achieved using the following reaction sequence (**Scheme 12**).



Scheme 12

To convert the triacetate (**4**) to the triflate (**14**) involved the selective deacylation of the phenol. This could only be achieved using a methanolic guanidine solution at -10 to -20°C.[66] At higher temperatures selectivity was lost. Traditionally mild methods for cleaving acetates, which included 5% or 10% citric acid and activated zinc in methanol, gave no selectivity.[67] Once the free phenol (**13**) had been formed, it was easily converted to the triflate (**14**) using the mild triflating agent N-phenyltriflimide and a base, either triethylamine or potassium carbonate.[68] Palladium catalysed couplings of the triflate (**14**) to the template systems could now be investigated, where we would expect selective coupling in the 4-position over the 1-position, based on steric factors. Details of this can be found in Section 4.2.3.

The IR spectrum of the phenol (**13**) was interesting in the respect that four absorptions in the carbonyl region were observed. These signals appeared at 1745, 1734, 1712 and 1693 cm^{-1}. The last two signals are lower than normal for an ester (1730-1715 cm^{-1}) due to hydrogen bonding of phenol to the adjacent oxygen of the ester (Figure 27).[69] Hydrogen bonding to the non-carbonyl oxygen was thought to be preferred as this interaction forms a more stable six-membered ring, rather than the eight-membered alternative. The matter was further complicated with what was thought to be Fermi resonance, doubling the number of expected signals from two to four.[70] Further

examples of hydrogen bonding of phenols to nearby esters are to be seen in the following sections.

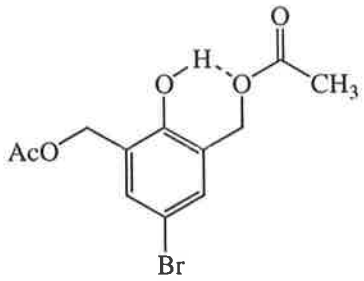
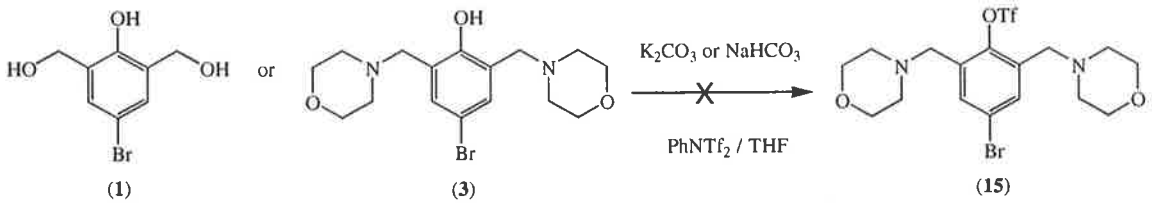


Figure 27. Hydrogen bonding present in the phenol (**13**).

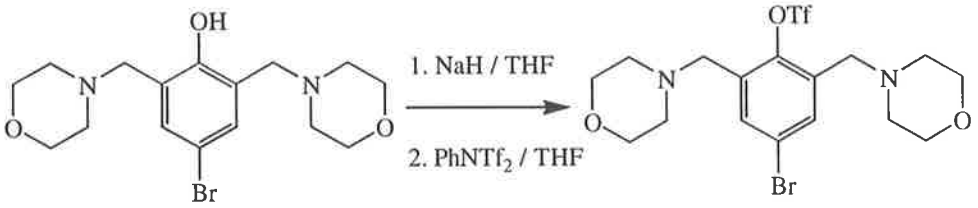
Mild triflation conditions were also applied to the 2,6-bis(hydroxymethyl)-4-bromophenol (**1**) and 2,6-bis(morpholinomethyl)-4-bromophenol (**3**) systems (**Scheme 13**). In both cases mild bases such as K_2CO_3 and $NaHCO_3$ were used along with $PhNTf_2$. These systems both failed to give any of the desired triflate (**15**).



(1) (3) (15)

Scheme 13

This lack of reactivity was thought to be due to the phenolic hydrogen of both (**1**) and (**3**) forming strong hydrogen bonds to the nearby heteroatoms. This spatial arrangement of the substrate makes attack of the base all the more difficult. A stronger and more nucleophilic base, sodium hydride, was reacted with (**3**) and the corresponding phenoxide trapped with $PhNTf_2$. This method was successful in giving the triflate (**15**) in 55% yield (**Scheme 14**).

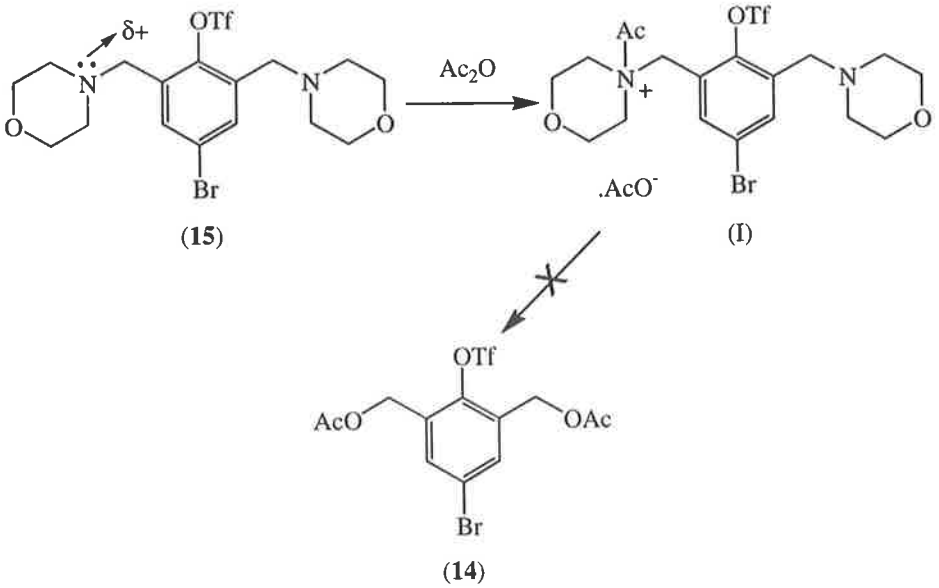


(3) **15**, 55%

Scheme 14

Conversion of the triflate (**15**) to the bis-acetoxymethyl compound (**14**) was then attempted by two methods. The first method involved refluxing the triflate (**15**) in acetic anhydride and a catalytic amount of acetic acid, and the second method involved

refluxing the triflate (**15**) in acetic anhydride along with a small amount of DMAP as a catalyst. In both cases no reaction was observed by tlc, the reaction conditions leaving the triflate unchanged. These reaction conditions favour S_N1 reactions,[71] under which the nitrogen of a morpholine ring may initially undergo acetylation to form the intermediate (I, **Scheme 15**). Subsequent heterolytic cleavage of the benzylic carbon-nitrogen bond would produce a benzylic carbocation. Comparison of the substrates of **Scheme 6** and **Scheme 15** indicated that the carbocation character of the benzylic carbon would be stabilised less by the electron withdrawing triflate, which was directly attached to the ring, than the electron donating hydroxyl group of the phenol. This suggested that the benzylic carbon-nitrogen bond of the triflate (I, **Scheme 15**) would undergo heterolytic cleavage less readily than the analogous intermediate for the phenol (**3**) thereby making the eventual transition to (**14**) unfavourable. It was expected that an analogous intermediate existed for the phenol (**3**) as the nitrogen was expected to be acetylated first rather than the phenol, due to its increased nucleophilicity.

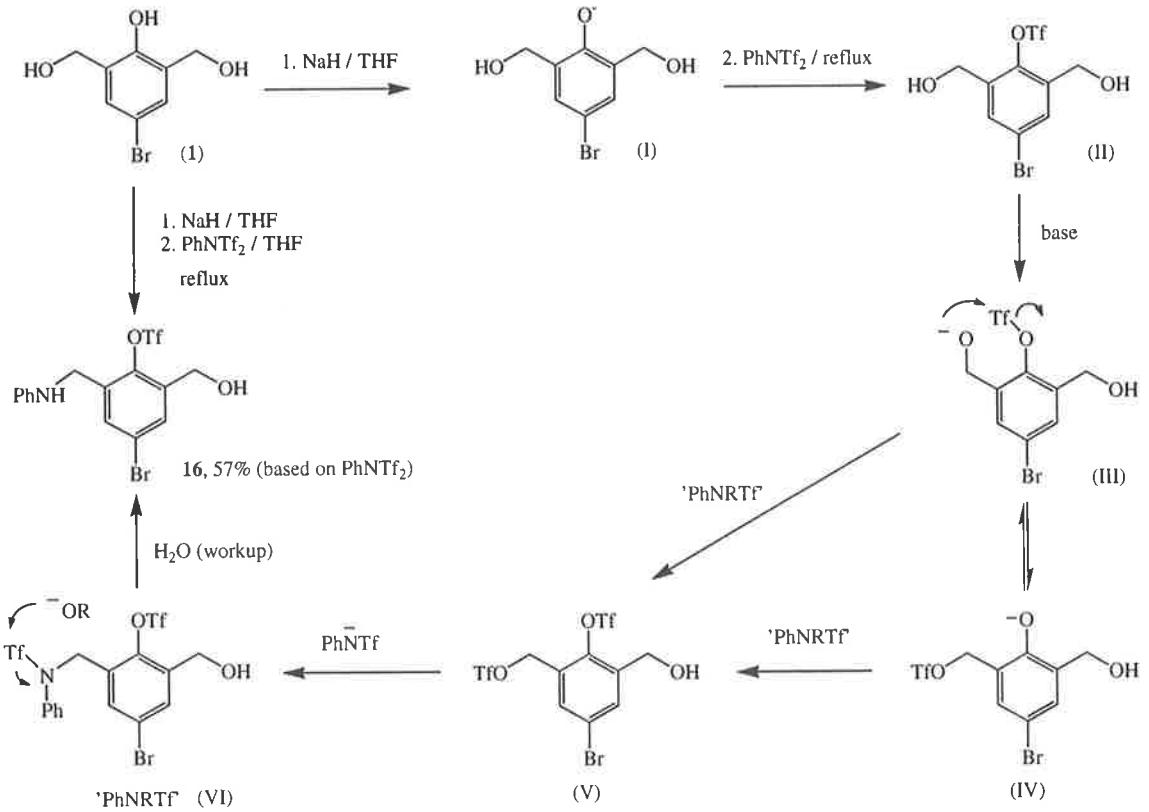


(**15**) (I) (**14**)

Scheme 15

The triflation of the bis-hydroxymethyl phenol (**1**) was investigated next. Application of the same reaction conditions as for (**3**) (1 equiv. NaH and 1.05 equiv. $PhNTf_2$) led, surprisingly, to the formation of the anilinomethyl triflate (**16**) in 57% yield based on N-phenyltriflimide. However, the formation of triflate (**16**) can be rationalised in the following manner (**Scheme 16**). Initially, reaction of (**1**) with NaH gave the phenoxide (I, **Scheme 16**). This was then trapped with $PhNTf_2$ to initially form the triflate (II, **Scheme 16**). At this stage the reaction mixture was still basic due to the

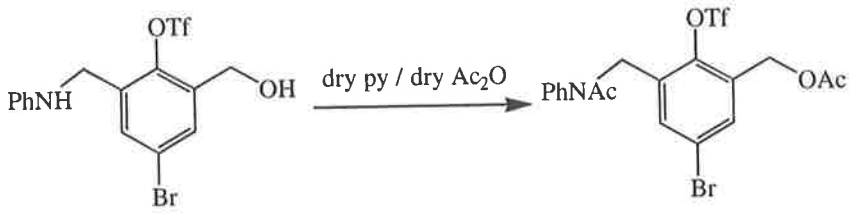
presence of left-over NaH and so one of the hydroxymethyl groups could also be triflated. This could be effected by intramolecular transfer of the triflate from the phenol to the hydroxymethyl group or by triflation through reaction with (VI, **Scheme 16**). In either case, the proposed intermediates (I-IV, **Scheme 16**) lead to the bis-triflate (V, **Scheme 16**), which could undergo attack by $Ph\bar{N}Tf$ producing intermediate (VI, **Scheme 16**), a possible triflating agent. It was unlikely that (VI, **Scheme 16**) was hydrolysed on workup as N-phenyltriflimide itself is stable to water for short periods of time. This suggested that the triflate (VI, **Scheme 16**) was consumed in the reaction, acting as a triflating reagent. The intermediate (VI, **Scheme 16**) could not be isolated and only the anilinomethyl compound (**16**) was the major product of the reaction, apart from baseline material.



Scheme 16

To confirm the structure of the anilinomethyl triflate (**16**), which was a colourless oil, an attempt was made to convert it to the diacetyl derivative (**Scheme 17**) which might have formed crystals suitable for x-ray analysis. Consequently, the anilinomethyl triflate (**16**) was acetylated under standard conditions by stirring it in a mixture of dry pyridine and dry acetic anhydride at room temperature. This gave the diacetyl derivative (**17**) in excellent yield. However, the derivative was a colourless oil

and could not be crystallised. Whilst the reaction outlined in **Scheme 16** showed that discrimination between the two hydroxymethyl arms of phenol (**1**) could be achieved, this class of monomers was not pursued any further due to the involved nature of their synthesis.



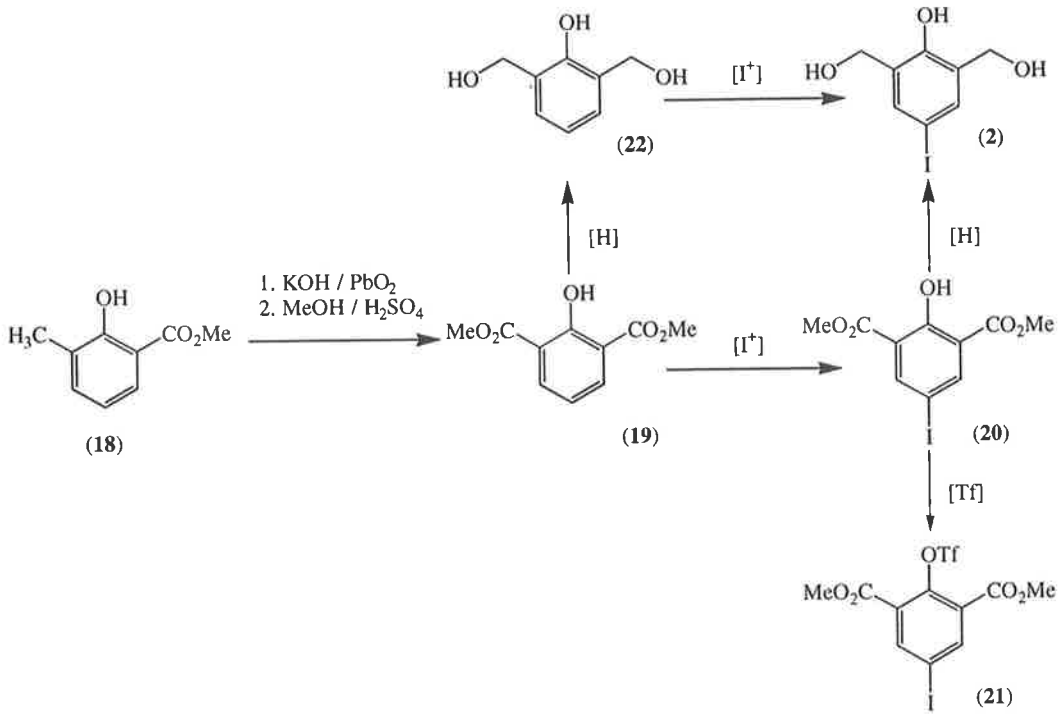
(**16**) **17**, 93%

Scheme 17

2.2. Isophthalate Derivatives

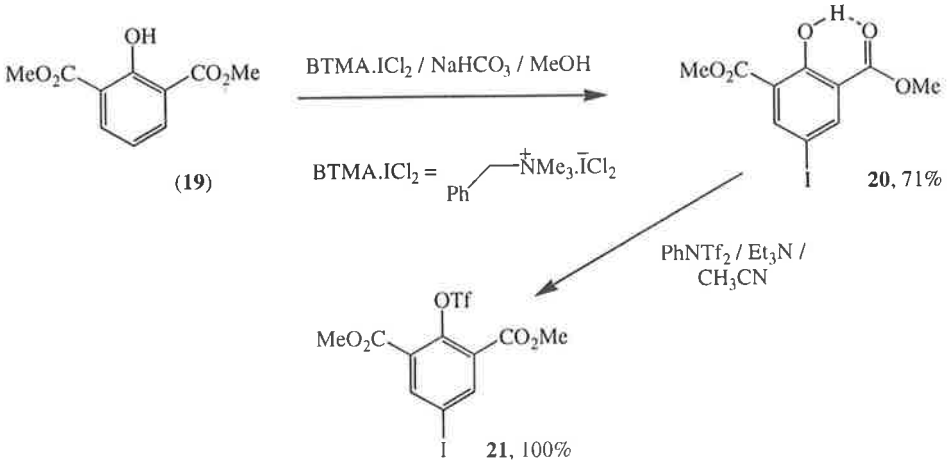
The isophthalate structure proved to be an excellent entry into a wide range of monomer compounds. Most compounds described in this section were based on 2-hydroxyisophthalic acid; the remainder on isophthalic acid itself.

The parent compound for this series of monomers was dimethyl 2-hydroxyisophthalate (**19**). This compound could be prepared from commercially available 2-hydroxy-3-methyl benzoic acid (**18**), in sizeable quantities, by literature procedures.[72,73] This material was quite synthetically flexible for several reasons. Firstly, the two ester groups could be reduced at various stages to the corresponding hydroxymethyl groups, for use as linker-arm precursors. Secondly, the phenol (**19**) could undergo direct iodination in the 5-position, for Pd catalysed coupling chemistry. Lastly, the iodo-phenol (**20**) could be converted to the triflate (**21**) for further Pd coupling. This shown schematically in **Scheme 18**.



Scheme 18

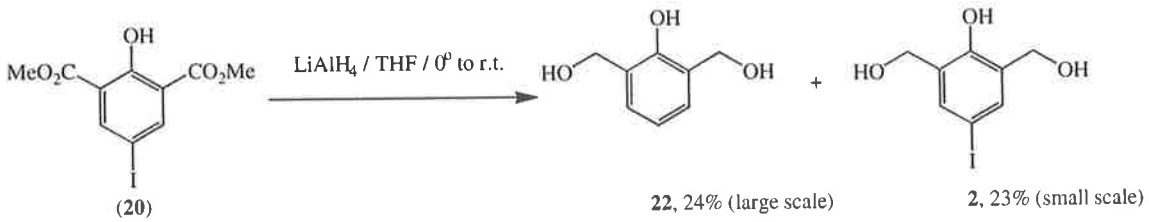
The iodination of diester (**19**) initially proved quite tricky. Several attempts at iodination, using standard literature procedures met with no success. These included: Chloramine-T/NaI in DMF, I_2/$NaHCO_3$ in methanol and *t*BuOCl/NaI in acetonitrile. In all cases, no reaction was observed at all. However, when the reagent BTMA.ICl_2[74] was used the iodinated product (**20**) could be isolated in 71% yield (**Scheme 19**). Conversion of the phenol was performed using N-phenyltriflimide and triethylamine in acetonitrile to the corresponding triflate (**21**) in a quantitative yield (**Scheme 19**). The coupling of triflate (**21**) to the standard template is discussed in Section 4.2.3.



Scheme 19

The IR spectrum of aryl-iodide (**20**) showed two distinct carbonyl absorptions at 1733 and 1681 cm^{-1}. As mentioned in a previous section, the lower absorption was indicative of hydrogen bonding of the phenol to an adjacent oxygen of the ester group, forming a six-membered ring. Two signals were also observed for the triflate (**21**), but this was thought due to Fermi resonance. Proton and carbon NMR spectra were consistent with the structures of the aryl-iodide (**20**) and the triflate (**21**), as were their microanalytical data.

The aryl-iodides (**20**) and (**21**) could now be coupled directly to the templates, and their ester groups reduced at a later stage or these groups could be reduced beforehand. This was attempted with the direct reduction of diester (**20**) with lithium aluminium hydride in THF at 0° (**Scheme 20**). An excess of reducing agent was used since the phenol reacts with the hydride source. On a small 20 milligram scale the reduction worked reasonably well provided that after the diester was added to the LAH, the suspension was allowed to warm gradually to room temperature over 3 hours. By NMR, integration of the benzyl peaks gave the ratio of 5-iodo (**2**):5-H (**22**) of 11:1. However, on a larger 300 milligram scale, under the same conditions, the ratio was reversed and increased to (**2**):(**22**)/1:29. The yields for the reduction were low too, due to the compounds streaking significantly on silica and having poor solubility in the chromatography solvents.

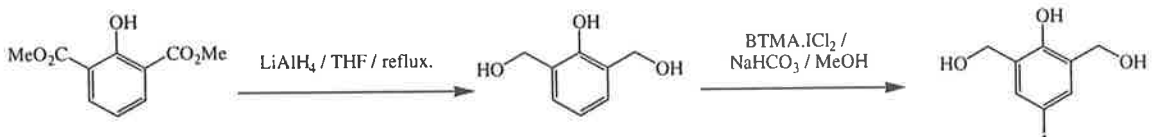


Scheme 20

A more successful approach for the formation of (**2**) was to perform the reduction on the parent diester (**19**) first, to form the intermediate (**22**), followed by iodination to give the aryl-iodide (**2**). This sequence is shown in **Scheme 21**. Reduction of diester (**19**) proceeded well with LAH in THF at reflex to give the phenol (**22**) in very high yields. This reduction was based on a modified literature procedure where the acetate of (**19**) was used for solubility in ether, along with LAH.[75] It was found that the lithium aluminium salts initially formed from the reaction of the phenol with LAH, were insoluble in ether which led to very low yields of product. However, by acetylating

phenol (**19**) ether solubility during the course of the reaction was maintained, enabling smooth reduction to the phenol (**22**). Our use of THF instead of ether eliminated these solubility problems, and so acetylation of (**19**) was not required. Iodination of the phenol was straightforward using the same conditions as for the diester (**20**) to give the aryl-iodide (**2**) in 89% yield (**Scheme 21**).

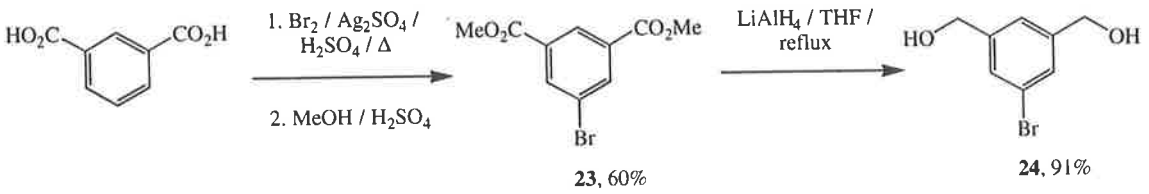
Of interest with the phenol (**22**) was enantiotropic polymorphism was observed with its melting point.[75] This is where there exists two (or more) crystalline forms which interchange reversibly on changing the temperature, and each form has its own stability range of temperature.[76] On heating, two distinct melting points were observed. The sample initially melted at 94.5-95.5°, and if the sample was removed from the hot-stage at this point, it crystallised immediately and melted at 98.0-99.0°. If this second form was removed at or above 99.0°, the sample crystallised slowly over 20 mins and melted at 94.0-95.0°, consistent with the first form. The published melting points were 94.7-95.2° for the first form and 98.2-98.4° for the second. The cycle could also be repeated on the same sample several times, and either form could be obtained at will.[75] This phenomenon was not observed for the phenols (**1**) and (**2**).



(**19**) **22**, 94% **2**, 89%

Scheme 21

A series of simpler monomers based on isophthalic acid were prepared to be used as trial systems throughout this work. Monomers based on the parent isophthalic acid underwent slightly different chemistry (**Scheme 22**). Initially, isophthalic acid was converted to dimethyl 5-bromoisophthalate (**23**) using a standard literature procedure.[77] This monomer could be directly coupled to the templates (Section 4.2.2) or the ester groups could be reduced beforehand. The reduction was performed to give the aryl-bromide (**24**) again using a standard literary procedure.[77]

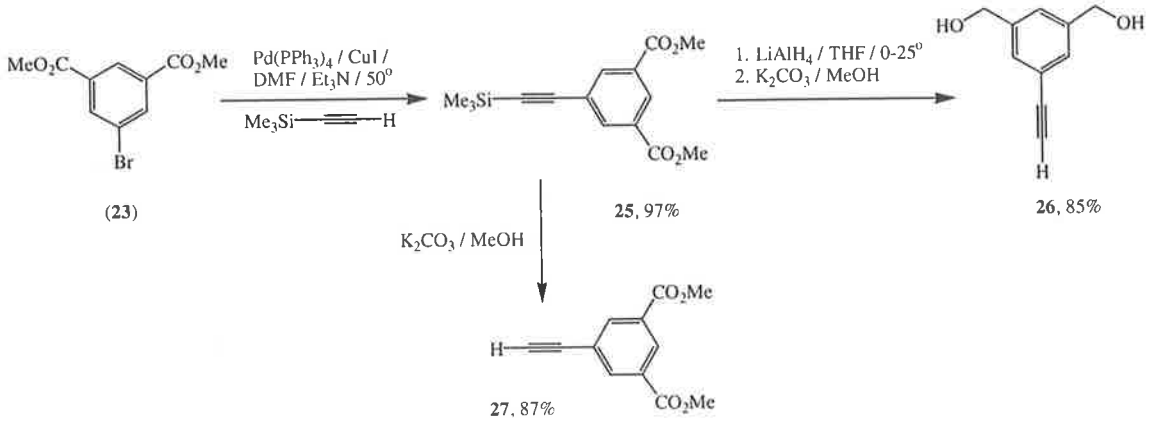


23, 60% **24**, 91%

Scheme 22

Monomers which were to be coupled to the 1,8-diiodo-10-methoxyanthracene template required the incorporation of a free ethynyl group. For the isophthalic system this was achieved with the synthesis of the bis-hydroxymethyl compound (**26**), shown in **Scheme 23**. The ester was initially coupled to trimethylsilylacetylene using standard Pd coupling chemistry to give the silyl-protected acetylene (**25**) in an excellent yield (for more detail on Pd catalysed coupling chemistry see Chapter 4).[78] The final steps involved selective reduction of the esters to the corresponding alcohols followed by mild deprotection of the acetylene using potassium carbonate in methanol. This gave the terminal alkyne (**26**) in a good yield of 85% for the two steps.[78] Reduction was performed at 0-25° to remove any possibility of reduction of the triple bond. Under these conditions complete selectivity was achieved. The terminal alkyne (**26**) is known in the literature, however it was synthesised from dimethyl 2-hydroxyisophthalate *via* the triflate.[78] The coupling of the bis-alcohol (**26**) is discussed in Section 4.3.

The last compound to be synthesised in this series was the terminal alkyne (**27**) (**Scheme 23**). The silyl-protected alkyne (**25**) was deprotected to the terminal alkyne (**27**) under the mild conditions of potassium carbonate in methanol with good yield. A coupling reaction involving this compound is described in Section 4.2.3.



(**23**) **25**, 97% **26**, 85%

27, 87%

Scheme 23

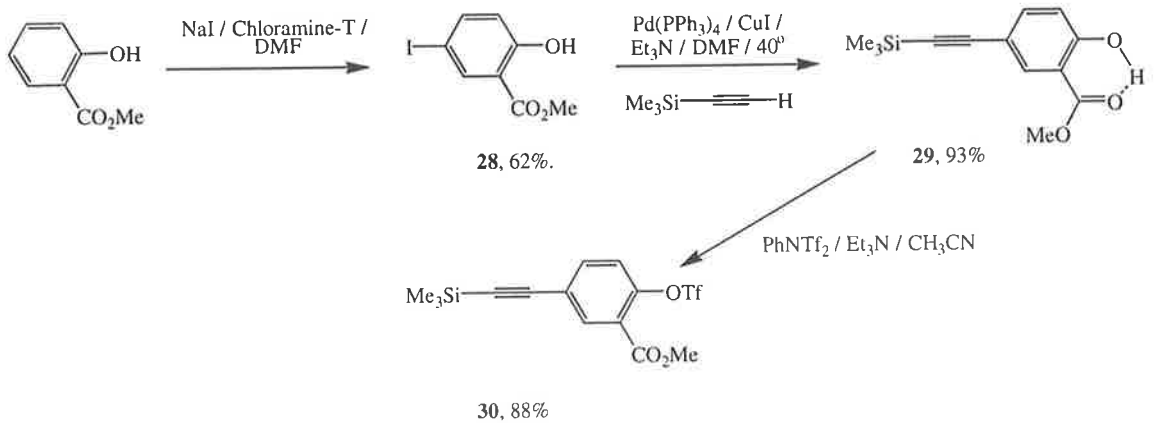
2.3. One-arm Monomers

The synthesis of the one-arm monomers was based around two key commercially available compounds, namely methyl salicylate and 3-iodobenzoic acid. The methyl salicylate derivatives had ethynyl groups introduced into the 4-position *via* the iodide since these one-arm compounds were mainly being coupled to the 1,8-diiodo-10-methoxyanthracene template. The 3-iodobenzoic acid derivatives were used as simple test compounds for the more complex salicylate monomers, and also for 'end-capping' some of the oligomer systems (Section 4.3.1).

2.3.1. The Salicylate Monomers

To introduce ethynyl groups to salicylate structure, methyl salicylate was firstly iodinated (**28**)[64] using a standard literature procedure and then coupled with trimethylsilylacetylene using standard Pd catalysed coupling chemistry to give the phenol (**29**).[79] More details on Pd catalysed coupling reactions can be found in Chapter 4. The coupling reaction was sluggish at room temperature (taking over 16 hrs to complete) and so a slightly elevated temperature of 40° was necessary to drive the reaction. Under these conditions the reaction was complete in 2 hrs. The IR spectrum of phenol (**29**) showed a lower than expected carbonyl absorption at 1681 cm^{-1}. This was due to hydrogen bonding of the phenolic proton to the nearby carbonyl group of the ester, which is known to lower carbonyl absorptions.

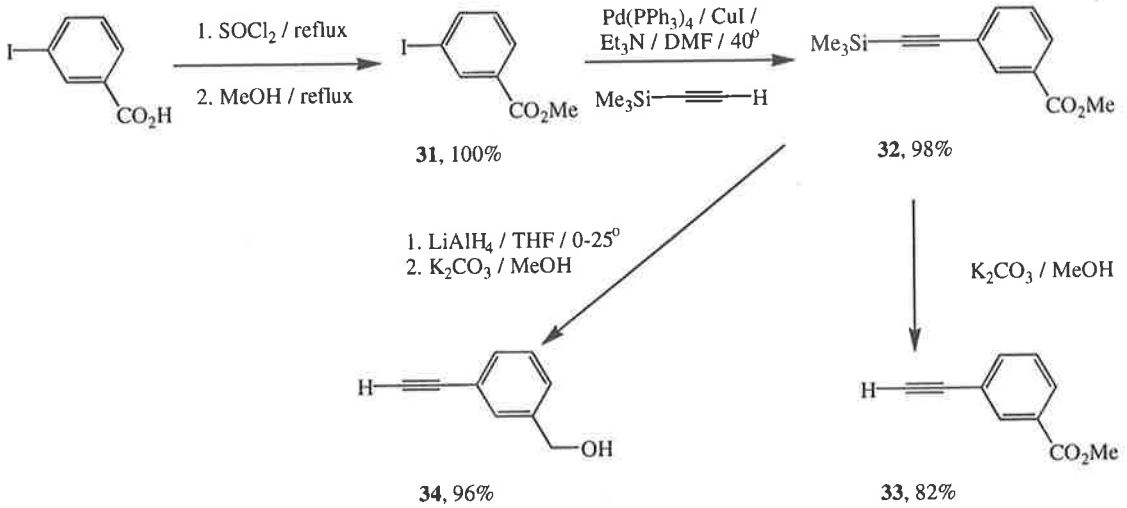
The phenol was then converted to the triflate using N-phenyltriflimide to give the highly functionalised triflate (**30**) which was used in the Section 4.3.1 for building the oligomer molecules.



Scheme 24

2.3.2. The 3-Iodobenzoic Acid Derivatives

Different chemistry was employed with the 3-iodobenzoic acid derivatives. The acid was initially esterified using standard procedures to give the methyl ester (**31**)[80] which was then coupled with trimethylsilylacetylene using the same conditions as for the phenol (**29**) to give the ester (**32**).[81] The ester was then used to synthesise two discrete monomers: the ester (**33**)[81] and the alcohol (**34**)[82], both of which contained unmasked ethynyl groups (**Scheme 25**). Compounds (**32-34**) are known in the literature however slightly different starting materials were used in all cases.



Scheme 25

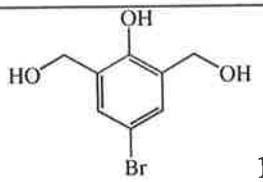
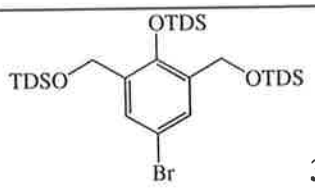
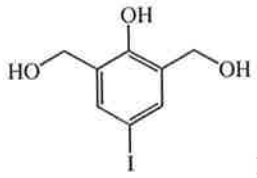
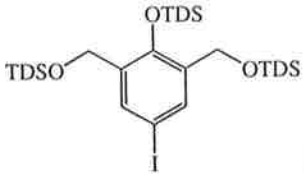
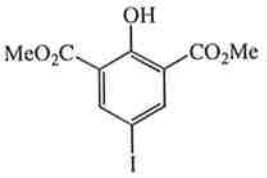
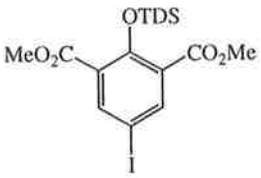
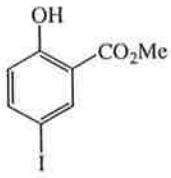
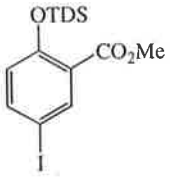
The trimethylsilylalkyne (**32**) was easily deprotected using potassium carbonate in methanol to give the ester (**33**) in good yield. The alcohol (**34**) was produced by firstly reducing the ester with lithium aluminium hydride in THF at 0-25° followed by deprotection of the crude intermediate alcohol by potassium carbonate in methanol. This gave the terminal acetylene in 96% yield for the two steps. Of note with this compound was that the methylene protons split into a doublet (*J* 5.6 Hz) due to coupling with the hydroxyl proton. No coupling was observed for the hydroxyl proton (broad singlet).

2.4. Protecting the Monomers

Results discussed in Chapter 4 showed that monomers had to possess non-polar solvating groups to make the monomer-template coupled systems easier to handle. This was achieved for a variety of monomers by converting the polar OH groups of the phenols and hydroxymethyl groups to the corresponding dimethylthexylsilyl (TDS) and

tert-butyldimethylsilyl (TBDMS) protected species. The results of these reactions are presented in Table 1. These reactions in general were straightforward using a slight excess of the silylating reagent and imidazole in dry DMF. Mild heating was required for substrates possessing hydroxymethyl groups (entries 1,2 and 4, Table 1), as silylation at room temperature for these substrates was slow. The formation of *t*-butyldimethylsilyl (TBDMS) ethers could also be achieved (entry 4, Table 1). In this case, the reaction was complete in 4 hrs with mild heating. Silylation of the phenols (**20**) and (**28**) did not require heating and could be performed at room temperature in 1.5-2 hrs with excellent yields. The difference in rate of reaction was clearly related to the pK_a of the hydroxyl groups, with the phenols being much more acidic (pK_a~8-11) than the hydroxymethyl groups (pK_a~16).[83] Of note with compounds (**35**) and (**36**), was that only 13 (instead of 15) signals could be observed in their ^{13}C NMR spectra due to the coincidence of signals for the methyl carbons of the thexyl moieties. The Pd catalysed coupling of these monomers to the templates is discussed in Section 4.2.1.

Table 1. The protection of the monomers as TDS and TBDMS ethers.

Entry	Substrate	Conditions[a]	Product	%Yield
1	 **1**	A	 **35**	92
2	 **2**	A	 **36**	93
3	 **20**	B	 **37**	99
4	 **24**	C	 **38**	93
5	 **28**	B	 **39**	82

[a] Conditions: (A) TDSCl/imidazole/dry DMF 3 hrs at 50°,

(B) TDSCl/imidazole/dry DMF 1.5-2 hrs at room temperature, and

(C) TBDMSCl/imidazole/dry DMF 4 hrs at 50°.

2.5. Summary

The work discussed in this section has yielded a multitude of monomers suitable for coupling to the various templates. These included a series of both the two-arm and one-arm monomers, the more soluble silyl protected monomers and finally an oligomeric two-unit system. The coupling reactions of these monomers are discussed in depth in Chapter 4.

3. Template Synthesis

The templates employed in this project gradually evolved from the simple 1,8-bis(ethynyl)anthracene (**40**) to the more complex adamantane derivative (**42**). This evolution took place as a result of information gleamed from the Pd catalysed coupling chemistry of Chapter 4. In short, it was found that the coupled monomer-template systems were difficult to handle and purify, owing to their low solubility in most organic solvents, and so it was necessary to incorporate functionality into the templates, specifically for solvation. The chemistry discussed in this chapter mainly relates to the introduction of large, non-polar groups into the anthracene system to aid in the handling of the monomer-template coupled systems. These templates are illustrated in Figure 28. Template (**43**) does not posses the ethynyl groups like the others (**40-42**), since the monomers coupled to it possessed the ethynyl link themselves (Section 4.3).

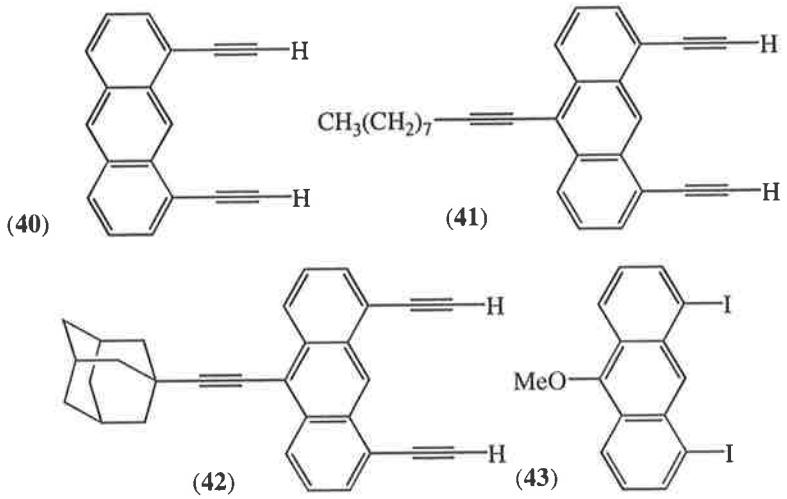
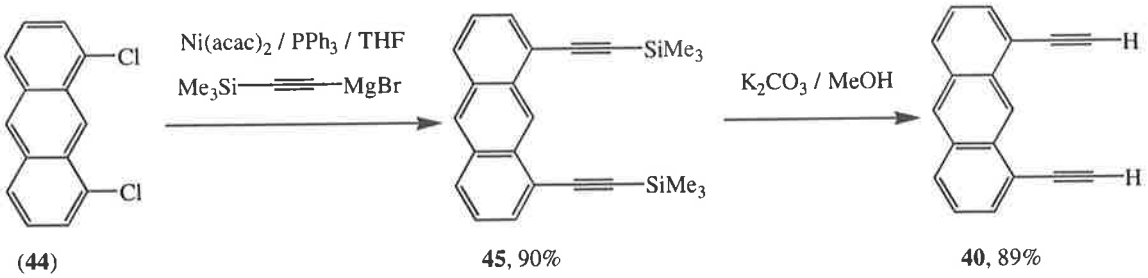


Figure 28. The template systems.

3.1. The Standard template

The first template system to be studied was the anthracene template 1,8-bis(ethynyl)anthracene (**40**), henceforth referred to as the standard template. This system was chosen first because gram quantities could be readily prepared from the starting material 1,8-dichloroanthracene (**44**) *via* the TMS protected intermediate (**45**) (**Scheme 26**).[84,85]



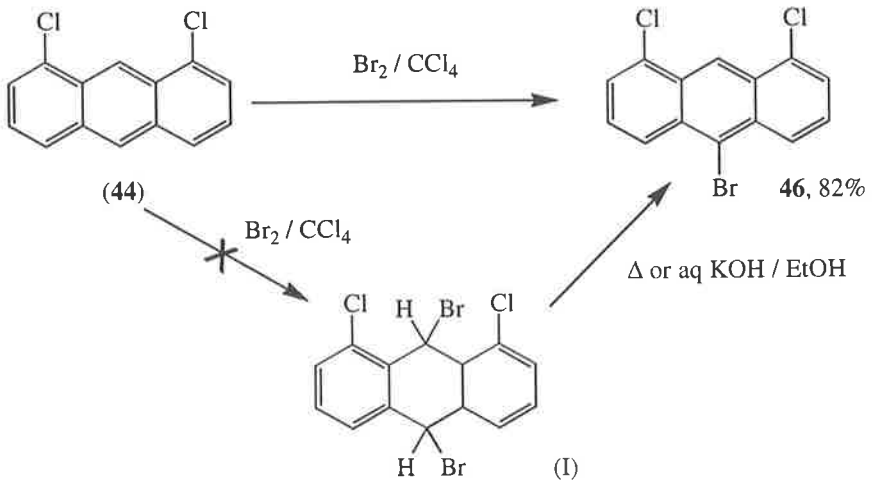
(**44**) **45**, 90% **40**, 89%

Scheme 26

The standard template (**40**) could be easily coupled with the monomer systems under mild conditions, as discussed in Chapter 4.

3.2. More Soluble Templates

The templates (**41**) and (**42**) shown in Figure 28 were both synthesised from 10-bromo-1,8-dichloroanthracene (**46**). The literature preparation for this compound is to treat 1,8-dichloroanthracene (**44**) with bromine in CCl_4 (**Scheme 27**), to form the intermediate 1,8-dichloro-9,10-dibromo-9,10-dihydroanthracene (I, **Scheme 27**).[86,87] The dibromide is then heated to liberate HBr, giving 10-bromo-1,8-dichloroanthracene (**46**).[87,88] Alternatively, the intermediate can be reacted with a potassium hydroxide solution to give the aryl-bromide (**46**). However, on trying this method it was found that treating 1,8-dichloroanthracene (**44**) with a solution of bromine in CCl_4 at room temperature proceeded directly to the aryl-bromide (**46**), and none of the intermediate (I, **Scheme 27**) was isolated. This procedure gave the desired bromide (**46**) in an excellent yield of 82% (**Scheme 27**).

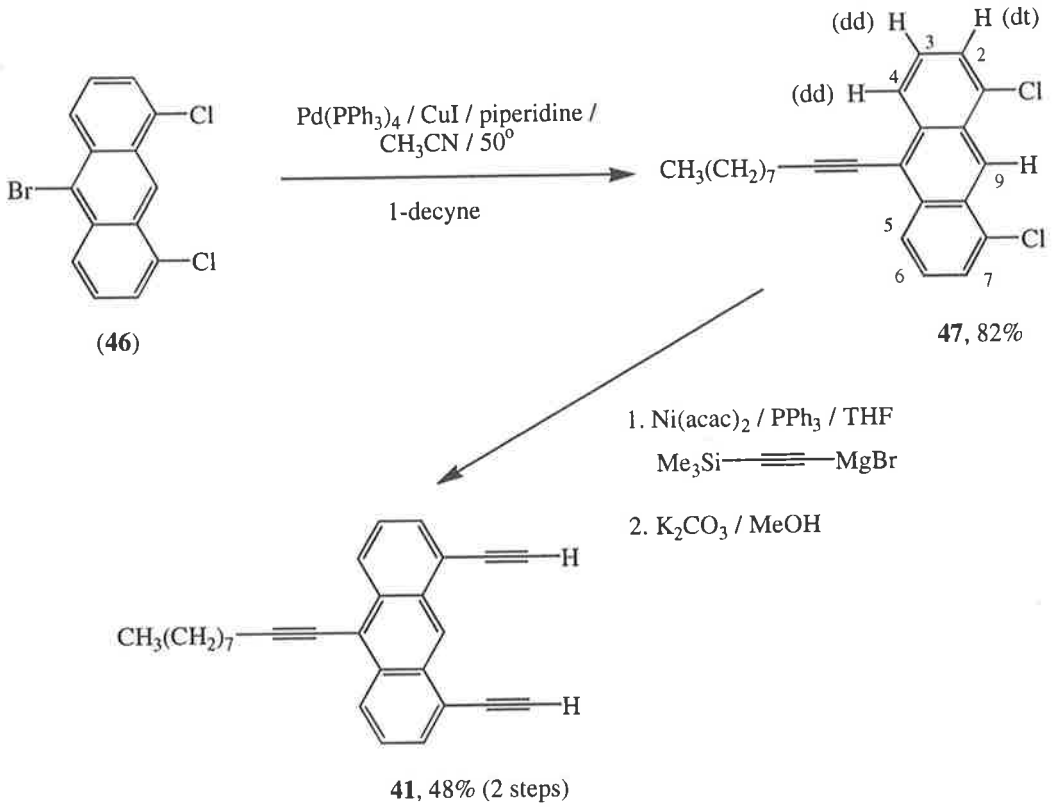


Scheme 27

Of note with this compound was the manner in which it melted. The experimental melting point of 200.0-201.5° was in good agreement with the literature melting point of 202°.[88] However, it was observed that the initial fine golden needles, obtained from recrystallisation from chloroform or acetic acid, fused together between 170-180° to form prisms. These prisms in turn melted sharply at 200.0-201.5°. These observations are consistent with monotropic polymorphism,[76] although there was no mention of this being observed in the literature.[88] This is where the prismatic form is stable at all temperatures below its melting point and never changes back to the needle form, and the needle form has a lower melting point, and is stable below that.

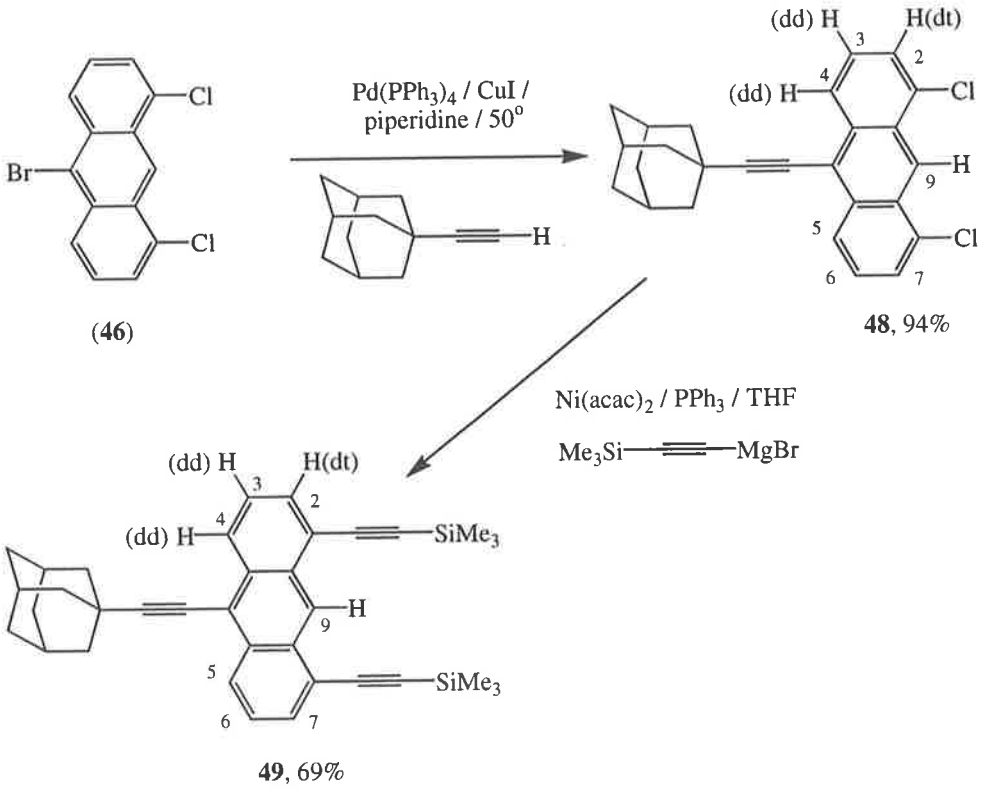
Whilst the melting point agreed with the published value, the issue of regiochemistry still had to be addressed since the experimental details of the aryl-bromide (**46**) were published before the advent of NMR. More recently, a carbon NMR study was performed on a series of naphthalene and anthracene compounds which included the aryl-bromide (**46**).[89] The 10-substituted anthracenes were assigned their regiochemistry based on the magnitude and multiplicity of the three bond (^3J) C-H coupling constants. Although no synthetic experimental details were presented in the paper, the δ_C, $^1J_{CH}$ and $^3J_{CH}$ values were consistent with our experimental values.[89]

The next step was to couple the aryl-bromide (**46**) to the respective acetylenes. The aryl-bromide (**46**) coupled readily to the commercially available 1-decyne under standard coupling conditions to give the dichloride (**47**) in good yield. Of note with the proton NMR spectrum of this compound was that long range coupling (^4J) was observed between protons H2,7 and H9 (J 1.1 Hz). This coupling was of the same magnitude as the meta-coupling of H2,7 to H4,5 (J 1.1 Hz). Hence, along with ortho-coupling to H3,6 (J 8.7 Hz), H2,7 appeared as a doublet of triplets. Long range and even meta-couplings are not always observed for these anthracene systems and the regiochemical assignment of the protons was based on published chemical shifts of analogous systems.[84] The dichloride (**47**) was then converted to the free template (**41**) using exactly the same coupling and deprotection chemistry as for the standard template (**40**). This is outlined below in **Scheme 28**.



Scheme 28

Similarly, the aryl-bromide (**46**) could be coupled to 1-ethynyl adamantane,[90] under standard Pd catalysed coupling conditions to give the corresponding dichloride (**48**) in an excellent yield. The dichloride (**48**) could then be converted to the TMS protected template using identical coupling chemistry as for template (**40**) to give the coupled system (**49**) in reasonable yield (**Scheme 29**). Long range and meta-coupling could be observed for both (**48**) and (**49**) in their proton NMR spectra. The coupled system (**49**) has, so far, not been deprotected to the free template (**42**). However, the mild deprotection conditions of potassium carbonate in methanol are expected to work well.

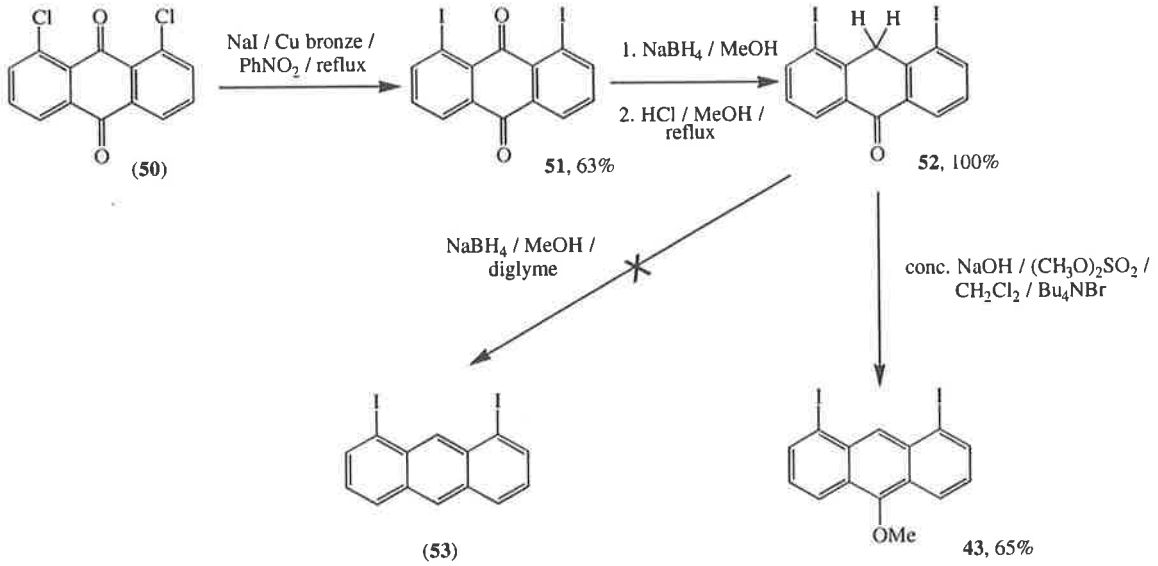


Scheme 29

Due to the involved synthesis of both 1-ethynyladamantane (a three step process),[90] and its coupled products, this template system was not pursued any further. The synthesis of the decyne functionalised template (**41**) was much less involved, and so template (**41**) was used to introduce solubility where necessary to the bis-coupled systems described in Chapter 4.

The final template to be synthesised was the known template (**43**).[91] In this case, no ethynyl groups needed to be introduced to the 1,8-positions, since these would be incorporated into the monomer and oligomer structures (see Chapter 2). Initially, the main synthetic target was the simpler 1,8-diiodoanthracene (**53**), as shown in **Scheme 30**. The commercially available 1,8-dichloroanthraquinone (**50**) could be converted to the corresponding diiodidoanthraquinone (**51**) in a reasonable yield, almost twice that stated in literature, when the hot filtration step in the workup was replaced with a Soxhlet extraction. The anthraquinone (**51**) could then be reduced to the anthrone (**52**) using the published conditions in a quantitative yield. However, the second reduction of the anthrone (**52**) to the anthracene (**53**) failed when attempted twice under the stated literature conditions.[91] Instead of pursuing this pathway further, the anthrone (**52**) was simply methylated under mild conditions to give the template (**43**) in sizeable quantities.

It was found that the methoxy group functioned quite well in adding a degree of solubility to the coupled monomer-template systems.



Scheme 30

3.3. Summary

The template systems that have been synthesised in this section, have been from both published literature work - templates (**40**)[84] and (**43**)[91] - and from novel organic synthesis, templates (**41**) and (**42**). Three of the templates (**41-43**) have been specifically synthesised to incorporate functional groups for solubility and the synthesis of these templates has worked efficiently. The subsequent use of these templates (**40-43**) is discussed next in Chapter 4.

4. Monomer-Template Coupling Chemistry

Once the monomer substrates and the templates had been synthesised, the next step in forming the cyclophanes was to couple the two units, forming the monomer-template coupled systems. This methodology was described in Chapter 1 and the corresponding outline of the reactions described in this section are shown below in Figure 29.

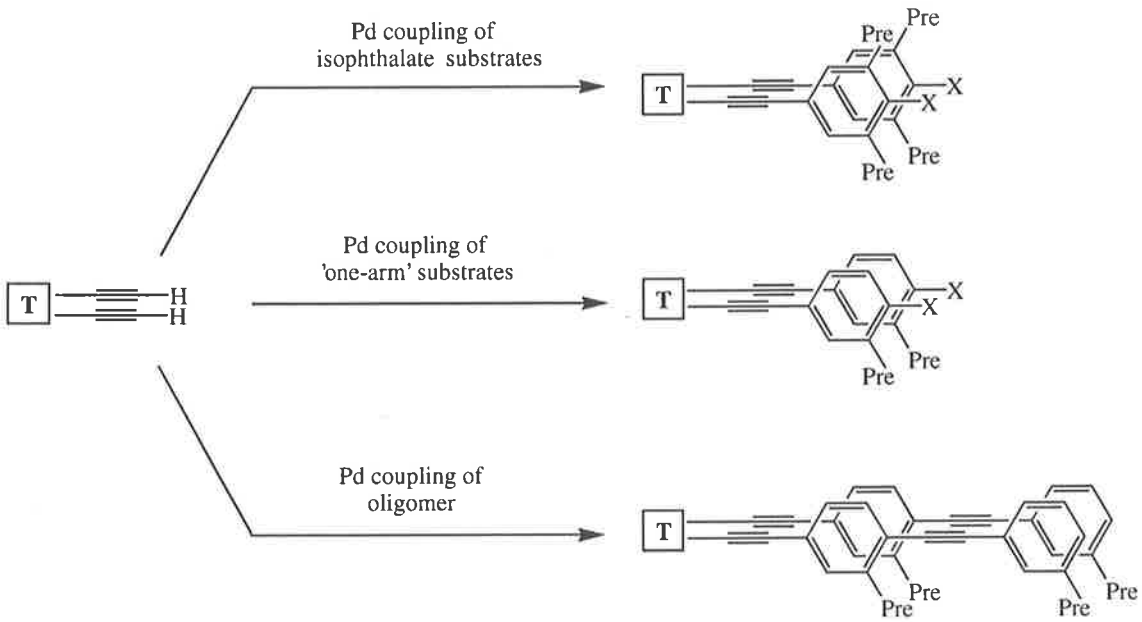


Figure 29. The coupling methodology, X=H, OR.

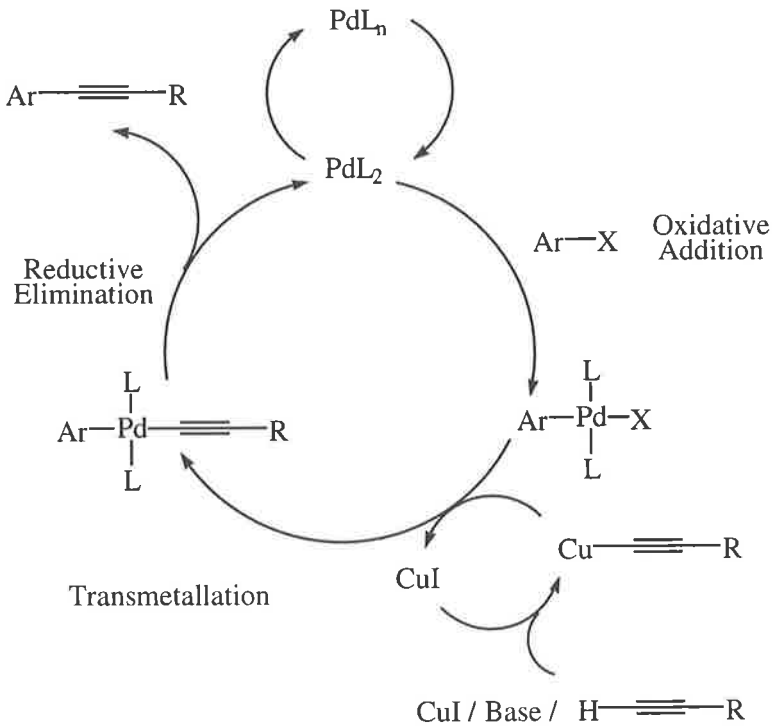
While there exists well established pathways to the formation of various templates, see Chapter 3, we have seen that their preparations can be quite involved. To prevent wastage of these valuable template materials, test coupling reactions were performed with the commercially available phenylacetylene. The coupled materials obtained from these reactions were themselves of value, as they were used in the testing of many of the required functional group transformations (Chapter 6).

4.1. Palladium Catalysed Coupling Reactions

Palladium catalysed coupling reactions of terminal alkynes to aryl-halides, or Sonogashira couplings as they are more commonly known, have been widely studied since the mid 1970's.[92,93] The general reaction profile is given below in **Scheme 31**.

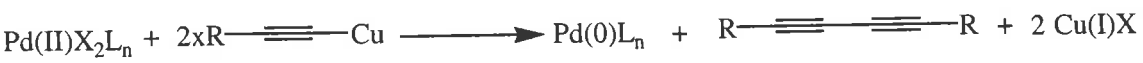
Scheme 31

Where X is a halogen (I, Br) or a halogen equivalent (OTf), the base is often an amine (e.g. Et_3N, piperidine, DBU) and 'Pd' refers to a palladium catalyst (e.g. $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_4$, $Pd_2(dba)_3$). These reactions involve a catalytic cycle consisting of three main processes. Firstly, oxidative addition of an aryl halide (or equivalent) to a zero valent palladium complex, followed by transmetallation with an *in-situ* generated copper acetylide. Finally, reductive elimination gives the coupled product and regenerates the Pd(0) catalyst (**Scheme 32**).[94,95,96]



Scheme 32

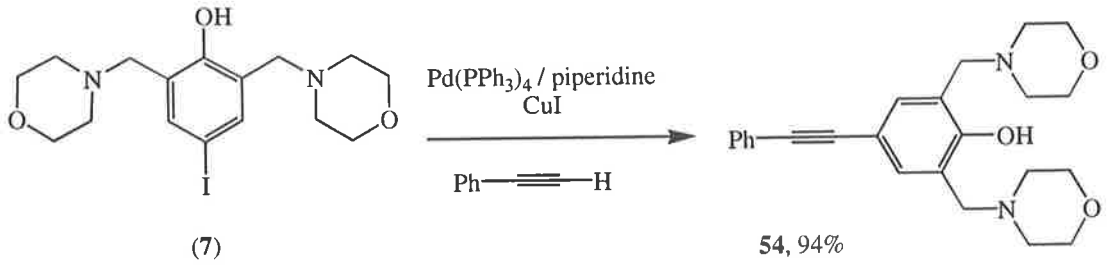
The order of reactivity for the oxidative addition of the aryl-halides or equivalents is I>Br≈OTf>Cl.[97,98] There exists a plethora of palladium catalysts available to the organic chemist, some of the more common ones being $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_4$ and $Pd_2(dba)_3$.[99] Generally, for the coupling reactions described in this thesis 0.1 equivalents of palladium catalyst and copper iodide were used, unless otherwise specified in the Experimental section (Chapter 10). If a Pd(II) catalyst is used, it is firstly reduced to Pd(0) before it enters the catalytic cycle.[95] This is achieved through homo-coupling of two equivalents of the copper acetylide as shown below (**Scheme 33**).



Scheme 33

4.2. Coupling to the Templates

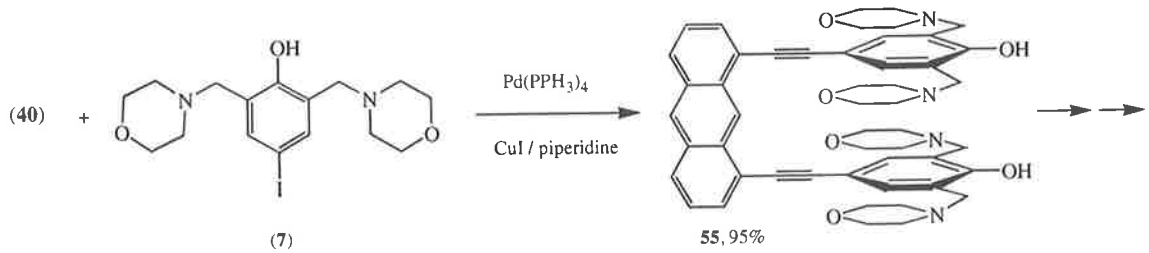
One of the first coupling reactions investigated was the of coupling of 2,6-bis(morpholinylmethyl)-4-iodophenol (**7**) to phenylacetylene in a trial reaction. This was performed using standard Pd catalysed coupling conditions (**Scheme 34**). The reaction proceeded well to give the desired product (**54**) in excellent yield.



(7) **54**, 94%

Scheme 34

Similarly, the standard template (**40**) was coupled to 2,6-bis(morpholinylmethyl)-4-iodophenol (**7**) (**Scheme 35**). This reaction proceeded smoothly to give the bis-coupled product (**55**) after one hour in 95% yield. Further transformations of this system can be found in Section 6.1.

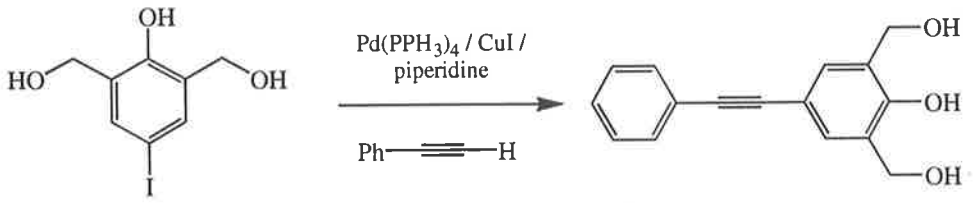


(7) **55**, 95%

Scheme 35

The next monomer that was to be coupled to the templates was the bis-hydroxymethyl (**2**). This compound was initially coupled to phenylacetylene, as shown in **Scheme 36**. The yield for this reaction was low due to the compound streaking on silica which led to losses on the column.

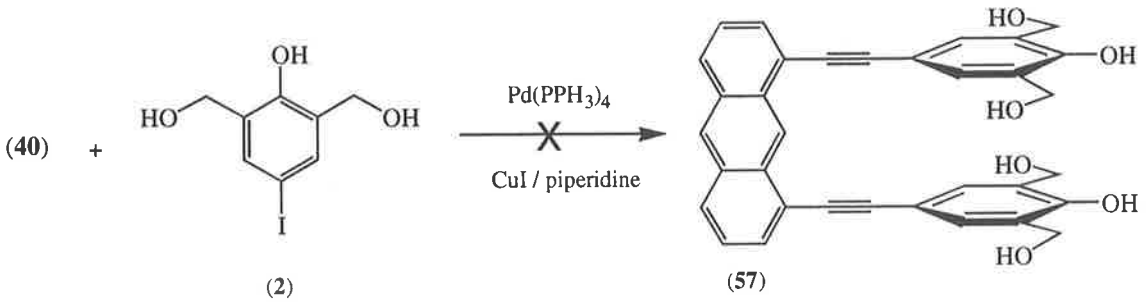
Of note with this compound was that no acetylene absorption was observed in the IR spectrum.* This is due to the vibrational symmetry or near symmetry of the molecule which makes the C≡C stretching frequency inactive in the infrared.[69]



(2) **56**, 46%

Scheme 36

When the corresponding reaction, however, was attempted with the standard template (**40**), none of the bis-coupled material (**57**) could be isolated (**Scheme 37**). The reaction was followed closely by tlc, which showed the disappearance of the starting materials followed by the concomitant appearance of material streaking near the baseline. Tlc using alumina produced the same results.



(2) (57)

Scheme 37

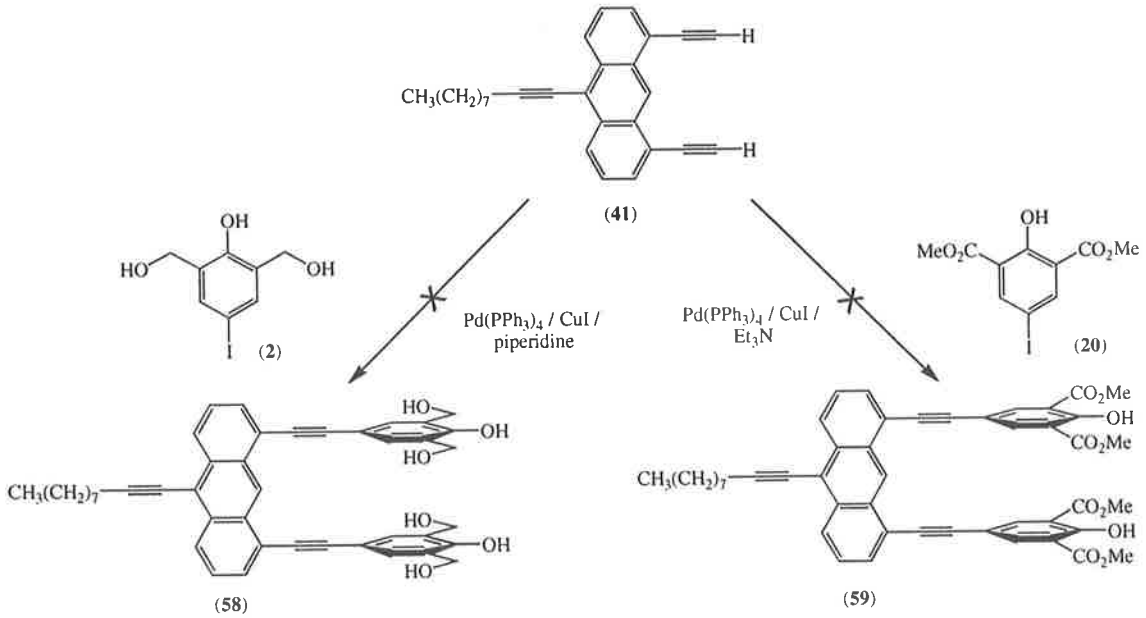
Similar results were obtained in attempting to couple the bis-hydroxymethyl compound (**2**) or the diester (**20**), to the more soluble template (**41**) (**Scheme 38**). It was thought that by using the more soluble template (**41**), tractability problems of the bis-coupled materials 'sticking' to the silica or alumina could be overcome. Usually

* The majority of bis-coupled materials showed no significant absorption in this region (2260-2150 cm^{-1}). If there was no other distinctive functional group, such as an ester, the IR spectrum was only performed when sufficient material was available. This rationale was also implemented for the compounds described in Chapters 6 and 7.

streaking in chromatography relates to the poor solubility of the materials in the solvent system. This was observed for many of the bis-coupled systems.

In the first case, the coupling of the bis-hydroxymethyl compound (**2**) to the template (**41**) to form the bis-coupled system (**58**) resulted in only baseline material being observed by tlc (on silica) after 1hr. Purification was attempted with squat chromatography on a very short column, but this resulted in complete loss of the coupled material as it appeared to 'stick' to the top of the silica even when the column was stripped with methanol.

In the second case, the coupling of the diester (**20**) to the template (**41**) to form the bis-coupled system (**59**) led to the formation of both the mono- and bis-coupled species when the reaction was followed by tlc and NMR (**Scheme 38**). However, it was observed that both species streaked heavily on silica and alumina resulting in the total loss of material when purification was attempted with squat chromatography on silica.

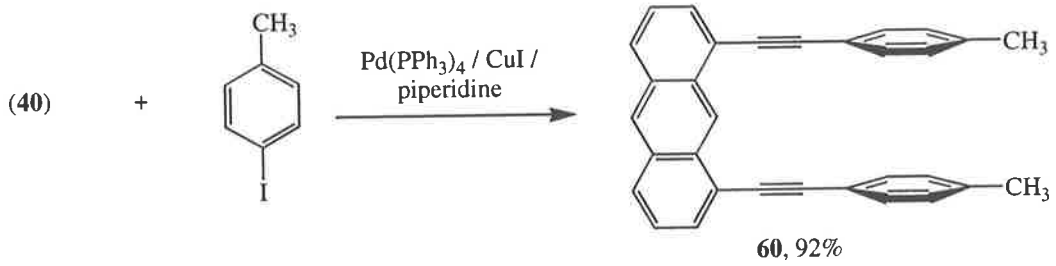


Scheme 38

Clearly there was a problem in coupling the monomers, in their present form, to both the standard and modified templates. To determine what part of the monomer's functionality was responsible, two trial reactions were performed using the standard template.

Firstly, to determine if polar functionalities were responsible, the non-polar 4-iodotoluene was coupled to the standard template (**40**). This coupling could be easily achieved using standard coupling conditions at room temperature to give the desired bis-

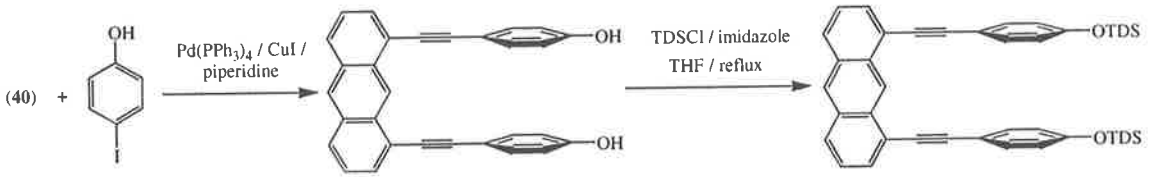
coupled material (**60**) in high yield (**Scheme 39**). The product could be handled easily, was taken up readily into halogenated solvents, and could be chromatographed without streaking. This reaction provided clear evidence that polar functionalities were the problem.



60, 92%

Scheme 39

To confirm this idea, 4-iodophenol was coupled to the standard template using the above conditions (**Scheme 40**). As expected, the mono- and bis-coupled materials streaked heavily on silica and alumina with the bis-coupled material streaking the most. The reaction was deemed complete in 1 hour and after workup, the crude reaction material was redissolved into THF and silylated with TDSCl and imidazole at reflux for 5 hrs (**Scheme 40**). In retrospect, from the results discussed in Section 2.4, better conditions would have been TDSCl/imidazole in DMF at room temperature. Nevertheless, the desired bis-coupled silylated material (**61**) was isolated in a reasonable yield. The product behaved very well on silica, with no streaking being observed.



(not isolated)

61, 52% (2steps)

Scheme 40

These reactions confirmed that the polar functionalities played a major role in the purification problems of the bis-coupled systems. The reactions also showed that the highly non-polar nature of the decyne substituted template (**41**) (and by inference the ethynyladamantane template (**42**)) could not be relied upon to solely overcome the tractability problems of the bis-coupled systems. It was clear that the monomers had to be more non-polar in nature to aid in the handling of these compounds and to prevent

the coupled systems 'sticking' to the silica. This was achieved through silylation of the monomers, as described in Section 2.4.

An alternative solution to the tractability problem was to use reverse phase silica for the purification of the bis-coupled systems, and indeed this technique was used to good effect for some of the compounds described below. However, the streaking of the bis-coupled materials still remained a problem in some cases, and this was due to lack of solubility of the materials in the chromatography solvent systems. Another problem with reverse phase silica is its expense, although it was effectively recycled many times by stripping the column several times with non-polar solvents.[100]

The exact reason why the bis-coupled materials 'stuck' to normal silica has yet to be determined. However, a working hypothesis is that there were cavitation effects in operation between the parallel rings of the coupled systems and the free hydroxyl groups on the surface of the silica (Figure 30). The silica used was Merck Silica gel 60 which had a pH range of 6.5-7.5. When the aromatic rings of these systems possessed polar groups, especially phenolic hydroxyl groups, strong binding interactions such as hydrogen bonding were present between the cavity of the coupled system and the silica. A similar argument could be put forward for alumina (neutral, pH 7.0±0.5) which also possessed surface hydroxyls. However, reverse phase silica has no free hydroxy groups as these have been silylated with long chain alkyl groups. This means little or no cavitation effects are possible, resulting in the compound behaving as normal on the tlc plate or column; solubility problems aside.

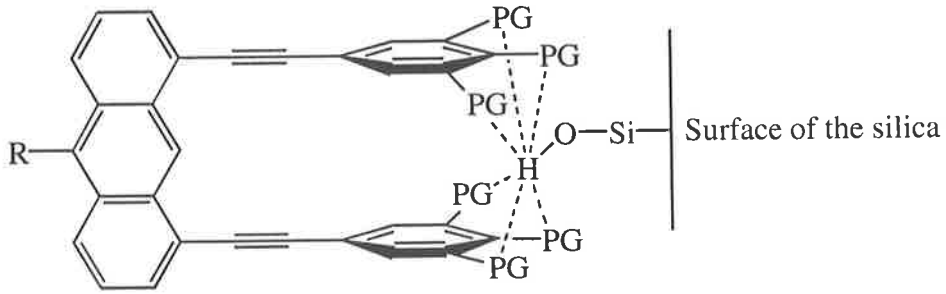
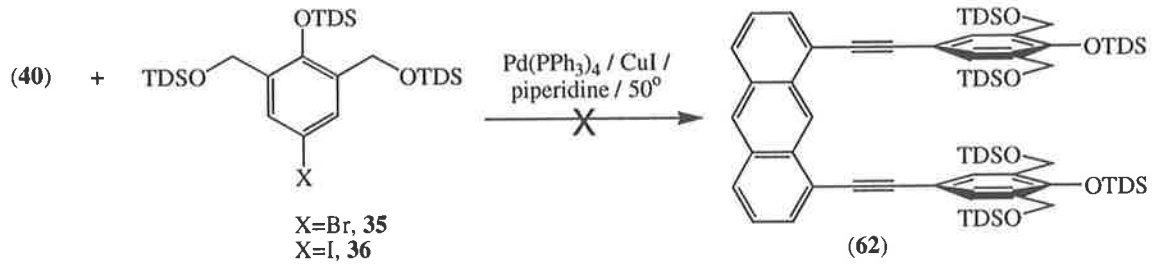


Figure 30. Possible cavitation effects of normal silica. PG = polar group: -CH_2OH, -OH or -CO_2Me; R=H, OMe, 1-decyne or 1-ethynyladamantane.

4.2.1. Coupling of the Silyl-Protected Monomers

Mixed results were obtained with the coupling of the silyl protected monomers (**35-39**) to the template systems (**Scheme 41**). Initially, attempts were made to couple the two tri-protected monomers (**35**) and (**36**) to the standard template (**40**) to form the bis-coupled system (**62**). The attempted coupling of the aryl-bromide (**35**) using standard Pd catalysed coupling conditions, and mild heating, resulted in decomposition of the template over 4 hrs, and the concomitant appearance of baseline material by tlc. The majority of the aryl-bromide was left unchanged in the reaction mixture.

The coupling of the aryl-iodide (**36**) produced slightly different results. The reaction mixture was again heated at 50° since the coupling at room temperature was observed to be slow. On heating the reaction mixture, the formation of a cascade of spots by tlc was observed after 2 hrs. After purification by flash chromatography the only major component to be identified was the de-iodinated starting material. Other fractions contained materials possessing complex proton NMR spectra. Decomposition of the template and/or the coupled products seemed to be likely in this case.



Scheme 41

Results from a low-level molecular modelling experiment also suggested that this reaction would be unfavourable. This can be observed in Figure 31 below where the large steric interactions between the coupled aromatic systems can be clearly seen. These interactions lead to the significant distortion (twisting) of the anthracene ring. The geometry optimisation was performed using the Spartan molecular modelling program using semi-empirical theory and the AM1 basis set. More details on molecular modelling of the bis-coupled systems and the cyclophanes can be found in Chapter 7.

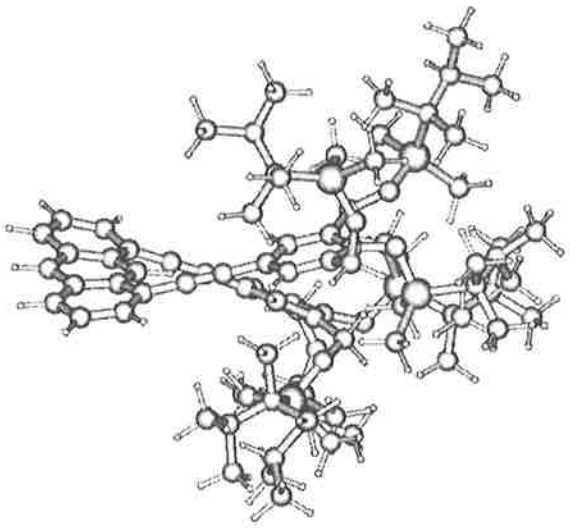
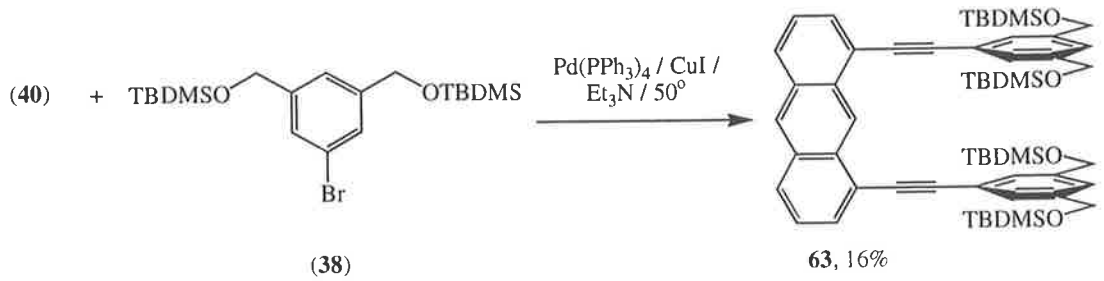


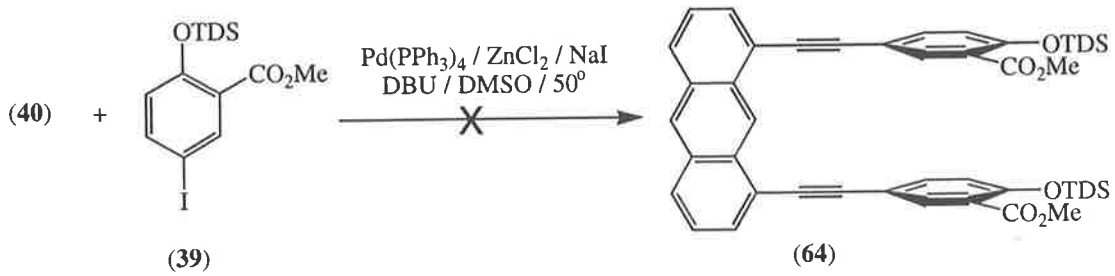
Figure 31. The optimised geometry of compound (**62**)

Slightly better results were obtained in coupling the aryl-bromide (**38**) to the standard template (**40**). In this case the corresponding bis-coupled material (**63**) could be formed in a low 16% yield (**Scheme 42**). The coupling wasn't 'clean', but produced two other close-running by-products in similar amounts to the bis-coupled material. The bis-coupled material was separated using reverse phase chromatography and the two by-products, which couldn't be separated from one another, were subjected to TDS silylating conditions to see if they were simply deprotected bis-coupled materials. By following the silylation by tlc it was clear that they weren't, since no movement was observed. After workup NMR showed multiple signals in the benzylic region suggesting that these materials were probably bis-coupled materials with one or more OTDS groups cleaved through homolytic cleavage at the benzyl positions (i.e. $ArCH_2OTDS \rightarrow ArCH_3$). This was unexpected since the reaction mixture was only heated at 50° for 1.5 hrs.



Scheme 42

The coupling of the one-arm aryl-iodide (**39**) to the standard template (**40**) to form the bis-coupled system (**64**) has only been attempted once without success (**Scheme 43**). It has to be noted that some new coupling chemistry was used in this case which is discussed in depth in the following chapter. The products of this reaction were complex in nature with two or more spots overlapping by tlc on both normal and reverse phase silica.

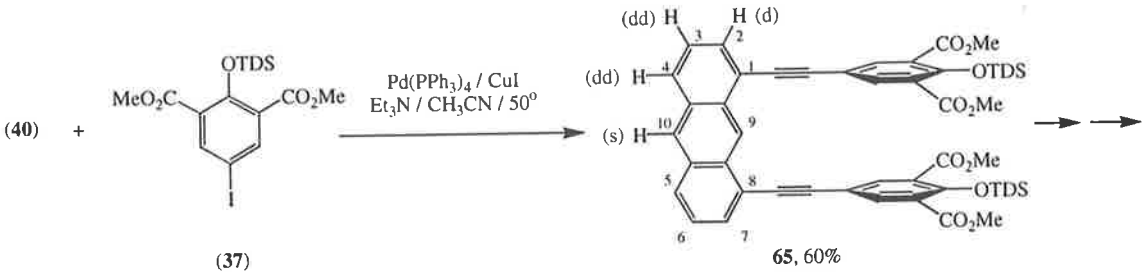


Scheme 43

The best results so far in coupling these protected monomers was with the coupling of the aryl-iodide (**37**) to the standard template. The coupling could be achieved under standard Pd catalysed coupling conditions to give the bis-coupled material (**65**) in 60% yield (**Scheme 44**). The yields for this reaction initially varied from 24-60% until it was realised that the saturated ammonium chloride solution used in the workup was rapidly cleaving the TDS group. This problem was overcome by eliminating the extractive workup altogether. The crude reaction mixture was firstly filtered through a short squat column of silica, concentrated, and then purified by flash chromatography on reverse phase silica. Further reactions of this system are discussed in Section 6.3.

Of note with this compound was that long range coupling (^4J) was observed between the protons of H4,5 and H10.[†] Consequently H4,5 was observed as a doublet of doublets (J 0.9 and 6.9 Hz) and H10 as a slightly broadened singlet. No meta-couplings between protons H2,7 and H4,5 were observed and no long range coupling was observed between H2,7 and H9.

[†] Similar long range couplings between H4,5 and H10 were observed for many of the bis-coupled systems of Chapters 4 and 6, and the cyclophanes of Chapter 7.



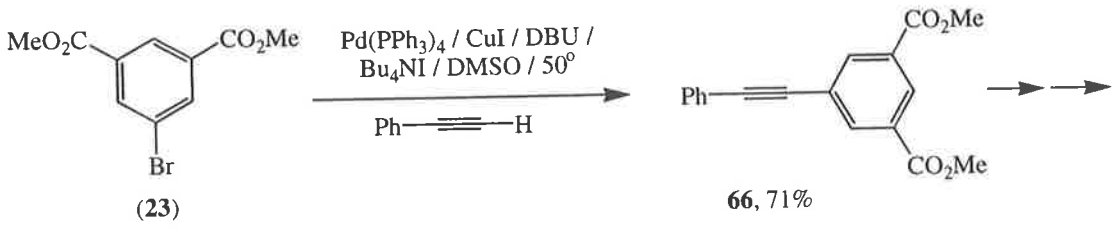
Scheme 44

4.2.2. Coupling of Non-Protected Monomers

The above results have shown that whilst it was better to protect the monomers before coupling, to aid in handling and purification, effectively carrying out the coupling reaction was often difficult. These difficulties arose from the large steric bulk of the monomers which certainly hindered the second monomer coupling to the template. This prolonged the reaction times which resulted in the decomposition of the templates, the monomers and/or the coupled systems.

Several non-protected monomers which had less steric bulk than the majority of the protected ones could be successfully coupled to the templates. Often the resulting bis-coupled materials were hard to handle and reverse phase silica was nearly always used for purification.

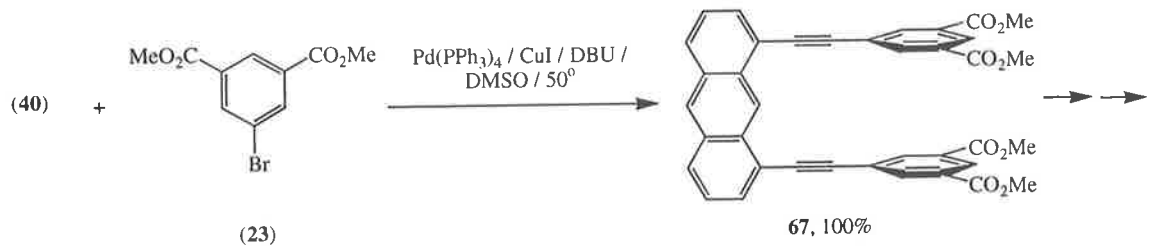
The diester (**23**) was initially coupled to phenylacetylene as a trial reaction (**Scheme 45**). The coupling used slightly modified conditions with Bu_4NI in DMSO at 50° giving the desired material in 71% yield, after recrystallisation. The modified conditions were used to increase rate of coupling, and are based on a published method where it was observed that iodide salts greatly accelerate the Pd catalysed coupling reactions.[101] Later reactions performed using the diester (**23**) have shown that Bu_4NI is not strictly needed, and that standard coupling conditions work fine. Further transformations of this coupled system are discussed in Section 6.3.



Scheme 45

The diester (**23**) was then coupled to the standard template (**40**) using solvent system containing DMSO and DBU along with the standard catalysts (**Scheme 46**). It was found that the coupling proceeds very slowly if DMSO is not used as a solvent. In one reaction, a solvent system consisting of acetonitrile and triethylamine was used, and after 3.5 hrs there was little mono- or bis-coupled material to be seen by tlc. However, the addition of a quantity of degassed DMSO (2mL added to the 3mL reaction suspension) resulted in the completion of the reaction in 0.5 hr.

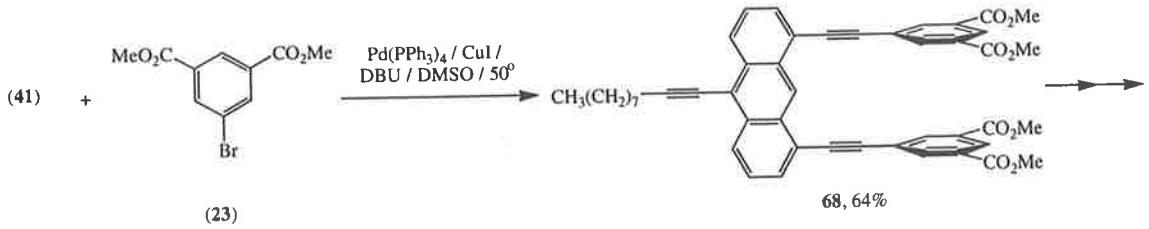
The bis-coupled material was difficult to handle, having limited solubility in organic solvents such as ether and halogenated solvents. Solubility in THF was good and this was exploited in the further transformations of tetra-ester (**67**). Nevertheless, good purification of the tetra-ester (**67**) could be achieved by using a short squat column with a dichloromethane/ethyl acetate solvent system to give the bis-coupled material in a quantitative yield. Further reactions of this bis-coupled material are discussed in Section 6.4.



Scheme 46

The diester (**23**) was then coupled to the more soluble template (**41**) in a bid to overcome the solubility problems. This was achieved by using the same conditions as above to give the bis-coupled product in 64% yield (**Scheme 47**). As expected, the bis-coupled material (**68**) was easy to handle with no solubility problems, however, the material did streak quite significantly on silica. Consequently, the product was purified using reverse phase chromatography with no problems to give the coupled material in good yield. This bis-coupled material (**68**) could also be synthesised using the new

coupling protocols, albeit in a lower yield. This is discussed in Section 5.4 and further transformation of this system are discussed in Section 6.4.

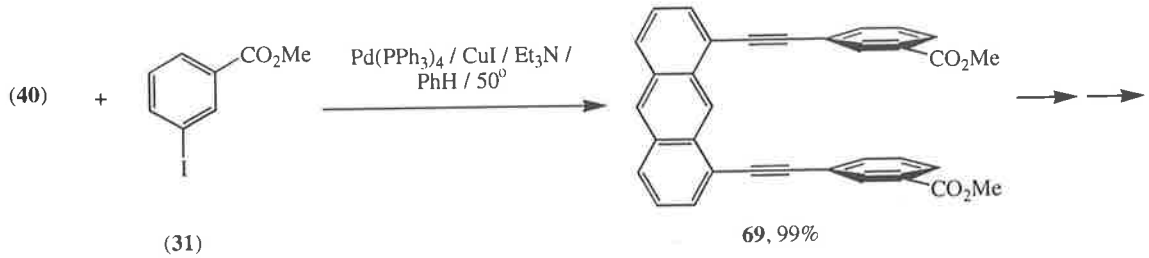


Scheme 47

The one-arm monomers could also be coupled to the anthracene templates. This was investigated with the coupling of the ester (**31**) to the standard template (**40**). The solvent system in this case was a mixture of benzene and triethylamine. This mixture was used since the mono- and/or bis-coupled materials were precipitating out of solution as the reaction progressed. In retrospect, a better solvent system would have been DMSO.

Heating was required for this coupling, not only for solvation, but to increase the rate of the second coupling. In general, due to steric factors associated with the bis-coupled systems, the coupling of the second substrate was slow, even for aryl-iodides and so mild heating was used in most cases. The yield for this reaction was excellent, near quantitative, (**Scheme 48**), and the reaction product was readily purified by squat chromatography.

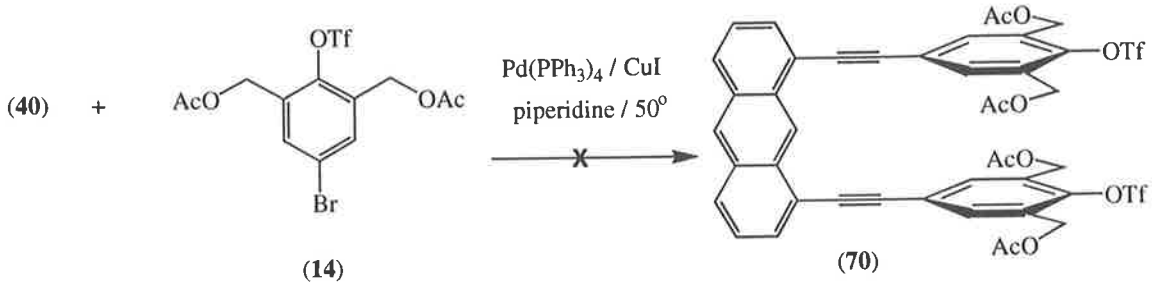
The handling properties of this compound, however, weren't good. The coupled material (**69**) had limited solubility in ether, ethyl acetate, halogenated solvents, and required THF or benzene as a solvent for the extractive workup. Strangely, this compound could be recrystallised from a THF/MeOH solution to give fine golden needles. Often the bis-coupled systems can't be recrystallised or provide powders at best. Further reactions of this bis-coupled system are discussed in Section 6.3.



Scheme 48

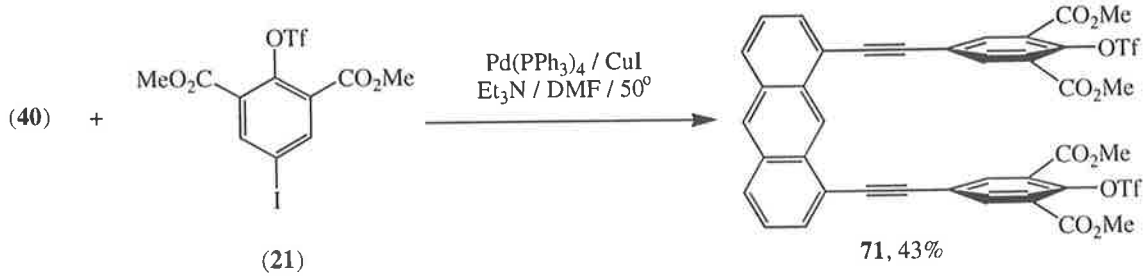
4.2.3. Regioselective Coupling Reactions

Investigations into regioselective coupling of the monomers was first attempted with the coupling of the triflate (**14**) to the standard template (**40**) (**Scheme 49**). Selective coupling in the 4-position was expected since the triflate is hindered by the two adjacent acetoxymethyl groups. Standard coupling conditions were used; $Pd(PPh_3)_4$ and CuI in piperidine at 50°. Unfortunately, no coupled product (**70**) could be isolated from this reaction as only baseline materials were observed by tlc after one hour. It was possible that the piperidine had reacted with the acetoxymethyl groups or that the triflate had decomposed. This reaction has yet to be repeated with a non-nucleophilic or hindered base due to the involved preparation of the triflate.



Scheme 49

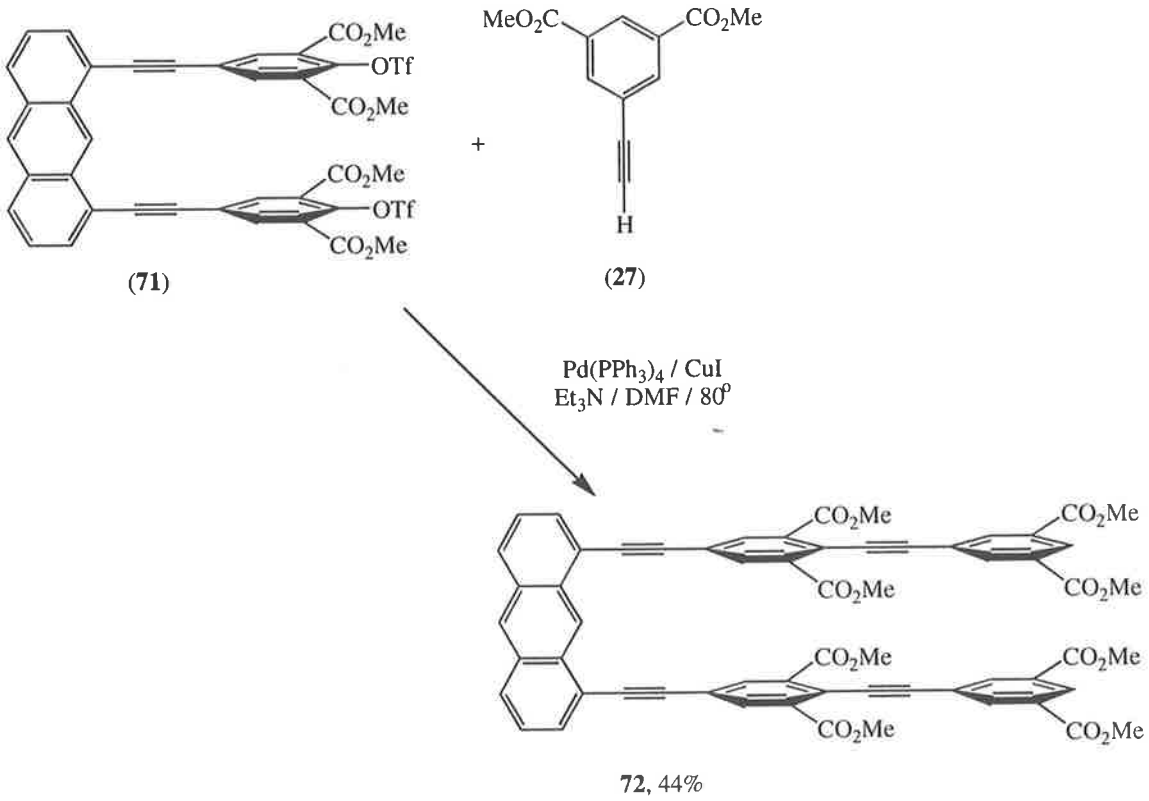
More success was obtained with the coupling of the triflate (**21**) to the standard template (**40**). Standard coupling conditions were used to effect this coupling, with mild heating being required as no coupling was observed after 1hr at room temperature (**Scheme 50**). The reaction produced many spots by tlc, but the dominant material present was the bis-coupled product (**71**). Good separation was achieved using reverse phase silica and gave the product in a respectable 43% yield. This reaction showed that 1,4-selectivity was possible with good yields.



Scheme 50

The bis-coupled system (**71**) was then further extended by coupling to the terminal alkyne (**27**) (**Scheme 51**). The same coupling conditions as in **Scheme 50** were

used except that the reaction temperature was increased to 80° to aid in the oxidative addition of the hindered triflate. Under these conditions the two-unit oligomer (**72**) could be produced in a reasonable yield of 44% after purification on normal silica. Solubility problems were encountered with this compound, as expected from previous results. It was found that the oligomer was only soluble to a significant degree in chloroform with partial solubility in dichloromethane and carbon tetrachloride. Other solvents such as ether, THF, DMSO, benzene and acetonitrile showed little or no solvation. Nevertheless, the reactions outlined in **Scheme 50** and **Scheme 51** highlighted the fact that regioselective coupling was possible between the iodide and the hindered triflate, and that further coupling to the triflate was possible.



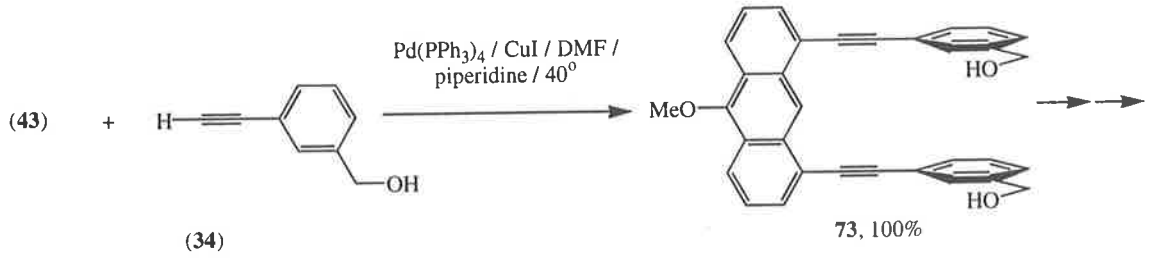
Scheme 51

4.3. Coupling to the OMe-Substituted Template

The last series of reactions in this section to be discussed are related to the coupling of various benzyl alcohols to the OMe-substituted template (**43**). The monomers in this case all contained a free ethynyl group for coupling to the template and the benzyl alcohols were in no way protected. In most cases this wasn't a problem

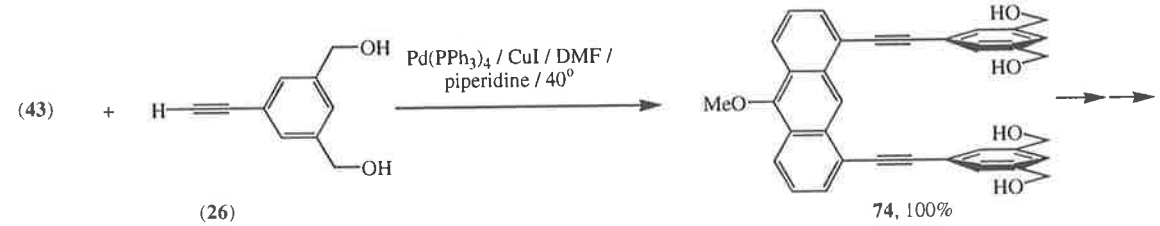
as purification and handling were manageable, and the alcohols were invariably converted to the corresponding non-polar bis-, tetrakis- or tetra-bromomethyl compounds.

Coupling of alcohol (**34**) to the template (**43**) was achieved using standard coupling conditions to give the bis-coupled material (**73**) in a quantitative yield (**Scheme 52**). Although the product streaked somewhat on silica, good purification could be achieved with squat chromatography. Conversion to the corresponding bromide is discussed in Section 6.4.



Scheme 52

The next monomer to be coupled was the bis-hydroxymethyl system (**26**). The same conditions were used as for (**73**) giving a quantitative yield of the bis-coupled system (**74**) (**Scheme 53**). Again the compound streaked on silica, but good separation could be achieved with a short squat column. Of interest with this compound was that the methylene protons coupled to the hydroxyl groups, as in the case of (**34**). Conversion of this material to the corresponding bromide is discussed in Section 6.4.



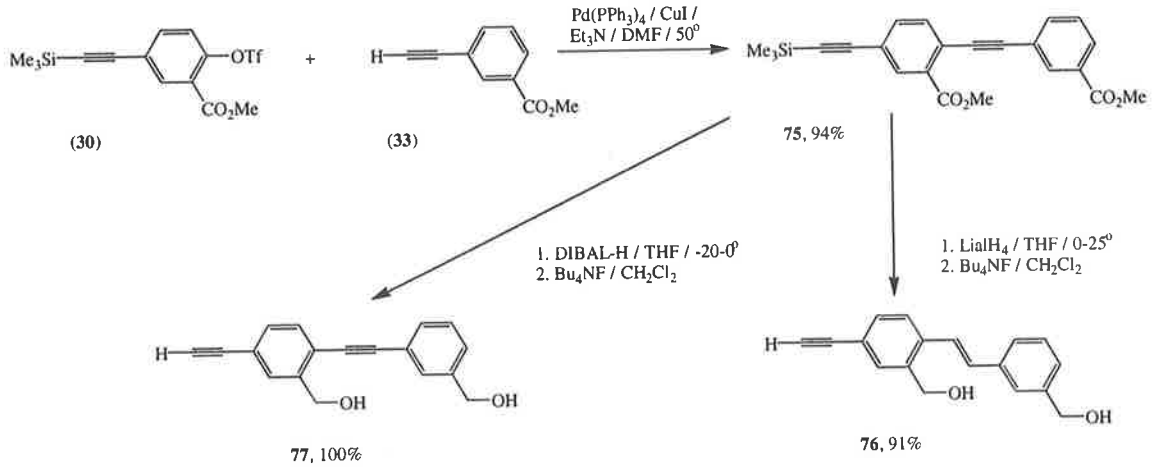
Scheme 53

4.3.1. The Formation and Coupling of a Two-Unit Oligomer

The results discussed earlier in this chapter and in Chapter 6 showed that once the monomers had been coupled to the templates, the resulting coupled systems were difficult to handle and purify, even with the more soluble silyl groups in place. As a consequence, it became important to perform the majority of functional group

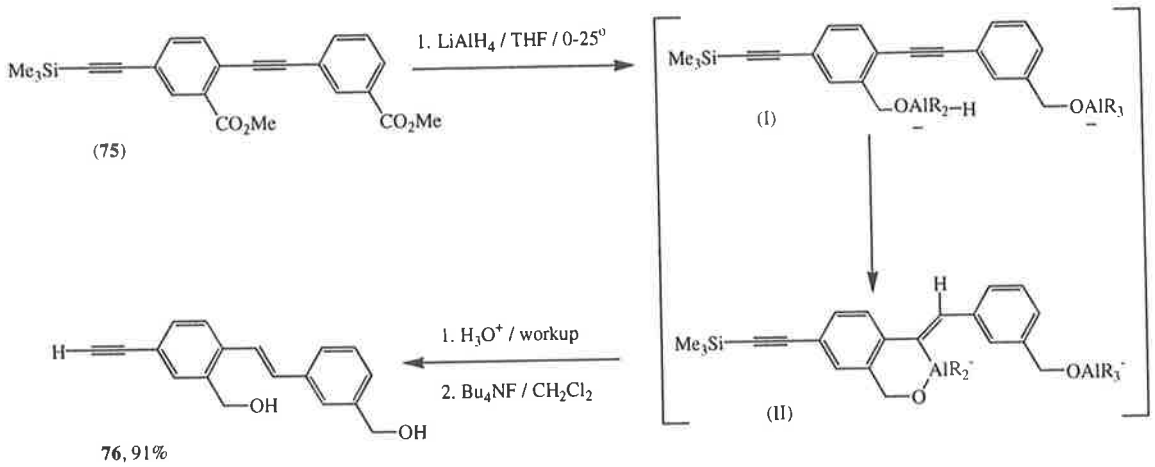
manipulations off the template. Once the monomer-template coupled systems had been formed only one or two synthetic steps should be necessary to achieve final cyclophane formation. Development of this methodology was started with the synthesis of the two-unit oligomer (**77**) using monomers previously synthesised in Section 2.3.1 and 2.3.2.

The first step in the synthesis of bis-hydroxymethyl compound (**77**) was the coupling of the triflate (**30**) to the ester (**33**). The ester (**33**) was used here as an 'end-capping' group since it does not contain any functionality in the 6-position for further Pd coupling chemistry, and the resulting oligomer (**75**) can be thought of as 'capped' at one end. The coupling of triflate (**30**) to the ester (**33**) was done using standard Pd catalysed coupling chemistry to give the diester (**75**) in a high yield of 94% (**Scheme 54**).



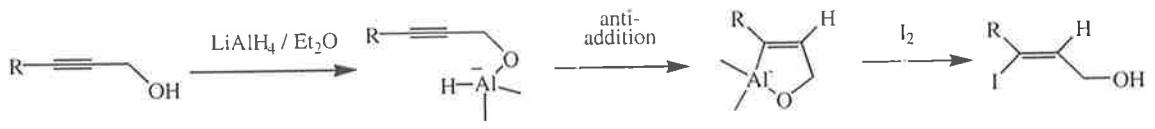
Scheme 54

Conversion of the diester (**75**) to the bis-hydroxymethyl compound (**77**) was initially attempted with lithium aluminium hydride at 0°, followed by deprotection with Bu_4NF. Unfortunately, the product isolated was in fact compound (**76**) where over-reduction had occurred, converting the triple bond to a double one. This process is facile, even at the lowered temperature since the intermediate alumino hydride (I, **Scheme 55**) is arranged such that donation of the hydrogen to the triple bond produces a stable six membered ring (II, **Scheme 55**) which hydrolyses upon workup (**Scheme 55**).



Scheme 55

These ideas are consistent with those in the literature, where propargyl alcohols have been reduced to allylic alcohols *via* anti-addition across the triple bond to produce five membered β-aluminoallyl alcohols (**Scheme 56**).[102] Evidence to support the assignment of the double bond as *trans* has been obtained with proton NMR spectroscopy where a homonuclear decoupling experiment has been performed. While only one of the initially presumed alkenyl protons was set apart from the other aromatic signals at δ 7.17 ppm (1H, d, *J* 16.2 Hz) decoupling of this proton produced a marked change to appearance of the aromatic/alkenyl multiplet at δ 7.24-7.56 ppm (7H, m). This signal was presumed to be alkenyl because of its large coupling constant, since aromatic coupling constants usually do not extend beyond 9 Hz.[103] The decoupling experiment showed a coalescent of two peaks in the normal spectrum, at δ 7.41 and 7.46 ppm, to a single peak at δ 7.43 ppm, indicating that the isolated alkenyl signal at δ 7.17 ppm coupled to a doublet in the aromatic/alkenyl multiplet, and no further coupling to any aromatic protons was observed. Measurement of the coupling constant (15.9 Hz) showed good correlation to the signal at δ 7.17 ppm (16.2 Hz), with the spin system being borderline first-order ($\Delta\nu/J$=4.8). In summary, the presence of the two alkenyl protons has been confirmed, and since their coupling constant was greater than 12 Hz, the double bond can be assigned *trans*.[103]



Scheme 56

The connection between the oligomer system and the propargyl alcohol cases is that the intermediate (I, **Scheme 55**) can be thought of as a pseudo-propargyl alcohol where a cis double bond has been inserted between the carbon bearing the oxygen and the triple bond (Figure 32(a)). The extra conjugation is required since the alternative alkynols, shown in Figure 32(b), have only been reduced under the forcing conditions of lithium aluminium hydride in diglyme/THF at 140° for 48-55 hrs.[104]

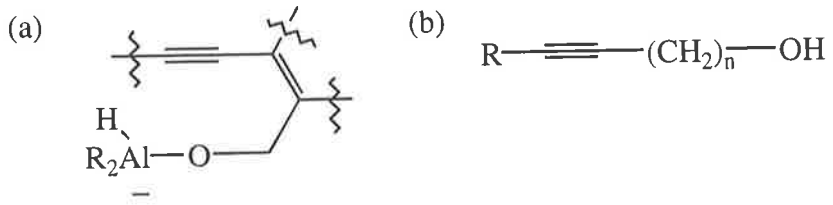
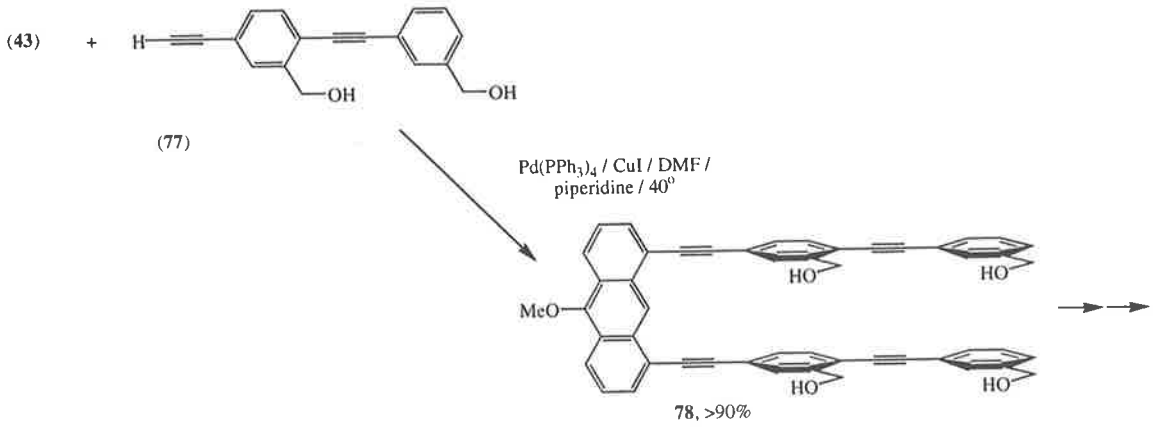


Figure 32. (a) The oligomer intermediate, (b) the alkynols (n=2-7).

The problem of the over-reduction was solved by using DIBAL-H at -20° in THF. Since DIBAL-H has only one hydride to donate, the intermediate alumino species cannot react further with the nearby triple bond. Carrying out the reaction at the low temperature prevented the DIBAL-H undergoing *cis* addition across the acetylene.[105] Reduction under these conditions, followed by deprotection with Bu_4NF worked well giving the desired bis-hydroxymethyl compound (**77**) in a quantitative yield from the ester (**75**). Both compounds (**76**) and (**77**) showed coupling of the methylene protons to the hydroxyl groups, as in the case of (**34**).

The coupling of the bis-hydroxymethyl compound (**77**) to the OMe-substituted template (**43**) was performed using standard coupling conditions, and the desired bis-coupled product (**78**) could be isolated in a good crude yield (**Scheme 57**). However, the solubility of this compound was poor. This could be seen in the extractive workup where a 3:1 mixture of ether:THF was required. The crude product that was obtained was not characterised but taken immediately on to the bromide, see Section 6.4.



Scheme 57

4.4. Summary

In this chapter we have seen the coupling of a wide range of monomers to three template systems. The coupling reactions employed have been by-and-large standard Pd catalysed coupling reactions, using the readily available $Pd(PPh_3)_4$ and CuI combination with a variety of organic solvents and bases.

The coupling reactions have shown that mild heating is usually required since the coupling of the second monomer was usually slow due to steric factors. The bis-coupled systems so formed could be quite difficult to handle in some cases, but these tractability problems have been generally overcome through the use of the silylated monomers, more soluble templates and reverse phase chromatography.

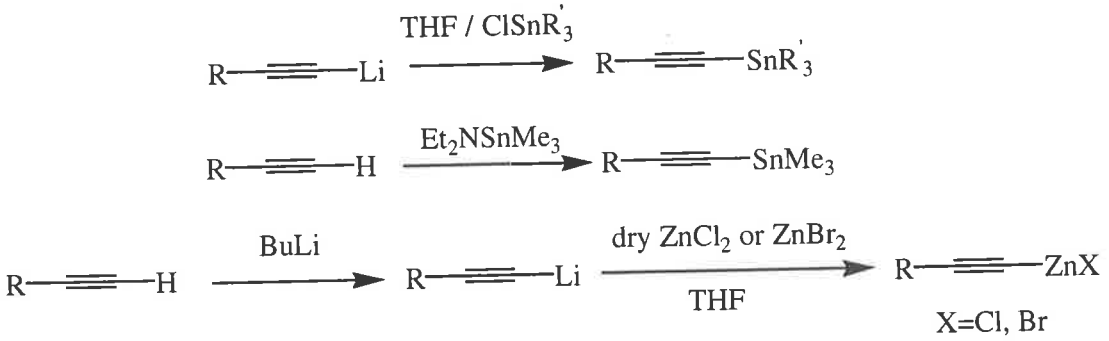
Regioselective palladium catalysed coupling was illustrated with the selective coupling of a monomer containing both aryl-iodide and aryl-triflate bonds, where the coupling was effected between the aryl-iodide bond and the template selectively. Further coupling was then shown to be possible between the aryl-triflate and another monomer to produce a two-unit oligomeric system.

The next stage in the synthesis of the cyclophanes lies with the functional group manipulations of the bis-coupled systems and these reactions are discussed in Chapter 6. However, let us digress for a moment as the results from the failed reactions outlined in **Scheme 41** eventually led to the discovery and development of some novel Pd catalysed chemistry involving zinc co-catalysts. These reaction are discussed next in Chapter 5.

5. New Coupling Chemistry

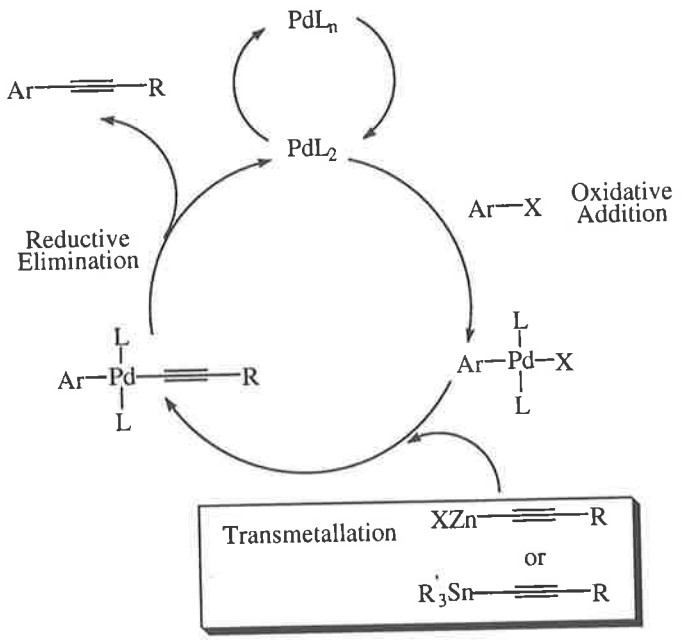
The Sonogashira-type coupling reactions discussed in the previous chapter highlighted the fact that mild conditions with short reaction times were necessary for the preparation of aryl-alkynes of the type shown in Figure 29 (page 45). Heating of the reaction mixtures over prolonged periods of time led to the decomposition of the templates and/or the aryl-halides. With this in mind, investigations were made into developing novel coupling conditions, that were mild, easy to use and produced minimal decomposition of substrates.

Couplings using the Sonogashira protocols infer the generation of copper acetylides in the catalytic cycle.[106] However, stoichiometric quantities of organometallic acetylides can be used instead including Sn, Al, B, Zn, Mg, Li and others.[95,106] The most commonly used stoichiometric reagents are the organotin and organozinc acetylides (**Scheme 58**). The organotin compounds are generally formed in one of two ways. The first method involves the reaction of a lithium acetylide with a trialkyl-tin halide.[107,108] The second method is to heat a terminal acetylene with a tin amide.[107,109] The organozinc compounds are generally prepared by deprotonation of the terminal alkyne using a strong organic base (e.g. BuLi) followed by transmetallation with anhydrous $ZnCl_2$[110,111] or $ZnBr_2$.[112]



Scheme 58

The mechanism of coupling is well known and is very similar to the catalytic cycle shown in **Scheme 32**, containing the sequential steps of oxidative addition, transmetallation and reductive elimination.[106] This is shown for the organometals below in (**Scheme 59**).



Scheme 59

The coupling of these organometallic species to aryl-halides generally works quite well.[110,112] However, the drawbacks are that the synthesis of these organometals usually require strong bases and consequently cannot be used with base sensitive substrates. Secondly, while the organotin compounds can be stored for some time, they cannot be stored indefinitely, and more so with the organozinc species which are generally made immediately prior to use.

In general, the functional group tolerance in the coupling of the organometals to the aryl-halides is very good. The aryl ring can accommodate a wide range of functionality, and this has been reviewed extensively in the literature.[95,106] The organozinc compounds are also known to couple at low temperatures (-20°), implying fast transmetallation.[113]

The use of co-catalysts in the terminal acetylene to aryl halide coupling reactions, as discussed in Section 4.1, has been generally limited to copper (I) species. The 'traditional' coupling method has been used extensively, since the ability to generate *in-situ* nucleophilic copper acetylides obviates the necessity of preparing and storing quantities of potentially unstable organometallic compounds.

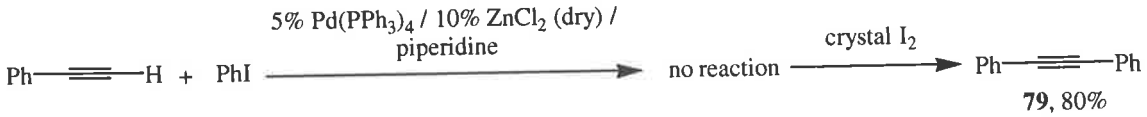
Recently a new catalytic coupling protocol has been published replacing copper iodide with silver iodide in DMF along with a bulky amine base.[114,115] Other silver salts such as silver nitrate, silver carbonate and silver triflate have also been used. These

conditions were used to couple vinyl triflates with terminal acetylenes,[115] and in the synthesis of epoxyenynes.[114,115] The use of the silver salts was required in the latter case, since the use of copper iodide led to the decomposition of the epoxyacetylenic starting materials. Mechanistically, silver acetylides are thought to be generated *in-situ*, and that these behave as other metal acetylides in the transmetallation step of the catalytic cycle.[115]

The lack of many alternatives to copper led us to look for novel coupling protocols using different metallic species. By using previously untried metallic salts as alternatives to copper iodide, it may be possible to effect a faster transmetallation step. Previous studies have shown transmetallation to be the rate determining step in many of the catalytic cycles.[116,117] By increasing the rate of transmetallation, coupling may be possible under milder conditions (e.g. lower temperature), leading to minimal decomposition of the template acetylenes during the coupling reactions. It was known from the literature that zinc acetylides readily couple to aryl-halides with a palladium catalyst,[110,112] and so the generation of these organozinc species (or their equivalents) *in-situ* would be an important step towards finding an alternative to the Sonogashira method. Our initial investigations have met with some success, the results of which were published recently and are presented below.[118]

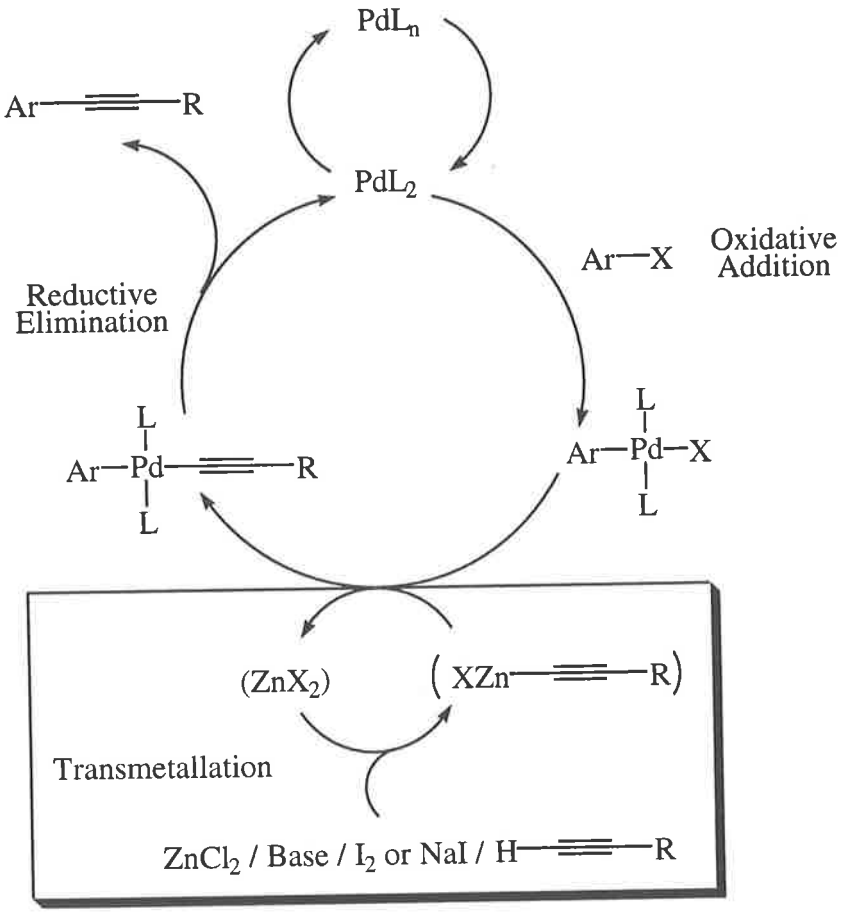
5.1. The Initial Discovery

The first reaction investigated was the coupling of iodobenzene with phenylacetylene. These substrates were chosen due to their activated nature towards Pd catalysed coupling, since the iodobenzene readily undergoes oxidative addition at room temperature, and the terminal acetylenic proton of phenylacetylene could be abstracted by bases commonly used for Pd catalysed couplings. The catalysts initially used were 5% $Pd(PPh_3)_4$ and 10% $ZnCl_2$ in degassed piperidine as both the solvent and base (**Scheme 60**). However, after the above reagents were added together, no reaction was observed after 4 hrs at room temperature. A crystal of iodine was then added and an immediate precipitation of a solid (piperidine hydroiodide) was observed with the reaction going to completion in 1 hr. An extractive workup followed by recrystallisation gave the expected product (**79**) (tolan) in 80% yield.



Scheme 60

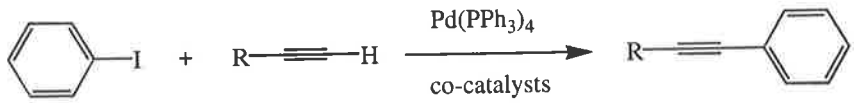
The addition of the iodine was crucial and was initially thought necessary due to the *in-situ* formation of ZnI_2. This in turn would react with the small equilibrium concentration of phenylacetylide in solution, forming a zinc acetylide *in-situ*. However, the results presented below show this isn't the case. Nevertheless, the possibility that a zinc acetylide or its equivalent was being formed, and that this was a reactive intermediate was an initial working hypothesis for further development. This idea is shown schematically in **Scheme 61**.



Scheme 61

5.2. Optimising the Conditions

The next step was to determine the optimum conditions for the coupling, varying the nature of the co-catalysts and the base. Thus, a series of coupling reactions as described in **Scheme 62** were investigated. Iodobenzene was used so that transmetallation was rate determining, not oxidative addition. These results are presented in Table 2.



Scheme 62

After the initial success of the first coupling (entry 1, Table 2), it was necessary to determine whether dry zinc chloride was essential. Using laboratory grade, undried zinc chloride directly from the supplier produced no marked effect on the yield (entry 2, Table 2). The reaction could also be performed using sodium iodide as the source of iodine, and it was equally efficacious (entry 3, Table 2). However, the reaction proceeded very slowly if no source of iodine was used. Of note is the fact that zinc iodide alone (entry 5, Table 2) did not promote the reaction as efficiently as the zinc chloride/sodium iodide combination, which meant that the requirement for iodine/iodide cannot simply be the formation of zinc iodide. Replacing piperidine as the solvent with DMF and using only 1.5 equivalents of piperidine did not alter the yield significantly (entry 6, Table 2). No reaction occurred in the absence of the palladium catalyst (entry 4, Table 2), or when triethylamine replaced piperidine as the solvent and base with the zinc chloride/sodium iodide combination (entry 7, Table 2). In going from piperidine (pK_a=11.12) to triethylamine (pK_a=10.72) the pK_a values only differed slightly,[119] but in terms of nucleophilicity, piperidine, which is a secondary amine, is more nucleophilic than the tertiary amine triethylamine. However, a slow reaction was observed when this combination was heated (entry 8, Table 2), or when DMAP was used in addition to triethylamine (entry 9, Table 2). These results suggested that a nucleophilic base was required. The traditional copper iodide method gave tolan in 100% yield after only 10 mins at room temperature (entry 10, Table 2) which meant that the zinc chloride/sodium iodide combination effects a slower coupling for these reactive substrates. Iodide was not the only nucleophile which was capable of promoting the transformation as azide worked equally well (entry 11, Table 2).

Table 2. The coupling of iodobenzene with phenylacetylene.[a]

Entry	Solvent/base	R	Co-catalysts[b,c]	Product	% Yield
1	Piperidine	Ph	$ZnCl_2$[d]/I_2	PhC≡CPh (**79**)[120]	80
2	Piperidine	Ph	$ZnCl_2/I_2$	〃	94
3	Piperidine	Ph	$ZnCl_2$/NaI	〃	94
4	Piperidine	Ph	$ZnCl_2$/NaI	〃	0[e]
5	Piperidine	Ph	ZnI_2	〃	34[f]
6	Piperidine	Ph	ZnI_2	〃	26[g]
7	Et_3N	Ph	$ZnCl_2$/NaI	〃	0
8	Et_3N	Ph	$ZnCl_2$/NaI	〃	34[h]
9	Et_3N/DMAP	Ph	$ZnCl_2$/NaI	〃	44[i]
10	Piperidine	Ph	CuI	〃	100
11	Piperidine	Ph	$ZnCl_2/NaN_3$	〃	100
12	Piperidine	C_4H_9	$ZnCl_2$/NaI	PhC≡CC_4H_9 (**80**)[121]	94
13	Piperidine	Me_3Si	$ZnCl_2$/NaI	PhC≡C$SiMe_3$ (**81**)[122]	100[f]
14	Piperidine	HC≡C$(CH_2)_4$	$ZnCl_2$/NaI	PhC≡C$(CH_2)_4$ (**82**)[123]	100
15	Piperidine	$HOCH_2$	$ZnCl_2$/NaI	PhC≡CCH_2OH (**83**)[92]	100

[a] 5% $Pd(PPh_3)_4$, base as solvent, room temperature, reaction time <1 hr. [b] In all cases 10% of each co-catalyst was used. [c] $ZnCl_2$ used without drying except where indicated. [d] $ZnCl_2$ dried under high vacuum. [e] Reaction without $Pd(PPh_3)_4$. [f] Reaction mixture stirred for 20 hrs. [g] DMF used as solvent with 3 equivalents of piperidine, reaction time 17 hrs. [h] Reaction mixture heated at 60° for 4 hrs. [i] Reaction mixture heated at 60° for 20 hrs.

In order to probe the scope of the reaction further, the optimum conditions of piperidine, zinc chloride and sodium iodide at room temperature were applied to the coupling of iodobenzene with a variety of acetylenes, (entries 12-15, Table 2). Each reaction gave an excellent yield of the expected product, and of note, the coupling of trimethylsilylacetylene (entry 13, Table 2) took 20 hrs at room temperature whereas all the other substrates took 1-3 hrs.

Of particular interest was the successful coupling of iodobenzene to propargyl alcohol (entry 15, Table 2). This reaction initially suggests that zinc acetylides are unlikely to be forming in solution, as if they were, they would be expected to react with the active hydrogen of the hydroxyl group to give zinc alkoxides (**Scheme 63**).[124] A similar argument can be put forward for the presence of water in the reaction mixture to give zinc hydroxides (entry 2, Table 2). The formation zinc alkoxides/hydroxides would effectively remove the co-catalyst from the reaction manifold since the zinc-oxygen bond (ΔHf^{o}_{298} =284.1 kJ/mol) is thermodynamically more stable than the zinc-carbon bond (ΔHf^{o}_{298} ≈201 kJ/mol for Et_2Zn).[125]

R=H, propargyl

Scheme 63

It could be argued that the zinc chloride/sodium iodide (or iodine) combination is simply acting as a Lewis acid, and that no zinc acetylides are forming at all. The co-catalysts may be able to increase the acidity of the acetylenic proton by π-coordinating to the triple bond thereby increasing the polarity of C–H bond. This has been observed for various salts including mercury, silver and the alkali metals.[126] By increasing the acidity of the terminal proton, the concentration of acetylide anions in solution would increase thereby increasing the rate of transmetallation and consequently the rate of the overall reaction. A similar argument could be put forward for the traditional copper iodide, as it too is a Lewis acid.

The zinc chloride/sodium iodide (or iodine) combination may act as a Lewis acid in a different manner by sequestering the halide from the oxidative addition adduct, forming a cationic palladium species along with a trihalozincate (Figure 33). Cationic palladium species being involved in the coupling mechanism have been postulated

previously,[127] and zincates containing three halogens or more are well known.[128] The formation of the cationic palladium species would facilitate transmetallation thereby increasing the rate of reaction. This alternative mechanism may also be in operation for the traditional copper iodide, however, little is known about the corresponding cuprate anions.[129]

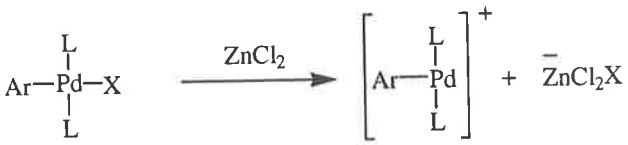


Figure 33. Formation of a cationic palladium species.

Whilst the above arguments disfavour the presence of zinc acetylides, their existence as reactive intermediates cannot be ruled out completely. Several reactive intermediates of the types shown in Figure 34 can be postulated, although no direct evidence to support these structures has yet been obtained. Here the coordinating amine is piperidine, but the incorporation of other nucleophilic amine bases might be envisaged. These proposed structures are based on evidence in the literature that organozinc compounds form strong complexes with amines such as TMEDA,[130] pyridine[131] and imidazole.[132] These amines facilitate the formation of some organozinc species.[131,133] The complexes so formed are thermally stable, and undergo slow hydrolysis[131] as compared to uncomplexed organozincs which generally undergo rapid hydrolysis.[124] In a detailed modelling study it has also been shown that imidazole is more strongly bound than water to Zn^{2+} species.[132] No di-alkynylzinc species have been proposed in Figure 34, however their existence cannot be discounted given the stability of di-alkynylzinc containing pendent dimethyl amino groups.[134]

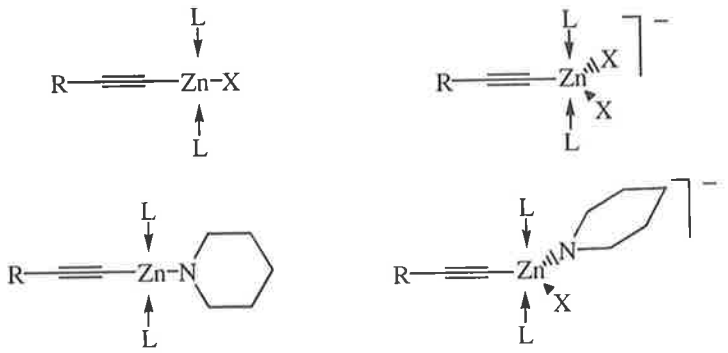
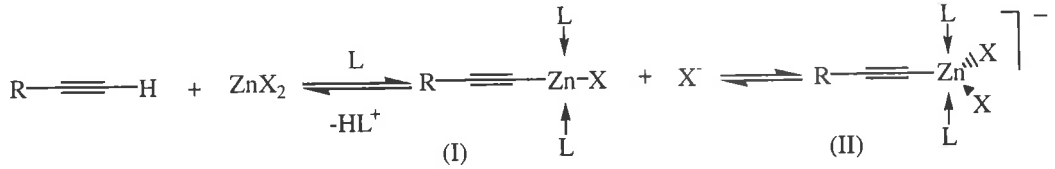


Figure 34. Possible reactive intermediates, L=piperidine, X=halogen

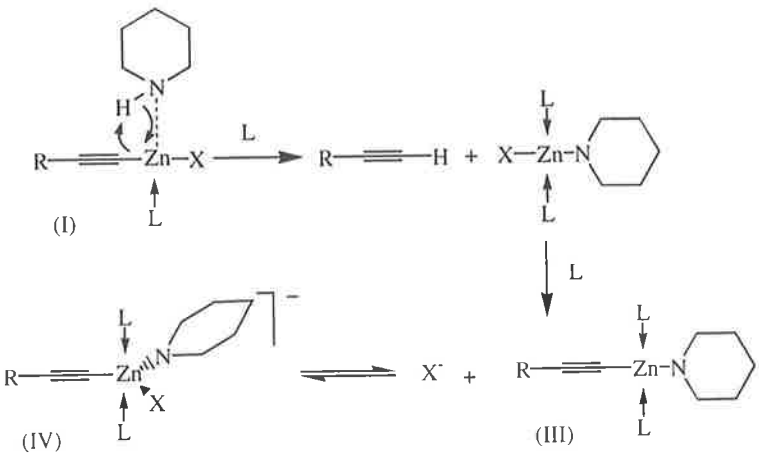
Intermediate (I, **Scheme 64**) could be produced from the reaction of a terminal acetylene with piperidine and a zinc halide (**Scheme 64**) to form a four-coordinate zinc species. The requirement of iodine/iodide source for these reactions to proceed suggests that (I, **Scheme 64**) is converted to (II, **Scheme 64**) in the presence of a halide, and that the penta-coordinate species undergoes transmetallation faster than (I, **Scheme 64**). This type of anion assistance in transmetallation has been observed with fluoride assisted palladium catalysed coupling reactions of organosilicon compounds.[135]



Scheme 64

Organozinc compounds of the type (I, **Scheme 64**) and (II, **Scheme 64**) could react further with piperidine, as the zinc-carbon bond can undergo protonolysis. The reactivity of the zinc-carbon bond towards active protons is high and this process occurs at ambient temperatures.[124] The reaction usually terminates at the mono-substituted stage since the remaining zinc-carbon bond is considerably less reactive.[124] A possible mechanism for the formation of (III, **Scheme 65**) and (IV, **Scheme 65**) is shown schematically below (**Scheme 65**). A similar mechanism could be proposed for the conversion of (II, **Scheme 64**) to (III, **Scheme 65**) and/or (IV, **Scheme 65**).

If the base being used does not possess an active hydrogen, such as DBU, then only the species (I, **Scheme 64**) and (II, **Scheme 64**) could be thought of as the reactive intermediates.

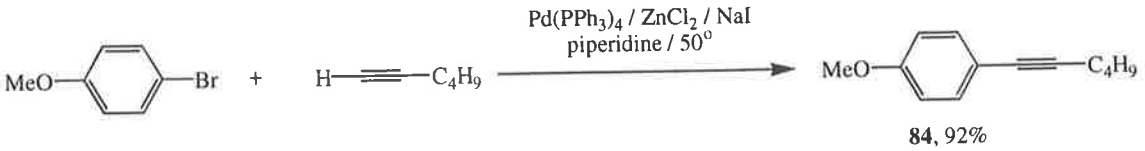


Scheme 65

Of the four structures shown as the reactive intermediate in the catalytic cycle, it can be reasoned that species (IV, **Scheme 65**) would be the most stable under the reaction conditions as it has four electron donating groups around the central zinc atom. It is envisaged that, as for (II, **Scheme 64**), reactive intermediate (IV, **Scheme 65**) would undergo faster transmetallation than (III, **Scheme 65**) based on anionic assistance of the halide. The stability of intermediates of the type (IV, **Scheme 65**) towards hydrolysis or reaction with alcohols (such as propargyl alcohol) is unknown. It is known, however, that di-organozincs undergo protonolysis with alcohols by the same mechanism as for primary and secondary amines.[124] However, since zinc-nitrogen coordinate bonds are stronger than zinc-oxygen coordinate bonds[132] and there may exist a solvent cage effect preventing or limiting the formation of the zinc-alkoxides and hydroxides, thereby allowing the formation of the intermediates depicted in Figure 34. Such arguments are speculative with the requirement of further physical and analytical studies to determine the reactive alkynylzinc intermediate/s in the catalytic cycle.

5.3. Non-Activated Substrates

The limits of this new protocol were then investigated with the coupling of two non-activated substrates, to probe the effects of the co-catalysts on oxidative addition and transmetallation. The first system involved the coupling of 4-bromoanisole to 1-hexyne. The 4-bromoanisole was considered to be a non-activated substrate towards oxidative addition to the Pd catalyst because aryl-bromides react less readily than aryl-iodides,[96,97] and the methoxy group increases the electron density on the electrophile thereby further hindering the oxidative addition. 1-Hexyne ($pK_a \approx 25$) was less reactive than the phenylacetylene ($pK_a \approx 23$) used in the previous section since its terminal proton was harder to abstract.[136] The optimum conditions of 5% $Pd(PPh_3)_4$/20% $ZnCl_2$/20% NaI in piperidine with a slight excess of 1-hexyne were used (**Scheme 66**). The reaction was heated at 50° for 16 hrs since no coupling was observed at room temperature. Extractive workup followed by flash chromatography gave the expected product (**84**)[137] in excellent yield. This result compares quite well to the traditional copper iodide case, where in a gas chromatography study, it has been shown that the CuI conditions go to 71% completion in 4-8 hrs.[118]

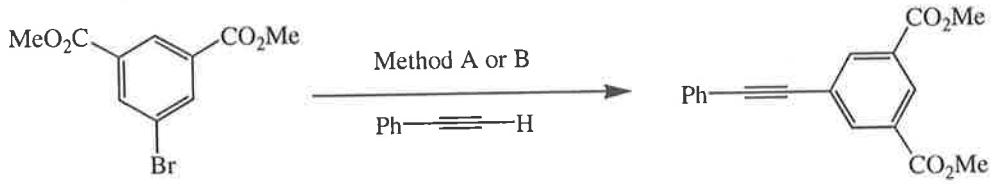


84, 92%

Scheme 66

This reaction using the zinc chloride/sodium iodide combination has been repeated in the above gas chromatographic study where the reaction was found to be complete in a similar time (4-8 hrs).[118] The presence of an anionic palladium species under the zinc chloride/sodium iodide conditions may account for the comparable rate of reaction since it is known that halides aid in the oxidative addition by forming anionic palladium (0) species in solution.[138,139] However, a quantitative kinetic study has yet to be performed on this or other non-activated systems to ascertain the exact nature of the rate determining step. Further studies on the type and effects of the added halides are discussed in the next section.

The coupling of dimethyl 5-bromo isophthalate (**23**) with phenylacetylene was also investigated under traditional Sonogashira conditions and with the zinc chloride/sodium iodide combination. The product was synthetically useful as a test system for various functional group manipulations, and these are discussed in Chapter 6. Two methods (A and B) were trialed in forming the diester (**66**), to investigate alternative coupling conditions (**Scheme 67**).[118]



(**23**)

66, 75% (Method A)
66, 70% (Method B)

Scheme 67

Method A involved the use of 5% $Pd(PPh_3)_4$/20% $ZnCl_2$/20% NaI in DMF but with 20% imidazole in addition to triethylamine as the bulk base. The reaction was heated at 60° for 16 hrs, and gave the product in 75% yield after an extractive workup and recrystallisation. The imidazole was the last component of the reaction mixture to be added and it resulted in an immediate precipitation of what was thought to be zinc imidazolate (which exists as a polymer).[140] The precipitation of the zinc imidazolate

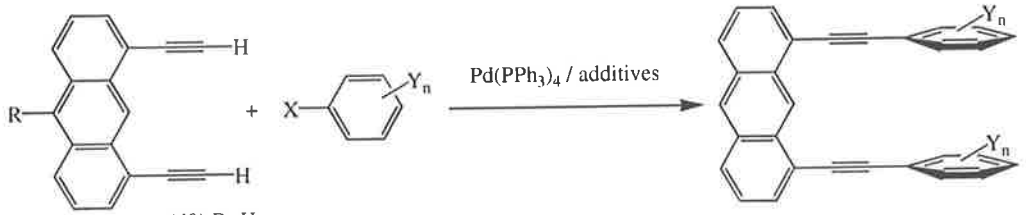
reduced the availability of the zinc catalyst, explaining why a long reaction time was necessary. It was thought that the use of imidazole could be substituted for the nucleophilic piperidine, which has the potential to react with the ester groups. Comparison to the CuI method was promising, with the traditional method giving the product in 71% yield in 1 hr to our method giving a yield of 75% in 16 hrs. The next method went part way to improve this issue.

Method B involved the use of 5% $Pd(PPh_3)_4$/20% $ZnCl_2$/20% NaI in DMF with excess DBU as the base. In this case, DBU was our nucleophilic base, and it was chosen as it would not form amide products with our diester (**23**) as piperidine might. By using DBU instead of triethylamine, a higher concentration of acetylide anions in solution could be formed as DBU was considerably more basic (pK_a=23.9 in CH_3CN)[141] than triethylamine (pK_a=18.46 in CH_3CN)[142]. Using these conditions gave a faster reaction than with method A, giving the product (**66**) in 70% yield after 3 hrs. Clearly these conditions were now comparable to that of the CuI method.

To summarise the results so far, the optimum conditions used are $Pd(PPh_3)_4$, laboratory reagent grade $ZnCl_2$ and NaI in piperidine as the solvent and base. If the substrates were sensitive to piperidine, the use of DBU as the base in DMF worked well. Further studies by the Crisp group in this area have found that $Pd(PPh_3)_4$ was the most appropriate palladium source to use.[118] The use of a nucleophilic base for this reaction was essential, and either NaI or iodine could be used in conjunction with $ZnCl_2$. Finally, as with the CuI method, heating was required for non-activated aryl-bromides.

5.4. Forming the Monomer-Template Coupled Systems

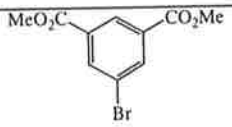
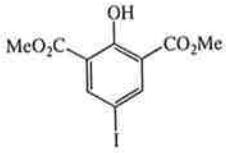
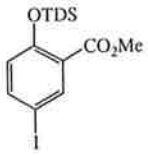
Taking this new coupling chemistry and applying it to coupling monomers with template has met with mixed success. The results of the reaction described in **Scheme 68** are presented below in Table 3.



(**40**) R=H
(**41**) R=1-decyne

Scheme 68

Table 3. Coupling of the monomers to the templates.

Entry	Template	Substrate	Additives	Base	Solvent	% Yield[a]
1	(**40**)	 (**23**)	$ZnCl_2$/NaI/ imidazole	Et_3N[b]	-	0
2	(**40**)	(**23**)	CuI	DBU	DMSO	100 (**67**)
3	(**40**)	 (**20**)	$ZnCl_2$/NaI/ imidazole	Et_3N[b]	-	0
4	(**41**)	(**20**)	CuI	Et_3N[b]	-	0
5	(**40**)	 (**39**)	$ZnCl_2$/NaI	DBU	DMSO	0
6	(**41**)	 (**23**)	$ZnCl_2$/NaI	DBU	DMSO	52[c] (**68**)
7	(**41**)	(**23**)	CuI	Et_3N	CH_3CN	64[c] (**68**)

[a] In all cases 10% $Pd(PPh_3)_4$ was used, at 50° for 3-24 hrs. [b] Base used as solvent.

[c] Reaction complete in 16 hrs.

The good results of coupling the diester (**23**) to phenylacetylene (**Scheme 67**) led us to attempt the coupling of the diester (**23**) to the standard template (**40**) (entry 1, Table 3). Following the reaction by tlc showed the reaction progressed slowly, and it appeared complete after 24 hrs. However, after an extractive workup with ether, very little material was obtained upon removal of the solvent. It was observed also that there was a large quantity of solid material that didn't dissolve in ether. This was initially thought to be the polymeric $Zn(Im)_2$. However, the solid probably contained the bis-

coupled product (**67**) as it had been shown earlier (entry 2, Table 3) (Section 4.2.2) that such compounds are difficult to handle with low solubility in most organic solvents. A better extractive solvent would have been chloroform or THF.

Similar results were obtained in coupling the diester (**20**) to the standard template (**40**) (entry 3, Table 3). However, upon workup the coupled material could be extracted using ether, but was lost on a squat column, the material streaking a great deal on silica. This result was reminiscent of the problems encountered in Section 4.2 where the tradition CuI coupling conditions were used (entry 4, Table 3) with the more soluble template (**41**).

Somewhat more promising results came out of the coupling of the protected monomer (**39**) with the standard template (**40**) (entry 5, Table 3). The coupling was observed to be very slow and the reaction was worked up after 16 hrs. Tlc showed that several compounds were overlapping on both normal and reverse phase silica, and consequently the bis-coupled material could not be purified to any significant extent. This coupling reaction has yet to be performed with the standard CuI catalyst for comparison.

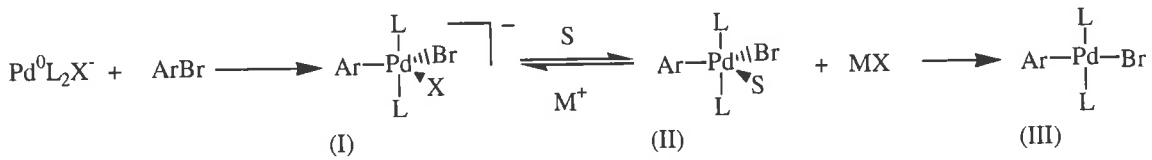
The best results using this new chemistry were obtained with the coupling of the diester (**23**) to the more soluble decyne functionalised template (**41**) (entry 6, Table 3). In this case the desired coupled product (**68**) could be obtained in 52% yield. By using the more soluble template the bis-coupled material could be handled easily and it did not streak to any significant extent on silica. This reaction also compared well to the tradition CuI method, where under standard conditions the yield of the product was 64% (entry 7, Table 3).

5.5. Subsequent Results from the Crisp Group

The precise mechanism of the zinc chloride/sodium iodide reaction remains unknown. To discern more information about the reaction, a series of qualitative experiments were performed using gas chromatography to determine the extent of the reaction.[118] Briefly, the coupling reaction shown in **Scheme 66** was investigated in depth and it was found that the palladium catalysts $Pd(PPh_3)_4$ and $Cl_2Pd(PPh_3)_4$ were equally efficacious. Also, the use of DMSO was favoured over DMF and gave fewer side products. However, the most interesting result to come out of this study, was the

effect of using zinc dust in place of zinc chloride. The complete conditions used were: zinc dust, NaI, DBU and triethylamine in DMSO at 60°. The reaction was complete in 2-3 hrs in a quantitative yield, and gave minimal reduction of the anisole or dimer formation of the acetylene.

The role of the co-catalysts was addressed in another study which looked at the 4-bromoanisole/1-hexyne coupling reaction by gas chromatography.[143] It was also found that the reaction was catalysed by addition of metallic salts, without $ZnCl_2$. For example, the reaction was catalysed when the co-catalyst was only NaCl, KCl or NaBr, to give respectable yields of 52-87% in 6-8.5 hrs. The ion-pairing of the salts was shown to be an important factor influencing the rate of the reaction. This process is shown schematically in **Scheme 69**. Tight ion pairs such as NaCl and LiCl produced a considerably faster rate than loose ion pairs such as tetrabutylammonium bromide. The nature of the cation in turn influences the rate of oxidative addition, and the overall rate of reaction, by its ability to sequester the halide from species (I, **Scheme 69**).[138] Cations from tight ion pairs will be able to sequester the halide faster than those of loose ion pairs, thereby aiding the conversion of (I, **Scheme 69**) *via* (II, **Scheme 69**) into (III, **Scheme 69**) and increasing the rate of oxidative addition. Further studies on activated substrates where oxidative addition is not the rate determining step need to be performed to determine the effect of these salts on transmetallation.



L=PPh_3 and S=solvent molecule

Scheme 69

5.6. Summary

The fortuitous initial discovery of the coupling of iodobenzene with phenylacetylene, under some quite novel conditions, has led the development of a new palladium catalysed coupling protocol. The conditions for coupling have been shown to be compatible with a wide range of functional groups to give good yields, and has been employed in the synthesis of one of the monomer-template coupled systems.

Studies within the Crisp group have shown that the nucleophilicity of the base is important and this would imply a coordination of the base to the zinc intermediate which either stabilises or activates the organozinc intermediate. The zinc salts may simply be acting as Lewis acids to increase the acidity of the terminal alkyne thereby facilitating coupling, or a more complex organozinc intermediate or intermediates may be involved. Other Lewis acids apart from those containing zinc have been shown to be effective, and in some cases the coupling proceeds in the absence of zinc.

6. Functional Group Manipulations

Once the monomers had been coupled to the template systems, the next step lay with the conversion of the precursor groups of these bis-coupled materials to suitable leaving groups. These leaving groups, which were generally bromides, were displaced in the following step to effect cyclophane formation. Other leaving groups apart from the bromides were investigated, and these included iodides and mesylates. The reactions discussed in this chapter are outlined below in Figure 35.

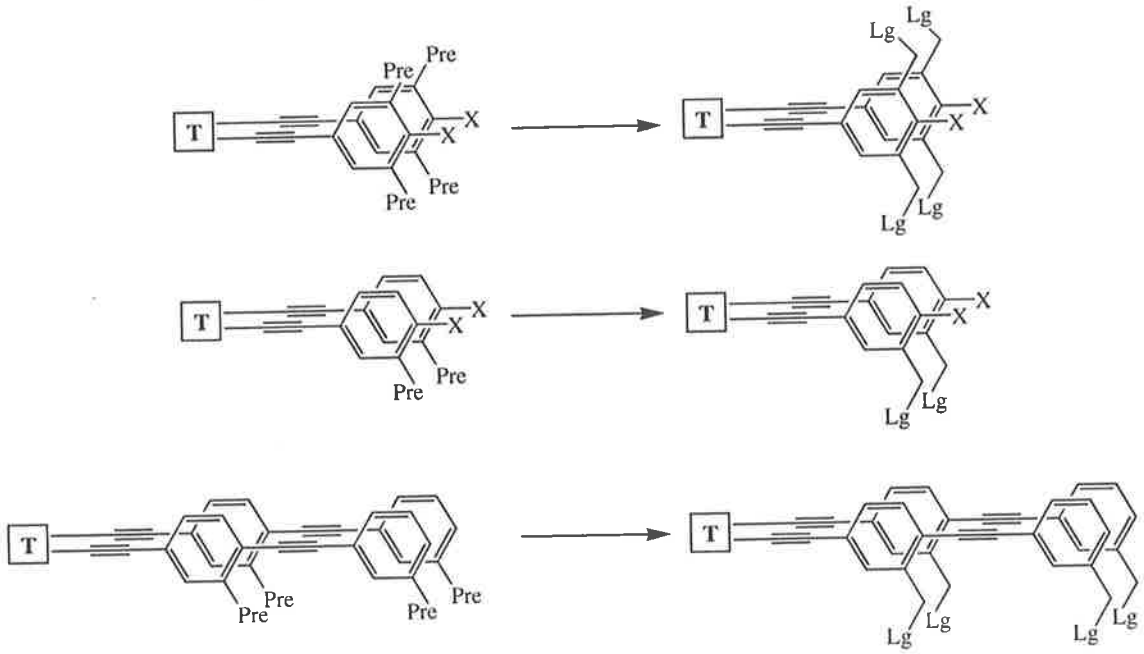


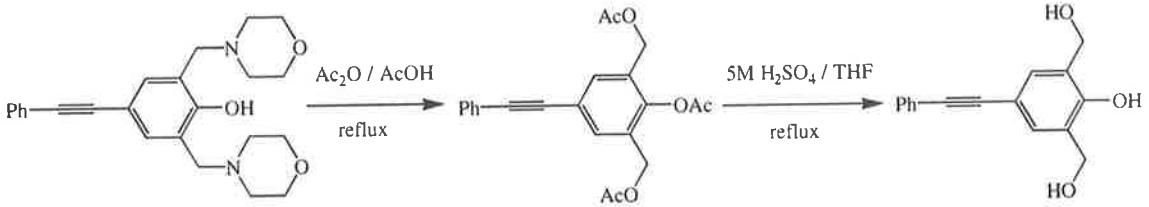
Figure 35. Conversion of precursor groups, X=H,OR; Lg=leaving group.

The products of the coupling reactions of Chapter 4 which used phenylacetylene to model the templates, have been used to test functional group manipulations of the bis-coupled systems.

6.1. Conversion of Mannich Bases

Initially, the conversion of the Mannich base (**54**) to the corresponding bis-hydroxymethyl compound, *via* the triacetate, was investigated (**Scheme 70**). Treatment of (**54**) with acetic anhydride and acetic acid at reflux successfully produced the tri-acetate (**85**) in 75% yield. Hydrolysis under basic conditions gave only partial hydrolysis using a range of conditions, including guanidine/MeOH, NaOMe/MeOH and

KOH/MeOH. Even with extensive heating of the reaction mixtures only one or at most two of the acetates could be cleaved, as suggested by tlc. No tri-hydroxy (**56**) could be isolated. Acidic conditions were then used. Hydrolysis was attempted by heating to reflux a THF solution of (**85**) with 10% citric acid, but there was no hydrolysis of the tri-acetate (**85**) after several hours. A small quantity of 5M H_2SO_4 was then added and reflux continued. Under these conditions complete hydrolysis could be achieved in 17 hrs to give the desired bis-hydroxymethyl compound (**56**) in 48% yield.

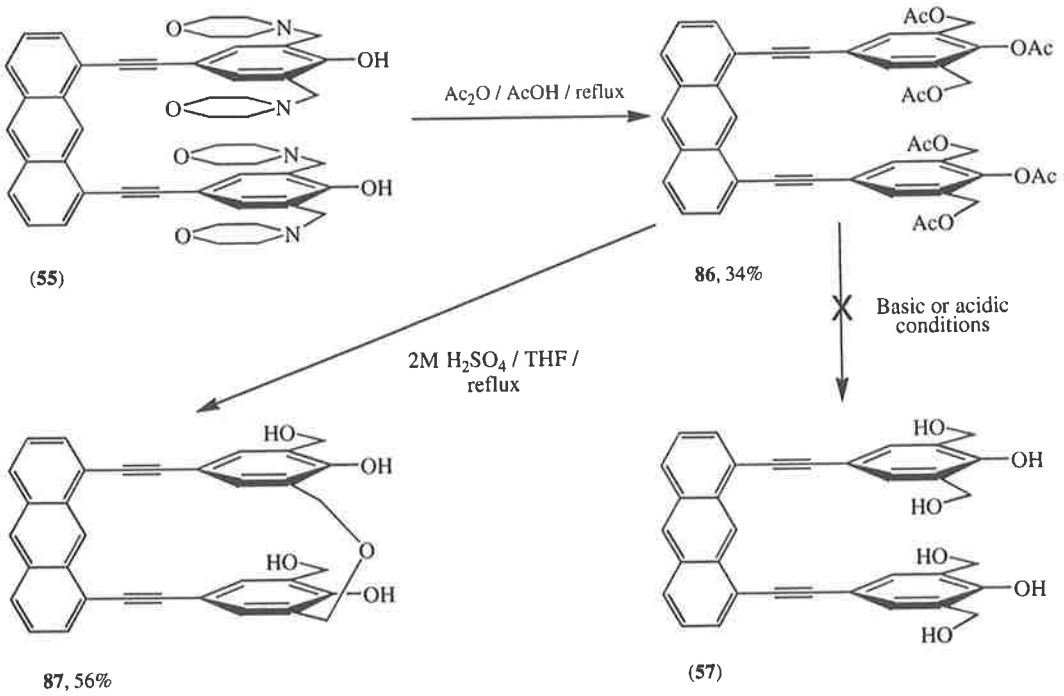


(**54**) **85**, 75% **56**, 48%

Scheme 70

These last two steps were synthetically important as they established the fact that the acetylenic functionality can remain intact under strongly acidic conditions while the linker-arm precursors were manipulated.

The above chemistry was then applied to the coupled system (**55**), shown in **Scheme 71**. The Mannich base (**55**) was first converted to the hexa-acetate (**86**) by reflux in acetic anhydride and a small amount of acetic acid. This gave the hexa-acetate (**86**) in a modest 34% after purification by flash column chromatography. The IR spectrum of this compound showed three carbonyl absorptions instead of the expected two. Two of the peaks were of similar intensity, suggesting Fermi resonance was responsible for the extra peak.

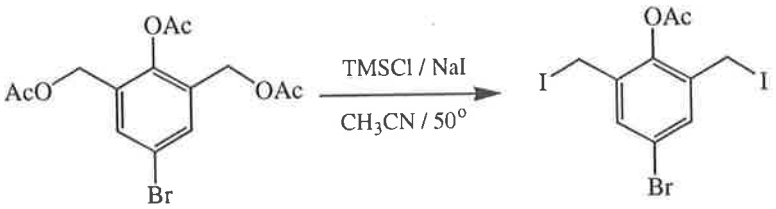


Scheme 71

Hydrolysis of the hexa-acetate (**86**) proved to be troublesome. Complete hydrolysis to form compound (**57**) could not be achieved under basic conditions. These included guanidine/MeOH, K_2CO_3/H_2O/MeOH and $LiOH/H_2O$/MeOH. This result was reminiscent of the test system (**85**) under basic hydrolysis. More success was obtained with acidic conditions. However, the reaction proceeded beyond complete hydrolysis to give a one-arm cyclophane (**87**). Presumably this arose through the displacement of a protonated hydroxymethyl group by the oxygen of an adjacent hydroxymethyl group. Confirmation of the structure was obtained by proton and carbon NMR, along with accurate mass spectrometry. In the proton spectrum (600 MHz), two singlets at δ 4.82 and δ 5.07 ppm of equal integration were observed for the two distinct benzyl groups, and two doublets at δ 7.93 ppm and δ 7.64 ppm (*J* 1.8 Hz) corresponding to the two aromatic protons of the cyclophane rings possessing meta-coupling with each other. The carbon spectrum showed 14 aromatic signals, consistent the proposed structure, and accurate mass value was in agreement with the calculated value. Apart from baseline material, the cyclophane was the sole product of the reaction, with no two-arm cyclophane being observed. The isolated cyclophane streaked extensively on silica, and had limited solubility in common organic solvents, resulting in the modest yield. It may be possible to completely cyclise (**87**) to the two-arm cyclophane with a stronger Lewis acid, however, this was not investigated.

6.2. Conversion of the Acetoxymethyl Groups

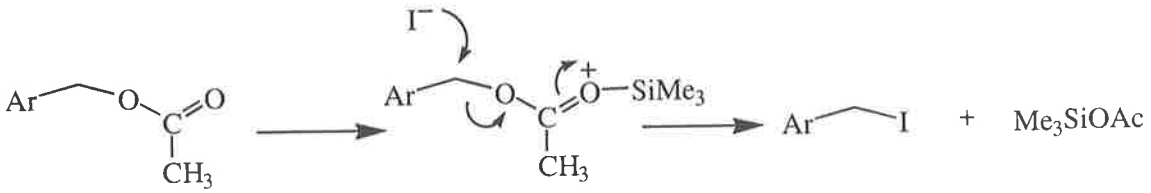
The difficulty of hydrolysing the acetoxymethyl groups of (**87**) led to the search for alternative ways of converting the acetates to good leaving groups. This was explored with the use of trimethylsilyliodide.[144,145,146,147] The use of this reagent was first investigated with the tri-acetate (**4**) (**Scheme 72**). The reagent was prepared *in-situ* by heating trimethylsilylchloride and sodium iodide in acetonitrile.[146] Over the course of the reaction sodium chloride precipitated from solution.



(**4**) **88**, 62%

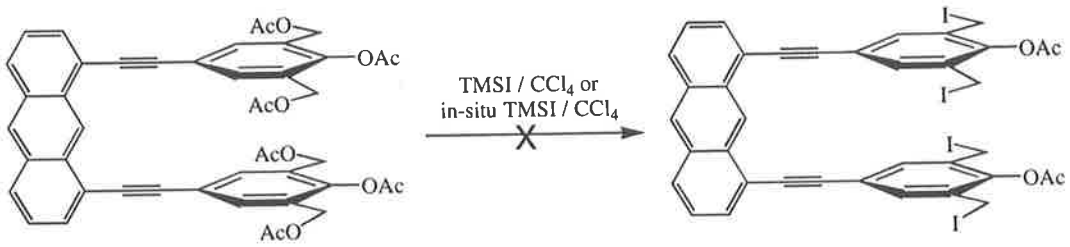
Scheme 72

This reaction only converted the acetoxymethyl groups and left the aryl acetate untouched. The mechanism to explain selectivity is outlined below in **Scheme 73**. Firstly, the trimethylsilyl group complexed with the acetate functionality and then the more nucleophilic iodide displaced the complexed acetate to give the iodomethyl compound and trimethylsilylacetate. With the aryl-acetate, complexation still occurs but no nucleophilic displacement was possible. Chloromethyl compounds are not observed with this reaction as formation of the iodomethyl compounds was driven by the precipitation of sodium chloride.



Scheme 73

Once the chemistry of this reaction had been established, it was then tried on the hexa-acetate (**86**). Two methods were trialed; the *in-situ* generation of trimethylsilyliodide in CH_3CN, and the addition of preformed trimethylsilyliodide in CCl_4 (**Scheme 74**). Unfortunately, none of the tetrakis-iodomethyl compound (**89**) could be isolated as both methods gave complex reaction products. Chromatographic separation of the more dominant products yielded complex materials by proton NMR. It was also possible that some of the reaction products had coincident R_fs.



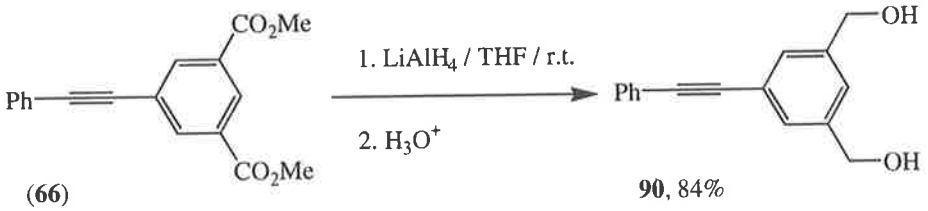
(86) (89)

Scheme 74

6.3. Reduction of the Esters

The result of the previous sections showed that a more amenable path to the synthesis of the compounds outlined in Figure 35 had to be found. One of the ways this was achieved was with the synthetic manipulations of the bis-coupled systems containing esters. These esters would first be reduced to the hydroxymethyl groups, and then converted to the respective halomethyl or mesylate compounds.

The reduction of the esters was first investigated with the test diester (**66**). Reduction proceeded quickly and selectively at room temperature, giving the desired bis-hydroxymethyl compound (**90**) in 84% yield (**Scheme 75**).



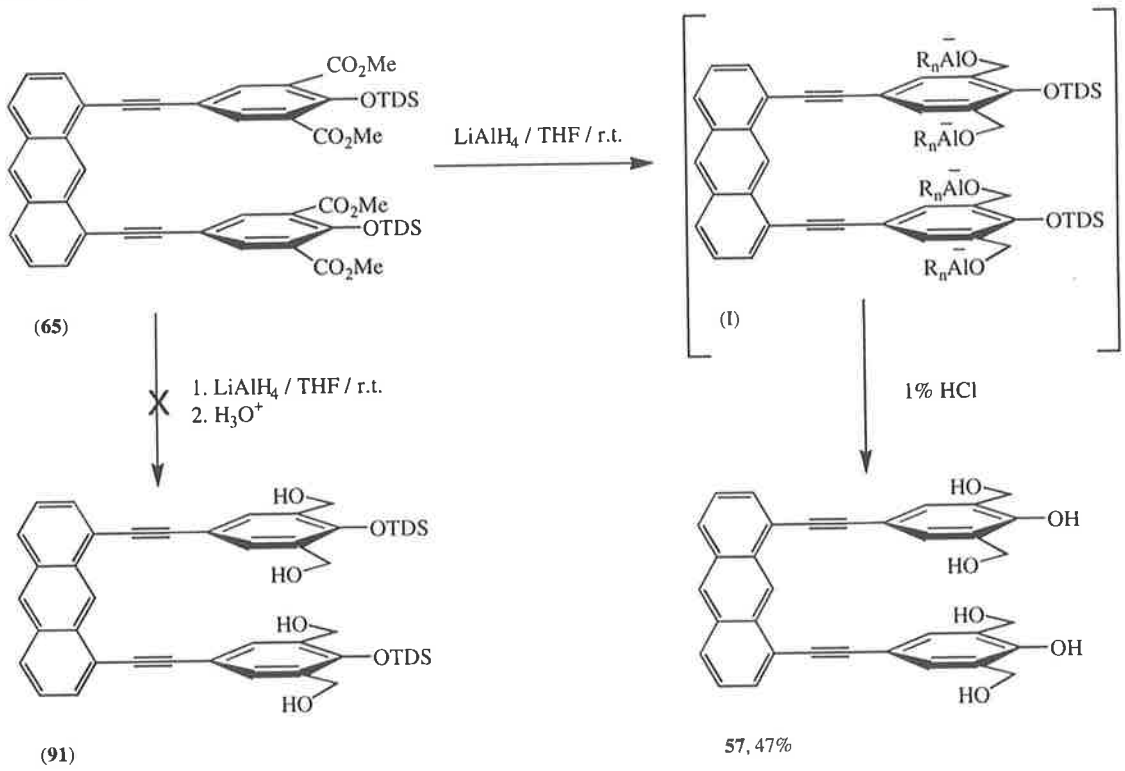
(**66**) **90**, 84%

Scheme 75

The next step was to apply this chemistry to the reduction of the bis-coupled systems. This was attempted with the tetra-ester (**65**). However, the protecting groups were cleaved during the acidic workup, using 1% HCl, failing to give silyloxy compound (**91**) (**Scheme 76**). Using milder acids, such as 10% citric or sat. NH_4Cl, failed to dissolve the gelatinous material containing the intermediate (I, **Scheme 76**), obtained after the reaction was quenched with water. Basic conditions failed in the same manner. These problems aside, complete reduction of the esters was achieved and the tetra-hydroxymethyl compound (**57**) was isolated after chromatography on reverse phase silica in 47% yield. As expected, from Chapter 4, the cleavage of the TDS groups made handling of this material difficult, and the reaction could only be followed with reverse

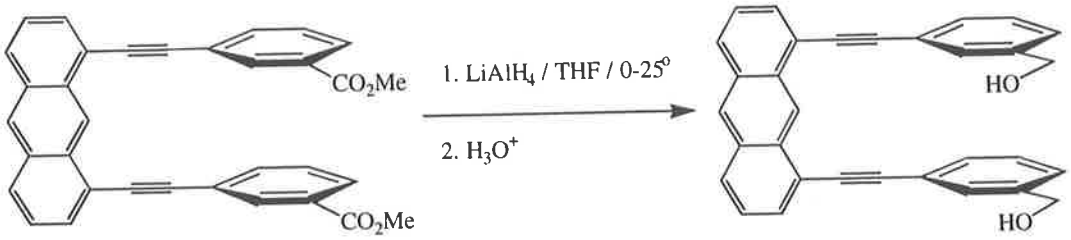
phase tlc plates since only a baseline spot was observed with normal silica. There remains the possibility of selectively re-protecting the isolated material, however this was anticipated to be difficult from the triflation studies of Section 2.1.4, where the neighbouring hydroxymethyl groups participated in the reaction under basic conditions.

The formation of the siloxy compound (**91**) would have been useful in the subsequent step to convert the hydroxymethyl groups to good leaving groups. The utility of compound (**91**) would have been in its discrimination between the hydroxyl groups of the phenols with that of the hydroxymethyl moieties. A method to circumvent this problem is discussed in the next section.



Scheme 76

The promising results of the above system led to the reduction being applied to the simpler diester (**69**). In this case, the diester could be reduced with LAH in THF at 0-25°, to give the desired product (**92**), in good yield after an acidic workup and purification on reverse phase silica (**Scheme 77**). The bis-hydroxymethyl compound (**92**) was not characterised, but taken directly on to the corresponding bromide, which is discussed in the next section.



(69) **92**, 81%

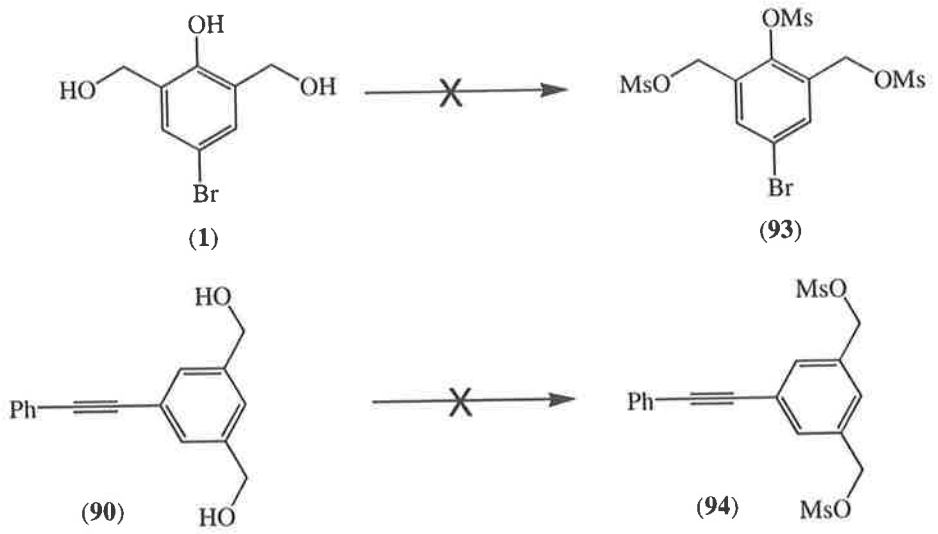
Scheme 77

6.4. Conversion of the Hydroxymethyl Groups

Apart from introducing hydroxymethyl-containing monomers directly to the templates (Section 4.3), the successful reduction of the bis-coupled systems containing esters, also generated a series of coupled systems containing hydroxymethyl groups which could now be converted to good leaving groups.

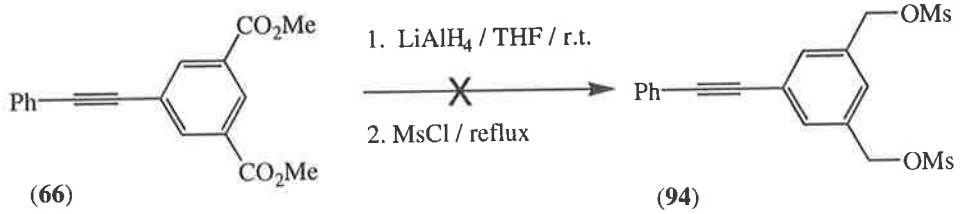
The types of leaving groups investigated were mesylates, iodides and bromides. Of these, the bromides were found to be the most amenable, both to synthesis and stability. However, let us first discuss the formation of the mesylates.

Two test compounds were initially used to determine suitable conditions for mesylation. These compounds were the bis-hydroxymethyl compounds (**1**) and (**90**) which were used in attempts to form the corresponding mesylates (**93**) and (**94**) respectively (**Scheme 78**). For both compounds several different conditions were trialed including pyridine/MsCl in CH_2Cl_2 or $CHCl_3$, MsCl with pyridine as solvent and base, and finally MsCl/Et_3N in CH_3CN. In every case, the disappearance of the starting materials could be seen with the concomitant formation of higher R_f materials. However, the product/s decomposed every time on silica with no materials being recovered from the columns.



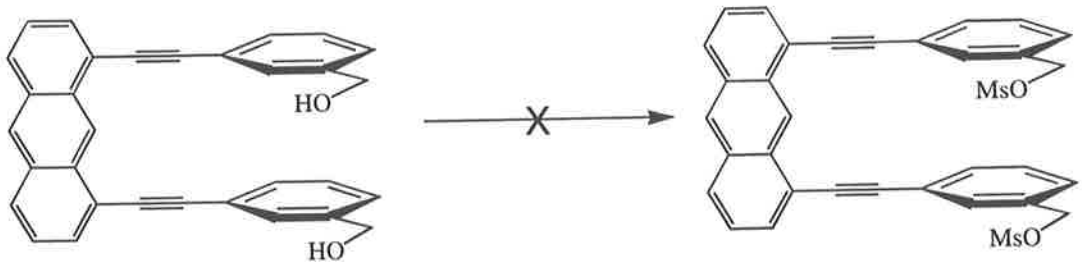
Scheme 78

Another method for forming the mesylate (**94**) was investigated. This time the diester (**66**) was reduced with LAH as in **Scheme 75**, but the reaction was quenched with MsCl and the reaction mixture refluxed for 12 hrs (**Scheme 79**). At the end of this time, one product spot dominated by tlc. However, as in the previous cases the material decomposed on silica.



Scheme 79

The evidence from the previous reactions did not bode well for trying to mesylate the bis-coupled systems. Nevertheless, mesylation was attempted on the bis-hydroxymethyl compound (**92**), using MsCl with pyridine as the solvent and base, or MsCl/pyridine in $CHCl_3$. In both cases, the product/s decomposed on silica and none of the bis-mesylate (**95**) could be isolated. It might have been possible to dispense with the purification step altogether and perform a direct displacement of the mesylates formed in solution with a nucleophile. This has been performed on allylic alcohols, converting them to allyl chlorides using $MsCl/Et_3N$ in CH_2Cl_2 followed by the addition of excess LiCl.[148] The substitution may also work with LiBr, however work in this area has not been investigated since a more direct route from the hydroxymethyl to the bromomethyl systems has been found, and is discussed later.

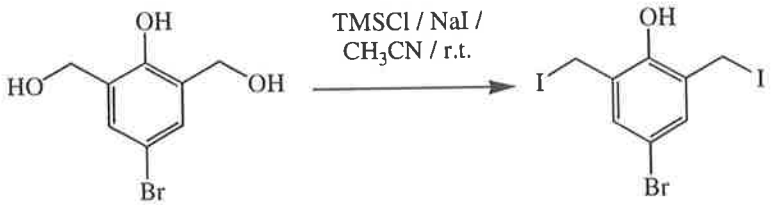


(92) (95)

Scheme 80

Alcohols can be converted to their corresponding alkyl halides with a wide variety of reagents.[149] The most common reagents used for these transformations are the halogen acids HX and the inorganic acid halides, such as $SOCl_2$, PCl_3, PCl_5, $POCl_3$ and PBr_3.[150] However, the use of the halogen acids can be precluded since they will add across the triple bonds of the bis-coupled systems.[151] Often the best way to effect a transformation lies with the use of the mildest reagents and conditions, and these were the methods of choice that were used below. With this in mind, the next type of leaving group that was investigated were the iodides.

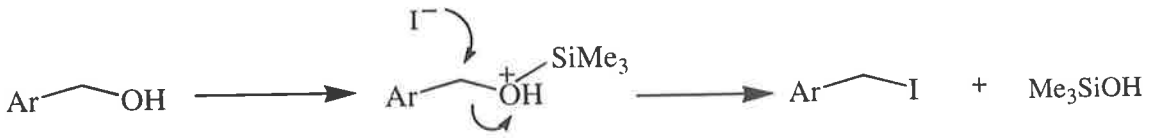
The first reaction investigated was the conversion of the bis-hydroxymethyl compound (**1**) to the bis-iodomethyl phenol (**96**). This type of reaction was similar to the conversion of the acetoxymethyl groups in **Scheme 72**. Here the same reagents were used, TMSCl/NaI/CH_3CN, at room temperature. Under these mild conditions the corresponding bis-iodomethyl phenol (**96**) could be produced in good yield after sublimation (**Scheme 81**).



(1) **96**, 64%

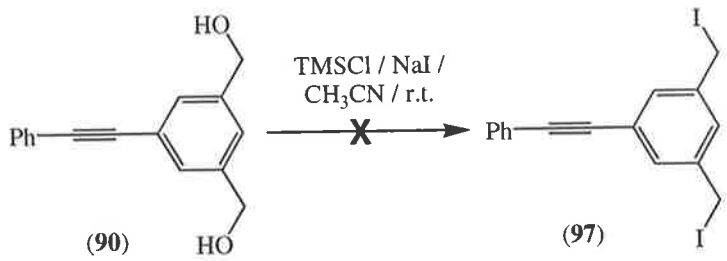
Scheme 81

The mechanism of this transformation was similar to that described in Section 6.2, where the TMS group co-ordinates to the oxygen of the alcohol, followed by displacement by the iodide to give the iodomethyl compound and TMS alcohol (**Scheme 82**).[146]



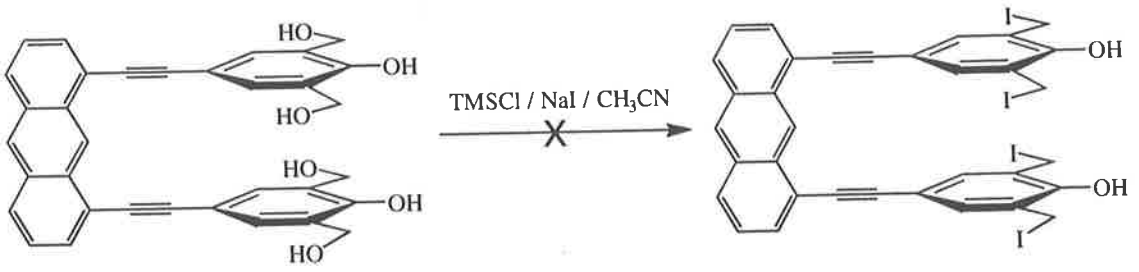
Scheme 82

However, when these conditions were used in an attempt to convert the bis-hydroxymethyl compound (**90**) to the corresponding iodide (**97**) none of the desired compound could be isolated (**Scheme 83**). Only a small amount of material could be isolated by flash chromatography. This material possessed a complex proton NMR spectrum and underwent decomposition in solution over several hours, with the appearance of a purple colour being observed. This might have been due to the formation of molecular iodine in solution, however the identity of the decomposition products or the isolated material was not pursued.



Scheme 83

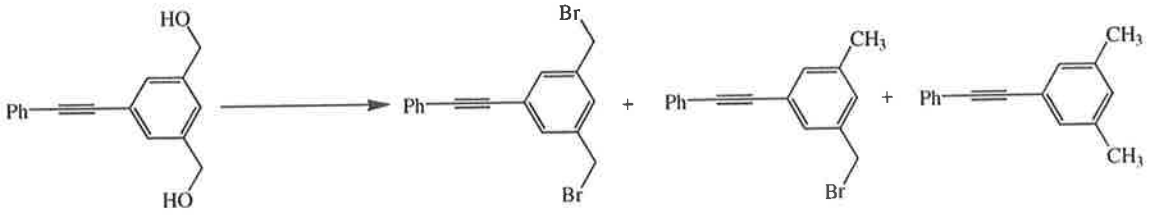
Similarly, application of this chemistry to the bis-coupled system (**57**) to form the tetrakis-iodomethyl compound (**98**) met with no success (**Scheme 84**). Initially, the same reagents and conditions were used as before and the reaction was deemed complete after 2 hrs. However, upon an extractive workup it was found that the product could not be taken up into solution with either ether or dichloromethane, but gave an intractable solid. This may have been expected with the large number of halogens on the one compound and with the two unprotected phenolic groups. With the handling of this material being difficult, and its stability in solution in doubt, these iodides were not pursued any further. Instead we turned to the bromides.



(57) (98)

Scheme 84

Once again a model system (**90**) was used to test reagents and conditions. A number of different conditions were tried to find the best way to form the bis-bromomethyl compound (**99**) (**Scheme 85**). These results are summarised in Table 4.



(90) **99**, 0-65% (100) (101)

Scheme 85

Table 4. Test conditions for making the aromatic (**99**).

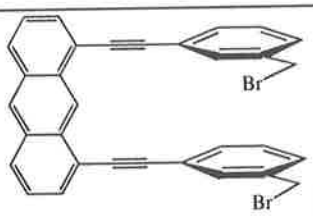
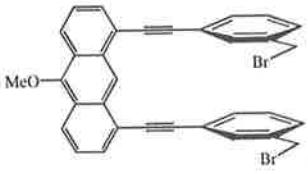
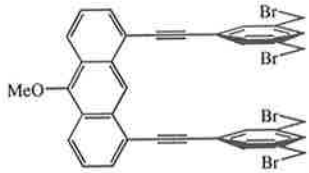
Entry	Conditions	Time (hrs)	Products	% Yield
1	PPh_3/CBr_4/ether/reflux	16	(**99**)	65
2	PPh_3/CBr_4/py/60°	1	decomp.	-
3	$PPh_3/CBr_4/CH_3CN$/50°	48	(**99**) + (**100**) + (**101**)	-
4	PBr_3/THF/reflux	16	(**99**)	26

The first set of conditions that were tried (entry 1,Table 4) were modelled on a literature procedure,[152] and gave the desired material in a reasonable yield. The reaction required heating to proceed, and was observed to be quite slow when followed by tlc. The next reaction (entry 2, Table 4) was based on a literature method also,[153] however when the reaction was followed by tlc, the disappearance of starting material did not result in a corresponding formation of product/s. Only baseline material was observed. The use of acetonitrile as a solvent (entry 3, Table 4) slowed the reaction dramatically,

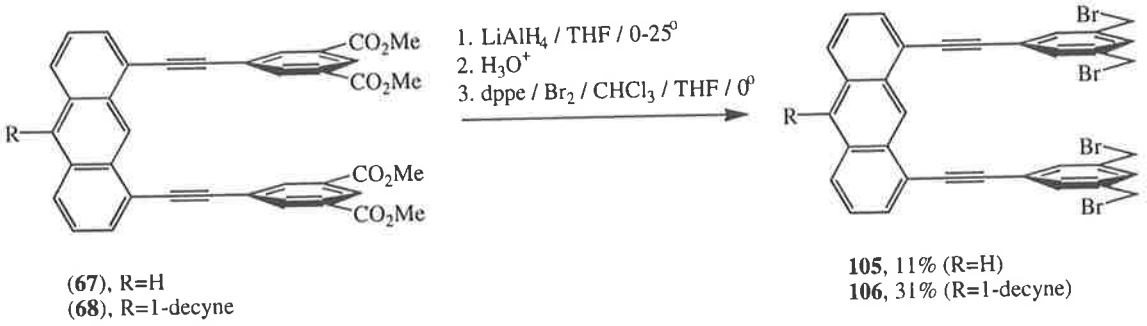
and the product (**99**) decomposed over the long period of heating to give a mixture dehalogenated materials (**100**) and (**101**). All three compounds (**99-101**) had the same R_f in a range of solvent systems. The constituents of the mixture were determined by mass spectrometry, as determination by proton NMR wasn't conclusive. The last reaction (entry 4, Table 4) gave the product in only a modest yield after flash chromatography.

Whilst the original reaction conditions appeared the best to use with the coupled systems, milder reaction conditions were found in the literature based on a dppe (bis-diphenylphosphinoethane)/Br_2[154,155] or a PPh_3/NBS[156] combination at 0° or below. For the dppe/Br_2 conditions the dppe.Br_2 complex was first formed by addition of a 2M solution of bromine in chloroform to a solution of dppe in chloroform at 0°, under anhydrous conditions. After the addition of the bromine was complete the substrate was then added in a dry THF/$CHCl_3$ solution, the THF being necessary for solubility. The PPh_3/NBS combination was much less involved, requiring only the addition of the two reagents along with the substrate to a dry THF solution of the alcohol at -20°, and allowing it to warm to 0°. Both of these conditions, especially the dppe/Br_2 combination (entries 1-2, Table 5), were found to work extremely well with the bis-coupled systems. The PPh_3/NBS method tended to give reduced yields (entries 3-4, Table 5), but both systems left the alkyne groups untouched, the dppe/Br_2 combination even being compatible with silyl protecting groups.[154] Both combinations, in general, gave complete conversion of starting materials in under an hour. The results of these reactions are summarised below in Table 5.

Table 5. Converting the hydroxymethyl alcohols to bromomethyl aromatics.

Entry	Substrate	Conditions	Product	% Yield
1	(**92**)	dppe/Br_2	 (**102**)	78
2	(**73**)	dppe/Br_2	 (**103**)	77
3	(**73**)	PPh_3/NBS		56
4	(**74**)	PPh_3/NBS	 (**104**)	64

In the case of some systems, the intermediate compounds containing hydroxymethyl groups were not isolated, but used crude in the subsequent bromination step. Two of these systems were the tetra-esters (**67**) and (**68**), which were first reduced with LAH at 0-25°, the reaction mixtures worked up in the usual fashion, the crude alcohols dried under high vacuum, and then brominated using the dppe/Br_2 combination (**Scheme 86**). Unfortunately, the corresponding tetrakis-bromomethyl compounds (**105**) and (**106**), could only be isolated in low to moderate yields. Explanations for the reduced yields rested with the tetrakis-bromomethyl compound (**105**) having significant solubility problems which contributed to the low yield after flash chromatography, and with the formation of the tetrakis-bromomethyl compound (**106**), a considerable amount of baseline material was observed when the reaction was followed by tlc. Of note with compound (**105**) was that no molecular ion, and as a result no accurate mass data, could be obtained for this compound despite trying both EI and LSIMS techniques. However, both proton and carbon NMR spectra were consistent with the structure of compound (**105**). The tetrakis-bromomethyl compound (**106**) could not be separated from close running materials by flash chromatography on normal or reverse phase silica. Consequently only accurate mass data could be obtained for this compound.

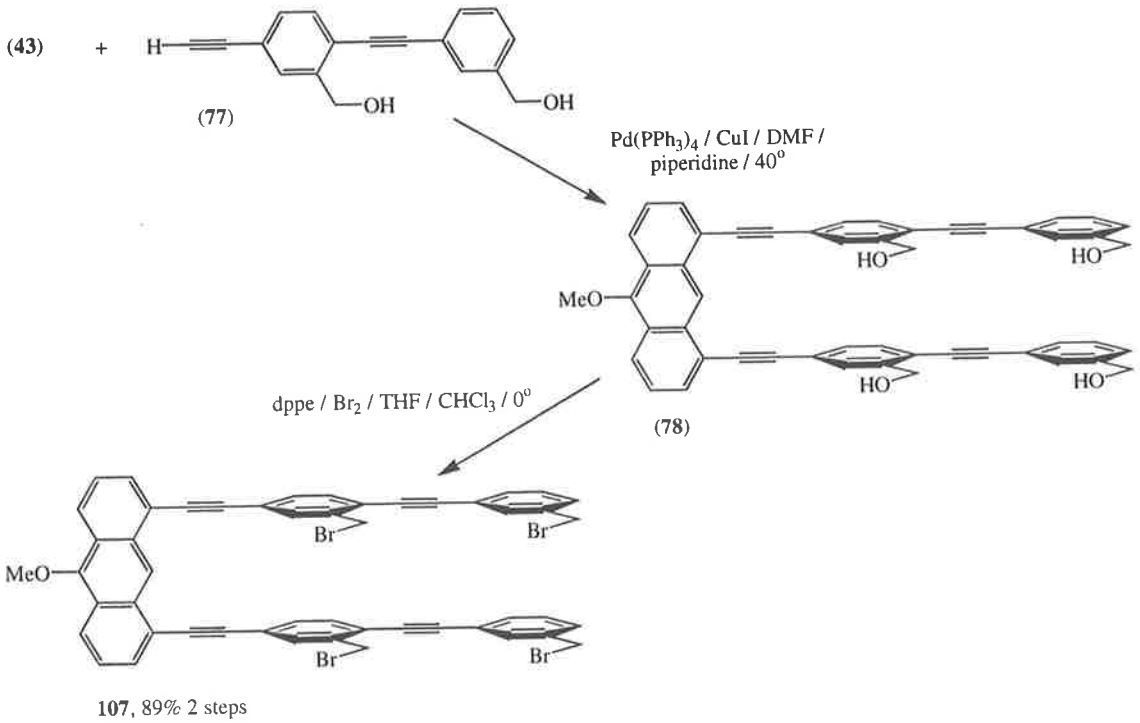


(**67**), R=H
(**68**), R=1-decyne

105, 11% (R=H)
106, 31% (R=1-decyne)

Scheme 86

A higher yield was obtained with the tetra-bromomethyl compound (**107**). The tetra-bromomethyl compound was obtained in 89% yield from the template (**43**) in two steps (**Scheme 87**). The oligomer (**77**) was first coupled to the template with Pd catalysed coupling chemistry (discussed earlier in Section 4.3.1) to form the intermediate (**78**), and then brominated with the dppe/Br_2 combination to give the tetra-bromomethyl compound (**107**). In this case, no solubility problems were encountered as for (**105**), and the tetra-bromomethyl compound (**107**) could be purified easily by normal flash chromatography.

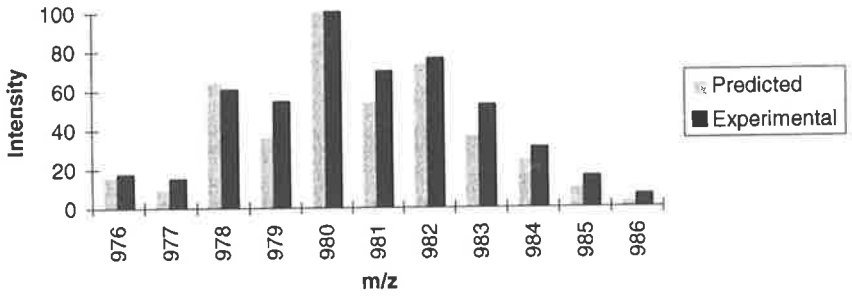


107, 89% 2 steps

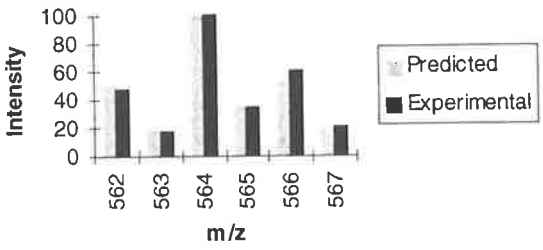
Scheme 87

All of the compounds in **Scheme 86**, **Scheme 87** and Table 5 were characterised by the proton and carbon NMR spectra where possible, and by accurate mass

spectrometry (except for compound (**105**)). The accurate mass data generally gave good correlations between the observed and predicted mass values. Similarly, good correlations were observed between the observed and predicted isotope pattern of the molecular ions. These distinctive patterns are due to the two isotopes of bromine, ^{79}Br and ^{81}Br, which have natural abundances of 49.5 and 50.5% respectively. Examples of the isotope distribution patterns are shown below for (**107**) in Graph 1 and for (**102**) in Graph 2. On occasion the formation of molecular ions could not be observed using electron-impact or electrospray techniques with the bis-coupled systems. However, this problem was generally overcome using liquid secondary ionisation mass spectrometry (LSIMS). The issue of producing sufficient quantities of molecular ions relative to background noise, may explain why there are slight deviations between the observed and predicted values in Graphs 1 and 2. The isotope patterns were generated using the program "Isotope Pattern Calculator Version 1.6.4".



Graph 1. The predicted and experimental isotope patterns for $C_{51}H_{32}Br_4O$ (**107**).



Graph 2. The predicted and experimental isotope patterns for $C_{32}H_{20}Br_2$ (**102**).

6.5. Summary

The results discussed in this chapter have shown that the conversion of the precursor groups of the bis-coupled systems to 'good' leaving groups was possible in the form of bromides. Other leaving groups such as mesylates and iodides were found to have limited stability in solution. Nevertheless, a series of bis-coupled systems were transformed into systems suitable for cyclophane formation by displacement of the alkyl bromides with a variety of nucleophiles. These reactions are discussed next in Chapter 7.

7. Cyclophane Formation

The last step in the formation of the cyclophanes lay with the double nucleophilic displacement of a range of nucleophiles on the bromomethyl groups. The nucleophiles investigated were sodium sulphide and sodium *p*-toluenesulphonamide. Transesterification was also investigated as a method of cyclophane formation with the tetra-ester (**65**).

Semi-empirical molecular modelling experiments were performed on some systems to assess the suitability of the linker-arm with regards to the introduction of strain into the geometry of the cyclophanes. These semi-empirical geometry optimisation experiments were carried out using the Spartan molecular modelling program with the AM1 basis set.

The formation of both one-arm and two-arm cyclophanes was investigated, along with a two-unit oligomeric system. The main scope of the reactions investigated in this chapter are outlined below in Figure 36.

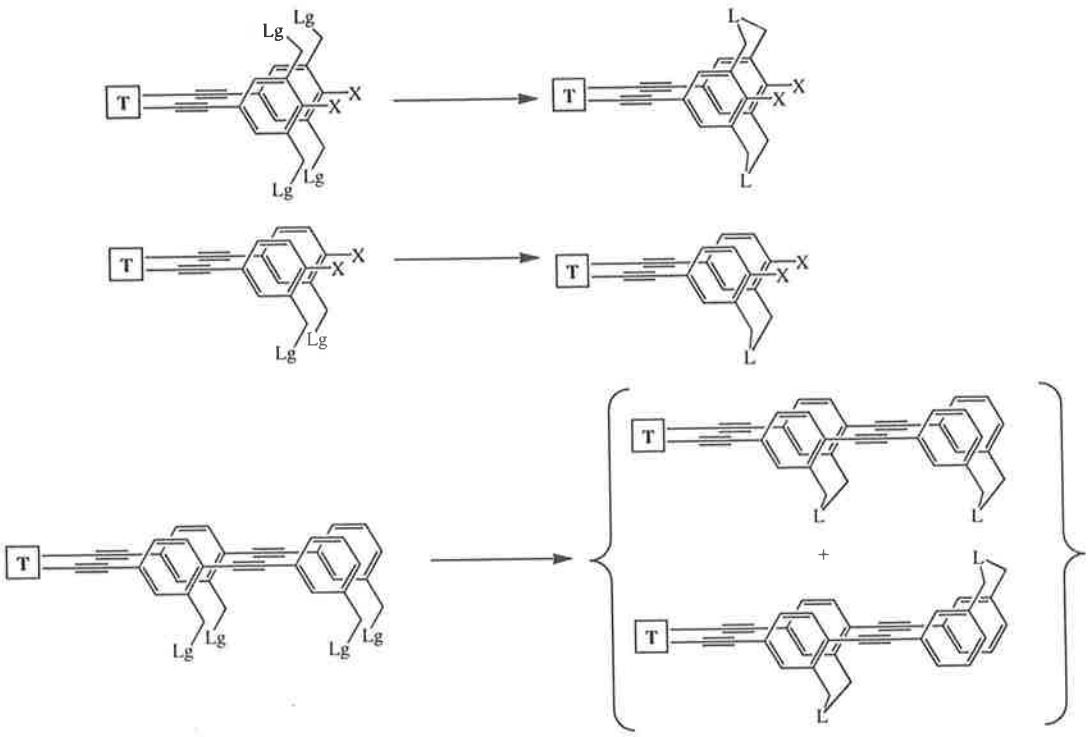
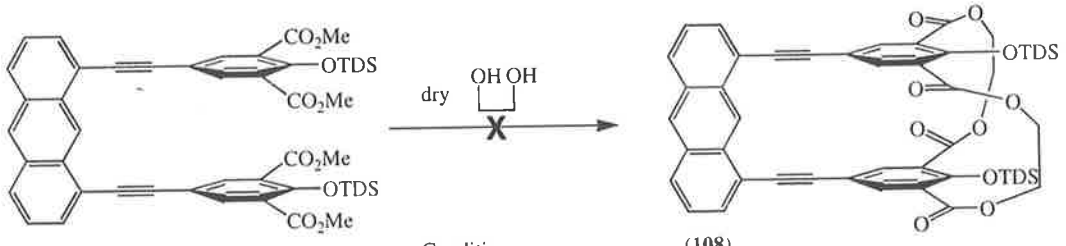


Figure 36. The main cyclophane formation reactions, X=H, OR; Lg=leaving group.

7.1. Transesterification Reactions

Attempts at making cyclophanes containing ester linkages were investigated under transesterification conditions with ethylene glycol (**Scheme 88**).[157] Several conditions were trialed with the reactions being kept under nitrogen, and followed by tlc and proton NMR. It was expected that there would be little difference between the proton NMR spectra of (**65**) and (**108**), however there should have been an observable difference in integration of the ester protons between the two compounds, 12H for (**65**) and 8H for (**108**). Initially, a hypernucleophilic acylation catalyst (DMAP) was used in an attempt to aid in the transesterification.[158,159] After reflux for two days only starting material was observed. In the second case, DMAP along with a mild base, potassium carbonate, and a phase transfer catalyst (Bu_4NHSO_4) were added to the reaction mixture. After stirring at room temperature for 24 hrs, again only starting materials were observed. Addition of an excess of stronger base, potassium hydroxide, resulted in an immediate colour change from yellow to orange. Tlc showed only mainly baseline material with some starting material still present after 12 hrs. After purification *via* a short squat column, proton NMR showed that the only isolable material to be starting material. The baseline product/s were expected to be either polymerised materials or desilylated compounds which, from results in Chapter 4, would 'stick' to the silica. There was also the possibility that under the strongly basic conditions hydrolysis had occurred to some extent, producing carboxylate salts which would have been observed by tlc as baseline material.

The final attempt at forming (**108**) was by using a Lewis acid, titanium *iso*-propoxide, to aid the transesterification, instead of DMAP. After stirring the reaction mixture for 48 hrs at room temperature, only starting material was observed by proton NMR.



(**65**) (**108**)

Conditions:
a) DMAP / $PhCH_3$ / reflux
b) DMAP / K_2CO_3 then xs KOH / Bu_4NHSO_4 / $PhCH_3$ / r.t.
c) $Ti(iPrOH)_4$ / $PhCH_3$ / r.t.

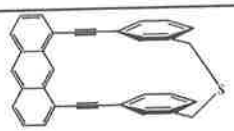
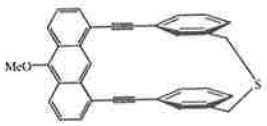
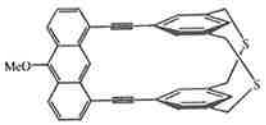
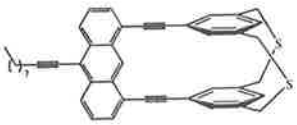
Scheme 88

7.2. Formation of the Thiacyclophanes

The next method investigated for forming cyclophanes was the double nucleophilic displacement of the sulphide anion on the bromomethyl compounds described in Chapter 6 to form thiacyclophanes. The results of these reactions are presented below in Table 6.

The first reaction investigated was with the formation of cyclophane (**109**). Initially, a solution of sodium sulphide was added to a solution of the bis-bromomethyl compound (**102**) in DMF (entry 1, Table 6). After stirring at room temperature for 3 hrs the reaction underwent an extractive workup and purification by reverse phase chromatography to afford the thiacyclophane (**109**) in 26% yield. A higher yield was obtained when sodium sulphide adsorbed on alumina (2.5 mmol/g)[160] was used (entry 2, Table 6), although an additional 2 equivalents of sulphide were added after 3 hrs since starting material was still present by tlc. Using the adsorbed sulphide reagent in conjunction with a dichloromethane/ethanol (5:1) solvent system eliminated the extractive workup, as on completion, the reaction mixture was simply filtered, concentrated and purified by chromatography (entries 2-8, Table 6). Purification was best attained by using reverse phase silica for thiacyclophane (**109**), however, chromatography on normal silica was adequate for the purification of thia- and dithia-cyclophanes (**110**) and (**111**), with some streaking observed due to limited solubility in the solvent systems. Only a modest increase in yield was observed by using high dilution techniques with the formation of thiacyclophane (**110**) (entries 3 and 4, Table 6). It was necessary to add an extra 3 equivalents of sulphide with the high dilution case, as starting material was still present by tlc an hour after addition of the bis-bromomethyl compound was complete. Without high dilution (entry 4, Table 6), the 3 equivalents were sufficient and the reaction was complete in 1 hour. This suggests, along with entry 2, that the adsorbed reagent starts to decompose after approximately an hour in solution.

Table 6. The formation of the thiacyclophanes.

Entry	Substrate	Reagent	Solvent (v/v)	Conc.[a]	Product/% Yield
1	(**102**)	$Na_2S.9H_2O$[b] 5 eq	DMF	1.77 mM[c]	 (**109**)/26
2	(**102**)	$Na_2S.Al_2O_3$ 2 eq	CH_2Cl_2/EtOH (5/1)	2.95 mM	(**109**)/50
3	(**103**)	$Na_2S.Al_2O_3$ 3 eq	CH_2Cl_2/EtOH (5/1)	Dilution[d]	 (**110**)/100
4	(**103**)	$Na_2S.Al_2O_3$ 3 eq	CH_2Cl_2/EtOH (5/1)	20.2 mM	(**110**)/85
5	(**104**)	$Na_2S.Al_2O_3$ 5 eq	CH_2Cl_2/EtOH (5/1)	3.21 mM	 (**111**)/trace(<1 mg)
6	(**106**)	$Na_2S.Al_2O_3$ 6 eq	CH_2Cl_2/EtOH (5/1)	1.87 mM	 (**112**)/0
7	(**107**)	$Na_2S.Al_2O_3$ 6 eq	CH_2Cl_2/EtOH (1/1)	0.71 mM	 (**113**)/intractable
8	(**107**)	$Na_2S.Al_2O_3$ 6 eq	DMF	5.1 mM	(**113**)/intractable

[a] Concentration of poly-bromomethyl compound in solution. [b] Reagent added as a 0.17 M solution. [c] Concentration of bis-bromomethyl compound in solution after reagent added. [d] High dilution used, 10.1 mM solution of bis-bromomethyl compound added over 2.5 hrs.

Limited success was obtained in forming the two-arm dithiacyclophane (**111**) (entry 5, Table 6). By using the similar conditions to entry 2 and 4 with a reaction time of only 1 hour, only a trace of dithiacyclophane (**111**) could be isolated. By tlc there were several faint spots above and below what was deemed to be the product spot, with the majority of the material being on the baseline. A similar result was obtained for the formation of dithiacyclophane (**112**) (entry 6, Table 6), however only baseline material was observed in this case by tlc when the reaction mixture was allowed to stir at room temperature overnight. These reactions (entries 5 and 6, Table 6) suggest that polymerisation is favoured over cyclophane formation for the two-arm systems, and that high dilution may be required. Finally, the attempt at forming dithiacyclophane (**113**), using the adsorbed reagent and the dichloromethane/ethanol solvent system (entry 7, Table 6) led to the precipitation of dithiacyclophane (**113**) or its intermediates, over a period of 1 hour. Following the reaction by tlc proved troublesome since the reaction mixture streaked on normal silica, alumina and reverse phase silica tlc plates, with a large variety of solvent systems. Only the consumption of the starting material (**107**) could be observed by tlc, with the concomitant formation of essentially one spot/streak of similar R_f to the starting material, and baseline products. Repetition of the reaction using DMF (entry 8, Table 6) led to similar results, except that the reaction mixture changed colour from yellow to blue/green on addition of the sulphide. The reaction was not complete after 3 hrs and an extra portion of sulphide was added to ensure completion. Solubility of the product was very poor in a wide range of organic solvents such that no NMR data could be obtained. Consequently the only analytical data obtained for the dithiacyclophane (**113**) was an accurate mass measurement which possessed good agreement between the experimental and predicted values.

The cyclophanes of Table 6, except for the dithiacyclophane (**113**), were each characterised by proton and carbon NMR, and also by accurate mass spectrometry. Proton NMR showed a characteristic upfield shift in the methylene protons in going from the poly-bromomethyl compounds (δ~4.2-4.6 ppm) to the thiacyclophanes (δ~3.4 ppm). Every methylene signal observed for the cyclophanes was a singlet, except (**111**) which was observed as an AB quartet (J 15.0 Hz). This result suggested that the two-arm cyclophane structure of (**111**) was more rigid than the one-arm systems as the linker-arms are less flexible causing the methylene protons to become diastereotopic.

The one-arm thia- and aza-cyclophanes (of Section 7.3), both undergo fast rotations on the NMR timescale about the aryl-alkyne bonds leading to a time-average signal (a singlet) being observed for the methylene protons. At low temperature one would expect a slowing of these rotations, and consequently an appearance of an AB quartet, as the each of the protons become trapped in a distinct chemical environment.

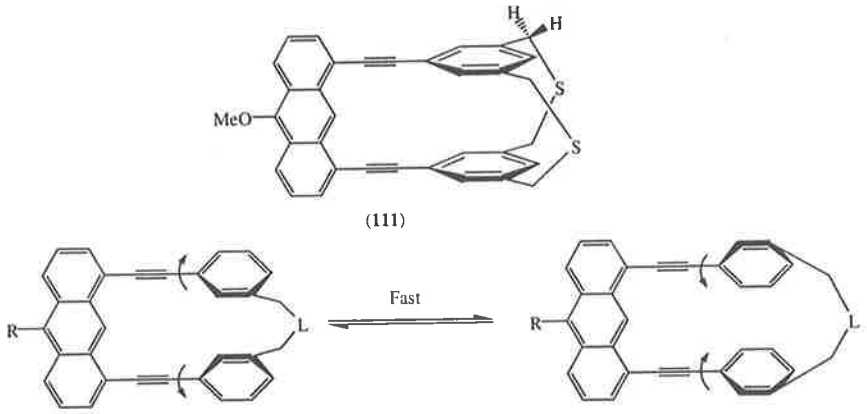


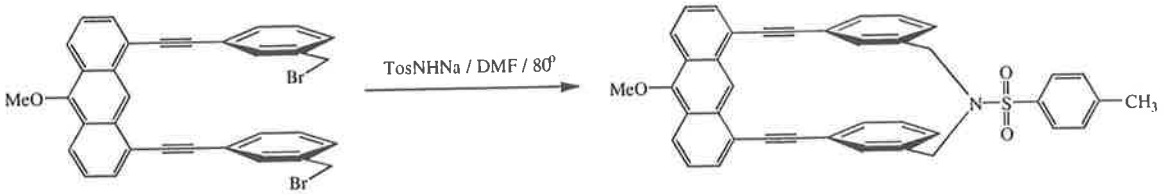
Figure 37. The rigid two-arm cyclophane (**111**), and the more flexible one-arm cyclophanes.

A variable temperature proton NMR experiment was performed in which the proton spectrum of (**110**) was obtained at 5° intervals between 25° and -55° in $CDCl_3$ (mp -64°). The results of this experiment showed no splitting or even broadening of the benzylic protons as the temperature was lowered to -55°. The benzylic protons were observed as a sharp singlet at δ 3.43 ppm. The experiment could have been repeated with a solvent possessing a lower melting point than $CDCl_3$. For example, d_4-MeOH and d_8-THF have melting points of -98° and -108° respectively. However, since no broadening was observed at -55° in $CDCl_3$, very little difference, if any, would be expected in the proton spectrum by reducing the temperature a further 30°. Consequently, the experiment was not repeated using a different solvent.

7.3. Formation of the Azacyclophanes

Formation of cyclophanes other than thiacyclophanes was investigated with the formation of azacyclophane (**114**) (**Scheme 89**). A modified literature procedure was used in which 1.5 equivalents of TosNHNa and the bis-bromomethyl compound (**103**) were stirred together in DMF under nitrogen with heating.[161] The reaction was complete in 1 hour. An extractive workup followed by chromatography on normal silica yielded

the azacyclophane (**114**) in a quantitative yield. Streaking on the silica was observed to be minimal with good solubility in organic solvents. However, the azacyclophane was observed to decompose in solution over several hours if left in the sunlight, and over several days if kept in the dark. The cyclophane also decomposed in the solid state over several weeks when kept on the bench in sunlight. Tlc analysis of a decomposed NMR sample showed the formation of a cascade of spots, and solids had precipitated out of the deuteriochloroform solution. Proton NMR showed complex aromatic and alkyl signals. The identification of the decomposition products was not pursued.



(103) **114**, 100%

Scheme 89

Due to the stability problems associated with this azacyclophane, the two-arm and two-unit analogues were not prepared.

7.4. Molecular Modelling of the Cyclophanes

Semi-empirical molecular modelling was performed on a variety of cyclophane structures to qualitatively determine the effect of the type of linker-arm on the geometry of the cyclophane, and whether or not it introduced a degree of strain to the system. Significant strain can be observed in a molecule with 'bending' associated with the template-alkyne-aryl bonds, and with 'bending' of the cyclophane aromatic ring itself. The template-alkyne-aryl bonds should ideally all be coplanar and the aromatic ring should be flat. A qualitative measure of the internal strain of a cyclophane could be obtained by considering the angle α (for two-arm cyclophanes), which takes into account the bending of the template-alkyne-aryl bonds, Figure 38(a). The smaller the angle α the less strain in the system with α ideally being equal to 0° for cyclophanes containing linker-arms of optimal length for the anthracene templates. For one-arm cyclophanes, molecular modelling showed none of the template-alkyne-aryl bonds were perturbed (α=0), but another angle β could be considered, Figure 38(b). This angle wasn't a measure of the strain in a system, but was a measure of the rotation about the

aryl-alkyne bonds and consequently was influenced by the length of the linker-arm. The longer the linker-arm, the smaller the value of β, and for two-arm cyclophanes β=0° due to the rigidity and symmetry of the two linker-arms. Ideally, β should be equal to 0° for all cyclophanes so that the oligomer structures possess cyclophane rings that are all parallel, as discussed in Chapter 1.

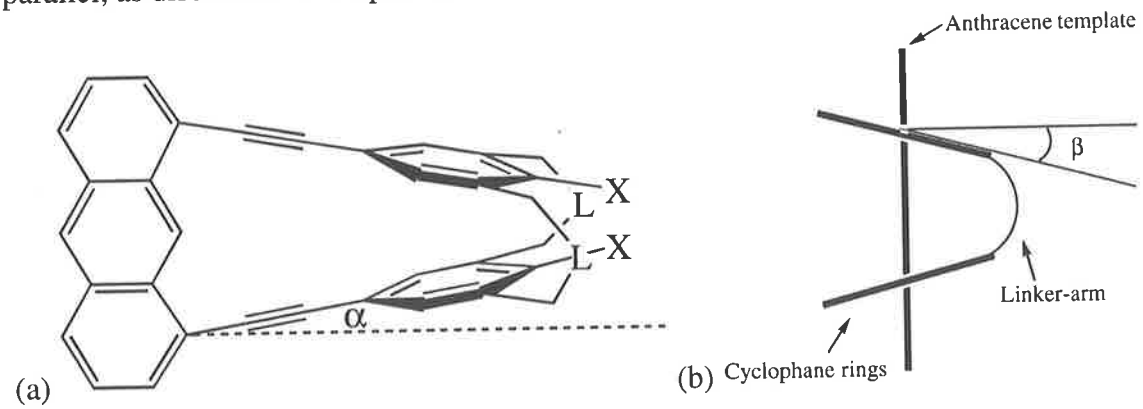


Figure 38. The internal strain of the cyclophanes for: (a) two-arm cyclophanes, and (b) one-arm cyclophanes.

The first cyclophanes to be modelled were the proposed 'ethylene-glycol linked' esters of Section 7.1. The optimised structures for (**65**) and (**108**) are shown below in Figure 39. Semi-empirical molecular modelling of the two systems qualitatively suggested that cyclophane formation would be possible, as there was no large degree of strain introduced to the cyclophane. However, there was some internal strain present in the cyclophane (**108**), with α=0° in the starting ester (**65**) going to ~12° for cyclophane (**108**). This is apparent in Figure 39(b), showing bending of template-alkyne-aryl bonds.

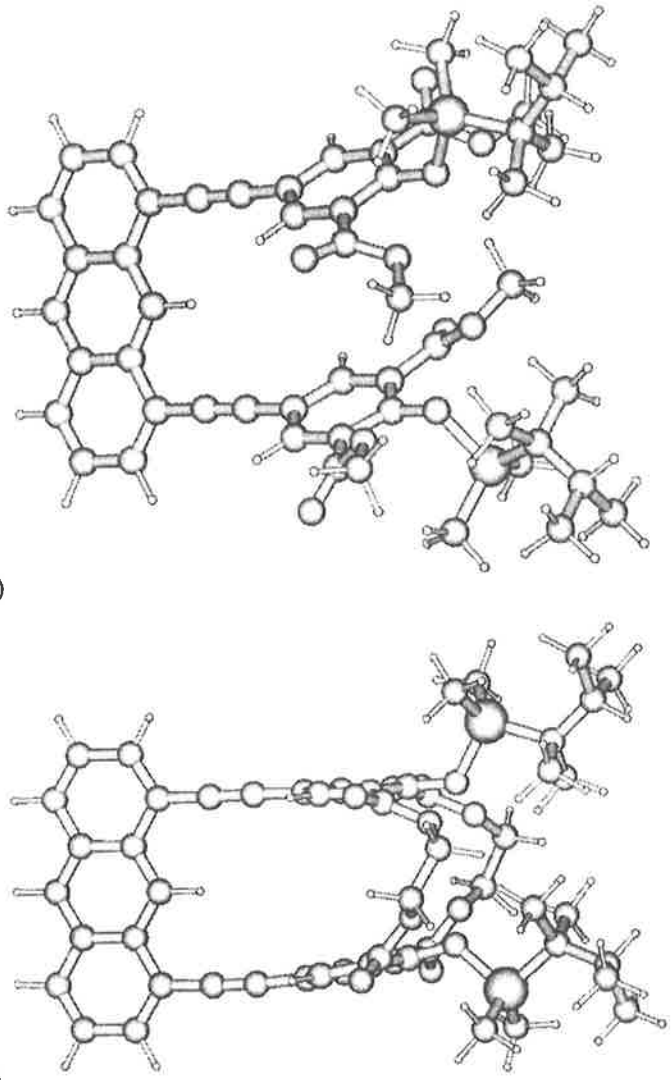
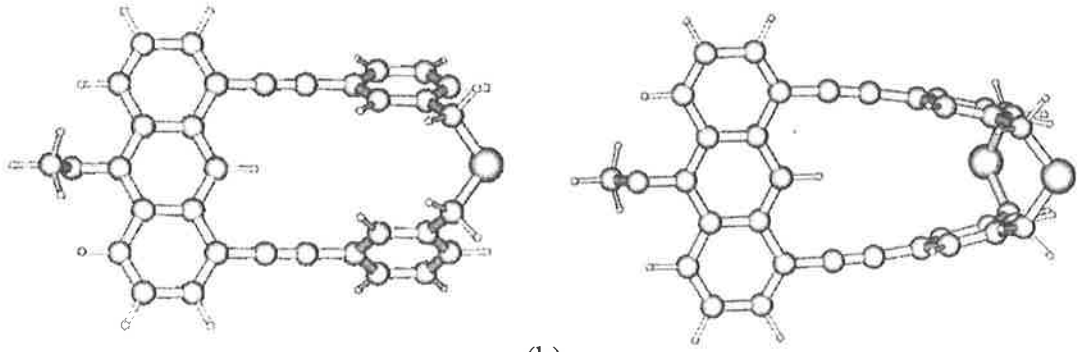


Figure 39. The optimised structures for: (a) tetra-ester (**65**), and (b) the cyclophane (**108**).

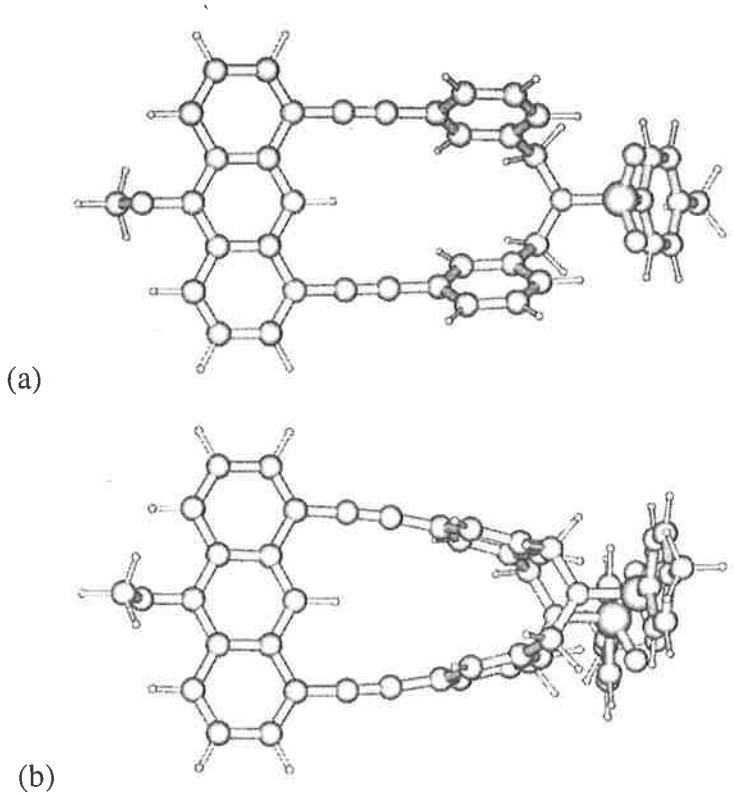
Semiempirical geometry optimisations were also performed on a range of thia- and azacyclophanes. The thiacyclophanes, which possess a three centre linker-arm (-CH_2SCH_2-), were found to introduce a significant degree of strain to the cyclophane structure. It appeared as though the linker-arm was not of a sufficient length to give parallel cyclophane rings, as can be seen in Figure 40(a) and Figure 40(b). For the thiacyclophane (**110**) $\beta \approx 26°$, and for the dithiacyclophane (**111**) the angle $\alpha \approx 8°$. These results support the experimental results of Section 7.2 where a low yield was obtained for the preparation of the dithiacyclophane (**111**).



(a) (b)

Figure 40. Thiacyclophane geometries: (a) one-arm cyclophane (**110**), and (b) two-arm cyclophane (**111**).

Similar results were obtained for the aza analogues of (**110**) and (**111**) which also possessed a three centre linker-arm (-CH_2(NTos)CH_2-). The azacyclophanes had similar α and β values to the thiacyclophanes analogues as azacyclophane (**114**) had an angle β=29°, Figure 41(a), and the two-arm azacyclophane (**115**) had $\alpha \approx 13°$, Figure 41(b).



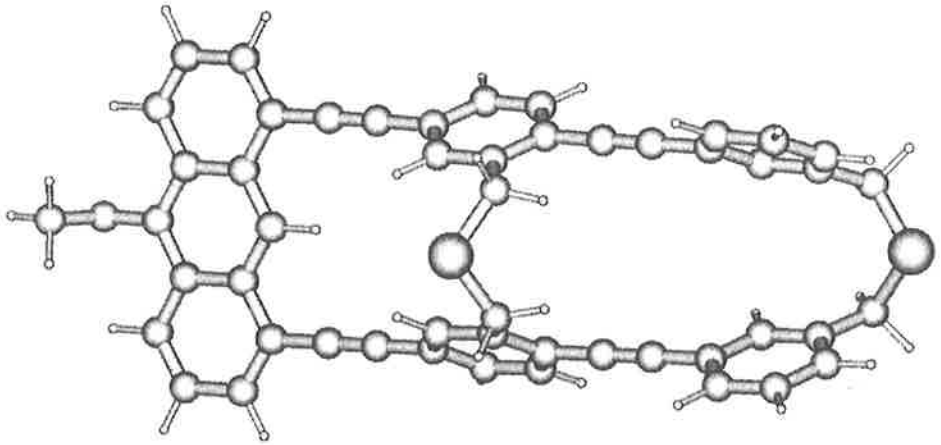
(a)

(b)

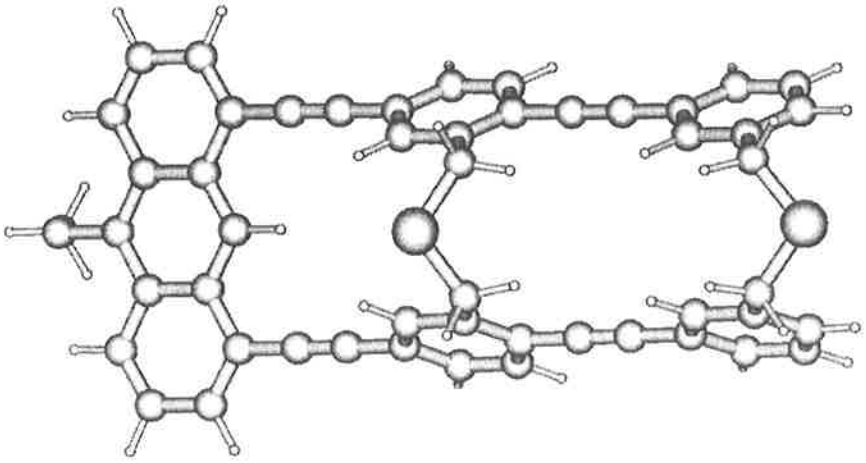
Figure 41. The azacyclophanes: (a) (**114**) and (b) (**115**).

The only two-unit oligomer to be discussed at this point is the thiacyclophane (**113**). It has two isomers, one with the linker-arms on opposite sides of the oligomer,

the other with both on the same side. Semi-empirical modelling showed that both had similar energies with the difference being less than 1 kJ/mol. This meant that both isomers are expected to be formed in the cyclisation reaction. Confirmation of this has yet to be investigated due to the intractability of the compound. These isomers both have the same β value of 22°.



(a)



(b)

Figure 42. The different isomers of oligomer (**113**): (a) opposite sides, and (b) same side.

7.5. X-ray Structure of an One-Arm Cyclophane

A crystal of the one-arm cyclophane (**110**) was grown from a slowly evaporating solution of the cyclophane in ethyl acetate, and its X-ray structure determined. The solid state structure is shown below in Figure 43.

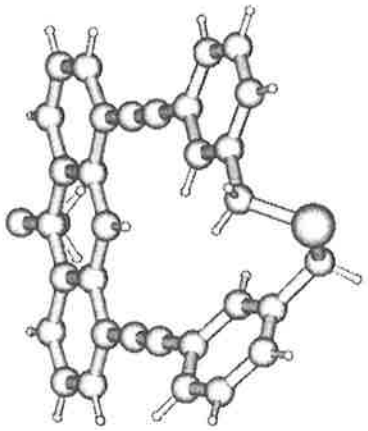


Figure 43. The X-ray structure of cyclophane (**110**).

Apart from unambiguously confirming the structure of cyclophane (**110**), the crystal structure showed several interesting features. The x-ray structure clearly showed the two aromatic rings were not parallel to one-another, and this was due to intermolecular π-π stacking between adjacent molecules in the crystal lattice. This can be observed where one of the aromatic rings of the cyclophane π-stacked with the anthracene ring of another molecular, forming a centrosymmetric dimer and distorting the parallelism of the cyclophane rings. The distance between the cyclophane and the anthracene rings was measured to be 3.5 Å, and was of typical magnitude for intermolecular π-π stacking interactions.[162]

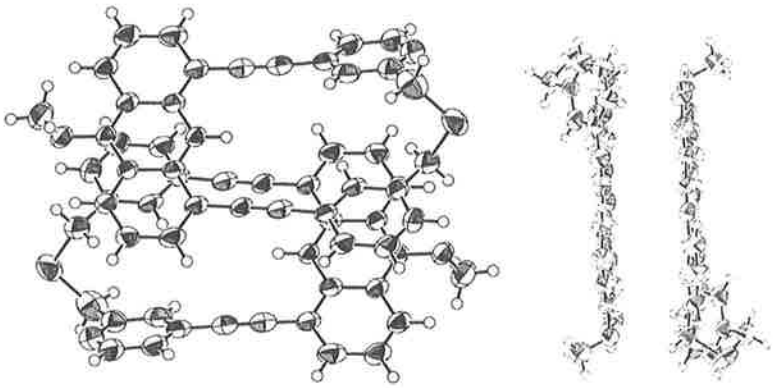


Figure 44. Two views of the centrosymmetric dimer.

The crystal structure also showed the linker-arm going from one side of the cyclophane to the other, and doesn't link the cyclophane together on the same side as might be expected from molecular modelling experiments. This 'distortion' arose from the intermolecular stacking, producing the unexpected geometry. Little bending of the

template-alkyne-aryl bonds was observed, with the angle α=-3.8° (negative angle represents bending contrary to that shown in Figure 38), and the angle β was meaningless with the solid state structure due to its distorted nature. This compared with the value of α=0° determined by molecular modelling (Section 7.4). However, comparisons are generally tenuous between the solid and gas phase (modelling) optimised geometries.

7.6. Summary

In this chapter the synthesis of several cyclophanes, including a two-unit oligomeric system, was discussed. It was found that the formation of thiacyclophanes from compounds containing bromomethyl groups was facilitated by sodium sulphide adsorbed onto alumina. Formation of azacyclophanes was also possible, although these compounds were found to have limited stability in solution and the solid state. Molecular modelling studies were performed on several cyclophanes to assess the degree of strain introduced to the system by the linker-arms. It was found that linker-arms of a longer length would be required to ensure the cyclophane rings were parallel. However, the synthetic pathways established for the synthesis of the cyclophanes described in this chapter could be readily adapted to prepare cyclophanes possessing longer linker-arms.

A crystal structure was obtained for one of the one-arm cyclophanes which showed the cyclophane rings to be non-parallel in the solid state. Pi-stacking was also observed between molecules, forming centrosymmetric dimers.

8. UV-Visible and Fluorescence Spectroscopy

8.1. UV-Visible Spectroscopy

The ultraviolet-visible (UV-Vis) spectra of organic compounds provide information about transitions between electronic energy levels. These transitions are generally between bonding or lone pair orbitals, and an unfilled non-bonding or anti-bonding orbital. The electronic processes that can occur in a molecule are schematically represented below in Figure 45.[163] Here only the first triplet (T), and first two singlet (S) states are shown. The subscript refers to the state number and the superscript refers to the vibrational mode. The absorption (A) of light by a molecule leaves it in any one of its numerous vibrational modes of one of its excited states. Generally, transitions from the ground state usually proceed to a singlet state with transitions from the ground state directly to a triplet state being forbidden.[163] The wavelengths (λ) of light that are absorbed can be considered a measure of the separation of the energy levels between the orbitals concerned. The range of wavelengths generally lies between 200 and 900 nm, and the spectra are generally measured using very dilute solutions of the organic compound (~10^{-4}-10^{-7}M).

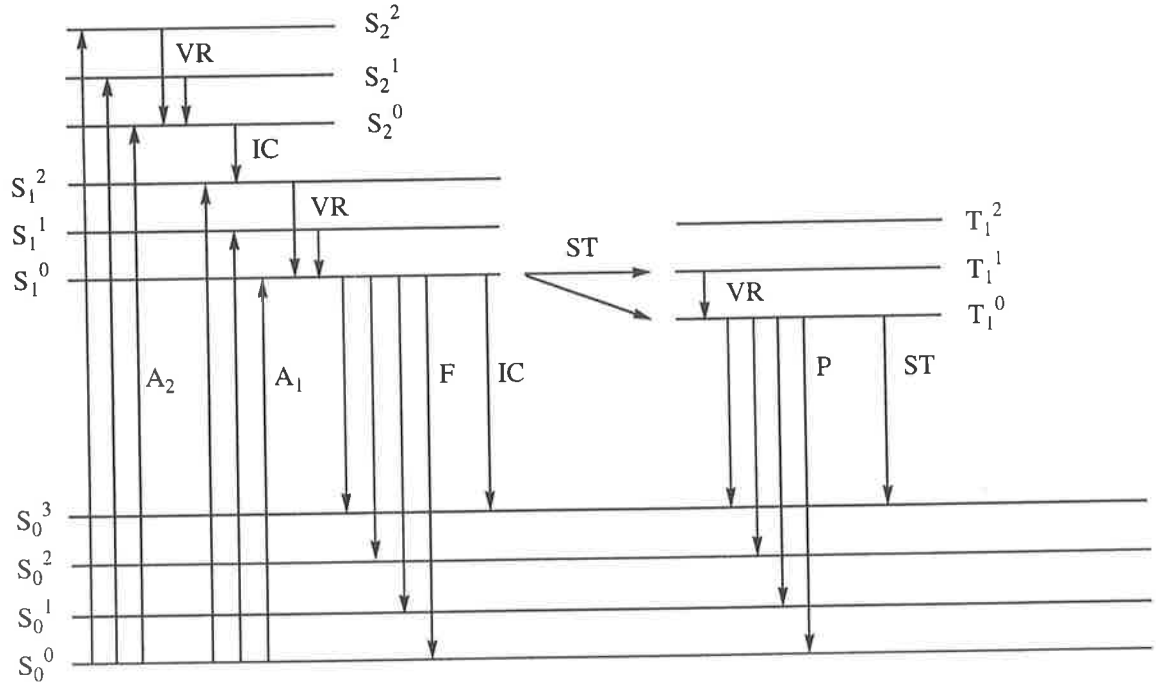


Figure 45. The ground and excited states of a molecule.

The absorbance (A) of a compound at a particular wavelength can be expressed using the Beer-Lambert law (Equation 2). Absorbance has no units. The remaining variables I_0 and I are the intensities of the incident and transmitted light respectively. The quantity ε is the molar absorption coefficient (1000 cm^2mol^{-1}), l is the length of the solution cell (cm), and c is the concentration of the solution ($molL^{-1}$).[164,165] Generally, values of ε are quoted without units.

$$A = \log_{10}\frac{I_0}{I} = \varepsilon.l.c \qquad (2)$$

The absorption of light leads to the excitation of electrons in a molecule which is accompanied by changes in the rotational and vibrational states. This means that the UV-Vis spectrum is observed as a series of broad peaks and not a line spectrum. However, due to solvent interactions, fine structure information is usually 'blurred' out to a smooth curve, but in the vapour phase or in non-polar solvents it can sometimes be observed. The observance of fine structure in aromatic systems can be increased by rigidifying the molecular framework.[40,165]

Generally, the longer the chromophore (the groups containing electrons responsible for absorption) the more intense the absorption with ε values of ~100 000 and the larger the value of λ_{max}. This is because with an increase in the number of electrons in the chromophore the energy difference between π and π^* becomes less and less. Generally, allowed transitions will have ε>10 000 whereas forbidden transitions have ε values below 1000.

The introduction of substituents directly onto an aromatic system can have varied effects.[165] Introduction of unsaturated groups such as alkenyl or alkynyl, generally result in a large bathochromic shift (a shift to longer λ), a decrease in fine structure and an increase in intensity. Methoxy or hydroxyl groups don't significantly alter the UV-Vis spectrum, although the hydroxyl groups can introduce some intense bands at long wavelengths.

The UV-Vis and fluorescence spectra of cyclophanes have been studied in detail as these compounds can possess interesting transannular interactions between the cyclophane rings.[32,33] These interactions arise when the linker-arms are short, typically two or three methylene units long, thereby introducing deformations to the aromatic rings. Deformation of the aromatic rings results in little fine structure being observed.

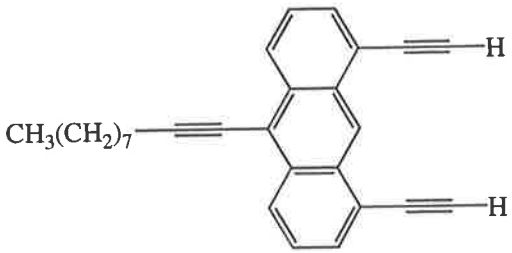
However, when the linker-arms are lengthened fine structure returns.[32a] Various charge-transfer complexes of cyclophanes have been prepared, usually with the electron deficient tetracyanoethylene (TNCE) molecule.[32b,166] These complexes generally show an absorption at lower wavelength than the uncomplexed cyclophane due to the charge transfer absorptions. Charge-transfer mechanisms can also exist between the cyclophane molecules themselves, without the addition of π-acids or π-bases. These intermolecular excited complexes are called excimers (*exc*ited homod*imers*). These complexes (C) form at high concentrations (~10^{-2} M), and are stabilised by both exciton resonance (*CC↔CC*) and charge-transfer configurations ($C^+C^-\leftrightarrow C^-C^+$).[32a,167] If two different solute molecules are involved in the complex then the excited complex is called an exciplex.[167] Excimers are characterised by their emission (fluorescence) spectra where there is generally a broad emission at a lower wavelength than the monomer emission. The emission is dependent on both temperature[167] and concentration.[168]

8.1.1. UV-Vis Spectra

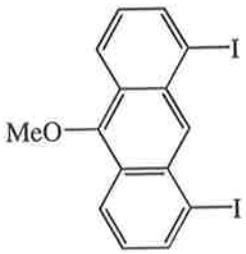
The UV-Vis spectra of several bis-coupled systems and cyclophanes are presented below. The spectra were recorded as dilute solutions (~10^{-5} M) in HPLC grade THF. The first group of compounds to be studied were the template systems, shown below in Figure 46. These spectra showed two distinct regions of absorption, both of which were related to the π electrons. The first region was a broad series of peaks centred about 390 nm resulting from π-π* transitions to low excited states (primary band), and the second was a quite sharp peak centred about 265 nm resulting from higher energy π-π* transitions (secondary band).[169,170] In general, the primary band contained more vibrational fine structure than the secondary, and this was observed for all the compounds described in this chapter. It was also noted that all the UV-Vis spectra possessed very similar absorptions to the parent compound anthracene with the differences being the wavelengths of the primary and secondary bands and the reduced amount of fine structure in the primary band.[170]

The templates shown below, whilst having similar primary and secondary band structures, differed substantially when considering the position of λ_{max}. The methoxy template (**43**), as expected, had the lowest λ_{max} at 408 nm (ε 10 000) due to the absence of the alkynyl groups which increase the length of the chromophore in other systems.

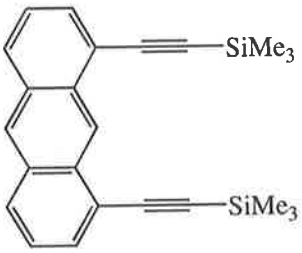
The TMS protected analogue of the standard template (**45**) possessed the next highest λ_{max} 412 nm (ε 24 000) followed by the two 10-substituted templates: the decyne template (**41**) 430 nm (ε 21 000) and the ethynyl adamantane template (**49**) 440 nm (ε 32 000). The longer λ_{max} of the 10-substituted templates as compared to the standard template was expected as these system possess a larger conjugated system.



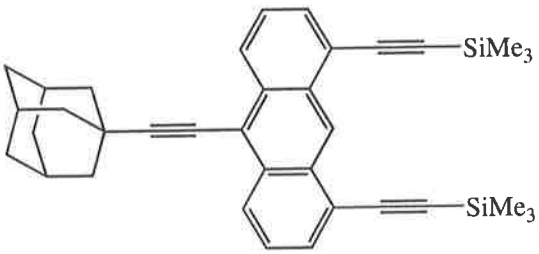
(**41**)



(**43**)



(**45**)



(**49**)

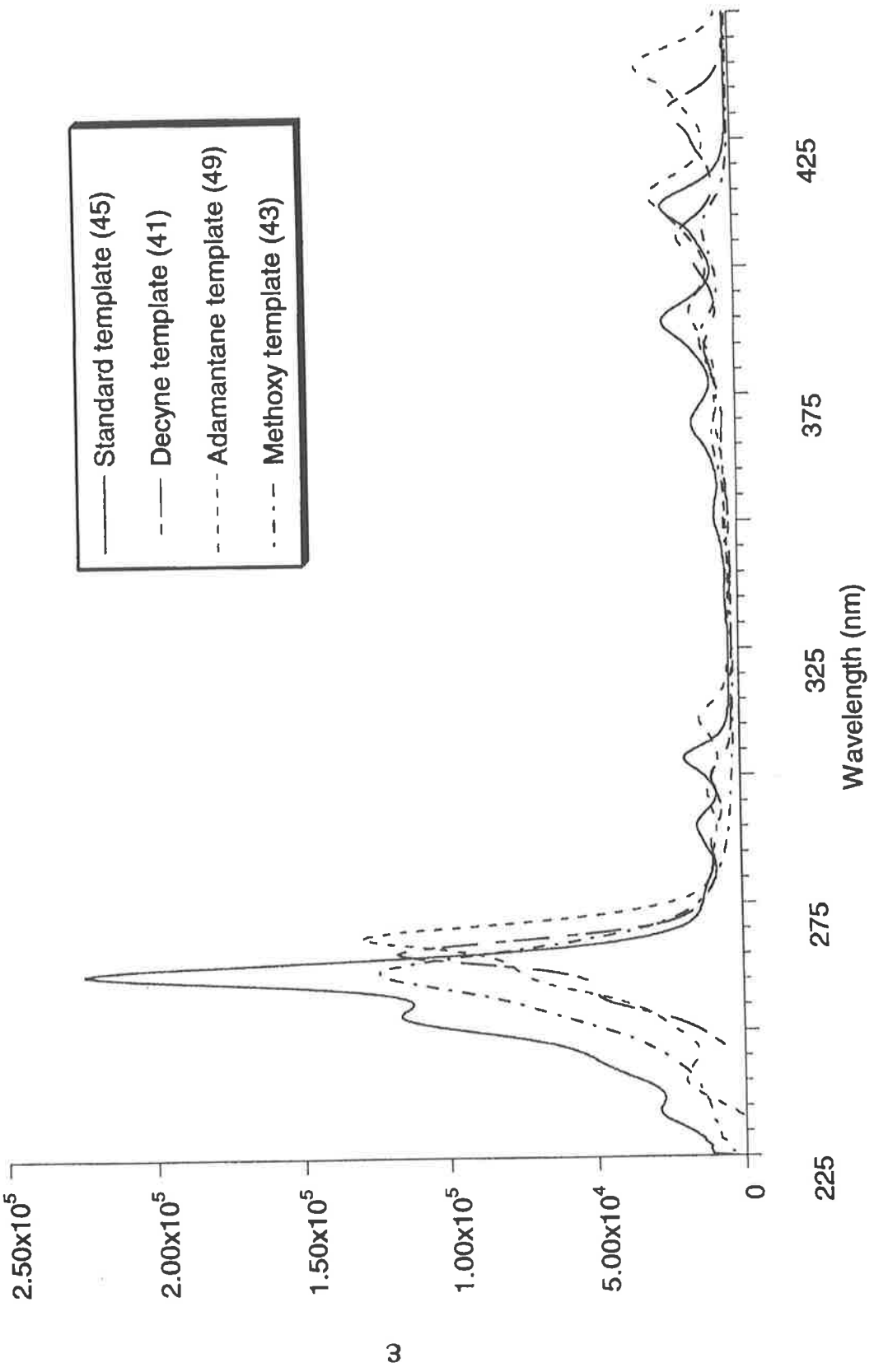


Figure 46. The UV-Vis spectra of the anthracene templates.

The next set of UV-Vis spectra belong to the bis-coupled systems (**60**) and (**61**) shown below in Figure 47. Both compounds possessed absorptions of similar wavelength and ε, with compound (**61**) possessing a slight higher λ_{max} 420 nm (ε 17 000) compared to (**60**), λ_{max} 418 nm (ε 22 000). This was due to the presence to the two siloxy auxochromes producing a slight bathochromic shift.

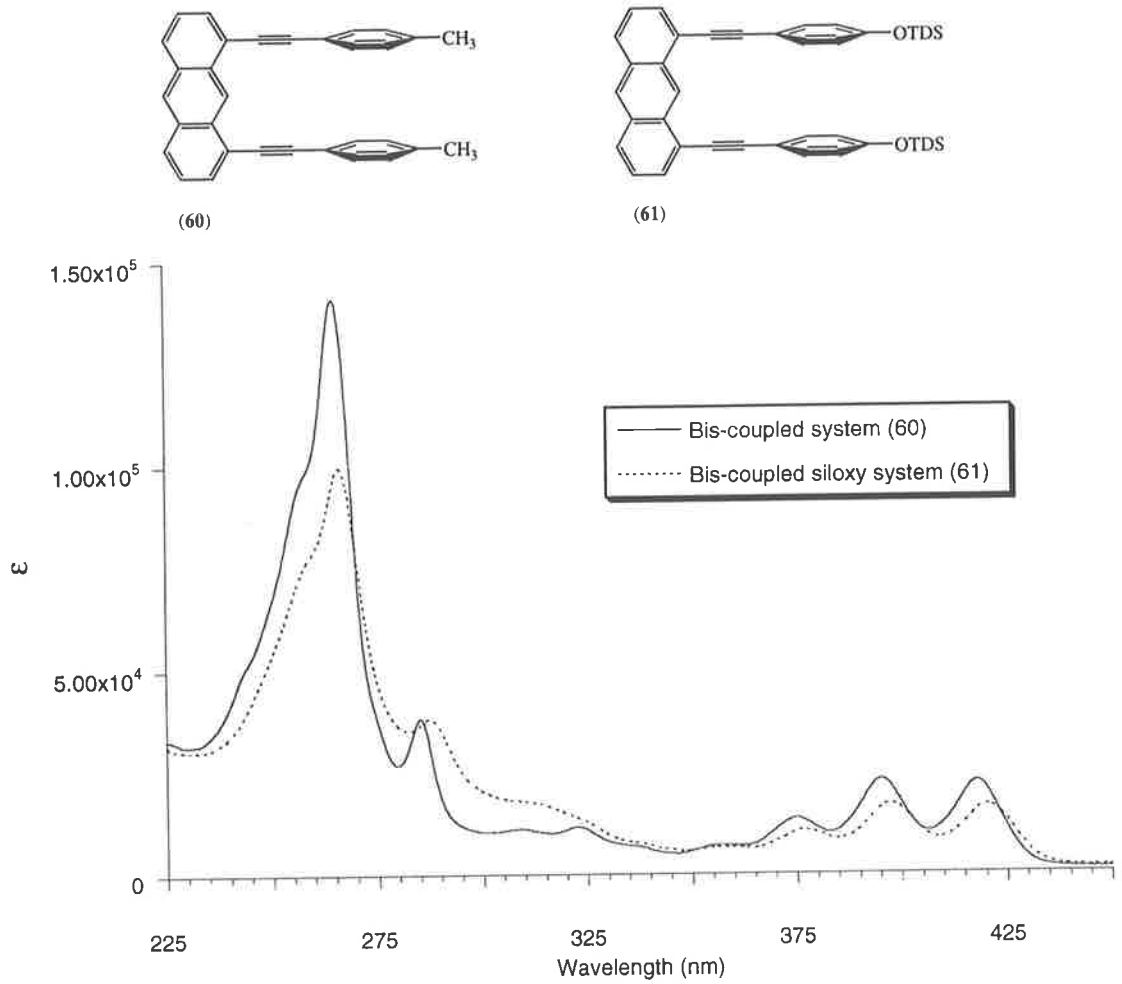


Figure 47. The UV-Vis spectra of the bis-coupled system of (**60**) and (**61**)

More interesting results were obtained with the bis-coupled ester containing systems (**65**), (**67**) and (**69**) (Figure 48). A trend could clearly be seen in going from the diester (**69**) λ_{max} 417 nm (ε 16 000) to the tetra-ester (**67**) λ_{max} 419 nm (ε 18 000) and finally to the protected tetra-ester (**65**) λ_{max} 423 nm (ε 20 000). Comparison of these λ_{max} values showed that additional ester groups conjugated to the ring systems produced a modest bathochromic shift. The spectrum of (**65**) had the longest λ_{max} due to the addition presence of the siloxy auxochromes.

This trend was also present in the secondary band with the smaller peaks on the longer-wavelength side showing more 'movement' to higher wavelengths than the main peaks.

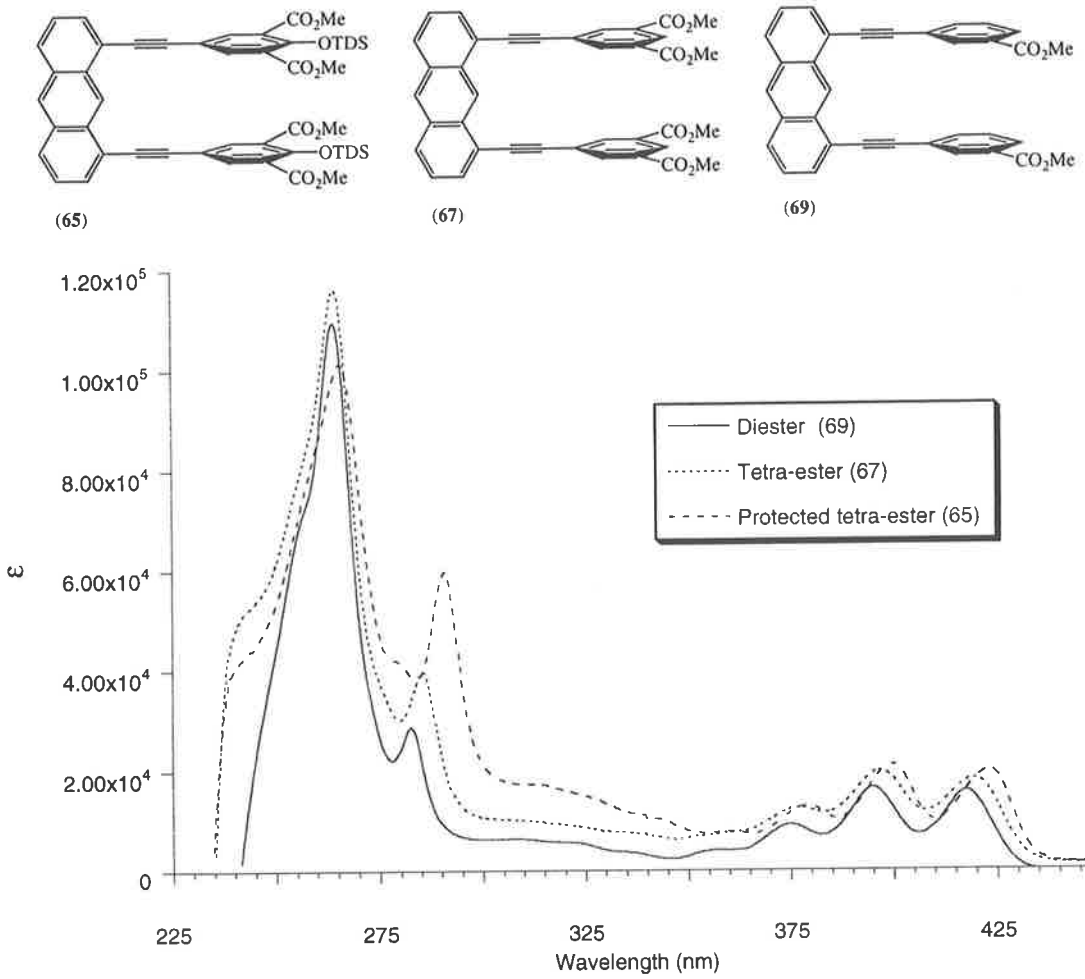


Figure 48. The UV-Vis spectra of the bis-coupled ester containing systems (**65**), (**67**) and (**69**).

A significant bathochromic shift can be seen in comparing the tetra-ester (**67**) with the octa-ester oligomer (**72**) λ_{max} 428 nm (ε 23 000) (Figure 49). Also, the smaller side peak of the tetra-ester λ 285 nm (ε 40 000) has now 'moved' to a longer wavelength λ 324 nm with higher intensity (ε 65 000). This feature can be seen in all the two-unit oligomer systems.

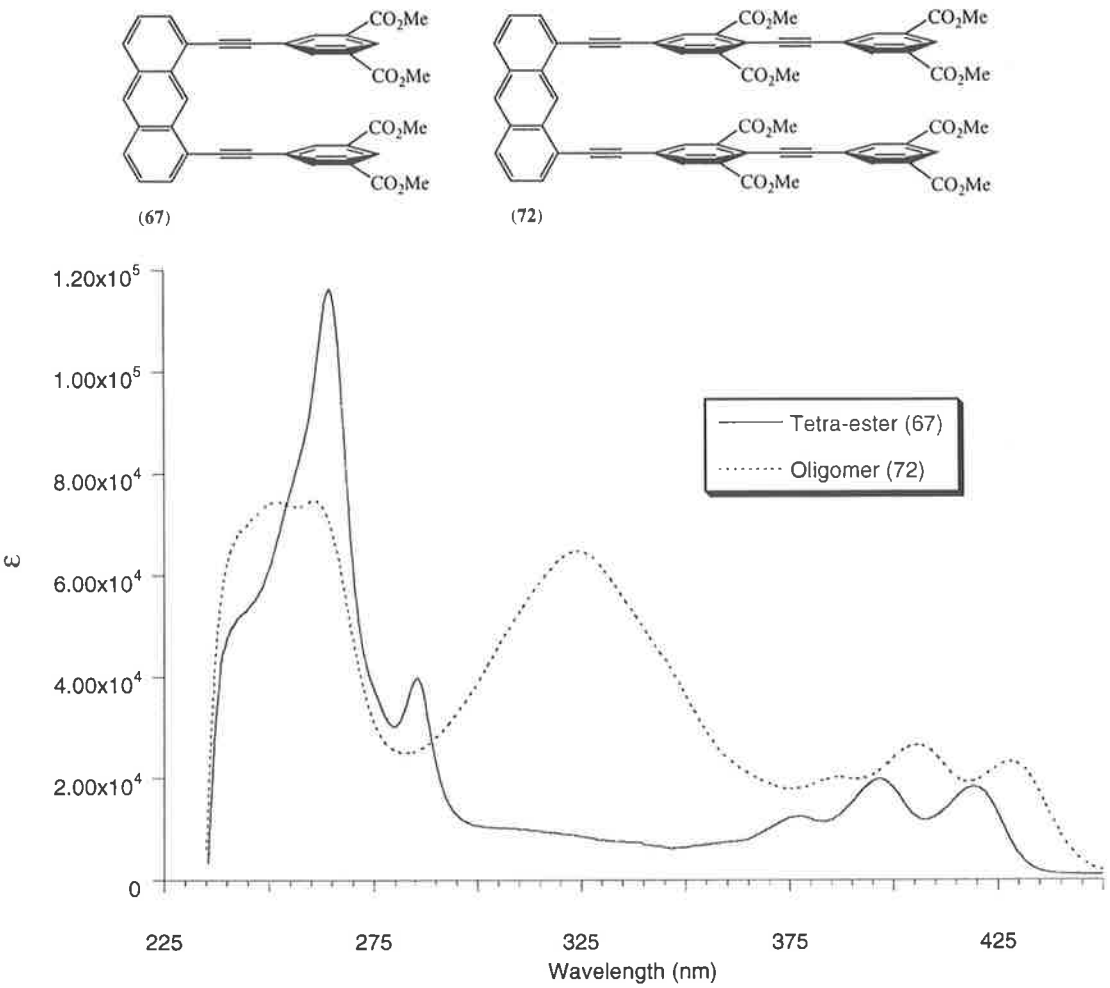


Figure 49. The UV-Vis spectra of the tetra-ester (**67**) and the oligomer (**72**).

The next set of compounds are related to the attempted hydrolysis of the hexa-acetate (**86**) described in Section 6.1 (Figure 50). Of the three compounds the hexa-acetate had the lowest λ_{max} 420 nm (ε 18 000) and the narrowest secondary band. The bis-coupled system (**57**) and the one-arm cyclophane (**87**) had broader secondary bands with more fine structure. This could be seen as the two additional shoulders on the main peak at λ ~235 nm and ~259 nm. Compounds (**57**) and (**87**) also had higher λ_{max} values of 423 nm (ε 13 000) and 427 nm (ε 12 000) respectively. This was due to the greater electron donating ability of the phenolic groups, as compared to the acetoxy groups, producing a slight bathochromic shift of 3 nm. The acetoxymethyl and hydroxymethyl groups are not conjugated to the aromatic rings and therefore do not directly influence the UV-Vis spectra in the range of wavelengths considered. Hydrogen bonding in compounds (**57**) and (**87**) may add a degree of rigidity to these systems, thereby increasing the through-conjugation between the aromatic rings and the anthracene

system. This would increase the effective length of the chromophore, and hence the λ_{max} values, for compounds (**57**) and (**87**) as compared to that of the hexa-acetate (**86**). The greater λ_{max} of the one-arm cyclophane (**87**), as compared to the other two compounds, may be due to the greater rigidity of the aromatic system with the presence of the ether linker-arm.

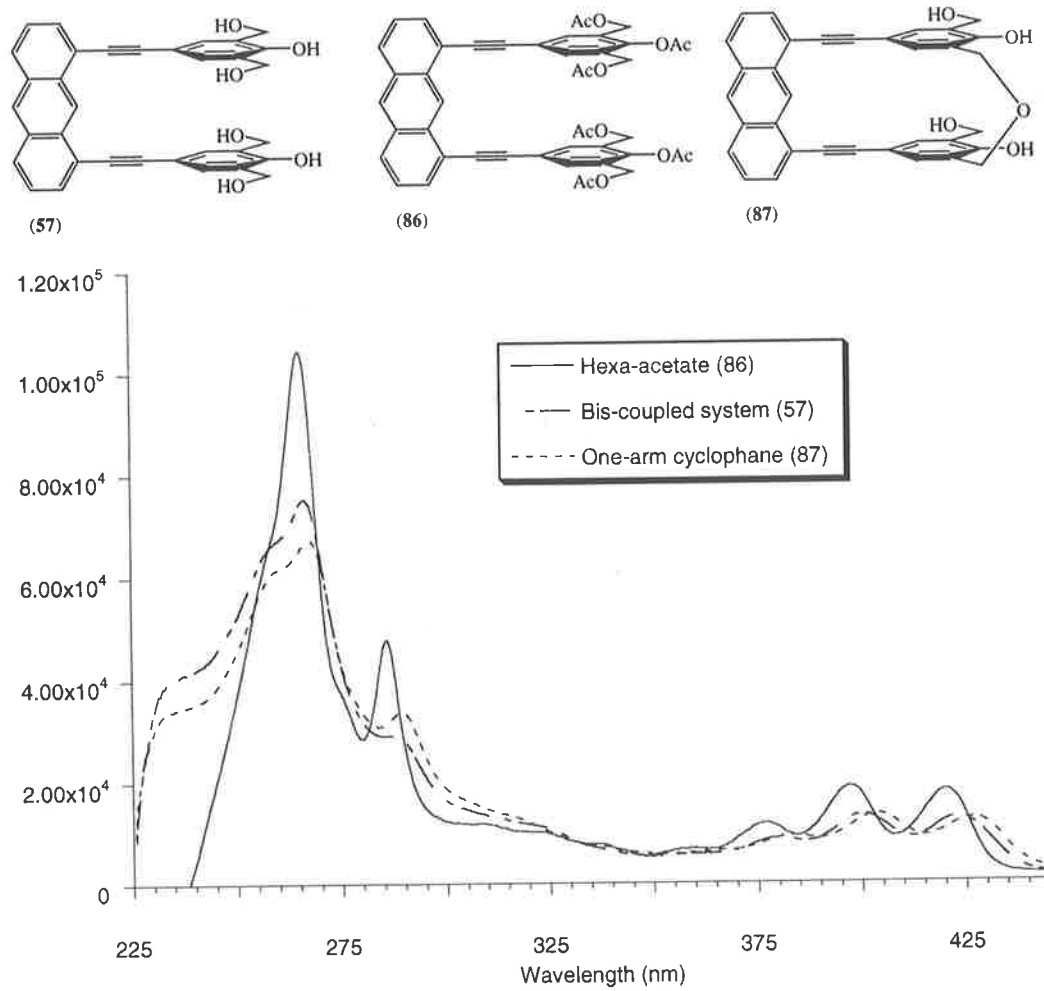
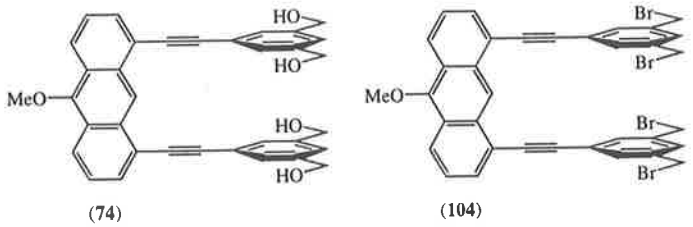


Figure 50. The UV-Vis spectra of (**57**), (**86**) and (**87**).

The bis-coupled systems based on the OMe-substituted template (**43**) all possessed values of λ_{max} greater than or equal to 430 nm. These values were all higher than those for analogous compounds based on the standard template (**40**). The first two systems to be investigated were the two-arm bis-coupled systems (**74**) and (**104**), shown below in Figure 51. Both compounds possessed the same λ_{max} 433 nm (ε 8 000 for (**74**)) and (ε 18 000 for (**104**)). Of note was that both had broad secondary bands and the absorption of the tetrakis-bromomethyl compound (**104**) λ 268 nm (ε 122 000) was

significantly larger than that for the tetrakis-hydroxymethyl compound (**74**) λ 268 (ε 59 000).



(74) (104)

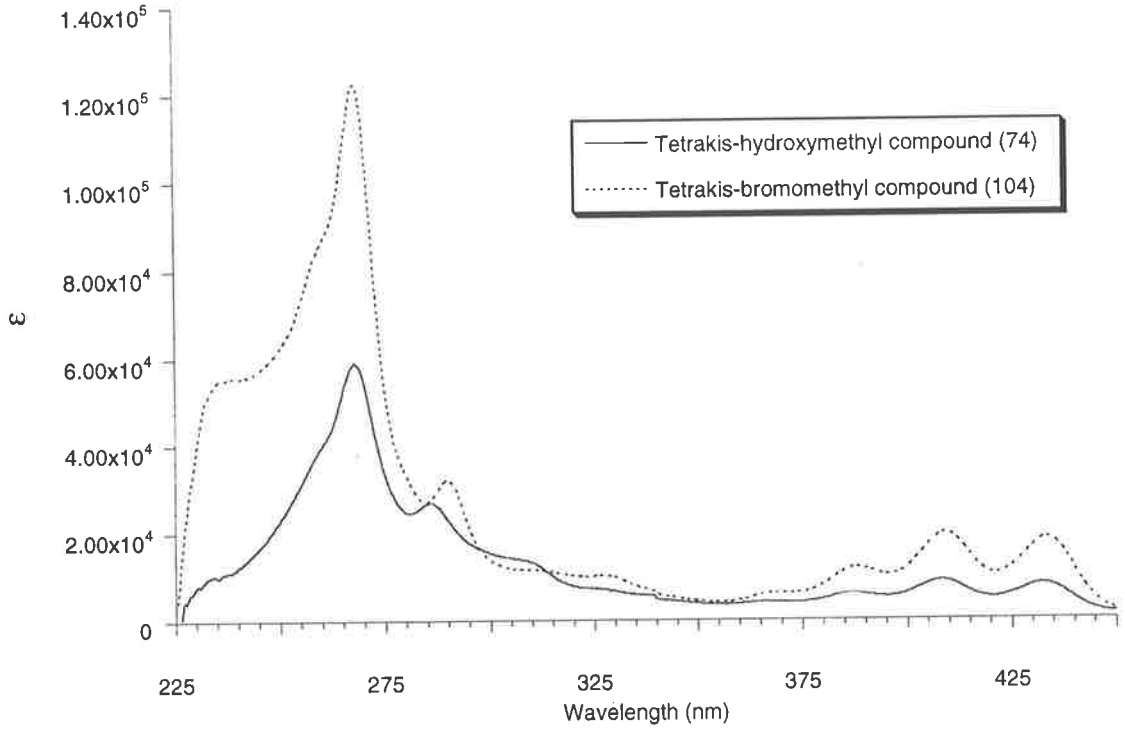


Figure 51. The UV-Vis spectra of the two-arm coupled systems (**74**) and (**104**).

The spectrum of the tetra-bromomethyl coupled oligomer (**107**) possessed some interesting features. The spectrum of the two-unit oligomer precursor (**77**) and of the octa-ester (**72**) are shown below in Figure 52 for comparison. The first item of note was the λ_{max} value of tetra-bromomethyl coupled oligomer (**107**), λ_{max} 430 nm (ε 25 000), being larger than the octa-ester (**72**) (λ_{max} 428 nm). This result suggested that the methoxy auxochrome produced a larger bathochromic shift than the combined effects of eight ester groups, directly conjugated to the aromatic rings. Also, the broad peak at 319 nm (ε 71 000) was comparable in size and shape to that of the octa-ester (**72**). This portion of the spectrum was similar to the spectrum of the two-unit oligomer precursor (**77**), except that less fine structure was to been seen for the tetra-bromomethyl coupled oligomer or the octa-ester.

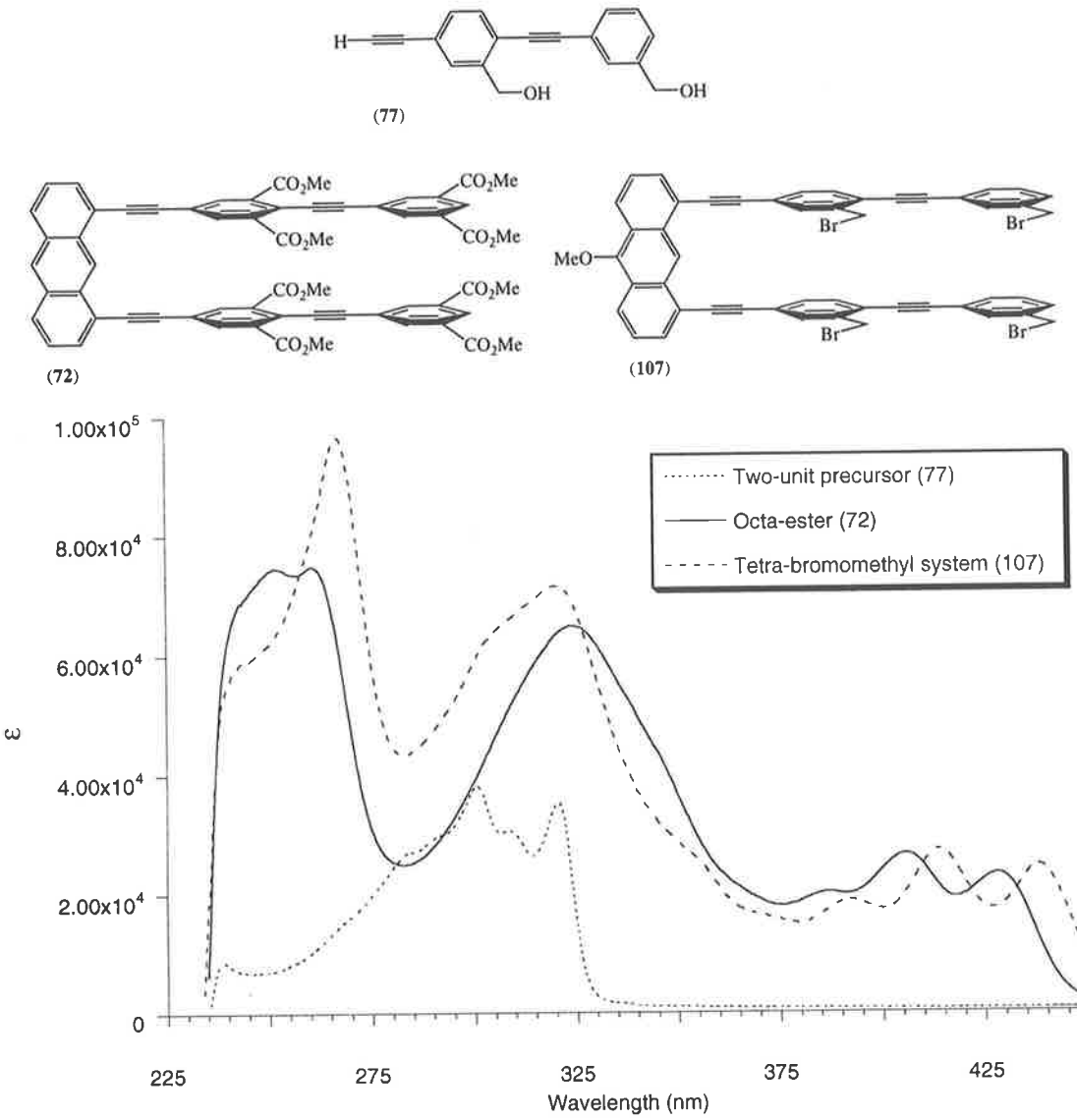


Figure 52. The UV-Vis spectra of the two-unit oligomeric systems.

The next set of compounds to be investigated were the one-arm systems containing the OMe-substituted template (Figure 53). All three compounds possessed near identical UV-Vis spectra, except for slight differences in intensity of absorption and λ_{max}. The order of λ_{max} values went from the bis-hydroxymethyl compound (**73**) λ_{max} 431 nm (ε 17 000), to the bis-bromomethyl compound (**104**), λ_{max} 432 nm (ε 21 000), and finally the cyclophane (**110**), λ_{max} 436 nm (ε 21 000). Unfortunately, no increase in fine structure of either band was observed for the cyclophane. The only indication of a more rigidified molecular structure, as compared to (**73**) and (**104**), was the increase in the λ_{max} value.

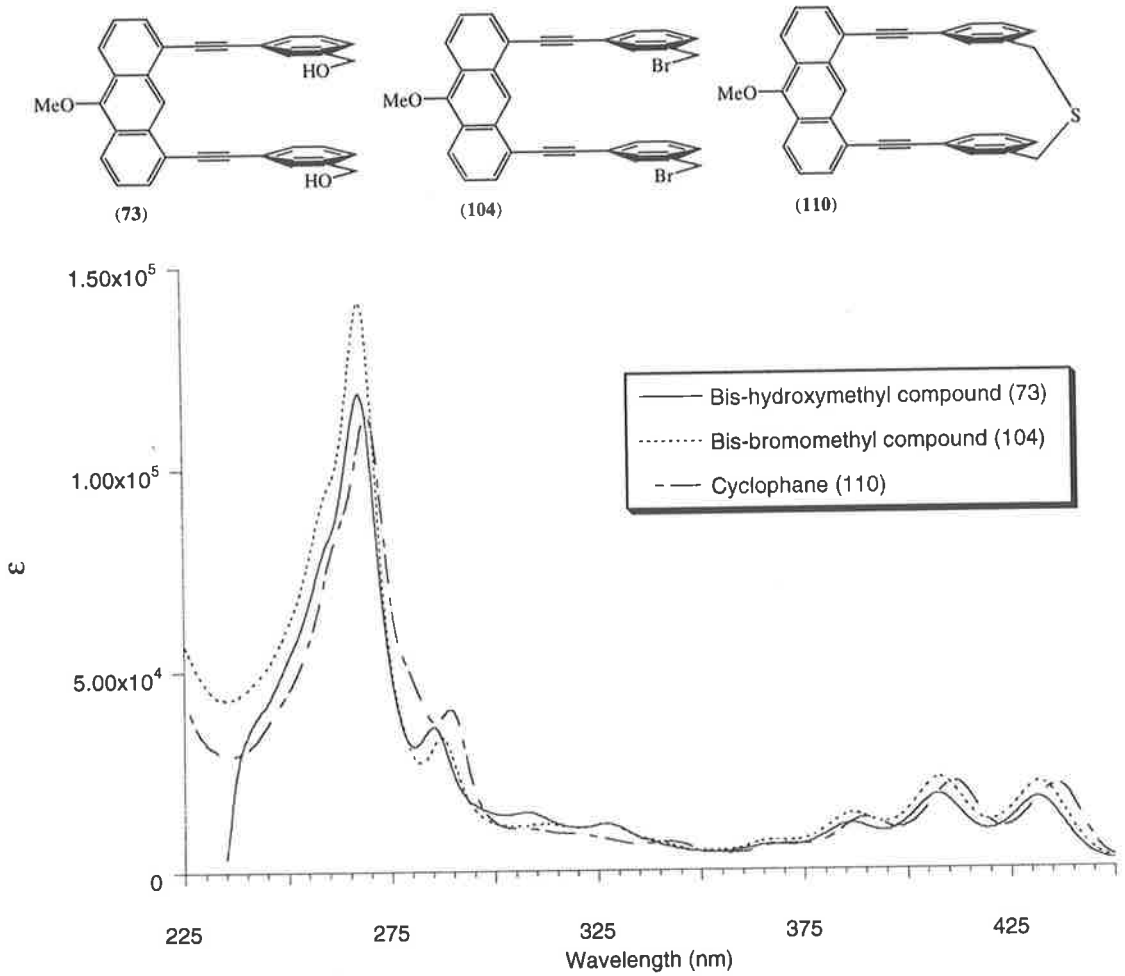


Figure 53. The UV-Vis spectra of the one-arm systems of the OMe-substituted template.

Similar results were obtained for the one-arm systems containing the standard template (Figure 54). Here the ε values for the cyclophane (**109**) were less than those for the bis-bromomethyl system (**102**). The λ_{max} values for these were close, with the cyclophane (**109**) having a slightly higher λ_{max}, 422 nm (ε 14 000), than that for the bis-bromomethyl compound (**102**), λ_{max} 418 nm (ε 14 000). Finally, no additional fine structure was observed for the cyclophane (**109**).

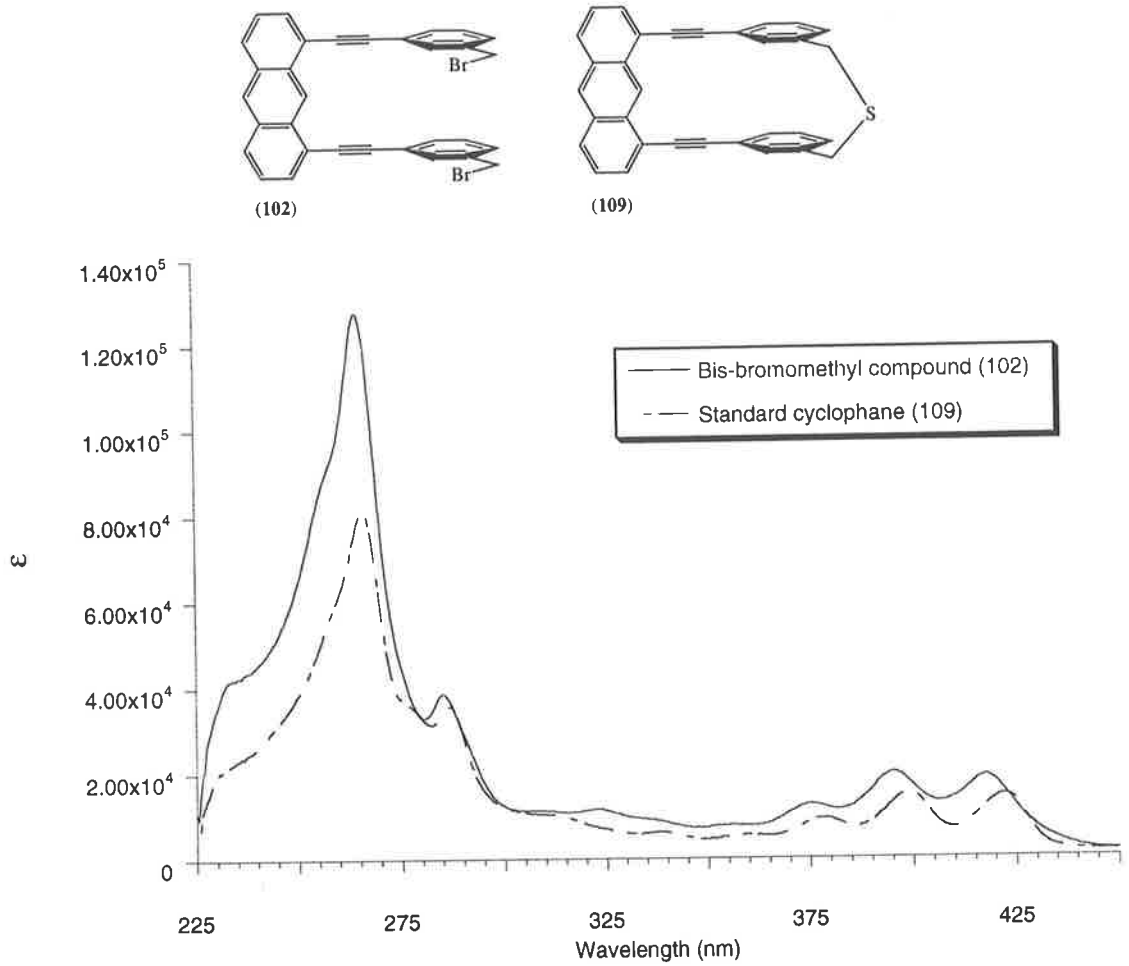


Figure 54. The UV-Vis spectra of the one-arm systems of the standard template.

8.2. Fluorescence Spectroscopy

Once a molecule exists in one of its excited states, it decays back to its ground state in a number of ways. It can undergo thermal relaxation which occurs at ~10^{-14} to 10^{-12} s or molecular luminescence which is much slower at ~10^{-8} s. Since thermal relaxation of a molecules' vibrational energy is much faster than luminescence, fluorescence and phosphorescence always originate from thermally equilibrated excited states in their lowest vibrational level.

Thermal relaxation involves both the vibrational relaxation (VR) and internal conversion (IC) of the excited states down to the lowest singlet state (Figure 45). Generally, these processes are radiationless since the excited electronic states are much closer together than are the ground and lowest excited state. This means that internal

conversion between excited states is efficient and precludes fluorescence, except between the ground state and the lowest excited state.

The lowest vibrational level of the lowest excited (singlet) state can further decay in one of three ways. Firstly, it may undergo internal conversion to the highest vibrational level of the ground state. This occurs with molecules containing many degrees of freedom, hence vibrational levels, and does not usually occur for the more rigid aromatic systems.

Secondly, the lowest excited state may undergo intersystem crossing (ST) to the lowest triplet state.[163] Intersystem crossing to the triplet state generally are of lower energy than the singlet states, and often there is overlap between the higher vibrational levels of the triplet state and the lowest excited singlet state. However, this process is classically forbidden but with quantum mechanical tunnelling, some population of the triplet states is possible. The lifetimes of these states are of the order of 10^{-8} s, and after thermally relaxing to the lowest triplet state, decay to the ground state through phosphorescence.

The last method of decay of the lowest excited singlet state is fluorescence (F). The molecule emits a quanta of visible or ultraviolet light and arrives in one of the ground state's vibrational levels. The molecule doesn't decay straight to the lowest vibrational level of the ground state since fluorescence occurs on the ~10^{-15} s timescale which means that vibrational relaxation cannot occur during transition. Once in a vibrational level of the ground state, the molecule undergoes radiationless vibrational relaxation to its lowest vibrational level.

The fluorescence spectrum reflects the vibrational structure of the molecule as all fluorescence arises from the transition of the same vibrational level of the lowest excited state to the various vibrational levels of the ground state. If the ground state and the lowest excited singlet state have similar vibrational structures, then the fluorescence and absorption spectra will be mirror images of each other with the fluorescence spectrum being on the longer wavelength side. Often this isn't the case since the ground and excited states have different charge distributions leading to different vibrational structures. Finally, the larger the chromophore, the larger the difference between the wavelength of fluorescence and the value of λ_{max} in the UV-Vis spectrum. This is

because the energy gap between the ground and excited states decreases with an increase in the degree of conjugation.

An example of the 'mirror image' effect that can be seen between the UV-Vis and fluorescence spectra is shown below in Figure 55 for the cyclophane (**109**). The mirror image resembles the primary band of the UV-Vis spectrum with three peaks clearly visible in the fluorescence spectrum. Often the fluorescence spectra of the bis-coupled systems show only two distinct peaks. No peaks are to be seen mirroring the secondary band since the secondary band does not result from the lowest excited state absorptions. The shoulders on the shorter-wavelength side (λ 389 and 410 nm) may be due to slight impurities in the solution, or imperfections in the cell, as the spectrum collected with a blank unfilled cell produced measurable peaks in these positions. Taking the difference spectrum between samples and the background (blank cell) resulted in negative peaks in this problem area and so the spectra shown below are the 'native' spectra without background subtraction.

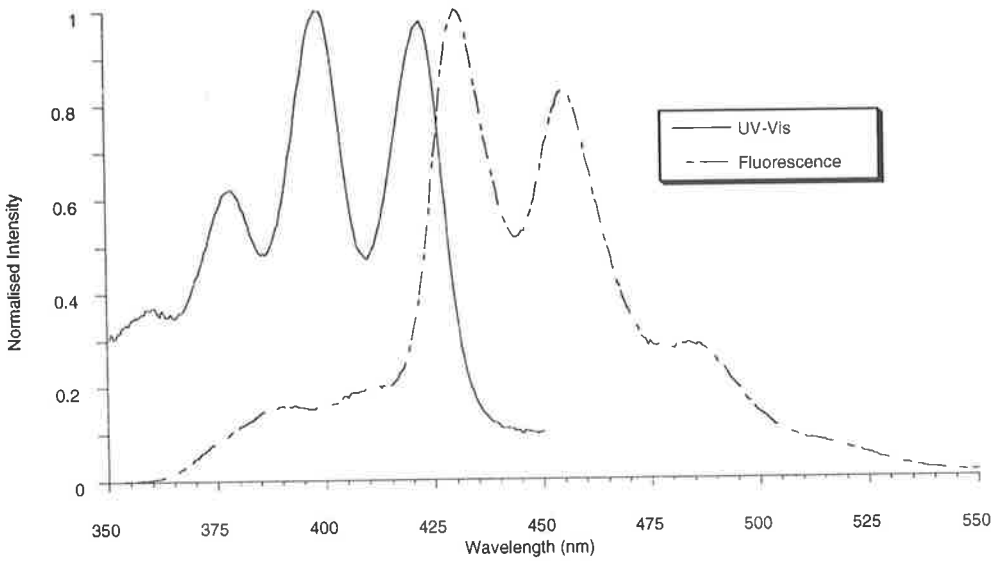
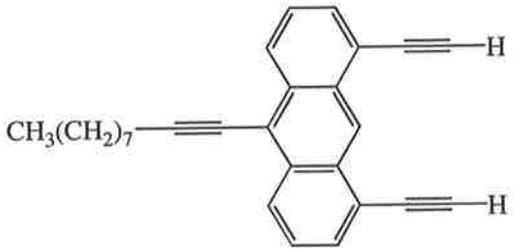


Figure 55. The 'mirror image' effect for cyclophane (**109**).

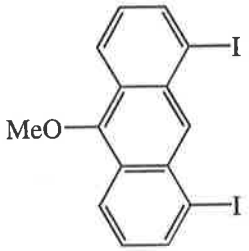
8.2.1. Fluorescence Spectra

The fluorescence spectra of several bis-coupled systems and cyclophanes are presented below with the y-ordinate normalised for comparison purposes. The spectra were recorded as dilute solutions (~10^{-5}-10^{-7} M) in HPLC grade THF, and two sets of data were taken and averaged for each spectrum. The first set of compounds to be

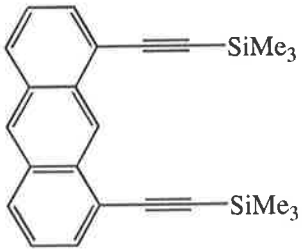
investigated were the template systems shown in Figure 56. The first item of note was that the order of position of the main peaks all mirror the λ_{max} values of their corresponding UV-Vis spectra. The wavelength difference between the λ_{max} values and the first peak of the fluorescence spectra were all between 7 or 8 nm.‡ The fluorescence spectrum of the OMe-substituted template possessed considerable more 'noise' than the other templates as it did not produce a good emission spectrum at concentrations up to 10^{-4} M. This accentuated the side peaks on the smaller wavelength side of the spectrum as compared to the main peak, which was quite broad.



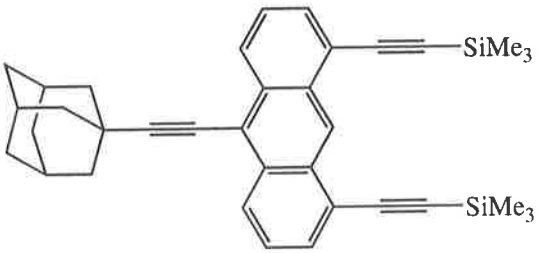
(**41**)



(**43**)



(**45**)



(**49**)

‡ The 'first peak' in all the fluorescence spectra was the first major peak with the smallest wavelength.

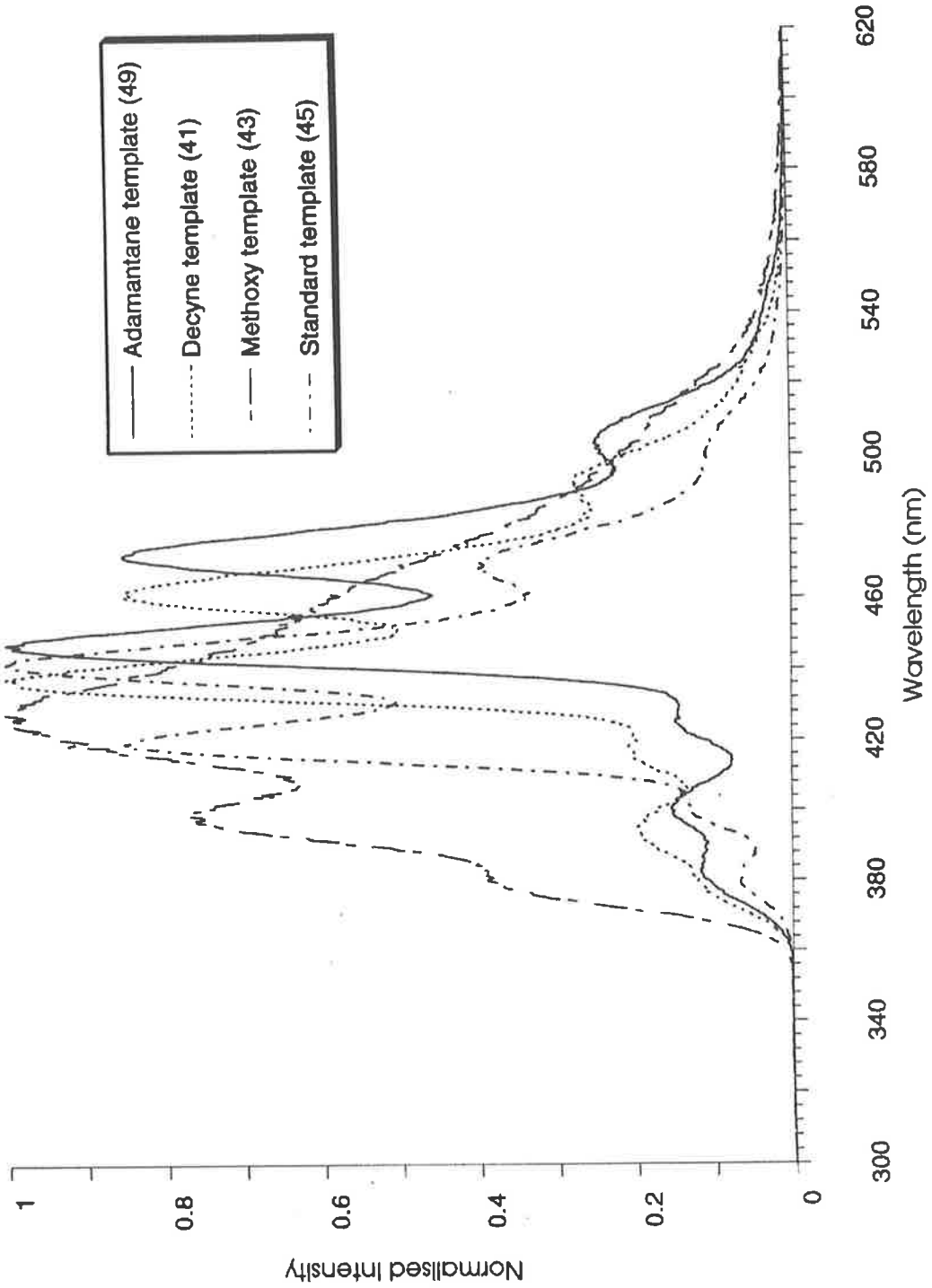


Figure 56. The fluorescence spectra of the template systems.

The next set of compounds to be studied were the bis-coupled systems (**60**) and (**61**) shown below (Figure 57). Little fine structure was to be observed in these spectra, the main peaks being all quite broad and the difference between their λ_{max} and the first peak fluorescence values were slightly higher than those of the templates, around 11 nm.

This was indicative of a more conjugated system, as expected with the two additional aromatic rings.

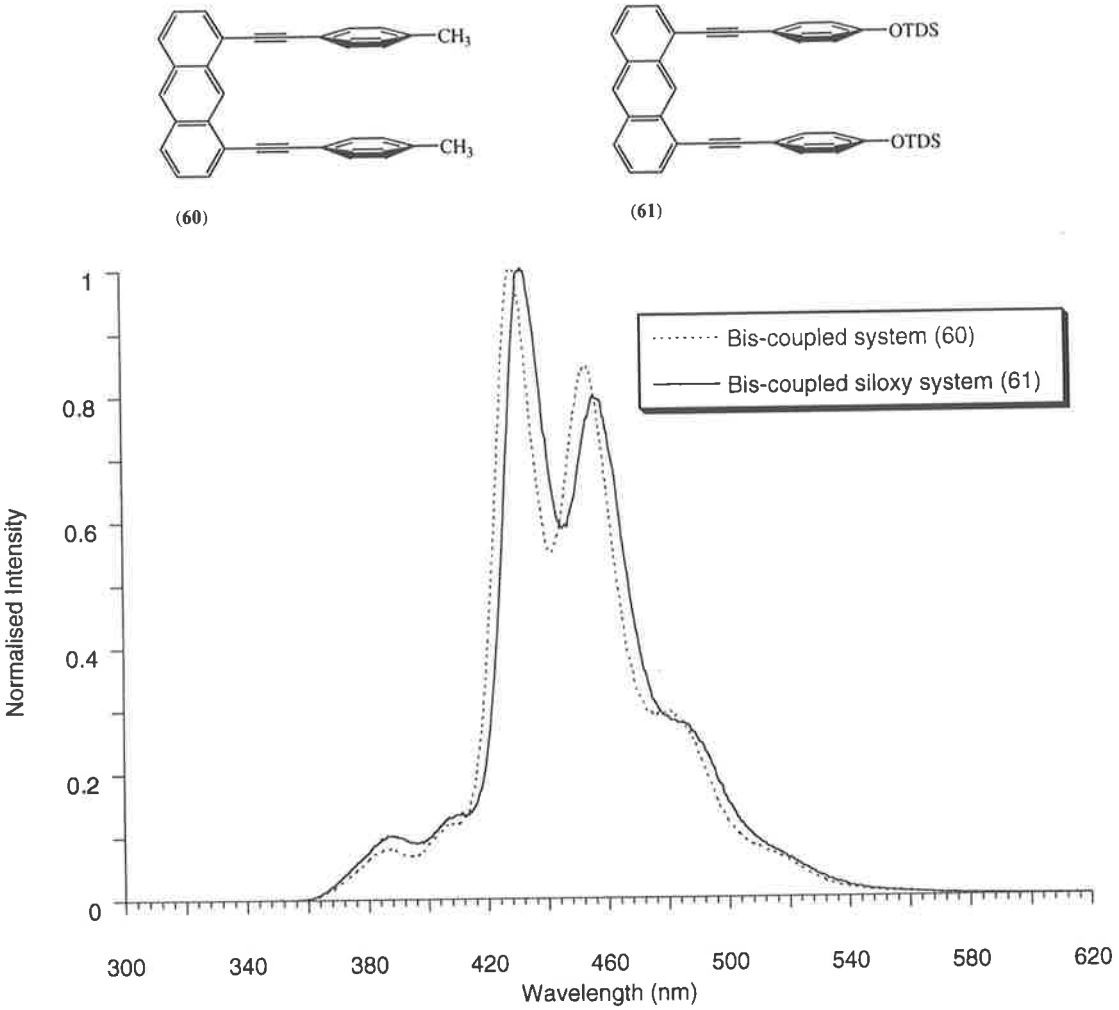


Figure 57. The fluorescence spectra of the bis-coupled systems (**60**) and (**61**).

Little difference was to be seen between the bis-coupled ester containing systems shown below in Figure 58. The differences between their λ_{max} and the first peak fluorescence values varied only slightly from 9 nm for (**67**) to 12 nm for (**69**) and (**65**).

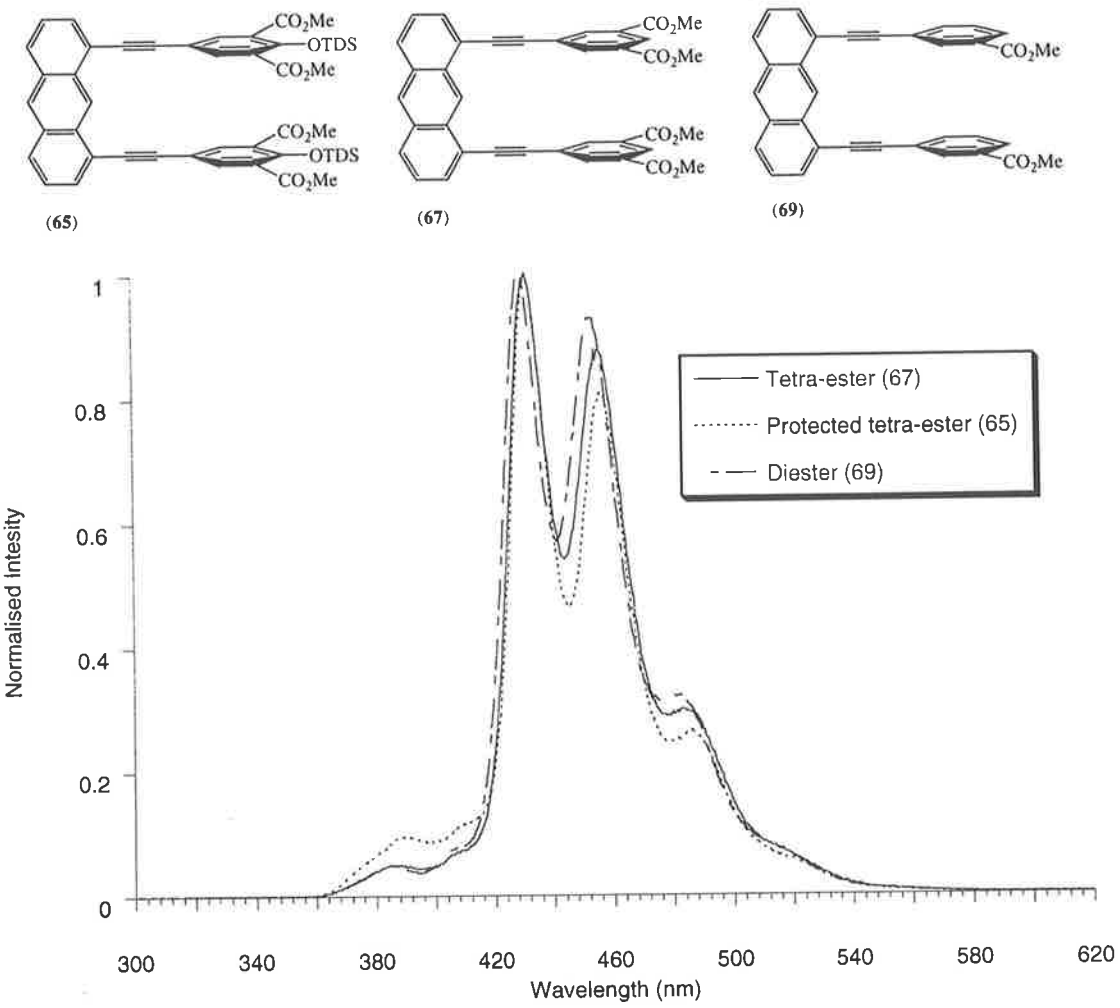


Figure 58. The fluorescence spectra of the bis-coupled ester containing systems (**65**), (**67**) and(**69**).

More interesting results were obtained for the tetra-ester (**67**) and octa-ester (**72**) systems (Figure 59). Considerably less vibrational structure was observed for the octa-ester as compared to the tetra ester. This suggested that the ground state of the octa-ester possessed more vibrational states and that these were close together in terms of energy. However, the difference between the λ_{max} and the first peak fluorescence value was higher for the octa-ester, 17 nm, compared to the tetra ester, 12 nm. This result was due to the larger conjugated system of the octa ester.

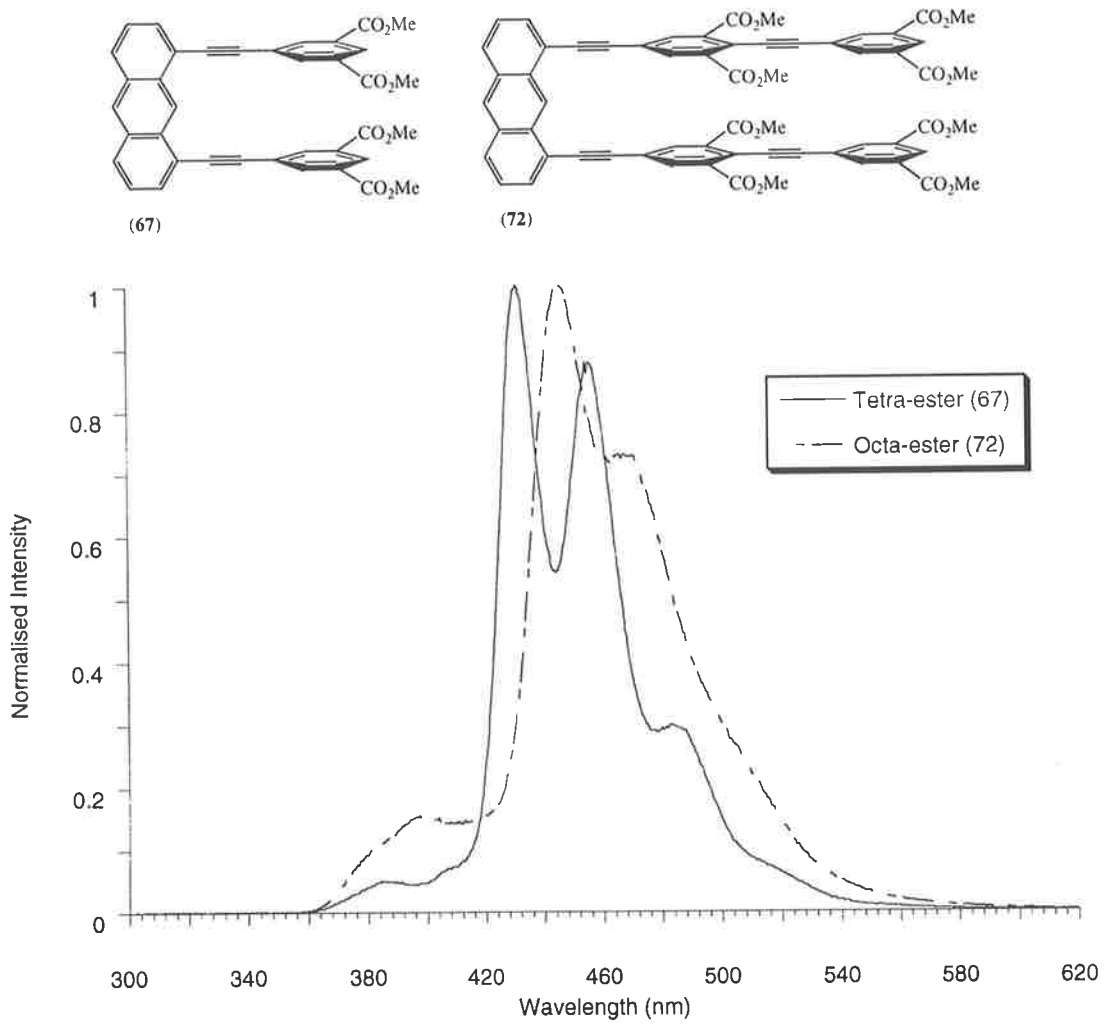


Figure 59. The fluorescence spectra of the tetra-ester (**67**) and octa-ester systems (**72**).

Significant differences were observed between the spectra of compounds (**57**), (**86**) and (**87**) (Figure 60). There was a considerable decrease in the amount of vibrational structure for bis-coupled system (**57**) and the one-arm cyclophane (**87**). Also, the bis-coupled system (**57**) possessed a very similar spectrum to the one-arm cyclophane (**87**) and both had very similar differences between the λ_{max} and the first peak fluorescence values, 21 nm and 19 nm respectively. These values differed markedly from the corresponding value for the hexa-acetate (**86**) of 9 nm, and suggested that compounds (**57**) and (**87**) possessed greater effective conjugation throughout the coupled system. This may be due to hydrogen bonding, holding the hydroxymethyl groups in a semi-rigid conformation thereby lessening the amount of rotation about the aryl-alkyne bond and increasing the effective conjugation of the molecule. The one-arm cyclophane would be expected to be even more rigid due to the ether linkage, and the

UV-Vis spectra of Section 8.1.1 support this hypothesis. However, comparisons between compounds (**57**) and (**87**) are tenuous as the results of molecular modelling experiments in Chapter 7 showed different molecular geometries and, by inference, different electronic configurations between the bis-coupled systems and the one-arm cyclophanes. This means that an increase in the difference between the λ_{max} and the first peak fluorescence value would not necessarily be observed in going from the bis-coupled system (**57**) to the one-arm cyclophane (**87**).

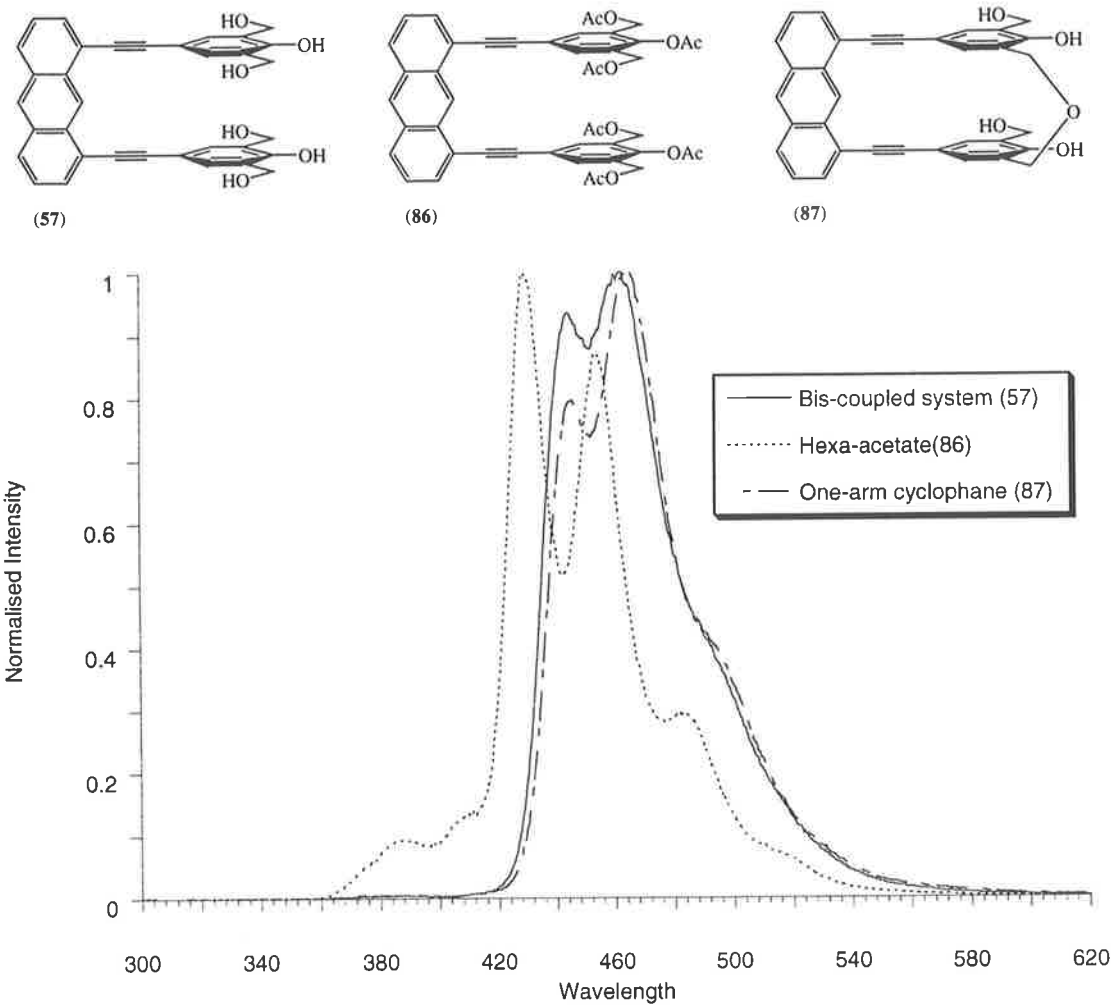


Figure 60. The fluorescence spectra of (**57**), (**86**) and (**87**).

The spectra of the bis-coupled systems (**74**) and (**104**) possessed a significant amount of noise (Figure 61). This could have been reduced by increasing the concentration of the solution, thereby increasing the intensity of the emission. Nevertheless, the main features of the spectra can clearly be seen below in Figure 61. Little vibrational structure was observed in either spectrum, but there was a marked

variation in the difference between the λ_{max} and the first peak fluorescence values, 12 nm for the tetrakis-hydroxymethyl compound (**74**) and 17 nm for the tetrakis-bromomethyl compound (**104**). Based on the argument for the previous systems in Figure 60, the tetrakis-hydroxymethyl compound would be expected to possess a higher difference between the λ_{max} and first peak fluorescence values. However, the reversal in order may be due to the larger steric bulk of the bromomethyl groups holding the two aromatic rings in a rigid conformation.

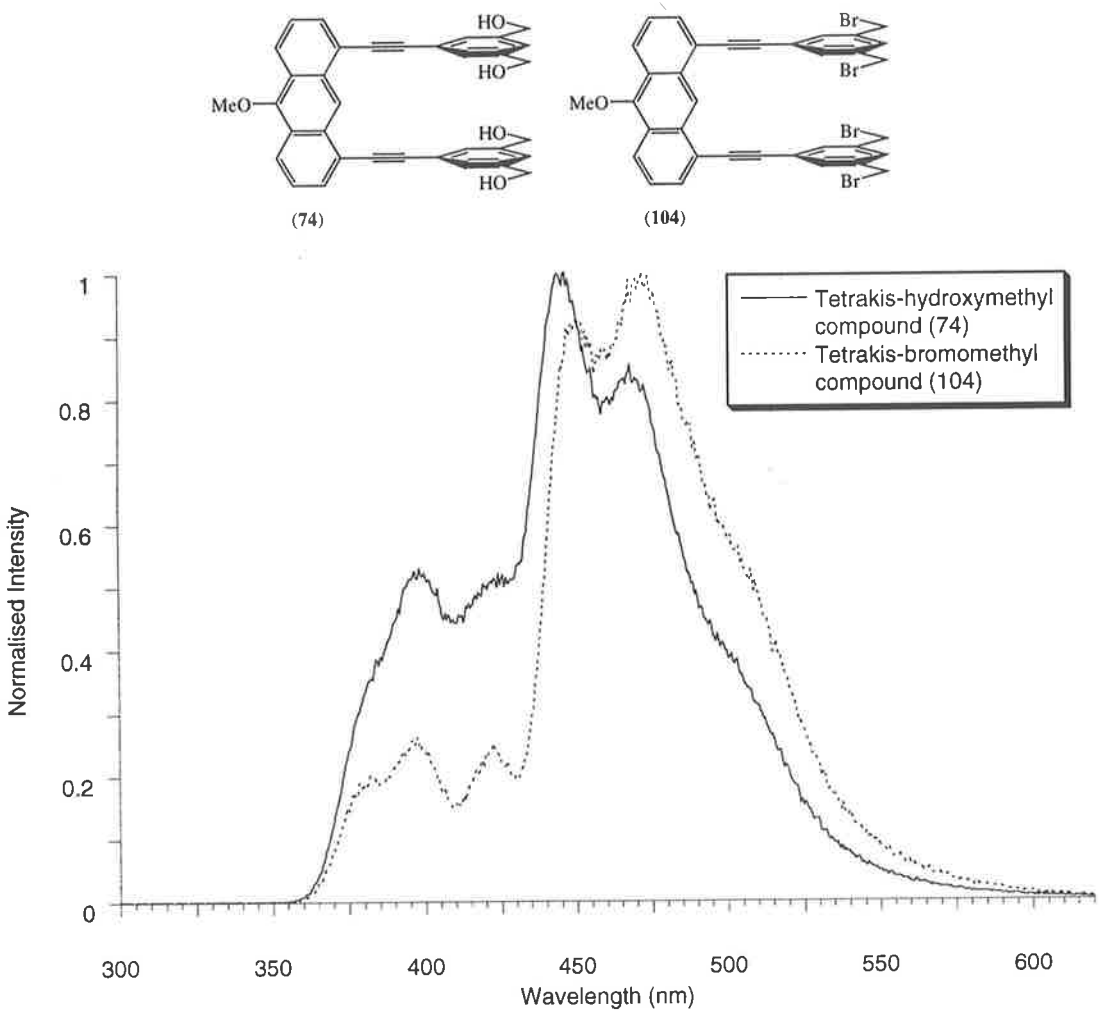


Figure 61. The fluorescence spectra of the two-arm bis-coupled systems (**74**) and (**104**).

The two-unit oligomeric system shown in Figure 62 all possessed broad peaks in their emission spectra. Some noise was also observed in the tetra-bromomethyl compound (**107**) spectrum and the octa-ester (**72**) has been included here for comparison. The two-unit precursor (**77**) possessed the lowest difference between the λ_{max} and first peak fluorescence value of 12 nm, as expected, and the other systems

possessed similar values of 17 nm for the octa-ester and 19 nm for the tetra-bromomethyl compound.

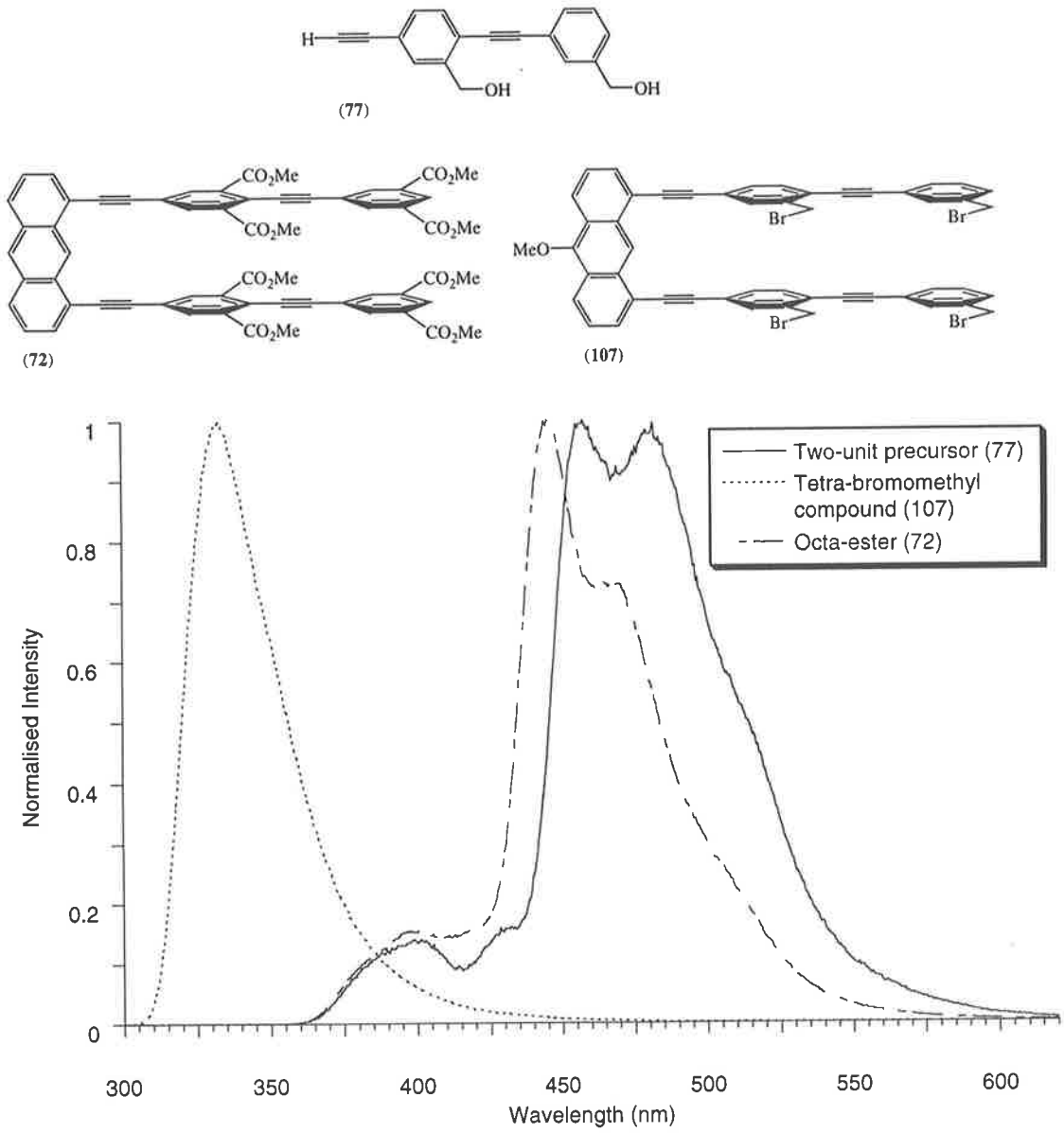


Figure 62. The fluorescence spectra of the two-unit oligomeric systems.

The spectra of the one-arm systems shown below in Figure 63 were very similar. All the peaks were broad, and the differences between the λ_{max} and first peak fluorescence values were similar as well, ranging from 13 nm for the cyclophane (**110**) to 16 nm for the bis-hydroxymethyl system (**73**). The bis-bromomethyl compound (**103**) had a value of 15 nm. The cyclophane was expected to have a higher value, based on previous arguments, but this wasn't the case.

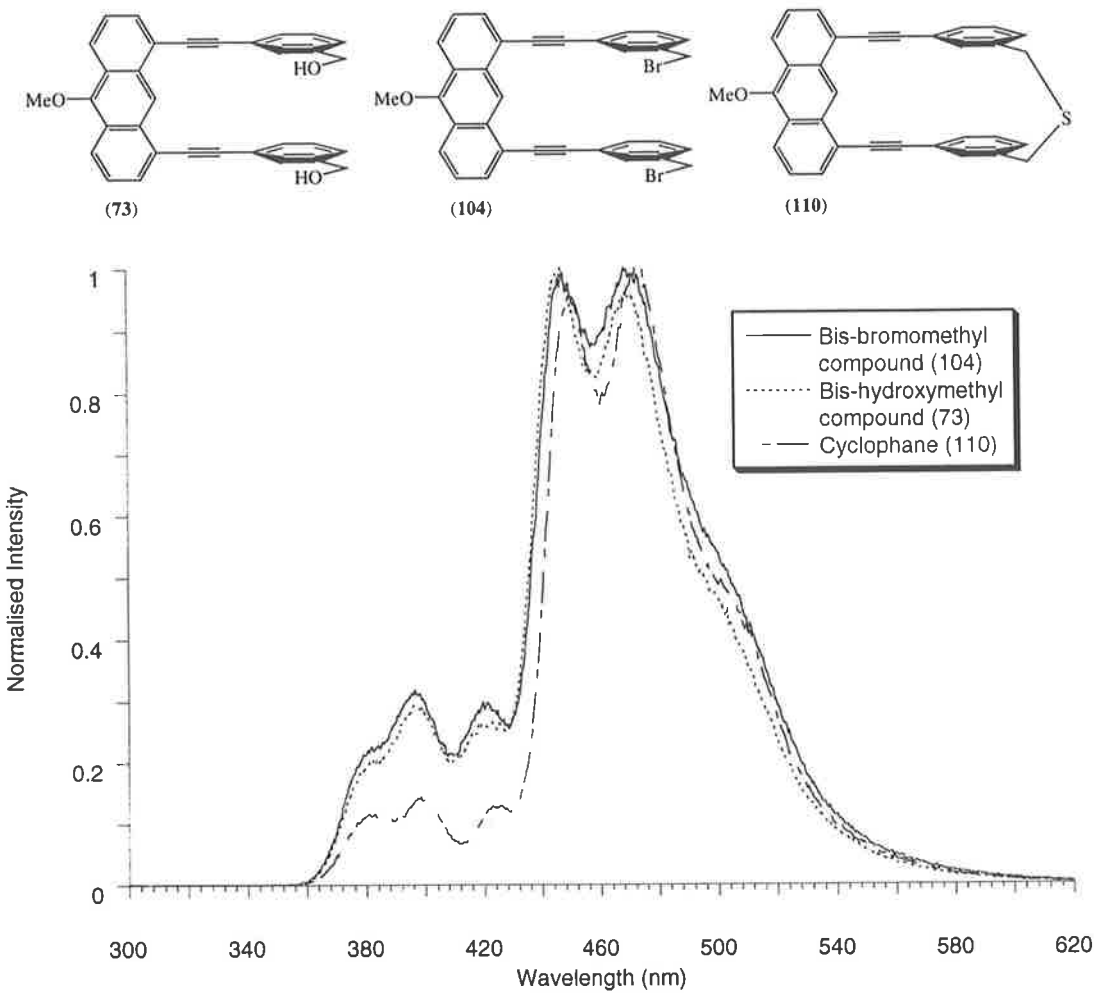


Figure 63. The fluorescence spectra of the one-arm systems of the OMe-substituted template.

The last set of compounds to be studied were the one-arm systems containing the standard template. In this case a marked difference was to be seen between the spectra. Considerable more vibrational structure was observed in the spectrum of cyclophane (**109**) than that of the bis-bromomethyl compound (**102**). In the spectrum of the bis-bromomethyl compound the second main peak was larger than the first, and the difference between the λ_{max} and first peak fluorescence values was larger for the bis-bromomethyl compound than for cyclophane. These results were similar to the analogous compounds in Figure 63.

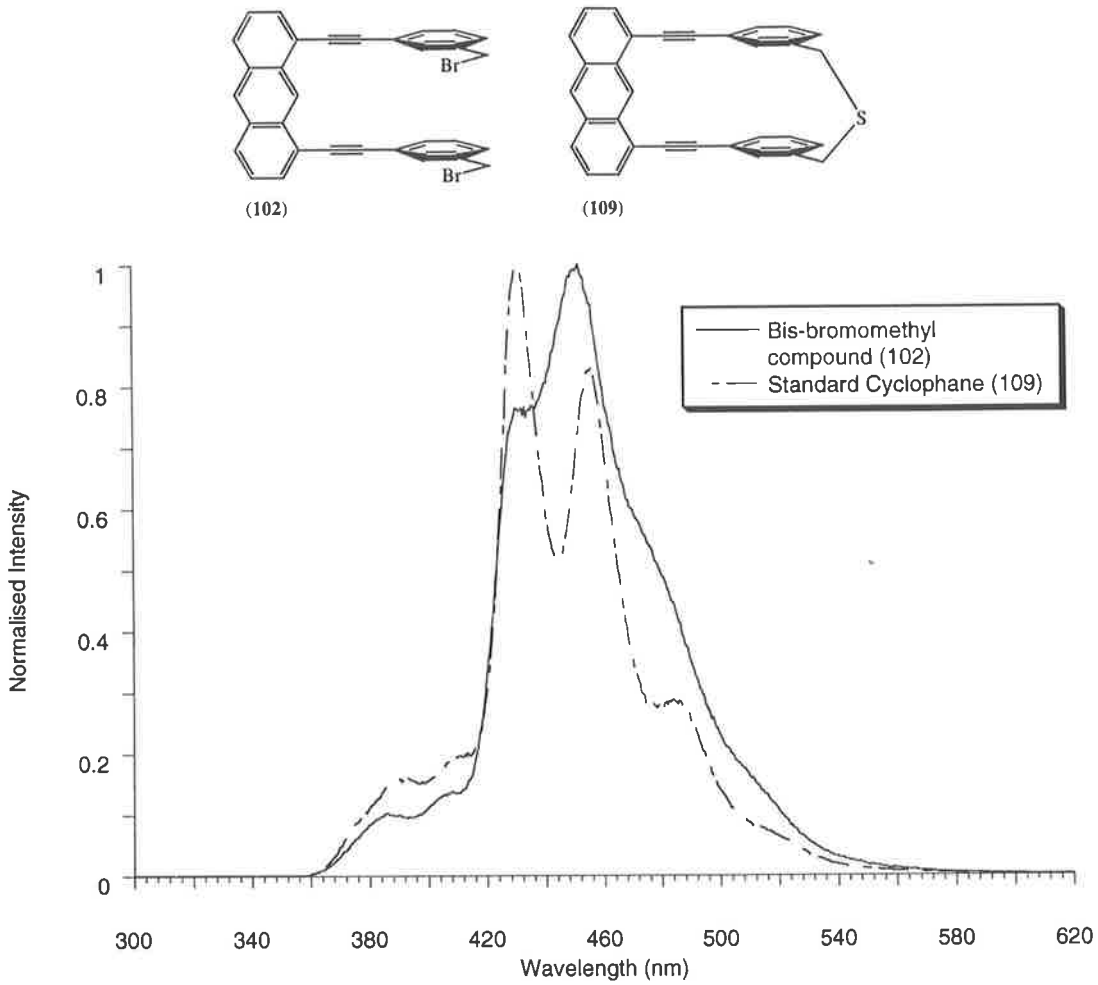


Figure 64. The fluorescence spectra of the one-arm systems of the standard template.

8.3. Summary

The UV-Vis and fluorescence spectra the bis-coupled and cyclophane systems have been recorded. These spectra have shown that vibrational structure was not always carried through from the UV-Vis to fluorescence spectra, and this was observed as a broadening of the fluorescence peaks. A trend was observed in the measure of the conjugation throughout a molecule, by considering the difference between the λ_{max} and first peak fluorescence values. This trend showed an increase in conjugation from the template systems to the bis-coupled systems, be they cyclophanes or otherwise, to finally the two-unit oligomer systems.

9. Conclusions and Future Work

A series of one-arm and two-arm monomers has been prepared (Chapter 2). These compounds have incorporated within them various linker-arm precursors (-CO_2Me or -CH_2OH); groups amenable to palladium catalysed coupling reactions (Br, I or ethynyl); and, in some cases, groups to aid in solubility (silyloxy groups).

Various anthracene template systems were synthesised (Chapter 3). Two of these templates were literature compounds, (**40**) and (**43**), and two others were novel 10-substituted systems, (**41**) and (**42**). Synthesis of the 10-substituted systems was achieved *via* the key steps of regioselective bromination of 1,8-dichloroanthracene in the 10 position and the subsequent regioselective palladium catalysed coupling of terminal alkynes to this functionalised position.

The one- and two-arm monomers were coupled to the template systems to form a series of bis-coupled systems (Chapter 4). The couplings were performed using Sonogashira coupling conditions. Solubility and purification problems were encountered for a number of the bis-coupled systems, however these were overcome by the introduction of silyloxy groups and by using reverse phase silica for purification.

A one-arm, two-unit oligomer was synthesised by the palladium catalysed coupling of two monomer units, the triflate (**30**) and alkyne (**33**) (Chapter 4). Subsequent reduction of the methyl esters to the corresponding hydroxymethyl groups could be achieved using DIBAL-H. The use of lithium aluminium hydride was found to reduce the esters as well as regiospecifically reducing the internal alkyne to a *trans* double bond. The oligomer was then successfully coupled to a template system (**43**).

The coupling of the triflate (**21**) to the template (**40**) showed that regioselective coupling was possible between an aryl-iodine bond versus a hindered aryl-triflate, and that the reaction proceeded in good yield (Chapter 4). Extension of this bis-coupled system (**71**) to the octa-ester (**72**) using a palladium catalysed coupling reaction with the monomer (**27**), showed that further coupling was possible to the hindered bis-triflate.

A new catalytic protocol was discovered and developed for the palladium catalysed coupling of aryl-halides to terminal alkynes (Chapter 5). The new protocol employed zinc salts and iodine/iodide co-catalysts in place of the traditional copper (I)

iodide. It was established that nucleophilic amine bases were required for these reactions. The new coupling conditions were successfully used for the preparation of various test and bis-coupled systems.

The linker-arm precursors of the bis-coupled systems were manipulated to form a series of compounds containing bromomethyl groups (Chapter 6). It was found that the corresponding iodomethyl and mesylate compounds were unstable and, in some cases, could not be isolated.

The bromomethyl compounds were then converted into a series of thia-, dithia- and aza-cyclophanes *via* double nucleophilic displacement reactions (Chapter 7). The formation of the thiacyclophanes (**109**) and (**110**) was best achieved using alumina absorbed Na_2S giving the cyclophanes in high yields. Conditions employing high dilution had little effect on the yield of the cyclophanes, and the addition of extra absorbed reagent was necessary to complete the reaction due to it decomposing over time in solution. The poor yields of the two-arm cyclophane (**111**) suggested that the three-unit linker-arms were too short for the anthracene template systems. Molecular modelling results supported this idea with significant 'bending' of the alkyne groups and the aromatic rings being observed for the two-arm dithia- and diaza-cyclophanes.

An x-ray crystal structure was obtained for the thiacyclophane (**110**) (Chapter 7). The structure showed the cyclophane rings to be non-parallel in the solid state, and that π-stacking was present between the molecules. This produced centrosymmetric dimers of the cyclophane in the solid state.

The corresponding one-arm azacyclophane (**114**) could be prepared in good yield from the bis-bromomethyl compound (**103**) (Chapter 7). However, this cyclophane was found to be unstable, and so the corresponding two-arm analogues or two-unit oligomeric systems were not prepared.

The UV-Vis and fluorescence spectra were obtained for many of the bis-coupled systems and cyclophanes. An increase in fine structure was not observed in the UV-Vis spectra of the cyclophanes, as compared to the unconstrained systems. However, an increase in conjugation was observed in going from the templates to the bis-coupled systems, and from the bis-coupled systems to the two-unit oligomeric systems. This was determined by considering the difference between the value of λ_{max} in the UV-Vis spectra and the λ value of the first main peak in the fluorescence spectra.

Future work associated with this project would involve the application of the chemistry described in this thesis to different template systems. Since it has been established that the three-unit linker-arm is too short for the anthracene systems, the use of templates with a shorter distance between the positions for coupling the monomer units to (cf. the 1,8-positions of the anthracene templates) would be preferred. Two possible template systems are shown below in Figure 65 where the R groups may be introduced to aid in solubility. The synthesis of these templates would be more involved as compared to the anthracene systems, and difficulties in the preparation and storage of the naphthalene systems may arise, based on previous work in the literature on similar compounds.[171] It would be expected that palladium catalysed coupling to the naphthalene and cyclohexyl templates would be more difficult than for the anthracene systems due to the increase in steric interactions between the aromatic rings of the corresponding bis-coupled systems. However, subsequent cyclophane formation would be easier than for the anthracene systems since the linker-arm precursors would be held closer together.

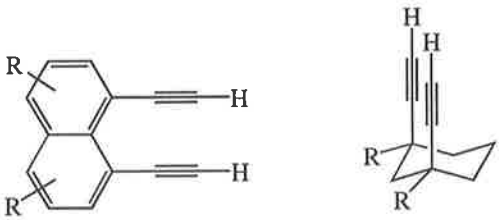


Figure 65. Two possible template systems.

Molecular modelling suggested that these templates would produce dithiacyclophanes with minimal stain in their systems, as can be seen in their optimised geometries. Two examples are shown below in Figure 66 for the two-arm dithiacyclophane of the naphthalene template, and also for the corresponding two-unit oligomeric system. Similar results would be expected for the cyclohexyl systems.

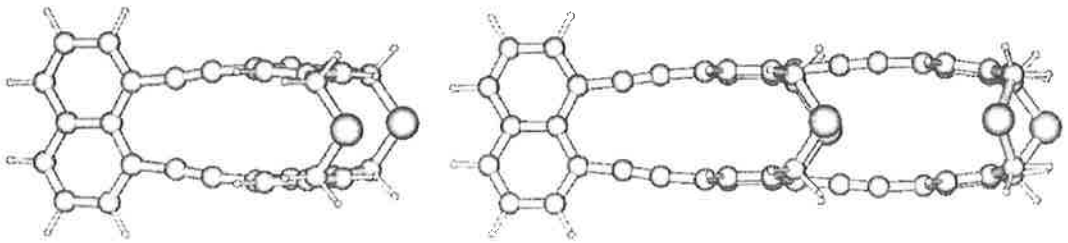


Figure 66. The two-arm cyclophanes of the naphthalene system.

An alternative to using different templates would be to increase the length of the linker-arm to reduce the strain present in the two-arm cyclophanes of Chapter 7. An example of this would be to insert two extra methylene units into the linker-arm to extend their length from the present three-units to five. Molecular modelling suggested that this would significantly reduce the amount of strain in the systems. The optimised geometry for a two-arm thiacyclophane is shown below in Figure 67.

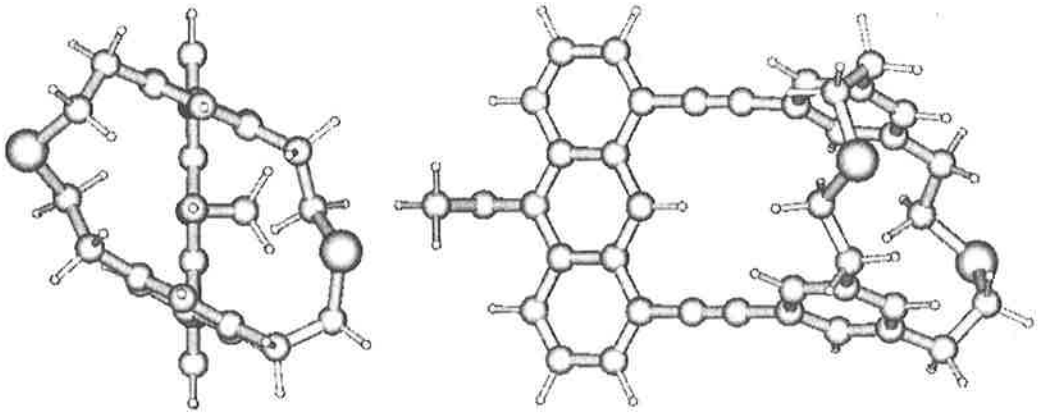


Figure 67. Different views of a longer linker-arm cyclophane.

By increasing the length of the linker-arm or by using 'smaller' templates, the reduction in the amount of strain in the cyclophanes may translate into an enhancement of the conjugation throughout the molecule. It is possible that the longer linker-arm systems may not be rigid enough to ensure increased conjugation by allowing significant rotations about the aryl-alkyne bonds.

Finally, nonlinear optical measurements would be made on a series of cyclophanes, and comparisons would be made between the differences in templates used, the length of the linker-arms and the length of the oligomer, based on their $\chi^{(3)}$ values.

10. Experimental

^{1}H NMR spectra were recorded at 600 MHz on a Varian Nova NMR spectrometer (105.87 MHz for ^{13}C), 300 MHz on a Varian Gemini NMR spectrometer (75.47 MHz for ^{13}C) or at 200 MHz on a Varian Gemini spectrometer (50.28 MHz for ^{13}C), using a dual 5mm $^{13}C/^{1}H$ probe. All spectra were recorded as dilute solutions in deuteriochloroform using tetramethylsilane as an internal standard; except where indicated. All multiplicities for proton NMR are abbreviated: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and br, broad. Regiochemical NMR assignments of protons was based on previously published chemical shift values for analogous strucutures.[84,91,103]

Melting points were determined on a Kofler hot-stage micro-melting point apparatus equipped with a Reichart microscope and are uncorrected.

Electron impact (EI) and fast atom bombardment (FAB) mass spectra were recorded at 70 eV on a Vacuum Generators ZAB 2HF mass spectrometer. Liquid secondary ionisation mass spectrometry (LSIMS) and accurate mass spectra were performed by the University of Tasmania mass spectrometric service.

Infrared spectra were recorded on a Hitachi 270-30 spectrometer, or a Perkin Elmer Spectrum BX, or a ATI Mattson Genesis FTIR as nujol mulls between sodium chloride plates; except where indicated.

Ultraviolet-visible (UV-Vis) spectra were recorded on a Varian Cary 2200 UV-VIS Spectrophotometer in THF. Fluorescence spectra were recorded on a Perkin Elmer LS 50B Luminescence Spectrophotometer in THF.

Elemental analyses were performed at the University of Otago, New Zealand.

Thin layer chromatography (tlc) was carried out using Merck Silica gel (Kieselgel) $60F_{254}$ on aluminium backed plates, Merck aluminium oxide 150 F_{254} (Neutral) on aluminium backed plates or with Whatman $KC_{18}F$ reverse phase tlc plates. Tlc plates were visualised using 253 nm ultraviolet light and/or by an acidic solution of 10% ammonium molybdate or 1% potassium permanganate solution. Flash and squat column chromatography was carried out using Merck Silica gel 60 (particle size 0.040-

0.063 mm) pH 6.5-7.5, Fluka aluminium oxide for chromatography 507 C neutral (100-125 mesh) pH 7.0±0.5 or with Waters preparative C18 (55-105 μm) reverse phase silica.

Solvents were purified and dried using standard laboratory procedures.[172] All organic extracts were dried over anhydrous magnesium sulphate. All solvents for palladium catalysed coupling reactions were degassed by the freeze-pump-thaw method and kept under an atmosphere of nitrogen.[172] All reactions involving anhydrous solvents were also kept under an atmosphere of nitrogen. 'Wet' ether refers to a water saturated solution of ether.

A typical extractive workup for the palladium catalysed coupling reactions involved addition of the reaction mixture to sat. NH_4Cl and extraction with two portions of organic solvent. The organic layers were then combined and washed once with water. Finally, the solvent was dried and removed.

The following compounds were prepared according to published procedures: methyl 5-iodosalicylate,[64] dimethyl 2-hydroxyisophthalate,[72,73] benzyltrimethyl-ammonium dichloroiodate,[74] dimethyl 5-bromoisophthalate,[77] 1,3-bis(hydroxymethyl)-5-bromobenzene,[77] 1,8-dichloroanthracene,[85] 1,8-diethynylanthracene,[84] ethynyladamantane[90], 1,8-diiodo-10-methoxyanthracene,[91] and sodium sulphide adsorbed on alumina (2.5 mmol/g).[160]

2,6-Bis(hydroxymethyl)-4-bromophenol (1)

To an aqueous solution of 25% NaOH (25 mL) containing *p*-bromophenol (8.65 g, 50 mmol) and methanol (12.5 mL) was added 38% formaldehyde solution (45 mL). The resulting mixture was heated at 70° for 1.5 hrs and then allowed to stir at room temperature for a further 36 hrs. A solution of acetic acid (12.5 mL) in water (25 mL) was then added and stirring was continued for 6 hrs at room temperature after which a white precipitate had formed. This was collected and recrystallised from ethyl acetate to give fine off-white needles (1.61 g, 14%); mp 150.0-151.0° (lit.[2] 163.0-164.0°, purification by sublimation); δ_H (300 MHz, d_6-acetone) 4.73 (4H, s, Ar**C**$\mathbf{H_2}$OH), 7.28 (2H, s, Ar**H**); δ_C (75.47 MHz, d_6-acetone) 61.4 (Ar**C**H_2OH), 111.7 (**Ar**Br), 129.3, 130.6, 153.5 (**Ar**OH); m/z (EI) 234 (M^+, ^{81}Br, 39%), 232 (M^+, ^{79}Br, 40%), 216 (84), 214 (87).

2,6-Bis(hydroxymethyl)-4-iodophenol (2)

To a solution of 2,6-bis(hydroxymethyl)phenol (**22**) (1.22 g, 7.92 mmol) in methanol (40 mL) was added $NaHCO_3$ (3.32 g, 39.61 mmol) and benzyltrimethylammonium dichloroiodate (2.90 g, 8.32 mmol). The resulting suspension was stirred at room temperature for 2hrs. The reaction mixture was concentrated *in vacuo* and then purified by squat column chromatography [dichloromethane/ethyl acetate 1/1 (v/v), R_f 0.50] to give the title compound as a fawn solid (1.98 g, 89%). A small sample was recrystallised from a methanol/water mixture as orange needles; mp 155.0-156.5°; Exact Mass Calcd for $C_8H_9IO_3$: 279.9598, Found 279.9608; δ_H (200 MHz, d_6-acetone) 4.72 (4H, s, ArC**H**$_2$OH), 7.46 (2H, s, Ar**H**); δ_C (50.28 MHz) 61.2, 81.5 (**Ar**I), 131.0, 135.4, 154.4 (**Ar**OH); m/z (EI) 280 (M^+, 37%), 262 (100).

2,6-Bis(morpholinomethyl)-4-bromophenol (3)

To a solution of *p*-bromophenol (8.65 g, 50 mmol) in acetic acid (10 mL) was added morpholine (9.60 mL, 110 mmol) and 38% formaldehyde solution (11 mL, 110 mmol). The resulting solution was then heated at 80° for 6 hrs. The reaction mixture was then taken up into dichloromethane (200 mL) and washed with water (100 mL), sat. $NaHCO_3$ (100 mL) and finally water (100 mL). The solution was dried and passed through a short squat column. The solvent was removed *in vacuo*, to yield a yellow solid (16.45 g, 82%); mp 115.0-115.5°; Anal. Calcd for $C_{16}H_{23}N_2O_3Br$: C, 51.76; H, 6.24; N, 7.54, Found: C, 52.03; H, 6.23; N, 7.42; δ_H (300 MHz) 2.53 (8H, t, *J* 4.6 Hz), 3.59 (4H, s, ArC**H**$_2$R), 3.74 (8H, t, *J* 4.6 Hz), 7.20 (2H, s, Ar**H**); δ_C (75.47 MHz) 52.7, 58.2, 66.3, 110.1 (**Ar**Br), 124.0, 130.8, 154.7 (**Ar**OH); m/z (EI) 372 (M^+, ^{81}Br, 40%), 370 (M^+, ^{79}Br, 41%), 285 (100), 283 (84).

1-Acetoxy-2,6-bis(acetoxymethyl)-4-bromobenzene (4)

A solution of 2,6-bis(morpholinomethyl)-4-bromophenol (**3**) (5.00 g, 13.5 mmol) in acetic anhydride (30 mL) and acetic acid (2 mL) was refluxed for 24 hrs. The reaction mixture was concentrated by rotary evaporation and the resulting red/brown oil taken up into dichloromethane (150 mL), washed with sat. $NaHCO_3$ (3x75 mL) and water (75 mL). The solvent was dried and removed *in vacuo* to give a red oil. This oil

was then shaken with a solution of 3% methanol in hexane (10 mL) for 5 mins before being placed in the fridge to crystallise overnight. The crude product was collected and recrystallised from hexane to give colourless needles (3.08 g, 64%); mp 81.0-82.0°; Anal. Calcd for $C_{14}H_{15}O_6$: C, 46.82; H, 4.21, Found: C, 46.73; H, 4.02; δ_H (300 MHz) 2.10 (6H, s, $ArCH_2OCOCH_3$), 2.35 (3H, s, $ArOCOCH_3$), 5.00 (4H, s, $ArCH_2R$), 7.57 (2H, s, Ar**H**); δ_C (75.47 MHz) 20.4, 20.7, 60.5, 119.4 (**Ar**Br), 131.1 (**Ar**CH_2OAc), 132.8, 146.3 (**Ar**OAc), 168.7 (**C**=O), 170.3 (**C**=O); m/z (FAB) 361 ($(M+H)^+$, ^{81}Br, 60%), 359 ($(M+H)^+$, ^{79}Br, 61%), 301 (13), 209 (13), 259 (16), 257 (17); ν_{max} (cm^{-1}) 1734, 1768 (C=O).

2,6-Bis(morpholinomethyl)phenol (5)

To a 38% formaldehyde solution (35.2 mL, 450 mmol) was added phenol (20.00 g, 210 mmol) followed by morpholine (38.6 mL, 440 mmol). The resulting suspension was stirred vigorously and heated at 50° for 15 hrs. Water (100 mL) and ethyl acetate (20 mL) was then added with cooling to 0°. Over 0.5 hr a white precipitate formed which was collected by vacuum filtration and washed with a solution of water/ethyl acetate (10:1) (100 mL). The solid was recrystallised from hexane to give the title compound as colourless plates (12.00 g, 20%); mp 123.5-124.5°; Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27, Found: C, 66.02; H, 8.07; δ_H (300 MHz) 2.51 (8H, t, *J* 4.6 Hz), 3.61 (4H, s, $ArCH_2R$), 3.71 (8H, t, *J* 4.6 Hz), 6.74 (1H, t, *J* 7.5 Hz, Ar**H**), 7.04 (2H, d, *J* 7.5 Hz, Ar**H**); δ_C (75.47 MHz) 53.1, 59.2, 66.7 ($ArCH_2R$), 118.5, 122.0 (**Ar**CH_2R), 129.0, 155.9 (**Ar**OH); m/z (EI) 292 (M^+, 75%), 205 (100).

1-Acetoxy-2,6-bis(acetoxymethyl)benzene (6)

A solution of 2,6-bis(morpholinomethyl)phenol (**5**) (4.69 g, 16 mmol) in acetic anhydride (20 mL, 196 mmol) was refluxed for 20 hrs. The reaction mixture was added to water (200 mL) and extracted with dichloromethane (3x100 mL). The organic extracts were combined and washed with sat. Na_2CO_3 (3x100 mL) followed by water (100 mL). The solvent was dried and remove *in vacuo* to give a colourless oil[57] (2.54 g, 57%); δ_H (300 MHz) 1.92 (6H, s, $ArCH_2OCOCH_3$), 2.20 (3H, s, $ArOCOCH_3$), 4.92 (4H, s, $ArCH_2OAc$), 7.12 (1H, t, *J* 7.6 Hz, 4-H), 7.30 (2H, d, *J* 7.6 Hz, Ar**H**); δ_C (75.47

MHz) 19.8, 20.1, 60.7 (Ar**C**H_2OAc), 125.8, 128.7, 130.1, 147.3 (**Ar**OAc), 168.5 (**C**=O), 169.9 (**C**=O); m/z (EI) 361 (M^+, ^{81}Br, 60%), 359 (M^+, ^{79}Br, 60%), 301 (^{81}Br, 18%), 299 (^{79}Br, 18%), 257 (^{81}Br, 19%), 259 (^{79}Br, 20%); ν_{max} (cm^{-1}) 1768, 1734 (C=O).

2,6-Bis(morpholinomethyl)-4-iodophenol (7)

Method A:

To a solution consisting of acetonitrile (16 mL) and water (5 mL) was added 2,6-bis(morpholinomethyl)phenol (**5**) (2.00 g, 6.85 mmol) and NaI (1.23 g, 8.22 mmol). The resulting solution was cooled to 0° and *t*-BuOCl (1 mL, 8.35 mmol) added dropwise *via* syringe. The reaction mixture was allowed to stir for a further 15 mins at 0° before being taken up into dichloromethane (50 mL) and washed with water (50 mL). The aqueous layer was re-extracted with dichloromethane (50 mL), the organic layers combined, washed with sat. $Na_2S_2O_3$ (2x50 mL) and finally water (50 mL). The solvent was dried and removed *in vacuo* to give a yellow oil. The product was purified by flash chromatography on silica gel [ethyl acetate, R_f 0.36] to give a colourless oil which crystallised upon addition of hexane to give an off-white solid (0.94 g, 33%).

Method B:

To a solution of 2,6-bis(morpholinomethyl)phenol (**5**) (2.00 g, 6.85 mmol) in dimethylsulphoxide (10 mL) was added NaI (1.23 g, 8.22 mmol) and chloramine-T trihydrate (2.32 g, 8.22 mmol) with stirring. The resulting suspension was heated at 50° for 45 mins after which time the reaction mixture was taken up into dichloromethane (50 mL) and washed with water (50 mL). The aqueous layer was re-extracted with dichloromethane (50 mL), the organic layers combined and washed with sat. $Na_2S_2O_3$ (2x50 mL) and water (50 mL). The solvent was dried and removed *in vacuo* to give a yellow oil. The product was purified by flash chromatography on silica gel [ethyl acetate, R_f 0.36] to give a colourless oil which was taken up into hot hexane and upon cooling gave off-white prisms (1.95 g, 68%); mp 108.0-109.0°; Exact Mass Calcd for $C_{16}H_{23}IN_2O_3$: 418.0755. Found: 418.0763; δ_H (300 MHz) 2.52 (8H, t, *J* 4.6 Hz), 3.59 (4H, s, ArC**H**$_2$R), 3.74 (8H, t, *J* 4.6 Hz), 7.34 (2H, s, Ar**H**); δ_C (75.47 MHz) 53.1, 58.5, 66.7, 113.1 (**Ar**I), 125.0, 137.3, 156.1 (**Ar**OH); m/z (EI) 418 (M^+, 44%), 331 (98).

2-(Morpholinomethyl)-4-iodophenol (8)

The procedure was analogous to that for (**3**) except that the solution was heated for 23 hrs at 50°. Purification by flash chromatography [dichloromethane/ethyl acetate 1/1 (v/v), R_f 0.41] gave the title compound as a colourless oil (15%); Exact Mass Calcd for $C_{11}H_{14}INO_2$: 319.0071, Found: 319.0066; δ_H (300 MHz) 2.56 (4H, br s), 3.65 (2H, s, ArC**H**$_2$R), 3.76 (4H, br s), 6.60 (1H, d, *J* 8.4 Hz), 7.28 (1H, d, *J* 2.1 Hz), 7.44 (1H, dd, *J* 2.1 and 8.4 Hz); δ_C (75.47 MHz) 52.7, 60.9, 66.6, 80.6 (**Ar**I), 118.5, 123.2, 137.1, 137.6, 157.4 (**Ar**OH); m/z (EI) 319 (M^+, 100%), 233 (28).

2,6-Bis(acetoxymethyl)-4-bromophenol (13)

A stock solution of 0.5M guanidine in methanol was prepared. Sodium (1.78 g, 77.4 mmol) was added to dry methanol (800 mL) under a nitrogen atmosphere. Once effervescence had ceased, guanidine hydrogencarbonate (14.20 g, 79 mmol) was added with stirring. After 1 hr the resulting white suspension was filtered and the 0.5M guanidine solution stored under nitrogen.

A solution of 1-acetoxy-2,6-bis(acetoxymethyl)-4-bromobenzene (**4**) (600 mg, 1.67 mmol) in methanol (8 mL) and dichloromethane (8 mL) was cooled to -25° before 0.5 M guanidine in methanol (3.34 mL, 1.67 mmol) was added over 0.5 hr. During this time the reaction temperature was kept between -20 and -25°. The reaction mixture was then allowed to stir for a further 3 hrs. Acetic acid (0.2 mL) was then added to quench the reaction. The reaction mixture was taken up into dichloromethane (75 mL) and washed with 5% NH_4Cl (40 mL) and water (40 mL). The solvent was dried and removed *in vacuo* to yield an off-white solid which was recrystallised from hexane to give the title compound as a colourless powder (353 mg, 67%); mp 82.0-83.0°; Exact Mass Cald for $C_{12}H_{13}O_5Br$: 315.9947, Found: 315.9948; δ_H (300 MHz) 2.13 (6H, s, $ArCH_2OCOC\mathbf{H}_3$), 5.10 (4H, s, ArC**H**$_2$OAc), 7.41 (2H, s, Ar**H**); δ_C (75.47 MHz) 20.8 (**C**$H_3CO_2CH_2Ar$), 61.8 (Ar**C**H_2OAc), 119.9 (**Ar**Br), 125.4, 134.1, 152.9 (**Ar**OH), 172.5 (**C**=O); m/z (EI) 318 (M^+, ^{81}Br, 8%), 316 (M^+, ^{79}Br, 8%), 216 (30), 214 (32); ν_{max} (cm^{-1}) 1745, 1734, 1712,1693 (C=O).

Phenyl-2,6-bis(acetoxymethyl)-4-bromo-trifluoromethylsulphonate (14)

Method A:

2,6-Bis(acetoxymethyl)-4-bromophenol (**13**) (100 mg, 3.16×10^{-4} mol), potassium carbonate (52 mg, 3.78×10^{-4} mol) and N-phenyltriflimide (136 mg, 3.78×10^{-4} mol) in THF (6 mL) were stirred together at room temperature for 16 hrs. The reaction mixture was taken up into dichloromethane (40 mL) and washed with 5% NH_4Cl (2x25 mL) and water (25 mL). The solvent was dried and removed *in vacuo* to give a colourless oil. The crude product was purified by flash chromatography [dichloromethane, R_f 0.49] to give the title compound as colourless oil which crystallised upon addition of pentane as colourless prisms (118 mg, 84%).

Method B:

2,6-Bis(acetoxymethyl)-4-bromophenol (**13**) (100 mg, 3.16×10^{-4}mol), triethylamine (0.02 mL, 3.16×10^{-4}mol) and N-phenyltriflimide (123 mg, 3.47×10^{-4} mol) in THF (6 mL) were stirred together at room temperature for 16 hrs. The reaction mixture was taken up into dichloromethane (40 mL) and washed with 5% NH_4Cl (2x20 mL) and water (20 mL). The solvent was dried and removed *in vacuo* to give a colourless oil which was taken up into boiling pentane to give colourless prisms on cooling (76 mg, 54%); mp 59.5°; Anal. Calcd for $C_{13}H_{12}BrF_3O_7S$: C, 34.76; H, 2.69, Found: C, 34.67; H, 2.46; δ_H (300 MHz) 2.15 (6H, s, $ArCH_2OCOC\mathbf{H}_3$), 5.20 (4H, s, $ArC\mathbf{H}_2OAc$), 7.63 (2H, s, Ar**H**); δ_C (75.47 MHz) 20.6 ($\mathbf{C}H_3CO_2CH_2Ar$), 60.0 ($ArCH_2OAc$), 118.4 (q, *J* 319 Hz, $\mathbf{C}F_3SO_2Ar$), 122.6 (**Ar**Br), 132.6, 133.3, 142.3 (**Ar**OTf), 170.2 (**C**=O); m/z (FAB) 451 ($(M+H)^+$, ^{81}Br, 4%), 449 ($(M+H)^+$, ^{79}Br, 4%), 391 (18), 289 (18), 301 (20), 299 (20); ν_{max} (cm^{-1}) 1746 (C=O).

Phenyl-2,6-bis(morpholinomethyl)-4-bromo-trifluoromethylsulphonate (15)

2,6-Bis(morpholinomethyl)-4-bromophenol (**5**) (500 mg, 1.35 mmol) in dry THF (5 mL) was added dropwise *via* syringe to a suspension of NaH (50 mg, 2.08 mmol) in dry THF (10 mL) at 0° under a nitrogen atmosphere. With the addition of (**5**) complete, N-phenyltriflimide (530 mg, 1.48 mmol) in dry THF (5 mL) was added *via* syringe and the suspension refluxed for 3 hrs. The reaction mixture was quenched by dropwise addition of water before being taken up into dichloromethane (50 mL) and washed with water (50 mL). The aqueous layer was re-extracted with dichloromethane (50 mL), the

organic layers combined and dried. The solvent was removed *in vacuo* and the resulting golden oil purified by flash chromatography on silica gel [dichloromethane/ethyl acetate 4/1 (v/v), R_f 0.50] to give the title compound as a colourless oil (374 mg, 55%); Exact Mass Calcd for $C_{17}H_{22}BrF_3N_2O_5S$: 505.0444, Found: 505.0464; δ_H (300 MHz) 2.45 (4H, t, *J* 4.3 Hz), 3.58 (4H, s, ArC**H**$_2$R), 3.71 (8H, t, *J* 4.6 Hz), 7.72 (2H, s, Ar**H**); δ_C (75.47 MHz) 53.2, 56.4, 66.5, 118.3 (q, *J* 321 Hz, **C**F_3SO_2R), 122.1 (**Ar**Br), 132.6, 134.1, 144.4 (**Ar**OTf); m/z 505 ($(M+H)^+$, ^{81}Br, 65%), 503 ($(M+H)^+$ [^{79}Br] and $(M-H)^+$ [^{81}Br], 89%), 501 ($(M-H)^+$, ^{79}Br, 25%).

2-(Anilinomethyl)-4-bromo-6-(hydroxymethyl)phenyl-trifluoromethanesulphonate (16)

2,6-Bis(hydroxymethyl)-4-bromophenol (**1**) (220 mg, 0.77 mmol) in dry THF (10 mL) was added dropwise *via* syringe to a suspension of NaH (17 mg, 0.77 mmol) in dry THF (5 mL) at 0° under a nitrogen atmosphere. Upon completion of addition of (**3**) the reaction mixture was allowed to warm to room temperature and was stirred for a further hour. N-phenyltriflimide (285 mg, 0.80 mmol) was then added and the suspension refluxed for 3 hrs. The reaction mixture was quenched by dropwise addition of 'wet' ether until no further effervescence was observed. The solvent was removed in vacuo and the resulting oil purified by flash chromatography on silica gel [dichloromethane, R_f 0.22] to give the title compound as a colourless oil which slowly solidified on standing (100 mg, 57% based on N-phenyltriflimide); mp 85.0-88.0°; Exact Mass Calcd for $C_{15}H_{13}BrF_3NO_4S$: 438.9718, Found: 438.9718; δ_H (200 MHz): 4.69 (2H, s, ArC**H**$_2$R), 4.96 (2H, s, ArC**H**$_2$R), 7.01 (1H, d, *J* 2.4 Hz, Ar**H**), 7.20-7.33 (6H, m, Ar**H**); δ_C (75.47 MHz) 50.8, 63.9, 111.5, 120.5 (q, *J* 324.4 Hz, ArOSO_2**C**F_3), 123.6, 126.7, 129.1, 129.2, 129.3, 130.6, 132.6, 136.4, 153.6; m/z (EI) 441 (M^+, ^{81}Br, 49%), 439 (M^+, ^{79}Br, 60%), 424 (^{81}Br, 31%), 422 (^{79}Br, 25%), 290 (^{81}Br, 40%), 288 (^{79}Br, 41%).

2-(Acetylanilinomethyl)-4-bromo-6-(acetoxymethyl)phenyl-trifluoromethanesulphonate (17)

A solution containing the triflate (**16**) (45 mg, 1.02×10^{-4} mol) in dry pyridine (2 mL) and dry acetic anhydride (0.5 mL) was stirred at room temperature for 16 hrs. The reaction mixture was concentrated *in vacuo* and purification by flash chromatography [dichloromethane, R_f 0.50] gave the title compound as a colourless oil (50 mg, 93%); δ_H (200 MHz) 2.06 (3H, s, ROCOC**H**$_3$), 2.32 (3H, s, ROCOC**H**$_3$), 4.81 (2H, br s, ArC**H**$_2$R), 4.93 (2H, s, ArC**H**$_2$R), 7.09 (1H, d, *J* 2.4 Hz, Ar**H**), 7.13-7.20 (2H, m, Ar**H**), 7.33-7.36 (3H, m, Ar**H**), 7.48 (1H, d, *J* 2.4 Hz, Ar**H**); δ_C (75.47 MHz) 20.5 (ROCO**C**H$_3$), 20.7 (ROCO**C**H$_3$), 51.8, 60.5, 118.3, 120.5 (q, *J* 324.5 Hz, ROSO$_2$**C**F$_3$), 129.0, 129.2, 129.5, 129.6, 131.5, 133.5, 134.3, 135.9, 147.0, 168.9 (C=O), 170.2 (C=O); m/z (EI) 525 (M^+, ^{81}Br, 28%), 523 (M^+, ^{79}Br, 27%), 483 (^{81}Br, 12%), 481 (^{79}Br, 12%); ν_{max} (cm^{-1}) (film) 1766, 1747 (C=O).

Dimethyl 2-hydroxy-5-iodoisophthalate (20)

To a solution of dimethyl 2-hydroxyisophalate (1.00 g, 4.76 mmol) in methanol (50 mL) was added $NaHCO_3$ (2.00 g, 10.48 mmol) and benzyltrimethylammonium dichloroiodate (1.74 g, 5.00 mmol). The resulting suspension was stirred at room temperature for 3 hrs, and then filtered and the solvent removed. The crude product was then taken up into chloroform (150 mL), washed with sat. $Na_2S_2O_3$ (100 mL) and brine (100 mL). The solvent was dried and removed to give the title compound as an off-white solid (1.13 g, 71%). A small sample was purified for analysis by sublimation at 85°/0.03 mmHg; mp 135.0-138.0° with rapid heating; Anal. Calcd for $C_{10}H_9O_5I$: C, 35.74; H, 2.70, Found: C, 35.98; H, 2.44; δ_H (300 MHz) 3.96 (6H, s, ArCO$_2$C**H**$_3$), 8.32 (6H, s, Ar**H**); δ_C (75.47 MHz) 52.7 (ArCO$_2$**C**H$_3$), 78.9 (**Ar**I), 118.6, 114.6, 161.2, 166.8 (**C**=O); m/z (EI) 336 (M^+, 100%), 304 (62), 273 (41), 246 (66); ν_{max} (cm^{-1}) 1733, 1681 (C=O).

Dimethyl 5-iodo-2-{[(trifluoromethyl)sulphonyl]oxy}isophthalate (21)

Dimethyl 2-hydroxy-5-iodoisophthalate (**20**) (200 mg, 5.95×10^{-4} mol), triethylamine (0.10 mL, 1.39×10^{-3} mol) and N-phenyltriflimide (276 mg, 7.74×10^{-4} mol) in dry CH_3CN (5 mL) were stirred together for 16 hrs at room temperature under

nitrogen. The reaction mixture was then concentrated *in vacuo* and then purified by flash chromatography [hexane/ethyl acetate 6/1 (v/v), R_f 0.36] to give the title compound as a colourless oil which crystallised upon addition of pentane as colourless needles (278 mg, 100%); mp 96.0-98.0°; Anal. Calcd for $C_{11}H_8F_3ISO_7$: C, 28.22; H, 1.72, Found: C, 28.43; H, 1.72; δ_H (300 MHz) 3.96 (6H, s, $ArCO_2C\mathbf{H}_3$), 8.46 (2H, s, Ar**H**); δ_C (75.47 MHz) 53.2 ($ArCO_2CH_3$), 92.1 (**Ar**I), 118.5 (q, *J* 321 Hz, $\mathbf{C}F_3SO_2Ar$), 127.5, 144.7, 146.2, 162.9 (**C**=O); m/z (EI) 468 (M^+, 100%), 437 (36), 404 (14), 373 (49); ν_{max} (cm^{-1}) 1739, 1726 (C=O).

2,6-Bis(hydroxymethyl)phenol (22)

To a suspension of lithium aluminium hydride (1.50 g, 39.47 mmol) in dry THF (50 mL) under nitrogen was added a solution of dimethyl 2-hydroxyisophthalate[72,73] in dry THF (50 mL) dropwise with stirring at room temperature. After addition was complete, the suspension was reflux for 1 hr. The reaction mixture was quenched with 'wet' ether and then added to 5% HCl (100 mL), followed by extraction with ether (2x50 mL). The organic layers combined, dried and the solvent removed. Recrystallisation from chloroform gave the title compound as colourless prisms (3.28 g, 94%); Enantiotropic polymorphism was observed, mp 94.5-95.5° (lit.[75] 94.7-95.2°); δ_H (300 MHz, d_6-acetone/$CDCl_3$) 4.72 (4H, 2, $ArC\mathbf{H}_2OH$), 6.72 (1H, t, *J* 7.5 Hz, Ar**H**), 7.03 (2H, d, *J* 7.5 Hz, Ar**H**); δ_C (75.47 MHz, d_6-acetone) 62.2 ($ArCH_2OH$), 119.9, 127.3, 127.8, 154.8 (**Ar**OH); m/z (EI) 154 (M^+, 69%), 136 (91), 135 (93), 107 (100).

Dimethyl 5-(trimethylsilylethynyl)isophthalate (25)

A solution of dimethyl 5-bromoisophthalate (**23**) (0.50 g, 1.83 mmol), $Pd(PPh_3)_4$ (0.10 g, 0.09 mmol), trimethylsilylacetylene (0.39 mL, 2.74 mmol) and CuI (17 mg, 0.09 mmol) in a degassed solvent system of triethylamine (1 mL)/DMF (4 mL) was stirred at 50° for 16 hrs. An extractive workup with ether (40 mL) gave a tan solid. Purification by sublimation at 80°/0.02 mmHg yielded the title compound as a colourless solid (0.52 g, 97%); mp 102.0-104.0° (no lit. mp)[78]; δ_H (300 MHz) 0.26 (9H, s, $RSi(C\mathbf{H}_3)_3$), 3.96 (6H, s, $ArCO_2C\mathbf{H}_3$), 8.29 (2H, d, *J* 1.2 Hz, Ar**H**), 8.61 (1H, t, *J* 1.2 Hz, Ar**H**); δ_C (75.47 MHz) -0.3 ($RSi(\mathbf{C}H_3)_3$), 52.4 ($ArCO_2\mathbf{C}H_3$), 96.7 (**C**≡C), 102.7

(**C**≡C), 124.3, 130.3, 130.8, 136.9, 165.6 (**C**=O); m/z (EI) 290 (M^+, 16%), 275 (100); ν_{max} (cm^{-1}) 2158 (C≡C), 1736 (C=O).

3,5-Bis(hydroxymethyl)ethynylbenzene (26)

A suspension of lithium aluminium hydride (16 mg, $4.14x10^{-4}$ mol) in dry THF (3 mL) was cooled to 0° under nitrogen, and then dimethyl 5-(trimethylsilylethynyl)-isophthalate (**25**) (60 mg, $2.07x10^{-4}$ mol) in dry THF (3 mL) was added with stirring. The resulting suspension was allowed to warm to room temperature over 0.5 hr. The reaction mixture was quenched with 'wet' ether and then added to sat. NH_4Cl (10 mL), followed by extraction with ether (2x10 mL). The organic layers combined, dried and the solvent removed to give a tan solid. The solid was taken up into methanol (5 mL) and potassium carbonate (20 mg, $1.45x10^{-4}$ mol) added. The resulting suspension was stirred for 15 hrs at room temperature, followed by concentration *in vacuo* and purification by squat column chromatography [ethyl acetate R_f 0.56] to give the title compound as golden oil which solidified on standing (38 mg, 85%). A sample was recrystallised from benzene to give fine colourless needles; mp 74.0° (no lit. mp)[78]; δ_H (300 MHz) 3.08 (1H, s, ArC≡C**H**), 4.70 (4H, s, Ar**C**H_2OH), 7.38 (1H, s, Ar**H**), 7.43 (2H, s, Ar**H**); δ_C (50.28 MHz, $CDCl_3/CD_3CN$) 63.7 (Ar**C**H_2OH), 76.8 (**C**≡C), 83.3 (**C**≡C), 121.8, 125.5, 129.0, 141.5; m/z (EI) 162 (M^+, 82%), 144 (19), 131 (39), 115 (100); ν_{max} (cm^{-1}) 3280 (C–H of ArC≡C–H).

Dimethyl 5-ethynylisophthalate (27)

A solution of dimethyl 5-(trimethylsilylethynyl)isophthalate (**25**) (200 mg, $6.90x10^{-4}$ mol) in methanol (10 mL) was stirred with potassium carbonate (10 mg, $7.25x10^{-5}$ mol) at room temperature for 2 hrs. The suspension was filter and the solvent removed *in vacuo* to give a fawn solid. The crude product was sublimed at 120°/0.02 mmHg to give the title compound as a colourless solid (130 mg, 87%); mp 130.0-131.0° with rapid heating; Anal. Calcd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62, Found: C, 65.96; H, 4.60; δ_H (200 MHz) 3.18 (1H, s, ArC≡C**H**), 3.96 (6H, s, $ArCO_2C\mathbf{H}_3$), 8.32 (2H, d, *J* 1.8 Hz, Ar**H**), 8.65 (1H, t, *J* 1.8 Hz, Ar**H**); δ_C (50.28 MHz) 52.5 ($ArCO_2\mathbf{C}H_3$), 79.1 (**C**≡C), 81.5 (**C**≡C), 123.2, 130.7, 131.0, 137.0, 165.5 (**C**=O); m/z (EI) 218 (M^+, 63%), 187

(100), 159 (18), 144 (19); ν_{max} (cm^{-1}) 3249 (C–H of ArC≡C–H), 2104 (C≡C), 1727 (C=O).

Methyl 2-hydroxy-5-(trimethylsilylethynyl)salicylate (29)

A solution of methyl 5-iodosalicylate (4.00 g, 14.39 mmol), $Pd(PPh_3)_4$ (0.16 g, 0.14 mmol), trimethylsilylacetylene (2.54 mL, 17.99 mmol) and CuI (27 mg, 0.14 mmol) in a degassed solvent system of triethylamine (5 mL)/DMF (10 mL) was stirred at 40° for 2 hrs. An extractive workup with ether (100 mL) gave a fawn solid. Purification by squat column chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.56] yielded the title compound as a colourless oil which solidified on standing (3.30 g, 93%). A small sample was recrystallised from a methanol/water mixture as pale yellow needles; mp 70.0-71.5° (no lit. mp)[79]; δ_H (200 MHz) 0.24 (9H, s, $RSi(\mathbf{C}H_3)_3$), 3.94 (3H, s, $ArCO_2\mathbf{C}H_3$), 6.88 (1H, d, *J* 8.6 Hz, Ar**H**), 7.50 (1H, dd, *J* 2.2 and 8.6 Hz, Ar**H**), 7.94 (1H, d, *J* 2.2 Hz, Ar**H**); δ_C (50.28 MHz) -0.2 ($RSi(\mathbf{C}H_3)_3$), 52.3 ($ArCO_2\mathbf{C}H_3$), 92.8 (**C**≡C), 103.9 (**C**≡C), 112.3, 114.2, 117.8, 133.8, 138.9, 161.6 (**Ar**OH), 169.9 (**C**=O); m/z (EI) 248 (M^+, 84%), 233 (76), 216 (49), 201 (100); ν_{max} (cm^{-1}) (neat) 1681 (C=O), 2158 (C≡C).

Methyl 5-(trimethylsilylethynyl)-2-{[(trifluoromethyl)sulphonyl]oxy}benzoate (30)

The procedure was analogous to that for (**21**) using the phenol (**29**) and purification was performed using flash chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.40] to give the title compound as a colourless oil (88%); Exact Mass Calcd for $C_{14}H_{16}O_5F_3SSi$: 381.0458, Found: 381.0421; δ_H (200 MHz) 0.26 (9H, s, $RSi(\mathbf{C}H_3)_3$), 3.96 (3H, s, $ArCO_2\mathbf{C}H_3$), 7.23 (1H, d, *J* 8.6 Hz, Ar**H**), 7.66 (1H, dd, *J* 8.6 and 2.2 Hz, Ar**H**), 8.15 (1H, d, *J* 2.2 Hz, Ar**H**); δ_C (50.28 MHz) -0.4 ($RSi(\mathbf{C}H_3)_3$), 52.7 ($ArCO_2\mathbf{C}H_3$), 98.1 (**C**≡C), 101.7 (**C**≡C), 118.7 (q, *J* 321 Hz, $\mathbf{C}F_3SO_2Ar$), 122.9, 124.2, 124.6, 136.2, 137.1, 147.6, 163.6 (**C**=O); m/z (LSIMS) 381 ($(M+H)^+$, 100%), 248 (46); ν_{max} (cm^{-1}) (neat) 1738 (C=O), 2164 (C≡C).

Methyl 3-iodobenzoate (31)

A solution of 3-iodobenzoic acid (1.00 g, 4.03 mmol) in thionyl chloride (10 mL) was refluxed for 2hrs with a calcium chloride guard tube affixed to the condenser. Excess thionyl chloride was remove *in vacuo*, the residue cooled to 0°, and then dry methanol (10 mL) was added gradually with stirring. The resulting solution was refluxed for 2 hrs. This was then concentrated *in vacuo* and the residue purified by a short squat column of silica [hexane/dichloromethane 4/1 (v/v), R_f 0.30] to give the title compound as a colourless oil which solidified on standing as colourless prisms (1.11 g, quantitative). A small sample was recrystallised from pentane as colourless needles; mp 48.0-49.0° (lit.[80] 50°, 54-55°); δ_H (300 MHz) 3.86 (3H, s, $ArCO_2C\mathbf{H}_3$), 7.12 (1H, t, *J* 7.8 Hz, Ar**H**), 7.81 (1H, d, *J* 7.8 Hz, Ar**H**), 7.94 (1H, d, *J* 7.8 Hz), 8.32 (1H, s, Ar**H**); δ_C (75.47 MHz) 52.2 ($ArCO_2\mathbf{C}H_3$), 93.7 (**Ar**I), 128.6, 129.9, 131.9, 138.3, 141.6, 165.4 (**C**=O); m/z (EI) 262 (M^+, 100%), 231 (95), 203 (29); ν_{max} (cm^{-1}) 1734 (C=O).

Methyl 3-(trimethylsilylethynyl)benzoate (32)

A solution of methyl 3-iodobenzoate (**31**) (10.00 g, 38.16 mmol), $Pd(PPh_3)_4$ (0.44 g, 0.14 mmol), trimethylsilylacetylene (6.46 mL, 45.81 mmol), triethylamine (10.62 mL, 76.34 mmol) and CuI (73 mg, 0.38 mmol) in degassed DMF (20 mL) was stirred at 40° for 16 hrs. An extractive workup with ether (200 mL) gave a fawn solid. Purification by squat column chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.43] gave the title compound as a colourless solid (8.69 g, 98%). A small sample was recrystallised from a methanol/water mixture was fawn needles; mp 52.0° (no lit. mp)[81]; δ_H (200 MHz) 0.29 (9H, s, $RSi(C\mathbf{H}_3)_3$), 3.95 (3H, s, $ArCO_2C\mathbf{H}_3$), 7.41 (1H, t, *J* 7.8 Hz, Ar**H**), 7.67 (1H, dt, *J* 7.8 and 1.6 Hz, Ar**H**), 8.00 (1H, dt, *J* 7.8 and 1.6 Hz, Ar**H**), 8.18 (1H, t, *J* 1.6 Hz, Ar**H**); δ_C (50.28 MHz) -0.3 ($RSi(\mathbf{C}H_3)_3$), 52.1 ($ArCO_2\mathbf{C}H_3$), 95.3 (**C**≡C), 103.9 (**C**≡C), 123.6, 128.3, 129.4, 130.3, 133.1, 135.9, 166.3 (**C**=O); m/z (EI) 232 (M^+, 43%), 217 (100), 201 (62); ν_{max} (cm^{-1}) 2157 (C≡C), 1732 (C=O).

Methyl 3-ethynylbenzoate (33)

A solution of methyl 3-(trimethylsilylethynyl)benzoate (**32**) (500 mg, 2.15 mmol) in methanol (20 mL) was stirred with potassium carbonate (30 mg, 0.22 mmol) at room temperature for 2 hrs. The solvent was removed *in vacuo* and the resulting tan solid was sublimed at 45°/0.03 mmHg to give the title compound as a colourless solid (76mg, 76%); mp 54.0-55.0° with rapid heating (lit.[81] 48-50°); δ_H (200 MHz) 3.13 (1H, s, ArC≡C**H**), 3.93 (3H, s, $ArCO_2C\mathbf{H}_3$), 7.41 (1H, t, *J* 7.8 Hz, Ar**H**), 7.66 (1H, dt, *J* 7.8 and 1.4 Hz, Ar**H**), 8.01 (1H, dt, *J* 7.8 and 1.4 Hz, Ar**H**), 8.17 (1H, t, *J* 1.4 Hz, Ar**H**); δ_C (50.28 MHz) 52.2 ($ArCO_2C\mathbf{H}_3$), 78.1 (**C**≡C), 82.5 (**C**≡C), 122.6, 128.5, 129.8, 130.5, 133.3, 136.3, 166.3 (**C**=O); m/z (EI) 160 (M^+, 60%), 159 (21), 129 (100), 101 (63); ν_{max} (cm^{-1}) 3311 (C–H of C≡C–H), 2106 (C≡C), 1732 (C=O).

3-(Hydroxymethyl)ethynylbenzene (34)

The procedure was analogous to that (**26**) except that 1% HCl was used in place of sat. NH_4Cl. Purification was performed using flash chromatography [hexane/ethyl acetate 2/1 (v/v), R_f 0.36] to give the title compound as a colourless oil[81] (96%); δ_H (200 MHz) 3.08 (1H, s, ArC≡C**H**), 4.56 (2H, d, *J* 5 Hz, $ArC\mathbf{H}_2OH$), 7.26-7.44 (4H, m, Ar**H**); δ_C (50.28 MHz) 64.2 ($Ar\mathbf{C}H_2OH$), 77.2 (**C**≡C), 83.5 (**C**≡C), 122.1, 127.3, 128.4, 130.4, 131.1, 141.2; m/z (EI) 132 (M^+, 100%), 131 (51), 103 (99); ν_{max} (cm^{-1}) 2104 (C≡C).

2,6-Bis[(dimethylthexyl)siloxymethyl]-4-bromo-2-(dimethylthexylsiloxy)-benzene (35)

A solution containing 2,6-bis(hydroxymethyl)-4-bromophenol (**1**) (100 mg, 0.43 mmol), dimethylthexylsilylchloride (0.51 mL, 2.58 mmol), imidazole (175 mg, 2.58 mmol) in dry DMF (4 mL) was stirred at 50° for 3 hrs. The reaction mixture was added to water (20 mL) and extracted with ether (2x20 mL). The organic layers were combined and washed with water (20 mL). The solvent was dried and removed *in vacuo* to give a yellow oil. Purification by flash chromatography [hexane/dichloromethane 5/1 (v/v), R_f 0.52] gave the title compound as a colourless oil (260 mg, 92%); Exact Mass Calcd for $C_{32}H_{62}O_3BrSi_3$: 657.3189, Found: 657.3176; δ_H (200 MHz) 0.14 (12H, s, $ArCH_2OSi(C\mathbf{H}_3)_2R$), 0.17 (6H, s, $ArOSi(C\mathbf{H}_3)_2R$), 0.90-1.00 (36H, m), 1.70 (3H, m),

4.67 (4H, s, ArC**H**$_2$OR), 7.49 (2H, s, Ar**H**); δ_C (50.28 MHz) (only 13 signals observed) -3.5, -1.6, 18.5, 20.3, 25.3, 25.7, 33.9, 34.1, 60.2 (Ar**C**H$_2$OR), 114.8 (**Ar**Br), 128.8, 134.2, 147.0; m/z (EI) 660 (M^+, ^{81}Br, 11%), 658 (M^+, ^{79}Br, 10%), 575 (^{81}Br, 25%), 573 (^{79}Br, 23%), 487 (^{81}Br, 88%), 485 (^{79}Br, 79%).

2,6-Bis[(dimethylthexyl)siloxymethyl]-4-iodo-2-(dimethylthexylsiloxy)benzene (36)

The procedure was analogous to that for (**35**) using 2,6-bis(hydroxymethyl)-4-iodophenol (**2**) and purification by flash chromatography [hexane/dichloromethane 5/1 (v/v), R_f 0.48] gave the title compound as a colourless oil (93%); Anal. Calcd for $C_{32}H_{63}O_3ISi_3$: C, 54.36; H, 8.98, Found: C, 54.63; H, 9.25; δ_H (300 MHz) 0.11 (12H, s, ArCH$_2$OSi(C**H**$_3$)$_2$R), 0.16 (6H, s, ArOSi(C**H**$_3$)$_2$R), 0.89-0.99 (36H, m), 1.70 (3H, m), 4.63 (4H, s, ArC**H**$_2$OR), 7.66 (2H, s, Ar**H**); δ_C (75.47 MHz) (only 13 signals observed) -3.6, -1.5, 18.5 (br), 20.4 (br), 25.3, 25.8, 34.0, 34.2, 60.1 (Ar**C**H$_2$OR), 85.2 (**Ar**I), 134.5, 135.1, 148.0; m/z (EI) 707 (M^+, 5%), 621 (18), 533 (34).

Dimethyl 5-iodo-2-[(dimethylthexyl)siloxy]isophthalate (37)

The procedure was analogous to that for (**35**) using the phenol (**20**) and 1.5 equivalents of both TDSCl and imidazole. The reaction mixture was stirred at room temperature for 2 hrs, and purification by flash chromatography [dichloromethane, R_f 0.36] gave the title compound as a colourless oil (99%); Anal. Calcd for $C_{18}H_{27}O_5ISi$: C, 45.19; H, 5.69, Found: C, 45.49; H, 5.49; δ_H (300 MHz) 0.00 (6H, s, ArOSi(C**H**$_3$)$_2$R), 0.94 (6H, d, *J* 6.9 Hz, (C**H**$_3$)$_2$CHR), 1.02 (6H, s, (CH$_3$)$_2$CHC(C**H**$_3$)$_2$SiR), 1.73 (1H, septet, *J* 6.9 Hz, (CH$_3$)$_2$C**H**R), 3.85 (6H, s, ArCO$_2$C**H**$_3$), 8.11 (2H, s, Ar**H**); δ_C (75.47 MHz) -2.8, 18.4, 20.0, 25.2, 33.6, 52.3, 82.6 (**Ar**I), 127.8, 143.1, 153.5, 165.4 (**C**=O); m/z (FAB) 479 ($(M+H)^+$, 8%), 463 (10), 393 (100); ν_{max} (cm^{-1}) 1745, 1722 (C=O).

3,5-Bis[(*t*-butyldimethyl)siloxymethyl]bromobenzene (38)

The procedure was analogous to that for (**35**) using the 1,3-bis(hydroxymethyl)-5-bromobenzene (**24**) and 2.2 equivalents of both TBDMSCl and imidazole. The reaction mixture was stirred for at 50° for 4 hrs, and purification by flash chromatography [hexane/dichloromethane 5/1 (v/v), R_f 0.33] gave the title compound as

a colourless oil (93%); Anal. Calcd for $C_{20}H_{37}O_2BrSi_2$: C, 53.91; H, 8.37, Found: C, 54.28; H, 8.52; δ_H (300 MHz) 0.07 (12H, s, $ArCH_2OSi(CH_3)_2tBu$), 0.92 (18H, $ArCH_2OSi(CH_3)_2C(CH_3)_3$), 4.67 (4H, s, $ArCH_2OR$), 7.18 (1H, br s, Ar**H**), 7.31 (2H, br s, Ar**H**); δ_C (75.47 MHz) -5.4, 18.3, 25.8, 64.2 ($ArCH_2OR$), 122.1, 122.3, 127.5, 143.7; m/z (EI) 446 (M^+, ^{81}Br, 14%), 444 (M^+, ^{79}Br, 12%), 389 (8), 387(8).

Methyl 5-iodo-2-[(dimethylthexyl)siloxy]benzoate (39)

The procedure was analogous to that for (**35**) using the phenol (**28**) and 1.5 equivalents of both TDSCl and imidazole. The reaction mixture was stirred at room temperature for 1.5 hrs, and purification by flash chromatography [hexane/dichloromethane 3/1 (v/v), R_f 0.38] gave the title compound as a colourless oil (82%); Exact Mass Calcd for $C_{16}H_{26}IO_3Si$: 421.0699, Found: 421.0689; δ_H (300 MHz) 0.22 (6H, s, $ArOSi(CH_3)_2R$), 0.91 (6H, d, *J* 6.9 Hz, $(CH_3)_2CHR$), 0.96 (6H, s, $(CH_3)_2CHC(CH_3)_2SiR$), 1.74 (1H, septet, *J* 6.9 Hz, $(CH_3)_2CHR$), 3.85 (3H, s, $ArCO_2CH_3$), 6.62 (1H, d, *J* 8.7 Hz, Ar**H**), 7.60 (1H, dd, *J* 2.4 and 8.7 Hz, Ar**H**), 8.01 (1H, d, *J* 2.4 Hz, Ar**H**); δ_C (75.47 MHz) -2.4, 18.4, 19.9, 25.1, 33.7, 51.9, 82.5 (**Ar**I), 122.9, 125.3, 139.8, 141.4, 154.7, 165.6 (**C**=O); m/z (EI) 420 (M^+, 7%), 405 (5), 335 (100); ν_{max} (cm^{-1}) 1725 (C=O).

10-Decynyl-1,8-diethynylanthracene (41)

To a solution of 1,8-dichloro-10-decynylanthracene (**47**) (400 mg, 1.04 mmol), $Ni(acac)_2$ (27 mg, 0.10 mmol) and PPh_3 (27 mg, 0.10 mmol) in dry THF (15 mL) was added a solution of (trimethylsilylethynyl)magnesium bromide (20 mL, 0.42 M in THF). The Grignard was prepared by the addition of a solution of ethylmagnesium bromide (10 mL, 0.84 M in THF) to trimethylsilylacetylene (1.30 mL, 9.19 mmol) in dry THF (10 mL) at 0°. The Grignard was warmed to room temperature over 2 hrs with vigorous gas evolution. After addition of the Grignard to (**47**), the resulting solution was refluxed for 17 hrs. The reaction mixture was quenched by cautious addition to sat NH_4Cl (100 mL). The organic layer was separated and the aqueous layer re-extracted with ether (2x50 mL). The organic layers were combined and washed with water (100 mL). The solvent was dried and removed to give a brown solid (400 mg) which was redissolved in a 1:1 THF:MeOH (20 mL) solvent system. Potassium carbonate was added (110 mg,

0.78 mmol) and the reaction mixture was stirred for 16 hrs at room temperature. The solvent was then removed, and purification by flash chromatography [hexane/dichloromethane 8/1 (v/v), R_f 0.36] gave the title compound as a yellow solid (188 mg, 48%). A small quantity was recrystallised from methanol as small orange/yellow prisms; mp 94.0-95.5°; Anal. Calcd for $C_{28}H_{26}$: C, 92.77; H, 7.23, Found: C, 92.52; H, 7.12; δ_H (300 MHz) 0.89 (3H, t, *J* 6.6 Hz), 1.32-1.81 (12H, m), 2.75 (2H, t, *J* 7.2 Hz), 3.62 (2H, s, ArC≡C**H**), 7.51 (2H, dd, *J* 6.9 and 8.7 Hz, Anthryl**H**), 7.80 (2H, d, *J* 8.7 Hz, Anthryl**H**), 8.57 (2H, d, *J* 6.9 Hz, Anthryl**H**), 9.42 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 14.1, 20.1, 22.6, 28.9, 29.1, 29.2 (br, 2 overlapping signals), 31.8, 76.8 (**C**≡C), 81.6 (**C**≡C), 82.8 (**C**≡C), 103.3 (**C**≡C), 120.0, 120.7, 123.8, 125.7, 128.4, 131.2, 131.8, 132.3; m/z (FAB) 363 ($(M+H)^+$, 17%), 362 (M^+, 30%); ν_{max} (cm^{-1}) 3291 (C–H of ArC≡C–H), 2214 (C≡C); UV-Vis (nm) 257 (49 000), 265 (117 000), 287 (10 000), 299 (10 000), 369 (5 000), 384 (10 000), 406 (19 000), 430 (21 000); Fluorescence (nm) 380, 393, 417, 438, 462, 494.

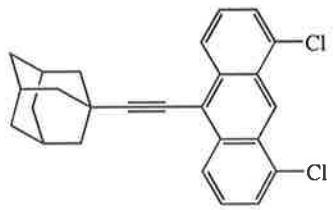
10-bromo-1,8-dichloroanthracene (46)

To a solution of 1,8-dichloroanthracene (3.45 g, 13.96 mmol) in CCl_4 (200 mL) was added a solution of bromine (3.60 mL, 69.83 mmol) in CCl_4 (15 mL) dropwise with stirring. A yellow precipitate formed during the addition of the bromine, and once addition was complete, the reaction mixture was stirred for a further 16 hrs at room temperature. The solvent and excess bromine was removed *in vacuo* and the residue recrystallised from acetic acid to give the title compound as fine golden needles (3.71 g, 82%); mp 200.0-201.5° (lit.[88] 202°); δ_H (300 MHz) 7.54 (2H, dd, *J* 7.2 and 9.0 Hz, Anthryl**H**), 7.68 (2H, d, *J* 7.2 Hz, Anthryl**H**), 8.48 (2H, d, *J* 9.0 Hz, Anthryl**H**); δ_C (75.47 MHz) 121.4, 123.5, 126.3, 127.0, 127.1, 129.6, 131.4, 132.7; δ_C (75.47 MHz, proton coupled) 121.5 (d, *J* 166.4 Hz), 125.5 (m), 126.4 (dd, *J* 166.7 and 9.1 Hz), 127.0 (dd, *J* 165.4 and 7.4 Hz), 127.1 (d, *J* 164.2 Hz), 129.6 (t, *J* 5.9 Hz), 131.4 (t, *J* 8.2 Hz), 132.6 (m); m/z (EI) 330 (M^+,$2x^{37}Cl^{81}Br$, 8%), 328 (M^+, $2x^{37}Cl^{79}Br$ and $^{35}Cl^{37}Cl^{81}Br$, 47%), 326 (M^+, $2x^{35}Cl^{81}Br$ and $^{35}Cl^{37}Cl^{79}Br$, 100%), 324 (M^+, $2x^{35}Cl^{79}Br$, 60%), 249 (3), 247 (5), 245 (8), 212 (13), 210 (50), 175 (30).

1,8-dichloro-10-decynylanthracene (47)

A solution containing 10-bromo-1,8-dichloroanthracene (**46**) (800 mg, 2.45 mmol), $Pd(PPh_3)_4$ (141 mg, 0.12 mmol), 1-decyne (0.46 mL, 2.57 mmol) and CuI (46 mg, 0.24 mmol) in a degassed solvent system of piperidine (8 mL)/acetonitrile (12 mL) was stirred at 50° for 16 hrs. An extractive workup with dichloromethane (100 mL) gave a yellow solid which was recrystallised from ethanol to give the title compound as small yellow prisms (780 mg, 82%); mp 54.0-55.0°; Anal. Calcd for $C_{24}H_{24}Cl_2$: C, 75.19; H, 6.31, Found: C, 75.23; H, 6.16; δ_H (300 MHz) 0.89 (3H, t, *J* 6.6 Hz), 1.31-1.82 (12H, m), 2.75 (2H, t, *J* 6.6 Hz), 7.47 (2H, d, *J* 7.2 and 8.7 Hz, Anthryl**H**), 7.64 (2H, dd, *J* 7.2 and 1.1 Hz, Anthryl**H**), 8.50 (2H, dt, *J* 8.7 and 1.1 Hz, Anthryl**H**), 9.24 (1H, s, Anthryl**H**); δ_C (75.47 MHz) (16 signals only) 14.0, 20.0, 22.6, 28.3, 29.1, 29.2, 31.8, 76.8 (**C**≡C), 103.6 (**C**≡C), 120.3, 120.8, 126.3, 126.4, 129.1, 132.9, 133.6; m/z (EI) 384 (M^+, ^{37}Cl, 66%), 382 (M^+, ^{35}Cl, 100); ν_{max} (cm^{-1}) 2214 (C≡C).

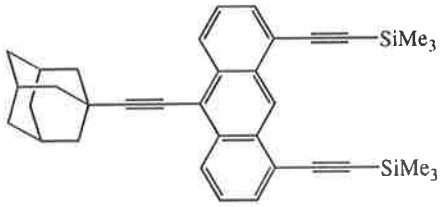
1-[2-(4,5-Dichloro-9-anthryl)-1-ethynyl]adamantane (48)



A solution containing 10-bromo-1,8-dichloroanthracene (**46**) (1.00 g, 3.07 mmol), $Pd(PPh_3)_4$ (0.35 g, 0.30 mmol), ethynyladamantane (0.59 g, 3.68 mmol) and CuI (0.05 g, 0.30 mmol) in degassed piperidine (15 mL) was stirred at 70° for 16 hrs. The reaction mixture was taken up in dichloromethane (100 mL) and washed with sat. NH_4Cl (100 mL). The aqueous layer was re-extracted with dichloromethane (100 mL), the organic layers combined and washed with water (100 mL). The solvent was dried and removed to give a brown solid. Purification by flash chromatography [hexane/dichloromethane 8/1 (v/v), R_f 0.50] gave the title compound as a yellow solid (1.17 g, 94%); mp 223.0-235.0°; Exact Mass Calcd for $C_{26}H_{22}Cl_2$: 404.1098, Found: 404.1097; δ_H (300 MHz) 1.82 (6H, br s), 2.10 (3H, br s), 2.20 (6H, br s), 7.46 (2H, dd, *J* 7.2 and 8.7 Hz, Anthryl**H**), 7.63 (2H, dd, *J* 7.2 and 0.9 Hz, Anthryl**H**), 8.46 (2H, dt, *J* 8.7 and 0.9 Hz, Anthryl**H**), 9.21 (1H,s, Anthryl**H**); δ_C (75.47 MHz) 27.9, 30.9, 36.3,

42.9, 75.6 (**C**≡C), 111.5 (C≡**C**), 120.3, 120.7, 126.3, 126.4, 127.4, 129.1, 132.9, 133.4; m/z (EI) 408 (M^+, $^{37}Cl^{37}Cl$, 13%), 406 (M^+, $^{37}Cl^{35}Cl$, 68%), 404 (M^+, $^{35}Cl^{35}Cl$, 100%); ν_{max} (cm^{-1}) 2209 (C≡C).

1-{2-[4,5-Bis(trimethylsilylethynyl)-9-anthryl]-1-ethynyl}adamantane (49)



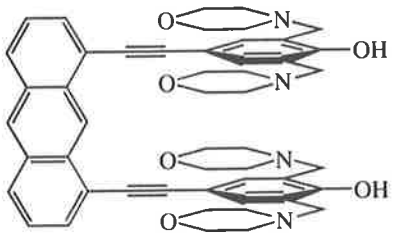
The procedure was analogous to that for (**41**) except that the intermediate solid was purified by flash chromatography [hexane/dichloromethane 8/1 (v/v), R_f 0.44] to give the title compound as a yellow solid (69%). A small quantity was recrystallised from *i*-PrOH as small yellow prisms; mp 230.0-232.0°; Anal. Calcd for $C_{36}H_{40}Si_2$: C, 81.76; H, 7.62, Found: C, 81.58; H, 7.77; δ_H (300 MHz) 0.37 (18H, s, ArC≡CSi(**CH**$_3$)$_3$), 1.81 (6H, br s), 2.09 (3H, br s), 2.19 (6H, br s), 7.48 (2H, dd, *J* 6.9 and 9 Hz, Anthryl**H**), 7.79 (2H, dd, *J* 6.9 and 0.9 Hz, Anthryl**H**), 8.53 (2H, dt, *J* 9 and 0.9 Hz, Anthryl**H**), 9.29 (1H,s); δ_C (75.47 MHz) 0.4, 28.1, 31.1, 36.4, 43.1, 75.8 (**C**≡C), 100.0 (**C**≡C), 103.6 (**C**≡C), 111.1 (**C**≡C), 119.8, 121.6, 123.8, 125.6, 128.1, 130.8, 132.1, 132.5; m/z (EI) 528 (M^+, 13%); ν_{max} (cm^{-1}) 2148 (C≡C); UV-Vis (nm) 240 (20 000), 261 (75 000), 269 (13 000), 297 (11 000), 311 (14 000), 371 (7 000), 391 (15 000), 414 (28 000), 440 (32 000); Fluorescence (nm) 382, 400, 425, 447, 473, 504.

2,6-Bis(morpholinomethyl)-4-(2-phenyl-1-ethynyl)phenol (54)

A solution of 2,6-bis(morpholinomethyl)-4-iodophenol (**7**) (1.00 g, 2.03 mmol), $Pd(PPh_3)_4$ (0.23 g, 0.20 mmol), phenyl acetylene (0.45 mL, 4.06 mmol) and CuI (38 mg, 0.20 mmol) in degassed piperidine (15 mL) was stirred at room temperature for 1 hr. An extractive workup with dichloromethane (60 mL) gave an orange/red oil. Purification by flash chromatography on silica gel [ethyl acetate, R_f 0.40] gave the title compound as a golden oil (0.83 g, 94%); Exact Mass Calcd for $C_{24}H_{28}N_2O_3$: 392.2100, Found: 392.2103; δ_H (300 MHz) 2.72 (8H, t, *J* 4.4 Hz), 3.80 (4H s, ArC**H**$_2$R), 3.92 (8H, t, *J* 4.4 Hz), 7.51 (5H, m, Ar**H**), 7.69 (2H, m, Ar**H**); δ_C (50.28 MHz) 53.1, 58.6, 66.6

($ArCH_2R$), 113.2, 122.5, 123.6, 127.7, 128.2, 131.3, 132.3, 156.6 (**Ar**OH); m/z (EI) 392 (M^+, 23%), 305 (100); ν_{max} (cm^{-1}) 2208 (C≡C).

1,8-Di{2-[3,5-bis(morpholinomethyl)-4-hydroxyphenyl]-1-ethynyl}anthracene (55)



A solution of 2,6-bis(morpholinomethyl)-4-iodophenol (**7**) (1.22 g, 2.92 mmol), $Pd(PPh_3)_4$ (0.16 g, 0.29 mmol), 1,8-diethynylanthracene (0.32 g, 1.39 mmol) and CuI (26 mg, 0.29 mmol) in degassed piperidine (15 mL) was stirred at room temperature for 1 hr. An extractive workup with dichloromethane (200 mL) gave an orange oil. Purification by flash chromatography on silica gel [acetone, R_f 0.43] yielded the title compound as a light orange oil (1.07 g, 95%); Exact Mass Calcd for $C_{50}H_{55}N_4O_6$: 807.4123, Found: 807.4246; δ_H (300 MHz) 2.46 (16H, t, *J* 4.2 Hz), 3.39 (8H, s, $ArCH_2R$), 3.71 (16H, t, *J* 4.2 Hz), 7.34 (4H, s, Ar**H**), 7.45 (2H, dd, *J* 6.9 Hz and 8.4 Hz, Anthryl**H**), 7.77 (2H, d, *J* 6.9 Hz, Anthryl**H**), 7.97 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.44 (1H, s, Anthryl**H**), 9.62 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 53.1, 58.7, 66.7 ($ArCH_2R$), 86.3 (**C**≡C), 95.2 (**C**≡C), 113.6, 121.9, 122.6, 124.2, 125.2, 127.3, 128.5, 130.0, 131.3, 131.6, 132.6, 156.7 (**Ar**OH); m/z (FAB) 807 ($(M+H)^+$, 5%), 806 (7); ν_{max} (cm^{-1}) 2192 (C≡C).

2,6-Bis(hydroxymethyl)-4-(2-phenyl-1-ethynyl)phenol (56)

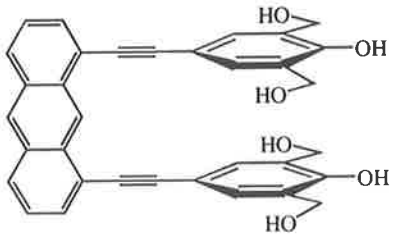
Method A:

A solution containing 2,6-bis(hydroxymethyl)-4-iodophenol (**2**) (140 mg, 4.16×10^{-4} mol), $Pd(PPh_3)_4$ (48 mg, 4.16×10^{-5} mol), phenylacetylene (0.09 mL, 8.33×10^{-4} mol) and CuI (16 mg, 8.33×10^{-4} mol) in degassed piperidine (3 mL) was stirred at room temperature for 1.5 hrs. An extractive workup with dichloromethane (40 mL) gave an orange oil. Purification by flash chromatography [dichloromethane/ethyl acetate 1/1 (v/v), R_f 0.48] gave the title compound as a colourless solid (59 mg, 46%).

Method B:

5M Sulphuric acid (2 mL) was added to a solution of 1-acetoxy-2,6-bis(acetoxymethyl)-4-(2-phenyl-1-ethynyl)benzene (**85**) (50 mg, 1.31×10^{-4} mol) in THF (7 mL). The resulting solution was refluxed for 17 hrs. The reaction mixture was concentrated by rotary evaporation, taken up into dichloromethane (30 mL) and washed with water (30 mL). The solvent was dried and removed to give a colourless oil which crystallised upon addition of chloroform. The solid was recrystallised from chloroform/hexane to give the title compound as colourless needles (13 mg, 48%); mp 125.0-126.0°; Exact Mass Calcd for $C_{16}H_{14}O_2$: 238.0994. Found: 238.0988; δ_H (300 MHz) 4.75 (4H, s, ArC**H**$_2$OH), 7.33 (5H, m, Ar**H**), 7.48 (2H, m, Ar**H**); δ_C (75.47 MHz) 61.7 (Ar**C**H$_2$OH), 88.3 (**C**≡C), 90.7 (C≡**C**), 115.4, 125.3, 128.9, 129.1, 129.6, 131.4, 132.4, 155.4 (**Ar**OH); m/z (LSIMS) 238 (M^+, 100%), 207 (14), 191 (28); ν_{max} (cm^{-1}) no significant absorption.

1,8-Di{2-[3,5-bis(hydroxymethyl)-4-hydroxyphenyl]-1-ethynyl}anthracene (57)



Pd catalysed coupling method:

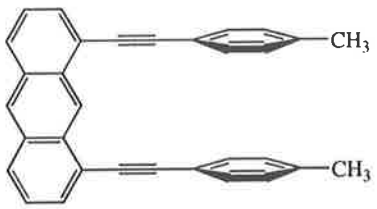
A solution containing 2,6-bis(hydroxymethyl)-4-iodophenol (**2**) (182 mg, 6.50×10^{-4} mol), $Pd(PPh_3)_4$ (36 mg, 3.10×10^{-5} mol), 1,8-diethynylanthracene (70 mg, 3.10×10^{-4} mol) and CuI (11 mg, 6.20×10^{-5} mol) in degassed piperidine (5 mL) was stirred at room temperature for 2 hrs. An extractive workup with THF (25 mL) gave a dark orange solid. Product lost on squat column of silica, solvents graded from ethyl acetate to methanol.

$LiAlH_4$ reduction method:

To a suspension of lithium aluminium hydride (2.63×10^{-4} mol) in THF (2 mL) was added the tetra-ester (**65**) in dry THF (3 mL) dropwise with stirring at room temperature. The suspension was allowed to stir for a further 3 hrs. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL), followed by extraction with ether (2x10 mL). The organic layers were combined, dried and the

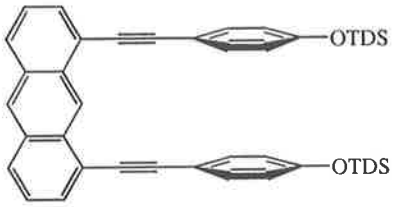
solvent removed. Purification by flash chromatography on reverse phase silica [acetonitrile/dichloromethane 2/1 (v/v), R_f 0.42] gave the title compound as a yellow film (8 mg, 47%); Exact Mass Calcd for $C_{34}H_{26}O_6$: 530.1729, Found: 530.1725; δ_H (300 MHz, $CDCl_3$/d_6-acetone) 4.62 (8H, s, Ar**C**H_2OH), 7.34 (4H, s, Ar**H**), 7.47 (2H, dd, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.74 (2H, d, *J* 6.9 Hz, Anthryl**H**), 8.00 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.48 (1H, s, Anthryl**H**), 9.55 (1H, s, Anthryl**H**); δ_C (75.47 MHz, $CDCl_3$/d_6-DMSO) 60.2 (Ar**C**H_2OH), 84.9 (**C**≡C), 94.8 (**C**≡C), 112.6, 120.8, 122.8, 124.5, 126.6, 126.7, 127.6, 129.4, 129.5, 130.3, 130.6, 154.1; m/z (LSIMS) 530 (M^+, 61%); ν_{max} (cm^{-1}) no significant absorption; UV-Vis (nm) 234 (40 000), 257 (60 000), 266 (75 000), 287 (28 000), 362 (6 000), 379 (9 000), 400 (13 000), 423 (13 000); Fluorescence (nm) 444, 462, 490.

1,8-Di[2-(4-methylphenyl)-1-ethynyl]anthracene (60)



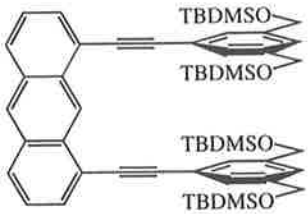
A solution containing 4-iodotoluene (43 mg, $1.95x10^{-4}$ mol), $Pd(PPh_3)_4$ (10 mg, $9.29x10^{-6}$ mol), 1,8-diethynylanthracene (21 mg, $9.29x10^{-5}$ mol) and CuI (4 mg, $1.86x10^{-5}$ mol) in a degassed solvent system of piperidine (0.5 mL)/acetonitrile (2 mL) was stirred for 0.5 hr at room temperature. An extractive workup with dichloromethane (25 mL) gave an orange solid. Purification by squat column chromatography [dichloromethane, R_f 0.38] followed by recrystallisation from ethanol gave the title compound as a fine golden needles (34 mg, 92%); mp 170.5-172.0°; Anal. Calcd for $C_{32}H_{22}O$: C, 94.55; H, 5.46, Found: C, 94.63; H, 5.41; δ_H (200 MHz) 2.38 (6H, s, Ar**C**H_3), 6.99 (4H, d, *J* 7.8 Hz, Ar**H**), 7.44-7.51 (6H, m, Ar**H**), 7.79 (2H, d, *J* 6.2 Hz, Anthryl**H**), 8.01 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.47 (1H, s, Anthryl**H**), 9.63 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 21.6, 87.0 (**C**≡C), 95.1 (**C**≡C), 120.2, 121.7, 124.2, 125.2, 127.4, 128.7, 129.1, 130.3, 131.4, 131.5, 131.7, 138.2; m/z (FAB) 407 ($(M+H)^+$, 56%), 406 (M^+, 100); ν_{max} (cm^{-1}) 2203 (C≡C); UV-Vis (nm) 257 (97 000), 264 (141 000), 285 (38 000), 308 (11 000), 323 (12 000), 355 (7 000), 375 (14 000), 395 (23 000), 418 (22 000); Fluorescence (nm) 386, 407, 429, 453, 480.

1,8-Di{2-[4-(dimethylthexyl)siloxyphenyl]-1-ethynyl}anthracene (61)



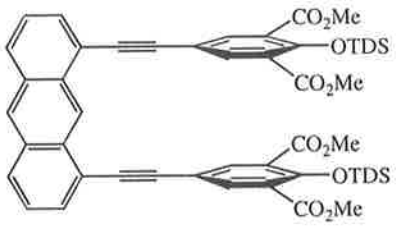
The procedure was analogous to that for (**60**) except for the use of 4-iodophenol in place of 4-iodotoluene, and the reaction mixture was stirred for 1 hr. After the extractive workup, the crude material was redissolved into dry THF (3 mL) along with dimethythexysilyl chloride (0.10 mL, 5.08×10^{-4} mol) and imidazole (40 mg, 5.88×10^{-4} mol). The resulting solution was refluxed for 4.5 hrs. The reaction mixture was cooled to room temperature, diluted with ether (10 mL) and washed with water (10 mL). The aqueous layer was re-extracted with ether (10 mL), the organic layers combined, dried and the solvent removed. Purification by flash chromatography [hexane/dichloromethane 5/1 (v/v), R_f 0.25] gave the title compound as a yellow oil which solidified on standing (16 mg, 52%); mp 124.0-128.0°; Exact Mass Calcd for $C_{46}H_{55}O_2Si_2$: 695.3742, Found: 695.3757; δ_H (300 MHz) 0.26 (6H, s, ArOSi(C**H**$_3$)$_2$R), 0.96 (6H, d, *J* 6.8 Hz, (C**H**$_3$)$_2$CHR), 0.97 (6H, s overlap with 0.96, (CH$_3$)$_2$CHC(C**H**$_3$)$_2$SiR), 1.75 (1H, septet, *J* 6.8 Hz), 6.74 (4H, AA' portion of AA'XX', Ar**H**), 7.46 (2H, dd, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.54 (4H, XX' portion of AA'XX', Ar**H**), 7.78 (2H, d, *J* 6.9 Hz, Anthryl**H**), 7.99 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.46 (1H, s, Anthryl**H**), 9.62 (1H, s, Anthryl**H**); δ_C (75.47 MHz) -2.3, 18.6, 20.1, 25.1, 34.0, 86.6 (**C**≡C), 95.0 (**C**≡C), 116.1, 120.3, 121.9, 124.2, 125.1, 127.3, 128.5, 130.2, 131.3, 131.5, 133.2, 156.0; m/z (LSIMS) 695 ($(M+H)^+$, 100%), 694 (M^+, 99); UV-Vis (nm) 258 (77 000), 266 (99 000), 287 (38 000), 314 (18 000), 357 (7 000), 377 (11 000), 397 (17 000), 420 (17 000); Fluorescence (nm) 387, 408, 432, 457, 485.

1,8-Di{2-[3,5-bis([*t*-*b*utyldimethyl]siloxymethyl)phenyl]-1-ethynyl}anthracene (63)



A solution containing 3,5-bis[(*t*-butyldimethyl)siloxymethyl]bromobenzene (**38**) (134 mg, 3.01×10^{-4} mol), $Pd(PPh_3)_4$ (31 mg, 2.65×10^{-5} mol), 1,8-diethynylanthracene (30 mg, 1.33×10^{-4} mol), triethylamine (0.10 mL, 1.38×10^{-3} mol) and CuI (2 mg, 1.05×10^{-5} mol) in degassed acetonitrile (3 mL) was stirred at 50° for 1.5 hrs. An extractive workup with ether (20 mL) gave an orange oil. Purification by flash chromatography on reverse phase silica [acetonitrile/dichloromethane 2/1 (v/v), R_f 0.20] yielded the title compound as a yellow oil (20 mg, 16%); Exact Mass Calcd for $C_{58}H_{82}O_4Si_4$: 954.5290, Found: 954.5284; δ_H (200 MHz) 0.07 (6H, s, $Si(CH_3)_2$), 0.92 (9H, s, $SiC(CH_3)_3$), 4.47 (8H, s, $ArCH_2OR$), 7.37 (6H, br s, Ar**H**), 7.48 (2H, dd, *J* 7 and 8.4 Hz, Anthryl**H**), 7.82 (2H, d, *J* 7 Hz, Anthryl**H**), 8.02 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.47 (1H, s, Anthryl**H**), 9.67 (1H, s, Anthryl**H**); δ_C (75.47 MHz) -5.6, 18.3, 25.9, 64.3 ($ArCH_2OR$), 87.3 (**C**≡C), 95.6 (**C**≡C), 121.7, 122.8, 124.0, 124.3, 125.3, 127.4, 127.9, 128.5, 130.6, 131.5, 131.6, 141.8; m/z (LSIMS) 955 ($(M+H)^+$, 100%), 954 (M^+, 98%), 897 (24), 823 (31).

1,8-Di{2-[4-(dimethylthexyl)siloxy-3,5-(methoxycarbonyl)phenyl]-1-ethynyl}-anthracene (65)



The procedure was analogous to that for (**63**) using the standard template (**40**) and aryl-iodide (**37**), and the reaction mixture was stirred at 50° for 0.5 hr. Instead of an extractive workup, the reaction mixture was filtered through a short squat column of silica, and the residue was washed with a 1:1 dichloromethane:ethyl acetate solution. The filtrate was concentrated *in vacuo* and further purification by flash chromatography on reverse phase silica [acetone/methanol (v/v), R_f 0.42] gave the title compound as a

yellow solid (60%). A small quantity was reprecipitated from *i*-PrOH as a fine yellow powder; mp 190.0-196.0°; Exact Mass Calcd for $C_{54}H_{63}O_{10}Si_2$: 927.3961, Found: 927.3886; δ_H (300 MHz) 0.00 (6H, s, $Si(CH_3)_2$), 0.96 (6H, d, *J* 6.6 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 1.03 (6H, s, $SiC(CH_3)_2$), 1.76 (1H, septet, *J* 6.6 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 3.77 (12H, s, $ArCO_2CH_3$), 7.49 (2H, dd, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.80 (2H, dd, *J* 0.9 and 6.9 Hz, Anthryl**H**), 8.03 (2H, d, *J* 8.4Hz, Anthryl**H**), 8.10 (4H, s, Ar**H**), 8.49 (1H, s, Anthryl**H**), 9.57 (1H, s, Anthryl**H**); δ_C (75.47 MHz) -2.9, 18.3, 19.9, 25.1, 33.6, 52.0, 88.4 (**C**≡C), 93.1 (**C**≡C), 116.4, 121.2, 123.9, 125.3, 126.3, 127.6, 129.1, 130.8, 131.2, 137.9, 153.8, 165.9 (**C**=O); m/z (EI) 418 (M^+, 44%), 331 (98); ν_{max} (cm^{-1}) 1735 (C=O); UV-Vis (nm) 243 (44 000), 265 (12 000), 285 (40 000), 379 (13 000), 400 (21 000), 423 (20 000); Fluorescence (nm) 389, 409, 432, 456, 486.

Dimethyl 5-(2-phenyl-1-ethynyl)isophthalate (66)

CuI Method:

A solution containing dimethyl 5-bromoisophthalate (200 mg, $7.33x10^{-4}$ mol), $Pd(PPh_3)_4$ (169 mg, $1.46x10^{-4}$ mol), Bu_4NI (540 mg, $1.47x10^{-3}$ mol), phenylacetylene (0.16 mL, $1.47x10^{-3}$ mol), DBU (0.33 mL, $2.19x10^{-3}$ mol) and CuI (41 mg, $2.19x10^{-4}$ mol) in degassed DMSO (5 mL) was stirred at 50° for 1 hr. The reaction mixture was added to water (50 mL) and extracted with dichloromethane (3x20 mL). The organic layers were combined, washed with sat. NH_4Cl (2x30 mL) and finally water (30 mL). The solvent was dried and removed to give a tan solid. Recrystallisation from hexane gave the title compound as off-white needles (144 mg, 71%).

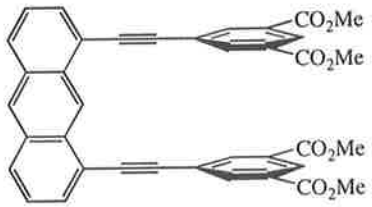
Zinc Co-catalyst Method A:

To a solution of dimethyl 5-bromoisophthalate (200 mg, $7.33x10^{-4}$ mol) in degassed DMF (3 mL) was added $Pd(PPh_3)_4$ (42 mg, $3.66x10^{-5}$ mol), phenylacetylene (0.09 mL, $8.21x10^{-4}$ mol), triethylamine (0.20 mL, $2.76x10^{-3}$ mol), undried $ZnCl_2$ (20 mg, $1.47x10^{-4}$ mol), NaI (22 mg, $1.47x10^{-4}$ mol) and imidazole (10 mg, $1.47x10^{-4}$ mol). The resulting suspension was then stirred at 60° for 16 hrs. An extractive workup with dichloromethane (40 mL) followed by squat column chromatography [dichloromethane, R_f 0.48] gave a fawn solid. Recrystallisation from hexane gave the title compound as fine colourless needles (160 mg, 75%).

Zinc Co-catalyst Method B:

To a solution of dimethyl 5-bromoisophthalate (200 mg, $7.33x10^{-4}$ mol) in degassed DMF (3 mL) was added $Pd(PPh_3)_4$ (42 mg, $3.66x10^{-5}$ mol), phenylacetylene (0.09 mL, $8.21x10^{-4}$ mol), DBU (0.20 mL, $1.34x10^{-3}$ mol), undried $ZnCl_2$ (20 mg, $1.47x10^{-4}$ mol) and NaI (22 mg, $1.47x10^{-4}$ mol). The resulting suspension was then stirred at 60° for 3 hrs. An extractive workup with dichloromethane (20 mL) gave a tan solid. Purification by flash chromatography [dichloromethane/hexane 2/1 (v/v), R_f 0.37] and then recrystallisation from hexane gave the title compound as colourless needles (150 mg, 70%); mp 115.0-116.0°; Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.80, Found: C, 73.59; H, 4.57; δ_H (300 MHz) 3.93 (6H, s, $ArCO_2CH_3$), 7.32-7.35 (3H, m, Ar**H**), 7.50-7.53 (2H, m, Ar**H**), 8.31 (2H, d, *J* 1.5 Hz, Ar**H**), 8.58 (1H, t, *J* 1.5 Hz, Ar**H**); δ_C (75.47 MHz) 52.4, 87.3 (**C**≡C), 91.2 (**C**≡C), 122.5, 124.4, 128.5, 128.9, 130.0, 130.9, 131.8, 136.5, 165.7 (**C**=O); m/z (EI) 294 (M^+, 100%), 263 (47), 235 (10), 220 (13); ν_{max} (cm^{-1}) 2214 (C≡C), 1722 (C=O).

1,8-Di{2-[3,5-di(methoxycarbonyl)phenyl]-1-ethynyl}anthracene (67)



Zinc Co-catalyst Method:

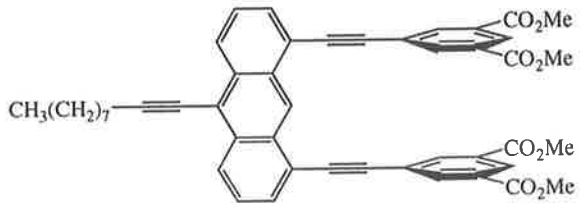
To a solution of dimethyl 5-bromoisophthalate (152 mg, $5.58x10^{-4}$ mol) in degassed DMF (3 mL) was added $Pd(PPh_3)_4$ (30 mg, $2.65x10^{-5}$ mol), 1,8-diethynylanthracene (60 mg, $2.65x10^{-4}$ mol), triethylamine (0.50 mL, $3.59x10^{-3}$ mol), undried $ZnCl_2$ (10 mg, $7.35x10^{-5}$ mol), NaI (10 mg, $6.66x10^{-5}$ mol) and imidazole (18 mg, $2.65x10^{-4}$ mol). The resulting suspension was then stirred at 60° for 24 hrs. An extractive workup with ether (40 mL) elicited only a trace amount of (**67**) by tlc.

CuI Method:

A solution containing dimethyl 5-bromoisophthalate (68 mg, $2.51x10^{-4}$ mol), $Pd(PPh_3)_4$ (14 mg, $1.21x10^{-5}$ mol), 1,8-diethynylanthracene (27 mg, $1.14x10^{-4}$ mol), DBU (0.20 mL, $1.34x10^{-3}$ mol) and CuI (5 mg, $2.63x10^{-5}$ mol) in degassed DMSO (5

mL) was stirred at 50° for 40 mins. An extractive workup with chloroform (30 mL) gave a yellow/orange solid. Purification by squat column chromatography [dichloromethane/ethyl acetate 5/1 (v/v), R_f ~0.50] yielded the title compound as a yellow solid (73 mg, 100%); mp 254.0-258.0°; Exact Mass Calcd for $C_{38}H_{26}O_8$: 610.1628, Found: 610.1583; δ_H (300 MHz) 3.83 (12H, s, $ArCO_2C\mathbf{H}_3$), 7.51 (2H, dd, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.83 (2H, d, *J* 6.9 Hz, Anthryl**H**), 8.06 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.30 (4H, d, *J* 1.8 Hz, Ar**H**), 8.49 (2H, t, *J* 1.8 Hz, Ar**H**), 8.50 (1H, s, Anthryl**H**), 9.57 (1H, s, Anthryl**H**); δ_C (75.47 MHz) (15 signals only) 52.3, 89.4 (**C**≡C), 93.1 (**C**≡C), 120.7, 123.9, 124.2, 125.2, 127.6, 129.5, 129.9, 130.8, 131.4, 131.5, 136.3, 165.1 (**C**=O); m/z (LSIMS) 611 ($(M+H)^+$, 69%), 610 (M^+, 100), 579 (39); ν_{max} (cm^{-1}) 2208 (C≡C), 1723 (C=O); UV-Vis (nm) 244 (53 000), 265 (116 000), 285 (40 000), 357 (7 000), 376 (13 000), 396 (20 000), 419 (18 000); Fluorescence (nm) 386, 407, 431, 456, 484.

1,8-Di{2-[3,5-di(methoxycarbonyl)phenyl]-1-ethynyl}-10-decynylanthracene (68)



CuI Method:

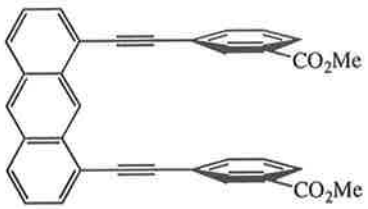
The procedure was analogous to that for (**67**) using the decyne template (**41**) and the dimethyl 5-bromoisophthalate. The reaction mixture was stirred at 50° for 3hrs and ether was used instead of chloroform in the extractive workup. Purification by squat column chromatography [dichloromethane/ethyl acetate 5/1 (v/v), R_f ~0.50] gave the title compound as a yellow solid (64%).

Zinc Co-catalyst Method:

To a solution of dimethyl 5-bromoisophthalate (83 mg, $3.04x10^{-4}$ mol) in degassed DMSO (4 mL) was added $Pd(PPh_3)_4$ (16 mg, $1.38x10^{-5}$ mol), 10-decynyl-1,8-diethynylanthracene (50 mg, $1.38x10^{-4}$ mol), DBU (0.20 mL, $1.33x10^{-3}$ mol), undried $ZnCl_2$ (4 mg, $2.94x10^{-5}$ mol) and NaI (4 mg, $2.66x10^{-5}$ mol). The resulting suspension was stirred at 50° for 16 hrs. An extractive workup with ether (30 mL) and purification

by squat column chromatography [as above] gave the title compound as a yellow solid (54 mg, 52%); mp 95.0-98.0°; Exact Mass Calcd for $C_{48}H_{42}O_8$: 746.2879, Found: 746.2879; δ_H (300 MHz) 0.90 (3H, t, *J* 6.6 Hz), 1.25-1.80 (12H, m), 2.78 (2H, t, *J* 7.5 Hz), 3.84 (12H, s, $ArCO_2C\mathbf{H}_3$), 7.58 (2H, dd, *J* 6.9 and 8.7 Hz, Anthryl**H**), 7.85 (2H, dd, *J* 0.9 and 6.9 Hz, Anthryl**H**), 8.29 (4H, d, *J* 1.8 Hz, Ar**H**), 8.48 (2H, t, *J* 1.8 Hz, Ar**H**), 8.62 (2H, dt, *J* 8.7 and 0.9 Hz, Anthryl**H**), 9.58 (1H, s, Anthryl**H**); δ_C (75.47 MHz) (only 24 signals observed) 13.9, 20.1, 22.6, 28.9, 29.1, 29.2, 31.8, 76.8 (**C**≡C), 89.4 (**C**≡C), 93.4 (**C**≡C), 103.5 (**C**≡C), 120.2, 121.2, 123.8, 124.2, 125.9, 128.5, 130.0, 130.8, 130.9, 131.0, 132.5, 136.4, 165.2 (**C**=O); m/z (FAB) 747 ($(M+H)^+$, 37), 746 (M^+, 42%), 715 (10); ν_{max} (cm^{-1}) 1730 (C=O).

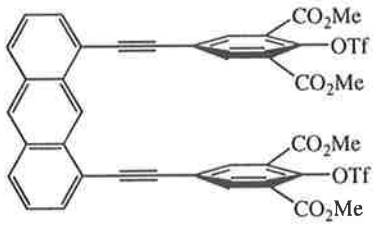
1,8-Di{2-[3-(methoxycarbonyl)phenyl]-1-ethynyl}anthracene (69)



A solution containing methyl 3-iodobenzoate (331 mg, 1.27 mmol), $Pd(PPh_3)_4$ (66 mg, 0.06 mmol), 1,8-diethynylanthracene (130 mg, 0.58 mmol) and CuI (11 mg, 0.06 mmol) in a degassed solvent system of triethylamine (2 mL)/benzene (5 mL) was stirred at 50° for 5 hrs. An extractive workup with THF (50 mL) gave an orange oil. Purification by squat column chromatography [dichloromethane, R_f 0.32] yielded the title compound as a yellow solid (281 mg, 99%). A small quantity was recrystallised from a THF/methanol mixture to give fine golden needles; mp 188.0-191.5°; Anal. Calcd for $C_{34}H_{22}O_4$: C, 82.58; H, 4.48, Found: C, 82.62; H, 4.42; δ_H (300 MHz) 3.85 (6H, s, $ArCO_2C\mathbf{H}_3$), 7.16 (2H, t, *J* 7.8 Hz, Ar**H**), 7.50 (2H, dd, *J* 7.2 and 8.7 Hz, Anthryl**H**), 7.67 (2H, dt, *J* 7.8 and 1.8 Hz, Ar**H**), 7.83 (2H, dd, *J* 7.2 and 1.2 Hz, Anthryl**H**), 7.96 (2H, dt, *J* 7.8 and 1.8 Hz, Ar**H**), 8.04 (2H, d, *J* 8.7 Hz, Anthryl**H**), 8.26 (2H, t, *J* 1.8 Hz, Ar**H**), 8.49 (1H, s, Anthryl**H**), 9.58 (1H, s, Anthryl**H**); δ_C (75.47 MHz) (only 17 signals observed) 52.1, 88.6 (**C**≡C), 93.9 (**C**≡C), 121.2, 123.8, 124.0, 125.3, 127.7, 128.5, 129.3 (br), 130.6, 130.8, 131.5, 131.6, 132.8, 135.9; m/z (EI) 494 (M^+, 100%), 463 (3); ν_{max} (cm^{-1}) 1737 (C=O); UV-Vis (nm) 265 (109 000), 283 (29 000),

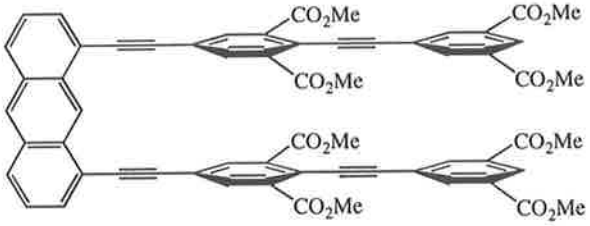
356 (4 000), 375 (9 000), 395 (16 000), 417 (16 000); Fluorescence (nm) 385, 407, 429, 453, 481.

1,8-Di{2-[3,5-di(methoxycarbonyl)-4-{[(trifluoromethyl)sulphonyl]oxy}phenyl]-1-ethynyl}anthracene (71)



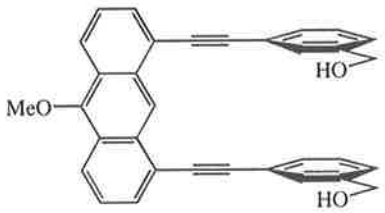
A solution containing dimethyl 5-iodo-2-{[(trifluoromethyl)sulphonyl]oxy}-isophthalate (**21**) (128 mg, 2.72×10^{-4} mol), $Pd(PPh_3)_4$ (16 mg, 1.38×10^{-5} mol), 1,8-diethynylanthracene (30 mg, 1.32×10^{-4} mol), triethylamine (0.40 mL, 2.86×10^{-3} mol) and CuI (2 mg, 1.00×10^{-5} mol) in degassed DMF (2 mL) was stirred at 50° for 9 hrs. An extractive workup with ether (40 mL) gave a yellow oil. Purification by flash chromatography on reverse phase silica [acetonitrile, R_f 0.38] yielded the title compound as a yellow solid (81 mg, 68%); mp 87.0-89.0°; Exact Mass Calcd for $C_{40}H_{24}O_{14}S_2F_6$: 906.0545, Found: 906.0539; δ_H (300 MHz) 3.90 (12H, s, $ArCO_2CH_3$), 7.53 (2H, dd, *J* 7.2 and 8.4 Hz, Anthryl**H**), 7.86 (2H, dd, *J* 7.2 and 0.9 Hz, Anthryl**H**), 8.09 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.32 (4H, s, Ar**H**), 8.52 (1H, s, Anthryl**H**), 9.42 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 53.0 ($ArCO_2CH_3$), 91.3 (**C**≡C), 91.7 (**C**≡C), 118.6 (q, *J* 324.5 Hz, $ArOSO_2CF_3$), 120.0, 123.2, 125.0, 125.2, 126.4, 128.0, 130.1, 131.1, 131.4, 131.9, 138.4, 145.3, 163.3 (**C**=O); m/z (LSIMS) 906 (M^+, 100%), 875 (19); ν_{max} (cm^{-1}) 1734 (C=O).

1,8-Di{2-[2-(4-[2-{3,5-di(methoxycarbonyl)phenyl}-1-ethynyl]-3,5-di(methoxycarbonyl)phenyl-1-ethynyl]-1-ethynyl}anthracene (72)



A solution containing the bis-triflate (**71**) (69 mg, 7.62×10^{-5} mol), $Pd(PPh_3)_4$ (18 mg, 1.56×10^{-5} mol), dimethyl 5-ethynylisophthalate (**27**) (35 mg, 1.61×10^{-4} mol), triethylamine (0.11 mL, 7.91×10^{-4} mol) and CuI (3 mg, 1.58×10^{-5} mol) in degassed DMF (3 mL) was stirred at 80° for 7 hrs. An extractive workup with dichloromethane (40 mL) gave a yellow solid. Purification by flash chromatography [dichloromethane/ethylacetate 9/1 (v/v), R_f 0.37] yielded the title compound as a yellow solid (35 mg, 44%); mp 294.0-296.0°; Exact Mass Calcd for $C_{62}H_{43}O_{16}$: 1043.2553, Found: 1043.2511; δ_H (300 MHz) 3.94 (12H, s, $ArCO_2CH_3$), 3.95 (12H, s, $ArCO_2CH_3$), 7.54 (2H, dd, *J* 7.2 and 8.7 Hz, Anthryl**H**), 7.84 (2H, d, *J* 7.2 Hz, Anthryl**H**), 8.09 (2H, d, *J* 8.7, Anthryl**H**), 8.18 (8H, m, Ar**H**), 8.44 (2H, t, *J* 1.8 Hz, Ar**H**), 8.53 (1H, s, Anthryl**H**), 9.58 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 52.4 ($ArCO_2CH_3$), 52.6 ($ArCO_2CH_3$), 87.6 (**C**≡C), 91.4 (**C**≡C), 93.3 (**C**≡C), 99.4 (**C**≡C), 120.7, 121.6, 123.0, 123.9, 124.3, 125.3, 127.7, 129.8, 130.3, 130.7, 130.8, 131.4, 131.5, 134.7, 135.8, 136.5, 165.2 (**C**=O), 165.4 (**C**=O); m/z (LSIMS) 1043 ($(M+H)^+$, 100%); ν_{max} (cm^{-1}) (CH_2Cl_2 solution) 1730 (broad C=O); UV-Vis (nm) 250 (74 000), 260 (75 000), 324 (65 000), 386 (20 000), 406 (27 000), 428 (23 000); Fluorescence (nm) 395, 445, 469.

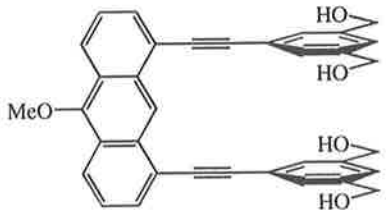
1,8-Di{2-[3-(hydroxymethyl)phenyl]-1-ethynyl}-10-methoxyanthracene (73)



A solution containing 1,8-diiodo-10-methoxyanthracene (**43**) (100 mg, 2.17×10^{-4} mol), $Pd(PPh_3)_4$ (25 mg, 2.17×10^{-5} mol), 3-(hydroxymethyl)ethynylbenzene (**34**) (60 mg, 4.56×10^{-4} mol) and CuI (4 mg, 2.17×10^{-5} mol) in a degassed solvent system of

piperidine (1 mL)/DMF (1 mL) was stirred at 40° for 2 hrs. An extractive workup with ether (20 mL) gave an orange oil. Purification by squat column chromatography [ethyl acetate/dichloromethane 2/1 (v/v), R_f 0.40] yielded the title compound as a yellow solid (102 mg, 100%). A small quantity was reprecipitated from a dichloromethane/hexane mixture to give a fluffy yellow powder; mp 91.5-93.0°; Exact Mass Calcd for $C_{33}H_{24}O_3$: 468.1725, Found: 468.1713; δ_H (200 MHz) 4.13 (3H, s, ArOC**H**$_3$), 4.33 (4H, s, ArC**H**$_2$OH), 7.17 (2H, t, *J* 8 Hz, Ar**H**), 7.25-7.49 (8H, m, Ar**H**), 7.75 (2H, dd, *J* 7.0 and 1.0 Hz, Anthryl**H**), 8.27 (2H, d, *J* 6.8 Hz, Anthryl**H**), 9.37 (1H, s, Anthryl**H**); δ_C (50.28 MHz) 63.6, 64.3, 87.8 (**C**≡C), 94.5 (**C**≡C), 119.8, 121.7, 123.0, 123.4, 124.5, 125.0, 127.0, 128.6, 130.1, 130.8, 130.9, 132.0, 141.3, 153.3; m/z (LSIMS) 468 (M^+, 100%); ν_{max} (cm^{-1}) no significant absorption; UV-Vis (nm) 268 (118 000), 284 (36 000), 307 (15 000), 327 (12 000), 366 (6 000), 386 (11 000), 407 (18 000), 431 (17 000); Fluorescence (nm) 381, 396, 420, 447, 470, 497.

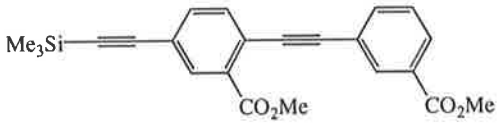
1,8-Di{2-[3,5-bis(hydroxymethyl)phenyl]-1-ethynyl}anthracene (74)



A solution containing 1,8-diiodo-10-methoxyanthracene (**43**) (100 mg, $2.17x10^{-4}$ mol), $Pd(PPh_3)_4$ (25 mg, $2.17x10^{-5}$ mol), 3,5-bis(hydroxymethyl)ethynylbenzene (**26**) (72 mg, $4.46x10^{-4}$ mol) and CuI (4 mg, $2.10x10^{-5}$ mol) in a degassed solvent system of piperidine (1 mL)/DMF (2 mL) were stirred together at 50° for 3 hrs. An extractive workup with ether (30 mL) gave a yellow solid. Purification by flash chromatography [ethylacetate/methanol 9/1 (v/v), R_f 0.49] yielded the title compound as a yellow solid (114 mg, 100%); mp 174.0-177.0°; Exact Mass Calcd for $C_{35}H_{28}O_5$: 528.1936, Found: 528.1942; δ_H (300 MHz, $CDCl_3$/d_6-DMSO) 3.94 (3H, s, ArOC**H**$_3$), 4.18 (8H, d, *J* 5.7 Hz, ArC**H**$_2$OH), 7.19 (4H, br s, Ar**H**), 7.30 (2H, dd, *J* 8.4 and 6.6 Hz, Anthryl**H**), 7.56 (2H, d, *J* 6.6 Hz, Anthryl**H**), 7.77 (2H, br s, Ar**H**), 8.08 (2H, d, *J* 8.4 Hz, Anthryl**H**), 9.15 (1H, s, Anthryl**H**); δ_C (75.47 MHz, CDCl3/d_6-DMSO) 62.6, 62.8, 86.3 (**C**≡C), 94.7 (**C**≡C), 118.6, 120.8, 121.7, 122.2, 123.5, 124.3, 124.8, 127.7, 130.1, 131.0, 141.7,

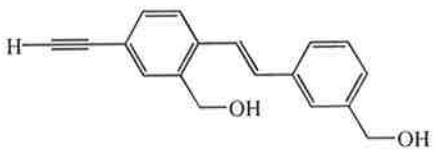
152.5; m/z (EI) 528 (M^+, 100%); ν_{max} (cm^{-1}) (film) 2203 (C≡C); UV-Vis (nm) 268 (59 000), 286 (27 000), 309 (14 000), 366 (4 000), 386 (6 000), 408 (9 000), 433 (8 000); Fluorescence (nm) 398, 422, 445, 468, 502.

Methyl 2-{2-[3-(methoxycarbonyl)phenyl]-1-ethynyl}-5-(trimethylsilylethynyl)-benzoate (75)



A solution containing triflate (**30**) (1.22 g, 3.21 mmol), $Pd(PPh_3)_4$ (185 mg, 0.16 mmol), methyl 3-ethynylbenzoate (**33**) (539 mg, 3.37 mmol) and CuI (31 mg, 0.16 mmol) in a degassed solvent system of triethylamine (4 mL)/DMF (8 mL) was stirred at 50° for 2 hrs. An extractive workup with ether (100 mL) gave a tan solid. Purification by flash chromatography [hexane/ethylacetate 5/1 (v/v), R_f 0.46] yielded the title compound as a colourless solid (1.18 g, 94%). A small sample was sublimed at 100°/0.05 mmHg to give a colourless powder; mp 106.0-107.5°; Anal. Calcd for $C_{23}H_{22}O_4Si$: C, 70.74; H, 5.68, Found: C, 70.64; H, 5.65; δ_H (300 MHz) 0.26 (9H, s, $Si(CH_3)_3$), 3.94 (3H, s, $ArCO_2CH_3$), 3.97 (3H, s, $ArCO_2CH_3$), 7.46 (1H, t, *J* 7.5 Hz, Ar**H**), 7.57 (2H, br s, Ar**H**), 7.45 (1H, dt, *J* 7.5 and 1.5 Hz, Ar**H**), 8.02 (1H, dt, *J* 7.5 and 1.5 Hz, Ar**H**), 8.09 (1H, br s, Ar**H**), 8.24 (1H, t, *J* 1.5 Hz, Ar**H**); δ_C (75.47 MHz) -0.2 ($Si(CH_3)_3$), 52.2 ($ArCO_2CH_3$), 52.3 ($ArCO_2CH_3$), 88.5 (**C**≡C), 95.0 (**C**≡C), 97.6 (**C**≡C), 103.4 (**C**≡C), 123.1, 123.3, 123.6, 128.5, 129.6, 130.6, 131.9, 132.8, 133.9,134.1, 134.6, 135.8, 165.7 (**C**=O), 166.3 (**C**=O); m/z (EI) 390 (M^+, 16%), 375 (18); ν_{max} (cm^{-1}) 2156 (C≡C), 1718 (C=O), 1704(C=O).

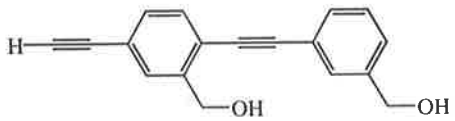
4-{(*E*)-2-[3-(hydroxymethyl)phenyl]-1-ethenyl}-3-(hydroxymethyl)ethynyl-benzene (76)



A suspension of lithium aluminium hydride (10 mg, $2.63x10^{-4}$ mol) in dry THF (3 mL) was cooled to 0° under nitrogen, and then diester (**75**) (50 mg, $1.28x10^{-4}$ mol) in

dry THF (3 mL) was added with stirring. The resulting suspension was allowed to warm to room temperature over 5 hrs. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL), followed by extraction with ether (2x10 mL). The organic layers combined, dried and the solvent removed to give a tan solid. The solid was taken up into dichloromethane (5 mL), Bu_4NF (60 mg, $1.92x10^{-4}$ mol) was added and the resulting solution stirred for 2 hrs at room temperature. The reaction mixture was concentrated *in vacuo* and purification of the residue by flash chromatography [dichloromethane/ethyl acetate 1/1 (v/v), R_f 0.39] yielded an off-white solid. Recrystallisation from a benzene/hexane mixture gave the title compound as fine off-white needles (30 mg, 91%); mp 138.0-139.0°; Exact Mass Calcd for $C_{18}H_{16}O_2$: 264.1150, Found: 264.1153; δ_H (300 MHz, CD_3CN) 3.43 (1H, s, ArC≡C**H**), 4.58 (2H, d, *J* 3.9 Hz, Ar**C**$\mathbf{H_2}$OH), 4.71 (2H, d, *J* 3.9 Hz, Ar**C**$\mathbf{H_2}$OH), 7.17 (1H, d, *J* 16.2 Hz, HC=C**H**), 7.13-7.48 (7H, m), 7.43 (1H, d, *J* 16.2 Hz), 7.68 (1H, d, *J* 8.1 Hz, Ar**H**); δ_C (50.28 MHz, $CDCl_3/CD_3CN$) 62.4, 64.6, 79.1 (**C**≡C), 84.3 (**C**≡C), 121.6, 125.4, 125.8, 126.3, 126.4, 127.3, 129.5, 131.8, 132.3, 132.4, 137.3, 138.1, 140.0, 143.4; m/z (LSIMS) 264 (M^+, 100%), 247 (78); ν_{max} (cm^{-1}) 3275 (C–H of ArC≡C–H).

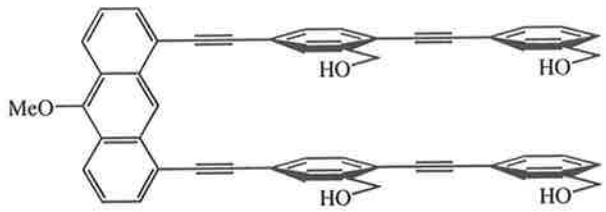
4-{2-[3-(Hydroxymethyl)phenyl]-1-ethynyl}-3-(hydroxymethyl)ethynyl-benzene (77)



A solution of diester (**75**) (19 mg, $4.87x10^{-5}$ mol) in dry THF (3 mL) was cooled to -20° and 1.5 M DIBAL-H in toluene (0.20 mL, $3.00x10^{-4}$ mol) was added with stirring. The resulting solution was allowed to warm to 0° over 0.5 hr. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL), followed by extraction with ether (2x10 mL). The organic layers combined, dried and the solvent removed to give a fawn solid. The solid was taken up into dichloromethane (3 mL) and Bu_4NF ($5.70x10^{-5}$ mol) added. The resulting solution was stirred for 15 mins at room temperature, followed by concentration *in vacuo* and purification by flash column chromatography [ethyl acetate/dichloromethane 1/1 (v/v), R_f 0.50] to give the title compound as a fawn solid (13 mg, 100%). A sample was recrystallised from a

benzene/hexane mixture to give fine pale yellow needles; mp 87.0-88.5°; Exact Mass Calcd for $C_{18}H_{14}O_2$: 262.0994, Found: 262.0998; δ_H (300 MHz) 3.20 (1H, s, ArC≡C**H**), 4.68 (2H, d, *J* 5.1 Hz, ArC**H**$_2$OH), 4.87 (2H, d, *J* 5.7 Hz, ArC**H**$_2$OH), 7.34-7.47 (5H, m, Ar**H**), 7.53 (1H, s, Ar**H**), 7.63 (1H, d, *J* 0.9 Hz, Ar**H**); δ_C (75.47 MHz) 62.0 (Ar**C**H$_2$OH), 63.5 (Ar**C**H$_2$OH), 78.5 (**C**≡C), 82.9 (**C**≡C), 85.7 (**C**≡C), 95.5 (**C**≡C), 120.9, 121.7, 122.3, 126.8, 128.1, 129.4, 129.8, 129.9, 130.1, 131.4, 141.6, 143.0; m/z (LSIMS) 262 (M^+, 100%), 245 (94); ν_{max} (cm^{-1}) 3321 (C–H of ArC≡C–H); UV-Vis (nm) 230 (8 000), 283 (27 000), 291 (30 000), 300 (38 000), 309 (31 000), 320 (35 000); Fluorescence (nm) 332.

1,8-Di{2-[2-(4-[2-{3-(hydroxymethyl)phenyl}-1-ethynyl]-3-(hydroxymethyl)phenyl)-1-ethynyl]-1-ethynyl}-10-methoxyanthracene (78)



A solution of 1,8-diiodo-10-methoxyanthracene (50 mg, $1.08x10^{-4}$ mol), $Pd(PPh_3)_4$ (13 mg, $1.13x10^{-5}$ mol), acetylene (**77**) (58 mg, $2.21x10^{-4}$ mol) and CuI (2 mg, $1.05x10^{-5}$ mol) in a degassed solvent system of piperidine (0.5 mL)/DMF (2 mL) was stirred at 40° for 1 hr. An extractive workup with a 3:1 ether:THF mixture (20 mL) gave a yellow solid. Purification by squat column chromatography [ethyl acetate, R_f 0.40] yielded the title compound as a yellow solid. The compound was not characterised but converted directly to the tetra-bromomethyl compound (**107**).

Diphenylacetylene (79)

Method 1:

To a solution of iodobenzene (0.20 mL, 1.78 mmol) in degassed piperidine (3 mL) was added $Pd(PPh_3)_4$ (105 mg, $8.93x10^{-5}$ mol) and phenylacetylene (0.20 mL, 1.82 mmol). The co-catalysts dry $ZnCl_2$ (50 mg, $3.67x10^{-4}$ mol) and a crystal of iodine were then added and the resulting suspension stirred at room temperature for 1 hr. An extractive workup with ether (40 mL) followed by recrystallisation from an ethanol/water mixture gave diphenylacetylene as colourless plates (255 mg, 80%).

Method 2:

The procedure was analogous to Method 1 except that undried zinc chloride (57 mg, $4.19x10^{-4}$ mol) was used (94%).

Method 3:

The procedure was analogous to Method 1 except that a co-catalyst combination of undried zinc chloride (57 mg, $4.19x10^{-4}$ mol) and sodium iodide (27 mg, $1.78x10^{-4}$ mol) was used (94%).

Method 4:

The procedure was analogous to Method 1 except that no palladium catalyst was added and the co-catalyst combination of undried zinc chloride (57 mg, $4.19x10^{-4}$ mol) and sodium iodide (27 mg, $1.78x10^{-4}$ mol) was used. No reaction was observed by tlc.

Method 5:

The procedure was analogous to Method 1 except that zinc iodide (57 mg, $1.78x10^{-4}$ mol) as co-catalyst was used and the reaction mixture was stirred at room temperature for 20 hrs (34%).

Method 6:

The procedure was analogous to Method 1 except that piperidine (0.53 mL, 5.34 mmol) and zinc iodide (57 mg, $1.78x10^{-4}$ mol) as co-catalyst in DMF (3 mL) were used and the reaction mixture was stirred at room temperature for 17 hrs (26%).

Method 7:

The procedure was analogous to Method 1 except that triethylamine (3 mL) was used as the solvent and base, with the co-catalyst combination of undried zinc chloride (57 mg, $4.19x10^{-4}$ mol) and sodium iodide (27 mg, $1.78x10^{-4}$ mol). The reaction mixture was stirred at room temperature for 20 mins. No reaction was observed by tlc.

Method 8:

The procedure was analogous to Method 1 except that triethylamine (3 mL) was used as the solvent and base, with the co-catalyst combination of undried zinc chloride (57 mg, $4.19x10^{-4}$ mol) and sodium iodide (27 mg, $1.78x10^{-4}$ mol). The reaction mixture was stirred at 60° for 4 hrs (34%).

Method 9:

The procedure was analogous to Method 1 except that triethylamine (3 mL) was used as the solvent and base, with the co-catalyst combination of undried zinc chloride

(57 mg, 4.19×10^{-4} mol), sodium iodide (27 mg, 1.78×10^{-4} mol) and DMAP (217 mg, 1.78 mmol). The reaction mixture was stirred at 60° for 20 hrs (44%).

Method 10:

The procedure was analogous to Method 1 except that the co-catalyst CuI (34 mg, 1.78×10^{-4} mol) was used (100%).

Method 11:

The procedure was analogous to Method 1 except that the co-catalyst combination of undried zinc chloride (57 mg, 4.19×10^{-4} mol) and sodium azide (12 mg, 1.78×10^{-4} mol) was used (100%); mp 59.0-60.0° (lit. 62.5°)[120]; δ_H (300 MHz) 7.33 (6H, m, Ar**H**), 7.54 (4H, m, Ar**H**); δ_C (75.47 MHz) 89.4 (**C**≡C), 123.4, 128.2, 128.3, 131.6; m/z (EI) 178 (M^+, 100%), 152 (7), 126 (4); ν_{max} (cm^{-1}) no significant absorption.

1-(1-Hexynyl)benzene (80)

The procedure was analogous to that for (**79**, **Method 1**) using iodobenzene and 1-hexyne, and the reaction mixture was stirred at room temperature for 2 hrs. An extractive workup with dichloromethane (40 mL) and purification by squat column chromatography [hexane/dichloromethane 3/1 (v/v), R_f 0.47] gave the title compound as a golden oil[121] (94%); δ_H (300 MHz)): 0.87 (2H, t, *J* 7.2 Hz), 1.51 (4H, m), 2.40 (2H, t, *J* 7.2 Hz), 7.26 (3H, m, Ar**H**), 7.39 (2H, m, Ar**H**); δ_C (75.47 MHz) 13.4, 19.0, 21.9, 30.8, 80.6 (**C**≡C), 90.4 (**C**≡C), 124.2, 127.4, 128.2, 131.6; m/z (EI) 158 (M^+, 41%), 143 (65), 129 (69), 115 (100); ν_{max} (cm^{-1}) 2231 (C≡C).

Trimethyl(2-phenyl-1-ethynyl)silane (81)

The procedure was analogous to that for (**79**, **Method 3**) using iodobenzene and trimethylsilylacetylene, and the reaction mixture was stirred at room temperature for 20 hrs. An extractive workup with dichloromethane (40 mL) and purification by squat column chromatography` [hexane/dichloromethane 5/1 (v/v), R_f 0.52] gave the title compound as a colourless oil[122] (100%); δ_H (300 MHz) 0.25 (9H, s), 7.30 (3H, m, Ar**H**), 7.47 (2H, m, Ar**H**); δ_C (50.28 MHz): -0.1, 93.9 (**C**≡C), 105.2 (**C**≡C), 123.2, 128.2, 128.5, 131.9; ν_{max} (cm^{-1}) (neat) 2160 (C≡C).

1,8-Diphenyl-1,7-octadiyne (82)

To a solution of iodobenzene (0.40 mL, 3.57 mmol) in degassed piperidine (3 mL) was added $Pd(PPh_3)_4$ (210 mg, $1.82x10^{-4}$ mol), 1,7-octadiyne (0.26 mL, 1.96 mmol), undried $ZnCl_2$ (100 mg, $7.12x10^{-4}$ mol) and NaI (54 mg, $3.56x10^{-4}$ mol). The resulting suspension was then stirred at room temperature for 3hrs. An extractive workup with dichloromethane (40 mL) gave a golden oil. The crude product was purified by flash chromatography [hexane/dichloromethane 3/1 (v/v), R_f 0.43] to give the title compound as a colourless oil (459mg, 100%). The spectroscopic data was consistent with published values.[123]

3-Phenyl-2-propyn-1-ol (83)

The procedure was analogous to that for (**79, Method 3**) using iodobenzene and propargyl alcohol, and the reaction mixture was stirred at room temperature for 45 mins. An extractive workup with dichloromethane (40 mL) and purification by flash chromatography [dichloromethane/ethyl acetate 10/1 (v/v), R_f 0.57] gave the title compound as a golden oil[92] (100%). δ_H (300 MHz) 4.49 (2H, br s), 7.26 (3H, m, Ar**H**), 7.43 (2H, m, Ar**H**); δ_C (75.47 MHz) 51.0, 85.3 (**C**≡C), 87.3 (**C**≡C), 122.5, 128.2, 128.3, 131.6; m/z (EI) 132 (M^+, 6%), 131 (9), 115 (4); ν_{max} (cm^{-1}) 2238 (C≡C).

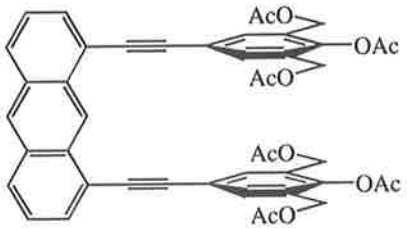
1-(1-Hexynyl)-4-methoxybenzene (84)

The procedure was analogous to that for (**79, Method 3**) using 4-bromoanisole and 1-hexyne, and the reaction mixture was stirred at 50° for 16 hrs. An extractive workup with dichloromethane (40 mL) and purification by flash chromatography [hexane/dichloromethane 5/1 (v/v), R_f 0.40] gave the title compound as a colourless oil[137] (92%). δ_H (200MHz): 0.94 (2H, t, *J* 6.8 Hz), 1.50 (4H, m), 2.39 (2H, t, *J* 6.8 Hz), 3.79 (3H, s), 6.80 (2H, AA' portion of AA'XX', Ar**H**), 7.30 (2H, XX' portion of AA'XX', Ar**H**); δ_C (75.47 MHz) 13.5, 19.0, 21.9, 30.9, 55.0, 80.2 (**C**≡C), 88.6 (**C**≡C), 113.8, 132.2, 132.8, 159.0; m/z (EI) 188 (M^+, 84%), 173 (41), 159 (29), 145 (100), 115 (27); ν_{max} (cm^{-1}) (neat) 2535 (C≡C).

1-Acetoxy-2,6-bis(acetoxymethyl)-4-(2-phenyl-1-ethynyl)benzene (85)

A solution of 2,6-bis(morpholinomethyl)-4-(ethynylphenyl)phenol (**54**) (883 mg, 2.25 mmol) in acetic anhydride (25 mL) and acetic acid (1 mL) was refluxed for 14 hrs. The reaction mixture was concentrated by rotary evaporation and the resulting oil taken up into dichloromethane (100 mL), washed with sat Na_2CO_3 (3x50 mL) and water (50 mL). The solvent was dried and removed *in vacuo* to give an off-white solid which was recrystallised from hexane to give the title compound as fine colourless needles (644 mg, 75%); mp 80.0°; Exact Mass Calcd for $C_{22}H_{20}O_6$: 380.1260, Found: 380.1260; δ_H (300 MHz): 2.07 (6H, s, $ArCH_2OCOC\mathbf{H}_3$), 2.32 (3H, s, $ArOCOC\mathbf{H}_3$), 5.02 (4H, s, $ArC\mathbf{H}_2OAc$), 7.33 (3H, m, Ar**H**), 7.50 (2H, m, Ar**H**), 7.58 (2H, s, Ar**H**); δ_C (75.47 MHz): 20.2 ($\mathbf{C}H_3COR$), 20.5 ($\mathbf{C}H_3COR$), 60.9 ($ArCH_2OAc$), 87.9 (**C**≡C), 90.2 (**C**≡C), 121.9, 123.0, 128.4, 128.6, 129.8, 131.7, 133.4, 147.5 (**Ar**OAc), 168.8 (**C**=O), 170.5 (**C**=O); m/z (EI) 380 (M^+, 16%), 338 (34), 278 (100), 236 (79); ν_{max} (cm^{-1}) 1741, 1761 (C=O).

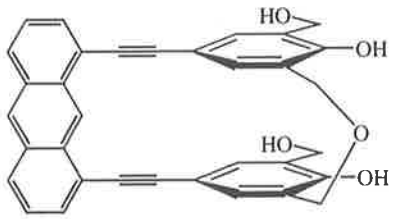
1,8-Di{2-[3,5-bis(acetoxymethyl)-4-acetoxyphenyl]-1-ethynyl}anthracene (86)



A solution of 1,8-di{2-[3,5-bis(morpholinomethyl)-4-hydroxyphenyl]-1-ethynyl}anthracene (**55**) (1.12 g, 1.39 mmol) in acetic anhydride (20 mL) and acetic acid (0.5 mL) was refluxed for 17 hrs. The reaction mixture was concentrated *in vacuo* and taken up into dichloromethane (100 mL), washed with sat. Na_2CO_3 (2x50 mL) and water (50 mL). The solvent was dried and removed to give an orange oil. Purification by flash chromatography on silica gel [dichloromethane/ethyl acetate 5/1 (v/v), R_f 0.36] gave the title compound as an orange solid (0.37 g, 34%); mp 52.5-55.0°; Exact Mass Calcd for $C_{40}H_{38}O_{12}$: 782.2363, Found: 782.2378; δ_H (300 MHz) 2.04 (12H, s, $ArCH_2OCOC\mathbf{H}_3$), 2.36 (6H, s, $ArOCOC\mathbf{H}_3$), 4.83 (8H, s, $ArC\mathbf{H}_2OAc$), 7.46 (2H, dd, *J* 7.2 Hz and 8.7 Hz, Anthryl**H**), 7.65 (4H, s), 7.80 (2H, d, *J* 7.2 Hz, Anthryl**H**), 7.98 (2H, d, *J* 8.7 Hz, Anthryl**H**), 8.41 (1H, s), 9.54 (1H, s); δ_C (75.47 MHz) 20.2 ($\mathbf{C}H_3OR$), 20.4

(**C**H$_3$OR), 60.6 (Ar**C**H$_2$OAc), 88.6 (**C**≡C), 93.6 (**C**≡C), 121.1, 121.7, 123.9, 125.2, 127.6, 129.3, 130.0, 130.8, 131.4, 131.5, 133.0, 147.4 (**Ar**OAc), 168.6(**C**=O), 170.3 (**C**=O) m/z (EI) 782 (M^+, 24%); ν_{max} (cm^{-1}) 1764, 1747, 1731 (C=O); UV-Vis (nm) 266 (109 000), 274 (37 000), 286 (48 000), 358 (7 000), 377 (12 000), 399 (19 000), 420 (18 000); Fluorescence (nm) 387, 410, 429, 454, 484.

1^2,5^2-Dihydroxy-1^3,5^3-bis(hydroxymethyl)-3-oxa-8(1,8)-anthracena-1,5(1,5)-dibenzacyclodeca-6,9-diynaphane (87)



A solution of the hexa-acetoxymethyl compound (**86**) (50 mg, $6.39x10^{-5}$ mol) in THF (3 mL) and 2M H_2SO_4 (1 mL) was refluxed for 48 hrs. The reaction mixture was diluted with ether (10 mL) and washed with water (20 mL). The aqueous layer was then extracted with ether (3x10 mL) and the organic layers combined, dried and the solvent removed. Purification by squat column chromatography [ethyl acetate, R_f 0.56] gave the title compound as a yellow solid (19 mg, 56%); mp >307.0° with decomposition; Exact Mass Calcd for $C_{34}H_{24}O_5$: 512.1624, Found: 512.1597; δ_H (600 MHz, d_6-acetone) 4.88 (4H, s), 5.07 (4H, s), 7.65 (2H, d, *J* 1.8 Hz, Ar**H**), 7.72 (2H, dd, *J* 7.2 and 8.4 Hz, Anthryl**H**), 7.93 (2H, d, *J* 1.8 Hz, Ar**H**), 8.03 (2H, d, *J* 7.2 Hz, Anthryl**H**), 8.28 (2H, d, *J* 8.4 Hz, Anthryl**H**). 8.84 (1H, s, Anthryl**H**), 9.61 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 62.6, 65.75, 86.4 (**C**≡C), 95.7 (**C**≡C), 114.4, 122.3, 123.8, 125.1, 125.9, 127.7, 128.7, 129.3, 131.2, 131.6, 131.7, 132.3, 133.1, 155.8; m/z (LSIMS) 512 (M^+, 30%), 495 (7); UV-Vis (nm) 235 (34 000), 259 (61 000), 268 (66 000), 290 (34 000), 361 (6 000), 382 (9 000), 403 (13 000), 427 (12 000); Fluorescence (nm) 446, 467, 490.

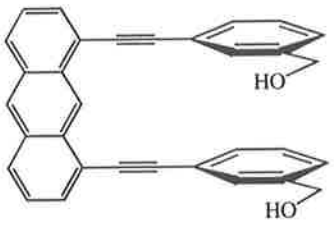
1-Acetoxy-2,6-bis(iodomethyl)-4-bromobenzene (88)

To a solution of 1-acetoxy-2,6-bis(acetoxymethyl)-4-bromobenzene (**4**) (1.00 g, 2.78 mmol) in acetonitrile (20 mL) was added trimethylsilylchloride (2.5 mL, 19.63 mmol) and NaI (2.51 g, 16.71 mmol). The resulting suspension was heated at 50° for 20 hrs. Reaction mixture was quenched by addition to sat. Na_2CO_3 (50 mL) and extracted with dichloromethane (2x50 mL). The organic layers were combined and washed with 5% $Na_2S_2O_3$ (50 mL) and finally water (50 mL). The solvent was dried and removed to give a tan solid which was recrystallised from methanol/water to give off-white needles (0.85 g, 62%); mp 190.5-192.0°; Anal. Calcd for $C_{10}H_9BrI_2O_2$: C, 24.27; H, 1.83, Found: C, 24.42; H, 1.90; δ_H (300 MHz) 2.48 (3H, s, ArOCOC**H**$_3$), 4.21 (4H, s, ArC**H**$_2$OAc), 7.46 (2H, s, Ar**H**); δ_C (75.47 MHz) -3.9 (Ar**C**H$_2$I), 20.6 (ArOCOCH$_3$), 119.4 (**Ar**Br), 133.4, 134.8, 146.2, 167.7 (**C**=O); m/z (EI) 496 (M^+, ^{81}Br, 17%), 494 (M^+, ^{79}Br, 17%), 454 (^{81}Br, 65%), 452 (^{79}Br, 65%), 369 (^{81}Br, 89%), 367 (^{79}Br, 90%), 327 (^{81}Br, 79%), 325 (^{79}Br, 81%), 199 (^{81}Br, 56%), 197 (^{79}Br, 54%); ν_{max}(cm^{-1}) 1749 (C=O).

1,3-Bis(hydroxymethyl)-5-(2-phenyl-1-ethynyl)benzene (90)

To a suspension of lithium aluminium hydride (69 mg, 2.04 mmol) in dry THF (15 mL) was added the diester (**66**) (300 mg, 1.02 mmol) in dry THF (15 mL) dropwise with stirring at room temperature. The suspension was allowed to stir for a further 1 hr. The reaction mixture was quenched with 'wet' ether and then added to 5% HCl (30 mL). The organic layer was separated, and the aqueous layer extracted with ether (2x30 mL). The organic layers combined, dried and the solvent removed to give a tan solid. Recrystallisation from a chloroform/hexane mixture gave the title compound as colourless needles (204 mg, 84%); mp 100.0-102.0°; Exact Mass Calcd for $C_{16}H_{14}O_2$: 238.0994, Found: 238.0988; δ_H (300 MHz) 4.70 (4H, s, ArC**H**$_2$OH), 7.33-7.36 (4H, m, Ar**H**), 7.45-7.46 (2H, m, Ar**H**), 7.51-7.54 (2H, m, Ar**H**); δ_C (75.47 MHz) 63.9 (Ar**C**H$_2$OH), 88.9 (**C**≡C), 89.1 (**C**≡C), 122.9, 123.0, 125.0, 128.1, 128.2, 128.5, 131.3, 141.7; m/z (EI) 238 (M^+, 100%), 207 (14); ν_{max} (cm^{-1}) no significant absorption.

1,8-Di{2-[3-(hydroxymethyl)phenyl]-1-ethynyl}anthracene (92)



A solution of the diester (**69**) (85 mg, 1.72×10^{-4} mol) in dry THF (10 mL) was added dropwise with stirring to a cooled suspension of lithium aluminium hydride (20 mg, 5.26×10^{-4} mol) in dry THF (3 mL) at 0°. The resulting suspension was allowed to warm to room temperature over 3 hrs with further stirring. The reaction mixture was quenched with 'wet' ether and then added to 1% HCl (10 mL). The organic layer was separated, and the aqueous layer re-extracted with ether (2x10 mL). The organic layers were combined, dried and the solvent removed. Purification by flash chromatography on reverse phase silica [acetonitrile/acetone 9/1 (v/v), R_f 0.41] gave the title compound as a yellow solid (50 mg, 81%); The compound was not characterised, but converted directly to the bis-bromomethyl compound (**102**).

2,6-Bis(iodomethyl)-4-bromophenol (96)

To a solution of 2,6-bis(hydroxymethyl)-4-bromophenol (**1**) (100 mg, 4.29×10^{-4} mol) in dry acetonitrile (3 mL) was added NaI (322 mg, 2.14×10^{-3} mol) and trimethylsilylchloride (0.24 mL, 1.88×10^{-3} mol). The resulting suspension was stirred at room temperature for 1.5 hrs. The reaction mixture was added to ether (20 mL), washed with water (20 mL) and the aqueous layer re-extracted with ether (20 mL). The organic layers were combined and washed with sat. $Na_2S_2O_3$ (20 mL). The organic layer was dried and the solvent removed. Purification by sublimation at 120°/0.01 mmHg gave the title compound as a fawn solid (124 mg, 64%); mp 155.5-157.0°; Exact Mass Calcd for $C_8H_7{}^{79}BrI_2O$: 451.7774, Found: 451.7745; δ_H (200 MHz) 4.36 (4H, s, Ar**C**$\mathbf{H_2}$I), 7.35 (2H, s, Ar**H**); δ_C (50.28 MHz) -0.7 (Ar**C**H_2I), 111.7, 128.8, 132.4, 151.5; m/z (EI) 454 (M^+, ^{81}Br, 32%), 452 (M^+, ^{79}Br, 32%), 200 (^{81}Br, 61%), 198 (^{79}Br, 61%).

1,3-Bis(bromomethyl)-5-(2-phenyl-1-ethynyl)benzene (99)

Method 1:

To a solution of the diol (**90**) (20 mg, 8.40×10^{-5} mol) in dry ether (4 mL) was added CBr_4 (61 mg, 1.85×10^{-4} mol) and triphenylphosphine (48 mg, 1.85×10^{-4} mol). The resulting solution was refluxed for 16 hrs. The solvent was removed *in vacuo* and the residue purified by flash chromatography [hexane/dichloromethane 8/1 (v/v), R_f 0.30] to give the title compound as a colourless oil which solidified on standing (20 mg, 65%).

Method 2:

A solution containing the diol (**90**) (30 mg, 1.26×10^{-4} mol), triphenylphosphine (150 mg, 5.73×10^{-4} mol) and CBr_4 (105 mg, 3.15×10^{-4} mol) in dry pyridine (3 mL) was heated at 60° for 1 hr. By this time only baseline material was observed by tlc.

Method 3:

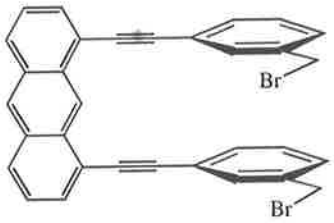
A solution containing the diol (**90**) (30 mg, 1.26×10^{-4} mol), triphenylphosphine (69 mg, 2.65×10^{-4} mol) and CBr_4 (105 mg, 3.15×10^{-4} mol) in dry acetonitrile (5 mL) was heated at 50° for 48 hrs. The solvent was removed *in vacuo*, and the residue passed through a short column of silica [dichloromethane, R_f 0.77]. Reprecipitation from hexane yielded an off-white powder containing an inseparable mixture of (**99**), (**100**) and (**101**) by tlc [hexane/dichloromethane 8/1 (v/v), R_f 0.30] (28 mg); δ_H (300 MHz) 4.46 (s), 4.52 (s), 7.34-7.38 (m), 7.48-7.52 (m); m/z (EI)) 366 (M^+, $^{81}Br^{81}Br$, 27%), 364 (M^+, $^{81}Br^{79}Br$, 54%), 362 (M^+, $^{79}Br^{79}Br$, 27%), 286 ((**100**), ^{81}Br, 22), 285 (^{81}Br, 98%), 284 ((**100**), ^{79}Br, 28), 283 (^{79}Br, 97%), 206 ((**101**), 33%).

Method 4:

A solution containing the diol (**90**) (30 mg, 1.26×10^{-4} mol) and PBr_3 (0.50 mL, 5.27×10^{-4} mol) in dry THF (2 mL) was refluxed for 16 hrs. The reaction mixture was added dropwise to sat. $NaHCO_3$ (10 mL) and the aqueous layer extracted with ether (2x10 mL). The organic layers were combined, dried and the solvent removed. Purification by flash chromatography [hexane/dichloromethane 3/1 (v/v), R_f 0.42] gave the title compound as a colourless oil which solidified on standing (8 mg, 26%). A small sample was sublimed at 100°/0.05 mmHg to give a colourless powder; mp 111.0-114.0°; Anal. Calcd for $C_{16}H_{12}Br_2$: C, 52.78; H, 3.32, Found: C, 52.75; H, 3.11; δ_H (300 MHz) 4.46 (4H, s, Ar**C**$\mathbf{H_2}$Br), 7.34-7.38 (4H, m, Ar**H**), 7.49-7.54 (4H, m, Ar**H**); δ_C (75.47 MHz) 32.0 (Ar**C**$\mathbf{H_2}$Br), 88.1 (**C**≡C), 90.4 (**C**≡C), 122.7, 124.5, 128.4, 128.6,

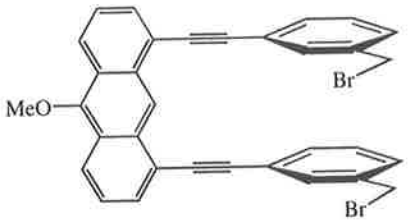
129.3, 131.6, 131.9, 138.6; m/z (EI) 366 (M^+, $^{81}Br^{81}Br$, 27%), 364 (M^+, $^{81}Br^{79}Br$, 54%), 362 (M^+, $^{79}Br^{79}Br$, 27%), 285 (^{81}Br, 98%), 283 (^{79}Br, 97%); ν_{max} (cm^{-1}) 2208 (C≡C).

1,8-Di{2-[3-(bromomethyl)phenyl]-1-ethynyl}anthracene (102)



A solution of dppe (32 mg, $7.95x10^{-5}$ mol) in dry dichloromethane (2 mL) was cooled to 0° before 0.2 M bromine in dichloromethane (0.80 mL, $1.59x10^{-4}$ mol) was added over 10 mins with stirring. The diol (**92**) (29 mg, $6.62x10^{-5}$ mol) in dry dichloromethane (3 mL) was then added and the reaction mixture allowed to warm to room temperature over 45 mins. The reaction mixture was then diluted with dichloromethane (20 mL) and washed with sat. $Na_2S_2O_3$ (20 mL). The aqueous layer was re-extracted with dichloromethane (20 mL), the organic layers combined, dried and the solvent removed. Purification by flash chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.48] gave the title compound as a yellow solid (29 mg, 78%); mp 129.0-131.5°; Exact Mass Calcd for $C_{32}H_{20}{}^{79}Br_2$: 561.9933, Found: 561.9910; δ_H (300 MHz) 4.31 (4H, s, ArC**H**$_2$Br), 7.12 (2H, t, *J* 7.5 Hz, Ar**H**), 7.36 (2H, dd, *J* 1.8 and 7.5 Hz, Ar**H**), 7.49 (2H, dd, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.60 (2H, t, *J* 1.8 Hz, Ar**H**), 7.82 (2H, dd, *J* 1.2 and 6.9 Hz, Anthryl**H**), 8.04 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.49 (1H, s, Anthryl**H**), 9.58 (1H, s, Anthryl**H**); δ_C (50.28 MHz) 32.6 (Ar**C**H$_2$Br), 88.3 (**C**≡C), 94.2 (**C**≡C), 121.3, 123.9, 124.0, 125.3, 127.6, 129.0, 129.1, 129.2, 130.8, 131.5, 131.6, 131.8, 132.0, 138.2; m/z (EI) 566 (M^+, $^{81}Br^{81}Br$, 61%), 564 (M^+, $^{81}Br^{79}Br$, 100%), 562 (M^+, $^{79}Br^{79}Br$, 48%), 404 (27); UV-Vis (nm) 235 (43 000), 264 (127 000), 285 (38 000), 322 (11 000), 356 (8 000), 375 (13 000), 395 (20 000), 418 (19 000); Fluorescence (nm) 386, 406, 432, 451, 477.

1,8-Di{2-[3-(bromomethyl)phenyl]-1-ethynyl}-10-methoxyanthracene (103)



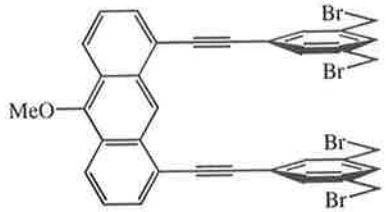
Method 1:

The procedure was analogous to that for (**102**) using the diol (**73**) and dry chloroform was used in place of dichloromethane. Purification by flash chromatography [hexane/dichloromethane 1/1 (v/v), R_f 0.47] gave the title compound as a yellow solid (198 mg, 77%).

Method 2:

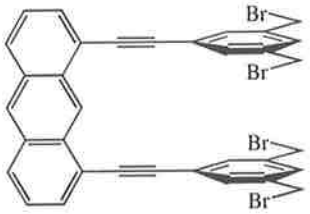
A solution of the diol (**73**) (50 mg, 1.07×10^{-4} mol) in dry THF (5 mL) was cooled to -20° before triphenylphosphine (59 mg, 2.14×10^{-4} mol) and NBS (40 mg, 2.24×10^{-4} mol) were added. The reaction mixture was then allowed to warm to room temperature over 2 hrs with stirring. The reaction was quenched by addition to sat. $NaHCO_3$ (20 mL), followed by extraction with ether (2x20 mL). The organic layers were combined, dried and the solvent removed. Purification by flash chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.30] gave the title compound as a yellow solid (35 mg, 56%); mp 135.0-137.0°; Exact Mass Calcd for $C_{33}H_{22}O^{79}Br_2$: 592.0038, Found: 592.0016; δ_H (200 MHz) 4.18 (3H, s, ArOC**H**$_3$), 4.31 (4H, s, ArC**H**$_2$Br), 7.14 (2H, t, *J* 7.6 Hz, Ar**H**), 7.34-7.38 (2H, m, Ar**H**), 7.45-7.59 (4H, m, Ar**H**), 7.81 (2H, dd, *J* 1 and 6.8 Hz, Anthryl**H**), 8.34 (2H, dt, *J* 1 and 7.8 Hz, Anthryl**H**), 9.40 (1H, s, Anthryl**H**); δ_C (50.28 MHz) 32.6, 63.7, 88.3 (**C**≡C), 94.4 (**C**≡C), 119.8, 121.6, 123.4, 123.9, 124.6, 125.1, 129.0, 129.1, 130.9, 131.8, 132.0, 132.1, 138.2, 153.5; m/z (LSIMS) 596 (M^+, $^{81}Br^{81}Br$, 58%), 594 (M^+, $^{81}Br^{79}Br$, 100%), 592 (M^+, $^{79}Br^{79}Br$, 44%); UV-Vis (nm) 268 (141 000), 287 (32 000), 312 (12 000), 327 (12 000), 366 (7 000), 386 (14 000), 408 (22 000), 432 (21 000); Fluorescence (nm) 381, 396, 420, 447, 470, 497.

1,8-Di{2-[3,5-bis(bromomethyl)phenyl]-1-ethynyl}-10-methoxyanthracene (104)



The procedure was analogous to that for (**103**, **Method 2**) using the tetrakis-hydroxymethyl compound (**74**), and allowing the reaction mixture to warm to room temperature over 1.5 hrs. Purification by flash chromatography [hexane/dichloromethane 3/2 (v/v), R_f 0.38] gave the title compound as a yellow solid (64%); mp 182.5-186.5°; Exact Mass Calcd for $C_{35}H_{24}O^{79}Br_4$: 775.8563, Found: 775.8587; δ_H (300 MHz) 4.18 (3H, s, ArOC**H**$_3$), 4.21 (8H, s, ArC**H**$_2$Br), 7.38 (2H, t, *J* 1.5 Hz, Ar**H**), 7.48 (4H, d, *J* 1.5 Hz, Ar**H**), 7.52 (2H, dd overlap with 7.48, *J* 6.9 and 8.7 Hz, Anthryl**H**), 7.82 (2H, d, *J* 6.9 Hz, Anthryl**H**), 8.35 (2H, d, *J* 8.7 Hz, Anthryl**H**), 9.37 (1H, s, Anthryl**H**); δ_C (50.28 MHz) 32.0, 63.7, 88.9 (**C**≡C), 93.8 (**C**≡C), 119.6, 121.3, 123.5, 124.4, 124.5, 125.0, 129.7, 131.0, 131.9, 132.0, 138.9, 153.5; m/z (LSIMS) 780 (within M^+ and $(M+H)^+$ cluster) (M^+, 100%); UV-Vis (nm) 238 (55 000), 268 (122 000), 290 (32 000), 313 (11 000), 328 (10 000), 367 (6 000), 388 (12 000), 409 (20 000), 433 (18 000); Fluorescence (nm) 381, 396, 422, 450, 471, 505.

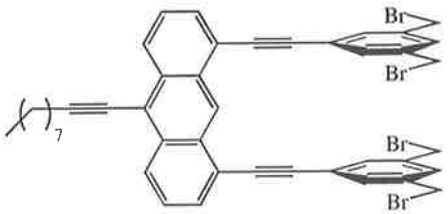
1,8-Di{2-[3,5-bis(bromomethyl)phenyl]-1-ethynyl}anthracene (105)



To a suspension of lithium aluminium hydride (18 mg, 4.79×10^{-4} mol) in dry THF (3 mL) was added the tetra-ester (**67**) (73 mg, 1.19×10^{-4} mol) in THF (6 mL). The resulting suspension was stirred at room temperature for 3 hrs. The reaction mixture was then quenched with 'wet' ether and then added to 1% HCl (10 mL). The organic layer was separated and the aqueous layer was extracted with ether (2x20 mL). The organic layers were combined, dried and the solvent removed. The crude material was not purified but used immediately in the following step.

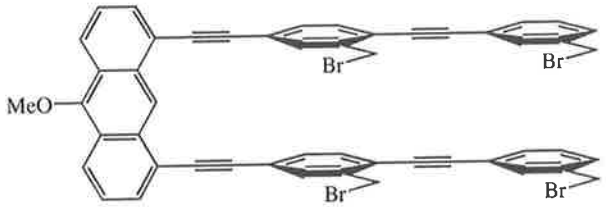
A solution of dppe (114 mg, 2.86×10^{-4} mol) in dry chloroform (10 mL) was cooled to 0° before 0.2 M bromine in chloroform (2.90 mL, 5.80×10^{-4} mol) was added over 10 mins with stirring. The reduced material from the first step dissolved in a dry solvent system of 1:1 THF:chloroform (6 mL) was then added and the reaction mixture allowed to warm to room temperature over 1 hr. The reaction mixture was then diluted with chloroform (20 mL) and washed with sat. $Na_2S_2O_3$ (20 mL). The aqueous layer was re-extracted with chloroform (20 mL), the organic layers combined, dried and the solvent removed. Purification by squat column chromatography [hexane/dichloromethane 2/1 (v/v), R_f 0.49] gave a yellow solid which contained the title compound (10 mg, ~11%); mp 200.0-208.0°; δ_H (300 MHz, $CDCl_3/d_6$-DMSO) 4.14 (8 H, s, ArC**H**$_2$Br), 7.32 (2H, t, *J* 1.5 Hz, Ar**H**), 7.43 (4H, d, *J* 1.5 Hz, Ar**H**), 7.44 (2H, dd overlap with 7.43, *J* 6.9 and 8.4 Hz, Anthryl**H**), 7.76 (2H, dd, *J* 0.9 and 6.9 Hz, Anthryl**H**), 8.00 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.45 (1H, s, Anthryl**H**), 9.48 (1H, s, Anthryl**H**); m/z (no molecular ion could be produced using EI or LSIMS); ν_{max} (cm^{-1}) no significant absorption.

1,8-Di{2-[3,5-bis(bromomethyl)phenyl]-1-ethynyl}-10-decynylanthracene (106)



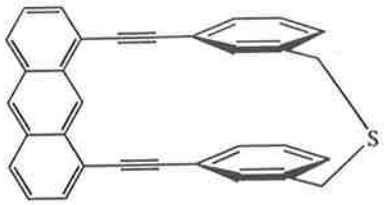
The procedure was analogous to that for (**105**) using the tetra-ester (**68**), and the reaction mixture was allowed to stir for only 25 mins in the second step (~31%). Purification by flash chromatography on either normal silica or reverse phase silica could not separate the title compound from close-running impurities. Consequently, multiple signals for the benzylic protons where observed in the proton NMR spectrum; Exact Mass Calcd for $C_{44}H_{38}{}^{79}Br_2{}^{81}Br_2$: 885.9670, Found: 885.9705; m/z (LSIMS) 886 (within M^+ and $(M+H)^+$ cluster) (M^+, 100%).

1,8-Di{2-[2-(4-[2-{3-(bromomethyl)phenyl}-1-ethynyl]-3-(bromomethyl)phenyl)-1-ethynyl]-1-ethynyl}-10-methoxyanthracene (107)



A solution of dppe (130 mg, 3.26×10^{-4} mol) in dry THF (10 mL) was cooled to 0° before 0.2 M bromine in chloroform (2.72 mL, 5.43×10^{-4} mol) was added over 10 mins with stirring. The crude tetra-hydroxymethyl compound (**78**) dissolved in dry THF (6 mL) was then added and the reaction mixture allowed to warm to room temperature over 1 hr. The reaction mixture was then diluted with chloroform (20 mL) and washed with sat. $Na_2S_2O_3$ (20 mL). The aqueous layer was re-extracted with chloroform (20 mL), the organic layers combined, dried and the solvent removed. Purification by flash chromatography [hexane/dichloromethane 1/1 (v/v), R_f 0.45] gave the title compound as a yellow solid (93 mg, 89% 2 steps); mp 180.0-183.0°; Exact Mass Calcd for $C_{51}H_{32}O^{79}Br_4$: 975.9189, Found: 975.9147; δ_H (300 MHz) 4.19 (3H, s, ArOC**H**$_3$), 4.37 (4H, s, ArC**H**$_2$Br), 4.55 (4H, s, ArC**H**$_2$Br), 7.18 (2H, t, *J* 8.1 Hz, Ar**H**), 7.31-7.56 (10H, m, Ar**H**), 7.64 (2H, d, *J* 1.5 Hz, Ar**H**), 7.82 (2H, dd, *J* 0.9 and 6.9 Hz, Anthryl**H**), 8.35 (2H, d, *J* 9 Hz, Anthryl**H**), 9.37 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 31.2, 32.6, 63.8, 86.7 (**C**≡C), 90.1 (**C**≡C), 94.3 (**C**≡C), 96.5 (**C**≡C), 119.7, 121.3, 123.0, 123.3, 123.6, 123.7, 124.5, 125.0, 128.9, 129.4, 120.9, 131.5, 131.6, 131.9, 132.1, 132.6, 132.7, 138.1, 139.6, 153.5; m/z (LSIMS) 980 (within M^+ isotope cluster) (M^+, 100%); UV-Vis (nm) 245 (60 000), 267 (96 000), 319 (71 000), 391 (19 000), 414 (27 000), 438 (25 000); Fluorescence (nm) 397, 430, 457, 480.

6-Thia-1(1,8)-anthacena-4,8(1,3)-dibenzacyclodeca-2,9-diynaphane (109)



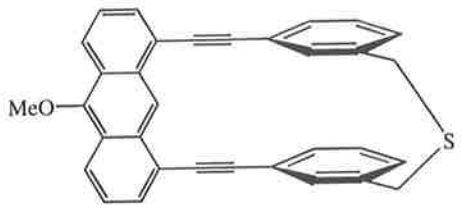
Method 1:

To a solution of the bis-bromomethyl compound (**102**) (10 mg, $1.77x10^{-5}$ mol) in DMF (5 mL) was sodium sulphide nonahydrate (20 mg, $8.33x10^{-5}$ mol) in water (0.5 mL). The resulting solution was stirred at room temperature for 3 hrs. The reaction mixture was added to water (20 mL), and extracted with ether (2x20 mL). The organic layers were combined, dried and the solvent removed. Purification by gravity column chromatography on reverse phase silica [acetonitrile/dichloromethane 5/1(v/v), R_f 0.29] gave the title compound as a yellow solid (2 mg, 26%).

Method 2:

To a solution of the bis-bromomethyl compound (**102**) (10 mg, $1.77x10^{-5}$ mol) in a solvent mixture of dichloromethane (5 mL) and ethanol (1 mL), was added $Na_2S.Al_2O_3$ (30 mg, $7.50x10^{-5}$ mol) and the resulting suspension stirred at room temperature for 3 hrs. The reaction mixture was filtered and the solvent removed *in vacuo*. Purification by gravity column chromatography on reverse phase silica [acetonitrile/dichloromethane 4/1 (v/v), R_f 0.44] gave the title compound as a yellow solid (4 mg, 50%); mp 230.0-233.0°; Exact Mass Calcd for $C_{32}H_{20}S$: 436.1303, Found: 436.1299; δ_H (300 MHz) 3.45 (4H, s, Ar**C**$\mathbf{H_2}$S**C**$\mathbf{H_2}$Ar), 7.44-7.62 (8H, m, Ar**H**), 7.86 (2H, dd, *J* 1.8 and 6.9 Hz, Anthryl**H**), 8.03 (2H, d, *J* 8.4 Hz, Anthryl**H**), 8.49 (1H, s, Anthryl**H**), 9.59 (1H, s, Anthryl**H**); δ_C (75.47 MHz) (only 16 signals observed) 33.1, 87.8 (**C**≡C), 94.6 (**C**≡C), 121.4, 122.9, 123.9, 125.2, 127.7, 129.1, 129.4, 129.5, 130.7, 131.3, 131.6, 132.6, 138.7; m/z (EI) 436 (M^+, 100%); ν_{max} (cm^{-1}) no significant absorption; UV-Vis (nm) 235 (24 000), 266 (80 000), 287 (35 000), 313 (10 000), 339 (6 000), 360 (5 000), 378 (9 000), 399 (15 000), 422 (14 000); Fluorescence (nm) 289, 410, 430, 456, 484.

1^{10}-Methoxy-6-thia-1(1,8)-anthacena-4,8(1,3)-dibenzacyclodeca-2,9-diynaphane (110)



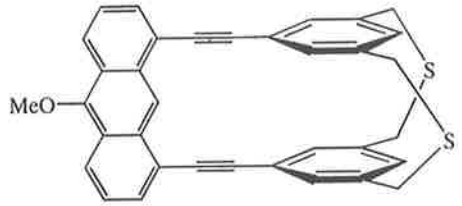
Method 1:

To a suspension of $Na_2S.Al_2O_3$ (60 mg, $1.52x10^{-4}$ mol) in ethanol (3 mL) was added the bis-bromomethyl compound (**103**) (30 mg, $5.05x10^{-5}$ mol) in dichloromethane (5 mL) *via* a syringe pump over 2.5 hrs. After addition was complete, the reaction mixture was allowed to stir for 0.5 hr before an extra quantity of $Na_2S.Al_2O_3$ (30 mg, $7.60x10^{-5}$ mol) was added and the suspension stirred for a further 1 hr. The reaction mixture was filtered and the solvent removed *in vacuo*. Purification by flash chromatography on silica [hexane/ethyl acetate 10/1 (v/v), R_f 0.39] gave the title compound as a yellow solid (24 mg, 100%).

Method 2:

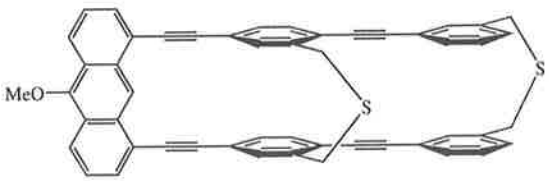
The procedure was analogous to that for (**109**, **Method 2**) using the bis-bromomethyl compound (**103**), and the reaction mixture was stirred at room temperature for 1 hr. Purification by flash chromatography on alumina [hexane/ethyl acetate 20/1 (v/v), R_f 0.50] gave the title compound as a yellow solid (85%). A small sample was recrystallised from an ethyl acetate/hexane mixture as small orange prisms; mp 236.0-238.5°; Exact Mass Calcd for $C_{33}H_{22}OS$: 466.1391, Found: 466.1386; δ_H (300 MHz) 3.43 (4H, s, $ArC\mathbf{H}_2SC\mathbf{H}_2Ar$), 4.16 (3H, s, $ArOC\mathbf{H}_3$), 7.42-7.59 (10H, m, Ar**H**), 7.84 (2H, d, *J* 6.9 Hz, Anthryl**H**), 8.31 (2H, d, *J* 8.7 Hz, Anthryl**H**), 9.39 (1H, s, Anthryl**H**); δ_C (75.47 MHz) 32.9, 63.6, 87.9 (**C**≡C), 94.8 (**C**≡C), 119.7, 121.8, 122.9, 123.2, 124.6, 125.0, 129.4, 129.5, 130.8, 131.5, 131.9, 132.7, 138.7, 153.5; m/z (EI) 466 (M^+, 98%), 451 (100); ν_{max} (cm^{-1}) no significant absorption; UV-Vis (nm) 269 (11 000), 289 (40 000), 343 (7 000), 369 (7 000), 390 (13 000), 411 (21 000), 436 (21 000); Fluorescence (nm) 380, 398, 423, 449, 473, 503.

4(1,8)-Anthracena-1,7(1,3,5)-dibenza-9,12-dithiabicyclo[5.3.3]trideca-2,5-diynaphane (111)



The procedure was analogous to that for (**109**, **Method 2**) using the bis-bromomethyl compound (**104**), and purification by flash chromatography on silica [chloroform/hexane 3/5 (v/v), R_f 0.48] gave the title compound as a yellow solid (trace <1 mg); Exact Mass Calcd for $C_{35}H_{24}OS_2$: 524.1269, Found: 524.1263; δ_H (300 MHz, $CDCl_3$/d_6-DMSO) 3.83 (4H, A portion of AB, *J* 15 Hz, $ArCH_AH_BSR$), 3.87 (4H, B portion of AB, *J* 15.0 Hz, $ArCH_AH_BSR$), 4.18 (3H, s, $ArOCH_3$), 7.10 (2H, br s, Ar**H**), 7.35 (4H, br s, Ar**H**), 7.50 (2H, dd, *J* 6.9 and 9.0 Hz, Anthryl**H**), 7.66 (2H, d, *J* 6.9 Hz, Anthryl**H**), 8.31 (2H, d, *J* 9.0 Hz, Anthryl**H**), 9.29 (1H, s, Anthryl**H**); m/z (EI) 524 (M^+, 100%).

14[10]-Methoxy-14(1,8)anthracena-1,11(1,2,4),4,8(1,3)-tetrabenza-6,18-dithiabicyclo[9.5.3]nonadeca-2,9,12,15-tetraynaphane (113)



Method A:

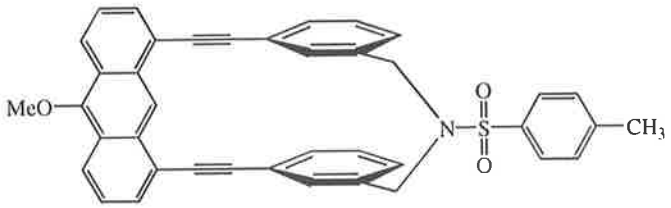
To a solution of the tetra-bromomethyl compound (**107**) (7 mg, $7.14x10^{-6}$ mol) in a solvent mixture of dichloromethane (5 mL) and ethanol (5 mL), was added $Na_2S.Al_2O_3$ (17 mg, $4.29x10^{-5}$ mol) and the resulting suspension stirred at room temperature for 1 hr. The reaction mixture was filtered through kenite and the residue washed with dichloromethane (100 mL). The solvent was removed *in vacuo* to give a bright yellow solid (6 mg) which contained the title compound.

Method B:

To a solution of the tetra-bromomethyl compound (**107**) (10 mg, $1.02x10^{-5}$ mol) in dry DMF (2 mL), was added $Na_2S.Al_2O_3$ (25 mg, $6.13x10^{-5}$ mol) and the resulting suspension stirred at room temperature for 6 hrs. After 3 hrs another quantity of

$Na_2S.Al_2O_3$ (25 mg) was added. The reaction mixture was filtered through a short column of silica and the residue washed with dichloromethane (100 mL). The solvent was removed *in vacuo* to give a bright yellow solid (9 mg) which contained the title compound; Exact Mass Calcd for $C_{51}H_{32}OS_2$: 724.1887, Found: 724.1894; m/z (EI) 724 (M^+, 100%).

1^{10}-Methoxy-6^1-(4-methylphenyl)sulphonyl-6-aza-1(1,8)-anthracena-4,8(1,3)-dibenzacyclodeca-2,9-diynaphane (114)



To a solution of the bis-bromomethyl compound (**103**) (22 mg, $3.70x10^{-5}$ mol) in dry DMF (3 mL) was added TosNHNa (11 mg, $5.55x10^{-5}$ mol) and the resulting solution stirred at 50° for 1 hr. The reaction mixture was added to water (20 mL) and extracted with ether (20 mL). The organic layers were combined, dried and the solvent removed. Purification by flash chromatography on silica [hexane/dichloromethane 1/1 (v/v), R_f 0.30] gave the title compound as a yellow solid (22 mg, 100%); mp 155.0-160.0°; Exact Mass Calcd for $C_{40}H_{29}O_3NS$: 603.1885, Found: 603.1927; δ_H (200 MHz) 2.48 (3H, s, ArC**H**$_3$), 4.17 (3H, s, ArOC**H**$_3$), 4.24 (4H, s, ArC**H**$_2$R), 7.18 (2H, dt, *J* 1.5 and 7.8 Hz, Ar**H**), 7.29-7.39 (4H, m, Ar**H**), 7.48-7.58 (6H, m, Ar**H**), 7.82-7.84 (4H, m, Ar**H**), 8.32 (2H, dt, *J* 1.2 and 8.7 Hz, Anthryl**H**), 9.34 (1H, s, Anthryl**H**); δ_C (105.87 MHz) (22 signals only) 21.6, 49.3, 63.7, 88.0 (**C**≡C), 94.4 (**C**≡C), 119.6, 121.6, 123.1, 123.2, 124.5, 124.9, 127.3, 129.2, 129.8, 131.2, 131.5, 131.9, 132.6, 135.8, 137.9, 143.6, 153.4; m/z (LSIMS) 604 ($(M+H)^+$ and isotopes of M^+, 73%), 603 (M^+, 100).

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Published Articles

1. Crisp, G.T., Turner, P.D. and Tiekink, E.R.T., *Zeit. Fur Krist.,* 1998, **213**, 385.

2. Crisp, G.T., Turner, P.D., Stephens, K.A., *J. Organomet. Chem.,* 1998, **570**, 219.

Crystal structure of 4-iodo-2,6-di(morpholinomethyl)phenol, $C_{16}H_{23}IN_2O_3$

G. T. Crisp, P. D. Turner and E. R. T. Tiekink

The University of Adelaide, Department of Chemistry, Australia 5005

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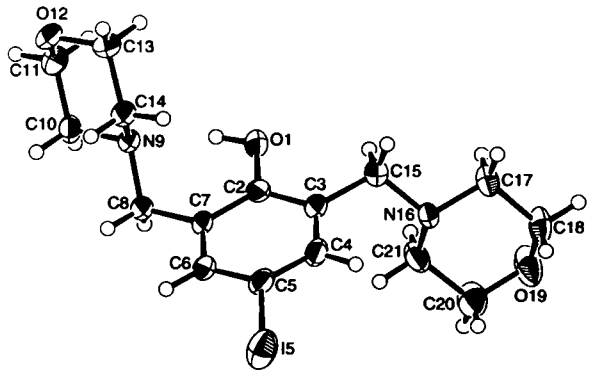

Source of material: Material prepared from phenol by initially reacting with morpholine and formaldehyde (see ref. 1) and then iodination (see ref. 2); mp 381 K – 382 K.
A significant intramolecular H-bond exists between O1–H and N9 with *d*(O1–H) 0.88 Å, *d*(H···N9) 1.97 Å, *d*(O1···N9) 2.753(5) Å and O1–H···N9 147°. This has the result that N9 of the morpholine ring is directed to the aromatic ring in order to facilitate the H···N interaction; i.e. C2/C7/C8/N9 is –49.7(6)° and C2/C3/C15/N16 is –134.7(5)°. The morpholine rings each adopt the chair conformation.

$C_{16}H_{23}IN_2O_3$, monoclinic, $P12_1/c1$ (No. 14), a =11.189(8) Å, b =10.810(5) Å, c =14.30(1) Å, β =94.58(6)°, V =1724.1 Å^3, Z =4, $R(F)$ =0.042, $R_w(F)$ =0.053.

Table 1. Parameters used for the X-ray data collection

Crystal:	colorless plate, size 0.22 x 0.37 x 0.45 mm
Wavelength:	Mo K_α radiation (0.7107 Å)
μ:	18.72 cm^{-1}
Diffractometer:	AFC6R
Scan mode:	ω/2θ
$T_{measurement}$:	293 K
$2\theta_{max}$:	55°
$N(hkl)_{unique}$:	2451
Criterion for I_o:	$F_o > 6\,\sigma(F_o)$
$N(param)_{refined}$:	200
Program:	TEXSAN

Table 2. Final atomic coordinates and displacement parameters (in Å^2)

Atom	Site	*x*	*y*	*z*	U_{iso}
H(1)	4*e*	0.5537	0.1323	0.2939	0.0923
H(4)	4*e*	0.1086	0.0537	0.3051	0.0522
H(6)	4*e*	0.3186	–0.1176	0.1243	0.0483
H(8a)	4*e*	0.5261	–0.0765	0.1300	0.0464
H(8b)	4*e*	0.5791	–0.0747	0.2360	0.0464
H(10a)	4*e*	0.7657	0.0119	0.1924	0.0477
H(10b)	4*e*	0.7126	0.0000	0.0867	0.0477
H(11a)	4*e*	0.8644	0.1467	0.0973	0.0656
H(11b)	4*e*	0.7964	0.2218	0.1720	0.0656
H(13a)	4*e*	0.6222	0.3241	0.1280	0.0602
H(13b)	4*e*	0.5682	0.3186	0.0223	0.0602
H(14a)	4*e*	0.5259	0.1086	0.0386	0.0502
H(14b)	4*e*	0.4621	0.1850	0.1150	0.0502
H(15a)	4*e*	0.2303	0.2689	0.3766	0.0579
H(15b)	4*e*	0.3465	0.2157	0.4332	0.0579
H(17a)	4*e*	0.2511	0.2668	0.5750	0.0564
H(17b)	4*e*	0.1327	0.3099	0.5158	0.0564
H(18a)	4*e*	0.0235	0.1603	0.5875	0.0737
H(18b)	4*e*	0.0882	0.2477	0.6647	0.0737
H(20a)	4*e*	0.2160	–0.0793	0.6262	0.0915
H(20b)	4*e*	0.0987	–0.0370	0.5653	0.0915
H(21a)	4*e*	0.2609	–0.0253	0.4752	0.0660
H(21b)	4*e*	0.3284	0.0631	0.5503	0.0660

Table 3. Final atomic coordinates and displacement parameters (in Å^2)

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
I(5)	4*e*	0.05110(3)	–0.12842(5)	0.14223(3)	0.0520(2)	0.1127(4)	0.0565(3)	–0.0118(2)	0.0083(2)	–0.0103(3)
O(1)	4*e*	0.4942(3)	0.1485(3)	0.3292(2)	0.052(2)	0.050(2)	0.042(2)	–0.007(2)	0.017(2)	–0.011(2)
O(12)	4*e*	0.7250(3)	0.2370(3)	0.0442(3)	0.062(2)	0.045(2)	0.060(2)	–0.007(2)	0.031(2)	0.009(2)
O(19)	4*e*	0.1543(5)	0.0819(4)	0.6627(3)	0.135(4)	0.074(3)	0.037(2)	0.032(3)	0.027(2)	0.004(2)
N(9)	4*e*	0.6012(3)	0.0851(3)	0.1692(3)	0.038(2)	0.032(2)	0.032(2)	0.000(2)	0.010(2)	0.002(2)
N(16)	4*e*	0.1950(3)	0.1454(3)	0.4739(3)	0.044(2)	0.033(2)	0.036(2)	0.005(2)	0.014(2)	–0.005(2)
C(2)	4*e*	0.3970(4)	0.0840(4)	0.2909(3)	0.055(3)	0.032(3)	0.030(2)	–0.005(2)	0.011(2)	0.002(2)
C(3)	4*e*	0.2847(5)	0.1042(4)	0.3248(3)	0.056(3)	0.034(3)	0.035(2)	0.001(2)	0.019(2)	0.005(2)

Table 3. (Continued)

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(4)	4*e*	0.1869(4)	0.0414(5)	0.2827(3)	0.045(3)	0.047(3)	0.040(3)	0.004(2)	0.017(2)	0.006(2)
C(5)	4*e*	0.2002(4)	−0.0377(5)	0.2089(3)	0.044(3)	0.049(3)	0.035(2)	−0.010(2)	0.009(2)	0.002(2)
C(6)	4*e*	0.3111(4)	−0.0611(5)	0.1762(3)	0.054(3)	0.039(3)	0.031(2)	−0.006(2)	0.015(2)	0.001(2)
C(7)	4*e*	0.4109(4)	−0.0016(4)	0.2178(3)	0.046(3)	0.032(3)	0.030(2)	0.001(2)	0.015(2)	0.004(2)
C(8)	4*e*	0.5342(4)	−0.0282(4)	0.1872(3)	0.050(3)	0.032(3)	0.037(3)	0.000(2)	0.015(2)	0.003(2)
C(10)	4*e*	0.7209(4)	0.0541(5)	0.1408(3)	0.041(2)	0.044(3)	0.040(3)	0.005(2)	0.013(2)	−0.002(2)
C(11)	4*e*	0.7865(5)	0.1692(5)	0.1165(4)	0.041(3)	0.058(4)	0.070(4)	−0.005(3)	0.022(3)	−0.005(3)
C(13)	4*e*	0.6108(5)	0.2721(5)	0.0727(4)	0.061(3)	0.037(3)	0.056(3)	−0.002(3)	0.018(3)	0.007(3)
C(14)	4*e*	0.5390(4)	0.1593(4)	0.0949(3)	0.046(3)	0.040(3)	0.038(3)	0.000(2)	0.010(2)	0.004(2)
C(15)	4*e*	0.2682(5)	0.1947(5)	0.4035(4)	0.061(3)	0.041(3)	0.050(3)	0.000(3)	0.024(3)	−0.004(3)
C(17)	4*e*	0.1741(5)	0.2397(5)	0.5455(4)	0.052(3)	0.050(3)	0.044(3)	0.012(3)	0.011(2)	−0.008(3)
C(18)	4*e*	0.1001(5)	0.1857(6)	0.6178(4)	0.075(4)	0.074(4)	0.031(3)	0.021(3)	0.017(3)	−0.004(3)
C(20)	4*e*	0.1744(7)	−0.0098(6)	0.5948(4)	0.122(6)	0.062(4)	0.048(3)	0.017(4)	0.031(4)	0.014(3)
C(21)	4*e*	0.2505(5)	0.0391(5)	0.5206(4)	0.081(4)	0.039(3)	0.048(3)	0.017(3)	0.016(3)	−0.003(3)

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